478. 4-*Substituted Steroids Derived by Rearrangement and Reduction of Cholestenone Enol Acetate.*

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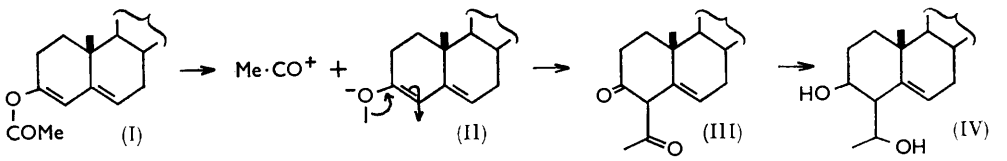
One of the diols produced by the simultaneous action of lithium aluminium hydride and aluminium chloride on cholestenone enol acetate is shown to be 4α-1′-hydroxyethylcholest-5-en-3β-ol. Another is probably 4β-1′-hydroxyethylcholest-5-en-3α-ol.

The simultaneous action of lithium aluminium hydride and aluminium chloride on the enol acetate (I) of cholest-4-en-3-one was previously reported [1] to yield 36% of material soluble in light petroleum [shown to be a mixture of cholest-4-ene (16%) and cholestenone (20%)] and 49% of material insoluble in light petroleum which, by crystallisation, yielded a

[1] Brown, *J.*, 1952, 2756.

molecular compound of two diols, designated (A) and (B). It was tentatively suggested that these diols were cholest-5-ene-3α,4β- and -3β,4α-diol, which at that time were unknown. This suggestion is now known to be incorrect, since Fieser and Stevenson [2] have prepared and proved the structure of cholest-5-ene-3β,4α-diol which differs from both the diols (A) and (B).

Since the reduction is carried out in the presence of aluminium chloride, the isomeric diols might be expected to arise by rearrangement of the enol acetate and subsequent reduction as shown in the annexed scheme. The rearrangement envisaged is formally analogous to the Fries rearrangement. The acetylium ion attacks the 4-position of the



enolate ion (II), evidence for the existence of which during the reduction of cholestenone enol acetate with lithium aluminium hydride has been advanced by Dauben and Eastham.[3] The resulting diketone (III) is reduced by lithium aluminium hydride to give the 4-1′-hydroxyethylcholest-5-en-3-ol structure (IV). The work described here substantiates structure (IV) for the diols (A) and (B).

This structure requires a molecular formula of $C_{29}H_{50}O_2$, whereas in the earlier paper [1] the analyses were calculated on the formula $C_{27}H_{46}O_2$. The differences in the carbon and hydrogen percentages calculated for the diols and their simple derivatives on the C_{27} and C_{29} formulæ are almost within the experimental error of analysis. However, the results now recorded show better agreement with the C_{29} formula and analyses of more complex derivatives [*e.g.*, the cyclic sulphite ester and two bromo-compounds of diol (B) and the toluene-*p*-sulphonate ester of diol (A)] allow a definite distinction and permit only the C_{29} formula.

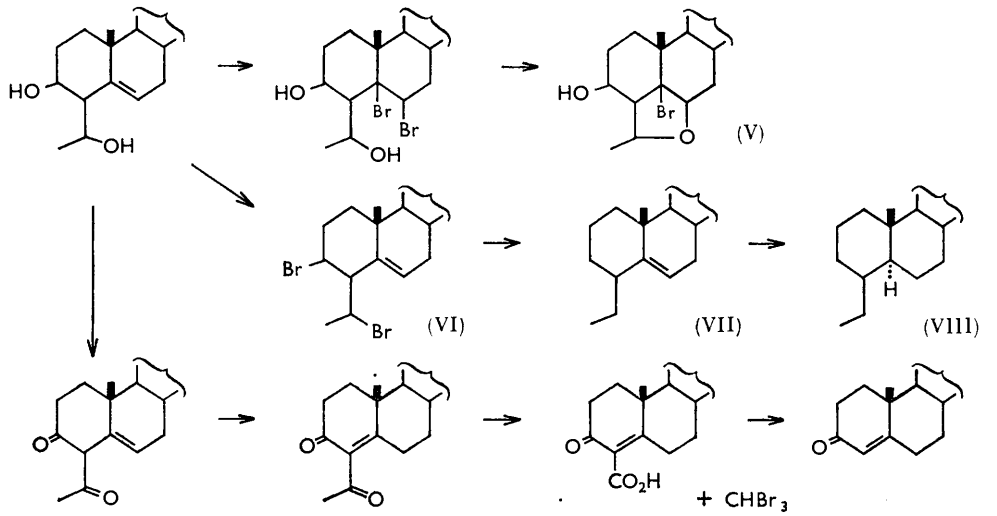
The presence [1] of a double bond in diol (B) has been confirmed by the observation that this diol reacts with bromine in chloroform. However, the only pure product isolated was a bromo-ether (V), formally derived by loss of hydrogen bromide from the diol dibromide. The difficulty experienced in hydrogenating this double bond [1] is explicable in terms of the proposed structure where a large hindering group is at position 4.

The suspected presence of a CH_3·CH·OH group in the diols led to the use of hypohalite as an oxidising agent. Both diols with potassium hypobromite in aqueous dioxan yielded cholest-4-en-3-one and the presence of bromoform in the products was demonstrated by a sensitive colour test.[4] The production of cholestenone indicates that the CH_3·CH·OH group is adjacent to a 3-hydroxyl group since oxidation and loss of bromoform must lead to a carboxylic acid which can readily lose carbon dioxide (see annexed scheme).[5] Further, the double bond must be in either the 4,5- or the 5,6-position; the latter is favoured by the negative rotations of the diols and their derivatives. Attachment of the CH_3·CH·OH group to the 2-position would explain the formation of cholestenone: however, degradation of diol (B) to a hydrocarbon and synthesis of the latter have shown that the attachment is at the 4-position in this diol.

Treatment of diol (B) with phosphorus tribromide gave the dibromo-compound (VI), which with lithium and liquid ammonia gave an ethylcholestene (VII) which melted over a range. A similar reduction of cholesteryl bromide gave material which melted over a

[2] Fieser and Stevenson, *J. Amer. Chem. Soc.*, 1954, **76**, 1728.
[3] Dauben and Eastham, *J. Amer. Chem. Soc.*, 1953, **75**, 1718.
[4] Clarke, " A Handbook of Organic Analysis," Edward Arnold and Co., London, 4th edn., 1926, p. 67.
[5] Cf. Simonsen and Ross, " The Terpenes," Cambridge Univ. Press, 1957, Vol. V, p. 451.

range below the m. p. of cholest-5-ene and had a more positive specific rotation than cholest-5-ene; repeated crystallisation of this material gave pure cholest-5-ene. Hydrogenation of the crude ethylcholestene over platinum in ether–acetic acid gave a hydrocarbon (VIII), $[\alpha]_D$ +6°, which melted sharply at 89—90°. It seems, from these observations, that reduction of an unsaturated halogeno-steroid by lithium and liquid ammonia may give rise to some of the saturated hydrocarbon along with the unsaturated hydrocarbon. The



saturated hydrocarbon (VIII) from diol (B), which differed from cholestane itself, was expected to be either 4α- or 4β-ethylcholestane, since reduction of a cholest-5-ene in acid solution usually leads to a *trans*-A/B ring junction.

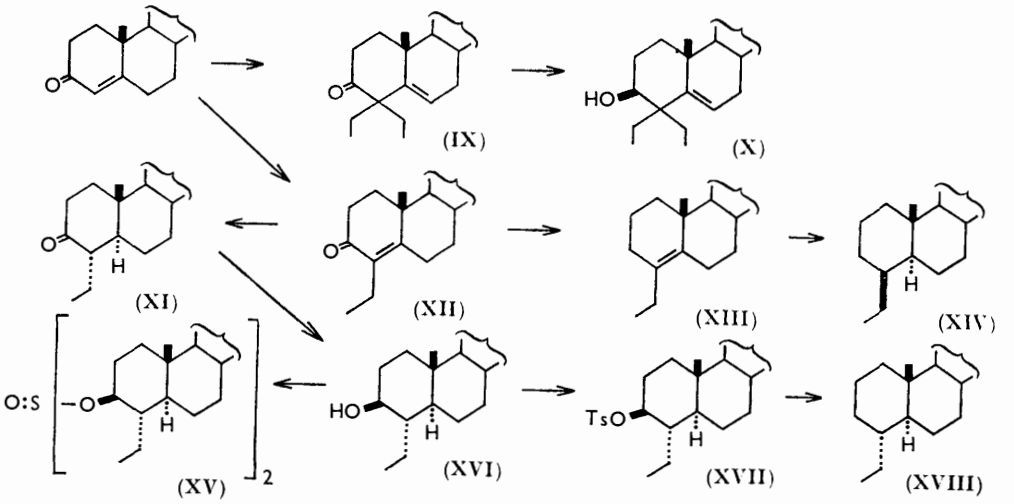
The two 4-ethylcholestanes have been synthesised in order to establish the structure and stereochemistry of the saturated hydrocarbon derived from diol (B). Despite statements to the contrary,[6-9] Atwater [10] has reported that steroidal 4-en-3-ones can be successfully monomethylated at the 4-position. By following Atwater's procedure, but using a higher dilution and a longer reaction time, we have ethylated cholest-4-en-3-one directly, using ethyl iodide and potassium in t-butyl alcohol, and we isolated 4-ethylcholest-4-en-3-one (XII) (54%), 4,4-diethylcholest-5-en-3-one (IX) (10%), and unchanged cholestenone (33%). The diethyl-ketone (IX) has zero rotation, but lithium aluminium hydride reduces it to 4,4-diethylcholest-5-en-3β-ol (X), $[\alpha]_D$ −57°.

Reduction of 4-ethylcholestenone as described by Djerassi *et al.*[9] gave 4α-ethylcholestan-3-one (XI), known to have this configuration by analogy with 4α-methylcholestan-3-one.[6,7] Further reduction of the ethylcholestanone gave 4α-ethylcholestan-3β-ol (XVI),[9] which even with hot thionyl chloride gave a sulphite ester (XV). However, reduction of the toluene-*p*-sulphonate (XVII) with lithium aluminium hydride gave 4α-ethylcholestane (XVIII), m. p. 89—90°, $[\alpha]_D$ +4·5°. The hydrocarbon obtained from diol (B) caused no depression of m. p. when admixed with 4α-ethylcholestane, and the two have almost identical specific rotations. This result establishes that the CH_3·CH·OH group in diol (B) is attached at the 4-position and has the α-configuration.

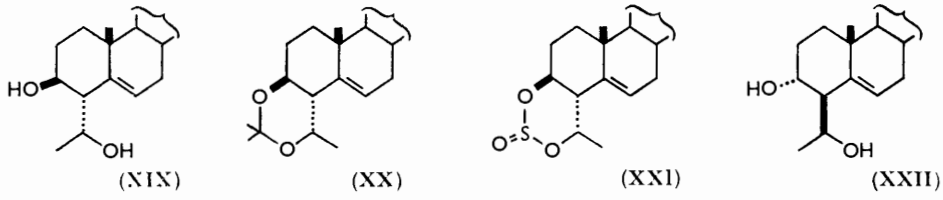
Reduction of 4-ethylcholest-4-en-3-one (XII) with lithium aluminium hydride and aluminium chloride [11] gave 4-ethylcholest-4-ene (XIII), which, on catalytic hydrogenation

[6] Meakins and Rodig, *J.*, 1956, 4679.
[7] Beton, Halsall, Jones, and Phillips, *J.*, 1957, 753.
[8] Mazur and Sondheimer, *J. Amer. Chem. Soc.*, 1957 **79**, 2906.
[9] Djerassi, Cais, and Mitscher, *J. Amer. Chem. Soc.*, 1958, **80**, 247.
[10] Atwater, *J. Amer. Chem. Soc.*, 1957, **79**, 5315.
[11] Broome and Brown, *Chem. and Ind.*, 1956, 1307.

in ether–acetic acid, afforded 4β-ethylcholestane (XIV), m. p. 75—77°, $[\alpha]_D$ +31°. This hydrocarbon is assigned this configuration since acidic conditions favour the formation of a cholestane system [12] and *cis*-addition of hydrogen then leads to a 4β-derivative.[13]



Consideration of the infrared spectra of the diols and their acetates in carbon disulphide has enabled the stereochemistry of the 3-hydroxyl groups to be deduced. The absorptions



recorded in Table 1 are due to C–O stretching vibrations and the work of Jones *et al.*,[14] Cole,[15] and Page [16] leads to the assignments of stereochemistry shown. Thus diol (B) is 4α-1′-hydroxyethylcholest-5-en-3β-ol (XIX). Further, the results recorded in Table 2

TABLE 1. *Infrared spectra of the diols and their acetates in* CS_2 *solution.*

Compound	Frequency (cm.$^{-1}$)	Confign. of 3-OH or 3-AcO-group	Compound	Frequency (cm.$^{-1}$)	Confign. of 3-OH or 3-AcO-group
Diol (A)	1006	axial, 3α	Diol (B) diacetate	1028	equat., 3β
Diol (B).....	1049	equat., 3β	Diol (A) diacetate	1242, 1211	axial, 3α
Diol (A) diacetate	1016	axial, 3α	Diol (B) diacetate	1242 only	equat., 3β

TABLE 2. OH *Stretching frequencies of the diols in* CS_2 *solution.*

		Absorption bands (cm.$^{-1}$)					Absorption bands (cm.$^{-1}$)		
Diol	Concn. (mg./ml.)	Free OH	Intramol. H-bond	Intermol. H-bond	Diol	Concn. (mg./ml.)	Free OH	Intramol. H-bond	Intermol. H-bond
A	9	3610m sh	—	—	B	9	3620w sh	3520m sh	3300m br
A	20	3610m sh	—	3310w br	B	20	3620w sh	3520m sh	3300s br
B	4	3620w sh	3520m sh	3300w br					

[12] Windaus, *Ber.*, 1919, **52**, 170.
[13] Mazur and Sondheimer, *J. Amer. Chem. Soc.*, 1958, **80**, 5220.
[14] Jones, Humphries, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1951, **73**, 3215.
[15] Cole, *J.*, 1952, 4969.
[16] Page, *J.*, 1955, 2017.

show that diol (B) is intramolecularly hydrogen-bonded, a conclusion confirmed by the consideration of a model of diol (B) and by the preparation of an isopropylidene compound (XX) and a cyclic sulphite ester (XXI).

The infrared evidence leads to the assignment of a 3α-configuration to one of the hydroxyl groups in diol (A) and, on the assumption that the CH_3·CH·OH group is attached at the 4-position as in diol (B), consideration of models shows that this group must be β-orientated if the compound is not to show intramolecular hydrogen bonding. In agreement, an isopropylidene compound was not obtained from the diol (A) (XXII) under the conditions which yielded one from diol (B).

Experimental

Rotations were determined for chloroform solutions at room temperature. Alumina was Spence's grade H or O, deactivated, when stated, with acetic acid. Light petroleum refers to the fraction of b. p. 40—60°.

Degradation of diols

Diol (A) (XXII).—This, 4β-1′-*hydroxyethylcholest-5-en-3α-ol*, has m. p. 179·5—180° (Found: C, 81·0; H, 11·5. $C_{29}H_{50}O_2$ requires C, 80·9; H, 11·6%). It gives a *diacetate*, m. p. 159—160° (Found: C, 77·1; H, 10·5. $C_{33}H_{54}O_4$ requires C, 77·0; H, 10·5%), and *ditoluene-p-sulphonate* (from ethanol–methanol), needles, m. p. 141·5—142°, $[\alpha]_D$ −25° (*c* 1·68) (Found: C, 70·3; H, 8·4; S, 8·7. $C_{43}H_{62}O_6S_2$ requires C, 70·0; H, 8·4; S, 8·7%), decomposing in 5 min. at 140°.

Diol (B) (XIX).—This, 4α-1′-*hydroxyethylcholest-5-en-3β-ol*, has m. p. 179—180° (Found: C, 81·1, 80·6; H, 11·5, 11·7)%, and gives a *diacetate*, m. p. 114—115·5° (Found: C, 76·9; H, 10·4%).

The two diols give a *molecular compound*, m. p. 196—197° (Found: C, 80·75, 81·0; H, 11·55, 11·4%). Both diols and the molecular compound gave a yellow colour with tetranitromethane in chloroform.

Bromo-ether (V) *from Diol* (B).—Diol (B) (249 mg.) in chloroform was treated dropwise with bromine in chloroform until a slight permanent colour was observed. After 2 hr. at room temperature the solvent was removed *in vacuo* and the residue crystallised several times from acetone. The *bromo-ether* (91 mg.) was obtained as colourless needles, m. p. 167—168·5° (Found: C, 68·35; H, 9·85. $C_{29}H_{49}BrO_2$ requires C, 68·35; H, 9·65%), $\nu_{max.}$ (in CS_2) 3400 (OH) and 1098 $cm.^{-1}$ (cyclic ether). The mother-liquors yielded crystals, m. p. 171—174°, whose analysis indicated that they contained both the bromo-ether and the diol dibromide.

Hypobromite Oxidation of the Diols.—To a solution of the diol (A or B) (368 mg.) in dioxan (35 ml.) was added a solution of potassium hypobromite prepared from bromine (1·90 g.), potassium hydroxide (1·06 g.), and water (25 ml.). The resulting suspension was stirred for 3 days. Excess of 2N-sulphuric acid was added and the products were removed in ether. The extract was washed with water, sodium thiosulphate solution, sodium carbonate solution, and water to neutrality. A portion (1 ml.) of this extract was boiled with a little pyridine and an equal volume of sodium hydroxide solution. The pyridine layer became deep red, indicating the presence of bromoform.[4] Control experiments showed that the other reagents present did not interfere with this test.

Evaporation of the extract gave a residue which was dissolved in ethanol and boiled with sodium iodide for 1·5 hr. Addition of water, extraction with ether, and evaporation of the washed extract gave an oil which was extracted with light petroleum. The residue, on recrystallisation, gave unchanged diol (18 mg.), m. p. and mixed m. p. 179—180°. The light petroleum extract was chromatographed on alumina (grade O), yielding, on elution with benzene, a yellow oil (230 mg.). Part of the oil was sublimed at 180°/0·5 mm.; the crystalline sublimate separated from acetone–methanol as needles, m. p. 79—80°, unchanged on admixture with cholest-4-en-3-one. The infrared spectrum in Nujol was identical with that of authentic cholestenone. The oil gave a 2,4-dinitrophenylhydrazone which separated from ethyl acetate–ethanol as red prisms, m. p. 229—231°; the mixed m. p. with cholestenone dinitrophenylhydrazone was 231—233°; the ultraviolet and infrared spectra were identical with those of cholestenone dinitrophenylhydrazone.

Action of Phosphorus Tribromide on Diol (B).—Phosphorus tribromide (1·97 g.) was added with shaking to a solution of diol (B) (1·01 g.) in chloroform (50 ml.). After 4 days. excess of

water was added and the product isolated by using chloroform. The crude product was washed with acetone to remove a gummy solid (85 mg.) and crystallised several times from ether–methanol. The *dibromo-compound* (VI) (280 mg.) was obtained as colourless needles, m. p. 96·5—98°, $[\alpha]_D$ +17° (*c* 1·08) (Found: C, 62·5; H, 8·5; Br, 28·7. $C_{29}H_{48}Br_2$ requires C, 62·6; H, 8·6; Br, 28·8%).

4α-*Ethylcholest-5-ene* (VII).—The above dibromo-compound (291 mg.) in ether (60 ml.) was added to lithium (480 mg.) in liquid ammonia (150 ml.) at −35°. After 2 hr. with stirring, ammonium chloride was added and the ammonia was allowed to evaporate. Addition of water and extraction with ether gave a colourless solid which was filtered through alumina (grade O) in light petroleum and crystallised from ethyl acetate–methanol, to yield a solid (153 mg.), m. p. 90—97°, $[\alpha]_D$ −37·5° (*c* 1·18). Three crystallisations from ethyl acetate gave 4α-*ethylcholest-5-ene* as needles, m. p. 103—107° (Found: C, 87·5; H, 12·3. $C_{29}H_{50}$ requires C, 87·45; H, 12·55%). The compound gave a deep yellow colour with tetranitromethane in chloroform.

4α-*Ethylcholestane* (VIII).—The crude 4α-ethylcholest-5-ene (60 mg.) in ether (5 ml.) and acetic acid (10 ml.) was hydrogenated at 19°/765 mm. over platinum oxide (50 mg.). Hydrogen uptake was complete after 2·5 hr. The product (58 mg.) gave no colour with tetranitromethane in chloroform. Filtration of a light petroleum solution through alumina (grade O; 5% deactivated) and recrystallisation from ethyl acetate–methanol gave 4α-ethylcholestane as flat needles, m. p. 89—90°, $[\alpha]_D$ +6° (*c* 0·77) (Found: C, 87·0; H, 13·05. Calc. for $C_{29}H_{52}$: C, 87·0; H, 13·0%). The m. p. was unchanged on admixture of the compound with synthetic 4α-ethylcholestane (see below).

Cholest-5-ene (by P. R. Brooks).—Cholesteryl bromide (720 mg.) in ether (280 ml.) was reduced, as above, with lithium (1·14 g.) in liquid ammonia (560 ml.). The product (593 mg.), m. p. 78·5—80·5°, $[\alpha]_D$ −35° (*c* 1·12), was thrice recrystallised from ether–methanol, to give cholest-5-ene (195 mg.), m. p. and mixed m. p. 91·5—92°, $[\alpha]_D$ −51° (*c* 1·07) (Found: C, 87·3; H, 12·05. Calc. for $C_{27}H_{46}$: C, 87·55; H, 12·45%).

Cyclic Sulphite Ester (XXI) *of Diol* (B).—Diol (B) (1·00 g.) was treated with thionyl chloride (2·00 g.). An immediate reaction occurred and the steroid dissolved. After 24 hr. at room temperature, excess of the reagent was removed under reduced pressure and the residue was filtered through alumina (grade O; 10% deactivated) in light petroleum. The resulting oil was chromatographed on alumina (grade O; 30 g.). Elution with light petroleum yielded an intractable yellow gum (166 mg.) which was not further investigated. Elution with light petroleum–benzene (1 : 1 v/v) gave a solid (633 mg.) which, on crystallisation from ether–methanol and then from acetone–methanol, gave the cyclic *sulphite* (XXI) as colourless prisms, m. p. 122·5—123·5°, $[\alpha]_D$ +41° (*c* 1·23) (Found: C, 73·1, 73·1; H, 10·3, 9·9; S, 6·4. $C_{29}H_{48}O_3S$ requires C, 73·1; H, 10·1; S, 6·7%), $\nu_{max.}$ (in CS_2) 1185 cm.$^{-1}$ (sulphite).

Isopropylidene Derivative (XX) *of Diol* (B).—A suspension of diol (B) (220 mg.) in a 2% solution of hydrogen chloride in acetone (50 ml.) was shaken for 3 hr., to yield a clear solution, which was kept at room temperature for 2 days. Powdered calcium carbonate (4·1 g.) was added with shaking until the mixture was neutral. Filtration and evaporation *in vacuo* gave an oil which was put on alumina (grade O) and eluted with light petroleum–benzene (1 : 1 v/v), to yield the *isopropylidene derivative* (XX) (132 mg.) as a solid which separated from acetone–methanol as needles, m. p. 112—113·5°, $[\alpha]_D$ +28° (*c* 1·27) (Found: C, 82·0; H, 11·5. $C_{32}H_{54}O_2$ requires C, 81·7; H, 11·5%).

After 48 hr. under the conditions used for diol (B), diol (A) was recovered unchanged (m. p. and mixed m. p. and infrared comparison) in 80% yield after recrystallisation.

Syntheses

4-*Ethylcholest*-4-*en*-3-*one* (XII).—To a stirred solution of potassium (1·75 g.) and cholest-4-en-3-one (10·0 g.) in dry, refluxing t-butyl alcohol (180 ml.) was added during 7 hr. ethyl iodide (4·10 g.) in t-butyl alcohol (600 ml.). The cold mixture was treated with water (200 ml.) and evaporated at 80° *in vacuo*. The residue was dissolved in ether, potassium iodide was separated by filtration, ether was evaporated from the filtrate, and the residue (10·4 g.) was put on alumina (grade H; 10% deactivated; 1 kg.) in light petroleum. Elution (500-ml. fractions) was as follows: (i) Fractions 1—5 (light petroleum) gave a viscous yellow oil (1·30 g.) whose infrared spectrum showed it to be chiefly dialkylated ketone with some monoalkylated product. (ii) Fractions 6—13 (light petroleum) gave crystals (5·32 g.). (iii) Fractions 14—16 (light

petroleum–benzene, 99 : 1 v/v) gave crystals (0·34 g.). (iv) Fractions 17—19 (light petroleum–benzene, 95 : 5 v/v) gave crystals (0·14 g.). (The infrared spectra of fractions 6—19 showed them to be chiefly monoalkylated ketone.) (v) Fractions 20—21 (benzene) gave crystals (3·30 g.), m. p. 79·5—80·5°, unchanged on admixture with the starting material (infrared spectrum identical with that of cholestenone).

Fractions 6—19 were recrystallised from acetone–methanol (1 : 1 v/v), to give 4-ethylcholestenone (4·38 g.), m. p. 85·5—86·5°, $[\alpha]_D$ +92° (*c* 1·8), $\lambda_{max.}$ (in EtOH) 251 mμ (log ε 4·21), $\nu_{max.}$ (in CS_2) 1675 cm.$^{-1}$. Djerassi *et al.*[9] report m. p. 87—89°, $\lambda_{max.}$ (in EtOH) 251 mμ (log ε 4·07). The *enol acetate* separated from acetone–methanol as needles, m. p. 103—104·5°, $[\alpha]_D$ −100° (*c* 0·92), $\lambda_{max.}$ (in EtOH) 237 mμ (log ε 4·34) (Found: C, 81·8; H, 11·05. $C_{31}H_{50}O_2$ requires C, 81·9; H, 11·0%).

The residue after evaporation of the mother-liquor from the above crystallisation was combined with fractions 1—5, dissolved in light petroleum, and put on alumina (grade H; 10% deactivated; 300 g.). Elution with light petroleum (300 ml. fractions) was as follows: (i) Fractions 1—6 gave a viscous yellow oil (0·985 g.) which from acetone–methanol (1 : 1 v/v) gave 4,4-*diethylcholest*-5-*en*-3-*one* (IX) (0·68 g.) as needles, m. p. 94·5—95°, $[\alpha]_D$ 0° (*c* 1·12) (Found: C, 84·1; H, 11·85. $C_{31}H_{52}O$ requires C, 84·5; H, 11·8%), $\nu_{max.}$ (in CCl_4) 1708 cm.$^{-1}$ (unconjugated C=O). (ii) Fractions 7—13 gave 4-ethylcholestenone (1·00 g.; from acetone–methanol), m. p. 85·5—86·5°.

4,4-*Diethylcholest*-5-*en*-3β-*ol* (X).—4,4-Diethylcholestenone (117 mg.) was reduced in the usual way with lithium aluminium hydride (500 mg.) in ether. The product separated from acetone as prisms (67 mg.), m. p. 107—108°, $[\alpha]_D$ −57° (*c* 0·91) (Found: C, 83·95; H, 12·5. $C_{31}H_{54}O$ requires C, 84·2; H, 12·3%), $\nu_{max.}$ (in CS_2) 3546 and 1027 cm.$^{-1}$ (β-OH). Jouanneteau and Mentzer [17] record m. p. 126° and $[\alpha]_D$ −56° for this alcohol which they obtained by reduction of an oil said to be 4,4-diethylcholest-5-en-3-one.

4α-*Ethylcholestan*-3-*one* (XI).—4-Ethylcholest-4-en-3-one (1·10 g.) in ether (50 ml.) was added dropwise during 10 min. to a stirred solution of lithium (0·55 g.) in liquid ammonia (200 ml.). After 20 min. solid ammonium chloride was added until the blue colour of the solution was discharged, ammonia was allowed to evaporate, and water (100 ml.) was added. Extraction with ether and crystallisation from methanol or ethanol gave the saturated ketone (0·81 g.) as plates, m. p. 120·5—121°, $[\alpha]_D$ +33° (*c* 3·83), $\nu_{max.}$ (in $CHCl_3$) 1720 cm.$^{-1}$. Djerassi *et al.*[9] report m. p. 120—122°, $[\alpha]_D$ +38°, $\nu_{max.}$ (in $CHCl_3$) 1720 cm.$^{-1}$.

4α-*Ethylcholestan*-3β-*ol* (XVI).—Reduction of the above saturated ketone (806 mg.) with lithium aluminium hydride (300 mg.) in ether gave, after chromatography on alumina (grade H; 10% deactivated) and recrystallisation from methanol, the alcohol (558 mg.) as needles, m. p. 146—147°, $[\alpha]_D$ +28° (*c* 1·39), $\nu_{max.}$ (in CS_2) 1034 cm.$^{-1}$ (β-OH) (Found: C, 83·2; H, 12·4. Calc. for $C_{29}H_{52}O$: C, 83·4; H, 12·5%). Djerassi *et al.*[9] record m. p. 141—143°, $[\alpha]_D$ +24°.

Action of Thionyl Chloride on 4α-*Ethylcholestan*-3β-*ol*.—4α-Ethylcholestan-3β-ol (286 mg.) in ether (10 ml.) was treated at −10° with thionyl chloride (42 mg.) and pyridine (55 mg.). After 1 hr. the precipitated pyridine hydrochloride was separated by filtration and washed with ether. Evaporation of the filtrate gave a solid which was heated for 1 hr. with thionyl chloride (42 mg.) and then crystallised twice from ethyl acetate, to give the *sulphite* (XV) (231 mg.) as needles, m. p. 172—173°, $[\alpha]_D$ 0° (*c* 1·35) (Found: C, 79·2; H, 11·9; S, 3·5. $C_{58}H_{102}O_3S$ requires C, 79·3; H, 11·6; S, 3·65%), $\nu_{max.}$ (in Nujol) 1205 cm.$^{-1}$ (sulphite).

Hydrolysis of the compound with aqueous mineral acid gave the original alcohol.

4α-*Ethylcholestan*-3β-*yl Toluene*-p-*sulphonate* (XVII).—A mixture of 4α-ethylcholestan-3β-ol (427 mg.), pyridine (5 ml.), and toluene-*p*-sulphonyl chloride (427 mg.) was kept at room temperature for 2 days. Addition of water (200 ml.) and ether extraction yielded the *toluene*-p-*sulphonate* which separated from ether–methanol as needles (445 mg.), m. p. 141—142°, $[\alpha]_D$ +30·5° (*c* 1·68) (Found: C, 75·7; H, 10·1; S, 5·7. $C_{36}H_{58}O_3S$ requires C, 75·8; H, 10·15; S, 5·6%), $\nu_{max.}$ (in Nujol) 1600 (aromatic), 1190, 1170 (sulphonate), 845, and 815 cm.$^{-1}$ (aromatic).

4α-*Ethylcholestane* (XVIII).—The above toluene-*p*-sulphonate (309 mg.) in tetrahydrofuran (50 ml.) was boiled under reflux for 4·5 hr. with lithium aluminium hydride (723 mg.). The mixture was worked up in the usual way, to yield an oil which was dissolved in light petroleum and filtered through alumina (grade O; 5% deactivated). The resulting 4α-*ethylcholestane* (218 mg.) separated from ethyl acetate–methanol as colourless needles, m. p. 89—90°, $[\alpha]_D$ +4·5° (*c* 2·48) (Found: C, 86·95; H, 13·1. $C_{29}H_{52}$ requires C, 87·0; H, 13·0%).

[17] Jouanneteau and Mentzer, *Compt. rend.*, 1958, **246**, 2495.

4-*Ethylcholest*-4-*ene* (XIII).—4-Ethylcholest-4-en-3-one (413 mg.) in ether (30 ml.) was added to a mixture of lithium aluminium hydride (0·15 g.) and aluminium chloride (1·0 g.) in ether (30 ml.). The mixture was boiled for 1·75 hr. and worked up in the usual way. The resulting oil in light petroleum was put on alumina (grade H; 15 g.). Elution with light petroleum (60 ml.) gave a colourless oil (333 mg.) which, after several crystallisations from ethyl acetate–methanol, gave 4-*ethylcholest*-4-*ene* (150 mg.) as needles, m. p. 49—50°, $[\alpha]_D$ +69° (*c* 1·36) (Found: C, 87·1; H, 12·7. $C_{29}H_{50}$ requires C, 87·45; H, 12·55%). The compound gave an intense yellow colour with tetranitromethane in chloroform.

4β-*Ethylcholestane* (XIV).—4-Ethylcholest-4-ene (198 mg.) was hydrogenated over Adams catalyst (199 mg.) at 20°/765 mm. in ether–acetic acid (1 : 3 v/v). Hydrogen uptake was complete after 15 min. Filtration and evaporation of the solvent yielded an oil which separated from ethyl acetate–methanol as needles (170 mg.), m. p. 73—76°. Filtration in light petroleum through alumina (grade H) and recrystallisation gave 4β-*ethylcholestane*, m. p. 75—77°, $[\alpha]_D$ +31° (*c* 1·04) (Found: C, 86·75, 87·2; H, 13·3, 12·95. $C_{29}H_{52}$ requires C, 87·0; H, 13·0%). The compound gave a very slight yellow colour with tetranitromethane in chloroform.

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