KETENES II

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Thomas T. Tidwell

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Dedicated to Sarah, for her inspiration and support

Contents

Preface

It was a century ago that Hermann Staudinger introduced ketenes to the world, and almost 50 years ago that I first encountered these beguiling reactive intermediates in my first course in organic chemistry, using a textbook written by the inimitable Louis Fieser. Ketenes are remarkable for the variety of ways in which they can be prepared, for their high chemical reactivity, and for the diverse range of useful products from their reactions. Ketenes have long been renown for their unique reactivity in [2+2] cycloaddition reactions giving a ready source of four membered ring compounds, their distinctive characteristic of undergoing facile dimerization, and the high stereoselectivity shown in many of their reactions.

The first edition of this book appeared 10 years ago, and even though ketene chemistry seemed at a high point at that time it was predicted "...in 2005, the opportunities for research will be even greater than they are today." As better methodology has been devised for ketene preparation and new applications have been found for this family the interest in their chemistry has steadily increased, and the developments over the past decade have exceeded my greatest expectations. This new edition incorporates 1,000 new references, some published in 2005, and to keep the text to a reasonable size just as many have had been dropped. The format of the previous work has proven to be useful and is retained, with 5 principal sections "Structure, Bonding, and Thermochemistry", Spectroscopy and Physical Properties", Preparation", Types of Ketenes", and "Reactions". The text has been completely rewritten with incorporation of new material, and all of the chemical equations and structural formulae have been redrawn in a uniform style. The extensive lists of known ketenes have not been continued because of space restraints, and because of the present capability of searching these online.

Much has been learned, but there is even a greater amount still to be discovered. Advances in experimental techniques have made many classes of ketenes into conveniently observable intermediates, but other challenges remain, particularly in the observation of highly reactive ketenes by methods such as NMR. Several classes of ketenes calculated to be stable are still unknown experimentally, and provide a continuing challenge. Many surprising new developments may be confidently awaited in the next decade.

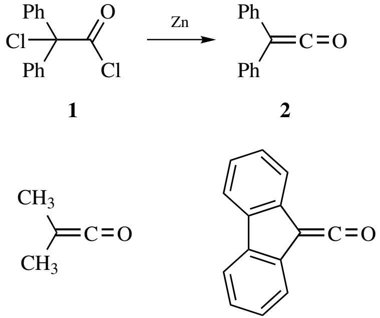
Thanks are due to the many enterprising chemists around the world who have provided the fascinating results which are reported here. I am particularly grateful to Peter Lillya, who graciously read the entire manuscript, and to Pat Woodcock for her invaluable help with the writing over many years. I apologize for all errors and omissions, for which I am solely responsible, and am grateful to those including reviewers of the first edition who have pointed out mistakes and provided ideas. My own contributions would have been impossible without my delightful and skillful coworkers and collaborators, especially Annette Allen, Huda Henry-Riyad, Nanyan Fu, Shinjiro Kobayashi, Andrei Fedorov, Katayoun Najafian, Kuangsen Sung, Wen-wei Huang, Mike Fenwick, Adel Rafai Far, Pat Moore, Romeo Marra, Jim Colomvakos, Ian Egle, Paul Renton, and many others.

FRENCH BEACH

British Columbia, July 2005

Introduction

The first ketene to be prepared and characterized was diphenylketene (**1**). It was made by Hermann Staudinger in 1905, while he was an instructor (*Unterrichts-Assistent*) at the Kaiser Wilhelms-Universtität in Strasbourg (then part of Germany), in the Organic Department of Johannes Thiele.[1] The preparation involved the reaction of 2-chorodiphenylacetyl chloride with zinc (equation 1) and, as recounted by Staudinger in his scientific autobiography,[2] was inspired by the preparation of the stable triphenylmethyl radical by Gomberg. Dimethylketene (**3**)[3] and dibenzopentafulvenone (**4**)[4] were soon prepared by the same method.



1 **2**

3 **4**

(1)

Shortly thereafter, N. T. M. Wilsmore at University College, London, prepared the parent ketene $CH_2{=}C{=}O$ (**5**) from the pyrolysis of acetic anhydride or acetone using a hot platinum wire.[5] Staudinger and Klever then prepared **5** from bromoacetyl bromide and zinc, and engaged in a brisk discussion with Wilsmore as to the priority for the discovery and as to whether ketene is best represented by $CH_2{=}C{=}O$ or $HC{\equiv}COH$, a possibility that had been mentioned by Wilsmore. This was decided in favor of Wilsmore's priority and the former structure.[7,8]

Staudinger was then successively "Associate Professor"[2] at the Technische Hochschule in Karlsruhe (1907–1912), Professor at the ETH in Zürich (1912–1926), and Professor in Freiburg (1926–1951). He summarized his early studies on ketenes in a monograph in 1912[9] and published further studies on ketenes through 1925. He then devoted his efforts to the study of macromolecules and was recognized for this work by the award of the Nobel Prize in Chemistry in 1953.

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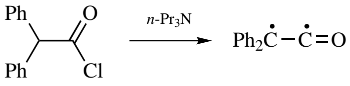
Wilsmore had been at the ETH in Zürich, and left there in 1903 for University College, London, where he subsequently became Assistant Professor. In 1912 he was appointed to the Chair of Chemistry at the new University of Western Australia and, owing to the demands of setting up a new department, made no more contributions to ketene chemistry.[10]

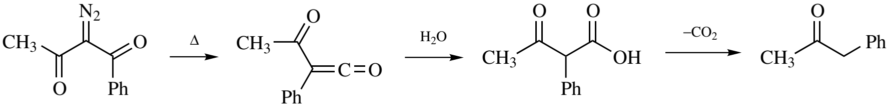
Edgar Wedekind missed the opportunity to discover ketenes while in Tübingen in 1901, when he treated $Ph_2CHCOCl$ (**6**) with *n*-Pr_3N, noted the formation of *n*-Pr_3NHCl, and proposed the formation of intermediate **7** (equation 2), which is equivalent to $Ph_2C{=}C{=}O$ (**2**).[11] However, Wedekind equivocated in his claim[12] and did not isolate the ketene, and this achievement was left for Staudinger in 1905.



6 **7**

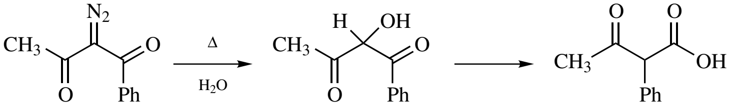
(2)

Ludwig Wolff in 1902 also generated ketenes as unobserved intermediates in what became known as the Wolff rearrangement,[13] but did not identify the intermediate as a ketene or adopt a ketene structure until 1912,[14] by which time ketenes were well-recognized intermediates. Wolff's experiment involved refluxing the diazo ketone **8** (formulated at that time as having a cyclic structure) in water, forming the ketene **9**, which led to the unobserved acid **10**, which underwent decarboxylation to give **11** (equation 3).[13] Wolff recognized that rearrangement had occurred and that the acid **10** was a key intermediate, but rather than ketene formation, he proposed that water addition occurred, giving **12**, which underwent a double migration forming **10**, and cited the analogy of the pinacol and benzilic acid rearrangements (equation 4).[13]



8 **9** **10** **11**

(3)



8 **12** **10**

(4)

The utility of ketenes in both laboratory and industrial practice was quickly recognized, and these species have been extensively utilized, including as intermediates in the manufacture of acetic acid and acetic anhydride, pharmaceutical intermediates, integrated circuits for computer chips, and paper coatings. Their study has attracted many of the sharpest minds in chemistry, among them Nobel laureates in addition to Staudinger including R. B. Woodward, E. J. Corey, Roald Hoffmann, R. G. W. Norrish, George Porter, K. Fukui, L. Ruzicka, V. Prelog, O. Diels, R. W. Holley, G. Natta, W. N. Lipscomb, A. Zewail, John Polanyi, Derek Barton, John Pople, R. F. Curl, Jr., F. S. Rowland, and George Olah.

Following publications of Staudinger's book,[9] there have been many reviews on ketenes, including reviews on specific topics.[15–31] Among these is a volume devoted to a detailed survey of the preparation of ketenes and their application in synthesis.[15] A more detailed description of the origins of ketene chemistry has been presented.[32]

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1

Structure, Bonding, and Thermochemistry of Ketenes

1.1 THEORETICAL AND COMPUTATIONAL STUDIES OF KETENES

Computational methods are increasingly used not only for the elucidation of the structures, energies, and properties of ketenes, but also as an adjunct to a wide variety of ketene studies. Consequently, the use of computational studies appears throughout this book and only a few of the more fundamental studies devoted to computation of ketene properties are noted here, while others are included in appropriate sections throughout the book.

A comprehensive review of theoretical studies on ketene appeared in 1980,[1] and this and other earlier studies[2,3] will not be repeated here. These provide the fundamental basis for understanding the properties of ketenes. The emphasis is now on the application of computational studies for understanding the properties of different types of ketenes and the myriad reactions that they undergo.

1.1.1 Molecular and Electronic Structure and Energy

The unique properties of ketenes derive from their cumulene structure, with the highest occupied molecular orbital (HOMO) perpendicular to the ketene plane and the lowest unoccupied molecular orbital (LUMO) in the ketene plane (Figure 1.1).[4] These reveal that ketene has substantial negative charge on oxygen and C_2, while there is positive charge on C_1 (the carbonyl carbon) in the ketene plane. As a consequence, electrophiles are expected to attack ketenes at oxygen or perpendicular to the ketene plane at C_2, while nucleophiles approach in the ketene plane at C_1.

HOMO LUMO

The important resonance structures for ketene are **1a–c**, and these predict the negative charge on C_2 and the positive charge on C_1. These resonance structures were used by Hannay and Smyth[5] to explain the dipole moment of ketene (1.45

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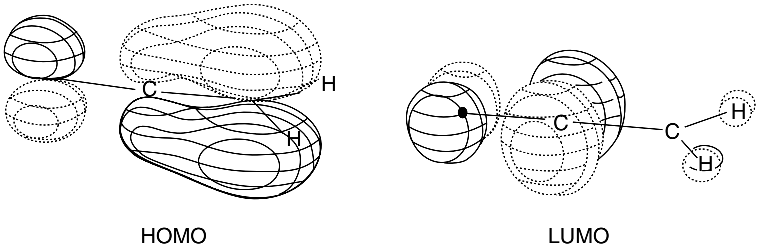
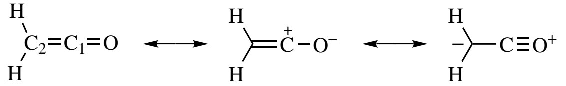


Figure 1.1 Frontier molecular orbitals of ketene (reproduced from reference 4 by permission of the American Chemical Society).

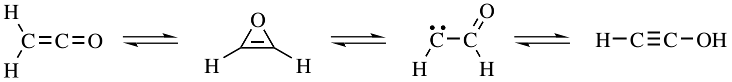
Debye [D]), which is less than those of formaldehyde (2.27 D) or acrolein (3.04 D), suggesting negative charge buildup on C_2 and the possibility of less negative charge on oxygen than in most aldehydes and ketones (Section 2.4). An alternative interpretation by Walsh[6] was that the sp hybridization of C_1 reduces the negative charge on oxygen, but this did not explain the propensity for electrophilic attack at C_2.



1a **1b** **1c**

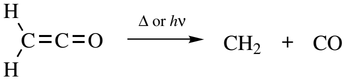
High-level *ab initio* calculations of the electronic states of ketene[7–10] have been reported. Calculated vertical excitation energies of ketene agree well with experimental values.[7] The calculation of the molecular structure and vibrational infrared (IR) spectrum of ketene, as calculated by post-Hartree-Fock and density functional theory methods, show that good agreement with experimental values can be obtained by either method.[9] *Ab initio* calculations of the electronic structures of $CH_2{=}C{=}O$ and C_3O_2 give the dipole polarizabilities of these molecules and the results provide a basis for predicting experimental properties.[10]

The structures and stabilities of the C_2H_2O isomers ketene (**1**), oxirene (**2**), formylmethylene (**3**), and hydroxyacetylene (**4**) and their interconversion by the Wolff rearrangement have been the subject of many computational studies (equation 1).[11–17] Investigations using (AM1) were particularly concerned with the possibility of competing hydrogen rearrangement[18] and the effects of substituents in aryl derivatives.[19] Calculations of the isomerization of vibrationally excited ketene via oxirene (equation 1) agree with experimental results.[20] This reaction has also been studied by density functional theory (DFT) methods, including the role of formylcarbene.[21] The nature of the stationary point of oxirene has been examined using a variety of density functional methods, and the results with the largest basis sets agree with previous high-level correlated methods that this species is an energy minimum.[22,23] This problem is discussed further in Section 3.3.



1 **2** **3** **4** (1)

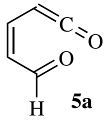
The dissociation of ketene into CH_2 and CO by photochemical or thermal methods (equation 2) is a classical problem in chemistry, particularly regarding the energy distribution and electronic states of the products (Sections 5.2, 5.3).[24,25]



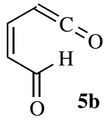
$$H_2C{=}C{=}O \xrightarrow{\Delta \text{ or } h\nu} CH_2 + CO \qquad (2)$$

1

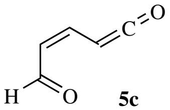
Examples of recent studies of ketenes include calculations of the structures, conformations and IR spectra of 5-oxo-2,4-pentadienal (**5**), and it was concluded that of the previously claimed structures, conformer **5a** does not exist as an energy minimum and that only **5b–d** occur.[26] Structures of the cyclized forms **6** and α-pyrone (**7**) were also calculated, as well as that for the transition state for the degenerate rearrangement of **5b** by hydrogen migration. Structures of hydroxycumulenones **8** were also calculated.[26] Structures, conformations, and vibrational spectra have been calculated for the haloacyl and acetyl ketenes **9**.[27,28] The dipole polarizabilities of ketene and carbon suboxide (C_3O_2) have also been calculated by *ab initio* methods.[10]



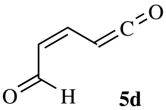
5a



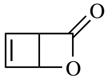
5b



5c



5d



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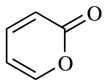

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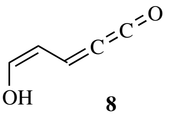

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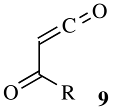
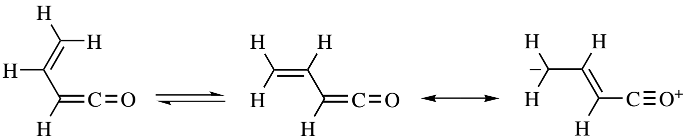


9 (R = F, Cl, Br, CH_3)

The moleculecular structure of vinylketene (**10**) has been of interest, and the C–C rotational barrier has also been determined by computations (equation 3).[29] The dipole moment and ^{13}C NMR (nuclear magnetic resonance) spectrum (Section 4.1.2) of **10** have been interpreted as showing the importance of electron delocalization to C_4, as shown in resonance structure **10a**.



s-cis-**10** *s-trans*-**10** **10a**

(3)

Molecular mechanics force fields for studies of ketenes have also been presented,[30] and the use of natural valence coordinates for ketene computations have been tested.[31]

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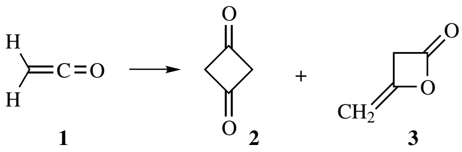
1.1.2 Theoretical and Computational Studies of Ketene Reactions

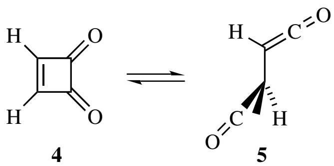
The mechanisms and energetics of many different reactions of ketenes have been analyzed by computational and theoretical methods and provide useful insights into the understanding of ketene reactivity. Many of these studies are included in later sections dealing with the preparation and properties of ketenes, but a brief survey of the approaches to some of the most common ketene reactions is presented here.

The dimerization of ketene (**1**) has been studied using *ab initio* molecular dynamics calculations, 1–5 which lead to the conclusion in the most recent calculation[1] that the β-lactone dimer **3** is the most stable, (equation 1),[1] with a free energy change of –5.5 kcal/mol, while formation of 1,3-cyclobutanone **2** has a free energy change of –4.5 kcal/mol. Previous calculations predicted a lower barrier for forming **3**,[2–5] in agreement with experiment. Dynamics calculations, however, predicted a lower barrier for formation of **2**, and appear to be less reliable in this regard.[1]

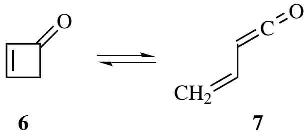


(1)

The equilibrium between cyclobuten-3,4-dione **4** and 1,2-bisketene **5**, which is shown by theory and experiment to have a twisted, almost perpendicular conformation, is considered in Section 4.9 (equation 2). Ring opening of cyclobutenone **6** to vinylketene **7** (equation 3) is discussed in Section 5.4.4, as well as the opening of the corresponding aza- and oxa-cyclobutenones to form imidoylketene (**8**) and formylketene (**9**), respectively.

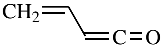


(2)



(3)

Computations using DFT have been used to examine the [4+2] and [2+2] cycloadditions of vinylketene (**7**), imidoylketene (**8**), and formylketene (**9**) with formaldimine (**10**).[6] For the [2+2] cycloaddition, both stepwise mechanisms involving zwitterionic intermediates and transition states for concerted reactions were located, and it was suggested that multiple transition states may be involved. For the [4+2] cycloadditions, both stepwise and concerted pseudopericyclic pathways were also calculated.[6]



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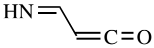

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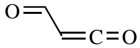
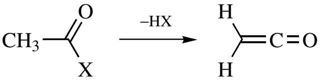


9

$CH_2{=}NH$

10

A theoretical study of the conversion of acetyl cyanide, acetyl isocyanide and acetyl fluoride (**11a–c**) to ketene and other products has also been reported (equation 4).[7,8]

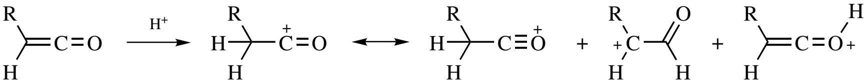


11 (X = CN, NC, F) **1**

(4)

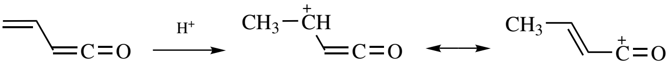
A DFT computational study of the [2+2] cycloaddition of ketene with $CH_2{=}CH_2$, $CH_2{=}O$, and $(C_5H_5)Re(O)_2{=}O$ discusses the role of orbital interactions, electrostatics, and repulsions due to the Pauli principle on the activation energies.[9]

Protonation of ketenes and bisketenes has been the subject of a number of studies.[10–15] Protonation of ketene (**1**) at C_2 forming the acylium ion **12** is strongly favored relative to protonation at C_1 forming α-formyl carbocation **13**, but for substituted ketenes **14**, strongly electron-donating substituents R enhance the possibility of formation of **13** (equation 5).[13,15] Protonation at oxygen forming **15** is not as favorable as protonation at C_2 in the cases studied. For vinylketene protonation at C_4 forming the allylic cation **16** is the lowest energy pathway (equation 6).[11]



14 (**1**, R = H) **12** **13** **15**

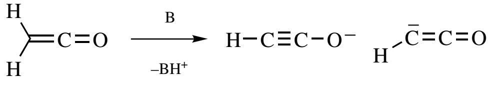
(5)



10 **16**

(6)

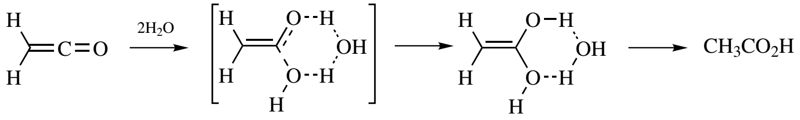
Proton abstraction from ketene (**1**) forming the ynolate anion **17** has been the subject of computational study, and the linear structure for **17** with negative charge delocalized between oxygen and C_2 is favored over a bent structure **18** that could have negative charge concentrated on C_2 (equation 7).[16,17]



1 **17** **18**

(7)

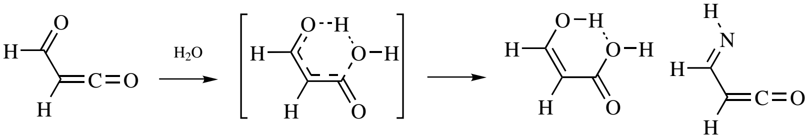
The hydration of ketene has been the subject of numerous computational studies, and reaction with two water molecules through a cyclic transition state **19** forming the acid enol **20** is favored over addition of a single H_2O molecule or addition of two H_2O molecules to the C–C double bond, forming acetic acid directly (equation 8).[18–21] This is the accepted mechanism for hydration of aldehydes and ketones forming hydrates in both experimental and theoretical studies.[22–25]



1 **19** **20**

(8)

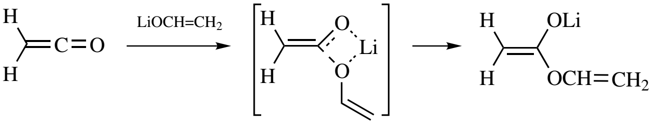
Reaction of formylketene (**21**)[26] with H_2O was predicted to occur with coordination of the H_2O to the formyl oxygen through pseudopericyclic transition state **22** forming **23** (equation 9).[26,27] Imidoylketene **24** was found to behave similarly[27]



21 **22** **23** **24**

(9)

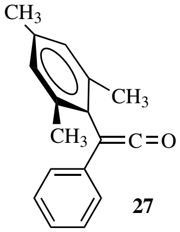
The reactions of LiH, and $LiCH_3$ with ketene are predicted to occur through initial lithium coordination to the ketenyl oxygen and then bond formation to the carbonyl carbon.[28] The addition of the lithium enolate of acetaldehyde was predicted to occur similarly, with C–O bond formation giving **25**, even though C–C bond formation gives a more stable product (equation 10).[29] This result was confirmed experimentally (Section 5.5.2.2)



1 **25** **26**

(10)

The structure of mesitylphenylketene **27** has been calculated at the HF/3–21G level and has been found to have a twisted structure of the mesityl perpendicular to the ketene plane, with the bond distances (**27a**) and bond angles (**27b**) shown.[30] The transition state for addition of MeLi was also calculated, and the preferential attack from the side of the mesityl group was explained by the perpendicular conformation adopted by this substituent to minimize steric interactions.[30]



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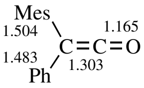
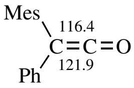


27a



27b

Other theoretical studies include the possible formation of metal-complexed ketenes from vinyl carbene complexes (Section 3.5),[31] radical cyclization of ketenes (Section 5.7),[32] and the reaction of ketenes with diazomethanes (Section 5.10).[33]

The structure of the complex of ketene with $Cr(CO)_4OH_2$ was calculated using the B3LYP(6-31)G$^+$) basis set for C, H, and O, and a double (ζ) basis set for Cr (Figure 3.1, Section 3.5).[15]

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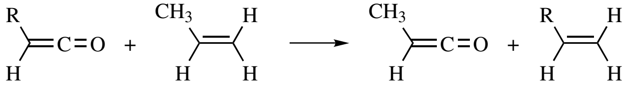
1.1.3 Substituent Effects on Ketenes

The effects of substituents on the stability of ketenes were studied by *ab initio* calculations of the structures and energies of the ketenes and isodesmic comparison with alkenes (equation 1).[1–3] The energy change (kcal/mol) in the conversion of a substituted ketene **1** and propene (**2**) to methylketene **3** and the substituted alkene **4** was taken as the stabilization energy (*SE*) of that substituent on ketenes (Table 1.1). The choice of CH_3 as the standard of comparison is arbitrary, but emphasizes that by this method many alkyl, alkenyl, and aryl groups (Me, cyclopropyl, CF_3, vinyl, phenyl) are calculated to have similar effects, and the *SE* values are small. The results are consistent using HF/3–21G, HF/6–31G*, and MP2/6–31G* level calculations, which produces confidence that the conclusions will not be affected by higher-level calculations.



1 **2** **3** **4** (1)

From a qualitative viewpoint, the *SE* values (Table 1.1) are consistent with experience, for example in the known stability of silyl-substituted ketenes and the high reactivity of haloketenes, especially fluoroketenes. This suggested a correlation with substituent electronegativity, and indeed, a reasonable correlation

TABLE 1.1 Comparative Calculated Stabilization Energies (kcal/mol) (MP2/6–31G*//MP2/6–31G* and HF/6–31G*//HF/6–31G*) for Ketenes RCH=C=O for the Isodesmic Reaction of Equation 1[1,3]

R	ΔE (MP2)	ΔE (HF)	χ_{BE}[a]
H	3.9	3.3	2.20
Li	30.1	27.9	1.00
BeH	19.6	18.1	1.47
BH_2	18.7	16.8	1.93
CH_3	0.0	0.0	2.56
NH_2	−9.3	−7.2	3.10
OH	−14.5	−14.2	3.64
F	−16.9	−17.2	4.00
Na	34.3	29.2	1.00
MgH	23.2	21.9	1.33
AlH_2	20.1	18.7	1.62
SiH_3	11.5	10.9	1.91
PH_2	6.3	6.3	2.17
SH	0.2	1.3	2.63
Cl	−7.7	−7.5	3.05
CF_3	—	−0.1	2.68
c-Pr	—	−1.8	2.56
$CH{=}CH_2$[b]	—	−0.2	2.61
CH=O[c]	5.4	3.6	2.60
Ph	—	0.9	2.58
CO_2H	—	4.7	2.66
C≡CH	0.5	0.2	2.66
CN	0.6	−0.4	2.69
$CH{=}C{=}CH_2$	—	−1.6	
CH=C=O	—	−5.3[d]	2.58
N=O	—	−0.1	3.06
NO_2	1.9	−3.2	3.22
N≡C[e]	—	−8.5	3.30

[a] Group electronegativity from refs. 4, and 5, except Pauling electronegativity for H.

[b] Transcoid.

[c] Ciscoid.

[d] For the process $(CH{=}C{=}O)_2 + (CH_2{=}CH)_2 \rightarrow 2\ CH_2{=}CHCH{=}C{=}O$.

[e] Isocyano.

(Figure 1.2) was found with the group electronegativities χ_{BE} provided by Boyd, Boyd, and Edgecombe (equation 2).[4,5] Thus, ketenes are expected to be stabilized by electropositive substituents, which are capable of σ-π electron donation from the R–C_2 bond to the carbonyl group, and destabilized by electronegative groups. Electronegative atoms such as O, N, and the halogens also have lone pairs of electrons, which have a repulsive interaction with C_2 of ketenes, which bears a high negative charge, as found by the computations, and as seen in the remarkably high field ^{13}C

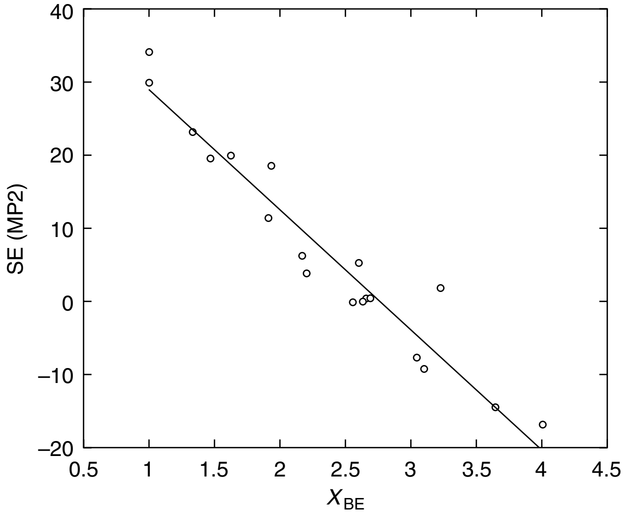
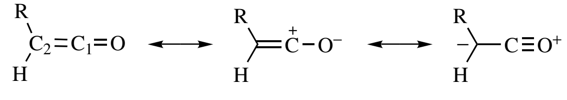


Figure 1.2 Plot of MP2/6–31G* calculated stabilization energies for substutued ketene versus substituent group electronegativities (X_{BE}).

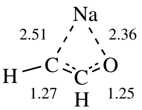
NMR shifts of this carbon (Section 2.1), and as expected by the resonance structure **1c**.

$$SE_{(\mathrm{MP2})} = -17.0_{\chi\mathrm{BE}} + 46.4 \quad (r = 0.97) \tag{2}$$



1a **1b** **1c**

As shown in Figure 1.2, there are some deviations from the correlation, and those for the substituents Na, BH_2 and CH=O are all significantly above the correlation line (obs: 34.3, 18.7, and 5.4, respectively, calculated from equation 2: 29.4, 13, and 2.2, respectively), indicating greater stabilization than expected from these substituents on the basis of their electronegativities. The extra stabilization of sodioketene (**5**) can be understood as arising from the bridged structure **5** calculated for this ketene (bond distances in Å shown), while boranylketene (**6**) and formylketene (**7**) are stabilized by conjugation.



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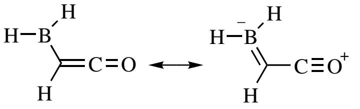

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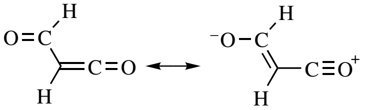
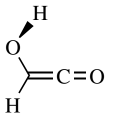


7

The nonplanar geometries of hydroxyketene (**8**) and aminoketene (**9**) are another structural feature revealed by the computations.[1,3] These ketenes with n-π donor groups adopt these conformations to minimize repulsive interactions between the π-electrons concentrated at C_2 and the lone pairs. The suggestion of a bonding interaction between the nitrogen lone pair and the carbonyl carbon in **9** was discounted, as the calculated bond order between these atoms is negative.[1]



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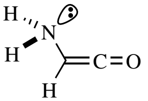
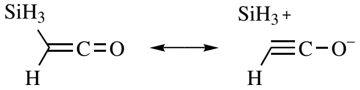


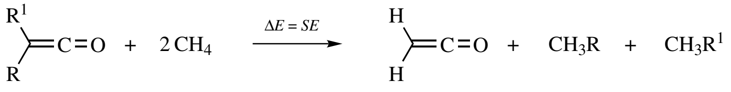
9

The stabilization of silylketenes **10** and others with electropositive substituents may be ascribed to hyperconjugative electron donation, as shown in **10a** (Section 4.5). This is an example of the β-silicon effect, as observed in β-silyl carbocations.[6]



10 **10a**

A limited study using computations at the G3(MP2)//B3LYP level for an isodesmic comparison of ketenes with substituted methanes was carried out, which included disubstituted ketenes (equation 3).[7] The results are given in Table 1.2. This treatment compares the substituent effects for ketenes to those for substituted methanes and also includes substituent effects on disubstituted ketenes.



$$\mathrm{R^1RC{=}C{=}O} + 2\,\mathrm{CH_4} \xrightarrow{\Delta E = SE} \mathrm{H_2C{=}C{=}O} + \mathrm{CH_3R} + \mathrm{CH_3R^1} \qquad (3)$$

11 **1** **12** **13**

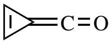
Because of the different references used, the results in Tables 1.1 and 1.2 are not directly comparable. The magnitudes of the ΔE values are larger for the comparisons in Table 1.1, and this is evidently due to the difference of the substituent effects in $RCH{=}CH_2$ as compared to RCH_3. In Table 1.1 the magnitude of the F/OH and F/Cl differences are 2.4 and 11.6 kcal/mol, respectively, compared to 6.4 and 6.2 kcal/mol, respectively, in Table 1.2. Thus, while the magnitude of the substituent effects is $F > OH > Cl$ for both sets, there are quantitative differences. More striking are the effects in the disubstituted ketenes (Table 1.2), which, rather

TABLE 1.2 Calculated Stabilization Energies (kcal/mol) (G3MP2//B3LYP) for Ketenes $RR^1CH{=}C{=}O$ for the Isodesmic Reaction of Equation 3[7]

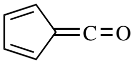
Ketene	ΔE (kcal/mol)
$HOCH{=}C{=}O$	−5.6
$MeOCH{=}C{=}O$	−6.1
$ClCH{=}C{=}O$	−5.8
$ClC(OH){=}C{=}O$	−4.3
$ClC(OMe){=}C{=}O$	−3.7
$FCH{=}C{=}O$	−12.0
$FC(OH){=}C{=}O$	−5.4
$FC(OMe){=}C{=}O$	−5.4

than being additive, are actually less for the disubstitued cases. This suggests that stabilizing effects are present when there are two electronegative substituents on C_2 of ketene. Further study to test the generality of this effect is warranted.

Substituent effects in ketenylketenes are considered in Section 4.9 and those in allenylketenes in Section 4.18.[8] Computational studies of antiaromatic destabilization in trifulvenone **14** and heptafulvenone **16**, and of aromatic stabilization of pentafulvenone **15**, are discussed in Section 4.1.10.[9,10]



14



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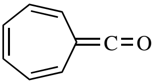

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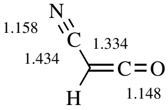
1.2 MOLECULAR STRUCTURE DETERMINATIONS

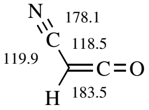
Molecular structures of many ketenes[1] have been examined experimentally by microwave,[2–15] electron diffraction,[16–18] and X-ray techniques,[19–27] and many more by computations at various theoretical levels. Experimental data for some simple ketenes are given in Table 1.3, with calculated values for comparison.

Structures have been determined using microwave spectroscopy for $CH_2{=}C{=}O$ (**1**),[2–6] $NCCH{=}C{=}O$ (**2**),[7] $FCH{=}C{=}O$ (**3**),[8,9] $ClCH{=}C{=}O$ (**4**),[10] $CH_3CH{=}C{=}O$ (**5**),[11] and $BrCH{=}C{=}O$ (**6**).[12] The microwave spectrum of vinylketene (**7**) was measured, but only the dipole moment was obtained from the data.[13] The microwave spectrum of $(CH_3)_2C{=}C{=}O$ (**8**) was measured and the structure obtained with the assumption of the same C=O bond length as in $CH_3CH{=}C{=}O$.[14] The ketene $Cl_2C{=}C{=}O$ (**9**) had a negligible dipole moment and the microwave spectrum could not be measured,[15] but the structure was determined using electron diffraction.[16] A molecular structure for thioketene ($CH_2{=}C{=}S$, **10**) was also determined.[17] The experimental bond distances, bond angles, and dipole moments obtained are summarized in Table 1.3, along with comparative computational results.

Gas phase pyrolysis of the acyl chloride with appropriate isotopic labeling at 750°C gave cyanoketene (**2**) with ^{2}H, ^{15}N, ^{13}N, carbonyl ^{13}C, or ^{18}O labeling for determination of the molecular structure by microwave spectroscopy.[7] The molecule had a dipole moment of 3.542(15) D, and the molecular structure was in reasonable agreement with the calculated structure (Table 1.3). See also Section 4.1.3.

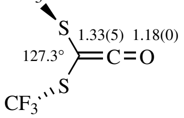


2a



2b

The gas phase molecular structure of $(CF_3S)_2C{=}C{=}O$ (**11**) has been determined by electron diffraction and displays C_2 symmetry, with the CF_3–S bonds perpendicular above and below the molecular plane.[18] This geometry is that predicted by molecular orbital calculations, and minimizes repulsion between the lone pairs on sulfur and the electron-rich HOMO at C_2 of the ketene.



11

TABLE 1.3 Experimental and Calculated (HF/6-31G*//HF/6-31G*)(Parentheses) Bond Distances, Bond Angles (Deg), and Dipole Moments of Ketenes $RR^1C_2C_1C{=}O$

R	R^1	C=O	$C_1{=}C_2$	C_2-R_1	C_2-R	OC_1C_2	RC_1C_2	RC_2R_1	$R_1C_2C_1$	μ (Debye)	Ref
H	H	1.164	1.3165	1.0800	1.0800	180.0	119.01	121.98	119.01	1.41	3
		1.1626	1.3147	1.0905	1.0905	180.0	118.27	123.46	118.27		2
		(1.145)	(1.306)	(1.075)		(180.0)	(119.3)	(121.4)	(119.3)	(1.63)	22
		(1.1681)	(1.3166)	(1.0745)	(1.0745)	(180.0)	(119.4)	(121.2)	(119.38)		2[a]
F	H	1.167	1.317	1.080	1.356	178.0	119.5	118.2	122.3	1.29	8,9
		(1.147)	(1.308)	(1.067)	(1.339)	(177.9)	(120.1)	(117.4)	(122.5)	(1.59)	22
		(1.181)	(1.323)	(1.074)	(1.363)	(178.1)	(120.0)	(117.7)	(122.3)		9[b]
Cl	H	1.161	1.316	1.082	1.726	180.0	120.9	119.3	119.8	1.2	10
		(1.142)	(1.308)	(1.068)	(1.731)	(179.2)	(120.5)	(118.7)	(120.8)	(1.39)	22
Br	H	1.162	1.316	1.082	1.880	180.0	118.5	120.6	120.9		12
CH_3	H	1.171	1.306	1.083[c]	1.518	180.5	122.6[d]	123.7	113.7	1.79	11
		(1.149)	(1.305)	(1.074)	(1.512)	(180.0)	(123.2)	(120.8)	(116.0)	(1.99)	22
NC	H	1.148	1.334		1.434	176.5	118.5	119.9		3.542(15)	7
		1.133	1.321	(1.072)	(1.424)	(178.7)		(121.3)	(120.6)	(3.72)	22
$CH{=}CH_2$	H									0.97	12
										(1.20)	22
Cl	Cl	1.160	1.299	1.726	1.726	180.0	120.4	119.2	120.4		16
		(1.161)	(1.306)	(1.726)	(1.726)	(180.0)	(120.7)	(118.6)	(120.7)	(0.07)	16a
CH_3	CH_3	1.171	1.300	1.514		180.0	120.6	118.8	120.6		14
CF_3S	CF_3S	1.18	1.33					127.3			18

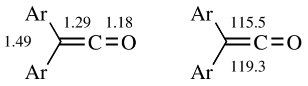
[a] MP3/6–31G**.

[b] MP2/4–31G**.

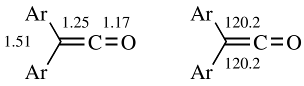
[c] For CH_3 C-H 1.083 ((1.084), 1.11.

[d] H–C–H 109.9, 108.8; H–C–C_2 111.1 (111.4).

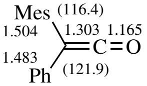
Structures have been obtained by X-ray studies of dimesitylketene (**12**) and bis(3,5-dibromomesityl)ketene (**13**).[19] Both structures have propeller conformations of the aryl groups, and in **12** these are nonequivalent, with dihedral angles of 48.8° and 56.8°, while in **13** these are equivalent, with dihedral angles of 56.8°. The structure of mesitylphenylketene **14** has been calculated at the HF/3–21G level, with the indicated bond distances and bond angles (parentheses).[20]



12 (Ar = 2,4,6-$Me_3C_6H_2$)

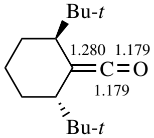


13 (Ar = 2,4,6-$Me_3C_6Br_2$)



14

Structures determined by X-ray for the aliphatic ketene **15**,[21] the alkenylketene **16** with a chromiun tricarbonyl complexed to the side chain,[22] and the tetraketene **17**[23] have also been reported. There are systematic differences in the ketenyl C=C bond lengths determined by X-ray, which are all between 1.25 and 1.29 Å, and those obtained by microwave spectroscopy or electron diffraction reported in Table 1.3, which are all greater than 1.30 Å, and those calculated at the MP2/6–31G* level, which are all also greater than 1.30 Å, with the exception of those to the highly electropositive Li, Na, and MgH substituents, none of which are known experimentally.[24,25]



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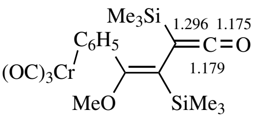

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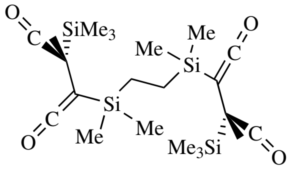
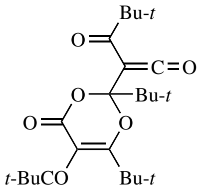


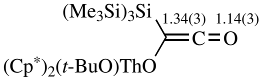
17

The X-ray structure of ketene **18**, derived from the dimerization of dipivaloylketene,[26] revealed that the ketenyl C=O and C=C bond lengths of 1.13 and 1.35 Å are distinctly shorter and longer, respectively, than the average of those of four previous ketene X-ray structure determinations of 1.18 and 1.28 Å, respectively, but are very similar to recently determined values of 1.14 and 1.34 Å for a (metal-oxy)silylketene **19**.[27] The shorter C=O and longer C=C bonds for **18** are consistent with acyl conjugation of the ketene as proposed for other acylketenes (**20**; see also Section 4.1.4), but the C–C bond length of the silylketene was not shortened, as could be expected by resonance structure **21**.



18

obs bond lengths (Å)		ketene bond lengths from literature
C=O	1.13 (1)	1.18, 1.17, 1.18, 1.18 (1.18)
C=C	1.35 (2)	1.29, 1.25, 1.28, 1.30 (1.28)



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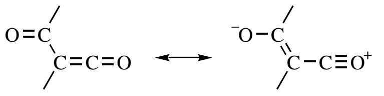

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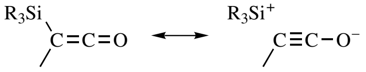
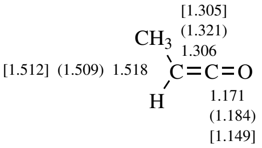


21

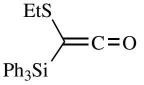
A molecular structure of $CH_3CH{=}C{=}O$ (**5**) calculated using the MP2/6–31G level (parentheses) shows no better agreement with experimental values than do previous HF/6–31G* calculations [brackets].[29]



5

Carbon suboxide C_3O_2 ($O{=}C{=}C{=}C{=}O$, **22**) has a quasilinear structure with a very small energy barrier for bending around the central carbon.[29–31] The structure of crystalline C_3O_2 has been determined by X-ray.[32]

Other molecular structures of ketenes have been determined by X-ray for the silyl stabilized ketene **23**,[33] and for a cobalt-complexed ketene.[34]



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1.3 THERMOCHEMISTRY OF KETENES

The determination of the thermodynamic properties of ketenes has been of continuing interest,[1–14] and these properties have been obtained by both experimental and computational methods. There have been significant differences in values from different sources, but resolution of these differences has apparently been achieved. Preferred values from the most recent reports for ketene, methylketene, and dimethylketene are given in Table 1.4, and a compilation of some of the other existing data is presented in Table 1.5.[1–21] The computational value for

TABLE 1.4 Thermodynamic Values for Simple Ketenes (kJ/mol; kcal/mol in brackets)

Ketene	ΔH^{o}_{f}	PA (kJ/mol) [kcal/mol]	GB (kJ/mol) [kcal/mol]	Ref
$CH_2=C=O$	−54±5 [−12.9]	822.9 ± 3.4 [195]	790.1 ± 1.5 [188]	2, 5, 22
$CH_3CH=C=O$	−66.9 [−16.0][21]	839.8 ± 3.6 [200.7]	809.6 ± 3.3 [193.5]	1, 2, 5, 21
		845.4 ± 4.8		7
$(CH_3)_2C=C=O$	−92	855 [204]		4, 6

TABLE 1.5 Experimental and Theoretical Heats of Formation and Proton Affinities (kJ/mol; kcal/mol in brackets)

	ΔH^{o}_{f298}	PA	Ref
$CH_2=C=O$	−52		6
	−54 ± 5 [−12.9]	822.9 ± 3.4 [195]	2, 5
	−47.7(−11.4)		15
	(−14.7)		16
	−100 ± 10		18
$CH_2=C=O^{+\bullet}$	875 [209]		4, 6
$CH_3C(+)=O$	658		6
$CH_3CH=C=O$	−68 [−16.3]		4, 6
	−97±5		1, 2
		845 ± 4.8	7
		834.1	20
	−95.5 [−22.8]		5
	−86.6 [−20.6]	853	12
	−65.1 ± 10		3
	−105 [−25]		17, 19
$CH_3CH=C=O^{\pm\bullet}$	795 [190]		6
	797.0		3, 4
$CH_3CH_2C(+)=O$	618 [148]		6
$(CH_3)_2C=C=O$	−92 [22]	855 (204)	4, 6
	−137 ± 5 [−32.7]		5
	−155 [−37]		19
$(CH_3)_2C=C=O^{+\bullet}$	726 (174)		4
	723 [173]		6
$(CH_3)_2CHC(\pm)=O$	583 [139]		6
$NCCH=C=O$	−100.4 [−24 ± 5]		10
$NCCH_2C(+)=O$	828 [198 ± 3]		10
$NCCH_2C(\bullet)=O$	133.8 [32 ± 1]		10
$NCCH=C=O^{+\bullet}$	1061 [253 ± 3]		10
$PhCH=C=O$	25.1 [6] (est)		19
$Ph_2C=C=O$	121 [29] (est)		19
$CH_2=CHCH=C=O$	16.7 [4]		14
$CH_2=CHCH=C=O^{+\bullet}$	816 [195]		14

TABLE 1.6 CBS–Q Calculated ΔH_f^{298} and ΔS^{298} for Ketenes and Bisketenes

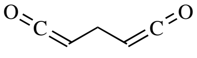
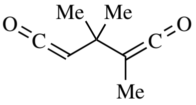
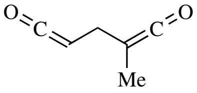
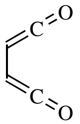
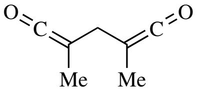
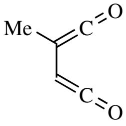
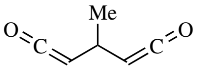
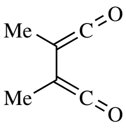
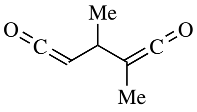
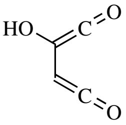
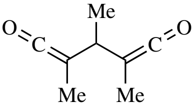
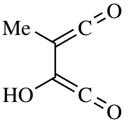
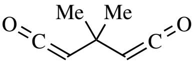
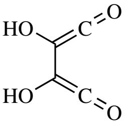
Ketene	ΔH_f^{298} (kcal/mol)	ΔS^{298} (cal/mol K)	Ketene	ΔH_f^{298} (kcal/mol)	ΔS^{298} (cal/mol K)
CH$_2$=C=O (**1**)	−11.34	57.47	MeOC(OH)=C=O (**17**)	−68.94	80.20
MeCH=C=O (**2**)	−15.14	68.20	MeC(OH)=C=O (**18**)	−44.90	75.73
EtCH=C=O (**3**)	−20.67	77.61	MeC(OMe)=C=O (**19**)	−40.15	84.34
i–PrCH=C=O (**4**)	−28.57	84.05	EtC(OH)=C=O (**20**)	−50.42	84.85
t–BuCH=C=O (**5**)	−37.75	87.66	*i*–PrC(OH)=C=O (**21**)	−58.29	91.63
Me$_2$C=C=O (**6**)	−21.73	74.92	*t*-BuC(OH)=C=O (**22**)	−68.88	95.04
MeCEt=C=O (**7**)	−27.97	85.84	EtC(OMe)=C=O (**23**)	−45.77	94.10
i–PrCMe=C=O (**8**)	−35.76	92.13	*i*-PrC(OMe)=C=O (**24**)	−54.08	100.17
t–BuCMe=C=O (**9**)	−44.87	95.68	*t*-BuC(OMe)=C=O (**25**)	−64.68	103.36
Et$_2$C=C=O (**10**)	−34.66	93.66	(HOCH$_2$)CH=C=O (**26**)	−51.60	77.65
i–PrCEt=C=O (**11**)	−42.52	101.41	(HOCH$_2$)CMe=C=O (**27**)	−58.53	85.64
t–BuCEt=C=O (**12**)	−51.76	104.35	(HOCHMe)CH=C=O (**28**)	−61.18	85.32
HOCH=C=O (**13**)	−35.82	67.30	(HOCHMe)CMe=C=O (**29**)	−68.83	94.02
MeOCH=C=O (**14**)	−31.33	75.68	(HOCMe$_2$)CH=C=O (**30**)	−72.47	88.83
(HO)$_2$C=C=O (**15**)	−73.22	70.23	(HOCMe$_2$)CMe=C=O (**31**)	−79.94	97.06
(MeO)$_2$C=C=O (**16**)	−67.74	86.97			
 **32**	−15.18	85.48	 **39**	−41.51	108.11
 **33**	−22.85	95.48	 **40**	−10.03	76.91
 **34**	−30.98	102.69	 **41**	−17.06	86.75
 **35**	−23.64	94.48	 **42**	−24.12	94.42
 **36**	−31.73	102.13	 **43**	−41.32	85.70

TABLE 1.6 (*Continued*)

Ketene	ΔH_f^{298} (kcal/mol)	ΔS^{298} (cal/mol K)	Ketene	ΔH_f^{298} (kcal/mol)	ΔS^{298} (cal/mol K)
 **37**	−39.88	110.27	 **44**	−48.89	94.76
 **38**	−32.93	97.07	 **45**	−72.35	92.25

ΔH_f^0 of -92 kJ/mol[4,6] for dimethylketene appears preferable to the experimental value of –137 kJ/mol,[5] as the latter value depends on reference values for other cations and a recently revised experimental value of $\Delta H^o{}_f$ for the propionyl cation necessitated a revision of the proton affinity for methylketene.[7] The trend in the values for the three ketenes also appears reasonable.

Based on an analysis of literature data, a revised value for the enthalpy of formation of ketene $\Delta H_f^0 = -100 \pm 10$ kJ mol^{-1} was proposed.[18] This differs significantly from the previously accepted value of $\Delta H_f^0 = -48$ kJ mol^{-1}, and further confirmation of this value appears warranted.

Heats of formation (kcal/mol values in parentheses) have been reported for the following species: NCCH=C=O (24±5), $NCCH_2C(+){=}O$ (198±3), $NCCH_2C(\bullet){=}O$ (32±1), and $NCCH{=}C{=}O^{+\bullet}$ (253±3).[7,10]

Sumathi and Green[11] have used MP2/6–31G*//MP2/6–31G* calculations to determine the heats of formation of 45 fairly simple monoketenes and bisketenes, as shown in Table 1.6. The calculated values were considered to be as accurate as the available experimental values and were used to derive group equivalents for the estimation of ΔH_f for other species.

Proton affinities (kJ/mol) of ketenes RCH=C=O for the groups R have been found by CBS-QB3 calculations as follows: H (820), CH_3 (844), NH_2 (917), OH (823), and F (793).[22] These results reflect the combined effect of the substituent on the stability of the ketene and on the cation $RCH_2C(+){=}O$ such that the least favorable protonation for R = F was attributed to the great instability of the cation, FCHC(+)=O, while the most favorable process was for $R = NH_2$, where the initial product was the dissociating complex $H_2NCH^+ \bullet\bullet\bullet C{=}O$.[22]

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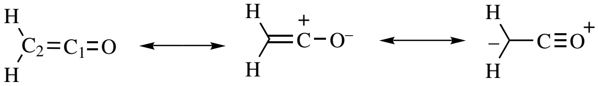
2 Spectroscopy and Physical Properties of Ketenes

The spectroscopy of ketenes has been discussed in previous reviews,[1,2] but as study of these species has gained momentum and experimental techniques have improved, there has been a great increase in the available data. Ketenes possess very distinctive IR absorptions near 2100 cm^{-1} and equally characteristic ^{13}C NMR chemical shifts for C_2 at remarkably high fields; these are very useful for providing definitive identification of these species.

2.1 NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

The ^1H chemical shift of ketene (**1**, $CH_2{=}C{=}O$) at δ 2.43–2.46 is at a remarkably high field for olefinic protons, and this may be attributed to the high electron density at C_2.[3–5] The large value for the geminal coupling constant $J_{H\text{-}H'}$ compared to that for $CH_2{=}CH_2$ (2.2 Hz) was attributed to favorable hyperconjugative interactions of the C—H bonds in ketene with the carbonyl π bond.[3] A compilation of ^1H chemical shifts and coupling constants for ketenes is given in Table 2.1.

Many diarylketenes have been isolated and characterized, and an extensive set of ^{13}C and ^{17}O NMR data is available for these compounds, as reported in Table 2.2.[11] The measurement of ^{17}O shifts at natural abundance is more convenient for ketenes than for many other carbonyl compounds. The ^{13}C chemical shifts are in the range of δ 178 to 203 ppm for the carbonyl carbon C_1 and 33–48 ppm for C_2. The very high field absorption for C_2 is characteristic of all ketenes and is attributed to the high negative charge density at this carbon, as confirmed by computations and illustrated by the characteristic ketenyl resonance structures **1a–c**. The C_2 shifts of these diaryl derivatives are at somewhat lower fields than for aliphatic and silyl substituted ketenes, which is the usual effect of α-aryl groups.



1a **1b** **1c**

Ketenes II, by Thomas T. Tidwell

TABLE 2.1 ^{1}H NMR Chemical Shifts and Coupling Constants for Ketenes $RR^1C{=}C{=}O$

R	R^1	δ (^{1}H)	J (Hz)	Other δ, J (Hz)	Ref
H	H	2.43[b]	15.8 (H, H′)		3
H	H	2.46			4
H	D	2.40	2.42 (H, D)		3
Me	H	2.67	7.4	1.56 (CH_3, $J = 7.4$)	4, 5
Et	H	2.80	6.9	2.04 (CH_2), 1.06 (CH_3, $J = 7.4$)	4, 5
i-Pr	H	2.82	5.7	2.49 (CH), 1.07 (CH_3, $J = 6.7$)	4, 5
t-Bu	H	2.81		1.19 (*t*-Bu)	4, 5
Me_3Si	H	1.65			10
EtHSi	H	1.65		3.0 (HSi–CH)	10
$(CD_3)_eSi$	H	1.70			10
t-$BuMe_2Si$	H	1.60			6
t-$BuPh_2Si$	H	2.07			6
Cl_3Si	H	2.84			10
$CH_3CH{=}CH$	H	3.95, 4.10 (*E*, *Z*)		9	
$CH_2{=}CH$	H	4.09	10	4.66 (*Z*), 4.95 (*E*), 6.06 (vinyl, $J = 11.0$, 18)	4, 5, 8
$CH_2{=}CH$	Me	1.76 (Me)		4.76, 4.77, 6.30 (vinyl $J = 11$, 16.6	4, 5
Me	Me	1.58, 1.65[c](Me)			4, 5, 10a

[a] $CDCl_3$ unless otherwise noted.

[b] 85% in TMS.

[c] CCl_4, ref. 10a.

TABLE 2.2 ^{13}C and ^{17}O NMR Chemical Shifts and Ketenyl IR Stretching Frequencies for $Ar^1ArC{=}C{=}O$ (data from ref. 11 unless otherwise noted)

		δ ^{13}C			
Ar^1	Ar	C_1	C_2	δ ^{17}O	IR (cm^{-1})
4-$Me_2NC_6H_4$	Ph	202.6	45.8	340	2088
4-$MeOC_6H_4$	Ph	202.0	45.7	339	2093 (2096)[d]
4-MeC_6H_4	Ph	201.7	46.4	340	2092
Ph	Ph	201.2	47.0	340	2094 (2100)[d]
4-Br C_6H_4	Ph	200.0	46.4	340	2095
4-Cl C_6H_4	Ph	200.1	46.2	341	2096
4-$O_2C_6H_4$	Ph	195.7	48.0	340	2100 (2109)[d]
$MesBr_2$[a]	$MesBr_2$[a]	178.7	55.8	310	2104
Mes[b]	Mes[b]	191.4	38.9	310	2096
C_6Me_5	C_6Me_5	191.3	41.9	301	2096
Tip[c]	Tip[c]	191.5	33.4	292	2095

[a] 2,4,6-Me_3-3,5-Br_2C_6.

[b] 2,4,6-$Me_3C_6H_2$.

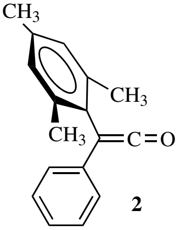
[c] 2,4,6-(*i*-$Pr)_3C_6H_2$.

[d] Data for $Ar^1{}_2C{=}C{=}O$ (ref. 17).

The data in Table 2.2 reveal that for ketenes 4-$XC_6H_4CPh{=}C{=}O$, substituents X have rather small effects on the shifts of C_1 and C_2, although there is a correlation of the shift of C_1 with σ_p for the groups X, $r = 0.995$.[11] The ^{17}O shifts are unaffected by the substituents X.

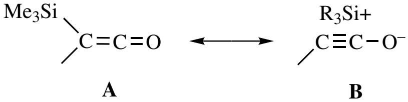
For the ketenes with highly substituted aryl groups there are significant changes in both the ^{13}C and ^{17}O shifts, and these are proposed to result from steric interactions.[11] The mechanism of this interaction was proposed to be a repulsive interaction between the bulky ortho substituents and the lone pairs on oxygen, which favored resonance structure **1c**, with increased electron density on C_2, giving rise to the higher field absorption at C_2 and the lower field for ^{17}O in these cases.

The three diarylketenes in Table 2.1 with bulky hydrocarbon substituents have ^{13}C shifts for both C_1 and C_2 that are at a higher field than for the less crowded compounds. This may be due to a twisted aryl ring in these compounds, as shown in the calculated structure for meistylphenyketene **2**.[12] This effect could arise from a lack of conjugation or the effect of the nearby methyl groups. For the compound with two 2,4,6-Me_3Br_2Ph substituents C_1 is at an even higher field, while C_2 is at the lowest field of the group.



2

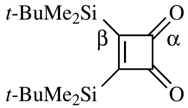
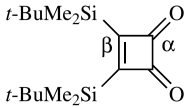
Results for other ketenes are collected in Table 2.3, and include a number of silyl substituted ketenes. Because of their high stability these compounds can usually be isolated, which permits convenient measurement of their spectra. Results for the ^{13}C, ^{17}O, and ^{29}Si NMR of silyketenes show a trend toward higher field shifts for C_1 and ^{17}O, and lower field shifts for ^{29}Si, compared to other silyl compounds bonded to sp^2 carbons (Table 2.3).[13,14] These results are consistent with "neutral hyperconjugation," as shown for resonance structures **A** and **B**, with a shift in electron density from the Si—C_2 bond to C_1 and O. Similar effects are seen in the ^{17}O and ^{29}Si spectra of ketones. Substituents RMe_2Si have similar effects on the C_1 and ^{17}O shifts for R = Me, *t*-Bu, Ph, but the group R does affect the ^{29}Si shifts.



The calculated chemical shifts of $Me_3SiCH{=}C{=}O$ (**3**) and $(CH_3)_2C{=}C{=}O$ (**4**) obtained using the (IGLO) method, basis set II, with MP2/6–31G* optimized geometries, are shown below and gave reasonable agreement with the experimental values, shown in parentheses.[13] In particular, the calculations reproduce the large

TABLE 2.3 ^{13}C, ^{17}O, and ^{29}Si NMR Chemical Shifts in $CDCl_3$ of Ketenes and IR Stretching Frequencies of Reference Compounds

Ketene	$\delta^{13}C$ C_1	C_2	$\delta^{17}O$	$\delta^{29}Si$	ν (cm^{-1})	Ref
$CH_2=C=O$	194.0	2.5			2133, 2142, 2151[a]	44
$MeCH=C=O$	200.0	10.9				44
$EtCH=C=O$	200.0	18.6				44
$(2\text{-Bu})CH=C=O$	200.2	31.3				25
$Me_2C=C=O$	204.9[a]	24.2	329[b]			5, 44
$MeEtC=C=O$	206.1	28.2				44
$t\text{-}Bu_2C=C=O$	203.1	51.9	330.6 (331.5)		2083	45, 46
$t\text{-}BuC(CO_2Me)=C=O$	191.8	50.0				42
$t\text{-}BuC(COBu\text{-}t)=C=O$	196.5	53.4				42
$(1\text{-Ad})_2C=C=O$	203.4	53.0			2035	18
$(CH_2)_2C=C=O$	206.1					
$PhCMe=C=O$	205.6	33.8				44
$PhCEt=C=O$	205.6	42.1				44
$Ph_2C=C=O$	201.3	47.0	340		2100[17]	7, 11
$CHCl=C=O$	166.2	70.1				43, 43a
$CMeCl=C=O$	168.9	85.0				43, 43a
$CBr_2=C=O$	178.6	98.5				7
$CH_2=CHCH=C=O$	200.2	28.6				8
$t\text{-}Bu_2P(S)C(Ac)=C=O$	170.2	9.5			2100	40
$(CF_3S)_2C=C=O$	171.8	18.8			2139	39
$(C_6F_5S)_2C=C=O$	172.6	31.4			2135	47
$(CF_3Se)_2C=C=O$	169.3	124.9			2127	37
$F_5SCMe=C=O$	196.8	72.4			2149	38
$(CF_3SO_2)_2C=C=O$	181.0	13.5			2139	37
$Me_3SiCH=C=O$	179.2	−0.1	255.0	−0.2	2112	10
$PhMe_2SiCH=C=O$	178.9	−0.7	256.1	−5.4	2114	20
$Me_3SiCPh=C=O$	182.5			−0.6		13
$t\text{-}BuMe_2SiCH=C=O$	180.0	−4.6				6
$t\text{-}BuPh_2SiCH=C=O$	178.5	−3.6				6

$(Me_3SiC{=}C{=}O)_2$	181.8	5.6	269.2 (269.0)[a]	3.2		13
$(t\text{-}BuMe_2SiC{=}C{=}O)_2$	182.2	4.3	270.5	10.6		13
$(PhMe_2SiC{=}C{=}O)_2$	180.9	5.9	270	−2.4	2080	13
$Me_2SiCH_2CO_2H$				3.8		13
$Me_3SiCH_2CO_2Et$				3.2[c]		13
$Me_3SiCH_2COCH_3$	206.8		536.7	1.6		13
	202.0		499.1	−8.4		13
	202.1			0.4		13
$Me_2C{=}O$ (acetone)	206.5		565.3 (571)[a]			13
$Me_3SiCH{=}CH_2$				−6.6		13
$Me_3SiC_6H_5$				−4.5		13
$t\text{-}BuMe_2SiCH{=}CH_2$				0.9		13
$CH_2{=}CHC(SiMe_3){=}C{=}O$	183.7	22.3			2085	48
$Me_2Si(CH{=}C{=}O)_2$	178.8	0.9	260.1	−3.3	2108, 2129	14
$MeSi(CH{=}C{=}O)_3$	178.0	1.8	263.9	−7.9	2108, 2136	14
$Me_5Si_2CH{=}C{=}O$	178.7	−2.4	252.2	−18.3, −18.8	2108	19
$(SiMe_2CH{=}C{=}O)_2$	178.2	−2.2	253.6	−18.6	2108, 2052	19
$(CH_2SiMe_2CH{=}C{=}O)_2$	179.0	−1.6	253.8	3.1	2115, 2052	19
$(Me_3Si)_2C{=}C{=}O$	1.668	1.7	211.2	−1.5	2085	19, 23
$1,4\text{-}C_6H_4(SiMe_2CH{=}C{=}O)_2$	178.9	−0.7	256.6	−5.4	2115	21

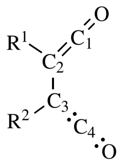
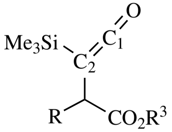
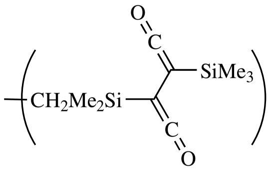


TABLE 2.3 (*Continued*)

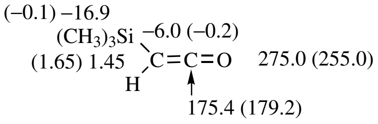
R^1	R^1	C_1	C_2	C_3	C_4		
Me_3Si	Ph	178.8	7.9	33.5	202.2	2093	25, 26
Me_3Si	$4\text{-}MeOC_6H_4$	178.4	7.4	31.9	204.2	2094	21, 36
Me_3Si	$4\text{-}MeC_6H_4$	178.3	7.1	32.6	203.1	2094	21, 36
Me_3Si	$4\text{-}AcC_6H_4$	177.5	7.0	34.2	198.1	2100	21, 36
$i\text{-}Pr_3Si$	Ph	178	11.9	33.5	201.6	2092	26, 36
Me_3Si	Me	180.6	10.7	18.9	204.2	2101	25, 26, 36
							
	R_3	C_1	C_2	C_3	C_4		
	$4\text{-}MeOC_6H_4$	179.8	46.4			2089	21
	Me	181.3	9.8			2085	27
	Et	180.9	10.8			2091	27
	i-Pr	181.0	11.0			2084	27
		181.4	4.4		3.4, 6.8	2089	22
		181.7	5.6				

---

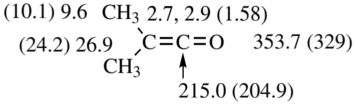
[a] CH_3CN solvent.

[b] Solid, argon matrix, and vapor, respectively.

effects of Si substitution on the chemical shifts for $^{13}C_1$ ($\Delta\delta$ calc 39.6, obs 25.7 ppm) and ^{17}O ($\Delta\delta$ calc 78.7, obs 74 ppm).



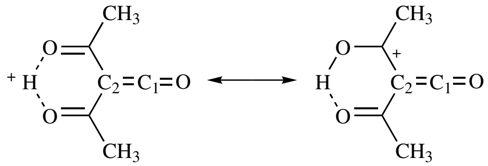
3



4

A continuing challenge is the measurement of NMR spectra of highly reactive, short-lived ketenes. There has been considerable progress in the measurement of IR spectra of such species, using either time-resolved IR (TRIR), matrix isolation, or measurements in dilute solutions with dry solvents, but NMR studies have not been as successful. There is a report of the generation of PhCH=C=O and measurement of the ^{13}C shift for C_2, but this requires confirmation.[15]

The ^{1}H and ^{13}C NMR spectra of the cationic diacylketene **5** show C_1 and C_2 at 169.7 and 78.0 Hz, respectively; $J_{CC} = 98.0$ Hz, with the IR absorption at 2200 cm^{-1}.[16]



5

Solid-state ^{13}C NMR spectra were measured for $CH_2{=}C{=}O$ and $O{=}C{=}C{=}C{=}O$.[16a]

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2.2 ULTRAVIOLET SPECTRA, PHOTOELECTRON SPECTRA, AND CHIROPTICAL PROPERTIES

The ultraviolet (UV) spectrum of ketene was first measured in 1924[1] and has been reviewed.[2] This showed the C=C $\pi \rightarrow \pi^*$ transition at 183 nm,[3] the C=O $\pi \rightarrow \pi^*$ transition at 215 nm ($\varepsilon = 80$),[4] and the n $\rightarrow \pi^*$ transition at 325 nm ($\varepsilon = 10$).[5,6] The UV spectrum of ketene has been recorded using a continuously tunable light source of synchrotron radiation.[7] The electronic states in the 140 to 220 nm cluster region have a predominantly Rydberg character and were described by coupled methods for excitation energies.[7] The absorption spectrum in this region was calculated from first principles based on a vibronic model and compared to the experimental spectrum.[8]

The UV spectra of a variety of ketenes and polyketenes are given in Table 2.4. The series of ketenes **1–3** with one, two, and three ketenyl groups, respectively, show UV absorption with maxima in the range 300 to 308 nm, with no significant effect of the position on the number of ketenyl groups attached to silicon but an increase in the extinction coefficient as the number of ketenyl groups increases.

Gas phase UV spectra showing the maxima have been reported for ketene (330 nm), methylketene (365 nm), ethylketene (355 nm), and dimethylketene (370 nm).[25] The vibrational progression of $CH_2{=}C{=}O$ suggests that the lowest singlet state is less than 61 kcal/mol above the ground state, while the energy of the lowest triplet in less than 55 kcal/mol.[26]

The photoelectron spectrum of bisketene **4** was found to be in good agreement with calculations for the twisted conformation shown.[27] Photoelectron spectra of **1-3** and other silylated mono- and bisketenes were also determined.[27,28]

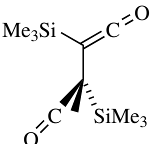

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TABLE 2.4 UV Spectra of Ketenes

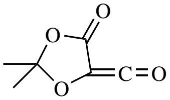
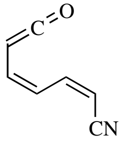
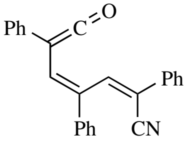
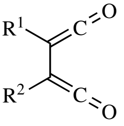
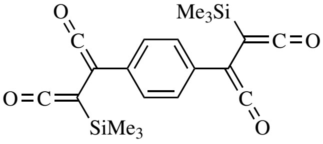
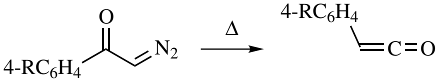
	$\lambda_{\max}$ (nm)	ε ($\mathrm{cm^2\ mol^{-1}}$)	Ref
$\mathrm{CH_2{=}C{=}O}$	183, 215, 325	(−), 80, (10)	1–6
$\mathrm{Me_2C{=}C{=}O}$	370		9
$\mathrm{Et_2C{=}C{=}O}$	378	13.3	9
$t\text{-}\mathrm{Bu_2C{=}C{=}O}$	225, 360	1,200, 11.6	10
$t\text{-}\mathrm{BuCH{=}C{=}O}$	360	13.2	10
$t\text{-}\mathrm{BuC(CO_2Et){=}C{=}O}$	228		10
$\mathrm{PhCH{=}C{=}O}$	360	13.2	10
$\mathrm{4\text{-}O_2NC_6H_4CH{=}C{=}O}$	495		35
$\mathrm{Ph_2C{=}C{=}O}$	350, 405, 399	(−), 310	11, 12
$\mathrm{(EtS)_2CH{=}C{=}O}$	288	6,000	13
$c\text{–}\mathrm{PrCPh{=}C{=}O}$	248, 395 ($\mathrm{CH_2Cl_2}$)		19
$\mathrm{PnCPh{=}C{=}O}$	260, 385 ($\mathrm{CH_2Cl_2}$)		19
$c\text{–}\mathrm{HxCPh{=}C{=}O}$	264, 388 ($\mathrm{CH_2Cl_2}$)		19
$c\text{–}\mathrm{PrC(Bu\text{–}}t\mathrm{){=}C{=}O}$	240, 373 ($\mathrm{CH_2Cl_2}$)		19
$c\text{–}\mathrm{Pr_2C{=}C{=}O}$	280, 376 ($\mathrm{CH_2Cl_2}$)		19
	~280		14
	13, 323 sh	15, 500, 12, 500	15
	221, 324	14,000, 11,500	15
$\mathrm{Me_3SiCH{=}C{=}O}$ (**1**)	213, 307	1,300, 30	10
$t\text{–}\mathrm{BuMe_2SiCH{=}C{=}O}$	292	35	10, 20
$\mathrm{PhMe_2SiCH{=}C{=}O}$	254, 309	200, 110	24
$\mathrm{Me_2Si(CH{=}C{=}O)_2}$ (**2**)	300	88	20
$\mathrm{MeSi(CH{=}C{=}O)_3}$ (**3**)	307	170	20
$\mathrm{MeSiC(CH{=}CH_2){=}C{=}O}$	233	9,000	34
$\mathrm{(Me_2Si)_2C{=}C{=}O}$	213, 278	1,000, 27	21
$\mathrm{Me_5Si_2CH{=}C{=}O}$	317	210	21
$\mathrm{(SiMe_2CH{=}C{=}O)_2}$	308	610	21
$\mathrm{(CH_2SiMe_2CH{=}C{=}O)_2}$	309	220	21
 $\mathrm{R^1, R^2}$			

TABLE 2.4 (*Continued*)

	λ_{max} (nm)	ε (cm^2 mol^{-1})	Ref
Me_3Si, Me_3Si (**4**)	325, 376	250, 107	16
t-$BuMe_2Si$, *t*-$BuMe_2Si$	326, 400	260, 80	16
Me_3Si, Ph	257		17, 18
i–Pr_3Si, Ph	260		17, 18
Me_3Si, 4-$MeOC_6H_4$	257		22
Me_3Si, 4-MeC_6H_4	257		22
Me_3Si, 4-$MeCOC_6H_4$	289		22
$PhMe_2Si$, $PhMe_2Si$	210 (sh)	16,000	23
 **4**	280		23

Thermolysis of the diazoacetophenones **5** at 500 °C gave the arylketenes **6** (equation 1), whose vertical ionization potentials (IP) were measured by photoelectron spectroscopy in the gas phase, and gave good agreement with values calculated at the B3LYP/6-31+G(d)//HF/6-31G(d) level.[29] It was proposed that the HOMO of these ketenes was destabilized by the presence of π-donor substituents at C–4 of the phenyl ring, thus leading to a lowered IP.[29]

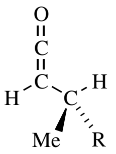


5 **6** (1)

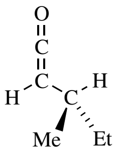
	IP (eV)	
R	**PE**	**Calc**
H	8.23	7.93
CH_3	8.22	7.68
CH_3O	7.91	7.36
Cl	8.29	7.94

Other measurements of photoelectron spectra of ketenes include $CH_2{=}CRCH{=}C{=}O$ (R = H, CO_2H),[30] haloketenes, and others.[31]

The conformational behavior of ketenes $CH_3CHRCH{=}C{=}O$ (**7**, R = H, Me, and EtO) was calculated at the B3LYP/6-31/+G**//B3LYP/6-31G* level, and chiroptical properties were calculated at the CIS/6-31+G* level.[32] The calculations indicated that the conformation with the C=O bond eclipsed by an α-hydrogen was of lowest energy, and the barriers for rotation around the C–C bond were 1.3 to 1.6 kcal/mol. The CD spectrum of (*S*)–**8** was measured at –13°C in CH_2Cl_2/pentane (λ_{max} = 363 nm) ^{1}H NMR δ 0.81 (t, 3, J = 7.3), 0.98 (d, 3, J = 6.7), 1.05–1.20 and 1.30–1.40 (ea 1, m), 2.13 (m, 1), and 2.75 (1, d, J = 6.9); ^{13}C NMR: δ 11.4 (CH_3), 21.4 (CH_3), 22.9 (CH), 28.2 (CH), 31.3 (CH_2), 200.2 (C=O). The effect of the alkyl substituent on the n-π^* Cotton effect sign obeyed a reverse octant rule, and there was agreement between the calculated and experimental chiroptical properties.[32] The effects of alkyl substituents on the chiroptical properties of bicyclo[2.2.1]heptylideneketenes **9** have also been examined.[33]



7 R = H, Me, EtO



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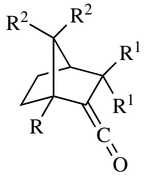

9

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2.3 INFRARED SPECTRA AND RAMAN SPECTRA

The IR spectrum of ketene has been the subject of continuing interest for a long time,[1–9] and the principal band assignments for $CH_2{=}C{=}O$, $CHD{=}C{=}O$, and $CD_2{=}C{=}O$ have been determined (Table 2.5).[2,4] Further investigations have included the combination bands and the vibrational and rotational spectrum.

Measurements of the vibrational spectrum and dipole moment of ketene have appeared, including the $\nu_2 + \nu_3$ and $\nu_2 + \nu_4$ bands at 3526 to 3528 cm^{-1} and at 3257 to 3277 cm^{-1}, respectively, from IR-UV double resonance photolysis.[5a]

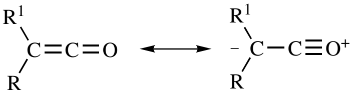
TABLE 2.5 IR Absorption Band Assignments for Ketenes (cm^{-1})

Mode	$CH_2{=}C{=}O^4$	$CH_2{=}C{=}O^{4a}$	$CD_2{=}C{=}O^2$
C-H (D) stretch	3071	3070.4	3115
C=O stretch	2152	2152.6	2150
CH_2 deformation	1388	1386.6	1293
C=C stretch	1118	1116.0	1022
C-H (D) stretch (antisymmetric)	3166	3165.4	2297
CH_2 rocking	977	977.8	815
CH_2 wagging	588	587.3	—
C=C=O bending	438	439.0	—
C=C=O bending (out of plane)	528	528.4	515

The IR spectra of ketenes showed a dependence of the position of the ketenyl band upon the medium, and for $CH_2{=}C{=}O$ this appears at 2151, 2142, and 2133 cm^{-1} in the vapor, the argon matrix, and the solid, respectively.[6] The Raman absorption of ketene was observed at 2049 cm^{-1}.[7]

The four fundamental IR bands for ketene below 1000 cm^{-1} have been obtained free from Coriolis contributions.[8,9] A detailed investigation of the IR spectrum of gaseous methylketene has also been reported.[10]

The ketenyl IR bands for ketenes $4\text{-}XC_6H_4CPh{=}C{=}O$ (Table 2.2, Section 2.1) are correlated with the σ_p substituent parameters ($r^2 = 0.978$).[11] The increase in the frequency is 7 cm^{-1} for X changing from MeO to NO_2, and for the disubstituted series $(4\text{-}XC_6H_4)_2{=}C{=}O$[11] this change is 13 cm^{-1}, showing an additivity of the effect. These trends are consistent with the proposal that electron acceptor substituents stabilize the resonance structure **1a** and lead to an increase in the frequency.



1 **1a**

A correlation derived from the IR frequencies of just five ketenes $R_2C{=}C{=}O$ (R = H, Cl, CH_3, CN, CH_3) was proposed between the frequencies and the *F* (field) and *R* (resonance) parameters of the substituents (equation 1).[12] This correlation indicated that the ketene frequency ν was increased by both effects.

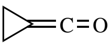
$$\nu(cm^{-1}) = 24F + 30R + 2141 \qquad (1)$$

A later correlation of computed IR frequencies found a modest correlation with a coefficient of 0.87 of the observed frequencies with the *F* parameter but no dependence on R (equation 2).[13]

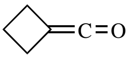
$$\nu(\text{cm}^{-1}) = 88F + 2141 \qquad (2)$$

IR spectra of a variety of ketenes[14] and bisketenes[15] formed by laser flash photolysis have been measured by TRIR spectroscopy, as well as many by conventional spectroscopy. Some of these are collected in Tables 2. Significant medium effects on these absorptions, including variations with solvent, have been observed.[6]

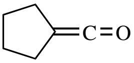
The ketenylidenecycloalkanes **2–4** all show doublet absorption of the ketenyl band in the IR, a result attributable to Fermi resonance.[16,18,29]



2 (2135, 2154 cm^{-1})

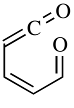


3 (2098, 2150 cm^{-1})

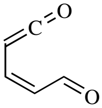


4 (2106, 2122 cm^{-1})

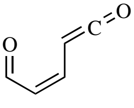
Ketene **5** labeled with ^{13}C in the carbonyl carbon displays four different IR bands at 2068, 2074, 2081, and 2089 cm^{-1} in an argon matrix at 8 K, attributed to the conformations **5a–d**, respectively.[17] As noted in Section 1.1.1 (ref. 26), it has been suggested that **5a** is not an energy minimum.



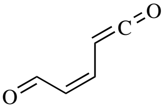
5a



5b

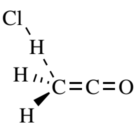


5c

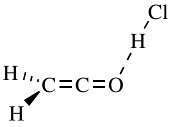


5d

The IR spectra of $CH_2{=}C{=}O$, $CH_3CH{=}C{=}O$, and $C_2H_5CH{=}C{=}O$ complexes in argon matrices are reported in Table 2.6 and were assigned to the structure **6** involving coordination of C_2.[18a–c] In xenon for $CH_2{=}C{=}O$ an additional band at 2134 cm^{-1} was assigned to structure **7**.[18a–c]



6



7

TABLE 2.6 IR Stretching Frequencies of Ketenes (cm^{-1})

Ketene	ν	Medium	Ref
$CH_2{=}C{=}O$	2151	gas phase	6
	2164	gas phase	5b
	2141	argon matrix	6
	2133	solid	6
$CHF{=}C{=}O$	2145	argon matrix	30
	2148	gas phase	30
	2148	argon matrix	30
$CHCl{=}C{=}O$	2151	argon matrix	30
	2150	gas phase	27
	2157	gas phase	30
$CHBr{=}C{=}O$	2148	argon matrix	30
$CHI{=}C{=}O$	2145	argon matrix	30
$CCl_2{=}C{=}O$	2160	gas phase	33
	2158	matrix	32
	2155	matrix	28
$CF_2{=}C{=}O$	2162	argon matrix	28a,b
$CH_2{=}C{=}O \bullet HCl$	2145	argon matrix	18a–c
	2142, 2134	xenon matrix	18a–c
$MeCH{=}C{=}O$	2140	gas phase	5b
	2130	solution	25
$MeCH{=}C{=}O \bullet HCl$	2127	argon matrix	30
$EtCH{=}C{=}O$	2134	gas phase	5b
$Me_2C{=}C{=}O$	2134	gas phase	5b
t–BuCH=C=O	2108	THF	60
t–$Bu_2C{=}C{=}O$	2090	film	63
t–BuC(Pr-*i*)=C=O	2090	CCl_4	59
t–BuC(Pr-*c*)=C=O	2097	CCl_4	59
c–$Pr_2C{=}C{=}O$	2106	CCl_4	59
MeOCH=C=O	2136	matrix	16a
EtOCH=C=O	2120	solution	70
PhCH=C=O	2117	isooctane	29
PhCH=C=O	2250	gas phase	65
$Ph_2C{=}C{=}O$	2094	$CHCl_3$	64
PhCMe=C=O	2135	THF	60
PhCEt=C=O	2130	CCl_4	60
PhC(Pr-*i*)=C=O	2096	CCl_4	59
PhC(Pr-*c*)=C=O	2102	CCl_4	59
PhC(Bu-*t*)=C=O	2097	CCl_4	59
E–PhCH=CHCH=C=O	2116	isooctane	29
E,Z–MeCH=CHCH=C=O	2118	CS_2	67
$CH_2{=}CHC(SiMe_3){=}C{=}O$	2085	solution	24
PhC≡CCH=C=O	2131	isooctane	29
$(NC)_2C{=}C{=}O$	2175	matrix	32
$(CF_3)_2C{=}C{=}O$	2196	matrix	34
$(EtS)_2C{=}C{=}O$	2160	solution	35
(*t*-BuS)$_2$C=C=O	2170	solution	35

TABLE 2.6 (*Continued*)

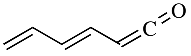
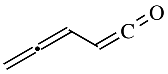
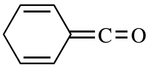
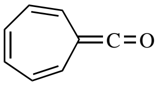
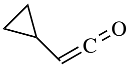
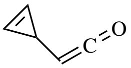
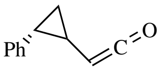
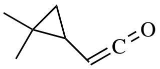
Ketene	ν	Medium	Ref
$(ArS)_2C{=}C{=}O$	2190	solution	35
$F_5SCH{=}C{=}O$	2177	film	31
$F_5SCMe{=}C{=}O$	2149	film	31
$F_5SCCl{=}C{=}O$	2175	vapor	31
$F_5SCBr{=}C{=}O$	2169	vapor	31
$CH_2{=}CHCH{=}C{=}O$	2118	toluene	22
$CH_2{=}CHCH{=}C{=}O$	2130	gas phase	22a
$Me_3SiCH{=}C{=}O$	2112	solution	36
$(CD_3)_3SiCH{=}C{=}O$	2122	gas phase	36
$(Me_3Si)_2C{=}C{=}O$	2085	solution	36
$Et_3SiC{=}C{=}O$	2115	solution	36
$Cl_3SiCH{=}C{=}O$	2165	gas phase	36
t-$BuMe_2SiCH{=}C{=}O$	2110	CCl_4	37
t-$BuPh_2SiCH{=}C{=}O$	2110	CCl_4	37
$EtO_2CCMe{=}C{=}O$	2137	gas phase	38
$MeCOCMe{=}C{=}O$	2121	gas phase	38
$MeCOCH{=}C{=}O$	2137	gas phase	38
t-$BuCOCH{=}C{=}O$	2140	gas phase	38
t-$BuCOCH{=}C{=}O$	2140	gas phase	38
$(C_6Cl_5)_2C{=}C{=}O$	2130		39
$(C_6F_5)_2C{=}C{=}O$	2140	CCl_4	40
$\bullet CH{=}C{=}O$	2023	matrix	41
$Ph_3P{=}C{=}C{=}O$	2080	KBr	42
	2111	toluene	22
	2117	toluene	22
	2101	toluene	21
	2101, 2103	toluene, matrix	22, 52
	2120	isooctane	20
	2110	matrix	4
	2121	isooctane	20
	2119	isooctane	20, 44

TABLE 2.6 (*Continued*)

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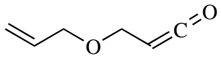
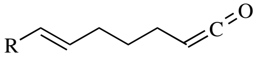
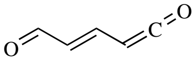
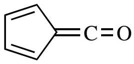
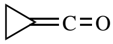
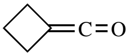
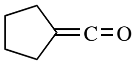
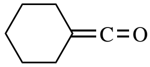
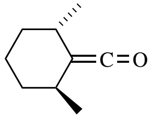
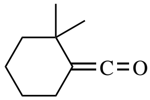
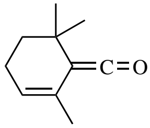
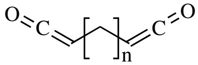
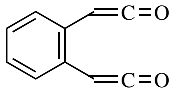
	2126	isooctane	54
 R = (H, Ph, *c*-Pr)	2119–2121	isooctane	20
	2117, 2129	matrix, *c*-C_6H_{12}	17
	2119, 2130	solution, matrix	18, 45
	2125, 2145	matrix	46
	2098, 2150	solution	16
	2106, 2122	hexane	29
	2100	CH_2Cl_2	68
	2106	CH_2Cl_2	69
	2100	THF	60
	2080[61], 2115[62]	film	61, 62
	2113–2114	hexane	55
	2115	toluene	19

TABLE 2.6 (*Continued*)

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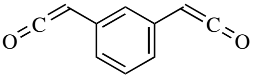
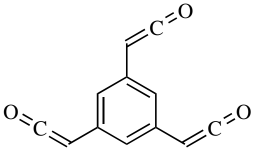
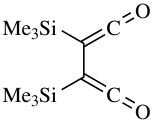
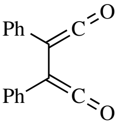
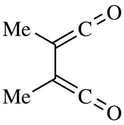
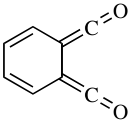
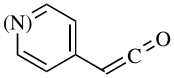
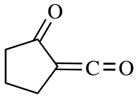
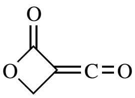
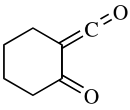
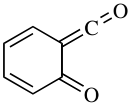
	2116, 2122	isooctane	19
	2115	hexane	66
	2084	$CDCl_3$	48
	2100, 2112	matrix	49
	2096, 2138	matrix	49
	2077, 2138	CH_3CN	50
	2128 (4); 2123 (3) 2123 (*anti*-2); 2132 (*syn*-2)		53, 53a
	2133	matrix	56
	2154, 2176	matrix	57
	2124	matrix	56
	2135	CH_3CN	51

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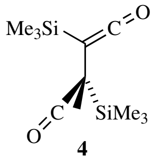
2.4 DIPOLE MOMENTS

The dipole moment of ketene was reported in 1946 as 1.45 D,[1] and the fact that this was less than the values for formaldehyde (2.27 D) and acrolein (3.04 D) provided evidence for the resonance structures of ketene, with high negative charge at C_2.[1] A highly precise value for the dipole moment of ketene of 1.42215(28) was obtained by a molecular beam electric resonance,[2] and microwave spectroscopy gave a value of 1.42429.[3] Dipole moments were also obtained for the three lowest-lying vibrational states ν_5, ν_6, ν_9 of ketene as 1.37408, 1.40433, and 1.42545 D, respectively.[3]

Dipole moments of many ketenes have been obtained computationally.[4] The ketene $CCl_2{=}C{=}O$ did not give a microwave spectrum, a result attributed to the absence of a dipole moment. A dipole moment was also measured for $CH_2{=}CHCH{=}CH{=}C{=}O$ (Section 4.1.2). Dipole moments of 2.7 and 1.8 D were measured for the bisketene **4** and $Me_3SiCH{=}C{=}O$, respectively, confirming the twisted structure of **4**.[6]



4

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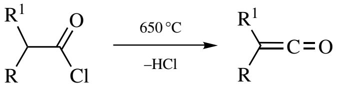
2.5 MASS SPECTROMETRY AND GAS PHASE ION CHEMISTRY

The mass spectrometry of ketenes has been reviewed.[1] Ketenes are conveniently prepared in the gas phase by thermolytic dehydrochlorination of acyl chlorides, and an extensive set of alkylketenes **2** was generated quantitatively by flash vacuum thermolysis of the acyl chlorides **1** at 650 °C with loss of HCl (equation 1), and their mass spectra were measured (Table 2.7).[2]



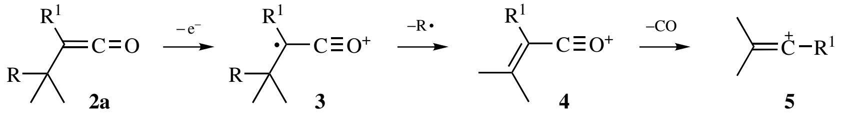
1 **2**

(1)

TABLE 2.7 Electron Impact Mass Spectra of Ketenes from Acyl Chlorides (Ref 2)

Ketene	Principal Fragment Ions (relative abundance in parentheses)
$CH_2{=}C{=}O$	42 (M^+, 100), 41 (M^+ –H, 25)
$MeCH{=}C{=}O$	56 (M^+, 100), 55 (M^+ –H, 21), 29 (MH^+ –CO, 25)
$EtCH{=}C{=}O$	70 (M^+, 100), 55 (M^+ $-CH_3$, 97), 41 (M^+ –COH, 48)
n-$PrCH{=}C{=}O$	84 (M^+, 34), 55 (M^+ $-C_2H_5$, 100)
n-$BuCH{=}C{=}O$	98 (M^+, 21), 55 (M^+ $-C_3H_7$, 100)
n-$PnCH{=}C{=}O$	112 (M^+, 25), 55 (M^+ $-C_4H_9$, 100)
i-$PrCH{=}C{=}O$	84 (M^+, 75), 69 (M^+ $-CH_3$, 80), 55 (M^+ $-C_2H_5$, 36) 41 ($C_3H_5{}^+$, 100)
s-$BuCH{=}C{=}O$	98 (M^+, 35), 69 (M^+ $-C_2H_5$, 100), 55 (M^+ $-C_3H_7$, 24)
t-$BuCH{=}C{=}O$	98 (M^+, 52), 83 (M^+ $-CH_3$, 100), 55 (M^+ $-C_3H_7$, 80)
$Me_2C{=}C{=}O$	70 (M^+, 100), 41 ($C_3H_5^+$ or C_2HO^+, 74)
n-$PrCMe{=}C{=}O$	98 (M^+, 46), 69 (M^+ $-C_2H_5$, 52), 41 (M^+ $-C_3H_7$, 100)
$EtCMe{=}C{=}O$	84 (M^+, 50), 69 (M^+ $-CH_3$, 16), 55 (M^+ $-C_2H_5$, 53), 41 (C_3H_5+, 100)
$Et_2C{=}C{=}O$	98 (M^+, 51), 83 (M^+ $-CH_3$, 19), 69 (M^+ –Et, 6), 55 (M^+ $-C_3H_7$, 100)

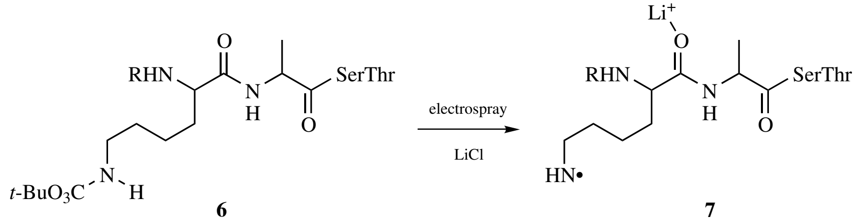
A characteristic feature of the mass spectra is the appearance of substantial molecular ion peaks M^+, which is due to the stabilization of the radical ions **3** formed, which have substantial acylium ion character (equation 2), as also noted by the ease of electron transfer from ketenes in solution (Section 5.1). The main fragmentation pathways of alkyl ketenes, as seen in Table 2.7, are β-cleavage giving conjugated cations **3**, with preferential loss of the larger R group, followed by further loss of CO forming vinyl cations **4** (equation 2).



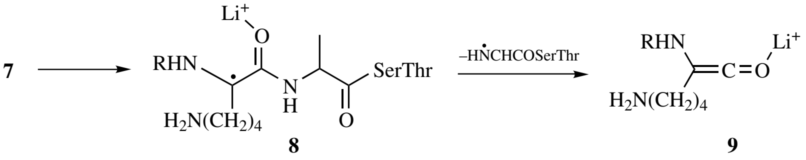
(2)

Many stabilized silyl-substituted ketenes have been isolated and found to give parent ions by (EI) mass spectrometry.[3–7] Loss of CO and of Me_3Si^+ are prominent processes observed.[3–7] Loss of alkyl groups from silicon in ketenes was also observed; thus, the parent ion from $PhMe_2SiCH{=}C{=}O$ results from loss of CH_3.[3–7] Mass spectra of some silylated bisketenes have also been reported.[6,7]

Because of their stabilized acylium ion structures, ketene radical cations are frequently formed by fragmentation of various precursors, and this has applications for structure analysis. The electrospray mass spectrum of peptide **6** functionalized with a peroxycarbamate function on the lysine sidechain proceeded by formation of aminyl radical **7** (equation 3), which abstracted hydrogen forming **8**, which gave cleavage to the ketenyl fragment **9** (equation 4).[8] This process was proposed as part of a strategy for directed fragmentation by free radical processes as a simplified method for protein analysis. Fragmentation of diacyl glycerophosphoethanolamine under low-energy, collision-activated dissociation with neutral loss of ketene was charge driven.[9]

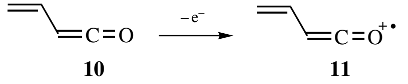


(3)

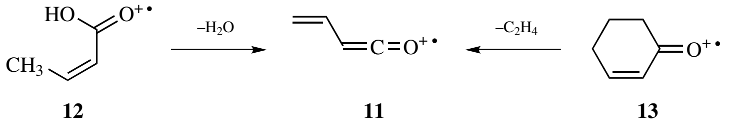


(4)

The 70 eV mass spectrum of vinylketene $CH_2{=}CHCH{=}C{=}O$ (**10**) gave a major parent ion **11** with a relative abundance of 67% compared to the fragment $C_2H_4{}^+$ (equation 5).[10] The ion **11** was also formed in the mass spectra of *Z*-crotonic acid **12** and of cyclohexenone **13** (equation 6).[11]

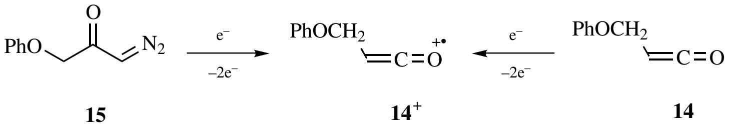


(5)



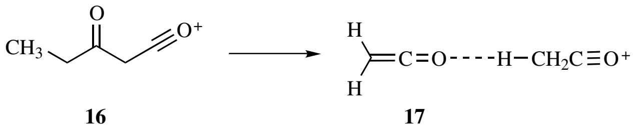
(6)

The mass spectrum of the ketene $PhOCH_2CH{=}C{=}O$ (**14**) generated by dehydrochlorination of the acyl chloride was observed and gave the same ion $\mathbf{14}^+$ formed by electron impact–induced Wolff rearrangement of **15** (equation 7).[12]



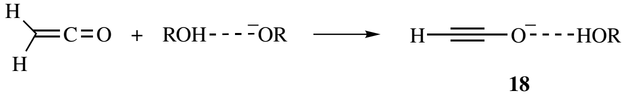
(7)

The kinetic energy release in the metastable fragmentation of $CH_2{=}C{=}O$[13,14] and the photoionization mass spectra of $CH_2{=}C{=}O$ and $CD_2{=}C{=}O$[15] have been studied. Ketene complexes with ionic species in the gas phase have been observed, including the complex **17** formed from **16** (equation 8).[16]

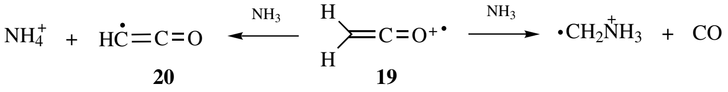


(8)

Ketene and alkoxide/alcohol ion pairs in the gas phase formed hydrogen-bonded ynolate ions **18** (equation 9).[17] The ketene radical cation **19** reacted with NH_3 in a selected ion flow tube (SIFT) by two reaction channels, including formation of the ketenyl radical **20** (equation 10).[18,19]

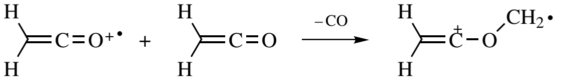


(9)



(10)

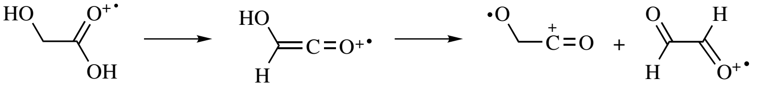
The ketene radical cation **19** was formed from the acetone radical ion,[20] and formed complexes detected in the gas phase with H_2O[21] and with acetone.[22] The reaction of **19** with ketene formed the distonic ion **20** (equation 11).[23]



19 **20**

(11)

The ketene complex $CH_2{=}NH_2^{+}\bullet\bullet\bullet CH_2{=}C{=}O$ (**21**) was formed in the 70 eV mass spectrum of $CH_3CONH(CH_2)_2CH_3$.[24] A complex of ketene with protonated acetone formed by rearrangement was also detected.[25] The molecular ion of $CH_3CH(OH)CH_2CO_2Me$ also formed a ketene complex.[26] The radical cation of hydroxyketene **22** was formed by dissociative electron ionization of glycolic acid, and formed the ions **23** and **24**, which fragmented, with formation of both CO and $CH_2{=}O^{+\bullet}$ (equation 12).[27]



22 **23** **24**

(12)

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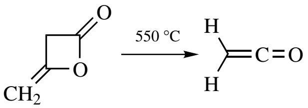
3 Preparation of Ketenes

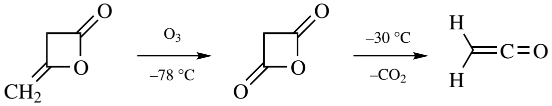
3.1 KETENES FROM KETENE DIMERS

Reviews of the chemistry of the ketene dimer have appeared.[1,2] Pyrolysis of ketene dimer (**1**) provides a simple synthesis of ketene (**2**) (equation 1).[3] The reaction of ozone with (**1**) gave the elusive malonic anhydride (**3**), and this formed ketene by loss of carbon dioxide (equation 2).[4,5]



(1)

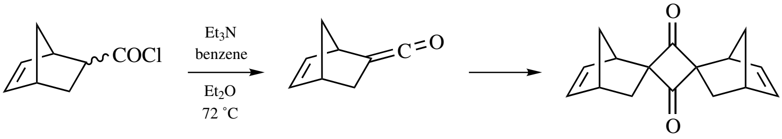
1 **2**



(2)

1 **3** **2**

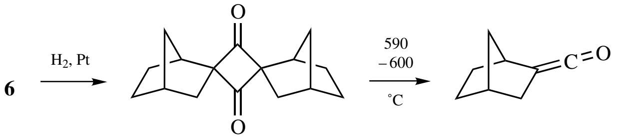
For preparation of norbornylideneketene (**8**), dimer **6** of ketene **5** was first made by treatment of 2-norbornenyl carbonyl chloride (**4**) with triethylamine (equation 3).[6] Hydrogenation gave (**7**), and flash vacuum pyrolysis at 590–600 °C gave ketene **8** (IR 2110 cm^{-1}), which was trapped at −78 °C (equation 4). Reaction of ketene **8** with diazomethane is discussed in Section 5.10.1. Dimethylketene has also been prepared by pyrolysis of the dimer.[7]



(3)

4 **5** **6** (73%)

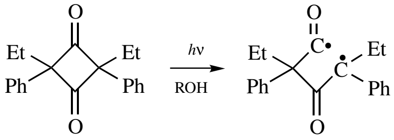
Ketenes II, by Thomas T. Tidwell



7 (78%) **8** (65%)

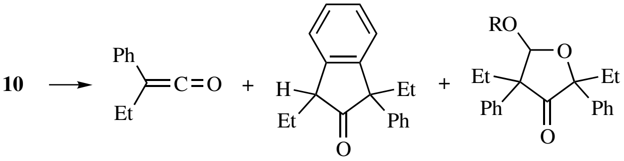
(4)

Photolysis of *cis* or *trans* cyclobutanedione **9** was suggested to give the diradical **10**, which formed only 5–12% yields of trapping products of ketene **11**, along with ketones **12** and **13** (equations 5, 6).[8] Photolysis of some dimers of dialkylketenes including **14** also gave the ketenes in yields of 20–30%.[9,10]



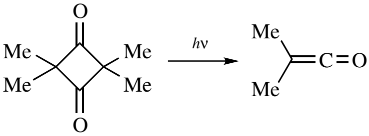
9 **10**

(5)



11 (5–12%) **12** **13**

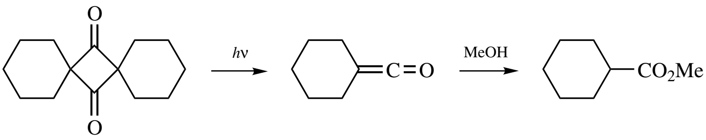
(6)



14 **15** (20–30%)

(7)

Photolysis of the cyclobutanedione (**16**) in CH_2Cl_2 gave pentamethyleneketene (**17**), as identified by IR absorption at 2100 cm^{-1} (equation 8).[11] Photolysis in MeOH gave the ester **3** in 20% yield (equation 8).[11] Tetramethyleneketene was formed in a similar fashion, but ketene formation was less efficient for smaller and larger ring sizes.[11]



16 **17** (IR 2100 cm^{-1}) **18** (20%)

(8)

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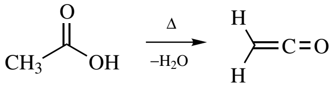
3.2 KETENES FROM CARBOXYLIC ACIDS AND THEIR DERIVATIVES

3.2.1 Ketenes from Carboxylic Acids and Anhydrides

3.2.1.1 Ketenes from Carboxylic Acids The direct preparation of ketene by the pyrolysis of acetic acid is not practical for laboratory use but has been used on an industrial scale (equation 1),[1] and the kinetics of acetic acid thermolysis forming ketene and other products have been reported.[2] The pilot-scale preparation of ketene by pyrolysis of acetic acid has been studied and enhanced by model-aided optimization.[3]



1

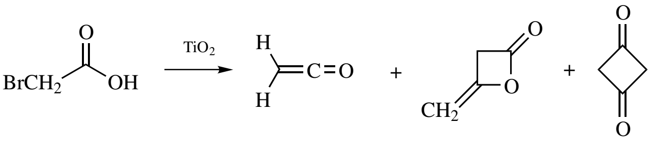
(1)

Many other procedures have been studied to effect this transformation. Catalytic dehydration of acetic acid to ketene on metal oxides can form ketene,[4,5] and the C_3 to C_5 carboxylic acids have been dehydrated with a catalyst to the corresponding ketenes over a packed bed of high surface area SiO_2 above 700 K,[6,7] The catalytic decomposition of acetic acid at -50 °C gave ketene, which was used to acetylate glycol monoethers.[8] The IR multiphoton dissociation of acetic acid gave ketene and water by one reaction channel, while decarboxylation to CH_4 and CO_2 accounted for roughly 35% of the total dissociation.[9] However, thermal and catalytic dehydration do not usually provide convenient laboratory preparations of ketene.

In the catalytic hydrogenation of acetic acid over zirconia to produce acetaldehyde, the formation of acetone was also observed, and it was proposed that the reaction involved removal of an α-hydrogen from the acetic acid, forming ketene, which could transfer CH_2 to acetic acid, forming acetone.[10]

Dehydration of acetic acid on UO_2 single crystals yields ketene,[11,12] and acetic acid and isobutyric acid on functionalized silica monoliths form ketene and dimethylketene, respectively.[13] Thermal decomposition of thulium acetate hydrate [$Tm(OAc)_3 \bullet 4H_2O$] forms ketene, acetic acetate, acetone, and methane.[14]

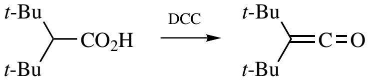
The reaction of bromoacetic acid on TiO_2 single crystal surfaces results in the formation of ketene and the ketene dimers **2** and **3** (equation 2).[15] Acetic acid on TiO_2 was found to form ketene near 290 °C.[16]



1 **2** **3**

(2)

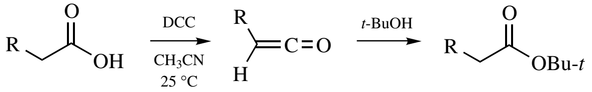
On a laboratory scale, the formation of ketenes from carboxylic acids may be achieved in certain cases. The very stable ketenes $t\text{-}Bu_2C{=}C{=}O$ (**4**) and $Me_3SiCH{=}C{=}O$ (**5**) were prepared by the direct dehydration of the carboxylic acids using dicyclohexyl carbodimide (DCC) (equation 3).[17]



4 (70%)

(3)

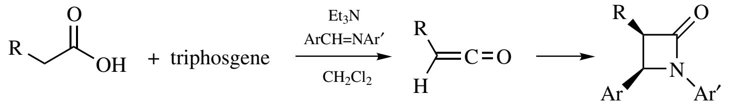
Reaction of carboxylic acids **5** with strongly electron-withdrawing α-substituents with DCC in the presence of crowded alcohols rapidly gave high yields of esters at room temperature via ketenes **6** (equation 4).[18,19] The formation of ketenes was implicated by the incorporation of deuterium when *t*-BuOD was used and by the formation of [4 + 2] cycloaddition of adducts of ketenes with DCC in some cases.[18,19] Competitive reactions showed that MeOH, EtOH, and *c*-PrOH reacted with $(EtO)_2POCH{=}C{=}O$ (**6a**) at almost equal rates, while *t*-BuOH was 15 times less reactive. Ketenes **6** generated in this way reacted selectively with methanol in preference to more acidic alcohols or many phenols.[20]



(4)

5 **6** R = $(EtO)_2PO$ (**a**), $EtCO_2$ (**b**), NC (**c**), 4–$CH_3C_6H_4SO_2$ (**d**)

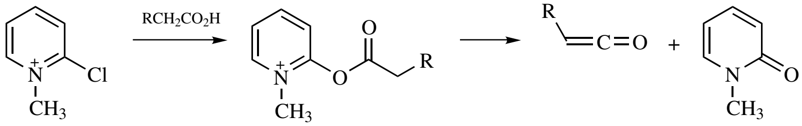
Triphosgene was used to react with carboxylic acids **5** to generate ketenes **7**, and in the presence of imines in dichloromethane at −40 °C it provided an efficient preparation of β-lactams **8** (equation 5).[21,22]



5 R = PhO, MeO, Phth, 2,4-$Cl_2C_6H_3O$ **7** **8** (65–95%)

(5)

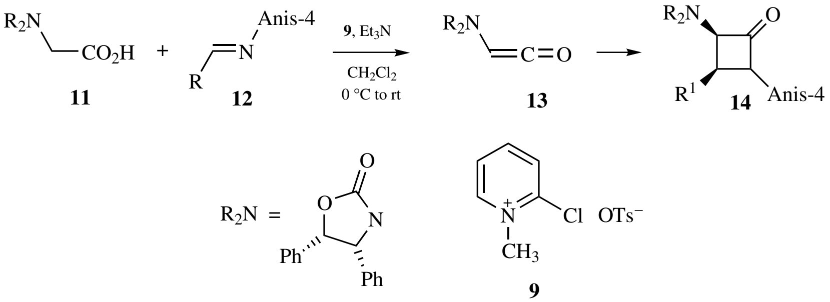
Mukaiyama's reagent **9** (2-choro-1-methylpyridinium tosylate or iodide)[23] effects the in situ dehydration of carboxylic acids to ketenes, and was suggested to react with the acids by formation of 2-pyridinium carboxylate esters, which gave ketenes and *N*-methylpyridone **10** (equation 6).[23]



9 **10**

(6)

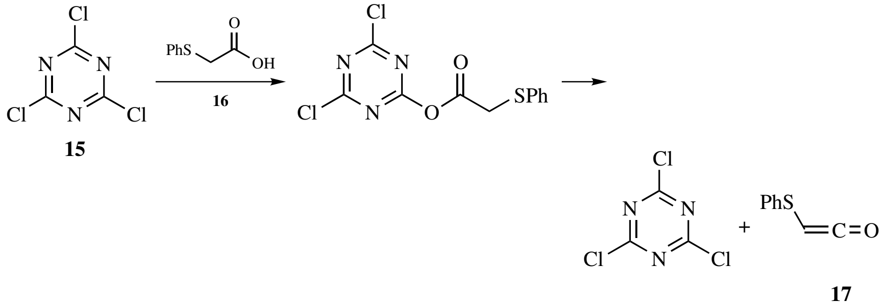
Optimized conditions using Mukaiyama's reagent for generation of ketene **13** from the optically active glycine-derived substrate **11** in the presence of imines **12** led to β-lactams **14** in yields of ≥90% and selectivities for the *cis*-product of 90 to 99% (equation 7).[24] These reactions were carried out under mild conditions with all the reagents present together, implicating the formation of ketene intermediates.[24] Mukaiyama's reagent has also been utilized on a solid support[25] as well as in solution[26,27] for ketene formation for reaction with imines forming β–lactams, and **9** was used for ketene generation for intramolecular cyclization.[28]



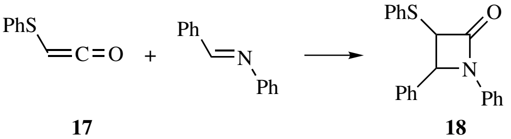
11 **12** **13** **14** **9**

(7)

Cyanuric chloride (**15**)[29,30] also served as a dehdrating agent for formation of a ketene or ketene equivalent, as in the reaction of the acid **16** forming phenylthioketene (**17**), which underwent [2 + 2] cycloaddition with the imine benzylideneaniline forming β-lactam **18** (equations 8, 9).[29,30]



(8)



(9)

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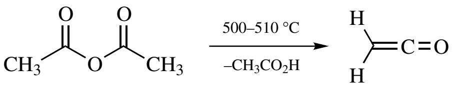
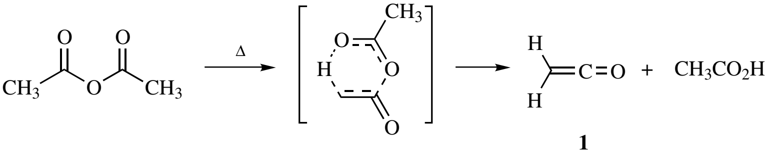
3.2.1.2 Ketenes from Acid Anhydrides Pyrolysis of acetic anhydride using a platinum wire was used by Wilsmore in the first preparation of ketene (equation 1).[1,2] Laboratory procedures using this method are available.[3]



1 (26%)

(1)

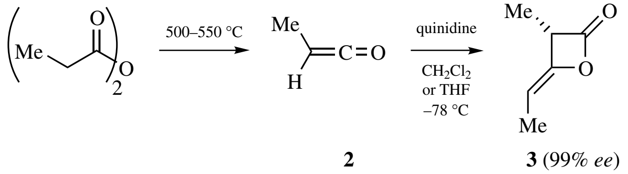
IR laser-powered pyrolysis (IRLPP) of acetic anhydride with SF$_6$ as a sensitizer has been used to generate $CH_2{=}C{=}O$ for direct IR observation.[4] The kinetics of the thermal unimolecular conversion of acetic anhydride to ketene and acetic acid were measured between 750 and 980 K and give Arrhenius parameters $A = 11.8\ s^{-1}$ and $E_a = 138$ kJ/mol, with $k = 10^{12.2}$ (exp -145 kJ/mol^{-1}/RT)s^{-1}.[4] *Ab initio* calculations favored a six-membered cyclic transition state with a barrier of 156 kJ/mol at the MP4 (SDTQ) level (equation 2).[5] Ketene formation from acetic anhydride with zeolite (BEA) in the presence of anisole gave 4-methoxyacetophenone.[6]



1

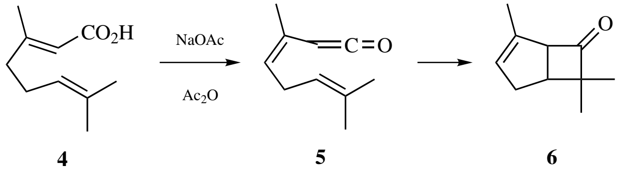
(2)

Methylketene (**2**) has been generated effectively from pyrolysis of propionic anhydride and has been obtained as a green solution usable for further reactions.[7] Trapping of the pyrolysis vapors in a solution of a catalytic amount of quinidine in (THF) or CH_2Cl_2 at −78 °C gave the dimer **3** with 99% ee (equation 3), and this could be reacted with amine nucleophiles to form chiral amides.[8]

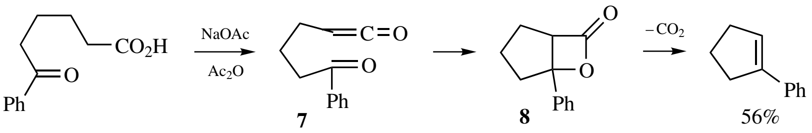


(3)

Carboxylic acid **4** reacted with sodium acetate in refluxing acetic acid (Perkin conditions) to form the acid anhydride, which yielded ketene **5**, which gave intramolecular [2 + 2] cycloaddition with the pendent alkenyl group forming cyclobutanone **6** (equation 4).[9–11] The β-lactone **8** was formed from the ketoketene **7** generated under these conditions, and underwent decarboxylation (equation 5).[12]

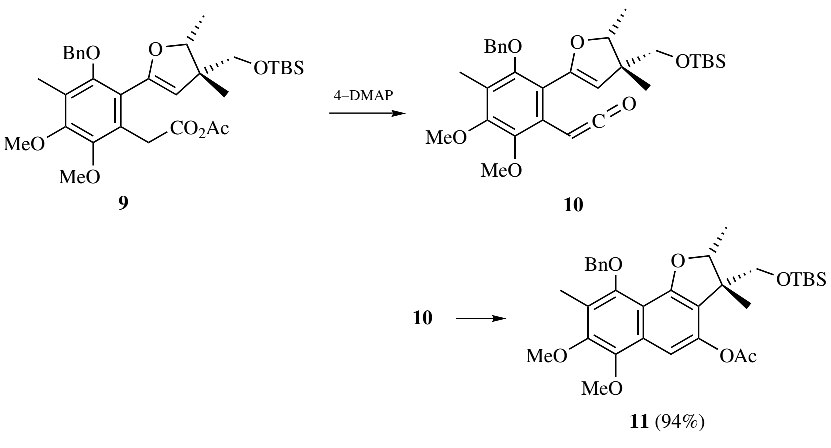


(4)



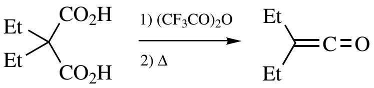
(5)

The base-induced formation of the ketene **10** from acid anhydride **9**, forming **11**, is a mechanistic pathway proposed in a total synthesis of furaquinocins (equation 6).[13]



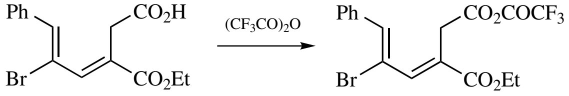
(6)

Ketenes such as **12** have been formed from malonic acids by conversion to mixed anhydrides with trifluoroacetic anhydride and thermolysis (equation 7).[14] Reaction of carboxylic acid **13** with trifluoroacetic anhydride formed the mixed anhydride **14** (equation 8). This led to the dienylketene **15**, which cyclized to phenol **16** (equation 9).[15] Anhydrides from carboxylic acids and ethyl chloroformate reacted similarly.[15]



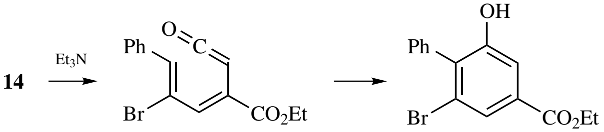
12 (56%)

(7)



13 **14**

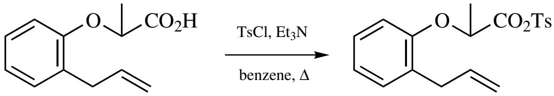
(8)



15 **16**

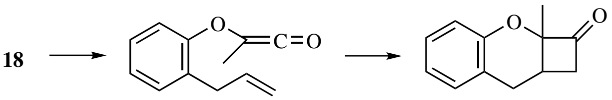
(9)

Mixed tosylate anhydrides have also been used to generate ketenes from carboxylic acids, as in the conversion of acid **17** with toluenesulfonyl chloride forming a mixed anhydride **18** (equation 10), which was converted to ketene **19**, which reacts by intramolecular [2 + 2] cycloaddition, forming cyclobutanone **20** (equation 11).[16–18] Mixed anhydrides **21** of cyclohexanecarboxylic acid with sulfonic acids gave cyclohexylideneketene (**22**) on pyrolysis (equation 12).[19] Similarly mixed anhydrides of CH_3SO_3H with carboxylic acids are reported to form ketenes on pyrolysis at 130 °C[20] or on reaction with Et_3N at 0 °C.[21]



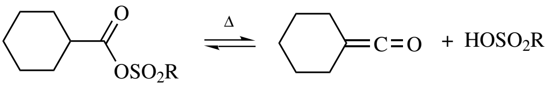
17 **18**

(10)



19 **20** (50%)

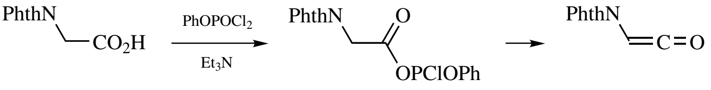
(11)



21 **22** (42%)

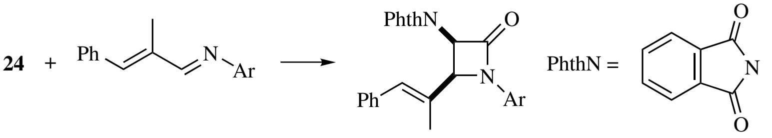
(12)

Reactions of carboxylic acids with phosphoryl chlorides allowed the in situ generation of ketenes,[22–27] which evidently formed from intermediate anhydrides, as in the conversion of the acid to anhydride **23**, forming ketene **24** (equation 13), which reacted by [2 + 2] cycloaddition with imines, forming β-lactams **25** (equation 14).[25]



23 **24**

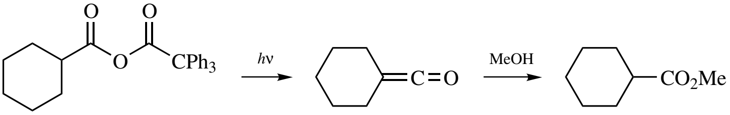
(13)



25 (80%, Ar = 4-MeOC$_6$H$_4$)

(14)

Photolysis of the mixed anhydride **26** formed ketene **22**, which was captured by methanol forming the ester **27** in a 70% yield (equation 15).[28]



26 **22** **27** (70%)

(15)

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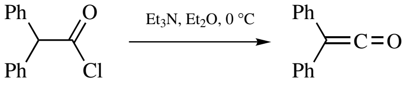
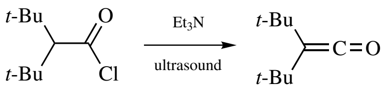
3.2.2 Ketenes from Acyl Halides and Activated Acids

The preparation and isolation of ketenes by dehydrohalogenation was confirmed by Staudinger in 1911,[1] although Wedekind had reacted diphenylacetyl chloride with *n*-Pr_3N in 1901 but failed to isolate the ketene.[2] This method has usually been successful for the isolation of ketenes only when these are stabilized by the presence of two bulky or aryl groups, as in the examples of diphenylketene (**2**, equation 1),[3] di-*tert*-butylketene (**4**, equation 2),[4] cycloheptylideneketene **6** (equation 3),[5] and 1,3,3-trimethylnorbornylidene-ketene (**8**, equation 4).[6] Ketene **4** was also prepared by dehydrochlorination at 80 °C with *n*–Bu_3N, IR 2090 cm^{-1} (Section 4.1.1).[6a]



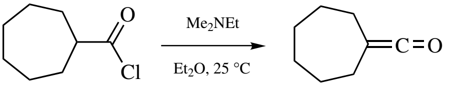
(1)

1 **2** (53–57%, IR 2100 cm^{-1})



(2)

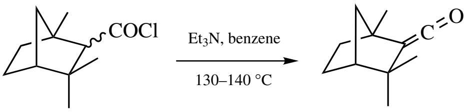
3 **4** **6** (86%)



(3)

5

6 (30%, IR 2102 cm^{-1})

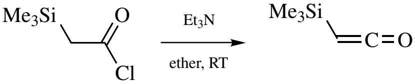


(4)

7

8 (19%)

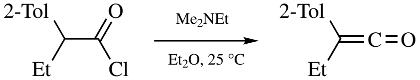
Dehydrochlorination was also successful in the preparation of the very stable trimethylsilyketene (**9**, equation 5).[7]



(5)

9 (48%)

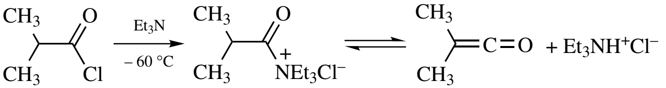
Other diarylketenes prepared by dehydrochlorination that have been isolated include bis(pentamethylphenyl)ketene,[8] ditipylketene (tiptyl is 2,4,6-triisopropylphenyl),[9,10] and bis(pentachlorophenylketene.[11] Alkyl(aryl)ketenes have also been isolated, including methyl(phenyl)ketene,[12] ethyl(phenyl)ketene,[13] and ethyl(2-tolyl)ketene (**10**, equation 6).[14]



(6)

10 (41%, IR 2081 cm^{-1})

The isolation of more reactive ketenes prepared by dehydrohalogenation may be difficult because of other reactions, such as dimerization. There is evidence that these reactions involve acylammonium intermediates and that the dehydrohalogenation step is reversible. Thus, in the reaction of isobutyryl chloride (**11**) with triethylamine at −60 °C, an IR absorption at 1810 cm^{-1} ascribed to the acylammonium salt **12** was observed, and a signal at δ 1.4 in the ^{1}H NMR was assigned as the ketene **13** (equation 7).[15,16]

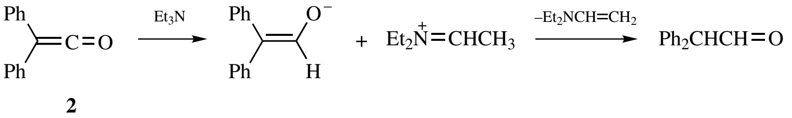


(7)

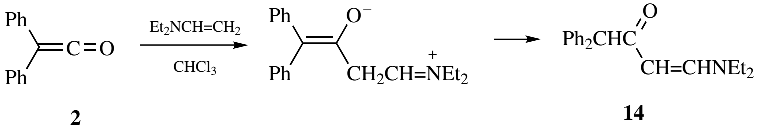
11 **12** **13**

In the preparation of diphenylketene (**2**, equation 1) by dehydrochlorination in refluxing chloroform, the by-product **14** was formed to the extent of 6–9%

(equations 8, 9).[17] The mechanism proposed for the formation of **14** involved initial hydride transfer to **2**, forming the corresponding enolate.[17]

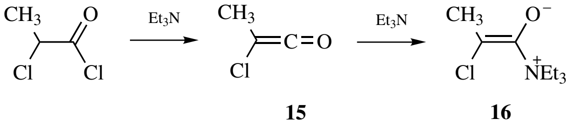


(8)



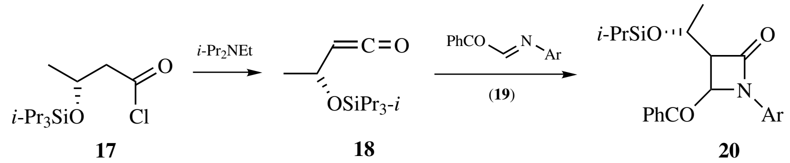
(9)

In esterifications using acyl chlorides RCOCl ($R = CH_3$, $ClCH_2$, $PhOCH_2$, and $PhCH_2$) with CH_3OD catalyzed by Et_3N ketene formation was shown to be competitive with direct addition in product formation.[18] The reaction of $CH_3CHClCOCl$ with Et_3N followed a complex path and was proposed to involve formation of $CH_3CCl{=}C{=}O$ (**15**), which added Et_3N, forming the zwitterion **16**, but the ketene was not observed even using stopped flow NMR (equation 10).[19] The formation of dimers of chloroketene and dichloroketene as unobserved products in Et_3N-catalyzed dehydrochlorination reactions is discussed in Section 4.4.2.



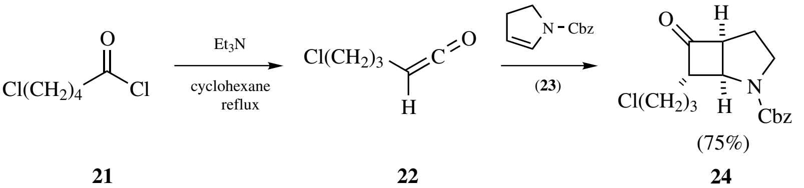
(10)

In the reaction of the chiral acyl chloride **17** in the presence of imine **19** catalyzed by *i*-Pr_2NEt, a strong band in the IR was observed at 2110 cm^{-1} due to ketene **18** (equation 11).[18] When the reaction was monitored by IR at −22 °C the appearance of the ketene and the slower formation of the β-lactam **20** were observed, and the kinetics were fit to the reaction of equation 11.[20]



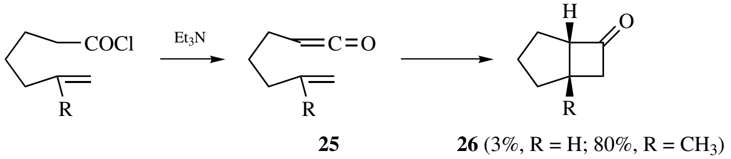
(11)

Reactive ketenes generated by dehydrochlorination are frequently trapped in situ with other reagents, and such processes can be convenient, giving high yields of products with high selectivity. An example is the dehydrochlorination of **21** forming 3-chloropropylketene **22**, which underwent [2 + 2] cycloaddition with the dihydropyrrole **23**, forming the cyclobutanone **24** (equation 12).[21]

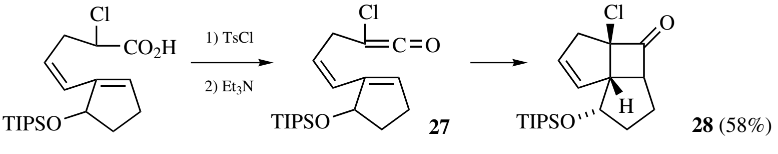


(12)

Efficient intramolecular [2 + 2] cycloadditions with pendant alkenyl groups also occur with reactive ketenes generated by dehydrochlorination. Cyclization of ketene **25** formed in this way proceeded in only a 3% yield with R=H, but for the more activated double bond with R=CH_3 the yield of **26** was 80% (equation 13).[22] The more reactive chloro-substituted ketene **27** gave a 58% yield of **28** when generated by activation of the acid with tosyl chloride and triethylaminc (equation 14).[23] This methodology was applied in synthesis using ketene **29** for the preparation of a precursor **30** to retigeranic acid (equation 15).[24] These reactions are relevant to the mechanism of ketene [2 + 2] cycloadditions, as they are geometrically restrained from a concerted $[_{\pi}2_s+_{\pi}2_a]$ pathway, and a $[_{\pi}2_a+_{\pi}2_a]$ pathway is forbidden, so a stepwise pathway is evidently followed.[25,26]



(13)



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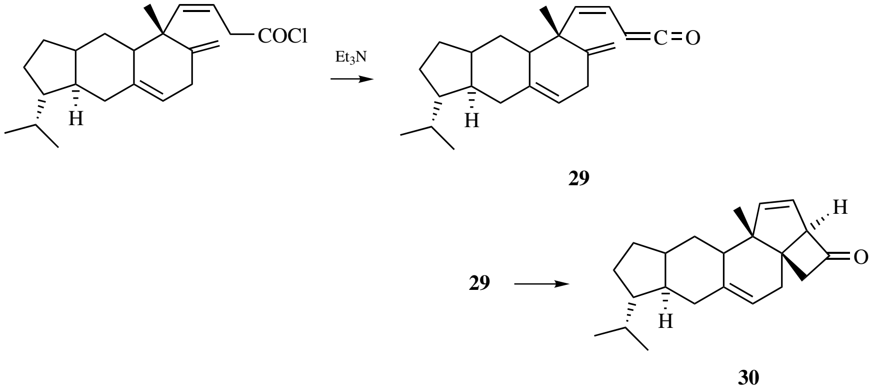
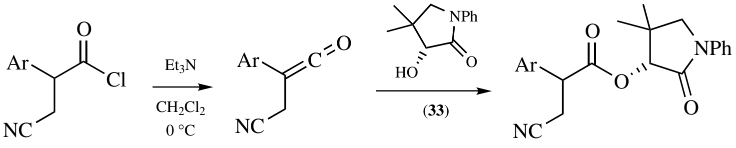


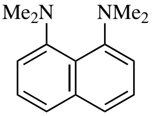
(15)

α-Aryl-α-cyanomethylketenes **32** generated by dehydrochlorination of the acyl chlorides **31** in the presence of either *R*- or *S*-*N*-phenylpantolactam (**33**) formed the cyano esters **34** in nearly quantitative yields with diastereomeric ratios up to 93:7 (equation 16).[27]

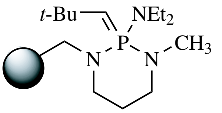


31 **32** **34** (16)

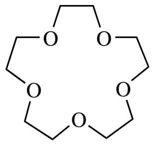
There have been significant improvements in the generation of ketene solutions by dehydrochlorination using the combination of a stochiometric base that reacts with the HCl generated and a catalytic amount of a trialkylamine that serves as a kinetic shuttle base.[28–31] The amine rapidly effects the dehydrochlorination and then transfers the proton to the stronger base, with regeneration of the catalytic base (Scheme 3.1). Bases that were screened included bis(1,8-dimethylamino)-naphthalene (**30**), NaH with 15-crown-5, K_2CO_3, and the polymer bound base BEMP, which is a triaminophosphonamide imine bound to a polymer support. The use of chiral tertiary amines permits catalytic asymmetric reactions of the ketenes.



30

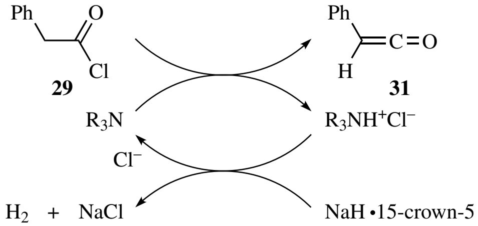


BEMP



15-crown-5

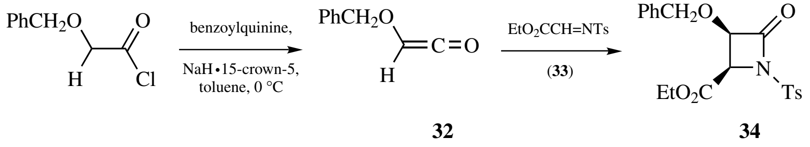
Of the bases, BEMP is insoluble and has the advantage that the ketene can be produced in solution by dehydrochlorination, either by passing the solution of the acyl chloride through a column containing BEMP or by stirring the two together and filtering off the ketene solution. However, K_2CO_3 and NaH are much cheaper, and for generation of ketenes such as phenyketene (**31**) react by a shuttle mechanism with dehydrohalogenation of the acyl chloride **29** by the amine R_3N, forming **31** in solution (Scheme 3.1).[28,29] The catalyst R_3N acts as a shuttle base in toluene



Scheme 3.1 Shuttle mechanism for formation of phenylketene (**31**) by dehydrochlorination using NaH and R_3N a shuttle base.

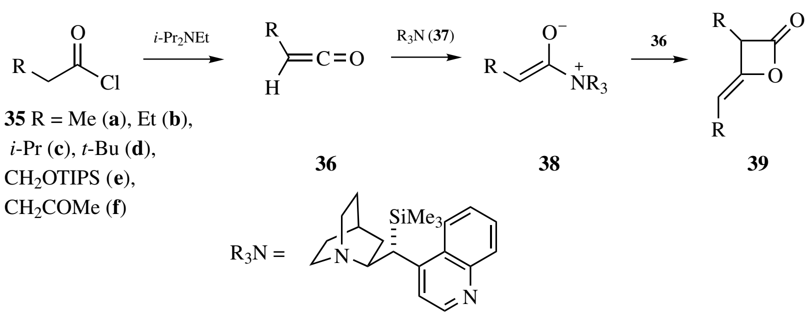
solution, forming the initial $R_3NH^+Cl^-$ salt, which transfers the proton to NaH, forming H_2 and regenerating R_3N. As described in Section 4.1.4, this methodology has been adapted to the generation of ketenes that were directly observable by IR. Other developments include the use of bases on solid supports[29] and insoluble K_2CO_3 for dehydrochlorination forming ketenes.[28–31]

When chiral amines such as benzoylquinine (BQ) are used as the shuttle base, these can catalyze asymmetric reactions of the ketene, as in the reaction of benzyloxyketene (**32**) with the imine **33**, forming the β-lactam **34** in 60% yield, 99% ee, and 8/1 *cis*/*trans* ratio (equation 17).[31] When 1,8-bis(dimethylamino)naphthalene (**30**) is used, the deprotonation of the acyl chloride may be reversible, and in some cases the reaction may go though an acylammonium ion and not a free ketene.[31]



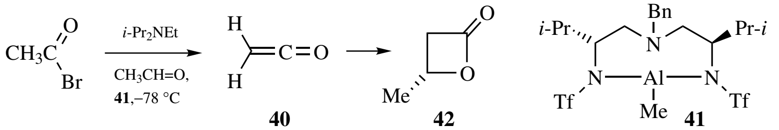
(17)

The use of other chiral alkaloid bases as catalyts also permitted asymmetric reactions of ketenes generated by dehydrochlorination of acyl chlorides **35**. In a careful study, the reaction of propionyl chloride (**35a**) with diisopropylethylamine (DIPEA) in CH_2Cl_2 at room temperature in the presence of trimethylsilylquinine (**37**) gave methylketene (**36a**), which formed the dimer **39a** in 79% yield and 94% *ee* (*R*) (equation 18).[32] Kinetic studies were consistent with rate-limiting ketene formation, with the stereoselectivity determined by complexation of the ketene with the chiral base forming **38**. Other ketenes **36** reacted similarly. Chiral ketene dimers **39** were shown to be valuable intermediates in a variety of synthetic procedures.[32]



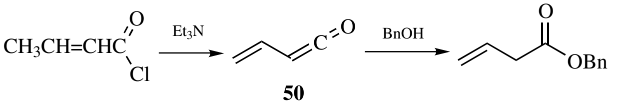
(18)

Ketene (**40**) generated by dehydrobromination of acetyl bromide in the presence of 10 mol % catalyst **41** reacted with acetaldehyde in situ and gave (*R*)-3-methylpropiolactone (**42**) in 92% yield, >98% *ee* (equation 19).[33] This intermediate was utilized in a total synthesis of the pharmacologically active natural product (−)-laulimalide.

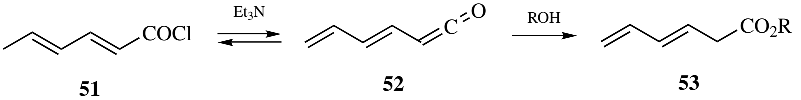


(19)

The reaction of the acyl chlorides derived from a series of acrylic acids with Et_3N in CH_2Cl_2 at −20 °C gave ketenes $CH_2{=}C(CH_3)CH{=}C{=}O$ (**43**), $CH_3CH{=}CHCH{=}C{=}O$ (**44**), $EtCH{=}CHCH{=}C{=}O$ (**45**), $CH_2{=}CHCH{=}CMe{=}C{=}O$ (**46**), $CH_3CH{=}CHCH{=}CMe{=}C{=}O$ (**47**), $CH_2{=}CHCBr{=}C{=}O$ (**48**), $CH_2{=}CMeCBr{=}C{=}O$ (**49**), and **50**, which upon addition of benzyl alcohol led to isolation of benzyl esters with a predominance of the β,γ-unsaturated isomers (equation 20).[34] A similar reaction is shown in Section 4.1.2. Reaction of **51** with Et_3N in the presence of alcohols led to significant amounts of the ketene **52**, as evidenced by the formation of deconjugated esters **53** (equation 21).[35]

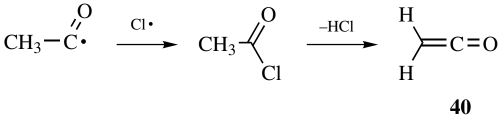


(20)



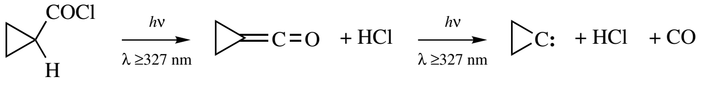
(21)

Photolyses of acetyl chloride,[36–38] acetyl bromide,[39] propionyl chloride,[40,41] and butanoyl chloride[42] in solid argon gave absorptions assigned to molecular complexes of the ketene with HCl or HBr. The IR spectra of $CH_2{=}C{=}O$ (**40**) in these complexes were practically unchanged from that of the free ketene, but the HCl and HBr stretching frequencies were significantly lower than those of the monomeric species in solid argon (see Section 2.3).[36–38] The propionyl chloride dissociation follows a concerted electrocyclic pathway, giving a T-shaped ketene-HCl complex.[40] The known reaction of $CH_3C(\bullet)O$ and Cl• radicals to give ketene (**40**) was examined theoretically and proposed to involve intermediate formation of acetyl chloride, which formed $CH_2{=}C{=}O$ and HCl (equation 22).[41]



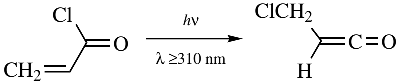
(22)

Photolysis of cyclopropanecarbonyl chloride (**54**) in an argon matrix at 15 K gave cyclopropylideneketene (**55**) and HCl, and it was proposed that upon further photolysis, decarbonylation to the complex of the carbene **56** and HCl was formed (equation 23).[42,43] Photolysis of matrix-isolated acrylyl chloride gave ketene **57** by a 1,3-chlorine migration (equation 24).[44]



54 **55** **56**

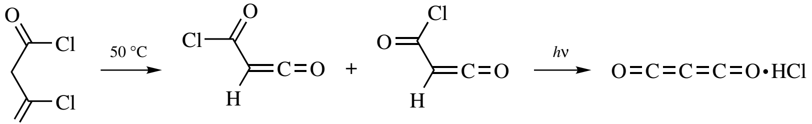
(23)



57

(24)

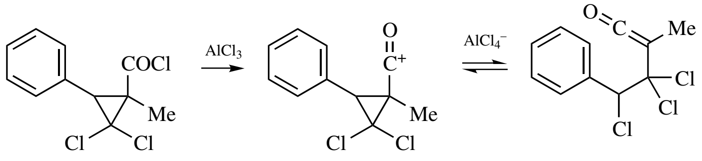
Thermolysis of malonyl dichloride at 50 °C gave chloroformylketene (**58**), for which two conformers were observed by IR in rare gas matrices (equation 25).[45] Further photolysis of **58** gave the complex **59** of C_3O_2 with HCl, and the barriers for the reaction in the ground state and the first excited state were calculated (equation 25).[45] The gas phase IR laser photolysis of CH_3COCl with SbF_6 leads to ketene formation, but in the presence of $W(CO)_6$ radical abstraction of Cl leading to $CH_3C(\bullet){=}O$ occurs.[46]



58a **58b** **59**

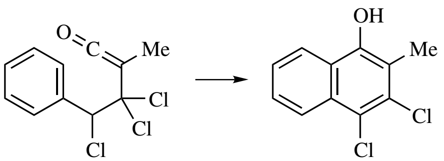
(25)

An unusual formation of ketene **61** from $AlCl_3$-catalyzed rearrangement of cyclopropyl acyl chloride **60** leading to formation of naphthol **62** has been proposed (equations 26, 27).[47] Inversion of configuration occurs upon treatment of the acid **63** with oxalyl chloride and the indole **64**. This was attributed to intervention of the ketene **65** or ketene iminium ion **66**, which formed the observed amide **67** (equation 28).[48] These reactions, possibly involving chloride loss and acylium ion formation, share some mechanistic characteristics with dehydrochlorination.



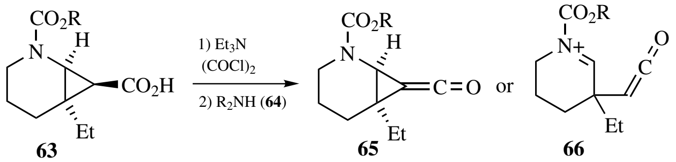
60 **61**

(26)

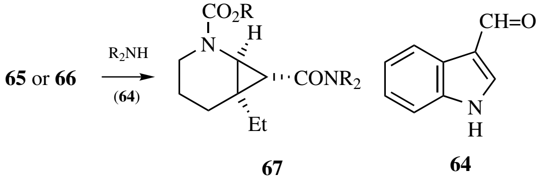


61 **62**

(27)

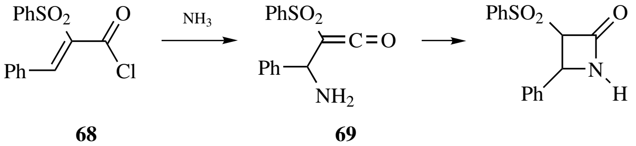


(28)



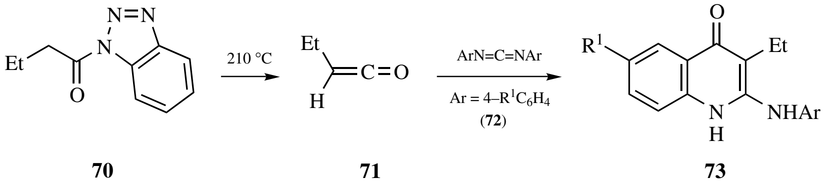
(29)

The addition of ammonia to 2-sulfonyl substituted propenoyl chloride **68** led to β-lactama, and was proposed to involve formation of ketene **69** by an addition-elimination sequence, although this were not detected directly (equation 30).[49] Stereoselectivity in the amine addition and formation of the resultant β-lactam was achieved with a chiral Lewis acid catalyst.[50]

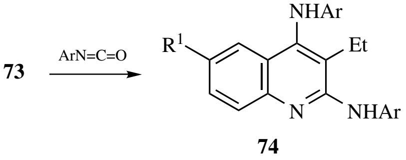


(30)

Thermolysis of 1-acetylbenzotriazole **70** with carbodimides **72** at 210 °C formed quinoline derivatives **73** by a process proposed to occur with formation of ethylketene (**71**) by an elimination process followed by reaction forming **73**, which reacted further with an isocyanate derived from **72** (equations 31, 32).[51]

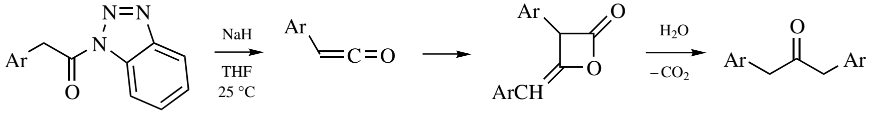


(31)



(32)

Reaction of arylacetyl benzotriazoles **75** with NaH was proposed to form arylketenes **76**, which gave dimers **77** that yielded 1,3-diarylacetones **78** upon hydrolysis and decarboxylation (equation 33).[52]



75 **76** **77** **78**

(33)

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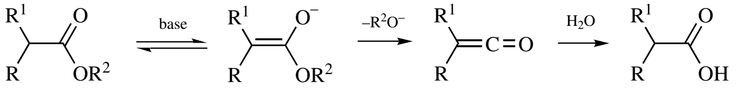
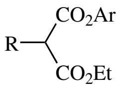
3.2.3 Ketenes from Esters

3.2.3.1 Ketenes from Ester Enolates Ester hydrolysis by the E1cB mechanism is a well-documented process in which a base removes a proton adjacent to the carbonyl group in an ester **1**, forming ester enolate **2**, and good alkoxy or aryloxy leaving groups depart, forming ketene intermediates **3**, which in water form acids **4** (equation 1).[1–5] This reaction has been studied computationally for ethyl acetate with a comparison of the free energy of reaction in water and in DMSO; the calculated $\Delta G^*_{\mathrm{sol}}$ value was only 6.0 and 8.4 kcal/mol greater for the E1cB mechanism (equation 1), respectively, compared to the $B_{AC}2$ mechanism of base attack at the carbonyl carbon.[6] It was expected that in crowded esters where access to the carbonyl group was hindered, the E1cB process could become dominant.[6]

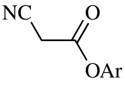


1 **2** **3** **4** (1)

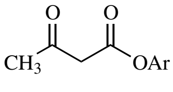
There is good evidence for this mechanism in the hydrolysis of aryl ethyl malonates **5**,[1] *o*-nitrophenyl cyanoacetate (**6**),[2] and aryl acetoacetates **7**, which form carboethoxy-, cyano-, and acetylketenes, respectively.[3] Evidence for this mechanism includes linear correlations of log*k* for hydrolysis of **7** with the pK_a of the phenolate leaving group,[3] an enhancement of the reaction by bulky substituents on the aryl leaving group,[7,8] and positive activation volumes, characteristic of dissociative processes.[9,10]



5



6



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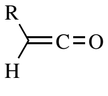
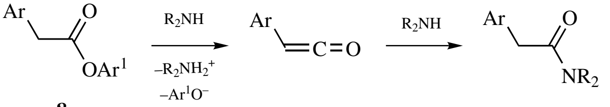


3 R = EtO_2C (**a**), NC (**b**), CH_3CO (**c**)

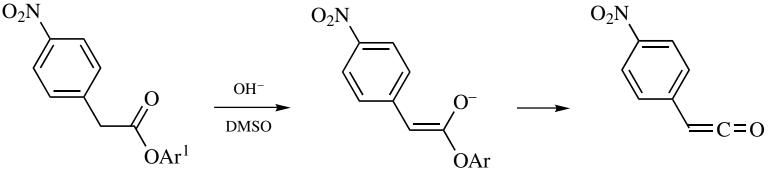
The reactions of aryl arylacetates **8** in CH_3CN with amines R_2NH were interpreted as proceeding through the formation of arylketenes **9** by the one-step E2 mechanism (equation 2).[11,12] For 4-nitrophenyl 4-nitrophenylacetate promoted by $R_2NH/R_2NH_2^+$ buffers in 70% CH_3CN/H_2O, the reaction was interpreted as involving concurrent E2 and E1cb mechanisms. Reactions of $Ph_2CHCO_2Ar^1$ were interpreted as involving similar processes.[13,14]



8 **9** **10**

(2)

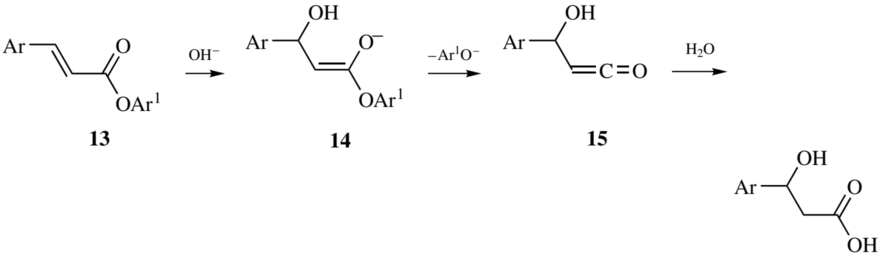
Reactions of aryl 4-nitrophenylacetates **8** (Ar = 4-$O_2NC_6H_4$) with OH^- in 80% DMSO/H_2O proceeded through formation of carbanion intermediates **11**, which were observed by UV and which formed 4-nitrophenylketene **12**, as evidenced by the correlation of the rate constants for carbanion decay with the σ^- constants of the aryl substituents with $\rho = 4.4$ (equation 3).[15] The UV absorption of **12** was observed with $\lambda_{max} = 495$ nm, and this was used to monitor the kinetics of hydration of **12** in this solution.[15] Similar mechanisms have been proposed for hydrolysis of **8** in 20% H_2O/CH_3CN.[16]



8 **11** **12**

(3)

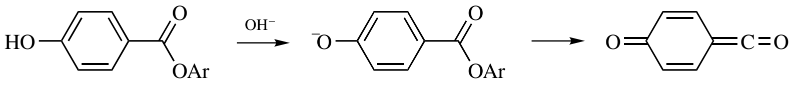
Conjugate addition of OH^- to arylacrylates **13** generated carbanion intermediates **14**, leading to E1cB ester formation of ketenes **15** (equation 4).[17]



13 **14** **15**

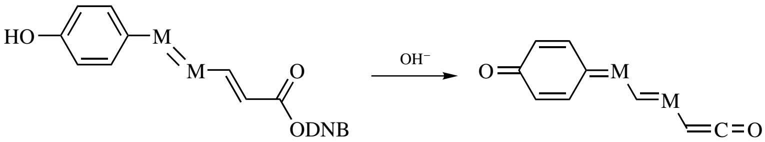
(4)

Basic hydrolysis of aryl 4-hydroxybenzoate esters **16** occurred by deprotonation of the phenolic hydroxyl, forming the oxoquinone methide **17** (equation 5).[18,19] Several homologues of this system were studied,[20–22] and the doubly vinylogous dinitrobenzoate esters **17a** and **17b** were proposed to react in basic solution, forming oxoquinone methides **17c** and **17d** (equation 5a).[23,24]



16 **17**

(5)



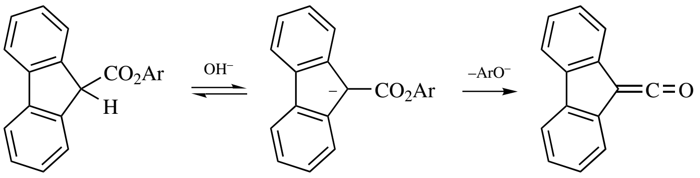
17a (M = CH)

17b (M = N)

17c,d

(5a)

Aryl fluorene-9-carboxylates **18** with electron-withdrawing aryl substituents (R = 3- or 4-NO_2, 4-CN, 4-Ac, 3- or 4-Cl) hydrolyzed by the E1cB mechanism, but for poorer leaving groups reacted by hydroxide attack at carbonyl carbon (equation 6).[25] The effects of micelles on the reactivity of **18** were also examined.[26]

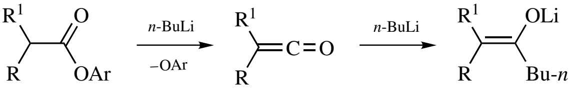


18 (Ar = RC_6H_4)

19

(6)

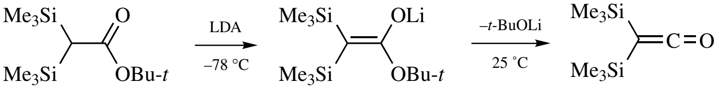
Crowded 2,6-di-*tert*-butyl-4-tolyl (BHT) esters of carboxylic acids (**20**) were deprotonated by *n*-BuLi forming ester enolates which expelled the aryloxide anion, forming ketenes **21**, which were captured by excess *n*-BuLi, forming ketone enolates **22** (equation 7).[27,28] The product enolates were captured by aldehydes to form aldols or by Me_3SiCl to give silyl enol ethers.[27,28]



20 (Ar = 2,6-*t*-Bu-4-MeC_6H_2) **21** **22**

(7)

The particularly stable bis(trimethylsilyl)ketene **24** was isolated from reaction of the ester **23** with LDA in a 60% yield (equation 8).[29]



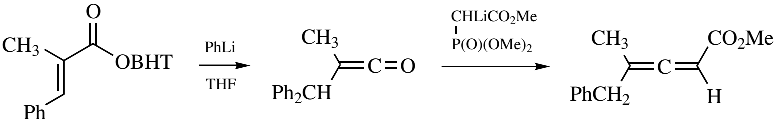
23

24 (60%)

(8)

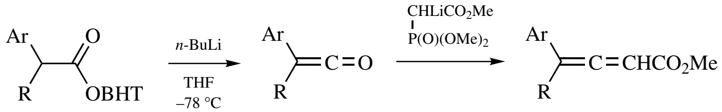
The ketene **26** formed from the BHT ester **25** by conjugate addition (*cf.* equation 4) was used to form the allene **27** by a ketene Wittig reaction (equation 9).[30] Reaction of BHT arylacetates **28** with *n*-BuLi formed enolates that gave the ketenes **29**, and upon addition of trimethyl phosphonoacetate ion in the presence of Sn^{2+} or

Zn^{2+} these gave allenes **30** (equation 10).[31] Ketenes generated from BHT esters were also trapped with stannyllithium reagents.[32]



25 **26** **27** (52%)

(9)

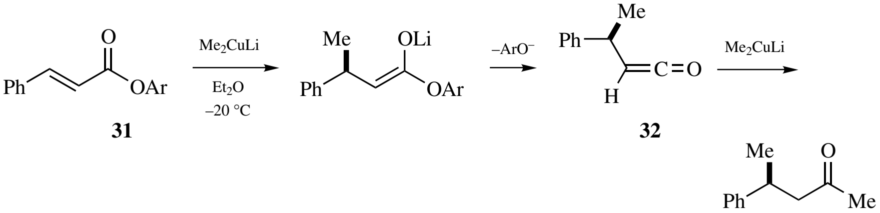


28 (Ar = Ph, 2-Naph; R = Me, Et, *i*-Pr) **29** **30**

(10)

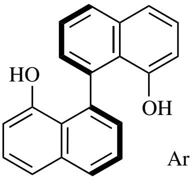
The formation of phenylketene PhCH=C=O by the dissociation of the enolate of $PhCH_2CO_2Pr$-*i* is reported in Section 4.1.4, including measurement of the ^{13}C NMR spectrum, but this report requires confirmation.

Asymmetric Michael addition to chiral binaphthyl cinnamate esters **31** gave ketenes **32**, which were trapped by Me_2CuLi to give optically active ketones **33** with high selectivity (equation 11).[33,34] Phenyl esters $PhCRCO_2Ph$ reacted with LDA and $ZnCl_2$ to give ketenes that were enantioselectively converted to allenes by a chiral phosphonate.[35]



31 **32** **33** (85%)

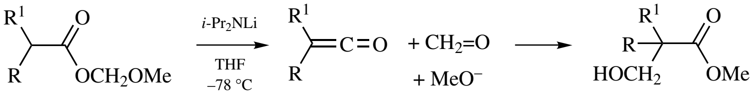
(11)



Ar

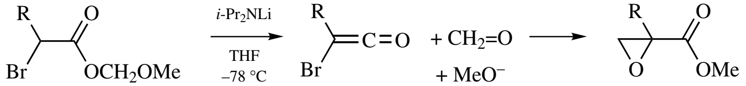
Additions of organolithiums to 4-methoxy-2,6-di-*tert*-butyl esters of naphthoic acids in the presence of chiral ligands resulted in asymmetric addition to the ring with ketene formation.[36] Reduction gave dihydronaphthalenes.[37]

Enolates of methoxymethyl esters **34** were proposed to fragment to ketenes **35**, formaldehyde, and methoxide, which recombined to give the aldol product **36** (equation 12).[38] With an β-bromo ester **37** the ketene **38** formed the glycidic ester **39** (equation 13).[38]



34 **35** **36**

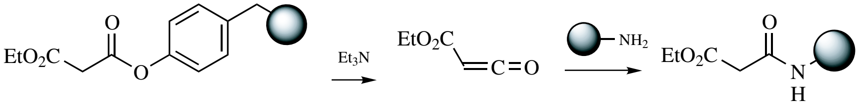
(12)



37 **38** **39**

(13)

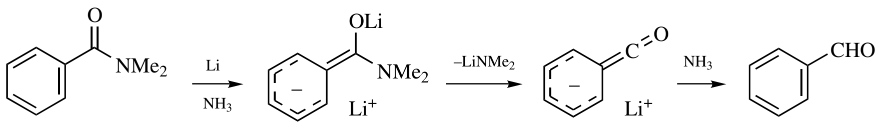
In an example of the three-phase test for reaction intermediates, the polymer-bound ester **40** with Et_3N in dioxane formed ketene **41**, which gave acylation of a polymer-bound amine (equation 14).[39]



40 **41** **42**

(14)

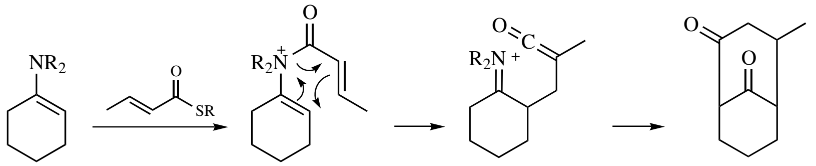
Birch reduction of the benzamide **43** was suggested to proceed through the amide enolate **44**, which formed the ketenyl anion **45**, leading to benzaldehyde **46** (equation 15).[40]



43 **44** **45** **46**

(15)

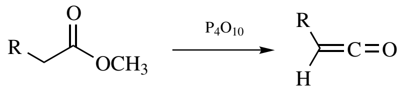
Reaction of cyclohexanone enamines **46a** with α,β-unsaturated thio esters and seleno esters leading to bicyclo[3.3.1]nonane-2,9-diones **46d** may have involved [3,3]-sigmatropic rearrangements of intermediate *N*-acylated enamines **46b** forming ketenes **46c**, which cyclized further and were hydrolyzed to the final products (equation 16).[41] This was analogous to the reactions of acyl chlorides previously observed.[42,43]



46a **46b** **46c** **46d** (32–68%)

(16)

A claim of formation of ketenes **47** as discrete intermediates by elimination from the corresponding esters (equation 16a)[44] requires independent confirmation, as these ketenes have eluded other efforts at preparation in solution and by every indication would be quite reactive.

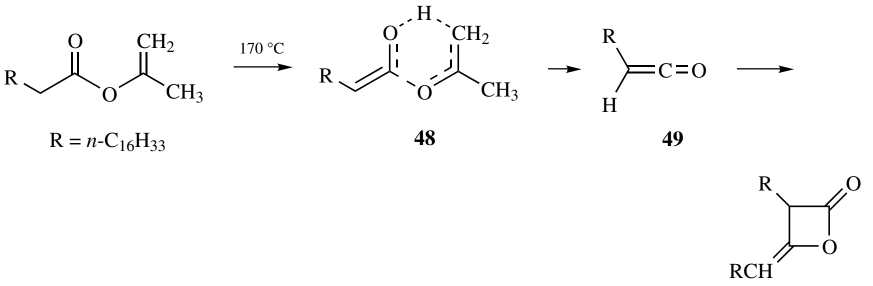


47 R = NO_2, R = CN (**3b**)

(16a)

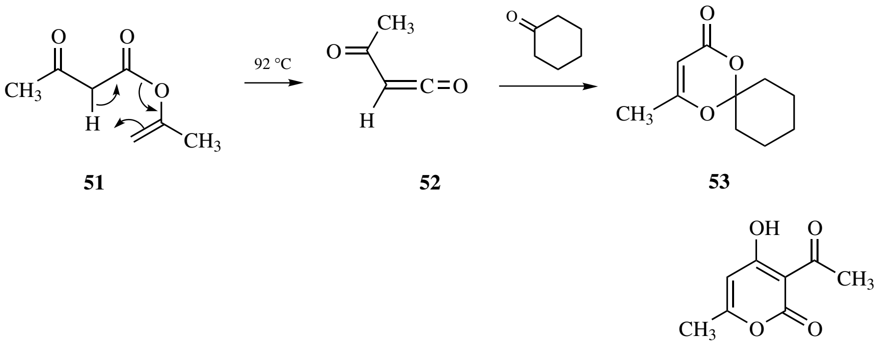
Treatment of aminonicotinic esters with base was proposed to give acylketenes that cyclized to 1,8-naphthopyridin-2-ones.[45] Acetoacetate esters of thiols, including *S*-acetoacetyl coenzyme A, were found to hydrolyze by the E1cB mechanism, implicating the formation of ketene intermediates.[46,46a]

3.2.3.2 Ketenes by Ester Pyrolysis Pyrolysis of isopropenyl esters was used to generate ketenes with long hydrocarbon chains through a mechanism involving the ester enol, as in the pyrolysis through the pericyclic transition state **48** forming *n*-hexadecylketene **49**, which was obtained as the dimer **50** (equation 17).[47] Isopropenyl acetoacetate (**51**) formed acetylketene (**52**) by a pericyclic process and was captured by cyclohexanone as the dioxinone **53** or the dimer **54** (equation 18).[48]



R = *n*-$C_{16}H_{33}$ **48** **49** **50**

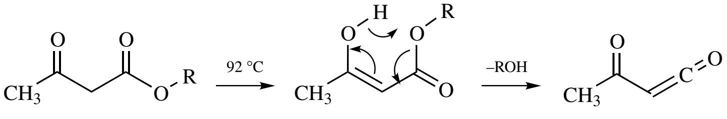
(17)



51 **52** **53** **54**

(18)

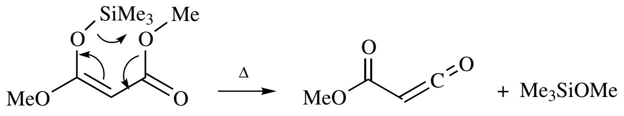
Pyrolysis of alkyl acetocetates **55** formed ketene **52** and the alcohol, and evidently proceeded through a pericyclic mechanism involving the ester enol **56** (equation 19).[49,50] Evidence for the pericyclic mechanisms comes from kinetic results in Table 3.1, which show significant accelerations in reactivity for the isopropenyl and *tert*-butyl esters.[49,50] The acceleration for the *tert*-butyl ester evidently arose from a steric effect favoring the dissociative mechanism.



55 **56** **52**

(19)

Pyrolysis of the trimethylsilyl ether of dimethyl malonate was also proposed to react through a pericyclic transition state, and formed carbomethoxyketene **57** (equation 20).[51] The acylketene **58** was proposed to be generated by thermolysis of the ester in alcohols and captured as the product of ester interchange (equation 21).[52,53]

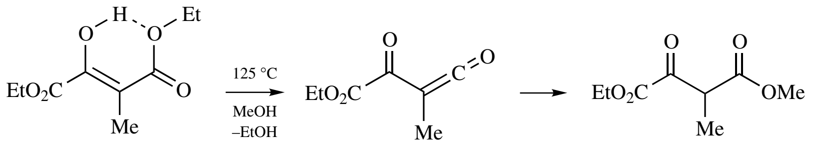


57

(20)

TABLE 3.1 Relative Rates of Thermolysis of Acetoacetates $CH_3COCH_2CO_2R$ in *n*-BuOH at 91.7 °C[50]

R	k_{rel}	R	k_{rel}	R	k_{rel}
Me	1.0	*i*-Pr	1.4	Isopropenyl[49]	7.3
Et	1.1	*t*-Bu	17		

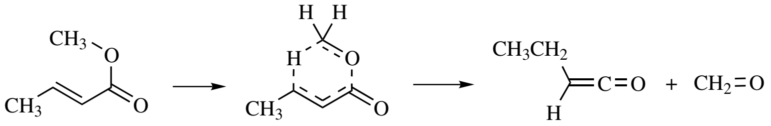


58

(21)

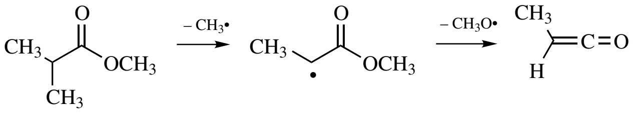
The titanium isopropoxide complex of $CH_3COCH_2CO_2Bu$-*n* underwent thermal decomposition to form acetylketene with deposition of TiO_2 as a thin film.[54]

Plasma dissociation of vinyl and saturated esters was found to give ketenes as detected by FTIR in the vapor, with bands near 2130 cm^{-1}.[55] Methyl crotonate (**59**) reacted by a pericyclic mechanism, forming ethylketene **60** (equation 22), while methyl isobutyrate (**61**) reacted by a radical mechanism, forming methylketene **63** (equation 23) and ketene **64** (equation 24).[55]



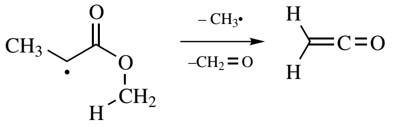
59 **60**

(22)



61 **62** **63**

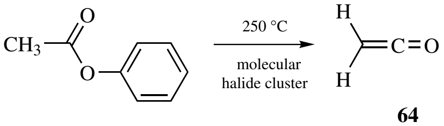
(23)



62 **64**

(24)

Heating of phenyl acetate in the gas phase over molecular halide clusters of Nb, Mo, Ta, and W at 250 °C led to the formation of phenol and ketene (equation 25).[56]

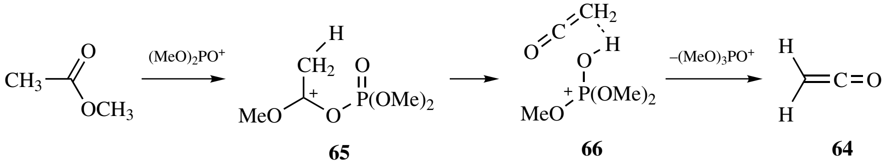


64

(25)

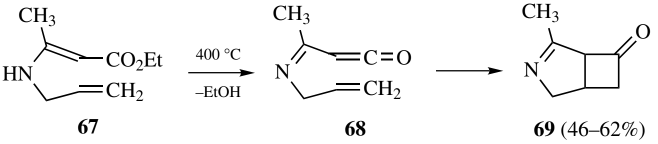
Gas phase reaction of phosphonium ions $(MeO)_2PO^+$ with aliphatic esters formed ketene (**64**).[57] This reaction was modeled by B3LYP/6-31G(d,p) calculations for methyl acetate–forming complex **65**, which formed the ketene complex

66 (equation 26).[57]



(26)

Pyrolysis of ester **67** gave ketene **68**, which cyclized to 3-azabicyclo[3.2.0] heptenones **69** (equation 27).[58]



(27)

Esterolysis melt polymerization using $CH_3CO_2ArCO_2CH_3$ suffers from color problems due to the formation of ketene. These problems can be avoided by using $PhCO_2ArCO_2CH_3$ for the preparation of polyesters.[59]

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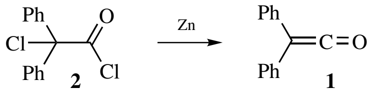
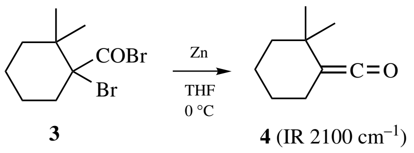
3.2.4 Ketenes by Dehalogenation of α-Halo Carboxylic Acid Derivatives

The initial preparation of diphenylketene (**1**) by Staudinger in 1905 involved the reduction of α-bromodiphenylacetyl bromide (**2**) with zinc (equation 1).[1,2] This procedure has been extensively utilized ever since, and has also been used for the preparation of 1,1- and 2,2-dinaphthylketenes.[3]



(1)

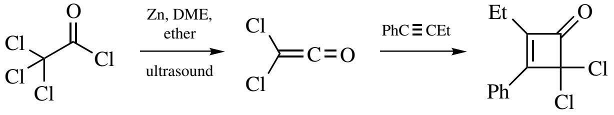
Improved yields for the preparation of methyl- and ethylketene were obtained by carrying out the zinc dehalogenation in THF with codistillation of the ketene and solvent under reduced pressure.[4] Removal of the ketene solution from the precipitated zinc salts has also been achieved by using syringe transfer, as in the preparation of a THF solution of ketene **4** from **3** (equation 2).[5]



(2)

In the formation of chloroketenes by dehalogenation for in situ [2 + 2] cycloadditions, complexation of the zinc salts with POCl$_3$[6,7] or dimethoxyethane[8] prior to workup has been recommended. This preparation of the highly reactive dichloroketene (**6**) for in situ trapping by the dehalogenation of trichloroacetyl chloride (**5**) has been described in *Organic Syntheses*.[7,8] Ultrasound served to activate zinc for formation of dichloroketene.[9] This has been utilized in cycloadditions with alkynes to give cyclobutenones **4**, which may be hydrolyzed to cyclobutenediones (equation 3).[9]

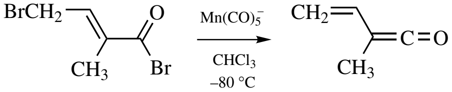
Various procedures for zinc activation have been utilized,[10–12] and activation using ultrasound[13] or simple heating[14] was found to be simple and quite effective.



5 **6** **7** (88%)

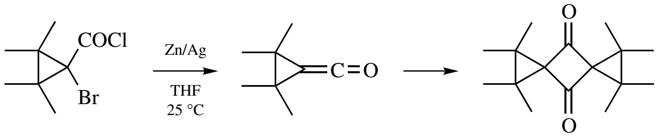
(3)

The metal ions Mn(CO)$_5^-$ and Cr(CO)$_4$NO$^-$ have proved to be very useful in the generation of small quantities of reactive ketenes at low temperatures and have permitted the measurement of ^{1}H NMR spectra of sensitive ketenes such as **8** (equation 4).[15–17] The use of Zn-Ag couple with the α-bromoacyl chloride **9** was utilized for the preparation of cyclopropylideneketene **10**, which formed the dimer **11** (equation 5).[18–20] Analogues of **10** were prepared by the same procedure.[18–20]



8 (80%)

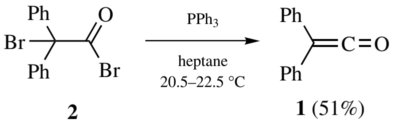
(4)



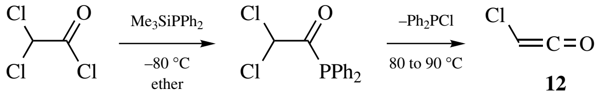
9 **10** **11** (50%)

(5)

An alternative procedure for debromination of α-bromodiphenylacetyl bromide (**2**) was treatment with triphenylphosphine, which gave diphenylketene (**1**, equation 6).[21] Chloroketene (**12**) was obtained by the reaction of dichloroacetyl chloride with Me$_3$SiPPh$_2$ at low temperature, forming the acylphosphine, followed by heating and trapping of the ketene at −80 °C (equation 7).[22] Reaction of **13** with Ph$_3$P gave dibromoketene (**14**), which was trapped with cyclopentadiene by [2 + 2] cycloaddition, forming **15** (equation 8).[23]



(6)



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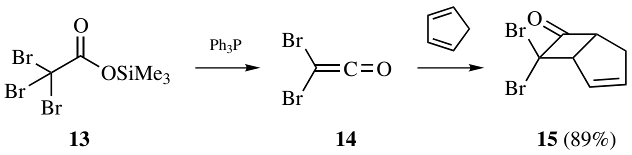
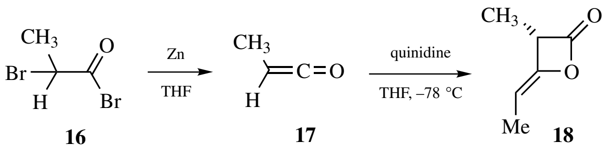


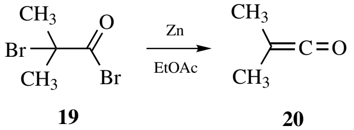
(8)

Formation of methylketene (**17**) by debromination of α-bromopropionyl bromide (**16**) in THF, with distillation of the product at room temperature and 110 Torr as it formed and treatment of the solution with quinidine at −78 °C, gave stereoselective formation of the dimer **18** as a solution in THF (equation 9).[24,25] The dimer was a useful synthon for further synthetic transformations.



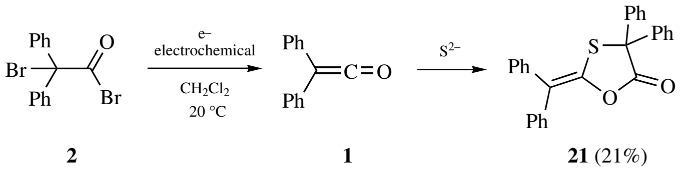
(9)

Dimethylketene (**20**) was prepared by debromination of 2-bromoisobutyryl bromide (**19**) with zinc in ethyl acetate and collected by distillation with heating at 300 torr as a solution in ethyl acetate (equation 9).[26]



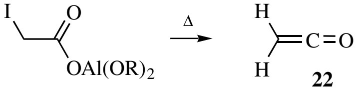
(10)

Electrochemical reduction of α-bromodiphenylacetyl bromide (**2**) formed diphenylketene (**1**) in almost quantitative yield, and in the presence of elemental sulfur this reaction was utilized in the synthesis of [1,3]oxathiolan-5-one **21**, proposed to result from reaction of **1** with S^{2-} (equation 11).[27]



(11)

Thermolyis of aluminium salts of iodoacetic acid was reported to form ketene (**22**), which was trapped in low yield as the ester (equation 12).[28]



22

(12)

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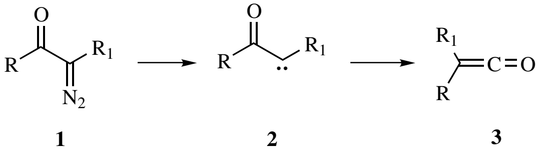
3.3 KETENES FROM DIAZO KETONES (WOLFF REARRANGEMENTS)

Wolff reported the first examples of the rearrangement of diazo ketones in 1902[1] but did not formulate the reaction as involving a ketene intermediate until later,[2] after this had been put forward by Schröter.[3] This reaction has proven to be of great value and mechanistic interest and has been frequently reviewed.[4–13] The reaction of diazo ketones **1** can occur thermally, by metal-catalyzed reaction, or photochemically, and in some cases forms a keto carbene intermediate **2** as a precursor to ketene **3** (equation 1).

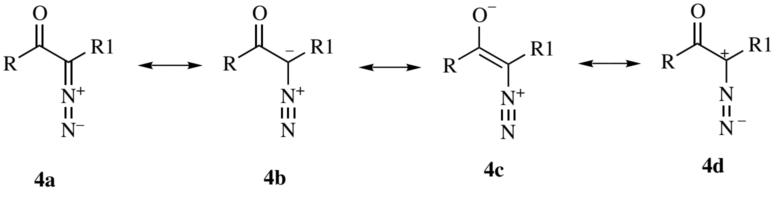


(1)

The electronic structure of diazo ketones may be represented by the resonance structures **4a–d** shown in Scheme 3.2, in which electron donation from the diazo group to the carbonyl group plays an important role. Structure **4d** is of negligible importance. These structures stabilize diazo ketones compared to other diazoalkanes, and predict the observed double bond character and restricted rotation in the central C-C bond between the two groups.

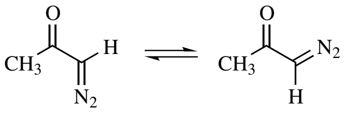
The effect of substituents on the structure and energy of diazo compounds and of diazirines has been studied by *ab initio* molecular orbital calculations.[14,15] These confirm the stabilizing effect of carbonyl groups on the diazo group.

The two conformers of diazoacetone (**5**) have been observed by ^{1}H NMR, and there is a barrier for intercoversion of *anti*-**5** to *syn*-**5** of 15.5 kcal/mol, with a 92:8 preference for *syn*-**5** at −40 °C (equation 2).[16] For $HCOCHN_2$ the *syn/anti* ratio is 69:31.[16] If the coplanarity and conjugation of the π-system is restricted by bulky groups (equation 3)[17,18] or by twisting of a ring system (equation 4),[19] then the substrates are much more labile and nitrogen loss occurs at a lower temperature. However, if the migrating group cannot occupy a position antiperiplanar to the departing nitrogen, then migration is inhibited, and methyl migration without ketene formation is dominant (equation 3).[17] However, upon photolysis in the gas phase, the yield of the ketene **7** is 40%.[18] The twisted seven-membered ring **9** promoted



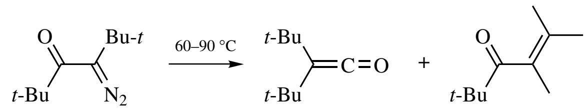
Scheme 3.2 Resonance structures for diazo ketones.

thermal Wolff rearrangement even at 20 °C, and the ketene **10** was observed by IR, with a reported frequency of 2200 cm^{-1} and was hydrolyzed to the acid in 48% overall yield (equation 4).[19] Similarly, photolysis of **12** formed the ketene **13** in 96% yield, while thermolysis gave the ketene in 85% yield (equation 5).[20]



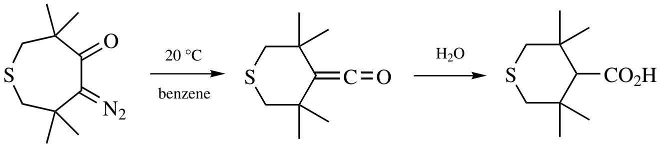
anti-**5** *syn*-**5**

(2)



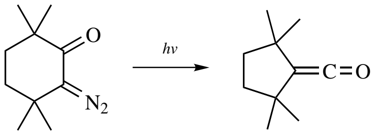
6 **7** (<3%) **8**

(3)



9 **10** **11** (48%)

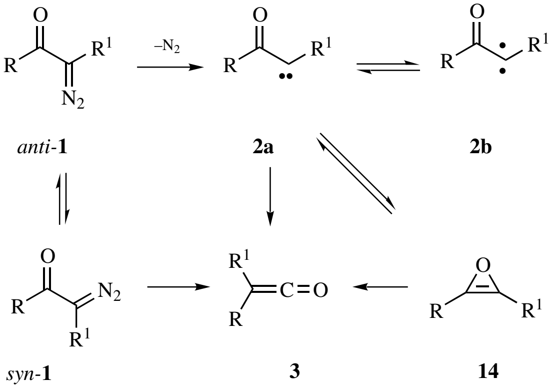
(4)



12 **13** (96%, IR 2090 cm^{-1})

(5)

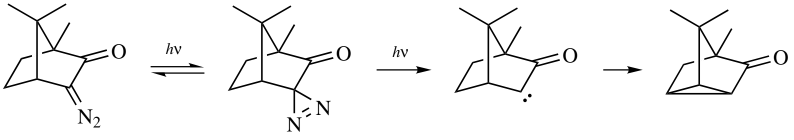
The mechanism of the Wolff rearrangement raises subtle questions regarding the intervention of possible reactive intermediates, and these have been pursued through increasingly sophisticated experimental and theoretical means. Possible pathways for the ketene **3** (Scheme 3.3) include equilibration of *syn*-**1** with *anti*-**1**



Scheme 3.3 Some possible steps in the Wolff rearrangement.

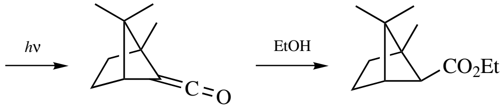
and initial loss of N_2 from *anti*-**1** forming singlet keto carbene **2a**, which may undergo spin inversion to a triplet carbene **2b**, which can reform **2a** or undergo some other reaction such as hydrogen abstraction. The singlet carbene **2a** can undergo Wolff rearrangement to the ketene **3**, which can also be formed in a concerted reaction from *syn*-**1**. The intervention of an oxirene intermediate **14** has been found to occur in some cases, as demonstrated for $R = Ph$, $R^1 = H$ by isotope labeling studies using ^2H, ^{13}C, and ^{18}O.[21] For $R = CF_3$, $R^1 = H$ migration forming the ketene was demonstrated, whereas for $R = CF_3$, $R^1 = CO_2Et$ a triplet carbene was formed and no Wolff rearrangement occurred.[22]

Besides ketene formation, other possible reactions of the singlet keto carbene **2a** are addition of a solvent, such as methanol, and addition to a carbon-carbon double bond forming a cyclopropane. In the case of diazocamphor (**15**), reversible photochemical rearrangement of the diazo group to the diazirine **16** has been observed, as well as intramolecular insertion by a concerted pathway or from the intermediate carbene **17** forming the tricylanone **18** (equation 6).[23] In ethanol the ketene **19** resulting from ring contraction by Wolff rearrangement formed the *exo*-ester **20** by proton transfer to the least hindered side (equation 7).[23]



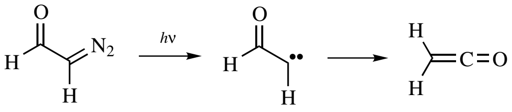
15 **16** **17** **18** (6)

15



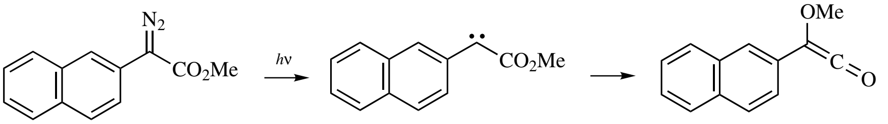
19 **20** (7)

Singlet carbene **22** is formed by laser flash photolysis of diazoacetaldehyde (**21**) in CH_2Cl_2 and has a lifetime determined as 0.15 to 0.73 ns, leading to ketene (**23**) (equation 8).[24] Other computational studies of the Wolff rearrangement are noted in Section 1.1.1.



21 **22** **23** (8)

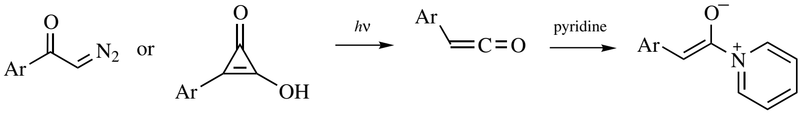
Photolysis of methyl α-diazo-(2-naphthyl)acetate (**24**) forming the carbene **25** and ketene **26** has been studied by three different groups.[25–27] Included were both solution phase and matrix isolation studies, and rearrangement of the carbene gave the ketene, with an IR band at 2096 cm^{-1} (equation 9). Detection of IR bands from both the singlet and triplet states of the spin-equilibrated carbene allowed a direct experimental estimate of the singlet/triplet energy gap in solution at ambient temperature.[26] The singlet carbene was preferentially stabilized in more polar solvents.[28]



24 **25** **26** (IR 2096 cm^{-1})

(9)

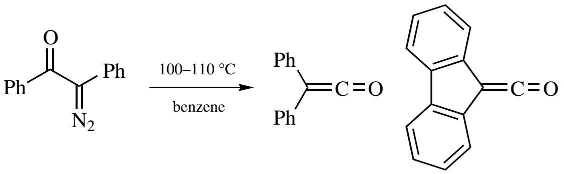
The intermediates generated from a series of aryl diazomethyl ketones **27** were compared to those from photolysis of arylhydroxycyclopropenones **28** by trapping with pyridine (equation 10).[29] The trapped species were identical, and since ketenes **29** were known to be formed in the latter reaction, it was concluded that these were also formed from **27** within the duration of the laser pulse (20 ns), so that any α-carbonylcarbene intermediates from **27** must have lifetimes shorter than this.



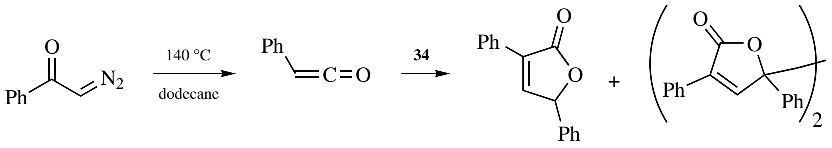
27 **28** **29** **30** (10)

3.3.1 Thermal Wolff Rearrangement

Diphenylketene has been prepared by thermal Wolff rearrangement (**32**, equation 11),[30] but with rare exceptions such as **13**,[20] thermal reactions are not useful for the preparation and isolation of ketenes from diazo ketones because of the occurrence of reaction between the ketenes and residual diazo ketone.[31–33] Even fluorenylideneketene (**33**) has apparently not been made preparatively by thermal Wolff rearrangement. Heating diazoacetophenone (**34**) led to the adduct **36** from combination of unreacted **34** with the derived phenylketene (**35**) (equation 12).[31] The dimer **37** from oxidation of **36** was also formed.[31]



31 **32** (64%) **33** (11)



34 **35** **36** (4%) **37** (24%)

(12)

The kinetics of thermal Wolff rearrangements forming substituted diarylketenes **40** from diazo ketones **38** and **39** (equation 13) have been measured, as shown in Table 3.2.[34] The effect of substituents X on the rates of thermal Wolff rearrangement of **38** were correlated by Hammett σ constants with a value of ρ of 0.75, while for **39** the rates were correlated by σ^+ constants with a value of ρ^+ of -1.49.[34] The diminished reactivity with electron donor substituents in **38** may have arisen from ground state stabilization due to electron donation to the carbonyl group, while the enhancement of the reactivity by electron donor substituents in **39** could have been due to weakening of the C-N bond, with negative charge on the N_2 moiety. The combination of substituent effects in the disubstituted diazo ketones **41** forming ketenes **42** produced substantial rate differences (equation 14 Table 3.3).[35]

TABLE 3.2 Relative Rates of Decomposition of 38 and 39 in *n*-Butyl Ether at 70 °C[34]

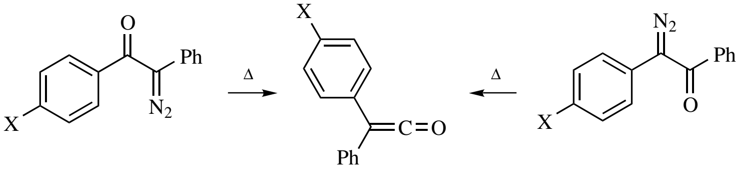
X (**38**)	k_{rel}	X (**39**)	k_{rel}
MeO	0.73	Me	3.04
Et	0.76	H	1.0
Me	0.80	F	1.92
H	1.0	Cl	0.74
F	1.29	Br	0.76
Cl	1.56	NO_2	0.071
Br	1.66		

TABLE 3.3 Relative Rates of Decomposition of 41,[35] 43, and 45[36,37]

X	Y	k_{rel}(**41**)[a]	Ar	R	k_{rel}(**43**)[b]
NO_2	MeO	220	4-Tol	Me	26.7
MeO	MeO	40	4-Tol	*i*-Pr	45.6
H	H	1.0	4-Tol	*t*-Bu	101
NO_2	NO_2	0.04	Mes[c]	*t*-Bu	306
MeO	NO_2	0.026	**45**		3.9
H	NO_2	0.022			

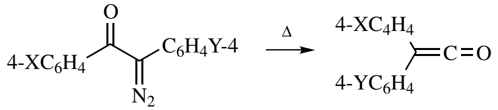
[a] In 1,2-dichloroethane.
[b] In dioxane, 101 °C.
[c] Mes is 2,4,6-$Me_3C_6H_2$.

Increasing steric bulk enhanced reactivity in the aryl alkyl diazo ketones **43**, forming ketenes **44** (equation 15, Table 3.3), as was observed for twisted alkyl systems, while **45**, which formed ketene **46**, was stabilized by efficient conjugation between the diazo group and the carbonyls (equation 16).[36,37]



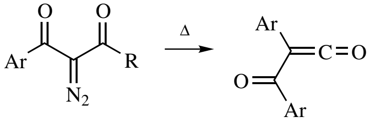
38 **40** **39**

(13)



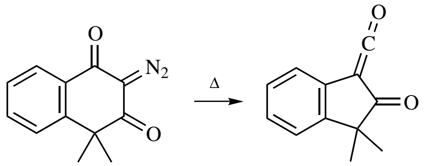
41 **42**

(14)



43 **44**

(15)



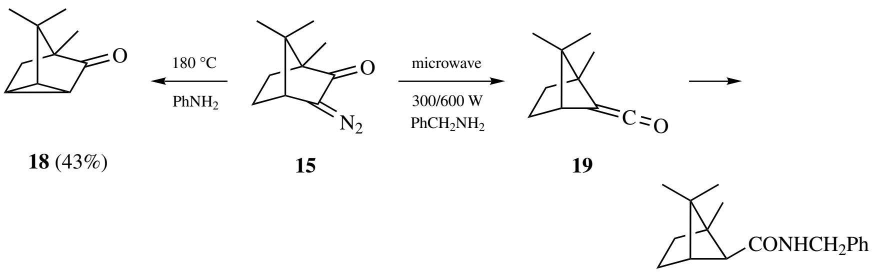
45 **46**

(16)

Other kinetic studies of Wolff rearrangement showed that phenyl groups were more activating than acyl groups for decomposition.[38,39]

Microwave-assisted Wolff rearrangement of diazo ketones gave significantly higher yields of ketene-derived products than did thermolysis.[40] Polar solvents were found to promote ketene formation, as the *Z*-conformers that lead efficiently to rearrangement have higher dipole moments than the *E*-conformers, so the former are favored in polar solvents. Even cyclic diazo ketones such as diazocamphor (**15**) that favor insertion forming **18** on thermolysis over formation of ketene **19** captured by benzylamine forming **47** gave much higher yields of capture of Wolff rearrangement products with microwaves than with thermolysis. This was attributed to the diazo ketone grouping adopting a conformation with a higher dipole moment aligned with the electric field of the microwaves, which was more favorable for

Wolff rearrangement (equation 17).[40]

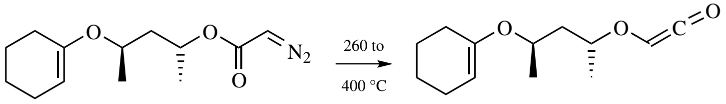


18 (43%) **15** **19**

47 (73%)

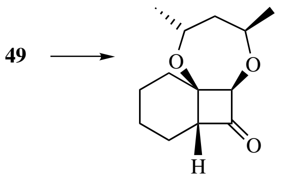
(17)

Flash vacuum pyrolysis at 260 to 400 °C of diazo ketone **48** with a tethered cyclohexenyl group formed ketene **49**, which led by [2 + 2] cycloaddition to **50** with a high degree of stereoselectivity (equation 18,19).[41–43] This method was also utilized for synthesis of optically active β-lactams.[41]



48 **49**

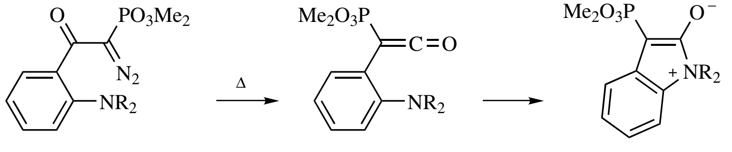
(18)



50 (79%, >99% de)

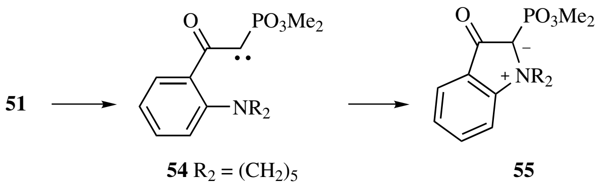
(19)

Thermal decomposition of phosphonate-substituted diazo ketones **51** produced competition between formation of ketene **52** followed by intramolecular attack by nitrogen on the ketene-forming zwitterion **53** (equation 20), and capture of an initial carbene **54** by nitrogen to form ylide **55** in yields from 0 to 45% (equation 21).[44,45] Intramolecular hydrogen transfer was proposed to occur for ketene **56**, leading to the intermediate **57**, which formed **58** (equation 22).[45–47] 2-Diazo-β-ketophosphonates **59** with Rh(II) catalysts were proposed to give ketenes **60**, which formed γ-lactones **61** (equation 23).[48]

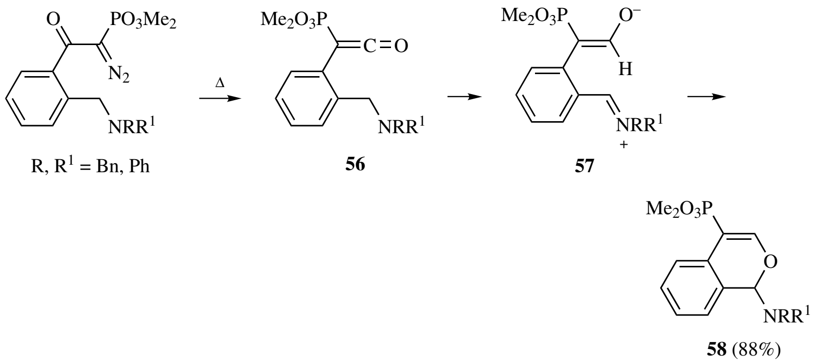


51 $R_2 = (CH_2)_4$ **52** **53** (88%)

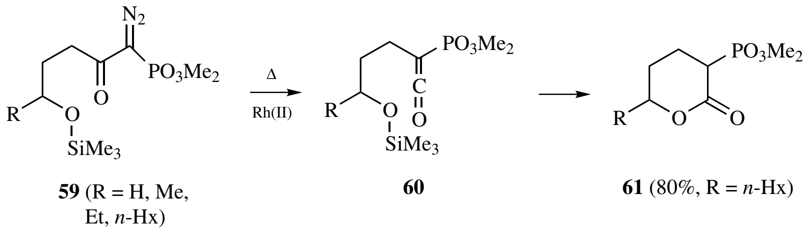
(20)



(21)

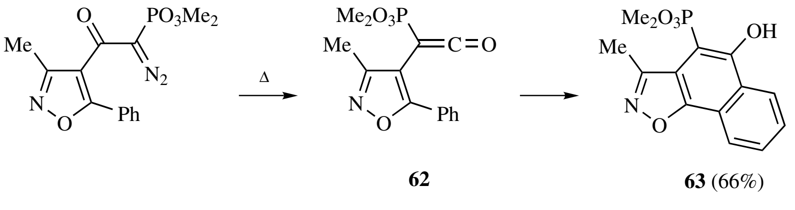


(22)



(23)

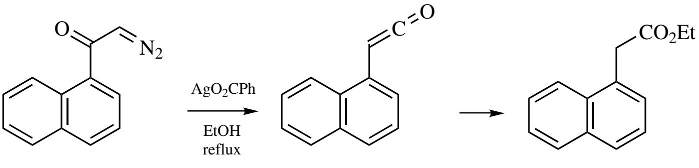
Isoxazole-substituted ketene **62** generated by Wolff rearrangement cyclized to fused derivatives **63** (equation 24).[45,47] These are also discussed in Section 4.6.



(24)

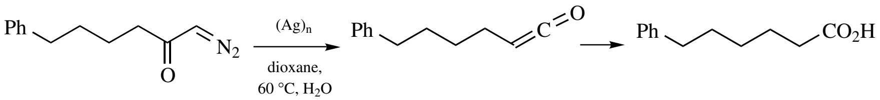
3.3.2 Catalyzed Wolff Rearrangement

Wolff rearrangement was enhanced by metal catalysts, particularly silver salts, as in the formation of diazo ketone **64** forming 1-naphthylketene (**65**), which is captured by the solvent ethanol, forming **66** (equation 25).[49] It has been proposed that in the presence of amines, silver nanoclusters are formed from silver benzoate that under these conditions are effective catalysts. This was confirmed by experiments using preformed silver nanoclusters with diazo ketone **67** in the generation of ketene **68** forming acid **69** (equation 26).[50]



64 **65** **66** (84–92%)

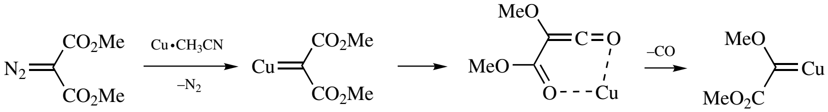
(25)



67 **68** **69** (80–91%)

(26)

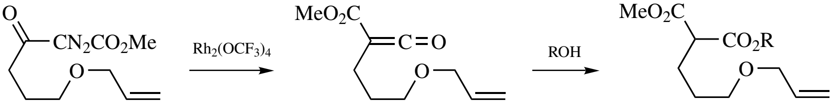
Diazomalonate esters with attached silver or copper ions introduced into the gas phase by electrospray ionization and subjected to collisional activation undergo Wolff rearrangement to unobserved ketene intermediates **70** followed by decarbonylation (equation 27).[51,52]



70

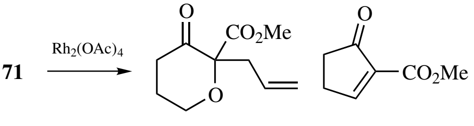
(27)

Rhodium catalysts with ligands from strong carboxylic acids promoted Wolff rearrangements of **71** to ketene **72** captured by allyl alcohol forming esters **73** in modest yields (equation 28) in competition with intramolecular reaction of **71** with the allyl ether moiety to give **74** and intramolecular C-H insertion to give **75** (equation 29).[53] Thus, $Rh_2(O_2CCF_3)_4$ gave **73**, **74**, and **75** in a 22:50:28 ratio, where **73** was derived from the ketene **72**, while with $Rh_2(OAc)_4$ the corresponding ratio was 0:60:40.[53]



71 **72** **73** (22%, R = allyl)

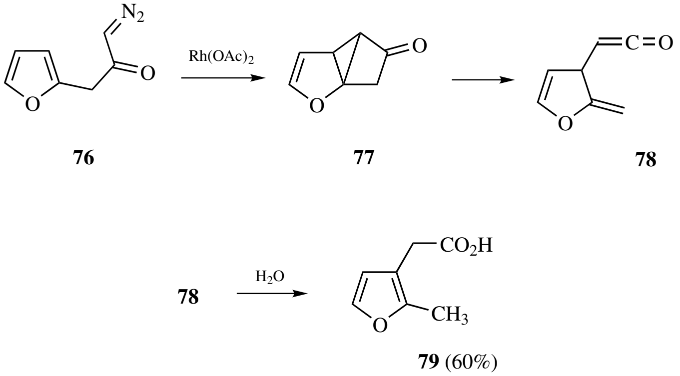
(28)



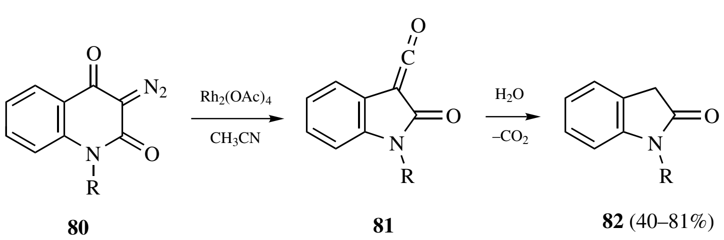
74 (50%) **75** (28%)

(29)

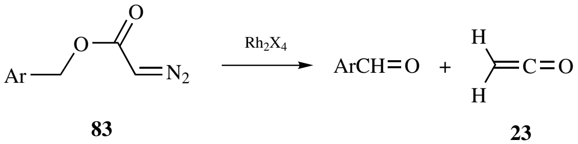
Reaction of $Rh_2(OAc)_4$ with the α-diazo ketones such as **76** led in some cases to products proposed to arise from initial carbenoid reaction forming **77** followed by vinylogous Wolff rearrangement to ketene **78** captured by methanol as the ester **79** (equation 30).[54] This was proposed not to involve rearrangement of an intermediate keto carbene, but rather insertion of the diazo carbon into a γ-alkenyl bond forming a bicyclo[2.1.0] pentane that underwent fragmentation to a ketene **78**, which is captured by water in 60% yield (equation 30).[55] Copper catalysis with $CuSO_4$, $Cu(OTf)_2$, or $Cu(AcAc)_2$ has also been used to promote the vinylogous Wolff rearrangement.[56] Photolysis of **76** gave the normal Wolff product in 92% yield, with only 8% of the **79**. Other examples of the vinylogous Wolff rearrangement are given in Section 3.4.2. Rhodium-catalyzed Wolff rearrangement of diazoquinolinediones **80** formed ketenes **81**, followed by hydration and decarboxylation to give oxindoles **82** in 40–81% yields (equation 31).[56] Rhodium-catalyzed cleavage of **83** into an aryl aldehyde and ketene (**23**) was a significant competing reaction during an attempted intramolecular cyclopropanation (equation 32).[57]



(30)

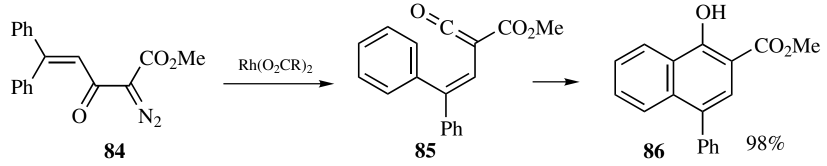


(31)



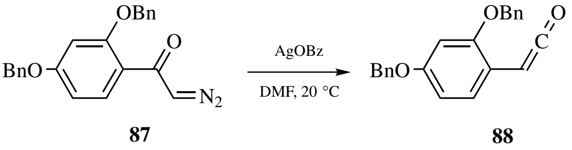
(32)

Arylalkenylketene **85** from rhodium octanoate catalyzed Wolff rearrangement of **84** cyclized to form naphthol **86** (equation 33).[58] A similar cyclization is reported in Section 5.4.4.

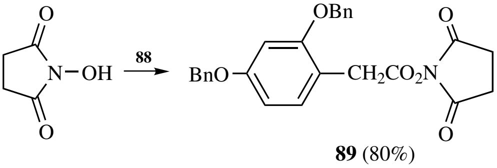


(33)

The catalyzed Wolff rearrangement of **87** proceeded through the unobserved ketene **88** (equation 34), which reacted with *N*-hydroxysuccinimide forming **89** (equation 35).[59] Ultrasound has been found to accelerate the silver benzoate–catalyzed Arndt-Eistert reaction of aryl and alkyl diazo ketones in methanol.[60] It was also found that diazo ketones derived from amino acids underwent Wolff rearrangement followed by cycloaddition with imines using microwave irradiation.[61] Even imines not substituted with aryl groups gave satisfactory reactions.

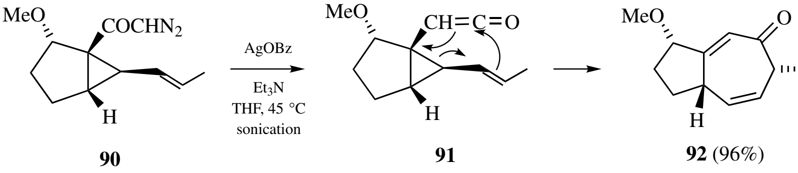


(34)



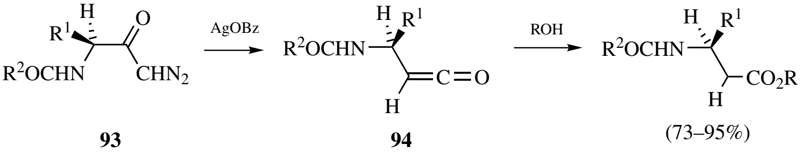
(35)

Ultrasonic irradiation of the vinylcyclopropyl diazo ketone **90** forming the ketene **91** was followed by a ketene-Cope reaction forming **92** in 96% yield (equation 36).[62,63] Several related examples were studied, and some similar reactions of cyclopropylketenes are shown in Section 4.1.5.



(36)

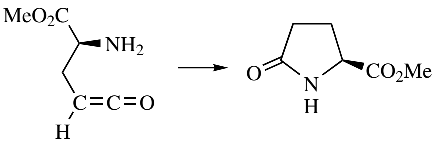
The silver benzoate–catalyzed Arndt-Eistert reaction has been used for the preparation of β-amino acids through the reaction of diazo ketones **93** to give the ketene intermediates **94** (equation 37).[64] In all cases there was complete retention of stereochemistry at the migrating carbon in the Wolff rearrangement,[64] but for $R^1 = Ph$ 10% of the enantiomer was formed during preparation of **93**.[64] β-Aminoketenes generated in this way reacted selectively with the less hindered hydroxy group of 3-methyl-1,3-dihydroxybutane,[65] and also showed selectivity in the acylation of 2-aminoethanol, isopropylidene-*D*-xylofuranose, sucrose, thymidine, and adenosine derivatives.[65] Cyclization of ketene **95** formed by a Wolff rearrangement led to proline precursor **96** (equation 38).[66] A similar cyclization was observed for ketenes derived from Ag^+-catalyzed Wolff rearrangement of RCH(NHTs)-CH_2COCHN_2.[66] The Ag^+-catalyzed Wolff rearrangement[67] proved useful in the Arndt-Eistert synthesis of *N*–Fmoc-β-homoamino acids.[68,69] The reaction was promoted by ultrasound[70] and could be used in polymer-supported synthesis.[71]



93 **94**

(37)

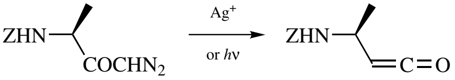
R^1, R^2: Me, BnO or *t*-BuO (**a**); Me, BnO or *t*-BuO (**b**); Bn, *t*-BuO (**c**); *t*-Bu, BnO (**d**); *t*-BuOCH$_2$, *t*-BuO (**e**); Me, *Z*-Ala (**f**); *i*-Pr, BnO (**g**)



95 **96**

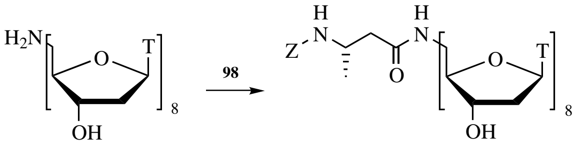
(38)

Ketenes **98** generated by Ag^+ or photochemical Wolff rearrangement of diazo ketones **97** (equation 39) reacted with 5′-amino-substituted oligonucleotides **99** to give oligoionucleopeptides (equation 40).[72] These reactions were also successful with polymer-supported oligonucleotides. Wolff rearrangement of the di-*O*-cyclohexylidene-*D*-arabino-hexulose diazo ketone **101** induced by Ag_2O gave ketene **102**, which formed the hexenic acid derivative **103** (equation 41).[73]



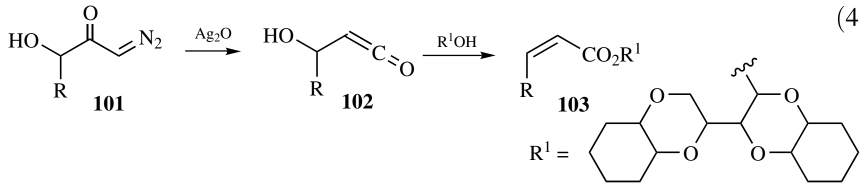
97 **98**

(39)



99 **100** (75%)

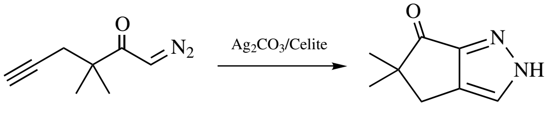
(40)



101 **102** **103**

(41)

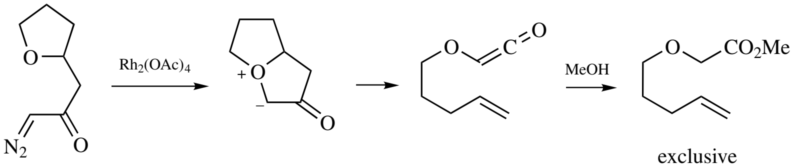
1-Diazo-3,3-dimethylalkyn-2-ones such as **104** with silver (I) catalyst did not give Wolff rearrangement, but instead gave intramolecular 1,3-dipolar cycloaddition leading to bicyclic pyrazoles **105** (equation 42).[74] In the absence of the geminal dimethyl groups, normal Arndt-Eistert products were observed upon reaction in EtOH.[74]



104 **105** (47%)

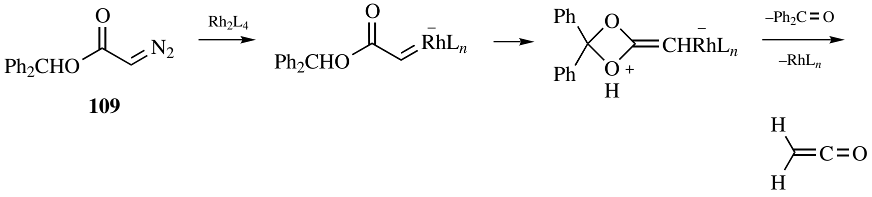
(42)

Reaction of the diazo ketone **106** with $Rh_2(OAc)_4$ in the presence of MeOH was proposed to proceed by formation of the oxonium ylide **107**, which opened to ketene **108**, which was trapped by MeOH to give the ester (equation 43).[75] This non-Wolff rearrangement was suggested to be of a hitherto unknown type. Dirhodium(II)-catalyzed reactions of secondary benzylic and allylic diazoacetates **109** may form ketones and ketene (**23**) by a non-Wolff mechanism (equation 44).[76] The formation of ketene was established by trapping with 2,5-dimethyl aniline.



106 **107** **108** exclusive product

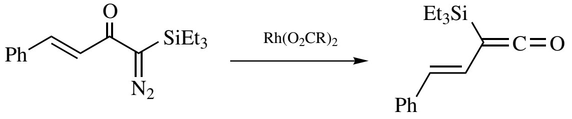
(43)



109 **23**

(44)

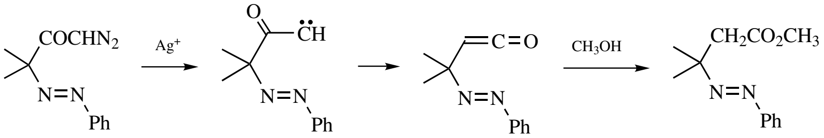
The reaction of acyl chlorides with trimethylsilyldiazomethane followed by thermolysis in the presence of alcohols gives Arndt-Eistert products without the need to use diazomethane.[77] Carboxylic acids activated as mixed anhydrides by reaction with ethyl chloroformate reacted with Me_3SiCHN_2 gave diazo ketones, and one of these was used in an Arndt-Eistert reaction catalyzed by Ag ion.[78] Reaction of carboxylic acids with DCC and Me_3SiCHN_2 gave diazoketones, but yields did not exceed 50%.[79] The Rh(II) octanoate-catalyzed reaction of Et_3Si-substituted diazo ketones provides an unusual route to silylketenes **110** in yields of 12–80% (equation 45).[79]



110 (33%)

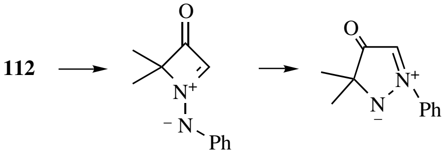
(45)

The AgO_2CPh-catalyzed reaction of **111** in CH_3OH gave products derived from the intramolecular capture of the ketocarbene **112**, as well as the capture by methanol of the ketene **113** from Wolff rearrangement (equations 46, 47).[80] The extremely hindered diazo ketone **115** was prepared from an acyl mesylate and gave Ag_2O-catalyzed Arndt-Eistert homologation via ketene **116** forming acid **117** in 35% yield based on the carboxylic precursor to **115** (equation 48) that was crucial to the synthesis of CP molecules.[81,82]

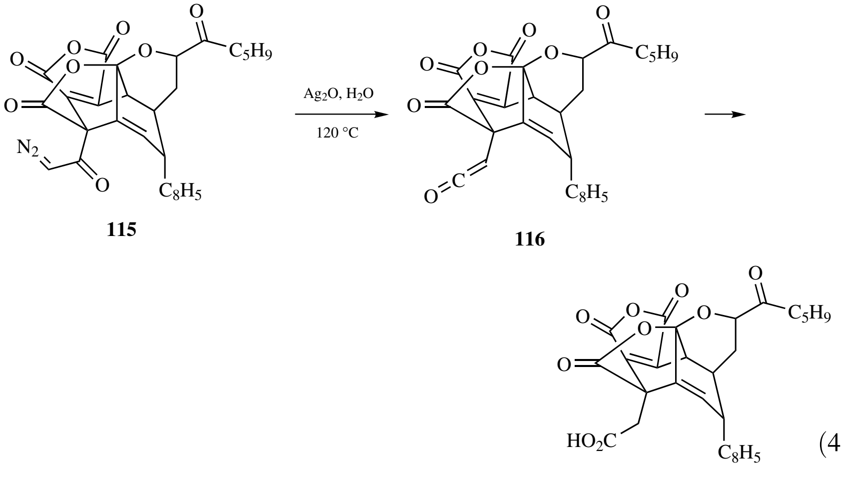


111 **112** **113** **114** (55%)

(46)



(47)

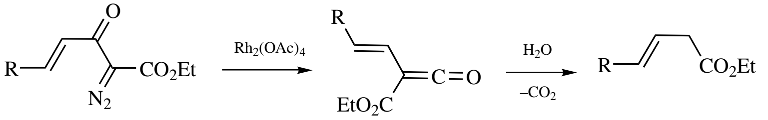


115 **116**

117 (>35%)

(48)

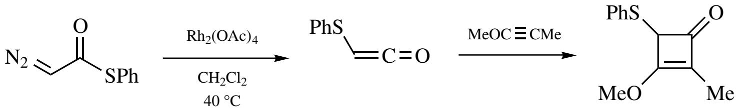
Diazo esters **118** reacted with rhodium II acetate in the presence of water to form β,γ-unsaturated esters **120** via ketenes **119** that underwent hydration and decarboxylation (equation 49).[83]



(49)

118 **119** **120** (67%, R = Ph)

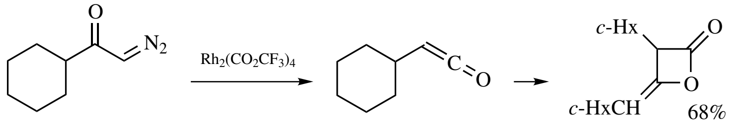
2-Diazothiol esters **121** reacted in rhodium-catalyzed processes to form thio-substituted ketenes **122** that were captured in [2 + 2] cycloaddition reactions with alkenes, dienes, imines, and alkynes (equation 50).[84]



(50)

121 **122** **123** (72%)

Cycloalkyl diazo ketones **124** reacted with $Rh_2(O_2CCF_3)_4$ to form ketene-derived products (dimers, 30–68%, and carboxylic acids, 12–35%), along with variable amounts of cyclization products.[85]

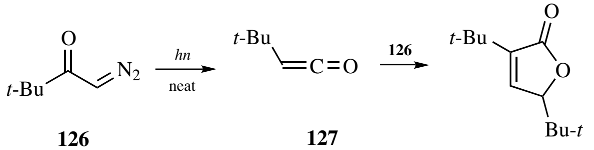


(51)

124 **125**

3.3.3 Photochemical Wolff Rearrangement

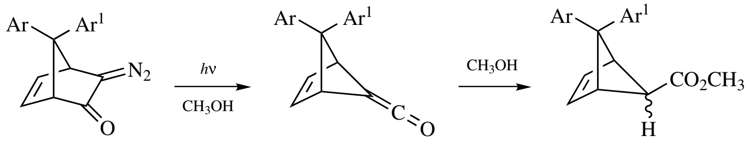
Horner and coworkers demonstrated that photolysis of diazo ketones gave efficient ketene formation,[86,87] but this method is not efficient for ketene isolation because of the possibility of photodecomposition of the formed ketene upon prolonged photolysis. Also, in concentrated solutions the ketenes can react with residual diazo ketone. Thus, while photolysis of neat diazopinacolone (**126**) formed *tert*-butylketene (**127**), this reacted with residual **126** to give lactone **128** in 62% yield (equation 52),[88] but in the presence of alcohols the derived esters were obtained. These problems were overcome in the preparation of **13** (equation 5).[20]



(52)

126 **127** **128** (62%)

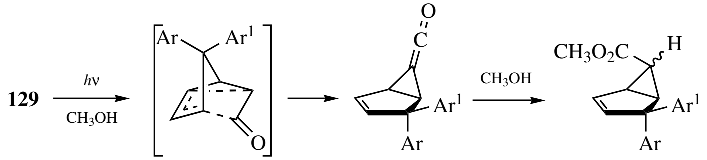
Photolysis of the stereoisomeric 7,7-diaryldiazo-norbornenyl ketones **129** gave both normal Wolff rearrangements forming ketenes **130** leading to esters **131** (equation 53) and vinylogous Wolff rearrangements forming ketenes **133** (equation 54).[89] In the formation of **131** ($Ar^1 = 2$-pyridyl) there was a 2/1 preference for *endo* protonation, showing that the 2-pyridyl group did not give major assistance for *exo* protonation.[89]



129 **130** **131** (34%)

(Ar, Ar^1 = Ph, 2-pyridyl)

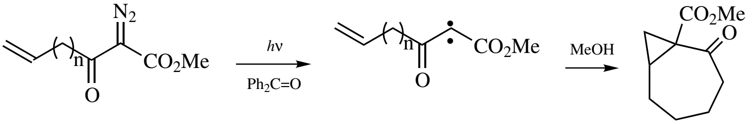
(53)



129 **132** **133** **134** (28–43%)

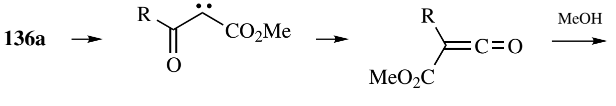
(54)

Photolysis of acyl diazo ketones **135** with alkenyl side chains sensitized with benzophenone in CH_3OH led to both cyclization products **137** arising from triplet ketocarbenes (**136a**) (equation 55) and Wolff rearrangement products from ketenes **138** resulting from conversion of the triplet ketocarbene to the singlet **136b** (equation 56).[90] For four CH_2 groups in the side chain the yield of cyclization product was 20% (equation 55), with 32% of ester **137b** from the ketene, and 37% insertion product (equation 56). With two and three CH_2 groups in the side chain, cyclization yields were 88 and 83%, respectively.[90]



135 (n = 4) **136a** **137a** (20%)

(55)

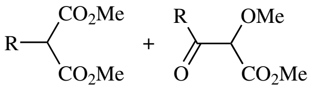


136a

136b **138**

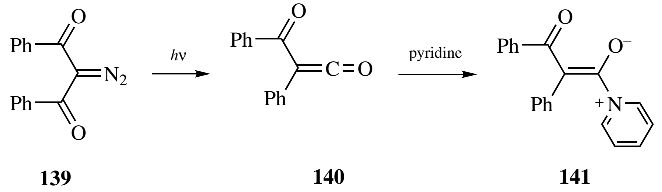
(R = CH_2=CH(CH_2)$_4$)

(56)



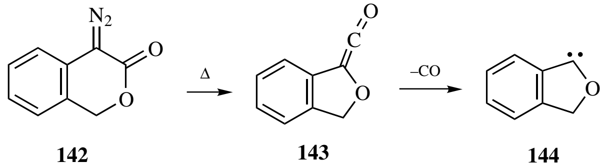
137b (32%) **137c** (37%)

Photolysis of the diazo ketone **139** resulted not only in the formation of ketene **140** (which was trapped as the pyridine ylide **141**) via a singlet pathway (equation 57), but also in the formation of a short-lived triplet of **139** that decayed back to the ground state.[91]

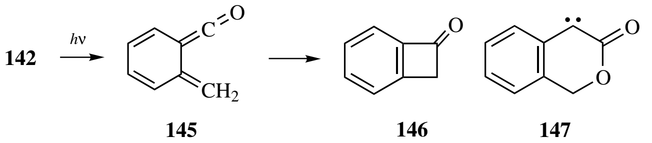


(57)

Thermal Wolff rearrangement induced with a CO_2 laser of **142** was proposed to give the oxygen-substituted ketene **143**, which underwent facile decarbonylation and eventual formation of **146** (equation 58).[92] Analysis of the photochemical reaction of **142** by TRIR spectroscopy showed that ketene **145** was produced faster than the time resolution of the instrumentation, and led to the hypothesis that **145** was formed directly from **142** without the intervention of carbene intermediate **147** (equation 59).[93] Some of **147** was formed in competition with **143** but was not a precursor to **143**.

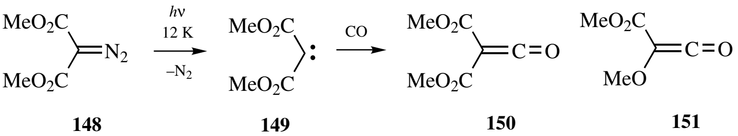


(58)



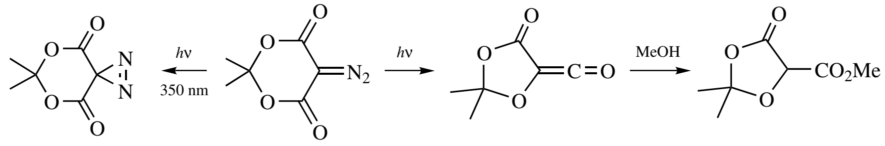
(59)

Photochemical Wolff rearrangement of **148** in a matrix was inhibited by the presence of CO or O_2, which react with the carbene **149** to form the ketene **150** with an IR band at 2166 cm^{-1} or a carbonyl oxide, respectively, instead of the ketene **151** (equation 60).[94] In solution, photolysis of **148** gave dimers of **151**, and the ketene was also trapped by [2 + 2] cycloaddition with cyclopentadiene.[95]



(60)

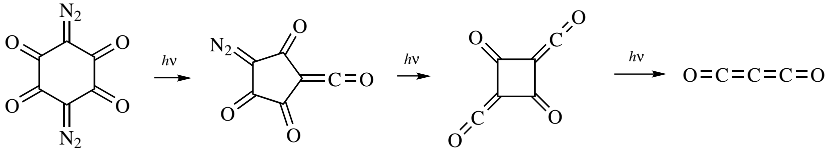
Photolysis of diazo Meldrum's acid (**152**) near the absorption maximum at 248 nm gave mainly Wolff rearrangement to ketene **154**, which formed ester **155** in methanol (equation 61).[96] Photolysis at 355 nm of **152**, however, gave almost exclusively formation of the diazirine **153** (equation 61).[96] Thermolysis of **153** resulted in reformation of **152**, whereas photolysis of **153** gave some **152** but mainly proceeded through a diacylcarbene leading to Wolff rearrangment. Photolysis of **152** in poly(methyl methacrylate) using picosecond IR detection led to formation within 20 ps of the keto ketene **154**, as detected by its IR absorption centered at 2161 cm^{-1} (equation 61).[97,98] This ketene was observed by picosecond IR spectroscopy at room temperature[97,98] and is similar to photoresist materials discussed in Section 4.1.10.



153 **152** **154** **155**

(61)

Photolysis of the bis(diazo)cyclohexanetetraone **156** in an Ar matrix at 17 K gave the diazo ketene **157**, with IR bands at 2165 and 2131 cm^{-1}. Upon further photolysis, this gave the cyclic diacylbisketene **158**, with IR bands at 2101 and 1747 cm^{-1}, and on further photolysis this gave carbon suboxide (C_3O_2, **159**) (equation 62).[99–101]

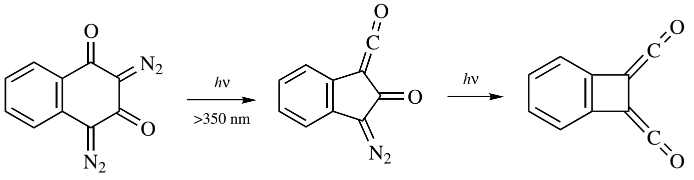


156 **157** **158** (IR 2102 cm^{-1}) **159**

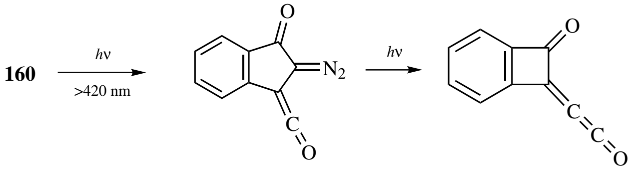
(62)

Photolysis of the bis(diazo) diketone **160**, which has two nonequivalent diazo ketone groupings, with light of >350 nm in an Ar matrix at 12 K, gave rise to a product with IR bands at 2142, 2088, 1690, and 1381 cm^{-1} that was assigned the structure **161** on the basis of the PM3 calculated IR frequencies of 2145 ($C{=}N_2$), 2061 ($C{=}C{=}O$), 1722 ($C{=}O$), and 1382 (indanone in-plane deformation) cm^{-1} (equation 63). Upon further photolysis this gave a band at 2152 cm^{-1} assigned to the bis(ketene) **162** (equation 63).[102] Irradiation of **160** in the matrix with light of >420 nm gave rise to IR bands at 2136, 2070, 1695, and 1468 cm^{-1} that were assigned to the structure **163** on the basis of the PM3 calculated IR frequencies of 2133 ($C{=}N_2$), 2056 ($C{=}C{=}O$), 1743 ($C{=}O$), and 1466 (5-ring in-plane deformation). Further photolysis led to bands at 2116 and 1780 cm^{-1} assigned to

164 (equation 64). The molecular orbital analysis of the PM3 calculations suggested the participation of higher excited states in these photoreactions.[102]

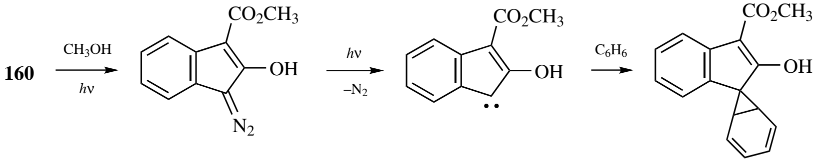


160 **161** **162** (63)

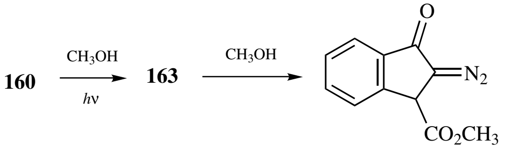


163 (IR 2056 cm^{-1}) **164** (IR 2116 cm^{-1}) (64)

Photolysis of **160** in benzene-MeOH led to products **166** and **167**, which were assigned to result from **165** and **163**, respectively (equations 65, 66). The yield of **165** was greatly favored when light of >420 nm was used.[103]

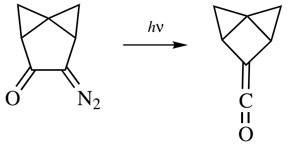


165 **166** (65)



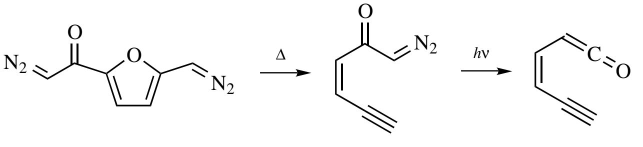
167 (66)

Photolysis of the diazoketone **168** in a matrix gave an IR absorption at 2117 cm^{-1} due to ketene **169**, although preparative experiments in solution in the presence of CH_3OH or Me_2NH gave products attributed to cleavage of the intermediate keto carbene (equation 67).[104,105] The structure of ketene **169** was calculated at the MP2/6-31G* level.[105]



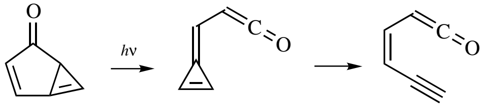
168 **169** (IR 2117 cm^{-1}) (67)

Heating of **170** with trapping of the volatile products in solid argon led to **171**, which upon photolysis gave the ene-yne ketene **172**, identified by its IR band at 2128 cm^{-1} (equation 68).[106] Photolysis of **173** also formed **172**, and deuterium labeling experiments favored a pathway through ketene **174** (equation 69).[106] The conformation shown for **174** was calculated to be the most favorable.



(68)

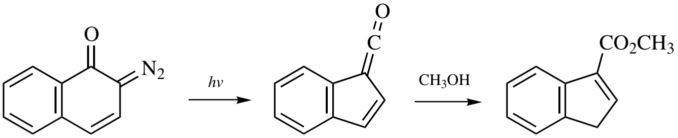
170 **171** **172** (IR 2128 cm^{-1})



(69)

173 **174** **172**

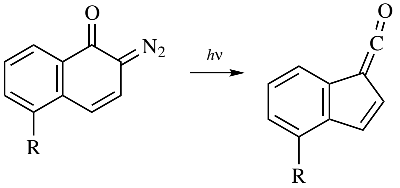
Photolysis of diazo ketone **175** in methanol forming the ketene **176**, which was captured as the methyl ester **177**, was achieved by near-IR photolysis with two-photon absorption inducing the Wolff rearrangement (equation 70).[107] Diazo ketone **175** was irradiated with an ultrafast pulsed laser operating at 800 nm, a wavelength with no spectral overlap with that of **175**. The yield of **177** as a function of the irradiation time was fit by an equation derived for two-photon photolysis, and the yield was also fit by an equation for two-photon absorption. This system was also utilized for two-photon photolithography.[107]



(70)

175 **176** **177**

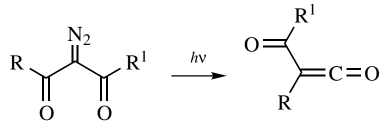
Long chain diazo ketones on water surfaces underwent Wolff rearrangement to give ketenes that undergo competitive hydration and dimerization.[108] Irradiation of **178** on a thin film with an electron beam induced formation of **179**,[109] and this may involve an initial ionization step analogous to mass spectrometry (equation 71).[110–112] Relative migratory aptitudes of substituents in diazo diketones **180** forming ketenes **181** have been compared for thermal photochemical and electron impact–induced Wolff rearrangement.[112]



(71)

178 **179**

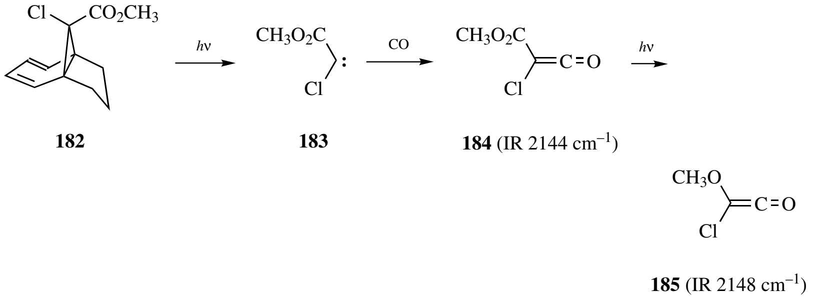
R = $PhCOC_6H_4OSO_2$



180 **181**

(72)

Photolysis of **182** in argon at 14 K gave carbene **183**, which was observed by IR and UV and reacted with CO to give ketene **184** (equation 73).[113] Photolysis of **184** also appeared to give a low yield of ketene **185**, as identified by the IR band at 2148 cm^{-1} (equation 73).[113] Calculations have been used to evaluate barriers to Wolff rearrangements in carbonyl carbenes, and the barriers are usually correlated with the exothermicities of the reactions.[114]

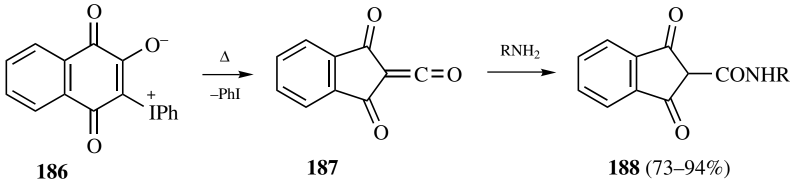


182 **183** **184** (IR 2144 cm^{-1}) **185** (IR 2148 cm^{-1})

(73)

3.3.4 Other Routes to Ketocarbene Rearrangements

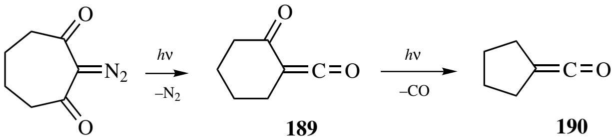
Aryliodonium ylides provided another route to the keto-carbene intermediates involved in the Wolff rearrangement. Refluxing **186** in CH_2Cl_2 with an equimolar amount of an amine was proposed to lead through the diacyl ketene **187**, forming amide **188** (equation 74).[115]



186 **187** **188** (73–94%)

(74)

Acylketene **189** generated in a matrix by Wolff rearrangement also underwent decarbonylation upon further photolysis and gave Wolff rearrangement leading to ketene **190** (equation 75).[116] Other examples of Wolff rearrangements from photolysis of ketoketenes were demonstrated.[116]



189 **190**

(75)

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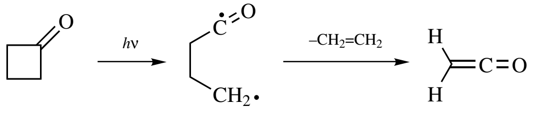
3.4 KETENES BY PHOTOCHEMICAL AND THERMOLYTIC METHODS

3.4.1 Ketenes from Cyclobutanones and Cyclobutenones

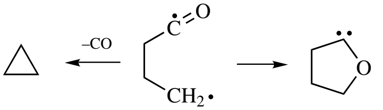
The ring openings of cyclobutanones to form ketenes[1] and of cyclobutenones to form vinylketenes[1,2] have been the subject of reviews and play an important part in the chemistry of cyclobutanes.[3–6]

The photochemical ring opening of cyclobutanone (**1**) is a classic problem in chemistry,[7,8] and the details of the Norrish type 1 photocleavage leading to diradical **2**, and the subsequent cleavage to either ketene (**3**) and ethylene (equation 1) or cyclopropane and carbon monoxide (CO), have been evaluated using femtosecond time-resolved mass spectrometry.[9] Further computational studies of the photochemical cycloreversion of cyclobutanone to form ketene and ethylene, as well as the competing decarbonylation giving cyclopropane and propene and formation of the oxocarbene, have been carried out (equation 2).[10]



1 **2** **3**

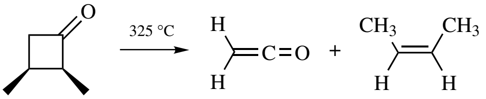
(1)



2 **4**

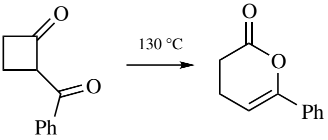
(2)

Thermolysis of the substituted cyclobutanone **5** gave stereoselective formation of *Z*-butene and ketene (equation 3),[11] while ring opening of the acyl cyclobutanone **6** gave complete conversion to the δ-lactone **7** (equation 4).[12] Vinylcyclobutanones gave ring-expanded enones in 45–81% yields at 145 to 190 °C,[13] but the intermediacy of ketenes in these reactions has not been proven.



5 **3**

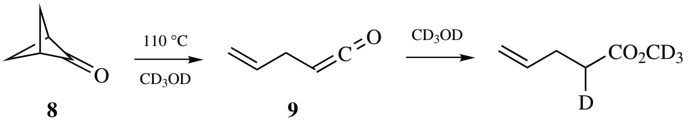
(3)



6 **7**

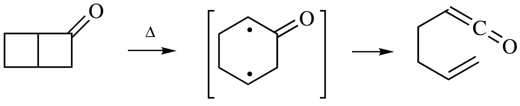
(4)

Strained cyclobutanones cleaved more readily to ketenes, and in the case of bicyclo [1.1.1]pentan-2-one **8** formed ketene **9** (equation 5),[14] while bicyclo[2.2.0]-hexanone **10** formed ketene **11** (equation 6).[15,16]



8 **9**

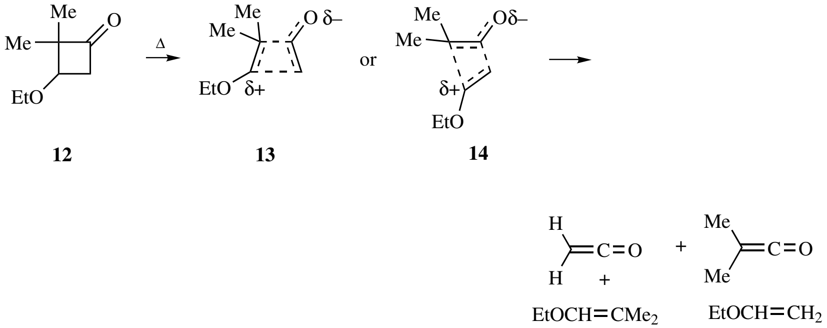
(5)



10 **11**

(6)

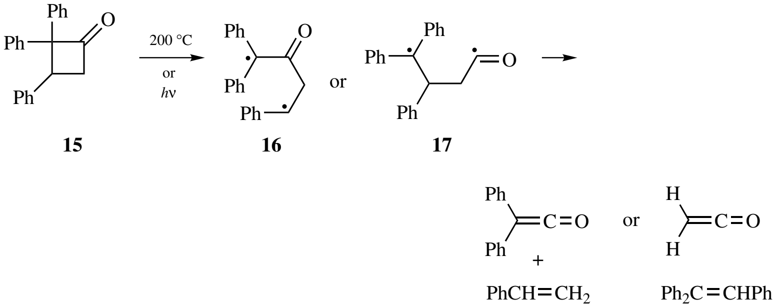
The kinetics of decomposition of substituted cyclobutanones in the gas phase from 192 to 285 °C have been measured, and as in the case of **12** these cleaved in two directions giving two sets of products (equation 7).[17–21] The results were interpreted as implicating two zwitterionic transition states, **13** and **14**, resembling the $[{}_{\pi}2_s+{}_{\pi}2_a]$ cycloaddition (Section 5.4.1) for ketene formation.



12 **13** **14**

(7)

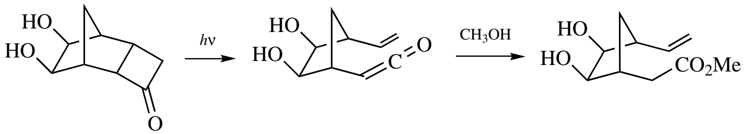
Thermal and photochemical cleavage of cyclobutanones may proceed in different directions, as with 2,2,3-triphenylcyclobutanone (**15**), which formed diphenylketene in the thermal reaction but ketene upon photolysis (equation 8).[22] The two reaction paths were proposed to involve isomeric biradicals **16** or **17,** respectively,[22] but zwitterions cannot be excluded.



15 **16** **17**

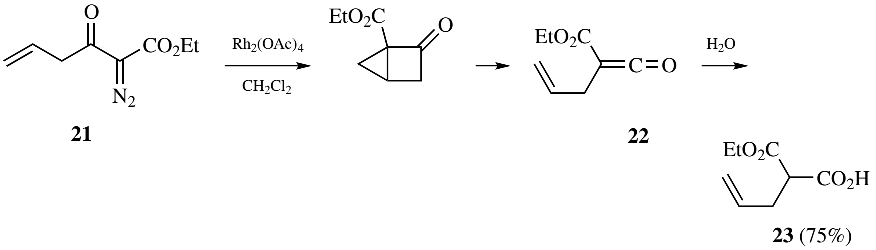
(8)

Photolysis of the cyclobutanone **18** gave the ketene **19**, which was trapped as the ester **20**, which was used in a synthesis of dihydrocleavamine (equation 9).[23] Treatment the diazo ketone **21** with $Rh_2(OAc)_4$ resulted in the formation of the acid **23** derived from the allylketene **22** in a reaction that may have involved a bicyclo[2.1.0]pentanone intermediate (equation 10).[24] This is an example of the vinylogous Wolff rearrangement (Section 3.3.2). Dichlorocyclobutenones **25** prepared by dichloroketene cycloaddition undergo photoelimination, forming dichloroalkenes in 54–65% yields and $CH_2{=}C{=}O$ (equation 11).[25]



18 **19** **20** (57%)

(9)



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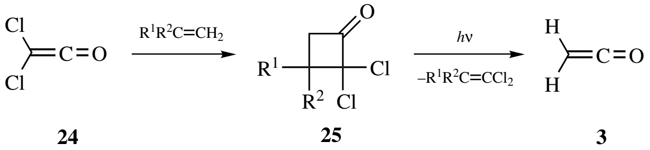
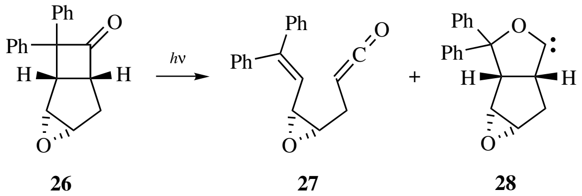


(11)

Photolysis of cyclobutanone **26** in MeOH occurred with ring opening to the vinylketene **27** as well as ring expansion to the oxocarbene **28** (equation 12), and these were captured as the MeOH addition products **29** and **30**, respectively (equation 13).[26]



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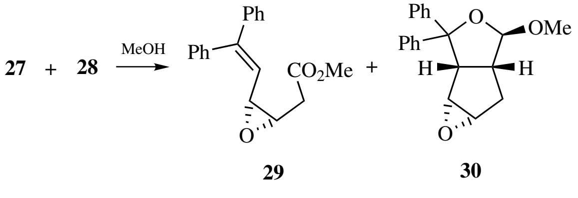
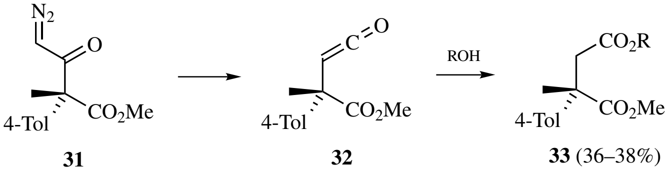


(13)

Thermolysis of the diazo ketone **31** with $PhCO_2Ag$ formed not only the normal ketene **32** trapped as the ester **33** (equation 14), but also the bicyclo[2.1.0]pentan-2-one **34**, which was an intermediate in the vinylogous Wolff rearrangement (Section 3.3.2), and opened to the ketene **35** (equation 15).[27]



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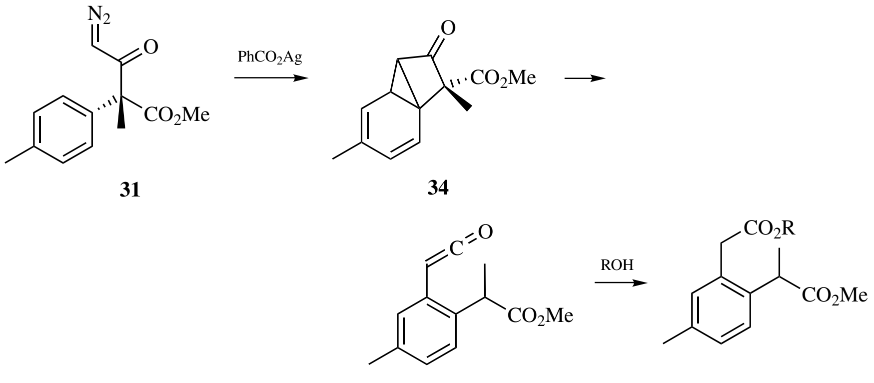
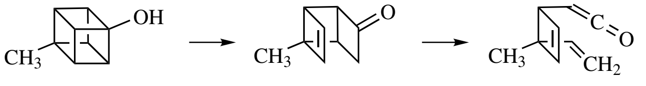


31 **34** **35** **36** (12–30%)

(15)

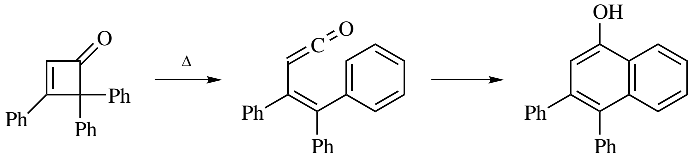
The hydroxycubane **37** reacted by homoketonization, forming the cyclobutanone **38**, which opened to the ketene **39** (equation 16).[28]



37 **38** **39**

(16)

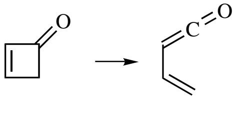
Thermal ring opening of 2,4,4-triphenylcyclobutenone **40** was found to give vinylketene **41**, which cyclized, forming naphthol **42** (equation 17).[28] This procedure has been found to be quite general and has been widely utilized in synthesis (Smith-Hoehn reaction).[2,4] The substrate **40** was itself prepared by diphenylketene cycloaddition with phenylacetylene.[29]



40 **41** **42**

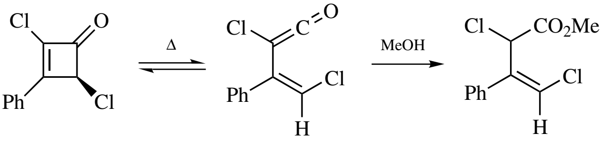
(17)

The ring opening of cyclobutenone (**43**), forming vinylketene (**44**), was studied computationally, and was found to be essentially thermoneutral, with a barrier of 21 kcal/mol (equation 18).[30] It was shown that optically active cyclobutenone **45** underwent racemization on heating in $CHCl_3$ at 100 °C at rates that could be conveniently measured (equation 19).[31] The reaction involved reversible ring opening to the vinylketene **46**, which was trapped with EtOH, forming **47** (equation 19).[31] Further investigation showed that thermolysis of **45** gave a preference for formation of *Z*-**46**, but upon prolonged reaction racemization occurred.[32] Photolysis of **45** preferentially formed *E*-**46**.[32]



(18)

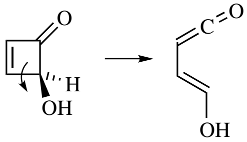
43 **44**



(19)

45 **46** **47**

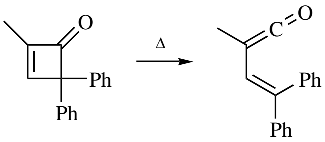
The torquoselectivity in the thermal ring opening of cyclobutenones **48** has been examined by theoretical means and proposed to occur with outward rotation of electron donor groups to form vinylketenes **49** (equation 20).[33]



(20)

48 **49**

Studies of solvent effects on the cyclobutenone ring opening of **50** ($R = Me$, $R^1 = H$) reveal that these were rather small (Table 3.4), with somewhat slower rates in solvents of greater polarity, as measured by the E_T values. This suggests that the rather polar enone starting material was stabilized in the polar solvent (equation 21).[34,35] In alcoholic solvents, **51** was trapped as the ester, but cyclized to the naphthol in nonnucleophilic solvents.[34,35]



(21)

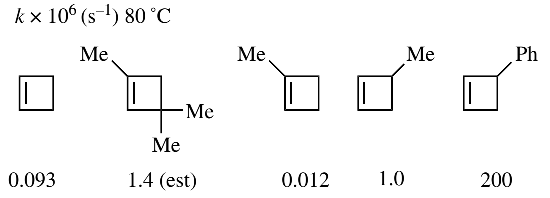
50 **51**

TABLE 3.4 Solvent Effects on Ring Opening of Cyclobutenone 50

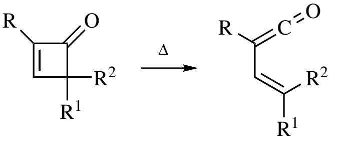
Solvent	E_T	$k \times 10^4$, s^{-1} (55 °C)
Cyclohexane	31.2	5.36
Benzene	34.6	4.14
EtOAc	38.1	2.53
DMF	43.8	1.75
HOAc	51.1	1.83
EtOH	51.9	2.01
MeOH	55.5	1.78

TABLE 3.5 Substituent Effects on Cyclobutenone Ring Opening

R	R^1	R^2	$k \times 10^6$ (s^{-1}) 80 °C
Me	Me	Me	1.1
Me	Me	Ph	90
Me	Et	Ph	33
Me	*i*-Pr	Ph	12.7
Me	Ph	Ph	2,430
Et	Ph	Ph	3,710
H	Ph	Ph	20,400



Changing the substituents on the cyclobutenones **51** has major effects on the reactivity in ring opening (equation 22), with a difference of a factor of 2 × 10^4 between the first and last entries (Table 3.5).[35]

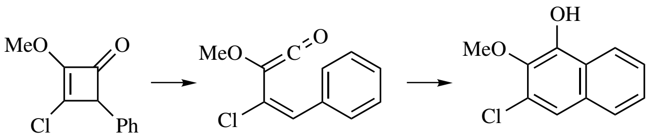


51 **52**

(22)

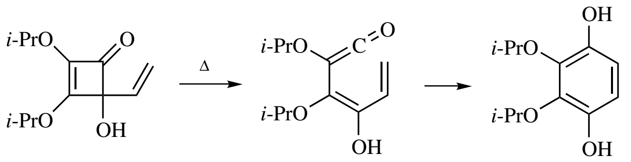
Other examples of these reactions are given in Sections 3.5 and 5.4.4.

Heating of **53** gave the ketene **54**, which formed the naphthol **55** (equation 23).[37] The vinylcyclobutenone **56** formed the ketene **57**, which gave hydroquinone **58**, used in the synthesis of echinochrome A (equation 24).[38] This reaction has also been used in the synthesis of naphthoquinones[39] and in heterocyclic analogues for conversion of diethyl squarate **59** to the furan-containing ketene **60** to form **61** (equation 25).[40] The analogous reaction of vinylcyclobutenone **62** proceeded via the ketene **63** to give **64**, which was converted to the antiparasitic monoterpene espintanol (equation 26).[41]



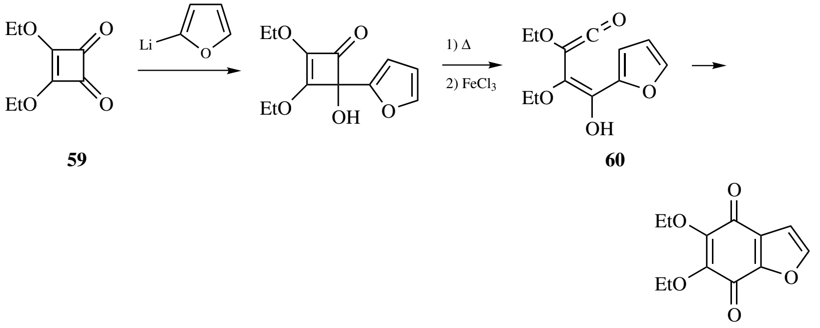
53 **54** **55** (81%)

(23)



56 **57** **58** (87%)

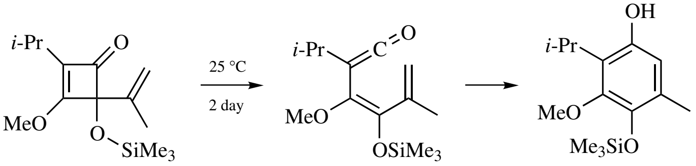
(24)



59 **60**

61 (84%)

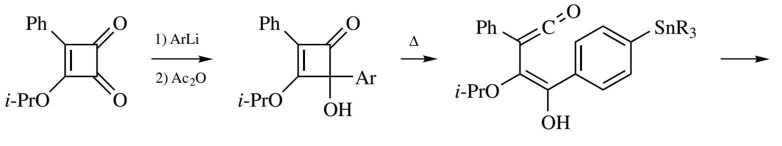
(25)



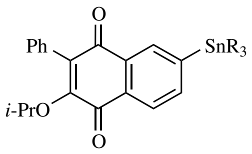
62 **63** **64** (77%)

(26)

Thermal rearrangement of cyclobutenone **66**, formed from the cyclobutenedione **65**, formed the vinylketene **67**, which cyclized and was oxidized by air to the naphthoquinone **68** (equation 27).[42] Conversion of **68** to **69** and thermolysis gave the new vinylketene **70** (equation 28), which cyclized to phenanthrene derivative **71** (equation 29).[42] This methodology was also adapted for the preparation of naphthoquinone-substituted porphyrins.[43]

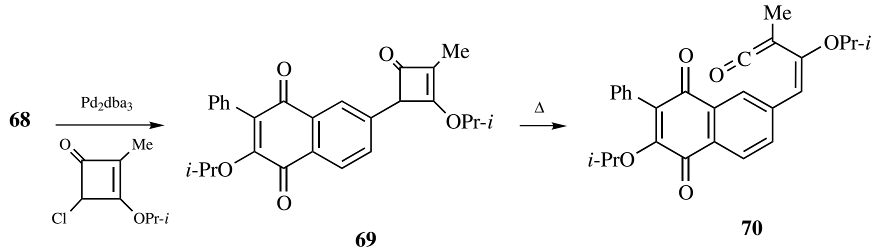


65 **66** (Ar = 4-*n*-Bu$_3$SnC$_6$H$_4$) **67** (R = *n*-Bu)

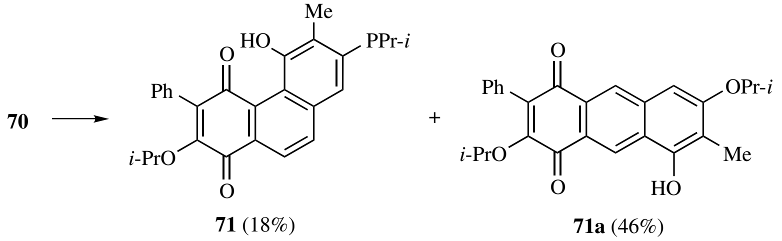


68 (R = *n*-Bu, 80%)

(27)



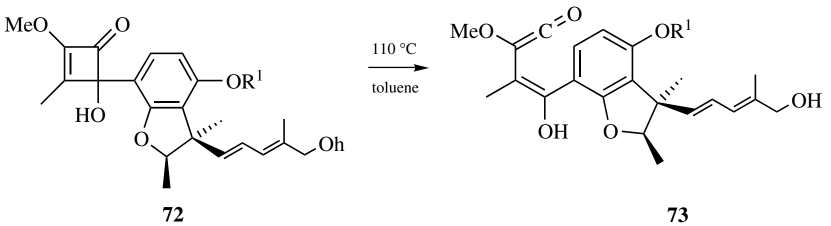
(28)



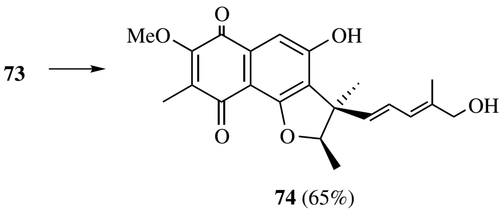
71 (18%) **71a** (46%)

(29)

Thermolysis of the cyclobutenone **72** (R = TBDMS, R^1 = TIPS) gave the vinylketene **73** (equation 30), which underwent cyclization and, after air oxidation of the product and removal of the protecting groups, gave furaquinocin E (**74**) (equation 31).[44]



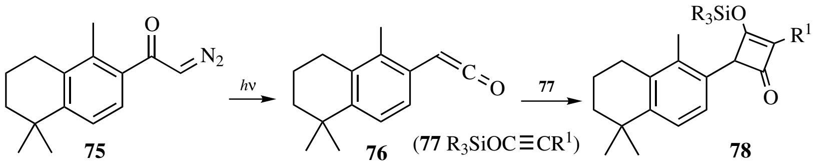
(30)



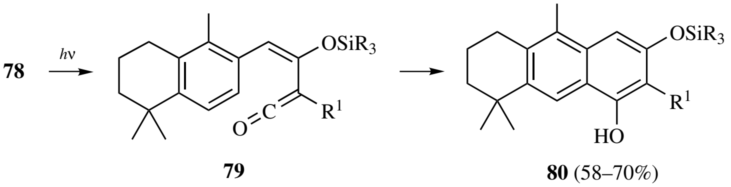
74 (65%)

(31)

Cycloaddition of ketene **76**, formed by a photochemical Wolff rearrangement of diazo ketone **75**, with alkynes **77** gave cyclobutenones **78** (equation 32), which on continued photolysis gave the ketenes **79**, which cyclized to **80** (equation 33).[45] Other polycyclic natural products and highly substituted naphthols were prepared using this methodology.[46,46a]

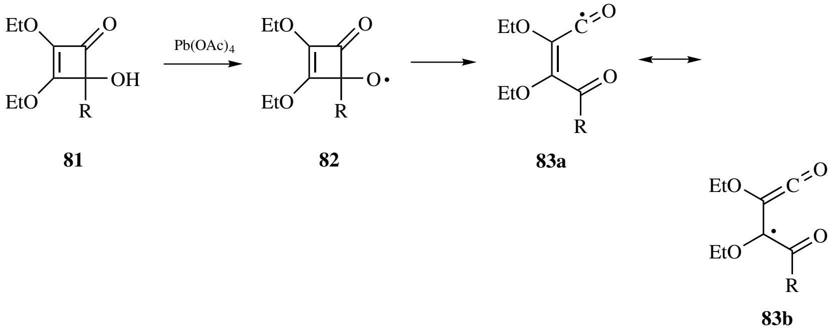


(32)



(33)

Oxidation of hydroxycyclobutenones **81** (R=Me, *n*-Bu, CH_2COPh, Ph, 2-furyl) with lead tetraacetate was proposed to form oxy radicals **82**, which upon ring opening gave acyl radical intermediates **83** (equation 34) that led to furanones **84a** and **84b** (equation 35).[47] The structures of the intermediate acyl radicals **83** were calculated using (UHF/PM3) methods.[47]



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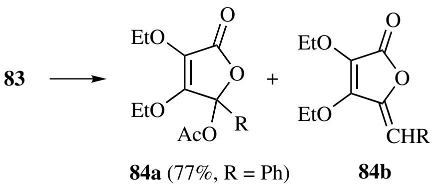
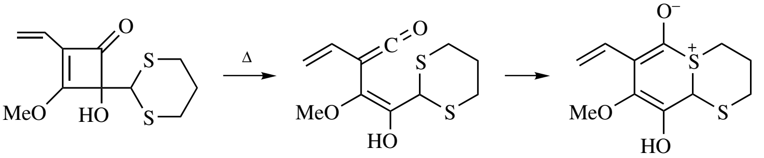


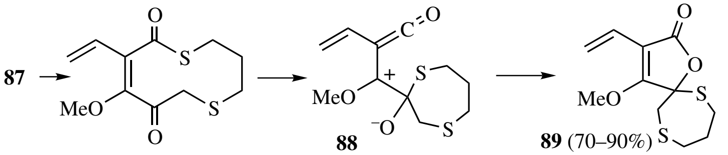
(35)

The ethenylcyclobutenone **85** underwent thermal ring opening forming divinylketene **86**, which was proposed to undergo migration of sulfur to form **89** (equations 36, 37).[48] The vinylcyclobutenone **90** formed the vinyl ene-yne ketene **91**, which gave **92** (equation 38).[49]



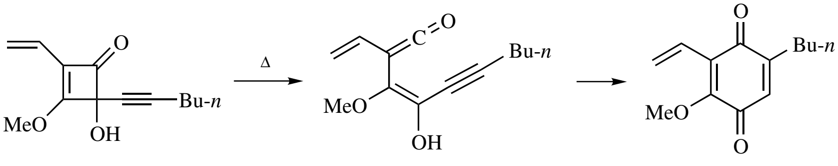
85 **86** **87**

(36)



88 **89** (70–90%)

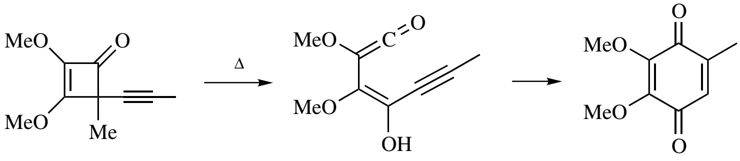
(37)



90 **91** **92** (49% from **90**)

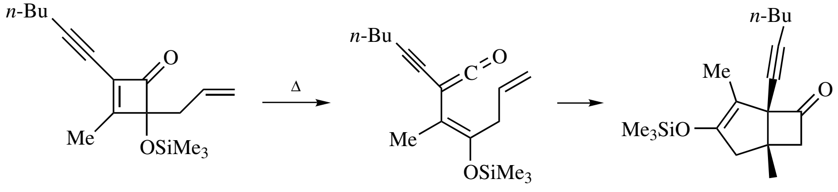
(38)

Ring opening of alkynylcyclobutenones **93** formed ketenes **94**, which cyclized, forming quinones **95** after oxidation (equation 39).[50] This was adapted using ^{2}H- and ^{13}C-labeled propynyl units to form labeled **95**, which was converted to ubiquinones.[50] Thermolysis of alkynylcyclobutenones **96** proceeded through alkynylketenes **97**, which cyclized by [2 + 2] cycloaddition to bicyclo[3.2.0]heptenones **98** (equation 40).[51]



93 **94** **95** (80–85%)

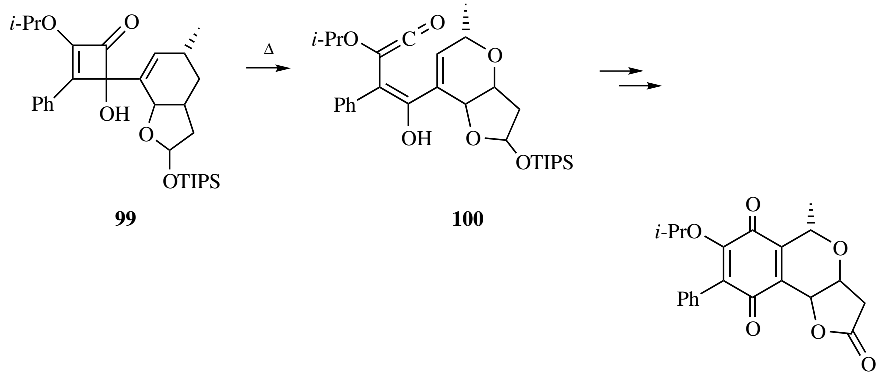
(39)



96 **97** **98** (98%)

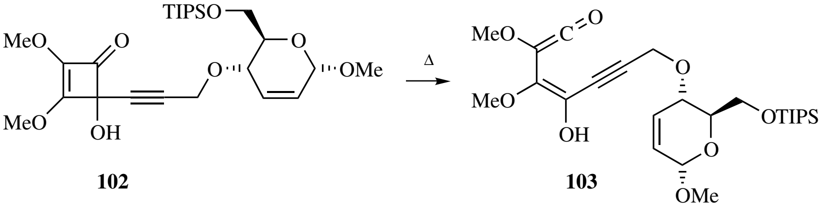
(40)

Ring opening of **99** gave ketene **100**, which reacted by ring closure on the pyran ring, forming **101** after deprotection and oxidation (equation 41).[52] The alkynylcyclobutenone **102** formed ene-yne ketene **103** (equation 42), which upon cyclization gave diradical **104**, which formed **105** by a radical cyclization and intramolecular hydrogen atom abstraction (equation 43).[53]



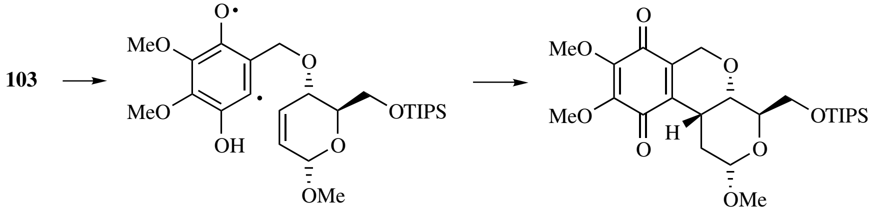
99 **100** **101** (68%)

(41)



102 **103**

(42)

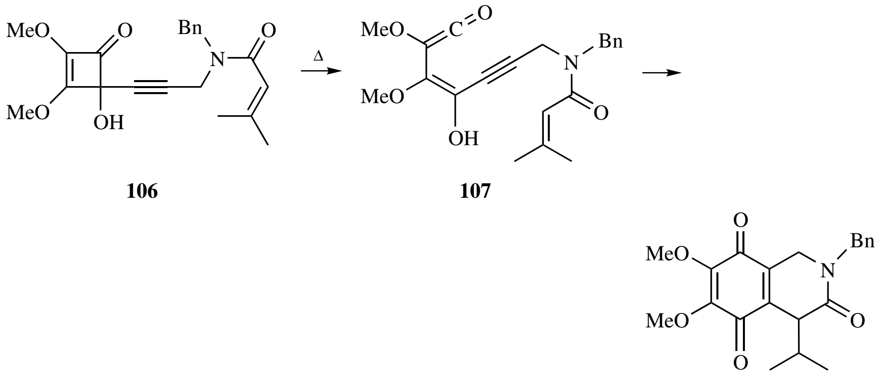


104 **105** (54%)

(43)

Other cyclizations of ene-yne ketenes were proposed for the synthesis of dihydroisoquinoline **108** from **106** through the intermediate ketene **107** followed by oxidation (equation 44),[53] and for the formation of dihydrobenzophenanthridine

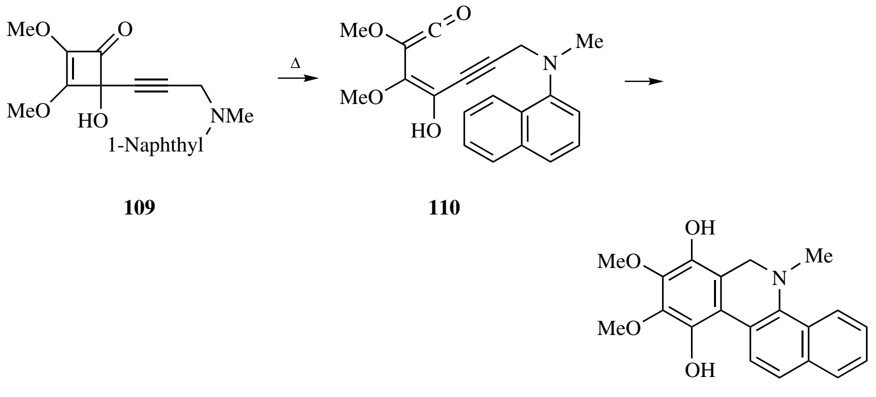
111 by ring opening of **109** to the ketene **110** (equation 45).[54]



106 **107**

108 (54%)

(44)

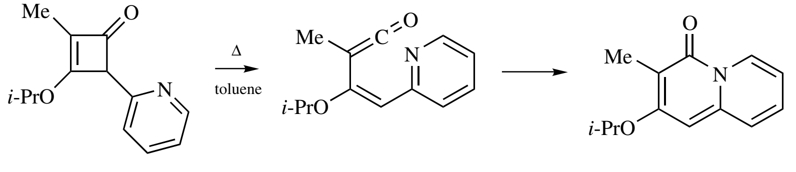


109 **110**

111 (66%)

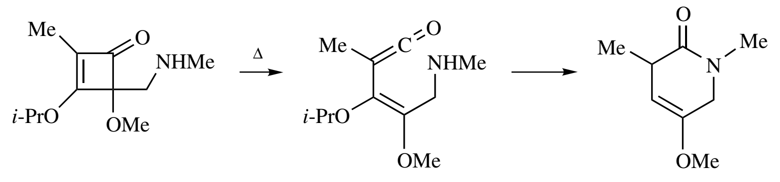
(45)

Ring opening of **112** gave ketene **113**, which formed **114** by electrocyclization on the pyridine ring (equation 46).[55] The aminoalkyl group in **116** reacted by an intramolecular nucleophilic addition forming dihydropyridone **117** (equation 47).[56] The in situ–generated 4-acylcyclobutenone **118** (equation 48) gave ring opening to ketene **119**, which formed γ-pyrone **120** (equation 49).[57] The dihydropyridine-substituted ketene **122** gave electrocyclization to dihydroquinoline **123** (equation 50), which was converted to a quinolinylquinone.[58]



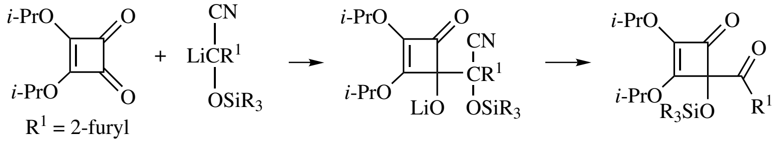
(46)

112 **113** **114** (62%)



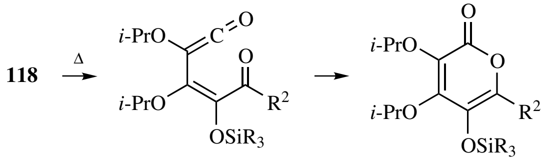
115 **116** **117** (75%)

(47)



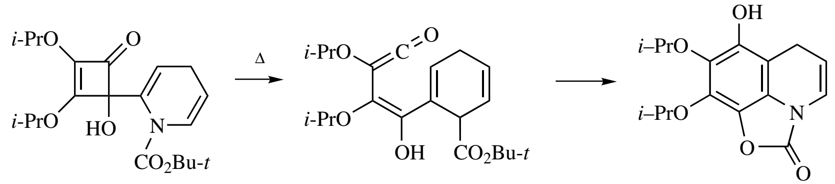
118

(48)



119 **120** (71%)

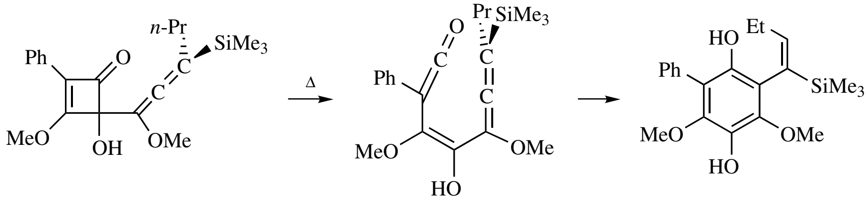
(49)



121 **122** **123** (53%)

(50)

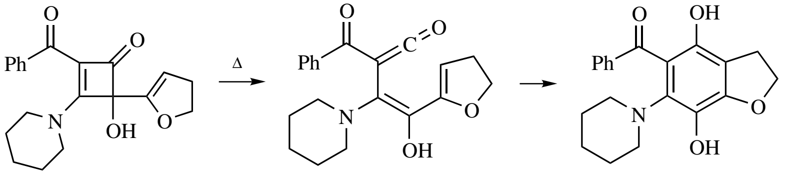
Allenylcyclobutenone **124** gave give torquoselective[33] ring opening with outward rotation of the OH group to form the ene-allenyl ketene **125**, that cyclized to a transient quinone methide that tautomerized to **126** (equation 51).[59]



124 **125** **126** (75%)

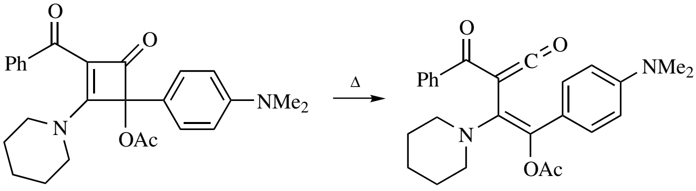
(51)

The 3-acyl-4-aminocyclobutenone **127** reacted by ring opening to ketene **128**, which cyclized to **129** (equation 52).[60] The 4-dimethylaminophenyl-substituted derivative **130** was proposed to form ketene **131**, which cyclized by an ionization and recombination of acetate ion to furan derivative **132** (equation 54).[60] Related cyclizations onto furan, thiophene, and pyrrole rings have also been observed,[61,62] including a xanthone synthesis.[62]



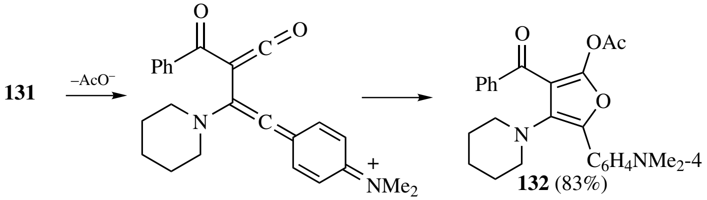
127 **128** **129** (94%)

(52)



130 **131**

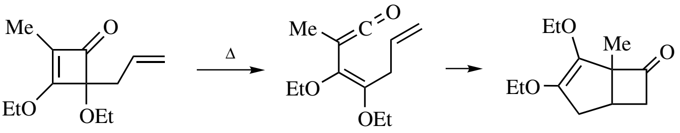
(53)



132 (83%)

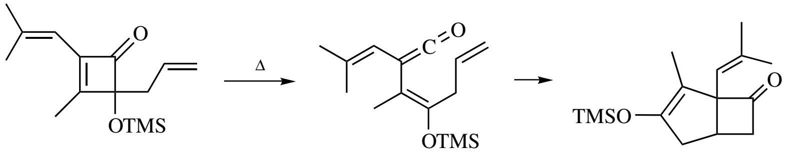
(54)

4-Allyl-4-ethoxycyclobutenone **133** on thermolysis gave the vinylketene **134**, which formed bicyclo[3.2.0]heptanone **135** through an intramolecular [2 + 2] cycloaddition reaction (equation 55).[63,64] Related substrates give similar cyclizations.[65–68] 2-Vinyl-4-allylcyclobutenone **136** formed divinylketene **137**, which gave vinyl bicyclo[3.2.0]heptenone **138** (equation 56).[67] 2-Dienyl-substituted cyclobutenone **139** gave ketene **140**, which cyclized to give phenol **141**, which formed benzofuran **142** with acid (equation 57).[68]



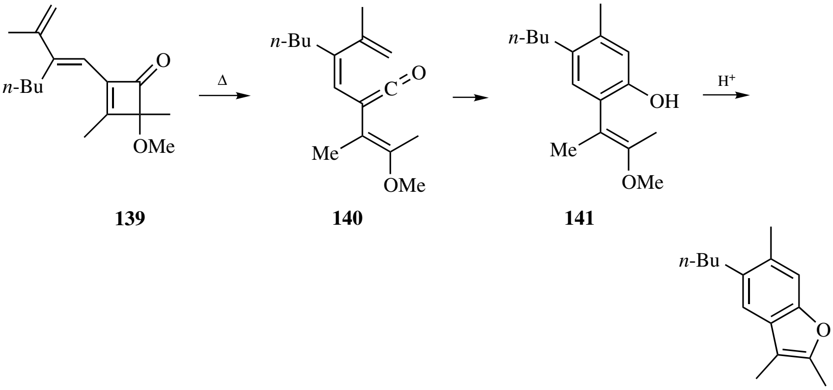
133 **134** **135** (98%)

(55)



136 **137** **138** (69%)

(56)



139 **140** **141**

142 (55%)

(57)

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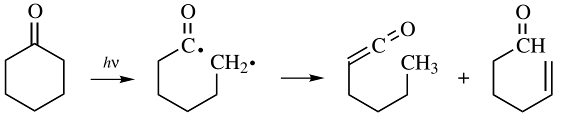
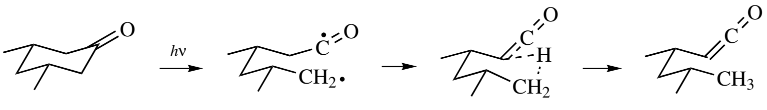
3.4.2 Ketenes from Photolysis of Cycloalkanones and Enones

Norrish Type I cleavage of cycloalkanones forms diradicals that can form an aldehyde or a ketene by intramoleclar hydrogen transfer,[1–7] and cyclohexanone (**1**) gave diradical **2** with low quantum efficiency that by hydrogen atom transfer formed *n*-butylketene (**3**), together with *n*-5-hexenal (**4**) in a ratio of 39:61 (equation 1).[4] Cyclopentanones gave low yields of ketenes upon photolysis compared to cylohexanones.[1–3] 3,5-Dimethylcyclohexanone (**5**) formed diradical **6**, where the transition state **7** to form ketene **8** was favored over **9** for aldehyde formation due to steric interactions in the latter (equation 2).[5]



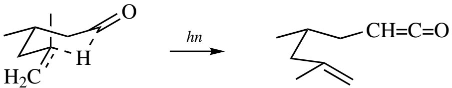
1 **2** **3** **4**

(1)



5 **6** **7** **8** (83%)

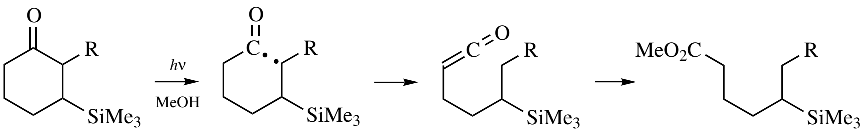
(2)



9 **9a** (17%)

(3)

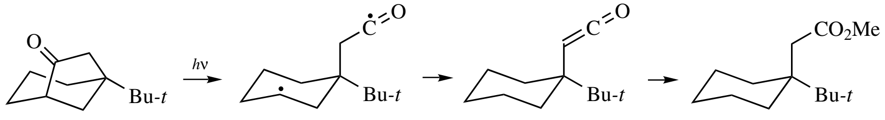
β-Silyl substituents have been proposed to enhance Norrish Type I cleavage of cyclic ketones **10** due to silicon stabilization of the resulting carbon radicals **11**, resulting in increased formation of ketenes **12**, which are captured by solvent (equation 4).[8–11] In substrates **10** with R = *tert*-butyl, enhancement of ring cleavage was observed for the equatorial R_3Si group.[11]



10 **11** **12** (43%, R = H)

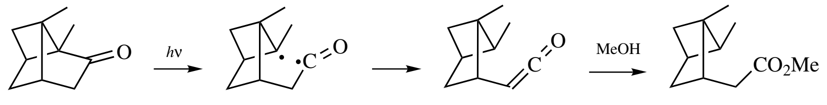
(4)

Bicyclic ketone **13** underwent hydrogen transfer resulting in efficient formation of ketene **15** from diradical **14** to the complete exclusion of aldehyde formation, which was hindered for steric reasons (equation 5).[12,13] The camphor analogue **16** formed the diradical **17**, which was similarly excluded from aldehyde formation, and gave ketene **18** captured as the ester **19** (equation 6).[14] Verbinone (**20**) upon photolysis gave ring opening to the diradical **21**, which formed the alkenylketene **22** identified by the IR absorption at 2120 cm^{-1} and by capture as the methyl ester **23** (equation 7).[15]



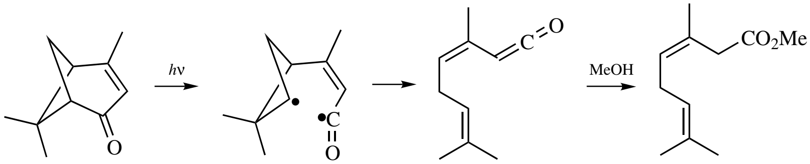
13 **14** **15** (96%)

(5)



16 **17** **18** **19**

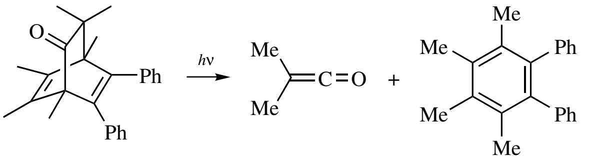
(6)



20 **21** **22** (IR 2120 cm^{-1}) **23** (21%)

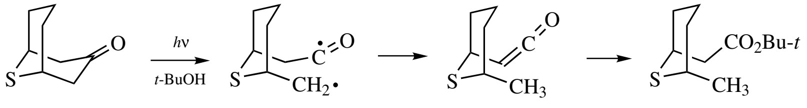
(7)

Photolysis of bicyclo[2.2.2]hexadienone **24** resulted in cycloreversion forming dimethylketene (**25**, equation 8).[16] Dibenzo derivatives of **24**[17–19] and a dihydro analogue[20] upon photolysis lead to several different types of ketenes.[17–19] Photolysis of the bicyclic keto sulfide **26** in *t*-BuOH gave predominantly Norrish Type I cleavage forming the biradical **27**, in which hydrogen atom abstraction to give the ketene **28** is facile, followed by ester formation (equation 9).[21]



24 **25** (83%)

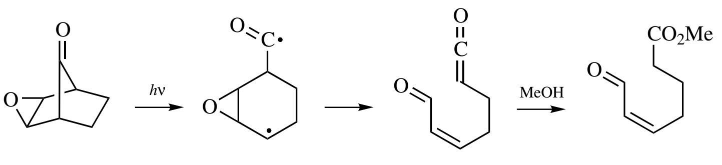
(8)



26 **27** **28** **29** (32%)

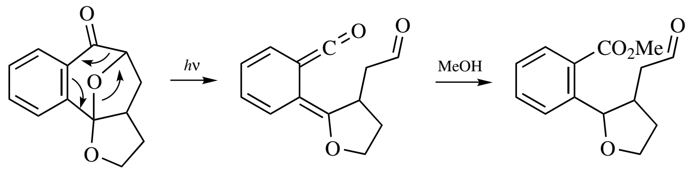
(9)

Photolysis of the epoxy bicyclo[2.2.1]hetan-7-one **30** formed the diradical **31**, which gave ketene-aldehyde **32**, identified by IR absorption at 2117 cm^{-1} (equation 10) and which was captured by MeOH forming ester **33**.[22] The cyclic acetal **34** upon photolysis was proposed to react in an electrocyclic process forming the ketene **35**, which was captured with MeOH to give **36** in 73% yield (equation 11).[23]



30 **31** **32** (IR 2117 cm^{-1}) **33**

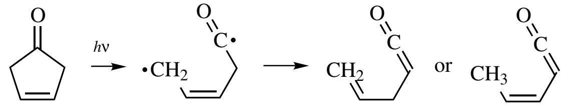
(10)



34 **35** **36** (73%)

(11)

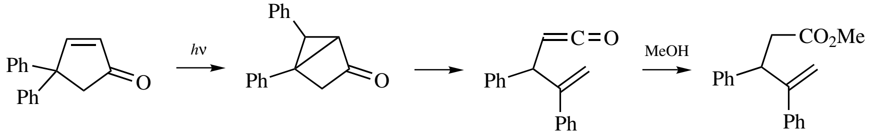
Photolysis of cyclopenten-4-one (**37**) gave a ketene intermediate with an IR band at 2121–2126 cm^{-1} in an argon matrix and 2066–2210 cm^{-1} in the gas phase, tentatively identified as **38a** or **38b** (equation 12).[24]



37 **38a** **38b**

(12)

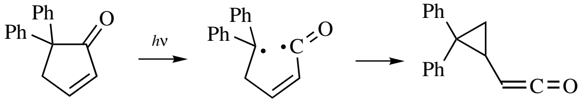
Photolysis of 4,4-diphenylcyclopentenone **39** led to the ketene **41**, observed by IR in a process proposed to occur by di-π-methane rearrangement to **41**, with capture of the ketene by methanol as the ester **42** (equation 13).[25] Photolysis of 5,5-diphenylcyclopent-2-en-1-one **43** gave cyclopropylketene **45**, identified by the IR absorption at 2110 cm^{-1}, and capture as the ester (equation 14).[26] Tetramethyleneketene **48** was identified by its IR absorption at 2100 cm^{-1} as the product from photolysis of the cyclopentenyl ketone **46** via fragmentation of the diradical **47** (equation 15).[27] Methanol treatment gave the methyl ester in 25% yield.[27]



39 **40** **41** **42**

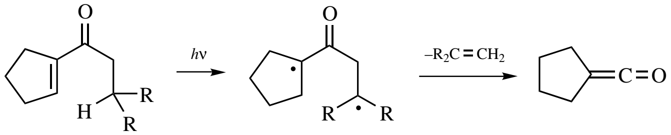
(IR 2110 cm^{-1})

(13)



43 **44** **45**

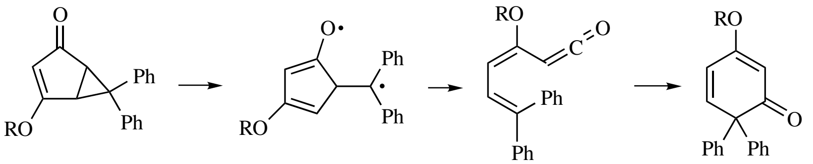
(14)



46 **47** **48**

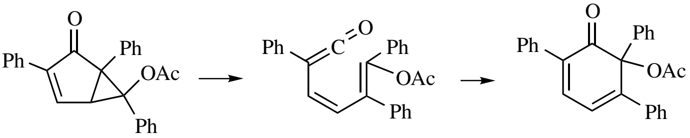
(15)

Solid phase photolysis of crystalline cyclopropanocyclopentenone **49** led to ketene **50**, as observed by NMR, and shown by its capture with nucleophiles and its cyclization to **51** on long standing (equation 16).[28] Photolysis of **52** gave ketene **53**, as evidenced by an IR band at 2091 cm^{-1} at $-196\,°C$ and cyclization to **54** (equation 17).[29] Photolysis of **55** formed **56**, captured by CH_3OH as the ester **57**, in a conversion assigned as a concerted $[2 + 2 + 2 + 2]$ cycloreaction (equation 18).[30]



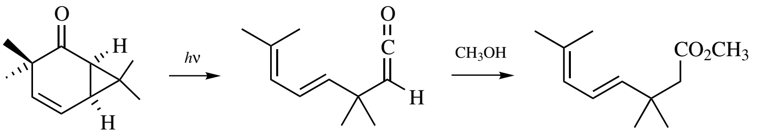
49 (R = Ph_2CH) **50** **51**

(16)



52 **53** (IR 2091 cm^{-1}) **54**

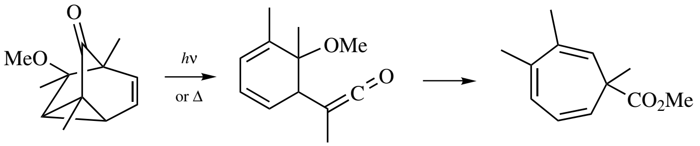
(17)



55 **56** (2110 $\mathrm{cm^{-1}}$) **57** (61%)

(18)

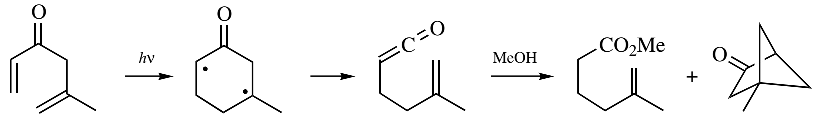
Photolysis of **58** gave ketene **59**, which was characterized by an IR band at 2105 $\mathrm{cm^{-1}}$, capture by diethylamine, and rearrangement to **60** with intramolecular MeO migration (equation 19).[31]



58 **59** (IR 2105 $\mathrm{cm^{-1}}$) **60** (31%)

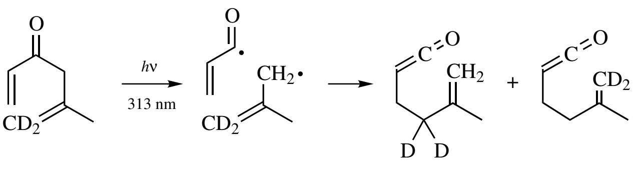
(19)

Photolysis of 5-methyl-1,5-hexadiene-3-one (**61**) gave cyclization to the diradical **62**, which opened to the 3-butenylketene **63** (the vinylogous Wolff rearrangement, Section 3.3.2), captured by MeOH as the ester **64** in 27% yield (equation 20).[32] There was competitive formation of the bicyclo[2.1.1]hexan-2-one **65** in 43% yield from **61**.[32] The use of deuterium labeling showed that in the conversion of **61**-d_2, in addition to the 1,6-electrocyclization (equation 20), at λ 313 nm there was also α-cleavage leading to the radical pair **66**, which gave recombination to both **67** and **68** (equation 21).[33] Studies with triplet sensitizers indicated that α-cleavage to **66** was a singlet process and that cyclization to **65** occurred from the triplet state of the ketone.[34]



61 **62** **63** **64** (27%) **65** (43%)

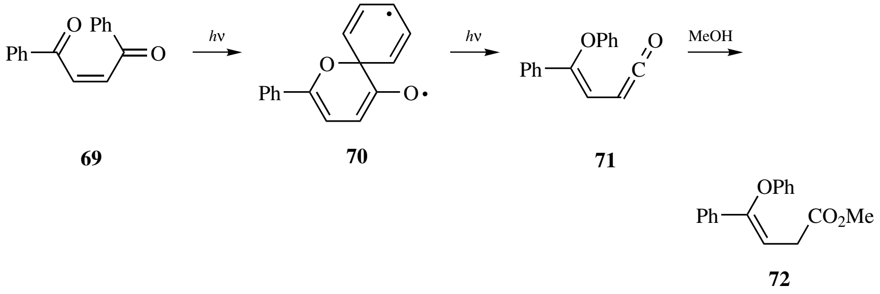
(20)



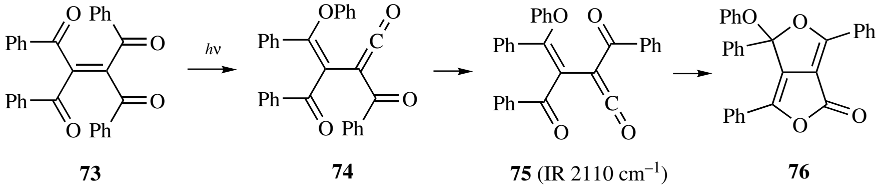
61-d_2 **66** **67** **68**

(21)

Photolysis of *Z*-dibenzoylethylene **69** in methanol is proposed to involve phenyl migration via **70**, forming ketene **71**, which was trapped with MeOH, giving the ester **72** (equation 22).[35–38] Photochemical rearrangement at 10 K of tetrabenzoylethylene **73**, forming **74**, was followed by bond rotation forming the conformer **75**, which cyclized to **76** (equation 23).[39]

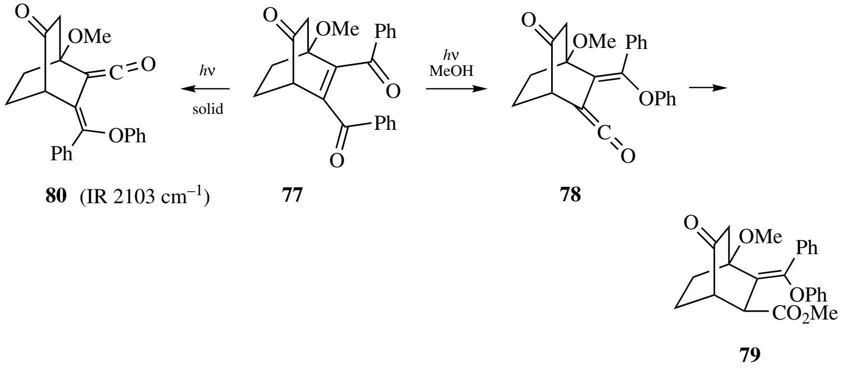


(22)

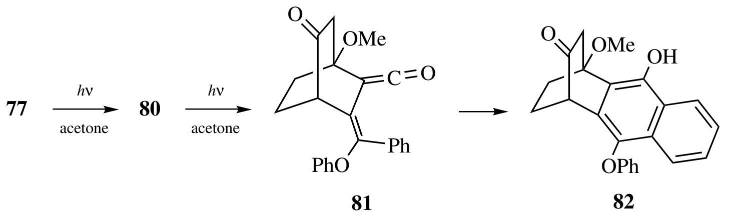


(23)

In a further study of the regioselectivity of the carbon-to-oxygen photo-phenyl migration in *Z*-1,2-dibenzoylethylenes to give alkenylketenes, it was found that photolysis of **77** in MeOH gave ketene **78** (equation 24), as evidenced by the ester **79** formed by MeOH trapping, while irradiation in the solid state gave ketene **80**, as evidenced by the IR band at 2103 cm^{-1} (equation 24) and trapping with MeOH.[40] Irradiation of **77** in acetone was proposed to give both **78** and **80** and the latter underwent further acetone-sensitized isomerization of the double bond to form the new ketene **81**, which cyclized to **82** (equation 25).[40]

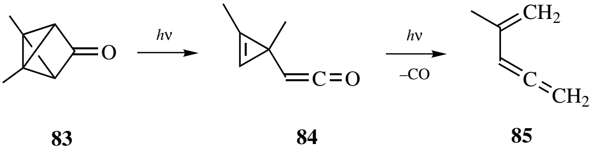


(24)

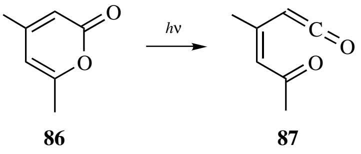


(25)

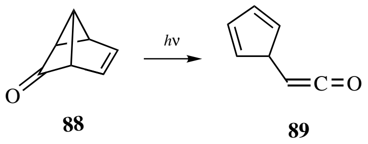
Photolysis of **83** in an Ar matrix led to the cyclopropenylketene **84**, as characterized by the IR band at 2105 cm^{-1}, and further photolysis resulted in decarbonylation and formation of the vinylallene **85** (equation 26).[41] Photolysis of the pyrone **86** gave some formation of ketene **87**, as evidenced by an IR band at 2120 cm^{-1} (equation 27).[41] Photolysis of **88** in an argon matrix gave a species tentatively identified as **89**, with an IR band at 2130 cm^{-1} (equation 28).[42]



(26)

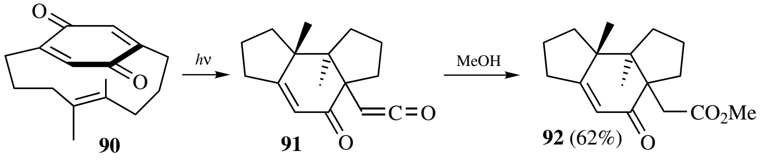


(27)



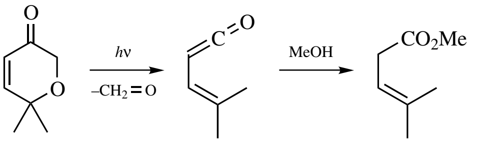
(28)

Photolysis of the 2,5-(*trans*-4-octenyl)-bridged p-benzoquinone **90** led to formation of the ketene **91**, detected by an IR band at 2110 cm^{-1} and capture as the ester **92** with MeOH (equation 29).[43]



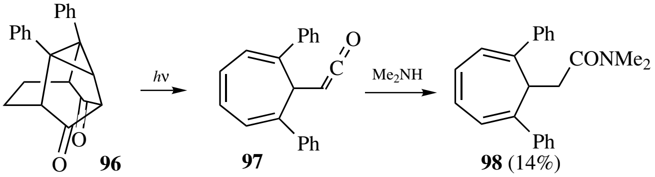
(29)

Photolysis of **93** gave a formal [4 + 2] cycloreversion to the ketene **94** with expulsion of formaldehyde and capture of the ketene by MeOH as the ester **95** (equation 30).[44]

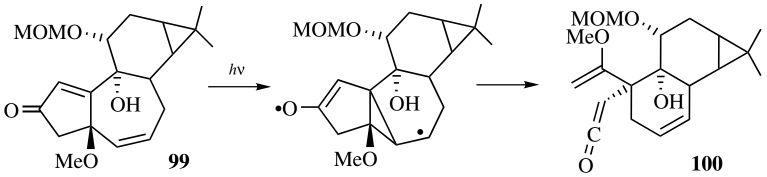


93 **94** **95** (70–80%) (30)

Photolysis of **96** was reported to form ketene **97**, which was trapped by Me_2NH, forming **98** along with other products (equation 31).[45] The photolysis of **99** was proposed to lead to a ketene intermediate **100** (equation 32) that cyclized, forming both a lactone and a spirocyclopentenone.[46]

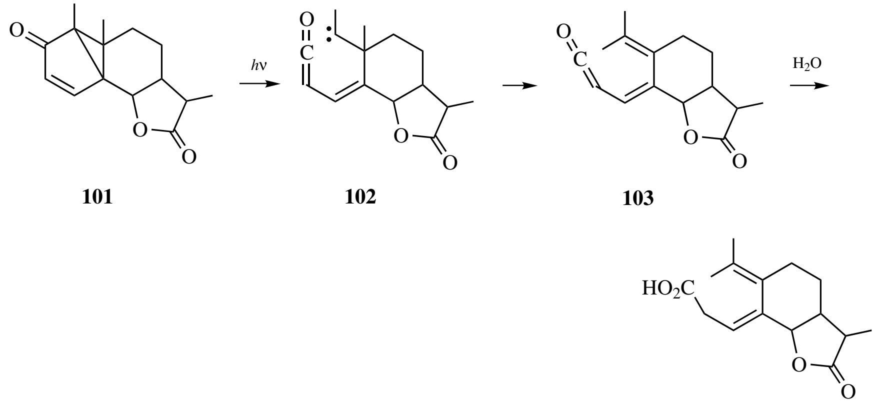


96 **97** **98** (14%) (31)



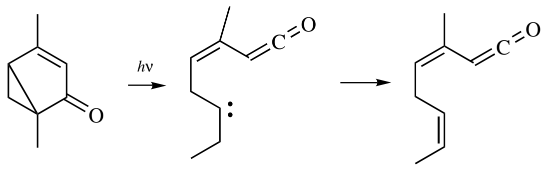
99 **100** (32)

A possible mechanism for the photochemical rearrangement of lumiphotosantonin (**101**) to photosantonic acid (**104**) involved the ketene-carbene **102** (equation 33),[47] and upon photolysis at −190 °C the IR of ketene **103** at 2113 cm^{-1} was observed.[48] The photolysis of umbellulone (**105**) at −190 °C gave rise to an IR band at 2113 cm^{-1} attributed to the ketene **106** (equation 34), which was trapped with CH_3OH. A similar ketene-carbene route was suggested for this reaction.[48] Concerted processes forming **103** and **106** directly without the intermediacy of the ketene carbenes were also considered possible.[48]



101 **102** **103** **104**

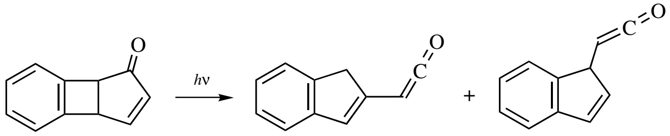
(33)



105 **106**

(34)

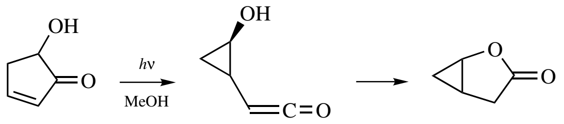
Photolysis of the cyclopentenone **107** in CH_3OH led to two methyl esters resulting from trapping of ketenes **108** and **109** in 7 and 34% yields, respectively (equation 35).[49] The structures for possible intermediates in these reaction pathways were suggested.[49]



107 **108** **109**

(35)

Photolysis of hydroxycyclopentenone **110** gave lactone **112**, which was proposed to form from (hydroxycyclopropyl)ketene **111** (equation 36).[50] The ketenes could not be trapped by CH_3OH and it was proposed that the cyclizations rates were even faster than solvent attack.



110 **111** **112** (8%)

(36)

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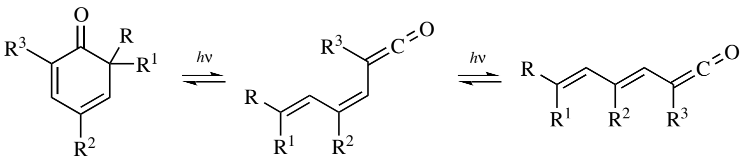
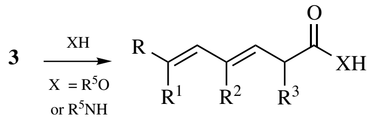
3.4.3 Ketenes from Cyclohexadienones and Other Cycloalkenones

The photochemical ring opening of cyclohexadienones (Barton-Quinkert reaction) was first reported in 1960[1] and provides a facile synthesis of complex molecules from readily available starting materials, even with the use of incandescent light.[2–6] Cyclohexadienones **1** absorb light at long wavelengths and undergo reversible ring opening to dienylketenes **2** and **3**, which can be observed spectroscopically and intercepted by nucleophiles such as alcohols or amines forming **4** (equations 1, 2).[6] Photochemical interconversion of the dienylketenes **2** and **3** may also occur.



1 **2** **3**

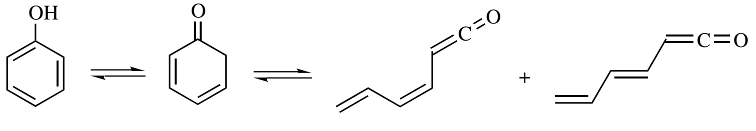
(1)



4

(2)

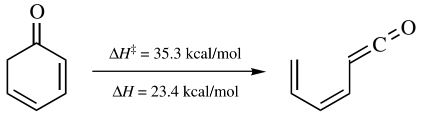
The energetics of the interconversion of phenol (**5**), 2,4-cyclohexadienone (**6**), and *Z*- and *E*-1,3,5-cyclohexatrien-1-one (**7**) have been studied computationally[7–11] at the B3LYP/6-31G//B3LYP/6-31G level (Scheme 3.4).[11]



5 (0) **6** (18.9) *Z*-**7** (36.8) *E*-**7** (35.4)

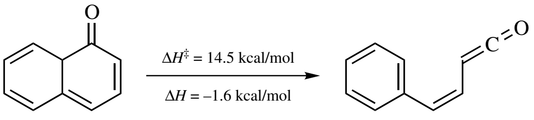
Scheme 3.4 Photoisomers of phenol and relative energies (kcal/mol).

Computations at the (U)B3LYP/6–31G* level of the interconversion of cyclohexadienone and dienylketenes through ring opening and closure indicate that whereas the parent cyclohexadienone **6** has a high barrier for forming the less stable dienylketene Z-**7** (equation 3), conversion of **8** to phenylvinylketene **9** is significantly more facile due to the gain in aromaticity (equation 4).[9,10] Cyclization of *Z*-**7** to the ketenylidenecyclopentenes **10** has also been examined.[11]



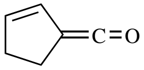
6 *Z*-**7**

(3)

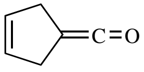


8 **9**

(4)

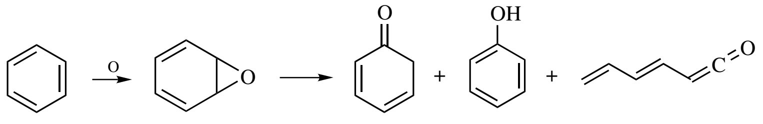


10a



10b

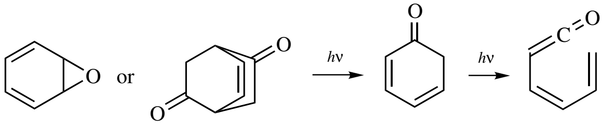
The reaction of benzene with oxygen atoms produced from ozone photolysis in an argon matrix at 12 K produces phenol (**5**), benzene oxide (**11**), 2,4-cyclohexadienone (**6**), and the ketene *E*- **7** (equation 5).[11] The ketene was identified by a series of IR bands from 2116 to 2133 cm^{-1}, and the conformation shown of the *E*-isomer was calculated to be the most stable. It was assumed that the initially formed *Z*-**7** would be photoisomerized to the more stable *E*-**7**.[11] The relative energies of phenol, **6**, and ketenes *Z*-**7** and *E*-**7** were calculated as 0, 18.9, 36.8 and 35.4 kcal/mol Scheme 3.4.[11] Similar oxidations were carried out with toluene, *m*- and *p*-xylene and mesitylene and ketene products were observed by IR.[12] The structures of these were assigned based on comparison of the observed with the calculated IR frequencies, including the examination of ^{18}O isotopomers.[12]



11 **6** **5** ***E*–7**

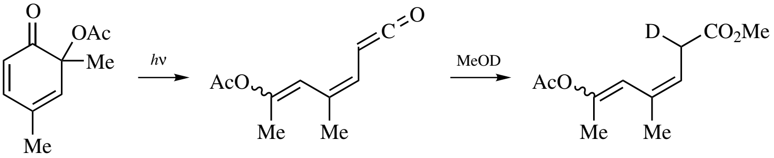
(5)

Photolysis of benzene oxide (**11**)[13] or the diketone **12**[14] formed the parent cyclohexadienone **6** and this was converted to dienylketene *Z*-**7** on further photolysis (equation 6).[13,14] The ketene *Z*-**7** was identified by its IR absorption at 2112 cm^{-1}, the UV spectrum, and capture by EtOH.[13,14] The substituted dienylketene **13** was generated by photolysis and trapped with MeOD, forming the ester (equation 7).[15]



11 **12** **6** *Z*-**7** (IR 2112 cm^{-1})

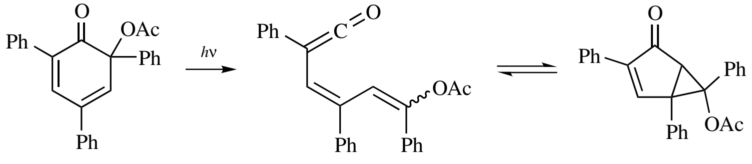
(6)



13

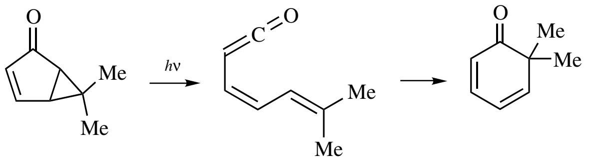
(7)

Dienylketene **15** from photolysis of cyclohexadienone **14** cyclized to bicyclo[3.1.0]hex-3-en-2-ones **16**, which underwent thermal ring opening back to **15** and **14** (equation 8).[16] Some isomeric analogues were also studied.[16] The formation of **19** from photolysis of **17** was similarly proposed to involve the intermediacy of the dienylketene **18** (equation 9).[17] Photolysis of **20** gave ketene **21** (IR 2100 cm^{-1}), which thermally reformed **20** together with **22** or was captured by amines, which were much more efficient in this process than alcohols (equation 10).[18]



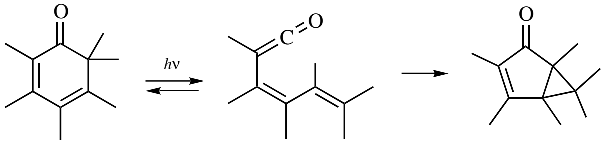
14 **15** **16**

(8)



17 **18** **19**

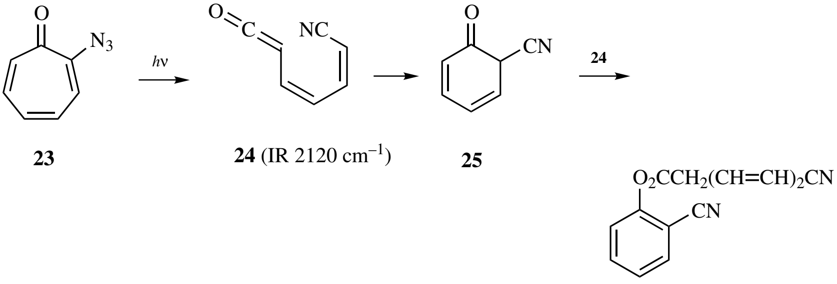
(9)



20 **21** **22**

(10)

1-Azidocycloheptatrienone **23** upon photolysis formed (4-cyanobutadienyl)ketene **24**, which cyclized to 6-cyanocyclohexadienone **25** (equation 11).[19,20] The ketene **24** was identified by its IR absorption at 2120 cm^{-1}, the UV spectrum, and capture by nucleophilic solvents. The half-life of **24** was 4 min at 22 °C and the major product was **26**, derived by acylation by **24** of the phenol from **25** (equation 11).[19,20] The 2,4,6-trimethyl analogue of **23** gave the corresponding dienylketene, which cyclized faster than **24** by a rate factor estimated as 10^3.[19,20]

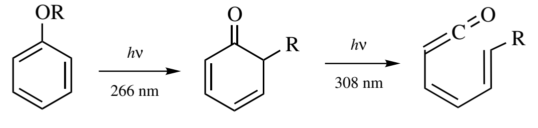


23 **24** (IR 2120 cm^{-1}) **25**

26

(11)

Laser photolysis of **27a** and of **27b** with 266 nm light gave transient species assigned as the cyclohexadienones **28a,b** (equation 12).[21] Photolyses of these transients with a 308 nm laser gave new transient species with absorption maxima at 270 nm and 330 nm, assigned as the dienylketenes **29a** and **29b**, respectively.[21] The longer-wavelength absorption of **29b** was attributed to conjugation of the acetyl substituent with the dienylketene.[21]

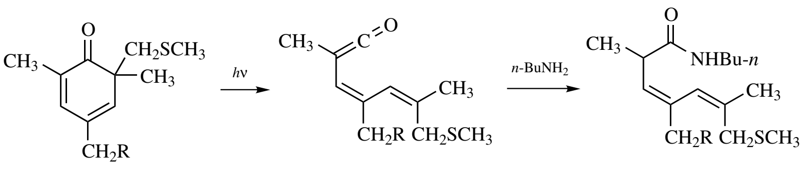


27a R = $PhCH_2$
27b R = CH_3CO

28a,b **29a,b**

(12)

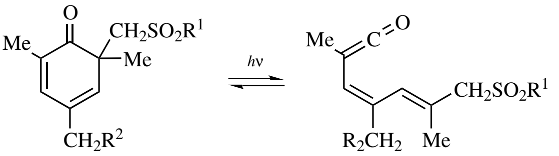
Photolysis of the cyclohexadienone **30** (R = H) with visible light in the presence of amines was proposed to form dienylketenes **31**, which then gave amides **32** in yields of 87–95% as *cis/trans* mixtures that were not separated (equation 13).[22] In a competition experiment, photolysis of **30** in the presence of *n*-BuNH$_2$ (1 equiv) and EtOH (5 equiv) gave amide and ester products in a 9.5:1 ratio, showing the much greater nucleophilicity of the amine. It was suggested that dienylketenes generated in this way would be useful for reactions with amine functions in enzymes.[22] Photolysis of **30** (R = SPh) with visible light in the presence of amines also gave amide products **32**.[23]



(13)

30 **31** **32**

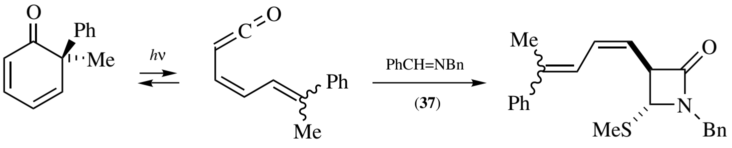
Photolysis of the water-soluble cyclohexadienones **33** in the presence of amino acids in aqueous solution was carried out at pH 10 so that free amino groups were present and resulted in selective capture of the ketenes **34** by the nucleophiles (equation 14).[24,25] Reaction of **34** with diamines gave the bisamides from reaction of two equivalents of the ketene.[26]



(14)

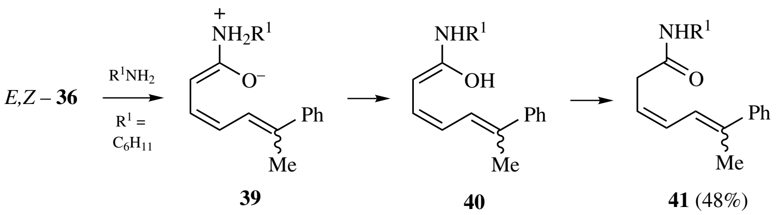
33 (R^2 = H, CO$_2$H, PO$_3$Me$_2$) **34** (83–100%)

Photolysis of chiral cyclohexadienone **35** gave the dienylketenes **36** (λ_{max} 305 nm, ε 5000), which either reverted to **35** or reacted with imine **37** in [2 + 2] cycloaddition reactions, forming β-lactam **38** (equation 15), or with nucleophiles (RNH$_2$, MeOH, EtOH), forming amide **41** (equation 16) or esters.[27] Two IR bands at 2102 and 2114 cm^{-1} were observed, suggesting that both the *E* and *Z* isomers of the ketene **36** were present. The ^{1}H NMR spectra of these species were observed and capture products from both were obtained. With excess cyclohexylamine there is a pseudo first order reaction of **36** assigned to formation of a zwitterionic intermediate **39** (λ_{max} 380 nm), which formed amide enol **40** and the amide **41** (λ_{max} 460 nm) (equation 16).[27]



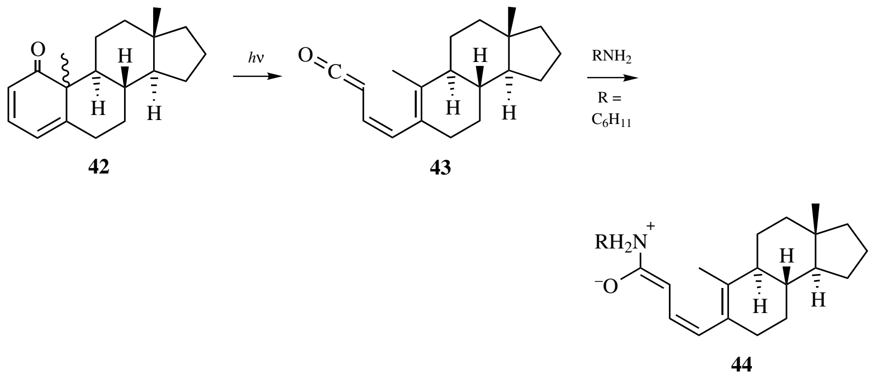
(15)

35 *E,Z*-**36** **38** (71%)

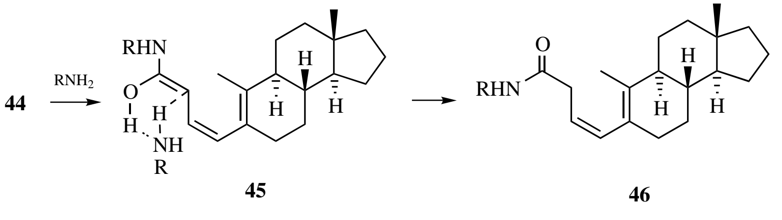


(16)

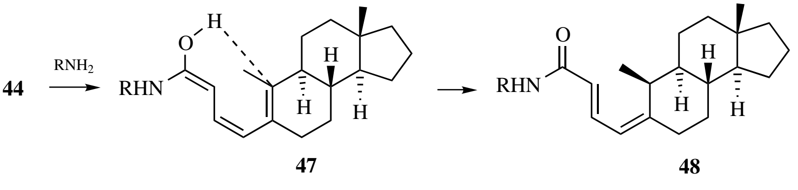
The ketone **42** underwent photochemical conversion to the dienylketene **43** as two conformational isomers, with IR absorptions at 2104 and 2118 cm^{-1}, respectively (equation 17).[28] Reaction of **43** with cyclohexylamine was proposed to form a zwitterionic intermediate **44**, which was converted to an enol amide **45** that formed amide **46** by a cyclohexylamine-assisted process (equations 17, 18) and **48** by an intramolecular reaction (equation 19).[28]



(17)

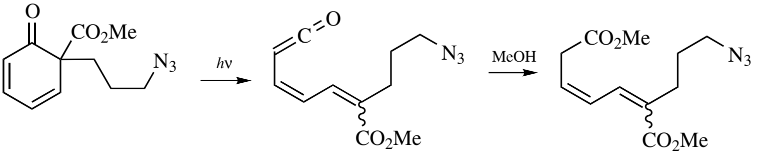


(18)



(19)

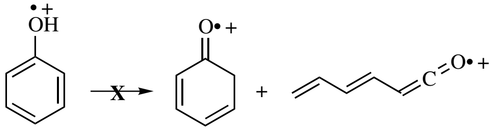
Photolysis of azidoalkylcyclohexendione **49** with 366 nm light gave dienylketene **50**, as evidenced by capture by MeOH as the ester **51** (equation 20).[29]



49 **50** **51**

(20)

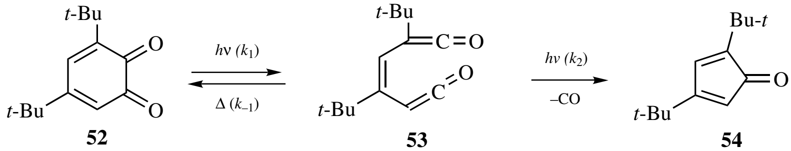
Gas phase chemical ionization of protonated anisole formed ionized phenol radical cation ($\mathbf{5}^{+}\bullet$), but rearrangement of this to the radical cations of cyclohexadienone **6** and of butadienylketene **7** was not observed (equation 21).[30] For the radical cation species the relative energies of phenol, cyclohexadiene and dienylketene *E*- **7** are calculated to be 0, 35 and 29 kcal/mol, respectively. Thus, the relative stabilities of cyclohexadienone and the dienylketene are reversed between the neutral species (Scheme 3.4) and the radical cation.



$\mathbf{5}^{+\bullet}$ $\mathbf{6}^{+\bullet}$ *E*-$\mathbf{7}^{+\bullet}$

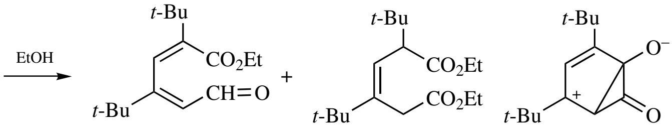
(21)

Laser photolysis of 3,5-di-*tert*-butyl-1,2-benzoquinone **52** in hexane, carbon tetrachloride, or acetonitrile gave rise to bisketene **53**, which was identified by its IR absorption at 2173 cm^{-1} and a UV absorption near 320 nm (equation 22).[31,32] Upon continued photolysis **53** underwent decarbonylation to give the cyclopentadienone **54** (equation 22). Kinetic analysis led to values of 5×10^{-4} s^{-1} for the rate constants k and k_2 and of 2×10^{-5} s^{-1} for k_{-1}. The addition of EtOH after 30 min photolysis led to immediate disappearance of **53** and formation of ester **55a** in the presence of a small amount of EtOH and of ester **55b** if a large amount of EtOH was added (equation 23). The formation of **54** from **53** may involve initial decarbonylation or possibly a zwitterion **56**.



52 **53** **54**

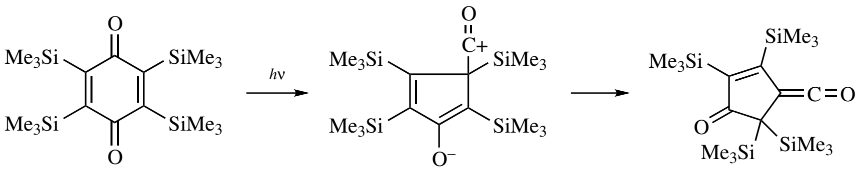
(22)



55a **55b** **56**

(23)

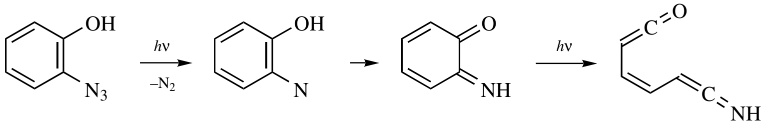
Photolysis of 2,3,5,6-tetra(trimethylsilyl)-1,4-benzoquinone (**57**) gave the ketene **59** (IR 2089 cm^{-1}) as pale yellow crystals in 21% yield (equation 24).[33] A zwitterionic intermediate **58** may have been formed.



57 **58** **59** (IR 2089 cm^{-1})

(24)

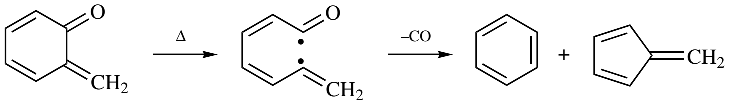
Photolysis of 6-imino-2,4-cyclohexadien-1-one (**60**) in an Ar matrix at 10 K in solid Ar gave the ketene **63**, identified by the ketenyl and keteniminyl IR absorptions at 2114 and 2031 cm^{-1}, respectively, which agreed with calculated absorption positions (equation 25).[34] Photolysis of the azidophenol **61** led to **62**, which gave a hydrogen shift to also form **60** (equation 25).[34,35]



61 **62** **60** **63** (IR 2114, 2031 cm^{-1})

(25)

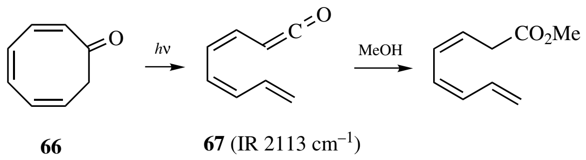
Thermolysis of *o*-quinone methide **64** at 760 to 1110 K gave benzene and fulvene and while the formation of the intermediate **65** with possible ketene character in this process was considered, a concerted pathway was favored (equation 26).[36]



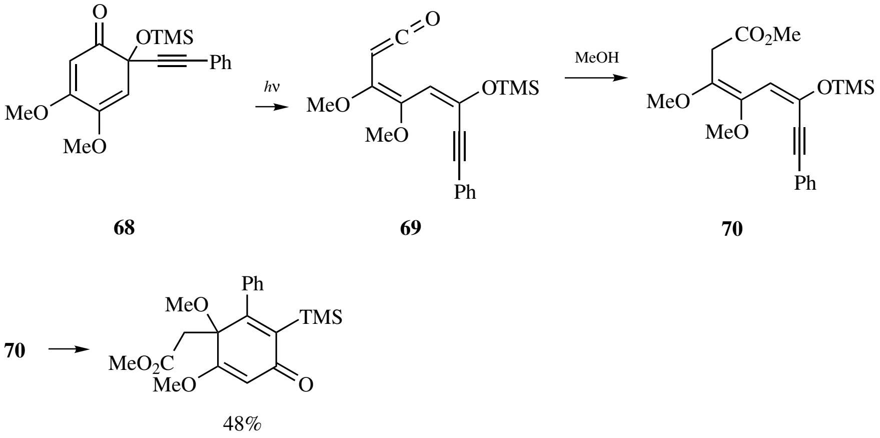
64 **65**

(26)

Photolysis of 2,4,6-cyclooctatrienone **66** gave the hexatrienylketene **67**, identified by its capture with CH_3OH[37] and by the IR band at 2113 cm^{-1} (equation 27).[38] The alkynyl-substituted cyclohexadienone **68** in MeOH gave the diene-yne ketene **69**, which was trapped as the methyl ester from cyclization of **70** (equation 28).[39]

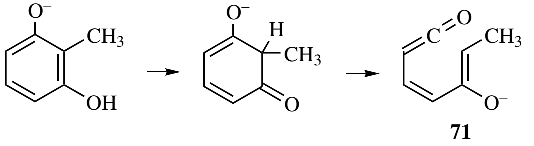


(27)

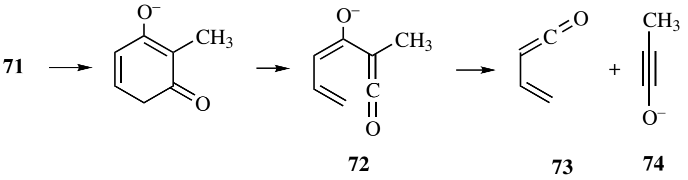


(28)

The gas phase collisionally activated dissociation (CAD) of *O*-deprotonated resorcinol and 2-, 4- and 5-methylresorcinols gave fragment ions consistent with *O* to *C* proton migration and ring opening to alkenylketene intermediates such as **71** that rearranged to the ketene **72**, which cleaved further to form species such as vinylketene (**73**) and the ynolate **74** (equations 29, 30).[40,41]

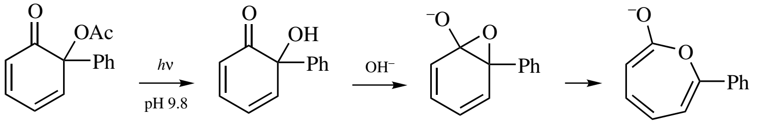


(29)

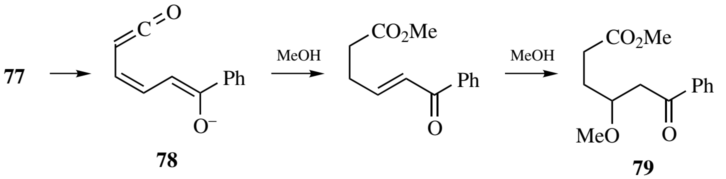


(30)

The photosolvolysis of the 6-acetoxycyclohexa-2,4-dienone **75** was proposed to involve formation of the benzene oxide **76**, which opened to the oxepin **77** (equation 31), which gave the ketene **78** leading to the final product, **79** (equation 32).[42]



75 **76** **77** (31)



78 **79** (32)

Photolysis of bridged cyclohept-2,4-dien-1-ones gave cyclopropylketenes identified by their IR bands in the range 2112–2120 cm^{-1} and their ^{1}H NMR signals in the range δ 2.62–3.33 at –80 °C in CD_2Cl_2 for the proton at C_2. Upon reaction with MeOH, these gave the corresponding ester in yields of 70–100%.[43]

Many examples of cyclization of metal-complexed dienylketenes are given in Section 3.5. See also Section 4.1.4

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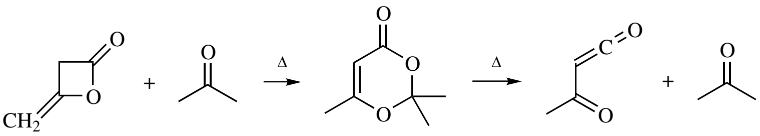
3.4.4 Ketenes from Dioxinones

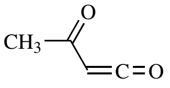
The chemistry of dioxinone **1**, a convenient precursor for acetylketene **2**, has been the subject of a short review.[1] Dioxinone **1** is a product of the reaction of diketene and acetone, and forms acetylketene (**2**) and acetone on thermolysis (equation 1). Even though the preparation of diketene in acetone was used on a large scale in industry, the formation of **1** was not recognized for a long time. The structure of **1** was elucidated in a collaboration involving Michael F. Carroll of the A. Boake Roberts Company and Alfred Bader of Aldrich Chemical Company using UV and IR analysis and later NMR,[2,3] and was one of the early offerings of the Aldrich Company.



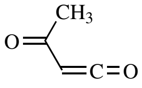
1 **2**

(1)

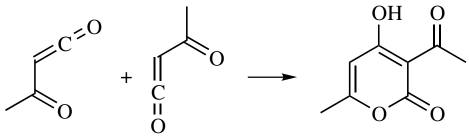
Dioxinones cleave on thermolysis or photolysis, with formation of an acylketene and a ketone.[4] Pyrolysis of **1** at 180–240 °C and trapping of the product in an argon matrix at 5–12 K showed the presence of **2** and acetone by IR (equation 2).[5] Ketenyl bands at 2135 and 2142 cm^{-1} suggested the presence of both the *s-cis* and *s-trans* conformations of **2**.[5] Dimerization of **2** proceeded by a [4 + 2] cycloaddition to form **3** (equation 2).[5] The stereochemistry of dioxinone formation has been studied by computational methods.[6]



2 *s-cis*



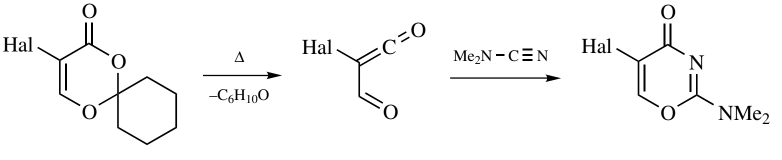
2 *s-trans*



2 **2** **3**

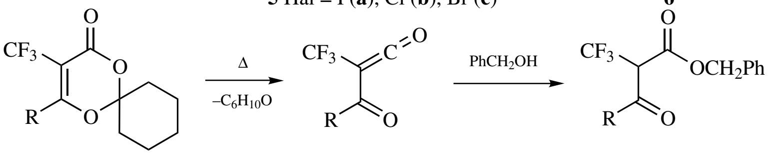
(2)

A variety of substituted acylketenes have been prepared from dioxinones, including halo derivatives **5** from 5-halodioxinones **4**, and these were trapped with dimethylcyanamide to give halooxazinones **6** (equation 3).[7,8] It was noted that the chloroketene **5b** formed more readily than the fluoro compound, and this is consistent with the known destabilization of ketenes by fluorine (Section 4.4.1). Trifluoromethyldioxinones **7** gave the α-trifluoromethylketenes **8**, which were trapped by benzyl alcohol (eqaution 4).[9]



4 **5** Hal = F(**a**), Cl (**b**), Br (**c**) **6**

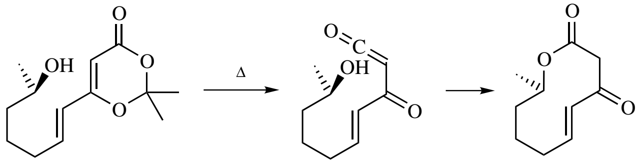
(3)



7 **8** **9**

(4)

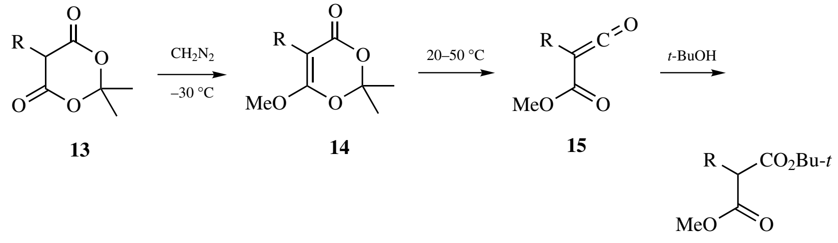
Dioxinones **10** with side chains bearing nucleophilic groups form acylketenes **11**, which cyclize by intramolecular attack (equation 5).[10] This reaction was also used to prepare eight-membered rings[11] and other medium ring-sized lactones.[12,13]



10 **11** **12** (68%)

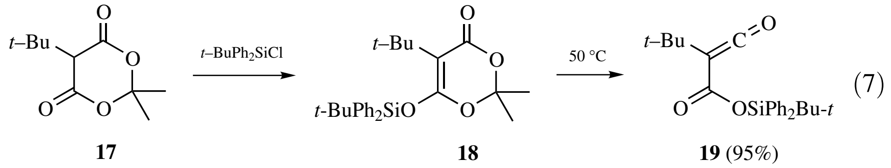
(5)

Treatment of various Meldrum acid derivatives **13** with diazomethane gave 6-methoxydioxinones **14**, which on thermolysis gave acylketenes **15** at 20–50 °C, as shown by trapping with *t*-BuOH and by observation of the characteristic IR absorptions at 2130–2149 cm^{-1} (equation 6).[14] These ketenes underwent gradual dimerization. Silylation of **17** gave **18**, which upon heating at 50 °C without solvent gave the persistent ketene **19**, with IR absorption at 2125 cm^{-1} (equation 7).[14]

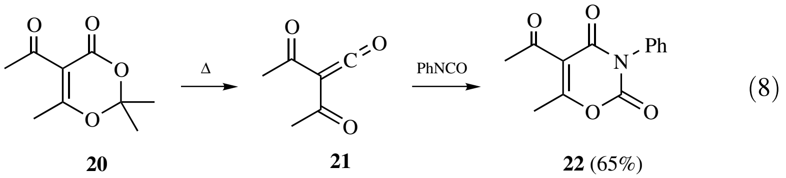


13 **14** **15** **16**

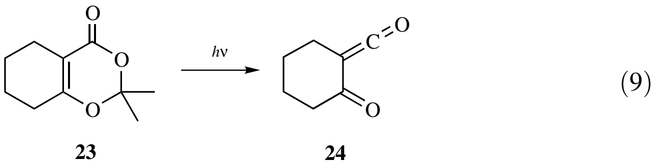
(6)

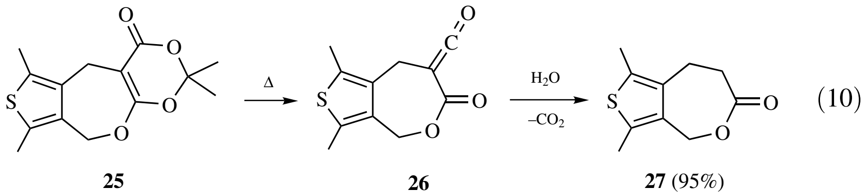


Thermolysis of acyldioxinone **20**, forming diacetylketene **21** in the presence of phenylisocyanate, gave [4 + 2] cycloaddition forming **22** (equation 8).[15]



Photolysis of the dioxinone **23** with 248 nm light provided a convenient source of the ketene **24** for measurement of the rate of hydration (equation 9).[16] Thermolysis of **25** gave the ketene **26**, which was hydrolyzed to the carboxylic acid that lost CO_2, forming **27** (equation 10).[17] The ketene was also trapped with t-BuOH.[17]





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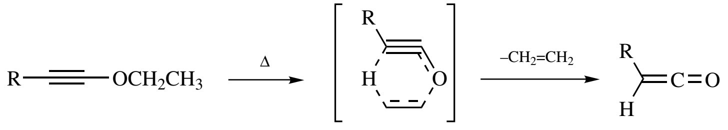
3.4.5 Ketenes by Thermolysis of Alkynyl Ethers

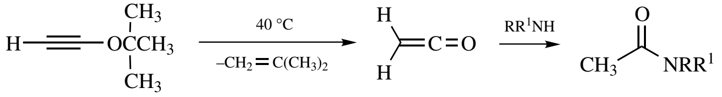
Thermolysis of alkynyl ethers provides a mild route for the preparation of a variety of alkynyl ethers. This procedure was discovered in 1954 by Ficini, who found that ethyl alkynyl ethers **1** on thermolysis underwent loss of ethylene to form active acylating agents.[1] These were originally proposed to be alkynyl alcohols,[1] but on further investigation they were shown to be ketenes **3**.[2–4] On the basis of deuterium isotope effect studies, the reactivity order *t*-BuO > *i*-PrO > EtO for alkoxy ethynyl ethers,[5] and other studies, the mechanism of the reaction is considered to involve concerted hydrogen atom transfer through a 6-membered ring transition state **2** (equation 1).[5]



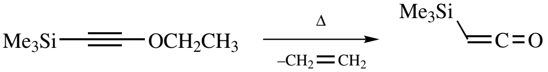
(1)

1 **2** **3**

tert-Butyl alkynyl ethers **4** underwent ketene formation at temperatures as low as 40 °C[6–8] and provided a route to ketene **5** itself, captured with amines (equation 2).[6–10] Thermally stable ketenes such as trimethylsilylketene **7** have been prepared and isolated by this procedure (equation 3),[7,7a] or the ketenes were trapped by reactions with nucleophiles or in [2 + 2] cycloadditions. Reaction of the ketene with the alkynyl ether precursor was often facile,[8] and this represents a severe limitation to this method, but if as in the case of silylketenes the products are stable neat, the reactions can be conducted using preparative gas chromatography and the products collected from the outlet after reaction in the chromatograph.

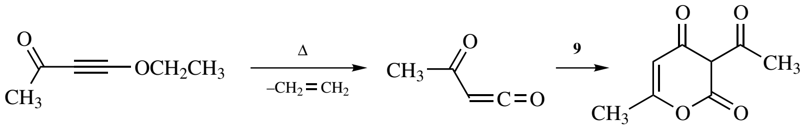


4 **5** (87–99%) (2)

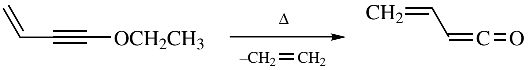


6 **7** (65%) (3)

This method has been used for the preparation of acetylketene (**9**) by the thermolysis of ethyl 3-oxo-1-butynyl ether (**8**), which formed the dimer in 77% yield (equation 4).[11] Vinylketene (**11**) was obtained by the thermolysis of but-3-en-1-ynyl ether (**11**) and was observed in the gas phase (equation 5).[12] Acylketenes with substituents Me_3Si, Me_3Ge, and Ph_2P were also prepared by alkynyl ether thermolysis.[12a]

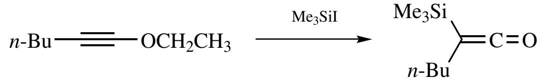


8 **9** 77% (4)

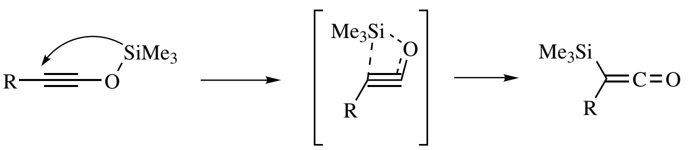


10 **11** (5)

Reaction of alkynyl ether **12** with trimethylsilyl iodide gave trimethylsilylketene **13** (equation 6).[13,14] The thermal rearrangement of trimethylsilyl alkynyl ether **14**, forming ketenes **16**, has been the subject of a computational study, and a mechanism with a concerted 1,3-silyl shift through the four-membered ring transition state **15** was presented, with retention of configuation at silicon (equation 7).[15]

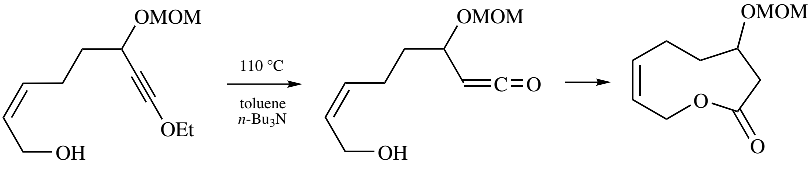


12 **13** (57%) (6)



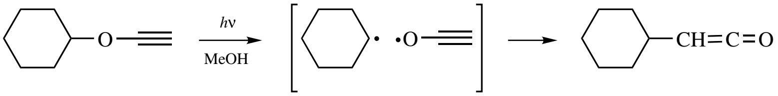
14 **15** **16** (7)

Ketene **18** formed by thermolysis of the alkynyl ether **17** with a functionalized side chain bearing a pendant hydroxyl group cyclized intramolecularly with formation of macrocyclic lactone **19** (equation 8).[16] Tri-*n*-butylamine (10 equiv) was added to facilitate cyclization.

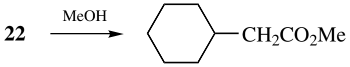


17 **18** **19** (30%) (8)

Photolysis of cyclohexyl ethynyl ether (**20**) in methanol gave a mixture of cyclohexanol (30–40%) and 32% methyl cyclohexyl acetate (**23**).[17] The corresponding reaction of the alkynyl ether from (+)-2-octanol gave 40% racemization in formation of the rearranged ester, and a mechanism involving the intermediacy of a radial pair **21** that formed cyclohexylketene (**22**) was proposed (equation 9).[17]

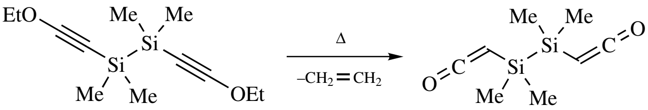


20 **21** **22** (9)



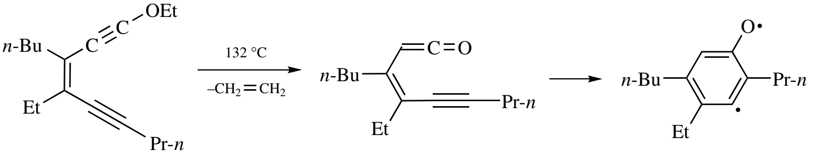
23 (32%)

Gas phase thermolysis of ethoxyalkynylsilanes has proven useful for the preparation of a variety of silylated ketenes and polyketenes,[18–20] including **25** from the dialkynyldisilane **24** (equation 10).[20]

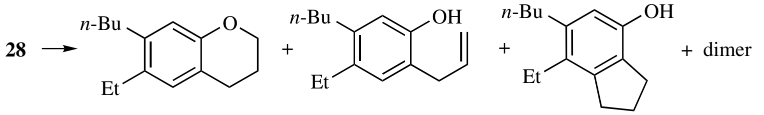


24 **25** (10)

Thermolysis of enediynyl ethyl ether **26** gave ene-yne ketene **27**, which cyclized to diradical intermediate **28** (equation 11), which formed **29a–d** (equation 12).[21] Other routes to ene-yne ketenes are discussed in Section 3.4.1, and use of an alkynyl ether to form an alkynylketene is considered in Section 4.1.3.



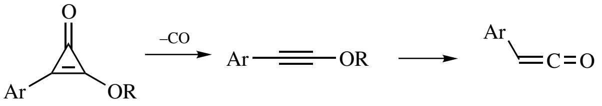
26 **27** **28** (11)



29a (39%) **29b** (8%) **29c** (7%) **29d** (14%)

(12)

Mass spectrometric analysis of aryl ethoxy, *i*-propoxy, and *t*-butoxycyclopropenones (**30**) led to loss of the elements of CO and alkenes and the observation of ions with ratios *m/z* corresponding to the corresponding hydroxyalkynes or the isomeric arylketenes **32** formed from intermediate ethynyl ethers **31** (equation 13).[22]



30 **31** **32**

(13)

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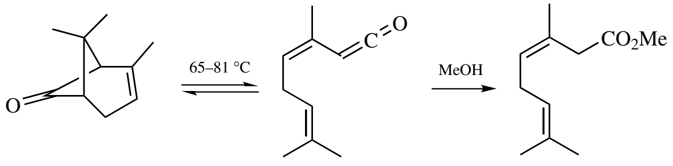
3.4.6 Ketenes from Other Thermolytic and Photochemical Routes

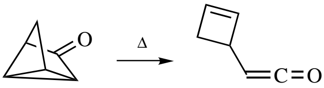
Ketenes are formed by a variety of other thermal and photochemical methods of unique character, and a selection of these are included in this section. Ketene itself is prepared by pyrolysis of acetone (Section 4.1). Thermal ring opening of (-)-chrysanthenone (**1**) caused racemization upon heating to 81 °C, and the intermediacy of the ketene **2** was inferred from the capture as the ester **3** upon refluxing **1** in MeOH (equation 1).[1–4] This example is a special case of cyclobutanone ring opening (Section 3.4.1).



(1)

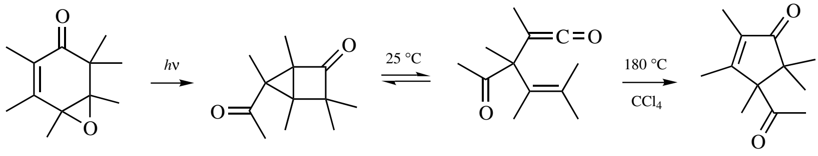
1 **2** **3**

The tricyclic ketone **4** opened the cyclopropane ring above 50 °C, giving cyclobutenylketene **5**, as evidenced by trapping experiments (equation 2).[5] Irradiation of **6a** gave diketone **6** at room temperature, which showed an IR absorption attributed to ketene **7** present at equilibrium, which formed **8** on heating to 180 °C (equation 3).[6] With MeOH, **6** was converted to **9** and **10** at room temperature (equation 4).[6] The failure of **7** to react with MeOH was attributed to the steric crowding present, as observed in similar examples.[6]



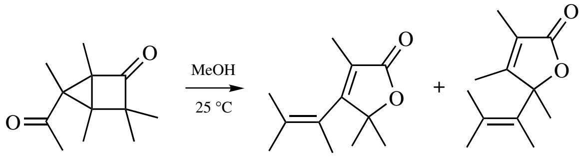
(2)

4 **5**



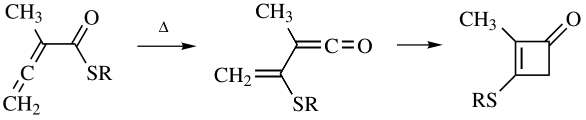
(3)

6a **6** (90%) **7** **8**



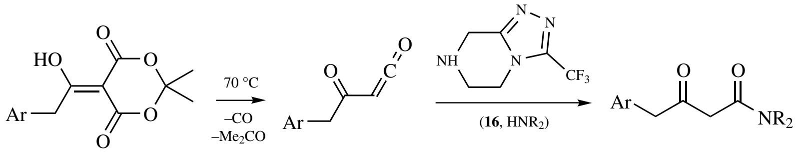
6 **9** **10** (4)

Migration of alkylthio or arylthio groups upon heating of allenyl thio esters **11** led via vinylketenes **12** to isolable cyclobutenones **13** (equation 5).[7]

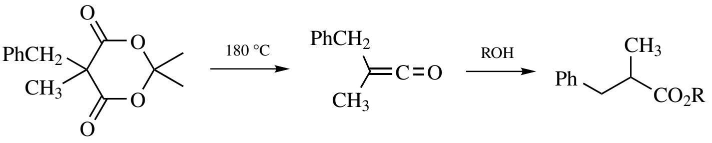


11 **12** **13** (5)

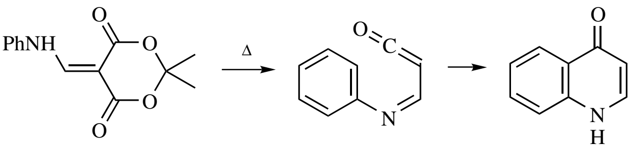
A thorough investigation of the thermolysis of Meldrum's acid derivative **14** at 70 °C showed that acylketene **15** was formed and trapped by amine **16**, forming the intermediate **17** used for drug development with 98% conversion (equation 6).[8] Generation of **15** in the presence of imines resulted in the formation of [2 + 2] or [4 + 2] cycloaddition products.[8] Heating of the Meldrum's acid derivative **18** in the presence of menthol at 180 °C was proposed to lead to ketene **19**, which formed the ester **20** in 90% yield (equation 7).[9] Thermolysis of Meldrum's acid derivative **21** formed ketene **22**, together with the cumulenone PhNHCH=C=C=O, as intermediates observed in a separate low-temperature experiment, and these cyclized to **23** (equation 8).[10] Other reactions of Meldum's acid derivatives are given in Sections 4.1.6 and 5.4.1.7.



14 Ar = 2,4,5-$C_6H_2F_3$ **15** **17** (98%) (6)

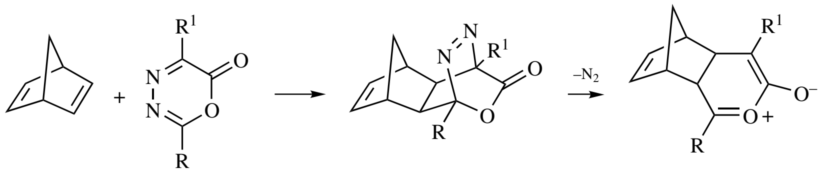


18 **19** **20** (7)



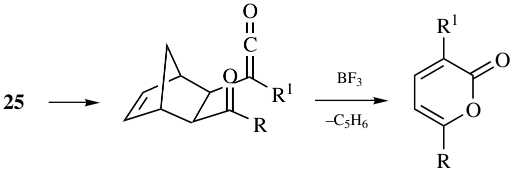
21 **22** **23** (90%) (8)

Norbornadiene gave [4 + 2] cycloaddition with 1,3,4-oxadiazin-6-ones **23** forming adducts **24**, which lost N_2 at room temperature to give acylketenes **26**, presumably via intermediates **25** (equations 9, 10).[11,12] The ketenes reacted by thermal loss of cyclopentadiene to form pyrones **27** (equation 10).



(9)

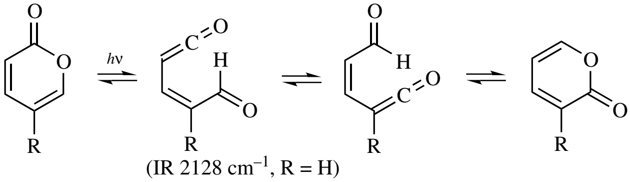
23 **24** **25**



(10)

26 **27** (52–65%)

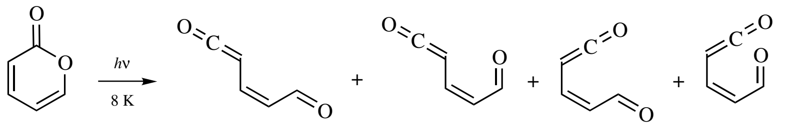
Photolysis of 2-pyrone (**28**, R = H) in a glass at 90 K formed the ketene **29**, identified by its IR absorption at 2128 cm^{-1} (equation 11) and its conversion to the ester with MeOH.[13] Thermolysis at 550–625 °C of **28** (R = Me, Br) resulted in conversion to the 3-substituted isomer **31**, while for R = CO_2Et **28** isomerized to **29**, and for R = ^2H a mixture of **28** and **31** were formed.[13,14] It was proposed that the isomerization occurs by hydrogen transfer interconverting **29** and **30** (equation 11).[13–16] Flash photolysis of **28** (R = H) gave **29**, IR 2128 cm^{-1}, with a half-life for reversion to **28** of 2.9 μs at room temperature.[16]



(11)

28 **29** **30** **31**

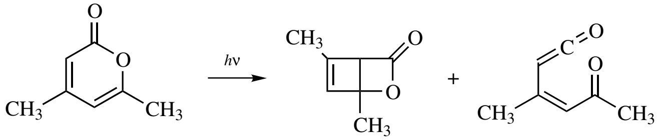
Photolysis of **32** labeled with ^{13}C at the carbonyl carbon gave the ketene **33**, which at 8 K in an Ar matrix gave IR absorption at 2068, 2074, 2081, and 2089 cm^{-1} attributed to the four conformers **33a–d** (equation 12).[17] As noted in Section 1.1.1 (ref. 26), it was concluded that **33d** is not an energy minimum structure. Upon further photolysis hydrogen transfer occurred, resulting in scrambling off the label to the aldehydic carbon, and with new ketene IR absorptions at 2121, 2129, 2133, and 2139 cm^{-1}.[17] With prolonged photolysis the ketenyl IR absorption disappeared.



32 **33a** **33b** **33c** **33d**

(12)

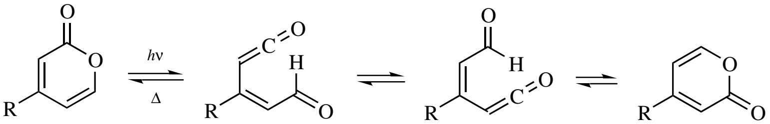
Similar photolysis with light of λ >285 nm of α-pyrone **32** in an argon matrix produced IR bands at 2108, 2124, 2130, and 2135 cm^{-1} assigned to two conformers of the *Z*-isomer of ketene **33**, and further irradiation showed conversion to the *E*-isomer with observed bands at 2122 and 2127 cm^{-1}.[18] The bands were assigned with the aid of B3LYP/6-311++G** computations. Photolysis of the 4,6-dimethyl isomer **34** with light of λ >315 nm gave valence isomerization to the Dewar bicyclo [2.2.0] isomer **35** as the major product to the extent of 90%, with only 5% of the ketene **36**, identified by its characteristic IR absorption at 2128.9 cm^{-1} (equation 13).[18]



34 **35** **36**

(13)

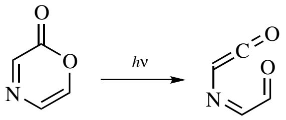
Thermolysis at 550–625 °C of the 5-methyl and 5-bromo pyrones (**37**, R = Me, Br) led to the isomeric 3-pyrones **39**,[13] while the 3-carboethoxypyrone isomerized to the 5-isomer (equation 14).[14] It was proposed that the isomerizations occur by hydrogen shifts via the isomeric ketenes **38** to form the more stable products.[13,14,20] The bicyclo[2.2.0] isomer of **37** (R=H) lost CO_2 upon photolysis to form cyclobutadiene.[21]



37 **38a** **38b** **39**

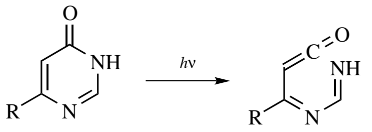
(14)

Oxazinone **40** (equation 15)[22] and pyrimidones **42** (equation 16)[23] gave similar photochemical ring opening, forming ketenes **41** and **43**, respectively.



40 **41**

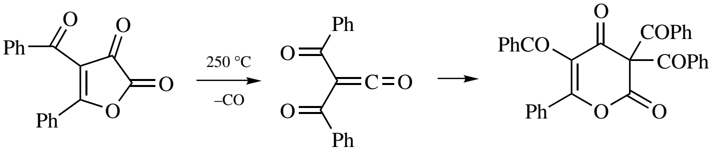
(15)



42 **43**

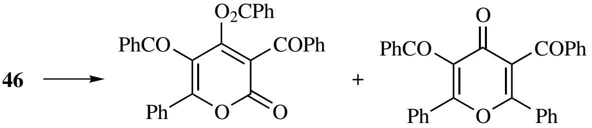
(16)

Thermolysis of furandione **44** formed dibenzoylketene **45**, trapped at low temperature and identified by the IR absorption at 2140 cm^{-1} at –196 °C (equation 17).[24–26] Upon warming, the products **47** and **48** were isolated, evidently formed from the dimer **46** (equation 18).



44 **45** **46**

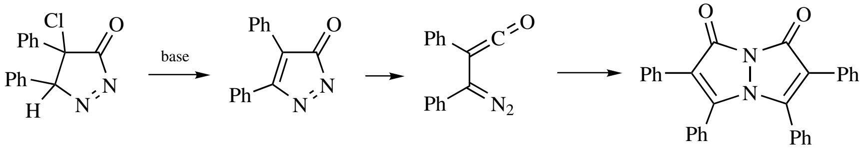
(17)



47 **48**

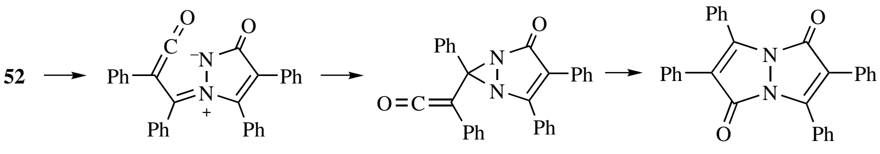
(18)

Dehydrochlorination of 4-chloropyrazolin-5-one **49** was proposed to form 1,2-diazacyclopentadienone **50**, which gave diazo ketene **51**, leading to bimane **52** (equation 19).[27] Thermal rearrangement of **52** to the *anti*-isomer **55** was proposed to involve initial formation of ketenes **53** and **54** (equation 19).[27] An alternative route to **50** was also reported.[28]



49 **50** **51** **52**

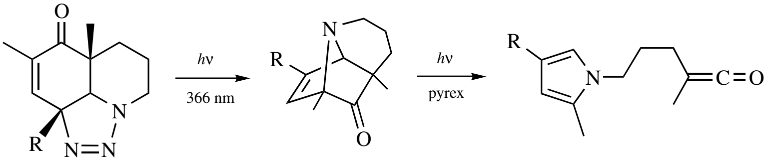
(19)



53 **54** **55**

(20)

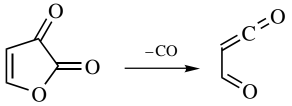
Photolysis of triazolines **56** at 366 nm gave tricyclic ketones **57**, which upon photolysis through pyrex formed pyrrole-substituted ketenes **58**, as evidenced by capture with MeOH and the formation of ketene dimers (equation 21).[29–31]



(21)

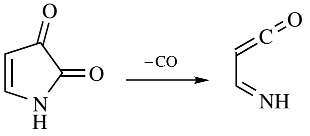
56 **57** **58**

Pathways for the pseudopericyclic decarbonylations of furandione **59** leading to ketene **60** and of **61** leading to ketene **62** have been calculated (equations 22, 23).[32] A detailed computational study, including changes in magnetic susceptibility and anisotropy to estimate the associated aromatization, indicated that pseudopericyclic reactions have at least one disconnection in the cyclic array of overlapping orbitals.[33] Photolysis of **63** in the presence of acetone was proposed to give an initial triplet that led to unobserved ketene **64**, which was trapped by alcohols or underwent decarbonylation (equation 17).[34]



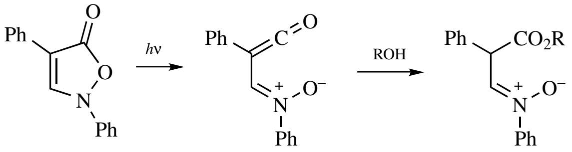
(22)

59 **60**



(23)

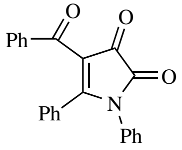
61 **62**



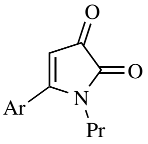
(24)

63 **64** **64** (28–36%)

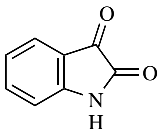
Determination by X-ray crystallography of the structures of **65–67** that undergo cheleotropic fragmentation forming ketenes, as in equation 23, showed that all three are planar and have bond elongations as expected for incipient pseudopericyclic fragmention, in accord with the structure correlation principle.[35] Compound **67** was the least reactive and, as expected, showed the lowest degree of distortion.[35]



65

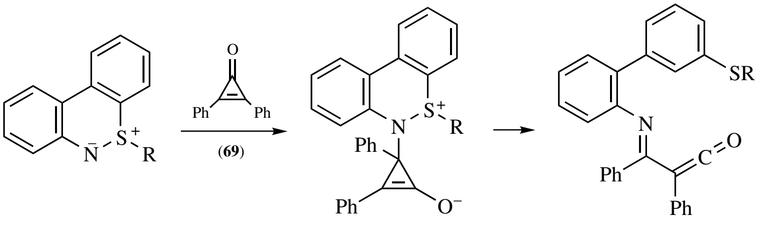


66



67

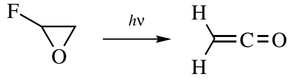
Reaction of diphenylcyclopropenone (**69**) with **68** was proposed to result in formation of ketene **71** from **70** (equation 25).[36] Ketene formation has been proposed for reactions of other nucleophiles with **69**.[37]



68 **70** **71**

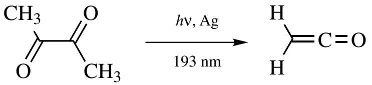
(25)

Gas phase IR irradiation of fluorooxirane (**72**) gave ketene (**73**) and HF (equation 26).[38,39] Photolysis of biacetyl on Ag(111) with 193 nm light formed ketene (**73**) from biacetyl in a process by cleavage to $CH_3C(\bullet){=}O$ and loss of H• that was competitive with decarbonylation (equation 27).[40,41] Electron activation of acetone on silver also produced ketene.[41]



72 **73**

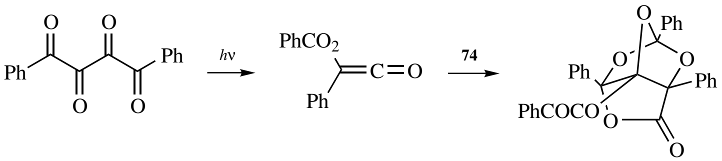
(26)



73

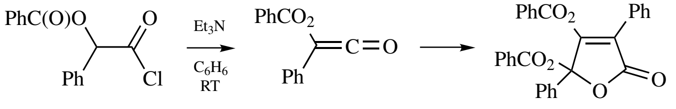
(27)

Irradiation of the tetraketone **74** in an argon matrix at 10 K gave an IR band at 2128 cm^{-1}assigned to ketene **75** (equation 28).[42] The ketene **75** reacted further with **74** to give the tricyclic dimer **76** (equation 28).[42] Ketene **75** generated independently by dehydrochlorination of the acyl chloride gave the dimer **77** (equation 28a).[42]



74 **75** (IR 2128 cm^{-1}) **76** (63%)

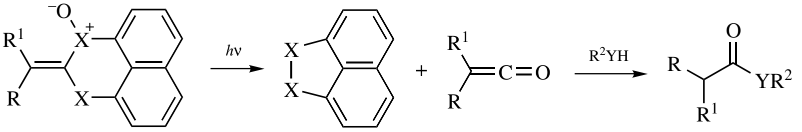
(28)



75 **77** (74%)

(28a)

Photolysis of the sulfoxide and selenoxide derivatives **78** gave ketenes **79**, which were observed by IR and trapped with alcohols and amines (equation 29).[43]



78 X = S, Se **79**

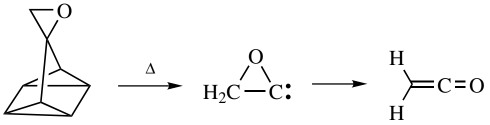
(29)

R,R^1 = Ph, Et, Me, H Y = O, NH

Photolysis at 193 nm[44] or pyrolysis[45] of furan gave ketene (**73**) and acetylene by one pathway, as well as other products (equation 30). Pyrolysis of **80** give oxiranylidene **81**, which was directly observed in an argon matrix and formed $CH_2{=}C{=}O$ (equation 31).[46]

(30)

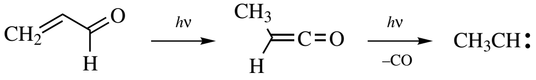
73



80 **81** **73**

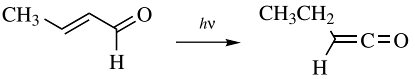
(31)

Photochemical isomerization of acrolein (**82**) to methylketene (**83**) by 193 nm light has been proposed[47–49]and examined by calculations.[50] Further photolysis of **83** to CH_3CH: and CO (equation 32) may compete with formation of C_2H_3 and CHO from **82**.[47] *E*-Crotonaldehyde (**84**) upon photolysis in the gas phase formed ethylketene (**85**), identified by its IR absorption at 2132 cm^{-1} (equation 33).[51,52] Photolysis of hydroxyacetone giving successive radical elimination via **86** forming ketene was studied computationally (equation 34).[53]



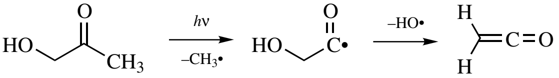
82 **83**

(32)



84 **85**

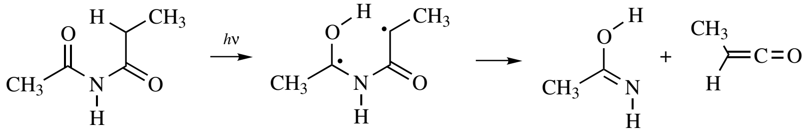
(33)



86 **73**

(34)

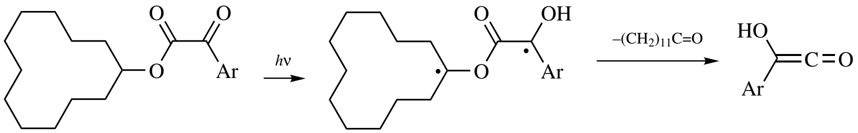
Photolysis of *N*-acetylpropanamide (**87**) in CH_3OD gave methyl propanoate containing one deuterium atom, thus implicating the formation of methylketene (**83**, equation 35).[54]



87 **83**

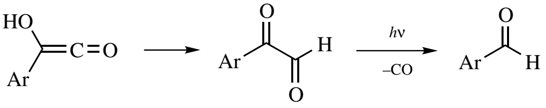
(35)

Photolysis of (2,4-dimethylbenzoyl)formate esters **88** resulted in formation of carbonyl compounds and hydroxyketenes **90** (equation 36).[56] The hydroxyketenes were proposed to tautomerize to aldehydes **91** that were photolyzed further to benzaldehydes (equation 37).[56]



88 **89** **90**

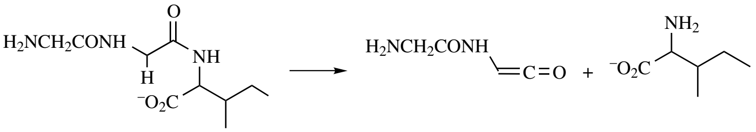
(36)



90 **91**

(37)

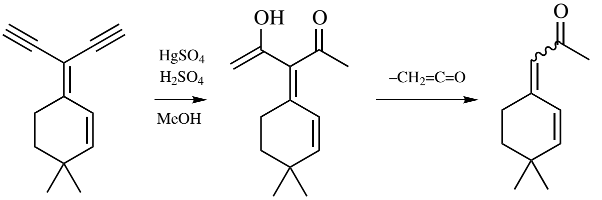
Gas phase collisional activation of deprotonated peptides **92** was proposed to give ketenes **93** (equation 38).[57]



92 **93**

(38)

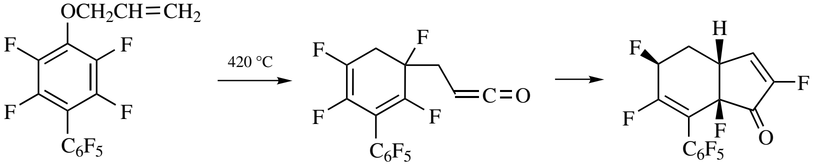
Hydration of 1,1-diethynyl diene **94** gave the dienone **96**, proposed to result from formal ketene elimination from the intermediate **95** (equation 39).[58]



94 **95** **96** (10%)

(39)

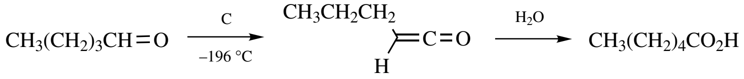
Pyrolysis of **97** at 420 °C gave **99**, proposed to form via ketene **98** in a multistep reaction (equation 40).[59]



97 **98** **99** (30%)

(40)

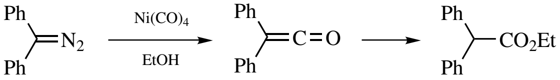
Carbon atoms reacted with butanal at –196 °C to form *n*-propylketene (**100**), as evidenced by the isolation of pentanoic acid after addition of H_2O (equation 41).[60] The reaction pathway was studied computationally.[60]



100

(41)

Diphenylketene **101** was formed from the reaction of diphenyldiazomethane with $Ni(CO)_4$ and trapped as the ester in 35–74% yields (equation 42).[61]



101

(42)

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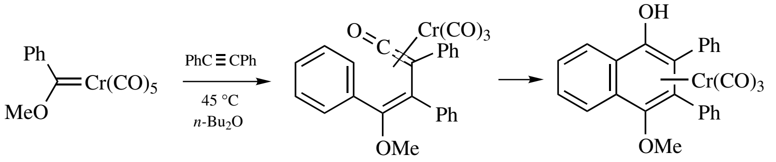
3.5 KETENES FROM METAL CARBENE COMPLEXES

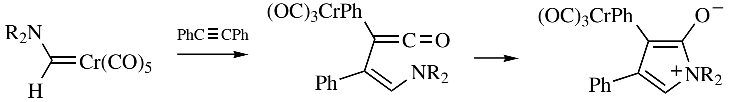
The discovery of the thermal reaction of chromium carbonyl carbene complexe **1** with alkynes leading to the formation of alkenylketene chromium complex **2**, which cyclized to naphthol complex **3**, was made by Dötz in 1975 (equation 1).[1] This process (Dötz reaction) was proposed to proceed through complex **2** on the basis of the reaction kinetics and the isolation of complexed products **3**.[2–5] The cyclization resembles a metal-complexed version of the cyclization of alkenylketenes generated from arylcyclobutenones (Smith-Hoehn reaction, Section 3.4.1), but the alkenylketene is assembled in situ (equation 1). This methodology has been frequently reviewed.[4–11]



(1)

1 **2** **3** (62%)

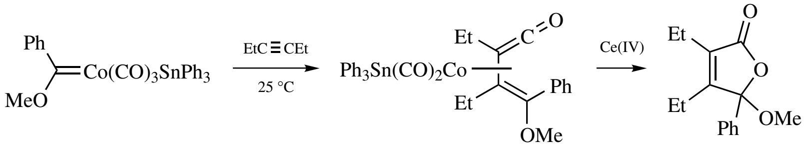
Reaction of the aminocarbene complex **4** with diphenylacetylene gave the zwitterion **6** with $Cr(CO)_3$ complexed to the phenyl, and the structure of this complex was determined by X-ray (equation 3).[12] Related complexes were obtained in yields of 48–80%.[12]



(2)

4 $R_2 = (CH_2)_5$ **5** **6** (60%)

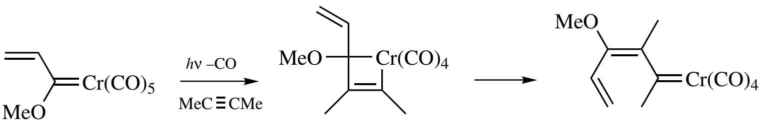
The cobalt complex **7** reacted with 3-hexyne at 25 °C to form the alkenylketene complex **8**, whose structure was determined by X-ray and which was oxidized by Ce(IV) to furanone **9** (equation 3).[13] These reactions also took place with molybdenum and tungsten complexes.



(3)

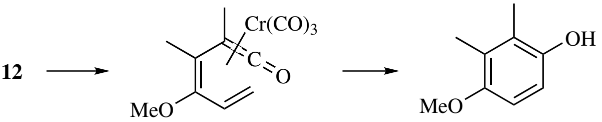
7 **8** **9** (58%)

A simplified mechanism has been presented[14] in which metathesis of the alkyne and a vinyl chromium complex **10** via complex **11** gives complex **12** (equation 4), which inserts CO to form the dienylketene complex **13**, which cyclizes to **14** (equation 5).



(4)

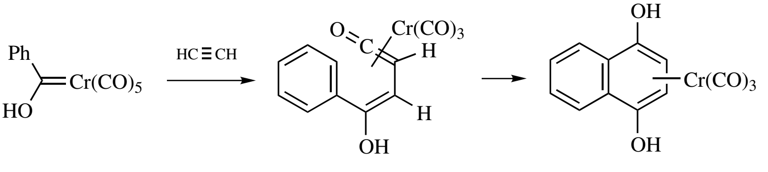
10 **11** **12**



(5)

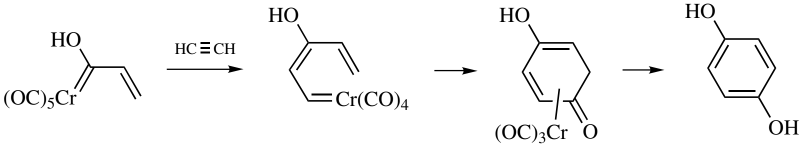
13 **14**

Density functional theoretical study of the reaction of aryl chromium carbene complex **15** with ethyne leading to complex **16**, which cyclized to naphthol **17** (equation 6), was used to elucidate the steps in the reaction.[15] However, other recent calculations have favored an alternative pathway reaction scheme in which complex **18** formed **19**, which cyclized to **20**, and the CO insertion occurred without the formation of a ketene complex (equation 7).[16,17]



(6)

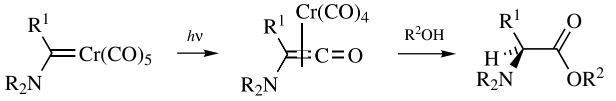
15 **16** **17**



(7)

18 **19** **20**

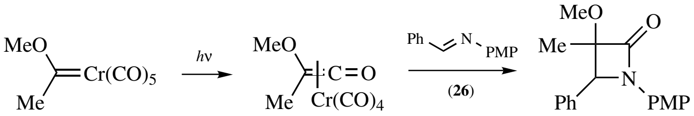
It was also found that photolysis of chromium carbene complexes with visible light gave species formulated as chromium complexes with ketenes, and that these species undergo typical ketene reactions including additions of nucleophiles, and [2 + 2] cycloadditions with imines forming β-lactams, and with alkenes forming cyclobutanones.[10,11] Thus, photolysis of aminocarbene chromium-complexes **21** with chiral auxiliaries on the nitrogen led to intermediate chromium complexed ketenes **22** that reacted with alcohols in an asymmetric synthesis of amino acid esters **23** (equation 8).[11] The mechanism has been studied computationally.[11a]



(8)

21 **22** **23**

Irradiation with visible light of the complex **24** formed the ketene complex **25** in the presence of imine **26** and gave the β-lactam **27** as a *cis/trans* mixture (equation 9).[18] A DFT study using B3LYP/6–31G* level computations found structures for the carbonylation of $(OC)_5Cr{=}CH_2$ forming the complex $(OC)_4Cr{\bullet}CH_2{=}C{=}O$, which formed a new complex with the imine $CH_2 = NH$ (Figure 3.1), and then the transition state for [2 + 2] cycloaddition.[18]



(9)

24 **25** **27**

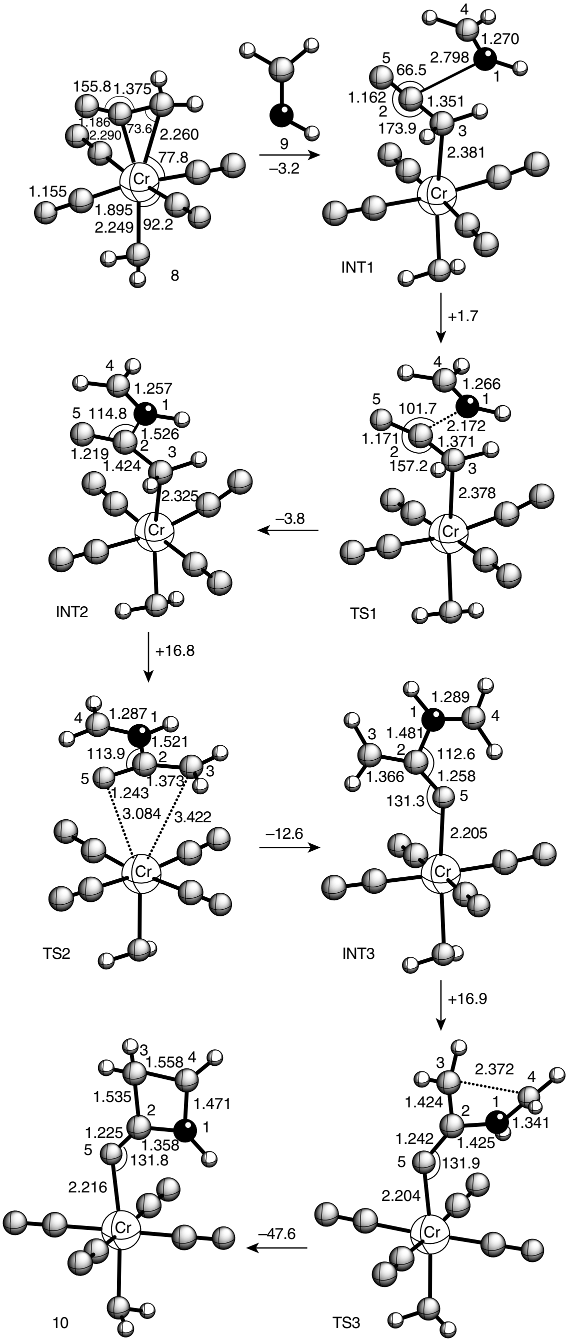
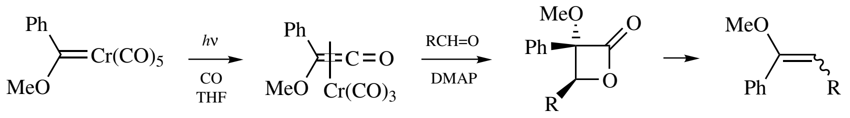


Figure 3.1 DFT-computed structures for reaction of ketene complex $(OC)_4Cr{\bullet}CH_2{=}C{=}O$ with imine $CH_2{=}NH$ (reproduced from ref. 18 with permission of the American Chemical Society).

Chromium-complexed ketene **29** from carbene complex **28** reacted with aldehydes, forming β-lactones **30** with significant *syn* selectivity (equation 10).[19] Electron-rich aldehydes (R = 4-anis, 2-furyl; 3-methyl-2-butenyl) gave alkenes **31** that resulted from decarboxylation of the β-lactones.[19]

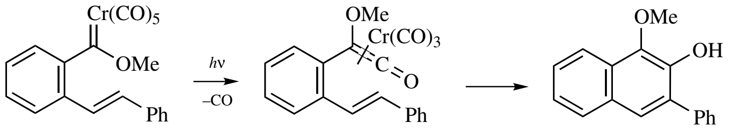


28 **29** **30** (33–55%, R = alkyl of Ph) **31** (43–61%, R = electron donor)

(10)

The UV photolysis of amine-substituted chromium carbene complexes in matrices at 12 K and with flash photolysis at room temperature resulted in CO loss, but ketene complexes were not observed.[20] This led to the conclusion that these complexes were not primary photoproducts but were formed in subsequent steps. Photolysis of the complex MeOCMe=Cr(CO)$_5$ (**24**) in argon and nitrogen matrices also showed no evidence of the formation of metal ketene complexes.[21]

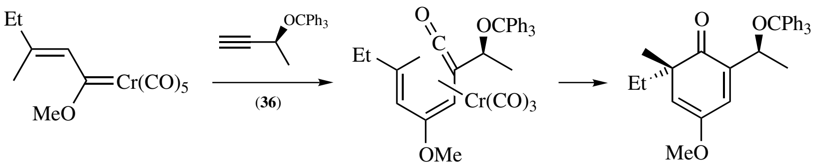
Photolysis of the complex **32** formed the ketene complex **43**, which cyclized to the naphthol **34** (equation 11).[22]



32 **33** **34** (42%)

(11)

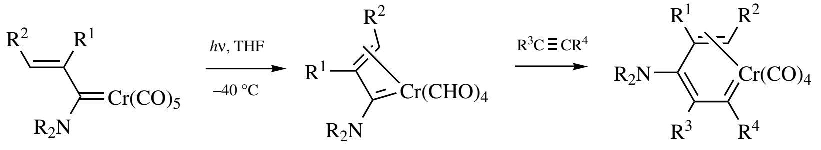
Reaction of complex **35** with the chiral alkyne **36** led to the ketene complex **37**, which gave the cyclohexadienone **38** with 92:8 *de* at the newly formed quaternary carbon (equation 12).[23]



35 **37** **38** (73%, 92:8 *de*)

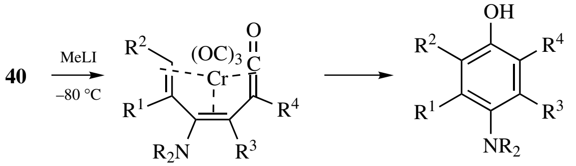
(12)

Experimental studies indicated that there was equilibration of regioisomeric vinyl carbene intermediates in benzannulation reactions.[24] The intermediates **39** and **40** formed from chromium carbene complex photolysis have been isolated and characterized at low temperature (equation 13) and led to typical phenolic products of Dötz reactions (equation 14).[25]



39 **40**

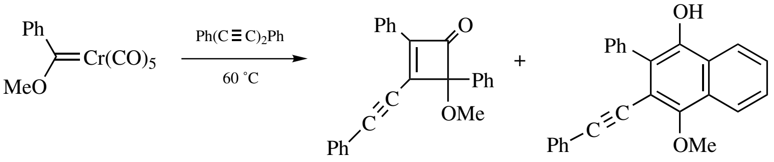
(13)



41 **42**

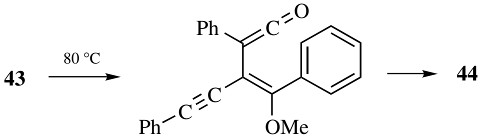
(14)

The reaction of carbene complex **28** with diynes led to mixtures of cyclobutenones **43** and naphthols **44** at 60 °C (equation 15), and heating of **43** at 80 °C also gave **44** (equation 16).[26] This latter process evidently involved the vinylketene **45**, suggesting that the formation of **44** from **43** may be metal assisted (equation 16).



28 **43** **44**

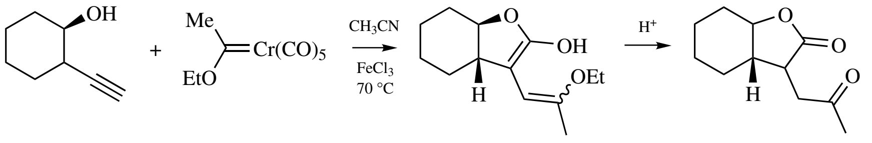
(15)



45

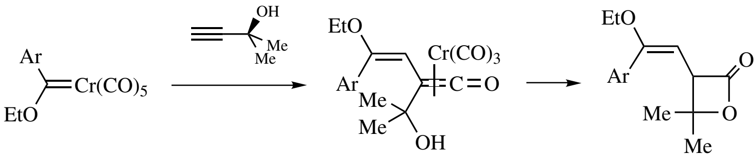
(16)

Reaction of hydroxyalkynylalkane **46** with chromium carbene complex **47** gave lactone **49**, which was used in natural product synthesis (equation 17).[27] Propargylic alcohols gave thermal reactions with chromium carbene complexes **50** to form β-lactones **52** in processes suggested to involve ketene complexes **51** (equation 18).[28] This reaction was found to be assisted by sonication.[29,30]



46 **47** **48** **49** (85%, 92:8 *dr*)

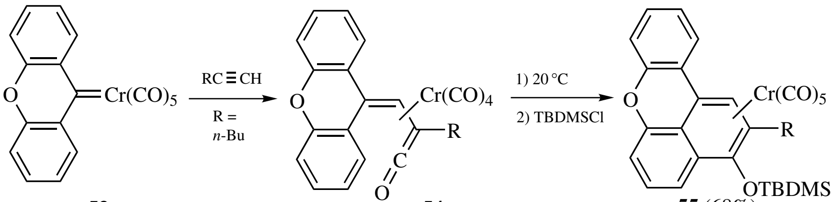
(17)



50 Ar = 2,6-$MeOC_6H_3$ **51** **52** (72%)

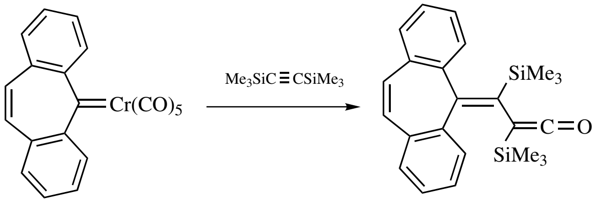
(18)

Chromium complex **53** and related derivatives prepared from the corresponding diazo compounds reacted with 1-hexyne via ketene complexes **54** to form **55** (equation 19).[31] Reaction of **56** with bis(trimethylsilyl)acetylene gave the ketene **57** with an IR band at 2077 cm^{-1}, isolated in 22% yield as the methyl ester (equation 20).[32]



53 **54** **55** (68%)

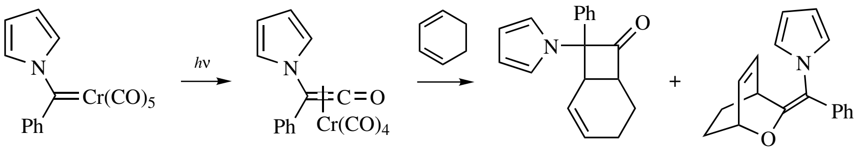
(19)



56 **57** (22%, IR 2077 cm^{-1})

(20)

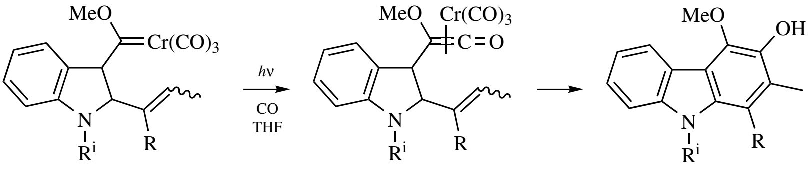
Chromium carbene complex **58** with a pyrrole substituent gave similar benzannulation reactions with alkynes, as well as ketene [2 + 2] cycloaddition with cyclohexadiene, forming **59** together with an unusual [4 + 2] reaction across a ketene carbonyl forming **60** (equation 21).[33]



58 **59** **60** (24%) **61** (18%)

(21)

3-(2-Vinyl)indolylcarbene complexes **62** gave ketene complexes **63**, which formed carbazole derivatives **64** used in the synthesis of carbazoquinocin (equation 22).[34]



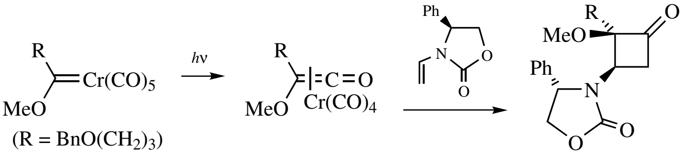
62 (R = *n*-Hp
R^1 = Bn, 4-MeOBn

63

64
(62–65%)

(22)

Photolysis of chromium carbene complex **65** in the presence of optically active ene carbamates proceeded through stereoselective [2 + 2] cycloaddition of ketene **66** to give cyclobutanone **67**, which was converted to a butenolide (equation 23).[35]



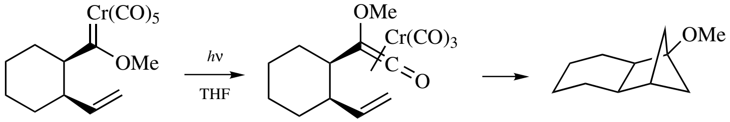
65

66

67 (58%,
92% de)

(23)

Intramolecular [2 + 2] cycloaddition of ketene intermediates **69** from chromium carbene complex **68** formed the bicyclo[2.1.1]hexane derivative **70** (equation 24).[36] Reaction between carbene complex **24** and diene-yne **71** gave ketene **72**, which formed bicyclo[3.1.1[heptan-6-ones **73** as a possible taxane A-ring synthon, in a 2:1 ratio with a cyclobutenone from [2 + 2] cycloaddition (equation 25).[36]

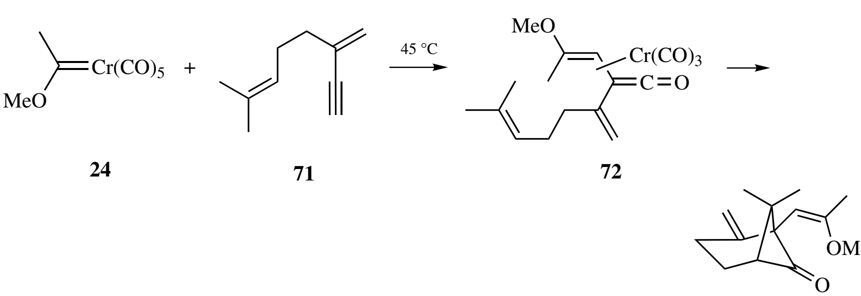


68

69

70 (78%)

(24)



24

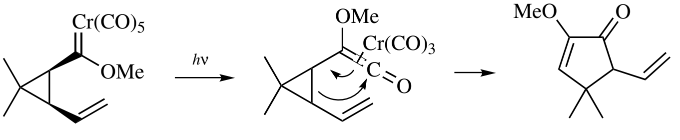
71

72

73 (63%)

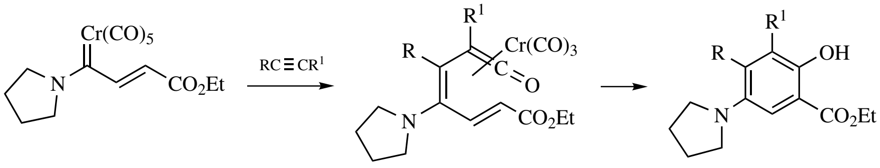
(25)

Vinylcyclopropyl carbene complex **74** gave a vinylcyclopropane rearrangement of the intermediate cyclopropylketene complex **75** to form cylopentenone **76** (equation 26).[36] A Dötz benzannulation reaction of a vinylcarbene complex was used as a step toward the the synthesis of kendomycin.[38] Carbene complex **77** with an alkenyl side chain bearing an electron withdrawing group formed ketenes **78**, which gave efficient cyclization to phenols **79** (equation 27).[39]



74 **75** **76** (83%)

(26)



77 **78** **79** (57–95%)

(27)

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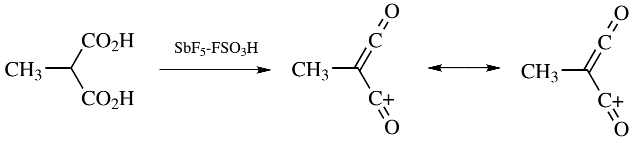
3.6 KETENE FORMATION FROM CATIONS AND FREE RADICALS

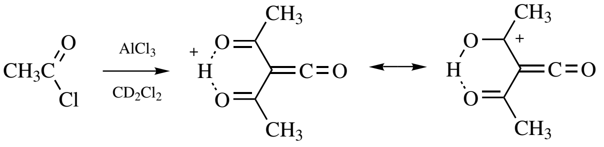
Ketenes are reactive toward acids, and their formation as recognizable intermediates in the presence of acids is rare. An exception occurs where intermediates with acylium ion character are formed, as in the reaction of methylmalonic acid or the dimethyl ester in SbF_5-FSO_3H forming **1**, as identified by the IR absorption at 2150 cm^{-1} and the ^{1}H NMR signal at δ 3.05 (equation 1).[1]



(1)

1 (IR 2150 cm^{-1})

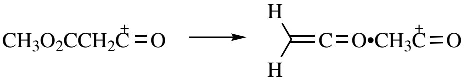
Acetyl chloride with $AlCl_3$ in CD_2Cl_2 formed protonated diacetylketene tetrachloroaluminate (**2**), which was characterized by IR absorption at 2100 cm^{-1} and by ^1H and ^{13}C NMR (equation 2).[2] Polyketenes are formed from acyl halides under similar conditions in reactions proposed to involve an equilibrium between ketene and acylium ions (Section 5.6).[3]



2 (IR 2100 cm^{-1})

(2)

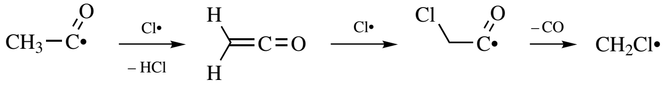
Gas phase dissociation of the malonate-derived cation **3** led to the ion-neutral complex **4** of ketene and acetylium ion (equation 3).[4]



3 **4**

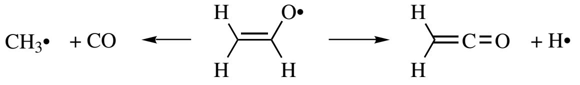
(3)

Ketenes are quite reactive toward free radicals, but there are reports of ketene formation from radical processes. Thus, kinetic measurements for the formation of ketene from the reaction of Cl• with acetyl radical **5** were obtained by IR spectroscopy, as well as the rate constant for Cl• addition to ketene forming chloroacetyl radical **6** (equation 4).[5] The vinyloxy radical **7** forms CH_3• and ketene by competitive processes (equation 5).[6] Other examples of ketene formation from $CH_3C(\bullet) = O$ (**5**) are given in Section 3.4.6.



5 **6**

(4)



7

(5)

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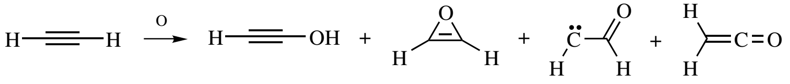
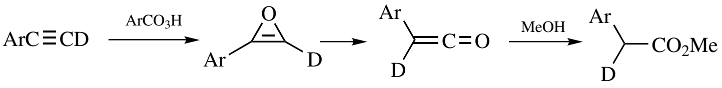
3.7 KETENES FROM OXIDATION OF ALKYNES

Ketene (**4**) is known to be formed by the oxidation of acetylene in a reaction important in studies of combustion, for which many steps are involved.[1] A DFT computational study examined this process and included the sequence of oxygen atom insertion into a C—H bond of acetylene forming ethynol (**1**), as well as addition to the triple bond forming oxirene (**2**) and formylcarbene (**3**), and the rearrangement of these species to ketene (equation 1).[1]



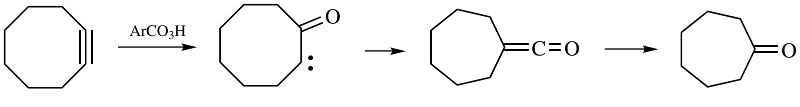
1 **2** **3** **4** (1)

Oxidation of arylalkynes with peracids was postulated to form ketenes, and reaction of 2-deuterobiphenylylacetylene **5** with *m*-chlorobenzoic acid in methanol gave the methyl ester **8**, consistent with formation of the oxirene **6** and the ketene **7** (equation 2).[2]



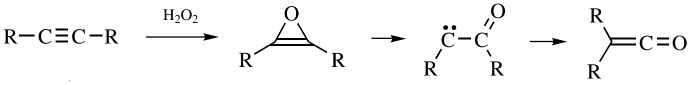
5 (Ar = PhC_6H_4) **6** **7** **8** (2)

Peracids oxidized phenylacetylene and diphenylacetylene to mixtures including ketene-derived products.[3,4] Similar reactions of cycloalkynes including cyclooctyne **9** gave products derived from keto carbene **10** and rearrangement to ketene **11**, which was further oxidized to cycloheptanone **12** (equation 3).[5]



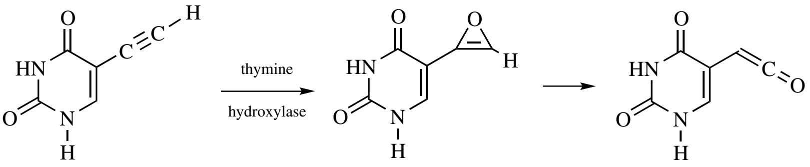
9 **10** **11** **12** (22%) (3)

The oxidation of alkynes **13** by H_2O_2 catalyzed by methylrhenium trioxide (CH_3ReO_3) formed α-diketones and carboxylic acids from reactions interpreted as involving oxirene intermediates **14** that underwent partial rearrangement via ketocarbenes to ketenes (equation 4).[6] Alkyne oxidation with the HOF•CH_3CN complex also gave products indicative of intermediate oxirene formation.[7]



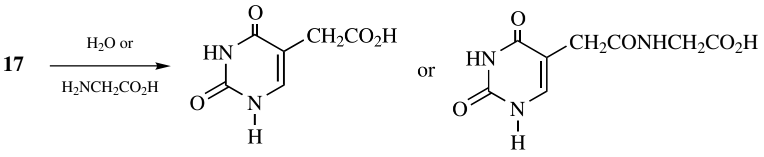
13 **14** (4)

Incubation of thymine hydroxylase with 5-ethynyluracil (**15**) gave 5-(carboxymethyl)uracil (**18**) and uracil-5-acetylglycine **19** and resulted in inactivation of the protein by covalent modification.[8,9] The formation of **18** and **19** was proposed to result from formation of an oxirene **16** and a ketene **17** (equations 5, 6). The protein inactivation resulted from reaction with the ketocarbene.



15 **16** **17**

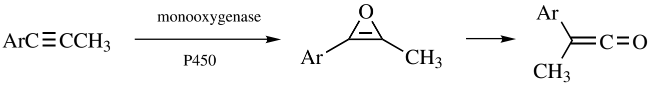
(5)



18 **19**

(6)

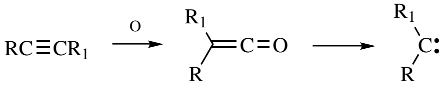
Arylpropynes $ArC{\equiv}CCH_3$ **20** acted as mechanism-based inhibitors of cytochrome P450-dependent monooxygenase enzymes, and were proposed to function by formation of oxirenes **21** that formed ketenes **22** by 1,2-methyl migration, as evidenced by the isolation of 2-arylpropionic acids (equation 7),[10] as had been proposed earlier.[11]



20 **21** **22**

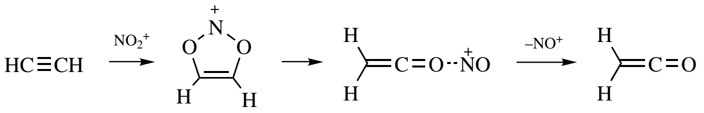
(7)

The reaction of alkynes **23** with oxygen atoms in the gas phase proceeded by formation of ketocarbenes that formed excited ketenes **24**, which then underwent decarbonylation, forming carbenes **25** (equation 8).[12] The photo-reaction of ethyne and propyne complexes with NO_2 in solid argon led to transfer of an oxygen atom and formation of $CH_2{=}C{=}O$ and $CH_3CH{=}C{=}O$, respectively, followed by decarbonylation, as monitored by FTIR.[13] Gas phase reaction of NO_2^+ with acetylene formed *O*-nitrosonium ion ketene complex **26**, which dissociated to ketene (equation 9).[14] Several pathways to this product were examined computationally.



23 **24** **25**

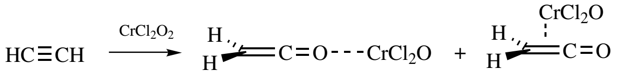
(8)



26

(9)

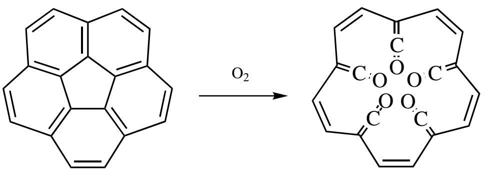
Acetylene reacted with $CrCl_2O_2$ in a matrix, and IR bands were observed at 2105 and 2195 cm^{-1}, and assigned to the end-on ketene complex **27** and the more stable ketene complex **28** with the C=C bond (equation 10).[15]



27 (IR 2105 cm^{-1}) **28** (IR 2195 cm^{-1})

(10)

Computational studies of possible products $C_{60}O_n$ that conceivably could be formed by the oxidation of the fullerene C_{60} included pentaketene $C_{60}O_5$ and hexaketene $C_{60}O_6$.[16] These were not among the more stable isomers but $C_{60}O_5$ was esthetically interesting, as illustrated for oxidation of the pentabenzocyclopentyl unit fragment of C_{60} **29** forming **30** (equation 11).[16]



29 **30**

(11)

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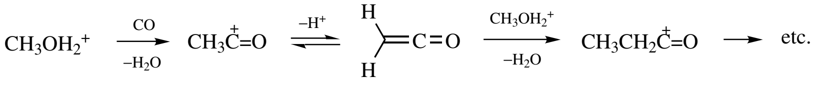
3.8 OTHER ROUTES TO KETENES

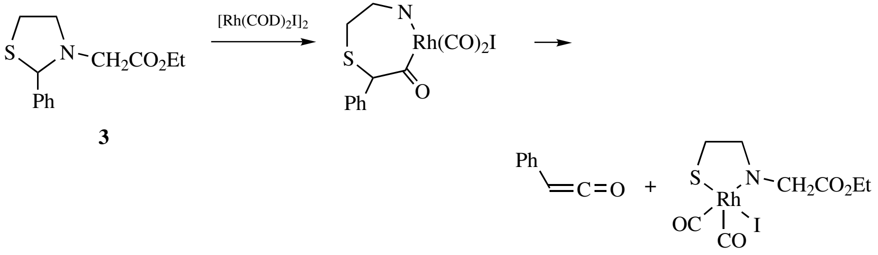
Ketene has been proposed as an intermediate in the H-ZSM-5 zeolite-catalyzed conversion of methanol to gasoline.[1] The mechanism put forward proceeded with generation of CO, which reacted with activated methanol, forming acylium ion **1**, which was reversibly deprotonated (equation 1).[1] Further conversion to higher acylium ions and ketenes occurred succesively, resulting in the formation of higher hydrocarbons. Ketene was also implicated by trapping as an intermediate in the conversion of synthesis gas to ethanol using Rh-Ti/SiO_2.[2,3] Reaction of $CH_2{=}CHCH{=}O$ on a Pt surface also formed some $CH_2{=}C{=}O$, together with some propene.[4,5] Metal oxide–catalyzed conversion of acetic acid to acetone was suggested to involve ketene formation on the catalyst surface.[5a]



1 **2**

(1)

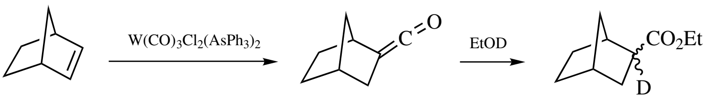
Ketene formation from the reaction of 1,3-thiazolidine **3** with CO in the presence of chloro(1,5-cyclooctadiene)rhodium(I) dimer and KI was shown to give elimination of phenylketene (**4**) in 8–10% yields, as evidenced by the observation of a ketene band at 2163 cm^{-1} in the IR, and capture as the ester with MeOH (equation 2).[6]



3 **4**

(2)

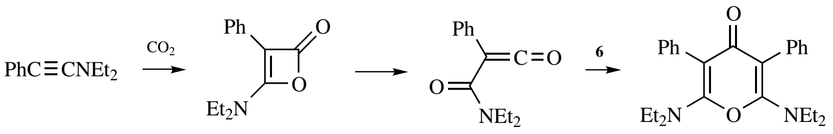
The formation of norbornylideneketene **5** during the ring-opening polymerization of norbornene using $W(CO)_3Cl_2AsPh_3)_2$ was demonstrated by trapping with EtOD (equation 3).[7]



5

(3)

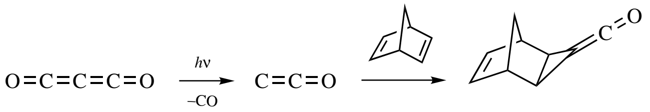
Ynamine **6** reacted with CO_2 and was proposed to form the unsaturated β-lactone **7**, which gave the acylketene **8** resulting from [2 + 2] cycloaddition, and reaction with a second molecule of **6** gave the observed product **8a** (equation 4).[8–10] Reactions of bis(ynamines) gave polymerization to poly(4-pyrones).[8]



6 **7** **8** **8a** (81%)

(4)

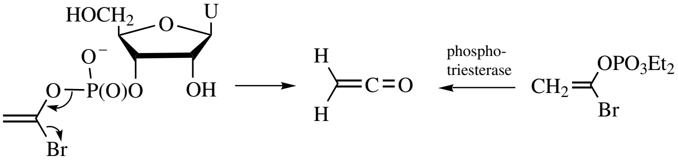
Formation of ketene **11** by addition of the carbene C=C=O (**10**) formed by photolysis of C_3O_2 (**9**) to norbornadiene has been suggested (equation 5).[11] No direct evidence for **11** was obtained, and further photolysis led to formation of a C_8H_8 hydrocarbon.[11] Other reactions of **10** forming ketenes are discussed in Section 4.11.



9 **10** **11**

(5)

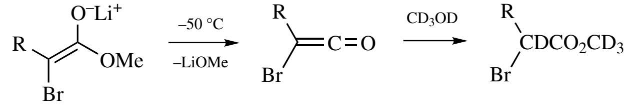
The possibility of formation of ketene (**2**) by α-elimination from α-bromoenol phosphates **12** by a mechanism-based inhibitor of ribonuclease A[12] and from **13** by inhibition of phophotriesterase has been considered (equation 6).[13]



12 **2** **13**

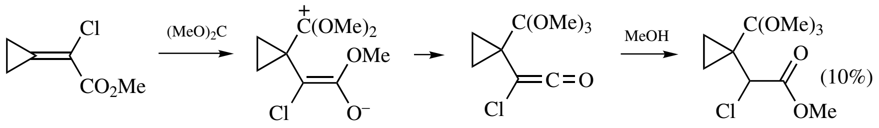
(6)

The α-elimination of methoxide from α-bromo ester enolate **14** forming ketene **15** was shown to occur by capture of the deuterated ester **16**, although to a small extent (equation 7).[14] The reaction of **17** with dimethoxycarbene to form **19** was proposed to involve formation of a ketene **18** by methoxide rearrangement (equation 8).[15] Gas phase α-elimination by collision-induced dissociation of **20** to form methylketene **21** has been observed (equation 9).[16]



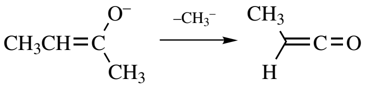
14 (R = n-C$_{14}$H$_{29}$) **15** **16** (6%)

(7)



17 **18** **19**

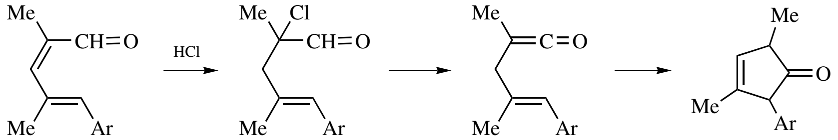
(8)



20 **21**

(9)

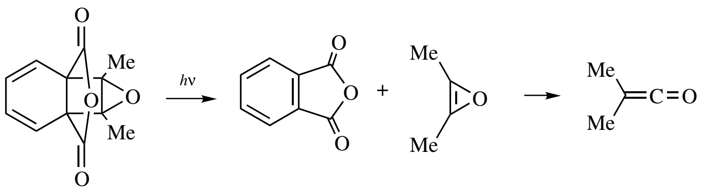
Reaction of the aldehyde **22** with concentrated HCl has been proposed to form the ketene **23** as an intermediate observed by ^{1}H NMR in THF through an addition/elimination sequence, leading to the ketone **24** (equation 10)[17] However, such an elimination appears unusual, and other mechanisms are possible, so further proof of the intermediacy of ketene **23** is required.



(Ar = 4-O$_2$NC$_6$H$_4$)
22 **23** **24**

(10)

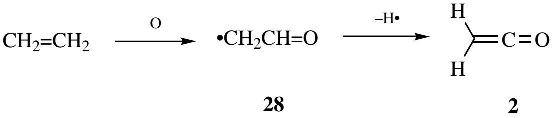
Photolysis of **25** in a matrix gives Me$_2$C=C=O (**27**), possibly through the oxirene **26** (equation 11).[18]



25 **26** **27**

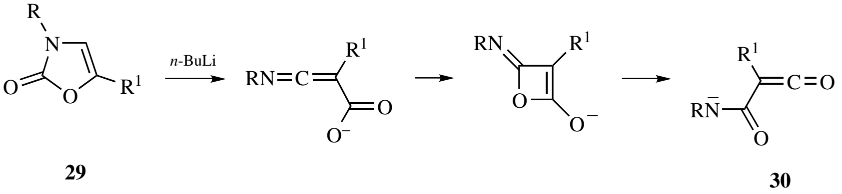
(11)

The formation of $CH_2{=}C{=}O$ (**2**) in the pyrolysis and oxidation of CH_4[19] and of $CH_2{=}CH_2$[20] has also been considered. Studies on oxidation of $CH_4/CH_2{=}CH_2$ mixtures using FTIR and UV detection, and including a reevaluation of previous results, gave strong evidence for ketene formation by the IR band observed at 2152 cm^{-1}, and also indicated that the formation of ketene was usually underestimated due to loss of ketene in sampling.[21] Ketene formation was also implicated in the oxidations of alkenes and alkynes, including combustion reactions. For example, ketene has been proposed as an intermediate in the reaction of acetylene with ozone,[22–24] and reaction of ethylene with oxygen atoms could form the enolic radical **28**, which gave ketene (equation 12).

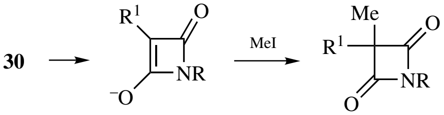


(12)

Reaction of isoxazol-5(2*H*)-ones **29** with bases was proposed to form ketene intermediate **30** (equation 13), which reacted with amines or cyclized and was trapped with CH_3I (equation 14).[25]

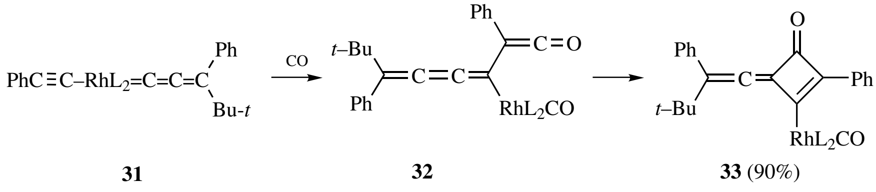


(13)



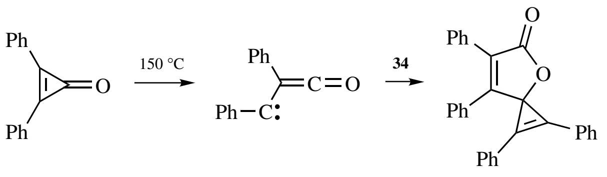
(14)

Reaction of **31** with CO, giving a possible ketene intermediate **32**, was proposed in the formation of **33** (equation 15).[26]



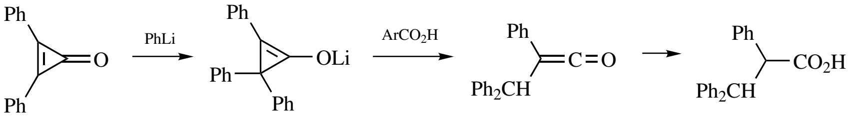
(15)

Thermolysis of diphenylcyclopropenone **34** gave a dimer with the probable structure **36**, which may have formed by ring opening to carbene-substituted ketene **35**, which reacted with **34** to form **36** (equation 16).[27] Addition of phenyllithium to **34** led to the formation of ketene **37** upon acidification, as evidenced by observation of the IR absorption at 2100 cm^{-1}, and isolation of the acid **38** (equation 17).[28] Reaction of **34** with Ph_3P gave ketene **39**, identified by formation of the methyl ester **40** (equation 18).[29]



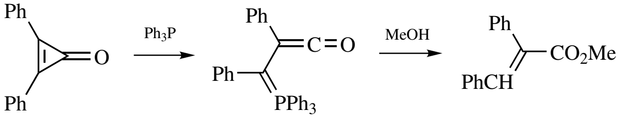
34 **35** **36** (40%)

(16)



34 **37** (IR 2100 cm^{-1}) **38** (18%)

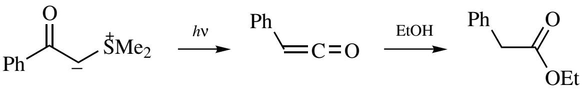
(17)



34 **39** **40**

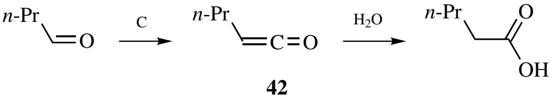
(18)

Phenylketene (**4**) was generated in EtOH by a Wolff-type rearrangement of the sulfur ylide **41** and isolated in 26% yield as the ethyl ester (equation 19).[30] Reaction of *n*-butanal with carbon atoms and hydrolysis gave some pentanoic acid, indicative of formation of *n*-propylketene **42** by insertion into the C=O bond (equation 20).[31]



41 **4**

(19)



42

(20)

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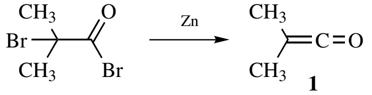
4 Types of Ketenes

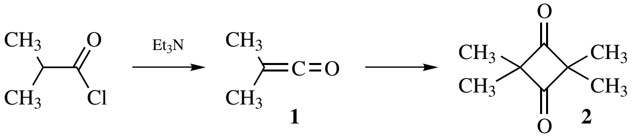
4.1 CARBON-SUBSTITUTED KETENES

4.1.1 Alkylketenes

The first report of an alkylketene was the preparation of dimethylketene (**1**) by Staudinger in his second publication on ketenes, which utilized the dehalogenation of α-bromoisobutyryl bromide (equation 1).[1] However, as acknowledged by Staudinger in this report, **1** had probably already been generated, but not identified, in studies by Wedekind and Weisswange, as reported in an unpublished dissertation in 1904.[1] In this study the reaction of isobutyryl chloride with triethylamine formed the dimer **2**.

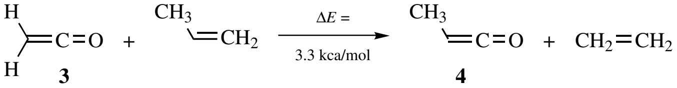


(1)



(2)

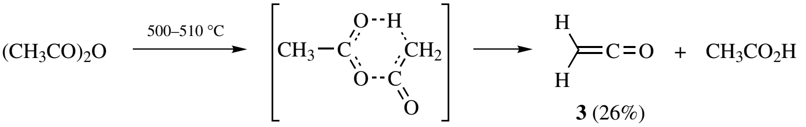
The parent ketene $CH_2{=}C{=}O$ (**3**) is included in the alkylketene family, and the thermodynamic stability of ketene and methylketene (**4**) compared to the corresponding alkenes was found by the isodesmic comparison of equation 3.[2,3] This indicated some thermodynamic destabilization compared to the alkene for methylketene (**4**), but although both ketene and methylketene dimerize readily, they do have some stability in solution and even briefly as neat liquids. This is in contrast to arylketenes such as phenylketene, which dimerize much more rapidly.



(3)

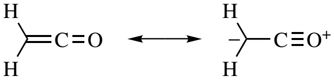
Ketenes II, by Thomas T. Tidwell

Ketene (**3**) is a noxious gas that was first prepared by Wilsmore in 1907[4] from the pyrolysis of acetic anhydride with a hot platinum wire through a likely cyclic transition state, and this method is still used today (equation 4).[5] Ketene was then prepared by Staudinger and Klever in low yield by the zinc dehydrohalogenation of bromoacetyl bromide with zinc.[6] There was some discussion as to whether ketene had the $CH_2{=}C{=}O$ structure or the alkynol structure $HC{\equiv}COH$, but this was soon decided in favor of the former.[7,8] The structure of ketene has been determined both by computations[9–11] and by microwave spectroscopy.[11,12] The preparation, properties, and uses of ketene have been reviewed.[13,14]



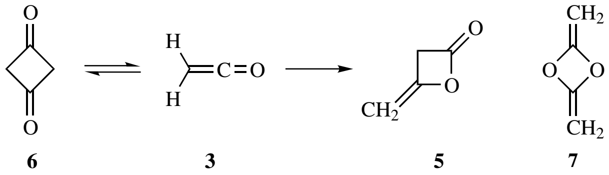
(4)

The ^1H NMR signal of ketene was reported as δ 2.47 (neat), $J_{H\text{-}H'} = 15.8$ Hz[15] and δ 2.46 ($CDCl_3$).[16] The large value for $J_{H\text{-}H'}$ compared to that for $CH_2{=}CH_2$ (2.2 Hz) was attributed to favorable hyperconjugative interactions of the C—H bonds in ketene with the carbonyl π bond.[15] The ^{13}C NMR shifts are δ 194.0 for C_1 (the carbonyl carbon) and 2.5 for C_2, $J_{C\text{-}H} = 171.5$ Hz.[17] The finding that the dipole moment of 1.45 D was less than those of formaldehyde and acrolein ($CH_2{=}CHCH{=}O$) of 2.27 and 3.04 D, respectively, led to the proposal of the importance of the resonance structure **3a** for ketene, with negative charge on C_2.[18,19] The remarkably high field ^{13}C chemical shift of this carbon gives vivid evidence of this effect. The distinctive ketenyl IR band was also found to vary with the medium, ranging from 2151, 2142, and 2133 cm^{-1} in the vapor, the argon matrix, and the solid, respectively.[20] The absorption of ketene in the Raman spectrum was observed at 2150 cm^{-1}.[21] The UV spectrum displayed the C=C π → π* band at 183 nm, the C=O π → π* band at 215 nm, and the n → π* band at 325 nm.[22]

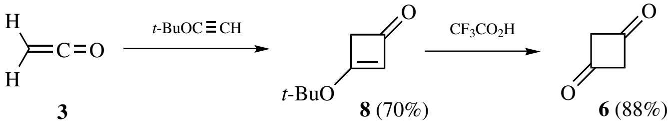


3 **3a**

On standing ketene forms the β-lactone dimer **5**, known as diketene, as the major product (equation 5). The debate about the structure of this material lasted for more than 40 years, and was finally settled as the structure **5** by a combination of chemical studies,[23] electron diffraction,[24] microwave spectroscopy,[25] and X-ray crystallography. [26,27] The β-lactone dimer **5** is a valuable chemical intermediate.[28,29] The dimerization was examined computationally,[30–32] and the diketone dimer **6** was calculated to be 1 kcal/mol more stable than the β-lactone **5**,[30] but as noted below, a later computation reversed this order. The unknown vinyl ether dimer **7** was predicted to be 32 kcal/mol less stable but capable of existence.[30] The diketone dimer **6** was prepared by hydrolysis of the cyclobutenone **8** (equation 6).[33]



(5)

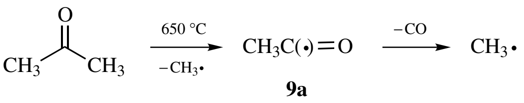


(6)

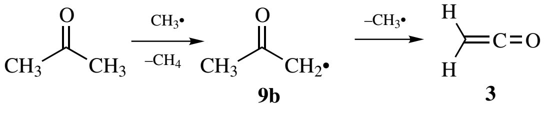
Dimerization in the absence of catalysts forms the isomeric dimers **5** and **6** in a 95:5 ratio.[34] This process has been studied further using *ab initio* molecular dynamics calculations, which led to the conclusion that the formation of the β-lactone dimer **5** is the result of thermodynamic control and that the formation of 1,3-cyclobutanone **6** has a lower barrier (equation 5).[35] Formation of the β-lactone dimer **5** has a calculated barrier of 31.5 kcal/mol and a free energy change of −5.5 kcal/mol, while formation of 1,3-cyclobutanedione **6** has a barrier of 26.4 kcal/mol and a free energy change of −4.5 kcal/mol.[35] This is contrary to the results of previous calculations, which predicted a lower barrier for forming **5** and greater stability of **6** compared to **5**.[30,36] In view of the known preference for formation of **5** it appears this is more stable, and has a lower barrier to its formation.

All ketenes react with nucleophiles, and the volatile parent is especially obnoxious and toxic.[13,14,37] *This compound should be regarded as highly dangerous and handled with care in a well-ventilated fume hood.*

Pyrolysis of acetone is an alternative laboratory procedure for the preparation of ketene, with heating of the acetone with burners in a glass tube[38,39] or with a metal filament (Hurd lamp).[40] This process occurs through a free radical chain mechanism involving the radicals **9a** and **9b** (equations 7, 8).



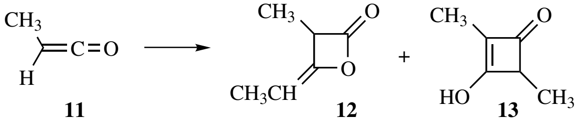
(7)



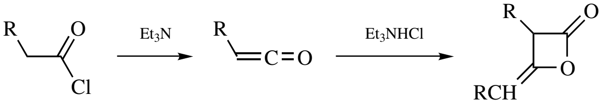
(8)

Alkylketenes usually have a light green or yellow color, and for *tert*-butylketene (**10**) this may be ascribed to the UV λ_{max} at 360 nm due to the n-π^* transition of the carbonyl.[22] The C=C absorption of alkylketenes is strong near 220 nm.[40a]

Monoalkylketenes typically undergo dimerization, and both methylene-β-lactone dimers and 1,3-diketone dimers are known. For methylketene (**11**) the structures of the lactone dimer **12** and the enolized diketone dimer **13** were established in 1950 by Woodward and Small (equation 9).[40b] Lactone dimers are formed by dehydrochlorination of acyl chlorides with triethylamine (equation 10),[41–44] and it has been suggested[45] that their formation is catalyzed by triethylamine hydrochloride, whereas the uncatalyzed reaction leads to 1,3-diketone dimers. Dimerization of methylketene (**11**)[46–48] with a chiral catalyst has been carried out with high stereoselectivity (Section 5.9).[48] The β-lactone dimers made from long-chain fatty acids have widespread application in paper sizing.[13]

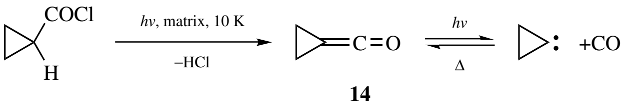


(9)

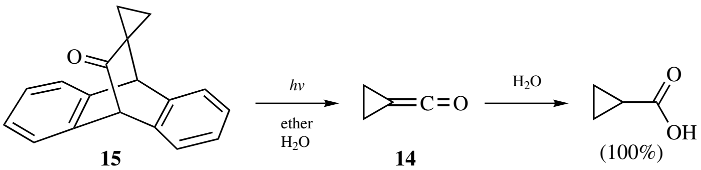


(10)

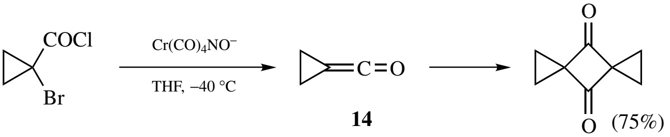
Cyclopropylideneketene (**14**) is a highly reactive species that has been observed in a solid argon matrix.[49] Photolysis of cyclopropanecarbonyl chloride in the matrix showed the presence of **14** by IR absorption at 2135 and 2154 cm^{-1}, and further photolysis caused dissociation to the carbene and CO, which reverted to the ketene thermally (equation 11).[49] Photolysis of the anthracene derivative **15** gave **14** in high yield (equation 11a).[50] Dehydrohalogenation with highly reduced metals also gave **14**, which was not observed but formed the dimer **15** (equation 12).[51] Dehalogenation of **16** with Zn/Ag gave tetramethylcyclopropylideneketene **17**, characterized as the dimer **18** (equation 13).[52,53]



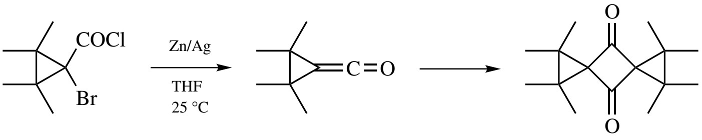
(11)



(11a)



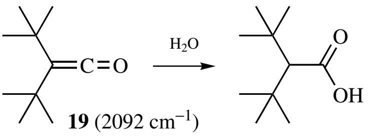
(12)



16 **17** **18** (50%)

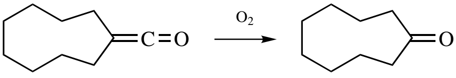
(13)

In contrast to the highly reactive **14**, di-*tert*-butylketene (**19**) is stable indefinitely as a neat liquid[54] and undergoes hydration rather slowly in pure water (equation 14),[55] although the reaction is catalyzed by acid.[56] The difference in the C—C—C bond angles of **19** and **14** is reflected in the difference in their ketenyl IR spectra, at 2092 cm^{-1} in the matrix[57] and 2090 cm^{-1} (film)[58] for **19** and at 2135 and 2154 cm^{-1} for **14**.[49] The low frequency for **19** is similar to that for octamethyleneketene (**20**) of 2095 cm^{-1} in CCl_4.[59] However, while **19** is apparently unreactive in air, **20** is readily oxidized to the ketone (equation 15).[59]



19 (2092 cm^{-1})

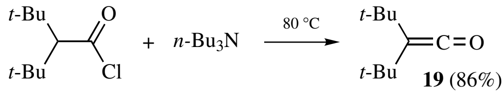
(14)



20 (IR 2095 cm^{-1})

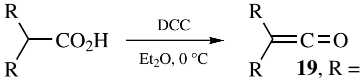
(15)

Di-*tert*-butylketene has been prepared by ultrasound-assisted dehydrochlorination of the acyl chloride with Et_3N,[60] dehydrochlorination with n-Bu_3N (equation 16),[58] dehalogenation of the α-chloroacyl bromide,[61] and dehydration of the acid with dicyclohexylcarbodiimide in a procedure also used to form di-1-adamantylketene **21** (equation 17).[62] Although preparation of **19** by the photochemical Wolff rearrangement in solution was inefficient, this was successful in the gas phase, in 40% yield, with the IR absorption at 2100 cm^{-1} (equation 24, vide infra).[63] This ketene has served as a valuable substrate for spectroscopic studies and for measurement of reactivity, including addition of electrophiles,[56] nucleophiles,[55] and an imine in [2 + 2] formation of a β-lactam.[64]



19 (86%)

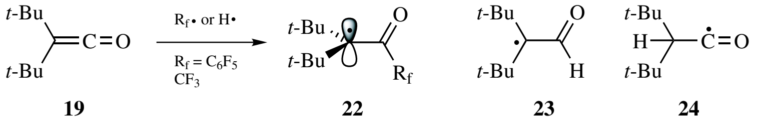
(16)



19, R = *t*-Bu (70%)
21, R = 1-Adamantyl (74%)

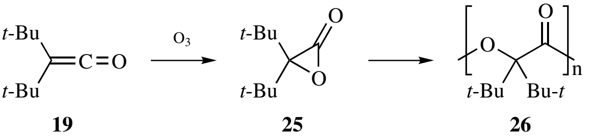
(17)

Di-*tert*-butylketene (**19**) reacted with perfluoroalkyl radicals at C_1, giving radicals that from their ESR spectra are interpreted as having perpendicular geometries **22** (equation 18).[65] Adducts of hydrogen atoms derived from HI adding to both C_1(**23**) and C_2 (**24**) of the ketene were also observed.[65] The radical **23** had a planar structure, and in **24** the C-H bond at C_2 was perpendicular to the singly occupied orbital (equation 18).[65]



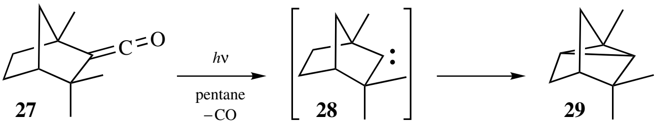
(18)

Reaction of ozone with di-*tert*-butylketene (**19**) at −78 °C gave a product in solution assigned as the α-lactone **25** on the basis of the ^{1}H NMR signal at δ 1.2 and the formation of polyester **26** upon warming (equation 19).[66]



(19)

The persistent bicyclic ketene **27** upon photolysis in hydrocarbon solvents gave the tricyclane **29**, evidently via decarbonylation to the carbene **28** and intramolecular insertion (equation 20).[67] Photolysis of **27** in CH_3OD at −60 °C formed **29** and the deuterated aldehyde **32** in a 1:1 ratio. The formation of **32** implicated photoprotonation of the ketene on the carbonyl carbon forming **30** and rearrangement to the carbocation **31** (equation 21).[67]



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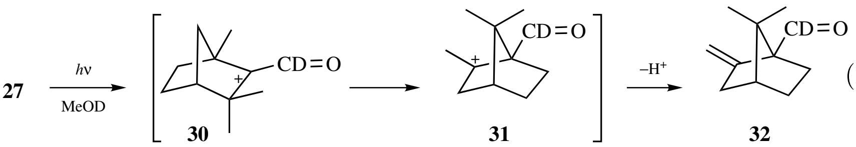
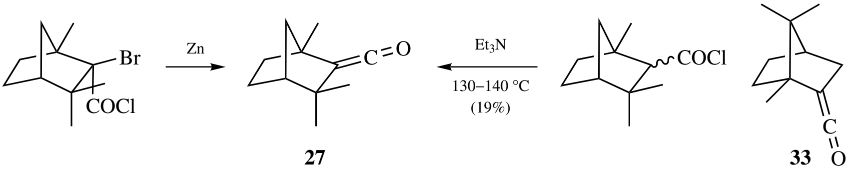


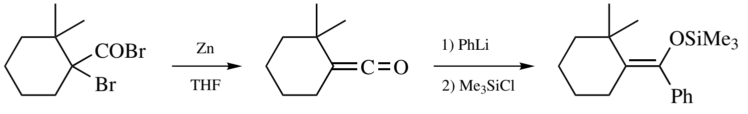
(21)

Ketene **27** was prepared by dehydrochlorination, as described in Section 3.2.2,[67] as well as by dehalogenation (equation 22).[68] The crowded camphorketene (**33**)[67] and **34** (equation 23)[69] have also been prepared by zinc dehalogenation. The latter ketene was reacted with phenyllithium and gave stereoselective addition from the least hindered side, forming **35** (equation 23).[69]



27 **33**

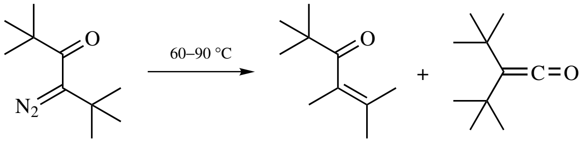
(22)



34 **35** (56%)

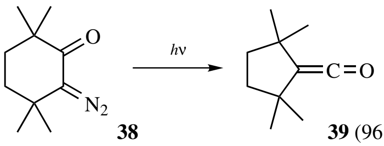
(23)

The low yield of di-*tert*-butylketene from thermolysis of diazo ketone **36** in which methyl migration forming the alkene **37** predominated arises from the unfavorable geometry for Wolff rearrangement in the conformation **36** in which the potential migrating group is *syn* to the departing N_2 (equation 24),[70] in contrast to the efficient formation of **39** from **38**, in which the migrating group is *anti* (equation 25).[71] Gas phase photolysis of *tert*-butyl *tert*-butyldiazomethyl ketone **36** gave di-*tert*-butylketene **19** in an improved 40% yield, a result attributed to different confomational populations in the gas phase, but the efficiency of product formation was still only 1/300th that of formation of **39**.[63]



36 **37** **19** <3%

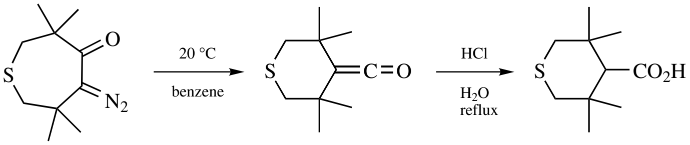
(24)



38 **39** (96%)

(25)

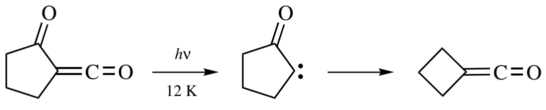
Thermal Wolff rearrangement of the thiadiazocycloheptanone **40** formed the ketene **41**, which is persistent at 20 °C, and was identified by its ketenyl IR absorption (equation 26).[72] The lability of the diazothiacycloheptanone was ascribed to twisting of the ring, which prevented conjugation in the diazo ketone grouping.



40 **41** (48%, IR 2200 cm^{-1})

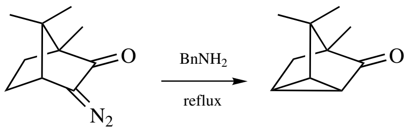
(26)

α-Ketoketenes may undergo decarbonylation, and matrix photochemical decarbonylation at 12 K of α-ketoketene **42** generated an α-keto carbene **43**, which underwent Wolff rearrangement to cyclobutylideneketene **44** (equation 27).[57] The ketene was identified by the IR doublet at 2098 and 2150 cm^{-1} and was captured with methanol at 100–140 K, giving methyl cyclobutanecarboxylate.[57] Ketene **44** was also generated by Wolff rearrangement of diazocyclopentanone and by pyrolytic dehydrochlorination.[57]

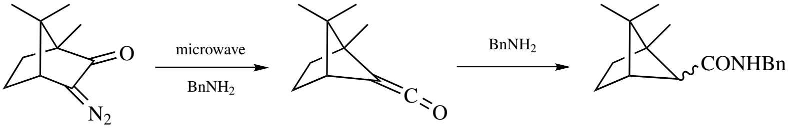


42 **43** **44** (IR 2098, 2150 cm^{-1}) (27)

Microwave irradiation was found to enhance the efficiency of thermal Wolff rearrangement, forming a variety of alkyl- and arylketenes.[73] Thus, diazocamphor (**45**)[74–76] or pinene-derived diazo ketones[77] underwent Wolff rearrangement upon photolysis,[75] but thermally or with transition metal catalysis **45** formed the tricyclanone **46** (equation 28).[73] However, with microwave irradiation in the presence of benzylamine, **45** underwent Wolff rearrangement to ketene **47**, which yielded **48** (equation 29).[73]

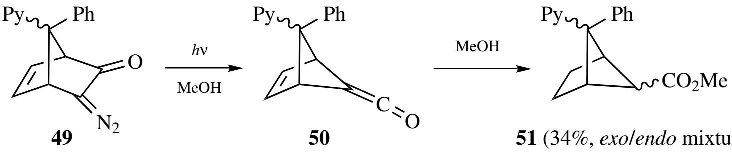


45 **46** (43%) (28)

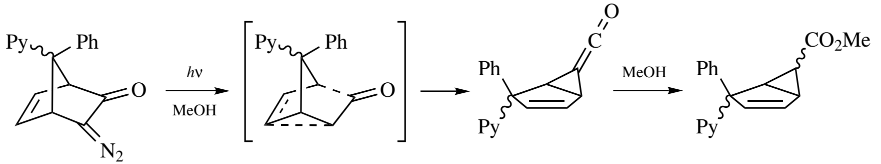


45 **47** **48** (73%, *exo*/*endo* 45/55) (29)

Photolysis of the 7,7-diarylbicyclo[2.2.1]hept-2-enes **49** gave normal Wolff rearrangement forming the ketenes **50**, which led to esters **51** from capture by MeOH in 34% yield from either isomer of **49**, and a preference for formation of *exo*-**51** (equation 30).[78] A second pathway was the vinylogous Wolff rearrangement via the transition state **52** forming ketenes **53**, which gave esters **54**, as well as some tricylane product (equation 31).[78]



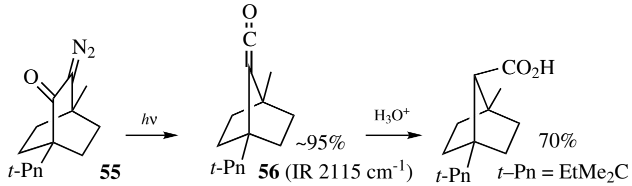
49 **50** **51** (34%, *exo*/*endo* mixtures) (30)



49 **52** **53** **54** (28–54%)

(31)

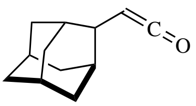
Photolysis of the diazo ketone **55** gave a 95% crude yield of an extraordinarily stable ketene **56**, IR 2115 cm^{-1}, UV λ_{max} (cyclohexane), 222 nm (ε 1260), that was stable to extraction with 1 *M* KOH but was hydrolyzed to the acid by heating with aqueous $HClO_4$ (equation 32).[79]



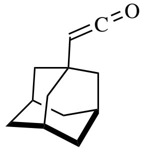
55 **56** (IR 2115 cm^{-1})

(32)

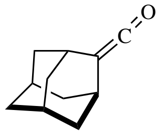
The adamantylketenes **57** and **58** were prepared by dehydrochlorination of the corresponding acyl chlorides, and **59** by dehalogenation of the α-bromo acyl chloride with zinc, and their ketenyl IR absorptions were observed in solution.[80] Derivatives of **57–59** were prepared, including the dimer of **59**.[80]



57 (IR 2120 cm^{-1})

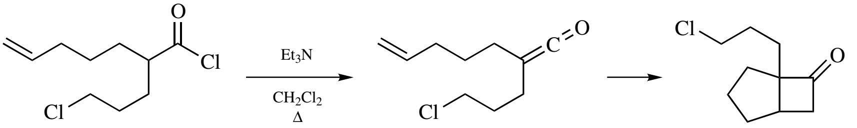


58 (IR 2120 cm^{-1})



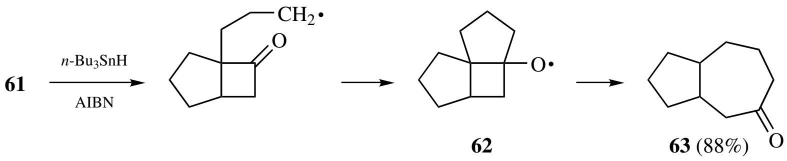
59 (IR 2110 cm^{-1})

Thermal intramolecular cyclization of ketene **60** generated from the acyl chloride gave cyclobutanone **61** (equation 33), which after chloride was exchanged for bromide, and then was converted via radical cyclization to **62**, followed by ring expansion to bicyclic ketone **63** (equation 34).[80a]



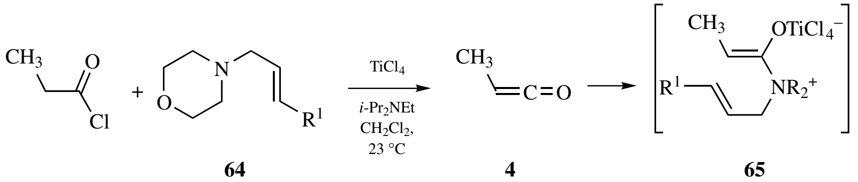
60 **61** (37%)

(33)

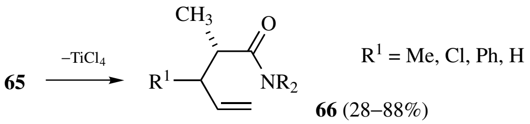


(34)

Methylketene (**4**) generated by dehydrochlorination reacted with allyl morpholines **64**, forming amides **66** with high selectivity (equations 35, 36).[81,81a] The reactions were envisaged as proceeding through a ketene aza-Claisen reaction through **65**, and were successful with catalysis by 5–10 mol% $Yb(OTf)_3$, $AlCl_3$, $Ti(OPr\text{-}i)_2Cl_2$, and $TiCl_4{\bullet}(THF)_2$.

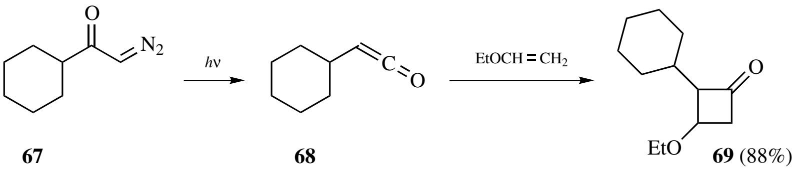


(35)



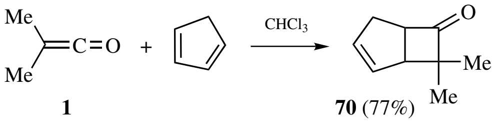
(36)

Direct photolysis of diazo ketone **67** in the presence of ethyl vinyl ether gave cyclohexylketene **68**, which reacted by [2 + 2] cycloaddition to form the cyclobutanone **69** (equation 37), whereas metal-mediated reactions of **67** gave cyclopropyl ketone products not derived from ketenes.[82]



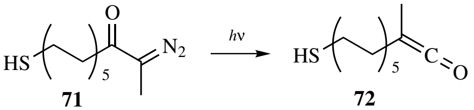
(37)

Dimethylketene (**1**) generated by dehydrochlorination gave [2 + 2] cycloaddition with cyclopentadiene to form the intermediate **70** used in leukotriene synthesis (equation 38).[83]



(38)

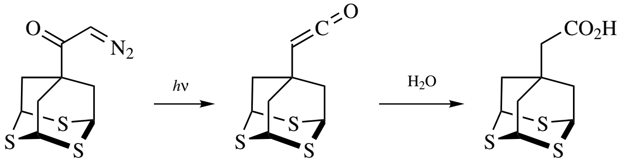
Photolysis of diazo ketone **71** as a monolayer on a gold surface upon photolysis gave the ketene **72**, which was trapped by CH_3OH, leading to an IR absorption indicating formation of the ester (equation 39).[84]



71 **72**

(39)

Photochemical Wolff rearrangement of the diazo ketone **73** adsorbed on a gold surface through the sulfur atoms gave ketene **74**, which was captured by water as the acid **75** (equation 40).[85] The ketene was also captured as the amide with *n*-octadecylamine and as a photoluminescent ester by capture with 1-hydroxymethylpyrene.[85]



73 **74** **75**

(40)

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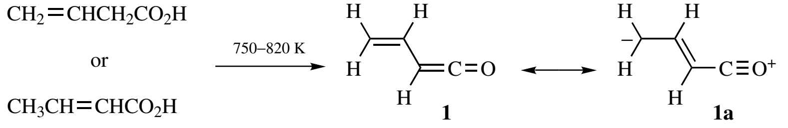
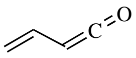
4.1.2 Alkenylketenes

Vinylketene (**1**) is the parent alkenylketene, and was generated by pyrolysis of vinylacetic acid or crotonic acid.[1] The dipole moment measured in the gas phase indicated that the *anti* conformation was favored (equation 1).[2] Computations confirmed that this was more stable than the *syn* conformation by 1.7 kcal/mol.[3–5] The gas phase photoelectron spectrum of **1** has also been measured,[1] as well as the ^{13}C NMR spectrum of the ketene formed by pyrolysis and collected at −196 °C in CS_2/$CDCl_3$.[6] This showed at −70 °C the ^{13}C shift of the CH_2 at δ 109, consistent with negative charge delocalization to the terminal CH_2, as shown in **1a**.[6]

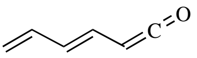


(1)

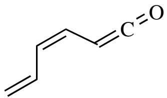
The vinylketene **1** and *E*-(1,3-butadienyl)ketene *E*-**2**[7] have been generated by dehydrochlorination of the acyl chlorides and directly observed by IR.[7] The same procedure gave the bis(alkenyl)ketene **3**[8] using 1,8-bis(dimethylamino)-naphthalene as a stoichiometric base and Et_3N as a catalytic shuttle base (see Section 3.2.2).[9] *Z*-(1,3-Butadienyl)ketene *Z*-**2** has been formed by photolysis of 2,4-cyclohexadienone **4** and identified by its IR[10] and UV[10,11] spectra (equation 2).



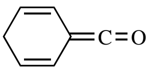
1 (IR 2118 cm^{-1})



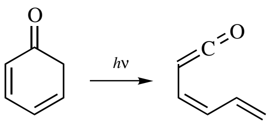
E-**2** (IR 2111 cm^{-1})



Z-**2** (IR 2111 cm^{-1})



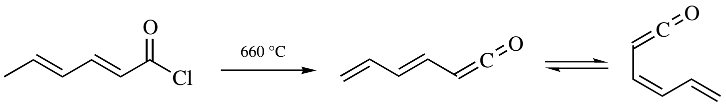
3 (IR 2101 cm^{-1})



4 *Z*-**2**

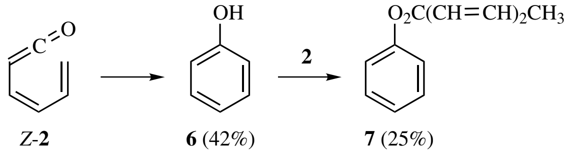
(2)

Flash vacuum pyrolysis of the hexadienoyl chloride **5** was reported to form an equilibrating mixture of *E/Z*-**2** (equation 3), as evidenced by the formation of phenol (**6**) and the ether **7** (equation 4).[12]



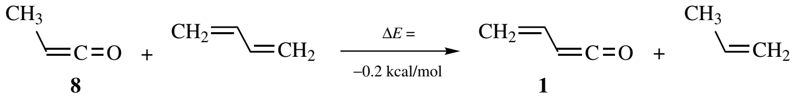
5 *E*-**2** *Z*-**2**

(3)

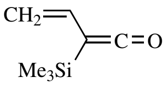


(4)

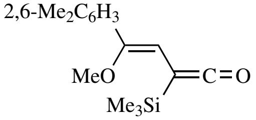
Computations at the MP2/6-31G*//MP2/6-31G* level using an isodesmic energy comparison are consistent with essentially equal stabilization of vinylketene (**1**) in comparison to methylketene (**8**), and with essentially equal conjugative stabilization in comparison to that of 1,3-butadiene (equation 5).[3–5] The vinyl substituent also enhances the reactivity of alkenylketenes, which are quite reactive toward many reagents. Trimethylsilyl substituents stabilize silylketenes, as they do other ketenes, and **9**[13] and **10**[14] are long-lived. The crowded ketene **11** was isolable and resistant to dimerization, but was reactive toward electrophiles and nucleophiles.[15]



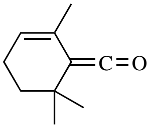
(5)



9 (IR 2112 cm^{-1})

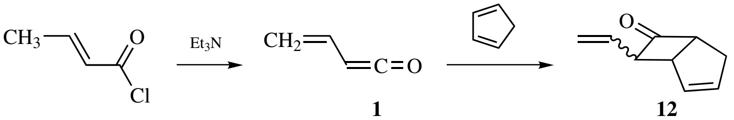


10

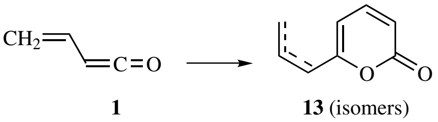


11 (IR 2115 cm^{-1})

Dehydrochlorination of crotonyl chloride by triethylamine formed vinylketene **1**, which was trapped in situ by cyclopentadiene in a [2 + 2] cycloaddition forming the bicyclo[3.2.0]heptene **12** (equation 6).[16,17] In the absence of trapping agents, dimerization to 2-pyrones **13** occurred (equation 7).[16,17]

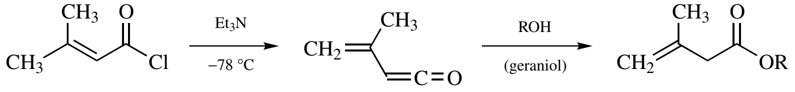


(6)

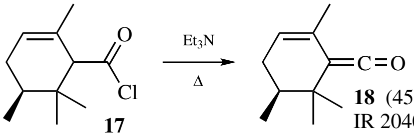


(7)

The reaction of β,β-dimethylacrylyl chloride (**14**) with triethylamine in CH_2Cl_2 at −78 °C was proposed to lead to the unobserved alkenylketene **15**, which was trapped in situ by geraniol, forming **16** (equation 8).[18] A similar reaction is shown in Section 3.2.2. The optically active and long-lived alkenylketene **18** was prepared by dehydrohalogenation of **17** (equation 9).[19] Chiroptical properties of ketenes are discussed in Section 2.2.

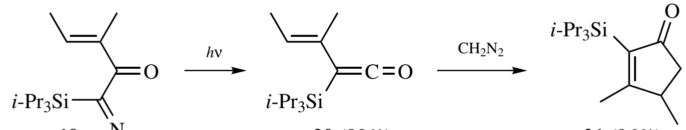


14 **15** **16** (99%) (8)

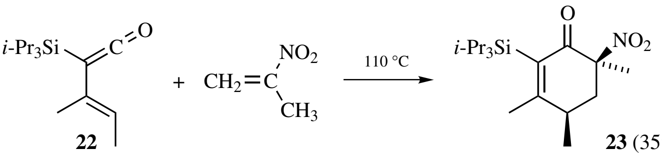


17 **18** (45%, IR 2040 cm^{-1}) (9)

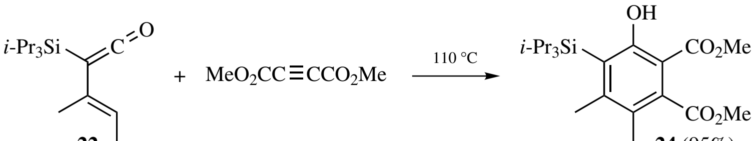
Photochemical Wolff rearrangement of diazo ketones **19** gave a general route to the formation of α-trialkylsilylalkenylketenes **20** (equation 10).[20–22] The reactions of **20** with diazoalkanes yielded cyclopentenones **21** (equation 10).[20] Alkenes and alkynes reacted by [4 + 2] cycloadditions with **22** formed in this way to give cyclohexenones **23** and phenols **24**, respectively (equations 11, 12)[21] Imines reacted with **22** by [4 + 2] cycloadditions to give δ-lactams **25** (equation 13).[22] Other reactions of **20** and some analogues are discussed in Section 4.5.



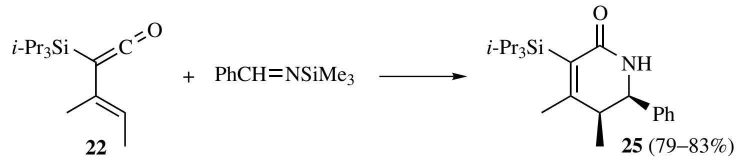
19 **20** (80%) **21** (96%) (10)



22 **23** (35%) (11)

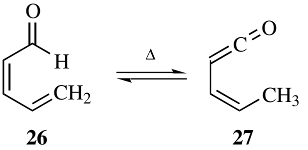


22 **24** (95%) (12)

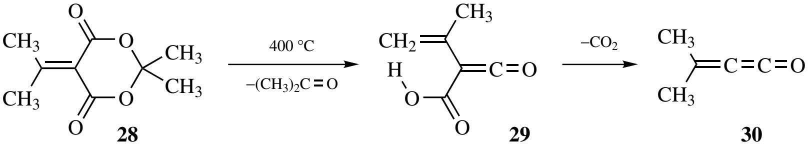

22 **25** (79–83%)

(13)

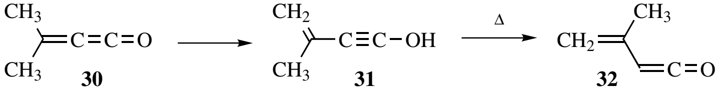
Additional reactions for formation of vinylketenes are discussed elsewhere, including Wolff rearrangements (Section 3.3), cyclobutenone and cyclohexadienone ring openings (Sections 3.4.1 and 3.4.3, respectively), and reactions of metal carbene complexes (Section 3.5). Ene reactions of dienylaldehyde **26** formed **27** (equation 14[23] and Sections 3.4.6 and 5.4.4), and thermolysis of Meldrum's acid derivative **28** formed **29**, which gave the cumulenone **30** (equation 15), which was converted through the ynol **31** to vinylketene **32** (equation 16).[24] The parent **1** was also formed from the gas phase thermolysis of ene-yne ethyl ether **33** (equation 17),[25] and vinylketenes were reported to be formed in the flash vacuum pyrolysis of spiro[2,3]hexan-4-ones based on the products from trapping with MeOH.[26]


26 **27**

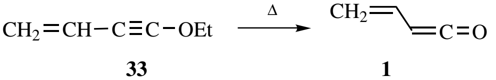
(14)


28 **29** **30**

(15)

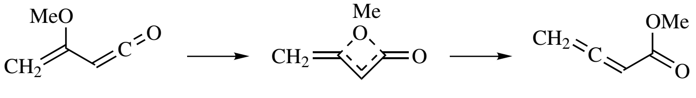

30 **31** **32**

(16)

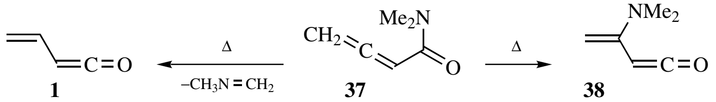

33 **1**

(17)

The barriers to rearrangements of vinylketenes **34** to acylallenes **36** have been calculated by *ab initio* methods, and the thermal migration of methoxy through transition state **35** has been shown experimentally (equation 18).[27,28] Allenyl amide **37** rearranged similarly, together with partial elimination upon flash vacuum thermolysis, to form a mixture of alkenylketenes **1** and **38** (equation 19).[28] The unobserved vinylketene **39** generated by a similar route rearranged to the observed **40** (equation 20).[29]

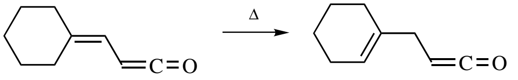

34 (IR 2138, 2142 cm^{-1}) **35** **36**

(18)



1 **37** **38**

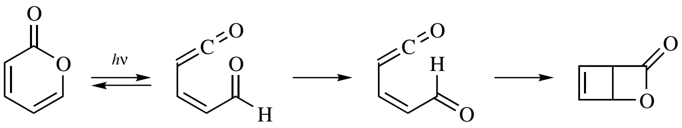
(19)



39 **40**

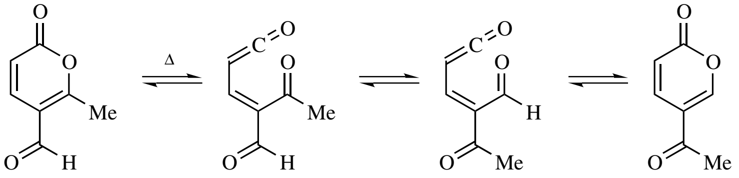
(20)

Calculations of the conformations of the 2-pyranone (**41**) photolysis product 5-oxo-2,4-pentadienal (**42**) and its cyclization to **43** indicated that the conformer **42a** was not a stable structure, but would close without a barrier to **41** (equation 21).[30] Pyrolysis of the 2-oxopyran-5-carboxaldehyde **44** led to an equilibrium mixture of the 2-pyridones **44**, **47**, and **49** involving the acylketenes **45**, **46**, **46a**, and **48** as unobserved intermediates (equations 22, 23).[31]



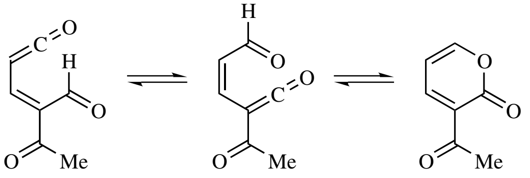
41 **42a** **42b** **43**

(21)



44 **45** **46** **47**

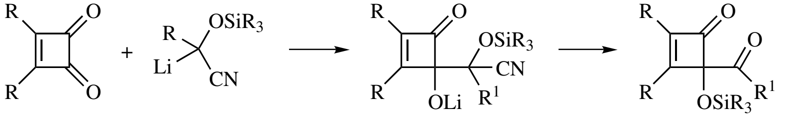
(22)



46a **48** **49**

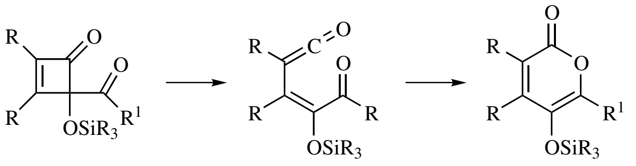
(23)

The cyclobutenedione **50** was proposed to react with RCLi(CN)OTBDMS, forming **51**, which underwent ring opening to the vinyl ketene **52** followed by cyclization to the 2-pyranone **53** (equations 24, 25).[32] Other examples of cyclobutenone ring openings forming vinylketenes are given in Section 3.4.1.



50 $R_3Si = t\text{-}BuMe_2Si$ **51**

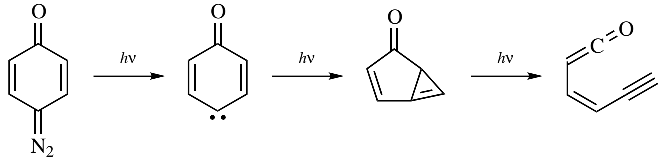
(24)



51 **52** **53**

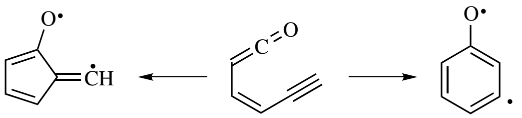
(25)

Matrix photolysis of the diazo ketone **54** gave the carbene **55** and the strained cyclopropene **56**, which on further photolysis gave the ene-yne ketene **57**, as identified by the matrix IR spectrum (equation 26).[33,34] The ring closures of the ene-yne ketene **57** through the Schmittel and Myers-Saito pathways, forming the diradical intermediates **58** and **59**, respectively, (see Section 3.4.1) have been studied computationally (equation 27).[35]



54 **55** **56** **57**

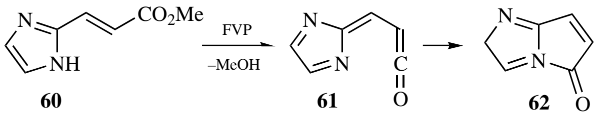
(26)



58 **57** **59**

(27)

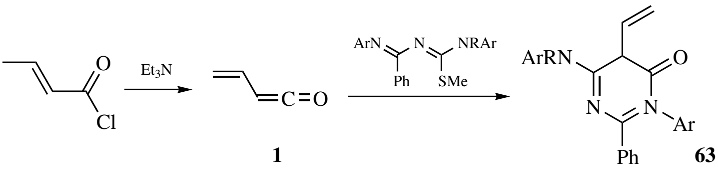
Flash vacuum pyrolysis (FVP) of the ester **60** was proposed to give the ketene **61**, which cyclized to **62** (equation 28).[36]



60 **61** **62**

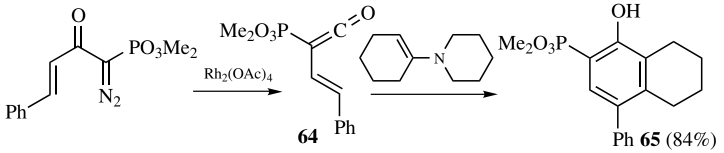
(28)

Vinylketene **1** generated by dehydrohalogenation gave [4 + 2] cycloaddition reactions with 1,3-diaza-1,3-butadienes, forming **63** (equation 29).[37] Wolff rearrangement gave **64**, which reacted by a [4 + 2] cycloaddition pathway with an eneamine, forming **65** (equation 30).[38]



1 **63**

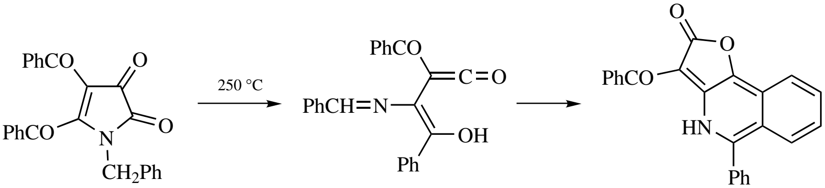
(29)



64 **65** (84%)

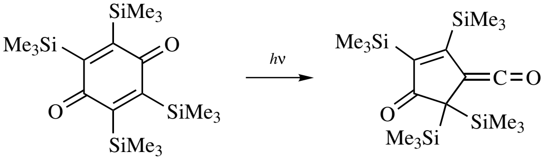
(30)

Thermolysis of **66** was proposed to give the ketene **67**, which underwent cyclization and dehydrogenation to give the observed **68** (equation 31).[39] Photolysis of the silylated *para*-benzoquinone **69** gave the ketene **70** as a yellow solid, IR 2089 cm^{-1} (equation 32).[40]



66 **67** **68**

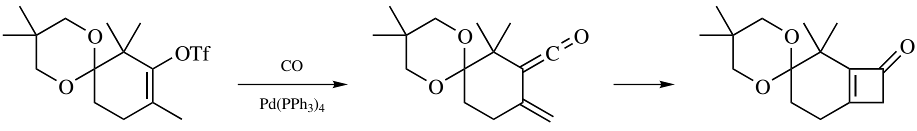
(31)



69 **70** (21%)

(32)

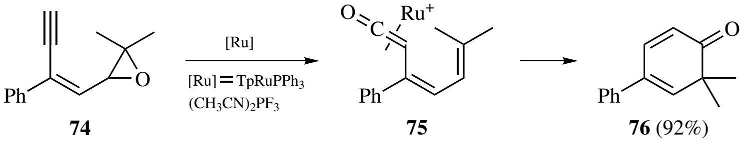
Carbonylation of the triflate **71** using Pd(PPh$_3$)$_4$ was proposed to form the ketene **72**, which cyclized to the cyclobutenone **73** (equation 33).[41] Heating **73** in MeOH gave the ring-opened ester in 80% yield.



71 **72** **73** (49%)

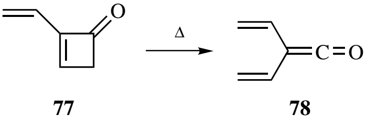
(33)

Reaction of the ene-yne-substituted epoxide **74** with the ruthenium catalyst TpRuPPh$_3$(CH$_3$CN)PF$_6$ [Tp=tris(1-pyrazolyl)borate] reacted through the Ru$^+$-coordinated dienylketene **75**, which cyclized to the dienone **76** (equation 34).[42] Several similar examples were also reported.[42] This method is discussed further in Section 4.8.4.



(34)

Examples of thermolysis of substituted analogues of vinylcyclobutenone **77** forming divinylketene **78** (equation 35) are shown in Section 3.4.1.



(35)

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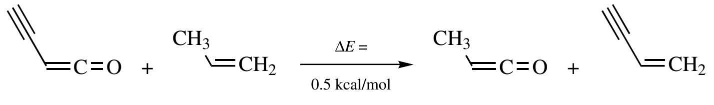
4.1.3 Alkynyl- and Cyanoketenes

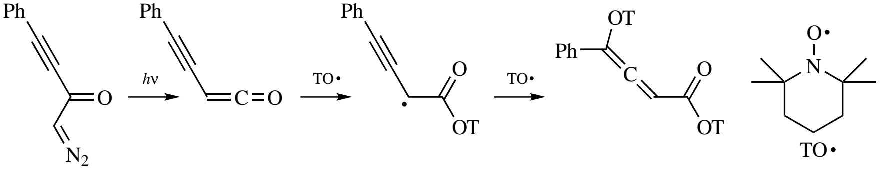
The alkynyl substituent was calculated at the MP2/6-31G*//MP2/6-31G* level to have almost exactly the same stabilization energy as the methyl group.[1–4] Known examples of alkynylketenes are quite reactive, and apparently no long-lived example has been reported, although these should be accessible.



(1)

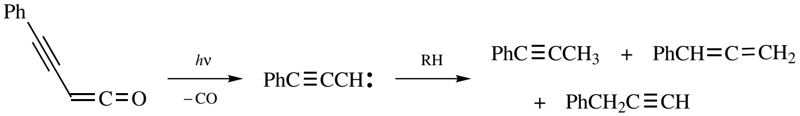
1 **2** **3** **4**

Phenylethynylketene (**6**) formed by photochemical Wolff rearrangement of the diazo ketone **5** using flash photolysis was detected by TRIR spectroscopy by the characteristic absorption at 2132 cm^{-1} in CH_3CN,[5] and by the use of conventional photolysis and detection in isooctane at 2131 cm^{-1} (equation 2).[6] The ketene **6** was trapped by the stable free radical TEMPO (TO•), forming the adduct **8** (equation 2).[6] Upon photolysis of **6** decarbonylation occurred, leading to the carbene **9**, which formed 1-phenylpropyne, phenylallene, and benzylacetylene (equation 3).[7]



5 **6** **7** **8**

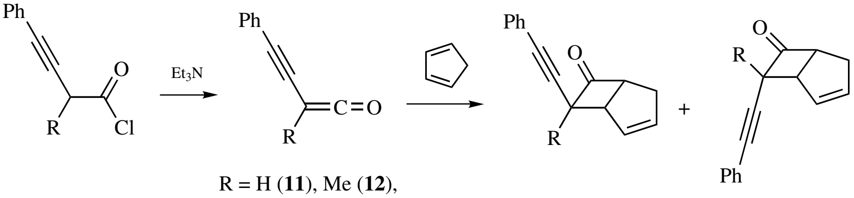
(2)



6 **9**

(3)

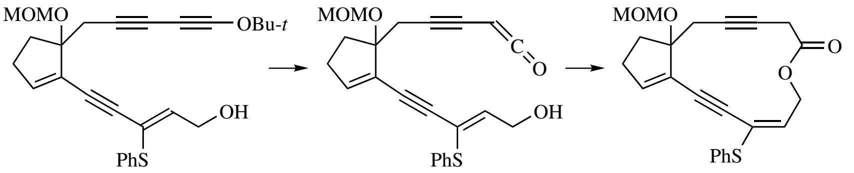
Dehydrochlorination of the acyl chlorides **10** in the presence of cyclopentadiene led to generation of the alkynylketenes **11–15**, which gave in situ [2 + 2] cycloaddition forming the adducts **16**, with the alkynyl group preferentially in the *exo* position as the only observed products (equation 4).[4,8] The smaller group preferentially occupied the *exo* position in these reactions, and this result illustrated the small steric requirements of the carbon-carbon triple bond.



10 R = H (**11**), Me (**12**), Et (**13**), *i*-Pr (**14**), *t*-Bu (**15**) **16** **17**

(4)

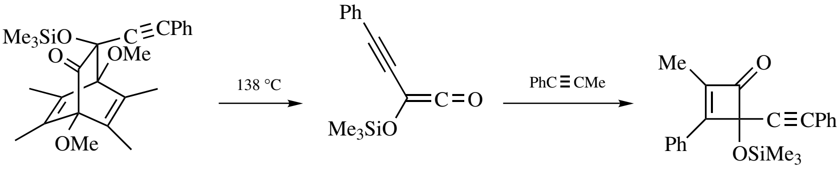
Heating of the 1-*tert*-butoxy-1,3-butadiyne **18** gave the macrolide **20** through intramolecular capture of the intermediate alkynylketene **19** (equation 5).[9] Analogous products were prepared by the same procedure,[9] and another similar procedure is given in Section 3.4.5.



18 **19** **20** (25%)

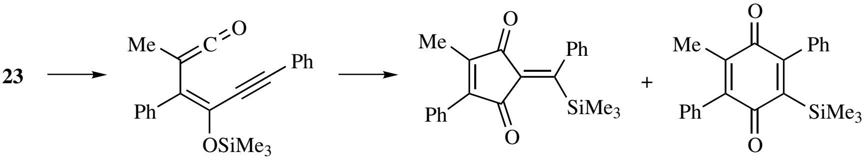
(5)

Thermolysis of the bicyclo[2.2.2]octadiene **21** in xylene at 138 °C was proposed to form alkynyl(trimethylsilyloxy)ketene **22**, which reacted with 1-phenylpropyne by [2 + 2] cycloaddition, forming cyclobutenone **23** (equation 6).[10] Under these reaction conditions **23** underwent ring opening, forming ene-yne ketene **24**, which cyclized to cyclopentene **25** and benzoquinone **26** (equation 7) via diradical intermediates **27** and **28**, respectively.[10] Formation of another ene-yne ketene is shown in Section 4.1.2.

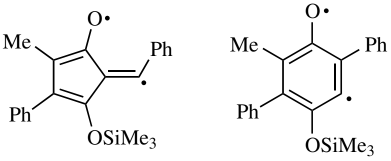


21 **22** **23**

(6)



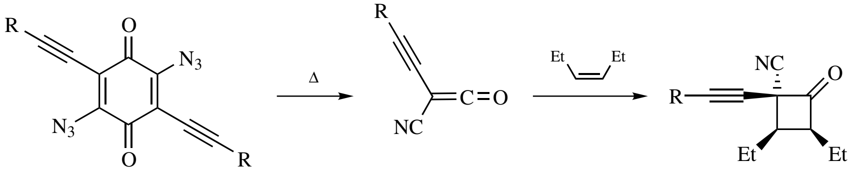
24 **25** (48%) **26** (12%)



27 **28**

(7)

Alkynylcyanoketenes **30** were generated by thermolysis of 2,5-dialkyl-3,6-diazidoquinones **29** and reacted with alkenes by [2 + 2] cycloaddition (equation 8).[11,12] There was retention of the alkene stereochemistry, and a 4:1 preference for the *cis* orientation of the alkynyl group and the adjacent ethyl substituent.[12]

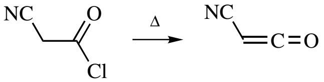


29 **30** **31** (60%, R = *n*-Bu)

(8)

The cyano group in cyanoketene (**32**) was calculated at the MP2/6-31G*//MP2/6-31G* level by isodesmic comparison, as in equation 1, to have a small stabilizing energy of −0.4 kcal/mol relative to the methyl group.[1–4] Cyanoketenes are, however, quite reactive, an attribute that arises from the small size of the substituent and the strong conjugative stabilization of transition states for reaction.

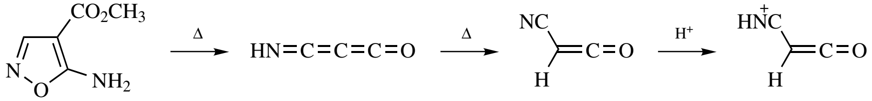
Cyanoketene (**32**) was prepared by pyrolysis of cyanoacetyl chloride (**33**) (equation 9), and the molecular structure was determined by microwave spectroscopy, showing a dipole moment of 1.542 *D* (Section 1.2).[13] The photoelectron spectrum of **32** was also measured.[13a] This ketene was shown to be short-lived in the condensed phase, contradicting a claim of the isolation of **32** as a liquid.[14] Cyanoketene was prepared from the reaction of cyanoacetylene with oxygen in an ice matrix and identified by the IR bands at 2224 (CN) and 2166 (C=C=O) cm^{-1}, which agreed with the calculated spectrum.[15]



33 **32**

(9)

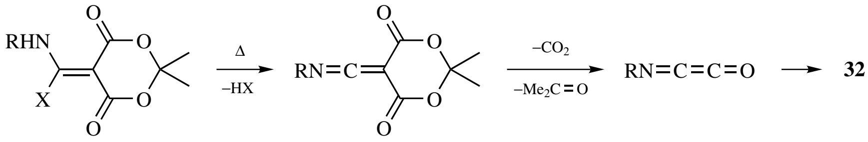
The cumulene **35** was prepared by pyrolysis of **34**, and rearranged to cyanoketene (**32**), which in the gas phase gave preferential protonation on nitrogen forming **36** (equation 9).[16]



34 **35** **32** **36**

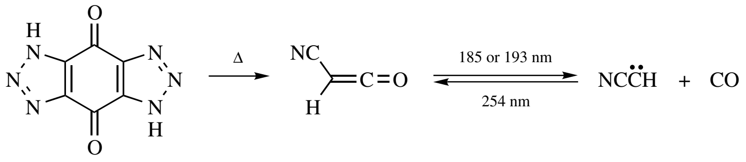
(10)

Flash vacuum thermolysis (FVT) of various cyanoacetic acid derivatives also yielded **32**, as identified by its strong IR absorption at 2163 cm^{-1} in an Ar matrix.[17] Similarly, FVT of Meldrum's acid derivatives **37** gave **32**, mainly from the iminopropadienone **38** (equation 11).[17] FVP of **39** with matrix isolation gave **32**, with the ketenyl IR band at 2162.8 cm^{-1} and the CN band at 2240.2 cm^{-1} (equation 12).[18] Photolysis of **32** in the matrix with 185 or 193 nm light gave decarbonylation and formation of cyanocarbene, and upon photolysis with 254 nm light this reformed **32** (equation 12).[18]



37 **38**

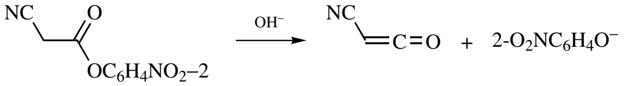
(11)



39 **32** (12)

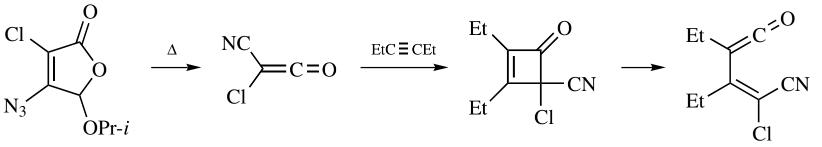
The heats of formation of **32** and its radical cation have been determined as 24 ± 5 and 253 ± 3 kcal/mol, respectively, and the heat of formation of the radical cation of $(NC)_2C{=}C{=}O$ (**40**) has been estimated as 300 kcal/mol.[19]

It was proposed that the basic hydrolysis of 2-nitrophenyl cyanoacetate (**41**) formed **32** on the basis of the enhanced rate of reaction compared to that expected for normal ester hydrolysis (equation 13).[20]

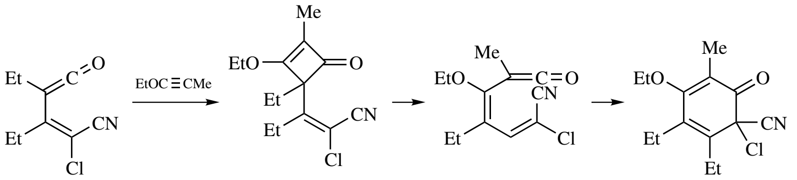


41 **32** (13)

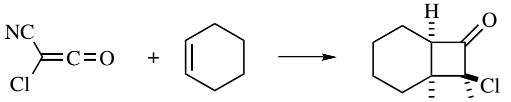
Chlorocyanoketene (**43**) was generated from pyrolysis of furanone **42** and reacted with 3-hexyne, forming cyclobutenone **44** (equation 14).[21–23] This gave ring opening even at ambient temperatures, forming vinylketene **45** (equation 14), which reacted by [4 + 2] cycloaddition with 1-ethoxypropyne to form cyclobutenone **46**, which opened to vinylketene **47** followed by cyclization to cyclohexadienone **48** (equation 15).[23] Cyclohexene reacted with **43** by [2 + 2] cycloaddition (equation 16).[23]



42 **43** **44** **45** (14)

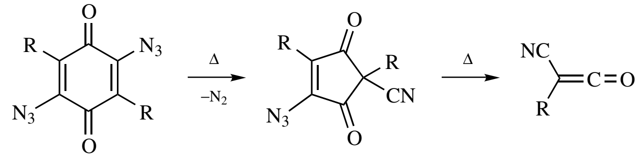


45 **46** **47** **48** (56%) (15)



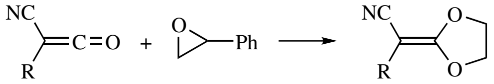
43 76% (16)

Pyrolysis of azidoquinones **49** gave a general route via cyanocylopentenediones **50** to form substituted cyanoketenes **51** (equation 17).[24–28] *tert*-Butylcyanoketene (**51a**, R=*t*-Bu) was obtained in benzene solution in 95% yield, and while not isolated was characterized by the IR bands at 2130 (C=C=O) and 2220 (CN) cm^{-1} and the ^{1}H NMR singlet at δ 0.75.[25] The reactions of **43** and of *tert*-butylcyanoketene (**51a**) with styrene oxide gave keteneacetals **52** (equation 18).[29]



49 **50** **51** R = *t*-Bu (95%), *i*-Pr, Ph, Me

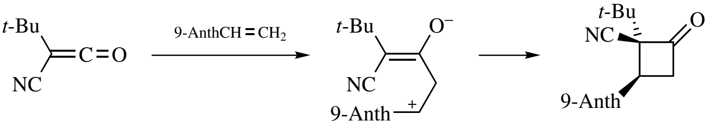
(17)



R = Cl (**43**), *t*-Bu (**51a**) **52**

(18)

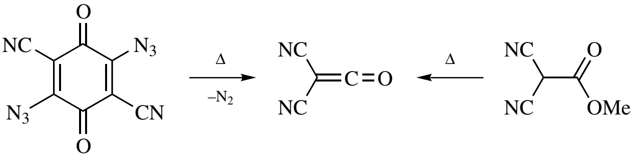
tert-Butylcyanoketene (**51a**) reacted with arylalkenes (aryl = phenyl, 1- and 2-naphthyl, anthracenyl) and gave cyclobutanones **53** with *cis*-stereochemistry of the *tert*-butyl with the phenyl and naphthyl groups but *trans* for *tert*-butyl with anthracenyl (equation 19).[30] The reaction was proposed to be concerted in the former two cases but stepwise in the latter.



51a **53**

(19)

Dicyanoketene (**40**) was prepared by thermolysis of dicyanodiazidoquinone **54**[28] and from FVP at 500 °C of methyl dicyanoacetate (**55**).[31] When trapped in an argon matrix, it was identified by the IR absorption at 2175 cm^{-1} (equation 20).[31] The synthetic utility of **40** was also explored.[28]



54 **40** (IR 2175 cm^{-1}) **55**

(20)

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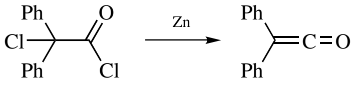
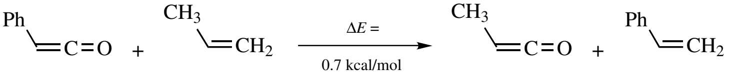
4.1.4 Aryl- and Heteroarylketenes

Diphenylketene (**1**) was the first ketene to be isolated and characterized, by Staudinger in 1905,[1] by the zinc reduction of α-chorodiphenylacetyl chloride (equation 1), and has been the most extensively utilized ketene. The fact that diphenylketene was isolable and relatively stable is evidently due to steric factors, as the bulky aryl groups hinder dimerization. The computed isodesmic comparison of equation 2[2–4] indicated that phenylketene is only slightly stabilized relative to methylketene. The stability of ketenes was correlated with the electronegativity of the substituents. Ketenes are stabilized by electropositive groups, and by conjugative π-electron acceptors, and destabilized by electronegative substituents,[2–4] and for phenyl the sum of these effects is near that of methyl. Ketenes **1** and **2** are highly activated by the phenyl groups and give facile reactions with nucleophiles and in cycloaddition reactions.



1

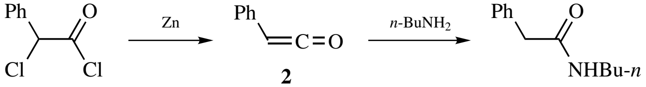
(1)



2 **3** **4** **5**

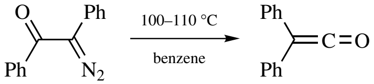
(2)

Phenylketene was prepared in 1911 from α-chlorophenylacetyl chloride by zinc dehalogenation and was detected by its color in solution.[5] The ketene was trapped with n-BuNH$_2$ (equation 3)[5] but polymerized upon attempted isolation by removal of the solvent. Both **1** and **2** were prepared in the gas phase by dehalogenation for measurement of their photoelectron spectra, and their conformations were determined by computation.[5a]



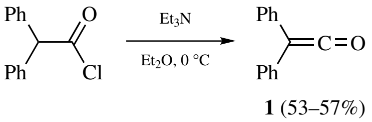
(3)

Procedures are reported in *Organic Syntheses* for the preparation of diphenylketene (**1**) by thermal Wolff rearrangement of the diazo ketone (equation 4)[6] and by dehydrochlorination of diphenylacetyl chloride (equation 5).[7] The latter procedure was also used to prepare **1** ^{13}C labeled in both carbons from $^{13}CO_2$, in 22% yield.[7a] When dehydrochlorination was carried out in refluxing chloroform, the by-product **6** was formed to the extent of 6–9% (equations 6, 7).[8] The mechanism proposed for the formation of **6** involved initial hydride transfer to **1**, forming the corresponding enolate.[8]



1 (64%)

(4)



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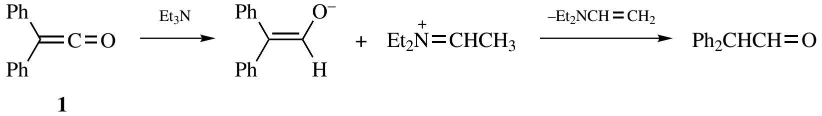

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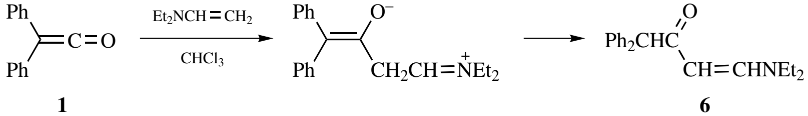
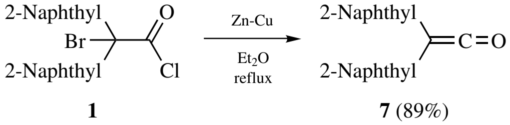


(7)

The original preparation of **1** was by reductive dehalogenation,[1,9] and this procedure has also been used for the preparation of di-(2-naphthyl)ketene **7** (equation 8).[10] Diphenylketene (**1**) has also been prepared by dehalogenation of α-bromodiphenylacetyl chloride with triphenylphosphine (equation 9).[11] The pyrolysis of diphenylketene acetal **8a** also gave **1** (equation 10).[12] Bis(pentafluorophenyl)ketene (**8b**) was prepared by direct dehydration of the acid (equation 11).[13]



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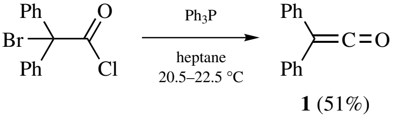

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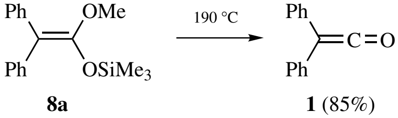

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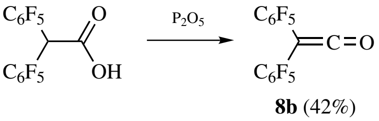
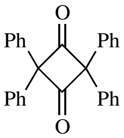
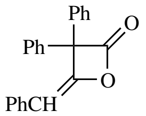


(11)

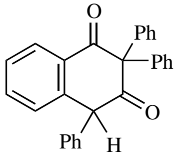
Three dimers of diphenylketene have been reported.[14] The 1,3-cyclobutanedione dimer **9a** was obtained from **1** and quinoline, while dimerization induced by sodium methoxide gave the β-lactone dimer **9b**, and heating of **1** at 100 °C in benzoyl chloride formed **9c**.[14]



9a

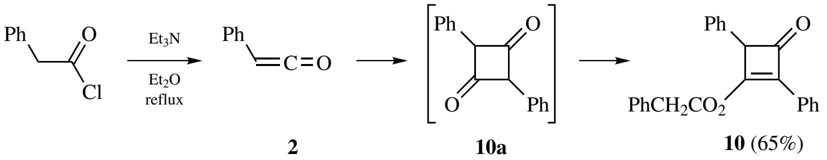


9b

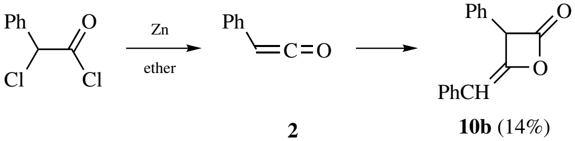


9c

The generation of phenylketene (**2**) by dehydrochlorination with triethylamine in ether led to formation of the acylated dimer **10** (equation 12).[15] This reaction evidently proceeded through formation of the 1,3-diketo dimer **10a**, followed by acylation of the enol. The enol has been obtained by basic hydrolysis of **10**.[15] The β-lactone dimer **10b** of phenylketene was isolated when the ketene was prepared by zinc dechlorination (equation 13).[16]

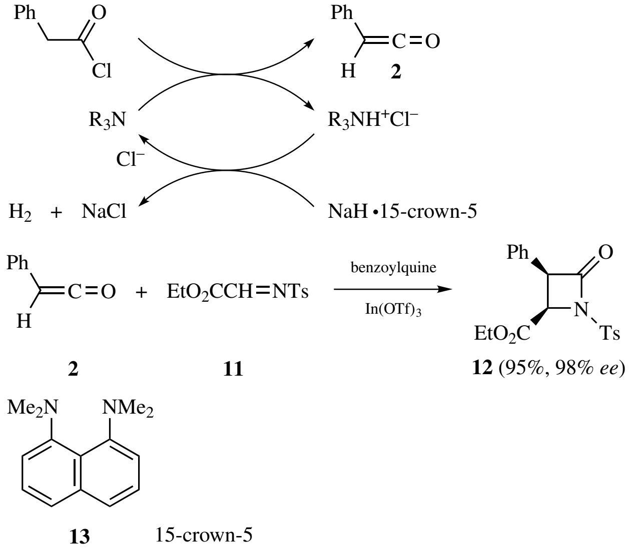


(12)



(13)

Solutions of phenylketene (**2**) for synthetic applications have been conveniently obtained by the protocol of Lectka, in which phenylacetyl chloride was reacted with a tertiary amine such as Et$_3$N or a chiral amine such as benzoylquinine as a kinetic shuttle base and stoichiometric bases such as NaH with 15-crown-6 or K$_2$CO$_3$ that reacted irreversibly (Scheme 4.1).[17,18] Chiral bases also acted as catalysts for stereoselective addition to the ketene, and with benzoylquinine together with In(OTF)$_3$ as an electrophilic cocatalyst, a [2 + 2] cycloaddition with imine **11**

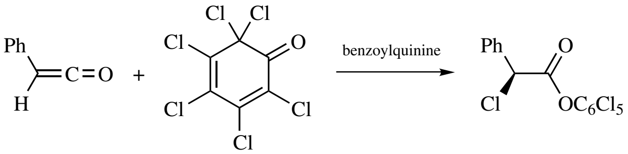


(14)

Scheme 4.1 Generation of phenylketene by dehydrochlorination with a shuttle base and NaH•15-crown-5.

gave the β-lactam product **12** in 95% yield, 98% *ee*, and 60/1 *dr* (equation 14).[17] The mechanism of the catalysis has been examined in detail.[17a] 1,8-Bis(dimethylamino)naphthalene (**13**) has also been used as a stoichiometric base, but may give reversible deprotonation forming phenylketene, so the ketene may not be involved in the product-forming step.[17]

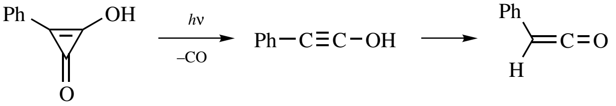
Reaction of **2** generated as in Scheme 4.1 with **14** gave stereoselective chlorination (equation 15). The procedure was also carried out with other bases, including sodium bicarbonate and polymer-bound triaminophosphonamide.[18]



2 **14** **15** (63%, 95% *ee*)

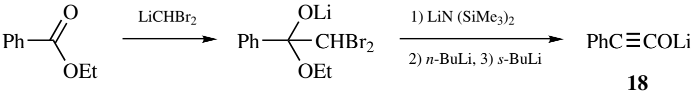
(15)

Phenylketene has also been generated from phenylethynol (**17**), which was formed by the photochemical decarbonylation of hydroxycyclopropenone **16** (equation 16).[19,20] The rearrangement was monitored by both TRIR spectroscopy[19] and UV spectroscopy.[20] This method was also utilized for the formation of other arylketenes whose kinetics of hydration to the carboxylic acids were monitored.[21] Phenylynolate (**18**) was formed by a procedure involving $LiCHBr_2$ addition to ethyl benzoate (equation 17) and reacted with ethanol to give the ester **19** by way of the ketene **2** (equation 18).[22–24] Other routes to **17** and **18** are given in Section 4.8.1.[25,26]



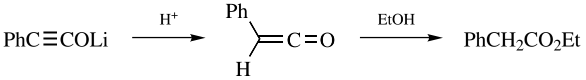
16 **17** **2**

(16)



18

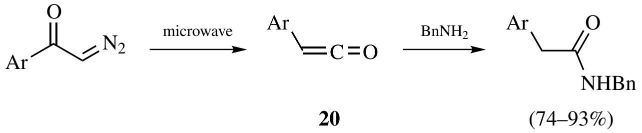
(17)



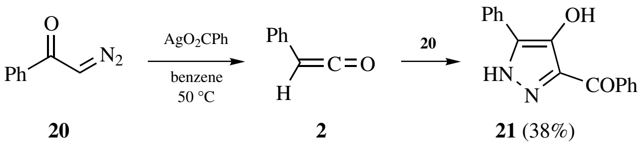
18 **2** **19** (71%)

(18)

Phenylketene (**2**) and other monoarylketenes $RC_6H_4CH{=}C{=}O$ **20** (R = 2-Me, 2-Cl, 2-I, 2-Br, 4-Me, 4-MeO) were generated by microwave-assisted Wolff rearrangement and captured with benzylamine (equation 19).[27] Generation of monoarylketenes from thermal Wolff rearrangement in the absence of trapping agents was not satisfactory because of the reaction of the ketene formed with the residual diazo ketone (equation 20).[28] An *Organic Syntheses* procedure describes the silver benzoate–catalyzed generation of 1-naphthylketene (**22**) and capture with ethanol (equation 21).[29]



(19)



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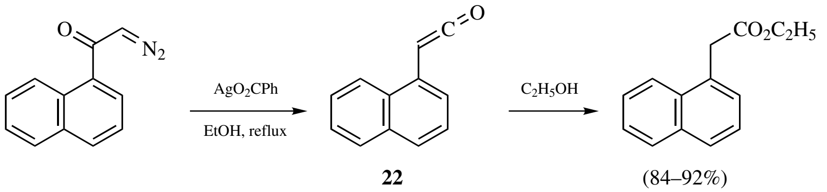
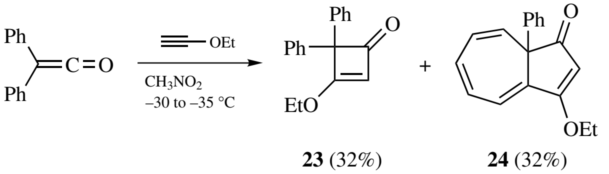


(21)

Diphenylketene (**1**) reacted with ethoxyacetylene to give a mixture of the [2 + 2] cycloaddition product **23** and the azulene derivative **24** (equation 22).[10,30,31] The cyclobutenone **23** was characterized as the naphthol **26** (equation 23) formed by thermal rearrangement of **23** via the intermediate ketene **25** (Smith-Hoehn reaction; see Section 3.4.1), while **24** was proposed to result from a net [2 + 2 + 2] cycloaddition forming the intermediate **27** from attack on the ketene and cyclization onto the aromatic ring.



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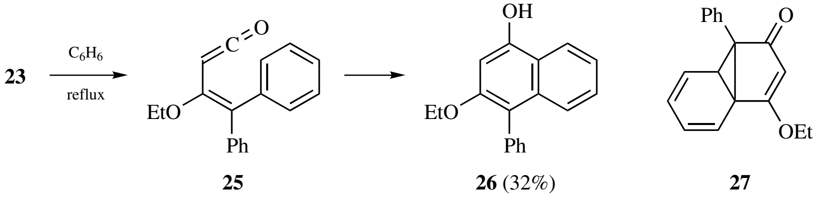
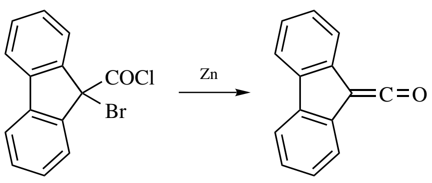


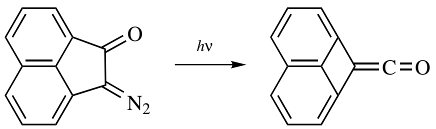
(23)

Dibenzofulvenone (**28**) is an analogue of diphenylketene that was prepared by Staudinger using dehalogenation by zinc reduction (equation 24).[32] Other examples of fulvenones are described in Section 4.1.10. Another diphenylketene analogue is **30**, which was formed by the photochemical Wolff rearrangement of diazo ketone **29** in a matrix and identified by the IR absorption at 2127 cm^{-1} (equation 25).[33,34] However, ketene **30** was not observed as a product from photolysis or thermolysis of **29** in solution.[34,35] Diazulenylketene (**30a**) was prepared by thermal Wolff rearrangement of the diazo ketone and trapped with MeOH (equation 25a).[36]



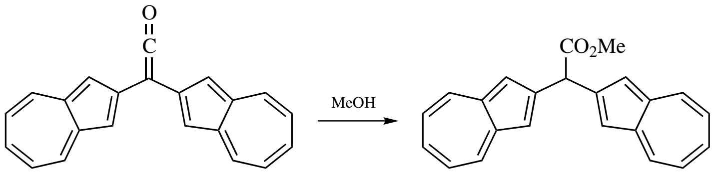
28

(24)



29 **30**

(25)



30a (35%)

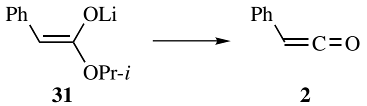
(25a)

Photolysis of phenyldiazomethane in an argon matrix doped with CO led to formation of a small amount of phenylketene (**2**), as identified by its IR band at 2115 cm^{-1} (equation 26).[37] 2-Naphthylcarbene reacted similarly with CO and formed 2-naphthylketene, with an IR band at 2121 cm^{-1}.[38] Phenylketene has been generated by Wolff rearrangement as a relatively long-lived intermediate and observed by IR in isooctane solution.[39,40]

2

(26)

The ester enolate **31** has been reported to form PhCH=C=O (equation 27) and NMR signals attributed to this species were reported,[41] but confirmation of these results is desirable.

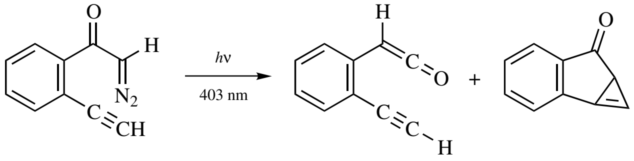


31 **2**

(27)

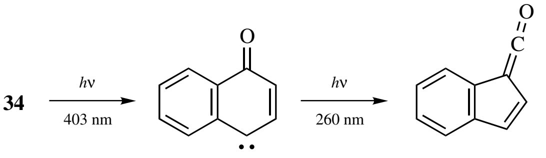
Photolysis at 403 nm of the diazo ketone **32** in an argon matrix at 10 K led to the ketene **33**, identified by its strong ketene IR bands at 2130, 2126, and 2121 cm^{-1}

(equation 28).[42] Bands were also observed for the cyclopropenyl ketone **34**, which on further photolysis gave the carbene **35**, which itself formed the fulvenone **36** on photolysis at 260 nm (equation 29).[42]



32 **33** **34**

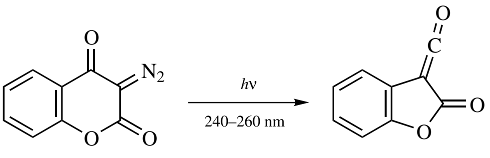
(28)



35 **36** (IR 2139 cm^{-1})

(29)

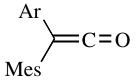
Photolysis of 3-diazo-4-oxocoumarin **37** and a variety of ring-substituted derivatives gave ketenes **38** studied for photolithographic applications (equation 30).[43] The reactivity of **38** in thin novolac films was monitored by the disappearance of the ketenyl IR absorptions near 2142 cm^{-1} to determine the reactivity with the phenolic groups in the resin. The kinetics were modeled using fractal mathematics, which are useful for studies in polymer systems. The reactivities increased with increasing electron-withdrawing power of substituents on the aryl rings, with retardations due to bulky groups near the ketenyl moiety, but an acceleration by a proximate benzyloxy group, which may have attracted the nucleophile. Recent developments in the theory of the mechanism of action of novolac-diazonaphthoquinone resists have been reviewed (see also Section 4.1.10.2).[44]



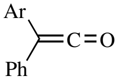
37 **38**

(30)

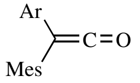
The mixed ketenes **39–43** with highly substituted aryl groups were prepared by dehydrochlorination of the acyl chlorides.[45–56] Thermolysis of **44** led to the isochromene **45** by hydride transfer (equation 31), and at a rate 100 times faster than the corresponding reaction of $Mes_2C{=}C{=}O$ (**46**).[50] The reaction of **46** with amines led to amide enols observable by NMR.[48,50] The kinetics of the addition of alcohols catalyzed by pyridine and bridged pyridines to $Mes_2C{=}C{=}O$ $C{=}O$ have been measured.[46]



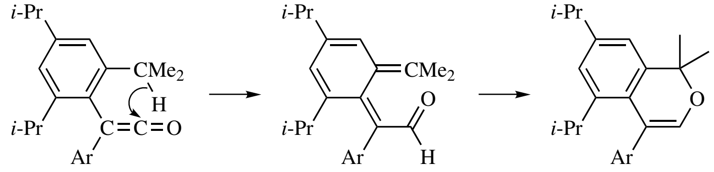
39 (Ar = 3-MeOMes)
40 (Ar = 4-*t*-Bu,2,6-diMeC_6H_2,
Mes = 2,4,6-$Me_3C_6H_2$)



41 (Ar = 2,4-$Me_2C_6H_3$)



42 (Ar = 3-MeOMes)
43 (Ar = 4-*t*-Bu,2,6-diMeC_6H_2)
46 (Ar = Mes)

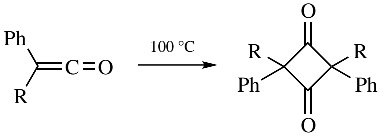


(31)

44 (Ar = 2,4,6-(*i*-Pr)$_3C_6H_2$)

45

Arylalkylketenes have been readily generated, usually from derivatives of α-arylalkanoic acids by the dehydrochlorination or dehalogenation routes. They are less reactive than arylaldoketenes, and can usually be isolated, but are still sensitive to moisture and react readily with many nucleophilic reagents. Arylalkylketenes **47** dimerized on heating to give cyclobutane-1,3-diones **48**, with an increasing proportion of the *cis* product with increasing size of the alkyl group (equation 32).[57] The preference for formation of the more crowded 4-membered ring product is a common feature of ketene cycloaddition chemistry, and is explained as resulting from perpendicular approach of the reacting species with the larger substituents in the least crowded position in the transition state, which, however, leads to more crowded products.

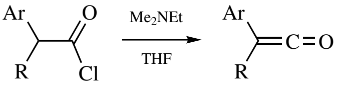


R	Me (**a**)	Et (**b**)	*i*-Pr (**c**)
cis/*trans*	20:80	62:38	100:0

(32)

47 **48**

Arylalkylketenes have been prepared by dehydrohalogenation of 2-alkyl-2-arylacetyl chlorides using Et_3N,[58] but **49a–c** were preparing using $EtMe_2N$ (equation 33).[59–61] These ketenes may usually be isolated but have sometimes been generated for reaction in situ for use in Wittig reactions.[62,63]

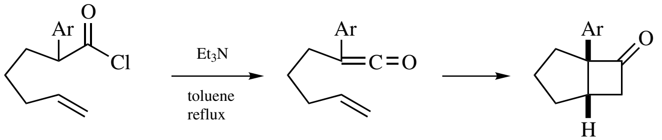


Ar, R: 2-Tol, Et (**49a**);
2-Anis, Me (**49b**);
N-Me-indolyl, Bn (**49c**)

(33)

47 **49** (21–42%)

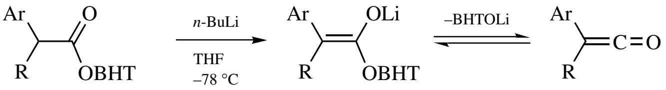
Intramolecular cyclization of aryl ketenes with remote double bonds provided a useful route to fused cyclobutanones.[64] Thus, dehydrohalogenation of 2-arylhept-6-enoyl chlorides (**50**) generated unobserved 2-aryl-2-pent-4-enylketenes **51**, which gave [2 + 2] cyclizations forming bicyclo[3.2.0]heptanones **52** (equation 34).[64]



(34)

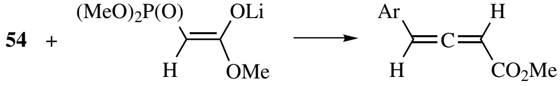
50a (Ar = Ph) **51a** **52a** (74%)
50b (Ar = 2-naphthyl) **51b** **52b** (88%)
50c (Ar = 2-furyl) **51c** **52c** (91%)

2,6-Di-*tert*-butyl-4-methylphenyl (BHT) esters of α-alkylarylacetates **53** were converted by *n*-BuLi in THF in the presence of ZnCl$_2$ or SnCl$_2$ to the corresponding ester enolates, which lost aryloxide anion to form ketenes **54** (equation 35).[65] The ketenes reacted with added lithium trimethyl phosphonoacetate **55**, forming allenes **56** through ketene Horner-Wadsworth-Emmons reactions (equation 36).[65]



(35)

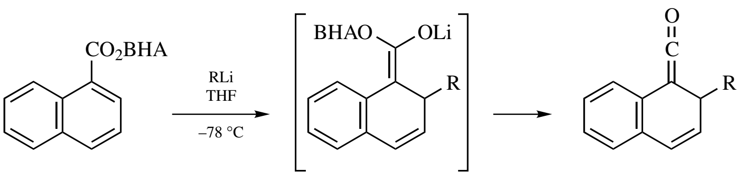
53 (Ar = Ph, 2-Naph; R = Me, Et, *i*-Pr) **54**



(36)

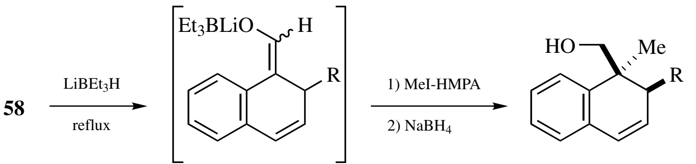
55 **56** (61–92%)

Reaction of 2,6-di-*tert*-butyl-4-methoxyphenyl (BHA) esters of 1- and 2-naphthalenecarboxylates **57** with organolithiums proceeded by addition to the naphthalene ring and elimination, giving ketenes **58** (equation 37).[66] The ketenes were converted in situ by lithium triethylborohydride to aldehyde enolates that were protonated or alkylated, followed by NaBH$_4$ reduction forming **59** (equation 38).[66]



(37)

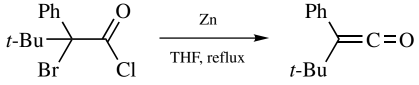
57 (BHA = 2,6-di-*t*-Bu$_2$-4-MeOC$_6$H$_2$) **58**
R = *n*-Bu, vinyl, Ph



(38)

59 (42–75%)

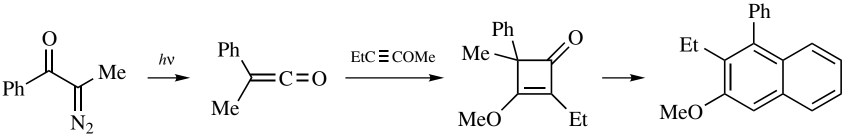
Zinc dehalogenation of PhCBr(*t*-Bu)COBr (**60**) was used to form phenyl(*tert*-butyl)ketene (**61**), which was isolated and characterized (equation 39).[67] The kinetics of hydration of this ketene were measured, and it was found to be less reactive in this nucleophilic attack by a factor of 1.4 × 10^4 compared to phenylketene.[67]



60 **61** (59%)

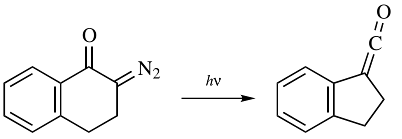
(39)

The formation of arylalkylketenes by Wolff rearrangement requires the preparation of unsymmetrical diazo ketones, usually from aryl carboxylic acids and substituted diazomethanes or from cyclic ketones. This method was used to form phenyl(methyl)ketene **47a** (equation 40) and 1-ketenylideneindane **62**, which underwent [2 + 2] cycloaddition with alkynyl ethers (equation 41).[68] Because of the susceptibility of ketenes to photochemical decarbonylation, these reactions are usually done with in situ capture of the ketenes.



47a (49%)

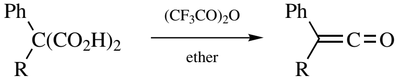
(40)



62

(41)

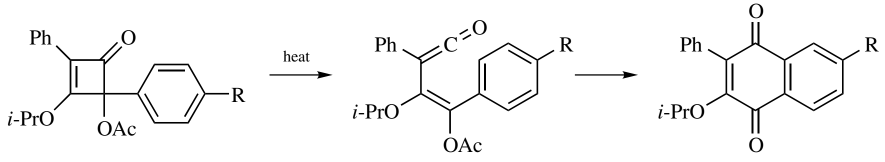
Treatment of 2-phenyl-2-alkylmalonic acids with trifluoroacetic anhydride gave phenylalkylketenes, and these were isolated by distillation (equation 42).[69,70]



R = Me (**a**), Et (**b**) **47a**, R = Me (98%)

(42)

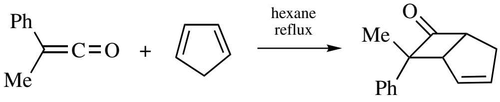
2-Arylcyclobutenone **63**, prepared by addition of the aryllithium to the cyclobutenedione, underwent thermal ring opening to give the unobserved arylvinylketene **64**, which cyclized, forming naphthoquinone **65** after air oxidation (Smith-Hoehn reaction; equation 43).[71,72]



63 (R = n-Bu$_3$Sn) **64** **65** (80%)

(43)

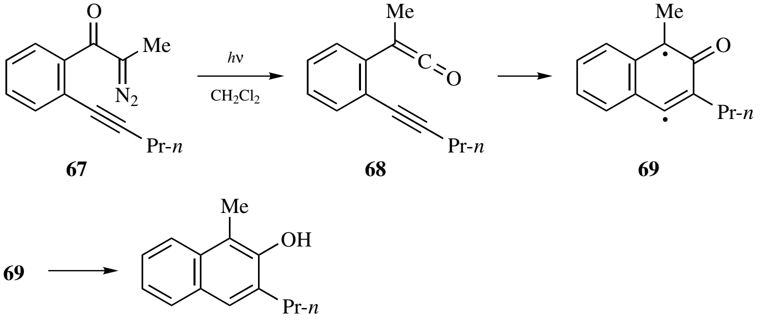
Phenyl(methyl)ketene (**47a**) gave [2 + 2] cycloaddition with a variety of alkenes with a preference between 1 and 2 for *endo* stereochemistry of the phenyl, but for cycloaddition with cyclopentadiene forming **66** the preference was greater than 20:1 (equation 44).[73]



47a **66** (85%)

(44)

Photochemical Wolff rearrangement of diazo ketone **67** formed the ketene **68**, which cyclized via the diradical intermediate **69**, leading to the naphthol **70** (equation 45).[74]

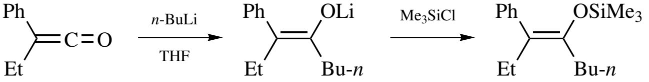


67 **68** **69**

(45)

70 (27%)

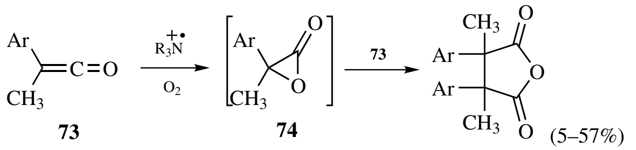
Addition of n-butyllithium to phenyl(ethyl)ketene (**47b**) took place with in-plane attack of the nucleophile on the least hindered side of the ketene opposite the aryl group forming the enolate **71**, which reacted with Me$_3$SiCl, forming Z-**72** (equation 46).[75]



47b **71** Z-**72** (77%)

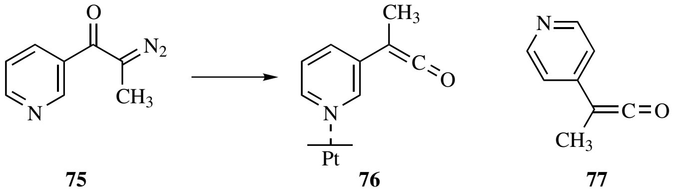
(46)

Electron transfer oxygenation of arylmethylketenes **73** was suggested to lead to α-lactone intermediates **74**, which reacted with another molecule of **73** to form succinic anhydrides (equation 47).[76] Ring opening of **74** to a zwitterion could also be involved.

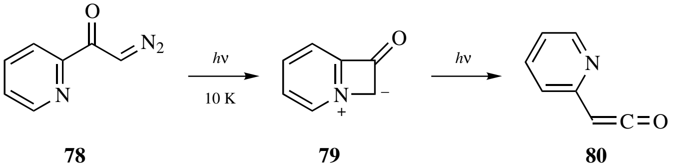


(47)

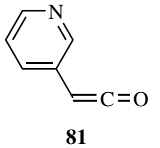
Wolff rearrangement of pyridyl diazo ketone **75** as a monolayer on a platinum surface gave 3-pyridyl(methyl)ketene **76** bound to the surface, as identified by the ketenyl IR absorption band at 2111 cm^{-1} (equation 48).[77] 4-Pyridyl(methyl)ketene **77** was formed in the same way. Photolysis of the diazo ketone **78** in an argon matrix at 10 K gave the ylide **79**, as identified by the IR spectrum which agreed with the DFT calculated spectrum, and which rearranged to 2-pyridylketene **80** upon further photolysis with light with λ >320 nm (equation 49).[78] Wolff rearrangement induced by FVP at 750 °C with trapping in an argon matrix at 10 K gave **80**, as identified by the IR bands at 2123 (*anti*-conformer) and 2132 cm^{-1} (*syn*-conformer).[78] The 2-, 3-, and 4-pyridyl ketenes **80**, **81**, and **82**, respectively, were formed by Wolff rearrangements in solution[79] and identified using TRIR spectroscopy by their absorption bands at 2127, 2125, and 2123 cm^{-1}, respectively. Their reactivity with *n*-BuNH$_2$ and with H$_2$O is considered in Section 5.5.2.3. Other preparations of pyridylketenes have been reported.[80–83]



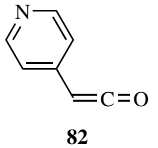
(48)



(49)

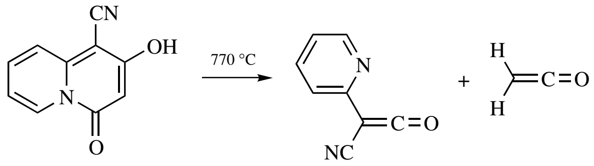


81



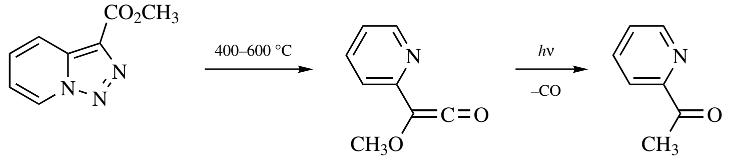
82

Flash vacuum thermolysis (FVT) of the quinolizine-4-one **83** led to the formation of 2-pyridylcyanoketene (**84**) as well as $CH_2{=}C{=}O$ (equation 50).[82] These were trapped in Ar at 20 K and identified by their ketenyl IR bands at 2149 cm^{-1} (*s*-Z-**84**) and 2141 cm^{-1}, respectively.[82] Similar thermolysis of the triazole **85** gave 2-pyridylmethoxyketene (**86**), IR 2114 cm^{-1}, which upon photolysis formed CO and 2-acetylpyridine (equation 51).[82] Photolysis of **85** in the matrix gave 2-pyridylketene (**80**) by the possible intermediacy of the diazo ester (equation 52).[83]



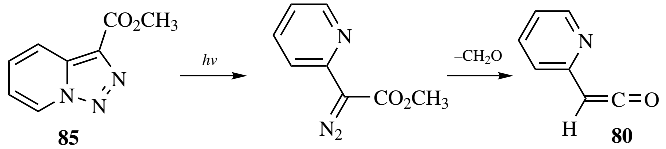
83 **84** (2149 cm^{-1})

(50)



85 *S-Z*-**86** (IR 2114 cm^{-1})

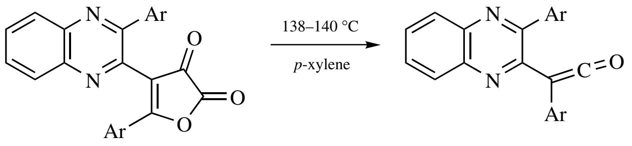
(51)



85 **80**

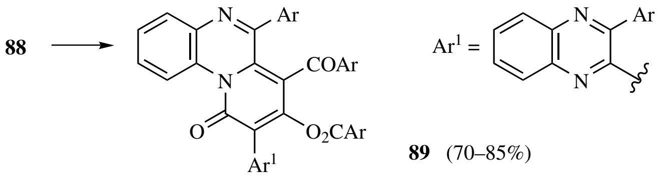
(52)

Furandiones **87** underwent decarbonylation at 138–140 °C, forming quinoxalinylketenes **88** (equation 53), which gave [4 + 2] dimerization with rearrangement, forming **89**,[84,85] or reacted with ketones by [4 + 2] cycloadditions.



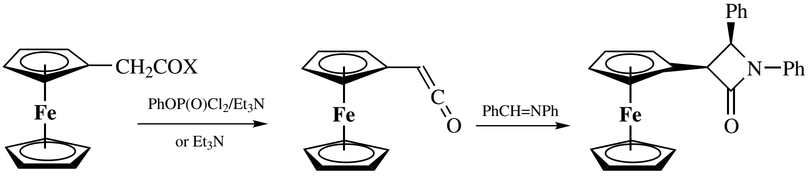
87 **88**

(53)



89 (70–85%)

Reaction of ferrocenylacetic acid **90** with $PhOP(O)Cl_2$ and Et_3N or of ferrocenylacetyl chloride **91** with Et_3N led to the formation of ferrocenylketene **92**, as evidenced by the in situ capture with imines forming β-lactams **93** (equation 54).[86] Photolysis of the diazo ketone **94** gave **92**, as observed by IR, and this was trapped by n-$BuNH_2$ or by the stable nitroxyl radical TEMPO (TO•), forming **95** and **96**, respectively.[87] Ferrocenylketenes have also been generated as unobserved intermediates in ring contraction of ferrocenyl diazo ketones.[88]

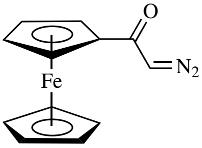


90 (X = OH)
91 (X = Cl)

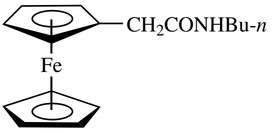
92

93 (65%)

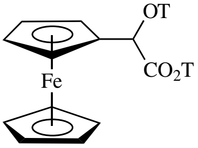
(54)



94

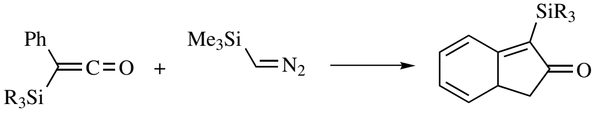


95



96

Aryl(trialkyl)silylketenes **97** have been generated by Wolff rearrangements, isolated as long-lived species by chromatography in yields of 52–89%, and found to react with trimethylsilyldiazomethane to yield indanone derivatives **98** (equation 55).[89] These reactions were proposed to proceed with initial [2 + 1] cycloaddition, as shown in Section 4.5.



97

98 (86%, R = i-Pr)

(55)

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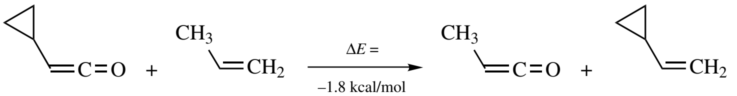
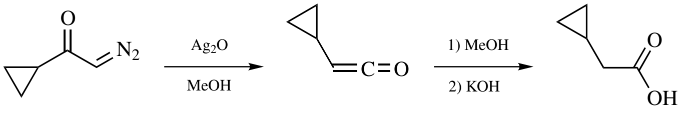
4.1.5 Cyclopropyl-, Cyclopropenyl-, and Oxiranylketenes

Cyclopropylketene is calculated by the HF/6-31G*//HF/6-31G* isodesmic energy comparison of equation 1 to be slightly less stable than methylketene.[1–3] The size of the cyclopropyl group is intermediate between those of the ethyl and isopropyl groups, and this offers a modest degree of steric protection.[4] The cyclopropyl group is highly strained, and when reaction pathways permit, ring opening may occur.

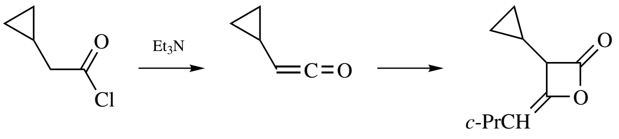


1 **2** **3** **4** (1)

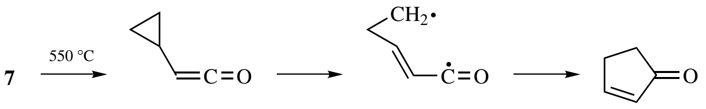
The original preparation of cyclopropylketene was by the Wolff rearrangement of diazo ketone **5** catalyzed by silver oxide in methanol, forming the methyl ester (equation 2).[5] Generation of **1** by dehydrochlorination of the acyl chloride **6** resulted in isolation of the dimer **7** (equation 3).[6] Pyrolysis of the dimer or of the ester *c*-PrCH$_2$CO$_2$Et at 550 and 600 °C, respectively, led to the formation of cyclopentenone **9**, evidently formed by rearrangement of **1** (equation 4).[6] This rearrangement may be considered to occur either through a diradical intermediate **8** or, alternatively, through a concerted process analogous to the vinylcyclopropane rearrangement, which in the case of the ketene **1** would be a pseudopericyclic process.



5 **1** **6** (47%) (2)

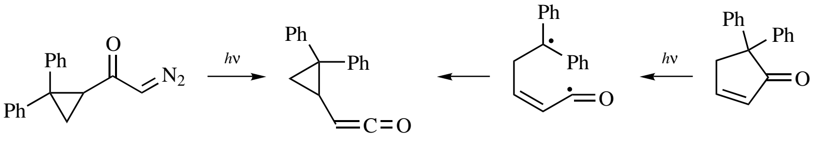


6 **1** **7** (3)

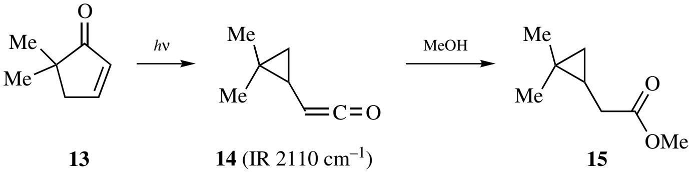


1 **8** **9** (4)

2,2-Diphenylcyclopropylketene (**10**) was generated by photochemical Wolff rearrangement of the diazo ketone in H$_2$O/CH$_3$CN and trapped as the acid. Photolysis of 4,4-diphenylcyclopentenone (**11**) also led to **10** through a process proposed to involve the biradical **12** (equation 5).[7] Photolysis of 4,4-dimethylcyclopentenone (**13**) in pentane gave rise to an IR absorption at 2110 cm^{-1} assigned to the ketene **14**, and trapping with methanol gave the ester **15** (equation 6).[7,8] These and other cyclopentenone cleavages were proposed to involve formation of diradical intermediates in the cyclopentenone-cyclopropylketene interconversion.[8]

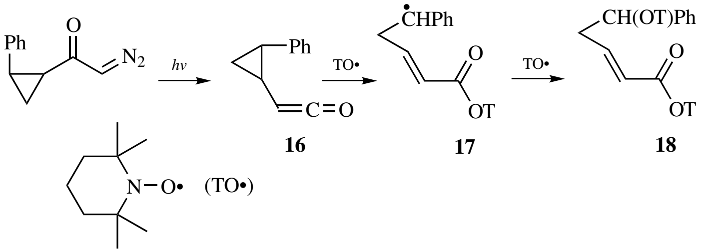


10 **12** **11** (5)



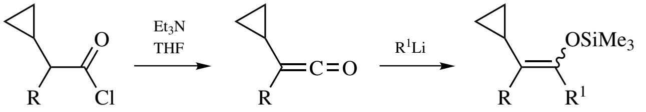
13 **14** (IR 2110 cm^{-1}) **15** (6)

Cyclopropylketenes **1**, **14**, and **16** were generated by photochemical Wolff rearrangements in hydrocarbon solvents, and their IR spectra with ketenyl bands at 2119–2120 cm^{-1} were measured under ambient conditions (equation 7).[9] The reaction of **16** with the aminoxyl radical TEMPO (TO•) gave the product **18** from ring opening to the intermediate radical **17** (equation 7).[9]



16 **17** **18** (7)

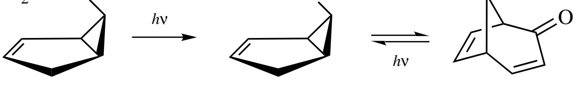
2-Phenyl-, 2-cyclopropyl-, and 2-*tert*-butyl-cyclopropylketenes **19a–c**, were prepared by dehydrochlorination of the acyl chlorides with triethylamine, and were obtained as stable and isolable products, with characteristic ketenyl IR bands at 2102, 2106, and 2097 cm^{-1}, respectively (equation 8).[10] Addition to **19a** of *n*-BuLi or *t*-BuLi led to enolates that upon capture with Me_3SiCl gave the silyl enol ethers **20** with 79:21 and 9:91 preferences for addition of RLi *anti* to phenyl, respectively (equation 8).[10]



(R = Ph, *c*-Pr, *t*-Bu) **19a–c** (32–55%) **20** (R = Ph, R^1 = *n*-Bu, *t*-Bu) (8)

Cyclopropylketene (**1**) was more reactive than *n*-BuCH=C=O toward H_2O by a factor of only 3.1 (Section 5.5.1.2).[11] There is no evidence for major rate enhancements in other additions to this species.

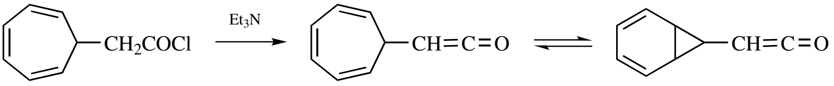
Photochemical Wolff rearrangement of diazo ketone **21** in THF gave the strained cyclopropylketene **22**, which cyclized to bicyclooctadienone **23** by Cope rearrangement (equation 9).[12] Ketene **22** was reformed by photolysis of **23** and observed by IR at 2112 cm^{-1} (neat film, −190 °C).[13] The ketene was trapped by methanol to give the ester in >90% yield, or in the absence of nucleophiles underwent thermal conversion back to **23**.[13] Other similar vinylcyclopropylketenes were generated by ring opening of bicycloheptadienones.[13]



21 **22** (IR 2112 cm^{-1}) **23** (9)

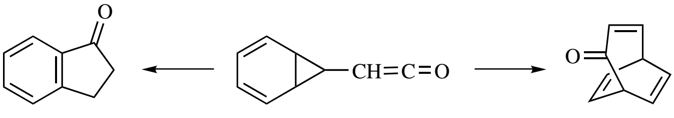
Dehydrochlorination of **24** gave the cycloheptatrienylketene **25**, which was proposed to be in equilibrium with the norcaradienylketene **26** (equation 10).[14]

Evidence for the presence of **26** was the isolation of the possible rearrangement products **27** and **28** in 44 and 40% yields, respectively (equation 11).[14]



24 **25** **26**

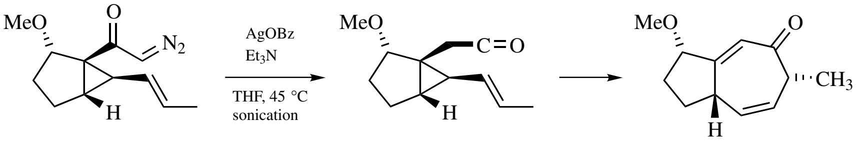
(10)



27 (44%) **26** **28** (40%)

(11)

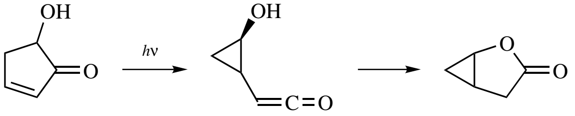
The ketene **30** formed by Wolff rearrangement of diazo ketone **29** using sonochemically assisted silver benzoate catalysis led to the cycloheptadienone **31** by ketene Cope rearrangement (equation 12).[15] Modeling of the reaction by DFT calculations allowed the prediction of the effects of substituents in order to design substrates that favor particular products (see also Section 3.3).[16]



29 **30** **31** (95%)

(12)

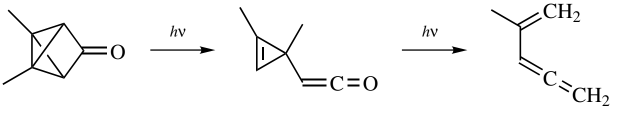
As noted in Section 3.4.2, photolysis of hydroxycyclopentenone **32** gave lactone **34**, which was proposed to form from (hydroxycyclopropyl)ketene **33** (equation 13).[17] The ketene was not trapped by CH_3OH, and it was proposed that the cyclization rate was even faster than that of solvent attack.



32 **33** **34**

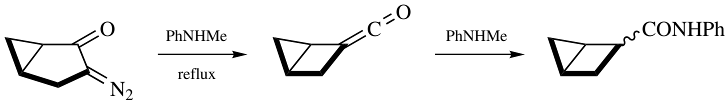
(13)

Photolysis of **35** in an Ar matrix, as also noted in Section 3.4.2, led to the dimethylcyclopropenylketene **36**, as characterized by the IR band at 2105 cm^{-1}, and further photolysis resulted in decarbonylation and formation of the vinylallene **37** (equation 14).[18]

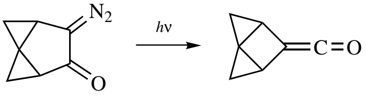


35 **36** **37** (14)

Ketene **39** was formed by thermolysis of the diazo ketone **38** in boiling *N*-methylaniline and was captured as the epimeric anilides **40** (equation 15).[19] The IR of **39** generated in a matrix was observed at 2140 cm^{-1}.[20] Photolysis of the diazo ketone **41** in a matrix gave rise to an IR band at 2117 cm^{-1} and provided evidence of the formation of ketene **42** by ring contraction (equation 16).[20] However, photolysis in solution in the presence of trapping agents such as CH_3OH or Me_2NH gave products of trapping of cleavage products of an intermediate keto carbene.

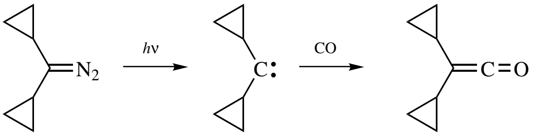


38 **39** (IR 2140 cm^{-1}) **40** (15)



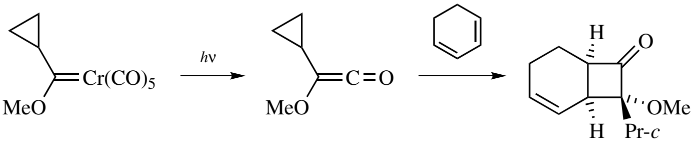
41 **42** (IR 2117 cm^{-1}) (16)

Dicyclopropylcarbene (**44**) was generated in a matrix by photolysis of dicyclopropyldiazomethane (**43**), and reacted with CO, forming dicyclopropylketene (**19b**), IR 2112 cm^{-1} (equation 17).[21]

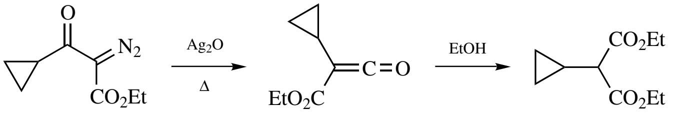


43 **44** **19b** (IR 2112 cm^{-1}) (17)

Photolysis of the cyclopropyl cabene metal complex **45** gave ketene **46**, which was trapped by cyclohexadiene in a [2 + 2] cycloaddition, forming **47** (equation 18).[22] Thermal Wolff rearrangement of the diazo ketone **48** proceeded with cyclopropyl group migration, forming the ketene **49**, which was isolated by distillation and reacted with ethanol to give the diethyl ester **50** (equation 19).[23,24]



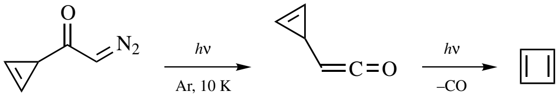
45 **46** **47** (48%) (18)



48 **49** **50** (43%)

(19)

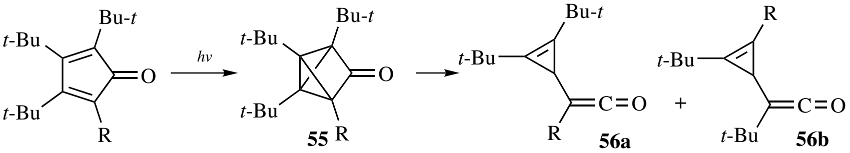
Cyclopropenylketene (**52**) was formed by Wolff rearrangement of the diazo ketone **51** in an argon matrix at 10 K and identified by the IR band at 2108 cm^{-1}.[25] Further photolysis of the ketene in the matrix led to decarbonylation and formation of cyclobutadiene (**53**, equation 20).[26]



51 **52** **53**

(20)

Upon photolysis at −78 °C the cyclopentadienones **54** reacted via the bicyclic ketones **55** and gave cyclopropenylketenes **56a**,**b**, as evidenced by the IR absorption at 2080 cm^{-1} (equation 21).[27,28] Upon treatment with $CuCl_2$ the ketenes reformed **54**.[27,28]

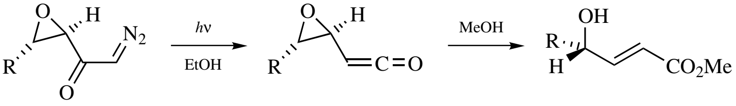


55 **56a** **56b**

54a-c
a (R = 1-Ad)
b (R = *t*-Bu)
c (R = *i*-Pr)

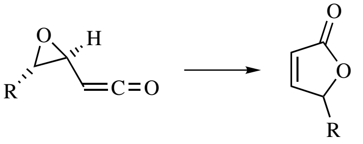
(21)

Oxiranylketenes **58** formed by photochemical Wolff rearrangements of diazo ketones **57** gave stereoselective ring opening on reaction with nucleophiles, forming unsaturated hydroxyl esters **59** (equation 22).[29] In the absence of nucleophiles, rearrangement to butenolactones **60** took place (equation 23).[30]



57 **58** **59** (90%, R = Ph)

(22)



58 **60** (90%, R = Ph)

(23)

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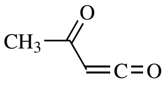
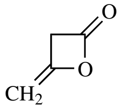
4.1.6 Acylketenes

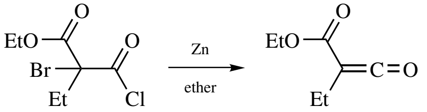
It was originally proposed in 1908 that acetylketene (**1**) was the structure of the ketene dimer,[1] but this was disproved, and in 1909 carboethoxy(ethyl)ketene (**4**) was prepared by dehalogenation of **3** in an ethereal solution as the first authentic acylketene (equation 1).[2] This family has been studied ever since, and general reviews of acylketenes have appeared,[3,4] as well as a brief review devoted to the chemistry of chlorocarbonylketenes.[5]



1

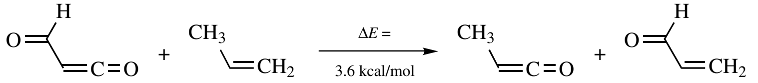


2

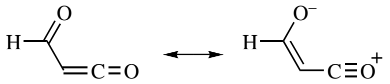


3 **4** (1)

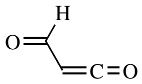
Formylketene (**5**) was calculated to be stabilized by 3.60 kcal/mol relative to methylketene by isodesmic energy comparison (equation 2).[6–8] This has been attributed to the conjugative stabilization between the ketenyl group and the formyl group, as represented by the resonance structure **5a**. The conformer *syn*-**5** was found[6,7] to be more stable than *anti*-**5** by 1.0 kcal/mol, and this was proposed to result from a favorable electrostatic interaction between the formyl oxygen and the ketenyl carbon.[6,7]



5 **6** **7** **8** (2)

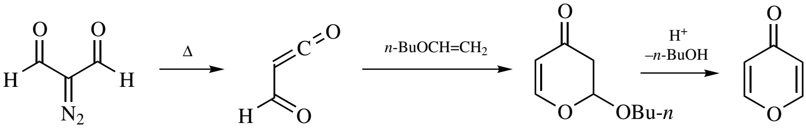


syn-**5** *syn*-**5a**



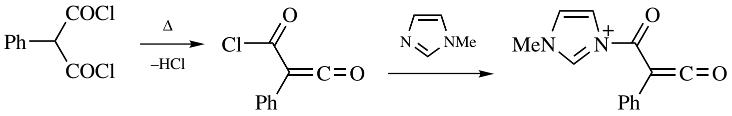
anti-**5**

Acylketenes have been prepared by a variety of routes. The parent formylketene **5** was formed by photochemical Wolff rearrangement of the diazo ketone **9** in an argon matrix at 10 K, and observed by IR as interconverting *syn* and *anti* forms, with IR bands at 2145 and 2142 cm^{-1}, respectively.[9] Thermolysis of **9** in refluxing *n*-butyl vinyl ether gave **5**, which reacted with the vinyl ether by a [4 + 2] cycloaddition forming **10**, which gave **11** by elimination (equation 3).[10]

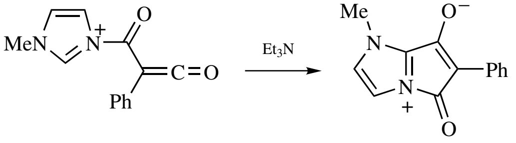


9 *syn*-**5** **10** (70%) **11** (96%) (3)

Chlorocarbonyl(phenyl)ketene (**13**) and related derivatives were formed by thermolysis of malonyl dichlorides **12** and are often isolable intermediates (equation 4).[5,11–13] These ketenes tended to react preferentially at the ketenyl group with nucleophiles.[11] Reaction of **13** with imidazole gave a solid product identified as **14** (equation 4), and this formed **15** on reaction with Et_3N (equation 5).[13]

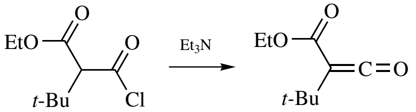


12 **13** **14** (4)

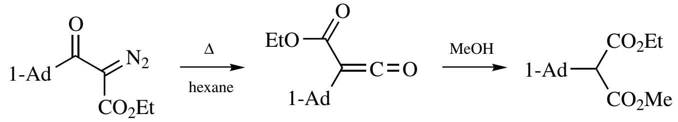


14 **15** (100%) (5)

Acylketenes with bulky substituents are long-lived, and *tert*-butyl(carboethoxy) ketene **16**, prepared by dehydrochlorination (equation 6), was persistent,[14] as were the corresponding methyl ester (IR 2129 cm^{-1})[15] and 1-adamantyl(carboethoxy) ketene (**17**), prepared as a solution in hexane by Wolff rearrangement (equation 7).[16]

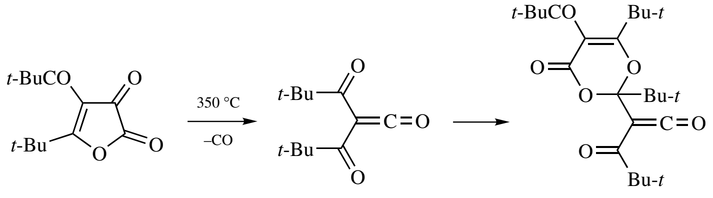


16 (73%, IR 2130 cm^{-1}) (6)



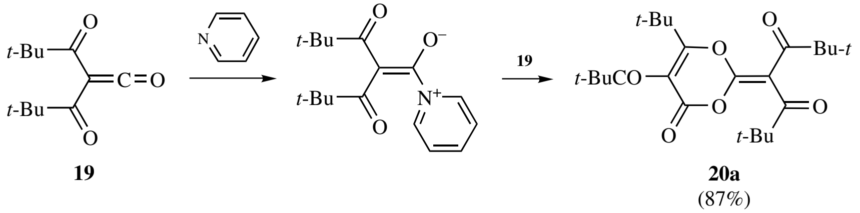
17 (IR 2120 cm^{-1}) (86%) (7)

Dipivalylketene **19** was prepared from pyrolysis of the furandione **18**, and while stable in solution at −20 °C, it reacted rapidly with MeOH to give the ester, and dimerized by a [4 + 2] pathway to give ketene **20** as a stable species, for which an X-ray structure was obtained (equation 8).[17] The diverse chemistry found for **20** included differing reactions with amines[18] and nucleophilic reactions leading to 2,4,6,8-tetraoxaadamantanes,[19] and this has been reviewed.[20] The mechanism of thermolysis of furandiones has been studied experimentally, using IR detection, and by computation.[21]



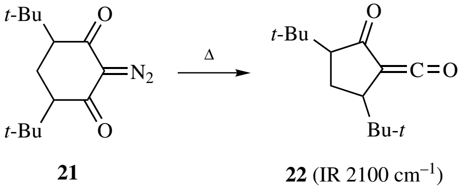
18 **19** (2138 cm^{-1}) **20** (88%) (IR 2115 cm^{-1}) (8)

An alternative mode of [4 + 2] dimerization of **19** across a C=O bond was induced by DMSO, *n*-Bu_3PO, or pyridine,[22] and was proposed to result from an intermediate zwitterion forming **20a** (equation 9).[22] Reactions of **19** with various RNH_2 reagents were observed.[23]



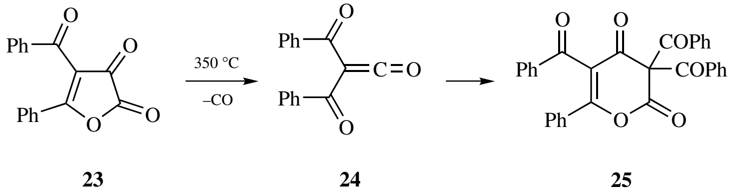
(9)

Stereoisomeric diazo ketones **21** formed the corresponding acylketenes **22** on thermolysis, and the ketenes were isolated and characterized (equation 10).[24] The stereochemistry of the reactions of **22** with alcohols and amines was examined.[24] Acyclic diazo ketones with bulky aryl groups reacted with alcohols or amines to form enols whose molecular dynamics were studied by NMR.[25]



(10)

Dibenzoylketene **24** was prepared from pyrolysis of the furandione **23** and trapped with amines,[26] and its IR absorption at 2140 cm^{-1} was observed in a matrix at −196 °C (equation 11).[27] On warming, **24** gave the dimer resulting from [4 + 2] cycloaddition forming **25**, and this led to **26** and **27** (equation 12).[27]



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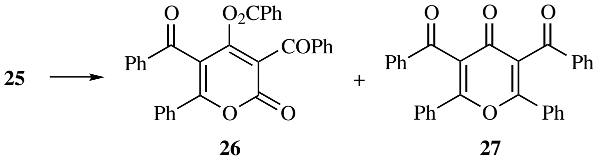
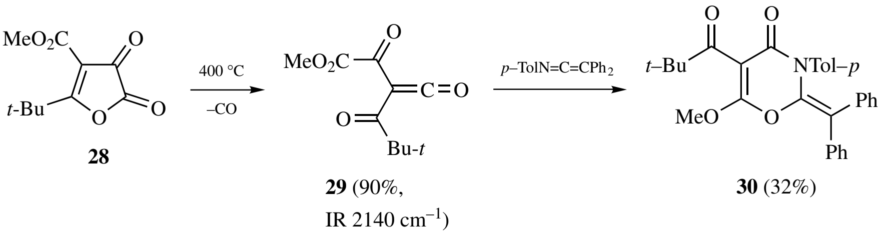


(12)

The diacylketene **29** was formed as a fairly persistent neat liquid by decarbonylation upon flash pyrolysis of furan-2,3-dione **28**, and gave [4 + 2] cycloaddition with a ketenimine involving reaction of the less hindered but normally less reactive ester carbonyl, forming **30** (equation 13).[28] When **29** was cogenerated with **31** the two ketenes underwent a [4 + 2] cycloaddition, forming **32** (equation 14).[29]



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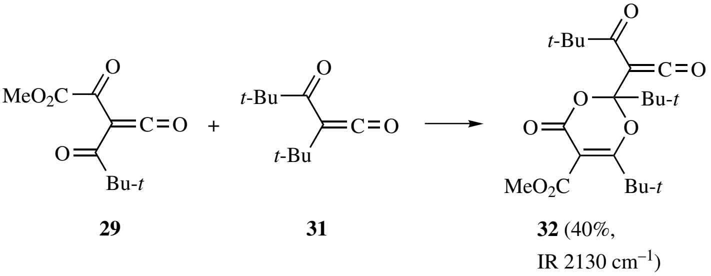
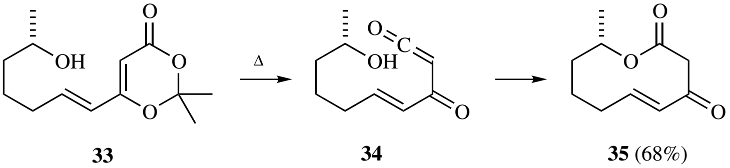


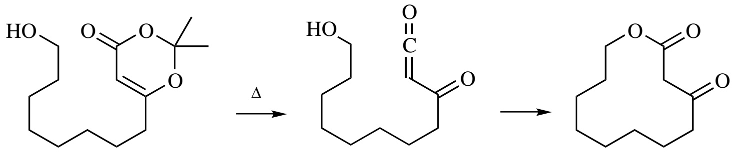
(14)

Acylketenes have also been generated by the thermolysis or photolysis of dioxinones.[30–35] For **33** with a side chain bearing a hydroxyl group forming the ketene **34**, this was a useful method for cyclization forming lactone **35** (equation 15).[31]



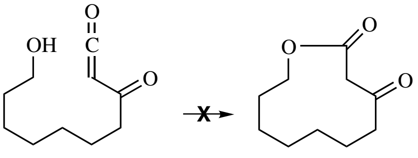
(15)

In other applications[36–39] of the cyclization of acylketenes generated by the thermolysis of dioxinones bearing hydroxy or amino side chains, macrocyclic lactones or lactams were formed. The dioxinone **36** formed ketene **37**, which gave not only the 12-membered ring lactone **38** in 28% yield, but also the dimeric and trimeric 24- and 36-membered lactones in 41 and 12% yields, respectively (equation 16).[36] Efforts to form an analogous 11-membered ring lactone **40** by thermolysis of ketene **39** (equation 17) were unsuccessful, and only dimeric, trimeric, and higher molecular weight lactones were observed. Thus, thermolysis of **41** to form ketene **42** gave a series of cyclic oligolides **43**, and for $n = 1–6$ these were isolated and characterized as 22- to 77-membered rings by ^{1}H and ^{13}C NMR and by mass spectroscopy (equation 18).[37]



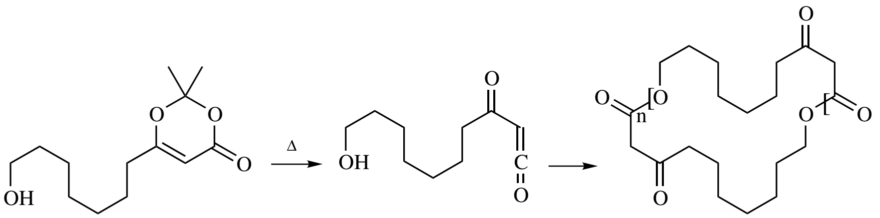
36 **37** **38** (28%)

(16)



39 **40**

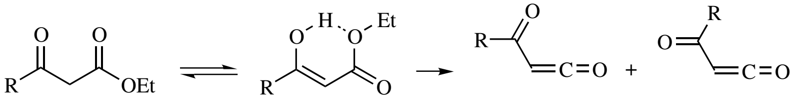
(17)



41 **42** **43**

(18)

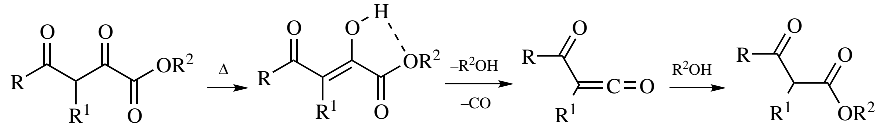
Flash vacuum thermolysis of β-keto esters **44** formed acylketenes **46** observed by IR spectrocopy at 12 K. It was proposed that these reactions involved initial enolization to **45**, as the more readily enolized substrates reacted more readily, and the residual starting material was enriched in the keto form (equation 19).[40–44]



44 (R = Me, *t*-Bu, 1-Ad) **45** *syn*-**46** *anti*-**46**

(19)

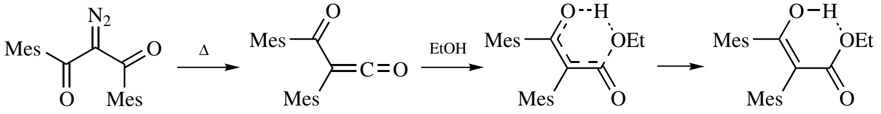
Pyrolysis of 2,4-diketo esters **47** at 170–190 °C took place with elimination and decarbonylation forming acylketenes **48**, which were captured by the alcohol forming esters **49** (equation 20).[45,46] The reactions were proposed to occur by pericyclic elimination with decarbonylation, and the stretching frequencies of the ketenes in the region 2120–2140 cm^{-1} were observed by GC-FTIR when the reactions were carried out at 280 °C.



47 **48** **49**

(20)

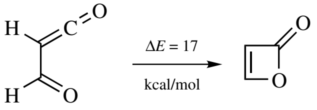
The addition of oxygen nucleophiles to acyl ketenes has the potential for in-plane attack on the side of the acyl oxygen through pseudopericyclic transition states, as in the reaction of ketene **50**, for which the transition state **51** leading to the enol ester **52** was proposed (equation 21).[25,47,48] A similar mechanism was put forward to account for the hydration of ketene **16**,[49] and this reaction was modeled with *ab initio* calculations.[49,50]



Mes = 2,4,6-$Me_3C_6H_2$ **50** **51** **52**

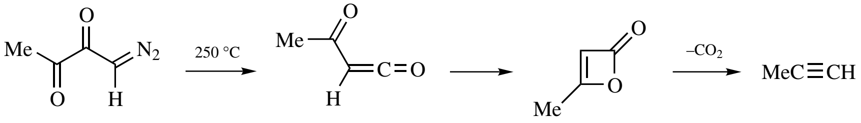
(21)

The cyclization of formylketene **5** to **53** was calculated to be endothermic by 17 kcal/mol (equation 22),[51] but cyclization of acetylketene **1** was proposed to occur to account for the products formed upon pyrolysis of **54** forming propyne via the intermediacy of **55** (equation 23).[52] FVP of **56** was proposed to form carbomethoxyketene (**57**), which was captured with benzyl alcohol (equation 24).[53]



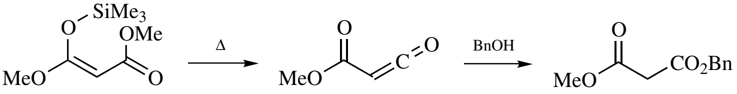
5 **53**

(22)



54 **1** **55**

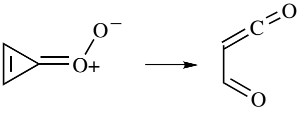
(23)



56 **57**

(24)

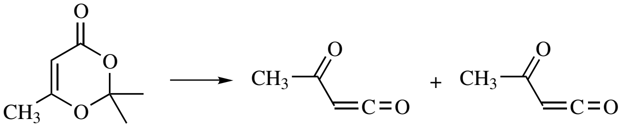
Isomerization of cyclopropenone carbonyl oxide **58** to formylketene **5** was calculated at the MRDCI + Q level to have a barrier of 32.0 kcal/mol and to be exothermic by 117.5 kcal/mol (equation 25).[54] The geometry and vibrational spectra of **5** were calculated using improved methodology.[55]



(25)

58 **5**

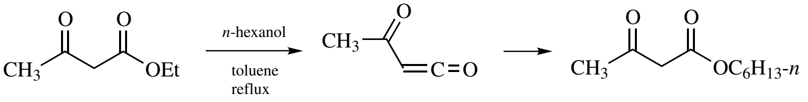
FVP of dioxinone **59** with matrix isolation gave IR spectra that exhibited bands due to two conformations of acetylketene (**1**), and these spectra were in good agreement with calculations (equation 26).[56] Photolysis gave new bands attributed to photochemically populated matrix sites.



(26)

59 *syn*-**1** *anti*-**1**

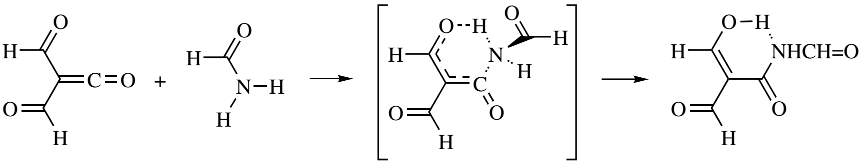
Transesterification of β-keto esters **60** with alcohols in refluxing toluene over aluminosilicates occurred by formation of acetylketene (**1**) as an intermediate, which led to the ester **61** (equation 27).[57]



(27)

60 **1** **61** (72%)

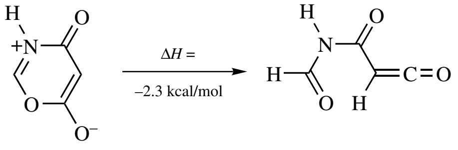
Computations of the reaction of diformylketene (**62**) with formamide found a preference for a one-step asynchronous reaction through a pseudopericyclic transition state **63** with the formyl group of the formamide above the plane leading to the product **64** (equation 28).[58] Computations for the reaction in benzene solvent indicated that there was little change compared to the gas phase in the structures.[58]



62 **63** **64**

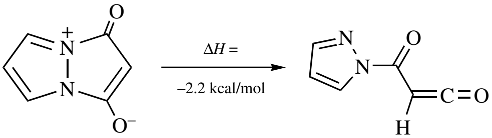
(28)

The formation of acylketenes **65** and **67** from the mesoionic species **64** and **66**, respectively, was calculated to be exothermic by about 2 kcal/mol in each case (equations 29, 30).[59] The formation of α-amidoketenes $R^1C(CONR){=}C{=}O$ from the reaction of alkynes with CO_2 is discussed in Section 3.8.



64 **65**

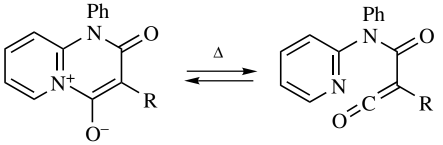
(29)



66 **67**

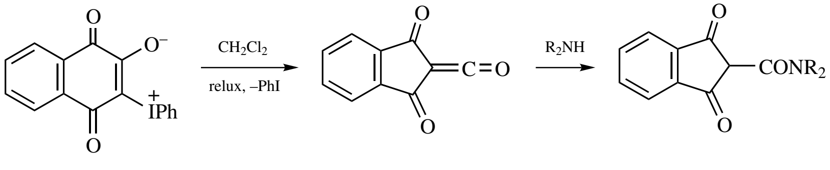
(30)

FVT of mesoionic species **68** and matrix isolation resulted in formation of the unobserved acylketenes **69**, which interconverted with **68** (equation 31).[60] Wolff-type rearrangements of aryliodonium ylides **70** provided a route to diacylketenes **71**, which were trapped with amines, giving amides **72** (equation 32).[61,62]



68 **69**

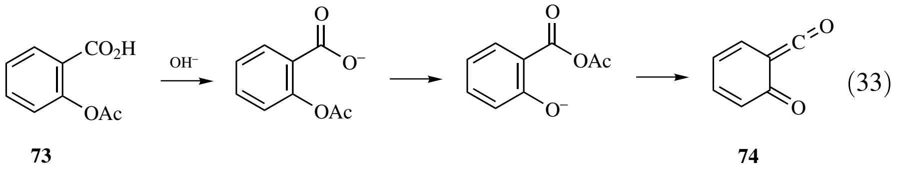
(31)



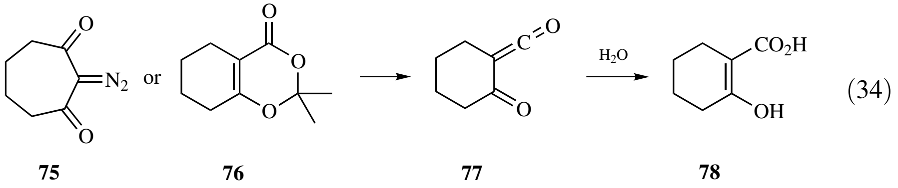
70 **71** **72** (73–94%)

(32)

The rapid hydrolysis of 2-acetoxybenzoic acid **73** was proposed[63] to occur with intramolecular catalysis, with formation of the unobserved acylketene **74** (equation 33), which formed an observed acid enol whose rate of ketonization was measured.[63] Ketene **77** was generated by photochemical Wolff rearrangement of the diazo ketone **75** and also by photolysis of the dioxinone **76**, and upon hydration formed **78** (equation 34).[64] The hydration to the enol and ketonization of the enol were studied and compared to the reactions of the corresponding 5-membered ring analogue.

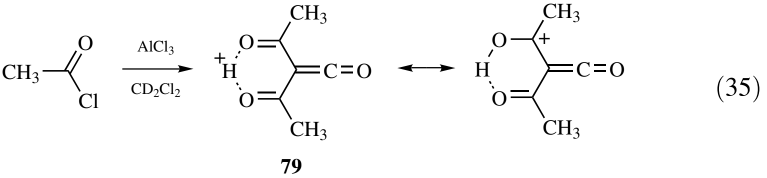


73 **74**



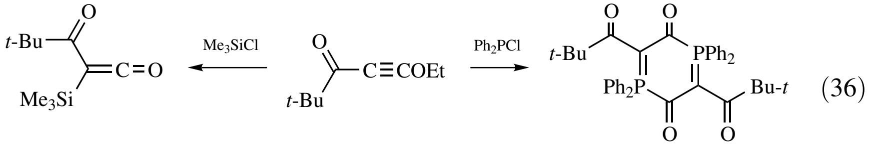
75 **76** **77** **78**

The reaction of acetyl chloride with $AlCl_3$ in CD_2Cl_2 formed protonated diacetyl-ketene tetrachloroaluminate (**79**), which was characterized by ^1H- and ^{13}C-NMR and by IR (equation 35).[65]



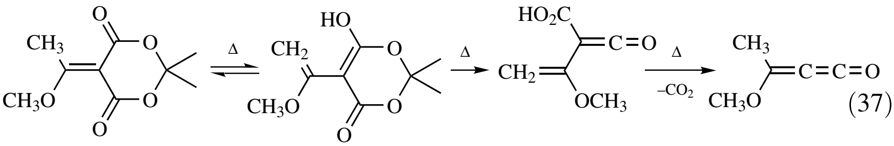
79

The reaction of pivaloylethoxyacetylene (**80**) with Me_3SiCl led to the acylketene **81**, and germanium halides reacted similarly, while Ph_2PCl formed the dimer **82** (equation 36).[66]



81 **80** **82**

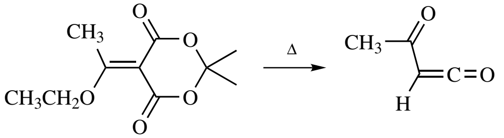
FVP of the Meldrum's acid derivative **83** gave the carboxylketene **84**, as identified by FTIR, and this underwent decarboxylation to **85** (equation 37).[67,67a] The corresponding ethoxy cumulated ketene was formed from **86** and then gave **87** (equation 38).[67a] An *Organic Syntheses* procedure for preparation of 2-alkyl-4-pyrones **90** involves heating of the Meldrum's acid derivative **88**, which was proposed to lose acetone to generate the acylketene **89**, which was captured by *n*-butyl vinyl ether followed by decarboxylation and acid-catalyzed elimination (equation 39).[68–70] A related generation of an acylketene from a hydroxymethylene Meldrum's acid derivative is shown in Section 3.4.6.[71]



83 **84** **85**

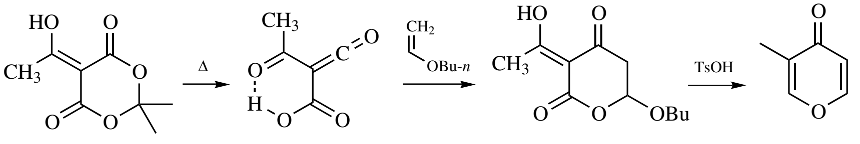
(IR 2153, 2150 cm^{-1})

(37)



86 **87** (IR 2143, 2133 cm^{-1})

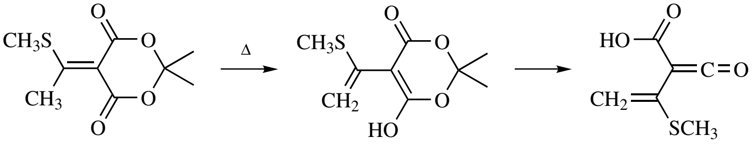
(38)



88 **89** **90** (61%)

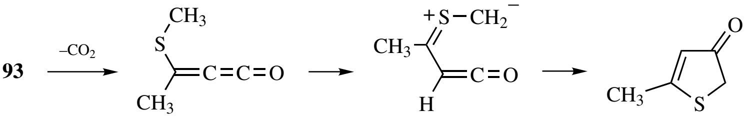
(39)

Reaction of the methylthio derivative **91** was proposed to form **92** and then the ketene **93** (equation 40), which led to the thiophene derivative **94** (equation 40a).[67a] Ketene **94a** from dioxinone **88** reacted with Boc(BocO)NH, leading to the β-keto hydroxamic acid **94b**, and was cyclized to a 3-isoxazole (equation 41).[72]



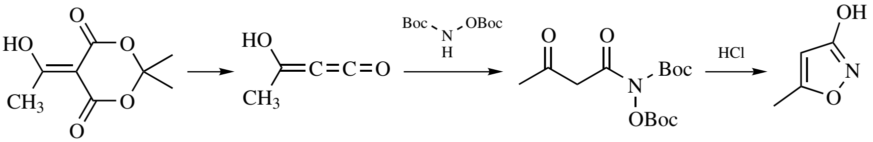
91 **92** **93**

(40)



94

(40a)

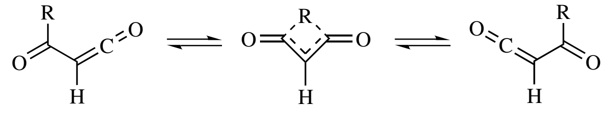


88 **94a** **94b** (74%)

(41)

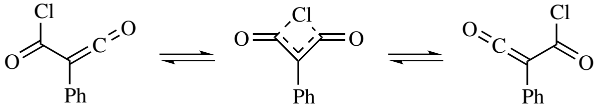
Intramolecular rearrangements in acylketenes **95** have been examined by *ab initio* molecular orbital calculations. Particularly for groups such as Me$_2$N and

MeS with lone pair electrons available for donation, these were predicted to occur at reasonable temperatures through a transition state **96** (equation 42).[73–75] 1,3-Shift of Cl in system **97** (equation 43) was also calculated[76] to be accelerated, as was a 1,5-Cl shift in O=C=CHCH=CHCCl=O (**99**) through the transition state **100** (equation 44). Measurements by ^{13}C NMR show the 1,3-Cl shift in **97** has $\Delta G^{\ddagger}$ of only 10.0 kcal/mol, in excellent agreement with the results of molecular orbital calculations (equation 43).[77] Calculations of the conformations and reactivities of a variety of acylketenes have also been reported.[78]



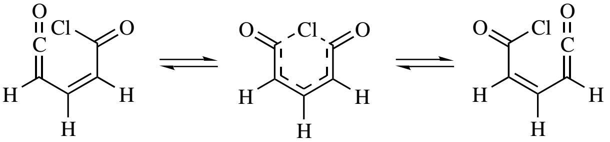
95 (R = Me_2N, MeS) **96** **95**

(42)



97 **98** **97**

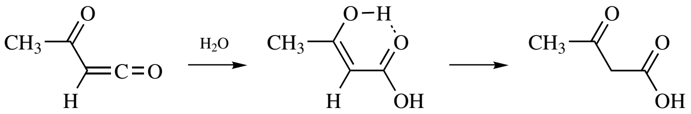
(43)



99 **100** **99**

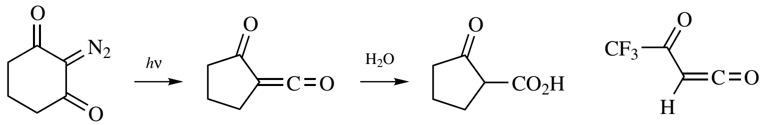
(44)

The kinetics of the hydration of acetylketene **1** generated by flash photolysis of the dioxinone **59** (equation 26) were measured, and this ketene was remarkably reactive, with a rate constant of $1.5 \times 10^6\,\mathrm{s}^{-1}$ at 25 °C.[79] The initial product was acetoacetic acid enol (**101**), which formed acetoacetic acid (**102**) by a process whose mechanism was also elucidated (equation 45).[79] These studies did not provide evidence regarding the carbonyl-assisted hydration of acetylketene, and this question is still unanswered. The cyclic analogue **104** prepared by Wolff rearrangement of the diazo ketone **103** had $k(H_2O) = 1.4 \times 10^6\,\mathrm{s}^{-1}$, almost identical to that of **1** (equation 46),[80] and the trifluoromethyl analogue **106** had a similar rate constant of $1.75 \times 10^6\,\mathrm{s}^{-1}$.[81]



1 **101** **102**

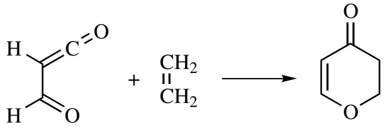
(45)



103 **104** **105** **106**

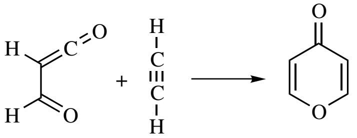
(46)

Calculations of the cycloaddition of formylketene (**3**) with ethylene showed that planar and nonplanar transition states to form **107** had almost equal energy, whereas the reaction with acetylene to form **108** favored a nonplanar transition state (equations 47, 48).[82]



3 **107**

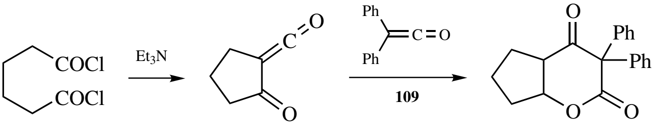
(47)



3 **108**

(48)

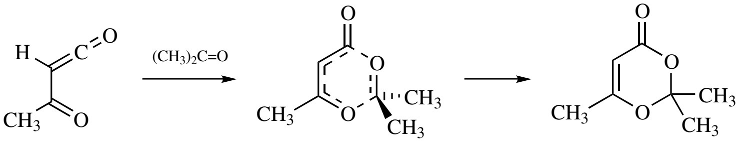
Dehydrochlorination of adipyl dichloride was proposed to form the acylketene **104**, which underwent [4 + 2] cycloaddition with diphenylketene (**109**) to give the adduct **110** (equation 49).[83]



104 **110**

(49)

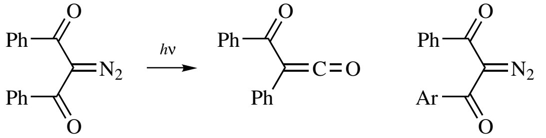
The transition state **111** for [4 + 2] cycloaddition of acetylketene **1** plus acetone forming the dioxinone **59** has been calculated to have the bonding atoms essentially coplanar (equation 50).[84] This geometry was expected for in-plane attack on the ketenyl moiety. Computational studies of the reaction of **1** with aldehydes bearing chiral substituents have shown this to proceed with Felkin-Anh stereoselectivity.[85]



1 **111** **59**

(50)

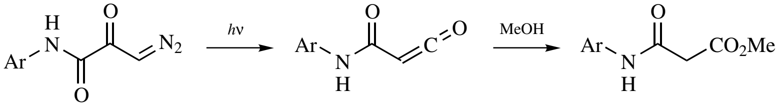
Photolysis of diazo diketone **112** formed phenylbenzoylketene (**113**), which reacted with amino acid derivatives (equation 51).[86] Photolysis of the diazo ketone **114** with an ionic side chain in the presence of DNA gave cleavage of the DNA at guanine.[86–88] Further examples of DNA cleavage by ketenes are given in Section 5.4.1.2.



112 **113** **114** (Ar = 4-$C_6H_4CONHCH_2CH_2NH_2$)

(51)

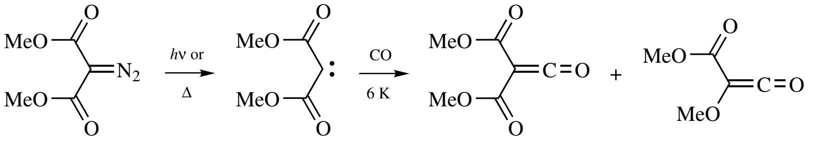
Photochemical Wolff rearrangements of diazo ketone derivatives **115** gave carboxamide-substituted ketenes **116** (equation 52) that were trapped by nucleophiles, and it was proposed that the diazopyruvyl derivatives could be attached to thiol groups of proteins to give photoactivatable cross-linking agents.[89]



115 **116** (10–72%)

(52)

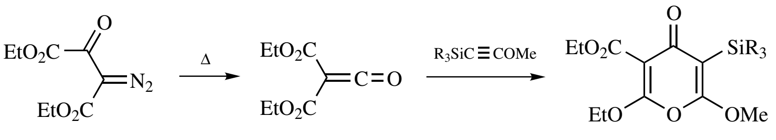
Diazo ketone **117** gave a photochemical or thermal reaction leading to formation of diacylketene **119** by carbene capture by CO in matrices at 6 K of the carbene **118** competitive with Wolff rearrangement, forming **120** (equation 53).[90]



117 **118** **119** (IR 2166 cm^{-1}) **120** (IR 2136 cm^{-1})

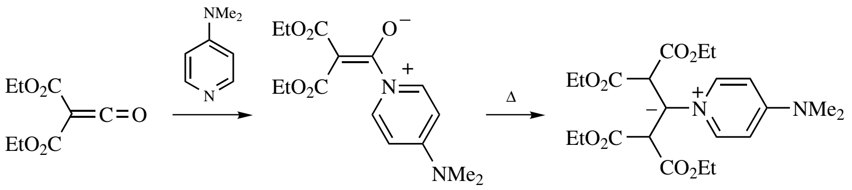
(53)

Staudinger and Herzel prepared di(carboethoxy)ketene **122** in 1916 as a distillable liquid by the Wolff rearrangement of diazo ketone **121** (equation 54).[91] This ketene reacted slowly with moisture and dimerized at room temperature,[92] and underwent [4 + 2] cycloaddition with a methyl silylalkynyl ether, forming **122a** (equation 54).[93] 4-Dimethylaminopyridine (DMAP) reacted with **122** to form the zwitterion **123** as a solid that formed **124** on heating (equation 55).[94]



121 **122** **122a** (39%)

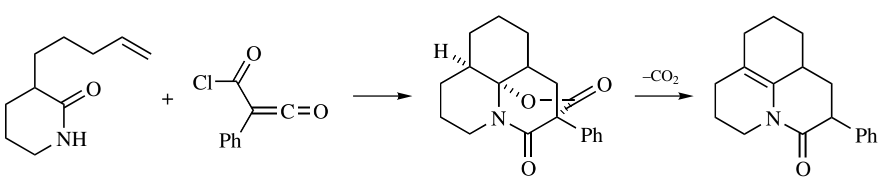
(54)



122 **123** (80%) **124** (65%)

(55)

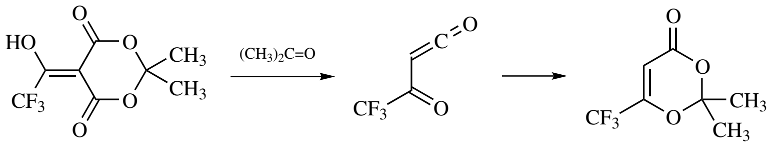
The reaction of **97** with 3-alkenyl δ-lactams **125** gave polycyclic lactones **126** that were thermally decarboxylated to **127** (equation 56).[95] The reaction of **97** with oximes formed heterocyclic mesomeric betaines.[96]



125 **97** **126** **127** (16%)

(56)

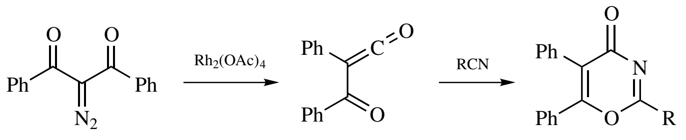
Trifluoroacetyl Meldrum's acid, which exists in the enol form **128**, reacted with acetone at room temperature to give the corresponding dioxinone **129** in a process proposed to involve trifluoroacetylketene (**106**, equation 57).[97]



128 **106** **129**

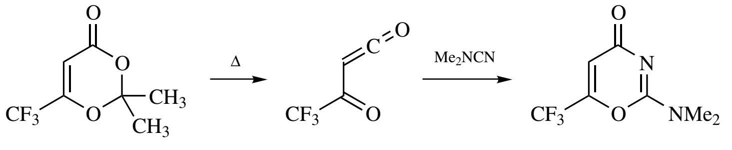
(57)

Dibenzoyldiazomethane with rhodium acetate formed benzoylphenylketene (**113**), which reacted with nitriles by [4 + 2] cycloaddition to form 1,3-oxazine-4-ones (**130**, equation 58).[97] Trifluoroacetylketene (**106**) from dioxinone **129** reacted with the nitrile **131** to give the 1,3-oxazin-4-one **132** (equation 59).[98]



113 **130** (76%)

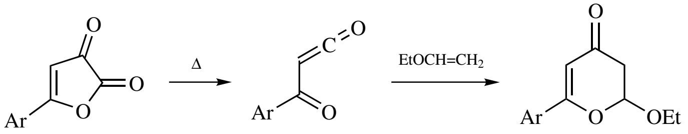
(58)



129 **106** **132** (46%)

(59)

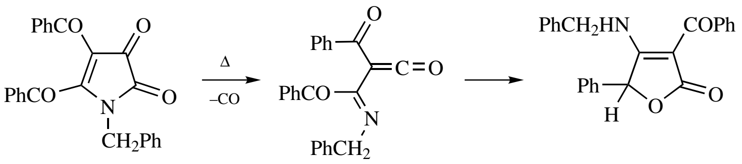
The reactivity of aroylketenes **134** formed by thermolysis of 5-aryl-2,3-dihydrofuran-2,3-diones **133** with ethyl vinyl ether, forming **135**, was enhanced by electron-withdrawing aryl substituents (equation 60).[99] Bis(4-methoxybenzoyl) ketene ($(4\text{-MeOC}_6H_4CO)_2C{=}C{=}O$) was generated by thermolysis of the 4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)furan-2,3-dione and reacted by [4 + 2] cycloadditions.[100] Reaction mechanisms of decomposition of **133** have been observed by IR study of the intermediates formed.[101]



133 **134** **135** (36–65%)

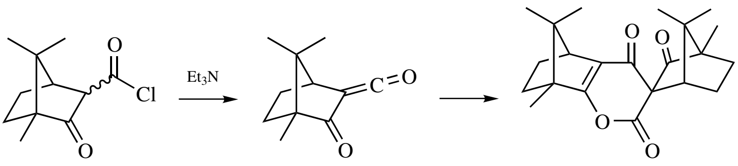
(60)

Thermolysis of **136** formed ketene **137**, which cyclized to **138** (equation 61).[102] Some related examples of acylketene formation from 2,3-dihydrofuran-2,3-diones were also examined.[103,104] Camphorketene **140** formed by dehydrochlorination of **141** gave the dimer **142** (equation 62), whose stereochemistry was established by X-ray crystallography.[105] The dimerization was reported to occur through a planar pseudopericyclic pathway.[105]



136 **137** **138**

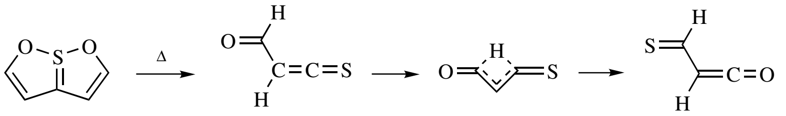
(61)



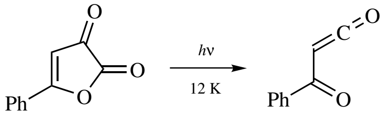
139 **140** **141**

(62)

Pyrolysis of **144** with matrix trapping permitted the observation of IR of formylthioketene **145**, which rearranged through the hydrogen migration transition state **146** to thioformylketene **147** (equation 63).[106] Matrix photolysis of furandione **148** gave benzoylketene (**149**) by extrusion of CO (equation 64).[107]



142 **143** (IR 1753 cm^{-1}) **144** **145** (IR 2141 cm^{-1}) (63)



146 **147** (64)

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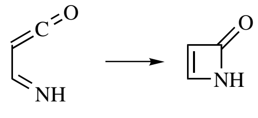
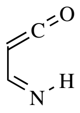
4.1.7 Imidoylketenes

Imidoylketenes resemble acylketenes in structure, but are quite reactive and are not normally observable intermediates. The structure of imidoylketene **1** and of its cyclization product, the azetinone **2**, were calculated at the HF/6-31G*//HF/6-31G* level, and the ring closure was found to be endothermic by 12.0 kcal/mol (equation 1).[1] *Ab initio* calculations of the various conformations of imidoylketene (**1a–d**) have been reported.[2]

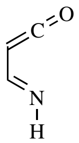


1 **2**

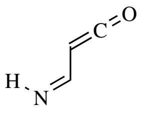
(1)



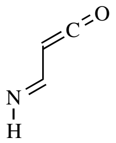
1a



1b

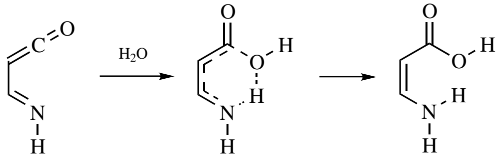


1c



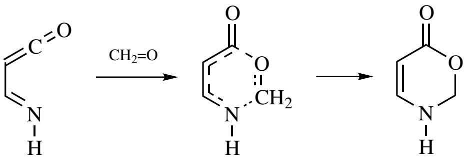
1d

Calculations of the structures and energies for the hydration of **1** forming **4** (equation 2), and [4 + 2] cycloaddition with formaldehyde forming **6** (equation 3), have been reported.[2] The reactions of equations 2 and 3 involve pseudopericyclic transition states **3** and **5**, respectively, which are essentially coplanar, but without continuous pi-electron delocalization, and these reactions are allowed for any number of electrons.



1 **3** **4**

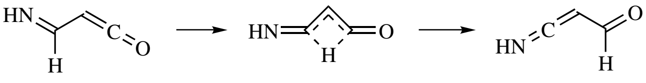
(2)



1 **5** **6**

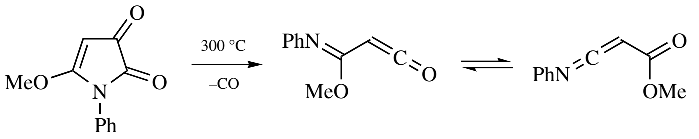
(3)

Imidoylketenes are isomers of acylketenimines. The 1,3-hydrogen shift of **1** to form ketenimine **8** is a pseudopericyclic process that has been studied computationally and involves the 4-membered ring transition state **7** (equation 4).[2]


1 **7** **8**

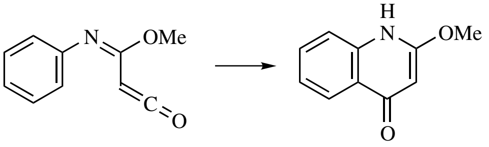
(4)

Experimentally, the interconversion of the imidoylketene **10** generated by FVP-induced decarbonylation of the pyrrolidione **9** forming the ketenimine **11** by methoxy group migration, was demonstrated by trapping of **11** in an argon matrix, with identification by low temperature IR spectroscopy and isolation from reaction at 350 °C (equation 5).[3,4] Similar rearrangements have been studied by MINDO/3.[5] The quinolone **12** was formed by Conrad-Limpach cyclization of imidoylketene **10** (equation 6).[6,7]



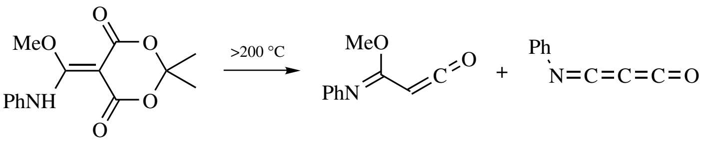
9 **10** (IR 2135 cm^{-1}) **11** (26%, IR 2050 cm^{-1})

(5)


10 **12** (67%)

(6)

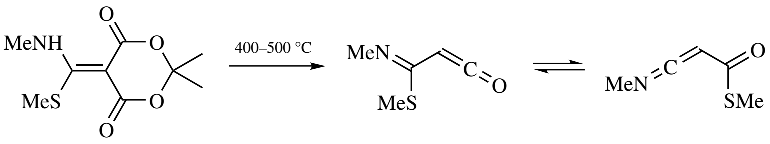
Ketene **10** and other analogues were also formed from Meldrum's acid derivatives such as **13** above 200 °C (equation 7).[4,8] The cumulenone **14** was also formed in this reaction, as identified by the IR bands at 2140 (sh) and 2222 cm^{-1} (equation 7).[4,8] Chemical generation of an imidoylketene was used in syntheses of pharmaceutically useful 4-arylquinolines.[9]



13 **10** **14**

(7)

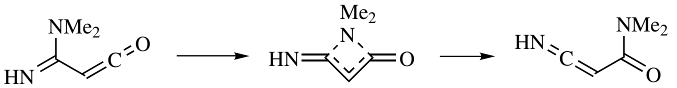
Pyrolysis of the analogous Meldrum's acid derivative **15** gave the imidoylketene **16**, which underwent reversible MeS group migration, forming the ketenimine (equation 8).[10] Imidoylketene **16** was also formed from the pyrrolidione analogous to **9**.[9] Cyclization of an imidoylketene to an azetin-2-one (cf. **2**) was also observed.[11]



(8)

15 **16** (IR 2132 cm^{-1}) (IR 2076 cm^{-1})

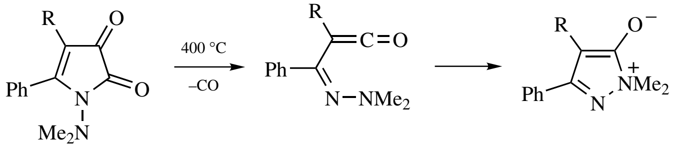
Computations at the B3LYP/6-311+G**//B3LYP/6-31G* level indicated that rearrangement of the α-imidoylketene **17** via the transition state **18** to the more stable α-oxoketenimine **19** has a low activation barrier of 62 kJ/mol or 14.8 kcal/mol (equation 9).[13]



(9)

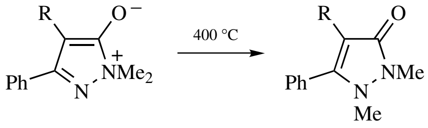
17 **18** **19**

FVT of **20a,b** formed the transient eneaminylketenes **21a,b** identifed by weak IR bands at 2130 and 2115 cm^{-1} in a matrix (equation 10).[14] The ketenes cyclized to pyrazolium oxides **22a,b** (equation 10), which underwent methyl migration to form **23a,b** (equation 11).[14]



(10)

20a,b (R = H, Me) **21a,b** (IR 2130 cm^{-1}, R = H) **22a,b**

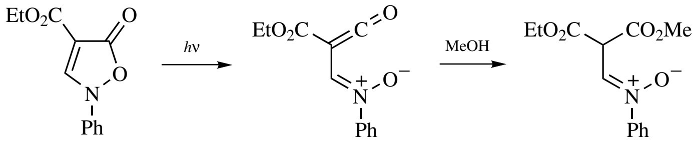


(11)

22a,b **23a,b**

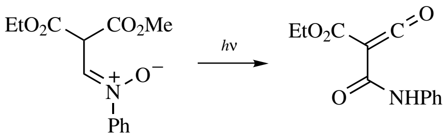
Zhou and Birney have carried out experimental and theoretical studies of dimerizations of imidoylketenes (see Section 5.4.3).[14,15]

Photolysis of 2-phenylisoxazol-5(2H)-one (**24**) gave the nitronate-substituted ketene **25**, as evidenced by the capture of the ester **27**, proposed to result from photochemical rearrangement of the methanol addition product **26** (equations 11, 12).[16]



24 **25** **26**

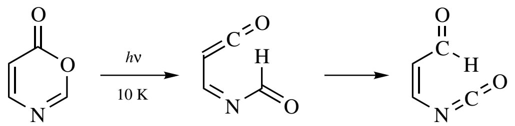
(12)



26 **27**

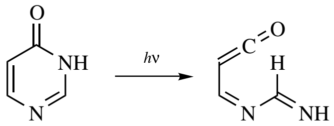
(13)

Photolysis of oxazinone **28** and substituted derivatives gave ketenes **29** observed spectroscopically at temperatures below −160 °C (equation 14).[17,18] These rearranged by hydrogen migration, forming isocyanates **30** (equation 14).[17,18] Matrix photolysis of pyrimidones **31** gave imino analogues **32** (equation 15).[19]



28 **29** (IR 2139 cm^{-1}) **30** (IR 2245 cm^{-1})

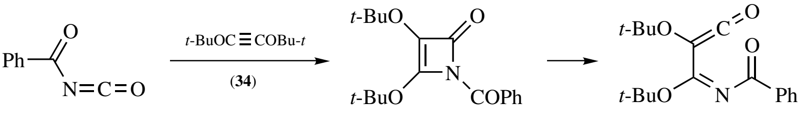
(14)



31 **32** (IR 2139 cm^{-1})

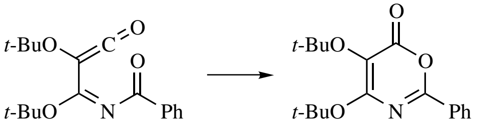
(15)

Cycloaddition of acylisocyanate **33** with the alkynyl ether **34** was proposed to form imidoylketene **36** (equation 16), which was converted to the observed **37** (equation 17).[20] The interconversion of the *N*-formylazetinone **38** to the iminoketene **39**, and the further ring closure to the 1,3-oxazinon-6-one **28**, were studied computationally (equation 18).[21]

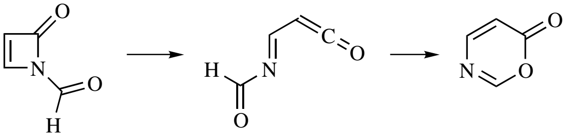


33 **35** **36**

(16)



36 **37** (17)



38 **39** **28** (18)

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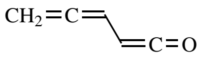
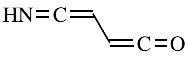
4.1.8 Cumulene-Substituted Ketenes

Cumulene-substituted ketenes include allenylketene **1**, keteniminylketene **2**, diazomethylketene **3**, and isocyanatoketene **4**. 1,2-Bisketenes are considered in Section 4.9.



1



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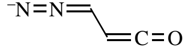

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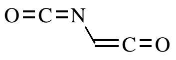
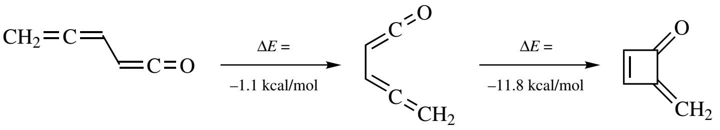


4

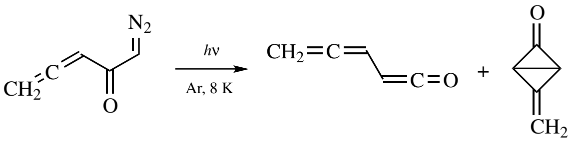
The structures and energies of allenylketene **1** and the cyclization product 4-methylenecyclobutenone **5** were calculated at the MP2/6-31G*//MP2/6-31G* level. The allenyl ketene *anti*-**1** was less stable than *syn*-**1** by 1.1 kcal/mol, which was less stable than **5** by 11.8 kcal/mol, with a barrier for ring closure to **5** of 33.7 kcal/mol (equation 1).[1–3]



anti-**1** *syn*-**1** **5**

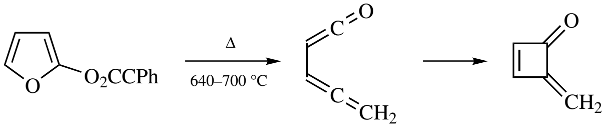
(1)

Photolysis of the diazo ketone **6** in an argon matrix was reported to form **1** as well as the methylenebicyclobutanone **7** (equation 2).[4] Pyrolysis of the furan **8** gave **1**, which formed **5** as the observed product (equation 3).[5]



6 **1** **7**

(2)

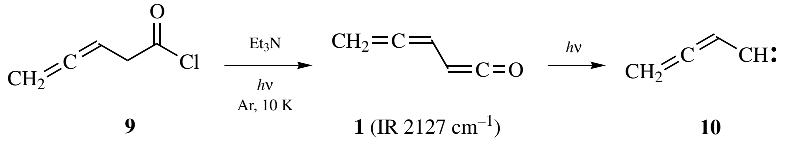


8 *syn*-**1** **5** (40%)

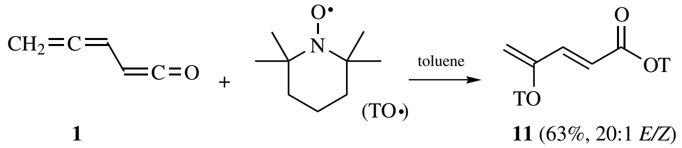
(3)

Photolysis of the acyl chloride **9** in an argon matrix gave the parent allenylketene **1**, identified by its IR band at 2127 cm^{-1} (equation 4).[6] Further photolysis gave the carbene **10**, and the structures of the ketene and carbene were calculated.[6] The reaction of **9** with 1,8-bis(dimethylamino)naphthalene in toluene also gave

1, observed by IR, and reaction of **1** with the aminoxyl radical TEMPO (TO•) gave the product **11** of diaddition with allylic rearrangement (equation 5).[7]

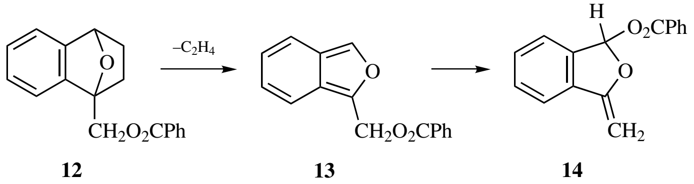


(4)

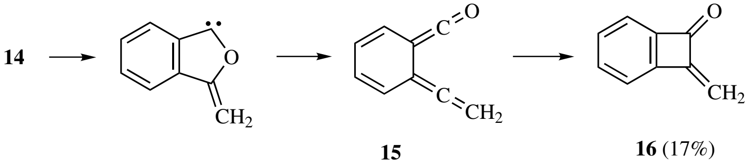


(5)

FVP of **12** was proposed to form the isobenzofuran **13**, which was converted by successive rearrangements to **14**, giving ketene **15**, which led to the observed **16**, along with 33% of isomeric products (equations 6, 7).[8] An analogous reaction gave **18** in 48% yield through the intermediacy of **17** (equation 8).[9]



(6)



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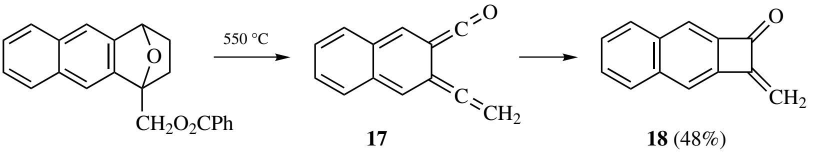


(8)

Photolysis of the cyclopentadienone **19** resulted in rearrangement forming the allenylketene **20**, identified by its IR absorption at 1890 and 2080 cm^{-1}, and further photolysis gave the cumulene **21** (equation 9).[10] Persistent allenylketenes **23** stabilized by Me_3Si groups were formed on photolysis of methylenecyclobutenones **22** (equation 10).[1] The X-ray structure of **23b** confirmed that these species prefer the coplanar *anti* conformation, as predicted by computations (Figure 4.1).[1] The use of the ketenyl and allenyl substituent stabilization parameters derived earlier allowed the prediction of the energy change for the reaction of equation 10, and

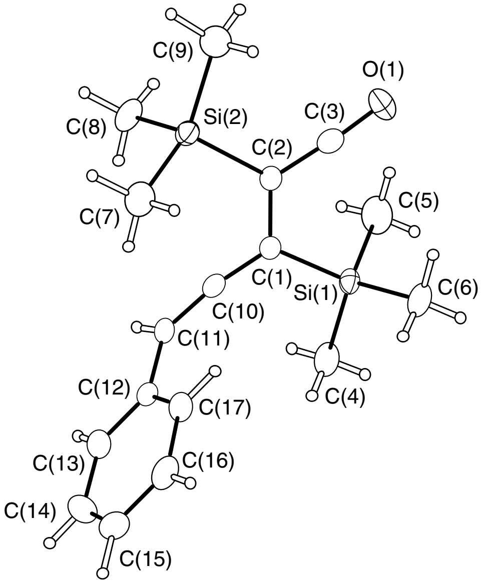
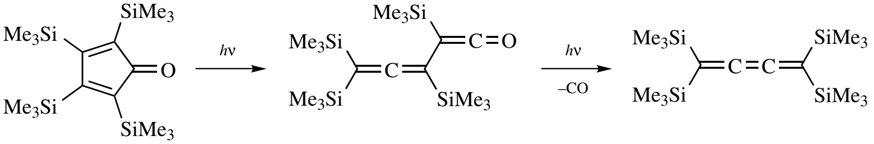


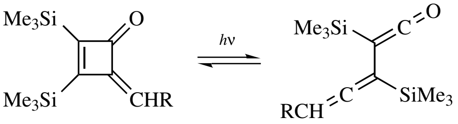
Figure 4.1 X-ray structure of **23b** (reprinted from reference 1 with permission of the American Chemical Society).

experimentally measured equilibrium constants were in reasonable agreement with these predictions.[1]



19 **20** **21**

(9)



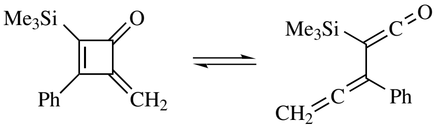
22

23 (**a**, R = H, IR 2080 cm^{-1};
b, R = Ph, IR 2080 cm^{-1};
c, R = CO$_2$Et, IR 2086 cm^{-1})

(10)

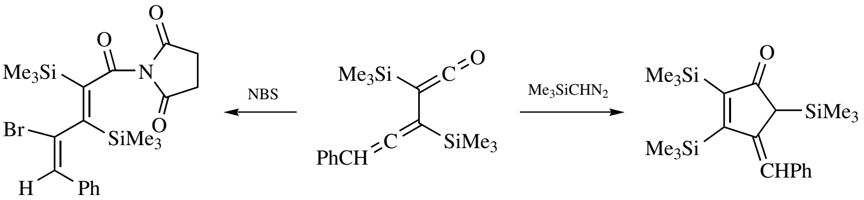
The phenyl-substituted allenylketene **25** was formed from **24**, and as expected was less stable relative to the cyclobutenone compared to **23** with R=H (equation 11).[1] The reactivities of **23b** and **25** in nucleophilic, electrophilic, and cycloaddition reactions have been examined.[11] Reaction of **23b** with NBS gave **26a** and reaction of **23b** with Me$_3$SiCHN$_2$ gave **26b** (equation 12), while reactions with

$CH_3CH{=}O$, $PhCH{=}O$, and TCNE gave **27**, **28**, and **29**, respectively.[11]



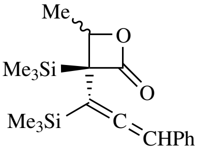
24 **25**

(11)

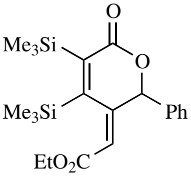


26a **23b** **26b**

(12)



27



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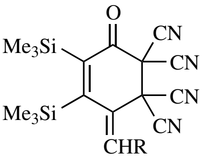
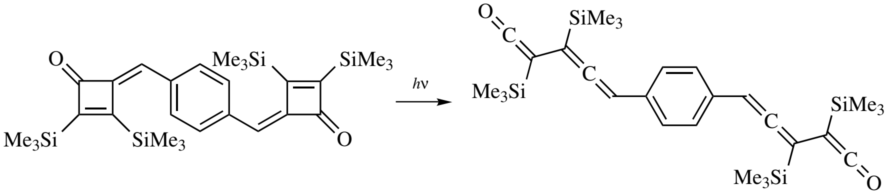


29

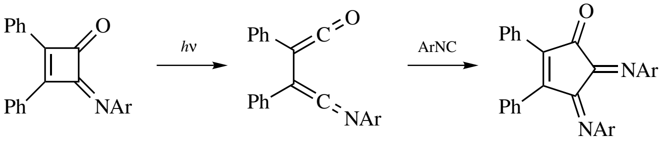
The bis(methylenecyclobutenone) **30** gave upon photolysis the bis(allenylketene) **31** as a 1:1 mixture of *dl* and *meso* isomers, which upon recrystallization gave a single isomer, with the ketenyl IR at 2080 cm^{-1} (equation 13).[1]



30 **31** (IR 2080, 1912 cm^{-1})

(13)

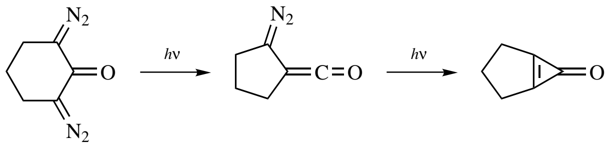
Photolysis of the cyclobutenone **32** with an arylisocyanide was proposed to result in formation of the keteniminylketene **33**, which led to **34** (equation 14).[12–14]



32 **33** (IR 2091, 2022 cm^{-1}) **34**

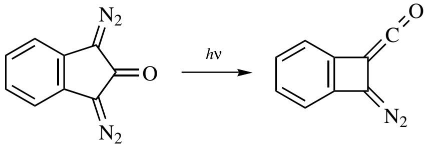
(14)

Diazoalkylketenes[15–18] have been observed at 8 K in argon matrices from the photolysis of bis(diazo) ketones, as in the conversion of **35** to **36**, which was identified by the IR absorption at 2118 and 2120 cm^{-1} and which gave the cyclopropenone **37** upon further photolysis (equation 15).[15] Photolysis of the benzannulated compound **38** gave the diazo ketene **39**, IR 2106 cm^{-1} (equation 16).[16]



35 **36** **37**

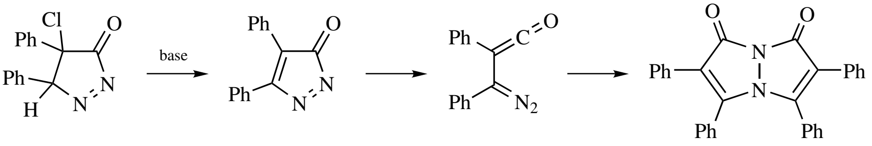
(15)



38 **39**

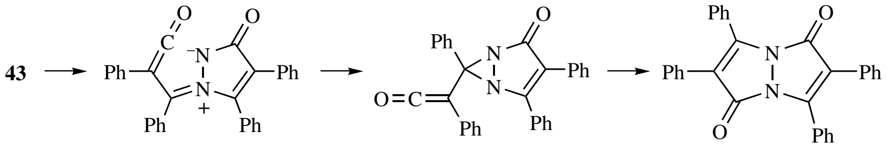
(16)

Dehydrochlorination of 4-chloropyrazolin-5-one **40** was proposed to form 1,2-diazacyclopentadienone **41**, which gave diazo ketene **42**, leading to bimane **43** (equation 17).[19,20] Thermal rearrangement of **43** to the *anti*-isomer **44** was proposed to involve initial formation of ketenes **45** and **46** (equation 18).[19,20]



40 **41** **42** **43**

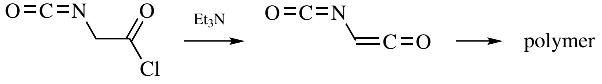
(17)



45 **46** **44**

(18)

Reaction of isocyanatoacetyl chloride **47** with triethylamine formed polymeric material, suggesting the intermediacy of isocyantoketene **48** (equation 19).[21]



47 **48**

(19)

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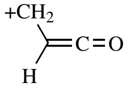
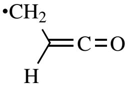
4.1.9 Ketenes with Charged, Radical, and Carbenic Side Chains

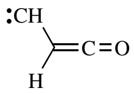
Ketenes with side chain carbocation (**1a**), radical (**1b**), or carbenic (**1c**) centers at the 3-position are known in a number of examples, consistent with a favorable electron donation from the ketenyl group to electron deficient centers, and display useful chemistry. Analogous carbanions (**1d**) are rare, as expected, due to an unfavorable interaction of ketenes with carbanionic centers. However, there has been no systematic study of these effects.



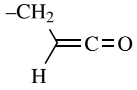
1a



1b

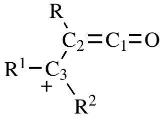


1c



1d

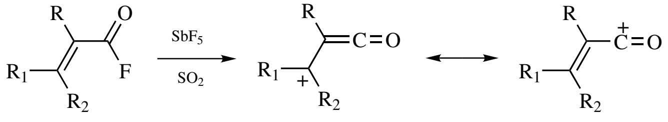
TABLE 4.1 ^{13}C NMR Chemical Shifts of Acylium Ions 2



2a

R	R^1	R^2	C_1	C_2	C_3
H	H	H	147.1	92.7	177.1
CH_3	H	H	151.5	84.3	202.6
CH_3	CH_3	H	154.2	79.0	223.0
H	H	CH_3	148.1	104.3	172.8
H	CH_3	CH_3	151.3	94.3	193.5
Ph	Ph	H	158.7	68.7	201.1
Ph	H	H	157.0	69.4	183.3
c-Pr	CH_3	H	160.4	71.2	227.0
COCl	H	H	146.7, 143.1	102.8	165.3, 162.0

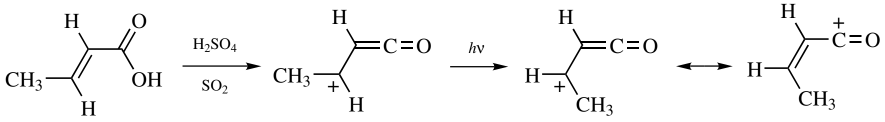
Carbocationic derivatives were generated from a series of acrylyl fluorides with SbF_5 in SO_2 forming the acylium ions **2**, which were characterized by ^{1}H NMR and IR (equation 1).[1] These had IR bands at 2210–2250 cm^{-1} for the ketenyl group and were reported to be at somewhat lower frequencies than for alkyl acylium ions, which were seen at 2205–2302 cm^{-1}.[1,2] These IR bands and the ^{1}H NMR shifts of CH_3 groups at R^1 and R^2 were interpreted as supporting a contribution from ketene resonance structure **2a**.[1,2] The observed ^{13}C NMR spectra of cations **2** are given in Table 4.1 and were interpreted in terms of the substantial ketenic character of these ions.[3]



2a **2b**

(1)

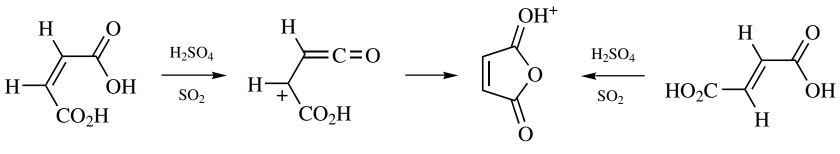
The cation *E*-**3** was generated from *E*-crotonic acid in H_2SO_4/SO_3, and the ^{13}C NMR spectrum showed very low field absorption at C_1 and C_3, consistent with significant positive charge development at these positions (equation 2).[4] Photolysis of *E*-**3** produced a spectrum attributed to *Z*-**3**.[4] No isomerization of *E*-**3** to *Z*-**3** was observed after several hours at room temperature, and it was suggested that there was no ketene character **3a** as opposed to acylium ion character **3b** for this ion.[4]



E-**3a** *Z*-**3a** *Z*-**3b**

(2)

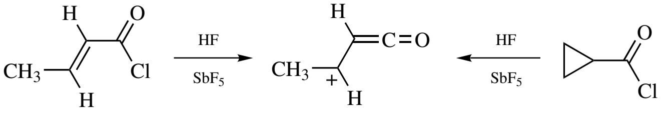
Both maleic acid (**4**) and fumaric acid (**5**) reacted in H_2SO_4/SO_3 to form *O*-protonated maleic anhydride **7** (equation 3).[4] The isomerization was proposed to occur through an intermediate ketenyl cation **6**.[4]



4 **6** **7** **5**

(3)

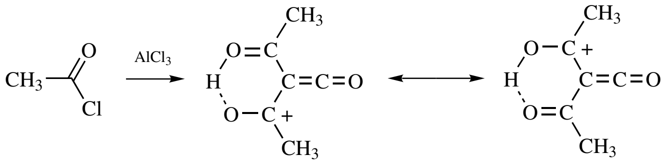
The reactions of crotonyl chloride in DF-SbF_5 were followed by ^1H NMR, and the deuterium content of the product ester was determined after quenching with MeOH.[5] It was concluded that vinylketene $CH_2{=}CHCH{=}C{=}O$ was likely not to be an intermediate in the reaction, but the ketenic cation **8** was implicated (equation 4).[5] Cation **8** was also formed from *c*-PrCOCl (**9**) in 1:1 HF-Sb_5 by protonation of the cyclopropane ring (equation 4).[6]



8 **9**

(4)

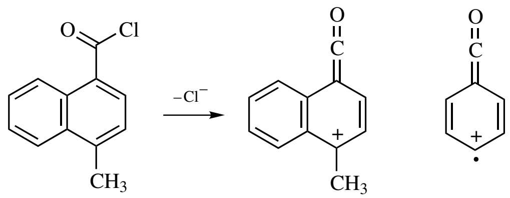
Acetyl chloride reacts with $AlCl_3$ in CD_2Cl_2, forming the cation **10** (equation 5), which was characterized by ^1H and ^{13}C NMR and by IR.[7]



10

(5)

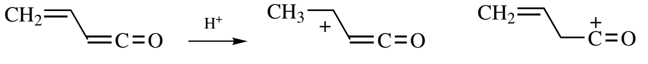
The solvolysis of naphthoyl chloride **11** has been proposed to occur through an acylium ion with a contribution of the ketenyl resonance structure **12** (equation 6).[8] Distonic dehydrobenzoyl radical cation **13** in the gas phase was reported to have similar ketenic character.[9]



11 **12** **13**

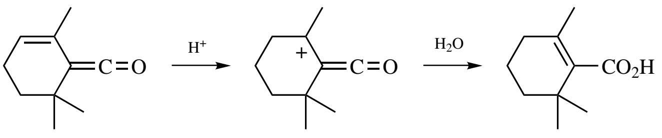
(6)

A computational study of the protonation of vinylketene **14** led to the prediction that attack at C_4 leading to the carbocation **15** was strongly favored over protonation at C_2 to form **16** (equation 7).[10] This was confirmed by experiment for the reaction of **17**, which gave initial formation of the cation **18** leading to the acid **19** (equation 8).[11] The nonconjugated acid that would result from protonation at C_2 was found to be more stable than **19**, so the latter did not form through equilibration.[11]



14 **15** **16**

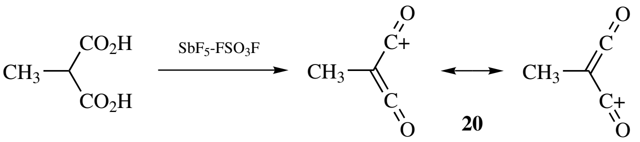
(7)



17 **18** **19**

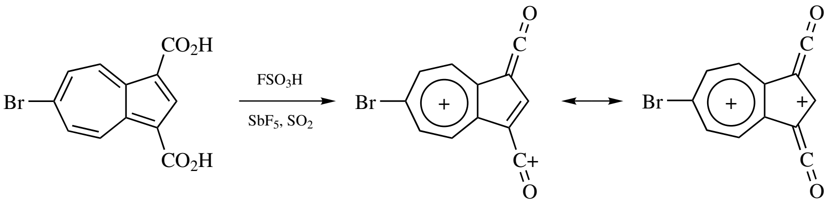
(8)

It was proposed that the reaction of methylmalonic acid or its dimethyl ester in SbF_5-FSO_3F gave rise to the ketenyl acylium ion **20**, as evidenced by the ^1H NMR signal at δ 3.05 and an IR band at 2170 cm^{-1} (equation 9).[12] Formation of the vinylogous analogue **22** from reaction of an azulene-1,3-dicarboxylic acid **21** was also proposed based on ^1H NMR evidence (equation 10).[13]



20

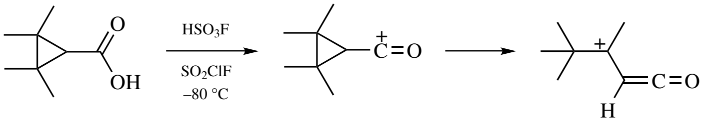
(9)



21 **22**

(10)

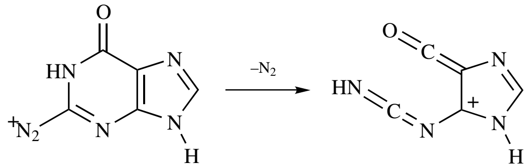
The reaction of acid **23** in FSO_3H/SO_2ClF gave rise to the acylium ion **24**, whose rearrangement to **25** was observed by ^1H NMR (equation 11).[14] Cation **25** was trapped with MeOH.



23 **24** **25**

(11)

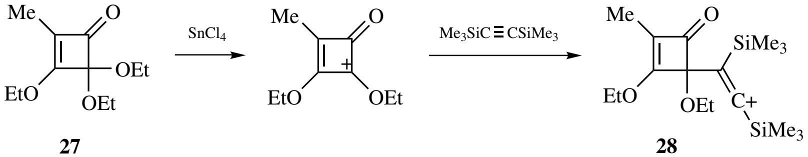
A theoretical study of the diazotization of guanine led to the proposal of a calculated structure **26** for the first ring-opened intermediate in the reaction (equation 12).[15]



(12)

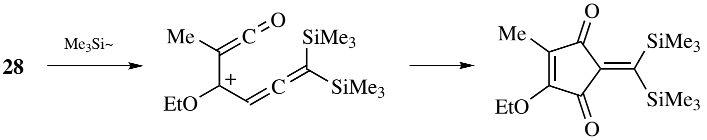
26

Reaction of cyclobutenone **27** with bis(trimethylsilyl)acetylene catalyzed by Lewis acids was proposed to occur via formation of cation **28** with silyl migration and ring opening to cationic ketene **29** and cyclization leading to **30** (equations 13, 14).[17] The reaction pathway was calculated with PM3 methods, and the ring closure step involved an in-plane p-orbital of the allenic moiety attacking the ketenyl group. Oxidation of cyclobutenones **31** with PhI(OAc)$_2$ was suggested to proceed with ring opening to the cationic ketenyl species **32**, which added methanol with ring closure (equation 15).[18]



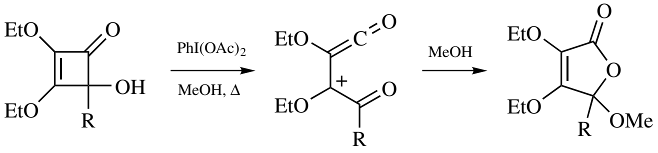
(13)

27 **28**



(14)

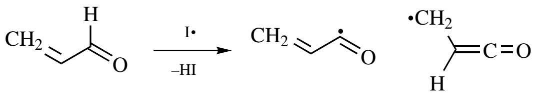
29 **30**



(15)

31 **32** (24–84%)

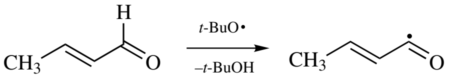
The possible formation of radical **1b** or of the bent acyl radical **33** during photolysis of acrolein could occur by direct bond fission or by abstraction, and reaction with iodine atoms led to an estimate of the carbonyl C-H bond strength that was similar to that of acetaldehyde (equation 15a).[18a,b] Based on this result and ESR data[19,20] the structure **33** is favored.



(15a)

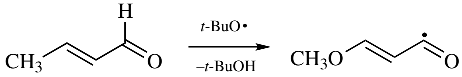
33 **1b**

Vinyl-substituted acyl radicals **34** and **35** were generated by hydrogen abstraction from aldehydes, but the ESR spectra of these species indicated that these were bent σ radicals, not ketenyl structures (equations 16, 17).[19,20] Photolysis of hexa-1,5-dien-3-ones such as **36** was proposed to form the radical pair **37**, which recombined to form ketene **38**, but the acyl radical in **37** also presumably would have σ character (equation 18).[21,22]



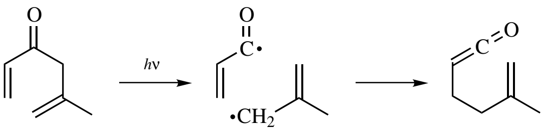
34

(16)



35

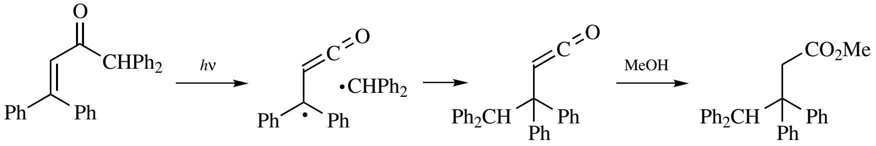
(17)



36 **37** **38**

(18)

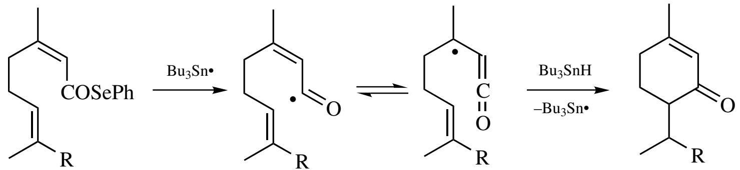
Photolysis of **39** was proposed to give cleavage to the radical pair **40**, and π character for the ketenyl radical in **40** was claimed, based on the expected conjugative ability of the phenyl groups (equation 19).[23] Recombination of the radical pair gave the ketene **41** observed by IR and captured with methanol, forming **42** (equation 19).[23]



39 **40** **41** **42** (30%)

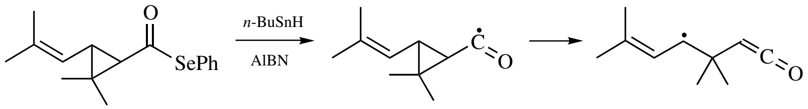
(19)

Reaction of selenyl esters **43** with *n*-Bu_3SnH-AIBN was proposed to give ketenyl radicals **44**, which cyclized to cyclohexenones **45** (equation 20).[24] The ester **46** was suggested to give the cyclopropylacyl radical **47** in hot benzene which formed the aldehyde **49** and the dimer **51**, while in MeOH the ester **50** was formed, although the timing of the dimerization and nucleophilic addition steps was not established (equations 21, 22).[25,28a] In a further experiment the selenyl ester **52** gave the ketone **56** by a pathway proposed to involve the radical intermediates **53**–**55** (equations 23, 24).[28b] An analogous reaction of an allenyl derivative gave a cyclooctadienone.[26]



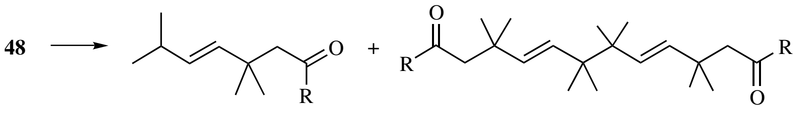
43 **44a** **44b** **45**

(20)



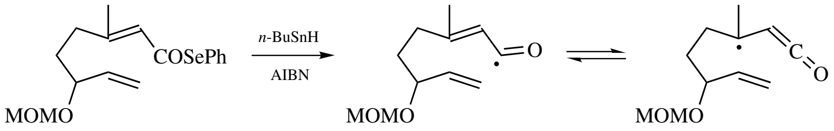
46 **47** **48**

(21)



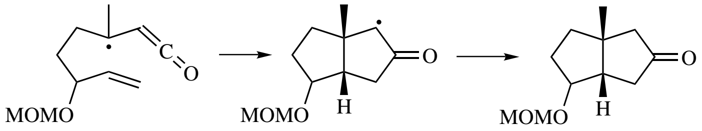
49 (R = H) **50** (R = OMe) **51** (78%, R = H)

(22)



52 **53** **54**

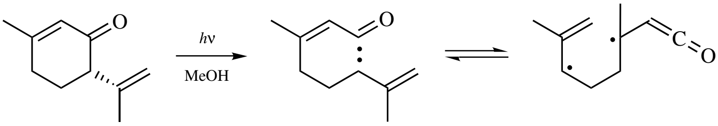
(23)



54 **55** **56** (76%)

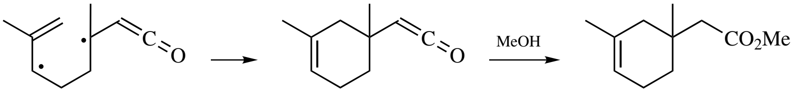
(24)

Precedent for the generation of vinyl acyl radicals was found in the photolysis of **57** in MeOH, which was proposed to form the diradicals **58** and **59**, leading to cyclization to the ketene **60**, which led to the observed product **61** (equations 25, 26).[27] The reactions of cyclopropylvinylacyl selenides with n-Bu_3SnH gave the corresponding acyl radicals, which underwent cyclopropyl ring opening and then radical cyclization of the ketenyl intermediates (equation 27).[28,28a,b]



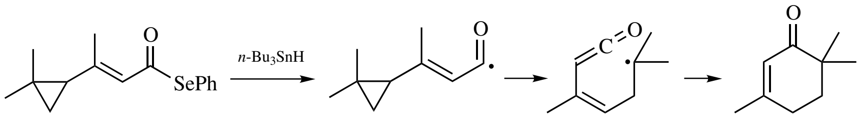
57 **58** **59**

(25)



59 **60** **61**

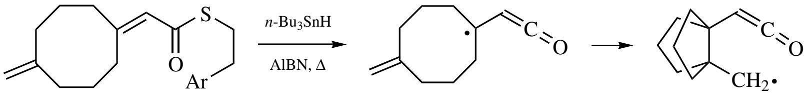
(26)



62 **63** **64** **65** (60%)

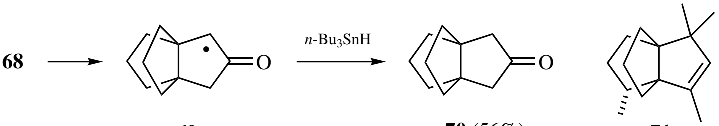
(27)

Reaction of the thioester **66** was proposed to give the ketenyl radical **67**, which reacted by an intramolecular 5-*exo* trig cyclization, forming the ketenyl radical **68**, which underwent a further intramolecular 5-*exo* trig cyclization leading to **69** and **70** (equations 28, 29).[29,30] An analogous sequence was used in a formal synthesis of (±)-modhephene **71**.[31] Tandem cyclization onto a cyclopentene was used in the preparation of pentalene.[30]



66 ($Ar = 2\text{-}IC_6H_4$) **67** **68**

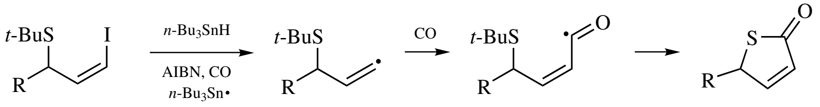
(28)



69 **70** (56%) **71**

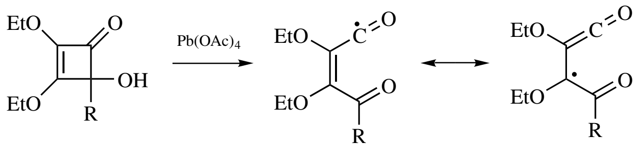
(29)

The addition of CO to vinyl radicals gives acyl radicals,[31a] and reaction of vinyl iodide **72** with n-Bu_3Sn• under pressure of CO gave vinyl radical **73**, which gave carbonylation to ketenyl radical **74**, which cyclized to thiolactone **75** (equation 30).[32] As discussed in Section 3.4.1, oxidation of hydroxycyclobutenone **31** led to vinyl acyl/ketenyl radicals **76** (equation 31).[33]



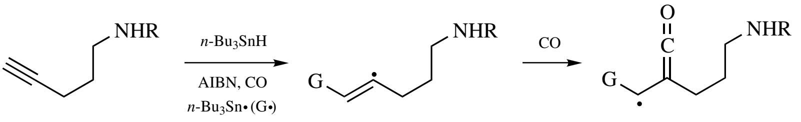
72 (R = n-Pn) **73** **74** **75** (60%)

(30)

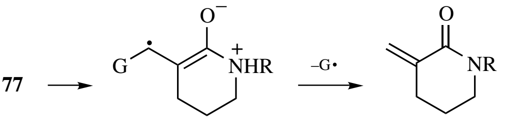


31 **76** (31)

An unusual amine cyclization occurred with the ketenyl radicals **77** generated from ω-amino terminal alkynes by free radical carbonylation (equation 32).[34] The reaction proceeded through addition of the radical *n*-Bu_3Sn• (G•) to the alkyne, forming a vinyl radical that combined with CO to form **77**. This cyclized, followed by partial destannylation, possibly with hydrogen atom transfer from an intermediate lactam enol, to give lactams **77a** (equation 33).

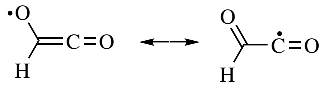


77 (32)

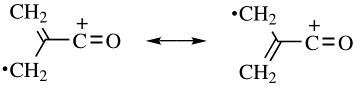


77a (21–71%) (33)

Ketene **78** with an oxyl radical side chain has been studied by computational means.[34a] Density functional calculations indicated that the distonic ion **79** has a structure with most of the positive charge at the carbonyl carbon and the unpaired spin delocalized over the allyl group.[35] The reactivity of **79** was studied by Fourier transform ion cyclotron resonance.[35]

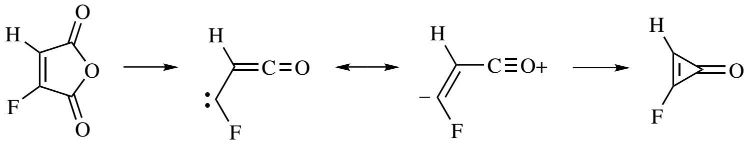


78



79

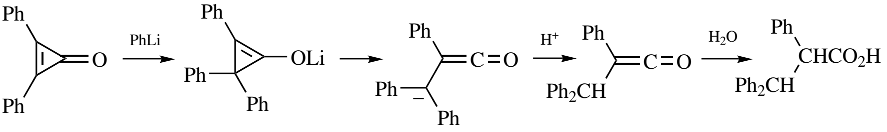
Photolysis of fluoromaleic anhydride **80** in an argon matrix led to IR bands ascribed to fluoro(ketenyl)carbene **81** and fluorocyclopropenone **82** (equation 34), which underwent further slow photolysis to fluoroacetylene and CO.[36] The ketene **81** was assigned the *syn*-conformation shown, although this was calculated to be slightly higher in energy than the *anti*-conformation, because of the high calculated barrier for interconversion of the conformers and the low barrier for conversion of *syn*- **81** to **82**.[36] The calculations suggested that resonance structures such as **81a** gave rise to the high conformational barriers.[36] Photochemical and thermochemical decomposition of maleic and dichloromaleic anhdyrides in matrices were also suggested to form ketenylcarbenes and cyclopropenes.[37]



80 **81** **81a** **82**

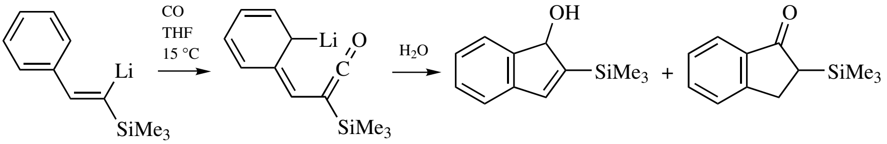
(34)

Ketenyl carbanions are rare, but a possible example **83** was proposed to result from phenyllithium addition to diphenylcyclopropenone, which upon acidification gave a transient IR absorption at 2100 cm^{-1} attributed to ketene **84**, and this added water to give **85** (equation 35).[38] Reaction of the vinyllithium compound **86** with CO was suggested to possibly involve a ketenyl carbanion **87** (equation 36).[39] Gas phase reaction of CO with the cyclopropenyl anion **88** was thought to involve the ketenyl carbanion **89** (equation 37).[39]



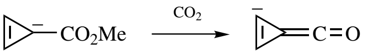
83 **84** (IR 2100 cm^{-1}) **85** (18%)

(35)



86 **87** (61%) (10%)

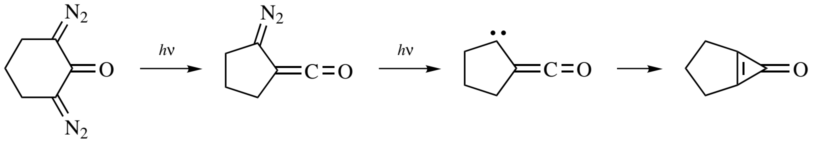
(36)



88 **89**

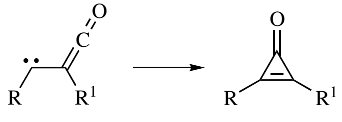
(37)

Photolysis of bis(diazo) ketone **90** forms the α-diazo ketene **91**, which on further photolysis gave ketenylcarbene **92** as the precursor to cyclopropenone **93** (equation 38).[41,42] The photolysis and thermolysis of 1,2-bisketenes may also lead to ketenylcarbenes (Section 4.9). Computations of the effects of the substituents on the energies of ketenylcarbenes **94** and the corresponding cyclopropenones **95** formed by ring closure have been reported (equation 39).[43,44]



90 **91** **92** **93**

(38)



94 **95** (39)

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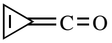
4.1.10 Fulvenones and Cumulenones

Fulvenones are α-oxo analogues of the well-studied fulvenes[1–3] and include triafulvenone (**1**), pentafulvenone (**2**), heptafulvenone (**3**), and nonafulvenone (**4**). Computational studies have evaluated the aromaticity of **1–4**, and by the criteria of aromatic stabilization energy (ASE), bond alternation, nucleus independent chemical shifts (NICS), and magnetic susceptibility exaltation (λ), **1** and **3** are antiaromatic, while **2** and **4** are aromatic.[4]



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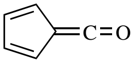

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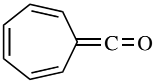

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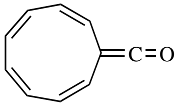
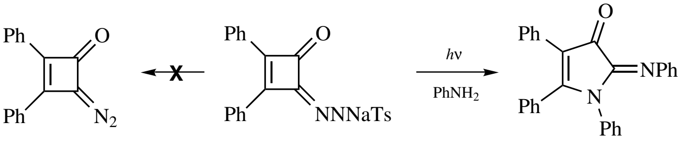


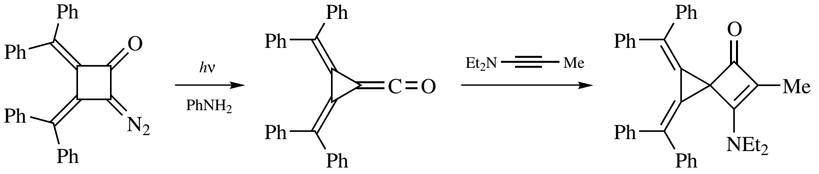
4

4.1.10.1 Triafulvenones Triafulvenone **1** was predicted to be strongly antiaromatic[1,4–6] and is unknown experimentally. Attempted preparation of the diazo ketone precursor **5** of the diphenyl analogue was unsuccessful and gave instead **6** (equation 1).[7] The diazo ketone **5** was also expected to have 4π electron antiaromatic character, which accounted for this result. Photolysis of **7** in the presence of 1-diethylaminopropyne gave a quantitative yield of N_2 and 30% of **9**, which may have formed from the ketene **8** (equation 2).[7] A possible carbanionic derivative of **1** is noted in Section 4.1.9.[8]



5 **6**

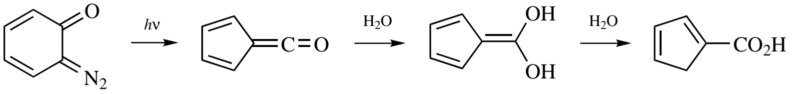
(1)



7 **8** **9**
(30%)

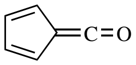
(2)

4.1.10.2 Pentafulvenones Pentafulvenone (**2**) was prepared by Süs in 1944 by Wolff rearrangement of the diazo ketone **10** and found to undergo hydration to the carboxylic acid **12** in aqueous solution (equation 3).[9] Kinetic investigations of this process led to the proposal that the reaction occurred with formation of intermediate enediol **11** (equation 3).[10] Pentafulvenones **2**, **13**, and **14** were each generated in hydrocarbon solvents by photolysis of the corresponding diazo ketones at ambient temperatures, and their ketenyl IR absorptions were measured by conventional methods at 2129, 2117, and 2110 cm^{-1}, respectively.[11] Their reactions with the aminoxyl radical TEMPO were also examined (Section 5.7).[11]

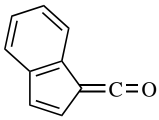


10 **2** **11** **12**

(3)



2



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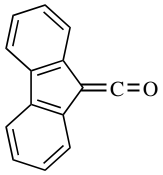
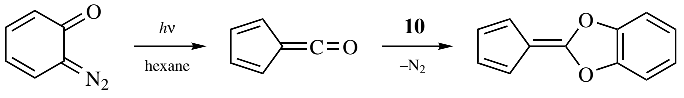


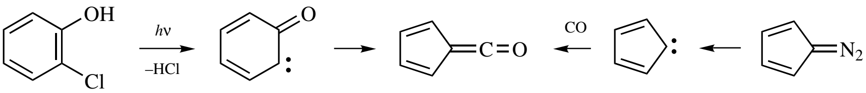
14

The yield of pentafulvenone **2** formed from photochemical Wolff rearrangement was diminished due to the formation of the dimeric product **15** formed by reaction of **2** with residual diazo ketone (equation 4).[11]

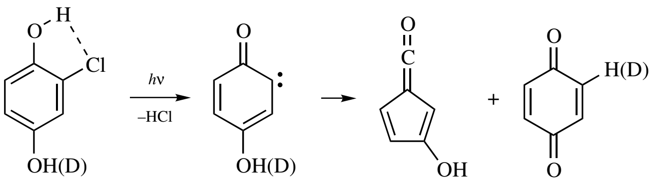


10 **2** **15** (4)

Photoreactions of 2-chlorophenol, isomeric dichlorophenols, and 2,4,5-trichlorophenol in matrices formed substituted α-ketocarbenes **16** that gave Wolff rearrangement to derivatives of **2** as detected by IR (equation 5).[12] Complexes of these pentafulvenones with HCL were also observed and their geometries derived from the vibrational shift.[12] The carbene **16** was also formed from photolysis of 2- bromophenol, and was observed by UV and rearrangement to **2**.[13] Ketene **2** was also formed by carbonylation of the carbene formed from the diazoalkane **17** in a matrix containing CO (equation 5).[14] Photolysis of chloro-*p*-hydroquinone in an argon matrix at 16 K gave formation of hydroxypentafulvenone **2a** as well as *p*-benzoquinone, proposed to form via the ketocarbene (equation 5a).[14a] Deuterium labeling showed that *p*-benzoquinone formed by migration of the hydrogen indicated (equation 5a).

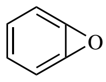


16 **2** **17** (5)

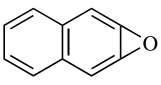


2a (IR 2126 cm^{-1}) (5a)

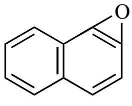
Theoretical studies of benzooxirene (**18**) and its benzo derivatives (**19a–c**) elucidated their conversion to ring-opened keto carbenes that rearranged to fulvenones (equation 5).[15,16]



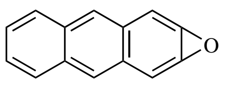
18



19a

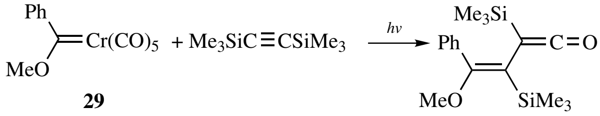


19b



19c

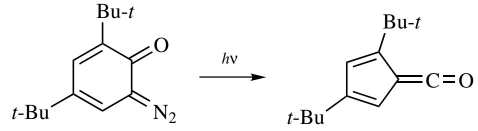
Photolysis of tetrabromodiazocyclopentadiene in an argon matrix gave the carbene **20**, which in the presence of CO formed the ketene **21**, identified by its IR band at 2163 cm^{-1} (equation 6).[17] The pentafulvenone **23** was formed by photolysis of the diazo ketone **22** in an Ar matrix (equation 7) and identified by its IR band at 2120 cm^{-1}.[18]



29

30 (70%)
IR 2089 cm^{-1}

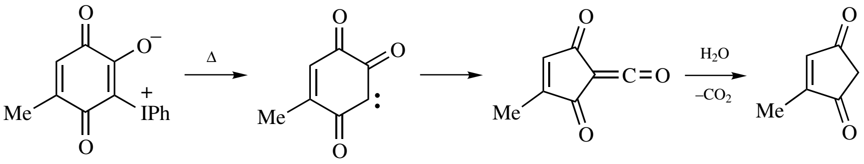
(6)



22 **23**

(7)

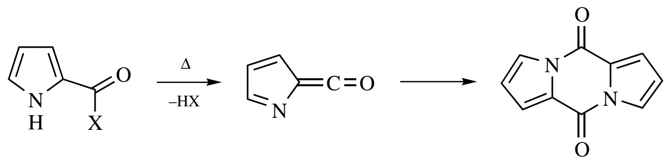
Thermolysis of the iodonium zwitterions **24** in refluxing acetonitrile was reported to lead via a possible carbene intermediate to the unobserved diacylfulvenone **25**, which in undried solvent formed the dione **25a** in 55% yield, presumably by a hydration/decarboxylation route (equation 8).[20,21] This reaction is also discussed in Section 4.1.6 with acylketenes.



24 **25** **25a** (55%)

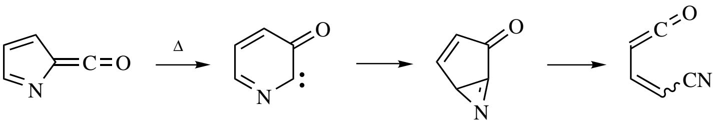
(8)

FVP of **26** gave elimination reactions forming azafulvenone **27**, identified by its IR band at 2148 cm^{-1} in an Ar matrix at 12 K, and the formation of dimer **28** (equation 9).[22] Pyrolysis of **26** at higher temperature gave reduced amounts of **27** and IR bands at 2142, 2139, and 2135.5 cm^{-1}, which were attributed to the cyanovinylketenes **30**, which were proposed to form by a retro-Wolff rearrangement to the keto carbene **29** (equation 10).[23] The ketenes were trapped with methanol.[23]



26 (X = OH, OCH_3, Cl) **27** (IR 2146 cm^{-1}) **28**

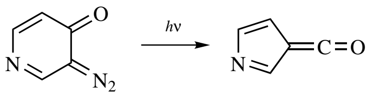
(9)



27 **29** **29a** **30**

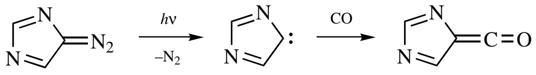
(10)

Low-temperature photochemical Wolff rearrangement of diazo ketone **31** in a matrix gave the azapentafulvenone **32** (equation 11).[22,23] Diazo compound **33** on photolysis in a matrix formed carbene **34**, which underwent carbonylation, forming **35** (equation 12).[24]



31 **32** (IR 2146 cm^{-1})

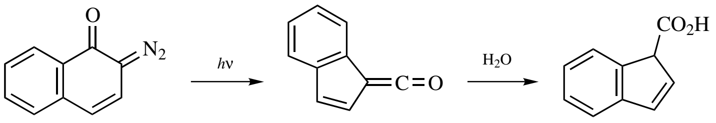
(11)



33 **34** **35** (IR 2153 cm^{-1})

(12)

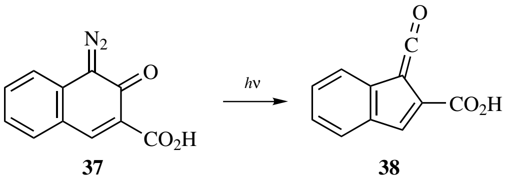
Hydration of fulvenone **13** to the acid **36** is the key reaction involved in its application in photolithography,[25–28] and the mechanism of this reaction in solution has received much attention (equation 13).[29–31] This transformation has also been achieved by two-photon absorption of light operating at 800 nm using an ultrafast pulse laser, which does not overlap with the absorption of the diazo ketone.[32] Derivatives of **13** have been used in the growth of well-aligned carbon nanotubes.[33]



13 **36**

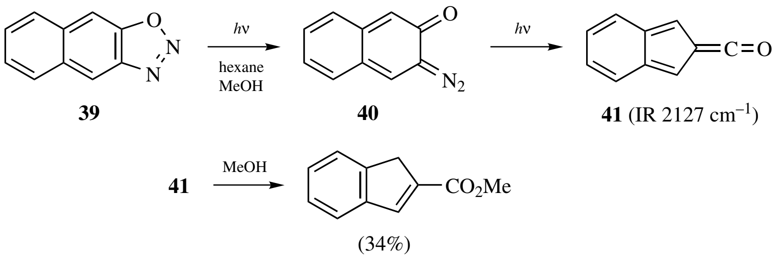
(13)

Matrix photolysis of **37** gave the indenylketene **38**, with a characteristic ketenyl IR band at 2142 cm^{-1} (equation 14).[36] Derivatives of **38** are also important in photoresists (Section 3.3.2).[34–37]



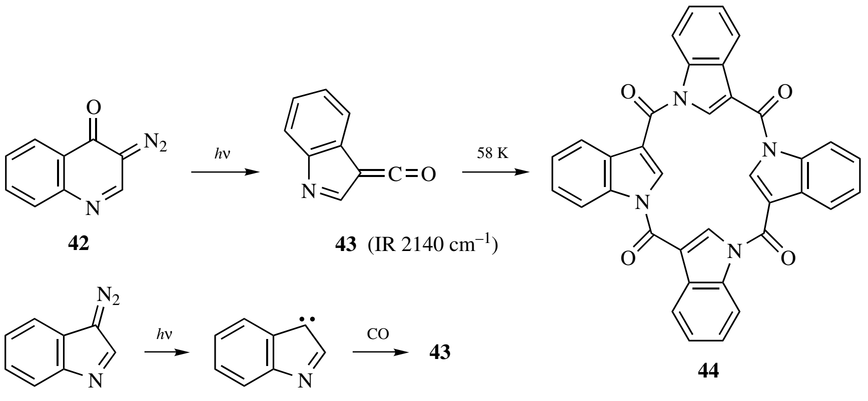
(14)

Photolysis of **39** gave the diazo ketone **40**, which was converted to benzopentafulvenone **41** by Wolff rearrangement in a matrix, as identified by IR and trapping with methanol (equation 15).[38] Benzopentafulvenone **41** was also formed by pyrolysis at 750 °C of 3-acetoxy-2-naphthoic acid and trapped in a matrix at −196 °C, as shown by the IR absorption at 2127 cm^{-1}.[39]



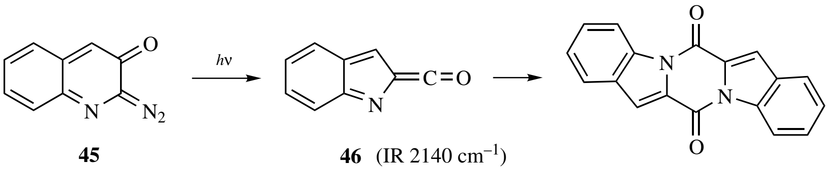
(15)

Wolff rearrangement of diazo ketone **42** gave azaindenylideneketene **43**, which formed the tetramer **44** (equation 16).[40,41] Addition of CO to the carbene in the matrix also gave **43**.[41]

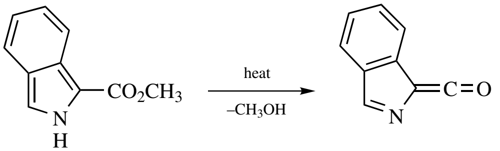


(16)

Photochemical Wolff rearrangement of **45** in a matrix gave **46**, which was observed by IR and formed the dimer **47** (equation 17).[40] FVP of **48** with elimination of methanol gave the ketene **49**, which was trapped in a matrix and observed by IR (equation 18).[42,43]

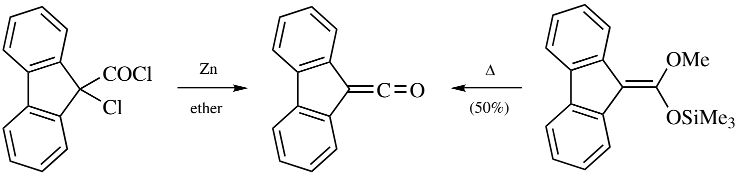


45 **46** (IR 2140 cm^{-1}) **47** (17)



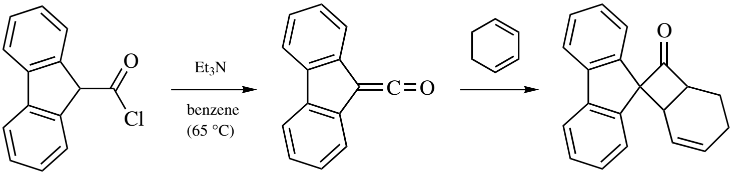
48 **49** (IR 2133 cm^{-1}) (18)

Dibenzofulvenone (fluorenylideneketene, **14**), an analogue of diphenylketene, is an isolable material that was first prepared by zinc dechlorination of the α-chloro acyl chloride **50** (equation 19).[44] Ketene **14** was also prepared by pyrolysis of the methyl trimethylsilyl ketene acetal **51** (equation 19),[45] and by Wolff rearrangement,[46,47] and gave a ketenyl IR band at 2121 cm^{-1} (CH_3CN)[46] and at 2114 and 2126 cm^{-1} (hexane).[11]



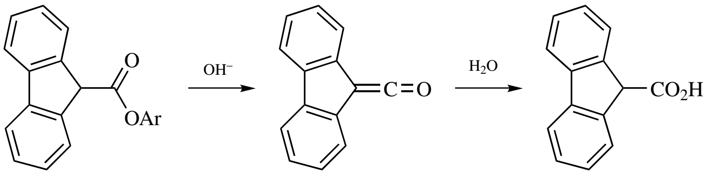
50 **14** **51** (19)

Preparation of **14** by dehydrochlorination of 9-fluorenylcarbonyl chloride (**52**) with triethylamine with in situ [2 + 2] cycloaddition with 1,3-cyclohexadiene gave **53** (equation 20).[48]



52 **14** **53** (62%) (20)

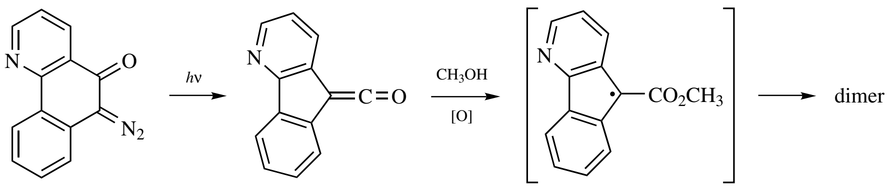
Base-catalyzed hydrolysis of esters **54** of 9-fluorenylcarboxylic acid possessing aryl leaving groups with electron-withdrawing substituents was proposed to involve ester enolate formation leading to ketene **14** (equation 21).[49,50] The ketene **14** formed by photolysis of the diazo ketone showed high reactivity with amines and H_2O (Section 5.5.1).[47,50]



54 **14**

(21)

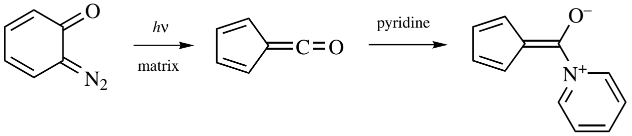
Wolff rearrangement of **55** in methanol gave the unobserved azafluorenylideneketene **56**, which reacted by methanol addition and oxidation to radical **57**, which then formed the dimer (equation 22).[51]



55 **56** **57**

(22)

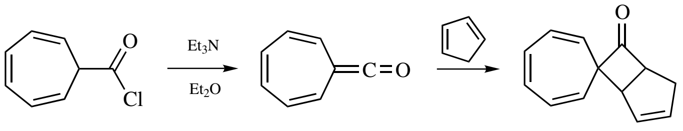
The highly reactive fulvenone **2** formed zwitterionic adduct **58** with pyridine in a matrix between 15 and 50 K (equation 23).[22] The fulvenones **13** and **14** behaved similarly.



2 (IR 2126 cm^{-1}) **58** (IR 1687 cm^{-1})

(23)

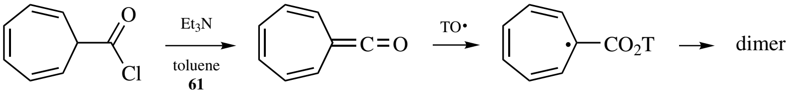
Heptafulvenone **3** generated by dehydrochlorination of **59** gave in situ [2 + 2] cycloaddition with cyclopentadiene, forming **60** (equation 24).[52]



59 **3** **60** (60%)

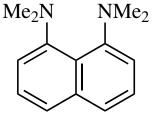
(24)

Dehydrochlorination of **59** with Et_3N and 1,8-bis(dimethylamino)naphthalene (**61**) gave **3**, identified by its IR band at 2101 cm^{-1} (equation 25).[53] The reactivity of **3** with the aminoxyl radical TEMPO was studied, and products from dimerization of an intermediate cycloheptatrienyl radical **62** were observed (equation 25).[53] Ketene **3** was also formed in a argon matrix by CO addition to the carbene and identified by the IR band at 2103 cm^{-1}.[54]



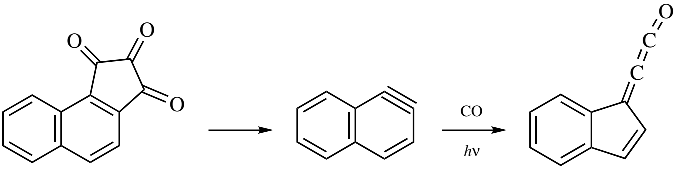
59 **3** **62**

(25)



61

Photolysis of the anhydride **63** gave the dehydronaphthalene, which upon photolysis added CO to give cumulenone **64** (equation 26).[55]



63 **64**

(26)

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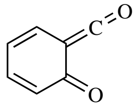
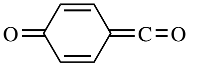
4.1.11 Oxoquinone Methides, Oxoxylylenes, and Related Species

Ketene analogues of quinone methides are oxoquinone methides **1** and **2**, while the oxoxylylenes **3** and **4** are analogues of xylylenes. These species tend to be highly reactive, and are of particular interest because of the opportunities for reactions involving interactions of the conjugated functional groups.



1



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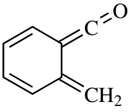

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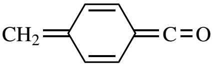
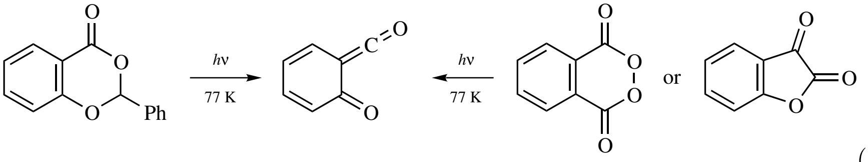


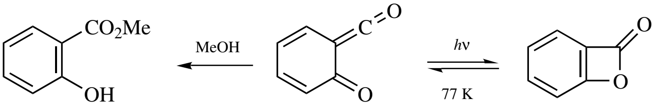
4

Oxoquinone methide **1** was first observed from photolysis of the benzodioxinone **5** in a matrix at 77 K, and identified by its IR absorption at 2118 cm^{-1} (equation 1),[1] and **1** was also formed by photolysis of phthalyl peroxide **6** or the furan-2,3-dione **7** (equation 1).[2] Photo interconversion of **1** and benzopropiolactone **8** was observed, with **8** favored by light of wavelength >340 nm and **1** favored by light of wavelength 315 nm (equation 2).[3] Reaction of **1** with methanol formed methyl salicylate

(**9**).[3] The chemistry of **1** has been reviewed.[4]

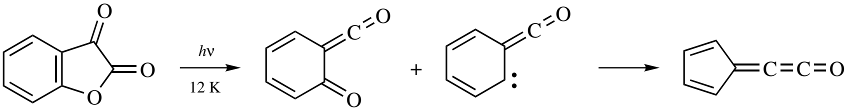


5 **1** (IR 2118 cm^{-1}) **6** **7** (1)



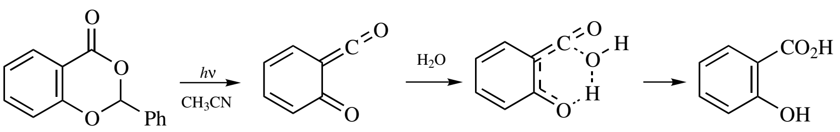
9 **1** (IR 2118 cm^{-1}) **8** (IR 1904 cm^{-1}) (2)

Photolysis of 1-benzofuran-2,3-dione (**7**) in an argon matrix at 12 K resulted in the loss of CO and formation of the α-oxoketene **1**, which was identified by its IR bands at 1605 and 2089–2105 cm^{-1} (equation 3).[5] Initial loss of CO_2 from **7** to form the carbene **10**, leading to the cumulenone **11**, was also observed (equation 3).[5] Photolysis of **5** in CH_3CN solution gave **1**, with a strong band at 2135 cm^{-1} observed by TRIR spectroscopy (equation 4).[6] Rate constants were measured for reaction of **1** with H_2O, MeOH, and Et_2NH at 22 °C of 1.5×10^7, 3.0×10^7, and 1.1×10^9 M^{-1} s^{-1}, respectively.[6] The pseudopericyclic transition state **12** for the reaction of **1** with H_2O leading to salicylic acid **13** was calculated at the MP2/6-31G*//HF/6-31G* level, but no transition structure was located at the MP2/6-31G* level.[6]



7 **1** **10** **11**

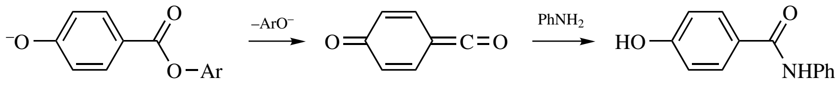
(3)



5 **1** (IR 2135 cm^{-1}) **12** **13**

(4)

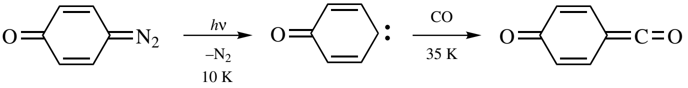
Evidence for the 1,4-oxoquinonemethide **2** came from the kinetics of base-catalyzed hydrolysis of 2,4-dinitrophenyl 4-hydroxybenzoate (**14**), which reacted 340 times faster than expected for the $B_{Ac}2$ mechanism, indicating the intervention of the E1cB pathway forming **2**, which was trapped by aniline, forming **15** (equation 5).[7]



14 (Ar = 2,4-$(O_2N)_2C_6H_3$) **2** **15**

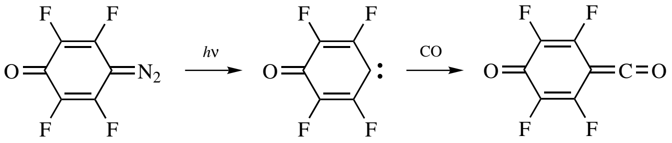
(5)

Photolysis of diazo ketone **16** in an Ar matrix doped with 1% CO at 10 K gave the carbene **17**, and when this was warmed to 35 K, addition of CO gave the ketene **2**, as identified by its IR band at 2110 cm^{-1} (equation 6).[8] Similarly, photolysis of the tetrafluoro analogue **18** gave the carbene **19**, and carbonylation in the matrix formed the ketene **20** with IR absorption at 2172 cm^{-1} (equation 7).[9] The tetrachloro analogue **20a** was formed similarly, with an IR absorption at 2132 cm^{-1}.[9]



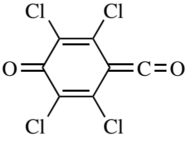
16 **17** **2** (IR 2110 cm^{-1})

(6)



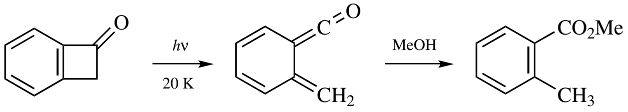
18 **19** **20** (IR 2172 cm^{-1})

(7)



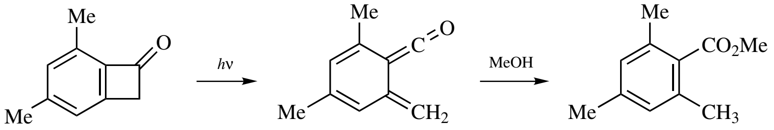
20a (IR 2132 cm^{-1})

Photolysis of benzocyclobutenone **21** in methanol or isopropanol gave the oxo-1, 2-xylylene **3**, which was trapped as the ester **22** (equation 8).[10,11] When generated by the photo reaction in an argon matrix at 20 K, **3** was identified by its IR absorption at 2120 cm^{-1}.[12,13] Generation of **3** by flash photolysis of **21** in water permitted measurement of the kinetics of hydration forming 2-toluic acid.[14] The rate of reaction of substituted derivative **3a** with nucleophiles were slowed due to hindrance to in-plane attack on the ketenyl group (equation 8a).[14a]



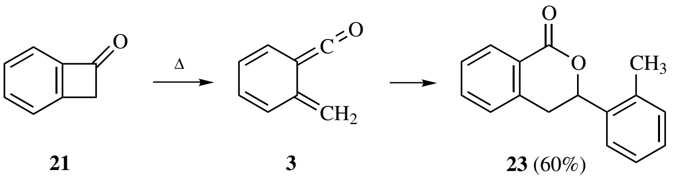
21 **3** (IR 2120 cm^{-1}) **22**

(8)

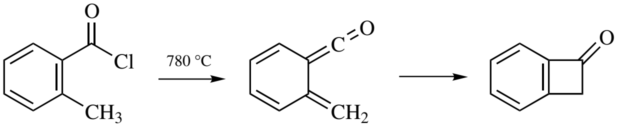


3a (8a)

Heating of neat benzocyclobutenone **21** with alcohols to form **3** gave esters **22**, as in equation 8, while heating of neat **21** gave the dimer **23** resulting from [4 + 2] cycloaddition (equation 9).[15] Thermolysis of toluyl chloride **24** at 780 °C formed **3**, leading to **21** (equation 10).[16]

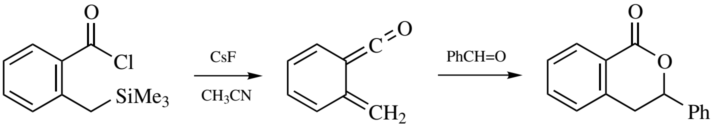


21 **3** **23** (60%) (9)

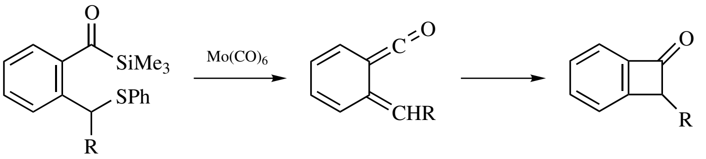


24 **3** **21** (80%) (10)

Reaction of 2-trimethylsilylmethylbenzoyl chloride (**25**) with anhydrous CsF gave **3**, which was trapped with benzaldehyde by a [4 + 2] cycloaddition, forming **26** (equation 11).[17–19] Substituted derivatives of **3** were formed similarly and gave [2 + 2] cycloadditions with alkenes.[17–19] The reaction of **27** with $Mo(CO)_6$ formed **28**, which gave benzocyclobutenones **29** (equation 12).[20]

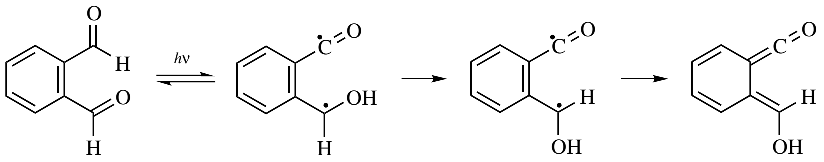


25 **3** **26** (38%) (11)



27 **28** **29** (74%, R = *n*-Bu) (12)

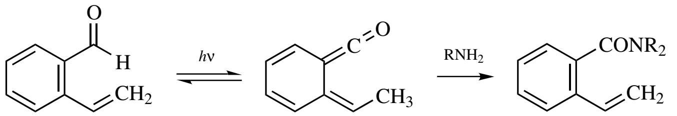
Photolysis of phthalaldehyde **30** formed **33** by a process proposed to involve reversible hydrogen atom transfer that formed **31**, which underwent bond rotation to **32**, which gave **33** (equation 13).[21,22] The structures **32** and **33** may differ in both electronic multiplicity and geometry.[21,22]



30 **31** **32** **33**

(13)

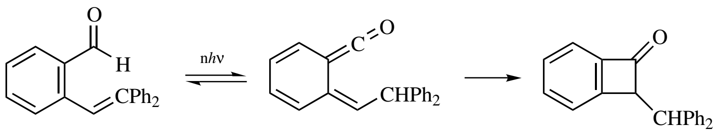
Irradiation of 2-vinylbenzaldehyde (**34**) gave the ketene methide **35**, detected by UV absorption at 380 nm and by IR bands at 2086 and 2098 cm^{-1} (equation 14).[23] In the presence of amines **35** gave amides **36**, and reacted slowly with methanol but did not react with dienophiles; this was attributed to rapid reversion of **35** back to **34**. Ionization of **34** by X-irradiation in argon matrices gave the radical cation of **35**.[23] Both **35** and its radical cation were also obtained from the corresponding methylbenzocyclobutenone.[24,25]



34 **35** **36**

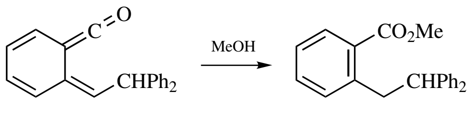
(14)

Photolysis of **37** under high-intensity laser jet conditions gave the unobserved fulvenone **38**, which either cyclized to **39** (equation 15), underwent photochemical decarbonylation, or, in the presence of MeOH, was trapped as the ester **40** (equation 16).[26] Because **37** did not form **38** upon photolysis at 350 nm but gave other products instead, it was proposed that the conversion of **37** to **38** was not symmetry allowed from the first excited state but occurred from a higher state.[26] Hydrogen transfer in *o*-vinylbenzaldehyde giving an analogue of **38** was shown to be reversible, and upon prolonged photolysis an unusual dimerization of the aldehyde eventually occurred.[27] Photolysis of aryl ketones and esters with ortho methyl groups led to analogous hydrogen transfers and formation of ketene derivatives.[28,29]



37 **38** **39** (12–16%)

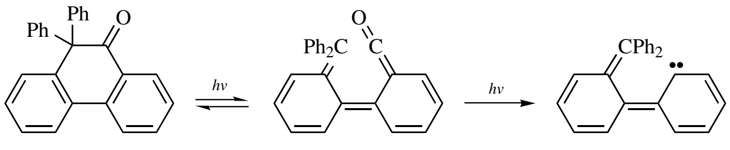
(15)



38 **40** (5–6%)

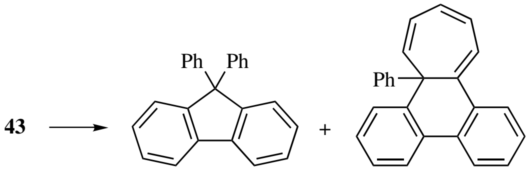
(16)

Photolysis of **41** under laser jet conditions was proposed to lead to the fulvenone **42**, which underwent photochemical decarbonylation to **43** and formation of **44a** and **44b** (equations 17, 18).[30] Under ordinary photolysis conditions no net reaction of **41** was observed, and this was attributed to rapid cyclization of **42** back to **41**.[30]



41 **42** **43**

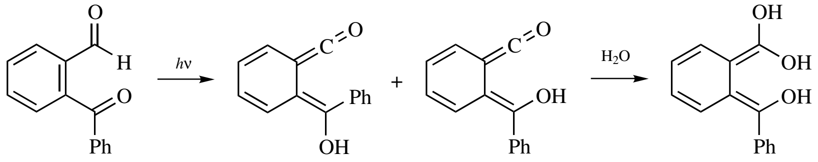
(17)



44a **44b**

(18)

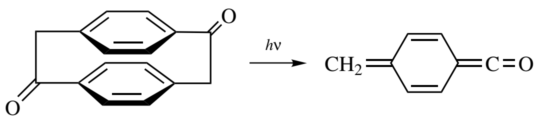
Photolysis of **45a** formed isomeric ketene enols *E/Z*-**45b**, each detected by UV. The *Z*-isomer rapidly decays, and with H_2O was proposed to form **45c** (equation 18a).[31]



45a *E*–**45b** *Z*–**45b** **45c**

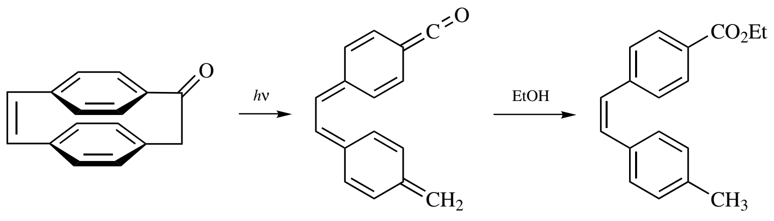
(18a)

3-Oxomethylenene-6-methylene-1, 4-cyclohexadiene (**4**) was the subject of a computational study,[33] and was prepared by photolysis of the [2.2]cyclophane **46** in an Ar matrix at 10 K and identified by the IR band at 2108 cm^{-1} (equation 19).[34] Photolysis of the unsaturated [2.2]cyclophane **47** gave **48**, which was trapped with EtOH, forming the ester **49** (equation 20).[34,35]



46 **4** (IR 2108 cm^{-1})

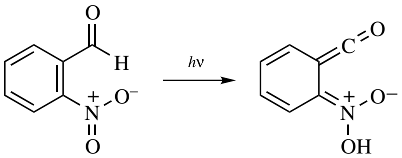
(19)



47 **48** **49**

(20)

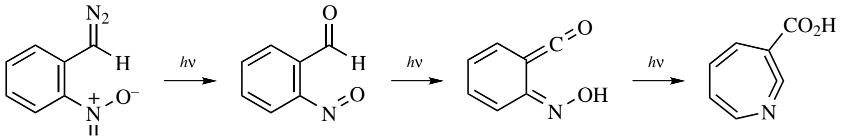
Many heteroatom analogues of the oxoquinonemethides have been studied. Thus, flash photolysis of 2-nitrobenzaldehyde (**50**) in benzene gave a product with a strong UV absorption near 450 nm assigned as the ketene **51**, which formed 2-nitrosobenzoic acid either unimolecularly or with catalysis by H_2O (equation 21).[36] Irradiation of **50** with X-rays in an argon matrix also gave **51**, as identified by the IR absorption at 2108 and 2115 cm^{-1}.[37]



50 **51** (IR 2108, 2115 cm^{-1})

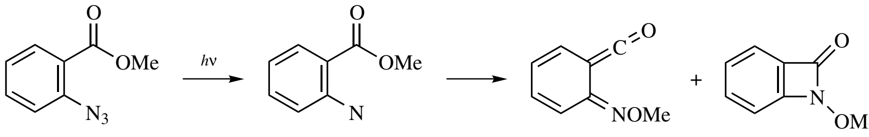
(21)

Photolysis of (2-nitrophenyl)diazomethane in an argon matrix at 10 K formed 2-nitrosobenzaldehyde (**52**), which upon further irradiation was interpreted as proceeding with formation of the ketene **53**, which rearranged to **54**, as assigned by the IR spectrum (equation 22).[38] Isomerization to *E*-**53** (IR 2114 cm^{-1}) was also observed.[38] Photolysis in an argon matrix of the azide **55** formed the nitrene **56**, leading to benzazetinone **58** and a geometrical mixture of ketenes **57**, identified by the IR absorption at 2088 and 2118 cm^{-1} (equation 23).[39]



52 **53** (IR 2116 cm^{-1}) **54**

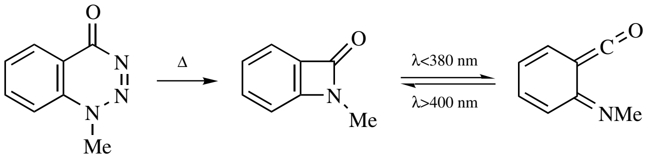
(22)



55 **56** **57** (IR 2088, 2118 cm^{-1}) **58**

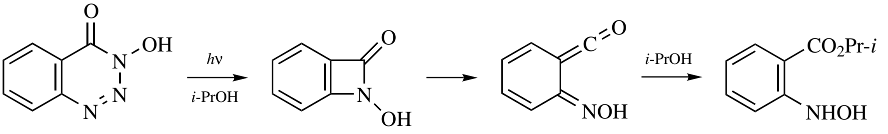
(23)

Thermolysis of 1,2,3-benzotriazin-4(1H)-one **59** with trapping in an argon matrix gave benzazetinone **60**, which upon photolysis gave the imino ketene **61** in a reversible process, as identified by the IR absorption at 2125 cm^{-1} (equation 24).[40] Formation of the NH derivative of **61** by pyrolytic routes has also been proposed, with formation of a dimer in 50% yield.[41,42] Photolysis of **62** in *i*-PrOH was proposed to form **63** and the ketene **64**, which was observed by UV and captured, forming the ester **65** (equation 25).[43]



59 **60** **61** (IR 2125 cm^{-1})

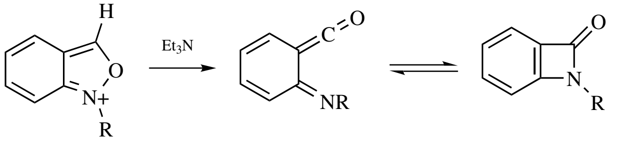
(24)



62 **63** **64** **65** (65%)

(25)

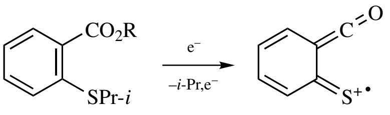
Elimination induced by Et_3N from **66** was proposed to lead to the unobserved imino ketenes **67**, which cyclized to **68** (equation 26).[44,45] It was proposed that photolysis of **68** gave **67** and that these were in thermal equilibrium, as indicated by the capture of **67** with alcohols or amines.[44]



66 (R = *t*-bu, 1-Ad) **67** **68** (97%, R = 1-Ad; (73%, R = *t*-Bu)

(26)

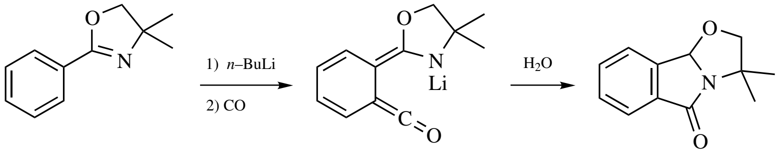
The mass spectrum of the esters **69** gave the ketene radical cation **70** as the base peak (equation 27).[46]



69 (R = Me, *i*-Pr) **70**

(27)

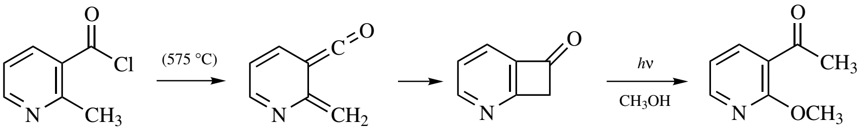
Lithiation of **71** and carbonylation was proposed to form the ketene **72**, which cyclized to **73** (equation 28).[47]



71 **72** **73** (91%)

(28)

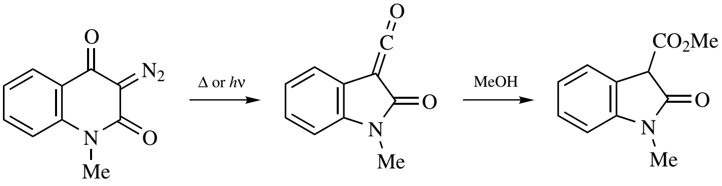
Pyrolysis of **74** at 575 °C was proposed to lead to the azafulvenone **75**, which at 10^{-4} torr formed **76** (equation 29),[48] but at a higher pressure of 10^{-2} torr and higher contact time only decarbonylation products were isolated. Photolysis of **76** in MeOH did not reform **75** but instead gave **77** quantitatively, resulting from MeOH addition at the bridgehead carbon adjacent to the nitrogen.[48]



74 **75** **76** (20%) **77**

(29)

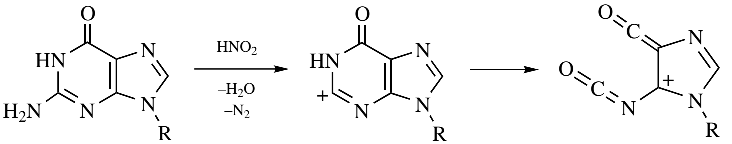
FVP or matrix photolysis of **78** gave the ketene **79**, identified by its IR bands at 2158, 2151, and 2147 cm^{-1} (equation 30).[49] This ketene also dimerized and was captured by MeOH.[49]



78 **79** (IR 2151 cm^{-1}) (90%)

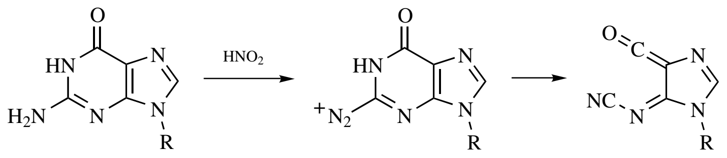
(30)

Nitrosative deamination of guanine (**80**) was reported to give the cationic ketene **82**, which was found by molecular orbital calculations to favor the resonance structure shown (equation 31; see also Section 4.1.9).[50,51] Studies using ^{18}O- labeled water for the nitrosative deamination of **80** showed the intermediacy of the diazonium ion **83**, which formed ketene **84** (equation 32), which upon hydration gave **85**, which cyclized to 2′-deoxyoxanosine **86** as the predominant reaction product (equation 33).[52–54]



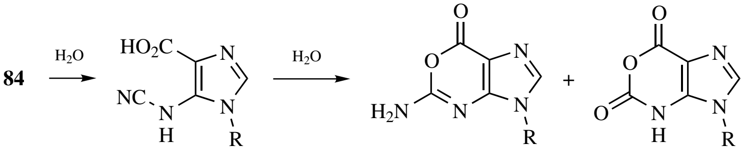
80 **81** **82**

(31)



80 (R = 2′deoxyribose) **83** **84**

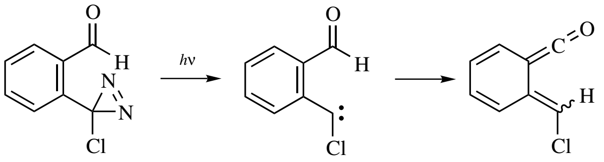
(32)



85 **86** **87**

(33)

Photolysis of diazirene **88** gave the carbene **89** which abstracted hydrogen, forming the ketenes *syn/anti*-**90**, IR 2093, 2105 cm^{-1} (equation 34).[55] Deuteration of the aldehydic hydrogen showed dramatically slowed conversion to the ketene in the matrix, a result attributed to quantum mechanical tunneling.[55]



88 **89** **90** (IR 2093, 2105 cm^{-1})

(34)

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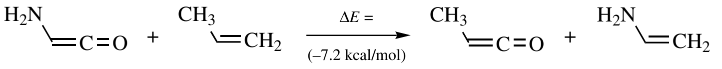
4.2 NITROGEN-SUBSTITUTED KETENES

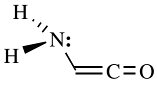
A diverse array of ketene substituents with nitrogen bonding directly to C_2 of the ketene have been studied, including amino, azido, nitroso, nitro, and azo, but substituted derivatives of the NH_2 group are the most common. Nitrogen is strongly electronegative; consequently, nitrogen-substituted ketenes are destabilized relative to alkyl-substituted analogues, as shown by the isodesmic energy comparison for aminoketene (**1**) of equation 1.[1,2] The effect of substituents on the stability of ketenes is correlated with the substituent group electronegativity, which accounts for the instability of aminoketene.[1,2]



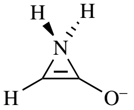
(1)

1 **2** **3** **4**

Aminoketene was calculated to have the structure **1a**, with the lone pair of electrons in the ketene plane facing in the direction of the carbonyl carbon. This has been interpreted as indicating destabilization of conformations with the nitrogen lone pair perpendicular to the ketenyl plane interacting with the C=C pi bond due to n-π electron repulsion.[1,2] An alternative interpretation, that there is a favorable interaction between the nitrogen lone pair and the carbonyl carbon, would suggest a shortening of the distance between the two atoms and a decrease in the N—C—C bond angle, which in the extreme would lead to the bridged structure **1b**. The HF/6-31G* calculated N—C—O bond angle of 118.6 deg was modestly less than the C-C-C bond angle for methylketene (**3**), suggesting that there may be some electrostatic attraction between nitrogen and the carbonyl carbon but not significant bridging.[1,2]

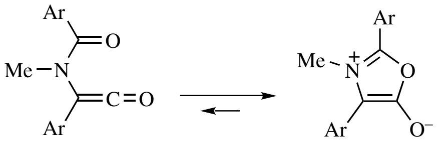


1a



1b

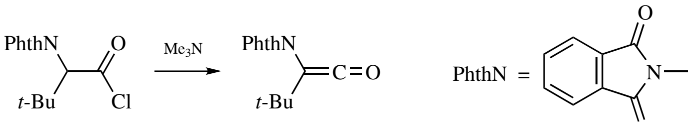
Benzoylated aminoketenes **5** have been suggested to be in equilibrium with oxazolium-5-oleate "münchnone" tautomers **6**,[3] which are the structures usually detected spectroscopically (equation 2).[4]



5 **6**

(2)

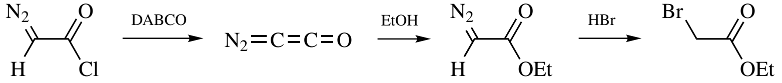
Phthalimido-*tert*-butylketene (**8**) was formed by the dehydrochlorination of acyl chloride **7** and is a persistent ketene obtained as a crystalline solid, mp 96–98 °C, IR 2134 cm^{-1} (equation 3).[5]



7 **8** (78%)

(3)

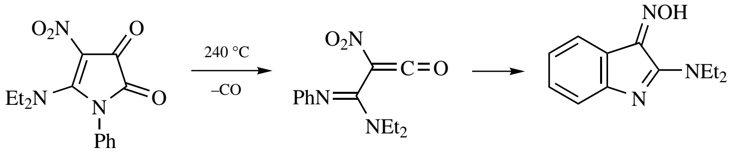
Diazoketene (**9**) was obtained by distillation of the product from diazoacetyl chloride (**8**) with DABCO (1,4-diazabicyclooctane) in ether, and was identified by the product obtained from reaction with EtOH followed by HBr (equation 4).[6]



8 **9** **10** **11**

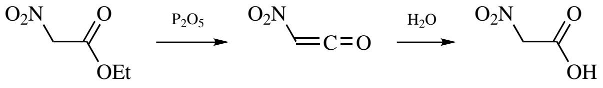
(4)

Nitroketenes are rare, despite the fact that this strongly conjugating group should stabilize ketenes, as was found in the computed structure[1,2] and as occurs for cyano and acyl groups. Pyrolysis of 4-nitropyrrolidione **12** was proposed to form the nitroketene **13**, which led to the observed indole **14** (equation 5).[7] Possible evidence for the formation of nitroketene **15** was claimed by heating methyl or ethyl nitroacetate with P_2O_5 and trapping the gas in H_2O to give the presumed $O_2NCH_2CO_2H$ in 8–15% yield, as determined by titration (equation 6).[8] No spectroscopic evidence for the formation of **15** was reported, and further study of this reaction is needed.



12 **13** **14** (82%)

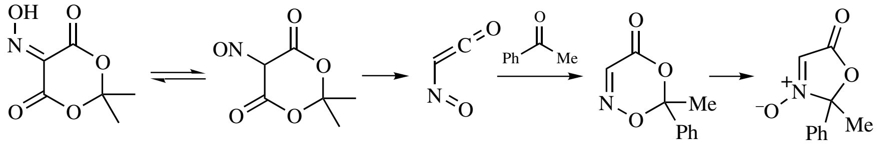
(5)



15 (8–15%)

(6)

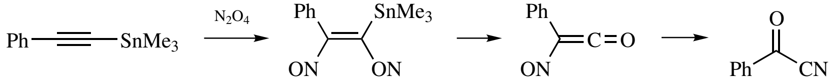
Nitrosoketene **17** has been generated by the thermolysis of nitroso Meldrum's acid (**16**) in toluene, and trapping with carbonyl compounds yielded nitrones **19**, which were proposed to arise from initial [4+2] cycloadducts **18** (equation 7).[9,10] The chiral [3 + 2] cycloadduct of **17** with *l*-menthone was used for the synthesis of the naturally occurring nonproteinogenic amino acid (2*S*,1′*S*)-(cyclopent-2-enyl)-glycine.[10] Observation of **17** in the gas phase showed the ketene band at 2146 cm^{-1} and a C=C band at 1314 cm^{-1}, in agreement with the calculated spectrum.[11] *Ab initio* molecular orbital studies of the cycloaddition of nitrosoketene (**17**) with carbonyl compounds favored a direct [3 + 2] reaction to form the nitrone **19** rather than an initial [4 + 2] formation of **18** followed by rearrangement to **19**.[12,13]



16 **17** **18** **19** (33%)

(7)

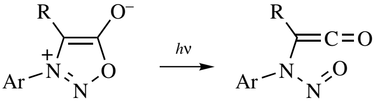
Reaction of phenyl(trimethylstannyl)acetylene with N_2O_4 results in addition of NO^+ and formation of nitroso(phenyl)ketene (**19a**) which is converted to benzoyl cyanide (equation 7a).[13a]



19a

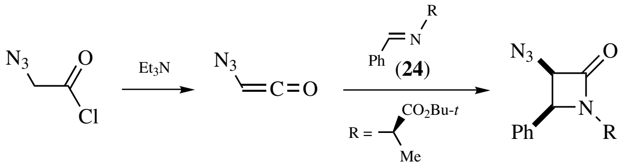
(7a)

Photolysis of "syndnones" **20** formed *N*-nitoso-*N*-(3-aryl)aminoketenes **21** (equation 8).[14] For **20** (Ar=Ph, R=alkenyl), photolysis in frozen solutions resulted in the formation of new absorption bands at 630 and 625 nm, respectively, attributed to the formation of ketenes **21** for which INDO calculated structures were reported.[15]



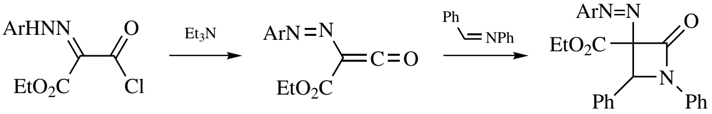
20 **21** (8)

Dehydrochlorination of azidoacetyl chloride (**22**) gave azidoketene (**23**),[16–18] which reacted in situ with the chiral imine **24**, forming the diastereomeric *cis* β-lactams **25** in a 51:49 ratio (equation 9).[17]

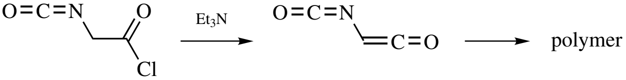


22 **23** **25** (80%) (9)

Azoketenes **27** were formed by dehydrochlorination of acyl chlorides **26** and trapped in [2 + 2] cycloadditions with imines, forming β-lactams **28** (equation 10), and by additions of alcohols and amines.[19,20] Dehydrochlorination of **29** was proposed to form isocyanatoketene (**30**), leading to cross-linked and oligomeric products (equation 11).[21]

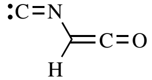


26 **27** **28** (6–29%) (10)

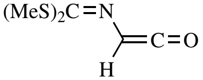


29 **30** (11)

Isocyanoketene CNCH=C=O[22] (**30a**) and the iminoketene $(MeS)_2C=NCH=C=O$[23] (**30b**) were proposed as intermediates formed by dehydrochlorination of the corresponding acyl chlorides, as evidenced by their capture by [2 + 2] cycloaddition with $Ph_2C=NPh$ as the β-lactams.

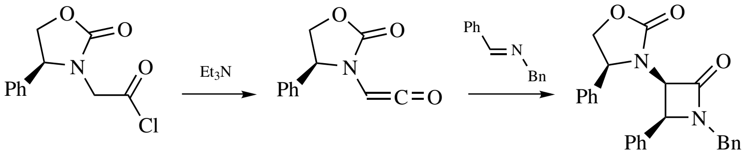


30a



30b

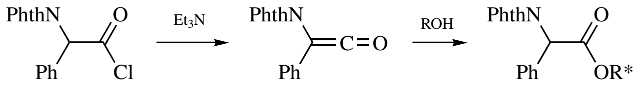
Nitrogen-substituted ketenes have found wide application, particularly in stereoselective [2 + 2] cycloadditions. For example, dehydrochlorination of **31** gave the chiral ketene **32**,[24,25] which reacted in situ with imines, giving β-lactams **33** with high diastereoselectivity (equation 12).[25]



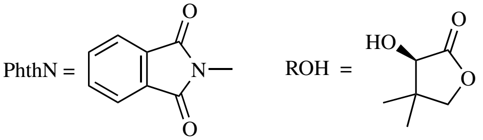
31 **32** **33**
(90%, 97:3 *dr*)

(12)

Phthalimidoketene **35** was generated by dehydrochlorination of the *N*-phthalyl acyl chloride **34** with Et$_3$N at −78 °C and utilized in stereoselective [2 + 2] cycloaddition with imines,[26] and addition of *R*-pantolactone (ROH) gave the ester **36** of phenylglycine in 98% *de* (equation 13).[27] Similar reactions are considered in Section 5.9. *N*-Tetrachlorophthalimidoketene generated from the acyl chloride with Et$_3$N also reacted with imines to give β-lactams.[28]

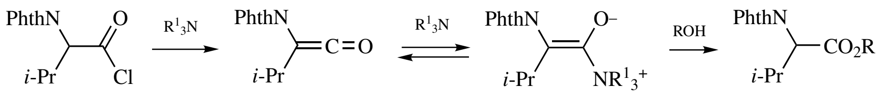


34 **35** **36** (90%)

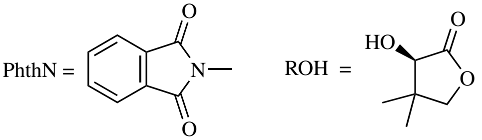


(13)

The reaction of the acid chloride of *N*-phthalyl valine (**37**) with various tertiary amines and *R*-pantolactone gave the unobserved valine-derived ketene **38**, which reacted with further amine to give the zwitterion **39**, which gave the ester **40** in 96% yield and 85% *de* with quinuclidine as the base (equation 14).[29]

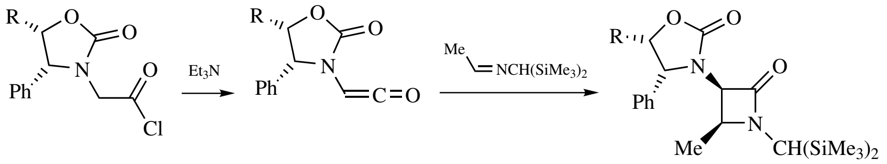


37 **38** *E/Z*-**39** **40** (96%)



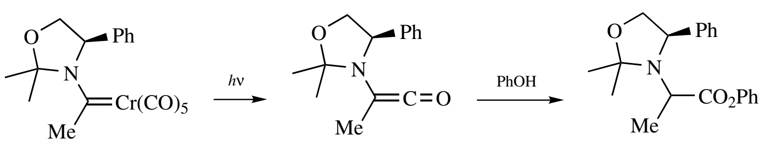
(14)

The reaction of chiral acyl chlorides **41** with Et$_3$N to give aminoketenes **42** followed by [2 + 2] cycloaddition with imines gave β-lactams **43** with high diastereoselectivities (equation 15).[30] Ketene equivalents **45** generated photochemically from chromium carbene complexes **44** reacted with alcohols to give esters **46** with high *de* (equation 16).[31] Reaction of the proline derivative **47** with Et_3N led through imine [2 + 2] cycloaddition of ketene **48** to the spiro γ-lactam **49** (equation 17), which was used to prepare peptidominetics.[32] The stereoselectivity of the reactions of the chiral derivative **50** is discussed in Section 5.4.1.7.[33]



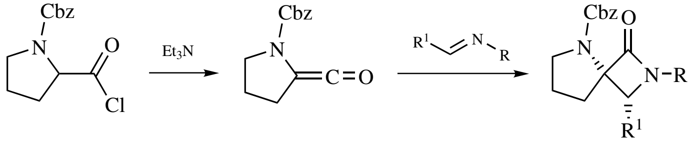
41 **42** **43** (65%, R = Ph)

(15)



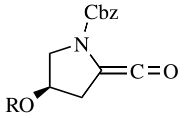
44 **45** **46** (55%)

(16)



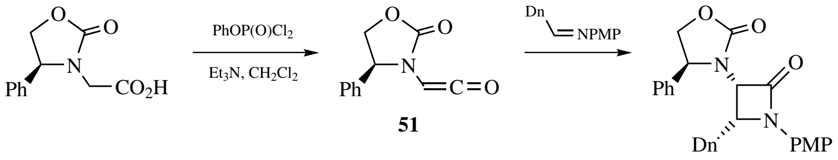
47 **48** **49** (63–83%)

(17)



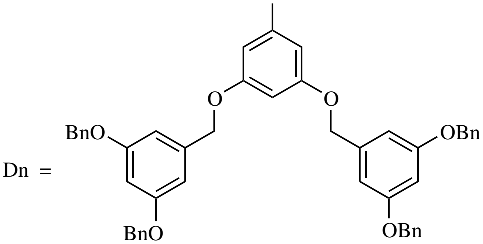
50 R = *t*-BuMe$_2$Si

Ketene **51** formed by dehydration reacted with a dendrimer-bound imine, forming dendrimer-bound β-lactam **52** (equation 18).[34]

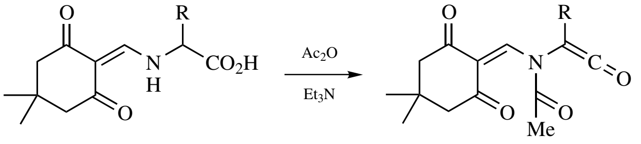


51 **52** (54–90%)

(18)

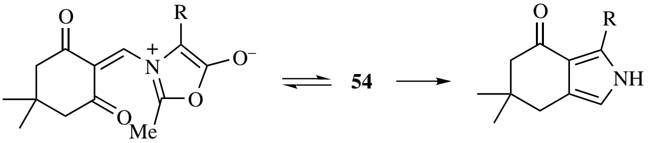


Heating eneamino acids **53** with acetic anhydride containing Et_3N giving dihydroisoindoles **56** was proposed to occur through ketenes **54** tautomeric with 1,3-oxazolium-5-olates (münchnones) **55** (equations 19, 20).[35] The reaction of acyl chlorides with imines and of CO with palladium catalysis provided a four-component synthesis of münchnones **57** (equation 21).[36]



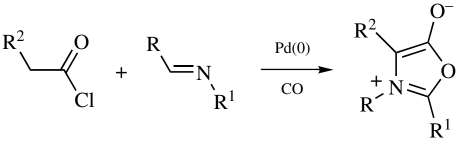
53 **54**

(19)



55 **56**

(20)



57 (32–93%)

(21)

As described in Section 2.5, the formation of aminoketene fragments from electrospray mass spectrometric peptide cleavage was proposed as a method for protein analysis.[37]

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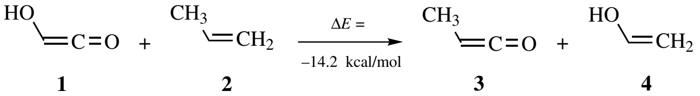
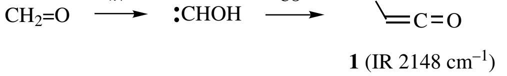
4.3 OXYGEN-SUBSTITUTED KETENES

Ketene **1** with the electronegative OH substituent was calculated by the isodesmic comparison of equation 1 at the MP2/6-31G*//MP2/6-31G* level to be destabilized by 14.5 kcal/mol relative to methylketene (**3**).[1,2] Ketenes are stabilized by electropositive substituents that can donate electrons by σ-π conjugation in the ketene plane to the carbonyl group, and are destabilized by π donors, and oxygen is disfavored by both mechanisms. The substituents OH, OCH_3, and O_2CCH_3 have calculated electronegativities of 3.55, 3.53, and 3.57,[3] respectively, and so by this criterion are all predicted to be essentially equally destabilizing, although the lower π-donating ability of the acetoxy group may make acetoxyketene more stable. Ketenes with these substituents are quite reactive, and are typically generated and used in situ for further transformations.

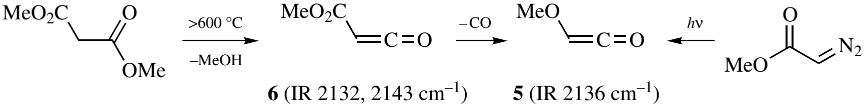


(1)

Photolysis of formaldehyde in a CO matrix was reported to cause a hydrogen shift in formaldehyde leading to hydroxy carbene, which underwent carbonylation forming **1**, as detected by its IR absorption at 2148 cm^{-1} (equation 2).[4] Methoxyketene (**5**) was formed by pyrolysis of dimethyl malonate above 600 °C by decarbonylation of the intermediate carbomethoxyketene **6**, with trapping in an argon matrix at 12 K, or by photolysis of methyl diazoacetate in the matrix, and was identified by its IR absorption at 2136 cm^{-1} (equation 3),[5] while ethoxyketene (**7**) had an absorption at 2120 cm^{-1}.[6]

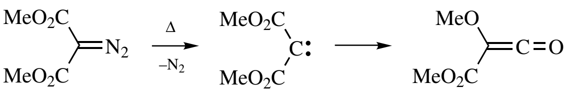


(2)



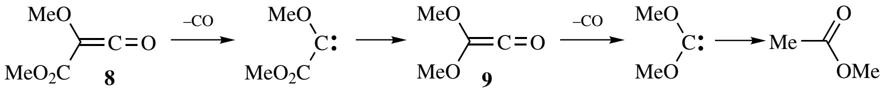
(3)

Gas phase pyrolysis of dimethyl diazomalonate was proposed to involve formation of the ketene **8** (equation 4), which underwent decarbonylation leading to dimethoxyketene **9** which also lost CO, leading to methyl acetate (equation 5).[7] Pyrolysis of diphenoxymalonic acid gave diphenoxyketene **10**, which reacted by [2 + 2] cycloaddition with $Ph_2C{=}NPh$, forming β-lactam **11** (equation 6).[8]

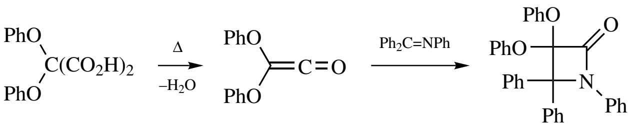


8

(4)



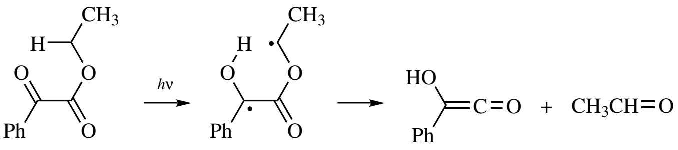
(5)



10 **11**

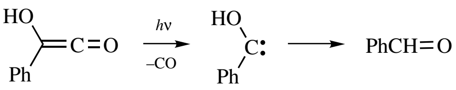
(6)

Photolysis of ethyl phenylglyoxylate **12** formed phenylhydroxyketene (**14**) to the extent of 80% by intramolecular cleavage via the diradical **13** (equation 7).[9] The ketene **14** was not observed but was proposed to undergo further photolysis with decarbonylation to the carbene **15**, which rearranged to the observed product benzaldehyde (equation 8).[9,10] This ketene was observed by TRIR spectroscopy at 2100 cm^{-1},[11] and a band at 1651 cm^{-1} was attributed to the triplet state of **12**.[11] Further investigations used step-scan FTIR for study of the reaction, with observation of the ketene band at 2105 cm^{-1}.[12]



12 **13** **14**

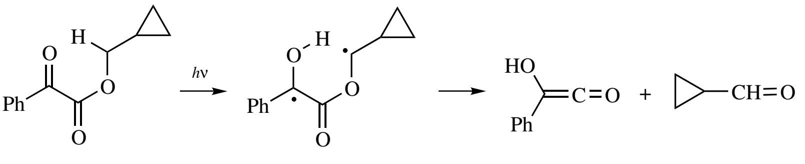
(7)



14 **15**

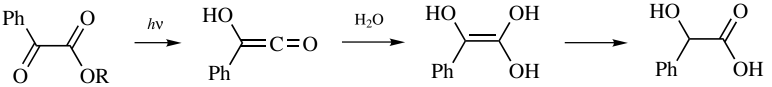
(8)

Photolysis of the ester **16** substituted with a cyclopropyl clock gave products resulting from cyclopropylcarbinyl radical ring opening, as well as benzaldehyde resulting from the formation of ketene **14** in a 44:56 ratio, and led to the estimate of a lifetime of 16 ns for the diradical **17** (equation 9).[13]



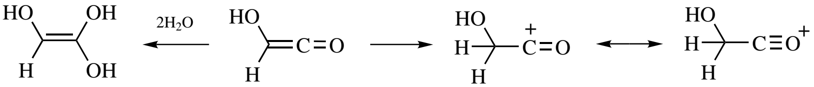
16 **17** **14**

Photolysis of *n*-butyl and isobutyl phenylglyoxalates $PhCOCO_2R$ (**18**) in aqueous solution gave **14** for kinetic studies of the hydration reaction, forming mandelic acid in a reaction proposed to proceed through formation of the acid enol **19** in water-, base-, and acid-induced reactions, which were interpreted as first forming the acid enol **19** (equation 10).[14–16] The rate constants for the water and base reactions at 25 °C $k(H_2O) = 5.51 \times 10^5\ s^{-1}$, $k(OH^-) = 2.33 \times 10^9\ M^{-1}\ s^{-1}$, and $k(H^+) = 5.45 \times 10^7\ M^{-1}\ s^{-1}$ are large for this highly reactive ketene compared to some model compounds (Table 4.2; data from Table 1, Section 5.5.1.2).



18 **14** **19**
R = *n*-Bu,*i*-Bu

Computational studies of the hydration of hydroxyketene (**1**) favored a pathway for protonation on C_2 forming the cation **20**, stabilized by the acylium resonance structure **21** (equation 11).[16] Addition of water dimer was favored to form the enediol **22** (equation 11),[16] consistent with the experimental results for **14** (equation 10).

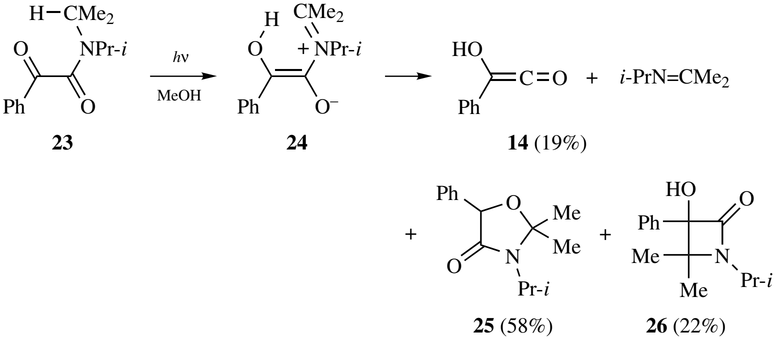


22 **1** **20** **21**

TABLE 4.2 Comparative Rate Data for Hydration of Ketenes PhCR=C=O

Ketene	$k(H_2O)\ s^{-1}$ (k_{rel})	$k(OH^-)\ M^{-1}\ s^{-1}$ (k_{rel})	$k(H^+)\ M^{-1}\ s^{-1}$ (k_{rel})
PhCH=C=O	4.77×10^3	1.22×10^6	Not detected
	1.0	1.0	
PhCMe=C=O	55.7	2.03×10^4	Not detected
	0.012	0.017	
PhC(OH)=C=O	5.51×10^5	2.33×10^9	5.45×10^7
	116	1900	

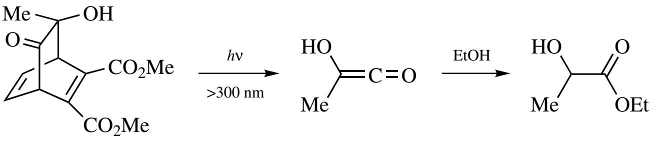
Photolysis of the pyruvyl amide **23** in methanol was interpreted to proceed with formation of the zwitterionic intermediate **24**, which underwent cleavage to the hydroxyketene **14**, which was trapped by methanol, as well as undergoing cyclization to the oxazolidin-4-one **25** and the β-lactam **26** (equation 12).[17,18] The formation of oxazolidin-4-ones was favored for substrates with small alkyl substituents.[17,18]



23 **24** **14** (19%) **25** (58%) **26** (22%)

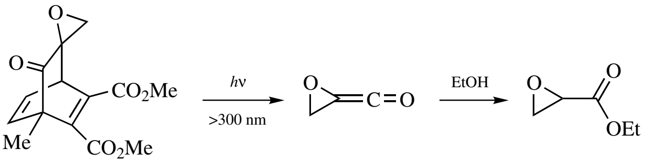
(12)

Photolysis of **27** and **29** in $CHCl_3$ containing ethanol gave the ketenes **28** and **30**, respectively, which were captured as the ethyl esters (equations 13, 14).[19] Another example of a bicyclo[2.2.2]octadiene cleavage giving an oxygen-substituted ketene is shown in Section 4.1.3.[20]



27 **28**

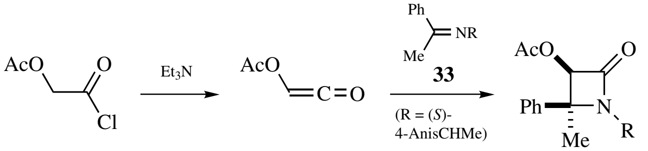
(13)



29 **30** (66%)

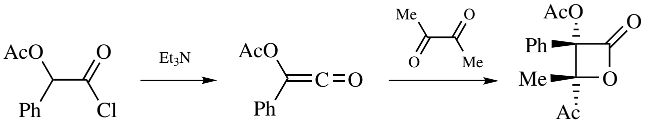
(14)

Acetoxyketene **32**, generated in situ by dehydrochlorination of **31**, reacted with imines **33**, giving β-lactams **34** used to produce the taxotere side chain (equation 15),[21] and also gave [2 + 2] cycloaddition with cyclopentadiene.[22] Acetoxy(phenyl)ketene **35** was also prepared by dehydrochlorination, and gave [2 + 2] cycloaddition with the carbonyl group of biacetyl, forming **36** (equation 16).[23]



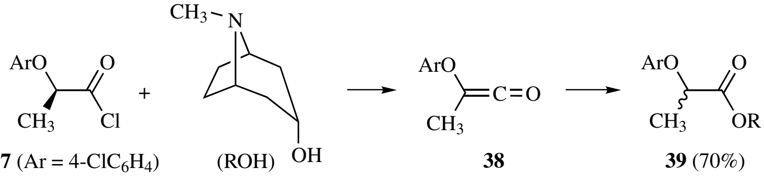
31 **32** **34** (64%)

(15)



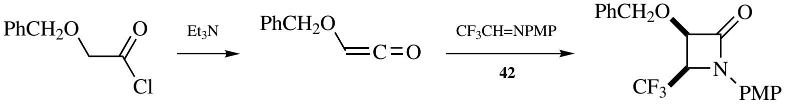
35 **36** (30%) (16)

Reaction of optically active acyl chloride **37** with the amino alcohol tropanol led to a racemic ester **39** by the intermediacy of ketene **38** (equation 17).[24] The use of tropanol hydrochloride prevented the racemization.

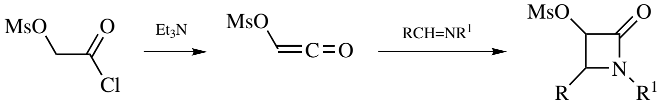


37 (Ar = 4-ClC$_6$H$_4$) (ROH) **38** **39** (70%) (17)

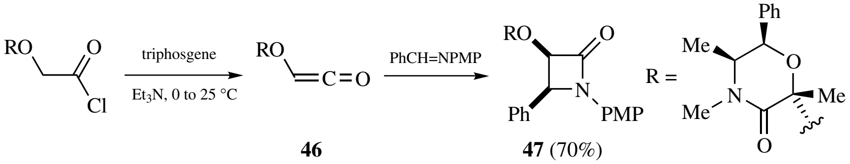
Dehydrochlorination of benzyloxyacetyl chloride (**40**) with Et$_3$N gave benzyloxyketene **41**, which was not observed but was trapped in a [2 + 2] cycloaddition with imine **42**, forming β-lactam **43** (equation 18).[25,25a] Reaction of **41** generated in this way in CH$_2$Cl$_2$ with the chiral amine *t*-BuCH=NCH(CH$_3$)Ph also gave the *cis*-lactam, but with no diastereoselectivity.[26] Methanesulfonyloxyketene MsOCH=C=O (**44**) has also been generated by the dehydrochlorination route and trapped with imines, forming **45** (equation 19).[27] Triphosgene was used to generate ketene **46** containing a chiral auxiliary for synthesis of an equal mixture of the diastereomeric *cis*-β-lactams **47**, which were readily separated into the optically pure forms by chromatography (equation 20).[28]



40 **41** **43** (50%) (18)



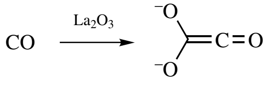
44 **45** (23–90%) (19)



46 **47** (70%)

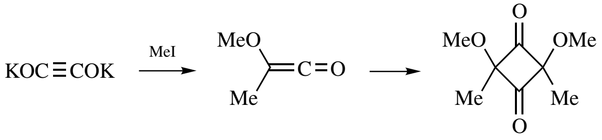
(20)

Deposition of CO on La_2O_3 gave a UV band at 300 nm and IR bands at 2075 and 1367 cm^{-1} ascribed to the anion **48** (equation 21).[29] Reaction of the potassium salt **49** with methyl iodide formed the ketene **50**, which gave the dimer **51** (equation 22).[30] Thermolysis of the alkynyl diether **52** yielded ketene **53**, which reacted with more of the alkyne **52** by [2+2] cycloaddition, forming the cyclobutenone **54** (equation 23).[30]



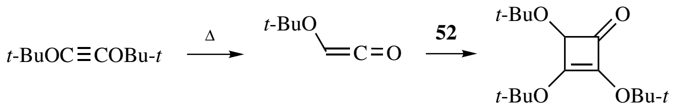
48

(21)



49 **50** **51**

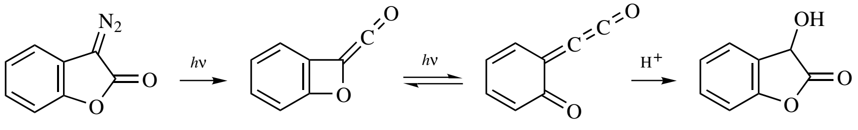
(22)



52 **53** **54**

(23)

Wolff rearrangement of diazo ketone **55** gave the ketene **56**, detected by UV spectroscopy, and this interconverted on photolysis with the cumulenone **57** (equation 24).[31] The major product from acid-catalyzed hydration was **57a**, proposed to form by protonation at C_2 of the cumuleneone.[31]

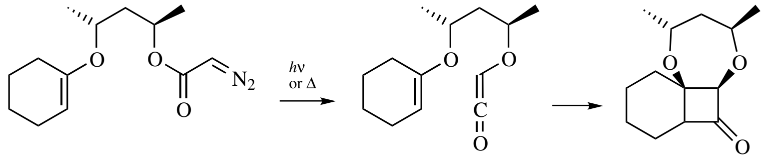


55 **56** **57** **57a**

(24)

Photochemical generation of oxygen-substituted ketenes by Wolff rearrangement has generally been inefficient, as oxygen is poor in migration and keto carbenes are formed that undergo extensive capture by solvent before oxygen migrates. Thus, photolysis of **58** gave ketene-derived products in 33% yield in solution (equation 25).[32] However, FVT in which the keto carbene was formed in the gas phase in the absence of solvent permitted enhanced Wolff rearrangement to ketene **59** and gave intramolecular [2 + 2] cyclization to **60** in 70% yield and

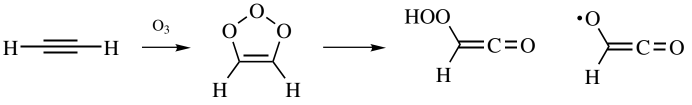
>99% *de* (equation 25).[32–34]



58 **59** **60**

(25)

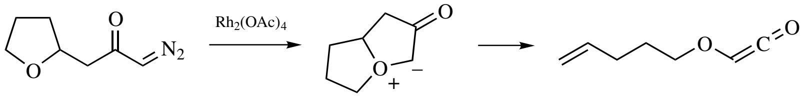
Computations gave the energetics for the reaction of acetylene with ozone, forming **61** and hydroperoxyketene **62** (equation 26).[35] Formation of the ketenyloxyl radical **63** has been considered.[36]



61 **62** **63**

(26)

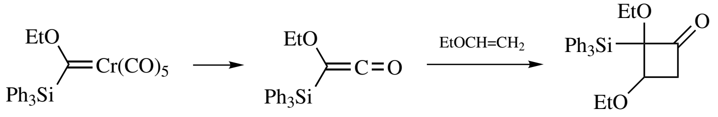
Rhodium-catalyzed cyclization of the diazo ketone **64** gave cyclization to the transient bicyclo[3.3.0]octan-3-one-1-oxonium-2-ylide **65**, which underwent sigmatropic and stereospecific [3 + 2] cycloreversion to the 4-pentenyloxyketene **66**, which was trapped with MeOH in 88% yield (equation 27).[37] The effects of different ring sizes and substituents were examined, and the mechanism was analyzed using DFT computations.[37]



64 **65** **66**

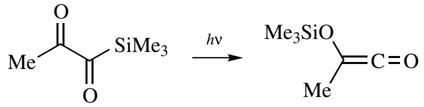
(27)

The ethoxy(triphenylsilyl)ketene **68** was prepared from metal carbene complexes **67** and trapped in situ by ethyl vinyl ether by [2 + 2] cycloaddition (equation 28).[38] Trimethylsilyloxy(methyl)ketene **70** was formed by photochemical rearrangement of silyldiketone **69** in a Vaseline mull and detected by the IR absorption at 2106–2108 cm^{-1} (equation 29).[39] Another silyloxy-substituted ketene is noted in Section 4.1.3.[40]



67 **68**

(28)



69 **70** (IR 2106–2108 cm^{-1})

(29)

Hydroxyl-substituted bisketenes are covered in Section 4.9.

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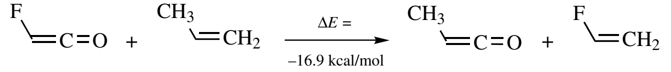
4.4 HALOGEN-SUBSTITUTED KETENES

4.4.1 Fluoroketenes and Fluoroalkylketenes

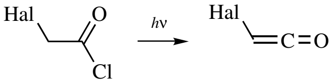
Fluoroketene (**1**) was calculated at the MP2/6-31G* level to be destabilized by 16.9 kcal/mol relative to methylketene by the isodesmic comparison of equation 1, and by this criterion is the least stable ketene of the group studied (Section 1.1.3).[1–3] The effect of substituents on the stability of ketenes was correlated with the substituent group electronegativity, which accounts for the instability of fluoroketene.[1,2]



1 **2** **3** **4**

(1)

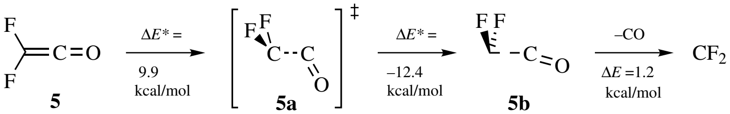
The ketenyl IR bands of $\mathrm{CFH{=}C{=}O}$ (**1**, 2142 cm^{-1})[4] and $\mathrm{CF_2{=}C{=}O}$ (**5**, 2162 cm^{-1}) have been reported.[5,6] Ketenyl IR frequencies measured in a single laboratory using laser pyrolysis elimination from acyl chlorides for $\mathrm{CHHal{=}C{=}O}$ $\mathrm{C{=}O}$ were 2145, 2151, 2148, and 2145 cm^{-1} for Hal = F, Cl, Br, and I (**1**, **6**, **7**, **8**, respectively) in matricies and 2148 and 2157 cm^{-1} for Hal = F and Cl, respectively, in the gas phase (equation 2).[7]



5 Hal = F(**1**), Cl(**6**), Br (**7**), I (**8**)

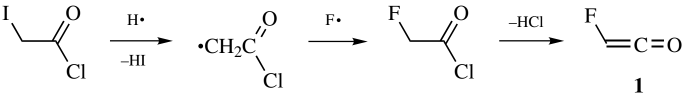
(2)

Fluoroketenes are remarkably reactive, and CFH=C=O (**1**) and CF_2=C=O (**5**) have not been directly observed in solution. The latter also rapidly underwent spontaneous decarbonylation, forming CF_2, but as described below, there is evidence that this species does have a short existence, and it has been generated, observed in a low-temperature matrix, and trapped. Recent computations indicated that this decarbonylation was exothermic by 2.3 kcal/mol with a barrier of 9.9 kcal/mol to transition structure **5a**, forming the CF_2•CO complex **5b**, which was 1.2 kcal/mol more stable than separated CF_2 and CO (equation 3).[8] Structural and thermodynamic data for **1** and **5** have also been obtained by computation.[9]



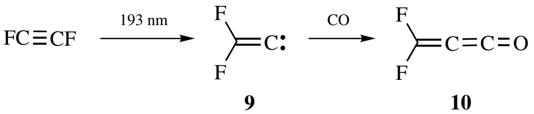
(3)

The reaction of hydrogen and fluorine atoms generated in a microwave discharge of H_2/CF_4 with ICH_2COCl formed activated FCH_2COCl, which gave CHF=C=O by loss of HCl (equation 4).[10]

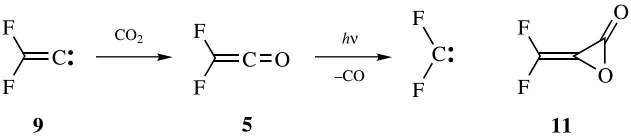


(4)

Photolysis of difluoroacetylene with 193 nm light in an Ar matrix at 10 K led to difluorovinylidene **9**, and in the presence of CO this formed the nonlinear cumulene-ketene **10** on warming to 35–42 K (equation 5).[11] Similar photolysis forming **9** at 7 K in a CO_2-doped Ar matrix that was annealed at 30 K gave difluoroketene (**5**), as identified by the IR bands at 2162, 1427, and 1274 cm^{-1} (equation 6).[5,6] Formation of **5** from **9** was proposed to involve electrophilic abstraction of an oxygen atom without formation of the lactone **11**. Irradiation of CF_2=C=O with light >550 nm led to decarbonylation, but the resultant CF_2 was not observed to react with CO.



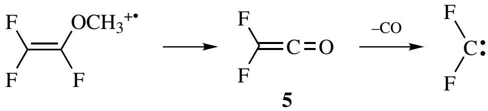
(5)



(6)

The B3LYP calculated C—C and C—O bond lengths of CF_2=C=O of 1.313 and 1.168 Å, respectively, are similar to those of CH_2=C=O, while the C—F bond length is 1.333 Å, and the F—C—F angle is 114.2°.[5,6]

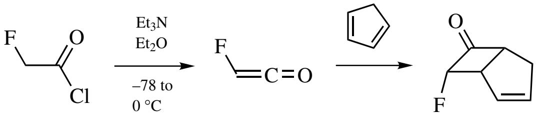
The mass spectrum of $CF_2{=}CFOCF_3$ also indicated the formation of $CF_2{=}C{=}O$, which was estimated to dissociate with a barrier of 10.0 kcal/mol (42 kJ/mol) in a process that was exothermic by 6.0 kcal/mol (25 kJ/mol) (equation 7).[12]



5

(7)

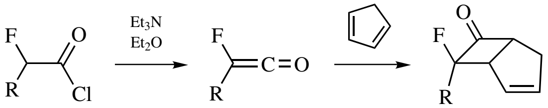
Fluoroketene generated by dehydrochlorination of fluoroacetyl chloride underwent [2 + 2] cycloaddition with cyclopentadiene, with a 10:1 preference for the *endo* fluorine in the product **12** (equation 8).[13]



1 **12** (32% *exo/endo* 1:10)

(8)

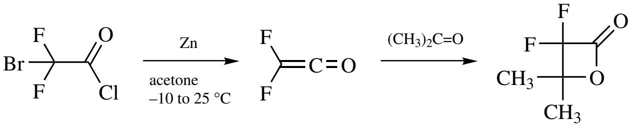
Substituted fluoroketenes $FCR{=}C{=}O$, R = Me, Ph, and CF_3 (**13a–c**) have been prepared by dehydrohalogenation of the acyl chlorides and, while not observed directly, were trapped by cyclopentadiene by [2 + 2] cycloadditions, forming cyclobutanones **14** (equation 9).[14] The products were formed with a preference for fluorine only in the *exo* position.[14]



13a–c (R = Me, Ph, CF_3) **14** (10–38%)

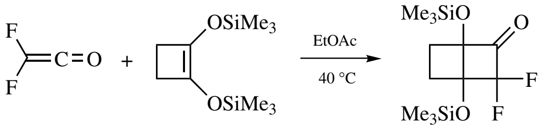
(9)

Reaction of $CBrF_2COCl$ in acetone with activated zinc, forming difluoroketene, took place with in situ trapping by [2 + 2] cycloaddition and formation of 2,2-difluoro-3,3-dimethylpropanolactone (**15**) in 50% yield (equation 10).[15] Difluoroketene was also trapped by trimethylsilyl vinyl ethers, forming **16** and **17** (equations 11, 12).[16,17]

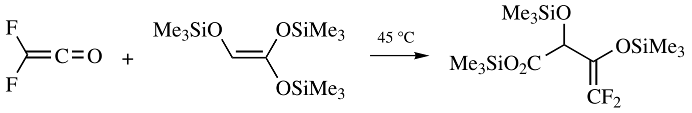


5 **15** (50%)

(10)

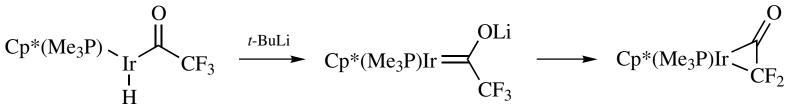


5 **16** (34%) (11)



5 **17** (60%) (12)

Reaction of the iridium complex **18a** with *tert*-butyllithium from −196 to −80 °C gave the complex **18b**, observed by NMR spectroscopy, which upon warming to 22 °C formed the difluoroketene complex **19**, with ^{13}C NMR signals at δ 207.2 (CO) and 178.0 (CF_2), and the ketenyl IR signal at 1725 cm^{-1} (equation 12a).[17a] The structure of **19** was confirmed by X-ray (Figure 4.2).[17a]



18a **18b** **19** (32%) (12a)

Acylfluoroketenes **21** were generated by photolysis at room temperature or thermolysis in refluxing aromatic solvents of fluorodioxinones **20** and captured as the oxazinones **22** by reaction with cyanamide (equation 13).[18] Photolysis of **20** (R=H)

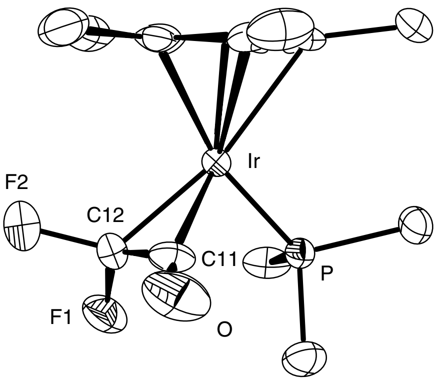
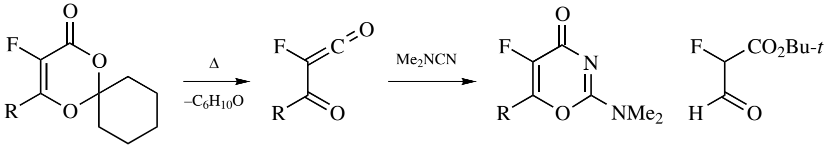


Figure 4.2 X-ray structure of difluoroketene complex **19** (reprinted from ref. 17a with the permission of Wiley VCH).

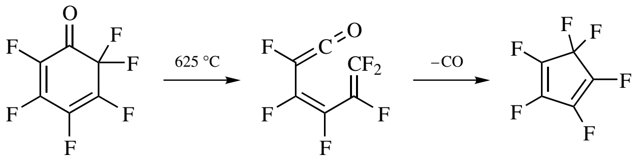
in *t*-BuOH generated **21a**, which gave the ester **23**, isolated as the semicarbazone, in 57% yield.[18]



20 **21a–d** (R = H, Ph, Me, CF_3) **22** (51–90%) **23**

(13)

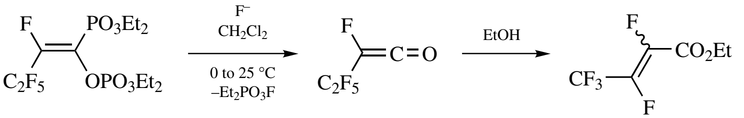
FVP of the hexafluorocyclohexadienone **24** together with some of the 2,5-dienone isomer was proposed to involve initial formation of the perfluoroketene **25**, which decarbonylated, forming the observed product perfluorocyclopentadiene **26**, trapped at −78 °C in 53% yield and 95% purity (equation 14).[19] The photochemical ring opening of cyclohexadienones is a well-known route to dienylketenes (Barton-Quinkert reaction; Section 3.4.3).



24 **25** **26** (53%)

(14)

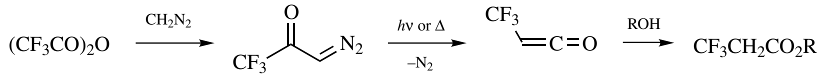
Reaction of the vinyl phosphate **27** with fluoride ion generated the unobserved fluoroketene **28**, which was captured by EtOH, giving the ester **29** (equation 15).[20]



27 **28** **29** (90% *E/Z* 82:18)

(15)

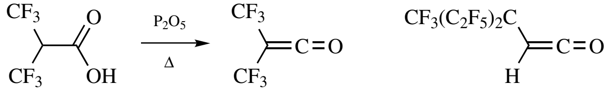
Fluoroalkylketenes also have unique properties, and are often considered together with ketenes with fluorine directly bonded to the ketenyl carbon. The reaction of trifluoroacetic anhydride with diazomethane gave a simple preparation of the diazo ketone **30**, which was characterized by ^1H, ^{13}C, ^{15}N, ^{17}O, and ^{19}F NMR spectroscopy (equation 16).[21] The *Z* conformation of **30** was calculated to be the most stable by 3.2 kcal/mol, and the EI mass spectrum obtained with minimal heating showed no formation of the ketene **31**, whereas with greater heating of **30** the mass spectrum of **31** was observed (equation 16).[21] The diazo ketone **30** has also been made from the acyl chloride with diazomethane and used to generate the ketene **31** in H_2O or alcohol for isolation of the acid or esters **32**.[22–24] The ketene **31** was detected by UV when formed by flash photolysis for measurement of the reactivity with water, and was found to be six times more reactive than *n*-BuCH=C=O (Section 5.5.1.2).[25] A study of the Wolff rearrangement of ^{13}C-labeled **30** showed no scrambling of the label, indicating that an oxirene intermediate was not formed.[25a]



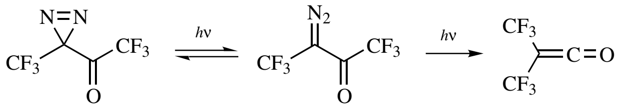
30 **31** **32** (16)

The structures and conformations of **31** and of $CHF_2CH{=}C{=}O$ (**33**) have been calculated by *ab initio* methods.[26]

Dehydration of the acid **34** by heating with P_2O_5 gave **35**, bp 5 °C, with a characteristic IR absorption at 2203 cm^{-1} (equation 17).[27,28] The perfluoroalkylaldoketene **36** was prepared similarly.[29] The ketene **35** was also formed by photochemical Wolff rearrangement of the diazo ketone **37** (equation 18).[30] The diazine **37a** also formed in a reversible reaction upon photolysis of **37** (equation 18).[30]

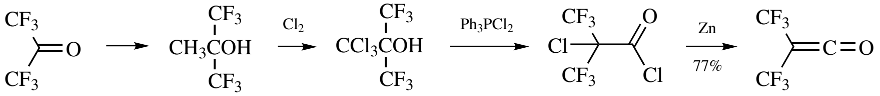


34 **35** (94%) **36** (17)



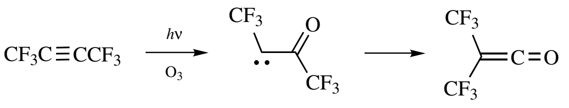
37a **37** **35** (18)

A new preparation of $(CF_3)_2C{=}C{=}O$ (**35**) beginning with hexafluoroacetone has been reported, which makes this species generally available (equation 19).[31] Previous preparations relied upon toxic starting materials that are not convenient. Photolysis of hexafluoro-2-butyne in a matrix containing O_3 led to formation of **35** by reaction of oxygen atoms forming an observable keto carbene, followed by a Wolff-type rearrangement (equation 20).[32] When CO was present in the matrix, addition to the keto carbene forming the acyl ketene **35a** was observed by IR (equation 20a).[32]



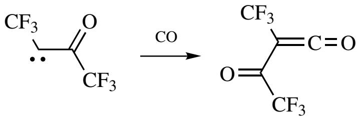
35

(19)



35

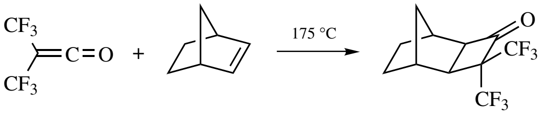
(20)



35a (IR 2181 cm^{-1})

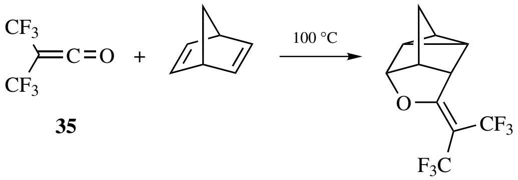
(20a)

The cycloaddition chemistry of bis(trifluoromethyl)ketene has been extensively investigated. Some of the reactions observed include [2 + 2] cycloaddition with norbornene forming **38** (equation 21),[33] norbornadiene forming **39** (equation 22),[34] and alkynes forming **40** (equation 23).[35] Pyrolysis of **40** proceeded with ring opening, forming the unobserved **41**, which reacted further to give products derived by fluoride migration with cyclization.[36]



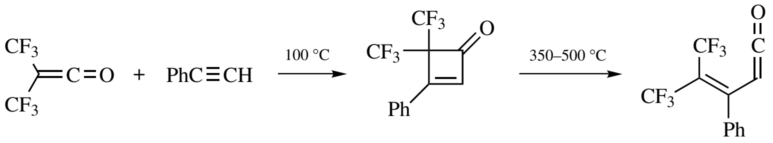
35 **38** (~100%)

(21)



35 **39** (81%)

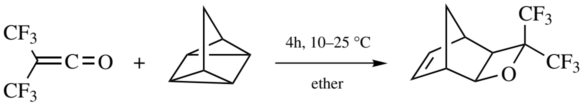
(22)



35 **40** (80%) **41**

(23)

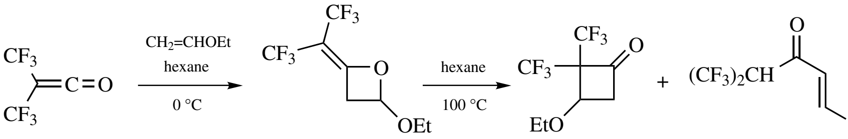
Bis(trifluoromethyl)ketene (**35**) undergoes [2 + 2 + 2] cyclization with quadricyclane (**41a**), forming **41b** in 92% yield under mild conditions (equation 23a).[37]



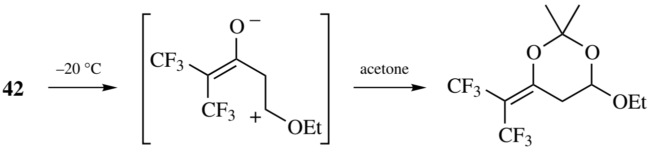
35 **41a** **41b** (92%)

(23a)

Reaction of **35** with ethyl vinyl ether in hexane at 0 °C gave the oxetane **42**, as detected by NMR. This isomerized at 50 °C to the cyclobutanone **43** and the enone **44**, isolated in 67% and 13% yields, respectively, when the cycloaddition was performed at 100 °C (equation 24).[38] Reaction in CH_2Cl_2 at −80 °C permitted isolation of crystalline **42** (mp −43 °C), which at −20 °C gave a deep blue intermediate assigned as the zwitterion **45** (equation 25). Reaction of **42** in acetone gave the adduct **46** from **45** (equation 25).[38]

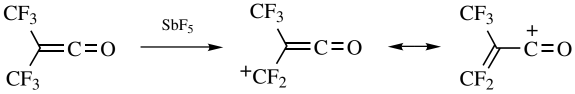


35 **42** **43** (92%) **44** (8%) (24)

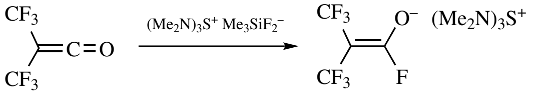


45 **46** (92%) (25)

Bis(trifluoromethyl)ketene **35** underwent ionization in SbF_5, forming the delocalized cation **47**, which was directly observed by NMR (equation 26).[39] The addition of fluoride ion to **35** gave the stable crystalline salt **48** (equation 27), which in the ^{19}F NMR showed nonequivalent CF_3 groups even at 75 °C, indicating a barrier to rotation of at least 19 kcal/mol in the enolate.[40]

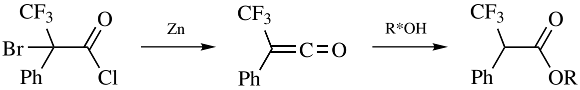


35 **47** (26)



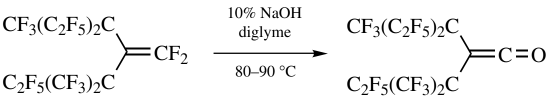
35 **48** (27)

Phenyl(trifluoromethyl)ketene (**49**) was prepared by dehalogenation, and the addition of chiral alcohols gave stereoselectivity in the formation of the new chiral center in the ester **50** (equation 28).[41]



49 **50** (28)

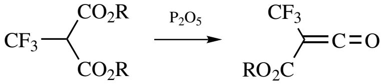
Hydrolysis of the perfluoroalkene **51** with aqueous NaOH solution formed the ketene **52**, which displayed characteristic IR absorption at $2160\,\mathrm{cm}^{-1}$ (equation 29).[42]



(29)

51 **52** (80%)

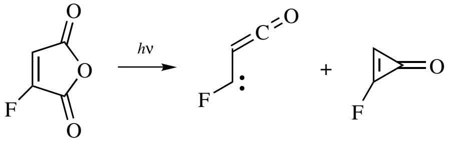
Trifluoromethylmalonate esters **53** react with P_2O_5, forming ketenes $CF_3C(CO_2R){=}C{=}O$ (**54**, equation 30).[43] These ketenes are thermally stable but react with both electrophilic and nucleophilic reagents.[43]



(30)

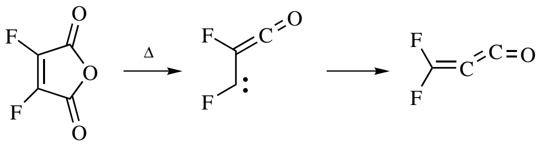
53 **54**

Photolysis of matrix-isolated fluoromaleic anhydride **55** in an Ar matrix gave fluoro(ketenyl)carbene **56** and fluorocyclopropenone (**57**) (equation 31; see also Section 3.8).[44] Difluoromaleic anhydride (**58**) upon pyrolysis was proposed to form the carbene **59**, which gave the nonlinear cumulene **10** (equation 32).[45]



(31)

55 **56** **57**



(32)

58 **59** **10**

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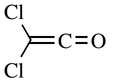
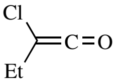
4.4.2 Chloro- and Bromoketenes

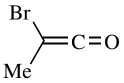
The study of haloketenes is a relatively recent development in ketene chemistry, even though attempts were made by early investigators to prepare these species, including dichloro-,[1] chloro(ethyl)-,[2] and bromo(methyl)ketenes **1**–**3**.[3] However, none of these ketenes were isolated, and only ill-defined products were obtained. Finally, in 1965–1966, haloketenes were proven to exist by their generation and capture in independent studies in three different laboratories,[4–6] but even then, these species were not directly observed. The haloketenes are highly reactive, and their synthetic utility quickly became apparent, particularly in [2 + 2] cycloadditions with alkenes, alkynes, imines, and other reagents. Their chemistry has been actively pursued ever since and has been discussed in earlier reviews.[7–9]



1

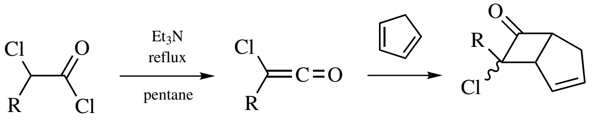


2



3

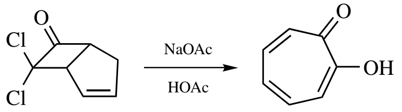
Chloroketenes are conveniently prepared by the dehydrochlorination of α-chloroalkanoyl chlorides and trapped by reactive alkenes such as cyclopentadiene by [2 + 2] cycloadditions, forming bicyclo[3.2.0]pent-2-ene-6-ones **8** (equation 1).[10] The adduct **8a** of dichloroketene was used in a simple and efficient preparation of tropolone **9** (equation 2).[11]Dichloroketene (**1**) formed by dehydrochlorination of dichloroacetyl chloride (**10**) also gave an efficient reaction with the highly reactive *trans*-cyclooctene to form the [2 + 2] cycloaddition product **11** (equation 3).[12]



R = H (**4**), Me (**5**),
Et (**2**), *i*-Pr (**6**),
Ph (**7**), Cl (**1**)

8 *endo/exo* >97/3
(R = H)

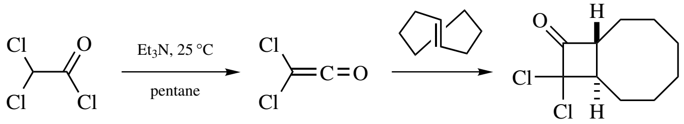
(1)



8a

9 (66%)

(2)



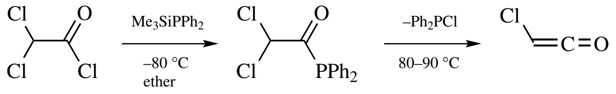
10

1

11 (ca.100%)

(3)

Chloroketene (**4**) was also obtained by the reaction of dichloroacetyl chloride (**10**) with Me_3SiPPh_2 at low temperature, forming **12**, followed by heating and trapping of the ketene at −80 °C for measurement of the ^{13}C NMR spectrum (equation 4).[13,13a]



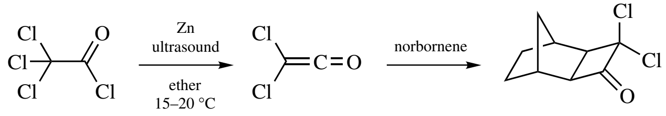
10

12

4 δ ^{13}C116.2 (C=O)
70.1 (CHCl)

(4)

Dichloroketene (**1**) has been prepared both by the dehydrochlorination of dichloroacetyl chloride (equations 1, 3)[10–12] and by the zinc dehalogenation of trichloroacetyl chloride, and in each case the ketene has been generated and used in situ.[7–9] A variety of methods are used for activating the zinc used for the dehalogenation, including the use of ultrasound[14.15] for the reaction with norbornene forming **13** (equation 5)[14] or simple heating.[16]

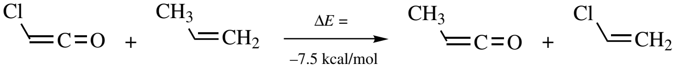


1

13 (75%)

(5)

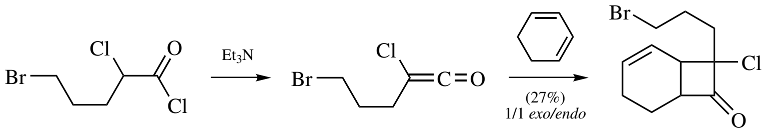
Halogen-substituted ketenes are now widely used in synthesis, but in almost all cases the ketenes are not observed in preparative studies. Even derivatives with ketene-stabilizing silyl substitutents have not been isolated. The high reactivity of halogen-substitued ketenes is in agreement with the results of *ab initio* calculations,[17,18] which indicate that chloroketene (**4**) is destabilized by 7.7 kcal/mol at the MP2/HF6-31G* level compared to methylketene (**14**) by isodesmic energy comparison (equation 6). This result was explained by the finding that ketenes are destabilized by electronegative substituents, and stabilized by electropositive groups, in agreement with the high reactivity of chloroketenes observed in practice.



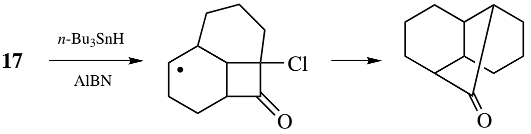
4 **14** (6)

This high reactivity also has made these species quite useful, especially as they can be prepared using inexpensive starting materials, and the products can be used in a variety of further transformations. The Wolff rearrangement method, which is widely used in the preparation of many types of ketenes, has not, however, found application in the preparation of halogen-substituted ketenes. For direct observation of halogen-substituted ketenes, generation in the gas phase or in low-temperature matrices have been successful, as well as preparation at low temperature in solution.[13,19]

Cycloaddition reactions of chloroketenes with alkenes gave chlorocyclobutanones that have been utilized in many synthetic transformations, as in the dehydrochlorination of the α-chloroacyl chloride **15**, forming ketene **16**, which reacted in situ with cyclohexadiene by [2 + 2] cycloaddition, forming **17** (equation 7).[20] Reaction of **17** with *n*-Bu_3SnH resulted in cyclization to the unobserved intermediate **18**, which formed the product **19** by rearrangement and dechlorination (equation 8).[21] Other related examples were observed.[22]

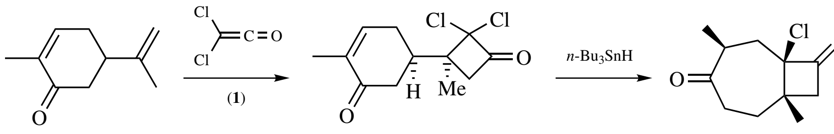


15 **16** **17** (27%)
1/1 *exo/endo* (7)



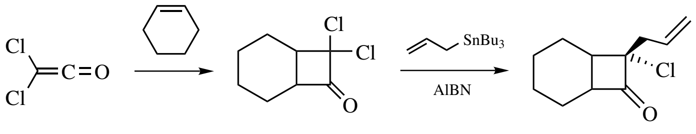
17 **18** **19** (53%) (8)

Dichloroketene (**1**) generated by zinc reduction reacted with the alkene **20**, forming the cyclobutanone **21**, which underwent reductive cyclization to **22** (equation 9).[23] Dichloroketene reacted with cyclohexene, forming the [2 + 2] cycloadduct **23** (equation 10), and this was converted to the rearranged ketone **25** (equation 11).[24,25]



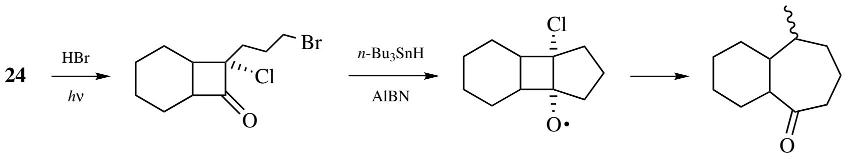
(9)

20 **21** **22**



(10)

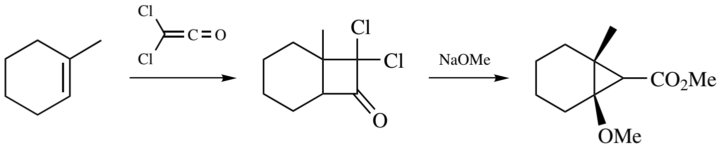
1 **23** (70–90%) **24** (51%)



(11)

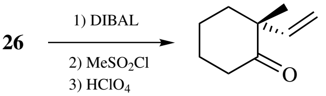
(43–48%) **25**

The dichloroketene adduct with 1-methylcyclohexene was converted to cyclopropyl carboxylate ester **26**, which was a precursor to vinylketones **27** (equations 12, 13).[26] The [2 + 2] cycloaddition of dichloroketene generated by dehydrochlorination with the silyl alkenyl ether **28**, forming **29**, was evaluated in a pilot plant scale reaction (equation 14), but was unsatisfactory due to problems with the subsequent dehalogenative ring expansion.[27]



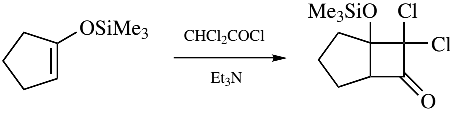
(12)

26 (75%)



(13)

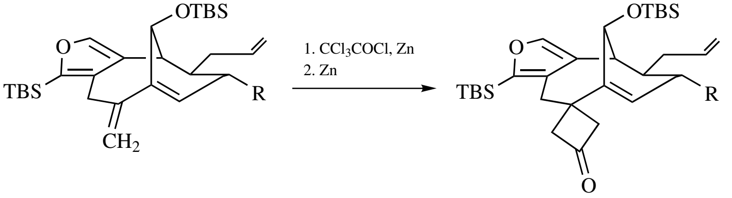
27 (63%)



(14)

28 **29** (~80%)

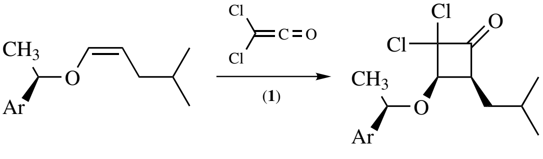
In the synthesis of the CP compounds, which are complex antibiotics, [2 + 2] cycloaddition of dichloroketene with the alkene **30** was followed by dechlorination with zinc to give **31**, which was converted to the final target (equation 15).[28]



30 (R = $(CH_2)_6OBn$) **31** (85%)

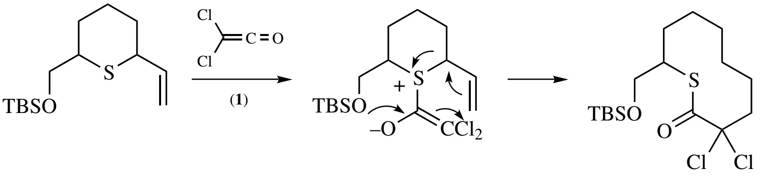
(15)

Other examples of $CCl_2{=}C{=}O$ cycloadditions included reactions with a vinyl ether forming **32** (equation 16),[29] addition to a carbohydrate derivative,[30] and reaction with 4-*m*-carboranyl-1-butene (Section 4.8.2).[31] The reaction with allyl-substituted thioether proceeded by nucleophilic attack and rearrangement, forming **33** (equation 17).[32] In [2 + 2] cycloadditions of **1**, ring opening could be suppressed by the substitution of DME for $POCl_3$ as the $ZnCl_2$ sequestering agent.[33] Allyl ethers react similarly. Reaction of a vinyl epoxide **34** was proposed to form **35**, which gave lactone **36** (equation 18).[33]



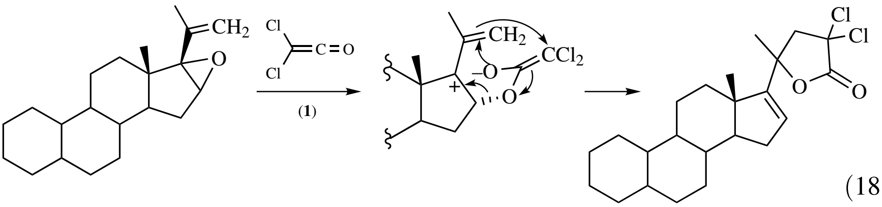
32 (>40%)

(16)



33
(75–85%)

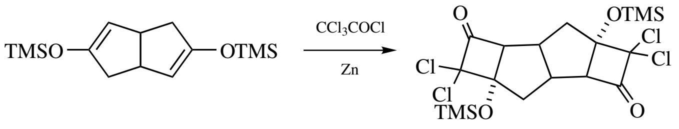
(17)



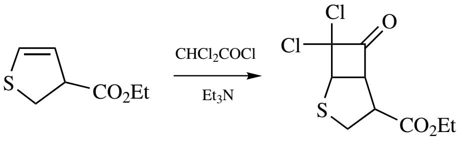
(18)

34 **35** **36** (85%)

Dichloroketene was used in reactions with bicyclo[3.3.0]octadiene **37**, forming **38** (equation 19),[35] and with dihydrothiophene **39**, forming **40** in the synthesis of a penicillin analogue (equation 20).[36]

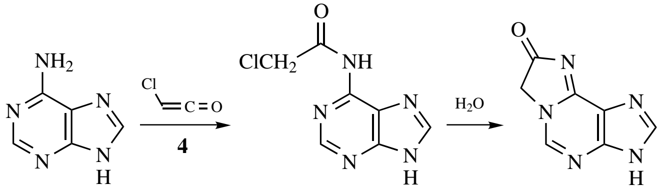


37 **38** (30%, two isomers) (19)



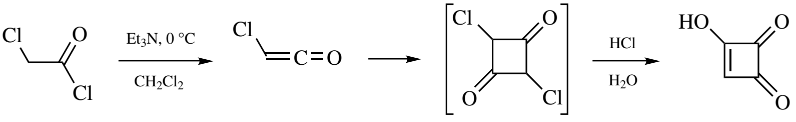
39 **40** (80%) (20)

To elucidate the possible role of chloroketenes as intermediates in halo olefin bioactivation and possible DNA binding, the reactions of **1** and **4** with adenine, cytosine, guanine, and thymine were examined. Thymine did not react, but adenine and cytosine gave stable adducts with both **1** and **4**, as demonstrated by analysis, and guanine reacted with **1**.[37] The adducts were identified as resulting from acylation of the exocyclic amino groups, as in the example of the formation of *N*-chloroacetyladenine (**42**) from adenine (**41**) (equation 21).[37] In H_2O at pH 7, **42** was cleaved back to **41** and also formed 1,*N*-6-acetylguanine **43** (equation 21).[37]



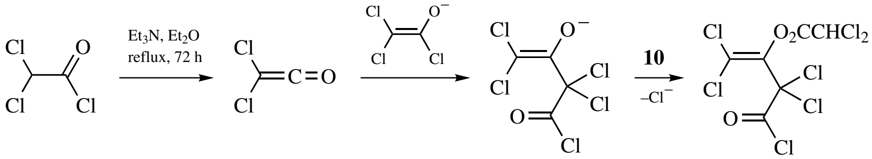
41 **42** **43** (21)

Dimers of chloroketene and dichloroketene have apparently not been isolated and characterized, but in situ hydrolysis of the product of dehydrochlorination of $ClCH_2COCl$ led to the isolation of **44** in 1.8% yield, and this implicated the formation and hydrolysis of the chloroketene dimer (equation 22).[38]



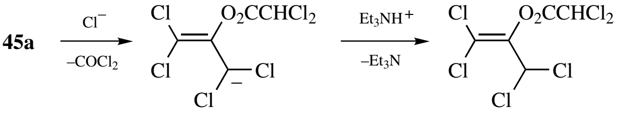
4 **44** (1.6%) (22)

Dehydrochlorination of dichloroacetyl chloride in ether at reflux over an extended time period led to the two oligomeric products **45b** and **45c**, proposed to form as shown in equations 22a–22c.[39]



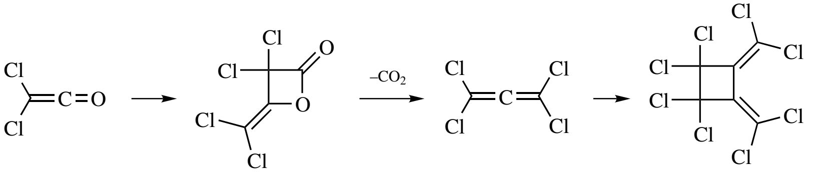
10 **1** **45a**

(22a)



45b (25.5%)

(22b)

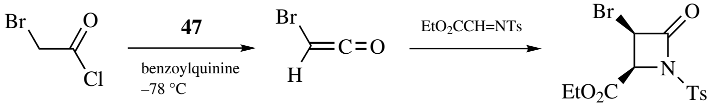


1 **45c** (3.6%)

(22c)

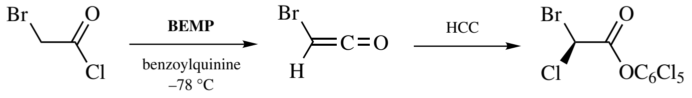
Experiments in which $CH_2ClCOCl$ and $CHCl_2COCl$ were reacted with Et_3N and CH_3OD resulted in the formation of methyl esters that were monodeuterated to the extent of 32 and 41%, respectively, suggesting that the esterification took place partially through ketene intermediates.[40]

Bromoketene (**46**) has been prepared by gas phase dehydrochlorination of bromoacetyl chloride at 700–800 °C and used for determination of the photoelectron spectrum.[41] The reaction of bromoacetyl chloride with 1,8-bis(dimethylamino)-naphthalene **47** as a strong stochiometric base and benzoylquinine as a shuttle base at −78 °C gave [2 + 2] cycloaddition with the imine $EtO_2CCH{=}NTs$ forming the β-lactam product **48** in 61% yield, 96% *ee*, and 98 : 2 *dr* (equation 23a).[42] However, it is not certain if bromoketene was a discrete intermediate in this reaction, as an enolate may have been involved.[42] Bromoketene generation was, however, carried out using the insoluble polymeric base (BEMP), and stereoselective chlorination was achieved using hexachlorocyclohexadienone (HCC) as the chlorinating agent. In this case, formation of the ketene was unambiguous (equation 23b).[43]

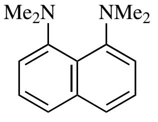


46 **48** (61%, 98% *ee,* 98/2 *dr*)

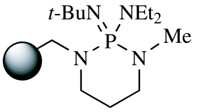
(23a)



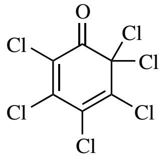
46 **49** (51%, 9% *ee*) (23b)



47

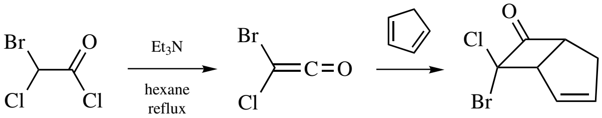


BEMP

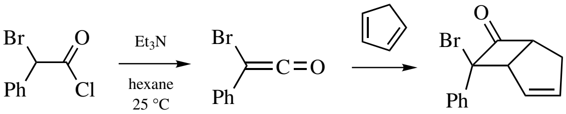


HCC

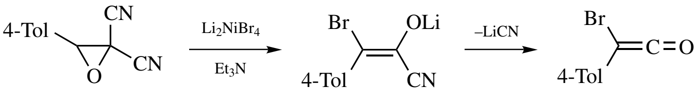
Dehydrochlorination of bromochloroacetyl chloride with triethylamine gave bromochloroketene (**50**), and this reacted in situ by [2 + 2] cycloaddition with cyclopentadiene, forming **51** in 60% yield, with selectivity for the bromo group in the *endo* position (equation 24).[8] Bromophenylketene (**52**) was also formed by dehydrochlorination, and reacted with cyclopentadiene to give **53** with the bromo group preferentially in the *exo* position (equation 25).[44] Bromoarylketenes (**56**) were also formed from 2,2-dicyano-3-aryloxiranes (**54**) via intermediates **55** (equation 26) and gave stereoselective reactions with chiral amines **57**, forming **58** (equation 27).[45]



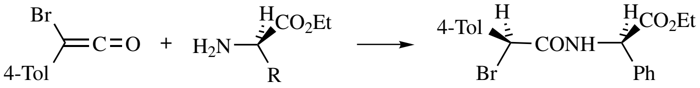
50 **51** (60%) (24)



52 **53** (63%) (25)



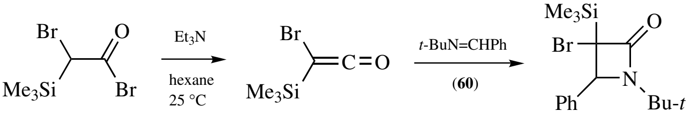
54 **55** **56** (26)



56 **57** (**i**, R = Me; **ii**, R = CH_2OH) **58** (**i**, 74%, 50% *de*, **ii**, 80%, >95% *de*) (27)

Bromotrimethylsilylketene (**59**) was prepared by dehydrobromination and reacted with imine **60** to form the β-lactam **61** (equation 28).[46] Ketene **59** was long-lived in solution, as evidenced by observation of the ketenyl IR band at

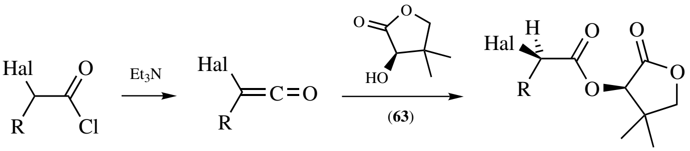
2114 cm^{-1}, but polymerized upon removal of the Et_3NHCl salt.[46]



59 (IR 2114 cm^{-1}) **61** (56%)

(28)

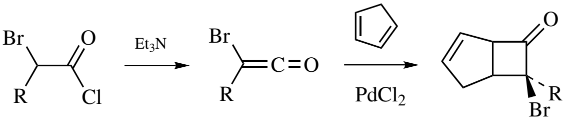
Alkylbromo- and alkyliodoketenes **62** generated by dehydrochlorination of α-bromoalkanoyl chlorides reacted with *R*-pantolactone (**63**) to give esters **64** with diastereoselectivities of 75 to >95% (equation 29).[47]



62 **64**

(29)

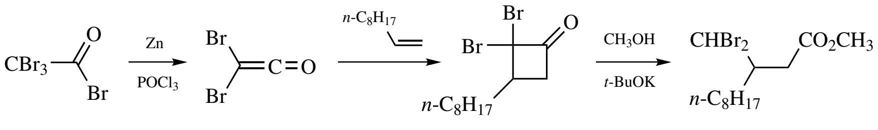
Palladium(II) complexes affect the *exo/endo* selectivity of [2 + 2] cycloadditions of bromo(alkyl)ketenes **66**, prepared by triethylamine dehydrochlorination of 2-bromoalkanoyl chlorides **65**, with cyclopentadiene forming bicyclo[3.2.0]hept-2-en-7-ones **67** (equation 30).[48,49] The palladium catalyst increased the yields of cycloaddition products from 23–58% to 42–91%, with a modest increase in the preference for *exo* alkyl groups in the products, although in most cases *endo* alkyl stereochemistry was still predominant.



65 (R = *n*-$Br(CH_2)_3$, *n*-alkyl) **66** **67**

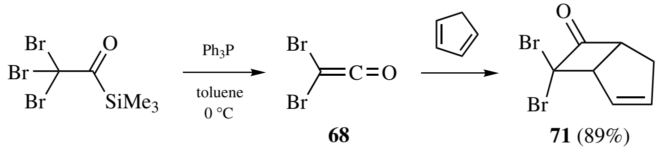
(30)

Dibromoketene (**68**) generated from zinc debromination of CBr_3COBr was captured by benzylamine, and when generated in the presence of alkenes such as *n*-decene gave dibromocyclobutanone **69**, which was cleaved by alkoxides to give β-dibromomethyl ester **70** (equation 31).[50] Reaction of trimethylsilyl tribromoacetate with triphenylphosphine formed dibromoketene, which reacted with cyclopentadiene, forming **71** (equation 32).[51]



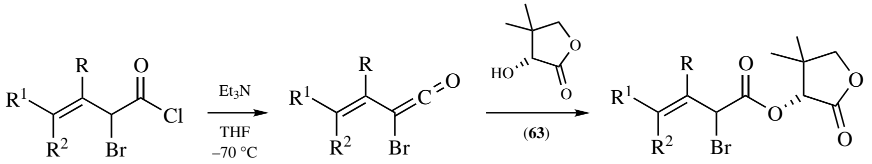
68 **69** (70%) **70** (71%)

(31)



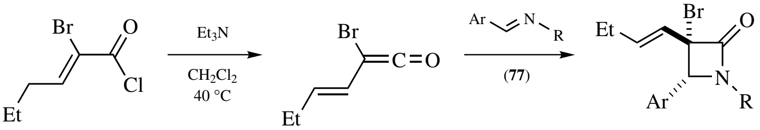
68 **71** (89%) (32)

α-Bromo-α-alkenylketenes **73** generated by dehydrochlorination of acyl chorides **72** reacted in situ with *R*-pantolactone (**63**), forming esters **74** with yields of 50–85% and diastereomeric ratios ranging from 72:28 to >95:5 (equation 33).[52] Displacement of the bromine by benzylamine forming α-amino esters was followed by further synthetic elaboration of the resulting products. The alkenylketenes **73** also gave [4 + 2] cycloadditions with imines forming 3-bromo-5,6-dihydropyridin-2-ones.[53] Dehydrochlorination of 2-bromo-2-hexenoyl chloride (**75**) with triethylamine gave the ketene **76**, which was captured in situ by imines **77** giving the bromo-substituted β-lactams **78** (equation 34).[54]



72 **73** **74** (50–85%)

(33)



75 **76** **78** (50–93%) (34)

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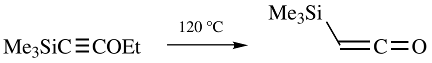
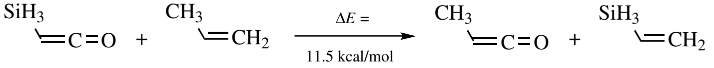
4.5 SILYL-, GERMYL-, AND STANNYLKETENES

Trimethylsilylketene (**1**) is a remarkably stable ketene that was first reported in 1965 from the pyrolysis of (trimethylsilyl)ethoxyacetylene (**2**) as an isolable oil with no apparent tendency toward dimerization (equation 1).[1,2] It was found to react readily with nucleophiles[1–3] and to undergo Wittig reactions forming allenes.[3]



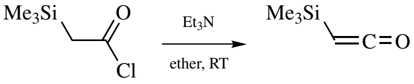
2 **1** (90%) (1)

A quantitative measure of the stabilization of ketenes provided by the silyl substituent was given by the MP2/6-31G*//MP2/6-31G* isodesmic energy change of 11.5 kcal/mol shown in equation 2.[4,5]

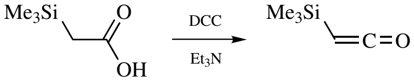


3 **4** **5** **6** (2)

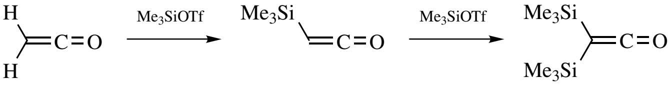
A review devoted to silylketenes has appeared,[6] as well as concise descriptions of the chemistry of $Me_3SiCH{=}C{=}O$[7] and $CH_2{=}CHC(SiMe_3){=}C{=}O$ (**7**).[8] An optimized procedure for the preparation of **1** by the alkynyl ether pyrolysis of equation 1 has been presented,[9] and pyrolysis of the *tert*-butoxy ether $Me_3SiC{\equiv}COBu$-*t* forming **1** proceeded at 50 °C.[10] Other preparations of **1** included the dehydrochlorination of the acyl chloride **8** (equation 3),[11] dehydration of trimethylsilylacetic acid **9** (equation 4),[12] and treatment of ketene with trimethylsilyl triflate, which reacted further with additional Me_3SiOTf to give $(Me_3Si)_2C{=}C{=}O$ **10** (equation 5).[13] Triethylsilylketene (**11**) was prepared by pyrolysis of the anhydride (equation 6)[11] and also by dehydrochlorination of the acyl chloride.[14]



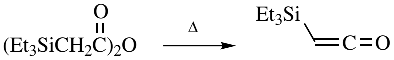
8 **1** (48%) (3)



9 **1** (63%) (4)

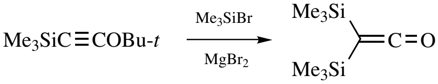


1 (63%) **10** (48%) (5)

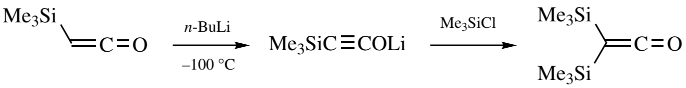


11 (80%) (6)

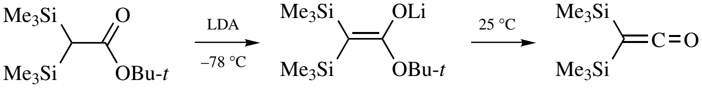
Bis(trimethylsilyl)ketene (**10**) has been prepared by treatment of the alkynyl ether **12** with Me_3SiBr (equation 7),[15,16] by reaction of Me_3SiCl with the ynolate **13** formed by deprotonation of **1** (equation 8),[17] by the E1cb elimination from the ester **14** (equation 9),[18] and from photochemical Wolff rearrangement of the diazo ketone **15** as a by-product in a reaction that evidently proceeded through the silene intermediate **16** (equation 10).[19]



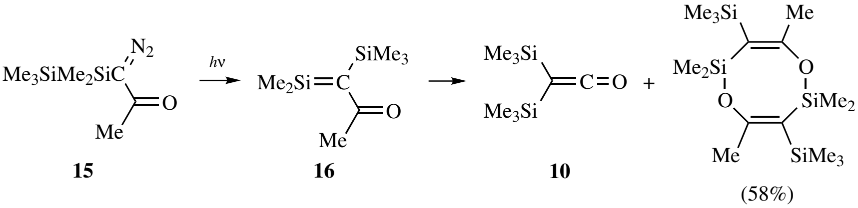
12 **10** (35%) (7)



1 **13** **10** (80%) (8)

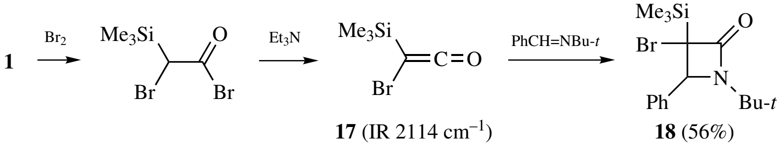


14 **10** (60%) (9)

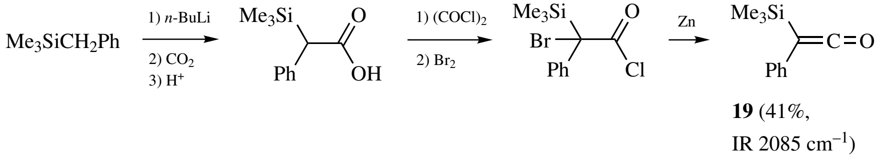


(10)

Bromotrimethylsilylketene **17** was formed by bromination/dehydrobromination of **1** and identified in solution by IR and trapped by [2 + 2] imine cycloaddition, forming the β-lactam **18** (equation 11),[20] Phenyltrimethylsilylketene **19** was prepared by dehalogenation of the β-bromoacyl chloride (equation 12),[21] while *n*-butyltrimethylsilylketene **20** was obtained from silylation of the alkynyl ether (equation 13),[22] and $Me_3SiC(Pr\text{-}i){=}C{=}O$[23] and $Me_3SiC(Hx\text{-}n){=}C{=}O$[24] were obtained similarly. Dehydrochlorination provided trimethylsilylvinylketene **21** in 39–50% yield starting from the acid (equation 14).[25] Ethyltrimethylsilylketene (**22**) was also obtained by dehydrochlorination (equation 15).[26]



(11)



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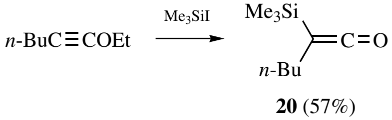

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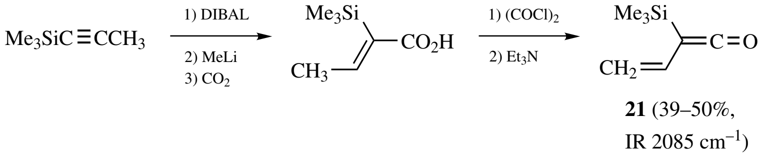

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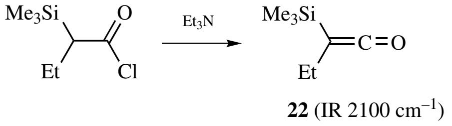
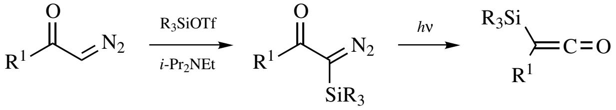


(15)

TABLE 4.3 Silylketenes from Photochemical Wolff Rearrangement (equation 16)

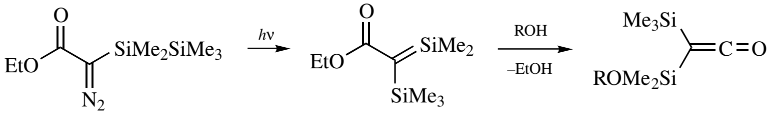
Ketene	R^1	R_3Si	Ketene	R^1	R_3Si
25a	Ph	Et_3Si (87%)	**25g**	*t*-Bu	*t*-$BuPh_2Si$ (26%)
25b	2-Thienyl	*i*-Pr_3Si (94%)	**25h**	*t*-Bu	*i*-Pr_3Si (38%)
25c	Me	Et_3Si (54%)	**25i**	Ph_2CH	*i*-Pr_3Si (71%)
25d	Me	*i*-Pr_3Si (49%)	**25j**	1-Ad	*t*-$BuMe_2Si$ (72%)
25e	*t*-Bu	*t*-$BuMe_2Si$ (50%)	**25k**	1-Ad	*t*-$BuPh_2Si$ (71%)
25f	*t*-Bu	*t*-$BuMe_2Si$ (39%)	**25l**	1-Ad	*i*-Pr_3Si (62%)

Silyl-substituted ketenes **25** were prepared from photochemical Wolff rearrangements of **24** obtained by silylation of diazo ketones **23** (equation 16).[27,28] Examples are shown in Table 4.3. The rather high energy of the UV absorption of the product silylketenes allows them to undergo minimal photodecarbonylation by the light used, contributing to the success of this procedure.



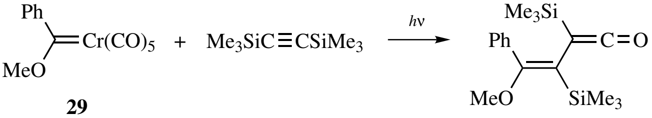
23 **24** **25** (16)

Photolysis of ethyl (pentamethyldisilanyl)diazoacetate (**26**) in alcohol solvents gave the bis(silyl)-substituted ketene **28** by a process that could have involved successive migration of Me_3Si, addition of ROH to the silene **27**, and loss of EtOH (equation 17).[29,30]



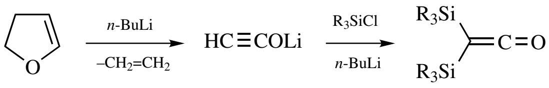
26 **27** **28** (R = Me. Et, *t*-Bu;
99%, R = Et, IR 2080 cm^{-1}) (17)

Silyl(alkenyl)ketene **30** was prepared in 20% yield from the chromium carbene complex **29** (equation 18), and in addition the $Cr(CO)_3$ complex of **30** was obtained from the same reaction in 52% yield.[31,32] Other preparations of silyketenes from metal carbene complexes are given in Section 3.5.



29 **30** (70%)
IR 2089 cm^{-1} (18)

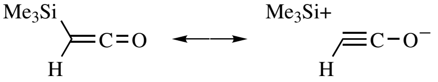
Dihydrofuran (**31**) reacted with *n*-BuLi, forming ynolate **32**, which was silylated by R_3SiCl and converted to a silyl ynolate that gave bis(silyl)ketenes **10** and **33a**,**b** (equation 19).[33]



(19)

31 **32** R = Me_3Si **10** (21%), Me_2HSi **33a** (28%), *t*-$BuMe_2Si$ **33b** (40%)

The extraordinary resistance to dimerization of trimethylsilylketene (**1**) was attributed by Brady and Cheng[34] to ground state stabilization arising from hyperconjugative electron donation from the C-Si bond to the carbonyl group, as represented by resonance structure **1a**. Such donation is made possible by the coplanarity of the C-Si bond and the carbonyl pi system.

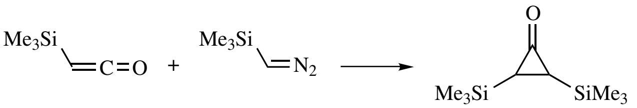


1 **1a**

An alternative explanation is that the stabilization of silylketenes was due to back electron donation from the pi system of the carbonyl group to *d* orbitals on silicon,[35] However, while electron-donation from C-Si bonds to electron-deficient centers is well documented, there is little support for such *d*-π bonding between carbon and silicon.[36–39] The explanation of Brady and Cheng,[34] namely, that the stabilization of ketenes by silyl substituents is due to the β-silicon effect,[36,38] is consistent with many aspects of silicon chemistry.

As noted in Section 5.5.1.1, trimethylsilyketene (**1**) is less reactive than ketene toward water by a factor of 160,[40] and this may also be attributed to the ground state stabilization of **1**.

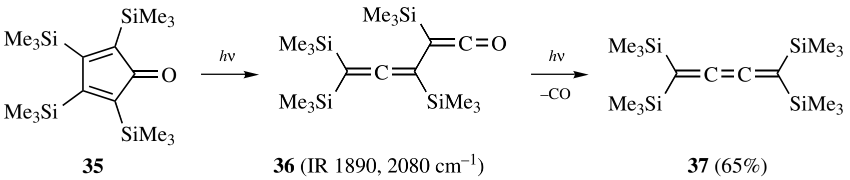
Silylketenes react with diazomethanes to form cyclopropanones and cyclobutanones, as in the formation of **34** by reaction of trimethylsilylketene **1** with trimethylsilyldiazomethane (equation 20).[21,41]



(20)

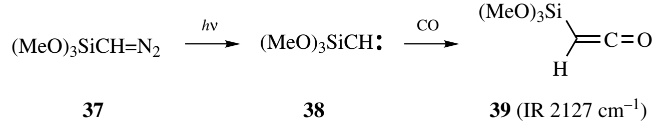
1 **34** (64%)

Photolysis in a matrix at 77 K of the cyclopentadienone **35** gave the allenylketene **36**, which was characterized by IR bands at 1890 and 2080 cm^{-1} and which formed the tetra(trimethyl)silylbutatriene **37** on further photolysis (equation 21).[42]



(21)

Photolysis of (trimethoxysilyl)diazomethane in an Ar matrix gave the carbene **38**, which was characterized by IR and UV spectroscopy, and when CO was included in the matrix, it reacted to give the ketene **39**, identified by its IR band at 2127 cm^{-1} (equation 22).[43] Photolysis of the diazo ester **40** with 300 nm light in toluene gave the housane derivative **41**, isolated in 68% yield, which upon thermolysis gave the ketene **43** in 20% yield, with a characteristic IR absorption at 2089 cm^{-1} (equation 23).[44] This transformation was proposed to occur by a [2 + 2] cycloreversion giving the silaethene **42**, which rearranged to **43** by a 1,3 OMe shift.[44]



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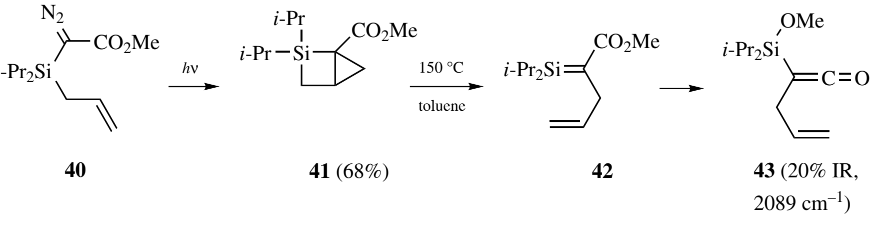
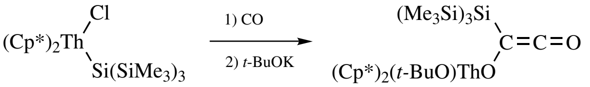


(23)

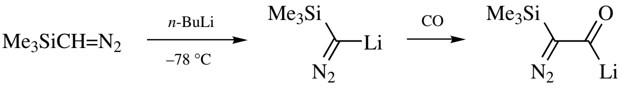
Carbonylation of the thorium complex **44** gave the silylated metalloxy ketene complex **45** with an X-ray crystal structure similar in its main dimensions to those of other ketenes (equation 24).[45] A complex of $Me_3SiCH{=}C{=}O$ (**1**) with a tantalum η^2-(C,O) complex was also obtained.[46] Carbonylation of the lithiated silyldiazomethane **46** was proposed to occur through a sequence involving diazo ketone **47**, azo ketene **48**, and ynolate **13** leading to the isolated ketene **50** (equations 25, 26).[47] Bis(trimethylsilyl)ketene **10** reacted with *t*-BuOK, forming potassium ynolate **51**, which combined with Ph_3SiCl, forming the mixed bis(trialkylsilyl) ketene **52** (equation 27).[48] Trimethylsilyldiazomethane was carbonylated with octacarbonyl dicobalt catalysis to trimethylsilylketene (**1**).[48a]



44 **45** (41%) (IR 2044 cm^{-1})

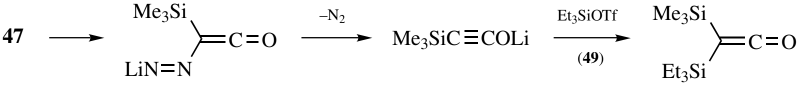
[C=O, 1.14(3); C=C, 1.34(3); C–OTh, 1.41(2)]

(24)



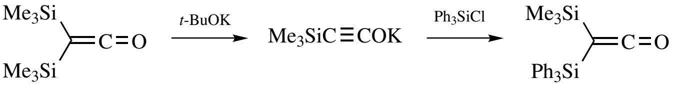
46 **47**

(25)



48 **13** **50** (85%, IR 2070 cm^{-1})

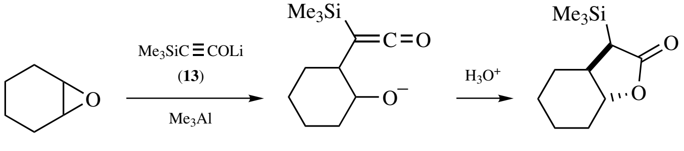
(26)



10 **51** **52** (76%)

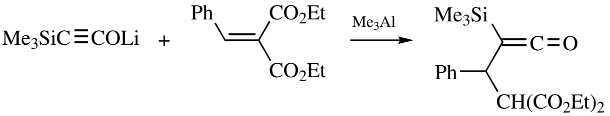
(27)

Lithium trimethylsilyl ynolate **13** added to epoxides in a reaction promoted with Me_3Al, forming ketenes **54** that cyclize to the observed lactones **55** (equation 28).[47] Diethyl benzalmalonate reacted with **13**, giving ketene **57** in 62% isolated yield (equation 29).[47]



53 **54** **55** (93%)

(28)

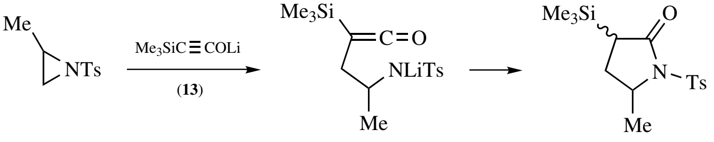


13 **57** (62%, IR 2082 cm^{-1})

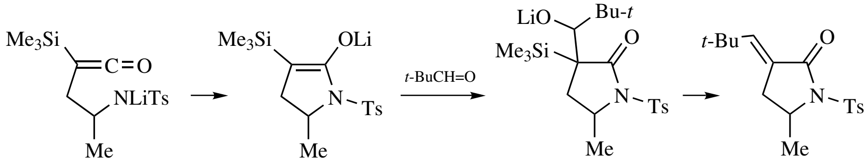
(29)

Propylene imine **58** reacted with **13** to give lactam **60** through a ketene intermediate **59** (equation 30).[49] This reaction was proposed to proceed through enolate intermediate **61** which was also trapped with pivaldehyde forming **62** which gave

63 by Peterson olefination (equation 31).[49] Aldimine **64** and **13** gave ketene intermediate **65**, which formed **66** (equation 32).[47]

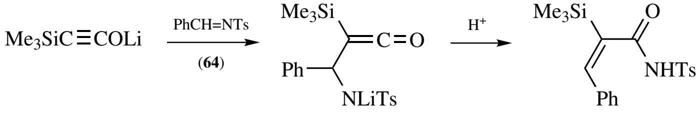


58 **59** **60** (65%) (30)



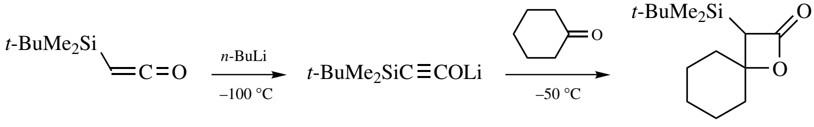
59 **61** **62** **63** (80%)

(31)

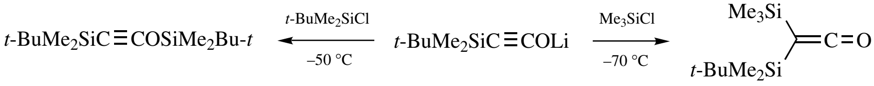


13 **65** **66** (68%) (32)

Following the procedure of equation 8,[17] the reaction of t-BuMe$_2$SiCH=C=O (**67**) with n-BuLi at −100 °C gave ynolate **68**, which reacted with cyclohexanone to give β-lactone **69** (equation 33).[50] Ynolate **68** reacted with Me$_3$SiCl at −70 °C to form ketene **70**, but reaction with t-BuMe$_2$SiCl and workup at −50 °C gave the ynol ether **71** (equation 34).[50] Reaction with Ph$_3$PbCl gave t-BuMe$_2$Si(Ph$_3$Pb)C=C=O in 85% yield.[50]



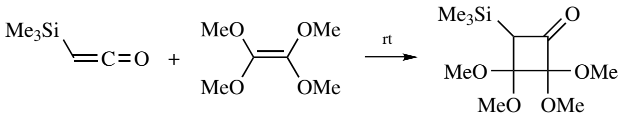
67 **68** **69** (52%) (33)



71 (65%) **68** **70** (96%)

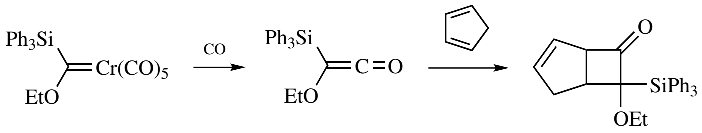
(34)

The [2 + 2] cycloaddition reaction of trimethylsilyketene with alkenes was usually unsuccessful,[3] but did take place with aldehydes to give oxetanones[3,51] and with tetralkoxyethylene to give cyclobutanone **72** (equation 35).[52] The ketene **73** prepared in situ from a carbene complex was more reactive, and gave [2 + 2] cycloaddition with reactive alkenes (equation 36).[53]



1 **72** (70%)

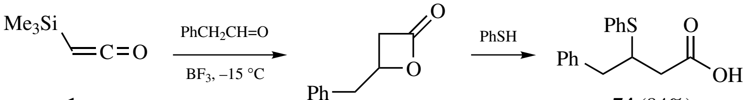
(35)



73 (58%)

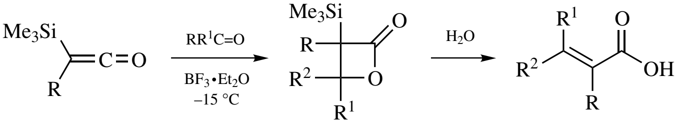
(36)

Trimethylsilylketene **1** gave [2 + 2] cycloaddition with aliphatic aldehydes, forming desilylated oxetanones (β-lactones) that reacted with thiols, forming acids **74** (equation 37).[54] Hydrolysis of oxetanones formed from silylketenes **75** gave substituted acrylic acids **76** (equation 38; see also Section 5.4.5).[55,56] Catalysis by $EtAlCl_2$ of oxetanone formation from $Me_3SiC(Hx\text{-}n){=}C{=}O$ and a chiral aldehyde in the synthesis of lipstatin has also been reported.[57] Reaction of $Me_3SiCH{=}C{=}O$ with aldehydes catalyzed by methylaluminoimidazolines gave preferential formation of *cis*-oxetanones in 32–85% yields and 30–83% *ee*.[58,59] Trimethylsilylketene gave [2 + 2] cycloaddition with cyclohexanecarboxaldehyde using the dichlorotitanium-TADDOL catalyst **77**, forming β-lactone **78** in 66% yield, 80% *ee* (equation 39).[60]



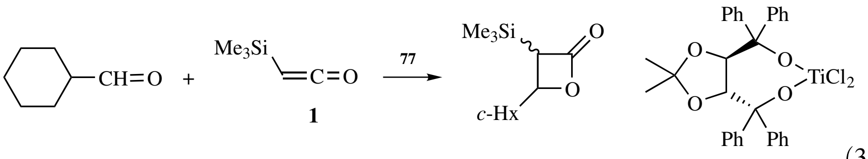
1 **74** (84%)

(37)



75 **76** (41–98%)

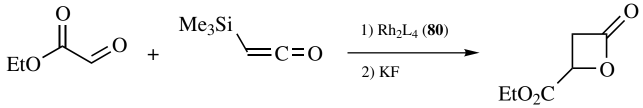
(38)



1 **78** (66%) **77**

(39)

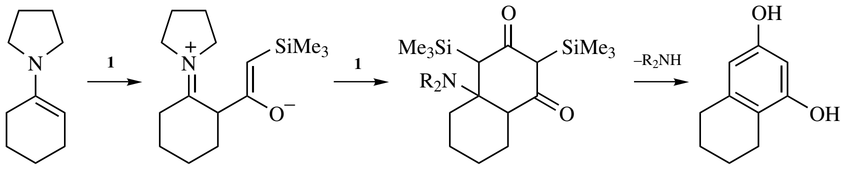
Trimethylsilylketene gave stereoselective [2 + 2] cycloaddition with ethyl glyoxylate (**79**) catalyzed by chiral dirhodium(II) carboxamidates (**80**), forming β-lactones **81** (equation 40).[61] A survey of chiral catalysts was carried out, and it was found that the addition of quinine as a cocatalyst gave up to 99% *ee* and shorter reaction times.[61]



79 **1** **81** (16–99%)

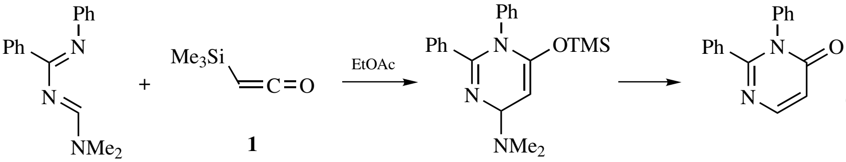
(40)

The combination of two equivalents of trimethylsilylketene with enamine **82** gave resorcinol derivatives **83** by the proposed mechanism shown, with silyl migration to oxygen (equation 41).[62] 1,3-Diaza-1,3-diene **84** reacted with **1** by [4 + 2] cycloaddition, forming 4(3*H*)-pyrimidone **85** (equation 42).[63] Reactions of trialkylsilylketenes **86** with Wittig reagents gave allenes **87** (equation 43).[64]



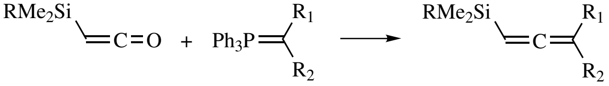
82 **83** (37%)

(41)



84 **1** **85** (94%)

(42)

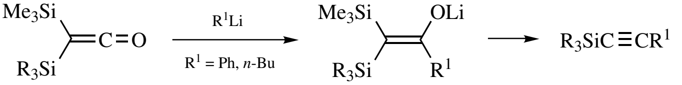


(98%, R = Me, R^1 = CN, R^2 = H)

86 **87**

(43)

Reaction of bis(silylated) ketenes **10**, **70**, and **88** with organolithium reagants formed *Z*- and *E*-α-silylenolates **89**, which equilibrated under the reaction conditions and in the presence of HMPA underwent a *syn*-Peterson elimination to give good yields of silylated alkynes **90** (equation 44).[65] Organocerium reagents reacted with silylketenes **91**, leading to silyl ketones **92** (equation 45).[66]

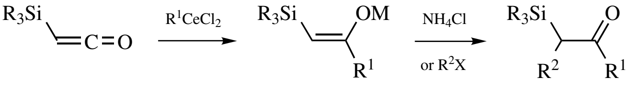


R_3Si = Me_3Si (**10**), *t*-$BuMe_2Si$ (**70**), Ph_2MeSi (**88**)

89

90 (78% from **70**, R^1 = *n*-Bu)

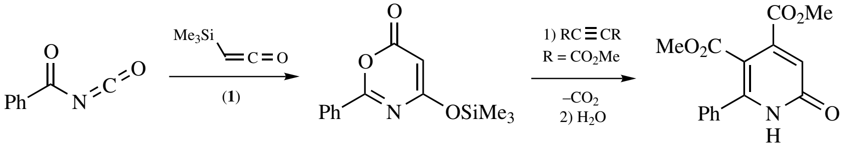
(44)



(45)

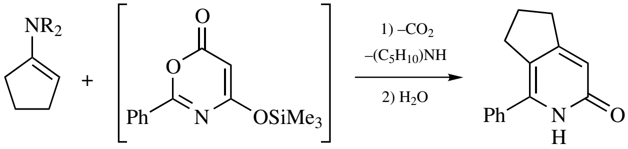
91 **92** (40–99%)

[4 + 2] Cycloaddition of trimethylsilylketene with benzoylisocyanate was proposed to form 4-trimethylsilyloxy-1,3-oxazin-6-one **93**, which reacted in situ with electron-deficient alkynes to give 2-pyridone **94** (equation 46)[67] and with enamine **95** to give bicyclic 2-pyridone **96** (equation 47).[68] Reaction of trimethylsilylketene (**1**) with α,*N*-diphenylnitrone gave oxindole **97** (equation 48), and reaction with *N*-benzylidenebenzylamine *N*-oxide gave **98** (equation 49).[69]



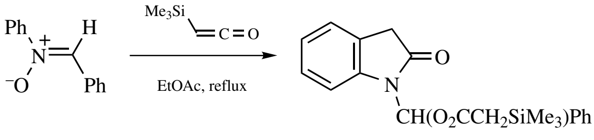
(46)

93 **94** (75%)



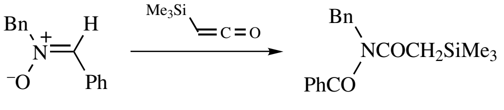
(47)

95 $R_2 = (CH_2)_5$ **93** **96** (77%)



(48)

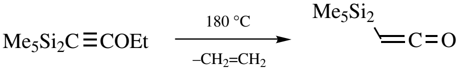
97 (77%)



(49)

98 (63%)

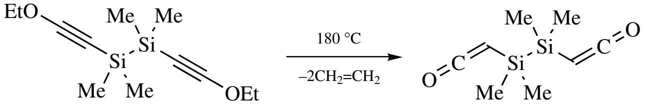
Pyrolysis of ethoxyalkynes gave the disilanylketene **99**, the disilanylbisketene **100**, and the 1,6-bisketene **101** as isolable, long-lived species that showed characteristic ketenyl NMR and IR spectra (equations 50–52).[70] The relative rates of hydration of **99**–**101** compared to $Me_3SiCH{=}C{=}O$ in 60% H_2O/CH_3CN at 25 °C were 1.9, 5.6, and 0.9, respectively.[70]



$$Me_5Si_2C{\equiv}COEt \xrightarrow[-CH_2=CH_2]{180\ °C} Me_5Si_2CH{=}C{=}O$$

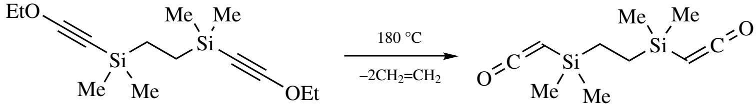
(50)

99 (IR 2108 cm^{-1})



100 (IR 2108, 2052 cm^{-1})

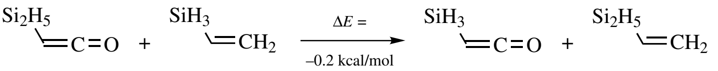
(51)



101 (IR 2115, 2052 cm^{-1})

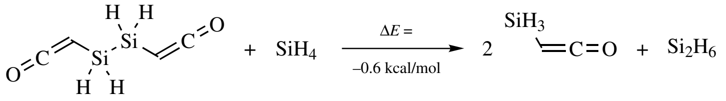
(52)

Isodesmic energy comparisons based on *ab initio* calculated energies at the RHF/6-31G*//RHF/6-31G* level indicated that the Si_2H_5 substituent has essentially the same ketene-stabilizing ability as SiH_3 (equation 53) and that each ketenyl group in $(SiH_2CH{=}C{=}O)_2$ had essentially the same stabilization as that in $SiH_3CH{=}C{=}O$ (equation 54).[70]



102 **3**

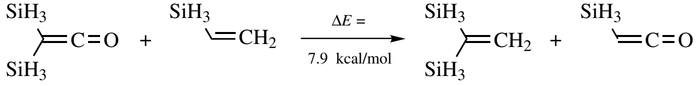
(53)



103 **3**

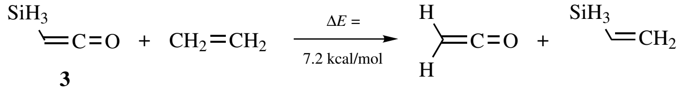
(54)

Isodesmic comparisons of $(SiH_3)_2C{=}C{=}O$ (**104**) and $SiH_3CH{=}C{=}O$ (**3**) (equations 55, 56) indicated that the stabilizing effects of the two silyl groups on this ketene are additive.[71] Both of the silyl groups also contributed to the upfield ^{17}O NMR chemical shifts seen in silylketenes, as $(Me_3Si)_2C{=}C{=}O$ (**10**), Me_3Si $CH{=}C{=}O$ (**1**), and $Me_2C{=}C{=}O$ have δ 211.2, 255, and 329, respectively.[70] There were also cumulative effects on the UV spectra of silylketenes, as $(Me_3Si)_2C{=}C{=}O$, $Me_3SiCH{=}C{=}O$, and *t*-$Bu_2C{=}C{=}O$ have their highest-wavelength UV λ_{max} at 278, 308, and 360 nm, respectively. This latter effect was attributed to an interaction of the ketenyl C-Si σ bond with the in-plane carbonyl π and π^* orbitals, lowering the energy of the former and raising the energy of the latter.[70] As there was little interaction with the *n* orbitals on oxygen, the net result was an increase in the $n \rightarrow \pi^*$ energy on silyl substitution.[70]



104 **3**

(55)

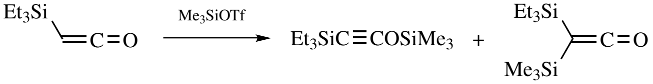


3

(56)

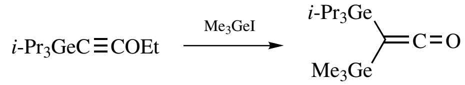
The hydration rate ratios k($CH_2{=}C{=}O$)/k($Me_3SiCH{=}C{=}O$) of 160 and k($CH_2{=}C{=}O$)/k[$(Me_3Si)_2C{=}C{=}O$] of 1030 indicated that both silyl groups decreased the reactivity of ketenes. This has been attributed to an electronic ground state stabilization of the ketenes,[40] while the smaller rate effect by a factor of 6 for the second Me_3Si group was a measure of the steric effect.[70]

Hydration of *t*-$BuMe_2SiCH{=}C{=}O$ (**70**) and $Et_3SiCH{=}C{=}O$ (**11**) has been used to prepare the corresponding acids.[72] The reaction of silylketene **11** with Me_3SiOTf produced a mixture of silyloxyalkyne **105** and mixed bis(silyl)ketene **50** (equation 57).[73] Bis(trialkylsilyl), silylgermyl, and bis(germyl)ketenes **107** were prepared by metalation of alkynyl ethers (equation 58).[74,75] A computational study of the thermal conversion of metallated alkyl alkynyl ethers $R_3MC{\equiv}COCHRCH_3$ to metallated ketenes $R_3MCH{=}C{=}O$ has been reported.[76]



11 **105** **50**

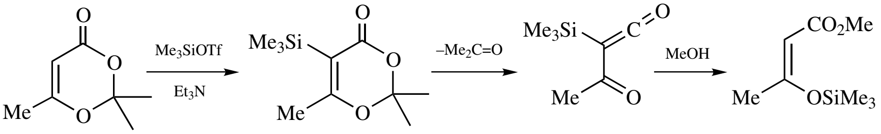
(57)



106 **107**

(58)

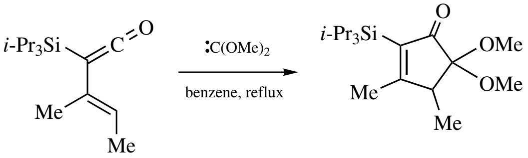
Silylation of Meldrum's acid produced the dioxinone **108**, which was unstable in solution at 0 °C and reacted with alcohols, amines, and thiols to produce acetoacetate derivatives, indicating the intermediacy of ketene **109** (equation 59).[13]



108 **109** (67%)

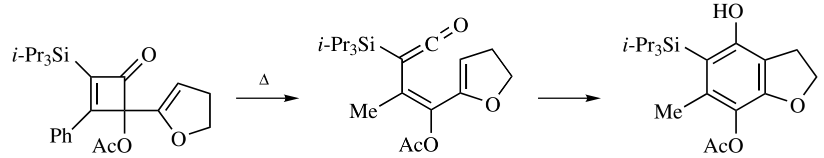
(59)

α-Silylated alkenylketenes **110** and some analogues gave [4 + 1] cycloadditions with various nucleophilic carbenes generated from oxadiazolines, forming cyclopentenones **111** (equation 60).[77] Other syntheses and reactions of some α-silylated alkenylketenes are discussed in Section 4.1.2. Trimethylsilyl-substituted dienylketene **113** was generated by thermolysis of cyclobutenone **112** (equation 61), as discussed in Section 3.4.1.[78]



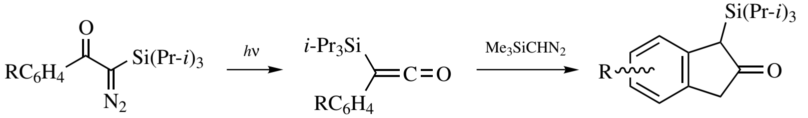
110 **111** (80%)

(60)



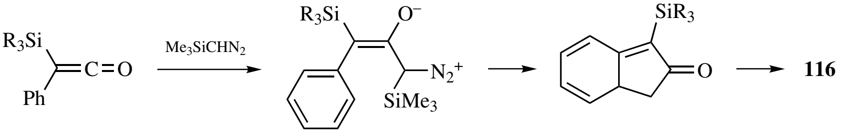
112 **113** **114** (67%) (61)

Trialkylsilyl(aryl)ketenes (**115**) from Wolff rearrangements reacted with trimethylsilyldiazomethane in a [4 + 1] annulation process, forming 2-indanones (**116**) (equation 62).[79] The reactions were proposed to involve initial attack of Me_3SiCHN_2 from the side of the ketene opposite the bulky silyl substituent forming an intermediate **117**, which could form **116** directly (equation 63) or react through a cyclopropanone or oxyallylic intermediate.[79]



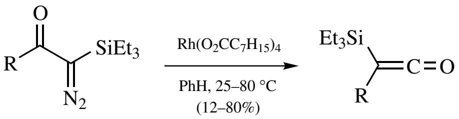
R = H, 2–Cl, 4–Br, 3–Me, 3–i–Pr, 4–MeO_2C

115 **116** (86%, R = H) (62)



115 **117** (63)

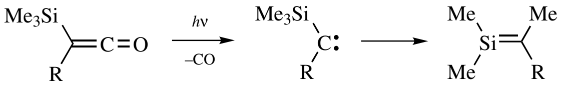
Reaction of silylated diazo ketones **118** with rhodium (II) octanoate gave silylketenes **119** that were purified by chromatography and characterized (equation 64).[80]



118 **119** (12–80%) (64)

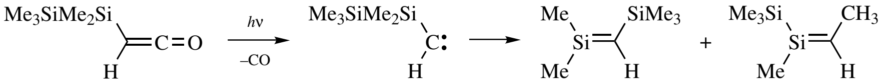
R = n–C_7H_{15} (a), $PhCHCH_3$ (b),
PhCH=CH (c),Ph (d), 4–Anis (e),
4–ClC_6H_4 (f), furanyl (g),
3–(N-Boc)quinolyl (h), 1–(O–Bn)ribosyl (i)

Photolysis of silyl-subtituted ketenes **1** and **10** proceeded by decarbonylation to carbenes **120**, which rearranged, providing a useful synthesis of transient silenes **121** that were captured by nucleophilies (equation 65).[81,82] The disilane-substututed ketene **99** gave the silenes **123** and **124** resulting from Me_3Si and Me migration in a 9:1 ratio (equation 66), and the reactivities of the silenes with nucleophiles were measured and compared.[81,82]



1 (R = H) **120** **121**
10 (R = Me_3Si)

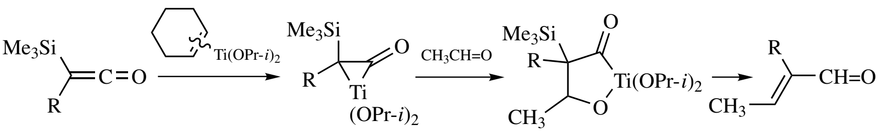
(65)



99 **122** **123** (90%) **124** (10%)

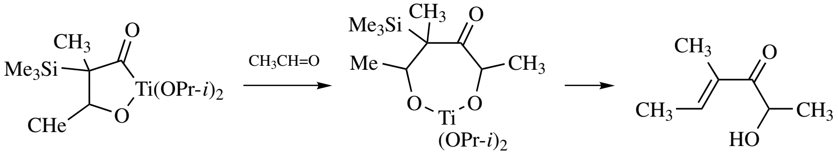
(66)

Reaction of *n*-decyltrimethylsilylketene (**125**) with the cyclohexene complex of Ti(O-PrO-*i*)$_2$ to form titanium complex **126** was proposed to insert added acetaldehyde forming **127**, which gave **128** (equation 67).[83] Complex **127** also added another molecule of acetaldehyde forming intermediate **129**, which underwent elimination, forming **130** (equation 68).[83]



125 (R = *n*-$C_{10}H_{21}$) **126** **127** **128** (6%)

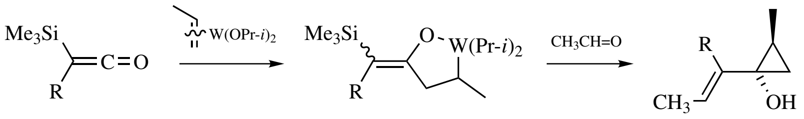
(67)



127 **129** **130** (33%)

(68)

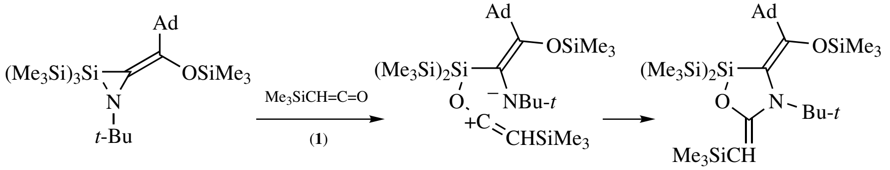
Reaction of **125** with the corresponding propene/tunsten complex was proposed to form the intermediate **129**, which reacted with acetaldehyde to form **130** (equation 69).[83]



125 (R = *n*-$C_{10}H_{21}$) **129** **130** (34%)

(69)

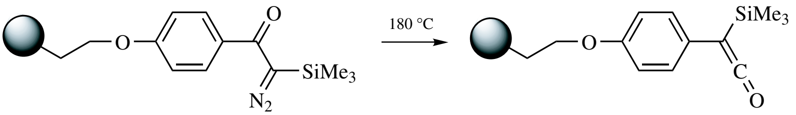
Trimethylsilylketene inserted into the silaaziridine **131** in a reaction proposed to involve attack of the ketenyl oxygen on silicon to form the zwitterionic intermediate **132**, which forms the product **133** (equation 70).[84] Examination of the product mixture by ^1H NMR showed complete conversion to **133** after 24 hours, but there was considerable decomposition upon chromatography.



131 **132** **133**

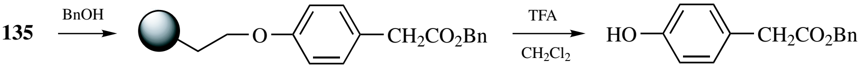
(70)

Thermal Wolff rearrangement of Wang resin-bound, silylated diazo ketone **134** was carried out in the absence of solvent by heating to 180 °C for 20 min to generate the polymer-bound ketene **135** (equation 71).[85] In the presence of benzyl alcohol the polymer-bound ester **136** was formed, and cleavage gave **137** in 63% yield (equation 72).[85] A resin with an aliphatic chain and ketene reactions with amines were also studied.[85]



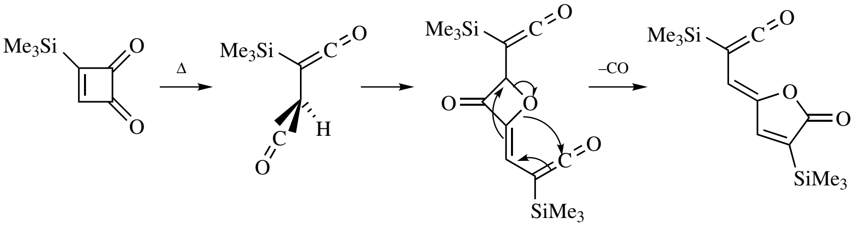
134 **135**

(71)



136 **137** (63%) (72)

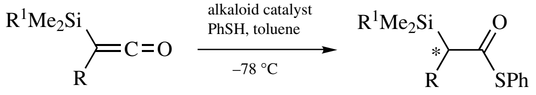
Thermal ring opening of trimethylsilylcyclobutenedione **138** formed bisketene **139**, which gave ketenyl lactone **141**, which could form through the intermediate [2 + 2] cycloaddition dimer **140** (equation 73).[86]



138 **139** **140** **141** (IR 2089 cm^{-1})

(73)

α-Substituted trimethylsilyl and phenyldimethylsilylketenes **142** were prepared by either dehalogenation or dehydrochlorination routes, and underwent stereoselective esterification with thiophenol catalyzed by cinchona alkaloids, forming α-silylthioesters **143** in 41–93% yields and enantiomeric excess of 79–93% (equation 74).[87]

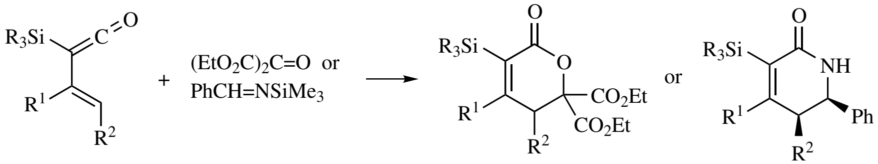


(74)

142 R′ = Me, Ph; R = Ph, 2-Naph
n-Pr, Bn, $(CH_2)_2CH{=}CH_2$

143

Silylated vinylketenes **144** generated by either Wolff rearrangement or cyclobutenone ring opening reacted by [4 + 2] cycloaddition with carbonyl compounds and with imines, forming α,β-unsaturated δ-valerolactones **145** and lactams **146**, respectively (equation 75).[88]



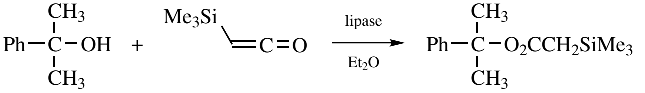
144

145 (77–94%)

146 (76–91%)

(75)

Lipase enzyme catalyzed acylation of alcohols in ether by trimethylsilylketene (**1**), triethylsilylketene (**11**), and dimethylphenylsilylketene gave esters in yields of 70–99% (equation 76).[89]



$$Ph-\underset{CH_3}{\overset{CH_3}{C}}-OH + Me_3Si{-}CH{=}C{=}O \xrightarrow[Et_2O]{\text{lipase}} Ph-\underset{CH_3}{\overset{CH_3}{C}}-O_2CCH_2SiMe_3 \qquad (76)$$

1

147 (97%)

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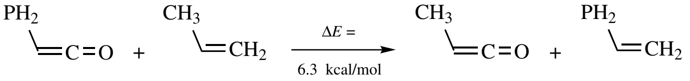
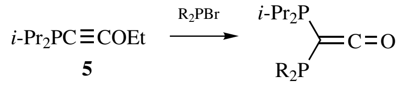
4.6 PHOSPHORUS-SUBSTITUTED KETENES

Phosphinyl-substituted ketenes are predicted to have substantial stabilization,[1,2] as shown by isodesmic comparison based on MP2/6-31G*//MP2/6-31G* calculated energies (equation 1).[2] However, ketenes substituted with P(III) are rare. Among the first examples were **6** and **7**, prepared from reaction of alkynyl ethers with phosphinyl halides (equation 2).[3] Ketene **6** was not stable even in solution, and on standing was converted to a complex mixture. However, the IR spectrum and the ^{31}P NMR spectrum supported the assigned structure. Ketene **7** was quite stable and was characterized by IR, ^{31}P NMR, and elemental analysis. Ketenes **9** and **10** were prepared similarly and are much more stable than **6** (equation 3).[3]



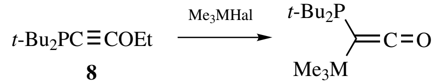
1 **2** **3** **4** (1)



5

6 (90%, R = i-Pr, IR 2100 cm^{-1})
7 (100%, R = C_6F_5, IR 2100 cm^{-1})

(2)

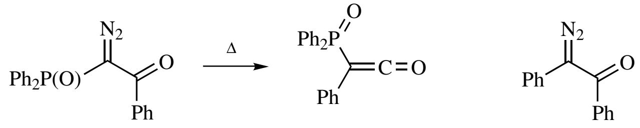


8

9 (M = Si, Hal = I, IR 2100 cm^{-1})
10 (M = Ge, Hal = Br, IR 2100 cm^{-1})

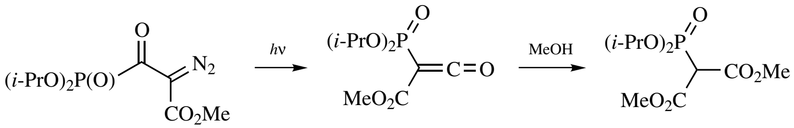
(3)

Ketenes substituted with P(V) include those with the $Ph_2P(O)$ and $(MeO)_2P(O)$ substituents formed by Wolff rearrangements (equations 4, 5).[4–6] The kinetics of thermal decomposition of the diazo ketone **11** forming ketene **12** were measured, and **11** was found to be less reactive than **13** by a factor of 22 (equation 4).[4,5] Ketene **12** was identified by the strong IR absorption at 2120 cm^{-1} upon photolysis in a novolac resin.[6] Photolysis of the diazo ketone **14** in hexane led to formation of the ketene **15**, as detected by its IR absorption at 2160 cm^{-1}, while photolysis in MeOH resulted in capture of the ketene, forming the symmetrical dimethyl malonate **16** in quantitative yield (equation 5).[7]



11 (k(rel) = 1.0
12 (IR 2120 cm^{-1})
13 k(rel) = 22

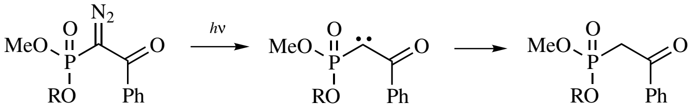
(4)



14
15 (IR 2160 cm^{-1})
16

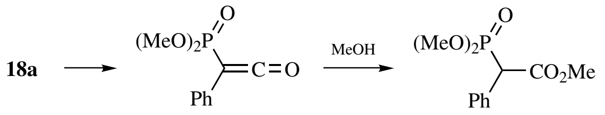
(5)

The phosphonate-substituted diazo ketone **17**, upon photolysis in MeOH, resulted in the formation of the products **19** and **21** derived from hydrogen abstraction by an intermediate carbene **18** (equation 6) and Wolff rearrangement to the ketene **20**, respectively (equation 7).[8] When R was methyl the ratio of the products **19a** and **21a** was near 1:1, but when R was Na the Na salt **17** gave almost exclusively Wolff rearrangement to the ketene **20b**.[8] The ketene **20a** was also generated in a matrix at 10 K by photolysis of **17a** (R=Me) and observed by IR near 2120 cm^{-1}, and was also formed by carbonylation in a matrix of the carbene **23** generated by photolysis of the diazo ketone **22** (equation 8).[9]



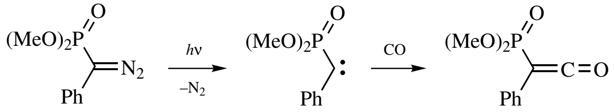
17 (**a**, R = Me; **b**, R = Na)
18
19 (33%, R = Me)

(6)



20a **21a** (41%)

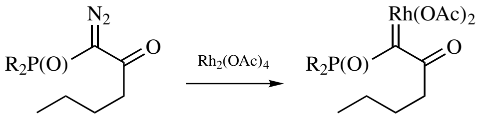
(7)



22 **23** **20a** (IR 2120 cm^{-1})

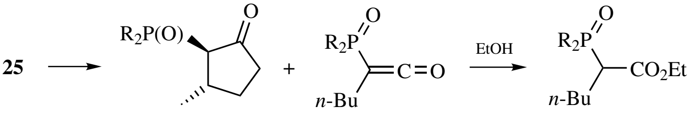
(8)

Reactions of the phosphonate **24a** and the phosphine oxide **24b** in refluxing CH_2Cl_2 containing rhodium(II) acetate gave mixtures of cyclized carbene insertion products **26** and ketenes **27**, as shown by reaction with ethanol forming **28** (equations 9, 10).[10] The formation of ketenes in $Rh_2(OAc)_4$-catalyzed reactions was unusual, and was interpreted in terms of the low electron-withdrawing character of the phosphorus substituents diminishing the electrophilic character and the tendency for insertion of intermediate rhodium carbene species **25**.[10]



24 (**a**, R = EtO; **b**, R = Ph) **25**

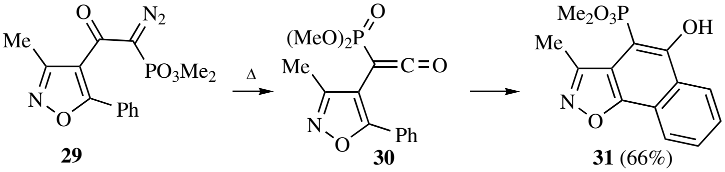
(9)



26 (**a**, 67%; **b**, 50%) **27** **28** (**a**, 30%; **b**, 45%)

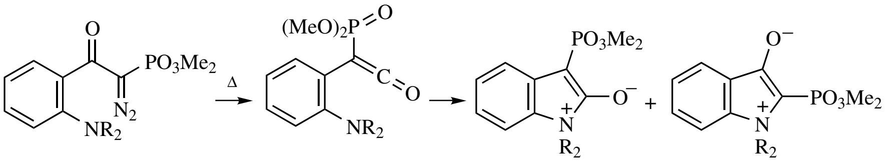
(10)

Thermal Wolff rearrangement of the diazo ketone **29** formed the phosphonato-substituted ketenes **30**, which could be trapped by MeOH or allowed to undergo intramolecular benzannulation reactions providing a variety of heterocycles (equation 11).[11] Diazo ketone **32** with a pendant *tert*-amino substituent upon thermolysis formed ketene **33**, which gave rise to a mixture of 2-oxindolinium enolate **34** as well as the product **35** from capture of the carbene in a 51:49 ratio (equation 12).[12] The structure of **34** was determined by X-ray.[12] These reactions are also discussed in Section 3.3.1.



29 **30** **31** (66%)

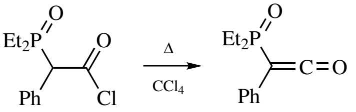
(11)



32 R = (CH$_2$)$_5$ **33** **34** (44%) **35** (43%)

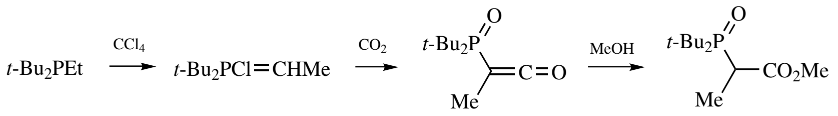
(12)

Thermal dehydrochlorination of the phosphoryl-substituted acyl chloride **36** by refluxing in CCl$_4$ provided a route to the diethylphosphonoketene **37** in 70% yield (equation 13).[13–15] Phosphine **38** reacted with carbon tetrachloride to form the chloro-substituted phosphorus ylides **39**, which reacted with CO$_2$ to form the phosphoryl-substituted ketene **40**, characterized by IR and NMR and trapped with MeOH, forming the ester **41** (equation 14).[14,15] The fluoro phosphorus ylide **42** reacted with CO$_2$ to form a fluorooxaphosphorane that on heating formed the ketene **43** (equation 15).[16,17]



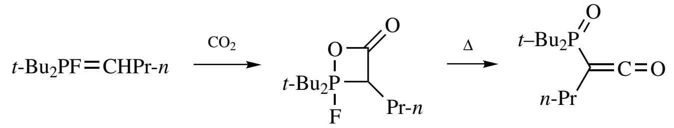
36 **37** (70%)

(13)



38 **39** **40** (IR 2100 cm^{-1}) **41**

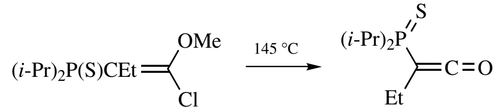
(14)



42 **43** (30%)

(15)

Heating of the vinyl ether **44** resulted in elimination of MeCl and formation of the ketene **45** in 92% yield, identified by the IR and NMR spectra (equation 16).[18] Trimethylsilyl iodide reacted with the alkynyl ether **46** to give the thiophosphorylketene **47** (equation 17).[19]

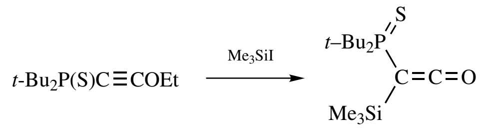


44 **45** (IR 2100 cm^{-1})

(16)

TABLE 4.4 Relative Rate Constants for Addition of 4-XC_6H_4OH to 48[20]

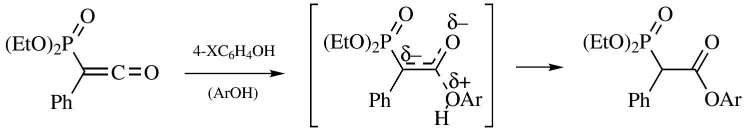
X	MeO	F	Cl	CH_3	H	CF_3S
k(rel)	23.6	10.1	4.4	8.0	4.2	1.0



(17)

46 **47** (~90%, IR 2100 cm^{-1})

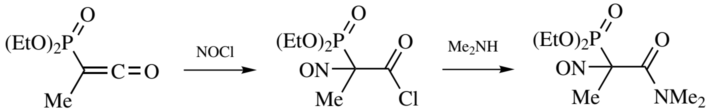
Phosphoryl-substituted ketenes underwent typical additions of nucleophiles such as water, alcohols, and amines. Kinetics of the reaction of ketene **48** with substituted phenols in CCl_4 have been reported, and showed greater reactivity with substituted phenols for π-donors and electronegative substituents (Table 4.4). Ketene **48** was also 2000 times more reactive toward phenol than was $Ph_2C{=}C{=}O$,[20] suggesting a high degree of carbanion character that would be stabilized by the $(EtO)_2P(O)$ substituent, so a mechanism involving a polar transition state **49** appeared to be involved (equation 18). This is consistent with the results of other studies of nucleophilic attack on ketenes (Section 5.5.1.2). The question of the preferred direction of in-plane attack on the ketene was unanswered.



(18)

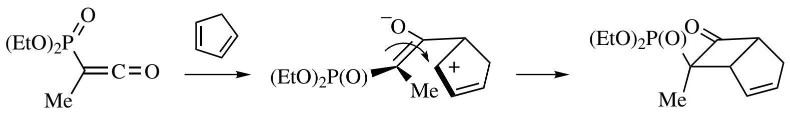
48 **49** **50** (70%, Ar = 4-$MeOC_6H_4$)

Addition of the electrophilic NOCl to **51** formed by dehydrochlorination gave **52**, which was converted to the amide (equation 19).[21] Ketene **51** also reacted by [2 + 2] cycloaddition with imines, forming β-lactams, and with cyclopentadiene formed **54**, which was assigned the configuration with the bulky phosphonate substituent in the *exo* position (equation 20).[22] This stereochemistry was contrary to the usual result of ketene cycloadditions, in which the larger substituent occupied the more crowded *endo* position as a result of the perpendicular approach of the ketene to the reacting double bond, and formation of the bond to C_2 of the ketene before this can rotate to a less crowded conformation (Section 5.4.1.2). The formation of **54** may indicate that a long-lived zwitterionic intermediate **53** was formed that had the opportunity to form the thermodynamically most stable product (equation 20).



(19)

51 **52** (41%)



51 **53** **54** (50%) (20)

Ketenylidene phosphoranes (phosphaketene ylides) **56** are a unique family of phosphorus-substituted ketenes, which can be formed by elimination from the carbomethoxy phosphorane **55** (equation 21).[23,24] The ketene **56** was a crystalline solid with a P-C_2-C_1 angle of 145.5 °, as determined from the X-ray structure.[23] Alkoxyethynylphosphines **58** formed by reaction of phosphorus halides R_2PHal with lithium acetylides **57** rearranged thermally to ketenylidenephosphoranes **59** upon heating (equation 22).[25,26]

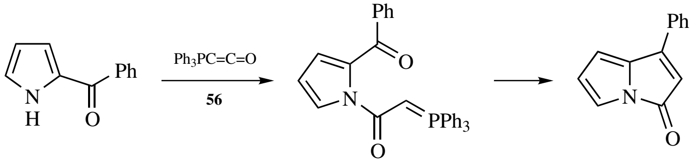
$$\mathrm{Ph_3P{=}CHCO_2Me} \xrightarrow{\mathrm{NaN[Si(Pr\text{-}\mathit{i})_3]_2}} \mathrm{Ph_3P{=}C{=}C{=}O} \longleftrightarrow \mathrm{Ph_3\overset{+}{P}{-}\overset{-}{C}{=}C{=}O} \qquad (21)$$

55 **56** (80%, IR 2080 cm^{-1})

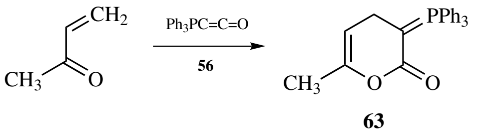
$$\mathrm{LiC{\equiv}COMe} \xrightarrow{\mathrm{R_2PhHal}} \mathrm{R_2PC{\equiv}COMe} \xrightarrow{\Delta} \mathrm{MeR_2PC{=}C{=}O} \qquad (22)$$

57 **58** **59** (90%, R = *t*-Bu)

Synthetic applications of phosphaketene ylides included additions to carbonyl groups,[27] Wittig reactions,[28–30] an addition-Wittig cyclization sequence of **56** converting benzoylpyrrole to **62** (equation 23),[29] and [4 + 2] cycloadditions with α,β-unsaturated carbonyl compounds (equation 24).[31]

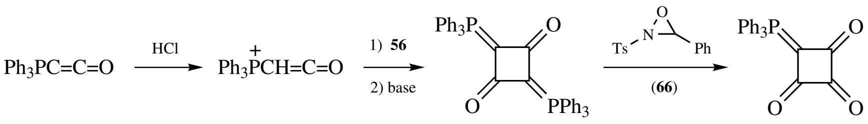


60 **61** **62** (43%) (23)



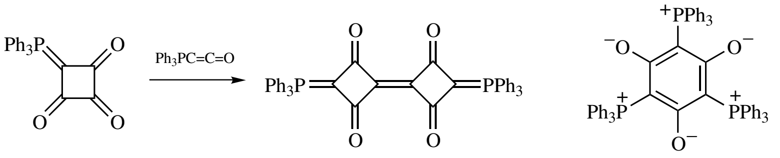
63 (24)

Protonation of the ketenylidenephosphorane **56** with HCl gave the cationic species **64**, which immediately underwent cycloaddition with another molecule of **56** to form the cyclobutanedione **65** (equation 25).[32] Oxidation of **65** with **66** gave the trione **67** (equation 25).[32] Reaction of **67** with **56** yielded **68** (equation 26).[32] The structures of **67** and **68** were determined by X-ray. The trimer **69** of **56** has also been prepared by reaction of **56** with HCl and has been described as a hybrid between a ketone and an ylide.[33]



56 **64** **65** **67** (75%)

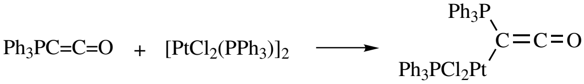
(25)



67 **68** (95–98%) **69** (30%)

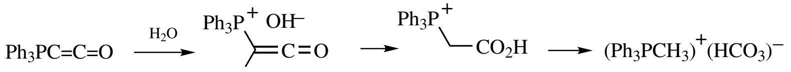
(26)

Reaction of **56** with Pt(II) complexes gave products such as **70** (equation 27), and a large number of related ketene and bisketene analogues were obtained (see also Section 4.9),[34–36] and their ^{13}C and ^{31}P NMR spectra were recorded.[37] Theoretical studies showed that the cycloaddition reactions of $H_2P{=}C{=}C{=}O$ occurred at the C—P bond.[38] The reaction of **56** with H_2O yielded **72**, and this was proposed to take place by initial proton transfer forming **71**, followed by hydration and decarboxylation (equation 28).[39]



56 **70** (IR 2072 cm^{-1})

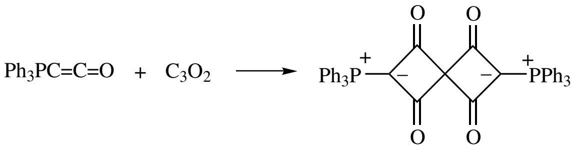
(27)



56 **71** **72** (73%)

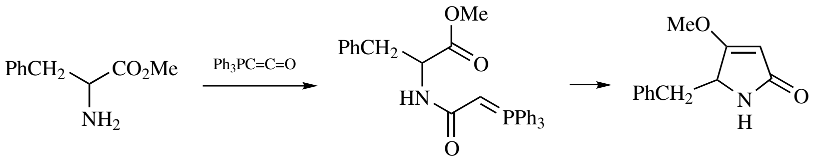
(28)

Cycloaddition of **56** with carbon suboxide led to the spiro tetraketoheptane derivative **73** (equation 29).[40] Reaction of **56** with esters bearing OH, NHR, or SH groups in the α-, β-, or γ-position gave five-, six-, or seven-membered heterocycles (equation 30).[41,42] Cyclization of **56** with **76** gave the spiro tetronate **77** (equation 31).[43]



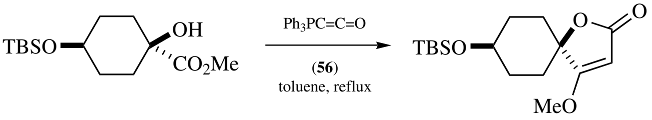
56 **73** (86%)

(29)



74 **75** (60%)

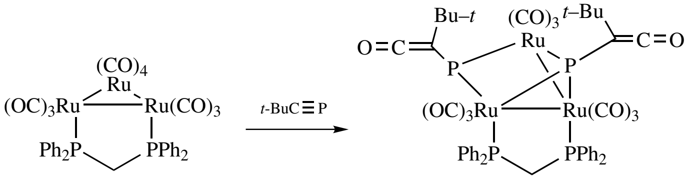
(30)



76 **77** (72%)

(31)

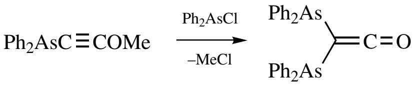
A unique phosphorus-substituted bisketene **78** has been prepared and its structure established by X-ray (equation 32).[44]



(32)

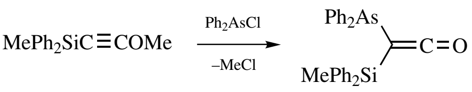
78 (27%, IR 2092 cm^{-1})

Arsenic-substituted ketenes have also been prepared.[45–47] The acetylenic ether **79** reacted with Ph_2AsCl to give the bis(arsenic)-substituted ketene **80**, which was purified by distillation (equation 33).[45] The silyl alkynyl ether **81** reacted similarly, forming the silylated and arsenic-substituted ketene **82** (equation 34), and Ph_3GeCl reacted with the ethyl ether analogue of **79** to form $Ph_2AsC(GePh_3){=}C{=}O$.[45]



(33)

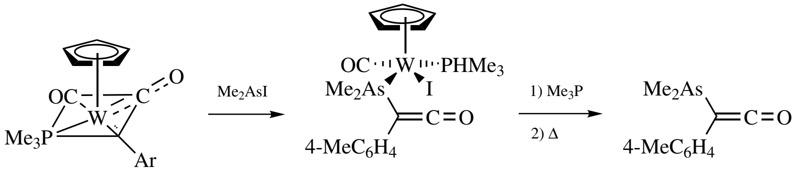
79 **80** (78%, IR 2078 cm^{-1})



(34)

81 **82** (96%, IR 2083 cm^{-1})

The tungsten complex **83** was converted to the ketene complex **84**, which reacted with Ph_3P to give the isolable free ketene **85** (equation 35).[45,46]



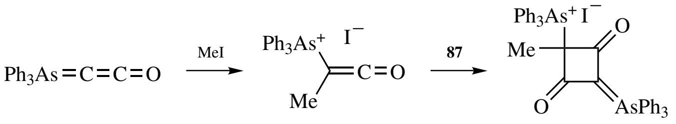
(35)

83 **84** (79%, IR 2095 cm^{-1}) **85** (IR 2074 cm^{-1})

Triphenylarsenylideneketene **87** was obtained as a crystalline solid by elimination from the ester **86** (equation 36) and reacted with methyl iodide to form the ketene **88**, which combined with **87** by [2 + 2] cycloaddition, forming **89** (equation 37).[48]

$$Ph_3As{=}CHCO_2Me \xrightarrow{NaN[Si(Si(Pr\text{-}i)_3]_2} Ph_3As{=}C{=}C{=}O \longleftrightarrow Ph_3\overset{+}{As}{-}\overset{-}{C}{=}C{=}O \qquad (36)$$

86 **87** (60%, IR 2030 cm^{-1})



(37)

87 **88** **89** (50%)

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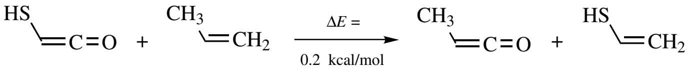
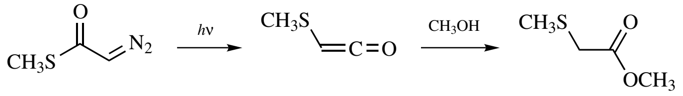
4.7 SULFUR-SUBSTITUTED KETENES

Mercaptoketene (**1**) was predicted by an isodesmic exchange reaction based on MP2/6-31G*//MP2/6-31G* calculated energies to be stabilized to the same extent as methylketene **3** (equation 1).[1,2] There has been relatively little study of this family, but there is considerable evidence that these ketenes are relatively easy to form and have appreciable stability. There is a rich chemistry of sulfur-substituted compounds, and further study of these ketenes appears warranted.



1 **2** **3** **4** (1)

Methylthioketene **6** was prepared by Wolff rearrangement upon direct photolysis of *S*-methyl diazothioacetate **5** in methanol with 310–380 nm light, resulting in the formation of the methyl ester **7** in 86% yield as the only observable volatile product (equation 2).[3] The ketene EtSCH=C=O (**8**) was also prepared by photochemical Wolff rearrangement and trapped with alcohols.[4] These results are in contrast to those obtained with photolysis of α-diazo esters and amides, which gave only 20–60% of Wolff rearrangement in solution,[4] and indicate a high migratory aptitude for the thiol group in Wolff rearrangement. The failure to trap **6** from the corresponding sensitized reaction was taken as evidence that Wolff rearrangement did not occur from a triplet carbene.[3]

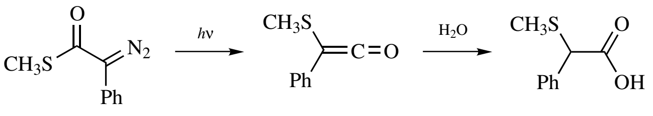


5 **6** **7** (86%) (2)

TABLE 4.5 Relative Hydration Reactivitities of PhCR=C=O in H_2O at 25 °C (data from Section 5.5.1)[5]

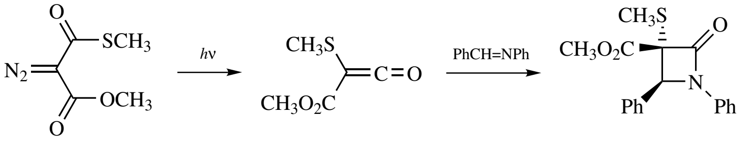
R	k(rel)(H^+)	k(rel)(H_2O)	k(rel)(OH^-)
OH	1.2×10^7	5.4×10^3	1.2×10^5
SCH_3	1.0	1.0	1.0
CH_3	—	0.55	1.1

Photolysis of methyl phenyldiazoacetate **8** in water formed (methylthio)phenylketene (**9**), which formed the acid **10** as the only detectable product by HPLC analysis (equation 3).[5] The kinetics of hydration of **9** were measured,[5] and the reactivity was found to be much less than that of PhC(OH)=C=O, and about the same as that of PhCMe=C=O, in acid-, neutral, and base-induced reactions (Section 5.5.1, Table 4.5).

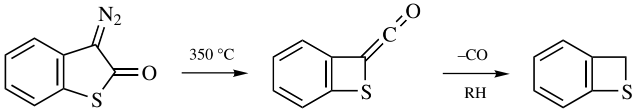


8 **9** **10** (3)

Photolysis of the diazomalonate derivative **11** gave the methylthio-substituted ketene **12**, as characterized by the IR absorption at 2120 cm^{-1} in $CDCl_3$, as well as by ^1H NMR (equation 3a).[6] No detectable product from methoxy group migration was observed, showing the much greater propensity for thio group migration, and the ketene was also trapped as the corresponding β-lactam **13** upon [2 + 2] cycloaddition with the imine PhN=CHPh (equation 3a).[6] Thermolysis of the diazo ketone **14** formed the ketene **15**, detected by photoelectron spectroscopy, which upon decarbonylation and hydrogen abstraction gave benzothiete **16** (equation 4).[7]

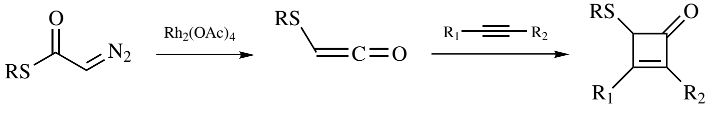


11 **12** (IR 2120 cm^{-1}) **13** (3a)



14 **15** **16** (80%) (4)

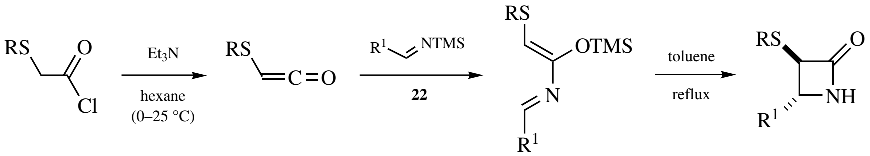
The $Rh_2(OAc)_4$-catalyzed reaction of α-diazo thiol esters **17** provided a general route to thio-substituted ketenes **18** that have been used in cycloadditions with alkenes, alkynes, and imines (equation 5).[8,9]



17 **18** **19** (14–92%)

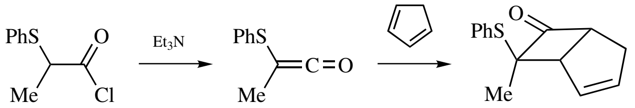
(5)

Ketenes RSCH=C=O (**21**) generated by dehydrochlorination of the acyl chlorides (**20**) reacted with imines **22** to give observable azadienes **23** that upon thermolysis form β-lactams **24** (equation 6).[10] For R^1 = PhCH=CH a six-membered ring dihydropyridone was formed from reaction of **21** and **22**.[10] Dehydrochlorination of **25** gave ketene **26**, which was trapped by imines or with cyclopentadiene (equation 7).[11]



20 (R = Ar, ArCH$_2$) **21** **23** **24** (15–50%)

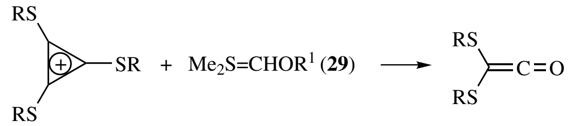
(6)



25 **26** **27** (86%)

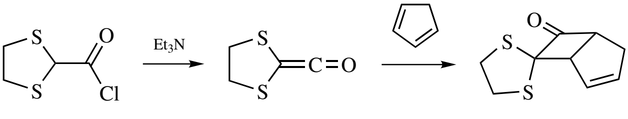
(7)

Reaction of the cyclopropenium cation **28** with the ylides **29** gave isolable ketenes **30** with two sulfur substituents, and these were sufficiently stable in MeOH that this was used as a solvent to measure their UV spectra (equation 8).[12] Dehydrochlorination of **31** gave ketene **32**, which was trapped in situ by [2 + 2] cycloaddition with cyclopentadiene (equation 9)[11,13] or with imines.[14]



28 R = Et, *t*-Bu, *t*-BuC$_6$H$_4$ **30**

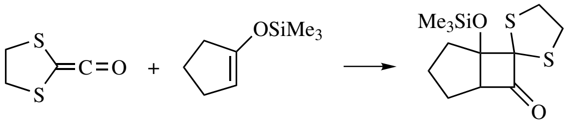
(8)



31 **32** **33** (70%)

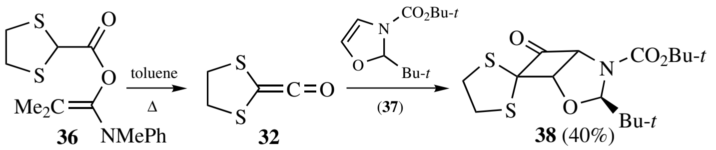
(9)

Ketene **32** also gave [2 + 2] cycloaddition with the silyl enol ether **34** and formed **35** (equation 10).[15] Thermolysis of **36** formed ketene **32**, which reacted with the alkene **37**, forming **38** (equation 11).[16]



32 **34** **35** (76%)

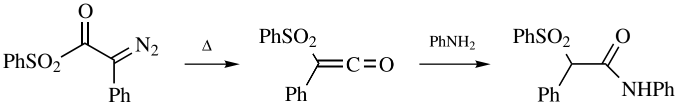
(10)



36 **32** **38** (40%)

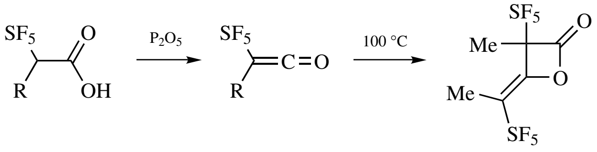
(11)

Wolff rearrangement of the diazo ketone **39** gave the phenylsulfonylketene **40** (equation 12).[17,18] A series of isolable SF_5-substituted ketenes **41** were prepared by dehydration of the carboxylic acids and dimerized upon heating (equation 13).[19]



39 **40**

(12)



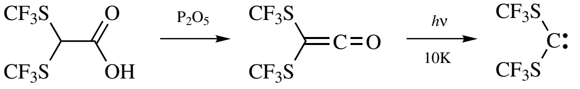
41 R = H (**a**), Me (**b**), Cl (**c**), Br (**d**)

42 (60%, IR 2149 cm^{-1}, R = Me)

(98%)

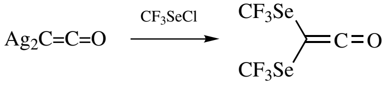
(13)

Dehydration of **43** gave **44** with strong UV absorption at 220 and 325 nm, and upon photolysis **44** was proposed to give the carbene **45** (equation 14).[20,21] The selenyl analogue **46** was obtained by dehydration in 45% yield and was also prepared from $Ag_2C{=}C{=}O$ (equation 15).[22] The ketene **47** was obtained by the unique method of CrO_3 oxidation of **44** (equation 16).[22]



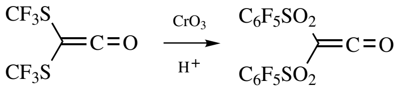
43 **44** (78%, IR 2141cm^{-1}) **45**

(14)



46 (45%, IR 2127 cm^{-1})

(15)

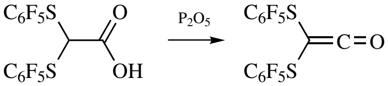


(16)

44 **47** (5%, IR 2139 cm^{-1})

The structure of the ketene $(CF_3S)_2C{=}C{=}O$ (**44**) has been determined by gas phase electron diffraction and was found to have C_2 symmetry, with the S-CF_3 bonds perpendicular above and below the molecular plane,[23] as previously predicted by *ab initio* calculations.[1] This structure was in agreement with the interpretation that there is a repulsion between substituent lone pairs and the electron-rich ketenyl HOMO perpendicular to the ketene plane at C_2, so that the favored conformation minimizes this interaction.

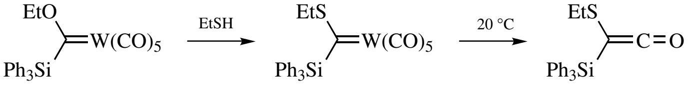
Ketene **49** was formed either from P_4O_{10} dehydration of the carboxylic acid **48** (equation 17) or by reaction of C_6F_5SCl with $Ag_2C{=}C{=}O$.[24] This ketene was a solid with a typical ketenyl IR band at 2135 cm^{-1} and ^{13}C NMR signals at δ 172.6 and 31.4 for C_1 and C_2 of the ketenyl group.



(17)

48 **49** (48%, IR 2135 cm^{-1})

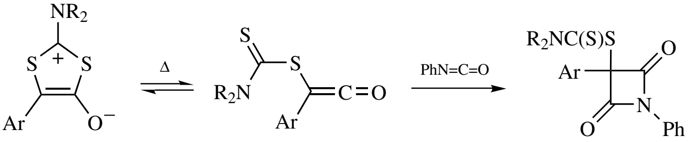
Reaction of the carbene complex **50** with thioethanol formed the unstable complex **50a**, which at 20 °C gave the ketene **51**, crystallized at −30 °C in 12% yield as a rather unstable material, characterized by the IR absorption at 2093 cm^{-1} and by ^{1}H NMR (equation 18).[25,26] The structure of the silyl-stabilized ketene **51** was determined by X-ray.[25]



(18)

50 **50a** **51** (12%, IR 2093 cm^{-1})

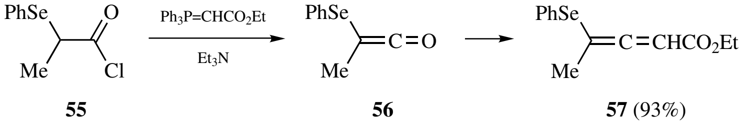
Heating of the mesoionic dithiole **52** was proposed to give rise to the unobserved ketene **53**, which was captured by PhNCO as the [2 + 2] cycloaddition product **54** (equation 19).[27]



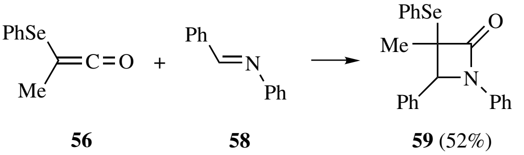
(19)

52 **53** **54** (93%)

Dehydrochlorination of the seleno-substituted acyl chloride **55** with Et_3N in the presence of a phosphorus ylide gave ketene **56** that was converted to allene **57** by Wittig reaction (equation 20).[28] The phenylselenylketene **56** reacted with an imine by [2 + 2] cycloaddition (equation 21).[29]



(20)



(21)

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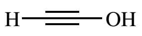
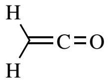
4.8 METAL-SUBSTITUTED KETENES

4.8.1 Ynols and Ynolates

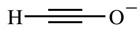
Ethynol **1** is a valence tautomer of ketene (**2**), and is the parent of the ynol, or hydroxyacetylene, family. Ynolates such as **3** are conjugate bases of both ketenes and ynols. Ethynol **1** has been generated in the gas phase by decarbonylation and neutralization of the radical cation of propiolic acid $HC{\equiv}CCO_2H$ using tandem mass spectrometry.[1] Photolytic ring opening of hydroxycyclobutenedione **4** to the bisketene **5** in an argon matrix at 12 K and subsequent photochemical decarbonylation also formed **1**, which was identified by its IR spectrum, and formed **2** upon further photolysis (equation 1).[2]



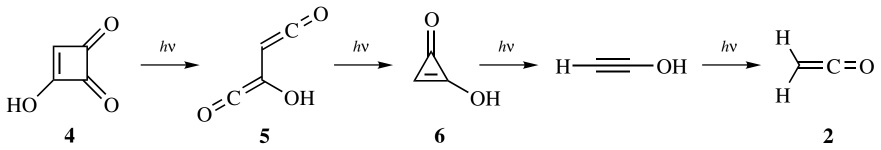
1



2

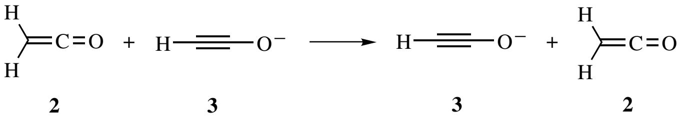


3

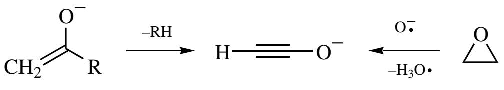


(1)

The identity reaction of proton exchange between ketene and the parent ynolate ion has been studied computationally and has a barrier of only 12.3 kcal/mol at the B3LYP level (equation 2).[3,4] This indicated effective conjugation in the transition state. Computational studies predicted ethynol to be remarkably acidic,[5] and the ethynolate ion **3** was readily produced in the gas phase by the collisional activation cleavage of enolates **7**[6] and by proton abstraction from ethylene oxide **8** (equation 3).[7] The gas phase acidity of ketene has been measured in the gas phase using the flowing afterglow method.[8]

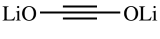


(2)

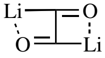


7 3 8 (3)

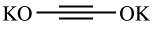
Computations at the MP2/G-31G*//HF/6-31G* level indicated that in the absence of solvent the C-lithiated structure CHLi=C=O would be more stable than the O-lithiated isomer HC≡COLi by 4 kcal/mol.[9] For $Li_2C_2O_2$ the bis(ynolate) structure LiOC≡COLi **9a** and the bicyclic structure **9b** were calculated to be of equal stability.[10] "Potassium dicarbonyl," **10**, is a well-studies species for which the structure KOC≡COK has been proposed.[11,12]



9a

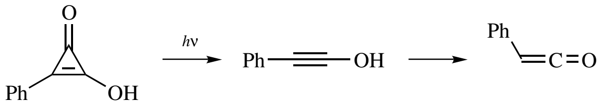


9b



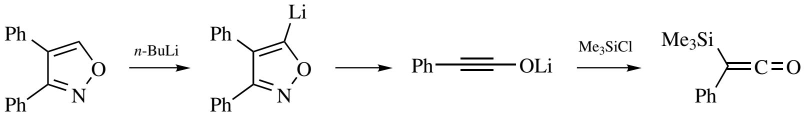
10

Photolysis of arylhydroxycyclopropenones provided a general route to arylethynols,[13] and irradiation of **11** gave phenylethynol (**12**), which was converted to phenylketene **13**. The kinetics of this conversion have been measured by TRIR spectroscopy (equation 4).[13a] Further studies of this reaction in aqueous solution using UV spectroscopy have also been carried out.[14,15]

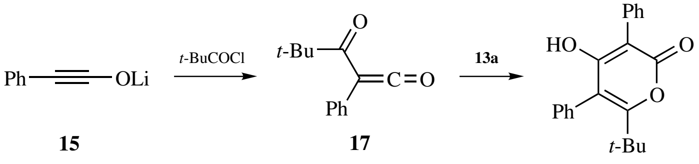


11 **12** **13** (4)

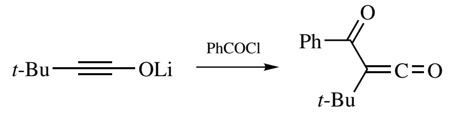
The chemistry of ynolate anions has been reviewed[16] and these species have been generated by a number of routes, including the reaction of isoxazole **14** with *n*–BuLi, forming phenylethynolate **15**, which reacted with Me_3SiCl, forming ketene **16** (equation 5).[17] Reaction of two molecules of **15** with *t*–BuCOCl proceeded through ketene **17**, forming pyrone **18** (equation 6).[18] The *tert*-butyl ynolate **19** reacted with benzoyl chloride to form the isolable acyl ketene **20** (equation 7).[18]



14 **15** **16** (41%, IR 2070 cm^{-1}) (5)



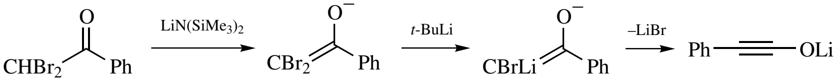
15 **17** **18** (28%) (6)



19 **20** (53%, IR 2103 cm^{-1})

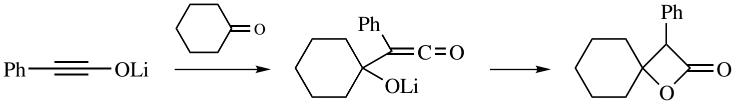
(7)

Deprotonation of α-haloenolate **21** led to dianion **22**, which formed ynolate **15** (equation 8), and this reacted with cyclohexanone to give β-lactones **23** (equation 9).[19] Esters reacted with CH_2Br_2 and strong bases through an optimized route to form the ynolate **15**, and upon reaction with ethanol this gave the homologated ester **24** (equation 10).[20–22]



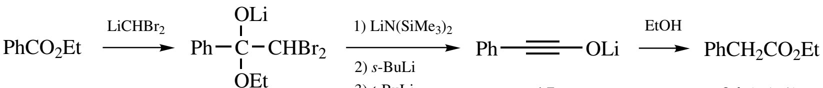
21 **22** **15**

(8)



15 **23** (43%)

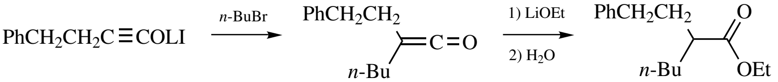
(9)



15 **24** (71%)

(10)

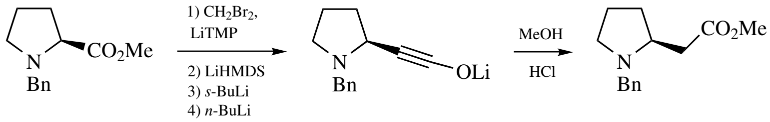
The ynolate **25** formed from the procedure of equation 10 was suggested to combine with *n*-BuBr (used to prepare *n*—BuLi) to form the ketene **26**, which reacted with LiOEt (from the starting ester) to give **27** as a by-product after hydrolysis (equation 11).[22] The use of *s*-BuLi avoided this problem.



25 **26** **27** (4%, by-product)

(11)

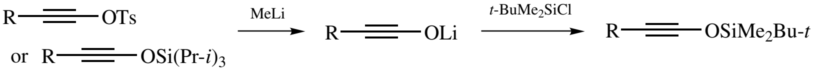
Ynolates prepared by the Kowalski procedures were used to prepare a variety of homologated amino acid esters, without significant racemization, as in the conversion of **28** to **30** (equation 12).[23]



28 **29** **30** (72%)

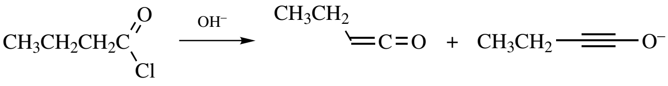
(12)

Ynolates **31** were also formed by reaction of alkynyl tosylates or of triisopropylsilyl or alkynyl *tert*-butyldimethylsilyl ethers with MeLi, and further reaction with silyl chlorides proceeded with *O*-silylation, forming alkynyl silyl ethers **32** (equation 13).[24,25] This is in contrast to the result of equation 5, where *C*-silylation occurred.

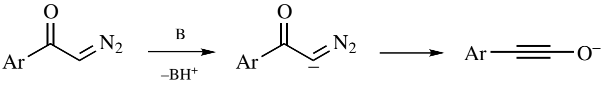


31 **32** (55%, R = *t*-Bu) (13)

The reaction of OH^- with acyl chlorides **33** in negative ion mass spectroscopy formed both ketenes **34** and ynolates **35** by E2-type eliminations (equation 14).[26] Negative ion Wolff rearrangement of deprotonated diazo ketones **36** has been used to generate aryl ynolates in the gas phase (equation 15).[27]

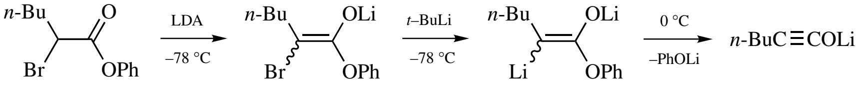


33 **34** **35** (14)



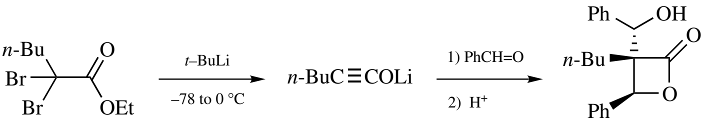
36 **37** (15)

The *n*-butyl ynolate anion **39**[28–40] has been generated from ester dianions formed from the α-bromo ester **38** (equation 16)[28] and from the α,α-dibromo ester **40** (equation 17).[29,30] Capture of **39** with TIPSCl gave the alkynyl silyl ether in 60% yield.[28] The ynolate reacted by [2 + 2] cycloaddition with benzaldehyde, forming β-lactone **41** (equation 17), and with imine **42**, forming β-lactam **43** after protonation (equation 18).[35]

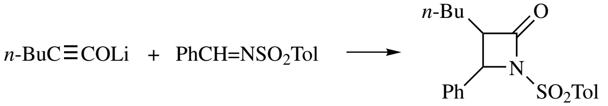


38 **39**

(16)



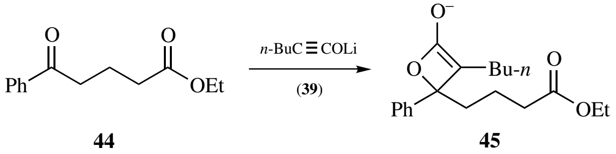
40 **39** **41** (69%) (17)



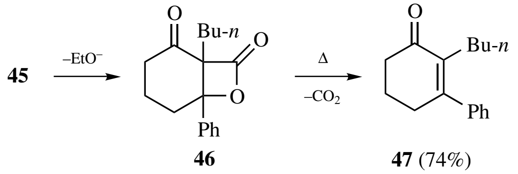
39 **42** **43** (58%) (18)

Ynolates were also generated by reaction of α,α-dibromoesters with lithium naphthalenide.[31] The ynolates react with silylating agents to give silyl ynol ethers[28] or silylketenes and with aldehydes to give β-lactones (equation 17)[28] or acrylic acids.[28,31] Reactions with ketones give stereoselective formation of trisubstituted acrylates,[30] while imines give β-lactams (equation 18)[35] and acrylamides,[36] in reactions that proceed through β-lactam enolates.

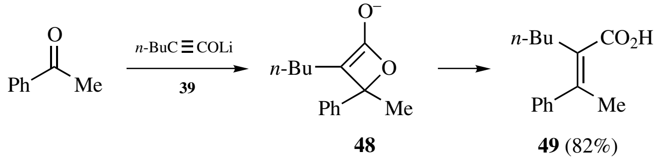
Keto ester **44** reacted with ynolate **39** through a Dieckmann-type reaction (equations 19, 20).[32,36] This reaction has also been utilized for cyclopentenone formation.[32,36,40] Reaction of ketones with ynolate **39** formed acrylic acids **49** proposed to form through β-lactone enolates **48** (equation 21).[30] The stereoselectivity of ring opening in this reaction was studied computationally.[34a]



(19)

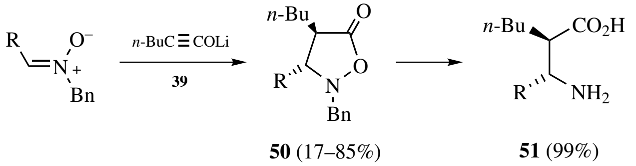


(20)

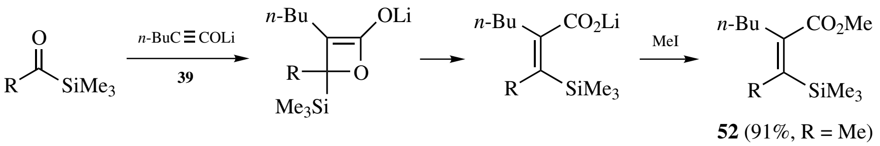


(21)

Ynolate **39** reacted with nitrones by a 1,3-dipolar cycloaddition forming 5-isoxazolidinones **50**, which were converted to β-amino acids **51** (equation 22).[38] Reaction of **39** with acylsilanes gave selective formation of *Z*-alkenes **52** (equation 23).[39]



(22)

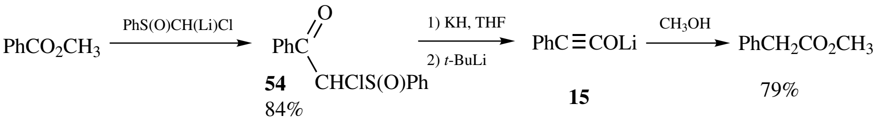


(23)

Phenyl ynolate **15** was generated by reaction of lithium phenylacetylide with *t*-BuOOLi, as evidenced by capture of the ketene dimer and $PhCH_2CO_2Et$ on reaction with EtOH and capture as the silyl ethynyl ether **53** (equation 24).[41,42]

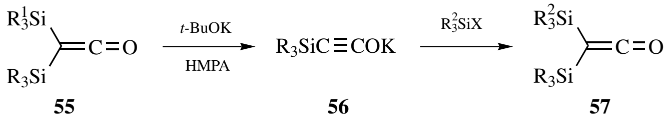
$$\mathrm{PhC{\equiv}CLi} + t\text{-}\mathrm{BuOOLi} \longrightarrow \underset{\mathbf{15}}{\mathrm{PhC{\equiv}COLi}} \xrightarrow{i\text{-}\mathrm{Pr_3SiCl}} \underset{\mathbf{53}\ (60\%)}{\mathrm{PhC{\equiv}COSi(Pr\text{-}}i)_3} \qquad (24)$$

In another route to ynolates, methyl benzoate was converted to the α-chloro α-sulfinyl ketone **54**, which reacted with potassium hydride followed by *tert*-butyllithium to form the phenyl ynolate **15**, which gave methyl phenylacetate on reaction with methanol (equation 25).[43,44]



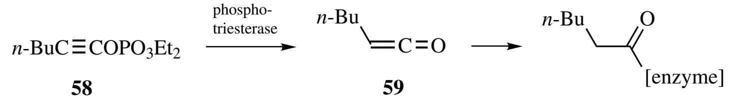
(25)

Bis(trialkylsilyl)ketenes **55** were desilylated by treatment with *t*-BuOK in the presence of HMPA, forming potassiuum ynolates **56**, and these could be converted to other bis(trialkylsilyl)ketenes **57** (equation 26).[45] (See also Section 4.5.)



(26)

Reaction of diethyl 1-hexynyl phosphate (**58**) with the enzyme phosphotriesterase resulted in inactivation of the enzyme. This was attributed to formation of *n*-butylketene **59**, which acylated the enzyme (equation 27).[46]



(27)

Generation of silylketenes from silyl ynolates is discussed in Sections 4.5 and 4.10.

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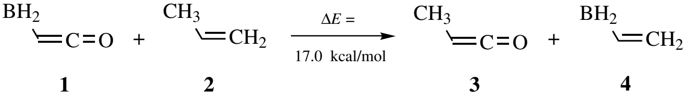
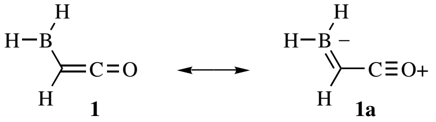
4.8.2 Boron-Substituted Ketenes

Computations at the MP2/6-31G*//MP2/6-31G* level of the energies of BH_2-substituted ketenes indicate that these species are stabilized by 17 kcal/mol relative to methylketene,[1,2] as indicated by isodesmic energy comparison (equation 1).[2] This stabilization exceeded that predicted by a correlation with substituent electronegativity, which was interpreted as indicating a favorable π-acceptor ability of the boron substituent shown in **1a** adding extra stability.[1,2]



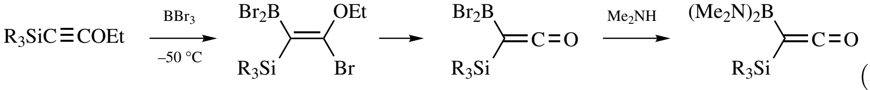
(1)



Boron-substituted ketenes are known in only a limited number of examples and are sensitive materials. Thus, despite their thermodynamic stabilization, their reactivity has limited their study.

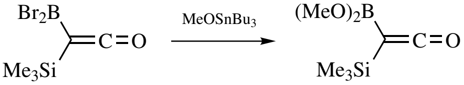
The reaction of alkynyl ethers **5** with BBr_3 gave ketenes **7** in a reaction proposed to involve the addition intermediate **6** (equation 2).[3,4] Reaction of the ketenes with amines or dialkylaminostannanes displaced the halides and gave aminoborane ketenes **8** (equation 2).[3,4] The substituents on boron in ketenes **7** were also replaced on reaction with alkoxystannanes to give ketenes **9** with alkoxyborane substituents (equation 3).[3] Trimethylsilylethynyl ethyl ether (**10**) reacted directly with

$(Me_2N)_2BBr$, forming **11** (equation 4).[4]



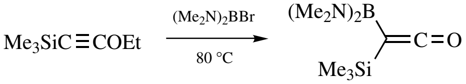
(2)

5 **6** **7** (62%, R = *i*-Pr, IR = 2100 cm^{-1}) **8** (64%, R = *i*-Pr, IR 2075 cm^{-1})



(3)

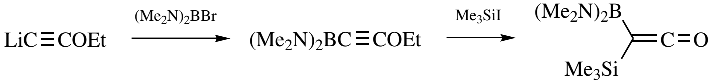
7 **9** (52%, IR 2080 cm^{-1})



(4)

10 **11** (43%, IR = 2070 cm^{-1})

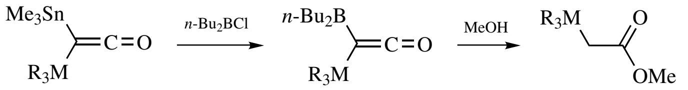
Aminoborane ether **12** was prepared and reacted with Me_3SiI, also forming ketene **11** (equation 5).[5]



(5)

12 **11**

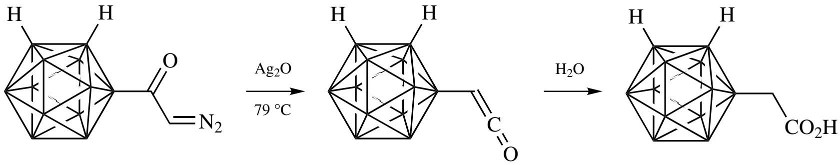
Boron also replaced tin substituents on stannylketenes **13** with a silicon or germanium substituent forming boron-substituted ketenes **14** (equation 6).[6,7] Methanol was added to **14** with cleavage of the boron-carbon bond (equation 6).[7]



(6)

13 M = Si (**a**), Ge (**b**) **14** **15** (85%, IR = 2090–2100 cm^{-1}, $R_3M = Me_3Ge$)

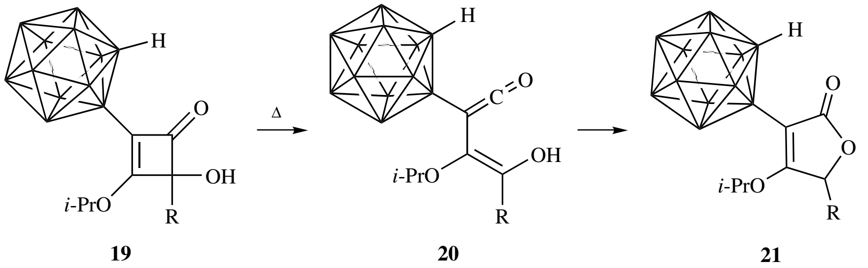
Thermal Wolff rearrangement of 3-diazoacetyl-*o*-carborane (**16**) with Ag_2O in aqueous dioxane at 70 °C formed the boron-substutued ketene **17**, which was hydrated to the acid **18** (equation 7).[8]



16 **17** **18**

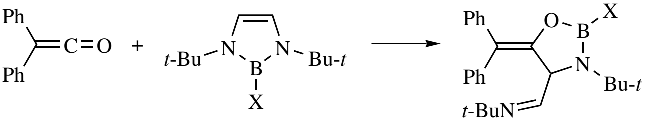
(7)

As discussed in Section 3.4.1, ring opening of carboranyl-substituted cyclobutenones **19** to carborane-substituted ketenes **20** with the ketenyl group bonded to carbon in the carborane led to formation of lactones **21** in "fair to good yields" (equation 8).[9]



(8)

Diphenylketene (**22**) reacted with 1,3-di-*tert*-butyl-2,3-dihydro-1*H*-1,3,2-diazaboroles **23** to form 1,3,2-oxaazaborolidines **24**, in a reaction proposed to be initiated by boron attack at the ketenyl oxygen (equation 8).[10]



(9)

22 **23** **24** (64–70%)

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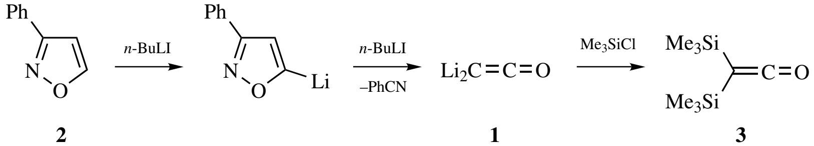
4.8.3 Other Metal-Substituted Ketenes and Metal Ketenides

Computations predict that ketenes with electropositive substituents will be stabilized, and this has been vividly demonstrated experimentally for the long-lived silicon, germanium, and tin-substituted ketenes (Section 4.5). Lithiumketene is predicted to be much more stabilized than the silylketenes,[1,2] but in solution has strong ionic character in an ynolate structure (Section 4.8.1). Boron is also predicted to be highly stabilizing, with covalent bonds to carbon, but in the examples known experimentally, stabilizing Group 4 substituents are also present, and the effect of the boron is not well defined (Section 4.8.2).

Computations also predict strong stabilization of ketenes RCH=C=O with R = Na, BeH, MgH, and AlH_2,[1,2] but these species are not known experimentally.

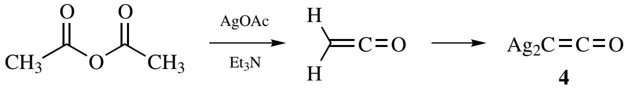
Dilithiumketene (**1**) was prepared by the reaction of **2** with *n*-BuLi and gave bis(trimethylsilyl)ketene (**3**) by reaction with Me_3SiCl (equation 1).[3]



2 **1** **3**

(1)

Metal ketenides represented as $M_2C{=}C{=}O$ are known for M = Ag, Cu, Au, and Hg.[4–9] Silver salts react with $CH_2{=}C{=}O$ to give the ketenide $Ag_2C{=}C{=}O$ (**4**), and this ketene was also generated in situ by reaction of acetic anhydride, silver acetate, and triethylamine (equation 2).[7,8] The structure of crystalline silver ketenide and the pyridine complex have been determined by X-ray powder diffraction.[8] The yellow monomer $Ag_2C{=}C{=}O$ (**4**) was proposed to exist briefly in solution, and then to form a polymeric precipitate that could not be redissolved. Bis(trifluoromethylselenyl)ketene (**5**) was prepared by the use of this reagent (equation 3).[10]



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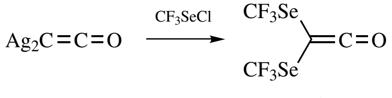
(2)

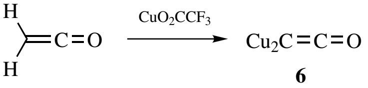


4 **5** (45%)

(3)

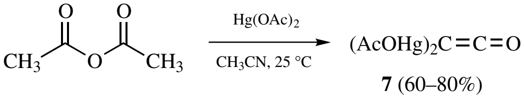
The reaction of acetone with a silver surface that had been oxidized by heating with oxygen gave surface bound ketenylidene (C=C=O), as identified by its strong IR band at 2026 cm^{-1}.[11] This is characteristic of metal ketenides, which typically absorb between 2015 and 2070 cm^{-1}.[4,5]

Copper ketenide **6** was prepared from ketene and CuO_2CCF_3 (equation 4).[9] The reaction of mercuric acetate and acetic anhydride gave the mercury derivative **7** (equation 5),[4] and the gold compound **8** was obtained from (1,4-oxathian)gold(I), 2,6-dimethylpyridine, and Et_3N (equation 6).[5,6]



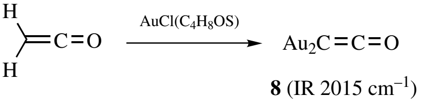
6

(4)



7 (60–80%)

(5)



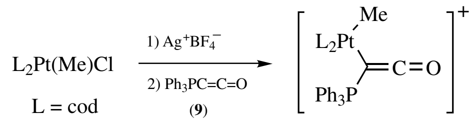
8 (IR 2015 cm^{-1})

(6)

Zirconium and hafnium ketenylidene complexes have also been prepared, and the X-ray structure of a zirconium complex was determined.[12]

Laser-ablated metal atoms (Nb,[13] Ta,[13] Zr,[14] Hf,[14] U,[15] and Th[16]) in solid neon reacted with CO to form carbonyls $M(CO)_n$ and insertion products (CMO) that reacted further under photolysis to form metal ketenides (OMCCO). The ketenyl IR absorptions were at 2065.5,[13] 2087.5,[13] 2046.4,[14] 2063.5,[14] and 2051.5[15] cm^{-1} for the Nb, Ta, Zr, Hf, and U ketenides, respectively. No such complex was reported for Th. Complexes isotopically labeled with ^{13}C and ^{18}O were also studied. Density functional calculations using BP86 and B3LYP functionals found C_s symmetric structures with bent (OMC) angles for these ketenes and reasonable agreement with the observed IR spectra.

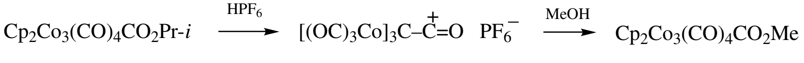
Ketenylidenetriphenylphosphorane (**9**) reacted with platinum complexes, forming platinum-substituted ketenes **10** (equation 7).[17,18] These compounds are stable solids, and a variety have been synthesized and characterized and their chemistry investigated (see also Section 4.6).[17,18]



10 (93%,
IR 2040 cm^{-1})

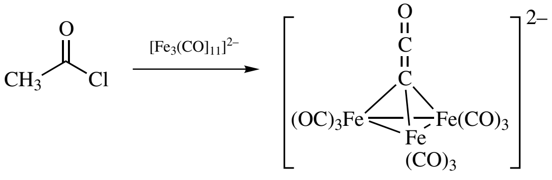
(7)

Reaction of the ester **11** in acid gave the metal acylium cluster **12**, which was observed by NMR, and captured with MeOH, forming **13** (equation 8).[19,20] Acetyl chloride reacted with a carbanionic iron carbonyl, forming $[(OC)_3Fe]_3C{=}C{=}O]^{2-}$ (**14**, equation 9),[21] and analogous cobalt and osmium compounds were also prepared.[22]



$$Cp_2Co_3(CO)_4CO_2Pr\text{-}i \xrightarrow{HPF_6} [(OC)_3Co]_3C\text{–}\overset{+}{C}{=}O\ \ PF_6^- \xrightarrow{MeOH} Cp_2Co_3(CO)_4CO_2Me \quad (8)$$

11 **12** (70%, IR 2040 cm^{-1}) **13** (97%)



14

(9)

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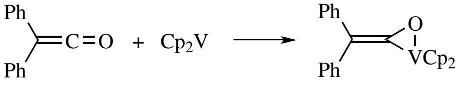
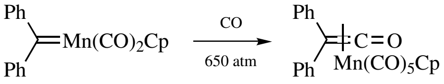
4.8.4 Metal-Complexed Ketenes

Metal complexes of ketenes have been prepared in a wide variety of structural forms, with metal coordination by either σ or π bonding.[1,2] Ketenyl complexes with a metal as one of the ketene substituents, and ketenylidene complexes in which the ketene carbon has only metals as substituents, are covered elsewhere. This section focuses on non-sigma bonded complexes, which may be formed by direct addition of the metal complex to the ketene (equation 1),[3] by carbonylation of metal carbene complexes (equation 2),[4–7] and by other routes. Often the bonding involves not only the ketenyl moiety but also the ketene substituents, as in the $Fe(CO)_3$ complex of a vinylketene (**6**). Reviews of the subject are available.[1,8–11] This chapter is not intended to be comprehensive or systematic, but only illustrative of some of the known examples. Further information is given in Sections 3.5 and 4.8.3.



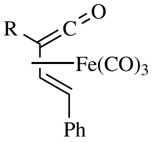
(1)

1 **2** ($Cp = C_5H_5$) **3**



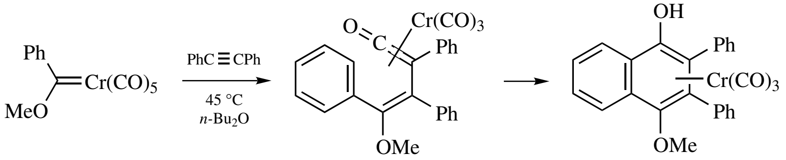
(2)

4 **5**



6

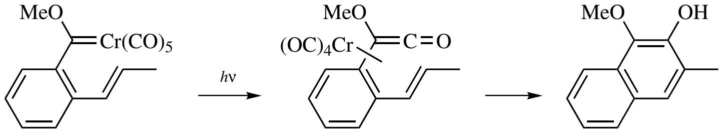
As described in Section 3.5, the Dötz reaction of photolysis of a metal carbene complex **7** in the presence of an alkyne has been proposed to form a metal-complexed alkenylketene **8**, which reacts further, for example by intramolecular cyclization forming **9** (equation 3).[5,6] The complexed ketenes have usually not been directly observed, but the products formed in some cases are still complexed with the metal.



(3)

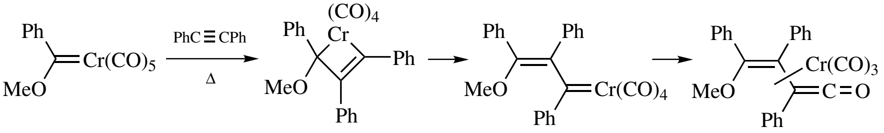
7 **8** **9** (62%)

A number of pathways for the course of these reactions have been presented.[12] For example, upon photolysis a chromium carbene complex **10** has been proposed to undergo direct insertion of CO forming ketene complex **11**, and this reacted by intramolecular [4 + 2] cycloaddition (equation 4). For the formation of **8** (equation 3), it was suggested that upon thermolysis of complex **7** in the presence of an alkyne metallocyclobutene **13** could form by displacement of CO by the alkyne, followed by ring opening to carbene complex **14**, which inserts CO, forming a metal-complexed alkenylketene **8** (equation 5).[6,12] Further studies of the mechanism of these reactions are presented in Section 3.5.



10 **11** **12** (23%)

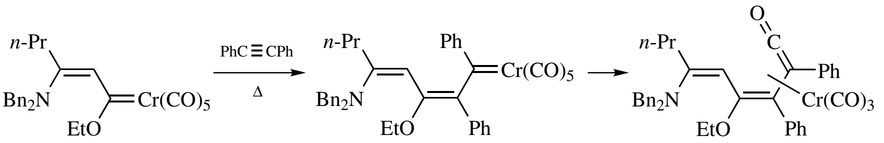
(4)



7 **13** **14** **8**

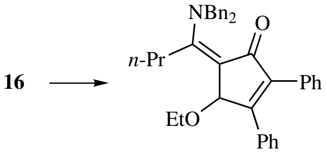
(5)

The structure of the complex of ketene with $Cr(CO)_4OH_2$ was calculated using the B3LYP/6-31G* basis set for C, H, and O and a double ζ basis set for Cr.[13] The reaction pathway for reaction of the complex with $CH_2{=}NH$ forming a β-lactam was also calculated.[13] Molecular orbital studies of the complex of $CH_2{=}C{=}O$ with $Pd(PR_3)_2$ indicated that bonding of Pd to C=C is favored, rather than to C=O, by 10–15 kcal/mol.[14] Reaction of the chromium carbene complex **15** with diphenylacetylene was proposed to give alkenylketene complexes **16** (equation 6), that cyclized to give the observed product **17** (equation 7).[15,16]



15 **16**

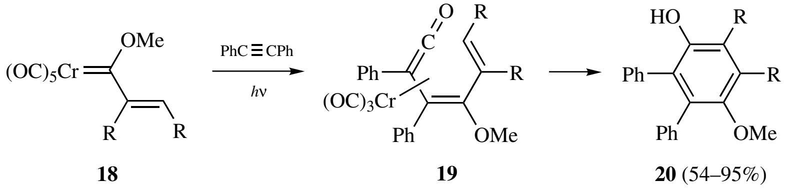
(6)



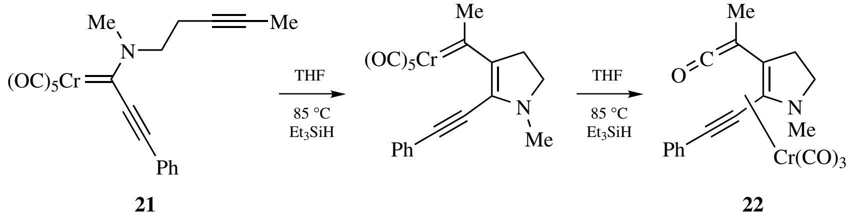
17 (68%)

(7)

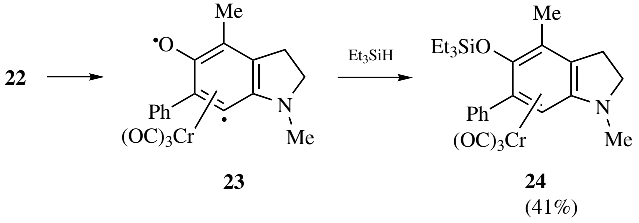
Photolysis of the alkenyl carbene complexes **18** in the presence of diphenylacetylene formed dienylketenes **19**, which cyclized to the phenols **20** with an enhanced yield using photolysis with a Xenon lamp (equation 8).[17] Cyclizations of metal complexes with two tethered alkynyl groups were carried out,[18] and amino-tethered bisalkynyl chromium carbene complex **21** was proposed to react to give the ene-yne ketene chromium complex **22** (equation 9), which cyclized via diradical intermediate **23** to give indoline **24** (equation 10).[19] The use of triethylsilane to capture the diradical helped to prevent demetallation.[19]



(8)

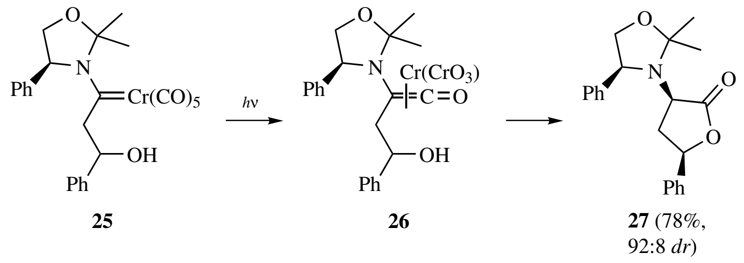


(9)



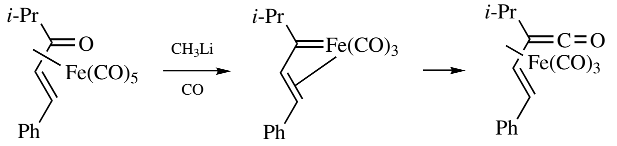
(10)

Photolysis of chiral hydroxycarbene complex **25** led to 4-hydroxy ketene **26** that cyclized to lactone **27**, and the major diastereomer was isolated (equation 11).[21] Other chiral auxiliaries were also employed in these reactions.[21]



(11)

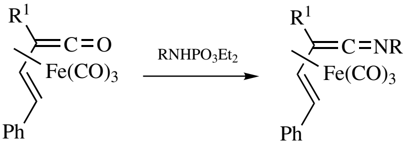
Alkenylketene complexes with iron tricarbonyl were formed by reaction of alkenylketones with alkyllithium reagents under an atmosphere of CO.[22] Iron carbene complexes have been suggested as intermediates in these processes.[22] Reaction of the enantiomerically enriched ketone complex **28** gave the ketene complex **30** with complete retention of stereochemistry, a result consistent with the intervention of a chiral carbene complex such as **29** (equation 12).[22] Upon purification the product **30** was obtained in 57% yield, 96% *ee*.[22]



(12)

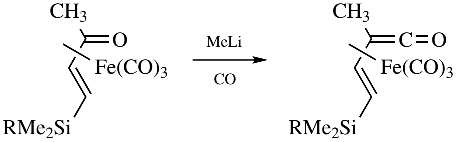
28 (*ee* 86%) **29** **30** (crude 86% *ee* 57% yield, 96% *ee* after purification)

Reaction of vinylketene tricarbonyl iron (0) complex **31** with phosphoramidates gave complexed ketenimine **32** in an aza-Wittig reaction (equation 13).[23] The reactions of **31** with dienophiles have also been examined.[24] Reaction of complexed vinyl ketone **33** with methyllithium gave the complexed vinylketene **34** (equation 14).[25] Reaction of vinyllithium reagents generated from vinylstannanes **35** with $Fe(CO)_5$ followed by reaction with EtOTf gave vinylketene iron complexes **36** (equation 15).[26] The sequence was also successful with PPh_3 replacing one of the CO ligands.



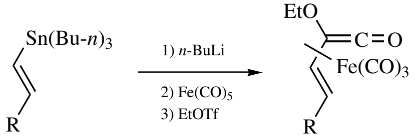
(13)

31 **32** (41–90%)



(14)

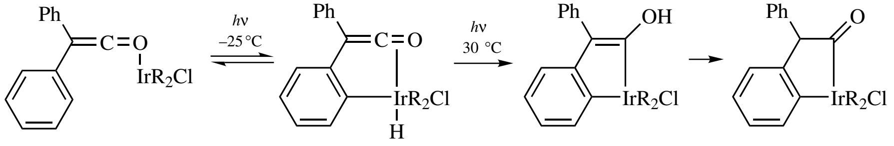
33 **34** (R = Me, 68%, *t*-Bu, 52%)



(15)

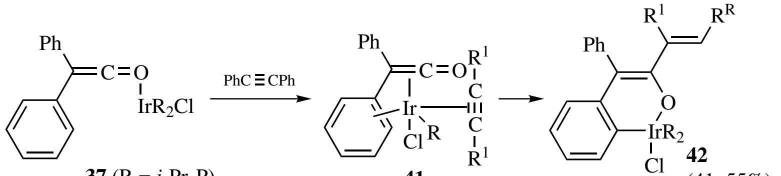
35 **36** (31–54%, R = Ph, Ph_3Si, *n*-Pn)

Photolysis of the iridium complex **37** at −25 °C gave **38**, which reformed **37** at ambient temperature, while photolysis of **38** at 28–30 °C gave the enol **39**, which isomerized to **40** on standing (equation 16).[27] Reaction of **37** with alkynes gave complexes **41**, which readily reacted further with C–C bond formation to give **42** (equation 17).[28] Iridium complex **43** was reversibly ionized to the carbene complex **44** by removal of chloride (equation 18).[29,30] A number of structures were compared,[31] and the chemistry of complex **43** has been modeled in a theoretical study.[32]



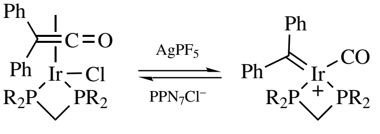
37 (R = *i*-Pr$_3$P) **38** (100%) **39** (78%) **40**

(16)



37 (R = *i*-Pr$_3$P) **41**

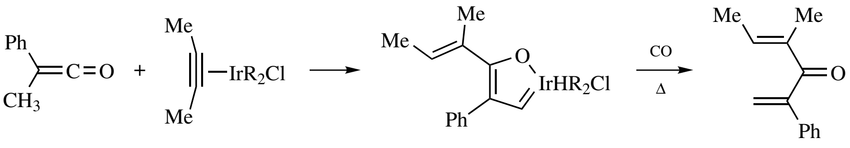
(17)



43 **44**

(18)

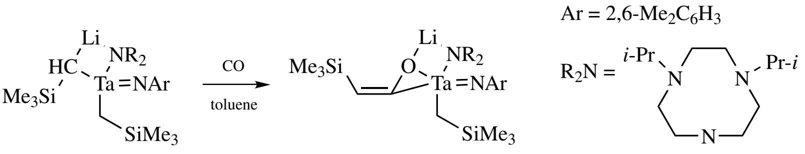
Excess phenyl(methyl)ketene (**45**) reacted with the iridium-alkyne complex **46**, forming **47** in 78% isolated yield in a double C–H activation of the CH_3 group of **45** (equation 19).[33] There was some polymerization of **45**. Heating of **47** under a CO atmosphere at 60–80 °C formed **48**, also in 78% yield (equation 19).[33]



45 **46** (R = (*i*-Pr$_3$)P$_2$ **47** (78%) **48** (78%)

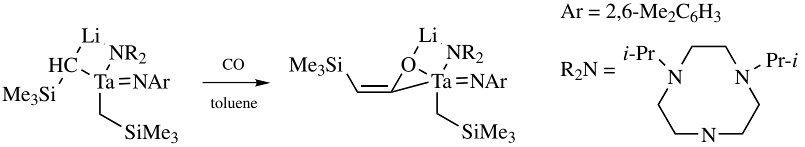
(19)

Reaction of the tantalum complex **49** with CO gave the ketenyl complex **50**, whose structure was confirmed by X-ray determination (equation 20).[34] Niobium ketene complexes **51** were prepared as *E* and *Z* isomers, but photoexcitation did not result in *E/Z* isomerization.[35] Vinyl complex **52** reacted on the double bond with cyclopentadiene in a Diels-Alder fashion and with free ketenes.[36] Other such niobium complexes have been prepared and studied.[37–39]



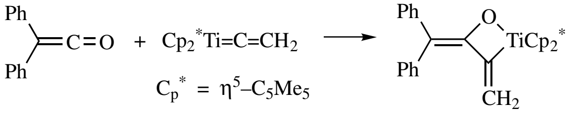
49 **50** (42%)

(20)



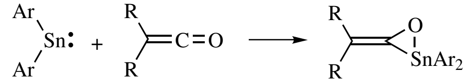
49 **50** (42%)

The complex **54** was formed by a [2 + 2] cycloaddition of diphenylketene (**53**) with a titanaallene (equation 21).[40] The stable diarylstannylene **55** reacted with ketenes in [2 + 1] cycloadditions, forming **56** (equation 22).[41] This reaction is also noted in Section 5.10.1. Reaction of acetylene with $CrCl_2O_2$ in an argon matrix at 7 K gave the end-on ketene complex **57**, identified by the IR band at 2095 cm^{-1}, as compared to the free ketene absorption at 2142 cm^{-1} (equation 23).[42]



53 **54**

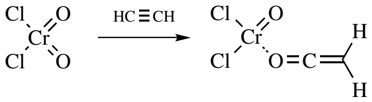
(21)



55 **56**

Ar = 2,4,6–$(CF_3)_3C_6H_2$

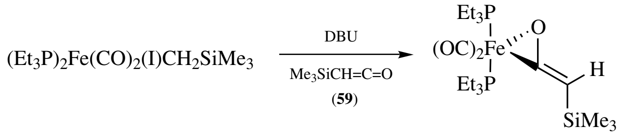
(22)



57 (IR 2095 cm^{-1})

(23)

The iron ketene complex **60** was prepared by the reaction of the metal complex **58** with trimethylsilylketene **59**, in 20% yield as determined by IR (equation 24).[43] Complex **60** was obtained independently in 95% yield and in better purity by the reaction of $(OC)_2Fe(PEt_3)_2N_2$ with $Me_3SiCH{=}C{=}O$, and was assigned the *E* configuration on the basis of the upfield shift of the olefinic proton. The reaction of **60** with CO liberated $Me_3SiCH{=}C{=}O$.



58 **60** (20%) (24)

Malonate esters were obtained in a low-yielding catalytic conversion of CH_2I_2 that was proposed to involve **61** forming a ketene complex **62** (equations 25, 26).[44]

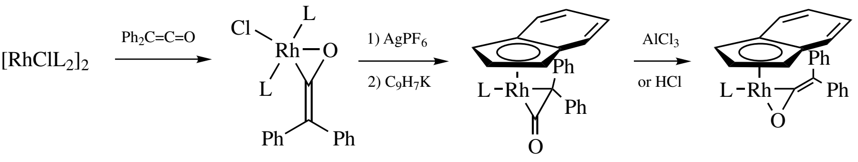
$$RhI(CO)(PEt_3)_2 \xrightleftharpoons{CH_2I_2} RhI_2(CO)(CH_2I)(PEt_3)_2 \xrightleftharpoons{CO} RhI_2(CO)(OCCH_2I)(PEt_3)_2 \tag{25}$$

61

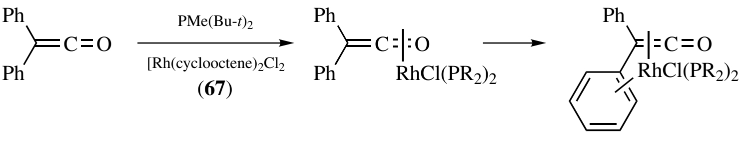
$$\mathbf{61} \rightleftharpoons [RhI_2(CO)(O{=}C{=}CH_2)]^+I^- \xrightleftharpoons{EtOH,\ CO} CH_2(CO_2Et)_2 \tag{26}$$

62

Reaction of **63** with $Ph_2C{=}C{=}O$ (**53**) gave the complex **64**, which was converted by potassium indenyl to **65**, which in turn was converted to **66**, the first example of a linkage-isomeric ketene complex (equation 27).[45] The ketenyl IR of **66** was at 1777 cm^{-1}, which is typical for such η^2(CO) complexes.[45] The structures of **65** and **66** were confirmed by X-ray crystallography. Reaction of $Ph_2C{=}C{=}O$ (**53**) with a mixture of a phosphine and Rh-cyclooctene complexes **67** gave complexes **68**, which were converted to complexes **69** at rates determined by the nature of the phosphine complex (equation 28).[46]

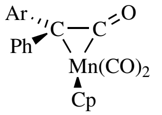


63 **64** **65** **66** (86%)
L = *i*–Pr$_3$P (27)



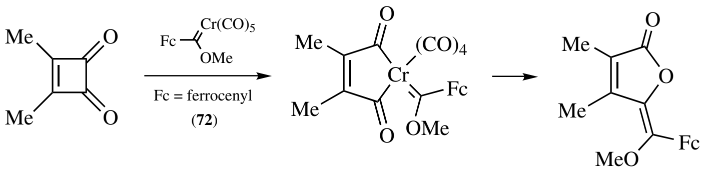
53 **68** **69** (28)

The manganese ketene complexes **70** and **71** were found by NMR studies to undergo both rotation around the ketene axis, interchanging the positions of the aryl groups, and exchange of the ketene CO with those on manganese.[47]

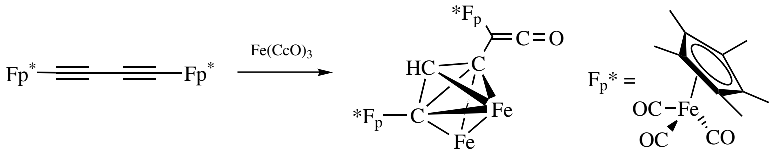


70 (Ar = $PhCC[CO_2(CO)_6]$)
71 (Ar = Ph)

Reaction of dimethylcyclobutenedione with ferrocenyl chromium carbene complex **72** has been proposed to form metal-complexed bisketene **73** as an intermediate leading to the lactone **74**, which was the only product observed from the cyclobutenedione (equation 29).[48] The unique organometallic-substituted ketene **76** was prepared from the dialkyne **75**, and the structure was confirmed by X-ray (equation 30).[49,50]

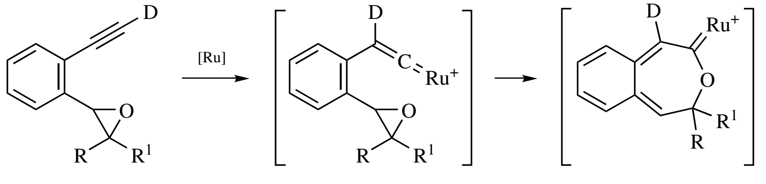


73 **74** (9%) (29)

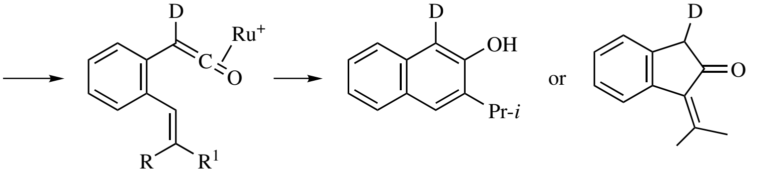


75 **76** (13%) (30)

Reaction of 2-ethynylphenyl epoxides **77** with the ruthenium catalyst $TpRuPPh_3(CH_3CN)_2PF_6$ [Tp = tris(1-pyrazolyl)borate] proceeded with high selectivity to give either 2-naphthols **81** (R = *i*-Pr, 81%) or 1-alkylidene-2-indanones **82** ($R = R^1$ = Me, 89%) (equations 31, 32).[51] The process was shown to proceed through the intermediacy of the metal-complexed ketene **80** by deuterium labeling of the alkyne, resulting in formation of **81** and **82** with rearranged label, and by capture of the ketene **80b** with *i*-butanol, giving the ester **83** in 90% yield (equation 33).[51] Ene-yne epoxides were similarly converted to complexed dienylketenes that formed cyclohexadienones (Section 4.1.2).[52]

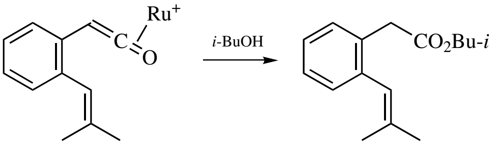


77 (**a**, R = *i*-Pr, R^1 = H; **b**, $R = R^1$ = Me) **78** **79** (31)



79 → **80** → **81** (72%, R = *i*-Pr, R^1 = H) or **82** (89%, R = R^1 = Me)

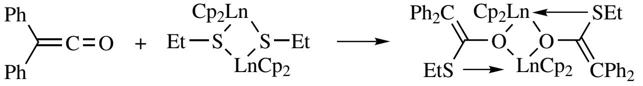
(32)



80b **83** (90%)

(33)

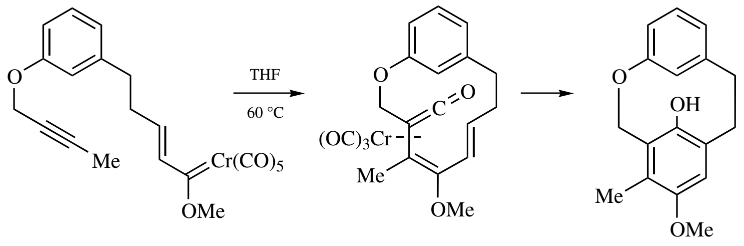
Complexation of diphenylketene (**53**) with the lanthanum complexes **84** gave insertion into the metal-sulfur bond, forming complexes **85** (equation 34).[53]



53 **84** Ln = Yb, Er, Sm, Y **85** (94–96%)

(34)

Intramolecular cyclization of a chromium carbene complex **86** gave a [2.2]-*meta*-cyclophane **88** through a ketene complex **87** (equation 35).[54]



86 **87** **88** (25%)

(35)

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4.9 BISKETENES

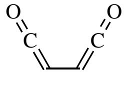
The simplest bisketene, C_2O_2, or CO dimer (**1**), has been the object of continuing theoretical[1,2] and experimental[3] examination, and while an energy minimum structure for this molecule has been calculated,[1] it is still unknown experimentally. It was concluded that this species is an intrinsically short-lived molecule that was predicted to dissociate rapidly to CO within a few nanoseconds.[3] Carbon suboxide, C_3O_2 (**2**), was the first bisketene that was prepared, and was discovered by Diels and Wolf in 1906,[4] only 1 year after the report of the first ketene, $Ph_2C{=}C{=}O$. Carbon suboxide, a stable, colorless gas with a linear structure, is discussed in Section 4.11. Ketene **3** has been described as a 1,2-bisketene, and **1** and **2** may correspondingly be classified as (0,0) and (1,1) bisketenes; **4–7** are the next higher homologues of this series, respectively. Staudinger and Kreis in 1923 reported a systematic effort to prepare the linear α,ω-bisketenes, but were unsuccessful in their attempt to prepare O=C=CHCH=C=O (**3**) by the double decarboxylation of **8** and obtained the bis(anhydride) **9** instead (equation 1).[5]

$O{=}C{=}C{=}O$

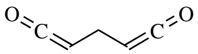
1 (0,0)

$O{=}C{=}C{=}C{=}O$

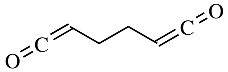
2 (1,1)



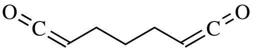
3 (1,2)



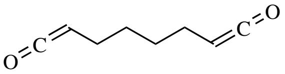
4 (1,3)



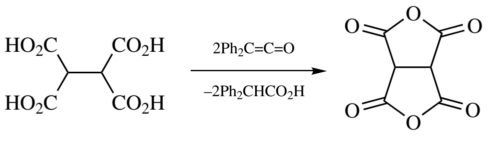
5 (1,4)



6 (1,5)

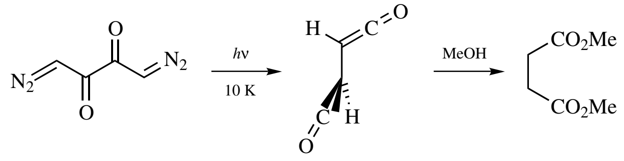


7 (1,6)

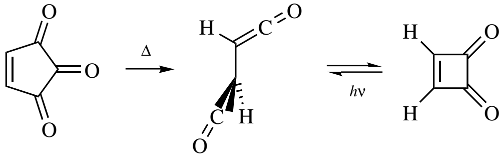


8 **9** (1)

The parent 1,2-bisketene **3** was generated by a double Wolff rearrangement of **10** in an argon matrix at 10 K, identified by its IR absorption at 2125 cm^{-1}, and captured by methanol as the succinate (equation 2).[6] Pyrolytic decarbonylation of the trione **11** also gave **3**, as evidenced by the formation of cyclobutenedione **12** in 9% yield (equation 3).[7] Photolysis of **12** in solution gave evidence for the formation of **3**, with IR absorption at 2120 cm^{-1} and the ^{1}H NMR signal at δ 3.20 (equation 3).[8] Reviews on cyclobutenedione chemistry have appeared.[8a,b]

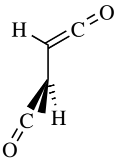


10 **3** (IR 2125 cm^{-1}) (2)

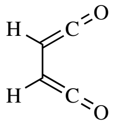


11 **3** **12** (3)

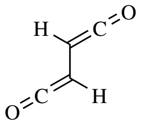
Initial computations at the RHF/3-21G level indicated that the bisketene **3a** was an energy minimum, 4.1 kcal/mol more stable than the cyclobutenedione **12**.[9] However, further computations at the MP2/6-31G*//MP2/6-31G* level showed that bisketene **3** was most stable in a twisted, almost perpendicular geometry, with energies relative to cyclobutenedione **12** for **3**, *cisoid* **3a**, and *transoid* **3b** of 2.9, 5.6, and 4.0 kcal/mol, respectively.[9a] The planar geometry was proposed to be disfavored because of the repulsion between C_2 of the two ketenyl moieties arising from the high π-electron density at these atoms and the absence of any favorable conjugative interaction between the two ketenyl groups.[9a] The preference for the twisted conformation of 1,2-bisketenes was confirmed by the X-ray structure of the silyl-substituted tetraketene **14** obtained from photolytic ring opening of the bis(cyclobutenedione) **13**, with dihedral angles of 119° between the adjacent ketenyl groups (equation 4).[10] The tetraketene **14** was thermodynamically stable to reversion to **13**, confirming the predictions based on theoretical calculations.[9] The measured dipole moment of 2.7 *D* of the bisketene **26** (vide infra)[10a] and the photoelectron spectrum[10a] also confirm that 1,2-bisketenes prefer twisted conformations.



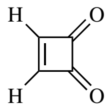
3



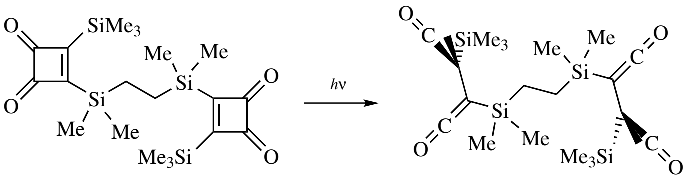
3a



3b



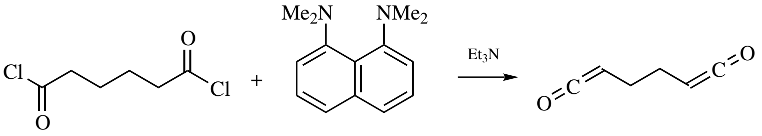
12



13 **14**

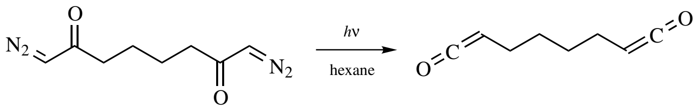
(4)

The 1,4-bisketene **5** was formed by the double dehydrochlorination of adipyl chloride **15** using 1,8-bis(dimethylamino)naphthalene (**16**) as a strong stochiometric base and Et_3N as a kinetic shuttle base (Section 3.2.2), and was identified by the IR absorption at 2114 cm^{-1} (equation 5) and by capture as the tetraadduct by the stable free radical TEMPO (Section 5.7).[11] The 1,5-bisketene **6** was prepared in a similar fashion.[11] The 1,6-bisketene **7** was prepared by a photochemical double Wolff rearrangement of bis(diazo ketone) **17**, identified by its IR absorption at 2120 cm^{-1}, and trapped with benzylamine as the diamide **18** (equations 6, 7).[11]

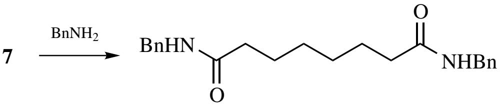


15 **16** **5** (IR 2114 cm^{-1})

(5)

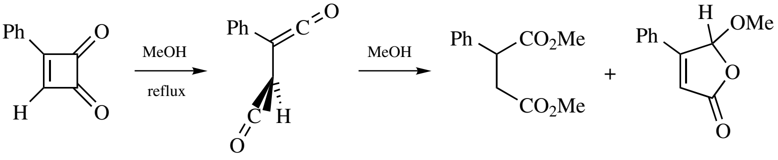


17 **7** (IR 2120 cm^{-1}) (6)

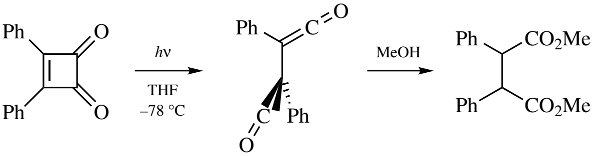


18 (47%) (7)

The monophenyl bisketene **20** was first generated by refluxing of the cyclobutenedione **19** in MeOH, which led to the succinate ester **21** and the lactone **22**, although there was some question about whether the products could arise from attack on **19** (equation 8).[12] Photolysis of 3,4-diphenyl-1,2-cyclobutenedione **22** in THF at −78 °C gave the bisketene **23**, as observed by the IR absorption at 2103 cm^{-1} that persisted for several days at −78 °C (equation 9).[13–16] Upon generation of **23** in MeOH at 77 K, IR bands at 2100 and 2112 cm^{-1} were observed, and at −80 °C these decayed, with concomitant formation of **24** (equation 9).[13]

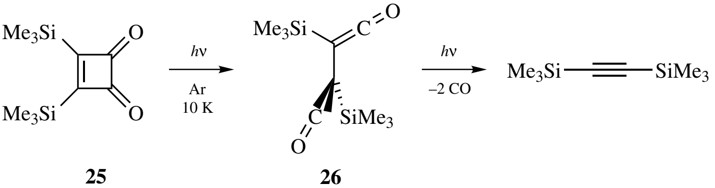


19 **20** **21** **22** (8)

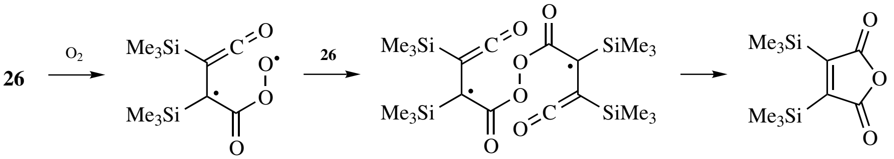


22 **23** (2103 cm^{-1}) **24** (9)

1,2-Bis(trimethylsilyl)cyclobutenedione **25** on thermal or photochemical ring opening gave the bis(trimethylsilyl)-1,2-bisketene **26** in a process that by MP2/6-31G*//MP2/6-31G* computations was exothermic by 5.0 kcal/mol (equation 10).[9a,17,18] The thermal conversion at 100 °C was quantitative, and **26** appeared to be stable indefinitely in the absence of moisture or oxygen, but on continued photolysis underwent decarbonylation, forming bis(trimethylsilyl)acetylene (equation 10).[17] Reaction of **26** with oxygen gave the maleic anhydride **28** in a reaction suggested to involve the peroxide intermediate **27** (equation 11).[17]



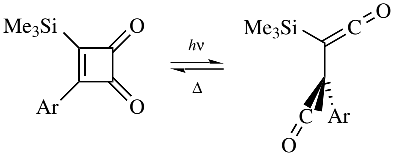
25 **26** (10)



27 **28**

(11)

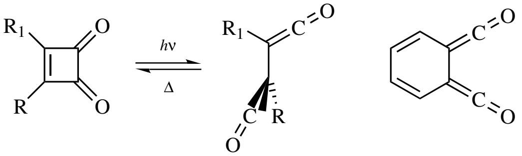
A series of aryl-substituted bisketenes **30** were generated photochemically, and the rates of their thermal conversion back to cyclobutenediones **29** were correlated with the $\sigma_p{}^+$ constants of the aryl substituents, with $\rho^+ = -1.10$ (equation 12).[19] The ketenes were predicted to be stabilized by electropositive substituents,[18] and the cyclobutenediones stabilized by electron donors. These effects were reflected in both the rates of ring closure and the amount of bisketene **30** present in thermal equilibrium with **29**.[19]



(12)

29 (Ar = 4-XC_6H_4) **30** (**a**) X = H, MeO (**b**), Me (**c**), Cl (**d**)

A larger group of 1,2-bisketenes **32** and others, including **33**, have been generated by photolysis of 1,2-cyclobutenediones **31**, and the kinetics of their ring closure (equation 13) were measured by UV or by TRIR spectroscopy, as reported in Table 4.6.[20,21] All of these bisketenes were identified by their characteristic IR bands (Table 4.6), and in a number of cases the rate constants for ring closure were intermediate between the faster rates that could be measured by TRIR spectroscopy and the slower rates that were accessible by conventional UV spectroscopy.



(13)

31 **32** **33**

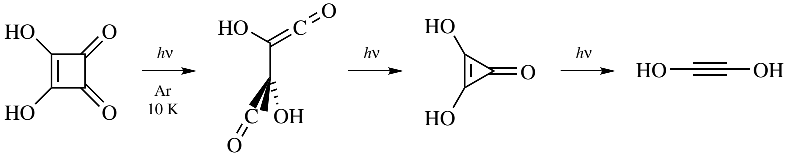
A study of 1,2-bisketene **32o** ($R = R^1 = PhMe_2Si$) showed that this had a rate of ring closure similar to that of the corresponding substrate with Me_3Si substituents, and there was no evidence for an interaction of the phenyl group with the ketene functionalities that would affect the rate of ring closure or of reaction with H_2O.[22] Similarly, there were no noticeable conjugative effects of phenyl on the ^{13}C, ^{17}O, or ^{29}Si NMR spectra of $PhSiMe_2CH{=}C{=}O$.[22]

TABLE 4.6 Rate Constants for Ring Closure of Bisketenes 28 in CH_3CN at 25 °C[20,21]

R, R^1		ν_1, ν_2 (cm^{-1})	k_{obs} (s^{-1})
H, Ph	**20**	2103, 2127	1.70×10^{-4}
Ph, Ph	**23**	2096, 2110	3.89×10^{-2}
Me, Me	**32a**	2092, 2114	3.60×10^{-2}
t-Bu, *t*-Bu	**32b**	2087, 2113	8.19×10^{-4}
Me_3Si, Me_3Si	**26**	2084	$(10^{-10})^b$
Me_3Si, Ph	**30a**	2093	2.03×10^{-6}
Me_3Si, Me	**32c**	2101	4.37×10^{-6}
Me, Ph	**32d**	2093, 2112	3.50×10^{-2}
PhS, PhS	**32e**	2112	5.62×10^{-3}
EtO, Me_3Si	**32f**	2090, 2104	1.77×10^{-3}
CN, Ph	**32g**	2116, 2140	8.51×10^{-2}
Cl, Cl	**32h**	2113, 2154	3.20×10^{3}
Br, Ph	**32i**	2105, 2132	0.137
Cl, MeO	**32j**	2098, 2142	2.97×10^{4}
t-BuO, *t*-BuO	**32k**	[a]	2.5×10^{4}
t-Bu, *i*-PrO	**32l**	2092, 2108	3.2×10^{4}
(t-$BuMe_2SiC{\equiv}C)_2$	**32m**	2111, 2119	4.23×10^{-3}
$(PhC{\equiv}C)_2$	**32n**	[a]	1.59×10^{-2}
	33	2072, 2128	1.9×10^{4}

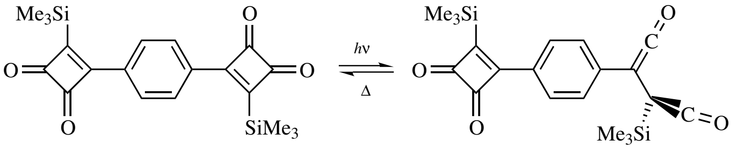
[a] Not measured.
[b] Estimated.

Photolysis of squaric acid (**34**) in an Ar matrix at 10 K gave IR bands at 2162, 2132, and 2092 cm^{-1}, attributed to the bisketene **35** (equation 14).[23] Further photolysis led successively to deltic acid **36** and dihydroxyacetylene (**37**). Attempted sublimation of **36** at 160 °C gave water and carbon suboxide O=C=C=C=O.[23]

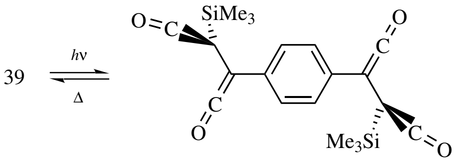


34 **35** **36** **37** (14)

Photolysis of the bis(dioxocyclobutenyl)benzene **38** gave the bisketene **39** (equation 15) and then the tetraketene **40** (equation 16), which was long-lived at room temperature but was converted thermally back to **39** and **38** in processes whose rates were measured using UV spectroscopy.[24]

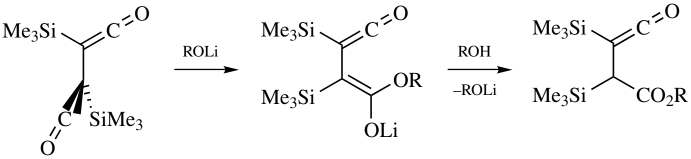


38 **39** (15)

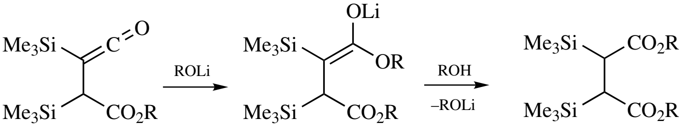


40 (16)

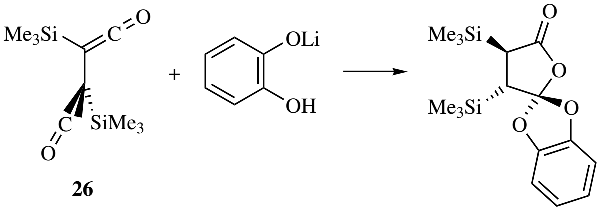
The reaction of bis(trimethylsilyl)-1,2-bisketene **26** with neat alcohols followed by rapid removal of the solvent permitted isolation of ketenyl esters **42**.[17] The reaction was catalyzed by added lithium alkoxide in a process suggested to proceed with formation of the enolate **41** (equation 17).[25] Further addition of alcohols to **26** catalyzed by lithium alkoxides was rapid and gave succinate esters **44** by the proposed intermediacy of **43** (equation 18).[25] The use of the alkoxide catalyst minimized desilylation, which was a predominant pathway in the prolonged reaction of **26** with alcohols in the absence of base. The efficient addition of alkoxides to the ketenyl carbonyl was attributed to lithium coordination to the ketenyl oxygen.[25] The monoanion of catechol reacted with **26** to give ortho esters **45** under similar conditions (equation 19).[25]



26 **41** **42** (17)

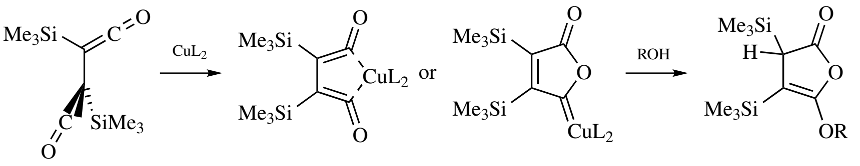


42 **43** **44** (45–72%) (18)



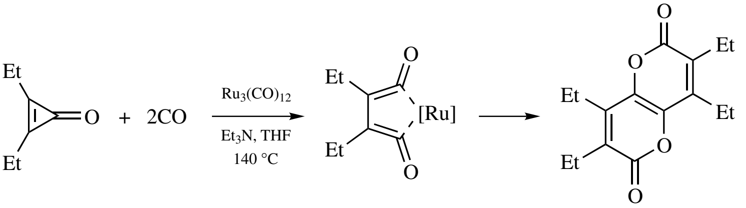
26 **45** (64%) (19)

The reactions of alcohols with bisketene **26** catalyzed by Cu(I) and Cu(II) complexes gave butenolide **48** in a process that may conceivably involve reaction of complexes **46** or **47** with the alcohol (equation 20).[26,27] Other bisketenes also formed butenolides.[26,27] Chiral ligands on the catalyst did not give enantioselectivity in the isolated **48**, a result attributed to racemization of the product.[27] An analogous ruthenium complex **50** was proposed to form in the reaction of diethylcyclopropenone (**49**) with $Ru_3(CO)_{12}$ forming the pyranopyrandione **51** (equation 21).[28]



26 **46** **47** **48** (98%, R = Et)

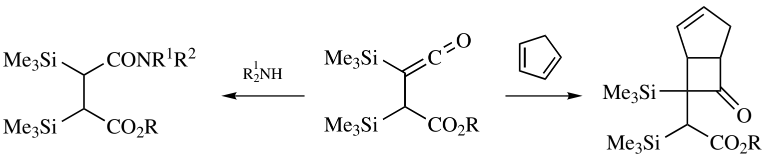
(20)



49 **50** **51** (70%)

(21)

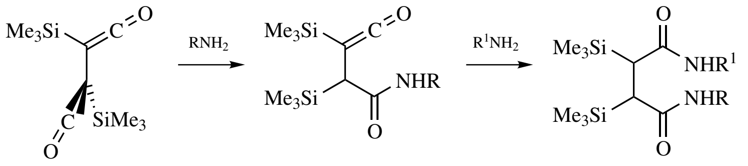
The reactions of **26** with alcohols catalyzed by chiral amines gave 19–34% *ee* in formation of ketenyl esters **42** (equation 17).[26,27] Catalysis of the addition of alcohols and other nucleophiles to **26** by lactams was effective but gave low % *ee*.[26,27] Ketenyl esters **42** reacted with amines to give ester amides **52** (equation 22),[26,27] with thiols to give mixed esters, and with cyclopentadiene to give the [2 + 2] cycloaddition product **53** (equation 22).[26,27]



52 (98%, R^1 = *i*-Pr) **42** **53** (71%, R = Et)

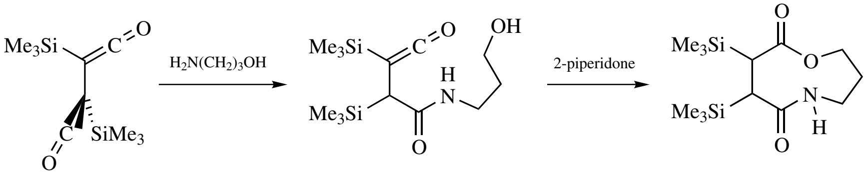
(22)

The bisketene **26** reacted rapidly with one equivalent of primary alkylamines to give selectively monoketenyl amides **54** that were isolated and fully characterized. These reacted with a second amine in a much slower process to give diamides **55** as *dl* and *meso* isomers that were separated by chromatography (equation 23).[29] The kinetics and mechanisms of these processes have been examined (Section 5.5).[29] Reaction of **26** with *R*-1-phenylethylamine gave a selectivity of 2:1 in formation of the new chiral center, and this product was purified by recrystallization to give **54** with a 98:2 *dr*.[30] There was high diastereoselectivity in the reaction of **54** with alcohols.[27,30] Reaction of **26** with 3-amino-1-propanol gave a ketenyl amide **56** that cyclized to **57** on catalysis with 2-piperidone (equation 24).[27] A single secondary amine reacted with **26** with cyclization to form aminodihydrofuranones **57a** (equation 24a).[31]



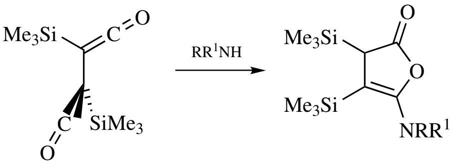
26 **54** (~95%, R = Bn) **55** (~90%, *dl* + *meso*)

(23)



26 **56** (>99%) **57** (78%)

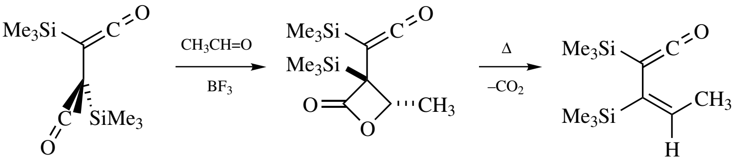
(24)



26 **57a** (97–99%)

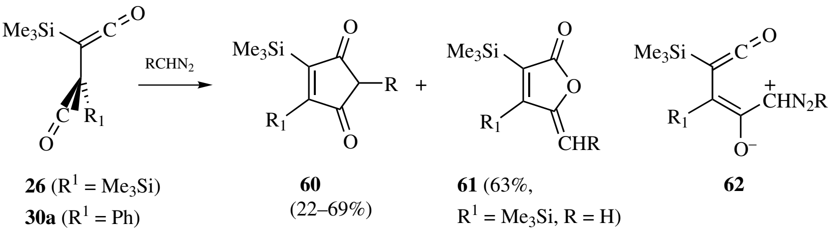
(24a)

Reaction of **26** with $CH_3CH{=}O$ catalyzed by BF_3 gave the β-lactone **58** as the only product detected, which on pyrolysis gave decarboxylation to the vinylketene **59** (equation 25).[32] The reaction of **26** and of the unsymmetrical bisketene **30a** with CH_2N_2 gave mixtures of cyclopentenediones **60** and lactones **61** (R = H), while Me_3SiCHN_2, and $PhCHN_2$ gave only **60** (equation 26).[32] The preference for formation of **60** with the bulkier substituted diazomethanes was attributed to in-plane attack on the ketenyl group from the side opposite the group R^1 forming the intermediate **62**. Dimethoxycarbene from **66** reacted with **26** to give cyclopentendione **67** (equation 27).[32] Heating the cyclobutenedione **68** to form the bisketene **69** resulted in formation of the isolable ketene product **71**, and was interpreted to proceed by [2 + 2] cyclodimerization to **70**, which reacted by decarbonylation and rearrangement to give **71** (equation 28).[8]

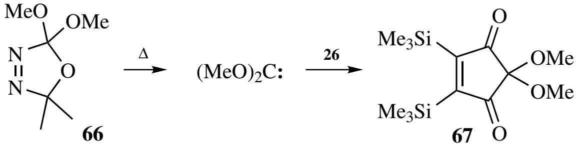


26 **58** (82%) **59** (35%)

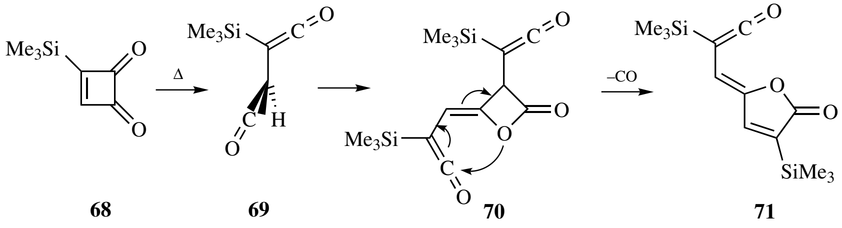
(25)



(26)

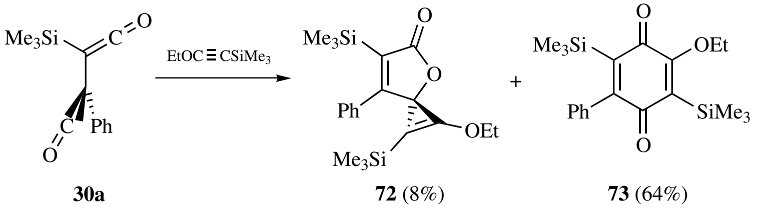


(27)



(28)

The nucleophilic alkyne $Me_3SiC{\equiv}COEt$ reacted with **30a** to give spiro-cyclopropenylfuranone **72**, and also reacted by [4 + 2] cycloaddition to form benzoquinone **73** (equation 29).[32] The metal complexed bisketene **74** analogous to **46** and **50** reacted with diarylalkynes to give **75** (equation 30).[33] The X-ray structure of complex **74** (Figure 4.3) showed C-C-O bond angles of 137.8 and 138.5 °, indicating a major diminution of ketenyl character, as also manifested by the IR stretching frequency of 1810 cm^{-1}.[34]



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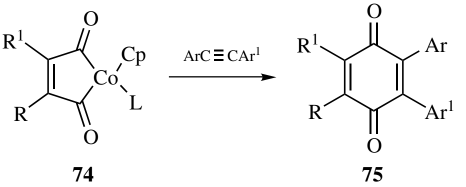


(30)

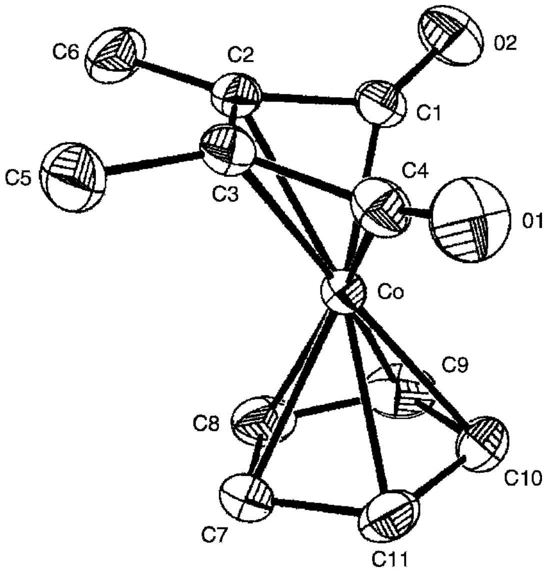
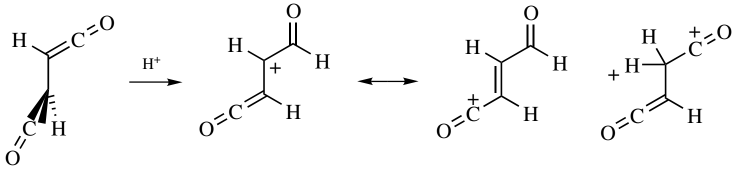


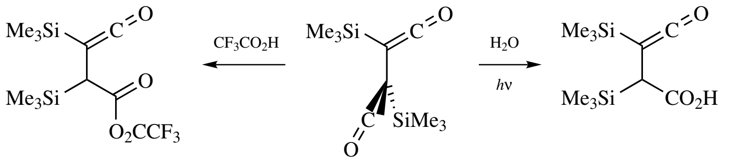
Figure 4.3 X-ray structure of **74** (reprinted from ref. 34 with permission of the American Chemical Society).

Molecular orbital calculations predicted a preference for electrophilic attack on C_1 of the 1,2-bisketene **3**. This was explained on the basis of the extended conjugation possible in the cation **76**, in contrast to the less extensive acylium conjugation possible in **77**, which would result from the usual electrophilic attack at C_2 of ketenes (equation 31).[35] Nevertheless, CF_3CO_2H addition and hydration of **26** during photolysis gave the products **77** and **78**, respectively, arising from protonation of C_2 (equation 32).[36] This result permitted the observation of the ketenyl acid **78**, which may also be formed as an unobserved intermediate during the neutral hydration of **26**.



3 **76** **77**

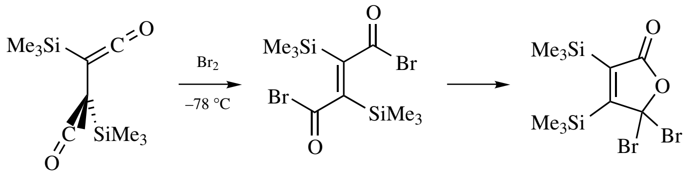
(31)



77 **26** **78**

(32)

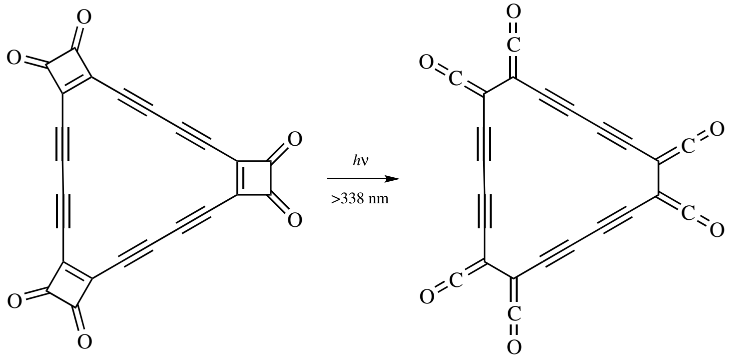
Reaction of **26** with Br_2 gave the fumaryl bromide **79** resulting from 1,4-addition, with the stereochemistry of **79** proven by X-ray crystallography (equation 33).[36] However, **79** was unstable and rearranged to the dibromofuranone **80** by an apparent ionization-recombination mechanism (equation 33).[36] The calculated transition structure for the reaction of **26** with Br_2 showed initial coordination of Br_2 to both carbonyl carbons, followed by rotation to the *trans* form.[36]



26 **79** **80**

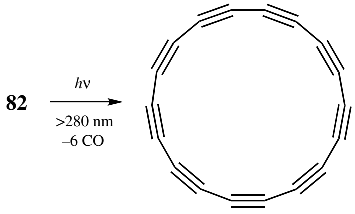
(33)

Photolysis of alkynylcyclobutenedione **81** at λ >338 nm gave rise to ketenyl IR absorption at 2115 cm^{-1}, attributed to hexaketene **82** (equation 34).[37] Further irradiation at λ >280 nm resulted in decarbonylation and possible formation of *cyclo*-C_{18} (**83**) (equation 35).[37] A molecule $C_{60}H_6(CO)_{12}$ containing six cyclobutenedione units on a bicyclic scaffold gave a negative-ion (ICR-LD) mass spectrum containing (among others) the $C_{60}^{\bullet -}$ ion, suggesting a decarbonylation pathway analogous to that of equation 34.[38]



81 **82**

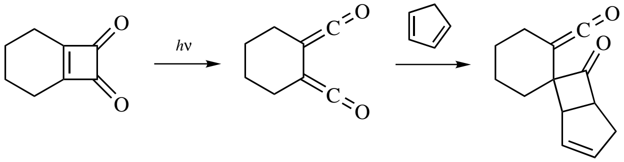
(34)



83

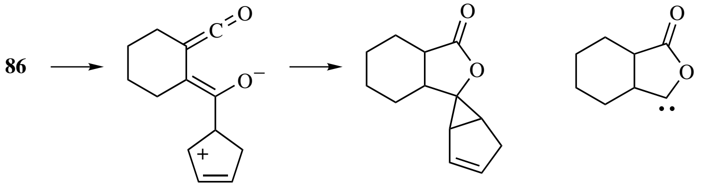
(35)

Photolysis of cyclobutenedione **84** in the presence of cyclopentadiene led to spiro adduct **88**. This could form either by [2 + 2] cycloaddition of the intermediate ketene **85**, forming **86** (equation 36), which rearranged with ring opening directly to **88**, or through an intermediate zwitterion **87** (equation 37).[39] Other cyclobutenediones and cyclobutanones[40] behaved similarly. Oxocarbene intermediates such as **89** isomeric with ketene **85** have been considered as reaction intermediates but have not been observed directly.



84 **85** **86**

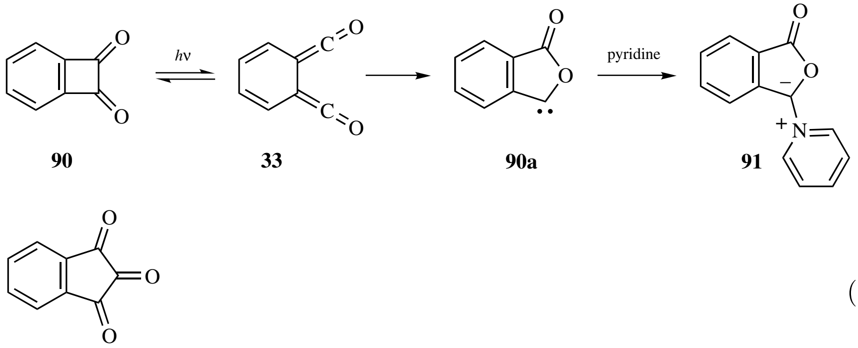
(36)



87 **88** **89**

(37)

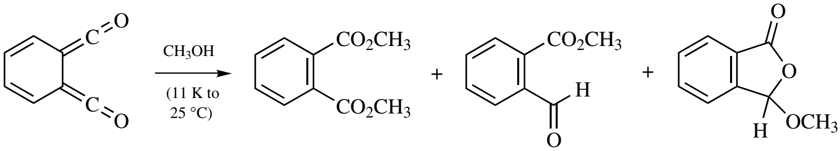
Photolysis of benzocyclobutenedione **90** formed the bisketene **33**,[41–43] detected by UV absorption at 380 nm[43] and by IR absorption at 2077 and 2138 cm^{-1} in a matrix at 11 K (equation 38).[42] Photolysis of **90** in solution using TRIR spectroscopy also gave **33**, with IR bands at 2072 and 2128 cm^{-1}, and reformation of **90** with a rate constant (Table 4.6) for ring closure of **90** back to **33** of $1.9 \times 10^4\ \text{s}^{-1}$, as measured by IR (equation 38).[20,21,43] In the presence of pyridine the ylide **91** with characteristic UV absorption was observed, and was attributed to capture of carbene **90a**, or reaction with **33** (equation 38).[43,44] High-intensity (laser jet) photolysis of the trione **92** in benzene formed the bisketene **33**, leading to an 11% observed yield of the dione **90**.[45] Photochemical generation of **33** in MeOH led to formation of the diester **93** as well as the products **94** and **95** from addition of a single MeOH (equation 39).[44]



90 **33** **90a** **91**

92

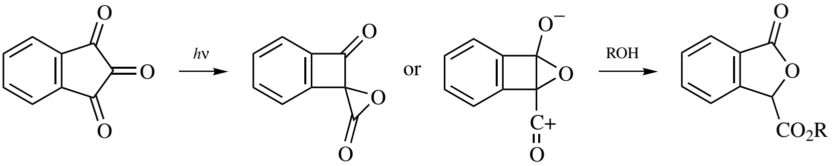
(38)



33 **93** **94** **95**

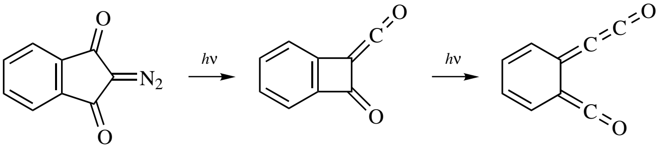
(39)

Photolysis of **92** in alcohol solutions was interpreted as involving the intermediates **96** or **97**, which gave the observed product **98** (equation 40).[46] Photolysis of **90** led to the formation of bisketene **33**, as indicated by TRIR spectroscopy,[21,47] but no absorption for the carbene **90a** was detected. The formation of **91** from **33** upon addition of pyridine argues against the intervention of the carbene **90a**, which has not been detected directly.[47] High-intensity laser photolysis of the diazo diketone **100** in CH$_3$OH was proposed to lead to **101** and then to **102** on the basis of capture of the corresponding esters (equation 41).[48]



92 **96** **97** **98**

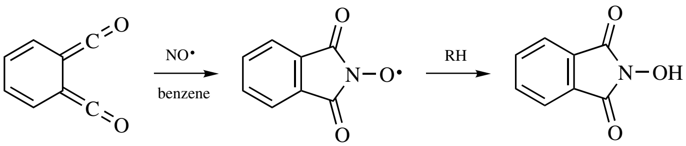
(40)



100 **101** **102**

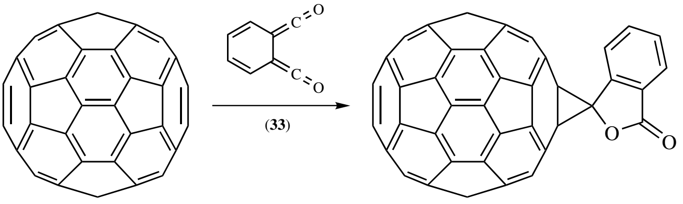
(41)

Photolysis of **90** forming **33** in the presence of the stable free radical NO gave **104**, proposed to form from nitroxyl radical **103** (equation 42).[49] Reaction of **33** with NO$_2$ by a [4 + 2] cycloaddition path was followed by loss of NO to give phthalic anhydride.[49] The bisketene **33** generated by photolysis reacted with C$_{60}$ to form the cycloaddition product **104a** (equation 42a).[50]



33 **103** **104** (4%)

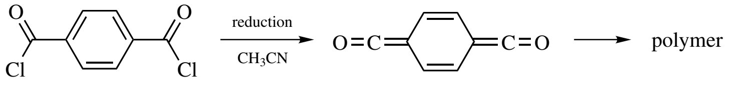
(42)



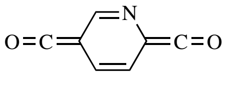
104a

(42a)

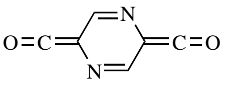
Electrochemical reduction of terephthalyl chloride **105** was proposed to form the bisketene **106**, which led to the observed polymer (equation 43).[51] The aza and diaza analogues **107** and **108** were suggested to form by similar routes.[51]



105 **106** (95%) (43)

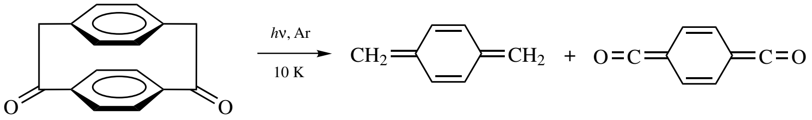


107



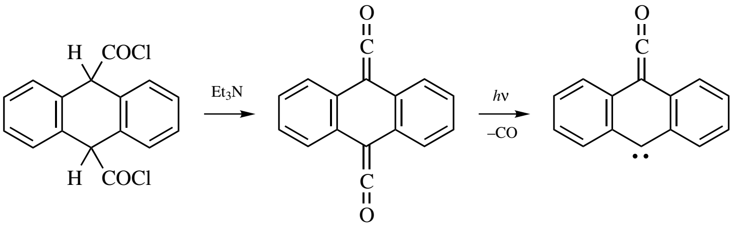
108

Photolysis of [2.2]paracyclophane-1,10-dione (**109**) in Ar at 10 K led to *p*-xylylene (**110**) and 1,4-dicarbonyl-2,5-cyclohexadiene (**106**), as identified by its IR band at 2082 cm^{-1} (equation 44).[52,52a] Further photolysis of **106** gave decarbonylation, but no further photo product could be identified. The RHF/6-31G (d,p) calculated structure of **106** gave the following bond distances (Å): C_1O (1.147), C_1C_2 (1.314), C_2C_3 (1.473), C_3C_4 (1.324), C_3H (1.075) and angles (degrees): $C_1C_2C_3$ (117.8 °), $C_2C_3C_4$ (121.1 °), C_3C_4H (120.1 °).[52] The calculated ketenyl IR band was at 2077 cm^{-1}. This was in contrast to the isomeric 1,2-bisketene **33**, which showed IR bands at 2077 and 2138 cm^{-1}, assigned to the coupled symmetric and antisymmetric vibrations of the ketene moieties, respectively.[52] For **106** the coupled vibration showed zero intensity.[52]

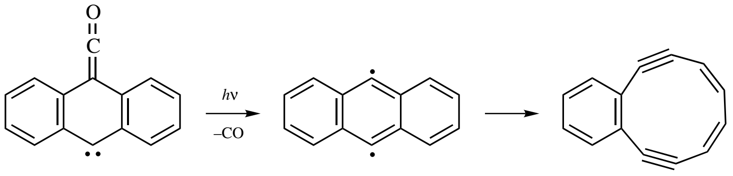


109 **110** **106** (IR 2082 cm^{-1}) (44)

The bisketene **112** was obtained as an isolable solid by dehydrochlorination of the acyl chloride **111**,[53] and upon photolysis in argon at 10 K led to the carbene ketene **113**, identified by the strong IR absorption at 2105.8 cm^{-1} (equation 45).[54] Further photolysis gave the presumed diradical intermediate **114**, which formed **115** (equation 46).[54]



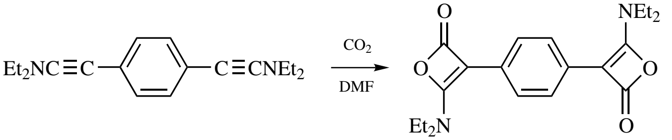
111 **112** (IR 2082 cm^{-1}) **113** (IR 2105.8 cm^{-1}) (45)



113 **114** **115**

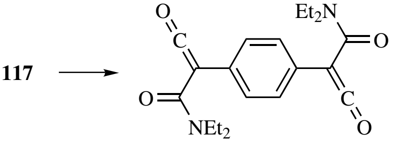
(46)

Reaction of 1,4-bis(diethylaminoethynyl)benzene **116** with CO_2 was proposed to form unsaturated β-lactone **117** (equation 47), which gave formal ring opening to bis(acylketene) **118** (equation 48).[55] This was not observed but reacted further with the ynamine by [4 + 2] cycloaddition to give observed bis(pyrone) **119** (equation 49).[55] Stepwise generation of the ketenyl groups seemed likely.[55]



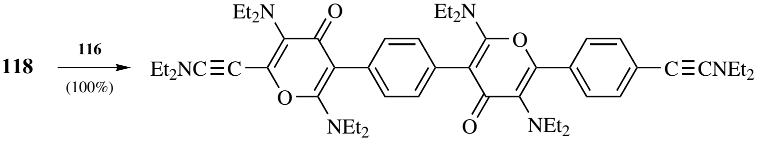
116 **117**

(47)



118

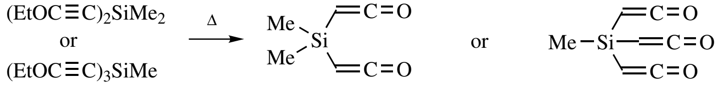
(48)



119

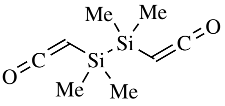
(49)

Thermolysis of the bis- and tris-(ethoxyethynyl)silanes formed 1,3-bisketene **121** and trisketene **122**, respectively (equation 50).[56] Both **121** and **122** were isolated as long-lived species, and *ab initio* molecular orbital calculations indicated that the ketenyl groups in these molecules were each stabilized as much by the silicon as in $Me_3SiCH{=}C{=}O$.[56] Analogous ethoxyalkyne decompositions gave the 1,4-bisketene **123**,[57] the 1,6-bisketene **124**,[57] and the 1,8-bisketene **125**.[22]

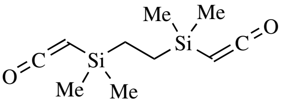


121 (75%, IR 2129, 2108 cm^{-1}) **122** (82%, IR 216, 2108 cm^{-1})

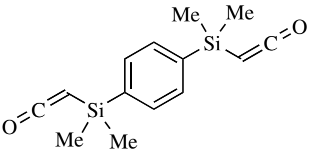
(50)



123 (IR 2108, 2052 cm^{-1})

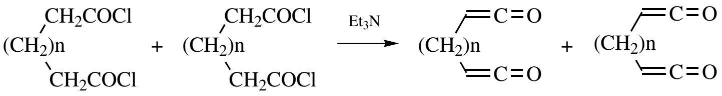


124 (IR 2115, 2052 cm^{-1})



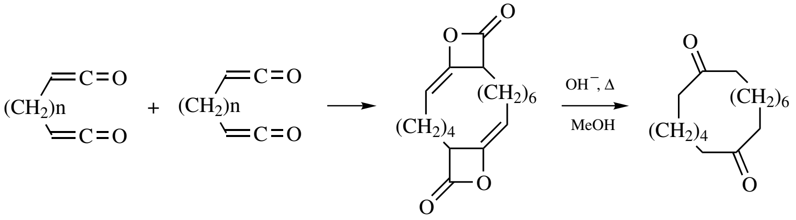
125 (IR 2115, 2052 cm^{-1})

The reaction of diacyl chlorides with Et_3N followed by hydrolysis and decarboxylation under basic conditions (Blomquist reaction)[58] has been applied with a 1:1 mixture of suberyl chloride (**126**) and sebacyl chloride (**127**) to give the mixed diketone **130** arising from the mixed dimer **129** together those from the homodimerization of the individual diacyl chlorides (equations 51, 52).[59] These reactions can be formulated as involving bisketenes **7** and **128** but may proceed through a stepwise formation of monoketenes instead.



126 (n = 4) **127** (n = 6) **7** (n = 4) **128** (n = 6)

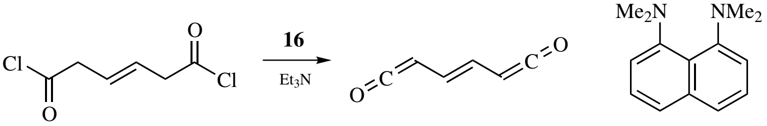
(51)



7 (n = 4) **128** (n = 6) **129** **130**

(52)

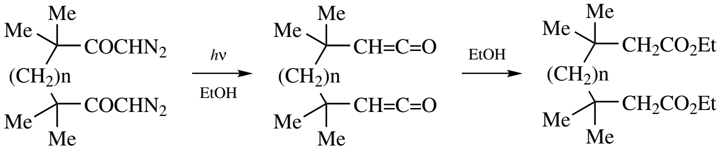
Dehydrochlorination of **133** with 1,8-bis(dimethylamino)naphthalene (**16**) as a stochiometric base and Et_3N as a catalytic shuttle base in toluene, as described above (equations 5–7),[11] gave 1,2-bis(ketenylidene)ethylene *E*-**134**, identified by IR absorption at 2118 cm^{-1} (equation 53).[60]



133 *E*–**134** (IR 2118 cm^{-1}) **16**

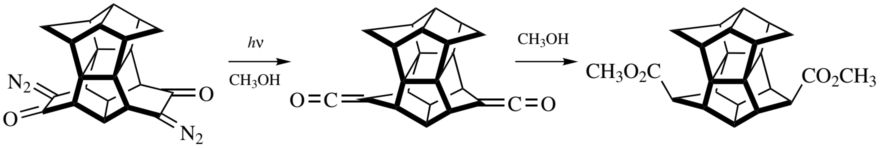
(53)

Photolyses of bis(diazo ketones) in the presence of nucleophiles may be represented as forming bisketenes. For example, the conversion of **135** could form **136**, which was trapped as the diester **137** (equation 54),[61] and in the pagodane system photolysis of the bis(diazo ketone) **138** formally gave the bisketene **139**, which was trappped as **140** (equation 55),[62] but these reactions were probably largely sequential. As noted above, bisketenes have been observed from photolysis of bis(diazo ketones) in the absence of trapping agents and directly observed in solution by IR (equation 6).[11]



135 **136** **137** (80%, n = 6,8)

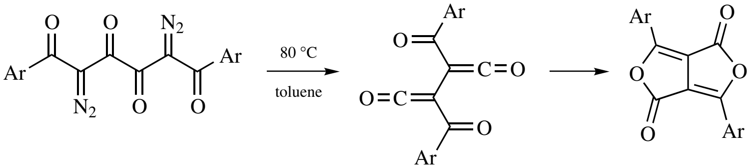
(54)



138 **139** **140** (90%)

(55)

Thermal Wolff rearrangement of the bis(diazo ketones) **142** led to products **144** that are formally derived from bisketenes **143** (equation 56).[63]

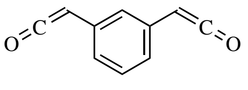


142 Ar = Ph, 4-Anis,
4-Tol, 4-ClC$_6$H$_4$

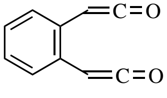
143 **144** (64–89%)

(56)

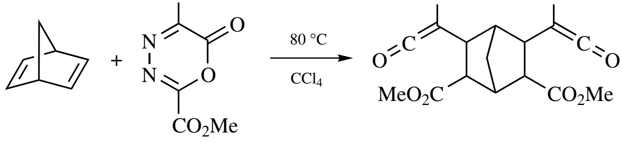
The aryl bisketenes **145** and **146** were generated by Wolff rearrangement and bis(dehydrochlorination), respectively, observed by IR, and trapped with TEMPO as the tetraaddition products.[64] Norbornadiene reacted by [4 + 2] cycloadditions with two molecules of **147** followed by loss of two N_2 molecules to form the isolable bisketene **148** (equation 57).[65]



145 (IR 2110 cm^{-1})



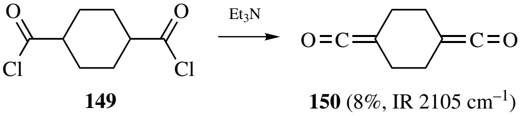
146 (IR 2115 cm^{-1})



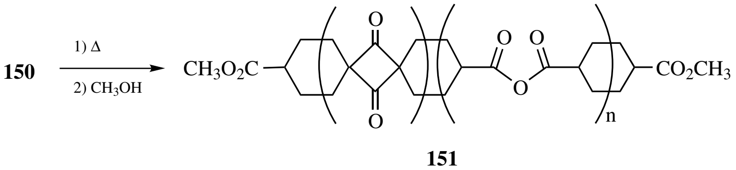
147 **148** (36%, IR 2105, 2095 cm^{-1})

(57)

Reaction of diacyl chloride **149** with Et_3N gave ketene **150** as an isolable but sensitive yellow solid (equation 58).[66] The ketene polymerized to give a polymer containing cyclobutanedione and acid anhydride units that formed **151** upon reaction with CH_3OH (equation 59).[67]



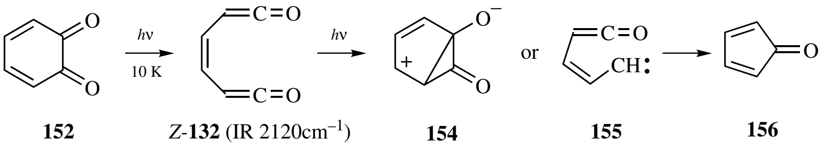
(58)



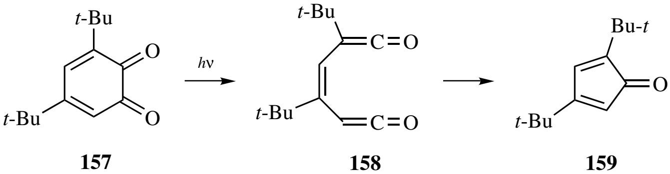
(59)

Other bisketenes are noted in Sections 3.4.3, 3.5, and 4.11.

Photolysis at λ >300 nm of benzoquinone (**152**) in an argon matrix at 10 K gave *Z*-bisketenylethylene (**134**), identified by its IR bands at 2105 and $2115\,cm^{-1}$, and further photolysis at 254 nm resulted in decarbonylation and formation of cyclopentadienone **156**, possibly by formation of the zwitterion **154** or the carbene **155** (equation 60).[68] Photolysis of the di-*tert*-butylquinone **157** gave the bisketene **158**, identified by its IR absorption at $2173\,cm^{-1}$, and this formed the isolable cyclopentadienone **159** (equation 61).[69]

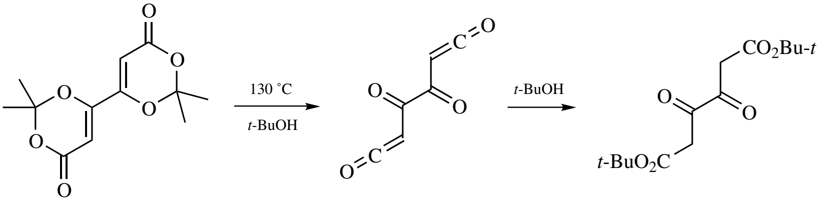


(60)



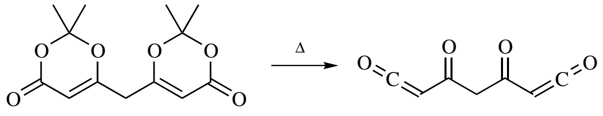
(61)

The bisdioxinones **160** and **163** are potential precursors to bisketenes **161** and **164**, respectively, but **160** upon heating with *tert*-butanol was shown to react sequentially to form **162** (equation 62).[70] Heating of bis(dioxinone) **163** in chlorobenzene gave products ascribed to intramolecular reactions of the bisketene **164** (equation 63).[71] The bis(cyclohexadienone) **165** gave **167** upon photolysis in methanol. This may have involved bisketene **166** on photolysis or sequential reaction as the major pathway (equations 64, 65).[72]



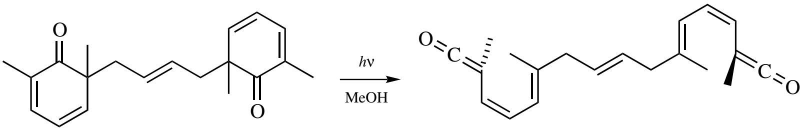
160 **161** **162** (94%)

(62)



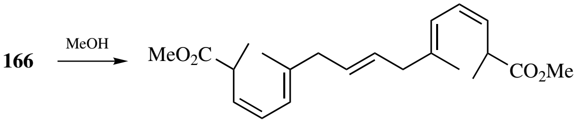
163 **164**

(63)



165 **166**

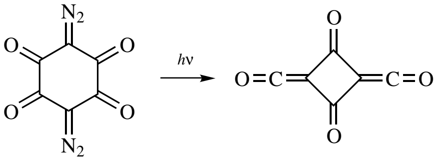
(64)



167 (48%)

(65)

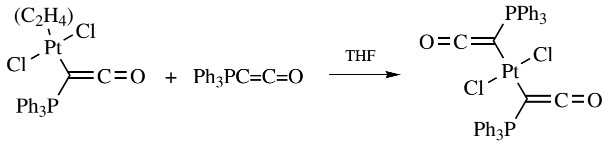
As noted in Section 3.3.2, photolysis of **168** in an Ar matrix at 17 K gave the cyclic diacylbisketene **169**, with IR bands at 2101 and 1747 cm^{-1} (equation 65a).[72a]



168 **169** (IR 2101 cm^{-1})

(65a)

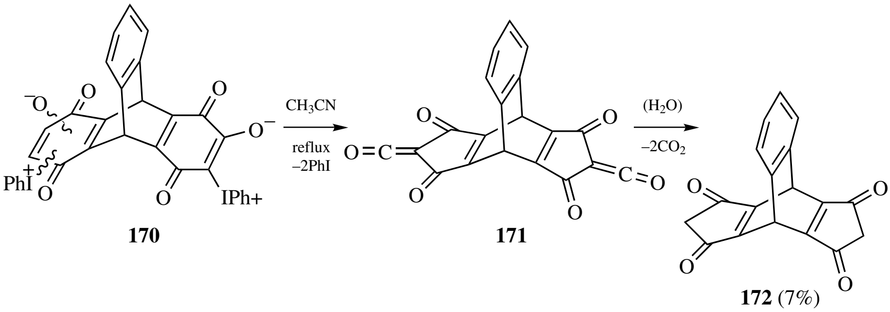
Reaction of the Pt ketenyl complex **168** gave the unique bisketene **169** (equation 66; see also Section 3.8).[73] The electronic structure of **169** has been examined by quasi-relativistic density functional computations.[74]



168 **169** (59%, IR 2062 cm^{-1})

(66)

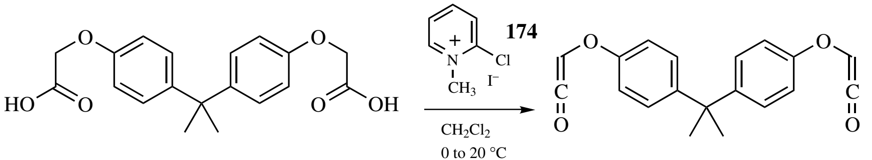
The bis(phenyliodonium) ylide **170** on thermolysis formally produced the bisketene **171**, which upon hydration and decarboxylation led to the tetraketone **172** (equation 67).[75]



170 **171** **172** (7%)

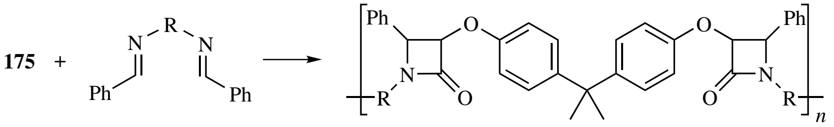
(67)

Dehydration of **173** with Mukaiyama's reagent **174** gave in a formal sense the bisketene **175** (equation 68), which reacted with the bisimine **176** to give the poly(2-azetidinone) **177** (equation 69).[76]



173 **175**

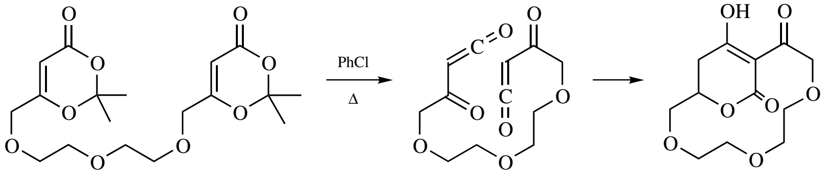
(68)



176 (R = [(CH$_2$)$_{12}$] **177**

(69)

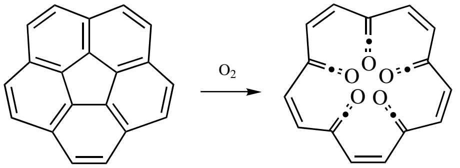
Thermolysis of the bis(dioxinone) **178** gave the polycycle **180**, which could result from the bisketene **179** (equation 70).[77]



178 **179** **180** (77%)

(70)

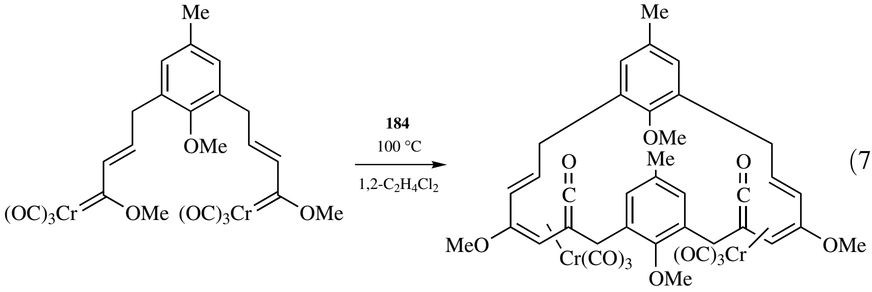
As noted in Section 3.7, computational studies of possible products $C_{60}O_n$ that conceivably could be formed by the oxidation of the fullerene C_{60} included pentaketene $C_{60}O_5$, as represented by the pentabenzocyclopentyl unit fragment of C_{60} **181** forming **182** (equation 71).[78]



181 **182**

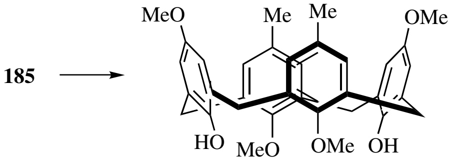
(71)

Bis(chromium carbene) complexes may also be represented as forming bisketene intermediates. Reaction of bis(chromium complex) **183** with the dialkyne **184** formally gave the bis(ketene) **185** (equation 72), which gave calixarene **185** (equation 73).[79] Other examples are given in Section 4.8.

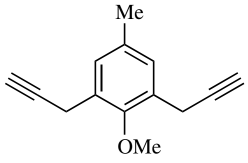


183 **185**

(72)



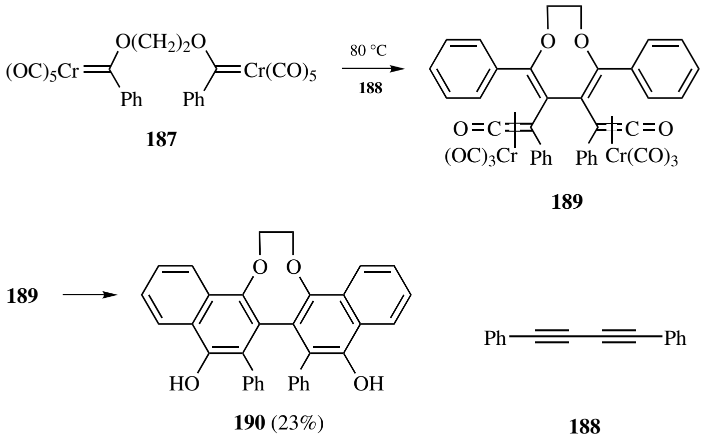
186 (36%)



184

(73)

The bis(chromium complex) **187** on heating reacted with the diyne **188**, formally giving the bis(ketene chromium complex) **189**, which formed **190** (equation 74).[80] As described in Section 3.5, an analogue of **187** was used to form a complexed bisketene that gave stereoselective bis[2 + 2] cycloaddition with a chiral imine. Other reactions of bis(ketene chromium complexes) are given in Section 3.5, and reactions of bis(diazo ketones) are given in Section 3.3.2.



(74)

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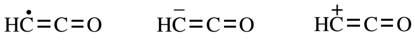
4.10 KETENYL RADICALS, ANIONS, AND CATIONS

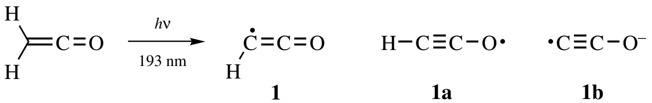
Ketenyl radicals, anions, and cations are considered to be structures with charge or radical character at C_2, as in **1**–**3**, respectively. Structure **2** is the ynolate ion and is also considered in Section 4.8.1. Electron transfer reactions of ketenes are considered in Section 5.1, and ketenes with charged, radical, or carbenic side chains are discussed in Section 4.1.9.



$H\dot{C}=C=O \qquad H\overset{-}{C}=C=O \qquad H\overset{+}{C}=C=O$

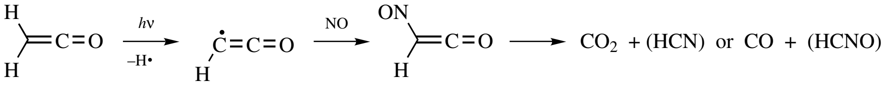
1 **2** **3**

The ketenyl radical **1** was produced by the laser photolysis of ketene with 193 nm light,[1,2] and was characterized by the measurement of the high-resolution IR spectrum[1] and examination by laser-induced fluorescence spectroscopy (equation 1).[2] The kinetics of reaction of **1** with NO were measured.[1] Computations indicated that the ketenyl radical **1** had a bent structure and that the ethynyloxy radical structure **1a** was not important.[3,4] The chemistry of **1** is of major significance, as it is implicated in the combustion of acetylene and the formation of soot. The formation of **1** and **3** in the combustion of acetylene has been evaluated by DFT calculations.[5] The gas phase acidity of **1** leading to the radical anion **1b** was also determined.[6]



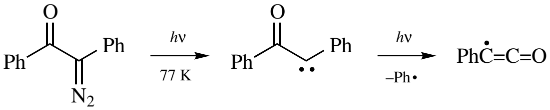
1 **1a** **1b** (1)

The ketenyl radical **1** was generated in the gas phase by photolysis of ketene and reacted with NO to form CO and CO_2 (equation 2).[7] The product branching ratio for formation of CO and CO_2 was 88:12, and the formation of CO was suggested to proceed via nitrosoketene (**4**) as a transient intermediate.[7] Photolysis of the diazo ketone **5a** in a matrix at 77 K gave rise to an ESR spectrum attributed to the phenylketenyl radical **6** formed by phenyl radical expulsion from the keto carbene **5** (equation 3).[8]



1 **4**

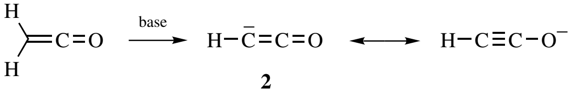
(2)



5a **5** **6**

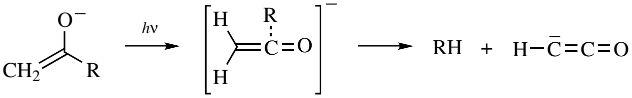
(3)

The ynolate ion **2** has been readily generated in the gas phase by the reaction of ketene with bases (equation 4),[9] and the bond dissociation energy and electron affinity have been determined.[9a] The ynolate anion was found to be highly stabilized, with a linear structure with the charge concentrated on oxygen.[10] IR multiple-photon activation of enolate ions in the gas phase was interpreted as causing formation of an anion-ketene complex **7** that formed ynolate anion (equation 5; see also Section 4.8.1).[11]



2

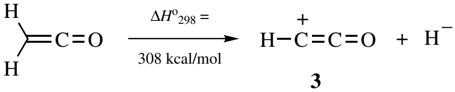
(4)



7 **2**

(5)

The hydride affinity of the ketenyl cation **3** was found to be 308 kcal/mol (equation 6),[12] and the activation energy for formation of **3** from the radical cation **8** of ethynol has been estimated as 68 kcal/mol (equation 7).[13] The cyano ketenyl cation **9** was proposed to form from C_3N^+ (equation 8).[14] Formation of the trimethylsilyl-substituted ketenyl cation **11** was proposed to occur upon photolysis of the diazo ester **10**, as evidenced by formation of the methyl ester **12** upon reaction with MeOH (equation 9).[15]



3

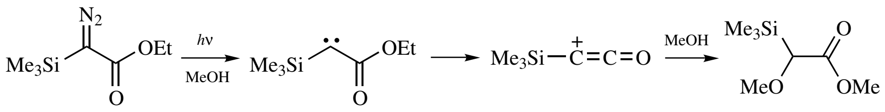
(6)

$$H-C\equiv C-OH^{+\bullet} \longrightarrow H-\overset{+}{C}=C=O + H\bullet \qquad (7)$$

8 **3**

$$^{+}N=C=C=C: \xrightarrow{O_2} N\equiv C-\overset{+}{C}=C=O \qquad (8)$$

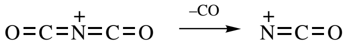
9



10 **11** **12**

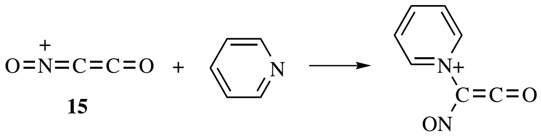
(9)

The cationic species **13** and **15** were generated in the gas phase, and **13** underwent decarbonylation to **14**, while **15** reacted with pyridine to form **16**, which rapidly lost CO (equations 10, 11).[16]



$$O{=}C{=}\overset{+}{N}{=}C{=}O \xrightarrow{-CO} \overset{+}{N}{=}C{=}O \qquad (10)$$

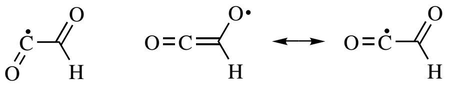
13 **14**



15 **16**

(11)

The structures and electronic configurations of the radicals **17** and **18** have been determined by high-level computaional studies.[17]



17 **18**

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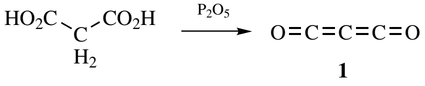
4.11 CUMULENONES

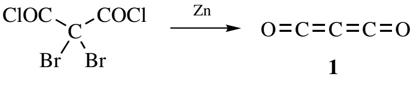
Cumulenones are considered to include carbon suboxide (**1**), methyleneketenes such as propadienone (**2**), and carbenic species such as **3**. The coverage in this section is not intended to be comprehensive, but rather to illustrate some of the diverse structural types that have been studied. Reviews of some of these compounds have appeared.[1,2]

$$\underset{\mathbf{1}}{O{=}C{=}C{=}C{=}O} \qquad \underset{\mathbf{2}}{CH_2{=}C{=}C{=}O} \qquad \underset{\mathbf{3}}{:C{=}C{=}O}$$

Carbon suboxide was first prepared in 1906 by Diels and Wolf by the dehydration of malonic acid (equation 1)[3] and in 1908 by Staudinger and Bereza by dehalogenation (equation 2).[4] The preparation and properties of **1** have been extensively studied and reviewed,[5] and only a few recent studies are noted here.



(1)

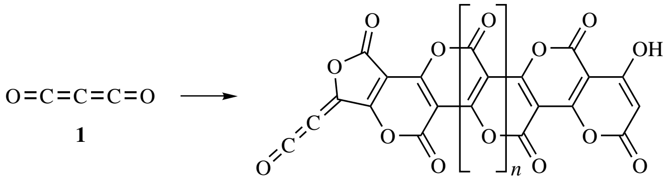


(2)

The carbon dioxides C_nO_2 with even numbers of carbons are less stable than those with odd numbers, and all attempts to prepare C_2O_2, the dimer of CO, have been unsuccessful.[6–10,13] There is evidence for C_4O_2 in an argon matrix[11] and in the gas phase,[12] and for the odd-numbered species C_5O_2[14] and C_7O_2[15] in matrices.

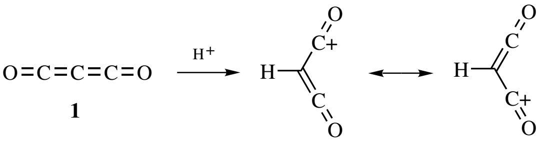
Carbon suboxide, C_3O_2, has a quasilinear structure with a very small energy barrier for bending around the central carbon, as discussed in Section 1.2. The structure of crystalline C_3O_2 has been determined by X-ray.[16]

Carbon suboxide undergoes spontaneous polymerization, forming a red to black solid found to have a degree of polymerization $n \approx 40$, with the polypyronic structure **4** as determined by X-ray (equation 3).[17]


1 **4**

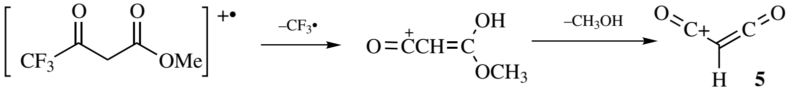
(3)

Ab initio calculations indicated that carbon suboxide is preferentially protonated on the central carbon to give **5**, which has a bent geometry (equation 4).[18,19] The proton affinity of 200 kcal/mol (791 kJ mol^{-1}) was determined[19] by Fourier transform mass spectrometry and was in good agreement with the calculated value of 200 kcal/mol (789 kJ/mol).[19] The oxygen-protonated isomer ($O{=}C{=}C{=}C{=}OH^+$) and the radical ($O{=}C{=}CH{-}C{=}O^{\bullet}$) have also been observed.[19] The generation of the complex of **1** and HCl from photolysis of matrix-isolated O=C=CHCOCl is noted in Section 5.6.1. Complexation of pyridine with C_3O_2 in a matrix has been found computationally and experimentally to produce T-shaped complexes, but not a zwitterion.[20] The use of **1** in synthesis has been briefly reviewed in the context of malonate chemistry.[21]


1 **5**

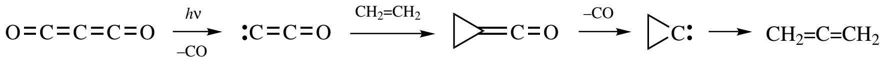
(4)

Ion **5** was also formed in the gas phase by electron ionization of methyl trifluoroacetoacetate. One route proposed for this conversion involved successive loss of $CF_3\bullet$ and methanol (equation 5).[22]


5

(5)

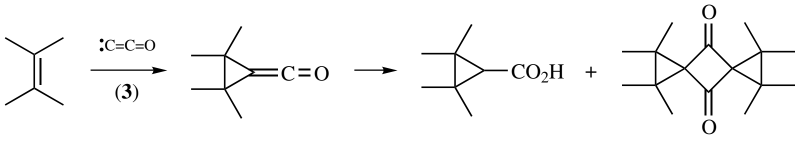
Upon photolysis in the gas phase carbon suboxide formed the triplet carbenic species **:**C=C=O (**3**), which reacted with ethylene, forming cyclopropylideneketene **6**, which underwent decarbonylation, forming the carbene **7**, which led to allene (equation 6).[23–26] The triplet electronic state of **3** was confirmed by direct observation in a matrix.[27]



1 **3** **6** **7**

(6)

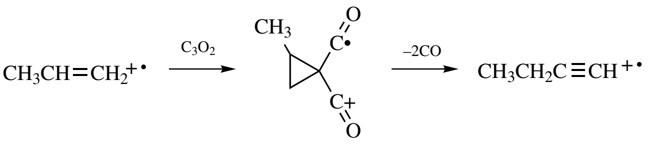
Upon photolysis of **1** in the gas phase generating **3** in the presence of tetramethylethylene, the ketene **8** was formed, as shown by the isolation of the acid **9** from hydration and the dimer **10** (equation 7).[28] The formation of **8** and **10** by a different route is discussed in Section 4.1.1. The use of **3** in the formation of tetrahedrane as a transient intermediate has also been reported.[29]



8 **9** **10**

(7)

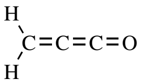
Reaction of carbon suboxide with propene radical cation was proposed to proceed by initial addition forming the distonic ion **11**, followed by loss of two CO's and rearrangement to give the radical cation of 1-butyne (equation 8).[30]



11

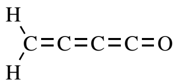
(8)

Computations of the structures and energies of the cumulenones **2**, **12**, and **13** have been reported.[31] At the highest levels of calculation, all of these structures showed significant bending in the heavy-atom chain. Dimethylpropadienone **16**, with an IR absorption at 2124 cm^{-1}, was obtained in a matrix by carbonylation of the carbene **15** obtained by photolysis of bisperester **14** (equation 9).[32] This species was also obtained by a low-temperature dehalogenation of **17** (equation 10).[33]



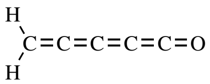
$H_2C{=}C{=}C{=}O$

2



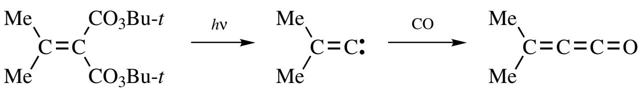
$H_2C{=}C{=}C{=}C{=}O$

12



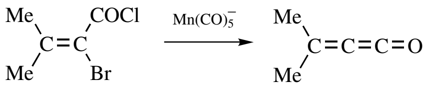
$H_2C{=}C{=}C{=}C{=}C{=}O$

13



14 **15** **16** (IR 2124 cm^{-1})

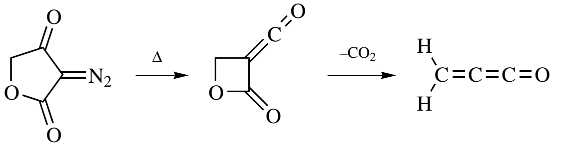
(9)



17 **16**

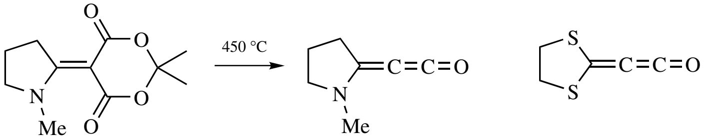
(10)

Propadienone (**2**) was formed by pyrolysis of diazo ketone **18** in a reaction suggested to give the acyl ketene **19**, which lost CO_2, forming **2**, which was trapped in an argon matrix and identified by IR absorption at 2125 cm^{-1} (equation 11).[34] The methyleneketene **21** obtained by pyrolysis of Meldrum's acid derivative **20** was the first member of this class obtained as a stable compound in solution at room temperature and was characterized by the ^{13}C NMR spectrum (equation 12).[35] Cumulenone **22** was prepared by a similar route and observed in solution at $-50\,°C$.[36,37] Methylene derivatives **23** of Meldrum's acid on FVP formed surprisingly stable iminopropadienones **24** that were isolated and characterized (equation 13).[38] A variety of nucleophilic additions to **24** were examined.[38,38a]



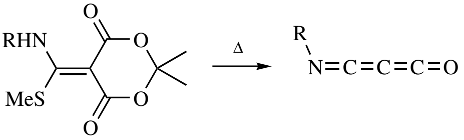
18 **19** **2** (IR 2125 cm^{-1})

(11)



20 **21** (IR 2080 cm^{-1}) **22**

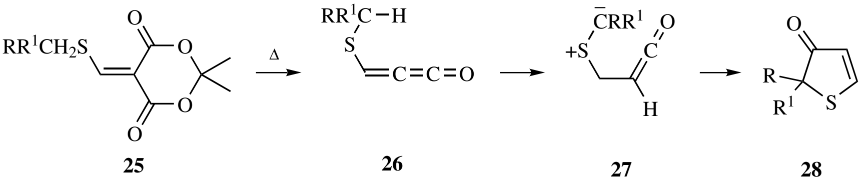
(12)



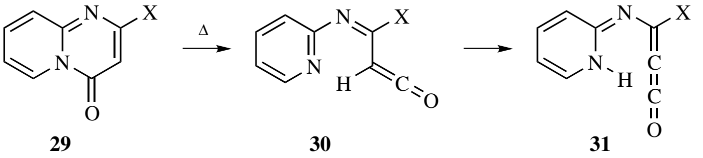
23 **24** (R = Ph, Me; IR 2247 cm^{-1})

(13)

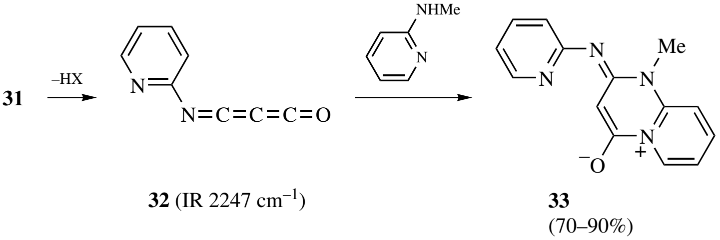
Pyrolyses of Meldrum's acids **25** were proposed to lead to thiosubstituted cumulenones **26**, which rearranged by hydrogen transfer to give ketenes **27**, which formed thiophene derivatives **28** (equation 14).[39–41] An analogous transformation is mentioned in Section 4.1.6. Pyrolysis of **29** was proposed to form the ketene intermediate **30**, which reacted through a dihydropyridylmethyleneketene **31** (equation 15) to form the iminocumulenone **32**, identified by a strong IR band at 2247 cm^{-1} (equation 16).[42] Reactions of **32** with 2-methylaminopyridine gave the mesoionic derivative **33** (equation 16).[42] Other reactions of **24** (R = neopentyl, mesityl, 2-*t*-BuC_6H_4) were studied.[43]



(14)

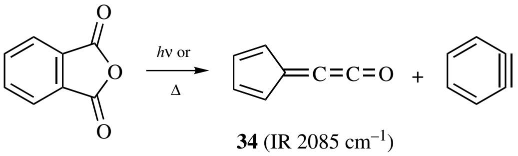


(15)



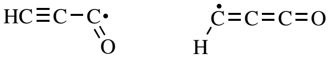
(16)

Pyrolysis or photolysis of phthalic anhydride gave benzyne as well as the cyclopentadienylideneketene **34**, characterized by its IR absorption at 2085 cm^{-1} (equation 17).[44] This IR absorption had earlier been assigned to benzyne, and the structure of **34** was determined by *ab initio* molecular orbital calculations.[45,46]



(17)

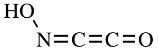
Photolysis of C_3O_2 produced C_5O, C_7O, and C_9O, and the structures of these species were determined from their rotational spectra with the assumption of linearity.[47] The radical HCCCO was calculated to have the alkynylacyl structure **35a**, 3.0 kcal/mol (12.5 kJ/mol) more stable than the ketenyl structure **35b**.[48–50]



$HC{\equiv}C{-}\dot{C}{=}O \qquad H{-}\dot{C}{=}C{=}C{=}O$

35a **35b**

The oxime **36** of the unknown C_2O_2 has been generated in an Ar matrix and identified by its IR spectrum.[51] The analogue O=C=C=S has been prepared from CO and CS.[52] The mass spectrum of C_3O_2 produces $C_2O_2^{+\bullet}$, and the latter species has been examined by tandem mass spectroscopy.[53]



36

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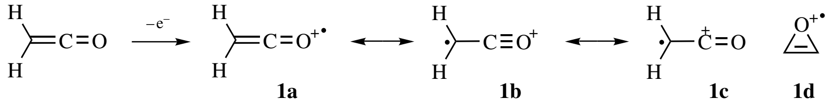
5 Reactions of Ketenes

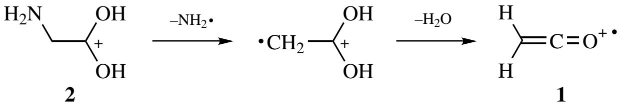
5.1 OXIDATION AND REDUCTION OF KETENES

Ketenes are susceptible to oxidation forming the radical cation **1** (equation 1),[1] and the photoelectron spectra of $CH_2{=}C{=}O$ and $CD_2{=}C{=}O$ forming $CH_2{=}C{=}O^{+\bullet}$ and $CD_2{=}C{=}O^{+\bullet}$ have been measured and the vibrational energies of the ions derived.[2] This process was favored by the relative ease of electron removal from the ketene HOMO and the stabilization of the acylium ion resonance structure **1b**. Addition of an electron to the high-lying LUMO is, however, quite difficult. The oxirene radical cation **1d** has been prepared from several sources as a stable species in the gas phase, but did not yield neutral oxirene by charge neutralization.[3]

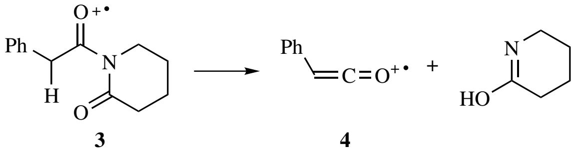


(1)

The ion $CH_2{=}C{=}O^{+\bullet}$ was also generated from the gas phase reaction of protonated glycine (equation 2).[4] The ion with *m/z* 118 in the 70 eV electron impact mass spectrum of (*N*-phenylacetyl)piperidin-2-one (**3**) has been identified as phenylketene radical cation **4** by its mass-analyzed kinetic energy spectrum (equation 3).[5] The interconversion of $HOCH{=}C{=}O^{+\bullet}$ and $HOCH{=}\dot{C}{-}O^-$ is noted in Section 2.4.



(2)

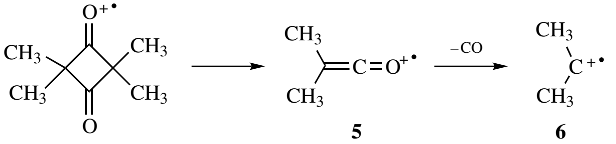


(3)

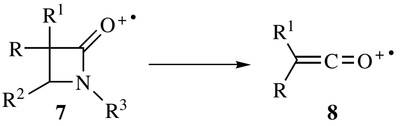
Ketenes II, by Thomas T. Tidwell

Recent experimental and calculated values of the heat of formation (ΔH_f^{298}) of methylketene radical cation $CH_3CH{=}C{=}O^{+\bullet}$ and of $(CH_3)_2C{=}C{=}O^{+\bullet}$ (**5**) are presented in Section 1.3.[6–8]

The electron impact mass spectrum of tetramethyl-1,3-cyclobutanone formed the dimethylketene radical cation **5**, which lost CO to form dimethylcarbene radical cation **6** (equation 4).[9] The formation of ketene radical cations **8** by electron impact–induced cleavage of β-lactams **7** has been examined (equation 5).[10,11] Other reports of the formation of ketene radical cations by mass spectrometry are given in Section 2.4.

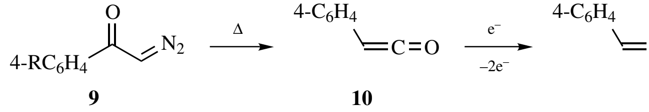


(4)



(5)

The photoelectron spectra of arylketenes **10**, which were generated by thermal Wolff rearrangements of diazo ketones **9** (equation 6), gave the lowest vertical ionization potentials that were compared to calculated values (Table 5.1).[12] The measured and calculated values showed the same trends, with distinctly lower values for the first and third IP values for the 4-MeO groups, interpreted as showing the higher coefficient for the HOMO at the 4-aryl position.



(6)

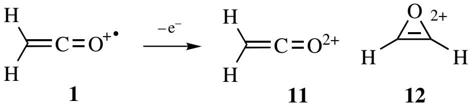
Further ionization of the ketene radical cation **1**, generated by 70 eV electron impact of ketene or by loss of H_2O from the molecular ion of acetic acid, formed the dication **11** by charge stripping in the mass spectrometer (equation 7).[13] The ion **11** could be generated in the gas phase, although it was very unstable and was expected to be highly oxidizing toward other molecules. Computations indicated

TABLE 5.1 Measured and Calculated Ionization Potentials of Arylketenes 10

R	IP (ev)	IP (eV)[a]	IP (eV)	IP (eV)[a]	IP (eV)	IP (eV)[a]
H	8.23	7.93	9.34	9.1	10.41	10.1
CH_3	8.22	7.68	9.36	9.0	10.17	9.8
CH_3O	7.91	7.36	9.22	9.1	9.56	9.4
Cl	8.29	7.94	9.25	9.3	9.74	9.8

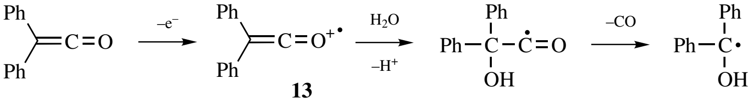
[a] Calculated by B3LYP/6-31+G(d)//HF/6-31G(d).

a planar structure and at the MP2/6-31G*//4-31G level a 27.2 kcal/mol greater stability than the oxirene structure **12**.[13]



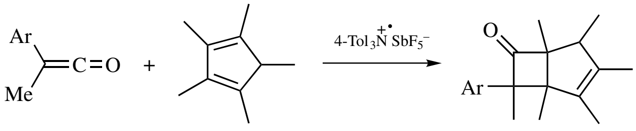
(7)

Electrochemical oxidation of diphenylketene forming the radical cation **13** in CH_3CN resulted in the formation of benzophenone, and could occur by attack of adventitious water (equation 8) or by a process including a Ritter-type reaction with the solvent.[14]



(8)

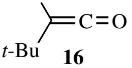
Oxidation potentials E_p (versus SCE) in CH_3CN were obtained by cyclic volltametry for 4-$MeOC_6H_4CMe{=}C{=}O$ (**14**, $E_p = 0.91$ V),[15,16] 4-$MeC_6H_4CMe{=}C{=}O$ (**15**, $Ep = 1.11$ V),[15,16] and *t*-$Bu_2C{=}C{=}O$ (**16**, $E_p = 1.44$ V)[17] and indicated that the ease of oxidation depended upon the electron donor abilities of the ketene substituents. The radical cations **14** and **15** generated by one electron oxidation of the ketenes with 4-$Tol_3N^{+\bullet}$ SbF_5^- as catalyst reacted with pentamethylcyclopentadiene (**17**) by [2+2] cycloaddition, forming **18** (equation 9).[15,16]



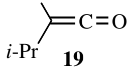
(9)

14 (Ar = 4-$MeOC_6H_4$) **17** **18**
15 (Ar = 4-MeC_6H_4)

In contrast to the frequent observations of ketene oxidations, reports of their reduction have been scarce. Attempted electrochemical reduction of ketenes **16** and **19–22** was unsuccessful, as no reduction was observed up to −3 eV. A reduction for $Ph_2C{=}C{=}O$ was observed at −2.06 eV, but no ESR spectrum for the radical anion could be observed.[18]



16



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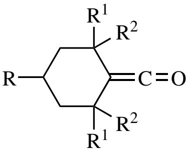
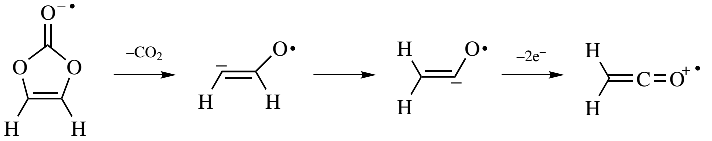


20 (R = H, $R^1 = R^2 =$ Me)
21 (R = R^1 = *t*-Bu, R^2 = H)
22 (R = R^1 = H, R^2 = *t*-Bu)

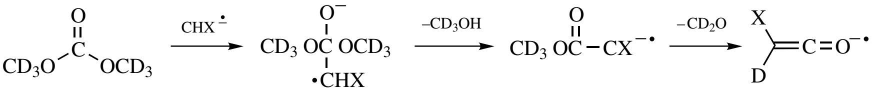
Evidence for the radical anion of ketene $CH_2{=}C{=}O^{-\bullet}$ (**25**) was obtained by the reaction of vinylene carbonate radical anion **23**, generated using low-energy electrons in the gas phase.[19,20] Anion **23** was suggested to lose CO_2, forming **24**, but rearrangement to **25** has a high barrier[19] and oxidation may be required to form **26** (equation 10).



23 **24** **25** **26**

(10)

Formation of haloketene radical anions **27** by carbene radical anion addition to dimethyl carbonate has been proposed (equation 11).[21] The direct observation of some fulvenone radical cations was reported (Section 4.1.10).



27 (X = Hal)

(11)

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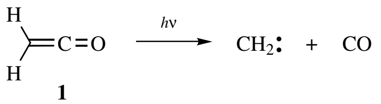
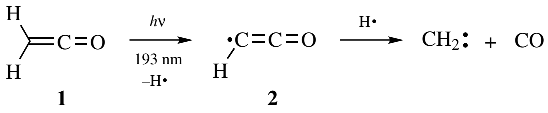
5.2 PHOTOCHEMICAL REACTIONS

The photodissociation of ketene (**1**) is a classic reaction that has been pursued continuously since 1934,[1] including an early study using the new technique of flash photolysis,[1a] and remains a frequently utilized and convenient source of methylene for mechanistic studies (equation 1). This topic has been periodically reviewed.[2–6]



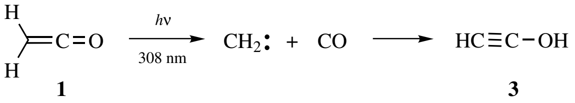
(1)

Photolysis of $CH_2{=}C{=}O$ with 193 nm light proceeded by four channels, including cleavage of a C–H bond rather than initial decarbonylation, followed by addition of H• to the resulting radical **2** (equation 2).[7] Formation of CH_2 occurred by two different channels and formation of **:**$C{=}C{=}O$ and H_2 was also identified.[7]



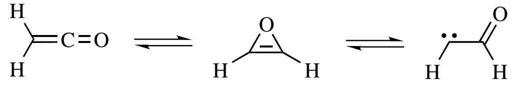
(2)

Photolysis of ketene in an argon matrix at 12 K with a 308 nm XeCl laser resulted in the formation of ethynol (**3**) (equation 3).[8] It was proposed that this isomerization involved excitation of the n → π* transition of ketene at 310 nm, followed by decarbonylation to CH_2 and CO, and then insertion of CO into the C–H bond of CH_2.



(3)

Photolysis of $^{14}CH_2{=}C{=}O$ led to formation of both ^{12}CO and ^{14}CO, attributed to formation of oxirene **4** (equation 4).[9] A slow increase in the yield of ^{14}CO suggested that the degree of scrambling was increasing with time, indicating that some of the oxirene was forming rearranged ketene.[9] Rearrangement of highly vibrationally excited ketene labeled with ^{13}C in the CH_2 group followed by dissociation to methylene and CO was also detected.[10–12]



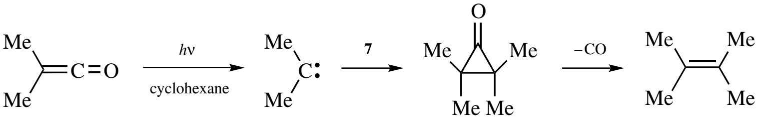
1 **4** **5**

(4)

Further studies of ketene photolysis have included consideration of internal conversion of photoexcited ketene,[13] measurement of rate constants for the unimolecular dissociation of ketene and deuterated ketene by photofragmentation in a cold jet (equation 1),[14] and study of the effects of K conservation.[15,16] In accord with expectations, the rate constant increased in a stepwise manner as the energy increased.[15] Other studies of ketene photodecomposition have appeared,[17–21] including high-level *ab initio* calculations of the reaction path and energetics for dissociation of singlet ketene.[22–25] The translational energy distribution of rotational states of CO from this process has been examined.[26,27] Other related studies have also been reported.[28–31]

Photolysis of the higher ketenes $MeCH{=}C{=}O$ (**6**)[32–34] and $Me_2C{=}C{=}O$ (**7**)[35–37] formed the corresponding carbenes, and in the gas phase $CH_2{=}CH_2$ and $MeCH{=}CH_2$, respectively, are the major products.[32,35]

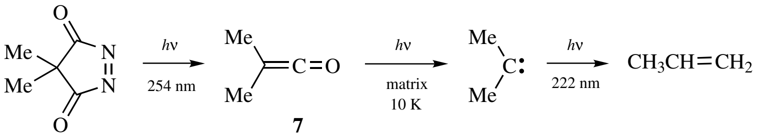
Photolysis of **7** in cyclohexane solution also gave $Me_2C{=}CMe_2$, which was proposed to form via the cyclopropanone **9**, which was observed by IR at 1840 cm^{-1} (equation 5).[36] The quantum yield for photodissociation of **6** was less than that for $CH_2{=}C{=}O$,[32] and for **7** the quantum yield for dissociation was unity for irradiation at 254 nm. However, for photolysis at 366 nm the quantum yield was pressure dependent, indicating formation of a long-lived, excited state.[35]



7 (IR 2124 cm^{-1}) **8** **9**

(5)

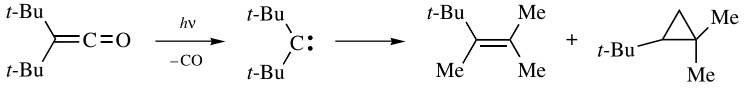
Dimethylketene (**7**) was formed in an argon matrix at 10 K by photolysis of dimethylpyrazolen-3,5-dione with 254 nm light or at greater than 570 nm (equation 6).[37] The ketene was essentially photostable in the matrix upon further photolysis at these wavelengths, but upon photolysis at 222 nm gave propene via dimethylcarbene (equation 6).[37]



7

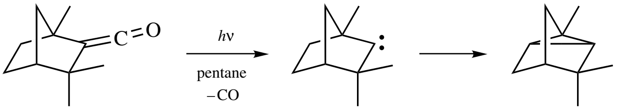
(6)

Photolysis of di-*tert*-butylketene (**10**) gave the carbene **11**, which formed **12** and **13** (equation 7).[38,39] The persistent ketene **14** upon photolysis in hydrocarbon solvents formed the carbene **15**, which gave the cyclopropane **16** by intramolecular insertion (equation 8).[40] Upon photolysis in CH_3OD at −60 °C, **16** and the deuterated aldehyde **18** were formed in a 1:1 ratio. The formation of **18** implicated photoprotonation of the ketene and rearrangement to the carbocation **17b** (equation 9).[40]



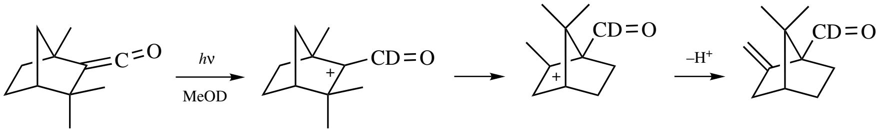
10 **11** **12** **13**

(7)



14 **15** **16**

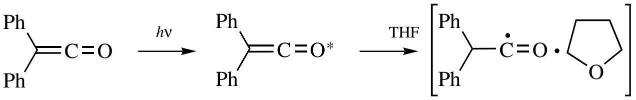
(8)



14 **17a** **17b** **18**

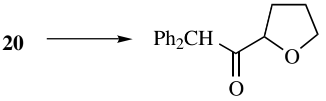
(9)

Photolysis of diphenylketene $Ph_2C{=}C{=}O$ (**19**) in several solvents gave products derived from diphenylcarbene, but in THF the diphenylacetyl derivative **21** was formed (equations 10, 11).[41] This was proposed to form by hydrogen abstraction by the photoexcited ketene, forming a radical pair that recombined (equation 10,11).[41] Multiphotonic reaction of dibenzoyldiazomethane (**22**) formed benzoylphenylketene (**23**), which underwent photochemical decarbonylation and Wolff rearrangement to diphenylketene, which in alcohol underwent decarbonylation to diphenylcarbene, which was protonated to the cation **24** (equation 12).[42]



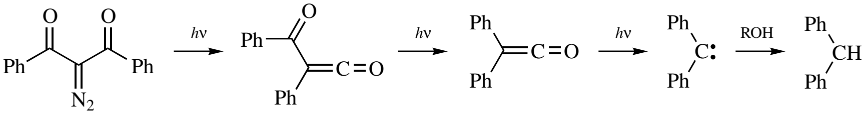
19 **19*** **20**

(10)



21

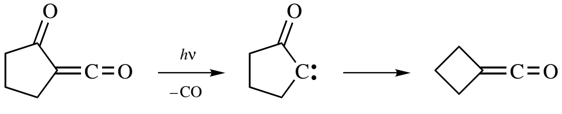
(11)



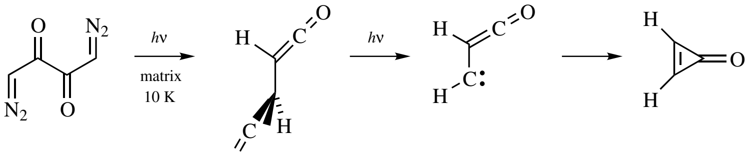
22 **23** **19** **24**

(12)

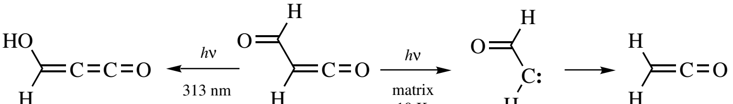
Photolysis of the acylketene **25** in an argon matrix resulted in decarbonylation and formation of trimethyleneketene **26** (equation 13).[43] Photolysis of the bis(diazo ketone) **27** in an argon matrix at 10 K led to the bisketene **28**, which upon photochemical decarbonylation formed cyclopropenone **29** (equation 14).[44] Photolysis of formylketene (**30**) under the same conditions gave ketene, as well as isomerization to the hydroxypropadienone **30a** (equation 15).[44]



25 **26** (IR 2098, 2150 cm^{-1}) (13)

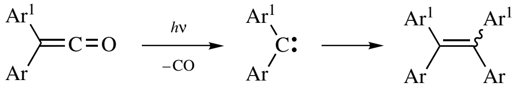


27 **28** **29** (14)



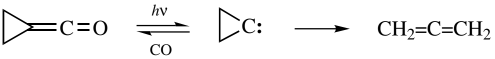
30a (IR 2128 cm^{-1}) **30** **5** **1** (IR 2142 cm^{-1}) (15)

Photolysis of dimesitylketene (**31**)[45] and (4-*tert*-butyl-2,6-dimethylphenyl)mesityl-ketetene **32**[46] led to decarbonylation to the carbenes, which dimerized to the alkenes **33** (equation 16). Photolysis of cyclopropylideneketene (**34**) in an argon matrix at 15 K gave reversible formation of CO and the carbene **35** and formation of allene (equation 17).[47]



(16)

31 ($Ar = Ar^1 = 2,4,6\text{-}Me_3C_6H_2$) **33** (19–52%)
32 ($Ar = 2,4,6\text{-}Me_3C_6H_2$, $Ar^1 = 2,6\text{-}Me_2\text{-}4\text{-}t\text{-}BuC_6H_2$)

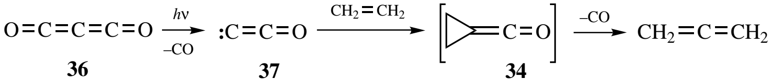


34 **35** (17)

Irradiation of liquid ketene with positive muons gave muonated methyl radical.[48] The photolysis of ketene/acetylene mixtures has been used to prepare propargyl radical (C_3H_3).[49]

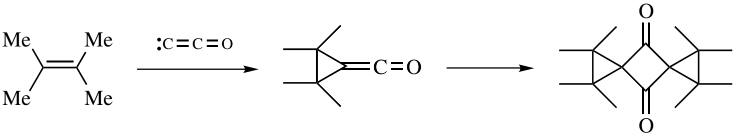
As described in Section 4.11, the photolysis of carbon suboxide (**36**) in the gas phase in the presence of ethylene, propene, and the butenes resulted in formation of the corresponding allenes, which arose from decarbonylation of C_3O_2, forming

:C=C=O (**37**), which added to the alkenes, forming transient cycloalkylidene ketenes such as **34** that lost CO, giving the allenes (equation 18).[50] Reaction in the presence of 2,3-dimethyl-2-butene formed the crystalline dimer **39** of the ketene **38** (equation 19).[51,52]



36 **37** **34**

(18)



38 **39**

(19)

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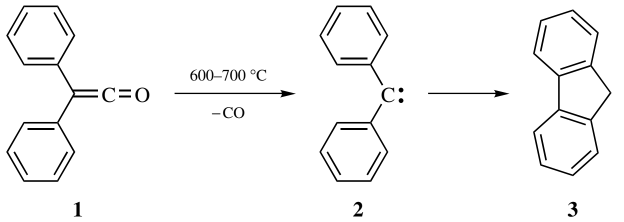
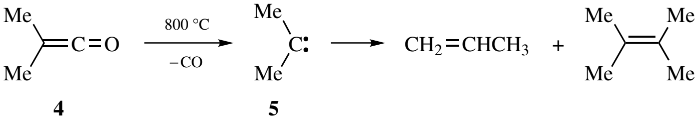
5.3 THERMOLYSIS REACTIONS

Staudinger and Endle observed in 1913 that diphenylketene (**1**) underwent thermolysis with loss of CO and formation of diphenylcarbene (**2**), which cyclized to fluorene (**3**) (equation 1).[1] It was also found that dimethylketene (**4**) on pyrolysis gave dimethylcarbene (**5**), which formed propene and tetramethylethylene (equation 2).[1] This work defined at an early date many of the fundamental reactions of carbene chemistry. Ketenes are available from a variety of sources that are suitable for carbene generation by thermal or photochemical processes and their full potential for carbene generation is yet to be exploited.

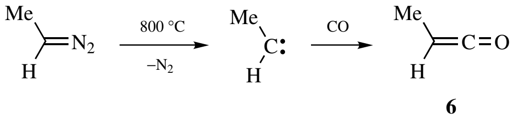


(1)



(2)

Thermal decarbonylation of ketenes is a reversible process, as has been shown in the gas phase thermolysis of azoethane for generation of methylcarbene in an atmosphere of CO, resulting in formation of methylketene **6** (equation 3).[2] There are also numerous examples of ketenes formed from carbenes in low-temperature matrices generated either in the gas phase and deposited in the matrix or by the photolysis of diazoalkanes in the matrix in the presence of CO, as in the formation dicyclopropylketene, and of **6a** (equation 3a).[4]



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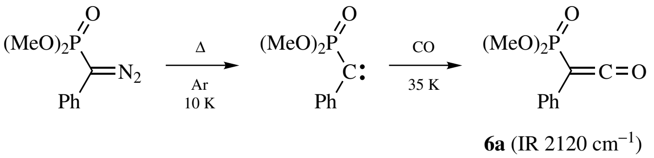
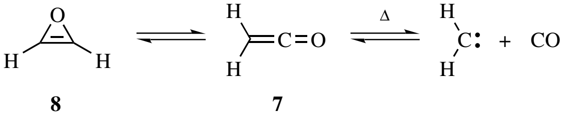


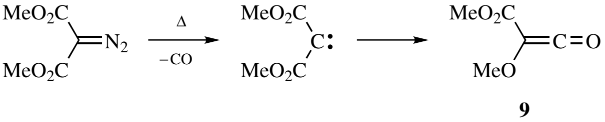
(3a)

A mechanism involving 36 reactions was developed for the high-temperature pyrolysis of ketene (**7**), including decarbonylation,[5,6] and atom isomerization of vibrationally excited ketene indicated the intermediacy of the oxirene intermediate **8** (equation 4).[7]



(4)

Pyrolysis of methyl diazomalonate at 280–640 °C formed ketene **9** (equation 5), which itself underwent thermal decarbonylation under the reaction conditions **10** and led to methyl acetate (equation 6).[8]



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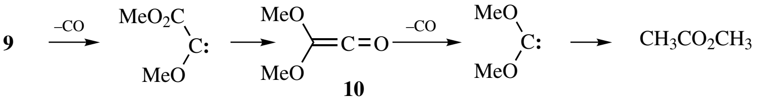
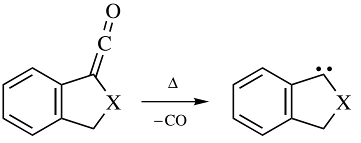


(6)

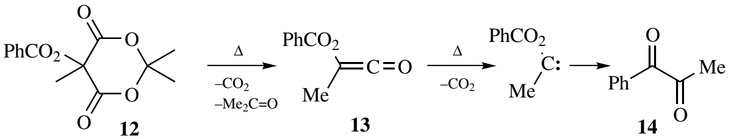
The MP2-calculated activation energy for decarbonylation of ketene **11a** exceeded that of ketene **11b** by 14.3 kcal/mol.[9] Ketene **11a** formed by thermal Wolff rearrangement was detected by photoelectron spectroscopy, but **11b** was not, suggesting that **11b** may have decarbonylated under the reaction conditions (equation 7).[9]



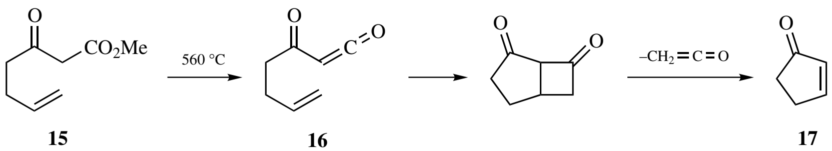
(7)

11a (X = S) **11b** (X = O)

Pyrolysis of the Meldrum's acid derivative **12** was proposed to form ketene **13**, which lost CO and formed **14** (equation 8).[10] The β-keto ester **15** lost MeOH at 560 °C, forming the acylketene **16**, which reacted by cyclization and ketene loss, leading to cyclopentenone **17** (equation 9).[11] Ketene **16** also underwent decarbonylation to give **18** (equation 10) in a 4:1 **17**/**18** ratio.[11]



(8)



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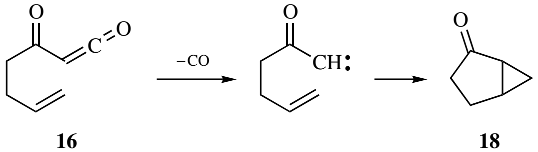
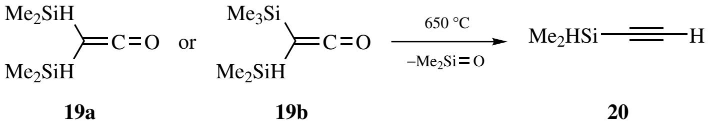


(10)

FVP of (dimethylhydridosilyl)ketenes **19** resulted in formation of the alkyne **20** (equation 11).[12] Pyrolysis of the diazo ester **21** gave the ketene **22**, which underwent decarbonylation to form acetophenone as the most abundant product (equation 12).[13] The thermal isomerization of ketene via an oxirene intermediate has been examined by computations.[14]



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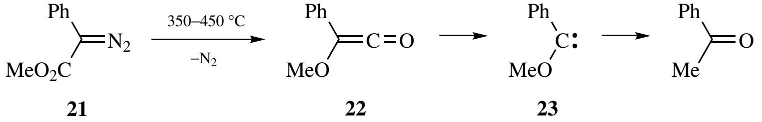

(12)

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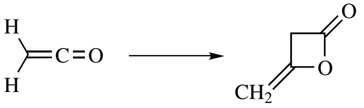
5.4 CYCLOADDITION REACTIONS OF KETENES

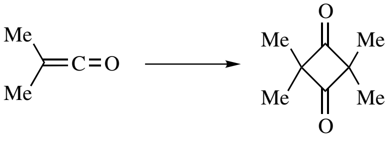
Cycloaddition reactions have been a characteristic feature of ketene chemistry from the very beginning, with the isolation of the ketene dimer (**1**) by Chick and

Wilsmore,[1,2] which was eventually shown to have the methylene-β-lactone structure **2** (equation 1). Dimethylketene (**3**) was found to form the symmetrical dimer **4** by Staudinger and Klever (equation 2).[3] Staudinger also found, soon after the initial report of the preparation of diphenylketene (**5**), that it reacted with cyclopentadiene to form an addition compound **6** that was later shown to result from net [2+2] cycloaddition,[4] and that it reacted with imines **7** to form the β-lactam **8** (equation 4) and with aldehydes to form β-lactone **9**, which, however, underwent decarboxylation, forming triphenylethylene (equation 5).[4,5] Since that time, cycloaddition has remained the most distinctive, useful, and intellectually challenging aspect of ketene chemistry.



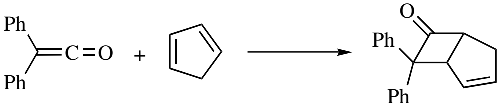
1 **2**

(1)



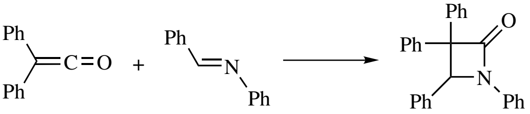
3 **4**

(2)



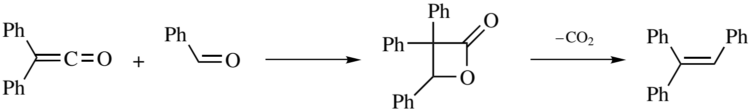
5 **6**

(3)



5 **7** **8**

(4)



5 **9**

(5)

Ketenes have a unique propensity for giving facile [2+2] cycloaddition reactions, even when other pathways are available, and give [4+2] cycloadditions only in unusual circumstances. This feature of ketene chemistry is of major importance for preparative purposes in that the reaction with alkenes and dienes gives cyclobutanones (equation 3), usually with a high degree of stereoselectivity, in a process of considerable synthetic utility. The reaction with imines forming β-lactams (equation 4) is the most straightforward method for the synthesis of these compounds, which have valuable applications in the synthesis of antibiotics (Section 5.4.1.7). Ketenes also usually give [2+2] cycloadditions with dienes, and [4+2] cycloadditions to give cyclohexenones are so rare that "ketene equivalents" are used to mimic the behavior of hypothetical ketenes that would react by this pathway.[6–8] Cycloaddition reactions of ketenes have been considered in a number of reviews.[9–18d]

Ketene cycloadditions often proceed with a high degree of stereoselectivity, which increases their value in synthesis and heightens interest in their reaction mechanisms. The proposal of the Woodward-Hoffmann rules,[19] and their eventual application to explain the distinctive [2+2] cycloaddition reaction mode and unusual stereoselectivity of ketenes, led to an intense period of investigation of many types of ketene cycloadditions. Ketene [2+2] cycloadditions became an important proving ground for testing theories of orbital symmetry control of organic reactivity, as their preferences for formation of the less stable products, often with complete selectivity, were predicted by theory.[19]

After several decades of intense study activity this field has reached maturity, but it still produces surprises. A notable example was the discovery that the canonical [2+2] cycloaddition of diphenylketene with cyclopentadiene did not proceed with initial cyclobutanone formation, but rather [4+2] cycloaddition to the C=O bond of the ketene (Sections 5.4.1.2, 5.4.1.3).

A great deal of the currently available experimental and computational evidence is consistent with many [2+2] cycloadditions of ketenes as proceeeding through concerted reactions governed by orbital symmetry. In particular, the reactions of ketenes with alkenes usually retain the stereochemistry of the alkene and often show stereoselectivity to form the least stable product. However, there are a number of cases where this does not occur and nonconcerted pathways are followed, and there is a suspicion that other seemingly well-established reactions may actually involve other transient intermediates, whose existence may be revealed by more careful examination.

The Woodward-Hoffmannn analysis of ketene cycloadditions[19] provided a theoretical basis for understanding ketene cycloaddition and greatly stimulated study in this field. It was suggested[19] that ketene cycloaddition with alkenes proceeded by the perpendicular arrangement of the two reactants, as shown in Figure 5.1, with both bonds to the alkenes being formed from the same side (*suprafacial*), while the bonds to the two carbons of the ketene were formed from opposite sides (*antarafacial*). The actual role of this process has been the subject of continuous debate and is still unsettled, as discussed below (Sec. 5.4.1.3). However, there is strong evidence that many ketene cycloadditions are not concerted, that is, that they proceed by a two-step process with formation of a zwitterionic intermediate. This latter process is also consistent with the stereospecific formation of the thermodynamically less stable products without loss of the stereochemistry of the reactants.

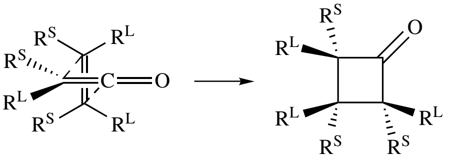


Figure 5.1 The [2+2] cycloaddition of ketene.

Thus, although the concerted pathway is consistent with the observed data in many cases, a stepwise process often provides at least an equally convincing explanation of the result.

Ketene cycloaddition is reversible as a useful process in only a few examples, including in the pyrolysis of the unsymmetrical dimer diketene to ketene (Section 3.1) and in the cleavage of some cyclobutanones to ketenes (Section 3.4.1).

Other important cycloaddition reactions of ketenes besides [2+2] cycloaddition to carbon-carbon double bonds are the [2+2] cycloaddition to imines (Section 5.4.1.7) and to carbonyl groups (Section 5.4.5), [3+2] and [4+2] cycloadditions (Sections 5.4.2 and 5.4.3), and [2+1] cycloadditions (Section 5.10).

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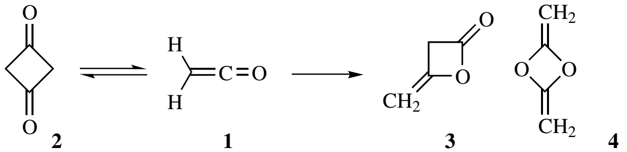
5.4.1 Intermolecular [2+2] Cycloaddition

5.4.1.1 Dimerization of Ketenes The tendency toward dimerization is perhaps the most characteristic feature of ketene chemistry, but [2+2] dimers have not been observed from silylketenes, ketenes with only halogen substituents (Section 4.4.2), or the highly substituted t–$Bu_2C{=}C{=}O$ or $(CF_3)_2C{=}C{=}O$. As discussed in Section 4.1.1, ketene (**1**) has three possible dimers, **2**–**4**, and dimerization in the absence of catalyst formed 1,3-cyclobutanedione **2** and the β-lactone dimer (**3**) in a 5:95 ratio (equation 6).[1] The most recent computations indicated that **3** is more stable by 1 kcal/mol.[2] The diketone dimer **2** was prepared selectively by hydrolysis of the vinyl ether **5** (equation 2),[3] while the bis(vinyl ether) dimer **4** is unknown.



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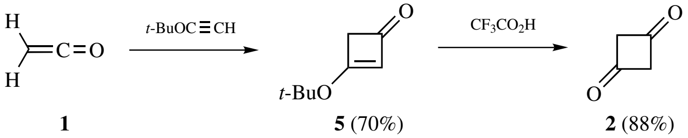
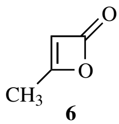


(2)

The structure of the dimer **3** was in doubt for almost 50 years and elicited the comment from workers in the field: "The extraordinary chemical behavior of the ketene dimers has lent exceptional interest to that class of substances, and the controversy which has raged for decades over the structures of the compounds is without parallel in the study of small molecules."[4] The final structural proof that the major dimer had the methylene-β-propiolactone structure, instead of one of a variety of others that had been considered (**2**, **4**, **6**–**8**), was based on chemical studies,[5] electron diffraction,[6] X-ray crystallography,[7,8] and the microwave spectrum[9] and there is an excellent review of the long controversy regarding this structure.[10] The dimer **3** is commercially available, serves as a laboratory precursor for monomeric ketene,[11] and is a valuable synthetic reagent in its own right.[10,12]



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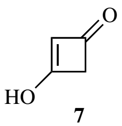

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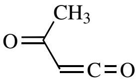
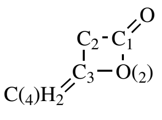


8

Previous computations on the dimers of ketene had indicated that the cyclobutanedione structure **2** was 1 kcal/mol more stable than the lactone structure **3**, which



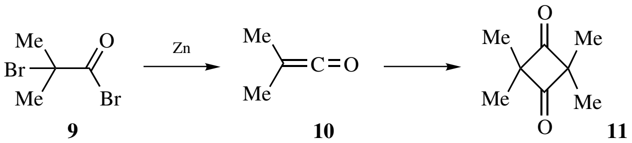
2

C_1C_2	[1.51]	(1.52)	1.536
C_2C_3	[1.54]	(1.52)	1.518
C_3C_4	[1.32]	(1.31)	1.334
C_1O_1	[1.22]	(1.19)	1.196
C_1O_2	[1.395]	(1.41)	1.395
C_3O_2	[1.47]	(1.41)	1.418

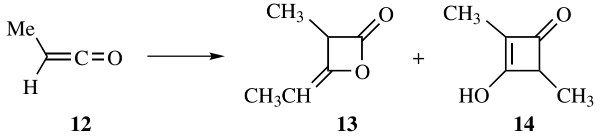
Scheme 5.1 Calculated and experimental bond distances in diketene (**2**). Electron diffraction data[6] in parentheses, X-ray results[7,8] in brackets, and calculated values.[2,14]

is 32 kcal/mol more stable than the unknown isomer **4**. The agreement of the calculated structures with experimental values was characterized as "only fair."[13] Further calculations of the structure of **3** at higher levels of theory[14] led to the conclusion that the theoretical bond lengths, which agree well with experimental microwave results,[9] were more accurate than early electron diffraction[6] and X-ray[7,8] values. The comparative values (Å) are shown in Scheme 5.1, with electron diffraction data[6] in parentheses, X-ray results[7,8] in brackets and the calculated values.[14]

Dimethylketene **10** was prepared by zinc dehalogenation in 1906 and formed the cyclobutanedione dimer **11** (equation 3).[15] Many monosubstituted ketenes ("aldoketenes") such as methylketene (**12**) tend to form both β-lactone dimers of type **13** and substituted derivatives of enolized cyclobutanedione analogous to **14**,[16,17] whereas disubstituted ketenes ("ketoketenes") usually form cyclobutanedione dimers analogous to **11** (equation 3).



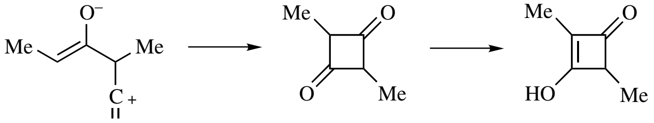
(3)



(4)

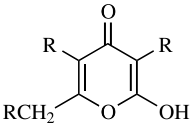
In the formation of dimers of monoalkylketenes such as methylketene (**12**) from the acyl chlorides and Et_3N, it was suggested that $Et_3NH^+Cl^-$ promoted formation of lactone dimers such as **13**,[18–20] whereas in uncatalyzed reactions cyclobutanediones such as **11** (equation 3) or the enolized forms **14** are formed (equation 4).[16] Lactone dimers prepared by dehydrochlorination of acyl chlorides derived from long-chain fatty acids have long been used in paper coatings (sizing).[21]

The lactone structure **13** for the liquid dimer of methylketene and the enolized 1,3-cyclobutanedione structure **14** for the crystalline, acidic dimer, were established in 1950 by Woodward and Small.[4] In a prescient mechanistic analysis, these authors pointed out that the dimerization would be favored to proceed by formation of zwitterionic intermediates such as **15**, forming **16**, which would be converted to the enol **14** (equation 5), and that attack on the C=C bond of ketenes would occur perpendicular to the ketene plane, while attack on the carbonyl would be in the plane.[4]



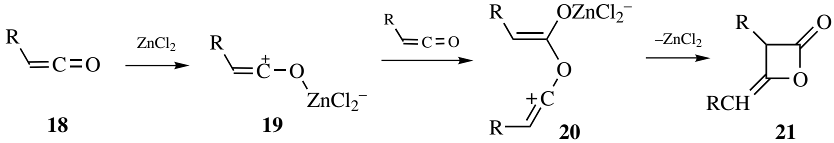
15 **16** **14** (5)

It has been suggested that, with the exception of $CH_2{=}C{=}O$ itself, the primary uncatalyzed dimerization pathway for both aldo- and ketoketenes is formation of cyclobutanedione derivatives of type **11** or **14**.[16] According to the Woodward-Hoffmann analysis, this would occur by a concerted $[_\pi 2_a + _\pi 2_s]$ cycloaddition (vide infra).[22] In the presence of acidic catalysts such as triethylammonium chloride or $ZnCl_2$, lactone dimers of type **13** or γ-pyrone type trimers (**17**) may be formed. Furthermore, it was demonstrated that in the presence of base the lactone dimers **13** revert to cyclobutanedione structures **14**.[16]



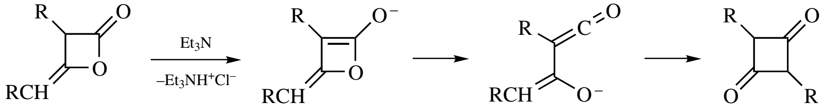
17

A rationalization of the effect of acid catalysts in promoting the formation of lactone structures was proposed in which the catalyst enhances the electrophilicity of the carbonyl carbon and assists nucleophilic attack by the carbonyl oxygen of a second ketene molecule (equation 6).[16]



18 **19** **20** **21** (6)

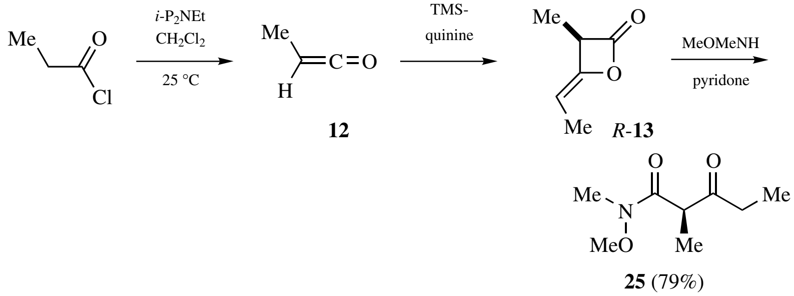
Base-catalyzed isomerization of lactones **21** was suggested[16] to occur by enolization and generation of ketene intermediates **23**, which cyclized to form **24** (equation 7). Trapping of **23** by a further ketene monomer could lead to pyrones **17**.



21 **22** **23** **24** (7)

Lactone dimers **21** with long-chain alkyl groups were originally incorrectly formulated as acylketenes.[18,19] On hydrolysis these dimers yielded β-keto acids that underwent decarboxylation in practical syntheses of long-chain ketones.[18,19]

The dimerization of methylketene (**12**) catalyzed by chiral amines gave enantioselective dimerization to **13** (54 to 98% *ee*).[23–28] For example, dehydrochlorination of propionyl chloride with diisopropylethylamine in CH_2Cl_2 at room temperature with 5 mol% trimethylsilylquinine as catalyst gave a 79% yield of the *R*-dimer **13**, isolated as the β-ketoamide **25** after reaction with methoxy(methyl)amine (equation 8).[23] The dimerization was proposed to proceed by addition of the chiral catalyst to **12**, forming a zwitterion **26** that reacted with a second molecule of **12**, forming **13** (equation 9).[24] Kinetic studies showed that methylketene formation from propionyl chloride was rate determining and that this reacted rapidly to form the dimer. It was also shown that methylketene generated thermolytically from propionic anhydride gave the same selectivity for dimer formation, indicating that the dimerization involved two ketene molecules, not propionyl chloride.[28]



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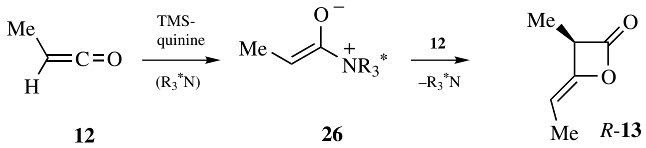
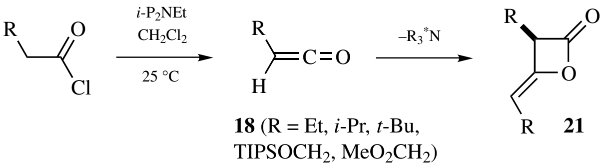


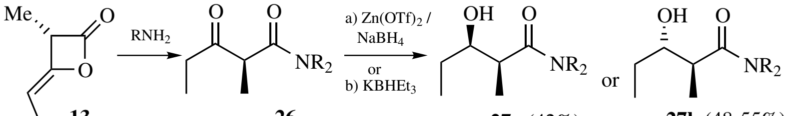
(9)

Dimers **21** of ketenes RCH=C=O (**18**, R = Et, *i*-Pr, *t*-Bu, $TIPSOCH_2$ [TIPS = *i*-Pr_3Si], MeO_2CCH_2) were prepared similarly in 58–88% yields and 91–96% *ee* (equation 10).[23]



(10)

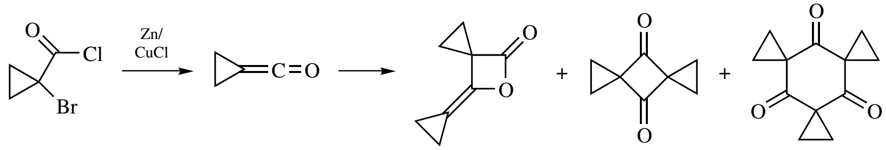
Amination of the methylketene dimer **13** formed **26**, and selective reduction gave either isomer of **27** (equation 11).[25] The dimer was also used in the preparation of pamamycin 621A.[28] A modified procedure involved production of methylketene by pyrolysis of propionic anhydride, enantioselective dimerization and opening of the dimer with lithium methyl(methoxy)amide.[27] The product was used in further synthesis of polypropionates.



13 **26** **27a** (42%) **27b** (48-55%)

(11)

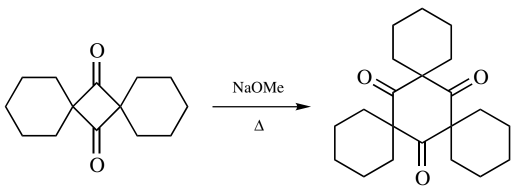
Reaction of the 2-bromo acyl chloride **28** with Zn/CuCl in CH_3CN with ultrasonication gave the unobserved ketene **29**, which formed isomeric dimers **30** and **31** together with the trimer **32** (equation 12).[29] Reaction of the free ketene gave only the dimer **30**,[30] and treatment of **30** with Lewis acids did not lead to isomerization to **31**.[29] Evidently, complexation with $ZnCl_2$ favored the formation of **31**.



28 **29** **30** (27%) **31** (28%) **32** (5%)

(12)

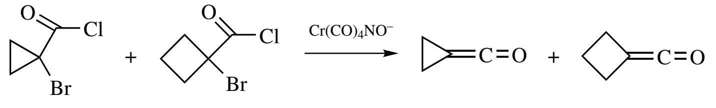
Treatment of the dimer of pentamethyleneketene with NaOMe led to the trimeric 1,3,5-cyclohexanetrione **33** (equation 13).[31] Treatment of $Me_2C{=}C{=}O$ (**10**) or its dimer **11** with a catalytic amount of NaOMe in refluxing toluene also led to a trimer,[32] and dimethyleneketene (**29**) and trimethyleneketene [$(CH_2)_3C{=}C{=}O$] (**34**) gave similar dimers and trimers (cf. equation 12).[31,32]



33

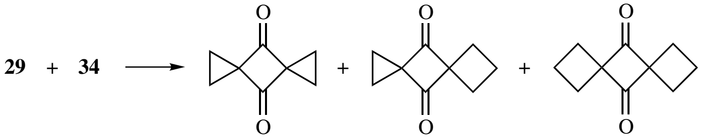
(13)

Dehalogenation of α-bromoacyl chlorides **28** and **28a** by the metal anions $Mn(CO)_5^-$ or $Cr(CO)_4NO^-$ formed the ketenes **29** and **34**, respectively (equation 14), and led to the respective dimers **31** and **35**.[33] When the two ketenes were cogenerated, there was a strong kinetic preference for formation of the mixed dimer **36** (equation 15).[33]



(14)

28 **28a** **29** **34**

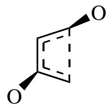


(15)

31 **36** (78%) **35** (2%)

Mixed ketene dimers have also been formed by the generation of haloketenes in the presence of $Me_2C{=}C{=}O$ (**10**), by the mixing of solutions of two different ketenes, and by the cogeneration of two different ketenes.[34,35] When two unsymmetrical ketenes reacted, equal amounts of the stereoisomeric mixed dimers were formed.[35]

Computational studies using several theoretical methods to analyze ketene dimerization predicted that the transition states **37** and **38** form the cyclobutanedione and β-lactone dimers **2** and **3**, respectively[2,36–38] Barriers of 36 kcal/mol for the formation of **2** and 32 kcal/mol for the formation of the major product **3** were found.[36] Both of these transition structures were nonplanar, with ring dihedral angles ranging from 23.1 to 55.7°.[36–38] The transition states were highly unsymmetrical and were interpreted as indicating nonsynchronous but concerted reactions.[36]



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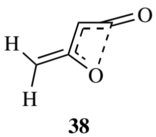
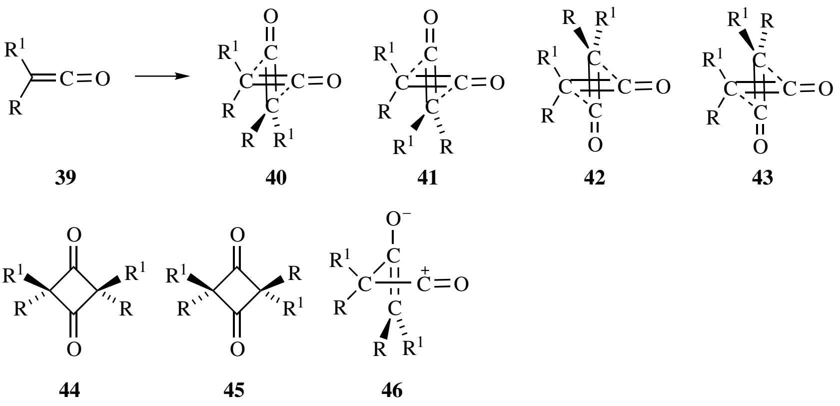


38

The transition state **38** involved interaction of the HOMO of one ketene (the C=C π MO) and the LUMO of the other ketene (the C=O π* MO), with negative charge development on oxygen.[36] This was lower in energy than **37**, in which both the positive and negative charge development was on carbon.[36] It was suggested that methyl substituents would tend to favor concerted dimerization, whereas electron-withdrawing groups would favor a stepwise process.[36] The



Scheme 5.2 Reaction pathways for [2+2] cyclodimerization of ketenes.

calculated[37,38] deuterium isotope effects on the product distribution were in good agreement with experimental values measured using natural abundance ^{2}H NMR spectroscopy of the dimer of $CDH{=}C{=}O$.[39]

The stereochemistry of the products of dimerization of unsymmetrical ketenes **39** according to Scheme 5.2 are summarized in Table 5.2.[40,41] These results were discussed in terms of the $[_{\pi}2_s+_{\pi}2_a]$ mechanism with transition states **40** and **41** leading to the *Z* dimer **44**, and **42** and **43** leading to the *E* dimer **45**. It was proposed that as group R^1 became progressively larger, **41** and **43** were increasingly favored. However, the trends in the results were not consistent and particularly with neopentyl(methyl)ketene the *trans* isomer was favored. It was concluded that these results are not definitive for establishing a $[_{\pi}2_s+_{\pi}2_a]$ mechanism.[41]

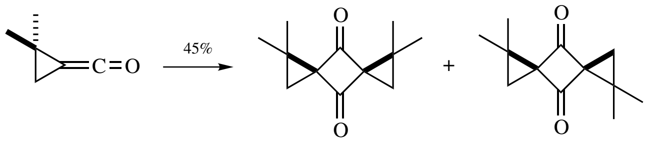
An alternative zwitterionic intermediate **46** with a strong interaction between the R groups could react with rotation of these groups away from one another, leading to the *trans* product **45**. This would, however, increase the interaction between groups R and R^1, and the balancing of these effects may explain why the results do not follow a clear trend.

Ketene **47** underwent dimerization to form the *syn* and *anti* dimers **48** and **49**[42–45] in a 1:9 ratio (equation 16).[45] This preference for the less crowded *anti* isomer was unusual and would not be predicted by the less hindered transition state **50** for a concerted $[_{\pi}2_s +_{\pi} 2_a]$ process. Possibly this behavior resulted from a zwitterionic intermediate **51** that underwent preferential formation of the less hindered

TABLE 5.2 Dimerzation of Ketenes to 44 and 45

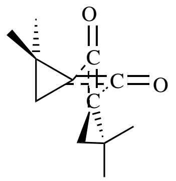
R	Ph	Ph	Ph	Ph	$PhCH_2$	$PhCH_2$	$PhCH_2$	*i*-Pr	*t*-$BuCH_2$
R^1	Me	Et	*i*-Pr	$PhCH_2$	Me	Et	*i*-Pr	Me	Me
44/45	20/80	62/38	100/0	73/27	60/40	58/42	64/36	76/24	23/77

anti isomer **49**.



(16)

47 **48** **49**



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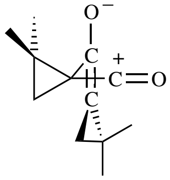
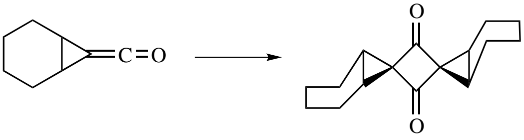


51

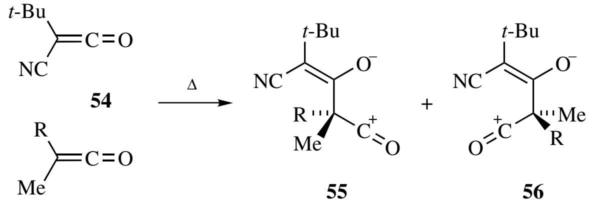
The reaction of **52** gave the *anti* dimer **53** (equation 17), whose structure was established by X-ray crystallography.[44,45] Just as in the reaction of **47**, this was not the product predicted by a concerted $[_{\pi}2_a + {}_{\pi}2_s]$ cycloaddition and a two-step process via a zwitterionic intermediate analogous to equation 5 may be involved. The reason that **47** and **52** gave more of the *anti* dimer compared to **39** (Table 5.2) may result from stabilization of the acylium ion by the cyclopropane ring, leading to a longer lifetime for **51**. The compact size of the cyclopropyl group may also reduce the steric interactions in the path to the *anti* product.



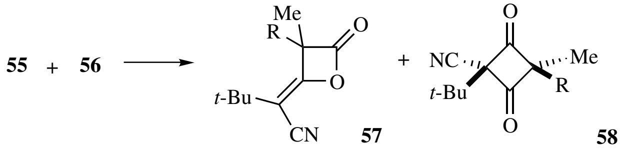
(17)

52 **53**

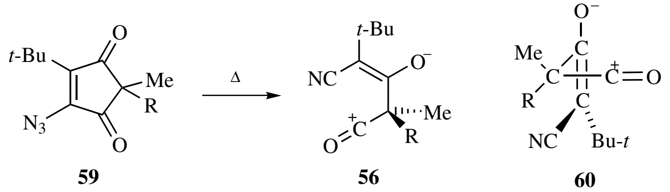
Moore and Wilbur[46,47] studied the reaction of *t*-BuC(CN)=C=O (**54**) with CH_2=C=O, MeCH=C=O, Me_2C=C=O, and MeEtC=C=O. In the first two examples β-propiolactone dimers **57** were formed, whereas the latter two formed cyclobutanediones **58** (equations 18, 19). These ketenes were proposed to react by a head-to-tail approach giving initially the zwitterionic intermediate **55**. When R = H this isomerized to **56**, and **55** and **56** formed **57** and **58**, respectively. The same intermediates were also generated from thermolysis of the corresponding 4-azido-5-*tert*-butylcyclopentene-1,3-diones **59** and gave the same products. Thus, these results were taken as showing unequivocally that for these highly polar ketenes, stepwise zwitterionic mechanisms were involved in the dimerizations.[40,46,47] The preference for formation of β-propiolactone-type dimers **57** of aldoketenes (R = H) would appear to arise from the lower barrier of conversion of **55** to **57** or to a lower barrier to formation of **57** directly from the ketenes. The structures were represented[46,47] with the ring-forming atoms in an essentially coplanar arrangement, but it would appear that steric interactions would favor that shown in **60** (equation 20), with little decrease in bonding efficiency.



(18)



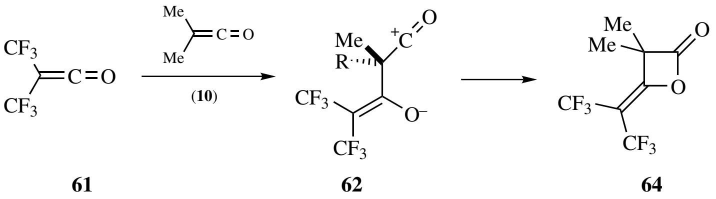
(19)



(20)

In the reaction of MeEtC=C=O there was very little selectivity in the formation of the dimer, with a 46:54 ratio of the *E/Z* isomers being observed. This lack of selectivity led Moore and Wilbur[46] to question if the products with high selectivity observed by Dehmlow et al. (Table 1)[40] were good evidence for a concerted pathway. As noted above, in later work Dehmlow et al. did not rule out stepwise processes.[41]

Bis(trifluoromethyl)ketene **61** did not dimerize thermally but was quite reactive toward other ketenes, reacting with $Me_2C{=}C{=}O$ (**10**) to form both cyclobutanediones and β-propiolactone-type dimers **64** and **65**, and with $CH_2{=}C{=}O$ and MeCH=C=O to form only β-propiolactone-type dimers.[48] The reactivity was explained in terms of steric hindrance in a zwitterionic intermediate **62** that allowed competitive formation of **63** leading to **65** (equations 21, 22).



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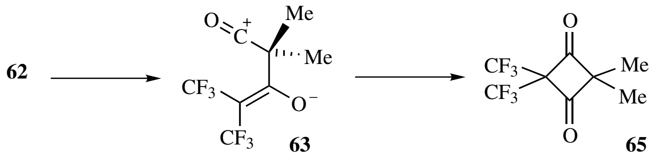
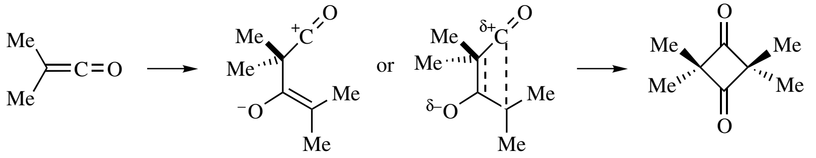


(22)

Huisgen and Otto[49] measured the solvent dependence of the dimerization rate of $Me_2C{=}C{=}O$ (**10**) by ^1H NMR and found good second-order kinetics, with a variation in substrate at 35 °C from 2.31×10^{-5} $M^{-1}s^{-1}$ in CCl_4 to 67.4×10^{-5} M^{-1} s^{-1} in CH_3CN. Relative rates were 1 (CCl_4), 2.00 (C_6H_6), 2.81 (C_6H_5Cl), 10.3 ($CDCl_3$), 11.3 (CH_2Cl_2), 15.1 (PhCN), and 29.2 (CH_3CN). This variation in rate gave a moderately good correlation with the solvent polarity parameter E_T. The reaction in PhCN gave $\Delta H^\ddagger = 10.8$ kcal/mol and $\Delta S^\ddagger = -42$ eu, suggesting an ordered transition state. These results were interpreted as showing less of an effect of solvent polarity on the rate than was expected for a zwitterionic transition state **66**, so a one-step reaction proceeding through a dipolar transition state **67** was favored (equation 23). However, both transition states **66** and **67** are expected to be stabilized qualitatively in polar solvents; furthermore, the reactant ketenes are quite polar. Hence, the magnitude and even the direction of the solvent effect on the rates by either transition state are difficult to predict. As pointed out,[49] the dipole moment of the product dione was zero, and a product-like transition state would be expected to show an inverse dependence of rate on solvent polarity. Both processes are also expected to have large negative entropies of activation, so quantitative criteria for differentiating the two are not available.



(23)

10 **66** **67** **11**

In summary, the evidence appears compelling that at least some mixed ketene dimerizations involving ketenes with substituents of very different polarities proceed through a two-step process involving zwitterionic intermediates. For dimerization of ketenes with similar polarities, the dimerizations occur either through one-step processes with a high degree of polar character or through two-step processes with zwitterionic intermediates.

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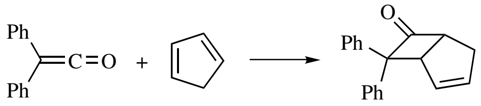
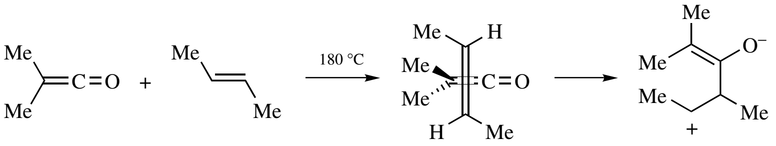
5.4.1.2 Cycloadditions with Alkenes and Dienes As noted in Section 5.4.1.1, the cycloaddition of diphenylketene (**1**) with cyclopentadiene to form cyclobutanone **2** was discovered very early[1,2] and is a characteristic ketene reaction. In this section, some prominent examples of the reaction are given, followed by a fuller discussion of some of the mechanistic features in Section 5.4.1.3. This process is reversible in only a few examples, and this method for forming ketenes is discussed in Section 3.4.1.



1 **2**

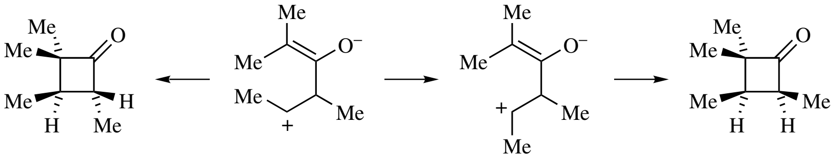
(1)

Diphenylketene gave cyclobutanones on reaction with ethylene, propene, and 1-hexene at temperatures of 85–115 °C.[3,4] Under these conditions *E*- and *Z*-2-butene reacted stereospecifically, with retention of the alkene stereochemistry, within the limits of ^1H NMR detection (4–6%).[3,4] Cycloaddition of these alkenes with $Me_2C{=}C{=}O$ (**3**) was carried out at 105 °C,[5] while *n*-BuCEt=C=O gave [2+2] cycloaddition with cyclohexene at 180 °C.[6] In the reaction of the 2-butenes with $Me_2C{=}C{=}O$ the *Z*-isomer reacted about twice as fast and gave a stereospecific reaction, whereas the less reactive *E*-isomer gave significant loss of the alkene stereochemistry (equations 2, 3).[5] The lower reactivity of *E*-2-butene provided evidence that the reaction occurred with a near-orthogonal approach of the ketene to the alkene double bond, as shown in **4** (equation 2), and the loss of stereochemistry was strong evidence for a stepwise process involving the zwitterion **5**, which underwent partial conversion to **6** to avoid steric crowding (equation 3).[5]



3 **4** **5**

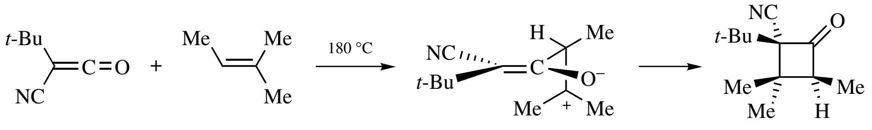
(2)



trans-**7** **5** **6** *cis*-**7**

(3)

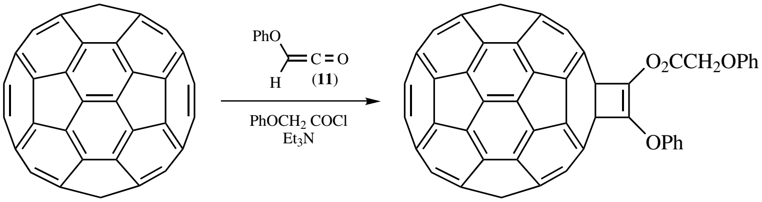
The cycloaddition of *t*-BuC(CN)=C=O (**8**) with 2-methyl-2-butene proceeded regio- and stereoselectively to form **10**, as shown by X-ray crystallography.[7] This reaction was interpreted[7] as occurring by a concerted pathway, but the results can also be explained by a pathway analogous to equation 2 in which the initial bond rotation in the intermediate **9** that determines the stereochemistry of the final product involves rotation of the cyano group away from the *syn* methyl (equation 4).



8 **9** *cis*-**10**

(4)

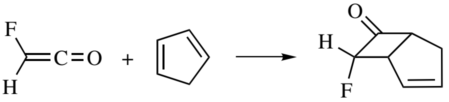
Preparative cycloadditions require sufficiently reactive Ketene and alkene partners. Thus the highly reactive phenoxyketene (**11**) generated by dehydrochlorination gave [2+2] cycloaddition with [60]fullerene forming **12** in a sequence including acylation of the initially formed cyclobutanone enol (equation 5).[8] Other aryloxyketenes reacted similarly, but there was no reaction with other less reactive ketenes.



12 (61%)

(5)

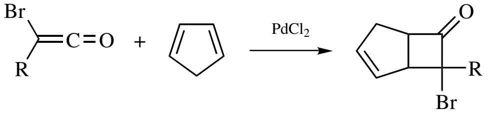
Reactive unsaturated groupings were usually required to trap the more reactive ketenes, which otherwise were consumed by self-reaction or other pathways. Dienes have been particularly useful in capturing many of the most reactive ketenes,[9–28] such as FCH=C=O (**13**, equation 6).[9,12,15] Electron-rich ketenophiles such as vinyl ethers[3,4,29] and imines are discussed in later sections.



13 **14**

(6)

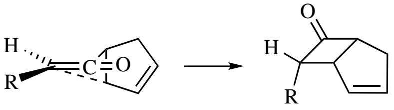
Palladium catalysis of the [2+2] cycloaddition to cyclopentadiene of ketenes RCBr=C=O (**15**) produced by the dehydrochlorination route forming **16** has been reported to give increased yields and selectivity (equation 7).[30] With longer-chain alkyl groups (C_8–C_{16}) as ketene substituents the bromine was exclusively in the less hindered *exo* position.



(7)

15 (R = *n*-alkyl) **16** (42–91%)

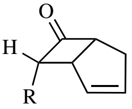
The frequent preference of the larger substituent for the *endo* position in this cycloaddition is a hallmark of ketene chemistry and has been taken as diagnostic evidence of the [$_\pi 2_s + _\pi 2_a$] mode of addition (equation 8). The transition state **17** shows that the substituent in the least hindered position in the transition state will occupy the *endo* position in the final product, which is seemingly more hindered. Bartlett[13] used the phrase “masochistic steric effect” to describe this situation, where the steric hindrance of a group was reversed between the transition state and the product.



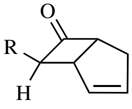
(8)

17 **18**

This simple picture was not as clear-cut as it seemed, as the *endo* isomer of **18** is not necessarily the least stable isomer, and indeed in many cases is more stable than the *exo* isomer. This was demonstrated by equilibration of the two isomers of **18**, in which the equilibrium product ratios in Table 5.3 were found.[9]



endo-**18**

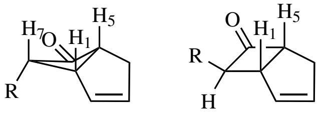


exo-**18**

TABLE 5.3 Product Percentages at Equilibrium for 7-Substituted Bicyclo[3.2.0]hept-2-en-6-ones 18[9]

R	*endo*	*exo*
F	88.7	11.3
Cl	86.7	13.3
CH_3	76.3	23.7
Et	64.4	35.6
i-Pr	56.9	43.1
t-Bu	9.6	90.4
Ph	67	33

The explanation for this unanticipated result[9] was that the cyclobutanone ring in **18** was not planar but puckered, and existed in the conformation depicted below for *endo*-**18**. This was established by an analysis of the ^{1}H NMR spectra, in particular the various H-H coupling constants. The preference for *endo*-**18** was explained by unfavorable steric interactions between the carbonyl group and H_1 and H_5 in the alternative conformation *exo*-**18**, and possibly by a favorable electronic interaction between H_5 and the carbonyl group in *endo*-**18** as well. The *endo* position in *endo*-**18** was more crowded, but this was offset for all but the *t*-butyl substituent by a preference of H_7 for the *exo* position so as to be orthogonal to the carbonyl group.[9] A stabilizing hyperconjugative interaction of the C-H_7 bond and the carbonyl may also be envisioned in this geometry.



endo-**18** *exo*-**18**

There was a strong solvent effect on the *exo/endo* methyl product ratio of the reaction of ketenes $CH_3CHal{=}C{=}O$ (Hal = Cl, Br) with cyclopentadiene, as shown in Table 5.4.[17] This result suggested that the formation of the less stable product in these reactions was not good evidence of a concerted mechanism. Further, this significant effect of solvent polarity may be taken as evidence that a polar zwitterionic intermediate was formed in the reaction, and that the partitioning of this intermediate between *exo* and *endo* products was affected by solvent polarity. The more polar solvents favored the *exo*-methyl isomer, and this effect may derive from a longer lifetime of a polar intermediate, favoring a more stable product.

The *exo/endo* stereochemical preference for cycloaddition was greatest for cyclopentadiene compared to some other alkenes (Table 5.5).[19] It has also been shown that cycloadditions of $MeCCl{=}C{=}O$ and $MeCBr{=}C{=}O$ with cyclopentadiene and cyclopentene gave similar selectivities.[18]

The fact that for many alkenes the *exo/endo* product ratio for ketene cycloadditions was insensitive to alkene structure, and rather close to 1, was evidence that

TABLE 5.4 Product Stereochemistry for [2+2] Cycloaddition of $CH_3CHal{=}C{=}O$ with Cyclopentadiene in Different Solvents[17]

Hal	Solvent	*exo*/*endo* (Me)	Hal	Solvent	*exo*/*endo* (Me)
Cl	hexane	1:4.3	Br	hexane	1.0:0.71
Cl	Et_3N	1:2.2	Br	Et_3N	1:0.28
Cl	$CHCl_3$	1:1.6	Br	CH_3CN	1:0.14
Cl	CH_3CN	1.0:0.59			

TABLE 5.5 ***Exo/endo*** **Product Ratios for [2+2] Cycloaddition of PhCMe=C=O in Hexane with Different Alkenes**[19]

Alkene	*exo/endo* (Me)
Cyclopentadiene	>20
$EtOCH{=}CH_2$	2.3
Dihydropyran	1.7
Cyclohexene	2
Cyclooctene	1

these cycloaddition transition states were not highly ordered. It was also notable that $EtOCH{=}CH_2$ and cyclohexene, expected to involve extremes in their sensitivity to solvent polarity, gave similar results.

Rate data for the reaction of $Ph_2C{=}C{=}O$ with some alkenes and dienes are given in Table 5.6.[23–25] In the reaction with isoprene and chloroprene the ratios of addition to the substituted and unsubstituted double bonds were 1.5:1 and 1:4, respectively.[24] The reactions were interpreted in terms of "near-concerted" processes,[24] but there was a very large accelerating effect for cyclopentadiene (3×10^4 relative to cyclopentene), which was well suited for conjugative stabilization in a polar transition state. The regiochemistry of the reaction of isoprene also showed a significant polar effect, with a preference for reaction at the more hindered double bond.

In the reaction of t-BuC(CN)=C=O (**8**) with $Me_2C{=}CHCH{=}CMe_2$ the adducts **19** and **20** were formed, and on heating in benzene containing 7% EtOH the proportion of **20** in the mixture increased from 67 to 85% (equation 9).[26] The formation of two products, and the apparent isomerization of **19** to **20**, were interpreted as showing that a zwitterionic intermediate was involved in the reaction that was not trapped by EtOH. In the reaction of **8** with **21** the initial product showed a 5:1 preference for **22**, but on prolonged heating **23** was the only product observed

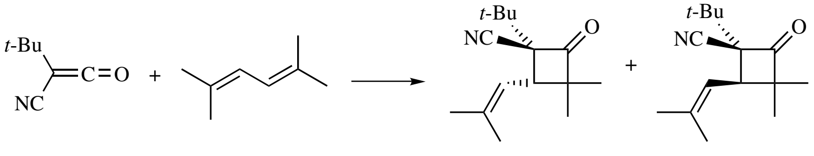
TABLE 5.6 Rate Constants for Reaction of $Ph_2C{=}C{=}O$ with Alkenes with Dienes ($M^{-1}\,s^{-1} \times 10^6$)[23–25]

Alkene	k_2 (40 °C, PhCN)	k_2 (30 °C, THF)
Cyclopentene	1.25	
$CH_2{=}CHCH{=}CH_2$		1.17
Cyclopentadiene	3.73×10^4	280
Cyclohexadiene	53.0	
E-$CH_3CH{=}CHCH{=}CH_2$	17.5	
Z-$CH_3CH{=}CHCH{=}CH_2$	9.3	
$CH_2{=}CMeCH{=}CH_2$	4.9	
Dihydropyran	23.5[a,b]	16.5

[a] In THF; 34 (toluene), 16 (n-PrCN), and 9.4 (DMF).[25]

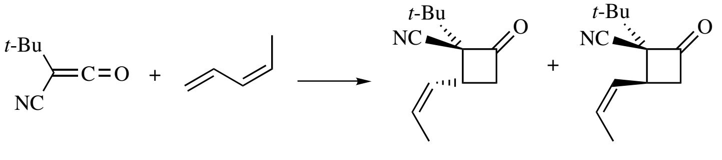
[b] $\Delta H^{\ddagger} = 9.1$ kcal/mol, $\Delta S^{\ddagger} = -43$ eu.

(equation 10).



8 **19** **20**

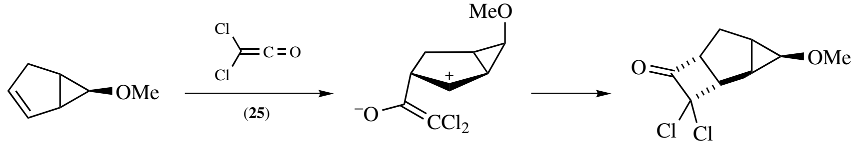
(9)



8 **21** **22** **23**

(10)

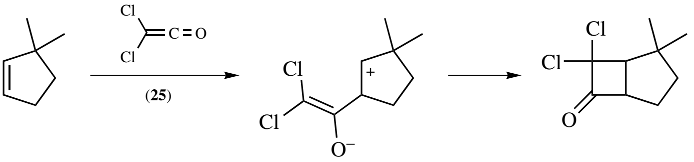
An illustration of the polar effect in ketene [2+2] cycloadditions was found in the reaction of dichloroketene (**25**) with the vinylcyclopropane **24** used in prostaglandin synthesis (equation 11).[31,32] The selectivity for formation of the product **27** was attributed to the stabilization of the positively charged carbon in transition state **26** by the adjacent cyclopropyl group.



24 **26** **27**

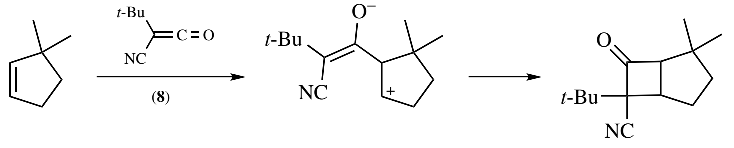
(11)

Cycloadditions of ketenes to 3,3-dimethylcyclopentene (**28**) show an interesting variation with ketene structure.[33] There was a reversal in the regiochemistry of the preferred product for $CCl_2{=}C{=}O$ (**25**, equation 12) compared to *t*-BuC(CN)=C=O (**8**, equation 13). The results were interpreted in terms of nonparallel approach of the reactants and concerted [2+2] processes, but could also be explained by stepwise processes. Thus, formation of zwitterionic transition states (or intermediates) would be favored by both steric and polar factors (equation 12). In equation 13 the most stable product was formed, and in a stepwise process this would involve initial formation of a bond at the most crowded carbon. This arrangement, however, minimized the interaction of the geminal dimethyl groups with the *tert*-butyl and was evidently the most favorable arrangement. Diphenylketene at 100 °C adds to **28** as in equation 12, but at 200 °C dissociates to the reactants with a half-life of 15–20 min.[33]



28 **29** **30**

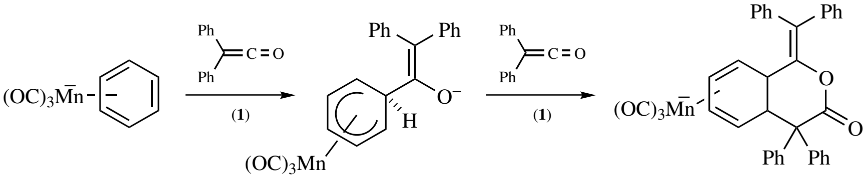
(12)



28 **31** **32**

(13)

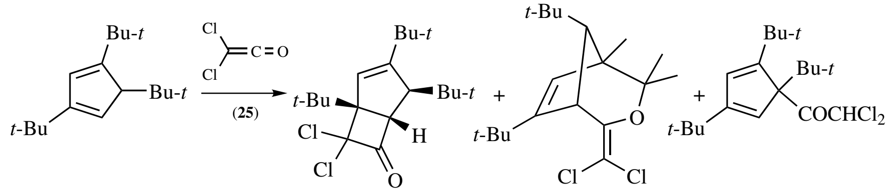
Diphenylketene (**1**) underwent [2+2+2] cycloaddition with the 18-electron η^4-arene complex $[Mn(\eta^4 C_6H_6)(CO)_3]^-$ $[Ph_3PNPPh_3]^+$ (**33**), possibly through the monoadduct **34**, to give the dihydroisochroman-3-one **35**, with the structure confirmed by X-ray (equation 14).[34]



33 **34** **35** (74%)

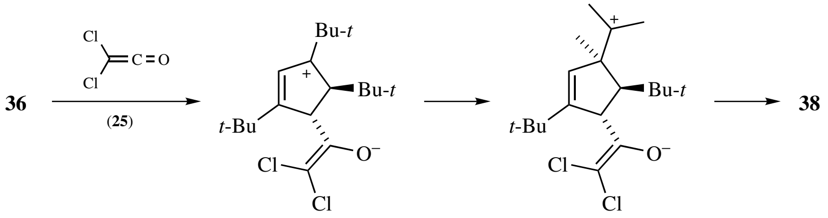
(14)

Reaction of 1,3,5-tri-*t*-butylcyclopentadiene (**36**) with dichloroketene (**25**) gave the adducts **37–39** (equation 15).[35] The [2+2] cycloadduct **37** (54%) formed when **25** was generated from $CHCH_2COCl$ and Et_3N, but **38** (60%) was formed when **25** was made from CCl_3COCl and Zn, and the latter reaction was proposed to involve $ZnCl_2$-promoted formation of a zwitterion that underwent rearrangement and cyclization (equation 16).[35] The formation of **39** was proposed to occur by several paths. Reaction of **36** with CHCl=C=O (**40**) gave the [2+2] cycloadduct **41**, which rearranged on heating to the [4+2] adduct **42** (55%, equation 17).[35] This was proposed to proceed through a diradical intermediate, but a zwitterionic intermediate as shown also appears to explain the results.

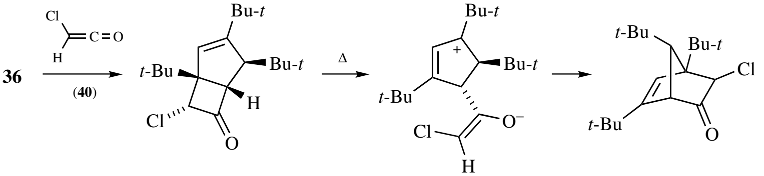


36 **37** **38** **39**

(15)



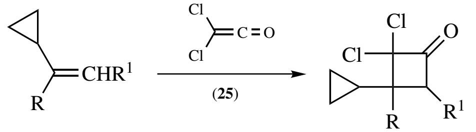
(16)



41 42

(17)

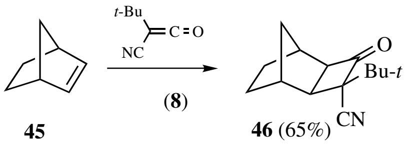
Cyclopropylalkenes **43** gave [2+2] cycloaddition with dichloroketene (**25**) without cyclopropane ring opening (equation 18).[36] Thus, while the regiochemistry for the reaction was consistent with positive charge development adjacent to the cyclopropyl in the transition state, it was not sufficient to induce ring opening.



43 **44** (50%, R = R^1 = *c*-Pr)

(18)

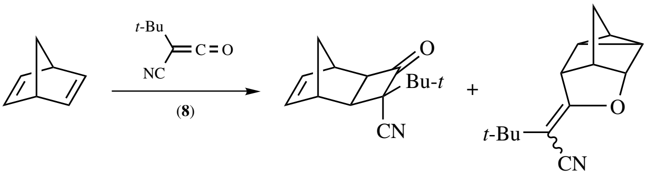
Norbornene (**45**) and other bicyclo[2.2.1]heptenes[37–41] gave [2+2] cycloaddition with *t*-BuC(CN)=C=O (**8**), with formation of adducts such as **46** with the *tert*-butyl group *syn* to the CH_2 bridge (equation 19).[37] This formation of the more crowded product was characteristic of ketene cycloadditions, and was consistent with a process in which the initial bond rotation that determined the product stereochemistry moved the cyano away from the congested norbornyl fragment (equation 19).



45 **46** (65%)

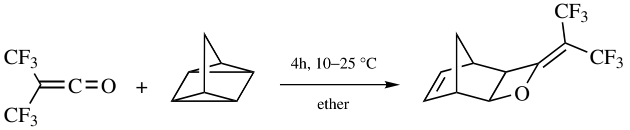
(19)

The reaction of *t*-BuC(CN)=C=O (**8**) with norbornadiene (**47**) led to both the [2+2] cycloaddition product **48** and the product of [2+2+2] cycloaddition to the ketene carbonyl **49** (equation 20).[40] These products arose from competing *exo* and *endo* attack of the ketene, and the ratio fo the two products showed little dependence on the solvent polarity, indicating that the two transition states had similar polarities.[40] The ketene $(CF_3)_2C{=}C{=}O$ (**50**) gave only a product analogous to **49** on reaction with norbornadiene,[42] whereas $CCl_2{=}C{=}O$ and *i*-PrCCl=C=O gave the product analogous to **48**,[43,44] as did MeCBr=C=O, but the latter ketene showed a solvent-dependent stereochemistry of the substituents in the product.[45] Ketene **8** reacted with 3,3-dimethylcyclopropene to give [2+2] cycloadducts and ring-opened products, while **50** gave only ring-opened products.[45] Reaction of bis(trifluoromethyl)ketene (**50**) with nortricylane **51** gave the cycloadduct **52** under mild conditions in 92% yield (equation 21).[46]



47 **48** **49**

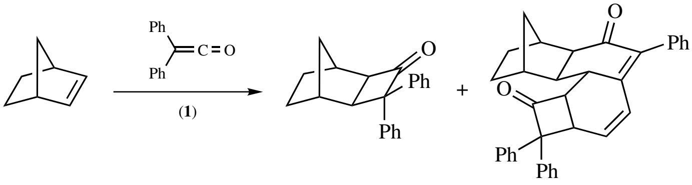
(20)



50 **51** **52** (92%)

(21)

Norbornene (**45**) reacted with diphenylketene (**1**) in refluxing benzene to produce the 1:1 adduct **53** (84%), but reaction with excess $Ph_2C{=}C{=}O$ led to a 5:1 ratio of **53** and the 2:1 adduct **54** (equation 22).[47]



45 **53** (45–56%) **54** (10–16%)

(22)

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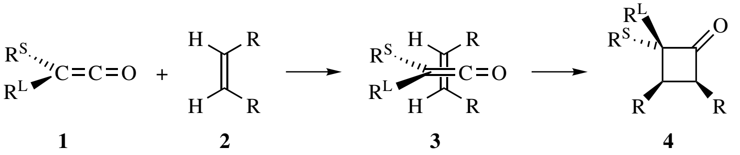
5.4.1.3 Mechanism of Ketene [2+2] Cycloadditions with Alkenes The facile [2+2] cycloaddition reaction of ketenes is a centerpiece of one of the classic mechanistic problems of organic chemistry, namely, the readiness of many alkenes to undergo thermal concerted [4+2] cycloaddition with dienes, whereas thermal [2+2] cycloadditions of ordinary alkenes are clearly stepwise, if they occur at all. The appearance in the mid-1960s of the Woodward-Hoffmann rules[1–3] had a profound effect on the chemical community and provided the explanation that $[_{\pi}4_s+_{\pi}2_s]$ cycloadditions were allowed by orbital symmetry, whereas $[_{\pi}2_s+_{\pi}2_s]$ processes were forbidden.

Experimentally, it was known that unsymmetrically substituted ketenes **1** with one substituent R^L more sterically demanding than the other reacted by [2+2] cycloaddition with alkenes **2** with more sterically demanding substituents on one side than the other to produce preferentially cyclobutanones **4** with the larger substituents on one side of the ring (equation 1). In many cases there was no loss of the original stereochemistry of the alkene. This was explained as resulting from an almost orthogonal approach of the ketene to the alkene with the smaller ketene substituent R^S approaching the less hindered side of the alkene and a transition state **3** with antarafacial bonding, so that initially the smaller substituent R^S moved away from the alkene, but with the result that the larger substituent R^L was *cis* to the larger alkene substituents in the product.



(1)

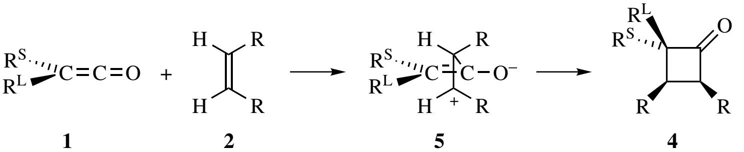
Woodward and Hoffmann[3] put forward the reasons for the tendency of ketenes to undergo concerted [2+2] cycloadditions as opposed to a [4+2] pathway. First, ketenes are powerful electrophiles; specifically, the π* C=O orbital is quite low in energy and very susceptible to nucleophilic attack. This carbon is also only disubstituted, which facilitates its reactivity even more by the absence of steric interactions. Thus, nucleophilic attack is greatly facilitated and takes place rapidly, usually resulting in [2+2] cycloaddition. However, the reactivity of the C=C linkage of the ketene in a concerted $[_\pi 4_s + _\pi 2_s]$ process is not facilitated by the carbonyl group so in this process the ketene resembles a normal alkene and is not very reactive. Only in unusual cases in which the intermediates are long-lived does [4+2] cycloaddition result, but probably not by concerted processes (Section 5.4.3).

Ketene cycloadditions played a key role in the acceptance of these proposals, as the $[_\pi 2_a + _\pi 2_s]$ cycloaddition is an allowed process. The existing data on ketene cycloadditions appeared to fit this proposal, and it was stated with authority regarding this mechanism that "the evidence is now conclusive that it is concerted."[3] Interestingly, the first publication on the subject stated, "it must be concluded that those cycloadditions which do occur in cases prohibited by our selection rules for concerted reactions must proceed through multistep mechansisms, (e.g., dimerization of allenes and ketenes. . . ."[1] However, after further analysis, it was realized that ketenes possessed structures permitting the $[_\pi 2_a + _\pi 2_s]$ cycloaddition.

The evident readiness of ketenes to react in this way, whereas ordinary alkenes do not, was explained by the proposal that the ketene transition state **3** was much more suitably disposed to the $[_\pi 2_s + _\pi 2_a]$ process than that for alkenes because of the lesser steric demands of the ketene, and also because of the favorable bonding interactions between both carbons of the alkene and the electron-deficient *p* orbital of the carbonyl carbon.

An alternative description suggested by Zimmerman in 1970 stated that this process was best described in Hückel-Möbius terms, and it allowed for six π-electron systems with no sign inversions or four π electrons with one sign inversion.[4,4a] This was described by Baldwin and Kapecki as involving a p orbital on oxygen[5] or as an (S+S+S) process, often given as an $[_\pi 2_s + (_\pi 2_s + _\pi 2_s)]$ pathway using the C=C and C=O π bonds of the ketene and the π bond of the alkene.[4,5] In this mechanism the major initial bond formation involves attack by the more nucleophilic of the alkene carbons on the carbonyl π-orbital at C_1 of the ketene. To a lesser extent the other carbon of the alkene carries out electrophilic attack on C_2 of the ketene. Thus, addition to the ketene involves nucleophilic attack at C_1 and electrophilic attack on the orthogonal orbital at C_2.

A counterproposal was made at the same time that instead of "a (more or less) synchronous cycloaddition," as proposed by Woodward and Hoffmann, cycloaddition of ketenes and alkenes occurred by a two-step reaction involving a dipolar intermediate.[6,7] This intermediate **5** was proposed to result from initial bond formation from the more nucleophilic carbon of the alkene, to the carbonyl carbon with an interaction between the cationic carbon and the enolate system of the dipolar intermediate (equation 2).[4,5] This mechanism also involved an initial almost orthogonal approach of the ketene to the alkene from the least hindered direction, and a second step with initial bond rotation at C_2 of the ketene so that the smaller substituent on the ketene moved away from the nearest alkene substituent. As the second bond formed, this brought the larger ketene and alkene substituents into a *cis* relationship (equation 2).

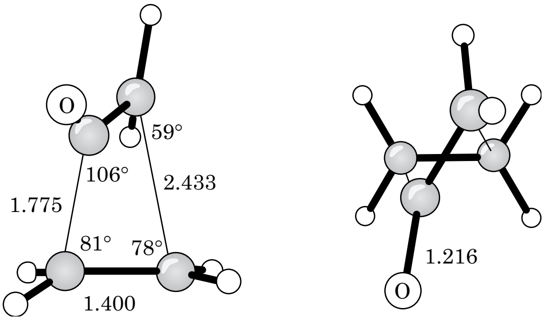


1 **2** **5** **4** (2)

Many of the experimental criteria that have been applied to the differentiation of concerted and stepwise reaction pathways for ketene cycloaddition are ambiguous, as an unsymmetrical concerted process and a stepwise process have many of the same features. In cases where there is a loss of stereochemical homogeneity in the alkene,[8,9] or where there is isolation, spectroscopic detection, or interception of an intermediate that lies on the cycloaddition pathway, there is unequivocal evidence for a stepwise process. Such intermediates have indeed been detected in a number of cycloaddition reactions of ketenes, as discussed below, and so these are known to be stepwise. The very high stereoselectivity observed in many ketene cycloadditions suggests that these reactions have all the features of concerted asynchronous reactions, but in some cases newer and better experimental methods could give more accurate measures of the degree of stereoselectivity and reexamination of some of these could be informative. Perhaps the best evidence for the occurrence of concerted processes is the failure to detect an intermediate in a number of high-level theoretical studies. However, even in these cases there is still doubt that the theoretical methods provide a sufficiently accurate description of reaction in solution. Thus, proof that ketene cycloadditions proceed by concerted pathways remains an elusive goal.

The types of evidence available regarding the mechanism of ketene [2+2] cycloadditions include (a) theoretical analysis, (b) stereochemistry, (c) isotope effects, (d) substituent effects, (e) solvent effects, (f) pressure effects and (g) activation parameters. However, as described below, the effects of substituents, solvent effects, pressure effects and activation parameters are expected to be similar for the two alternative mechanisms under consideration, as both are bimolecular and lead to a polarized transition state. Similarly, both mechanisms have similar stereochemical outcomes, although it has often been argued that very high retention of configuration of the alkene stereochemistry is indicative of a concerted process.

There have been many theoretical studies of the mechanism of ketene cycloadditions,[10–22] and these studies are helping to define the possible variations in the transition states and the factors that influence them. The studies emphasize the



Scheme 5.3 Calculated MP2/6-31G* transition state for [2+2] calculation of ketene and ethylene (reprinted from reference 14 with permission of Wiley VCH).

effects of substitutents on the ketenes and alkenes which can cause significant changes in the energetics of the reactions.

Wang and Houk[13] calculated the geometry and energy of the transition state for the [2+2] cycloaddition of ketene and ethylene at the MP2/6-31G* level and found a highly asymmetric geometry (Scheme 5.3).[14] The forming bond length of the carbonyl carbon is 1.78 Å, while that of the second forming bond is 2.43 Å.

This reaction was also studied by Bernardi et al.[12] at the 4-31G level. The authors reported one transition state resembling that shown in Scheme 5.3 formed by attack in the ketene plane. These authors also located a second transition state similar in energy to the first but with attack of the ethylene perpendicular to the ketene plane.

Both of these studies emphasized the highly asynchronous nature of the reaction.[12,13] The carbonyl carbon of the ketene interacts strongly with both ethylene carbons.[14] Mulliken population analysis shows an increase in negative charge on oxygen ($\Delta q = -0.16$) and a concomitant increase in positive charge on the weakly bonding carbon from ethylene ($\Delta q = +0.22$), showing the zwitterionic character of the structure.[13]

High-level *ab initio* molecular orbital calculations for the cycloaddition reaction between ketene and cyclopentadiene gave predicted reaction energies (MP4SDQ + ZPVE) for the products **8–12**, as shown (kcal/mol), with calculated activation energies (CCSD(T) + ZPVE) given in parentheses (Figure 5.2).[25] The [4+2] cycloaddition product **8** was predicted to be the most stable, but the barrier for formation of the [2+2] product **9** was less by 12.0 kcal/mol.[25] However, these studies did not include the [4+2] product **13** from addition to the C=O bond.

The transition state for the [4+2] reaction forming **8** had almost equal bond formation to the ketene carbonyl carbon C_1 and to C_2, with bond distances of 2.187 and 2.276 Å, respectively and the reaction was described as a synchronous

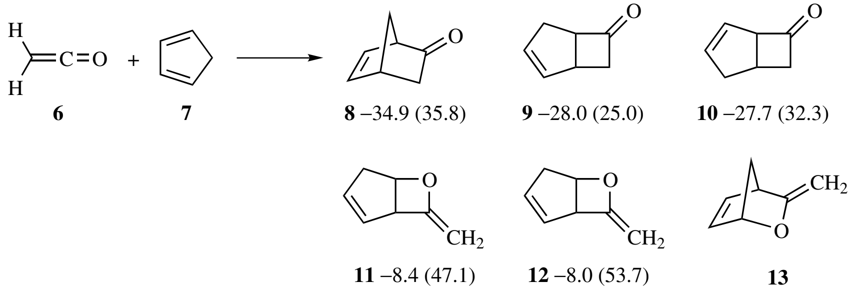
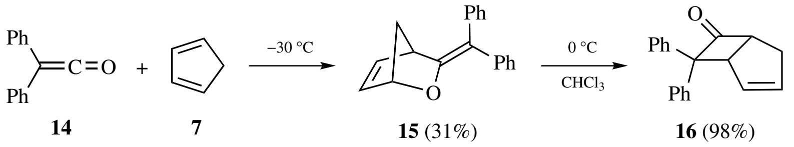


Figure 5.2 Calculated MP4SDQ/6-31G*//MP2/6-31G* reaction energies (kcal/mol) for cycloaddition of ketene (**6**) with cyclopentadiene (**7**), with activation energies, (kcal/mol) in parentheses.

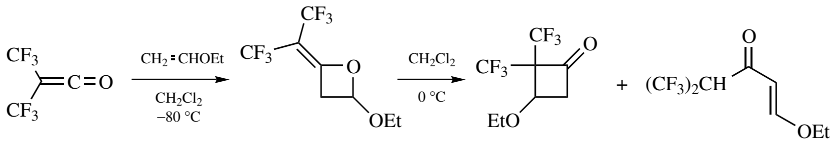
concerted process.[25] By contrast, the transition state for the [2+2] cycloaddition forming **9** had major bond formation to C_1, with a bond distance of 1.636 Å and no bond to C_2. There was a net charge transfer from the cyclopentadienyl moiety to the ketene of 0.4 electron.

However, a major reevaluation of ketene/alkene cycloaddition chemistry has been necessitated by the finding that the kinetically favored pathway in the prototypical reaction of diphenylketene (**14**) with cyclopentadiene at −20 °C in CH_2Cl_2 is [2+2] cycloaddition with the carbonyl group forming **15** (equation 3).[26,27] Upon warming, **15** was converted by a [3,3] sigmatropic Claisen rearrangement to the previously observed cyclobutanone **16**, as reported in the very first example of a ketene/alkene cycloaddition.[28,29] Reactions of $Ph_2C{=}C{=}O$ with acyclic 1,3-dienes also gave mixtures of [4+2] and [2+2] cycloadducts.[27] Theoretical analyses of these pathways have also been carried out.[26,27,30]



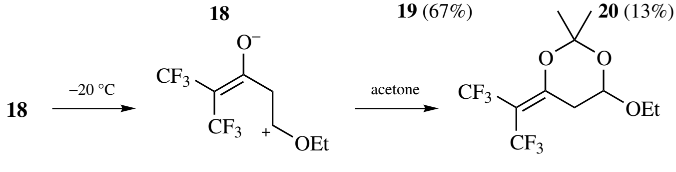
(3)

A [4+2] cycloaddition to the C=O bond of a ketene has also been found for the reaction of $(CF_3)_2C{=}C{=}O$ (**17**) and $EtOCH{=}CH_2$.[31] Reaction in hexane at 0 °C gave the oxetane **18** as detected by NMR, and this isomerized at 50 °C to the cyclobutanone **19** and the enone **20**, isolated in 67 and 13% yields, respectively, when the cycloaddition was performed at 100 °C (equation 4).[31] Reaction in CH_2Cl_2 at −80 °C permitted isolation of **18**, which at −20 °C gave a deep blue intermediate assigned as the zwitterion **21**. Reaction of **18** in acetone gave the adduct **22** from **21** (equation 5).[31]



(4)

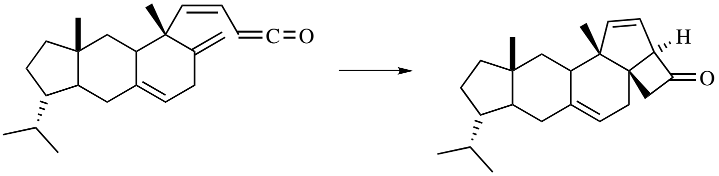
17 **18** **19** (67%) **20** (13%)



(5)

21 **22** (92%)

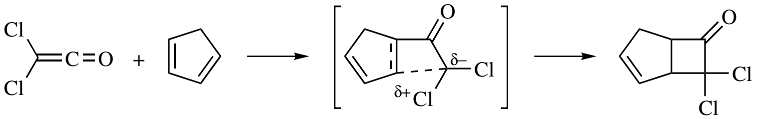
Evidence for nonconcerted mechanisms in some cases comes from studies of intramolecular [2+2] cycloadditions of ketenes with alkenes, which have revealed examples that proceed quite readily by net $[_\pi 2_s + _\pi 2_s]$ stereochemistry (Section 5.4.4). For example, cyclization of the ketene **23** derived by dehydrochlorination forming **24** was evidently stepwise, for a concerted $[_\pi 2_a + _\pi 2_a]$ *syn* addition was electronically forbidden, and an allowed $[_\pi 2_s + _\pi 2_a]$ reaction was not geometrically feasible (equation 6).[32]



(6)

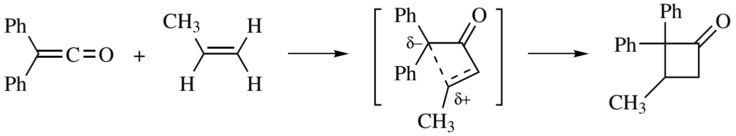
23 **24**

The regiochemistry of ketene [2+2] cycloaddition with alkenes is almost invariably that expected for a species with dipolar charge, as shown by the examples of dichloroketene (**25**) addition to cyclopentadiene (equation 7) or to propene (equation 8).[33] Perturbation theory predicts this regiochemistry, in that bonding occurs between the carbonyl carbon of the ketene, the atom with the highest coefficient in the LUMO and the carbon of the alkene with the highest coefficient of the HOMO. Bonding between these atoms also produces the most stabilized zwitterionic intermediate, which leads to the products shown in equations 7,8.



(7)

25 **7** **26** **27**



(8)

14 **28**

TABLE 5.7 Rate Constants for Reaction of Alkenes with $Ph_2C{=}C{=}O$ (k_2, $M^{-1}\ s^{-1}$) in PhCN at 40.3 °C[35,39]

Alkene	$k_2 \times 10^4$	Alkene	$k_2 \times 10^4$
1-Pyrolidinoisobutene	2.4×10^5	$PhC(OMe){=}CH_2$	12
2,3-Dihydrofuran	1.04×10^3	*E*-*n*-$PrOCH{=}CHCH_3$	0.6
Cyclopentadiene	372	$EtOCH{=}CMe_2$	0.29
2-Ethoxypropene	227	$PhCH{=}CH_2$	0.23
1-Morpholinoisobutene	169	$PhCMe{=}CH_2$	0.038
Z-*n*-$PrOCH{=}CHCH_3$	110	Cyclopentene	0.0125
$EtOCH{=}CH_2$	45	$CH_2{=}CHCN$	No reaction
Z-EtOCH=CHMe	109[a]	*Z*-EtOCH=CHPr-*i*	117[a]
E-EtOCH=CHMe	1.29[a]	*E*-EtOCH=CHPr-*i*	0.742[a]
Z-EtOCH=CHEt	1.28[a]	*Z*-EtOCH=CHBu-*t*	3.6[a]
E-EtOCH=CHEt	1.20[a]	*E*-EtOCH=CHBu-*t*	0.054[a]

[a] Reference 35.

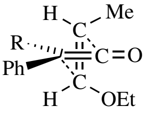
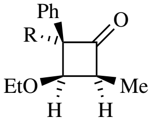
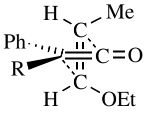
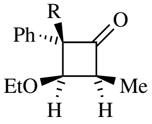
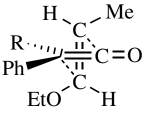
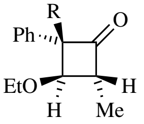
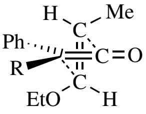
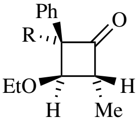
The stereochemistry of addition is such that the largest substituents on the ketene and alkene are almost always in the *syn* position on the cyclobutanone.[34–39] However, as discussed in Section 5.4.1.2, this product is also sometimes the thermodynamically most stable isomer. *Z*-Alkenes are also significantly more reactive than the *E*-isomers toward $Ph_2C{=}C{=}O$ (Tables 5.7–5.9).[34,35,39] and $Me_2C{=}C{=}O$ (Table 5.10).[40] These results are explained by an intermediate or transition state **5** in which the more nucleophilic carbon C_1 attacks the carbonyl carbon in the ketene plane and the more bulky C_β terminus of the ketene is directed away from the alkene substituents (equation 2). For convenience this structure is often represented with an orthogonal alignment of the ketene and alkene, but theoretical studies indicate that the carbonyl carbon will tilt more closely toward the more nucleophilic carbon of the alkene, with C_2 of the ketene skewed toward the other alkene carbon as in Scheme 5.3, and also higher above the ketene plane than the carbonyl carbon. A $[_\pi2_s + _\pi2_a]$ or $[_\pi2_s + (_\pi2_s + _\pi2_s)]$ pathway from **5** leads to a *cis* disposition of all three R groups in the product, as is usually observed (equation 2).

The reaction of *t*-BuC(CN)=C=O (**29**) with *Z*- and *E*-cyclooctene forming **30a** and **30b**, respectively, provided an impressive example of the stereoselectivity of ketene cycloadditions.[36] In each case the reaction gave retention of the cyclooctene

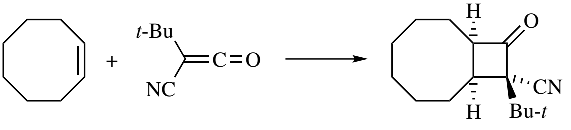
TABLE 5.8 Rate Constants for [2+2] Cycloaddition of Enol Ethers with $Ph_2C{=}C{=}O$ at 23 °C ($s^{-1}\ M^{-1} \times 10^6$)[40]

Enol Ether	k_2 (*Z*)(CCl_4)	k_2 (*Z*)($CDCl_3$)	k_2 (*E*)(CCl_4)	k_2 (*E*)($CDCl_3$)
MeOCH=CHMe	48	880	0.303	5.6
MeOCH=CHEt	73	732	0.483	3.8
EtOCH=CHMe	258	2050	2.2	13
EtOCH=CHEt	173	2530	1.48	8.58

TABLE 5.9 Partial Rate Constants (k_2, s^{-1} M^{-1} × 10^6) for Reaction of Z- and *E*-Ethoxypropene with PhCR=C=O in PhCN at 40 °C[34]

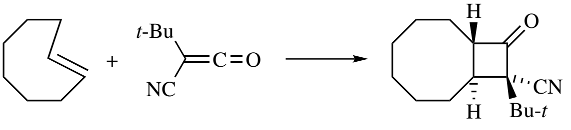
	 **31a**  **32a**	 **31b**  **32b**	 **31c**  **32c**	 **31d**  **32d**
R = Me	985	130	61	—
Et	77	65	3.5	0.40
n-Pr	65	62	2.4	0.35
i-Pr	—	26	0.022	0.13
t-Bu	—	5.1	—	0.028

configuration and led to the stereoisomer with the *t*-butyl in the seemingly less stable position *cis* to the alkyl group (equations 9, 10). These results appear consistent with a concerted [$_\pi 2_s + _\pi 2_a$] cycloaddition whereas free zwitterionic intermediates would seem to easily convert to a more stable isomer if formed. Dichloroketene also adds stereospecifically to *Z*- and *E*-cyclooctenes.[37]



(**29**) (**30a**)

(9)



(**29**) (**30a**)

(10)

The reactivity of $Ph_2C{=}C{=}O$ with alkenes in PhCN decreased by a factor of 10^7 as the alkene structure became less electron rich (Table 5.7).[39] Comparable kinetic data were found for reactions of enol ethers with $Ph_2C{=}C{=}O$ in CCl_4 and $CDCl_3$ (Table 5.8).[40] The span of reactivities was quite large and shows convincingly that very large polar effects are present in these reactions. The very high reactivity of the enamines in particular argues that zwitterionic intermediates are involved in these processes, as does the formation of noncyclized products in the reactions of some very nucleophilic alkenes. This evidence is discussed in Section 5.4.1.7.

The *Z/E* rate ratios in Table 5.8 varied from 115 to 160 in CCl_4 and from 150 to 295 in $CDCl_3$, confirming the greater reactivity of *cis* alkenes. The ratio $k(CDCl_3)/k(CCl_4)$ varied from 5.7 to 18.5, showing a significant polar solvent effect on these reactions.

The reactions of the *Z*- and *E*-1-ethoxypropenes with PhCR=C=O proceed quantitatively to the cyclobutanones.[34] On the assumption that the products resulted exclusively from stereospecific $[_{\pi}2_a+_{\pi}2_s]$ reactions through the complexes **31** shown, the rate and product data were quantitatively separated into the individual rate constants shown in Table 5.9.[34]

The influence of R on the rates of the processes proceeding through the reaction complexes **31b** and **31d** was attributed both to the varying electronic properties of R and to a remote steric effect in which the more bulky groups R affected the conformation of the phenyl and increased steric repulsions in the transition states.[34] Because the electronic properties of these R groups varied much less than their steric bulk, the latter factor would appear to be most important.

The relative reactivities of $Me_2C{=}C{=}O$ with alkenes determined by competitive techniques (Table 5.10)[41] are generally consistent with the rate constants reported in Tables 5.7–5.9, although the latter sets cover a wider range of reactivities. The relative reactivities also show a large rate difference $k(EtOCH{=}CH_2)/k(PhCH{=}CH_2) = 89$ that argues for highly polar transition states, at least for the vinyl ether.

Cycloaddition rate constants of $Ph_2C{=}C{=}O$ with 1,1-diarylethylenes and substituted styrenes (Table 5.11) gave linear Hammett plots with the σ constants of the aryl substituents with ρ values of -0.78 and -0.73, repectively.[5] These reactions were all first order in both $[Ph_2C{=}C{=}O]$ and the alkene, but whereas the styrenes gave cyclobutanones, the diphenylethylenes gave adducts containing two molecules of $Ph_2C{=}C{=}O$ and one of the alkene.[42] It was proposed that the rate-limiting step for the latter reaction was a [2+2] cycloaddition to form a cyclobutanone followed by reaction with a second ketene. However, the structure of the final product and the

TABLE 5.10 Relative Reactivities in [2+2] Cycloaddition of $Me_2C{=}C{=}O$ with Alkenes at 100 °C[41]

Alkene	k(rel)	Alkene	k(rel)
Z-2-butene	1.0	$PhCH{=}CH_2$	0.1
Z-2-pentene	1.0	$4\text{-}MeOC_6H_4CH{=}CH_2$	2.6
1-butene	0.44	$4\text{-}MeC_6H_4CH{=}CH_2$	1.8
isobutene	0.124	$4\text{-}ClC_6H_4CH{=}CH_{28}$	0.36
E-2-butene	8×10^{-4}	Cyclobutene	0.009
E-2-pentene	10^{-3}	Cyclopentene	0.19
1,3-butadiene	2.64	Cyclohexene	0.068
2-Me-2-butene	0.016	Cycloheptene	0.06
$Me_2C{=}CH_2$	No reaction	Cyclooctene	0.92
$EtOCH{=}CH_2$	8.9	Methylenecyclopropane	1.81
$n\text{-}BuOCH{=}CH_2$	9.0	$EtOC{\equiv}CH$	23.7

TABLE 5.11 Rate Constants for Reaction of $Ph_2C{=}C{=}O$ with $(4\text{-}XC_6H_4)_2C{=}CH_2$ and $4\text{-}XC_6H_4CH{=}CH_2$ at 120 °C in PhBr[45]

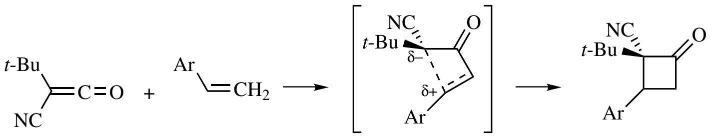
	$k(s^{-1} \times 10^{-4})$	$k(s^{-1} \times 10^{-4})$
X	$Ar_2CH{=}CH_2$	$ArCH{=}CH_2$
CF_3	0.0167	2.85
Cl	0.0863	7.82
H	0.113	7.00[a]
CH_3	0.212	9.43

[a] 6.66 ($1,2\text{-}Cl_2C_6H_4$), 6.50 ($[ClCH_2CH_2]_2O$), and 6.03 (DMF).

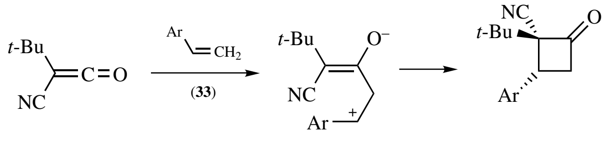
details of the reaction have evidently not been settled. The [2+2] cycloaddition of $Me_2C{=}C{=}O$ with substituted styrenes (Table 5.10) gave a ρ value of -1.4,[41] indicative of modest charge development.

The large rate differences observed with the structural variations shown in Tables 5.7–5.10 are indicative of a high degree of positive charge buildup on the alkene. The substituent effects of the styrenes noted are more modest, and overall these trends are less than those observed in alkene protonations in water.[43] Thus, the $EtOCH{=}CH_2/PhCH{=}CH_2$ rate ratio for the latter reaction is 10^5 and the ρ^+ value for styrene protonation is -2.9.[43]

The kinetics of the cycloaddition of *tert*-butylcyanoketene (**29**) with styrenes **33** gave a good correlation with $\sigma_p{}^+$ parameters with $\rho^+ = -2.48$ ($r = 0.998$), but not with σ_p values, and gave stereoselective formation of the less stable products **35** (equation 11).[44] Thus, the response of the reactivity of **29** to the styrene substituents, as measured by the $\sigma_p{}^+$ value, was considerably more than for the corresponding reactions of dimethylketene at 100 °C and diphenylketene at 120 °C, which gave ρ values of -1.4 and -0.73, respectively. These results, and the failure to intercept any zwitterionic intermediates, were interpreted in terms of a one-step concerted but nonsynchronous cycloaddition involving an unsymmetrical transition state **34** with a high degree of zwitterionic character.[44] A stepwise process was proposed for the reaction of **29** with styrenes with 4-MeO, 4-F and 4-Cl substituents.[45,46] For Ar = 9-anthryl **37** was the only observed product, and this was attributed to a stepwise process proceeding through intermediate **36** due to the bulk and electron-donor ability of the 9-anthryl group (equation 12).[46]



29 **33** **34** **35** (11)



29 **36** **37** (12)

TABLE 5.12 Rates of Reaction of t-BuC(CN)=C=O with 4-$XC_6H_4CH=CH_2$ in C_6H_6 at 25 °C ($M^{-1}\ s^{-1} \times 10^3$)[44]

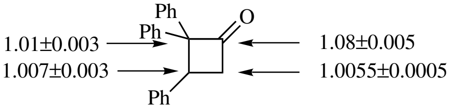
X	k_2	X	k_2
MeO	121	H	1.59
n-Bu	5.92	4-Br	0.571
Me	9.78		

Sizable negative entropies of activation of [2+2] ketene cycloadditions[39,42,44] are consistent with bimolecular processes proceeding by either concerted pathways or through zwitterionic intermediates.[47]

Solvent effects on ketene cycloaddition reveal a rate ratio $k(CH_3CN)/k$(cyclohexane) of 160 for the reaction of $Ph_2C=C=O$ with n-$BuOCH=CH_2$.[39] The comparable ratio for the same two solvents for the reaction of TCNE with n-$BuOCH=CH_2$ is about 2600.[48–50] The latter reaction is established to be stepwise, and there is a qualitative resemblance between the magnitudes of the solvent effects of the two processes.

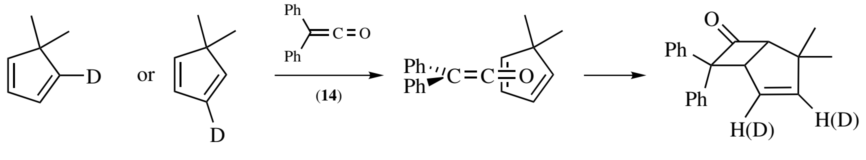
Isotope effects on ketene cycloadditions have been intensely studied but do not lead to unequivocal interpretations of the mechanism. For the reaction of $Ph_2C=C=O$ with styrene, intermolecular competition studies indicated that k_H/k_D was 0.91 for the CH_2 carbon of styrene, consistent with a hybridization change from sp^2 to sp^3, but for C_1 k_H/k_D was 1.23.[45] For the reaction of $Me_2C=C=O$ with $PhCD=CH_2$ k_H/k_D at C_1 was found to be 0.80,[41] in disagreement with the other results.[5,51,53]

A further study of isotope effects involved all four possible $Ph_2C=C=O$ and $PhCH=CH_2$ structures monolabeled with ^{14}C in the alkene carbons, as well as E and Z PhCH=CHD.[54] The k_H/k_D isotope effects were the same at 0884 ± 0.006, in agreement with the results of Baldwin and Kapecki.[5] The $k(^{12}C)/k(^{14}C)$ isotopes ranged from 1.0055 to 1.08, as shown in **34**. These isotope effects were interpreted as consistent with significant negative charge buildup on oxygen, greater bond breaking than formation at the carbonyl carbon, and essentially equal bond making and breaking at the other carbons.[54]



34

The reaction of $Ph_2C=C=O$ (**14**) with the selectively deuterated 5,5-dimethylcyclopentadienes **34** and **35** showed the ratio of formation of the product **37** with nondeuterated and deuterated double bonds k_H/k_D to be 0.84 ± 0.02 for **34** and 1.0 ± 0.01 for **35** (equation 13).[55] The large inverse isotope effect for **34** was interpreted as indicating that substantial bond formation occurred at C_1 in the transition state, with a change in hybridization from sp^2 to sp^3, whereas the absence of a substantial isotope effect for **35** was interpreted as showing that there was little bond formation or change in hybridization at C_2.[55] Thus, these results favored a stepwise mechanism, and the transition state was depicted with the "usual" orthogonal geometry, **36**, with the diphenyl carbon of the ketene raised further above the diene plane than the carbonyl carbon to minimize steric interactions.[55]



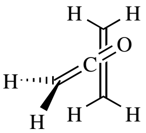
34 **35** **36** **37**

(13)

The effect of pressure on ketene cycloadditions also indicted a decrease in volume in the transition state, but did not provide a definitve differentiation between concerted and stepwise mechanisms.[56]

Theoretical study of the ketene-imine cycloaddition supports a two-step process involving a zwitterionic intermediate for this reaction, as discussed in Section 5.4.1.7.[17,18] The courses of the [2+2] cycloadditions of ketene with ethylene, methylenimine, and formaldehyde were compared by MP2/6-31G* calculations of the transition states and by intrinsic reaction coordinate examination of the approach to the transition states.[19,30] All three reactions are characterized by an approach of the reactants that is skewed slightly from the orthogonal, and give transition states with skewed geometries with activation barriers of 26.9, 30.8, and 24.9 kcal/mol, for ethylene, methylenimine, and formaldehyde, respectively.

The ketene-ethylene complex has been directly observed and its structure determined by microwave spectroscopy (**38**).[57] This was reported to be "remarkably similar" to that calculated by Yamabe et al.[19] for the early stages of the reaction.[57]



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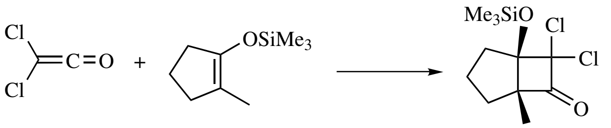
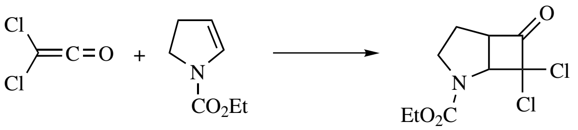
5.4.1.4 Cycloaddition of Ketenes with Nucleophilic Alkenes The cycloaddition of ketenes with strongly nucleophilic alkenes such as vinyl ethers are predisposed to favor formation of zwitterionic intermediates, and there is evidence for this process in different examples. Nucleophilic attack on the ketene leads to a transition state with a high degree of enolate character, but a freely rotating zwitterionic intermediate is usually not formed, as the stereochemistry of the alkene is often preserved and the addition is also usually stereospecific at C_2 of the ketene to give in many cases the thermodynamically least stable cyclobutanone derivative.

Examples of [2+2] cycloadditions with nucleophilic alkenes include the reaction of dichloroketene (**1**) prepared by zinc dehalogenation with the silyl vinyl ether **2** forming the cyclobutanone **3** (equation 1).[1] Dichloroketene prepared by dehydrochlorination reacted similarly with the eneamide **4**, forming **5** (equation 2).[2] The chloroalkylketene **6** prepared by dehydrochlorination reacted with **4** by [2+2] cycloaddition to give **7**, which was converted to **8** (equation 3).[3] Related examples have been observed.[4–5a]



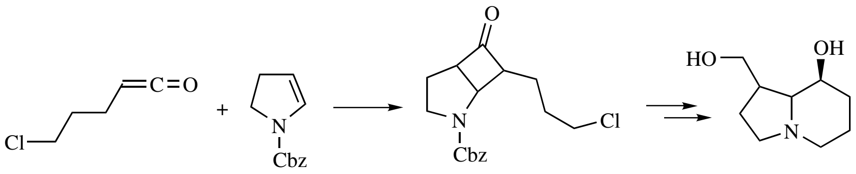
1 **2** **3** (85%)

(1)



1 **4** **5** (92%)

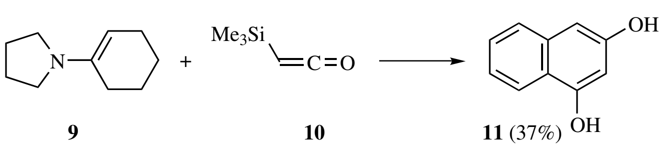
(2)



6 **4** **7** (59%) **8** (69%)

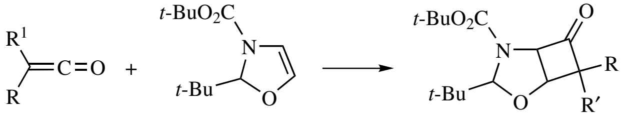
(3)

The eneamine **9** reacted with two molecules of trimethylsilylketene **10** to form **11** in a reaction proposed to involve an intermediate zwitterion that reacted with **10** (equation 4).[6] The reaction of ketenes **12** with **13** gave mainly the regioisomer **14** (equation 5), a result attributed to steric and not electronic control.[7] Other electrophiles preferentially attack **13** at C–5. Cycloadditions of dichloroketene (**1**) from dehydrochlorination with the vinyl ether **15** gave **16**, which was converted by dechlorination and Beckmann rearrangement, forming pyrrolidinone **17** (equation 6).[8]



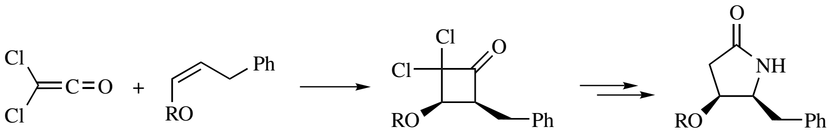
9 **10** **11** (37%)

(4)



12 **13** **14**

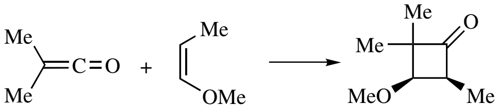
(5)



1 **15** (R* = ArCHMe) **16** (69%, 94:6 *dr*) **17** (82%)

(6)

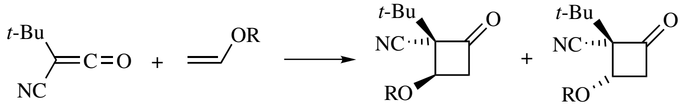
The [2+2] cycloaddition of $Me_2C{=}C{=}O$ (**18**) with *E*-MeOCH=CHMe gave the cyclobutanone **19** with retention of the alkene stereochemistry (equation 7).[9] Similar results were found for a variety of enol ethers $ROCH{=}CHR^1$ with $Ph_2C{=}C{=}O$.[10–12] Kinetic data for some of these reactions are given in Tables 5.7–5.9 in Section 5.4.1.3.



18 **19**

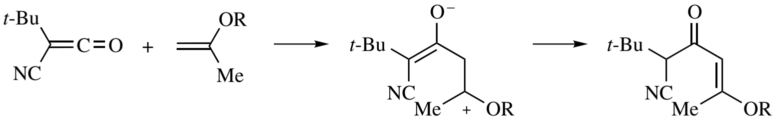
(7)

The [2+2] cycloaddition of *t*-BuC(CN)=C=O (**20**) with $CH_2{=}CHOEt$ and $CH_2{=}CHOAc$, however, did not proceed with 100% stereoselectivity, but gave *cis/trans* ratios in the product cyclobutanones **2** of 3:1 for EtO and CN and 3.5:1 for AcO and CN (equation 8).[13] The products from reaction of **20** with isopropenyl acetate and benzoate **22** formed from zwitterionic intermediates, as hydride transfer resulting in acyclic products **24** occurred, or acyl transfer, and not ring closure (equation 9).[13]



20 **21a** **21b**

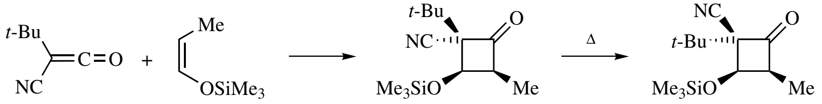
(8)



20 **22** **23** **24**

(9)

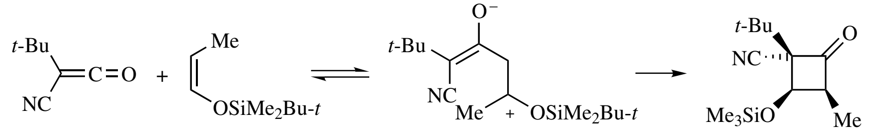
The [2+2] cycloaddition of the silyl enol ether *Z*-$Me_3SiOCH{=}CHMe$ **25** with **20** showed higher reactivity than for the *E*-alkene and a high degree of stereoselectivity forming **26** (equation 10).[14] The product from *E*-**25** was also formed stereoselectively and was stable upon heating, while on heating the product **26** was converted to **27** (equation 10)



20 **25** **26** **27**

(10)

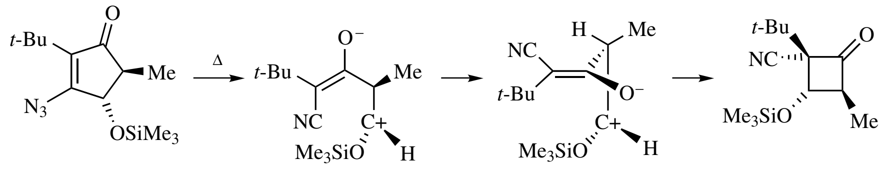
By contrast, the *E*-isomer of *t*-BuMe$_2$OCH=CHMe (**28**) was more reactive toward **20** than the *Z*-isomer, although the cyclobutanone products from each were still formed with high stereoselectivity. It was proposed[14] that the reason for the low reactivity of *Z*-**28** was that a zwitterionic intermediate **29** was being formed reversibly, and that ring closure of **29** was rate determining, implying that the formation of **29** was reversible (equation 11).[14] Presumably the bulk of the *t*-Bu group made ring closure to **30** slow.



20 Z-**28** **29** **30**

(11)

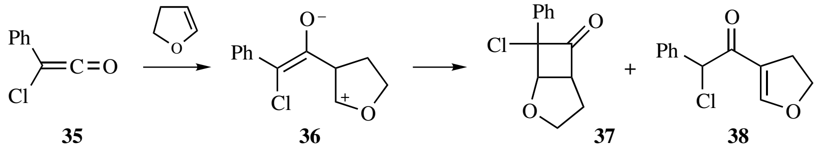
Confirmatory evidence that the reactions proceeded by zwitterionic intermediates was obtained from thermolysis of the azide *trans*-**31**, which gave the product **34**.[14] It was proposed that the reaction of **31** gave **32**, which underwent bond rotation to **33** followed by closure to **34** (equation 12).[14] Reaction of *Z*-**31** in refluxing benzene gave **26**, **27**, and **34** in relative yields of 40, 5, and 50% respectively. The same products were formed from the reaction of **20** with **25** under the same conditions.



E-**31** **32** **33** **34**

(12)

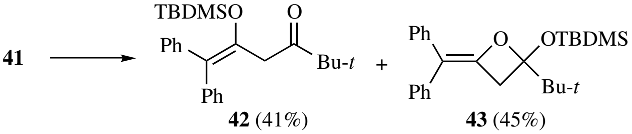
The reaction of chloroketenes with silyl enol ethers, 1,1-dialkoxyalkenes and 1,1-disilyloxyalkenes gave [2+2] cycloaddition in some cases, acyclic products in others, or mixtures of the two.[15–19] The reaction of phenylchloroketene (**35**) with 4,5-dihydrofuran gave a 75% yield of the cycloaddition product **37**, along with 15% of the acyclic product **38**, suggesting the formation of the zwitterionic intermediate **36** (equation 13).[20]



35 **36** **37** **38** (13)

Rearrangement also occurred in the reaction of $Ph_2C{=}C{=}O$ (**39**) and the silyl vinyl ether **40** forming **42** and the product of [2+2] addition to the C=O bond **43** (equations 14, 15).[20] The formation of **43** was found to be reversible to the reactants and on prolonged heating was converted to **42**, and the zwitterion **41** was proposed as an intermediate (equations 14, 15).[20]

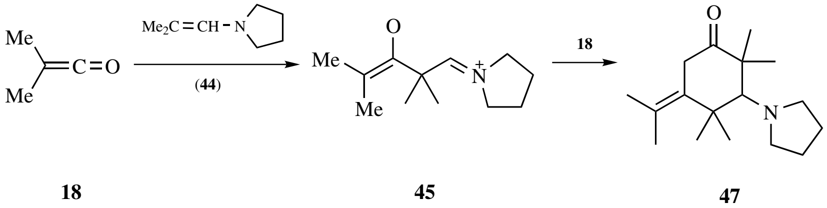
(14)



(15)

Cycloaddition of $CH_2{=}CH_2$ with $Ph_2C{=}C{=}O$ (**39**) and other ketenes with tetramethoxyethylene gave variable amounts of oxetane products from addition to the C=O bond along with cyclobutanones.[21–23]

The reaction of $Me_2C{=}C{=}O$ (**18**) with *N*-isobutenyl pyrrolidine (**44**) gave the [2+2] cycloadduct **46** and the product **47** resulting from reaction of two molecules of ketene (equation 16).[24] The kinetics were dissected into two concurrent processes, one involving competition of intermediate **45** for ring closure to **46** and reaction with a second molecule of **18** to give **47**, and a separate direct formation of **46** (equation 17).[24] The formation of mixed products from ketene reactions with eneamines has also been found in other examples.[25,26]



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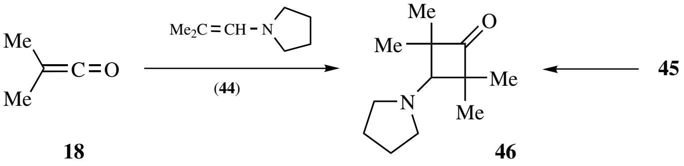

(17)

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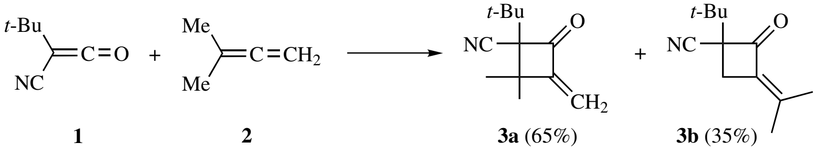
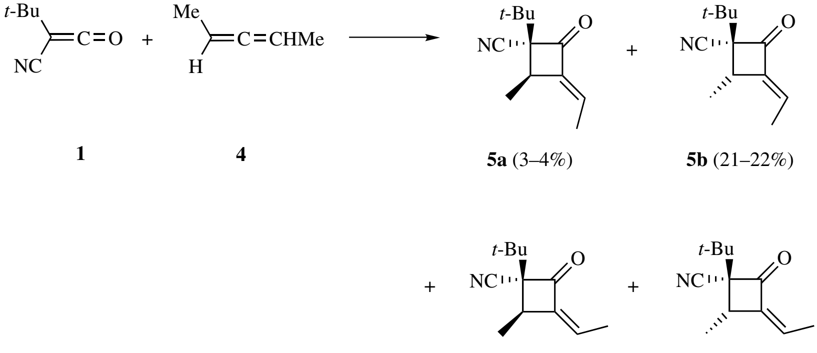
5.4.1.5 Cycloaddition of Ketenes with Allenes Ketenes react readily with allenes by [2+2] cycloaddition pathways, and these have some interesting stereochemical outcomes. The reactions of *tert*-butylcyanoketene (**1**) have been extensively examined; this reacted with dimethylallenes **2** and **4** to form the isomeric 2-methylenecyclobutanones **3** and **5**, respectively (equations 1, 2).[1–3]

Tetramethylallene (**6**) reacted with **1** to give a single product **7** (equation 3).[1–3]



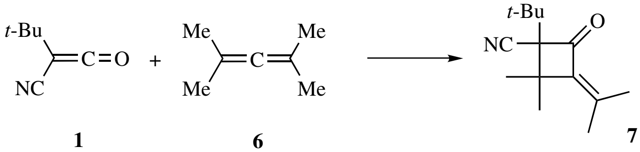
1 **2** **3a** (65%) **3b** (35%) (1)



1 **4** **5a** (3–4%) **5b** (21–22%)

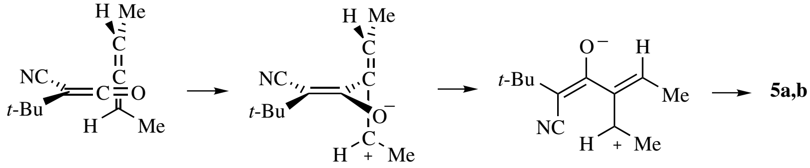
(2)

5c (34–38%) **5d** (37–41%)

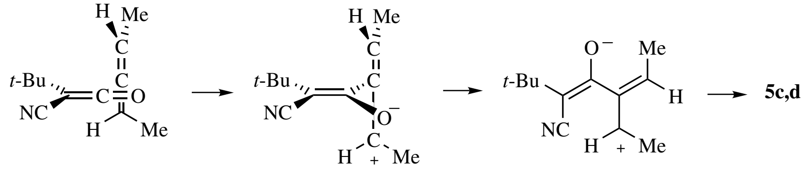


1 **6** **7** (77%) (3)

Reaction of optically active **4** gave optically active **5a,b**, but **5c,d** were racemic.[2] To explain these results, a mechanism involving initial encounter complexes **8** and **11** were proposed, with little preference because of the minimal steric effects involved.[1–3] Bond formation from **8** gave the zwitterion **9**, which formed optically active **5a**, or by bond rotation formed achiral intermediate **10**, which led to to **5a**,**b** (equation 4). Encounter complex **11** formed **12** and **13**, which gave rise to optically active **5b** and racemic **5c,d**, respectively (equation 5).[1–3]

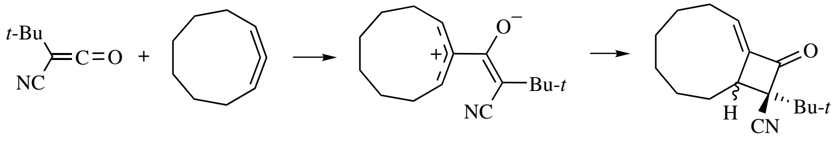


8 **9** **10** (4)



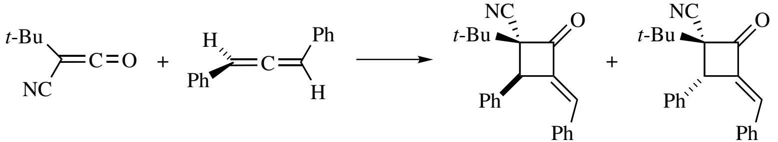
11 **12** **13** (5)

Optically active 1,2-cyclononadiene **14** gave [2+2] cycloaddition with *t*-BuC(CN=C=O (**1**) to form a 2:3 mixture of the *cis/trans* stereoisomeric adducts **16** (equation 6).[4] Both of the products were optically active, although the optical purities were not established. The results were interpreted as involving a zwitterion **15** (equation 6).[1,4]



1 **14** **15** **16** (6)

Optically active 1,3-diphenylallene (**17**) gave [2+2] cycloaddition with *t*-BuC(CN)=C=O to form only cyclobutanones **18** and **19**, with the *E* configuration of the phenylvinyl groups (*anti* to the carbonyl) analogous to **5a**,**b**, and both were optically active (equation 7).[5,6] These results were interpreted[1] in terms of the formation of two encounter complexes resembling **8** and **11** and similar formation of chiral zwitterions. However, the greater steric interactions with the phenyl groups prevented the formation of the *Z*-stereoisomers corresponding to **5c**,**d**.



1 **17** **18** **19** (7)

The reactions of $Me_2C{=}C{=}O$[7,8] with a large number of allenes have been studied, as well as reactions of other ketenes with allenes.[9] The allenes included symmetrically and unsymmetrically substituted examples, and the reactions often formed all of the possible stereoisomeric products. The reaction pathways appear to be consistent with the processes shown above (equations 4, 5). The reaction rates and product distributions for various ketene/allene pairs were interpreted as involving formation of uncharged species by bonding between the sp carbons of the ketene and the allene.[10]

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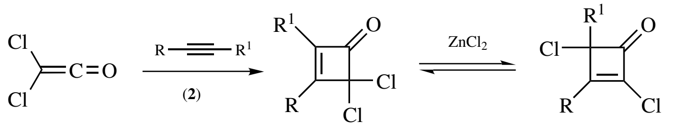
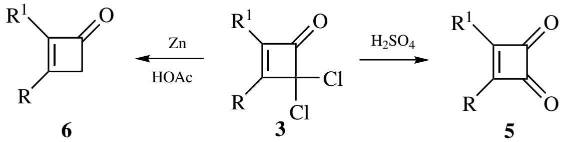
5.4.1.6 Cycloaddition of Ketenes with Alkynes Reactive ketenes substituted with electronegative groups gave [2+2] cycloaddition with nonactivated alkynes to form cyclobutenones.[1,2] This reaction provides a major route for the preparation of cyclobutenones, which form vinylketenes upon ring opening (Section 3.4.1). For example, dichloroketene (**1**) generated by zinc dehalogenation reacted with 2-butyne, 3-hexyne, or 1-hexynes **2** to form adducts **3**, which underwent isomerization in situ induced by the $ZnCl_2$ present to an equilibrium mixture with **4** (equation 1).[2,3] Hydrolysis of **3** with acid gave cyclobutenediones **5** (equation 2),[2,3] which may be used to prepare bisketenes (Section 4.9). Cyclobutenones **3** and **4** were reduced with zinc and acetic acid to cyclobutenones **6** (equation 2).[2,3] *tert*-Butylcyanoketene reacted with a variety of alkyl- and arylalkynes to give cyclobutenones,[4] and dimethylketene (**7**) gave [2+2] cycloaddition to alkynyl ether **8** forming cyclobutenone **9** (equation 3).[5]



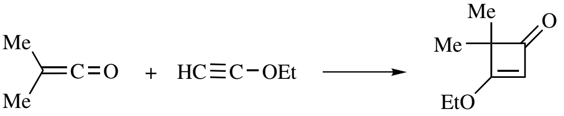
1 **3** **4**

(1)



6 **3** **5**

(2)

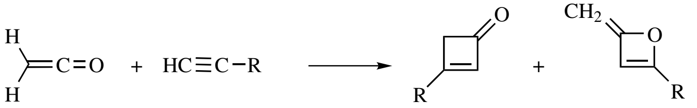


7 **8** **9** (83%)

(3)

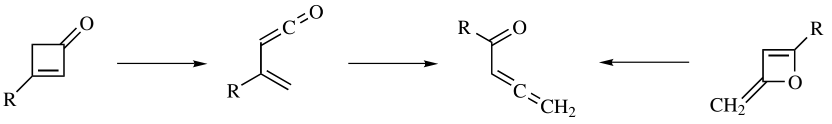
A computational study of [2+2] cycloaddition reactions of ketene (**10**) with alkynes **11** examined the formation of cyclobutenones **12** and oxetes **13** and the dependence of the reactions on the alkynyl substituents R (equation 4).[6] The cyclobutenones **12** can undergo ring opening to vinylketenes **14**, which can rearrange to acylallenes **15**, which can also be formed by ring opening of the oxetes

13 (equation 5).[6]



10 **11** **12** **13**

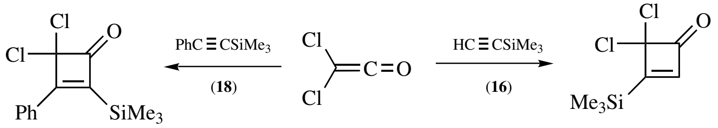
(4)



12 **14** **15** **13**

(5)

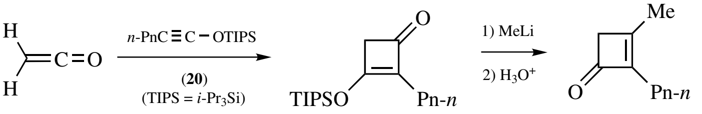
The reaction of trimethylsilylacetylene (**16**) with dichloroketene (**1**) gave mainly the product **17** resulting from electrophilic attack at the nonsilicon-substituted carbon of the alkyne, contrary to the usual direction of electrophilic substitution on this alkyne (equation 6).[7] However, this carbon does have the highest coefficient of the HOMO of $SiH_3C{\equiv}CH$.[7] With $PhC{\equiv}CSiMe_3$ (**18**) electrophilic attack occurs at the silylated carbon, in accord with the expected stability of an intermediate with positive charge adjacent to phenyl (equation 6).[7]



19 **1** **17**

(6)

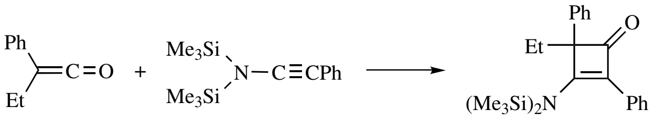
The reactive alkyne 1-triisopropylsilyloxyheptyne (**20**) reacted with ketene (**10**) to give 3-silyloxycyclobutenone **21** (equation 7).[8] 1-Ethoxyheptyne was less reactive toward **10** than was **20**. Reaction of **21** with MeLi followed by acid gave cyclobutenone **22** (equation 7).[8]



10 **21** **22**

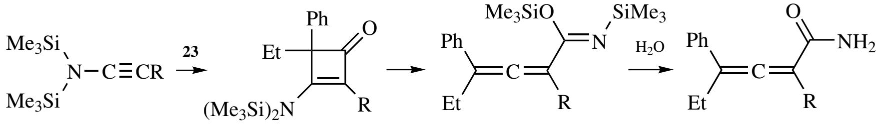
(7)

The reaction of *N*,*N*-bis(trimethylsilyl)ynamine **24** with ketene **23** led to the formation of cyclobutenone **25** (equation 8).[9] However, reaction of the *n*-butyl analogue **26** with **23** gave 24% of **27**, together with the allenic amide **29** (35%) resulting from ring opening and rearrangement followed by hydrolysis of the initial product **28** (equation 9).[9]



23 **24** **25** (86%)

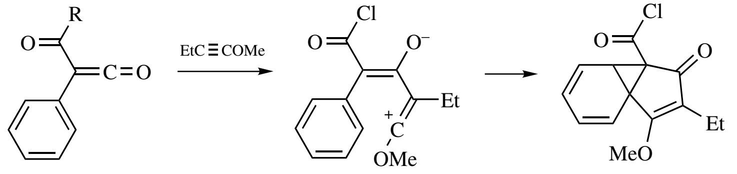
(8)



26 (R = *n*-Bu) **27** (24%) **28** **29** (35%)

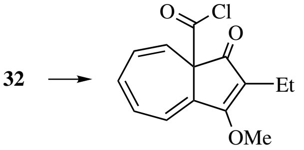
(9)

Acylketene **30** (R = Cl) generated by dehydrochlorination reacted with 1-methoxybutyne, leading to azulenone **33** (equations 10, 11).[10] With **30** (R = EtO) the [4+2] cycloadduct **37** was the major product (equation 12).[10] On the basis of the observed solvent and substituent dependence of the product distribution, the zwitterionic intermediate **31** from **30** (R = Cl) was proposed to undergo cyclization on the phenyl ring leading to **33** (equations 10, 11), whereas with **30** (R = EtO) the zwitterion **34** cyclized to the cyclobutenone **35**, followed by ring opening to **36** leading to the pyrone **37** (equation 12).[10] The reaction of **30** with other alkynyl ethers was also studied.[10]



30 (R = Cl) **31** **32**

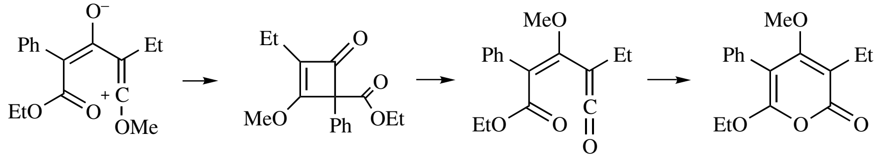
(10)



32 →

33 (79%)

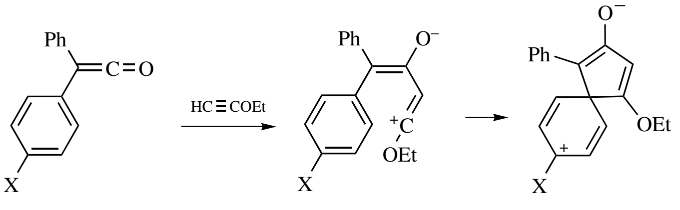
(11)



34 **35** **36** **37**

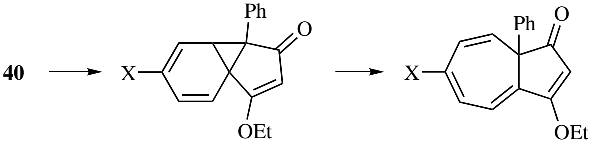
(12)

Diarylketenes **38** and ethoxyacetylene also reacted to form azulenones in a process formulated as involving cycloaddition of the zwitterionic intermediate **39**, which gave **40**, leading to **41** and the azulene derivatives **42** (equations 13, 14), as well as cyclobutenones from [2+2] cycloadditions.[11,12] There was a preference for attack on the ring bearing an electron-donating substituent (MeO, Me) but not an electron-withdrawing group (Cl, Br, CO_2Et). The intermediate norcaradienes corresponding to **32** were isolated in the reaction of 1-naphthylphenylketene, di-(2-naphthyl)ketene, and di-(1-naphthyl)ketene with EtOC≡CH.[12] The vinylketenes **43** and **44** gave only [2+2] cycloaddition products with HC≡COEt.[12]



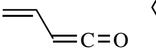
38 **39** **40**

(13)

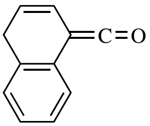


41 **42**

(14)

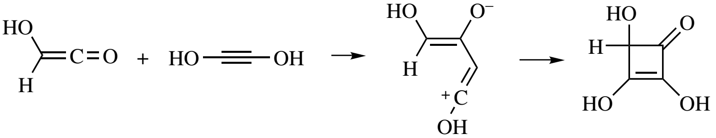


43



44

The [2+2] cycloaddition of hydroxyketene (**45**) with dihydroxyacetylene (**46**) was studied computationally using MNDO, and the reaction was predicted to proceed with formation of a zwitterionic intermediate **47** leading to the cyclobutenone **48** (equation 15).[13] The structure of the complex of acetylene and ketene in the gas phase has been examined by microwave spectroscopy and found to be planar, with a 25° tilting of the axes of the molecules (Figure 5.3).[14]



45 **46** **47** **48**

(15)

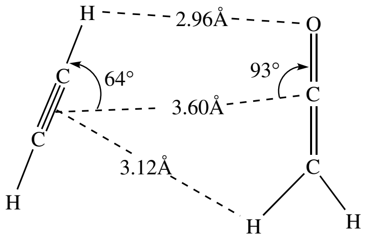
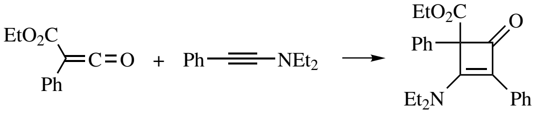


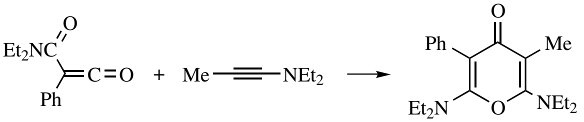
Figure 5.3 Ketene-acetylene complex as determined by microwave spectroscopy (reprinted form ref. 12 with permission of the American Chemical Society)

Carboethoxy and carboxamido ketenes (**49**, **52**, and **55**) reacted with alkynylamines to give cyclobutenones by [2+2] cycloaddition (equation 16), pyrones by [4+2] cycloaddition (equation 17), and allenes (equation 18), depending upon the particular substrates.[15,16] Vinylketenes also gave allenes and other products on cycloaddition with alkynylamines, together with cyclobutenones.[17–20]



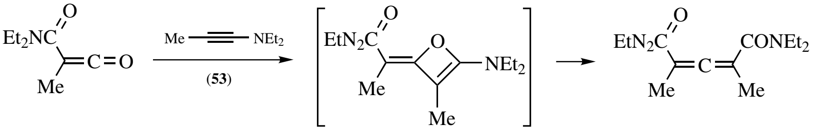
49 **50** **51**

(16)



52 **53** **54**

(17)



55 **56**

(18)

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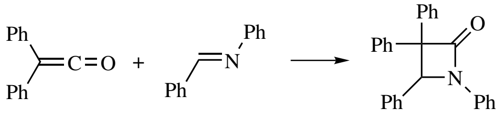
5.4.1.7 Cycloaddition of Ketenes with Imines The reaction of diphenylketene (**1**) and benzanilide forming the β-lactam **2** was discovered by Staudinger in 1907 (equation 1).[1] This [2+2] cycloaddition of ketenes with imines (Staudinger reaction) provides a facile and versatile preparation of β-lactams, and because of the importance of these derivatives it has been of continuing and increasing interest and has been frequently reviewed.[2–11]

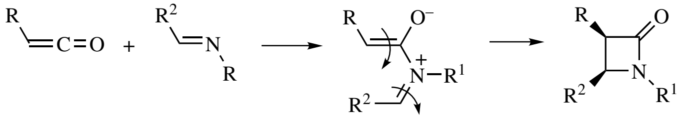


1 **2**

(1)

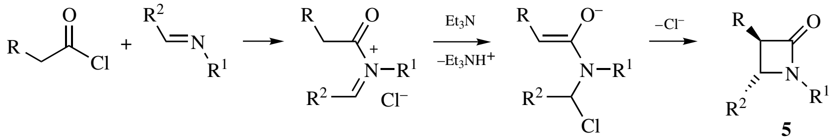
The [2+2] cycloaddition reaction is usually carried out with in situ generation of the ketene from the acyl chloride in the presence of the imine. With no base such as triethylamine present, the reaction could take place without the formation of a ketene by attack of the imine on the acyl chloride.

Calculations at the B3LYP/6-31G* level indicated that when the ketene was preformed by adding the acyl chloride slowly to a tertiary amine/imine mixture, stepwise formation of zwitterion **3** followed by conrotatory ring closure gave the *cis* product **4**, in agreement with experimental findings (equation 2).[12] When the tertiary amine was added to the acyl chloride/imine mixture, an intermediate formed that led through an S_N2 reaction giving *trans* product **5**, also in agreement with experimental results (equation 3).[13]



3 **4**

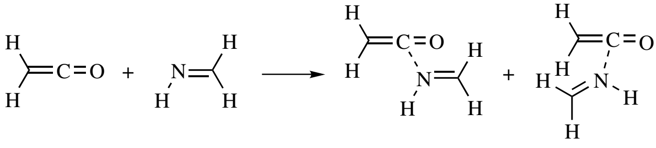
(2)



5

(3)

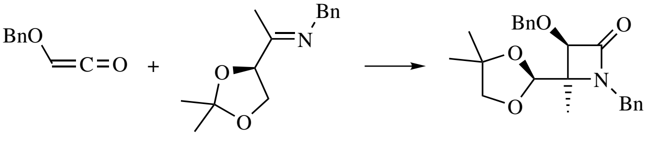
The mechanism of the reaction has been the subject of increasingly refined computational studies.[13–15] A mechanistic scheme derived using a (CASPT2) and (CASSCF) approach identified two directions of approach of the imine to the ketene in the reaction (equation 4).[13] This was proposed as a starting point for more detailed calculations, including substituent and solvent effects to predict the product stereochemistry.[13] The thermodynamic stability of the cycloaddition of vinylimine ($CH_2{=}C{=}NH$) to ketene forming 3- and 4-methylene-β-lactams was also examined by computational means.[14]



6 *trans* *gauche* (4)

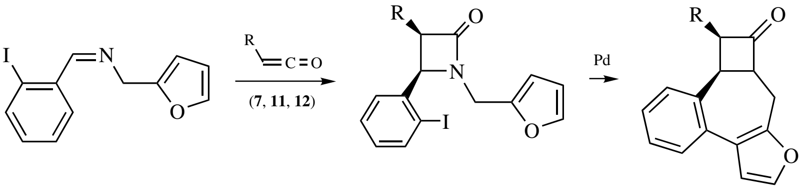
The enantioselective synthesis of β-lactams is an area of great interest,[15] as also discussed in Section 5.9, and has been applied to the synthesis of α- and β-amino acids.[16] Thermally induced isomerization of the initial *cis*-β-lactams **4** to form the *trans* isomers has been found, and has provided evidence for reversible formation of zwitterions **3** that form the thermodynamically more stable products.[17] Large polycyclic aryl *N*-substituents on the imines also favored *trans* products.[18]

Benzyloxyketene (**7**) reacted with ketenimine **8**, forming the *cis*-lactam **9** as a single isomer (equation 5), and this was further converted to β-amino acids.[19]



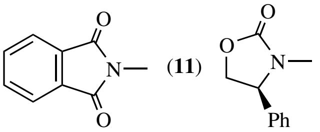
7 **8** **9** (80%) (5)

Cycloaddition of ketenes **7**, **11**, and **12** with imines **10** gave β-lactams **13** that upon palladium-catalyzed cycloaddition gave polycyclic β-lactams **14** (equation 6).[20] Phenoxyketene (**16**) reacted with the chirally substituted imine **15** to give a 17:83 mixture of β-lactams **17** (equation 7).[21]

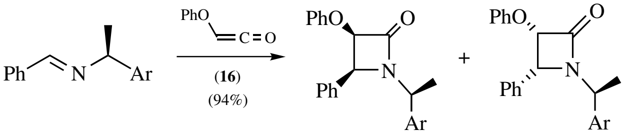


10 **13** (82%, R = BnO) **14** (52%) (6)

R = $PhCH_2O$ (**7**)



(**11**) (**12**)

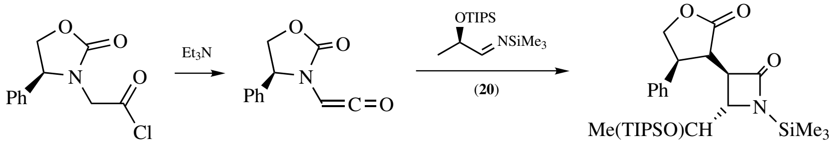


15 (Ar = 2,6-$C_6H_3Cl_2$) **17** **18**

(7)

Solvent effects on the stereoselectivity of ketene-imine cycloaddition reactions have been studied by *ab initio* molecular orbital calculations,[22] and this subject has been reviewed.[23] The reaction of fluoroketene with $H_2NCH{=}NH$ was studied by computation.[24] Calculations have been interpreted as favoring a concerted pathway for the ketene-imine cycloaddition, but other interpretations favor stepwise processes, as noted above.[25] Ketene cyclizations with carbohydrate derived imines have been studied by (AM1) calculations.[26]

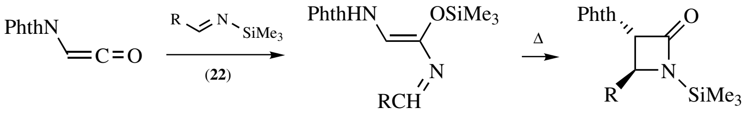
Stereoselectivity in imine [2+2] cycloadditions with ketenes has been examined by the use of chiral substituents on both the ketene and the imine.[27,28] The imine $(Me_3Si)_2CHN{=}CH_2$ is a stable and isolable compound that reacted with chiral ketenes to provide 4-unsubstituted β-lactams in a single step.[29] The [2+2] cycloaddition of chiral ketene **19** formed by dehydrochlorination with the chiral imine **20** gave **21** (equation 8) in a two-step reaction with an observable intermediate (cf. **23**, equation 9), and a variety of related examples were observed.[30]



19 **21** (59%, 9:1 *dr*)

(8)

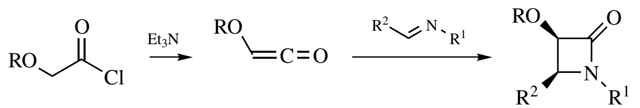
Phthimidolketene (**11**) reacted with *N*-trimethylsilylimines **22** to give observable intermediates **23**, which at reflux cyclized to *trans*-β-lactams **24** that were suggested to form with silyl migration (equation 9).[31] The silyl group was subsequently removed by hydrolysis. These reactions have been studied computationally.[32] These two-step cycloadditions were also found to proceed with microwave assistance under solvent-free conditions,[33] and the stereochemistry changed when the ketene substituent was varied from benzyloxy to benzoyloxy.[34] Diastereoselective synthesis of β-lactams was also carried out with an *N*-(α-thiophenyl)benzyl (PhSCHAr) protecting group removable by oxidation.[35]



11 **23** **24** (63%, 1:1 *dr*)

(9)

Oxygen-substituted ketenes **7**, **16**, and **26** generated in situ by dehydrochlorination of **25** reacted with haloalkyl-substituted imines **27** forming azetidinones **28**, which gave ring-opened products upon treatment with NaOMe (equation 10).[36]



25

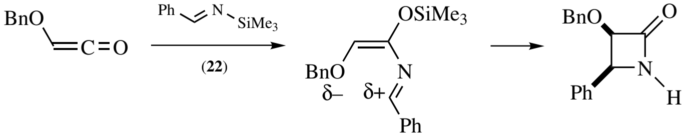
7 (R = Bn)
16 (R = Ph)
26 (R = Me)

27 ($R^2 = R^3R^4CCl$ or $HalCH_2CMe_2$)

28 (60%,
R = Ph,
R^1 = *i*-Pr,
$R^2 = CMe_2Cl$)

(10)

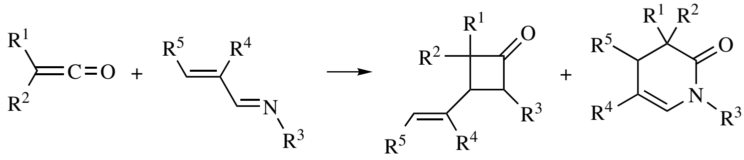
Benzyloxyketene (**7**) generated by dehydrochlorination reacted with **22** with a facile cyclization step forming the *cis* product **30**, and the stereochemistry was proposed to arise from a two-step reaction with an electrostatic interaction between the oxygen and the imine carbon stabilizing the *E*-*anti*-azadiene **29** (equation 11).[37]



7 **29** **30** (81%)

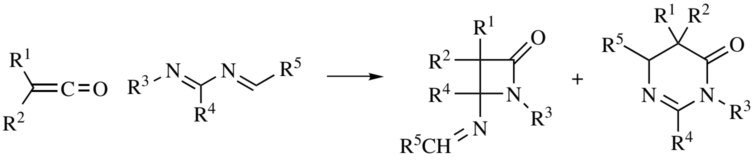
(11)

The effects of the solvent and of the substituents on ketenes **31** and vinylimines **32** undergoing cycloaddition have been studied computationally and experimentally for selectivity in forming the [2+2] product **33** and the [4+2] product **34** (equation 12).[38] Reactions of trisubstituted imines with disubstituted ketenes gave β-lactams with quaternary carbons.[39] The reactivity of ketenes **31** to give both [2+2] and [4+2] cycloadditions with 1,3-diaza-1,3-butadienes **35**, forming **36** and **37** has been studied computationally (equation 13).[40]



31 **32** **33** **34**

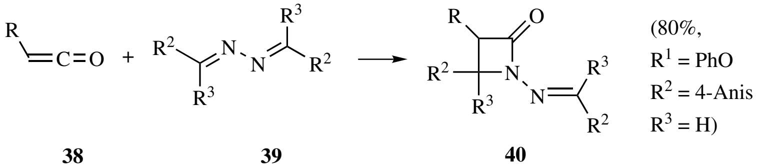
(12)



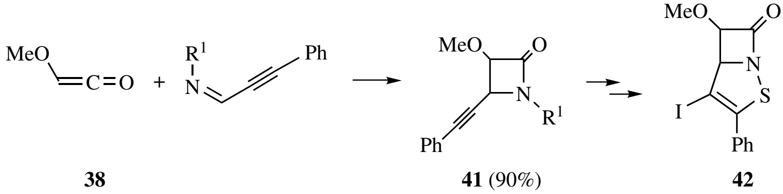
31 **35** **36** **37**

(13)

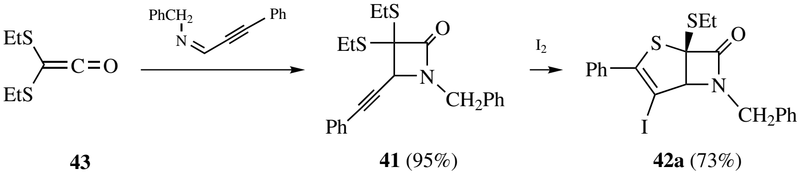
N-Imino-β-lactams (**40**) were formed from the reaction of 2,3-diaza-1,3-dienes **39** with ketenes **38** from a variety of precursors (equation 14) and are useful in further synthetic transformations.[41] The reaction of alkynylimines with ketenes **38**, forming β-lactams **41** followed by cyclization, led to unusual "inversely fused" bicyclic lactams **42** (equation 15).[42,43] The ketene $(EtS)_2C{=}C{=}O$ (**43**) was used to prepare **42a** (equation 15a).[43]



(14)

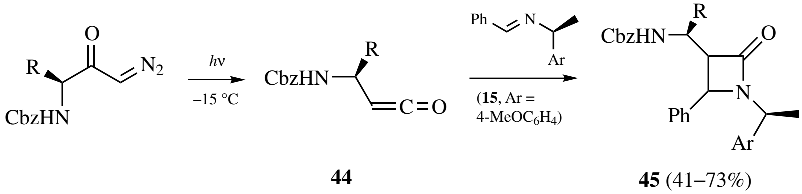


(15)

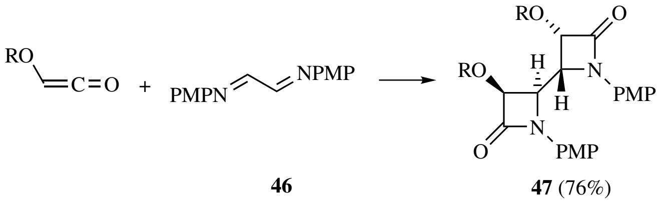


(15a)

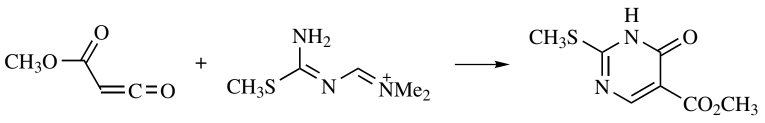
Ketene **44** generated by Wolff rearrangement reacted with imines to give β-lactams **45**,[44,45] and the use of an oxidatively removable chiral auxiliary on the imine **15** gave significant selectivity (equation 16).[46] Reactions of ketenes with peptide-derived imines gave peptidic lactams.[47] Oxygen-substituted ketenes **7**, **16**, **25**, and **30** generated by dehydrochlorination reacted with diimines **46** to form bis-β-lactams **47** (equation 17).[48] Carbomethoxyketene (**48**) gave [4+2] cycloaddition with the cationic triazapentadienium iodide **49** forming **50** (equation 18).[49]



(16)



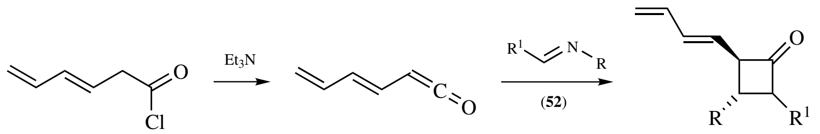
(17)



48 **49** **50** (82%)

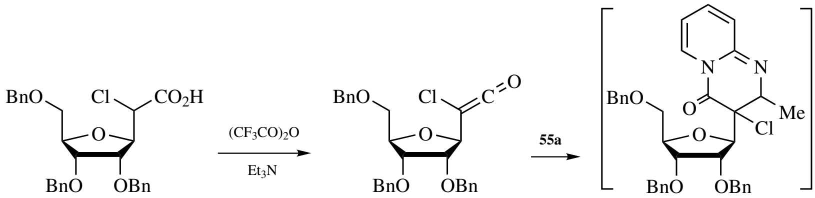
(18)

The diastereoselectivities in other ketene-imine cycloadditions have been studied,[50–52] including reaction of dienylketene **51**[51–53] with **52** to form **53** (equation 19),[52] and in [4+2] cycloadditions of **51**[52,53] and other ketenes with 1,3-diazabutadienes forming 5-dienyl pyrimidones.[53–55] Dehydration of the furanose-substituted carboxylic acid **54** by elimination from the mixed trifluoroacetic anhydride was proposed to generate the ketene **55**, which reacted with **55a** by a [4+2] cycloaddition to form the unobserved intermediate **55b** (equation 20), which was converted to *C*-nucleosides **56** and **56a** (equations 20, 20a).[56] The product **56a** was suggested to arise from hydroysis and decarboxylation of **55b**.[56]



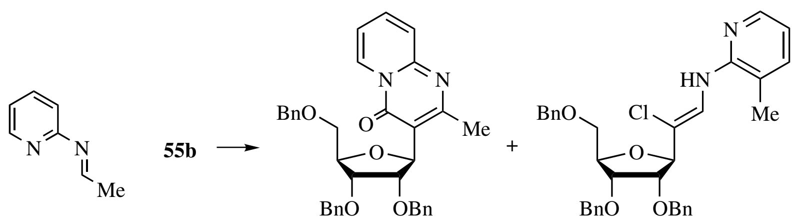
51 **53**

(19)



54 **55** **55b**

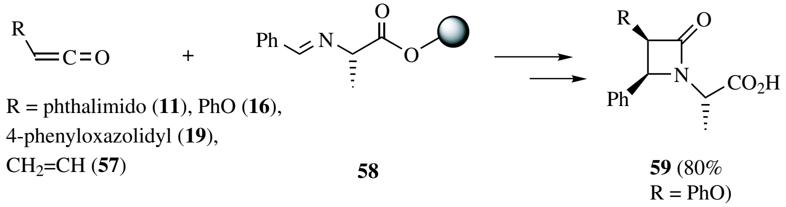
(20)



55a **56** (17%) **56a** (47%)

(20a)

Polymer-supported imine **58** gave high diastereoselectivities to form β-lactams **59** on reaction with ketenes **11**, **16**, **19**, and **57** generated by dehydrochlorination in solution, with removal of the β-lactams from the resin with 3% CF_3CO_2H (equation 21).[57] Polymer-bound aryl imines (polymer)$NHCOC_6H_4CH{=}NR$ reacted similarly with AcOCH=C=O (**60**).[58] Imines bound to soluble polyethylene glycols gave β-lactams upon reaction with PhOCH=C=O (**16**).[59] Rink-resin-bound imines reacted with ketenes **7**, **16**, and **60** to give β-lactams in 60–68% yields.[60]


R = phthalimido (**11**), PhO (**16**),
4-phenyloxazolidyl (**19**),
CH_2=CH (**57**)

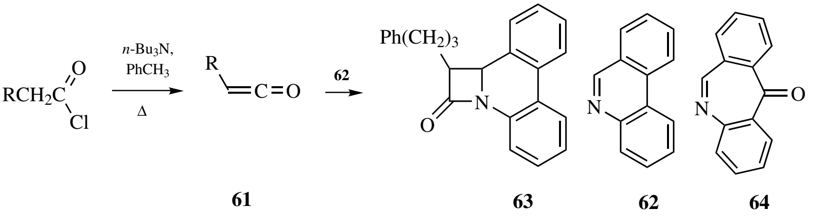
58

59 (80%
R = PhO)

(21)

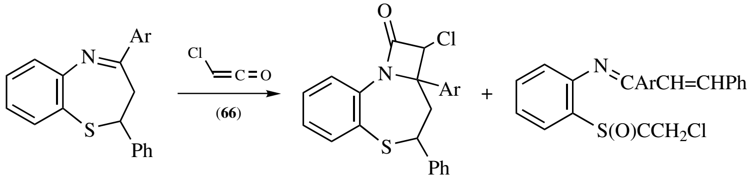
Benzyloxy ketene **7** underwent [2+2] cycloaddition with the (fluoroalkyl)acetaldimines $R_fCH{=}N(C_6H_4OMe\text{-}4)$ where $R_f = CF_3$, CF_2H, and CF_2Cl in yields Of 55–72%.[61] Diacylimines $(RCO)(R^1CO)C{=}NPh$ reacted with a variety of ketenes to give β-lactams.[62]

5-Phenylvaleryl chloride was heated with *n*-Bu_3N to generate ketene **61**, which reacted with phenanthridine (**62**) to give **63** as a mixture of *cis* and *trans* isomers in only 7% yield (equation 22),[63] but reaction with **64** gave the *trans* β-lactam in 47% yield.[63] Ketenes with electron-withdrawing substituents gave much better yields of β-lactams on reaction with **62**.[64] Chloroketene (**66**) reacted with 1,5-benzothiazepine **65** to give β-lactams **67** at room temperature but ring-opened products **68** at reflux (equation 23).[65] The structures of some ketene adducts with pyridine-*N*-oxides and dihydropyridines were determined by X-ray crystallography.[66]


61
R = $Ph(CH_2)_3$

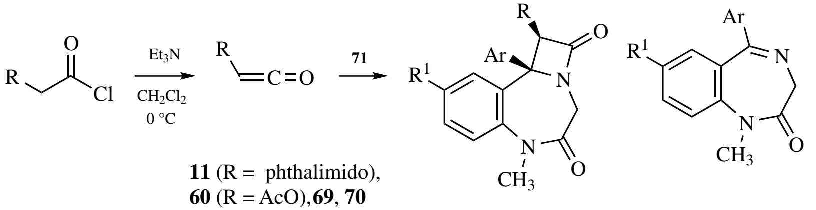
63 **62** **64**

(22)


65 **67** **68**

(23)

Ketenes generated by dehydrochlorination gave [2+2] cyclization with 1,4-benzodiazepines **71** and formed novel β-lactams **72** in yields of up to 95% (equation 24).[67]

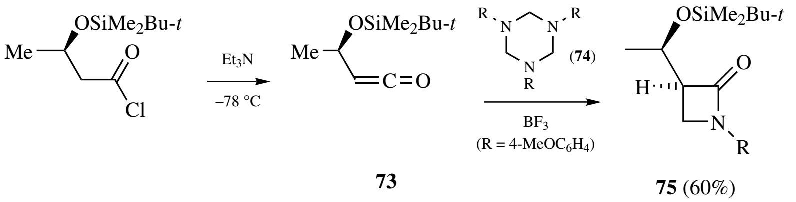

11 (R = phthalimido),
60 (R = AcO),**69**, **70**
(R = phenyl- and
diphenyloxazolidinones

72
(26–95%)

71

(24)

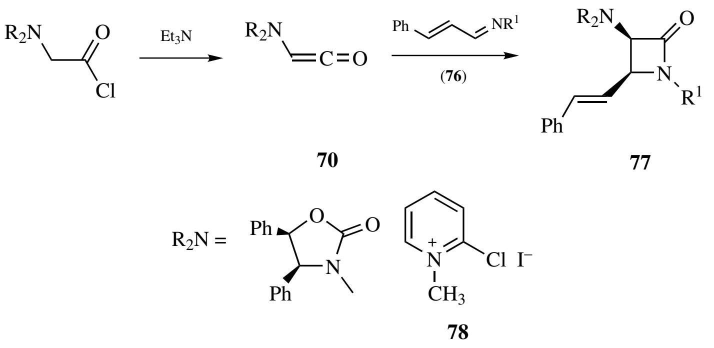
Reaction of the ketene **73** generated in situ with the imine equivalent **74** gave 85% selectivity for the desired β-lactam **75**, with a 60% yield of the two stereoisomers (equation 25).[68] The triazine **74** and BF_3 acted as an imine equivalent.



73 **75** (60%)

(25)

The diphenyloxazolidinyl-substituted ketene **70** reacted with imines **76** to give β-lactams **77** in 60–71% yield and 97% *de* (equation 26).[69,70] Further reactions converted **77** to carbacephen intermediates. Phthalimidoketene (**11**) was also generated using Mukaiyama's salt (**78**, Section 3.2.1) for conversion of **76** to the cycloadduct **77** ($R_2N = PhthN$) in 89% yield.[70]

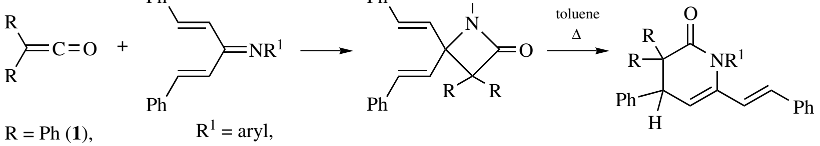


70 **77**

78

(26)

Diphenylketene (**1**) and dimethylketene (**79**) reacted with the divinylimines **81** to form [2+2] adducts **82** that underwent [1,3] sigmatropic rearrangements forming the [4+2] adducts **83** on heating (equation 27).[71] Dichloroketene (**80**) reacted with **81**, giving the [4+2] adduct **83** directly.[71]

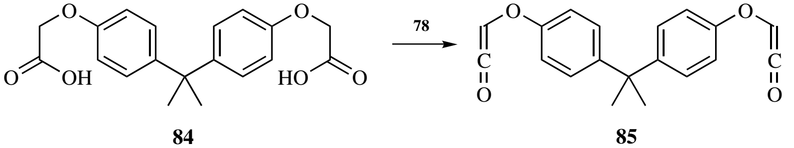


R = Ph (**1**), Me (**79**), Cl (**80**) R^1 = aryl, alkyl, Me_2N **81** **82** (76–98%) **83** (99%)

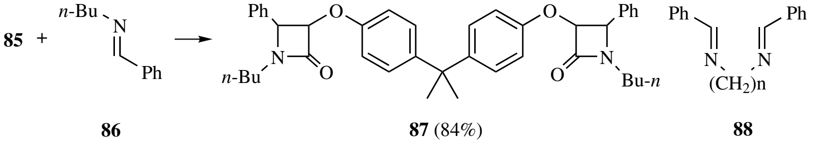
(27)

Reaction of the diacid **84** with Mukaiyama's reagent **78** generated the formal bisketene **85** (equation 28) that reacted with the imine **86** and gave the dilactam

87 (equation 29).[72] Reaction of **85** with a bis(amine) **88** formed a polymer with β-lactams in the amine chain, as shown in Section 4.9.[72]

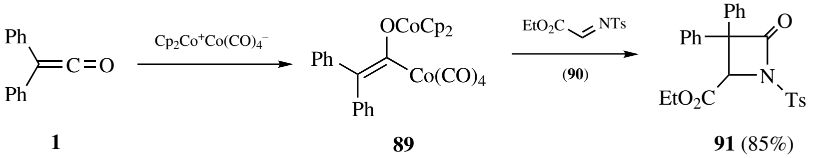


(28)



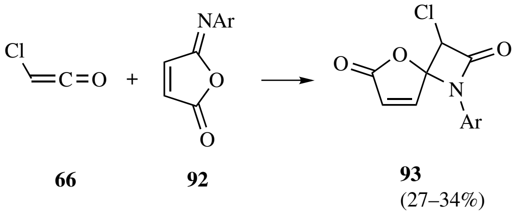
(29)

Diphenylketene (**1**) did not react with TsN=CHCO$_2$Et (**90**) at room temperature, but 5% Cp$_2$Co$^+$Co(CO)$_4$$^-$ catalyzed the rapid formation of **91** in a reaction proposed to involve the intermediate **89** (equation 30).[73]

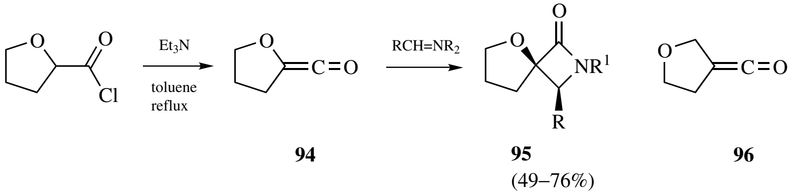


(30)

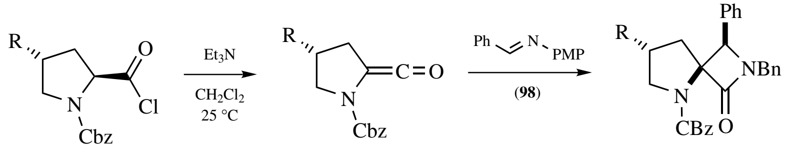
Chloroketene (**66**) generated by dehydrochlorination reacted with the imine **92**, with formation of the spiro-β-lactam **93** (equation 31).[74] This reaction has been employed in the total synthesis of spirocyclic β-lactam alkaloids isolated from marine sources.[75] Tetrahydrofuran-derived spiro-β-lactams **95** were formed from ketene **94** (equation 32).[76] Isomeric ketene **96** behaved in the same manner.[76] Imines bearing chiral substituents gave high diastereoselectivities up to 95:5.[77] The reaction of chiral proline–derived ketenes **97** with imine **98** gave *cis*-stereoselectivity forming **99** (equation 33).[78] Computational modeling of the reaction using DFT methods was also carried out with ketene **100** reacting with the imine **101** forming **102** (equation 34), and also for the reaction of **100** with the chiral imine **103**.[76]



(31)



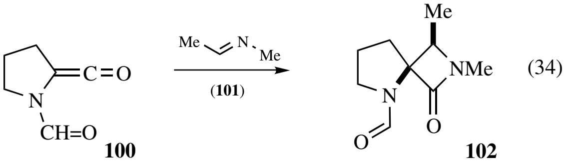
(32)



97
R = H (**a**), R = *t*-BuMe$_2$SiO (**b**),
t-BuPh$_2$SiO (**c**), MsO (**d**)

99 (60–70%)

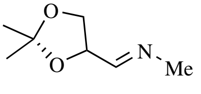
(33)



100

102

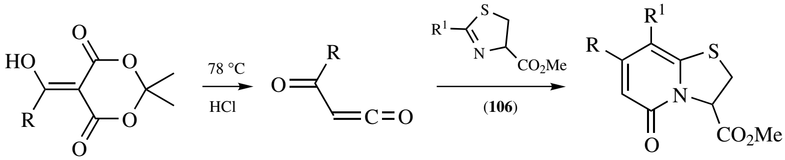
(34)



103

(34)

Acylketenes **105** generated from Meldrum's acid derivatives **104** reacted with β-thiazolines (**106**) to form 2-pyridinones **107** (equation 35).[79]



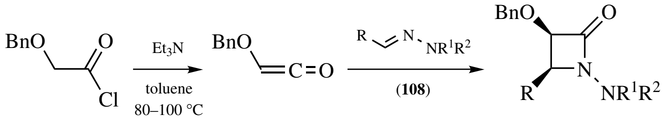
104

105

107 (92–100%)

(35)

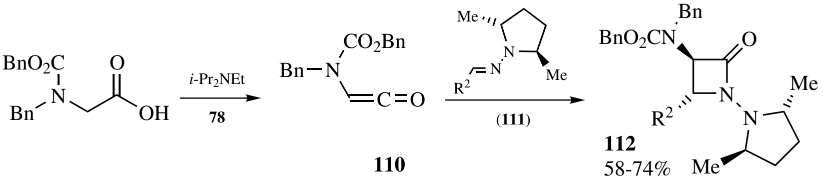
N,N-Dialkylhydrazones **108** acted as the imine component in [2+2] cycloadditions with benzyloxyketene (**7**) forming *cis*-azetidinones **109** (equation 36).[80] However, the chiral *N,N*-dialkylhydrazones **111** reacted with the ketene **110** generated from the acid with Mukaiyama's salt (**78**) and *i*-Pr$_2$NEt to give the *trans*-azetidin-2-ones **112** as single diastereomers (equation 37).[81] The formation of *trans* products was in contrast to the *cis*-selectivity observed with benzyloxyketene, and was interpreted as involving formation of a zwitterionic intermediate that, because of a steric barrier to conrotatory closure to the *cis*-adduct, instead underwent a C=N bond isomerization before conrotatory closing to the *trans* product (equation 38).



7

109 (53–97%)

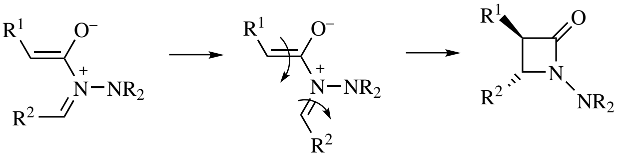
(36)



110

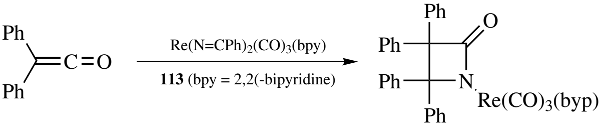
112
58-74%

(37)



(38)

The transition metal-substituted imine *N*-rhenaimine **113** gave a remarkably fast [2+2] cycloaddition with diphenylketene (**1**) forming **114** even at −78 °C (equation 39).[82] The structure of the product was confirmed by X-ray and examined by DFT computations.



(39)

1 **114**

Other studies of ketene-imine cycloadditions forming β-lactams include the use of imines derived from *D*-glucose,[83] and imines substituted with chiral chromium tricarbonyl–complexed arenes.[84]

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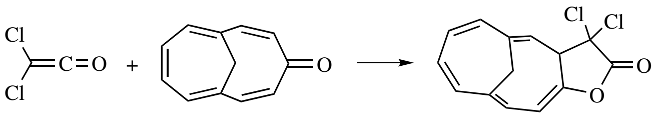
5.4.2 [3+2] Cycloadditions of Ketenes

[3+2] Ketene cycloadditions are 1,3-dipolar additions leading to 5-membered rings, and this area has been reviewed.[1]

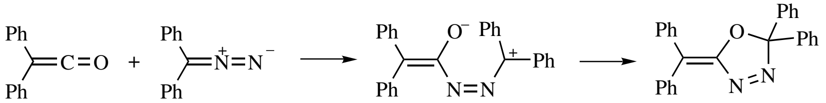
Dichloroketene (**1**) generated by dehydrochlorination reacted with the bridged cycloundecapentaenone **2** by a [3+2] cycloaddition to the ketenyl C=C bond, forming **3** (equation 1).[2]



1 **2** **3**

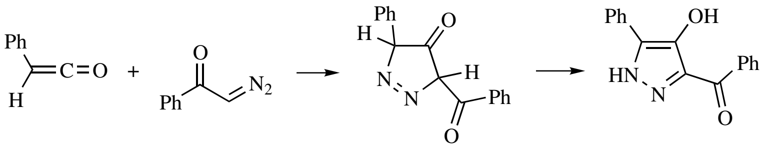
(1)

Diazoalkanes are 1,3-dipoles that give [3+2] cycloadditions with ketenes, as in the reaction of diphenylketene (**4**), which reacted with diphenyldiazomethane (**5**) to form **7** in a reaction that could be concerted or could proceed through a zwitterionic intermediate **6** (equation 2).[3] Phenylketene (**8**) generated from diazoacetophenone (**9**) with silver benzoate and triethylamine formed the [3+2] cycloadduct **10** by reaction of **8** with **9**, followed by tautomerization to **11** (equation 3).[4]



4 **5** **6** **7**

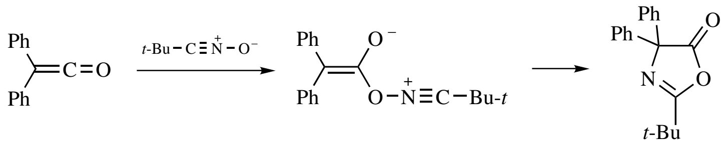
(2)



8 **9** **10** **11**

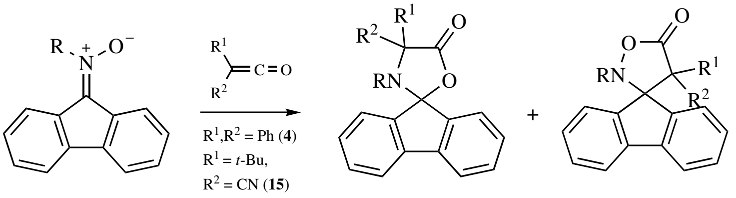
(3)

tert-Butylcyanide *N*-oxide reacted with **4** to give a [3+2] adduct assigned as **12**, proposed to form with rearrangement by ring closure and ring opening (equation 4).[5,6] Dimethylketene (**13**) reacted with 2,4,6-trimethylbenzonitrile *N*-oxide to give a product analogous to **12**.[7] Nitrone **14** reacted with **4**, **15**, and **16** ($R^1 = t$-Bu, $R^2 = CO_2Et$), forming mixtures of **17** and **18** in 52–78% yields (equation 5).[8,9]



4 **12**

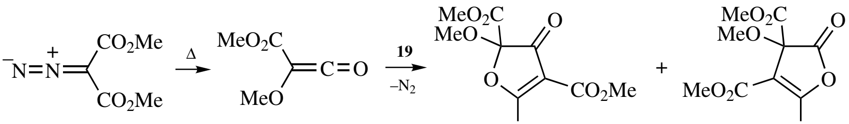
(4)



14 **17** **18**

(5)

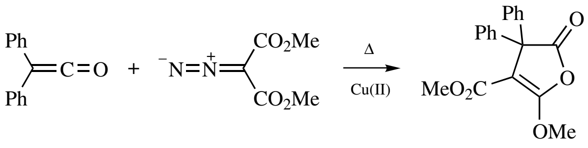
Thermolysis of dimethyl diazomalonate (**19**) formed a mixture of **21** and **22** in a process that could be envisioned to involve [3+2] cycloaddition of the ketene **20** with **19** in two regiochemical directions, with expulsion of nitrogen (equation 6).[10–12] Other examples of ketene [3+2] cycloadditions with the precursor diazo ketones are shown in Sections 3.1.3, 3.3.1, and 4.1.10.2.



19 **20** **21** (25%) **22** (5%)

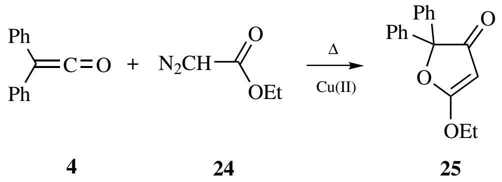
(6)

In further examples preformed ketene **4** gave [3+2] cycloadditions with diazo ester **19**, forming **23** (equation 7),[12] and **24**, forming **25** (equation 8),[13] while the silylketene **28** reacted with the diazo ester precursor **27**, forming **29** (equation 9).[14]

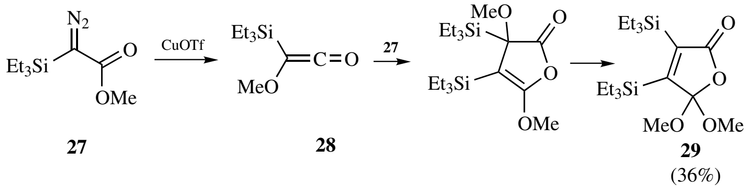


4 **19** **23**

(7)

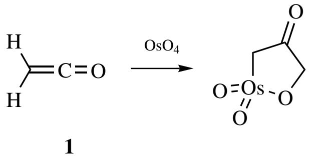


(8)

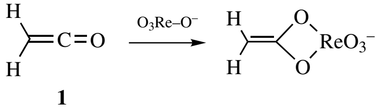


(9)

A theoretical study of ketene cycloadditions with some metal oxides has appeared.[15] Osmium tetroxide was reported to react by a [3+2] process (equation 10), while $O_3Re{-}O^-$ gave [2+2] addition to the carbonyl group (equation 11) and $MeReO_3$ gave [2+2] addition to the C=C bond (equation 12).[15]



(10)



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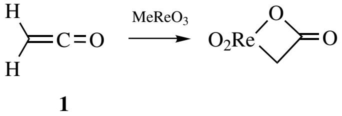

(12)

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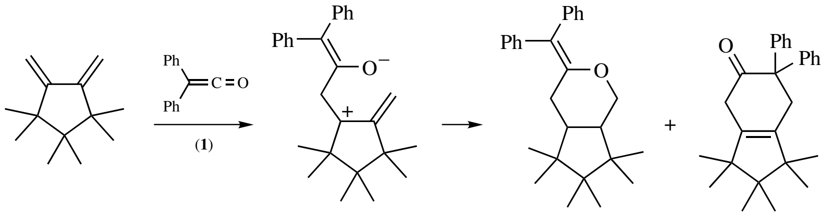
5.4.3 [4+2] Cycloadditions

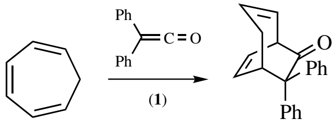
Preparative cycloaddition chemistry of ketenes is dominated by net [2+2] cycloadditions, and examples of [4+2] cycloadditions are rather limited. However, as noted above (Sec. 5.4.1.3), there are cases where [4+2] products have been formed as the initial intermediates, but then isomerize to [2+2] cycloaddition products.

In the reaction of diphenylketene (**1**) with the congested diene **2**, [2+2] cycloaddition was hindered by steric crowding and the products **4a** and **4b** from net [4+2] cycloaddition to the C=C and C=O bonds of the ketene were observed. The formation of both could have occurred through the zwitterionic intermediate **3** (equation 1).[1]

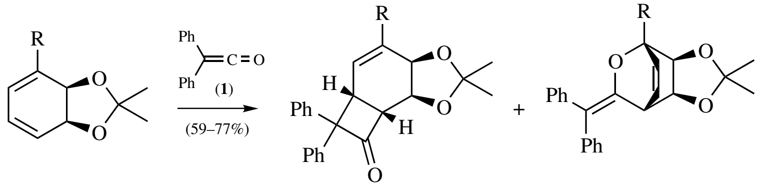


2 **3** **4a** (35%) **4b** (35%) (1)

Cycloheptatriene reacted with diphenylketene (**1**) by a net [4+2] cycloaddition to the C=C bond of the ketene, forming **5** as the only observed product, but in only 11% isolated yield (equation 2).[2] The cyclohexadienes **6** and **7** reacted with diphenylketene, forming the [4+2] and [2+2] products **8** and **9** in 44:56 and 90:10 ratios, respectively (equation 3).[3,4] Heating of **8** caused partial isomerization to **9**, suggesting that the [4+2] product **8** was the kinetic product.[3,5] With R = Br only the product **9** was formed (equation 3).[6]



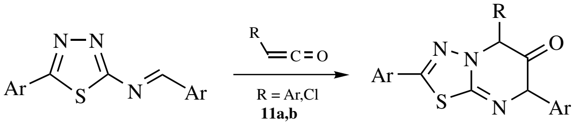
5 (11%) (2)



6 (R = H), **7** (R= F) **8** **9**

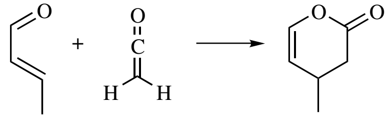
(3)

A variety of heteroatom-containing dienes underwent [4+2] cycloadditions with ketenes yielding heterocycles. Thus, formation of [4+2] cycloaddition products **12** occurred from ketenes **11** and arylimino-1,3,4-thiadiazoles **10** (equation 4).[7] Lactone formation from reaction of ketene (**13**) with α,β-unsaturated aldehydes has long been known (equation 5),[8] and reaction with 1,3-diazadiene **15** forms **16** after elimination of dimethylamine (equation 6).[9] Reaction of the tautomer **16a** with ketene similarly gives **17** (equation 7).[10]



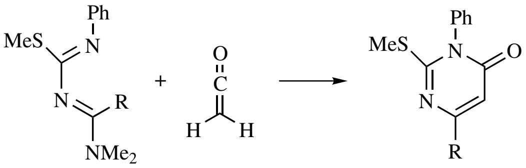
10 **12** (75–95%)

(4)



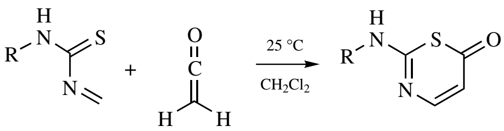
13 **14** (95%)

(5)



15 **13** **16** (47–98%)

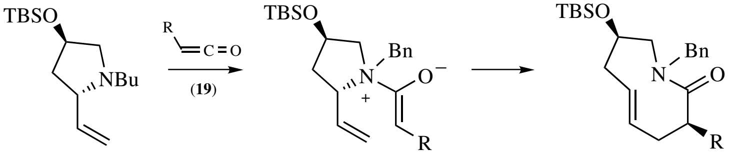
(6)



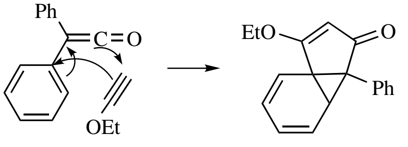
16a **13** **17**

(7)

Reaction of the allylic amine **18** and RCH_2COCl with Me_3Al and K_2CO_3 occurred with aza-Claisen rearrangement, and may involve generation of ketenes **19** that form **20**, leading to **21** by a net [4+2] type cycloaddition (equation 8).[11] The reaction of diphenylketene (**1**) with ethoxy ethynyl ether proceeded by a [2+2+2] pathway, as shown by **22**, to form **23** (equation 9).[12] Naphthylketenes reacted similarly (Section 5.4.1.6).[12]

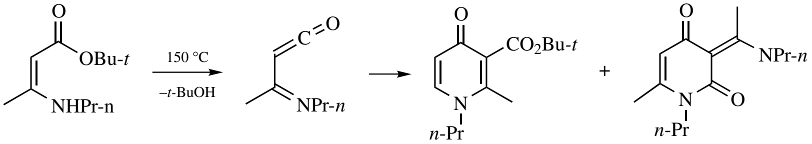


18 **20** **21** 70–95% (8)



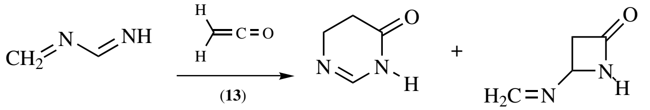
22 **23** (9)

Experimental and theoretical studies showed that imidoylketenes **25** formed by pyrolysis of acrylate esters **24** reacted by [4+2] cycloaddition pathways with planar, pseudopericyclic transition states, forming **26a** by reaction with **24** and **26b** by dimerization and rearrangement (equation 10).[13,14]



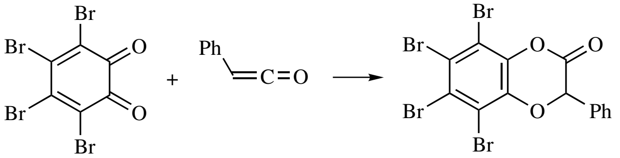
24 **25** **26a** (24%) **26b** (30%) (10)

The [4+2] and [2+2] cycloadditions of ketene (**13**) with 1,3-diazabutadiene forming **27a** and **27b** have been studied by DFT calculations (equation 11).[15]

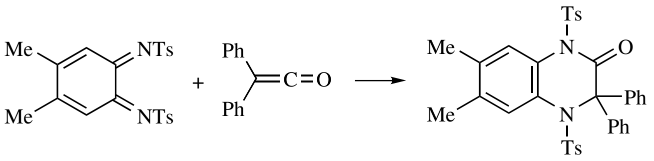


27a **27b** (11)

1,2-Benzoquinones reacted by [4+2] cycloadditions with aryl- or alkylketenes generated in situ by thermal Wolff rearrangements, forming **28** (equation 12).[16,17] The analogous bis(imines) **29** reacted similarly to form **30** (equation 13).[18]



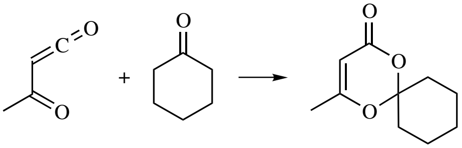
11a **28** (12)



(13)

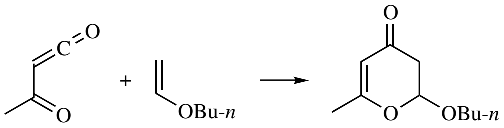
29 **1** **30** (90%)

Acylketenes often have given [4+2] cycloadditions, as in the reaction of acetylketene (**31**) with cyclohexanone to give dioxinone **32** (equation 14), and with *n*-butyl vinyl ether, forming **33**, used in the synthesis of sugars (equation 15).[19] Benzonitrile reacted with the acylketene **34**, forming **35** (equation 16).[20]



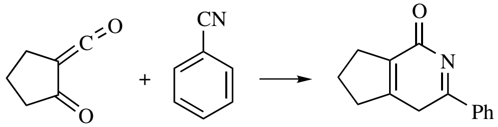
(14)

31 **32**



(15)

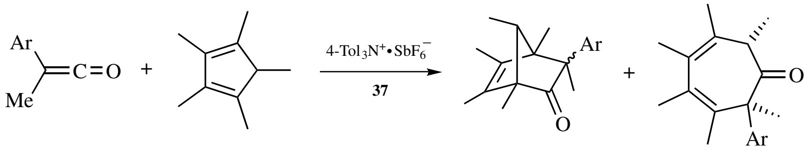
31 **33**



(16)

34 **35** (56–66%)

Ketenes **36** ordinarily react with pentamethylcyclopentadiene, giving [2+2] cycloaddition forming cyclobutanones, but in the presence of the oxidant **37** formed [4+2] adducts **38** via the ketene radical cation (equation 17).[21,22] The cycloheptadieneone **39** was also formed by protonation of the diene, [2+2] cycloaddition, and rearrangement (Section 5.6.2).



(17)

36 **38** **39**

As pointed out in Section 5.4.1.3, several reactions that result in net [2+2] cycloaddition between ketenes and dienes begin with an initial formation of a transient [4+2] cycloaddition to the ketene carbonyl. Other examples of this reaction may be found.

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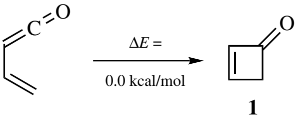
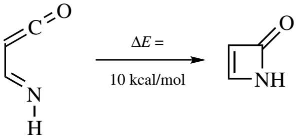
5.4.4 Intramolecular Cycloaddition of Ketenes

Intramolecular cycloadditions of ketenes are often facile and have significant synthetic utility. The ring closures of vinyl-, imidoyl-, or acylketenes forming 4-membered rings were calculated at the MP4SDQ/6-31G**//HF/6-31G* level to be thermoneutral for formation of cyclobutanone (**1**) (equation 1) and endothermic by 10 and 17 kcal/mol, respectively, for formation of the azetone (**2**) and oxetone (**3**), respectively (equations 2, 3).[1] An example of preparative cyclobutenone formation was cyclization of the vinylketene **5** formed by Wolff rearrangement of diazo ketone **4** to give **6** (equation 4).[2]



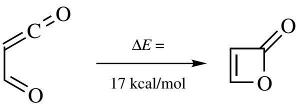
1

(1)



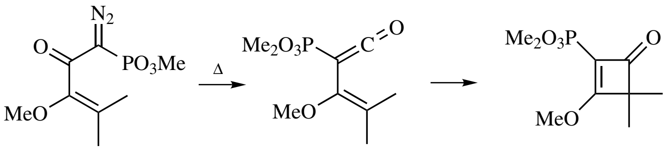
2

(2)



3

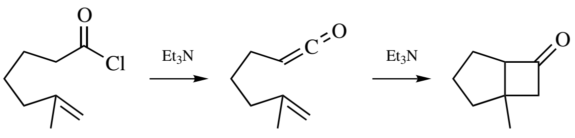
(3)



4 **5** **6** (75%)

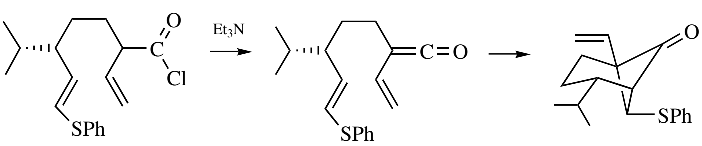
(4)

Cyclobutanone formation by intramolecular ketene cyclization has also been widely studied and was the subject of several reviews.[3–5] For example, the ketene **7** generated by dehydrochlorination cyclized to the cyclobutanone in 80% yield (equation 5).[6] In an application of intramolecular ketene [2+2] cycloaddition in synthesis of a precursor to (-)-salsolene oxide, the ketene **9** formed by dehydrochlorination of **8** gave intramolecular cycloaddition to form **10** (equation 6).[7] Generation of allenylketenes **13** by dehydration of carboxylic acids **11** using Mukaiyama's reagent **12** resulted in [2+2] cycloaddition, forming **14** and **15** (equation 7).[8]



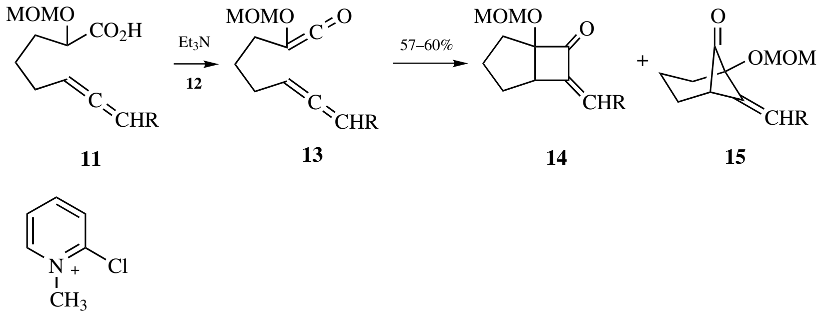
7 80%

(5)



8 **9** **10** (57%)

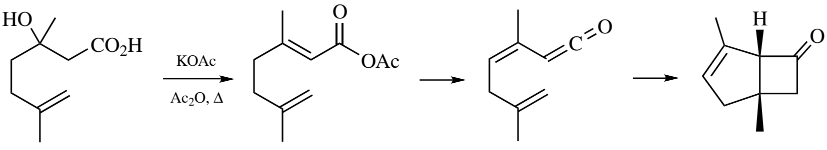
(6)



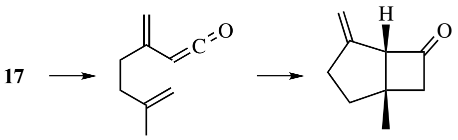
11 **13** **14** **15** (7)

12

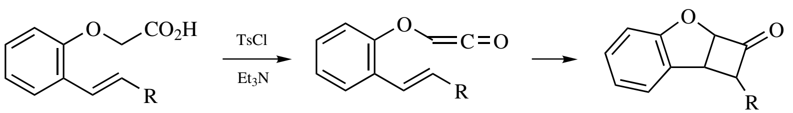
The reaction of 3-hydroxy-6-dimethyl-6-heptenoic acid (**16**) with potassium acetate and acetic anhydride (Perkin conditions)[9–14] led to bicyclo[3.2.0]hept-3-en-6-ones **19** and **21**, useful in synthesis,[12] and evidently involved formation of **17**, which underwent competitive elimination to ketenes **18** and **20**, which then cyclized (equations 8, 9).[12] Conversion of the acid **22** to the mixed anhydride and in situ elimination gave (2-alkenylphenoxy)ketene **23**, which formed the tricyclic system **24** (equation 10).[13]



16 **17** **18** **19** (79%) (8)

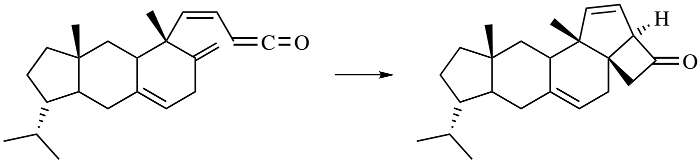


20 **21** (3%) (9)



22 **23** **24** (74%, R = Me) (10)

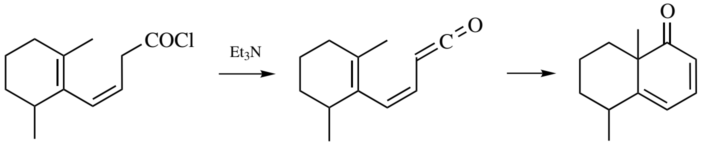
The reactivity in cyclizations forming cyclobutanones was influenced by both the reactivity of the ketene and the nucleophilicity of the alkene. Thus, the alkenyl group in **18** (equation 8) favors cyclization, as does the activating oxygen substituent in ketene **23** (equation 10). Cyclizations such as the conversion of the ketene **25** derived by dehydrochlorination, forming **26**, were evidently stepwise, for a concerted [$_\pi 2_a + _\pi 2_a$] *syn* addition would be electronically forbidden and an allowed [$_\pi 2_s + _\pi 2_a$] reaction would not be geometrically feasible (equation 11).[15]



(11)

25 **26** (80%)

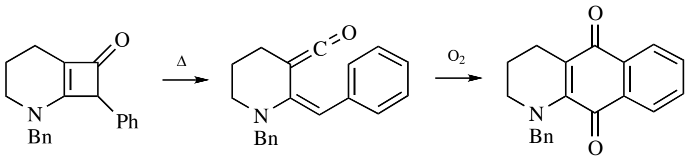
Dehydrochlorination of **27** formed the ketene **28**, which gave a six-electron electrocyclic ring closure to a 1:1 mixture of the isomers **29** in a useful synthesis of polycyclic rings (equation 12).[16–19] This cyclization of dienylketenes to cyclohexadienones is the reverse of the Barton-Quinkert photochemical ring-opening reaction (Section 3.4.3).



(12)

27 **28** **29** (44%)

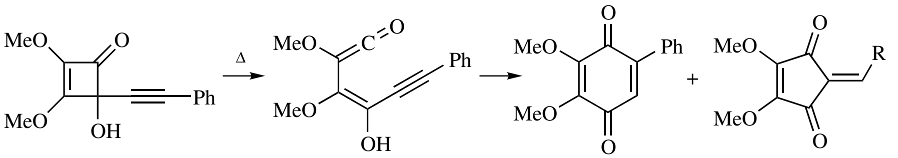
Cyclobutenone **30** underwent thermal ring opening to form the β-phenylalkenylketene **31**, which cyclized to the naphthyl quinone **32** (equation 13).[20] Similar cyclization onto naphthyl groups gave phenanthrols, and these reactions are examples of the Smith-Hoehn reaction (Section 3.4.1). β-Arylalkenylketenes that underwent similar cyclization were also generated from the reaction of chromium carbene complexes with alkynes (Section 3.5).[21] Other examples of such cyclizations were observed with ketenes generated by Wolff rearrangement (Section 3.3.1).



(13)

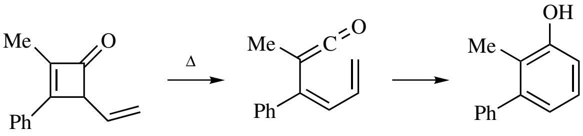
30 **31** **32** (89%)

The ene-yne-substituted ketene **34** generated by thermolysis of the alkynylcyclobutenone **33** cyclized to form the quinone **35**, together with the cyclopentendione **35a** (equation 14).[22] Photolysis of **33** gave an isomeric ene-yne ketene in which the vinyl OH group added to the ketene, forming a lactone.[22] The dienylketene **37** generated by thermolysis of vinylcyclobutenone **36** formed the phenol **38** (equation 15).[23]



33 **34** **35** (21%) **35a** (46%)

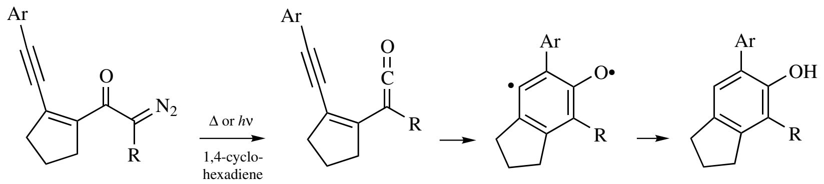
(14)



36 **37** **38** (75%)

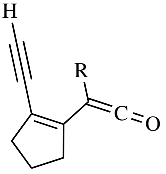
(15)

Thermolysis or photolysis of the diazo ketones **39** gave indanols **42** proposed to form by intramolecular cyclization of the intermediate ene-yne ketenes **40**, giving diradicals **41** (equation 16).[24] Calculations at the HF/6-31G* level for the *s-trans* and *s-cis* conformers **40a** and **40b** showed that there was a preference for *s-trans* of 0.53 and 1.40 kcal/mol for R = Me and H, respectively. The lesser preference for **40a** in the case of R = Me was attributed to steric repulsion between the alkyne bond and the Me group, and the resulting higher proportion of **40b** for R = Me led to the higher yield of cyclization to indanol **42** in this case. Related α-diazo ketones with DNA binding groups R gave improved DNA-cleaving activity compared to R = Me.[24] Further examples of DNA cleavage by ketenes are given in Section 4.1.6.

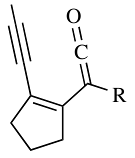


39 **40** **41** **42** (21–67%)

(16)



40a



40b

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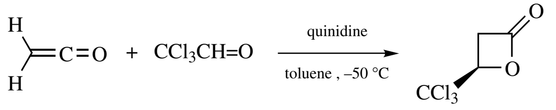
5.4.5 Cycloaddition of Ketenes with Carbonyl Groups

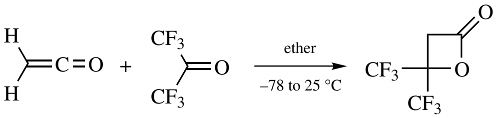
The [2+2] cycloaddition of ketenes with carbonyl groups forming β-lactones has long been known and is a valuable experimental tool because of the synthetic utility of the products.[1–5] This method has acquired increasing prominence because of the development of methods that give high stereoselectivity in the formation of new chiral centers. A striking early example was the addition of trichloroacetaldehyde to ketene catalyzed by a chiral tertiary amine to give the β-lactone **1** with high stereoselectivity (equation 1).[6,7]



(1)

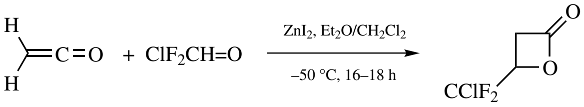
1 **1** (89%, 98% *ee*)

Ketene underwent [2+2] cycloaddition with the electrophilic carbonyl group in hexafluoroacetone forming the β-lactone **2** (equation 2),[8] and formed **3** with chlorodifluoroacetaldehyde in a reaction promoted with a Lewis acid catalyst (equation 3).[9]



(2)

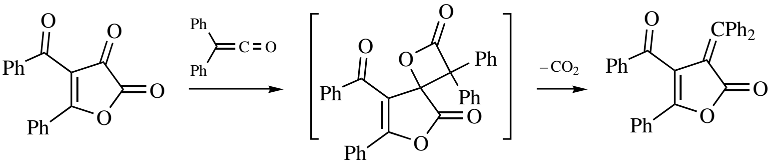
2 (96%)



(3)

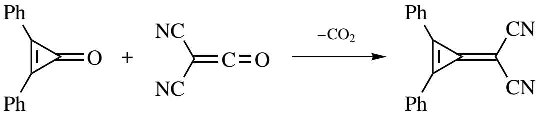
3 (55%)

The β-lactones formed by ketene cycloadditions are prone to decarboxylation, and the cycloaddition provides a means of olefination of carbonyl groups, as in the conversion of **4** to **5** using diphenylketene (equation 4)[10] and the formation of **6** using dicyanoketene (equation 5).[11]



(4)

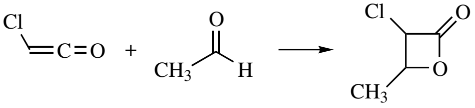
4 **5**



(5)

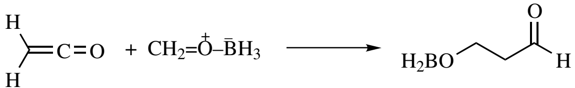
6 (26%)

Ketene [2+2] cycloaddition with carbonyl groups has been studied by computational methods.[12,13] These studies included eight different gas phase and solution transition states for the reaction of chloroketene with acetaldehyde, forming **7** (equation 6).[12] It was found that the formation of *trans*-2-oxetanones was favored in the absence of catalyst, whereas the presence of catalyst favored the *cis* isomer, in agreement with experiment.[12] Theoretical study of BF_3 catalysis showed that coordination to the aldehyde carbonyl was favored, with a major reduction in the activation energy for C—C bond formation, while inclusion of solvent in the computation was shown to lead to an earlier transition state.[14] The interaction with BH_3 favored C—C bond formation and hydride donation to carbon, forming **8** (equation 7).[14]



7

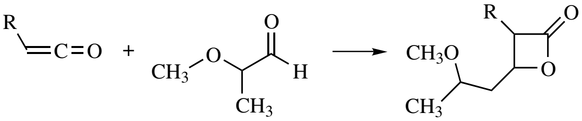
(6)



8

(7)

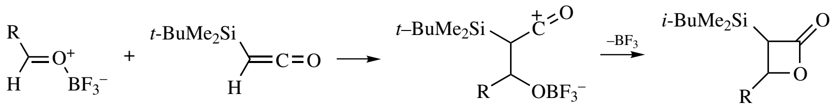
Extensive theoretical studies of stereocontrol in [2+2] cycloadditions between ketenes and the aldehyde $CH_3OCH(CH_3)CH{=}O$ forming **9** included the effects of lithium cation catalysis (equation 9).[15] In the uncatalyzed reactions highly asynchronous concerted $[_2\pi_S+(_2\pi_S+_2\pi_S)]$ transition states were favored.



9

(8)

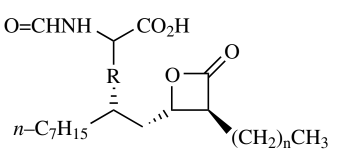
The development of catalytic, enantioselective methods has increased the utility of β-lactone formation by ketene cycloaddition with carbonyl groups.[16] The stereoselectivity of the BF_3-catalyzed cycloaddition of cyclohexanecarboxaldehyde with ketene **10** (equation 9) has been studied both computationally and by measurement of the ^{13}C kinetic isotope effects.[17] The reaction gave >90% yields of **12** as a *cis*/*trans* mixture with a diastereoselectivity that varied from 2.7–3.1:1 at 23 °C to 1.3:1 at −21 °C.[17] Distinctly different ^{13}C kinetic isotope effects were observed for the two diastereomers, which were both interpreted as forming from the stepwise process of equation 9. The first step forming **11** was rate limiting for formation of the *trans* product, whereas the second step forming **12** from **11** was rate limiting for formation of the *cis* product.



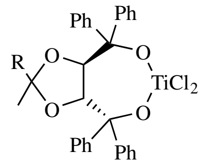
10 **11** **12**

(9)

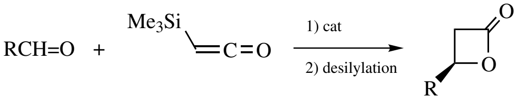
The reaction of silylketenes with carbonyl compounds leading to β-lactones served as an alternative to the Wittig reaction[18] and supplied precursors for studies of ring cleavage of the lactones.[19] This reaction was also used to prepare five different panclicins **13**, which are pancreatic lipase inhibitors containing β-lactone rings.[20] Chiral catalysts such as the Ti-TADDOL derivatives **14** catalyzed the cycloaddition of aldehydes with $Me_3SiCH{=}C{=}O$ with high stereoselectivity (equation 10).[21]



13



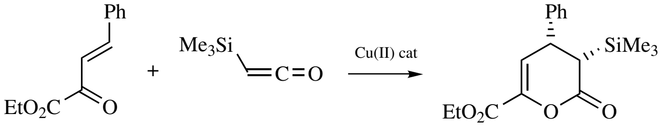
14



49–78%

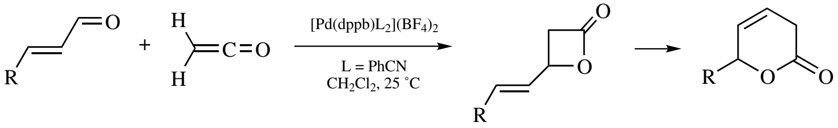
(10)

Bis(oxazoline)-Cu(II) complexes catalyzed stereoselective [4+2] cycloaddition of ethyl cinnamate with trimethylsilyketene, forming **15** (equation 11)[22] (see also Section 4.5). Such reactions have been reviewed.[23] A new in situ ketene generation with an optically active catalyst has been developed for β-lactone formation (Section 5.9).[24] Palladium catalysts promoted formation of isolable β-lactones **17** from $CH_2{=}C{=}O$ and 4-substituted vinyl aldehydes **16**, and these were isomerized to 3,6-dihdyro-2-(*H*)pyran-2-ones **18** (equation 12).[25,26]



(11)

15 (96%)



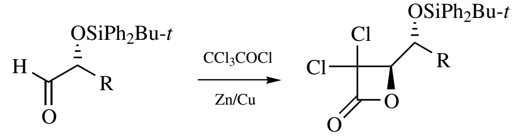
16 (R = Ar, *n*-Pr, H)

17 (96%, R = H)

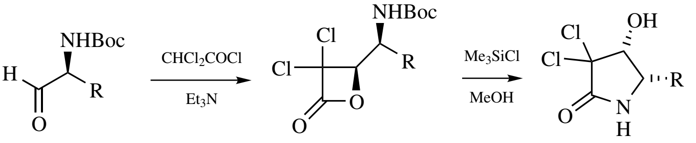
18 (77%, R = Ph)

(12)

Reaction of dichloroketene generated by zinc dechlorination or dehydrochlorination with optically active α-silyloxy or α-amino aldehydes gave only single diastereomers of the β-lactones **19** or **20**, respectively (equations 13, 14).[27] The ketene *n*-$C_6H_{13}C(SiMe_3)=C=O$ reacted with these aldehydes to give the analogous products, with the stereochemistry established by X-ray analysis.[28]

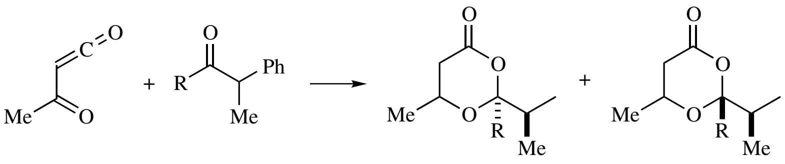


R = Me, *i*-Pr, *i*-Bu, Ph **19** (85%) (13)



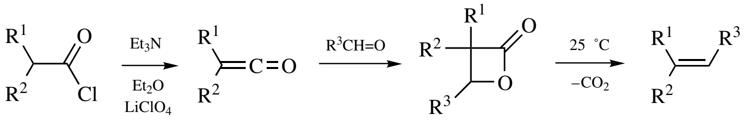
R = $PhCH_2$, *i*-Pr **20** 85% R = *i*-Pr (14)

The [4+2] cycloaddition of acetylketene formed by FVP with trapping by chiral racemic aldehydes **21**, forming dioxinones **21a** and **21b**, proceeds stereoselectively, favoring the product **21a** by factors of 2.0–6.3:1.0, as predicted by the Felkin-Anh model (equation 15).[29] The pseudopericyclic transition state for this reaction has been calculated.[29]



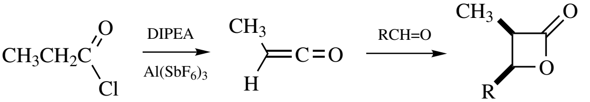
21 (R = H, Me, Et) **21a** **21b** (15)

The reaction of acyl chlorides **22** with Et_3N in 5 M $LiClO_4$ in diethyl ether gave ketenes **23**, which reacted in situ with aldehydes at 0 °C, forming β-lactones **24** (equation 16).[15,30] The reaction mixtures were stirred at room temperature, and the intermediate oxetanones **24** underwent decarboxylation to give alkenes or dienes (equation 16).[30] Both steps of this olefination sequence were proposed to be promoted by this highly polar aprotic medium.[30] The adduct **24a** ($R^1 = R^2 = Me$, $R^3 = 4\text{-}O_2NC_6H_4$) did not undergo decarboxylation under these conditions, and for $R^1 = R^2 = H$ acids $R^3CH{=}CHCO_2H$ were formed.



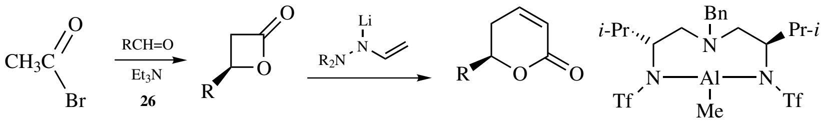
22 **23** **24** (40–81%) (16)

The reactions of acyl halides with aldehydes induced by diisopropylethylamine (DIPEA) in the presence of $Al(SbF_6)_3$ catalyst gave β-lactones **25** with high *cis/trans* product ratios (equation 17).[31–36] Mechanistic studies implicated ketene intermediates in these reactions. The lactones gave β-hydroxy esters in catalyzed reactions with alcohols. Chiral catalyst **26** for cycloaddition of $CH_2{=}C{=}O$ gave optically active β-lactones **27**, which were converted to **28** (equation 18).[35]



25 (65–80%)

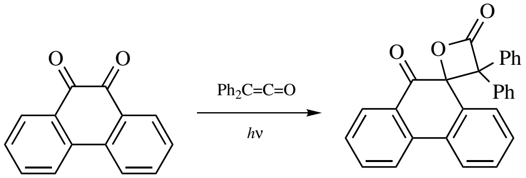
(17)



27 **28** (68-81%) **26**

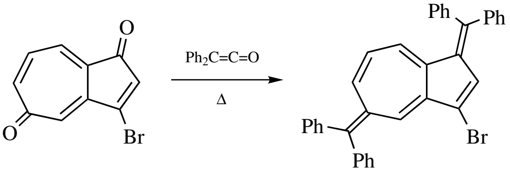
(18)

Photochemical cycloaddition of diphenylketene to phenanthrenequinone gave **28** (equation 19).[37] Thermal reaction of the 1,5-azulenequinone **29** with $Ph_2C{=}C{=}O$ formed the corresponding quinodimethane **30** through [2+2] cycloaddition and loss of CO_2 (equation 20).[38]



28

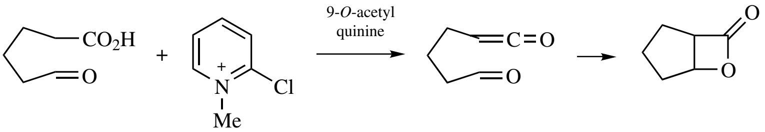
(19)



29 **30**

(20)

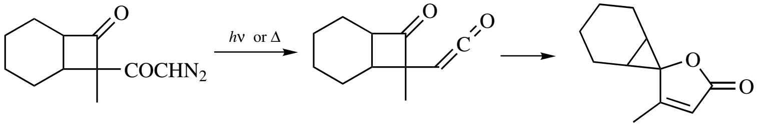
Ketene **32** containing an aldehyde carbonyl group was generated from aldoacid **31** with Mukaiyama's reagent and gave intramolecular cycloaddition forming **33** in 86–92% *ee*, using 9-*O*-acetylquinine as catalyst (equation 21).[39,40] There were earlier reports of such intramolecular cycloadditions.[41–45]



31 **32** **33** (52%, 92% *ee*)

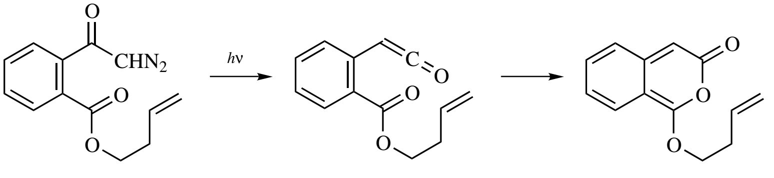
(21)

2-Ketenylcyclobutanones **34** generated by Wolff rearrangement gave lactones **35** by carbonyl addition with rearrangement (equation 22).[46] The intermediate ketenes were observed by IR at 2120 cm^{-1} and −50 °C and were trapped with alcohols. The aryl ketene **35** cyclized to pyrone **36** (equation 23).[47] Further examples of formation of γ-pyrones are given in Section 4.1.2.



34 **35** (70%)

(22)



35 **36** 78%

(23)

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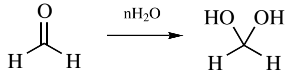
5.5 NUCLEOPHILIC ADDITION TO KETENES

5.5.1 Mechanisms of Hydration of Ketenes

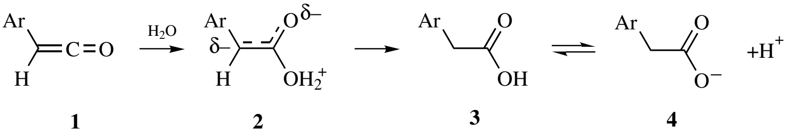
The hydration of carbonyl compounds forming 1,1-diols has been found by experimental[1] and computational[2–4] studies to involve multiple water molecules in which water clusters effect net hydroxide addition to the carbonyl carbon and proton addition to the carbonyl oxygen through hydrogen-bonded arrays (equation 1).



(1)

Most ketenes are too reactive for measurements using conventional spectroscopy of the rate constants for addition of nucleophiles such as water to preformed ketenes, although early interpretations of hydration indicated that enediols were formed as the first intermediates.[5,6] Studies using relatively unreactive ketenes in organic solvents containing small amounts of water permitted measurements of rate constants that were more than first order in water concentration[7–14] but did not provide satisfactory interpretations of the details of the reactions.[15]

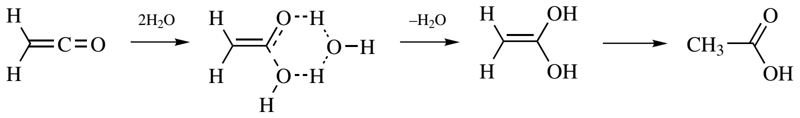
Initial quantitative measurements of the reactivity of arylketenes **1** generated by Wolff rearrangements using flash photolysis of diazo ketones in wholly aqueous media were carried out by measuring the change in conductivity due to the ionization of the substituted phenylacetic acids formed (equation 2).[16] The arylketenes showed a dependence of the measured rate constants log$k(H_2O)$ on the σ^n constants of the aryl substituents with a value of $\rho = 1.19$, indicating negative charge development in the transition state **2** near the aryl group. The reactivity of ketene (**5**) itself was then studied, and was found to be much less reactive than the arylketenes.[17] This also indicated a significant conjugative stabilization by the aryl groups in the transition state for ketene hydration. Activation parameters $\Delta H^{\ddagger} = 10.3$ kcal mol^{-1} and $\Delta S^{\ddagger} = -16$ cal deg^{-1} mol^{-1} and a solvent isotope effect $k(H_2O)/k(D_2O) = 1.9$ were measured.[17] The value of $\Delta S^{\ddagger}$ is consistent with an associative mechanism, and the solvent isotope effect is consistent with nucleophilic water attack.



(2)

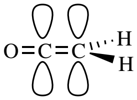
1 **2** **3** **4**

Computational studies of the hydration of $CH_2{=}C{=}O$ (**5**)[18–24] were generally in accord with the description for hydration of other carbonyl compounds,[1–4] and for addition of two water molecules a cyclic transition state **6** leading to the enol **7** of acetic acid was preferred (equation 3). A significantly higher barrier was found for addition of a single water molecule, as confirmed by the most recent computation.[22] Structures with larger numbers of water molecules have also been considered,[19,21] and the enol **7** in solution would also be solvated by further water molecules. For the parent ketene **5**, addition using two water molecules to the C=C bond giving acetic acid directly was calculated to be close in energy to addition to the C=O bond, but for substituted ketenes in which stabilization of a polar transition state would be possible, as in equation 2, addition to the carbonyl group would be favored. The kinetics of ketene hydration have been examined computationally by "No Barrier Theory," and this gave a reasonable estimate of the known rate constant.[24] A theoretical study of the addition reactions of a single molecule of H_2O, H_2S, NH_3, HF, and HCN to ketene provided comparative information[25] but was not the best description of the reaction with multiple solvent molecules.

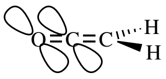


5 **6** **7** (3)

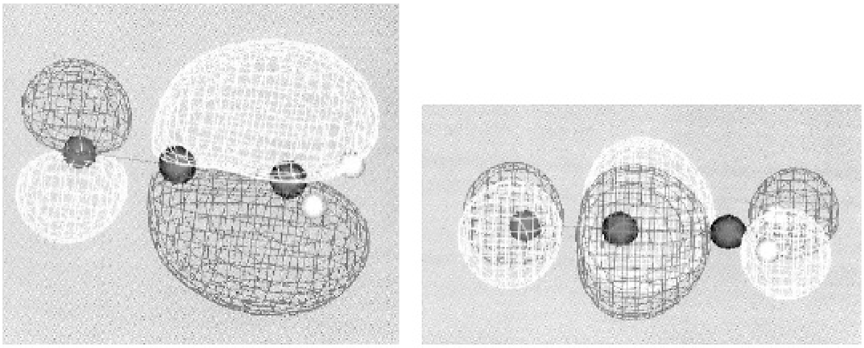
The ketene HOMO is perpendicular to the ketene plane with negative charge at C_2 and oxygen, whereas the LUMO is in plane with positive charge at C_2, the carbonyl carbon (Figure 5.4).[26,27] Electrophilic addition to the C=C bond occurs on the HOMO and would require out-of-plane attack at the π bond perpendicular to the ketene plane in **5a**, and nucleophilic addition to the carbonyl group of ketene would involve attack at the LUMO in-plane π bond in **5b**.



5a



5b



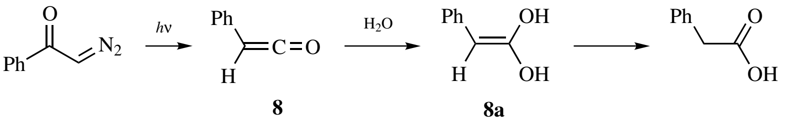
HOMO LUMO

Figure 5.4 Frontier molecular orbitals of ketene.

Experimental measurements of the gas phase hydration of ketene showed an uncatalyzed surface reaction, and a homogeneous reaction between ketene with one water molecule catalyzed by a single acetic acid molecule, but did not allow a definite conclusion as to the mechanism.[28] Experimental studies of the gas phase dehydration of acetic acid to ketene have also been carried out,[22,29] and when the direct elimination to ketene and initial acid enol formation were compared, the latter process was found to be favored.[29]

The hydration reactions of a number of ketenes have been studied by measuring the decrease in the UV absorption of the ketene, and the derived rate constants are collected in Table 5.13. For a few examples, the ketenes were sufficiently stable so that the reactions have been carried out by adding the prepared ketene to either a wholly aqueous or a partially aqueous solvent mixed with an organic component.[30–35] Extrapolations permitted estimates of ketene reactivities in purely aqueous solutions from measurements in mixed solvents. Flash photolysis in water of suitable precursors, usually diazo ketones, has been used for the generation of more reactive ketenes in situ, and the kinetics have been monitored by UV spectroscopy.[36–46] These include the kinetics of hydration of ketene (**5**) generated from diazoacetaldehyde ($N_2CHCH{=}O$) in acid, neutral, and base solution.[38,40]

The formation of intermediate ethene-1,1-diols (ketene hydrates) was first proposed by Staudinger and Meyer in 1922.[5] Experimentally, acid enol intermediates have been observed for hydration of some ketenes by UV spectroscopy,[41–45] including the reaction of phenylketene (**8**), forming the acid enol **8a**, and then phenylacetic acid (equation 4).[45,46] Interestingly, when the absorption changes in the UV for this reaction were monitored at 260 nm, initial increase in absorbance followed by decay was observed, and it was concluded that the initial rise in absorption did not represent the hydration of the phenylketene, but rather that the subsequent decrease in absorption was due to conversion of **8** to **8a**.[45]



(4)

The hydration with ^{18}O-labeled H_2O of crowded arylketenes and diphenylketene resulted in incorporation of more than one ^{18}O in the product diarylacetic acid, indicating that the hydration was reversible (equation 5).[47] This result was confirmed by the observation of ^{18}O incorporation in the recovered ketene.[47] The hydration of bis(2,4,6-triisopropylphenyl)ketene (**9a**) has been shown to involve reversible formation of the 1,1-enediol **10**, which was directly observed as a long-lived species in solution by NMR (equation 5).[48,49] Acid enols $Ar_2C{=}C(OH)_2$ (**10**, Ar = 2,4,6-$Me_3C_6H_2$ and C_6Me_5) from the hydration of the corresponding ketenes **9** have also been observed as reasonably long-lived intermediates in solution.[50] In the hydration of $PhC(OH){=}C{=}O$ (**11**) an acid-catalyzed term was detected that was interpreted as indicating the formation of the acid enol **13**, but the mechanism of this process

TABLE 5.13 Hydration Rate Constants for Ketenes at 25 °C

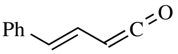
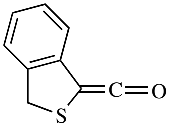
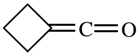
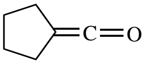
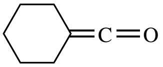
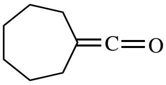
Ketene	k_{H}^{+},	k_{H_2O}, s^{-1}	k_{OH^-}, $M^{-1}s^{-1}$	$\frac{k_{H_2O}}{k_{D_2O}}$	$\frac{k_{H^+}}{k_{H_2O}}$ (M^{-1})	$\frac{k_{OH^-}}{k_{H_2O}}$ (M^{-1})	Ref.
$CH_2=C=O$	1.01×10^4	44, 36.5	5.26×10^4	1.59	276		17, 38
n-$BuCH=C=O$	3.98×10^3	99.4	3.29×10^4	1.88	40	330	36
$ArCH=C=O$, Ar=							
$4\text{-}O_2NC_6H_4$		49.5×10^3					16
$4\text{-}NCC_6H_4$		25.6×10^3					16
$4\text{-}ClC_6H_4$		9.6×10^3					16
$4\text{-}FC_6H_4$		5.9×10^3					16
C_6H_5		4.77×10^3	1.22×10^6	1.44		260	16, 36
C_6F_5		2.76×10^3	1.13×10^6	1.42		409	63
$4\text{-}CH_3OC_6H_4$		2.9×10^3	1.13×10^6			390	58
$4\text{-}CH_3C_6H_4$		3.8×10^3					16
1-Naphthyl		2.95×10^3	1.25×10^6	1.25		420	58
Mesityl	4.7^d	1.10×10^2	6.78×10^4	1.51	0.042	620	52, 58
$2,4,6\text{-}(MeO)_3C_6H_2$		8.28	4.34×10^3			520	58
2-Pyridyl		1.1×10^4					46
3-Pyridyl		2.5×10^4					46
4-Pyridyl		5.0×10^4					46
$Me_3SiCH=C=O$		0.254					33
$CF_3CH=C=O$		6×10^2					39
c-$PrCH=C=O$		304	2.48×10^5	2.58		816	39
$PhC\equiv CCH=C=O$	1.61×10^5	7.15×10^4	1.98×10^7	2.84	2.2	277	39
	2.09×10^4	5.76×10^3	2.31×10^6	2.09	3.6	401	39
$O=C=C=C=O$	0.195	1.45×10^{-2}		2.20			64
$CH_3SCPh=C=O$	4.67	1.02×10^2	1.89×10^4	1.59	0.046	232	62
		2.21×10^5	1.66×10^7	1.20		75	71
$HOCPh=C=O$	5.45×10^7	5.51×10^5	2.33×10^9	1.49	9.9	4200	41
$PhCOCPh=C=O$		6.29×10^3					39, 71
t-$BuCH=C=O$	4.77×10^3	14.6	1.68×10^4	2.01	327		31, 38
$Et_2C=C=O$		8.26^a					31
	3.13×10^5	4.09×10^2			765		63
	2.14×10^4	1.11×10^2	2.14×10^4	3.39	193	350	63
	2.78×10^3	23.0	6.24×10^3	2.04	121	271	31, 63
		23.5	6.08×10^3	1.91		259	63

TABLE 5.13 (*Continued)*

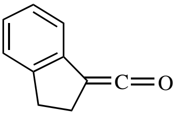
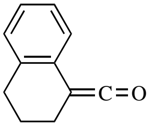
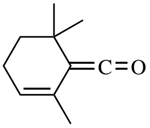
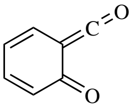
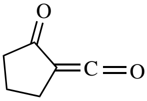
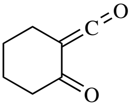
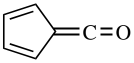
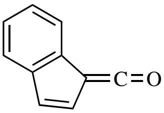
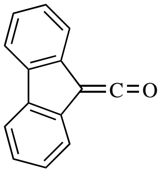
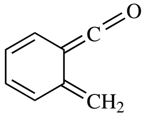
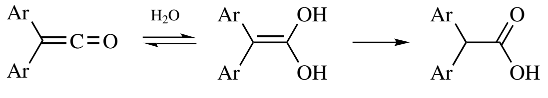
Ketene	k_H^+,	k_{H_2O}, s^{-1}	k_{OH^-}, $M^{-1}s^{-1}$	$\frac{k_{H_2O}}{k_{D_2O}}$	$\frac{k_{H^+}}{k_{H_2O}}$ (M^{-1})	$\frac{k_{OH^-}}{k_{H_2O}}$ (M^{-1})	Ref.
t-$Bu_2C{=}C{=}O$	434	1.57×10^{-4}			2.8×10^6		30, 31
c-$Pr_2C{=}C{=}O$		13.4^a					34
$Ph_2C{=}C{=}O$		275	6.11×10^4	1.27		220	36
$MeCPh{=}C{=}O$		55.7	2.03×10^4	1.55	36		63
$EtCPh{=}C{=}O$		10.3	6.05×10^3	1.48		587	63
c-$PrCPh{=}C{=}O$		11.1^a					34
i-$PrCPh{=}C{=}O$		1.23^a					32
t-$BuCPh{=}C{=}O$		0.370^a					32
		1.96×10^3	8.42×10^5	1.18		430	63
		103	6.30×10^4	1.60		612	63
	7.03	2.97×10^{-4}	0.104	2.32	2.4×10^4	350	32
t-$BuC(CO_2Et){=}C{=}O$		0.124		1.48			35
t-$BuC(COBu$-$t){=}C{=}O$		2.35×10^{-4}		1.37			35
$CH_3COCH{=}C{=}O$		1.54×10^6	1.86×10^8	1.11		120	72
$CF_3COCH{=}C{=}O$		1.75×10^6		0.88			51
		8.2×10^{8a}					78
		1.4×10^6	7.5×10^7		54		73
		3.45×10^4	1.08×10^7				77
		9.0×10^5	4.8×10^7			53	37, 63
		1.2×10^6	3.8×10^{7c}	1.32		36	55, 63

TABLE 5.13 (*Continued*)

Ketene	k_H^+,	k_{H_2O}, s^{-1}	k_{OH^-}, $M^{-1}s^{-1}$	$\frac{k_{H_2O}}{k_{D_2O}}$	$\frac{k_{H^+}}{k_{H_2O}}$ (M^{-1})	$\frac{k_{OH^-}}{k_{H_2O}}$ (M^{-1})	Ref.
		1.07×10^5	3.47×10^6	1.35		35	57
	1.44×10^5	1.35×10^5	9.26×10^6		1.46		76
$Mes_2C{=}C{=}O^a$		0.68^a					50
$(Me_5C_6)_2C{=}C{=}O^a$		0.16^a					50
$(Me_3Si)_2C{=}C{=}O^a$		2.46×10^{-4a}					69
$(Me_3SiC{=}C{=}O)_2{}^a$		0.307^a					82
$Me_2Si(CH{=}C{=}O)_2{}^a$		3.34×10^{-2}					70
$Me_3SiCH{=}C{=}O$	542	3.23×10^{-3}	70		1.7×10^5	2.1×10^4	33
$PhMe_2SiCH{=}C{=}O^a$		5.40×10^{-3}					68
t-$BuMe_2SiCH{=}C{=}O^a$		9.58×10^{-4}					68
$Me_5Si_2CH{=}C{=}O^a$		9.31×10^{-3}					69
$(SiMe_2C{=}C{=}O)_2{}^a$		1.52×10^{-2}					69
$(CH_2SiMe_2CH{=}C{=}O)_2{}^a$		5.19×10^{-3}					69

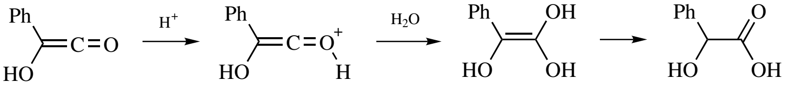
[a] Extrapolated.

has not been explained (equation 6).[41]



9 (**a**, Ar = 2,4,6-*i*-$Pr_3C_6H_2$) **10** **11**

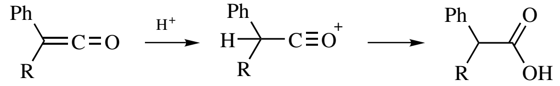
(5)



11 **12** **13** **14**

(6)

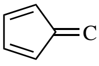
The hydration of mesitylketene (**15**, 2,4,6-$Me_3C_6H_2CH{=}C{=}O$) generated by flash photolysis revealed acid-catalyzed, neutral, and OH^--catalyzed reactions.[52] The arylketenes $PhCR{=}C{=}O$ (**16**, R = *i*-Pr, *c*-Pr, *t*-Bu) previously were shown to undergo acid-catalyzed hydration by proton transfer to C_2 with formation of the intermediate acylium ions **17** (equation 7).[32,34] The acid-catalyzed hydration requires rather high acid concentrations, a result attributed to ground state stabilization by aryl, as well as destabilization of the positively charged transition state by aryl.[32]



16 R = *i*-Pr (**a**), *c*-Pr (**b**), *t*-Bu (**c**) **17** **18**

(7)

The fulvenones **19**,[37] **20**,[53–56] and **21**[57] were found to be very reactive in neutral hydration, a result attributable to the cyclopentadienyl anion character of the transition states for water addition. A rate constant of 1.6×10^8 M^{-1} s^{-1} for addition of cyanide ion to **19** was also measured.[37]



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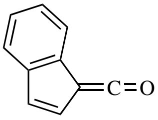

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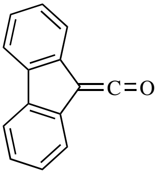
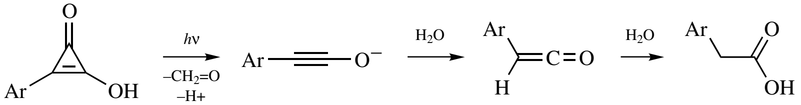


21

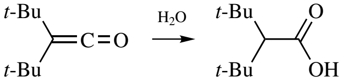
Flash photolysis of arylhydroxycyclopropenones **22** in aqueous solution formed ynolates **23** that were converted to arylketenes **24**, whose rates of hydration were measured (equation 8).[58] The identity of the ketenes was confirmed by comparison with the species formed by photochemical Wolff rearrangements.[58]



22 (Ar = Ph, 1,3,5-$Me_3C_6H_2$, 1-naphthyl, 1,3,5-$(MeO)_3C_6H_2$, 4-$MeOC_6H_4$) **23** **24** **25**

(8)

Alkylketenes were significantly less reactive in hydration than arylketenes (Table 5.13), with a rate ratio k_{rel}(PhCH=C=O/*n*-BuCH=C=O) = 500. Di-*tert*-butylketene (**26**) was less reactive than *t*-BuCH=C=O by a factor of 10^5, a result attributed to steric hindrance on both sides of the carbonyl carbon to in-plane attack of water (equation 9).[31]



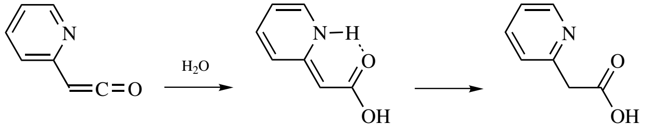
26

(9)

A collection of rate constants has been reported for the neutral hydration of a number of alkylketenes obtained from flash photolysis[59,60] and dialkylketenes measured by stop-flow methods.[61] These results were plausibly interpreted in terms of in-plane attack of water on the ketenes, but certain unusual features of the data, including the report of a rate constant measured by stop-flow for *t*-Bu_2C=C=O in 10% H_2O/CH_3CN with a half-life greater than 1 year suggest that confirmation of these results would be desirable.

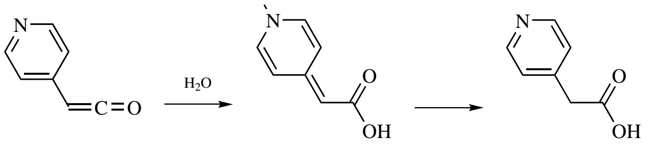
The solvent isotope effects of the hydroxide ion–catalyzed hydration of a series of ketenes are all weakly inverse ($k_{OH}^{-}/k_{OD}^{-} = 0.76$–$0.97$), and this was suggested as a mechanistic criterion for this reaction.[62] There was a linerar correlation between log$k$(H_2O) and log$k$(OH^-) for ketene hydration, which was also suggested to be diagnostic for ketene hydration.[63] A deviation from the correlation was noticed for PhC(OH)=C=O (**11**), suggesting that the mechanistic assignment for this reaction required revision.[63]

The hydration of 2- and 4-pyridylketenes (2- and 4-**27**) generated by photochemical Wolff rearrangement, forming pyridylacetic acids **29**, have been found to involve intermediate carboxymethylenedihydropyridines 2- and 4-**28**, with a strong intramolecular hydrogen bond in 2-**28** (equations 10, 11).[46] 3-Pyridylketene (3-**27**) reacted with formation of the intermediate acid enol 3-**29** (equation 12).[46]



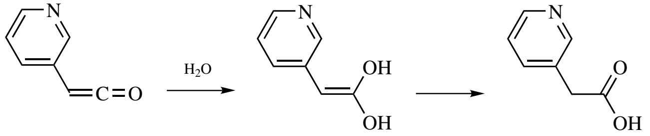
(10)

2-**27** 2-**28** 2-**29**



(11)

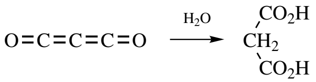
4-**27** 4-**28** 4-**29**



(12)

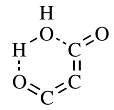
3-**27** 3-**30** 3-**29**

The rate of hydration of carbon suboxide (O=C=C=C=O, **31**) forming malonic acid (**32**) has been measured (equation 13), and the reaction was also studied using *ab initio* calculations.[64] Complexes of C_3O_2 with H_2O (**33**) and NH_3 (**34**) in argon matrices were studied by FTIR spectroscopy, and calculations of the structures of these pre-reactive complexes suggested that they could lead to initial 1,4-addition.[65] A new theoretical study of the hydration of C_3O_2 has appeared,[66] and computed values for the proton affinity of 765 to 801 kJ/mol[64,66] are in reasonable agreement with the experimental value of 791 kJ/mol.[67]



$$O=C=C=C=O \xrightarrow{H_2O} CH_2(CO_2H)_2 \qquad (13)$$

31 **32**



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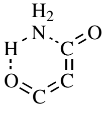

34

Further studies of ketene hydration include those of acetylketene (Section 4.1.6, ref. 11), α-oxoketenes (Section 4.1.10), and disilanylketenes (Section 4.5).

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5.5.2 Mechanisms of Amination of Ketenes

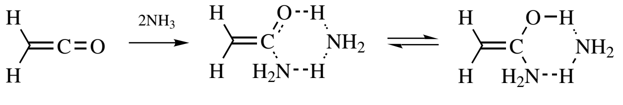
Reactions of ketenes with amines are quite facile and have long been of preparative use (Section 5.5.3.3). Computational study of the reaction of ketene (**1**) revealed that reaction with two molecules of NH_3 was favored over reaction with a single NH_3 molecule and proceeded through a transition state **2a**, followed by addition to the C=O bond leading to a complexed amide enol **2b** (equation 1).[1,2] Transition

TABLE 5.14 Hydration Rates of Ketenes in H_2O/CH_3CN at 25 °C

Ketene	% H_2O	k_H^+, $M^{-1}s^{-1}$	k_{H_2O}, s^{-1}	k_{OH}^-, $M^{-1}s^{-1}$	$\frac{k_{H_2O}}{k_{D_2O}}$	$\frac{k_H^+}{k_{H_2O}}$ (M^{-1})	$\frac{k_{OH}^-}{k_{H_2O}}$ (M^{-1})	Ref.
t-BuCH=C=O	20%	135	0.0873	1.7×10^3				31
Ph_2C=C=O	20%		4.17					50
Mes_2C=C=O	50%		0.162					50
$(Me_5C_6)_2C$=C=O	50%		4.26×10^{-2}					50
Et_2C=C=O	50%		0.357		1.59	145^b	790	31
c-Pr_2C=C=O	50%		0.406					34
c-PrCPh=C=O	20%		0.297					34
i-PrCPh=C=O	50%	0.120	0.0424^a	58.4	1.67	2.8	1400	32
t-BuCPh=C=O	50%	0.488	0.00997	46.7		49	4700	32
t-Bu_2C=C=O	50%	3.6						31
Me_3SiCH=C=O	50%	542	3.23×10^{-3}	70		1.7×10^5	2.1×10^4	33
$(Me_3SiC$=C=$O)_2$	50%		0.307					82
$PhMe_2SiCH$=C=O	50%		5.40×10^{-3}					68
t-$BuMe_2SiCH$=C=O	50%		9.58×10^{-4}					68
Me_5Si_2CH=C=O	50%		9.31×10^{-3}					69
$(SiMe_2C$=C=$O)_2$	50%		1.52×10^{-2}					69
$(CH_2SiMe_2CH$=C=$O)_2$	50%		5.19×10^{-3}					69
$Me_2Si(CH$=C=$O)_2$	50%		3.34×10^{-2}					70

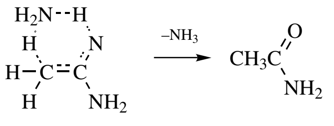
[a] Extrapolated.
[b] 9.0 °C.
[c] 5 °C.
[d] Ref. 7.

structure **3** was found for tautomerization of **2b** to the product acetamide. The pathway for reversal of the formation of the amide enol **2b** to reform ketene was lower in energy than conversion of **2b** to product, suggesting that the formation of **2b** could be reversible. An alternative pathway involving direct addition of NH_3 to the C=C bond forming acetamide directly was thermodynamically 22.6 kcal/mol more favorable than the formation of **2b** but had a barrier that was 12.8 kcal/mol higher than for formation of **2b**.



1 **2a** **2b**

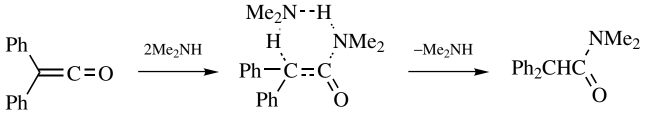
(1)



3

(2)

Early kinetic studies of ketene amination by Satchell et al.[3–6] found that the rate of reaction of Ph_2C=C=O (**4**) with anilines in benzene and of dimethylketene in ether was dependent on both [amine] and [amine]^2, and the results were interpreted as showing that the reaction occurred by an amine-assisted concerted addition to the C=C bond (equation 3). The reaction of $Ph_2C{=}C{=}O$ (**5**) in H_2O with a variety of different amines followed by UV spectroscopy showed a much greater reactivity for the amines compared to reaction with H_2O but no systematic dependence of the reactivity on amine basicity.[7] These results were interpreted as demonstrating rate-limiting addition of the amines to the ketene C=O bond forming an amide enol, with an attenuation of reactivity of the more basic amines due to hydrogen bonding to the H_2O (equation 4).[7] For the ketenes $Ar_2C{=}C{=}O$ (Ar = mesityl, Me_5C_6, and 2,4,6-i-$Pr_3C_6H_2$) amide enols have been observed by IR and UV as rather long-lived intermediates.[2,8,9] The kinetics of the reactions were first order in [amine], indicating that attack of a single amine molecule was rate determining.[2]



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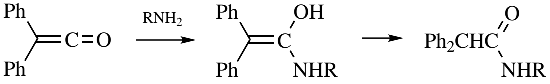
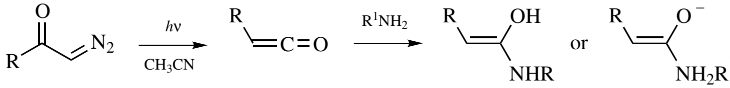
(3)



4

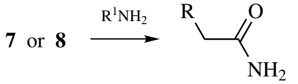
(4)

Measurements of the kinetics of amination of a variety of ketenes **6** by TRIR spectroscopy in CH_3CN were carried out by flash photolysis of the diazo ketones **5**, generating the ketenes which were identified by their characteristic IR absorption near 2100 cm^{-1}.[10] The kinetics of the reactions of the ketenes were monitored by the disappearance of the characteristic ketenyl IR absorption and showed a first-order dependence of the rates on [amine]. New transients were formed with the same rate constants as the ketene decay, and had IR absorption near 1750 cm^{-1} that also decayed with a first-order dependence on [amine]. These second transient intermediates were assigned as having the structures either of amide enols **7** or of zwitterions **8** and decayed to amides **9**[10–12] (equations 5, 6). The measured rate constants for amination are given in Table 5.15. The bimolecular rate constants k_2 for the ketenes varied from 4.6×10^5 M^{-1} s^{-1} for t-BuCH=C=O with Et_2NH to 1.6×10^9 M^{-1} s^{-1} for $4\text{-}O_2NC_6H_4CH{=}C{=}O$ with piperidine and were approaching the diffusion controlled limit.



5 **6** **7** **8**

(5)



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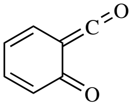
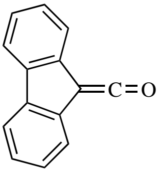
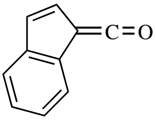
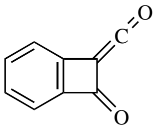
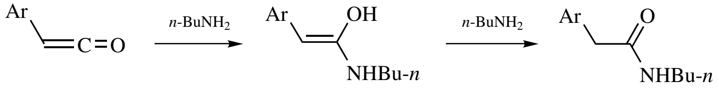
(6)

TABLE 5.15 Bimolecular Rate Constants for the Reaction of Ketenes with Amines in CH_3CN at 23–25 °C

Ketene	Et_2NH	$(CH_2)_5NH$[a]	i-$PrNH_2$	n-$BuNH_2$	$BnNH_2$	Ref
t-BuCH=C=O	4.6×10^5	6.7×10^6	7.7×10^5	1.6×10^6	7.5×10^5	10
$PhMe_2SiCH=C=O$	4.2×10^{4c}			2.3×10^5		15
PhCH=C=O	4.8×10^8	5.0×10^8	1.2×10^8	3.3×10^8	1.4×10^8	10
$4\text{-}MeOC_6H_4CH=C=O$	3.3×10^8	5.1×10^8	9.5×10^7	2.2×10^8	9.2×10^7	10
$4\text{-}NCC_6H_4CH=C=O$	9.5×10^8	1.4×10^9	5.8×10^8	8.7×10^8	5.8×10^8	10
$4\text{-}O_2NC_6H_4CH=C=O$	9.5×10^8	1.6×10^9	8.1×10^8	1.1×10^9	7.0×10^8	10
PhCH=CHCH=C=O	4.9×10^8	8.0×10^8	1.6×10^8	5.1×10^8	1.7×10^8	10
$PhC\equiv CCH=C=O$	1.1×10^9					10
2-PyridylCH=C=O				2.2×10^8		13
3-PyridylCH=C=O				3.8×10^8		13
4-PyridylCH=C=O				3.7×10^9		13
$Ph_2C=C=O$	1.2×10^7	1.5×10^7	4.4×10^6	1.1×10^8	5.4×10^7	10
PhCOCPh=C=O	2.1×10^7	3.8×10^7	9.4×10^6	2.3×10^7	1.1×10^7	10
 **21**	1.1×10^9					12
 **29**	7.6×10^7	1.8×10^8				11, 21
 **28**	1.0×10^9	1.9×10^9				21
 **30**	1.1×10^9	3.5×10^9				21

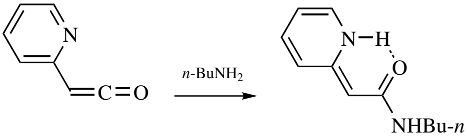
[a] Piperidine.
[b] Average value.
[c] Morpholine.

Phenylketene (**10a**) and n-$BuNH_2$ reacted with formation of the amide enol **11a** observed by IR, and this formed the amide **12a** in an amine-catalyzed reaction (equation 7).[10] 3- and 4-Pyridylketene (**10b,c**) reacted similarly, but 2-pyridylketene (**10d**) formed an intermediate that decayed with an amine-catalyzed rate constant that was slower than those of **10a–c** by factors near 10^7.[13] This was determined to be the intramolecularly hydrogen-bonded amide 2-methylene-1,2-dihydropyridine **13** (equation 8) on the basis of the long, wavelength UV absorption similar to that of the model compound **14**,[14] and not that of the amide enol **11d**,[13,14] which would have a different UV spectrum. Calculations using DFT methods indicated the dihydropyridine **13** to be 3.5 kcal/mol more stable than the amide enol **11d**, which in turn was 17 kcal/mol more stable than the structure **11e** without the intramolecular hydrogen bond.[14]



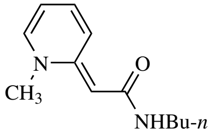
(7)

10 Ar = Ph (**a**), 3-Py (**b**). 4-Py (**c**) **11** **12**



(8)

10d **13**



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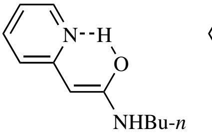
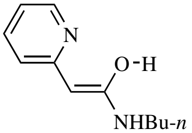
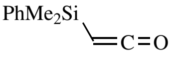


11d



11e

Kinetic studies of the less reactive ketene $\mathrm{PhMe_2SiCH{=}C{=}O}$ (**15**) in $\mathrm{CH_3CN}$ showed that this followed the rate equation 9, with second- and third-order terms in [amine] and a very large dependence of rate on the amine basicity.[15] Thus, for $\mathrm{PhMe_2SiCH{=}C{=}O}$ the rate ratio $k_{\mathrm{obs}}^{n\text{-}\mathrm{BuNH_2}}/k_{\mathrm{obs}}^{\mathrm{CF_3CH_2NH_2}}$ at 0.02^3 M amine was 10^7 ($\mathrm{p}K_{\mathrm{BH}}{}^{+}$ values for n-$\mathrm{BuNH_2}$and $\mathrm{CF_3CH_2NH_2}$ are 10 and 5, respectively).[15] The ketene t-BuC(Pr-i)=C=O (**16**) was very unreactive, and gave a rate constant for amination in neat n-$\mathrm{BuNH_2}$.[15]



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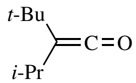


16

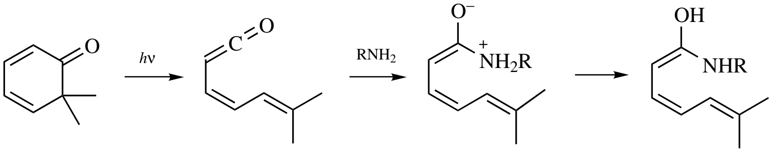
$$k_{\mathrm{obs}} = a[\mathrm{amine}]^2 + b[\mathrm{amine}]^3 \qquad (9)$$

These kinetic results were interpreted in terms of a mechanism analogous to that found by the theoretical studies, with reversible formation of an amide enol from reaction of ketene with two amine molecules, followed by irreversible amide formation in steps catalyzed either by a third amine molecule (equation 10) or by a basic solvent (equation 11). The observation of only a first-order dependence on [amine] in earlier studies[7,10] that used more reactive ketenes as substrates was attributed to irreversibility of the initial ketene-amine reaction, so that the subsequent steps involving additional amine molecules did not affect the rate of ketene disappearance, although the amine-catalyzed conversion of long-lived but irreversibly formed intermediate was directly observed by TRIR spectroscopy.[10]

$$\text{ketene} + 2\ \text{amine} \rightleftharpoons \text{ketene} \bullet 2\ \text{amine} \longrightarrow \text{product} \qquad (10)$$

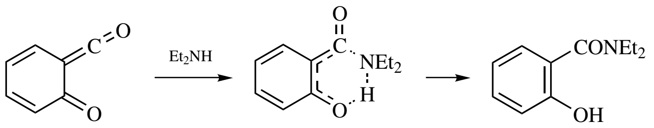
$$\text{ketene} \bullet 2\ \text{amine} \longrightarrow \text{product} \qquad (11)$$

The amination of dienylketene **18** formed by photolysis of cyclohexadienone **17** showed the consecutive formation of two distinct intermediates during the conversion of the ketene to the amide, as observed by UV, and this was interpreted as formation of an initial zwitterion **19**, which then formed an amide enol **20** (equation 12).[16] Long-lived zwitterionic species have been observed to form from ketenes and tertiary amines (vide infra), although in calculations of gas-phase structures, such zwitterions with hydrogens on the nitrogen atoms are not energy minima and only amide enol structures have been found as minima.[1] In studies by IR only one intermediate between the ketene and the amide has been detected, and whether or not zwitterions are involved as observable intermediates in aminations with primary and secondary amines is a subtle and unanswered question.



17 **18** **19** **20** (12)

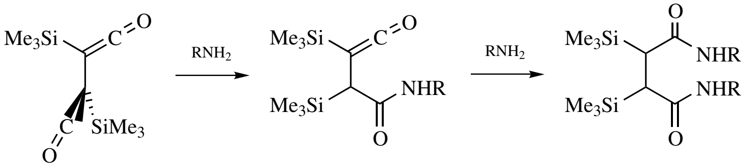
Amination of ketene **21** with Et$_2$NH gave a rate constant in CH$_3$CN at 25 °C of $k_2 = 1.2 \times 10^9\ \text{M}^{-1}\ \text{s}^{-1}$ or near the diffusion limit.[12] By analogy with theoretical studies of the reaction of **5** with H$_2$O and of O=CHCH=C=O with NH$_3$, this reaction may proceed through the cyclic transition state **22** and lead to a stable aromatic product. However, the ketene **30** (Table 5.15) has a comparably large amination rate constant[21] but would lead to an antiaromatic product by this mechanism.



21 **22** (13)

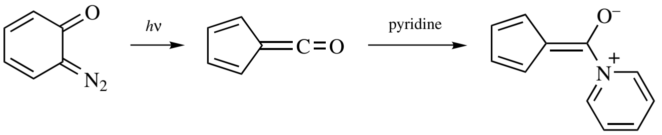
The 1,2-bisketene **23** reacted rapidly with amines, with high selectivity for initial formation of isolable ketenylamides **24**, which reacted with a second amine, in a step slower than the first by factors of nearly 10^4, to form the diasteriomeric succinamides **25** (equation 14).[19] The kinetics of the first step were also fit by equation 10, with terms in $[\text{amine}]^2$ and $[\text{amine}]^3$. Reaction of the ketenylamide **24** with a different second amine gave mixed diamides, while reaction of **24** with MeOH gave a mixed ester amide. The latter reaction showed evidence for a rate enhancement and selectivity in formation of the diastereomeric product, indicating assistance by the amido function in enhancing the attack by MeOH.[19] For *n*-BuNH$_2$, addition to

24 (R = *n*-Bu) showed the absence of a higher-order term in *n*-$BuNH_2$, also suggesting assistance by the carboxamido group.[19]



23 **24** **25** (14)

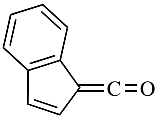
Tertiary amines such as pyridine reacted with ketenes including pentafulvenone (**26**), generated by photolysis of the diazo ketone in a matrix, forming zwitterionic species **27** that was directly observed by its IR absorption at 1683 cm^{-1} (equation 15).[18,20] Ketenes **28** and **29** gave similar behavior.[21] The kinetics of the reaction of ketenes with tertiary amines have also been measured,[10,11] with rate constants that are lower than those of comparable secondary amines by factors near 10^4.[10,11] These lower rate constants may reflect the absence of hydrogen-bonding interactions, as depicted in equation 1 for the tertiary amines, and also steric barriers with the more substituted nucleophiles. The kinetics of the reactions of **28**–**30** with both secondary and tertiary amines have been measured using laser flash photolysis with UV detection.[21]



(15)

26 (IR 2126 cm^{-1})

27 (IR 1683 cm^{-1})



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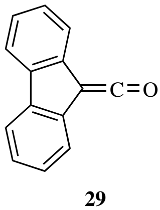

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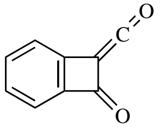
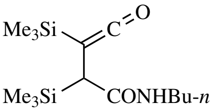
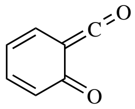
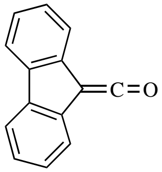
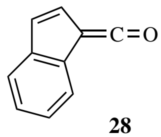
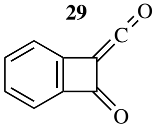


30

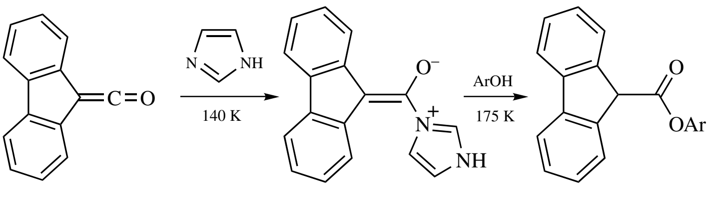
Comparative reactivity data for different ketenes with 0.1 M *n*-$BuNH_2$ are summarized in Table 5.16. In a previous consideration of the reactivity of $Ph_2C{=}C{=}O$ compared to $Me_2C{=}C{=}O$, it was suggested that the greater reactivity of the former arises from the ability of the aryl groups to stabilize developing negative charge in the (TS) for amination. This view has been criticized,[2] as the transition states leading to amide enols were evidently felt not to possess much charge separation. However, there is a difference in rate constants by a factor of 17 for 4-pyridylketene compared to 4-anisylketene, and $PhCH{=}C{=}O$ is 200 times more reactive than *t*-$BuCH{=}C{=}O$ (Table 5.16). These differences provide strong evidence for the importance of conjugative stabilization in the transition state for amination.

TABLE 5.16 Comparative Rate Constants (s^{-1}) for Reactions of Ketenes in CH_3CN with 0.1 M n-$BuNH_2$ (ca. 25 °C)[d]

	k (s^{-1})		k (s^{-1})
t-BuCH=C=O	1.6×10^5	$PhMe_2SiCH{=}C{=}O$	6.06×10^{3a}
PhCH=C=O	3.3×10^7	t-BuC(Pr-i)=C=O	4.57×10^{-3a}
$4\text{-}MeOC_6H_4CH{=}C{=}O$	2.2×10^7	$(Me_3SiC{=}C{=}O)_2$ (**7**)	4.1×10^{4b}
$4\text{-}O_2NC_6H_4CH{=}C{=}O$	1.1×10^8	$NCC_6H_4CH{=}C{=}O$	8.7×10^7
PhC≡CHCH=C=O	1.1×10^{8b}	$Ph_2C{=}C{=}O$	1.1×10^7
2-PyridylCH=C=O	2.2×10^7	3-PyridylCH=C=O	3.8×10^7
4-PyridylCH=C=O	3.7×10^8		
PhCH=CHCH=C=O	54.1×10^7		0.211^a
 **21**	1.1×10^{8b}	 **29**	7.6×10^{6c}
 **28**	1.0×10^8	 **30**	1.1×10^{8c}

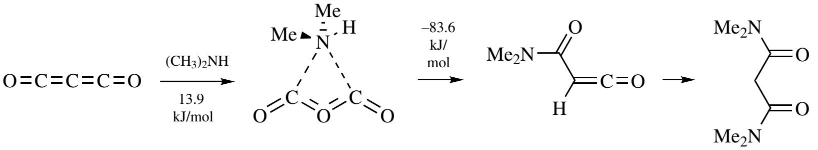
[a] Ref. 15.
[b] Ref. 10.
[c] Et_2NH, ref. 21.
[d] Data from Table 5.15

Ketene **29** was generated together with imidazole and a phenolic resin by photolysis of the diazo ketone on a thin film at 10 K and observed by the IR absorption at 2110 cm^{-1}.[22] Upon warming to 140 K, an absorption at 1635 cm^{-1} grew in and was assigned to the ylide **31**. At 175 K this began to be replaced by an absorption at 1750 cm^{-1} assigned to the ester **32** (equation 16).[22] In the absence of imidazole, reaction of the ketene with the phenolic resin was observed only at 250 K.[22]



29 IR 2110 cm^{-1} **31** **32** IR 1750 cm^{-1} (16)

Molecular complexes of C_3O_2 (**26**) with NH_3, $(CH_3)_2NH$, $(CH_3)_3N$, and 4-(dimethylamino)pyridine were observed, and were converted at 40 K to zwitterionic products.[23] Computations for the reaction with $(CH_3)_2NH$ showed formation of the complex **29** with a barrier of 13.0 kJ/mol that formed the ketene **30** in a step that was exothermic by 83.6 kJ/mol and led to tetramethyl malonamide (**31**, equation 17).[23]



(17)

26 **29** **30** **31**

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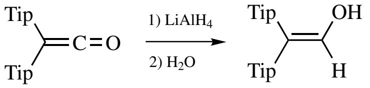
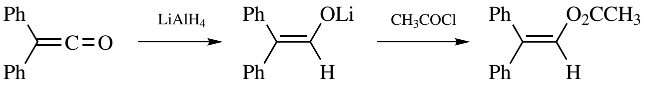
5.5.3 Nucleophilic Addition to Ketenes: Preparative Aspects

5.5.3.1 Hydride Reduction Ketenes have been found to be reduced by hydrides, although this reaction has been studied only occasionally. The reaction of bis(2,4,6-triisopropylphenyl)ketene ("ditipylketene," **1**) with $LiAlH_4$ gave the stable enol **2** (equation 1).[1] Reaction of diphenylketene (**3**) with $LiAlH_4$ formed the enolate **4**, which was acetylated with acetyl chloride, forming the vinyl ester **5** (equation 2).[2] Reduction with $LiBEt_3H$ of the ketene **7** formed in situ from **6** gave an enolate that was alkylated and reduced further to **8** (equation 3).[3,4]



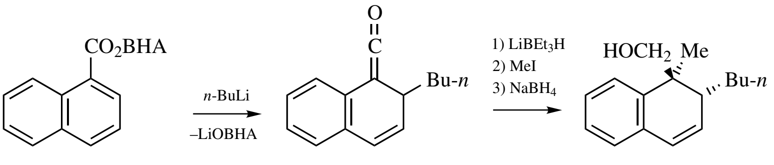
1 (Tip = 2,4,6-i-$Pr_3C_6H_2$) **2**

(1)



3 **4** **5**

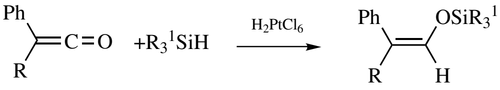
(2)



6 (BHA = 2,6-(t-$Bu)_2$-4-$MeOC_6H_2$) **7** **8** (75%)

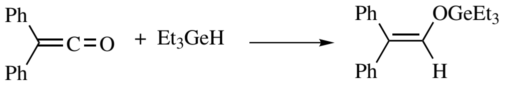
(3)

The reduction of ketenes by silanes,[5] germanes,[6] and stannanes[7] gave silyl, germyl, and stannyl enol ethers, respectively (equations 4–6). Hydrides of platinum and cobalt gave similar reactions.[7]



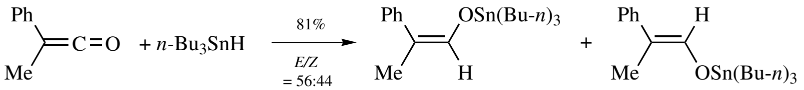
9 (R = Et, Ph, n-Pr, n-Bu) **10** (80%, R = Et, *E/Z* = 48:52)

(4)



(5)

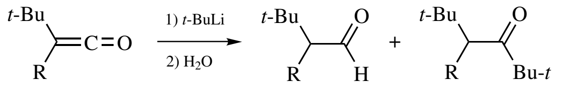
11 **12** (80%)



(6)

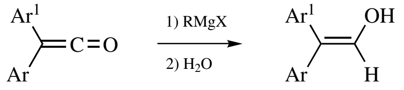
13 *Z*-**14** *E*-**14**

tert-Butyllithium and Grignard reagents reacted with crowded aliphatic ketenes **15** both by hydride donation forming aldehydes **16** and by alkyl group transfer forming ketones **17** (equation 7).[8,9] *tert*-Butyl and isopropyl Grignard reagents reacted with ketenes **18** containing bulky aryl groups by hydride transfer, giving stable enols **19** after hydrolysis (equation 8).[10,11]



(7)

15 (R = *t*-Bu, *i*-Pr) **16** **17**

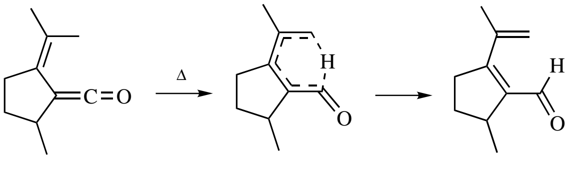


(8)

18 (Ar = Ph, Mes; Ar^1 = Mes, Duryl
R = *t*-BuLi, *i*-Pr)

19 (86%, Ar = Ar^1 = Mes,
R = *t*-Bu)

Intramolecular hydride transfer occurred upon thermolysis of ketene **20**, forming **21** (equation 9).[12] Other hydride reactions of ketenes are shown in Section 3.4.6.[13]



(9)

20 **21** (40%)

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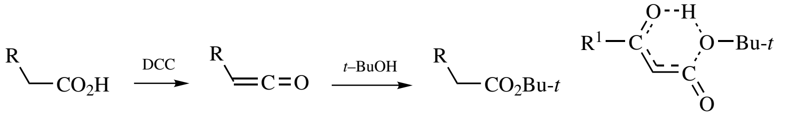
5.5.3.2 Reaction of Oxygen Nucleophiles with Ketenes Addition of oxygen nucleophiles is a characteristic reaction of ketenes. It plays a major role in the Arndt-Eistert chain elongation of carboxylic acids (Section 3.3) and has been extensively utilized in stereoselective additions to ketenes by either chiral alcohols or achiral alcohols with chiral catalysts (Section 5.9). The mechanism of ketene hydration has been actively pursued (Section 5.5.1).

Tricyclic pyridine bases catalyzed the addition of alcohols to ketenes, and enhanced the selectivity for acylation of primary alcohols in comparison to secondary alcohols[1–3] and for selective acylation of polyols.[4] The selectivities of ketenes generated by Wolff rearrangements for polyfunctional nucleophiles are noted in Section 3.3.1.

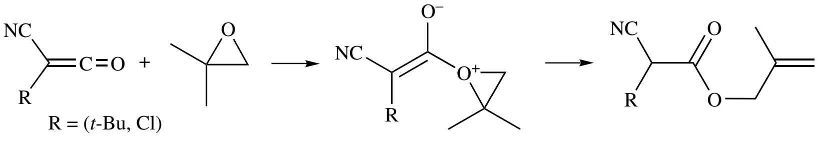
Ketenes **2** bearing conjugatively electron-withdrawing substituents generated from the reaction of carboxylic acids **1** with carbodiimides gave facile acylation of crowded alcohols (equation 1).[5] It was proposed that $EtO_2CCH{=}C{=}O$ (**2a**), $(EtO)_2(O)PCH{=}C{=}O$ (**2b**), and $EtO_2CC(Me){=}C{=}O$ (**2e**) reacted through a pseudopericyclic transition state, as in **4**, which was insensitive to the steric bulk of the alcohols.[5]



1 **2** **3** (75–100%) **4** (1)

R = EtO_2C (**a**); $(EtO_2O(P)$ (**b**), CN (**c**), 4-$TolSO_2$ (**d**)

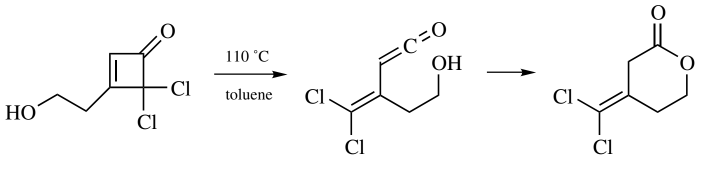
Reaction of cyanoketenes **5** with dimethyloxirane (**6**) gave allyl esters **8**, which were proposed to form by an ene-like reaction, (equation 2).[6]



R = (*t*-Bu, Cl)

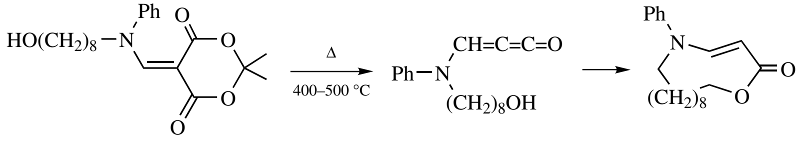
5 **6** **7** **8** (2)

Intramolecular additions of hydroxyl groups to ketenes have provided routes to a variety of lactones. Thus ring opening of dichlorocyclobutenone **9** formed vinylketene **10**, which cyclized to lactone **11** (equation 3).[7] Meldrum's acid derivative **12** formed ketene **13** at 400–500 °C, and this cyclized to **14** (equation 4).[8]



9 **10** **11** (67%)

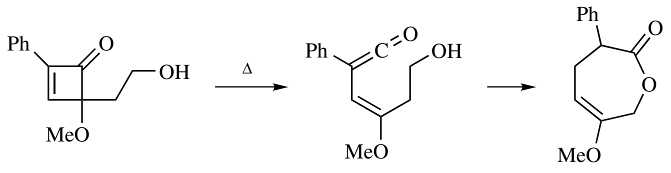
(3)



12 **13** **14** (75%)

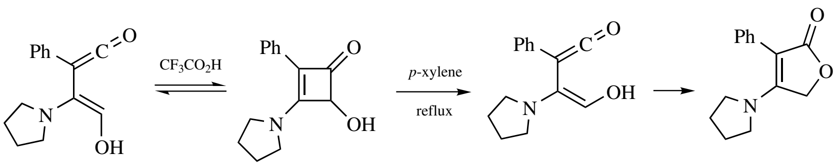
(4)

Ring opening of cyclobutenone **15** gave the vinylketene **16**, which cyclized to the lactone **17** (equation 5).[9] 4-Hydroxycyclobutenone **18** obtained from the corresponding cyclobutenedione by reduction with $NaBH_4$ was refluxed in *p*-xylene with 1.1 eq of CF_3CO_2H to form the intermediate ketene *E*-**19**, which cyclized to the lactone **20** (equation 6).[10] The acid catalyst increased the rate of reaction, which was proposed to be slowed by the favored but reversible ring opening of **18** to the *Z*-alkenylketene *Z*- **19**.[10] As noted in Section 3.4.1, electron donor substituents such as OH in **18** favor outward rotation of the substituent forming *Z*-**19**.[11]



15 **16** **17** (60%)

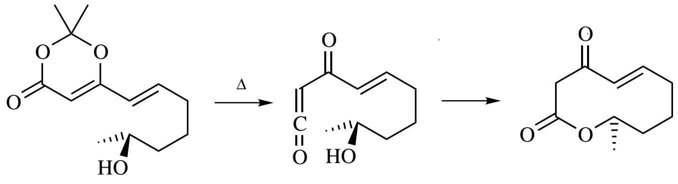
(5)



Z-**19** **18** *E*-**19** **20** (68%)

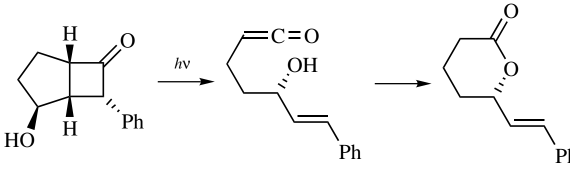
(6)

Thermolysis of the dioxinone **21** formed the acylketene **22**, which gave the lactone **23** (equation 7).[12] Photolysis of cyclobutanone **24** formed the ketene **25**, which cyclized to the lactone **26** (equation 8).[13] Photolysis of the chromium carbene complex **27** proceeded through the ketene **28** to lactone **29** (equation 9).[14]



21 **22** **23** (68%)

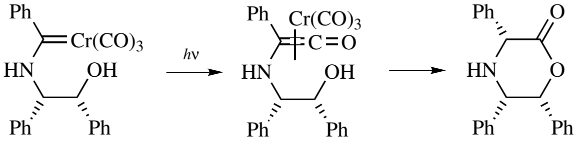
(7)



(89%)
E/Z 87:13

(8)

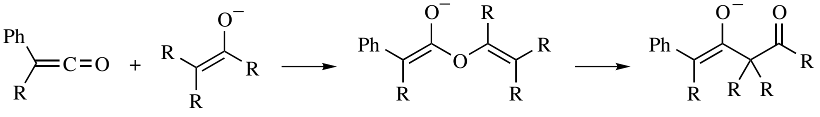
24 **25** **26**



(9)

27 **28** **29** (81%)

Arylketenes **30** reacted with enolates **31** with a kinetic preference for attack of the enolate oxygen, forming **32**, but on prolonged reaction these were then converted to the thermodynamically more stable products **33** of C-acylation which on hydration gave **34** and **35**, respectively (equations 10, 11).[15,16]



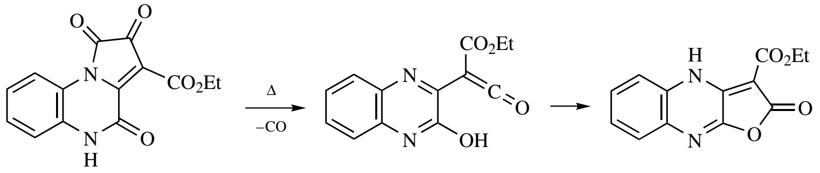
(10)

30 **31** **32** **33**

(11)

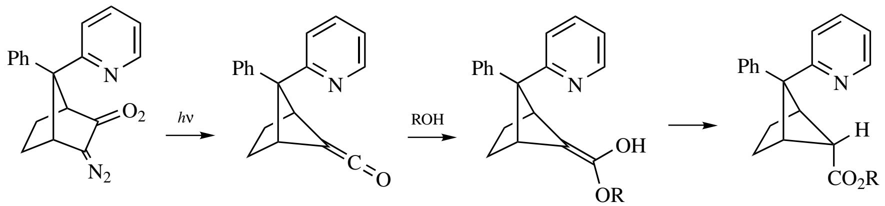
34 **35**

Thermolysis of **36** took place with decarbonylation to form the ketene **37**, which cyclized to **38** (equation 12).[17] Wolff rearrangement of diazo ketone **39** formed ketene **40**, which reacted with methanol or water, forming the enol **41**, which underwent protonation with a preference for forming **42** (equation 13).[18] The preference for proton delivery from the more hindered side with MeOH and H_2O was attributed to the smaller reagents assisting by hydrogen bonding to the pyridyl nitrogen.[18]



36 **37** **38**

(12)

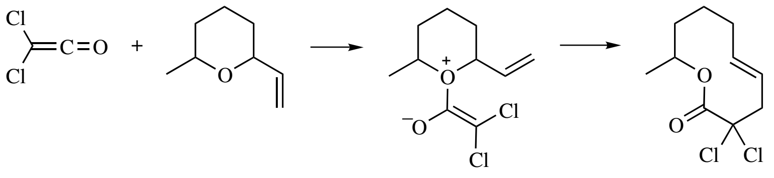


39 **40** **41** **42**

R = MeOH (89:11)
H_2O (92:8) *t*-BuOH (40:60)

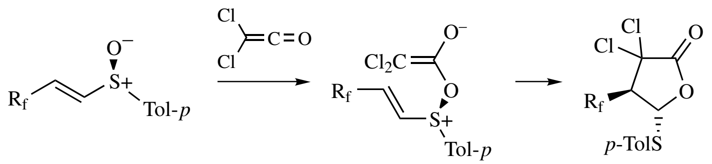
(13)

Dichloroketene **43** formed in situ by zinc dechlorination reacted with the allylic ether **44**, forming a zwitterionic intermediate that underwent [3,3] sigmatropic rearrangement to give the lactone **45** (equation 14).[19] Such addition of allylic ethers to ketenes forming zwitterionic species that rearranged by [3.3] sigmatropic rearrangement have been reviewed, and are referred to as the Bellus-Claisen or Malherbe-Bellus rearrangement.[20] Optically active sulfoxides **46** reacted similarly to give butyrolactones **47** in high enantiomeric purity (equation 15).[21]



43 **44** **45**
(55%)

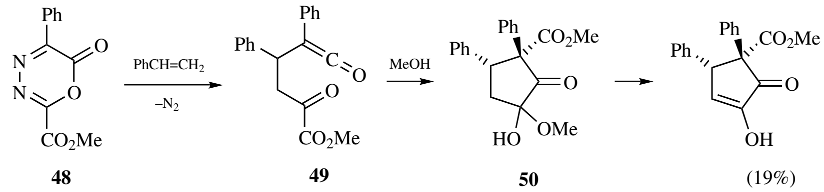
(14)



46 **47** (51%,
$R_f = CF_3$)

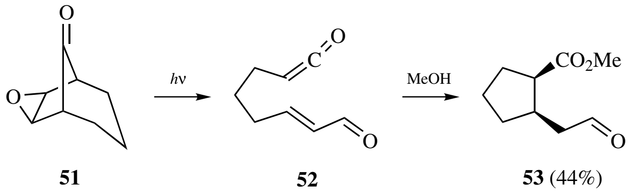
(15)

Diazine **48** reacted with styrene by a [4+2] cycloaddition followed by loss of nitrogen to give ketene **49**, and this was captured by methanol in a Dieckmann-like reaction giving **50** (equation 16).[22] Photolysis of **51** was proposed to give the ketene **52**, which added methanol with cyclization, forming **53** (equation 17).[23]



48 **49** **50** (19%)

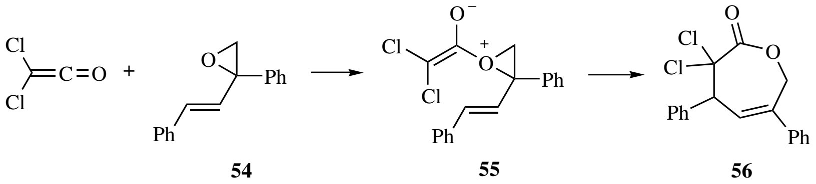
(16)



51 **52** **53** (44%)

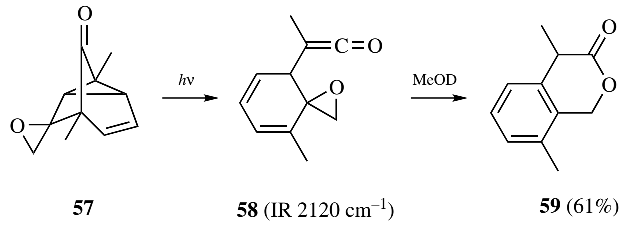
(17)

Dichloroketene reacted with the epoxide **54** via the zwitterion **55**, forming the caprolactone **56** (equation 18).[24] Photolysis of **57** formed the ketene **58**, identified by the IR band at 2120 cm^{-1}, and this cyclized to **59** without incorporation of deuterium from MeOD (equation 19).[25] The oxiranylketene **61** was similarly formed by photolysis of **60** and could be captured by MeOH, but in benzene gave the cyclization product **62** (equation 20).[26]



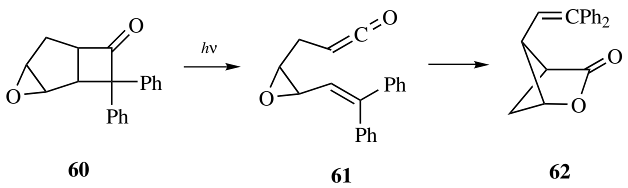
54 **55** **56**

(18)



57 **58** (IR 2120 cm^{-1}) **59** (61%)

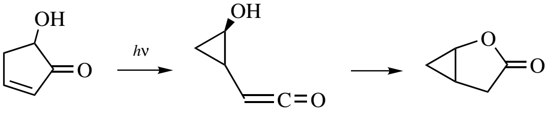
(19)



60 **61** **62**

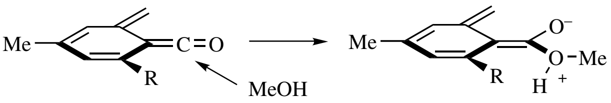
(20)

As noted in Section 3.4.2, photolysis of hydroxycyclopentenone **63** gave lactone **65** in low yield, and this was proposed to form from (hydroxycyclopropyl)ketene **64** (equation 21).[27] The ketene could not be trapped by CH_3OH, and it was proposed that the cyclization rate was faster than that of solvent attack.



63 **64** **65** (8%) (21)

The reactivity of ketenes **66** with MeOH (1 M in ether) was decreased by more than a factor of 10^3 for R = Me compared to R = H, which demonstrated steric retardation of in-plane by the oxygen nucleophile (equation 22).[28]



65 **65** (22)

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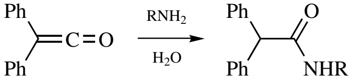
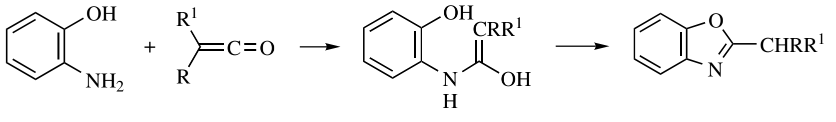
5.5.3.3 Reaction of Nitrogen Nucleophiles and Electrophiles with Ketenes Reaction with nitrogen nucleophiles, especially with amines, is a characteristic reaction of ketenes, with nucleophilic attack in the ketene plane on the carbonyl carbon. Various mechanistic and preparative aspects of these reactions are presented in Sections 4.1.4, 5.5.2, and 5.9. Imines typically react with ketenes by [2+2] cycloadditions, forming β-lactams in a valuable synthetic reaction (Section 5.4.1.7). Amines are much more reactive with ketenes than is H_2O, as illustrated by the reaction of diphenylketene generated by Wolff rearrangement, which reacted more readily with the amines in aqueous solution, although H_2O was present in much higher concentration (equation 1).[1]

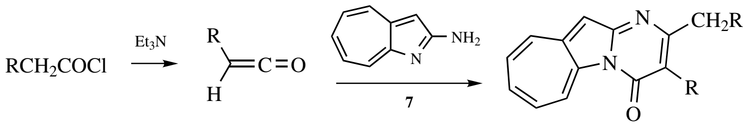


1 **2** (1)

Difunctional amines reacted with ketenes by several pathways. 2-Aminophenol (**3**) reacted with ketenes **4**, forming 2-substituted benzoxazoles **6**, evidently through the intermediate amide enols **5** (equation 2).[2] 2-Amino-1-azaazulene (**7**) reacted with two molecules of CHCl=C=O or PhCH=C=O (**8a,b**), generated in situ from the acid chlorides and Et_3N and gave fused heterocycles **9** (equation 3).[3] This reaction presumably involved initial acylation of the NH_2 group followed by reaction with a second molecule of **8**. Pyrido[1,2-a]pyrazines **10** reacted with in situ-generated ketenes **11**, forming **12**, with replacement of the imino group of **10** (equation 4).[4]



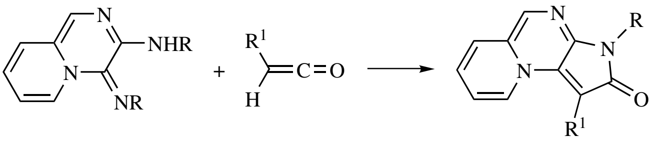
3 **4** **5** **6** (52–83%) (2)



8 (R = Ph, Cl)

9 (34%,
R = Cl)

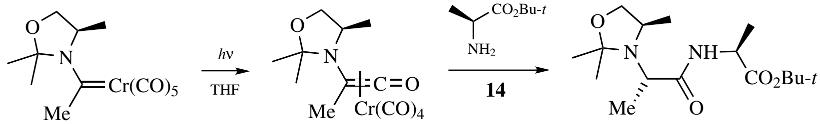
(3)



10 **11** **12**

(4)

Reaction of a chiral amino acid derivative **14** with a chromium-complexed ketene **13** formed **15** with some diastereoselectivity (equation 5).[5] Other examples of stereoselective reactions of ketene with amines are given in Section 5.9.

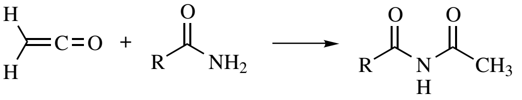


13

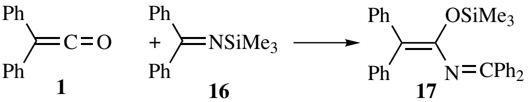
15 (80%, 82:18 *dr*)

(5)

Amides are acylated by reaction with ketene (equation 6).[6] Silylated imine **16** reacted with diphenylketene **1**, forming the *O*-silylated product **17** (equation 7),[7] and the silylated amine **18** gave the *C*-silylated product **19** with ketene (equation 8).[8] Reactions of PhCMe=C=O (**19a**) with $LiNMe_2$ and capture of the enolate with Me_3SiCl gave the silyl enol ethers **19b** in an *E/Z* ratio of 1.8:1 (equation 8a).[9]

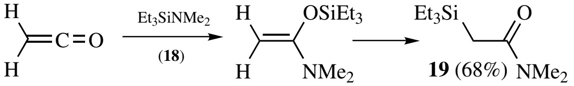


(6)



1 **16** **17**

(7)



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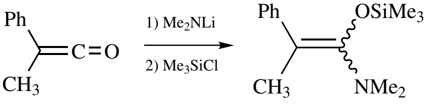
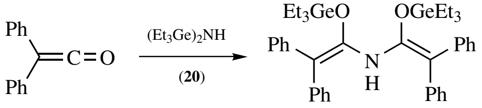


19a **19b**

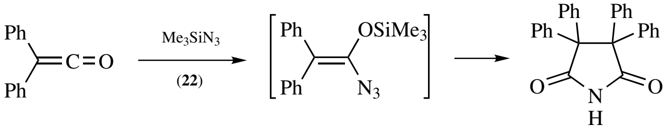
(8a)

The germylamine **20** reacted with two molecules of **1**, forming the *O*-germylated product **21** (equation 9),[10] and the silyated azide **22** formed **23** (equation 10).[11]



1 **21** (47%)

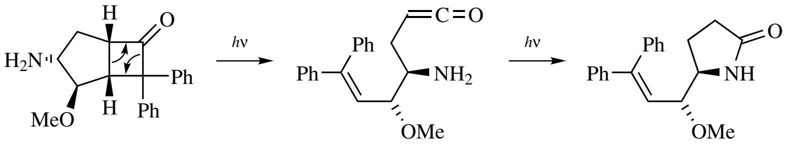
(9)



1 **23** (50%)

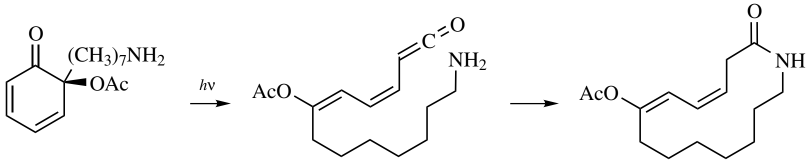
(10)

Intramolecular reactions of pendant amino groups with ketenes provided a route to lactams by the photolysis of the cyclobutanone **24**, forming ketene **25**, which cyclized to **26** (equation 11).[12] Photolysis of the cyclohexadienone **27** generated the ketene **28**, which formed the lactam **29** (equation 12).[13] The 2-carboxamidophenylketene **31** generated by Wolff rearrangement of **30** cyclized to **32** (equation 13.[14] Ketenes with pendant amino functions generated by thermolysis of alkynyl ethers gave efficient cyclization to macrocyclic lactams.[15]



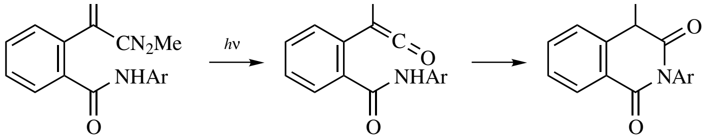
24 **25** **26**

(11)



27 **28** **29** (5–17%)

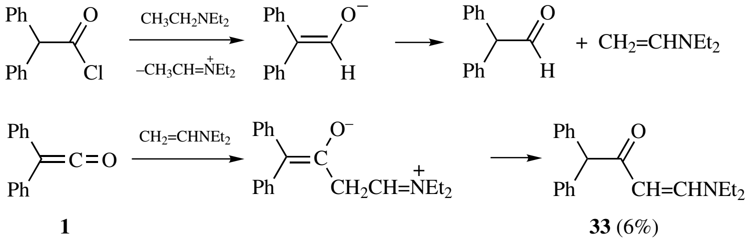
(12)



30 ($Ar = 4\text{-}O_2NC_6H_4$) **31** **32**

(13)

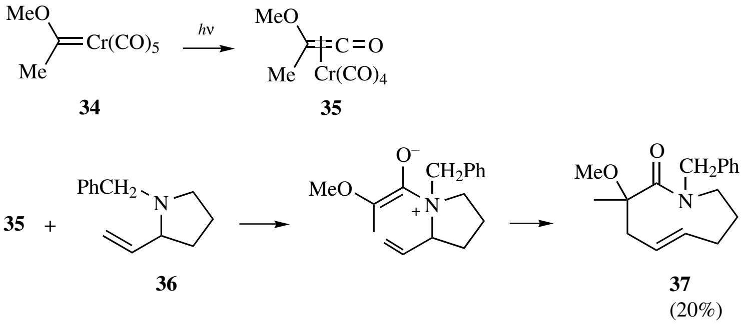
Tertiary amines react with ketenes by diverse pathways. In the preparation of diphenylketene (**1**) by reaction of $Ph_2CHCOCl$ and Et_3N under reflux a 6% yield



Scheme 5.4

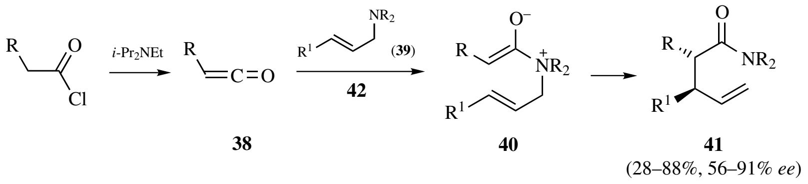
of the enone **33** was formed, which was suggested to arise from an initial hydride transfer from Et_3N to $Ph_2C{=}C{=}O$ (Scheme 5.4).[3]

Photolysis of chromium carbene complex **34** in the presence of tertiary allylic amines **36** was proposed to proceed by generation of the chromium complexed ketene **35**, which reacted with the amine, leading to a zwitterionic aza-Cope rearrangement to form the unsaturated lactam **37** (Scheme 5.5).[16]

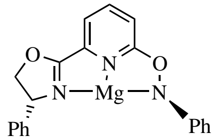


Scheme 5.5

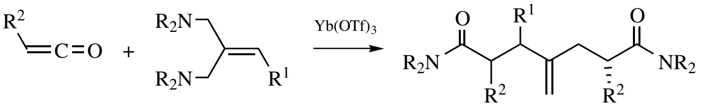
Ketenes **38** generated in situ from acyl chlorides and *i*-Pr_2NEt gave a Lewis acid–catalyzed reaction with allyl amines **39**, forming **41** through a route envisioned to proceed through **40** and a Claisen rearrangement (equation 14).[17] (cf. Section 5.5.3.2). The use of a chiral Lewis acid catalyst such as **42** in this process gave high enantioselectivity for formation of **41**.[18] The use of allyl diamines **43** in this sequence gave highly selective formation of diamides **44** (equation 15).[19]



(14)

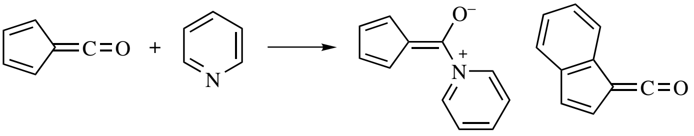


42

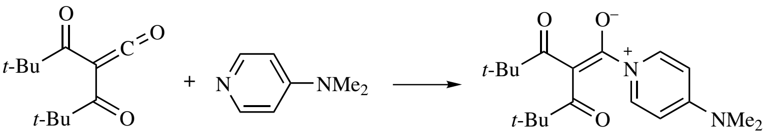


43 **44** (70–99%) (15)

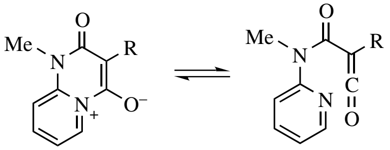
Pyridine reacted with ketenes including fulvenones **45a** and **45b** to form observable ylides **46** (cf. **91**, Section 4.9; equation 16, Section 5.5.2) (equation 16).[20] The structures and bonding in these species have been studied by theoretical means.[21] Bimolecular kinetics of the addition of pyridine to fulvenones in matrices forming complex **46** have been described by the methods of Kohlrausch kinetics.[22] 4-(Dimethylamino)pyridine (DMAP) was added to the acylketene **47**, forming zwitterion **48** as a yellow solid (equation 17).[23,24] Pyrido pyrimidinylium olates **49** were prepared and characterized, and were proposed to react through their acyl-ketene forms **50** (equation 18).[25,26]



45a **46** **45b** (16)

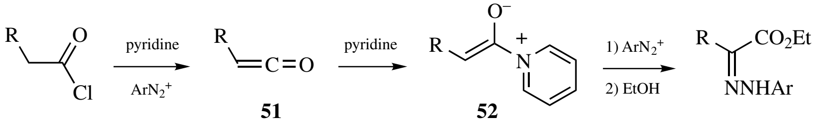


47 **48** (77–85%) (17)



49 **50** (18)

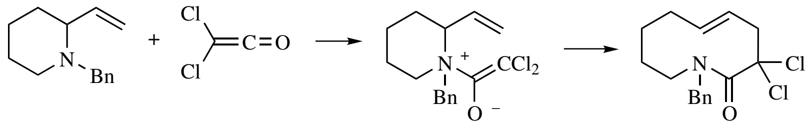
Reaction of acyl chlorides with pyridine and diazonium salts was proposed to proceed by formation of ketenes **51** with formed ylides **52** by nucleophilic attack by pyridine (equation 19).[27] This was followed by electrophilic attack of aryldiazonium ions with **52** to form hydrazones (equation 19).[27]



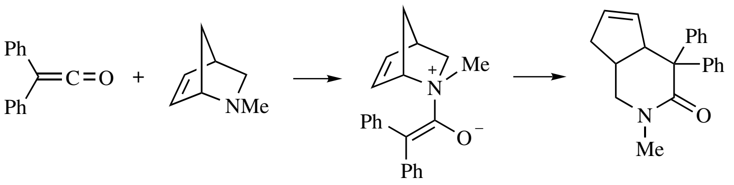
51 **52** (19)

R = n–$C_{14}H_{29}$, $PhCH_2$,
$(CH_2)_8CH{=}CH_2$, i–Pr, CH_2CH_2Cl

Reaction of the tertiary allylamine **53** with dichloroketene gave a zwitterionic intermediate **54**, which then rearranged to the azacyclodecane **55** (equation 20).[28] In a similar reaction, diphenylketene **1** reacted with **56** through the proposed intermediate **57** to form **58** (equation 21).[29,30]

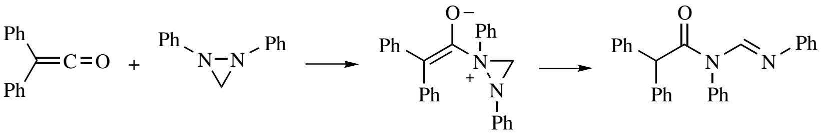


53 **54** **55** (96%) (20)



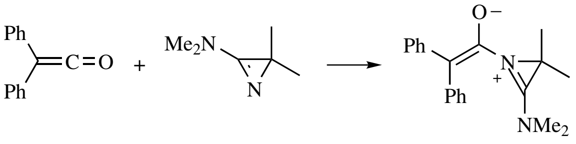
1 **56** **57** **58** (53%) (21)

Diazarane **59** reacted with diphenylketene through the intermediacy of **60** to form **61** (equation 22),[31] while azirene **62** gave **63** (equation 23), leading to **64**–**67** (equation 24).[32] Azirene **69** reacted with *tert*-butyl(isopropyl)ketene (**68**) to form **70**, which gave **71** (equation 25).[32]

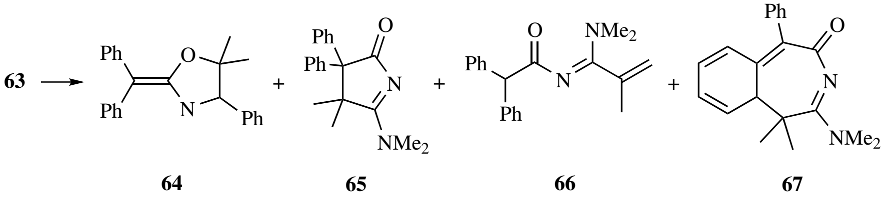


1 **59** **60** **61**

(22)



1 **62** **63** (23)



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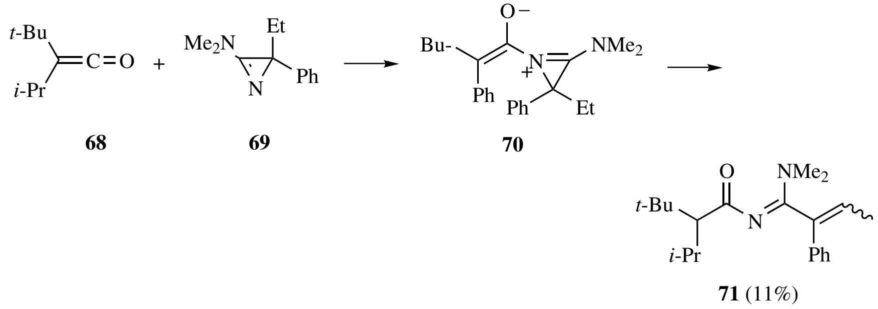
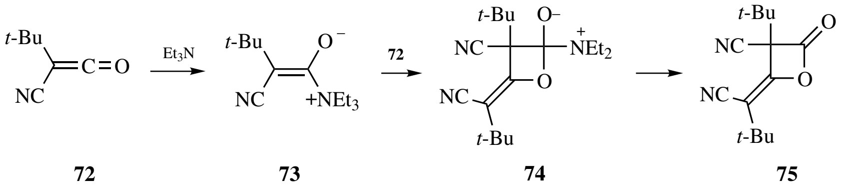
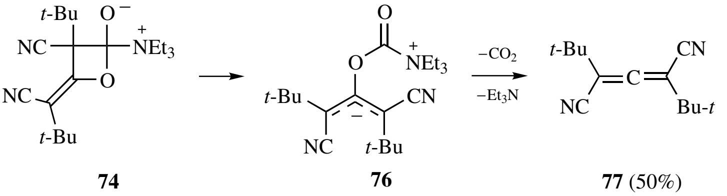


(25)

Dimerization of *tert*-butyl(cyano)ketene **72** did not occur thermally, but 0.1 equivalent of Et_3N catalyzed formation of the dimer **75** through the intermediacy of zwitterion **73** (equation 26).[33] The allene **77** was also formed, and could result from conversion of **74** to **76** followed by decarboxylation (equation 27).[33]

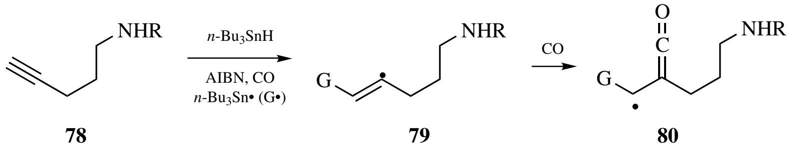


(26)

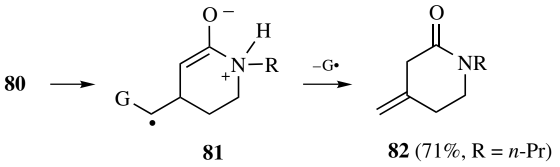


(27)

An unusual amine cyclization occurred with the ketenyl radicals **79** generated from ω-amino terminal alkynes **78** by free radical carbonylation (equation 28).[34] The reaction proceeded through addition of the radical n-$Bu_3Sn\bullet$ (G•) to the alkyne forming **79**, which combined with CO to form **80**. This cyclized to **81**, which underwent partial destannylation, possibly with hydrogen atom transfer from an intermediate lactam enol (equation 29).



(28)



(29)

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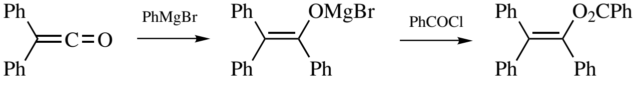
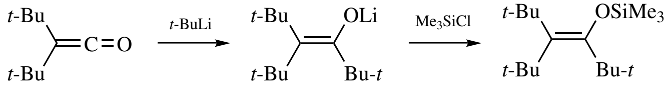
5.5.3.4 Carbon and Silicon Nucleophiles The addition of Grignard reagents to ketenes was demonstrated by Staudinger in 1907,[1] and it was then shown by Gilman and Heckert that the enolate **2** formed by addition of phenylmagnesium bromide to diphenylketene (**1**) could be trapped as the enol ester **3** (equation 1).[2]



1 **2** **3** (1)

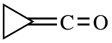
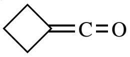
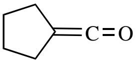
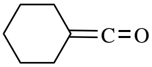
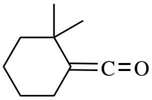
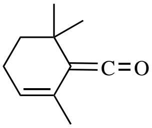
Surveys of the reactions of ketenes with Grignard reagents[3] and organolithium reagents[4] have been presented, and reactions of ketenes with organolithium reagents are summarized in Table 5.17.[5–11]

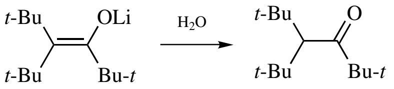
Di-*tert*-butylketene (**4**) is crowded and unreactive, but addition of *tert*-butyllithium formed the enolate **5**, which reacted with Me_3SiCl and gave the silyl enol ether **6** (equation 2), and with water formed the ketone **7** (equation 3).[12] Efforts to enolize the ketone **7** were unsuccessful, so the ketene addition route was the only proven way to form **6**.[12]



4 **5** **6** (2)

TABLE 5.17 Ketene Reactions with Organolithium Reagents

Ketene	RLi	Ref
$EtMeC{=}C{=}O$	$MeLi$, $PhCH_2Li$	8
i-$PrMeC{=}C{=}O$	$MeLi$, n-$BuLi$, $PhCH_2Li$	8
t-$BuMeC{=}C{=}O$	$MeLi$, n-$BuLi$, $PhCH_2Li$	8
$Me_2C{=}C{=}O$	n-$BuLi$, $PhC{\equiv}CLi$	8
$Et_2C{=}C{=}O$	n-$BuLi$	8
t-$Bu_2C{=}C{=}O$	$PhLi$	7
t-$Bu_2C{=}C{=}O$	t-$BuLi$	12
	n-$BuLi$, $PhLi$, $PhCH_2Li$	8
	$PhCH_2Li$	8
	$PhCH_2Li$	8
	$PhCH_2Li$	8
$(Me_3M)_2C{=}C{=}O$ M= Si, Ge, Sn	$MeLi$, n-$BuLi$, $PhLi$	9, 10
$Mes_2C{=}C{=}O$	i-$PrLi$, t-$BuLi$	34
$PhMeC{=}C{=}O$	n-$BuLi$	5
$PhEtC{=}C{=}O$	n-$BuLi$	5
$Ph(i\text{-}Pr)C{=}C{=}O$	n-$BuLi$, t-$BuLi$	6
$Ph(t\text{-}Bu)C{=}C{=}O$	n-$BuLi$, t-$BuLi$	6
	$PhLi$	5
	$PhLi$	11

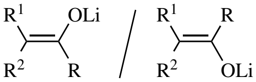
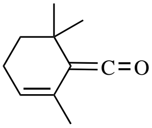


5 **7** (3)

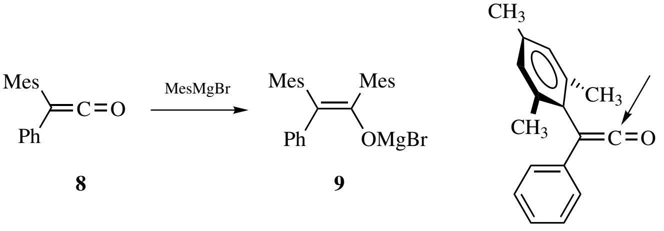
Reactions of unsymmetrical disubstituted ketenes with organometallic reagents showed a preference for attack of the nucleophile from the least hindered side of the ketene, as summarized in Table 5.18.

In the addition of MesMgBr to mesitylphenylketene **8** there was a 3:1 preference for attack on the side of the mesityl group of the ketene forming **9**, a result ascribed to the adoption of a conformation **8a** in which the mesityl was nearly perpendicular to the ketene plane, so approach to the carbonyl carbon in the ketene plane from this

TABLE 5.18 Stereoselectivity in Addition of Organometallic Reagents to Ketenes $R^1R^2C{=}C{=}O$

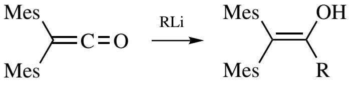
R^1	R^2	RLi		Ref
t-Bu	H	*t*-BuLi	>(95/5)	5
Et	Me	MeLi	1.7/1	7
i-Pr	Me	MeLi	7.0/1	7
t-Bu	Me	MeLi	>(99/1)	7
t-Bu	*i*-Pr	*t*-BuLi	>(95/5)	6
Ph	Me	*n*-BuLi	>(95/5)	5
Ph	Et	*n*-BuLi	>(95/5)	5
Ph	Et	Me_3SiLi	>(95/5)	6
Ph	*i*-Pr	*t*-BuLi	1/4	6
Ph	*t*-Bu	*t*-BuLi	>(5/95)	6
Ph	*c*-Pr	*n*-BuLi	79/21	6
Ph	*c*-Pr	*t*-BuLi	9/91	6
Ph	*c*-Pn	*n*-BuLi	88/12	6
Ph	*c*-Hx	*n*-BuLi	56/44	6
		$CH_2{=}CHCH_2MgCl$	9/1	11
Et	Me_3Si	*n*-BuLi	>(5/95)	5
Et	Me_3Si	$CH_2{=}CHLi$	>(5/95)	5
Et	Me_3Si	$HC{\equiv}CLi$	>(5/95)	5

direction was less hindered (equation 4).[13] The transition state for this reaction was modeled by *ab initio* calculations.[13]



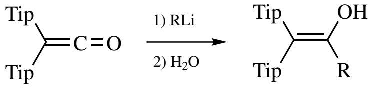
8 **9** **8a** (4)

Reactions of diarylketenes with highly substituted benzene rings gave stable enols, as in the example of dimesitylketene (**10**) forming **11** (equation 5).[14,15] Ditipylketene (**12**) reacted similarly with MeLi and *t*-BuLi to give the stable enols **13a** and **13b**, respectively (equation 6).[14] The reaction of dimesitylketene **10** with alkenyl- and alkynyllithium compounds formed dienols and yne-enols (equation 5) for studies of one-electron oxidation chemistry.[15]



10 **11**

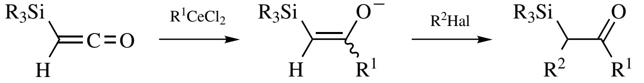
(5)



12 **13a,b** (R = Me, *t*-Bu)

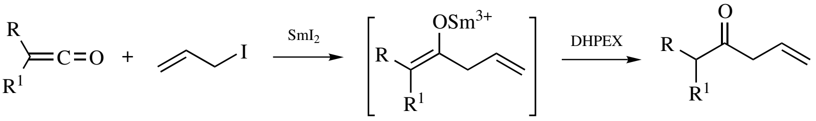
(6)

Organocerium reagents were added to silylketenes **14** to generate enolate anions **15**, which reacted with NH_4Cl or alkyl halides to give α-silylketones **16** (equation 7).[16,17] Samarium iodide–promoted addition of allyl iodide to unsymmetrical disubstituted ketenes **17** gave enolates **18**, which were protonated enantioselectively with a chiral alcohol to ketones **19** (equation 8).[18,19]



14 **15** **16** (10–99%)

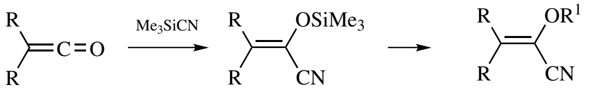
(7)



17 **18** **19** (21–79%)

(8)

The reaction of Me_3SiCN with ketenes **1**, **20**, and **21** was proposed to take place by a $[\pi_2{+}\pi_2{+}\sigma_2]$ cycloaddition forming silyl enol ethers **22**, which were converted to the corresponding enol sulfonates, carboxylates, or phosphates (equation 9).[20] *tert*-Butylisocyanide reacted with diphenylketene (**1**), forming the intermediate **23**, which gave **24** (equation 10).[21]

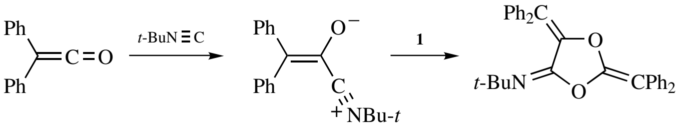


R = Ph (**1**), H (**20**), Me (**21**)

22

$R^1 = R^2SO_2, R^2CO,$
$(EtO)_2PO$ (22–91%)

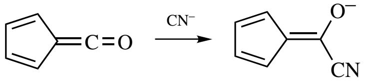
(9)



1 **23** **24** (88%)

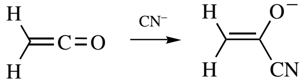
(10)

The kinetics of addition of cyanide ion to pentafulvenone (**25**) in aqueous NaOH were measured, with a rate constant at 24 °C $k(\mathrm{CN}^-) = 1.6 \times 10^8\ \mathrm{s}^{-1}\ \mathrm{M}^{-1}$, which was three times greater than the corresponding rate constant for reaction with OH^- (equation 11).[22] However, the product of the reaction could not be isolated.[22] *Ab initio* computations at the MP2/6-31+G*//MP2/6-31+G* level for the attack of cyanide anion on the ketenes **20** and **28–30** show that in all cases the product enolates from in-plane attack leading are favored over those from perpendicular attack and also have lower barriers for reaction (equations 12–15).[23] In the case of **30** the barrier for perpendicular attack was only 2.8 kcal/mol higher than for in-plane attack, and this was suggested to be due to some incipient aromatic stabilization in the transition state.[23]



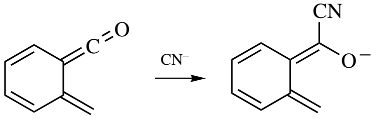
25 **26**

(11)



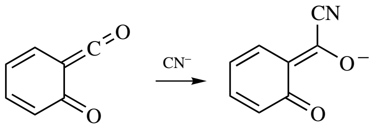
20 **27**

(12)



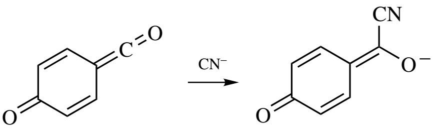
28

(13)



29

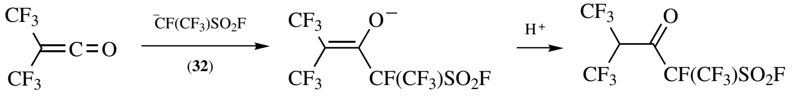
(14)



30

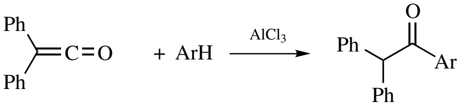
(15)

Addition of the fluoro carbanion **32** to bis(trifluoromethyl)ketene **31** resulted in formation of the ketone **34** (equation 16).[24] Friedel-Crafts reaction of diphenylketene (**1**) was induced by aluminum chloride, forming **35** (equation 17),[25,26] and **1** added to furan **36** without catalyst (equation 18).[27]

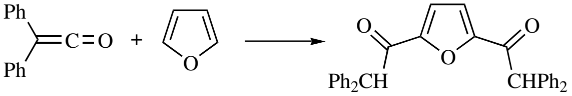


31 **33** **34** (57%)

(16)

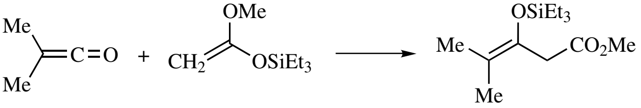


1 **35** (17)

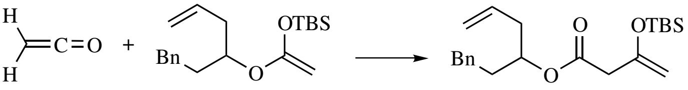


1 **36** **37** (18)

Ketene acetal **38** added to dimethylketene (**21**) formed the vinyl silyl ether **39** (equation 19).[28] Ketene (**20**) generated by dehydrochlorination reacted with the ketene acetal **40** to form the silyl vinyl ether **41** in 98% yield (equation 20).[29] The product **41** was utilized for an oxonia-Cope Prins cyclization.[29] Enolates reacted with ketenes by initial attack on oxygen followed by rearrangement to the product of nucleophilic attack by carbon (equation 10, Section 5.5.3.2).

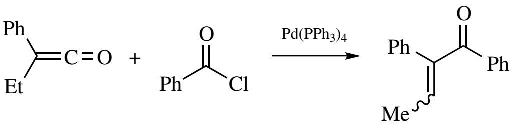


21 **38** **39** (85%) (19)

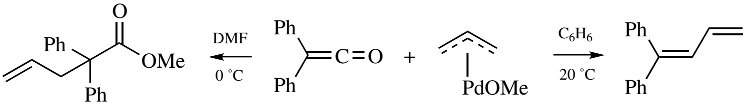


20 **40** **41** (98%) (20)

Phenylethylketene (**42**) reacted with aroyl chlorides in a reaction catalyzed by $Pd(PPh_3)_4$ with decarbonylation and bond formation at C_1 of the ketene, forming **43** (equation 21),[30] while diphenylketene (**1**) reacted with allylpalladium complex **44** with carbon-carbon bond formation at C_2 and either decarbonylation in benzene, forming **45**, or ester formation in DMF, forming **46** (equation 22).[31]



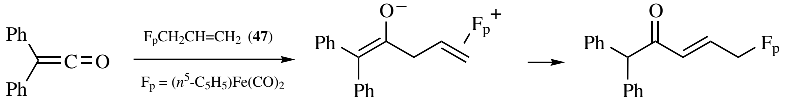
42 **43** (46%) (21)



46 **1** **44** **45** (72%) (22)

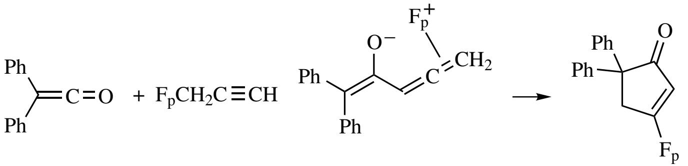
Allyl and propargyl iron complexes **47** and **50**, respectively, were interpreted as adding at C_1 of diphenylketene (equations 23, 24).[32,33] Reaction of $Ph_2C{=}C{=}O$

with diazoborole **53** gave complexes **54** (equation 25).[34]



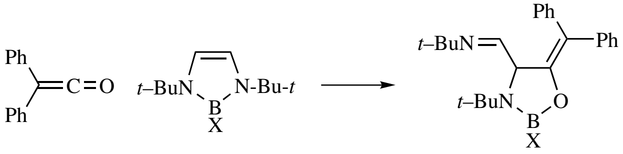
1 **48** **49**

(23)



1 **50** **51** **52**

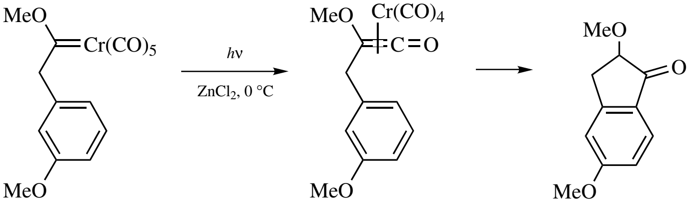
(24)



1 **53** **54**

(25)

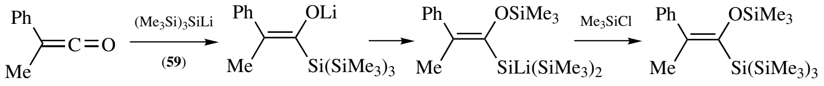
Chromium-complexed ketene **56** generated by photolysis of the chromium-carbene complex **55** underwent attack by the electron-rich aromatic side chain in an intramolecular Friedel-Crafts acylation (equation 26).[35]



55 **56** **57**

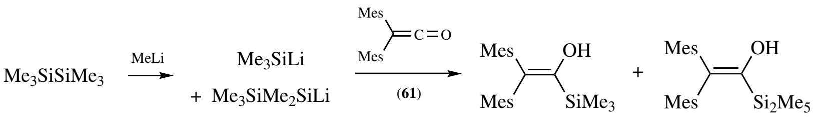
(26)

Tris(trimethylsilyl)silyllithium (**59**) reacted with PhCMe=C=O (**58**) to give the enol ether **60**, proposed to form by silyl exchange (equation 27).[36] The formation of **60a** was demonstrated by quenching experiments.[36] Reaction of **59** with $(Me_3Si)_2C{=}C{=}O$ gave the ynolate $Me_3SiC{\equiv}COLi$.[37] Reaction of hexamethyldisilane with MeLi formed both Me_3SiLi, and Me_3SiMe_2SiLi, and addition of this mixture to dimesitylketene (**61**) gave the enols **62** and **63** (equation 28).[37,38]



58 **60a** **60** (69%)

(27)



62 **63**

(28)

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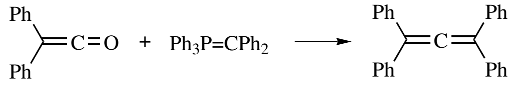
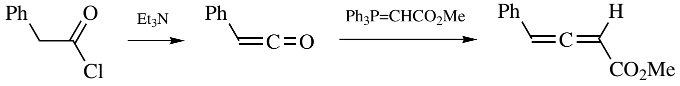
5.5.4 Wittig-Type Reactions

Diphenylketene (**1**) was found to react with the phosphorus ylide **2** to form tetraphenylallene (**3**) by Lüscher in the laboratory of Staudinger in 1922 (equation 1).[1,2] This reaction was later developed by Wittig and Haag,[3] and the Horner-Emmons reaction of carboethoxyphosphonium ylides was applied to ketenes generated in situ from acyl chlorides[4,5] for the reaction of phenylketene (**4**) forming **5** (equation 2), and *tert*-butylketene (**6**) forming **7** (equation 3).[6,7]



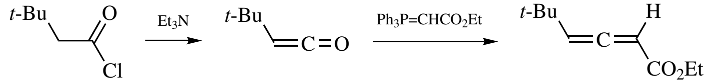
(1)

1 **2** **3**



(2)

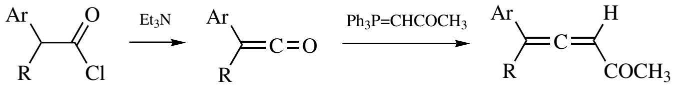
4 **5** (23%)



(3)

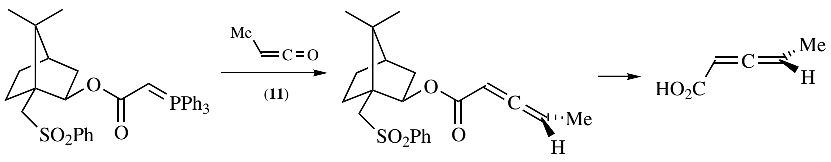
6 **7** (55%)

Allenyl ketones **9** were also prepared from arylketenes **8** by this method (equation 4).[8] Phosphorane **10** with a chiral auxiliary attached reacted with methylketene (**11**) for formation of chiral allene **12** (equation 5).[9]



(4)

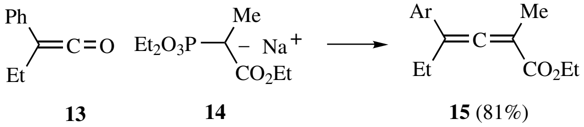
8 **9**



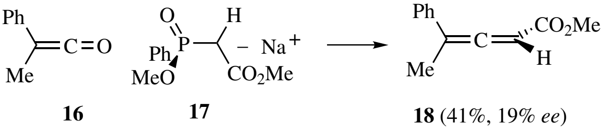
(5)

10 **12** (62%) **12**

Phosphonate anion **14** reacted with ketene **13** to form allene **15** (equation 6).[10–15] Ketene ($CH_2=C=O$) reacted with phosphonate anions to give terminal allenes.[17,18] Reaction of the optically active phosphinylacetate anion **17** with ketene **16** gave the enantiomerically enriched allene **18** (equation 7).[14]

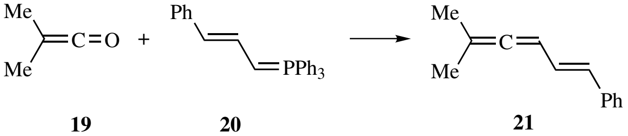


(6)

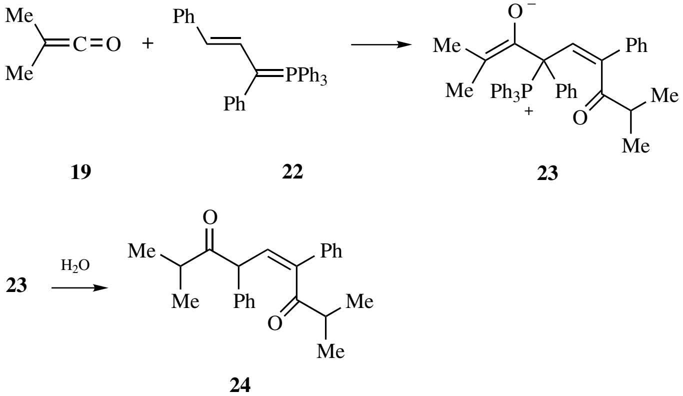


(7)

Vinyl phosphorane **20** reacted with dimethylketene **19** to give the vinylallene **21** (equation 8), but the α-phenyl analogue **22** reacted with two moles of **19** to form **24** after hydrolysis (equation 9).[19]

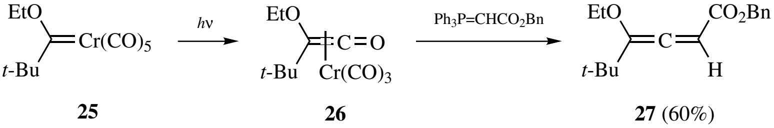


(8)



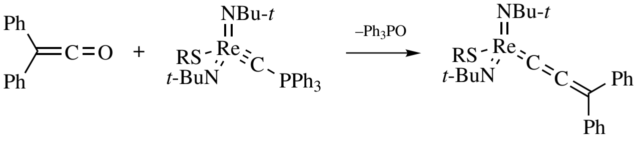
(9)

The chromium alkoxycarbene complex **25** upon photolysis gave the chromium-complexed ketene **26**, which gave a Wittig reaction forming allene **27** (equation 10).[20] In some cases the allenes formed in this way were not isolated but were hydrolyzed to the corresponding ketones.[20]



(10)

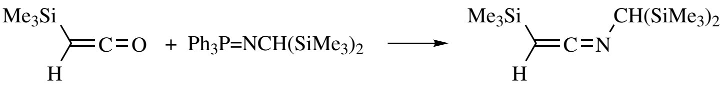
Wittig reaction of diphenylketene (**1**) with the phosphonioalkylidene rhenium (VII) complex **28** provided an expeditious route to the allenylidene rhenium (VII) complex **29** (equation 11).[21] The structure of **29** was confirmed by X-ray analysis.



1 **28** (R = 1-adamantyl) **29** (36%)

(11)

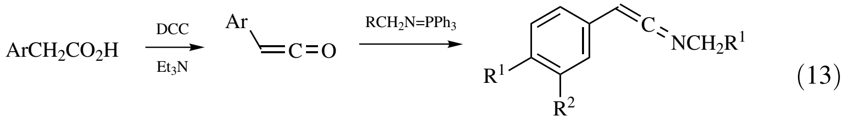
The reaction of ketenes with iminophosphoranes to give aza-Wittig reactions was discovered by Staudinger and Hauser[22] and has been used to prepare ketenimines.[23] This procedure was applied to the reaction of trimethylsilylketene (**30**) with bistrimethyliminophosphorane (**31**) and gave the ketenimine **32** (equation 12).[24] Diphenylketene gave a similar reaction.[24]



30 **31** **32** (56%)

(12)

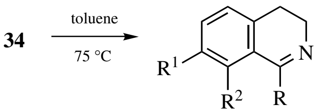
Arylketenes **33** generated by dehydration of phenylacetic acids with DCC/Et_3N in THF at 0 °C reacted with iminophosphoranes to give ketenimines **34** that underwent cyclization to dihydroisoquinolines **35** (equations 13, 14).[25] Pyrimidone **38** was obtained by the aza-Wittig reaction of PhCH=C=O (**4**) with **36**, with cyclization of the intermediate **37** (equation 15).[26]



Ar = $R^1R^2C_6H_3$

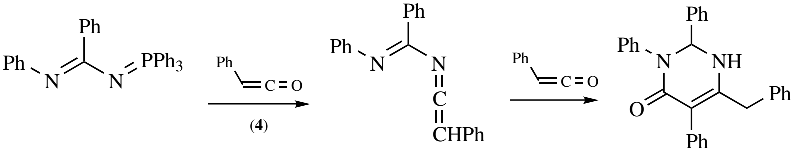
33 **34**

(13)



35 (24–78%)

(14)

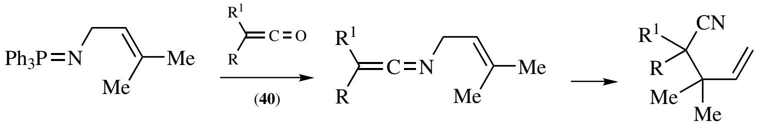


36 **37** **38** (71%)

(15)

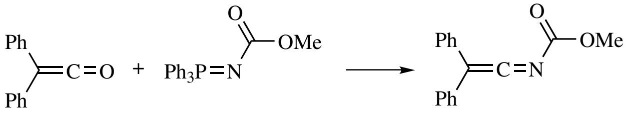
Allyliminophosphorane **39** reacted with ketenes **40**, forming ketenimines **41**, which gave aza-Claisen rearrangements to **42** (equation 16).[27] Diphenylketene

(**1**) reacted with the acyliminophosphorane **43** to form the acylketenimine **44** (equation 17).[28]



39 **41** **42** (41–60%)

(16)



1 **43** **44** (76%)

(17)

As discussed in Section 4.6, phosphaketene ylide $Ph_3P{=}C{=}C{=}O$ reacts with nucleophiles at the carbonyl carbon, forming reactive acyl Wittig reagents.

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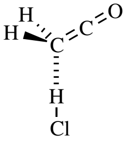
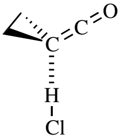
5.6 ELECTROPHILIC ADDITION TO KETONES

5.6.1 Protonation of Ketenes

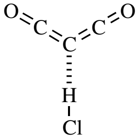
In agreement with the known electronic distribution of ketenes with negative charge at oxygen and C_2, complexes of HCl with $CH_2{=}C{=}O$ (**1a**), $(CH_2)_2C{=}C{=}O$ (ketenylidenecyclopropane, **1b**), and C_3O_2 (carbon suboxide, **1c**) have been characterized by FTIR matrix spectroscopy and *ab initio* calculations as T-shaped species involving electrophilic proton addition to C_2 of the ketene, as in **1a**–**c**.[1] For C_3O_2 a linear complex with hydrogen bonding to oxygen was calculated to be slightly more stable, but the observed spectra were more compatible with the T-structure **1c**.[1] Theoretical studies of the HCl and HF complexes were reported.[2] These complexes serve as models for proton addition to ketenes.



1a

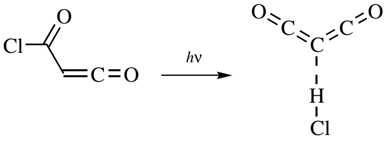


1b



1c

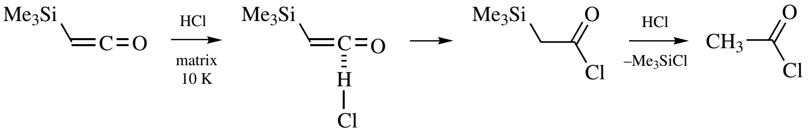
As noted in Section 3.2.2, photolyses of acetyl chloride and acetyl bromide in solid argon gave rise to IR spectra attributed to ketene complexes with HCl and HBr respectively.[3–5] While the HCl and HBr IR absorptions differed significantly from those of the monomers, the ketene IR was essentially unchanged. Complexes of HCl and C_3O_2 were prepared directly,[6] or by matrix photolysis of chlorocarbonylketene **2** forming **1c** (equation 1).[7] Studies of protonation of C_3O_2 are reported in Section 3.2.2.[8,9]



(1)

2 **1c**

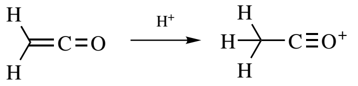
The addition of HCl to trimethylsilylketene in a matrix has been studied by IR, and shows formation of an initial complex **1b** with the ketene IR band shifted to 2110 cm^{-1}. Upon warming, this forms the addition product **1c**, and then cleavage of the C—Si bond and formation of acetyl chloride (equation 1a).[9a]



(1a)

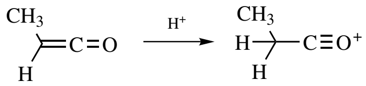
1a (IR 2120 cm^{-1}) **1b** (IR 2110 cm^{-1}) **1c** **1d**

As discussed in Section 1.1.2, gas phase protonation of ketene (**3**) and methylketene (**5**) has been extensively examined experimentally and theoretically and occurs on C_2, forming the acylium ions **4** and **6**, respectively, which are stabilized by π-electron donation from oxygen (equations 2, 3).[10–18] Protonation of ketenes RCH=C=O (R=NH_2, OH, and F) were also considered.[18a] The proton affinity of **3** is −195 kcal/mol (equation 2),[19] while that of **5** is −201 kcal/mol (equation 3).[20] The difference may be attributed to stabilization of **6** by the methyl group, but this difference is attenuated by the strong stabilization by oxygen.



(2)

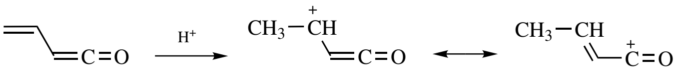
3 **4**



(3)

5 **6**

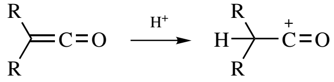
The energetics of the addition of hydrogen halides to CH_2=C=O (**3**) and Me_2C=C=O (**7**) to give C– and O—protonated ketene ion pairs were examined, and it was concluded that C-protonation was more favorable.[23] Calculations of the protonation of vinylketene (**8**) indicated that protonation at C_4 is favored by 15.8 kcal/mol relative to protonation at C_2 (equation 4).[24] The resulting ion **9** has an allylic resonance structure with acylium ion character.



(4)

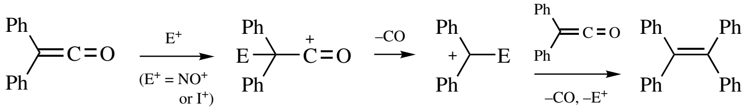
8 **9**

Protonation of diphenylketene (**10**) and di-*tert*-butylketene (**11**) in FSO_3H-SbF_5/SO_2ClF at −60 °C gave the corresponding acylium ions **12**, as detected by their ^{13}C NMR signals for CO^+ at δ 154.7 and 155.3, respectively (equation 5).[25] Reaction of Ph_2C=C=O (**11**) with $NOBF_4$ or I_2 led to the formation of Ph_2C=CPh_2, which may be attributed to decarbonylation of the acylium ion and reaction of the resulting cation **12a** with **10** (equation 5a).[25]



10 (R = Ph), **11** (R = *t*-Bu) **12**

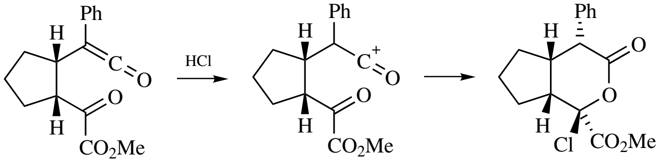
(5)



10 **12a**

(5a)

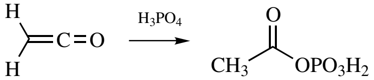
The γ-oxoketene **13** added HCl, leading to the δ-chloro-γ-lactone **15**, which resulted from protonation forming **14** or alternatively by protonation on oxygen followed by cyclization (equation 6).[26,27]



13 **14** **15** (33%)

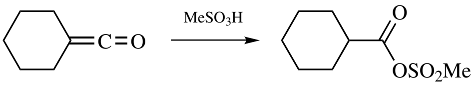
(6)

Addition of anhydrous acids to ketenes permitted the formation of mixed anhydrides, including acetyl dihydrogen phosphate **16**, from ketene (equation 7).[28] Addition of CH_3SO_3H to ketenylidenecyclohexane (**17**) gave the mixed anhydride **18** (equation 8).[29] Carboxylic acids also added to ketenes to give anhydrides.[30,31]



3 **16**

(7)

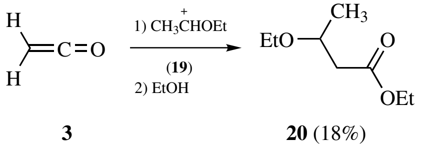


17 **18** (98%)

(8)

α-Alkoxy carbocations **19** generated from $CH_3CH(OAc)OEt$ and $ZnCl_2$ added to C_2 of ketene, forming **20** (equation 9).[32] Reactions of dichloroketene (**21**) with acetals **22** catalyzed by $ZnCl_2$ gave β-alkoxy esters **23** and were proposed to involve initial nucleophilic attack by the acetal oxgyen with Lewis acid activation of the ketene to give an enolate that combined with the carboxonium ion (equation 10).[33] Chiral 1,3-dioxolanes **24** reacted similarly with phenylketene (**25**) to form 1,4-dioxepan-5-ones **26** with high stereoselectivity (equation 11).[33] These reactions may alternatively be depicted as involving initial attack of carboxonium ions at C_2

of the ketene, but the low reactivity of the electron-poor dichloroketene makes this unlikely.



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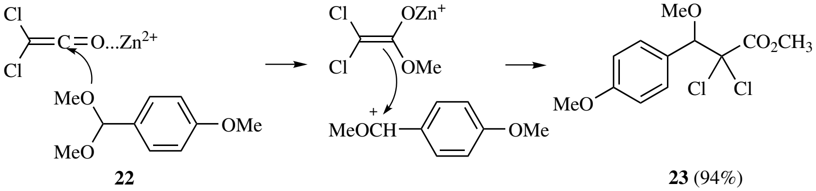

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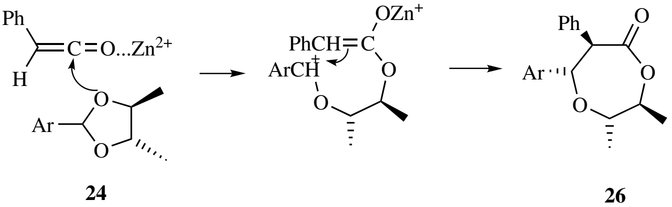
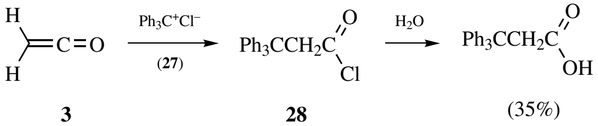


(11)

Triphenylmethyl cation **27** added to C_2 of ketene, forming **28** (equation 12).[34] The addition of **27** to diphenylketene (**11**) gave the acylium ion **29**, which formed the observed pentaphenylethyl cation **30** by decarbonylation (equation 13).[25]



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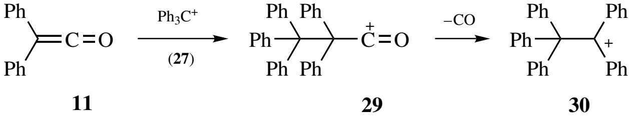
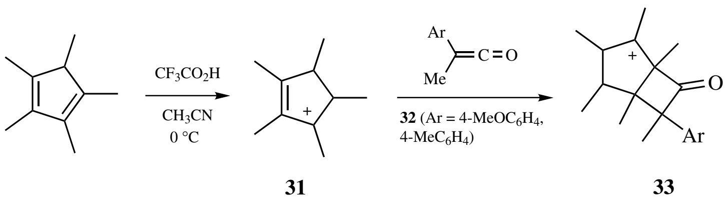
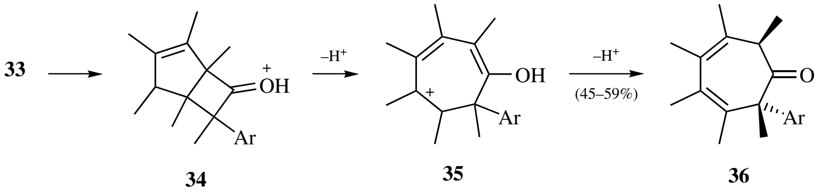


(13)

Carbocation **31** generated from protonation of pentamethylcyclopentadiene reacted with alkyl(aryl)ketenes **32** proposed to give a [2+2] cycloadduct **33** (equation 14), leading to formation of cycloheptenediones **36** (equation 15).[35]

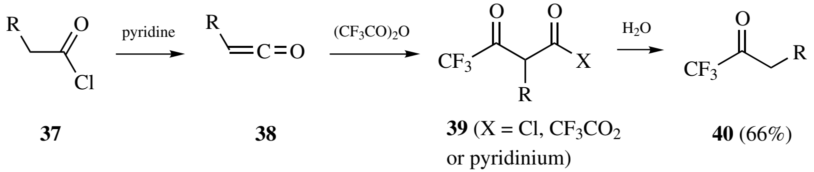


(14)



(15)

Reaction of acyl chlorides **37** with pyridine and trifluoroactic anhydride (TFAA) was proposed to involve formation of ketenes **38** that underwent electrophilic attack by TFAA to give β-trifluoroacetylacetic acid derivatives **39** that decarboxylated, forming trifluoromethyl ketones **40** (equation 16).[36] Addition of MeOH trapped **38** as the esters. Quenching of the reactions with dienophiles led to formation of heterocycles **42** that evidently result from cycloaddition reactions of intermediate acylketenes **41** formed by elimination from **39** (equation 17).[36–38]



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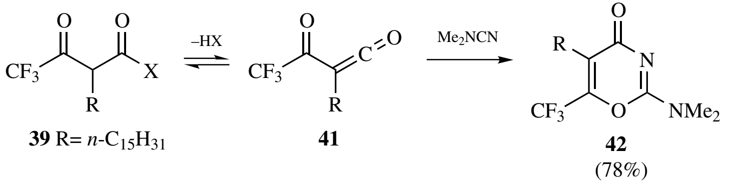
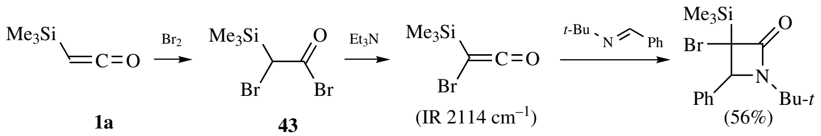
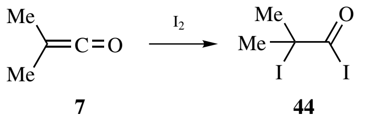


(17)

Halogens and analogous reagents add readily to ketenes; for example, the addition of bromine to trimethylsilylketene (**1a**) formed **43**, which was dehydrobrominated to the bromoketene that was identified by IR but could not be isolated, but was trapped by imine [2+2] cycloaddition (equation 18).[39] Iodine added similarly to dimethylketene (**7**, equation 19).[40] Rate constants for the latter reaction and for bromination of $Ph_2C{=}C{=}O$ (**10**) have been reported,[40] as well as for bromination of some silylated ketenes (Section 4.5).

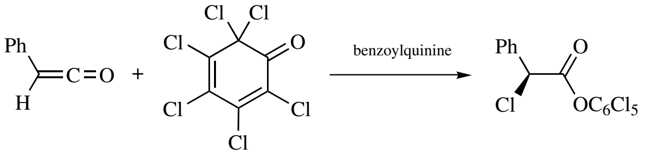


(18)



(19)

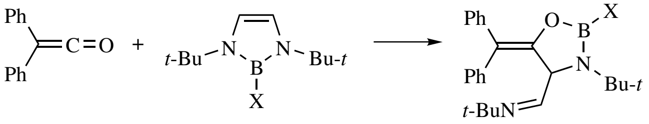
Phenylketene (**25**) was generated in toluene by dehydrochlorination, and reacted with hexachlorocyclohexadienone **45** as a mild chlorinating agent and with benzoylquinine as a chiral catalyst to give stereoselective formation of the α-chloro ester **46** (equation 20).[41–43a]



(20)

25 **45** **46** (63%, 95% *ee*)

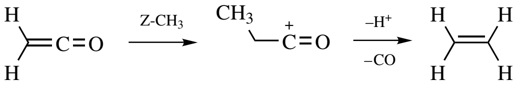
Hydroboration of ketene in the gas phase produced a product with the mass of a 1:1 addition compound, and an adduct with the structure $H_2BCH_2CH{=}O$ was proposed, possibly with some coordination between boron and oxygen.[44] Diphenylketene (**11**) reacted with 1,3-di-*tert*-butyl-2,3-dihydro-1*H*-1,3,2-diazaboroles **47** to form 1,3,2-oxaazaborolidines **48** in a reaction proposed to be initiated by boron attack at the ketenyl oxygen (equation 21).[45]



(21)

11 **47** **48**

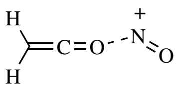
Transfer of a methyl cation derived from methanol to ketene has been proposed as a step in the zeolite-promoted methanol to gasoline (MTG) conversion (equation 22).[46]



(22)

3

The rate constant for ketene protonation in the gas phase has been calculated,[47] and the structure of the nitosonium adduct with ketene (**49**) was determined by computation.[48]



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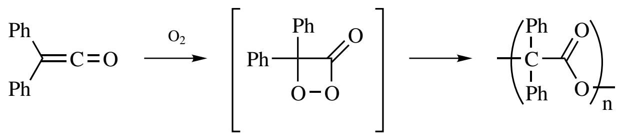
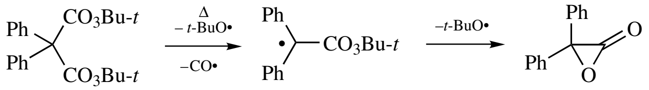
5.6.2 Oxygenation of Ketenes

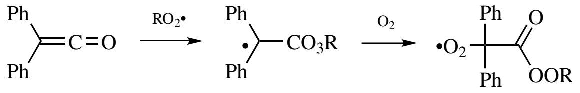
Diphenylketene (**1**) was observed to react with oxygen when it was first prepared, and was found by Staudinger et al. in 1925 to form a polyester product **3**, which was proposed to arise from an initial cyclic peroxide **2** (equation 1).[1] Later study showed that the same product was formed from the bis(perester) **4**, which was proposed to form the radical **5**, which cyclized to the α-lactone **6** (equation 2).[2] It was suggested that the conversion of **1** to **3** also proceeded through **6**, which formed as shown in equations 3 and 4.[2]



1 **2** **3** (1)

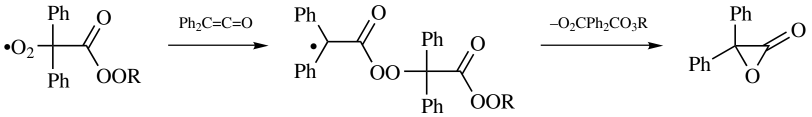


4 **5** **6** (2)



1 **5** **7**

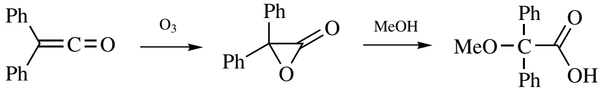
(3)



7 **8** **6**

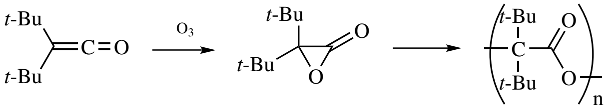
(4)

The reaction of **1** with ozone at −78 °C also gave **3**, and this reaction was also interpreted as proceeding through the α-lactone **6**, which could be captured by reaction with MeOH as the α-methoxy acid **9** (equation 5).[3] Addition of ozone to di-*tert*-butylketene (**10**) gave the α-lactone **11**, which was identified by its ^{1}H NMR spectrum at −60 °C and which formed the polymer **12** on warming (equation 6).[3]



1 **6** **9** (60%)

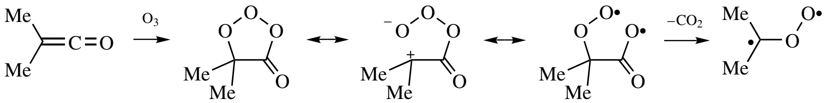
(5)



10 **11** **12** (91%)

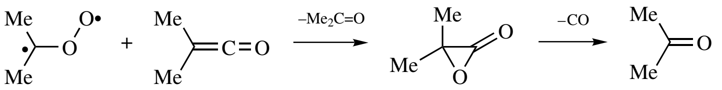
(6)

Upper limits for the rate constants of reactions of ozone with ketene (**13**), methylketene (**14**), ethylketene, and dimethylketene (**15**) gave relative rates of 1, 700, 10^3, and 4×10^4, respectively.[4] Wall and radical reactions complicated the analysis, but the reaction of dimethylketene (**15**) forming the trioxide **16** with zwitterionic and singlet diradical character leading to diradical **17** was proposed (equation 7). Transfer of oxygen between **15** and **17** led to the α-lactone **18**, which underwent decarbonylation to the ketone **19** (equation 8).[4] Enhancement of the reaction by methyl substituents was contrary to what was found for nucleophilic attack at C_1, but was consistent with reactions involving a transition state with positive charge or free radical development at C_2.



15 **16** **17**

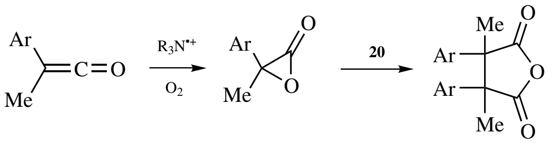
(7)



17 **15** **18** **19**

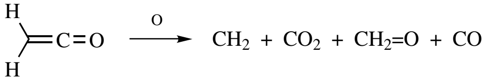
(8)

Electron-transfer oxygenation of arylalkylketenes **20** initiated by aminium salts gave succinic anhydrides **22** in a process proposed to involve combination of **20** with α-lactones **21** formed from the ketenes (equation 9).[5]

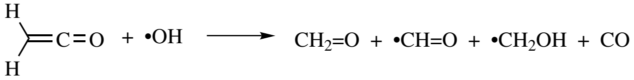


20 **21** **22** (9)

Computer simulation of an 85-step mechanism of the reaction of $CH_2{=}C{=}O$ (**23**) with O_2 in the temperature range 1050–2050 K was used to derive rate expressions for steps including ketene oxygenations (equations 10, 11).[6] Some of these reactions were also involved in acetylene combustion,[7] and the mechanism of the reaction of C_2H with O_2 has been studied theoretically.[8–10]

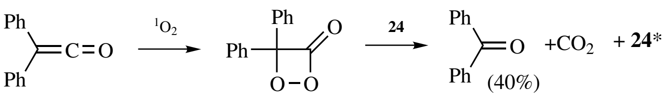


23 (10)



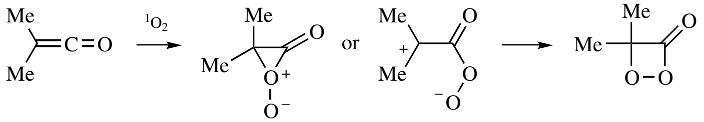
23 (11)

Diphenylketene (**1**) reacted with singlet oxygen generated from $(PhO)_3PO_3$, and in the presence of 9,10-bis(phenylethynyl)anthracene (**24**) there was chemiluminescent emission from **24**, with formation of $Ph_2C{=}O$ and CO_2 (equation 12).[11] It was proposed that Staundinger's peroxide **2** was formed. This was identified by the distinctive IR absorption at 1870 cm^{-1} and was found to react with **24**, forming the observed products and excited **24**.[11]



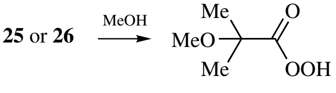
1 **2** (IR 1870 cm^{-1}) **24** = 9,10-bis(ethynylphenyl)anthracene (12)

α-Peroxylactones such as **27** were also formed from $^1O_2$ reaction with ketenes ($Me_2C{=}C{=}O$ (**15**), *t*-BuCH=C=O, *n*-BuCH=C=O, *n*-PrCMe=C=O, *n*-BuCPh=C=O, and $(CF_3)_2{=}C{=}O$) as well as with **1**, and these were purified at −20 °C and the structures confirmed by their ^1H NMR and IR spectra (equation 13).[12,13] Kinetic measurements and reaction of the ketenes with $^1O_2$ were consistent with the proposed reaction pathway (equation 13).[12] Reaction in the presence of MeOH resulted in the formation of α-methoxyperacetic acid **28** (equation 14), so the reactions were interpreted as involving either a perepoxide **25** or a zwitterion **26**, and not direct formation of the α-peroxylactone **25** (equation 14).[14]



(13)

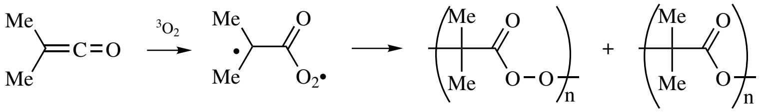
15 **25** **26** **27**



(14)

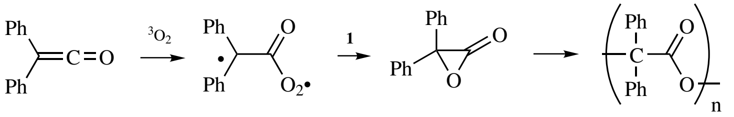
28 (20%)

Additional study[14,15] of the reactions of ketenes with triplet oxygen confirmed and extended the work of Staudinger et al.[1] Reaction of $Me_2C{=}C{=}O$ (**15**) with $^3O_2$ in ether at −20 °C gave the poly(peroxyester) **29** (96%) and the polyester **29a** (4%), while $Ph_2C{=}C{=}O$ (**1**) gave no poly(peroxyester), 70% polyester **3**, and 30% $Ph_2C{=}O$ and CO_2.[14] Reaction of $Me_2C{=}C{=}O$ (**15**) in MeOH gave $HOOCMe_2$-CO_2Me as the only major product, while $Ph_2C{=}C{=}O$ (**1**) gave a significant amount of $Ph_2C(OMe)CO_3H$.[14] These results and others were interpreted as showing that $Me_2C{=}C{=}O$ (**15**) reacted with $^3O_2$ to form diradical **30**, which polymerized to **29** (equation 15), whereas $^1O_2$ formed perepoxide **25** and/or zwitterion **26**, which were captured by MeOH (equations 13, 14). Diradicals such as **30** can undergo conversion to **25/26**, and the poly(peroxyesters) can decompose to ketones and CO_2. The diradical **31** from $Ph_2C{=}C{=}O$ (**1**) formed a zwitterion analogous to **25/26**, which reacted with **1** to form the α-lactone **2**, which gave the polyester **3** (equation 16).



(15)

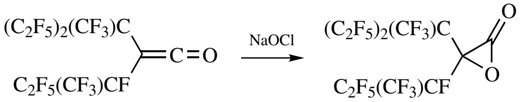
15 **30** **29** **29a**



(16)

1 **31** **2** **3**

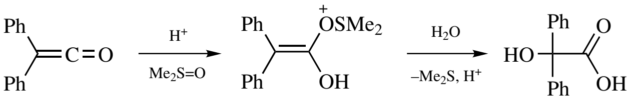
The conversion of other ketenes to ketones by oxygen has been observed,[16–18] as well as the reactions of ketenes with ozone and peracids forming polyesters and ketones.[19–21] The perfluorinated ketene **32** gave the stable α-lactone **33** (equation 17).[22]



(17)

32 **33**

The reaction of diphenylketene (**1**) with DMSO and aqueous acid was proposed to occur with nucleophilic attack at C_1 forming **34**, which gave benzilic acid (equation 18).[23] Iodosobenzene (PhIO) reacts with **1** to form polyester **3**,[24] and this presumably also occurs via nucleophilic attack at C_1, followed by formation of α-lactone **2**.



1 **34** **35** (88%) (18)

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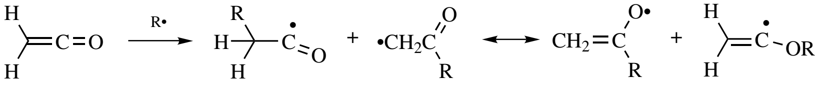
5.7 RADICAL REACTIONS OF KETENES

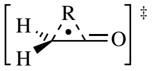
A theoretical study of the reaction of H, CH_3, OH, F, SiH_3, and Cl radicals with $CH_2{=}C{=}O$ (**1**) forming the products **2a–c** by addition to C_2, C_1, and oxygen of the ketene, respectively, gave good agreement with available data on the relative stabilities of the products and of the barriers for attack (Table 5.19).[1] The results for H• and CH_3• were similar, with little selectivity for attack at C_1 and C_2, and there was little difference between the relative energies of the isomeric products. For HO•, F•, and Cl• the product enolic radicals from attack at C_1 were significantly more stable than the products for attack at C_2, but small barriers for attack at C_1 were calculated, while none were found for attack at C_2, so selectivity for attack at C_2 was predicted, in agreement with experimental results. For SiH_3• a preference for attack at C_2 was predicted, and this radical was also predicted to be the most stable. These studies were confirmed by further calculations for H•,[2] Cl•,[3] OH•,[4] and F•[5] radical addition to ketene and product radicals.



1 **2a** **2b** **2c** (1)

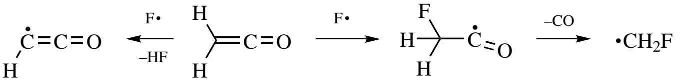
The results in Table 5.19 show barriers for rearrangement from the less stable enolic radical **2b** to acyl radical **2a** of 42.1 kcal/mol for R = H, and for rearrangement of the less stable acyl radicals **2a** to the more stable enolic radical **2b** of 27.6 and 4.6 kcal/mol for R = F and Cl, respectively.

TABLE 5.19 B3LYP/6-31G*//B3LYP/6-31G* Calculated Energy Changes (kcal/mol) for Additions of Radicals R• to $CH_2{=}C{=}O$[a]

	$RCH_2\dot{C}{=}O$ (**2a**)			$\bullet CH_2C(O)R$ (**2b**)			$CH_2{=}\dot{C}OR$ (**2c**)	
R	ΔE_{ts}	ΔE^0	ΔE_{ts}^{Rearr}	ΔE_{ts}^{Perp}	$\Delta E_{ts}^{in\text{-}plane}$	ΔE^0	ΔE_{ts}	ΔE^0
H	0.5	−44.2	2.6	5.4	6.6	−39.5	13.4	−9.3
CH_3	9.3	−29.7		11.9	8.5	−31.4	22.5	10.0
OH		−32.6		3.8		−54.7		
F		−50.1	−22.5			−69.2		
SiH_3	3.3	−20.6		9.2	6.3	−4.2	11.2	−12.9
Cl		−20.5	−15.9	−13.4		−28.6		

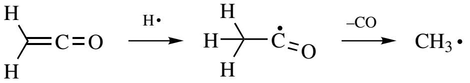
[a] Energy differences relative to the separated reactants in each case.

The reactions of F, Cl, and OH radicals with ketene were monitored using a flow system with far IR detection of the reaction products.[6] The predominant pathways observed with F• were radical addition to the CH_2 group, forming **3** followed by decarbonylation, and hydrogen abstraction forming the ketenyl radical **4** (equation 2).[6] The radicals Cl• and HO• behaved similarly.[7–10] Experimentally, reaction of ketene with H• occurred by addition to C_2, forming the radical **5**, and led to formation of CH_3• (equation 3).[11] The rate constants for addition of F•,[7] Cl•,[7] and H•[11] to ketene were measured. Reaction with O atoms with several ketenes occurred primarily at C_1, leading to formation of CO_2, and for **1** could involve an intermediate **6** with diradical or zwitterionic character (equation 4).[12]



4 **3**

(2)



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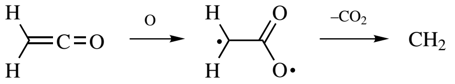
(3)

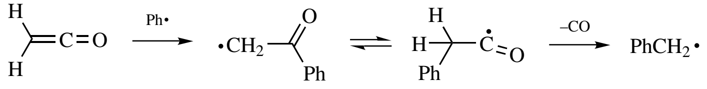


6

(4)

The kinetics of the reactions of the radicals •CN and •N=C=O with ketene in the gas phase were measured, and occurred predominantly by C-C bond formation followed by decarbonylation yielding $NCCH_2$• and •CH_2NCO, respectively.[13] Hydrogen abstraction forming HCN and HNCO, respectively, together with the radical •CH=C=O, was a minor or negligible reaction channel.[13]

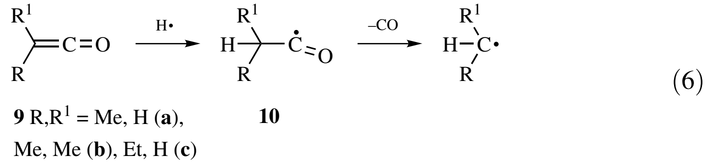
The kinetics of addition of phenyl radicals to ketene were measured by monitoring the IR spectrum of the phenyl radical, and showed that the reaction occurred by addition and not hydrogen abstraction, as there was no measurable isotope effect for reaction of CD_2=C=O.[14] Computational studies indicated that addition could occur at either C_1 or C_2, forming either **7** or **8**, respectively, and the radicals formed could interconvert with a low low barrier leading to decarbonylation with formation of $PhCH_2$• (equation 5).[14]



1 **7** **8**

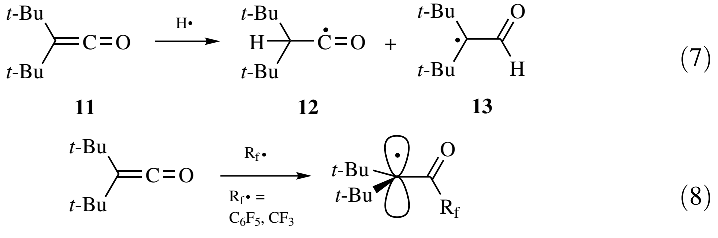
(5)

Hydrogen atoms reacted with methylketene, dimethylketene, and ethylketene (**9**) forming alkyl radicals and CO, and evidently led to radical intermediate **10** (equation 6).[15,16]


9 R,R^1 = Me, H (**a**), Me, Me (**b**), Et, H (**c**)

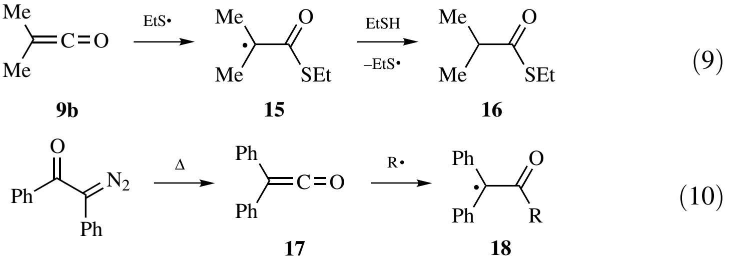
10

Addition of H• radical to di-*tert*-butylketene (**11**) in solution gave both the acyl radical **12** and the enolic radical **13**, as identified by ESR (equation 7).[17] The acyl radical was assigned as having a σ structure and decayed rapidly by decarbonylation, forming $t\text{-}Bu_2CH\bullet$. Addition of C_6F_5 or CF_3 radicals to di-*tert*-butylketene (**11**) gave the radicals **14**, which were assigned as having perpendicular conformations from their ESR spectra (equation 8).[17] This acyl radical conformation was favored because of the steric crowding in a planar conjugated structure.


11 **12** **13**

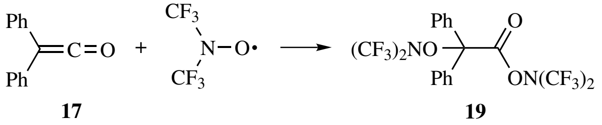
11 **14**

Ethanethiol added to dimethylketene (**9b**) in solution in a radical initiated chain process with radical attack at C_1 forming the intermediate **15**, which formed the thioester **16** (equation 9).[18] Radical addition was proposed to occur to C_1 of diphenylketene (**17**) formed by thermolysis of azabenzil, giving rise to radical **18**, detected by ESR (equation 10).[19]

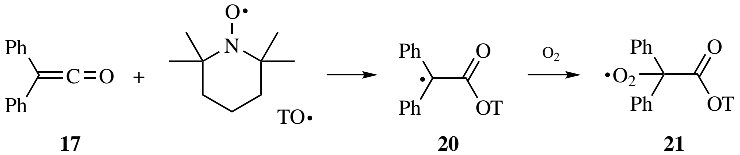

9b **15** **16**

17 **18**

The addition of the nitroxyl radical $(CF_3)_2NO\bullet$ to $Ph_2C{=}C{=}O$ (**17**) formed the 1.2-diaddition product **19** (equation 11).[20] The less reactive nitroxyl radical 2,2,6,6-tetramethylpiperidinyloxy (TEMPO, TO•) also reacted with diphenylketene (**17**) but did not add a second TEMPO (equation 12).[21] On standing in air, reaction with oxygen formed the peroxide **22**, whose structure was confirmed by X-ray determination.[21] This result indicated that the nitroxyl radical added initially at C_1 of the ketene, forming the intermediate radical **20**, which was presumably in equilibrium with the unsymmetrical dimer, and upon exposure to O_2 formed the peroxide (equations 12, 13).[21]



(11)



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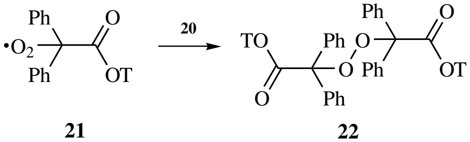
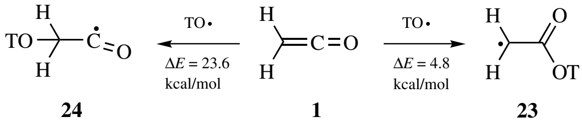


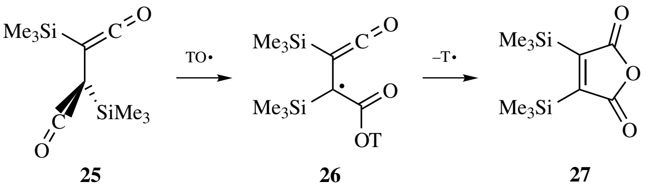
(13)

Computations at the B3LYP/6-31G* level indicated that while addition of HO• to ketene to form $HOCH_2C(\bullet){=}O$ and $\bullet CH_2CO_2H$ was predicted to be exothermic by 32.6 and 54.7 kcal/mol, respectively (Table 5.19),[1] the corresponding reactions of aminoxyl radical ($H_2NO\bullet$) or of the 2,2,6,6-tetramethylpiperidinyloxy (TEMPO, TO•) were calculated to be much less exothermic, but still with a strong preference for addition at C_1 compared to C_2, with ΔE of 4.8 and 23.6 kcal/mol for formation of **23** and **24**, respectively (equation 14).[22] Thus, addition at C_1 was predicted to be favored, in agreement with with the experimental results for **17**.[21]



(14)

At elevated temperatures TEMPO reacted with the bisketene **25** to give the anhydride **27** in a reaction suggested to involve radical attack on the carbonyl carbon (equation 15).[21] The reactions of a number of other ketenes with TEMPO have been studied, and a linear correlation (Figure 5.5) between $\log k_2(TO\bullet)$ and the measured rate constants for hydration $\log k(H_2O)$ at 25 °C was found (equation 16).[22–24]



(15)

$$\log k_2(\text{TEMPO}) = 1.22 \log k(H_2O) - 4.93 \qquad (16)$$

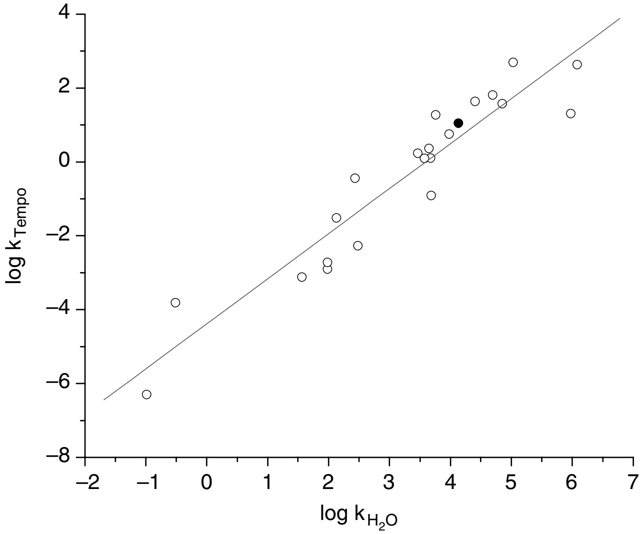
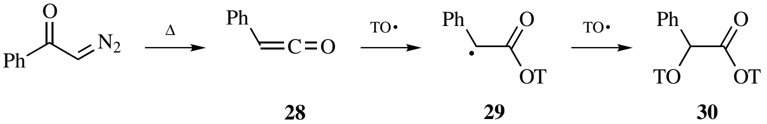


Figure 5.5 Logk_2(TEMPO) versus log k(H_2O) for ketenes.

Phenylketene (**28**) generated in situ by Wolff rearrangement or dehydrochlorination of the acyl chloride in the presence of TEMPO gave 1,2-diaddition of two molecules of TEMPO to form **30** (equation 17).[23] Butadienylketene (**31**) reacted by 1,6-addition (equation 18),[32] while dienylketene **33** was proposed to form the observed ester **35** by hydrogen abstraction from an intermediate radical **34** (equation 19).[30] Pentafulvenone (**36**) formed **37** and **38** by complex reaction pathways (equation 20).[28] Other ketenes whose reactions with TEMPO were examined include 1-naphthylketene,[25] cyclopropylketene,[27] 4-butenylketene,[26] allenylketene,[32] and (phenylethynyl)ketene.[26]



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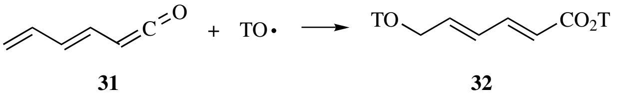

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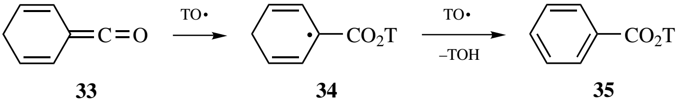

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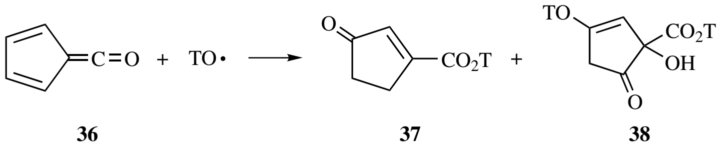
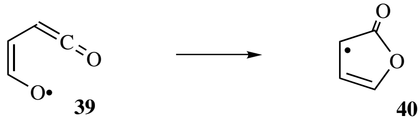


(20)

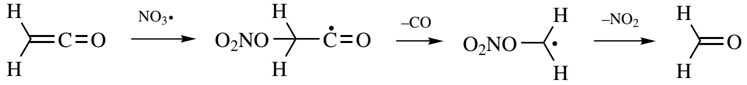
Cyclization of **39** with radical addition to the ketenyl group forming **40** was studied computationally for comparison to experimental results (equation 21).[33] Other intramolecular reactions of radicals with ketenes are shown in Section 4.1.9.



39 **40**

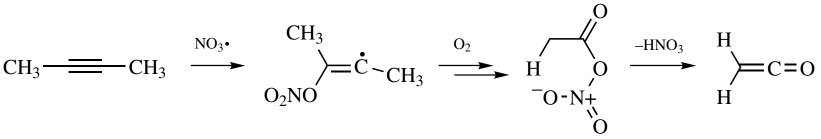
(21)

Addition of the nitrate radical to ketene (**1**) was proposed to occur by formation of the acyl radical **41**, which fragmented to formaldehyde (equation 22).[34] Ketene (**1**) was formed during the reaction of 2-butyne with NO_3 and was proposed to arise from acetyl nitrate **42**, which eliminated nitric acid (equation 23).[34]



1 **41**

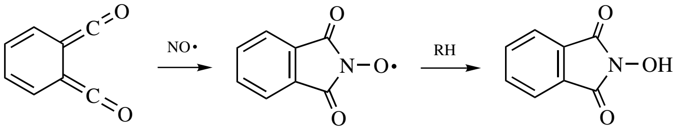
(22)



42 **1**

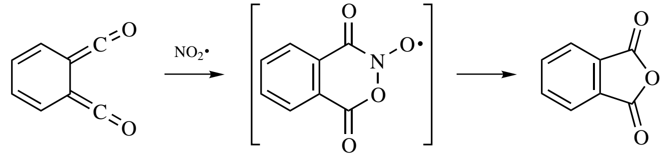
(23)

Bisketene **43** reacted with NO by [4+1] cycloaddition, forming the nitroxyl radical **44**, which led to **45** (equation 24), and with NO_2, forming phthalic anhydride through the proposed intermediate **46** (equation 25).[35]



43 **44** **45**

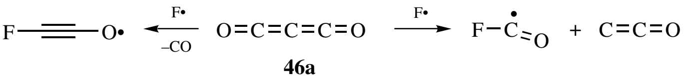
(24)



43 **46**

(25)

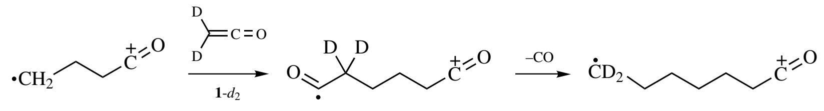
Fluorine atoms reacted with carbon suboxide **46a** to form CO. The possible first steps may have involved F addition or CO abstraction (equation 26).[36]



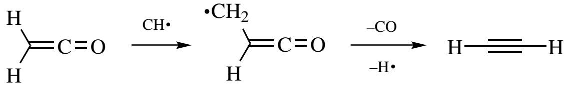
$$F{-}C{\equiv}O\bullet \xleftarrow[-CO]{F\bullet} O{=}C{=}C{=}C{=}O \xrightarrow{F\bullet} F{-}\dot{C}{=}O + C{=}C{=}O \qquad (26)$$

46a

The distonic species **47** formed in the gas phase from cyclobutanone added to dideuteroketene (**1**-d_2), forming **48**, which then lost CO (equation 27).[37] Reaction of CH with ketene to give CO, C_2H_2, and H• was proposed to proceed by insertion, forming intermediate **49** (equation 28).[38]

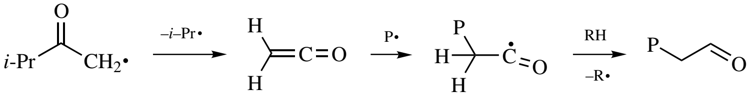


47 **48** (27)

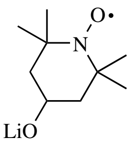


1 **49** (28)

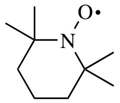
It was proposed that during polymerization of *N*-vinylpyrrolidinone in 3-methylbutan-2-one, enolic radicals **50** were formed that cleaved, forming ketene and isopropyl radicals, and that the ketene subsequently was attacked by the polymerizing chain **P•**, forming acyl radical **51**, which abstracted hydrogen, giving aldehyde **52** (equation 29).[39] Anionic polymerization of ethyl(phenyl)ketene was initiated by the nitroxyl radical **53**, forming a polymer with a nitroxyl end group.[40] Heptafulvenone **54** reacted with TEMPO (TO•) to form the dimer **55** and the *o*-, *m*-, and *p*-substituted benzaldehydes **56** by radical processes (equation 30).[32]



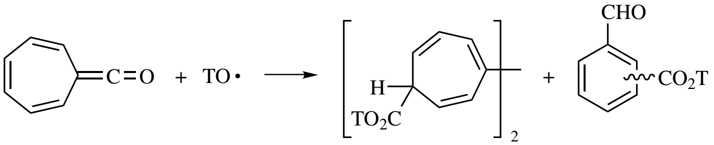
50 **1** **51** **52** (29)



53



TO•



54 **55** **56** (30)

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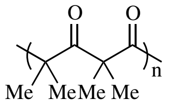
5.8 POLYMERIZATION OF KETENES

Polymers derived from ketenes were first observed by Wedekind[1] and by Staudinger,[2,3] and this provided an impetus for the further development of polymer chemistry. The formation of high polymers from ketenes was examined systematically by Natta, et al.,[4,5] and this work has been reviewed.[6–9] Types of ketene polymers include those formed by 1,2-additions of the C=C bonds (**1**) and of the C=C bonds (**2**), which are poly(ketones) and poly(acetals), respectively, and esters **3** that have both types of linkages. All three have been prepared from $Me_2C{=}C{=}O$ (**4**) by appropriate choice of catalyst and solvent (equations 1–3).[4]



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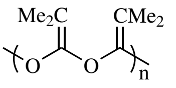

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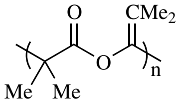
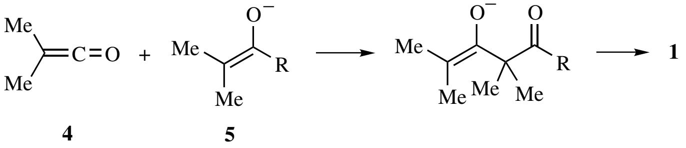


3

The formation of **1** by polymerization of **4** with $AlBr_3$ in toluene was proposed to involve formation of enolate **5**, which added **4** (equation 1), while **2** was formed from **4** by *n*-BuLi in ether (equation 2). The formation of **3** took place when $AlEt_3$ in toluene was used as the catalyst (equation 3).[4,7,10,11]



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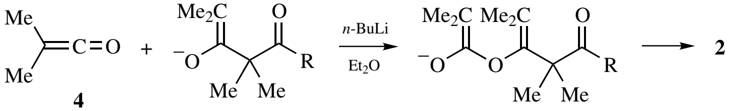
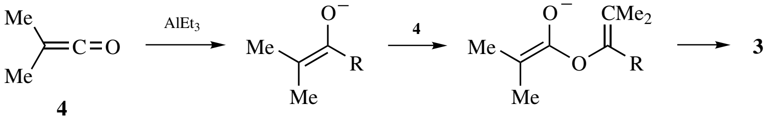


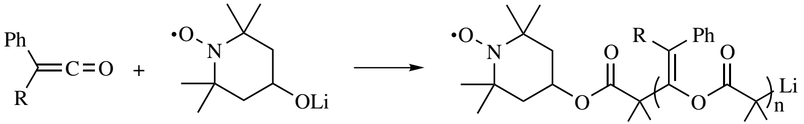
(2)



(3)

Ketene was polymerized by La(OPr-*i*)$_3$, probably in a process involving a lanthanum enolate.[12] This species served to initiate methyl methacrylate polymerization.[12] This catalyst also formed a copolymer of diethylketene and methyl methacrylate.[13] Cationic polymerization of dimethylketene has been reported,[14] as well as radiation cryopolymerization of ketene, which was proposed to proceed by an anionic mechanism.[14a]

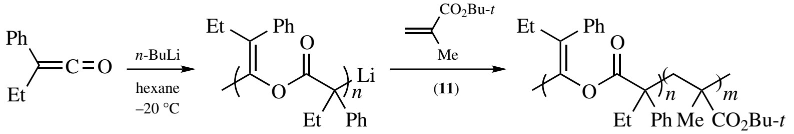
Arylalkylketenes **6** have also been polymerized,[15–21] and anionic living polymerization initiated with alkoxy anion **7** containing a stable tetramethylpiperidinyl radical gave **8** tagged with a radical end group (equation 4).[15]



6 **7** **8**

(4)

Polymerization of phenyl(ethyl)ketene **9** in THF at −20 °C initiated by *n*-BuLi gave a living polymer **10** that could be quenched by MeOH.[16] Alternatively, the addition of further ketene to the living polymer gave renewed polymerization, or the addition of *tert*-butyl methacrylate (**11**) gave block polymer **12** (equation 5).[19]

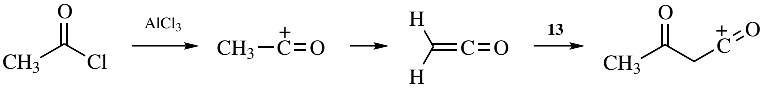


9 **10** **12**

(5)

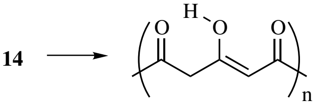
Diphenylketene has also been polymerized using EtLi or *t*-BuLi.[21] Ketenes also form copolymers with other carbonyl compounds[22,23] or with isocyanates.[24]

Polyketene (**15**), the polymer of ketene, was formed by the reaction of acetyl chloride with AlCl$_3$, and was proposed to result from deprotonation of the acylium ion **13** forming ketene, which then reacted with **13** forming **14**, followed by addition of ketene monomers leading to **15** (equation 6).[25] Polyketene has also been formed by acid polymerization of the ketene acetal CH$_2$=C(OHx-*n*)$_2$ followed by mild hydrolysis of the resulting acetal.[26] Polyketene was found to be extensively enolized, with interesting conducting properties.[27]



13 **14**

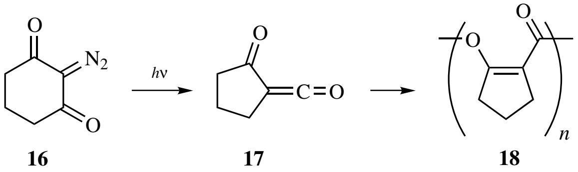
(6)



15

(7)

Ketoketenes **17** formed by photolysis of 2-diazo-1,3-diketones **16** in Et_2O polymerize to polyesters **18** (equation 8).[28] A variety of polymers have been prepared from carbon suboxide (C_3O_2).[29,30] Carbon suboxide spontaneously forms a low-molecular-weight polymer, as discussed in Section 4.11.[31] The formation of polymers from other bisketenes is mentioned in Section 4.9.



(8)

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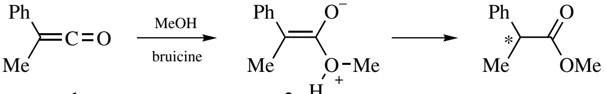
5.9 STEREOSELECTIVITY IN KETENE REACTIONS

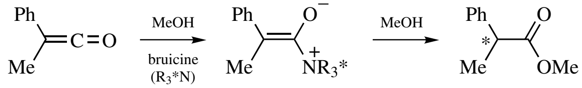
Additions to ketenes often involve the generation of new chiral centers. The search for stereoselectivity in these reactions was initiated in 1919 by Weiss, who added the chiral alcohol menthol to phenyl-*p*-tolylketene and claimed to have observed diastereoselectivity in formation of the ester.[1] This was, however, improbable and was later disproved.[2,3] Despite this initial setback, there has been continuing interest and rapidly increasing success in the search for methods to achieve stereoselectivity in ketene reactions, and the subject has been frequently reviewed.[3–11]

Further studies of stereoselective addition of alcohols to ketenes have involved the use of chiral alcohols, chiral catalysts, and chiral auxiliaries. Appreciable stereoselectivity in the addition of methanol to phenylmethylketene (**1**) catalyzed by the chiral base brucine forming the ester **3** was achieved by Pracejus in 1960 (equation 1).[12] There was a 25% excess of the *S*-(+) ester at $-110\,^{\circ}$C and a 10% excess of the *R*-(-) ester at 80 °C. Selective protonation of a zwitterionic intermediate **2** was proposed,[5,12,13] but more recently, addition of the catalyst to the ketene forming an enolate that undergoes stereoselective protonation has been suggested for many but not all such reactions (equation 2).[8,10,11] Optically active amines bound to polymers were also effective catalysts for this reaction.[15,16] A chiral dendritic diamine gave enantioselective protonation in the reaction of PhCMe=C=O (**1**) with MeOH.[17] The enantioselective protonation of enolates derived from ketenes has been reviewed.[6] A chiral azaferrocene catalyst (vide infra) promoted the stereoselective addition of CH_3OH to PhCEt=C=O.[10,11]



1 **2** **3**

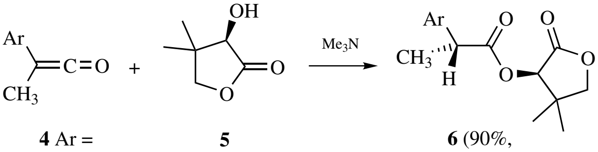
(1)



1 **2a** **3**

(2)

Addition of the chiral alcohol pantolactone (**5**) to the arylmethylketene **4** generated from the acyl chloride with a tertiary amine has been found to give diastereoselectivities as high as 99% in forming 2-arylpropionates **6** (equation 3).[18,19] Many variations of the reaction of chiral alcohols with ketenes have been studied,[20–33] and a detailed computational investigation has been carried out.[30,31] Other unsymmetrical ketenes such as $R_2NCR{=}C{=}O$,[24,25] arylhaloketenes RCHal=C=O,[28] and phenyltrifluoromethylketene (**7**) with chiral alcohol **8** forming **9** gave more modest stereoselectivity (equation 4).[29]

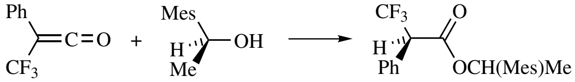


4 Ar = 3-$C_6H_5COC_6H_4$

5

6 (90%, 99.5% *R*)

(3)



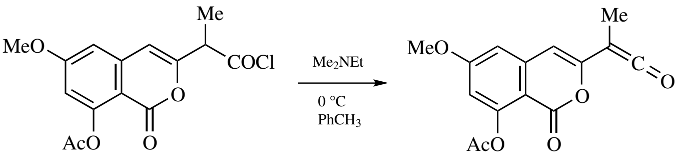
7

8 Mes = 2,4,6-$Me_3C_6H_2$

9 (13% *de*)

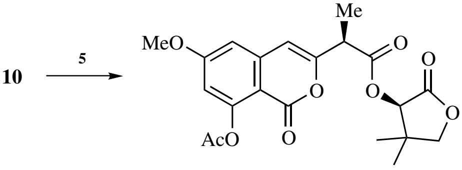
(4)

The ketene **10** generated by dehydrochlorination reacted with (*R*)-pantolactone **5** to give the ester **11** in 85% yield, 94% *de* (equations 5, 6).[34]



10 (IR 2119 cm^{-1})

(5)



11 (85%, 94% *de*)

(6)

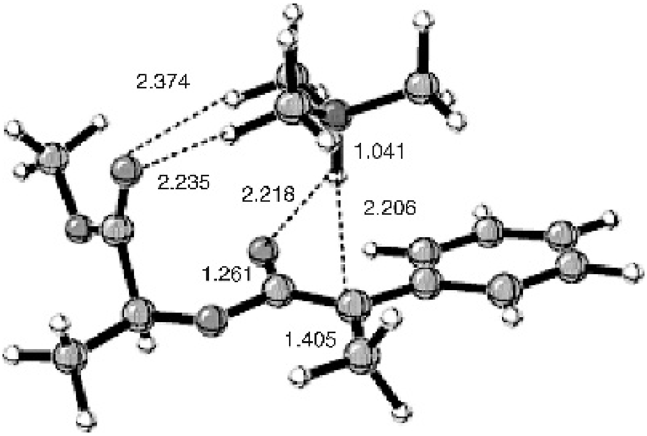
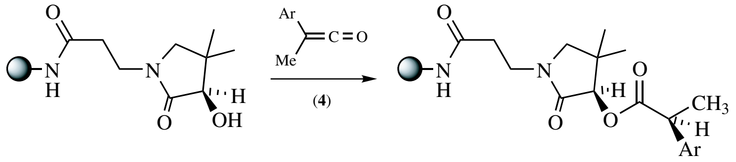


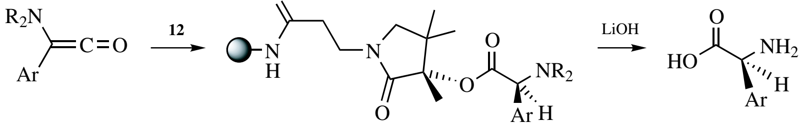
Figure 5.6 Favored transition state calculated for proton transfer to carbon in the esterification of methyl(phenyl)ketene by methyl (*S*)-lactate catalyzed by trimethylamine (reprinted with permission of the American Chemical Society).

A computational study at the B3LYP/6-31G* level of the reaction of $PhCMe{=}C{=}O$ (**1**) with methyl (*S*)-lactate lactate and Me_3N found initial complexes, TS for alcohol addition *syn* to the Me group of **1** forming a zwitterionic intermediates, and TS for proton transfer to the α-carbon.[31] The important final TS involves a favorable C—H—O hydrogen bond from the lactate carbonyl to a methyl C—H (Figure 5.6).[31] This model accounts for the observed stereoselectivity of (*S*)-pantolactone to methyl(phenyl)ketene.

Additions of the polymer-bound alcohol **12** with $ArCMe{=}C{=}O$ (**4**) gave esters **13** (equation 7), which were saponified to give the chiral acids in >99% yield and *ee* >80%.[32] The free chiral alcohol was also recovered from the reaction. Reaction of **12** with phthalimido ketenes **14** formed esters **15a**, which upon cleavage gave 2-aryl-3-amino propionic acids **15b** with 75–88% *ee* (equation 8).[33] Sugars reacted with aryl(methyl)ketenes **4**, forming esters that after hydrolysis gave α-propionic acids with *dee* up to 78%.[35]

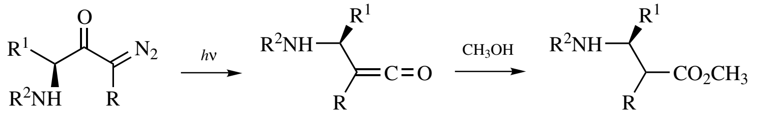


12 **13** (7)



14 (R_2 = phthalyl) **15a** **15b** (63–68%) (8)

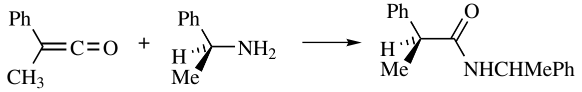
Chiral ketenes **17** from Wolff rearrangements of amino acid–derived diazo ketones **16** reacted stereoselectively with CH$_3$OH in the generation of the new chiral center in **18** (equation 9).[36] Other chiral ketenes also gave stereoselective reaction with achiral alcohols.[37,38]



(9)

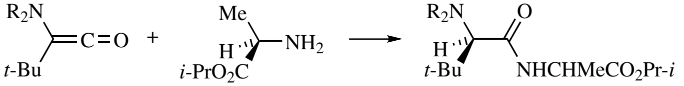
16 **17** **18** (25–77%)

In a pioneering study of the reaction of the chiral amines, *S*-(-)-1-phenylethylamine (**19**) with the ketene **1** in toluene at −100 °C gave the *S,S*-amide **20** with 60% *de* (equation 10).[39] The addition of the isopropyl ester of *R*-alanine (**22**) to ketene **21** gave the *RR*-amide **23** in 63% *de* (equation 11).[39] The dienylketene **25** generated by photolysis of **24** also gave stereoselectivity in reaction with *d*-ephedrine (equation 12).[40]



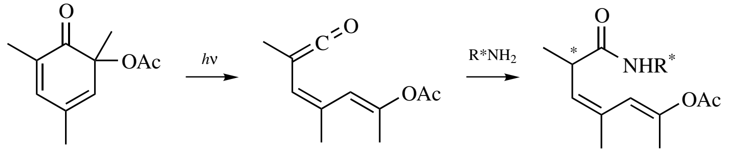
(10)

1 **19** **20** (60% *de*)



(11)

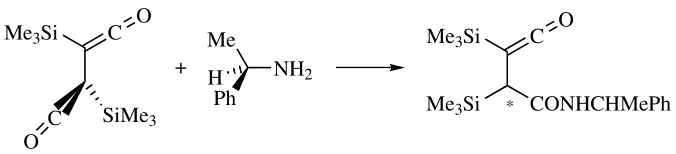
21 (R$_2$ = phthalyl) **22** **23** (63% *de*)



(12)

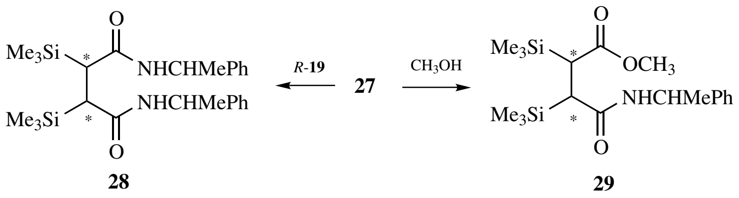
24 **25** **26** (94%, 70:30 *dr*)

The reaction of *R*-1-phenylethylamine (*R*-**19**) to bisketene **26** gave the ketenylamide **27** with significant selectivity (equation 13), and this was enriched to >90% *ee* with one recrystallization.[41] The reaction of **27** with a second *R*-1-phenylethylamine (*R*-**19**) forming **28** also had 2/1 selectivity, and MeOH addition generating **29** proceeded with 96:4 *dr* (equation 14).[41]



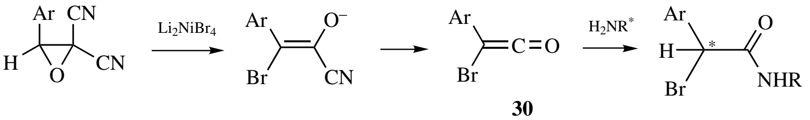
(13)

26 *R*-**19** **27**



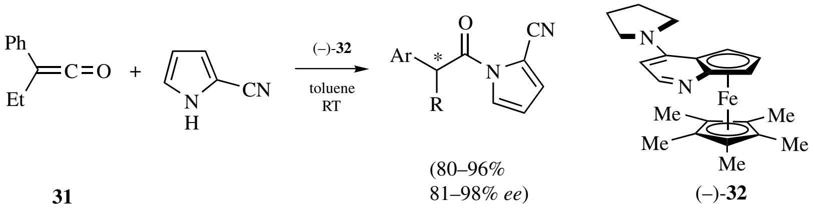
(14)

Chiral amino acid esters added to ketenes ArCBr=C=O (**30**), generated in situ from 3-aryl-2,2-dicyanooxiranes, and gave amides with significant diastereoselectivity (equation 15).[42] High diastereoselectivity (98:2) was also observed for the Et_2Zn-catalyzed reaction of (*S*)-(+)-3-hydroxytetrahydrofuran with phenyl(methy)ketene (**1**), with 78% yield.[43]



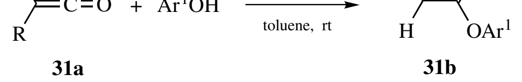
(15)

Phenyl(ethyl)ketene (**31**) and 2-cyanopyrrole in the presence of catalyst **32**[10,11,44–46] gave stereoselective amination forming the amide (equation 16).[45] The stereoselectivity was proposed to arise from proton transfer to an amide enolate by the protonated catalyst.[11,45] A number of ketenes ArCR=C=O and amines were examined, and the cyanopyrrole gave the highest stereoselectivity of the amines.[45]

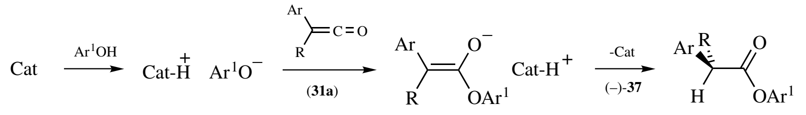


(16)

In studies of esterification of ketenes **31a** with phenols ArOH catalyst (-)-**32** gave esters **31b** with *ee* of 35–91%, with the highest *ee* with 2-*tert*-butylphenol (equation 16a).[46a] A variety of ketenes with this phenol gave *ee* of 79–94% and yields of 66–97%. The mechanism proposed for this process involved deprotonation of the phenol, phenoxide attack on the ketene forming an enolate, and proton transfer from the resulting ion pair forming **38** (equation 16b).[46a] Ketenes **31a** also reacts with aldehydes $Ph_2CHCH=O$ with catalysis by (−)-**32** to give stereoselective formation of enol esters.[46b]



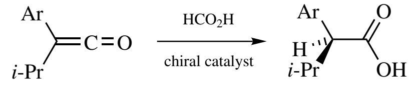
(16a)



(16b)

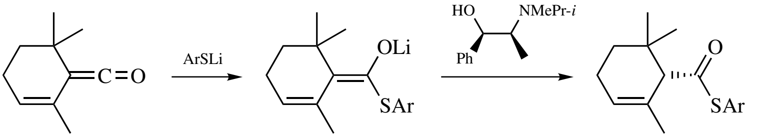
(–)-**32** **31b**

The reaction of carboxylic acids with ketenes **33** catalyzed by chiral amines gave stereoselective formation of α-aryl carboxylic acids **34** (equation 17).[47] Chiral alcohols were used to protonate enolate **36** formed from addition of arylthiophenoxides to ketene **35**, and gave stereoselectivity in the formation of **37** (equation 18).[48]



(17)

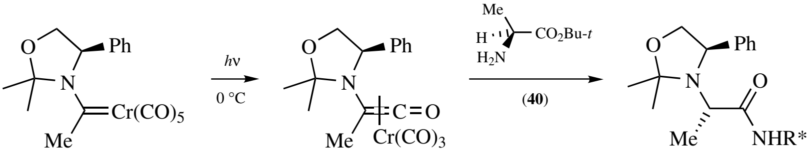
33 **34**



(18)

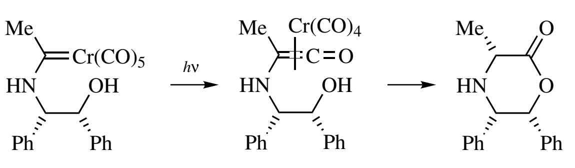
35 **36** **37** (81–87%)

Photolysis of the optically active amino-substituted chromium carbene complex **38** gave the chromium-complexed ketene **39**, which reacted with the chiral amino acid ester **40** to give the amide **41** with 98:2 *dr* (equation 19).[49] This procedure was adapted for solid-state peptide synthesis.[50] Stereoselective cyclization of the chromium-complexed ketene **42** formed by carbene complex photolysis gave the lactone **43** (equation 20).[51] Other examples of stereoselective reactions of chromium-complexed ketenes have been reported.[52,53]



(19)

38 **39** **41** (56–88%)

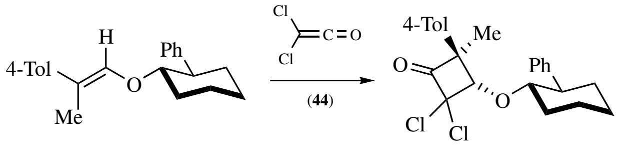


(20)

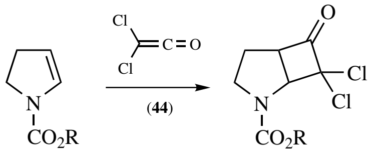
42 **43** (60%, 90% *de*)

Ketenes characteristically give high stereoselectivity in [2+2] cycloaddition reactions, so reactions with reagents containing preexisting chiral centers permit further stereochemical control. For example, dichloroketene **44** gave greater than

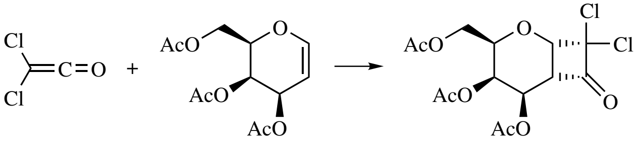
90% *ee* in cycloaddition with **45**, forming the cyclobutanone (equation 21).[54,55] The selectivity was attributed to shielding of one face of the double bond by the phenyl.[54,55] Enecarbamates **46** with chiral auxiliary groups R reacted with **44** with selectivity of up to 4:1 in the formation of diastereomeric products **47** (equation 22).[56] Dichloroketene also added selectively to the optically active carbohydrate enol ether **48**, forming **49** (equation 23).[57]



45 (92%) (21)

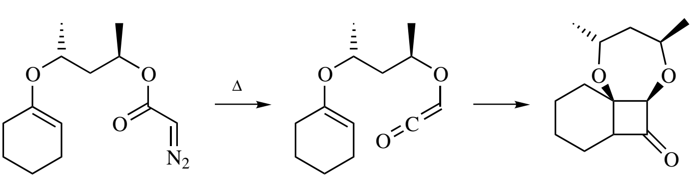


46 **47** (77–88%) (22)



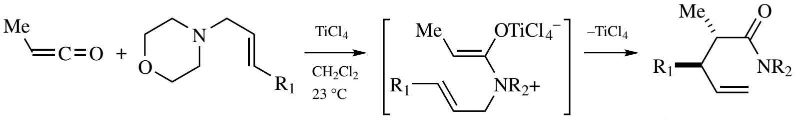
44 **48** **49** (95%) (23)

Ketene **51** generated by photochemical Wolff rearrangement of diazo ketone **50** gave stereocontrolled intramolecular [2+2] cycloaddition (equation 24).[58] The cyclobutanone **52** was the only stereoisomer detected (>99% *de*) over the temperature range 195 to 423 K, and the lack of temperature dependence indicated the entropy control of the stereochemical outcome. The Wolff rearrangement of the ester was characteristically inefficient, with isolated yields of 10–33%, but generation of the ketene by an elimination route also gave **52** as the only stereoisomer.[58–60] However, Wolff rearrangement by vacuum flash pyrolysis gave the product in 70% yield with undiminished stereoselectivity, as the intermediate carbene avoided intermolecular hydrogen atom transfer.[59,60]



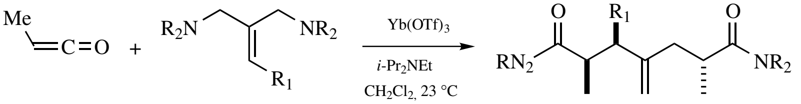
50 **51** **52** (70%) (24)

Methylketene **53** generated by dehydrochlorination reacted with allyl morpholines **54**, forming amides **55** with high selectivity for the isomer shown (equation 25).[61] The reactions were envisioned as proceeding through a ketene aza-Claisen reaction reaction as shown, and were successful with catalysis by 5–10 mol%. Yb(OTf)$_3$, AlCl$_3$, Ti(OPr-*i*)$_2$Cl$_2$, or TiCl$_4$•(THF)$_2$. Nitrogen-, oxygen-, and sulfur-substituted ketenes were also successfully used in this procedure.



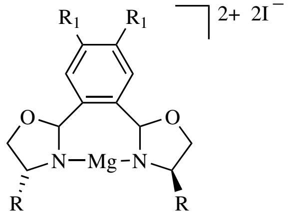
53 **54** **55** (R^1 = Me, Cl, Ph, H; 76–90%) (25)

Allylic diamine **56** reacted successively with two molecules of methylketene (**53**), forming **57** in a cascade process depicted as occurring by two iterations of the aza-Claisen rearrangement (equation 26).[62] The first reaction was considered to occur with the R$_2$N group *trans* to R^1. Reaction for R$_2$N = morpholine and R^1 = Me gave a 97% yield with a 98:2 preference for the product shown. The reaction was also successful for benzylketene. The catalyst **58** promoted this reaction with high stereoselectivity.[63] Use of the chiral catalysts **58** and **59** gave the product **57** in yields of up to 88% and up to 91% *ee*.[63]

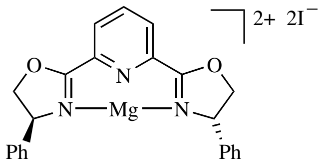


53 **56** **57** (26)

(R$_2$N = morpholine, pyrrolidine, piperidine; R^1 = Me, Cl, OBz, CN, SPh)

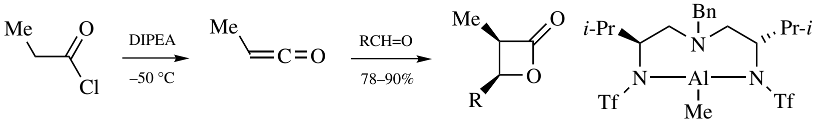


58
[Mg•Arbox](1)$_2$



59
[Mg•pybox](1)$_2$

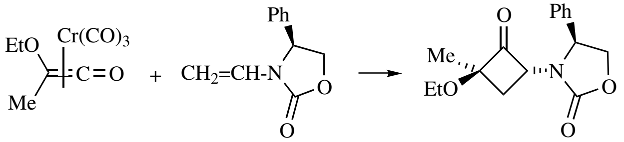
Methylketene (**53**) generated by dehydrochlorination of propionyl chloride by diisopropylethylamine (DIPEA) underwent [2+2] cycloadditions with aldehydes catalyzed by Al(SbF$_6$)$_3$, forming β-lactones **60** with high *cis/trans* product ratios (equation 27).[64–68] Stereoselectivity was achieved with the chiral catalyst **61**, giving *ee* of 90–94%.[65,66] This reaction was improved using benzotrifluoride as solvent, which resulted in precipitation of the ammonium salt.



(27)

53 **60** **61**

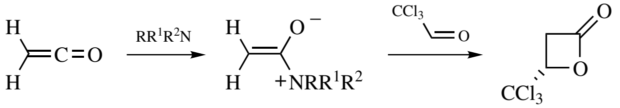
High stereoselectivity in [2+2] cyclization was achieved with the chromium-complexed ketene **62** generated by photolysis of the carbene complex EtOC-Me=$Cr(CO)_5$, which reacted with the enamine **63** bearing a chiral substituent to form **64** (equation 28).[69] Asymmetric benzannulations of chromium carbene complexes with chiral auxiliaries have also been observed.[70]



(28)

62 **63** **64**

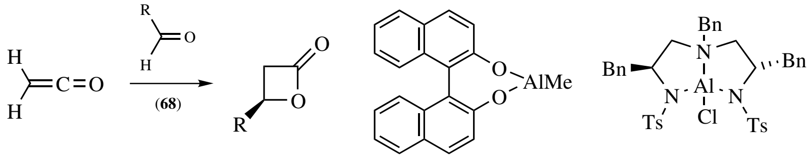
Ketenes gave effective [2+2] cycloaddition to aldehydes, and the reaction of $CH_2=C=O$ (**65**) with chloral catalyzed by optically active tertiary amines proceeded with high stereoselectivity, forming the β-lactone **67** (equation 29).[71–73] The stereoselectivity was attributed to formation of the chiral zwitterion **66** that reacts with chloral.



(29)

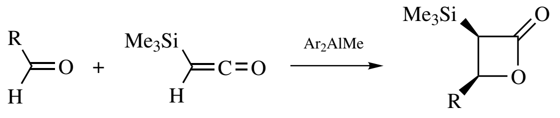
65 **66** **67** (95%, 98% *ee*)

Reactions of ketene with aldehydes **68** to form oxetanones **69** catalyzed by chiral 1,1′-binaphthalene-2,2′-diol aluminum catalysts **70** gave up to 56% *ee*, while the catalyst **71** gave up to 92% *ee* (equation 30).[74,75] Trimethylsilylketene (**73**) underwent [2+2] cycloaddition with aldehyde **72** promoted by a chiral catalyst Ar_2AlMe, forming **74** with high diastereoselectivity (equation 31).[76]



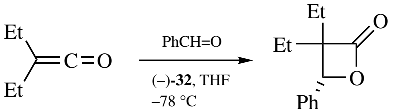
(30)

65 **69** (33–91%) **70** **71**



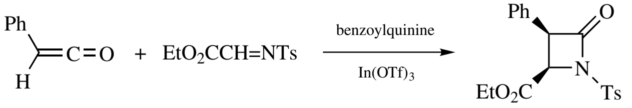
72 (R = *c*-Hx) **73** **74** (88%, 90:10 *dr*) (31)

Asymmetric synthesis using diethylketene (**75**) with catalyst (-)-**32** gave formation of the β-lactone with a quarternary carbon in 92% yield, 91% *ee* (equation 32).[77] The unsymmetrical ketene *i*-PrCMe=C=O (**76**) reacted with 91% *ee*, 48% yield, and 4.5:1 selectivity for the *cis*-lactone.[77]

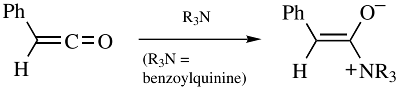


75 (92%, 91% *ee*) (32)

The asymmetric synthesis of β-lactams by [2+2] cycloaddition of ketenes with imines has received increasing attention.[9,78] Phenylketene (**77**) underwent stereoselective [2+2] cycloaddition with the imine **78** catalyzed by the chiral base benzoylquinine, and with In(OTf)$_3$ as an electrophilic cocatalyst gave the β-lactam product **79** in 95% yield, 98% *ee*, and 60/1 *dr* (equation 33).[79] Mechanistic analysis led to the conclusion that the benzoylquinine (R$_3$N) formed the zwitterionic enolate **80**, which reacted with the metal-coordinated imine (equation 34).[79,80] This reaction is discussed in more detail in Section 4.1.4. Molecular mechanics calculations have been used to predict the enantioselectivity of ketene [2+2] cycloadditions forming β-lactams.[81]

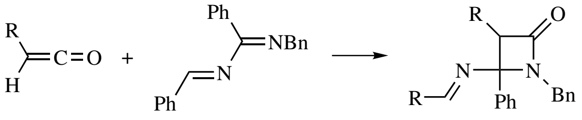


77 **78** **79** (95%, 98% *ee*) (33)

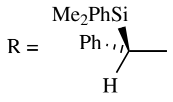


77 **80** (34)

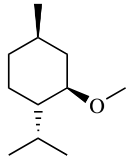
The chiral ketenes **81a–c** reacted with 1,3-diazabuta-1,3-diene by intermolecular [2+2] cycloadditions forming β-lactams with diasteriomeric excesses of 10, 10, and >95%, respectively (equation 35).[82] Chiral ketenes **81a,c** were also used for stereoselective [2+2] cycloadditions with imines RN=CR^{1}R^2 for the construction of chiral β-lactams with quarternary centers.[82a]



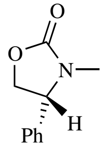
81 54–95% (35)



(**81a**)

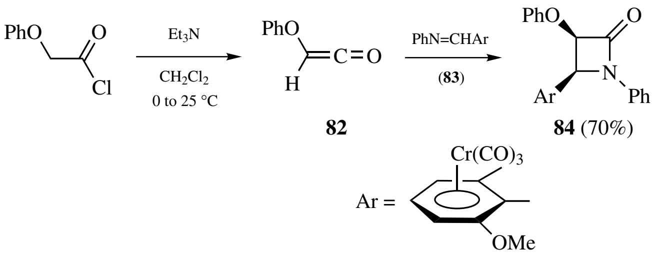


(**81b**)



(**81c**)

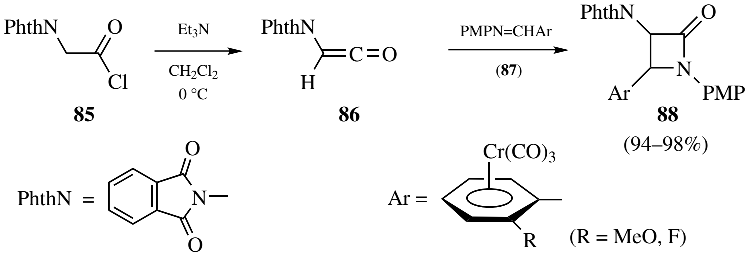
Chiral imines derived from *D*-glucose have been used in asymmetric synthesis of β-lactams by [2+2] ketene cycloadditions.[83] A chiral imine derived from (-)-ephedrine was also used.[84] Imines **83** with chiral chromium tricarbonyl complexes as substituents reacted with phenoxyketene (**82**) generated by dehydrochlorination forming the chiral β-lactam **84** (equation 36).[85]



(36)

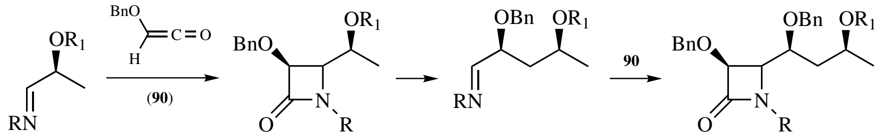
Ketenes **1**, **31**, and **31a** (Ar = Ph, R = *i*-Bu) reacted with imines and catalyst (−)-**32** to give β-lactams with ~10:1 *cis/trans* preference and 89–98% ee with Ar CH = NTs,[86] and 80:20 to 98:2 *trans/cis* preference and 63–99% ee with $Ar^1CH = NTf$.[87]

Arylimines **87** complexed with chromium tricarbonyl were used in completely stereoselective [2+2] cycloadditions forming β-lactams **88** with phthalimidoketene **86** generated from the acyl chloride **85** (equation 37).[88]



(37)

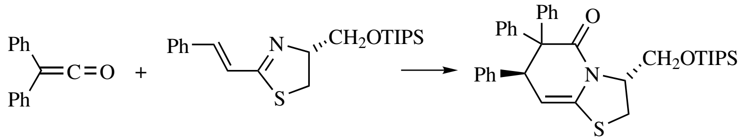
Benzyloxyketene (**90**) gave [2+2] cycloaddition to chiral imine **89** with formation of β-lactams **91** that was converted to imines **92**, which reacted again with **90**, forming the further β-lactams **93**, which were used in the synthesis of 1,3-polyols (equation 38).[89]



89 **91** **92** **93** (75%)

(38)

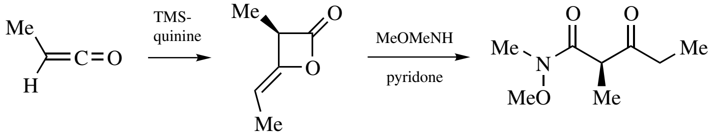
Diphenylketene (**94**) gave [4+2] cycloaddition with chiral 2-alkenyloxazolines and 2-alkenylthiazolines (**95**) with complete stereoselectivity in the formation of **96** (equation 39).[90] Stereoselective [3,3] Claisen rearrangements of the zwitterionic intermediates from ketene reactions with allylic ethers, thioethers, and amines to ketenes have been reviewed[91] and are discussed in Section 5.5.3.2.



94 **95** **96** (52%)

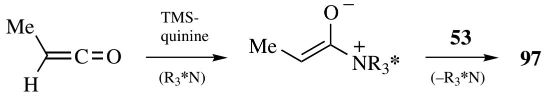
(39)

The dimerization of methylketene (**53**) generated by dehydrochlorination of propionyl chloride with diisopropylethylamine in CH_2Cl_2 at room temperature with 5 mol% trimethylsilylquinine as catalyst gave a 79% yield of the *R*-dimer **97** with 97% *ee*, isolated as the β-ketoamide **98** after reaction with methoxymethylamine (equation 40).[92] The dimerization was proposed to proceed by formation of a zwitterion **99** that reacted with a second molecule of **53**, forming **97** (equation 41).[92] Kinetic studies showed that formation of **53** from propionyl chloride was rate determining, with rapid formation of the dimer. Generation of **53** by pyrolysis of propionic anhydride gave the same selectivity for dimer formation, indicating that the dimerization involved two ketene molecules, and not propionyl chloride.



53 **97** **98** (79%
97% *ee*)

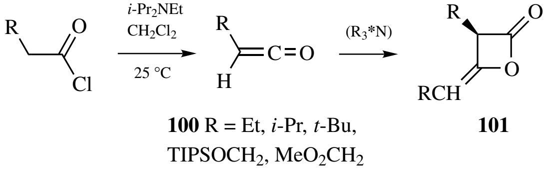
(40)



53 **99**

(41)

Dimers **101** of ketenes RCH=C=O (**100**, R = Et, *i*-Pr, *t*-Bu, $TIPSOCH_2$, MeO_2CCH_2, respectively) were prepared similarly in 58–88% yields, 91–96% *ee* (equation 42).[92]



(42)

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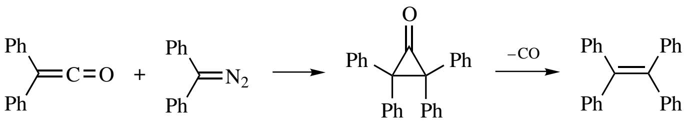
5.10 OTHER ADDITIONS TO KETENES

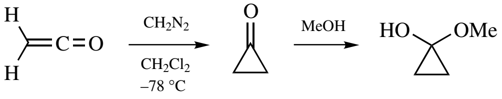
5.10.1 Reaction with Diazomethanes

The reaction of diphenylketene (**1**) with diphenyldiazomethane was found by Staudinger and Reber to form tetraphenylethylene (**3**), evidently through the formation of tetraphenylcyclopropanone (**2**) followed by decarbonylation (equation 1).[1] With less highly substitututed ketenes and diazoalkanes, a variety of more stable cyclopropanones have been prepared from the reactions of ketenes and diazoalkanes,[2–12] including the parent **5** from ketene, obtained in solution, and trapped with MeOH, giving a solution of the hemiacetal (equation 2).[4,5] Tetramethylcyclopropanone (**7**) was obtained in a similar fashion from dimethylketene (**6**, equation 3),[6] and methyl-,[6] 2,2-dimethyl-,[6] and trimethylcyclopropanone[8] were also prepared.



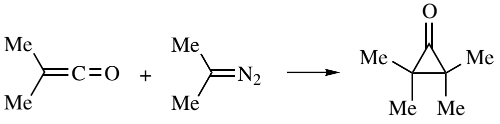
1 **2** **3**

(1)



4 **5** (90%) 98%

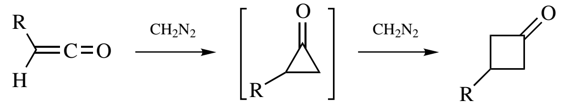
(2)



6 **7**

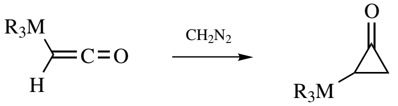
(3)

Cyclobutanones may be are formed in these reactions from insertion reactions of the diazoalkanes with the cyclopropanones, as in the conversion of **8** to **9** (equation 4).[8,9] Trimethylsilylketene (**10a**) and trimethylgermylketene (**10b**) gave the cyclopropanones **11** with diazomethane (equation 5),[10] and **10a** reacted with trimethylsilyldiazomethane to form **12**[13] (equation 6).[10–14]



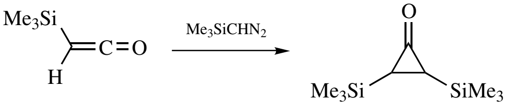
(4)

8 (**a** R = *t*-Bu, **b** R = *i*-Pr) **9**



(5)

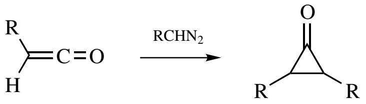
10 (**a** R$_3$M = Me$_3$Si, **b** R$_3$M = Et$_3$Ge) **11** (50%, R = Me$_3$Si)



(6)

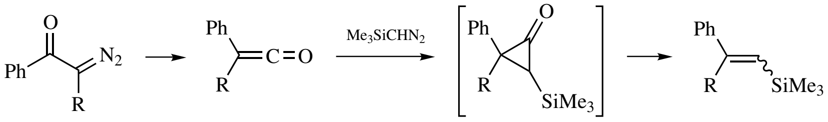
10a **12** (64%)

The reactions of *t*-BuCH=C=O (**8a**) and CH$_3$CH=C=O (**13**) with *t*-BuCHN$_2$ and CH$_3$CHN$_2$ to give cyclopropanones **14** have been studied experimentally (equation 7),[15] and the mechanisms of these processes have been elucidated with *ab initio* molecular orbital calculations.[15] Arylketenes **15** prepared by Wolff rearrangements reacted with Me$_3$SiCHN$_2$ through intermediate cyclopropanones **16** that underwent decarbonylation to give trimethylsilyl-substituted styrenes **17** (equation 8).[16]



(7)

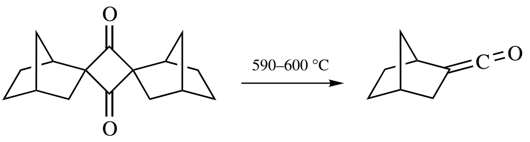
8a (R = *t*-Bu) **13** (R = Me) **14** (R = *t*-Bu, Me)



(8)

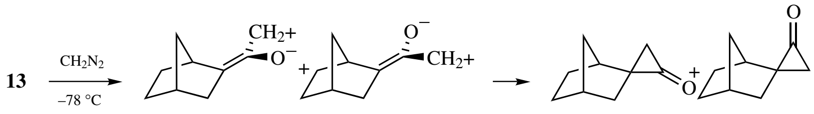
15 **16** **17** (12–60%)

Norbornylideneketene **19** was generated by pyrolysis of the dimer **18** (Section 3.1) and collected at 196 K (equation 9).[17] Reaction of **19** with diazomethane at 195 K gave the products **21a** and **21b** in a 1.6:1 ratio (equation 10).[17] The low preference for *exo* attack was not consistent with initial attack at C$_2$ of the norbornyl skeleton, but could have arisen from in-plane nucleophilic attack of the diazomethane at the carbonyl carbon to give oxyallyls **20a** and **20b**, which closed to **21** (equation 10). At higher temperatures **21a** and **21b** interconverted, and eventually reached an 0.8:1 equilibrium ratio.[17]



18 **19** (65%)

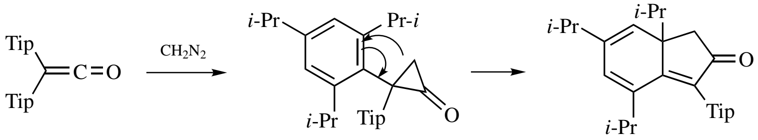
(9)



20a **20a** **21a** **21b**

(10)

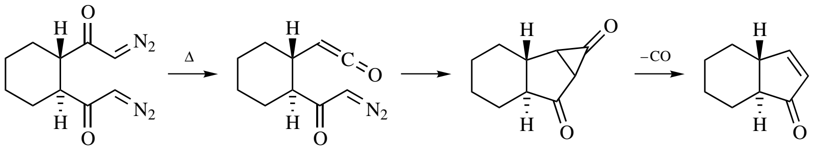
Reaction of bis(2,4,6-triisopropylphenyl)ketene **22** with diazomethane formed the unobserved cyclopropanone **23**, which rearranged to the isolated product **24** (equation 11).[18]



22 (Tip = 2,4,6-(i-Pr)$_3$C$_6$H$_2$) **23** **24**

(11)

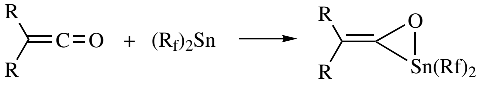
Thermolysis of the bis(diazo ketone) **25** was proposed to involve formation of ketene **26**, which reacted with the remaining diazo group, forming cyclopropanone **27**, followed by decarbonylation to give the enone product **28** (equation 12).[19]



25 **26** **27** **28**

(12)

Reaction of the stable diarylstannylene **30** with ketenes **29** gave three-membered stannocycles **31** (equation 13).[20] This reaction is also noted in Section 4.8.4.

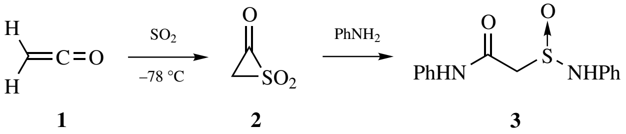


29 **30** R$_f$ = 2,4,6-(CF$_3$)$_3$C$_6$H$_2$ **31**

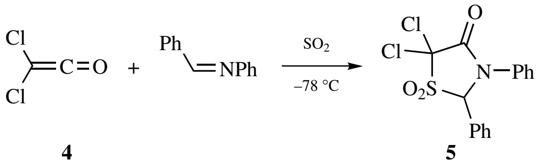
(13)

5.10.2 Reaction with Sulfur Dioxide

Sulfur dioxide reacted with ketene (**1**) at −78 °C to form a white solid that was identified as the cyclic adduct **2** on the basis of the ^1H NMR singlet observed at δ 2.30 at −67 °C in SO_2 and the formation of **3** upon reaction with aniline (equation 1).[21] Reaction of **1** with azines was also reported.[22] Dichloroketene (**4**) reacted with SO_2 and benzanilide to form **5** (equation 2).[23]

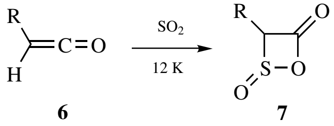


(1)



(2)

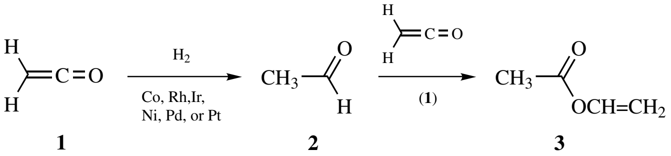
In contrast to the thermal [2 + 1] cycloaddition of ketenes with SO_2, the photochemical reaction in matrices at 12 K with **6** was found to give [2+2] cycloadducts **7** (equation 3).[24]



(3)

5.10.3 Hydrogenation of Ketenes

Ketene (**1**) is hydrogenated to acetaldehyde (**2**) using Group 9 (Co, Rh, Ir) or Group 18 (Ni, Pd, Pt) metal catalysts.[25] Reaction of acetaldehyde prepared in this way with further ketene provides a route to vinyl acetate (**3**) (equation 1).[26]



(1)

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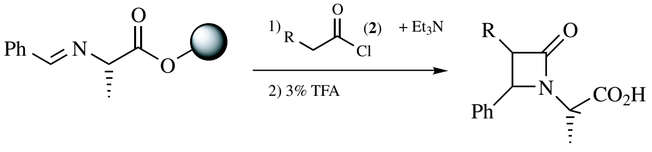
5.11 KETENE REACTIONS USING POLYMER SUPPORTS

Ketene reactions using polymer-supported reagents as well as reactions of polymer-supported ketenes have proven to be useful in synthetic and mechanistic studies, and a review of ketenes in polymer-assisted synthesis has appeared.[1]

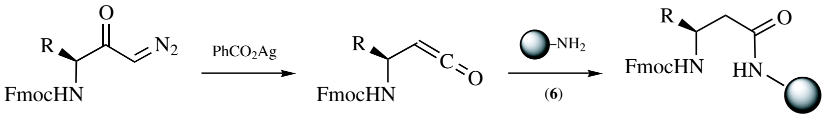
Solid phase–supported imines **1** derived from amino acids gave high diastereoselectivities in reactions with ketenes generated in solution from acyl chlorides **2** forming β-lactams **3** with *dr* ranging from 55:45 to 100:0 after cleavage from the resin (equation 1).[2] β-Lactams formed similarly in the solid phase have been converted to quinolones[3] and subjected to Suzuki and Heck cross-coupling reactions.[4]

Imines attached to soluble polyethylene glycol supports also formed β-lactams upon reaction with ketenes.[5] Resin-attached peptides **6** are acylated by ketenes **5** generated from Fmoc-protected, amino acid–derived diazo ketones **4**, forming **7** with β-amino acids added to the peptide chains in purities >90% (equation 2).[6] See also Section 3.3.1.[7] Soluble polymer supports have also been utilized in β-lactam formation.[8] Ketenes **8** formed by dehydrohalogenation reacted with Rink resin–supported imines **9**, giving resin-bound β-lactams **10** that were cleaved at nitrogen, yielding **11** (equation 3).[9]



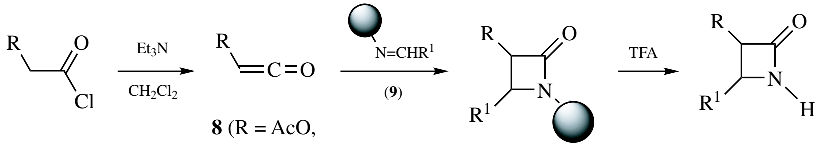
(1)

1 **3** (62–80%)



(2)

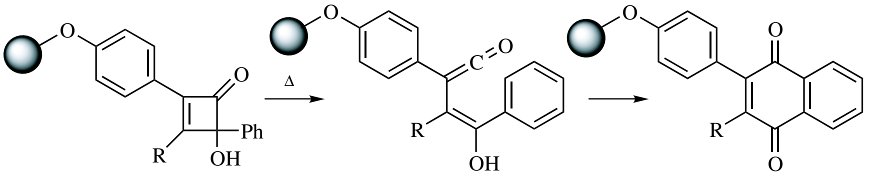
4 **5** **7** (80–95%)



(3)

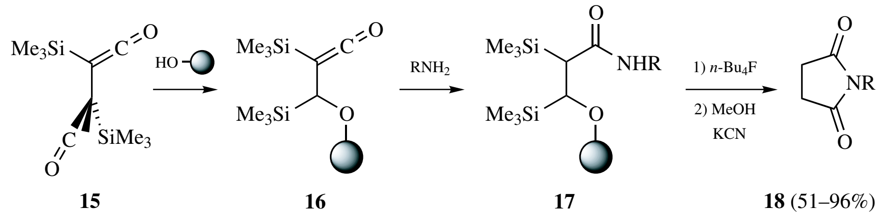
8 (R = AcO, PhO, BnO, PhthN) **10** **11** (55–97%)

Solid-supported cyclobutenones **12** upon ring opening formed supported alkenylketenes **13** (equation 4).[10] The ketenes were not observed directly but they participated in the formation of a variety of products, including cyclization to naphthoquinones **14** in 30–50% yields after cleavage from the resin (equation 4).[10] Ketene **16** prepared from bisketene **15** and monomethyl poly(ethylene glycol) was used in the preparation of succinamides **18** and 4-pyridones (equation 5).[11]



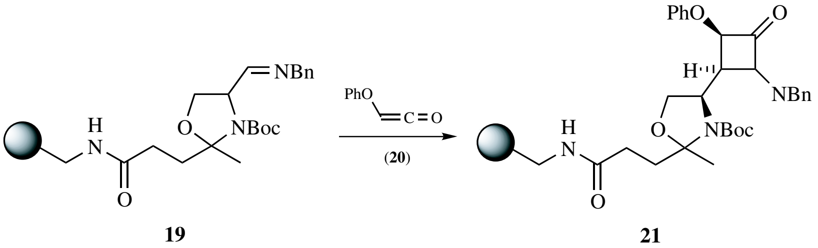
12 **13** **14** (30–50%)

(4)

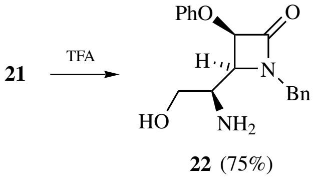


(5)

The chiral solid–supported imine **19** reacted with phenoxyketene (**20**) generated by dehydrochlorination of the acyl chloride to form the supported β-lactam **21** with high stereoselectivity (equation 6).[12] Cleavage from the resin gave the free β-lactam **22** (equation 7).[12]

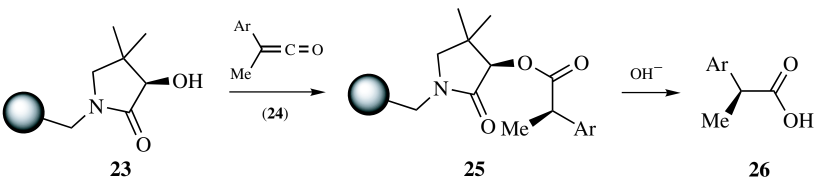


(6)



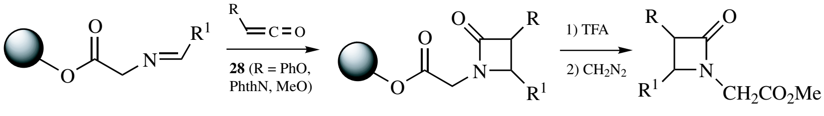
(7)

Ketenes ArCMe=C=O (**24**) generated in solution reacted with polymer-supported alcohols **23** to give stereoselective formation of esters **25**, which upon saponification gave optically active 2-arylpropionic acids **26** (equation 8).[13] Additions of polymer-supported chiral alcohols to aryl(phthalimidomethyl)ketenes provided a route to β-amino acid derivatives.[14]



(8)

Anionic polymerization of ethylphenylketene on polystyrene beads has been used in solid-supported synthesis of poly(methylmethacrylate).[15] Imine-substituted Wang resin **27** gave [2+2] cycloaddition with ketenes **28** formed by dehydrochlorination, yielding polymer-bound β-lactams **29** that were cleaved to yield the free β-lactams **30** (equation 9).[16]



(9)

27 **29** **30** (36–78%)

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