943. *Calciferol and its Relatives. Part VI.*[1] *A Degradation of 7-Oxocholesteryl Acetate to Some Des-AB-cholestane Derivatives.*

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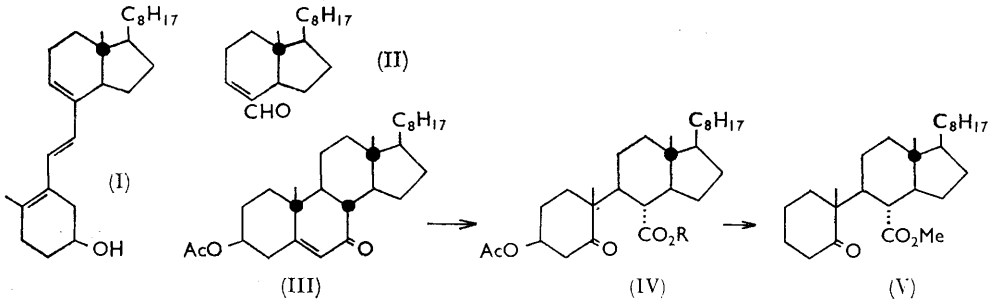
A route from 7-oxocholesteryl acetate to the aldehyde (II) and some other des-AB-cholestane derivatives is described. The isomerisation of the conjugated ester (XVII; R = Me) to the unconjugated ester (XIX; R = Me) indicates that in these *trans*-hydrindanes conformational factors operate similar to those which determine that Δ^2-*trans*-9-methyloctalins are more stable than their Δ^1- or Δ^3-isomers.

As part of a series [2] of studies on the synthesis of 9,10-seco-sterols we projected a synthesis [3] of tachysterol (I) from a monocyclic fragment representing ring A and a bicyclic fragment (II) representing rings C and D. We chose in the first instance to prepare the bicyclic fragment (II) by removing rings A and B from cholesterol, and in this and the following Paper we describe two different approaches to this degradative problem. The starting point for the present experiments was 7-oxocholesteryl acetate (III), available [4] in good yield by allylic oxidation of cholesteryl acetate.

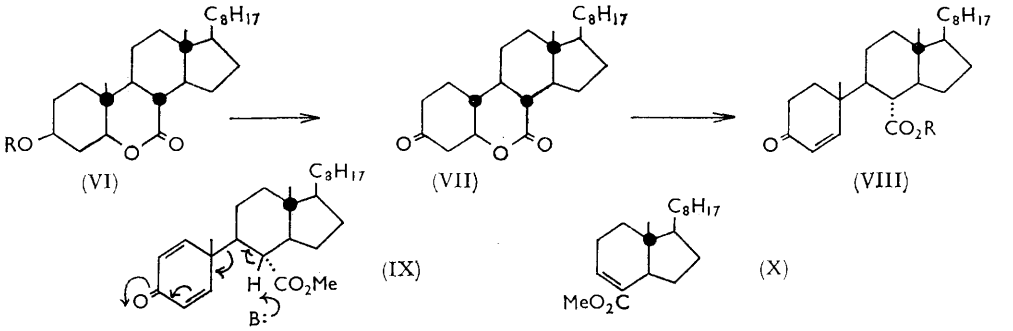
In preliminary studies [5] we ozonised the acetate (III) and obtained the crystalline seco-acid (IV; R = H). This and some of its derivatives have since been described by Jacobs and Brownfield.[6] Since in our work the acid was required for preparative purposes we gave some attention to the conditions of the ozonolysis; under those described in the Experimental part the acid was formed in 65% yield.

[1] Part V, Harrison, Hurst, Lythgoe, and Williams, *J.*, 1960, 5176.
[2] Harrison and Lythgoe, *J.*, 1958, 837, 843, and earlier Papers.
[3] Preliminary account: *Tetrahedron Letters*, 1963, 1413.
[4] Heusler and Wettstein, *Helv. Chim. Acta*, 1952, **35**, 284.
[5] Günther, Ph.D. Thesis, Leeds, 1958.
[6] Jacobs and Brownfield, *J. Amer. Chem. Soc.*, 1960, **82**, 4033.

Thermal elimination of acetic acid from the ester (IV; R = Me), and hydrogenation of the product, gave the δ-keto-ester (V). By carrying out a reversed Michael reaction on the corresponding δ-keto-aldehyde, Cornforth and his colleagues [7] obtained 2-methylcyclohexanone, and we hoped similarly to obtain from the ester (V) the same product,



together with the bicyclic ester (X). However, the δ-keto-ester (V) proved too stable to be readily decomposed in this manner. We then made some attempts to obtain the dienone ester (IX) because, in theory, its fragmentation under the influence of base into *p*-cresol and the ester (X) should be assisted by the energy of incipient aromatisation of ring A. Reduction with sodium borohydride transformed the acid (IV; R = H) into the acetoxy-lactone (VI; R = Ac), regarded as belonging to the 5α-series. From it the hydroxy-lactone (VI; R = H) and the keto-lactone (VII) were prepared. Treatment with alkali converted the latter into the unsaturated ketone (VIII; R = H). Attempts to introduce a Δ^1-double bond into the lactone (VII) were not immediately successful, and, since the yields in this reaction sequence were only moderate, we did not persist in attempts to obtain the dienone ester (IX). Results described later in this Paper make it improbable that base-catalysed reactions of any but the mildest would yield the desired bicyclic ester (X).



The *en bloc* removal of ring A from the keto-acid (IV; R = H) having proved impracticable, stepwise removal of the component atoms was next studied. Heating the acid with acetic anhydride containing sodium acetate caused enol lactone formation and also elimination of the acetoxy-group to give a homoannular diene (XI), $\lambda_{max.}$ 274 mμ. This provided a means for removing four of the carbon atoms of ring A. Alder and Rickert [8] showed that cyclohexa-1,3-diene and methyl acetylenedicarboxylate form an adduct which decomposes at moderate temperatures, giving ethylene and dimethyl phthalate. The adduct from the diene (XI) showed no absorption in the near ultraviolet in agreement with the structure (XII). At the temperature of boiling decalin it isomerised

[7] Cornforth, Hunter, and Popjak, *Biochem. J.*, 1953, **54**, 590.
[8] Alder and Rickert, *Annalen*, 1936, **524**, 180; Pines and Kozlowski, *J. Amer. Chem. Soc.*, 1956, **78**, 3776.

nearly quantitatively, giving an aryl ester (XIII) which was readily hydrolysed to 3-hydroxyphthalic acid and 9β-isopropenyl-des-AB-cholestan-8α-carboxylic acid (XIII; R = H).

This acid was an important substance for our purposes, since it contained the required bicyclic system, bearing at positions 8 and 9 groups suitable for manipulation in the desired sense. At this stage, Fieser and his associates [9] described the closely related acid (XIV) (" duoannelic acid ") which they obtained in *ca.* 4% yield from the products of oxidation of cholesterol with dichromate and acetic acid. The steps by which it arose in this oxidation were not clear, but its degradation by hypobromite to a dibasic acid $C_{20}H_{34}O_4$, together with its proton magnetic resonance spectrum, established its structure as (XIV; R = H). We obtained the same acid (XIV; R = H) by oxidising the methylenic acid (XIII; R = H) with Lemieux's [10] reagent or, better, by ozonolysis, and this provides independent confirmation of its structure. Since cholesterol is cheap, Fieser's method is the more convenient way of preparing small quantities of the acid (XIV; R = H), although the yield using our route is much higher, being nearly 40% from 7-oxocholesteryl acetate.

Continuing the degradation, the methyl ester (XIV; R = Me) was converted by reaction with trifluoroperacetic acid into the acetoxy-ester (XV; R = Ac). From this, the hydroxy-ester (XV; R = H) was obtained by Zemplén [11] methanolysis, and 9β-hydroxy-des-AB-cholestan-8α-carboxylic acid by alkaline hydrolysis. At first, we attempted to convert the hydroxy-ester (XV; R = H) into the unsaturated ester (XVII; R = Me) by pyrolysis of the benzoate. The reaction product was a mixture whose spectral characteristics showed that only about 20—30% of the desired conjugated ester was present. The major component was the methyl ester of the unconjugated acid (XIX; R = H), and this acid was isolated after hydrolysis.

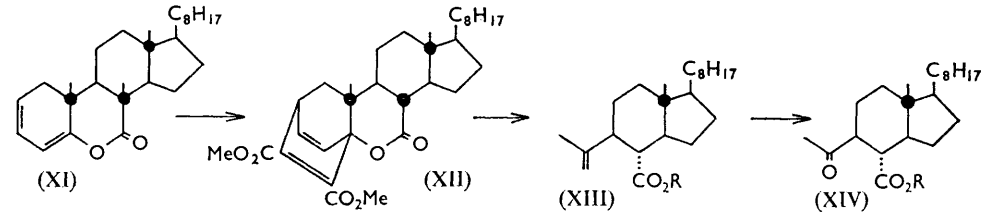
Next we tested an ionic elimination; in contrast to the pyrolytic *cis*-elimination the two eliminated groups had then to be related *trans* to each other, so the hydroxy-ester (XV; R = H) was first changed into its C(9)-epimer (XVI; R = H) by using Chang and Blickenstaff's [12] method. The 9α-hydroxy-ester (XVI; R = H) was then converted into the benzenesulphonate, which was warmed with aqueous ethanolic potassium hydroxide (2 mol.). This gave a product which was separated into neutral and acidic fractions. The acidic fraction gave the crystalline conjugated acid (XVII; R = H), from which the methyl ester was obtained by reaction with diazomethane. The neutral fraction consisted mainly of the methyl ester (XVII; R = Me), but the spectral data showed some contamination with the unconjugated ester (XIX; R = Me). The crude product was, however, pure enough for use in the next step of the sequence. The amount of unconjugated ester in the product increased considerably when more reagent or a longer reaction time were used. This was attributed to the isomerisation of the conjugated ester by the base present; when the pure ester (XVII; R = Me) and 0·12N-methanolic sodium methoxide were warmed together, spectroscopic observations showed that in 7½ hours over 80% was transformed into the unconjugated ester (XIX; R = Me).

It was next necessary to reduce the conjugated ester (XVII; R = Me) to the primary allylic alcohol (XVIII). Use of lithium aluminium hydride gave only moderate yields of this alcohol, because the conjugated double bond was reduced to an appreciable extent. We obtained better results when the reduction was carried out with a solution of lithium aluminium hydride to which 1 mol. of alcohol had been added; the effective reagent was presumably lithium aluminium monoethoxyhydride. This reagent has also been successfully used in this laboratory for other reductions of conjugated esters where saturation of the ethylenic link is a complicating factor, and it may prove to be generally useful for this

[9] Fieser, Huang, and Goto, *J. Amer. Chem. Soc.*, 1960, **82**, 1688.
[10] Lemieux and von Rudloff, *Canad. J. Chem.*, 1955, **33**, 1701, 1710.
[11] Zemplén and Kunz, *Ber.*, 1923, **56**, 1705.
[12] Chang and Blickenstaff, *J. Amer. Chem. Soc.*, 1958, **80**, 2906.

purpose. The allylic alcohol (XVIII) was characterised as the *p*-nitrobenzoate. Oxidation with manganese dioxide converted the alcohol into the syrupy aldehyde (II), $\lambda_{max.}$ 235 mμ, characterised as the semicarbazone.

The superior thermodynamic stability of the unconjugated ester (XIX; R = Me) over its conjugated isomer, noted above, requires comment. This and some of our other



observations on des-AB-cholestane derivatives appear to reflect the fact that in a *trans*-hydrindane system bearing an angular methyl group, introduction of a double bond into the six-membered ring at a point adjacent to a ring junction imposes more strain than when the double bond is separated from the ring junction by one saturated carbon atom. The effect is well-known in 9-methyl-*trans*-octalin derivatives; its conformational origins have been discussed by Corey [13] and by Turner [14] and their respective collaborators. It has indeed already been pointed out [14] that the heat of hydrogenation of 3α-hydroxy-Δ^{11}-cholenic acid is abnormally high, but this example is a complicated one, the double bond affecting a *trans*-decalin as well as a *trans*-hydrindane system. The behaviour of the des-AB-cholestane derivatives now described provides clear evidence of the operation of the effect in simple hydrindane systems.

Experimental

Optical rotations refer to solutions in chloroform except where otherwise stated.

Ozonolysis of 7-Oxocholesteryl Acetate.—Ozonised oxygen (4·5% O_3 v/v; flow rate, 4 g. O_3/hr.) was passed through a suspension of the ketone (5 g.) in ethyl acetate (125 c.c.) and glacial acetic acid (50 c.c.) at −30°, until the solution became clear (37 min.). The solution was then allowed to attain room temperature, glacial acetic acid (75 c.c.), water (25 c.c.) and 30% hydrogen peroxide (7 c.c.) were added, and the solution was heated under reflux for 1 hr. Material from three such experiments was combined, diluted with water, extracted with ether, and the ether phase washed successively with water, 0·25N-potassium hydrogen carbonate, 2N-sulphuric acid, and water, and finally evaporated. Crystallisation of the residue from light petroleum (b. p. 40—60°) gave the seco-acid (IV; R = H) (5·75 g.), m. p. 158° (lit.,[6] 159—159·5°) (Found: C, 73·0; H, 9·8. Calc. for $C_{28}H_{46}O_5$: C, 72·7; H, 10·0%).

To the mother-liquor material, dissolved in 80% acetic acid (60 c.c.), 50% periodic acid (2·4 c.c.) was added, and after 4 hr. the product was extracted with ether, and the ether solution washed as before, dried, and evaporated to a gum. This was triturated with ice-cold 0·5N-sodium carbonate, and the mixture extracted with ether. The acidic fraction, isolated from the aqueous sodium carbonate phase in the usual manner, provided more crystalline seco-acid (0·54 g.). The mother-liquor material was cyclised as described below, and gave the enol lactone (XI) (2·80 g.). This is equivalent to 3·95 g. of the seco-acid (VI), the effective yield of which is thus 65%.

[13] Corey and Sneen, *J. Amer. Chem. Soc.*, 1955, **77**, 2505.
[14] Turner, Meador, and Winkler, *J. Amer. Chem. Soc.*, 1957, **79**, 4122.

The Keto-ester (V).—The seco-acid (IV; R = H) (500 mg.) was converted by brief treatment with diazomethane in the usual way into its methyl ester, a part of which (460 mg.) was heated at 0·07 mm. and 160—220° during 30 min.; distillation took place at the latter temperature. Crystallisation of the distillate from methanol gave the unsaturated ester (yield 70%), m. p. 56·5—57·5° (Found: C, 77·45; H, 10·45. Calc. for $C_{27}H_{44}O_3$: C, 77·8; H, 10·55%). This compound has been described [6] as an oil. Our material had $\lambda_{max.}$ 230 mμ (ε 6700). Alkaline hydrolysis gave the corresponding acid, m. p. 177—179°, $\lambda_{max.}$ 228 mμ (ε 6200) (Found: C, 76·7; H, 10·35. Calc. for $C_{26}H_{42}O_3$: C, 77·6; H, 10·5%). Jacobs and Brownfield [6] record for this compound m. p. 164—165°.

Hydrogenation (5% palladised charcoal) of the above unsaturated ester in methanol gave a virtually quantitative yield of the keto-ester (V) as needles (from dilute ethanol), m. p. 80° (Found: C, 77·55; H, 11·0. Calc. for $C_{27}H_{46}O_3$: C, 77·5; H, 11·1%). Jacobs and Brownfield [6] give m. p. 71·2—72·6° for this compound.

The Hydroxy-lactone (VI; R = H).—The seco-acid (IV; R = H) (2 g.), dissolved in ethyl acetate (10 c.c.) and ethanol (14 c.c.), was reduced at 0° by the gradual addition of sodium borohydride (0·6 g.) during 30 min. After 2 hr. the excess of reagent was destroyed with 2N-hydrochloric acid (40 c.c.), the solution was extracted with ether, and the ether phase was washed with aqueous sodium carbonate and with water, and dried and evaporated. The residual *acetoxy-lactone* (VI; R = Ac) separated from alcohol as crystals (1·1 g.) m. p. 148—149° (Found: C, 75·45; H, 10·3. $C_{28}H_{46}O_4$ requires C, 75·3; H, 10·4%). Some starting material (0·14 g.) was recovered from the sodium carbonate phase by acidification.

The above lactone (2·1 g.), ethanol (10 c.c.) and 2N-aqueous potassium hydroxide (20 c.c.) were refluxed together for 15 min. The cooled and diluted mixture was ether-extracted, after which acidification and isolation with chloroform gave the *hydroxy-lactone* (VI; R = H) as crystals (1·5 g.) (from ethanol), m. p. 160—161° (Found: C, 77·25; H, 10·8. $C_{26}H_{44}O_3$ requires C, 77·2; H, 11·0%).

The Unsaturated Keto-acid (VIII; R = H).—The above hydroxylactone (0·3 g.) in pyridine (2 c.c.) was added to chromium trioxide (0·3 g.) in pyridine (3 c.c.). After 48 hr. at room temperature the solution was poured into water (100 c.c.). Ether extraction, and evaporation of the washed and dried extract provided material which on crystallisation from alcohol yielded the *keto-lactone* (VII) (120 mg.), m. p. 186—187° (Found: C, 77·4; H, 10·35. $C_{26}H_{42}O_3$ requires C, 77·6; H, 10·45%).

When this material (0·29 g.) and 10% aqueous potassium hydroxide (50 c.c.) were refluxed together for 30 min., and the acidic material isolated in the usual way and crystallised from light petroleum (b. p. 60—80°), there was obtained the *keto-acid* (VIII; R = H) (0·21 g.) m. p. 122°, $\lambda_{max.}$ 230 mμ (ε 13,000) (Found: C, 77·6; H, 10·25. $C_{26}H_{42}O_3$ requires C, 77·6; H, 10·4%).

6-*Oxa-cholesta*-2,4-*dien*-7-*one* (XI).—Crude crystalline seco-acid (VI; R = H) (9·45 g.; m. p. 153°) was heated under reflux with acetic anhydride (250 c.c.) containing freshly fused sodium acetate (150 mg.) for 16 hr. After the acetic anhydride had been removed under reduced pressure, the residue was treated with a little ethanol, and then ether (250 c.c.), and the solution was washed with water, dried, and evaporated. Crystallisation from methanol gave the enol lactone (6·4 g.) m. p. 113—114°, $[\alpha]_D^{28}$ +72°, $\lambda_{max.}$ 274 mμ (ε 7700), $\nu_{max.}$ 1760 (δ-lactone), 1656 and 1595 cm.$^{-1}$ (conjugated double bonds) (Found: C, 81·4; H, 10·25. $C_{26}H_{40}O_2$ requires C, 81·3; H, 10·4%).

Chromatography of the mother-liquor material on silica gel (50 g.) and elution with light petroleum (b. p. 40—60°) containing 40% v/v benzene gave more enol lactone (272 mg.); total yield, 85%.

Alder–Rickert Reaction on the Enol Lactone (XI).—The enol lactone (7·13 g.) and methyl acetylenedicarboxylate (3·35 g.) were heated together under nitrogen, the time-temperature relation being as follows: 20 min. (80°); 40 min. (104°); 80 min. (128°); 100 min. (140°); 140 min. (160°). The mixture was then allowed to cool and unchanged acetylenic ester was removed by evaporation with acetone, finally *in vacuo*. Crystallisation of the residue from light petroleum (b. p. 40—60°) gave the *adduct* (XII) (5·0 g.), m. p. 155·5° (Found: C, 73·25; H, 8·8. $C_{32}H_{46}O_6$ requires C, 73·0; H, 8·75%). It showed no specific absorption above 225 mμ. Chromatography of the mother-liquor material on Florisil (50 g.; deactivated with 10% water) and elution with benzene gave an oil (3·94 g.) which crystallised from methanol at −10° giving the *aryl ester* [XIII; R = $C_6H_3(CO_2Me)_2$] (3·07 g.), m. p. 82° (Found: C, 72·8; H, 8·6%).

For isomerisation, the adduct (XII) (8·72 g.) was heated under reflux in decalin (105 c.c.)

for 2 hr. Removal of the decalin, and crystallisation of the residue from methanol gave the aryl ester (8·452 g.), m. p. 82°. The overall yield of this material from the enol lactone (XI) was 81%.

9β-*Isopropenyl-des*-AB-*cholestan*-8α-*carboxylic Acid* (XIII; R = H).—The above aryl ester (13·7 g.) and a solution of potassium hydroxide (78 g.) in water (120 c.c.) and ethanol (300 c.c.) were kept together under reflux for 2½ hr., after which some ethanol (200 c.c.) was removed under reduced pressure. The solution was diluted with water and extracted with ether, the ether being re-extracted with water. The combined aqueous phases were acidified and extracted thrice with benzene; the benzene was washed with water, dried, and evaporated. Evaporation gave a crystalline residue (8·51 g.; 97%) of material pure enough for the next step. Crystallisation from aqueous ethanol gave the pure *acid* (XIII; R = H), m. p. 91·5°, $[\alpha]_D^{18}$ +35° (Found: C, 79·05; H, 11·25. $C_{22}H_{38}O_2$ requires C, 79·0; H, 11·4%).

9β-*Acetyl-des*-AB-*cholestan*-8α-*carboxylic Acid* (XIV; R = H).—Ozonised oxygen (4·5%; flow rate 4·6 g. O_3/hr.) was passed through a solution of the acid (XIII; R = H) (6·478 g.) in methylene chloride (320 c.c.) at −20° for ½ hr. The solution was evaporated to dryness under reduced pressure at 16°; the residue was dissolved in glacial acetic acid (100 c.c.), and zinc dust (8 g.) was added with cooling. When the mixture had been shaken for 20 min., peroxides were found absent, and the zinc was removed and washed with more acetic acid. Dilution with an equal volume of water gave the required acid (5·771 g.; 89%), m. p. 140·5°; pure material separated from light petroleum (b. p. 40—60°) and had m. p. 145° (lit.,[9] m. p. 145—145·5°) (Found: C, 74·75; H, 10·55. Calc. for $C_{21}H_{36}O_3$: C, 74·95; H, 10·7%).

Methyl 9β-*Hydroxy-des*-AB-*cholestan*-8α-*carboxylate* (XV; R = H).—The keto-acid (XIV; R = H) (9·5 g.) was converted into the crude methyl ester by reaction with diazomethane. The ester, in methylene chloride (50 c.c.) was stirred with anhydrous disodium hydrogen phosphate (40 g.) whilst a solution of trifluoroperacetic acid, obtained by the addition of 85% hydrogen peroxide (2·5 c.c.) to trifluoroacetic anhydride (12 g.) in methylene chloride (25 c.c.) with thorough cooling and shaking, was added slowly. After the exothermic reaction was over, the mixture was heated under reflux for 30 min., then cooled and filtered, the sodium phosphate being well washed with methylene chloride. The filtrate was washed with 10% aqueous potassium carbonate and then with water, dried, and evaporated.

A solution of the residue in ethanol (25 c.c.) and glacial acetic acid (5 c.c.), containing Girard's reagent T (3·5 g.) was heated under reflux for 1 hr., then cooled and added to ether (1 l.) and light petroleum (b. p. 40—60°; 1 l.), and the solution washed thrice with water (700, 500 and 250 c.c.). When the combined aqueous phases were heated to 100° for 30 min. with concentrated hydrochloric acid (25 c.c.) and then cooled and the product isolated with ether, there was recovered crude crystalline methyl ester (XIV; R = Me) (2·0 g.) suitable for re-oxidation without further purification. Evaporation of the ether-petroleum phase from the Girard separation gave the acetoxy-ester (XV; R = Ac) (7·5 g.) as a gum.

The acetoxy-ester (24·35 g.) was kept under reflux for 2 hr. in absolute methanol (800 c.c.) containing sodium methoxide (from 3 g. sodium), moisture being excluded. Glacial acetic acid (9 c.c.) was then added, and the solution was concentrated to 100 c.c., then diluted with ether (600 c.c.), and the ether washed with water. Concentration of the ether to a small volume gave the hydroxy-ester (XV; R = H) (18·5 g.), m. p. 121°, pure enough for use in the next steps. Taking into account the recovered starting material, the yield of the ester (XV; R = H) from the acid (XIV; R = H) was 80%. Recrystallisation from ether gave pure *methyl* 9β-*hydroxy-des*-AB-*cholestan*-8α-*carboxylate*, m. p. 123·5° (Found: C, 73·75; H, 11·15. $C_{20}H_{36}O_3$ requires C, 74·1; H, 11·1%), $\nu_{max.}$ 1730 cm.$^{-1}$ (ester).

Hydrolysis with aqueous alcoholic potassium hydroxide provided the corresponding *acid*, which separated from light petroleum (b. p. 40—60°) and had m. p. 133—135°, $[\alpha]_D^{19}$ +32·4° (Found: C, 73·7; H, 10·8. $C_{19}H_{34}O_3$ requires C, 73·5; H, 11·0%).

Pyrolysis of the Benzoate (XV; R = CO·Ph).—The methyl ester (XV; R = H) (154 mg.) was benzoylated in the usual manner with pyridine (1 c.c.) and benzoyl chloride (0·14 c.c.) during 16 hr. at room temperature, which gave an oil (200 mg.), $\nu_{max.}$ 1740 (normal ester) and 1720 cm.$^{-1}$ (conjugated ester). This benzoate (600 mg.) was pyrolysed in glass at 365° for 10 min.; benzoic acid distilled over. The distillate and the residue were combined and dissolved in ether, and the ether was washed with sodium hydrogen carbonate and with water, and then dried and evaporated. The residual gum showed absorption in the ultraviolet at 222 mμ, and in the infrared at 1740 (normal ester) and 1720 cm.$^{-1}$ (conjugated ester), but the

relevant intensities indicated that the content of the conjugated ester did not exceed 30%. Hydrolysis with methanolic sodium hydroxide gave acidic material from which an impure crystalline acid, m. p. 74—78° was obtained by crystallisation from methanol at low temperatures. It showed no specific absorption near 220 mμ, and was an impure sample of the unconjugated acid (XIX; R = H), m. p. 78—81° (see below).

*9α-Hydroxy-des-*AB*-cholestan-8α-carboxylic Acid.*—To the hydroxy-ester (XV; R = H) (18·59 g.) in pyridine (50 c.c.), benzenesulphonyl chloride (25 c.c.) was added with cooling, and after the mixture had been kept for 18 hr., it was cooled whilst water (100 c.c.) was added. The product was extracted with ether, and the ether was washed successively with 2N-sulphuric acid, aqueous sodium carbonate, and water, and then dried and evaporated. The residual benzenesulphonate (25·78 g.) formed an oil. It was kept at 118° for 15½ hr. with dimethylformamide (1 l.) containing water (20 c.c.). The solvent was then removed under reduced pressure, giving a residue which was extracted with ether, and the ethereal solution was washed as above with dilute sulphuric acid, aqueous sodium carbonate, and water, and dried and evaporated. The residual oil (18·6 g.) was heated under reflux in absolute methanol (800 c.c.) containing sodium methoxide (from 2·2 g. sodium) for 15 min., then glacial acetic acid (6 c.c.) was added, and most of the methanol was removed. The product, after extraction with ether, which was washed, dried, and evaporated, formed an oil (17·5 g.) $\nu_{max.}$ 1740 and 1710 cm.$^{-1}$ (esters). It was dissolved in light petroleum (b. p. 40—60°) and the solution chromatographed on Florisil (600 g., deactivated by addition of 10% water). Elution was conducted with light petroleum (b. p. 40—60°) containing 5% and 10% of benzene, with benzene alone, and finally with ether. Rechromatography of the fraction eluted by light petroleum —10% benzene was necessary. In this way there were obtained three fractions; the most readily eluted or "petroleum fraction" formed an oil (5·34 g.); the next, or "benzene fraction" formed an oil (10·57 g.); the least readily eluted, or "ether fraction" formed a crystalline solid. It was identified as the hydroxy-ester (XV; R = H) which had escaped benzenesulphonylation, presumably; it was pure enough to be re-cycled.

Hydrolysis of the "petroleum fraction" with aqueous alcoholic potassium hydroxide gave *des-*AB*-cholest-9-en-8α-carboxylic acid* (XIX; R = H), as crystals (from methanol) m. p. 78—81° (Found: C, 78·2; H, 11·15. $C_{19}H_{32}O_2$ requires C, 78·0; H, 11·0%).

Similar hydrolysis of the "benzene fraction" (10·57 g.) gave *9α-hydroxy-des-*AB*-cholestan-8α-carboxylic acid* (8·59 g.), which separated from light petroleum (b. p. 40—60°) as crystals, m. p. 107—108°, $[\alpha]_D^{19}$ +12·7° (Found: C, 73·5; H, 11·0. $C_{19}H_{34}O_3$ requires C, 73·5; H, 11·0%).

*Des-*AB*-cholest-8(9)-en-8-carboxylic Acid* (XVII; R = H).—The above 9α-hydroxy acid (7·52 g.) was converted into the methyl ester by reaction with diazomethane in the usual way. The ester (7·71 g.) was treated with benzenesulphonyl chloride (10 c.c.) in pyridine (20 c.c.) at room temperature for 64 hr. which afforded the *benzenesulphonate* (XVI; R = SO_2·Ph) (9·14 g.), m. p. 95° (Found: C, 67·0; H, 8·6; S, 7·15. $C_{26}H_{40}O_5S$ requires C, 67·2; H, 8·6; S, 6·9%).

To a solution of this material (8·5 g.) in ethanol (116 c.c.), 5% aqueous potassium hydroxide (52 c.c.) was added, and the mixture was heated under reflux for 1 hr., and then concentrated to half volume under reduced pressure. The product was isolated with ether, and separated in the usual way into acidic and neutral fractions. Crystallisation of the acidic fraction from methanol gave the *acid* (XVII; R = H) (2·7 g.), m. p. 120—121°, $[\alpha]_D^{17}$ —17·3°, $\lambda_{max.}$ 224 mμ (ε 9100) (Found: C, 77·8; H, 11·0. $C_{19}H_{32}O_2$ requires C, 78·0; H, 11·0%). The mother-liquor contained a mixture (1·1 g.) of this acid and its unconjugated isomer; it showed $\lambda_{max.}$ 222 mμ (ε 4500).

The neutral fraction formed an oil (1·5 g.) which showed $\lambda_{max.}$ 221 mμ (ε 7500). The oily, but essentially pure methyl ester (XVII; R = Me), obtained by brief reaction of the acid with diazomethane had $\lambda_{max.}$ 219 mμ (ε 9100). The crude ester thus contained *ca.* 80% of the conjugated isomer.

The Allylic Alcohol (XVIII).—To a solution of lithium aluminium hydride (2·2 g.) in ether was added absolute ethanol (0·266 g.) in ether (total volume of solution, 100 c.c.). A portion (1 c.c.) of this reagent was added to a stirred solution of the conjugated ester (XVII; R = Me) (0·53 g.) in ether (5 c.c.). After 1 hr. a further portion (1 c.c.) of the reagent was added, and this process was continued until a total of 4 c.c. had been used. After the cautious addition of water the aluminium salts were filtered off, washed with water and ether, and the filtrate was extracted with more ether. Evaporation of the dried ethereal solution gave an oil (0·52 g.).

Reaction with *p*-nitrobenzoyl chloride (1·1 g.) in pyridine (7 c.c.) gave the p-*nitrobenzoate* of the alcohol (XVIII) which separated from ethanol as crystals (0·48 g.) m. p. 103° (Found: C, 73·05; H, 8·5; N, 3·25. $C_{26}H_{37}NO_4$ requires C, 73·0; H, 8·8; N, 3·3%).

8-*Formyl-des*-AB-*cholest*-8(9)-*ene*.—The above *p*-nitrobenzoate was hydrolysed in the usual manner to the oily alcohol. A solution of the alcohol (0·45 g.) in ether (85 c.c.) was shaken for 1½ hr. with manganese dioxide (6·2 g.). Filtration and evaporation gave a colourless oil (0·351 g.), $\lambda_{max.}$ (in EtOH) 235 mμ (ε 11,400), $\nu_{max.}$ 2675, 1680 and 1625 cm.$^{-1}$. Reaction of a portion with semicarbazide acetate gave the *semicarbazone* as crystals (from ethanol), m. p. 194—195°, $[\alpha]_D^{18}$ −35·6° (in AcOH), $\lambda_{max.}$ (in EtOH) 268 mμ (ε 26,400) (Found: C, 72·25; H, 10·6; N, 12·75. $C_{20}H_{35}N_3O$ requires C, 72·1; H, 10·5; N, 12·6%). Attempted regeneration of the aldehyde from its semicarbazone by the pyruvic acid method caused partial isomerisation to unconjugated aldehyde, as shown by the ultraviolet and infrared data.

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