310. *Steroids and Walden Inversion. Part XLVII.* 5α-Cholestan-1-one, A-Nor-5α-cholestan-1-one, and Some Derivatives Thereof.*

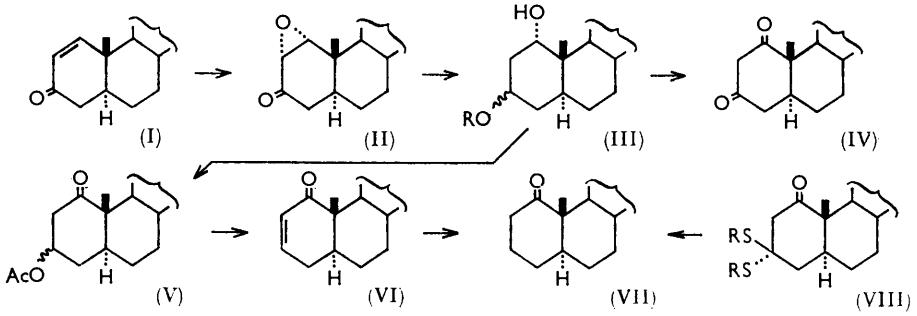
By C. W. Shoppee, S. K. Roy, and (in part) B. S. Goodrich.

5α-Cholestan-1-one has been prepared from 5α-cholest-1-en-3-one by way of 5α-cholestane-1,3-dione. Bromination of 5α-cholestan-1-one gives the 2α-bromo- and 2,2-dibromo-ketones, dehydrobrominated respectively to 5α-cholest-2-en-1-one and its 2-bromo-derivative, which may be interconverted.

1ξ-Amino-5α-cholestane, by deamination, gives 5α-cholestan-1α-ol and a mixture of 5α-cholest-1- and -2-ene; the epimeric 1-amino-5α-cholestane could not be obtained.

A-Nor-5α-cholestan-1-one has been prepared from 5α-cholest-1-ene by oxidative ring-fission to the 1,2-seco-1,2-dicarboxylic acid and pyrolysis of its barium salt; 1β-amino-A-nor-5α-cholestane, by deamination, affords A-nor-5α-cholestan-1β-ol and A-nor-5α-cholest-1-ene.

5α-Cholestan-1-one (VII) was first prepared by Striebel and Tamm [1] from 5α-cholest-1-en-3-one (I) by conversion into the 1α,2α-epoxide (II) and reduction to a mixture of 3-epimeric 5α-cholestane-1,3-diols (as III; R = H); chromatographic separation, partial acetylation at $C_{(3)}$, and oxidation of the diol 3-monoacetates (as III; R = Ac) with chromium trioxide, gave the 3-epimeric acetoxy-ketones (as V), converted by treatment with aluminium oxide into 5α-cholest-2-en-1-one (VI), hydrogenated to 5α-cholestan-1-one (VII). This ketone has also been obtained by Plattner, Fürst, and Els,[2] starting from a mixture of 5α-cholest-1- and -2-ene.



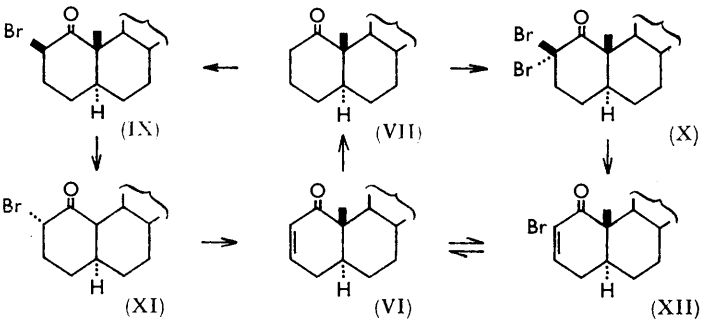
We have prepared 5α-cholestan-1-one (VII) by Striebel and Tamm's method but we found chromatographic separation of the mixture of unchanged epoxide (II), 1α,3α-diol, and 1α,3β-diol (as III; R = H) difficult and tedious; further, we were unable to achieve the essential nearly quantitative partial 3-acetylation of the 1α,3β-diol (the major product) as described by Striebel and Tamm. In an attempt to improve the preparative procedure, we examined the reaction of a synthetic 1 : 1 mixture of the epimeric diols (as III; R = H) with thionyl chloride in pyridine, whereby only the *cis*-diaxial 1α,3α-diol should yield a cyclic sulphite;[3] however, apart from chromatographically easily eluted non-crystalline material, <15% of the 1α,3β-diol could be recovered. We next investigated the oxidation of the epimeric diols, and finally found that by brief oxidation with a standard solution of chromium trioxide in sulphuric acid [4] in acetone–ether under nitrogen at 10—15° conversion

* Part XLVI, *J.*, 1960, 4874.

[1] Striebel and Tamm, *Helv. Chim. Acta*, 1954, **37**, 1094.
[2] Plattner, Fürst, and Els, *Helv. Chim. Acta*, 1954, **37**, 1399.
[3] Plattner, Segré, and Ernst, *Helv. Chim. Acta*, 1947, **30**, 1432.
[4] Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548.

into 5α-cholestane-1,3-dione † (IV), m. p. 171°, $[\alpha]_D$ +108°, $\nu_{max.}$ 1695, 1725 cm.$^{-1}$, $\lambda_{max.}$ 256 (log ε 4·1), could be effected. The β-diketone condensed readily with toluene-ω-thiol to give the crystalline dibenzyl 3-thioketal (VIII; R = CH_2Ph), $\nu_{max.}$ 1715 cm.$^{-1}$, a process probably assisted by bonding of the 11α-hydrogen atom with the 1-carbonyl group; desulphurisation with deactivated Raney nickel [2,5] in ethanol then furnished 5α-cholestan-1-one (VII), $\nu_{max.}$ 1712 cm.$^{-1}$.

5α-Cholestan-1-one (VII), on acid-catalysed monobromination in acetic acid, gave 2α-bromo-5α-cholestan-1-one (XI), accompanied by some 2,2-dibromo-5α-cholestan-1-one (X). According to Corey,[6] the initial monobromination product should be the axial 2β-bromo-ketone (IX) (cf. ref. 7), which in the presence of hydrogen bromide passes by reduction and rebromination into the more thermodynamically stable, equatorial 2α-



bromo-ketone (XI). We attempted to obtain the 2β-bromo-ketone (IX) by base-catalysed bromination in acetic acid,[8] and by bromination in acetic acid in presence of hydrogen peroxide, but the ketone (VII) failed to react under these conditions. Acid-catalysed dibromination of 5α-cholestan-1-one (VII) gave the 2,2-dibromo-ketone (X) as the major product together with the 2α-bromo-ketone (XI); an excellent separation could be effected by chromatography on silica gel and elution with pentane and pentane–ether.

Refluxing the 2α-bromo-ketone (XI) with *s*-collidine under nitrogen for 1 hr. gave the αβ-unsaturated ketone (VI).[1] The 2,2-dibromo-ketone (X) under similar conditions was rapidly (10 min.) converted in 90% yield by ionic elimination (2βBr/3αH: *trans*, diaxial) into 2-bromo-5α-cholest-2-en-1-one (XII), and this was reduced by zinc in ethanol to the

Compound	$\nu_{max.}$ (cm.$^{-1}$)	$\Delta\nu$	$\lambda_{max.}$ (mμ)	$\Delta\lambda$	Halogen conformn.
5α-Cholestan-1-one	1712	—	297	—	
2α-Bromo-5α-cholestan-1-one	1727	+15	292 infl	−5	eq
2,2-Dibromo-5α-cholestan-1-one	1725	+13	320	+23	eq + ax
5α-Cholest-2-en-1-one	1692	—	222	—	
2-Bromo-5α-cholest-2-en-1-one	1700	+8	254	+32	—
5α-Cholestan-3-one	1718	—	286	—	
2α-Bromo-5α-cholestan-3-one	1733	+15	282	−4	eq
2,2-Dibromo-5α-cholestan-3-one	1735	+17	294	+8	eq + ax
5α-Cholest-1-en-3-one	1684	—	230	—	
2-Bromo-5α-cholest-1-en-3-one	1697	+13	256	+26	—

αβ-unsaturated ketone (VI). 2-Bromo-5α-cholest-2-en-1-one (XII) was also obtained from 5α-cholest-2-en-1-one (VI) by conversion into the crude 2,3-dibromide (cf. ref. 7) (2β,3α- and/or 2α,3β-dibromide) and passage of this through aluminium oxide.

† Since this paper was written, this dione has been reported by Tamm and Albrecht (*Helv. Chim. Acta*, 1960, **43**, 768), as also have compounds (IX), (X), (XI), and (XVIII) (m. p. 75°, [α] +11°, $\nu_{max.}$ 1727—1730 cm.$^{-1}$ in CH_2Cl_2) by Sigg and Tamm (*Helv. Chim. Acta*, 1960, **43**, 1402).

[5] Spero, McIntosh, jun., and Levin, *J. Amer. Chem. Soc.*, 1948, **70**, 1907; Rosenkranz, Kaufmann, and Romo, *ibid.*, 1949, **71**, 3689.

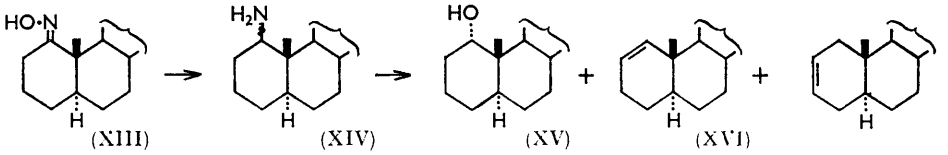
[6] Corey, *J. Amer. Chem. Soc.*, 1954, **76**, 175.

[7] Alt and Barton, *J.*, 1954, 4284.

[8] Crowne, Green, Evans, and Long, *J.*, 1956, 4354.

The infrared and ultraviolet spectra of 5α-cholestan-1-one and the related compounds described above support the structures assigned; they are summarised in the annexed Table, which gives for comparison the corresponding values for 5α-cholestan-3-one and related compounds.

Although optical rotatory dispersion measurements in methanol–hydrochloric acid [9] show a considerable degree of steric retardation of the 1-keto-group by the adjacent axial angular methyl group, 5α-cholestan-1-one (VII) gives a 2,4-dinitrophenylhydrazone [10] and under forcing conditions gives a single ketoxime in 75% yield. The oxime (XIII) failed to undergo the Beckmann change under a variety of experimental conditions, and, surprisingly, by reduction with sodium–alcohol, lithium aluminium hydride in ether, or hydrogen–platinum in acetic acid, gave the same 1ξ-amino-5α-cholestane (XIV), characterised as the nicely crystalline acetyl derivative. Deamination of this base (XIV) in 50% aqueous acetic acid at 20° gave 5α-cholestan-1α-ol (XV) (40%) (identified by direct comparison and by its infrared absorption spectrum; unaccompanied by 5α-cholestan-1β-ol), together with an unsaturated hydrocarbon (60%), whose infrared [11] and ultraviolet [10] absorption spectra indicated a mixture of 5α-cholest-1-ene (XVI) and the more stable 5α-cholest-2-ene.[1,2,10-12]



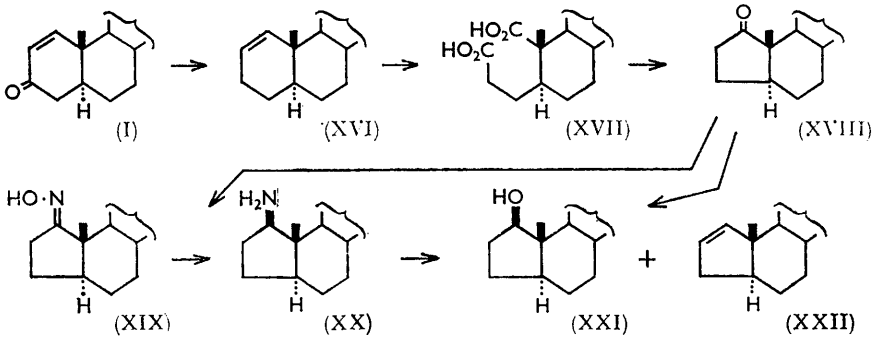
We have as yet been unable to prepare the 1-epimer of the base (XIV), so that the configuration of the amino-group is uncertain. It is known that rear-side α-attack is general in ring A; thus 5α-cholest-1-,[10] -2-,[13] -3-,[14] and -4-ene [15] afford α-epoxides; at $C_{(1)}$ there is additionally the steric influence of the adjacent angular β-methyl group, so that reduction of the π-component of the C=N linkage in the oxime (XIII) would be expected preferentially to furnish 1β-amino-5α-cholestane (as XIV; NH_2 equatorial). It must, however, be noted that reduction of 5α-cholestan-1-one by sodium and alcohol affords a mixture from which 5α-cholestan-1β-ol (OH equatorial) can be isolated in ~65% yield, although 5α-cholestan-1α-ol (XV; OH axial) predominates when lithium aluminium hydride is used.[1,2,10]

On the other hand, deamination of amino-steroids has been found [16] to be conformationally specific—equatorial amines react with retention of configuration to give the appropriate equatorial alcohols in nearly quantitative yield, whilst axial amines react, also with retention of configuration, to yield the appropriate axial alcohols accompanied by much unsaturated hydrocarbon. If this stereochemical pattern is carried over from positions 2, 3, 4, 6, and 7 to position 1, then deamination of the 1-amino-steroid (XIV) to give axial 5α-cholestan-1α-ol (XV) and 5α-cholest-1-ene (XVI) indicates that the base is 1α-amino-5α-cholestane (as XIV; NH_2 axial).

A-Nor-5α-cholestan-1-one (XVIII) has been prepared as follows. 5α-Cholest-1-ene (XVI), obtained from 5α-cholest-1-en-3-one (I) by reduction with lithium aluminium hydride to the 3β-alcohol, conversion of this into the 3β-chloride, and further reduction

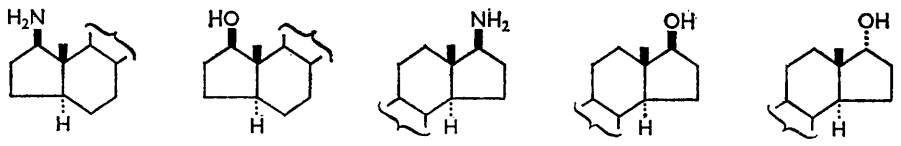
[9] Djerassi, personal communication; cf. Djerassi, Mitscher, and Mitscher, *J. Amer. Chem. Soc.*, 1959, **81**, 947.
[10] Henbest and Wilson, *J.*, 1956, 3289.
[11] Henbest, Meakins, and Wood, *J.*, 1954, 800.
[12] Turner, Meador, and Winkler, *J. Amer. Chem. Soc.*, 1957, **79**, 4122.
[13] Fürst and Plattner, *Helv. Chim. Acta*, 1949, **32**, 275.
[14] Fürst and Scotoni, *Helv. Chim. Acta*, 1953, **36**, 1332.
[15] Shoppee, Howden, Killick, and Summers, *J.*, 1959, 630.
[16] Shoppee, Evans, and Summers, *J.*, 1957, 97; Evans and Summers, *ibid.*, p. 906; Shoppee, Cremlyn, Evans, and Summers, *ibid.*, p. 4364.

with lithium aluminium hydride,[10] was ozonised and the resulting 1,2-seco-1,2-dialdehyde oxidised to 1,2-seco-5α-cholestane-1,2-dioic acid (XVII). Pyrolysis of the barium salt yielded A-nor-5α-cholestan-1-one (XVIII), m. p. 74—76°, $[\alpha]_D$ +16°, $\nu_{max.}$ 1740 cm.$^{-1}$.



The ketone (XVIII) was reduced by sodium in alcohol, lithium aluminium hydride in ether, or hydrogen–platinum in acetic acid, to a single alcohol, regarded as A-nor-5α-cholestan-1β-ol (XXI). The ketoxime (XIX) similarly, by reduction with sodium in pentanol, lithium aluminium hydride, or hydrogen–platinum, gave the non-crystalline base, 1β-amino-A-nor-5α-cholestane (XX) characterised as the acetyl derivative. Deamination of the base (XX) in 50% aqueous acetic acid at 20° gave 80% of A-nor-5α-cholestan-1β-ol (XXI) (identified by direct comparison and by its infrared absorption spectrum), accompanied by 20% of a non-crystalline unsaturated hydrocarbon, probably A-nor-5α-cholest-1-ene (XXII).

In the absence of any other criterion, the configurations assigned to the amine (XX) and the alcohol (XXI) are based on Klyne's [17] principle of enantiomeric types. The molecular rotatory contribution of the 1-hydroxyl group in (XXI) is opposite in sign to that of the hydroxyl group in 5α-androstan-17β-ol [5,18] (as XXIV) and of like sign to that



$[M]_D$	−14°	−19°	$[M]_D$	+24°	+36°	−22°
$[M]_D$ A-nor-5α-cholestane	+90	+90	$[M]_D$ 5α-androstane	+2	+2	+2
$\Delta[M]_D$	−104	−109	$\Delta[M]_D$	+22	+34	−24

of the hydroxyl group in 5α-androstan-17α-ol [18] (as XXV); similarly, the molecular rotatory contribution of the 1-amino-group in (XX) is opposite in sign to that of the amino-group in 17β-amino-5α-androstane [19] (XXIII). Approximate correspondences in magnitude are not to be expected, since the rotatory contribution of the 1-keto-group in A-nor-5α-cholestan-1-one (XVIII) is only −53° whereas that of the enantiomeric 17-keto-group in 5α-androstan-17-one is +266°.

It appears that deamination of the 1β-amine (XX) proceeds with retention of configuration accompanied by elimination. This agrees with the prediction [19] that 1β-substituted A-norsteroids should possess equatorial character in the same way as 17β-substituted steroids. It should be noted, however, that deamination of 17β-amino-5α-androstane (as

[17] Klyne, *J.*, 1952, 2916.
[18] Shoppee, *Chem. and Ind.*, 1950, 454.
[19] Shoppee and Sly, *J.*, 1959, 345.

XXIII) gives 5α-androstan-17β-ol (as XXIV) in high yield[19] unaccompanied by 5α-androst-16-ene.

Experimental

For general experimental directions see *J.*, 1959, 345. $[\alpha]_D$ refer to $CHCl_3$ solutions; ultraviolet absorption spectra were measured on a Hilger Uvispek spectrophotometer for EtOH solutions, and infrared absorption spectra on a Perkin–Elmer model 21 double-beam or on an Infracord instrument for CCl_4 solutions.

5α-Cholest-1-en-3-one (I).—2α-Bromo-5α-cholestan-3-one (m. p. 167—168°; 60 g.) was refluxed with *s*-collidine (200 ml.) in a current of dry nitrogen at 210° for 2 hr.; nitrogen was passed in for 0·5 hr. before heating and during cooling. The usual working up gave 5α-cholest-1-en-3-one (44 g., 95%), which crystallised spontaneously, and was purified by elution from aluminium oxide (1200 g.) with benzene–hexane (1 : 9 and 1 : 4; 16 × 500 ml.), and finally by recrystallisation from aqueous ethanol; it had m. p. 96—98°.

5α-Cholestane-1α,3α- and -1α,3β-diol (as III; R = H).—The above ketone (20 g.; m. p. 96—98°) by treatment with 30% hydrogen peroxide (68 ml.) and N-sodium hydroxide (200 ml.) in dioxan (800 ml.) at 20° for 20 hr. gave 1α,2α-epoxy-5α-cholestan-3-one (16 g.), m. p. 122—124° (from ethanol). The epoxide (16 g.) in ether (250 ml.) was treated with a suspension of lithium aluminium hydride (8 g.) during 30 min. After 3 hours' refluxing, isolation in the usual way gave the mixed diols (15·5 g.), which were chromatographed on aluminium oxide (500 g.) in hexane, 750 ml. portions of eluant being used. Elution with ether–benzene (1 : 9) gave fractions 1—16 containing unreduced epoxide (1·8 g.), whilst ether–benzene (1 : 4) gave fractions 17—21 consisting of epoxide and 1α,3α-diol (800 mg.); further use of ether–benzene (1 : 4) gave fractions 22—35, yielding 5α-cholestane-1α,3α-diol (4 g.) as needles, m. p. 209—211°, from ether–ethanol. Finally, use of chloroform–ether and methanol–chloroform gave fractions 36—41, affording 5α-cholestane-1α,3β-diol (8·8 g.) as prisms, m. p. 154—156°, from ethanol.

5α-Cholestane-1,3-dione (IV) [B.S.G.].—(*a*) 5α-Cholestane-1α,3α-diol (300 mg.), dissolved in acetone (50 c.c.) and a little ether, was stirred under nitrogen at 10° with a standard solution[4] of chromium trioxide in sulphuric acid (0·6 ml.). After 5 min., the green solution was diluted with water, and acetone removed at 12 mm.; extraction with ether, washing with water, drying, and evaporation gave *5α-cholestane-1,3-dione* (250 mg.) which had m. p. 174°, $[\alpha]_D$ +108° (*c*, 1·0), $\nu_{max.}$ 1695, 1725 cm.$^{-1}$, $\lambda_{max.}$ 256 mμ (log ε 4·1), after crystallisation from ether–pentane (Found: C, 81·0; H, 11·4. $C_{27}H_{44}O_2$ requires C, 80·9; H, 11·1%); it gave no colour with aqueous-alcoholic ferric chloride.

(*b*) 5α-Cholestane-1α,3β-diol (530 mg.), similarly oxidised, gave the 1,3-diketone (370 mg.), having m. p. and mixed m. p. 173° after chromatographic purification on Davison silica gel (45 g.) in hexane with elution with benzene–hexane (1 : 1).

3,3-Di(benzylthio)-5α-cholestan-1-one (VIII).—5α-Cholestane-1,3-dione (m. p. 172—174°; 110 mg.) was treated with toluene-ω-thiol (1 ml.) and 72% perchloric acid (2 drops) at 0° for 10 min. Ether-extraction and the usual working up gave *3,3-di(benzylthio)-5α-cholestan-1-one* (120 mg.), m. p. 145—147°, raised by recrystallisation from ethanol to m. p. 149—150°, $\nu_{max.}$ 1712 cm.$^{-1}$ (C=O) (Found: C, 77·8; H, 9·4. $C_{41}H_{58}OS_2$ requires C, 78·05; H, 9·7%).

5α-Cholestan-1-one (VII).—The mercaptal (VIII) (70 mg.) in ether (20 ml.) and ethanol (10 ml.) was treated with deactivated Raney nickel[2,5] at 80° for 3 hr. Filtration and evaporation of the filtrate gave a colourless oil (40 mg.), which was chromatographed on aluminium oxide (3 g.) prepared in pentane. Elution with ether–pentane (1 : 99) gave 5α-cholestan-1-one (20 mg.), m. p. and mixed m. p. 83—86°, $\nu_{max.}$ 1712 cm.$^{-1}$, after crystallisation from ether–methanol. Optical rotatory dispersion measurements, kindly made by Professor C. Djerassi, Stanford University, in methanol and methanol–hydrochloric acid at 29° show that the 1-carbonyl group is incapable of forming an acetal: $[\alpha]_{700}$ +65°, $[\alpha]_{589}$ +118°, $[\alpha]_{332}$ +388°, $[\alpha]_{317}$ +366°, $[\alpha]_{275}$ +1140° (shoulder), $[\alpha]_{250}$ +1511°, $[\alpha]_{240}$ +1780° (*c* 0·099 in methanol); and $[\alpha]_{700}$ +80°, $[\alpha]_{589}$ +112°, $[\alpha]_{332}$ +386°, $[\alpha]_{317}$ +362°, $[\alpha]_{275}$ +1115° (shoulder), $[\alpha]_{250}$ +1459°, $[\alpha]_{245}$ +1528° (*c* 0·099 in methanol–hydrochloric acid).

2α-Bromo-5α-cholestan-1-one (XI) *and 2,2-Dibromo-5α-cholestan-1-one* (X).—(*a*) 5α-Cholestan-1-one (150 mg.) in acetic acid (20 ml.) was treated with bromine (66 mg., 1·05 mol.) in acetic acid (2 ml.) and a few drops of a solution of hydrogen bromide in acetic acid at 20° for 16 hr. Water (10 ml.) was then added and after 12 hr. the crystals were collected, dried in a vacuum

(160 mg.), and chromatographed on Davison silica gel (15 g.; 100—200 mesh; W. R. Grace and Co., Baltimore, Maryland, U.S.A.) in pentane (b. p. 30—40°). Elution with ether–pentane (1 : 200; 3 × 100 ml.) gave *2,2-dibromo-5α-cholestan-1-one* (40 mg.), as needles (from chloroform–methanol), m. p. 165—167°, $[\alpha]_D$ +22° (*c* 0·65), $\nu_{max.}$ 1725 cm.$^{-1}$, $\lambda_{max.}$ 320 mμ, optical rotatory dispersion $[\alpha]_{900}$ +175°, $[\alpha]_{589}$ +221°, $[\alpha]_{345}$ −576°, $[\alpha]_{285}$ +2195°, $[\alpha]_{270}$ +1900° (*c* 0·057 in methanol at 27°) [Found (after drying at 20°/0·05 mm. for 5 hr.): C, 60·3; H, 8·15. $C_{27}H_{44}Br_2O$ requires C, 59·6; H, 8·1%]. Further elution with ether–pentane (1 : 150; 3 × 100 ml.) gave *2α-bromo-5α-cholestan-1-one* (70 mg.), plates (from chloroform–methanol), m. p. 154—156°, $[\alpha]_D$ +91° (*c* 0·8), $\nu_{max.}$ 1727 cm.$^{-1}$, $\lambda_{infl.}$ 292 mμ, optical rotatory dispersion $[\alpha]_{700}$ +79°, $[\alpha]_{589}$ +114·5°, $[\alpha]_{295}$ +726°, $[\alpha]_{265}$ +515°, $[\alpha]_{260}$ +408° (*c* 0·05 in dioxan at 25°) [Found (after drying at 20°/0·05 mm. for 5 hr.): C, 69·55; H, 9·75. $C_{27}H_{45}BrO$ requires C, 69·7; H, 9·75%]. Finally, elution with ether–pentane (1 : 200; 2 × 100 ml.) gave 5α-cholestan-1-one (20 mg.), m. p. and mixed m. p. 85·5° (from methanol).

(*b*) 5α-Cholestan-1-one (200 mg.) was similarly treated with bromine (5 mol.) in acetic acid at 20° for 5 days. The product (260 mg.) likewise was chromatographed on silica gel (30 g.) in pentane to give 2,2-dibromo-5α-cholestan-1-one (140 mg.), m. p. and mixed m. p. 165—167°, and 2α-bromo-5α-cholestan-1-one (90 mg.), m. p. and mixed m. p. 155—156°.

5α-Cholest-2-en-1-one (VI).—(*a*) 2α-Bromo-5α-cholestan-1-one (100 mg.) was refluxed with *s*-collidine (1 ml.) under nitrogen for 1 hr. The usual working up gave an oil (80 mg.), which was chromatographed on aluminium oxide (3 g.) in hexane. Elution with benzene–hexane (1 : 9) yielded 5α-cholest-2-en-1-one, having m. p. and mixed m. p. 68—69°, $[\alpha]_D$ +123° (*c* 0·8), $\nu_{max.}$ 1692 cm.$^{-1}$, $\lambda_{max.}$ 222 mμ (log ε 3·9), after crystallisation from methanol.

(*b*) 2-Bromo-5α-cholest-2-en-1-one (60 mg.) was refluxed with zinc dust in ethanol for 10 hr. Isolation of the product in the usual way and chromatography as under (*a*) gave 5α-cholest-2-en-1-one (40 mg.), m. p. and mixed m. p. 69° (from methanol).

2-Bromo-5α-cholest-2-en-1-one (XII).—2,2-Dibromo-5α-cholestan-1-one (30 mg.) was refluxed with *s*-collidine (0·5 ml.) for 10 min. under nitrogen, which was used to displace air before the reaction and during cooling of the mixture. The usual isolation procedure gave a solid (25 mg.), which by crystallisation from chloroform–methanol yielded *2-bromo-5α-cholest-2-en-1-one*, m. p. 123—125°, $[\alpha]_D$ +140° (*c*, 0·7), $\nu_{max.}$ 1700 cm.$^{-1}$, $\lambda_{max.}$ 254 mμ [Found (after drying at 15°/0·1 mm. for 5 hr.): C, 69·95; H, 9·3. $C_{27}H_{43}BrO$ requires C, 70·0; H, 9·3%].

(*b*) 5α-Cholest-2-en-1-one (100 mg.) in ether (7 ml.) was treated dropwise with bromine (41·5 mg.) in acetic acid (1 ml.) at 0°. After being left overnight, the mixture was poured into water, and the ethereal extract worked up to give crude 2,3-dibromo-5α-cholestan-1-one (130 mg.); this was dissolved in ether–pentane (1 : 9) and filtered through a column of aluminium oxide (5 g.), and the column was eluted with pentane to give 2-bromo-5α-cholest-2-en-1-one as plates (from chloroform–methanol), m. p. and mixed m. p. 123—125°, $\lambda_{max.}$ 254 mμ.

5α-Cholestan-1-one Oxime (XIII).—The ketone (2 g.) was refluxed with hydroxylamine hydrochloride (3 g.) and sodium acetate trihydrate (4 g.) in ethanol (70 ml.) for 4 hr. and isolated in the usual way. Recrystallisation from methanol gave the *oxime* (1·6 g.), m. p. 151—153° [Found (after drying at 80°/0·05 mm. for 4 hr.): C, 80·65; H, 11·1; N, 3·6. $C_{27}H_{47}NO$ requires C, 80·7; H, 11·45; N, 3·4%].

1ξ-Amino-5α-cholestane (XIV).—(*a*) The ketoxime (250 mg.) in refluxing pentanol (50 ml.) was saturated with sodium during 3 hr. After a further hour, the base was isolated by way of the ether-insoluble hydrochloride to give *1ξ-amino-5α-cholestane* as a hygroscopic oil (240 mg.), b. p. 170—180°/0·001 mm., $[\alpha]_D$ +90° (*c*, 0·6) (Found: C, 82·05; H, 12·1. $C_{27}H_{49}N,\frac{1}{2}H_2O$ requires C, 82·6; H, 12·6%), characterised as the *acetyl derivative* which had m. p. 218—220°, $[\alpha]_D$ +35° (*c*, 0·9), after recrystallisation from methanol [Found (after drying at 100°/0·05 mm. for 5 hr.): C, 80·9; H, 11·65; N, 3·25. $C_{29}H_{51}NO$ requires C, 81·05; H, 11·95; N, 3·25%]. Like the acetate of 5α-cholestan-1α-ol, which resisted prolonged heating with 3% methanolic potassium hydroxide and could only be hydrolysed by use of lithium aluminium hydride,[2] the acetyl derivative was resistant to acid and to alkaline hydrolysis.

(*b*) The ketoxime (100 mg.) in ether (30 ml.) was refluxed with an excess of lithium aluminium hydride for 4 hr. The above working up gave an oil, converted by acetic anhydride into 1ξ-acetamido-5α-cholestane, m. p. and mixed m. p. 218—220°.

(*c*) The ketoxime (100 mg.) was hydrogenated with platinum oxide (50 mg.) in acetic acid (20 ml.); after 3 hr. the base was isolated in the above way as an oil (100 mg.) converted by acetic anhydride into 1ξ-acetamido-5α-cholestane, m. p. and mixed m. p. 218—220°.

Deamination of the Base (XIV).—1ξ-Amino-5α-cholestane (200 mg.) in a mixture of 50% acetic acid and dioxan (1 : 1) was treated dropwise with a solution of sodium nitrite (500 mg.) in 50% acetic acid, with stirring at 20°. After 24 hr. the mixture was basified with 4N-sodium hydroxide, and the product, isolated in the usual way, refluxed with 5% methanolic potassium hydroxide for 0·5 hr. The product (200 mg.) was chromatographed on aluminium oxide (6 g.) in pentane. Elution with pentane gave a hydrocarbon (120 mg.), which did not crystallise satisfactorily but gave a yellow colour with tetranitromethane in chloroform and is probably 5α-cholest-1-ene mixed with 5α-cholest-2-ene. Further elution with benzene–hexane (1 : 2) gave 5α-cholestan-1α-ol (70 mg.), alone or mixed with a genuine specimen exhibiting the double m. p. 95°/105—106°,[1] $[\alpha]_D$ +36° (*c* 0·7) (after crystallisation from methanol); its infrared absorption spectrum was identical with that of the genuine specimen.

5α-*Cholest*-1-*ene* (XVI).—5α-Cholest-1-en-3-one (m. p. 96—98°; 20 g.) was reduced with lithium aluminium hydride in ether for 3 hr. to 5α-cholest-1-en-3β-ol (17 g.), m. p. 129—131° (from ethanol); this was converted with thionyl chloride in benzene at 20° into 3β-chloro-5α-cholest-1-ene (10·5 g.), m. p. 94—100° (from acetone), which on reduction with lithium aluminium hydride in ether for 16 hr. gave, after filtration through aluminium oxide in pentane and crystallisation from acetone, 5α-cholest-1-ene (6·5 g.), m. p. 65—69°. The hydrocarbon was purified by conversion into the 1α,2β-dibromide (7 g.), m. p. 132—134° (from ethyl methyl ketone), and regeneration with zinc dust in acetic acid; extraction with pentane and filtration of the extract through aluminium oxide gave 5α-cholest-1-ene (3·6 g.), having m. p. 69—70°, $[\alpha]_D$ +13° (*c* 0·9), after recrystallisation from acetone (cf. ref. 10).

1,2-*Seco*-5α-*cholestane*-1,2-*dioic Acid* (XVII).—A solution of 5α-cholest-1-ene (m. p. 69—70°; 10 g.) in pure chloroform (230 ml.) was ozonised at −10° for 2 hr.; water (5 ml.) was then added and chloroform removed at 30—40°/10 mm., to afford a colourless semi-solid product. Water (5 ml.) was added and the ozonide heated to 80° during 15 min.; the mixture was dissolved in acetone (600 ml.) and oxidised with a standard solution of chromium trioxide in sulphuric acid [4] (15 ml.) at 20° overnight. After removal of chromium sulphate by filtration and of acetone under reduced pressure, the residue was taken up in ether, and 1,2-seco-5α-cholestane-1,2-dioic acid (6 g.) isolated by four-fold extraction with 2N-sodium hydroxide, acidification with 2N-hydrochloric acid, and extraction with ether as a glass, m. p. 110—130°.

A-*Nor*-5α-*cholestan*-1-*one* (XVIII).—The 1,2-seco-diacid (XVII) (6 g.) in 60% ethanol was neutralised with vigorous stirring by N-potassium hydroxide (phenolphthalein), and barium chloride (4 g.) in water (25 ml.) was added. The barium salt was filtered off, washed with ethanol and with ether, dried, and pyrolysed at 400—450°/1 mm. for 4 hr. The distillate (3 g.) crystallised and was purified by chromatography on aluminium oxide (150 g.) in hexane. Elution with benzene–hexane (1 : 4; 10 × 100 ml.) and recrystallisation from methanol furnished A-*nor*-5α-*cholestan*-1-*one* (1 g.) as needles, m. p. 74—76°, $[\alpha]_D$ +16° (*c* 0·9), $\nu_{max.}$ 1740 cm.$^{-1}$ [Found (after drying at 20°/0·05 mm.): C, 83·85; H, 11·9. $C_{26}H_{44}O$ requires C, 83·8; H, 11·9%].

This gave its *oxime* (XIX), m. p. 170—172° (from ethanol) [Found (after drying at 80°/0·02 mm. for 4 hr.): C, 80·3; H, 11·8; N, 3·65. $C_{26}H_{45}NO$ requires C, 80·55; H, 11·7; N, 3·85%].

A-*Nor*-5-α-*cholestan*-1β-*ol* (XXI).—(*a*) A-Nor-5α-cholestan-1-one (75 mg.) was hydrogenated with platinum oxide (25 mg.) in acetic acid (7 ml.) during 2·5 hr. The product, isolated in the usual manner, was an oil (80 mg.), which was chromatographed on aluminium oxide (2·5 g.) in hexane. Elution with benzene–hexane (1 : 2, 3 × 25 ml.; and 1 : 1, 4 × 25 ml.) gave A-*nor*-5α-*cholestan*-1β-*ol* (60 mg.) as prisms, double m. p. 89—91°/101—103°, $[\alpha]_D$ −5° (*c* 0·7) (after crystallisation from methanol) [Found (after drying at 60°/0·05 mm. for 4 hr.): C, 83·4; H, 12·35. $C_{26}H_{46}O$ requires C, 83·4; H, 12·35%].

(*b*) The A-nor-ketone (100 mg.) was refluxed with lithium aluminium hydride (60 mg.) in ether (25 ml.) for 2 hr. The usual isolation procedure furnished an oil (95 mg.), which by chromatography as under (*a*) gave A-nor-5α-cholestan-1β-ol (70 mg.), double m. p. and mixed double m. p. 90—91°/101—103°, $[\alpha]_D$ −5° (*c* 0·8) (after crystallisation from methanol).

1β-*Amino*-A-*nor*-5α-*cholestane* (XX).—The ketoxime (XIX) (200 mg.) in refluxing pentanol was saturated with sodium during 3 hr.; after a further hour, the base was isolated in the usual way and through the ether-insoluble hydrochloride, to give 1β-*amino*-A-*nor*-5α-*cholestane*, b. p. 200—220°/0·15 mm., $[\alpha]_D$ −5° (*c* 0·9) (Found: C, 83·3; H, 12·4. $C_{26}H_{47}N$ requires C, 83·55; H, 12·6%), and converted with acetic anhydride into the *acetyl derivative*, m. p. 201°, $[\alpha]_D$ +33°

(*c* 0·8) (from aqueous ethanol) [Found (after drying at 80°/0·03 mm. for 5 hr.): C, 80·8; H, 11·85. $C_{28}H_{49}NO$ requires C, 80·7; H, 11·85%].

Reduction of the ketoxime with lithium aluminium hydride in ether or its hydrogenation with platinum oxide in acetic acid gave the same 1β-amine, characterised in each case as the acetyl derivative, m. p. and mixed m. p. 201°.

Deamination of the Base (XX).—1β-Amino-A-nor-5α-cholestane (100 mg.) in a mixture of 50% acetic acid and dioxan (1 : 1) was treated dropwise with stirring with sodium nitrite (250 mg.) in 50% acetic acid overnight at 20°. After basification with 4N-sodium hydroxide, the product was extracted with ether and refluxed with 5% methanolic potassium hydroxide for 0·5 hr. Chromatography of the product (95 mg.) on aluminium oxide (3 g.) in pentane, and elution with pentane, gave a hydrocarbon, probably A-nor-5α-cholest-1-ene (20 mg.), as an oil, giving a yellow colour with tetranitromethane in chloroform. Further elution with benzene–pentane (1 : 2 and 1 : 1) yielded A-nor-5α-cholestan-1β-ol (70 mg.), double m. p. and mixed double m. p. 90°/101—103° with the specimen prepared as above, $[\alpha]_D$ −5° (*c* 0·8), whose infrared absorption spectrum was identical with that of the earlier material.

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