Photoinduced Transformations. Part 41.[1] Photo-Beckmann Rearrangement of Some Cholestan-3-one Oximes with Methyl Groups attached to the α-Carbon

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Methylation of 4,4-dimethyl-5α-cholestan-3-one with methyl iodide and base gave 2α,4,4-trimethyl-5α-cholestan-3-one and 2,2,4,4-tetramethyl-5α-cholestan-3-one as the major products. The photoreactions of 4,4-dimethyl-5α-cholestan-3-one oxime and 2α,4,4-trimethyl-5α-cholestan-3-one oxime afforded the corresponding 3-aza- and 4-aza-lactams, respectively, arising by a Beckmann-type rearrangement. In these photorearrangements no products resulting from α-fission are formed. These results contrast with those of the acid-catalysed reaction in which products resulting from second-order Beckmann rearrangement predominate.

ONE of the features of the photo-Beckmann rearrangement, a reaction valuable in synthesis, is that in contrast with the Beckmann rearrangement, the photorearrangement is rarely accompanied by products resulting from α-fission.[2,3] This paper describes the preparation of four steroid ring-A lactams (8), (9), (13), and (14) which have methyl substituents α to the amide functions. These were required for studies on the circular dichroism of lactams,[4] and were prepared by the photoreactions of 4,4-dimethyl-5α-cholestan-3-one oxime[5] (7) and 2α,4,4-trimethyl-5α-cholestan-3-one oxime (11).

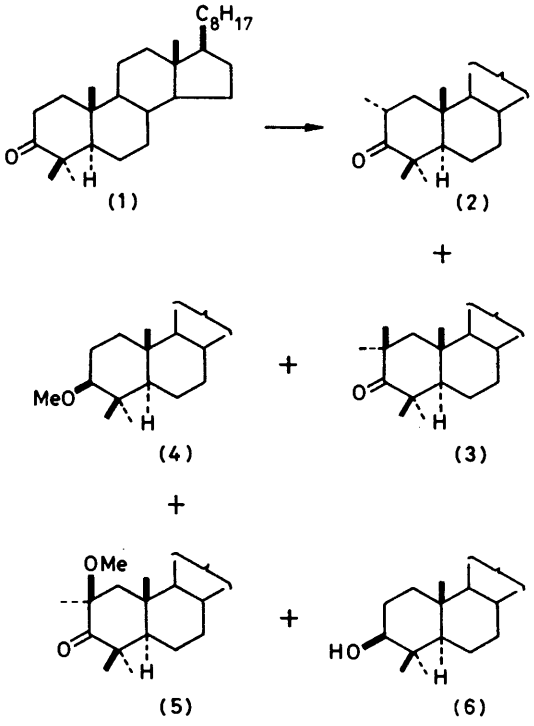
RESULTS

Preparation of the Substrates.—2α,4,4-Trimethyl-5α-cholestan-3-one (2) was prepared in 21% yield by the reaction of 4,4-dimethyl-5α-cholestan-3-one (1)[6] with methyl iodide in boiling t-butyl alcohol in the presence of potassium t-butoxide. 2,2,4,4-Tetramethyl-5α-cholestan-3-one (3) (24%), two new minor products, 3β-methoxy-4,4-dimethyl-5α-cholestane (4) and 2ξ-methoxy-2ξ,4,4-trimethyl-5α-cholestan-3-one (5), and a trace amount of 3β-hydroxy-4,4-dimethyl-5α-cholestane (6)[6] were also formed (Scheme 1). The structures of these compounds, together with the conformation of ring A of the three ketones (2), (3), and (5), are based on the following spectral (see also Experimental section) and chemical evidence.

Signals in the n.m.r. spectrum of the 3-ketone (2) due to a proton and a methyl group attached to C-2 appeared as a multiplet centred at τ 7.23 and a doublet at τ 8.98 (*J ca.* 4 Hz) as confirmed by double resonance. Thus, irradiation at the frequency of the centre of the latter signal caused a collapse of the former to a broad doublet with *J* 7.5 Hz. The coupling constant of the proton at C-2 and chemical shift of that at C-19 are only consistent with a 2α-methyl group in a chair form[7] of ring A.

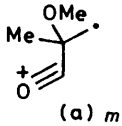
The mass spectrum of the ketone (3) exhibited the molecular ion as the base peak; however, that of the ketone (5) showed a molecular ion of only low abundance.

The n.m.r. spectra of these ketones, (3) and (5), exhibited three-proton singlets at τ 9.22 and 9.29 due to the protons at C-19. These chemical shifts deviate considerably from those predicted by the additivity of chemical shifts[7] since the signals due to all the tertiary methyl groups other than 18-H of the chair ketones (1)[8] [τ 9.37 (18-H) and 8.98 (19-H, C-4-Me)] and (2) appeared at lower field than τ 8.96 (the introduction of methyl or methoxy groups at C-2 should cause these signals to move further downfield). These considerable upfield shifts prove that the conformation in ring A of the ketones (3) and (5) is not a chair but an unspecified boat

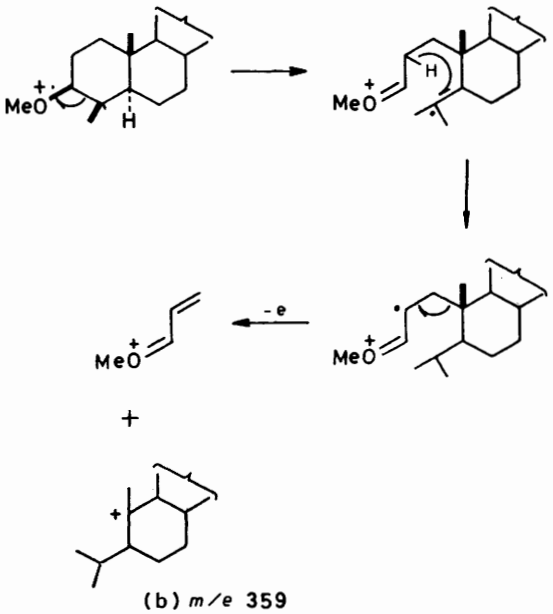


SCHEME 1

in which 19-H is within a shielding cone of the 3-oxo-group. The prominent peaks in the mass spectrum of (5) were those at *m/e* 430 (10%), 114 (26), 100 (48), and 99 (100). The fragment having *m/e* 100 may have structure (a).



(a) *m/e* 100



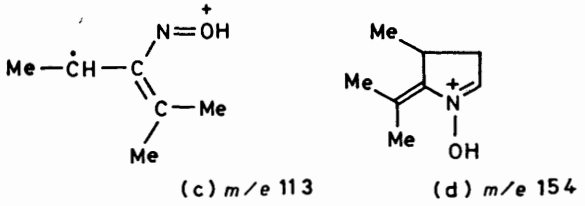
SCHEME 2

The methoxyketone (5) is probably formed by reaction of the ketone (2) with iodine to afford a 2α-iodide followed by reaction with methoxide ion.

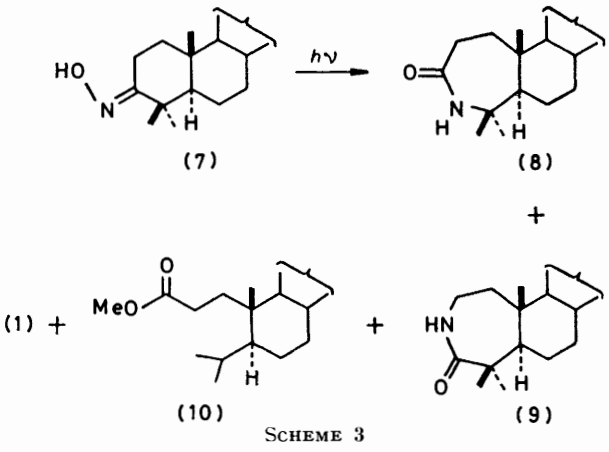
Product (4) was identified by spectral means; its structure was confirmed by its preparation from methylation of the 3β-ol (6). The mass spectrum of (4) exhibited an intense molecular ion (47%) and a base peak at *m/e* 359. The structure and genesis of the base peak (b) may be as shown in Scheme 2. The effect of substitution at C-4 on the mass spectral fragmentation of 3β-methoxy-5α-cholestane [9] is apparent.

The oximes (7) and (11) were prepared by the standard method. Oximation of the hindered ketone (3) failed even under severe conditions.

The fragmentation behaviour of the oxime (11) was in complete analogy with that of the oxime (7) and the structures of the base peak at *m/e* 113 and a prominent peak at *m/e* 154 (34%) can be (c) and (d), respectively,



as assigned by Goldsmith *et al.*[10] The ^{1}H n.m.r. spectrum of the oxime (7) showed a one-proton broad doublet at τ 6.83 (*J* 13 Hz) which was assigned to the 2α-H deshielded by the hydroxyimino-group.[3] This confirmed the *syn* configuration of the hydroxy-group with respect to the C-2–C-3 bond in a chair conformation of ring A. The conformation of ring A of the ketone (2) was a chair (as discussed above), while that of the oxime (11) was found by ^{1}H n.m.r. to be a boat. The spectrum exhibited a one-proton broad multiplet centred at τ 6.74, and a three-proton doublet at τ 8.86 (*J* 4.5 Hz), assigned by double resonance to a proton and a methyl group, respectively, at C-2: irradiation at the frequency of the centre of the multiplet changed the three-proton doublet at τ 8.86 to a singlet, while irradiation at the frequency of the doublet at τ 8.86 changed the multiplet to a broad signal. A model of the oxime (11) indicates that if ring A takes a chair form a proton attached to C-2 would not be deshielded by the *syn* hydroxyimino-group to such an extent, since the 2β-proton is not eclipsed by the C=N group. However, if ring A takes a boat conformation, the 2β-proton is eclipsed by the C=N group and should be deshielded by the *syn* hydroxyimino-group. Thus, a multiplet at τ 6.74 can be assigned to the 2β-proton and ring A should be in an unspecified boat conformation with the hydroxyimino-group *syn*-oriented with respect to the C-2–C-3 bond. The chemical shift of the proton at C-19 of the oxime (11) can also be reasonably explained in terms of a boat conformation for ring A but not by a chair. Thus, a signal due to 19-H of the oxime (11) was found at τ 9.31. If ring A of the oxime (11) is a chair, a signal due to 19-H should be found at lower field than that (τ 9.10) observed for

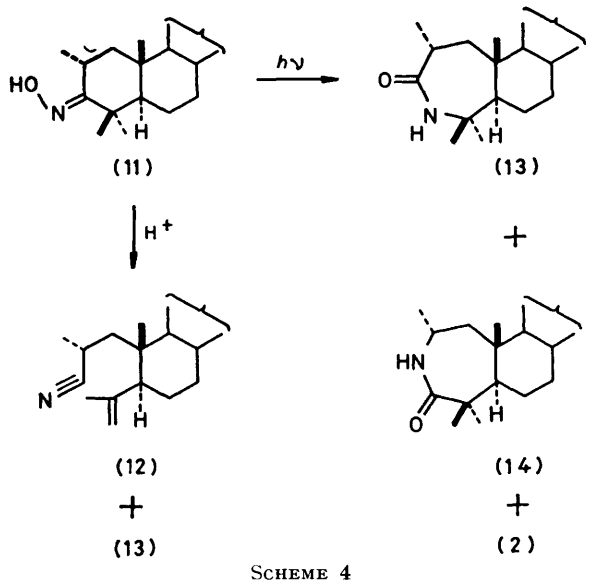


SCHEME 3

5α-cholestan-3-one oxime,[1] ring A of which is a chair. In fact, the reverse is true, proving that ring A of the oxime (11) is an unspecified boat form. Considerable shielding of the 19-H is attributable mainly to the C=N group.

Acid-catalysed and Photo-Beckmann Rearrangements (*Schemes* 3 *and* 4).—Beckmann rearrangement of the oxime (7) with toluene-*p*-sulphonyl chloride in pyridine under reflux has previously been reported to yield 4a,4a-dimethyl-4-aza-A-homo-5α-cholestan-3-one (8) (8.5%) and 4-methyl-4-methylene-3,4-seco-5α-cholestane-3-nitrile (85%).[5]

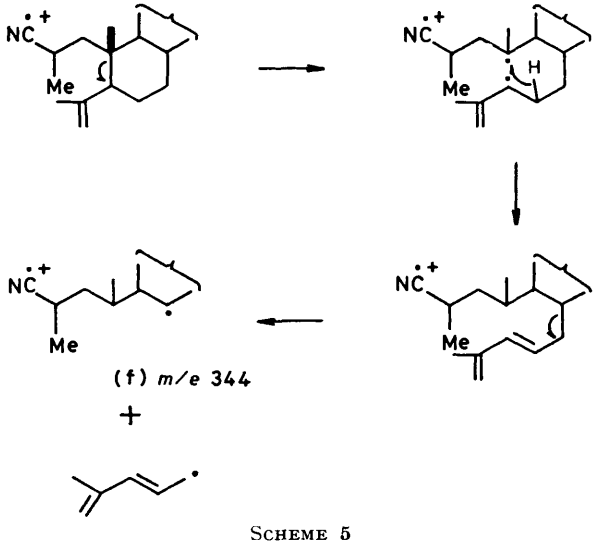
Beckmann rearrangement of the oxime (11) in dioxan with thionyl chloride at room temperature afforded 2α,4-dimethyl-4-methylene-3,4-seco-5α-cholestane-3-nitrile (12), together with a very low yield of 2α,4a,4a-trimethyl-4-aza-A-homo-5α-cholestan-3-one (13) (Scheme 4). The structure of (12) was confirmed by its mass, i.r., and n.m.r. spectra. The mass spectrum exhibited the



SCHEME 4

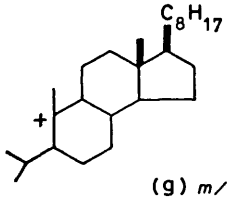
molecular ion as the base peak (*m/e* 435) and contained only two other intense peaks (e) and (f) over *m/e* 100, at *m/e* 312 (45%) and 344 (61). Accurate mass measurements showed that the ions (e) and (f) were due to $C_{22}H_{34}N^+$ (*m/e* 321.369 5) and $C_{24}H_{42}N^+$ species (344.335 2). The ion (e) thus arises from trivial loss of the C-17 side chain.[11] The structure and genesis of the ion (f) may be as depicted in Scheme 5. On the other hand, irradiation of 4,4-dimethyl-5α-cholestan-3-one oxime (7) (2.3×10^{-3}M), by a procedure similar to the photoreaction of cholestane oximes previously reported,[3] afforded methyl 4-methyl-2,3-seco-5α-cholestane-2-carboxylate (10) (16%), 4a,4a-dimethyl-4-aza-A-homo-5α-cholestan-3-one (8) (4%), and a new lactam, 4a,4a-dimethyl-3-aza-A-homo-5α-cholestan-4-one (9) (6%) (Scheme 3).

Photolysis of a solution of 2α,4,4-trimethyl-5α-cholestan-3-one oxime (11) (1.6×10^{-3}M) afforded a

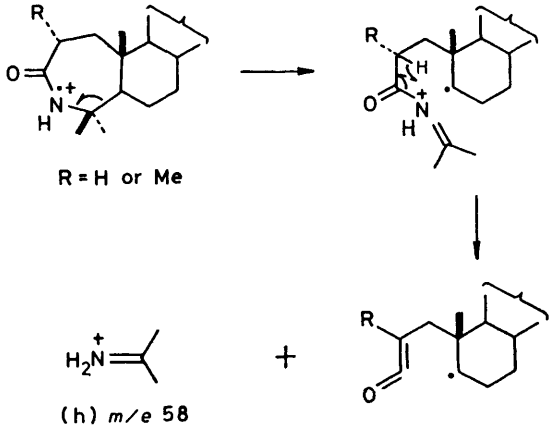


SCHEME 5

complex mixture of products. Preparative t.l.c. afforded 2α,4a,4a-trimethyl-4-aza-A-homo-5α-cholestan-3-one (13) (11%) and a new lactam 2α,4a,4a-trimethyl-3-aza-A-homo-5α-cholestan-4-one (14), (4%) together with the parent ketone (2) (2%) (Scheme 4). The structure of these products followed from their i.r., n.m.r., and mass spectra (see Experimental section). The mass spectrum



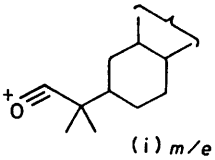
of the ester (10) exhibited a base peak at *m/e* 359. The structure of this ion may be (g). The mass spectra of lactams (8) and (13) showed a common base peak at *m/e* 58 with no other ions having an abundance >8%. This spectrum contrasts with the reported fragmentation of 4-aza-A-homo-5α-cholestan-3-one (12) in which



SCHEME 6

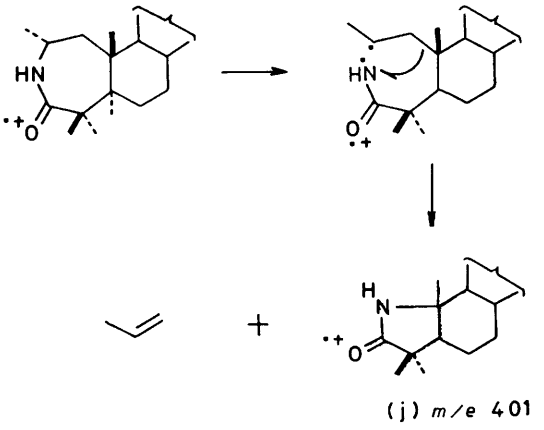
the molecular ion was the base peak. The structure and genesis may be rationalized as in Scheme 6.[12] In contrast to the 4-aza-lactams, the molecular ions in the mass spectra of the 3-aza-lactams (9) and (14) were in much greater abundance (61.1 and 35.5% respectively). The fragmentation of 3-aza-A-homo-5α-cholestan-4-one has been discussed.[13] The present results show that the introduction of methyl groups at C-2 and C-5 had a significant effect on the mode of fragmentation [13] in the mass spectrum of 3-aza-A-homo-5α-cholestan-4-one. Thus, in contrast to 3-aza-A-homo-5α-cholestan-4-one, the [M^+ — ring D] ion (*m/e* 274) of lactams (9) and (14) was not significant [6.0% in lactam (9) and 0.9% in (14)]. The lactam (9) exhibited a base peak at *m/e* 387 and an intense ion of *m/e* 386 (93.6%). However, the intensity of the ion with *m/e* 386 in the lactam (14) was only 9.4% and the only intense ions over *m/e* 120 in (14) were those of *m/e* 428 ($M^+ - CH_3$, 11.8%) and 401 (29.3). The structure of the ion may be (i), as suggested by Budzikiewicz *et al.*[13]

Accurate mass measurement (*m/e* 401.368 2) showed that the ion of *m/e* 401 in (14) was due to a $C_{27}H_{47}NO^+$ species. The suggested genesis and structure of this species (j) is depicted in Scheme 7. The abundance of



(i) *m/e* 386

this ion was only 7.3% in the lactam (9) and thus the effect of the 2α-methyl group in lactam (14) for the cleavage of the C-2–N bond is apparent. The n.m.r. spectra of the lactams (13) and (14) are consistent with a chair conformation for ring A as shown for caprolactam [14] and related fused systems.[15] Dreiding models of lactams (13) and (14) indicate that the dihedral angles



(j) *m/e* 401

SCHEME 7

between the C(2)-βH–C(1)-αH and the C(2)-βH–C(1)-αH in their chair conformations are *ca.* 90 and 150° respectively. These dihedral angles require $J_{2\beta,1\alpha} \simeq 0$ Hz and $J_{2\beta,1\beta} \simeq 7$—12 Hz. The n.m.r. spectrum of the lactam (13) showed a multiplet at τ 7.26 (2β-H) which collapsed to a broad doublet (*J* 6 Hz) by irradiation at the frequency of the centre of a doublet (τ 8.88) due to the 2α methyl group. Similarly, the n.m.r. spectrum of the lactam (14) showed, after D_2O exchange, a multiplet at τ 6.14 (2β-H) which changed to a broad singlet ($W_{\frac{1}{2}}$ 9 Hz) by irradiation at the frequency of the centre of the 2α methyl (τ 8.81). These splittings after decoupling can be taken as $J_{2\beta,1\beta} + J_{2\beta,1\alpha}$ and are in agreement with those expected for chair conformations.* It is noted that the 10β methyl resonances of lactams (8) and (9) are shifted to lower field by 0.04 and 0.11 p.p.m., respectively, by introduction of a 2α methyl. It is very probable that ring A of lactams (8) and (9) is also in a chair conformation.

In the present photoreactions, nitriles from second-order photo-Beckmann rearrangements, major products in acid-catalysed Beckmann rearrangements, were not formed. The results thus indicate the contrast between photo- and ordinary-Beckmann rearrangement and show the advantage of the photo-Beckmann rearrangement in synthesis.

* A boat and a twisted chair (formed by a flip of the C-2 of the chair) cannot be excluded purely on the grounds of n.m.r. spectra. Thus, the dihedral angle between the 2β-H and the 1α-H and that between the 2β-H and the 1β-H for the boat are *ca.* 10 and 110 which requires *J* values of *ca.* 8—10 and 1—2 Hz respectively. The dihedral angles between the corresponding protons for the twisted chair are 100 and 20° which require *J* values of *ca.* 0—0.5 and 7—9 Hz respectively. The observed *J* values do not significantly deviate from these values. However, models show that these conformations are clearly less favourable.

EXPERIMENTAL

For instruments used and general procedure see ref. 3. I.r. spectra were determined for Nujol mulls with a JASCO IRA-1 spectrometer. Low resolution mass spectra were determined with a Hitachi JMS-D 300 spectrometer (source temperature 180 °C; ionizing voltage 70 eV unless stated otherwise) by the staff of the Faculty of Pharmaceutical Sciences of this University. Only significant peaks higher than *m/e* 300 and fragment peaks of relative intensities over 30% in ions lower than *m/e* 300 are mentioned. High-resolution mass spectra were recorded with a Hitachi RMU 7MF double focusing mass spectrometer (direct inlet system; source temperature 180 °C; ionizing voltage 70 eV).

4,4-Dimethyl-5α-cholestan-3-one Oxime (7).[5]—To a solution of 4,4-dimethyl-5α-cholestan-3-one (1) (1.228 g) in ethanol (500 ml), a solution of hydroxylamine hydrochloride (1.531 g) containing sodium acetate trihydrate (1.514 g) in water (12 ml) was added. The solution was stirred at 28 °C for 30 min. The solvent was removed and the residue extracted with diethyl ether. Usual work-up gave a residue which was recrystallized from diethyl ether–methanol (yield 1.02 g). The pure sample had m.p. 208—209° (lit.,[5] 207—209°); $\nu_{max.}$ 930, 947, and 3 332 cm^{-1}; τ 9.39 (3 H, s, 18-H), 8.92, 8.98, or 9.05 (3 H, s, 19-H), 6.83 (1 H, br d, *J* 13 Hz, 2α-H), and two of 8.92, 8.98, and 9.05 (3 H, s, C-4-Me).

The Photo-Beckmann Rearrangement of the Oxime (7).—The oxime (7) (387 mg) in methanol (400 ml) was irradiated with a 12-W low-pressure mercury arc in an atmosphere of nitrogen until the oxime disappeared (19 g). Removal of the solvent under reduced pressure afforded a residue, examination of which by t.l.c. (benzene–diethyl ether, 10 : 1) showed three major compounds. The two less mobile compounds were the lactams (8) and (9). The product was subjected to preparative t.l.c. using benzene–diethyl ether (1 : 1). The most mobile fraction (201 mg) was a gum, its n.m.r. spectrum showing its major part to be a seco-ester containing several minor products. This was again subjected to preparative t.l.c. (solvent, benzene–hexane 4 : 3) to yield a second mobile fraction (70 mg). This was recrystallized from methanol to yield *methyl 4-methyl-2,3-seco-5α-cholestane-2-carboxylate* (10) as needles (63 mg), m.p. 60.5—61°, $[\alpha]_D^{19}$ +6.3° (*c* 0.01, chloroform) (Found: C, 80.75; H, 12.3. $C_{30}H_{54}O_2$ requires C, 80.65; H, 12.3%); $\nu_{max.}$ 1 648 (ester C=O); τ 9.36 (3 H, s, 18-H), 9.17 (3 H, s, 19-H), and 6.34 (3 H, s, OMe); *m/e* (70 eV, source temp. 185°) 446 (M^+, 8.9%), 431 ($M^+ - CH_3$, 3.8), 403 (8.4), 360 (30.5), 359 (100), 333 (7.6), 331 (18.0), 81 (39.1), 69 (35.2), 55 (34.0), and 43 (31.8). Of the two less mobile fractions, the more mobile one (29 mg) was recrystallized from diethyl ether–dichloromethane to afford 4a,4a-dimethyl-3-aza-A-homo-5α-cholestan-4-one (9) (23

mg), m.p. 190—191°, $[\alpha]_D^{19}$ +37.4 (*c* 1.2, $CHCl_3$); $\nu_{max.}$ 1 646 (amide I), 3 077, 3 205, 3 281 (lactam NH), 1 418, 1 368, 1 355, and 1 345 cm^{-1}; τ 9.37 (3 H, s, 18-H), 9.03 (3 H, s, 19-H), 6.57 and 7.00 (2 H, each br s, 2-H), 8.74 and 8.80 (each 3-H, s, 4a-Me), and 4.10 (1 H, br s, NH); *m/e* 429 (M^+, 61.1%), 414 ($M^+ - CH_3$, 19.4), 412 (17.2), 387 (100), 386 (93.6), 358 (23.4), 316 (15.1), 315 (28.9), 287 (18.8), 99 (36.7), 95 (38.4), 70 (41.9), 69 (48.3), 57 (36.9), 55 (49.5), 45 (22.6), 44 (26.6), 43 (63.0), and 41 (38.2). A less mobile fraction (58 mg) was recrystallized from diethyl ether–dichloromethane to afford 4a,4a-dimethyl-4-aza-A-homo-5α-cholestan-3-one (8) (15 mg), m.p. 226—229° (lit.,[5] 228—229°); $\nu_{max.}$ 1 631 and 1 663 (amide I) and 3 240 cm^{-1} (NH); τ 9.38 (3 H, s, 18-H), 8.98 (3 H, s, 19-H), 7.76 (2 H, m, 2α- and 2β-H), 8.67 and 8.79 (each 3 H, s, 4a-Me), and 4.38 (1 H, s, NH); *m/e* 429 (M^+, 3.7), 414 ($M^+ - CH_3$, 1.6), 401 (0.3), and 58 (100).

Reaction of 4,4-*Dimethyl*-5α-*cholestan*-3-*one with Methyl Iodide in the Presence of Potassium t-Butoxide*.—To the 3-ketone (4.0 g) and potassium t-butoxide [from potassium (6.1 g) and t-butyl alcohol (100 ml)] in t-butyl alcohol (50 ml) and dry benzene (30 ml), was added methyl iodide (60 ml). The solution was refluxed for 66 h. After the addition of water, the solution was extracted with dichloromethane (2 l) and the organic layer worked up as usual. The crude product (3.9 g) was subjected to column chromatography (Wako gel C-200, 120 g; hexane–benzene 1 : 1 as eluant) to afford three fractions (A, B, and C). The first fraction A (894 mg), which showed three spots on t.l.c., was recrystallized from acetone–methanol to afford 2,2,4,4-*tetramethyl*-5α-*cholestan*-3-*one* (3) (494 mg), m.p. 90—91°. An analytical specimen was obtained by further recrystallization and had $[\alpha]_D^{19}$ +41.8° (*c* 0.99, $CHCl_3$) (Found: C, 84.2; H, 12.3. $C_{31}H_{54}O$ requires C, 84.1; H, 12.3%); $\nu_{max.}$ 1 699 (C=O) and 1 041 cm^{-1}; τ 9.35 (3 H, s, 18-H), 9.22 (3 H, s, 19-H), two of 8.82, 8.86, 8.87, and 8.93 (each 3-H, s, 2-Me), and two of 8.82, 8.86, 8.87, and 8.93 (each 3-H, s, 4-Me); *m/e* 442 (M^+, 100%), 427 ($M^+ - CH_3$, 18.2), 357 (10.5), 302 (32.7), 287 (37.6), 123 (32.4), 109 (40.2), 95 (51.6), 83 (49.3), 81 (44.0), 69 (43.2), 57 (35.4), 55 (43.0), and 43 (42.2). The residue from the filtrate and the second fraction (1.5 g) were combined and were subjected again to column chromatography using hexane–benzene (1 : 1) to afford six fractions (1—6). Fraction 1 (390 mg) was subjected to preparative t.l.c. (Wako gel B-5F; benzene–hexane 2 : 3) to afford three fractions. The most mobile fraction (49 mg) was recrystallized from diethyl ether–methanol to afford 3β-methoxy-4,4-dimethyl-5α-cholestane (4), m.p. 106—108°. The next most mobile fraction (259 mg) was subjected again to preparative t.l.c. using hexane–benzene (1 : 1) as eluant to afford the 3-ketone (3) and 2α,4,4-trimethyl-5α-cholestan-3-one (2). The third most mobile fraction (76 mg) was the 3-ketone (2) which could not be obtained in a crystalline form; τ 9.34 (3 H, s, 18-H), 8.96 (3 H, s, 19-H), 7.23 (1 H, m, 2β-H), 8.98 (3 H, d, *J* 4 Hz, 2α-Me), and 8.86 and 8.96 (each 3 H, s, 4-Me); $\nu_{max.}$ 1 730 (C=O), 1 285, 1 118, 1 069, and 736 cm^{-1}. Fraction 2 (650 mg) was subjected to preparative t.l.c. (benzene–hexane 1 : 1) to afford the 3-ketones (3) (135 mg) and (2) (486 mg). Fraction 3 (329 mg) was the nearly pure 3-ketone (2). Fraction 4 (390 mg) was subjected to preparative t.l.c. (benzene–hexane 1 : 2) to afford two fractions. The more mobile fraction (123 mg) was the 3-ketone (2). The less mobile fraction (247 mg) was an unidentified gum. Fraction 5 (174 mg) was recrystallized from diethyl ether–methanol to afford 2ξ-*methoxy*-2ξ,4,4-*trimethyl*-5α-*cholestan*-3-*one* (5) (84 mg), m.p. 103—104°, $[\alpha]_D^{20}$ +80.6° (*c* 1.0, $CHCl_3$) (Found: C, 80.95; H, 11.75. $C_{31}H_{54}O_2$ requires C, 81.15; H, 11.85%); $\nu_{max.}$ 1 706 (C=O), 1 066, and 716 cm^{-1}; τ 9.37 (3 H, s, 18-H), 9.29 (3 H, s, 19-H), one of 8.77, 8.77, and 8.94 (each 3 H, s, 2-Me), two of 8.77, 8.77, and 8.94 (each 3 H, s, 4-Me), and 6.94 (3 H, s, 2ξ-OMe); *m/e* (70 eV, source temp. 175°) 458 (M^+, 4.8%), 443 (M^+, 0.5), 430 ($M^+ - CO$, 10.3), 428 (6.3), 393 (5.8), 373 (6.8), 100 (47.7), and 99 (100). Fraction 6 (170 mg) was an unidentified gum. Thus, the total yields of the 3-ketones (2) and (3) from fractions A and B were 938 (24%) and 850 mg (21) respectively. Fraction C (91 mg) was recrystallized from diethyl ether–methanol to yield 4,4-dimethyl-5α-cholestan-3β-ol (6) (130 mg), identical with an authentic specimen.

4,4-*Dimethyl*-3β-*methoxy*-5α-*cholestane* (4).—To 4,4-dimethyl-3β-hydroxy-5α-cholestane (100 mg) in benzene (4.4 ml), was added potassium metal (44 mg) and the mixture was refluxed for 0.5 h under nitrogen. Methyl iodide (2 ml) was added and the solution was refluxed for *ca.* 40 h during which time methyl iodide (16 ml) was added to the solution in 8 doses. After methanol had been added to the cooled solution, the solvents were removed under reduced pressure. The residue was extracted with diethyl ether and the ethereal solution worked up as usual. The residue was recrystallized from diethyl ether–methanol to afford the 3β-*methoxycholestane* (4) (62 mg), m.p. 106—108° (Found: C, 83.5; H, 12.55. $C_{30}H_{54}O$ requires C, 83.65; H, 12.65%); $[\alpha]_D^{22}$ +24.3° (*c* 0.99 $CHCl_3$); $\nu_{max.}$ 1103 (C–O) and 1 187 cm^{-1}; τ 9.36 (3 H, s, 18-H), 9.22 (3 H, s, 19-H), 7.35 (1 H, dd, *J* 3.9 and 11.4 Hz, 3α-H), 9.06 and 9.14 (each 3 H, s, 4-Me), and 6.64 (3β-OMe); *m/e* 430 (M^+, 47.0%), 415 ($M^+ - CH_3$, 7.3), 398 ($M^+ - CH_3OH$, 28.6), 383 ($M^+ - CH_3 - CH_3OH$, 20.1), 359 (100), 135 (55.5), 123 (40.4), 121 (31.7), 109 (48.7), 107 (31.0), 95 (72.2), 83 (35.1), 81 (60.1), 71 (34.4), 69 (60.7), 57 (47.9), 55 (51.4), 43 (47.1), and 41 (35.7).

2α,4,4-*Trimethyl*-5α-*cholestan*-3-*one Oxime* (11).—The 3-ketone (2) (938 mg), hydroxylamine hydrochloride (1 g), and sodium acetate hydrate (1 g) in ethanol (120 ml) and water (10 ml) were refluxed for 24 h. After removal of a part of the solvent, the solution was extracted with dichloromethane. The organic layer was washed with water and dried (Na_2SO_4). Removal of the solvent left a residue (892 mg) which was recrystallized from diethyl ether–methanol to yield the oxime (542 mg). The residue from the filtrate was subjected to preparative t.l.c. with benzene to afford three fractions (A, B, and C). The most mobile fraction (67 mg) was crude recovered ketone. The second most mobile fraction (187 mg) was recrystallized to afford the oxime (148 mg). Fraction C (36 mg) was an unidentified gum. The total yield was 71%. The *oxime* (11) had m.p. 183—184°, $[\alpha]_D^{21}$ +15.0° (*c* 1.0, $CHCl_3$) (Found: C, 81.2; H, 12.1; N, 3.15. $C_{30}H_{56}NO$ requires C, 81.2; H, 12.05; N, 3.15%); $\nu_{max.}$ 3 280 (OH), 1 130, and 935 cm^{-1}; τ 9.38 (3 H, s, 18-H), 9.31 (3 H, s, 19-H), 6.74 (1 H, m, 2β-H), 8.86 (3 H, d, *J* 4.5 Hz, 2α-Me), and 8.70 and 8.81 (each 3 H, s, 4-Me); *m/e* 443 (M^+, 13.7%), 428 ($M^+ - CH_3$, 7.8), 427 ($M^+ - O$, 8.8), 426 ($M^+ - OH$, 9.5), 154 (31.1), and 113 (100).

Beckmann Rearrangement of 2α,4,4-*Trimethyl*-5α-*cholestan*-3-*one Oxime* (11).—To the oxime (11) (101 mg) in dry dioxan (5 ml) at 15 °C was added thionyl chloride (0.1 ml). The solution was stirred for 15 min and then poured into

water. The solution was extracted with dichloromethane and the organic layer worked up as usual. The residue (106 mg) was subjected to preparative t.l.c. with benzene–diethyl ether (1 : 1) as eluant to afford two fractions. A very mobile crystalline fraction (36 mg) was recrystallized from diethyl ether–methanol to afford 2α,4-*dimethyl*-4-*methylene*-3,4-*seco*-5α-*cholestane*-3-*nitrile* (12) (21 mg), m.p. 101—101.5°, $[\alpha]_D^{20}$ +50.9° (*c* 1.0, $CHCl_3$) (Found: C, 83.25; H, 12.05; N, 3.5. $C_{30}H_{51}N$ requires C, 84.65; H, 12.1; N, 3.3%); $\nu_{max.}$ 2 222 (CN) and 894 cm^{-1} (C=CH_2); τ 9.32 (3 H, s, 18-H), 9.10 (3 H, s, 19-H), 7.24 (2 H, dd, *J* 11 and 6 Hz, 2-H), 8.70 (3 H, d, *J* 7.1 Hz, 2-Me), 8.28 (3 H, s, 4-Me), and 5.15 and 5.38 (each 1 H, d, *J* 1.5 Hz, 4-methylene); *m/e* 425 (M^+, 100%), 410 ($M^+ - CH_3$, 13.5), 344 (61.2), 329 (18.1), 312 (45.4), 95 (47.0), 83 (34.2), 82 (30.6), 81 (52.3), 71 (30.4), 69 (46.6), 57 (48.6), 55 (51.2), 43 (46.0), and 41 (34.6). The less mobile crystalline fraction (60 mg) was recrystallized from dichloromethane–methanol to afford 2α,4a,4a-trimethyl-4-aza-A-homo-5α-cholestan-3-one (13), identical with a specimen obtained by the photo-Beckmann rearrangement.

Photo-Beckmann Rearrangement of 2α,4,4-*Trimethyl*-5α-*cholestan*-3-*one Oxime* (11).—The oxime (11) (536 mg) in methanol (750 ml) was irradiated in a nitrogen atmosphere for 43 h. After removal of the solvent, the residue was subjected to preparative t.l.c. (benzene–diethyl ether 1 : 1) to afford four fractions. The most mobile fraction (186 mg) was a mixture of several products including seco-esters and the parent ketone (10 mg). The second most mobile (69 mg) and the least mobile fractions (120 mg) were unidentified gums. The third fraction (241 mg) was subjected again to preparative t.l.c. (benzene–diethyl ether 1 : 1) to afford four fractions. The most and least mobile fractions (5 and 35 mg respectively) were unidentified gums. The second most mobile fraction (33 mg) was recrystallized from diethyl ether–methanol to afford 2α,4a,4a-*trimethyl*-3-*aza*-A-*homo*-5α-*cholestan*-4-*one* (14) (24 mg), m.p. 166.5—167.5°, $[\alpha]_D^{18}$ −15.1° (*c* 0.35, $CHCl_3$) (Found: C, 79.8; H, 12.05; N, 3.25. $C_{30}H_{53}NO$ requires C, 81.2; H, 12.05; N, 3.15%); $\nu_{max.}$ 3 293 and 3 247 (lactam NH), 1 638 (lactam C=O), 1 015, and 719 cm^{-1}; τ 9.34 (3 H, s, 18-H), 8.92 (3 H, s, 19-H), 6.14 (2 H, m, 2-H), 8.81 (3 H, d, *J* 6.0 Hz, 2-Me), 8.72 and 8.79 (each 3 H, s, 4a-Me), and 4.32 (1 H, d, *J* 4.5 Hz, NH); *m/e* 443 (M^+, 35.3%), 428 (11.8), 401 (29.3), 400 (14.2), 69 (30.8), 58 (37.4), 57 (36.8), and 44 (100). The third fraction (85 mg) was recrystallized from dichloromethane–methanol to afford 2α,4a,4a-trimethyl-4-aza-A-homo-5α-cholestan-3-one (13) (57 mg), m.p. 209—210°, $[\alpha]_D^{18}$ −3.5° (*c* 1.0, $CHCl_3$) (Found: C, 81.05; H, 12.25; N, 3.2. $C_{30}H_{53}NO$ requires C, 81.2; H, 12.05; N, 3.15%); $\nu_{max.}$ 3 286 (OH), 1 657 (lactam C=O), and 723 cm^{-1}; τ 9.35 (3 H, s, 18-H), 8.94 (3 H, s, 19-H), 7.26 (2 H, m, 2-H), 8.88 (3 H, d, *J* 6.8 Hz, 2-Me), 8.78 and 8.67 (each 3 H, s, 4a-Me), and 4.15 (1 H, s, NH); *m/e* 443 (2.6%), 428 ($M^+ - CH_3$, 0.9), 400 (3.9), 386 (3.4), and 58 (100).

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