Photoinduced Transformations. Part 36.[1] Stereochemical Integrity of the Terminus of the Migrating Carbon in the Photo-Beckmann Rearrangements of Some Cholestanone Oximes

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Analysis of the products of the photo-Beckmann rearrangement of four isomeric cholestanone oximes and an A-nor-cholestanone oxime, in all of which the hydroxyimino-group is in the terminal ring A, has shown that in each case only two structurally isomeric lactams are formed, in combined yields of 25—53%, together with a small amount of the parent and an isomeric ketone. In all the lactams formed, the chirality of the migrating groups is retained. Although the differences in the amounts of the two isomeric lactams formed in each photorearrangement were very small, the lactams obtained by migration of the more substituted carbon centre were always produced in slightly larger amount, and the difference was greater in the case of cholestan-1-one oximes than with cholestan-4- and -6-one oximes. On the basis of these and previous results, the pathway of the photo-Beckmann rearrangement of most alicyclic ketone oximes may be understood in terms of a simple scheme involving transformation of excited singlet oxime into an oxaziridine intermediate followed by reorganization of the singlet excited intermediate to the lactams in a fully concerted manner. In all the present photorearrangements, no products of photo-Beckmann fission were formed; this shows the synthetic utility of this photorearrangement. ^{1}H N.m.r. spectra of the oximes are discussed.

We have previously [2] reported that the photo-Beckmann rearrangements of 5α- and 5β-cholestan-6-one oximes in methanol afford a pair of structurally isomeric lactams in both of which the chirality of the migrating group is retained. Although the difference in the amounts of the two isomeric lactams formed in each photoreaction was small, the lactams obtained by migration of the more substituted carbon centre were always produced in slightly larger amount. Moreover, the presence of oxygen in the solution did not affect the formation of the lactams. On the basis of these results we proposed that the lactams were formed *via* a concerted reorganization of an excited singlet oxaziridine intermediate. Although this pathway appeared to operate generally for all aliphatic and alicyclic ketones and aldehydes, we subsequently found an exception to this rule. Irradiation of *O*-acetylandrosterone oxime afforded a pair of lactams epimeric at C-13, although the yields were very low.[3] We interpreted this exception in terms of another mode of the breakdown of the oxaziridine intermediate: *viz.* oxaziridines which can afford a stable ionic or radical species by cleavage rearrange through an intermediate in which the migrating group becomes free of the migration terminus. The results of the rearrangement of the oximes of androsterone and 13α-androsterone could be rationalized in terms of this mode.[3]

However, as noted previously,[2] further examination of the stereochemistry of the reaction with various steroidal substrates was needed to specify the structural requirements for concerted or non-concerted breakdown of the oxaziridine intermediates.

We now report further investigations of the configurational integrity of the terminus of the migrating carbon centre in the photo-Beckmann rearrangement of 5α- and 5β-cholestan-4-one oximes (1) and (6), 5α- and 5β-cholestan-1-one oximes (9) and (14), and A-nor-5β-cholestan-3-one oxime (25). 5α- and 5β-Cholestan-4-one oximes (1) and (6) were studied because although the immediate environments of the hydroxyimino-groups are similar to those of 5α- and 5β-cholestan-6-one oximes, the hydroxyimino-groups in the oximes (1) and (6) are in the terminal ring. This situation is comparable with androsterone oxime and differs from the 5α- and 5β-6-one oximes. 5α- and 5β-Cholestan-1-one oximes (9) and (14) were selected because one of the potentially migrating carbon centres in these oximes was tetrasubstituted. This was also analogous to androsterone oxime but differed from it in that the hydroxyimino-groups were in a six-membered ring. Finally, A-nor-5β-cholestan-3-one oxime (25) was chosen because the hydroxyimino-group was in a five-membered ring. This situation is analogous to that in androsterone oxime but differs in that the potentially migrating carbon centre is trisubstituted.

The Cholestanone Oximes (1),[4-6] (6), (9),[4,7] and (14) *and the* A-*Norcholestanone Oxime* (25).[8]—All the parent ketones were prepared by the reported method with some modification when necessary. A-Nor-5β-cholestan-3-one [9] was prepared by decarboxylation of the hydroxy-acid (22)[10] with sodium bismuthate [11] to afford a known A-

[1] Part 35, H. Takahashi, M. Ito, and H. Suginome, *Chem. Letters*, 1977, 241.
[2] H. Suginome and H. Takahashi, *Tetrahedron Letters*, 1970, 5119; *Bull. Chem. Soc. Japan*, 1975, **48**, 582.
[3] H. Suginome and T. Uchida, *Tetrahedron Letters*, 1973, 2293; *Bull. Chem. Soc. Japan*, 1974, **47**, 687.
[4] C. W. Shoppee, R. E. Lack, and S. K. Roy, *J. Chem. Soc.*, 1963, 3767.
[5] A. Windaus, *Ber.*, 1920, **53**, 488.
[6] C. W. Shoppee, R. J. W. Cremlyn, D. E. Evans, and G. H. R. Summers, *J. Chem. Soc.*, 1957, 4364.
[7] C. W. Shoppee, S. K. Roy, and B. S. Goodrich, *J. Chem. Soc.*, 1961, 1583.
[8] C. W. Shoppee, R. W. Killick, and G. Kruger, *J. Chem. Soc.*, 1962, 2275.
[9] C. W. Shoppee and G. H. R. Summers, *J. Chem. Soc.*, 1952, 2528; A. Windaus, *Ber.*, 1912, **45**, 1316; 1919, **52**, 170.
[10] G. H. Whitham and J. A. F. Wickramasinghe, *J. Chem. Soc.*, 1965, 5416.
[11] B. Camerino and U. Valcavi, *Gazzetta*, 1963, **93**, 723, 735; B. Camerino, B. Patelli, and R. Sciaky, *ibid.*, p. 1165.

nor-5α-cholestan-3-one (23) with a small amount of the 5β-isomer, followed by isomerization with base. The chemical shifts of the 19-H and the 18-H of the six ketones (2), (3), (10), (15), (23), and (24) are given in Table 3. The oximes were prepared by the standard method. Only the oximes (6) and (14) were hitherto unreported. 5α-Cholestan-6-one,[2] 5β-cholestan-1-one, and A-nor-5β-cholestan-3-one reacted much more slowly with hydroxylamine than the other ketones; oximations at room temperature did not proceed at a detectable rate. With the exception of 5β-cholestan-6-one,[2] which afforded a mixture of *E*- and *Z*-oximes, all the ketones afforded a single oxime.

The ^{1}H n.m.r. spectra (Table 1) of the four oximes (1),

TABLE 1

N.m.r. parameters (100 MHz) for the oximes in $CDCl_3$ solution [chemical shifts (τ) and splittings (Hz; in parentheses)]

Oxime	18-H	19-H	2α-H	3β-H	3α-H	OH
(1)	9.32	9.20		6.63br (d) (6.9)		
(6)	9.34	8.92			6.62br (d) (12.0)	
(9)	9.33	8.94	6.67br (d) (9.5)			1.22br (s)
(14)	9.37	8.77	6.64br (d) (10.9)			0.17 (s) ($W_{\frac{1}{2}}$ 3.9)
(25)	9.33	8.92	7.56 (m)			

(6), (9), and (14) each exhibited a one-proton broad doublet at *ca.* τ 6.6 ascribable to a proton α to the hydroxyimino-group.[2] Dreiding models show that these protons deshielded by the hydroxyimino OH are the 2α-protons in the oximes (9) and (14), the 3β-proton in the oxime (1), and the 3β-proton in the oxime (6); all these protons are nearly eclipsed by the C=N bond. On the basis of these results the hydroxyimino OH groups were concluded to be in the *E*-configuration, as depicted. Geminal coupling constants were significantly smaller than those of methane. Dreiding models of the oximes (1), (6), (9), and (14) revealed that if the conformations of these oximes are as depicted in the Schemes, the dihedral angle between the β-lobe of the π-bond and the C(3)–H_α bond in the oxime (1) is *ca.* 165°. Similarly, dihedral angles between the α-lobe and C(3)–H_α in the oxime (6), the α-lobe and C(2)-H_β in the oxime (9), and the β-lobe and C(2)–H_β in the oxime (14) are 80, 165, and 80°, respectively. Based on these dihedral angles, π-bond contributions of *ca.* 0 to 1 Hz to the methane geminal coupling constant (12.4 Hz) are expected for the oximes (1), (6), (9), and (14).[12] This afforded the expected values of J_{gem} = 12.4—13.4 Hz for the geminal coupling constants of the four oximes. A considerable deviation from the expected value in the case of the oxime (1) is noted.*

In contrast with the six-membered ring ketone oximes, no deshielded proton signal was observed at τ *ca.* 6.6 in the ^{1}H n.m.r. spectrum of A-nor-5β-cholestan-3-one oxime (25). This is expected since a Dreiding model exhibited no proton adjacent to the hydroxyimino-group eclipsed by the C=N bond. However, the *E*-configuration of the hydroxyimino-group is certain on the basis of the reported result of the Beckmann rearrangement,[8] which we have confirmed.

Beckmann Rearrangements.—We needed the lactams which would be produced in the photo-Beckmann rearrangement for direct comparisons.

The Beckmann rearrangement of the oximes (1) and (9) has already been reported to yield 4a-aza-A-homo-5α-cholestan-4-one (4) as well as 1-aza-A-homo-5α-cholestan-2-one (11) and 1,10-seco-5α-cholest-10(19)-eno-1-nitrile (13) [$\Delta^{10(19)}$].[4] We confirmed that the Beckmann rearrangement of the oxime (1) in dioxan–thionyl chloride afforded 4a-aza-A-homo-5α-cholestan-4-one (4) as the sole product.

We also found that the yield of the lactam (11) was significantly improved (55%) by carrying out the rearrangement in dioxan as the solvent, at the expense of the nitrile (13), the product of a second-order Beckmann rearrangement.

The Beckmann rearrangement of the oxime (6) in dioxan with thionyl chloride at room temperature afforded a new lactam (7), m.p. 170—172°, as the sole product in 84% yield. The structure of the new lactam (7), A-homo-4a-aza-5β-cholestan-4-one was confirmed by spectroscopic means, especially the ^{1}H n.m.r. data (Table 2). Treatment of the oxime (14) under the same conditions afforded another new lactam (16), m.p. 114—117°, in 35% yield together with a nitrile (21) resulting from second-order Beckmann rearrangement (18%). The structure of the new lactam (16), 1-aza-A-homo-5β-cholestan-2-one, was evident from the n.m.r. spectrum (Table 2).

Photo-Beckmann Rearrangements.—The photo-Beckmann rearrangements were carried out under the same procedure as the photo-Beckmann rearrangement of cholestan-6-one oximes previously reported.[2] Methanol was used as solvent, and the concentration of the oximes was slightly different in each experiment since none of the oximes was very soluble to methanol and the photoreactions were undertaken with almost saturated solutions.

5α-Cholestan-4-one oxime (1) (*Scheme* 1). Irradiation of a solution of the oxime (1) (3.6×10^{-3} M) afforded 5α-cholestan-4-one (2) [13] (2%), 5β-cholestan-4-one (3) [13] (5%), 4a-aza-A-homo-5α-cholestan-4-one (4) [4] (29%), and a new

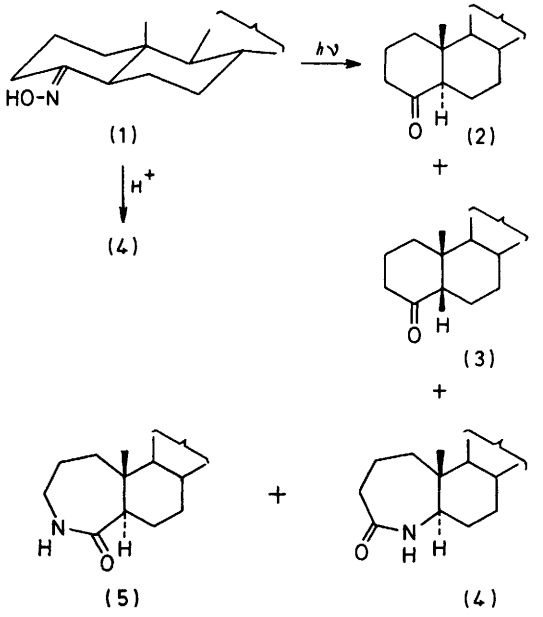
* In 5α-cholestan-6-oxime, the 7β-H is deshielded by the hydroxyimino group. The dihedral angle between the β-lobe of the π-bond and the C(7)–Hβ bond is *ca.* 80° and a π-bond contribution of *ca.* 0—1 Hz to the methane geminal coupling constant is expected. This affords an expected value of $J_{gem} \simeq$ 12.4—13.4 Hz (the value 11.4 Hz was given mistakenly in our previous paper [2]), in good agreement with the observed C-7 methylene geminal coupling constant (13.5 Hz). In one of the 5β-cholestan-6-one oximes, a π-bond contribution to the C-7 methylene geminal coupling constant was also 0—1 Hz [dihedral angle between the β-lobe of the π-bond and C(7)–Hβ *ca.* 80°.] This afforded an expected value of $J_{gem} \simeq$ 12.4 Hz. The observed coupling constant was 10.5 Hz.[2]

[12] M. Barfield and D. M. Grant, *J. Amer. Chem. Soc.*, 1963, **85**, 1899; S. Sternhell, *Quart. Rev.*, 1969, **23**, 236.

[13] H. B. Henbest and T. I. Wrigley, *J. Chem. Soc.*, 1957, 4596; C. W. Shoppee, M. E. H. Howden, R. W. Killick, and G. H. R. Summers, *ibid.*, 1959, 630.

lactam (5) (24%). The structure (5) was confirmed by the n.m.r. spectrum [τ 6.81br (s, $W_{\frac{1}{2}}$ 18.0 Hz, NCH_2) and 7.54 (q, J 4.5 and 12.0 Hz, CH·CO)].

5β-*Cholestan-4-one oxime* (6) (*Scheme* 2). This oxime



SCHEME 1

(3.6×10^{-3} M) similarly afforded 5β-cholestan-4-one (3) (5%), 5α-cholestan-4-one (2) (3%), and unchanged oxime as relatively mobile fractions in preparative t.l.c. A less mobile fraction afforded 4a-aza-A-homo-5β-cholestan-4-one (7) (20%), identical with a specimen obtained by Beckmann rearrangement, and a new lactam (8), m.p. 126—129° (18%), identified by its n.m.r. spectrum.

5α-*Cholestan-1-one oxime* (9) (*in the presence or absence of oxygen*) (*Scheme* 3). Irradiation of a solution of the oxime (9) (3.6×10^{-3} M) and separation of the products by adsorption chromatography afforded unchanged oxime, 5α-cholestan-1-one [14] (10) (9%), a new lactam (12), m.p. 154—157° (14%), and 1-aza-A-homo-5α-cholestan-2-one (11) [4] (21%), successively. Compound (12), $C_{27}H_{47}NO$, was apparently 2-aza-A-homo-5α-cholestan-1-one (12), as shown by i.r. and the n.m.r. spectra (Table 2).

The two lactams (11) and (12) were also obtained in 8 and 7% yields together with a 64% yield of the parent ketone (10) when a solution of the oxime (9) saturated with oxygen was irradiated.

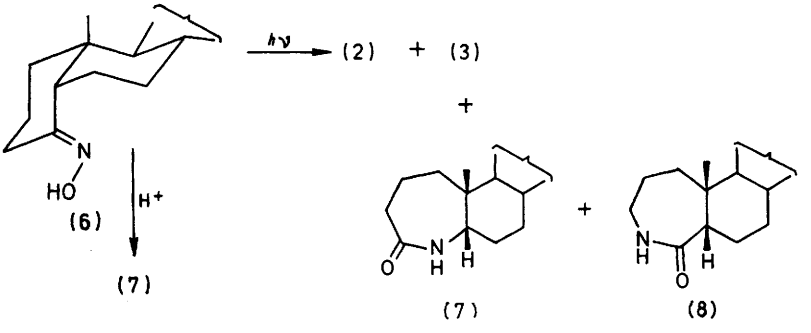
5β-*Cholestan-1-one oxime* (14) (*Scheme* 4). The oxime (14) (2.8×10^{-3} M) similarly afforded an amorphous compound (18) (5%) as one of the first fractions. I.r. and n.m.r. spectra disclosed that this was a crude seco-ester (18), contaminated by a trace of a seco-aldehyde (19) [τ 0.26 (s, CHO) and 5.39 (d, J 4.7 Hz, :CH)]. Other products from the most mobile fraction were 5β-cholestan-1-one (15) [15] (6%) and unchanged oxime.

TABLE 2

N.m.r. parameters (100 MHz) for the lactams in $CDCl_3$ solution [chemical shifts (τ) and splittings (Hz; in parentheses)]

Lactam	18-H	19-H	3-H	5a- or 5-H	NH
(4)	9.33	9.13	7.59 (t)	6.78 (m)	4.68br (s) ($W_{\frac{1}{2}}$ 12.0)
(5)	9.32	9.11	6.81br (s) ($W_{\frac{1}{2}}$ 18.0)	7.54 (g) (4.5 and 12.0)	3.63br (s) (18.0)
(7)	9.34	9.06	7.45 (m)	6.59 (quint)	3.97 (d) (6.6)
(8)	9.33	8.92	6.73 (m)	7.58br (d) ($W_{\frac{1}{2}}$ 8.4)	3.96br (s) ($W_{\frac{1}{2}}$ 15.6)
(11)	9.32	8.76	7.51br (t) ($W_{\frac{1}{2}}$ 13.5)		4.17 (s)
(12)	9.33	8.78	6.98 (m), 6.62 (m)		4.30 (t) (6.6)
(16)	9.33	8.68			4.41 (s)
(17)	9.33	8.63	6.84br (s) ($W_{\frac{1}{2}}$ 25.5)		3.59 (q) (7.9 and 5.2)
(26)	9.33	8.99		6.73br (s) ($W_{\frac{1}{2}}$ 7.2)	3.66br (s)
(27)	9.32	8.94	[2-H 6.78 (m)]		4.03br (s) ($W_{\frac{1}{2}}$ 10.5)

The following fraction afforded 1-aza-A-homo-5β-cholestan-2-one (16), identical with a specimen obtained by Beckmann rearrangement (22%), and a new lactam (17),



SCHEME 2

m.p. 127—129°, in 10% yield, identified on the basis of n.m.r., i.r., and mass spectra.

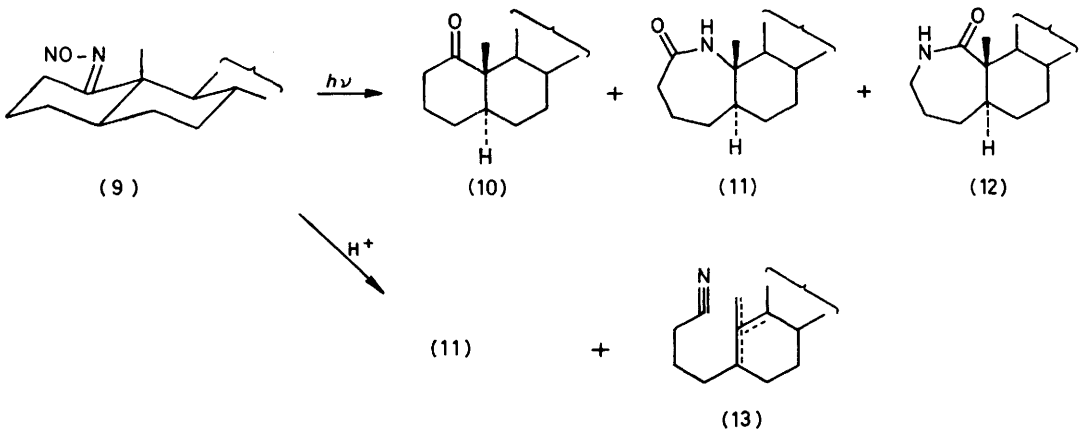
The last fraction afforded an amorphous compound (7%). Its mass spectrum revealed an intense molecular ion peak at *m/e* 401 (39%; base peak *m/e* 18) corresponding to the molecular formula $C_{27}H_{47}NO$. On the basis

[14] C. Djerassi, D. H. Williams, and B. Berkoz, *J. Org. Chem.*, 1962, **27**, 2205.

[15] E. Glotter, M. Weissenberg, and D. Lavie, *Tetrahedron*, 1970, 3857.

of i.r., mass, and n.m.r. spectra an amide structure (20) is assigned. Its i.r. spectrum exhibited bands at 1 629, 1 666, 3 204, and 3 368 cm^{-1} due to aliphatic $CONH_2$.

A-*Nor*-5β-*cholestan*-3-*one oxime* (25) (*Scheme* 5). Irradiation of this oxime led to a complex mixture from which the following were obtained by t.l.c.: a seco-ester

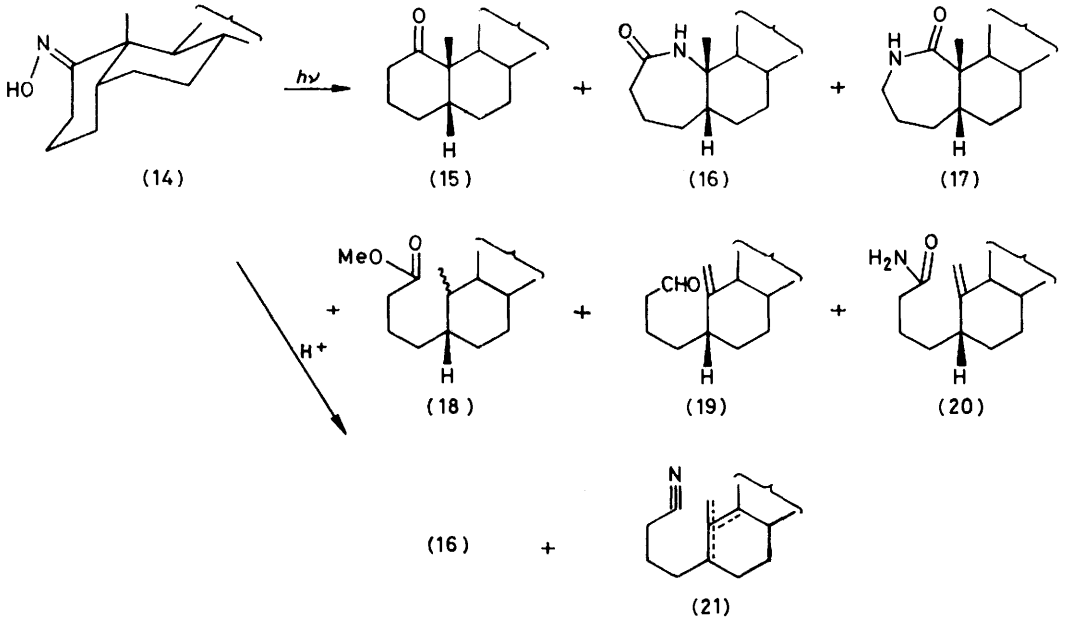


SCHEME 3

The mass spectra showed distinct fragment ion peaks at *m/e* 59 (60%) and 315 (26%). The former is typical of aliphatic amides with a C_3 chain,[16] and can be attributed to the Mclafferty rearrangement of a γ-hydrogen atom of the amide chain (Scheme 6). The latter fragment must have stemmed from the elimination of an olefin (Scheme 7). In addition the spectrum exhibited a series of typical fragments due to C-17 substituted steroids [17] at *m/e* 386 (*M* − 15) (21%), 288 (*M* − C_8H_{17}) (20%), and 246 (29%). The n.m.r. spectrum exhibited a signal at τ 5.38 (d, *J* 4.5, $:CH_2$) and no 19-H resonance.

(28) (6%), A-nor-5β-cholestan-3-one (24) [9] (7%), unchanged oxime, 4-aza-5β-cholestan-3-one (26) [8] (13%), and 3-aza-5β-cholestan-4-one (27) (12%).[8]

Mass Spectra of the Lactams.—In the electron impact mass spectra of all the lactams obtained an intense molecular ion peak was present [base peak for the lactams (4), (5), (7), (26), and (27)]. The fragmentation patterns could be explained by competition between two decomposition modes, those characteristic of amides and those due to general fragmentation of the cholestane framework.[16] All eight seven-membered lactams and two



SCHEME 4

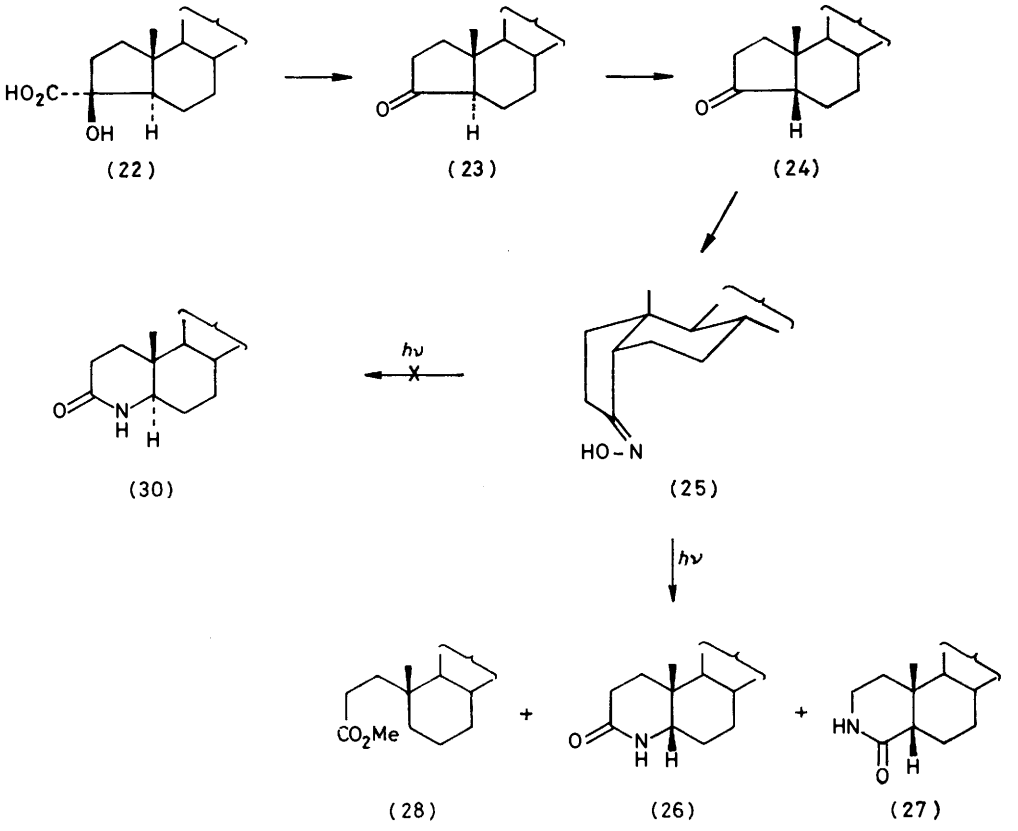
[16] H. Budzikiewicz, C. Djerassi, and D. H. Williams, 'Mass Spectrometry of Organic Compounds,' Holden-Day, San Francisco, 1967, p. 336.

[17] H. Budzikiewicz, C. Djerassi, and D. H. Williams, 'Structure Elucidation of Natural Products by Mass Spectrometry,' Holden-Day, San Franciso, 1964, p. 94.

six-membered lactams exhibited an intense $M - CH_3$ peak. Comparisons of isomeric pairs of the lactams, *e.g.* the lactams (11) and (12) or (16) and (17), show no favoured ejections of the angular 10-methyl group in the

DISCUSSION

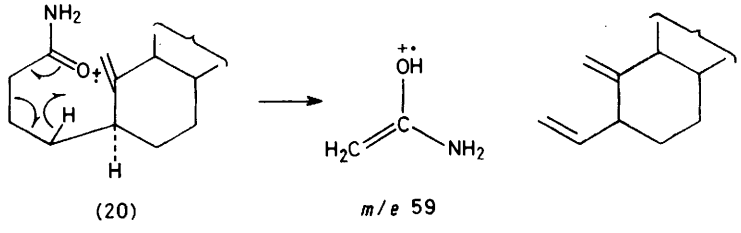
The results of the photo-Beckmann rearrangements of 5α- and 5β-cholestan-4-one oximes (1) and (6) were entirely parallel with our previous result with 5α- and 5β-choles-



SCHEME 5

lactams (11) and (16). This behaviour contrasts with the reported difference in fragmentation pattern between 3β-methoxy-17-aza-5α-androstan-16-one and 3β-methoxy-16-aza-5α-androstan-17-one: the former exhibited a very intense $M - CH_3$ peak due to the iminium

tan-6-one oximes.[2] The differences in the amounts of the two isomeric lactams from each oxime were very small [1 : 1.1 for 5α-cholestan-4-one oxime (2) and 1 : 1.2 for 5β-cholestan-4-one oxime (6)] but the lactams obtained by migration of the more substituted carbon [*e.g.*



SCHEME 6

species whereas the latter showed such a peak to only a minor extent.[18] Thus, in the six- or seven-membered steroidal lactams, the $M - CH_3$ peak has little diagnostic value for distinguishing these two structural isomers.[19]

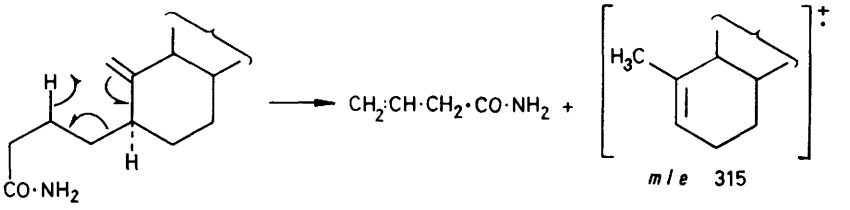
(4) and (7) rather than (5) and (8)] were always produced in slightly larger amount. These results also were parallel with the cases of 5α- and 5β-cholestan-6-one oximes [2] and monocyclic ketone oximes.[20] The formation of 5β-cholestan-4-one (3) (2%), which is less stable than the parent 5α-ketone, in the photo-Beckmann rearrangement

[18] H. Budzikiewicz, F. Compernolle, K. V. Cauwenberghe, K. Schulze, H. Wolf, and G. Quinkert, *Tetrahedron*, 1968, **24**, 6797.

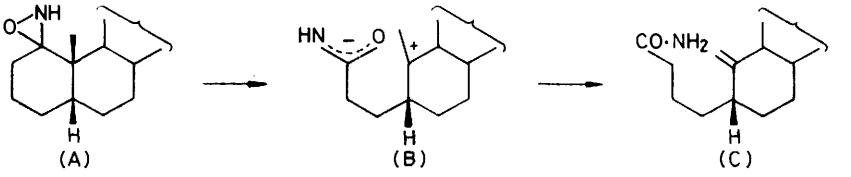
[19] H. Suginome, submitted for publication in *J.C.S. Perkin I*.

[20] M. Cunningham, L. S. N. Lim, and G. Just, *Canad. J. Chem.*, 1971, **49**, 2891.

of 5α-cholestan-4-one oxime (1) is of interest. This ketone must have been formed *via* a photochemical α-cleavage–recombination sequence [21] from 5α-cholestan-4-one (2) generated from an oxaziridine intermediate.

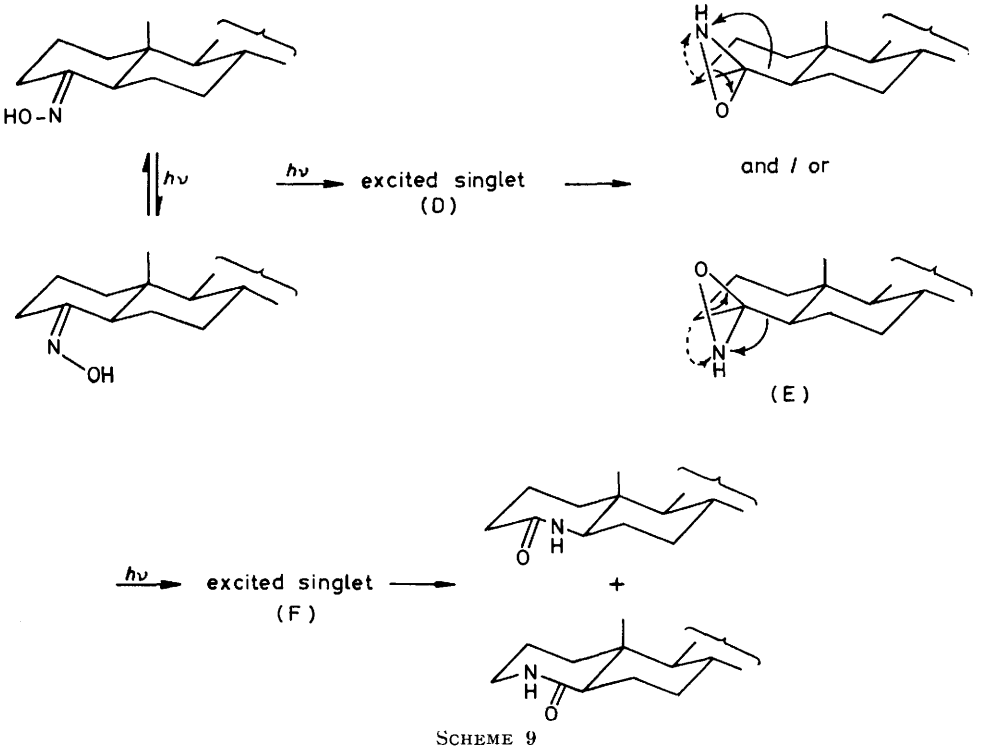


SCHEME 7



SCHEME 8

The photo-Beckmann rearrangement of 5α- and 5β-cholestan-1-one oximes (9) and (14) also afforded two lactams, (11) and (12), or (16) and (17), in which the chirality of the migrating centres is retained. These observations discount our previous explanation that an exceptional stereochemical outcome in the photo-Beckmann rearrangement of *O*-acetylandrosterone oxime may be due merely to the single factor that one of the migrating carbon centres is tetrasubstituted.[3] It is notable that the unsaturated amide (20) was formed in the case of 5β-cholestan-1-one oxime (9), whereas the formation only of saturated amides, probably due to ring cleavage of an intermediate oxaziridine, has been reported previously.[20,22–25,*] This amide is most probably produced by breakdown of the oxaziridine intermediate (A) *via* a cleaved species such as (B) (Scheme 8).



SCHEME 9

Other products (18) and (19) were apparently produced from photochemical cleavage of the parent ketone (15).

In the photoreactions of the oximes (9) and (14) the

* Ring-opened radical species such as postulated by Just *et al.*[26] may also lead to lactams.

[21] H. Wehrli and K. Schaffner, *Helv. Chim. Acta*, 1962, **45**, 385.
[22] R. T. Taylor, M. Douek, and G. Just, *Tetrahedron Letters*, 1966, 4143.
[23] Y. Kobayashi, *Bull. Chem. Soc. Japan*, 1973, **46**, 3467.
[24] G. Just and M. Cunningham, *Tetrahedron Letters*, 1972, 1151.
[25] B. L. Fox and H. M. Rosenberg, *Chem. Comm.*, 1969, 1115.
[26] G. Just and L. S. Ng, *Canad. J. Chem.*, 1968, **46**, 3382.

differences in amounts of the two isomeric lactams produced in each case were greater than those for 5α- and 5β-cholestan-6-one oximes and 5α- and 5β-cholestan-4-one oximes (1) and (6) [1 : 1.5 for (9) and 1 : 2.2 for (14)].

The result of the photo-Beckmann rearrangement of A-nor-5β-cholestan-3-one oxime (24) is particularly significant. Thus, if the photorearrangement involved any ring-opened species, the lactam predominantly formed would be the more stable AB-*trans*-lactam (30). However, the sole lactam isolated was the lactam with an AB-*cis*-junction. Thus the chirality of the migrating group was again retained. All the foregoing results confirmed that our earlier suggestion with regard to the mode of the photochemical reorganization of the oxaziridine intermediate to give lactams is not confined to the steroid ring B oximes, but is also valid for terminal ring ketone oximes.

On the basis of the present results, together with those of other investigators,[2,20,22-24] the pathway of the photo-Beckmann rearrangement of alicyclic ketone oximes may be understood in terms of a rather simple scheme (Scheme 9).[27] Singlet excited oximes (D) are rapidly transformed into intermediate oxaziridines (E). These oxaziridines (E) undergo excitation to a singlet state (F), and this is reorganized to give lactams (4) and (5) without a further intermediate. Photochemical $E \rightleftharpoons Z$ transformations, which may occur from either singlet or triplet state,[28] are seen to proceed faster than oxaziridine formation, since there was no significant difference in yields of the lactams in the photo-Beckmann rearrangements of the *E*- and *Z*-isomers of an oxime.[2] The presence of oxygen in the oxime photoreaction slightly lowers the yields of lactams, as previosly noted.[2] This is probably due to reactions[29] between oxygen and the oxaziridine intermediate rather than partial physical quenching of triplet excited oxaziridine.* This mechanism differs from the proposed mechanisms of the Beckmann rearrangement of aromatic aldehyde oximes[30] and styryl ketone oximes.[31]

Although we consider that the proposed pathway may operate generally for most aliphatic ketones and aldehydes, there may be some exceptions, such as androsterone oxime (see above.) In these cases, cleaved radicals generated from the oxaziridine intermediate seem to be particularly stabilized, and the lactams appear to be formed by ring closure of these species.[3,26]

In the photo-Beckmann rearrangement of all the steroidal substrates we have examined, no nitriles from the second-order photo-Beckmann rearrangement[32] were isolated, nor were even detected in the crude photolysates, whereas the corresponding ground-state Beckmann rearrangement afforded moderate amounts of nitriles (13) and (21). This property should be of value when the photo-Beckmann rearrangement is used in synthesis.

* A large quenching effect of oxygen in the photo-Beckmann rearrangement of adamantanone oxime has been reported.[32b]

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EXPERIMENTAL

For instruments used and general procedure see ref. 33. Silica gel 60 (Merck; 70—230 mesh) was used for column chromatography unless stated otherwise. Dotite spectrosol methanol (Wako) was used as solvent for the photoreactions.

5α-Cholestan-4-one oxime (1) had m.p. 218—221 °C (from ether–methanol) (lit.,[4] 221—223°; lit.,[5] 205°; lit.,[6] 221—223°), $\nu_{max.}$ 3 254 (OH), 935, and 956 cm^{-1}; for n.m.r. see Table 1.

5β-*Cholestan*-4-*one Oxime* (6).—To the solution of 5β-cholestan-4-one (80 mg) in methanol (50 ml), a solution of hydroxylamine hydrochloride (113 mg) containing sodium acetate trihydrate (115 mg) in a small volume of water was added. The clear solution was stirred at room temperature for 20 h. The solvent was removed and the residue was extracted with ether. The usual work-up afforded a residue (70 mg, 92%), which yielded the *oxime* (6), m.p. 123—125 °C (from methanol) (Found: C, 80.6; H, 11.9; N, 3.7. $C_{27}H_{47}NO$ requires C, 80.75; H, 11.8; N, 3.5%); $\nu_{max.}$ 3 307 (OH), 953, 936, 924, 900, and 859 cm^{-1}; for n.m.r. see Table 1.

5α-Cholestan-1-one oxime (9) had m.p. 153—154.5° (from methanol) (lit.,[4] 152°; lit.,[7] 151.0—153.0°), $\nu_{max.}$ 3 296 (OH), 1 650 (C=N), and 932 cm^{-1} (N–O); for n.m.r. see Table 1.

5β-*Cholestan*-1-*one* (15).—This ketone was prepared by the method of Glotter *et al.*[15] from cholesta-1,4,6-trien-3-one, obtained in our experiments by dehydrogenation of cholest-4-en-3-one with chloranil to cholesta-4,6-dien-3-one,[34] followed by dehydrogenation with dichlorodicyanobenzoquinone.[35] 1α,2α-Epoxycholesta-4,6-dien-3-one, prepared by epoxidation of cholesta-1,4,6-trien-3-one (30% H_2O_2 and methanolic 10% NaOH), had m.p. 111.0—112.5° (lit.,[15] 108—110°) (from MeOH–Et_2O); τ 9.22 (s, 18-H), 8.81 (s, 19-H), 655 (dd, *J* 1.8 and 4.5 Hz, 2-H), 6.40 (d, *J* 4.5 Hz, 1-H), 4.34br (s, $W_{\frac{1}{2}}$ 4.5 Hz, 4-H), and 3.91 (s, 6- and 7-H). Hydrogenation of this epoxide over 5% Pd–$CaCO_3$ gave 1α-hydroxy-5β-cholestan-3-one, m.p. 117—121° (lit.,[15] 114—115°); τ 9.31 (s, 18-H), 8.78 (s, 19-H), and 6.38 (dd, *J* 7.1 and 8.8 Hz, 1β-H). This was transformed into amorphous 5β-cholestan-1α-ol by successive treatment with tosyl hydrazide in methanol and sodium borohydride; τ 9.35 (s, 18-H), 8.85 (s, 19-H), and 6.68 (m, 1β-H). The 5β-cholestan-1α-ol was converted into 5β-cholestan-1-one with Jones reagent; m.p. 104.0—104.5° (lit.,[15] 101—102°); for n.m.r. see Table 3.

Although the literature[15] records an overall yield of 45% from 1α-hydroxy-5β-cholestan-3-one, an improved yield (82%) could be achieved by immediate oxidation of crude 1α-hydroxy-5β-cholestan-3-one obtained by the reduction with sodium borohydride.

5β-*Cholestan*-1-*one Oxime* (14).—To the ketone (700 mg) in methanol (350 ml) was added aqueous hydroxylamine

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hydrochloride (6 g) and sodium acetate trihydrate (6 g). The mixture was refluxed for 22 h. After the addition of water, crystals of the crude oxime (707 mg) were collected and dissolved in ether. The solution was washed with water, dried (Na_2SO_4), and evaporated to leave the crude oxime, which was dissolved in ether. To this solution n-hexane was added and the mixture was set aside for a week in a refrigerator to afford the oxime (14) (507 mg), m.p. 81—84°. A specimen recrystallized from acetone had m.p. 86—88 °C (Found: C, 80.75; H, 11.8; N, 3.5. $C_{27}H_{47}NO$ requires C, 80.85; H, 11.85; N, 3.45%); for n.m.r. see Table 1.

A-*Nor*-5α-*cholestan*-3-*one* (23) *by Oxidative Decarboxylation of* 3-*Hydroxy*-A-*nor*-5α-*cholestane*-3-*carboxylic Acid* (22).—The acid (22) (1.9 g) [τ 9.33 (18-H) and 9.02 (19-H)] and sodium bismuthate (16.2 g) in aqueous 75% acetic acid (140 ml) were stirred for 2 h at room temperature. To the mixture was added methylene chloride (300 ml), and then slowly aqueous 40% KOH. The suspension was filtered and the aqueous layer extracted again with methylene chloride. The combined organic layers were washed with water, dried (Na_2SO_4), and evaporated. The residue was recrystallized from acetone–methanol to yield A-nor-5α-cholestan-3-one (23) (587 mg).

Isomerization of A-*Nor*-5α-*cholestan*-3-*one* (23).—A-Nor-5α-cholestan-3-one (587 mg) in methanolic 5% KOH (50 ml) was stirred for 1.5 h at room temperature. After addition of acetic acid (3 ml), the solvent was removed by distillation and the residue was dissolved in ether. The solution was washed with sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and evaporated, and the residue was recrystallized from acetone–methanol to afford 520 mg of A-nor-5β-cholestan-3-one (24).[9]

A-Nor-5β-cholestan-3-one oxime (25) had m.p. 125—127° (from acetone) (lit.,[8] 123—127°); $\nu_{max.}$ 854, 895, 926, 947, and 3 296 cm^{-1} (OH).

Beckmann Rearrangement of the Oximes.—General procedure. To a solution of the oxime (1), (6), (9), or (14) in dioxan (oxime : dioxan 50 mg : 1 ml) was added freshly purified thionyl chloride (0.01 ml for 50 mg of oxime) at room temperature. The solution was stirred for 5 min [for (1) and (6)] or 20 min [for (9) and (14)] at room temperature. The mixtures from the oximes (1) and (6) were poured into water. To the mixtures from the oximes (9) and (14) was added aqueous sodium hydrogen carbonate. The aqueous solutions were extracted with ether [for (1), (6), and (9)] or chloroform [for (14)]. The extracts were worked up as usual. The residues were either recrystallized or subjected to adsorption chromatography.

TABLE 3

N.m.r. data (100 MHz) of ketones in $CDCl_3$ (τ values)

Ketone	18-H	19-H
(2)	9.33	9.24
(3)	9.35	8.88
(10)	9.34	8.84
(15)	9.36 *	8.85 †
(23)	9.32	9.25
(24)	9.33	8.84

* Lit.,[15] 9.37. † Lit.,[15] 8.87.

5α-*Cholestan*-4-*one oxime* (1). The crystalline residue (54 mg, 90%) from the oxime (60 mg) was recrystallized from acetone to yield the pure 5α-lactam (4), m.p. 227—228° (lit.,[4] 220—222°); $\nu_{max.}$ 1 675 (lactam C=O), and 3 105 and 3 235 cm^{-1} (lactam NH); for n.m.r. see Table 2; *m/e* 401 ($M^{+\cdot}$, 100%), 386 (27), 95 (16), 81 (14), 69 (18), and 56 (41).

5β-*Cholestan*-4-*one oxime* (6). The crystalline residue (42 mg, 84%) from the oxime (50 mg) was recrystallized from acetone to yield pure A-*homo*-4a-*aza*-5β-*cholestan*-4-*one* (7) (26 mg), m.p. 170—172° (Found: C, 80.7; H, 11.85; N, 3.5. $C_{27}H_{47}NO$ requires C, 80.75; H, 11.8; N, 3.5%); $\nu_{max.}$ 1 648 and 1 670 (lactam C=O), and 3 217 cm^{-1} (lactam NH); for n.m.r. see Table 2; *m/e* 401 ($M^{+\cdot}$, 100%), 386 (32), 95 (22), 81 (20), 69 (31), and 56 (69).

5α-*Cholestan*-1-*one oxime* (9). The product from the oxime (200 mg) was chromatographed on a silica gel column (7 g). Elution with benzene afforded an oily substance (25 mg). The n.m.r. spectrum indicated that this was virtually a single nitrile (13), τ 9.32 (s, 18-H), 9.10 (s, 19-H), 7.67 (t, *J* 5.1 Hz, 2-H_2), and 5.36 (d, *J* 12.0 Hz, 10-CH_2); $\nu_{max.}$ 889 (C=CH_2), 1 640 (C=C), and 2 245 cm^{-1} (C≡N). Elution with benzene–ether (5 : 1) then afforded the lactam (11) (110 mg, 55%), m.p. 136—138° (from methanol) (lit.,[4] 138°); $\nu_{max.}$ 1 651 (lactam C=O), and 3 088, 3 274, and 3 312 cm^{-1} (lactam NH); for n.m.r. see Table 2; *m/e* 401 ($M^{+\cdot}$, 88%), 386 (44), 247 (36), 138 (100), 125 (33), and 95 (38).

5β-*Cholestan*-1-*one oxime* (14). The product (112 mg) from the oxime (99 mg) was subjected to column chromatography on silica gel (2 g). Elution with benzene–ether (50 : 1) afforded a first fraction (18 mg) which was a nitrile containing an olefinic double bond; $\nu_{max.}$ 1 640 (C=C), 2 268 (C≡N), and 891 cm^{-1} (C=CH_2); τ 9.32 (3 H, s, 18-H), 5.3 br (2 H, s, 10-CH_2), and 7.66br (s, 2-H_2). Further elution with ether–benzene (1 : 5) afforded crude 1-*aza*-A-*homo*-5β-*cholestan*-2-*one* (16) (35 mg), m.p. 117—119° (from acetone) (Found: C, 80.6; H, 11.85; N, 3.55. $C_{27}H_{47}NO$ requires C, 80.75; H, 11.8; N, 3.5%); $\nu_{max.}$ 1 649 (lactam C=O) and 3 295 cm^{-1} (NH); for n.m.r. see Table 2; *m/e* 401 ($M^{+\cdot}$, 61%), 386 (28), 138 (100), 125 (32), 95 (40), and 70 (20).

Beckmann Rearrangement of A-*Nor*-5β-*cholestan*-3-*one Oxime* (25).—To the oxime (100 mg) in pyridine (2 ml) was added freshly purified thionyl chloride (0.05 ml) at 0 °C. The solution was stirred for 1 h and 10% sodium hydroxide solution (2 ml) added. After addition of water, the solution was extracted with ether. The ethereal solution was worked up and the residue was purified by column chromatography to afford the lactam (26) (41 mg), m.p. 196—199° (lit.,[8] 193—196°); $\nu_{max.}$ 1 620 and 1 972 (lactam C=O), and 3 207 cm^{-1} (NH); for n.m.r. see Table 2; *m/e* 387 (100%), 372 (16), 262 (16), 232 (16), 56 (83), and 55 (25).

Photo-Beckmann Rearrangements.—General procedure. A methanolic solution of the oxime was irradiated with an 18 W low-pressure mercury arc until the oxime had disappeared or nearly disappeared. Removal of the solvent under reduced pressure afforded a residue which was dissolved in ether or chloroform. The solution was washed with water, dried, and evaporated and the residue was subjected to preparative t.l.c. (Wakogel F5 unless stated otherwise) or column chromatography. The lactams were identified by direct comparison.

5α-*Cholestan*-4-*one oxime* (1). The oxime (400 mg) in methanol (350 ml) was irradiated for 8 h 40 min. The product was subjected to preparative t.l.c. (chloroform–ether, 4 : 1). The most mobile fraction (77 mg) was further subjected to column chromatography (3 mg). Elution with benzene afforded 5β-cholestan-4-one (3) (8 mg, 2%) (after recrystallization from acetone–methanol) and 5α-cholestan-4-one (2) (20 mg, 5%), successively. The second most mobile compound (115 mg, 29%) was 4a-aza-A-homo-5α-cholestan-4-one (4), m.p. 227—228 °C (from methanol). The third most mobile fraction (96 mg, 24%) was 4-*aza*-A-*homo*-5α-

cholestan-4α-one (5), m.p. 203—206° (from methanol). (Found: C, 80.85; H, 11.6; N, 3.4. $C_{27}H_{47}NO$ requires C, 80.75; H, 11.8; N, 3.5%); $\nu_{max.}$ 1 659 (lactam C=O), and 3 073 and 3 268 cm^{-1} (NH); for n.m.r. see Table 2: *m/e* 401 (100), 386 (35), 246 (57), 139 (26), 126 (50), and 113 (75). Later fractions (125 mg) were a complex mixture not containing any lactam.

5β-*Cholestan-4-one oxime* (6). The product (434 mg) from 7 h irradiation of the oxime (400 mg) was subjected to preparative t.l.c. (choroform–ether, 4 : 1). Column chromatography on silica gel (4 g) of the most mobile fraction (121 mg) afforded 5β-cholestan-4-one (3) (19 mg, 5%) and a mixture of 5α-cholestan-4-one (2) and unchanged 5β-oxime (46 mg). Yields of 5α-cholestan-4-one and the oxime estimated from n.m.r. spectra were 9.5 mg (3%) and 37 mg.

The second most mobile fraction (180 mg) was subjected again to preparative t.l.c. (benzene–ether, 1 : 4; two developments) to afford first 4-*aza*-A-*homo*-5β-*cholestan*-4a-*one* (8) (67 mg, 18%) and then 4a-aza-A-homo-5β-cholestan-4-one (7) (73 mg, 20%). A pure specimen of the lactam (8) was obtained by adsorption chromatography and recrystallization from acetone; m.p. 126—129° (Found: C, 80.4; H, 11.95; N, 3.45. $C_{27}H_{47}NO$ requires C, 80.75; H, 11.8; N, 3.5%); $\nu_{max.}$ 1 669 (lactam C=O), and 3 225 and 3 092 cm^{-1}; for n.m.r. see Table 2; *m/e* 401 (74), 386 (40), 246 (32), 139 (11), 126 (100), and 113 (73). The less mobile fractions (125 mg) did not contain any lactams and were complex mixtures of several products probably containing amides.

5α-*Cholestan-1-one oxime* (9). The oxime (400 mg) in methanol (280 ml) was irradiated for 7.5 h. The amorphous product (418 mg) was subjected to column chromatography. Elution with benzene afforded unchanged oxime (55 mg) and then the parent ketone (10) (31 mg, 9%). Elution with benzene–ether (5 : 1) afforded 2-aza-A-homo-5α-cholestan-1-one (11) (49 mg, 14%) and then 1-*aza*-A-*homo*-5α-*cholestan*-2-*one* (12) (73 mg, 21%). Elution with ether afforded 93 mg of a complex mixture of less mobile compounds which did not contain any lactams. The lactam (12) had m.p. 154—157° (from acetone) (Found: C, 80.3; H, 11.8; N, 3.4. $C_{27}H_{47}$-NO requires C, 80.75; H, 11.8; N, 3.5%); $\nu_{max.}$ 1 651 (lactam C=O), and 3 084, 3 151, 3 252, and 3 303 cm^{-1} (lactam NH); for n.m.r. see Table 2; *m/e* 401 (87%), 386 (41), 247 (34), 138 (100), 125 (34), and 95 (37).

5β-*Cholestan-1-one oxime* (14). The oxime (400 mg) in methanol (350 ml) was irradiated for 6.5 h. The product (417 mg) was subjected to preparative t.l.c. (chloroform–ether, 5 : 1). Six fractions (A—F) were obtained. The most mobile fraction A (64 mg) was subjected to column chromatography on silica gel (2 g). Elution with hexane–benzene afforded a seco-ester (18) (21 mg, 5%) containing a trace of a seco-aldehyde (19) and 5β-cholestan-1-one (15) (22 mg, 6%), $\nu_{max.}$ 1 704 cm^{-1} (C=O), successively. The seco-ester (18) showed $\nu_{max.}$ (neat) 1 749 cm^{-1} (CO_2Me); τ 9.35 (s, 18-H), 7.69 (t, *J* 6.6 Hz, 2-H_2), and 6.34 (s, CO_2Me). The aldehyde showed τ 0.26 (CHO) and 5.39 (d, *J* 4.9 Hz, 10-CH_2).

Fraction B (49 mg) was subjected to column chromatography on silica gel (2 g). Elution with benzene and benzene containing increasing amounts of ether afforded unchanged oxime (8 mg) together with a more mobile unidentified substance (17 mg). Fraction C (99 mg) was almost pure 1-aza-A-homo-5β-cholestan-2-one (16). This was subjected to column chromatography on silica gel (3 g). Elution with benzene–ether containing an increasing amount of ether afforded the lactam (16) (86 mg, 22%), which was recrystallized from acetone (yield 44 mg).

Fraction D (45 mg) was 2-*aza*-A-*homo*-5β-*cholestan*-1-*one* (17) and was purified by column chromatography on silica gel (2 g) and recrystallization from acetone (yield 38 mg, 10%); m.p. 127—129° (Found: C, 80.3; H, 11.75; N, 3.2. $C_{27}H_{47}NO$ requires C, 80.75; H, 11.8; N, 3.5%); $\nu_{max.}$ 1 649 (lactam C=O) and 3 295 cm^{-1} (NH); for n.m.r. see Table 2; *m/e* 401 (18%), 386 (18), 247 (34), 126 (29), 99 (15), 96 (100), and 43 (21).

Fraction E (26 mg) did not contain any lactams and was not examined further. Fraction F (38 mg) was purified by column chromatography on silica gel (1 g) to afford (27 mg, 7%) an amorphous seco-amide (20); $\nu_{max.}$ 1 629 and 1 666 ($CONH_2$), and 3 204 and 3 368 cm^{-1} (NH_2); τ 9.34 (s, 18-H), 5.38 (d, *J* 4.5 Hz, 10-CH_2), 4.00, and 4.35br (s, CO·NH_2).

Photo-Beckmann Rearrangement of 5α-*Cholestan*-1-*one Oxime* (9) *in the Presence of Oxygen*.—The oxime (402 mg) was dissolved in methanol (280 ml) and oxygen was bubbled through for 1 h. Then the solution was irradiated for 7 h. The mixture (375 mg) was subjected to column chromatography. Elution with benzene afforded unchanged oxime (127 mg) and then the parent ketone (170 mg). Elution with benzene–ether (1 : 1) afforded the 1-aza-lactam (11) (21 mg) and the 2-aza-lactam (12) (19 mg).

Photo-Beckmann Rearrangement of A-*Nor*-5β-*cholestan*-3-*one Oxime* (25).—The oxime (400 mg) in methanol (350 ml) was irradiated for 9 h. T.l.c. of the product (404 mg) revealed at least eight spots. Preparative t.l.c. on Wakogel B-5 (benzene–ether, 1 : 3) gave six fractions (A—F). The most mobile fraction A (196 mg) was again purified by adsorption chromatography on silica gel (4.5 g). Elutions with hexane and then hexane containing increasing amounts of benzene afforded successively a seco-ester (28) (22 mg, 6%), the 5β-ketone (24) (23 mg, 7%) and unchanged oxime (45 mg). The amorphous seco-ester was identified by the n.m.r. spectrum: τ 6.33 (3 H, s, CO_2Me), 9.10 (3 H, s, 19-H), 9.34 (3 H, s, 18-H), and 7.67—7.83 (m, CO·CH_2). Column chromatography on silica gel (2 g) of fraction B (22 mg) afforded a major homogeneous fraction (11 mg) but its structure was not clarified. Fraction C (34 mg) was subjected to adsorption chromatography on silica gel (1.5 g). Elution with ether–benzene (1 : 1) afforded an unidentified amorphous compound (12 mg). Fraction D (50 mg) was purified by column chromatography on silica gel (2 g). Elution with benzene–ether (7 : 3) afforded 3-aza-5β-cholestan-4-one (27) (41 mg, 12%), m.p. 165—168° (from acetone) (lit.,[8] 168—170°); $\nu_{max.}$ 1 618 and 1 656 (C=O), and 3 319 and 3 199 cm^{-1} (NH); for n.m.r. see Table 2; *m/e* 387 (100%), 372 (23), 232 (31), 112 (93), 81 (11), and 55 (16). Fraction E (53 mg) was purified by column chromatography on silica gel (2 g). Elution with benzene–ether (1 : 3) afforded 4-aza-5β-cholestan-3-one (26) (46 mg, 13%). The least mobile fraction F (40 mg) was an unidentified gum.

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