702. *Aza-steroids. Part V.** 1-, 2-, 3-, *and* 4a-*Aza*-A-*homo*-5α-*cholestane and* 6-*Aza*-B-*homo*-5α-*cholestane.*

By C. W. Shoppee, Ruth E. Lack, and S. K. Roy.

The five aza-steroids named above have been prepared by Beckmann rearrangement of the appropriate ketoximes. The formation from 5α- and A-nor-5α-cholestan-1-one oxime of abnormal cleavage products has been observed and is briefly discussed.

We reported previously [1] that in a small-scale experiment 5α-cholestan-1-one oxime (I) failed to undergo Beckmann rearrangement. We now find that (I) on treatment with thionyl chloride at −20° gives approximately equal amounts of the normal rearrangement product (1-aza-A-homo-5α-cholestan-2-one) (II) and the abnormal "second-order Beckmann" cleavage product (III).

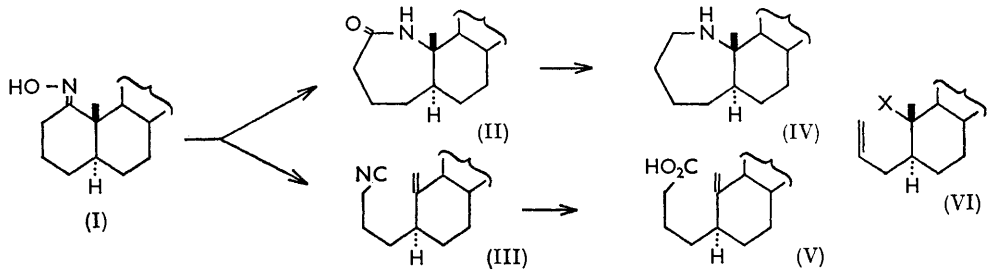
The ε-lactam (II) exhibits $\nu_{max.}$ 3220 (NH), 1652, 1648 cm.$^{-1}$ [CO(–NH)] and the low m. p. 138°; it is unusually soluble in ether, which probably accounts for the failure to detect it in the original experiment.[1] The lactam is reduced by lithium aluminium hydride in tetrahydrofuran to crystalline 1-aza-A-homo-5α-cholestane (IV), which shows a weak infrared peak at 3170 cm.$^{-1}$ (NH), is a weak base since it does not abstract carbon dioxide from the atmosphere during brief exposure, and was characterised as the *N*-acetyl derivative.

The 1,10-seco-1-cyano-compound (III) exhibits infrared maxima at 2237 (C≡N) and 1631, 895 cm.$^{-1}$ (>C=CH_2) and is hydrolysed under relatively mild conditions by potassium

* Part IV, *J.*, 1962, 2275.

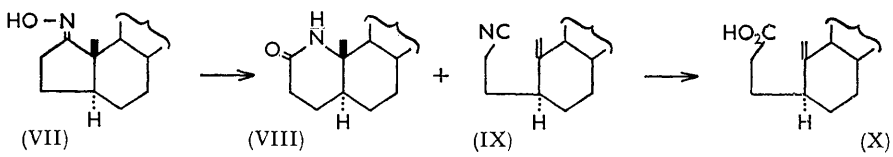
[1] Shoppee, Roy, and Goodrich, *J.*, 1961, 1583.

hydroxide to the carboxylic acid (V), which exhibits infrared maxima at 1630 and 895 cm.$^{-1}$ (>C=CH$_2$) and does not evolve carbon monoxide with warm concentrated sulphuric acid. These observations exclude the 1,2-seco-10-cyano-structure (VI; X = CN) and the corresponding structure (VI; X = CO_2H) containing a tertiary carboxyl group.



On the accepted basis of *trans*-interchange in molecular rearrangements, the configuration of 5α-cholestan-1-one oxime is accordingly (I; OH *anti* to 10β-Me) and the structure of the derived ε-lactam is (II). This conclusion is supported by the preparation (see below) of 2-aza-A-homo-5α-cholestane (XVII), which is different from 1-aza-A-homo-5α-cholestane (IV).*

On treatment with thionyl chloride at −20° A-nor-5α-cholestan-1-one oxime [1] (VII) similarly furnished the normal Beckmann rearrangement product, 1-aza-5α-cholestan-2-one (VIII) (35%), accompanied by the unrearranged 1-cyano-1,10-seco-compound (IX) (50%) which exhibited infrared maxima at 2235 (C≡N) and 1630, 894 cm.$^{-1}$ (>C=CH$_2$) and was hydrolysed without difficulty by 4N-potassium hydroxide to the carboxylic acid (X). A-Nor-5α-cholestan-1-one oxime thus has the configuration (VII; OH *anti* to 10β-Me).

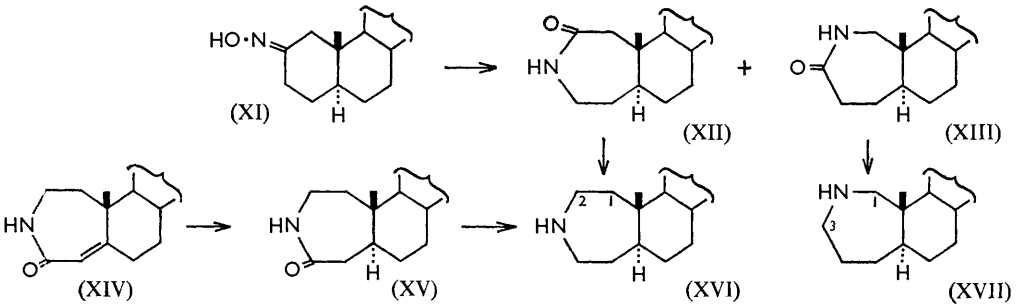


5α-Cholestan-2-one oxime (XI) appeared to be homogeneous with a sharp m. p. unaltered on recrystallisation from ethanol or on repeated chromatography. A solution of the oxime in thionyl chloride at −20° must, however, contain both the *syn*- and the *anti*-form since the product of Beckmann rearrangement under these conditions consisted of 3-aza-A-homo-5α-cholestan-2-one (XII) and 2-aza-A-homo-5α-cholestan-3-one (XIII), which were readily separated by chromatography.

The lactam (XII) was reduced by lithium aluminium hydride in tetrahydrofuran to 3-aza-A-homo-5α-cholestane [2] (XVI), which was characterised as the *N*-acetyl derivative, m. p. 111—113° (lit.,[2] 109—111°). This aza-steroid (XVI) was also obtained from 3-aza-A-homocholest-4a-en-4-one [3] (XIV); hydrogenation with palladium–charcoal in ethanol gave the saturated lactam (XV), which was reduced by lithium aluminium hydride in tetrahydrofuran to 3-aza-A-homo-5α-cholestane (XVI), again characterised as the acetyl

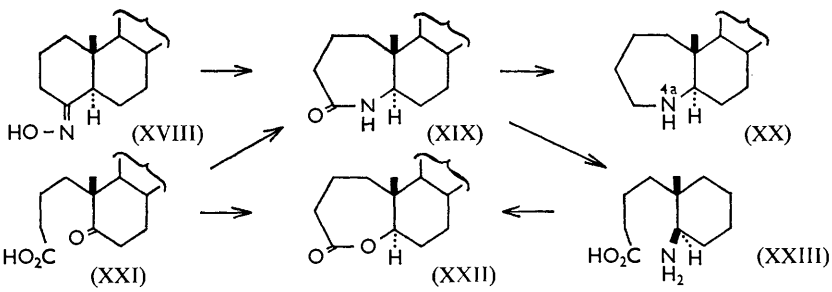
* Beckmann rearrangement of 9-acetyl-*cis*-decalin oxime with concentrated sulphuric acid or polyphosphoric acid at 20° involves inversion of configuration but reaction with toluene-*p*-sulphonyl chloride in pyridine at 20° gives a 92% yield of uninverted (*cis*-)amide (Hill and Chortyk, *J. Amer. Chem. Soc.*, 1962, **84**, 1064). That our lactam (II) was produced by the action of thionyl chloride at −20° seems to exclude the possibility, suggested by a Referee, that it is the 10α-methyl compound derived by a Ritter reaction from the 10-cation corresponding to (III). A similar argument applies to lactam (VIII) (below).

[2] Shoppee and Sly, *J.*, 1958, 3458.
[3] Shoppee, Krüger, and Mirrington, *J.*, 1962, 1050.



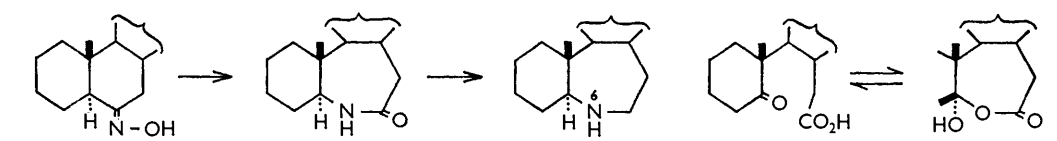
derivative. Similar reduction of the lactam (XIII) yielded 2-aza-A-homo-5α-cholestane (XVII), characterised as the *N*-acetyl derivative, m. p. 142—144°.

Treatment of 5α-cholestan-4-one oxime [4,5] (XVIII) with thionyl chloride at —20° gave



a single normal Beckmann rearrangement product, 4a-aza-A-homo-5α-cholestan-4-one (XIX), exhibiting infrared maxima at 3194 (NH) and 1670 cm.$^{-1}$ (C=O), unaccompanied by an abnormal product. The lactam (XIX), on reduction with lithium aluminium hydride, gave the crystalline 4a-aza-A-homo-5α-cholestane (XX).

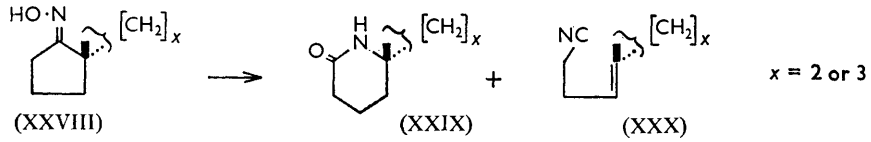
The structures of the lactam (XIX) and the aza-steroid (XX) have been established by hydrolysis of the former with ethanolic 5N-hydrochloric acid under pressure at 100° to the hydrochloride of the ε-amino-acid (XXIII), deaminated by aqueous nitrous acid at 20° to the analogous ε-hydroxy-acid, which cyclised at once to the ε-lactone (XXII). This, like the synthetic specimen prepared from the keto-acid [6] (XXI) by reduction with sodium borohydride, could not be induced to crystallise; the infrared spectra were, however, identical. The structure of the lactam (XIX) is confirmed by its synthesis in poor yield from the oxime of the keto-acid (XXI) by reduction with sodium in boiling ethanol. The configuration of 5α-cholestan-4-one oxime (XVIII; OH *anti* to 5α-H) follows from the structure of the lactam (XIX).



5α-Cholestan-6-one oxime (XXIV), on treatment with thionyl chloride at —20°, rearranged to a single lactam regarded as 6-aza-B-homo-5α-cholestan-7-one (XXV), showing infrared maxima at 3192 (NH) and 1668 cm.$^{-1}$ (C=O), unaccompanied by an abnormal product. The lactam (XXV) was reduced by lithium aluminium hydride to a

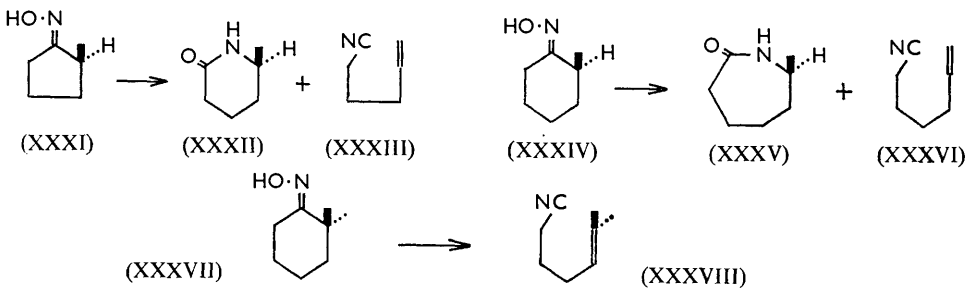
[4] Windaus, *Ber.*, 1920, **53**, 488.
[5] Shoppee, Cremlyn, Evans, and Summers, *J.*, 1957, 4364.
[6] Lettré, *Z. physiol. Chem.*, 1933, **221**, 73; cf. Grasshof, *ibid.*, 1934, **223**, 249.

crystalline aza-steroid regarded as 6-aza-B-homo-5-cholestane (XXVI). It was not possible to convert the lactam (XXV) into the analogous lactone, because hydrolysis to the related amino-acid could not be effected even under drastic conditions; further the keto-acid [7-10] (XXVII) resisted oximation (cf. ref. 9) and possibly exists as the 5α-hydroxy-7→5β-lactone. The structures (XXV) and (XXVI) are therefore provisional and based on the assumption that the oxime (XXIV; OH *anti* to 5α-H) is the more stable and less sterically hindered geometrical isomer.



(XXVIII) (XXIX) (XXX)

The cause of the production of ω-cyano-olefins from the 1-ketoximes (I and VII), in contrast with the 4-ketoxime (XVIII) and the 6-ketoxime (XXIV), is not clear. The simplest tertiary ketoxime, pinacolone oxime, $Me{\cdot}C(:N{\cdot}OH){\cdot}CMe_3$, is reported [11] to give only the normal Beckmann rearrangement product *N*-t-butylacetamide, but the expected abnormal products methyl cyanide, b. p. 80°, and isobutene, b. p. −7°, could have escaped observ-

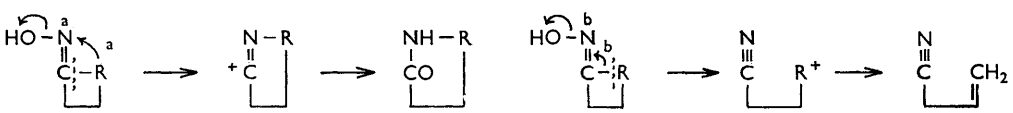


(XXXI) (XXXII) (XXXIII) (XXXIV) (XXXV) (XXXVI)

(XXXVII) (XXXVIII)

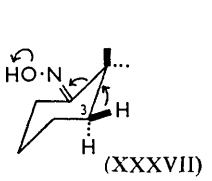
ation; however, the tertiary alicyclic ketoximes (XXVIII) of spiro[4,4]nonan-1-one and spiro[4,5]decan-1-one with thionyl chloride afford the δ-lactams (XXIX) accompanied by the ω-cyano-olefins (XXX).[12] A tertiary carbon atom adjacent to the hydroxyimino-group is not an essential molecular feature because simple alicyclic ketoximes yield abnormal products. With thionyl chloride, cyclopentanone oxime furnishes δ-valero-lactam and but-3-enyl cyanide, and cyclohexanone oxime gives 6-hexanolactam and pent-4-enyl cyanide, whilst 2-methylcyclopentanone oxime (XXXI) furnishes 6-methyl-2-piperidone (XXXII) and pent-4-enyl cyanide (XXXIII), and 2-methylcyclohexanone oxime (XXXIV) gives the lactam (XXXV) and the cyanide (XXXVI); [13] but 2,2-dimethyl-cyclohexanone (XXXVII) yields only 5-methylhex-4-enyl cyanide (XXXVIII).[14]

The formation of lactams and ω-cyano-olefins in the Beckmann rearrangement of ketoximes appears to correspond to the two modes of heterolysis of the bond C–R: [15]



[7] Windaus and Resau, *Ber.*, 1914, **47**, 1229.
[8] Windaus, *Ber.*, 1920, **53**, 488.
[9] Lettré, *Z. physiol. Chem.*, 1933, **218**, 67.
[10] Dauben and Fonken, *J. Amer. Chem. Soc.*, 1956, **78**, 4736.
[11] Scholl, Weil, and Haldermann, *Annalen*, 1904, **338**, 1.
[12] Hill and Conley, *Chem. and Ind.*, 1956, 1314.
[13] Donaruma and Heldt, *Org. Reactions*, 1960, **11**, 26 et seq., 96, 98, 103.
[14] Conley, Frainier, and Nowak, Abs. Amer. Chem. Soc. Meeting, Sept. 1959, 7P.
[15] Ferris, *J. Org. Chem.*, 1960, **25**, 12.

Since oxime geometry determines the product in normal Beckmann rearrangements, the covalency changes (a) must be concerted. In the formation of ω-cyano-olefins, the electron displacements (b) may be concerted or consecutive. If the displacements (b) are concerted, the stereoelectronic requirement should be a *trans*-coplanar arrangement of the C_γ–H bond broken (in R) to the C_β–C_α bond cleaved. In 2,2-dimethylcyclohexanone oxime (XXXVII) the equatorial $C_{(3)}$–hydrogen atom satisfies this requirement, but in 5α-cholestan-1-oxime-(I) only axial 5α- and 9α-hydrogen atoms, and in β-amyrenone oxime [16] (XXXIX) only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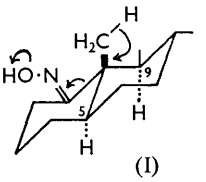
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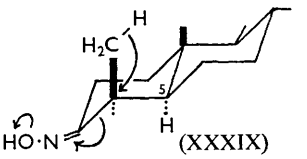
(XXXIX)

an axial 5α-hydrogen atom, are available, so that *trans*-elimination of a proton from an axial methyl group is preferred. If, on the other hand, the displacements (b) are consecutive, the same ω-cyano-olefin should arise with equal ease from both geometrical isomers of a ketoxime, since the stereochemical distinction between *syn*- and *anti*-forms should disappear in the intermediate iminium cation; there appears to be no suitable example recorded in the literature with which to test the matter.

Experimental

For general experimental directions, see *J.*, 1958, 3458. $[\alpha]_D$ are for $CHCl_3$ solutions. Ultraviolet absorption spectra were measured for EtOH solutions in a Perkin-Elmer model 4000 A spectrophotometer, and infrared absorption spectra were determined on a Perkin-Elmer model 421 or, for Nujol mulls, on an Infracord spectrophotometer.

Rearrangement of 5α-Cholestan-1-one Oxime (I).—5α-Cholestan-1-one oxime (m. p. 152°; lit.,[1] 151—153°) (1 g.), cooled in carbon dioxide–acetone, was treated with purified thionyl chloride (10 c.c.), previously cooled to the same temperature. The brown solution was at once poured slowly into 4N-potassium hydroxide (50 c.c.) at 20°. The aqueous layer was decanted and the product dissolved in pentane and chromatographed on aluminium oxide (30 g.) in pentane. Elution with ether–benzene (1 : 19) gave 1,10-*seco*-5α-*cholest*-10(19)-*eno*-1-*nitrile* (III) (360 mg.), b. p. 150—160°/0·2 mm. (Found: C, 84·1; H, 11·8. $C_{27}H_{45}N$ requires C, 84·5; H, 11·8%). Further elution with ether–benzene gave only traces of oil, but use of ether gave the crude lactam (505 mg.), which was rechromatographed on alumina (15 g.). Elution with ether–benzene (1 : 1) gave dark amorphous material, but use of ether gave 1-*aza*-A-*homo*-5α-*cholestan*-2-*one* (II) (285 mg.), m. p. 138° (from ether) [Found (after drying at 80°/0·5 mm. for 4 hr.): C, 80·4; H, 12·1. $C_{27}H_{47}NO$ requires C, 80·7; H, 11·7%].

1-*Aza*-A-*homo*-5α-*cholestane* (IV) [R. E. L.].—The lactam (II) (100 mg.) was refluxed with lithium aluminium hydride (500 mg.) in ether for 48 hr. The excess of the reagent was decomposed with moist ether and finally with water; the precipitate of aluminium hydroxide was repeatedly extracted with chloroform, and the combined ether–chloroform extracts were worked up in the usual way, to give 1-*aza*-A-*homo*-5α-*cholestane* (IV) (90 mg.), which crystallised spontaneously and, when recrystallised from methanol, had m. p. 84° [Found (after drying at 20°/0·5 mm. for 4 hr.): C, 83·5; H, 12·75. $C_{27}H_{49}N$ requires C, 83·65; H, 12·75%]. The N-*acetyl derivative*, prepared by using acetic anhydride–pyridine at 20° overnight, had m. p. 80° after recrystallisation from methanol [Found (after drying at 20°/0·5 mm. for 4 hr.): C, 81·1; H, 11·8. $C_{29}H_{51}NO$ requires C, 81·05; H, 11·95%].

1,10-*Seco*-5α-*cholest*-10(19)-*en*-1-*oic Acid* (V).—The cyanide (III) (50 mg.) was refluxed in ethanol (5 c.c.) with 4N-potassium hydroxide until evolution of ammonia ceased (4 hr.). Dilution gave an insoluble potassium salt, which was acidified; the acid was isolated by extraction with ether and crystallised when rubbed with ether–pentane; two recrystallisations from ether–pentane gave 1,10-*seco*-5α-*cholest*-10(19)-*en*-1-*oic acid*, m. p. 154—156°, $\nu_{max.}$ 1630,

[16] Whitham, *J.*, 1960, 2016.

895 cm.$^{-1}$ (>C=CH_2) [Found (after drying at 60°/0·3 mm. for 6 hr.): C, 80·95; H, 11·5. $C_{27}H_{46}O_2$ requires C, 80·6; H, 11·5%].

Rearrangement of A-*Nor*-5α-*cholestan*-1-*one Oxime* (VII).—A-Nor-5α-cholestan-1-one oxime [1] (m. p. 170—172°) (200 mg.) was treated with purified thionyl chloride (3 c.c.) in a bath of solid carbon dioxide–acetone. The pale yellow solution was then poured into 4N-potassium hydroxide (50 c.c.) at 20°, and the product (180 mg.), isolated in the usual way, was chromatographed on aluminium oxide (6 g.) in hexane. Elution with benzene afforded 1,10-*seco*-A-*nor*-5α-*cholest*-10(19)-*eno*-1-*nitrile* (IX) (100 mg.) as a solid, which after distillation at 150°/0·2 mm. and recrystallisation from aqueous ethanol as the hemihydrate had m. p. 105—107° [Found (after drying at 60°/0·3 mm. for 4 hr.): C, 82·5; H, 11·4. $C_{26}H_{43}N,\frac{1}{2}H_2O$ requires C, 82·45; H, 11·7%]. Further elution with ether and chloroform–ether furnished 1-*aza*-5α-*cholestan*-2-*one* (VIII) (70 mg.), m. p. 176—177°, $\nu_{max.}$ 3200 (NH), 1650 cm.$^{-1}$ [CO(–NH)] [Found (after drying at 80°/0·2 mm. for 6 hr.): C, 80·5; H, 11·6. $C_{26}H_{45}NO$ requires C, 80·55; H, 11·7%].

1,10-*Seco*-A-*nor*-5α-*cholest*-10(19)-*en*-1-*oic Acid* (X).—The cyanide (IX) (60 mg.) was refluxed in ethanol (5 c.c.) with 4N-potassium hydroxide until ammonia was no longer evolved (4 hr.). The product was isolated by dilution, acidification, and extraction with ether. Two recrystallisations from ether–pentane yielded the *acid* (X), m. p. 133—135° [Found (after drying at 60°/0·3 mm. for 6 hr.): C, 80·7; H, 11·7. $C_{26}H_{44}O_2$ requires C, 80·35; H, 11·4%].

Rearrangement of 5α-*Cholestan*-2-*one Oxime* (XI) [R. E. L.].—5α-Cholestan-2-one oxime (m. p. 198°; lit.,[5,17] m. p. 200°) (1 g.) was treated with purified thionyl chloride (10 c.c.) as above. The pale yellow solution was at once poured into 4N-potassium hydroxide (50 c.c.) at 20°; the aqueous layer was decanted, and the product dissolved in pentane, worked up in the usual way, and chromatographed on aluminium oxide (30 g.) in pentane. Elution with pentane and with benzene gave no material, and use of ether yielded dark amorphous material; elution with chloroform–ether (1 : 20) gave 2-*aza*-A-*homo*-5α-*cholestan*-3-*one* (XIII) (220 mg.); this had m. p. 181—182° and $\nu_{max.}$ 3300 (NH), 1670 cm.$^{-1}$ [CO(–NH)] after recrystallisation from ether [Found (after drying at 80°/0·5 mm. for 4 hr.): C, 80·5; H, 12·0. $C_{27}H_{47}NO$ requires C, 80·7; H, 11·8%]. Further elution with chloroform–ether (1 : 1) afforded 3-*aza*-A-*homo*-5α-*cholestan*-2-*one* (XII) (450 mg.), having m. p. 216—217° and $\nu_{max.}$ 3300, 3195 (NH), 1670 cm.$^{-1}$ [CO(–NH)], after recrystallisation from ether [Found (after drying at 100°/0·5 mm. for 4 hr.): C, 80·4; H, 12·0%]. A mixture of (XII) and (XIII) in approximately equal parts had m. p. 155—160°.

2-*Aza*-A-*homo*-5α-*cholestane* (XVII) [R. E. L.].—The lactam (XIII) (50 mg.) was refluxed with an excess of fresh lithium aluminium hydride (250 mg.) in tetrahydrofuran (50 c.c.) for 48 hr. Destruction of the reagent and isolation of the product as described above furnished 2-aza-A-homo-5α-cholestane (40 mg.) as an oil, $\nu_{max.}$ 3300 cm.$^{-1}$ (NH) but no peak at 1665 cm.$^{-1}$. The N-*acetyl derivative*, prepared by using acetic anhydride–pyridine at 20° for 12 hr., had m. p. 142—144°, $\nu_{max.}$ 1635 cm.$^{-1}$ [NH(–CO)], after crystallisation from methanol [Found (after drying at 60°/0·5 mm. for 4 hr.): C, 81·2; H, 11·85. $C_{29}H_{51}NO$ requires C, 81·05; H, 11·95%].

3-*Aza*-A-*homo*-5α-*cholestane* (XVI) [R. E. L.].—(*a*) The lactam (XII) (50 mg.) similarly gave 3-*aza*-A-*homo*-5α-*cholestane* (XXI) (40 mg.) as an oil, $\nu_{max.}$ 3300 cm.$^{-1}$ (NH) (no peak at 1670 cm.$^{-1}$). The *N*-acetyl derivative, prepared as usual, had m. p. 113—115°, $\nu_{max.}$ 1635 cm.$^{-1}$ [NH(–CO)], after crystallisation from methanol [Found (after drying at 40°/0·5 mm. for 4 hr.): C, 81·0; H, 11·9%].

(*b*) The Δ^{4a}-lactam (XIV) was prepared from cholest-4-en-3-one *syn*-oxime, m. p. 152—153°, as described [3] and had m. p. 252—255° (lit.,[3] 250—254°). It was hydrogenated with palladium–charcoal in ethanol to give 3-aza-A-homo-5α-cholestan-4-one (XV), m. p. 294—295° (lit.,[3] 294—296°). The ε-lactam (XV) (150 mg.) was refluxed with an excess of a fresh specimen of lithium aluminium hydride (500 mg.) in tetrahydrofuran (100 c.c.) for 48 hr. Working up as described above yielded 3-aza-A-homo-5α-cholestane (XVI) (95 mg.), $\nu_{max.}$ 3300 cm.$^{-1}$, no peak at 1670 cm.$^{-1}$, as an oil that gave the acetyl derivative, m. p. and mixed m. p. 111—112° with preparation (*a*).

Rearrangement of 5α-*Cholestan*-4-*one Oxime* (XVIII).—(*a*) 5α-Cholestan-4-one oxime (m. p. 221—223°; lit.,[4,5] 205°, 221—223°) (1·5 g.) was dissolved in purified thionyl chloride (10 c.c.) as above. The pale yellow solution was then slowly poured into 4N-potassium hydroxide (150 c.c.) at 20°. The colourless solid was filtered off, washed with water and with aqueous ethanol, dried in a vacuum-desiccator, and crystallised from chloroform–methanol, to give

[17] Fürst and Plattner, *Helv. Chim. Acta*, 1949, **32**, 275.

4a-*aza*-A-*homo*-5α-*cholestan*-4-*one* (XIX) (1·2 g.), m. p. 220—222° [Found (after drying at 80°/0·05 mm. for 4 hr.): C, 80·5; H, 11·7; N, 3·6. $C_{27}H_{47}NO$ requires C, 80·7; H, 11·8; N, 3·5%].

(*b*) The oxime (200 mg.) was dissolved in pentane (20 c.c.) and treated at 20° under anhydrous conditions with thionyl chloride (0·2 c.c.) in pentane (4 c.c.). After 6 hr., the mixture was poured into pure anhydrous chloroform and saturated with dry ammonia, and the precipitated ammonium chloride was filtered off. Evaporation of the filtrate *in vacuo* gave a yellow semi-solid material which was triturated with ether; the colourless solid product was filtered off, washed with ether, and crystallised from ethanol, to yield the lactam (XIX) (90 mg.), m. p. and mixed m. p. 220—222°.

4a-*Aza*-A-*homo*-5α-*cholestane* (XX).—The lactam (XIX) (500 mg.) was refluxed with lithium aluminium hydride (1 g.) in ether (400 c.c.) for 48 hr. The excess of the reagent was destroyed with moist ether; repeated extraction of the precipitate of aluminium hydroxide with ether, and evaporation of the combined, dried ethereal extracts gave an oil (460 mg.),which rapidly crystallised. Two recrystallisations from methanol gave 4a-*aza*-A-*homo*-5α-*cholestane* (XX), m. p. 90—92°, $[\alpha]_D$ +9° (*c* 0·5) [Found (after drying at 20°/0·05 mm. for 4 hr): C, 83·7; H, 12·6; N, 3·9. $C_{27}H_{49}N$ requires C, 83·65; H, 12·75; N, 3·6%]. Acetylation as above gave the N-*acetyl derivative*, m. p. 148—149° (from acetone) [Found (after drying at 60°/0·05 mm. for 6 hr.): C, 80·95; H, 12·05; N, 3·3. $C_{29}H_{51}NO$ requires C, 81·05; H, 11·95; N, 3·25%].

Acid Hydrolysis and Deamination of 4a-*Aza*-A-*homo*-5α-*cholestan*-4-*one* (XIX).—The lactam (XIX) (100 mg.) was heated with 10N-hydrochloric acid (1 c.c.) and ethanol (1 c.c.) in a sealed tube at 100° for 16 hr. Evaporation in a vacuum then gave 5-amino-4,5-seco-5α-cholestan-4-oic acid hydrochloride (XXIII), m. p. 155—160°, which was deaminated as described by Shoppee and Sly [2] with sodium nitrite in 50% acetic acid at 20° for 16 hr. The usual isolation procedure gave 5-hydroxy-4,5-seco-5α-cholestan-4-oic acid 4→5-lactone (XXII), $\nu_{max.}$ (in Nujol) 1715 cm.$^{-1}$ [CO(−O−)], as an oil whose infrared spectrum was identical with that of an authentic specimen.

5-*Hydroxy*-4,5-*seco*-5α-*cholestan*-4-*oic Acid* 4→5-*Lactone* (XXII).—5-Oxo-4,5-secocholestan-4-oic acid [6] (XXI), prepared from cholest-4-ene [m. p. 81·5°; lit.,[18] 82—83·5°; (purified through the 4β,5α-dibromide, m. p. 117°)], on ozonolysis in acetic acid and subsequent oxidation with hydrogen peroxide gave a product that was reduced with sodium borohydride in methanol to the lactone (XXII), identical with the foregoing preparation.

Reduction of 5-*Oxo*-4,5-*secocholestan*-4-*oic Acid Oxime:* 4a-*Aza*-A-*homo*-5α-*cholestan*-4-*one* (XIX).—The oxime (m. p. 165°; lit.,[6] 165—166°) (150 mg.) in refluxing ethanol (15 c.c.) was treated with sodium (1 g.) during 2 hr. The usual working up gave a solid (120 mg.), which was chromatographed on aluminium oxide (4 g.) in hexane. Elution with ether–hexane (2 : 3; 2 × 100 c.c.) gave semi-solid material (50 mg.); then elution with ether and chloroform–ether gave 4a-aza-A-homo-5α-cholestan-4-one (XIX) (60 mg.), m. p. and mixed m. p. 220—222° (from ethanol).

Rearrangement of 5α-*Cholestan*-6-*one Oxime* (XXIV).—(*a*) 5α-Cholestan-6-one oxime (m. p. 197—198°; lit.,[19,20] 195°, 196—198°) (3 g.) was dissolved in purified thionyl chloride (30 c.c.) as above. The yellow solution was at once slowly poured into 4N-potassium hydroxide (300 c.c.) at 20°. The pale yellow solid was filtered off, washed with water and with aqueous ethanol, dried in a vacuum-desiccator, and chromatographed on aluminium oxide (90 g.) in hexane. Elution with ether–hexane (1 : 1) yielded some unchanged oxime, but use of ether–hexane (>1 : 1) and ether gave a colourless solid, which on recrystallisation from ethanol afforded 6-*aza*-B-*homo*-5α-*cholestan*-7-*one* (XXV), m. p. 175—176°, $[\alpha]_D$ +52° (*c* 0·6) [Found (after drying at 60°/0·03 mm. for 4 hr.): C, 80·7; H, 11·4; N, 3·7. $C_{27}H_{47}NO$ requires C, 80·7; H, 11·8; N, 3·5%].

(*b*) The oxime (200 mg.) in pentane (20 c.c.) was treated with thionyl chloride (0·2 c.c.) in pentane (4 c.c.) under anhydrous conditions at 20° for 6 hr. The procedure (*b*) given for 5α-cholestan-4-one oxime then yielded a colourless solid (90 mg.), which was recrystallised from ethanol, to give 6-aza-B-homo-5α-cholestan-7-one, m. p. and mixed m. p. 174—176°.

6-*Aza*-B-*homo*-5α-*cholestane* (XXVI).—The lactam (XXV) (500 mg.) was refluxed with

[18] Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2406.
[19] Windaus and Dalmer, *Ber.*, 1919, **52**, 162.
[20] Shoppee, Evans, and Summers, *J.*, 1957, 97.

lithium aluminium hydride (1 g.) in ether (400 c.c.) for 48 hr. Working up [as for 4a-aza-A-homo-5α-cholestane (XX)] then gave an oil, which soon crystallised; two recrystallisations from moist methanol yielded 6-*aza*-B-*homo*-5α-*cholestane* (XXVI), m. p. 74—76°, $[\alpha]_D$ +69° (*c* 0·6) [Found (after drying at 20°/0·05 mm. for 4 hr.): C, 83·9; H, 13·0. $C_{27}H_{49}N$ requires C, 83·65; H, 12·75%]. The N-*acetyl derivative*, prepared as above, had m. p. 100—103°, $[\alpha]_D$ +46° (*c* 0·7) (from aqueous acetone) [Found (after drying at 20°/0·05 mm. for 4 hr.): C, 81·5; H, 11·9; N, 3·3. $C_{29}H_{51}NO$ requires C, 81·05; H, 11·95; N, 3·25%].

5-*Oxo*-5,6-*secocholestan*-6-*oic Acid* (XXVII).—Cholest-5-ene [18,21] (2 g.) was ozonised in chloroform (60 c.c.) at −10° for 2 hr.; after removal of the solvent under reduced pressure, the ozonide was dissolved in acetic acid–ethyl acetate (1 : 1) and treated with water (10 c.c.) and 30% hydrogen peroxide (1 c.c.) at 20° for 18 hr. The usual extraction procedure gave 5-oxo-5,6-secocholestan-6-oic acid as an oil,[7-10] $\nu_{max.}$ 1705 cm.$^{-1}$. The acid (1 g.) resisted oximation by hydroxylamine (1·4 g.) and sodium acetate trihydrate (2 g.) in boiling ethanol (30 c.c.) for 24 hr.

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[21] Mauthner and Suida, *Monatsh.*, 1894, **15**, 85.