Photoinduced Molecular Transformations. Part 149.[1] Stereospecific Photoadditions and Photorearrangements of the Oximes of Some Steroidal α,β-Unsaturated Cyclic Ketones and Their Deuterio Derivatives

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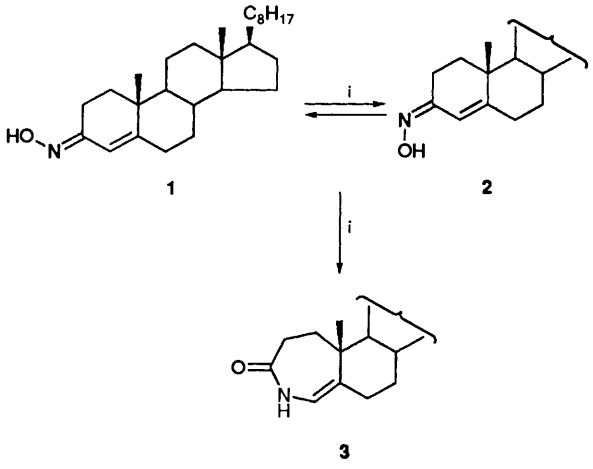
The photolysis of several steroidal cyclic α,β-unsaturated ketone oximes as model substrates in methanol showed that these excited oximes react in either one of two ways, depending upon their structural features. Thus, while the excited oximes, such as those of 5α-cholest-4-en-6-one and the 5-en-4-one oxime, having their C=C bond at their ring junction, lead to the corresponding enamides (15–40%) arising from a photorearrangement, the excited oximes, having their C=C bond at their non-ring junction (such as the oximes of 5α-cholest-2-en-1-one and the 3-en-2-one), principally lead to photoisomerization to form transient *trans* geometrical isomers from which stereospecific additions of proton or methanol to their *trans* C=C bond take place.

The irradiation of (*E*)-5α-cholest-2-en-1-one oxime in benzene–acetic acid (94:6) gave 1-aza-4a-homo-5a-cholest-3-en-2-one arising from a regioselective photorearrangement, while irradiation of the oxime in methanol gave 3β-methoxy-5α-cholestan-1-one arising from photoaddition in low yield. Thus, organic acid accelerates the photorearrangement to the lactam in competition to the α-fission.

In contrast to these photochemical transformations, ground-state Beckmann rearrangements of (*E*)-cholest-4-en-6-one oxime and (*E*)-cholest-5-en-4-one oxime, having their C=C bond at their ring junction, under the standard conditions gave the corresponding cyclic enamines. Treatment of (*E*)-5α-cholest-2-en-1-one oxime under the standard conditions of the Beckmann rearrangement, however, gave an unsaturated nitrile as well as the corresponding enamide. The regioselectivities of the formation of cyclic enamine and enamides in the photo- and nonphoto-rearrangements, as well as the structure–photoproduct correlation of the oximes, are discussed.

Our previous study concerning photoreactions of the oximes of α,β-unsaturated cyclic ketones using a number of steroidal oximes as a model substrate disclosed that two principal photoinduced reactions, a photorearrangement to the corresponding lactams and *cis*-to-*trans* isomerization of the α,β-unsaturated double bond, take place competitively in protic solvents.[2–5] Thus, while the photoreaction of (*E*)- and (*Z*)-cholest-4-en-3-one oximes **1** and **2** in methanol gave an enamine **3** as the exclusive lactam arising from a regiospecific photorearrangement[2] (Scheme 1), irradiation of 5α-cholest-1-en-3-one oxime **4** and its 5β-isomer **9** in methanol did not give any unsaturated lactams that arise from the photo-Beckmann-type rearrangement, but gave, respectively, 1β-methoxy-5α-cholestan-3-one oxime **5** (X = H) and its 1α,5β-isomer **10** (X = H),

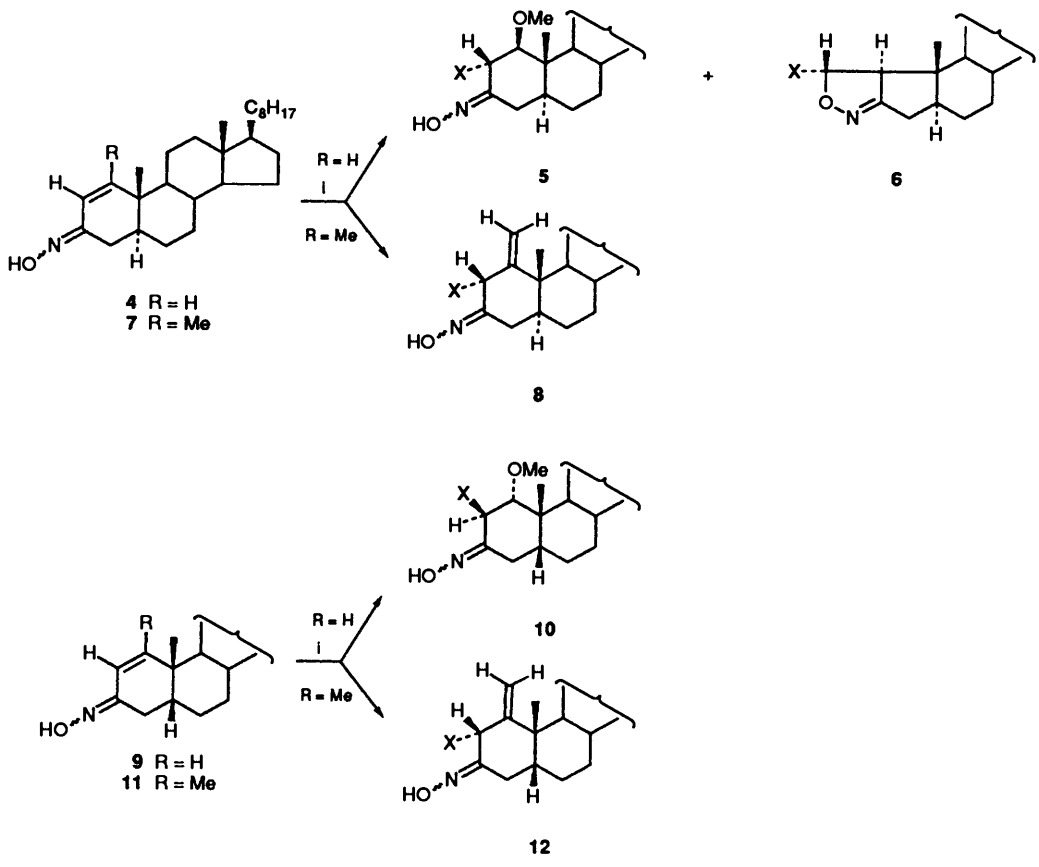


Scheme 1 *Reagents and conditions:* i, MeOH, *hv*

arising from a stereospecific *syn* addition of methanol to the photogenerated strained *trans* C=C bond of the enone oximes from their less hindered side (Scheme 2).[3,5] An isoxazole **6** (X = H) arising from a skeletal photorearrangement was the by-product in the photoreaction of the oxime **4** (Scheme 2). Deuterium-labelling studies of these processes established that the addition of methanol to the *trans* C=C bond of the oximes and the photorearrangement to the isoxazole **6** are stereospecific; the hydroxy-group protons of methanol in the photolysis of 5α-oxime **4** is attached to the 2α-position (X in **6**) of photoproduct **6**, while a proton of methanol in the photolysis of 5β-oxime **9** is attached to the 2β-position (X in **10**) of adduct **10**.

Irradiation of 1-methyl-5α-cholest-1-en-3-one oxime **7** and its 5β-isomer **11** in methanol, on the other hand, gave almost exclusively 1-methylene-5α-cholestan-3-one oxime **8** (X = H) and its 5β-isomer **12** (X = H), respectively, arising from a photodeconjugation of the α,β-unsaturated enone oximes into the β,γ-enone oximes.[4,5] Deuterium-labelling studies again established the stereospecific incorporation of the hydroxylic protons of methanol to products **8** and **12** in these photoreactions; the hydroxylic proton of the methanol is attached to the 2α-position of product **8** in the photolysis of the 5α-isomer, while the hydroxylic proton is incorporated into the 2β-position of product **12**.

Of these behaviours of steroidal α,β-unsaturated oximes towards light irradiation, it was especially notable that excited steroidal α,β-unsaturated oximes such as cholest-4-en-3-one oxime **1**[2] gave exclusively an enamine lactam **3** which is inaccessible by thermal Beckmann rearrangement. Thus, we felt that further elaboration of some fundamental behaviour of excited steroidal oximes is worthwhile from the viewpoint of the synthesis of azasteroids to which many biologically active molecules belong.[6,7]



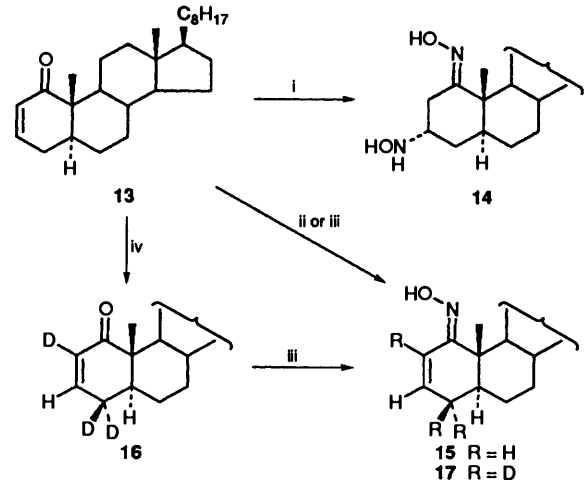
Scheme 2 *Reagents and conditions:* i, MeOH, *hv*

We have thus examined the photoreactions of oximes **15**, **19**, **20**, **26**, **32** and **34** of cholest-2-en-1-one, cholest-3-en-2-one, cholest-2-en-4-one, cholest-4-en-6-one and cholest-5-en-4-one and the deuteriated derivatives **17** and **27**, in order to obtain additional information concerning the effects of altering the structure of the starting oximes. The principal structural features of these oxime substrates are that: (a) the carbon–carbon double bond of oximes **15**, **19** **20** and **26** is located at their non-ring junction in ring A, (b) oxime **15** has a tertiary carbon centre adjacent to the hydroxyimino group and (c) the carbon–carbon double bond of oximes **32** and **34** is located at their ring junction.

Results

Preparation of (E)-5α-*Cholest-2-en-1-one Oxime* **15**, (E)- *and* (Z)-5α-*Cholest-3-en-2-one Oximes* **19** *and* **20**, (E)-5α-*Cholest-2-en-4-one Oxime* **26** *and their Deuterio Derivatives* **17** *and* **27**, (E)-*Cholest-4-en-6-one Oxime* **32**, *and* (E)-*Cholest-5-en-4-one Oxime* **34**.—The title steroidal oximes **15**, **19**, **20**, **26**, **32** and **34** used as substrates in the present photoreactions were synthesized as outlined in Schemes 3–7. Oximation of 5α-cholest-2-en-1-one **13**,[8–10] prepared from 1α,2α-epoxy-5α-cholestan-3-one by a Wharton reaction,[7] in a mixed solvent of ethanol and water gave 3α-hydroxyamino-5α-cholestan-1-one oxime **14** exclusively. A conjugate addition of hydroxylamine to the α,β-unsaturated double bond of enone **13** apparently takes place in preference to an addition to the carbonyl group under these conditions. The oximation of the enone **13** in ethanol in the absence of water under reflux gave oxime **15** in poor yield. Finally, oximation of the enone in pyridine at room temperature gave oxime **15** in high yield as the exclusive product.

The deuteriation of enone **13** with methan[^{2}H]ol and sodium in diethyl ether under reflux by the standard method gave 2,4,4-

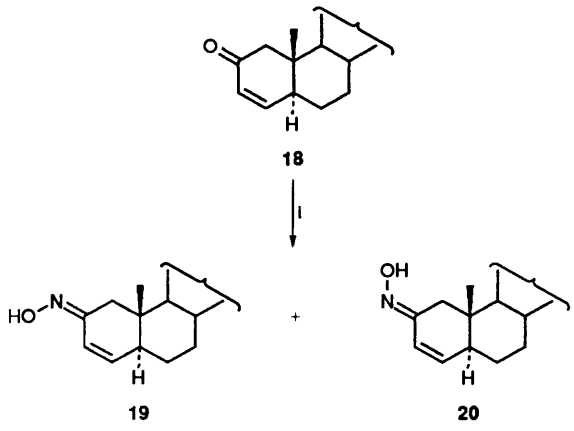


Scheme 3 *Reagents and conditions:* i, NH_2OH·HCl–NaOAc·$3H_2O$–EtOH, reflux; ii, NH_2OH·HCl–NaOAc·$3H_2O$–EtOH, room temp.; iii, NH_2OH·HCl–pyridine, room temp.; iv, MeOD–Et_2O–Na, reflux

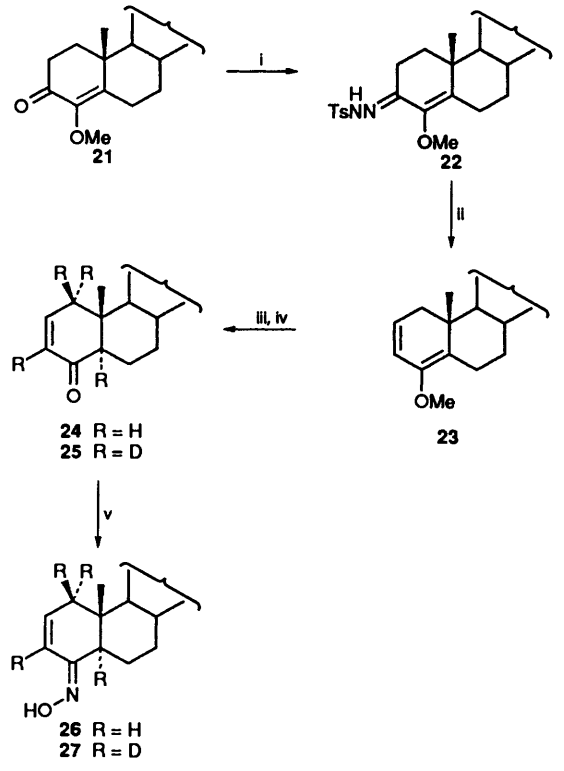
trideuterio-5α-cholest-2-en-1-one **16**. The oximation of trideuterio enone **16** with hydroxylamine hydrochloride in pyridine gave (*E*)-trideuterio enone oxime **17**.

Oximation of 5α-cholest-3-en-2-one **18** (prepared according to the method of Nakano and colleagues[11]) by the standard method gave a 1 : 1 mixture of the corresponding (*E*)- and (*Z*)-oximes **19** and **20** (Scheme 4). Attempted preparation of a trideuterio derivative of the enone **18** by the standard procedure was unsuccessful.

Finally, 5α-cholest-2-en-4-one **24** was prepared from 4-methoxycholest-4-en-3-one **21** according to the method of Patel and Reusch,[12] as outlined in Scheme 5. Thus, application of the



Scheme 4 *Reagents and conditions:* i, NH_2OH·HCl–NaOAc·$3H_2O$–EtOH, room temp.

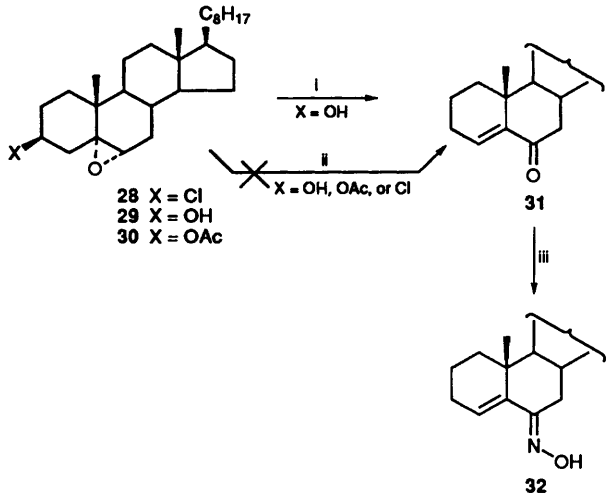


Scheme 5 *Reagents and conditions:* i, $TsNHNH_2$–EtOH, reflux; ii, MeLi–Et_2O, reflux; iii, SiO_2H^+; iv, NaOMe–MeOD, reflux; v, NH_2OH·HCl–NaOAc·$3H_2O$–EtOH, room temp.

Shapiro reaction to 4-methoxycholest-4-en-3-one **21**[13] gave 4-methoxycholesta-2,4-diene **23** *via* a tosylhydrazone **22**. Spontaneous acidic hydrolysis of the diene **23** over silica gel during preparative TLC (PLC) separation gave enone **24**.[14] Oximation of enone **24** by the standard method gave the corresponding (*E*)-oxime **26**.

The deuteriation of enone **24** with methan[^{2}H]ol and sodium in diethyl ether under reflux by the standard method gave 1,1,3,5-tetradeuterio-5α-cholest-2-en-4-one **25**. Oximation of deuterio enone **25** gave the corresponding oxime **27**.

The preparation of two oximes, **32** and **34**, of cholest-4-en-6-one **31** and cholest-5-en-4-one **33** has already been recorded in the literature.[15] The preparation of one of the parent enones, cholest-4-en-6-one **31**, first prepared by Reich *et al.*,[16] has subsequently been reported by four groups of workers.[17] The latest method is that by Ahmad *et al.*, reported in 1985.[17d] They reported that this enone **31** can be prepared in excellent yields by reaction of 3β-chloro-, 3β-hydroxy-, or 3β-acetoxy-5,6α-epoxy-5α-cholestane (**28**, **29** or **30**), with phenyl isocyanate in dimethylformamide (DMF) in the presence of LiCl as a catalyst (Scheme 6).[17d] We, however, failed to obtain this enone in our

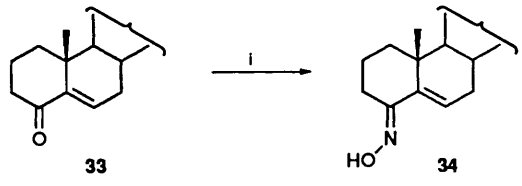


Scheme 6 *Reagents and conditions:* i, $MgBr_2$·$3Et_2O$–Et_2O–benzene, reflux; ii, PhNCS–LiCl–DMF, reflux; iii, NH_2OH·HCl–pyridine, room temp.

several repetitions of their work. The reason for this failure has not yet been clarified. We found that this enone was most conveniently prepared by treatment of 5,6-epoxy-5α-cholestan-3β-ol **29** with $MgBr_2$ according to a procedure reported by Turner.[17a]

Cholest-5-en-4-one **33**[18] in the present experiment was prepared according to a method reported by Shoppee and colleagues[17b] from cholest-4-ene in 5 steps.

Oximation of these enones, **31** and **33**, by the standard method gave the corresponding oximes, **32** and **34**[15] (Schemes 6 and 7). The ^{1}H NMR spectrum of cholest-4-en-6-one oxime **32**



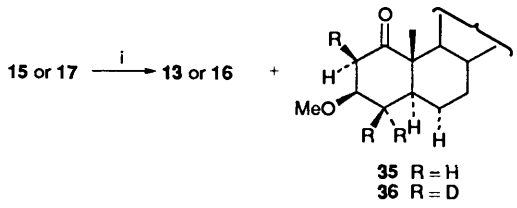
Scheme 7 *Reagents and conditions:* i, NH_2OH·HCl–pyridine, room temp.

exhibited two doublet signals, at δ 3.30 (*J* 14.7 and 4.4 Hz), and at δ 5.86 (*J* 3.3 and 4.0 Hz), assignable to the 7-H$^\beta$ and 4-H. The downfield shift of the signal due to the 7-H$^\beta$, attributable to the deshielding by the hydroxy group of the oxime, indicated the (*E*) configuration of the oxime **32**. The ^{1}H NMR spectrum of cholest-5-en-4-one oxime **34** similarly exhibited two double doublet signals, at δ 3.30 (*J* 12.7 and 2.6 Hz) and at δ 5.87 (*J* 5.4 and 2.4 Hz), assignable to the 3-H$^\beta$ and 6-H. The downfield shift of the signal due to the 3-H$^\beta$ by deshielding due to the hydroxy group of the oxime indicated that the hydroxyimino group had an (*E*) configuration, as was expected.

Electronic Spectra of Enone Oximes **15**, **19**, **20**, **26**, **32** *and* **34**.[19]—Electronic spectra of (*E*)-5α-cholest-2-en-1-one oxime **15** and (*E*)-5α-cholest-2-en-4-one oxime **26** in methanol exhibited an absorption maximum at 229–232 nm (ε 9000–9500 dm^3 mol^{-1} cm^{-1}) assignable to their π ⟶ π* transition while those of (*E*)- and (*Z*)-5α-cholest-3-en-2-one oximes **19** and **20** in methanol exhibited the absorption maximum at 236 nm with a much higher intensity (ε 18 700). Similarly, the electronic

spectra of the two oximes **32** and **34** in methanol exhibited an absorption maximum at 224 nm (ε 6700) and 234 nm (ε 7800), respectively, assignable to their $\pi \longrightarrow \pi^*$ transitions.[19]

Photoreactions of (E)-*Cholest-2-en-1-one Oxime* **15** *and its Trideuterio Derivative* **17** (*Scheme* 8).—The photoreaction of oxime **15** in methanol (3.8×10^{-3} mol dm^{-3}) was carried out with a low-pressure mercury arc generated by a Rayonet RPR photochemical chamber reactor, as described in previous papers.[2-5] A solution of oxime **15** in methanol placed in a quartz vessel was irradiated under nitrogen for 10 h at room temperature to give the parent enone **13** (6.2%) as well as another product **35** (4.5%) by PLC (Scheme 8).

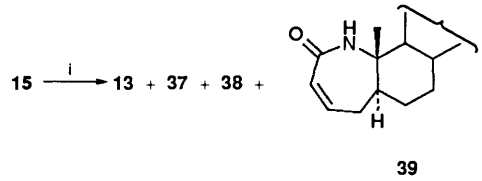


Scheme 8 *Reagents and conditions:* i, MeOH, *hv*, room temp.

The molecular formula of product **35** was established to be $C_{28}H_{48}O_2$ by high-resolution mass spectrometry (HRMS). The IR spectrum showed the presence of a 6-membered cyclic ketone. This product was shown to be 3β-methoxy-5α-cholestan-1-one on the basis of the ^1H NMR spectrum which exhibited a singlet due to the methoxy group at δ 3.33, a signal at δ 2.60 (ddd, J 1.7, 5.6 and 11.2), assignable to 2-H^{α}, and signals for 2-H^{β} and 3-H^{α}. The configuration of the methoxy group was further confirmed to be β on the basis of the results of the following photoreaction of oxime **17** labelled with deuterium.

The photoreaction of 5α-[2,4,4-$^2H_3$]cholest-2-en-1-one oxime **17** in methanol under the above mentioned conditions gave a mixture of products from which the parent enone **16** and its methanol adduct **36** were isolated in 7.6 and 2.8% yield, respectively. The ^1H NMR spectrum of the trideuterio adduct **36** exhibited a doublet at δ 2.58 (1 H, J 5.3 Hz), a singlet at δ 3.33 (3 H) and a doublet at δ 3.35 (1 H, J 5.3 Hz). These chemical shifts and coupling constants indicated that the signals are assignable to the equatorial 2-H^{α}, the equatorial 3β-methoxy group and the axial 3-H^{α}, respectively.

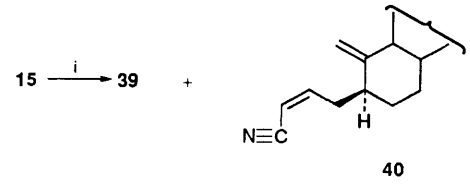
The photoreaction of oxime **15** in benzene containing glacial acetic acid (94 : 6) for 3 h under the conditions mentioned above, however, gave different results (Scheme 9): the photolysis



Scheme 9 *Reagents and conditions:* i, benzene–AcOH, *hv*, room temp.

resulted in a 78% conversion of the oxime and gave a product mixture which comprised at least four products, apart from the recovered oxime **15** (PLC). The second mobile fraction was the parent enone **13** (13.3%) and the fourth mobile fraction was a new compound, which was chracterized as 1-aza-4a-homo-5α-cholest-3-en-2-one **39** (13%) by combustion analysis, mass spectrometry and spectral analysis. Extraction of the most mobile product **37** and the third mobile product **38** from the TLC plates with a solvent gave the parent enone **13** (13.3%) and the starting oxime **15** (17.9%). These products are thus unstable and are converted into the parent enone and the oxime **15** during extraction from the TLC plates. No evidence concerning the structures of these products is available, although products **37** and **38** might be an imine and a (*Z*)-oxime, respectively.

Beckmann Rearrangement of (E)-*Cholest-2-en-1-one Oxime* **15** (*Scheme* 10)—It is known that only cyclic enamides can be obtained by Beckmann rearrangement of a mixture of (*E*)- and (*Z*)-cholest-4-en-3-one oximes, where *E*/*Z* isomerization takes place prior to C $\longrightarrow$ N migration. Beckmann rearrangement of (*E*)-cholest-2-en-1-one oxime **15** should thus give an enamide. Treatment of the oxime with thionyl dichloride in 1,4-dioxane, in fact, gave the expected lactam **39** in 16% yield. The nitrile **40**



Scheme 10 *Reagents and conditions:* i, $SOCl_2$–1,4-dioxane, room temp.

(40%) arising from a Beckmann fission was an accompanying product. The ^1H NMR spectrum indicated that the (*Z*) stereochemistry of the original carbon–carbon double bond of the oxime was retained in the nitrile.

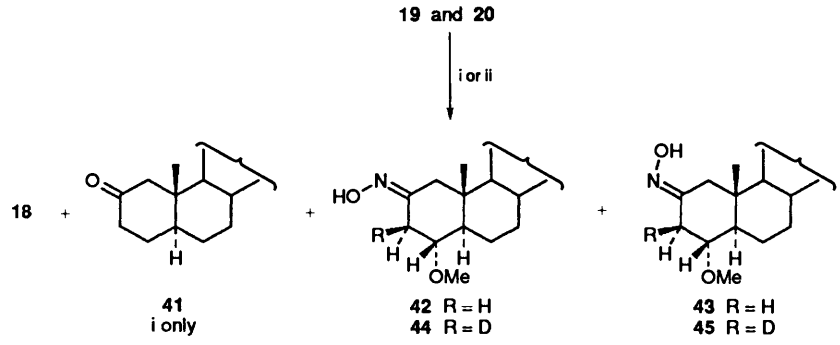
Photoreaction of (E)- *and* (Z)-*Cholest-3-en-2-one Oximes* **19** *and* **20**.—(a) *In methanol* (*Scheme* 11). The photoreaction of the (*E*)- and (*Z*)-oximes **19** and **20** in methanol under the same conditions as in the photolysis of oxime **15** for 4 h gave the parent enone **18** (4%), 5α-cholestan-2-one **41** (3%) and two new products, **42** (14.3%) and **43** (9.5%). The mass, IR and ^1H NMR spectral results of these products indicated that products **42** and **43** were (*Z*)- and (*E*)-4α-methoxy-5α-cholestan-2-one oximes, respectively, arising from the addition of methanol to the double bond. Details concerning the analysis of the structures are given in the Experimental section.

(b) *In methan*[^{2}H]*ol*. In order to establish the stereochemistry of the addition of methanol to the enone oxime **19**, photoreaction of the oxime in methan[^{2}H]ol was carried out. Irradiation of the oxime **19** in methan[^{2}H]ol under the above mentioned conditions thus resulted in only a 43% conversion of the oxime, and gave much better yields of 5α-cholest-3-en-2-one **18** (24%), (*Z*)-3β-deuterio-4α-methoxy-5α-cholestan-2-one oxime **44** (37%) and its (*E*)-isomer **45** (13%).

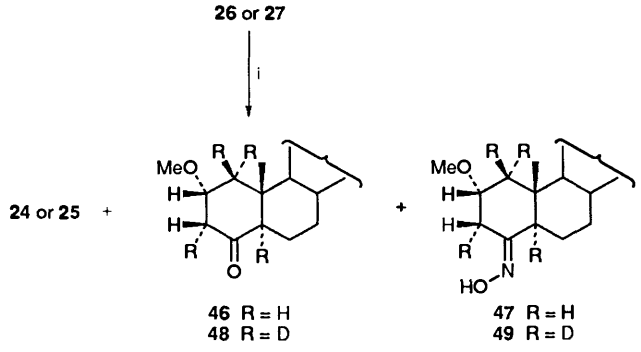
Incorporation of the deuterium and methoxy groups into the 3β and 4α positions of oximes **44** and **45** was established by ^1H NMR spectroscopy; signals due to the 4β-protons of deuterio oximes **44** and **45** appeared as triplets (J 10.4) at δ 3.02 and 3.05, respectively, while the corresponding signals of oximes **42** and **43** appeared as a double triplet at δ 3.02 (J 5.3 and 10.4) and at 3.05 (J 5.0 and 10.2), respectively.

Photoreaction of (E)-*Cholest-2-en-4-one Oxime* **26** *in Methanol*.—Photoreaction of oxime **26** in methanol under the same conditions as mentioned above for 8 h gave the parent enone **24** (10.7%) and two products, **46** and **47**, in 4.5 and 5.4% yield, respectively (Scheme 12). HRMS indicated the molecular formulae of these products to be $C_{28}H_{48}O_2$ and $C_{28}H_{49}NO_2$, respectively. Spectroscopic analyses of these products then established that products **46** and **47** were 2α-methoxy-5α-cholestan-4-one and (*E*)-2α-methoxy-5α-cholestan-4-one oxime, respectively. Details concerning the analysis of the structures are given in the Experimental section.

Photoreaction of (E)-1,1,3,5-*Tetradeuterio-5α-cholest-2-en-4-one Oxime* **27** *in Methanol*.—The stereochemistry of the



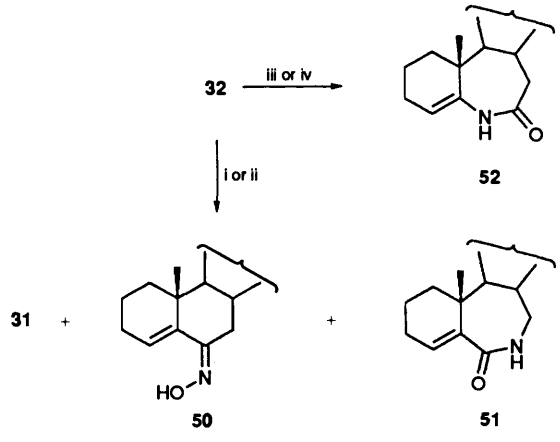
Scheme 11 *Reagents and conditions:* i, MeOH, *hv*; ii, MeOD, *hv*



Scheme 12 *Reagents and conditions:* i, MeOH; *hv*

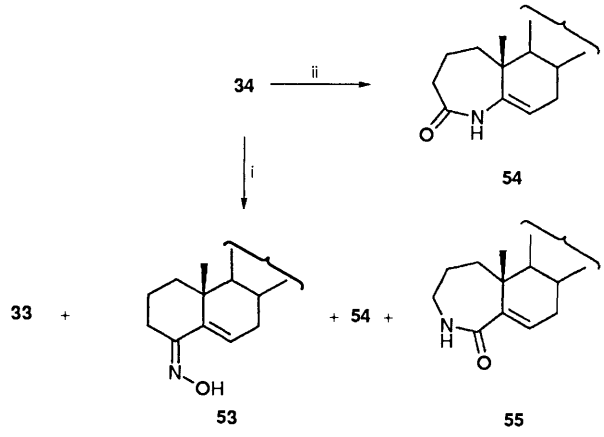
addition of methanol to the enone oxime **26** was then established by the photolysis of oxime **27** labelled with deuterium. Thus, the irradiation of labelled oxime **27** in methanol under the above mentioned conditions gave the parent deuterio enone **25** (12.6%), 1,1,3α,5-tetradeuterio-2α-methoxy-5α-cholestan-4-one **48** (5.0%), and (*E*)-1,1,3α,5-tetradeuterio-2α-methoxy-5α-cholestan-4-one oxime **49** (5.4%). The stereochemistry of the incorporation of methanol into the 2α and 3β positions of oxime **27** was established by ^{1}H NMR spectroscopy; signals due to the 2β-position of deuterio oxime **49** appeared at δ 3.36 (d, *J* 5.3), while the corresponding signal of unlabelled oxime **47** appeared at δ 3.36 as a multiplet.

Photoreaction of the Oximes **32** *and* **34** (*Schemes* 13 *and* 14).—



Scheme 13 *Reagents and conditions:* i, MeOH, *hv*; ii, benzene–AcOH (94:6), *hv*; iii, $SOCl_2$–dioxane, room temp.; iv, $POCl_3$–pyridine, room temp.

Irradiation of (*E*)-cholest-4-en-6-one oxime **32** in methanol (3.1×10^{-3} mol dm^{-3}) for 4 h resulted in a 96% conversion of the oxime and gave cholest-4-en-6-one **31** (33%) and two other products, **50** (15%) and **51** (15%). Product **50** was identified as



Scheme 14 *Reagents and conditions:* i, MeOH, *hv*; ii, $SOCl_2$–1,4-dioxane, room temp.

(*Z*)-cholest-4-en-6-one oxime on the basis of ^{1}H NMR, IR and mass spectral evidence. The molecular formula, $C_{27}H_{45}NO$, of product **50**, established by combustion analysis and mass spectrometry, indicated that the product was an isomer of the starting oxime **32**. Its IR spectrum showed a band at 3340 cm^{-1} assignable to the hydroxyimino group. Its ^{1}H NMR spectrum exhibited a broad doublet signal at δ 2.41 (*J* 9.9 Hz) and a double doublet signal at δ 5.96 (*J* 2.7 and 4.9 Hz) assignable to the 7-H$^\beta$ and 4-H. A comparison of the chemical shifts of these signals with those of the corresponding signals of the (*E*)-oxime **32** mentioned above indicated an upfield shift of the 7-H$^\beta$ signal (Δδ +0.89 ppm) and a downfield shift (Δδ −0.10 ppm) of the 4-H signal. These results clearly indicated that product **50** was (*Z*)-cholest-4-en-6-one oxime.

The molecular formula of product **51** was also established to be $C_{27}H_{45}NO$ by HRMS. The IR, ^{1}H NMR, mass and UV spectra of product **51** indicated that it was 7-aza-7a-homo-cholest-4-en-6-one. Its IR spectrum exhibited the presence of a lactam group. Apart from the signals due to 18-H$_3$ and 19-H$_3$, the ^{1}H NMR spectrum exhibited four signals (each 1 H) at δ 2.86 (ddd, *J* 14.3, 3.7 and 10.3 Hz), 3.03 (ddd, *J* 14.3, 7.2 and 2.0 Hz), 5.92 (dd, *J* 3.7 and 7.2 Hz) and 6.02 (t, *J* 3.7 Hz) assignable to the 7a-H$^\alpha$, 7a-H$^\beta$, 7-H and 4-H. Its UV spectrum in methanol exhibited an intense absorption maximum at 206 nm (ε 16 000) attributable to an enone chromophore.

The photolysis of oxime **32** in benzene containing glacial acetic acid (94:6) under the above mentioned conditions for 3 h converted 77% of the oxime and gave lactam **51** in better yield (39%) with the parent enone **31** (15%) and (*Z*)-oxime **50** (27%).

Irradiation of (*E*)-cholest-5-en-4-one oxime **34** in methanol (3.8×10^{-3} mol dm^{-3}) under conditions similar to those of oxime **32** for 10 h converted 93% of the oxime to give the parent enone **33** (17.0%) and three other products: **53** (11.6%), **54** (9.8%) and **55** (29.5%). An unstable product **53** was identified

as (*Z*)-cholest-5-en-4-one oxime based on ^{1}H NMR and IR spectral analyses. HRMS indicated its molecular formula to be $C_{27}H_{45}NO$. Its IR spectrum showed a band attributable to the hydroxyimino group. Its ^{1}H NMR spectrum exhibited a double doublet signal at δ 5.98 (*J* 2.2 and 5.9 Hz) and a broad doublet at δ 2.43 (*J* 13) assignable to 6-H and 3-H$^{\beta}$. Each signal appeared 0.11 ppm downfield and 0.87 ppm upfield from the signals due to the 6-H and 3-H$^{\beta}$ of (*E*)-oxime **34**, respectively. These results were in agreement with the structure of product **53** being the (*Z*)-isomer of oxime **34**.

HRMS confirmed that products **54** and **55** were also isomers of oxime **34**. Their IR, ^{1}H NMR, mass, and UV spectra indicated that these products were 4a-aza-4a-homocholest-5-en-4-one and 4-aza-4a-homocholest-5-en-4a-one, respectively, which could readily be distinguished by means of their IR and ^{1}H NMR spectra; the ^{1}H NMR spectrum of product **54** exhibited a broad doublet (1 H) at δ 5.54 and a broad singlet (1 H) at δ 6.89 assignable to the olefinic 6-H and NH while that of product **55** exhibited a multiplet (2 H) at δ 3.19, a double doublet (1 H) at δ 5.96 and a broad singlet (1 H) at δ 6.45 assignable to the C-3 methylene protons attached to the NH, the olefinic 6-H and NH, respectively. The absence of a signal due to the methylene protons attached to an NH in the spectrum of compound **54** and the presence of such a signal in the spectrum of compound **55** clearly indicated the assigned structures for products **54** and **55**. These assignments were further supported by their electronic spectra. As expected, the intensity of the absorption maximum of enamine **54** was about a half of that of enamide **55** as in enamine **52** (see below).

Beckmann Rearrangement of the Oximes **32** *and* **34**.—In our previous paper[2] we reported that, regardless of the configuration of its hydroxyimino group, only a cyclic enamine **3** can be obtained in a Beckmann rearrangement of cholest-4-en-3-one oxime **1**, where *E*/*Z* isomerization takes place prior to C→N migration. It would thus be interesting to confirm the products of the Beckmann rearrangement of oximes **32** and **34**, both of which adapt the configuration of their hydroxyimino groups so as to satisfy the conditions for formation of the enamine.

Treatment of oxime **32** with either thionyl dichloride in 1,4-dioxane or phosphoryl trichloride in pyridine gave a single lactam **52** in 46 or 56% yield. The structure was found to be 6-aza-7a-homocholest-4-en-6-one, an enamine, by spectral analysis (see Experimental section).

Similar treatment of oxime **34** with thionyl dichloride in 1,4-dioxane again gave a single product (60%) which was identical with the enamine **54** obtained from the photoreaction. Examination of the products obtained by Beckmann rearrangement of the oximes **32** and **34** by TLC showed that neither of the cyclic enamides, **51** and **55**, the products in the photoreaction, were formed.

Discussion

The foregoing results concerning the photoreactions of oximes **15**, **19**, **20** and **26** of cholest-2-en-1-one, cholest-3-en-2-one and cholest-2-en-4-one in methanol have shown that no unsaturated lactam[2] arising from a Photo-Beckmann-type rearrangement was formed, and that the principal products **35**, **42**, **43**, **46** and **47** are those arising from the addition of methanol to the α,β-unsaturated double bond of the oximes. These results are nearly parallel to those obtained in the photoreaction of the oxime **4** of cholest-1-en-3-one previously reported by us.[2,3]

The foregoing studies also disclosed the contrasted behaviours of oximes **32** and **34** of cholest-4-en-6-one and cholest-5-en-4-one in the photoreactions in methanol; the excited oximes result in the formation of cyclic enamides **51** and **55** arising from photorearrangements in up to 39% yield and the excited oxime of cholest-5-en-4-one **33** also gives a cyclic enamine **54** as a by-product. These results are nearly parallel to those obtained in the photoreaction of oximes of cholest-4-en-3-one and -5-en-7-one previously reported by us,[2] although the regioselectivity in the formation of the lactams is the reverse of the previous examples.[2]

The results reported in this and previous papers[2-5] have thus indicated that the excited oximes of fused α,β-unsaturated cyclic ketones react in either of two directions, depending upon their structural features: while the excited enone oximes, such as those of cholest-4-en-3-one and -5-en-7-one,[2] having their C=C bond at their ring junction, result in the formation of the corresponding lactams arising from their photorearrangement, those generated from the enone oximes having their C=C bond at their non-ring junction (such as oximes of cholest-1-en-3-one,[3-5] -2-en-1-one, -2-en-4-one and -3-en-2-one) lead to an isomerization of the C=C bond to a twisted *trans* double bond, from which the products arose by a stereospecific *syn* addition of methanol.

The present study also disclosed that while photolysis of the oximes of cholest-4-en-3-one and -5-en-7-one in methanol gave only cyclic enamines,[2] the photoreaction of oximes **32** and **34** of cholest-4-en-6-one and -5-en-4-one gave selectively cyclic enamides, **51** and **55**, although an enamine **54** was formed as the by-product in the case of the photolysis of oxime **34**. Thus, the regioselectivity in the formation of the lactams in the photorearrangement of oximes **32** and **34** was the reverse of the examples which we previously found.[2] The specific formation of cyclic enamide has also been reported in the photorearrangement of 17β-hydroxyandrosta-1,5-dien-3-one oxime.[20]

The present work has also shown that while excited cholest-2-en-1-one oxime in methanol resulted in no rearrangement to lactam, the addition of acetic acid accelerated the formation of cyclic enamide **39** in accord with a previous report.[2]

The factor which controlled these regioselectivities is still obscure. The different regioselectivity, however, may originate from a stereoelectronic effect; the relative geometry between a lone pair on the nitrogen and the migrating C–C bond in the oxaziridine intermediate generated from these oximes may be such that it favours migration of the C–C bond to give amides. The simultaneous formation of both enamine and cyclic enamides, **54** and **55**, may indicate the involvement of two isomeric oxaziridine intermediates.

A deuterium-labelling study concerning the photoadditions of oximes **15**, **19**, **20** and **26** established that the addition of methanol takes place in a stereospecific manner, as in the case of our previous observations concerning the photoaddition of methanol in the oximes of cholest-1-en-3-ones.[3,5]

The pathways for the formation of the methanol adducts (such as **35**, **42**, **43**, **46** and **47**) from the excited α,β-enone oximes (**15**, **19**, **20** and **26**) should be parallel to those for the formation of methanol adducts **5** and **10** from oximes **4** and **9** (Scheme 2). Thus, irradiation of deuteriated oximes **17** and **27** (in methanol) as well as oximes **19** and **20** (in methan[^{2}H]ol) generates twisted ground-state intermediates **17t**, **19t**, **20t** and **27t** in which the C=C bonds are twisted by more than 90°, *via* either singlet or, more likely, triplet excited oximes (Fig. 1). A nucleophilic *syn* addition of either methanol or methan[^{2}H]ol to the reactive *trans* double bonds of the intermediates from the front side of each molecule gives the observed adducts **36**, **44**, **45**, **48** and **49**, in agreement with the results of the deuterium-labelling studies. The attack of methanol or methan[^{2}H]ol to the double bond of intermediates **17t**, **19t**, **20t** and **27t** from the rear side is blocked by the fused ring. In the photolysis of oxime **17**, only the methanol adduct of the parent enone **16** was obtained in low yield. This product most probably arose from a secondary

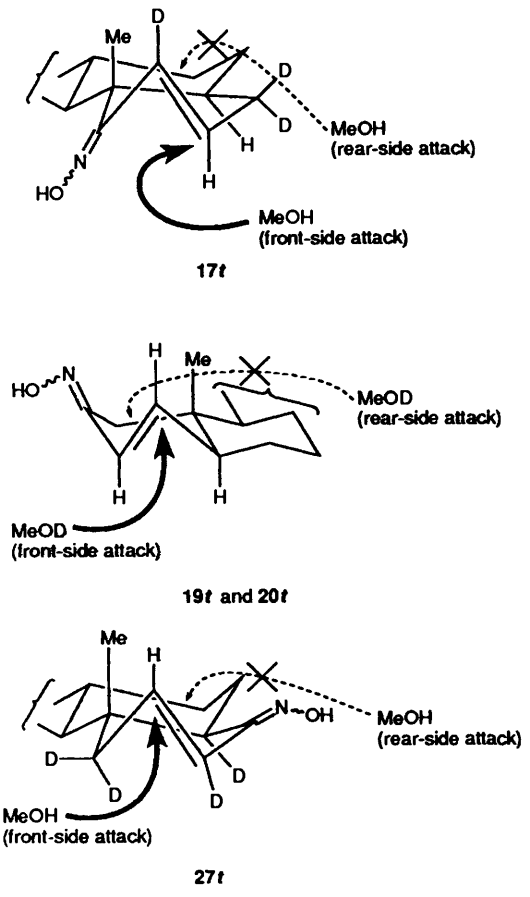


Fig. 1 Ground-state intermediates in the addition of methanol to oximes **17**, **19**, **20** and **27**

photochemical decomposition of the initially formed methanol adduct. The energy of the excited oximes, having their double bond at their ring junction, principally dissipates so as to isomerize their C=C bond in preference to rearranging to the lactams. Energy dissipation through this $Z \rightarrow E$ isomerization is, however, prohibited in the excited oximes having their C=C bond at the ring junction, resulting instead in a rearrangement to the lactams.[2,7a,19] The formation of a cyclic enamide in the photorearrangement of 17β-hydroxyandrosta-1,5-dien-3-one oxime, reported by Bonet and colleagues,[20] might seem to be an exception. In this case, however, a new strain introduced by the presence of the C=C bond at the C(5) position of the oxime may make the photochemical geometrical isomerization of the C=C bond at the C(1) position less easy than in the case of cholest-1-en-3-one oxime.[3]

While the ground-state Beckmann rearrangement of oxime **15** gave a mixture of lactam **39** by rearrangement and nitrile **40** by Beckmann fission, the photoreaction gave no nitrile arising from α-fission, in spite of the fact that it had a tertiary carbon centre adjacent to the hydroxyimino group. The present results again indicated that, in contrast to the ground-state reaction, α-fission rarely takes place in the photoreaction, as we had previously found.[21]

A survey of the past literature concerning the Beckmann rearrangement of α,β-unsaturated ketone oximes indicates that there are a number of examples[22] in which alkyl groups are apt to migrate more readily to the nitrogen centre if *syn–anti* isomerization of the geometry of the hydroxyimino group takes place faster than C ⟶ N migration under the experimental conditions, although the vinyl group seems to migrate more readily to electron-deficient centres.[23]

However, a normal migration of a vinyl group has been observed in oximes, in which the geometry of the hydroxyimino group for vinyl migration is preserved under the experimental conditions, and the overlap of the p-orbitals of the vinyl group and the emptying orbital generated on the nitrogen atom by the loss of the leaving group is not hindered.[24]

The foregoing results showed that Beckmann rearrangements[25] of (*E*)-cholest-4-en-6-one oxime **32** and (*E*)-cholest-5-en-4-one oxime **34** gave enamines **52** and **54**, as expected from the geometry of the hydroxyimino group. The results are in contrast with those of the Beckmann rearrangement of cholest-2-en-1-one oxime **15** and cholest-4-en-3-one oxime **1**.[2,22a–d]

Whatever is the cause of the regioselectivity of the photorearrangements of oximes **32** and **34**, the formation of the enamide lactams (such as **51** and **55**), which are not accessible by Beckmann rearrangements, at room temperature should demonstrate the usefulness of photoreactions for the preparation of azasteroids.

Experimental

M.p.s were determined using a Yanaco micro m.p. apparatus and are uncorrected. The IR spectra were determined for Nujol mulls (unless stated otherwise) with either a Hitachi 285 grating infrared spectrophotometer or a JASCO IR 810 infrared spectrophotometer. The ^{1}H NMR spectra of compounds **13**–**22**, **24**–**27**, **35**, **36** and **42**–**49** were determined using a JEOL JNM-JX 270 FT high-resolution spectrometer operating at 270 MHz (δ_H) (solvent $CDCl_3$: $SiMe_4$ as internal reference). The ^{1}H NMR spectra of compounds **31**, **32**, **39**, **40** and **50**–**55** were determined with either a Hitachi R90 H high-resolution spectrometer operating at 90 MHz, a JEOL JNM-FX 200 FT NMR spectrometer operating at 200 MHz, or a JEOL JNM-GX 270 FT NMR spectrometer operating at 270 MHz (solvent $CDCl_3$; $SiMe_4$ as internal reference). The *J*-values are given in Hz. UV Spectra were measured with a JASCO U best-30 instrument. The mass spectra of the enones and oximes were determined either with a JEOL JMS-HX110 or a JMS-DX303 spectrometer (70 eV). The mass spectra of compounds **28**–**34** and **52**–**55** were determined with either a JEOL model JMS-300 mass spectrometer, a JEOL model JMA-2000 mass data analysis system, or a JEOL JMS-O1SG-2 mass spectrometer. Elemental analyses were performed at the Faculty of Pharmaceutical Sciences of this University. PLC was carried out on a Merck Kieselgel 60 PF_{254}. Column chromatography was carried out using Merck Kieselgel 60. The photoreaction was carried out with a low-pressure Hg arc generated by Rayonet RPR photochemical reactor.

Cholest-2-en-1-one **13**.[10]—This enone **13** was prepared from 5α-cholestan-3-one in 4 steps; its trimethylsilyl enol ether was treated with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) according to a procedure reported by Fleming and Paterson[9] to give cholest-1-en-3-one [δ_H(270 MHz) 0.67 (3 H, s, 18-H_3), 1.05 (3 H, s, 19-H_3), 5.78 (1 H, dt, *J* 2.0 and 10.2, 2-H) and 6.64 (1 H, dt, *J* 3.4 and 10.2, 3-H)]. Its conversion into 1α,2α-epoxy-5α-cholestan-3-one, followed by the Wharton reaction according to the procedure of Djerassi *et al.*,[8] gave cholest-2-en-1-one **13**.[10]

2,4,4-*Trideuterio-5α-cholest-2-en-1-one* **16**.—To a solution of 5α-cholest-2-en-1-one **13** (100 mg, 0.26 mmol) in diethyl ether (1.0 cm^3) and MeOD (3.5 cm^3) was added sodium (12 mg, 0.52 mmol). The solution was heated under reflux for 2 days. After evaporation of the solvent, the residue was dissolved in diethyl ether. The solution was neutralized with 5% hydrochloric acid, washed successively with water and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent gave a crude trideuterio derivative **16** (100 mg). This product was subjected to

PLC [(5:1) hexane–ethyl acetate] to give trideuterio enone **16** (67 mg). This was recrystallized from acetone–methanol to give pure enone **16** (63 mg, 62.7%), m.p. 66.5–67.5 °C; δ_H(270 MHz) 0.67 (3 H, s, 18-H_3), 1.05 (3 H, s, 19-H_3) and 6.64 (1 H, s, 3-H).

(E)-3α-*Hydroxyamino*-5α-*cholestan*-1-*one Oxime* **14**.—Enone **13** (50 mg, 0.13 mmol), hydroxylamine hydrochloride (37 mg, 0.53 mmol), and sodium acetate trihydrate (71 mg, 0.52 mmol) were dissolved in ethanol (1.7 cm^3) containing water (0.1 cm^3). The solution was heated under reflux for 3 h and was then poured into water–ice to give crystals, which were collected by filtration. The crystals were dissolved in diethyl ether. The ethereal solution was washed with brine and dried over anhydrous $MgSO_4$. The product (58 mg) was crude (E)-3α-*hydroxyamino*-5α-*cholestan*-1-*one oxime* **14** (58 mg), m.p. 179.5–181.0 °C (from $CHCl_3$); ν_{max}/cm^{-1} 3320 (NHOH), 1333, 1032, 941, 924 and 915; δ_H(270 MHz) 0.67 (3 H, s, 18-H_3), 1.07 (3 H, s, 19-H_3), 2.03 (1 H, dd, *J* 3.5 and 13.4, 2-H^β), 3.49 (1 H, br s, 3-H^β) and 3.51 (1 H, d, *J* 19.1, NH); *m/z* 432 (M^+, 3.4%), 430 (29.4), 414 (28.1), 413 (31.2), 400 (46.1), 399 (97.3), 397 (82.3), 383 (29.4), 382 (37.8), 121 (53.3) and 43 (100) (Found: C, 73.3; H, 11.2; N, 6.3. $C_{27}H_{48}N_2O_2 \cdot 1/2\ H_2O$ requires C, 73.42; H, 11.40; N, 6.34%).

(E)-*Cholest*-2-*en*-1-*one Oxime* **15**.—(a) *In pyridine*. Enone **13** (497 mg, 1.29 mmol), hydroxylamine hydrochloride (615 mg, 8.86 mmol) and pyridine (22 cm^3) were stirred together for 24 h. To the solution was added more hydroxylamine hydrochloride (367 mg, 5.28 mmol); the solution was then stirred for 17 h. Water was added to the solution; the crystals, collected by filtration, were dissolved in diethyl ether. The ethereal solution was worked up in the usual manner to give a crude crystalline product (510 mg). This product was subjected to PLC (benzene) to give two fractions. The less mobile fraction (142 mg) was the starting enone and the more mobile fraction (340 mg, 92.2% based on the converted enone) was the *oxime* **15**, m.p. 153.0–154.0 °C (from Me_2CO); ν_{max}/cm^{-1} 3290 (OH), 952 and 938; δ_H(270 MHz) 0.69 (3 H, s, 18-H_3), 0.99 (3 H, s, 19-H_3), 6.10 (1 H, ddd, *J* 10.3, 4.5 and 2.5, 3-H) and 6.63 (1 H, d, *J* 10.2, 2-H); *m/z* 399 (M^+, 23.1%), 384 (44.1), 382 (100) and 149 (58.0); λ_{max}(MeOH)/nm 228 (ε 9080) (Found: C, 81.0; H, 11.4; N, 3.6. $C_{27}H_{45}NO$ requires C, 81.14: H, 11.35; N, 3.51%).

(b) *In ethanol*. Enone **13** (50 mg, 0.13 mmol), hydroxylamine hydrochloride (51 mg, 0.73 mml) and sodium acetate trihydrate (58 mg, 0.43 mmol) were dissolved in ethanol (3 cm^3). The solution was heated under reflux for 3 h and was then poured into water–ice. The crystals collected by filtration were dissolved in diethyl ether. The ethereal solution was first washed successively with water and brine, and dried over anhydrous Na_2SO_4. The product was subjected to PLC to give (*E*)-cholest-2-en-1-one oxime **15** (7 mg, 13.5%).

(E)-2,4,4,-*Trideuterio*-5α-*cholest*-2-*en*-1-*one Oxime* **17**.—A solution of 2,4,4-trideuterio enone **16** (60 mg, 0.15 mmol) and hydroxylamine hydrochloride (57 mg, 0.82 mmol) in pyridine (4 cm^3) was stirred for 12 h at room temperature. The solution was then poured into water. The crystals collected by filtration were dissolved in diethyl ether. The solution was then neutralized with 5% hydrochloric acid, washed successively with water and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent gave crude oxime **17**. This oxime was subjected to PLC [(5:1) benzene–diethyl ether] to give trideuterio enone oxime **17** (41 mg, 68.1%), m.p. 153.0–154.0 °C; δ_H(270 MHz) 0.69 (3 H, s, 18-H_3), 0.99 (3 H, s, 19-H_3) and 6.09 (1 H, s, 3-H).

Cholest-4-*en*-6-*one* **31**.[17]—This unsaturated ketone[16] was prepared in 36% yield by treatment of 5,6α-epoxy-5α-cholestan-3β-ol **29** with $MgBr_2$ according to a procedure reported by Turner,[17a] m.p. 105–106 °C (from MeOH) (lit.,[17a] 107–108 °C); δ_H(90 MHz) 0.70 (3 H, s, 18-H_3), 0.96 (3 H, s, 19-H_3) and 6.38 (1 H, t, *J* 3.7, 4.H).

(E)-*Cholest*-4-*en*-6-*one Oxime* **32**.—A solution of cholest-4-en-6-one **31** (104 mg) and hydroxylamine hydrochloride (123 mg) in pyridine (4.4 cm^3) was stirred for 20.5 h at room temperature. After the addition of water to the solution, crystals were collected by filtration. The solution was extracted with diethyl ether. The crystals were dissolved in diethyl ether. The combined ethereal solution was worked up in the usual manner. The crude oxime was recrystallized from methanol to give oxime **32** (83 mg, 77%), m.p. 154–162 °C (lit.,[3] 163–165 °C); ν_{max}/cm^{-1} 3246 (OH), 1298, 953, 920 and 803; δ_H 0.67 (3 H, s, 18-H_3), 0.93 (3 H, s, 19-H_3), 3.30 (1 H, dd, *J* 14.7 and 4.4, 7-H^β) and 5.86 (1 H, dd, *J* 3.3 and 4.0, 4-H); *m/z* 399 (M^+, 4.9%), 384 (13.6), 382 (6.1), 368 (6.8), 356 (18.7) and 111 (100); λ_{max}(MeOH)/nm 224 (ε 6700).

Photoreaction of (E)-*Cholest*-2-*en*-1-*one Oxime* **15**.—(a) *In methanol*. A solution of the oxime **15** (75 mg, 0.19 mmol) in methanol (50 cm^3) was flushed with nitrogen and was then irradiated for 10 h. The solvent was removed by a rotary evaporator. The product was then subjected to PLC with (7:1) hexane–ethyl acetate to afford three products. The most mobile product (5.5 mg, 6.2%) was the parent ketone **13**. The next mobile fraction (4.3 mg) could not be characterized. The least mobile fraction was 3β-*methoxy*-5α-*cholestan*-1-*one* **35** (2.8 mg, 4.5%); ν_{max}/cm^{-1} (neat) 1709 (C=O); δ_H(270 MHz) 0.65 (3 H, s, 19-H_3), 1.14 (3 H, s, 18-H_3), 2.60 (1 H, ddd, *J* 1.7, 5.6 and 11.2, 2-H^α), 2.69 (1 H, dd, *J* 0 and 11.2, 2-H^β), 3.33 (3 H, s, OMe) and 3.35 (1 H, m, 3-H^α); *m/z* 416 (M^+, 30.3%), 384 [(M − MeOH)$^+$, 20.3], 369 [(M − MeOH − Me)$^+$, 11.7], 230 (12.7), 154 (23.8), 93 (30.6), 81 (33.6), 69 (27.7), 57 (47.3) and 43 (100) (Found: M^+, 416.3667 $C_{28}H_{48}O_2$ requires M, 416.3642).

(b) *In benzene–glacial acetic acid* (94:6). A solution of the oxime **15** (50 mg) in benzene–glacial acetic acid (43 cm^3) was flushed with nitrogen and was then irradiated for 3 h. The product mixture was then subjected to PLC with benzene to give five fractions (A to E in order of their mobility). The second mobile fraction (B; 11 mg) was the recovered oxime.[15] The third mobile fraction (C; 5 mg, 13.3% based on the converted oxime) was cholest-2-en-1-one **13**. Fraction E (24 mg) was again purified by PLC with (1:1) benzene–diethyl ether to give 1-*aza*-4a-*homo*-5α-*cholest*-3-*en*-2-*one* **39** (5 mg, 13% based on the converted oxime), m.p. 144.5–145.5 °C (from MeOH); ν_{max}/cm^{-1} 3250 and 3200 (NH), 1677, 1626 (COC=C), 1227 and 815; δ_H(270 MHz) 0.69 (3 H, s, 19-H), 1.11 (3 H, s, 18-H_3), 5.89 (1 H, d, *J* 12.54, 3-H), 6.08 (1 H, br s, NH) and 6.19 (1 H, ddd, *J* 3.3, 5.0 and 12.5, 4-H); *m/z* (JEOL JMS-DX300) 399 (M^+, 7.2%), 384 [(M − Me)$^+$, 13.8], 136 (65.7), 122 (100), 107 (23.0), 93 (33.9), 81 (12.9) and 67 (13.0) (Found: C, 80.2; H, 11.6; N, 3.6. $C_{27}H_{45}NO \cdot 1/4H_2O$ requires C, 80.24; H, 11.35; N, 3.47%). Extraction of fraction A with ethyl acetate gave more cholest-2-en-1-one **13** (5 mg, 13.3% based on converted oxime); extraction of fraction D gave more of the starting oxime **15** (7 mg).

Photoreaction of 2,4,4,-*Trideuterio Enone Oxime* **17** *in Methanol*.—A solution of oxime **17** (41 mg, 0.10 mmol) in methanol (27 cm^3) was flushed with nitrogen and was then irradiated as in the case of oxime **15** to give the parent enone **16** (3 mg, 7.6%) and 2β,4,4-trideuterio-3β-methoxy-5α-cholestan-1-one **36** (1.2 mg, 2.8%), δ_H(270 MHz) 0.65 (3 H, s, 18-H_3), 1.14 (3 H, s, 19-H_3), 2.58 (1 H, d, *J* 5.3, 2-H^α), 3.33 (3 H, s, 3β-OMe) and 3.35 (1 H, d, *J* 5.3, 3-H^α).

Beckmann Rearrangement of (E)-*Cholest*-2-*en*-1-*one Oxime* **15**.—To a solution of the oxime **15** (50 mg, 0.13 mmol) in 1,4-

dioxane (2 cm^3) under nitrogen was added thionyl dichloride (0.03 cm^3) dropwise. The solution was stirred for 40 min at room temperature. After the addition of water, the solution was extracted with diethyl ether. The extract was washed successively with aq. 5% Na_2CO_3, water, and brine, and was then dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a product mixture (40 mg), which was subjected to PLC (benzene) to give three fractions. The most mobile fraction (19 mg, 40%) was an *unsaturated nitrile* **40**, m.p. 106–110 °C (from MeOH); ν_{max}/cm^{-1} 2217 (C≡N), 1645 and 1623; δ_H(270 MHz) 0.68 (3 H, s, 18-H_3), 2.48 (1 H, m, one of C=CCH_2), 2.71 (1 H, m, one of C=CCH_2), 4.61 (1 H, s, 19-H), 4.74 (1 H, s, 19-H), 5.36 (1 H, d, *J* 11.0, C=CHC≡N) and 6.54 (1 H, ddd, *J* 11.0, 6.6 and 8.1, CH_2CH=CH); *m/z* 381 (M^+, 24%), 366 (28.6), 315 (26.9), 268 (58.4), 226 (90.2) and 57 (100) (Found: C 84.8; H, 11.5; N, 3.7. $C_{27}H_{43}N$ requires C, 84.97; H, 11.36; N, 3.67%).

The next mobile fraction (5 mg) was the recovered oxime **15**. The most polar fraction (13 mg, 16%) was the lactam **39**, which was identical with the lactam obtained from the photoreaction.

5α-*Cholest*-3-*en*-2-*one* **18**.—Enone **18** was prepared according to a method from the literature.[11] M.p. 106.5–107.5 °C (from hexane) (lit.,[9] 112–113 °C); ν_{max}/cm^{-1} 1671 (CO–C=C); δ_H(270 MHz) 0.66 (3 H, s, 18-H_3), 0.87 (3 H, s, 19-H_3), 2.07 (1 H, d, *J* 16.6, 1-H^α), 2.31 (1 H, ddd, *J* 3.1, 5.3 and 13.2, 5-H^α), 2.55 (1 H, d, *J* 15.84, 1-H^β), 5.96 (1 H, dd, *J* 3.3 and 9.9, 3-H) and 6.57 (1 H, dd, *J* 2.0 and 10.2, 4-H).

(E)- *and* (Z)- 5α-*Cholest*-3-*en*-2-*one Oximes* **19** *and* **20**.—A solution of 5α-cholest-3-en-2-one **18** (100 mg, 0.26 mmol), hydroxylamine hydrochloride (102 mg, 1.47 mmol) and sodium acetate trihydrate (130 mg, 0.96 mmol) in ethanol (5 cm^3) was stirred for 24 h at room temperature. Removal of the solvent gave crystals, which were dissolved in diethyl ether–water. The organic layer was washed successively with water and brine, and was dried over anhydrous Na_2SO_4. Removal of the solvent gave a product, which was subjected to PLC [(5:1) benzene–ethyl acetate] to give two oxime isomers, **19** and **20**. The more mobile oxime (37.8 mg, 36.4%) was (Z)-*oxime* **19**, m.p. 171.0–172.5 °C (from acetone); ν_{max}/cm^{-1} 3324 (OH), 1639 and 1630 (C=C–C=N); δ_H(270 MHz) 0.66 (3 H, s, 18-H_3), 0.78 (3 H, s, 19-H_3), 2.47 (1 H, d, *J* 14.5, 1-H^β), 5.90 (1 H, dd, *J* 1.8 and 10.1, 3-H) and 6.76 (1 H, dd, *J* 3.0 and 9.9, 4-H); *m/z* 399 (M^+, 8.8%), 383 (100), 368 [(M − Me)$^+$, 38.0], 314 (19.2), 120 (68.2), 106 (75.2), 71 (82.1), 55 (88.3) and 43 (98.9); λ_{max}(MeOH)/nm 236 (ε 18 700) (Found: C, 81.0; H, 11.5; N, 3.5. $C_{27}H_{45}NO$ requires C, 81.14; H, 11.35; N, 3.51%).

The less mobile product **20** was (E)-5α-*cholest*-3-*en*-2-*one oxime* (40.7 mg), m.p. 225–228 °C (from Me_2CO); ν_{max}/cm^{-1} 3320 (OH), 1638 and 1619 (C=C–C=N); δ_H(270 MHz) 0.66 (3 H, s, 18-H_3), 0.78 (3 H, s, 19-H), 3.19 (1 H, d, *J* 16.8, 1-H^β), 5.78 (1 H, dd, *J* 1.7 and 9.9, 3-H) and 6.07 (1 H, dd, *J* 2.6 and 9.6, 4-H); *m/z* 399 (M^+, 54.0%), 382 [(M − OH)$^+$, 100], 366 (6.5), 287 (23.6), 121 (18.6), 107 (22.9), 95 (37.9), 81 (35.1), 69 (37.5), 57 (49.7) and 43 (55.7) (Found: C, 80.85; H, 11.25; N, 3.6%).

Photolysis of (E)- *and* (Z)-5α-*Cholest*-3-*en*-2-*one Oximes* **19** *and* **20**.—(a) *In methanol.* Solutions of the oximes (75 mg, 0.19 mmol) in methanol (50 cm^3) were flushed with nitrogen and irradiated for 4 h to give four fractions (A, B, C and D in order of their mobility on PLC). The most mobile fraction (A; 2 mg, 3%) was identical with 5α-cholestan-2-one **41**. The second mobile fraction (3 mg, 4%) was the parent 5α-cholest-3-en-2-one **18**. The third mobile fraction (12 mg, 14%) was (Z)-4α-*methoxy*-5α-*cholestan*-2-*one oxime* **42** (11.6 mg, 14.3%), m.p. 159.5–162.0 °C (from Me_2CO–MeOH); ν_{max}/cm^{-1} 3214 (OH), 1665 (C=N) and 1092; δ_H(270 MHz) 0.64 (3 H, s, 18-H_3), 0.72 (3 H, s, 19-H_3), 2.35 (1 H, dd, *J* 1.0 and 13.2, 1-H^β), 3.02 (1 H, dt, *J* 5.3 and 10.4, 4-H^β) 3.38 (3 H, s, 4-OMe) and 3.89 (1 H, ddd, *J* 1.0, 5.3 and 13.7, 3-H^β); *m/z* 431 (M^+, 17.8%), 399 [(M − OMe)$^+$, 44.8], 382 [(M − OMe − OH)$^+$, 29.3], 273 (15.0), 219 (14.4), 107 (22.6), 95 (38.4), 81 (38.5), 71 (44.7), 55 (74.5) and 43 (100) (Found: M^+, 431.3743. $C_{28}H_{49}NO_2$ requires M, 431.3751).

The most polar fraction (7.7 mg, 9.5%) was (E)-4α-*methoxy*-5α-*cholestan*-2-*one oxime* **43** (7.7 mg, 9.5%), ν_{max}/cm^{-1} 3216 (OH), 1702, 1658 (C=C–C=N) and 1094; δ_H(270 MHz) 0.65 (3 H, s, 18-H_3), 0.73 (3 H, s, 19-H_3), 2.88 (1 H, ddd, *J* 1.3, 5.0 and 13.9, 3-H^β), 3.05 (1 H, dt, *J* 5.0 and 10.2, 4-H^β) 3.35 (3 H, s, 4-OMe) and 3.40 (1 H, dd, *J* 1.3 and 13.2, 1-H^β); *m/z* 431 (M^+, 100%), 416 [(M − Me)$^+$, 12.2], 399 [(M − OMe)$^+$, 89.9], 382 [(M − OMe − OH)$^+$, 53], 273 (24.7), 115 (26.4), 95 (42.8), 81 (43.1), 71 (50.1), 55 (76.9) and 43 (85.5) (Found: M^+, 431.3757).

(b) *In methan*[^{2}H]*ol.* A mixture of oximes **19** and **20** (57.5 mg, 0.14 mmol) in methan[^{2}H]ol (33 cm^3) was subjected to photolysis to give five fractions in order of their mobility on a TLC plate. The most mobile fraction (5.8 mg, 24.2% based on the converted oxime) was the parent enone **18**. The second fraction (15.2 mg) was recovered (*Z*)-5α-cholest-3-en-2-one oxime **19**. The third fraction (17.4 mg) was its (*E*)-isomer **20**. The fourth fraction (9.9 mg, 36.8% based on the converted oximes) was (Z)-3β-*deuterio*-4α-*methoxy*-5α-*cholestan*-2-*one oxime* **44**, m.p. 174.0–175.5 °C (from Me_2CO); ν_{max}/cm^{-1} 3262 (OH) and 1669; δ_H(270 MHz) 0.65 (3 H, s, 18-H_3), 0.72 (3 H, s, 19-H_3), 2.35 (1 H, d, *J* 13.5, 1-H^β), 3.02 (1 H, t, *J* 10.4, 4-H^β) and 3.38 (s, 3 H, 4α-OMe); *m/z* 432 (M^+, 1.1%), 415 [(M − OH)$^+$, 1.7], 400 [(M − MeOH)$^+$, 13.8], 383 (27.9), 229 (12.6), 157 (22.6), 121 (60.4), 107 (49.9), 95 (54.4), 69 (59.4), 55 (82.7) and 43 (100) (Found: M^+, 432.3801. $C_{28}H_{48}DNO_2$ requires M, 432.3847).

The most polar fraction (3.6 mg, 13.4% based on the converted oxime) was the isomeric (E)-3α-deuterio-4α-methoxy-5α-cholestan-2-one oxime **45**, m.p. 148.5–150.0 °C (from acetone–methanol); ν_{max}/cm^{-1} 3240 (OH), 1720 and 1657; δ_H(270 MHz) 0.65 (3 H, s, 18-H_3), 0.73 (3 H, s, 19-H_3), 3.05 (1 H, t, *J* 10.4, 4-H^β), 3.35 (3 H, s, 4-OMe) and 3.40 (1 H, d, *J* 13.2, 1-H^β); *m/z* 432 (M^+, 79.8%), 417 [(M − Me)$^+$, 15.5], 400 [(M − Me − OH)$^+$, 100], 383 (70.6), 274 (13.1), 121 (16.5), 107 (19.3), 95 (25.0), 81 (26.1), 69 (25.3), 57 (36.5) and 43 (52.7) (Found: M^+, 432.3819).

4-*Methoxycholest*-4-*en*-3-*one* **21**.—This enone was prepared in 58.7% yield from cholest-4-en-3-one according to the published method.[13] M.p. 131.0–132.5 °C (from MeOH–Me_2CO) (lit.,[11] 133–135 °C); ν_{max}/cm^{-1} 1605 and 1675 (C=C–C=O), 1100 and 1080; δ_H(270 MHz) 0.70 (3 H, s, 18-H_3), 1.18 (3 H, s, 19-H_3), 3.04 (1 H, ddd, *J* 2.7, 4.1 and 14.9, 6-H^β) and 3.59 (3 H, s, OMe).

4-*Methoxycholest*-4-*en*-3-*one Tosylhydrazone* **22**.—A solution of enone **21** (452 mg, 1.1 mmol) and tosylhydrazine (235 mg, 1.2 mmol) in absolute ethanol (4 cm^3) under nitrogen was heated under reflux for 5 h. Removal of the solvent gave crystals, which were dissolved in water–diethyl ether. The ethereal layer was washed successively with water and brine, and was dried over anhydrous Na_2SO_4. Evaporation of the solvent gave tosylhydrazone **22** (687 mg, 98.2%), m.p. 151.0–152.5 °C (from Me_2CO); ν_{max}/cm^{-1} 3218 (NH), 1600 (C=N) and 1188; δ_H(270 MHz) 0.67 (3 H, s, 18-H_3), 1.00 (3 H, s, 19-H_3), 2.40 (3 H, s, Me) 2.97 (1 H, ddd, *J* 2.3, 4.6 and 13.7, 6-H^β), 3.52 (3 H, s, OMe), 7.29 (2 H, d, *J* 8.2, ArH) and 7.88 (2 H, d, *J* 8.2, ArH); *m/z* (by JEOL JMS DX300) 398 [(M − TsNHN)$^+$, 9.8%], 383 [(M − TsNHN − Me)$^+$, 4.5], 247 (7.7), 185 (24.9), 135 (47.7), 91 (100), 65 (44.3) and 44 [Found: (M − $C_7H_8O_2N_2S$)$^+$, 398.3560. $C_{28}H_{46}O$ requires *m/z* 398.3537].

5α-*Cholest-2-en-4-one* **24**.[14]—To a solution of crude tosylhydrazone **22** (622 mg, 1.1 mmol) in dry diethyl ether (50 cm^3) was added methyllithium (1.5 mol dm^{-3} ethereal solution) (4.3 cm^3, 6.6 mmol) dropwise. The solution was then heated under reflux for 18 h. To this solution was added aq. ammonium chloride and the solution was stirred. The ethereal layer was washed successively with water and brine, and was dried over anhydrous Na_2SO_4. Evaporation of the solvent gave crude 4-methoxycholesta-2,4-diene **23** (488 mg). This diene was subjected to PLC [(5:1) hexane–ethyl acetate] to give directly 5α-cholest-2-en-4-one **24** (127 mg, 30.4% from enone **21**), m.p. 84.5–85.0 °C (from Me_2CO) (lit.,[14b] 89 °C; lit.,[14c] no description of m.p.); ν_{max}/cm^{-1} 1679 and 1621 (C=C–C=O); δ_H(270 MHz) 0.66 (3 H, s, 18-H_3), 0.85 (3 H, s, 19-H_3), 2.41 (1 H, dd, *J* 5.9 and 18.8, 5-H^{α}), 5.98 (1 H, br dd, *J* 3.0 and 10.2, 3-H) and 6.79 (1 H, ddd, *J* 2.3, 5.9 and 10.2, 2-H).

(E)-5α-*Cholest-2-en-4-one Oxime* **26**.—A solution of cholest-2-en-4-one **24** (100 mg, 0.26 mmol), hydroxylamine hydrochloride (102 mg, 1.47 mmol) and sodium acetate trihydrate (130 mg, 0.96 mmol) in ethanol (5 cm^3) was stirred for 18 h at room temperature. Removal of the solvent gave a residue, which was dissolved in a mixture of diethyl ether and water. The organic layer was washed successively with water and brine, and was then dried over anhydrous Na_2SO_4. Removal of the solvent gave crude oxime **26** (113 mg), which was recrystallized from acetone to give pure *oxime* (102 mg, 98.5%), m.p. 203.0–205.0 °C; ν_{max}/cm^{-1} 3272 (OH), 1685 and 1642 (C=C–C=N); δ_H(270 MHz) 0.66 (3 H, s, 18-H_3), 0.78 (3 H, s, 19-H_3), 6.15 (1 H, ddd, *J* 2.3, 5.6 and 10.2, 2-H) and 6.77 (1 H, dd, *J* 2.6 and 10.2, 3-H); *m/z* 399 (M^+, 74.1%), 382 [$(M - OH)^+$, 41.4], 368 (100), 120 (51.9), 106 (60.6), 95 (40.7), 81 (42.7), 55 (61.2) and 43 (82.9); λ_{max}(MeOH)/nm 232 (ε 9500) (Found: C, 81.05; H, 11.4; N, 3.4. $C_{27}H_{45}NO$ requires C, 81.14; H, 11.35; N, 3.51%).

1,1,3,5-*Tetradeuterio-5α-cholest-2-en-4-one* **25**.—To a solution of 5α-cholest-2-en-4-one **24** (150 mg, 0.39 mmol) in dry diethyl ether (1.5 cm^3)–methan[^{2}H]ol (4.5 cm^3) was added sodium metal (18 mg, 0.78 mmol). The solution was heated under reflux for 2 days. The residue obtained by removal of the solvent was dissolved in diethyl ether and neutralized with 5% hydrochloric acid. The solution was washed with brine and dried over anhydrous Na_2SO_4. Removal of the solvent gave crude deuterio ketone **25** (148 mg). Recrystallization from acetone gave pure *deuterio ketone* **25** (118 mg, 77.7%), m.p. 85.0–86.0 °C; ν_{max}/cm^{-1} 1650 and 1675 (C=C–CO); δ_H(270 MHz) 0.66 (3 H, s, 18-H_3), 0.85 (3 H, s, 19-H_3) and 6.78 (1 H, s, 2-H); *m/z* 388 (M^+, 11.2%), 373 [$(M - Me)^+$, 14.2], 233 (100), 135 (57.5), 123 (61.3), 113 (73.1), 99 (71.9), 55 (72.2) and 43 (74.1) (Found: M^+, 388.3636. $C_{27}H_{40}D_4O$ requires M, 388.3633).

(E)-1,1,3,5-*Tetradeuterio-5α-cholest-2-en-4-one Oxime* **27**.—The deuterio ketone **25** (118 mg, 0.30 mmol), hydroxylamine hydrochloride (115 mg, 1.65 mmol), and sodium acetate trihydrate (143 mg, 1.05 mmol) in ethanol were stirred for 18 h at room temperature. The reaction mixture was worked up as described for the preparation of oxime **26** to give *deuterio oxime* **27** (120 mg, 98.1%), m.p. 202.5–205.5 °C (from Me_2CO); ν_{max}/cm^{-1} 3328 (OH), 1667 and 1620 (C=C–C=N); δ_H(270 MHz) 0.66 (3 H, s, 18-H_3), 0.78 (3 H, s, 19-H_3) and 6.14 (1 H, s, 2-H); *m/z* 403 (M^+, 9.3%), 386 [$(M - OH)^+$, 24.5], 372 (47.1), 248 (19.1), 232 (20.2), 162 (40.3), 123 (57.5), 109 (86.0), 55 (84.6) and 43 (100) (Found: M^+, 403.3763. $C_{27}H_{41}D_4NO$ requires M, 403.3742).

Photoreaction of (E)-5α-*Cholest-2-en-4-one Oxime* **26**.—A solution of oxime **26** (75 mg, 0.19 mmol) in methanol (50 cm^3) was flushed with nitrogen, and was then irradiated under nitrogen for 8 h. The product mixture was subjected to PLC [(7:1) hexane–ethyl acetate] to give three products. The most mobile product (7.8 mg, 10.7%) was the parent enone **24**. The second mobile product (3.6 mg, 4.5%) was 2α-*methoxy-5α-cholestan-4-one* **46**, m.p. 95.0–96.5 °C (from MeOH–Me_2CO); ν_{max}/cm^{-1} 1711 (C=O); δ_H(270 MHz) 0.66 (3 H, s, 18-H_3), 0.71 (3 H, s, 19-H_3), 2.84 (1 H, ddd, *J* 1.8, 5.3 and 12.9, 3-H^{β}), 3.35 (3 H, s, 2-OMe) and 3.57 (1 H, tt, *J* 5.3 and 10.9, 2-H^{β}); *m/z* 416 (M^+, 88.2%), 401 [$(M - Me)^+$, 21.9], 384 (38.7), 343 (87.3), 230 (59.4), 95 (70.3), 81 (77.9), 55 (92.6) and 43 (100) (Found: M^+, 416.3672. $C_{28}H_{48}O_2$ requires M, 416.3656).

The most polar fraction (4.2 mg, 5.4%) was (E)-2α-*methoxy-5α-cholestan-4-one oxime* **47**, m.p. 184.5–186.5 °C (from Me_2CO–MeOH); ν_{max}/cm^{-1} 3274 (OH), 1709, 1670 and 1097; δ_H(270 MHz) 0.65 (3 H, s, 18-H_3), 0.74 (3 H, s, 19-H_3), 2.20 (1 H, dd, *J* 4.3 and 12.5, 3-H^{α}), 3.36 (1 H, m, 2-H^{β}), 3.38 (3 H, s, 2-OMe) and 3.86 (1 H, dd, *J* 5.3 and 12.5, 3-H^{β}); *m/z* 431 (M^+, 28.0%), 414 [$(M - OH)^+$, 6.6], 399 [$(M - OH - Me)^+$, 100], 382 (44.3), 368 (47.5), 121 (29.2), 106 (31.8), 95 (32.4), 81 (35.0), 55 (50.8) and 43 (77.7) (Found: M^+, 431.3761. $C_{28}H_{49}NO_2$ requires M, 431.3751).

Photoreaction of (E)-*Tetradeuterio-5α-cholest-2-en-4-one Oxime* **27**.—Deuterio oxime **27** (50 mg, 0.12 mmol), as a solution in methanol (33 cm^3), was subjected to photolysis under conditions similar to those for oxime **26**, to give three products. The most mobile compound (9.1 mg, 12.6%) was the parent deuterio enone **25** (9.1 mg, 12.6%). The second most mobile compound (3.9 mg, 5.0%) was 1,1,3α,5-*tetradeuterio-2α-methoxy-5α-cholestan-4-one* **48**, m.p. 95.0–96.5 °C (from MeOH–Me_2CO); ν_{max}/cm^{-1} 1711 (C=O) and 1082; δ_H(270 MHz) 0.65 (3 H, s, 18-H_3), 0.70 (3 H, s, 19-H_3), 2.81 (1 H, d, *J* 5.3, 3-H^{β}), 3.35 (3 H, s, 2-OMe) and 3.55 (1 H, d, *J* 5.3, 2-H^{β}); *m/z* 420 (M^+, 100%), 405 [$(M - Me^+$, 15.6], 387 (36.4), 343 (83.3), 316 (37.4), 234 (27.1), 95 (27.0), 81 (29.0), 55 (37.7) and 43 (63.4) (Found: M^+, 420.3886. $C_{28}H_{44}D_4O_2$ requires M, 420.3894). The most polar product (4.4 mg, 5.4%) was (E)-1,1,3α,5-*tetradeuterio-2α-methoxy-5α-cholestan-4-one oxime* **49**, m.p. 185.5–187.5 °C (from MeOH–Me_2CO); ν_{max}/cm^{-1} 3340 (OH), 1737, 1686 and 1261; δ_H (270 MHz) 0.65 (3 H, s, 18-H_3), 0.74 (3 H, s, 19-H_3), 3.36 (1 H, d, *J* 5.3, 2-H^{β}), 3.38 (3 H, s, 2-OMe) and 3.83 (1 H, d, *J* 5.3, 3-H^{β}); *m/z* 435 (M^+, 17.8%), 418 [$(M - OH)^+$, 6.6], 403 [$(M - OH - Me)^+$, 100], 385 (36.8), 371 (35.0), 109 (28.9), 95 (29.7), 69 (33.4), 55 (43.7) and 43 (56.5) (Found: M^+, 435.4009. $C_{28}H_{45}D_4NO_2$ requires M, 435.4003).

Photoreaction of (E)-*Cholest-4-en-6-one Oxime* **32**.—(a) *In methanol.* A solution of oxime **32** (49 mg, 0.12 mmol) in methanol (40 cm^3) in a quartz tube was irradiated for 4 h. The products which were subjected to PLC [(2:1) benzene–diethyl ether] gave four fractions (A, B, C and D in order of their mobility on a TLC plate). The most mobile fraction (A; 15 mg, 33% based on the converted oxime) was the parent enone **31**. Fraction B (7 mg, 15%) was (Z)-*oxime* **50**, m.p. 152–158 °C (from MeOH); ν_{max}/cm^{-1} 3340 (OH), 976 and 928; δ_H(90 MHz) 0.66 (3 H, s, 18-H_3), 0.95 (3 H, s, 19-H_3), 2.41 (1 H, d, *J* 9.9, 7-H^{β}) and 5.96 (1 H, dd, *J* 2.7 and 4.9, 4-H); *m/z* 399 (M^+, 3.9%), 384 (13.2), 368 (4.3), 356 (16.8) and 111 (100) (Found: M^+, 399.3490. $C_{27}H_{45}NO$ requires M, 399.3500).

Fraction C (2 mg) was the starting oxime **32**. Fraction D (17 mg) was again subjected to PLC [(1:1) ethyl acetate–diethyl ether] to give the *amorphous lactam* **51** (7 mg, 15%), ν_{max}/cm^{-1} 3420 (NH) and 1639 (CONH); δ_H 0.69 (3 H, s, 18-H_3), 1.08 (3 H, s, 19-H_3), 2.86 (1 H, ddd, *J* 14.3, 3.7 and 10.3, 7a-H^{α}), 3.03 (1 H, ddd, *J* 14.3, 7.2 and 2.0, 7a-H^{β}), 5.92 (1 H, dd, *J* 3.7 and 7.2, NH) and 6.02 (1 H, t, *J* 3.7, 4-H); *m/z* 400 [$(M + 1)^+$, 31.8%], 399 (M^+, 100), 384 [$(M - Me)^+$, 12.4], 371 (11.7), 151 (39.3) and 123 (46.9); λ_{max}(MeOH)/nm 206 (ε 16 000) (Found: M^+, 399.3490).

(b) *In benzene–glacial acetic acid* (94:6). A solution of the oxime **32** (53 mg, 0.13 mmol) in the mixed solvent (42.6 cm^3) was flushed with nitrogen and was then irradiated. The product was subjected to PLC [(2:1) benzene–diethyl ether] to give four fractions (A, B, C and D in order of their mobility on PLC). Fraction A was again subjected to PLC [(1:1) benzene–dichloromethane] to give the parent ketone **31** (6 mg, 15% based on the converted oxime). Fraction B was (*Z*)-oxime **50** (11 mg, 27%). Fraction C was the starting (*E*)-oxime **32** (12 mg). Fraction D was again subjected to PLC [(1:1) ethyl acetate–diethyl ether] to give lactam **51** (16 mg, 39%).

Beckmann Rearrangement of (E)-*Cholest-4-en-6-one Oxime* **32**.—(a) *With thionyl dichloride*. To a solution of oxime **32** (52 mg, 0.13 mmol) in 1,4-dioxane (2 cm^3) was added thionyl dichloride (0.03 cm^3). The solution was stirred for 50 min at room temperature. Water was added to this solution. The reaction mixture was extracted with diethyl ether. The extract was washed successively with aq. 5% Na_2CO_3 and water, and was then dried over anhydrous $MgSO_4$. Removal of the solvent gave a product (31 mg), which was subjected to PLC [(2:1) benzene–diethyl ether] to give *cyclic enamine* **52** (24 mg, 46%) as a gum, ν_{max}/cm^{-1} 3390 (NH), 1659 (CONH) and 1651; δ_H 0.68 (3 H, s, 18-H_3), 0.96 (3 H, s, 19-H_3), 5.54 (1 H, t, *J* 3.6, 4-H) and 7.14 (1 H, br s, NH); *m/z* 400 [(M + 1)$^+$, 32.0%], 399 (M^+, 100), 371 (16.9), 328 (14.8), 151 (15.5) and 123 (27.5); λ_{max}(MeOH)/nm 211 (ε 6200) (Found: M^+, 399.3523. $C_{27}H_{45}NO$ requires M, 399.3500).

(b) *With* $POCl_3$. To a solution of the oxime **32** (50 mg, 0.13 mmol) in pyridine (~0.1 cm^3) was added a mixture of $POCl_3$ (0.32 cm^3) in pyridine (0.7 cm^3) at 0 °C. The solution was stirred for 4 h at room temperature and was then acidified by addition of conc. hydrochloric acid (0.14 cm^3). To the solution was added water–ice; the reaction mixture was extracted with diethyl ether. The extract was worked up in the usual manner. The product was subjected to PLC to give two fractions. The more mobile fraction (22 mg) could not be characterized. The less mobile fraction (28 mg, 56%) was lactam **52** described above.

(E)-*Cholest-5-en-4-one Oxime* **34**.—This α,β-unsaturated ketone oxime[3] was prepared by the standard method. M.p. 172–174 °C (from Me_2CO) (lit.,[3] 168.170 °C); δ_H(270 MHz) 0.68 (3 H, s, 18-H_3), 0.94 (3 H, s, 19-H_3), 3.30 (1 H, dd, *J* 12.7 and 2.6, 3-H^β) and 5.87 (1 H, dd, *J* 5.4 and 2.4, 6-H); *m/z* 399 (M^+, 63.0%), 382 [(M − OH)$^+$, 31.2], 356 (100) and 331 (26.4); λ_{max}(MeOH)/nm 234 (ε 7800).

Photo-Beckmann Rearrangement of (E)-*Cholest-5-en-4-one Oxime* **34**.—A solution of the oxime **34** (120 mg) in methanol (80 cm^3) was irradiated for 10 h under nitrogen. The product was subjected to PLC [silica gel; (7:1) dichloromethane–diethyl ether] to give five fractions [A (19 mg), B (8 mg), C (13 mg), D (11 mg), and E (33 mg) in order of their mobility on a TLC plate]. Fraction A (17.0%) was the parent ketone **33**. Fraction B was the starting oxime **34**. Fraction C (11.6%) was unstable, amorphous (Z)-*cholest-5-en-4-one oxime* **53**, δ_H(270 MHz) 0.69 (3 H, s, 18-H_3), 0.95 (3 H, s, 19-H_3) and 5.98 (1 H, dd, *J* 2.2 and 5.9) (Found: M^+, 399.3492. $C_{27}H_{45}NO$ requires M, 399.3500); Fraction D (9.8%) was 4a-*aza*-4a-*homocholest-5-en-4-one* **54**, m.p. 169–171 °C (from Me_2CO); ν_{max}/cm^{-1} 3156 (NH) and 1688 and 1676 (lactam C=O); δ_H(270 MHz) 0.68 (3 H, s, 18-H_3), 1.01 (3 H, s, 19-H_3), 5.54 (1 H, br d, 6-H) and 6.89 (1 H, br s, NH); *m/z* 399 (M^+, 100%), 384 [(M − Me)$^+$, 20.3], 342 (14.1), 108 (27.0), 96 (18.5), 55 (25.1) and 43 (29.7); λ_{max}(MeOH)/nm 221 (ε 6500) (Found: M^+, 339.3498).

Fraction E (29.5%) was 4-*aza*-4a-*homocholest-5-en*-4a-*one* **55**, m.p. 178–180 °C (from Me_2CO); ν_{max}/cm^{-1} 3192 (NH) and 1657 and 1639 (lactam C=O); δ_H(270 MHz) 0.68 (3 H, s, 18-H_3), 1.04 (3 H, s, 19-H_3), 3.19 (2 H, m, 3-H_2), 5.96 (1 H, dd, *J* 2.2 and 5.5, 6-H) and 6.45 (1 H, br s, NH); λ_{max}(MeOH)/nm 217 (ε 14 000) (Found: M^+, 339.3495).

Beckmann Rearrangement of (E)-*Cholest-5-en-4-one Oxime* **34**.—To a solution of the *E*-oxime (50 mg) in 1,4-dioxane (2 cm^3) was added thionyl dichloride (0.1 cm^3); the solution was then stirred for 5 min at room temperature. The reaction mixture was worked up as in the previous case. The crude product was subjected to PLC [silica gel; (4:1) dichloromethane–diethyl ether] to give the enamine **54** (30 mg, 60%) obtained by the photorearrangement described above.

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