not change the m.p.; $[\alpha]_D^{25}$ +254° (CH_3OH); $\lambda_{max}^{CH_3OH}$ 241 mμ (ε = 18,600).

Anal. Calc'd for $C_{26}H_{30}ClNO_4 \cdot {}^1/_2CH_3OH$: C, 67.43; H, 6.83. Found: C, 67.79; H, 6.75.

1,4-Pregnadien-17α-ol-3,11,20-trione-21-(p-dimethylaminophenyl)nitrone (III). The reaction was carried out according to Leanza and coworkers.[2] From 4.52 g. of II there was obtained 3.78 g. of dark red plates of III, m.p. 182–183° (dec.). Recrystallization from aqueous methanol did not change the m.p.

Anal. Calc'd for $C_{29}H_{34}N_2O_5$: C, 70.99; H, 6.99; N, 5.71. Found: C, 71.26; H, 7.37; N, 5.62.

1,4-Pregnadien-21-al-17α-ol-3,11,20-trione Hydrate (IV). The procedure of Leanza and coworkers[2] was followed. Just prior to the crystallization of IV an orange oil precipitated and the latter was separated by decantation. From 2.88 g. of nitrone (III) there resulted 0.80 g. of IV as yellow needles, m.p. 220–230° (dec.) (capillary); $[\alpha]_D^{25}$ +166° (CH_3OH); λ_{max}^{EtOH} 238 mμ (ε = 15,800).

Anal. Calc'd for $C_{21}H_{24}O_5 \cdot 2H_2O$: C, 64.27; H, 7.19. Found: C, 64.55; H, 7.06.

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Conversion of Tigogenin and Neotigogenin into 16,22-Epoxycholest-25-en-3β-ol and 16,22-Epoxycholestan-3β-ol

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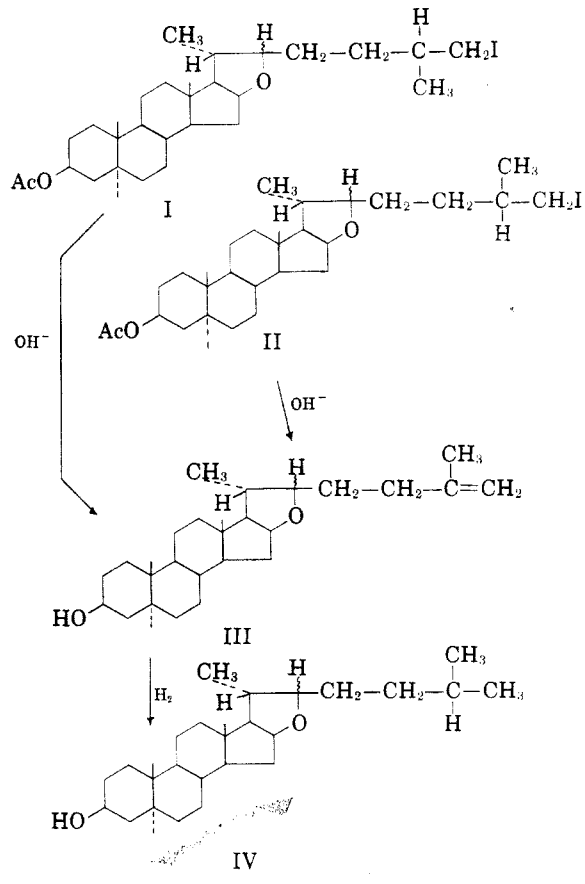
During the course of studies on the synthesis of some amino derivatives of dihydrotigogenin and dihydroneotigogenin, the 26-deoxy-26-iodo derivatives[1] of these dihydrosapogenins were prepared as intermediates. These compounds, 26-deoxy-26-iododihydrotigogenin acetate (I) and 26-deoxy-26-iododihydroneotigogenin acetate (II), were found to be extremely sensitive to base, readily undergoing simultaneous deacetylation and dehydrohalogenation to yield the common 26-deoxy-Δ^{25}-dihydro derivative (16,22-epoxycholest-25-en-3β-ol), III. Catalytic hydrogenation of III led to 16,-22-epoxycholestanol, IV. The epoxycholestanol (IV) was also obtained by the lithium aluminum hydride reduction of dihydrotigogenin 26-tosylate.

Scheer, *et al.*[2] have transformed the $C_5\beta$-sapogenin derivatives, dihydrosarsasapogenin and dihydrosmilagenin into 16,22-epoxycoprostanol by the lithium aluminum hydride reduction of the 26-tosylates of the respective dihydrosapogenins, but conversion of the $C_5\alpha$, C_{25}-epimeric sapogenins, tigogenin and neotigogenin into 16,22-epoxycholest-25-en-3β-ol and 16,22-epoxycholestan-3β-ol has hitherto been unreported.



EXPERIMENTAL[3]

16,22-Epoxycholest-25-en-3β-ol (III). 26-Deoxy-26-iododihydrotigogenin acetate[1] (I) (200 mg.) was dissolved in 20 cc. of methanolic potassium hydroxide (5%) and refluxed for 1 1/2 hours. The solution was partially concentrated *in vacuo* and water was added to the residue. The resulting crystalline precipitate (145 mg.), m.p. 134–138° was purified by chromatography over alumina. Elution with 0.5% methanol in ether yielded 112 mg. of III, which, after crystallization from dilute methanol and recrystallization from ether-hexane, yielded needles of m.p. 138–140°, $[\alpha]_D^{20}$ +3.7° (CH_3OH) λ_{max}^{Nujol} 2.90, 3.08 μ (hydroxyl); 6.05, 11.30 μ ($R_1R_2C{=}CH_2$).

Anal. Calc'd for $C_{27}H_{44}O_2$: C, 80.94; H, 11.07. Found: C, 80.64; H, 10.88.

Treatment of 26-deoxy-26-iododihydroneotigogenin acetate (II) in the same manner afforded III of m.p. 138–140°. The substance agreed in all properties (m.p., mixture m.p., infrared spectra, derivatives) with the compound obtained from I.

When I and II respectively were refluxed with methanolic potassium hydroxide (2%) for 75 minutes, each gave III in about 70% yield. Some dehydrohalogenation occurs also with potassium bicarbonate in methanol.

The *benzoate* of III crystallized from ether-methanol, m.p. 137–140°.

Anal. Calc'd for $C_{34}H_{48}O_3$: C, 80.90; H, 9.59. Found: C, 80.68; H, 9.65.

The *3,5-dinitrobenozate* crystallized from benzene-methanol, m.p. 201–205°.

(1) Sato and Latham, Jr., *J. Am. Chem. Soc.*, in Press.

(2) Scheer, Kostic, and Mosettig, *J. Am. Chem. Soc.*, **77**, 641 (1955).

(3) All melting points were taken on the Kofler block and are uncorrected. We are indebted to Dr. W. C. Alford and his associates for the microanalyses and to Mr. H. K. Miller, all of this Institute, for the spectrophotometric measurements.

Anal. Calc'd for $C_{34}H_{46}N_2O_7$: N, 4.71. Found: N, 4.77.

16,22-Epoxycholestan-3β-ol (IV). A solution of 0.162 g. of slightly impure III (from I) in 6 cc. of acetic acid was hydrogenated with 0.052 g. of Adams' catalyst at atmospheric pressure. After a rapid consumption of 1 mole equivalent of hydrogen, the uptake ceased. The catalyst was removed and the solution was made alkaline with dilute alkali. The precipitate was extracted with ether and after solvent removal the product was crystallized from dilute ethanol, m.p. 150–153.5°. Recrystallization from dilute acetone gave needles of m.p. 152–153.5°, $[\alpha]_D^{20}$ −5.8° ($CHCl_3$).

Anal. Calc'd for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.77; H, 11.53.

Reduction of III obtained from II gave the identical product IV.

The *benzoate* of IV, after several recrystallizations from methanol-ether, formed rods of m.p. 154.5–156°.

Anal. Calc'd for $C_{34}H_{50}O_3$: C, 80.58; H, 9.95. Found: C, 80.86; H, 10.03.

16,22-Epoxycholestan-3β-ol (IV) *from the lithium aluminum hydride reduction of dihydrotigogenin 26-tosylate.* The oily dihydrotigogenin 26-tosylate prepared in the manner of Scheer, *et al.*[2] was reduced directly with lithium aluminum hydride according to their directions. The crude product (228 mg.) then was chromatographed over alumina and the fraction eluted with benzene-ether (4:1) was crystallized from dilute ethanol to form rods of m.p. 148–152°. Recrystallization from dilute acetone raised the m.p. to 152–153°. The compound was identical in every respect with IV, obtained from the reduction of III.

A compound of m.p. 95–97° (35 mg. crystallized from abs. ethanol) was obtained from the fraction eluted earlier with benzene-hexane (1:1). It is presumably the 3-deoxy derivative, 16,22-epoxycholestane, formed by the reduction of the 3,26-ditosylate (by-product in the tosylation). Its infrared spectrum showed no hydroxyl band.

Anal. Calc'd for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 83.97; H, 11.95.

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Preparation of a Crystalline 22-Bromo-24,24-diphenylchol-23-ene

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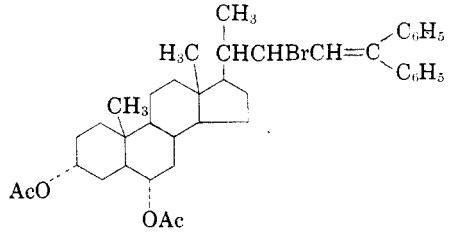
The 22-bromo-24,24-diphenylchol-23-ene derivatives are intermediates in the degradation of the side chain of bile acids.[1] They are very unstable compounds and usually dehydrobrominate immediately after being formed in the reaction between 24,24-diphenylchol-23-ene and N-bromosuccinimide. The only 24,24-diphenylchol-23-ene derivative reported is the 3α,12α-diacetoxy-22-bromo-24,24-diphenylchol-23-ene.[2] This compound was obtained only in a crude form and decomposed when further purification was attempted.

In the course of their studies on the side chain degradation of hyodesoxycholic acid, Hoehn and coworkers reacted 3α,6α-diacetoxy-24,24-diphenyl-23-ene and N-bromosuccinimide in carbon tetrachloride solutions.[3] The reaction mixture was illuminated with a 150-watt floodlight while being refluxed 15 minutes.

Re-investigating this process we found by using a pure 3α,6α-diacetoxy-24,24-diphenylchol-23-ene and a petroleum ether fraction boiling from 60–80° (Skellysolve B) as solvent that illumination of the reaction mixture was not necessary. The bromination proceeded smoothly and the 22-bromo derivative was stable even after several hours of refluxing. A crude bromo compound was isolated from the petroleum ether solution. It was crystallized from cyclohexane and ether and a pure, crystalline 3,6-diacetoxy-22-bromo-24,24-diphenylchol-23-ene[1] was obtained. To confirm the 22 position of the bromine the crystalline compound was dehydrobrominated by refluxing it with sodium acetate in acetic acid. The dehydrobromination product was found to be pure 3α,6α-diacetoxy-24,24-diphenylchol-21,23-diene by absorption spectra measurements.[4] This finding indicates that the bromine was a substituent on the 22 carbon atom of the crystalline bromo derivative.



I

EXPERIMENTAL

3α,6α-Diacetoxy-24,24-diphenylchol-23-ene[3] (20 g.) was dissolved in 500 ml. of Skellysolve B, 7.2 g. of N-bromosuccinimide and 3.6 g. of sodium bicarbonate were added, and the mixture was refluxed for 1.5 hours with constant stirring. The reaction mixture was cooled to room temperature, filtered, and the residue (succinimide) was washed with 80 ml. of Skellysolve B. The combined filtrates were kept overnight in the cold. A precipitate was formed which was removed by filtration. The filtrate was evaporated under reduced pressure from a water-bath at 25°. The brown residue weighed 10 g. and had a bromine content of 9.95% (Calc'd for I: 11.83%).

Five g. of this product was dissolved by heating in 30 ml. of cyclohexane. The solution was filtered and the filtrate was kept overnight in the cold; needles were formed which were

(1) Ch. Meystre, H. Frey, A. Wettstein, and K. Miescher, *Helv. Chim. Acta*, **27**, 1815 (1944).

(2) Ch. Meystre, L. Ehnann, N. Neher, and K. Miescher, *Helv. Chim. Acta*, **28**, 1252 (1945).

(3) R. B. Moffett, J. E. Stafford, J. Linsk, and W. H. Hoehn, *J. Am. Chem. Soc.*, **68**, 1857 (1946).

(4) 3α,6α-diacetoxy-24,24-diphenylchol-21,23-diene was prepared by L. Rubin, Research Department, Canada Packers, Ltd. by repeated recrystallizations of the dehydrobrominated reaction product of 3α,6α-diacetoxy-24,24-diphenylchol-23-ene and N-bromosuccinimide until a constant extinction coefficient ($E_{1\,cm.}^{1\%}$ 464 at 360 mμ) was obtained. The authors wish to thank Dr. Rubin for communicating to them the value of this extinction coefficient.