3-Hydroxy-Δ^3-cholesten-2-one (IIIa).—A mixture of diosphenols IIIa and IIIb was prepared according to the procedure of Ruzicka, *et al.*[7b] Upon shaking an ether solution of this mixture with cold 20% potassium hydroxide, an insoluble potassium salt formed and was filtered and washed with ether. A suspension of this salt in dilute hydrochloric acid was extracted with ether. Evaporation of the dried ether extracts and crystallization of the residue from petroleum ether gave IIIa, m.p. 143–145° (reported m.p. 144–145°); $\lambda_{max}^{CCl_4}$ 2.92, 5.98 and 8.25 μ; n.m.r. absorption at 4.32 and 4.45 τ (doublet J = 2.5 c.p.s.) in carbon tetrachloride solution.

2-Hydroxy-Δ^1-cholesten-3-one (IIIb).—A solution of diosphenol IIIa (400 mg.) in glacial acetic acid (3 ml.) containing a little concentrated hydrochloric acid (0.1 ml.) was heated on a steam bath for 10 min. Upon cooling, a solid precipitated and was crystallized from ethyl acetate to give IIIb (60 mg.), m.p. 161–162° (reported m.p. 160–162°); $\lambda_{max}^{CCl_4}$ 2.93, 6.00 and 11.65 μ; n.m.r. absorptions at 3.82 and 4.32 τ have equal areas.

The mother liquor exhibited three low field resonances at 3.78, 4.12 and 4.45 τ, the areas of which indicate a mixture of 18% IIIb and 82% IIIa. The downfield shift of the hydroxyl absorption (4.32 τ in pure IIIb to 4.12 in the mixture) is characteristic of mixtures of these diosphenols and implies intermolecular hydrogen bonding. A shift of the carbonyl stretching frequency in the infrared to 6.02 μ agrees with this suggestion.

Evidence for Cholestane-2,3-dione (IIIc).—Diosphenol IIIa is not stable in the crystalline state and yellows upon standing at room temperature or in the refrigerator. After 2 weeks it melted at 105–125°, and after a month the yellow solid melted at 70–75°. The infrared spectrum of this low-melting substance showed weak absorption at 2.94 and 6.02 μ and strong absorption at 5.78 and 5.89 μ. Very weak peaks at 3.86, 4.19 and 4.44 τ were observed in the n.m.r. spectrum; when compared with the area of the methyl resonance at 8.37 τ, these combined low field absorptions represent about 10% diosphenol.

A 50-mg. sample of the low melting yellow substance was converted to a potassium salt by shaking with 20% potassium hydroxide. Diosphenols were isolated by treating the salt with dilute hydrochloric acid followed by ether extraction. The crude solid thus obtained (35 mg.) was crystallized from petroleum ether to yield IIIa (20 mg.), m.p. 140–142°, identified by mixture melting point and infrared spectrum. The mother liquors showed strong absorption just above 6.00 μ in the infrared.

3-Methoxy-Δ^3-cholesten-2-one (IV).—A mixture of diosphenols IIIa and IIIb (560 mg.) was dissolved in methanol (40 ml.) containing sodium hydroxide (200 mg.) and then refluxed with dimethyl sulfate (2.5 g.) for 20 hr. The reaction mixture was diluted with water and then worked up by ether extraction in the usual manner. Evaporation of the dried ether portions yielded a yellow oil (550 mg.), which was chromatographed on 30 g. of neutral alumina. The first materials to be eluted were oils (150 mg.) exhibiting saturated carbonyl absorption in the infrared. Elution with benzene gave IV (230 mg.), m.p. 153–155°; $\lambda_{max}^{CCl_4}$ 5.96, 6.18 and 8.40 μ; $\lambda_{max}^{C_2H_5OH}$ 266 mμ (log ϵ 3.9); n.m.r., 4.83 τ (doublet) and 6.49 τ (area ratio 1:2.9). An analytical sample, m.p. 157–158°, was prepared by crystallization from aqueous ethanol.

Anal. Calcd. for $C_{28}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.71; H, 11.33.

Elution with ether gave 60 mg. of recovered diosphenols.

Rate-Controlled Methylation of Diosphenols IIIa and IIIb. A.—A freshly prepared and crystallized sample of IIIa (200 mg.) was dissolved in dry benzene (20 ml.) and treated with sodium hydride (50 mg. of a 52.8% dispersion in mineral oil) at reflux for 45 min. When the hydride was added, a flocculent solid formed concurrently with gas evolution. Methyl iodide (2 ml.) was added and the mixture was refluxed an additional 20 hr. Excess sodium hydride was decomposed by a few drops of ethanol and the reaction mixture was diluted with water and extracted with ether. Unchanged diosphenol (70 mg.) was removed as the potassium salt, formed by shaking the ether extracts with 20% potassium hydroxide. The residue obtained by evaporation of the ether extracts was chromatographed on neutral alumina (15 g.) yielding 88 mg. of a solid, upon elution with ether. Crystallization of this material from aqueous ethanol gave 60 mg. of needles, m.p. 121–131°, having an infrared spectrum identical to that of IV. The n.m.r. spectrum showed a very weak resonance at 4.20 τ and stronger absorptions at 4.90 τ (doublet) and 6.48 τ (OCH_3). The ratio of the areas of the vinyl hydrogen doublet to the methoxyl singlet indicated this material to be 94% IV. Additional attempts to remove the small amount of II apparently present by further chromatography or crystallization failed.

B.—A freshly prepared and crystallized sample of IIIb (54 mg.) dissolved in 15 ml. of dry benzene was refluxed with sodium hydride (7 mg. of the oil dispersion) for 50 min. After the addition of methyl iodide (1 ml.) to the reaction mixture reflux was continued for 20 hr. The work-up paralleled the previous procedure and, after chromatography, two crystalline fractions were isolated. Although the melting point ranges of these fractions were different (105–140° and 50–105°), the infrared spectra were very similar to each other and to authentic II + IV mixtures. The combined fractions totaled 52 mg. and exhibited absorption at 4.14, 4.81 (doublet) and 6.52 τ (OCH_3) in the n.m.r. spectrum. A comparison of the areas of the vinyl hydrogen resonances suggested that this material was a mixture of 44% II and 56% IV.

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The Synthesis of Δ^5-Cholestene-3β,19-diol *via* the 3,5-Cyclosterol Rearrangement. A Novel Route to 19-Nor Sterols

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The synthesis of the Δ^5-3β,19-dihydroxy steroid system is of interest because of its use as an intermediate in the preparation of physiologically active 19-nor steroids[1] and as a precursor in the synthesis of certain C-19 oxygenated naturally occurring steroids.[2] We have achieved a synthesis of this system by utilizing the 3,5-cyclosterol[3a] rearrangement of 3α,5α-cyclo-6β,19-oxidocholestane (II).[3b]

The hydrolytic rearrangement of 3α,5α-cyclo-6β-ol steroids to the corresponding 3β-Δ^5-sterols is well known.[3,4] The high solvolytic rate and stereospecificity observed in this reaction are accommodated by postulation of an intermediary nonclassical homoallylic cation. By analogy, it was anticipated that application of this rearrangement to a 3α,5α-cyclo-6β,19-oxido steroid (A) would lead to intramolecular transfer of the 6β oxygen to C-19 resulting in the homoallylic ion (B). Subsequent attack by solvent at C-3 would yield the corresponding 3β-substituted 19-hydroxy-Δ^5-steroid (C).

Such a reaction sequence was realized experimentally and represents a simple and potentially general route to Δ^5-3β,19-dihydroxy steroids.

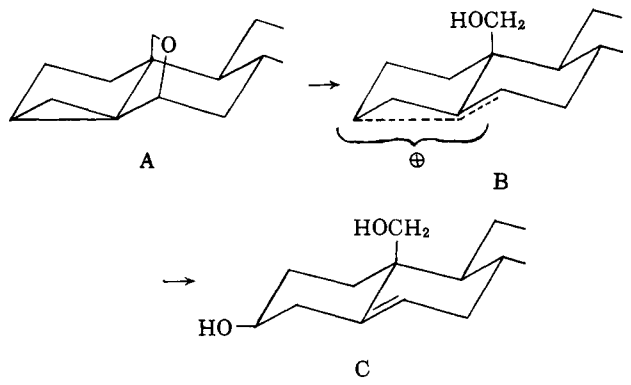
Treatment of 3α,5α-cyclocholestan-6β-ol (I) in dry benzene with lead tetraacetate and dry calcium carbonate led to a 25% yield, based upon recovered starting

(1) A. Bowers, R. Villotti, J. A. Edwards, E. Denot, and O. Halpern, *J. Am. Chem. Soc.*, **84**, 3204 (1962).

(2) L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, pp. 727–809.

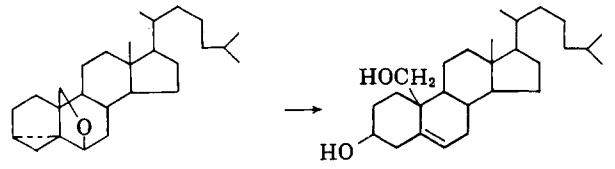
(3) (a) E. S. Wallis, E. Fernholz, and T. Gephardt, *J. Am. Chem. Soc.*, **59**, 137 (1937); (b) K. Tanabe, *et al.*, have published the preparation and rearrangement of 6β,19-oxido-3α,5α-cycloandrostan-17-one [K. Tanabe, R. Takasaki, K. Sakai, R. Hayashi, and Y. Morisawa, *Chem. Pharm. Bull.* (Tokyo), **10**, 1126 (1962)].

(4) E. M. Kowower and S. Winstein, *J. Am. Chem. Soc.*, **78**, 4347 (1956).



material, of 3α,5α-cyclo-6β,19-oxidocholestane (II).[1,5-7] The structural assignment is based upon composition, infrared and nuclear magnetic resonance spectra. The infrared spectrum (carbon tetrachloride) of II had a band at 11.08 μ which is characteristic of the 6β,-19-oxido bridge.[1] The n.m.r. spectrum[8] of the oxide lacked the C-19 methyl signal of starting *i*-steroid and was further characterized by the C-19 methylene multiplet centered at 6.23 τ,[9] J_{AB} = 12 c.p.s., δ_{AB}, 0.13 p.p.m. (2H); the unresolved C-6 multiplet at 6.68 τ (1H); and the cyclopropyl C-4 methylene centered at 9.75 τ (2H).

Treatment of 3α,5α-cyclo-6β,19-oxidocholestane (II) with a trace of sulfuric acid in aqueous acetone for two hours yielded Δ⁵-cholestene-3β,19-diol (II) in 80% yield. The identity of this material was proved by comparison with a known sample (melting point, mixture melting point, infrared) prepared by the method of Bowers.[1]



II III

Experimental[10]

3α,5α-Cyclo-6β,19-oxidocholestane (II).—Lead tetraacetate 4.68 g. (0.107 mole) was recrystallized from benzene and dried *in vacuo* for 3 hr. It was dissolved in 250 ml. of dry benzene and 50 g. (0.5 mole) of anhydrous calcium carbonate was added. The resulting reaction mixture was kept at reflux for 1 hr. and then a solution of 3α,5α-cyclocholestan-6β-ol, 8.2 g. (0.021 mole) in 100 ml. of dry benzene was added in one portion. After 18 hr. at reflux the reaction was filtered and the benzene solution was washed with saturated potassium iodide solution. The resulting two-phase system was filtered from the insoluble lead oxide and the benzene layer was separated and washed with water. After drying, the benzene solution was concentrated *in vacuo*, yielding a gummy product weighing 4.24 g.

Chromatography was carried out using Merck neutral alumina. Elution with hexane–benzene yielded crystalline material which was recrystallized from acetone affording 600 mg., m.p. 79–80°, $[\alpha]_D$ +65° (*c* 1.4).

Anal. Calcd. for $C_{27}H_{44}O$: C, 84.21; H, 11.53. Found: C, 84.48; H, 11.52.

Further elution with benzene–ether and pure ether yielded 3α,5α-cyclocholestan-6-one, cholesteryl acetate, and finally unchanged 3α,5α-cyclocholestan-6β-ol.

Δ⁵-Cholestene-3β,19-diol (III).—A solution of 3α,5α-cyclo-6β,19-oxidocholestane (0.10 g.) in 20 ml. of acetone was treated with 1.0 ml. of water and 0.5 ml. of 1 *N* sulfuric acid. After standing for 2 hr. at room temperature, the solution was neutralized with saturated sodium bicarbonate solution and extracted with ether. The combined ether extracts were washed with water and concentrated to dryness under reduced pressure.

Recrystallization of the crude product from methanol yielded 85 mg., m.p. 147–149°, $[\alpha]_D$ −30° (*c* 1). This material was identical with an authentic sample prepared by the method of Bowers.[1]

Acknowledgment.—The authors wish to thank Professor Paul von R. Schleyer of Princeton University for supplying the nuclear magnetic resonance data. The generosity of Dr. James C. Orr of Syntex Company is acknowledged for supplying us with a reference sample of III.

(5) M. S. Heller, H. Wehrli, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **45**, 1261 (1962).

(6) The crude reaction product showed acetate bands in the infrared (carbon tetrachloride) at 5.78 and 8.20 μ. Presumably the acetate arises from acetolysis of either 3α,5α-cyclocholestan-6β-ol (I) or 3α,5α-cyclo-6β,19-oxidocholestane (II); the acetic acid forms as the oxidation proceeds. Calcium carbonate was used in the oxidizing system in order to minimize the solvolytic reaction by buffer action. Tanabe, *et al.*, (see ref. 3b) report a 25% yield in the formation of 6β,19-oxido-3α,5α-cycloandrostan-17-one by lead tetraacetate oxidation of 3α,5α-cycloandrostan-6β-ol-17-one without buffer. Although a control experiment in our system has not been carried out, the result of Tanabe indicates that buffering may not be necessary. This point is currently under investigation.

(7) Formation of the 6β,19-oxido bridge from a 3α,5α-cyclo-6β-ol is consistent with bond formation occurring directly between the axial hydroxyl group and C-19 methyl with retention of configuration at C-6.

(8) The n.m.r. spectrum was determined in carbon tetrachloride solution relative to tetramethylsilane as internal standard. A Varian A-60 spectrophotometer was used operating at 60.0 Mc.

(9) G. V. D. Tiers, *J. Chem. Phys.*, **62**, 1151 (1958).

(10) All melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer infracord spectrophotometer. N.m.r. spectra were determined on a Varian A-60 spectrophotometer operating at 60.0 Mc. using carbon tetrachloride with tetramethylsilane as internal standard. Optical rotations were obtained in chloroform solution. Microanalysis were carried out by George I. Robertson, Florham Park, N. J.

The Preparation of Chloromethyl Vinyl Ketones

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Halomethyl vinyl ketones have been prepared mainly by the direct halogenation of methyl vinyl ketones,[1] by the action of diazomethane on vinyl acyl halides,[2] and by the addition of halogenated acyl halides to acetylene and ethylene derivatives in the presence of aluminum trichloride.[3]

In view of the possible synthetic and biological use[4] of these compounds, we report our observations on the reaction of aldehydes[5] with triphenylchloracetonylphosphorane (I) (following).

$$\underset{\text{I}}{Ph_3P{=}CHCOCH_2Cl} + RCHO \longrightarrow Ph_3P{=}O + RCH{=}CH{-}COCH_2Cl$$

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(5) Reactions of this type have been reviewed by U. Schöllkopf, *Angew. Chem.*, **71**, 260 (1959).