sample prepared by method a or with citrostanone and the infrared spectra of all the three materials were identical.

The chromatography fractions eluted with benzene gave 52 mg. of 4α-methylstigmastan-3β-ol (VIIa) with m.p. 178–184°. Two crystallizations from methanol yielded a pure sample, m.p. 186–187°, undepressed on admixture with a specimen prepared by the method described below.

4α-Methylstigmastan-3-β-ol (VIIa).).—A solution of 75 mg. of 4α-methylstigmastan-3-one (VI) in 15 cc. of dry ether was added to 100 mg. of lithium aluminum hydride in 10 cc. of ether and the mixture was heated under reflux for 1 hr. Decomposition with dilute sulfuric acid, isolation with ether and crystallization from methanol gave 61 mg. of 4α-methylstigmastan-3β-ol (VIIa), m.p. 187–188°, $[\alpha]_D + 28°$. The m.p. was undepressed on admixture with a sample of citrostanol and the infrared spectra were absolutely identical.

The **acetate VIIb** was prepared by means of acetic anhydride and pyridine (overnight, room temperature). Two crystallizations from methanol gave a pure sample, m.p. 143–144°, $[\alpha]_D + 38°$. Identity with citrostanol acetate was established by mixture m.p. determination and infrared comparison.

Acetaldehyde from Citrostadienol. (a) By Ozonolysis.—A stream of 3% ozonized oxygen was passed through a solution of 200 mg. of citrostadienol in 20 cc. of carbon tetrachloride at 0° for 25 minutes. Water (10 cc.) then was added and the mixture was distilled into a cooled solution of 200 mg. of 2,4-dinitrophenylhydrazine in 6 cc. of ethanol and 14 cc. of 40% aqueous sulfuric acid. The resulting precipitate was collected, washed with water, dried, dissolved in benzene and chromatographed on 15 g. of alumina. The benzene fractions on evaporation and crystallization from ethanol furnished 32 mg. (30%) of acetaldehyde 2,4-dinitrophenylhydrazone with m.p. 162–164°. The m.p. was undepressed on admixture with an authentic sample (m.p. 162–164°) and the infrared spectra were completely identical.

(b) By Successive Hydroxylation and Periodic Acid Cleavage.—Osmium tetroxide (125 mg.) was added to a solution of 100 mg. of citrostadienol acetate in 10 cc. of dry dioxane and the mixture was allowed to stand at room temperature in the dark for 48 hr. A stream of hydrogen sulfide was then passed through the mixture for 15 minutes, the black precipitate was removed and the product was isolated by means of ethyl acetate. It then was dissolved in 10 cc. of dioxane and a solution of 250 mg. of periodic acid hydrate in 2 cc. of water was added. After being left overnight at room temperature, the solution was distilled into a cooled solution of 100 mg. of dinitrophenylhydrazine in 3 cc. of methanol and 7 cc. of 40% aqueous sulfuric acid. The resulting precipitate, on purification as in the ozonolysis experiment, yielded 42 mg. (88%) of acetaldehyde 2,4-dinitrophenylhydrazone with m.p. 163–164°, undepressed on admixture with an authentic sample.

4α-Methylstigmastane-3β,7α,8α,24,28-pentol 3,7,28-Triacetate (IXb) and the Acetoxy-diketo-aldehyde XI.—A solution containing 95 mg. of citrostadienol and 130 mg. of osmium tetroxide in 15 cc. of pyridine was allowed to stand for 48 hr. in the dark. The pyridine was evaporated under reduced pressure and the residue was boiled for 90 minutes with 1.5 g. of sodium sulfite in 10 cc. of water and 10 cc. of ethanol. The product was then isolated with ether and ethyl acetate and one-half of the resulting crude pentol IXa was acetylated with 1.5 cc. of pyridine and 1.5 cc. of acetic anhydride overnight at room temperature. The acetate was isolated with ether in the usual way and chromatographed in benzene on 5 g. of alumina. The only crystalline material was eluted with ether and on crystallization from ether–pentane yielded the pentol triacetate IXb as needles with m.p. 221–222°.

Anal. Calcd. for $C_{36}H_{60}O_8$ (pentol triacetate IXb): C, 69.64; H, 9.74. Calcd. for $C_{34}H_{58}O_7$ (pentol diacetate Xb): C, 70.55; H, 10.10. Found: C, 69.55; H, 9.77.

The second half of the crude pentol IXa was dissolved in 4 cc. of glacial acetic acid, and 300 mg. of lead tetraacetate in 20 cc. of acetic acid was added. After being allowed to stand overnight at room temperature, the mixture was diluted with water and the product was isolated with ether. The resulting material was acetylated with acetic anhydride in pyridine at room temperature and the product was again isolated with ether. The acetate was dissolved in pentane–benzene (2:1) and chromatographed on 5 g. of alumina. The substance eluted with benzene on crystallization from ether–pentane gave the acetoxy-diketo-aldehyde XI as plates with m.p. 151–153°, showing a well defined aldehyde band in the infrared (ν_{max} 2793 cm.$^{-1}$).

Anal. Calcd. for $C_{30}H_{48}O_5$: C, 73.73; H, 9.90. Found: C, 73.53; H, 9.88.

REHOVOTH, ISRAEL

[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE, THE WEIZMANN INSTITUTE OF SCIENCE]

Synthesis of 4α-Methyl-Δ^7-steroids. The Interrelationship of Cholesterol, Citrostadienol and Lophenol

BY YEHUDA MAZUR AND FRANZ SONDHEIMER

RECEIVED JULY 7, 1958

The methylation of Δ^7-cholesten-3-one (II) has been shown to proceed at C-4 and to result in 4α-methyl-Δ^7-cholesten-3-one (III). Reduction of the latter with lithium aluminum hydride yielded 4α-methyl-Δ^7-cholesten-3β-ol (IVa). The last mentioned substance also was obtained from the citrus sterol citrostadienol (I) by partial ozonolysis to 4α-methyl-Δ^7-cholesten-3β-ol-24-one (VIIIa), followed by reduction of the 24-keto group through Wolff–Kishner reduction. The 4α-methyl-Δ^7-cholesten-3β-ol (IVa) obtained by either route proved to be identical with the cactus sterol lophenol to which structure IVa had been assigned. It is shown that the molecular rotation contribution of the 24-ethylidene group in citrostadienol is anomalous and it is proposed that the $\Delta^{24(28)}$-double bond in the citrus sterol exists in the opposite configuration to that in the algae sterols fucosterol and sargasterol. The suggestion is made that the grain oil sterol α_1-sitosterol is the $\Delta^{24(28)}$-isomer of citrostadienol.

We recently have shown the citrus sterol citrostadienol to be 4α-methyl-24-ethylidene-Δ^7-cholesten-3β-ol (I).[1] It seemed to us to be of interest to interrelate this substance with an authentic Δ^7-cholestene derivative by converting it through removal of the 24-ethylidene group to 4α-methyl-Δ^7-cholesten-3β-ol (IVa) and to synthesize the latter. This scheme, the realization of which is described in this paper, became of additional interest when it was announced that 4α-methyl-Δ^7-cholesten-3β-ol (IVa) is obtainable from two natural sources: the cactus constituent lophenol was shown to be IVa[2] and the latter structure also was assigned tentatively to a sterol isolated from rat feces,[3] although the two natural products did not seem to be identical.[2]

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[1] Y. Mazur, A. Weizmann and F. Sondheimer, THIS JOURNAL, **80**, 1007, 6293 (1958).

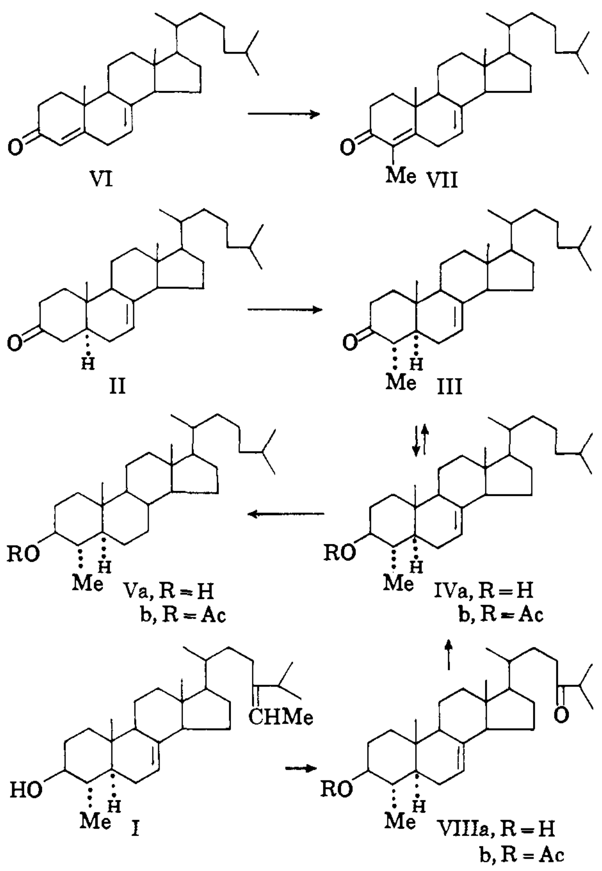
[2] C. Djerassi, J. S. Mills and R. Villotti, *ibid.*, **80**, 1005 (1958).

[3] W. W. Wells and D. H. Neiderhiser, *ibid.*, **79**, 6569 (1957).

Whereas there can be no doubt about the structure of lophenol, the reasons for assigning the 4α-methyl structure IVa to the rat sterol were ambiguous, being based on biogenetic considerations and on the fact that direct monomethylation of Δ^7-cholesten-3-one (II) with methyl iodide and potassium *t*-butoxide in *t*-butyl alcohol and subsequent lithium aluminum hydride reduction had yielded the natural sterol. In fact, the monomethylation of Δ^7-cholesten-3-one (II) would be expected to yield the 2α- rather than the 4α-methyl isomer, by analogy with the corresponding methylation of cholestan-3-one.[4,5] However, it was apparent to us that the sterol from rat feces could be neither pure 2α-methyl- nor pure 4α-methyl-Δ^7-cholesten-3β-ol, since the physical properties of the corresponding saturated compound (m.p. 153–155°; acetate, m.p. 99–101°) were rather different from those of 2α-methylcholestan-3β-ol (m.p. 139–140°; acetate, m.p. 107–108°)[4] and of 4α-methylcholestan-3β-ol (m.p. 163–164°; acetate, m.p. 128–129°).[4]

We first decided to re-investigate the direct monomethylation of Δ^7-cholesten-3-one (II)[6] by means of methyl iodide and potassium *t*-butoxide in *t*-butyl alcohol under the conditions used with cholestan-3-one.[4] The resulting monomethylated ketone, isolated in 37% yield, was reduced with lithium aluminum hydride and the product was purified through the insoluble digitonide in order to obtain the 3β-hydroxy fraction. The compound thus obtained in 62% yield appeared to be the 4α-methyl rather than the 2α-methyl derivative since acetylation caused a positive rather than a negative shift in the molecular rotation.[4] Catalytic hydrogenation of this acetate over platinum in acetic acid containing hydrochloric acid smoothly yielded a saturated acetate which proved to be identical in every respect with 4α-methylcholestan-3β-ol acetate (Vb) and the corresponding saturated free alcohols Va were also identical. Consequently the unsaturated alcohol is 4α-methyl-Δ^7-cholesten-3β-ol (IVa) and the ketone from which it was derived is 4α-methyl-Δ^7-cholesten-3-one (III). Introduction of a Δ^7-double bond into cholestan-3-one therefore causes methylation to occur at C-4 instead of C-2 (presumably because the 3-keto group enolizes toward C-4 instead of C-2) and the structural assignment made without proof by Wells and Neiderhiser[3] is actually correct.

Before the above direct route to 4α-methyl-Δ^7-cholesten-3-one (III) was worked out, we investigated the monomethylation at C-4 of $\Delta^{4,7}$-cholestadien-3-one (VI)[7] with methyl iodide and potassium *t*-butoxide in *t*-butyl alcohol, as reported for Δ^4-3-keto steroids.[8] The reaction yielded the required 4-methyl-$\Delta^{4,7}$-cholestadien-3-one (VII) with the characteristic ultraviolet maximum at 250 mμ.[8] The yield was, however, so poor that the reduction of the Δ^4-double bond was not investigated.



Citrostadienol (I) was degraded to IVa as follows. The $\Delta^{24(28)}$-double bond could be cleaved without affecting the Δ^7-bond through ozonolysis at −70° in ethyl acetate containing pyridine.[9] Reduction of the ozonide with Raney nickel yielded 4α-methyl-Δ^7-cholesten-3β-ol-24-one (VIIIa), further characterized as the acetate VIIIb. Reduction of the 24-ketone VIIIa by the Huang-Minlon modification of the Wolff–Kishner reduction smoothly led to 4α-methyl-Δ^7-cholesten-3β-ol (IVa) which on acetylation furnished the acetate IVb and on oxidation with chromium trioxide in pyridine[10] the ketone III. The three substances IVa, IVb and III prepared by this route proved to be identical in every respect with those synthesized from Δ^7-cholesten-3-one (II).

4α-Methyl-Δ^7-cholesten-3β-ol (IVa) and the acetate IVb prepared by the above two methods agree well in physical properties with those reported for lophenol and its acetate[2] and their respective identity was proved by direct infrared comparison and

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(4) Y. Mazur and F. Sondheimer, THIS JOURNAL, **80**, 5220 (1958).

(5) M. Mousseron, F. Winternitz and A. C. de Paulet, *Compt. rend.*, **245**, 1859 (1957); see also H. J. Ringold and G. Rosenkranz, *J. Org. Chem.*, **21**, 1333 (1956).

(6) Δ^7-Cholesten-3-one (II) was prepared most conveniently by hydrogenating 7-dehydrocholesterol over Raney nickel (*cf.* G. D. Laubach and K. J. Brunings, THIS JOURNAL, **74**, 705 (1952); W. V. Ruyle, E. M. Chamberlin, J. M. Chemerda, G. E. Sita, L. M. Aliminosa and R. L. Erickson, *ibid.*, **74**, 5929 (1952)) and oxidizing the resulting Δ^7-cholesten-3β-ol with chromium trioxide in pyridine (footnote 10). This oxidizing procedure was found to be superior to the use of the Oppenauer reagent, chromic acid in acetic acid (W. Buser, *Helv. Chim. Acta*, **30**, 1379 (1947)) or sodium dichromate in benzene and acetic acid (L. F. Fieser, THIS JOURNAL, **75**, 4395 (1953)).

(7) A. Windaus and O. Kaufmann, *Ann.*, **542**, 218 (1939); R. Antonucci, S. Bernstein, D. Giancola and K. J. Sax, *J. Org. Chem.*, **16**, 1453 (1951).

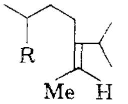
(8) F. Sondheimer and Y. Mazur, THIS JOURNAL, **79**, 2906 (1957); N. W. Atwater, *ibid.*, **79**, 5315 (1957).

(9) *Cf.* P. Bladon, H. B. Henbest, E. R. H. Jones, G. W. Wood and G. F. Woods, *J. Chem. Soc.*, 4890 (1952); G. Slomp and J. L. Johnson, THIS JOURNAL, **80**, 915 (1958).

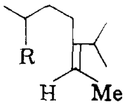
(10) G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, *ibid.*, **75**, 422 (1953).

mixture melting point determination.[11] The sterol from rat feces appears to be inhomogeneous and further discussion regarding its structure must await its obtention in the pure state. In a private communication Dr. Wells kindly informed us that he has purified the corresponding saturated alcohol and has shown it to be identical with our authentic 4α-methylcholestan-3β-ol (IVa).[4] The rat feces sterol therefore does possess the 4α-methylcholestane carbon skeleton.

The presently described degradation of citrostadienol to 4α-methyl-Δ^7-cholesten-3β-ol (IVa), taken together with the previously reported full hydrogenation to 4α-methylstigmastan-3β-ol, provides completely unequivocal evidence for the structure and stereochemistry at all centers of the citrus sterol with one exception. The only ambiguity lies in the fact that the ethylidine grouping at C-24 may exist in one of the two possible configurations IX and X. We are not able at present to assign one of these configurations to citrostadienol. It is of interest to note however that whereas the molecular rotation contribution of the 24-ethylidene group in citrostadienol [*M*D (citrostadienol) − *M*D (4α-methyl-Δ^7-cholesten-3β-ol)] is +90, the corresponding contribution of the 24-ethylidene group in the algae sterols fucosterol (24-ethylidene-Δ^5-cholesten-3β-ol) and sargasterol (24-ethylidene-Δ^5-20-isocholesten-3β-ol) is −18[12] and −27,[13] respectively. This difference leads us to the belief that fucosterol and sargasterol possess the ethylidene group in one configuration, whereas in citrostadienol this group is in the opposite configuration.



IX



X

We have previously pointed out[14] that α_1-sitostanol, the full hydrogenation product of the doubly unsaturated steroid α_1-sitosterol,[15] shows physical properties almost identical with those of 4α-methyl-stigmastan-3β-ol and the two are doubtless identical. α_1-Sitosterol itself, though very similar in most properties and reactions to citrostadienol, shows a considerably lower optical rotation and the same is true for its derivatives. The low rotation probably is not due to contamination with an unmethylated Δ^5-steroid such as β-sitosterol (*cf.* footnote 14) since the Δ_1-value (the difference in molecular rotation between the alcohol and the acetate) for α_1-sitosterol agrees reasonably well with the Δ_1-values for the various 4α-methyl-Δ^7-3β-hydroxysteroids described in this paper (see Table I). The Δ_1-values for unmethylated steroids are negative (Table I) and α_1-sitosterol is therefore apparently a pure 4-methyl sterol. The molecular rotation difference between α_1-sitosterol and 4α-methyl-Δ^7-cholesten-3β-ol (IVa) is −21, in excellent agreement with the contribution of the 24-ethylidene group in fucosterol and sargasterol. We therefore now wish to suggest that α_1-sitosterol is 4α-methyl-$\Delta^{7,24(28)}$-stigmastadien-3β-ol (I), differing from citrostadienol only in the configuration of the $\Delta^{24(28)}$-double bond. This problem is being further investigated.

TABLE I

MOLECULAR ROTATION DATA OF 4α-METHYL-Δ^7-3β-HYDROXY-STEROIDS AND THEIR ACETATES AND OF UNMETHYLATED STEROIDS (IN $CHCl_3$)

Compound	$[M]^{OH}_D$	$[M]^{OAc}_D$	Δ_1
4α-Methyl-Δ^7-cholesten-3β-ol (IVa)	+ 12	+115	+103
4α-Methyl-Δ^7-cholesten-3β-ol-24-one (VIIIa)	+ 12	+114	+102
Citrostadienol (I)	+102[a]	+202[a]	+100
α_1-Sitosterol	− 7[15a]	+134[15a]	+141
Δ^5-Stigmasten-3β-ol (β-Sitosterol)	−149[b]	−178[b]	− 29
Δ^7-Stigmasten-3β-ol (γ-Spinastenol)	+ 46[c]	+ 36[c]	− 10

[a] A. Weizmann and Y. Mazur, *J. Org. Chem.*, **23**, 832 (1958). [b] D. H. R. Barton, *J. Chem. Soc.*, 813 (1945). [c] D. H. R. Barton and J. D. Cox, *ibid.*, 1354 (1948).

Acknowledgments.—We are grateful to Dr. W. W. Wells (University of Pittsburgh, School of Medicine) for interesting correspondence. We also wish to thank Prof. C. Djerassi (Wayne State University, Detroit) for samples of lophenol and derivatives, and Dr. B. A. Hems (Glaxo Ltd., Greenford, Middlesex) for a gift of 7-dehydrocholesterol.

Experimental[16]

Δ^7-Cholesten-3-one (II).—A solution of 0.55 g. of Δ^7-cholesten-3β-ol (m.p. 122–123°)[6] in 10 cc. of dry pyridine was added to 0.5 g. of chromic acid in 10 cc. of pyridine and the mixture was allowed to stand at 24° for 16 hr. Ice and water were added and the product was isolated by means of ether. The resulting material in pentane solution was chromatographed on 15 g. of alumina. The fractions eluted with pentane–benzene (1:1) gave 0.38 g. of Δ^7-cholesten-3-one which on crystallization from methanol showed m.p. 146–147°, $[\alpha]_D$ +25°; reported[6] m.p. 146–148°, $[\alpha]_D$ +25°.

Methylation of Δ^7-Cholesten-3-one (II).—A solution of 195 mg. (5 millimoles) of potassium in 17 cc. of *t*-butyl alcohol was added to a boiling solution of 1 g. (2.6 millimoles) of Δ^7-cholesten-3-one (II) in 20 cc. of benzene. Methyl iodide (1 cc.) in 5 cc. of benzene then was added and the mixture was boiled under reflux for a further 20 minutes. It was cooled, ice was added and the product was isolated with ether in the usual way. The crystalline material which resulted was chromatographed in pentane solution on 40 g. of alumina. Elution with pentane yielded 360 mg. (37%) of 4α-methyl-Δ^7-cholesten-3-one (III) which on crystallization from methanol gave 285 mg. of the analytically pure material as needles with m.p. 139–140°, $[\alpha]_D$ +12°; a sample of lophenone (reported[2] m.p. 122–124°, $[\alpha]_D$ +12°)

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[11] Although the melting point of our 4α-methyl-Δ^7-cholesten-3-one (m.p. 139–140°, $[\alpha]_D$ +12°) is rather higher than that reported for lophenone (m.p. 122–124°, $[\alpha]_D$ +12°),[2] the infrared spectra were found to be practically identical and a mixture of the two showed an intermediate melting point. The discrepancy is perhaps due to polymorphism.

[12] D. H. R. Barton, *J. Chem. Soc.*, 813 (1945).

[13] K. Tsuda, R. Hayatsu, Y. Kishida and S. Akagi, THIS JOURNAL, **80**, 921 (1958).

[14] Y. Mazur, A. Weizmann and F. Sondheimer, *Bull. Research Council Israel*, **7A**, 82 (1958).

[15] *Cf.* (a) E. S. Wallis and E. Fernholz, THIS JOURNAL, **58**, 2446 (1936); (b) S. Bernstein and E. S. Wallis, *ibid.*, **61**, 2308 (1939).

[16] Melting points are uncorrected. The alumina used for all chromatograms was Merck acid-washed alumina. Rotations were determined at room temperature in chloroform solution. Ultraviolet spectra were taken in 95% ethanol solution on a Unicam model S.P. 500 spectrophotometer and infrared spectra in potassium bromide pellets on a Baird double-beam recording spectrophotometer with sodium chloride prism. Analyses were carried out in our microanalytical laboratory under the direction of Mr. Erich Meier.

showed m.p. 118–120°[17] and a mixture of the two exhibited m.p. 124–138°. The infrared spectra were essentially identical.

Anal. Calcd. for $C_{28}H_{46}O$: C, 84.35; H, 11.63. Found: C, 84.56; H, 11.65.

The next fractions eluted with pentane gave 160 mg. of crystalline material with m.p. 134–142° which could not be purified by crystallization and which was shown by rechromatography to be a mixture of Δ^7-cholesten-3-one and 4α-methyl-Δ^7-cholesten-3-one. Lastly, pentane–benzene (9:1) yielded 390 mg. of unchanged Δ^7-cholesten-3-one with m.p. 145–147°, $[\alpha]_D$ +25°.

4α-Methyl-Δ^7-cholesten-3β-ol (IVa).—A solution of 100 mg. of 4α-methyl-Δ^7-cholesten-3-one (III) in 10 cc. of ether was added dropwise to a suspension of 200 mg. of lithium aluminum hydride in 10 cc. of ether. The mixture was boiled under reflux for 1 hr. and then was decomposed by the careful addition of ice and dilute hydrochloric acid. Isolation with ether afforded 96 mg. of material which was dissolved in 25 cc. of ethanol and treated with a solution of 1 g. of digitonin in 50 cc. of 90% ethanol. The precipitated digitonide was collected after 16 hr., dissolved in the minimum of pyridine and diluted with ether. The precipitate was removed, washed with ether and the filtrates were evaporated. The resulting material (75 mg.) on crystallization from methanol yielded 62 mg. of 4α-methyl-Δ^7-cholesten-3β-ol (IVa) with m.p. 146–147°, $[\alpha]_D$ +3°; reported[2] for lophenol m.p. 149–151°, $[\alpha]_D$ +5°. There was no m.p. depression on admixture with a sample of lophenol with m.p. 145–146° (determined by us)[17] and the infrared spectra were completely identical.

Anal. Calcd. for $C_{28}H_{48}O$: C, 83.93; H, 12.08. Found: C, 83.68; H, 12.10.

The acetate IVb was obtained by means of acetic anhydride and pyridine (overnight at room temperature) and after crystallization from methanol showed m.p. 114–115°, $[\alpha]_D$ +26°; reported[2] for lophenol acetate m.p. 119–121°, $[\alpha]_D$ +28°. There was no m.p. depression on admixture with a sample of lophenol acetate with m.p. 114–115° (determined by us)[17] and the infrared spectra were identical.

Anal. Calcd. for $C_{30}H_{50}O_2$: C, 81.39; H, 11.38. Found: C, 81.25; H, 11.29.

Catalytic Hydrogenation of 4α-Methyl-Δ^7-cholesten-3-ol Acetate (IVb).—A solution of 50 mg. of the acetate IVb in 20 cc. of acetic acid containing 1 drop of concentrated hydrochloric acid was shaken in hydrogen over 10 mg. of platinum oxide. After 1 hr. another 1 drop of hydrochloric acid was added and the hydrogenation was allowed to proceed overnight. The catalyst was then removed, water was added to the filtrate and the product was isolated with ether. Chromatography on 4 g. of alumina, followed by crystallization of the fractions eluted with pentane–benzene (9:1) from methanol, gave 4α-methylcholestan-3β-ol acetate (Vb) with m.p. 128–129°, $[\alpha]_D$ +40°; reported[4] for Vb m.p. 128–129°, $[\alpha]_D$ +41°; reported[4] for 2α-methylcholestan-3β-ol acetate m.p. 107–108°, $[\alpha]_D$ −33°. There was no m.p. depression on admixture with an authentic sample of Vb[4] and the infrared spectra were identical.

Hydrolysis of the hydrogenation product (15 mg.) with methanolic potassium hydroxide (20 cc., 3%) for 1 hr. under reflux, followed by isolation with ether and crystallization from methanol, yielded 4α-methylcholestan-3β-ol (Va) with m.p. 162–164°, $[\alpha]_D$ +26°. Identity with an authentic sample (m.p. 163–164°, $[\alpha]_D$ +27°)[4] was established in the usual way.

Methylation of $\Delta^{4,7}$-Cholestadien-3-one (VI).—A solution of 191 mg. (0.5 millimole) of $\Delta^{4,7}$-cholestadien-3-one (VI)[7] in 25 cc. of *t*-butyl alcohol was added to a boiling solution of 30 mg. (0.77 millimole) of potassium in 27.5 cc. of *t*-butyl alcohol. Methyl iodide (71 mg., 0.5 millimole) in 15 cc. of *t*-butyl alcohol then was added dropwise to the boiling solution during 3 hr. After being boiled for a further 0.5 hr., the mixture was cooled, water was added and the product was isolated with ether in the usual way. The resulting material was dissolved in pentane and chromatographed on 10 g. of alumina. Five fractions (total weight, 32 mg.) eluted with pentane–benzene (9:1) showed ultraviolet maxima at 248–250 mμ (ε 10,500–14,100). They were combined and after crystallization from methanol yielded 20 mg. (10%) of 4-methyl-$\Delta^{4,7}$-cholestadien-3-one (VII) with m.p. 124–125°, $[\alpha]_D$ +24°, λ_{max} 250 mμ (ε 15,600), ν_{max} 1670 cm.$^{-1}$.

Anal. Calcd. for $C_{28}H_{44}O$: C, 84.78; H, 11.18. Found: C, 84.63; H, 11.12.

Ozonolysis of Citrostadienol (I) to 4α-Methyl-Δ^7-cholesten-3β-ol-24-one (VIIIa).—A saturated solution of ozone in ethyl acetate (30 cc.) at −70° was added to a solution of citrostadienol (100 mg.) and pyridine (8 mg.) in ethyl acetate (150 cc.) at the same temperature. The solution was allowed to stand at −70° for 10 minutes, Raney nickel (*ca.* 1 g.) then was added and the mixture was boiled under reflux for 20 minutes. The mixture was cooled, the metal was removed and washed with ethyl acetate. The combined filtrates were evaporated under reduced pressure and the residue, dissolved in 20 cc. of benzene–pentane (1:1), was chromatographed on 4 g. of alumina. The first fractions eluted with benzene yielded 9 mg. of recovered citrostadienol with m.p. 160–162°. Further elution with benzene afforded 22 mg. of 4α-methyl-Δ^7-cholesten-3β-ol-24-one (VIIIa) with m.p. 130–133°. The analytical sample was obtained by crystallization from acetone and showed m.p. 134–135°, $[\alpha]_D$ +3°, ν_{max} 1706 cm.$^{-1}$.

Anal. Calcd. for $C_{28}H_{46}O_2$: C, 81.10; H, 11.18. Found: C, 79.95; H, 11.16.

The acetate VIIIb (acetic anhydride, pyridine, overnight at room temperature) on crystallization from methanol showed m.p. 116–118°, $[\alpha]_D$ +25°, ν_{max} 1736 and 1706 cm.$^{-1}$.

Anal. Calcd. for $C_{30}H_{48}O_3$: C, 78.89; H, 10.59. Found: C, 78.80; H, 10.51.

Wolff-Kishner Reduction of 4α-Methyl-Δ^7-cholesten-3β-ol-24-one (VIIIa) to 4α-Methyl-Δ^7-cholesten-3β-ol (IVa).—A solution of 36 mg. of 4α-methyl-Δ^7-cholesten-3β-ol-24-one (VIIIa), 3.3 cc. of 100% hydrazine hydrate and 3.0 g. of potassium hydroxide in 33 cc. of diethylene glycol was boiled under reflux for 1.5 hr. The open flask was then heated until the internal temperature had reached 200° and the temperature was kept there under reflux for a further 1 hr. The product was isolated with ether and chromatographed on 4 g. of alumina. The crystalline fractions eluted with benzene on crystallization from methanol yielded 28 mg. of 4α-methyl-Δ^7-cholesten-3β-ol (IVa) with m.p. 145–146°, $[\alpha]_D$ +2°, identified with the above-described sample and with lophenol through mixture m.p. determination and infrared comparison. Acetylation yielded the acetate IVb with m.p. 113–114°, $[\alpha]_D$ +25°, identified with the above-described sample in the usual way.

4α-Methyl-Δ^7-cholesten-3-one (III) by Oxidation of 4α-Methyl-Δ^7-cholesten-3β-ol (IVa).—A solution of 15 mg. of the alcohol IVa in 0.5 cc. of pyridine was added to 15 mg. of chromic acid in 0.5 cc. of pyridine and the mixture was allowed to stand overnight at room temperature. Water was then added and the product was isolated with ether. The resulting material was dissolved in pentane–benzene (9:1) and filtered through 2 g. of alumina. Two crystallizations from methanol yielded 9 mg. of 4α-methyl-Δ^7-cholesten-3-one (III) with m.p. 138–140°, $[\alpha]_D$ +11°. Identity with the above-described sample was established through mixture m.p. determination and infrared comparison.

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[17] Our melting points were determined in capillary tubes, whereas Djerassi, *et al.* (footnote 2), determined the melting point of lophenol and derivatives on a Kofler block. This fact explains the slightly higher melting points reported in footnote 2 to those found by ourselves.