Stereochemical Aspects of the Photo-Beckmann Rearrangement. Stereochemical Integrity of the Terminus of the Migrating Carbon in the Photo-Beckmann Rearrangements of 5α- and 5β-Cholestan-6-one Oximes[1]

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The Beckmann rearrangement of either *syn*-5β-cholestan-6-one oxime or *anti*-5β-cholestan-6-one oxime with polyphosphoric acid at 90° takes place prior to the *syn-anti* equilibration of these isomers. In the photo-Beckmann rearrangement a pair of lactams, in both of which the original configurations of C_α with respect to the oximino-group of the starting oximes were retained, was produced irrespective of the configuration of the oximino-group of the starting oxime. The difference of the amounts between two isomeric lactams formed in each photolysis is small but the lactams due to the migration of the more substituted carbon are produced always in a slightly larger amount than those due to the migration of the less substituted carbon. Oxygen does not affect the formation of lactams. All these results indicate a concerted reorganization of an excited singlet oxaziridine intermediate, hydrogen-bonded with protic solvent molecule (s), into the corresponding lactams. During these studies, the photochemical epimerization of 5β-steroid-6-one into the 5α-isomer by α-cleavage-recombination sequence was observed.

Since the first report of the photo-Beckmann rearrangement of arylaldoximes by de Mayo[2] further examples with a variety of oximes have been recorded during this decade. The types of oximes investigated include alicyclic ketone oximes,[3a,3c-3f,6,7] naphthalenone oximes,[3b] aliphatic ketone oximes,[3a] styryl ketone oximes,[3g] and α,β,γ,δ-unsaturated aldehyde oxime.[3h]

The mechanistic aspects of this intriguing and potentially useful photochemical rearrangement have been discussed for arylaldoximes,[4] naphthalenone oxime,[3b] styrylketone oximes[3g] and alicyclic ketone oximes.[3c-3e] Common mechanistic features with respect to the formation of amides from all the types of oximes cited above are as follows.

The formation of amides takes place *via* oxaziridine intermediates which are formed rapidly from the excited oximes. This excited state was proved to be a singlet for the arylaldoxime rearrangement[4] and later for the styryl ketone oxime rearrangements.[3g]

Protic solvents, without exception, considerably accerelated the formation of amides from oximes. The photolysis of some steroidal ketone oximes in an aprotic solvent such as benzene does not afford lactams but the parent ketones.[5] In some instances, even alcohol is not sufficient and an acid such as AcOH is needed to cause the rearrangement.[3c]

These observations were taken as evidence that a protonation may be involved at some stage of the rearrangement[3b,3g] or that the oxaziridine formation may proceed *via* a polarized excited state.[3b,3d,3g] Several other features of the mechanism of the amide formation, however, do not conform with hypothesis based on a single mechanism for the all types of oximes and the correct mechanism and the excited species involved for each type of oxime must await further elaboration.

We wish to report here a study of the stereochemical aspects of the over-all rearrangement which had previously been disclosed by us only as a brief communication.[6] Since our publication, similar results were reported by Just and his colleagues.[7] We believe this aspect of the rearrangement is important both from the synthetic and mechanistic point of view.

We have chosen 5α- and 5β-cholestan-6-one oximes as the substrates for this study.

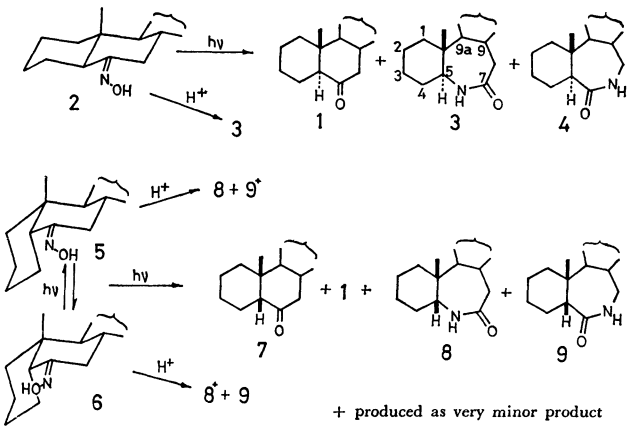
Results

Preparation of Cholestan-6-one Oximes. It was found that the oximation of 5α-cholestan-6-one **1** proceeds at an undetectable rate at room temperature. On the other hand, at reflux temperature, the oximation afforded only a single known oxime **2**.[8-10]

In contrast to the 5α-cholestan-6-one, the oximation of 5β-cholestan-6-one **7** at room temperature proceeded readily and afforded a mixture of two isomeric oximes. These oximes could be separated by preparative tlc to afford the more polar amorphous oxime **5** and the less polar crystalline oxime **6**, mp 144—146 °C, approximately in the ratio of 3 : 1. The methanolic solution of the *syn* isomer or that of the *anti* isomer was set aside for 48 hr at room temperature and examination of the solution by tlc indicated that virtually no *syn* to *anti* nor any *anti* to *syn* isomerization took place under these conditions. However, it has been found that benzene solutions of neither the *syn* isomer nor the *anti* isomer are as stable as methanolic solutions and a significant amount of *syn* isomer is produced from *anti* (and *vice versa*) after 48 hr at room temperature. The observed stability of the configuration of the oximino group in MeOH would probably be associated with the hydrogen bonding between the oximino-group and the protic solvent or with the higher dielectric constant of MeOH.[11]

The Configuration of Cholestan-6-one Oximes: The configuration of the oximino-hydroxyls of the three oximes **2**, **5** and **6** were established both by the Beckmann rearrangement and ^1H NMR spectra.

5α-Cholestan-6-one Oxime 2: In view of the fact that a single oxime is formed it would be reasonable to assume[9b] that the oximino group of **2** will possess the less sterically hindered and more stable *anti* configuration with respect to the C_5–C_6 bond since the interaction between the 4-methylene group and the OH group in both the initial adduct and the oxime in oximation reaction seems considerable.[12] The treat-



Scheme 1.

ment of **2** with PPA[13] afforded a known lactam **3**[9b] as the sole product in 65% yield. This lactam was confirmed as 6-aza-*B*-homo-5α-cholestan-7-one by ^{1}H NMR (Table 2). On this basis it was established that the configuration of the oximino group of **1** was *anti* with respect to the C_5–C_6 bond.

Hydrogens attached to a carbon α to an oximino-group are known to appear downfield,[14] in the ^{1}H NMR spectrum. The NMR spectrum of the oxime **2** exhibited a quartet centered at τ 6.69 (J=13.5 and 3.8 Hz) (Table 1) which may be assignable to a proton α to the oximino-group. This should be the 7β proton on the basis of the examination of the Dreiding model of **2** together with the coupling constants required by the model. The model of the oxime **2** reveals that the dihedral angle between the oximino π bond and the adjacent methylene group is about 74° and a π-bond contribution of approximately 0—1 Hz to the methane geminal coupling constant (12.4 Hz) is expected.[15] This affords the anticipated value of $J_{gem}\simeq 11.4$ Hz for the C-7 protons which is close to the observed geminal coupling constant. Moreover, the dihedral angle between the C_7–βH and the C_8–βH is about 55° and a small splitting of 3.8 Hz is also consistent with the above assignment.

Since the Beckmann rearrangement indicates that the configuration of the oximino-group of **2** is *anti* with respect to the C_5–C_6 bond, it is concluded that a proton H_α, *syn* to the oximino OH of saturated oximes should appear generally downfield from its *anti*-counterpart and this downfield shift of a proton is caused by the oximino OH.

*5β-Cholestan-6-one Oximes (**5** and **6**)*: The configurations of the oximino-groups of the 5β-cholestan-6-one oximes are not able to be differentiated merely from their NMR spectra. Assuming that the preferred conformations of the B-rings of **5** and **6** are chair forms, the 7β–H of the *anti* form should appear as a quartet with $J_{7\alpha,7\beta}\simeq 12$ Hz and $J_{7\beta,8\beta}\simeq 2$—3 Hz and the 5β–H of the *syn* form should also appear as a quartet with $J_{5\beta,4\beta}\simeq 2$ Hz and $J_{5\beta,4\alpha}\simeq 9$—11 Hz.

Table 1. The NMR data of oximes (τ, *J* (Hz), $CDCl_3$, TMS, 100 MHz)

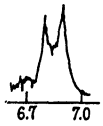
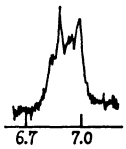
Oxime	18-H	19-H	7β-H	5β-H	
2	9.34	9.25	6.69 (q) (3.8 and 13.5)	—	
5	9.36	9.17	6.84 (d) (<1 and 10.5)	—	
6	9.36	9.17	—	6.92 (q) (4 and 11)	

Table 2. The NMR data of lactams (τ, *J* (Hz), $CDCl_3$, TMS, 100 MHz)

Lactam	18-H	19-H	8-H	5-H	NH
3	9.35	9.17	—	6.76 (q) (4.0 and 11.0)	4.48 (d) (5.5)
4	9.33	9.11	6.90 ~7.03 (m)	7.44 (q) (5.0 and 11.5)	3.96 (broad)
8	9.34	9.03	—	7.70 (d) (8.0)	3.8 (broad)
9	9.32	8.97	7.02 (b. s) (W_H=11)	—	3.85 (broad)

The NMR spectrum of **5** revealed a one proton doublet at τ 6.84 (J=10.5 Hz, Fig. in Table 1) with a small splitting of less than 1 Hz in each signal and the NMR spectrum of the oxime **6** revealed a one-proton quartet centered at τ 6.92 (J=4 Hz and 11 Hz, Fig. in Table 1). These signals are attributable to a proton α to the oximino-groups but it is not possible to distinguish between the *syn* and *anti*-isomers from the above figures of the coupling constants. Therefore, we carried out Beckmann rearrangements of the two oximes to obtain more reliable evidence for the configurations of the oximino hydroxyls of **5** and **6**.

Treatment of **5** with PPA afforded a single crystalline lactam **8** (IR), mp 95—100 °C, in 80% yield. The NMR spectrum of **8** revealed a broad one-proton doublet at τ 7.70 (J=8.0 Hz) (Table 2). Decoupling the signals at τ 8.35 caused a collapse of the doublet at τ 7.70 into a broad singlet. These data are consistent with those required for the 5β-proton of 6-aza-*B*-homo-5β-cholestan-7-one.

Beckmann rearrangement of **6** using the same proced ure used for **5** afforded an amorphous compound **9**, $C_{27}H_{47}ON$, isomeric with **8** in 90% yield. This was a lactam (IR) and the NMR spectrum of **9** (Table 2) was in agreement with the 7-aza-*B*-homo-5β-cholestan-6-one structure.

It has frequently been pointed out that care must be exercised in relating the stereochemistry of oximes with the lactams derived from the Beckmann rearrangement since *syn anti* isomerization is catalyzed by the reagents used for the Beckmann rearrangement[16,17] and the position of and rate of attaining the *syn* to *anti* equilibrium are temperature dependent.

The distinction among three lactams **3**, **8** and **9** could be readily made with the aid of the different chemical shifts of the 10β-methyl protons in their NMR spectra. Examination of the NMR spectrum of the crude product (see Fig. 1 in Experimental) from the Beckmann rearrangement of **5** indicated the presence of a small amount of **9** (revealed by a pair of weak signals at τ 8.97 and τ 9.32) and the NMR spectrum of the crude product from **6** (see Fig. 2 in Experimental) showed the presence of a small amount of **8** (revealed by a pair of weak signals at τ 9.03 and τ 9.34). The appearance of these signals in the products indicated that the equilibration from *syn* to *anti* or from *anti* to *syn* took place to some extent prior to the Beckmann rearrangement under our experimental conditions. However, it is apparent that the rearrangement of either oxime **5** or **6** is faster than the equilibration of these isomers.

On the basis of these results we concluded that the configurations of the oximino-hydroxyl of the oxime **5** and the oxime **6** are respectively *anti* and *syn* with respect to the C_5–C_6 bond.

Photo-Beckmann Rearrangement of Cholestan-6-one Oximes: The photo-Beckmann rearrangements of all three oximes **2**, **5**, and **6** were carried out in methanolic solution under a N_2 atmosphere at room temperature using a 15-W low pressure Hg arc lamp dipped in the solution. The progress of the photolysis was traced by tlc.

*Photolysis of 5α-Cholestan-6-one Oxime **2***: The photolysis of **2** in dry methanol (3.56×10^{-3} M) for 27 hr resulted in partial transformation of the oxime. Since further irradiation was found to cause secondary photochemical decomposition of the initial products the irradiation was stopped at this stage. Examination of the product by tlc revealed that several products were produced but these were able to be divided into four fractions by preparative tlc (see Experimental). The major part of the least polar fraction was found to be 5α-cholestan-6-one (8% as a ketone) by examination of its spectra. The second least polar fraction (6% as an oxime) was found to be the crude oxime. The third least polar fraction was further separated into two fractions by preparative tlc, using a different solvent system. Of these, the less polar fraction (11% as a lactam) afforded a compound **4** which melted at 110—114 °C after recrystallization from ethanol and the more polar fraction (15% as a lactam) afforded a lactam which was identical with the lactam **3**. Product **4** was also a lactam with the molecular formula $C_{27}H_{47}ON$ but was not identical with either the lactam **8** or the lactam **9** and the NMR spectrum of **4** (Table 2) was consistent with the 7-aza-*B*-homo-5α-cholestan-6-one structure. The 10β-Me protons appeared at τ 9.11 which is 0.06 ppm downfield from those of the isomeric 6-aza-lactam **3**.

*Photolyses of 5β-Cholestan-6-one Oximes **5** and **6***: The *syn*-oxime **6** in dry methanol (5.0×10^{-3} M) was then photolyzed and examination of the progress of the photolysis by tlc indicated that a rapid photostationary state between the *syn* and *anti* forms was established. Tlc examination of the reaction mixture after 3 hr revealed the presence of nearly equal amounts of *syn* and *anti* forms in the solution. The photolysis was stopped after 12 hr irradiation. The reaction mixture was analyzed by preparative tlc as in the case of 5α-cholestan-6-one oxime to afford two gummy ketone fractions, which yielded crystalline 5α-cholestan-6-one (3%) and crystalline 5β-cholestan-6-one (7%), the recovered oxime, and a lactam fraction in order of increasing polarity.

The NMR spectrum of the lactam fraction revealed the presence of sharp peaks at τ 8.97 and τ 9.03. This immediately suggested the presence of 6-aza-*B*-homo-5β-cholestan-7-one and 7-aza-*B*-homo-5β-cholestan-6-one. Preparative tlc of this mixture afforded the lactam **8** (24%) and the lactam **9** (17%). In addition, a fraction considerably less polar than the ketones was also obtained. Judged by the spectra this gum was 5,6-seco-cholestan-6-oic acid methyl ester derived from α-cleavage of the 6-ketone.[18] Nearly the same results were obtained when the photolysis was started with the anti-oxime. The results in this case were as follows; 5α-cholestan-6-one (3%), 5β-cholestan-6-one (5%), 6-aza-*B*-homo-5β-cholestan-7-one (30%) and 7-aza-*B*-homo-cholestan-6-one (12%).

Throughout these photolyses, it was found that the disappearance of the oxime and the appearance of the lactams were faster in the 5β-series than the 5α-series and the yields of lactams were higher in the 5β-series although no quantitative studies were undertaken.

Photo-Beckmann Rearrangement of 5β-Cholestan-6-one Oxime in the Presence of Oxygen: In order to obtain some information on the properties of the excited oxaziridine

from which the observed lactams are formed, the photolysis was carried out in the presence of oxygen. Oxygen is believed to remove triplet state species by both chemical and physical quenching.[19] A mixture of *syn* and *anti* 5β-oximes was chosen as the substrate, since, when compared with the 5α-oxime, the results of the reaction with this substrate were found to contain less by-products.

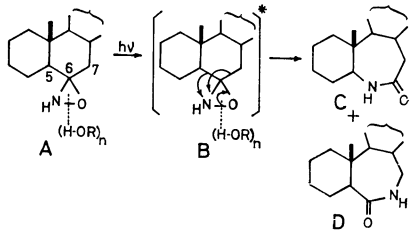
The photolysis of a methanolic solution of 5β-oximes (3.7×10^{-3} M) in the presence of O_2 afforded crystalline 5α-ketone (1%), crystalline 5β-ketone (7%), 6-aza-*B*-homo-5β-cholestan-7-one (16%, amount eluted from tlc) and 7-aza-*B*-homo-5β-cholestan-6-one (14%, amount eluted from tlc) and 4% of the starting oximes were recovered.

Discussion

In the foregoing part we have shown that in the photo-Beckmann rearrangements of 5α- and 5β-cholestan-6-one oximes, when we start off from 5β-oxime, lactams retaining the 5β-configuration are produced but from 5α-epimer only those having the 5α-configuration are formed. Through these experiments, the lactam part of the products was very carefully examined but we were unable to detect any lactams in which the initial configuration at C_α to the oximino-group of the starting oximes was reversed. It should also be noted that in the present results two isomeric lactams due to the migration of the tri-substituted carbon (C_5) and the di-substituted carbon (C_7) were produced in each case and the relative amounts of two lactams were not significantly different in the photolysis of **2** and in the photolysis of **5** or **6**, although in all the photolyses some preference for the migration of tri-substituted carbon over that of disubstituted carbon was shown.

The present results suggest that the reorganization from the oxaziridine intermediate to lactams occurs in a fully concerted manner (*e.g.*, A→B→C and D). At the time of our preliminary publication, we suggested that this mechanistic pathway might operate generally for all aliphatic ketones and aldehydes. However, we subsequently found[20] an exception to that rule. We found that the photolysis of androsterone oxime afforded an epimeric pair of lactams at the 13–Me, although the yields were very poor.

In order to get a general and consistent picture of the mechanistic pathway in regard to the migration step of the saturated oximes, we considered two possibilities for the mode of formation of a lactam from oxaziridine. The first was the migration through the intervention of an ionic or radical intermediate[20] in which bond between oxaziridine ring carbon and the migrating α-carbon (*e.g.*, C_5–C_6 bond or C_6–C_7 bond in A) is cleaved. According to this mechanistic view the present results with cholestan-6-one oxime might be rationalized by considering the involvement of a similar ion pair or radical pair intermediate which is configurationally stable. However, this unifying mechanism for all the saturated ketone oximes fails to interpret the small difference in migratory aptitude between C_5 and C_7 in the present case and in several other cases, *i.e.*, 3α,5-cyclo-5α-cholestan-6-one oxime,[3f] unsymmetrically α-substituted cyclohexanone oxime[7] and norcamphor oxime.[3d] These observation would be better explained if we assumed the formation of lactams *via* a concerted breakdown of the oxaziridines (Scheme 2).



Scheme 2.

This would mean that a dual mechanism is operative in the saturated oximes, depending upon their structural features in the immediate environment of the relevant oximino group. The oxime which can afford a stable ionic or radical species by cleavage would be able to rearrange through an intermediate in which the migrating group becomes free of the migration terminus. The rearrangement of the oximes of androsterone and 13α-androsterone perhaps fall in this category. On the other hand, oximes of cholestan-6-ones, menthone, isomenthone and norcamphor bear the tri-substituted migrating carbon within the framework of the six-membered ring and oxaziridines formed from these oximes would rearrange to afford lactams *via* a concerted breakdown of the oxaziridines.

No meaningful difference between the *syn*-oxime and the *anti*-oxime of 5β-cholestan-6-one was observed with respect to the photolysis products. This shows a fast establishment of photostationary states between *syn* and *anti* prior to substantial progress of the photorearrangement. On the other hand, we could not detect even a trace of the *syn*-form of 5α-cholestan-6-one oxime during the photolysis of *anti* 5α-cholestan-6-one oxime. This difference between 5α-6-one oxime and 5β-6-one oxime is readily understandable since it is inferred that, in the 5α-steroid-6-one oximes, the energy difference between the *syn* form and the *anti* form is large and the thermal relaxation from photogenerated *syn* to *anti* should be very fast. In contrast, in the 5β-steroid-6-one oximes, the energy difference between *syn* and *anti* is not as large and both forms are isolatable species at room temperature.

With regard to the properties of the excited oxaziridine, the result of the photolysis of 5β-cholestan-6-one oxime in the presence of oxygen would imply that a) no radical intermediate would be involved in the present photo-Beckmann rearrangement and b) the formation of lactams from the oxaziridine takes place in its singlet state. The former result is contrasted with the reported case of adamantanone oxime in which the intervention of a radical intermediate at some stage was inferred.[3c] The latter results differ from the case of styrylketone oximes in which a triplet state of protonated oxaziridine rearranges to afford lactams. All the present results of the photolysis are consistent with our original proposal that lactam is formed *via* a concerted breakdown of the oxaziridine.[6]

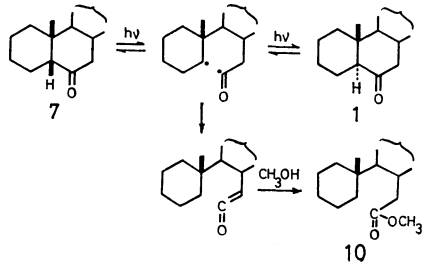
During the photo-isomerization experiments it was observed that the rate of disappearance of the oxime **5** or **6** was considerably faster than that of the oxime **2** and the yields of lactams were much higher than those of the oxime **2**. The faster rates observed in A/B *cis* oxime **5** or **6**, when compared with A/B *trans* oxime **2**, could be mainly attributed to the relief of steric compression due to nonbonded interactions of 2α- and 4α-axial hydrogens with 7α- and 9α-axial hydrogens in going from oxaziridine intermediates formed from the oxime **5** or **6** to the lactam **8** and **9**. With regard to the role of protic solvents in the rearrangement, in all the examples of photo-Beckmann rearrangements described, protic media or organic acids as solvents are reported to be essential.

Mukai and co-workers recently proposed that the excited triplet species of a protonated oxaziridine is involved in the formation of the corresponding lactams from styryl ketone oxime.

In our case the role of methanol would be associated with influencing the rate or efficiency of an electronic energy transfer process, by making hydrogen bonds between the unshared electrons of excited oxaziridines and methanol molecule(s), in the reorganization from excited oxaziridines to lactams. When the protic solvents are absent the excited singlet oxaziridines would lose their singlet energy by various physical deactivation processes prior to their rearrangement to lactams.

The isolation of 5α-cholestan-6-one together with 5β-cholestan-6-one in the photolysis of the 5β-cholestan-6-one oximes would demand an explanation. It was rather difficult to explain the isolation of these isomeric ketones in terms of the initial isomerization of 5β-oximes into 5α-oxime through an α-cleavage-recombination process followed by the decomposition of these oximes into the 5α- and 5β-ketones. The isolation of of both 5α and 5β ketones could be better explained if we assumed an initial formation of 5β-cholestan-6-one either via collision between ground state oxazirdine molecules[3g] or via other routes, including a photochemical one followed by isomerization into the 5α-one via a photochemical α-cleavage-recombination sequence (Scheme 3). This is supported by the results of the separate irradiation of 5β-cholestan-6-one in dry methanol containing dioxane. The solution in a quarz vessel was irradiated for 3 hr with a 15-W low pressure Hg arc lamp. Separation of the product by preparative tlc afforded 5α-ketone (13%), and 5,6-seco-cholestan-6-oic acid methyl ester **10** (14%), together with the original 5β-ketone (44%).

This isomerization is the second case of a photochemical isomerization of a steroidal ketone by an α-cleavage-recombination sequence. The first case of isomerization of steroidal ketone was reported by Butenandt *et al.*,[21] who found that steroidal 17-ketones epimerize at C-13,[22] and later the reversibility of the process was clarified by Schaffner.[23]



Scheme 3.

Experimental

All mps were determined with a Yanagimoto-type hot stage and are uncorrected. Unless stated otherwise, IR spectra were determined in Nujol using a JASCO model IR-E spectrophotometer. The NMR spectrum of oxime **2** was measured on a JEOLCO-JNM-PS-100 high resolution NMR spectrometer in $CDCl_3$ solution using TMS as an internal reference. Other NMR spectra were taken at Japan Electric & Varian Ltd. Wako gel B-5 was used for preparative tlc.

5α-Cholestan-6-one Oxime 2: This was prepared according to the literature procedure. mp 197—201 °C (lit, mp 204—206 °C,[10] mp 195 °C,[8] mp 196—198 °C,[9a] mp 197—198 °C[9b]); IR: 3272 cm^{-1} (OH), 1669 cm^{-1} (C=N), 896, 923, 947 cm^{-1}.

Beckmann Rearrangement of 5α-Cholestan 6-one Oxime 2: 5α-Oxime (94 mg) was added to PPA (Koso Chemical Co., Ltd. Tokyo) (1 g) kept at 100 °C. The reaction mixture was heated at 110—115 °C for 15 min. After being cooled the reaction mixture was neutralized with 10% Na_2CO_3 solution (10 ml) and extracted with ether. The ethereal solution was worked up as usual. Removal of the solvent left a residue which was recrystallized from acetone to yield 61 mg of lactam **3**. mp 173—175 °C (lit,[9b] mp 175—176 °C); IR: 1669 cm^{-1} (lactam C=O), 3230 cm^{-1}, 3090 cm^{-1} (lactam NH); Mass: *m/e* 401 (M^+).

Anti-5β-cholestan-6-one Oxime 5 and syn-5β-Cholestan-6-one Oxime 6: 5β-Cholestan-6-one (320 mg), hydroxylamine hydrochloride (450 mg) and NaOAc (320 mg) in 95% aqueous EtOH (30 ml) were stirred for 2 hr at room temperature. The solvent was removed under reduced pressure and the residue was extracted with ether. Usual work-up of the ethereal solution afforded an amorphous residue (350 mg). Preparative tlc of the residue (305 mg) using benzene as the solvent gave two fractions. The less polar fraction (120 mg) was recrystallized from acetone yielding 63 mg of *syn*-oxime **6**. mp 144—146 °C. (Found: C, 80.82; H, 11.85; N, 3.66%; Calcd for $C_{27}H_{47}ON$: C, 80.73; H, 11.80; N, 3.49%) Mass: *m/e* 401 (M^+); IR: 3276 cm^{-1} (OH), 1656 cm^{-1} (C=N), 925, 942, 954 cm^{-1}. The more polar fraction (249 mg) which was contaminated with a small amount of the less polar fraction was purified twice by preparative tlc ($CHCl_3$/ether—4/1 in vol.) to yield 68 mg of *syn*-oxime **6** and amorphous *anti*-oxime **5**. It was difficult to obtain the *anti*-oxime completely free from the *syn*-form, since during elution with acetone and $CHCl_3$ in the preparative tlc **5** seemed to undergo slight *anti-syn* isomerization. Analysis of *anti-oxime* **5**: (Found: C, 80.82; H, 11.77; N, 3.44%; calcd for $C_{27}H_{47}ON$: C, 80.73; H, 11.80; N, 3.49%).

Beckmann Rearrangement of syn-5β-Cholestan-6-one Oxime 6: Freshly prepared **6** (26 mg) was added to a small amount of PPA kept at 90 °C. The mixture was stirred for 5 min at that temperature and then cooled by ice. The reaction mixture was neutralized with 10% aqueous Na_2CO_3 solution and the solution was extracted twice with ether. Usual work-up of the ethereal solution left amorphous compound **9** (20 mg). The Me proton part of the NMR spectrum of this is shown in Fig. 2. The lactam **8** was removed by preparative tlc. (Found: C, 79.36; H, 11.57; N, 3.22%; Calcd for $C_{27}H_{47}ON$: C, 80.73; H, 11.80; N, 3.49%);

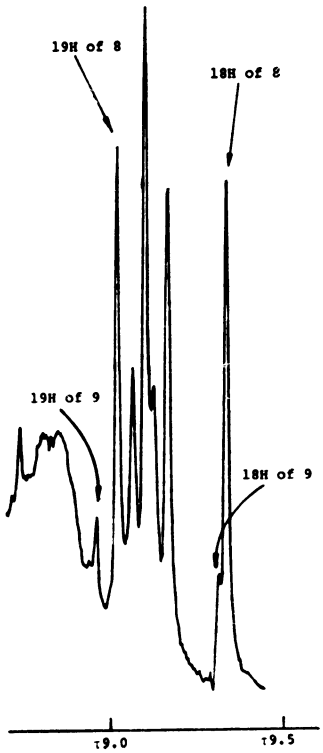


Fig. 1. NMR spectrum of crude **8**.

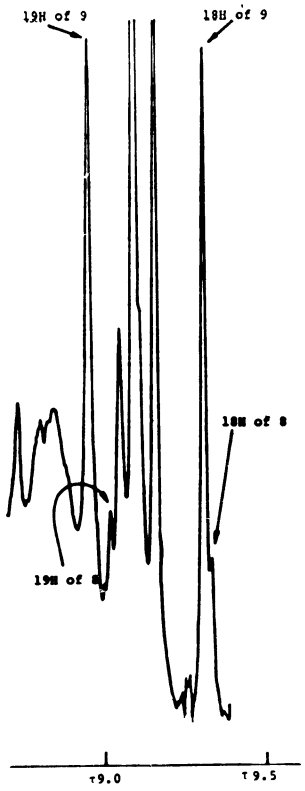


Fig. 2. NMR spectrum of crude **9**.

IR: ($CHCl_3$) 1643 cm^{-1} (lactam C=O), 3210 cm^{-1}, 3410 cm^{-1} (lactam NH).

Beckmann Rearrangement of anti-*5β-Cholestan-6-one Oxime 5*: Compound **5** (20 mg) was added to a few drops of PPA kept at 90 °C. The mixture was stirred for 5 min at that temperature. After being cooled by ice the reaction mixture was neutralized with 10% Na_2CO_3 solution and the solution was extracted twice with ether. Work up of the ethereal solution in the usual manner left 18 mg of an oily residue. The Me proton part of the NMR spectrum of this is shown in Fig. 1. This residue was purified by preparative tlc and then recrystallized from EtOH to yield lactam **8**. mp 76—80 °C.* (Found: C, 80.27; H, 11.94; N, 3.29%; Calcd for $C_{27}H_{47}ON$: C, 80.73; H, 11.80; N, 3.49%); IR: ($CHCl_3$) 1645 cm^{-1} (lactam C=O), 3390 cm^{-1} (lactam NH).

Photo-Beckmann Rearrangement of 5α-Cholestan-6-one Oxime 2: Oxime **2** (500 mg) in dry MeOH (350 ml) was irradiated for 23 hr. Examination of the reaction products by tlc revealed the presence of four major spots and these were separated by preparative tlc to afford 4 fractions A, B, C, and and D ($CHCl_3$/ether; 10/1 in vol.) in order of increasing polarities. The amount of fraction A was 40 mg and the major part of this was found to be 5α-cholestan-6-one. Recrystallization of fraction B (28 mg) from acetone afforded only 4 mg of the starting oxime. Fraction C (150 mg) was found to be a mixture of two compounds and this fraction gave two spots on a tlc with a mixed solvent of equal volumes of $CHCl_3$ and ether. Preparative tlc of the mixture with this solvent system afforded two compounds. The less polar and amorphous substance (53 mg) afforded 40 mg of crystals of 7-aza-*B*-homo-5α-cholestan-6-one. mp 110—114 °C. (Found: C, 79.12; H, 11.58; N, 3.77%; Calcd for $C_{27}H_{47}ON$: C, 80.73; H, 11.80; N, 3.49%); IR: 1656 cm^{-1} (lactam C=O), 3270 cm^{-1}, 3530 cm^{-1} (lactam NH). The more polar and crystalline compound (75 mg) melted at 174—179 °C and was identical with 6-aza-*B*-homo-5α-cholestan-7-one obtained from a Beckmann rearrangement of oxime **2**. Fraction D (80 mg) did not contain any lactam and was not examined further.

Photo-Beckmann Rearrangement of syn-*5β-Cholestan-6-one Oxime 6*: Oxime ***6*** (500 mg) in dry MeOH (250 ml) was irradiated for 12 hr. After removal of the solvent under reduced pressure, tlc of the residue revealed the formation of several products. However, there were two major spots. Preparative tlc ($CHCl_3$/ether; 4/1) afforded four fractions A, B, C and D in order of increasing polarity. Fraction A (198 mg) was again submitted to preparative tlc (benzene) and afforded 4 fractions. The NMR spectrum of the least polar fraction showed that this fraction was most probably 5, 6-seco ester. The polarities of the second and the third least polar fractions were close together and the second least polar fraction (30 mg) afforded 15 mg of crystals which were identical with 5α-cholestan-6-one. The third least polar fraction (100 mg) afforded 5β-cholestan-6-one (34 mg).

Fraction B was mainly crude starting material. The amorphous fraction C (229 mg) was again submitted to preparative tlc ($CHCl_3$/ether; 4/1) and afforded 120 mg of lactam **8** and 83 mg of lactam **9**. The most polar fraction D did not contain any lactams and was not examined further.

Photo-Beckmann Rearrangement of anti-*5β-cholestan-6-one Oxime 5*: Freshly prepared anti-5β-cholestan-6-one oxime (500 mg) in dry MeOH (300 ml) was photolyzed in the same manner as the *syn*-isomer. After 11 hr examination of the products by tlc revealed that nearly all the starting oxime had disappeared. After removal of the solvent the residue was extracted with ether. The ethereal solution was washed and dried as usual. The residue was separated by preparative tlc. Using the procedure employed for the *syn*-oxime, pure 5α-cholestan-6-one (13 mg) was obtained from 20 mg of crude fraction. In addition 22 mg of pure 5β-cholestan-6-one was obtained from 30 mg of crude 5β-compound. From the lactam part, 150 mg of lactam **8**

* Recorded previously as mp 95—100 °C.

and 90 mg of crude lactam **9** were obtained and the latter was recrystallized from ethanol to yield 59 mg of pure compound.

*The Photo-Beckmann Rearrangement of 5β-Cholestan-6-one Oxime, **5** and **6**, in the Presence of Oxygen*: A mixture of *syn* and *anti* isomers of 5β-cholestan-6-one oxime (420 mg) in dry methanol (280 ml) was photolyzed for 17.5 hr while dry oxygen was bubbled slowly. After removal of the solvent under reduced pressure the residue was dissolved in $CHCl_3$ and the solution was washed twice with H_2O, dried and evaporated. Another 300 mg of oxime in dry methanol (200 ml) was photolyzed under comparable condition and the solution was treated as above. The residues from these two photolyses were submitted to preparative tlc. The first preparative tlc was carried out with a mixed solvent of $CHCl_3$ and ether (4/1 in vol.). This enabled us to separate the mixture into two major fractions, a less polar fraction A (300 mg) and a more polar fraction B (300 mg). Between these two major bands on the tlc plate, several minor products were observed but these did not contain any lactams and were not examined further.

Fraction A was again submitted to preparative tlc with benzene and afforded four fractions A_1, A_2, A_3 and A_4 in order of increasing polarity. Fraction A_1 (120 mg) was amorphous and it was found to be 5, 6-seco-cholestan-6-oic acid methyl ester on the basis of its IR spectrum. The crystalline fraction A_2 (30 mg) was recrystallized from acetone to yield 5 mg of pure 5α-cholestan-6-one. The crystalline fraction A_3 (70 mg) was recrystallized from acetone to yield 30 mg of pure 5β-cholestan-6-one. The most polar fraction A_4 (30 mg) was found to be a mixture of the starting oximes.

Fraction B was also submitted to further preparative tlc with a mixed solvent of $CHCl_3$ and ether (5/1). Development was carried out twice. This afforded 70 mg of lactam **8** and 60 mg of lactam **9**.

The Photo-isomerization of 5β-Cholestan-6-one: 5β-Cholestan-6-one (80 mg) in dry methanol (25 ml) and dry dioxane (5 ml) was irradiated with a 15-W low pressure Hg arc lamp under an argon atmosphere. After 3 hr irradiation, examination of the solution revealed the formation of a fair amount of 5α-cholestan-6-one, which was less polar than 5β-cholestan-6-one, and a material considerably less polar than these ketones (R_f=0.88, benzene solvent). The solvent was then removed and the residue was submitted to preparative tlc and afforded a gum (16 mg), 5α-cholestan-6-one (10 mg) and 5β-cholestan-6-one (35 mg). The IR spectrum of the gum revealed it to be an ester (ester C=O, 1740 cm^{-1}, $CHCl_3$). The NMR spectrum showed a three-proton singlet at τ 6.34 ($COOCH_3$) two three proton singlets at τ 9.08 (19-H) and τ 9.32 (18-H) and a two-proton triplet at τ 7.44 ($-CH_2$ adjacent to $COOCH_3$). On the basis of these data, the gum should be 5,6-seco-cholestan-6-oic acid methyl ester.

The signals due to the 10β-methyls and the 13β-methyls of the 5α-isomer[24] and the 5β-isomer in the NMR spectra appeared at the following positions:

	19-H (τ)	18-H (τ)
5α-isomer ($CDCl_3$)	9.27	9.34
(CCl_4)	9.30	9.34
5β-isomer ($CDCl_3$)	9.17	9.35

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