Tetrahedron Letters No. 24, pp. 2201-2203, 1971. Pergamon Press. Printed in Great Britain.

1-HYDROXY-7-METHYLENE BICYCLO[3.2.1]OCTANE: A GIBBANE-STEVIOL C/D RING MODEL

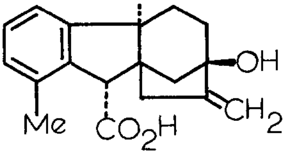
Frederick E. Ziegler and James A. Kloek[1]

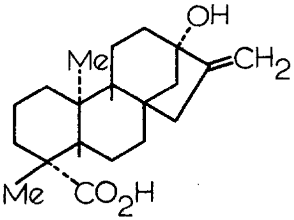
Sterling Chemistry Laboratory, Yale University
New Haven, Connecticut 06520

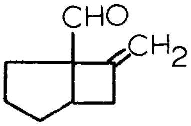
(Received in USA 20 April 1971; received in UK for publication 17 May 1971)

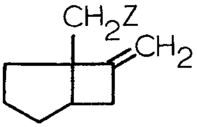
A variety of methods for the construction of the 1-hydroxy-7-methylene bicyclo[3.2.1] octane ring system have been developed and applied to the synthesis of gibbane synthons[2,3], epiallogibberic acid (1)[4], steviol (2)[5], and hibaene[6]. This Letter details a sequence of transformations applicable to the construction of this ring system as illustrated by the synthesis of the parent compound, 1-hydroxy-7-methylene bicyclo[3.2.1]octane (5c).

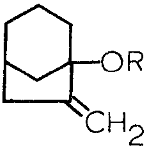
Photoaddition (450 W Hanovia lamp, sealed pyrex tube, room temperature, nitrogen atmosphere) of allene to 1-cyclopentene-1-carboxaldehyde[7] in ether solution afforded a single regioisomer, 1-formyl-7-methylene bicyclo[3.2.0]heptane (3)[8]: 41% yield; bp 63-70° (7 mm); ir (CCl_4) 1710, 1670 cm^{-1}; nmr (CCl_4) δ4.90 (2H,m,=CH_2) and 7.90 (1H,s,-CHO). The regiospecificity is in accord with the photoaddition of allene[9] to α,β unsaturated ketones. The product was accompanied by the formation of an appreciable quantity of ether soluble non-distillable material. Photolysis at low temperature had only a slight ameliorating effect upon the yield of the photoadduct. Reduction of the photoaldehyde with ethereal lithium aluminum hydride afforded 1-hydroxymethyl-7-methylene bicyclo[3.2.0]heptane (4a): 69% yield; bp 78-84° (7 mm); nmr (CCl_4) δ3.15 (1H,s,-OH), 3.66 (2H,s,-CH_2O-), and 4.79 (2H,m,=CH_2); p-nitrobenzoate, mp 71-73°. Exposure of the alcohol to pyridine/p-toluenesulphonyl chloride at 0° produced the corresponding tosylate 4b, mp 74-76°, in 80% yield. Solvolysis of the tosylate in 10% sodium acetate-acetic acid at 118° for five hours gave rise to 1-acetoxy-7-methylene bicyclo[3.2.1]octane (5a): 46% yield; bp 88-96° (7 mm); ir (CCl_4) 1735 cm^{-1}; nmr (CCl_4) δ1.96 (3H,s,-OAc) and 4.85 (2H,m,=CH_2). When the solvolysis was conducted for shorter periods of time, the internal return tosylate 5b was present at the expense of the acetate 5a[10]. Reduction of the acetate 5a with ethereal lithium aluminum hydride provided 1-hydroxy-7-methylene bicyclo[3.2.1]octane (5c): ir (CCl_4) 3600,

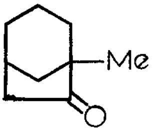

1


2


3


4a, Z=OH
b, Z=OTs


5a, R=Ac
b, R=Ts
c, R=H


6

3550-3200 cm^{-1}; nmr (CCl_4) δ3.95-4.35 (1H,broad s,-OH), 4.95 (1H,s,=C$\underline{H}_1H_2$), and 5.15 (1H,s,=C$H_1\underline{H}_2$). Rearrangement of acetate 5a with 20% hydrochloric acid-tetrahydrofuran resulted in the formation of 1-methyl-7-oxo bicyclo[3.2.1]octane 6:[13] ir (CCl_4) 1745 cm^{-1}; nmr (CCl_4) δ0.92 (3H,s). Thus,this rearrangement,well known to the chemistry of this system[6,11], coupled with the chemical shifts and multiplicity of the methylene protons[12] in unsaturated alcohol 5c, establish the mode of regiospecificity in photoadduct 3.

The application of this reaction in synthesis is currently under investigation.

We wish to acknowledge the National Science Foundation (GP-11273) and the National Cancer Institute, National Institutes of Health (CA-08869) for generous support of this work.

References

1. National Institutes of Health Predoctoral Fellow, 1968-1971.
2. G. Stork, S. Malhotra, H. Thompson, and M. Uchibayashi, J. Amer. Chem. Soc., 87, 1148 (1965).

3. E. J. Corey, M. Narisada, T. Hiraoka, and R. A. Ellison, *J. Amer. Chem. Soc.*, 92, 396 (1970).

4. K. Mori, M. Matsui, and Y. Suniki, *Tetrahedron Lett.*, 429 (1970).

5. K. Mori, Y. Nakahara, and M. Matsui, *Tetrahedron Lett.*, 2411 (1970); J. F. Cook and J. R. Knox, *Tetrahedron Lett.*, 4091 (1970).

6. R. A. Bell, R. E. Ireland, and L. N. Mander, *J. Org. Chem.*, 31, 2536 (1966).

7. Ozonolysis of cyclohexene in methanol followed by decomposition of the reaction mixture with dimethyl sulfide [J. J. Pappas, W. P. Keavney, G. Gancher, and M. Berger, *Tetrahedron Lett.*, 4273 (1966)] provided adipaldehyde rich in its acetal. Hydrolysis of the acetal mixture with 5% hydrochloric acid followed by distillation at aspirator pressure from p-toluenesulphonic acid gave 1-cyclopentene-1-carboxaldehyde and water. Drying of the mixture followed by redistillation provided the aldehyde in 47% yield from cyclohexene.

8. All new compounds gave correct combustion analyses. All melting points are corrected.

9. P. E. Eaton, *Tetrahedron Lett.*, 3695 (1964); R. W. Guthrie, Z. Valenta, and K. Wiesner, *Tetrahedron Lett.*, 4645 (1966); K. Wiesner, I. Jirkovsky, M. Fishman, and C. A. J. Williams, *Tetrahedron Lett.*, 1523 (1967); P. Sunder-Plassman, P. H. Nelson, P. H. Boyle, A. Cruz, J. Iriarte, P. Crabbe, J. A. Zderic, J. A. Edwards, and J. Fried, *J. Org. Chem.*, 34, 3779 (1969); and R. B. Kelly and J. Zamecnik, *Chem. Commun.*, 1102 (1970).

10. G. N. Taylor, Ph.D. Thesis, Yale University, 1968; W. G. Dauben, J. L. Chitwood, and K. V. Scherer, Jr., *J. Amer. Chem. Soc.*, 90, 1014 (1968); W. G. Dauben and J. L. Chitwood, *J. Org. Chem.*, 34, 726 (1969); ibid., *J. Amer. Chem. Soc.*, 92,1624 (1970).

11. B. E. Cross, *J. Chem. Soc.*, 4670 (1954).

12. J. R. Hanson, *J. Chem. Soc.*, 5036 (1965).

13. The nmr and ir spectra of 6 were identical with the spectra (kindly supplied by Professor Ernest Wenkert) of a sample prepared by an independent route; E. Wenkert, B. L. Mylari, and L. L. Davis, *J. Amer. Chem. Soc.*, 90, 3870 (1968).