Cushing, G. Watunya, and D. W. Reutter for skilled technical assistance.

References and Notes

(1) J. Chatt and H. R. Watson, *J. Chem. Soc.*, 2545 (1962) used a similar reaction to prepare a red-brown complex reported to be $Fe(dmpe)_2$. We have been able to isolate a second product from our reaction which fits the description of Chatt's compound, but is actually $[\{Fe(dmpe)_2\}_2(\mu\text{-dmpe})]$. Both products, separated by selective crystallization from pentane, are isolated in about 40% yield. This complex is also isolated from the reaction of $Fe(dmpe)_2H(C_{10}H_7)$ with ½ dmpe. To date, four-coordinate zero-valent iron complexes have been postulated,[10,11] but not observed.

(2) J. Chatt and J. M. Davidson, *J. Chem. Soc.*, 843 (1965) reported the preparation of $(C_{10}H_7)RuH(dmpe)_2$ and $(C_6H_5)RuH(dmpe)_2$ by Na reduction in the presence of $C_{10}H_8$ or C_6H_6.

(3) U. A. Gregory, S. D. Ibekwe, B. T. Kilbourn, and D. R. Russell, *J. Chem. Soc. A*, 1118 (1971).

(4) Species of the type $Fe(dmpe)_2HR$ are identified as cis or trans by the presence of ABCD or A_4 spin systems in the $^{31}P\{^1H\}$ NMR; trans species of deuterated analogues appear as 1:1:1 triplets.

(5) T. Herskovitz of this department has made similar observations in a different system.

(6) C. A. Tolman, unpublished results in cyclohexane.

(7) This is the highest field shift reported for a transition metal ethylene complex: see C. A. Tolman, A. D. English, and L. E. Manzer, *Inorg. Chem.*, **14**, 2353 (1975).

(8) C. A. Tolman, *J. Am. Chem. Soc.*, **96**, 2780 (1974); S. D. Ittel, *ibid.*, submitted for publication.

(9) C. A. Tolman, *J. Am. Chem. Soc.*, **92**, 2956 (1970).

(10) E. L. Muetterties and J. W. Rathke, *J. Chem. Soc., Chem. Commun.*, 850 (1974).

(11) H. H. Karsch, H.-F. Klein, and H. Schmidbaur, *Angew. Chem., Int. Ed. Engl.*, **14**, 637 (1975).

(12) Independently prepared in this laboratory; identified by an assignment of the $^{31}P\{^1H\}$ NMR.

(13) Contribution No. 2390 from E. I. du Pont de Nemours and Company.

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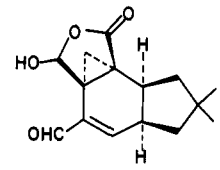
Total Synthesis of Marasmic Acid

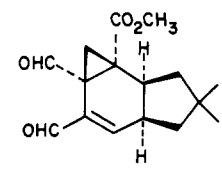
Sir:

Marasmic acid (**1**),[1] one of the many fungal metabolites isolated from the *Basidiomycetes*, has been the target of recent synthetic attempts. In their work, de Mayo and his colleagues synthesized methyl isomarasmate (**2**), which differs from the natural product in the stereochemistry of the polycyclic ring system.[2] During the course of our work, Wilson and Turner reported studies in which a Diels–Alder reaction was utilized for construction of the hydrindane ring system, and described an intermediate which was regarded as possessing the skeleton of marasmic acid.[3] We now wish to report the results of our own, independently conceived work on the Diels–Alder approach to marasmic acid, which has led to the first total synthesis of the molecule, and further, places the stereochemical assignments of Wilson and Turner in serious jeopardy.[4]

Our initial approach to marasmic acid involved Diels–Alder addition of an acetylenic dienophile to diene acetal **6**, which was synthesized in the following manner. Aldehyde **3**, available by the ring contraction method of Magnusson and Thoren,[5] was transformed to the diethyl acetal **4**,[6] bp 74.5–75.5 °C (4.5 mm), in 95% yield by treatment with triethyl orthoformate and a catalytic amount of *p*-toluenesulfonic acid in ethanol (24 h at room temperature). The acetal **4** was allowed to react with ethyl vinyl ether and anhydrous zinc chloride in ethyl acetate (24 h at room temperature) and the resulting ethoxy acetal, without isolation, was subjected to the action of sodium acetate in aqueous acetic acid[7] (4 h at 90 °C), affording the diene aldehyde **5**,[6] bp 68–69 °C (1 mm), in 93% yield. Treatment of **5** with trimethyl orthoformate in methanol containing a catalytic amount of ammonium nitrate gave the dimethyl acetal **6**,[6] bp 82–85 °C (2 mm), in 86% yield.



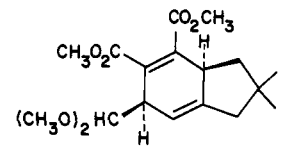
1



2

R

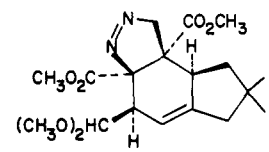
3 –CHO
4 $-CH(OCH_2CH_3)_2$
5 $-CH{=}CHCHO$
6 $-CH{=}CHCH(OCH_3)_2$
18 $-CH{=}CHCH_2OH$



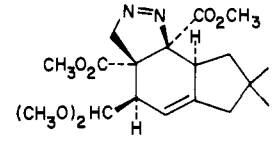
7

Diels–Alder reaction of **6** with dimethyl acetylenedicarboxylate was quite slow, requiring 8 days at 110 °C, but the adduct **7** was formed in high yield. When **7** was allowed to contact a sixfold excess of ethereal diazomethane, a 4:1 mixture of pyrazolines **8**[6] and **9**,[6] mp 117–118 °C (hexane–acetone), was formed over a period of 14 days. Irradiation of the mixture of pyrazolines in ether solution (Pyrex filter) gave, after column chromatography on silica gel, a single cyclopropane, **10**,[6] mp 79–79.5 °C (hexane), in 60% overall yield from **6**.

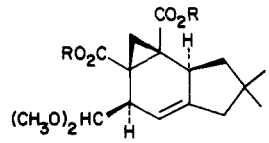
Saponification of **10** with sodium hydroxide in aqueous methanol (48 h, 90 °C) provided diacid **11** as a white foam in 97% yield. The diacid, without purification, was warmed with acetic anhydride (30 min, 55 °C), affording the anhydride **12**,[6] mp 106.5–107.5 °C (hexane), in 96% yield. Reduction of **12** with disodium tetracarbonylferrate in tetrahydrofuran[8] gave a 1:1 mixture of the lactols **13** and **14**. Treatment of this lactol mixture with acetic anhydride (2 h, 90 °C), followed by column chromatography on silica gel, gave lactol acetates **15**,[6] mp 115–116.5 °C (hexane), and **16**,[6] mp 125–128.5 °C (hexane), in 31% combined yield from **12**. Saponification of **15** with potassium carbonate in wet methanol gave pure **13**, mp 96–99 °C (hexane–methyl acetate), in 95% yield. Hydrolysis of the acetal moiety of **13** with tetrahydrofuran–10% aqueous HCl (1:1) afforded (to our surprise![4]) isomarasmic acid (**17**),[6] mp



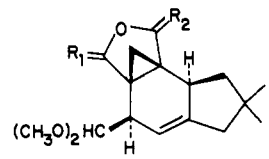
8



9

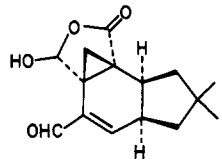


10 R = CH_3
11 R = H

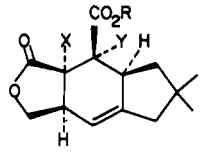


	R_1	R_2
12	=O	=O
13	H,OH	=O
14	=O	H,OH
15	H,OAc	=O
16	=O	H,OAc

140–144 °C (hexane–methyl acetate), in 40% yield. Treatment of **17** with excess ethereal diazomethane gave methyl isomarasmate (**2**), identical by ir (CCl_4) and ^1H NMR ($CDCl_3$) with that prepared by de Mayo.[9] Although an explanation for the exclusive addition of diazomethane to what appears to be the more hindered side of **7** is not readily available, it is the establishment of the isomarasmic stereochemistry for cyclopropane **10** that places in doubt the assignment of the marasmic acid skeleton to the similar cyclopropane obtained by Wilson and Turner, also via a pyrazoline.[10]

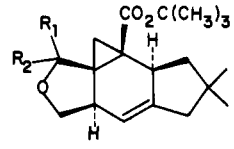


17

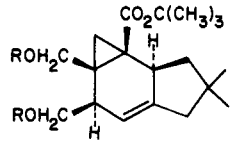


	X	Y	R
20	CH_2Br	H	H
21	H	CH_2Br	H
22	CH_2Br	H	$C(CH_3)_3$
23	H	CH_2Br	$C(CH_3)_3$

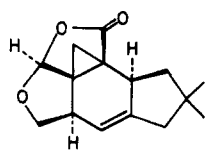
In a second approach to marasmic acid, diene aldehyde **5** was reduced with diisobutylaluminum hydride in benzene, giving the known alcohol **18**[3,6] in 91% yield. Diels–Alder reaction of **18** with bromomethylmaleic anhydride (**19**)[12] in methylene chloride solution (24 h at room temperature) gave a 1:1 mixture of the lactone acids **20**,[6] mp 172–174 °C (hexane–ether), and **21**,[6] mp 177–177.5 °C (hexane–ether). The crude mixture of acids (in methylene chloride solution) was esterified with isobutylene in the presence of *p*-toluenesulfonic acid (4 days at room temperature), affording the *tert*-butyl esters **22** and **23**,[6] mp 139.5–140.5 °C (hexane–ether). Treatment of this mixture of esters with potassium *tert*-butoxide in benzene–*tert*-butyl alcohol (15 min at room temperature) produced the cyclopropane **24**,[6] mp 81.5–83.5 °C (hexane), in 44% overall yield from **18.**



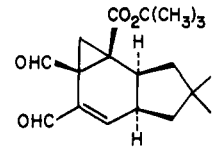
24 $R_1, R_2 = O$
25 $R_1 = OH, R_2 = H$



26 R = H
27 R = COCl



28



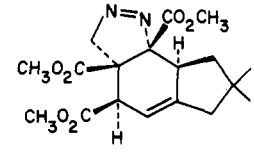
29

Reduction of **24** with diisobutylaluminum hydride in toluene (4 h at −78 °C) afforded the hemiacetal **25**, which could be converted to lactone **28**,[6] mp 87–88 °C (hexane), by exposure to trifluoroacetic acid (65% overall yield from **24**). Reduction of hemiacetal **25** with sodium borohydride in methanol provided the diol **26**[6] (67% overall yield from **24**). Addition of an ether solution of **26** containing 2 equiv of quinoline to an excess of ethereal phosgene at 0 °C provided the dichloroformate **27** in 95% yield. Treatment of **27** with dry dimethyl sulfoxide, followed by 2.1 equiv of triethylamine at room temperature,[13] afforded dialdehyde **29**, mp 111–115 °C (hexane–ethyl acetate), in 25% yield after column chromatography on silica gel. De-esterification of **29** with trifluoroacetic acid in benzene solution completed the synthesis, giving (±)-marasmic acid (**1**)[14] (50% yield) identical with that derived from natural sources[15] by ir ($CHCl_3$), ^1H NMR ($CDCl_3$), uv (95% C_2H_5OH), and mass spectra.[16]

Acknowledgment. This work was generously supported by the National Institutes of Health through Grant 5R01 GM 04229-22.

References and Notes

(1) (a) Isolation: F. Kavanaugh, A. Hervey, and W. J. Robbins, *Proc. Natl. Acad. Sci. U.S.A.*, **35**, 343 (1949); (b) Structure determination: J. J. Dugan, P. de Mayo, M. Nisbet, J. R. Robinson, and M. Anchel, *J. Am. Chem. Soc.*, **88**, 2838 (1966). (c) X-ray structure: P. D. Chadwick and G. A. Sim, *Chem. Commun.*, 431 (1971).
(2) D. Helmlinger, P. de Mayo, M. Nye, L. Westfelt, and R. B. Yeats, *Tetrahedron Lett.*, 349 (1970).
(3) S. R. Wilson and R. B. Turner, *J. Org. Chem.*, **38**, 2870 (1973).
(4) The stereochemical deductions of Wilson and Turner were in the main based upon steric arguments which paralleled our own during the planning stages of our work, and which we regard as reasonable even now. Consequently, the fact that the pertinent reactions follow the opposite course from that independently predicted by both groups poses a theoretical problem of much interest.
(5) G. Magnusson and S. Thoren, *J. Org. Chem.*, **38**, 2870 (1973).
(6) A satisfactory combustion analysis has been obtained for this compound or a suitable derivative thereof.
(7) O. Isler and P. Schudel, *Adv. Org. Chem.*, **4**, 128 (1963).
(8) Y. Watanabe, M. Yamashita, T. Mitsudo, M. Tanaka, and Y. Takegami, *Tetrahedron Lett.*, 3535 (1973).
(9) We are grateful to Dr. P. de Mayo for providing us with copies of his spectra.
(10) Wilson and Turner obtained a single pyrazoline, which they believed should have the structure i;[4] some support for this structure was subsequently



i

put forward on the basis of NMR studies with a lanthanide shift reagent;[11] it now appears that the assumptions underlying these arguments should be re-examined.
(11) S. R. Wilson and R. B. Turner, *J. Chem. Soc., Chem. Commun.*, 557 (1973).
(12) R. A. Laursen, W. Shen, and K. G. Zahka, *J. Med. Chem.*, **14**, 619 (1971).
(13) D. H. R. Barton, B. J. Garner, and R. H. Wightman, *J. Chem. Soc.*, 1855 (1964).
(14) Synthetic marasmic acid (racemic) has mp 171–171.5 °C (hexane–ethyl acetate) in an evacuated capillary. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.62; H, 6.99.
(15) We are grateful to Dr. P. de Mayo for a sample of (+)-marasmic acid from natural sources, which we recrystallized twice from hexane–ethyl acetate, mp 172–173 °C [lit.[1b] mp 173–174 °C (ethyl acetate)] in an evacuated capillary.
(16) Although ir spectra in KBr showed minor differences, the solution ir, NMR, uv, and the mass spectra were superimposable.
(17) NSF Predoctoral Fellow (1972–1975).

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Received December 15, 1975

An Electrochemical Determination of the pK_a of Isobutane

Sir:

We have described[1,2] the use of electrochemical data in a thermodynamic cycle to determine the pK_a's of triarylmethanes, cycloheptatriene, and various cyclopropenes. The cycle used involved a number of steps:

$$RH \rightarrow ROH \rightarrow R^+ \xrightarrow{e} R\cdot \xrightarrow{e} R^- (\rightarrow RH)$$