over sodium sulfate–potassium carbonate, yielded 3.80 g (95%) of crude acetate upon removal of solvent at reduced pressure. This acetate was of sufficient purity (>99% by vpc analysis on a Carbowax 20M on 70/80 Anakron ABS column and nmr analysis) to be used in subsequent reactions without further purification: ir (neat) ν 3080, 2980, 2860, 2885, 1728, 1615, 1375, 1240, 1052, 714 cm^{-1}; nmr (100 MHz, CCl_4) δ 5.68 (doublet of doublets J = 6, 2 Hz, 1 H), 5.38 (doublet of doublets, J = 6, 2 Hz, 1 H), 5.01 (doublet of triplets, J = 6, 6 Hz, 1 H), 3.35 (m, 1 H), 2.66 (m, 2 H), 1.96 (s, 3 H), 2.2–1.3 (m, 5 H).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.40; H, 8.78.

Preparation of *cis*-2,7-Bicyclo[3.3.0]octadiene (7).—Acetate **12** (2.2 g, 0.0132 mol) was pyrolyzed by dropwise addition onto a 40-cm Pyrex column packed with Pyrex glass beads heated to 475° in a slow nitrogen flow. The product was trapped directly into a receiver cooled to −78°, diluted with pentane, washed once with water, once with 5% $NaHCO_3$, and once with saturated NaCl, and dried over anhydrous Na_2SO_4. Subsequent removal of solvent by distillation through a 10-cm Vigreux column, followed by distillation of the residue, yielded 1.12 g (0.0106 mol, 80% based on acetate lost) of diene **7** and 0.30 g of recovered acetate **12**. The product was pale yellow; a colorless sample having an identical ir spectrum was obtained by chromatography on alumina with pentane elution. The ir spectrum of **7** was identical with that previously reported;[15] nmr (100 MHz, CCl_4) δ 5.54 (m, 4 H), 3.66 (doublet of multiplets, J = 7.5 Hz, 1 H), 3.1–2.5 (complex multiplet, 2 H), 2.55 (doublet of multiplets, J = 7.5 Hz, 1 H), 2.04 (doublet of multiplets, J = 15 Hz, 2 H).

Preparation of Tetracyclo[3.3.0.0^{2,4}.0^{3,7}]octane (1). A. Photolysis in Pentane.—A stirred solution of 2.45 g (2.29 × 10^{-2} mol) of diene **7** in 250 ml of olefin-free pentane was purged with nitrogen for 30 min, then irradiated under nitrogen with an unfiltered 450-W Hanovia high-pressure mercury lamp using a water-cooled quartz probe. Monitoring the reaction by vpc on a β,β'-oxydipropionitrile on 30/60 Chromosorb P (AW) column indicated a buildup of a new volatile component at the rate of about 1% per hour. At the end of 16 hr, however, conversion stopped. The solution, somewhat yellow and containing a solid material, was passed through a short alumina column, and the resulting clear solution was repurged and irradiated again as above. The new volatile component again grew at the rate of 1% per hour until it was 35% of the starting diene after 40 hr total irradiation. Further manipulation of the solution as above produced no further increase in the ratio of product to starting diene **7**. The yield of **1** as indicated by an internal vpc reference was 8%.

The product was isolated by removal of *ca.* 99% of the pentane by distillation through a 40-cm spinning band column, followed by extraction of the residue with an equal volume of saturated $AgNO_3$. Vpc analysis of this procedure indicated no loss of product relative to an internal norbornane standard, whereas diene **7** was completely removed. The resulting pentane solution was subjected to preparative gas chromatography on a β,β'-oxydipropionitrile on 30/60 Chromosorb P (AW) column, the single product being identified as desired hydrocarbon **1**. Unreacted diene **7** was recovered by dilution of the $AgNO_3$ solution with a tenfold volume of water and extraction by pentane.

B. Photolysis in Ether.—A solution of 2.50 g (2.43 × 10^{-2} mol) of diene **7** was taken up in 250 ml of commercial anhydrous ether, purged with nitrogen, and irradiated as described above. Monitoring the reaction indicated conversion of **7** to **1** at a rate of 0.5% per hour until the ratio of **7**:**1** was **38**:**62** as measured by vpc integration. The resulting yellow solution was concentrated by distillation of the ether through a 40-cm Vigreux column, the residue yielding pure **1**. The yield as determined by an internal norbornane vpc reference was 35%.

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Registry No.—**1**, 4582-22-3; **7**, 41164-14-1; **11**, 41164-15-2; **12**, 40132-71-6.

(15) W. v. E. Doering and W. R. Roth, *Tetrahedron*, **19**, 715 (1963).

The Synthesis of Cyclic 2-Enones from Cyclic 1,3 Diketones[1a]

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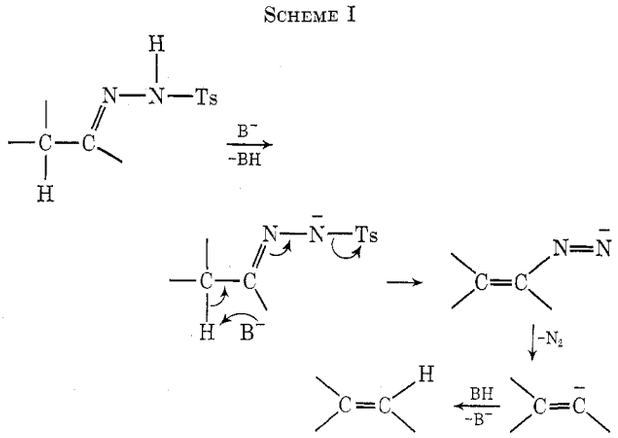
It has previously been shown that tosylhydrazones are converted into alkenes upon treatment with a strong base such as lithium aluminum hydride,[2] lithium hydride,[3] sodium amide,[4] or alkyllithium.[5] We have found that cyclic 1,3 diketones can be converted into cyclic 2-enones through treatment of their monotosylhydrazones with weak base. This new synthetic method is a simple, safe procedure for preparation of substituted cyclic 2-enones.

The mechanism for strong base conversion of tosylhydrazones into alkenes suggested by Shapiro[6] is outlined in Scheme I. Since the acidic sulfonamide proton (pK_a = 8.5)[7] is presumably removed first, removal of the α proton with concomitant loss of *p*-toluenesulfinate anion requires a strong base.

SCHEME I



If the α proton were more acidic than the sulfonamide proton, however, the reaction should proceed in the presence of a weak base. Since cyclic 1,3 diketones have sufficiently acidic α protons, they would be expected to undergo such a reaction.

5,5-Dimethylcyclohexane-1,3-dione (**1**, pK_a = 5.2)[8] was converted into 5,5-dimethyl-2-cyclohexen-1-one (**3**) in 52% yield on heating the crude monotosylhydrazone (**2**) in aqueous potassium carbonate solution. Enone **3** was also obtained in 53% yield from purified

(1) (a) This work was supported in part by grants from the California State University, Fullerton Foundation; (b) NSF Undergraduate Research Participant.

(2) L. Caglioti and M. Magi, *Tetrahedron Lett.*, 1261 (1962); L. Caglioti and M. Magi, *Tetrahedron*, **19**, 1127 (1963).

(3) L. Caglioti, P. Grasselli, and G. Maina, *Chim. Ind. (Milan)*, **45**, 559 (1963); L. Caglioti, P. Grasselli, and A. Selva, *Gazz. Chim. Ital.*, **94**, 537 (1964).

(4) W. Kirmse, B.-G. von Bülow, and H. Schepp, *Justus Liebigs Ann. Chem.*, **691**, 41 (1966).

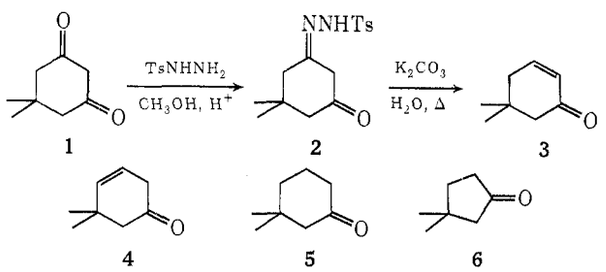
(5) R. H. Shapiro and M. J. Heath, *J. Amer. Chem. Soc.*, **89**, 5734 (1967); G. Kaufman, F. Cook, H. Shechter, J. Bayless, and L. Friedman, *ibid.*, **89**, 5736 (1967).

(6) R. H. Shapiro, *Tetrahedron Lett.*, 345 (1968).

(7) J. W. Powell and M. C. Whiting, *Tetrahedron*, **7**, 305 (1959).

(8) G. S. Hammond in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, p 453.

2. In addition to **3**, a small amount of the 3,4 isomer (**4**), 3,3-dimethylcyclohexanone (**5**), and 3,3-dimethylcyclopentanone (**6**) were identified in the product mixture.



1 2 3

4 5 6

2-Methyl-2-cyclohexen-1-one (**7**) was synthesized in 41% yield from 2-methylcyclohexane-1,3-dione (**8**). Also, small amounts of 2-methylcyclohexanone (**9**) and 2-methyl-2-cyclohexen-1-ol (**10**) were formed. 2-Cyclohexen-1-one (**11**) was prepared in 15% yield from cyclohexane-1,3-dione (**12**). In addition to **11**, a lower yield of the 3,4 isomer (**13**), cyclohexanone (**14**), cyclopentanone (**15**), and 2-methylcyclopentanone (**16**) were formed in the reaction.[9]

In preliminary experiments carried out in a similar fashion with methyl 2-cyclohexanonecarboxylate and ethyl acetoacetate, cyclohexanone and acetone were formed through decarboxylation.

Experimental Section[10]

5,5-Dimethyl-2-cyclohexen-1-one (**3**).—The following procedure for the preparation of **3** is typical for the conversion of cyclic 1,3 diketones into cyclic 2-enones.

A.—In a round-bottom flask were placed 2.80 g (20.0 mmol) of **1**, 3.83 g (20.6 mmol) of tosylhydrazide, 50 ml of anhydrous methanol, and three drops of concentrated H_2SO_4. After standing overnight at room temperature, the methanol was removed *in vacuo*, 22.1 g (160 mmol) of potassium carbonate and 250 ml of water were added, and the solution was heated to steam distil the product. The largely aqueous distillate was saturated with NaCl and extracted with ether (3 × 30 ml), and the ether was washed with saturated NaCl solution and dried ($MgSO_4$). The solvent was removed *in vacuo* to give an oil, 1.41 g, which gc analysis (FFAP) showed to be a mixture: 90% **3** (52% yield based on **1**),[11] 2% **4**, nmr (CCl_4) δ 1.10 (s, 6, 2 CH_3), 2.33 (s, 2, CCH_2CO), 2.80 (s, 2, $CH{=}CHCH_2CO$), 5.78 (s, 2, $CH{=}CH$), ir (CCl_4) 5.83 μ, 5% **5**,[12] 2% **6**,[13] and 0.5% solvent. Components in the reaction mixture were separated for spectral analysis using preparative gc (SF-96 and FFAP).

B.—Enone was also prepared from purified **2**. A solution of 2.05 g (14.6 mmol) of **1**, 2.84 g (15.2 mmol) of tosylhydrazide, 50 ml of methanol, and two drops of concentrated HCl was allowed to stand overnight at room temperature. Solvent was removed *in vacuo*, and the residue was recrystallized from methanol–benzene to give **2**: crop 1, 3.30 g (71.2%), mp 208.5–209.0° dec; crop 2, 0.39 g (8.0%), mp 205.0–206.5° dec [ir (mull) 6.23, 6.31, 6.45, 7.58 (SO_2), and 8.70 μ (SO_2); nmr [$(CD_3)_2SO$] δ 0.90 [s, 6, $C(CH_3)_2$], 1.92 (s, 2, CH_2), 2.08 (s, 2, CH_2), 2.38 (s, 3, $ArCH_3$), 5.10 (s, 1, CH), 7.40 (d, 2, J = 8.5 Hz, ArH), 7.71 (d, 2, J = 8.5 Hz, ArH), 8.61 (s, 1, NH), and 9.71 (s, 1, NH); analytical sample from methanol, mp 213.5–214.0° dec[14]].

Anal. Calcd for $C_{15}H_{20}N_2SO_3$: C, 58.41; H, 6.54; N, 9.09. Found: C, 58.15; H, 6.53; N, 8.99.

Using a procedure similar to that in part A, 6.17 g (20.0 mmol, mp 209.0–209.7° dec) of **2** with 22.0 g (159 mmol) of K_2CO_3 gave 1.42 g of an oil which was shown by gc analysis (SF-96) to consist of 93% **3** (53% yield based on **2**), 3% **4**, less than 1% **5**, 3% **6**, and 1% solvent.

3,3-Dimethylcyclopentanone (**6**).—3-Methyl-2-cyclopenten-1-one, which was prepared from 2,5-hexanedione,[15] was converted into **6** through 1,4 addition of methylmagnesium iodide.[16]

A solution of methylmagnesium iodide in ether prepared from 10.1 g (71.3 mmol) of methyl iodide and 1.76 g (72.5 mmol) of magnesium was combined with 0.10 g (0.5 mmol) of anhydrous cuprous chloride, and the mixture was cooled in an ice–salt bath. 3-Methyl-2-cyclopenten-1-one, 5.03 g (52.4 mmol), in 10 ml of dry ether was added dropwise over 9 min while stirring and cooling. Saturated NH_4Cl solution and diluted HCl were added, and the ether layer was separated. The aqueous phase was extracted once with ether, and the combined ether extracts were washed with water and saturated Na_2CO_3 and NaCl solutions and dried ($MgSO_4$). After filtration and removal of the solvent *in vacuo*, the residue was distilled in a short-path still at a bath temperature of 140° (24 Torr) to give 0.75 g of distillate. The nmr spectrum indicated that the distillate was impure. A pure sample of **6** was obtained through preparative gc (FFAP): nmr (CCl_4) δ 1.11 (s, 6, 2 CH_3), 1.95 (s, 2, CH_2), 1.55–2.40 (AA′BB′ multiplet, 4, CH_2CH_2); ir (CCl_4) 5.74 μ; semicarbazone mp 177.4–179.2° (lit.[17] mp 178°).

2-Methyl-2-cyclohexen-1-one (**7**).—Enone **7** was prepared following the typical procedure. Diketone **8**, 0.631 g (5.00 mmol), mp 206.0–206.8°,[18] and 0.940 g (5.04 mmol) of tosylhydrazide were combined to give crude tosylhydrazone. Steam distillation of a solution of tosylhydrazone with 5.50 g (39.8 mmol) of K_2CO_3 gave an oil, 0.247 g, which gc analysis (FFAP) demonstrated to be a mixture: 91% **7** (41% yield based on **8**), nmr (CCl_4) δ 1.72 (broad, 3, CH_3), 1.76–2.55 (m, 6, CH_2CH_2-CH_2), 6.67 (broad, 1, CH), ir (CCl_4) 5.94 μ, semicarbazone mp 207.5–209.1° (lit.[19] mp 207–208°), 1% **9**,[20] 7% **10**,[21] and less than 1% solvent. Components were separated for spectral analysis using preparative gc (FFAP).

An analytical sample of the monotosylhydrazone of **8** was recrystallized from methanol, mp 192.7–193.1° dec.

Anal. Calcd for $C_{14}H_{18}N_2SO_3$: C, 57.12; H, 6.16; N, 9.52. Found: C, 57.08; H, 6.21; N, 9.40.

2-Cyclohexen-1-one (**11**).—Using the typical procedure, 2.24 g (20.0 mmol), mp 104.5–105.1°,[22] of **12** and 3.72 g (20.0 mmol) of tosylhydrazide were converted to the crude tosylhydrazone. Steam distillation of a solution of the tosylhydrazone with 22.14 g (160 mmol) of K_2CO_3 gave 0.361 g of an oil. The oil was analyzed by gc (FFAP) and shown to be a mixture: 81% **11** (15% yield based on **12**), nmr (CCl_4) δ 1.73–2.55 (m, 6, CH_2CH_2-CH_2), 5.87 (pair of t, 1, J = 1.5 and 10 Hz, CH), 6.95 (pair of t, 1, J = 4 and 10 Hz, CH), ir (CCl_4) 5.95 μ,[23] 2% **13**, 4% **14**,[13] 12% of what appeared to be a mixture of **15** and **16** on the basis of nmr and ir spectra, and 1% solvent. Components were separated by preparative gc (FFAP) for spectral analysis. When a sample of the mixture of **15** and **16** from preparative gc was

(9) Ring contractions have also been observed in the Clemmensen reduction of 1,3 diketones; *cf.* A. N. Dey and R. P. Linstead, *J. Chem. Soc.*, 1063 (1935).

(10) Melting points were determined using a Thomas-Hoover capillary melting point apparatus and are corrected. Infrared spectra were recorded using a Perkin-Elmer Model 137 spectrometer. Nmr spectra were obtained using a Varian A-60A spectrometer with tetramethylsilane as an internal standard. Gas chromatography was carried out using a Varian Aerograph Model 90-P3 gas chromatograph with a 5 ft × 0.25 in. 10% FFAP or 10% SF-96 on 60–80 Chromosorb W column except where indicated. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

(11) Identified by spectroscopic comparison with an authentic sample prepared from **1**: W. F. Gannon and H. O. House, *Org. Syn.*, **40**, 14 (1960).

(12) Identical with the product of catalytic hydrogenation of **3** in ethanol over 5% Pd/C.

(13) Identified by spectroscopic comparison with an authentic sample.

(14) Cyclic 1,3 diketones and their derivatives exist primarily in the enol form: A. J. Fatiadi, *J. Org. Chem.*, **35**, 831 (1970).

(15) R. M. Acheson and R. Robinson, *J. Chem. Soc.*, 1127 (1952).

(16) The procedure of G. Büchi, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, **31**, 241 (1948), was followed.

(17) T. Henshall, *J. Soc. Chem. Ind.*, **62**, 127 (1943).

(18) A. B. Mekler, S. Ramachandran, S. Swaminathan, and M. S. Newman, *Org. Syn.*, **41**, 56 (1961).

(19) F. C. Whitmore and G. W. Pedlow, Jr., *J. Amer. Chem. Soc.*, **63**, 758 (1941).

(20) Identical with the product of catalytic hydrogenation of **7** in methanol over 5% Pd/C, and the infrared spectrum agrees with the published spectrum of **9**: C. J. Pauchert, "The Aldrich Library of Infrared Spectra," Aldrich Chemical Co., Milwaukee, Wis., 1970, p 198.

(21) Identical with the product of lithium aluminum hydride reduction of **7** at low temperature.

(22) J. C. Sircar and A. I. Meyers, *J. Org. Chem.*, **30**, 3206 (1965).

(23) The infrared spectrum agrees with the published spectrum; see ref 20, p 204.

analyzed on a diisodecyl phthalate column, two components in about equal amounts with retention times identical with those of **15** and **16** were found. Nmr and ir spectra of a mixture of authentic **15** and **16**[24] in the same ratio agreed with the spectra obtained from the preparative gc sample. Compound **13** could not be isolated free of **14**, but the nmr of the mixture had the characteristic absorption of a 3,4-unsaturated ketone: nmr (CCl_4) δ 2.43 ($CCH_2C{=}O$), 2.78 ($CH{=}CHCH_2C{=}O$), 5.79 ($CH{=}CH$), the remaining CH_2 was obscured by **14**.

An analytical sample of the monotosylhydrazone of **12** was recrystallized from methanol, mp 208.3–209.0° dec.

Anal. Calcd for $C_{13}H_{16}N_2SO_3$: C, 55.69; H, 5.75; N, 9.99. Found: C, 55.75; H, 5.62; N, 10.25.

Registry No.—**1**, 126-81-8; **2**, 41189-09-7; **3**, 4694-17-1; **4**, 41189-10-0; **6**, 20500-49-6; **7**, 1121-18-2; **8**, 1193-55-1; **8** monotosylhydrazone, 41189-12-2; **11**, 930-68-7; **12**, 504-02-9; **12** monotosylhydrazone, 41189-13-3; **13**, 4096-34-8; tosylhydrazide, 1576-35-8; 3-methyl-2-cyclopenten-1-one, 2758-18-1; methyl iodide, 74-88-4.

(24) Compound **16** was synthesized from 2-carbethoxycyclopentanone: F. C. Case and E. E. Reid, *J. Amer. Chem. Soc.*, **50**, 3062 (1928).

Sterol Metabolism. XXV. Cholesterol Oxidation by Singlet Molecular Oxygen[1]

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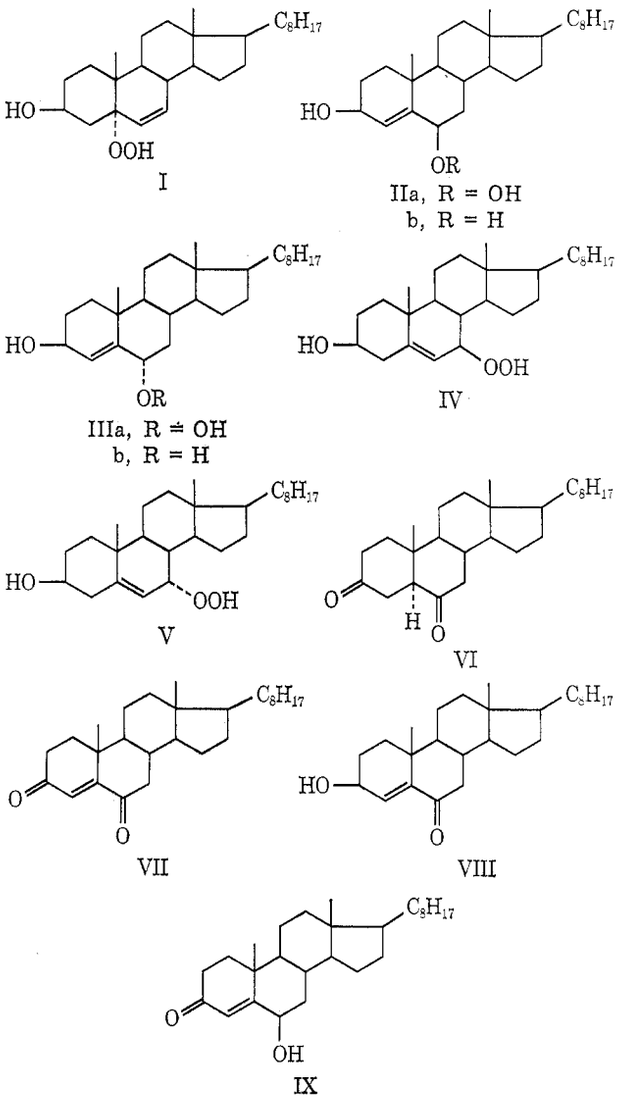
In seeking improved access to cholesterol 20α-hydroperoxide[3] implicated in the biosynthesis of pregnenolone from cholesterol[4] we examined a variety of oxidation reactions of cholesterol, among which was the well-known photosensitized oxidation in solution by excited-state (singlet) molecular oxygen. This reaction is considered to proceed by a cyclic ene mechanism with little ionic character[5] to yield 3β-hydroxy-5α-cholest-6-ene 5-hydroperoxide (I)[6] as major product. We establish herein that the epimeric 3β-hydroxycholest-4-ene 6-hydroperoxides IIa and IIIa are also formed in low yield (1–2%) but that the epimeric cholesterol 7-hydroperoxides IV and V are not formed.

The structures of the new 6-hydroperoxides IIa and IIIa were established by sodium borohydride reduction to the respective diols IIb and IIIb in the usual manner.[3] A B-ring chair conformation for IIa in which the 6β-hydroperoxide bond has quasiaxial character was supported by proton spectra in which the 6α proton appeared as a doublet of doublets coupled moderately and weakly ($J_{6\alpha,7\alpha}$ = 4.5, $J_{6\alpha,7\beta}$ = 2 Hz) to the vicinal 7α and 7β protons. Absence of strong 1,2-diaxial coupling between the 6α proton and either 7 proton together with the strong 1,3-diaxial effects of the



6β-hydroperoxide group on the chemical shift of the C-19 angular methyl group protons (shifted paramagnetically $\Delta\delta$ 0.15 ppm from their position in cholest-4-en-3β-ol[7]) additionally support this conformational assignment for IIa. Quasiaxial character for the 6β-hydroperoxide bond of IIa is thus analogous to the previously demonstrated quasiaxial character of the 6β bond of 6β-hydroperoxycholest-4-en-3-one[8] and of the 3β,6β-diol IIb.[9] The epimeric 6α-hydroperoxide IIa is accordingly the quasiequatorial epimer, a constant B-ring chair conformation being assumed for IIa and IIIa.

The quasiaxial IIa was not epimerized under reac-

(1) Paper XXIV: J. I. Teng and L. L. Smith, *J. Amer. Chem. Soc.*, **95**, 4060 (1973). Financial support of this work by the Robert A. Welch Foundation, Houston, Texas, and the U. S. Public Health Service (research grants AM13520, HE-10160, and NS-08106) is gratefully acknowledged. A preliminary account of this work has been made; *cf.* M. J. Kulig and L. L. Smith, Abstracts of Papers, 165th National Meeting of the American Chemical Society, Dallas, Texas, April 8–13, 1973, No. ORGN-078.

(2) Robert A. Welch Foundation Postdoctoral Fellow, 1971–1973.

(3) J. E. van Lier and L. L. Smith, *J. Org. Chem.*, **35**, 2627 (1970).

(4) (a) J. E. van Lier and L. L. Smith, *Biochim. Biophys. Acta*, **210**, 153 (1970); **218**, 320 (1970); (b) J. E. van Lier and L. L. Smith, *Biochem. Biophys. Res. Commun.*, **40**, 510 (1970).

(5) A. Nickon and J. F. Bagli, *J. Amer. Chem. Soc.*, **81**, 6330 (1959); **83**, 1498 (1961).

(6) (a) G. O. Schenck, *Angew. Chem.*, **69**, 579 (1957); (b) G. O. Schenck, K. Gollnick, and O.-A. Neumüller, *Justus Liebigs Ann. Chem.*, **603**, 46 (1957); (c) G. O. Schenck and O.-A. Neumüller, *ibid.*, **618**, 194 (1958); (d) G. O. Schenck, O.-A. Neumüller, and W. Eisfeld, *ibid.*, **618**, 202 (1958).

(7) Published proton spectra for cholest-4-en-3β-ol were used for comparison; see (a) I. McClenaghan and P. J. Sykes, *Chem. Commun.*, 800 (1968). (b) C. R. Narayanan and K. N. Iyer, *Tetrahedron Lett.*, 3741 (1965).

(8) J. I. Teng, M. J. Kulig, L. L. Smith, G. Kan, and J. E. van Lier, *J. Org. Chem.*, **38**, 119 (1973).

(9) The quasiaxial conformation for IIb is supported by its more mobile nature in comparison with IIIb on partition chromatographic systems in which axial alcohols generally migrate more rapidly than do equatorial alcohols. The diol IIb is more mobile than IIIb on both paper[10a] and gas–liquid (3% OV-1,[10b] 2% OV-210, and 3% SP-2401 reported herein) partition chromatographic systems.

(10) (a) L. L. Smith, *J. Amer. Chem. Soc.*, **76**, 3232 (1954); (b) J. E. van Lier and L. L. Smith, *Anal. Biochem.*, **24**, 419 (1968).