Carbene Chemistry

FROM FLEETING INTERMEDIATES TO POWERFUL REAGENTS

Edited by Guy Bertrand

MARCEL DEKKER

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The editor dedicates this book to his daughters
MARINE and MANON

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Preface

Robert A. Moss

If the reader will permit, I'd like to recall a short presentation that I made many years ago (in 1965) as a very young Assistant Professor to a 1-day Symposium on Carbene Chemistry held at Lewis College near Chicago. I vividly remember looking out at the first row and noting Jack Hine, William Doering, Phil Skell, and Gerhard Closs seated next to each other. At the time, I was petrified, but today, with the perspective afforded by 37 years, I recall the scene with gratitude that my first independent work could be presented before the founders of modern carbene research. Jack Hine's marvelous studies of the mechanism of haloform hydrolysis implicated dihalocarbenes as the key intermediates. Doering and Skell then established the electrophilicity of dichlorocarbene and dibromocarbene (respectively) in the archetypal carbene/alkene addition reaction. Doering also demonstrated the ferocious reactivity of methylene in carbon-hydrogen insertion reactions, while Skell explored the crucial experimental link between the stereochemistry of carbene/alkene addition reactions and the carbene's electronic state. Shortly thereafter, Closs demonstrated that various covalent lithium halide complexes of carbenes displayed much of the chemistry associated with carbenes but were not, in fact, free divalent carbon species. He called these carbene mimics "carbenoids", initiating an area of research that can now be seen to merge with studies of the structurally more well-defined metallocarbenes or carbene complexes.

The pioneering studies of Hine, Doering, Skell, and Closs were assimilated and integrated in several important texts. The classic early books of Hine (*Divalent Carbon*) and Kirmse (*Carbene Chemistry*) were followed by the volumes of Jones and Moss (*Carbenes, and Reactive Intermediates*). In the late 1980's, came the encyclopedic Houben-Weyl volumes, *Carbene(oide) Carbine*, edited by Manfred Regitz. And, in the past decade, three volumes of *Advances in Carbene Chemistry*, edited by Udo Brinker have been published. Numerous reviews on various aspects of carbene chemistry were interspersed between these important texts. Carbene chemistry has prospered and matured. Carbenes are no longer exotic mechanistic curiosities. Rapid kinetic techniques have made it possible to directly visualize them; state of the art computational methods now facilitate quite accurate calculations of their structures, energies, and spectroscopic properties. We are now in an era of “designer carbenes”, where precise synthetic use can be made of these highly energetic, but readily modulated intermediates.

Carbenes: From Fleeting Intermediates to Powerful Reagents highlights several aspects of the current scene. Moss traces the evolution of our understanding of carbenic philicity from electrophilic to nucleophilic and, finally, ambiphilic carbenes. Sander demonstrates how matrix isolation can be used to study exceptionally reactive electrophilic carbenes. Platz describes the use of pyridine ylides to follow reactions of carbenes on the micro to nanosecond time scale by laser flash photolysis. Tomioka shows how successive approximation in molecular design makes possible the synthesis of long-lived triplet carbenes. Bertrand and Alder each explore fine tuning of carbenic substituents to fabricate isolable singlet carbenes that retain key aspects of carbenic reactivity. Schrock and Dotz and Jahr illustrate the chemistry and synthetic utility of metal carbene complexes. Finally, Koga and Iwamura examine applications of carbenes in material science, specifically their magnetic properties.

In each case, our well-developed understanding of the relation between carbenic structure and reactivity permits us to harness the innate reactivity of very diverse divalent carbon species, converting them from “reactive intermediates” to useful reagents. The subtle control of carbenic reactivity demonstrated in the following pages is a tribute to years of incisive experimentation by many scientists. The four “founders” would be very pleased.

Robert A. Moss
Louis P. Hammett Professor
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Introduction

by R. R. Schrock

Carbenes, the simplest being CH_2, have fascinated and challenged chemists for decades. Although many carbenes are relatively short-lived, the generation and reactions of many carbenes can be controlled to a significant degree today. One way to "tame" a carbene is to attach heteroatoms to the carbene carbon; such species in fact can be isolated. In 1964 Fischer and Maasböl reported a different method of "taming" a carbene, by attaching it to a transition metal; the "metal-carbene complex", $(CO)_5W{=}C(Ph)OMe$, was prepared by a method that did not involve trapping of the carbene. Hundreds of examples of compounds that contain a heteroatom-stabilized (usually O or N) carbene ligand appeared in the next few years. The reactivity of these "low oxidation state" or "Fischer-type" carbene complexes led to the characterization of these species as "electrophilic carbene" complexes in which the M-C bond is polarized δ- on the metal and δ+ on the carbene carbon. Almost ten years later new types of carbene complexes (of tantalum) were isolated that did not contain any stabilizing heteroatoms; even a methylene complex could be isolated. However, the metal in these circumstances appeared to be in its highest possible oxidation state with the "carbene" behaving more like a dianion, with the metal-carbon bond being a full double bond, and with the metal-carbon bond being polarized δ+ on the metal and δ- on the carbene carbon. Therefore these species were called alkylidene complexes. One of these new species, $(Me_3CCH_2)_3Ta{=}CHCMe_3$, bore an obvious structural relationship to a phosphorus ylide and was remarkably thermally stable, melting at ~70°C and *distilling* readily in a good vacuum. In subsequent years many researchers attempted to put known and newly discovered carbene complexes into the "low" or "high" oxidation state category. However, many species defied and continue to defy such easy categorization. These categories are now recognized as extremes. But it was the reactivity patterns of carbene complexes that caught the imagination of chemists, and in particular the use of easily prepared Fischer-type complexes as stoichiometric reagents for making unusual organic molecules quickly, and the use of high

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oxidation state complexes (especially of Mo and W) as catalysts for the olefin metathesis reaction. Soon thereafter it was found that even “unstabilized”carbene complexes of later transition metals, in particular ruthenium carbene complexes, could be isolated and were not only relatively stable toward air and water, but still highly reactive in olefin metathesis reactions. Finally, although carbene complexes of metals such as copper are rare, they are believed to be intermediates in metal-catalyzed reactions involving diazo compounds that have become attractive for the synthesis of cyclopropanes. Yes, the carbene has been “tamed” by binding it to a transition metal, but wholly new and exciting reactions have been made possible that are helping to change the way some organic chemists approach organic syntheses. Clearly we have come far in the last four decades in terms of transition metal carbene chemistry. Two of the articles in this volume provide some flavor of what that journey has produced.

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Chapter 1

Matrix Isolation of Highly Electrophilic Carbenes

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1.1 BACKGROUND

The direct spectroscopic characterization of highly reactive carbenes has always been a challenge to physical organic chemistry. Over the past decades two complementary techniques proved to be most powerful to achieve this ambitious goal: time resolved absorption spectroscopy and matrix isolation spectroscopy. In solution at room temperature typical carbenes such as diphenylcarbene have lifetimes in the nanosecond regime. Nanosecond time resolved absorption spectroscopy is nowadays available in many laboratories and allows to follow the kinetics of carbene reactions. A large number of absolute reaction rates and carbene lifetimes have been recorded that way. [1] In most cases the spectroscopic information of this method is limited to the UV-vis region, although recently time resolved IR spectroscopy has also been used to observe carbenes. [2]

An entirely different approach to characterize carbenes is to immobilize these species in solid matrices – rare gas matrices or organic glasses – at very low temperatures (generally at 77 K or below). [3] This can most easily be achieved by freezing a solution of a photochemical carbene precursor in a solvent that forms an organic glass and generate the carbene photochemically. Alternatively, the carbene precursor and a large excess of a rare gas can be deposited on top of a spectroscopic window to form a matrix. Under these conditions carbenes are kinetically stabilized, since the thermal energy at low temperatures is not high enough to cross activation barriers larger than a few kcal/mol. In addition, the diffusion of molecules in the solid state is largely reduced, and therefore bimolecular reactions are suppressed.

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Spectroscopically clear solid solutions (organic glasses) are only achieved if the solvent does not crystallize, which drastically limits usable solvents. Due to the high reactivity of most carbenes only inert solvents (e. g. MTHF, methylcyclohexane, special Freon mixtures) can be used, and the most reactive carbenes can not be stabilized in organic glasses at all. Extremely electrophilic carbenes such as the fluorinated oxocyclohexadienylidenes (vide infra) rapidly react even in Freon at 4 K. The method of choice in these cases is the isolation of carbenes in low temperature inert gas matrices. The matrix isolation technique was developed almost fifty years ago by Pimentel et al. [4] and Norman and Porter. [5] Highly reactive carbenes have been among the first targets that were investigated using this technique [6] and meanwhile a large number of carbenes has been spectroscopically characterized in inert gas matrices. [3,7,8] In general, these matrices are generated by co-condensation of a photochemical carbene precursor (in many cases diazo compounds) with a large excess (typically 1 : 1000 – 2000) of the inert gas on top of a cold spectroscopic window. Alternatively, reactive species can be generated by flash vacuum pyrolysis of the precursor, followed by trapping of the products with a large excess of inert gas in a matrix. Flash vacuum pyrolysis has been proven to be less suitable for the generation of carbenes (only the most stable carbenes can be produced with that method), and in most cases the photochemical synthesis is the method of choice.

The most important matrix materials are argon or nitrogen, but neon, krypton and xenon are also used in special applications. The matrix gas determines the temperature range in which the matrix can be used. Below of about one third of the boiling temperature of the matrix material the matrix is very rigid and diffusion of trapped species is extremely slow. Above this temperature diffusion is more rapid and bimolecular reactions can be observed, as long as the thermal activation barrier is small enough. The usable temperature is limited by evaporation of the matrix into the high vacuum system. In practice, neon matrices are only usable to 8 K, and diffusion of trapped small molecules becomes rapid above 4 K. Xenon matrices, on the other hand, allow matrix temperatures up to 70 K without rapid evaporation. In argon matrices diffusion – and therefore bimolecular reactions – of small trapped molecules is induced by warming to 30 – 35 K. Above 40 K argon matrices evaporate rapidly.

Matrix isolation not only allows to the stabilization of carbenes for spectroscopic characterization, but also is a very powerful tool to study bimolecular reactions of carbenes under carefully selected conditions. A typical matrix experiment consists of several steps: photochemical or thermal generation of the carbene, investigation of the photochemistry at selected wavelength using monochromatic light, doping the matrix with a second reactant (e. g. molecular oxygen, CO, HCl), warming to induce bimolecular reactions, and investigation of the photochemistry of the thermal products. It is important to note that matrix isolation is basically a preparative technique, although using unusual conditions. The aim is to synthesize intermediates in high yields in sequential steps and to characterize these species spectroscopically.

A wide variety of spectroscopic methods, e. g. UV-vis, ESR, fluorescence, can be combined with the matrix isolation technique. However, by far the most important spectroscopic tool in inert gas matrices is IR spectroscopy. Due to the lack of interactions between isolated molecules and only weak interactions between trapped molecules and the matrix host, the IR absorptions of matrix isolated molecules are comparatively sharp (typical half widths in argon are about 2 cm^{-1}). In addition, rotations of molecules – except for very small molecules such as H_2O – are suppressed and thus all the intensity of an absorption is concentrated in a single line. This leads to an increase in sensitivity and spectral resolution of matrix IR spectra. In most cases the band positions are not much shifted relative to the gas phase values, and thus can be directly compared with data calculated by standard methods of computational chemistry. In fact, the tremendous increase in computational power and the improvement of algorithms, especially the development of powerful and reliable functionals for the DFT method, has let to an enormous improvement in the reliability of the results from matrix isolation studies. A good agreement between matrix IR spectra and vibrational data calculated using DFT or high level ab-initio calculations is meanwhile regarded as a "proof" for the existence of a compound. Especially the characterization of carbenes has profited tremendously from this successful interplay between experiment and theory.

1.2 THE CONCEPT OF PHILICITY

The philicity of singlet carbenes is an important concept to classify carbenes that was systematically studied by Moss. [9-11] The relative reactivity (selectivity) of a series of singlet carbenes in cyclopropanation reactions with electron rich and electron poor carbenes was used to quantify the carbene philicity. An empirical carbene philicity scale with a parameter m_{CXY} (where X and Y are the substituents at the carbene center) was defined (Figure 1). Electrophilic carbenes show m_{CXY} values below 1, nucleophilic carbenes above 2, and ambiphiles are between. [10] Ambiphilic carbenes act as an electrophile towards electron-rich alkenes and as a nucleophile towards electron-poor alkenes. The m_{CXY} values obey an empirical linear free energy relationship with the Taft substituent parameters σ_R^+ and σ_I. This allows to estimate the m_{CXY} values of unknown carbenes.

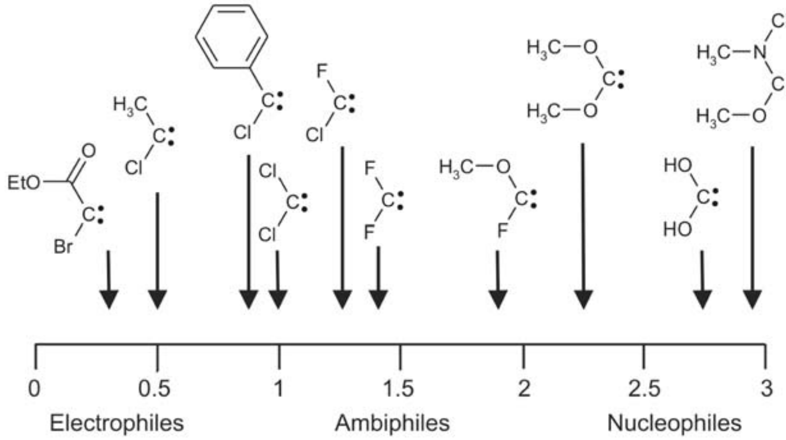


Figure 1. Carbene philicity spectrum as defined by Moss [10].

$$m_{CXY} = -1.10\sum_{X,Y}\sigma_R{}^{+} + 0.53\sum_{X,Y}\sigma_I - 0.31$$

A general problem in measuring m_{CXY} values is that only singlet ground state carbenes can be used, since the mechanism for cyclopropanation reactions with triplet carbenes is different (stepwise reaction via diradicals). Thus, only few studies on the philicity of triplet carbenes have been published. [12,13] Most singlet ground state carbenes contain σ-accepting and π-donating substituents such as halogen, oxygen, or nitrogen. Since these substituents lead to more nucleophilic carbenes, and most electrophilic carbenes have triplet ground states, strongly electrophilic carbenes are not easily accessible by this method.

A theoretical approach based on FMO theory was also proposed by Moss. [10] The differential orbital energies (differences of LUMO and HOMO energies of carbenes and alkenes) were correlated with the m_{CXY} values. If for a given carbene CXY the $\mathrm{LUMO}_{\mathrm{CXY}}$ – $\mathrm{HOMO}_{\mathrm{alkene}}$ differential energy was smaller than the $\mathrm{LUMO}_{\mathrm{alkene}}$ – $\mathrm{HOMO}_{\mathrm{CXY}}$ differential energy, the carbene CXY was considered to react as an electrophile toward this set of alkenes. For a nucleophilic carbene an inverse ordering of differential energies was expected. Indeed, in a number of cases a qualitative agreement between FMO predictions and the empirical carbene selectivity scale was observed. A major problem is that the LUMO energies depend very much on the theoretical method used and can not directly be compared to experimental values.

To overcome this problem we recently suggested to correlate the ionization potential (IP) and the electron affinities (EA) of carbenes with the carbene philicity. [14] IP and EA of carbenes can in principle be measured by negative ion photoelectron spectroscopy (NIPES), and data of a series of simple carbenes and vinylidenes were published by Lineberger et al. [15-23] The experimental data allow to evaluate the reliability of theoretical methods for the calculation of IP and EA. As shown in Table 1, there is a decent agreement between the experimental EA and calculations of the vertical EA of carbenes. The calculated adiabatic EAs are systematically too large by ca. 0.3 eV. However, if the adiabatic EAs are corrected by this value the agreement with the experiment is even better.

Table 1. Experimental and calculated electron affinities of a series of fluorinated carbenes and vinylidenes. Deviation of calculated EA from measured in parentheses.

Carbene	NIPES[a] EA	B3LYP[b] EA$_{\text{(calc, ad)}}$[c]	B3LYP[b] EA$_{\text{(calc, vert., neutral)}}$[d]	B3LYP[b] EA$_{\text{(calc, vert., anion)}}$[e]
FHC:	0.56	0.80 (0.24)	0.47 (-0.09)	1.20 (0.64)
Cl_2C:	1.60	1.89 (0.29)	1.46 (-0.14)	2.45 (0.85)
F_2C:	0.18	0.55 (0.37)	-0.02 (-0.20)	1.25 (1.07)
H_2C=C :	0.49	0.66 (0.17)	0.56 (0.07)	0.76 (0.27)
HFC=C:	1.72	1.96 (0.24)	1.98 (0.26)	2.33 (0.61)
F_2C=C:	2.26	2.53 (0.27)	2.16 (-0.10)	2.95 (0.69)

[a]Experimental EA from negative ion photoelectron spectroscopy (NIPES). [b]EA calculated at the B3LYP/6-311++G(d,p) level of theory. [c]Adiabatic EA. [d]EA at the geometry of the neutral carbene. [d]EA at the geometry of the anion.

Figure 2 shows the EAs and IPs, calculated at the B3LYP/6-311++G(d,p) level of theory for a number of carbenes. Typical stable nucleophilic carbenes show both small EAs and a low IPs and are located at the lower right quadrant of the diagram. Thus, nucleophilicity can be correlated with the IP, where a small IP means a large nucleophilicity. Electrophilic carbenes, on the other hand, have large EAs and large IPs, and are located at the opposite corner. Carbenes at the lower left corner of the diagram such as CF_2 are neither particularly nucleophilic nor electrophilic and in general of low reactivity. Carbenes at the upper right corner with a large EA and low IP have a small HOMO – LUMO gap and thus in general a triplet ground state. Although this scheme is still quite crude, it allows to classify carbenes and can serve as a guide on the search of carbenes with unusual properties.

The diagram shows two carbenes with a very high EA that are expected to be highly electrophilic: difluorovinylidene $F_2C{=}C$: **1b** as an example of an electrophilic singlet ground state carbene with an EA of 2.26 eV

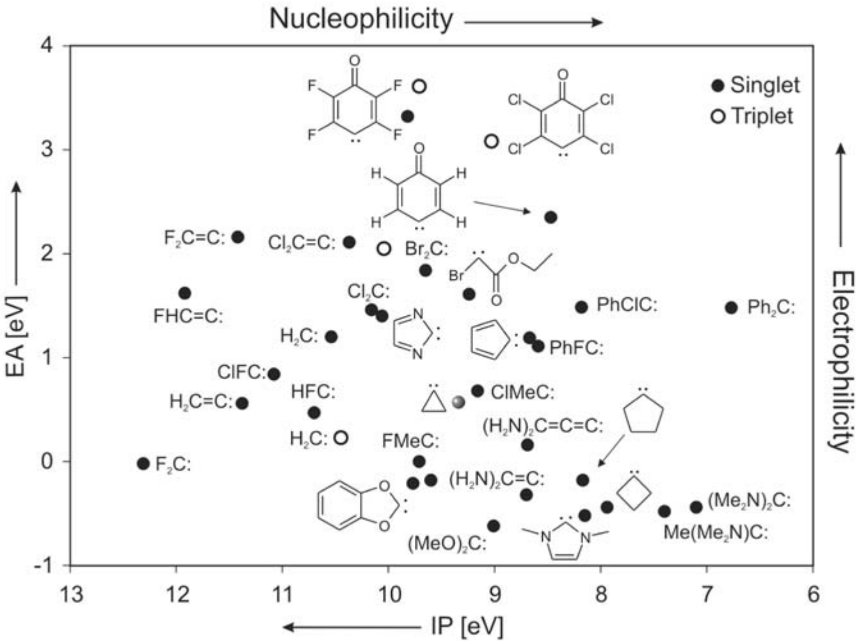
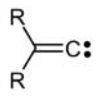


Figure 2. EA and IP of a series of carbenes calculated at the B3LYP/6-311++G(d,p) level of theory.



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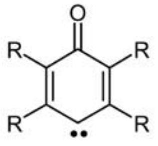

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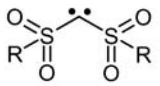

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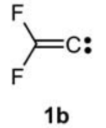
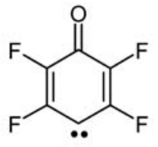


1b



2b

(experimental) [21] and 4-oxo-2,3,5,6-tetrafluorocyclohexadienylidene **2b** as a highly electrophilic triplet ground state carbene with an EA of 3.32 eV (B3LYP) [14]. In our search for carbenes with even higher electrophilicity we found that B3LYP calculations predict bis(sulfonyl)carbenes **3** to have EAs above 4 eV. These highly electrophilic carbenes have been studied in detail in our laboratory and are described in this chapter.

1.3 DIFLUOROVINYLIDENE

Vinylidenes **1** are in general very short lived intermediates that can only indirectly be identified by trapping reactions. The lifetime of these species is limited by the rapid migration of one of the substituents to give the corresponding acetylenes. For the parent vinylidene **1a** (R = H) *ab-initio* calculation predict a barrier of less than five kcal/mol, [24-26] and the lifetime in the gas phase was estimated to be in the order of picoseconds. [18,27] The barrier for the migration of halogen atoms, in particular fluorine atoms, is considerably higher, and the corresponding alkynes are thermodynamically destabilized by halogen substitution. This leads to both kinetic and thermodynamic stabilization of halogenated vinylidenes. This effect is most pronounced with fluorine substitution, and the barrier for the migration of a fluorine atom in **1b** was estimated to 35 – 40 kcal/mol (Figure 3). [28] Difluorovinylidene **1b** should be kinetically stable towards rearrangement and, as long as intermolecular reactions are excluded, isolable even at higher temperatures. It was thus our primary target for the matrix isolation of a vinylidene.

The electronic structure of vinylidenes differs mainly from that of other carbenes by the presence of an additional, low lying π orbital (Figure 4). Thus, while in carbenes two electrons can be placed in two close lying orbitals resulting in one triplet and three singlet electronic configurations, in vinylidenes four electrons share three close lying orbitals. However, since all known vinylidenes have singlet ground states, and since the p orbital at the carbene carbon is considerably higher in energy than the olefin π orbital and the σ carbene orbital, most of the chemistry can be understood by discussing the singlet $^1A_1$ configuration with filled π and σ orbitals and a vacant p orbital. This vacant p orbital (LUMO) lies in the plane of the substituents, in contrast to the most stable configuration of singlet carbenes, where the vacant p orbital is perpendicular to the plane of the substituents.

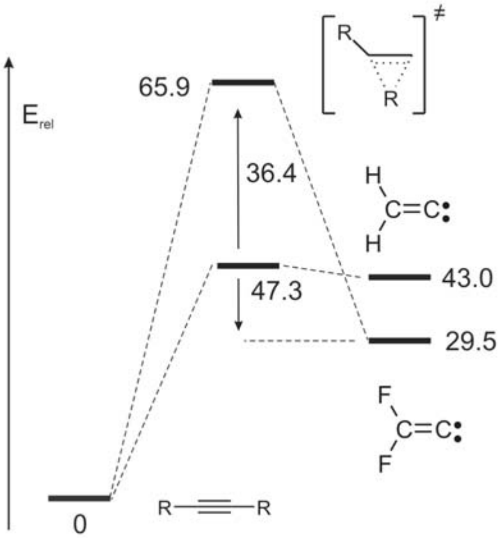
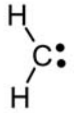
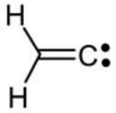
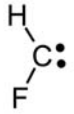
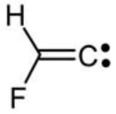
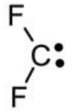
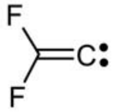


Figure 3. Reaction coordinate diagram for the rearrangement of vinylidene **1a** and difluorovinylidene **1b**.

Table 2. Singlet-triplet splittings ΔE_{ST} and electron affinities EA of the parent and the fluorinated carbenes and vinylidenes.

Carbene	ΔE_{ST} (kcal/mol)	EA (eV)	Vinylidene	ΔE_{ST} (kcal/mol)	EA (eV)
	-9.08	0.630		47.5	0.490
	14.9	0.542		30.4	1.718
	57	0.179		21.3	2.255

It is interesting to compare the influence of the fluorine substituents on the singlet triplet splitting ΔE_{ST} and the ionization potential EA in the vinylidenes $R_2C{=}C$: with that in the carbenes R_2C: (Table 2). [29,30] The σ accepting and π donating capability of fluorine atoms results in a stabilization of the in-plane σ orbital at the carbene carbon atom of R_2C: and destabilization of the π orbital, thus stabilization of the singlet state. While in H_2C: the triplet ground state is 9.08 kcal/mol more stable than the lowest singlet state, in F_2C: the singlet state lies 57 kcal/mol below the triplet. [19,20] The EA is reduced from 0.63 eV in H_2C: to 0.18 eV in F_2C:, again showing the π donating capability of fluorine atoms.

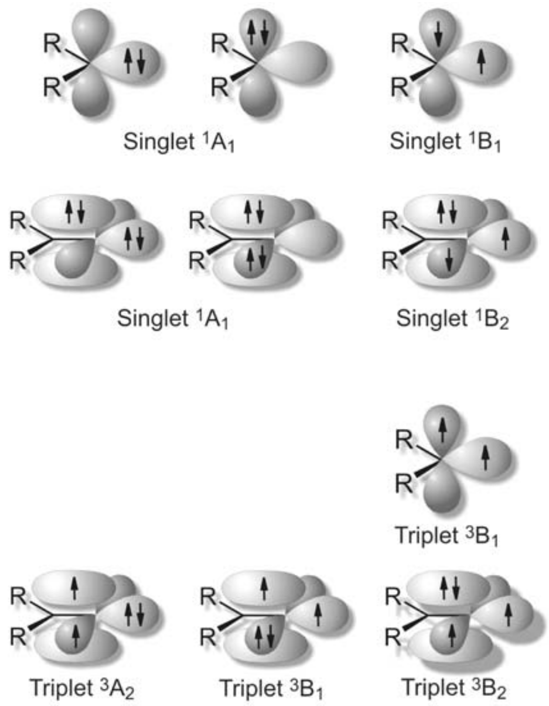
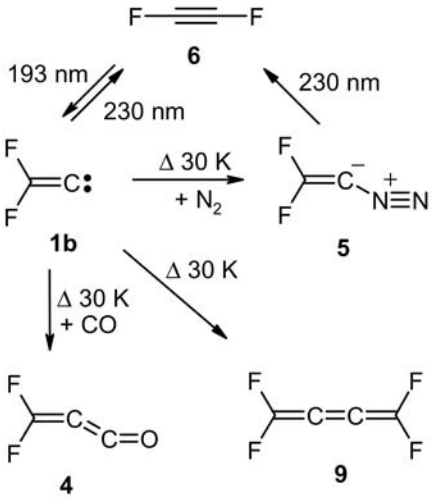


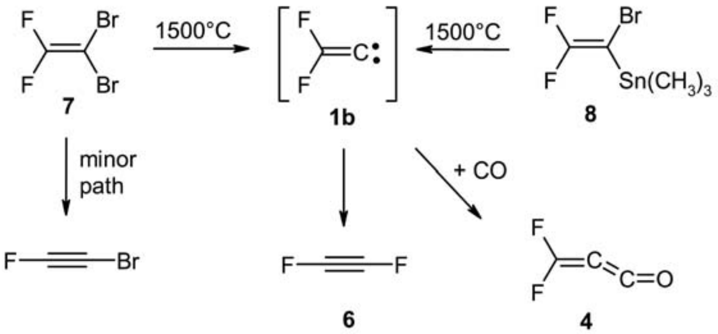
Figure 4. Important electronic configurations of carbenes and vinylidenes.

In $H_2C{=}C$: **1a** the singlet state lies 47 kcal/mol below the triplet. In contrast to the carbenes, fluorine substitution destabilizes the singlet state, although not enough to become the ground state. In $F_2C{=}C$: **1b** the singlet triplet splitting is reduced to 21 kcal/mol, which corresponds to a stabilization of the singlet state relative to the triplet state by 26 kcal/mol. [21] The EA, on the other hand, increases with fluorine substitution from 0.49 eV (**1a**) to 2.26 eV (**1b**), and thus **1b** is expected to be a highly electrophilic singlet carbene with interesting chemical properties. The reverse influence of fluorine (and other halogen) substitution in vinylidenes compared to carbenes reflects the in plane vs. out of plane position of the substituents with respect to the vacant p orbital.

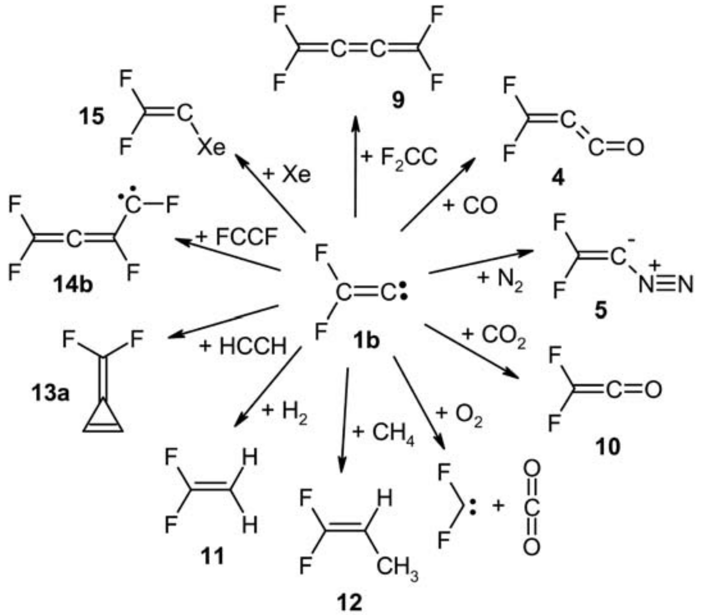
The extreme reactivity expected for **1b** reduces the number of suitable precursors for the matrix isolation of this species. Difluoropropadienone **4** as a precursor of **1b** was thoroughly investigated by Brahms and Dailey. [31] In argon at 10 K propadienone **4** proved to be photochemically stable and **1b** was not formed. However, in the presence of ^{13}CO the label was incorporated into **4**, and irradiation in a nitrogen matrix produced about 2% of difluorodiazoethene **5**. These results indicate that vinylidene **1b** indeed is produced during the photolysis of **4**, however, since **1b** and CO are formed in the same matrix cage, a rapid thermal recombination leads back to **4**. In the presence of N_2 **1b** is trapped and the diazo compound **5** is generated. Thus, due to the high thermal reactivity of **1b** towards CO the photochemical generation of **1b** from matrix-isolated **4** is very inefficient and does not allow the direct spectroscopic characterization of **1b**.



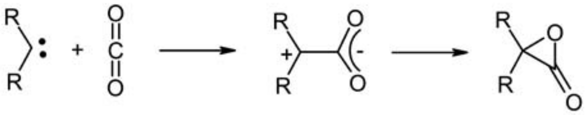
Alternatively, flash vacuum pyrolysis with subsequent trapping of the products in low temperature matrices of **4** or other thermal precursors should lead to matrix-isolated **1b**. Under these conditions **1b** and the by-products are isolated in separate matrix sites and thus the thermal recombination is prevented. Several attempts for the thermal generation of **1b** were reported, however, in all cases difluoroacetylene **6** was found as the only C_2F_2 species. Thus, pulse pyrolysis of dibromodifluoroethylene **7** or the stannyl compound **8** produces **6** as the main product. [32] If CO is added in the gas phase, propadienone **4** is generated as an additional product, which indicates that **1b** is formed as a reactive intermediated in the gas phase that is long-lived enough to be trapped by CO.

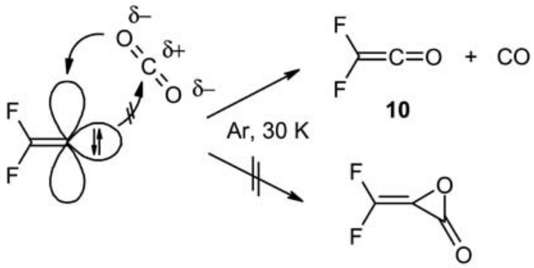


The only method that allowed the matrix isolation of **1b** so far is the vacuum UV photolysis of difluoroacetylene **6**. [33] Difluoroacetylene **6** exhibits a UV absorption with a maximum < 200 nm that shows a tailing to 250 nm. Irradiation of matrix-isolated **6** with the 193 nm light of an ArF excimer laser produces a new species in high yields that was identified as vinylidene **1b**. All fundamental IR vibrations of **1b** were observed experimentally, and band positions and relative intensities could be nicely reproduced by DFT and *ab-initio* calculations.



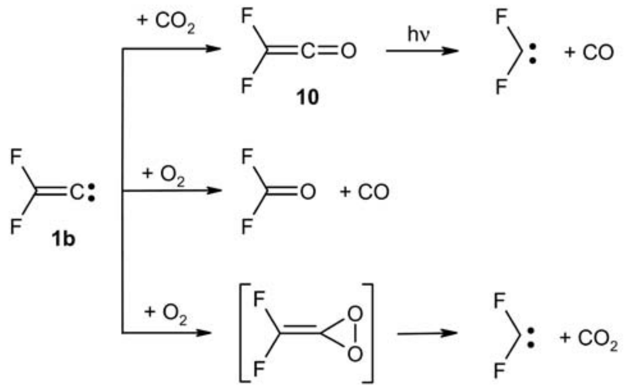
This simple synthesis of vinylidene **1b** allowed to study its reactions with a variety of small molecules. [30] To allow bimolecular reactions in rigid inert gas matrices, at least one of the reactants has to diffuse in the matrix. As described above, the diffusion of small molecules can be controlled by the matrix temperature. Vinylidene **1b** is completely stable in an argon matrix at 10 K, however, if the matrix is allowed to warm above 30 K, all IR absorptions of **1b** disappear and absorptions of tetrafluorobutatriene **9**, are growing in. [34] This clearly demonstrates that in an argon matrix at 35 K vinylidene is mobile enough to diffuse and that the barrier for the dimerization is zero or close to zero.





If the matrix is doped with ca. 1% CO or N_2, warming to 35 K produces only small amounts of butatriene **9**, and the main products are now propadienone **4** or diazo compound **5**, respectively. Both the reactions of **1b** with CO and N_2 are highly exothermic and occur without an activation barrier. As a matter of fact, since in most experiments the argon matrix is contaminated with traces of N_2 from small leaks in the vacuum system, the formation of **5** during warm-up of matrices containing **1b** is hard to avoid. According to calculations, both adducts show large deviations from linearity. Propadienone **4** exhibits a CCO angle of 140° and diazo compound **5** a CNN bond angle of 120°. [31,34,35]

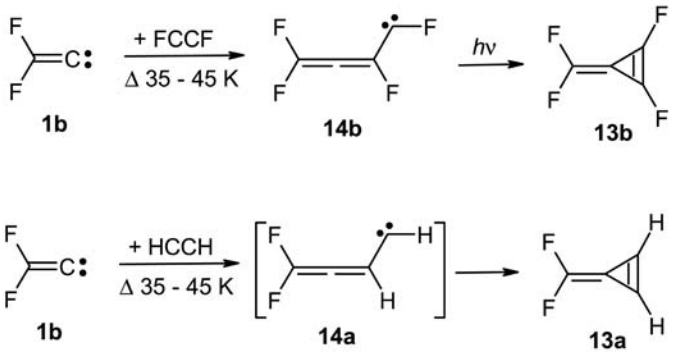
The reaction of carbenes with CO_2 under the conditions of matrix isolation allows to qualitatively estimate the philicity of carbenes. [36] The initial step of this reaction is the nucleophilic attack of the carbene at the CO_2 carbon atom. The primary adduct subsequently rearranges to give an α-lactone which is easily identified by IR spectroscopy. [36] Since carbenes act as a nucleophile in this reaction, the reactivity increases with increasing carbene nucleophilicity, and electrophilic carbenes like **2a** (R = H), despite being of very high reactivity towards a variety of reactants (see below), can not be carboxylated. We thus expected **1b** also to be unreactive towards CO_2 and were surprised that **1b** rapidly reacted in CO_2-doped argon matrices.



The product, however, is not the expected α-lactone, but rather difluoroketene **10** and CO are formed. [37] Obviously, vinylidene **1b** abstracts an oxygen atom from CO_2 without a noticeable activation barrier, a reaction which is estimated by DFT calculations to be exothermic by 38 kcal/mol. This unprecedented reactivity very clearly demonstrates the enormous electrophilicity of **1b**. The reaction is governed by the low-lying LUMO which interacts with the lone pairs at the CO_2 oxygen atoms and not by the vinylidene HOMO. Difluoroketene **10** is a highly labile intermediate that in an almost thermoneutral reaction fragments to CF_2 and CO. Unsuccessful attempts for the synthesis of **10** were reported in the literature, [38] and in all cases only the fragmentation products CF_2 and CO were found.

The reaction of **1b** with molecular oxygen also differs from that of other carbenes. [8] In O_2-doped argon matrices carbenes react with $^3O_2$ to give carbonyl *O*-oxides as the primary products. For triplet carbenes this reaction in general is very fast (controlled by the diffusion of the trapped species in the matrix) while singlet carbenes react much slower in a formally spin-forbidden reaction. [39,40] The oxidation of difluorovinylidene **1b** with $^3O_2$ results in a complex product mixture with CF_2, C_2F_4, CO_2 , COF_2 and CO as the major products, indicating secondary fragmentation reactions. [37] The primary products of the addition of O_2 to **1b**, a carbonyl oxide or a dioxirane, were not observed. Presumably these species directly fragment to CF_2 and CO_2 or CF_2O and CO. Secondary thermal reactions of the various intermediates subsequently lead to the observed product mixture.

The high electrophilicity of **1b** is also demonstrated by the barrierless insertion into H_2, D_2, CH_4, and CD_4 to produce the difluoroolefins **11** and **12**, respectively.[41] A rapid insertion into H-H and C-H bonds is only expected for highly electrophilic singlet carbenes. [14] Recently Zuev and Sheridan reported that triplet carbenes and open-shell singlet carbenes also insert into H_2 in low temperature matrices, but not into D_2. [42] Since calculations predict an activation barrier of several kcal/mol for these reactions, a tunneling mechanism was proposed. Singlet closed-shell carbenes were not observed to insert into H_2 under similar conditions. This clearly demonstrates the exceptional reactivity of vinylidene **1b**, which readily inserts into both H_2 and D_2. This is backed by calculations at the MP2 or DFT level of theory which predict for the insertion of **1b** into H-H and C-H bonds very shallow or no activation barriers, while for the parent vinylidene **1a** substantial barriers are expected. [41]



Interesting reactions of **1b** are additions to acetylene HCCH and difluoroacetylene FCCF. The reaction with HCCH directly leads to the methylenecyclopropene **13a**, and no other intermediates are observed. [43] In contrast, the reaction with FCCF yields allenylcarbene **14b** as the primary thermal product. Visible light irradiation is required to induce the rearrangement to the corresponding methylenecyclopropene **13b**. This clearly demonstrates that the formation of the methylenecyclopropene is a two-step reaction with carbene **14b** as an intermediate.

With more than 80 kcal/mol, according to B3LYP calculations, the formation of **14b** is very exothermic, while the cyclization of **14b** to **13b** releases only 18 kcal/mol. The fluorine substituent at the carbene center in **14b** leads to a highly stabilized ground state singlet carbene. In contrast, carbene **14a** is expected to have a triplet ground state, and according to DFT calculations the singlet state is not even a minimum on the potential energy surface. Thus, even if the reaction mechanisms of the addition of **1b** to HCCH and FCCF are similar, carbene **14a** would be formed in a spin-allowed reaction in its singlet state and rapidly rearrange to **13a** rather than produce triplet **14a** via intersystem crossing. Indeed, calculations by Cremer [44] indicate that the addition of vinylidene **1a** to HCCH proceeds via a structure similar to an allenylcarbene, which, however, is no stationary point on the potential energy surface.

Table 3. IR data of difluorovinylidene **1b** in neon and argon matrices and in argon matrices doped with 0.5% krypton and xenon, respectively, after annealing at 40 K. The experimental data are compared with results from a CCSD(T) calculation.

Sym.	Assignment	CCSD(T)[a]	Neon	Argon	Krypton	Xenon[b]
a_1	ν_1, C=C str	1693	1678	1672	1669/1670	1620
	ν_2, C-F str sym	927	918/921	916/918	915	898
	ν_3, CF_2 scissors	512		511		
b_1	ν_4, C-F str asym	1287	1268/1271	1264/1267	1262/1264	1220
	$\nu_2 + \nu_5$	1247	1254 ?	1245	1244/1246	
	ν_5, CF_2 rock	323		(334)		
b_2	ν_6, CF_2 wag	560		552		

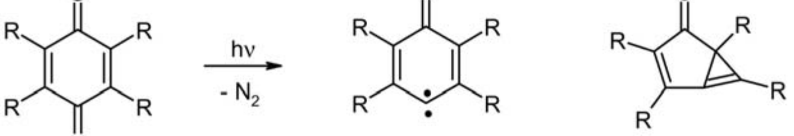
[a] Ref. [45]. b Ref. [46]

The ultimate reaction of an electrophilic carbene would be the formation of noble gas adducts, e. g. the reaction with xenon should lead to R_2C=Xe (a “xenone”). Since **1b** was generated in argon matrices, and the IR data of **1b** in argon are nicely reproduced by theoretical calculations for **1b** in the gas phase, the interaction between **1b** and argon obviously does not exceed usual matrix effects. In solid neon matrix effects are expected to be smaller, and indeed the IR absorptions are slightly closer to the calculated data (Table 3). The largest effect was observed for the C=C str. vibration which is shifted from 1672 cm^{-1} in argon to 1678 cm^{-1} in neon, the CCSD(T) calculated [45] value is 1693 cm^{-1}.

Xenon has a lower ionization potential than argon, and thus there should be a chance for a reaction with **1b**. Irradiation of difluoroacetylene in solid xenon at 10 K with the 193 nm light of an ArF excimer laser, however, was very disappointing, since under these conditions the FCCF did not rearrange, and no trace of the vinylidene **1b** was formed. This could be due to the filtering effect of the xenon matrix. Therefore, we repeated the experiment using FCCF in an argon matrix "capped" with solid xenon. The light had now to pass the xenon layer before photolyzing the FCCF. Now the FCCF rapidly rearranged to **1b**, clearly excluding a filtering effect of xenon. Finally, the experiment was repeated using a 0.5% xenon-doped argon matrix. Irradiation of FCCF at 10 K produced **1b** in high yields. Subsequent annealing of the matrix at 40 K resulted in a decrease of all IR absorptions assigned to **1b** and formation of a new product **15**, obviously a thermal adduct between **1b** and xenon. [46] All vibrations in this adduct are significantly shifted, the largest shift of 52 cm^{-1} (compared to argon) was found for the C=C stretching vibration. According to *ab-initio* calculations, the adduct **15** is highly bent with Xe-C-C bond angle of approximately 100° and stabilized by a few kcal/mol. Although this is definitely not a "xen-one", it is an interesting charge-transfer complex with a distinct IR spectrum, again revealing the reactivity of **1b**.

1.4 4-OXO-2,3,5,6-TETRAFLUOROCYCLOHEXADIENYLIDENE 2B

It is interesting to compare the reactivity of difluorovinylidene **1b**, a prototype of a highly electrophilic singlet carbene, with that of an electrophilic triplet carbene. 4-Oxo-cyclohexadienylidenes **2** are electron-deficient triplet carbenes, and a large number of these species was investigated in our laboratory. [47] Here we describe the most electrophilic of these cyclohexadienylidenes, the 4-oxo-2,3,5,6-tetrafluorocyclohexadienylidene **2b** with a calculated EA of 3.32 eV in its triplet ground state. [48,49]

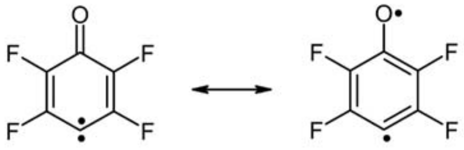


2a R = H
2b R = F

16

The 4-oxocyclohexadienylidenes **2** are readily synthesized in inert gas matrices by visible light irradiation of the corresponding matrix-isolated diazo compounds (quinone diazides). The parent carbene **2a** and many derivatives form photostationary equilibria with highly strained cyclopropenes **16**. [50,51] This type of rearrangement is not observed for the perfluorinated carbene **2b**, which makes the investigation of its chemistry simpler. According to DFT calculations, the closed shell $^1A'$ symmetrical singlet state is 3.9 kcal mol^{-1} higher and the open shell $^1B_1$ symmetrical singlet 7.4 kcal mol^{-1} higher in energy than the $^3B_1$ triplet state. [48] The fluorine substitution does not change the relative energies of $^3B_1$ ground and $^1B_1$ excited state. However, the closed-shell singlet state in **2b** is strongly stabilized (planar form: 7.8 kcal/mol) so that the C_s-symmetrical $^1A'$ state becomes lower in energy than the open-shell $^1B_1$ state, whereas in **2a** the open-shell singlet is more stable than the closed-shell singlet.

The prediction of a triplet ground state for **2b** was verified by the observation of its triplet ESR spectrum in solid argon at 15 K. [49] In organic glasses, even Freon, at 4 K only radicals but no triplet carbene was observed. This demonstrates the higher reactivity of **2b** compared to **2a**, which can be easily detected after irradiation of the diazo precursor as a powder sample [52] or in an organic glass. The electronic structure of **2b** can be described in terms of a carbenic and a diradicaloid resonance structure with one electron localized in the σ-plane (similar to a phenyl radical) and one electron delocalized in the π-system (similar to a phenoxyl radical).

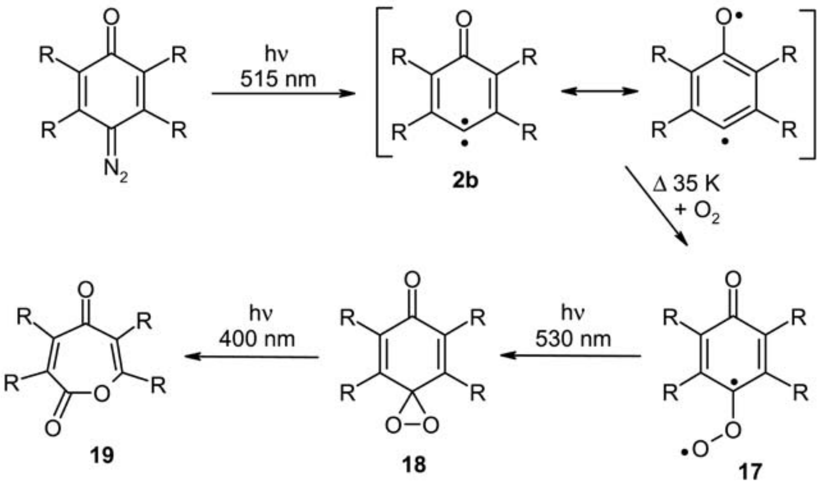


2b

The reaction of **2a** with N_2 is predicted by DFT calculations to be strongly endothermic, while that of **2b** is predicted to be exothermic, indicating a large destabilization of the carbene with respect to the diazo compound by the fluorine substitution. Despite this, the thermal reaction between **2b** and N_2 could not be observed, presumably because of a thermal activation barrier for this formally spin-forbidden reaction. The reaction of both carbenes **2a** and **2b** with CO to give the corresponding ketenes, on the other hand, proceeds rapidly on annealing CO-doped argon matrices. [48]

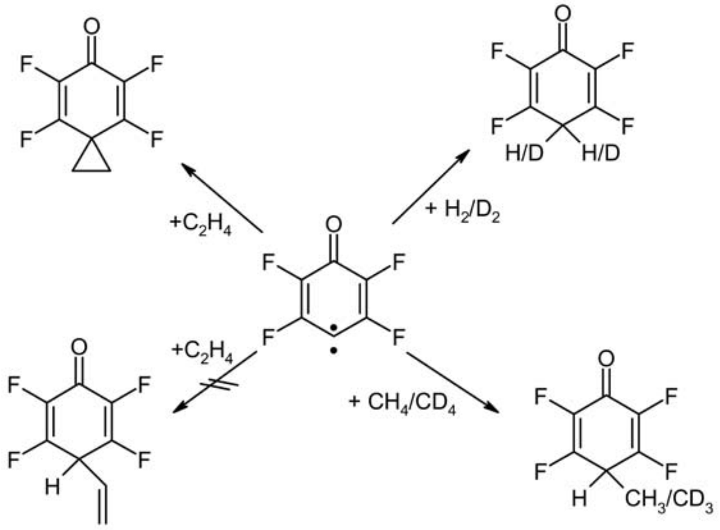
The thermal reaction of **2b** with molecular oxygen produces, as expected for a triplet ground state carbene, the quinone *O*-oxide **17**. This carbonyl oxide is extremely photo-labile and irradiation with red light rapidly produces the spiro dioxirane **18**, which on shorter wavelength irradiation yields the lactone **19**.

Thus, the reaction of triplet carbenes with $^3O_2$ seems to be largely independent of the philicity of the carbene and always leads to a carbonyl oxide.



The insertion reaction of **2a** into H_2 but not into D_2 under the conditions of matrix isolation has been recently described. [53] In contrast to **2a**, however, the fluorinated carbene **2b** also rapidly inserts into D_2 which indicates its increased electrophilicity. According to DFT calculations, this insertion proceeds on the singlet surface without barrier and is highly exothermic. The thermal insertion of matrix-isolated triplet carbenes into H_2 but not into D_2 was taken by Sheridan and Zuev as an indication for a tunneling mechanism. This indicates that carbene **2b** inserts into H-H and C-H bonds without assistance by a tunneling mechanism. This leaves us with the question at which point along the reaction coordinate the intersystem crossing from the triplet to the singlet surface takes place. A possible interpretation would be that the singlet – triplet splitting in **2b** is even smaller than predicted by the calculations and the singlet state is thermally populated to a certain amount even at temperatures below 40 K.

The reaction of carbene **2b** with ethylene exclusively leads to the cycloaddition reaction (formation of a cyclopropane) and not to a C-H insertion. This is in accordance with DFT calculations which predict a small thermal activation barrier for the insertion of **2b** into a C-H bond at an sp^2 hybridized carbon atom, whereas there is no barrier for the addition of **2b** to the double bond of ethylene to give a triplet diradical. The diradical is expected to have a very small singlet triplet splitting, and ISC to the singlet diradical should readily lead to ring-closure to the cyclopropane.



Carbene **2b** rapidly reacts with acetylene to vinylcarbene **20** as the primary thermal product. [49] This carbene to carbene reaction could be directly followed by ESR spectroscopy. The extensive delocalization of the unpaired π-electron in **20** results in a small zero-field splitting parameter D of 0.2047 cm^{-1} and an intense red color. Carbene **20** is thermally stable at cryogenic temperatures but rapidly rearranges to spiro-cyclopropene **21** on irradiation into the visible absorption. Thus, as with vinylidene **1b**, the reaction of carbene **2b** with acetylene to the corresponding cyclopropene is a two-step reaction with a carbene as the primary intermediate. The major difference is that the reaction of triplet **2b** with acetylene produces triplet carbene **20** and the photochemical ring-closure to **21** requires an ISC step to the singlet surface. In the case of the reaction of **1b** with acetylene no triplet species is involved and the whole reaction sequence proceeds on the singlet surface. Independent of the spin state of the carbene, the first step is the electrophilic addition of the carbene to one of the acetylene carbon atoms forming a second carbene in a spin allowed reaction. This carbene can be trapped as an intermediate if it is a stable singlet on the singlet path or triplet on the triplet path. The ring-closures of these carbenes require an additional thermal or photochemical activation. [49]

In contrast to the singlet vinylidene **1b,** the triplet carbene **2b** does not form a complex with xenon that exhibits a distinct IR spectrum. The formation of such a weakly bound complex requires a vacant, low lying orbital of a closed-shell singlet carbene as in **1b**. The lowest closed shell singlet state of **2b** is 3.9 kcal mol^{-1} above the triplet, which is about the expected stabilization energy of the complex.

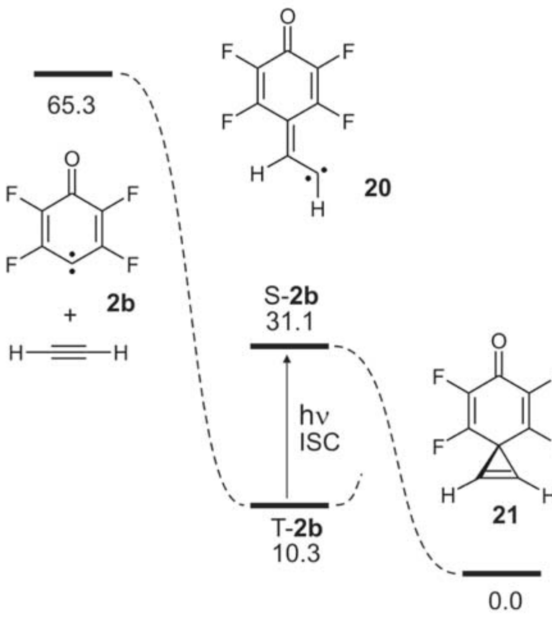
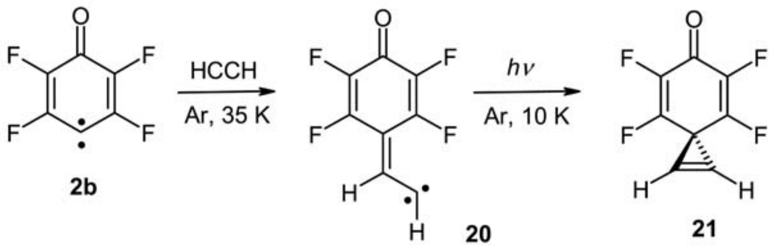
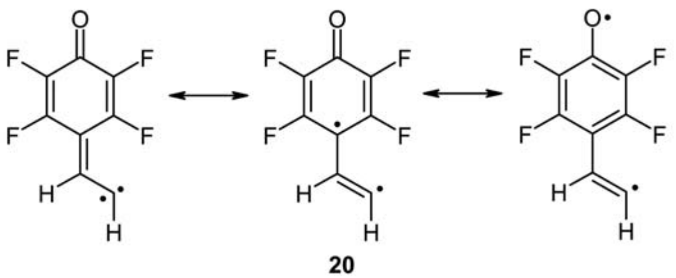


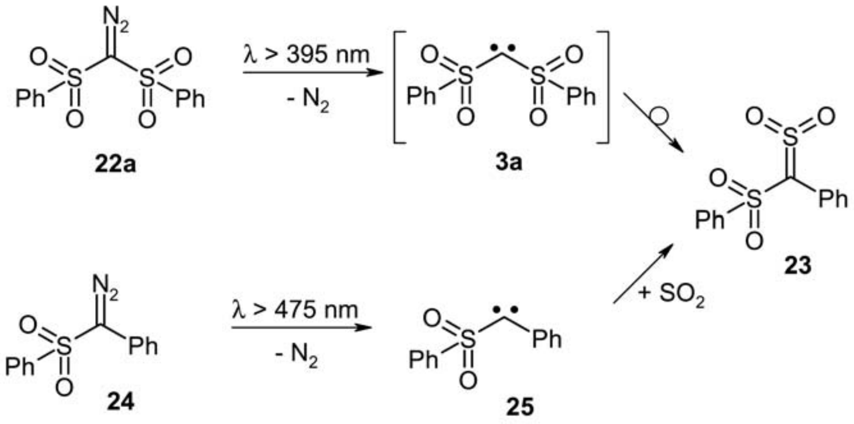
Figure 5. Energetics of the reaction of carbene **2b** with acetylene calculated at the B3LYP/6-311++G(d,p) level of theory.





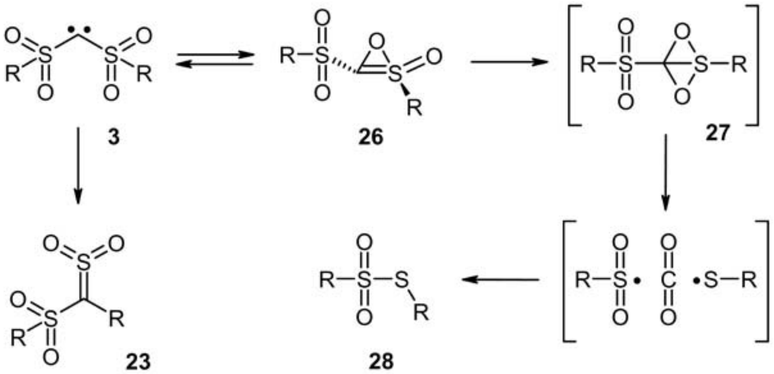
1.5 SULFONYL CARBENES

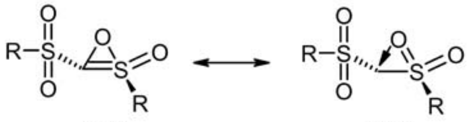
The sulfonyl substituent is another powerful electron withdrawing group that should result in highly electrophilic carbenes. Indeed, DFT calculations predict very high electron affinities for sulfonylcarbenes **3**: for the triplet ground states of $(HSO_2)HC$: and $(HSO_2)_2C$: electron affinities of 2.1 and 4.5 eV, respectively, were calculated. [54] Thus, bissulfonylcarbenes should be among the most electrophilic carbenes and exhibit unusual reactivities. Another point of interest is that the diazo precursors **22** of these carbenes are used as key components of new photoresists for deep UV lithography. [55,56] During photolysis of these photoresists sulfonic acids are formed which are capable of crosslinking acid sensitive compounds in negative tone materials. Although it is very likely that sulfonyl carbenes play an important role in the production of the sulfonic acids, only few systematic studies on the chemistry of these carbenes have been published. [54,55,57] In our laboratory the photochemistry of a series of sulfonyl diazomethanes **22** was investigated in argon matrices.



A typical example is the phenyl-substituted derivative **22a**. [54] Photolysis in an argon matrix results in a product mixture with sulfene **23** as one of the major products. Sulfene **23** is formed via rearrangement of carbene **3a** (hetero Wolff-Rearrangement), which, however, could not be observed spectroscopically in the matrix. The assignment of **23** was confirmed by an independent synthesis from diazo compound **24** via carbene **25**. In SO_2-doped matrices this carbene is rapidly trapped under formation of **23**.

Another indirect hint for the formation of carbene **3a** as an intermediate comes from trapping studies in solution. In hydrocarbons, e. g. cyclohexane, the major products are formed by insertion of **3a** into C-H bonds. In acetonitrile, on the other hand, compounds of type **28** are the main products.




26 A **26** B

Carbenes **3** could not be detected in low temperature matrices, irrespective of the substituent R. However, together with sulfene **23** other products were formed which, based on comparison of experimental with calculated IR spectra, were tentatively assigned to the oxathiirene oxides **26**. These compounds can either be regarded as an interesting new class of highly strained heterocycles (structure **26** A) or as intramolecularly stabilized singlet carbenes **3** (structure **26** B). The calculated CO bond length of 1.728 and 1.655 Å in the three-membered rings of *cis* and *trans* **26**, respectively, is much longer than expected for typical CO single bonds and indicates the importance of resonance structure **26** B. Still another unusual structure – the doubly bridged **27** – has been predicted by the calculations to be an energy minimum. This structure can explain the loss of CO_2 from carbene **3** – which requires the migration of two oxygen atoms from sulfur to carbon – and formation of **28**. The lowest singlet and triplet states of **3** and the cyclic structures **26** and **27** are all close in energy and at room temperature thermally accessible. This explains the strong temperature and solvent dependence of the products obtained from irradiation of diazo compounds **22**. These results show the limits in synthesizing ever more electrophilic carbenes: interactions between substituents with lone pairs and the vacant π orbital at the carbene center results in intramolecularly stabilized singlet carbenes or carbenoids. These species, although still high in energy, lack the specific properties of electrophilic carbenes.

1.6 CONCLUSION

Highly electrophilic carbenes are extremely reactive intermediates with interesting chemical properties. The electrophilicity of these carbenes can be linked to the electron affinity, which is easily obtained from DFT calculations. The vinylidene **1b** and the cyclohexadienylidene **2b** are prototypes of electrophilic singlet and triplet carbenes. The reactivity of these carbenes prevents their stabilization in organic glasses even at 4 K. Insertions into H-H and C-H bonds are rapid, irrespective of the spin state of the carbene and the temperature of the solvent. There is no indication that tunneling plays a role in this processes and for the singlet states zero or very small barriers are predicted. The only way to isolate these molecules is therefore the matrix isolation in rare gas matrices. The reactivity of singlet closed shell carbenes such as **1b** is completely governed by the low-lying LUMO, which results in unprecedented reactions such as the abstraction of an oxygen atom from CO_2 or the formation of a complex with xenon. As a triplet carbene is sometimes called a “1,1-diradical”, a singlet carbene can be looked upon as a “1,1-zwitterion” with both electrophilic and nucleophilic reactivity. If the electrophilicity of a carbene is enhanced as in **1b**, many aspects of the reactivity of the carbene resemble that of a carbocation. The general reactivity of triplet carbenes also increases with increasing electrophilicity, however, since an empty, low lying orbital is missing, the general pattern of reactivity is still that of typical triplet carbenes.

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Chapter 2

Observing Invisible Carbenes By Trapping Them with Pyridine

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2.1. BACKGROUND

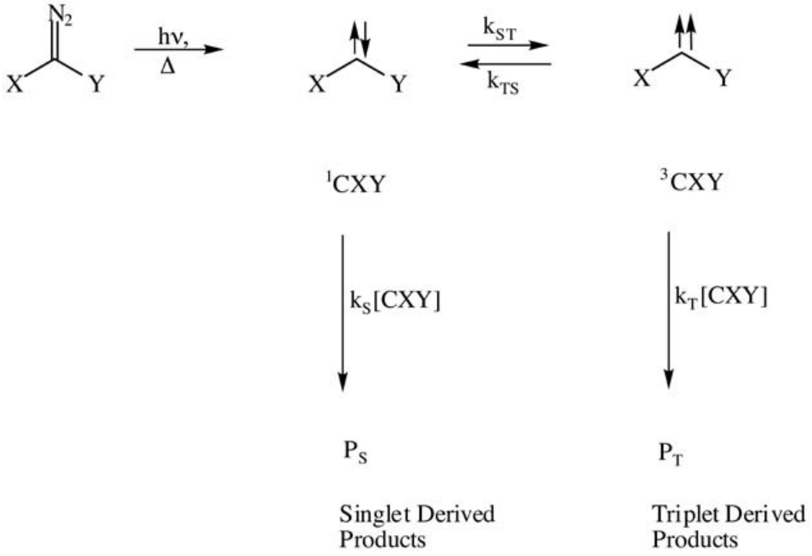
As stated by Hine [1] in his classic book:

"The most important reaction intermediates in organic chemistry are probably those containing carbon in an abnormal valence state. Only four types of such intermediates are common. Three types, carbonium ions, carbanions, and free radicals, are trivalent-carbon derivatives in which the trivalent carbon atom bears a positive charge, a negative charge, and no charge (but an unpaired electron), respectively. Methylenes, uncharged divalent-carbon derivatives, comprise the fourth type, which may be subdivided into singlets (containing no unpaired electrons) and triplets (containing two unpaired electrons)."

There were a few isolated attempts to generate CH_2 in the nineteenth century [2] but many chemists credit the origins of modern carbene chemistry to Staudinger's work published in 1911. [3] There was phenomenal growth in carbene chemistry beginning in 1950 and in fact the term "carbene" was coined around this time by Doering, Woodward and Winstein in a famous nocturnal taxi ride. [4]

In the 1950s and 1960s chemists learned how to generate carbenes from haloform, diazirine and diazo compound precursors as transient intermediates in solution. [1,5,6] The chemists of this era identified the products of carbene reactions and learned how to make these reactions synthetically useful. They postulated a framework for carbenes (Scheme 1) with ground or low lying triplet states which is still the starting point in all mechanistic discussions.

At that time, it was not possible to measure any of the rate constants of Scheme 1 directly but in some cases it was possible to measure ratios of rate constants or to determine if spin equilibration was much faster or slower than intermolecular reactions. Organic chemists could then only dream of determining the absolute rate constants of Scheme 1. This would become possible around 1980 with the invention of laser flash photolysis with nanosecond (ns) time resolution. But successful application of this tool would require knowledge of the electronic spectra of singlet and triplet carbenes. Low temperature spectroscopy was enormously helpful in this regard.



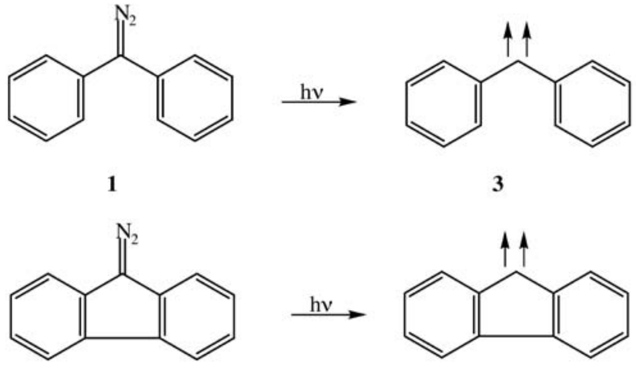
Scheme 1

2.2 MATRIX ISOLATION SPECTROSCOPY

In the 1960s chemists searched for ways to directly detect carbenes to further understand their geometric and electronic structure. Diphenyldiazomethane (**1**) and diazofluorene (**2**) (DAF) as solutions or crystals were frozen to cryogenic temperatures (4-77K). Photolysis of these samples produced diphenylcarbene (**3**) and fluorenylidene, (**4**) respectively, in their triplet ground states as persistent species. [7]

Researchers at Bell Laboratories and The University of Chicago developed the matrix-EPR spectroscopic technique and applied it in elegant ways to the study of diaryl and arylcarbenes. [7] Wasserman and co-workers [8] used EPR spectroscopy to demonstrate that triplet methylene has a bond angle of 135^0 as first predicted by Foster and Boys. [9] EPR spectroscopy is now a standard tool for the study of triplet carbenes.

Singlet and triplet methylene have been observed in the gas phase and their electronic spectra recorded. [10] Unfortunately, gas phase spectroscopy of carbenes is limited to very simple species. Arylcarbenes have never been spectroscopically detected in the gas phase despite numerous attempts. This is unfortunate because high resolution gas phase spectroscopy could, in principle, yield important structural information about these molecules.



1 3

2 4

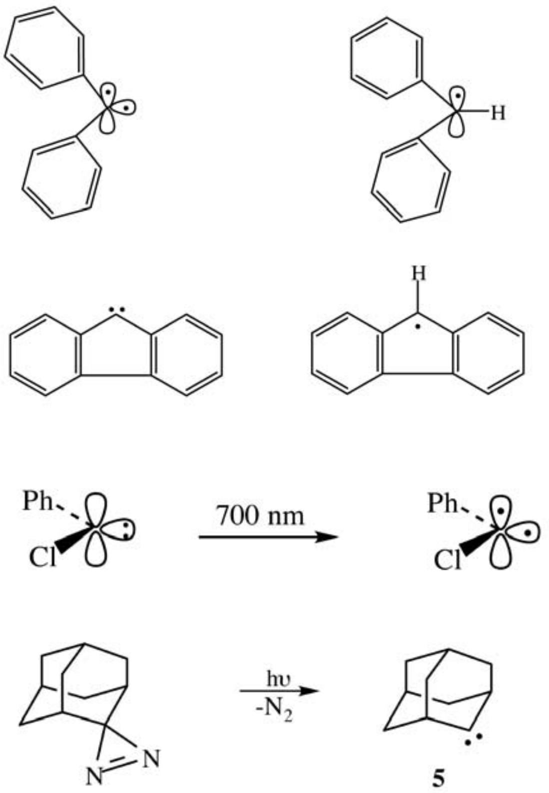
2.3 MATRIX ABSORPTION SPECTROSCOPY

As mentioned previously, arylcarbenes such as diphenylcarbene and fluorenylidene which have triplet ground states have been prepared as persistent in organic glasses at 4-77K. In addition to their EPR spectra, their electronic spectra were recorded. [11] The spectra of triplet diarylcarbenes are very similar to the related radicals and are dominated by transitions involving their extended π systems.

Arylhalocarbenes have singlet ground states. They are easily prepared as persistent species in organic glasses at 77K. They have strong π,π^* transitions in the UV region which are ideal for laser flash photolysis (LFP) studies. [12] They also have a broad, weak HOMO-LUMO transition in the visible region.[13]

Although this band is not useful in LFP experiments because of its low molar absorptivity, it can be observed in matrices when the carbene is persistent and a reasonable concentration of the carbene can be produced.

A good example of this is the carbene admantylidene (**5**). [14] Its broad HOMO-LUMO absorption at 590 nm can be observed when the carbene is frozen in argon but cannot be detected upon LFP of its diazirine precursor.

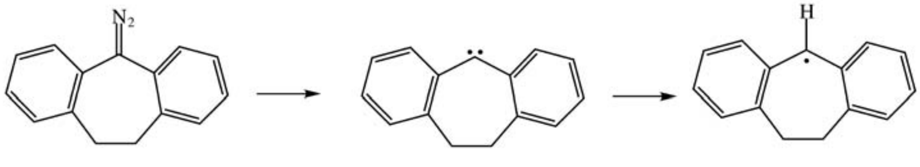


5

In general, non aromatic ground state singlet carbenes do not have useful chromophores for laser flash photolysis studies.

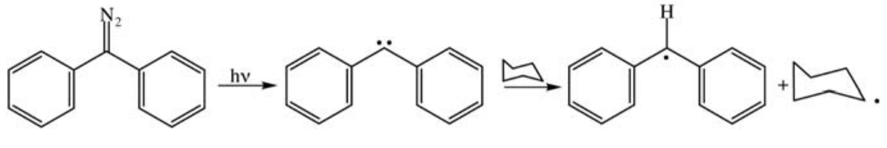
2.4 FLASH PHOTOLYSIS STUDIES OF CARBENES

In the late 1960s, Moritani and coworkers [15] reported studies of diazo compound **6** by flash photolysis methods. They were able to detect triplet carbene **7** and radical **8** several microseconds after the flash but did not measure the absolute rate constant of this transformation.



6 **7** **8**

The first absolute rate constant of a carbene reaction in solution was reported by Closs and Rabinow in 1976. [16] Upon photolysis of diphenyldiazomethane **1** in benzene with a conventional flash lamp, a transient spectrum with $\lambda_{max} \approx$ 300 nm was detected. This absorption was assigned to triplet diphenylcarbene **3** because of the correspondence of this spectrum with that previously obtained for this carbene in a low temperature matrix.[11] Upon flash photolysis of diphenyldiazomethane in cyclohexane the transient spectrum of the known spectrum of benzhydryl radical **9** ($\lambda_{max} \approx$ 334 nm) was produced. Carbene abstraction of hydrogen from the solvent proceeded faster than the time resolution of their spectrometer (20 μs).



1 **3** **9**

In benzene (which is inert towards **3**) Closs and Rabinow measured the absolute rate constant of reaction of triplet carbene with itself, with dienes and with methanol.

2.5 EARLY LASER FLASH PHOTOLYSIS STUDIES OF CARBENES

By 1980, there was still only one study, that of Closs and Rabinow,[16] that reported the absolute rate constant of a carbene reaction. This was about to change dramatically, as Moss and Turro [12] began their studies of arylhalocarbenes, Schuster's group studied fluorenylidene, [17] and Griller and Scaiano studied different reactions of the aforementioned carbenes. [18] These studies utilized the new technique (for physical-organic chemists) of nanosecond time resolved laser flash photolysis (LFP).

A Laser Flash Photolysis (LFP) apparatus involves at its heart the crossing of two beams of light (the pump and the probe) inside an optical cuvette containing a solution of precursor (diazirine or diazo compound) in solvent. The probe beam is comprised of polychromatic light whose intensity is constant for a few milliseconds (Figure 1). The pump beam is a short intense burst of monochromatic laser radiation. In an ideal experiment the laser radiation is absorbed entirely by precursor (the solvent should be transparent to the laser light). Excimer (XeCl) laser radiation of 308 nm works well for aryl diazo compounds; nitrogen (337 nm), KrF excimer (351 nm), or Nd-YAG (355 nm) radiation work well for diazirines. Absorption of laser radiation converts the precursor into the carbene of interest. In an ideal experiment the carbene will have an intense absorption in a spectral region far removed from that of the absorption of the diazo precursor and the products formed upon decay of the carbene transient.

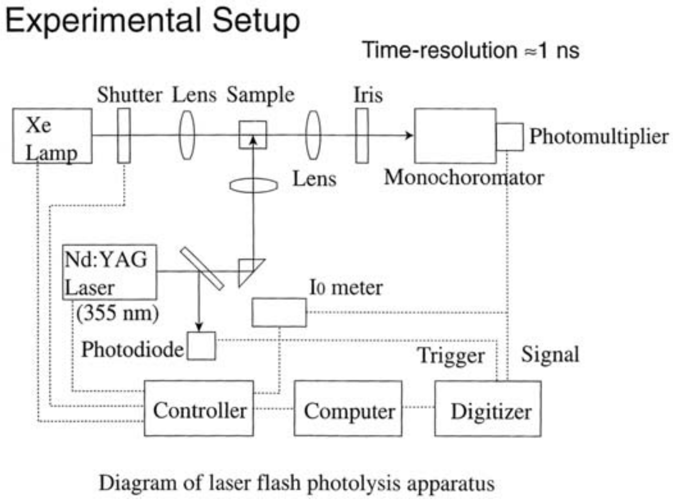


Figure 1. A typical apparatus for laser flash photolysis studies.

In a typical LFP experiment the computer will first activate a transient digitizer (an analog to digital or A/D converter). This device converts the analog signal exiting the photomultiplier tube (PMT) detector into a digital format that can be read later by the computer. The computer then opens a shutter and the polychromatic light of the arc lamp passes through the sample. A monochrometer (MC) is set to the absorption maximum of a species of interest. It is this light level which is measured by the PMT detector. In the case of diphenylcarbene in cyclohexane, the monochrometer can be set to 314 mm where the carbene **3** absorbs more intensely than radical **9**, or more conveniently to 332 nm, where the benzhydryl radical **9** principally absorbs. When the shutter opens, monitoring light strikes the PMT to produce a "pre laser pulse" signal level. A few milliseconds later the laser pulse strikes the sample and converts precursor to carbene. As the precursor and carbene have different molar absorptivity at the wavelength selected by the monochrometer, the amount of light striking the PMT and the resultant signal exiting the PMT changes suddenly (the few ns time resolution of the spectrometer). The signal out of the PMT then evolves according to the disappearance of the carbene and the growth of its reaction product and their relative absorbances.

Table 1. Bimolecular Rate Constants for the Reaction of Diphenylcarbene with Various Substrates at 300 K [19]

Substrate	Solvent	k, $M^{-1}s^{-1}$
Carbon tetrachloride	cyclohexane	$(3.6 \pm 0.4) \times 10^5$
tetrahydrofuran	cyclohexane	$(2.0 \pm 0.3) \times 10^5$
tetrahydrofuran	benzene	$(1.4 \pm 0.2) \times 10^5$
cyclohexne	cyclohexane	$(2.8 \pm 0.1) \times 10^5$
cyclooctene	cyclohexane	$(3.3 \pm 0.3) \times 10^5$
1-octene	cyclohexane	$(1.0 \pm 0.1) \times 10^6$
2,3-dimethyl-2-butene	cyclohexane	$(2.1 \pm 0.3) \times 10^5$
styrene	cyclohexane	$(1.4 \pm 0.3) \times 10^6$
1,4-cyclohexadiene	cyclohexane	$(1.0 \pm 0.1) \times 10^7$
1,3-cyclohexadiene	cyclohexane	$(2.6 \pm 0.2) \times 10^6$
1,5-cyclohexadiene	cyclohexane	$(2.0 \pm 1.2) \times 10^6$
1,3-cyclooctadiene	cyclohexane	$(2.8 \pm 0.1) \times 10^5$
1,3-octadiene	cyclohexane	$(1.5 \pm 0.1) \times 10^6$
chloroform	cyclohexane	$(8.4 \pm 0.9) \times 10^5$
triethylamine	cyclohexane	$(3.4 \pm 1.4) \times 10^5$

Diphenyldiazomethane **1**, triplet diphenylcarbene **3** and benzhydryl radical **9** all have significant absorption between 300-340 nm. In practical terms the exciting laser wavelength and monitoring wavelength are only a few nm apart which (a) increases the chance that the laser pulse can blind the detector, (b) means that the sample is optically dense at the monitoring wavelength and (c) that the signals contain contributions from the bleaching of the precursor, the formation and decay of the carbene, and the formation and decay of the reaction product, the benzhydryl radical.

Despite these complications, graduate student Linda Hadel and Dr. J. C. Scaiano (then of the NRCC in Ottawa) and I were able to obtain useful signals of triplet diphenylcarbene in cyclohexane. [19] The system can be analyzed because triplet DPC is much more reactive towards hydrogen atom donors than is benzhydryl radical; thus the time scales of reaction of these two species are very different and can be monitored separately.

The hydrogen atom abstraction reactions of DPC involve the lower energy, in plane hybrid orbital of the carbene. The carbene consequently has a reactivity closer to phenyl rather than to benzhydryl radical.

Our group was able to obtain hydrogen atom transfer rate constants (Table 1) with typical organic solvents and their Arrhenius Activation parameters (Table 2). The parameters are quite low for atom transfer reactions and we concluded that QMT contributes to the solution phase reactions. [20]

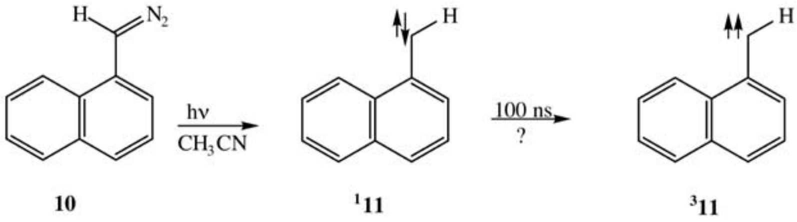
Table 2. Arrhenius Parameters for the Decay of Diphenylcarbene in Various Solvents [19]

Solvent	*T* Range K	Ea, kcal/mol	log A/s^{-1}
toluene	264-343	3.2 ± 0.7	8.0 ± 0.5
cyclohexane	276-327	2.5 ± 0.4	7.5 ± 0.3
cyclohexene	267-339	3.0 ± 0.3	8.7 ± 0.2
cyclopentane	234-317	2.9 ± 0.3	7.9 ± 0.2

2.6 1-NAPHTHYLCARBENE AND FLUORENYLIDENE

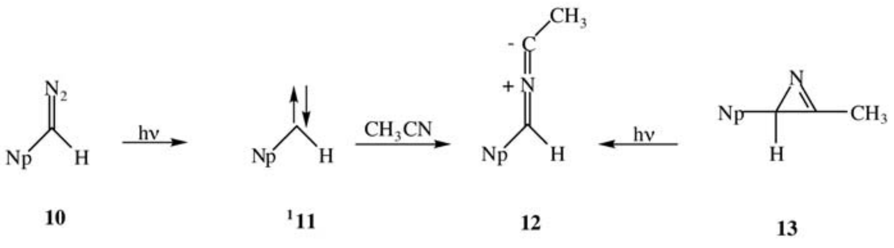
Our work with diphenylcarbene had some technical issues due to overlapping absorptions but was nevertheless straightforward, as the matrix spectrum of the triplet carbene was available and the spectrum of benzhydryl radical was known. Our work with 1-naphthylcarbene and fluorenylidene, however, was initially much more confusing.

LFP of 1-naphthyldiazomethane (**10**) in acetonitrile, the first solvent we studied, produced a transient spectrum with λ_{max} = 386 nm. The transient was formed in an exponential process with a time constant of 100 ± 10 ns and decayed over several microseconds. Our initial impulse was to attribute the transient absorbing at 386 nm to triplet 1-naphthylcarbene formed from invisible singlet 1-naphthylcarbene ^{1}**11** with a time constant of 100 ns. [21]



λ max=386 nm

Additional work soon discredited this postulate. The 386 nm transient could not be detected in other solvents. No transient was detected upon LFP of **10** in benzene or hexafluorobenzene. In cyclohexane, a transient with λ_{max} = 367 nm was formed 144 ns after the laser pulse. Only in nitrile solvents were transient absorption bands observed near 400 nm. The definitive experiment was performed by Linda Hadel who demonstrated that the pseudo-first order rate constant of formation of the 386 nm absorbing transient was linearly dependent on the concentration of acetonitrile. This proved that the transient is formed by reaction of an invisible species which reacts with acetonitrile. The observable transient was ylide **12** formed by capture of ^{1}**11**. The same transient was formed by LFP of azirine **13**.



Np = 1-Naphthyl

Ylides of singlet 1-naphthylcarbene (^{1}**11**) with acetone, triethylamine and pyridine were soon observed. [21] Fluorenylidene was also found to react with coordinating solvents to form ylides. [22]

The transient spectra of neither singlet nor triplet 1-naphthylcarbene have ever been observed upon LFP of **10**. The kinetics of these invisible carbenes were obtained from the growth of their ylide reaction products and not by direct observation of either singlet or triplet 1-naphthylcarbene.

2.7 PROBE KINETICS

The study of the 1-naphthylcarbene system is an example of the use of "probe kinetics," first employed in great detail by Scaiano and coworkers in the study of radicals and biradicals. [23]

Consider a reactive species A formed by LFP of a suitable precursor. Species A can react to form B with rate constant k_{AB}.

$$\mathrm{A} \xrightarrow{k_{AB}} \mathrm{B} \tag{1}$$

If neither A nor B has a useful chromophore, it is not possible to obtain k_{AB} by direct observation. However, the LFP experiment can be repeated in the presence of probe molecule P which reacts with A with rate constant k_{AP} to form AP. Under these conditions, [P] >> [A] and the kinetics are pseudo first order.

$$\mathrm{AP} \xleftarrow{k_{AP}[\mathrm{P}]} \mathrm{A} \xrightarrow{k_{OBS}} \mathrm{B} \tag{2}$$

Furthermore,

$$-\frac{d[\mathrm{A}]}{dt} = k_{AB}\,[\mathrm{A}] + k_{AP}\,[\mathrm{P}][\mathrm{A}] \tag{3}$$

$$\text{and } A_t = A_o \exp\left(-k_{AB} - k_{AP}[\mathrm{P}]\right), \tag{4}$$

where A_t and A_0 are the concentrations of A at time t and time equal zero, respectively. What about the formation of probe product AP? Under these conditions equation (5) is valid.

Integration yields equation (6).

$$+\ \frac{dAP}{dt} = k_{AP}[P][A] = k_{AP}[P]A_o \exp(-k_{AB} - k_{AP}[LP]) \tag{5}$$

$$[AP]_t = \frac{k_{AP}[P]}{k_{AP} + k_{AP}[P]} \exp(-k_{AB} - k_{AP}[P]) \tag{6}$$

Thus AP is formed exponentially with an observed rate constant k_{obs} as shown in equation (7).

$$k_{obs} = k_{AB} + k_{AP}[P] \tag{7}$$

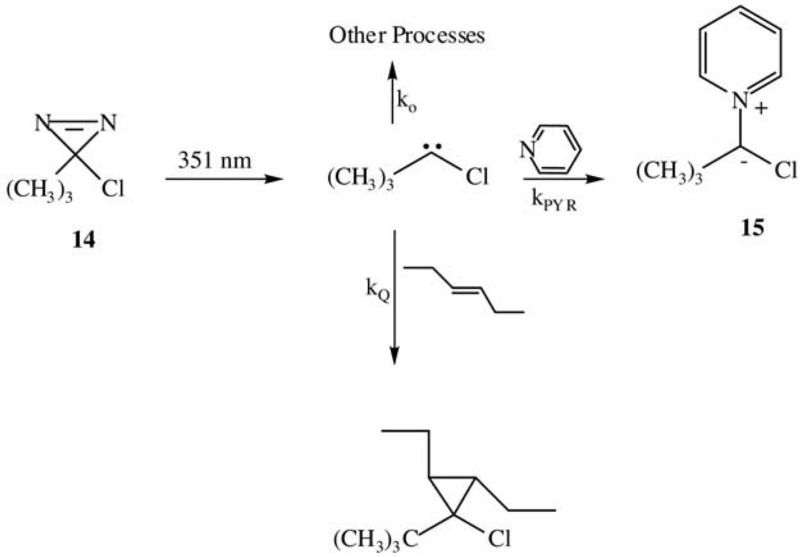
Thus the observed rate constant of formation of probe product AP depends on both k_{AB} and $k_{AP}[P]$.

Typically k_{obs} will be measured as a function of [P]. A plot of k_{obs} versus [P] will be linear with slope k_{AP} and intercept k_{AB}. In this manner one can measure k_{AB} even though reactive intermediate A and reaction product B are both spectroscopically invisible!

The situation with 1-naphthylcarbene is by no means unique. The "invisibility" of singlet and triplet non-aromatic carbenes makes studying their kinetics even more challenging. In fact, in our opinion the most interesting carbenes lack useful chromophores for laser flash photolysis studies.

In 1988 [24] then post-doctoral student Ned Jackson conjectured that pyridine would be the ideal carbene probe reagent for the following reasons: (1) Pyridine has no appreciable absorption at 308, 337, 351 or 355 mm, typical laser wavelengths used to excite precursors. (2) Pyridine is a strong, unhindered Lewis Base and should react with carbenes with very large rate constants. (3) The pyridine ylides would have intense absorptions in the visible region and should have microsecond lifetimes. Jackson, Soundararajan, Platz and Liu demonstrated the utility of pyridine ylides to study of the kinetics tertiary-butylchlorocarbene. [24] LFP of diazirine **14** in toluene fails to give a detectable transient. LFP (351 mm) of the same diazirine in toluene containing 10% pyridine produced the intense transient spectrum of ylide **15**. The transient is formed in an exponential process following the laser pulse, which can be analyzed to yield observed rate constant of formation, k_{obs}. The magnitude of k_{obs} is linearly dependent on the concentration of pyridine. The slope of the plot is k_{pyr}, the absolute rate constant of reaction of the carbene with pyridine. The intercept of the plot is k_o, where k_o is the sum of all first order and pseudo-first order processes which consume tert-butylchlorocarbene in toluene, in the absence of pyridine. The carbene lifetime (τ), in the absence of pyridine, is simply $1/k_o$.

In the absence of pyridine, tert-butylchlorocarbene can undergo two types of intramolecular rearrangements, react with diazirine precursor to form azine or react with solvent. It can also react with an olefinic trap to give a cyclopropane adduct. Analysis of the product mixture by Moss and Liu [25] gives the ratio of rate constants of these processes. As the alkene trapping reaction rate constant is known, the other rate constants of reaction of the invisible species tert-butylchlorocarbene can be deduced.

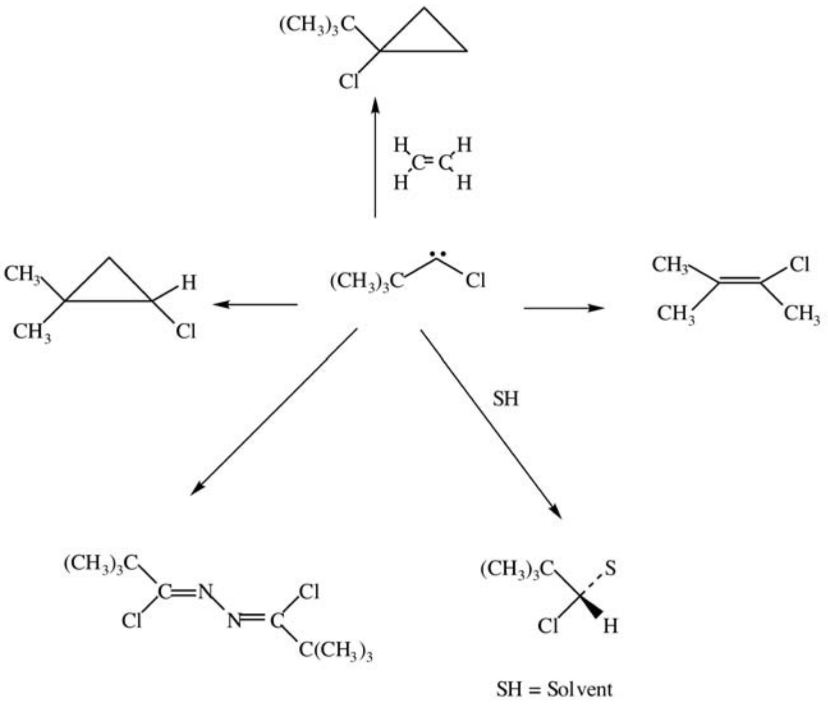


In Scheme 2, the observed rate constant of ylide formation k_{obs} is related to elementary rate constants by equation (8).

$$k_{obs} = k_o + k_{pyr}\,[\text{pyridine}] + k_Q\,[\text{trans-3-hexene}] \qquad (8)$$

To obtain k_{pyr}, one measures k_{obs} at several pyridine concentrations. To obtain the rate constant of carbene reaction with a quencher, Q, one holds the concentration of pyridine constant and varies the quencher concentration. A plot of k_{obs} versus [Q] is now linear with slope k_Q. For tert-butylchlorocarbene and trans-3-

heptene, $k_Q = 4.28 \pm 0.82 \times 10^7 M^{-1}s^{-1}$. [24] Even though neither the carbene nor the cyclopropane product is detected in this experiment, one can use the pyridine ylide probe to obtain the rate constant using the Scaiano probe technique. [23]



Scheme 2

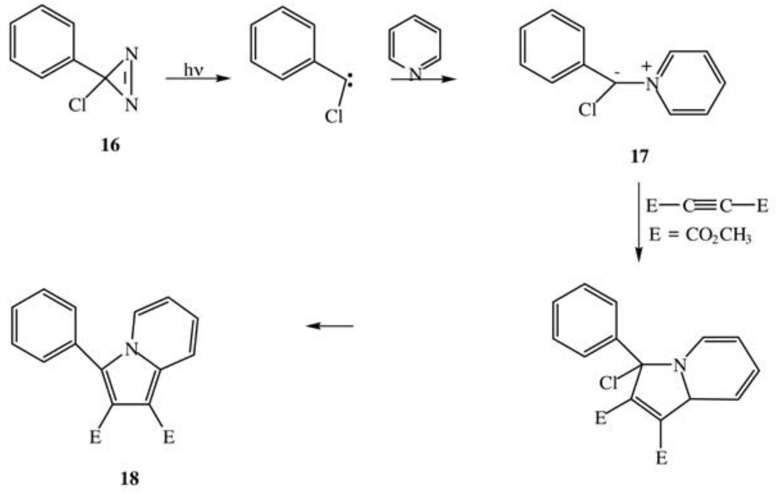
Pyridine ylide methodology is not needed to visualize chlorophenylcarbene but, as expected, LFP of chlorophenyl diazirine **16** in the presence of pyridine produces expected ylide **17**. Michelle Jones studied k_{pyr} for this reaction as a function of solvent. The reaction is slightly faster in non-polar solvents (Table 3) but the effect is small. [26]

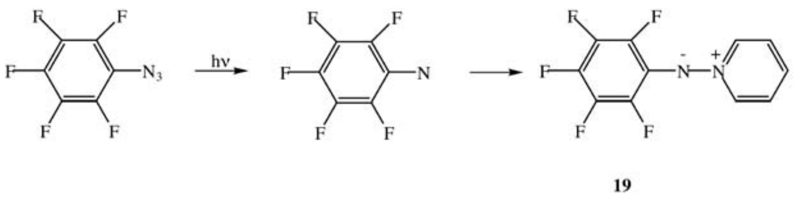
Upon photolysis of chlorophenyl diazirine **16** in the presence of both pyridine and dimethylacetylene dicarboxylate, adduct **18** is produced. This provides further evidence that the transient spectrum is due to ylide **17**. [24]

Russell Poe demonstrated that photolysis of perfluorophenyl azide in pyridine produces ylide **19** with λ_{max} = 390 nm. This ylide is isolable and its structure obtained by x-ray crystallography. [27]

Table 3. The Effect of Solvent Dielectric upon the Absolute Rate Constant for Reaction of Phenylchlorocarbene with Pyridine at 293 K [26]

Solvent	ε	***k*** **($M^{-1}s^{-1}$)**
hexane	1.89	$(7.56 \pm 0.93) \times 10^8$
toluene	2.38	$(3.74 \pm 0.38) \times 10^8$
ethyl acetate	6.02	$(2.94 \pm 0.36) \times 10^8$
∝,∝,∝-trifluorotoluene	9.18	$(4.20 \pm 0.32) \times 10^8$
o-dichlorobenzene	9.93	$(5.37 \pm 0.64) \times 10^8$
2-butanone	18.5	$(4.73 \pm 1.06) \times 10^8$
propionitrile	27	$(3.58 \pm 0.35) \times 10^8$
acetonitrile	36.2	$(2.90 \pm 0.40) \times 10^8$
sulfolane	44	$(2.90 \pm 0.30) \times 10^8$



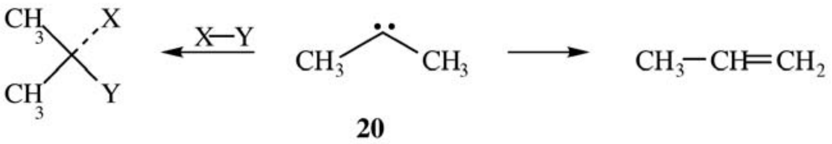


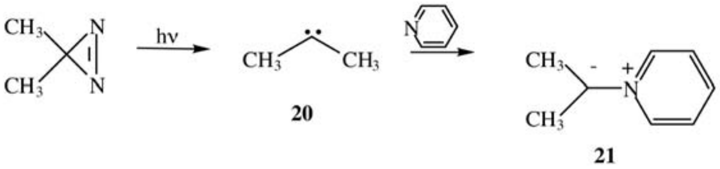
In recent years, numerous alkyl, alkylhalo, dialkyl and carbonylcarbenes, all of which lack useful chromophores, have been studied by using pyridine ylides. [28] Many of these studies are most concerned with the intercept term $k_{o,}$ the goal being to obtain rate constants of well known unimolecular carbene rearrangements. The major findings of one such study will be presented briefly. The coverage is not comprehensive and deals with only a few processes of interest to the author.

2.8 1,2-HYDROGEN MIGRATION REACTIONS

Little evidence for bimolecular chemistry of dimethylcarbene (**20**) and other simple alkyl and dialkylcarbenes is available. The conventional wisdom before 1990 was that the highly exothermic ($-H \approx 60 - 70$ kcal/mol) rearrangements of these carbene proceeded so rapidly as to preclude their capture by trap X-Y.

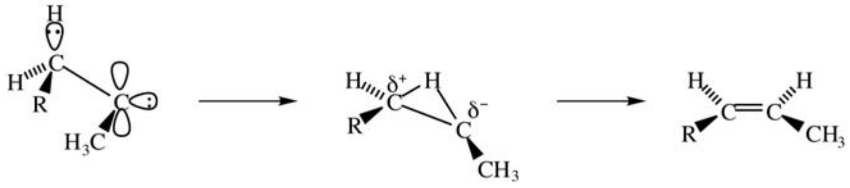
As capture rate constants are about 10^9 M^{-1} s^{-1} and [trap] can be up to10M, conventional wisdom predicted that **20** must have a lifetime of ≤ 10 ps.





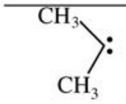
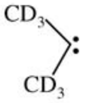
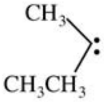
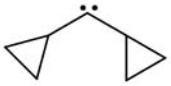
Nevertheless, David Modarelli found that LFP of dimethyldiazirine in pentane containing pyridine did indeed produce pyridine ylide **21**. [29] Modarelli also found that perdeuteromethylcarbene and ethylmethylcarbene, but not methylcarbene, were trappable with pyridine (Table 4).

Modarelli was not able to resolve the growth of the ylide absorption of **21** but was able to estimate the carbene lifetimes from plots of $1/\Delta A_y$ versus 1/[pyridine] where ΔA_y is the transient absorption of the ylide, and assuming a value of k_{pyr} of 1×10^9 M^{-1} sec^{-1}.



R = H, CH_3

Table 4. Dialkylcarbene Lifetimes at Ambient Temperature [29]

Carbene	Solvent	Lifetimes, ns[a]	k_D/k_H
	pentane	21	
	α,α,α–triflourotoluene	27	
	acetonitrile	8	
	acetonitrile-d_3	9	1.07
	chloroform	6.8	
	chloroform-d	7.3	1.08
	pentane	67	
	pentane	2	
	pentane	0.5	
	pentane	2.4	
	cyclohexane	14	
	cyclohexane-d_{12}	21	
	acetonitrile-d_3	14	
	chloroform-d	4	
	pentane	21	
	pentane	22	
	pentane	32	

[a]Assuming $k_{PYR} = 1 \times 10^9 M^{-1}s^{-1}$

Using this technique, Modarelli demonstrated that the lifetime of DMC was tens of nanoseconds, or thousands of times longer than previously thought. Modarelli's work and Michelle Sugiyama's [30] work with alkylaryl carbenes demonstrated that polar solvents accelerated the 1,2-hydrogen migration, as the transition state to rearrangement is more polar than the carbene itself. We accept the classical view that a C-H bond eclipses the empty *p*-orbital of dimethylcarbene **20**. Calculations show that this hyperconjugation is sufficiently strong to tilt the HCC bond angle from tetrahedral to about 100° in dimethylcarbene. [31]

A hydrogen atom and a pair of electrons migrate from carbon to leave behind a partial positive charge on carbon (see Figure 2).

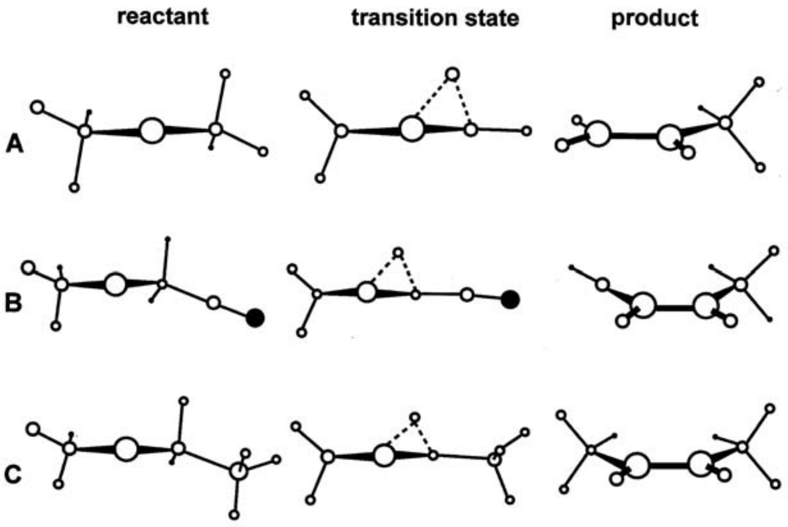
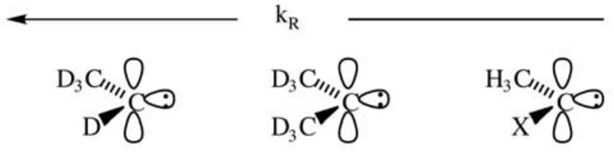


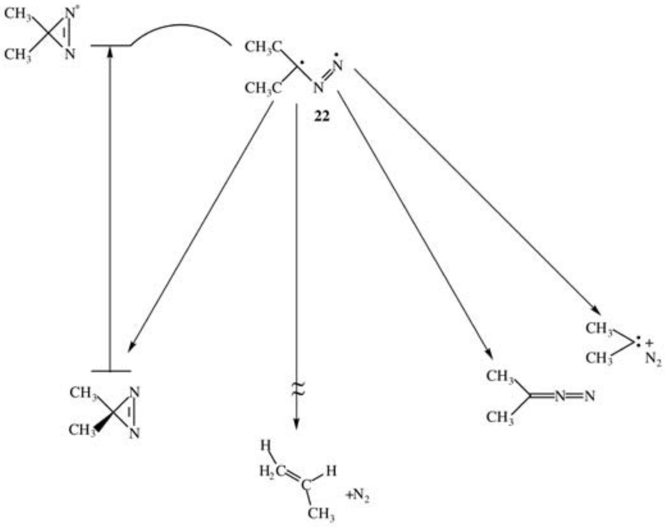
Figure 2. The calculated transition state for 1,2 hydrogen migration in dimethylcarbene. Reprinted with permission from Ford, F.; Yuzawa, T.; Platz, M.S.; Matzinger, S.; Fülscher, M. *J. Am. Chem. Soc.*, **1998**, *120*, 4430.



$X = Cl, F, OCH_3$

Ethylmethylcarbene rearranges more rapidly than does DMC because the migrating C-H bond is weaker in ethylmethylcarbene and the developing positive charge in the transition state is better stabilized when R = CH_3 than when R = H.

Perdeuterodimethylcarbene [32] rearranges about a hundred times more slowly than perdeuteromethylcarbene. We believe this is a result of ground state destabilization of the monoalkylcarbene. Ground state DMC-d6 resembles a secondary carbocation; ground state methylcarbene-d4 resembles a primary carbocation, which is less stable and more reactive than the secondary carbocation analog. Heteroatom substitution greatly stabilizes the pseudo cationic, carbene center and the rate or rearrangement is dramatically reduced.



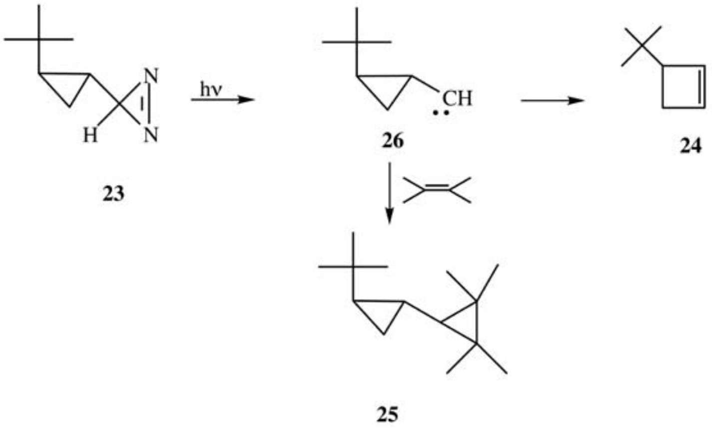
Scheme 3

If alkylcarbenes are so long lived, why had they not been routinely intercepted in good yield in previous studies? The answer is that dimethyldiazirine and dimethyldiazomethane are inefficient carbene precursors. The 300-350 nm transition of diazirines involves promotion of an electron into a non-binding orbital on nitrogen (the nitrogen lone pair) to a π-orbital. [33] This state (S_1, n → π*) is a few kcal/mol below S_2 (an n → * state), which can also be thought of as biradical **22**. Biradical **22** can reform dimethyldiazirine, isomerize to dimethyldiazomethane, eliminate nitrogen to form dimethylcarbene, or as we propose migrate a hydrogen to form propene in concert with loss of nitrogen. [34]

Photolysis of dimethyldiazirine produces a relatively small amount of carbene. The major decay route is the formation of propene, without the intermediacy of dimethylcarbene. This mechanism was supported by isotope effect studies on the diazirine fluorescence and yield of carbene. [34]

There are two experiments worthy of note that support this general scheme. Haiyong Huang [35] photolyzed diazirine **23** in $CF_2ClCFCl_2$ and obtained cyclobutene **24** along with products derived from carbene reaction with solvent. When a trap such as tetramethylethylene (TME) is present, carbene adduct **25** is formed.

As expected the yield of adduct **25** increases with increasing [TME], however, the yield of cyclobutene **24** is unchanged. [35] Thus, the simple mechanism of Scheme 4 cannot be correct. The "apparent" product of carbene rearrangement is not formed from the trappable carbene. Scheme 5 provides a better interpretation of the data. Once again a diazirinyl biradical (**27**) is postulated which can either form carbene **26** or form cyclobutene **24**.

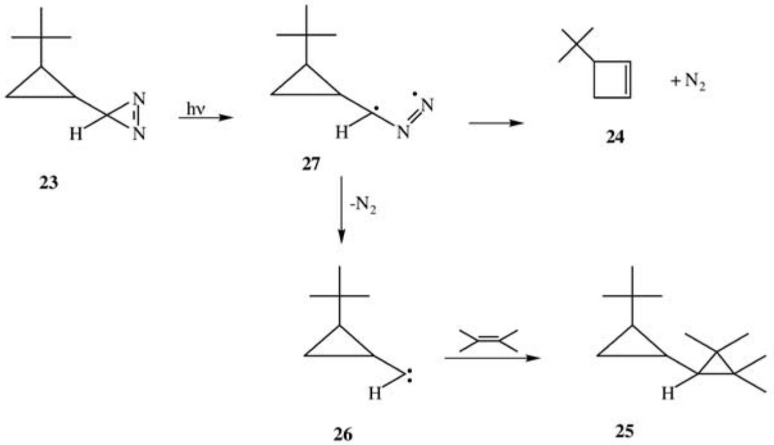


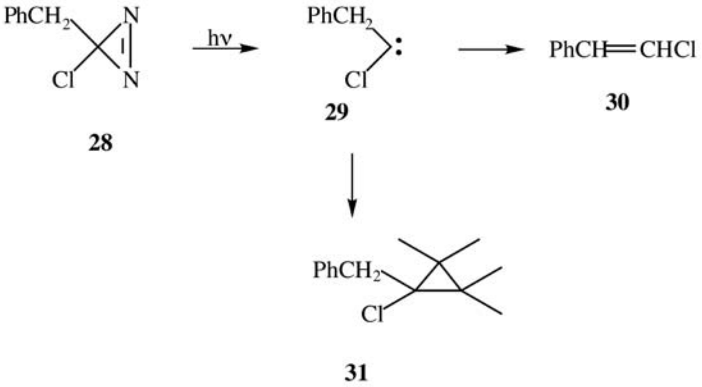
Scheme 4

Tomioka, Liu and Bonneau studied the photolysis of benzylchlorodiazirine **28**. [36] In the presence of trap it forms adduct and α-chlorostyrenes, the apparent product of carbene rearrangement (Scheme 6). They discovered, however, that plots of the ratio of yields of **31/30** were clearly not linear and they realized that Scheme 6 was incorrect.

Manisha Nigam demonstrated that different results were obtained with Johnston's precursor **32**. [37]

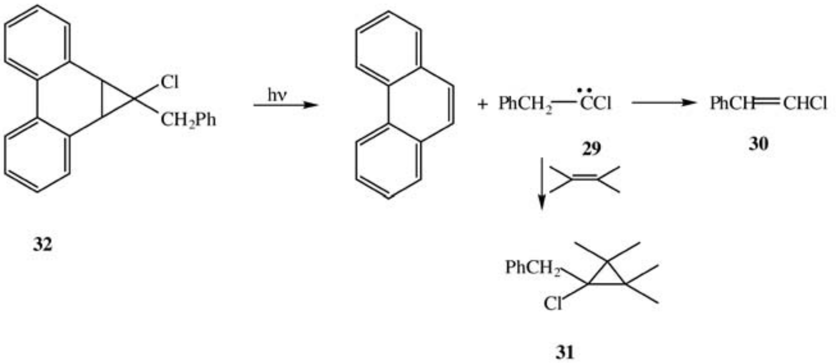
With the non-nitrogenous precursor **32**, a linear plot of **31**/**30** versus [TME] was obtained. The photochemistry of **32** is simple. The photochemistry of **19** we believe involves a "Rearrangement in Excited State" (RIES) mechanism via biradical **33**. [38]

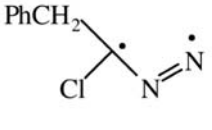




After the inefficiency of nitrogenous precursors of dimethylcarbene was understood, an alternative source of this carbene was sought. Igor Likhotvorik synthesized compound **34** which forms indane and dimethylcarbene upon photolysis. [39]

Although the desired photochemistry is still inefficient, it is a straightforward matter to measure the yield of indane.[39] Assuming that the yield of DMC and indane are equal, one can learn the efficiency of trapping the carbene before it can all rearrange to propene. The results, given in Table 5, demonstrate that DMC is efficiently intercepted with nucleophilic traps.





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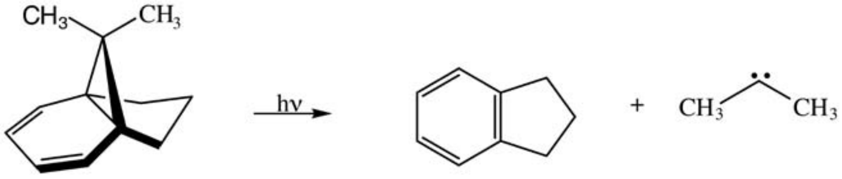

34

As mentioned previously, Modarelli was not able to resolve the formation of DMC-dimethylcarbene-pyridine ylide **21** (Figure 3) following excimer laser (20 ns pulse width) LFP of dimethyldiazirine in pyridine containing solution. [29] Francis Ford was able to resolve ylide formation (Figure 4) using a Nd: YAG laser (355 nm, 35 mJ, 150 ps pulse width). [31] Thus it was possible to measure k_{obs} following the laser pulse in $CF_2ClCFCl_2$, α, α, α-trifluoromethylbenzene and perfluorohexane. As usual, k_{obs} was measured as a function of [pyridine] (Figures 5-7) to yield values of k_o and k_{pyr}.. These measurements were repeated as a function of temperature to yield the Arrhenius parameters of Table 6 (see also Figure 3).

Table 5. Yields of dimethylcarbene and its insertion products [39]

Solvent	**Yield of DMC (%)**[a]	**Insertion Product**	**Yield (%)**
Cyclohexane	15-20[a]	Isopropylcyclohexane	4[b]
Benzene	13-15	Cumene	0.1[b]
Cyclohexylamine	6	Isopropylcyclohexyl amine	80[b]
Isopropanol	10	Diisopropyl ether	70[b]
Isobutylene	7	1,1,2,2-Tetramethylcyclopropane	33[c]

[a] The yield of dimethylcarbene was determined relative to the amount of indane formed upon irradiation.
[b] Yields of insertion products of dimethylcarbene were calculated from GC data using calibration with the corresponding reference compounds.
[c] Yield calculated by NMR.

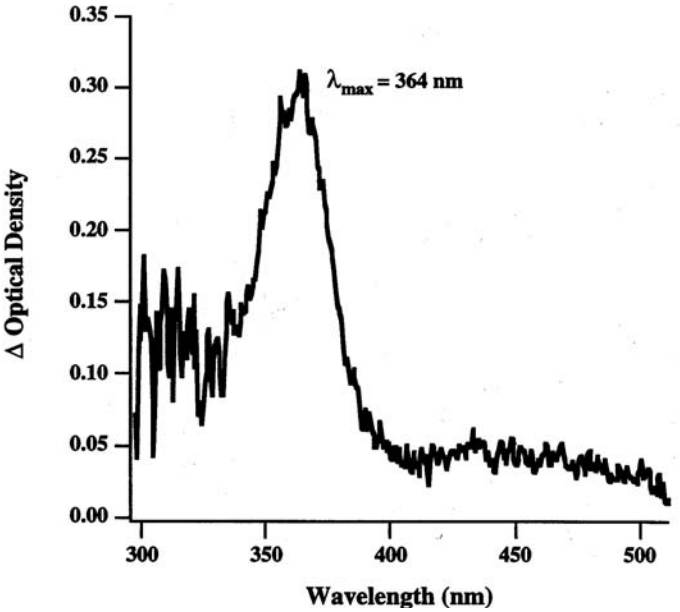

Figure 3. The transient absorption spectrum of ylide 21 produced by LFP of dimethyldiazirine in Freon-113 at ambient temperature. Reprinted with permission from Ford, F.; Yuzawa, T.; Platz, M.S.; Matzinger, S.; Fülscher, M. *J. Am. Chem. Soc.*, **1998**, *120*, 4430.

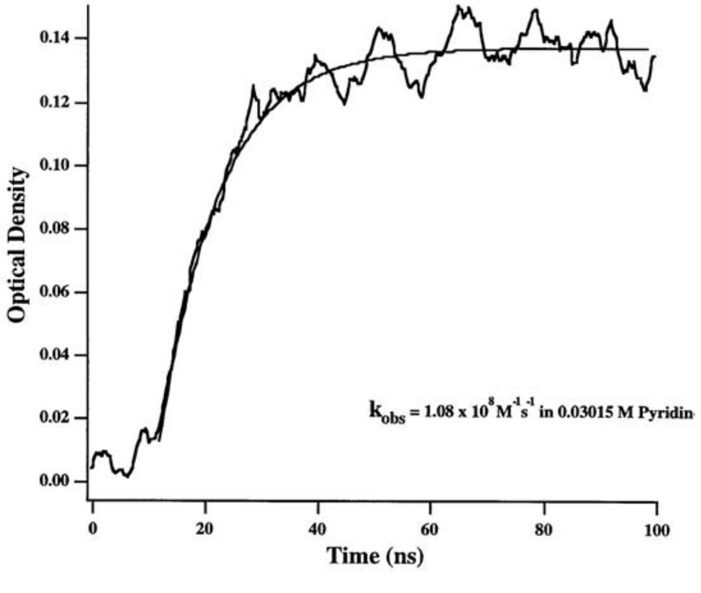

Figure 4. Growth of ylide **21** absorbance following laser flash photolysis of dimethyldiazirine in the presence of pyridine. Reprinted with permission from Ford, F.; Yuzawa, T.; Platz, M.S.; Matzinger, S.; Fülscher, M. *J. Am. Chem. Soc.*, **1998**, *120*, 4430

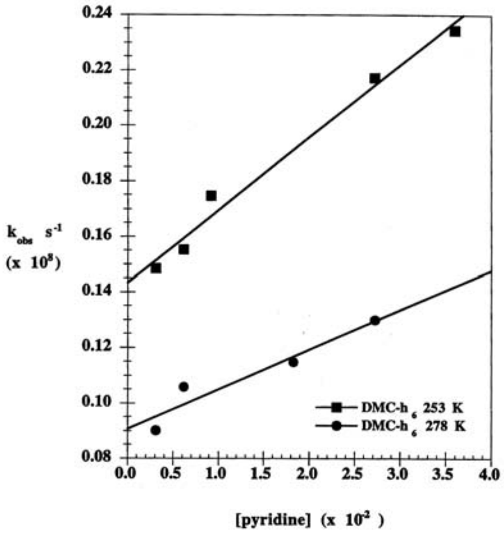

Figure 5. Plots of observed rate constant of ylide formation versus pyridine concentration obtained by LFP of dimethyldiazirine in trifluoromethylbenzene at two temperatures. Reprintedwith permission from Ford, F.; Yuzawa, T.; Platz, M.S.; Matzinger, S.; Fülscher, M. *J. Am. Chem. Soc.*, **1998**, *120*, 4430.

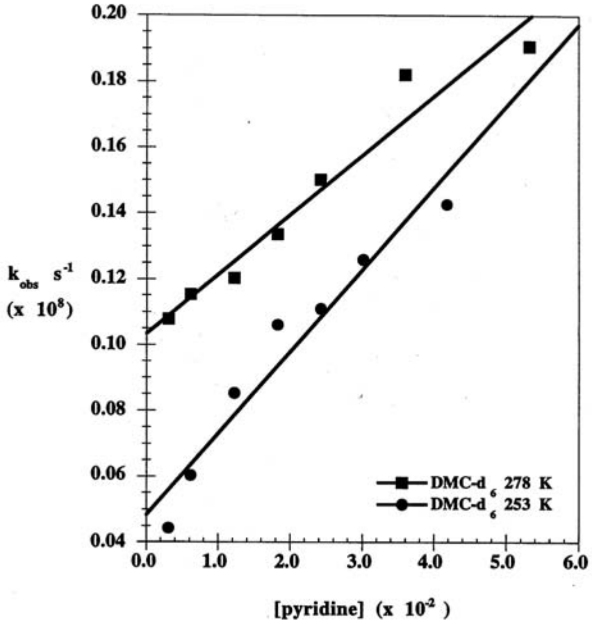

Figure 6. Plots of observed rate constant of ylide formation versus pyridine concentration obtained by LFP of dimethyldiazirine-d6 in trifluoromethylbenzene at two temperatures. Reprinted with permission from Ford, F.; Yuzawa, T.; Platz, M.S.; Matzinger, S.; Fülscher, M. *J. Am. Chem. Soc.*, **1998**, *120*, 4430.

Table 6. Activation Parametes of the Reactions of DMC and DMC-d6 Determined from the Intercepts (kR + kRX[RX]) of Plots of kOBS versus Pyridine Concentration. [31]

	DMC			**DMC-d6**		
Solvent	**Ea (kcal/mol)**	**ΔS≠ (298 K) (kcal/mol^{-1}K^{-1})**	**log A**	**Ea (kcal/mol)**	**ΔS≠ (298 K) (kcal/mol^{-1}K^{-1})**	**log A**
$Cl_2CFCClF_2$	3.11 ± 0.05	-9.6± 0.7	10.7 ± 0.3	3.36 ± 0.05	-9.6 ± 0.7	10.7 ± 0.3
$C_6H_5CF_3$	2.90 ± 0.05	-11.0 ± 0.7	10.4 ± 0.03	3.85 ± 0.05	-8.2 ± 0.07	11.0 ± 0.03
C_6F_{14}	2.56 ± 0.05	-12.8 ± 0.7	5.63 ± 0.03	-2.7 ± 0.7	-2.7 ± 0.7	12.2 ± 0.3

Modarelli's work stimulated high level quantum chemical calculations by a number of groups. These calculations predicted classical barriers of 5–7 kcal/mol for the 1, 2-hydrogen migration of dimethylcarbene **20**. [31,40] The activation barriers of **20** measured by Ford (Table 6) are all substantially lower than the calculated barrier. In $CF_2ClCFCl_2$ and α, α, α--trifluorotoluene the measured barriers are too low, in part, because **20** decays by both reaction with solvent and by the desired rearrangement process; thus $k_o = k_R + k_{SH}$ [SH].

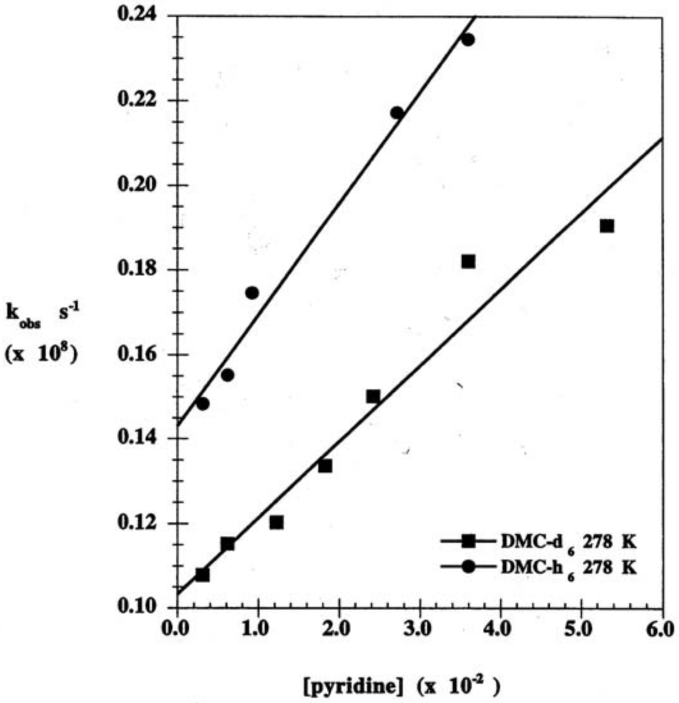

Figure 7. Plots of observed rate constant of ylide formation versus pyridine concentration obtained by LFP of dimethyldiazirine and dimethyldiazirine-d6 in Freon-113. Reprinted with permission from Ford, F.; Yuzawa, T.; Platz, M.S.; Matzinger, S.; Fülscher, M. *J. Am. Chem. Soc.*, **1998**, *120*, 4430.

When we started working with pyridine ylides we thought we would not be able to measure k_R by nanosecond spectroscopy because the reactions would be complete in picoseconds. Ironically we cannot measure k_R in many solvents because the reaction is not much faster than carbene reaction with solvent!

Perfluorohexane was the least reactive solvent we could imagine. Low Arrhenius parameters were still obtained for dimethylcarbene in perfluorohexane (Figure 8) but values close to those predicted were obtained for perdeuteromethylcarbene (**20**-d6). From this we concluded that quantum mechanical tunneling contributes to the 1, 2-hydrogen shift reaction of dimethylcarbene but has a smaller contribution to the rearrangement of the perdeuterated isotopomer. [31]

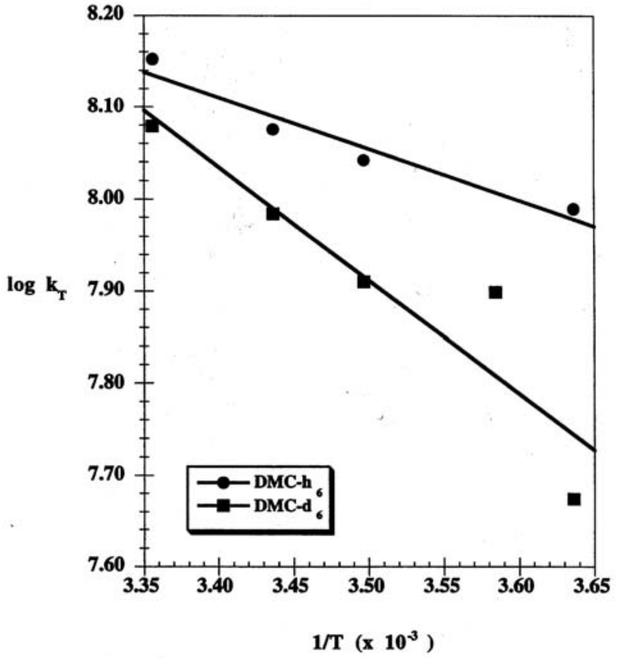

Figure 8. Arrhenius treatments of the intercepts of plots of the observed rate constant of ylide formation versus pyridine concentration obtained by LFP of dimethyldiazirine and dimethyldiazirine-d6 in perfluorohexane. Reprinted with permission from Ford, F.; Yuzawa, T.; Platz, M.S.; Matzinger, S.; Fülscher, M. *J. Am. Chem. Soc.*, **1998**, *120*, 4430.

In summary, the pyridine ylide method has told us quite a lot about 1,2-hydrogen migration reactions of invisible carbenes. We learned that simple alkyl and dialkyl carbenes are true intermediates with nanosecond lifetimes. The pyridine ylide method revealed that the rate of rearrangement of alkylcarbenes are influenced by the cationic stabilizing power of X (k_R increases as X = H < CH_3

< phenyl < halogen). We learned that the rate of rearrangement is accelerated by increasing solvent polarity and by placing alkyl groups on the carbon bearing the migrating hydrogen. Finally, it was discovered that quantum mechanical tunneling contributes to the 1,2-hydrogen migration process – all this without ever detecting the carbenes directly!

This in turn led us to realize that alkyldiazirine and diazo compounds are inefficient precursors of alkylcarbenes and suffer rearrangements in their excited states.

2.9 CONCLUSION

The probe kinetic methodology developed by Scaiano [23] to study radicals and biradicals by laser flash photolysis (LFP) methodology is readily extended to carbenes. LFP (308, 337, 351, or 355 nm) of diazirine or diazo compounds in the presence of pyridine produces carbenes, which generally react rapidly ($k_{pyr} \approx 10^9 M^{-1} sec^{-1}$) to form ylides. [28,29] Ylides are much easier to monitor than the carbenes because they have intense UV-Vis absorption and microsecond lifetimes. Pyridine ylide methodology has enabled LFP studies of alkyl, dialkyl, alkylhalo, dihalo and carbonylcarbenes. It is now a standard tool and will be used as long as LFP studies of simple carbenes are performed.

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Chapter 3

Carbenic Philicity

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3.1. BACKGROUND

3.1.1 Introduction

When I was a first year graduate student at the University of Chicago in 1961, Professor M.J.S. Dewar asked me to prepare a review of Jack Hine's pioneering studies of haloform hydrolysis.[1] Hine had demonstrated that the basic hydrolysis of (e.g.) chloroform proceeded via dichlorocarbene; Eq. 1-3.

$$CHCl_3 + OH^- \rightleftharpoons CCl_3^- + H_2O \tag{1}$$

$$CCl_3^- \rightleftharpoons :CCl_2 + Cl^- \tag{2}$$

$$:CCl_2 + OH^-(H_2O) \longrightarrow \longrightarrow CO + 2Cl^- \tag{3}$$

I further learned that Doering and Hoffmann had shown that CCl_2 could be trapped by alkenes to yield cyclopropanes, Eq. 4, [2] and Skell [3]and Doering [4] had then demonstrated that CBr_2 and CCl_2 preferentially reacted with more highly alkylated alkenes; i.e., these carbenes were *electrophilic*.

(4)

I found all of this very exciting and, as part of my qualifying examinations, prepared a research proposition dealing with carbenic reactivity. I had read

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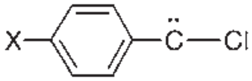
Louis P. Hammett's classic textbook *Physical Organic Chemistry*, [5] which opened vistas of a quantitative approach to organic reactivity. It seemed to me that linear free energy relationships might be usefully applied to quantitate carbenic reactivity. For example, although carbenes added to alkenes too rapidly to determine absolute rate constants for these addition reactions, [6] Skell [3] and Doering [4] showed that their reactivity could be described in terms of relative rate constants.

In this approach, alkenes *a* and *b* competed for an insufficiency of carbene. From the product mole ratio of the corresponding cyclopropanes (corrected for the mole ratio of the initial alkenes), one obtained the relative reactivity (approximately equal to the relative rate contant), k_a/k_b, of the carbene toward the selected alkene pair.

I thought that one might be able to combine this method with Hammett's σ, ρ approach. One could react a series of *p*-substituted arylcarbenes or arylhalocarbenes (e.g., **1**) with a fixed pair of alkenes, and then plot log (k_a/k_b)



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for each carbene vs. σ_X. The resulting correlation would give a ρ value that would indicate how the carbene's electrophilicity varied with the electronic effects originating at substituents X.

This idea seems quite rudimentary today, but in 1961 I thought it was novel. My examiners judged it adequate, passed me, and told me to select a research advisor. When I found that Professor Gerhard L. Closs was interested in carbene reactions, my choice was easily made. I began to study carbenic reactivity with him in 1961, [7] and have, at least in part, maintained an active interest in this research area ever since.

3.1.2 Empirical correlation of carbenic reactivity [8]

Our early efforts to quantitate carbenic reactivity again followed a path blazed by Doering and Skell. We "measured" the *selectivity* of carbene CXY by determining relative reactivities for its addition reactions with members of a "standard" set of alkenes:

$Me_2C{=}CMe_2$, $Me_2C{=}CHMe$, $Me_2C{=}CH_2$, *cis*-$MeCH{=}CHMe$,
trans-$MeCH{=}CHMe$

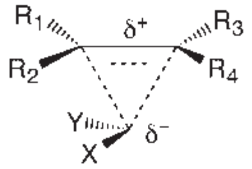
Within this set, the reactivity of isobutene was assigned as 1.0, and the reactivities of the other alkenes toward CXY were measured relative to isobutene. Data of this sort are illustrated for CF_2, CCl_2, and CBr_2 in Table 1. [9-12] (A very large collection of relative reactivity data for many carbenes appears in ref. 11).

Note that for each carbene in Table 1 the reactivity order of the alkenes is $Me_2C{=}CMe_2 > Me_2C{=}CHMe > Me_2C{=}CH_2 > MeCH{=}CHMe$. The most highly alkylated olefin reacts most rapidly, consistent with electrophilic selectivity by the carbenes, and in accord with the classical transition state **2**. [3,4,13,14] Here, the vacant (positive) p orbital of sp^2-hybridized singlet [15] carbene **3** "leads"the attack on the alkene's p electrons, net electron density is transferred from the π bond to the carbene, and positive charge is imposed on the olefinic carbon atoms. Alkyl substituents (electron releasing by inductive and hyperconjugative effects) mitigate the positive charge, stabilize the transition state, and render the alkene more reactive to carbene addition.

Table 1. Relative Reactivities of Carbenes with Alkenes (25 °C)

	relative reactivity		
alkene	CF_2[a]	CCl_2[b]	CBr_2[c]
$Me_2C{=}CMe_2$	15.4	8.98	4.0
$Me_2C{=}CHMe$	3.93	3.12	2.6
$Me_2C{=}CH_2$[d]	1.00	1.00	1.00
cis-MeCH=CHMe	0.061	0.27	0.44
trans-MeCH=CHMe	0.069	0.18	0.35

[a] Data from ref. 9 and 10. [b] Data from ref. 11. [c] Data from ref. 12. [d] The relative reactivity of isobutene = 1.00 by definition.



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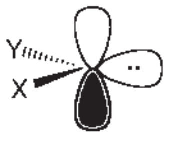

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To further characterize the selectivity of carbene CXY, we can compare its discrimination between the olefins of the standard set with that of CCl_2, which we designate the "standard carbene." We plot the logarithms of the relative reactivities for CXY against analogous data for CCl_2 (with the relative reactivities all adjusted to the standard alkene, isobutene, $k_o = 1.00$), and then determine the slope of the correlation line, m_{CXY}. We call m_{CXY} the "carbene selectivity index," defined as the least-squares slope of log $(k_i/k_o)_{CXY}$ vs. log $(k_i/k_o)_{CCl_2}$. [8,9,16,17] The m_{CXY} values for the carbenes of Table 1, determined in this manner, are $m_{CF_2} = 1.48$, $m_{CCl_2} = 1.00$ (by definition), and $m_{CBr_2} = 0.65$. [8,17] An example of the determination of m_{CBr_2} appears in Fig. 1. At face value, these results suggest that CF_2 discriminates about 1.5 times as well, while CBr_2 discriminates somewhat more than half as well, as CCl_2 between the olefins of the standard set.

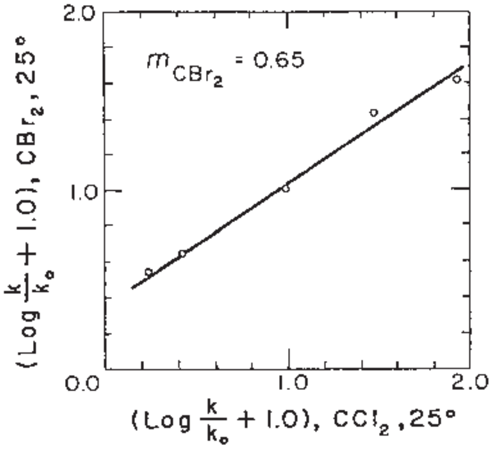


Figure 1. Determination of m_{CBr_2}: log (k/k_o) for CBr_2 vs. log (k/k_o) for CCl_2. Relative rates were multiplied by 10. The slope of the correlation, 0.65, is m_{CBr_2}; cf., Table 1. Reprinted with permission from ref. 12.

Similar numerical measures of of carbene/alkene discrimination had been previously obtained, [4,18,19] but we collected our m_{CXY} data at a single temperature (25 °C), only in hydrocarbon solvents, and generated the carbenes by methods likely to yield free, uncomplexed carbenes (rather than carbenoids [7,20]). Our data was therefore mutually comparable, and we were thus able to take another step in the quantitation of carbenic selectivity.

We assembled 9 experimentally determined values of m_{CXY}: CF_2 (1.48), CFCl (1.28), CCl_2 (1.00), PhCF (0.89), PhCCl (0.83), PhCBr (0.70), CBr_2 (0.65), MeCCl (0.50), and BrCCOOEt (0.29). Multiple linear regression analysis [21] of the dependence of m_{CXY} on the resonance ($\sigma_R{}^+$) and inductive (σ_I) substituent constants of X and Y (for CXY) then afforded the dual substituent parameter correlation, Eq. 4, in which $\Sigma_{X,Y}$ stands for the sum of the appropriate σ constants [21] for the substituents of CXY. [8,9,17]

$$m_{\mathrm{CXY}} = -1.10\sum_{X,Y}\sigma_R{}^+ + 0.53\sum_{X,Y}\sigma_I - 0.31 \tag{4}$$

Eq. 4 enabled an empirical analysis of carbenic selectivity (or philicity). (1) It correlated the selectivities of many of the carbenes that had been studied up to 1976. [8,17] (2) It quantitated the qualitative concepts of carbene-alkene addition reactions that were prevalent. (3) Most importantly, it could be used to estimate the selectivity of new carbenes. (4) It led to the identification of *ambiphilic* carbenes. (5) It would later be found to parallel conclusions drawn from ab intio electronic structure calculations of carbene-alkene addition reactions. Let's examine features (1) – (4); ab initio calculational results will be considered below, in Section 2.1.

(1) Eq. 4 does a good job of correlating the selectivities of its basis carbenes. Figure 2 shows the correlation of the experimental m_{CXY} values with the values calculated from Eq. 4. The largest deviation between the observed and calculated m_{CXY} values occurs with CBr_2 (Δm = 0.17) and represents a differential steric effect between CCl_2 and the larger CBr_2. [12] Inclusion of a steric term in Eq. 4 does not greatly improve the correlation, however, suggesting that the equation mainly expresses differential electronic effects of the carbenes on which it is based. [8,17]

(2) Eq. 4 indicates that increasing electron donation by resonance ($\sigma_R{}^+$), and increasing inductive withdrawal (σ_I) by carbene substituents X and Y, *both* enhance the selectivity of CXY. The coefficients of the $\sigma_R{}^+$ and σ_I terms are, respectively, negative and positive; the signs of the σ parameters of resonance donating and inductively withdrawing groups are also negative and positive, respectively. Therefore such groups (as carbenic substituents X and Y) will make positive contributions to m_{CXY}; i.e., they will enhance the selectivity of the carbene relative to that of CCl_2.

In terms of transition state **2**, we can see that *electrophilic* selectivity will be greatest when strong resonance interactions of X and Y with the carbenic carbon evoke correspondingly strong π-electron donation by the alkene, leading to the polarization depicted in **2**. Then, electron-donating alkyl substituents will mitigate the resulting positive charge on the alkene carbon atoms, while inductively withdrawing carbenic substituents will lessen the accumulation of negative charge on the carbenic center. The qualitative picture of electrophilic carbene addition to alkenes represented by transition state **2** is nicely mirrored by Eq. 4.

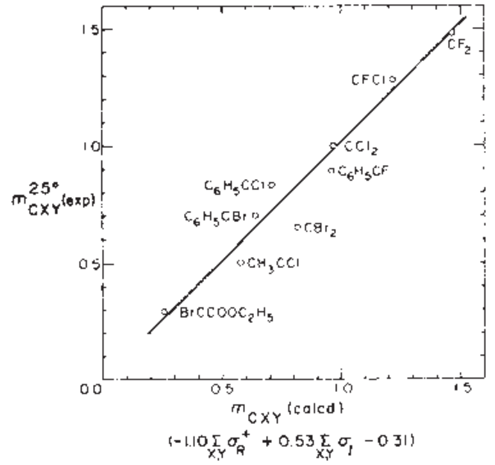
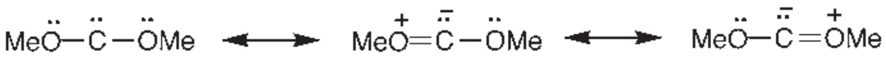


Figure 2. Slopes (m_{CXY}) of log (k_i/k_o) for CXY vs. log (k_i/k_o) for CCl_2 vs. σ_R^+ and σ_I; see Eq. 4. Reprinted with permission from ref. 8.

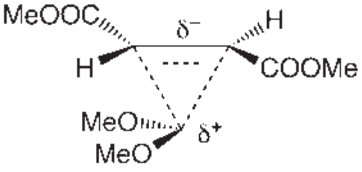
(3) Suppose we want to use Eq. 4 to estimate m_{CXY} values for new carbenes, particularly highly selective ones. According to the equation, we need to choose strongly resonance-donating substituents X and Y, for which σ_R^+ is large and negative. Good choices would be NMe_2, OMe, F, and Cl, with σ_R^+ = -1.75, -1.02, -0.57, and –0.36, respectively. [21] We can then calculate the anticipated m_{CXY} values for $MeOCNMe_2$, $(MeO)_2C$, MeOCF, and MeOCCl using appropriate σ_R^+ and σ_I substituent constants in Eq. 4. We obtain values of 2.91, 2.22, 1.85, and 1.59, respectively, for these 4 carbenes, each of which is predicted to be more selective than CF_2, where m_{CF2}(obsd) = 1.48. [8]



$$\mathrm{Me\ddot{O}{-}\ddot{C}{-}\ddot{O}Me} \longleftrightarrow \mathrm{Me\overset{+}{O}{=}\overset{-}{\ddot{C}}{-}\ddot{O}Me} \longleftrightarrow \mathrm{Me\ddot{O}{-}\overset{-}{\ddot{C}}{=}\overset{+}{O}Me}$$

4

These results immediately raised a problem. Dimethoxycarbene is so strongly stabilized by resonance (**4**) that it does not add to highly alkylated olefins such as $Me_2C{=}CMe_2$ or $Me_2C{=}CHMe$. Rather, this carbene adds to styrene and such electron-deficient olefins as diethyl maleate or fumarate, and ethyl cinnamate, [22] as well as aryl isocyanates and isothiocyanates. [23] In fact, $(MeO)_2C$ is a prime example of a *nucleophilic* carbene. Its "vacant" carbenic p orbital is involved in 2p-2p π bonding with electron pairs of the adjacent methoxy groups, so that electrophilic properties are suppressed at the carbenic center. Instead, the carbene's reactivity is defined by the electron pair residing in the sp^2 orbital on the carbenic center (cf., **3**). The carbene behaves as a nucleophile. We might represent the transition state for its reaction with dimethyl fumarate as **5**. Note the reversal of polarity relative to **3**, the transition state for electrophilic carbene addition. In the nucleophilic case, **5**, *negative* charge builds up on the olefinic carbon atoms and electron withdrawing substituents are necessary to disperse the charge. When such groups are absent, or electron donating alkyl groups are present, the activation energy for the addition of $(MeO)_2C$ is too high, and the carbene dimerizes to tetramethoxyethene, rather than add to the alkene. An excellent review of the nucleophilic chemistry of $(MeO)_2C$ and $MeOCNMe_2$ has been offered by Warkentin. [24]



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The results with dimethoxycarbene highlight an inherent deficiency of Eq. 4: it is an empirical correlation of parameters normalized to the electrophilic carbene, CCl_2. Its electrophilic heritage means that although the equation can predict m_{CXY} values for highly resonance stabilized, nucleophilic carbenes such as $(MeO)_2C$ or Me_2NCOMe, these are "virtual" selectivity indexes. The nucleophilic carbenes simply do not add to the alkenes of the "standard set." However, the equation helps us define the m_{CXY} regions in which electrophilic and nucleophilic carbenes reside. The electrophilic species, which react appropriately with the standard alkenes of Table 1, exhibit m_{CXY} values between 0.29 (BrCCOOEt) and 1.48 (CF_2). The nucleophilic carbenes, typified by $(MeO)_2C$, display $m_{CXY} \geq 2.2$. What philicity can we then expect for carbenes with m_{CXY} between 1.5 and 2.2?

(4) If there is not to be a discontinuity between electrophilic and nucleophilic behavior, then there should exist *ambiphilic* cabenes. Operationally, these

species should exhibit electrophilic selectivity with electron-rich alkenes and nucleophilic selectivity with electron-poor alkenes. [8] Our preceeding discussion suggests that ambiphilic carbenes should have $1.5 < m_{\mathrm{CXY}} < 2.2$, which means that MeOCCl, m_{CXY}(calcd) = 1.59, is a prime candidate for ambiphilicity.

Table 2. Relative Reactivities of an Ambiphilic Carbene

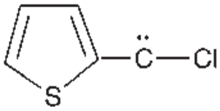
	k_{rel} for CXY		
alkene	MeOCCl[a]	MeCCl[b]	CCl_2[c]
$Me_2C{=}CMe_2$	12.6	7.44	78.4
$Me_2C{=}CH_2$	5.43	1.92	4.89
tr-MeCH=CHMe[d]	1.00	1.00	1.00
$CH_2{=}CHCOOMe$	29.7	0.078	0.060
$CH_2{=}CHCN$	54.6	0.074	0.047

[a] From ref. 25 (25 °C). [b] From ref. 26 (25 °C). [c] From ref. 26 (80 °C).
[d] Standard olefin.

Indeed, MeOCCl fulfills this prediction. [25] In Table 2, we present the relative reactivities of MeOCCl, MeCCl, and CCl_2 toward a set of alkenes which includes electron-rich olefins ($Me_2C{=}CMe_2$, $Me_2C{=}CH_2$) and electron-poor olefins ($CH_2{=}CHCOOMe$, $CH_2{=}CHCN$), with *trans*-MeCH=CHMe as the standard olefin. [8,25,26] The selectivity of MeOCCl clearly accords with our expectations for ambiphilicity: the k_{rel} sequence $Me_2C{=}CMe_2{>}Me_2C{=}CH_2{>}$*tr*-MeCH=CHMe is common to electrophilic carbenes [11] (see Table 1), whereas the high reactivities of MeOCCl toward $CH_2{=}CHCOOMe$ and $CH_2{=}CHCN$ are appropriate to a nucleophilic carbene. Moreover, this selectivity pattern differs dramatically from the behavior expressed by MeCCl ($m_{\mathrm{CXY}} = 0.50$) or CCl_2 ($m_{\mathrm{CXY}} = 1.0$). The latter species display a clear electrophilic selectivity over all 5 olefins of Table 2.

Our empirical analysis of selectivity in the carbene/alkene cyclopropanation reaction has now furnished both a quantitative index of selectivity and examples of the three types of carbene philicity: electrophilicity (exemplified by CCl_2), ambiphilicity (represented by MeOCCl), and nucleophilicity (exemplified by $(MeO)_2C$).

The selectivities of many other carbenes have been characterized and their respective m_{CXY} values assigned either experimentally or calculated by the use of Eq. 4. Among the experimentally defined species are PhCBr ($m = 0.70$), [27] PhCCl ($m = 0.83$), [28] PhCF ($m = 0.96$), [29] MeSCCl ($m = 0.91$), [30] and CFCl ($m = 1.28$). [9] More recent determinations include thiophenylchlorocarbene (**6**), for which $m_{CXY} = 0.95$, [31] and propynylbromocarbene (**7**), for which $m_{CXY} = 0.48$ (at -10 °C). [32] At least from their m_{CXY} values, and their behavior toward the alkenes of Table 1, these carbenes should be considered electrophiles (see however, below).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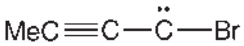

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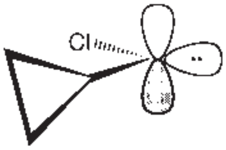
Another interesting electrophilic carbene is trifluoromethylchlorocarbene, CF_3CCl, which exhibits $m_{CXY} \sim 0.19$. [33] Notice that the electron withdrawing CF_3 substituent decreases the carbene's ability to discriminate between simple alkenes relative to MeCCl ($m_{CXY} = 0.50$). Substitution of CF_3 for CH_3 in RCCl appears to make the carbene less selective. Presumably, replacement of the electron donating methyl substituent by the electron withdrawing trifluoromethyl group destabilizes RCCl, a conclusion supported by ab initio calculations. [33]



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Cyclopropylchlorocarbene (**8**) should have $m_{CXY} = 0.73$ as calculated from Eq. 4. However, as determined experimentally from the measured relative reactivities, $m_{CXY} = 0.41$. [34] Close analysis, including ab initio calculations, reveal that in order to add to alkenes, steric demands require the cyclopropyl unit of carbene **8** to twist away from the "bisected" conformation shown in **8** (where stabilizing electronic interactions of cyclopropyl σ bonds and the vacant carbenic p orbital are optimal) to the "twisted" conformation depicted in **9** (where the electronic interaction is diminished). [35] The effective m_{CXY} value for **9** could be estimated as ~ 0.48, similar to the experimental value (0.41); whereas the m_{CXY} associated with **8** is calculated to be 0.81, similar to the value derived from Eq. (4) (0.73). [34] Thus the experimental and computational studies suggest that cyclopropylchlorocarbene adds to the olefins of Table 1 as a "twisted" electrophile, best represented by structure **9**.

Other *ambiphiles* characterized by experiment include phenoxychlorocarbene [36] (PhOCCl) and phenoxyfluorocarbene (PhOCF). [37] PhOCCl has m_{CXY} = 1.49 as calculated from Eq. 4, [36] nearly identical to that of CF_2, m_{CXY} = 1.48 (experimental) or 1.47 (calculated). [8] Despite the well expressed electrophilicity of CF_2, [9] PhOCCl behaves as an ambiphile; cf., Table 3. [38] Thus, m_{CXY} (calcd) = 1.49 already marks an empirical boundary for ambiphilic carbenes, at least as viewed through the "lens" defined by the alkenes in Tables 2 and 3. PhOCF has m_{CXY} (calcd) = 1.74, considerably higher than that of PhOCCl, and 0.15 higher than that of the "first" ambiphile, MeOCCl (Table 2). The data of Table 3 indicate that PhOCF also behaves as an ambiphile.

Table 3. Relative Reactivities of PhOCCl and PhOCF

	k_{rel} for CXY	
alkene	PhOCCl[a]	PhOCF[b]
$Me_2C{=}CMe_2$	8.3	7.14
$Me_2C{=}CH_2$	20.3	14.3
n-$C_4H_9CH{=}CH_2$[c]	1.00	1.00
$CH_2{=}CHCOOMe$	10.3	18.7
$CH_2{=}CHCN$	15.3	33.6

[a] From ref. 36 and 37 (25 °C). [b] From ref. 37 (50 °C). [c] Standard alkene.

3.1.3 Other empirical measures of carbenic reactivity

3.1.3.1 Hammett correlations

One can also characterize the reactivity and selectivity of carbenes using the venerable Hammett σρ linear free energy methodology. [5,39] Additions of CXY could be examined with a series of ring-substituted styrenes, $ArCH=CH_2$. Relative reactivities could be obtained, with styrene itself as the standard olefin, and then log k_{rel} could be plotted against the appropriate σ constant for each substituted styrene substrate. The slope of the resulting correlation is the Hammett ρ value for the carbene addition.

For example, Figure 3 illustrates this type of determination carried out for CF_2 at 80 °C. The various styrene substituents are indicated on the Figure, and $\rho = -0.57$.

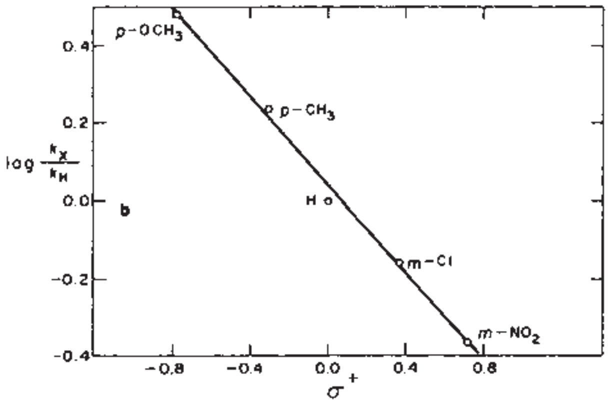


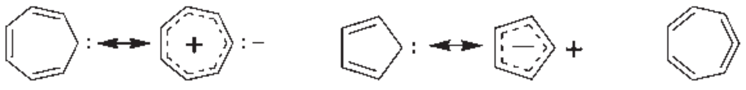
Figure 3. Plot of log (k_X/k_H) vs. σ^+ or σ_m for the addition of CF_2 to $ArCH=CH_2$ (80 °C). Reprinted with permission from ref. 9.

A negative value of ρ indicates that the reaction is accelerated by electron-donating substituents; that is, positive charge develops on the olefinic carbon atoms in the addition reaction's transition state (see **2**), which is then mitigated (and the energy of the transition state lowered) by electron release from the aromatic ring and its substituent. That means that CF_2 behaves as an *electrophile* in its addition to these styrene substrates, the same conclusion that we reached for the olefins on the basis of m_{CXY} (see above and Table 1).

Hammett ρ values have been similarly determined for many other carbene additions to styrenes. [40] Thus, $\rho = -0.62$ (vs σ^+) for CCl_2 at 80 °C. [41] CCl_2 is also electrophilic to styrenes. Note, however, that $m_{CF_2}/m_{CCl_2} = 1.48/1.00 = 1.48$, whereas ρ_{CF_2}/ρ_{CCl_2} = -0.57/-0.62 = 0.92; the selectivity of CF_2 is greater than that of CCl_2 toward the set of alkenes in Table 1, but slightly less than that of CCl_2 toward styrene substrates. This suggests that the charge distributions are quite different in the transitions states (**2**) for the additions of CCl_2 or CF_2 to alkenes where R_i = alkyl, as compared to carbene additions to styrenes, where R_1 = Ar, $R_2 = R_3 = R_4$ = H. A general attempt to correlate ρ_{CXY} with $\sigma_R{}^+$ and σ_I of X and Y would require coefficients other than those employed in Eq. 4; a different interplay of resonance and inductive effects governs the selectivity of CXY toward alkyl-substituted olefins and aryl-conjugated substrates such as styrenes.

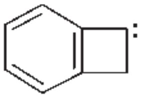
Other electrophilic carbenes characterized by Hammett ρ values include $Me_2C{=}C{=}C{:}$ (ρ = -0.95), [42] and $Me_2C{=}C{:}$ (ρ = -0.75 [43] or –0.64 [44]). Dimethylvinylidene has been carefully surveyed by Gilbert and Giamalva, [44] who note that the method of carbene preparation (Is the carbene free or complexed?), the nature of the solvent, as well as the temperature, all affect the magnitude of ρ. [44] Production of $Me_2C{=}C{:}$ from a diazoalkene precursor at –78 °C affords ρ = -0.64; [44] generation by α-elimination from $Me_2C{=}CHOTf$ and *t*-butoxide at –20 °C gives ρ =-0.75; [43] and the species generated by reacting $Me_2C{=}CBr_2$ with MeLi at –40 °C displays ρ = -4.3 (vs. σ^+). [44] Presumably the latter reaction involves a carbenoid ($Me_2C{=}CLiBr$), but the hugely different value of ρ cautions us that the empirical characterization of carbenic reactivity demands that carbenes be generated in comparable solvents, at similar temperatures, and by methods most likely to yield free carbenes.

What about a *nucleophilic* carbene, for which negative charge should build up on the olefinic carbon atoms during the carbene addition; cf. **5**? With $ArCH{=}CH_2$ substrates, electron-withdrawing aryl substituents would stabilize such a transition state and the ρ value should be positive. There are several examples of this phenomenon. For example, cycloheptatrienylidene, **10**, adds to *p*-substituted styrenes with ρ = +1.02 - 1.05 (vs. σ) consistent with a nucleophilic selectivity that seems to implicate the "aromatic" resonance form **10a** as an important feature of the carbene. [45] It is satisfying to compare this result with ρ = -0.76 (vs. σ) or –0.46 (vs. σ^+) for additions to styrenes of cyclopentadienylidene, **11**, where contributions of the cyclopentadienide form (**11a**) would render the carbene electrophilic. [46] However, these conclusions are too facile. There is reason to believe that the chemistry attributed to **10** might in fact be due to its allenic isomer **12**. [47] And the electronic structure of **11** is also more complicated than the simple depiction above. [48]



10 **10a** **11** **11a** **12**

Other carbenes which exhibit nucleophilic behavior include benzocyclobutenylidene (**13**), [49] bicyclo[3.2.1]octa-2,6-dien-4-ylidene (**14**), [50] and bicyclo [3.2.1]octa-2-en-4-ylidene (**15**), [50] with reported ρ values (vs. σ) of +1.57, +0.25, and +0.68, respectively. In all cases, computations suggest either an excess of negative charge on the carbenic center or a high-lying HOMO (essentially the carbene lone pair), which account for the carbenes' nucleophilicity toward styrenes.



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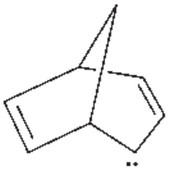

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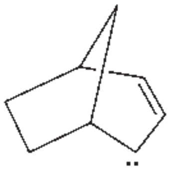

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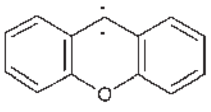
Can the ρσ treatment identify ambiphilic carbenes? The answer is affirmative. The additions of PhOCCl, a known ambiphile (see Table 3), were studied with a series of substituted styrenes. The k_{rel} data (and substituents) were: 1.95 (*p*-MeO), 1.32 (*p*-Me), 1.00 (H), 1.17 (*p*-Cl), 1.42 (*p*-CF_3) , 1.33 (*m*-NO_2). [51] Clearly, PhOCCl selects among the first 3 substrates as an electrophile (preferring the electron-rich *p*-methoxystyrene), but it selects among the last 4 substrates as a nucleophile (preferring the electron-poor *p*-trifluoromethyl- and *m*-nitrostyrenes.) Figure 4, which depicts a plot of log (k_{rel}) vs. σ^+ or σ constants, makes the point dramatically.

It is a "broken" Hammett plot, in which the minimum k_{rel} occurs with styrene itself (*i.e.*, where the substituent, H, is the minimum on the electron-donation/electron-withdrawal scale). Broken Hammett correlations are traditionally interpreted to signify a change in reaction mechanism as a function of changes in the substituents' electronic properties. Here, the "change in mechanism" mirrors the ambiphilicity of PhOCCl: the carbene behaves as an electrophile toward electron-rich styrenes, but as a nucleophile toward electron-poor styrenes. Very similar behavior toward styrenes is revealed by MeOCCl, [52] also known to be an ambiphile on the basis of its behavior toward other alkenes (see above, and Table 2).

We should also note in passing that *triplet* carbenes also seem to react with substituted styrenes with ambiphilic selectivity. Thus, both triplet 9-xanthylidene, **16**, [53] and diphenylcarbene, **17**, [54] add to X-$C_6H_4CH{=}CH_2$ (X = *p*-MeO, *p*-Me, H, *p*-Cl, *p*-Br, and *m*-Br), and afford "broken" Hammett patterns with k_{rel} minima at X = H (σ = 0.0). The "ambiphilicity" of these triplet species is distinct from that of the singlet carbenes, MeOCCl or PhOCF, discussed above. The philicity of the latter can be understood by molecular orbital analysis of their concerted cycloadditions to alkenes (as discussed in Section 2.1, see below), whereas the ambiphilicity of **17** (or **16**) can be understood in terms of the electron-donating or electron-withdrawing substituent stabilization of the benzylic radical center in (triplet) 1,3-diradical **18**, which must be an intermediate in the addition of triplet Ph_2C to $ArCH{=}CH_2$. [53,54] Prresumably, **18** can be stabilized by either electron-donating or electron-withdrawing substituents.



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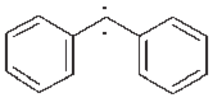

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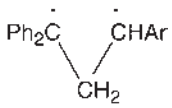

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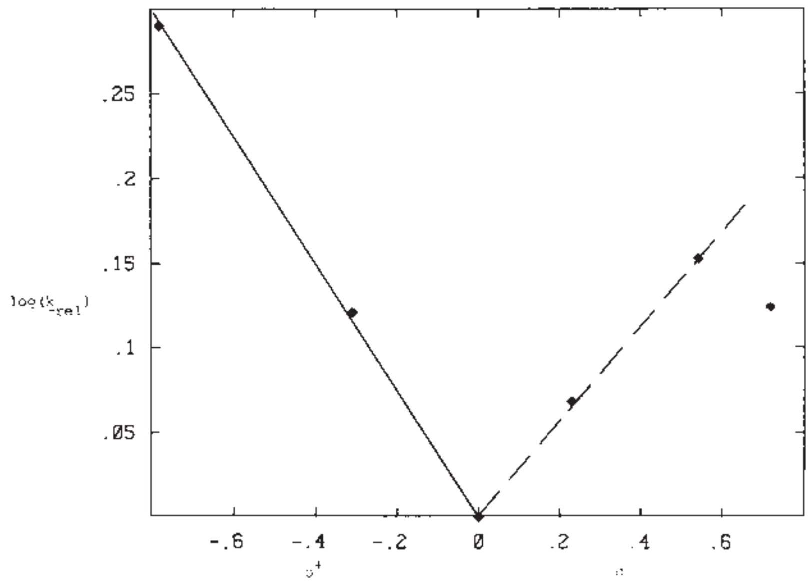
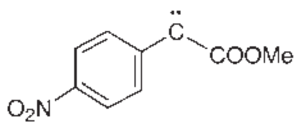


Figure 4. A "broken" Hammett correlation: log (k_{rel}) vs. σ^+ or σ for additions of PhOCCl to X-$C_6H_4CH{=}CH_2$. The solid line correlates data for X = *p*-MeO, *p*-Me, and H; the dashed line correlates data for H, *p*-Cl, and *p*-CF_3. The point for *m*-NO_2 has been excluded. Reprinted with permission from ref. 51.

A particularly interesting use of the Hammett relation to examine carbenic philicity was proved by Tomioka, *et. al.* [40] These scientists determined k_{rel} for the additions of carbenes **19** and **20** to a series of substituted styrenes. Although these carbenes possess triplet ground states, their additions to styrene probably proceed via the initially formed singlet carbenes. For carboxylate ester carbene **19**, log (k_{rel}) data affords ρ = -0.75, but carboxylate carbene **20** gives ρ = +0.35. Thus, **19** adds to the styrenes as an electrophile, whereas **20** behaves as a nucleophile. The reversal of philicity is attributed to an α-lactone-type electron donation from the carboxylate group of **20** (cf., **20a**) which ties up the vacant p orbital of carbene **20** and leads to excess carbanionic (nucleophilic) character at the carbene center; ester carbene **19**, in which such interaction cannot occur, remains an electrophilic species. [40]



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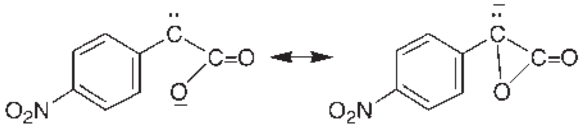


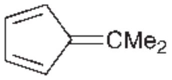
20 **20a**

Finally, what of my early idea of reacting a series of arylcarbenes (X-C_6H_4CH) with a fixed pair of olefins, and correlating log (k_a/k_b) vs. σ_X (see Section 1.1)? I actually carried out such experiments during my doctoral research. For example with carbene substituents X = *p*-MeO, *p*-Me, H, *p*-Cl, and *m*-Cl, and the olefin pair isobutene/*trans*-butene, the log (k_{rel}) data is correlated by σ constants to give ρ = +0.3. [7] We can interpret this result as the difference of the ρ values for carbene addition to isobutene vs. *trans*-butene, where the ρ for isobutene is more positive than that for *trans*-butene. It is difficult to interpret this data further. A clearer picture emerges with the use of *absolute* rate constants for carbene/alkene addition reactions. Those experiments will be described below in Section 2.2.

3.1.3.2 Other philicity measures

Several "special" substrates have been employed to sharpen empirical measures of philicity. For instance, 6,6-dimethylfulvene (**21**) is attacked by electrophilic carbenes (e.g., CCl_2) at its endocyclic π bonds, affording *m*-chlorostyrene derivatives (e.g., **22**) after cyclopropanation, rearrangement, and loss of HCl. [55] On the other hand, nucleophilic carbenes [$(MeO)_2C$] and the ambiphilic carbene, MeOCCl, add to **21** at its exocyclic π bond, affording spiro[2.4]heptadiene products **23** (X=OMe or Cl). [56] These results can be understood in terms of frontier molecular orbital theory, which will be discussed in some detail in Section 2.1. Briefly, electrophilic carbenes strongly interact with the highest occupied molecular orbital (HOMO) of **21**, which distributes its electron density over the endocyclic "butadiene" fragment of **21**. Nucleophilic $(MeO)_2C$

most strongly interacts with the lowest unoccupied molecular orbital (LUMO) of **21**, which is most explicit at the exocyclic π bond. The *exo*-attack of MeOCCl appears to be a function of the very large LUMO coefficient at C_6 of substrate **21**. Thus, the regiochemistries of the CCl_2, MeOCCl, or $(MeO)_2C$ additions to dimethylfulvene reflect the carbenes' philicities, and can be understood in terms of molecular orbital theory. [56]



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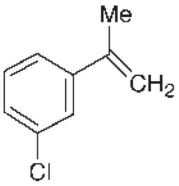

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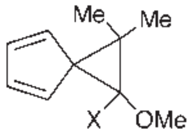

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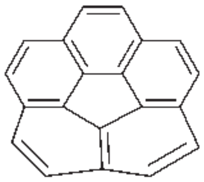
Related observations include the addition of CCl_2 to corannulene, **24**, which gives mainly **25**, albeit in low (8%) yield. [57] Note that the attack of CCl_2 occurs at a "radial" rather than a "peripheral" π bond. The regiochemistry appears to be governed by the electrophilic carbene's preference to attack the substrate's HOMO at a site with a high orbital coefficient, and the HOMO of corannulene has its largest orbital coefficients at the interior carbon atoms. [57] CBr_2 and CI_2 also give low yields of adducts analogous to **25**. [57]



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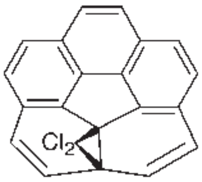

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Dihalocarbene addition to **24** is related to the addition of carbenes to C_{60}, Buckminsterfullerene, which occurs across a C_6-C_6 junction to give methanofullerenes, in preference to addition across the fullerene C_6-C_5 junction. [58] 2-Adamantanylidene,[58] PhCCl, [58] and CCl_2, [59] also behave in this manner. Interestingly, nucleophilic $(MeO)_2C$ also attacks a fullerene C_6-C_6 junction. [60] Fullerene is a strongly electrophilic substrate, [61] and does not differentiate electrophilic (CCl_2) from nucleophilic carbenes on the basis of the regiochemistry of their additions.

3.1.4 And yet…

By about 1980, a reasonable empirical understanding of carbenic philicity seemed to be at hand; electrophiles, ambiphiles, and nucleophiles had been identified and could be assigned m_{CXY} or ρ_{CXY} values that reflected the magnitude and character of their selectivity during their additions to alkenes. And yet, our rationalization of these reactions only in terms of relative reactivities and linear free energy relations was surely incomplete.

Consider, for example, the phenylhalocarbenes, PhCX. Observed (and calculated) values of m_{CXY} were PhCF, 0.89 (0.96); PhCCl, 0.83 (0.71); PhCBr, 0.70 (0.64), [8] situating PhCX firmly within the electrophilic family of carbenes ($m_{CXY} < 1.49$). And yet, PhCCl added readily to electron poor alkenes. [62] We examined the relative reactivities of PhCF and PhCCl toward the alkenes of Table 3, and compared the results to analogous data for electrophilic MeCCl ($m_{obsd} = 0.50$) and ambiphilic MeOCCl ($m_{calcd} = 1.59$). These comparisons appear in Table 4. [63]

Table 4. Relative Reactivities of PhCF, PhCCl, MeCCl, and MeOCCl[a]

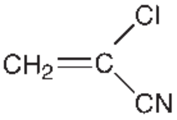
	k_{rel} for CXY			
alkene	PhCF[b]	PhCCl[c]	MeCCl[d]	MeOCCl[e]
$Me_2C{=}CMe_2$	33.2	25.5	7.44	12.6
$Me_2C{=}CH_2$	6.67	5.00	1.92	5.43
tr-MeCH=CHMe[f]	1.00	1.00	1.00	1.00
$CH_2{=}CHCOOMe$	0.74	0.50	0.078	29.7
$CH_2{=}CHCN$	0.80	0.55	0.074	54.6

[a] At 25 °C; ref. 63. [b] From ref. 29. [c] From ref. 64. [d] From ref. 26. [e] From ref. 25. [f] Standard alkene.

PhCF and PhCCl appear to be electrophilic: their selectivities resemble that of MeCCl in that all three carbenes are less reactive toward methyl acrylate and acrylonitrile than *trans*-butene. Moreover, PhCF and PhCCl certainly differ from ambiphilic MeOCCl, which is much more reactive toward the electron-poor alkenes than it is toward *trans*-butene. And yet, the electron deficient alkenes are *much* less reactive than *trans*-butene with MeCCl, but only 20 – 50% less reactive with PhCX.

We also determined Hammett ρ values for the additions of PhCF and PhCCl to a series of *p*-substituted styrenes (X = MeO, Me, H, Cl, CF_3). [63] The results were ρ = -0.22 (PhCF) and –0.32 (PhCCl), in agreement with electrophilic behavior for these carbenes.

Nevertheless, the use of relative reactivities to characterize carbenic philicity is restrictive; the apparent philicity is related to the alkenes selected for the relative reactivity measurements. What if the set of alkenes were expanded by the addition of an even more electron-deficient alkene? Such a test was applied in 1987 [65], using α-chloroacrylonitrile, **26**, which is more π-electron deficient than acrylonitrile, **27**. We found that PhCF or PhCCl added 15 or 13 times, respectively, more rapidly to **26** than to **27**. In preferring the more electron-deficient olefin, the carbenes exhibited nucleophilic character. However, because they also behave as electrophiles toward other alkenes (Table 4), they must in reality be ambiphiles. In fact, we now realize that all carbenes have the potential for nucleophilic reactions with olefins; the crucial factor is whether the carbene's filled σ orbital (HOMO)/alkene vacant π* orbital (LUMO) interaction is stronger than the carbene's vacant p orbital (LUMO)/alkene filled π orbital (HOMO) interaction in the transition state of the addition reaction. [63]



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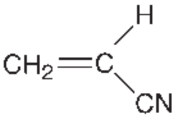

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It was clear that we needed a better theoretical framework to parallel and permit interpretation of carbenic philicity. Two crucial developments occurred around 1980: the application of ab initio computational methods and frontier molecular orbital (FMO) theory to carbene/alkene addition reactions, and the measurement of *absolute* rate constants for these reactions by laser flash photolysis (LFP). Together, these approaches greatly clarified our understanding of carbenic selectivity and philicity, and defined the current "state of the art."

3.2 STATE OF THE ART [66]

3.2.1 Theoretical background

3.2.1.1 FMO and ab initio studies

FMO theory [67] was successfully applied to the rationalization of electrophilic, nucleophilic, and ambiphilic behavior in 1,3-dipolar cycloaddition and Diels-Alder reactions. [68] The availability of orbital energies computed for a variety of CXY, [69] enables a similar rationalization of carbenic reactivity and philicity. It was from my colleagues Ken Houk (then of Louisiana State University, now of UCLA) and Karsten Krogh-Jespersen (of Rutgers University) that I learned how incisively FMO theory could help us to understand carbenic philicity. My collaborations with each of these excellent scientists have greatly enriched my understanding of carbenic reactivity.

The addition of a singlet carbene to an alkene involves simultaneous interactions of the vacant carbenic p orbital (LUMO) with the filled alkene π orbital (HOMO), and of the filled carbenic σ orbital (HOMO) with the vacant alkene π* orbital (LUMO). [70] These interactions are illustrated in Figure 5, where the orbital symmetries are also shown.

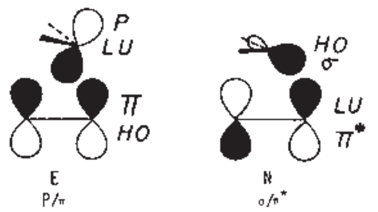


Figure 5. HOMO-LUMO interactions in carbene/alkene cycloadditions. Left, carbene p/alkene π; right, carbene σ/alkene π*. Reprinted with permission from ref. 66.

A singlet carbene is inherently *both* an electrophile and a nucleophile, what is behaviorally decisive is whether, in the carbene/alkene addition transition state, it is the LUMO(carbene)/HOMO(alkene) or HOMO(carbene)/LUMO(alkene) interaction (cf., Fig. 5) which dominates and determines the electronic distribution. If the former interaction dominates, the carbene will exhibit *electrophilic* selectivity; if the latter interaction is more important, *nucleophilic* selectivity will be observed. If both interactions are comparable, the carbene will display an *ambiphilic* selectivity pattern, in which it acts as an electrophile toward electron-rich alkenes, but as a nucleophile toward electron-poor alkenes. [8,69]

$$\Delta\varepsilon_E = \varepsilon^{LU}_{CXY} - \varepsilon^{HO}_{C=C} = p - \pi \tag{5}$$

$$\Delta\varepsilon_N = \varepsilon^{LU}_{C=C} - \varepsilon^{HO}_{CXY} = \pi^* - \sigma \tag{6}$$

How can we use these ideas in (at least) a semi-quantitative fashion? The dominant orbital interaction of Fig 5 will be determined both by the comparative extents of orbital overlaps and by the differential energies of the two FMO interactions. [67-70] Neglecting overlap for now, we can express the differential orbital energies as in Eq. 5 and 6, where Eq. 5 represents the electrophilic (E) interaction and Eq. 6 the nucleophilic (N) interaction. [66] These differential orbital energies appear in the denominators of the expression for ΔE, the stabilization energy gained when the carbene and alkene FMO's interact in the transition state. Therefore, the *smaller* differential orbital energy makes the *larger* contribution to ΔE, and will determine the philicity of the addition reaction. [8,66,69]

Let us qualitatively illustrate the application of these ideas. Consider the addition of an electrophilic carbene (e.g., CCl_2) to an electron rich olefin (e.g., butyl vinyl ether). Schematically, we can represent the FMO situation as shown in Figure 6 (E case). Here the differential energy of the carbene(LUMO)/alkene(HOMO), p - π interaction is smaller than the alternative alkene(LUMO)/carbene(HOMO), π* - σ interaction, and the former term dominates. Suppose we now replace the olefin's electron donating methoxy substituent with an electron withdrawing cyano group. This will stabilize and lower the energy of the olefin's π and π* orbitals. If we also select a nucleophilic carbene (e.g., $(MeO)_2C$), we obtain the situation represented in Figure 6 (N case), where the alkene(LUMO)/carbene(HOMO), π* - σ interaction dominates and the addition reaction is nucleophilic.

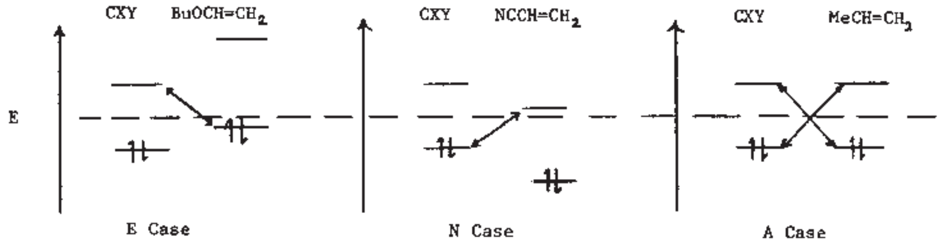
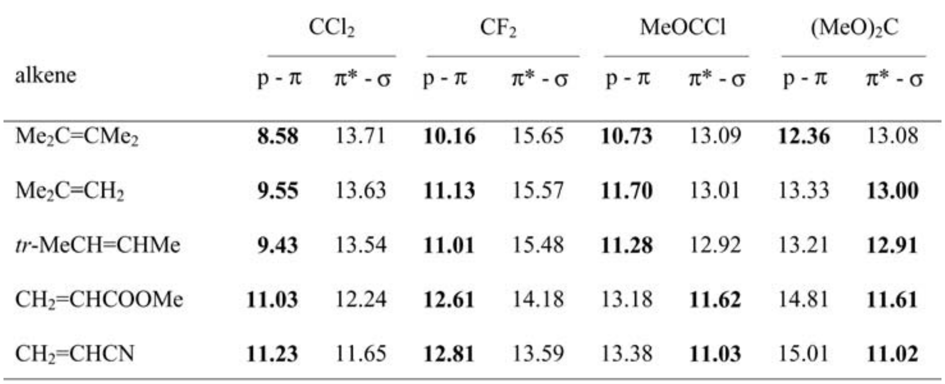


Figure 6. Schematic representations of relative FMO energies for electrophilic (E), nucleophilic (N), and ambiphilic (A) carbene/alkene additions.

Finally, consider the addition of an experimentally ambiphilic carbene (MeOCCl) to a simple alkene (e.g., propene). Now the carbene and alkene FMO's are roughly in balance; both differential FMO energies will be comparable. This is depicted in the "A Case" of Fig. 6. Now changing the alkene's Me substituent to BuO will raise both the π and π* orbital energies of the alkene, and convert the A Case to the N Case; i.e., the addition reaction will become electrophilic. Alternatively, changing propene's Me substituent to CN will convert the A Case to the N Case; the addition reaction will become nucleophilic. Of course, these imaginary manipulations describe the behavior of an ambiphilic carbene, and the expression of these thought experiments is represented by the relative reactivities of MeOCCl collected in Table 2.

Table 5. Differential Orbital Energies for Carbene/Alkene Additions



	CCl_2		CF_2		MeOCCl		$(MeO)_2C$	
alkene	p - π	π* - σ	p - π	π* - σ	p - π	π* - σ	p - π	π* - σ
$Me_2C{=}CMe_2$	**8.58**	13.71	**10.16**	15.65	**10.73**	13.09	**12.36**	13.08
$Me_2C{=}CH_2$	**9.55**	13.63	**11.13**	15.57	**11.70**	13.01	13.33	**13.00**
tr-MeCH=CHMe	**9.43**	13.54	**11.01**	15.48	**11.28**	12.92	13.21	**12.91**
$CH_2{=}CHCOOMe$	**11.03**	12.24	**12.61**	14.18	13.18	**11.62**	14.81	**11.61**
$CH_2{=}CHCN$	**11.23**	11.65	**12.81**	13.59	13.38	**11.03**	15.01	**11.02**

[a] The differential orbital energies are defined in Eqs. 5 and 6. For alkene and carbene orbital energies and references, see references 8 and 69

If we neglect orbital overlap, FMO analysis enables semi-quantitative characterization of the olefinic selectivity of any carbene using orbital energies to estimate the LUMO(carbene)/HOMO(alkene) and LUMO(alkene)/HOMO(carbene) differential energies for a series of CXY/alkene reactions. [8,66,69] Experimental values of π and π* orbital energies are available for many alkenes, and p and σ orbital energies can be calculated by ab initio methods for CXY. [69] Although it is somewhat primative to combine calculated and uncalculated carbene orbital energies with experminental values for alkenes, the results do seem to reflect reality.

In Table 5, we present the differential orbital energies, $\Delta\varepsilon_E$ and $\Delta\varepsilon_N$, as defined in Eqs. 5 and 6, for the additions of electrophilic (CCl_2, CF_2), ambiphilic

(MeOCCl), and nucleophilic [$(MeO)_2C$] carbenes to the alkenes of Tables 2 and 4. [8] For CCl_2 and CF_2, p - π ($\Delta\varepsilon_E$) is uniformly lower than π* - σ ($\Delta\varepsilon_N$) across the substrate set; the LUMO(carbene)/HOMO(alkene) interaction dominates, and these carbenes should be electrophilic in most accessible experimental situations (cf., Tables 1 and 2). For $(MeO)_2C$, however, the differential orbital energies are dominated by the π* - σ ($\Delta\varepsilon_N$) term; this carbene's additions to most alkenes should be nucelophilic. [22-24,71,72] MeOCCl, on the other hand, is clearly predicted to be an ambiphile by Table 5, and this is supported by the selectivity data in Table 2. Note, in Table 5, that the additions of MeOCCl are governed by $\Delta\varepsilon_E$ = p - π when the alkenes are electron rich (high-lying π orbitals), but are dominated by $\Delta\varepsilon_N$ = π* - σ when the alkenes bear electron withdrawing groups, which lower both π* and π orbital energies. There is a *crossover* or "mechanism change" from predominantly electrophilic to nucleophilic addition as we proceed from $Me_2C{=}CMe_2$ to $CH_2{=}CHCN$ substrates. This is experimentally reflected in a parabolic or ambiphilic selectivity pattern. [66]

Table 6. Carbenic Philicity and FMO Energies

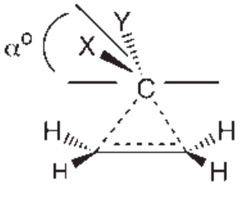
carbene	ε_{HO},[a] eV	ε_{LU},[a] eV	exptl philicity[b]
CF_2	-13.4	1.9	E
CCl_2	-11.4	0.31	E
MeOCCl	-10.8	2.5	A
MeOCPh	-9.4	2.4	A
PhOCF	-11.8	2.6	A
MeOCMe	-9.4	4.0	N
$(MeO)_2C$	-10.6	4.3	N

[a] The oxacarbenes are considered only in their trans configurations. Orbital energies are computed at the 4-31G level after geometry optimization at the STO-3G level: see refs. 37, 69, 72, and 73. [b] Predominant experimental philicity; E = electrophilic, A = ambiphilic , N = nucleophilic.

In general, electrophilicity is favored by a low-lying HOMO or σ orbital, which makes electron donation by the carbene unfavorable, and by a low-lying, accessible LUMO or p acceptor orbital. Conversely, carbenic nucleophilicity is favored by a high-lying HOMO, for efficient electron donation, and a high-lying inaccessible LUMO. [66]

If we adhere to a common set of alkene substrates, as in Table 5, carbenic philicity can be approximated simply by inspection of the ab initio computed carbene FMO energies, cf., Table 6. [66,73] Thus, CF_2 is forced to be an electrophile; its extremely low-lying σ HOMO contains electrons that are simply unavailable for donation. It cannot readily function as a nucleophile. CCl_2, conversely, is electrophilic by dint of its low-lying LUMO, which can easily accept electrons from (e.g.) an electron-rich alkene. MeOCCl, MeOCPh, and PhOCF have σ and p (HOMO and LUMO) orbitals that fall at "intermediate" energies, either ($\Delta\varepsilon_E$) or ($\Delta\varepsilon_N$) can dominate their additions, depending on the alkene, with an attendant ambiphilic reactivity pattern. Finally, the high-lying, relatively inaccessible LUMO's of MeOCMe [73] and $(MeO)_2C$, [72] together with their "middling" donor HOMO's, enable strongly nucleophilic selectivity.

Carbenic FMO energies for a dozen carbenes were computed by Rondan *et al.*, [69] who found a good linear correlation between ε_{LU} (4-31G) and m_{CXY} (from Eq. 4). Thus, as the energy of the vacant carbenic p orbital rises, m_{CXY} rises; i.e., the carbene becomes *less* electrophilic, passing through ambiphilicity to nucleophilicity. Another striking philicity indicator described by Rondan is the tilt angle (α) of the CXY plane with respect to the plane of the substrate olefin in the transition state for CXY addition to (e.g.) ethene; cf., **28**. [8,69] In a "purely" electrophilic transition state, only the carbene p orbital (LUMO) would impinge on the ethene's π orbitals and α would be 0°. Conversely, in a purely nucleophilic attack, only the carbenic σ orbital (HOMO) would interact with the ethene's π* orbital; α = 90°. The STO-3G computed values for α in **28** are CCl_2 (36°); CF_2 (43°), FCOH (48°), and $C(OH)_2$ (58°). [69] We see that α increases as the carbene moves from electrophilic (CCl_2, CF_2), to ambiphilic (FCOH), to nucleophilic ($C(OH)_2$): α parallels philicity.



28

3.2.1.2 Other theoretical approaches

Of course, while Ken Houk, Karsten Krogh-Jespersen, and I were applying FMO theory to carbene/alkene additions, other investigators were also analyzing these reactions from a theoretical perspective. Here, we will briefly consider several of these reports.

Schoeller and Brinker applied single electron perturbation theory to carbene/alkene additions and elaborated a construct that was almost indentical to our FMO analysis. [74] Schoeller also focused on estimating LUMO(carbene)/HOMO(alkene) and LUMO(alkene)/HOMO(carbene) differential energies, and derived a "selectivity index", S, which roughly paralleled m_{CXY}, and predicted the electrophilicity of the dihalocarbenes and the nucelophilicity of (e.g.), $C(NH_2)_2$, $C(OH)_2$, and $C(SMe)_2$. [74]

In 1988, Platz, *et al*. published a highly detailed study of the addition of arylchlorocarbenes (ArCCl) to a wide variety of electron-rich and electron-poor alkenes. [75] Absolute and relative rates of carbene/alkene additions were measured, and the ambiphilicity of ArCCl additions was noted, in agreement with our conclusions; see Section 1.4, above. [65] The ambiphilicity was expressed over a wide range of alkenes, which included diethyl fumarate as a very electron-poor alkene. To rationalize their data, Platz, *et al.* also used FMO arguments, deriving SE_{ts}, the stabilization energy for the addition reaction transition state, which depended on the usual differential FMO energies and the average ratio between p/π and σ/π* resonance integrals. [75] A plot of log *k* (where *k* is the absolute rate of the carbene/alkene addition determined by LFP) vs SE_{ts} was roughly linear for the additions of PhCCl to many alkenes. Thus, the FMO analysis was reaffirmed in its applicability to ArCCl, and the need for inclusion of the nucleophilic LUMO(alkene)/HOMO(carbene) component in the analysis was emphasized. Moreover, when log *k* was plotted against the "π molecular electronegativity" of the alkenes (defined as the average of the alkene's π and π* orbital energies, taken as ½ the sum of the ionization potential and the electron affinity), a roughly U-shaped (parabolic), ambiphilic correlation was obtained. The ambiphilicity of PhCCl, first recognized from relative reactivity studies with α-chloroacrylonitrile, [65] nicely emerged from this FMO analysis. [75]

Kostikov and his colleagues have focused on the additions of halocarbenes to dienes, trienes, and styrenes. They found that the reactivity of CCl_2 toward these substrates could be satisfactorily correlated with the localization energies of the CH_2 unit of the terminal double bond, calculated by the SCF PPP method as the difference between the energies of the π electrons of the substrate and the carbocation formed from it after detachment of the CH_2. [76] This correlation treated CCl_2 as an electrophile and basically followed the energy of the alkene's HOMO. It was found that the carbene's electrophilic reactivity tracked the availability of substrate HOMO electrons as measured by their IP (ionization potential). [18,76,77]

Zollinger examined the empirical correlation equation for m_{CXY} (Eq. 4) in the context of dual substituent parameter equations for a number of other, unrelated reactions (e.g., the loss of nitrogen from ArN_2^+). [78] Eq. 4 was thus shown to be one of a family of equations that can be derived to separate the influences of substituent resonance and field (inductive) effects on chemical reactivity. These equations trace back to Taft's formulation, Eq. 7, in which separate ρ and σ terms are used to represent the field and resonance electronic properties of substituents. [79] Zollinger points out that our m_{CXY} version of this expression is one of few dual substituent parameter equations in which the signs of the resonance and field terms are *opposed* (cf., Eq. 4, where the coefficients are –1.10 and +0.53, respectively). We have discussed the meaning of this opposition in Section 1.2, above.

$$\log (k_x/k_o) = \rho_F\,\sigma_F + \rho_R\,\sigma_R \qquad (7)$$

Fujimoto and Fukui analyzed carbene/alkene addition reactions using the method of paired interacting orbitals, in which one does not need to assume dominant contributions of the FMO's at the beginning of the analysis. [80] The method, which tracks electron redistribution during the reaction, was applied in detail to the addition of CH_2 to ethene, and then applied to additions of CCl_2, CClF, CF_2, CFOH, and $C(OH)_2$ to the same substrate. One pair of interacting orbitals, equivalent to carbene p-alkene π was important for the CCl_2 and CClF additions, which had early, electrophilic transition states and low activation energies. With CFOH and $C(OH)_2$, however, this interaction was less important; instead σ/p orbital mixing of the carbene was required to obtain addition, which occurred via a late, higher energy transition state. [80]

A new parameter, λ, was defined which represents the "capacitance" for electron acceptance by unoccupied molecular orbitals of CXY (mainly the $2P_y$ atomic orbital. $(\lambda_{CXY} - \lambda_{CCl_2})$ was found to be proportional to m_{CXY} for a variety of carbenes, including MeCCl, CFCl, CF_2, MeOCF, MeOCCl, and $(MeO)_2C$. [80]

Mendez and Garcia-Garibay analyzed carbene/alkene charge transfer by density functional theory and ab initio methods. [81] Electrophilicity and nucleophilicity were assessed by calculating ΔN, which represented charge transfer between the carbene and alkene; cf., Eq. 8. Here, μ is the chemical potential taken as –(I+A)/2, where I represents ionization potential, and A represents electron affinity. η is the "hardness" of the alkene or carbene, defined as (I-A)/2.

In the addition of the carbene to the alkene, electron density is transferred from regions of high μ (low electronegativity) to regions of low μ (high electronegativity). [81]

$$\Delta N = \frac{1}{2}\frac{(\mu_{alk} - \mu_{carb})}{(\eta_{alk} - \eta_{carb})} \tag{8}$$

For any carbene, ΔN from alkene to carbene increased as the alkene became more electron rich. ΔN also varied with the carbene. Carbenes with electron donor substituents supported carbene to alkene charge transfer. In fact, the ΔN paramenter ordered most ambiphilic and nucleophilic carbenes in agreement with m_{CXY}.

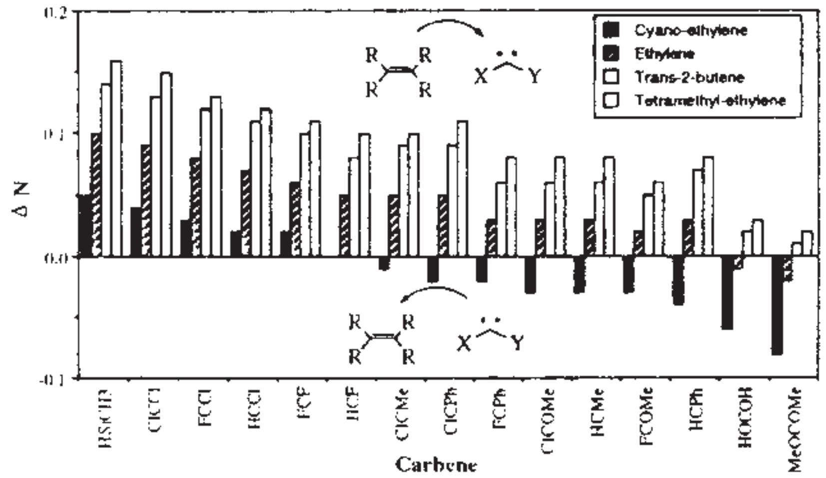


Figure 7. Histogram of charge transfer (ΔN) calculated for the additions of CXY to alkenes. Negative values of ΔN indicate electron density transfer from the carbene to the alkene. Adapted with permission from ref. 81.

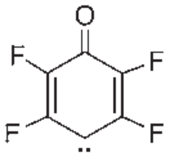
Figure 7 depicts the computed ΔN values for 15 carbenes adding to 4 alkenes. The alkenes include $Me_2C{=}CMe_2$, *trans*-MeCH=CHMe, $CH_2{=}CH_2$, and $CH_2{=}CHCN$, thus spanning electron-rich to electron-poor substrates. The carbenes span electrophiles (CCl_2, CFCl, CF_2), ambiphiles (MeOCCl, MeOCF), and nucleophiles ($C(OH)_2$, $C(OMe)_2$). The philicities measured by ΔN [81] are found to be in reasonable accord with conclusions that we reached on the basis of m_{CXY} or FMO considerations. [8,66,69] Thus, from Fig. 7, we see that (e.g.) CCl_2, CFCl, and CF_2 are "electrophilic" in the sense that ΔN is positive; i.e., electron transfer is from alkene to carbene for all 4 olefinic substrates. Other carbenes, such as PhCCl, PhCF, MeOCCl, and MeOCF are ambiphilic; they are electrophilic toward $Me_2C=CMe_2$, but nucleophilic toward $CH_2=CHCN$ (where ΔN is negative, and electron density is transferred from carbene to alkene). Note that the nucleophilic behavior toward $CH_2=CHCN$ increases with increasing m_{CXY}: $(MeO)_2C$ exhibits a much more negative ΔN toward $CH_2=CHCN$ than do MeOCF, MeOCCl, or PhCCl. [81] In this sense, the ΔN method of characterizing carbenic philicity parallels the m_{CXY} categorization.

Finally, Sander has analyzed carbenic philicity in terms of DFT (B3LYP) computed electron affinities (EA) and ionization potentials (IP) of the carbenes. [82] The EA represents the carbene's ability to accept electrons (i.e., its electrophilicity), whereas the carbene's IP reflects its ability to donate electron density (i.e., its nucleophilicity). Where comparisons are possible, there is qualitative agreement between the EA/IP and m_{CXY} analyses of carbenic philicity. Thus, nucleophilic $(MeO)_2C$ has a very low EA (-0.62 eV) and a middling IP (9.01 eV); it should be a good electron donor, but a poor electron acceptor. Dichlorocarbene, with EA = 1.46 eV and IP = 10.16 eV, should be a better electron acceptor and a poorer electron donor than $(MeO)_2C$; i.e., it should be much more electrophilic. Thus, according to Sander, [82] nucleophilic carbenes are characterized by low IP's and low EA's; electrophilic carbenes, conversely, have high IP's and high EA's. [83]

An advantage of Sander's method is that EA and IP can be calculated for any carbene, and do not depend (as does m_{CXY}) on a specific set of alkenes or carbenes. Thus, Sander is able to examine species he refers to as "super-electrophilic" carbenes. [82] These include difluorovinylidene, **29** [84] and 4-oxo-2,3,5,6-tetrafluorocyclohexa-2,5-dienylidene, **30**, a highly electrophilic triplet carbene. [85] With EA = 2.26 (observed) or 2.56 eV (computed), [84] carbene **29** is electrophilic enough to insert into the C-H bond of methane, and even the H-H bond of hydrogen at temperatures as low as 40 K. This type of reactivity is also observed [85] with **30** (computed EA = 3.61 eV). [82]

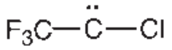
$F_2C=C\!:$

29

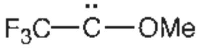


30

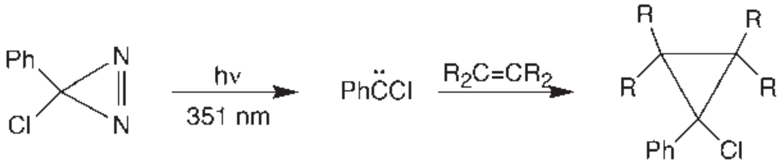
Of course, the electrophilicity of **29** and **30** is enhanced by their highly electronegative fluorine atoms which are strongly electron withdrawing by the inductive effect. Something similar operates with trifluoromethylchlorocarbene, **31**, and trifluoromethylmethoxycarbene, **32**. The trifluoromethyl group is a strong inductively electron withdrawing group (σ_I = 0.38 or 0.45), and its influence makes carbene **31** much more electrophilic than CCl_2 or MeCCl. The observed m_{CXY} values for **31**, MeCCl, and CCl_2 are ~0.19, 0.50, and 1.00, respectively. [33] Carbene **32** shows very little selectivity between $Me_2C{=}CHMe$, $MeEtC{=}CH_2$, or $CH_2{=}CHCN$, even though its non-fluorinated counterpart MeCOMe (see below) is a selective nucleophilic carbene. Again, the trifluoromethyl group has increased the electrophilicity and reactivity of a carbene. [86] Carbene **32** is of further interest as a "push-pull" carbene, which bears a resonance-donating MeO group and an inductively-withdrawing CF_3 group. Nevertheless, it does not exhibit unusual stability; rather, it is very reactive towards alkenes. As we will see below, replacement of the methoxy group by $(R_2N)_2P$ leads to a very highly stabilized push-pull carbene. [87]


$F_3C-\ddot{C}-Cl$

31


$F_3C-\ddot{C}-OMe$

32



(9)

3.2.2 *Absolute rate constants for carbene/alkene additions*

3.2.2.1 *Historical note*

When I was a graduate student measuring carbene/alkene relative reactivities at the University of Chicago in 1962, I used to dream about the possibility of directly determining the *absolute* rate constant for the addition of a carbene to an alkene. The ability to obtain absolute rate constants would enable us to undertake a really detailed study of the structure/reactivity relationship for carbenes, and thus provide a deeper understanding of carbenic philicity. The problem, however, was that carbene/alkene additions in solution were too fast to measure. Flash photolysis, in which a short burst of light is used to generate a transient species whose lifetime is then followed spectroscopically, was limited by the duration of the light pulse to species with lifetimes in the msec-µsec range; too slow for singlet carbene/alkene additions in solution.

In 1976, Closs and Rabinow reported the use of flash photolysis to measure the rate constant for the addition of (triplet) diphenylcarbene (Ph_2C) to butadiene in benzene at 25 °C: $k = 6.5 \times 10^5$ $M^{-1}s^{-1}$. [88] This exciting result was the first condensed-phase carbene/alkene addition rate constant. However, the addition reactions of most singlet carbenes were expected to be significantly faster than that of bulky triplet Ph_2C, too fast for the conventional flash lamp employed in Closs's experiment with its μsec light pulse.

In 1979, during a Gordon Conference coffee break, Professor Nicholas J. Turro of Columbia University informed me that he had assembled a laser flash photolysis (LFP) unit. The laser provided light pulses of 10-20 nsec duration, short enough to permit the study of transients with lifetimes in the submicrosecond realm. Nick Torro suggested that we collaborate on a study of carbene/alkene additions, and asked me to suggest an appropriate place to start. I suggested at once that we study phenylchlorocarbene, PhCCl. We were very familiar with its chemistry; it was easily generated by photolysis of the readily available phenylchlorodiazirine (Eq. 9); it added efficiently to alkenes; and because of the phenyl group, the carbene would possess a usable UV spectrum to permit us to follow its kinetics.

And so, in the Autumn of 1979, my students prepared phenylchlorodiazirine; froze it in a Dry-Ice Dewar flask; and, despite the prohibition of explosives, drove it from New Jersey, through the Lincoln Tunnel into New York City and on to Columbia. The LPF experiment worked at once. That same morning, we acquired the UV spectrum of PhCCl at 25 °C in isooctane solution, and were soon able to study its kinetics. [89] Thus began a delightful and productive collaboration.

Simultaneously, Gary Shuster, at the University of Illinois, investigated the chemistry of fluorenylidene by LFP. [90] Although rate constants for the reactions of singlet and triplet fluorenylidene with olefins were obtained, Schuster's investigations were not aimed at the question of carbenic philicity. Our experimental programs therefore proceeded along divergent paths.

3.2.2.2 *Quantitative results*

To deterimine the absolute rate for addition of PhCCl to $Me_2C{=}CMe_2$, Eq. 9, one generates the carbene by LFP of the diazirine in isooctane that contains a specific concentration of the substrate olefin. A pseudo-first-order rate constant can then be determined for the decay of the carbene by following the time-dependent loss of its UV absorbance at 320 nm. (Conventional photolysis and product analysis establishes that the reaction gives the expected cyclopropane product.) Next, one varies the concentration of olefin and repeats the LFP experiment, determining a new k_{obs} for carbene decay. Finally, a correlation of k_{obs} vs. olefin concentration gives a straight line, whose slope is the second order rate constant, k_{abs}, for the addition of PhCCl to $Me_2C{=}CMe_2$; 1.3 x 10^8 M^{-1} s^{-1} in this case. [89]

Table 7. Absolute Rate Constants for Additions of PhCX to Alkenes[a,b]

alkene	PhCF	PhCCl	PhCBr
$Me_2C{=}CMe_2$	1.6 x 10^8	2.8 x 10^8	3.8 x 10^8
$Me_2C{=}CHMe$	5.3 x 10^7	1.3 x 10^8	1.8 x 10^8
tr-MeCH=CHEt	2.4 x 10^6	5.5 x10^6	1.2 x 10^7
n-$BuCH{=}CH_2$	0.93 x 10^6	2.2 x10^6	4.0 x 10^6
$CH_2{=}CHCN$	2.3 x 10^6	7.0 x 10^6	1.1 x 10^7
$CH_2{=}CClCN$	1.2 x 10^8	2.1 x10^8	3.3 x 10^8
“spread”[6]	172	127	95

[a] Data from refs. 65, 66, and 91. [b] Rate constants are in L/(mol s) and were determined in alkene/hydrocarbon solutions at 23-25 °C by LFP. Reproducibilities are ±10-15%. [c] Defined as the rate constant ratio for additions to $Me_2C{=}CMe_2$ vs. n-$BuCH{=}CH_2$.

With LFP methodology, we were thus able to obtain k_{abs} values for the additions of many carbenes to various alkenes. In general, we were gratified to find that the k_{abs} values responded to structural variations in both the carbenes and alkenes in accord with previous conclusions drawn from relative reactivity studies. Examples of k_{abs} for PhCX additions are collected in Table 7. [65,66,91]

Note firstly that each PhCX clearly displays ambiphilic reactivity toward the set of alkene substrates: k_{abs} is high for additions to electron-rich ($Me_2C{=}CMe_2$) and electron-poor ($CH_2{=}CClCN$) alkenes, and at a minimum with the monosubstituted alkene, 1-butene. The ambiphilicity of PhCX clearly emerges from the k_{abs} data and accords with conclusions from relative reactivity studies (Section 1.4, above).

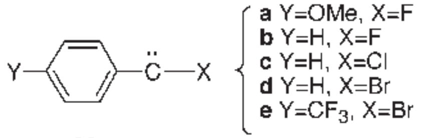
Even though the reactions of Table 7 are very fast, there is selectivity; k_{abs} ranges from near diffusion control (PhCBr + Me_2C=CMe_2) over a span of ~400 (PhCF + *n*-BuCH=CH_2). For each alkene, k_{abs} (*reactivity*) is in the order PhCBr > PhCCl > PhCF, the inverse of the anticipated carbene stability order based on halogen lone pair interactions with each carbene's vacant 2p orbital. [8,69] Moreover, as measured by the ratio of k_{abs} for Me_2C=CMe_2 vs. *n*-BuCH=CH_2 (the "spread") [92] the *selectivities* of the carbenes are in the order PhCF > PhCCl > PhCBr, indicating a reactivity-selectivity correlation of the "normal" or inverse type. [91] We have reviewed much of our absolute rate constant work with PhCX in other locations, to which the reader is referred. [93,94]

With the ability to measure absolute rate constants, we are in a position to follow changes in k_{abs} as a function of reaction temperature, and thus to derive activation energies for the additions of carbenes to alkenes. Our first experiments involved PhCCl and the initial 4 alkenes of Table 7. [95] With *trans*-pentene and 1-butene, we found activation energies of ~1 kcal/mol for the addition of PhCCl. Surprisingly, for tetramethylethylene and trimethylene, E_a was *negative* (-1.7 and –0.8 kcal/mol, respectively). [95] In these cases, the observed rate of carbene to alkene addition increased as temperature decreased! The preexponential (*A*) factors for the additions were low ($2 \times 10^7 – 6 \times 10^7$ M^{-1} s^{-1}), indicating substantially negative activation entropies for these reactions.

Our initial explanation of the negative activation energies postulated that the carbene-alkene additions involved the intermediate and reversible formation of loose carbene/alkene change-transfer complexes. The partitioning of these intermediates between cyclopropane formation and reversion to PhCCl and alkene would determine the observed rate constants and their temperature dependence. [95] However, although carbene-arene π complexes do appear to modulate the chemistry of some carbenes in solution, carbene-alkene complexes have not been supported by theoretical studies. [96]

A second explanation for the negative activation energies was offered by Houk *et al*. [97] They computed ΔH as function of reactant separation for the additions of CBr_2, CCl_2 and CF_2 to Me_2C=CMe_2 and Me_2C=CH_2. They also modeled ΔS for these reactions and derived values of ΔG. They found that in the addition of a very reactive carbene (CBr_2) to a reactive alkene (Me_2C=CMe_2), ΔH decreased continually along the reaction coordinate because the reaction was so exothermic (i.e., $\Delta H^‡$ and E_a were negative). However, there was a free-energy barrier to addition ($\Delta G^‡ > 0$) because of a dominant and unfavorable entropy of activation. The origin of the unfavorable entropy was mainly the loss of translational, vibrational, and rotational entropy encountered as the carbene and alkene reached the transition state for the addition reaction. For a more stable carbene (CF_2), E_a, and $\Delta H^‡$ were positive, and added to the $\Delta G^‡$ barrier, but entropy was still important. [97]

Houk's results both accounted for the negative activation energies and also called attention to the pivotal role of entropy in carbenic additions, a feature identified previously by Skell, [19] and also by Giese. [98] In order to broaden the scope of the experimental data, we determined the absolute rates and activation parameters for the additions of arylhalocarbenes **33a-e** to $Me_2C=CMe_2$ and n-$BuCH=CH_2$. [99] The k_{abs} values ranged from 1.7×10^9 M^{-1} s^{-1} for **33e**/$Me_2C=CMe_2$ to 5.0×10^4 M^{-1} s^{-1} for **33a**/n-$BuCH=CH_2$, a factor of 3400 at 25 °C. Classical ideas about carbenic reactivity were upheld: the most stabilized carbene, **33a** (with electron donating X and Y), reacted most slowly, whereas the least stabilized carbene, **33e** (with electron withdrawing Y), reacted most rapidly. With either alkene substrate, the order of carbenic reactivity was **33e** > **33d** > **33c** > **33b** > **33a**; i.e., the inverse of carbene stabilization by substituents X and Y. And, with each carbene, the more electron-rich alkene, $Me_2C=CMe_2$, reacted about 100 times faster than the monoalkylated n-$BuCH=CH_2$. [99]



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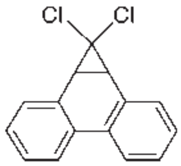
In accord with Houk's ideas, all of the reactions were dominated by $\Delta S^‡$: for additions of **33e** – **33a** to $Me_2C=CMe_2$, $\Delta S^‡$ ranged from –22 to –27 e.u.; for additions to n-$BuCH=CH_2$, the span was –25 to –29 e.u. Free energy barriers were 5.0 kcal/mol for the fastest reaction (**33e** + $Me_2C=CMe_2$), increasing to 11 kcal/mol for the slowest reaction (**33a** + n-$BuCH=CH_2$). $\Delta H^‡$ was –1.6 kcal/mol, increasing to 2.5 kcal/mol, respectively, for these two reactions.

Despite the dominance of entropy in these reactive carbene addition reactions a kind of "defacto enthalpic control" operates: the entropies of activation are all very similar, so that in any comparison of the reactivities of alkene pairs (i.e., k_{rel}), the rate constant ratios reflect differences in $\Delta\Delta H^‡$, which ultimately appear in $\Delta\Delta G^‡$. Thus carbenic *philicity*, which is the pattern created by carbenic *reactivity*, behaves in accord with our qualitative ideas about structure/reactivity relations, as modulated by substituent effects in both the carbene and alkene partners of the addition reactions. [66,99]

3.2.2.3 Some benchmark carbenes

It is of interest to examine the philicities of some important carbenes as defined by k_{abs} measurements. We can simultaneously get a sense of the overall reactivity of these carbenes, which is not possible using relative reactivity data alone.

Consider first CCl_2, perhaps the archetypal carbene. [1,2] Chateauneuf and Johnson succeeded in generating CCl_2 by the 266 nm LFP of its phenanthrene adduct, **34**. [100] k_{abs} values ($M^{-1}\ s^{-1}$) were determined for CCl_2 additions to $Me_2C{=}CMe_2$ (3.8 x 10^9), $Me_2C{=}CHMe$ (2.2 x 10^9), *trans*-pentene (6.3 x 10^7), cyclohexene (3.5 x 10^7), and 1-hexene (1.1 x 10^7). CCl_2 clearly appears to be an electrophile (as we concluded from k_{rel} data, see above Tables 1, 2, 5, and 6). Its reactivity is rather similar to that of PhCCl (*cf.*, Table 7), although CCl_2 is more selective: k_{rel} for $Me_2C{=}CMe_2$/*n*-$BuCH{=}CH_2$ is 345 for CCl_2 vs. 127 for PhCCl. CCl_2 also remains electrophilic even when electron-poor olefins ($CH_2{=}CHCN$) are brought into play (Table 2), because of its very accessible LUMO (Table 6).



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What about the classic ambiphile, MeOCCl? In Table 8, we summarize k_{abs} values for MeOCCl, determined by a combination of absolute and relative rate measurements. [101] Also included are analogous data for PhCOMe, [102] MeCOMe, [73] and $MeCOCH_2CF_3$. [103] For MeOCCl, we note that the ambiphilic reactivity pattern emerges from the absolute rate constants of Table 8 as clearly as it does from the relative rate constants of Table 4: high reactivity toward electron-rich or electron-poor alkenes, but low reactivity toward alkenes of intermediate electron density. However, whereas the relative rate data can only inform us about the carbene's selectivity pattern, the absolute rate data reveals the carbene's true reactivity. In fact, k_{abs} for the addition of MeOCCl to *trans*-butene (3.3 x $10^2\ M^{-1}\ s^{-1}$) is the lowest bimolecular rate constant yet measured for a carbene/alkene addition in solution. [101] And with 1-hexene, only 5% of MeOCCl addition was observed; this reaction is so slow that other competitive processes prevail. [101]

Comparison of k_{abs} for the MeOCCl/$Me_2C{=}CMe_2$ addition (4.2 x $10^3\ M^{-1}\ s^{-1}$) with that for the analogous CCl_2 addition (3.8 x $10^9\ M^{-1}\ s^{-1}$) [100] shows that the MeO for Cl substituent change between the two carbenes has led to a decrease of 9 x 10^5 in k_{abs} for MeOCCl! Strong resonance donation by the MeO group to the vacant carbenic p orbital (cf., **4**), raises that orbital's energy (ε_{LU} = 2.5 eV, Table

6) compared to CCl_2 ($\varepsilon_{LU} = 0.31$ eV). With substrate $Me_2C{=}CMe_2$, the resulting dominant LUMO(carbene)/HOMO(alkene) differential energies are 10.73 eV for MeOCCl and 8.58 eV for CCl_2 (Table 5). Because these differential orbital energies are inversely related to the stabilization of the respective addition transition states, the CCl_2 addition will have a considerably lower activation energy and occur much more rapidly, as we in fact observe. The other k_{abs} values for the MeOCCl additions of Table 8 are also much lower than those for CCl_2[100] or (e.g.) PhCCl (Table 7). For example, with the electron-poor substrate $CH_2{=}CClCN$, the k_{abs} values for MeOCCl and PhCCl are 5.6×10^5 and 2.1×10^8 M^{-1} s^{-1}, respectively.

Table 8. Absolute Rate Constants for Ambiphilic and Nucleophilic Carbenes [a]

alkene	MeOCCl[b]	PhCOMe[c]	MeCOMe[d]	$MeCOCH_2CF_3$[e]
$Me_2C{=}CMe_2$	4.2×10^3			
$Me_2C{=}CHMe$			4.7×10^3	
$Me_2C{=}CH_2$	1.8×10^3	4.0×10^4	4.8×10^3	9.0×10^5
tr-MeCH=CHEt	3.3×10^2	3.8×10^3	2.2×10^3	5.9×10^6 [f]
n-$BuCH{=}CH_2$		2.8×10^3		
$CH_2{=}CHCOOMe$	9.8×10^3	6.6×10^5	7.9×10^5	2.5×10^7
$CH_2{=}CHCN$	1.8×10^4	1.7×10^6	1.5×10^6	8.9×10^7
$CH_2{=}CClCN$	5.6×10^5	3.4×10^7	4.9×10^7	4.8×10^8

[a] Rate constants in M^{-1} s^{-1}, determined at 23-25 °C in hydrocarbon solvents. [b] Data from ref. 101. [c] Data from refs. 65, 101, and 102. [d] Data from refs. 73 and 101. [e] Data from ref. 103. [f] At -28 °C.

Similar results emerge from k_{abs} studies of PhCOMe. [102] The k_{abs} data of Table 8 reveal this carbene to be an ambiphile that is somewhat more reactive than MeOCCl. A better reactivity comparison is between PhCOMe and PhCCl (Table 7). Again the MeO for Cl substituent switch "cools" the carbene; PhCOMe is less reactive than PhCCl.

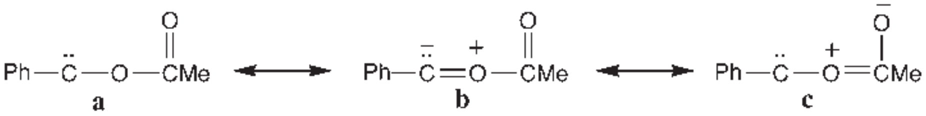
However, PhCOMe has m_{CXY}(calcd) = 1.34. According to our empirical analysis of carbenic selectivity (Section 1.2), it should be an electrophile because its m_{CXY} selectivity index lies between 0.29 and 1.48. What's wrong? FMO analysis and ab initio calculations support the ambiphilicity of PhCOMe. [102] The computed HOMO and LUMO energies of the carbene (Table 6) are similar to those of MeOCCl, and the actual computed differential orbital energies [102] accord with the ambiphilic/nucleophilic reactivity pattern displayed by k_{abs} in Table 8. Clearly, the empirical analysis of philicity based on m_{CXY} is not exact. It is helpful and intuitively satisfying, but qualitative. The FMO/computational approach is more precise, and it naturally rationalizes the observed behavior of all the carbenes we have thus far considered.

An analogous situation holds for MeCOMe: m_{CXY} calculated from Eq. 4 is 1.21, but the reactivity displayed by MeCOMe (Table 8) is effectively nucleophilic; the k_{rel} for CH_2=CClCN vs. *trans*-butene is 22,300. [73] Reference to Table 6 indicates that (trans) MeCOMe has ε_{HO} = -9.4 eV and ε_{LU} = 4.0 eV. The combination of a relatively high-lying, filled donor orbital, and a high-lying, poorly accessible vacant p orbital makes MeCOMe a good nucleophile and an ineffective electrophile. [73,104] Note that comparison of MeCOMe with MeOCCl involves a Me for Cl substituent switch. As we would expect, MeCOMe is ~100 times more reactive (as a nucleophile) than MeOCCl toward electron-poor alkenes (compare the k_{abs} values in Table 8).

An interesting example of reactivity "fine-tuning" is also contained in Table 8. Compare k_{abs} data for MeCOMe and $MeCOCH_2CF_3$. [103] Both are nucleophilic, but the latter carbene is more reactive than MeCOMe. Both the OMe and OCH_2CF_3 substituents stabilize the carbenic p orbital by resonance donation, but the OCH_2CF_3 substituent is less effective (than OMe) overall because of its inductively withdrawing CF_3 subunit. $MeCOCH_2CF_3$ is therefore less stabilized than MeCOMe, and more reactive, as expressed by k_{abs}. An analogous instance of fine tuning is observed on comparison of k_{abs} values for MeOCCl and CF_3CH_2OCCl additions; both carbenes are ambiphiles, but the latter is more reactive. [101]

A final example of fine-tuning is afforded by the acyloxycarbenes; e.g., phenylacetoxycarbene, PhCOAc. [105] Absolute and relative rate constants for alkene addition reactions of PhCOAc are displayed in Table 9, where the data are compared to those for PhCOMe (Table 8).

From the k_{rel} data of Table 9, we can see that although both carbenes are ambiphilic, the nucleophilic properties of PhCOMe (as revealed by its reactivity toward the electron-poor alkenes) are much more pronounced than those of PhCOAc. However, from the k_{abs} values, we observe that PhCOAc is somewhat more reactive than PhCOMe. Thus, PhCOAc is both more reactive and less (nucleophilically) selective than PhCOMe. A simple explanation takes note of the resonance representation for PhCOAc, **35**. [105] Here, the typical methoxy group resonance donation (cf., **4**) also operates for PhCOAc, as represented by contributor **35b**. However, the strength of electron donation to the carbenic center is *reduced* because of the acetyl group; cf., contributor **35c**. With PhCOMe, of course, the methoxy resonance donation is of normal strength, so that the carbene is more stabilized, less reactive, and more selective than PhCOAc. [105] A more detailed (FMO) analysis of these reactions is in accord with these simple arguments. [105]



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Hammett studies are also possible with k_{abs} data. [106] Thus, additions of p-X-PhCCl (X = CF_3, Cl, H, Me, MeO) were conducted with $Me_2C{=}CMe_2$, $Me_2C{=}CHMe$, *trans*-MeCH=CHEt, and n-BuCH=CH_2. The k_{abs} values were determined by LFP and correlated with the σ^+_p parameters of X. For each alkene, a correlation was obtained with $\rho = 1.4 – 1.6$. With these alkylethylene substrates, the carbene additions were accelerated by electron withdrawing X subsitituents in ArCCl. The simplest interpretation is that such substituents destabilize the carbene, and make it both more electrophilic and more reactive. For example, k_{abs} for the addition of p-X-PhCCl to $Me_2C{=}CHMe$ increases from 7.7×10^6 to 6.8×10^8 M^{-1} s^{-1} as X is altered from MeO to CF_3. [106] With n-BuCH=CH_2 as the substrate, the analogous k_{abs} are 1.3×10^5 vs. 1.8×10^7 M^{-1} s^{-1}.

Similar results were reported by Platz *et al*. [75] Interestingly, positive ρ values were observed not only for reactions of ArCCl with (e.g.) 1-pentene (+1.3), and 1-hexene (+1.3), but also with electron deficient alkenes, (e.g.) diethyl fumarate (+ 0.45) and ethyl acrylate (+0.75). The Hammett rho values thus suggest that these latter carbene additions are electrophilic, even though the selectivity and reactivity of PhCCl toward the set of alkenes in Table 7 is clearly parabolic and ambiphilic. One does note, however, that the electrophilicity of the additions, expressed by ρ, decreases as the alkenes become less electron-rich. Thus ρ decreases from +2.49 for butyl vinyl ether, to +1.3 for 1-pentene, to +0.45 for diethyl fumarate. [75] A more detailed explanation, based on the Houk enthalpy/entropy analysis, [97] has been offered. [75]

Absolute rate constants are also helpful in assessing the reactivity of nucleophilic carbenes such as $(MeO)_2C$. [72] As discussed above (Sections 1.2 and 2.1), dimethoxycarbene is so strongly stabilized by resonance donation from its methoxy substituents (cf., **4**) that it dimerizes rather than add to electron rich alkenes. [72] The carbene does, however, add as a nucleophile to electron deficient alkenes: LFP affords k_{abs} for $(MeO)_2C$ additions to CH_2=CHCN (~1 x 10^3 M^{-1} s^{-1}) and CH_2=CClCN (5.0 x 10^5 M^{-1} s^{-1}). [72] Comparisons to the rate constants for the analogous additions of MeCOMe (Table 8), show that $(MeO)_2C$ reacts ~100 – 1000 times more slowly than MeCOMe. Although both are nucleophilic carbenes, the additional methoxy substituent stabilizes $(MeO)_2C$, relative to MeCOMe, and leads to a lower addition rate.

Table 9. Absolute Rate Constants for PhCOAc and PhCOMe[a]

	PhCOAc[b]		PhCOMe[c]	
alkene	k_{abs}	k_{rel}	k_{abs}	k_{rel}
$Me_2C=CH_2$	1.45 x 10^6	6.3	4.0 x 10^4	10.6
tr-MeCH=CHMe	2.3 x 10^5	1.00	3.8 x 10^3	1.00
CH_2=CHCOOMe	1.2 x 10^6	5.2	6.6 x 10^5	172.
CH_2=CHCN	3.54 x 10^6	15.	1.7 x 10^6	445.
CH_2=CClCN	5.1 x 10^7	220.	3.4 x 10^7	8950.

[a] At 25 °C. [b] Relative reactivities refer to *trans*-butene. [b] Data from ref. 105 [c] Data from refs. 65, 101, and 102.

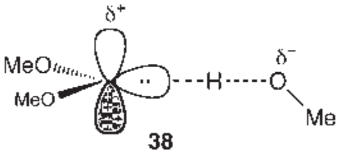
Although we have restricted our discussions of carbenic philicity to carbene/alkene addition reactions, the use of other substrates can also be informative. For example, both MeCOMe and $(MeO)_2C$ react with (oligomeric) methanol in pentane to give the formal O-H insertion products, **36** and **37**, respectively. [72,73] As we would expect, the reaction of MeCOMe (7 x 10^9 M^{-1} s^{-1}) is more rapid than that of $(MeO)_2C$ (2.5 x 10^6 M^{-1} s^{-1}). Further study of the reactions of $(MeO)_2C$ with a wide range of hydroxylic substrates shows that log k_{abs} is inversely proportional to the pK_a of ROH, affording a Brønsted relation with α = -0.66. [107] Furthermore, from the absolute rate constants for $(MeO)_2C$ reactions with MeOH and MeOD, the primary kinetic isotope effect for the O-H (O-D) "insertion" reaction is 3.3. [108] From these data, the transition state for the $(MeO)_2C$/MeOH reaction can be rendered as **38**, which represents the nucleophilic carbene as a Lewis base accepting a proton from the “acidic” alcohol. [107] In contrast, the transition state for the reaction of an electrophilic carbene with an alcohol may feature a dominant interaction of the carbene’s vacant p orbital with the alcohol’s oxygen lone pair. [107]

$MeCH(OMe)_2$

36

$HC(OMe)_3$

37



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3.2.3 *Nucleophilic carbenes*

In Section 1.2, we indicated that the nucleophilic properties of dimethoxycarbene could be put to synthetic use; for example in the synthesis of heterocyclic compounds by reactions with isocyanates and isothiocyanates. [23,24] It is worth noting that analogous chemistry is being elaborated by Rigby’s group for the bis(alkylthio)carbenes; e.g., (n-PrS)$_2$C. [109] Obviously, the nucleophilic properties of $(RS)_2C$ parallel those of $(MeO)_2C$. Moreover, further manipulation of the alkythio groups in the products of $(RS)_2C$ reactions opens substantial synthetic opportunities. [109]

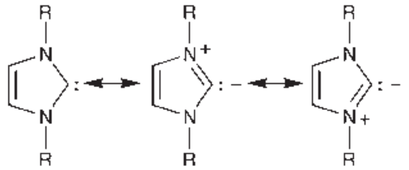
How stable can carbenes become as a result of resonance electron donation? We have seen that CF_2 and $(MeO)_2C$ are significantly stabilized in this manner. The Periodic Table suggests that the even less electronegative, first row element, nitrogen, should be a better overall donor than either oxygen or fluorine, and therefore that $(R_2N)_2C$ should be an even more stabilized carbene than $(MeO)_2C$. Indeed, bis(amino)carbenes are so stabilized that, beginning with the work of Arduengo, [110] many examples have actually been isolated. [111] Arduengo’s initial stable carbene, **39** (R = 1-adamantyl), [110] is thermodynamically stabilized by resonance, and kinetically stabilized by the bulky, sterically shielding 1-adamantyl groups that flank the carbenic center. It is a crystalline solid that *melts* at 240 – 241 °C. [110] It is a nucleophilic carbene that reacts with perfluorophenyl iodide to produce a reverse ylide. [112a] Saturated analogues of **39** undergo C-H insertion reactions with acidic substrates like acetylene, methylsulfones, and acetonitrile. [112b]

We will present only a very brief discussion here concerning stable, nucleophilic carbenes because this topic is dealt with at length in the chapter by Guy Bertrand elsewhere in this volume.

Interestingly, the imidazolylidene structure of **39** is not essential to the isolability of bis(amino)carbenes; Alder *et al.* prepared bis(diisopropylamino)carbene,

40. [113] Carbenes such as **39** and **40** are Lewis bases with high pK_a values. For example, the pK_a of **41** is 24 in DMSO-d_6, signifying a very strong, neutral base. [114]

Bertrand's approach to the stable carbene problem has been to search for a most delicate balance of stability and reactivity, such that the essential reactions expected of a carbene are not lost. Carbene **42**, for example is a distillable red oil that behaves as a nucleophilic carbene despite its phosphaacetylene contributing resonance form; it undergoes addition to electron poor olefins (e.g., dimethyl fumarate). The very electron-rich bis(diisopropylamino)phosphino substituent damps the carbene's electrophliic properties by resonance donation into the carbenic p orbital. [115] These phosphinosilylcarbenes are therefore best described by phosphorus vinyl ylide structures with a lone pair on carbon (cf., **42**, second contributor). [116]

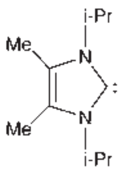


39

$[(i\text{-}C_3H_7)_2N]_2C:$

40

Carbene **42** adds to a variety of electron deficient olefins, and even to styrene;[117] with *p*-substituted styrenes, the nucleophilicity of these additions can be observed (for **42** with cyclohexyl replacing isopropyl). [117] Moreover, additions of **42** to *Z*- and *E*-2-deuteriostyrene are stereospecific with respect to the styrene substituents, as anticipated for singlet carbene additions. [117] Thus, the isolable phosphinosilylcarbenes are nucleophiles, but retain the essential reactivity expected of such carbenes.



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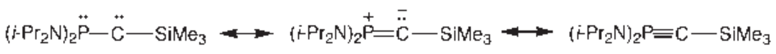
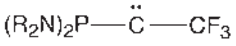


$(i\text{-}Pr_2N)_2\ddot{P}\text{—}\ddot{C}\text{—}SiMe_3 \longleftrightarrow (i\text{-}Pr_2N)_2\overset{+}{P}\text{=}\overset{-}{\ddot{C}}\text{—}SiMe_3 \longleftrightarrow (i\text{-}Pr_2N)_2P\equiv C\text{—}SiMe_3$

42

Finally, we note that Bertrand *et al.* have made excellent use of the "push-pull" motif to produce the isolable carbene, **43** (R = cyclohexyl). [87] Although

43 dimerizes in pentane, it is stable at low temperature in solutions of electron donor solvents (THF, ether, toluene). The carbene then adds to electron poor alkenes (methyl acrylate, dimethyl fumarate), and inserts into the Si-H bond of triethylsilane. [87]



$$(R_2N)_2P-\ddot{C}-CF_3$$

43

3.3 CONCLUDING REMARKS

It is surely a long journey from the voracious electrophilic reactivity of methylene (CH_2), which Doering “classed as the most indiscriminate reagent known in organic chemistry,” [118] to the isolable nucleophilic carbenes of Arduengo and Bertrand. In this chapter, I have tried to describe my own journey between these two stations, describing many of the stops and interesting scenary along the route.

Clearly, by the appropriate choice of substituents, carbenic stability, reactivity, and philicity can be simultaneously varied, while the delicate interrelations of these properties can be understood in empirical and, more precisely, in theoretical terms. The kinetic range of the carbene reactions that we have considered is enormous; the rate constants span 9 or more orders of magnitude. From this perspective, it is remarkable that the classical “tools” of physical organic chemistry, resonance and inductive effects, and Hammett relationships, provide such a satisfactory qualitative rationalization of the entire picture. Augmented by modern experimental methods such as LFP, and theoretical tools (FMO and computational methods), we are now able to understand and manipulate carbenic philicity in an intellectually satisfying and synthetically useful manner.

This chapter is dedicated to the memory of Professor Gerhard L. Closs.

ACKNOWLEDGMENT

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This chapter is dedicated to the memory of Professor Gerhard L. Closs.

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Chapter 4

Approach to A Persistent Triplet Carbene

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PROLOGUE

When I started to teach organic chemistry at the undergraduate level at Mie University in my early thirties, I was intrigued by the story of how Gomberg inadvertently came upon a triphenylmethyl, the first relatively stable radical. I assumed that all the students in my class would also be impressed by the anecdote not simply because their teacher was telling it so enthusiastically but because it really sounded exciting. The story can be summarized as follows;

*About a century ago, Gomberg attempted to prepare hexa(phenyl)ethane(**2**) by treating a solution of triphenylmethyl chloride (**1**) with silver or zinc. He obtained a yellow solution of a stable species whose properties, though, did not appear compatible with those expected from a hydrocarbon like hexa(phenyl)ethane. For example, the solution would decolorize rapidly when exposed to air, or treated with iodine or a number of other materials known to react with organic radical. Gomberg concluded in his paper of 1900 [1]: "The experimental evidence ··· forces me to the conclusion that we have to deal here with a free radical, triphenylmethyl,* $(C_6H_5)_3C$ *(**3**) (* Scheme 1*).*

These were bold words at that time. Although the possible existence of free radicals had been postulated more than fifty years before, all attempts to prepare them had failed. In addition, the success of Kekulé and Couper's structural theory in accounting for virtually all known organic chemistry in terms of tetravalent carbon had eliminated the possibility of free radicals in the minds of prac-

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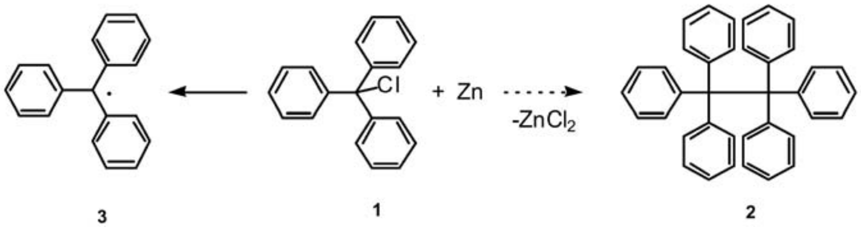
ticing chemists. [2] This conceptual framework culminated in Ostwald's 1896 pronouncement: "It took a long time before it was finally recognized that the very nature of organic radicals is inherently such as to preclude the possibility of isolating them". [3]



Scheme 1

Ostwald's view was widely held and considered final by most investigators in the field at the time. Therefore Gomberg's interpretation was not initially accepted. Gomberg himself clearly knew that he was on to something important when he ended his paper with the sentence, " the work will be continued, and I wish to reserve the field to myself ". [1] However, it soon attracted the attention of a large number of chemists and in the next few years, papers on triphenylmethyl appeared from many laboratories. To put it in modern context, triphenylmethyl combined the novelty of something like bucky balls with controversial nature of something like polywater or cold fusion. [4] The area of triarylmethyl chemistry quickly expanded, and free radicals have since become a major area of organic chemistry.

When I was promoted to full professor in my early forties, I realized that I had 20 years ahead of me to pursue my research. I thought that I should use those two decades to tackle something very challenging. At that time, I was deeply involved in the chemistry of carbenes and related species. I was very fascinated by the perplexing reactions displayed by the exotic divalent species.

Naturally I had a chance to study the history of carbenes, [5] which can be summarized as follows:

"The very first attempts to generate carbene were made at a time when the quadrivalency of carbon was not yet established. Thus Duma (1835) [6] and Renault (1839) [7] tried to dehydrate methanol by means of phosphorus pentoxide or concentrated sulfuric acid. A second period of carbene research was initiated by the discovery of isonitrile and fulminic acid derivatives in the late 19th century. Nef, stimulated by his own work in this field, attempted to inter-

pret organic reactions in terms of a 'general methylene theory', [8] in which carbenes play an important role. He even announced that carbenes would become available in the near future. Obviously, he thought that carbenes, once prepared, would be stable compounds."

It is very interesting to recognize here that two chemists, one having discovered a stable trivalent carbon (radical) and the other hoping to isolate a divalent carbon (carbene) were working simultaneously at the turn of century. One may wonder if either of them was inspired by each other's reports and might have attempted to stabilize carbenes or even to isolate them. However, it was only in the 1950's that carbenes started to be recognized as a unique type of intermediate giving characteristic reactions not encountered with radicals known in the organic chemists' community. Since then, research on carbenes has rapidly expanded and has made important contributions to both preparative and theoretical chemistry. [9] Nevertheless, almost no attempts were made to stabilize carbenes until 1980s. This realization pushed me select this as one of our projects.

Of course, there are similarity and dissimilarity between radicals and carbenes. Carbenes have two free electrons. Depending on the relative orientation of their spins, two electronic states are possible. In the singlet state, the spins are antiparallel, giving rise to a diamagnetic compound; the electronic configuration and magnetic properties of singlet carbenes are not related to those of radicals. In a triplet carbene, the two spins are parallel, making it paramagnetic. It is obvious then that next lower-coordinate cousin of Gomberg's radical corresponds to a triplet carbene. Therefore when we started the project, we decided to put focus on the triplet state of carbenes. More specifically, it was our initial hope to realize a stable triplet carbene by the centennial anniversary of the Gomberg's monumental report of 1900.

We soon learned that this is a really challenging project.

4.1 BACKGROUND

The carbene carbon is linked to two adjacent groups by covalent bonds, and possesses two nonbonding electrons which may have antiparallel spins (singlet state) or parallel spins(triplet state). Therefore, before starting work on the project, we needed to plot our strategy to stabilize only the triplet state, leaving the singlet one essentially intact. I should emphasize here that this requirement is specific to this project. It is usually not necessary in order to stabilize other "simple" transient species and, hence, makes the method rather complicated. Thus we needed to analyze the factors influencing the stability of both electronic states.

4.1.1 Factors influencing the stability of each electronic state of carbenes

4.1.1.1 The thermodynamic stability

If the carbene unit were linear, it should have two degenerate *p* orbitals, and Hund's first rule would predict a triplet ground state. Because the carbene unit is not linear, the two orbitals become different. The orbital perpendicular to the plane defined by the three atoms is designated as "*p*", while that parallel to this plane is called "σ". The σ orbital will acquire s character and thereby become stabilized while the *p* remains largely unchanged. Actually, most carbenes are not linear, and the ground state multiplicity depends upon the relative energy of the singlet and triplet states.

The four lowest energy configurations of carbene have electronic configuration described as $\sigma^1 p^1$, σ^2, or p^2. The electron spins in the $\sigma^1 p^1$ configuration may be paired, a singlet, or parallel to form a triplet, while the σ^2 and p^2 configurations must be electron-paired singlet. Thus, the triplet state has $\sigma^1 p^1$ configuration, while σ^2 is generally thought to be the lowest energy configuration for the singlet (Figure 1).

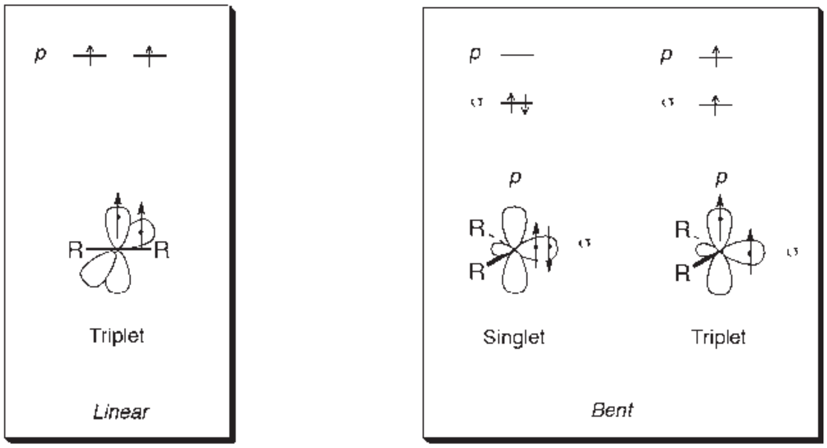


Figure 1. Linear and bent carbenes

In a singlet state σ^2 or p^2 carbene, the electron-electron coulomb repulsion would be severe, since two electrons are constrained to the same small MO. On the other hand, the triplet configuration is stabilized by relief of the coulomb repulsion and "exchange repulsion"; however, the separation of electrons into different MOs does not come without a cost. Thus, the magnitude of the energy difference between the triplet and singlet states (the singlet-triplet splitting, ΔG_{ST}) [10] is roughly equal to the electron-electron repulsion minus the energy required to promote an electron from the σ to the *p*-nonbonding orbital. In other words, as the energy separation between σ and *p* states increases, the promotion energy becomes large enough to overcome the repulsion energy, while if the spacing is small, the species will still have a triplet ground state. The small difference between the energies of S_0 and T_1 may easily be overturned by the effects of substituents on the carbene center. The factors which influence the spacing can be analyzed in terms of electronic and steric effects.

4.1.1.2 Electronic effects.

Because of more favorable overlap, the interaction of the carbon 2*p* orbital with substituent *p* or π orbitals is expected to dominate. The σ (*sp*^{n}) orbital which lies in the nodal plane of the substituent *p* or π orbital will only interact with substituent σ orbitals, and then only weakly. Its energy is thus mostly unperturbed by the substituent.

According to Fleming, [11] substituents interacting with a π system can be classified into three classes, namely X (p-electron donors such as $-NR_2$, -OR, -SR, -F, -Cl, -Br, and -I), Z(p-electron acceptors such as -COR, -SOR, $-SO_2R$, -NO, and $-NO_2$), and C(conjugating such as alkenes, alkynes or aryl groups).

As shown in Figure 2(a), an X substituent, which has a *p* orbital, or other suitable doubly occupied orbital which will interact with the π bond, raises the 2*p* orbital of the carbene, thereby increasing the separation of the 2*p* and *sp*^{n} (σ) orbitals. The ground state of an X-substituted carbene becomes singlet. Many carbenes in this class are known. The most familiar are halo carbenes. [12]

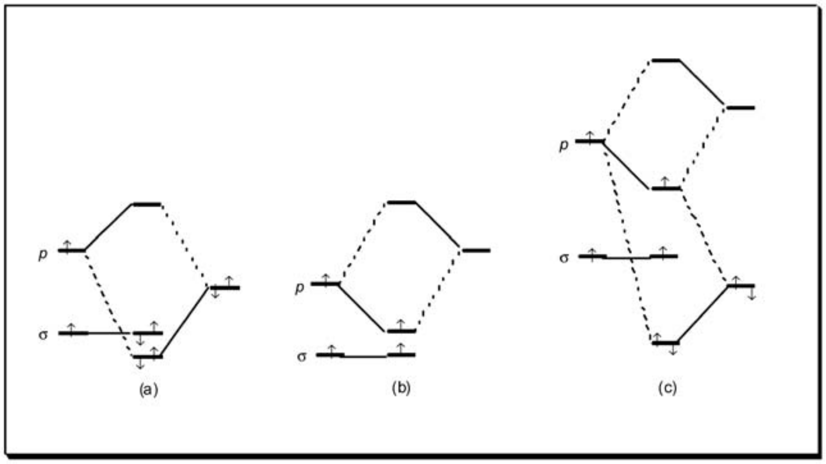


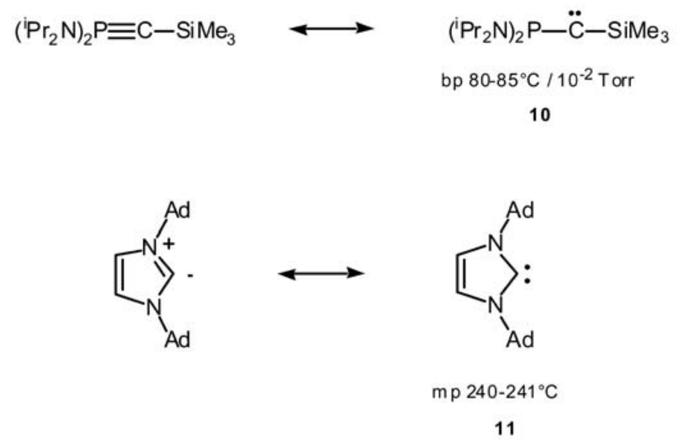
Figure 2. A carbene center interacting with (a) an X substituent, (b) a Z substituent, and (c) a C substituent

Z and C substituents having a *p* or π^* orbital and evenly spaced π and π^* orbitals, respectively, on the other hand, either lower the $2p$-sp^n gap or leave it about the same as shown in Figure 2(b) and (c). In either case, the ground state for these carbenes is expected to be T_1 although the magnitude of ΔG_{ST} may vary. It has been demonstrated by EPR studies that most aryl and diarylcarbenes have triplet ground states. [9,13]

The predictions have been experimentally demonstrated. For instance, a series of cyclic aromatic carbenes incorporated into a presumably planar ring of five or six atoms have been investigated. [14] The carbene bond angle of those examples containing a five-membered ring is expected to be constant (vide infra), and the diversity of chemical behavior must then be primarily associated with electronic changes. ΔG_{ST} of each carbenes has been estimated from the rate constants of each electronic states and is summarized in Figure 3. It is clear that electron-donating and -withdrawing groups have an opposite influence on the magnitude of ΔG_{ST}. For instance, for mesityl(bora)anthrylidene (**4**), which is at one extreme among those carbenes studied, the aromatic LUMO is significantly lowered by the presence of the vacant aromatic orbital of the boron and thus mixed with the carbene *p* orbital. This interaction lowers the energy of this non-bonding orbital, thus resulting in an increase in ΔG_{ST} . An analogous explanation is applied for analysis of 9-xanthylidene (**9**) , another extreme carbene, where the occupied aromatic orbital is raised by the electron-donating ability of oxygen and is mixed with the carbene *p*-orbital. In this case, the splitting of the orbitals in the mixed state is sufficiently increased beyond that of a prototype carbene to make ΔG_{ST} negative. Other aromatic carbenes (**5-8**) fall into intermediates positions in this range.

Figure 3. Effects of substituents on singlet-triplet energy gap of cyclic diarylcarbenes.

An extreme example in which the single state is stabilized by electron-donating substituents is seen in the recent isolation of singlet carbenes; in 1988, phosphinocarbene (**10**) was isolated as a stable yellow oil which can be distilled at 80-85 ^{o}C/10^{-2} Torr [15] and in 1991, imidazole-2-ylidene (**11**) was isolated as stable crystals that melt above 100 $^{\circ}$C [16] (Scheme 2).



Scheme 2

4.1.1.3 *Steric effects*

The magnitude of ΔG_{ST} is expected to be sensitive to the carbene-carbon bond angle. A linear carbene has two degenerate *p* orbitals, which is calculated to provide the maximum value of ΔG_{ST}. Bending the carbene removes the orbital degeneracy and reduced ΔG_{ST}. As the carbene-carbon bond angle is further contracted, the σ-orbital achieves stronger *s*-character and consequently moves even lower in energy. The smaller the bond angle, the more energy it takes to promote an electron from the σ to the *p*-orbital, and the smaller ΔG_{ST} becomes.

This is shown more quantitatively by calculations for methylene (Figure 4) [17]. The calculations predict that the energy of singlet methylene will drop below that of the triplet state for carbenes with bond angles less than about 100°. On the other hand, theory also suggests that opening of the central angle strongly destabilizes the singlet state but requires very little additional energy for the triplet, thus making ΔG_{ST} larger.

In accordance with this prediction, cyclopropenylidene has been shown to have a singlet ground state, [18] while diadamantylidene has a triplet ground state. [19] Although the bond angle effect is not always easily separated from other electronic effects, the ground state multiplicities of these two carbenes are principally determined by the central angle.

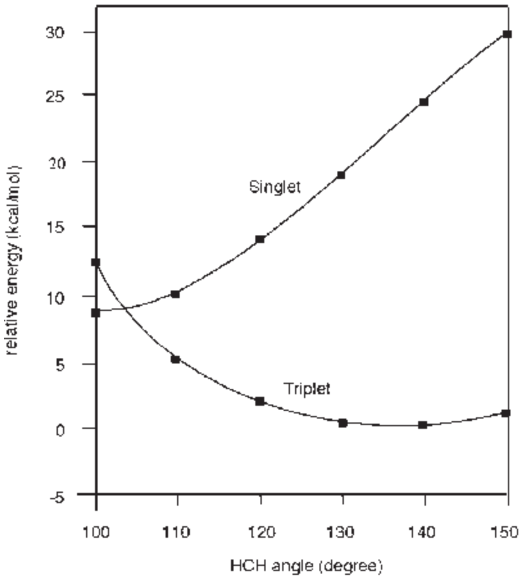


Figure 4. Change in the relative energy of singlet and triplet methylene with respect to <HCH at Becke 3LYP/TZ2P.

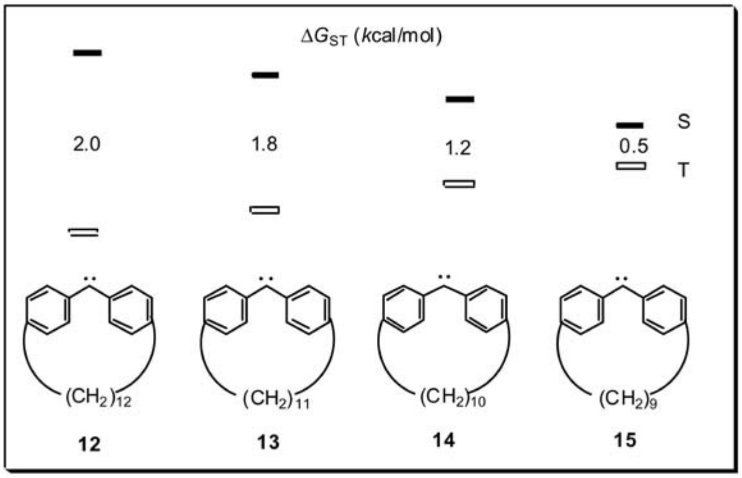


Figure 5. Effect of ring size on singlet-triplet energy gap of cyclophane diphenylcarbenes.

This prediction has been tested for arylcarbene systems more systematically by studying the effect of the ring size on the reactivity of cyclophane diarylcarbenes(**12-15**), where the phenyl rings are linked by alkyl chains of 9 to 12 methylene units (Figure 5). [20] As n decreases, the bond angle at the carbene center becomes smaller, and the phenyl rings are oriented toward each other. Thus, the singlet states should become stabilized with respect to their triplet states as a function of decreasing ring size. This is exactly what is observed.

4.1.1.4 Kinetic stabilization

Reactive species can also be stabilized kinetically. This is usually achieved by retarding the decay processes of the species in question. Steric protections, where sterically bulky substituents are introduced around the reactive center in order to prevent it from reacting with external reagents, are the most frequently employed method.

Examination of the relationship between the structure and reactivity thus far studied has shown that electronic effects usually play an important role in stabilizing the singlet state and that the singlet state undergoing thermodynamic stabilization becomes less reactive due to the contribution of ylidic character to such an extent that it can be isolated under ambient conditions. While the triplet states are also stabilized by electronic effects with respect to the singlet state and their reactions through the upper-lying singlet state may be suppressed, their intrinsic reactivities through unpaired electrons are not expected to be decreased so much. In this light, kinetic stabilization using steric protectors should be more effective for generating persistent triplet carbenes. Moreover, the introduction of sterically bulky groups around the carbenic center must expand the carbene bond angle, which result in the thermodynamic stabilization of the triplet states with respect to the singlet.

This method was shown to be very useful by Zimmerman and Paskovich in 1964 in their attempts to prepare a hindered divalent species completely unreactive towards external reagents. They generated bis(2, 4, 6-trimethylphenyl)carbene (**31a**, Scheme 6) and bis(2, 4, 6-trichlorophenyl)carbene (**40a**, Scheme 12). [21] Although those carbenes were not stable enough to be isolated, they exhibited unusual chemical properties. Thus, in solution at room temperature, these carbenes did not react with the parent diazo compound to give azine but dimerized instead to give tetrakis(aryl)ethylene (**32a** and **42a**) in 70-80% yield. Bis(2, 4, 6-trimethylphenyl)carbene decayed by attack at an *ortho*-methyl group to form benzocyclobutene (**33a**) at a higher temperature, a reaction that is not observed for 2-methyldiphenylcarbenes under similar conditions.

The formation of olefinic dimerization products as the main product is rare in the decomposition of diazo compounds while the formation of ketazine is virtually omnipresent. The authors explained these data by assuming that the hindered diarylcarbenes do not have accessible singlet counterparts, since the singlet would require a smaller carbene angle and incur severe aryl-aryl repulsion, and that, as a result of severe steric hindrance and consequent resistance to external attack by solvent, the hindered triplet diarylcarbene concentration builds up to the point where dimerization occurs.

The chemistry found for those carbenes is thus in sharp contrast with that found for other diarylcarbenes and is interpreted in terms of steric effects, which kinetically stabilize triplet states to a significant degree.

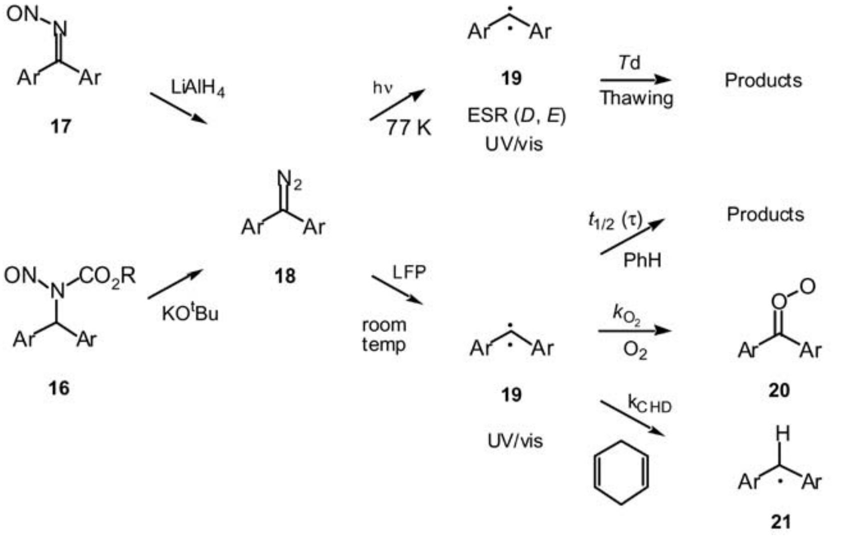
4.1.2 Strategy to stabilize triplet carbenes

These considerations clearly suggest that kinetic stabilization is a far better way to stabilize the triplet states of carbenes than the thermodynamic one. It is also important to note that thermodynamic stabilization usually results in the perturbation of electronic integrity of the reactive center, as has been seen in the case of phosphinocarbene (**10**) and imidazol-2-ylidene (**11**), while kinetic stabilization affects the original electronic nature only slightly. According to the definition, a carbene is a molecule where the two unpaired electrons can be localized on one carbon center. Therefore, if the unpaired electrons are excessively delocalized, one may wonder, whether one should still call the species a carbene. [22] In this regard, a carbene stabilized by steric protection can only be regarded as a “real” stable carbene. On the other hand, a triplet carbene attracts attention from practical viewpoints; because of its unusual high spin state for an organic molecule, triplet carbenes are regarded as an attractive spin source for organomagnetic materials. Thus it is important to create triplet carbenes while maintaining the spin integrity.

4.1.3 Method

Carbenes are conveniently generated from nitrogenous precursors such as diazo compounds [23] or diazirines [24] upon irradiation or thermolysis, which takes place very cleanly and efficiently. Therefore, it is possible to generate carbenes even at very low temperature in rigid matrix once those precursors are prepared. This makes it very easy to assign and characterize the carbenes spectroscopically, which is a very important point since we will then have to assign only triplet states of carbenes and to estimate their stability.

The first step of the research was to establish the method to prepare the precursors. We decided to use diazo compounds as precursors as they have been much better investigated than other nitrogenous compounds. It was not easy, however, to prepare highly congested diazomethanes (**18**). Fortunately, the methods developed by Zimmerman and Paskovich [21] , that is, either acyl cleavage of the corresponding *N*-alkyl-*N*-nitorosourethane (**16**) by potassium *tert*-butoxide or reduction of *N*-nirosoketimine (**17**) with $LiAlH_4$ were found to be very useful to prepare the required diazo precursors (Scheme 3).



Scheme 3

Once desired diazomethanes were prepared, they were irradiated in rigid organic glasses, e.g., 2-methyltetrahydrofuran (MTHF), at 77K. The photoproducts showed a fine-structure EPR line shape characteristic of randomly oriented triplet molecules with a large *D* value attributable to one-center nπ spin-spin interaction at a divalent carbon of triplet carbenes (**19**). The EPR signals were analyzed in terms of zero-field splitting (ZFS) parameters, *D* and *E* values, which give us information on the molecular and electronic structure of triplet carbenes. [25] The *D* value is related to the separation between the unpaired electrons and *E* value is a measure of the difference of the magnitude of the dipole interaction along the *x* and *y* axes. More plainly, the more the two electrons are delocalized with conjugated π systems, the smaller the *D* value will be. On the other hand, increasing the bond angle at the carbene center leads to a smaller value for *E* . The irradiation was then monitored by optical spectroscopy under identical conditions, which enables us to observe and characterize the UV-vis spectra of the triplet carbenes (**19**). Thermal stability of triplet carbenes can be estimated by measuring the temperature (*Td*) at which the triplet signals completely disappeared when thawing the matrix containing triplet carbenes.

In order to estimate the stability of triplet carbenes (**19**) under ambient conditions, laser flash photolysis (LFP) [26] was carried out on the precursor diazomethanes (**18**) in solution at room temperature. The transient absorption bands formed upon the flash were recorded by a multi-channel detector. These bands were assigned to the triplet carbenes (**19**) by comparison with those obtained in matrix at low temperature. The kinetic information was then available by monitoring the decay of the transient absorption with oscillographic tracer. When triplet carbenes decayed unimolecularly, which is often so, lifetime (τ) can be determined. However when the decay did not follow a single exponential, which is sometimes the case, τ cannot be determined. In this case, a half-life ($t_{1/2}$) is estimated from the decay curve as a rough measure of the stability.

The half-life ($t_{1/2}$) is just a measure of lifetime and cannot be regarded as a quantitative scale for reactivity. *Td* cannot also be taken as such a scale unless the decay process is demonstrated to be essentially the same over the carbenes studied. In this respect, the rate constant of the triplet carbene with a typical triplet quencher can be employed as a more quantitative scale of the reactivity. It is well documented that carbenes with triplet ground states are readily trapped with oxygen or a good hydrogen donor such as 1,4-cyclohexadiene (CHD) to generate the corresponding carbonyl oxides [27] or radicals, [26] respectively, which are also detected by LFP techniques. Therefore, the rate constants of the trapping reactions, i.e., k_{O_2} or k_{CHD}, are obtained by plotting the observed pseudo first-order rate constant of the formation of the carbonyl oxides or radicals as a function of [O_2] or [CHD], respectively. These rate constants are used as a more quantitative scale to estimate the reactivities of the triplet carbenes.

4.2 STATE OF THE ART

After establishing our strategy and method, we started our project, which is still in progress. I will describe the path we have followed. [28]

4.2.1 Triplet diphenylcarbenes (DPCs)

The first prototype triplet carbene we chose is diphenylcarbene (DPC) as it has been the most extensively studied of diarylcarbenes and abundant basic data are available. [9] The pioneering studies by Zimmerman and Pakovich on sterically congested DPCs [21] eased our way into this completely new field for us. We prepared diphenyldiazomethanes (DDMs) carrying several functional groups at the *ortho* positions introduced to protect triplet carbene centers and generated the corresponding DPCs upon photo-irradiation.

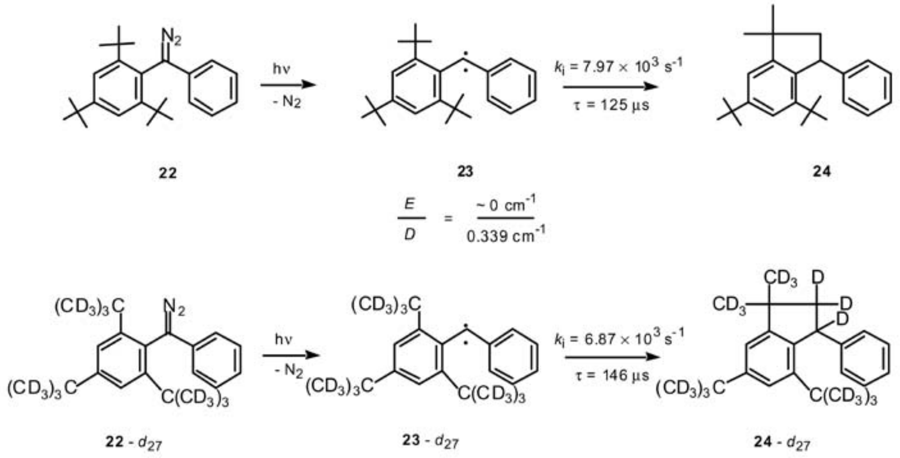
4.2.1.1 Triplet DPCs protected by alkyl groups

Kinetic protectors we first investigated were alkyl groups since it was our initial hope to stabilize and hopefully isolate triplet carbene consisting of only hydrocarbons. However, the use of alkyl groups as effective kinetic protectors was supposed to be very difficult in the light of the strong affinity of carbenes for electrons since they react even with very weak sources of electrons, e. g., C-H bond σ electrons.

(a) Tert-butyl group

Tert-butyl group is known as one of the most effective kinetic protectors and many reactive molecules have been stabilized and isolated by using this group. For instance, the divalent center of silylenes and germylenes, the heavy atom analogues of carbenes, have been shown to be blocked by *tert*-butyl groups. [29]

Photolysis of [2, 4, 6-tris(*tert*)butylphenyl](phenyl)diazomethane (**22**) results in the formation of 4, 6-di(*tert*)butyl-1, 1-dimethyl-3-phenylindane (**24**) almost exclusively, which is most probably produced from the photolytically generated carbene (**23**) as a result of insertion into the C-H bonds of *tert*-butyl groups at the *ortho* position (Scheme 4). LFP of **22** in degassed benzene in the presence of benzophenone as a triplet energy sensitizer produced transient absorption bands (340 nm) ascribable to the triplet carbene (^{3}**23**), which followed a first-order decay($k_i = 7.97\text{x}10^3\ \text{s}^{-1}$ at 20 °C). This means that ^{3}**23** decays mainly by abstracting hydrogen intramolecularly from the methyl group of *o*-*tert*-butyl to form the indane (**24**). The lifetime was estimated to be 125 μs, which is only 60 times longer than that observed for “parent” DPC (τ = 2 μs) under the identical conditions. [30]



Scheme 4

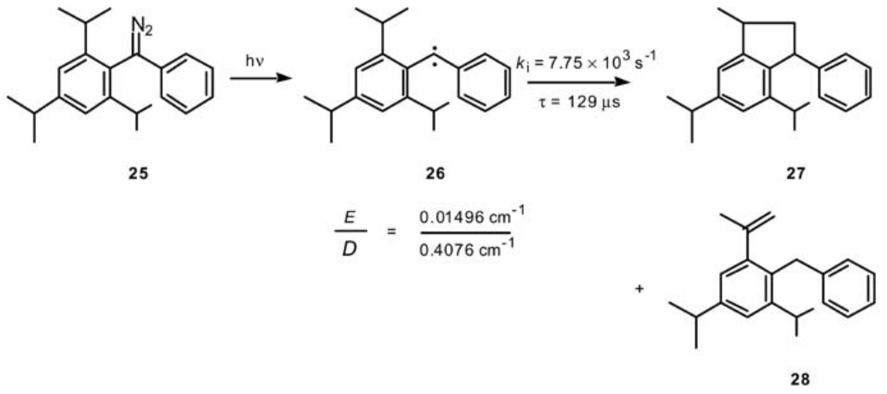
It is interesting that the carbene was not trapped intermolecularly even by methanol, which is known to be an excellent scavenger for most carbenes. This suggests that the carbene center is almost completely blocked from external reagents.

One of ways to increase the lifetime of carbene decaying by abstracting hydrogen is to use kinetic deuterium isotope effects (KDIEs). Thus, we prepared [2, 4, 6-tris(*tert*-perdeuteriobutyl)phenyl](phenyl)diazomethane (**22**-d_{27}) and generated the deuterated carbene (**23**-d_{27}). This carbene also produced the indane (**24**-d_{27}) almost exclusively and decayed unimolecularly ($k_i = 6.87 \times 10^3$ s^{-1}, $\tau = 146$ μs, at 20 °C). KDIE is disappointingly small ($k_H / k_D = 1.16$) in this case, and the lifetime is not increased significantly (Scheme 4). [31]

The observations suggest that *tert*-butyl groups, which have been successfully used to protect many reactive centers, are almost useless to stabilize triplet carbene center.

(b) Isopropyl group

Isopropyl group appears to be an attractive kinetic protector for carbene in this respect since it is not expected to be in too much close contact with carbene center when introduced at the *ortho* position of DPC but it is still able to block the center from external reagents.



Scheme 5

Irradiation of a degassed benzene solution of (2,4,6-triisopropylphenyl)-phenyldiazomethane (**25**) at room temperature afforded phenylindan (**27**) and diphenylmethane (**28**) in a 10:1 ratio (Scheme 5). It is probable that **27** is produced from the photolytically generated carbene (**26**), which underwent insertion into the C-H bonds of isopropyl methyl groups at the *ortho* positions. The formation of **28**, on the other hand, can be explained in terms of H abstraction of ^{3}**26** from the methine of the *o*-isopropyl group, followed by H migration in the resulting diradical. [32]

LFP of a degassed benzene solution of **25** in the presence of benzophenone again produced a transient absorption (320 nm) ascribable to triplet carbene **26**, which must be generated by denitrogenation of triplet excited state of **25**. The decay of the transient band due to ^{3}**26** followed a first-order kinetic (k_i = 7.75x10^{-3} s^{-1}), which is again in accordance with the product analysis data, showing that intramolecular H abstraction leading to **27** and **28** is the main decay pathway for triplet carbene (^{3}**26**). [32] The lifetime was estimated to be 129 μs, which is essentially the same as that of ^{3}**26** (τ = 120 μs).

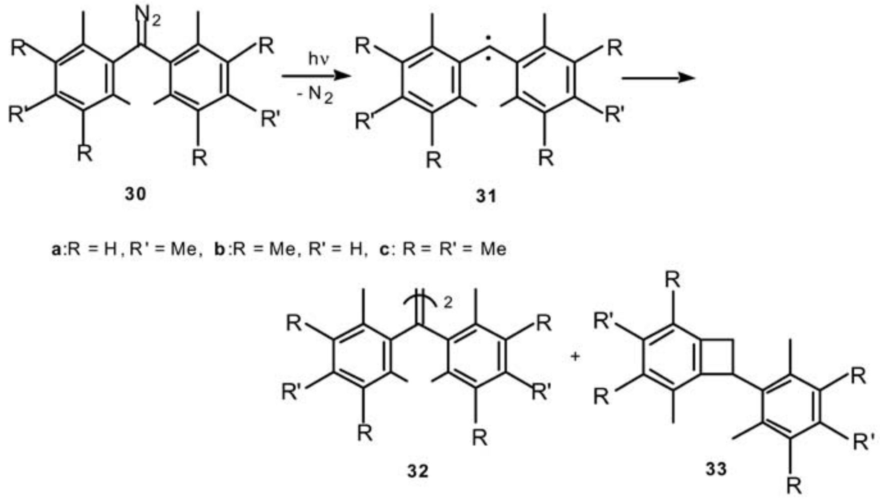
The comparison of the data between two carbenes reveals intriguing and unique nature required for kinetic protectors of triplet carbenes. Thus, significant *E* values of ^{3}**26**, as opposed to the essentially zero *E* values for ^{3}**23** under identical conditions, clearly suggest that steric congestion around the carbene center in ^{3}**26** is less severe than that in ^{3}**23**, as expected. Nevertheless, *o*-isopropyl groups can act as kinetic protector of triplet DPC comparable to the sterically bulkier *tert*-butyl group.

(c) Methyl group

Methyl group is the smallest alkyl group and is generally not considered as an effective kinetic protector. However, the results using *tert*-butyl and isopropyl groups as protectors suggest that a proper distance between H on alkyl groups and the carbene center is essential for the alkyl group to be an effective protector. In this respect, the *o*-methyl group is expected to be a good shielding group toward the triplet carbene center.

This has been already shown by Zimmerman and Paskovich [21] in the chemistry of bis(2,4,6-trimethylphenyl)carbene, which results in the formation of carbene dimer, suggesting that decay pathways of the hindered carbene are suppressed both inter- and intramolecularly and, hence, the concentration builds up in solution to the point where dimerization occurs (Scheme 6).

LFP of the precursor diazomethane (**30a**) in degassed benzene produced a transient band (330 nm) easily ascribable to the triplet carbene (^{3}**31a**) , which disappeared more slowly than those of *tert*-butylated (**23**) and isopropylated DPCs (**26**). The decay kinetics of the transients indicate that the absorption at 330 nm decays within 1 s to generate a new species with a maximum around 370 nm, which is too long-lived to be monitored by our system. The decay of the initial bands is kinetically correlated with the growth of the secondary species. Product analysis of the spent solution showed the presence of **32a** and **33a**. We assign the initially formed transient with a maximum at 330 nm to carbene and the second to *o*-quinodimethane (**34a**). The latter species is probably formed as a result of the 1,4-H shift from the *o*-methyl to the carbene center of ^{3}**31a** and undergoes cyclization leading to benzocyclobutene (**33a**) (Scheme 7). The decay rate (k_d) of the carbene was determined to be 1.1x10 s^{-1}, while the growth rate (k_i) was 1.5 s^{-1}. From the decay curve, a half-life ($t_{1/2}$) of ^{3}**31a** was estimated to be ca. 160 ms, while the lifetime (τ) based on k_i was 666 ms. [31,33] This is roughly more than three orders of magnitude greater than DPCs protected by *tert*-Bu or isopropyl groups. The observations showing that the smallest group exhibits the largest effect to shield triplet carbene center reveal a unique requirement for a kinetic protector toward the carbene center.

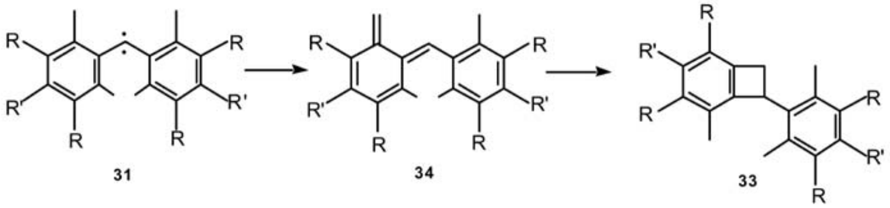


	32	33
a	96 %	4 %
b	54 %	46 %
c	4 %	96 %

Scheme 6

We wanted to take advantage of this group to increase the stability of DPCs by using the buttressing effect. It is well-known that, in 1,2-disubstituted benzene derivatives, introduction of substituents in the 3-position exerts a very large effect on the rate of appropriate reactions, which are considered in light of the importance of bond-bending; the 3-substituents "buttress" the 2-substituents. [34,35] It is expected, then, that protection of the carbenic center by *ortho* substituents will be greatly strengthened by the introduction of another group at the 3-position. Thus we investigated the effects of the *m*- and *p*-methyl groups on the reactivities of bis(2,6-dimethylphenyl)carbenes.

Irradiation of bis(2,3,5,6-tetramethylphenyl)diazomethane (**30b**) and bis(2,3,4,5,6-pentamethylphenyl)diazomethane (**30c**) generated the corresponding DPCs (Scheme 6), which are characterized by EPR. Inspection of the data in Table 1 indicates that *E*/*D* values steadily decrease as more methyl groups were introduced into the aromatic rings, suggesting that the carbene angle expands due to increased steric interaction between the four *o*-methyl groups in going from **31a** to **31b** to **31c**. This should lead to larger ΔG_{ST}.



Scheme 7

The reactions observed with **31b** and **31c** forming tetra(aryl)ethylene (**32**) and benzocyclobutene (**33**) were analogous to those observed with **31a**, but the product distributions were significantly different. While **31a** underwent dimerization almost exclusively, the formation of cyclobutene increased as more methyl groups were introduced. Carbene **31c** produced **33c** as major product at the expense of the dimer (**32c**).

LFP of **30b** in degassed benzene also generated transient bands ascribable to the triplet carbene (^{3}**31b**), which decayed rather slowly to generate a new species due to *o*-quinodimethane (**34b**). The decay of ^{3}**31b** is kinetically correlated with the growth of **34b**. The decay rate was determined to be 1.6 s^{-1}, while the growth rate was 2.2 s^{-1}. From the decay curve, the half-life ($t_{1/2}$) of ^{3}**31b** was determined to be ca 410 ms, while the lifetime based on k_i was estimated to be 455 ms.

On the other hand, ^{3}**31c** decayed unimolecularly almost exclusively with k_i of 4.1 s^{-1} (τ = 180 ms), in accordance with the product analysis results (Table 1).

These observations are interpreted as reflecting the difference in the extent of steric crowdedness around the carbene center between the three carbenes. Thus, in **31b**, each of the four *o*-methyl groups is buttressed by four additional *m*-methyl groups. Therefore, the carbene center in **31b** is surrounded by the *o*-methyl groups more tightly than in **31a**. Thus, **31b** is shown to be longer-lived than **31a**. On the other hand, the steady increase in k_i and the formation of benzocyclobutene as going from **31a** to **31c** clearly suggests that the *o*-methyl groups are brought closer to the carbene center by the buttressing methyl groups and hence the carbenic center thus interacts more easily with the *o*-methyl groups. Thus, **31c** decays unimolecularly by abstracting H from the *o*-methyl group to generate *o*-quinodimethane almost exclusively and hence becomes shorter-lived. [31]

Table 1. ZFS parameters[a] and kinetic data[b] for polymethylated DPCs (**31**)

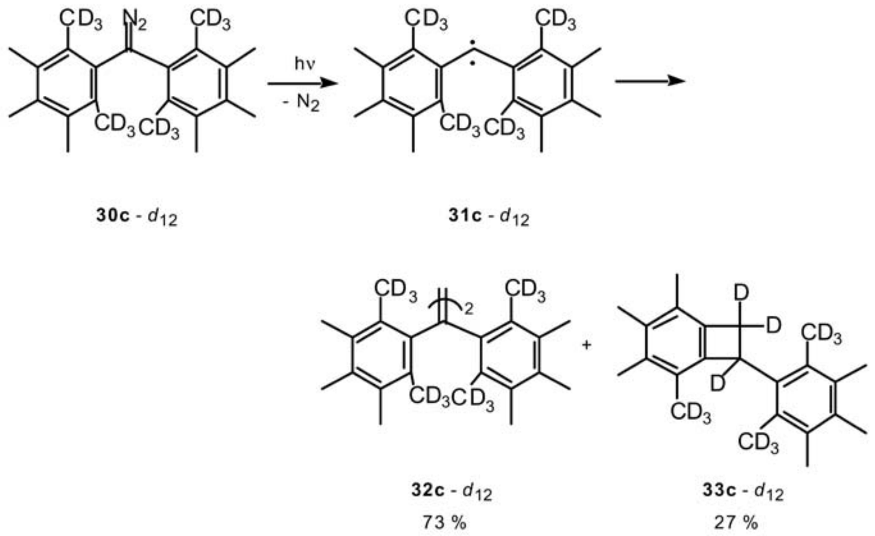
Carbene	D	E	k_i	$t_{1/2}$	k_{O_2}	k_{CHD}
	cm^{-1}		s^{-1}	ms	M^{-1} s^{-1}	
31a	0.3551	0.0116	1.5	160	2.0×10^8	4.6×10^2
31b	0.3805	0.0106	2.2	410	7.1×10^7	3.4×10
31c	0.3636	0.0095	4.1	180	1.0×10^8	9.8×10
31c - d_{12}	—	—	0.85	1,100	—	—

[a] In 2-methyltetrahydrofuran (MTHF) at 77 K.
[b] In benzene at room temperature.

The buttressing effects are thus shown to effectively strengthen the *ortho* group protection of the reactive center. However, in the case of methyl groups which are potentially reactive toward the carbene, the *o*-methyl groups become more efficient intramolecular quenchers as a result of buttressing, thus decreasing carbene persistence. One of the best ways to quench this process is, again, to use KDIE. Thus we generated, by photolysis of the corresponding diazo compound, bis[2,6-di(trideuteriomethyl)-3,4,5-trimethylphenyl]carbene which also afforded both benzocyclobutene and a carbene dimer. However, reflecting the KDIEs, the product ratios are significantly changed; the dimer was formed as a major product at significant expense of benzocyclobutene (Scheme 8).

LFP of **30c**-d_{12} in degassed benzene resulted in essentially the same transient bands that were observed for the protio analogue. The kinetic behavior is distinctly different between these two carbenes, however. Thus, the growth rate and optical yield of the deuterated *o*-quinodimethane were very small compared to those of the protio analogue. The growth rate of *o*-xylylene from **31c**-d_{12}, which is equal to the intramolecular D abstraction rate constant (k_D), was determined to be 0.85 s^{-1}. The KDIE based on the absolute rate constants, i.e., k^H_i/ k^D_i, is calculated to be 4.76. From the decay curve of the carbene, the half-life ($t_{1/2}$) of **31c**-d_{12} was estimated to be 1 s, while the lifetime based on k^D_i was 1.25 s

(Table 1). Thus the KDIE observed for methylated DPC is much larger than that observed for *tert*-butylated DPC (**23**), and a triplet carbene having a lifetime over 1 second is realized for the first time. [31]



Scheme 8

The other method to further stabilize kinetically protected triplet DPCs is to use the electronic (thermodynamic) effect of *para*-substituents. It is well-documented in radical chemistry that the abilities of various substituents to delocalize the spin on a carbon radical play an important role. [36, 37] Thus we generated bis(2,6-dimethylphenyl)carbene (**31a**) having a series of substituents at *para* positions and studied the effect of *para*-substituents on the stability of the carbene (Table 2, Scheme 9, Figure 6). [38-40]

The zero-field splitting parameters, *D* and *E*, were measured in matrices of different viscosities and analyzed in terms of a sigma-dot (σ•) scale, which is a nonkinetic measure of radical-stabilizing effects based on hyperfine coupling constants in the benzylic radical. [41] Fairly good correlation with σ• was found for the *D* values of ^{3}**31a** in its minimum energy geometry (Figure 6). This indicates that the unpaired electrons on the hindered DPCs are also delocalized by para-substituents depending on the radical-stabilizing power. [38] The stabilities of ^{3}**31a** were estimated either by measuring *Td* or by analyzing the decay kinetic of ^{3}**31a** in a degassed solution at room temperature.

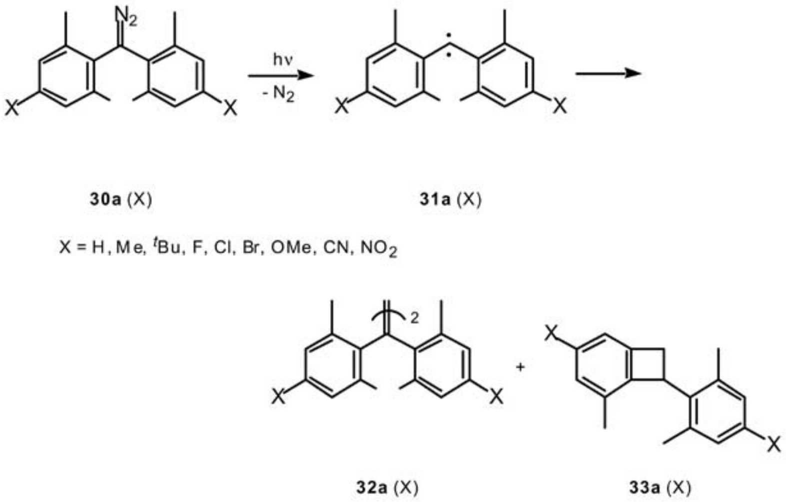
Table 2. ZFS parameters[a] and kinetic data[b] observed for bis(2,6-dimethyl-4-X-phenyl)carbenes (**31a**)

X in **31a**	*D*	*E*	*Td*[c]	$2k/\varepsilon l$	$t_{1/2}$	k_{O_2}	k_{CHD}
	cm^{-1}		K	s^{-1}	ms	$M^{-1}\ s^{-1}$	
H	0.355	2.8×10^{-6}	140	1.4×10	180	1.5×10^{8}	9.4×10
Me	0.331	2.6×10^{-6}	120	1.1×10	160	2.8×10^{8}	4.5×10^{2}
^{t}Bu	0.328	2.6×10^{-6}	170	5.8	500	1.8×10^{8}	3.0×10^{2}
F	0.344	2.8×10^{-6}	120	5.8×10	60	1.7×10^{8}	4.4×10^{2}
Cl	0.326	2.5×10^{-6}	120	4.0×10	100	1.1×10^{8}	1.8×10^{2}
Br	0.327	2.5×10^{-6}	120	2.2×10	50	9.7×10^{7}	1.4×10^{2}
OMe	—	—	120	1.3×10^{2}	20	3.1×10^{8}	1.2×10^{2}
CN	0.283	2.7×10^{-6}	180	1.8×10	590	3.1×10^{7}	1.3×10^{2}
NO_2	0.259	2.7×10^{-6}	170	—	—	—	—

[a] The values observed in triacetin (TA) matrix at 200 K, where carbene undergoes geometrical relaxation.
[b] In benzene at room temperature.
[c] Td is measured in 2-methyltetrahydrofuran (MTHF)matrix.

A significant increase in the stability is observed for **31a (**X = *t*Bu**)** and **31a (**X = CN**),** as evidenced by a significantly higher *Td* value in matrix as well as the longer half-life ($t_{1/2}$) in solution at room temperature observed for those two carbenes. [39, 40] In the case of **31a (**X = CN**)**, a significant decrease in *D* value is also noted, indicating that the unpaired electrons are delocalized more extensively by the CN group at the *p*-position. Thus, the extended stability can be explained in terms of thermodynamic factors as a result of spin delocalization. This indicates that the kinetically stabilized triplet carbenes can be further stabilized by spin-delocalizing substituents at *para* positions. However, the significant effect of *para*-*tert*-butyl group cannot be explained similarly since the $\sigma\cdot$ of this group is not large. Moreover, the inspection of *Td* and $t_{1/2}$ as a function of *D* value suggests that the correlation is rather poor.

The rate constant of the triplet carbene with a typical quencher such as O_2 and 1,4-cyclohexadiene can be employed as a more quantitative measure of the reactivity. However, neither k_{O_2} nor k_{CHD} appreciably correlated with the *D* value (Table 2). Presumably, simple linear correlations with spin delocalization factors may not be expected for the reaction of triplet carbenes (diradicals) to form the corresponding monoradicals since the extents of the delocalization of unpaired electrons should be different between the two states. An additional complexity may arise from mixings of the singlet state in the reaction on the triplet energy surface. The effects of substituents on the energy difference between the singlet and triplet states and spin-orbit coupling efficiencies are taken into account in this case.



Scheme 9

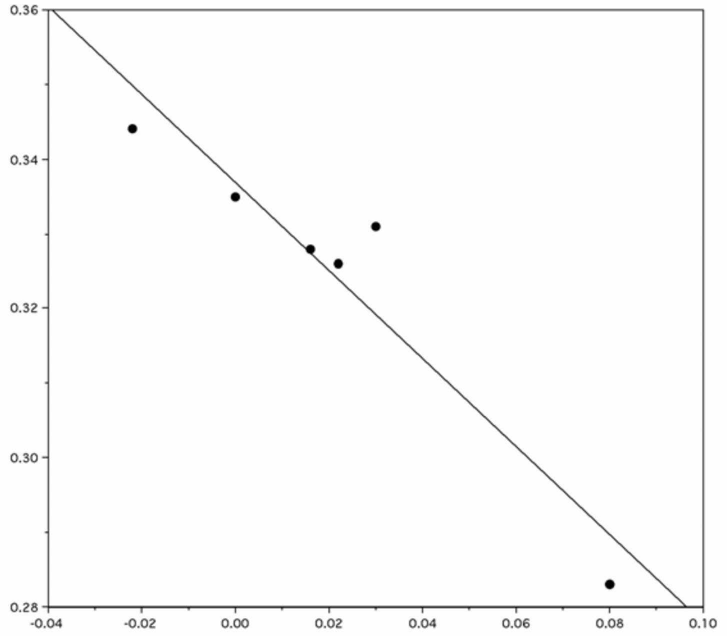
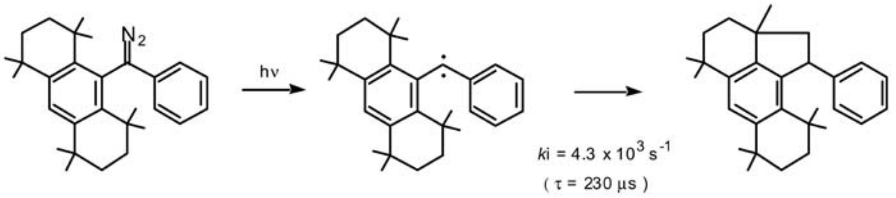


Figure 6. The plot of the D values for bis(2,6-dimetyl-4-X-phenyl)carbenes (**31a**) observed in triacetin (TA) at 200 K against $\sigma_{\alpha}\bullet$

(d) Bicycloalkyl Groups

Our studies thus far clearly suggest that acyclic alkyl groups encounter a limitation when used as protecting groups for triplet carbene center since, as they are brought closer to the carbene center in order to shield it from the external regents, they are more easily trapped by the reactive center that they are expected to protect. In this light, it is crucial to develop a protecting group that is sterically congesting but unreactive toward triplet carbenes. Cyclic alkyl groups are expected to exert as a better protector since the distance between H on the alkyl group and carbene center can be restricted to an extent that retards decay pathway of the carbene by abstracting H. For instance, 9-[(1,1,4,4,5,5,8,8-octamethyl)(octahydro)anthryl](phenyl)carbene (**36**) decayed by undergoing H abstraction from the methyl groups to form indane derivatives as in the case of *tert*-butylated DPC (**23**). However, the intramolecular H abstraction rate constant is determined to be $k_i = 4.3 \times 10^3\ s^{-1}$ ($\tau = 230\ \mu s$), [42] approximately half of the corresponding constant for **23** (Scheme 10).



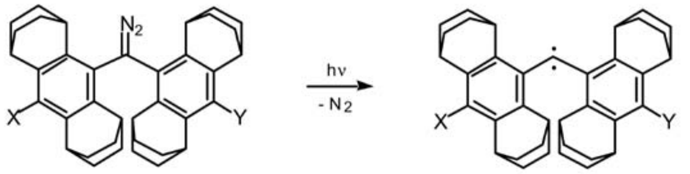
35 **36** **37**

$$\frac{E}{D} = \frac{0.01496\ cm^{-1}}{0.4076\ cm^{-1}}$$

Scheme 10

Bicycloalkyl groups are more attractive since bridgehead C-H bonds are much less susceptible to H abstraction [43] and yet the bridging chains will act as protectors. Thus, we generated bis [octahydro-1,4:5,8-di(ethano)anthryl]carbene (**39**) [44, 45] (Scheme 11) which showed a significantly smaller *E*/*D* value (0.0265) than that observed for "parent" DPC (*E*/*D* = 0.0464) and even than **31b**, an open-chain "counterpart" of **39**. This suggests that the central angle of **39** is significantly expanded because of the steric influence of the bicyclohexyl groups. LFP studies have shown that triplet **39** exhibited a transient band around 320-330 nm and a weak broad band around 480 nm. The transient absorption bands decayed in second-order kinetics ($2k/\varepsilon l = 8.4\ s^{-1}$), but no new absorption was formed (Table 3). The approximate half-life of ^{3}**39** is estimated in the form of half-life, $t_{1/2}$, to be 1.5 s, which is to be compared with that of ^{3}**31b** ($t_{1/2}$ =

0.41 s). Thus, the formation of all-hydrocarbon triplet carbenes having a half-life over a second under normal conditions was realized for the first time. The difference in the stability between the two carbenes is probably ascribable to that in the decay pathway between the two.



38 **39**

a : X = Y = H, **b** : X = Y = Br, **c** : X = Br, Y = CN

Scheme 11

Spectroscopic and product studies clearly suggest that the H migration is one of the prominent decay pathways for **31b,** but this process is a less prominent decay pathways for **39**. It has been shown that the intramolecular H migration is rather sensitive to the distance between the migrating H and the carbene center. The distances calculated (UPM3) for **31b** and **39** are 2.38 and 2.67Å, respectively. On the other hand, the diradical centers of the 1,4-diradical generated as a result of the H migration in **31b** would be stabilized by benzylic resonance, while, in the 1,4-diradical from **39**, such resonance stabilization is not expected for the radical center on the bridgehead carbon atom. These considerations suggest that the H migration is not likely to be a prominent decay pathway for **39,** as compared with the open-chain counterpart **31b**.

Table 3. ZFS parameters[a] and kinetic data[b] observed for carbenes (**39**)

Carbene	X	Y	D	E	Td^c	$t_{1/2}$ (τ)	k_{O_2}	k_{CHD}
			cm^{-1}		K	s	M^{-1} s^{-1}	
39a	H	H	0.400	0.0106	150	(1.5)[d]	2.3×10^8	3.6×10^2
39b	Br	Br	0.404	0.0098	200	2.8	1.7×10^8	1.8×10^2
39c	Br	CN	0.372	0.0087	180	1.4	1.2×10^8	6.7×10

[a] In 2-methyltetarhydrofuran (MTHF) at 77 K.
[b] In benzene at room temperature.
[c] Td is measured in 2-methyltetrahydrofuran (MTHF) .
[d] Lifetime.

The dimerization of **39** seems to be a more likely decay process, as the decay kinetics of **39** follows second-order kinetics. However, all attempts to isolate and/or detect the expected dimer of **39** have been unsuccessful; irradiation of **38** in a degassed benzene always resulted in complex mixtures from which no particular products were isolated. This may suggest that there is severe restriction during dimerization, and, hence, the reaction cannot end up with a final stable product.

Inspection of the optimized geometry indicates that dimerization of the carbene center of **31b** is hindered but still attained, as the facing methyl groups can rotate about one another in order to minimize the interaction potential during dimerization. The relatively easy isolation of the dimer of **31b** supports this view. On the other hand, in **39**, the flexible motion of bulky and rigid "three-dimensional" bicyclic substituents during the dimerization is not attained.

Thus, bicyclohexyl groups act as an ideal kinetic protector of triplet carbene not only by quenching the intramolecular H-donating process but also by forcing steric restriction during the dimerization of the carbene center.

It should be noted here that the reactivity (k_{O_2} or k_{CHD}) of **39** toward typical triplet quenchers (O_2 or CHD) is somewhat higher than that of **31b** (Table 3). Comparison of the optimized geometries between **39** and **31b** obtained by the AM1/UHF method reveals that there is slightly more space around carbene center in **39** than in that in **31b**. This suggests that **39** is subject to the attack of a small particle such as hydrogen more easily than **31b**.

The substituents at the *para*-position of **39** exhibit subtle but distinct effects on the reactivity on **39** (Table 3). Thus, the D values of **39** appreciably decrease when a strong spin-delocalizing substituent, i.e., the 4-CN group ($\sigma^{\bullet}_{\alpha} = 0.040$) is introduced, although a moderate spin-delocalizing group, i.e., 4-Br ($\sigma^{\bullet}_{\alpha}$ for 4-Cl $= 0.011$), has only a slight effect on the D value. As spin-delocalizing groups are introduced at *para*-positions, carbenes tend to become more stable, judging from Td and $t_{1/2}$ values. The rate constants of **39** with typical triplet carbene quenchers such as oxygen and 1,4-cyclohexadiene also show that the reactivity of **39** decreases as more spin-delocalizing groups are introduced. [45]

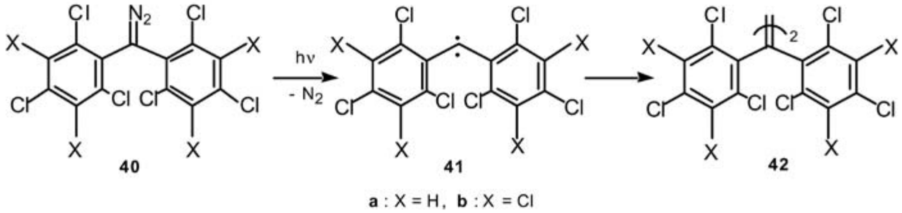
4.2.1.2 Triplet DPC protected by halogens

Alkyl groups are attractive kinetic protectors for triplet carbenes in order to realize persistent all-hydrocarbon triplet species. However, they are potentially reactive toward triplet carbenes and hence will not be able to shield the reactive center completely. In this respect, we need to explore protecting groups which are almost completely unreactive toward triplet carbenes. Halogens are generally reactive toward the singlet state of carbene but are not reactive with the triplet. For instance, the CIDNP studies on the reactions of carbenes with trichloromethane clearly indicate that, whereas a singlet carbene preferentially abstracts chlorine most probably by way of chloronium ylide intermediate, the corresponding triplet carbenes exclusively undergo H abstraction. [46]

Moreover, the enormous effect of perchlorophenyl groups on the stability of arylmethyl radicals has been well-documented by a series of reports by Ballester and his coworkers. [47] Thus, perchlorotriphenylmethyl has been shown to have its half-life on the order of 100 years in solution at room temperature in contact with air and has therefore been termed as an inert free radical. Even perchlorodiphenyl(chloro)methyl has been shown to be stable. [48] In this light, perchlorophenyl group may easily be expected to exerts a similar stabilizing effect on triplet DPCs.

(a) Chloro group

We first measured the stability of bis(2,4,6-trichlorophenyl)carbene [21,49] Zimmerman generated in 1964. Transient absorption due to ^{3}**41a,** however, was found to disappear disappointingly quickly (within ca 100 ms). The decay was found to be second order, in accordance with the product analysis data, showing that dimerization to form ethylene is the main decay pathway for ^{3}**41a** under these conditions. From the decay curve, the dimerization rate constant (k_d) was determined to be 1.2 x 10^7 M^{-1} s^{-1}. [49] The half-life was determined to be 18 ms, which is four orders of magnitude greater than that observed for parent DPC but is ca. one-tenth of that of ^{3}**31a** (Scheme 12, Table 4).



Scheme 12

Perchlorinated DPC ^{3}**41b** [49] also gave carbene dimer when generated in degassed benzene and decayed according to second-order kinetics. The dimerization rate constant (k_d) was found to be 2.5 x 10^6 M^{-1} s^{-1}, which is approximately one order of magnitude smaller than that determined for ^{3}**41a**. The observation suggests that the dimerization rate is sharply decreased as four additional chlorine groups are introduced at the meta positions, obviously due to the buttressing effect. The rough lifetime in the form of half-life is, however, estimated to be 28 ms.

On the other hand, k_{CHD} increases ableit slightly as more chlorine atoms are introduced. This is somewhat surprising in the light of the marked decrease in the dimerization rate by the four meta buttressing chloro substituents, as noted above, and is understood to indicate that electrophilicity of the carbene center is increased as more chlorine groups are introduced on the phenyl rings (Table 4). Thus, the attack of a bulky substrate, e.g., chlorinated DPC, on the carbenic center must be severely restricted while the rate of abstraction of a very small H atom from a very efficient H donor is still controlled by the electrophilicity of the carbenic center.

Table 4. ZFS parameters[a] and kinetic data[b] observed for polychlorinated DPCs (**41**)

Carbene	D	E	$t_{1/2}$	k_d	k_{CHD}
	cm^{-1}		ms	M^{-1} s^{-1}	
41a	0.364	0.0115	18	1.2×10^7	3.5×10^3
41b	0.409	0.0139	28	2.5×10^6	6.2×10^3

[a] In 2-methyltetrahydrofuran (MTHF) at 77 K.
[b] In benzene at room temperature.

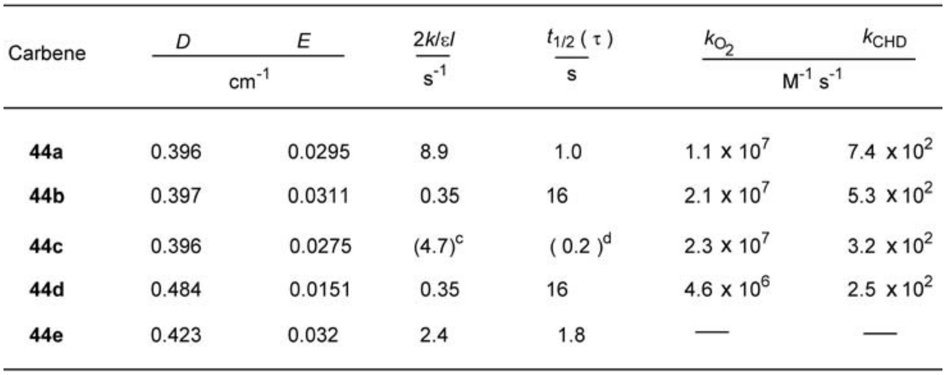
Perchlorophenyl groups, which exhibit the enormous effect on the stability of arylmethyl radicals, have only a slight effect on the stability of DPCs. The facts suggest how unstable triplet DPCs are and how much more difficult it is to stabilize than arylmethyl radicals.

(b) Bromo Group

Bromine groups appear to be more promising as a protecting group toward triplet carbene center because the van der Waals radius is similar to that of methyl (Br, 1.85 Å; Me 1.75 Å) and, more importantly, the C-Br bond length (1.85 Å) is longer than C-C (Me) (1.50 Å). [50] This suggests that the *o*-bromo groups can hang over the reactive site more effectively. In addition, the value of $\zeta\iota$, which gives a measure of the strength of the spin-orbit interaction, is increased rather dramatically in going from chlorine (586 cm^{-1}) to bromine (2,460 cm^{-1}). [51] This suggests that the intersystem crossing from the nascent singlet carbene to the triplet should be accelerated by introducing a bromine atom.

Bis(2,4,6-tribromophenyl)carbene [52-54] (**44a**)was easily generated by photolysis of the precursor diazomethane and was characterized by EPR spectra (Scheme 13). The triplet carbene generated in a degassed solution at room temperature decayed very slowly, persisting for at least 30s. The decay is found to be second order ($2k/\varepsilon l$= 8.9 s^{-1}). The rough lifetime is estimated in the form of the half-life, $t_{1/2}$, to be 1 s (Table 5).

Table 5. ZFS parameters[a] and kinetic data[b] observed for polybrominated DPCs (**44**)



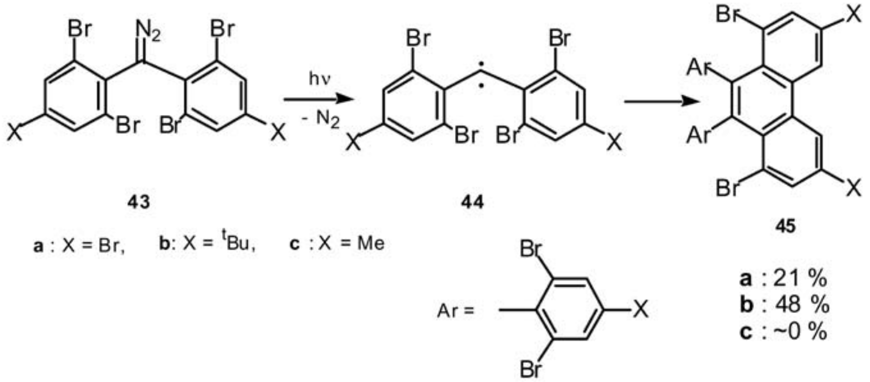
Carbene	D	E	$2k/\varepsilon l$	$t_{1/2}$ (τ)	k_{O_2}	k_{CHD}
	cm^{-1}		s^{-1}	s	$M^{-1}\ s^{-1}$	
44a	0.396	0.0295	8.9	1.0	1.1×10^7	7.4×10^2
44b	0.397	0.0311	0.35	16	2.1×10^7	5.3×10^2
44c	0.396	0.0275	(4.7)[c]	(0.2)[d]	2.3×10^7	3.2×10^2
44d	0.484	0.0151	0.35	16	4.6×10^6	2.5×10^2
44e	0.423	0.032	2.4	1.8	—	—

[a] In 2-methyltetrahydrofuran (MTHF) at 77 K.
[b] In benzene at room temperature.
[c] Uimolecular deday.
[d] Lifetime.

The reaction patterns observed for ^{3}**44a** were analogous to those observed with chlorinated and methylated DPCs. However, the structure and yield of the dimer were notably different from those observed for other persistent DPCs, e.g., **31** and **41**, which produced tetra(aryl)ethylenes in fairly good yield (~80 %). Thus, generation of ^{3}**44a** in a degassed benzene solution resulted in the formation of a tarry matter, from which a relatively small amount (20 %) of dimeric product was isolated. The dimer was identified as a phenanthrene derivatives (**45**) rather than a simple carbenic dimer, tetra(aryl)ethylenes. A possibility is that triplet carbenes undergo dimerization to form tetra(aryl)ethylenes, which subsequently cyclize to lead to phenanthrene. The fact that the carbene dimer is formed in a complicating form in surprisingly smaller amount suggests that the carbene center is effectively blocked by four *o*-Br groups.

The observations clearly indicated that bromine groups shield the carbene center better than methyl groups, as expected. One may wonder whether through-space interaction between the triplet carbene center and the *o*-bromine groups may play a role in stabilizing the triplet. EPR data clearly indicate, however, that there is no such interaction at least in matrix at low temperature. PM3 calculations also support the idea.

Anomalous effects of *para*-substituents on the stabilities of triplet brominated DPC were observed in this case (Scheme 13, Table 5). [53, 54] LFP studies show that bis(2,6-dibromophenyl)carbene ^{3}**44b** having *tert*-butyl groups at *para* positions decayed very slowly, much slower than that of ^{3}**44a**; it took more than 200 s before all the signals due to ^{3}**44b** disappeared completely. The decay was again found to be the second order ($2k/\varepsilon l = 0.36$ s^{-1}), and $t_{1/2}$ was estimated to be 16 s, suggesting that ^{3}**44b** is some 20 times longer-lived than ^{3}**44a**. In marked contrast, bis(2,6-dibromophenyl)carbene ^{3}**44c** having methyl groups at *para* positions decayed rather rapidly within 1 s. The decay was found to be the first-order in this case, and the lifetime is estimated to be 0.21 s ($t_{1/2} = 0.22$ s).



Scheme 13

What is the origin for this anomalous effects of *para*-substituents? The inspection of ZFS parameters clearly indicates that there are no significant change in *E*/*D* values as the *para* substituents are changed. The observations indicate that the *para* substituents do not have much effects on the geometries of ^{3}**2**, as expected. The reactivities of ^{3}**44** toward typical triplet quenchers, i.e., oxygen and 1,4-cyclohexadiene are also not significantly affected by the *para* substituents (Table 5).

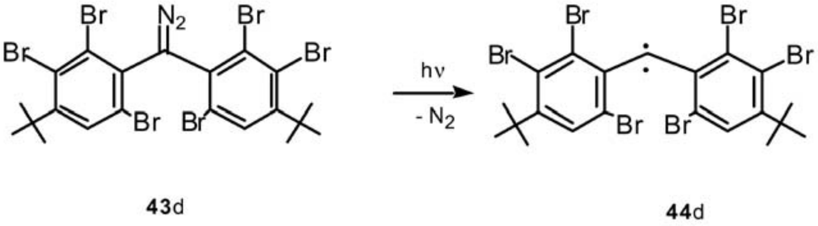
These observations clearly support a naïve idea based on intuition that the para substituents exerts almost no effects around the remote carbenic center of

^{3}**44**, at least in terms of the steric congestion. Furthermore, electronic effects do not seem important enough to change the reactivity of ^{3}**44** so significantly in the light of rather small distribution in the Hammett as well as spin-delocalizing substituent constants.

Benzene is recognized as a very unreactive solvent, especially for triplet carbenes; hence, the most reactive counterparts under these conditions must be the triplet carbenes themselves. However, the products obtained from the photolysis in benzene consist of a highly complex mixture containing small amounts of carbene dimers. It is then possible that the simple dimerization of ^{3}**44** at the carbenic center must suffer from severe steric repulsion and, therefore, the carbene is forced to react at the other positions. The most probable reactive sites are the aromatic rings, where spin can be delocalized.

Trityl radicals are known to undergo either methyl *para* or *para*-*para* coupling, depending on the substituent patterns. [55] Thus, it is likely that the brominated DPCs also undergo similar coupling. The coupling reactions of trityl radicals are not suppressed by "reactive" substituents.

For instance, (*p*-bromophenyl)diphenylmethyl undergoes methyl-*para* coupling. [56] On the other hand, tri(*p*-tolyl)methyl undergoes rapid disproportionation to yield tri(*p*-tolyl)methane and a quinoid compound that rapidly polymerizes. [57] However, the coupling at the *para* positions is retarded by *tert*-butyl group at this position. [58]



Scheme 14

Thus, the rather large stabilizing effects of *tert*-butyl groups at the-*para* positions on the lifetime of ^{3}**44** compared to the bromo and methyl groups are compatible with the effect of substituents observed in the coupling reaction of trityl radicals. The complexity of the product observed in the reaction of ^{3}**44** may be partly due to the complexity associated with the coupling reactions. It is to be noted that the yield of the "dimer" increases up to 50 % when 4-bromine groups are replaced with 4-*tert*-butyl groups but that essentially no dimeric product is obtained for the 4-methylated derivative.

In order to increase the stability of the brominated DPCs **44**, we examined the buttressing effect by introducing two more bromine groups at the *meta* positions of ^{3}**44b** (Scheme 14, Table 5). The results are somewhat contrary to those expected; **44d** also decayed in the second order, but the decay rate was essentially the same with that of ^{3}**44c** under the same condition (Scheme 14). [54] The quenching rate constants of ^{3}**44d** by oxygen and CHD were not significantly changed compared to ^{3}**44c** either. The observations suggest that the buttressing effect, which exerted a significant effect on the reactivity of triplet polymethylated and polychlorinated DPCs, has only a slight influence on the reactivity of triplet polybrominated systems.

Semi-empirical calculations provided intriguing results. [54] The optimized geometries calculated by PM3/UHF suggested that ^{3}**44b** has almost a linear (α=179.82°) and perpendicular (θ=89.9°) structure. Asimilar optimization of ^{3}**44d** resulted in three main conformers, i.e., I (α=167.9°, θ=75.7°), II (α=170.0°, θ=80.8°), and III (α=179.4°, θ=89.7°), which were very close in energy (± 0.04 kcal/mol). Although two conformers (^{3}**44d** – I and ^{3}**44d** – II) have a definitely smaller bond angle (α) than in ^{3}**44b**, the third one (^{3}**44d** – III) has essentially the same α and θ as ^{3}**44b**. However, the distances from the carbene carbon to the *o*-bromo groups are notably different between the two carbene systems. This distance in ^{3}**44b** is 3.057Å. On the other hand, the distances to the two bromine groups are marginally different in all three conformers of ^{3}**44d**; the distances to the 2-bromine group, which should be buttressed by 3-bromine, in I, II and III are 3.236, 3.228 and 3.200Å, respectively, while those to 2-bromine are 2.996, 3.005, and 3.054Å.

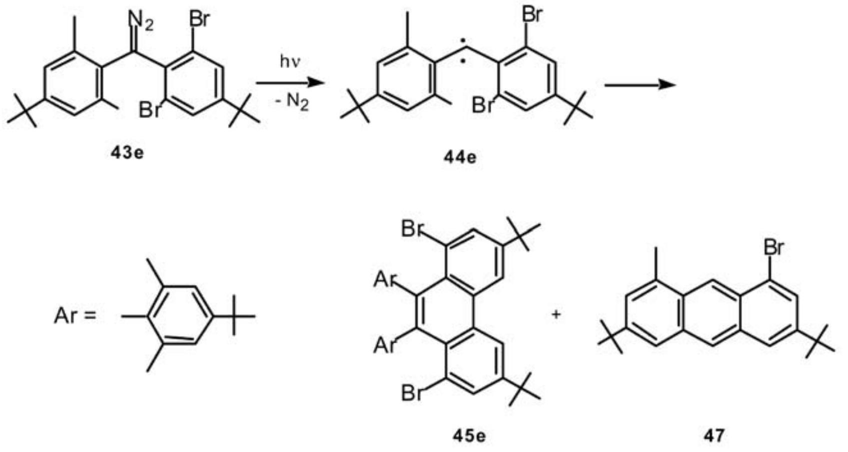
This means that 2-bromine groups, which are expected to get closer to the carbenic center than 6-bromine, are actually moving in the opposite direction. Therefore, the carbenic center in ^{3}**44d** is not as tightly protected as expected. A closer inspection of the geometry revealed that the benzene ring in ^{3}**44d** is distorted probably due to steric repulsion between the two adjacent bromine groups at the 2 and 3 positions, and that the two bromine groups are tilted, one up, one down, with respect to the benzene plane, by approximately 2°. Therefore, the buttressed 2-bromine group is forced to move away from the carbenic center and, hence, cannot block it from external reagents more effectively than the unbuttressed 6-bromine group.

The member of the bromine group that is spherically symmetrical interacts with each other with little directional factor. Therefore, the benzene ring must become distorted when two bromine groups are introduced at the adjacent position. On the other hand, in the case of methyl group, a hydrogen atom, bound to carbon, is only conically symmetrical, and the interaction potential of this hydrogen atom with another atom will depend on the particular point on the carbon-hydrogen bond to which the other atom approaches. Therefore, the two methyl groups at adjacent position can be accepted on the benzene ring without causing severe distortion by simply rotating around each other to minimize the interaction potential. This will result in the restraint of free rotation of the *ortho* methyl group and bring the methyl group closer and tighter around the carbenic center. Electronic repulsion between the two adjacent substituents should also be more significant for electronegative bromine groups than neutral methyl groups.

(c) Possible synergetic effects of bromine and methyl groups

The results show that bromine and methyl groups can both serve as effective kinetic protectors toward the triplet carbene, but they seem to shield the center in a different fashion, as expected from the difference in shape and size. In the case of dimesitylcarbene (**31a**), for instance, the directional factor is an important one, and, hence, van der Waals potential functions for the interaction between methyl groups at the *ortho* positions are not simple. They can rotate around each other harmonically to diminish the interaction potential between the hydrogens. Such a directional factor is less important in polybrominated diphenylcarbenes, as we saw already in the previous section. On the other hand, electronic properties of the two groups are different. From these considerations, it is very intriguing to generate ^{3}DPC protected by the both substituents and investigate their reactivities in order to examine the possible synergetic effects of the two kinetic protectors on the stability of ^{3}DPC. Above all things, almost nothing is known concerning the reactivity of sterically congested DPCs bearing unsymmetrical kinetic protectors.

(2,6-Dibromo-4-*tert*-butylphenyl)(2,6-dimethyl-4-*tert*-butylphenyl)carbene (**44e**) showed the ZFS parameters, which are not intermediate between the two, but very much like those of ^{3}**44b** (Scheme 15, Table 5). [54] The thermal stability of ^{3}**44e**, as judged from *Td*, is comparable to that of ^{3}**44b** but is much higher than that of ^{3}**31a** (X = ^{t}Bu). However, the behaviors of ^{3}**44e** in solution at room temperatures were found to be comparable to that of ^{3}**31a** (X = ^{t}Bu) rather than to those of ^{3}**44b**. The half-life ($t_{1/2}$) of ^{3}**44e** in degassed benzene is estimated to be 1.8 s, which is one order of magnitude smaller than that of ^{3}**44b** and comparable to that of ^{3}**31a** (X = ^{t}Bu). *o*-Quinodimethane was also generated as a result of intramolecular H transfer as ^{3}**44e** decayed. The rate constant of the H transfer was estimated to be 0.58 s^{-1}, which is comparable to that observed with ^{3}**31a** (X = ^{t}Bu) (k_i = 0.62 s^{-1}). Thus, ^{3}**44e** is shown to decay, at least in part, by abstracting hydrogen from the *o*-methyl group, while main decay pathway for ^{3}**44b** is dimerization. This intramolecular reaction channel available for ^{3}**44e** explains the difference in lifetime between the two carbenes. Product analysis results producing **47** (Scheme 15) also supported the idea.



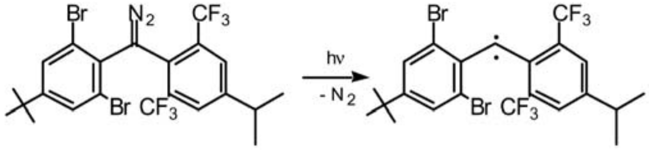
Scheme 15

The results suggest that DPC protected by unsymmetrical groups of a different nature undergoes little extra stabilization as a result of possible synergetic effects of the two groups, but exhibits a hybrid character depending on the conditions; the configurations and stabilities of ^{3}**44e** in the low temperature matrix are dominantly affected by the bromine substituents, while the kinetics in the solution phase are controlled by the methyl substituents. This can be explained in terms of the dependence of quenching processes possible for ^{3}**44e** on the conditions. Presumably, at low temperature, the main quenching pathway for ^{3}**44e** is dimerization to form the carbene dimer. The carbene center in ^{3}**44e** is well protected by the two *o*-bromine groups and the two *o*-methyl groups. The methyl groups in ^{3}**44e** are fixed more tightly than those in ^{3}**31a** (X = ^{t}Bu) as the substituents on the opposite side are spherically symetrical bromine group and, hence, ^{3}**44e** become thermally more stable than ^{3}**31a** (X = ^{t}Bu). On the other hand, when the temperature is raised, intramolecular H abstraction, which usually requires higher activation energy, [21] becomes allowed as well and starts to compete with the dimerization. Thus, the reactivity of ^{3}**44e** is affected by the reactive methyl groups at higher temperature.

4.2.1.3 Triplet DPC protected by trifluoromethyl group

The trifluoromethyl group has been regarded as an ideal kinetic protector of carbenes since it is much bigger than methyl and bromine groups, and, more importantly, C-F bonds are known to be almost the only type of bond unreactive toward carbenic center. [59] For instance, trifluoromethylated DPCs generated in gas phase at high temperature (350°C/10^{-4} Torr) gave trifluoromethylated fluorene derivatives as a result of carbene-carbene rearrangement with CF_3 group intact even at this high temperature. [60]

However it is almost impossibly difficult to prepare a precursor diphenyldiazomethane bearing four *ortho* CF_3 groups. Therefore ,we decided to use the sterically less demanding protectors in combination with CF_3 groups. The precursor we were able to prepare is diphenyldiazomethane (**48**), which has two *ortho* bromine groups in addition to two CF_3 groups (Scheme 16).



48

49

τ = 9.0 min

Scheme 16

Triplet carbene (**49**) [61] was easily characterized by EPR spectra recorded by irradiating the diazomethane precursor in MTHF glass at 77 K. The triplet signals were found to be persistent even at a significantly higher temperature. For instance, a significant decay of the triplet signals began only at 210 K in MTHF. In more viscous solvents, ^{3}**49** was able to survive at much higher temperature. In triacetin, for instance, no appreciable changes were observed even at 230 K. A measurable decay of the signals was observed only at 273 K (0°C), where the “first-order” half-life ($t_{1/2}$) was approximately 10 min (Table 6).

Table 6. ZFS parameters[a] and kinetic data[b] observed for DPCs (**49**) protected by CF3 and Br groups

Carbene	D	E	k_1	$t_{1/2}$ (τ)	k_{O_2}	k_{CHD}
	cm^{-1}		s^{-1}	s	M^{-1} s^{-1}	
49	0.383	0.0247	1.9×10^{-3}	(540) [c]	8.6×10^5	1.0×10
(**44b**	0.397	0.0311	0.35[d]	16	2.1×10^7	5.34×10^2) [e]

[a] In 2-methyltetrahydrofuran (MTHF) at 77 K.

[b] In benzene at room temperature.

[c] Lifetime.

[d] In 2k/εl. See Table 5.

[e] The data for **44b** in Table 5 are included for comparison purpose.

To estimate the lifetime of triplet carbene **49** under our standard condition, i.e., in degassed benzene at 20°C, LFP of **48** was carried out. However, the lifetime of ^{3}**49** was too long to be monitored by the LFP system, and a conventional UV/vis spectroscopic method was more conveniently employed in this case. The transient signals due to ^{3}**49** did not disappear completely even after 1 h under these conditions. The decay was analyzed as a sum of two exponential decays (k_1 = 1.9 x 10^{-3} s^{-1}; τ_1 = 9.0 min and k_2 = 1.0 x 10^{-5} s^{-1}; τ_2 = 1,602 min). [62] Since the half-life estimated by dynamic EPR studies is in the order of 10 min, we assume that the first-decaying component is assigned to the triplet carbene, while slower-decaying one assigned to secondary product formed during the decay pathway of the triplet carbene. Thus, a triplet carbene having lifetime over several minutes was realized for the first time. [61]

The rate constants of ^{3}**49** with typical triplet quenchers, i.e., oxygen and 1,4-cyclohexadiene were estimated and compared with those observed for the longest-lived triplet carbene known thus far. It is clear that reactivities decrease by approximately 2 orders of magnitude as two *o*-bromine groups in ^{3}**49** are replaced with two CF_3 groups.

The decay pathway of this carbene is of great interests in connection with its stability. Final products after “complete” decomposition of the precursor consisted of many components, from which no particular product including carbenic dimers was isolated. When the photolysis was carried out in a degassed C_6D_6 solution sealed in an NMR tube and was monitored by ^{1}H NMR, a new signal appeared at the initial stage of the irradiation but did not grow significantly even though the starting compound decomposed. The product signals gradually disappeared, when the sample was allowed to stand overnight, to give complex mixtures. Since triplet signals decay exponentially, it is likely that the carbene decomposes intramolecularly.

4.2.2 Triplet polynuclear aromatic carbenes

Introduction of aryl groups on methylene results in a significant decrease in *D* values; thus *D* decreases from 0.69 to 0.515 on going from methylene to phenylcarbene. [13] The *D* values decrease further as the aromatic ring is changed from phenyl to 1-naphthyl to 9-anthryl. Similar trends are seen in diarylcarbene systems. The *D* values of DPC, di(1-naphthyl)carbene and di(9-anthryl)carbene are 0.4055, 0.3157 and 0.113 cm^{-1}, respectively. [13] These data clearly suggest that the unpaired electrons are more extensively delocalized as the number of the aromatic rings is increased, and hence the triplet states are thermodynamically more stabilized.

While several diarylcarbenes with polynuclear aromatic rings such as naphthalene and anthracene have been generated and characterized spectroscopically, the chemistry of these carbenes has not been systematically studied yet.

4.2.2.1 Dinaphthylcarbenes (DNC)

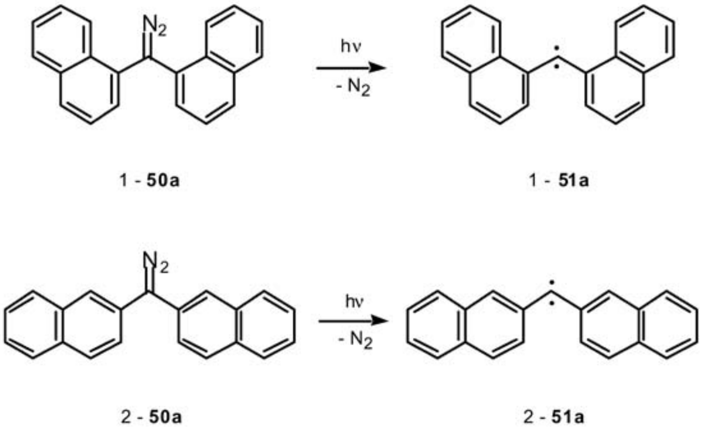
A comparison of the data avaibable on the reaction of mononaphthylcarbenes shows that 1-naphthylcarbene exhibits lower reactivity and possesses a smaller ΔG_{ST}, thus showing a higher singlet character. Two key molecular structural differences are responsible for the observed difference in the reactivity. First, the 1-position of the naphthyl moiety has the largest HOMO orbital coefficient. This will lead to a greater stabilization of the singlet carbene center by the π-p overlap, thus making ΔG_{ST} smaller. A second factor is the interaction between the carbene center and the *peri*-hydrogen in the 1-isomer, which makes it less reactive than the 2-isomer. In order to examine how these two factors influence the sterically more congested diaryl systems, we generate two dinaphtylcarbenes, i.e., bis(1-naphthyl)- and (1-**51a**) bis(2-naphthyl)carbenes (2-**51a**), and examined their reactivities (Scheme 17, Table 7). [64]

Table 7. ZFS parameters[a] and kinetic data[b] observed for dinaphthylcarbenes (**51**)

Carbene	D	E	Td[c]	$2k/\varepsilon l$	$t_{1/2}$ (τ)	k_{O_2}	k_{CHD}
	cm^{-1}		K	s^{-1}	μs	M^{-1} s^{-1}	
1 - **51a**	0.323	0.0105	100	7.4×10^4	70	1.7×10^9	1.2×10^4
2 - **51a**	0.383[d]	0.0182[d]	80	(1.2×10^6)[e]	(0.83)[f]	$> 10^{10}$	5.0×10^6
	0.397[d]	0.0158[d]					

[a] In 2-methyltetrahydrofuran (MTHF) at 77 K.
[b] In benzene at room temperature.
[c] *Td* is measured in 2-methyltetrahydrofuran (MTHF)matrix.
[d] Due to geometrical isomers, two sets of signals are observed.
[e] Unimolecular decay.
[f] Lifetime.

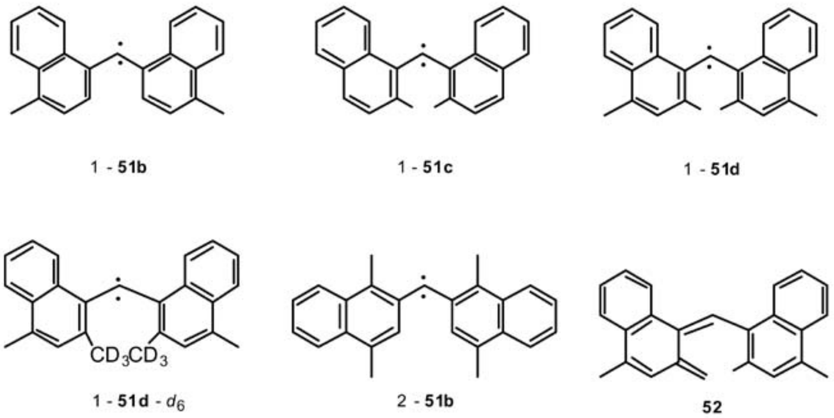
The ZFS parameters clearly suggest that the unpaired electrons are more delocalized and the central angle is more expanded in the 1-isomer (1-**51a**) than in the 2-isomer (2-**51a**). Taking into account the smaller loss of aromatization energy in the resonance structure for the 1-isomer than the 2-isomer, it is obvious that the unpaired electrons are more extensively delocalized in 1-**51a** than in 2-**51a**. In addition, the steric interaction between the carbene center and *peri*-hydrogen in the 1-isomer is expected to increase the carbene bond angle more than in the 2-isomer. Actually, the ZFS parameters for the 2-isomer are very similar with that reported for DPC, indicating the electronic and molecular structures of the two carbenes are similar. The difference in thermal stabilities of the two isomers reflects that in the structure. The 1-isomer is far more stable than the 2-isomer, as judged from *Td* in matrix and $t_{1/2}$ in a degassed benzene solution at room temperature. It is noteworthy that the 1-isomer decayed in a second-order kinetics, while the decay of the 2-isomer was unimolecular. Actually, from the spent solution of LFP using the diazomethane in benzene, bis(2-naphthyl)phenylmethane, formally an insertion product of 2-**51a** into the C-H bond of benzene, is isolated as the main product, while no particular products including the expected tetra(naphthyl)ethylene were isolated in the case of 1-**51a**.



Scheme 17

The kinetic data obtained using typical triplet quenchers should be more reliable to estimate the reactivity difference between the two carbenes especially in this case in which the two carbenes decay in different pathways. The data, especially that the rate constant for H abstraction from CHD observed with the 2-isomer are two orders of magnitude greater than that of the 1-isomer, clearly indicate that the 1-isomer is considerably less reactive than the 2-isomer (Table 7).

The above studies reveal that triplet bis(1-naphthyl)carbene (1-**51a**) is more than two orders of magnitude longer-lived than triplet DPC. This suggests that dinaphthylcarbene can serve as a more promising prototype diarylcarbene for persistent carbenes than DPC. Naturally, one would expect that the lifetime of DNC could be elongated by introducing appropriate kinetic protectors around the carbene centers. Thus, a series of DNCs having methyl groups on aromatic rings are generated (Scheme 18, Table 8). [64]



Scheme 18

Table 8. ZFS parameters[a] and kinetic data[b] observed for DNCs (**51**) protected by Me groups.

Carbene	D	E	Td^c	$2k/\varepsilon l$	$t_{1/2}$	k_{O_2}	k_{CHD}
	cm^{-1}		K	s^{-1}	s	$M^{-1}\ s^{-1}$	
1 - **51b**	0.320	0.0108	90	1.1×10^5	28	1.9×10^9	6.6×10^4
1 - **51c**	0.326	0.0089	110	1.0×10^4	1,400	6.5×10^8	2.8×10^3
1 - **51d**	0.249^d 0.218^d	0.0053^d 0.0053^d	105	—	100,000	1.0×10^8	3.6×10
1 - **51d** - d_6	0.327	0.0099	—	3.6×10^3	265,000	—	—
2 - **51a**	0.347^d 0.348^d	0.0173^d 0.0141^d	95	5.2×10^3	58	1.7×10^9	1.8×10^5

[a] In 2-methyltetrahydrofuran (MTHF) at 77 K.
[b] In benzene at room temperature.
[c] *Td* is measured in 2-methyltetrahydrofuran (MTHF)matrix.
[d] Due to geometrical isomers, two sets of signals are observed.

The ZFS parameters of methylated DNCs in MTHF glass at 77 K indicate that *E*/*D* values steadily decrease as one introduces more methyl groups on the aromatic rings. It is interesting to note that the *E*/*D* values decrease significantly when methyl groups are introduced at position 2 of the 1-DCN (1-**51c**: *E*/*D* = 0.0273) but decrease further when two more methyl groups are introduced at position 4 (1-**51d**: *E*/*D* = 0.0245~0.0215). Furthermore, $t_{1/2}$ in degassed benzene at room temperature indicates that ^{3}DNC is significantly stabilized by the 2-methyl groups but further more stabilized when two more methyl groups are introduced at position 4, while ^{3}1-DNC is only slightly stabilized by the 4-methyl groups themselves. This can be understood to indicate that, as the carbene center is more sterically shielded, simple dimerization at the carbene site suffers from severe steric repulsion and the carbene is hence forced to react at the sites where spin can be delocalized. Increased stability in 1–**51d** compared to 1–**51c** can then be ascribable to the suppression of this coupling pathway. The reactivities toward typical triplet quenchers, however, also decrease in this order. For instance, k_{CHD} decrease approximately two orders of magnitude in going from 1–**51c** to 1–**51d**.

This suggests that increased stability in benzene cannot be simply ascribable to the decrease in the reaction site in its dimerization reaction but to the inherent decrease of the reactivities of the carbene center.

It is interesting to note here that the LFP of 1–**50d** in degassed benzene generated secondary transient species ascribable to *o*-quinodimethane (**52**) as 1–**51d** decayed. In marked contrast, 1–**51c** decayed monotonously without showing any sign of *o*-quinodimethane. These observations suggest that, while both 1–**51c** and 1–**51d** carry 2-methyl groups, 1–**51d** can decay by abstracting hydrogen from the methyl group; however, this process is not involved in the decay pathway for 1–**51c**.

This difference can be simply explained by invoking the buttressing effect. 4-Substituents are usually expected to exert a small steric effect on the 2-substituent, especially without 3-substituents. However a recent reestimation of the buttressing effects in methyl-substituted benzoic acid derivatives has revealed that this effect is not zero even in 2,5-dimethyl derivative, the interaction between more distant groups being neglected. [65]

The effect is expected to be more significant for 4-methyl group of naphthalene than that in benzene due to the presence of *peri*-hydrogen in the former case. Thus, the 2-methyl groups in 1–**51d** are brought closer to the carbene center than those in 1–**51c**, and the carbene center in 1–**51d** is hence more tightly blocked by 2-methyl groups than that in 1–**51c**.

Similar effects of methyl groups are also noted for the kinetics of the 2-isomer of the carbene. Thus, on going from 2–**51a** to 2–**51b**, the lifetime increased approximately two orders of magnitude, and k_{CHD} decreased by one order of magnitude. However, the significantly shorter lifetime in benzene and the larger reactivities toward the triplet quencher of 2–**51b** as opposed to 2–**51c** again can be ascribable to the difference in the steric role of *peri*-hydrogens between the two carbenes.

Since one of the decay pathways of 1–**51d** is an intramolecular H abstraction from methyl groups at position 2, it is probable to extend the lifetime by using KDIEs. Thus we prepared bis[1-(2,6-dimethylnaphthyl)]diazomethane bearing fully deuterated 2-methyl groups and studied the kinetics of the carbene therefrom.

The LFP of the diazomethane generated transient absorption band assignable to triplet carbene (1-**51d**-d_6) which decayed monotonously. The decay of 1–**51d**-d_6 followed second order kinetics and the lifetime in the form of half-time was estimated to be 256 ms, which is some three times greater than that of the protio analogue (1–**51d)**. No new absorption band ascribable to *o*-quinodimethane was detected to the limit of our LFP time scale and detection. This is partly because the intramolecular H migration is not the exclusive pathway even for the decay of the protio analogue. The highest limit for rate constant for *D* transfer is roughly estimated to be < 1 s^{-1}.

"Parent" ^{3}1-DNC has lifetime of 70 ms, which is some 30 times larger than "parent" ^{3}DPC. This is obviously due to the effect of *peri*-H, which not only stabilizes triplet state with respect to the singlet but also acts as a kinetic protector toward carbene center. EPR data suggest that ^{3}1-DNC is significantly less bent than ^{3}DPC. In spite of the increased stability of the unsubstituted ^{3}1-DNC compared to ^{3}DPC, the effect of methyl groups as a kinetic protector on the stability of the triplet state is rather disappointingly small. Since basic skeletons between DNC and DPC are not exactly the same, an exact counterpart between the two cannot be found. However, the reactivity of ^{3}1-**51d** can be compared with triplet dimesitylcarbene (**31a**) if the *peri*-hydrogens at 8 positions are assumed to act as one of the hydrogens of the *o*-methyl groups in ^{3}**31a**. The van der Waals radius of methyl groups may be estimated to be larger than that of the net C_8 substituent. However, this comparison is fairly valid since the *peri*-Hs are expected to be fixed tightly in the same plane as the carbene carbon, while hydrogens on the *o*-methyl groups are rather flexible.The *E*/*D* values clearly support the idea. This value for ^{3}1-**51d** (E/D=0.019) is significantly smaller than that for ^{3}**31a** (E/D=0.033), suggesting that ^{3}1-**51d** is less bent than ^{3}**31a**. Nevertheless, the lifetime of ^{3}1-**51d** ($t_{1/2}$=100 ms) is not larger than that of ^{3}**31a** ($t_{1/2}$=160 ms)

4.2.2.2 Di(9-anthryl)carbene

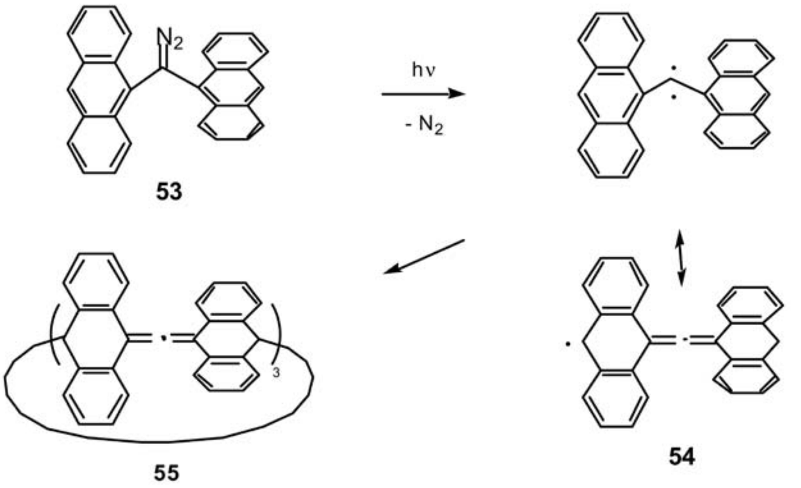
Among the many triplet diarylcarbenes known, triplet di(9-anthryl)carbene (**54**) is unique as it shows the smallest *D* (0.113 cm^{-1}) and *E* (0.0011 cm^{-1}) values ever reported. [66] This means that the carbene has almost linear and perpendicular geometry with extensive delocalization of the unpaired electrons into the anthryl portions of the molecule. [67] The extensive delocalization is expected to stabilize this carbene thermodynamically, while the perpendicular geometry of the anthryl group stabilize the carbene center kinetically, through shielding with the four *peri*-hydrogens. That is, the electronic factor and the molecular structure of the molecule seem ideal for the formation of a stable triplet carbene.

The carbene (**54**) was first generated in 1971 and characterized by EPR. [66] EPR measurements were made by irradiating powdered samples of a solid solution of di(9-anthryl)diazomethane (**53**) in di(9-anthryl)ketone. As reported by Wasserman and coworkers, “the observations were made to 210°C; the half-life of the triplet signals at 200°C was 7 min”. This might suggest that the carbene is very stable. However, toward to the end of the paper, the authors also mentioned that “the stability is due to the rigidity of the environment and not to an intrinsic lack of reactivity.”

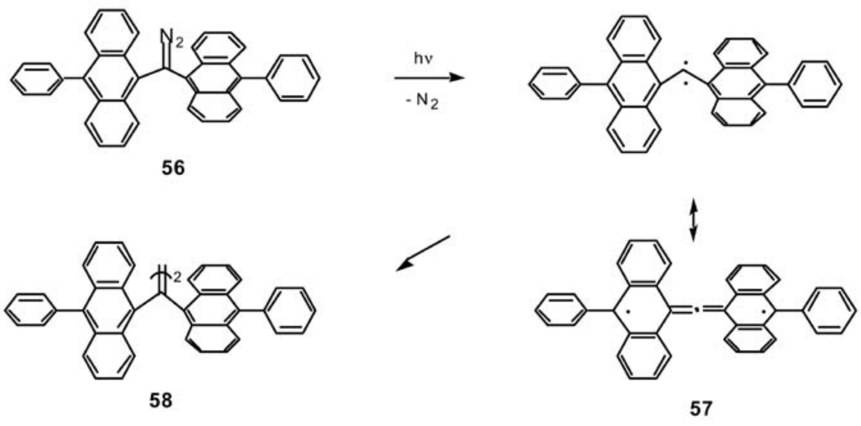
Actually, in spite of those highly favorable structural factors, ^{3}**54** is very ephemeral [68]: its lifetime in degassed benzene is 0.5 μs [69] which is shorter even than that of parent triplet DPC. Product analysis studies have shown that ^{3}**54** forms a trimer of dianthrylcarbene (**55**) as the main product (50-60 %) (Scheme 19). [70] The structure of the trimer is characterized as the one formed as a result of a three-fold coupling at position 10 of the carbene in a cyclic way. This observation suggest that delocalization of the unpaired electrons in ^{3}**54** leads to their leaking out from the carbene center to position 10, where sufficient spin density builds up for the trimerization to take place. At the same time, the lack of formation of olefin-type dimers through coupling two units of ^{3}**54** at their carbene centers indicates that the carbene center itself is indeed well shielded and stabilized.

The above observations indicate that the stability of ^{3}**54** would increase if the trimerization reaction were somehow suppressed. Thus, we attempted to generate a dianthrylcarbene having a substituent at position 10 to block the reactivity there. Usually, *tert*-butyl group is the best substituent for such a blocking group, but we found that *tert*-butyl group at position 10 of anthryl ring is very sensitive to an acid and easily removed during procedure employed to prepare the precursor diazo compound. Thus we used the phenyl group as a blockage, which turns out to be a very effective blocker. [71]

Triplet carbene generated by photolysis of bis[9-(10-phenyl)anthryl]-diazomethane (**56**) in MTHF glass at 77 K gave EPR signals very similar to those observed for dianthrylcarbene (Scheme 20). The ZFS parameters (D = 0.105 cm^{-1}, E = 4.4 x 10^{-4} cm^{-1}) derived from the signals are essentially the same with those obtained for ^{3}**54**. This indicates that the phenyl groups are not in the same plane as the anthryl rings owing to the repulsion between *ortho*- and *peri*-hydrogens. The EPR signals of **54** and **57** differ only in their thermal stability. When the 2-MTHF glass containing **54** was warmed gradually, the signals due to **54** started to disappear at around 90 K, whereas no significant decay of the signals of ^{3}**57** was observed up to 240 K. The signal of **57** started to decay only at around 270 K (~0°C), but was still visible when heating to 300 K (~27°C).



Scheme 19

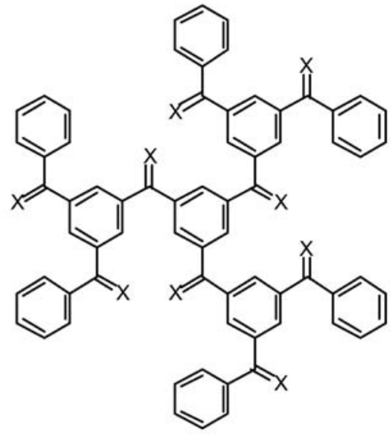


Scheme 20

To probe the stability of ^{3}**57** under normal conditions, **56** was photolyzed in degassed benzene at room temperature. The bands due to ^{3}**57** decayed cleanly, showing isosbestic points, and very slowly, persisting for more than 3 hours before disappearing completely. The decay curve was analyzed in terms of second-order kinetics ($2k/\varepsilon l = 5.2 \times 10^{-4}\ s^{-1}$). The half-life for ^{3}**57** was estimated to be 19 min. This is the longest-lived triplet carbene thus far generated in our research group.

4.2.3 Toward persistent high-spin polycarbenes

Triplet carbenes are regarded as one of the most effective spin sources. This is because the magnitude of the exchange coupling between the neighboring centers is large and the photolytic production of polycarbenes is possible even in solid solution at cryogenic temperature under helium to make in situ magnetic measurements easy if poly(diazo) precursors are available. [72, 73] Actually Iwamura and his coworkers have prepared a “starburst” type nonadiazo compound, 1,3,5-tris[[3’,5’-bis[phenyl(1,1-diazanediyl)methyl]phenyl](1,1-diazanediyl)benzene (**59**), and have demonstrated that the nine diazo groups are photolyzed therefrom at low temperature to give pentadecet ground state (**60**)(Scheme 21). [74] However, those systems lack the stability for characterization under ambient conditions and have an inherent drawback for further extension to usable magnetic materials. Moreover, the synthesis of the precursor diazo compounds become more difficult and laborious as the number of carbene units increases.



$$\mathbf{59}\ (X = N_2) \xrightarrow[-\,9N_2]{h\nu} \mathbf{60}\ (X = \mathbf{:}\,)$$

Scheme 21

In order to overcome these difficulties for realization of usable macroscopic spins, we have to find a way to stabilize triplet carbene centers and then to connect them in ferromagnetic fashion.

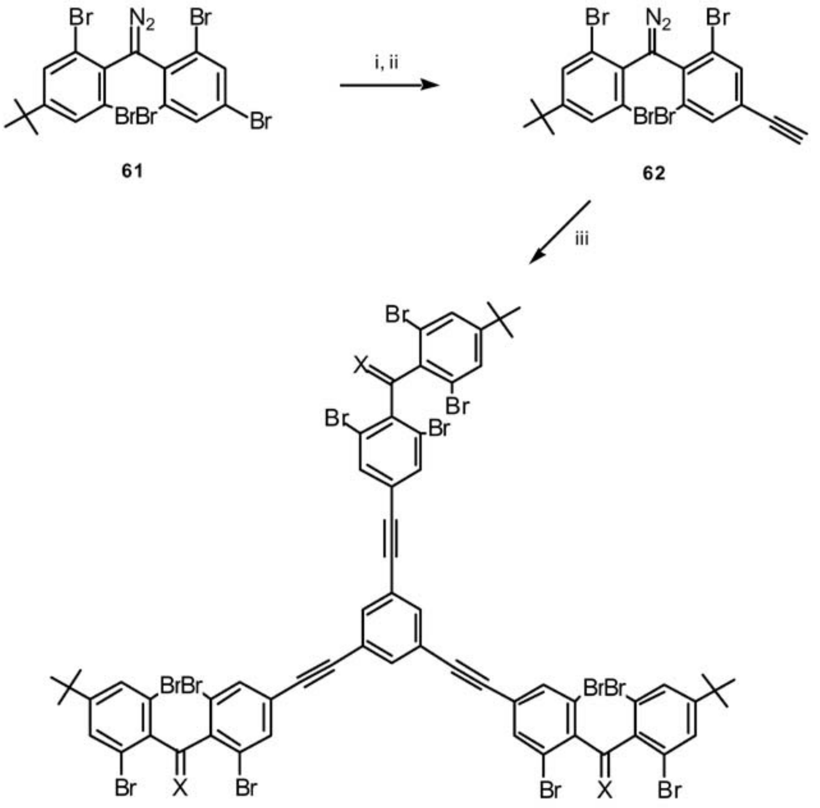
As we have fairly stable triplet carbenes, the next step should be to explore a way to connect them while retaining a robust π-spin polarization. The topology-mediated molecular design of neutral organic high-spin systems of π-conjugation has been well established in the field of purely organic magnetics. [72] In order to use polybrominated triplet DPCs as persistent spin units and to construct as high spins as possible, we designed 1,3,5-tris(ethynyl)phenyl as a two-dimensional linker.

The reaction scheme to realize the coupling of the persistent carbene precursor **64** is summarized in Scheme 22. [75] Diazo groups are generally labile, and, hence, these groups are usually introduced at the last step of the synthesis when preparing not only mono(diazo) but also poly(diazo)compounds. [74] Application of this strategy to these highly sterically congested diazo compounds, prepared mostly by base treatment of *N*-nitrosocarbamates, is almost impossibly difficult. Fortunately, however, the polybromodiphenyldiazomethanes **61** and **62** were found to be stable enough to survive in the presence of Pd (0) and Cul under Sonogashira coupling reaction conditions. [76] This is obviously due to the fact that the four bromine groups at the ortho positions which effectively protect the carbene center from the external reagents also are able to protect equally effectively the diazo carbon.

Moreover, each of the four ortho carbons is also protected from the approach of external reagents by these bromine groups. This enabled us to introduce connecting groups at the para position of the monomer diazo compound (e.g. **61**) to give the functionalized monomer **62** and then to connect it to an appropriate linker satisfying the topological requirement for intramolecular ferromagnetic spin alignment. Thus, we were able to introduce an ethynyl functional group very selectively at the *para* position in a reasonable yield. Deprotection of the trimethylsilyl group proceeded almost quantitatively to give **62**. Subsequent coupling with 1,3,5-triiodobenzene took place smoothly to produce tris(diazo) compound **63**, where three carbene precursor units were properly introduced so as to generate tris(carbene) (**64**) connected in a ferromagnetic fashion. [73]

Photolysis of **63** in MTHF glass at 5 K gave a fine-structure EPR spectrum which was different from that observed by the photolysis of the corresponding monodiazomethane. The salient features of organic high-spin species apparently failed to appear in the observed spectrum. Canonical peaks dominate in the g~2 range, and the key peaks appearing in the wings away from the g~2 region are only vague. It is obvious that conventional cw EPR spectroscopy fails to give evidence of the spin identification of the tris(carbene).

In order to identify the spin multiplicity of the tris(carbene), field-swept Two-Dimensional Electron Spin Transient Nutation (2D-ESTN) spectroscopy was invoked. [77] This technique is based on pulsed FT EPR spectroscopic method and is capable of elaborating straightforward information on electronic and environmental structures of high-spin species even in amorphous materials, something which conventional cw EPR cannot provide. The nutation spectra unequivocally demonstrated that the observed fine structure spectrum is due to a spin-septet state.



63 (X = N_2)
iv
64 (X = **:**)

(i) Me_3 SiC = CH/$(Ph_3P)_2PdCl_2$/Cul:
(ii) KOH/MeOH;
(iii) 1,3,5-$I_3C_6H_3/(Ph_3P)_2PdCl_2$/Cul
(iv) hν (λ > 300nm)

Scheme 22

A nutation peak arising from any doublet species of by-products was not detected showing a remarkable chemical stability of the tris(carbene) **64**. Furthermore, the marked thermal stability of **64** manifested itself during the annealing process. A significant change in the EPR signal shape was observed when the matrix temperature was raised above 140 K and maintained for 15 minutes. New fine-structure signals were irreversible with temperature and characteristic of the small fine-structure constants. They were also shown to originate in a septet ground state by 2D-ESTN spectroscopy. This is in sharp contrast with that observed for septet-state benzene-1,3,5-tris(phenylmethylene), which has been shown to be persistent only up to 85 [78] and 50 K [79] in rigid glasses.

These studies indicate that the diazo compounds prepared to generate persistent triplet carbenes are also very persistent and, hence, survive during the further chemical procedures to functionalize these precursor molecules to be building blocks for persistent high-spin polycarbenes. The building blocks thus prepared are very useful since they can be introduced very easily on the properly designed π-toplogical linkers *ad libitum*. Moreover, the undesirable bimolecular side reactions which generate chemical defects among the topologically controlled high-spin ($S = 1$) centers for extended spin alignment are rigorously avoided. These findings open a new door to the design and preparation of new persistent high-spin molecules for more practical organic ferromagnetics.

4.3 CONCLUDING REMARKS

Our seemingly “never-ending” attempts to isolate triplet carbenes are still in progress. Thus, this is still a progress report, not the final summation of our effort to isolate triplet carbenes. We still do not know how much longer we will have to go from here. All we have learned until now is just how reactive the species are.

One can learn how unstable carbon “radical” species become when the coordinate number changes from three to two. The tricoordinate species, radicals, is serendipitously isolated by Gomberg simply by introducing three phenyl rings. Diphenylcarbene, a dicoordinate counterpart, first generated by Staudinger only about ten years later, is ephemeral, more reactive even than methyl, “parent” radical. Perchlorotriphenylmethyl has its halflife on the order of 100 years in solution at room temperature. Even perchlorodiphenylmethyl is stable. However, a divalent counterpart, perchlorodiphenylcarbene, has a halflife of only 18 ms.

It is easy to see how difficult it is to stabilize triplet carbene. It is not stabilized by a polar effect, either internally or externally, since it is electronically neutral species. Only spin-delocalizing substituent may be useful to stabilize it. It has only two substituents, meaning that it has only two handles one can manipulate to stabilize it.

Nevertheless, we managed to increase the lifetime to the extent that you can "see" it at least for a while under normal conditions. We also found an important clue to further increase the stability. A really stable carbene cannot be generated from the diazo precursor prepared according to the Scheme 3 since this diazo compound should have a space to allow the chemical procedure for introducing the diazo functional group. In other words, the carbene generated from such a diazo precursor should also have the space to be quenched by accepting a reagent externally. We found, more or less by chance, that the kinetic protectors introduced around diazo carbon in order to protect the carbene therefrom also are able to protect the diazo carbon equally effectively. This means that we will be able to introduce a secondary protector after the diazo group is introduced. The idea is shown to work very well. For instance, we have been able to prepare, by the addition of benzyne to di(9-dianthryl)diazomethane, di(trypticyl)diazomethane , which is otherwise impossible to prepare.

Our efforts will still go on until we reach to a stable triplet carbene.

EPILOGUE

"Somehow, I can't believe that there are any heights that can be scaled by a man who knows the secret of making dream come true. This special secret, it seems to me, can be summarized in four Cs ;they are curiosity, courage, confidence and constancy. And the greatest of all is confidence. When you believe in a thing, believe in it all the way implicitly and unquestionably."

-Walt Disney-

ACKNOWLEDGMENTS

I am grateful to my colleagues named in the references and those currently in my group for their time-consuming and pains-taking efforts without which this work would not have been done. I also appreciate the support of the Ministry of Education, Science, Culture, Sports, Science and Technology, Japan for this research.

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Chapter 5

Diaminocarbenes: Exploring Structure and Reactivity

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5.1 BACKGROUND

5.1.1 Introduction

Carbenes were the latecomers to the company of stable examples of organic reaction intermediates. The 100th anniversary of Gomberg's discovery of the stable triphenylmethyl radical was celebrated in 2000, and Gomberg and others were familiar with the triphenylmethyl carbocation by 1910. Stable anions derived from hydrocarbons like the fluorenyl anion were being investigated by Conant and McEwan in the decade 1930-40, but the first isolable species which might be considered to be carbenes were not reported until 1988 by Bertrand [1] and 1991 by Arduengo. [2] The phosphinocarbene **1** described by Bertrand has always been somewhat controversial, since it can also be viewed as a phosphaacetylene, but there was really no possibility of mistaken identity with the diaminocarbene **2**. The history of earlier attempts to prepare diaminocarbenes has been reviewed by Arduengo. [3]; Wanzlick just missed out, in the 1960s, on making the first example of a stable diaminocarbene. The first stable crystalline diaminocarbene, **2**, had large adamantyl groups flanking the carbene centre, and the isolation of **3** the following year, was just as important in stimulating interest, because it showed that steric protection was not required for carbenes of this type to survive against dimerisation.

Since 1991, diaminocarbenes have been extensively explored although, as we shall see, fundamental questions concerning their structure and reactivity remain unanswered. The area has been the subject of several excellent reviews [4,5,6],

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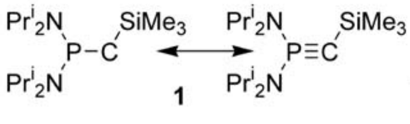
and this short chapter cannot attempt a similar comprehensive coverage. The emphasis here will be on the exploration of the range of stability of diaminocarbenes, and their structure, bonding, and reactivity towards dimerisation, protonation, and oxidation.



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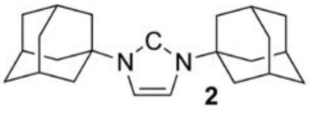

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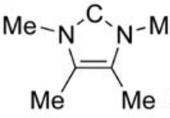

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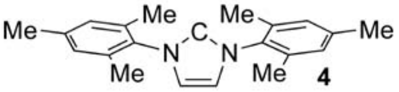

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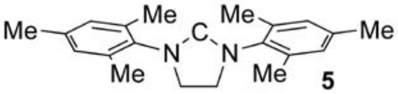

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Organometallic chemists had discovered many metal complexes of diaminocarbenes well before the isolation of **2**, and Herrmann and Kocher [4] pointed out that by 1997 complexes of diaminocarbenes with 48 elements across the periodic table were known. The most explosive growth in that area has probably occurred since then however, with the realisation that diaminocarbenes possess extremely valuable properties as ligands for transition metal in catalytically-active complexes. Carbenes like **4** and **5** are replacing the ubiquitous phosphines as ligands of choice for a wide variety of important reactions. In alkene metathesis, complexes containing these ligands show high reactivity while tolerating a range of functional groups. [7-12] Complexes containing these ligands have been applied to Heck, [13,14] Suzuki, [15-17] and other cross-coupling reactions, [18] and in many cases it has been shown that they permit coupling to be done using cheap aryl chlorides. Complexes containing these ligands have also been applied to important reactions like hydroformylation. [19] This area has been reviewed, [20] but beyond giving the leading references above, it will not be discussed further in this chapter.

We found [21] that diaminocarbenes form complexes with lithium (also discovered by others [22,23]), sodium, and even potassium ions. Since this has a substantial effect on the preparation and behaviour of the carbenes in solution, complexation with the alkali metals will be described in section 2.2.

5.1.2 How we became interested

My group has had a longstanding interest in strong bases, dating back to the discovery of Proton Sponge®, [24] and we had followed this by finding still more powerful uncharged bases. [25,26] Arduengo prepared **2** and **3** by deprotonation of imidazolium salts with strong bases like NaH/KOBu^t, and we therefore wondered what the pK_a of these imidazolium ions might be. For preparative purposes, sterically hindered bases are frequently required and this could be easily provided in varying degrees in diaminocarbenes, including the provision of adjacent chirality. Moreover, we hoped that the well-known higher barriers to proton transfer to carbon bases, [27] as compared to oxide and amide bases, might provide the basis for improved enantioselectivity in proton transfers. In practice, our hopes in this direction were largely dashed by the high nucleophilicity of the diaminocarbenes. Chiral diaminocarbenes also gave poor enantioselectivity in deprotonation reactions. [28] Nevertheless, the properties of these species had intrigued us by this time, and we began to ask questions such as:

1. Was aromaticity required for imidazol-2-ylidene stability?
2. Were rings required at all?
3. How much steric hindrance was required to create sustainable diamino carbenes?

This chapter is an account of our search for answers to these questions.

5.2 STATE OF THE ART

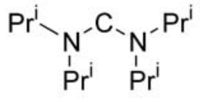
5.2.1 The generation of diaminocarbenes

Two principal methods have been used to generate diaminocarbenes (i) deprotonation of formamidinium or imidazolium salts, and (ii) desulfurisation of thioureas. These will be discussed in turn followed by a review of some lesser-known methods; some methods that we believe have potential will also be mentioned.

5.2.1.1 Deprotonation methods

Deprotonation of tetraalkylformamidinium or N,N-dialkylimidazolium ions is by far the most popular way to generate diaminocarbenes. A major advantage of this method is that deprotonation is a rapid reaction, even at low temperatures, so that carbenes that may be unstable to dimerisation can be prepared. As will be discussed later, N,N-dialkylimidazolium ions have pK_a values of around 24 in DMSO, and so strong anionic bases are required. In their original work, the Arduengo group used NaH or KH in THF, usually in the presence of additives like $KOBu^t$ or DMSO (to generate the soluble dimsyl anion). Herrmann [29] reported that sodium amide in liquid ammonia/THF at –40 ºC was effective for the preparation of imidazol-2-ylidenes.

In general alkoxide and hydride bases are not useful for the preparation of imidazolidin-2-ylidene and open chain diaminocarbenes, although Arduengo prepared the imidazolidin-2-ylidene **5** [30] and a thiazol-2-ylidene [31] using NaH. This is partly because the formamidinium ions probably have higher $\mathrm{pK_a}$ values than imidazolium ions (see the discussion of proton affinities in section 2.3.3), but mainly because the precursor formamidinium ions (including dihydroimidazolium ions) are much more susceptible to addition of nucleophilic species than the aromatic imidazolium ions. Thus we found that sodium dimsyl did not deprotonate the tetra-isopropylformamidinium ion but added, ultimately producing an unsaturated sulfoxide as shown in Scheme 1.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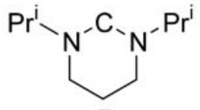
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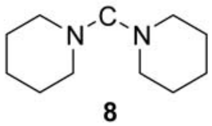
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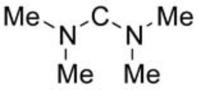
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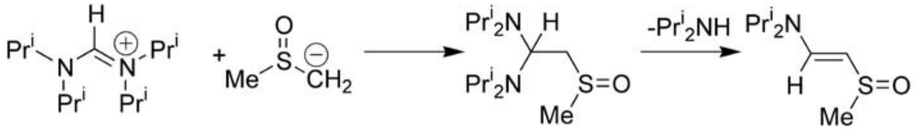
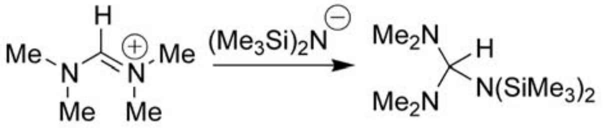


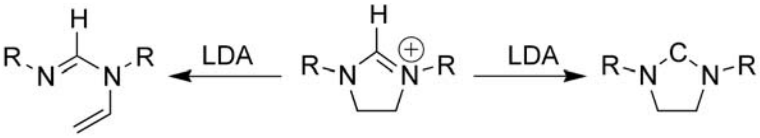
Scheme 1



Scheme 2

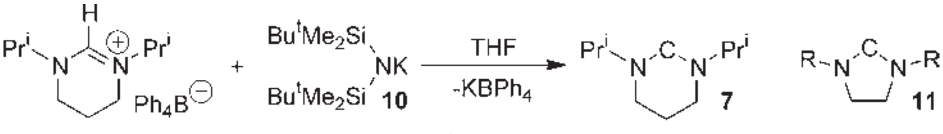
It is therefore generally necessary to use hindered alkali amide bases to prepare non-aromatic diaminocarbenes. Lithium diisopropylamide (LDA), lithium 2,2,6,6-tetramethylpiperidide (LiTMP), and lithium, sodium or potassium hexamethyldisilazide (HMDS) are the reagents of choice, although in some case *t*-butyllithium gives good results. All of these bases work well for hindered diaminocarbenes like **6** and **7**, but even the HMDS bases begin to fail for the least hindered carbenes like **8** and **9**. Thus the major reaction of the tetramethylformadinium ion with LiHMDS is addition, as shown in Scheme 2. [32] HMDS bases are not as hindered as is often thought, due to the long N-Si bonds, and these bases are significantly more nucleophilic than LDA or LiTMP. The latter are therefore usually the bases of choice for the preparation of the least hindered diaminocarbenes.

We recently encountered yet another side reaction during the preparation of unhindered imidazolidin-2-ylidenes. LDA and LiTMP react by deprotonation of a methylene group to give products containing vinyl groups, as shown in Scheme 3. [33] This side reaction does not occur with six-membered ring or open chain formamidinium ions, and presumably results from the increased acidity of the methylene protons in dihydroimidazolium ions, due to their proximity to the partially positively charged nitrogens. This competing deprotonation is much less apparent when disilazide bases are used, perhaps because they are rather weaker bases than the dialkylamides.



Scheme 3

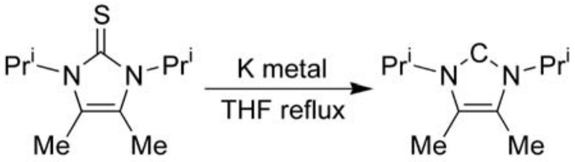
These various problems led us to believe that a more hindered base derived from di-*t*-butyltetramethyldisilazane (DTBTMDS) [34] might have ideal properties for the generation of unhindered diaminocarbenes. The lithium derivative is readily prepared using *n*-BuLi, and this does lead to extremely clean generation of several unhindered diaminocarbenes, which are however lithium complexes, as will be discussed in section 2.2. We have found recently that it is possible to generate the potassium derivative **10** (KDTBTMDS) by reaction with KH in THF under sonication. We also find that if a tetraphenylborate salt of the amidinium precursor is used, $KBPh_4$ precipitates from THF, leaving a metal-free solution of carbene **7**, where we know the chemical shift for the free carbene and its potassium ion complex in THF, (Scheme 4). [33] We are currently studying the application of this method to analogues of **7** with smaller alkyl groups and to the series of imidazolidin-2-ylidenes **11** (R = Me. Et. *i*-Pr, *t*-Bu)



Scheme 4

5.2.1.2 Desulfurisation

Kuhn and Krantz in 1993 reported [35] that 1,3-diisopropyl-4,5-dimethylimidazole-2-thione reacted with potassium metal to give the imidazol-2-ylidene (Scheme 5).

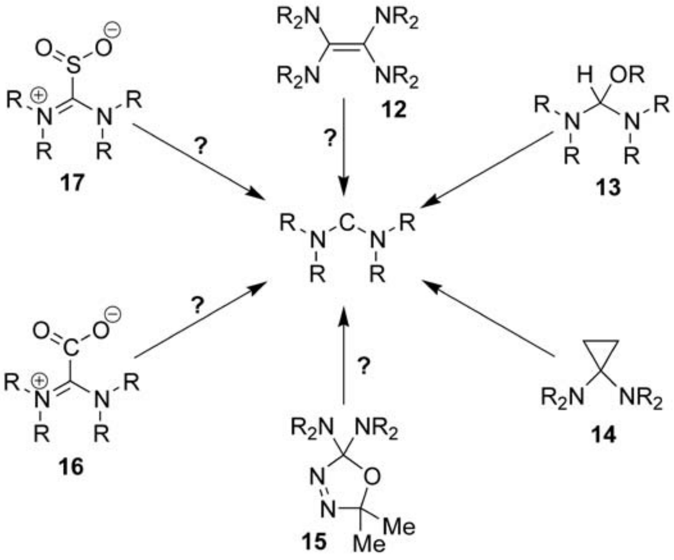


Scheme 5

This reaction has been used subsequently by several groups for the generation of diaminocarbenes. Denk's group [36] have reported the preparation of the series of imidazolidin-2-ylidenes **11** (R = Me, Et, *i*-Pr, *t*-Bu) by this method. The di-*t*-Bu compound is stable, but the other carbenes dimerise. We were interested in studying the rates of dimerisation of these carbenes in the absence of metal ion complexation, and this method looked attractive, since the other product is potassium sulfide (insoluble in THF). We confirmed that this desulfurisation method generated carbenes free of metal ion complexation by preparing carbene **7**. However, in our hands, the potassium/thione reaction was too slow and we only observed the dimers for **11** (R = Me, Et. *i*-Pr). We experimented with the use of sodium/potassium alloy, the use of sonication, and the addition of electron-transfer reagents like 4,4-di-*t*-butylbiphenyl to accelerate the reaction, but without success. [37] We have no explanation for this discrepancy, but warn that this heterogeneous reaction may be hard to reproduce.

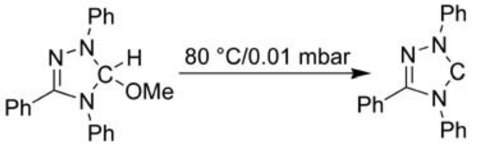
5.2.1.3 Thermolytic and photolytic methods

Perhaps the simplest conceivable route to diaminocarbenes is the thermolyis of dimers (derivatives of tetrakis(dialkylamino)ethene, **12** in Scheme 6). This reaction, and the controversy surrounding it, will be discussed in section 2.4, but no examples of successful preparation of diaminocarbenes by this process are known. However diaminocarbenes, and especially imidazol-2-ylidenes, are relatively stable thermally and so pyrolytic methods might be an attractive way to generate these carbenes free of metal ion complexation. The 1,2-shift to give an amidine is certainly exothermic, but has been predicted to have an activation energy of around 170 kJ/mol even for hydrogen migration, and one example of a 1,2-silyl shift has been shown to be intermolecular. [38]



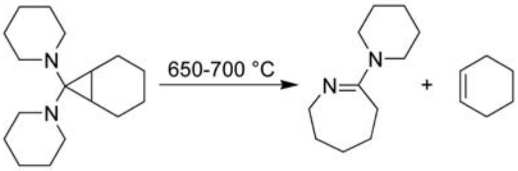
Scheme 6

Of many other potential precursors (see Scheme 6), we are only aware of two methods that have been experimentally tested. Enders reported the thermolysis of a methanol adduct led to a good yield of a triazol-2-ylidene, Scheme 7. [39,40] This looks an attractive route but has been little used; the required alkoxydiaminomethanes, **13** in Scheme 6, are extremely acid-sensitive.



Scheme 7

1,1-Bis(dialkylamino)cyclopropanes, **14** in Scheme 6, are potential carbene precursors in what amounts to the reverse of the usual reaction of carbenes with alkenes. Vilsmaier, Kristen and Tetzlaff reported [41] that the flash vacuum pyrolysis of several 7,7-bis(dialkylamino)bicyclo[4.1.0]heptanes gave cyclohexene and amidines resulting from rearrangement of diaminocarbenes, Scheme 8. It seems possible that suitable substitution on the cyclopropane could lead to lower thermolysis temperatures at which the carbenes could survive and be trapped at low temperatures.



Scheme 8

Thermolysis of the unknown 7,7-bis(dialkylamino)norbornadienes should proceed at much lower temperatures by analogy with the generation of $(MeO)_2C$ from the corresponding dimethoxy-compounds, and **15**, Scheme 6, would be expected to be excellent sources of diaminocarbenes by analogy with the Warkentin precursors of alkoxyaminocarbenes. [42,43]

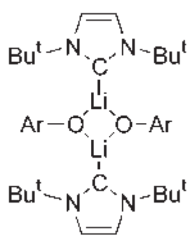
Maier and Endres showed [44] that irradiation of imidazole-2-carboxylic acid, matrix-isolated at 10 K, with a wavelength of 254 nm leads to decarboxylation and the formation of a complex between the parent imidazol-2-ylidene and carbon dioxide Maier applied a similar approach to the formation of the parent thiazol-2-ylidene. [45] This matrix-isolation approach is the only practical route to diaminocarbene derivatives with hydrogen substituents on the amino groups and it would be valuable to generate diaminocarbene itself this way. The precursor amidinoformic acid is known, [46] but is apparently too insoluble in suitable media for the matrix method to be applied. Both diaminocarbene [47] and the parent imidazol-2-ylidene [48] have been detected by neutralisation-reionisation mass spectroscopy.

A CO_2 adduct of one imidazol-2-ylidene is known (1,3-diisopropyl-4,5-dimethylimidazolium-2-carboxylate). It is surprisingly stable thermally - it was purified by sublimation at 90 ºC, [49] but thermolysis of **16**, Scheme 6, still appears an attractive proposition.

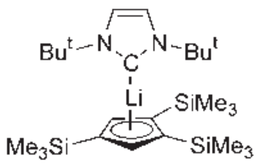
Formamidinesulfinic acid is commercially available and exists as the zwitterion (formally the SO_2 adduct of diaminocarbene), but fully alkylated derivatives, **17**, Scheme 6, are apparently unknown. However it is interesting to note that, in a very old reaction, [50] imidazol-2-thiones are oxidized to imidazolium ions by nitric acid. Diaminocarbene-SO_2 adducts and diaminocarbenes are likely intermediates.

5.2.2 Complexation with alkali metals

The first X-ray evidence for a carbene-lithium adduct, **18**, obtained by Arduengo and Tamm, was reported in a paper by Boche *et al*.. [51] Although full details of this structure have not appeared, the imidazol-2-ylidenes in **18** have N-C bond lengths and N-C-N angles which are very similar those in the free carbene. Other reported lithium complexes include **19**, [22] and a homoleptic complex containing two of the anionic tripod ligands **20** wrapped around two lithium ions. [23]



18
(Ar = 2,4,6-trimethylphenyl)



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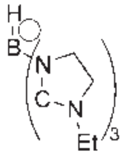

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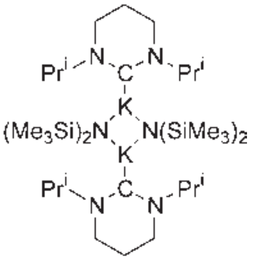


21

We noticed that the ^{13}C NMR chemical shift of the carbene centre in 1,3-diisopropyl-3,4,5,6-tetrahydropyrimid-2-ylidene **7** was sensitive to the presence of alkali metal ions derived from the base used to generate it. Carbene **7** does not dimerise and can be distilled, and the ^{13}C NMR chemical shift of the free carbene occurs at 236.1 ppm in toluene-d_8, but is shifted upfield to 216.8 in the presence of excess LiHMDS, 221.3 in the presence of excess NaHMDS, and 226.7 with excess KHMDS. Somewhat smaller shifts were observed with all three metal ions for a typical imidazol-2-ylidene carbene. We were also able to get the X-ray structure of the dimeric potassium complex **21**. [21,52] The K...C distance is 3.00 Å, so the interaction is essentially ionic, and the structure of the carbene is probably very little disturbed.

These results are interesting in themselves, but they are perhaps most significant in demonstrating that the generation of carbenes by deprotonation with strong anionic bases carrying alkali metal counterions will produce complexed species. Carbenes which dimerise like **8**, **9,** and **11** (R = Me, Et, *i*-Pr) can only be observed in solution, and it is an open question how much the observed properties are influenced by the complexation. This problem will be discussed further in sections 2.3 and 2.4, but we have been concerned for some time with trying to find ways to generate the simplest diaminocarbenes under conditions where metal complexation is absent. Some of these have been discussed in section 2.1.1. Another possible method is to sequester the metal ion into a stronger complex. Addition of 12-crown-4 to solutions of carbene **7** complexed to Li ions led to a reversal of the upfield shift, but only as far as 224 ppm, suggesting the formation of a tertiary complex involving both the crown and the carbene.

5.2.3 The structure and properties of diaminocarbenes

In early studies of stable diaminocarbenes, it was suggested that π-donation from the two nitrogen lone pairs into the empty p orbital on the carbene centre might not be important. [53,54] This view was challenged from a theoretical standpoint by Apeloig [55] and Frenking, [56] but it was not until acyclic diaminocarbenes were prepared that a fuller experiment assessment could be made.

5.2.3.1 Structures; bond lengths and angles

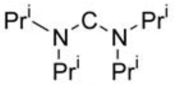
A striking feature of the imidazol-2-ylidenes is the small N-C-N bond angles (around 100-102°). These angles are smaller than in the imidazolium ion precursors; and this trend, which is reproduced by good quality calculations, continues with the saturated imidazolidin-2-ylidenes right through to the comparison of acyclic diaminocarbene **6** (121°) [57] and its precursor **22** (133°). [58]

The N-$C_{(carbene)}$ bond lengths in diaminocarbenes range from 1.35-1.38 Å, longer than for their protonated precursors (1.28-1.33 Å). These bond lengths are consistent with some double bond character, but they do not allow an accurate assessment of this important parameter.

5.2.3.2 Rotational barriers

Dynamic ^{1}H NMR behaviour was observed for bis(diisopropylamino)carbene **6**, and for the precursor amidinium ion **22**, corresponding to exchange of isopropyl group environments. [57] The barrier for **6** was 53 kJ/mol, almost the same as for **22** (55 kJ/mol). A major part of this exchange process must involve rotation about the N-$C_{(carbene)}$ bond so, if these results are taken at face value, there appears to be a substantial π-component to these bonds in the carbene, which must be viewed largely as an ylid. As noted above however, the N-$C_{(carbene)}$ bond length in **6** is 1.37 Å, significantly longer than the corresponding bond in **22** (1.32 Å), suggesting a greater difference in bond order than revealed by the dynamic NMR results.

We were subsequently able to measure the corresponding barriers for the bis(dimethylamino)carbene **9** (44 kJ/mol) and the tetramethylamidinium ion **23** (65 kJ/mol), and these barriers paint a rather different picture. [59] The barrier for amidinium ion **23** is higher than for **22**, which seems reasonable, since there must surely be more strain in the near-planar ground state of **22** than **23**, and this will be relieved during rotation, but the lower barrier for **9** compared with **6** is harder to understand. We know that **9** is probably complexed to Li in these solutions (it cannot be isolated), and this might be the cause of the discrepancy. However, B3LYP/6-31G*calculation of the barriers ($\Delta G^\ddagger$) for **9**, **23**, and a Li$^+$ complex of **9** gave 45, 73, and 62 kJ/mol respectively. The calculations are for the gas phase, but they do not support the idea that Li complexation would lower the barrier for **9**.



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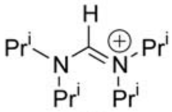

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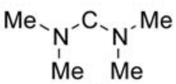

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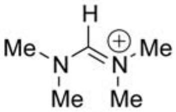

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We are presently inclined to believe that **9** rotates as a free species, and therefore that the data for this series is more representative. In the tetraisopropyl series, there may also be significant barriers for rotation about the N-Pr^i bonds, and with their significant differences in bond angles, this could be different for **6** and **22**.

5.2.3.3 pK_as and proton affinities

Singlet carbenes can be viewed as the conjugate bases of secondary carbocations, and so the pK_as and proton affinities of diaminocarbenes are of fundamental interest. As mentioned in section 1.2, we were able to measure the pK_a of 2,4-diisopropyl-3,4-dimethylimidazol-2-ylidene on the DMSO scale as 24. Unfortunately attempts to measure the pK_a of non-aromatic diaminocarbenes on the same scale have not been successful, due to side reactions (see Scheme 1).

At present the only way to evaluate the basicity of various diaminocarbenes is from calculated proton affinities (PA). The data in Figure 1 are from B3LYP/6-31G* calculations; [59,60] Dixon and Arduengo [53] report a calculated value for the parent imidazol-2-ylidene of 1076.5 kJ/mol at the MP2 level, in good agreement with the DFT result. Methylation of the nitrogen atoms raises the PA substantially, as may be expected, but it is surprising that the removal of the double bond in the imidazolidin-2-ylidene **11**, R = Me, cases no change in the PA. The loss of aromaticity applies to both the carbene and the protonated species, but the greater electron donating ability of the saturated CH$_2$CH$_2$ bridge might have been expected to have an effect.

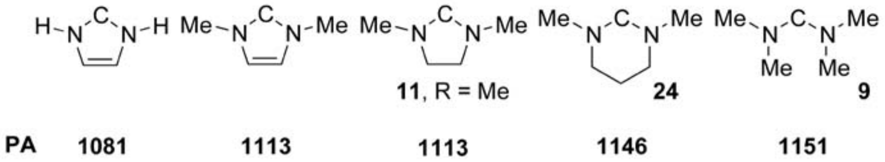


Figure 1 Calculated proton affinities for diaminocarbenes.

The PAs for the six-membered ring and open chain carbenes are substantially higher then the five-membered ring species. This is probably a consequence of the larger N-C-N angles, 105.2º for **11**, R = Me, 115.2º for **24**, and 119.7º for **9**. In accord with the discussion in section 2.3.1, the calculated angles for the protonated species are larger in all cases, 114, 125 and 131º respectively.

Bases on the PA data above, the pK_a values for six-membered, and acyclic carbenes may be from 2-6 pK_a units higher than for imidazol-2-ylidenes, and this may explain some of the increased difficulties with the generation of these species (see section 2.1.1).

5.2.3.4 ^{13}C NMR shifts

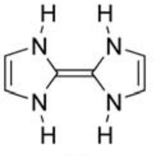
A striking feature of diaminocarbenes is the unusually low field ^{13}C chemical shifts for the carbene centre. These shifts can be predicted with reasonable accuracy by GIAO calculations. [59] They are actually at the high end of what may be expected for singlet carbenes - the calculated chemical shift for singlet methylene itself is about 1300 ppm downfield from TMS. [61] These extreme shifts arise mainly from a paramagnetic (deshielding) contribution due to a low-lying $n \rightarrow \pi^*$ transition, which in turn is related to the singlet/triplet gap.

In a practical sense, these shifts are very useful for confirming the formation of a diaminocarbene, even though the signal is sometimes broadened and the intensity is often very low. The chemical shifts range from 210-220 ppm downfield from TMS for the aromatic imidazol-2-ylidenes, to 235-245 for imidazolidin-2-ylidenes, and 255.5 for **9**. The shifts are decreased by complexation of the carbene centre, as noted in section 2.2.

5.2.4 The dimerisation of diaminocarbenes

5.2.4.1 Equilibria – what carbenes will dimerise?

Simple unhindered imidazol-2-ylidenes are thermodynamically stable towards dimerisation to tetraazafulvalenes. This extraordinary fact needs to be fully appreciated at the outset of any discussion of the kinetics and mechanism of diaminocarbene dimerisation. Replacing the four hydrogens of ethylene with two RN-CH=CH-NR bridges leads to the complete disappearancce of the >700 kJ.mol bond energy of the C=C double bond! This can be seen as the consequence [62] of the enormous stabilisation of the singlet state of each imidazol-2-ylidene. Part of this stabilisation arises for the aromaticity of imidazol-2-ylidene, and Heinemann and Thiel [63] calculated the singlet-triplet gap to be 354 for imidazol-2-ylidene, 290 for imidazolidin-2-ylidene, and 245 kJ/mol for diaminocarbene itself. This leads to estimates of the C=C bond strengths of **25**, **26** and **27** to be 4, 130, and 222 kJ/mol respectively. Besides the effects of aromaticity, the singlet/triplet gap decreases sharply as the N-C-N angle increases. This potentially has important consequences for the properties of acyclic diaminocarbenes. Gibbs free energies (at the MPS/6-311G(2D) and B3LYP/6-311G(2D) levels) for dimerisation of a number of carbenes, including those giving **25**, **26** and **27**, have been reported recently. [64]



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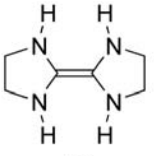

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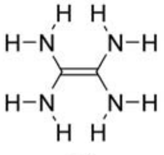

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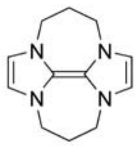
The most convincing experimental proof of the weakness of the C=C in tetraazafulvalenes comes from Taton and Chen's elegant experiments. [65] The tightly constrained **28** exists as the tetraazafulvalene, whereas the homologue **29** with longer tethers dissociates into a biscarbene. Perhaps equally remarkable is the fact that the central C=C bond in **28** is of normal length (1.337 Å), even though the strength of this bond can be only a few kJ/mol.



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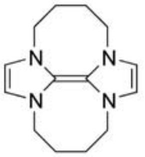

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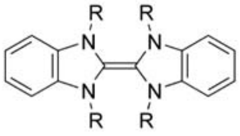

30, R = Et
31, R = CH_2CHMe_2

Benzoimidazol-2-ylidenes lose less aromatic stabilisation than imidazol-2-ylidenes when they dimerise, and unhindered examples exist as dimers at ambient temperatures. However, two studies have demonstrated that equilibria can be established at higher temperatures. Dissociation of dimer **30** in

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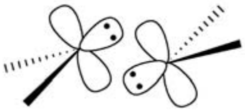
diglyme-d_{14} was observed in the temperature range 313 – 383 K; the thermodynamic parameters for dissociation of are $\Delta H^o = 57.3 \pm 2.5$ kJ/mol and $\Delta S^o = 127 \pm 7$ J mol^{-1} K^{-1}. [66] The more sterically-hindered dimer **31** dissociates in solution at ambient temperature, reaching an equilibrium of 90% carbene and 10% dimer after 24 hours. [67]

The equilibrium for unhindered diaminocarbenes that lack any aromatic stabilisation undoubtedly lies on the side of the dimer. Steric hindrance will not only thermodynamically destabilise the dimer, but is also likely to increase the kinetic barrier to dimerisation, so it is currently uncertain how much steric hindrance is required for to prevent dimerisation. All one can say at present is that bis(diisopropylamino)carbene **6**, 1,3-diisopropyl-3,4,5,6-tetrahydropyrimid-2-ylidene **7**, and imidazolidin-2- ylidene **11**, R = *t*-Bu show no signs of dimerising, whereas dipiperidinylcarbene **8**, bis(dimethylamino)carbene **9**, and five-membered ring carbenes **11** (R = Me, Et, *i*Pr) do so.

5.2.4.2 Kinetic barriers to dimerisation

Singlet carbenes cannot dimerise by a least motion, head-to-head, approach, as was first pointed out by Hoffmann, Gleiter, and Mallory in 1970. [68] The filled sp^2 lone pair orbital needs to approach the empty p orbital of the other carbene, as shown in **32** below. This general mechanism has been confirmed by calculations of varying sophistication over the years. One thorough study suggested that there might be a barrier of 170 kJ/mol to the dimerisation of H_2C. [69]



32

We have studied the dimerisation of several diaminocarbenes by density functional calculations; the transition states for dimerisation of diaminocarbene itself and for the tetramethyl derivative **9** have been reported. [59] Results for saturated five and six-membered ring carbenes are included in Table 1, [60] and the transition states for these (which have C_2 symmetry) are shown in Figure 2. The differences in the energy required for the reverse reaction are quite striking; Thus although there is undoubtedly steric hindrance in tetrakis(dimethylamino)ethylene, it is more stable relative to the carbene than the non-alkylated derivative. This may be due to destabilisation of

Table 1 Energetics for dimerisation of diaminocarbenes from B3LYP/6-31G* calculations.

Carbene	Dimer bond energy	$E^{\ddagger}$ for dimerisation	$E^{\ddagger}$ for dissociation
Diaminocarbene	182	46	228
9	210	48	258
11, R = Me	120	39	159
24	105	73	178

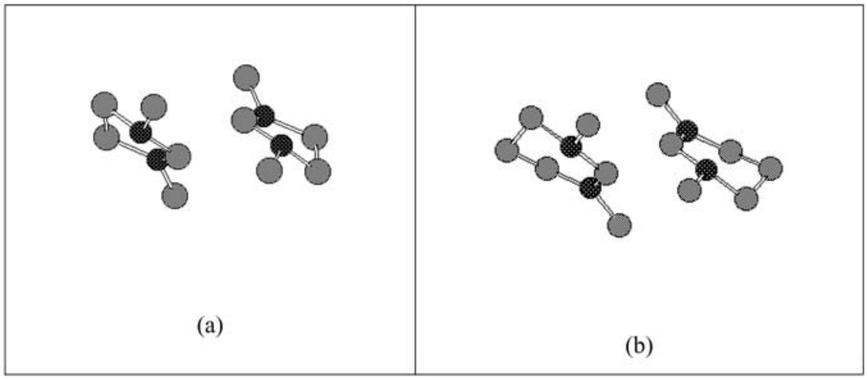
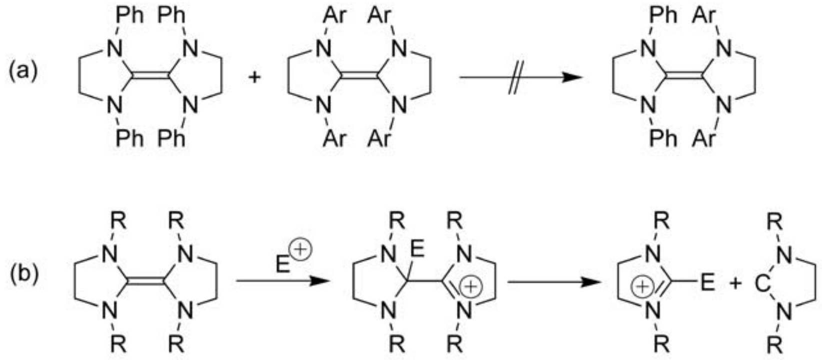


Figure 2 Transition states for dimerisation of (a) 1,3-dimethylimidazolidin-2-ylidene, (**11**, R = Me) and (b) 1,3-dimethyltetrahydropyrimid-2-ylidene, **24**, from B3LYP/6-31G* calculations (hydrogen atoms have been omitted for clarity).

the bis(dimethylaminocarbene **9** because of the expanded N-C-N angle. Dissociation of tetrakis(dimethylamino)ethylene would require prohibitively high temperatures, but this may not be the case for dissociations which give five- and six-membered ring carbenes.

In his early paper, Wanzlick proposed that tetraaminoethylenes dissociated reversibly to generate diaminocarbenes in order to account for the reaction of the former with electrophiles to give products apparently derived from the carbene. However, in 1964 Lemal [70] showed that typical tetraaminoethylenes did not dissociate, even under much more drastic conditions than used by Wanzlick, by carrying out a negative crossover experiment, Scheme 9(a), Ar = *p*-tolyl. Lemal proposed that the reactions with electrophiles proceeded by electrophilic attack on the dimer which then dissociated (Scheme 9(b)) into one equivalent of product and one of carbene, subsequently also attacked by E^+. Denk *et al.*, [71] recently carried out some related crossover experiments and claimed to find crossover under conditions similar to or milder than those used by Lemal. This work has been subsequently challenged by Lemal, [72] who showed that no crossing over took place when the reactions were run in the presence of potassium hydride, to prevent electrophilic catalysis. Lemal pointed out that a trace impurity, however nefarious, could not prevent the occurence of unimolecular dissociation, and therefore could not prevent crossover. On the other hand it could catalyse crossing over, for example by the mechanism in Scheme 9(b). It seems therefore that unimolecular tetraaminoethylene dissociation has not been convincingly observed so far, although our calculations do suggest that the formation of imidazolidin-2-ylidenes by this process may be a practical method at higher temperatures.



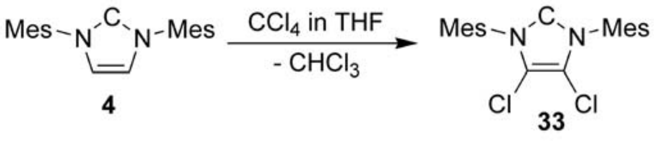
Scheme 9

In conclusion, there is no satisfactory experimental data concerning the actual barrier to dimerisation of a diaminocarbene. In their study of equilibration of benzoimidazol-2-ylidenes with dimers, Hahn *et al*. [67] proposed that this was due to unimolecular dissociation, but Liu and Lemal [66] were more cautious, suggesting electrophilic catalysis might be occurring.

We were initially astonished to find that simple diaminocarbenes like **8** and **9** survived for hours at ambient temperature in THF-d_8. We studied the kinetics of dimerisation of **9** over a range of temperatures. The reaction is cleanly second order, with E=77.7 kJ/mol, and log A=10.6 mol^{-1} s^{-1}, giving $\Delta G^{\ddagger}$=89.9, $\Delta H^{\ddagger}$ =75.2, and $\Delta S^{\ddagger}={}^{-}49.7$ J mol^{-1} s^{-1}. The observed $\Delta H^{\ddagger}$ is clearly much greater than predicted by calculations (Table 1), which refer to the gas phase, of course. While solvent effects may play their part, we believe the major reason for the slow dimerisation of **9** in THF-d_8 solution is that it is present as a Li complex; the results above were obtained with **9** generated using LiTMP and the solutions were 2M in [Li]. We have so far been unable to generate this carbene in the absence of metal ion coordination, although we have confirmed that adding extra LiTMP slowed the dimerisation still more.

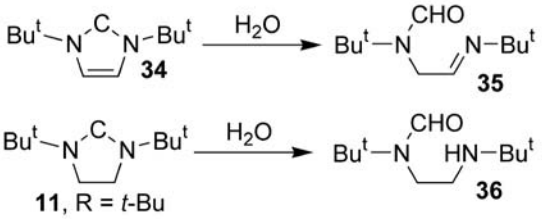
5.2.5 Air-stable carbenes; the reactions of diaminocarbenes with water and oxygen

Arduengo [73] has described the preparation of **33**, which is stable in the presence of chloroform (typical diaminocarbenes would be protonated) and survives as a solid in air for two days. The stability of this carbene towards both water and oxygen is remarkable. Stability towards water implies a substantially reduced pK_a, which may be explained by the electron-withdrawing effects of the chloro substituents, but the stability towards oxygen is perhaps more surprising, since it has been generally assumed that all diaminocarbenes react with (triplet) oxygen to give urea derivatives.



Scheme 10

However Denk *et al*. [74] recently reported that carbenes **34** and **11**, R = *t*-Bu, are inert towards dry (triplet) oxygen. When exposed to moist air, they only produce the hydrolysis products **35** and **36** (Scheme 11). Hydrolysis of **11**, R = *t*-Bu is instantaneous, but for **34**, hydrolysis takes days to become noticeable This suggests a significant difference in pK_a between these two carbenes, contrary to what might be expected from the proton affinities for related carbenes described in Section 2.3.3.

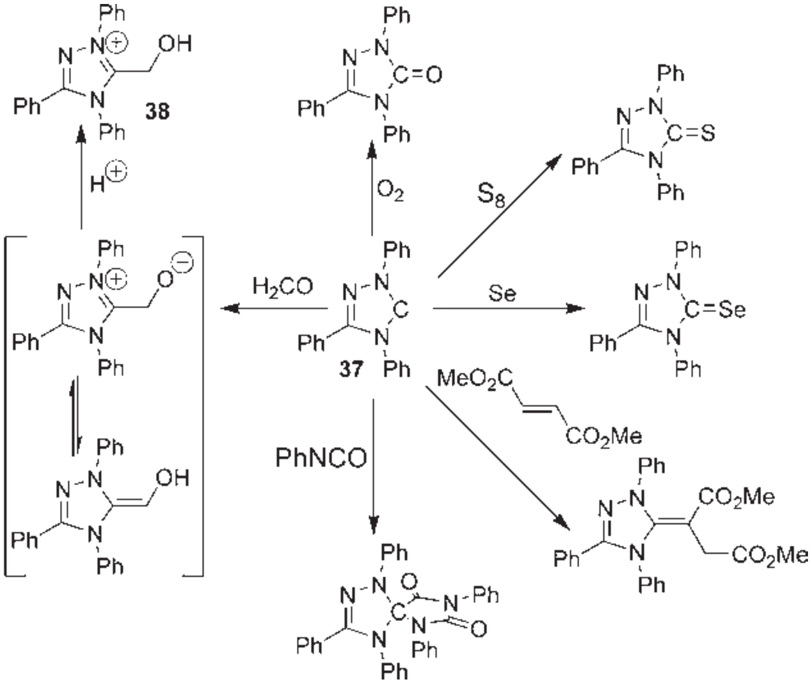


Scheme 11

It will be interesting to see how general this behaviour is. Enders [39,40] reported that triazol-2-ylidene **37** reacted with oxygen, sulfur and selenium to give the expected urea derivatives in 54%, 98%, and 88% yields respectively (Scheme 12). The reaction with sulfur in benzene to give thiourea derivatives is rapid and is often used as a test of carbene formation. It is presumably initiated by nucleophilic attack by the carbene on S_8.

5.2.6 Nucleophilic reactions of diaminocarbenes

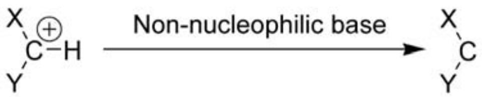
All the other known organic reactions of diaminocarbenes show them to be powerful nucleophiles and bases. Thus they do not react with normal alkenes to give cyclopropanes, but only with electrophilic alkenes and carbonyl groups. The reaction with electrophilic alkenes like methyl fumarate (Scheme 12) might proceed via the cyclopropane, but a Michael addition followed by proton shift seems a good alternative. Reaction with heterocumulenes like phenyl isocyanate leads to double addition via a zwitterionic intermediate. Reaction with formaldehyde to give **38** probably proceeds via an intermediate that can tautomerise as shown, since the reaction leads to a benzoin-type condensation when only a catalytic amount of **37** is used. This serves as a reminder that triazolium, thiazolium, and imidazolium ions act as efficient catalysts for various coupling reactions in basic media. These reactions certainly rely on the nucleophilic properties of the corresponding carbenes, as was first recognised for thiamine pyrophosphate by Breslow more than 40 years ago. [75]



Scheme 12

5.2.7 Postscript – related species

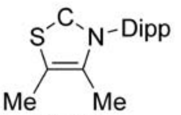
Singlet carbenes can be viewed as the conjugate bases of secondary carbocations, as was noted in section 2.3.3, and this idea (Scheme 13) provides a strong incentive to explore the generation of related species.



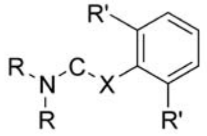
Scheme 13

The X = Y = NR_2 case probably does represent the best scenario for stability for both the carbocation and the carbene. This is not only due to the strongly electron-donating character of the NR_2 groups but also because the presence of four R groups provides the best steric protection. Nevertheless other heteroatoms can be considered, especially in conjunction with nitrogen, and systems with X

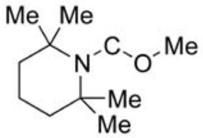
= SR, Y = NR_2 and X = OR, Y = NR_2 are known. An important extension which has recently been realised is the case where X = an aryl group, Y = NR_2.



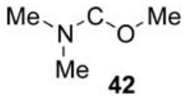
39, Dipp=
2,6-diisopropylphenyl



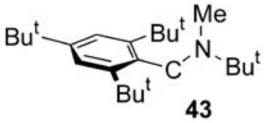
40a, X=S, R=*i*-Pr, R'=Me
40b, X=O, R=*i*-Pr, R'=Me
40c, X=O, R=*i*-Pr, R'=*t*-Bu
40d, X=O, R=Me, R'=*t*-Bu



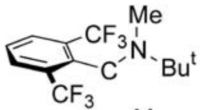
41



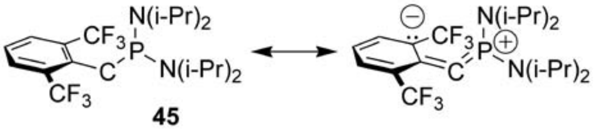
42



43



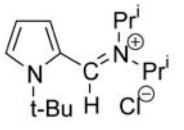
44



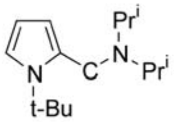
45

The first system of this type to be reported was the thiazol-2-ylidene **39**, which could be isolated as a crystalline solid, but which was converted to its dimer in the presence of traces of protic acids. [31] X-ray structures of both **39** and its dimer were obtained. We were able to generate the non-aromatic analogue **40a** and several X = OR, Y = NR_2 species **40b-d** and **41** by deprotonation reactions. Crystal structures of **40c** and its protonated precursor were obtained. The $C_{carbene}$-O bond lengthens much more than the $C_{carbene}$-N bond on going from the protonated precursor (1.321 Å) to carbene **40c** (1.379 Å), and it probably has very little π-character in **40c**. The length of the $C_{carbene}$-N bond is typical of iminium ions in the protonated precursor (1.283 Å), and while it does lengthen in **40c** (1.319 Å), it is still short enough to suggest strong π-bonding and ylidic character. This is supported by the high barrier to $C_{carbene}$-N bond rotation in **40b** (>88 kJ/mol), and it is clear that most of the π-bonding to the carbene centre comes from the nitrogen atom in these species. Much simpler X = OR, Y = NR_2 species, **42**, have been invoked to explain the exchange of methine protons in dimethylformamide dimethyl acetal in methanol-d_4, [76] and can be generated from 2-alkoxy-2-amino-Δ^3-1,3,4-oxadiazolines, as described in section 2.1.3, [42,43] but cannot be observed by NMR or isolated.

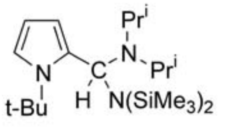
Bertrand and co-workers have prepared several stable species of the X = aryl, Y = NR_2 type. The arylaminocarbene **43** is stable at –50 ºC, but inserts into a *t*-Bu group at higher temperatures. Arylaminocarbene **44** is stable enough for X-ray study, and shows a C-$C_{carbene}$-N angle of 121.0º, very similar to that for **40b** (118.8º). The electron-withdrawing 2,6-bis(trifluoromethyl)phenyl group might have been expected to induce some allenic character, as appears to be the case with **45**, where the C-$C_{carbene}$-P angle is 162.1º.



46

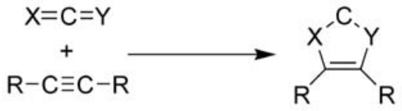


47



48

We attempted to prepare an X = aryl, Y = NR_2 species where the aryl group was a strongly electron-donating pyrrolyl group. Deprotonation of **46** with Li TMP led to the dimer of carbene **47**, while deprotonation with Li HMDS gave the adduct **48**. Treatment of **48** with sulfur gave the thioamide that might be expected from **47**. We suspect that **48** is in equilibrium with low concentrations of **47**, but have been unable to observe the ^{13}C NMR signal for the carbene. [77]



Scheme 14

Finally, it is interesting to note a completely different approach to 5-membered ring carbenes, through 3π + 2π cycloaddition reactions (Scheme 14). [78,79] Hartzler and others [80,81] first suggested this process for reactions of CS_2 in the early 1970. Since the carbene may react further with the heterocumulene (see section 2.6), it is not clear if this route could be used to make isolable carbenes. However it remains a intriguing possibility; a recent theoretical study [82] shows that reaction with HC≡CH is more exothermic for carbodiimide than for CS_2, but has a higher barrier (152 vs 134 kJ/mol).

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Chapter 6

Stable Versions of Transient Singlet Carbenes

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6.1 BACKGROUND

When I started to do research, in 1975, I felt that one of the most attractive challenges for a chemist dedicated to synthetic work was to generate experimental results that put into question existing theoretical conepts.

In the fifties, the theoreticians Pitzer [1] and Mulliken [2] had postulated the so-called "*double-bond rule*": the elements beginning with the second long period should not, under normal conditions, form stable compounds exhibiting (p-p)π bonds. And indeed, by 1975, only a very few compounds featuring a doubly bonded main group element were known: the phosphamethine cyanine cations **1** (Dimroth, 1964), [3] the phosphabenzenes **2a,b** (Märkl, 1966; [4] Ashe, 1971) [5] and the iminophosphane **3** (Niecke, 1973). [6] No derivative featuring a double bond between two main group elements was known, and most of the researchers thought that compounds featuring a triple bond would ever be known or accessible. However, it is important to note that, in 1961, Gier [7] reported that the simplest phosphaalkyne **4** was formed, from phosphine in a rotating electric arc struck between graphite electrodes, and survived the chromatographic purification. This work, was by far too early (!) and this great pioneer was only recognized much later.

This short introduction explains why I first tried to synthesize compounds featuring either a phosphorus-phosphorus double bond or a phosphorus-carbon triple bond.

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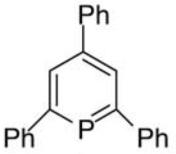
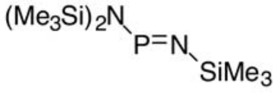
In fact, my group was not quick enough and not really lucky. Becker [8] and Yoshifuji [9] succeeded in the synthesis of the phosphaalkyne **5** and diphosphene **6**, respectively, in 1981, a few months before we obtained the same compounds in Toulouse. However, in the case of the diphosphene **6**, we were able to prove that we were not so late compared to Yoshifuji (now, one of my best friends), since a few months after his paper appeared, we published [10] the correct ^{31}P NMR chemical shift for **6** (+493 ppm, instead of -59 ppm, reported by Yoshifuji).

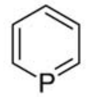
1
(1964)



2a
(1966)



3
(1973)



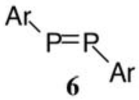
2b
(1971)

H−C≡P

4
(1961)

t-Bu−C≡P

5
(1981)



$Ar{-}P{=}P{-}Ar$

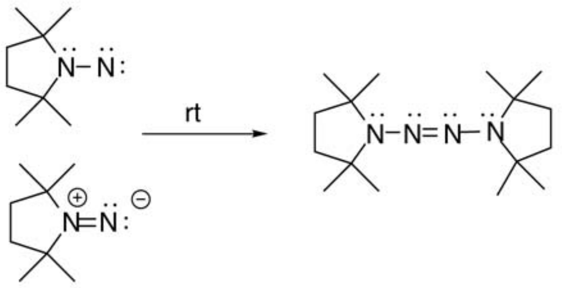
6
(1981)

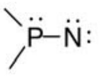
After these somewhat dissapointing events, I decided to look for a new challenge, as far as possible from the main stream. I thought about the possibility of synthesizing species that defie the "*octet rule*". Among them, carbocations and radicals were already well known, and therefore, we started a program dealing with nitrenes and carbenes. Of course, I wanted to use what I have learnt in main group chemistry and thought about the possibility of stabilizing such electron-deficient species with main group elements, and especially with phosphorus. We were encouraged by the results of Peter Dervan [10] of 1978-1982. He reported that, in contrast to the other types of nitrenes, aminonitrenes (diazenes) such as **7**, have a singlet ground state and, providing that they have sterically hindered substituents, were stable for days at -78°C. Their unusual stability was explained by the double-bond character of the nitrogen-nitrogen bond (**7b**), but importantly for a synthetic chemist, diazenes behave as "normal" nitrenes as shown below.

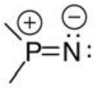
We thought that using a phosphino group, instead of the amino group, would enhance the stability of the corresponding nitrene because of the possibility of forming, not just a double bond as shown in **8b**, but a triple bond as in **8c**.

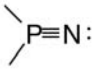
7a

7b



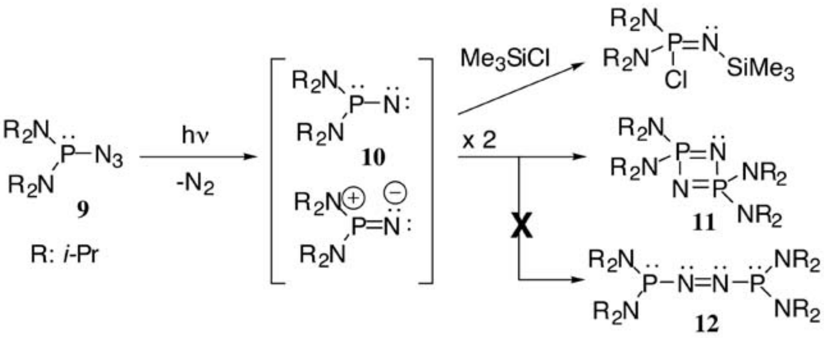

8a


8b


8c

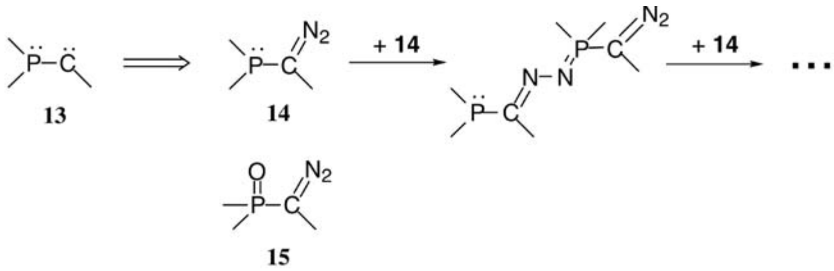
Since the obvious precursors for **8** were the very explosive azidophosphines, [12] we decided, before starting the experimental work, to ask my colleague Georges Trinquier to perform some calculations. [13] He found out that H_2PN would have indeed a singlet ground state, some 6 kcal/mol below the triplet state, and that the delocalization of the lone pairs, $n_\pi(P)$ into $p_\pi(N)$ and to some extent $n_\pi(N)$ into $\sigma^*(P)$, would occur. In other words, as we guessed, the phosphorus-nitrogen bond would be close to a triple bond (**8c**) or, more precisely, a dative double bond.

We thus investigated the photochemical behavior of the azidophosphine **9**, possessing bulky diisopropylamino substituents. Unfortunately, the desired compound **10** was not stable enough to be isolated. We also realized that the chemical behavior of **10** was very different from that of a nitrene, but rather close to to that expected for a phosphonitrile. [14] Of particular interest, it did not dimerize to give the corresponding azo compound **12**, as for the diazene **7**, but to give the cyclic [2+2] head-to-tail dimer **11**. [15]



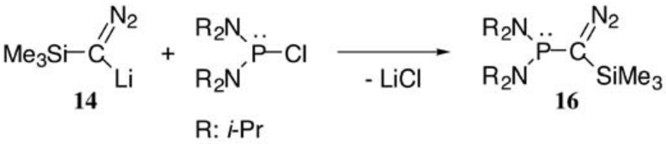
Although our aim of preparing a stable nitrene was not reached, these results were considered as important. [16] This was the first evidence for the transient formation of a compound featuring a hypervalent low coordinated phosphorus atom engaged in a pseudo-triple bond (**10**). The cyclodiphosphazene **11** was the first example of a heterocyclobutadiene, and **10** and **11** are the smallest members of the polyphosphazene family. In an article in C&E News, [16] it was noted that **11** "may shed new light on question of equilibria among monomers, ring, and chains in phosphazenes. Such equilibria could be important in understanding the formation of commercial polyphosphazene resins". Some fifteen years later, we should admit that we have not learnt much about polyphosphazenes, but there are now many examples of heterocyclobutadienes, which are σ*-anti-aromatic systems. [17]

The next goal became obvious: the synthesis of a phosphinocarbene **13**. Diazo derivatives are classical precursors of carbenes. However, although λ^5-phosphorus substituted diazo derivatives **15** were well documented, [18] no examples of derivatives **14** possessing a diazo group bonded to a λ^3-phosphorus atom were reported. We thought that this class of compounds, like phosphine azides, could be very unstable due to possible intermolecular reactions of the diazo moiety with the phosphorus lone pair. [19]



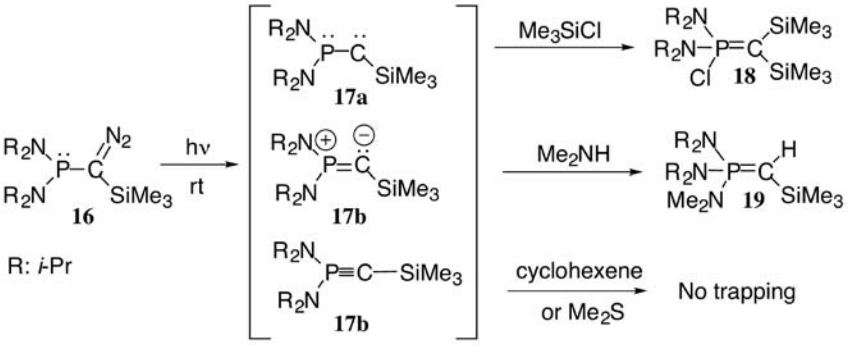
Scheme 2

To prevent this so-called Staudinger-Meyer reaction, it was necessary to protect the phosphorus center using bulky substituents. By analogy with our results with the phosphinonitrene **10**, it was clear that phosphinocarbenes **13** would be polarized $P^{\delta+}$-$C^{\delta-}$, and therefore amino groups at P and a trimethylsilyl group at C, seemed to be good choices. Therefore, we prepared the [bis(diisopropylamino)phosphino]-(trimethylsilyl)diazomethane **16**, by reacting the lithium salt of the trimethylsilyldiazomethane with the corresponding chlorophosphine. [20]



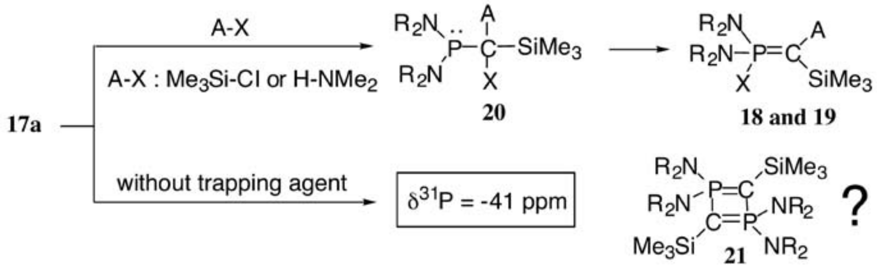
Scheme 3

We first studied the photolytic behavior of the diazo **16** in the presence of trimethylchlorosilane and dimethylamine. [20] The choice of the trapping agent was again dictated by our results with the phosphinonitrene **10**. Clean reactions occurred and adducts **18** and **19** were obtained. Adding to the fact that no trapping reactions occured in the presence of cyclohexene and dimethylsulfur, we concluded that phosphinocarbene **17a** was best regarded as a phosphorus vinyl ylide **17b** or even a phosphaacetylene **17c**.



Scheme 4

We made several mistakes in this paper, [20] and most of them were due to the fact that we were not aware enough to the literature concerning carbene chemistry and also because we were not ambitious enough. We were phosphorus chemists and wanted to prepare the first derivative featuring a λ^5-phosphorus atom engaged in a triple bond. It was obvious for a carbene chemist that our compound **17** was a nucleophilic carbene and could not react with electron rich trapping agents such as cyclohexene or dimethyl sulfur. We only recognised later [21] that, although the formation of **18** and **19** resulted at first glance from a 1, 2-addition of A-X reagents across the polarised PC-multiple bond of **17b** or **17c**, it is more likely that a carbene insertion into the A-X bonds takes place, giving **20**, which subsequently undergoes a rearrangement; such 1,2-shifts have already been exemplified. [22]

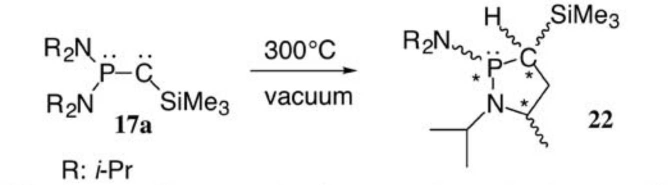


Scheme 5

We were so focussed on the PC multiple bond character of **17**, that in a footnote of the preliminary communication, [20] we wrote: *"According to the* ^{31}*P NMR, besides numerous products, a major species (*$\delta^{31}P = -41$ *ppm) was formed, in the absence of trapping agents or in the presence of cyclohexene or dimethylsulfur. However, because of the extreme instability of this compound (may be the four-membered ring dimer* ***21****), we have not been able to characterize it"*. Fifteen years later, we know that phosphinocarbenes never dimerize by a [2+2] process to give the corresponding four-membered ring of type **21**! Lastly, and more importantly, we needed three years to realize that the major species was indeed **17**, and providing that the work is conducted in the total absence of moisture, it was possible to isolate it.

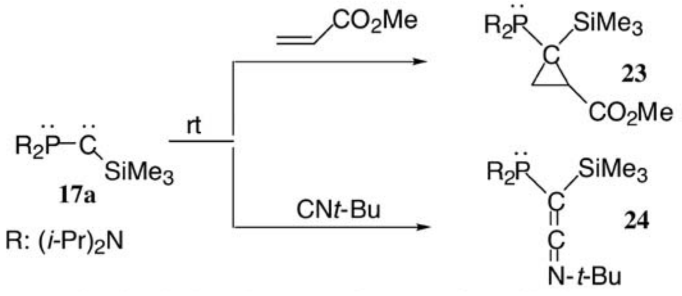
Thus, in 1988, we published a full paper entitled: *"Analogous α,α'-bis-carbenoid triply bonded species: Synthesis of a stable* λ^3*-phosphinocarbene-*λ^5*-phosphaacetylene"*. [21] Again, we were focussed on the multiple bond nature of our compound **17**. However, in the last paragraph, we reported that pyrolysis of **17** at 300°C under vacuum, afforded the five-membered heterocycle **22** (as a mixture of four diastereomers), probably via the insertion of the singlet carbene

17a into a carbon-hydrogen bond of an isopropyl substituent. *We were starting to realise that we had in hands the first stable carbene !*



Scheme 6

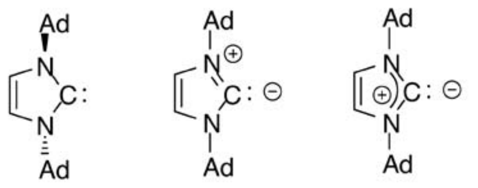
In the following months, we read a lot on carbene chemistry, and in 1989 we published a paper entitled: *"[Bis(diisopropylamino)phosphino]trimethylsilyl-carbene: A stable nucleophilic carbene"*. [23] We found that **17** readily underwent at room temperature the classical cyclopropanation reaction with electron-poor olefins such as methyl acrylate leading to **23** in high yield. Moreover, it appeared that **17** also cleanly reacted with *tert*-butyl isocyanide to give the ketene imine **24** in 90% yield: this was an example of carbene-carbene-like coupling reaction.



Scheme 7

These results seemed important to us, but it is only in 1991, when Arduengo published a paper entitled: *"The first bottle-able carbene"* [24] that our work began to be recognized, although Arduengo has never been convinced that, structurally, **17** was a carbene. [25] The main reasons were the large angle at carbon and the possible resonance structure **17b** and **17c** involving a PC multiple bond. However, already in 1980, Linus Pauling [26] established that σ-donor substituents (such as phosphorus) broadened the bond angle in singlet carbenes:

dilithio-, diboryl- and disilyl-carbenes are even predicted to be linear in the singlet state! Moreover, all the diaminocarbenes, including Arduengo carbene **25**, are stable also as the result of the electronic delocalization of the nitrogen lone pairs. In other words, in contrast to Arduengo statements, [24,25] diaminocarbenes are best described by the resonance form **25b** or better **25c**.



25a 25b 25c

In the last ten years, it has been shown that although bis(amino)carbenes such as **25** do not behave as classical transient singlet carbenes (no cyclopropanation reaction, no 1,2-shift, no C-H insertion...), they are wonderful ligands for transition metals which have very high catalytic activities. [27] Their three center four π electron system makes them strong σ-donor and poor π-attractor. In other words, they constitute a new class of Lewis base. Despites these facts, in the last two highlights of *Angew. Chem.* [28] devoted to stable carbenes, only bis(amino)carbenes were considered, without any mention of our work! This prompted us, to work harder and harder to demonstrate that our carbene **17** was a true carbene, and that it was even possible to obtain other types of stable carbenes, which are closer to the transient species.

6.2 STATE OF THE ART

Throughout this section, I will try to explain the how and why of the progress that has been made.

a) Structure of (phosphino)(silyl)carbenes

For more than ten years, only spectroscopic data and contradictory *ab initio* calculations [29] were available concerning the precise electronic structure of (phosphino)(silyl)carbenes. The quest for crystals, suitable for an X-ray diffraction study, has been the task of many of my talented coworkers. However, it is only in 2000, that one of my Japanese student succeeded. He obtained colorless crystals of the carbene **26** (mp = 122°C). [30]

The molecular structure of **26** shows that the ring and the PCSi fragment are coplanar (maximum deviation from the best plane: 0.03 Å), that the PC bond length [1.532(3) Å] is short, and that the PCSi framework is bent [152.6(3)°]. The presence of a strongly polarized $P^{\delta+}C^{\delta-}$ fragment is suggested by the short $SiC_{carbene}$ [1.795 Å compared with 1.86-1.88 Å for $Si\text{-}CH_3$] and PN bond distances [1.664(2) Å]. These data indicate an interaction of the phosphorus lone pair with the formally vacant orbital of the carbene and might suggest that the carbene lone pair interacts with the σ* orbitals of both the silyl and the phosphino groups (negative hyperconjugation). Therefore, at that stage, form **26a** could be ruled out, but all the others were reasonable.

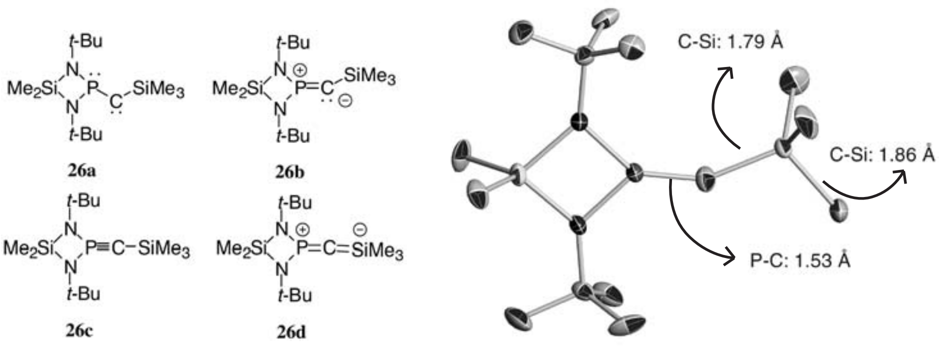


Figure 1. ORTEP diagram of the carbene 26

In order to have more of an insight into the electronic nature of (phosphino)(silyl)carbenes, an ELF analysis [30] of the model compound **27** $[(H_2N)_2PCSiH_3]$ was carried out and led to a rather different conclusion. First, in agreement with previous theoretical studies, we found a bent structure for the energy minimum of **27**, however the linear structure was only 1 kcal/mol higher in energy. For the ground state bent form (Figure 2a), the lone pair on the carbon atom is directed away from both the phosphorus and silicon, indicating that neither the triple bond (**27 c**) nor the cumulene (**27 d**) structure is the best formulation for (phosphino)(silyl)carbenes.

Since the PC double bond is clearly evident, **27** has to be regarded as the phosphavinylylide (**27 b**). Importantly, the isosurfaces representing the PC double bond are bent towards phosphorus, indicating that the phosphorus is reluctant to delocalize its lone pair into the formally vacant orbital of the carbene center. This will explain the observed reactivity (vide infra). Interestingly, the linear form of **27** (Figure 2b) also features the typical pattern for a PC double bond. The stretched shape of the isosurface is an indication of SiC double bond character, and since this isosurface is perpendicular to that attributed to the PC double bond, the linear form of **27** is best described by the cumulenic structure (**27 d**).

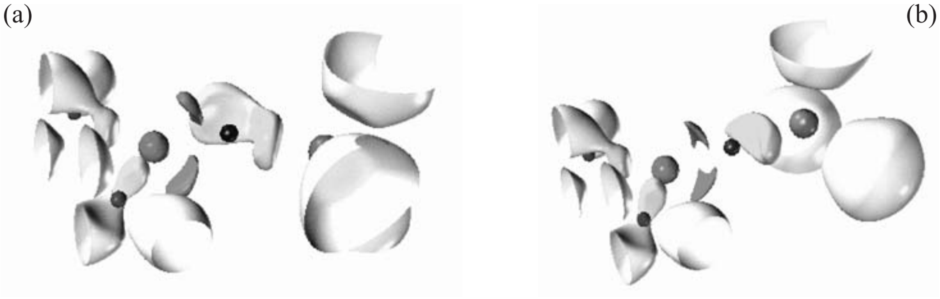


Figure 2. ELF plot of model compound 27

In summary, the phosphino group clearly acts as π-donor substituent, while to some extent the silyl acts as π-attractor due to the aptitude of silicon for hypervalency: (phosphino)(silyl)carbenes are push-pull carbenes.

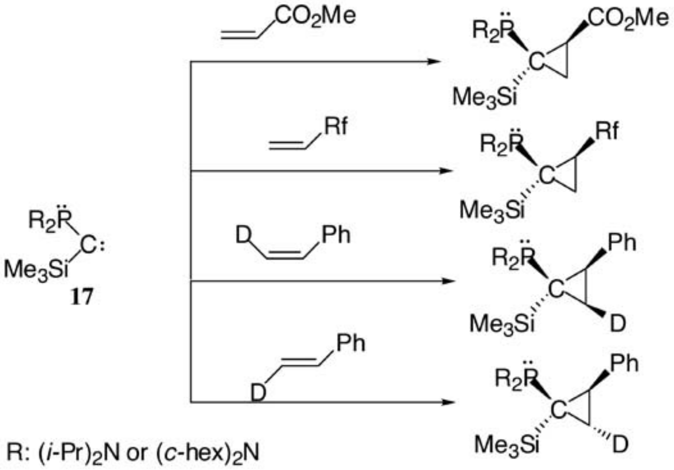
When compared to nitrogen, phosphorus is much more reluctant to achieve a planar configuration with sp^2 hybridization. [31,32] The ensuing smaller stabilizing effect of phosphorus compared to nitrogen is illustrated by the small singlet-triplet gap predicted for the (phosphino)(silyl)carbenes (5.6-13.9 kcal/mol) [29] compared to that calculated for acyclic as well as cyclic diaminocarbenes (58.5-84.5 kcal/mol). [33] This means that the commitment of the lone pair to donation into the vacant orbital on the divalent carbon atom is less definitive for phosphorus than for nitrogen and thus, the phosphinocarbenes retain more of a divalent-carbon behavior. This is well illustrated by their reactivity.

b) Reactivity of (phosphino)(silyl)carbenes

We are going to discuss the similarities and differences observed for the reactivity of (phosphino)(silyl)carbenes compared to the transient nucleophilic carbenes, using the most typical carbene reactions. However, we would also like to demonstrate that these stable species have allowed the synthesis of original types of compounds, which would hardly be available from other precursors.

c) Cyclopropanation and related reactions

In a recent paper, [34] Krogh-Jespersen, Yan and Moss wrote: "The addition of a carbene to an alkene with the formation of a cyclopropane is perhaps the most fundamental of cycloaddition reactions, as well as a basic component of the synthetic armamentarium*"*. Indeed, cyclopropanation reactions involving transient carbenes [35] or even transition metal carbene complexes have been widely studied. [36] Both singlet and triplet transient carbenes undergo cyclopropanation reactions, although with a totally different mechanism, which is apparent from the stereochemistry of the reaction: with singlet carbenes the stereochemistry about the original carbon-carbon double bond is maintained, while with triplet carbenes the stereochemical information is lost. [37] Additionally, for all types of carbene, including transition-metal-carbene complexes, intermolecular cyclopropanation usually occurred in poor to moderate diastereoselectivity (*syn*- versus *anti*-attack). [38]



Scheme 8

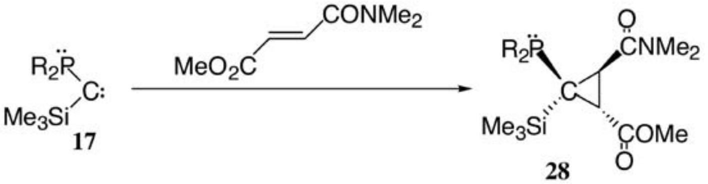
In one of our first papers, [23] we used the cyclopropanation reaction of **17** with methyl acrylate to demonstrate the carbene nature of our compound. But it was only last year that we decided to study the stereochemistry of this type of reaction. [39] The stable (phosphino)(silyl)carbenes **17** react efficiently with most of the electron-poor alkenes such 3,3,4,4,5,5,6,6,6-nonafluorohex-1-ene or (*Z*)- and (*E*)-2-deuterostyrene to give the corresponding cyclopropanes in good yields. The stereochemical outcome was such that all monosubstituted alkenes gave exclusively the *syn* isomer (with respect to the phosphino group), and the addition of disubstituted alkenes was totally stereospecific.

The stereospecificity observed with (*Z*)- and (*E*)-2-deuterostyrene present convincing evidence for the concerted nature of cyclopropanation reaction and therefore the genuine singlet carbene nature of stable phosphanylsilylcarbenes. The diastereoselectivity is at first glance surprising. Indeed, it is clear that steric factors cannot govern the observed selectivity since the bis(amino)phosphino group is at least as sterically demanding as the trimethylsilyl group. Since the *syn*-selectivity observed with the carbenes **17** is not due to steric factors, the obvious other possibility is to invoke orbital control. Because **17** is a nucleophilic carbene, the more dominant orbital interaction, in the transition state, is between the HOMO$_{carbene}$ and the LUMO$_{alkene}$, but this set of orbitals does not explain the observed *syn*-selectivity. However, in the course of computational and experimental work on the addition of carbenes to alkenes, the significance of a second pair of orbital interactions in the addition geometry has been pointed out. [40] Thus, we believe that the secondary orbital interaction LUMO$_{carbene}$ - HOMO$_{alkene}$ explains the selectivity observed. Due to the donation of the phosphorus lone pair, the LUMO$_{carbene}$ has some π*(PC) character and shows significant bonding overlap between the phosphorus center and the alkene substituent, as indicated schematically in the following scheme. In other words, like the *endo* selectivity in the Diels-Alder reaction, [41] the high stereoselectivity observed could be rationalized on the basis of favourable "secondary orbital interactions".

HOMO$_{carbene}$- LUMO$_{olefine}$ **LuMO$_{carbene}$- HOMO$_{olefine}$**

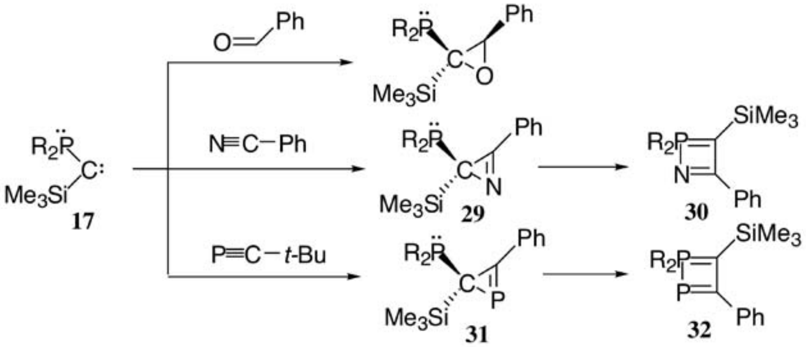
Figure 3. HOMO-LUMO interaction between a (phophino)(silyl) carbene and styrene

The effectiveness of the secondary orbital interactions on the selectivity of cyclopropanation reactions was demonstrated by the exclusive formation of **28** in the reaction of **17** with (*E*)-$Me_2NCOCH{=}CHCO_2Me$. Simple Hückel calculations show that the highest coefficient of the HOMO of the alkene is located at the amido group, and thus despite the smaller steric demand of the ester group, the amido substituent lies *syn* with respect to the phosphino group.



Scheme 9

Reactions related to cyclopropanation can also be carried out with (phosphino)(silyl)carbenes. For example, benzaldehyde reacts with **17** at 0°C leading to the corresponding epoxide, again as only one diastereomer. [23] Even more striking are the reactions with benzonitrile and *tert*-butylphosphaalkyne which lead initially to the azirine **29** [42] and phosphirene **31**. [43]

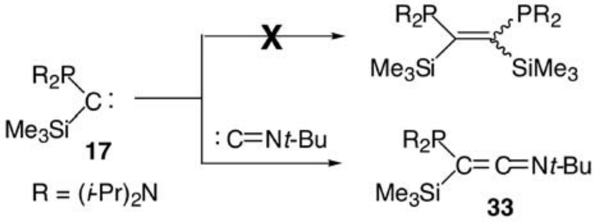


Scheme 10

Both three-membered heterocycles subsequently undergo ring expansion reactions affording azaphosphete **30** [42,44] and diphosphete **32**, [43] respectively. This is a new route for the synthesis of heterocyclobutadienes, [17] and this demontrates the usefulness of (phosphino)(silyl)carbenes for the synthesis of original species.

c) Carbene dimerization

In the Carter and Goddard formulation, [45] the strength of the C=C double bond resulting from the dimerization of singlet carbenes should correspond to that of a canonical C=C double bond (usually that of ethene) minus twice the singlet-triplet energy gap for the carbene. Since this gap is rather small for (phosphino)(silyl)carbenes, it is rather surprising that, to date, there has been no report of dimerization, nor of genuine carbene-carbene coupling reactions to give the corresponding alkenes. However, it appears that *tert*-butyl isocyanide is one of the very rare reagents that react with almost all of the stable phosphinocarbenes reported so far. [23,46] For example, it reacts with **17**, even at -78°C, affording the ketenimine **33** in 90 % yield. [23] Note that transient carbenes are well known to react with isonitriles to give the corresponding ketenimines. [47]

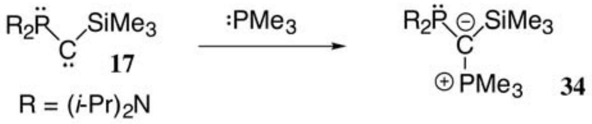


Scheme 11

The great reactivity of isonitriles towards phosphinocarbenes, while no carbene dimerization occurs, can easily be explained in terms of steric factors: the reactive site of RN=C: is comparatively unhindered.

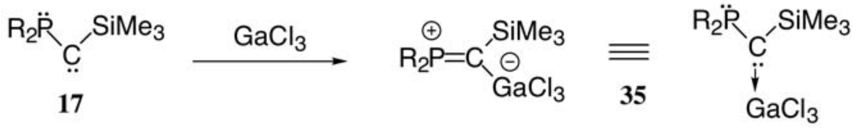
c) Reactions with Lewis bases and acids

Transient electrophilic carbenes are known to react with Lewis bases to give *normal ylides*. For example, carbene-pyridine adducts have been spectroscopically characterized and used as a proof for the formation of carbenes, [48] while the reaction of transient dihalogenocarbenes with phosphines is even a preparative method for C-dihalogeno phosphorus ylides. [49] Stable diamino carbenes do not undergo such reaction. However, we have recently shown that instantaneous and quantitative formation of the corresponding phosphorus ylide occurred when one equivalent of trimethylphosphine was added at 0 °C to a pentane solution of the carbene **17.** The formation of the phosphorus ylide **34** is of particular significance since it is certainly the most striking evidence for the presence of an accessible vacant orbital at the carbene center, as expected for a singlet carbene.



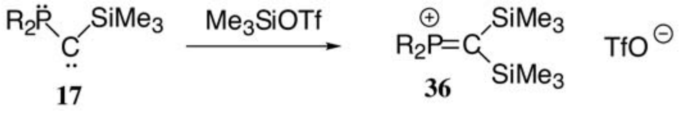
Scheme 12

Little is known about the reactivity of transient carbenes with Lewis acids, but because of the presence of the lone pair, singlet carbenes are expected to give carbene-Lewis acid adducts, the so-called *reverse ylides*. [51] As expected, both diaminocarbenes and (phosphino)(silyl)carbenes undergo such a reaction. Note that compound **35** can be considered as a carbene-gallium complexe. [52]



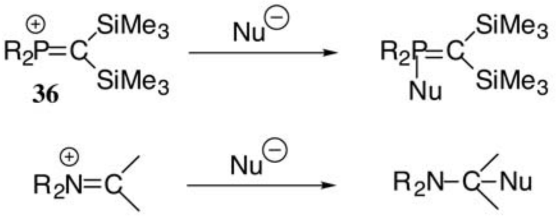
Scheme 13

The most interesting results have been obtained using cationic Lewis acids. Indeed, in 1989 we showed that addition of trimethylsilyl triflate to the carbene **17** led to the so-called methylenephosphonium cation **36**, which was the first example of a stable tricoordinated phosphorus cation. [53] This compound features a short phosphorus-carbon double bond (1.62 Å) and trigonal planar phosphorus and carbon centers, as expected for a compound isovalent and isoelectronic with olefins; however, the double bond is dramatically twisted (60°).

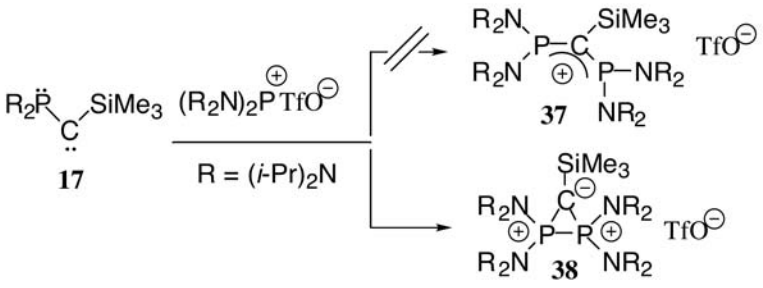


Scheme 14

The salt **36** is the phosphorus analogues of iminium salts, the well known aminocarbocations. However, because of the electropositivity of phosphorus, the phosphorus atom is positively charged and the nitrogen atom negatively charged, while for iminium salts the reverse polarity is observed (despite the usual writing). [54] Moreover, phosphorus can be hypervalent. The consequences of the preceding remarks are apparent in the reaction of **36** with nucleophiles, which react at phosphorus and not at carbon as observed for iminium salts.



Scheme 15

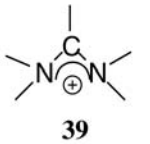


Scheme 16

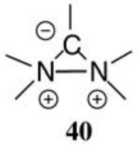
We recently decided to exploit the differences observed between amino- and phosphino-carbocations to prepare what we called *“a cyclic carbanionic valence isomer of a carbocation”*! [55] In other words we generated a carbocation, which spontaneously underwent a transformation into a carbanion. How is it possible?

The idea was simple. Since nucleophiles react at the phosphorus center of the phosphinocarbocation **36**, it was quite reasonable to think that a similar *intramolecula*r reaction will occur. Based on this, we synthesized the diphosphinocarbocation **37**, which indeed isomerized into its desired valence isomer **38**, featuring a carbanionic center.

Before going further, note that quantum chemical calculations predicted the amidinium salt **39** (R = R' = H) to be 541 kJ/mol more stable than its unknown cyclic valence isomer **40**.



39



40

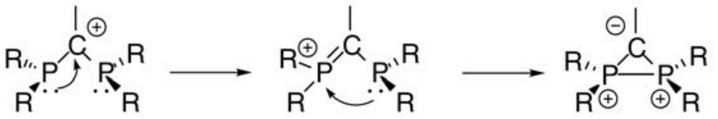
Several factors easily explain the reverse order of stability observed in the phosphorus (**37** less stable than **38**) and nitrogen series (**39** more stable than **40**):

Factor (a): A stable allylic structure of type **37** or **39** (a 3-center-4π-electron system) implies a large singlet-triplet energy separation, which amounts to 379 kJ/mol for the parent compound **39** but only 163 kJ/mol for **37** (R = R' = H). This is due mainly to the much smaller inversion barrier at nitrogen (21 kJ/mol) than at phosphorus (146 kJ/mol), which favors π-bonding. In addition, π-bonds between phosphorus and carbon are much weaker than those for nitrogen (P=C: 188 kJ/mol; N=C: 271 kJ/mol), which disfavors the allylic structure **37**.

Factor (b): Phosphorus-carbon bonds are longer than nitrogen-carbon bonds (P-C: 1.89 Å; N-C: 1.47 Å), and thus the ring strain energy in **38** is smaller than in **40**.

Factor (c): Due to the presence of an accessible σ* orbital at phosphorus, compound **38** can benefit from σ*-aromaticity, [56] although this type of stabilization is far weaker than that resulting from π-aromaticity, which is present in the well known cyclopropenium salts.

Derivative **38** can be considered as resulting from a "cascade stabilization"of the electron deficient carbocation center. As in the case of monophosphino-carbenium ions such as **36**, the first phosphorus atom gives electrons to the carbocationic center and becomes positively charged and therefore, highly electrophilic. The second phosphorus atom then acts as a Lewis base towards the first.



38

Scheme 17

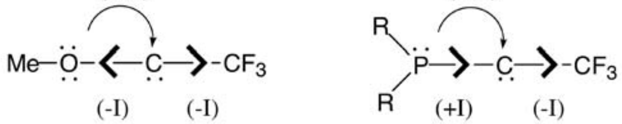
This type of transformation of a cationic center into an anionic center is unlikely to be unique and should be of significant synthetic utility. For example, preliminary calculations predict that the corresponding diphosphino nitrenium ions should exist in the cyclic form, with a negatively charged nitrogen atom.

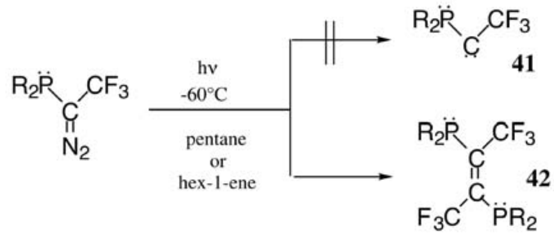
The synthesis of **38** is the most recent example of the use of stable (phosphino)(silyl)carbenes for the synthesis of original species, but we do hope to find further exciting species in the next future.

d) New stable versions of transient singlet carbenes

As already mentioned, although (phosphino)(silyl)carbenes have been for a long time the only stable carbenes featuring most of the reactivity of classical transient carbenes, they received little attention from organic chemists. We think that this is due to the presence of heavier main group elements. Therefore, we tried to move increasingly closer to «organic» carbenes. We first succeeded in replacing the silyl group by alkyl and aryl group, [57] and very recently, we have been able to synthesize a stable carbene featuring no phosphorus and no silyl substituents, but amino and aryl substituents : here we are, we have a stable «organic» carbene!

Let first summarize our results concerning (phosphino)(alkyl or aryl)carbenes. Again, we based our approach on the Pauling prediction [26] that substituents of opposing electronic properties (the so-called push-pull effect) should stabilize singlet carbenes by preserving the electroneutrality of the carbene centre. The validity of this approach was also investigated by Moss [59] and Dailey, [60] who independently studied the methoxytrifluoromethylcarbene (MeO-C-CF_3). This derivative was, however, highly unstable and electronically indiscriminate in its reaction with alkenes. This behavior was attributed to the pull inductive effect (-I) of the CF_3 group, which predominates over the push resonance effect (+M) of the MeO group. Recognizing that the methoxy group also has a pull inductive effect (-I), we chose to introduce a phosphino group in its place. This substituent features both resonance (+M) and inductive push (+I) effects and, in addition, provides considerably greater steric bulk.





Scheme 18

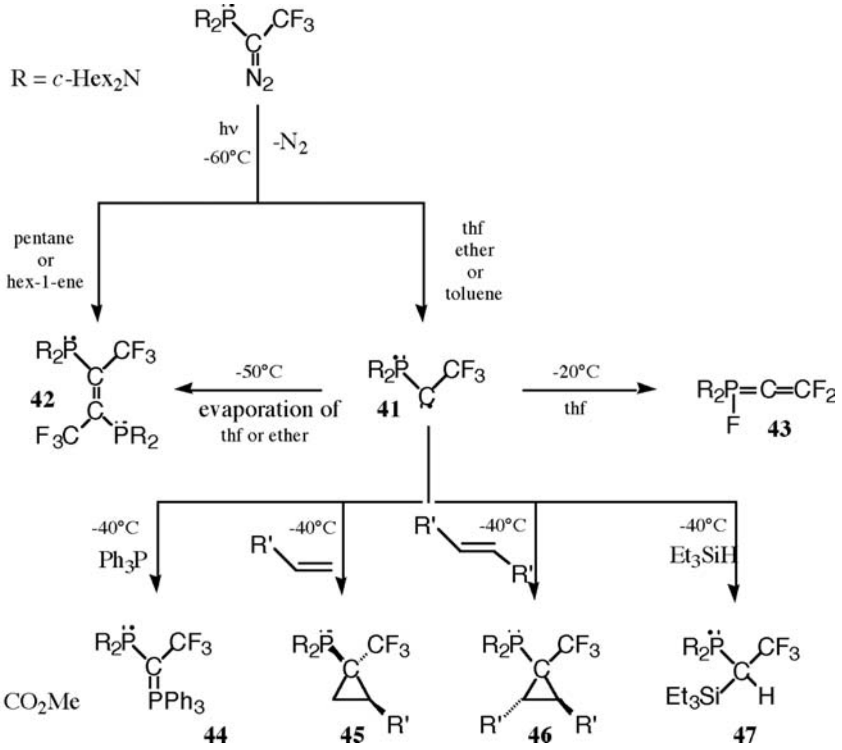
Photolysis (300 nm) of [bis(dicyclohexylamino)phosphino](trifluoromethyl)-diazomethane at -60°C in pentane does not afford carbene **41** but its dimer **42**, which precipitates from the solution as orange crystals (75 % yield).

We then investigated the photolysis in donor solvents, using the well-known Platz' method for observing "invisible" carbenes through ylide formation. [48] Irradiation of the diazo precursor in tetrahydrofuran or diethylether under the same experimental conditions (300 nm, -60°C) cleanly generated the desired carbene **41** which is stable for days in solution at -30°C, and was characterized spectroscopically. Evaporation of the solvent, even at -50°C, resulted in dimerization generating exclusively the alkene **42**. In contrast, upon warming the thf solution of **41** to -20°C, a clean rearrangement occurs affording the cumulene **43**, with no trace of the carbene dimer **42** being observed. These observations are in perfect agreement with previous work on transient carbenes. It has been shown that the extent of 1,2-migration processes increases, relative to intermolecular reaction (like the dimerization leading to **42**), as the solvent is changed from an alkane to a donor solvent. [61]

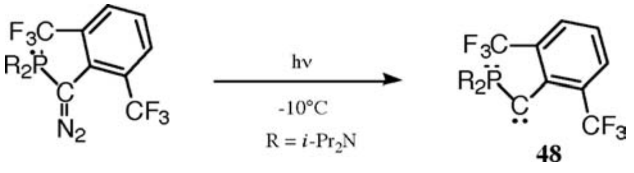
To confirm the interaction of thf and ether with the carbene **41**, and therefore the Lewis acid character of the carbene, we treated the thf solution of **41** at -40°C with triphenylphosphine, a strong Lewis base. As expected, the phosphorus ylide **44** was obtained and isolated in near quantitative yield.

Even subtle effects observed with transient carbenes can be reproduced with **41**. Jones, [61] Moss, [62] and Goodman [63] recently showed that transient singlet carbenes (such as chlorocarbenes) interact weakly with aromatics, but not with simple olefins. For example, this interaction led to an extension of the benzylchlorocarbene lifetime from 23 ns (isooctane) to 285 ns (benzene). [62] Similarly, we found that photolysis of the diazo precursor in hex-1-ene at -60°C led to the carbene dimer **42**, while in toluene we obtained the carbene **41**, which is stable up to -30°C.

(Phosphino)(trifluomethyl)carbene **41** does not react with electron-rich alkenes but cleanly undergoes cyclopropanation reactions (toluene, -78°C) with methyl acrylate and dimethyl fumarate, demonstrating its nucleophilic character. The corresponding cyclopropanes **45** and **46** were isolated in 80 and 60% yield, respectively, as only one diastereomer. Lastly, carbene **41** is reactive enough to insert at -40°C into the silicon-hydrogen bond of triethylsilane to afford phosphine **47** in 58% yield. [64]



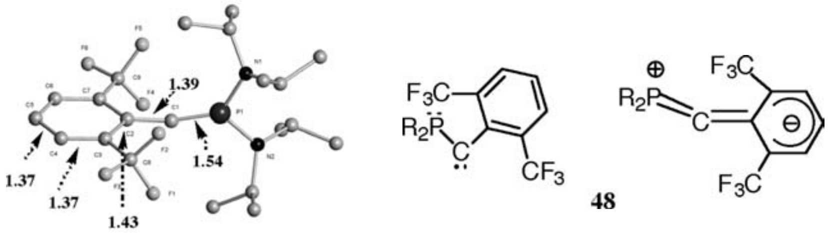
Scheme 19



Scheme 20

At that stage, we found necessary to increase the stability of such monoheteroatom substituted carbene and we investigated the possibility of replacing the σ-attracting CF_3 group (-I) by the bulky 2,6-bis(trifluoromethyl)phenyl group, which is both a σ- and a π-attractor (-I, -M). For all solvents used, photolysis of the diazo precursor at -10°C afforded the corresponding carbene **48**, which is stable for weeks at room temperature both in solution and in the solid state (melting point 68-70 °C).

The molecular structure of **48** shows that the phosphorus atom is in a planar environment and the P1-C1 bond length [1.544(3) Å] is short, as expected because of the donation of the phosphorus lone pair into the carbene vacant orbital. The aromatic ring is perpendicular to the C1P1N1N2 fragment allowing the delocalization of the carbene lone pair into the ring. This -M effect of the aromatic, is evident from the large P1-C1-C2 bond angle [162.1(3)°], the short C1-C2 bond length [1.390(4) Å], and the long C2-C3 and C2-C7 bond distances compared to the other bonds of the ring. In other words, the push-pull carbene **48** can be formulated as a cumulene.



48

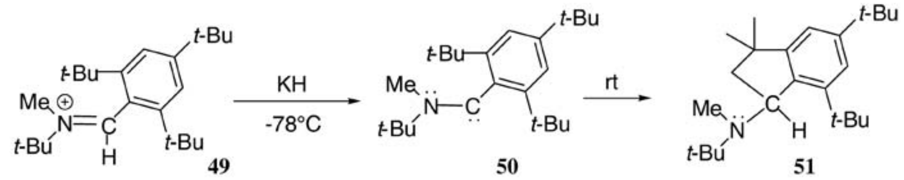
Figure 4. Molecular structure of carbene 48

This work bridged to some extent the gap between the classical, highly reactive transient carbenes and their stable counterparts. It demonstrated that push-pull stabilization was very effective for preparing carbenes featuring high thermodynamic stability, without destroying their typical carbene reactivity.

The important remaining question was: To what extent can the degree of carbene pertubation be further decreased without precluding isolation at room temperature? One of the challenges was to use only one electro-active substituent

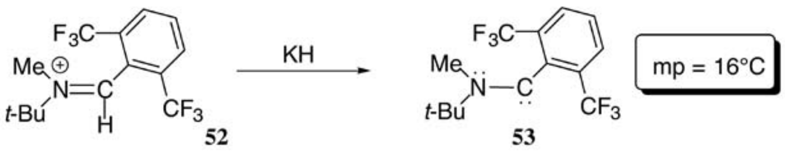
As already mentionned, the push-pull carbenes **41** and **48** follow Pauling's prediction, [26] with two substituents of opposite electronic properties being capable of stabilizing singlet carbenes by preserving the electroneutrality of the carbene center. It was thus tempting to use a single substituent, which on its own would be both an electron donor and an electron acceptor. In other words, was it possible to isolate carbenes featuring a *spectator* substituent ?

As the electronically active group, the amino group was the obvious choice: it is a good π-donor and σ-attractor. We initially prepared the iminium salt **49**, bearing a bulky *tert*-butyl group at nitrogen and a 2,4,6-tri-*tert*-butylphenyl group at carbon. Subsequently, **49** was deprotonated with potassium hydride at –78°C in tetrahydrofuran, which cleanly led to the formation of (amino)(aryl)carbene **50**. The signal observed at δ = 314.2 ppm in the ^{13}C NMR spectrum is the most deshielded signal ever observed for a carbene center. [27] The carbene **50** is stable for days in solution at –50°C but undergoes a classical C-H insertion reaction at room temperature; within a few hours, the 4,6-di-*tert*-butyl-1,1-dimethyl-3-(methyl-*tert*-butylamino)indan **51** was obtained as the major product. [65]



Scheme 21

In order to prevent the subsequent reaction of the carbene center, we replaced the ortho-*tert*-butyl groups of the aryl ring by trifluoromethyl substituents: C-F bonds are inert towards insertion of any type of carbene. [60,66] Following the same procedure as described above, the (amino)(aryl)carbene **53** was prepared from the corresponding iminium salt **52**. Since the insertion reaction is no longer possible and the dimerization is precluded on steric grounds, the carbene **53** could be isolated at room temperature in almost quantitative yield. The ^{13}C NMR resonance for the carbene carbon has a similar chemical shifts (303 ppm) to that of **50**, suggesting analogous electronic structure.



Scheme 22

It is interesting to compare the molecular structure of **53** with that of the push-pull (phosphino)(aryl)carbene **48**. [57] The nitrogen atom is in a planar environment and the N-$C_{carbene}$ bond length (1.283 ± 0.003 Å) is short [even shorter than that observed for diaminocarbenes(1.32 - 1.37 Å)], which indicates a strong donation of the nitrogen lone pair into the vacant carbene orbital. In marked contrast with the cumulenic system **48**, the $C_{carbene}$-C_{ipso} bond distance is long (**53**: 1.45 Å; **48**: 1.39 Å) and the carbene bond angle acute (**53**: 121.0°; **48**: 162.1°). These data clearly indicate that the potentially π-accepting 2,6-bis(trifluoromethyl)phenyl group does not interact with the carbene lone pair of **53** and is therefore a *spectator*.

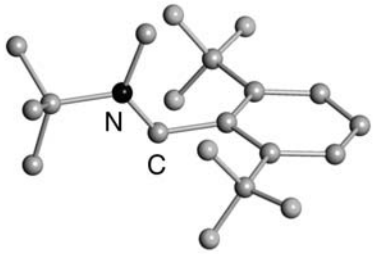


Figure 5. Molecular structure of carbene 53

6.3 CONCLUDING REMARKS

When we started our carbene project, it was a common statement that carbenes only occured as reactive intermediates: this is no longer valid. Up to the last months, the number and variety of stable carbenes have been limited by the perceived necessity for two strongly interacting substituents: our most recent work establishes that only a single electron-active substituent is necessary to isolate a carbene. Therefore a broad range of these species will soon be readily available, which will open the way for new synthetic developments and applications in various fields. Note that despite the limited number of stable carbenes known, these species have already found applications even on a large scale. [67]

Although new knowledge has been accumulated over the last two decades, many challenges are still to be achieved in the particular field of stable carbenes. After the synthesis of persistent triplet carbenes by Tomioka, [68] the preparation of stable non-heteroatom-substituted singlet carbenes is an exciting and realistic goal. In such compounds the singlet-triplet gap would be very small and the isolation of a carbene in both the singlet and the triplet state would be a spectacular achievement, but isn't it an inaccessible dream? [69]

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Chapter 7

The Discovery and Development of High Oxidation State Alkylidene Complexes

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In 1964 Fischer and Maasböl reported that the reaction of phenyl lithium with $W(CO)_6$ followed by addition of acid and then diazomethane gave a "metal-carbene" complex (**1**). [1] Hundreds of compounds that contain a heteroatom-stabilized (usually O or N) carbene ligand were published in the next few years.[2] In these 18 electron species the carbene ligand is best viewed as a singlet carbene which binds to the metal as a σ donor/π acceptor ligand analogous to CO. However, as a consequence of multiple bonding between the carbene carbon atom and the heteroatom, the metal-carbon bond is not a full double bond. In such species the carbene carbon is attacked by nucleophiles, and the heteroatom by electrophiles, a fact that has led to the characterization of these species as "electrophilic carbene" complexes in which the M-C bond is polarized δ- on the metal and δ+ on the carbene carbon. The most highly stabilized carbene in the family of heteroatom-stabilized carbenes is one that contains two nitrogen atoms (e.g., in **2**). Hundreds of compounds that contain diaminocarbenes have been prepared, largely of late transition metals.[3-5] Such strongly stabilized carbenes are believed to bind to a metal as almost pure σ donors. In fact, many carbenes of this type are known to be stable in the metal-free state. [6] In most circumstances it is appropriate to view a carbene ligand that contains one or two heteroatoms bound to the carbene carbon as being neutral, with a varying degree of metal-carbon double bond character. The tungsten in **1** therefore is best viewed as W(0). In the early 70's a large volume of work on heteroatom-stabilized carbene complexes was carried out. [2,3] Since that time heteroatom-stabilized carbene complexes have become

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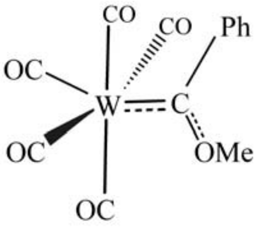
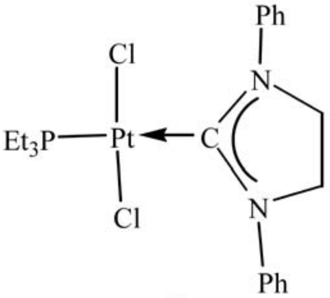
increasingly important as stoichiometric reagents for the synthesis of small organic molecules. [7-9]

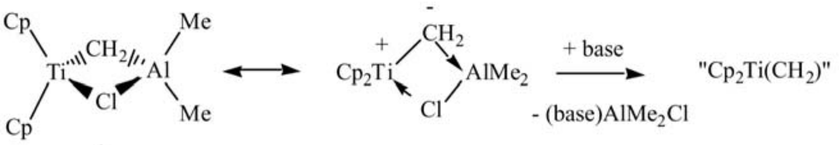


1



2

In 1973 at the Central Research Department of E. I. duPont de Nemours and Company the organometallic chemistry of titanium and tantalum was being explored. F. N. Tebbe discovered that the reaction between Cp_2TiCl_2 and excess $AlMe_3$ gave methane and **3** (Eq. 1). [10] Although the methylene is bridging between Ti and Al, later work suggested that **3** could serve as a source of "$Cp_2Ti(CH_2)$" in the presence of a base that would form an adduct with $AlMe_2Cl$. [11] One could argue that the Ti-CH_2 bond is polarized δ+ on Ti and δ- on carbon, exactly the opposite of a heteroatom-stabilized carbene complex, on the basis of the fact that the methylene ligand appears to be generated by "deprotonation" of a Ti-CH_3 species with an $AlCH_3$ species. Interestingly, compound **3** was shown to react with ethylene to give propylene into which the methylene had been incorporated. [10]

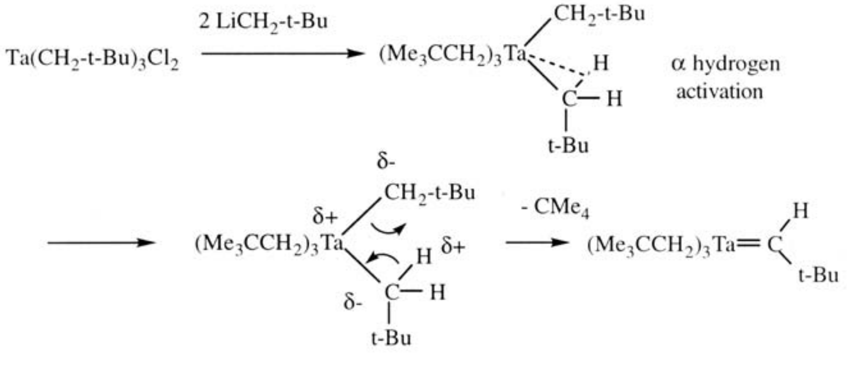


3

(1)

Tantalum (and niobium) methyl/chloride combinations containing a maximum of three methyl groups, e.g., $TaMe_3Cl_2$, [12] were the only alkyl complexes of tantalum that existed in 1973. Such species were prepared from $ZnMe_2$

and $TaCl_5$ in pentane. Extensive work by Schmidbaur [13] on pentaalkyls and alkylidene trialkyls of phosphorus and arsenic provided the author with inspiration to view tantalum as "metallic phosphorus," i.e., to attempt to prepare similar complexes of tantalum, e.g., pentamethyltantalum. Additional impetus came from a report that same year of the synthesis of hexamethyltungsten. [14] The reaction between $TaMe_3Cl_2$ and two equivalents of LiMe indeed produced pentamethyltantalum, [15] although it melted and decomposed above ~0°C. It was shown to decompose in a complex intermolecular fashion, [16] which in retrospect is not unexpected given the 10 electron count at the metal and the relatively sterically unprotected nature of a methyl group. Therefore larger alkyls were employed in an attempt to prevent intermolecular decomposition. The reaction between TaR_3Cl_2 and two equivalents of LiR when $R = CH_2Ph$ gave red crystalline $Ta(CH_2Ph)_5$, a species that was found to be much more stable than $TaMe_5$. [16] When $R = CH_2CMe_3$ a similar reaction did not yield $Ta(CH_2CMe_3)_5$, but $(Me_3CCH_2)_3Ta{=}CHCMe_3$ (Eq. 2), a "tantalum ylide" that bears an obvious structural relationship to a phosphorus ylide, along with neopentane. [17] $(Me_3CCH_2)_3Ta{=}CHCMe_3$ is quite stable thermally, melting at ~70°C and *distilling* readily in a good vacuum. It is sensitive to oxygen, water, and a variety of functionalities, among them the organic carbonyl functionality, with which it reacts in a Wittig-like manner to yield polymeric $(Me_3CCH_2)_3Ta{=}O$ and the expected olefin. [18] All of these properties are reminiscent of phosphorus ylides [13] and further suggest that the alkylidene ligand is present in its closed shell dianionic configuration and that tantalum therefore is in the 5+ oxidation state. It cannot be overstated how important to the development of high oxidation state alkylidene chemistry is the principle of employing bulky covalently bound ligands in order to stabilize pseudotetrahedral species against bimolecular decomposition, and the investigation of neopentyl complexes in particular.

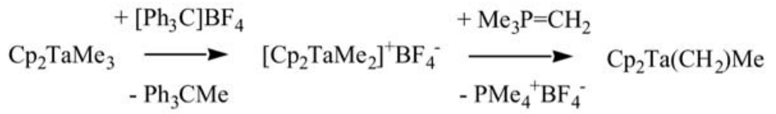


(2)

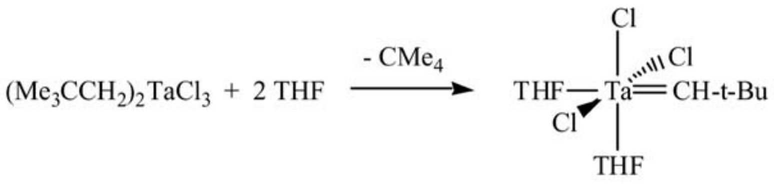
The neopentyl ligand was chosen over the more popular and less expensive trimethylsilylmethyl ligand on the basis of the fact that reactions involving trimethylsilylmethyl reagents and Nb and Ta halides were known to yield dimeric species with the formulation $[(Me_3SiCH_2)_2M(CSiMe_3)]_2$. [19,20] As a consequence of the longer C-Si bonds, the trimethylsilyl ligand does not produce as crowded an environment at a metal center, and consequently is also more susceptible to *inter*molecular α hydrogen abstraction reactions. $(Me_3SiCH_2)_3Ta{=}CHSiMe_3$ can be prepared below -30°C, but it readily decomposes bimolecularly to yield $[(Me_3SiCH_2)_2Ta(CSiMe_3)]_2$ above ~0°C. [21,22]

In an effort to stabilize tantalum methyl species by employing more bulky "ancillary" ligands, the reaction between $TaMe_3Cl_2$ and two equivalents of TlCp was employed to give Cp_2TaMe_3. [23] Addition of trityl tetrafluoroborate to Cp_2TaMe_3 led to what could be called a "tantalonium" salt, as shown in Eq. 3. This cationic species was deprotonated by a phosphorus ylide to yield the hoped-for "tantalum ylide," $Cp_2Ta(CH_2)Me$. [23] (Note that $[Cp_2TaMe_2]^+$ is a better acid than PMe_4^+!) This methylene complex was stable enough at room temperature to isolate and characterize completely. It also could be demonstrated convincingly that it behaved as if the $Ta{=}CH_2$ bond were polarized $\delta+$ on Ta and $\delta-$ on the methylene carbon. For example, $Cp_2Ta(CH_2)Me$ would react with $AlMe_3$ to yield $Cp_2TaMe(CH_2AlMe_3)$; $Cp_2TaMe(CH_2AlMe_3)$ also could be prepared by treating Cp_2TaMe_3 with $AlMe_3$ in toluene, a reaction that is proposed to yield $[Cp_2TaMe_2][AlMe_4]$ in the first step, followed by deprotonation of a Ta-Me group by an Al-Me group. It also was shown to decompose in a *bimolecular* fashion to yield an ethylene complex. [24] It was clear from X-ray studies [25] (and later neutron diffraction studies [26]) that the tantalum-carbon bond was a full double bond, judging from the difference between the Ta-Me bond length (2.25Å) and the $Ta{=}CH_2$ bond length (2.02Å). The metal is in its highest possible oxidation state in this circumstance also. Therefore, one can argue that an alkylidene ligand bound to a metal such as Ta(5+) is isoelectronic with an imido (M=NR) or an oxo (M=O) ligand. [27]

It soon became apparent that neopentyl ligands in d^0 complexes of Ta promote steric crowding and consequently are subject to a distortion that opens up the $Ta\text{-}C_\alpha\text{-}C_\beta$ angle and pushes the α hydrogens toward the metal. In a highly electrophilic metal complex such as hypothetical $Ta(CH_2CMe_3)_5$, which has a total of only 10 electrons in bonding and nonbonding metal-based orbitals, the electrons in a CH_α bond are attracted toward the metal and the α hydrogen thereby "activated" (Eq. 2). As a consequence H_α becomes relatively acidic. (Interaction of a C-H electron pair with the metal later came to be called an α "agostic" interaction. [28]) Migration of an α proton to a nearby nucleophilic neopentyl α carbon atom generates alkane and the Ta=C bond. This proposed "α hydrogen abstraction," can be viewed as essentially an intramolecular deprotonation reaction in this case. However, metal-carbon bond homolysis followed by abstraction of a hydrogen radical is a viable alternative in a crowded circumstance, and tends to be the preferred result when the metal-carbon bond and the presumed agostic interaction are weaker, e.g., for niobium. Therefore, α hydrogen abstraction tends to be observed in an intramolecular fashion most often for Ta, Mo, W, and Re. [29] The methyl ligand is the least sterically protected and the least prone to be activated intramolecularly via an α agostic interaction. Therefore the conditions that are required to induce α abstraction in a methyl complex often result in even more rapid decomposition of the methylene species that is formed; observation of methylene species by an α abstraction reaction therefore is rare. Finally, α hydrogen abstraction can be induced by addition of a base. For example, $Ta(CH_2CMe_3)_2Cl_3$ is stable in pentane, but rapidly turns purple in THF as 14 electron $Ta(CHCMe_3)(THF)_2Cl_3$ (Eq. 4) is formed quantitatively. [30] It is presumed that binding of THF to the tantalum center leads to an increase in steric crowding and to subsequent acceleration of the α hydrogen abstraction reaction.



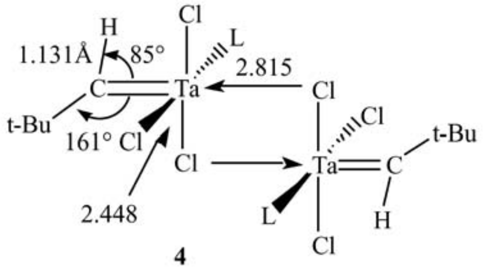
$$Cp_2TaMe_3 \xrightarrow[\text{- }Ph_3CMe]{+\ [Ph_3C]BF_4} [Cp_2TaMe_2]^+BF_4^- \xrightarrow[\text{- }PMe_4{}^+BF_4^-]{+\ Me_3P{=}CH_2} Cp_2Ta(CH_2)Me \qquad (3)$$



(4)

An important feature of "high oxidation state" alkylidene complexes that do not attain an 18 electron count about the metal was documented in a neutron diffraction study of $[Ta(CH\text{-}t\text{-}Bu)Cl_3(PMe_3)]_2$ (**4**). [31] In this compound the Ta=C bond (1.90 Å) was found to be ~0.10 Å shorter than expected, the Ta=C-C angle to be 161°, and the Ta=C-H angle to be only 85°, i.e., the alkylidene is distorted through an α agostic interaction, one that is driven sterically to some extent by the bulk of the t-butyl group. Therefore H_α could be said to be bonded to an orbital that has high p character on carbon, as if C_α were essentially sp hybridized. This is the reason why both J_{CH} (~90 Hz) and ν_{CH} (~2600 cm^{-1})

are unusually low in this, and in a variety of other electron deficient d^0 alkylidene complexes. The Ta-alkylidene bonding in this situation can be viewed either in terms of a three-center, six electron bond (**A**) or in the extreme even as a protonated triple bond (**B**). The short Ta-C bond can be rationalized on the basis of either description **A** or **B**. On the basis of description **B**, especially, one would expect the α proton in neopentylidene complexes of tantalum to be relatively acidic. In fact, it was found quite early that the reaction between $Ta(CH\text{-}t\text{-}Bu)(CH_2\text{-}t\text{-}Bu)_3$ and butyllithium gave "$[(Me_3CCH_2)_3Ta{\equiv}CCMe_3]^-$" (Eq. 5). [32] Other (neutral) tantalum alkylidyne complexes formed by α hydrogen abstraction reactions followed, [33,34] although the alkylidyne ligand became much more prominent in the chemistry of Mo, W, and Re.



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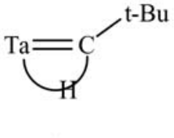
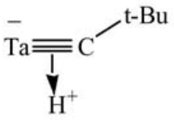


A



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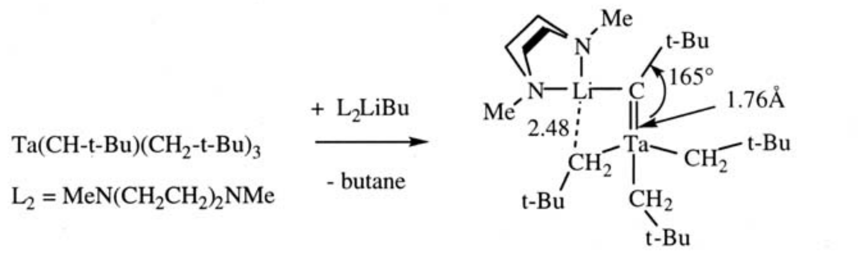


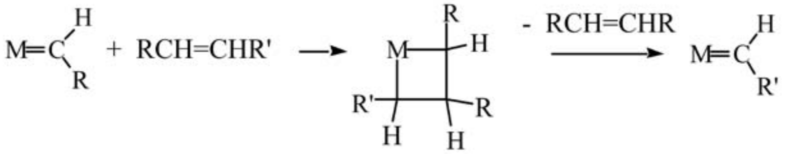
(5)

In the 1970's an intense interest in the olefin metathesis reaction [35] served as a driving force for research concerning metal-carbon double bonds. In its simplest form the olefin metathesis reaction consists of a redistribution of alkylidene components of olefins (Eq. 6). It was known to be promoted by tungsten, molybdenum, and rhenium, although at the time the catalytic reactions were "black boxes," with nothing known about the mechanism or the detailed nature of the catalyst. Among the proposals was one that consisted of a reaction between an alkylidene complex (or carbene complex at that time) and an olefin to give a metallacyclobutane intermediate, from which an olefin could be lost and a new alkylidene complex formed, [36] as shown in

Eq. 7. Although tantalum was not among the metals that were found to be most active for metathesis of olefins, the radically new tantalum alkylidene complexes offered the first opportunity to test the proposed mechanism of olefin metathesis with an observable alkylidene complex.

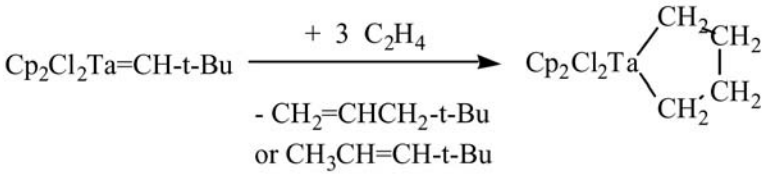
$$2\ \mathrm{RCH{=}CHR'} \rightleftharpoons \mathrm{RCH{=}CHR} + \mathrm{R'CH{=}CHR'}\ . \qquad (6)$$

(cis and trans equilibrated also)



(7)

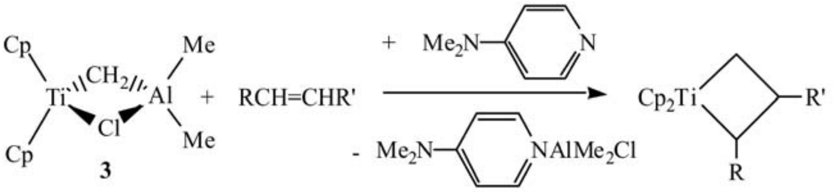
Among the first species to be explored was TaCp(CH-t-Bu)Cl_2. [37] It reacts with terminal olefins to give products of rearrangement of an intermediate tantalacyclobutane complex, plus tantalacyclopentane complexes formed from the incipient tantalum(III) complex and two equivalents of olefin (e.g., as shown in Eq. 8). [38] A second key observation was that while complexes such as Ta(CH-t-Bu)$Cl_3(PMe_3)_2$ reacted with olefins similarly to yield products of rearrangement of unobservable intermediate tantalacyclobutane complexes, complexes such as Ta(CH-t-Bu)Cl(PMe_3)(O-t-Bu$)_2$ led to productive metathesis of cis-2-pentene. [39,40] This was the first time that productive metathesis of a simple olefin starting with a well-characterized carbene complex had been observed. Unfortunately, the analogous intermediate ethylidene and propylidene complexes could *not* be observed; they apparently rearranged quickly to give ethylene and propylene, respectively. Presumably this is the reason (in part) why tantalum catalysts for the olefin metathesis reaction could not be prepared using various recipes that are successful for Mo or W. [35]



(8)

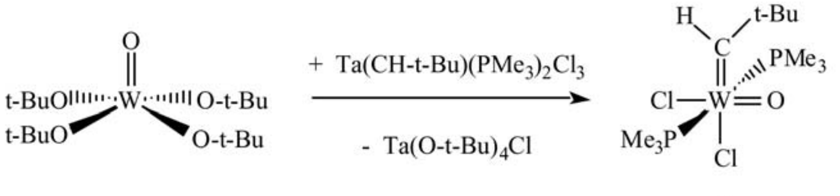
Metallacyclobutane complexes of titanium began to make an appearance in 1980. [41-44] (A titanacyclo*butene* complex was prepared from **3** in 1979.

[45,46]) It was found that titanacyclobutanes could be prepared by removing the aluminum from **3** with a strong Lewis base in the presence of an olefin, as shown in Eq. 9. These metallacycles were stable with respect to rearrangement to an olefin via a β hydride process, and showed a tendency to generate intermediate alkylidene complexes *in situ*. They ultimately proved to be useful as catalysts for the ring opening metathesis polymerization of a variety of strained olefins. [47,48] It should be noted that the "masked" titanium methylene complex **3** (Eq. 1) was shown to be a catalyst for the non-productive, degenerate metathesis of terminal olefins (methylene exchange). [45]



(9)

Even though alkoxides appeared to "turn on" metathesis by tantalum alkylidenes, [39] there was considerable doubt as to what alkylidene complexes of tungsten might be prepared, i.e., what combination of ligands would successfully maintain the 6+ oxidation state. It also was questionable as to whether alkylidenes that contain one or more protons on the β carbon atom would be stable with respect to rearrangement of that alkylidene to an olefin. One compound that was thought to be a plausible target (before the importance of a pseudotetrahedral coordination sphere was realized) was $(Me_3CO)_4W{=}CHCMe_3$. The reaction shown in Eq. 10 was an attempt to prepare that compound via exchange of an oxo ligand on tungsten with an alkylidene ligand on tantalum. [49,50] Formation of **5** instead suggested that the oxo/alkylidene combination was a favorable one. The 18 electron count in **5** is a consequence of π donation of one electron pair on the oxo ligand to the metal. Compound **5** turned out to be a catalyst for the metathesis of terminal, as well as internal olefins (in benzene), but only in the presence of a trace of $AlCl_3$. For the first time, the new alkylidene complexes could be observed; in several cases, including $W(O)(CH_2)(PMe_3)_2Cl_2$, they could be isolated. [39] In the presence of one equivalent of $AlCl_3$ in dichloromethane $W(O)(CH\text{-}t\text{-}Bu)(PEt_3)_2Cl_2$ yielded a complex that appeared to be $[W(O)(CH\text{-}t\text{-}Bu)(PEt_3)_2Cl][AlCl_4]$, and in the presence of two equivalents of $AlCl_3$ an analogous dicationic species. [51] Both would metathesize terminal and internal olefins in dichloromethane slowly (up to ~100 turnovers in 24 h). It was also shown that $W(O)(CH\text{-}t\text{-}Bu)(PEt_3)Cl_2$ could be isolated and that it would metathesize cis-2-pentene, although its activity was short-lived. [49]



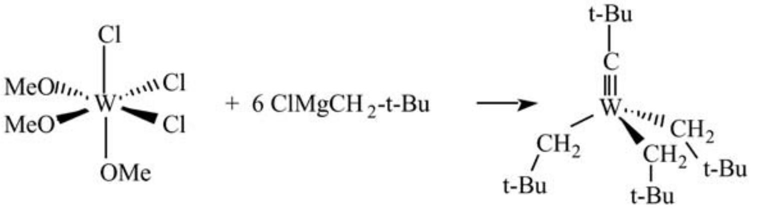
5

(10)

At approximately this time, important advances were made in the laboratories of J. A. Osborn at Strasbourg. [52-56] He found that addition of various Lewis acids to oxo complexes yielded metathesis catalysts. [56] These were found to be transformed into oxo-free alkylidene complexes, $W(CH\text{-}t\text{-}Bu)(OCH_2\text{-}t\text{-}Bu)_2Cl_2$ (Eq. 11). [52] These in turn were transformed by Lewis acids into cations of the type $[W(CH\text{-}t\text{-}Bu)(O\text{-}t\text{-}Bu)_2X]^+$ (e.g., as AlX_4^- salts) that were fully active for metathesis of internal olefins and which produced observable alkylidene intermediates. [52] These were the first studies in which *rapid* metathesis of olefins analogous to classical "black box" systems was observed, along with new alkylidenes, starting with a known d^0 alkylidene complex. Alkoxides (usually neopentoxides) were found to be crucial to the preparation and reactivity of tungsten-based metathesis catalysts of this type. Other important "oxo-free" tungsten alkylidene catalysts were developed later in the laboratories of Basset. [57,58]

$$W(OAlCl_3)(OCH_2R)_2(CH_2R)_2 \xrightarrow[-\ CH_3R]{-\ [AlOCl]_x} \underset{R\,=\,t\text{-}Bu}{W(CHR)(OCH_2R)_2Cl_2} \qquad (11)$$

In 1978 it was reported that reactions between neopentyllithium and WCl_6 or $MoCl_5$, "reducing" conditions analogous to those employed to prepare olefin metathesis catalysts *in situ*, [35] gave extraordinary compounds with the formula $(Me_3CCH_2)_3M{\equiv}CCMe_3$ in low yields (25% and 15%, respectively). [59] These were the first high oxidation state alkylidyne complexes, [60,61] which were to play more than one important role in the development of alkylidene chemistry. A higher yield (55%) route to the tungsten complex was developed later, as shown in Eq. 12. $(Me_3CCH_2)_3W{\equiv}CCMe_3$ is a volatile, yellow, crystalline compound that melts at approximately 70°C and that can be distilled *in vacuo*, properties that are reminiscent of $(Me_3CCH_2)_3Ta{=}CHCMe_3$. α Abstraction could be induced in $W(C\text{-}t\text{-}Bu)(CH_2\text{-}t\text{-}Bu)_3$ in neat PMe_3 to yield a compound in which a neopentyl, a neopentylidene, and a neopentylidyne ligand are found in the same complex (Eq. 13). The tungsten-carbon bond lengths, W-C-C bond angles, and magnitude of coupling of C_α to ^{183}W are all consistent with the multiplicity of the metal-carbon bond in question.



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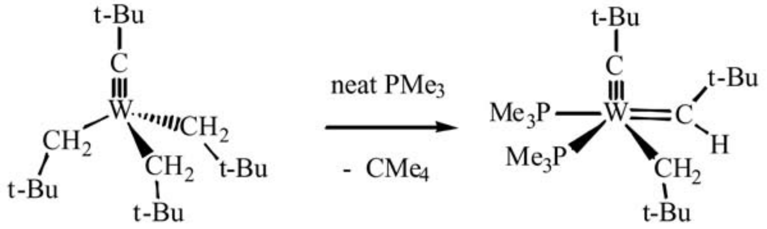


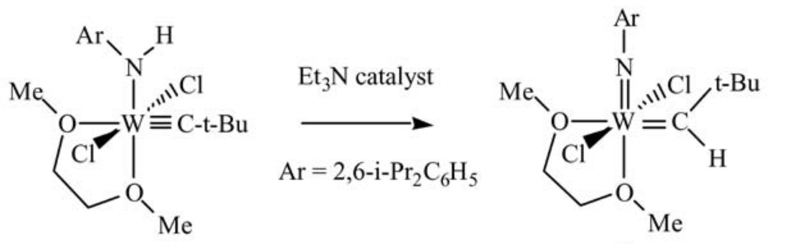
(13)

W-C = 2.26 Å W-C-C = 125° J_{CW} = 80 Hz
W=C = 1.98 Å W=C-C = 150° J_{CW} = 120 Hz
W≡C = 1.81 Å W≡C-C = 175° J_{CW} = 210 Hz

$$W(O)(CH\text{-}t\text{-}Bu)(PEt_3)_2Cl_2 \xrightarrow[-\ C_2Cl_4\ -\ Et_3PHCl]{+\ C_2Cl_6} W(C\text{-}t\text{-}Bu)(Et_3P{=}O)Cl_3 \tag{14}$$

Investigation of the reaction between $W(O)(CH_2)(PEt_3)_2Cl_2$ and hexachloroethane shown in Eq. 14 led to the formation of trichloride compounds that contained a neopentylidyne ligand. [62] Several key observations were made. First, $[Et_4N][W(C\text{-}t\text{-}Bu)Cl_4]$ could be prepared by treating $W(C\text{-}t\text{-}Bu)(CH_2\text{-}t\text{-}Bu)_3$ with ethereal HCl in the presence of tetraethylammonium chloride in ether. Secondly, the reaction between $[Et_4N][W(C\text{-}t\text{-}Bu)Cl_4]$ and three equivalents of lithium t-butoxide gave $W(C\text{-}t\text{-}Bu)(O\text{-}t\text{-}Bu)_3$, a pale yellow, pentane soluble, thermally stable, and sublimable species. Thirdly, several of these compounds, especially W(C-t-Bu)(O-t-Bu)$_3$, would react rapidly with alkynes to give new analogous alkylidyne species; in fact, W(C-t-Bu)(O-t-Bu)$_3$ would metathesize unsymmetric internal alkynes with remarkable facility. (Metathesis of alkynes was known, [63] but the reaction was slow and the active species were not known. However, Katz had suggested [64] that some metal-carbon triple bond should be able to add to carbon-carbon triple bonds to produce metallacyclobutadiene intermediates in such a reaction.) Bulky alkoxide ligands were again an important feature of the chemistry. The chemistry of alkylidyne complexes of tungsten developed rapidly. [61] Other trialkoxide neopentylidyne complexes of tungsten were soon prepared and shown to be successful initiators of alkyne metathesis. Tungstacyclobutadiene intermediates were not observed in the tri-t-butoxide system, but trigonal bipyramidal tungstacyclobutadiene complexes were observed when the alkoxide was more electron-withdrawing, e.g., OR = O-2,6-i-Pr$_2$C$_6$H$_3$ (OAr), OCH(CF$_3$)$_2$, or OCMe(CF$_3$)$_2$. A wide variety of molybdenum neopentylidyne complexes of the type Mo(C-t-Bu)(OR)$_3$ (OR = O-t-Bu, OCMe(CF$_3$)$_2$, OCMe$_2$(CF$_3$), or OAr) were also prepared from Mo(C-t-Bu)Cl$_3$(dme). [65] The OCMe(CF$_3$)$_2$, OC(CF$_3$)$_3$, and OAr complexes proved to be excellent catalysts for the metathesis of internal alkynes, but molybdacyclobutadiene complexes were rarely observed. The lessons learned from studies of alkylidyne complexes and alkyne metathesis, in particular the dramatic effect on the reaction upon changing the electron-withdrawing ability of the alkoxide ligands, were invaluable for the further development of alkylidene chemistry of Mo and W. [66]

In order to slow the intermolecular decomposition of a tungsten alkylidene complex, syntheses of alkylidene complexes that contain a sterically bulky imido ligand in place of an oxo ligand, in particular N-2,6-i-Pr$_2$C$_6$H$_3$, were designed. In this effort W(C-t-Bu)Cl$_3$(dme) played an important role. Treatment of W(C-t-Bu)Cl$_3$(dme) with ArNH(TMS) (where Ar = 2,6-i-Pr$_2$C$_6$H$_3$) yielded W(C-t-Bu)(NHAr)Cl$_2$(dme), which could be converted into the related imido alkylidene complex **6** by moving an α proton from nitrogen to carbon with the aid of a base, as shown in Eq. 15. [67,68] The movement of a proton from nitrogen to carbon is distantly related to the α abstraction reactions that gave rise to alkylidene and alkylidyne complexes. Addition of bulky alkoxide ligands to **6** (OR = OCMe$_3$, OCMe(CF$_3$)$_2$, O-2,6-i-Pr$_2$C$_6$H$_3$, etc.; Eq. 16) gave the four-coordinate 14 electron species **7** (assuming donation of an electron pair from the imido ligand); for steric reasons neither dimethoxyethane nor chloride is retained in the coordination sphere of **7**. The sterically bulky nature of all four ligands in four-coordinate W(NAr)(CHCMe$_3$)(OR)$_2$ also prevented bimolecular decomposition of the electronically unsaturated four-coordinate neopentylidene complex, a theme that harkens back to the thermally stable compounds $(Me_3CO)_3W{\equiv}CCMe_3$ and $(Me_3CCH_2)_3Ta{=}CHCMe_3$.



6

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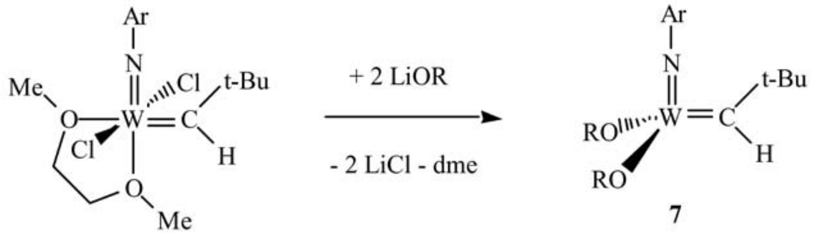
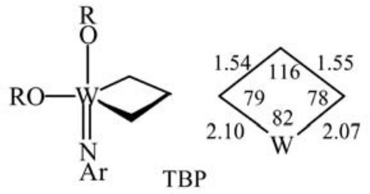
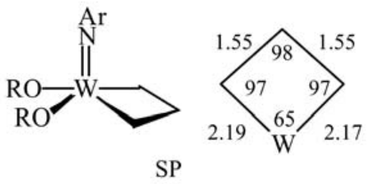


7

(16)

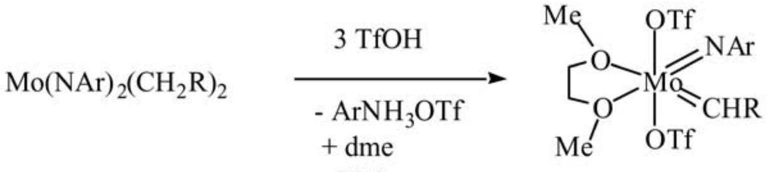


8a



8b

Compounds of type **7** proved to be remarkably active catalysts for the metathesis of internal olefins. [44,68,69] The activity of such species for the metathesis of ordinary internal olefins (e.g., *cis*-2-pentene) appeared to maximize for the $OCMe(CF_3)_2$ species. New alkylidene complexes such as $W(NAr)(CHPh)[OCMe(CF_3)_2]_2$ could be isolated, and in some cases trigonal bipyramidal (TBP) tungstacyclobutane intermediates were stable enough to be observed and isolated. On the basis of this work it was proposed that the rate of reaction of alkylidene complexes with olefins correlated directly with the electron-withdrawing ability of the alkoxide, as found in acetylene metathesis systems described earlier. In many circumstances trigonal bipyramidal or square pyramidal tungstacyclobutane intermediates could be observed. [44] In any system in which ethylene could be formed, unsubstituted metallacycles could form, e.g., trigonal bipyramidal **8a** and/or square pyramidal **8b**. They proved to be especially stable toward loss of ethylene for a variety of alkoxides. Methylene complexes of the type $W(NAr)(CH_2)(OR)_2$ could not be observed because of their high reactivity and tendency to decompose readily in a bimolecular fashion. However, alkylidenes that contain β protons could be observed and did not appear to rearrange readily to olefins.



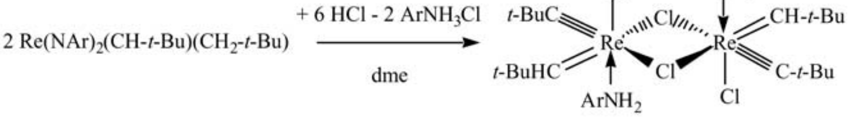
9

(17)

Attention then was focussed on molybdenum [65,70] in the hope that molybdenum would be more tolerant of functionalities than tungsten; molybdenum also was considerably cheaper than tungsten. Molybdenum complexes analogous to **7** could be prepared from $Mo(C\text{-}t\text{-}Bu)Cl_3(dme)$, but since $(Me_3CCH_2)_3Mo{\equiv}CCMe_3$ (from which $Mo(C\text{-}t\text{-}Bu)Cl_3(dme)$ was prepared) could not be prepared on a large scale reliably, a new approach was clearly needed. The solution turned out to be the reaction shown in Eq. 17 (R = t-Bu or CMe_2Ph). [71] This reaction is remarkable for several reasons, one of them being the relative stability of **9** toward additional triflic acid. The intermediate in the reaction is believed to be $Mo(NAr)(CH_2\text{-}t\text{-}Bu)_2(OTf)_2$, a five-coordinate species that contains two neopentyl groups and three other bulky ligands, and in which the metal is undoubtedly highly electron deficient. Therefore, α hydrogen abstraction to give $Mo(NAr)(CH\text{-}t\text{-}Bu)(OTf)_2$ is facile. The four-coordinate species then coordinates dimethoxyethane strongly, leading to an 18 electron species if electron pair donation from the imido ligand is included. Although **9** is relatively unreactive toward triflic acid, it is relatively reactive toward even alkoxides that are poor nucleophiles (e.g., $LiOCMe(CF_3)_2$). This reaction sequence continues to be the favored method of synthesis of a wide variety of molybdenum imido neopentylidene or neophylidene ($Mo{=}CHCMe_2Ph$) complexes of the type $Mo(CH\text{-}t\text{-}Bu)(NAr)(alkoxide)_2$. A variety of other imido groups have been employed, [72] a fact that becomes important later when a fine tuning of catalysts, e.g., for asymmetric metathesis reaction (see later), is desired. Molybdenum complexes of the type $Mo(NAr)(CHCMe_3)(OR)_2$ also proved to be highly active for the metathesis of olefins, especially when the alkoxide ligand is the highly electron-withdrawing $OCMe(CF_3)_2$ ligand. One advantage of Mo versus W is that molybdacyclobutane intermediates generally lose olefin more readily than tungstacyclobutane intermediates; therefore molybdacyclobutanes cannot serve as sinks or traps in a metathesis reaction.

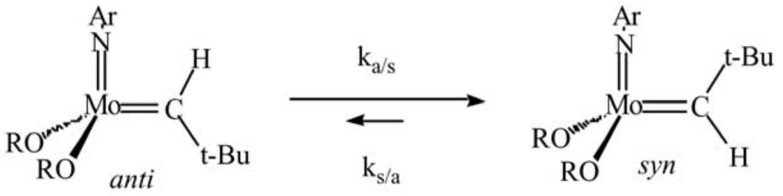
By this time it had become clear that electron deficient, reactive, four-coordinate species that contain multiple metal-carbon bonds and bulky ligands could be synthesized and isolated. But could this chemistry be extended to "Re(VII)," and if so, what would the Y^{3-} ligand be in (for example) a hypothetical $Re(Y)(CHCMe_3)(OR)_2$ complex, and how would that species be prepared? The only sterically protected Y^{3-} ligand that seemed feasible was an alkylidyne ligand. Indeed $Re(CHCMe_3)(CCMe_3)(CH_2CMe_3)_2$ was found to be a stable species, [73,74] one that completed the list of neutral pseudotetrahedral high oxidation state complexes of Ta, Mo, W, and Re that are derived only from neopentyl ligands. A complex that contained alkoxides in place of two neopentyl groups, $Re(CH\text{-}t\text{-}Bu)(C\text{-}t\text{-}Bu)(O\text{-}t\text{-}Bu)_2$, [73,74] was prepared, but it proved unreactive toward representative olefins. (At that time the importance of electron-withdrawing alkoxides in metathesis was not fully appreciated.) The reactions shown in Eq. 18 and 19 ultimately led to starting materials for the synthesis of $Re(CHCMe_3)(CCMe_3)(OR)_2$ complexes in which OR could be varied widely. [75-77] The reaction in Eq. 19 is remarkable in the degree to which α protons on carbon and nitrogen are mobile, and because in this circumstance the lowest energy form contains a rhenium-carbon triple bond, not a rhenium-nitrogen pseudo triple bond. $Re(CHCMe_3)(CCMe_3)[OCMe(CF_3)_2]_2$ complexes ultimately proved to be active for olefin metathesis, although the reactions are not as rapid as those for known Mo and W species, [77] and there appeared to be some new complications in some circumstances. [78]

$$Re(NAr)_2(py)Cl_3 \xrightarrow[-\ 1.5\ ZnCl_2\ -\ py\ -\ CMe_4]{1.5\ Zn(CH_2\text{-}t\text{-}Bu)_2} \underset{(Ar = 2,6\text{-}i\text{-}Pr_2C_6H_3)}{Re(NAr)_2(CH\text{-}t\text{-}Bu)(CH_2\text{-}t\text{-}Bu)} \qquad (18)$$



(19)

An important feature of all four-coordinate Mo, W, and Re alkylidene complexes is the formation of *syn* isomers, in which the alkylidene substituent points toward the imido (Mo or W) or alkylidyne (Re) ligand, or *anti* isomers, in which the alkylidene substituent points away from the imido or alkylidyne ligand (e.g., Eq. 20). The *syn* isomer is normally the one observed in the solid state and in solution in Mo or W complexes. However, the rate at which these two isomers interconvert by rotation about the metal-carbon bond in Mo and W species can vary dramatically as a function of the OR ligand, from $k_{s/a}$ ~1 s^{-1} in the case of OR = $OCMe_3$ to $k_{s/a}$ ~10^{-5} s^{-1} for OR = $OCMe(CF_3)_2$ in Mo imido complexes. [79] Therefore both *syn* and *anti* species must be considered in any reaction scenario. Important questions include whether a reaction involving the alkylidene ligand in either isomer is faster or slower than the rate of interconversion of *syn* and *anti* isomers, and whether one isomer is much more reactive than the other.



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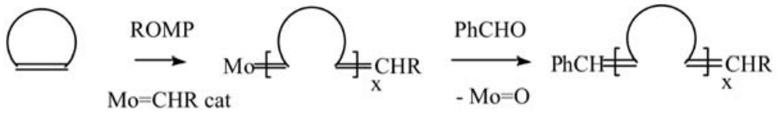
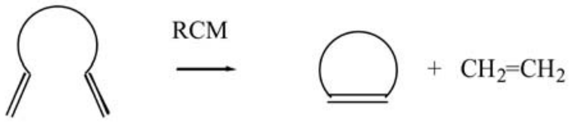


(21)

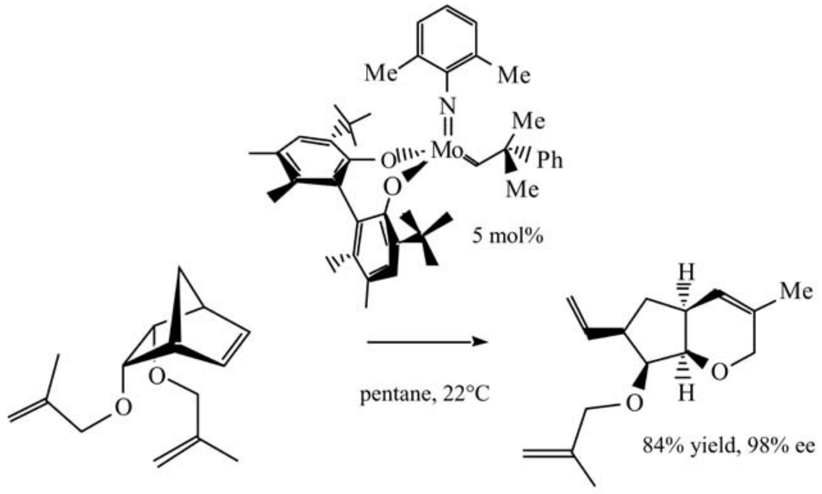
Several variations of the basic metathesis reaction have been explored with $Mo(NAr)(CHCMe_3)(OR)_2$ catalysts. [69,80] In Ring-Opening Metathesis Polymerization (or ROMP) reactions (first investigated using titanacyclobutane complexes [47,48] and later tungsten imido alkylidenes [81] as catalysts) a cyclic olefin such as a norbornene is attacked by the alkylidene to give a metallacyclobutane that opens to give a new alkylidene into which the cyclic species has been incorporated. [47,81-84] If this step is irreversible the new alkylidene can react with more cyclic olefin in a similar manner to form a polymer having repeating units that consist of the “opened” cyclic olefin (Eq. 21). If no intermediate of this type decomposes during the process then such ROMP reactions are “living.” Consequently another monomer can be added after consumption of the first monomer and block copolymers prepared. The polymer also can be cleaved from the metal in a Wittig-like reaction with a benzaldehyde. One of the more enlightening fundamental findings in this area was the elucidation of the origin of *cis* or *trans* double bonds in the ROMP polymer, and control of tacticity, i.e., the stereochemical relationship between neighboring repeat units in the ROMP polymer. It was found that the *syn* isomer gave rise to *cis* double bonds in the polymer, while the *anti* isomer gave rise to *trans* double bonds in the polymer. [79] It was also shown that catalysts of the type Mo(NAr)($CHCMe_3$)(rac-diolate), where rac-diolate is a racemic chiral diolate such as a binaphtholate, can control the tacticity of the polymer to a remarkable degree by enantiomorphic site control. [85] In the process it also was proven that an all *cis* polymer was isotactic, while an all *trans* polymer was syndiotactic. [86] Perhaps most interesting from a fundamental point of view was the fact that the *anti* isomer in one circumstance was estimated to be ~10^5 times more reactive than the *syn* isomer, even though the *anti* isomer could not be observed at any point before or during the ROMP reaction. [79] The first enantiomerically pure molybdenum imido alkylidene complex was prepared in 1993 and employed for ROMP, [86] although these “TADDOL” derivatives did not appear to be as stable as 3,3’-disubstituted biphenoxide or binaphtholate derivatives.

Another important variation of a metathesis reaction is Ring-Closing Metathesis or RCM, a simplified generic example of which is shown in Eq. 22. RCM reactions catalyzed by Mo(NAr)($CHCMe_2Ph$)[$OCMe(CF_3)_2]_2$ were shown in 1992 to be a remarkably facile and “clean” means of forming a variety of cyclic olefins. [87] Many papers have appeared in the last several years in which Mo(NAr)($CHCMe_2Ph$)[$OCMe(CF_3)_2]_2$ is the catalyst for RCM, [80] although the catalyst of choice for many RCM reactions since ~1995 has been one of a variety of ruthenium carbene complexes, [88-95] which are best viewed as Ru(II) species.



(22)

Important recent additions to the arsenal of molybdenum catalyst systems are those that contain a variety of enantiomerically pure biphenolate or binaphtholate ligands [85] and one of several different imido ligands. Such species have been shown to catalyze a variety of enantioselective ring-closing, ring-opening, and cross metathesis reactions efficiently. [96] An example is shown in Eq. 23. [96f] (Analogous enantiomerically pure catalysts that contain the {(R,R)-1,2-$[OC(CF_3)_2CH_2]_2C_5H_8\}^{2-}$ ligand were found to be inefficient catalysts in several kinetic resolutions of comparable substrates. [97,98]) The modular nature of molybdenum catalysts (i.e., the ability to vary the imido and diolate ligands) is an important asset that leads to maximum efficiency. Rapid interconversion of *syn* and *anti* isomers [96e] allow both isomers to be available for enantioselective reactions. Asymmetric metathesis reactions hold considerable promise as a means of relatively quickly preparing enantiomerically pure organic compounds from simple starting materials; in many cases such products could not be prepared readily by any other combination of methods. [96h]



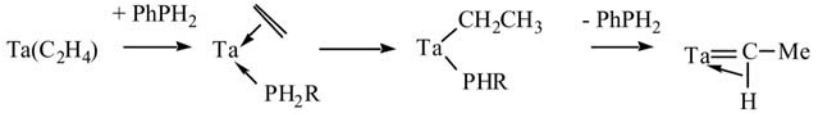
(23)

Molybdenum imido alkylidene complexes also have been employed for a variety of other catalytic reactions of interest to the organic or polymer chemist, among them selective cross-couplings of olefins, [99] polymerization of terminal alkynes, [100-102] step-growth polymerization of dienes, [103,104] and cyclopolymerization of 1,6-heptadiynes. [105-107]

It is clear that electron-withdrawing alkoxides in $M(NAr)(CHR)(OR')_2$ complexes dramatically increase the rate of reaction of an olefin with the M=CHR bond. In fact, no other X ligands in $M(NAr)(CHR)X_2$ complexes are as successful as alkoxides for sustained metathesis activity, [66] either because they are not bulky enough to stabilize an electron deficient metal center and prevent bimolecular decomposition (e.g., halides) or because they donate too much electron density to the metal in a σ and/or π fashion (e.g., amides or thiolates). A recent example is Mo(NAr)(CHR)(diamide) where the diamide is a N,N'-disubstituted-2,2'-bisamido-1,1'-binaphthyl ligand; no ready reaction was observed between this complex and ethylene or even benzaldehyde. [108]

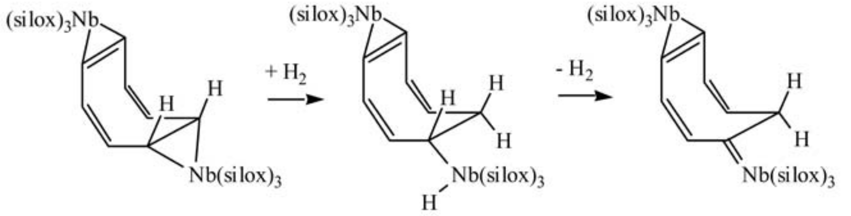
Alkylidene complexes are now known for all metals in groups 4, 5, and 6, plus rhenium. For example, it was shown that "$Cp_2Ti(CH_2)$" could be trapped with a phosphine to give species of the type $Cp_2Ti(CH_2)(PR_3)$, [44,109] the first titanium alkylidene complex of this general type having been observed in 1986. [110] By far the most rare are alkylidene complexes of Zr, [111-113] Hf, [114] V, [115-117] and Cr [118,119] In the vast majority of cases alkylidene complexes have been prepared by α hydrogen abstraction reactions, although other methods have been devised (see below), and some of them have been unpredictable. [119] Only complexes that contain Mo, W, or Re will metathesize olefins in any sustained manner. Few high oxidation state alkylidene complexes have been employed for stoichiometric organic reactions, the exception being titanium alkylidenes of the type "$Cp_2Ti(CHR)$," which are generated *in situ*. Such intermediates have become important reagents in organic chemistry in the last ten years, especially for Wittig-like reactions of the alkylidene. [120-127]

High oxidation state alkylidene complexes have been prepared by methods other than α abstraction, two examples being alkylidene transfer from phosphorus [115,128-130] and rearrangement of a 3,3-diphenylcyclopropene. [131,132] Some recent results suggest that it is possible to prepare d^0 alkylidene complexes from olefins themselves, the very opposite reaction that was thought in the past to limit the stability of alkylidenes that contain β hydrogen atoms in some circumstances. For example, the ethylidene complex, $[N_3N]Ta{=}CHMe$ ($[N_3N]^{3-} = [(Me_3SiNCH_2CH_2)_3N]^{3-}$) has been prepared by a phenyl phosphine catalyzed rearrangement of ethylene via the mechanism shown in Eq. 24. [133] Rearrangement of an olefin to an alkylidene was proposed to be favorable in this case because of the strong α agostic interaction in all alkylidene complexes of this type, as suggested by the dramatically low values for J_{CH} (~75Hz). The bimetallic alkene/alkyne complex shown in Eq. 25 has been shown to rearrange to the bimetallic alkylidene/alkyne complex upon heating, a conversion that also is catalyzed by molecular hydrogen. [134] It was also found that $(silox)_3Nb$(1-butene) rearranged to $(silox)_3Nb$(1-butylidene) in 8.5 h at 155 °C!



(24)

The mechanism or mechanisms are believed to involve formation of an alkyl followed by selective α hydrogen abstraction to give an alkylidene, as shown in Eq. 25, although it is not yet known what factor or factors tip the energetic balance in favor of the alkylidene in these examples. Selective α hydrogen elimination and abstraction have been observed in other circumstances, especially those in which β processes are sterically blocked. [135-138] These unusual findings lend credence to the possibility that alkylidene complexes might be able to form directly from olefin complexes and reduced metal complexes in some circumstances.



(25)

What I have attempted to trace here are highlights of the discovery and development of high oxidation state alkylidene complexes. The first review of high oxidation state alkylidene complexes was published in 1986. [29] A second review appeared in 1991. [44] Various aspects of chemistry involving d^0 alkylidene complexes have been covered in other articles. [66,69,80,83,139] A comprehensive review of d^0 alkylidene and alkylidyne complexes in the last decade (1991 to 2001) has also appeared recently. [119] Although theoretical studies of high oxidation state alkylidene complexes and olefin metathesis reactions catalyzed by them have not been discussed here, such studies have been numerous and have played a significant role in understanding high oxidation state species and their reactions. [140]

In order that the reader may gain some perspective I have listed in Table 1 the most significant developments in high oxidation state alkylidene chemistry from my point of view according to the year when the first report was published. I was aware of the actual timing of Tebbe's contributions and have made that clear in the text.

ACKNOWLEDGEMENTS

I thank the chemistry division of the National Science Foundation for supporting research on multiple metal-carbon bonds for many years and the many graduate and postdoctoral students who have dedicated their time and talent to this area of research.

Table 1. Some significant developments in the area of high oxidation state alkylidene chemistry.

1974	Synthesis of Ta(CH-t-Bu)(CH_2-t-Bu)$_3$	[17]
1975	Synthesis of $Cp_2Ta(CH_2)(CH_3)$	[23,25]
	Deprotonation of a Ta neopentylidene to give a Ta neopentylidyne	[32]
1976	Wittig-like reactivity of Ta and Nb alkylidenes	[18]
1978	Synthesis of $Cp_2Ti(CH_2AlMe_2Cl)$	[10]
	Bimolecular decomposition of Ta methylene	[24]
1979	Degenerate metathesis of terminal olefins by $Cp_2Ti(CH_2AlMe_2Cl)$	[45]
	Neutron diffraction confirmation of alkylidene H_α interaction with metal	[31]
	Reaction of Ta alkylidene with olefins and metallacycle rearrangement	[38]
	Synthesis of a titanacyclobutene	[45]
1980	Synthesis of W oxo alkylidene and metathesis of olefins	[49]
	Metathesis of internal olefins by Nb and Ta alkoxide complexes	[39]
	Synthesis of a titanacyclobutane	[41]
1982	Observation of W alkylidene cations and rapid metathesis of internal olefins	[52]
	Synthesis of Re neopentylidenes and neopentylidynes	[73]
1986	Synthesis of a well-defined, active W imido alkylidene catalyst	[67]
	Observation of Ti alkylidenes from titanacyclobutane	[110]
	ROMP using titanacyclobutanes	[48]
1987	ROMP by W alkylidenes	[81]
	Synthesis of well-defined Mo imido alkylidene metathesis catalysts	[65]
1988	ROMP by Mo alkylidenes	[70]
1992	Ring-closing by Mo catalysts	[87]
1993	Synthesis and use of chiral Mo-based ROMP initiators	[86]
	The first stable zirconium alkylidene	[111]
	Metathesis of olefins by rhenium alkylidenes	[77]
1994	Rearrangement of Ta olefin complex to alkylidene complex	[133]
	The first vanadium alkylidene	[115]
1996	Kinetic resolution with enantiomerically pure Mo catalyst	[97]
	The first chromium alkylidene	[118]
1998	Efficient asymmetric ring-closing metathesis	[96a]
2001	Rearrangement of Nb olefin complex to alkylidene complex	[134]
	The first hafnium alkylidene	[114]

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Chapter 8

Fischer Carbene Complexes in Organic Synthesis

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8.1. BACKGROUND

8.1.1 Introduction

8.1.1.1 Classification of Carbene Complexes

Carbene complexes [1] contain a divalent carbon species ("carbene") coordinated to a transition metal center *via* a formal carbon to metal double bond. The interaction with the metal accounts for a dramatic increase in stability of the carbene species which can be generated, stored and handled at ambient temperature. Based on the nature of the metal, its oxidation state and its coligand sphere, two types of carbene complexes are to be distinguished: *Fischer*-type metal carbenes typically contain a late transition metal (groups 6 to 8) in a low oxidation state, which is additionally coordinated by ligands featuring good π-acceptor properties (*e.g.* carbon monoxide). The carbene carbon atom behaves as an electrophilic center and is usually stabilized by π-donation from heteroatoms (*e.g.* oxygen or nitrogen). In contrast, a typical *Schrock*-type metal carbene (see chapter 7) is characterized by an early or middle transition metal (groups 3 to 6) in a higher oxidation state bearing efficient donor-coligands. This results in a reversed polarity of the carbene to metal bond and imposes considerable nucleophilicity onto the carbene carbon atom. As indicated in Figure 1, *Fischer* carbene complexes are known for a wide variety of metals. The broadest application in organic synthesis based on stoichiometric reactions, however, have gained the group 6 metal carbenes, especially the pentacarbonyl chromium

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complexes which are easy to prepare and – in some cases – even commercially available.

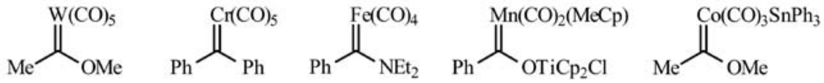
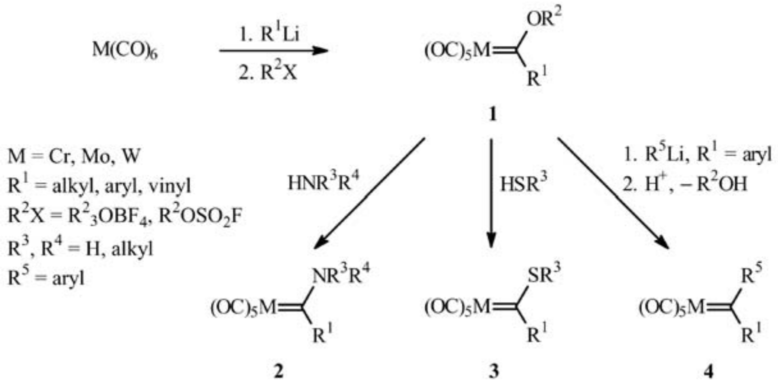


Figure 1. Selected examples of *Fischer*-type carbene complexes.

8.1.1.2 Synthesis of Fischer-type Carbene Complexes

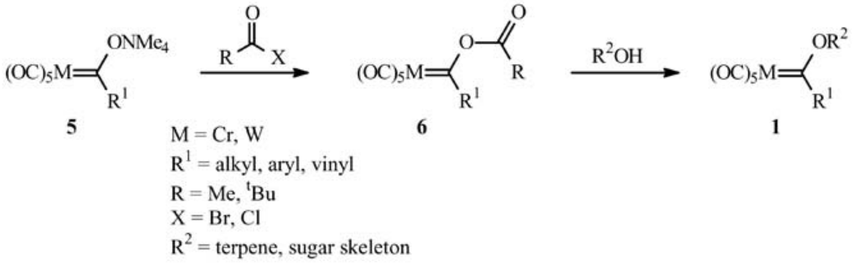
The most general approach to *Fischer* carbene complexes involves the nucleophilic addition of an organolithium reagent to a metal carbonyl yielding an acyl metalate which is subsequently alkylated by treatment with hard electrophiles such as trialkyloxonium salts or alkyl fluorosulfates providing alkoxycarbene complexes **1**. [2] Limitations of this reaction sequence are the availability of the organolithium compound and the alkylation reagent. The alkoxy group may be replaced for amino, thio or aryl substituents to give aminocarbene, thiocarbene and diarylcarbene complexes **2**, **3** and **4**, respectively (Scheme 1).



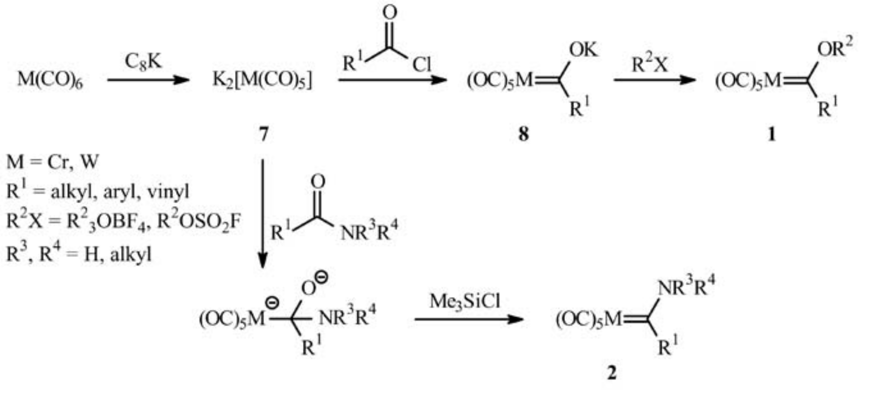
Scheme 1. *Fischer* route to metal carbene complexes.

More complex alkoxy substituents may be introduced by an acylation-alcoholysis sequence (Scheme 2). [3] Typically, this method involves the conversion of the lithium acyl metalate into the tetramethylammonium salt **5** which upon low-temperature acylation affords the thermolabile acyloxycarbene complex **6** as a strongly electrophilic reactive intermediate; subsequent alcoholysis generates the alkoxycarbene complex **1**. This route is the standard procedure for the synthesis of optically active carbene complexes from chiral alcohols (*e.g.* terpene or sugar auxiliaries).

Alternatively, the metal carbonyl may be subjected to an "umpolung" into an organometallic nucleophile which adds to an organic electrophile to give the carbene complex. In this approach – developed by *Hegedus* and *Semmelhack* – the metal carbonyl is reduced with C_8K providing the pentacarbonyl dianion **7**; it adds to acid chlorides to afford acyl metalates **8** which undergo alkylation to alkoxycarbene complexes **1** as mentioned before. This strategy can be extended to the synthesis of aminocarbene complexes **2**, where the metal carbonyl dianion **7** is added to carboxylic amides in the presence of trimethylsilylchloride as a deoxygenating reagent (Scheme 3). [4]



Scheme 2. Alkoxycarbene complexes *via* an acylation-alcoholysis sequence.



Scheme 3. *Hegedus-Semmelhack* approach to carbene complexes.

8.1.1.3 Reactivity of Fischer Carbene Complexes

The isolation of stable metal-coordinated carbenes which can be filled in bottles (although under inert gas) has stimulated the vision of synthetic-organic and physical-organic chemists that this type of compounds might serve as an easy to get and easy to handle source of free carbenes. So far, however, there is no evidence for a free carbene in a synthetically useful reaction of a *Fischer*-type carbene complex. In contrast, early experiments demonstrated that the metal-carbonyl bond is distinctly weaker than the metal-carbene bond. As a consequence, most of the C-C bond forming reactions start with a decarbonylation, and carbon-carbon bond formation occurs within the coordination sphere of the metal which – in some cycloaddition examples – may be regarded as a template keeping the substrates in a geometry favourable for interligand coupling. In other examples, the metal carbonyl fragment plays the role of an organometallic functional group which activates the carbene or even the adjacent carbon atom for subsequent specific reactions.

The characteristic reactivity pattern of carbonyl(carbene) complexes is illustrated in Figure 2. The most prominent feature – revealed by a low-field ^{13}C-NMR shift of up to 400 ppm, a value characteristic for carbenium ions – is the pronounced electrophilicity of the carbene carbon atom which favours the attack of carbon and heteroatom nucleophiles (**A**). Electrophiles may add to the heteroatom carbene substituent (*e.g.* oxygen) (**B**) what is the first step in the transformation of metal carbenes to metal carbynes. [5] As a consequence of the electrophilicity of the carbene carbon the acidity of α-CH groups is significantly enhanced; deprotonation by strong bases generates metal carbene anions which may be applied as *C*-nucleophiles to aldol-type reactions (**C**). Finally, carbonyl ligands undergo a thermal or photochemical substitution for other types of ligands (*e.g.* phosphines, alkenes, alkynes) which allows for a modification of the coligand sphere (**D**). This reactivity pattern demonstrates that the behaviour of metal carbenes is based on either ligand-centered or metal-centered reactions.

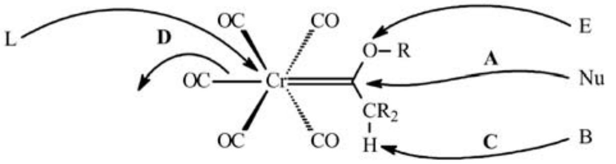


Figure 2. Reactivity pattern of carbonyl(carbene) complexes.

8.1.2 Ligand-Centered Reactions

8.1.2.1 Cleavage of the Metal-Carbene Bond

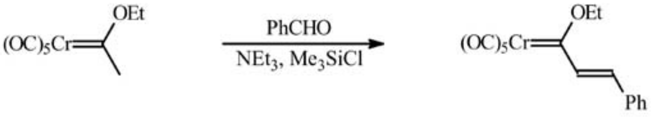
There are several methods to release the carbene ligand from the metal, but in no case the intermediacy of free carbenes has been established. The thermal decomposition of carbene complexes generally results in a dimerization of the carbene ligand to give alkenes. The replacement of the carbene ligand by carbon monoxide, tertiary phosphines or amines is a less drastic way to cleave the metal-carbene bond and, in principle, allows for a recovery of the low-valent metal species.

Widely used is the oxidative cleavage of the metal-carbene bond, formally replacing the chromium pentacarbonyl fragment by the isolobal oxygen atom. The oxidation is easy to carry out and results in high chemical yields but is accompanied by oxidized metal waste. Among various oxidizing agents, cerium(IV) compounds have found the widest synthetical application. [6] Reductive cleavage by hydrogenolysis leads to saturated hydrocarbons and requires much more drastic conditions. [7]

8.1.2.2 Carbon-Carbon Bond Formation via Metal Carbene Anions

α-Hydrogen atoms in the carbene ligand display a remarkable acidity; the methoxy(methyl)carbene complex features a pK_a value of about 8. [8] Therefore, alkylcarbene complexes can be deprotonated by alkoxide bases or organolithium reagents. The resulting carbene complex anions may be isolated as air-stable bis(triphenylphosphine)iminium salts.

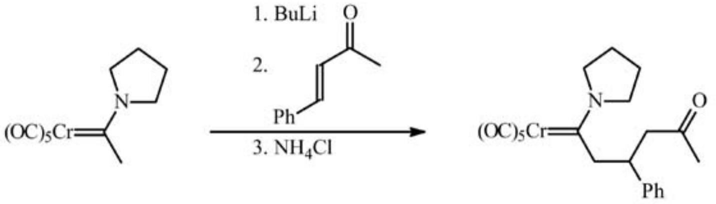
The metal carbene anions represent *C*-nucleophiles which can be applied to aldol-type reactions. The first aldol reactions were performed with stoichiometric amounts of carbene complex anions; [6a] later it turned out that higher yields are obtained when the reaction is run under equilibrating conditions (Scheme 4). [9] Clean aldol reactions generally require non-enolizable aldehydes. Nevertheless, an aldol condensation involving an enolizable aldehyde has been reported using catalytic amounts of base. [10]



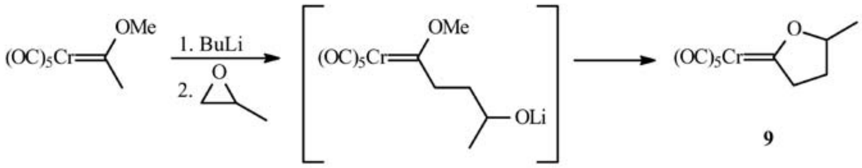
Scheme 4. Aldol condensation of an alkylcarbene complex under equilibrating conditions.

Anions of aminocarbene complexes undergo *Michael* additions to α,β-unsaturated carbonyl compounds leading to 1,4-adducts (Scheme 5). [11]

Carbene complex anions are suitable *C*-nucleophiles for the ring-opening of oxiranes. The resulting alkoxide intermediates undergo a subsequent cyclization to give 2-oxacyclopentylidene complexes **9** (Scheme 6). Unsymmetrically substituted epoxides are attacked by the carbene anion at the less hindered carbon atom.



Scheme 5. *Michael* addition of an aminocarbene complex anion to an enone.



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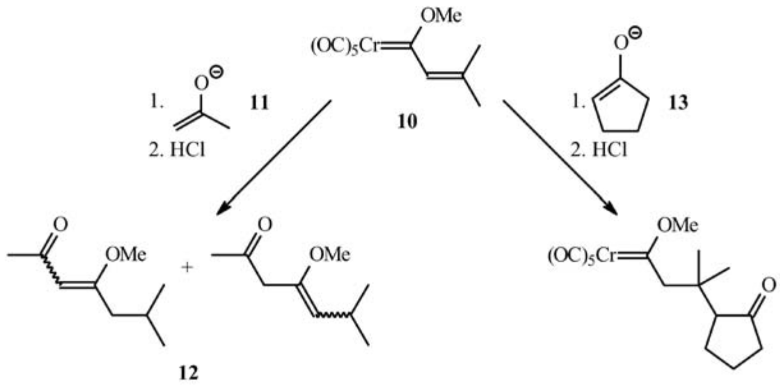
Scheme 6. Synthesis of oxacyclopentylidene complexes.

8.1.2.3 Addition of Nucleophiles

The nucleophilic addition to the carbene carbon has been utilized in numerous synthetical applications. Alkoxycarbene complexes are readily accessible starting materials and undergo addition of thiols, [12] primary or secondary amines [13] or aryllithium compounds [14] leading to alkylthio- (or arylthio-), amino- or arylcarbene complexes (Scheme 1). The mechanism of the aminolysis reaction has been studied in detail and has been found to resemble that of the aminolysis of esters. [15] Chiral amines allow the synthesis of optically active aminocarbene complexes. [16] The incorporation of more bulky amines or of chiral alcohol auxiliaries into the carbene ligand requires an even more electrophilic metal carbene center as provided in acyloxycarbene complexes.



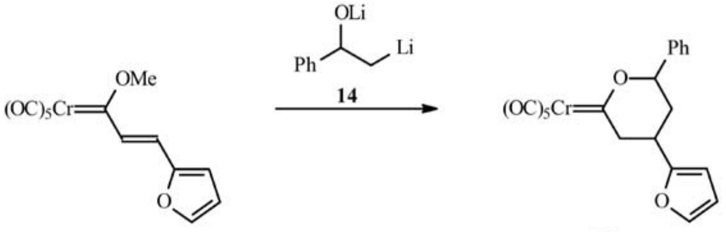
Scheme 7. Addition of enolates to α,β-unsaturated carbene complexes: 1,2- *versus* 1,4-addition.

The addition of carbon nucleophiles to the carbene carbon atom generates a new C–C bond. Organolithium reagents add to alkoxycarbene complexes to give alkyl metalates which undergo alkoxide elimination upon addition of acid or exposure to silica gel and thus may serve as precursors for non-heteroatom-stabilized diarylcarbene complexes (Scheme 1). [14b]

In alkenyl- and alkynylcarbene complexes the addition of nucleophiles to the carbene carbon competes with the addition to the β-carbon of the conjugated C-C multiple bond. [17] The regioselectivity of the addition of amines to alkynylcarbene complexes is temperature dependent; 1,2-addition is favoured by lower temperatures. [17c] Enolates turned out to be efficient *C*-nucleophiles for *Michael* addition reactions to unsaturated metal carbenes. The product distribution may depend on steric factors as shown in Scheme 7 for the addition of different enolates to alkenylcarbene complex **10**. The less bulky acetone enolate **11** adds to the carbene carbon; protonation of the primary addition product results in demetalation and in the formation of a mixture of isomeric enones **12**. In contrast, the more bulky cyclopentanone enolate **13** adds to the less shielded vinylic position.

Dianions such as dilithium species **14** undergo a sequential 1,4- and 1,2-addition; 1,4-addition of the carbanion and 1,2-addition of the alkoxide to the vinylcarbene complex afford the 2-oxacyclohexylidene complex **15** as a mixture of *cis*/*trans* isomers (Scheme 8). [18]

Nucleophilic multiple bond systems primarily add to the carbene carbon atom and subsequently insert into the metal-carbene bond. [19] Enamines, ynamines and cyanamides react cleanly with alkoxycarbene complexes **16** to give amino(vinyl)carbene complexes (Scheme 9); less nucleophilic ynethers, however, require metal carbenes with enhanced electrophilic properties such as the thermolabile tungsten benzylidene **17** to push the alkyne insertion to completion (Scheme 10). The *E* configuration generally prevails in the newly formed vinylic C=C bond. [20]



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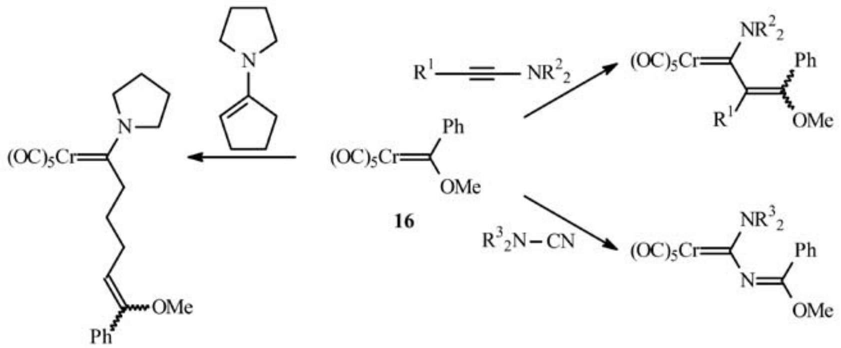
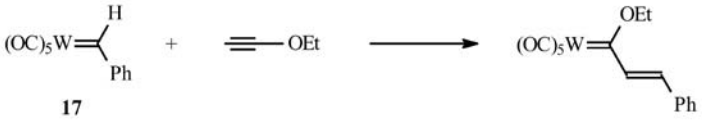
Scheme 8. Sequential 1,4- and 1,2-addition to an α,β-unsaturated carbene complex.

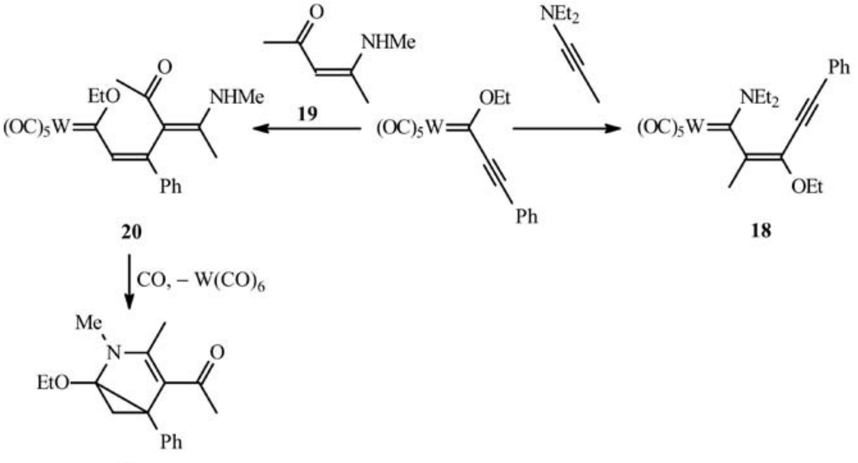
Whereas the insertion of ynamines into a metal-alkynylcarbene bond to give **18** is initiated by a nucleophilic attack at the carbene carbon atom, [21] the less nucleophilic ("softer") β-acyl enamine **19** rather adds to the ("softer") β-carbon of the alkynylcarbene ligand to give 1-metala-1,3,5-hexatriene **20** which upon thermolysis in unpolar solvents undergoes cyclization and demetalation to homopyrrole **21** (Scheme 11). [22]



Scheme 9. Insertion of α,β-unsaturated nucleophiles into the metal-carbene bond.



Scheme 10. Ynether insertion into the metal-carbene bond.

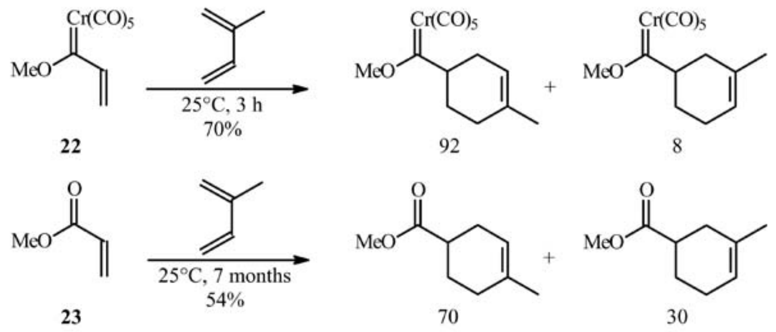


Scheme 11. Reaction of alkynylcarbene complexes with ynamines and enamines.

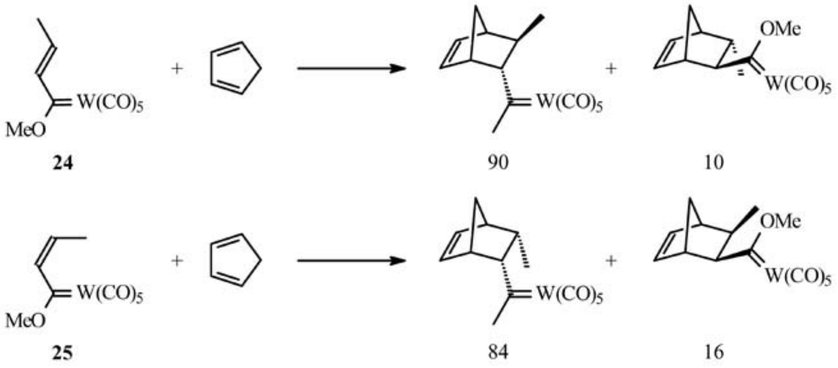
8.1.2.4 Cycloaddition Reactions with Metal Auxiliaries

The carbonylmetal fragment turns vinylcarbene ligands into potent π-systems for cycloaddition reactions. Most efforts have concentrated on their role as dienophiles in *Diels-Alder* reactions. Early studies indicated that – in comparison to its isolobal analogue methyl acrylate **23** – reactivity and regioselectivity of the methoxy(vinyl)carbene complex **22** are significantly increased and are comparable to those observed for an $AlCl_3$-assisted *Diels-Alder* reaction (Scheme 12). [23]

Moreover, the presence of the metal auxiliary may increase the stereoselectivity of the cycloaddition. Reaction of the isomeric tungsten propenylcarbene complexes **24** and **25** with cyclopentadiene afforded good chemical yields (> 85%) combined with an *endo*/*exo* selectivity of 90:10 for the *trans* complex **24** and of 84:16 for the *cis* isomer **25** (Scheme 13). [24] For comparison, the isolobal *trans*-methyl crotonate gave an *endo*/*exo* ratio of 54:46 under thermal conditions which was improved to 93:7 in the presence of aluminium trichloride.



Scheme 12. Comparative *Diels-Alder* reaction of carbene complex **22** and its isolobal analogue.



Scheme 13. Stereoselective *Diels-Alder* reactions of carbene complexes.

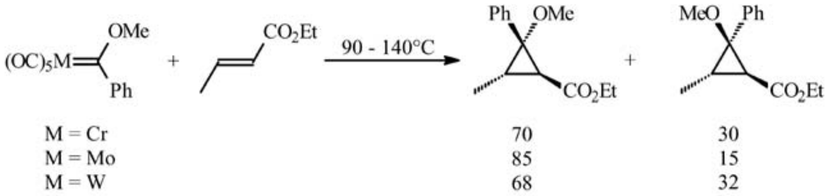
Alkynylcarbene complexes reveal similarly increased rates in their reactions with 1,3-dienes when compared to their organic analogues. [25] *Diels-Alder* reactions with inverse electron demand in which the diene is part of the carbene ligand are rare. [26] Examples for stereoselectively conducted *Diels-Alder* reactions of difluoroboroxycarbenes are presented in section 2.3 of this review.

Beyond *Diels-Alder* reactions, α,β-unsaturated carbene ligands have been applied to [3+2]-cycloadditions with 1,3-dipoles, [27] thermal [2+2]-cycloadditions with electron-rich alkenes (enol ethers, ketene acetals) [26] and in intramolecular *Pauson-Khand* reactions. [28]

8.1.3 Metal-Centered Reactions

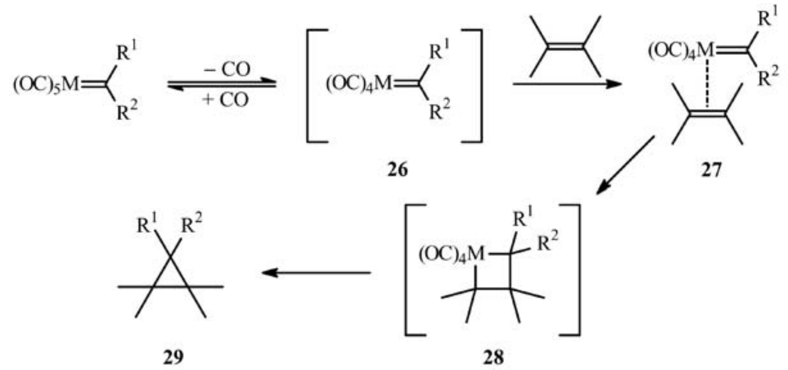
8.1.3.1 Cyclopropanation of Alkenes

The carbene ligand in metal carbenes may be transferred to alkenes to give cyclopropanes. Early [2+1]-cycloaddition reactions of this type revealed that the isomeric ratio of the cyclopropanes formed depends on the metal used. These results indicate that the metal is involved in the product-forming step, and consequently exclude the intermediacy of free carbenes (Scheme 14). [29] This idea was further supported by an (even low) transfer of chirality from a chromium carbene – bearing an optically active phosphine ligand – to the resulting cyclopropane. [30] Moreover, an efficient cyclopropanation of electron-rich and electron-deficient alkenes requires different reactions conditions, suggesting that different mechanisms are operative in these transformations. The cyclopropanation with carbene complexes is stereospecific; the configuration of the alkene is retained in the cycloadduct.

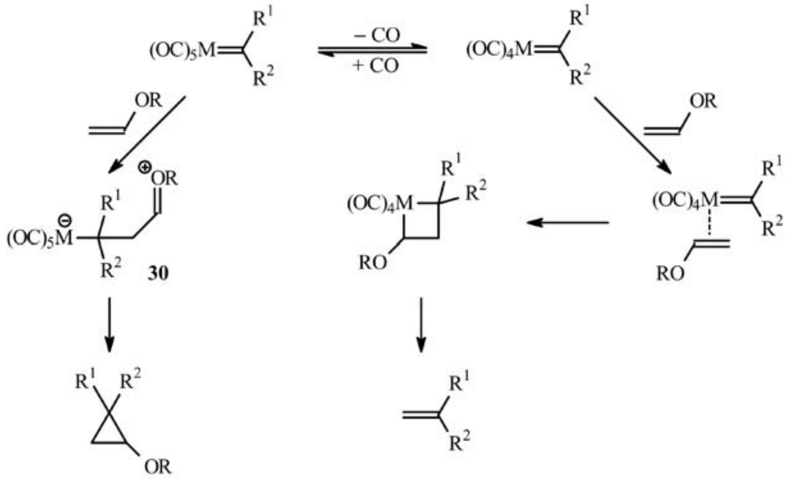


Scheme 14. Cyclopropanation of an unsymmetrically substituted electron-deficient alkene.

The cyclopropanation of α,β-unsaturated esters requires elevated temperatures (≥ 90°C) allowing a rapid CO exchange in the carbonyl(carbene) complex. Thus, a reasonable mechanism involves a decarbonylation preequilibrium followed by the coordination of the alkene to the coordinatively unsaturated tetracarbonyl intermediate **26**. The resulting alkene(carbene) complex **27** may rearrange to a metalacyclobutane **28** which undergoes reductive elimination to give the cyclopropane **29** (Scheme 15). [31]



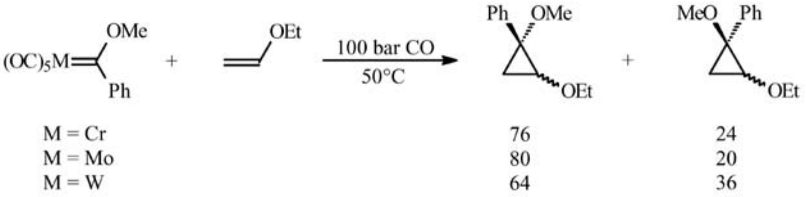
Scheme 15. Proposed mechanism for the cyclopropanation of electron-deficient alkenes.



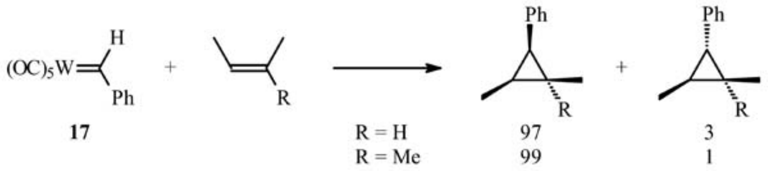
Scheme 16. Proposed mechanism for the cyclopropanation of electron-rich alkenes.

The cyclopropanation of electron-rich alkenes requires modified reaction conditions. Warming a solution of a metal carbene and an enol ether at atmospheric pressure results in the formation of an alkene which apparently is formed in an olefin metathesis reaction. However, good yields of cyclopropanation products are obtained under CO pressure. Under these conditions the nucleophilic alkene is supposed to add to the carbene carbon to generate zwitterion **30** in which the metal-coordinated carbon atom undergoes an either front-side or back-side attack at the former α-enol ether carbon atom (Scheme 16). [32] Again the isomeric ratios of the cyclopropanes formed reflect the role of the metal used (Scheme 17). [29c,33]

The cyclopropanation of non-functionalized alkenes requires even stronger electrophilic metal carbenes as provided by non-heteroatom-stabilized group 6 carbene complexes **17** or cationic iron carbene complexes; the reaction is highly *syn*-selective (Scheme 18). Iron carbenes bearing optically active phosphine ligands allowed for an efficient enantioselective cyclopropanation. [34]

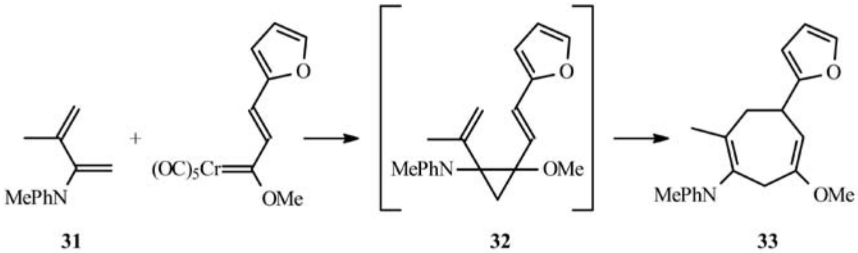


Scheme 17. Cyclopropanation of an electron-rich alkene.



Scheme 18. Cyclopropanation of a non-functionalized alkene.

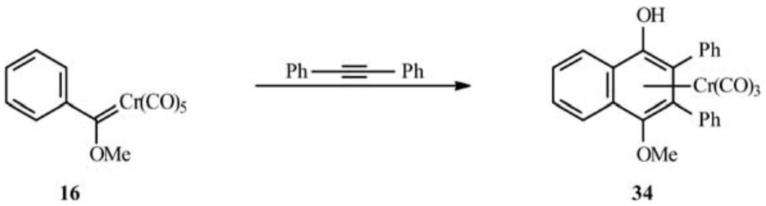
The cyclopropanation protocol can be applied to 1,3-dienes as well. [35] Electron-deficient 1,3-dienes yield vinylsubstituted cyclopropanes upon [2+1]-cycloaddition with *Fischer* carbene complexes. [36] In particular cases, however, the three-membered cycloadducts are rather unstable and susceptible to a *Cope* rearrangement as outlined in Scheme 19 for an electron-rich diene: [37] Carbene transfer to the more electron-rich C=C bond in diene **31** generates the *cis*-divinylcyclopropane **32** which undergoes a spontaneous ring expansion to give cycloheptadiene **33** in a regio- and stereoselective one-pot reaction. A similar reaction sequence has been applied in the synthesis of dihydroazepines from aza-1,3-dienes. [38]



Scheme 19. Cycloheptatrienes *via* cyclopropanation of 1,3-dienes and *Cope* rearrangement.

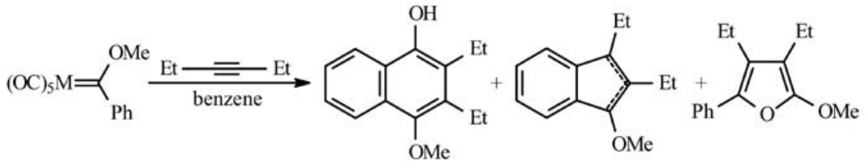
8.1.3.2 [3+2+1]-Benzannulation

Probably the most important stoichiometric application of metal carbenes in organic synthesis refers to their reaction with alkynes. Pentacarbonylchromium complexes bearing alkoxy(aryl- or alkenyl)carbene ligands react with alkynes to give densely substituted arenes **34** which remain coordinated to a $Cr(CO)_3$-fragment (Scheme 20). [39] This unique type of cycloaddition reaction assembles the α,β-unsaturated carbene ligand (C_3-synthon), the alkyne (C_2-synthon) and a carbonyl ligand (C_1-synthon) at the $Cr(CO)_3$-fragment which serves as a template for a stepwise interligand coupling. Chromium is the metal of choice for this type of annulation which occurs with considerable chemo-, regio- and stereoselectivity.



Scheme 20. Chromium-templated benzannulation of arylcarbenes.

The product distribution depends significantly on the nature of the metal, the heteroatom substitution in the carbene ligand, the solvent used and the work-up conditions. Along with the predominating benzannulation, competing paths are leading to [3+2]-cycloaddition; the formation of furans and cyclobutenones has been observed to varying extents. The role of the metal template is shown in Scheme 21. The reaction of methoxy(phenyl)carbene complexes of chromium, molybdenum and tungsten (**16**, **35** and **36**) with 3-hexyne in benzene afforded after demetalative workup hydroquinone **37**, indenes **38** and furan **39**. [40] The greatest chemoselectivity was found for the chromium complex **16** which produced the hydroquinone **37** almost exclusively. The molybdenum and tungsten analogues led to indenes **38** as the major products along with varying amounts of furan **39**. Apart from group 6 metal carbenes, manganese [41] and ruthenium [42] complexes have been reported to undergo a similar benzannulation either under more drastic thermal or photochemical conditions.

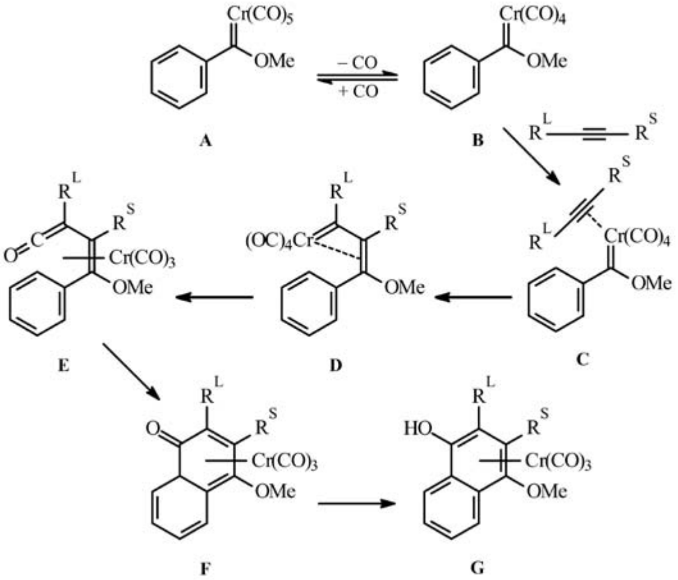


	37	38	39
16 M = Cr	> 98.3	< 0.7	< 1.0
35 M = Mo	6.3	77.9	15.8
36 M = W	3.2	90.5	6.3

Scheme 21. Role of the metal template in carbene-alkyne cyclization reactions.

The solvent may also influence the product distribution. [43] The reaction of chromium carbenes with alkynes in donors solvents like ethers or in benzene reveals a strong preference for benzannulation whereas non-coordinating solvents such as hexane or polar solvents such as DMF increase the yields of cyclopentannulation products. A strongly coordinating solvent like acetonitrile leads to the formation of moderate yields of cyclobutenones.

The competition of benzannulation and pentannulation significantly depends on the donor ability of the carbene ligand. Substitution of alkoxy for amino groups in the carbene ligand increases the thermal stability of the metal-carbonyl bond which hampers both the primary decarbonylation and the CO incorporation into the final product. As a consequence, annulation of chromium amino(aryl)carbenes requires elevated temperatures (≥ 90°C) and affords cyclopentannulation products (indenes). *N*-Acylation (*e.g.* by Boc) reduces the donor properties of the amino substituent and thus favours again the benzannulation. The competition of benzannulation *versus* cyclopentannulation also depends on the concentration and the temperatures applied; [43] less dilute solutions and low temperatures favour benzannulation over cyclopentannulation.



Scheme 22. Proposed mechanism of the [3+2+1]-benzannulation.

Based on experimental and kinetic studies, a mechanism has been proposed for the benzannulation which is also consistent with more recent theoretical calculations (Scheme 22, Figure 3). The initial and rate-determining step of the benzannulation is a reversible decarbonylation of the pentacarbonyl(carbene) complex **A** affording the coordinatively unsaturated tetracarbonyl complex **B**. This is in accordance with the observation that the reaction is suppressed in the presence of external carbon monoxide [44] and the decarbonylation equilibrium was later supported by a kinetic study. [45] Furthermore an η^1:η^3-vinylcarbene complex analogue **I**, corresponding to reaction intermediate **B**, has been isolated during the reaction of an alkenylcarbene complex. [46] Subsequent coordination of the alkyne gives an η^2-alkyne complex **C**; structural analogues displaying an intramolecular alkyne coordination (complex **II**) are known and have been characterized by X-ray. [47]

The subsequent steps of the reaction are too fast in order to allow further kinetic investigation. A previously proposed 16-electron chromacyclobutene intermediate arising from a formal [2+2]-cycloaddition of the alkyne ligand aross the metal-carbene bond was later discarded as a result of theoretical studies which support a direct insertion of the alkyne into the metal-carbene bond to generate an 18-electron valence-isomer, the η^3-vinylcarbene complex **D**. [48] A related species **III** has been isolated from the reaction of an aminocarbene complex. [46] Subsequent insertion of a carbonyl ligand leads to an η^4-vinylketene complex **E**, of which structural analogues as enaminoketene complex **IV** have been synthesized. [49] Electrocyclic ring closure affords the cyclohexadienone complex **F** which tautomerizes to give the naphthol complex **G**. A cyclohexadienone complex **V** has been isolated from the reaction of a molybdenum alkenylcarbene complex. [50]

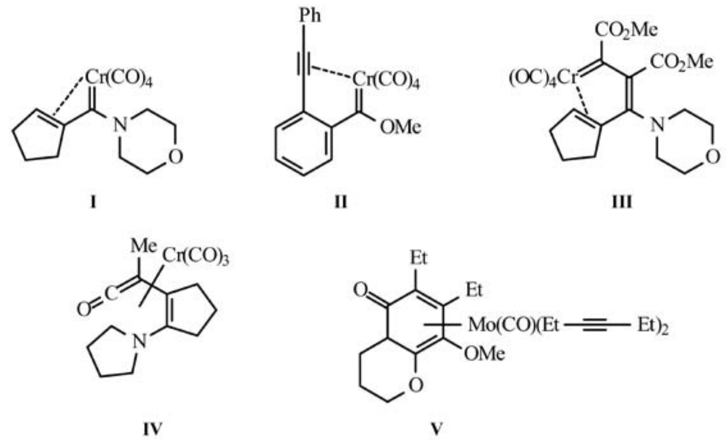
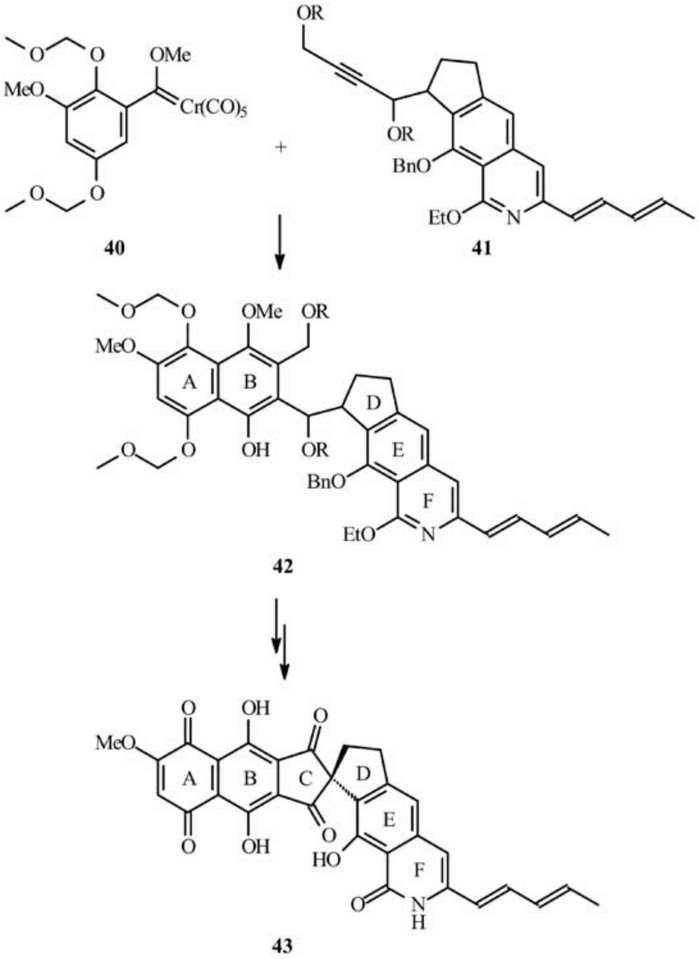


Figure 3. Isolated structural analogues of benzannulation intermediates.

The benzannulation is typically performed under mild thermal conditions in the temperature range of 45 to 60°C and gives yields up to 92%. Alternative reaction procedures include a photoinduced decarbonylation as the initial step which allows benzannulations under low-temperature conditions. However, because of the lower selectivity due to the presence of other photosensitive intermediates, photoinduced benzannulations gained synthetic importance only in cases where the thermal protocol fails. [51] In a few examples the benzannulation was promoted by high intensity ultrasound or was carried out under dry state absorption conditions. [52] Although these alternative techniques may lead to comparable yields in shorter reaction times in some cases, they do not allow the isolation of tricarbonylchromium complexes of the hydroquinoid benzannulation products, but instead give the corresponding quinones after oxidative workup.



Scheme 23. Benzannulation approach to fredericamycin A.

Beyond the chemoselectivity, the regioselectivity of the alkyne incorporation is another important criterion for the synthetic value of the benzannulation. The regiocontrol mainly arises from steric factors which favour a coupling of the alkyne carbon bearing the less bulky alkyne substituent with the carbene carbon atom. Therefore, the regioselection is virtually complete for terminal alkynes which lead to a benzannulation product bearing the alkyne substituent next to the phenolic group. Unsymmetrical dialkylalkynes afford regioisomeric mixtures; the ratio of regioisomers depends on the relative steric bulk of the alkyl substituents. [53]

As a consequence of the unsymmetric substitution pattern encountered in the arene ring (OH *versus* OR) formed upon benzannulation the chromium complexes bear a plane of chirality. Complexes of this type are powerful reagents in stereoselective synthesis, and approaches directed towards diastereoselective benzannulation will be addressed in section 2.1 of this review.

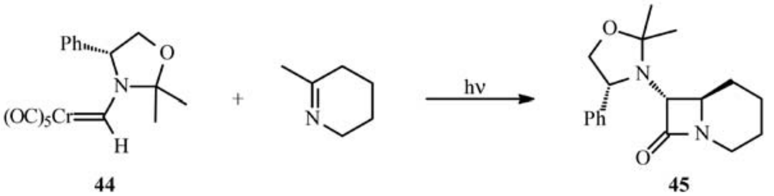
The benzannulation provides a straightforward access to densely functionalized arenes and as such has been applied to the synthesis of more complex arene skeletons. Earlier applications to natural product synthesis concentrated on vitamins, [54-56] steroids [57] and antibiotics. [58] A more recent strategy to the antibiotic and antitumour agent fredericamycin A incorporated the benzannulation as the key step of the total synthesis. [59] Benzannulation of the oxygenated arylcarbene complex **40** with the properly functionalized alkyne **41** gave a 35% yield of a single regioisomer **42** which was subjected to a final spirocyclization to give the target molecule **43** (Scheme 23).

8.1.3.3 Photochemistry of Chromium Carbene Complexes

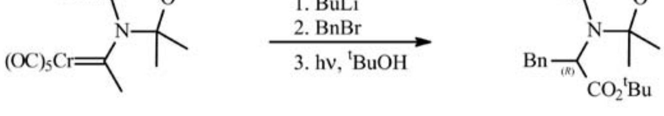
The bifunctionality of carbonyl(carbene) complexes stimulated further efforts to take advantage of both types of ligands as building blocks for organic synthesis. Based on earlier observations on the photolability of metal carbonyls *Hegedus* discovered that UV-irradiation into the metal to ligand charge transfer (MLCT) band of chromium carbene complexes generates a species featuring ketene-like reactivity. [60] This species may be described as a metalacyclopropanone or a metal-coordinated ketene and is considered to result from an insertion of a *cis*-CO ligand into the metal-carbene bond. [61] The ketene species derived from alkoxy- or aminocarbene complexes can be trapped *in situ* by either [2+2]-cycloaddition (especially with imines) or by protic nucleophiles (such as alcohols). Limitations have been observed for carbene complexes bearing two heteroatoms or potent π-acceptor groups next to the carbene carbon atom. Since neither free ketenes nor products derived thereof have been detected along the generation and subsequent reactions of the ketene species, these reactions are considered to occur within the coordination sphere of the metal.

One synthetic aspect of metal carbene photochemistry refers to [2+2]-cycloaddition reactions of the ketene intermediates with imines or alkenes to give β-lactams or cyclobutanones, respectively. Irradiation of chromium alkoxycarbene complexes in the presence of various imines leads to the formation of β-lactams. In most cases this is a smooth and high-yield process displaying very good diastereoselectivity. Chiral auxiliaries at the nitrogen allow for excellent diastereomeric excesses provided that rigid cyclic imines such as thiazolines [62] or imidazoles [63] are used. This photoprotocol can be extended to aminocarbene complexes, and thus can be applied to the synthesis of biologically active β-lactams which generally bear an amino group and a hydrogen at C-3. Photolysis of suitable aminocarbene complexes such as **44** in the presence of various imines affords lactams **45** in high yield and excellent diastereoselectivity (mostly ≥ 97% d.e.) (Scheme 24). [64] This method has found application in an efficient synthesis of α-alkyl α-aminoacids using oxazine as the imine component. [65]

Another application of photogenerated metal coordinated ketenes is based on the addition of protic nucleophiles and has been exploited in the synthesis of amino acids and peptides. [66] As usual, the reactive intermediate is generated by photolysis of an aminocarbene complex **46**, which may be α-alkylated in a previous step. The oxazolidine auxiliary applied successfully inducing asymmetry in the β-lactam formation, allowed an enantioselective synthesis of amino acids. Since both enantiomers of the auxiliary may be obtained from the corresponding phenyl glycine enantiomer, natural (*S*) and non-natural (*R*) amino acid esters **47** are accessible *via* this route (Scheme 25). A recent review on synthetical applications of chromium carbene photochemistry has been published. [1i]



Scheme 24. Photoassisted formation of β-lactams from chromium carbene complexes.



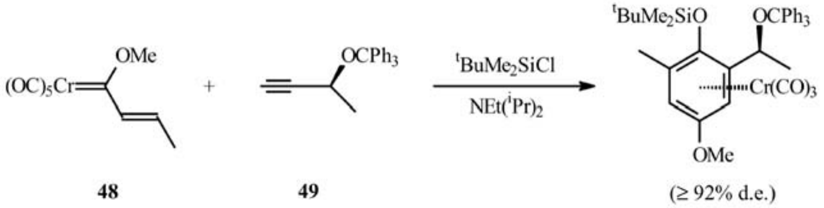
Scheme 25. Synthesis of enantiopure amino acids *via* photolysis of chromium carbene complexes.

8.2 STATE OF THE ART

8.2.1 Asymmetric Benzannulation Reactions

The chromium-templated coupling of alkenyl- or arylcarbene, alkyne and carbonyl ligands generates arene tricarbonylchromium complexes as primary benzannulation products which – based on their unsymmetric substitution pattern – bear a plane of chirality. Chiral arene complexes are powerful reagents in stereoselective synthesis; however, the preparation of pure enantiomers is a lengthy and often tedious procedure, and thus diastereoselective benzannulation appears to be an attractive alternative. In order to lure the chromium fragment to one or the other face of the arene formed, chiral information may be incorporated in the carbene complex or the alkyne.

Benzannulation of alkenylcarbene complexes such as **48** with α-chiral proargylic ethers **49** resulted in diastereofacial selection the degree of which was strongly dependent on the substitution pattern of the carbene ligand and the steric bulk of the ether oxygen substituent (Scheme 26). [67]



Scheme 26. Diastereoselective benzannulation with an α-chiral propargylic ether.

A more general approach concentrates on the chiral modification of the carbene ligand. Some examples based on a chiral carbene carbon side chain are depicted in Figure 4. [68] The reaction of alkoxy- and amino(cyclohexenyl)carbene complexes with 1-pentyne afforded diastereomeric tetralin complexes in moderate yields. [69] The sense of stereoselection was found to depend on the substitution pattern of the cyclohexenyl substituent. Whereas 5-methyltetralin derivatives were obtained in low preference for the *syn* complex, a higher preference for the *anti* diastereomer was observed synthesizing the 8-methyltetralin complexes **50** (Scheme 27). [69]

The most versatile and promising approach to pure enantiomers is based on chiral alcohol auxiliaries incorporated into the carbene ligand *via* the acylation-alcoholysis sequence. Several chiral secondary alcohols have been screened for their ability of diastereoinduction. [70] The best performance (80% d.e.) within a series of terpenoid alcohol auxiliaries was observed for (−)- and (+)-menthol (Scheme 28). The diastereomeric excess depends on the solvent and decreases when *tert*-butyl methyl ether is substituted for less polar hydrocarbon solvents. Compared with arylcarbene complexes the menthol auxiliary is much less efficient with alkenylcarbene complexes which only gave d.e. values below 20%. [70b] Attempts to improve the diastereoselection by means of chiral amine auxiliaries met with similar little success. [71]

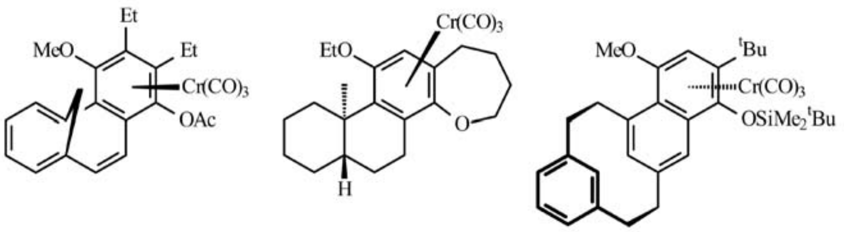
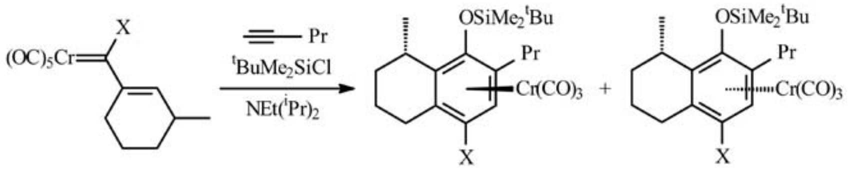


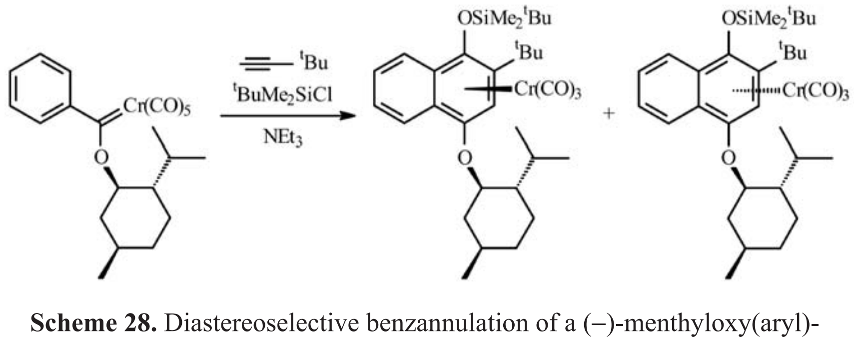
Figure 4. Asymmetric induction by chiral carbene carbon substituents.



50

X = OMe	76	24
$X = NMe_2$	91	9

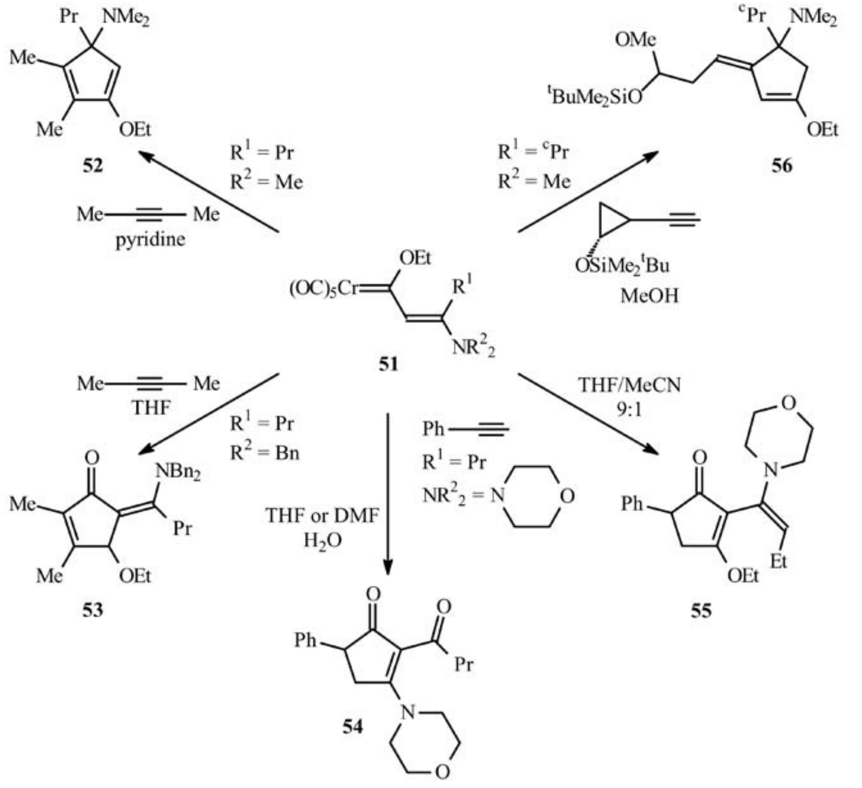
Scheme 27. Diastereoselective benzannulation of chiral methylcyclohexenylcarbene complexes.



Scheme 28. Diastereoselective benzannulation of a (−)-menthyloxy(aryl)-carbene complex.

2.2 Synthesis of Five-Membered Carbocycles

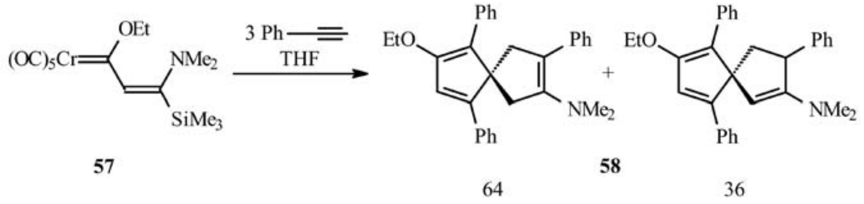
An annulation of chromium arylcarbenes by alkynes without CO-insertion leads to five-membered rings. It has been observed as a side reaction along the benzannulation which may become predominant depending on the nature of the carbene heteroatom substitution pattern, [72] the metal [40] and its coligands [73] and the solvent [43] used. In this respect, indene derivatives have been obtained from arylcarbene complexes of chromium and tungsten. [73,74]



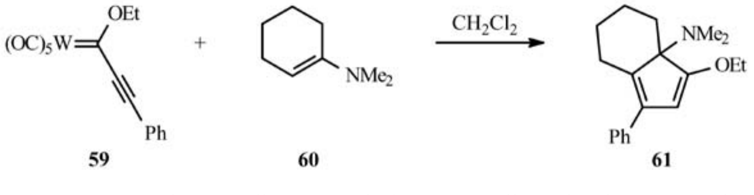
Scheme 29. Coupling of β-aminoalkenylcarbene complexes with alkynes.

More general recent approaches focused on chromium *E*-β-aminovinylcarbenes **51** which gave various cyclopentanoid substitution patterns upon reaction with alkynes (Scheme 29). [1g] Good yields of cyclopentadienes as **52** are obtained in hexane or if efficient donor solvents like pyridine or acetonitrile and a slow addition of the alkyne are applied. [1g] Cyclopentenones **53** result from the carbene-alkyne coupling performed in refluxing THF or dimethoxyethane. [75] Addition of minor amounts of acetonitrile leads to the formation of isomeric compounds **55** if carbene complex **51** contains a hydrogen atom in the allylic position of the alkenylidene ligand. [75b] 3-Aminocyclopentenones **54** may be obtained, when the cycloaddition is performed in wet THF or DMF. [76] Conjugated alkylidenecyclopentenes are formed with cyclopropylalkynes in methanol, **56** was obtained as a mixture of diastereomers with low stereoselectivity (17% d.e.). [77]

The reaction of silyl-β-aminovinylcarbene complex **57** with 3 equivalents of phenylacetylene results in an unexpected spirocyclization to give a mixture of spiro[4.4]nonatriene isomers **58** which differ in the position of one double bond (Scheme 30). [78] A mechanism of this unprecedented reaction has to take into account that the connectivity originating from the carbene complex **57** is lost along the spirocyclization. [79]



Scheme 30. Spiro[4.4]nonatrienes from β-aminoalkenylcarbene complexes.

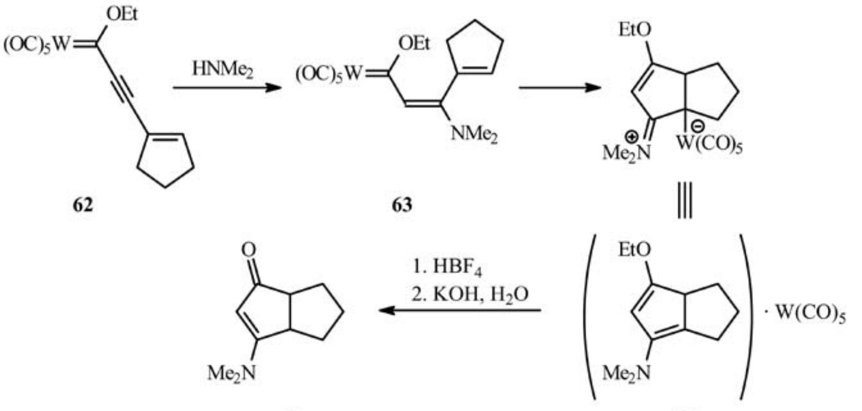


Scheme 31. Cyclopentadiene annulation of an alkynylcarbene complex with an enamine.

The carbene complex starting materials mentioned above include an enamine structure which is coupled with an alkyne. *Vice versa*, the coupling of alkynylcarbene complexes with enamines leads to cyclopentanoid products as well. The complementary reaction of tungsten alkynylcarbene complex **59** with enamine

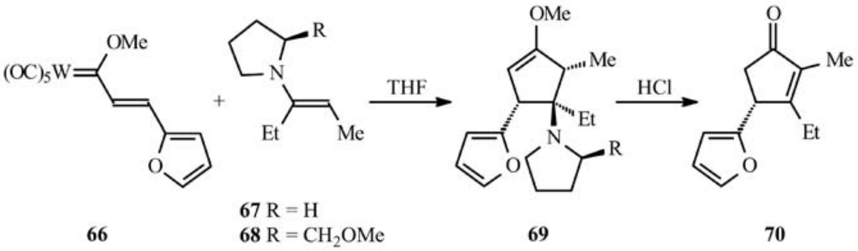
60 gave the cyclopentadiene **61** in high regioselectivity (Scheme 31). [80] The corresponding chromium carbene complex afforded the same product in a somewhat lower yield. [80] The method has been extended to several cyclic enamines; a suggested mechanism is based on an initial *Michael* addition of the enamine to the alkynylcarbene complex followed by an intramolecular hydrogen transfer to a metalahexatriene species. [81]

In a related process, 4-amino-1-metala-1,3,5-hexatrienes such as **63** – accessible from the addition of secondary amines to 2-(1-cyclopentenyl)ethynylcarbene complexes **62** – undergo a spontaneous cyclization to an η^1-cyclopentadiene species **64** (Scheme 32). [82] The uncoordinated cyclopentadiene could not be isolated on a preparative scale; instead cyclopentenone **65** was obtained upon subsequent treatment with HBF_4 and aqueous KOH. [82]

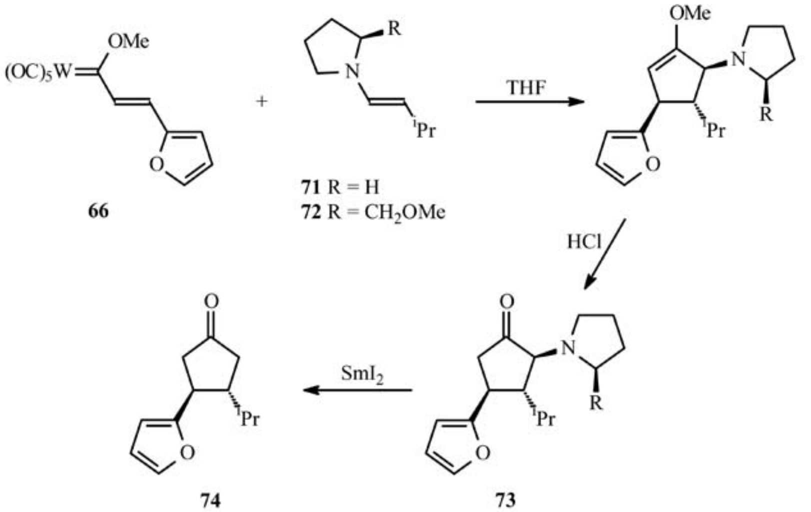


Scheme 32. η^1-Cyclopentadiene complexes as precursors for cyclopentenones.

Cyclopentanoids may also arise from the reaction of alkenylcarbene complexes with enamines. As shown in Scheme 33, tungsten carbene **66** reacts with enamines **67** and **68** to afford the enol ethers **69** which give cyclopentenone **70** upon acidic hydrolysis. [83] The formation of **69** generates two carbon-carbon bonds and three stereogenic centers with remarkable regio- and stereoselectivity. The reaction of enamine **67** results in a racemic mixture of **70**; the chiral enamine **68**, however, adds to carbene complex **66** to give enantiomerically enriched (87% e.e.) cyclopentenone **70**.



Scheme 33. Enantiocontrolled cycloaddition of enamines to alkenylcarbene complexes.

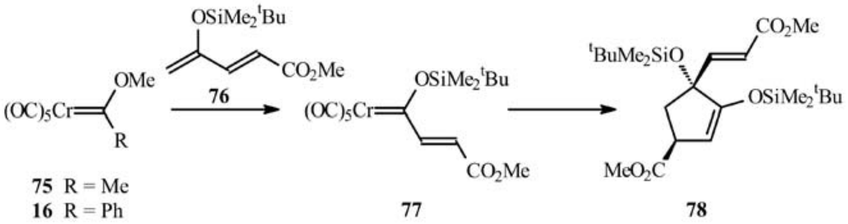


Scheme 34. Enantioselective formation of cyclopentanones from alkenylcarbene complexes and chiral enamines.

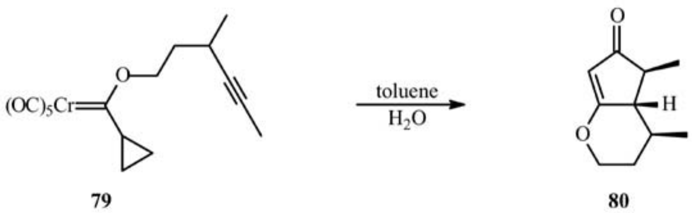
The regioselectivity of the cycloaddition is controlled by the substitution pattern of the enamine. A reversed regiochemistry is observed for enamines such as **71** or **72** which provide an access to amino-substituted cyclopentanones **73**; subsequent deamination gives cyclopentanone **74** (Scheme 34). [83] Again, achiral **71** generates a racemic mixture of **74**, whereas the reaction of **72** provides **74** almost enantiomerically pure (> 99% e.e.).

Cyclopentenol ethers **78** bearing a quaternary carbon center are formed from the reaction of an alkenylcarbene complex and an alkene. The reaction sequence is believed to start with an olefin metathesis of a carbene complex (**75** or **16**) and dienol ether **76** to give vinylcarbene complex **77** (Scheme 35). [84] Subsequent [3+2]-cycloaddition of the vinylcarbene and a second molecule of **76** affords the cyclopentene **78**. The reaction proceeds with high regio- and diastereoselectivity, leading to vinylcyclopentene **78** in 80 - 90% d.e.

Cyclopentenones have been also obtained from alkoxy(cyclopropyl)carbene complexes and alkynes *via* a cyclopentadienone intermediate. [85] The intramolecular version of this type of reaction has been studied intensively. [86] More recent studies focused on the role of a stereogenic center in the intramolecular cyclization process. [87] It turned out that high stereoselectivites can be achieved if the reaction is performed in aqueous toluene; for instance, the cyclization of complex **79** yields a 90:5:5:0 mixture of the four possible diastereoisomers in an overall yield of 70%. The three contiguous stereogenic centers in the major isomer **80** are formed in a *trans*-*trans* configuration (Scheme 36).



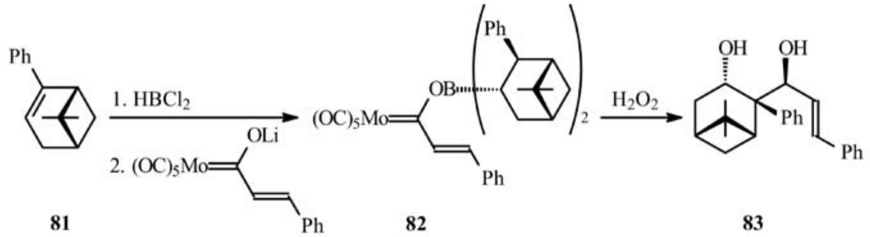
Scheme 35. Formation of vinylcyclopentenes *via* an olefin metathesis-[3+2]-cycloaddition sequence.



Scheme 36. Stereocontrolled intramolecular cycloaddition with a cyclopropylcarbene complex.

8.2.3 Synthetic Applications of Boroxycarbene Complexes

The coordination of an oxophilic metal to the oxycarbene side chain offers the possibility to tune the properties and the reactivity of the carbene complex. A review on metalloxycarbene complexes has been published recently; [88] among them boroxycarbene complexes have received the widest attention and have been applied to organic synthesis. Their reactivity strongly depends on the boron coordination sphere as demonstrated for dialkyl- and difluoroboroxycarbene complexes.



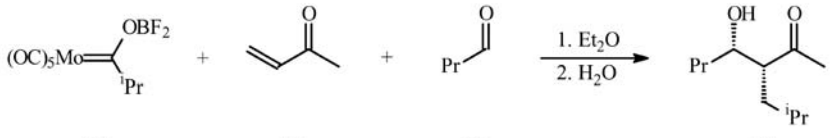
81 **82** **83**

Scheme 37. Regio- and diastereoselective transformation of terpenes into 1,3-diols.

Upon warming to room temperature dialkylboroxycarbene complexes were transformed into oxaborolane derivatives. [89] This reaction involves an insertion of the carbene ligand into the boron C_β–H bond accompanied by the loss of the metal fragment. Further oxidation of the oxaborolane yielded 1,3-diols as a mixture of diastereomers with low stereoselectivity (< 40% d.e.). Chiral dialkylborane derivatives bearing a tertiary C_β–H bond revealed excellent diastereoselectivities (up to > 99% d.e.) depending on the substitution pattern of the carbene complex. [89] By this methodology a series of terpenes such as **81** have been modified into the corresponding 1,3-diols (**83**) *via* boroxycarbene complexes (**82**) in good yield and with excellent stereoselectivity (Scheme 37). [90]

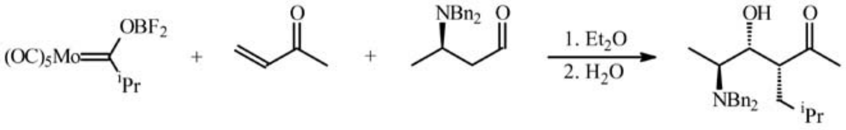
Radical reactions in synthetic organometallic chemistry are rare but gain increasing importance. A recent example demonstrated that molybdenum difluoroboroxycarbenes may serve as radical precursors and allow to generate acyl radicals under mild reaction conditions. [91] Coupling of molybdenum difluoroboroxycarbene **84** to vinylketone **85** and aldehyde **86** leads diastereoselectively to *syn*-β-hydroxyketone **87** (Scheme 38). Using the chiral aldehyde **88** a diastereofacial selectivity of more than 99% d.e. was observed for the formation of **89** (Scheme 39).

Difluoroboroxycarbene complexes have been further applied to stereoselective *Diels-Alder* reactions. The [4+2]-cycloaddition of alkenyl(difluoroboroxy)-carbene chelate **90** with 2-amino-1,3-dienes **91** afforded the spirocyclic carbene complex **92** with variable diastereoselectivity (Scheme 40). [92] An extension of this reaction to chiral aminodiene **93** led to the cycloadduct **94** featuring three stereogenic centers including a quaternary carbon in moderate yields but with high asymmetric induction (Scheme 41). [92]



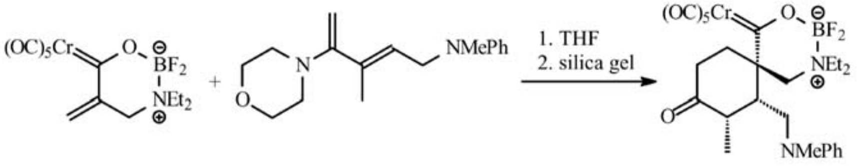
84 **85** **86** **87**

Scheme 38. Molybdenum difluoroboroxycarbene complexes in radical coupling reactions.



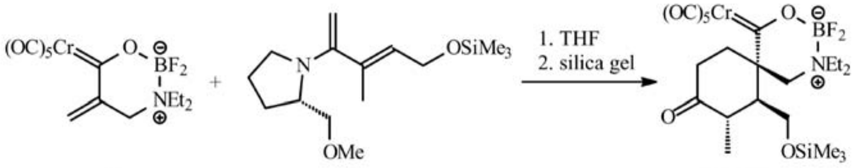
84 **85** **88** **89**

Scheme 39. Asymmetric radical coupling reaction with molybdenum boroxycarbenes.



90 **91** **92** (100% d.e.)

Scheme 40. *Diels-Alder* reaction of a chelated alkenyl-(difluoroboroxy)carbene complex.



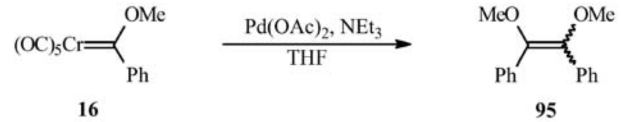
90 **93** **94** (93% e.e.)

Scheme 41. Enantioselective *Diels-Alder* reaction with a difluoroboroxycarbene complex.

8.2.4 Group 6 Metal Carbenes in Catalytic Carbene Transfer Reactions

Although the first carbene transfer from a *Fischer* carbene complex to another metal (*e.g.* iron or group 10 metals) has been reported already three decades ago and has been exploited in the synthesis of organometallic dinuclear and cluster complexes, [93] applications in organic synthesis became evident only recently. Beyond stoichiometric reactions [94] catalytic transmetalation of carbene complexes opens a promising area in organic synthesis. [95]

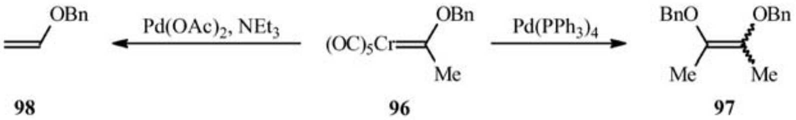
The dimerization of chromium-coordinated carbene ligands typically requires temperatures above 120°C. Whereas the addition of catalytic amounts of $Rh_2(OAc)_4$ allows to only a minor decrease in temperature to 100°C, the dimerization occurs already at room temperature under palladium catalysis. [95a,96] When the reaction of chromium arylcarbene **16** was promoted by $Pd(OAc)_2$ (10 mol-%) in the presence of NEt_3 using THF as a solvent, a mixture of isomeric carbene dimers **95** was obtained with an *E*/*Z* ratio of 2:1 (Scheme 42). The effects of the catalyst load, phosphine additives, the reaction temperature, the solvent and a series of other palladium catalysts have been investigated systematically, but did not reveal significant changes. [96]



16 **95**

Scheme 42. Palladium-catalyzed carbene dimerization of an arylcarbene complex.

In contrast, the nature of the catalyst has a dramatic influence concerning the dimerization of methylcarbene ligands such as present in **96**. Scheme 43 illustrates the remarkable chemoselectivity resulting from the presence of catalytic amounts of $Pd(OAc)_2/NEt_3$ or $Pd(PPh_3)_4$, respectively. Whereas the latter induces specifically the carbene dimerization to give an *E*/*Z* mixture of ene diether **97**, the $Pd(OAc)_2/NEt_3$ system effects a base-induced hydrogen migration to give enol ether **98**.

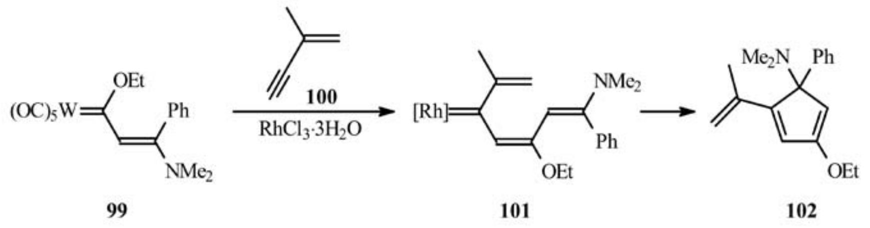


98 **96** **97**

Scheme 43. Chemoselectivity of palladium catalysts in carbene dimerization and hydrogen migration reactions.

The transmetalation strategy was applied to the synthesis of conjugated polyenes and enediyne derivatives from suitable metal carbene precursors; bis-carbene complexes undergo an intramolecular reaction to give cyclic dimerization products. A mechanistic rationale for the catalytic cycle includes the transmetalation of a chromacyclobutane to a palladacyclobutane intermediate in the key step of the reaction. [96]

The transmetalation is compatible with more elaborate carbene ligands. A recent example demonstrates the enhanced reactivity of β-aminovinylcarbene complex **99** towards enynes such as **100** when the group 6 metal is substituted for rhodium. It is remarkable that even the tungsten carbenes which generally are among the least reactive carbene complexes in metal centered processes are activated for C-C bond formation by this procedure. In the presence of catalytic amounts of a rhodium complex, a sequence of enyne insertion and π-cyclization occurs at ambient temperature to give vinylcyclopentadiene **102** (Scheme 44). [97] $RhCl_3 \cdot 3H_2O$ in methanol, $[(Cod)RhCl]_2$ and $[(OC)_2RhCl]_2$ turned out to be similar efficient catalysts. A π-cyclization of a rhodaoctatetraene intermediate **101** – which could be isolated in one case [97c] – generated by transmetalation of the chromium or tungsten analogue has been suggested as the key step of the reaction. [97]

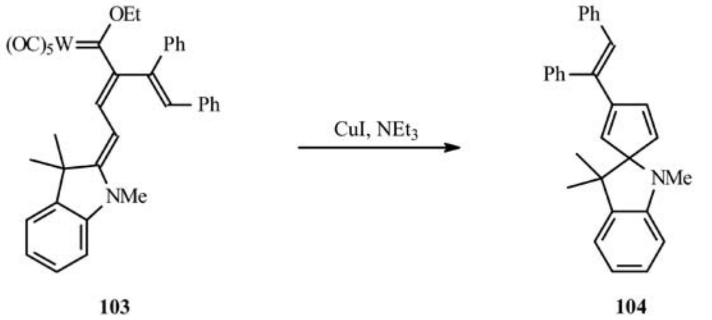


Scheme 44. Rhodium-catalyzed reactivity enhancement of a *Fischer* carbene complex.

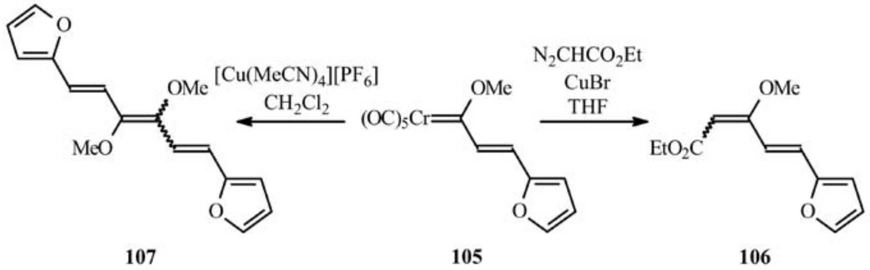
Apart from palladium and rhodium, copper(I) compounds have been shown to catalyze reactions of *Fischer* metal carbenes. As an example, the π-cyclization of tungsten carbene complex **103** to the spirocyclic vinylcyclopentadiene **104** has been found to be strongly enhanced in the presence of CuI and NEt_3 (Scheme 45). [97c]

A very recent report highlights the cross-coupling of *Fischer* carbene complexes with ethyl diazoacetate to give push-pull alkenes such as **106** at ambient temperature using 15 mol-% CuBr as a catalyst (Scheme 46); [98] alkyl-, alkenyl- (**105**) and arylcarbenes provided comparable good chemical yields.

Whereas no stereocontrol of the configuration of the double bond formed was observed with methoxycarbene complex **105**, its menthyloxycarbene analogue **108** afforded exclusively the *E* stereoisomer. The chemoselectivity of the reaction strongly depends on the nature of the catalyst: In the presence of 15 mol-% of $[Cu(MeCN)_4][PF_6]$, a dimerization of the methoxycarbene ligand was observed favouring the *E* isomer in a 10:1 ratio. (Scheme 46). [98]



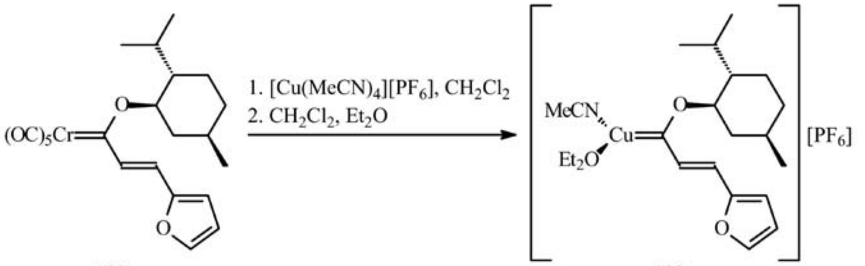
Scheme 45. Copper-catalyzed cyclization of a *Fischer* carbene to a spirocyclopentadiene.



Scheme 46. Copper-promoted carbene dimerization and cross-couping.

Finally, when chromium (−)-menthyloxycarbene **108** was exposed to 50 mol-% $[Cu(MeCN)_4][PF_6]$, a copper bis-carbene complex was formed along with acetonitrile(pentacarbonyl)chromium. Using dichloromethane and diethyl ether as solvents, a colour change occurred and crystals of copper(I) carbene complex **109** were deposited (Scheme 47). [98] So far, there has been only a single report on the synthesis of a stable copper(I) carbene complex. [99]

Under the conditions of crystallization of copper carbene complex **109**, the carbene ligand tends to be retransferred to chromium while the vacant coordination site at copper is occupied by diethyl ether. [98] The X-ray structure of **109** provides a rare example of a tricoordinated metal center. Both copper containing species, the bis-carbene and the mono-carbene **109**, undergo a carbene dimerization in the presence of tributylphosphine to yield (1*E*,3*E*,5*E*)-1,3,5-trienes in a process analogous to the formation of **107**. [98]



108 **109**

Scheme 47. Synthesis of a copper(I) carbene complex *via* transmetalation of a stable chromium percursor.

8.3 OUTLOOK

Over the past 35 years *Fischer* carbene complexes have been developed from organometallic curiosities to valuable reagents in organic synthesis. Their impact on carbon-carbon bond formation arises from both the pronounced electrophilicity of the carbene carbon attached to a metal carbonyl fragment and the α-CH acidity of alkyl carbene substituents. Beyond the role of the metal-carbene moiety as a novel organometallic functional group the metal center may act as a template which assembles a choice of coligands in a proper geometrical relation favourable for a stepwise interligand coupling. Both types of reactions offer promising perspectives for the stereoselective synthesis of functionalized acyclic and unsaturated cyclic compounds. A very recent aspect aims at an *in situ* transmetalation which allows the modification of a stable and storable group 6 metal carbene to a more reactive carbene complex derived from precious metals. This approach is expected to add a new aspect to metal carbene based catalysis, an area which is highlighted by olefin metathesis [100] (in particular ring closing metathesis (RCM); see also chapter 7) and the multi-facetted chemistry arising from rhodium carbene intermediates. [101]

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Chapter 9

From High-spin Polycarbenes To Carbene-based Magnets

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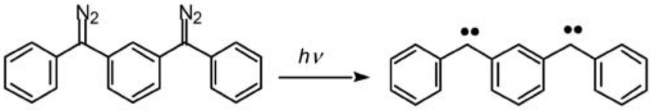
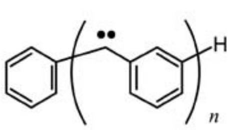
9.1 BACKGROUND

The chemistry of high-spin polycarbenes started in 1967 when two groups led by K. Itoh [1] and E. Wasserman [2] reported independently their findings that *m*-phenylene-dicarbene **1c** generated by the photolysis of diazo compound **1d** has a ground quintet state. Prior to this report, A. M. Trozzolo and coworkers [3] had found in 1963 that the corresponding *p*-phenylenedicarbene has a singlet ground state. The high-spin and low-spin ground states for a pair of the *m*- and *p*-phenylenedicarbenes established experimentally not only the topological symmetry control of the ground spin states of the dicarbenes but also a basis for design of super-high-spin polycarbenes.



1d **1c**



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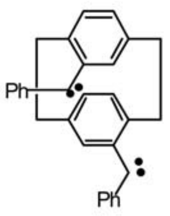
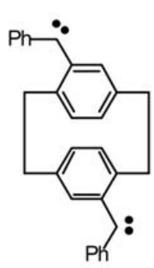
Actually one-dimensional polycarbenes like **2** ($n = \infty$) were subsequently proposed as prototypes of organic ferromagnets by N. Mataga [4]. No experimental challenge to this possiblity had appeared for more than a decade, when H. Iwamura and T. Sugawara at the Institute for Molecular Science (IMS) in Okazaki set out in the early eighties to prepare a systematic series of such polycarbenes and characterize their magnetic properties. Tetra- and pentadiazo compounds, precursors to tetra- and pentacarbenes **2**(n = 4 and 5), were prepared and the ground state spin mutiplicity (S) for their photoproducts were comfirmed by analyzing their epr fine structures. [5] This work was carried out in collaboration with K. Itoh and coworkers who were specialists for epr studies on high-spin species. This type of epr experiment requires that the samples be oriented (e.g., in a host crystal) for the measurements and cannot be applied to any sample. On the other hand, randomly oriented epr spectra for carbenes in frozen solutions, which are commonly used, showed many signals in the field range 100 – 500 mT and all signals tended to gather at $g = 2$ as the number of carbene centers increase. This means that, as the number of the carbene centers increases, the amount of information obtained from epr spectra decreases. For the determination of high-spin states of the generated carbenes, especially with $S > 6$, we therefore needed a convenient method other than epr spectral measurements. How can we determine the S value in the ground state for high-spin carbene ? One possible answer was a measurement of the field dependence of magnetization(M) in a frozen solution. For the purpose, we irradiated the sample through a window at the bottom of a Faraday-type magnetic balance and measured the magnetic moment of the photo-generated polycarbenes in situ. The successful proof of tetra- and pentacarbenes **2** (n = 4 and 5) by using this method encouraged us very much and we were led into the studies of hexacarbenes and dendritic high-spin polycarbenes. This method of using *M vs H/T* plots, established by T. Sugawara, proved to be a versatile tool for characterizing a number of 2D super high-spin polycarbenes and carbene-metal complexes, although the instrument was switched from a Faraday balance to a SQUID magneto/suceptometer sometime later.

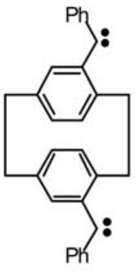
We not only pursued realization of a real magnet by using various polycarbenes, but also continued to investigate the fundamental magnetic properties of organic polycarbenes: through-bond and through-space interactions between triplet carbenes. As models for a stacking interaction between triplet carbene molecules in solid samples, we prepared dicarbenes **3** by taking advantage of the [2,2]paracyclophane skeleton and found by means of their epr fine structures that it is only the ortho and para stackings that lead to the parallel alignment of the spins of the neighboring molecules.[6] Since this provided the first experimental test for the McConnel theory II, [7] this paper received a high reputation.



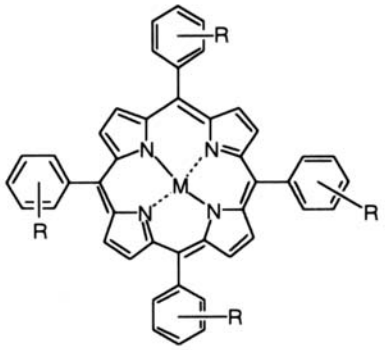
Ortho **3** ($S = 2$)

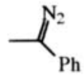


meta **3** ($S = 2$)



para **3** ($S = 0$)



4; R =  or H

M = H_2, Zn(II), Cu(II) etc.

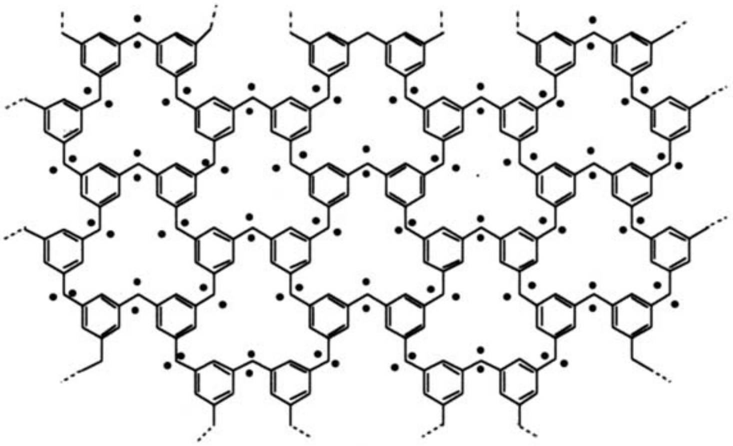
When N. Koga began with the subject of the magnetism in H. Iwamura's group at IMS in 1985, he wanted to make new types of high-spin carbene systems and started the studies on the magnetic properties of tetraphenylporphyrin derivatives **4** and their metal complexes having one to four carbene centers. He wished to elucidate three subjects: 1) the various types of carbene-carbene exchange interactions through a porphyrin ring, [8] 2) the carbene-metal ion magnetic interaction in metalloporphyrin, and 3) the magnetic interaction between carbene and photoexcited triplet porphyrin. After a while, he realized that he should thought more carefully about his own work before starting. Interesting and beautiful epr spectra were obtained in three subjects as expected and their works were submitted to international journals. However, all this work was rejected for the reason that you should simulate the spectra theoretically or you should prove the existence of a high-spin state by any additional procedure other than the epr measurement. For example, in the heterospin system of carbene-metalloporphyrin, the spectra were due neither to isolated triplet carbene nor to the addition of isolated carbene and metal ion but were due to the high-spin carbene species produced by the magnetic coupling between carbene and copper(II) ion. However, it was difficult to draw a conclusion concerning the quartet carbene species. The failure to publish the work on the photoexcited high-spin species by subject 3) epecially dissappointed Koga. The idea, the formation of a photoexcited high-spin species, appeared recently in the works by others. Since then, all data were kept in the cabinet of our office.

From this failure, we learned that we have to selectively apply the appropriate spin source to a model study or a high-spin study. In the beginning of this work on a high-spin molecule, we were often asked why we used the carbene as a spin source. Carbenes are unstable reactive intermediates and difficult to handle. We answered that we should be able to obtain spin-quantum number S twice as high in carbenes as in the corresponding free radicals. A quintet state sounded good compared with triplet one, when presenting the our work in a symposium. It was very attractive for us chemists to aim for high-spin molecules. However, we soon realized that carbenes were not suitable for the model study on the magnetic coupling. In particular for the model study, we were asked how and to what extent they are interacting. To answer this question, it is nesessary to have the sign and absolute values of exchange coupling parameter J for a intra- and intermolecular coupling and the information of the molecular and crystal structure to understand J values. In most cases, the model compounds using carbenes cannot give us both of them; it can tell us only the sign of J in a lucky case. Since carbenes are usually obtained by photolysis of the corresponding diazo precursor and cannot survive the high temperature region (> 77 K), we could not populate the less stable states thermally. It was also difficult to perform structure analysis of carbenes by X-ray diffraction. We therefore quit using a carbene as an organic spin source for a model coupound.

In 1987, we moved to the University of Tokyo and had an opportunity to expand our research strategy, focusing more directly on the construction of molecular based magnets by employing persistent radicals,[9] i.e., polyaminoxyl radicals, in place of carbenes as an organic spin source. In order to look for useful magnetic couplers for the construction of the spin network, we used model compounds having persistent aminoxyl radicals and found various ferromagnetic coupling units other than the *m*-phenylene (this area is, however, outside of this chapter).[10] At that time, a report by J. S. Miller [11] had just appeared on the charge-transfer salts of decamethylferrocene and TCNE that undergo the magnetic transition to a ferromagnetic state at 4.8 K. During the following years, some crystals of organic radicals showing transition to bulk magnets below 2 K were reported successively (M. Kinoshita [12] 1991, A. Rassat [13] 1992, and T. Nogami [14] 1993).

It became much clearer that the following three conditions have to be satisfied for the realization of high-temperature-T_c ferromagnets. [15]

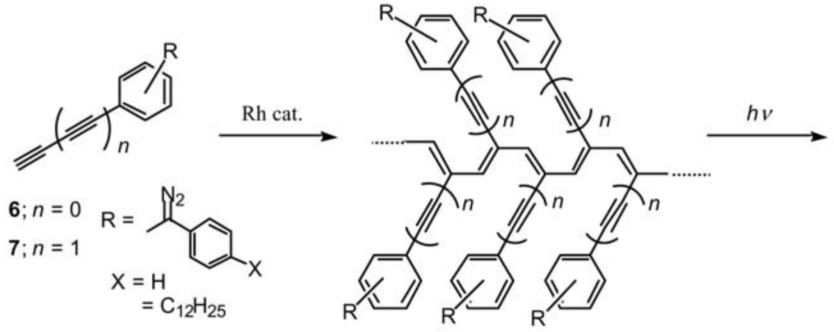
1. assemblage of many unpaired electrons,
2. stronger exchange coupling among the neighboring radical centers, and
3. the spins in one-dimensional chain cannot order at finite temperature; two- and thee-dimensional network structures are indispensable.



5

Therefore, our target molecule should be like honey-comb **5** instead of **1c** and **2**. This structure is a modified one of the original polyradical proposed by N. Mataga [4] in 1968. Since there is no preparative method available to such a structure, we designed hexa- and nonadiazo compounds and the dendritic polydiazo compounds which have a partial structure of the above honey-comb network and prepared their diazo precursors. Photoproducts of hexa- and nonadiazo compounds gave the corresponding polycarbenes with $S = 6$ and 9, respectively, in good agreement with theory. These molecules served as the highest-spin organic molecules ever prepared [16] (This record of $S = 9$ in a pure organic molecule was overcome by A. Rajca [17] in 1998). However, more branched dendritic polydiazo compounds did not give expected S values of 9 and 12, respectively. Our student, who spent 3 years on the synthesis of them, called this failure "a wall of $S = 10$". Very much frustrated with the latter results and unable to construct polycarbenes like **5**, we left the dendritic polycarbene business in 1995.

At the same time as the work on dendritic carbenes, we had started in 1989 the work on π-conjugated polymers carrying carbenes or persistent radicals as pendants. [18] We expected the construction of 1D chain structure by polymerization of monomer at once and the formation of the super high-spin chain after irradiation. We selected poly(phenylacetylene) and poly(phenyldiacetylene) as conjugated polymers which are easily obtained by the polymerization in the presence of catalyst. Especially, phenyldiacetylenes were known to undergo polymerization in solid state, which make us feel the new type of function for the magnetism. For the purpose, we designed 1-ethynyl-4-(a-diazobenzyl)benzene **6** and its diethynyl dereivatives **7** as monomers based on the model experiments. Four years later after repeating the improvements many times, we obtained a beautiful red colored polymer film which has a molecular weight of 20 x 10^4 without untouched diazo moieties. However, its magnetic property after irradiation of polymer film was miserable. It showed only limited correlation over 2~3 units. This study taught us many valuable lessons, such as the importance of information of molecular structure, intermolecular magnetic interaction, etc. At this turning point, we moved into heterospin systems consisting of carbenes and magnetic metal ions for the construction of extended spin networks.



By1993 we saw the limitation of our approach toward the construction of the purely organic ferromagnets and lost interest in model studies on the magnetic coupling. One day, when we were chatting about our research works, Iwamura told Koga that we had performed a large number of the model studies. It was enough for him. Lets move to a real molecular-based magnet. [19] What was the main problem at present for the construction of a magnet? One answer was how we can make a spin network having 1D, 2D, and 3D structures. We failed to make even an infinite linear chain such as **2** ($n = \infty$) in a purely organic spin system. We decided to leave purely organic spin systems for a while and to use metal ions to make the spin network through the coordination bond. [20]

When we planned to use heterospin systems consisting of metal 3d spins and organic 2p spins for the construction of spin-network, we remembered the supramolecular chemistry studied extensively by using pyridines- and polypyridines - metal ions. Especially the work of J.-M. Lehn, [21] J.-P. Sauvage,[22] and P. Stang [23] impressed us. It did not take time for us to reach the idea as shown in Figure 1 where the first metal complex is coordinatively unsaturated.

In our heterospin system,[24] photogenerated carbenes play an important role as magnetic coupler in addition to the organic spin source. Let me explain it using Figure 2. Two metal ions do not talk to each other before irradiation, while they start to talk through the generated carbene after irradiation. Therefore, we call diazo-pyridine(s) compounds "photoresponsive magnetic couplers" (PMC). According to our laboratory notebook, the first measurement of a powder sample of 1:1 complex of Mn(hfac)$_2$ coordinated with our first PMC was carried out on a Faraday balance on June 3 in 1994.

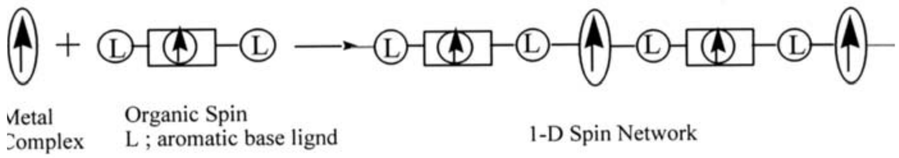


Figure 1. Strategy for the construction of 1D spin network in hetero-spin system.

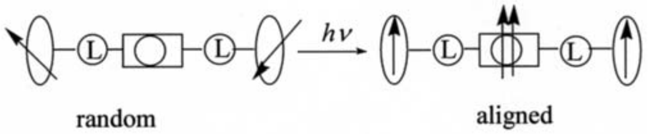


Figure 2. Role of carbene as a photoresponsive magnetic coupler (PMC).

Even with the effort it took for us to set-up our Faraday balance for the measurement of a high-spin carbene molecule, the set-up was not convenient and we needed a lot of experience and special techniques to handle and control the apparatus. Therefore, we always felt the necessity of a convenient new procedure equipped with irradiation system in place of a Faraday balance for investigating magnetic properties of carbenes. From the late eighties, SQUID magneto/susceptometer became commercially available at a reasonable price (still expensive) and relatively easy to obtain. It was easy to operate even for us, not specialists in magnetism. We planned to use SQUID magneto/susceptometer and collaborated with Quantum Design, Inc. to make a new sample holder which would allow irradiation of the sample inside a SQUID apparatus from an outside light source. We obtained a preliminary result by using the first-made sample holder. On the occasion of our move to Kyushu University, furthermore, we made an additional improvement to the sample folder for the irradiation system. The present system, which consists of an optical fiber and an argon-ion laser, shortened the irradiation and data-collection time to less than one-tenth of the previous one.

Our attempts to super-high-spin molecules in hetero-spin systems proceeded slowly but smoothly until the one dimensional spin network by combination of M(hfac)$_2$ and pyridine-carbene. [25] As mentioned before, our final goal is the molecular based magnet, requiring the construction of a two- or three-dimensional spin networks. In order to increase the dimension of linear chain network, we considered the simple scheme shown in Figure 3. We placed organic spins having a branched structure at the diverging point of spin network and focused our effort to the construction of 2D and/or 3D spin network.

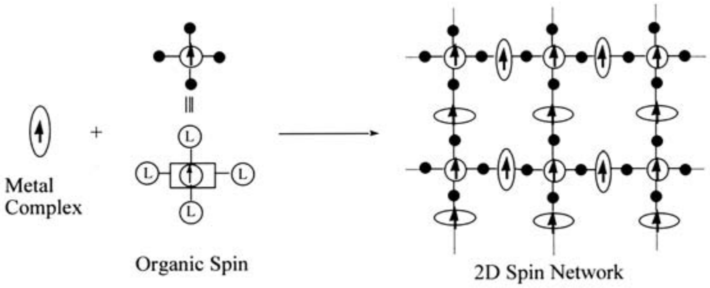


Figure 3. Strategy for the construction of 2D spin networks.

Various branched PMCs were designed and the first PMC for them was made in 1995. Since then, we have spent a lot of time for the preparation of a single crystal of 2:3 complex of M(hfac)$_2$ with PMC. The molecular and crystal structure of the sample gave us critical information to understand the magnetic behavior in detail. Unfortunately, however, we could not obtain enough size of single crystals for X-ray structure analysis. We were forced to change the strategy or the target.

From the middle of 1990s, various metal clusters having slow magnetic relaxation time have been reported as single-molecule magnets (or superparamagnets) [26] and spin glasses [27]. These have become a current topic in molecular magnetism; in terms of their characteristic properties in comparison with bulk magnets, there is no long range magnetic ordering. We felt that we could apply our strategy to these compounds. In 1999, we decided to investigate the magnetic properties under frozen solution conditions, which were similar to the one used for the formation of high-spin polycarbene in early stage of our work. We thought of forming assemblies consisting of branched PMC and M(hfac)$_2$ in frozen solutions and expected that they exhibit interesting magnetic behaviors. Actually, we could succeed in the observation of a spin glass-like magnetic behavior after irradiation under frozen solutions. [28] To the best of our knowledge, the photochemical formation of the spin-glass character and the development of hysteresis due to the spin-glass *in a frozen solution* are the first example. This work will suggest a new approach to the single-molecule magnets by employing an anisotropic metal.

Although the present work deviates somewhat from our final goal, we are convinced that a self-assembly having an interesting magnetic behavior in frozen solution will develop into a new field of magnetism.

9.2 STATE OF THE ART

Our carbene work aiming at the construction of molecular based magnets can be classified into two approaches, pure organic spin system [23] and heterospin system, In this section, we will present specific main works in both approaches in historical order.

9.2.1 Pure Organic Spin System

9.2.1.1 Linear Type of High-spin Polycarbenes [5]

Polydiazo compounds having four and five diazo groups connected by *m*-phenylene units were prepared and their photoproducts, **2** (n = 4 and 5), were confirmed to be nonet and undecet ground state, respectively.

9.2.1.1.1 Synthesis

Diazo compounds, precursors to carbenes, were prepared by the oxidation with active manganese(IV) oxide (or mercury(II) oxide) of the corresponding hydrazones which in turn were obtained from the corresponding ketones by the reaction with anhydrous hydrazine (or hydrazine monohydrate). This method was employed for the introduction of the diazo groups in most of our compounds as a standard procedure. As a typical example of synthesis, a route for pentadiazo compound, a precursor of **2** (*n* = 5) is summarized in Figure 4.

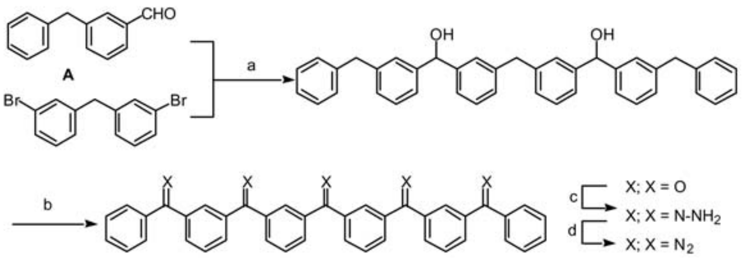


Figure 4. Reagents and Conditions: (a) 1) *n*- BuLi, Ether, 2) **A**, (b) $Na_2Cr_2O_7$, AcOH, 43 % (c) N_2H_4, $N_2H_4{\cdot}HCl$, DMSO, 90 °C, 98 %; (d) HgO, EtOK, EtOH, CH_2Cl_2, 14 %

9.2.1.1.2 Determination of High-spin State for the Generated Carbenes

It was confirmed by two measurements individually, (a) epr fine structure analysis and (b) determination of magnetization, that the carbenes **2** (*n* = 4 and 5), generated by photolysis of the diazo compounds were nonet and undecet ground states, respectively. In these measurements, diazo compounds in a benzophenone host crystal were employed as samples. Here, we demonstrated the results for only tetracarbene **2** (*n* = 4) in both measurements.

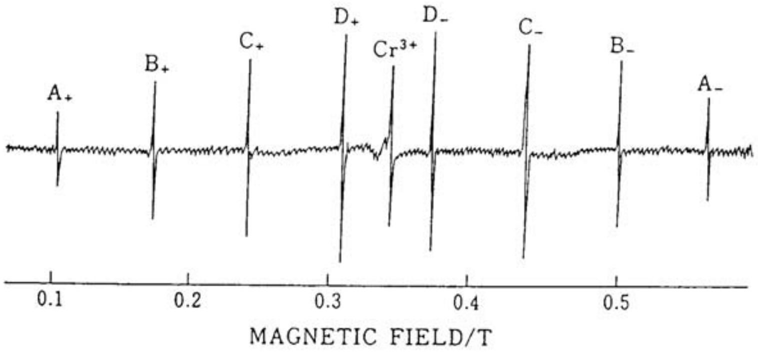


Figure 5. Oriented X-band epr spectrum after irradiation of tetradiazo compound, a precursor of **2** (*n* = 4) in a benzophenone crystal.

(a) Orientated epr spectra measurement. A mixed single crystal of the precursor diazo compound in benzophenone was placed in an epr cavity and irradiated at cryogenic temperature. The molecules of the generated tetracarbene **2** ($n = 4$) was effectively oriented within the host crystals and the epr fine structure was obtained as shown in Figure 5, when one of the principal axes of the fine structure tensor was oriented along the magnetic field. This epr spectrum clearly indicated the photochemical formation of a nonet ground state species.

(b) Magnetization Measurement on a Faraday Balance. Field dependence of magnetization (M) after irradiation of the a benzophenone crystal sample under conditions similar to the one for epr measurement was measured in the field range 0 - 50 kOe at 2.1 and 4.2 K on a Faraday balance.

The experimental data were rationalized in terms of the Brillouin function $B_J(x)$ for magnetization:

$$M = NgJ\mu_B B_J(x) \qquad \text{where} \qquad B_J(x) = \frac{2J+1}{2J}\coth\left(\frac{2J+1}{2J}x\right) - \frac{1}{2J}\coth\left(\frac{x}{2J}\right) \qquad (1)$$

$$x = gJ\mu_B H/(k_B T)$$

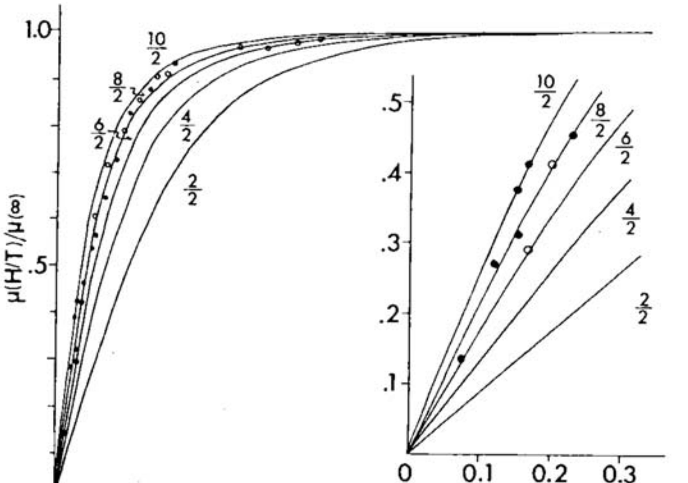
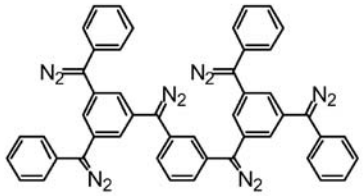


Figure 6. Field dependence of magnetization (M) at 2.1 (●) and 4.2 (○) K after irradiation of tetradiazo compound, a precursor to **2** ($n = 4$) in a benzophenone crystal.

An M vs. H/T plot is shown in Figure 6 together with the theoretical curves with $J = S = 2/2$, $4/2$, $6/2$, $8/2$, and $10/2$ in Eq. 1. Although the experimental data were rather scattered, the data roughly followed the theoretical curve with $S = 8/2$.

9.2.1.2 Dendrimer and Its Analogous High-spin Polycarbenes [16]

We designed six polydiazo compounds, **8**- **13**, which have partial structures of the honey-comb network **5**. The array-shape, cyclic, and dendritic structures were expected to produce high-spin polycarbenes after irradiation.



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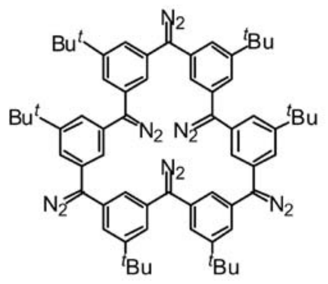

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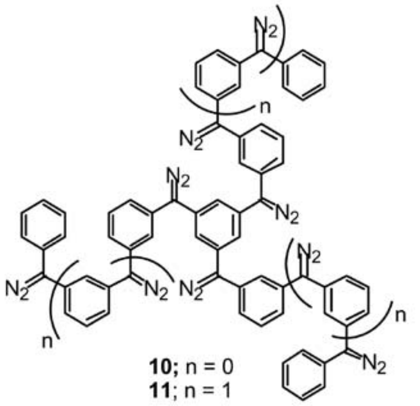
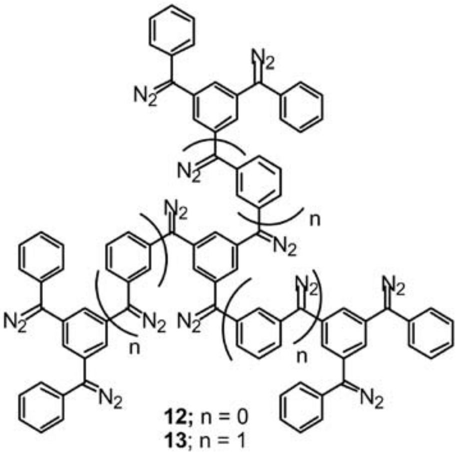


10; n = 0
11; n = 1



12; n = 0
13; n = 1

9.2.1.2.1 Synthesis

Hexaketones, precursors of **8**, **9**, and **10**, were synthesized from *m*-bromobenzaldehyde, calix[6]arene, and tribromobenzene, respectively. In the synthetic sequence for dendritic polydiazo compounds, **11**, **12**, and **13**, the key reaction was a cyclo trimerization reaction of aryl ethynyl ketone to form 1,3,5-triaroylbenzene. By repeating cyclotrimerization twice, we succeeded in the synthesis of dodecadiazo compound **13** which was the highest number we synthesized. The preparative route to **13** is summarized in Figure 7.

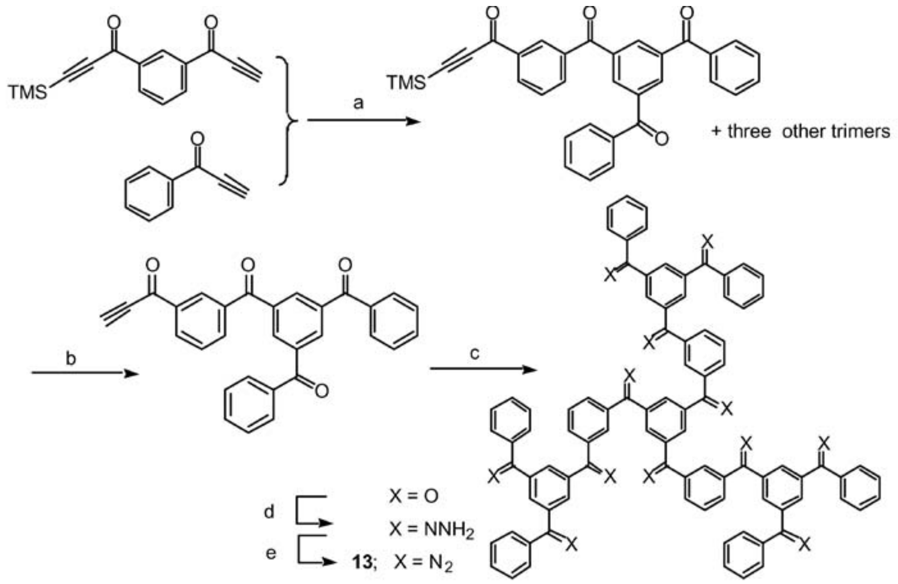


Figure 7. Reagents and Conditions: (a) Et2NH, Toluene, GPC, 31 %; (b) KF, MeOH, -20°C, 96 %; (c) Et_2NH, Toluene, 35 %; (d) N_2H_4, $N_2H_4{\cdot}HCl$, DMSO, 90 °C, 63 %; (e) HgO, EtOK, EtOH, CH_2Cl_2, 24 %

9.2.1.2.2 Determinations of High-spin State for Dendritic Carbenes

Polycarbenes generated by photolysis of the corresponding polydiazo compounds **8-13** were expected to be tridecet ($S = 12/2$), tridecet ($S = 12/2$), tridecet ($S = 12/2$), nonadecet ($S = 18/2$), nonadecet ($S = 18/2$), and pentacoset ($S = 24/2$) ground states, respectively. Magnetization (M) before and after irradiation of diazo compounds **8-13** in frozen MTHF solutions at various temperatures in field range of 0 – 5 T were measured on a Faraday balance. Field dependence of difference in M's between before and after irradiation for diazo compounds **11** are demonstrated together with theoretical curves (equation 1) in Figure 8. The experimental data for **11** traced the theoretical curve with $S = 9$, indicating that nonacarbene with a nonadecet ground state was produced after irradiation. Similarly, from the M vs. H/T plots after irradiation of diazo compound **8-10**, the generated polycarbenes were determined to have a tridecet ground state ($S = 6$). On the other hand, field dependence of M for nonadiazo compound **12** under similar conditions suggested the formation of the species with $S = 7$ instead of the expected $S = 9$. The highest branched dodecadiazo compound **13** also gave the dependence of M similar to the one for **12**. In compounds 12 and **13** having more branched structures, two carbene centers, especially terminal carbenes, might be generated in close proximity to each other and undergo facile intramolecular recombination.

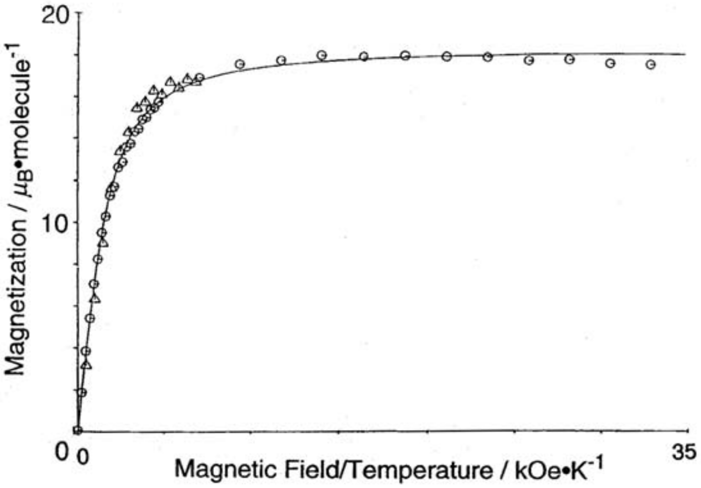


Figure 8. Field dependence of magnetization after irradiation of **11** in a frozen MTHF solution. The theoretical curve with $S = 9$ is shown by a solid line.

9.2.2 Heterospin System Consisting of Carbene and Metal Ion

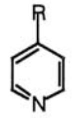
In this section on the heterospin system, we will discuss three subjects: 1) the magnetic coupling between the metal ion and organic spins through pyridine chromophores, 2) the photochemical formation of ferri- and ferrimagnetic chain (1D), and 3) the attempt to create frozen solution magnets (a carbene-based magnet).

9.2.2.1 Strategy in heterospin system for Molecular Based Magnet

In the requirement for the construction of the molecular-based magnets, we pointed out previously that we first have to align as many spins as possible *ferro- or ferrimagnetically.* This means that the spins align parallel or antiparallel, respectively. Second, the *exchange coupling has to be strong*; the sites of the spins must be as close as possible through the π-conjugated systems. The extended structure must be *two- and/or three dimensions in mesoscopic scale*. The first and second conditions, ferro- or ferrimagnetically, have been investigated experimentally and theoretically by using various kinds of two-spin models, and the magnetic couplings between spins can be predicted correctly in most cases. At the present stage, the most difficult problem is the last one, on the 2D and/or 3D in mesoscopic scale. The problem is how to construct the 2D and/or 3D spin-network. One promising approach is to employ the heterospin system consisting of 2p spins in organic radicals and 3d spins in metal ions. Our strategy for the construction of 2D and/or 3D spin-network in heterospin system based on our fundamental experiments is to use the metal ions to help build the 2D and/or 3D structures and to use the organic spins make spin-networks. For this purpose, we selected pyridines having diazo moieties for a precursor to carbene, as a photoresponsive magnetic coupler (PMC). Various combinations of pyridines and metal ions have been used as the building block for the supramolecular architecture and have been reported to form one-, two-, and three-dimensional assemblies in solutions. Therefore, spin-networks having many types of structures are expected to form by these combinations.

9.2.2.2 Exchange Coupling between Metal Ion and Carbene Center [29, 30]

To investigate magnetic coupling between the carbene and the metal ion through a pyridine ligand, 4-pyridylphenyldiazomethane **14d** was prepared as a model PMC together with other pyridines, 2,2'-bipyridines and terpyridines. As it is difficult to quantitively estimate magnetic coupling $J_{R\text{-}M}$ for carbene complexes, 4-pyridyl derivatives having an aminoxyl, which is a persistent organic radical, were also prepared for the quantitative analysis of $J_{R\text{-}M}$. Coordinatively unsaturated bis(hexafluoroacetylacetonato)manganese(II) and –copper(II), Mn- and Cu(hfac)$_2$, were employed as metal ions.



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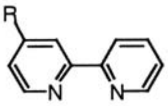

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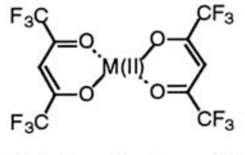
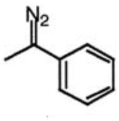
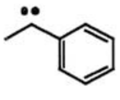
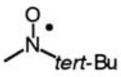


M(hfac)$_2$; M = Mn and Cu ...

R = d, c, and NO

d =


c =


NO =


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By mixing two solutions of M(hfac)$_2$; M = Mn(II) and Cu(II), and **14d** by a 1:2 ratio, the complexes of [M(hfac)$_2$·(**14**)$_2$] were obtained as single crystals. Similarly, the 1:1 complex of [M(hfac)$_2$·**15d**] was prepared. The molecular structures and crystal packing of all complexes were revealed by X-ray crystal structure analysis. The manganese and copper ions in all complexes reside in the center of symmetry of distorted octahedrons. Molecular structures of [Cu(hfac)$_2$·(**14d**)$_2$] and corresponding aminoxyl complex, [Cu(hfac)$_2$·(**14NO**)$_2$] are shown in Figure 9.

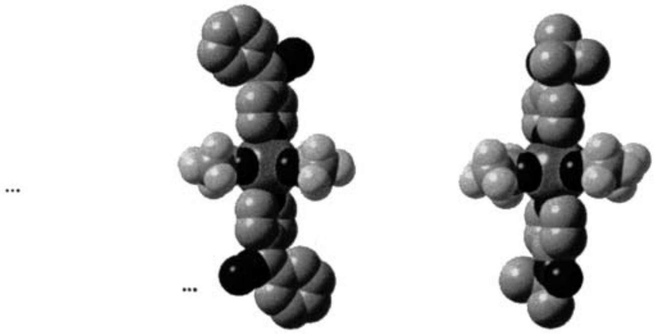


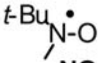
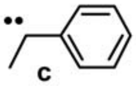
Figure 9. Molecular Structures of [Cu(hfac)$_2$·(**14d**)$_2$](left) and [Cu(hfac)$_2$·(**14NO**)$_2$] (right)

The magnetic properties before and after irradiation of the samples of [Mn- and Cu(hfac)$_2$·(**14d**)$_2$] were investigated by SQUID magneto/susceptometry. When irradiation started, the values of the magnetic moment at 5 K in a constant field of 5 kOe gradually decreased (for the Mn complex) and increased (for the Cu complex). The obtained temperature dependence of $\chi_{mol}T$ values below 100 K after irradiation for 5 hr may suggest that anti- and ferromagnetic interactions take place in the manganese and copper complexes, respectively.

After finishing these measurements, we realized the intrinsic problems associated with the use of carbene in a model. 1) The light from laser can not penetrate into a crystalline sample and leaves photolysis of diazo moiety incomplete. 2) We can use only the experimental data in temperature range ca. 10 –50 K for analyzing the magnetic coupling within a complex molecule: below the temperature region, the intermolecular antiferromagnetic interactions often become predominant (< 10 K) and the generated carbene centers start to decompose chemically above those temperatures. Therefore, their observations are not enough to conclude the magnetic coupling between metal ion and carbene centers through pyridine rings.

In order to understand the magnetic coupling quantitatively, temperature dependence of $\chi_{mol}T$ values for thermally stable [Mn- and Cu(hfac)$_2$·(**14NO**)$_2$] were investigated under similar conditions. The obtained $\chi_{mol}T$ vs. T plots were analyzed by means of theoretical equations for the three spin model consisting of metal ions; Mn(II) and Cu(II) with $S = 5/2$ and 1/2, respectively, and two aminoxyls with $2 \times S = 1/2$. The obtained exchange coupling parameters ($J_{R\text{-}M}$) in unit of temperature (1 K = 1.987 cal/mol) for [Mn- and Cu(hfac)$_2$·(**14c**)$_2$], [Mn- and Cu(hfac)$_2$·(**14NO**)$_2$] and the corresponding 2,2'-bipyridine complexes are summarized in Table 1.

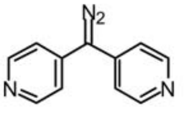
Table 1. Exchange Coupling Constants ($J_{R\text{-}M}$) in Various Metal Complexes

	R =	 NO	 c
[M(hfac)$_2$·**14**$_2$]	Mn	-12.4 K	-18 K
	Cu	+60.4	+
[M(hfac)$_2$·**15**]	Mn	-20.2 K	-
	Cu	+69.4	+

The difference in magnetic properties between the manganese and copper complexes was explained by the difference of their magnetic orbitals of metal ions; d_{xy}, d_{yz}, d_{xz}, $d_{x2\text{-}y2}$, and d_{z2} for Mn(II) ion and $d_{x2\text{-}y2}$ for Cu(II) ion. In the former, some of the d- orbitals containing the unpaired elelctron can overlap with the π-obital of the ligand, while, in the latter, the $d_{x2\text{-}y2}$ orbital is orthogonal to the ligand π-obital.

9.2.2 .3 One Dimensional Structure [25]

For the construction of spin-network having a chain structure, we designed diazodi(4-pyridyl)methane **16** and didiazo compound **17** as PMCs and prepared.



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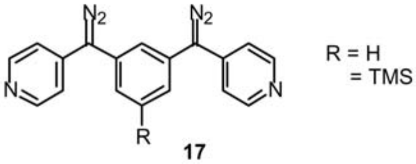

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The 1:1 manganese(II) and copper(II) complexes, [Mn- and Cu(hfac)$_2$·**16**] and [Mn- and Cu(hfac)$_2$·**17**] were prepared by the procedure in a manner similar to the one for model complexes. In both metal complexes of [Mn- and Cu(hfac)$_2$·**16**], two kind crystals, complex **a** and **b**, were obtained by using different solvents for the recrystallization. [25b, 25c] Crystal structures for manganese complexes **a** and **b** are shown in Figure 10.

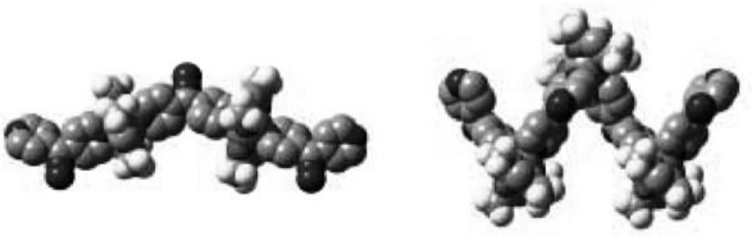


Figure 10. Crystal Structures of 1:1 Complexes [Mn(hfac)$_2$· **16**] in **a** *trans* (left) and **b** *cis* (right) Conformations

Two pyridine groups in **16** of complexes **a** and **b** coordinate with different manganese ion in *trans* and *cis* configuration to form zig-zag and spiral structures, respectively. In copper complexes, only complex **a** was analyzed and its crystal structure was close to the one for complex **a** for manganese. The single crystal of the 1:1 complex of Cu(hfac)$_2$coordinated with **17**, [Cu(hfac)$_2$·**17**],[25d] was also obtained and its crystal structure was revealed by X-ray structure analysis to have a helical 1D chain having the *trans* coordinations of pyridine groups.

The magnetic properties before and after irradiation of the microcrystalline samples (~ 0.6 mg) of [Mn- and Cu(hfac)$_2$·**16**] and [Mn- and Cu(hfac)$_2$·**17**] were investigated by SQUID magneto/susceptometry under conditions similar to those for the experiments of model complexes. The temperature dependence of $\chi_{mol}T$ values before and after irradiation of [Cu(hfac)$_2$·**16**] is shown in Figure

11. Before irradiation, the $\chi_{mol}T$ values of [Cu(hfac)$_2$·**16**] were nearly constant at 0.42 emu·K·mol^{-1} in whole temperature range. These values are consistent with $\chi_{mol}T = 0.375$ emu·K·mol^{-1} calculated for a dilute paramagnetic copper(II) of $S = 1/2$, indicating that the d electron spins of copper(II) ions are magnetically isolated. When irradiated with an Ar laser ($\lambda = 514$ nm), a drastic difference of the thermal behaviors of $\chi_{mol}T$ values below 230 K were observed in the copper complexes. On cooling from 240 K, $\chi_{mol}T$ values of copper complex **a** and **b** continuously increased from 230K and reached a maximum value of 7.43 and 18.2 emu·K·mol^{-1} at 14 and 3.0 K, respectively, and started to decrease somewhat towards 2 K. The data were analyzed theoretically by the method based on a model of the $S = 1/2$ and $S = 2/2$ Heisenberg ferromagnetic chain to give $J/k_B = +66.8$ K and $g = 2$ for complex **b** of [Cu(hfac)$_2$·**16**]. The observed sign of exchange coupling between the carbenes and the metal ion is consistent with that prescribed by model complexes. After annealing above 240 K, the thermal behavior in the complex became similar again; the $\chi_{mol}T$ values traced the horizontal line before irradiation. Similarly, the formation of ferrimagnetic chain due to the antiferromagnetic interaction after irradiation of the 1:1 complex of [Mn(hfac)$_2$·**16**] was observed.

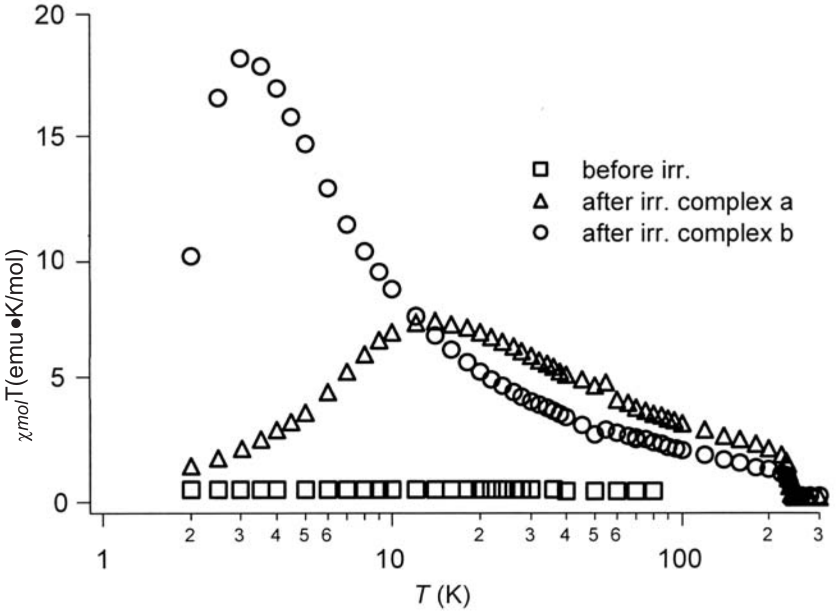


Figure 11. Temperature dependence of $\chi_{mol}T$ for 1:1 complex **a** and **b** of [Cu(hfac)$_2$ ·**16**] before and after irradiation.

Our entire results on the construction of 1D-spin network of [M(hfac)$_2$ ·**16**] are summarized in Figure 12. PMC, diazodi(4-pyridyl)methane **16**, and M(hfac)$_2$ were mixed by 1:1 ratio to form a 1D chain structure which was revealed by X-ray analysis. Before irradiation, the metal ions in a chain were magnetically isolated and the spins of metal ion aligned randomly. When irradiation started, the generated carbene centers interacted with both side of metal ions; ferro- and antiferromagnetically for copper(II) and manganese(II) complexes, to form ferro- and ferrimagnetic chain. Exactly speaking, π electrons and the two electrons of a carbene center interact. From the peak $\chi_{mol}T$ values in $\chi_{mol}T$ vs. T plots, we can estimate the ordering over ca. 6 and 15 units for the complex **a** and **b** of [Cu(hfac)2·**16**] and ca. 40 units in [Mn(hfac)2·**16**] along the chains.

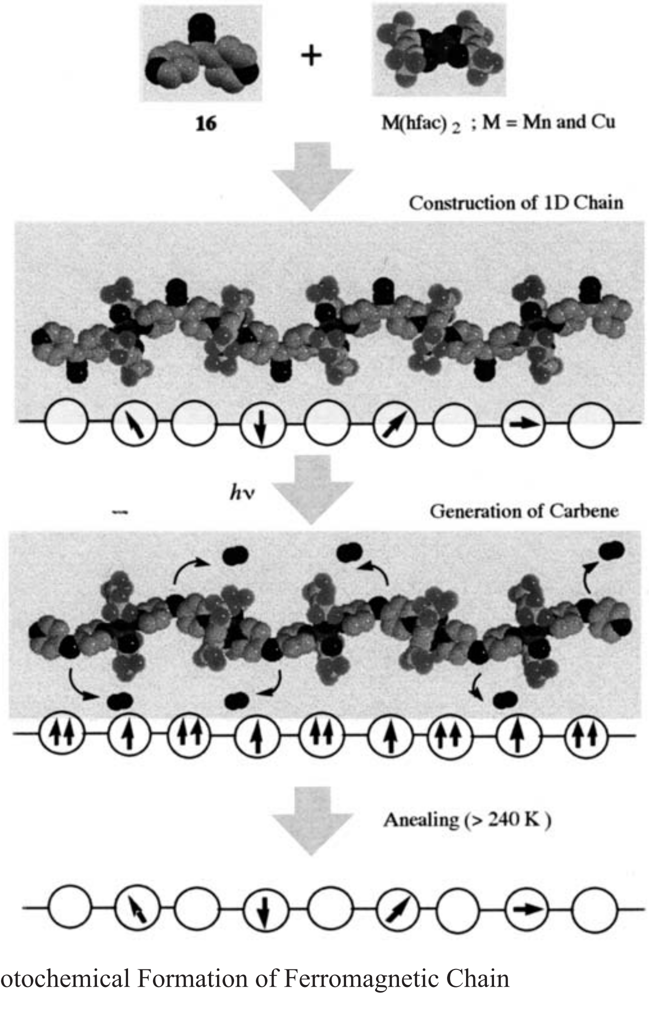


Figure 12. Photochemical Formation of Ferromagnetic Chain

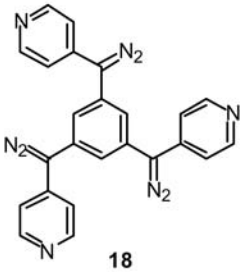
These correlation lengths should be taken as minimum estimates since $\chi_{mol}T$ values are not free from saturation at the 50 mT employed for the measurement, nor from the antiferromagnetic interchain interaction. After annealing above 240 K, carbene decomposed chemically and the spins of the metal ion returned back to be random.

Although this finding is not directly related to the magnetism, these experiments gave us, carbene chemists, a surprising discovery. It is the abrupt change of the $\chi_{mol}T$ values observed at 230 K. Taking the temperature independence of $\chi_{mol}T$ above 240 K and in a consecutive measurement after leaving the sample at 300 K into account, we interpret the abrupt change of the $\chi_{mol}T$ values at 240 K as indicating the disappearance of the generated carbene centers by chemical reactions. It is worth noting that, whereas the carbene species generated in model complexes [M(hfac)$_2$·(**14**)$_2$] disappeared at 90 K, those in the crystal of [M(hfac)$_2$·**16**] survived temperatures as high as 230 K. The observed stability of the carbene centers is novel and most probably due to kinetic protection in the stiff crystal lattice of the metal complex.

The success of the construction of the1D-spin network proved that our strategy is correctly directed toward the development of molecular based magnets and encouraged us very much. This experiment suggests that the construction of the 2D and/or 3D structures will lead to the achievement of creating the corresponding spin network, which should be magnetic; this is our goal.

9.2.2.4 Attempts at 2D- and/or 3D-Spin Networks in Frozen Solutions [28]

When it is considered that 2D and/or 3D-structures go beyond the line structure of the simple 1D case, a suggestion presents itself; the number of pyridyl group in PMC should be increased. Based on this answer, we designed tridiazo- and tripyridyl compound **18** and pentadiazo and tetrapyridyl compound **19** as new PMCs.



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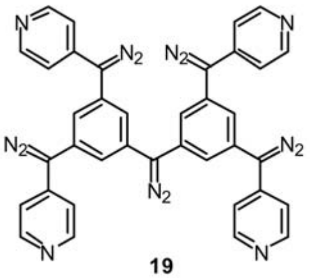

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They are prepared by the standard method and crystallized in appropriate solvents. Their molecular structures were determined by X-ray structure analysis. We first confirmed that the generated carbenes in molecules of PMCs interacted ferromagnetically by means of the field dependence of magnetization (*M*) as described above. When the experimental data for **18** and **19** is put into *M/Ms* vs. *H* plots and traced with theoretical curves, the best fits give $S = 6/2$ and 10/2, indicating that all carbene centers interact ferromagnetically to produce septet and undecet species, respectively. Each carbene center in PMCs was also expected to interact ferromagnetically with copper(II) ions through the pyridine rings in the complex with Cu(hfac)$_2$.

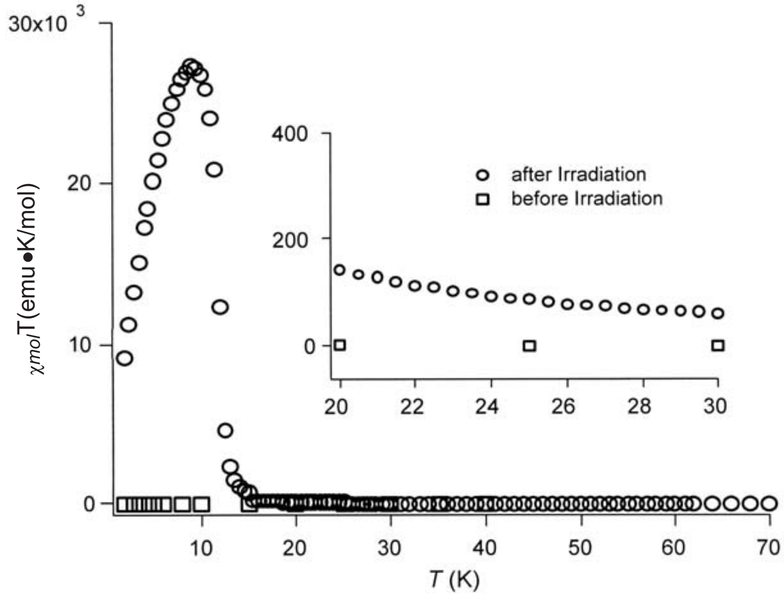

Figure 13. Temperature dependence of $\chi_{mol}T$ values after irradiation of a 3:2 mixture (20 mM) of Cu(hfac)$_2$ and **18** in a frozen solution. The inset shows the enlarged view in the temperature range of 20-30 K.

The magnetic properties before and after photolysis of self-assemblies consisting of Cu(hfac)$_2$ and **18** were studied by means of SQUID magneto/susceptometer. In these experiments, 50 μl of solutions of Cu(hfac)$_2$ in MTHF and **18** in MTHF-CH$_2$Cl$_2$ (4:1) by 2:3 molar ratio were employed as the sample for SQUID measurements. The light from an argon ion laser (λ = 514 nm) was used and the irradiation of the sample was performed in a sample room inside SQUID apparatus. Photolysis of the samples was confirmed to have taken place quantitatively by taking the difference of absorptions at 492 nm due to the diazo moieties before and after SQUID measurements. Saturation magnetization values (M_{sat}) obtained from the following experiments ranged 92.4-95.7 % of the theoretical ones. Magnetic properties before and after irradiation of self-assembled complexes, consisting of 3:2 mixture of Cu(hfac)$_2$ and **18** *in a frozen solution*, were investigated by the measurements of dc and ac magnetic susceptibilities. The $\chi_{mol}T$ vs. T plot in the dc magnetic measurement is shown in Figure 13. The results strongly suggest that the magnetic properties after irradiation are spin-glass-like.

Although it is very difficult to reveal the structure of the self-assemblies formed in frozen solution, we may assume that they have a multi-dimensional network structure. We took advantage of our hetero-spin system and could successfully construct complexes having spin-glass-like magnetic properties [27] by the simple procedure of mixing the two components in solutions and freezing them below 30 K followed by irradiation.

9.3 CONCLUDING REMARKS

When we aim at the construction of the molecular based magnets (bulk magnets), we are required to align as many spins as possible, parallel or antiparallel (ferro- and antiferromagnetically, respectively), in 2D- and/or 3D structures on a mesoscopic scale. To fulfill this requirement, we ignored the chemical stability of the triplet carbene and selected it as a spin source in our study for the following reasons. Diarylcarbene has a versatile skeletal and electronic structure in which two aryl groups are attached to the carbene center and the π-spin is effectively delocalize on the rings. This fact led us to a hetero-spin system smoothly by replacing the terminal phenyl rings in a pure polycarbene network with pyridyl rings. The most important benefit from the use of carbene as spin source is the addition of photoresponsiveness to the magnetism; the carbene is generated by the *photolysis* of the diazo precursor. However, the use of carbene is a double-edged sword in experimental work. We obtain the function of photoresponsiveness at the expense of the quantitativeness in the experiment; it is very difficult to photolyze a sample completely in most cases, especially in a solid state. Sometimes it becomes a fatal drawback in our fundamental study for the magnetism, as mentioned before.

In the area of molecular based magnets, it is widely accepted that the new magnets will never replace conventional magnets made by metals, metal oxides, alloys, etc.. Instead they should have additional functions such as the response to light, pressure, electric current, pH, etc. Thus, our magnets will reveal magnetism only in the part exposed to light and are expected to be applied as high-resolution photomagnetic devices in the materials science of the next generation.

In the study of the magnetism, we must always pay attention to the ferromagnetic impurity, especially for the study in a low concentration. This is one of the reasons why everyone in our field tends to use samples for which the molecular and crystal structure is elucidated by X-ray analysis. Carbenes are free from such a worry about ferromagnetic impurity, because we can easily know the origin of the observed magnetic moments by comparison before and after irradiation and/or those before and after annealing. This fact makes it possible to study the magnetism under frozen solution condition.

We began from the study of the high-spin hydrocarbon polycarbenes in frozen solutions. In the transition period from polycarbenes to carbene-based magnets, we made a number of trial-and-error experiences and learned that we should not approach the random system, such as the frozen solution condition. Now, we are using frozen solution conditions again for a carbene-based magnet. We hope we are going in the right direction.

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