517. *Reduction of* 5β-*Methyl*-3- *and* -6-*oxo*-19-*nor*-5β-*cholest*-9(10)-*enes by Metal Hydrides.*

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Reduction of 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3-one with sodium in ethanol and lithium aluminium hydride gave 5β-methyl-19-nor-5β-cholest-9(10)-ene-3α,6β- and-3β,6β-diol respectively. Similar reduction of 3β-methoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-6-one gave mainly the 6α-alcohol. The infrared spectra of 3β-methoxy-5-methyl-19-nor-5β-cholest-9(10)-ene and its derivatives, and treatment of 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3β-yl toluene-*p*-sulphonate with acetate are described.

Reduction of steroid ketones by lithium aluminium hydride or by sodium borohydride or related compounds generally produces almost exclusively one of the possible epimeric alcohols. This has been expressed in a rule,[1] which is an oversimplification, that sterically hindered and unhindered ketones on hydride reduction give mainly axial and equatorial alcohols respectively. The stereochemical outcome of hydride reduction on rigid structures of the steroid type certainly seems to be governed principally by steric effects coupled with size of the reagent, solvating power of the solvent, and temperature. Thus, recently [2,3] it has been postulated that the steric influence of neighbouring groups determines the direction of approach of the reagent to the carbonyl group and the relative stability of the equatorial and the axial intermediate transition complexes.[4] With "unhindered" ketones the reagent can approach with equal ease from either side, the intermediate

[1] Barton, *J.*, 1953, 1027.
[2] Dauben, Fonken, and Noyce, *J. Amer. Chem. Soc.*, 1956, **78**, 2579.
[3] Dauben, Blanz, Jiu, and Micheli, *ibid.*, p. 3752.
[4] See the criticisms of Hardy and Wicker, *ibid.*, 1958, **80**, 640.

complex adopts the more stable equatorial conformation (non-bonded interactions at a minimum), and the equatorial alcohol is furnished on hydrolysis. For " hindered " ketones the less stable axial complex may result if the energy of activation necessary to form the equatorial complex is considerable, owing to marked steric compression when the reagent approaches from the hindered side of the carbonyl group (compare the reduction of 3-keto- with that of 4-, 6-, and 11-keto-steroids). The greater selectivity shown by sodium borohydride and lithium tri-t-butoxyaluminium hydride and various analogues also clearly depends on the effective size of the reducing anion.[5] Moreover, these hydride reductions are considered to be bimolecular replacements so that steric factors should operate.[6]

To test further the influence of steric factors in reduction by metal hydrides and to obtain information about the stereochemistry of 5β-methyl-19-nor-5β-cholest-9(10)-ene-3β,6β-diol[7] (Westphalen's diol) (I; R = H) we have examined the reduction of its 3- and 6-oxo-derivatives.

Treatment of 3β,6β-diacetoxy-5β-methyl-19-nor-5β-cholest-9(10)-ene (I; R = Ac) with 0·26% methanolic potassium hydroxide for 35 minutes under reflux, furnished Westphalen's diol (I; R = H) (45%), the 6β-monoacetate (II) (24%), a mixture of (II) and the 3β-monoacetate (V) (25%), and some unchanged diacetate (6%). Under the conditions whereby 3β,6β-diacetoxycoprostane is partially hydrolysed to 6β-acetoxycoprostan-3β-ol,[8] Westphalen's diacetate is completely hydrolysed. Acetylation of the mixture of monoacetates (II and V) regenerated the diacetate (I; R = Ac), but chromatography of the mixture was difficult and the 3β-monoacetate (V) was obtained only in small yield. The same products were obtained by partial acetylation of the diol (I; R = H). The structure of 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3β-ol was confirmed by its conversion into the known 6β-acetoxy-3β-methoxy-5β-methyl-19-nor-5β-cholest-9(10)-ene[9,10] (III; R = Ac) by silver oxide in boiling methyl iodide. Hydrolysis of the 6β-acetate (III; R = Ac) gave the 6β-alcohol (III; R = H) which on oxidation with chromium trioxide in pyridine gave 3β-methoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-6-one[10] (IV). Similar oxidation of the 6β-monoacetate (II) yielded 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3-one (VI; R = Ac).

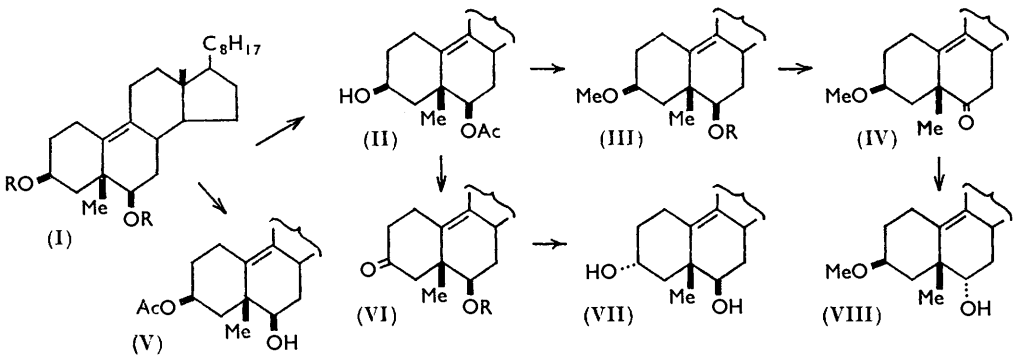
Reduction of 3β-methoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-6-one (IV) with sodium in ethanol or with lithium aluminium hydride gave only the 6α-alcohol (VIII). Sodium borohydride and sodium–ethanol reduced 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3-one (VI; R = Ac) exclusively to the 3β-alcohol (II; R = Ac) and mainly to the 3α,6β-diol (VII) respectively. Ellis and Petrow[11] also report reduction with lithium aluminium hydride of 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10),11-dien-3-one as giving the 3β-alcohol. These results contrast surprisingly with the findings[12] that metal hydrides reduce the corresponding 5β-cholestanones to alcohols of opposite configuration * but can be readily explained by an examination of the conformation of rings A and B in 5β-methyl-19-nor-5β-cholest-9(10)-ene-3β,6β-diol (I; R = H).

The stereochemistry of structural details in Westphalen's diol is to some extent still based on indirect evidence (cf. Ellis and Petrow[11]). Thus the 5-methyl group is assumed to be β-orientated and this is undoubtedly correct since the formation of the diacetate

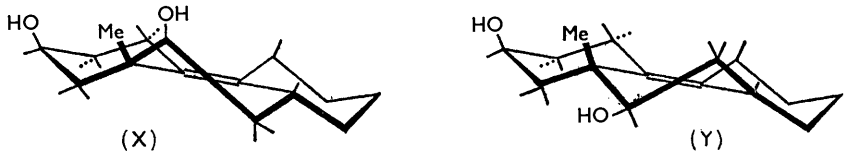
* Reduction of 17α-ethyl-17β-hydroxy-5α,10α-estran-3-one[30] by sodium borohydride to the 3β-alcohol appears to be the only example where an axial alcohol is formed predominantly by hydride reduction of a 3-keto-steroid.

[5] Wheeler and Mateos, *Canad. J. Chem.*, 1958, **36**, 1431.
[6] Trevoy and Brown, *J. Amer. Chem. Soc.*, 1949, **71**, 6675; Eliel, *ibid.*, p. 3970; Kenner and Murray, *J.*, 1950, 406.
[7] Westphalen, *Ber.*, 1915, **48**, 1064.
[8] Jones, Lewis, Shoppee, and Summers, *J.*, 1955, 2876.
[9] Davies and Petrow, *J.*, 1951, 2211.
[10] Shealy and Dodson, *J. Org. Chem.*, 1951, **16**, 1427.
[11] Ellis and Petrow, *J.*, 1952, 2246.
[12] Shoppee and Summers, *J.*, 1950, 687; Wheeler and Mateos, *Canad. J. Chem.*, 1958, **36**, 1049.

(I; R = Ac) by forced dehydration of 3β,6β-diacetoxy-5α-cholestan-5-ol involves 1,2-rearrangement with consequent inversion at the migration terminus $C_{(5)}$.[13] Additional evidence has recently been provided by Aebli, Grob, and Schumacher [14,15] who found that equilibration of 5β-methyl-19-nor-5β-cholest-9(10)-ene derivatives under acidic conditions



yielded the $\Delta^{9,11}$-isomers, which were shown to contain a *cis*-union of rings A and B. Therefore, the 3β- and the 6β-hydroxyl group in Westphalen's diol possess the axial conformation.



If ring B is assumed to have the more stable " half-chair " conformation [16] the molecule can be represented diagrammatically as either X or Y. Conformation Y may be excluded, since the above reduction studies indicate that the 6β-hydroxyl in this series is axial; in conformation Y it would be equatorial.

With respect to ring B the 5-methyl group and 8-hydrogen atom now adopt the quasi-equatorial and the quasiaxial conformation respectively. The 6-carbonyl group in 3β-methoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-6-one (IV) is subject to relatively little steric compression on the β-face [1,2-Me (quasiequatorial) and 1,3-H (quasiaxial) interactions], a consequence of the flattening of ring B by the 9(10)-double bond. On the other hand there is significant hindrance on the α-face due to the axial 7- and 4-hydrogen atoms (1,2 and 1,3-H interactions), and thus β-approach of the metal hydride ion is favoured. This also explains the ready hydrolysis of the 6β-acetoxy-group in the attempted partial hydrolysis described above. Formation of the axial 3β-alcohol indicates that the usual unhindered β-approach of the metal hydride ion to position 3 (cf. 5β-cholestan-3-one and its derivatives) is now impeded. The summation of steric interference to β-approach now amounts to two (1,3) interactions due to the axial 1-hydrogen atom and 5-methyl group and exceeds that of the α-face where hindrance is due to two (1,2-H) interactions.

It is informative to compare these observations with the reduction of some 6-keto-steroids, possessing different structural environments about $C_{(6)}$. 6-Keto-steroids of the A/B-*trans*-series are reduced by lithium aluminium hydride, predominantly by rear α-side attack, to the axial 6β-alcohol,[17] though similar reduction of the axial 7α-bromo-derivative

[13] de la Maere, *Ann. Reports*, 1950, **47**, 143.
[14] Aebli, Grob, and Schumacher, *Helv. Chim. Acta*, 1958, **41**, 774.
[15] Grob and Schumacher, *ibid.*, p. 924.
[16] Barton, Cookson, Klyne, and Shoppee, *Chem. and Ind.*, 1954, 21.
[17] Shoppee and Summers, *J.*, 1952, 3361.

yields the epimeric alcohols in approximately equal amounts.[18] In contrast 5α-cholest-4-en-6-one is exclusively reduced to 5α-cholest-4-en-6α-ol:[19,20] rings A and B in this ketone are considerably flattened by the presence of both the double bond, and the carbonyl group and carbon atoms 3—7 are coplanar. The 10-methyl group (quasiaxial) has now less retarding influence on the top β-side approach of the aluminohydride anion and in the absence of other steric factors the more thermodynamically stable, quasiequatorial alcohol is therefore formed.

In the A/B-*cis* series, where ring A protudes from the α-face of the molecule, the proximity of the α-orientated, axial C–H bonds at positions 4 and 7, and the 4,5-bond might be expected to impede approach of the aluminohydride ion from the rear α-side to such an extent as to reverse the result obtained with the A/B-*trans*-ketone. However, a model shows that a line perpendicular to the carbonyl linkage lies near the 10-methyl group but remote from the above axial bonds. Thus α-approach is subject to less steric retardation than β-approach, and again the 6β-axial alcohol should be the main product. This has been shown to be the case; reduction of 5β-cholestan-6-one,[20] 3β-substituted 5β-cholestan-6-ones,[24] and 6-oxo-5α-cholanic acid (preparation described later) gave the 6β-axial alcohol in quantitative yield. On the other hand 5β-hydroxy-5α-cholestan-6-one [20] on reduction gives the 5β,6α-diol exclusively, a result which can be best explained in terms of an intramolecular process brought about by $OAlH_3^-$ in the conformation (Z). A similar suggeston has been given by Klyne [22] for the conversion of 17α-hydroxy-20-ketones into 17α,20α-diols by lithium aluminium hydride. Similarly, the reduction of 5α-hydroxycholestan-6-one [20,21] and its derivatives gives the 5α,6β-diols.*

A comparison of the carbon–oxygen stretching frequencies of the methoxyl group in 3β-methoxy-5β-methyl-19-nor-5β-cholest-9(10)-enes and 3α- and 3β-methoxy-5β-cholestanes [23] confirms the axial conformation of the 3β-substituent in the former compounds (cf. Table)

C–O *stretching frequencies* (*cm.*$^{-1}$) *of the methoxyl group* (CS_2 *solutions*).

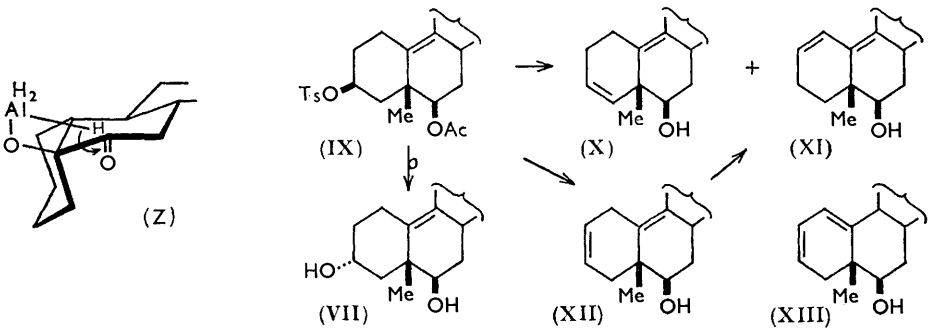
5β-Cholestane deriv.	ν	3β-Methoxy-5β-methyl-19-nor-5β-cholest-9(10)-ene deriv.	ν
3α-OMe	1100	6-One	1091
3β-OMe	1086	6β-OH and 6α-OH	1088
		6β-OAc and unsubst.	1089

Indirect evidence confirming the presence of the 9,10-double bond has been obtained from an investigation of 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3β-yl toluene-*p*-sulphonate (IX). The ester (IX) was formed only under forcing conditions, as with androstan-17β-ol [24] and 3α-chloro-5β-cholestan-6β-ol [25] where the hydroxyl groups are subject to considerable steric compression. The ester (IX) with potassium acetate in acetic acid at 95° yielded 5β-methyl-19-nor-5β-cholest-9(10)-ene-3α,6β-diol (VII) and an oil, $[\alpha]_D$ +128°, which from its analysis and elution characteristics appeared to be a monohydroxy-compound; it is undoubtedly produced by elimination of the 3β-toluene-*p*-sulphonate group and could be either the 3,9(10)-dien-6β-ol (X) or the 2,9(10)-dien-6β-ol (XII). Our experimental evidence favours formula (X). Thus the product showed ultraviolet absorption maxima at 208 (ε 7600), 237 (ε 980) and 254 mμ (ε 670) and was unchanged after brief treatment of the compound with hydrochloric acid in ethanol.

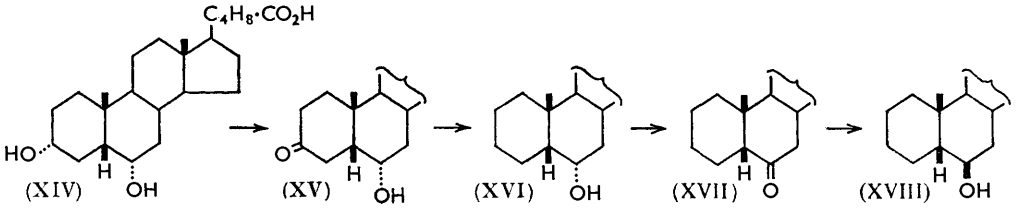
* Introduction of a 7,8-double bond does not alter this result. Lithium aluminium hydride reduces 3β-acetoxy-5α-hydroxy-ergosta-7,22-dien-6-one to ergosta-7,22-diene-3β,5α,6β-triol.

[18] Henbest and Wrigley, *J.*, 1957, 4596.
[19] Becker and Wallis, *J. Org. Chem.*, 1955, **20**, 353.
[20] Jones, Lewis, Shoppee, and Summers, *J.*, 1955, 2876.
[21] Reich, Walker, and Collins, *J. Org. Chem.*, 1951, **16**, 1753.
[22] Klyne, *Ciba Foundation Colloquia*, 1953, **7**, 127.
[23] Page, *J.*, 1955, 2017.
[24] Elks and Shoppee, *J.*, 1953, 241.
[25] Shoppee, Bridgwater, Jones, and Summers, *J.*, 1956, 2492.

The absorption band at 208 mμ indicated the presence of an unconjugated diene, which must be (X), since (XII) would isomerise to a conjugated diene (XI) or (XIII) under the experimental conditions. The extinction coefficient of an unconjugated diene containing an exocyclic double bond and an endocyclic double bond is of the order 9600—10,500; [26] the slightly lower value obtained indicates impurity in the material. The absorption



bands at 245 mμ, together with those of lower intensity at 237 and 254 mμ, are consistent with the presence of the heteroannular diene (XI). The value calculated by Woodward's methods [27] for the principal absorption band of 5β-methyl-19-nor-5β-cholest-1,9(10)-dien-6β-ol is 244 mμ, in agreement with the experimental value of 245 mμ. The extinction coefficient 980 corresponds to the presence of 4—6% of diene in the original mixture. These results confirm that the view the elimination product consists essentially of the 3,9(10)-diene (X).



6-Oxo-5β-cholanic was prepared as follows: Oxidation of hyodeoxycholic acid (XIV) with *N*-bromosuccinimide gave 6α-hydroxy-3-oxo-5β-cholanic acid (XV), previously obtained by partial hydrolysis of methyl diacetoxyhyodeoxycholate and oxidation of the resultant 6α-monoacetate with chromium trioxide.[28] Fieser and Rajagopalan [29] reported that the 3α-hydroxyl groups in cholic and deoxycholic acid are unaffected by *N*-bromosuccinimide in sodium hydrogen carbonate in acetone or acetic acid solution. Wolff–Kishner reduction of the acid (XV) gave 6α-hydroxy-5β-cholanic acid [28] (XVI) which with diazomethane gave an oily methyl ester, $[\alpha]_D$ +5°. Acid (XVI) with chromium trioxide in acetic acid furnished the known 6-oxo-5β-cholanic acid (XVII) which with sodium borohydride and then diazomethane yielded only methyl 6β-hydroxy-5β-cholanate (XVIII), m. p. 112—114°, $[\alpha]_D$ +52°.

Experimental

$[\alpha]_D$ refer to chloroform solutions.

Partial Hydrolysis of 3β,6β-*Diacetoxy*-5β-*methyl*-19-*nor*-5β-*cholest*-9(10)-*ene*.—The diacetate (4·35 g.) in methanol (1200 ml.) was treated with a cold solution of potassium hydroxide (4·5 g.)

[26] Dorfmann, *Chem. Rev.*, 1953, **53**, 47.
[27] Woodward, *J. Amer. Chem. Soc.*, 1942, **64**, 72.
[28] Hoehn, Linsk, and Moffett, *ibid.*, 1946, **68**, 1855.
[29] Fieser and Rajagopalan, *ibid.*, 1949, **71**, 3935.

in methanol (500 ml.). The solution was refluxed for 35 min., cooled, just acidified with concentrated hydrochloric acid, basified with ammonia, evaporated to small bulk in a vacuum, and worked up in the usual manner. The product, a colourless oil, was chromatographed on aluminium oxide (120 g.) prepared in pentane. Elution with benzene–pentane (1 : 1; 2 × 400 ml.) and benzene (2 × 400 ml.) gave unchanged starting material (244 mg.), m. p. and mixed m. p. 126—128° (from acetone–methanol). Elution with ether–benzene (1 : 4; 3 × 400 ml.) gave a solid (1·05 g.) which crystallized from acetone, to give 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3β-ol, m. p. 142—144°, $[\alpha]_D$ +89° (*c* 1·3) [Found (after drying at 80°/0·05 mm. for 4 hr.): C, 78·4; H, 11·1. Calc. for $C_{29}H_{48}O_3$: C, 78·3; H, 10·9%]. Aebli, Grob, and Schumacher [14] give m. p. 148—149°, $[\alpha]_D$ +89·2°. Further elution with ether–benzene (1 : 4, 2 × 400 ml.; and 1 : 1, 4 × 400 ml.) yielded a solid (1·1 g.; Fraction A), m. p. 135—160°, and elution with chloroform–methanol furnished 5β-methyl-19-nor-5β-cholest-9(10)-ene-3β,6β-diol, m. p. 80°, $[\alpha]_D$ at 118° (from acetone–methanol).

Fraction A was rechromatographed on aluminium oxide (30 g.). Elution with ether–benzene (1 : 9; 6 × 100 ml.) gave 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3β-ol, m. p. 143—146° (from acetone). Elution with ether–benzene (1 : 4, 4 × 100 ml.; and 1 : 1, 3 × 100 ml.) and crystallization from acetone furnished a solid, m. p. 133—138°, which with boiling acetic anhydride gave starting material. Further elution with ether–benzene (1 : 1; 4 × 100 ml.) gave a solid, m. p. 155—167° (343 mg.), which after four recrystallisations from acetone–methanol furnished 3β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-6β-ol as needles, m. p. 173—174°, $[\alpha]_D$ +113° (*c* 1·0) [Found (after sublimation at 150°/0·05 mm.): C, 78·2; H, 10·75. Calc. for $C_{29}H_{48}O_3$: C, 78·3; H, 10·9%]. Aebli, Grob, and Schumacher [14] give m. p. 169—170°, $[\alpha]_D$ +108·5°.

Partial Acetylation of 5β-*Methyl*-19-*nor*-5β-*cholest*-9(10)-*ene*-3β,6β-*diol*.—The diol (5·98 g.) in pyridine (33 ml.) was treated with acetic anhydride (1·5 ml.) for 14 hr. at 18°. Working up in the usual manner gave a brown oil which was chromatographed on aluminium oxide (180 g.) prepared in benzene. This led to diacetate (1 g.), 6β-monoacetate (1·08 g.), 3β-monoacetate (128 mg.), mixture of 3β- and 6β-monoacetates (1·97 g.), and diol (2·29 g.).

6β-*Acetoxy*-5β-*methyl*-19-*nor*-5β-*cholest*-9(10)*en*-3-*one*.—A solution of 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3β-ol (938 mg.) in pyridine (10 ml.) was added to chromium trioxide (950 mg.) in pyridine (10 ml.), and the mixture left for 12 hr. at 25°. The oily product was chromatographed on aluminium oxide (28 g.). Elution with pentane–benzene gave a colourless oil (583 mg.) which solidified under methanol in several days, to give 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3-one, double m. p. 55—58°, 78—80°, $[\alpha]_D$ +37° (*c* 1·1) [Found (after distillation at 185°/0·05 mm.): C, 77·9; H, 10·5. Calc. for $C_{29}H_{46}O_3$: C, 78·7; H, 10·5%]. Aebli, Grob, and Schumacher [14] give m. p. 79—80°, $[\alpha]_D$ +44°.

The ketone (329 mg.) in ether–methanol (1 : 1; 20 ml.) was treated with sodium borohydride (130 mg.) in methanol (4 ml.). After 2 hr. at 18°, the usual isolation furnished a product which on chromatography on aluminium oxide (10 g.) with elution by ether–benzene (1 : 9 and 1 : 4) gave 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3β-ol (243 mg.), m. p. and mixed m. p. 140—142° (from acetone).

5β-*Methyl*-19-*nor*-5β-*cholest*-9(10)-*ene*-3α,6β-*diol*.—Sodium (2 g.) was added to a solution of 6β-acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3-one (200 mg.) in boiling ethanol (30 ml.); after refluxing for 1·5 hr. the solution was poured into water and worked up in the usual way, to give an oil (155 mg.). With boiling acetic anhydride this gave a yellow oil which was chromatographed on aluminium oxide (5·5 g.). Elution with pentane (40 ml.) and pentane–benzene (1 : 4; 6 × 200 ml.) furnished a colourless oil (86 mg.) (fraction A). Elution with benzene (40 ml.) gave 3β,6β-diacetoxy-5β-methyl-19-nor-5β-cholest-9(10)-ene (20 mg.), m. p. and mixed m. p. 124—125° (from methanol).

Fraction A (73 mg.) was treated with lithium aluminium hydride in boiling ether for 30 min.; it gave a colourless oil (58 mg.) which was chromatographed on aluminium oxide (2 g.). Elution with benzene, ether, and methylene chloride furnished some oil (15 mg.), and elution with methylene chloride–methanol (4 : 1) gave 5β-*methyl*-19-*nor*-5β-*cholest*-9(10)-*ene*-3α,6β-*diol* (40 mg.) as an oil, $[\alpha]_D$ +100° (*c* 1·1) [Found (after distillation at 160°/0·05 mm.): C, 80·5; H, 11·3. $C_{27}H_{46}O_2$ requires C, 80·5; H, 11·5%].

6β-*Acetoxy*-3β-*methoxy*-5β-*methyl*-19-*nor*-5β-*cholest*-9(10)-*ene*.—6α-Acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3β-ol (220 mg.) was treated with silver oxide (220 mg.; freshly prepared), boiling methyl iodide (3·2 ml., freshly distilled). After 7 hr. the solution was filtered, ether was

added, and the whole washed with saturated sodium sulphite solution and then water, dried, and evaporated. The product crystallized from methanol to give needles, m. p. 118—120°. Treatment with lithium aluminium hydride in boiling ether gave 3β-methoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-6β-ol as needles, m. p. 107—108° (from methanol). Shealy and Dodson [10] give m. p. 107—107·5°, $[\alpha]_D$ +118·5°.

3β-Methoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-6-one.—3β-Methoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-6β-ol (460 mg.) in pyridine (4 ml.) was treated with chromium trioxide (460 mg.) in pyridine (4 ml.). After 17 hr. at 25°, the product was chromatographed on aluminium oxide (14 g.). Elution with benzene gave the 6-ketone as needles, m. p. 63—64° (152 mg.) (Shealy and Dodson [10] give m. p. 64·5—65·6°) (from acetone–methanol); elution with ether gave starting material (180 mg.).

3β-Methoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-6α-ol.—(*a*) 3β-Methoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-6-one (140 mg.) was treated with lithium aluminium hydride in boiling ether for 30 min. The product was chromatographed on aluminium oxide (4 g.). Elution with benzene and ether–benzene (15 eluates) furnished oils of [α] +20° and +24°. The product was *3β-methoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-6α-ol*, $[\alpha]_D$ +20° (*c* 1·5) [Found (after distillation at 165°/0·05 mm.): C, 80·7; H, 11·4. $C_{28}H_{48}O_2$ requires C, 80·7; H, 11·6%].

(*b*) The methoxy-ketone (1 g.) in ethanol (20 ml.) was refluxed with sodium (5 g.) for 2 hr. Isolation in the usual way gave an oil which was chromatographed on aluminium oxide (30 g.). Elution with ether (7 × 100 ml.) gave 3β-methoxy-5β-nor-5β-cholestan-9(10)-en-6α-ol as an oil, $[\alpha]_D$ +22° (*c* 1·1). The infrared spectra of eluates 1 and 7 and the specimen obtained in method (*a*) were identical.

6β-Acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3β-yl Toluene-p-sulphonate.—6β-Acetoxy-5β-methyl-19-nor-5β-cholest-9(10)-en-3β-ol (910 mg.) in pyridine (10 ml.) was treated with toluene-*p*-sulphonyl chloride (1 g.). After 18 hr. at 20° and 14 hr. at 34° the usual working up gave the *toluene*-p-*sulphonate* as needles, m. p. 130—132°, $[\alpha]_D$ +75° (*c* 1·1) (from acetone–methanol) [Found (after drying at 20°/0·05 mm. for 12 hr.): C, 72·2; H, 8·9. $C_{36}H_{54}O_5S$ requires C, 72·2; H, 9·1%].

The 3β-toluene-*p*-sulphonate (540 mg.) was refluxed with potassium acetate (6 g.) in acetic acid (25 ml.) for 3·25 hr. The oily product was treated with lithium aluminium hydride in boiling ether. The reduction product (348 mg.) was chromatographed on aluminium oxide (12 g.). Elution with benzene and ether–benzene furnished an oil (235 mg.), $[\alpha]_D$ +128° [Found (after distillation at 150°/0·05 mm.): C, 83·3; H, 11·3. Calc. for $C_{27}H_{44}O$: C, 84·3; H, 11·5%], $\lambda_{max.}$ 208 (ε 7600), 237 (ε 915), 245 (ε 980), and 254 mμ (ε 670). This consists of a mixture of 6β-hydroxy-5β-methyl-19-nor-5β-cholest-2,9(10)- and 3,9(10)-diene.

Elution with methanol–methylene chloride furnished 5β-methyl-19-nor-5β-cholest-9(10)-ene-3α,6β-diol as an oil, $[\alpha]_D$ +88° (*c* 1·0) [Found (after distillation at 160°/0·05 mm.): C, 80·5; H, 11·3. Calc. for $C_{27}H_{46}O_2$: C, 80·5; H, 11·5%].

6α-Hydroxy-3-oxo-5β-cholanic Acid.—Hyodeoxycholic acid (1 g.) in aqueous acetone (75 ml.) was treated with *N*-bromosuccinimide (1·2 g.) and left for 30 min. at 25°; the resultant gum, crystallized from ethyl acetate, gave 6α-hydroxy-3-oxo-5β-cholanic acid as prisms, m. p. 188—190°, $[\alpha]_D$ +17° (*c* 1·0). Hoehn, Linsk, and Moffett [28] give m. p. 196·5—198°, $[\alpha]_D$ +16°.

6α-Hydroxy-5β-cholanic Acid.—6α-Hydroxy-3-oxo-5β-cholanic acid (380 mg.) was refluxed with hydrazine (1·3 ml.) and potassium hydroxide (760 mg.) in ethanol for 30 min.; ethylene glycol (26 ml.) was added, aqueous ethanol removed by distillation, and the temperature raised to 196°. After 3 hr. the mixture was allowed to cool, poured into water, acidified with 2N-hydrochloric acid, and extracted with ether. The oil obtained was crystallized from acetone to furnish 6α-hydroxy-5β-cholanic acid as plates, m. p. 203—212°, $[\alpha]_D$ +10° (*c* 0·9 in dioxan) [Found (after sublimation at 180°/0·05 mm.): C, 76·6; H, 10·8. Calc. for $C_{24}H_{40}O_3$: C, 76·55; H, 10·7%]. Hoehn *et al.*[28] report m. p. 221—222°, $[\alpha]_D$ +8·5° (in dioxan). The methyl ester, prepared with diazomethane, was an oil, $[\alpha]_D$ +5°.

6-Oxo-5β-cholanic Acid.—6α-Hydroxy-5β-cholanic acid (342 mg.) in dioxan (5 ml.) and acetic acid (30 ml.) was treated with chromium trioxide (415 mg.) in acetic acid (25 ml.). After 14 hr. at 20°, the mixture was poured into water; the precipitate, after filtration and drying, crystallized from ether–pentane to give 6-oxo-5β-cholanic acid, m. p. 142—146°, $[\alpha]_D$ −39° (*c* 1·0 in dioxan). Hoehn *et al.*[28] report m. p. 138—140°, $[\alpha]_D$ −41·5° (in dioxan).

Methyl 6β-Hydroxy-5β-cholanate.—6-Oxo-5β-cholanic acid (104 mg.) in moist ether–methanol was treated with sodium borohydride (40 mg.). After 2·25 hr. at 20° the product was isolated

as an oil which was esterified with ethereal diazomethane. The oily product was chromatographed on neutral aluminium oxide (3 g.). Elution with ether–benzene (3 : 7) and crystallization from methanol furnished *methyl* 6β-*hydroxy*-5β-*cholanate* as needles, m. p. 112—114°, $[\alpha]_D$ +52° (*c* 0·4) [Found (after distillation at 120°/0·05 mm.): C, 77·3; H, 11·1. $C_{25}H_{42}O_3$ requires C, 76·9; H, 10·8%].

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