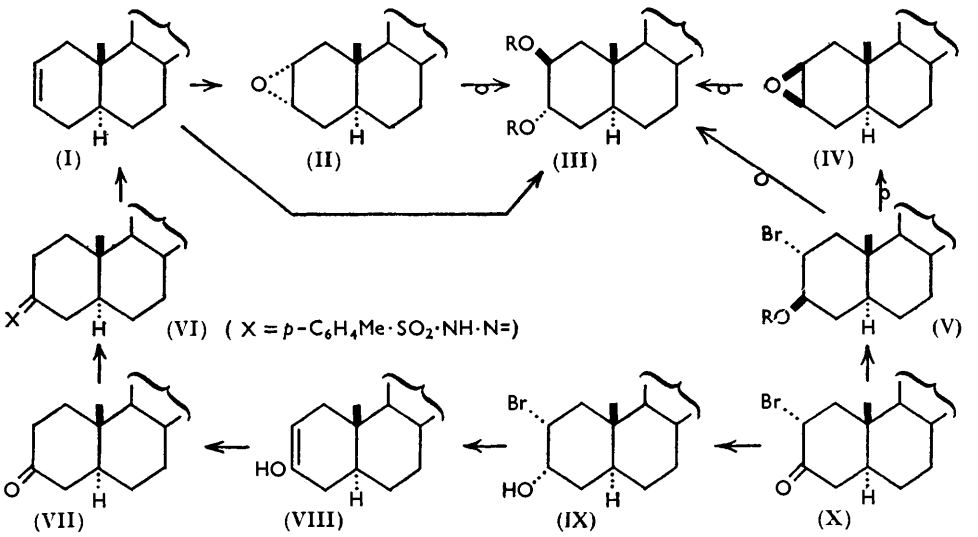
605. *Steroids and Walden Inversion. Part XXXVII.* The Epimeric Cholestane-2 : 3-diols.*

By C. W. Shoppee, D. N. Jones, and G. H. R. Summers.

The four epimeric cholestane-2 : 3-diols have been prepared by methods which permit the assignment of configuration.

In connexion with other studies, we required specimens of the four epimeric cholestane-2 : 3-diols and knowledge of their configurations; before the commencement of this work, only cholestane-2β : 3α-diol (III; R = H) had been described, and methods of preparation are now given for the other three epimerides.

Marker and Plambeck,[1] by oxidation of cholest-2-ene (I) with peracetic acid, obtained cholestane-2β : 3α-diol (III; R = H), m. p. 201°, characterised as the diacetate (III; R = Ac), m. p. 133—135°. Fürst and Plattner,[2] from cholest-2-ene (I) and perbenzoic acid, obtained 2α : 3α-epoxycholestane (II), which by hydrolysis gave a crude diol, m. p. 160—180°, from which was obtained a pure diacetate, m. p. 135°, $[\alpha]_D$ +57°; Hattori and Kawasaki[3] claimed that hydrolysis with ethanolic hydrochloric acid afforded a pure diol,



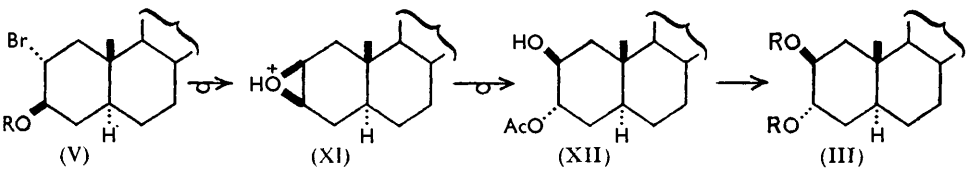
m. p. 159—161°, which they formulated as the 2β : 3α-diol (III; R = H), giving a diacetate, m. p. 135°. Since the only correlation between the products furnished by the three methods is the consistent m. p. recorded for the diacetates, we have repeated the reactions. Cholest-2-ene (I), conveniently prepared from cholestan-3-one (VII) by treatment of the toluene-*p*-sulphonylhydrazone (VI) with sodium hydroxide in refluxing diethylene glycol, with peracetic acid gave cholestane-2β : 3α-diol (III; R = H), m. p. 200—202°, $[\alpha_D]$ +33° (diacetate, m. p. 133—135°, $[\alpha]_D$ +56°), whilst 2α : 3α-epoxycholestane (II) by hydrolysis with sulphuric acid in aqueous acetone yielded an amorphous product, m. p. 145—150°, giving by acetylation and repeated crystallisation a diacetate, m. p. 133—135°, $[\alpha]_D$ +55°, undepressed on admixture with the above specimen. The diacetates displayed identical infrared spectral patterns with bands at (*a*) 1736 (ester CO

* Part XXXVI, *J.*, 1957, 97.

[1] Marker and Plambeck, *J. Amer. Chem. Soc.*, 1939, **61**, 1332.
[2] Fürst and Plattner, *Helv. Chim. Acta*, 1949, **32**, 275.
[3] Hattori and Kawasaki, *J. Pharm. Soc. Japan*, 1937, **57**, 160.

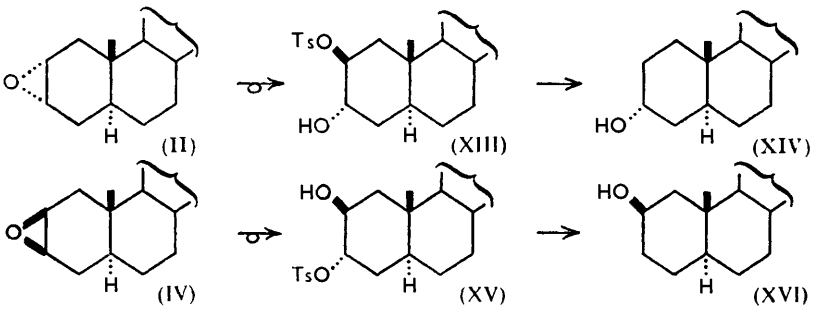
group [4]), (*b*) 1463, 1456, and 1449 (CH_2 and CH_3 deformation bands), and (*c*) 1240 and 1226 cm.$^{-1}$. Similar results were obtained when the epoxide (II) was cleaved with periodic acid.

An alternative route to the 2β : 3α-diol (III; R = H) is from 2α-bromocholestan-3-one (X), which by reduction with sodium borohydride gives 2α-bromocholestan-3β-ol (V; R = H) accompanied by 2α-bromocholestan-3α-ol (IX). A feature of the chromatographic separation of these bromohydrins was the elution of the equatorial epimeride (V) before the axial epimeride (IX), also found by Corey,[5] an inversion of the order reported by Fieser and Huang,[6] and a contravention of the expected elution order, *viz.*, axial alcohol before the equatorial epimeride.[7,8] Fieser and Ettore [9] have, however, also observed a case of anomalous chromatographic behaviour of bromohydrins involving methyl 3α-acetoxy-4β-bromocholanate (3α-OAc; equatorial), which is eluted from aluminium oxide before its axial 3β-acetoxy-epimeride. The 2α-bromo-3α-alcohol (IX) was characterised by acetolysis, probably *via* the enol (VIII), to cholestan-3-one (VII); the 2α-bromo-3β-alcohol (V; R = H) was characterised by catalytic hydrogenation with palladium–charcoal in ethanol containing potassium hydroxide to afford cholestanol, and by dehydrobromination yielded 2β : 3β-epoxycholestane (IV), hydrolysed by sulphuric acid to cholestane-2β : 3α-diol (III; R = H).



(V) (XI) (XII) (III)

As a possible route to cholestane-2α : 3β-diol (XX; R = H), acetolysis of the 2α-bromo-3β-alcohol (V; R = H) was examined. Treatment with potassium acetate in boiling acetic acid gave the acetate (V; R = Ac) and the diacetate (III; R = Ac), which by hydrolysis yielded cholestane-2β : 3α-diol (III; R = H). The inversion of configuration at $C_{(2)}$ and $C_{(3)}$ may be regarded as involving the conjugate acid (XI) of the 2β : 3β-epoxide (IV), with subsequent acetolysis to afford the diaxial 2-monoacetate (XII), hydrolysed to cholestane-2β : 3α-diol (III; R = H).



(II) (XIII) (XIV)

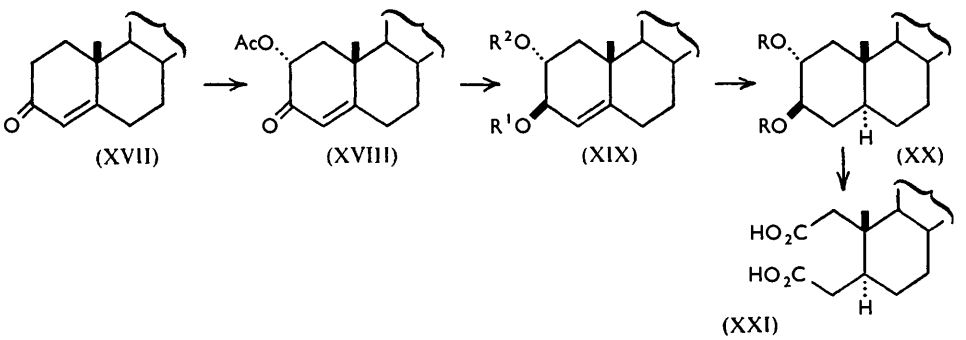
(IV) (XV) (XVI)

The 2β : 3α-configuration assigned to the diol, m. p. 200—202°, $[\alpha]_D$ +33°, is consistent with the rule of diaxial fission of steroid epoxides,[10,11] and is further supported by the reactions of the epoxides (II) and (IV) with ethereal toluene-*p*-sulphonic acid.[12] 2α : 3α-Epoxycholestane (II) gave 3α-hydroxycholestan-2β-yl toluene-*p*-sulphonate (XIII),

[4] Jones, Williams, Whalen, Humphries, and Dobriner, *J. Amer. Chem. Soc.*, 1948, **70**, 2024; 1949, **71**, 241; cf. Page, *J.*, 1955, 2017.
[5] Corey, *J. Amer. Chem. Soc.*, 1953, **75**, 4832.
[6] Fieser and Huang, *ibid.*, p. 4837.
[7] Barton, *J.*, 1953, 1027.
[8] Brooks, Klyne, and Miller, *Biochem. J.*, 1953, **54**, 212.
[9] Fieser and Ettore, *J. Amer. Chem. Soc.*, 1953, **75**, 1700.
[10] Fürst and Plattner, Abs. XII Internat. Congr. Pure Appl. Chem., 1951, p. 409.
[11] Alt and Barton, *J.*, 1954, 4284.
[12] Criegee and Stanger, *Ber.*, 1936, **69**, 2753.

converted by prolonged treatment with lithium aluminium hydride into *epi*cholestanol (XIV), whilst 2β : 3β-epoxycholestane (IV) yielded 2β-hydroxycholestan-3α-yl toluene-*p*-sulphonate (XV), converted by extended treatment with lithium aluminium hydride into cholestan-2β-ol (XVI),[2,13,14] characterised by oxidation to cholestan-2-one.*

Cholestane-2α : 3β-diol (XX; R = H) was obtained as follows. Cholest-4-en-3-one (XVII) by oxidation with lead tetra-acetate gave 2α-acetoxycholest-4-en-3-one (XVIII),[14,16] in which configuration at $C_{(2)}$ is established.[17] Seebeck and Reichstein [16] by exhaustive catalytic hydrogenation of the ketone (XVIII) and subsequent hydrolysis, obtained a crude diol, m. p. 150—157°, oxidised by chromium trioxide to 2 : 3-*seco*cholestane-2 : 3-dioic acid (XXI). By use of sodium borohydride we converted 2α-acetoxycholest-4-en-3-one (XVIII) into 3β-hydroxycholest-4-en-2α-yl acetate (XIX; R^1 = Ac, R^2 = H), hydrolysed to cholest-4-ene-2α : 3β-diol (XIX; $R^1 = R^2$ = H), in which configuration at $C_{(3)}$ is assigned on the grounds (*a*) that reduction of cholest-4-en-3-one with sodium borohydride furnishes at least 70% of the 3β-epimeride,[18] and (*b*) that substituents at $C_{(2)}$ do not affect the stereochemical course of hydride reduction of a 3-carbonyl group.[19] Hydrogenation of cholest-4-en-2α : 3β-diol (XIX; $R^1 = R^2$ = H) with platinum in acetic acid gave cholestane-2α : 3β-diol (XX; R = H), m. p. 204°, $[\alpha]_D$ +18°, whilst hydrogenation of the diacetate (XIX; $R^1 = R^2$ = Ac) with platinum in ethyl acetate yielded cholestane-2α : 3β-diol diacetate (XX; R = Ac). The 2α : 3β-diol (XX; R = H), on oxidation with chromium trioxide in acetic acid, afforded 2 : 3-*seco*cholestane-2 : 3-dioic acid (XXI). The diol, m. p. 118°, reported by Hattori and Kawasaki [3] thus cannot be cholestane-2α : 3β-diol, unless they were dealing with a polymorph; they give no optical rotation.



(XVII) (XVIII) (XIX) (XX) (XXI)

Since this sequence of reactions was completed, 2α-acetoxy-5α : 22*a*-spirost-4-en-3-one (as XVIII) has been converted into 5α : 22*a*-spirostane-2α : 3β-diol (as XX; R = H) by catalytic hydrogenation of the double bond and reduction of the carbonyl group with lithium aluminium hydride.[19]

Cholestane-2α : 3α-diol (XXII; R = H) was obtained from cholest-2-ene (I) by treatment with osmium tetroxide; configuration is assigned by analogy, since a survey of a large number of reactions shows that attack by bulky entities on the α-face of the steroid nucleus, especially in ring A, is subject to less steric retardation than on the

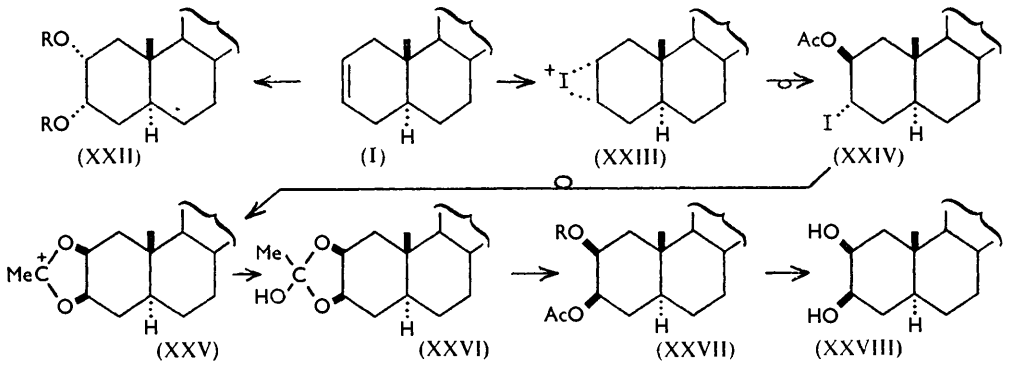
* Reduction of monotoluene-*p*-sulphonates of diaxial *trans*-1 : 2-diols with lithium aluminium hydride may occur by a base-catalysed elimination, giving an epoxide, since epoxides stable to lithium aluminium hydride have been isolated; [15] providing the rule of diaxial fission applies to epoxide reduction, the stereochemical arrangement of the free hydroxyl group will be unaffected.

[13] Ruzicka, Plattner, and Furrer, *Helv. Chim. Acta*, 1944, **27**, 727.
[14] Fieser and Romero, *J. Amer. Chem. Soc.*, 1953, **75**, 4716.
[15] Goering and Serres, *ibid.*, 1952, **74**, 5908.
[16] Seebeck and Reichstein, *Helv. Chim. Acta*, 1944, **27**, 948.
[17] Sondheimer, Kaufmann, Romo, Martinez, and Rosenkranz, *J. Amer. Chem. Soc.*, 1953, **75**, 4712.
[18] Shoppee, Agashe, and Summers, unpublished work.
[19] Herran, Rosenkranz, and Sondheimer, *J. Amer. Chem. Soc.*, 1954, **76**, 5531.

β-face,[20,21] and Wendler and Slates [22] have recently described the similar reaction of 5α : 22*a*-spirost-2-en-12-one (as I) to give 2α : 3α-dihydroxy-5α : 22*a*-spirostan-12-one (as XXII).

Cholestane-2β : 3β-diol (XXVIII) was obtained by a new method for *cis*-hydroxylation of olefins, first envisaged by Prevost and recently reported by Ginsburg; [23] cholest-2-ene (I), by treatment with iodine and silver acetate in moist acetic acid, gave, after acetylation and chromatography, a 50% yield of cholestane-2β : 3β-diol diacetate (XXVII; R = Ac) together with 3% of cholestane-2α : 3α-diol diacetate (XXII; R = Ac). Hydrolysis of the 2β : 3β-diacetate by treatment with lithium aluminium hydride furnished cholestane-2β : 3β-diol (XXVIII).

The almost exclusive production of the 2β : 3β-diol requires a mechanism involving the initial formation, by electrophilic attack of iodine, of a 2α : 3α-iodonium ion (XXIII), analogous to the 2α : 3α-bromonium ion postulated by Alt and Barton [11] as an intermediate in the addition of bromine to cholest-2-ene to give mainly the diaxial 2β : 3α-dibromocholestane. In a similar way, analogous to the diaxial fission of epoxides, the iodonium ion (XXIII) reacts with an acetate anion with inversion at $C_{(2)}$ to give the diaxial 2β-acetoxy-3α-iodide (XXIV). Separation of the 3α-iodine atom as the anion with participation of the 2β-acetoxyl group, and so with inversion at $C_{(3)}$, affords the cation (XXV), converted by traces of water [24] into the orthoacetate (XXVI), which readily rearranges to the 3β-monoacetate (XXVII; R = H).



The results of Knowles and his collaborators [25] indicate that trisubstituted steroid double bonds fail to react with iodine and silver acetate; we find that cholesterol reacts with difficulty, to give, after acetylation and chromatography, 5% of cholestane-3β : 5 : 6α-triol 3 : 6-diacetate [26,27] and 5% of cholestane-3β : 5 : 6β-triol 3 : 6-diacetate.[26,27]

The constants of the four diols and diacetates are collected in the Table.

*Cholestane-2 : 3-diols and their diacetates.**

	2α : 3α-Diol	2β : 3β-Diol	2β : 3α-Diol	2α : 3β-Diol
M. p.	216—219° (212—214°)	176—177° (174—177°)	200—202° (197—200°)	204—205° (212—214°)
$[\alpha]_D$	+31° (+32°)	+38° (+43°)	+33° (+42°)	+18° (+28°)
	Diacetate	Diacetate	Diacetate	Diacetate
M. p.	134°/135°	112°/119°	133—135°	106—107°
$[\alpha]_D$	+29°	+38°	+56°	−27°

* Since this paper was submitted, Henbest and Smith (*J.*, 1957, 926) have prepared the four diols. Their data are included in parentheses in our table.

[20] Fishman and Djerassi, *J. Amer. Chem. Soc.*, 1955, **77**, 4291.
[21] Tamasaki, Rosnati, Fieser, and Fieser, *ibid.*, p. 3308.
[22] Wendler and Slates, *Chem. and Ind.*, 1955, 167.
[23] Ginsberg, *J. Amer. Chem. Soc.*, 1953, **75**, 5746.
[24] Winstein and Buckles, *ibid.*, 1942, **64**, 2787.
[25] Barkley, Farrer, Knowles, Raffelson, and Thompson, *ibid.*, 1954, **76**, 5014.
[26] Ellis and Petrow, *J.*, 1939, 1078.
[27] Prelog and Tagmann, *Helv. Chim. Acta*, 1944, **27**, 1867.

Experimental

For general experimental direction, see *J.*, 1957, 97. $[\alpha]_D$ are in $CHCl_3$ unless otherwise stated. Infrared absorption spectra were determined in CS_2 on a Perkin-Elmer double-beam instrument.

Cholest-2-ene.—(*a*) Cholestan-3-one, m. p. 127° (1 g.), in ethanol (20 c.c.) was heated with toluene-*p*-sulphonyl hydrazide (630 mg.) and concentrated hydrochloric acid (1 c.c.) under reflux for 1 hr. The mixture was poured into water and extracted with ether, and the extract washed with 2N-hydrochloric acid, 2N-sodium carbonate, and water, dried, and evaporated; the *toluene*-p-*sulphonylhydrazone* had m. p. 172—174° (decomp.), $[\alpha]_D$ +30° (*c* 1·0), after recrystallisation from ether [Found (after drying at 95°/0·02 mm.): C, 76·3; H, 10·2. $C_{34}H_{54}O_2N_2S$ requires C, 76·35; H, 10·2%]. The hydrazone (450 mg.) was refluxed with sodium hydroxide (450 mg.) in diethylene glycol for 4 hr.; the brown solution was poured into water, and worked up to yield an oil, which by filtration of a pentane solution through aluminium oxide and crystallisation of the resulting solid from acetone–methanol gave cholest-2-ene, m. p. 71—72°, $[\alpha]_D$ +66°.

(*b*) A mixture of 2α-bromocholestan-3α- and -3β-ol (see below), obtained by reduction of 2α-bromocholestan-3-one with sodium borohydride,[5,6] was refluxed with zinc dust in acetic acid for 40 min., and after being worked up yielded cholest-2-ene, m. p. 72°, $[\alpha]_D$ +66° (cf. ref. 11).

2α-Bromocholestan-3α- and -3β-ol.—2α-Bromocholestan-3-one (2·57 g.) in ether (100 c.c.) was treated with a solution of sodium borohydride (484 mg.) in moist methanol (80 c.c.) at 25° for 2 hr. Chromatography of the product on a column of neutral aluminium oxide [28] (75 g.) prepared in pentane gave by elution with benzene (6 × 250 c.c.) cholestan-3-one (502 mg.), m. p. and mixed m. p. 127°. Elution with ether–benzene (1 : 9; 7 × 250 c.c.) gave an oil (1·19 g.) which crystallised from methanol in needles, m. p. 65—80°, unchanged by drying at 50°/0·05 mm. for 4 hr., but giving by repeated azeotropic distillation with benzene 2α-bromocholestan-3β-ol, m. p. 109—111°, $[\alpha]_D$ +13° (*c* 1·2), after recrystallisation from acetone; a portion (115 mg.) was characterised by hydrogenation with palladium–charcoal in ethanol (14 c.c.) containing potassium hydroxide (104 mg.) to cholestan-3β-ol, double m. p. 125°/140°,[29] after crystallisation from acetone–methanol, undepressed on admixture with a genuine specimen. Further elution with ether–benzene (1 : 9; 8 × 250 c.c.) gave a solid (555 mg.), m. p. 100—118°; this material was rechromatographed on a column of neutral aluminium oxide (10 g.), prepared in benzene; then elution with ether–benzene mixtures furnished 2α-bromocholestan-3α-ol, m. p. 116—118°, $[\alpha]_D$ +34° (*c* 1·4), after recrystallisation from acetone; a portion (267 mg.) by acetolysis with freshly fused potassium acetate (3·6 g.) in boiling acetic acid (25 c.c.) for 11·5 hr. gave a product separated by chromatography on neutral aluminium oxide and elution with benzene–pentane mixtures into cholestan-3-one (164 mg.), m. p. and mixed m. p. 125—127° after recrystallisation from acetone–methanol, and, by elution with ether–benzene (1 : 9), unchanged 2α-bromocholestan-3α-ol, m. p. and mixed m. p. 113—116° after recrystallisation from acetone.

Cholestane-2β : 3α-diol.—(*a*) Cholest-2-ene (3 g.), dissolved in acetic acid (50 c.c.), was heated on a steam-bath and treated with 30% hydrogen peroxide (3 c.c.) added during 1 hr. with stirring. The mixture was poured into water and extracted with ether, and the extract washed thrice with water, 2N-sodium carbonate, and water, dried, and evaporated. The product was hydrolysed with boiling 5% ethanolic potassium hydroxide (120 c.c.) for 45 min.; after addition of a little water, the solution was saturated with carbon dioxide, ethanol removed in a vacuum, and the product isolated and recrystallised from methanol to give cholestane-2β : 3α-diol, m. p. 200—202°, $[\alpha]_D$ +33° (*c* 1·2). Acetylation with acetic anhydride–pyridine at 20° for 14 hr. gave the diacetate, m. p. 133—135°, $[\alpha]_D$ +56° (*c* 1·1), after crystallisation from acetone–methanol.

(*b*) 2α : 3α-Epoxycholestane [2,3] (m. p. 100—102°, $[\alpha]_D$ +37°; 200 mg.) in acetone (45 c.c.) and water (5 c.c.) was treated with 2N-sulphuric acid (10 drops) at 20° for 48 hr. After neutralisation with 2N-sodium carbonate, the solution was evaporated in a vacuum, and the residue dried by repeated azeotropic distillation with benzene. Attempted crystallisation

[28] Reichstein and Shoppee, *Discuss. Faraday Soc.*, 1949, **7**, 305.
[29] Shoppee, *J.*, 1946, 1145.

from acetone gave an amorphous solid, m. p. 145—150°, which was acetylated with boiling acetic anhydride; the resultant oil crystallised from acetone–methanol, and after two recrystallisations furnished cholestane-2β : 3α-diol diacetate, m. p. 133—135°, $[\alpha]_D$ +55° (*c* 0·7). This specimen and that prepared under (*a*) gave no m. p. depression, and displayed identical infrared spectra [in CCl_4 at 2908 (2910), 2836 (2832), 1737 (1734), 1363 (1364), 1240, 1224, 1028 cm.$^{-1}$; in CS_2 at 1736 (1735), 1463, 1452, 1445 (1444), 1361 (1362), 1240, 1227 (1226), 1027 cm.$^{-1}$].

(*c*) 2β : 3β-Epoxycholestane [2] (m. p. 87—89°, $[\alpha]_D$ +50°; 56 mg.) was treated in acetone (11 c.c.) and water (1·2 c.c.) with 2N-sulphuric acid (2 drops) at 20° for 48 hr. Working up as under (*b*) gave an amorphous solid, m. p. 145—150°, which by acetylation with boiling acetic anhydride and crystallisation of the product thrice from acetone–methanol afforded cholestane-2β : 3α-diol diacetate, m. p. and mixed m. p. 133—135°, $[\alpha]_D$ +55° (*c* 0·7).

(*d*) 2α-Bromocholestan-3β-ol (m. p. 109—111°; 1·02 g.) was refluxed with freshly fused potassium acetate (12 g.) in acetic acid (68 c.c.) for 14 hr. The mixture was poured into water and extracted with ether, and the extract washed with water, 2N-sodium carbonate, and water, dried, and evaporated, to give an oil (970 mg.), which was chromatographed on a column of neutral aluminium oxide (30 g.) prepared in pentane. Elution with benzene–pentane (1 : 1; 5 × 100 c.c.) gave a colourless oil (366 mg.), which crystallised from acetone–methanol to afford 2α-bromocholestan-3β-yl acetate, m. p. 101—102°, $[\alpha]_D$ −81° (*c* 1·4) (lit.,[6] m. p. 106—107°, $[\alpha]_D$ −82°); on treatment with lithium aluminium hydride in ether at 0° for 30 minutes, this regenerated the starting material, m. p. and mixed m. p. 108—110°. Elution with benzene (3 × 100 c.c.) and with ether–benzene (1 : 19; 4 × 100 c.c.) gave an oil (222 mg.), which crystallised from acetone to yield cholestane-2β : 3α-diol diacetate, m. p. and mixed m. p. 133—135°, $[\alpha]_D$ +55° (*c* 1·0), hydrolysed by treatment with lithium aluminium hydride in ether at 36° for 30 min. to cholestane-2β : 3α-diol, m. p. and mixed m. p. 198—200°, $[\alpha]_D$ +31° (*c* 1·1). Further elution with ether–benzene (1 : 4; 3 × 100 c.c.) gave 2α-bromocholestan-3β-ol, m. p. and mixed m. p. 108—110°.

*3α-Hydroxycholestan-2β-yl Toluene-*p*-sulphonate.*—2α : 3α-Epoxycholestane (m. p. 100—102°; 412 mg.), dissolved in ether (10 c.c.), was treated with a solution of toluene-*p*-sulphonic acid (190 mg.) in ether (15 c.c.) at 20° for 14 hr. The solution was poured into water, ether (100 c.c.) added, and the ethereal layer separated, washed with 2N-sodium carbonate and with water, dried, and evaporated, to give an oil (590 mg.) which crystallised after being stirred with acetone and set aside at 0° for 48 hr. Two recrystallisations from ether–hexane gave *3α-hydroxycholestan-2β-yl toluene-*p*-sulphonate*, m. p. 150—151°, $[\alpha]_D$ +23° (*c* 1·1) [Found (after drying at 20°/0·05 mm. for 18 hr.): C, 73·1; H, 9·8. $C_{34}H_{54}O_4S$ requires C, 73·1; H, 9·75%]. The toluene-*p*-sulphonate (210 mg.) was treated with excess of lithium aluminium hydride in ether at 36° for 19 hr.; the solid product obtained by working up in the usual way crystallised from acetone to furnish cholestan-3α-ol, m. p. and mixed m. p. 182—184°.

*2β-Hydroxycholestan-3α-yl Toluene-*p*-sulphonate.*—2β : 3β-Epoxycholestane (m. p. 87—89°; 295 mg.), in ether (10 c.c.), was similarly treated with toluene-*p*-sulphonic acid (140 mg.) in ether (15 c.c.) at 20° for 10 hr., to yield *2β-hydroxycholestan-3α-yl toluene-*p*-sulphonate*, m. p. 149—150°, $[\alpha]_D$ +41° (*c* 1·5) [Found (after drying at 16°/0·05 mm. for 12 hr.): C, 73·2; H, 9·55. $C_{34}H_{54}O_4S$ requires C, 73·1; H, 9·75%], depressed to 138° on admixture with 3α-hydroxycholestan-2β-yl toluene-*p*-sulphonate. 2β-Hydroxycholestan-3α-yl toluene-*p*-sulphonate (270 mg.) was treated with excess of lithium aluminium hydride in ether at 36° for 12 hr., to give, after the usual working up, a solid (184 mg.) which was chromatographed on neutral aluminium oxide (6 g.) prepared in pentane; elution with benzene gave cholestan-2β-ol, m. p. 151—153°, $[\alpha]_D$ +34° (*c* 1·1) (lit.,[2,11] m. p. 152—154°, $[\alpha]_D$ +33°). The alcohol (61 mg.) in acetic acid (5 c.c.) was treated with a 2% solution of chromium trioxide in 98% acetic acid (1 c.c.) at 25° for 12 hr.; the product (59 mg.) by crystallisation from acetone–methanol yielded cholestan-2-one, m. p. 126—128°, $[\alpha]_D$ +48° (*c* 1·0) (lit.,[2,11] m. p. 130°, $[\alpha]_D$ +51°). The m. p. was depressed to 105° by admixture with cholestan-3-one, m. p. 127°.

Cholest-4-ene-2α : 3β-diol.—2α-Acetoxycholest-4-en-3-one [16] (m. p. 141—142°, $[\alpha]_D$ +66°; 279 mg.) in ether (9 c.c.) was treated with a solution of sodium borohydride (105 mg.) in moist methanol at 20° for 3 days. The usual isolation procedure furnished a solid, which was chromatographed on aluminium oxide (8 g.) prepared in benzene. Elution with ether–benzene mixtures gave an oil (52 mg.) but elution with methylene chloride yielded a solid (170 mg.) which by recrystallisation from methanol gave *cholest-4-ene-2α : 3β-diol*, m. p. 174°, $[\alpha]_D$ +38° (*c* 1·1) [Found (after drying at 50°/0·05 mm. for 18 hr): C, 80·4; H, 11·6. $C_{27}H_{46}O_2$ requires

C, 80·5; H, 11·5%]. The diol (50 mg.) with acetic anhydride–pyridine at 18° for 14 hr. gave, after the usual working up and crystallisation from methanol, the *diacetate*, m. p. 111—112°, $[\alpha]_D$ −60·5° (*c* 1·6) [Found (after drying at 80°/0·05 mm. for 1 hr.): C, 76·3; H, 10·4. $C_{31}H_{50}O_4$ requires C, 76·5; H, 10·4%].

Cholestane-2α : 3β-diol.—(*a*) Cholest-4-ene-2α : 3β-diol (36 mg.) in acetic acid (10 c.c.) was hydrogenated with platinum oxide (36 mg.) (uptake of H_2 complete in 10 min.). The usual isolation procedure afforded a solid, which, after purification by elution from aluminium oxide with methylene chloride and recrystallisation from methanol, gave *cholestane-2α : 3β-diol*, m. p. 204—205°, $[\alpha]_D$ +17° (*c* 1·0) [Found (after drying at 60°/0·05 mm. for 18 hr.): C, 80·0; H, 12·0. $C_{27}H_{48}O_2$ requires C, 80·1; H, 11·95%]. A mixture with cholestane-2β : 3α-diol, m. p. 200—202°, produced a depression of m. p. to 190—197°.

(*b*) Cholest-4-ene-2α : 3β-diol diacetate (114 mg.) in ethyl acetate (10 c.c.) was hydrogenated with platinum oxide (44 mg.). After uptake of hydrogen had ceased (5 hr.), the product was isolated in the usual way, and purified by chromatography on aluminium oxide. Elution with benzene–pentane (1 : 4) and crystallisation from methanol gave *cholestane-2α : 3β-diol diacetate*, m. p. 106—107°, $[\alpha]_D$ −27° (*c* 1·2) [Found (after drying at 50°/0·05 mm. for 1 hr.): C, 76·4; H, 10·8. $C_{31}H_{52}O_4$ requires C, 76·2; H, 10·7%]. The diacetate (45 mg.) by treatment with lithium aluminium hydride in ether at 36° for 30 min. and working up in the usual way, gave cholestane-2α : 3β-diol, m. p. 204—208°, $[\alpha]_D$ +18° (*c* 0·8) after crystallisation from acetone. The mixed m. p. with the specimen prepared as under (*a*) was 204—205°.

The 2α : 3β-diol (78 mg.) in acetic acid (8·5 c.c.) was oxidised with chromium trioxide (76 mg.) in 98% acetic acid (4·5 c.c.) at 25° for 12 hr. The acidic product (34 mg.) was isolated in the usual way, and thrice recrystallised from ether–pentane gave 2 : 3-*seco*cholestane-2 : 3-dioic acid, m. p. and mixed m. p. 196—197°.

Cholestane-2α : 3α-diol.—Cholest-2-ene (738 mg.) in ether (15 c.c.) was treated with osmium tetroxide (500 mg.) in ether (60 c.c.) at 15° for 14 days. Ether was removed and the black residue refluxed with aqueous-ethanolic sodium sulphite for 2 hr. The cooled suspension was filtered, the residue was washed with hot ethanol, and the combined filtrate and washings were evaporated in a vacuum. The product was extracted with ether, washed with 2N-sodium hydroxide containing mannitol, and with water, dried, and evaporated. The white solid, by crystallisation from chloroform–acetone and sublimation, furnished *cholestane-2α : 3α-diol*, m. p. 216—219°, $[\alpha]_D$ +31° (*c* 1·2) [Found (after sublimation at 180°/0·05 mm.): C, 79·9; H, 11·75. $C_{27}H_{48}O_2$ requires C, 80·1; H, 11·95%]. The diol (145 mg.) with boiling acetic anhydride gave, after crystallisation of the product from acetone–methanol, the *diacetate*, m. p. 134—135°, $[\alpha]_D$ +29° (*c* 1·5) [Found (after drying at 80°/0·05 mm. for 4 hr.): C, 76·2; H, 10·6. $C_{31}H_{52}O_4$ requires C, 76·2; H, 10·7%]. The m. p. was depressed to 110° on admixture with cholestane-2β : 3α-diol diacetate, m. p. 133—135°.

Cholestane-2β : 3β-diol.—Cholest-2-ene (811 mg.) in acetic acid (110 c.c.) containing water (1·5 c.c.) was treated with silver acetate (1·29 g.), and powdered iodine (755 mg.) added in one portion. The mixture was stirred vigorously at 45° for 3 hr., then cooled to 30°, and excess of sodium chloride added. The red solution was filtered and evaporated in a vacuum, and the residue dissolved in ether; the ethereal solution was washed with sodium hydrogen carbonate solution, sodium thiosulphate solution, and water, dried, and evaporated. Acetylation of the product with boiling acetic anhydride and the usual working up gave an oil (1 g.), which was chromatographed on aluminium oxide (30 g.) prepared in pentane. Elution with benzene–pentane (1 : 19; 8 × 100 c.c.) afforded *cholestane-2β : 3β-diol diacetate*, double m. p. 112°/119°, $[\alpha]_D$ +38° (*c* 1·2) [Found (after drying at 80°/0·05 mm. for 1 hr.): C, 76·1; H, 10·5. $C_{31}H_{52}O_4$ requires C, 76·1; H, 10·5%], after crystallisation from acetone–methanol. Further elution with benzene–pentane (1 : 19; 4 × 100 c.c.) gave material (385 mg.) consisting essentially of the diacetate. The diacetate (270 mg.) was hydrolysed by treatment with excess of lithium aluminium hydride in ether at 36° for 30 min.; the solid product, obtained after the usual working up, crystallised from acetone to furnish *cholestane-2β : 3β-diol*, m. p. 176—177°, $[\alpha]_D$ +38° (*c* 1·0) [Found (after drying at 80°/0·01 mm. for 4 hr.): C, 79·8; H, 11·7. $C_{27}H_{48}O_2$ requires C, 80·1; H, 12·0%]. Acetylation with boiling acetic anhydride gave the 2β : 3β-diacetate, m. p. and mixed m. p. 132—133°.

Hydroxylation of Cholesterol with Silver Acetate and Iodine.—Cholesterol (1 g.) in acetic acid (55 c.c.) containing water (1·5 c.c.) with silver acetate (1·69 g.) at 50—55° was treated with powdered iodine (0·96 g.) added in portions with stirring during 30 min. The mixture was

stirred at 50° for 40 min. and then at 95° for 3 hr. The product, isolated as above, was acetylated with boiling acetic anhydride, and chromatographed on aluminium oxide (25 g.) prepared in pentane. Elution with benzene–pentane mixtures (11 × 100 c.c.) gave an oil (234 mg.). Elution with benzene (3 × 100 c.c.) and with ether–benzene (1 : 9; 2 × 100 c.c.) afforded a solid, which by repeated crystallisation from ether–methanol gave cholestane-3β : 5 : 6α-triol triacetate (62 mg.), m. p. and mixed m. p. 181—185°, whilst further elution with ether–benzene (1 : 4; 4 × 100 c.c.) gave cholestane-3β : 5 : 6β-triol triacetate (59 mg.), m. p. and mixed m. p. 163—165°, after repeated crystallisation from methanol.

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UNIVERSITY COLLEGE, SWANSEA.
DEPARTMENT OF ORGANIC CHEMISTRY,
THE UNIVERSITY, SYDNEY.

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