Photo-induced Transformations. Part LXI.[1] Syntheses of Some Six-membered and Eight-membered Lactams of the B-Homo- and A-Nor-B,B-dihomocholestane Series by the Photo-Beckmann Rearrangement

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The syntheses of 3-aza-B-homo-5α-cholestan-4-one, 4-aza-B-homo-5α-cholestan-3-one, 6-aza-A-nor-B,B-dihomo-5α- and 5β-cholestan-7-one, and 7-aza-A-nor-B,B-dihomo-5α- and 5β-cholestan-6-one by the photo-Beckmann rearrangement of the oximes of A-nor-B-homo-5α-cholestan-3-one and A-nor-B-homo-5α and 5β-cholestan-6-one are described. An A/B *trans* ring-junction stereochemistry of the parent ketones was deduced by estimating the relative stabilities of the principal conformers of the A/B *cis*- and *trans*-isomers of the A-nor-B-homocholestan-3-ones and A-nor-B-homocholestan-6-ones by molecular mechanics calculations.

OUR previous studies on the photo-Beckmann rearrangement of several types of steroidal ketone oximes in methanol established that two isomeric lactams arising from the migration of either of the two carbon centres adjacent to the hydroxyimino-group are formed in moderate-to-good yield with retention of chirality.[2] We noted the synthetic potential of this photo-reaction which can be carried out in neutral media and at room temperature.

In this paper we report the preparations of two aza-B-homocholestanes (6) and (7), in which the amide group forms part of ring A, and four aza-A-nor-B,B-dihomocholestanes (11), (12), (15), and (16), in which the amide group forms part of ring B, by the photo-Beckmann rearrangement of A-nor-B-homo-5α-cholestan-3-one oxime (5) and A-nor-B-homo-5α- and 5β-cholestan-6-one oximes (10) and (14), respectively.

A-Nor-B-homo-5α-cholestan-3-one (4),[3] A-nor-B-homo-5α-cholestan-6-one (9),[4] and A-nor-B-homo-5β-cholestan-6-one (13),[4] intermediates for the preparations of the oximes, were obtained by the photochemical method reported by Swiss investigators for the preparation of 17β-acetoxy-A-nor-B-homoandrostan-3- and 6-one[5] (Scheme 1). The ketone (4) has already been prepared by this method[3] but the configuration at C-5 was not assigned. The two ketones (9) and (13) have already been synthesized by the treatment of 5β-cholestane-4β,5-diol 4-tosylate or 5α-cholestane-4α,5-diol 4-tosylate, respectively, with potassium t-butoxide in t-butyl alcohol.[4]

Irradiation of 4β,5-epoxy-5β-cholestan-3-one (1)[6] in dioxan with an Hanovia 450 W high-pressure mercury arc through a Vycor filter for 70 h gave 6-hydroxy-A-nor-B-homocholest-5-en-3-one (2) in 61% yield. Treatment of the ketone with acetic anhydride and pyridine gave crystalline 6-acetoxy-A-nor-B-homocholest-5-en-3-one (3) in 82% yield. Hydrogenolysis of this enol acetate with Pd–C catalyst gave crystalline A-nor-B-homo-5α-cholestan-3-one (4)[3] in 27% yield. Refluxing a solution of the ketone (4) with potassium t-butoxide in t-butyl alcohol under nitrogen did not cause racemization at C-5 and the starting ketone (4) was recovered unchanged. Thus, compound (4) is more stable than its 5-epimer since no formation of any isomeric ketone was detected by t.l.c. An inspection of a Dreiding model of compound (4), together with the fact that the more stable A-nor-B-homocholestan-6-one epimer is the 5α-epimer (9) (*vide infra*), suggested that ketone (4) is almost certainly the 5α-isomer. Empirical force-field calculations confirmed the assignment quantitatively.

Calculations on the 5α- and 5β-isomers of A-nor-B-homocholestane were performed using the 'MM2' program (QCPE 395)[7] to deduce the principal conformations with energy minima for each isomer. The ORTEP stereodrawings of the A/B-ring portions of the two principal conformers of the 5α- [(4)-A and (4)-B] and 5β-isomers [iso-(4)-A and iso-(4)-B] are shown in Figure 1 and their calculated energies are listed in Table 1. The results show that the (4)-B conformer, in which ring B is in a *quasi*-chair form, is the most stable of the four isomers and is some 2 kcal mol^{-1} † more stable than iso-(4)-B, ring B of which is in a *quasi*-boat form. The

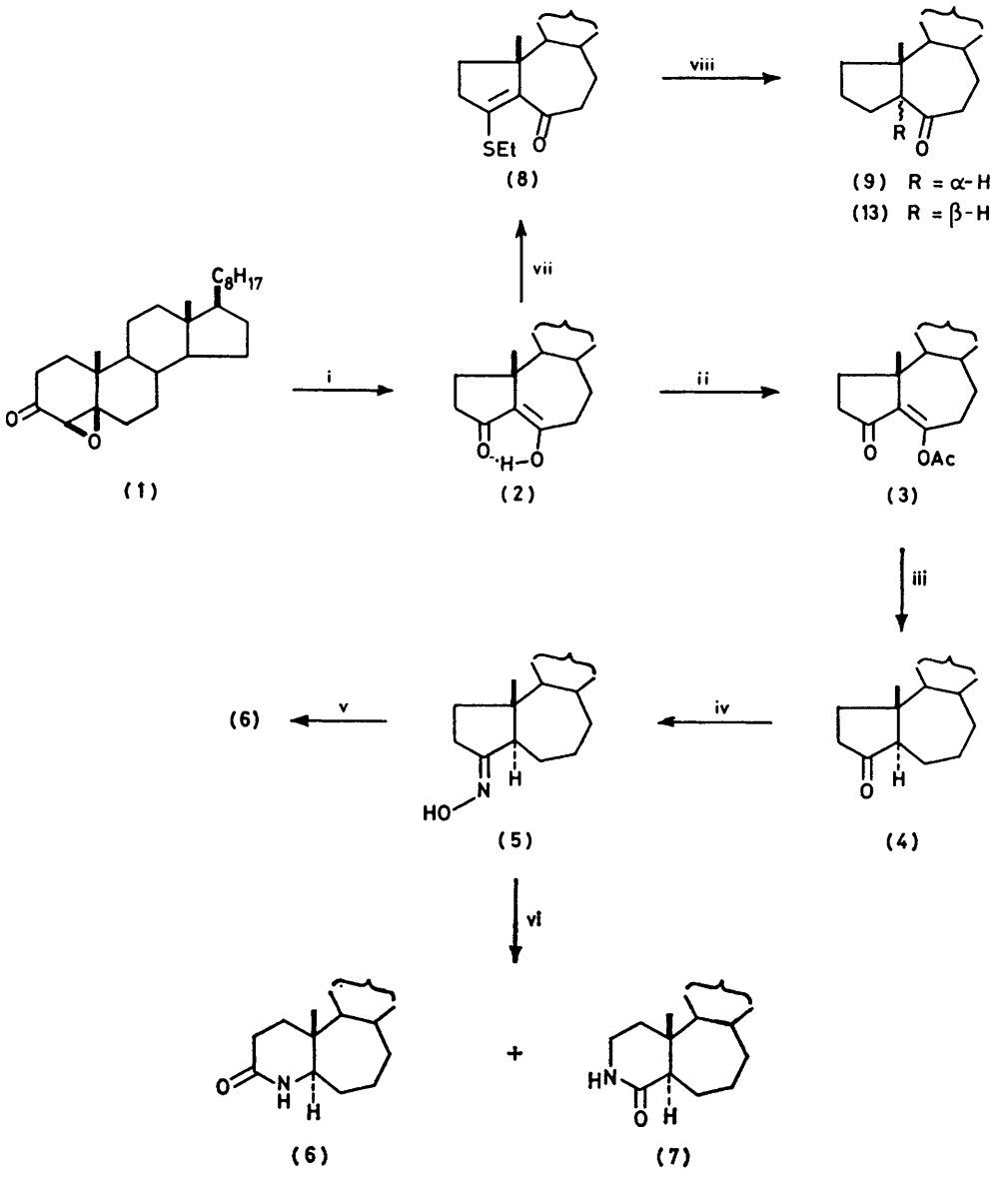
TABLE 1

Enthalpies and strain energies (kcal mol^{-1}) and conformer populations of A-nor-B-homo-5α- and 5β-cholestan-3-ones (25 °C) and -6-ones (100 °C) calculated by the MM2 force-field programme

Conformer	Strain energy	$\Delta H_f°$	$\Delta\Delta H_f°$	Population (%)
(4)-A	45.40	−124.37	2.89	0.7
(4)-B	42.51	−127.26	0.00	95.6
iso-(4)-A	45.35	−124.42	2.84	0.8
iso-(4)-B	44.57	−125.20	2.06	2.9
(9)-A	61.62	−123.82	3.55	0.6
(9)-B	58.08	−127.37	0.00	69.9
(13)-A	59.51	−125.94	1.43	10.1
(13)-B	59.03	−126.42	0.95	19.4

population of each conformer, which was obtained by assuming that all of them are in equilibrium at 25 °C, is also listed in Table 1. The ratio of the 5α- to the 5β-isomer is 96 : 4 and this is in agreement with the results obtained from equilibration with base.

† 1 cal = 4.184 J.



SCHEME 1 *Reagents*: i, *hν*, dioxan; ii, Ac_2O, pyr; iii, H_2, 10% Pd–C, benzene; iv, $H_2NOH{\cdot}HCl$, NaOAc, EtOH; v, H^+, dioxan; vi, *hν*, MeOH; vii, EtSH, AcOH, H^+; viii, Raney–Ni, EtOH

The Beckmann rearrangement of oxime (5) [3] in dioxan with thionyl chloride gave a new lactam (6) as the sole product in 75% yield, the structure of which was confirmed as 4-aza-B-homo-5α-cholestan-3-one (6) by ^1H n.m.r. and other spectroscopic data (see Table 2). On the other hand the photo-Beckmann rearrangement of oxime (5) in methanol with a low-pressure mercury arc for 24 h gave the lactam (6), identical with a specimen obtained by the Beckmann rearrangement, together with the isomeric crystalline lactam (7). The structure of the new lactam (7) was established as 3-aza-B-homo-5α-cholestan-4-one on the basis of its ^1H n.m.r., i.r., and mass spectra. The ^1H n.m.r. spectrum showed a 2 H multiplet at δ 3.35—3.21 due to its C-2 methylene group. The hydrogen on C-5 of both lactams (6) and (7) should be α-oriented on the supposition that both the Beckmann and the photo-Beckmann rearrangements take place while retaining the original configurations of the migrating centres of the starting oximes.[2] The yields of (6) and (7) were 44 and 16%, respectively. Only a small amount (2%) of the parent ketone (4) was formed in this photoreaction.

We then turned our attention to the photo-Beckmann rearrangement of A-nor-B-homo-5α- and 5β-cholestan-6-one oximes. The enolone (2) was transformed into 3-ethylthio-A-nor-B-homocholest-3-en-6-one (8) in 75% yield by treatment with ethanethiol in glacial acetic acid containing hydrochloric acid. This vinyl sulphide (8) was treated with Raney Nickel to yield a mixture of the 5α-ketone (9) and the 5β-ketone (13) in 26 and 13%

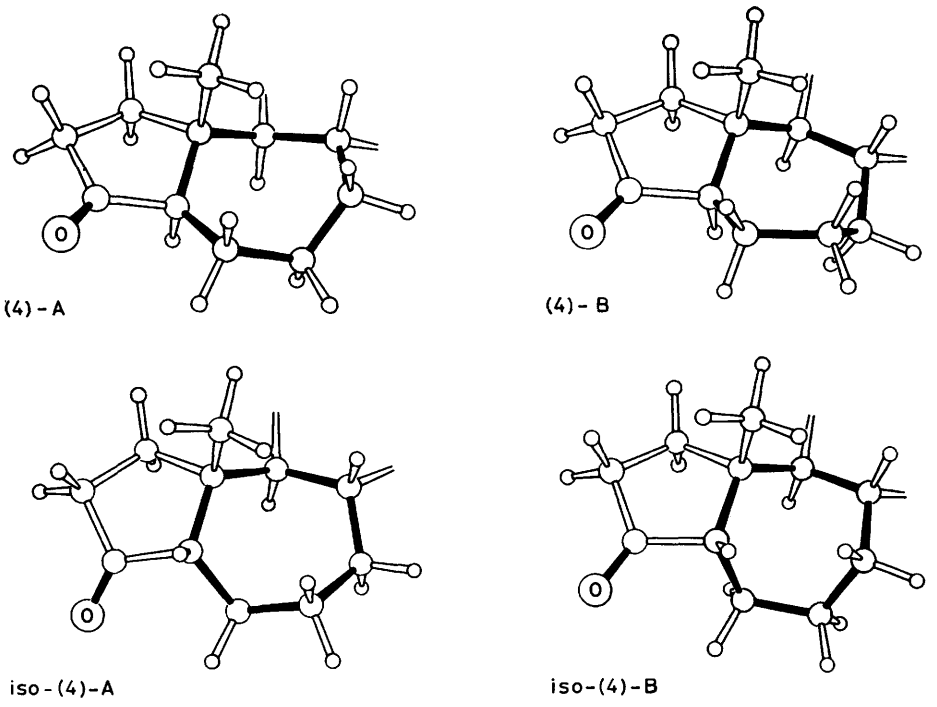


FIGURE 1 ORTEP stereodrawings of the major conformers of the ketone (4) and its 5β-isomer (rings A and B only shown)

isolated yield, respectively. The configuration of these ketones at C-5 has already been proved by Nussim and Mazur on the basis of chemical evidence.[4] They also found that the two ketones are equilibrated when heated either at 100 °C in acid solution or with potassium t-butoxide in t-butyl alcohol; the ratio of the two ketones (9) and (13) in the equilibrium mixture is 4 : 1. In order to examine the validity of our results on the configuration at the C-5 of A-nor-B-homo-5α-cholestan-3-one by means of molecular mechanics calculations, we also carried out the calculations to obtain principal conformations with energy minima for both the 5α-(9) and 5β-(13) ketones

TABLE 2

^{1}H N.m.r. parameters δ of 3- and 4-aza-B-homocholestanone and 6- and 7-aza-A-nor-B,B-dihomocholestanone derivatives in $CDCl_3$ solution (δ/Hz)

Compd.	5-H	18-H_3	19-H_3	7-H (13)(14) 7a-H (15)(16)	Others
(6)	3.43br. (d) [a] (9)	0.67 (s)	0.92 (s)		6.75br. (s, NH) ($w_{\frac{1}{2}}$ 4.5) 2.34—2.19 (2 H, m, 2-H_2)
(7)		0.67 (s)	0.96 (s)		6.77br. (s, NH) ($w_{\frac{1}{2}}$ 12.0) 3.35—3.21 (m, 2-H_2)
(13)	3.98br. (t) [a] (7.5)	0.62 (s)	0.87 (s)	2.89—*ca.* 2 [b] (m)	6.54 (d, NH) (9.0)
(14)	*ca.* 2.32 [b]	0.64 (s)	0.95 (s)	3.18—2.87 (m)	6.11 (t) (6.0)
(15)	4.12 (d) [a] (7.5)	0.68 (s)	0.86 (s)	2.16—*ca.* 2.1 [b] (m)	5.69 (d, NH) (9.0)
(16)	*ca.* 2.54 [b]	0.69 (s)	0.98 (s)	3.45—3.02 (m)	5.85 (d) (6.0)

[a] After treatment with D_2O. [b] Overlapped with other proton signals.

TABLE 3

^{1}H N.m.r. parameters δ for A-nor-B-homocholestane and 6- and 7-aza-A-nor-B,B-dihomocholestanone derivatives in $CDCl_3$ solution (δ/Hz)

Compd.	5-H	18-H_3	19-H_3	Others
(2)	—	0.69 (s)	1.11 (s)	
(3)	—	0.74 (s)	1.23 (s)	2.22 (s) (OAc)
(4)		0.68 (s)	0.84 (s)	
(5)		0.68 (s)	0.83 (s)	
(8)	—	0.72 (s)	1.18 (s)	
(9)	3.05br. (t) (7.5)	0.69 (s)	0.69 (s)	
(10)	3.02 (dd) (5.4 and 9.0)	0.69 (s)	1.06 (s)	
(11)	2.60 (t) [a]	0.68 (s)	0.72 (s)	
(12)	2.74 (dd) [a]	0.68 (s)	1.00 (s)	

[a] Overlapped with 7a-H signal.

and to estimate the population of each conformer. Steric energies of each of the two principal conformers of the two ketones are listed in Table 1 and the ORTEP drawings of the A/B-ring portions of two principal conformers [(9)-A and (9)-B] of the 5α-ketone and two principal conformers of the 5β-ketone [(13)-A and (13)-B] are shown in Figure 2. The most stable conformer of the four is the *trans* conformer (9)-(B), in which ring-B is in a *quasi* chair conformation; it is *ca.* 1 kcal mol^{-1} more

stable than the *cis* conformer (13)-B. Populations of each conformer, calculated by assuming that all the conformers are in equilibrium at 100 °C, are also listed in Table 1. The calculated 7 : 3 ratio of the 5α- and 5β-isomers is in good agreement with the experimental results quoted above.

These ketones afforded a single oxime each, (10) and (14) respectively, by the standard method at room temperature. The ^{1}H n.m.r. spectra of these oximes show no signal at *ca.* δ 3.4 (deshielded by the hydroxyimino-group) which is usually found in 6-membered-ring ketone oximes.[2] The Beckmann rearrangement of the oxime (10) with thionyl chloride in dioxan afforded a new lactam in 89% yield without any accompanying formation of the isomeric lactam (Scheme 2). The structure of the lactam was confirmed as 6-aza-A-nor-B,B-dihomo-5α-cholestan-7-one (11) on the basis of its i.r., n.m.r., and mass spectra. Thus, the geometry of the hydroxyimino-group was confirmed to be *anti*. The Beckmann rearrangement of oxime (14) with thionyl chloride likewise gave an amorphous new lactam in 67% yield (Scheme 2), the structure of which was established as 6-aza-A-nor-B,B-dihomo-5β-cholestan-7-one (15) on the basis of i.r., mass, and ^{1}H n.m.r. spectral evidence. As in the case of the oxime (10) no isomeric lactam was formed, confirming the *anti*-configuration of the hydroxyimino-group.

Irradiation of a methanolic solution of the oxime (10) for 86 h afforded lactam (11) and a new isomeric lactam (12) in 13 and 25% yields, respectively, which were isolated by preparative t.l.c. (Scheme 2). The former compound was identical with that obtained by Beckmann rearrangement of the oxime (10) and the structure of (12) was confirmed as 7-aza-A-nor-B,B-dihomo-5α-cholestan-6-one on the basis of i.r., mass, and ^{1}H n.m.r. spectral evidence. The ^{1}H n.m.r. spectrum showed a 2 H multiplet at δ 2.87—3.18 due to its C-7a methylene group. Similarly, photolysis of a methanolic solution of the oxime (14) for 60 h and separation of the products by preparative t.l.c. afforded two lactams, 6-aza-A-nor-B,B-dihomo-5β-cholestan-7-one (15) and 7-aza-A-nor-B,B-dihomo-5β-cholestan-6-one (16), both in 25% yield (Scheme 2). The former compound was shown to be identical with the lactam obtained by the ground-state Beckmann rearrangement of the oxime (14). The structure of the latter was established on the basis of i.r., mass, and ^{1}H n.m.r. spectral results. The 2 H multiplet at δ 3.02—3.45 in the n.m.r. spectrum is assigned to the C-7a methylene protons adjacent to the imino-nitrogen atom. The hydrogen on C-5 of the lactams (11) and (12) should again be α-oriented, and those of (15) and (16) should be β, on the basis of the established stereochemistry [2] of both the Beckmann and the photo-Beckmann rearrangements. It should be noted that structures of the lactams (11) and (12) and those of the lactams (15) and (16) can be clearly distinguished by their mass spectra. Thus, the mass spectra of lactams (11) and (15) revealed their base peak at *m/e* 69 and the prominent ion of *m/e* 373 (M^+ — CO). High-resolution mass spectrometry confirmed that the elemental compositions of these ions are $C_3H_3NO^+$ and $C_{26}H_{47}N^+$, respectively. The genesis of the former ion can reasonably be explained in terms of the assigned structures (11) and (15) and is depicted in Scheme 3. On the other

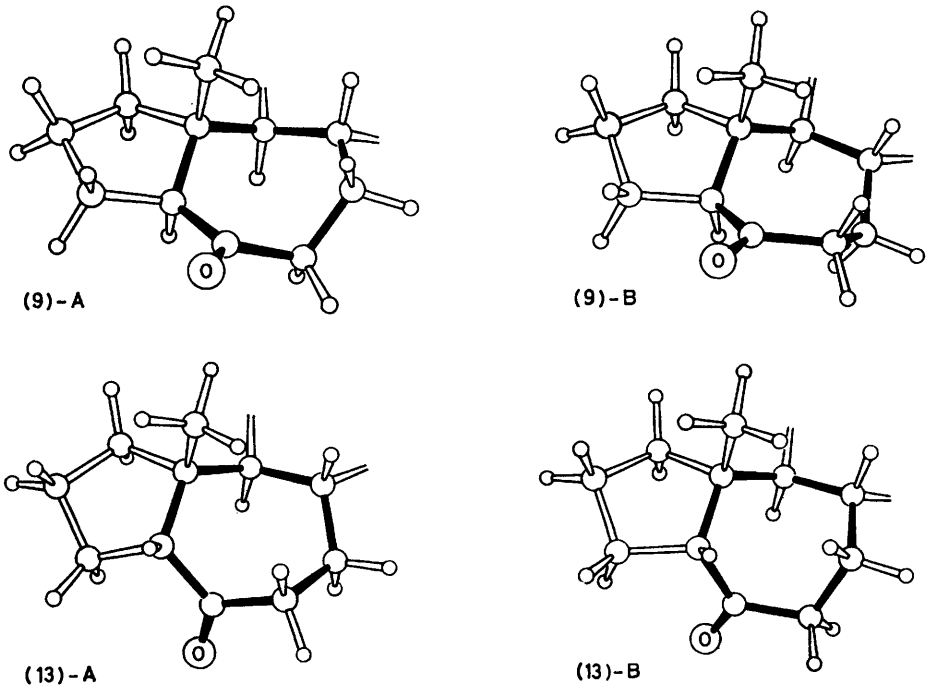
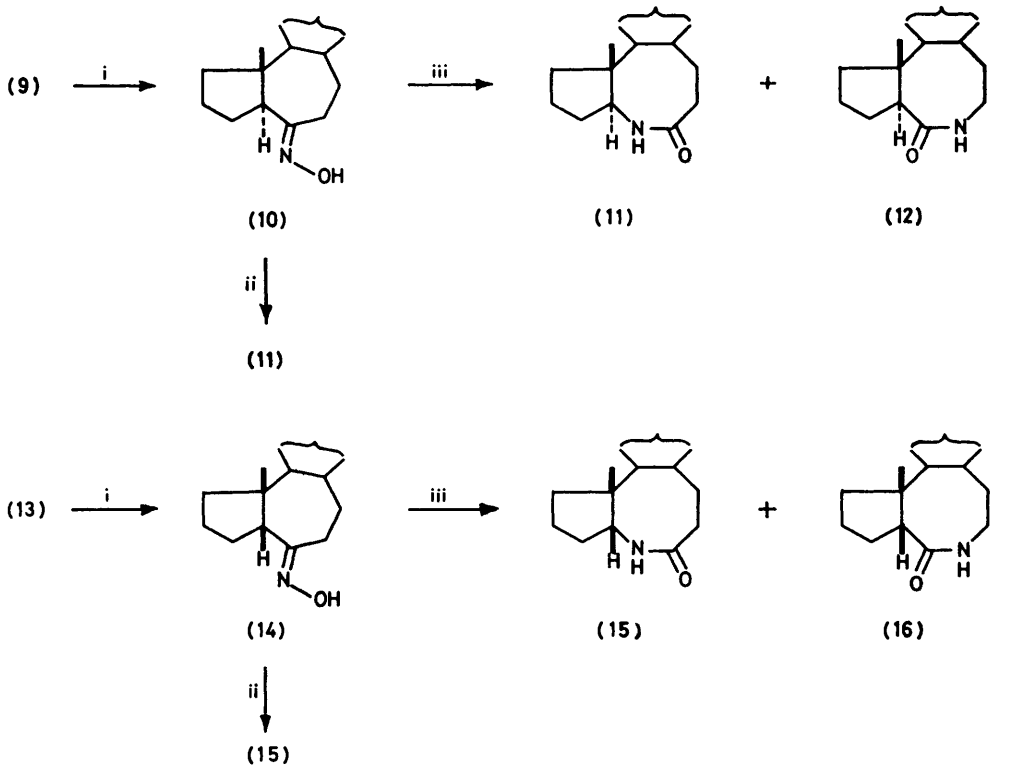
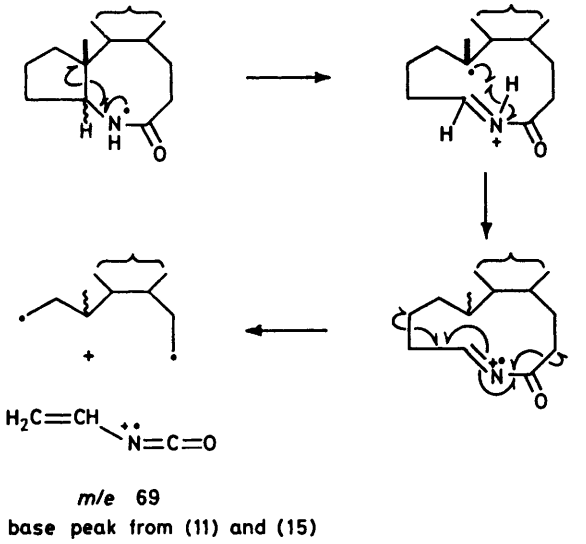


FIGURE 2 ORTEP stereodrawings of the major conformers of the ketones (9) and (13) (rings A and B only shown)



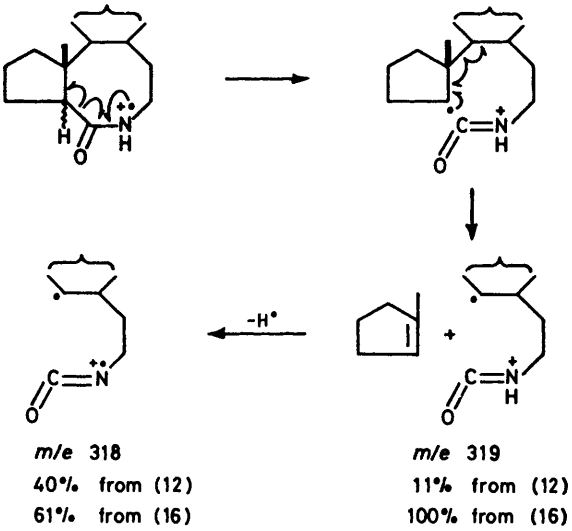
SCHEME 2 *Reagents*: i, H_2NOH·HCl, NaOAc, EtOH; ii, H^+, dioxan; iii, *hν*, MeOH

hand, the mass spectrum of lactam (16) showed prominent peaks due to the molecular ion (100%) and the prominent ions at *m/e* 318, and the base peak due to the ion *m/e* 319.



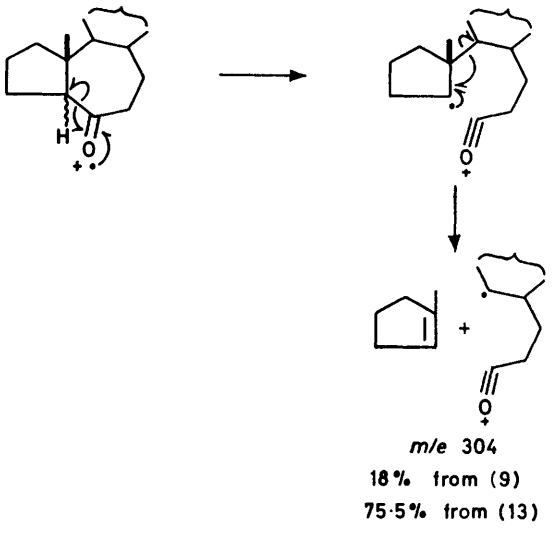
SCHEME 3 Proposed mechanism for the formation of the ion of *m/e* 69 in the mass-spectral fragmentation of lactams (11) and (15)

Accurate mass measurements confirmed that the latter two species have the constitution $C_{21}H_{36}NO^+$ and $C_{21}H_{37}NO^+$, and their formation from the molecular ion can be explained in terms of the assigned structure (16) as arising from expulsion of ring A as shown in Scheme 4. The mass spectrum of the lactam (12) showed the molecular ion as the base peak and the ion at *m/e* 318, although it was less prominent than that for lactam (16). A close analogy to this mode of fragmentation was found in the electron-impact mass spectra of A-nor-B-homo-5α- and 5β-cholestan-6-ones (9) and (13) as shown in Scheme 5. Both ketones revealed a prominent ion of *m/e* 304 due to



SCHEME 4 Proposed mechanism for the formation of ions of *m/e* 318 and 319 in the mass-spectral fragmentation of lactams (12) and (16)

a species of $C_{21}H_{36}O^+$ which arises from the expulsion of ring A from the molecular ion.



SCHEME 5 Proposed mechanism for the formation of the ion of *m/e* 304 in the e.i. mass-spectral fragmentation of the ketones (9) and (13)

EXPERIMENTAL

I.r. spectra were determined for Nujol mulls with a JASCO IRA-1 spectrophotometer. Low-resolution mass spectra of compounds (4), (6), (7), (8), (10), and (14) were recorded with a Hitachi JMS-D 300 spectrometer (ion-source temperature 180 °C, ionizing voltage 70 eV) by the laboratory for mass spectrometric analysis, the Faculty of Pharmaceutical Sciences, Hokkaido University. Low-resolution mass spectra of compounds (3), (5), (9), (11)—(13), (15), and (16) and the high-resolution mass spectra were recorded with a Hitachi JMS-D 300 spectrometer (70 eV) by the laboratory for mass spectrometric analysis, the Faculty of Agriculture, Hokkaido University. M.p.s were determined with a Yanagimoto micro m.p. apparatus. ^1H N.m.r. spectra were determined with a JEOL PS 100 high-resolution spectrometer (solvent $CDCl_3$; $SiMe_4$ as internal reference). U.v. spectra were determined with a Hitachi 124 double-beam spectrophotometer. The ^1H n.m.r. data are listed in Tables 2 and 3. T.l.c. was carried out on Wako-gel B-5 plates. Optical rotations were measured for chloroform solutions with a JASCO DIP-SL automatic polarimeter. Elemental analyses were performed by the staff of the Faculty of Pharmaceutical Sciences.

Preparation of 6-*Hydroxy*-A-*nor*-B-*homocholest*-5-*en*-3-*one* (2).—The epoxy-ketone (1) [6] (13.5 g) dissolved in dioxan (2.7 l) under nitrogen was irradiated with a Hanovia 450 W high-pressure mercury arc lamp with a Vycor filter for 70 h. Evaporation of the solvent gave a product which was recrystallized from acetone to yield the *enone* (2) (8.3 g, 61%), m.p. 92—94 °C; $[\alpha]_D^{22}$ +58.7° (*c* 1.03); (Found: C, 80.85; H, 11.1. $C_{27}H_{44}O_2$ requires C, 80.94; H, 11.07%); $\nu_{max.}$ 3 400br (OH), 1 600—1 650br (C=O), 1 228, 1 044, 905, and 875 cm^{-1}; $\lambda_{max.}$ (dioxan) (ε) 290 nm (9 900).

Acetylation of Compound (2).—The enone (200 mg) and acetic anhydride (2.5 ml) in pyridine (2.5 ml) were stirred for 6 d at room temperature. The solution was poured into ice–water to give crystals which were filtered off and recrystallized from methanol to yield 6-*acetoxy*-A-*nor* B-*homocholest*-5-*en*-3-*one* (3) (66 mg), m.p. 64.0—65.5 °C. Column chromatography of the residue obtained by evaporation of the filtrate (Wako C-200 silica gel, 4 g) with hexane–benzene (1 : 3 v/v) as eluant, followed by gradient elution with the mixed solvent with decreasing amounts of hexane, and finally with pure benzene, afforded the starting enone (12 mg) and a further crop of the acetate (116 mg), giving a total yield of the acetate (3) of 82%; (Found: C, 78.55; H, 10.55. $C_{29}H_{46}O_3$ requires C, 78.68; H, 10.47%); $\nu_{max.}$ 1 763 (OAc), 1 730 (C=O), 1 642 (C=C), 1 207, 1 151, 1 036, 887, and 860 cm^{-1}; $\lambda_{max.}$ (EtOH) (ε) 252 nm (10 000); *m/e* (rel. intensity) 442 (M^+, 0.2%), 400 (16.7), 382 (18.1), 151 (40.8), 138 (100), and 123 (37.1).

A-*Nor*-B-*homo*-5α-*cholestan*-3-*one* (4) *by Hydrogenolysis of the Enol Acetate* (3).—The enol acetate (3) (3.34 g) in benzene (167 ml) containing 10% Pd–C (3.34 g) was stirred under hydrogen for one week. After removal of the catalyst the solvent was evaporated off to yield a product (2.84 g) which was subjected to column chromatography (Wako C-200 silica gel, 120 g). Elution with hexane, hexane containing increasing amounts of benzene, and finally with pure benzene, gave four fractions A (80 mg), B (1.23 g), C (90 mg), and D (1.30 g) in order of increasing polarity. Fraction A was an unidentifiable mixture. Fraction B contained the required product. Fraction C was a mixture containing some of the required product. Fraction D was the starting acetate (3). Fraction B was recrystallized from acetone to yield pure compound (4) in 27% yield, m.p. 124—125 °C (lit.,[6] m.p. 123 °C); $[\alpha]_D^{19}$ −74.1° (*c* 1.0) {lit.,[6] $[\alpha]_D^{20}$ −80 ± 5° (*c* 0.2, dioxan)} (Found: C, 83.6; H, 12.1. Calc. for $C_{27}H_{46}O$: C, 83.87; H, 11.99%); $\nu_{max.}$ 1 732 cm^{-1} (C=O); *m/e* (rel. intensity) 386 (M^+, 78.0%), 371 ($M^+ - CH_3$, 6.7), 232 (100), and 231 (95.9). A racemization experiment was attempted by dissolving compound (4) (20 mg) in t-butyl alcohol (7 ml) containing potassium t-butoxide and then refluxing the solution under nitrogen for 2 h. The solution was worked up as usual. Examination of the product by t.l.c. showed a single spot due to the starting ketone. The ^1H n.m.r. spectrum of the product was also identical with that of the starting ketone.

anti-A-*Nor*-B-*homo*-5α-*cholestan*-3-*one Oxime* (5).—The ketone (4) (1.07 g), hydroxylamine hydrochloride (1.32 g), and sodium acetate monohydrate (1.34 g) in ethanol (120 ml) containing a few drops of water were stirred for 2 h at room temperature. The solvent was removed under reduced pressure and the product was extracted with aqueous diethyl ether. The organic layer was separated and worked up as usual to yield the crude oxime (880 mg), recrystallization of which from Et_2O–MeOH gave the pure oxime (5) (681 mg), m.p. 188—189 °C (lit.,[6] m.p. 180—181 °C). (Found: M^+, 401.3670. Calc. for $C_{27}H_{47}NO$, *M*, 401.3658), $\nu_{max.}$ 3 240 (OH) and 951 cm^{-1}; *m/e* (rel. intensity) 401 (M^+, 23.7%), 384 (M^+ − OH, 100), 110 (19.7), 109 (22.2), and 57 (32.9).

Beckmann Rearrangement of the Oxime (5).—To the oxime (5) (103 mg) in dioxan (3 ml) was added thionyl chloride (0.5 ml) at room temperature and the solution was stirred for 20 min. After the addition of water the solution was extracted with a mixture of diethyl ether and 5% aqueous sodium hydrogen carbonate. The ethereal layer was separated and worked up as usual to afford the crude lactam (6) (101 mg) which was recrystallized from diethyl ether to yield the pure *lactam* (77 mg), m.p. 207—208 °C; $[\alpha]_D^{23.5}$ +13.5° (*c* 0.99) (Found: C, 80.55; H, 12.0; N, 3.6. $C_{27}H_{47}NO$ requires C, 80.73; H, 11.80; N, 3.49%); $\nu_{max.}$ 1 674 cm^{-1} (C=O); *m/e* (rel. intensity) 401 (M^+, 100%) and 386 ($M^+ - CH_3$, 17.2).

Photo-Beckmann Rearrangement of the Oxime (5).—The oxime (300 mg) in methanol (Wako special grade, 200 ml) was irradiated with a low-pressure mercury arc (Rayonet preparative photochemical reactor RPR 208) under nitrogen for 24 h. After the removal of solvent the product was subjected to preparative t.l.c. with development with 4 : 1 CH_2Cl_2–Et_2O. The plate was developed three times and two fractions A (87 mg) and B (173 mg) were obtained. The more mobile fraction A was again subjected to preparative t.l.c. (development with benzene) to give the starting oxime (27 mg) and the parent ketone (6 mg). Fraction B, which was a mixture of two lactams, was again subjected to preparative t.l.c. with 4 : 1 CH_2Cl_2–Et_2O. The plate was developed three times to yield a more mobile fraction [44 mg, 16% based on (5) consumed] which was recrystallized from diethyl ether to give 3-*aza*-B-*homo*-5α-*cholestan*-4-*one* (7), m.p. 165—170 °C; $[\alpha]_D^{24}$ −12.2° (*c* 0.97) (Found: M^+, 401.3661. $C_{27}H_{47}NO$ requires *M*, 401.3656); $\nu_{max.}$ 3 185—3 594br and 1 653 cm^{-1} (C=O); *m/e* (rel. intensity) 401 (M^+, 100%) and 386 ($M^+ - CH_3$, 19.1).

The less mobile fraction (119 mg, 44%) was recrystallized from diethyl ether to yield crystals which were identical in every respect with the lactam (6) obtained by the Beckmann rearrangement.

3-*Ethylthio*-A-*nor*-B-*homocholest*-3-*en*-6-*one* (8).—The diketone (2) (992 mg) and ethanethiol (4 mg) in glacial acetic acid (20 ml) containing concentrated hydrochloric acid (10 drops) were stirred for 2 d at room temperature. The solution was extracted with aqueous diethyl ether. The organic layer was separated and washed twice with 5% aqueous sodium hydrogencarbonate and twice with water and dried (Na_2SO_4). After removal of the solvent the residue (1.15 g) was subjected to column chromatography (Wako C-200 silica gel, 45 g). Elution with hexane and then with hexane containing an increasing amount of benzene gave three fractions, the first of which (129 mg) was crude 3,6-diethylthio-A-nor-B-homocholesta-2,5- (or 3,6-) diene. This was recrystallized from acetone to yield the pure *compound* (75 mg). The second fraction (45 mg) was recovered starting enone. The most polar fraction [790 mg, 75% based on (2) reacted] was the sulphide (8) which was recrystallized from acetone to yield pure 3-*ethylthio*-A-*nor*-B-*homocholest*-3-*en*-6-*one* (606 mg, 55%), m.p. 114.0—115.0 °C (Found: C, 78.2; H, 10.85; S, 7.25. $C_{29}H_{48}OS$ requires C, 78.32; H, 10.88; S, 7.19%); $\nu_{max.}$ 1 634 cm^{-1} (C=O); $\lambda_{max.}$ (dioxan) (ε) 311 nm (11 800); *m/e* (rel. intensity) 444 (M^+, 19.1%), 415 ($M^+ - C_2H_5$, 100), 383 (65.4), and 167 (44.8).

A-*Nor*-B-*homo*-5α- *and* 5β-*cholestan*-6-*ones* (9) *and* (13) *by Hydrogenolysis of Compound* (8).—The vinyl sulphide (8) (3.08 g) in absolute ethanol (300 ml) was hydrogenated in the presence of Raney nickel (prepared from *ca.* 48% Wako Raney nickel) for 2 d. After removal of the catalyst the solvent was evaporated off and the residue was subjected to column chromatography (Wako C-200 silica gel, 90 g). Elution with hexane, then with hexane containing increasing amounts of benzene, and finally with benzene gave, in order of elution, three fractions, A, B, and C. The first fraction (A; 610 mg) was recrystallized from acetone to yield A-nor-B-homo-5β-cholestan-6-one (13) (353 mg, 26%), m.p. 99—100 °C (lit.,[4] m.p. 94—95 °C); *m/e* (rel. intensity) 386 (M^+, 100%), 368 (19.3), 304 (M^+ — five-membered ring A carrying C-10 methyl, 75.5; Found: *m/e* 304.2759. Calc. for $C_{21}H_{36}O^+$: 304.2765), 150 (59.3), 109 (40.0), 108 (27.0), 107 (28.0), 95 (43.7), 82 (43.2), 81 (61.3), 69 (28.3), 67 (33.5), 55 (58.5), and 43 (36.5). The second fraction (B; 1.27 g) was recrystallized from acetone to yield A-nor-B-homo-5α-cholestan-6-one (9) (0.70 g, 13%), m.p. 87.5—88.5 °C (lit.,[4] m.p. 86.0—88.0 °C); *m/e* (rel. intensity) 386 (M^+, 84.7%), 368 ($M^+ - 18$, 18.8), 304 (M^+ — five-membered ring A carrying 10-methyl, 18.4; Found: *m/e* 304.2765. Calc. for $C_{21}H_{36}O^+$: 304.2765), 231 (29.8), 150 (34.9), 109 (100), 95 (38.3), 81 (55.1), 69 (25.6), 67 (28.4), 55 (54.6), and 43 (33.4). Fraction C (133 mg) was a mixture of compounds bearing hydroxy-groups.

A-*Nor*-B-*homo*-5α-*cholestan*-6-*one Oxime* (10).—The ketone (9) (599 mg), hydroxylamine hydrochloride (751 mg), and sodium acetate monohydrate (751 mg) in ethanol (60 ml) containing a few drops of water were stirred at room temperature for 16 h. The solution was extracted with aqueous diethyl ether and the organic layer was separated and worked up in the usual way to afford the crude oxime (10) which was recrystallized from diethyl ether to yield the pure *oxime* (457 mg), m.p. 219—221 °C; (Found: C, 80.85; H, 11.95; N, 3.6. $C_{27}H_{47}NO$ requires C, 80.73; H, 11.80; N, 3.49%); $\nu_{max.}$ 3 300 (OH) and 975 cm^{-1}; *m/e* 401 (M^+, 21.1%), 385 (M^+ — OH, 37.2), 384 ($M^+ - H_2O$, 100), 244 (10.2), 139 (31.0), 136 (20.2), 81 (26.9), and 55 (23.8).

A-*nor*-B-*homo*-5β-*cholestan*-6-*one Oxime* (14).—In a similar manner, the ketone (13) (306 mg), hydroxylamine hydrochloride (376 mg), and sodium acetate monohydrate (376 mg) in ethanol (30 ml) containing a small amount of water were stirred at room temperature for 2 d. After work-up the crude product was purified by passage through a column of silica gel (Wako C-200, 15 g) to yield the amorphous *oxime* (290 mg) (Found: M^+, 401.3652. $C_{27}H_{47}NO$ requires *M* 401.3655); $\nu_{max.}$ 3 287 (OH) and 947 cm^{-1}; *m/e* (rel. intensity), 401 (M^+, 42.8%), 385 (M^+ — O, 25.1), 384 (M^+ — OH, 67.2), 369 (29.7), 360 (15.3), 319 (42.4), 302 (16.6), and 81 (100).

Beckmann Rearrangement of Oxime (10).—The oxime (10) (119 mg) and thionyl chloride (0.5 ml) in dioxan (6 ml) were stirred at room temperature for 4 h. The solution was worked up in the usual way and the residue was subjected to preparative t.l.c. (Wako-gel B-5-F) with 4 : 1 CH_2Cl_2–Et_2O as developer to give two major fractions, the more mobile of which (45 mg) was recovered oxime. The less mobile fraction [66 mg, 89% based on (10) consumed] was 6-*aza*-A-*nor*-B,B-*dihomo*-5α-*cholestan*-7-*one* (11) which crystallised on treatment with MeOH–Et_2O, m.p. 119—120.5 °C (Found: M^+, 401.3671. $C_{27}H_{47}NO$ requires *M*, 401.3658); $\nu_{max.}$ 3 191 and 3 060 (NH), 1 731 and 1 658 (CO), 1 280, 1 122, and 1 182 cm^{-1}; *m/e* (rel. intensity) 401 (M^+, 4.9%), 373 (M^+ — CO, 20.1; Found: *m/e* 373.3686. $C_{26}H_{47}N^+$ requires 373.3706), 235 (4.1), 152 (9.0), 139 (10.5), 110 (31.2,) 97 (37.5), 81 (18.4), 69 (100; Found: *m/e* 69.0131. $C_3H_3NO^+$ requires 69.0211), 57 (17.9), 56 (40.0), 55 (23.3), and 43 (46.3).

Photo-Beckmann Rearrangement of the Oxime (10).—The oxime (10) (300 mg) in methanol (200 ml) under nitrogen was irradiated in a Rayonet preparative photochemical reactor (RPR-208) with a low-pressure mercury arc for 86 h. After removal of solvent the residue was subjected to preparative t.l.c. (Wako-gel B-5-F) with 4 : 1 CH_2Cl_2–Et_2O as developer to give three fractions (A, B, and C) in order of decreasing mobility. Fraction A (70 mg) was a mixture of the starting oxime and the parent ketone. Fraction B (76 mg, 25%) was 7-*aza*-A-*nor*-B,B-*dihomo*-5α-*cholestan*-6-*one* (12) which was further purified by preparative t.l.c. but could not be induced to crystallize (Found: M^+, 401.3674. $C_{27}H_{47}NO$ requires *M*, 401.3658); $\nu_{max.}$ (neat), 3 382—3 233 and

3 073 (NH), 1 730 and 1 662 (CO), 1 462, 1 377, 1 282, and 736 cm^{-1}; *m/e* (rel. intensity) 401 (M^+, 100%), 319 (10.6), 318 (40.0), 290 (8.6), 109 (36.1), 95 (22.0), 81 (45.0), 71 (20.6), 69 (20.1), 67 (18.2), 55 (34.5), and 43 (27.9). Fraction C (38 mg, 13%) was the lactam (11), identical with the sample obtained by the Beckmann rearrangement of compound (10).

Beckmann Rearrangement of Oxime (14).—The oxime (14) (60 mg) and thionyl chloride (0.3 ml) in dioxan (5 ml) were stirred at room temperature for 3 h and the mixture was then worked up as for the 5α-isomer. The product (66 mg) was subjected to preparative t.l.c. with 4 : 1 benzene–Et_2O as developer to give 6-*aza*-A-*nor*-B,B-*dihomo*-5β-*cholestan*-7-one (15) (67%) which was further purified by a second preparative t.l.c. (Found: M^+, 401.3678. $C_{27}H_{47}NO$ requires *M*, 401.3657); $\nu_{max.}$ (neat), 3 285br and 3 051 (OH), 1 731 and 1 637 (CO), 1 466, 1 384, and 1 045 cm^{-1}; *m/e* 401 (M^+, 13.3%), 373 ($M^+ - CO$, 28.1; Found: *m/e* 373.3715. $C_{26}H_{47}N^+$ requires 373.3708), 235 (8.3), 152 (13.9), 139 (15.4), 110 (29.6), 97 (37.7), 70 (57.5), 69 (100; Found: *m/e* 69.0147. C_3H_3NO requires 69.6212), 55 (17.6), and 43 (34.4).

Photo-Beckmann Rearrangement of Oxime (14).—The oxime (14) (230 mg) in methanol (154 ml) under nitrogen was irradiated in a Rayonet preparative photochemical reactor (RPR-208) with a low-pressure mercury arc for 60 h. The solution was worked up in the usual way to afford the crude product which was subjected to preparative t.l.c. with benzene–Et_2O (4 : 1) as developer to yield four fractions (A, B, C, and D) in order of decreasing mobility. Fraction A (17mg) was the parent ketone. Fraction B (16 mg) was an unidentifiable gum. Fraction C (58 mg, 25%) was 7-*aza*-A-*nor*-B,B-*dihomo*-5β-*cholestan*-6-*one* (16) which was purified by preparative t.l.c. (Found: M^+, 401.3612. $C_{27}H_{47}NO$ requires *M*, 401.3655); $\nu_{max.}$ 3 308br (OH), 1 733 and 1 655 (CO), 1 295, 1 101, and 1 052 cm^{-1}; *m/e* (rel. intensity) 401 (M^+, 68.5%), 319 (100; Found: *m/e* 319.2842. $C_{21}H_{37}NO^+$ requires 319.2872), 318 (60.6; Found: *m/e* 318.2881. $C_{21}H_{36}NO^+$ requires 318.2796), 290 (61.5), 263 (28.9), 95 (37.1), 81 (59.6), 69 (87.4), 57 (38.9), 55 (73.0), and 43 (81.2). Fraction D (57 mg, 25%) was found to be identical with lactam (15) prepared by the Beckmann rearrangement of oxime (14).

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