Stereospecific Tricyclization of a Polyolefinic Acetal

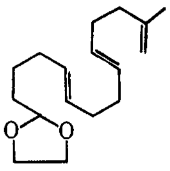
Sir:

The Stork–Eschenmoser hypothesis, which implies that the stereospecificity of the biocyclization of squalene may be a consequence more of intrinsic stereoelectronic factors than of enzymatic conformational control, has been validated only for the formation of bicyclic systems from acyclic substrates.[1,2] Attempts to test the idea and to use it to advantage synthetically for producing tricarbocyclic systems have thus far failed; *i.e.*, in those instances where material of the predicted configuration has been isolated, it has been formed in low yield as a minor reaction product.[3] Another case in point is our unreported study of the acetolysis of the *p*-nitrobenzenesulfonate, mp 44.5–46.0° (*Anal.* Found: C, 61.9; H, 7.3), of *trans,trans*-13-methyl-5,9,13-tetradecatrienol (described below) which gives, after hydrolysis, *trans,anti,trans*-2-methylperhydrophenanthren-2-ol in 2.8% yield. Thus all results have been uniformly discouraging.

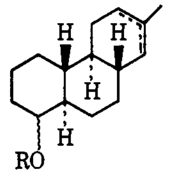
Nevertheless, we have continued to examine other systems and are now pleased to disclose what appears to be the first example of the stereoselective production of a tricarbocyclic system of "natural" configuration as the major product of reaction of an open-chain polyolefinic substrate. In addition to its theoretical significance, this finding promises to have synthetic utility.

The present study evolved from the discovery that acetals with appropriately juxtaposed olefinic bonds undergo facile acid-catalyzed ring closure to form mono-[4] and bicyclic[5] products in high yield. Now we report on the cyclization of the acetal I which was produced as follows. The benzyl ether of 5,9-decadiynol[6] was converted, by the action of butyllithium, into its anion, which was alkylated with 3-methyl-3-butenyl tosylate.[7] Treatment of the resulting enediyne with sodium in ammonia effected concomitant reduction of the two acetylenic bonds and hydrogenolysis of the ether to give *trans,trans*-13-methyl-5,9,13-tetradecatrienol (*Anal.* Found: C, 81.1; H, 11.9). The corresponding aldehyde, which was easily prepared in high yield by the excellent method of Barton,[8] was converted, by reaction with ethylene glycol in the presence of a trace of oxalic acid, into the acetal I (*Anal.* Found: C, 76.9; H, 10.4).

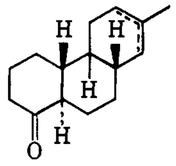
When a dilute solution of this acetal in benzene was treated with 1 mole equiv of stannic chloride[9] at 0–5° for 17 min, there was obtained, after chromatography, an 89% yield of monohydric alcohol fraction[10] which, as shown below, consisted mainly of the tricyclic unsaturated alcohols II (R = CH_2CH_2OH). The hydroxyethyl side chain was efficiently eliminated by forming the tosylate II (R = CH_2CH_2OTs) which, without purification, was treated with sodium iodide and zinc dust[11] in dimethoxyethane to produce ethylene and an alcoholic fraction, mainly II (R = H). The latter material was oxidized with Jones reagent[12] affording a mixture of ketones, mainly III. Treatment of this product with methanolic potassium hydroxide (under conditions which were shown by deuterium exchange experiments to give complete enolate equilibration) effected no change in its infrared spectrum or vapor phase chromatographic pattern; therefore the A/B ring fusion of the tricyclic ketones, and of their precursors, is assigned the more stable *trans* configuration.



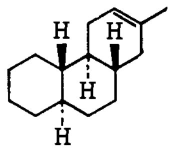
I



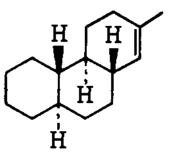
II



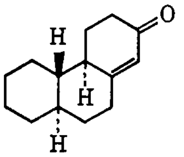
III



IV



V



VI

Wolff–Kishner reduction of the aforementioned ketone fraction afforded a mixture of hydrocarbons which was shown, by capillary vpc analysis, to contain two major components comprising 51 and 20% of the total product. These two substances were isolated by preparative vpc and shown to be the *trans,anti,trans*-methyldodecahydrophenanthrenes IV and V, respectively, by infrared and mass spectral comparison with authentic substances. The latter specimens were prepared by sodium in ammonia reduction of the unsaturated ketone VI[13] to give the *trans,anti,trans*-perhydro

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[1] See W. S. Johnson, *Pure Appl. Chem.*, 7, 317 (1963), *et seq.*

[2] *Cf.* W. S. Johnson, N. P. Jensen, and J. Hooz, *J. Am. Chem. Soc.*, **88**, 3859 (1966).

[3] See, for example, the acid-catalyzed cyclization of $(CH_3)_2C=CH(CH_2)_2C(CH_3)=CH(CH_2)_2C(CH_3)=CH(CH_2)_2CH=CHCO_2CH_3$, which gave the *trans,anti,trans*-perhydrophenanthrene derivative in 5–10% yield (A. Eschenmoser, D. Felix, M. Gut, J. Meier, and P. Stadler in "Ciba Foundation Symposium on the Biosynthesis of Terpenes and Sterols," G. E. W. Wolstenholme and M. O'Connor, Ed., J. and A. Churchill, Ltd., London, 1959, p 224). Eschenmoser states: "apart from it [the tricyclic material] and from a similarly small amount of crystalline bicyclic dihydroxy compound, the main product of the reaction consists of an intractable oily mixture. It seems that with polyenes of this complexity, acid-catalysed cyclization ceases to be a useful reaction from the preparative point of view."

[4] W. S. Johnson and H. C. Dunathan, to be reported.

[5] W. S. Johnson, J. J. Swoboda, and A. van der Gen, to be reported.

[6] W. S. Johnson, D. M. Bailey, R. Owyang, R. A. Bell, B. Jaques, and J. K. Crandall, *J. Am. Chem. Soc.*, **86**, 1959 (1964).

[7] K. L. Servis and J. D. Roberts, *ibid.*, **87**, 1331 (1965).

[8] D. H. R. Barton, B. J. Garner, and R. H. Wightman, *J. Chem. Soc.*, 1855 (1964).

[9] *Cf.* D. J. Goldsmith, *J. Am. Chem. Soc.*, **84**, 3913 (1962).

[10] The vapor phase chromatogram of this material showed a multiplicity of poorly resolved peaks; therefore, purification at this stage did not appear promising.

[11] *Cf.* H. B. Dykstra, J. F. Lewis, and C. E. Boord, *J. Am. Chem. Soc.*, **52**, 3396 (1930).

[12] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

[13] D. K. Banerjee, S. Chatterjee, and S. P. Battacharya, *J. Am. Chem. Soc.*, **77**, 407 (1955). We prepared this substance by a different approach, namely Birch reduction of the corresponding aromatic substance (VI with ring C aromatic and a methoxy in place of the keto group) (*Anal.* Found: C, 83.4; H, 9.2), which was produced by Raney nickel desulfurization of the thioketal, mp 107.5–108.5° (*Anal.* Found: C, 66.6; H, 7.1; S, 20.8), of *trans*-1-keto-7-methoxy-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (W. S. Johnson, A. R. Jones, and W. P. Schneider, *ibid.*, **72**, 2395 (1950)).

ketone, mp 20.5–22.0° (*Anal.* Found: C, 81.2; H, 10.6), which was then treated with methyllithium followed by iodine-catalyzed dehydration. The major and minor products were identified as IV and V, respectively, by examination of the width at half-height of the nmr signal for the vinyl proton.[2]

We have not yet found evidence for the presence of any other tricyclic materials. Spectral data on the ketone mixture suggested the presence of up to 16% of bicyclic material as determined by signals in the nmr for the terminal methylene group and no significant absorption in the infrared for *trans*-disubstituted olefinic bonds. Moreover, we have unequivocally demonstrated the absence of the *trans,anti,cis* isomers of IV and V in the hydrocarbon mixture by establishing the nonidentity of any of the vpc peaks with those of authentic samples.[14] It is therefore evident that the major product of the cyclization of the acetal I is tricyclic material which appears to be formed stereospecifically with respect to the ring fusions. We are now examining the possibility of producing higher polycyclic systems by this approach.

Acknowledgment. We wish to thank the National Institutes of Health, the National Science Foundation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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[14] A mixture of authentic hydrocarbons was prepared by catalytic hydrogenation of the unsaturated ketone VI to give the *trans,anti,cis*-perhydro ketone, mp 45–47.5° (*Anal.* Found: C, 81.5; H, 10.8), which was then treated with methyllithium followed by iodine-catalyzed dehydration.

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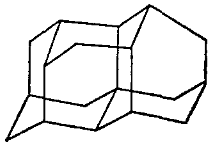
Triamantane

Sir:

The name "triamantane" has been proposed for I, "the third member of an adamantalogous series whose three-dimensional ultimate is diamond."[1] Adamantane[2] (II) and diamantane[3] (formerly called "congressane")[1] (III) have been prepared from isomeric precursors by rearrangements catalyzed by strong Lewis acids. By means of this approach we believe we have succeeded in synthesizing triamantane (heptacyclo-$[7.7.1.1^{3,15}.0^{1,12}.0^{2,7}.0^{4,13}.0^{6,11}]$octadecane, Ib).[4]

A seven-ring hydrocarbon, $C_{18}H_{24}$, was needed as starting material for I. One of the cyclooctatetraene dimers, mp 38.5° (IV),[5] is heptacyclic and can be elaborated to the desired C and H level. This was accomplished by Simmons–Smith cyclopropanation[6] to V, followed by reductive cleavage of both cyclopropane rings.[7] These reactions were followed by gas chromatography and by observing features of the infrared, nmr, and mass spectra. The exact composition of the penultimate material, VI, is not known with certainty, but this is not at all important for the present purposes since any $C_{18}H_{24}$ heptacyclic hydrocarbon might well serve as a rearrangement precursor for triamantane. Assignment of general structure VI has been made on the basis of the expected mode of cleavage of cyclopropane rings,[7] the intense m/e 240 peak in the mass spectrum, and the evidence for the presence of methyl groups (band near 1375 cm^{-1} in the infrared; resonances at 1.0 ± 0.2 ppm in the nmr (measured in δ units) of area one-fourth of the total).



Ia

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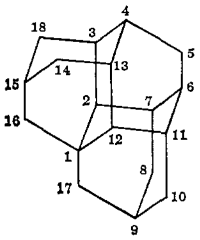

Ib

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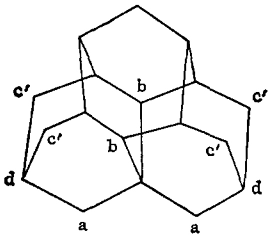
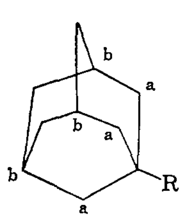
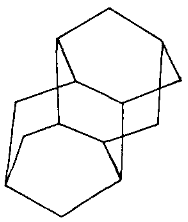


Ic

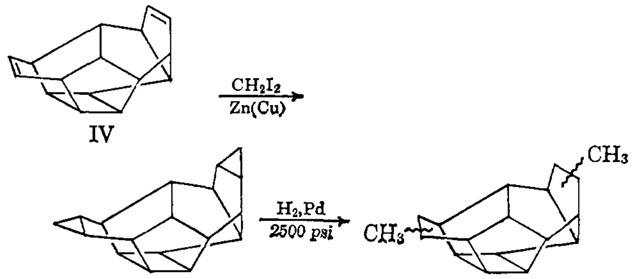


II, R = H
VII, R = C_2H_5



III

(a, +0.28 ppm, b, −0.12 ppm)



IV
V
VI

The rearrangement of VI to I was carried out in CS_2 solution under an HBr atmosphere using a 1.3- to 3-fold weight excess of an $AlBr_3$ "sludge" catalyst, prepared from $AlBr_3$ and *t*-BuBr.[8] After an initial treatment at 25°, heating at 100° for 4–6 days completed the reaction. Crystals of I could be obtained consistently in 2–5.2% yields from VI (mp 221–221.5° from acetone; *cf.* diamantane, mp 236–237°,[3] adamantane, mp 268–269°[10]). *Anal.* Calcd for $C_{18}H_{24}$: C, 89.98; H, 10.02. Found: C, 89.93; H, 10.24.

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[1] O. Vogl, B. C. Anderson, and D. M. Simons, *Tetrahedron Letters*, No. 4, 415 (1966).

[2] P. von R. Schleyer and M. M. Donaldson, *J. Am. Chem. Soc.*, **82**, 4645 (1960).

[3] C. Cupas, P. von R. Schleyer, and D. J. Trecker, *ibid.*, **87**, 917 (1965); I. L. Karle and J. Karle, *ibid.*, **87**, 918 (1965).

[4] IUPAC name supplied by Mr. Wallace F. Sliwinski, private communication.

[5] Review: G. Schröder, "Cyclooctatetraen," Verlag Chemie GmbH, Weinheim, Germany p 60.

[6] H. E. Simmons and R. D. Smith, *J. Am. Chem. Soc.*, **80**, 5323 (1958); **81**, 4256 (1959); R. S. Shank and H. Shechter, *J. Org. Chem.*, 24, 1825 (1959).

[7] Review: R. L. Augustine, "Catalytic Hydrogenation," Marcel Dekker, Inc., New York, N. Y., 1965, pp 133–134.

[8] This catalyst, invented by Williams,[9] has properties similar to that described by A. Schneider, R. W. Warren and E. J. Janoski, *J. Org. Chem.*, 31, 1617 (1966). With it, 10% yields of diamantane (III) can now be obtained from norbornene dimer.[3,9]

[9] V. Z. Williams, Jr., A.B. Thesis, Princeton University, 1965.

[10] Review: R. C. Fort, Jr., and P. von R. Schleyer, *Chem. Rev.*, **64**, 277 (1964).