Photo-induced Molecular Transformations. Part 87.[1] Regiospecific Photo-Beckmann Rearrangement of Steroidal α,β-Unsaturated Ketone Oximes: Synthesis of Some Steroidal Enamino Lactams

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While it is well known that the Beckmann rearrangement of steroidal cyclic α,β-unsaturated ketone oximes lead to the exclusive formation of enone-type lactams regardless of the initial geometry of their hydroxyimino group, the photolysis of three isomeric cholestenone oximes, (*E*)- and (*Z*)-cholest-4-en-3-one oximes, (*E*)-2,2-dimethylcholest-4-en-3-one oxime, and (*E*)-cholest-5-en-7-one oxime in protic solvents has shown that in each case an enamine-type lactam is the sole product (yield ≤33%), no enone-type lactam being formed. This regiospecific photo-rearrangement may be of value for the preparation of these enamine-type lactams which cannot be achieved by the Beckmann rearrangement.

Our previous studies[2] and the studies by Just and his colleagues[3] on the photoreaction of a number of cyclic ketone oximes have disclosed that the photolysis of five-membered cyclic ketone oximes,[2a,b] a six-membered cyclic ketone oxime,[2c–e] seven-membered cyclic ketone oximes,[2f] a cyclopropyl ketone oxime,[2g] a β,γ-cyclopropyl ketone oxime,[2h] a β,γ-unsaturated ketone oxime,[2i] and bicyclo[2.2.1]heptanone oximes[1] in protic solvents generally give a pair of structurally isomeric lactams in fair yield regardless of the geometries of their hydroxyimino group: the difference in the yields between the two isomeric lactams formed in the each photoreaction is not appreciable.† Our studies have also established that the chirality of the migrating group centre in the starting oximes is retained in the lactams formed.[2c,d] A further feature of the photoreaction of oximes revealed by our studies is that, in contrast to the Beckmann rearrangement, the photorearrangement is rarely accompanied by any products arising from α-fission.[2d–i]

In contrast to the work devoted to these saturated ketone oximes, only sporadic study has been carried out on the behaviour of excited α,β-unsaturated ketone oximes. Beugelmanns and his colleague have reported that the photolysis of cholest-4-en-3-one oxime in benzene gave the parent ketone in a 50% yield as the only product identified.[4] Mukai and his colleagues have reported[5] the results of the photoreactions of 1,1-dimethylnaphthalenone oxime and styryl ketone oxime which are better considered to be aromatic ketone oximes. Bonet and his colleagues subsequently reported[6] that the photolysis of 17β-acetoxyandrost-1,5-dien-3-one oxime in methanol gave 17β-hydroxy-4-aza-A-homandrosta-1,5-dien-3-one arising from a photo-Beckmann rearrangement.

We now report the results of the photolysis of three steroidal α,β-unsaturated cyclic ketone oximes, a mixture of (*E*)- and (*Z*)-cholest-4-en-3-one oximes (**1**) and (**2**), 2,2-dimethylcholest-4-en-3-one oxime (**6**), and cholest-5-en-7-one oxime (**12**). We have found that these oximes generally give only enamine-type lactams after photolysis in protic solvents.

Results

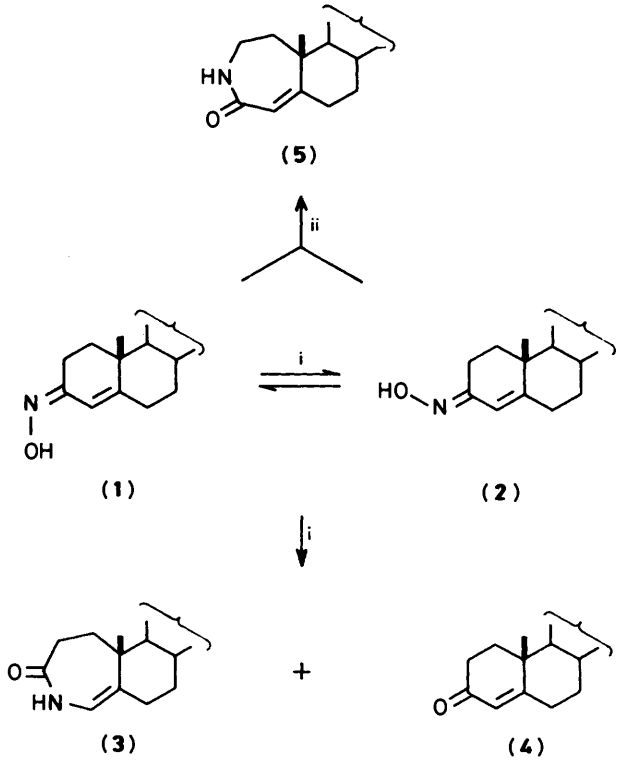
Preparation of α,β-Unsaturated Cyclic Ketone Oximes (**1**), (**2**), (**6**), *and* (**12**) *for the Photolysis.*—Oximation of cholest-4-en-3-one gave a mixture of (*E*)- and (*Z*)- oximes (**1**) and (**2**).[7] They were separable by preparative t.l.c. although on t.l.c. they undergo ready isomerization. A 57:43 mixture of (*E*) and (*Z*) forms obtained by recrystallization from acetone–methanol was used for the photoreaction. A hitherto unknown 2,2-dimethylcholest-4-en-3-one (**9**) was prepared in 70% yield by a kinetically controlled methylation[8] of cholest-4-en-3-one (**4**) with methyl iodide in the presence of potassium t-butoxide in dry THF. The oximation of the ketone in the presence of sodium hydroxide in ethanol–benzene under reflux gave the *E*-isomer (**6**) exclusively while oximation of cholest-5-en-7-one by the standard method also gave only *E*-isomer (**12**).[9]

Photo-reactions of the Oximes (**1**) *and* (**2**), (**6**), *and* (**12**) (*Schemes* 1—3).—The photoreactions of the oximes were carried out in methanol, in acetic acid, and in benzene containing a small amount of acetic acid with a low-pressure mercury arc generated by a Rayonet RPR photochemical chamber reactor.

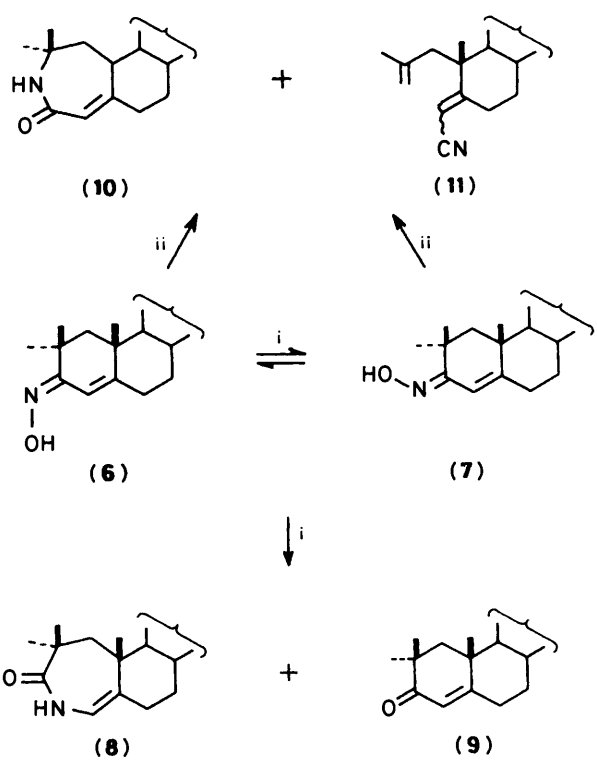
Irradiation of a mixture of (*E*)- and (*Z*)-cholest-4-en-3-one oxime (**1**) and (**2**) in methanol (3.3×10^{-3}M) for 7.5 h gave a 45% conversion and the isolation of product (**3**; $C_{27}H_{45}NO$) (33% yield) and the parent ketone (**4**) (51%). On the basis of ^{1}H n.m.r., u.v., i.r., and mass spectral evidence (see Experimental section) product (**3**) was identified as 4-aza-A-homocholest-4a-en-3-one. The photolysis in glacial acetic acid took place at a much faster rate. All the oxime was consumed after irradiation for 16 h, although only low yields of the lactam (**3**) (4%) and the parent ketone (11%) were isolated from the crude product mixture which largely consisted of ill-defined products. The photolysis of the oxime in benzene containing glacial acetic acid (94:6, v/v) also took place at a faster rate than in methanol and irradiation for 2.5 h gave a 59% conversion of the oxime from which the lactam (**3**) (25% yield) and the parent ketone (10%) were isolated. In these photolyses, the period of irradiation was kept to a minimum in order to avoid any secondary decomposition of the lactams. Careful t.l.c. examination of the products from this photolysis indicated that no isomeric 3-azalactam[7] had been formed.

The photolysis of (*E*)-2,2-dimethylcholest-4-en-3-one oxime (**6**) in benzene containing glacial acetic acid (15:1) was carried out under similar conditions. Again, an enamine-type lactam, 2,2-dimethyl-4-aza-A-homocholest-4a-en-3-one (**8**) was obtained as the only lactam (25% yield) together with ketone (**9**) (13%), the starting oxime (31%), and a hitherto unknown (*Z*)-oxime (**7**) (24%). The configuration of the hydroxy group of

† The results of photolysis of a steroidal 17-keto steroid oxime is exceptional and gives an epimeric pair of lactams: H. Suginome and T. Uchida, *Tetrahedron Lett.*, 1973, 2289; *Bull. Chem. Soc. Jpn.*, 1974, **47**, 687.



Scheme 1. *Reagents and conditions:* i, *hν*–MeOH or *hν*–$MeCO_2H$; ii, $SOCl_2$

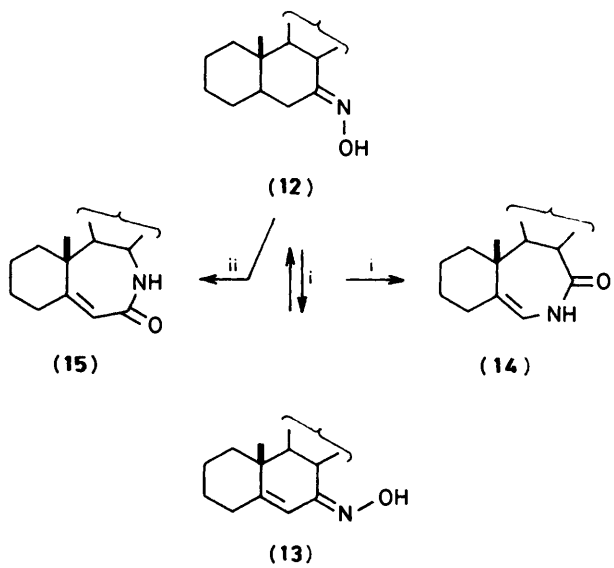


Scheme 2. *Reagents and conditions:* i, *hν*–MeOH or *hν*–$MeCO_2H$; ii, $SOCl_2$

the (*Z*)-oxime was deduced from the ^1H n.m.r. spectrum which showed signals due to 2β-Me (δ 1.30) and 2α-Me (δ 1.42) at considerably lower fields than the corresponding proton signals of the (*E*)-isomer. The olefinic proton also appeared at an appreciably higher field than the olefinic proton of the (*E*)-isomer. The photolysis in methanol gave a lower yield of the lactam (**8**) (18%) and a higher yield of the parent ketone (24%).

A similar photolysis of (*E*)-cholest-5-en-7-one oxime (**12**) in benzene containing acetic acid (94:6) for 3.5 h under the above conditions again gave an enamine-type lactam (**14**) (28% yield based on a consumed oxime), as the sole product. Spectroscopy established the structure of the lactam as 7-aza-B-homocholest-5-en-7a-one. The reaction was very clean and none of the parent ketone nor the isomeric lactam (**15**) was detected by means of t.l.c.

Finally, we investigated the effect of oxygen on the photorearrangement of α,β-unsaturated ketone oximes. Irradiation of (*E*)- and (*Z*)-cholest-4-en-3-one oxime (**1**) and (**2**) in methanol saturated with oxygen for 6 h gave the lactam (**3**) (18%) and the parent ketone (**4**) (50%). It is interesting to note that while the NH proton signal for each of the three steroidal enamine-type lactams, (**3**), (**8**), and (**14**) was a doublet with *J* 6 arising from coupling with the adjacent olefinic proton, the NH proton signal for all three enone-type lactams, (**5**), (**10**), and (**15**), was a broad singlet.



Scheme 3. *Reagents and conditions:* i, *hν*–MeOH or *hν*–$MeCO_2H$–benzene; ii, $SOCl_2$

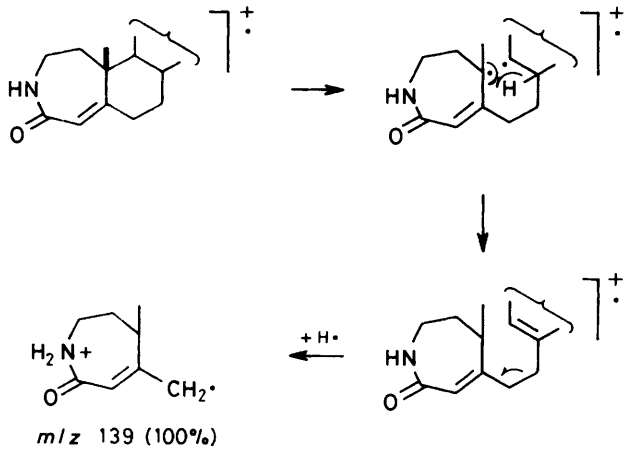
Beckmann Rearrangement of the Oximes.—Shoppee and his co-workers obtained only enone-type lactams by Beckmann rearrangements of a mixture of isomeric cholest-4-en-3-one oximes (**1**) and (**2**)[7] and cholest-5-en-7-one oxime (**12**).[9] Treatment of the oximes (**1**) and (**2**) and the oxime (**12**) with thionyl chloride in dioxane gave, respectively, an enone-type lactam (**5**) (46% yield)[7] (Scheme 1) or (**15**) (69% yield)[9] (Scheme 3); t.l.c. of the product mixture showed the absence of any enamino lactams. A similar treatment of the oxime (**6**) gave an enone-type lactam (**10**) (58% yield) together with an unsaturated nitrile (**11**) arising from a Beckmann fission. On the basis of ^1H n.m.r., u.v., i.r., and mass spectral results (see Experimental section) compounds (**10**) and (**11**) were identified as 2,2-dimethyl-3-aza-A-homocholest-4a-en-4-one and 4-cyano-2-methyl-3,4-secocholesta-2,4-diene. As described below, a hitherto unreported *Z*-isomer of 2,2-dimethylcholest-4-en-3-one

oxime (**7**) can be obtained by irradiation of its (*E*)-isomer (**6**). Treatment of the *Z*-isomer (**7**) with thionyl chloride in dioxane gave again only the enone-type lactam (**10**) (67%), no trace (t.l.c.) of the enamine-type lactam being present.

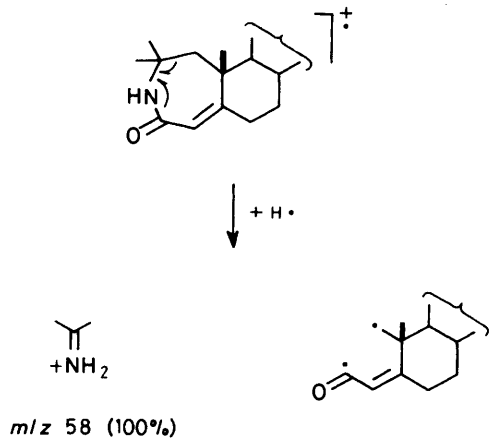
Mass Spectral Fragmentations of Unsaturated Lactams Obtained.—Some interesting mass spectral fragmentations were observed for the lactams obtained in the present study.

For example, while the mass spectrum of the enone-type lactam (**5**) showed an ion at *m/z* 139 as its base peak, the mass spectrum of the enamine-type lactam (**3**) showed the molecular ion as the base peak. The hypothetical genesis and the structure of the ion at *m/z* 139 is outlined in Scheme 4.

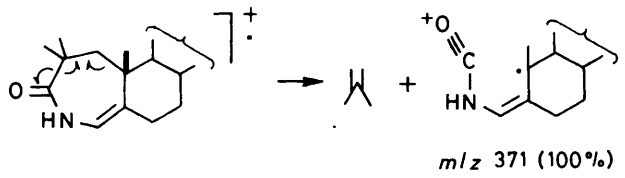
The mass spectra of the enone-type lactam (**10**) and enamine-type lactam (**8**) showed ions at *m/z* 58 and *m/z* 371 as their base peaks respectively. The geneses of these ions are outlined in Schemes 5 and 6.



Scheme 4.

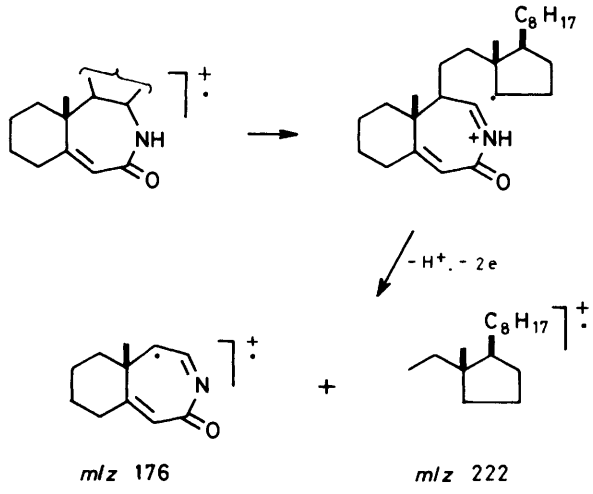


Scheme 5.



Scheme 6.

Finally the mass spectrum of enone-type lactam (**15**) showed the ion at *m/z* 222 as the base peak, with a prominent ion at *m/z* 176. Probable geneses of these ions are outlined in Scheme 7.



Scheme 7.

Discussion

The foregoing studies indicate that in contrast to the photorearrangement of cyclic ketone oximes, the photorearrangement of excited α,β-unsaturated ketone oximes in protic solvents takes place regioselectively to give only enamine-type lactams arising from the migration of their trigonal carbon to their nitrogen. It is almost certain that these lactams are formed *via* oxaziridines as their intermediate, as is the case in photochemical formation of amides from styryl ketone oximes[5] and benzaldehyde oxime,[10] since, although we were unable to isolate oxaziridines, we did observe the formation of iodine on treatment of irradiated methanolic solutions of the oximes with potassium iodide.[11]

Mukai and his colleagues[5] have shown that oxygen inhibits the photochemical formation of lactams in acetic acid and, therefore, the photochemical formation of amides from styryl ketone oxime, which may better be regarded as an aromatic ketone oxime, takes place *via* an excited triplet state of a protonated oxaziridine formed from an excited singlet oxime; and also that acids such as acetic acid necessary for the protonation of oxaziridines are indispensable for the rearrangement of the triplet excited oxaziridine to amides.

The foregoing results with the steroidal α,β-unsaturated ketone oximes revealed that acetic acid is not indispensable for the photorearrangement of the oximes to the lactams, although a protic solvent is required. We also confirmed that the presence of oxygen does not prohibit the photochemical formation of enamine-type lactams. These kinds of behaviour parallel the results we found for the formation of the lactams from excited saturated ketone oximes.[2d] The observed diminished yield is better regarded as due to a secondary decomposition of the lactam (**3**) under the conditions of the photolysis in the presence of oxygen rather than a partial physical quenching. Bonet *et al.* have already shown that enamine-type lactams readily react with oxygen to give unstable 1,2-dioxetanes.[12] Thus, we conclude that the formation of the lactams from steroidal α,β-unsaturated cyclic ketone oximes takes place *via* the reorganization of the excited singlet oxaziridines which are formed from excited singlet oximes, as with saturated cyclic ketone oximes.[2d]

Why the trigonal carbon centres in these oxaziridines

predominantly migrate over their tetrahedral carbon centres is, however, not clear at the present stage, although a stereoelectronic factor (the relative geometry between the nitrogen lone pair and the migrating C–C bond in the oxaziridine intermediates) is likely to play an important role in this selective migration. The generality of the regioselectivity of the photoreaction found in the present study, however, needs to be tested on more substrates since the specific formation of an enone-type lactam in the photorearrangement of 17β-hydroxyandrosta-1,5-dien-3-one acetate oxime has been reported by Bonet and his colleagues.[6] It has been reported that the steroidal cyclic α,β-unsaturated ketone oximes[7,13–16] are reactive only in their *E* configurations under the conditions of Beckmann rearrangements and the steroidal cyclic enamine-type lactams are not obtainable by the Beckmann rearrangement. Our experiments again confirmed this. There are also many reports on the migratory aptitude of the non-steroidal cyclic α,β-unsaturated ketone oximes. These investigations[17–24] indicate that the alkyl group is generally apt to migrate over the vinyl group in 5- or 6-membered cyclic ketone oximes although *syn-anti* isomerization under the conditions of the rearrangement makes the argument on the direction of the migration rather complex or sometimes unambiguous. The exclusive or competitive vinyl migrations have been found in mono- or fused cyclic ketone oximes[19,21,23] in only a few cases.* A lower rate of the vinyl migration in cyclic ketone oximes is probably attributed to geometrical constraints which prohibit overlap of the orbitals of the vinyl group and the empty orbital generated on the nitrogen atom.

Lactam formation as a result of alkyl migration from the oximes with a sterically unfavourable configuration was interpreted either in terms of isomerization of the hydroxyimino group prior to migration of the trigonal carbon or the intervention of iminium cations, the geometrical constraint of which prevents vinyl migration.

Exclusive formation of the enone-type lactam (**10**), from the oxime (**7**) in our case, can be explained clearly in terms of transformation of the (*Z*)-isomer to a more stable (*E*)-isomer prior to intramolecular migration of the trigonal carbon to the nitrogen of the (*Z*)-isomer.

The synthesis of the first steroidal enamine-type lactam, 4-benzyl-4-azacholest-5-en-3-one was achieved by reaction of 5-oxo-3,5-seco-4-norcholestan-3-oic acid with benzylamine by Woodward and his colleagues.[25] Several 4-substituted 4-azacholest-5-en-3-ones were then synthesized by the same method.[26]

Barton and his colleagues have recently reported that *N*-methyl derivatives of enamine-type lactams can be obtained by treatment of cyclic *N*-methylnitrones with toluene-*p*-sulphonyl chloride in pyridine.[27]

Whatever the cause of the regioselectivity of the rearrangement, the one-step formation of the *N*-unsubstituted steroidal enamine-type lactams by photorearrangement of oximes under neutral conditions at room temperature, may be useful for the preparation of azasteroids.

One of the unique features of excited oximes we found[1,2d,h,i,j] is that they rarely give any products arising from α-fission.† The present experiments again confirmed this behaviour: while the thermal Beckmann rearrangement of (*E*)-2,2-dimethylcholest-4-en-3-one oxime (**6**) gave the unsaturated nitrile (**11**), the photoreaction of the oxime (**6**) afforded no nitrile giving only the lactam (**8**).

Experimental

M.p.s were determined with a Yanagimoto micro m.p. apparatus. I.r. spectra were determined for Nujol mulls with a Hitachi-Perkin-Elmer Model 125 spectrophotometer. ^{1}H N.m.r. spectra were determined with a JEOL PS 100 high resolution spectrometer operating at 100 MHz (δ_H) (solvent $CDCl_3$; $SiMe_4$ as internal reference) unless we state otherwise. The ^{13}C n.m.r. spectrum was determined with a JEOL JNM-FX-100 spectrometer (solvent $CDCl_3$:$SiMe_4$ as internal reference). U.v. spectra were determined with a Hitachi 124 double-beam spectrophotometer. Mass spectra were determined with JEOL JMS-D 300 spectrometer (70 eV) either in the Faculty of Pharmaceutical Sciences of this University, or in the Faculty of Agriculture. Elemental analyses were performed in a laboratory for analysis in the Faculty of Pharmaceutical Sciences. T.l.c. was carried out on Merck silica gel 60 PF 254 containing gypsum for preparative t.l.c.

(E)- *and* (Z)-*Cholest-4-en-3-one Oximes*.—Cholest-4-en-3-one (**4**) (3 g), hydroxylamine hydrochloride (3.5 g), and sodium acetate trihydrate (3.5 g) in ethanol (300 ml) were stirred for 0.5 h at room temperature. Work-up of the solution gave a product (2.75 g) which was recrystallized from acetone–methanol to yield a 43:57 (^{1}H n.m.r.) mixture of (*E*)- and (*Z*)-oxime, m.p. 159—160 °C [lit.,[6] m.p. 152—153 °C, 2:3 mixture of (*E*)- and (*Z*)-oxime]; $\lambda_{max.}$(MeOH) 241 nm (ε 15 350). This mixture was subjected to preparative t.l.c. with benzene–diethyl ether (4:1) to yield (*E*)-isomer (**1**) and (*Z*)-isomer (**2**). Isomer (**1**): $\nu_{max.}$($CHCl_3$) 3 196 (br, OH), 1 639 (C=N), 1 216, and 952 cm^{-1}; δ 0.79 (3 H, s, 18-H), 1.10 (3 H, s, 19-H), and 6.47 (1 H, s, 4-H); *m/z* (rel. intensity) 399 (M^+, 10.6%), 383 (30.0), 139 (27.7), and 123 (100). Isomer (**2**): $\nu_{max.}$(Nujol) 3 208 (br, OH), 1 633 (C=N), and 970 cm^{-1}; δ 0.69 (3 H, s, 18-H), 1.05 (3 H, s, 19-H), and 5.76 (1 H, s, 4-H); *m/z* (rel. intensity) 399 (M^+, 23.4%), 383 (36.2), 139 (37.7), and 123 (100).

Preparation of 2,2-*Dimethylcholest-4-en-3-one* (**9**).—To cholest-4-en-3-one (**4**) (5 g) and methyl iodide (9.4 ml) in dry THF (50 ml) cooled at −65 to −70 °C (solid CO_2–MeOH), potassium t-butoxide (8.5 g) in dry THF (50 ml) was added over a period of 30 min. Water was then added and the solution was neutralized with 2M hydrochloric acid. The resulting solution was extracted with diethyl ether. The organic layer was worked up to give a product mixture which was subjected to column chromatography (Wako, activated alumina, 300 mesh). Elution with benzene gave three fractions. The first eluted fraction was recrystallized from ethanol to yield 2,2-dimethylcholest-4-en-3-one (**9**) (3.75 g, 70%), m.p. 99—100 °C (Found: C, 84.4; H, 11.7. $C_{29}H_{48}O$ requires C, 84.40; H, 11.72%); $\nu_{max.}$ 1673 and 1618 cm^{-1} (α,β-unsaturated carbonyl); λ_{max}(methanol) 243 nm (ε 14 300); δ 0.69 (3 H, s, 18-H), 1.09 (3 H, s, 19-H), 1.15 (3 H, s, 2-CH_3), 1.25 (3 H, s, 2-CH_3), and 5.31 (1 H, s, 4-H); *m/z* (rel. intensity) 412 (M^+, 50.5), 398 (M^+ − 14, 85.4), 369 (17.3), 356 (49.4), 342 (75.4), 229 (100), and 138 (98.2%).

(E)-2,2-*Dimethylcholest-4-en-3-one Oxime* (**6**).—The enone (3 g), hydroxylamine hydrochloride (3.5 g), and sodium hydroxide (3.3 g) in ethanol (100 ml) and benzene (30 ml) were heated under reflux for 2 h. The solution was worked up and the crude oxime recrystallized from ethanol to yield a pure (*E*)-oxime (**6**) (2.7 g, 87%), m.p. 158—159 °C (Found: C, 81.4; H, 11.6; N, 3.5. $C_{29}H_{49}NO$ requires C, 81.44; H, 11.55; N, 3.28%); $\nu_{max.}$ 3 225 (OH), 1 639 (C=N), and 952 cm^{-1} (N–O);

* An acyclic ketone oxime, pregn-16-en-20-one oxime is reported to give an amide as a result of vinylic migration during Beckmann rearrangement: G. Rosenkrankz, O. Mancera, F. Sondheimer, and C. Djerassi, *J. Org. Chem.*, 1956, **21**, 520.

† A highly substituted tri-t-butylcyclohexadienone oxime and a highly strained 7,14-cyclodihydrocodeinone oxime have been reported to give, exceptionally, α-fission products on irradiation (R. Okazaki, M. Watanabe, and N. Inamoto, *Tetrahedron Lett.*, 1977, 4515; M. Bös and W. Fleischhacker, *Liebigs Ann. Chem.*, 1982, 112).

$\lambda_{max.}$(methanol) 240 nm (ε 14 300); δ 0.66 (3 H, s, 18-H), 1.13 (9 H, s, 19-H and 2,2-dimethyl), and 6.41 (1 H, s, 4-H); *m/z* 427 (M^+, 24.2), 413 ($M^+ - 14$, 48.7), 396 ($M^+ - 31$, 43.2), and 151 (100%).

(E)-*Cholest-5-en-7-one Oxime* (**12**).—Cholest-5-en-7-one (3 g), hydroxylamine hydrochloride (3.5 g), and sodium acetate trihydrate (3.5 g) in ethanol (300 ml) were stirred for 5 h and then heated under reflux for 4 h. Work-up of the solution gave a crude (*E*)-oxime. This was recrystallized from acetone–methanol to yield the pure oxime (**12**) (2.8 g), m.p. 182—184 °C and then 185.5 °C (lit.,[8] m.p. 177—180 °C); $\nu_{max.}$ 3 268br (OH), 1 638 (C=N), 958, and 900 cm^{-1}; $\lambda_{max.}$ 237 nm (ε 13 300); δ 0.70, (3 H, s, 18-H), 1.11 (3 H, s, 19-H), and 6.49 (1 H, s, 6-H); *m/z* 399 (M^+, 93.4), 384 ($M^+ - CH_3$, 100), and 382 ($M^+ - OH$, 76.2%).

Photo-Beckmann Rearrangement of Cholest-4-en-3-one Oxime (**1**) *and* (**2**).—(a) *In methanol.* A mixture of (*E*)- and (*Z*)-cholest-4-en-3-one oximes (100 mg) in methanol (30 ml) was irradiated with a low pressure mercury arc generated by a Rayonet RPR photochemical reactor for 7.5 h. The solvent was removed with the aid of a rotary evaporator and the photolysate was subjected to preparative t.l.c. with benzene–diethyl ether (6:1) to afford four fractions A, B, C, and D in the order of their mobility on the t.l.c. plate. Fraction A (23 mg, 51% based on a consumed oxime) was the parent ketone. Fraction B (30 mg) was a (*Z*)-oxime. Fraction C (25 mg) was (*E*)-oxime. Fraction D (15 mg, 33% based on consumed oxime) was 4-aza-A-homocholest-4a-en-3-one (**3**) which was recrystallized from acetone; m.p. 224—228 °C (decomp.) (Found: M^+, 399.3491. $C_{27}H_{45}NO$ requires M^+, 399.3499); $\nu_{max.}$ 3 336, 3 206, and 3 106 (NH), 1 688, 1 664, and 1 633 (CONHCH=C), 1 205, and 1 160 cm^{-1}; $\lambda_{max.}$(MeOH) 243 nm (ε 9 430); δ 0.67 (3 H, s, 18-H), 1.08 (3 H, s, 19-H), 5.49 (1 H, d, *J* 6 Hz, 4a-H), and 6.78 (1 H, d, *J* 6 Hz, NH); *m/z* 399 (M^+, 100) and 384 (M^+ – Me, 29%).

(b) *In glacial acetic acid.* A mixture of oximes (373 mg) in glacial acetic acid (350 ml) was irradiated under a nitrogen atmosphere for 16 h at room temperature. The solvent was removed by a rotary evaporator (bath temp. −50 °C) with added benzene. The residue was dissolved in dichloromethane to remove some insoluble material which had collected and then dissolved in 5% aqueous sodium hydroxide. The dichloromethane solution gave a product mixture. The sodium hydroxide solution was shaken with dichloromethane and the aqueous layer was neutralized with 2M hydrochloric acid to give unidentified colourless crystals (7 mg). The product mixture was subjected to preparative t.l.c. with benzene–diethyl ether (6:1) to give 4-aza-A-homocholest-4a-en-3-one (**3**) (16.5 mg, 4.4%) and the parent ketone (41 mg, 11%). There were a large number of ill-defined products more polar than these first products but an attempt to separate these into their components was unsuccessful.

(c) *In glacial acetic acid benzene.* A mixture of (*E*)- and (*Z*)-oxime (117 mg) in a mixed solvent of benzene (94 ml) and glacial acetic acid (6 ml) was irradiated as described above for 2.5 h. After work-up as described above, the residue was subjected to preparative t.l.c. to give four fractions in the order of their mobility. Fraction A (7 mg, 10% yield based on the consumed oxime) was the parent enone. Fraction B (36 mg) was an(*Z*)-oxime. Fraction C (10 mg) was an (*E*)-oxime. Fraction D (17.5 mg, 25% yield based on the consumed oxime) was 4-aza-A-homocholest-4a-en-3-one (**3**).

(d) *In oxygen-saturated methanol under an atmosphere of oxygen.* Oxygen was bubbled through a mixture of oximes (100 mg) in methanol in a quartz vessel for 0.5 h. The solution was irradiated for 6 h under an atmosphere of oxygen and worked up as above to yield the lactam (**3**) (7 mg, 18%) and the parent ketone (**4**) (20 mg, 50%). The starting oxime (60 mg) was recovered.

Photo-Beckmann Rearrangement of (E)-2,2-*Dimethylcholest-4-en-3-one Oxime* (**6**).—*In methanol.* The oxime (**6**) (427 mg) in methanol (300 ml) was irradiated for 9 h under a nitrogen atmosphere as with the cholest-4-en-3-one oxime. After removal of solvent, the residue was subjected to preparative t.l.c. with benzene to yield five fractions: A (38 mg), B (52 mg), C (205 mg), D (40 mg), and E (73 mg) in the order of their decreasing mobility. Fraction B was the parent enone (24%). Fraction C was the starting (*E*)-oxime (48%). Fraction D was 2,2-dimethyl-4-aza-A-homocholest-4a-en-3-one (**8**) which was recrystallized from acetone, m.p. >300 °C (Found: M^+, 427.3797. $C_{29}H_{49}NO$ requires *M*, 427.3812); $\nu_{max.}$ 3 300br (NH), 1 696—1 661 (CONHCH=C), 1 119, 910, and 736 cm^{-1}; δ 0.67 (3 H, s, 18-H), 1.15 (3 H, s, 19-H), 1.21 (6 H, s, 2,2-Me_2), 5.44 (1 H, d, *J* 6 Hz, 4a-H), and 6.65 (1 H, d, *J* 6 Hz, NH); *m/z* (rel. intensity) 427 (M^+, 26.4), 412 ($M^+ - CH_3$, 6.4), and 371 (100%).

In benzene–glacial acetic acid. The oxime (151 mg) in benzene (120 ml) and glacial acetic acid (8 ml) was irradiated for 2 h under the conditions described above. The solution was worked up and the product subjected to preparative t.l.c. with a 7:1 mixture of benzene and diethyl ether to give four fractions: A (9 mg), B (47 mg), C (36 mg), and D (17 mg). Fraction A was the parent enone (13% based on consumed oxime). Fraction B was the starting (*E*)-oxime. Fraction C was the (*Z*)-oxime (**12**) formed by isomerization; this was recrystallized from acetone to yield a pure specimen, m.p. 145—147 °C. When the melt was heated further it turned into crystals of (*E*)-isomer and again melted at 178—179 °C; δ 0.69 (3 H, s, 18-H), 1.13 (3 H, s, 19(H), 1.30 (3 H, s, 2β-Me), 1.42 (3 H, s, 2α-Me), and 5.64 (1 H, s, 4-H). Fraction D was 2,2-dimethyl-4-aza-A-homocholest-4a-en-3-one (**8**) (25%, based on consumed oxime).

Photo-Beckmann Rearrangement of (E)-*Cholest-5-en-7-one Oxime.*—The oxime (**12**) (364 mg) in benzene (300 ml) and glacial acetic acid (19 ml) was irradiated with a low-pressure mercury arc generated by a Rayonet RPR photochemical reactor for 3.5 h under an atmosphere of nitrogen. The solvent was removed with the aid of a rotary evaporator and the residue was subjected to preparative t.l.c. with chloroform to give four fractions: A (11 mg), B (24 mg), C (201 mg), and D (73 mg) in the order of their mobility on t.l.c. plate. Fractions A and B were unidentified gums. Fraction C was the starting (*E*)-oxime. Fraction D was a mixture of 7-aza-B-homocholest-5-en-7a-one (**14**) and (*Z*)-oxime (**13**). This mixture was again subjected to preparative t.l.c. with a 6:1 mixture of benzene and diethyl ether to give the (*E*)-oxime (**12**) (19 mg) and a less mobile lactam (**14**) (40 mg, 28%) which was recrystallized from acetone, m.p. 178—180 °C (Found: M^+, 399.3505. $C_{27}H_{45}NO$ requires *M*, 399.3500); $\nu_{max.}$(Nujol) 3 260 (NH), 1 642 (C=O), 963, and 905 cm^{-1}; δ 0.68 (3 H, s, 18-H), 1.19 (3 H, s, 19-H), 5.48 (1 H, d, *J* 6 Hz, 6-H), and 6.86 (1 H, d, *J* 6 Hz, NH); *m/z* 399 (M^+, 100), 384 (M^+ – Me, 85.5), and 124 (66.3%).

Beckmann Rearrangement of Cholest-4-en-3-one Oxime (**1**) *and* (**2**).—To the mixture of (*E*)- and (*Z*)-cholest-4-en-3-one oxime (343 mg) in dioxane (20 ml), thionyl chloride (0.2 ml) was added and the solution was stirred for 20 min at room temperature. The reaction mixture was then neutralized with 5% aqueous sodium carbonate and the solution worked up. The crude product was subjected to preparative t.l.c. with benzene–diethyl ether (6:1) to afford two fractions. The more mobile fraction (68 mg) was a 1:3 mixture of (*E*)- and (*Z*)-oximes. The less mobile fraction (126 mg, 46%, based on converted oxime) was 3-aza-A-homocholest-4a-en-4-one which was recrystallized

from chloroform–diethyl ether; it had m.p. 244—246 °C (decomp.) (lit.,[6] m.p. 250—254 °C; lit.,[11] m.p. 251—253 °C); $\nu_{max.}$ 3 292, 3 172, and 3 042 (NH), 1 665, 1 640, and 1 600 (NHCOCH=C), 1 026, 995, 911, 871, and 861 cm^{-1}; $\lambda_{max.}$(MeOH) 220 nm (ε 15 350); δ 0.67 (3 H, s, 18-H), 1.10 (3 H, s, 19-H), 3.17 (2 H, br s, $W_{\frac{1}{2}}$ 15 Hz, 2-CH_2), 5.67 (1 H, s, 4a-H), and 6.92 (1 H, br s, $W_{\frac{1}{2}}$ 14 Hz, NH); *m/z* 399 (M^+, 17.1), 384 (M^+ − Me, 6.6), 371 (4.5), 356 (5.0), 155 (45.9), and 139 (100%).

Beckmann Rearrangement of (E)-2,2-*Dimethylcholest*-4-*en*-3-*one Oxime* (**6**).—To the oxime (300 mg) in dioxane (10 ml), thionyl chloride (0.2 ml) was added and the solution was stirred for 20 min. The solution was neutralized with 5% aqueous sodium carbonate and then worked up. The residue was subjected to preparative t.l.c. with benzene to give two fractions, A and B. The more mobile fraction A (25 mg, 8.5%) was an amorphous unsaturated nitrile; $\nu_{max.}$($CHCl_3$) 2 212 (C≡N) and 904 cm^{-1}; δ (90 MHz), 0.68 (3 H, s, 18-H), 1.29 (3 H, s, 19-(H), 1.77 (3 H, s, 2-CH_3), 4.76, 4.94 (each 1 H, br s, 2-methylene), and 5.25 (1 H, s, 4-H); *m/z* 409 (M^+, 32.3), 394 (M^+ − CH_3, 10.0), 354 [M^+ − $CH_2C(CH_3)$=CH_2, 100], 242 (57.6), 95 (74.9), 57 (94.4), 55 (79.4), and 43 (73.0%). The less mobile fraction B (175 mg, 58%) was purified once by passing it through an alumina column (Wako, activated alumina, 300 mesh) and then recrystallized from acetone to yield 2,2-dimethyl-3-aza-A-homocholest-4a-en-4-one (**10**), m.p. 166—167 °C (Found: C, 81.15; H, 11.4; N, 3.55. $C_{29}H_{48}NO$ requires C, 81.44; H, 11.55; N, 3.28%); $\nu_{max.}$($CHCl_3$) 3 178 (NH), 1 655 and 1 615 (CO=C), and 1 234 cm^{-1}; δ 0.69 (3 H, s, 18-H), 1.22 (3 H, s, 19-H), 1.29 and 1.33 (each 3 H, s, 2,2-Me_2), 5.75 (1 H, s, 4a-H), and 6.33 (1 H, br s, NH); $\lambda_{max.}$(MeOH) 221 nm (ε 12 550); *m/z* (rel. intensity) (70 eV) 427 (M^+, 14.6), 412 (M^+ − CH_3, 50.4), 167 (23.8), and 58 [100%, $\overset{+}{N}H_2$=$C(CH_3)_2$].

Beckmann Rearrangement of (Z)-2,2-*Dimethylcholest*-4-*en*-3-*one Oxime* (**7**).—The (*Z*)-oxime (55 mg) was subjected to the Beckmann rearrangement under similar conditions to those employed for the (*E*)-oxime to yield the lactam (**10**) (35 mg, 63%). No isomeric enamine-type lactam was detected in the product.

Beckmann Rearrangement of (E)-*Cholest*-5-*en*-7-*one Oxime* (**12**).—To the oxime (**12**) (311 mg) in dry dioxane (10 ml), thionyl chloride (0.2 ml) was added. The solution was stirred for 20 min at room temperature and then neutralized by the addition of 5% aqueous sodium carbonate and worked up. The product was passed through alumina (Wako activated alumina, 300 mesh) and then recrystallized from acetone–methanol to yield 7a-aza-B-homocholest-5-en-7-one (**15**), m.p. 207—208 °C (lit.,[8] m.p. 208—211 °C); $\nu_{max.}$ 3 236, 3 156, 3 006 (NH), 1 650, 1 609 (C=C–CO), 1 211, 881, 873, and 983 cm^{-1}; $\lambda_{max.}$(MeOH) 220 nm (ε 22 350); δ 0.68 (3 H, s, 18-H), 1.22 (3 H, s, 19-H), 3.26 (1 H, br s, $W_{\frac{1}{2}}$ 18 Hz, 8β-H), 5.56 (1 H, br s, $W_{\frac{1}{2}}$ 9 Hz, NH), and 5.65 (1 H, s, 6-H); *m/z* 399 (M^+, 76.2), 384 (M^+ − CH_3, 13.1), 222 (100), and 176 (58.2%).

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