The Constitution of Conessine. Part VIII. Reaction of Cholesteryl Toluene-*p*-sulphonate with Liquid Ammonia.*

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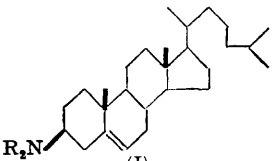
[Reprint Order No. 5914.]

The ammonolysis of cholesteryl toluene-*p*-sulphonate yields 3α-amino-cholest-5-ene and dicholesterylamines or isomers in addition to 3β-amino-cholest-5-ene and 6β-amino-3 : 5-*cyclo*cholestane which have already been described as products of the reaction.

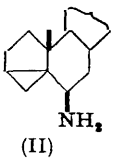
The reaction of cholesteryl toluene-*p*-sulphonate with liquid ammonia was first investigated by Julian, Magnani, Meyer, and Cole (*J. Amer. Chem. Soc.*, 1948, **70**, 1834) who obtained cholesterylamine, $C_{27}H_{47}N$ (I; R = H), and 6-amino-3 : 5-*cyclo*cholestane (II), the constitution of which was established by degradation to 3β-chlorocholestan-6-one. The same two products were obtained by Haworth, McKenna, and Powell (*J.*, 1953, 1110), together with a third base, m. p. 190°. Methylation of the mixture of amines left after separation of the 3 : 5-*cyclo*-base (II) yielded 3β-dimethylaminocholest-5-ene (I; R = Me)

* Part VII, *J.*, 1954, 967.

and an isomeric base, m. p. 70—71°; the same two methylated products were obtained from the reaction of cholesteryl toluene-*p*-sulphonate with dimethylamine. The constitution of the former, (I; R = Me), was firmly established by infra-red, ultra-violet, and optical rotation data, by Hofmann degradation to cholesta-3 : 5-diene (Haworth, McKenna, and Whitfield, *J.*, 1953, 1102; Favre, Haworth, McKenna, Powell and Whitfield, *ibid.*, p. 1115), and by hydrogenation to 3β-dimethylaminocholestane (III) (Dodgson and Haworth, *J.*, 1952, 167). This work was regarded as affording evidence for structure (I; R = H) for cholesterylamine, as the latter appeared to have yielded the dimethylamino-derivative (I; R = Me) on methylation, while the base of m. p. 190° was thought to correspond (after methylation) to the product of m. p. 70—71°. Further, on the basis



(I)



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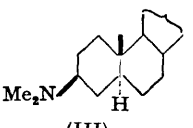
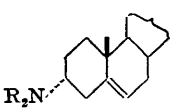


(III)

of Shoppee's generalisation (*J.*, 1946, 1147) it was thought unlikely that these new amines, and likewise a corresponding series encountered with a pregnane framework, carried an α-orientated basic group at $C_{(3)}$ (as in IV). The latter supposition appeared to be borne out by hydrogenation of the base, $C_{29}H_{51}N$, m. p. 70—71°; the product, $C_{29}H_{53}N$, m. p. 73—74°, was not identical with 3α- or 3β-dimethylaminocholestane, and from a further generalisation (quoted by, *inter alia*, Fieser and Fieser, "Natural Products related to Phenanthrene," Reinhold Publ. Corp., New York, 1949, p. 545) it was thought unlikely that hydrogenation of (IV; R = Me) would yield predominantly the coprostane derivative (V; R = Me). It appeared desirable, however, to re-examine the ammonolysis reaction and the bases of undetermined structure.

While this work was in progress, Šorm, Lábler, and Černý (*Chem. Listy*, 1953, **47**, 418) reported that the tertiary base, m. p. 73—74°, independently obtained by the method described above, was also formed on reaction of dimethylamine with coprostan-3β-yl toluene-*p*-sulphonate; the base, m. p. 73—74°, is thus 3α-dimethylaminocoprostane (V; R = Me), derived by hydrogenation of 3α-dimethylaminocholest-5-ene (IV; R = Me); a more detailed treatment of the stereochemistry of these and other steroidal amines has recently * (*Chem. Listy*, 1954, **48**, 1058) been given by the Czech authors. The Hofmann degradation of the base, m. p. 70—71°, to cholesta-3 : 5-diene previously described by Haworth, McKenna, and Powell (*loc. cit.*) is in accord with the formulation (IV; R = Me)



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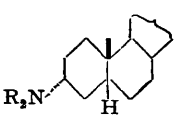

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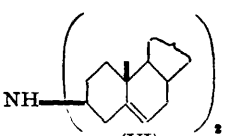

(VI)

and we have found that the infra-red (maxima at 796, 827, and 1660 $cm.^{-1}$; cf. Haworth, McKenna, and Whitfield, *loc. cit.*; Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402) and ultra-violet absorption ("end absorption" similar to that of 3β-dimethylaminocholest-5-ene; cf. Haworth, McKenna, and Whitfield, *loc. cit.*; Bladon, Henbest, and Wood, *J.*, 1952, 2737) and optical rotation ["Δ value" (Barton and Klyne, *Chem. and Ind.*, 1948, 755) of the unsaturated amine relative to 3α-dimethylaminocholestane is −223°, while the value for the epimeric 3β-dimethylaminocholest-5-ene relative to 3β-dimethylaminocholestane is −227°] support this structure. It thus appeared that in the reaction of cholesteryl toluene-*p*-sulphonate with ammonia (or dimethylamine) some inversion at $C_{(3)}$ occurred, and that hydrogenation of 3α-substituted Δ^5-steroids could

* In correspondence (June, 1953) Drs. Šorm and Lábler assigned structure (IV; R = Me) to the base, $C_{29}H_{51}N$, m. p. 70—71°, and kindly informed us that stereochemical considerations were not dealt with in their earlier paper as they were still working on this subject.

lead to A/B-*cis*-dihydro-derivatives predominantly. Examples of the formation of coprostanes by hydrogenation of 3α-substituted cholest-5-enes are given by Lewis and Shoppee (*Chem. and Ind.*, 1953, 897; 1954, 933).

Other examples of each phenomenon have recently been observed. Thus the reaction of cholesteryl toluene-*p*-sulphonate with diethyl sodiomalonate in boiling toluene yields some cholest-5-en-3α-yl-malonic ester in addition to the isomeric 3β- and 3 : 5-*cyclo*-compounds (Shoppee and Stephenson, *J.*, 1954, 2230; cf. Kaiser and Svarz, *J. Amer. Chem. Soc.*, 1949, **71**, 517, and earlier papers). The three reaction products of cholesteryl chloride with benzylamine were similarly formulated * by Vavasour, Bolker, and McKay (*Canad. J. Chem.*, 1952, **30**, 933); and we have recently established (unpublished work) that the reaction between pregn-5-en-3β-yl toluene-*p*-sulphonate and dimethylamine, and that between pregn-5 : 20-dien-3β-yl toluene-*p*-sulphonate and methylamine (Haworth, McKenna, and Powell, *loc. cit.*), also proceed with inversion, in the first instance virtually exclusively so.

In our re-examination of the products of the ammonolysis of cholesteryl toluene-*p*-sulphonate it was not found possible to repeat the preparation of the base, m. p. 190°; instead, a base $C_{54}H_{91}N$, m. p. 250° (decomp.), $[\alpha]_D$ −31°, of which the earlier product was probably an impure specimen, was obtained by chromatography or fractional crystallisation, together with an isomer, m. p. 172°, $[\alpha]_D$ −9°. These bases are probably isomeric dicholesterylamines (VI) (or perhaps one nucleus may have the 3 : 5-*cyclo*-structure); their formation is favoured by longer reaction times (up to 20 hours at 95°). Fractions, m. p. *ca.* 90°, also obtained by chromatography of the ammonolysis mixtures appeared to consist essentially of 3α- and/or 3β-aminocholest-5-ene. Direct isolation of pure samples of these epimeric bases proved difficult, but their *N*-acetyl derivatives were easily separated by fractional crystallisation. 3β-Acetamidocholest-5-ene readily yielded cholesterylamine (I; R = H) on hydrolysis with alcoholic potassium hydroxide; hydrolysis of the 3α-acetamido-epimer gave a basic oil which could not be crystallised but yielded 3α-dimethylaminocholest-5-ene (IV; R = Me) on methylation. Hydrogenation of 3α-acetamidocholest-5-ene did not yield predominantly the A/B-*cis*-dihydro-derivative as in the case of the related tertiary base; instead, 3α-acetamidocholestane was obtained, together with an approximately equal proportion of a second acetyl derivative, presumably 3α-acetamidocoprostane. 3α-Acetamidocholestane was prepared for comparison by acetylation of the ammonolysis product of cholestan-3β-yl toluene-*p*-sulphonate.

The epimeric 3-aminocholest-5-enes readily afforded *iso*propylidene derivatives on recrystallisation from acetone, which was somewhat unexpected. The infra-red absorption curve of neither derivative exhibited a band in the region characteristic of C=O stretching in non-conjugated ketones (*ca.* 1700—1750 cm.$^{-1}$) but a strong band which may be ascribed to C=N stretching (Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 227) rather than C=C stretching appeared in each case at 1660 cm.$^{-1}$. 3α- and 3β-*iso*Propylideneaminocholest-5-ene were readily converted into the appropriate acetamido- and dimethylamino-compounds. Hydrolysis with dilute hydrochloric acid gave the expected yield (*ca.* 70%, corresponding to trial runs) of acetone (as 2 : 4-dinitrophenylhydrazone) and the corresponding primary amine. Only by this procedure have we been able to obtain pure samples of 3α-aminocholest-5-ene (IV; R = H).

6β-Amino-3 : 5-*cyclo*cholestane (II) was isolated as before (Julian, Magnani, Meyer, and Cole, *loc. cit.*; Haworth, McKenna, and Powell, *loc. cit.*) from the ammonolysis mixtures; the melting point (85°) is higher than was previously recorded (77—79°). The ratio of 3 : 5-*cyclo*-amine to total bases formed by ammonolysis varied to some extent with the conditions : lower temperatures or shorter heating gave more *cyclo*-base. The stereochemical orientation at $C_{(6)}$ of this amine has not been determined by previous workers,

* Professor C. W. Shoppee has kindly sent us the MSS. of two papers; in one it is conclusively demonstrated that some inversion at $C_{(3)}$ takes place in this reaction, and additional evidence is presented on some allied substitutions at $C_{(3)}$ likewise accompanied by inversion. In the second paper is described the preparation of cholesterylamine by degradation of the corresponding carboxylic acid, a synthesis which furnishes additional evidence of stereochemical configuration of the amine (I; R = H).

but from analogy with similar rearrangement products (Shoppee and Summers, *J.*, 1952, 3361) it may be assigned the β-configuration as in (II). Methylation of the primary amine, $C_{27}H_{47}N$, with formaldehyde and formic acid yielded a basic oil, $[\alpha]_D$ +54°, from which a hydrochloride, $C_{29}H_{51}N,HCl,H_2O$, m. p. 166—167° (m. p. 206—207°, $[\alpha]_D$ +44°, when anhydrous) was prepared; this tertiary base is probably identical with an oily amine, $[\alpha]_D$ +61° (hydrochloride, m. p. 198°, $[\alpha]_D$ +45°) prepared by Šorm, Lábler, and Černý (*loc. cit.*) from cholesteryl toluene-*p*-sulphonate and dimethylamine and ascribed a 3 : 5-*cyclo*-structure by them. Some cholesterol was also isolated from the methylation mixture. Treatment of the tertiary base in acetone with methyl iodide yielded cholesteryl iodide and tetramethylammonium iodide in addition to the expected quaternary salt; the last-named product, however, was unaffected when heated in acetone with or without addition of methyl iodide.

The alkaloid conessine has a 5 : 6-double bond and it seems likely (Haworth, McKenna, and Whitfield, *loc. cit.*) that the acetic–sulphuric acid conversion into the isomer *neo*-conessine involves this unsaturated centre. Attempts were therefore made to isomerise 3β-dimethylaminocholest-5-ene by similar treatment, but complications were introduced by the low solubility of this base in the acid medium, and no definite product was isolated.

Experimental

Specific rotations were determined in $CHCl_3$.

Ammonolysis of Cholesteryl Toluene-p-*sulphonate.*—The ester was heated for 5—20 hr. at 90—95° with a large excess of liquid ammonia, and the basic reaction products were separated as previously described (Julian, Magnani, Meyer, and Cole, *loc. cit.*; Haworth, McKenna, and Powell, *loc. cit.*) into two fractions with hydrochlorides respectively soluble and insoluble in ether.

Base, m. p. 250°, *and Isomer, m. p.* 172°.—Mixed bases from hydrochlorides (5·3 g.) insoluble in ether, from an ammonolysis which had proceeded for 15 hr. at 95°, were chromatographed on alumina (Spence's Type H activated at 160° for 10 min.; 100 g.); on elution with light petroleum (b. p. 40—60°) a fraction (1 g.), m. p. 170—235°, was obtained, which on recrystallisation from the same solvent yielded a *base* as colourless needles (0·2 g.), m. p. 250° (decomp.), $[\alpha]_D$ −31° (*c*, 2·5) [Found: C, 86·0; H, 12·2; N, 2·1%; *M* (Rast), 753. $C_{54}H_{91}N$ requires C, 86·1; H, 12·1; N, 1·9%; *M*, 753]. Further elution with ether–chloroform gave a waxy solid (3·3 g.), m. p. 90—98° with previous softening; this fraction (epimeric 3-amines) resisted further attempts at direct purification. The mother-liquors from recrystallisation of the base, m. p. 250°, yielded an isomeric *base* as colourless needles (0·25 g.), m. p. (from methanol) 168—170°, raised to 172°, $[\alpha]_D$ −9° (*c*, 1·8), on further recrystallisation [Found: C, 85·8; H, 12·1; N, 1·9%; *M* (Rast), 765]. This amine was occasionally obtained from early chromatographic fractions and, like the isomer of m. p. 250°, was also isolated by fractional crystallisation of the total ether-insoluble hydrochlorides from methanol, in which the hydrochlorides of the higher-melting C_{54} amines were least soluble.

Treatment of the base, m. p. 250°, with boiling acetic anhydride gave an N-*acetyl* derivative, which separated from acetone in small colourless needles, m. p. 179° (Found: C, 83·6; H, 11·7. $C_{56}H_{93}ON$ requires C, 84·5; H, 11·7%). Methylation of the base (50 mg.) with formic acid (90%; 1 c.c.) and formaldehyde (40%; 1 c.c.) for 7·5 hr. at 100° yielded the N-*methyl* derivative as an oil (53 mg.) which on crystallisation from ether–acetone formed colourless prismatic needles, m. p. 159°, $[\alpha]_D$ −37° (*c*, 2·4) (Found: C, 85·7; H, 12·3; N, 1·8. $C_{55}H_{93}N$ requires C, 86·0; H, 12·1; N, 1·8%). Treatment of the base, m. p. 250° (43 mg.), in ether (20 c.c.) with N-hydrochloric acid (10 c.c.) and sodium nitrite (0·5 g.) for 7 hr. at 0° gave a product (8 mg.), colourless needles (from ether), m. p. 260° (depressed to 232—236° on admixture with the original amine), which gave a positive Liebermann nitroso-reaction.

The amine, m. p. 172°, described above yielded an N-*methyl* derivative, colourless plates (from ether–methanol), m. p. 186°, depressed to 169° on admixture with the base of m. p. 172° (Found: N, 1·7. $C_{55}H_{93}N$ requires N, 1·8%).

N-iso*Propylidene Derivatives of Epimeric* 3-*Aminocholest-5-enes from Ammonolysis Mixture.*—Bases (2 g.) with ether-insoluble hydrochlorides, from an ammonolysis which had proceeded for 5 hr. at 90°, on fractional crystallisation from acetone yielded successively crude C_{54} amine (50 mg.), m. p. 248—250° (decomp.), 3β-iso*propylideneaminocholest-5-ene* in colourless needles (0·35 g.), m. p. 136—138° raised to m. p. 140° on further recrystallisation, $[\alpha]_D$ −33° (*c*, 3·6) (Found: C, 84·4; H, 11·7; N, 3·7. $C_{30}H_{51}N$ requires C, 84·7; H, 12·0; N, 3·3%), and

3α-iso*propylideneaminocholest-5-ene* in colourless prisms (0·8 g.), m. p. 80—94° raised to m. p. 96° on further recrystallisation, $[\alpha]_D$ +7° (*c*, 3·7) (Found: C, 84·3; H, 11·7; N, 3·3%).

3β-*iso*Propylideneaminocholest-5-ene and the derived 3β-aminocholest-5-ene described below, but not the 3α-epimers, readily yielded precipitates with digitonin in alcohol. Acetylation and methylation of the 3β-*iso*propylidene derivative gave respectively 3β-acetamidocholest-5-ene, colourless plates (from methanol), m. p. 238°, undepressed on admixture with a sample obtained as described below, and 3β-dimethylaminocholest-5-ene, colourless needles (from acetone), m. p. and mixed m. p. 148°. Similar treatment of 3α-*iso*propylideneaminocholest-5-ene yielded 3α-acetamido-, colourless needles (from acetone), m. p. 180°, and 3α-dimethylamino-cholest-5-ene, colourless plates (from acetone), m. p. 68°, both undepressed on admixture with authentic specimens.

Epimeric 3-Acetamidocholest-5-enes from Ammonolysis Mixture.—Bases (2 g.) with ether-insoluble hydrochlorides from an ammonolysis (which had run for 7 hr. at 90°) in ether (5 c.c.) were treated with acetone (50 c.c.), the insoluble crude C_{54} amines were separated, and the residue was treated with boiling acetic anhydride for 10 min. Fractional crystallisation of the product (1·0 g.) from methanol gave 3β-acetamidocholest-5-ene as colourless plates (0·15 g.), m. p. 236—238° raised to m. p. 240—241° on further recrystallisation (Windaus and Adamla, *loc. cit.*, give m. p. 243—244°; Julian, Magnani, Meyer, and Cole, *loc. cit.*, give m. p. 238—242°), $[\alpha]_D$ −43° (*c*, 3·5). The mother-liquors yielded 3α-acetamidocholest-5-ene as colourless needles, (0·6 g.), m. p. 160—170° raised to m. p. 184° on recrystallisation from acetone, $[\alpha]_D$ −53° (*c*, 4·7) (Found: C, 81·1; H, 11·7; N, 3·3. Calc. for $C_{29}H_{49}ON$: C, 81·5; H, 11·5; N, 3·3%). Vavasour, Bolker, and McKay (*loc. cit.*) give m. p. 188—189°.

3β-*Aminocholest-5-ene.*—(*a*) 3β-*iso*Propylideneaminocholest-5-ene (59 mg.) was treated under reflux with 2N-hydrochloric acid (20 c.c.) for 1 hr.; steam-distillation then yielded acetone [2 : 4-dinitrophenylhydrazone (22 mg., 68%), m. p. and mixed m. p. 120—122°]. In a trial run at similar concentrations, 71% of acetone was recovered as 2 : 4-dinitrophenylhydrazone. The basic product (37 mg.) from the hydrolysis mixture was recrystallised from methanol and distilled at 140° (bath)/0·01 mm., and the 3β-aminocholest-5-ene obtained as colourless needles, m. p. 96°, $[\alpha]_D$ −34° (*c*, 2·7) (Found: N, 3·5. Calc. for $C_{27}H_{47}N$: N, 3·6%). The m. p. rose to 100—160° after the base had been kept for some time in a stoppered tube. Windaus and Adamla (*loc. cit.*) record m. p. 98° for this base, and Julian, Magnani, Meyer, and Cole (*loc. cit.*) give m. p. 89—94°, $[\alpha]_D$ −26°. Acetylation and methylation gave the acetyl and dimethyl derivative, m. p. 234—235° and 147—148° respectively.

(*b*) 3β-Acetamidocholest-5-ene (100 mg.) was treated with ethanolic potassium hydroxide (20%; 10 c.c.) for 27 hr. at 140°, and the basic reaction product crystallised from methanol. The colourless needles of 3β-aminocholest-5-ene had m. p. 92—94°.

3α-*Aminocholest-5-ene.*—3α-*iso*Propylideneaminocholest-5-ene (44 mg.) was hydrolysed by the method described above, yielding acetone (74% as 2 : 4-dinitrophenylhydrazone) and 3α-*aminocholest-5-ene* (32 mg.), colourless needles [on sublimation at 160° (bath)/0·01 mm.], m. p. 100—101°, $[\alpha]_D$ −44° (*c*, 2·8) (Found: N, 3·6. $C_{27}H_{47}N$ requires N, 3·6%), which was conveniently purified through the *hydrochloride*, colourless plates from methanol–ether, m. p. 288—290° (Found: Cl, 8·2. $C_{27}H_{47}N,HCl$ requires Cl, 8·4%). Vavasour, Bolker, and McKay (*loc cit.*) give m. p. 220—230° for this salt. On admixture of the amine, m. p. 100—101°, with the *iso*propylidene derivative, m. p. 96°, the mixed m. p. was 80—92°. After being kept for some time in a stoppered tube, the base had m. p. 96—110°. Acetylation and methylation of the base gave the acetyl and dimethyl derivatives, m. p. 180—182° and 67—69° respectively.

Hydrogenation of 3α-Acetamidocholest-5-ene.—The acetyl compound (87 mg.) in acetic acid (5 c.c.) was hydrogenated in presence of 15% palladised charcoal (60 mg.) (uptake at 27°/730 mm., 7·1 c.c. Calc. for one double bond, 5·2 c.c.). Fractional crystallisation of the product from ether gave colourless needles (30 mg.) of 3α-acetamidocholestane, m. p. 213—214° undepressed on admixture with an authentic specimen prepared as described below, and colourless needles (40 mg.) of an *isomer*, m. p. 180—181° (Found: C, 81·0; H, 11·8; N, 3·3. $C_{29}H_{51}ON$ requires C, 81·1; H, 11·9; N, 3·3%) depressed to 160—174° on admixture with 3α-acetamidocholest-5-ene, m. p. 184°.

3α-*Acetamidocholestane.*—Cholestan-3β-yl toluene-*p*-sulphonate (Stoll, *Z. physiol. Chem.*, 1932, **207**, 147) (500 mg.) was heated with excess of liquid ammonia for 10 hr. at 90°; the basic reaction product on acetylation gave 3α-acetamidocholestane (140 mg.) which separated from acetone in colourless needles, m. p. 215—216°, $[\alpha]_D$ +33° (*c*, 1·3) (Found: C, 80·9; H, 11·8; N, 2·9%).

Methylation of 6β-*Amino*-3 : 5-cyclo*cholestane.*—Ether-soluble hydrochlorides from the

ammonolysis of cholesteryl toluene-*p*-sulphonate yielded on basification the primary 3 : 5-*cyclo*amine, colourless needles (from pentane), m. p. 84—85°, $[\alpha]_D$ +36° (*c*, 5·5) (Found : C, 84·1; H, 12·3; N, 3·2. Calc. for $C_{27}H_{47}N$: C, 84·2; H, 12·2; N, 3·6%). Julian, Magnani, Meyer, and Cole (*loc. cit.*) give m. p. 77—79°, $[\alpha]_D$ +34°. Methylation of the primary amine (1 g.) with formaldehyde and formic acid in the usual way yielded an oil (1·1 g.), $[\alpha]_D$ +37°, which was chromatographed in light petroleum (b. p. 40—60°; 25 c.c.) on alumina (Spence's Type H neutralised with ethyl acetate, washed with water, and reactivated at 240°; 16·5 g.). A basic oil (0·8 g.), $[\alpha]_D$ +48°, was obtained, followed by colourless needles (0·09 g.), m. p. 120—132°, raised to 146—147° on recrystallisation from methanol and undepressed on admixture with cholesterol; for further characterisation the acetate was prepared; it had m. p. 112—113°, undepressed on admixture with cholesteryl acetate. The basic oil was purified by further chromatography until the $[\alpha]_D$ value was +51°, and then converted into the hydrated *hydrochloride*, colourless rods (from acetone), m. p. 166—167° (rapid heating) (Found : C, 74·5; H, 11·8. $C_{29}H_{51}N,HCl,H_2O$ requires C, 74·4; H, 11·6%), m. p. 206—207° (slow heating, or after drying at 60—80°/0·05 mm. over P_2O_5), $[\alpha]_D$ +44° (*c*, 2·6) [Found (in anhydrous salt) : C, 77·6 H, 11·7 N, 2·8; Cl, 7·5. Calc. for $C_{29}H_{51}N,HCl$: C, 77·4; H, 11·6; N, 3·1; Cl, 7·9%]. The 6β-dimethylamino-3 : 5-*cyclo*cholestane on recovery from the hydrochloride had b. p. 164—166°/0·05 mm., $[\alpha]_D$ +54° (*c*, 1·3). This base (75 mg.) in dry acetone (10 c.c.) was refluxed with dry methyl iodide (5 c.c.) for 3·5 hr., the solvents were evaporated, and the residue was extracted with ether (25 c.c.); the extract yielded cholesteryl iodide (20 mg.), colourless rods (from acetone), m. p. 104·5—105° (Found : C, 65·3; H, 9·0; I, 25·3. Calc. for $C_{27}H_{45}I$: C, 65·3; H, 9·1; I, 25·6%) undepressed on admixture with a specimen prepared by the method of Burckhardt, Helferich, and Günther (*Ber.*, 1939, **72**, 338). The residue from the methylation, after extraction with ether, was separated by trituration with acetone (10 c.c.) into a residue of tetramethylammonium iodide (15 mg.) which sublimed with some decomposition at 340°/760 mm. (Found : I, 63·2. Calc. for $C_4H_{12}NI$: I, 63·2%) and was converted into the picrate, m. p. 321° (Found : N, 18·3. Calc. for $C_{10}H_{14}O_7N_4$: N, 18·6%) (Kohn and Grauer, *Monatsh.*, 1913, **34**, 1751, give m. p. 318—320°), and *6β-dimethylamino-3* : 5-cyclo*cholestane methiodide*, colourless needles (from acetone), m. p. 206—207° (Found : C, 64·5; H, 9·7; N, 2·5; I, 22·3. $C_{30}H_{54}NI$ requires C, 64·9; H, 9·7; N, 2·5; I, 22·9%).

We thank the Department of Scientific and Industrial Research for a maintenance allowance (to L. H. C. L.), and Imperial Chemical Industries Limited for a grant towards the expenses of the investigation.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, November 25th*, 1954.]