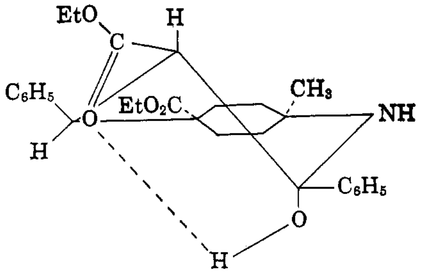
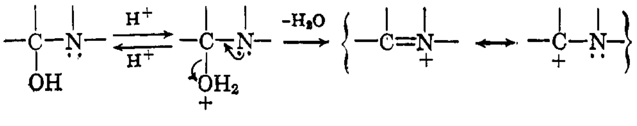
located at about 3.05 p.p.m. shows the reciprocal diaxial coupling. 2,4-Diphenyl-3-carbethoxy-5-acetyl-6-methyl-1,4-dihydropyridine (IIb) was used as a model compound in this investigation.



III

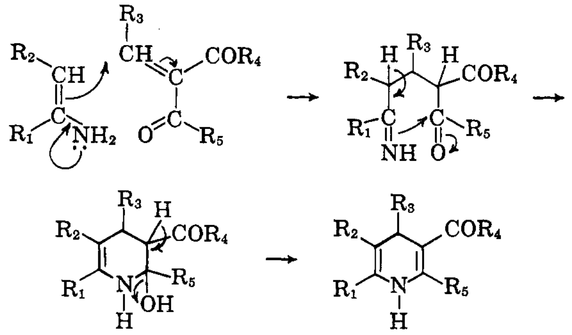
Molecular models of III show the ring hydrogen at position 3 to be well shielded by the two flanking phenyl groups.

The compound is completely resistant to dehydration at 56° over P_2O_5 *in vacuo* for 1 week, and shows no signs of decomposing below its melting temperature of 206.5–207.0°, although decomposition does accompany melting. Cold, dilute acid readily converts it to the corresponding 1,4-dihydropyridine (IIa), the reaction probably being assisted by the adjacency of nitrogen to the carbinol carbon.



The important role of the sterically hindered hydrogen in the stability of Ia was further emphasized when the synthesis of Ic was attempted under reaction conditions identical with those employed in the formation of Ia, but starting instead with ethyl β-aminocinnamate and ethyl benzylideneacetoacetate. *No Ic was obtained from the reaction mixture.* The only compound isolated was IIa. The hydrogen atom in question in Ic should be *cis* to a phenyl on C-4 and to a *methyl* on C-2, the reduction in steric hindrance apparently favoring base-catalyzed elimination in this instance.

The structure of Ia would then seem to indicate that the *initial step* in ring formation is Michael addition



and would tend to rule out Schiff base formation prior to ring closure, an alternate mechanism not excluded by the work of Berson and Brown.[7] Though the latter mechanism would lead to a 3,4-dihydropyridine, such compounds would be expected to isomerize under the usual reaction conditions to the more stable 1,4-dihydro structure.

Experimental[8]

Starting Materials.—Ethyl β-aminocrotonate,[9] ethyl benzylidenebenzoylacetate,[10] ethyl benzylideneacetoacetate,[10] and ethyl β-aminocinnamate[11] were prepared by known methods and freshly distilled prior to use.

2-Hydroxy-2,4-diphenyl-3,5-dicarbethoxy-6-methyl-1,2,3,4-tetrahydropyridine (Ia).—This compound, m.p. 206.5–207.0° dec. (lit.[4b] m.p. 190–192°), was prepared in 78.4% yield by the method of Palit and Chatterjea.[4b]

Anal. Calcd. for $C_{24}H_{27}NO_5$: C, 70.39; H, 6.65; N, 3.42. Found: C, 70.24; H, 6.61; N, 3.42.

2,4-Diphenyl-3,5-dicarbethoxy-6-methyl-1,4-dihydropyridine (IIa). A.—Treatment of 5.0 g. of Ia dissolved in ethanol with cold, dilute nitric acid produced IIa in 64% yield: m.p. 130–132° (aqueous ethanol), $\lambda\lambda_{max}$ 245 mμ (log ϵ 4.28) and 360 (3.88), NH at 3405 cm.$^{-1}$.

Anal. Calcd. for $C_{24}H_{25}NO_4$: C, 73.64; H, 6.43; N, 3.58. Found: C, 73.60; H, 6.25; N, 3.75.

B.—A mixture of 12.1 g. (0.06 mole) of ethyl benzylideneacetoacetate, 13.5 g. (0.07 mole) of ethyl β-aminocinnamate, 12.1 ml. of absolute ethanol, and 1.2 ml. of diethylamine was allowed to stand at 50–60° for 3 days. Yellowish white crystals (9.5 g., 40.9% yield) of m.p. 130.5–131.5° were obtained after several recrystallizations from aqueous ethanol. The product had an infrared spectrum identical with that of the material obtained in A and melted undepressed with it.

2,4-Diphenyl-3-carbethoxy-5-acetyl-6-methyl-1,4-dihydropyridine (IIb).—A mixture of 9.0 g. (0.046 mole) of ethyl β-aminocinnamate and 8.4 g. (0.045 mole) of benzylideneacetylacetone was heated on a steam bath for 20 hr. The resulting solution was dissolved in 250 ml. of ether and allowed to dry over anhydrous calcium chloride for 1 hr. After filtration, the ether was evaporated and the resulting thick red-orange liquid was triturated with small amounts of ether. This treatment produced 11.6 g. (67.9%) of yellow crystals melting at 162.0–163.5° after repeated recrystallizations from aqueous ethanol: λ_{max} 263 mμ (log ϵ 4.33) and 375 (4.04), NH at 3365 cm.$^{-1}$.

Acknowledgment.—This work was supported by a faculty research award provided from a National Science Foundation Grant to California State College at Long Beach. We are indebted to Eugene A. Pier of Varian Associates for the n.m.r. data.

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(7) J. A. Berson and E. Brown, *J. Am. Chem. Soc.*, **77**, 444 (1955).

(8) Melting points were determined on a Fisher-Johns apparatus and are not corrected. Ultraviolet spectra were taken in methanol and the infrared spectra in chloroform. The n.m.r. spectra were of deuteriochloroform solutions with tetramethylsilane added to act as an internal reference. Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside 77, N. Y.

(9) S. Glickman and A. Cope, *J. Am. Chem. Soc.*, **67**, 1017 (1945).

(10) E. F. Pratt and E. J. Werble, *ibid.*, **72**, 4638 (1950).

(11) R. Lukes and J. Kloubek, *Collection Czech. Chem. Commun.*, **25**, 607 (1960). Infrared and ultraviolet spectra indicate this compound to exist principally as the *cis*-chelated enamine rather than the imine as reported in this reference. See B. Witkop, *J. Am. Chem. Soc.*, **78**, 2873 (1956), for a discussion of spectra of imine-enamine systems.

1,5-Dibromoadamantane-2,6-dione Synthesis and Rearrangement to Tricyclo[3.3.0.0^{3,7}]-octane-1,3-dicarboxylic Acid

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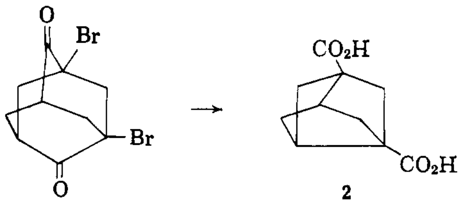
1 5-Dibromoadamantane-2,6-dione (**1**) was synthesized and rearranged by base to a dicarboxylic acid which we believe is tricyclo[3.3.0.0^{3,7}]octane-1,3-dicar-

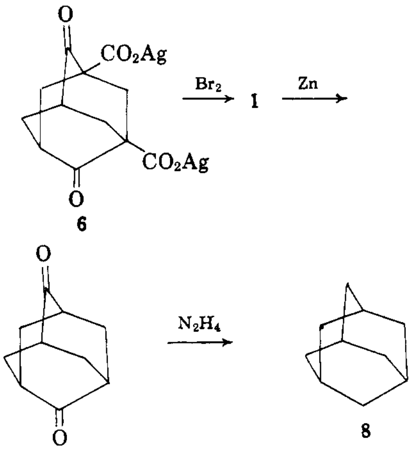


1

2

boxylic acid (2), the first compound with a tricyclo-$[3.3.0.0^{3,7}]$octane ring system.[1]

Disilver 2,6-diketoadamantane-1,5-dicarboxylate[2] (6) was treated with bromine to give the *bis*-α-bromo ketone 1. To confirm the structure of 1, it was reduced to adamantane-2,6-dione (7) with zinc and 7 was reduced to adamantane[3] (8) with hydrazine.



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8

The dibromodione rearranges smoothly in hot, alcoholic potassium hydroxide to a bromine-free dicarboxylic acid. This rearrangement probably proceeds in two distinct steps. At room temperature, a substance (m.p. 197–198°) results with an elemental analysis corresponding roughly to that required for the half-rearranged compound. The second step is slower because of increased steric strain and the negative charge on the carboxylate group.

The diacid 2 was assigned its structure on the basis of its infrared and n.m.r. spectra and the behavior of similar α-bromo ketones.[4] No carbon–carbon unsaturation bands are present in the infrared nor vinyl hydrogen peaks in the n.m.r.[5] The n.m.r. spectrum[6] has four peaks in the aliphatic hydrogen region: τ 7.03, 7.74, 7.97, and 8.17. The integrated areas are 1:1:2:1. Assigned structure of the diacid 2 has five pairs of equivalent hydrogens, but overlapping of two pairs would account for the spectrum.

Experimental

Disilver 2,6-Diketoadamantane-1,5-dicarboxylate.—A solution of 89 g. (0.35 mole) of 2,6-diketoadamantane-1,5-dicarboxylic acid in 750 ml. of methanol was neutralized with 10% KOH–water. The solution was then made slightly acidic with a few drops of dilute nitric acid and a solution of 120 g. (0.70 mole) of $AgNO_3$ in 420 ml. of methanol, and 210 ml. of water was added dropwise. Disilver 2,6-diketoadamantane-1,5-dicarboxylate was collected on a filter, washed with methanol–water, and dried at 60° (2 mm.) for 24 hr. The dry product (169 g., calculated 165 g.) was used without further purification.

1,5-Dibromoadamantane-2,6-dione.—To a solution of 40 g. (0.25 mole) of bromine in 100 ml. of dry carbon tetrachloride was added 50 g. (0.11 mole) of disilver 2,6-diketoadamantane-1,5-dicarboxylate. Carbon dioxide evolved immediately. The solution was stirred at room temperature for 0.5 hr. and was then heated under reflux for 3 hr. The reaction mixture was cooled to room temperature and the suspended solid (70 g.) was collected on a filter. This solid was extracted for 9 days with hot chloroform and the mixture of 1,5-dibromoadamantane-2,6-dione and unidentified acid impurities (25.3 g.), which was obtained, was washed with a saturated, aqueous $NaHCO_3$ solution for 2 hr. at room temperature. The insoluble 1,5-dibromoadamantane-2,6-dione (15.5 g., 45% yield) was collected and recrystallized once from ethyl acetate. It has m.p. 319–320°, sealed tube; $\lambda_{max}^{HCCl_3}$ 5.75 μ.

Anal. Calcd. for $C_{10}H_{10}Br_2O_2$: C, 37.30; H, 3.13; Br, 49.64. Found: C, 37.58; H, 2.92; Br, 49.33.

Adamantane-2,6-dione.—Zinc amalgam was prepared by shaking 20 g. of mossy zinc, previously washed with dilute hydrochloric acid, in a solution of 1 g. of $HgCl_2$ in 50 ml. of 0.25 *N* hydrochloric acid.

The amalgam was washed with water and was heated under reflux with 336 mg. (1.04 mmoles) of 1,5-dibromoadamantanedione in 78 ml. of acetic acid and 1 ml. of water for 24 hr. The reaction mixture was filtered and the filtrate was diluted with water and extracted continuously with ether for 3 days. The crude adamantanedione (94 g.), which was obtained, was treated with 5 ml. of 1% aqueous NaOH (24 hr.), and the resulting mixture was saturated with CO_2 and concentrated to dryness. The residue was extracted with acetone and the soluble portion was heated at 100° (1 mm.). White, crystalline adamantane-2,6-dione (63 mg., 37% yield, m.p. 313–314.5°, sealed tube) sublimed and had $\lambda_{max}^{HCCl_3}$ 5.75 μ.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.56; H, 7.19.

Adamantane.—A solution of 95 mg. (0.58 mmoles) of adamantane-2,6-dione, 0.5 ml., 85%, hydrazine hydrate, 1 drop of acetic acid, and 3 ml. of triethylene glycol was heated in an oil bath at 108° for 3 hr. The temperature of the bath was then gradually raised to 160°. The solution was cooled to room temperature and 0.8 g. of sodium methoxide and 2 ml. of methanol were added. The reaction mixture was now slowly heated to 180° (3 hr.), and the adamantane which sublimed was collected and resublimed. The resublimed adamantane (33 mg., 42% yield) melted at

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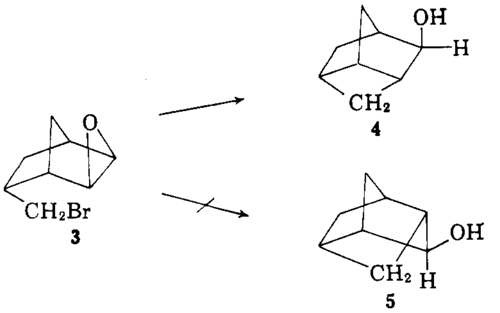
[1] R. R. Sauers and R. A. Parent, *J. Org. Chem.*, **28**, 605 (1963). When **3** was treated with sodium, the major product was tricyclo$[3.2.1.0^{3,6}]$octane (**4**) and not the tricyclo$[3.3.0.0^{3,7}]$octane (**5**).



3

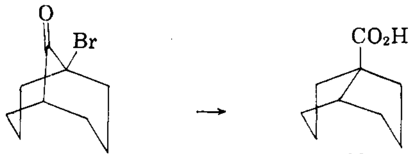
4

5

[2] V. Prelog and R. Siewerth, *Ber.*, **74**, 1644 (1941).

[3] S. Landa and V. Machacek, *Collection Czech. Chem. Commun.*, **5**, 1 (1933). For reviews of adamantane chemistry, see H. Stetter, *Angew. Chem.*, **66**, 217 (1954); **74**, 361 (1962).

[4] The rearrangement of α-bromo ketones (Favorskiĭ rearrangement) has been reviewed: A. S. Kende, *Org. Reactions*, **11**, 261 (1960). Of particular interest is the fact that 1-bromobicyclo[3.3.1]nonan-9-one (**9**) rearranges to bicyclo[3.3.0]octane-1-carboxylic acid (**10**); A. C. Cope and M. E. Synderholm, *J. Am. Chem. Soc.*, **72**, 5228 (1950); A. C. Cope and E. S. Graham, *ibid.*, **73**, 4702 (1951).



9

10

[5] Unsaturation would have been likely had the dibromodione rearranged to a different product.

[6] We are indebted to E. I. du Pont de Nemours and Co. for the use of their Varian A-60 n.m.r. spectrometer.

268.5° (lit.[3] m.p. 268–270°). Its structure was confirmed by infrared[7]: $\lambda_{max}^{HCCl_3}$ 3.50, 3.80, 6.90, 7.35, 9.05 10.30, and 12.50 μ.

Tricyclo[3.3.0.0^{3,7}]octane-1,3-dicarboxylic Acid.—To a solution of 1.0 g. KOH, 2 ml. of water, and 2 ml. of ethanol was added 430 mg., (1.33 mmoles) of 1,5-dibromoadamantane-2,6-dione. The resulting solution was refluxed for 4 hr. and acidified with dilute hydrochloric acid. The solution was concentrated to dryness and the residue was extracted with acetone. Tricyclo[3.3.0.0^{3,7}]octane-1,3-dicarboxylic acid (226 mg., 86% yield, m.p. 200–204°) was obtained. This was recrystallized from toluene–ethanol to get an analytical sample (m.p. 215–215.5°): λ_{max}^{KBr} 2.95, 3.33, 3.71, 3.85, 5.85, 6.75, 7.10, 7.60, 7.75, 8.20, 8.55, 9.16, 11.25, and 13.35 μ.

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.18; neut. equiv., 98.1. Found: C, 61.29; H, 6.10; neut. equiv. 98.2.

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[7] We are indebted to V. Prelog, Swiss Federal Institute of Technology, Zurich, Switzerland, who provided a sample of adamantane for comparison purposes.

The Preparation and Nuclear Magnetic Resonance Spectrum of the Cyclic Sulfite of 1,1-Dimethylol-3-cyclopentene

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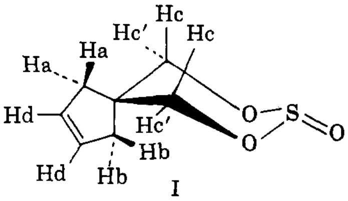
The pyramidal geometry of bonds attached to sulfur in organic sulfites has recently been confirmed by Lauterbur[1] and Pritchard.[2] In addition to the evidence obtained from the n.m.r. spectra of several cyclic sulfites they isolated two geometrical isomers of propylene sulfite[2] and three geometrical isomers of the cyclic sulfite derived from 2,4-pentanediol.[1] Hellier[3] has recently reported a study of trimethylene sulfite from which he draws the somewhat surprising conclusion that the sulfur–oxygen double bond assumes almost exclusively an axial conformation.

The pyramidal nature of the sulfite group imposes a magnetic asymmetry upon these molecules which is absent in the corresponding cyclic carbonates.[4] This may give rise to complex n.m.r. spectra.

As part of a study of small-ring spiran compounds the cyclic sulfite of 1,1-dimethylol-3-cyclopentene was prepared. This paper presents the evidence for its structure. Unequivocal proton assignments were made by employing isotopic substitution.

An isomeric mixture of diesters[5] containing 1,1-dicarbethoxy-3-cyclopentene was reduced with lithium aluminum hydride. From the reaction mixture 1,1-dimethylol-3-cyclopentene was isolated. The n.m.r. spectrum of the diol showed that double bond migration had not occurred during the reduction. It showed the following features given in τ-values (assignments shown in parentheses): 7.82, 4 protons (ring methylenes); 6.37, 4 protons (–C*H*$_2$OH); 6.24, broad, 2 protons (–O*H*); 4.40, 2 protons (vinyl hydrogen). The diol was converted to the cyclic sulfite (I) by treatment with thionyl chloride. The infrared spectrum showed a strong band at 1190 cm.$^{-1}$ attributed to the S=O bond. The n.m.r. spectrum of I shows the following features given in τ-values (assignments shown in parentheses): 8.62 and 7.57, partially resolved doublets, 2 protons each (hydrogens a and b); two doublets centered at 6.90 and 5.50, 2 protons each (hydrogens c and c′; and a complex multiplet centered at 4.77, 2 protons (d hydrogens). The coupling constant $J_{cc'}$ is 11 c.p.s.



I

In order to confirm that the doublets at τ 6.90 and 5.50 arise from the coupled protons c and c′, the corresponding cyclic sulfite with deuterium at c and c′ was prepared. A pure sample of 1,1-dicarbethoxy-3-cyclopentene was reduced with lithium aluminum deuteride to 1,1-dimethylol-d_4-3-cyclopentene. The n.m.r. spectrum shows, in addition to the broad hydroxyl absorption at τ 6.77[6] (2 protons), two singlets at τ 7.80 and 4.38 corresponding to the allyl and vinyl ring protons, respectively. The ratio of integrated areas for these two peaks is 2:1. Quantitative removal of the singlet at τ 6.37 confirms the assignments for the undeuterated diol. The deuterated diol was converted to the corresponding cyclic sulfite with thionyl chloride. The n.m.r. spectrum is identical with that for the undeuterated sulfite with the exception that the two doublets at τ 6.90 and 5.50 are quantitatively removed.

The results of this study are in agreement with those reported by Arbuzov[4] regarding the structure of the sulfite derived from 2,2-dimethyl-1,3-propanediol. In calculating the effect of the electric field of the sulfite group on the various proton chemical shifts, he has assumed that the S=O group is in an equatorial conformation. Clearly, additional experimental work is needed to resolve the conformational uncertainty in six-membered ring cyclic sulfites.

Experimental[8]

1,1-Dimethylol-3-cyclopentene.—An isomeric mixture of diesters[9] (206 g., 0.971 mole) containing 1,1-dicarbethoxy-3-cyclopentene and 1,1-dicarbethoxy-2-vinylcyclopropane was dissolved in 500 ml. of anhydrous ether. This solution was added dropwise with stirring over a 5-hr. period to a suspension of 46.0 g. (1.21 moles) of lithium aluminum hydride in 600 ml. of an-

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[1] P. C. Lauterbur, J. G. Pritchard, and R. L. Vollmer, *J. Chem. Soc.*, 5307 (1963).

[2] J. G. Pritchard and P. C. Lauterbur, *J. Am. Chem. Soc.*, **83**, 2105 (1961).

[3] D. G. Hellier, J. G. Tillett, H. F. Van Woerden, and R. F. M. White, *Chem. Ind.* (London), **50**, 1956 (1963).

[4] B. A. Arbuzov, Y. Y. Samitov, and R. M. Mamina, *Proc. Acad. Sci. USSR*, **143**, 186 (1962).

[5] K. C. Murdock and R. B. Angier, *J. Org. Chem.*, **27**, 2395 (1962).

[6] Recent reports[7] indicate that substitution of deuterium for hydrogen at one position in a molecule can cause upfield shifts in resonance frequencies for the remaining hydrogens. Although we observe an upfield shift for the hydroxyl proton in the deuterated diol, the magnitude is much too large to be caused by a deuterium isotope effect and we attribute this shift to changes in concentration.

[7] (a) E. I. Snyder, *J. Phys. Chem.*, **67**, 2873 (1963); (b) G. V. D. Tiers, *J. Chem. Phys.*, **29**, 963 (1958); (c) H. S. Gutowsky, M. Karplus, and D. Grant, *ibid.*, **31**, 1278 (1959); (d) H. S. Gutowsky, *ibid.*, **31**, 1683 (1959).

[8] All melting points are corrected. Boiling points are uncorrected. Infrared spectra were determined on a Perkin-Elmer Model 321 infrared recording spectrophotometer unless otherwise noted. N.m.r. spectra were determined on a Varian Model A-60 spectrometer. Analyses were performed by West Coast Analytical Laboratories, Inc.

[9] K. C. Murdock and R. B. Angier, *J. Org. Chem.*, **27**, 2395 (1962).