17. *Steroids and Walden Inversion. Part XXXVI.* The Mechanism of Deamination.*

By C. W. Shoppee, D. E. Evans, and G. H. R. Summers.

Deamination in aqueous acetic acid of saturated steroid equatorial amines yields the appropriate equatorial alcohols with retention of configuration, in quantitative yields; this behaviour corresponds exactly with that of the equatorial amines 1-amino-*trans-trans*-decalin and 2-amino-*cis-trans*-decalin.

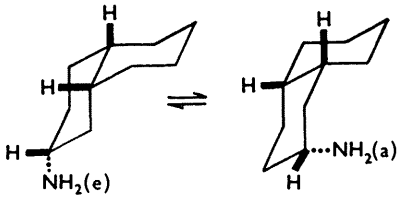
Deamination of saturated steroid axial amines affords the appropriate axial alcohols with retention of configuration, unaccompanied by the epimeric alcohols, but accompanied by much elimination, the olefins so formed conforming, not to the Hofmann rule, but to the Saytzeff rule. This behaviour is the reverse of that of the axial amines 1-amino-*cis-trans*-decalin and 2-amino-*trans-trans*-decalin which undergo substitution mainly with inversion.

Simple acyclic primary amines have been shown by Hughes, Ingold, and their co-workers [1] by configurational and kinetic studies to undergo deamination through the formation of a diazonium ion; this decomposes by an S_Ni process involving a carbonium ion to afford, by racemisation and some inversion, an alcohol of predominantly inverted configuration together with unsaturated hydrocarbons:

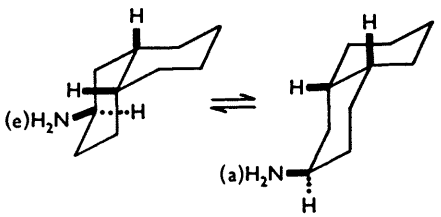
$$\text{L-R·NH}_2 + \text{HNO}_2 \longrightarrow \text{L-R·NH·NO} \longrightarrow \text{L-R·}\overset{+}{\text{N}}\equiv\text{N} \longrightarrow \overset{+}{\text{R}} \longrightarrow \text{D-ROH} + \text{DL-ROH} + \text{Olefins}$$

The deamination of alicyclic primary amines does not follow this simple pattern. In the *cyclo*pentane series both epimeric amines are deaminated with inversion accompanied by elimination,[2] but in the *cyclo*hexane series one epimeric amine is deaminated with predominant retention of configuration, whilst the other reacts with predominant inversion of configuration, and much elimination.[3, 4, 5] Mills [6] and Bose,[7] and subsequently Dauben *et al.*,[8] have shown that deamination of amino*cyclo*hexanes, aminodecalins, and the 4- and 5-amino-*cis*-indanes is conformationally specific; equatorial amino-groups react with retention of configuration, whilst axial amino-groups react with inversion of configuration and with elimination.

The flexibility of the *cyclo*hexane and *cis*-decalin ring systems allows a substituent to assume either an equatorial or an axial conformation:



2-Amino-*cis-cis*-decalin †



2-Amino-*trans-cis*-decalin †

* Part XXXV, *J.*, 1956, 4821.

† Each structure represents one of a pair of stereoisomers.

[1] Brewster, Hiron, Hughes, Ingold, and Rao, *Nature*, 1950, **166**, 178; Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell & Son, Ltd., London, 1953, pp. 396 *et seq.*

[2] Hückel, Gross, and Doll, *Rec. Trav. chim.*, 1938, **57**, 555; Hückel and Kupka, *Chem. Ber.*, 1956, **89**, 1694.

[3] Read, Cook, and Shannon, *J.*, 1926, 2223; Read and Robertson, *J.*, 1927, 2168; Read and Walker, *J.*, 1934, 308; Johnston and Read, *J.*, 1935, 1138.

[4] Hückel, *Annalen*, 1938, **533**, 1.

[5] Claudon, *Bull. Soc. chim. France*, 1950, 627.

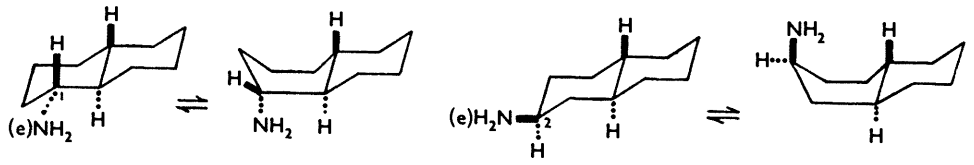
[6] Mills, *J.*, 1953, 260.

[7] Bose, *Experientia*, 1953, **9**, 256.

[8] Dauben, Tweit, and Mannerskantz, *J. Amer. Chem. Soc.*, 1954, **76**, 4420.

Mills [6] suggested that the existence of partial axial character, resulting from such interconversion, is indicated by deamination with partial inversion accompanied by elimination.

Mills [6] further suggested that deamination of a uniquely equatorial amino-group would occur with complete retention and without elimination, but stated that " the concept of a purely equatorial amino-group cannot at present be illustrated by examples." Such examples appear to be provided by the 1- and 2-amino-*trans*-decalins; * but *trans*-decalin has a rigid structure only if the possibility is excluded of conversion of a chair-form into a boat-form,[9] which transforms an equatorial amino-group into a quasi-axial amino-group:



Dr. Mills has informed us (letter of March 12th, 1956) that it was this possibility that led him to regard the 1- and the 2-amino-*trans*-decalins as incompletely equatorial in character, and so to make the statement cited above. Our results (see below) indicate that such partial quasi-axial character is probably not a factor in the stereochemical course of the deamination of 1- and 2-amino-*trans*-decalins as disclosed by the work of Hückel [4] and Dauben.[8] 1-Amino-*trans-trans*-decalin and 2-amino-*cis-trans*-decalin react to give alcohols with 100% retention of configuration; 1-amino-*cis-trans*-decalin and 2-amino-*trans-trans*-decalin react mainly with inversion (27%) but with some retention (3%), and with production of isomeric octalins (70%).

The rigidity of the accepted conformations of the steroid nucleus in coprostane and cholestane permits the preparation of amino-derivatives possessing purely equatorial or purely axial character. Examples are provided by the epimeric 6- and 7-amino-cholestanes, wherein double locking of ring B by rings A and C operates. We have therefore examined the stereochemical course of deamination of a series of epimeric steroid amines of established configuration. These deaminations are found partly to reproduce the conformational pattern characteristic of the amino*cyclo*hexanes and amino-*trans*-decalins, with one striking difference; whilst the equatorial steroid amines afford the appropriate equatorial alcohols in quantitative yield, the axial steroid amines react with ***retention*** of configuration to yield the appropriate axial alcohols, accompanied by elimination, which becomes exclusive at $C_{(6)}$ (see Table).

The preparation of the amines (I—IV), (VII), and (VIII), has been described and their configurations have been established by partial syntheses.[10, 11, 12] Cholestan-6β-ylamine (VI) was prepared by reduction of cholestan-6-one oxime and 6-nitrocholest-5-ene with lithium aluminium hydride, whilst reduction of the oxime with sodium and ethanol gave cholestan-6α-ylamine (V), identical with a base described by Vanghelovici and Vasiliu; [13] the configurations of the amines (V) and (VI), although evident from the methods of preparation, are supported by measurements of the basicities.[14] 3β-Hydroxycholestan-6β-ylamine (X) and its epimer (IX) [15] have been prepared similarly from 3β-acetoxycholestan-6-one and 3β-acetoxy-6-nitrocholest-5-ene.

It is of interest to compare these results with previous work, excluding from consideration the more complicated cases which involve the presence of reactive neighbouring

* The m. p.s 141° and 88° given by Mills [6] (p. 273, lines 22, 23) for the acetyl derivatives of 1- and 2-amino-*trans*-decalin relate to the *cis*-compounds. The correct figures [8] are: 1-acetamido-*trans-trans*-decalin, m. p. 182°, and 2-acetamido-*cis-trans*-decalin, m. p. 163°.

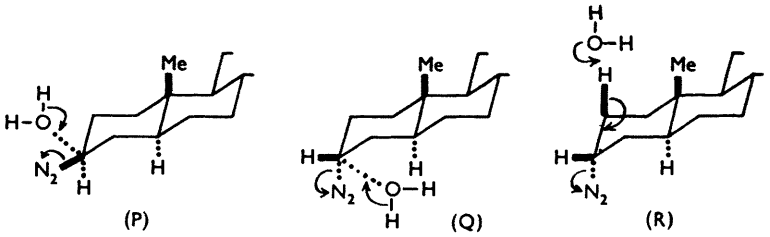
[9] Shoppee, *J.*, 1946, 1138.
[10] Pierce, Shoppee, and Summers, *J.*, 1955, 690.
[11] Richards, Shoppee, Sly, and Summers, *J.*, 1956, 1054.
[12] Shoppee, Evans, Richards, and Summers, *J.*, 1956, 1649.
[13] Vanghelovici and Vasiliu, *Bull. Soc. chim. Romania*, 1935, **17**, 249.
[14] Bird and Cookson, *Chem. and Ind.*, 1955, 1479.
[15] Barnett, Ryman, and Smith, *J.*, 1946, 528.

groups.[16, 17] It seems highly probable that the initial stage of all deaminations in aqueous acid is nitrosation by dinitrogen trioxide [18, 19, 20] leading to the formation of a diazonium ion. The complete retention of configuration observed in the deamination of equatorial steroid amines appears to exclude a true carbonium ion as successor to the diazonium ion; this conclusion is supported by the complete retention of configuration now disclosed by

Amine		Conform. of NH_2-group	Product of substitution	Product of elimination
Cholestan-3α-ylamine	(I)	a	Cholestan-3α-ol (45%, cholestan-3β-ol (0%)	Cholest-2-ene (54%)
Cholestan-3β-ylamine	(II)	e	Cholestan-3α-ol (0%), cholestan-3β-ol (99%)	—
Coprostan-3α-ylamine	(III)	e	Coprostan-3α-ol (92%), coprostan-3β-ol (0%)	—
Coprostan-3β-ylamine	(IV)	a	Coprostan-3α-ol (0%), coprostan-3β-ol (46%)	Coprost-3-ene (50%)
Cholestan-6α-ylamine	(V)	e	Cholestan-6α-ol (97%), cholestan-6β-ol (0%)	—
Cholestan-6β-ylamine	(VI)	a	—	Cholest-5-ene * (99%)
Cholest-5-en-3α-ylamine	(VII)	a	—	Cholesta-3 : 5-diene (70%)
Cholest-5-en-3β-ylamine	(VIII)	e	Cholesterol (100%), *epi*Cholesterol (0%)	—
3β-Hydroxycholestan-6α-ylamine	(IX)	e	Cholestane-3β : 6α-diol (98%), cholestane-3β : 6β-diol (0%)	—
3β-Hydroxycholestan-6β-ylamine	(X)	a	—	Cholesterol (95%)

* Probably contains some cholest-6-ene.

deamination of axial steroid amines, because the stereochemical distinction between epimerides would otherwise disappear. The critical stage must therefore involve the diazonium ion, and preservation of configuration appears to depend on the formation of pyramidal transition states (P, Q) during attack of a water molecule † on the diazonium ion, provided that a mechanistically bimolecular process is under observation.

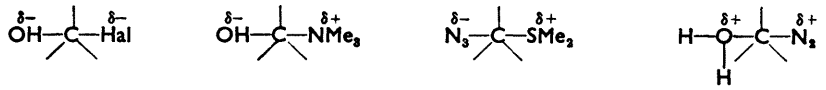


The transition states of the bimolecular replacements of halogen by hydroxyl,[22] of the trimethylammonium group by hydroxyl,[23] and of the dimethylsulphonium group by the azide group [24] form a sequence showing that electrostatic forces are relatively unimportant

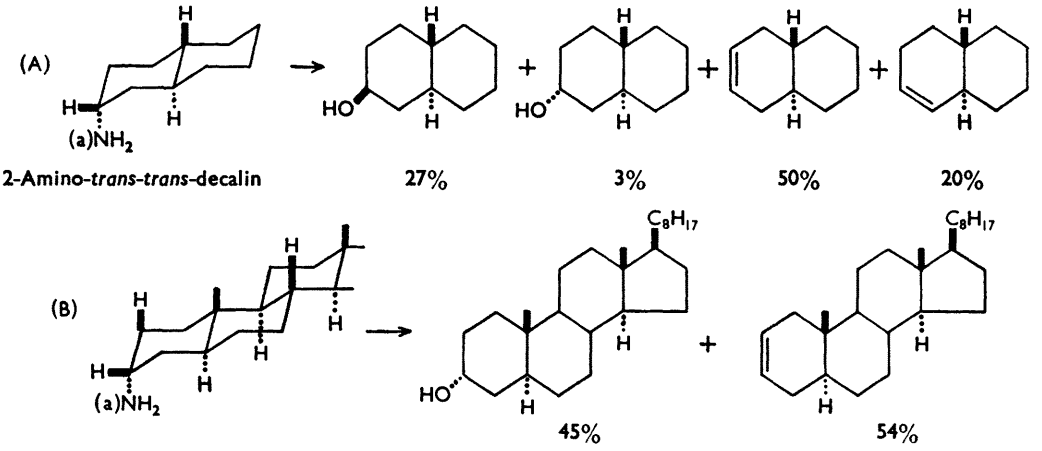
† Or an acetic acid molecule.[21]

[16] McCasland, *J. Amer. Chem. Soc.*, 1951, **73**, 2293.
[17] Cremlyn, Gamaise, and Shoppee, *J.*, 1953, 1847.
[18] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1940, p. 294.
[19] Hughes, Ingold, and Ridd, *Nature*, 1950, **166**, 642.
[20] Austin, Hughes, Ingold, and Ridd, *J. Amer. Chem. Soc.*, 1952, **74**, 555.
[21] Roberts, Lee, and Saunders, *J. Amer. Chem. Soc.*, 1954, **76**, 4501.
[22] Cowdrey, Hughes, Ingold, Masterman, and Scott, *J.*, 1937, 1252.
[23] Read and Walker, *J.*, 1934, 308.
[24] Harvey, Hughes, and Ingold, unpublished work: cf. *op. cit.*, ref. 1, p. 380.

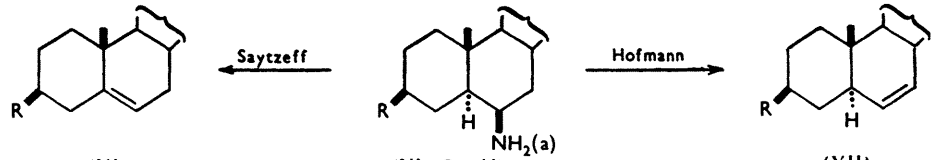
by comparison with the exchange forces between the bonds which are maintained and the bonds which undergo alteration :



Since the state of electrification is trivial, there appears to be no reason why bimolecular replacement of the diazonium ion group should not also take place with inversion and so complete the above sequence. We are unable to offer any satisfactory explanation (*e.g.*, β-hydrogen intervention, which appears here to be impossible) of the complete retention of configuration now observed experimentally in the deamination of saturated amines of the steroid series unless an internal replacement of S_N2 type is involved. Neither are we able to account for the surprising difference in behaviour observed between 2-amino-*trans*-*trans*-decalin (reaction A : inversion) and cholestan-3α-ylamine (reaction B : retention), since the structures are formally identical apart from a rigid extension of the molecule away from the site of reaction in the latter case :



The regular occurrence of elimination with axial steroid amines and its absence with equatorial steroid amines is consistent with the representation of the reaction as a base-induced *E*2 process (R) as suggested by Mills.[6] Bimolecular elimination from diazonium ions should follow the Hofmann rule in so far as polar factors control the course of reaction; our results conflict with the Hofmann rule and conform to the Saytzeff rule. Thus, cholestan-6β-ylamine (VI; 6β-NH_2/5α- or 7α-H : *trans*, *anti*, diaxial) yields cholest-5-ene (XI; R = H) probably containing a little cholest-6-ene (XII; R = H), whilst 3β-hydroxycholestan-6β-ylamine (X) gives only 3β-hydroxycholest-5-ene (XI; R = OH).



A preliminary examination of the epimeric 7-aminocholestanes [25] indicates that the equatorial 7β-amine is deaminated with retention of configuration to give cholestan-7β-ol

[25] Shoppee, Cremlyn, D. E. Evans, and Summers, unpublished work.

unaccompanied by olefin, whereas the 7α-amine (7α-NH_2/6β- or 8β-H : *trans, anti*, diaxial) is deaminated with retention to give cholestan-7α-ol and cholest-7-ene (Saytzeff orientation), although some cholest-6-ene (Hofmann orientation) may also have been formed.

The observed preference for elimination in the Saytzeff orientation does not appear to rest on steric requirements [26] since the attacking base (the water molecule) and the group eliminated (the diazonium ion group) are constant features. If the decomposition of axial steroid diazonium ions were an *E*1 process, the polar influences summarised in the Saytzeff rule would control the direction of elimination in harmony with the experimental observations. A kinetic test appears difficult to apply,[6] but the occurrence of elimination only with axial amines, which alone possess the geometry required for minimisation of the activation energy, is highly suggestive of a bimolecular mechanism.

Experimental

For general experimental directions, see preceding paper. $[\alpha]_D$ are in $CHCl_3$ unless otherwise stated. Ultraviolet absorption spectra were determined in EtOH on a Unicam SP 500 spectrometer with corrected scale, and infrared absorption spectra in CS_2 on a Perkin–Elmer double-beam instrument.

Deamination of Cholestan-3α-ylamine.—Cholestan-3α-ylamine (1·05 g.) in 50% aqueous acetic acid (40 c.c.) was treated with a solution of sodium nitrite (2 g.) in 50% aqueous acetic acid (20 c.c.) and left for 18 hr. Isolation in the usual way yielded an oil (940 mg.) which was chromatographed on aluminium oxide (30 g.). Elution with pentane gave an oil (460 mg.) which by crystallisation from ether–acetone furnished cholest-2-ene, m. p. and mixed m. p. 68°. Elution with benzene gave a solid (380 mg.) which by recrystallisation from ethanol gave cholestan-3α-ol, m. p. and mixed m. p. 184—185°. Elution with methanol yielded an oil (90 mg.) converted by boiling acetic anhydride into 3α-acetamidocholestane, m. p. 217—218°.

Deamination of Cholestan-3β-ylamine.—Cholestan-3β-ylamine (500 mg.) in 50% acetic acid (20 c.c.) and dioxan (5 c.c.) was treated with sodium nitrite (1 g.) in 50% acetic acid (10 c.c.). The solution was vigorously shaken for 10 min., left overnight, then poured into water, and the product was extracted with ether. The resulting oil was hydrolysed with 5% methanolic potassium hydroxide for 1 hr., yielding an oil (485 mg.) which was chromatographed on aluminium oxide (15 g.). Elution with benzene gave a solid (390 mg.) which by recrystallisation from ethanol afforded cholestan-3β-ol, m. p. and mixed m. p. 137—140°. Elution with acetone yielded an oil (90 mg.) which with boiling acetic anhydride gave 3β-acetamidocholestane, m. p. 244°.

Deamination of Coprostan-3α-ylamine.—Coprostan-3α-ylamine (320 mg.) in 50% acetic acid (20 c.c.) was treated with sodium nitrite (600 mg.) in 50% acetic acid (20 c.c.) and left for 18 hr. Working up in the usual manner gave an oil (310 mg.) which was chromatographed on aluminium oxide (10 g.). Elution with benzene afforded a solid (165 mg.) which by recrystallisation from acetone gave coprostan-3α-ol, m. p. and mixed m. p. 117—118°. Elution with ether and acetone furnished an oil (130 mg.) whence by acetylation 3α-acetamidocoprostane, m. p. 217°, was obtained.

Deamination of Coprostan-3β-ylamine.—Coprostan-3β-ylamine (170 mg.) in 50% acetic acid (20 c.c.) and dioxan (6 c.c.) was treated with sodium nitrite (500 mg.) in 50% acetic acid (15 c.c.) and left overnight. The solution was worked up in the usual manner to yield an oil (150 mg.) which was chromatographed on aluminium oxide (6 g.). Elution with pentane afforded an oil (25 mg.) which by crystallisation from ethyl acetate gave coprost-3-ene, m. p. and mixed m. p. 48°, $[\alpha]$ +21° (*c*, 1·1). Elution with benzene afforded an oil (23 mg.) which by crystallisation from acetone gave coprostan-3β-ol, m. p. and mixed m. p. 99—100°. Elution with chloroform and ethanol yielded an oil (100 mg.) which with boiling acetic anhydride and crystallisation from acetone yielded 3β-acetamidocoprostane, m. p. 172°.

Cholestan-6α-ylamine.—Cholestan-6-one oxime (m. p. 195°; 500 mg.) in refluxing propan-2-ol (20 c.c.) was treated with sodium until a saturated solution was formed. The solution was worked up in the usual manner and basic material isolated as the ether-insoluble hydrochloride, which by treatment with ammonia afforded cholestan-6α-ylamine, b. p. 140°/0·02 mm., needles

[26] Brown and Moritani, *J. Amer. Chem. Soc.*, 1953, **75**, 4112.

(from pentane), m. p. 125—127°, $[\alpha]_D$ +38·5° (*c*, 0·8). With acetic anhydride in ether at 15° it gave a solid which by recrystallisation from methanol furnished 6α-acetamidocholestane, double m. p. 117—118° and 185—187°, $[\alpha]_D$ +62° (*c* 0·67).

Deamination of Cholestan-6α-ylamine.—Cholestan-6α-ylamine (150 mg.) in 50% acetic acid (20 c.c.) and dioxan (3 c.c.) was treated with sodium nitrite (0·5 g.) in 50% acetic acid (20 c.c.), vigorously shaken for 15 min., left overnight, poured into water, and extracted with ether. The oily product was hydrolysed with 5% methanolic potassium hydroxide for 1 hr. and worked up in the usual way, to yield an oil (145 mg.) which by crystallisation from methanol gave cholestan-6α-ol, m. p. and mixed m. p. 129° (122 mg.). Chromatography of the residue on aluminium oxide gave, by elution with ether, cholestan-6α-ol (17 mg.).

Cholestan-6β-ylamine.—(*a*) 6-Nitrocholest-5-ene (3 g.) was treated with lithium aluminium hydride in refluxing ether (60 c.c.) for 3 hr. Excess of reagent was destroyed with water at 0°; the precipitated aluminium oxide was filtered off and continuously extracted with ether. After evaporation of the total ethereal extract, the basic product was isolated *via* its hydrochloride. Crystallisation from ethanol gave cholestan-6β-ylamine, m. p. 94—96°, $[\alpha]_D$ +6·3° (*c*, 1·28) (Found, after drying at 50°/0·03 mm. for 12 hr.: C, 83·5; H, 12·4. Calc. for $C_{27}H_{49}N$: C, 83·7; H, 12·65%). With acetic anhydride in boiling ether it gave 6β-*acetamidocholestane*, rods (from ether), m. p. 189—190°, $[\alpha]_D$ −13° (*c*, 1·37) (Found, after sublimation at 190—200°/0·01 mm.: C, 81·3; H, 11·8. $C_{29}H_{51}ON$ requires C, 81·05; H, 11·95%).

(*b*) Cholestan-6-one oxime (400 mg.) in ether (25 c.c.) was refluxed with lithium aluminium hydride for 17·5 hr. Working up in the usual way gave an oil which was acetylated with acetic anhydride in boiling ether; the solid product (340 mg.) was chromatographed on aluminium oxide (10 g.). Elution with benzene (5 × 40 c.c.) gave a solid (290 mg.) which on recrystallisation from ethanol furnished 6β-acetamidocholestane, m. p. 188—190°, $[\alpha]_D$ −12° (*c*, 0·7). Elution with benzene–ether (9 : 1) (2 × 40 c.c.) gave a solid (25 mg.), m. p. 170—185°, whilst further elution with the same solvent mixture gave a solid, m. p. 183—187° (15 mg.) undepressed on admixture with 6α-acetamidocholestane.

Deamination of Cholestan-6β-ylamine.—Cholestan-6β-ylamine (510 mg.) in 50% acetic acid (20 c.c.) and dioxan (20 c.c.) was treated overnight with a solution of sodium nitrite (1 g.) in 50% acetic acid (20 c.c.). The solution was worked up in the usual manner to yield an oil (480 mg.) which was chromatographed on aluminium oxide (15 g.). Elution with pentane gave an oil (340 mg.) which from ether–methanol gave an amorphous solid, m. p. 60—84°, $[\alpha]_D$ −74° (*c*, 0·9). Elution with ether–benzene (1 : 9) gave an oil (130 mg.) which with pyridine–acetic anhydride at 15° overnight afforded 6β-acetamidocholestane, m. p. and mixed m. p. 186—187° from acetone. The hydrocarbon (340 mg.) eluted with pentane was rechromatographed on aluminium oxide (15 g.), whence pentane (5 × 50 c.c.) eluted a series of oils which by crystallisation from ether–methanol gave a mixture, m. p. 72—90°, $[\alpha]_D$ −70° (*c*, 1·2), of cholest-5-ene and -6-ene.

Deamination of Cholest-5-en-3α-ylamine.—This amine (30 mg.) in 50% acetic acid (7 c.c.) and dioxan (2 c.c.) with sodium nitrite (150 mg.) in 50% acetic acid (3 c.c.) during 16 hr. at 20° afforded an oil (23 mg.) which on chromatography on aluminium oxide (1 g.) and elution with pentane gave an oil (20 mg.) which by crystallisation from acetone–methanol gave cholesta-3 : 5-diene as needles, m. p. 78—79°, $[\alpha]_D$ −115° (*c*, 0·6).

Deamination of Cholest-5-en-3β-ylamine.—The 3β-ylamine (700 mg.) in 50% acetic acid (40 c.c.) was treated with sodium nitrite (2 g.) in 50% acetic acid (30 c.c.) at 20° for 16 hr., giving a semi-solid (685 mg.) which was left with pyridine–acetic anhydride overnight. Chromatography on aluminium oxide (20 g.) and elution with benzene–pentane (1 : 9) gave a solid (573 mg.) which by crystallisation from ether–methanol gave cholesteryl acetate, m. p. and mixed m. p. 113—115°. Elution with chloroform gave a solid (99 mg.) which by recrystallisation from chloroform–methanol afforded 3β-acetamidocholest-5-ene, m. p. and mixed m. p. 240—243°.

3β-*Hydroxycholestan-6β-ylamine.*—(*a*) 6-Nitrocholesteryl acetate (500 mg.) in ether (100 c.c.) was refluxed with lithium aluminium hydride (300 mg.) overnight. Isolation of the product in the usual manner and acetylation with pyridine–acetic anhydride at 15° for 16 hr. afforded a solid (466 mg.) which was chromatographed on aluminium oxide (15 g.). Elution with benzene–pentane (1 : 1) and crystallisation from ethyl acetate–methanol afforded 6-nitrocholesteryl acetate, m. p. 101—102° (166 mg.). Elution with ether–benzene (1 : 9—1 : 4) gave a white solid (270 mg.) which by recrystallisation from aqueous acetone furnished 6β-*acetamido*-3β-*acetoxycholestane*, fine needles, m. p. 172—174°, $[\alpha]_D$ −18° (*c*, 1·2) (Found, after drying at 100°/0·02 mm. for 12 hr.: C, 76·1; H, 11·1. $C_{31}H_{53}O_3N$ requires C, 76·3; H, 10·8%).

(*b*) 3β-Acetoxycholestan-6-one oxime (m. p. 208°; 1 g.) in ether (100 c.c.) was refluxed with lithium aluminium hydride for 24 hr. Isolation of the product in the usual manner gave an oil, which solidified under pentane and on crystallisation from methanol gave 3β-hydroxycholestan-6β-ylamine, m. p. 128—130°, $[\alpha]_D$ −5·6° (*c*, 1·2); five analyses, by two analysts, were unsatisfactory (Found: C, 78·2—79·3; H, 11·3—12·05. Calc. for $C_{27}H_{49}ON$: C, 80·3; H, 12·25%), and we believe this to be due to rapid absorption of water and/or carbon dioxide. Acetylation with hot acetic anhydride gave an oil which was chromatographed on aluminium oxide. Elution with benzene–pentane (1 : 4) gave an oil which by crystallisation from pentane gave 6β-acetamido-3β-acetoxycholestane, as fine needles changing to rods on storage, m. p. 177—178°, unchanged on admixture with the above specimen.

Deamination of 3β-*Hydroxycholestan*-6β-*ylamine*.—3β-Hydroxycholestan-6β-ylamine (1·18 g.) in 50% acetic acid (20 c.c.) was shaken with sodium nitrite (1·23 g.) in 50% acetic acid (20 c.c.) for 0·5 hr., then left overnight and the product, an oil, isolated in the usual manner. After hydrolysis with lithium aluminium hydride in ether, the isolated solid (1 g.) was chromatographed on aluminium oxide (30 g.). Elution with benzene (10 × 100 c.c.) gave a solid (701 mg.) which crystallised from ether–methanol as needles, m. p. 147—148°, undepressed on admixture with cholesterol. Elution with ether and ether–chloroform gave an oil (230 mg.) which with boiling acetic anhydride gave 6β-acetamido-3β-acetoxycholestane, m. p. 174—177° from pentane.

3β-*Hydroxycholestan*-6α-*ylamine*.—3β-Acetoxycholestan-6-one oxime (0·5 g.) in ethanol (50 c.c.) was treated with sodium until the solution became saturated. Working up in the usual way gave a gel which was dried and washed with boiling pentane and ether, affording amorphous 3β-hydroxycholestan-6α-ylamine, m. p. 166—168°, $[\alpha]_D$ +11° (*c*, 2·1) [Found, after sublimation at 220—230°/0·02 mm. (at Zürich): C, 79·6; H, 12·4. Calc. for $C_{27}H_{49}ON$: C, 80·3; H, 12·25%). Acetylation with boiling acetic anhydride gave an oil; chromatography on aluminium oxide and elution with benzene–pentane (1 : 1) gave an oil which by crystallisation from pentane (with cooling) gave needles, m. p. 168—172°, and by recrystallisation afforded 6α-*acetamido*-3β-*acetoxycholestane*, m. p. 176—178°, $[\alpha]_D$ +15° (*c*, 1·0) (Found, after drying at 100°/0·03 mm. for 8 hr.: C, 76·0; H, 10·8. $C_{31}H_{53}O_2N$ requires C, 76·3; H, 10·8%). The mixed m. p. with 6β-acetamido-3β-acetoxycholestane was 169—187°.

Deamination of 3β-*Hydroxycholestan*-6α-*ylamine*.—3β-Hydroxycholestan-6α-ylamine (75 mg.) in 50% acetic acid (5 c.c.) was treated with sodium nitrite (300 mg.) in 50% acetic acid (10 c.c.). Working up in the usual way followed by hydrolysis with lithium aluminium hydride gave a solid (65 mg.) which by crystallisation from acetone gave cholestane-3β : 6α-diol, m. p. and mixed m. p. 214—217°.

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