Photoinduced Molecular Transformations. Part 133.[1] New Photoinduced Deconjugation of Steroidal α,β-Unsaturated Cyclic Ketone Oxime into the β,γ-Unsaturated Isomer involving Stereospecific Proton Transfer.[2]

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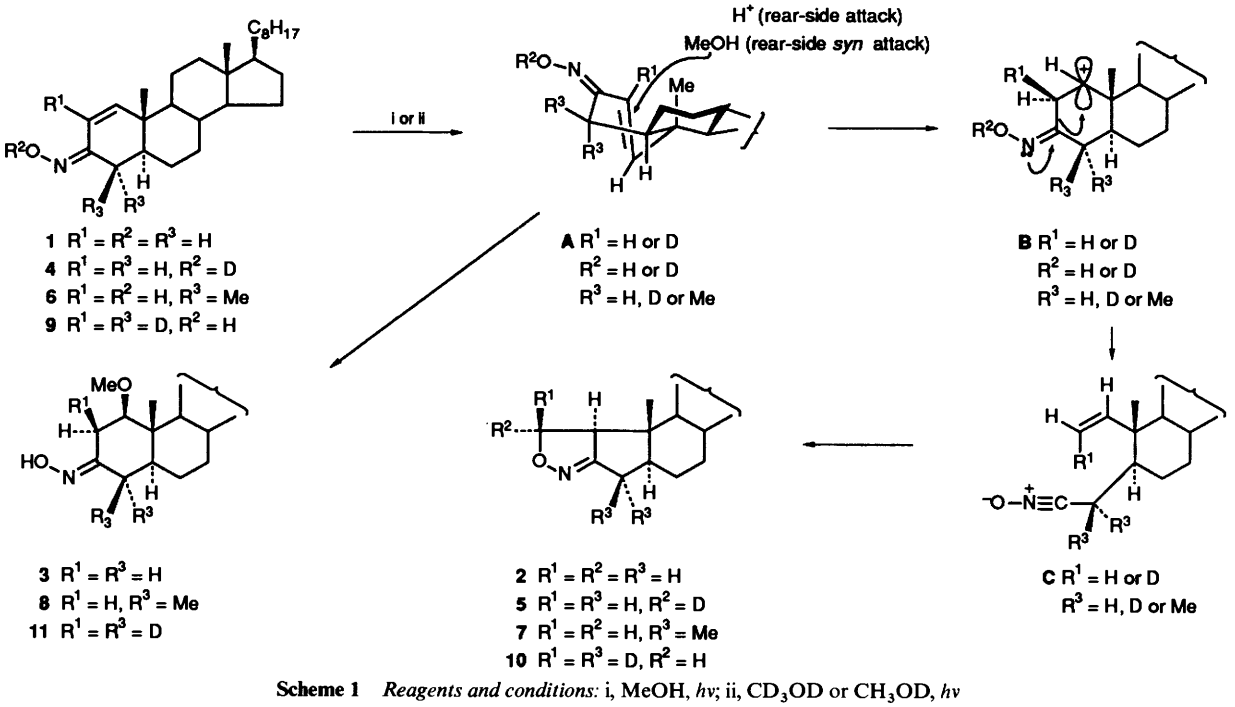
Irradiation of 1-methyl-5α-cholest-1-en-3-one oxime or its 4,4-dimethyl derivative in either a protic or an aprotic solvent gave 1-methylene-5α-cholestan-3-one oxime or the corresponding 4,4-dimethyl derivative, arising from an unprecedented photodeconjugation of α,β-enone oximes into the β,γ-isomers. Neither the expected isoxazole derivative (a product in the photoreaction of 5α-cholest-1-en-3-one oxime or its 4,4-dimethyl derivative) nor the unsaturated lactam that arises from a photo-Beckmann rearrangement was formed. Deuterium-labelling studies on the photoreactions of 1-methyl-5α-cholest-1-en-3-one oxime established that either a proton or a deuteron is stereospecifically introduced at the 2α-position of the steroidal oxime in this photodeconjugation. A pathway which involves the sterospecific addition of either a proton or deuteron to the photogenerated, twisted double bond of the oximes from the rear side of the steroidal framework, followed by the loss of a proton or deuteron from the 1-methyl group of the resulting carbocation intermediate, is proposed regarding the formation of β,γ-unsaturated oximes from the excited α,β-unsaturated oximes.

In a previous paper,[3] we reported on a novel stereospecific photorearrangement and stereospecific addition of methanol in steroidal α,β-unsaturated cyclic ketone oximes. Thus, the irradiation of 5α-cholest-1-en-3-one oxime **1** or its 4,4-dimethyl derivative **6** in either a protic or an aprotic solvent gave 4′α,5′-dihydro-4-nor-5α-cholestano[2,1-*c*]isoxazole **2** or the corresponding 3,3-dimethyl derivative **7** arising from an unprecedented photorearrangement. 1β-Methoxy-5α-cholestan-3-one oxime **3** and its 4,4-dimethyl derivative **8**, arising from an unprecedented photoaddition of methanol to the double bond of the enone oximes, were the accompanying products in both of these photoreactions, and no lactams were formed (as outlined in Scheme 1).

Deuterium-labelling studies of the photoreactions of 5α-cholest-1-en-one oxime **1** and its trideuteriated derivative **9** established that either a deuteron or a proton is stereospecifically introduced at the 2α-position of the steroidal oxime in these phototransformations; photolysis of the deuterio oxime **4** (prepared by dissolution of oxime **1**) gave the 5′α-deuterioisoxazole **5** and photolysis of [2,4,4-$^2H_3$]cholest-1-en-3-one oxime **9** in methanol resulted in formation of the trideuterioisoxazole **10** and methanol adduct **11**, in which a proton was stereospecifically introduced at the 5′α- or 2α-position, respectively.

The formation of the isoxazoles **2**, **5**, **7** and **10** from the excited oximes **1**, **4**, **6** and **9**, based on these labelling studies, is outlined



Scheme 1 *Reagents and conditions:* i, MeOH, *hν*; ii, CD_3OD or CH_3OD, *hν*

in Scheme 1. The photorearrangement involves an unprecedented stereospecific addition of either a proton or a deuteron to the photogenerated, twisted double bond of the oximes **A** from the rear side, followed by fragmentation of the resulting carbocation **B** and an intramolecular 1,3-dipolar addition of the nitrile oxide intermediate **C**. The mechanism for the photoaddition of methanol is also outlined in Scheme 1. It involves a stereospecific *syn* addition of methanol to the photoregenerated, twisted, ground-state double bond of the oximes **A** from the rear side.

As stated in our previous paper, photochemical transformations (in general) and phototransformations, such as described here (in particular), which can be achieved solely with photons in the presence of a solvent, have great potential utility in organic synthesis. We therefore decided to investigate more thoroughly the structure–product relationship in the photoreaction of steroidal α,β-unsaturated cyclic ketone oximes. Steroids are excellent probes for investigating organic photoreactions.

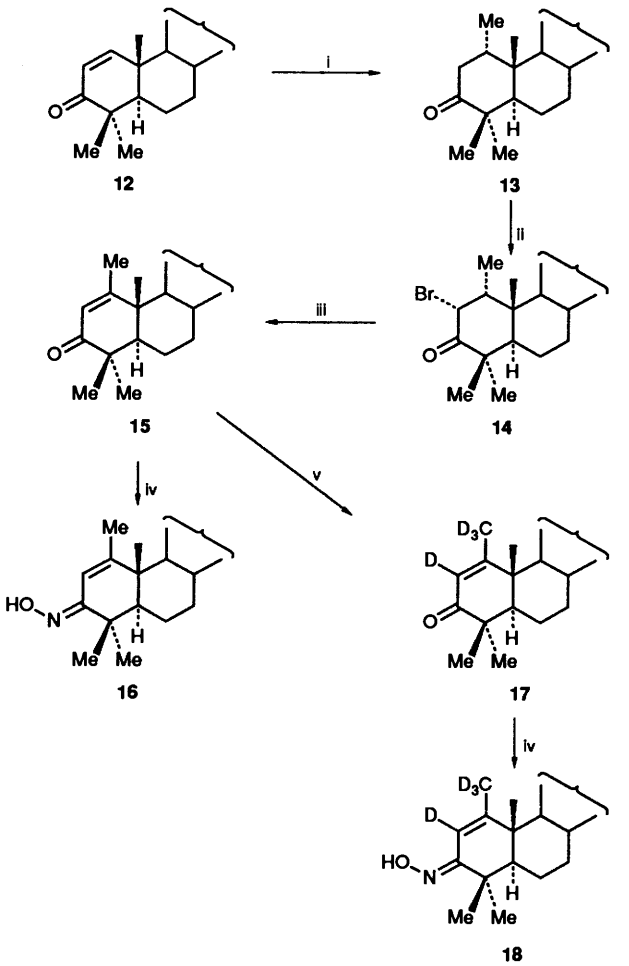
Following our previous paper, we report here on details concerning the effects of the substitution of the hydrogen attached to the β-carbon of the α,β-unsaturated cyclic ketone oximes, **1**, **6** and **9**.[2]

We have found that the effect of replacement of the β-hydrogen of the C–C double bond of the oxime by a methyl group is profound, and that irradiation of β-methyl-α,β-unsaturated oximes **16**, **18** and **22** in either a protic or an aprotic solvent results in an unprecedented isomerization of the α,β-unsaturated double bond to the β,γ-isomer involving the stereospecific addition of a proton.

Results

Preparation of 1-*Methyl-α,β-unsaturated Cyclic Ketone Oximes* **16**, **18**, **22** *and* **23**.—The substrates, (*E*)-1,4,4-trimethylcholest-1-en-3-one oxime **16**, (*E*)-2-deuterio-4,4-dimethyl-1-trideuteriomethyl-5α-cholest-1-en-3-one oxime **18**, and (*E*)- and (*Z*)-1-methyl-5α-cholest-1-en-3-one oximes **22** and **23** used for our study of the photoreaction were synthesized as outlined in Schemes 2 and 3. Conjugate addition of a methyl group to 4,4-dimethylcholest-1-en-3-one **12**[4] with lithium dimethylcuprate[5] in diethyl ether at room temperature gave 1α,4,4-trimethyl-5α-cholestan-3-one **13** in 93% yield. The monobromination of trimethyl-5α-cholestan-3-one **13** with pyridine hydrobromide perbromide[6] in glacial acetic acid at 60 °C gave 2α-bromo-1α,4,4-trimethyl-5α-cholestan-3-one **14** in 91% yield. The configuration of the 2α-bromo substituent of the ketone **14** was established by a nuclear Overhauser enhancement (NOE) measurement. Enhancements of the signal areas of the 1β-H (δ 2.37) and 2β-H (δ 5.57) were observed when the signal due to the 10β-Me was irradiated. The 2α-bromo steroid **14** was then subjected to dehydrobromination by treatment with calcium carbonate in *N*,*N*-dimethylacetamide (DMA)[7] under reflux for 20 h to give 1,4,4-trimethyl-5α-cholest-1-en-3-one **15** in 91% yield. Heating of the enone **15** with hydroxylamine and sodium acetate in ethanol under reflux gave the corresponding *E*-oxime **16** in 89% yield. Deuteriation of enone **15** with ethan[^{2}H]ol and sodium for 20 h at room temperature gave 2-deuterio-4,4-dimethyl-1-trideuteriomethyl-5α-cholest-1-en-3-one **17**. Oximation of this tetradeuteriated ketone **17** using the procedure described for enone **15** gave the corresponding *E*-oxime **18** (Scheme 2).

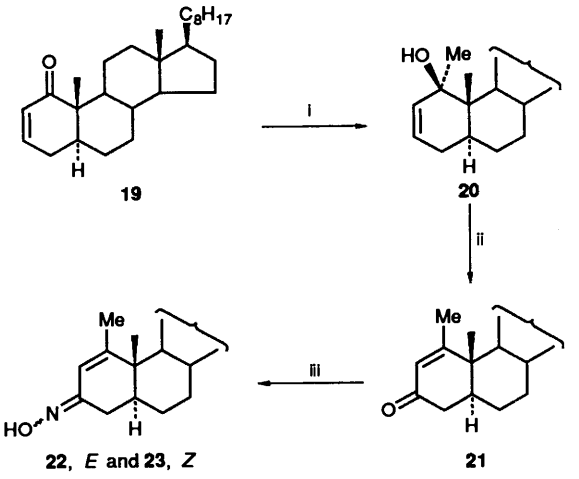
We then synthesized 1-methyl-5α-cholest-1-en-3-one **21**[8] through methylation of 5α-cholest-2-en-1-one **19**[9,10] with methyllithium followed by oxidation of the resulting allylic alcohol **20** with pyridinium chlorochromate (PCC), since a series of the above mentioned reactions for the synthesis of 1-methyl enone **15** failed to give 1-methyl enone **21** Thus,



Scheme 2 *Reagents and conditions:* i, Me_2CuLi–Et_2O, 0 °C; ii, pyridine·HBr·Br_2, AcOH, 60 °C; iii, $CaCO_3$, DMA, reflux; iv, NH_2OH·HCl, EtOH, AcONa, reflux; v, EtOD, Na

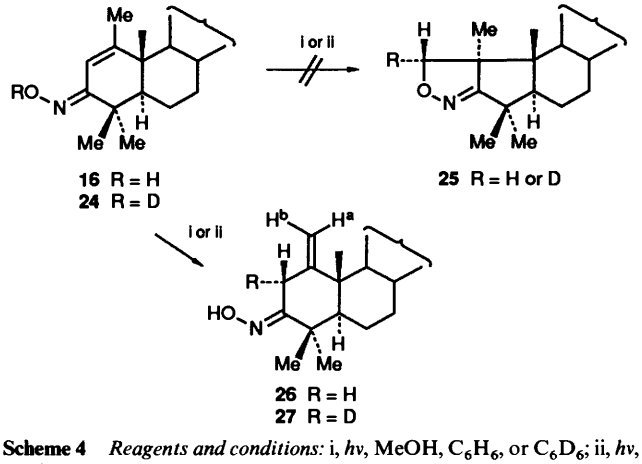
treatment of 5α-cholest-2-en-1-one **19** with methyllithium in tetrahydrofuran (THF) gave 1α-methyl-5α-cholest-2-en-1β-ol **20**. Oxidation of the allylic alcohol **20** with PCC[11] in refluxing dichloromethane for 24 h gave the enone **21**[3] in 50% yield (from enone **19**). Oximation of the enone **21** by the standard method at room temperature gave a mixture of the *E*- and *Z*-oxime **22** and **23** in 88% yield (Scheme 3).

Photoreactions of Oxime **16** (*Scheme* 4).—Photoreactions of oxime **16** in methanol were carried out with a low-pressure mercury arc generated by a Rayonet RPR photochemical chamber reactor, as described in a previous paper.[3] Thus, a solution of oxime **16** (140 mg) in methanol in a quartz vessel was irradiated under nitrogen for 4 h at room temperature to give a *single* product **26** in 69% yield. Combustion analysis and mass spectrometry of product **26** indicated that it was an isomer of the starting oxime. Its IR spectrum indicated the presence of a hydroxyimino group. Its NMR spectrum exhibited two singlets, at δ 4.68 (1 H) and 4.92, assignable to the exomethylene protons; two doublets, at δ 3.27 (1 H) and 3.43 (1 H) with *J* 17.6 Hz, were each assignable to the isolated methylene protons flanked by the two trigonal carbons. It also exhibited a singlet (3 H) at δ 1.03 assignable to the 19-H_3. These spectral results, together with a consideration of the possible pathways for its formation, indicated that product **26** was (*E*)-4,4-dimethyl-1-methylene-5α-cholestan-3-one oxime. NOE measurements in conjunction with the molecular model



Scheme 3 *Reagents and conditions:* i, MeLi, THF; ii, PCC, CH_2Cl_2; iii, NH_2OH·HCl, EtOH, AcONa

of product **26** established that the two singlets at δ 4.68 and 4.92 in the ^1H NMR spectrum arise from H^a and H^b of the exomethylene protons of product **26** (Scheme 4), and that the

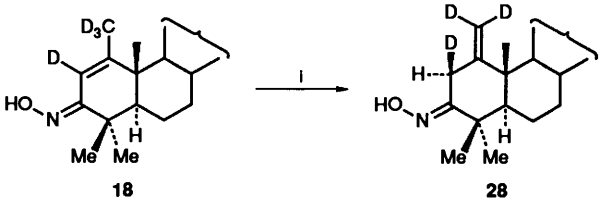


Scheme 4 *Reagents and conditions:* i, *hv*, MeOH, C_6H_6, or C_6D_6; ii, *hv*, MeOD

two doublets at δ 3.27 and 3.43 in the spectrum arise from 2α-H and 2β-H, respectively. Irradiation of the doublet at δ 3.27 resulted in an enhancement of the singlet at δ 4.92 as well as the doublet at δ 3.43. Irradiation of the singlet at δ 1.03 (19-H_3) resulted in an enhancement of the singlet at δ 4.68 as well as the doublet at δ 3.27. Moreover, irradiation of the doublet at δ 3.43 resulted in an enhancement of the singlet at δ 1.03 (19-H_3) as well as the doublet at δ 3.27. Neither the expected isoxazole derivative **25** nor the unsaturated lactam that arises from the photo-Beckmann rearrangement was found in the product. An identical product was obtained when a benzene solution of oxime **16** was irradiated for 7 h or a hexadeuteriobenzene solution of oxime **16** was irradiated for 8 h, and was obtained in 89 and 75% yield, respectively.

Deuterium-labelling Experiments on the Photodeconjugation of Oxime **16** *and its Tetradeuterio Derivative* **18**.—When the hydroximino proton of oxime **16** was exchanged by deuterium by dissolution in methan[^2H]ol to give intermediate **24** and the resulting solution irradiated under the above mentioned conditions, a *single* monodeuteriated product **27** was obtained. The ^1H NMR spectrum exhibited a signal at δ 3.39 as a singlet and a signal (3 H) at δ 1.03 also as a singlet assignable to 2-H and 19-H respectively. It also exhibited a doublet (1 H) at δ 4.68 and a singlet (1 H) at δ 4.92 assignable to H^a and H^b of the methylene group (Scheme 4). The configuration of 2-H in product **27** was then established to be β by means of NOE measurements; irradiation of the singlet at δ 1.03 (19-H_3) resulted in an enhancement, of the signal areas due to 2-H and to H^a. Irradiation of the signal due to 2-H of product **27** resulted in an enhancement of signal area due to the 19-H_3 and H^b. Moreover, irradiation of the signal due to H^b (δ 4.92) resulted in an enhancement of the signal areas of H^a and 2-H. Therefore, the deuteron is stereospecifically incorporated into the 2α position in compound **27**.

On the other hand, when tetradeuteriated oxime **18** was photolysed in methanol under the conditions described above, a *single* trideuteriated photoproduct **28** was obtained (Scheme 5).

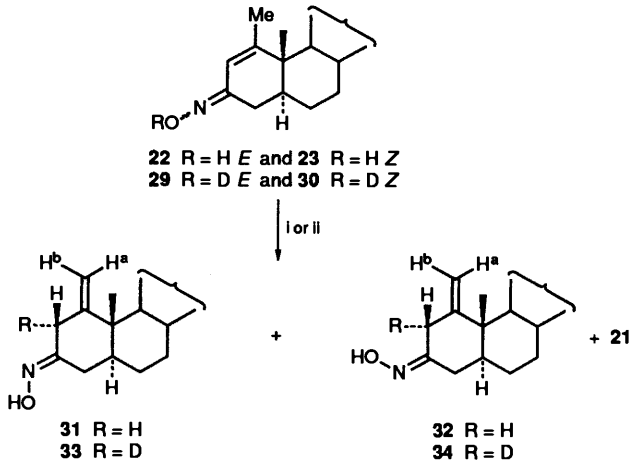


Scheme 5 *Reagents and conditions:* i, *hv*, MeOH

The ^1H NMR spectrum of product **28** exhibited a singlet at δ 3.24 assignable to 2-H. The configuration of the incorporated 2-H in product **28** was again assigned to be α by means of NOE measurements; irradiation of 19-H_3 resulted in no enhancement of 2-H and, conversely, irradiation of 2-H resulted in no enhancement of 19-H_3.

Photoreaction of Oximes **22** *and* **23**.—We then examined the photoreaction of (*E*)- and (*Z*)-1-methyl-5α-cholest-1-en-3-one oximes **22** and **23** in order to examine the effects of the dimethyl groups attached to C-4 of oximes **16** and **18**. Photoreaction of a mixture of the *E* and *Z* oximes, **22** and **23**, in methanol under the conditions described above gave a 1:1 mixture of the *E* and *Z* oximes, **31** and **32**, in 60% yield (based on the consumed oxime) with accompanying formation the enone **21** (20%). The molecular formula of oximes **31** and **32** was shown to be $C_{28}H_{47}NO$ by high-resolution mass spectrometry. The ^1H NMR spectrum of the mixture of isomeric oximes indicated two singlets (each ½ H) at δ 4.65 and δ 4.67, assignable to 1′-H^a of either the *E* and *Z* or the *Z* and *E* isomer. It also exhibited a singlet at δ 4.85 (1 H) assignable to 1′-H^b of the *E* and *Z* isomers. In addition to these signals it also exhibited four doublets at δ 2.81, 2.88, 3.09 and 3.77 (each ½ H) with *J* 16.1, 15.6, 15.6 and 16.1 Hz. These doublets are assignable to the 2β-H of *Z*-isomer **32**, the 2α-H of *E* isomer **31**, the 2β-H of *E* isomer **31** and the 2α-H of *Z* isomer **32**, respectively. The assignment of the last signal (δ 3.77) is based on its considerable downfield shift compared with the corresponding signal of isomer **31**. This shift is attributable to a deshielding by the hydroxyimino group. The spectrum also exhibited a double-doublet signal at δ 3.00 (½ H) with *J* 3.4 and 16.6 Hz, ascribable to the 4α-H of *E* isomer **31**. Its downfield shift due to deshielding by the hydroxyimino group confirms the geometry. A comparison of the ratio of the signals due to the two isomers indicated the ratio of the isomers to be 1:1.

Deuterium-labelling Experiments on the Photodeconjugation of Oximes **22** *and* **23**.—A deuterium-labelling study of the photodeconjugation of oximes, **22** and **23**, was then carried out. Irradiation of oximes **29** and **30** in methan[^2H]ol under the conditions described for the deuterium labelling of oxime **16** gave a 1:1 mixture of the *E* and *Z* isomers of monodeuteriated 1-methylene-5α-cholestan-3-one oxime, **33** and **34** in 60% yield (based on the consumed oximes) with accompanying formation of the parent ketone **21** (12%) (Scheme 6). The ^1H NMR



Scheme 6 *Reagents and conditions:* i, *hv*, MeOH; ii, *hv*, MeOD

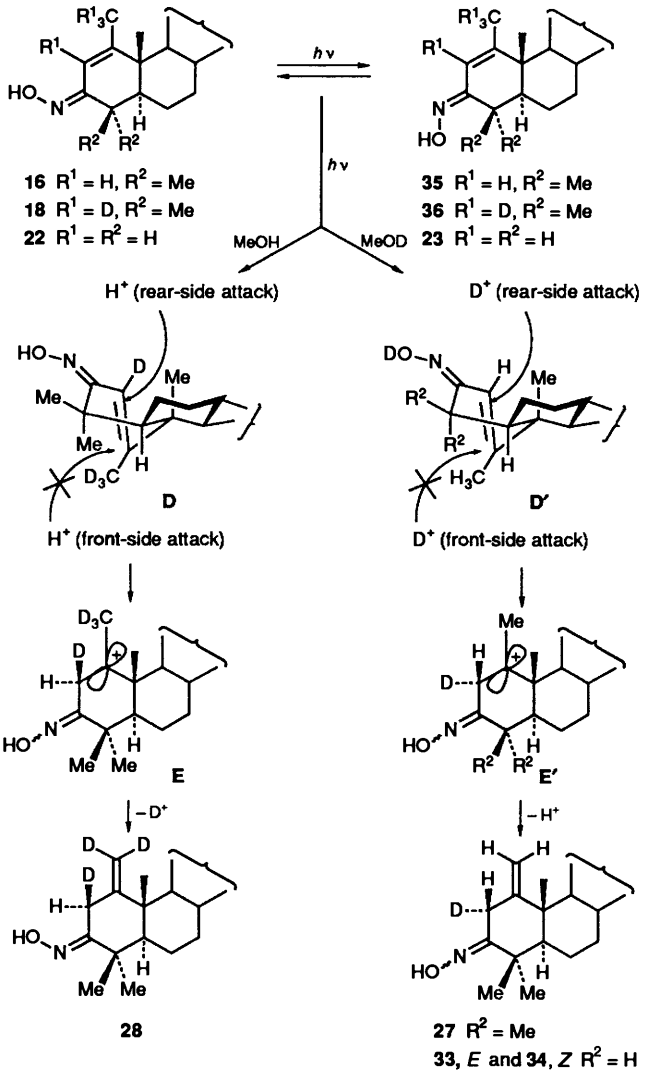
spectrum of oximes **33** and **34** exhibited an absence of signals attributable to their 2α-H and the presence of two singlets, at δ 2.80 and 3.07, ascribable to the 2β-H of isomers **33** and **34**. Details concerning further spectral analysis are given in the Experimental section. This experiment firmly established that the deuterium is stereospecifically incorporated into the C-2α position of the two oxime isomers, **33** and **34**.

These results are entirely parallel to those obtained regarding the photodeconjugation of the 4,4-dimethyl derivatives, **16** and **18**.

Pathways of the Photodeconjugation of Enone Oximes **16**, **18** *and* **22** (*Scheme* 7).—The pathways leading to the β,γ-enone oximes (such as **27**, **28**, **33** and **34**) from the excited α,β-enone oximes (**16**, **18** and **22**) are outlined in Scheme 7. Irradiation of oximes (such as **16**, **18**, **22**, **35**, **36** and **23**) in a protic or an aprotic solvent generates a ground-state intermediate, **D** or **D′** in which the C=C bond is twisted by more than 90°, *via* either singlet or triplet excited *Z* and *E* oximes The stereospecific protonation or deuteriation with either the hydroxyimino proton or the protic solvent then takes place at C-2 of the intermediate, **D** or **D′**, from the *rear side* of the steroidal framework to give carbocation **E** or **E′**.[3] The approach of a proton or deuteron from the front side of the steroids is blocked by the ring. The proton, which is attached to C-2α, can be supplied from either the hydroxyimino proton or the protic solvent in either an intra- or an intermolecular manner. The mechanism for the formation of this carbocation intermediate, **E** or **E′**, is entirely analogous to that involved in the photorearrangement of enone oximes **1**, **6** and **9** to isoxazoles **2**, **5**, **7** and **10** (as outlined in Scheme 1 [3]).

While fragmentations leading to the formation of isoxazoles **2**, **5**, **7** and **10** take place from the carbocation intermediate **B** generated from the excited enones **1**, **6** and **9** (Scheme 1), the loss of either a proton or a deuteron takes place in preference to fragmentation from the carbocation intermediate, **E** or **E′**, generated from the excited 1-methyl enones **16**, **18** and **22** (Scheme 7).

The results reported in this paper provide confirmation of the intervention of carbocations, such as **B**, in the photorearrangement of enone oximes such as compounds **1**, **6** and **9** to isoxazoles **2**, **5**, **7** and **10** as outlined in Scheme 1.



Scheme 7

Experimental

M.p.s were determined with a Yanagimoto m.p. apparatus and are uncorrected. The IR spectra were determined for Nujol mulls (unless stated otherwise) with either a Hitachi 285 grating IR spectrophotometer or a JASCO IR 810 IR spectrophotometer. The ^1H NMR spectra were determined with either a Hitachi R90H high-resolution spectrometer operating at 90 MHz, a JEOL JNM-GX 270 FT high-resolution spectrometer operating at 270 MHz, or a JEOL JNM-EX 400 FT high-resolution spectrometer operating at 400 MHz (solvent $CDCl_3$; $SiMe_4$ as internal reference), unless stated otherwise. The mass spectra were determined with either a JEOL JMS-DX 300 or a JMS-OISG-2 spectrometer (70 eV). The UV spectra were measured with a JASCO Ubest-30 UV/VIS spectrophotometer. Elemental analyses were performed at the Faculty of Pharmaceutical Sciences. Preparative TLC (PLC) was carried out on Merck silica gel 60 PF_{254} (Art 7747). Column chromatography was carried out with silica gel 60 (Art 7734).

1α,4,4-*Trimethyl*-5α-*cholestan*-3-*one* **13**.—To a solution of copper(I) iodide (514 mg, 27 mmol) in diethyl ether (10 cm^3) at 0 °C under nitrogen was added (dropwise) methyllithium (3.6 cm^3) (1.5 mol dm^{-3} diethyl ether solution). After the solution had been stirred for 15 min a solution of enone **12**[4] (520 mg, 1.26 mmol) in diethyl ether (9 cm^3) was added. The reaction mixture was stirred for 1 h. After addition of saturated aq. ammonium chloride to the solution, the organic layer was separated. The aqueous layer was extracted with diethyl ether. The combined

ethereal solutions were washed successively with water and saturated brine, and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave 1α-methyl ketone **13**, which was subjected to PLC (CH_2Cl_2) to give pure *ketone* **13** (504 mg, 93%), m.p. 116–117 °C (from methanol–acetone); ν_{max}/cm^{-1} 1710 (C=O); δ(270 MHz) 0.67 (3 H, s, 18-H_3) 0.83 (3 H, d, *J* 7.0, 1α-Me), 1.037 and 1.043 (each 3 H, each s, 4-Me_2), 1.19 (3 H, s, 19-H_3) and 3.00 (1 H, dd, *J* 5.7 and 15.2, 2β-H); *m/z* 428 (M^+, 100%), 413 [$(M - Me)^+$, 28.3], 357 (25.7), 343 (21.4), 315 (27.1), 287 (36.7), 274 (22.7), 273 (27.9) and 95 (77.9) (Found: C, 83.8; H, 12.5. $C_{30}H_{52}O$ requires C, 84.04; H, 12.23%).

2α-Bromo-1α,4,4-trimethyl-5α-cholestan-3-one **14**.—Pyridine hydrobromide perbromide (164 mg, 0.51 mmol), prepared according to the procedure of Djerassi and Scholz,[6] was added to a solution of the trimethyl ketone **13** (150 mg, 0.75 mmol) in glacial acetic acid (3.6 cm^3) at 60 °C. This solution was stirred for 1 h before the solvent was removed (rotary evaporator). To the residue were added water and diethyl ether. After separation of the organic layer, the aqueous layer was extracted with diethyl ether. The combined organic layers were washed successively with saturated aq. sodium carbonate, water, and finally saturated brine; they were then dried over anhydrous magnesium sulfate. Evaporation of the solvent gave *bromo ketone* **14** in almost quantitative yield. After purification by PLC (CH_2Cl_2), the product was recrystallized from methanol–diethyl ether to give an analytical specimen, m.p. 118.0–119.5 °C; ν_{max}/cm^{-1} 1729 (C=O); δ(270 MHz) 0.68 (3 H, s, 18-H_3), 0.91 (3 H, d, *J* 7, 1α-Me), 1.09 (3 H, s, 4-Me), 1.13 (3 H, s, 4-Me), 1.32 (3 H, s, 19-H_3), 2.37 (1 H, dq, *J* 5 and 7, 1β-H) and 5.57 (1 H, d, *J* 5, 2β-H); *m/z* 506 [$(M + 2)^+$, 16.0%], 508 (M^+, 16.0), 493 [$(M - Me)^+$, 6.4], 427 (86.0), 81 (65.5), 69 (100), 57 (59.2) and 43 (50.0) (Found: C, 70.8; H, 10.5; Br, 15.5. $C_{30}H_{51}BrO$ requires C, 70.84; H, 10.30; Br, 15.71%).

1,4,4-Trimethyl-5α-cholest-1-en-3-one **15**.—Calcium carbonate (2 g, 20 mmol) was added to a solution of DMA (12 cm^3). The solution was heated under reflux for 20 h, and was then filtered through Celite before water and diethyl ether were added. After separation of the organic layer, the aqueous layer was extracted with diethyl ether. The combined organic layers were washed successively with 0.5 mol dm^{-3} hydrochloric acid, water and finally saturated brine, and then dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a gummy *1-methyl enone* **15**, which was purified by PLC (CH_2Cl_2) (762 mg, 91%), m.p. 49–52 °C; ν_{max}(neat)/cm^{-1} 1672 (C=O); δ(270 MHz) 0.71 (3 H, s, 18-H_3), 1.075 (6 H, s, 4-Me and 19-H_3), 1.109 (3 H, s, 4-Me), 2.06 (3 H, d, *J* 1.1, 1-Me) and 5.76 (1 H, d, *J* 1.1, 2-H); *m/z* 426 (M^+, 48.2%), 411 [$(M - Me)^+$, 17.4], 398 [$(M - CO)^+$, 100], 383 (28.0), 316 (46.6), 203 (42.6), 151 (46.4), 135 (67.7), 107 (49.0), 96 (80.3) and 43 (76.0) (Found: M^+, 426.3883. $C_{30}H_{50}O$ requires *M*, 426.3862).

1,4,4-Trimethyl-5α-cholest-1-en-3-one Oxime **16**.—The enone **15** (185 mg, 0.937 mmol), hydroxylamine hydrochloride (170 mg, 2.45 mmol) and sodium acetate (130 mg, 1.6 mmol) in ethanol (9 cm^3) were heated under reflux for 18 h. The solution was worked up as in the previous case. The oxime was purified by PLC [(8:1) benzene–diethyl ether] to give pure *oxime* **16** (169 mg, 89%), m.p. 180–181 °C (from acetone) (Found: C, 81.7; H, 11.65; N, 3.25. $C_{30}H_{51}NO$ requires C, 81.57; H, 11.64; N, 3.62%); ν_{max}/cm^{-1} 3236 (OH); δ(90 MHz) 0.69 (3 H, s, 18-H_3) 1.01 (3 H, s, 19-H_3), 1.14 (6 H, s, 4-Me_2), 2.02 (3 H, d, *J* 1.1, 1-Me) and 6.43 (1 H, d, *J* 1.1, 2-H); *m/z* 441 (M^+, 65.3%), 424 [$(M - OH)^+$, 50.7], 398 (21.1), 328 (29.4), 310 (19.4), 247 (18.1), 180 (56.5), 167 (100) and 95 (65.9); λ_{max}(MeOH)/nm 236 (ε 11 700).

Photoreaction of (E)-1,4,4-Trimethylcholest-1-en-3-one Oxime **16**.—(a) *In methanol.* A solution of enone oxime **16** (140 mg, 0.689 mmol) in methanol (70 cm^3) in a quartz vessel was flushed with nitrogen. The solution was irradiated with a low-pressure mercury arc in a Rayonet photochemical reactor for 4 h under nitrogen. Evaporation of the solvent (rotary evaporator) gave a product, which was purified by PLC [(8:1) benzene–diethyl ether] to give *4,4-dimethyl-1-methylene-5α-cholestan-3-one oxime* **26** (97 mg, 69%) (Found: C, 81.3; H, 11.6; N, 3.2%; M^+, 441.3965. $C_{30}H_{51}NO$ requires C, 81.57; H, 11.64; N, 3.17%, *M*, 441.3971), m.p. 172–174 °C (from acetone); ν_{max}/cm^{-1} 3262 (OH), 1637 (C=N), 947 and 893; δ(270 MHz) 0.69 (3 H, s, 18-H_3), 1.03 (3 H, s, 19-H_3), 1.14 (6 H, s, 4-Me_2), 3.27 (1 H, d, *J* 17.6, 2-H), 3.43 (1 H, d, *J* 17.6, 2-H) and 4.68 and 4.92 (each 1 H, s, =CH_2); *m/z* 441 (M^+, 52%), 424 (36) and 43 (100).

(b) *In deuteriomethanol.* The enone oxime (70 mg, 0.344 mmol) in methan[^{2}H]ol (40 cm^3) was heated under reflux for 5 min under nitrogen. The solution was then irradiated for 3.5 h as mentioned above. After evaporation of the solvent, the product was purified by PLC [(5:1) benzene–diethyl ether] to give *2α-deuterio-1-methylene-5α-cholestan-3-one oxime* **27** (50 mg, 71%), m.p. 169–172 °C (from acetone); ν_{max}/cm^{-1} 3260 (OH), 1635 (C=N), 950 and 933; δ(270 MHz) 0.69 (3 H, s, 18-H_3), 1.03 (3 H, s, 19-H_3), 1.14 (6 H, s, 4-Me_2), 3.39 (1 H, s, 2β-H), 4.68 (1 H, d, *J* 1.0, H^a) and 4.92 (1 H, s, H^b); *m/z* 442 (M^+, 50.7%), 425 [$(M - OH)^+$, 42.2], 167 (61.0), 95 (64.1), 81 (60.6), 69 (67.8), 55 (82.7) and 43 (100) (Found: M^+, 442.4042. $C_{30}H_{50}DNO$ requires *M*, 442.4034).

(c) *In benzene.* A solution of the enone oxime (140 mg) in dry benzene (70 cm^3) under nitrogen was irradiated under the conditions mentioned above for 7 h. Evaporation of the solvent gave a mixture of products, which were subjected to PLC [(8:1) benzene–diethyl ether] to give β,γ-enone oxime **26** (88 mg, 63%) and the starting oxime **16** (41 mg, 29% recovery). The yield of the β,γ-enone oxime based on consumed oxime was 89%.

(d) *In hexadeuteriobenzene.* A solution of the enone oxime (70 mg) in [$^2H_6$]benzene (30 cm^3) was irradiated for 8 h under the conditions mentioned above. The solvent was removed to give a mixture of products. This mixture was subjected to PLC [(5:1) benzene–diethyl ether] to give β,γ-enone oxime **26** (49 mg, 70%) and the starting oxime **16** (5 mg, 7% recovery). The yield of β,γ-enone oxime based on consumed oxime was 75%.

2-Deuterio-4,4-dimethyl-1-trideuteriomethyl-5α-cholest-1-en-3-one **17**.—Sodium metal (50 mg, 2.17 mmol) was added to ethan[^{2}H]ol (13 cm^3) under nitrogen. To this solution was added (dropwise) a solution of the enone **15** (490 mg, 1.15 mmol) in anhydrous diethyl ether (5 cm^3). The solution was then stirred for 20 h at room temperature. After addition of glacial acetic acid (0.25 cm^3), the solution was filtered through Celite. The filtrate was concentrated and again filtered through Celite. Evaporation of the solvent gave crude tetradeuterio enone **17** (581 mg), which was recrystallized from methanol–acetone; δ(90 MHz) 0.71 (3 H, s, 18-H_3), 1.08 (6 H, s, 4-Me_2) and 1.10 (3 H, s, 19-H_3); *m/z* 430 (M^+, 39.8%).

2-Deuterio-4,4-dimethyl-1-trideuteriomethyl-5α-cholest-1-en-3-one Oxime **18**.—Tetradeuterio enone **17** (500 mg), hydroxylamine hydrochloride (1.8 g, 25.8 mmol) and sodium acetate (1.4 g, 17.2 mmol) in ethanol (25 cm^3) were heated under reflux for 3 h. The reaction mixture was worked up in the usual way. The crude oxime was purified by PLC [(8:1) benzene–diethyl ether] to give pure *tetradeuterio oxime* **18** (397 mg, 90%), m.p. 184–187 °C (from acetone); ν_{max}/cm^{-1} 3212 (OH) and 973; δ(270 MHz) 0.69 (3 H, s, 18-H_3), 1.01 (3 H, s, 19-H_3) and 1.14 (6 H, s, 4-Me_2); *m/z* 445 (M^+, 34%), 428 [$(M - OH)^+$, 28], 275

(9) and 43 (100) (Found: M^+, 445.4206. $C_{30}H_{47}D_4NO$ requires *M*, 445.4222).

Photoreaction of Tetradeuterio Enone Oxime **18**.—A solution of enone oxime **18** (100 mg, 0.224 mmol) in methanol (60 cm^3) was irradiated under nitrogen for 2.5 h, as mentioned above. After evaporation of the solvent, the product was subjected to PLC [(8:1) benzene–diethyl ether] to give *oxime* **28** (65 mg, 65%), m.p. 160–163 °C (from acetone); ν_{max}/cm^{-1} 3278 (OH) and 934; δ(270 MHz) 0.69 (3 H, s, 18-H_3), 1.03 (3 H, s, 19-H_3), 1.13 (6 H, s, 4-Me_2) and 3.24 (1 H, s, 2α-H); *m/z* 444 (M^+, 67.6%), 427 [(M − OH)$^+$, 68.5], 155 (61.4), 95 (71.7), 81 (64.7), 69 (74.5), 57 (93.3) and 43 (100) (Found: M^+, 444.4154. $C_{30}H_{48}D_3NO$ requires *M*, 444.4159).

5α-*Cholest*-2-*en*-1-*one* **19**.—This enone was prepared by the oxidation of 5α-cholest-1-en-1α-ol, prepared from 5α-cholest-1-en-3-one through its epoxidation,[9] followed by Wharton reaction[10] with PDC. The overall yield from 5α-cholest-1-en-3-one was 40%. M.p. 74–78 °C (from acetone) (lit.,[9] 58 °C; lit.,[10] 58–60 °C); δ(90 MHz) 0.83 (3 H, s, 18-H_3), 1.14 (3 H, s, 19-H_3), 5.78 (1 H, d, *J* 10.1, 2-H) and 6.5–6.8 (1 H, m, 3-H).

1α-*Methyl*-5α-*cholest*-2-*en*-1β-*ol* **20**.—To a solution of 5α-cholest-2-en-1-one **19** (713 mg, 1.86 mmol) in dry THF (30 cm^3) at −78 °C was added (dropwise) methyllithium (5% in hexane) (6 cm^3) for 3 h. The solution was neutralized by the addition of 2 mol dm^{-3} hydrochloric acid, and the solvent was evaporated off. The residue was extracted with diethyl ether. The organic layer was washed successively with 2 mol dm^{-3} hydrochloric acid, water, and brine, and was then dried over anhydrous sodium sulfate. Evaporation of the solvent gave crude 1α-methyl-5α-cholest-2-en-1β-ol **20**, which was immediately subjected to oxidation to enone **21**.

1-*Methyl*-5α-*cholest*-1-*en*-3-*one* **21**.—To a solution of the above mentioned crude allylic alcohol **20** in dichloromethane (37 cm^3) was added PCC (704 mg). The solution was heated under reflux for 24 h. After addition of diethyl ether, the solution was filtered through Celite. The filtrate was washed first with water, and then with brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave crude *enone* **21** (371 mg, 50%), m.p. 55–58 °C (from acetone) (Found: C, 83.9; H, 11.8. $C_{28}H_{46}O$ requires C, 84.35; H, 11.63%); ν_{max}/cm^{-1} 1670 and 1603 (conjugated C=O), 1337, 1285, 1172 and 849; δ(270 MHz) 0.72 (3 H, s, 18-H_3), 1.05 (3 H, s, 19-H_3), 2.07 (3 H, d, *J* 1.0, 1-Me), 2.18 (1 H, dd, *J* 13.5 and 18.1, 4β-H) and 5.71 (1 H, br s, 2-H); *m/z* 398 (M^+, 23.9%), 383 [(M − Me)$^+$, 3.1], 356 [(M − CH_2=C=O)$^+$, 5.7], 300 (7.7), 285 (11.9), 136 (100) and 123 (61.6).

(E)- *and* (Z)-1-*Methyl*-5α-*cholest*-1-*en*-3-*one Oximes* **22** *and* **23**.—A solution of enone **21** (97 mg, 0.24 mmol), hydroxylamine hydrochloride (111 mg) and sodium acetate trihydrate (111 mg) in ethanol (7 cm^3) was stirred for 3 h at room temperature. To the residue obtained upon removal of the solvent was added water. The mixture was then extracted with diethyl ether. The solution was washed successively with water and brine, and dried over anhydrous sodium sulfate to give a mixture of *E* and *Z* *oximes* (86 mg, 88%), m.p. 164–165 °C (from methanol–acetone) (Found: C, 81.2; H, 11.5; N, 3.4. $C_{28}H_{47}NO$ requires C, 81.29; H, 11.45; N, 3.39%); ν_{max}/cm^{-1} 3278 (OH), 1702 and 1631 (C=C–C=N); δ(400 MHz) 0.71 (3 H, s, 18-H_3 of *E* and *Z*), 0.91 (3 H, s, 19-H_3 of *E* and *Z*), 1.98 (3 H, s, 1-Me of *E* and *Z*), 2.20 (1 H, dd, *J* 13.2 and 18.3, 4β-H of *E*), 2.32 (1 H, dd, *J* 13.2 and 18.3, 4β-H of *Z*), 2.68 (1 H, dd, *J* 4.9 and 18.6, 4α-H of *E*), 5.77 (1 H, s, 2-H of *E*) and 6.47 (1 H, s, 2-H of *Z*); *m/z* 413 (M^+, 100%), 396 [(M − OH)$^+$, 52.8], 152 (26.1) and 139 (39.2).

Photodeconjugation of 1-*Methyl*-5α-*cholest*-1-*en*-3-*one Oximes* **22** *and* **23**.—(a) *In methanol*. A solution of enone oximes **22** and **23** (31 mg, 0.075 mmol) in methanol (20 cm^3) in a quartz vessel was flushed with nitrogen. The solution was then irradiated by a low-pressure mercury arc in a Rayonet photochemical reactor for 3 h under nitrogen. Evaporation of the solvent (rotary evaporator) afforded a product, which was subjected to PLC [(5:1) benzene–diethyl ether] to give three fractions. The most mobile fraction (6 mg, 20%) was the parent enone **21**. The second mobile fraction (2 mg, 3%) was the recovered starting material. The most polar fraction (19 mg, 60% based on the consumed oxime) was a 1:1 *mixture of* E and Z β,γ-*oximes* **31** and **32**, m.p. 134–137 °C (from acetone–methanol) (Found: M^+, 413.3675. $C_{28}H_{47}NO$ requires *M*, 413.3658); ν_{max}/cm^{-1} 3278 (OH), 1637 (C=N) and 898 (C=CH_2); δ(400 MHz) 0.70 (3 H, s, 18-H_3), 1.01 and 1.02 (each $\frac{3}{2}$ H, each s, 19-H_3 of *E* and *Z* isomers), 2.81 ($\frac{1}{2}$ H, d, *J* 16.1, 2β-H of *Z*), 2.88 ($\frac{1}{2}$ H, d, *J* 15.6, 2α-H of *E*), 3.00 ($\frac{1}{2}$ H, dd, *J* 3.4 and 16.6, 4α-H of *E* **31**), 3.09 ($\frac{1}{2}$ H, d, *J* 15.6, 2β-H of *E*), 3.77 ($\frac{1}{2}$ H, d, *J* 16.1, 2α-H of *Z*), 4.65 ($\frac{1}{2}$ H, s, 1′-H^a of *E* or *Z*), 4.67 ($\frac{1}{2}$ H, s, 1′-H^a of *Z* or *E*) and 4.85 (1 H, s, 1′-H^b of *E* and *Z*); *m/z* 413 (M^+, 100%), 396 [(M − OH)$^+$, 63.0], 383 (5.7), 151 (36.2) and 138 (32.0).

(b) *In methan*[^{2}H]*ol*. A solution of enone oximes **22** and **23** (40 mg, 0.097 mmol) in methan[^{2}H]ol (26 cm^3) in a quartz vessel was flushed with nitrogen and then irradiated for 3 h under the conditions mentioned above. Three fractions [the parent ketone **21** (5 mg, 12%), the starting material (1 mg, 3%), and a 1:1 mixture of (*E*)- and (*Z*)-2α-deuterio-1-methylene-5α-cholestan-3-one oximes **33** and **34** (24 mg, 60% based on the consumed oximes)] were obtained, as in the case of the photoreaction in methanol. The 1:1 mixture of oximes **33** and **34** had m.p. 135–137 °C (from acetone–methanol) (Found: M^+, 414.3718. $C_{28}H_{46}DNO$ requires *M*, 414.3721); ν_{max}/cm^{-1} 3290 (OH), 1638 (C=N) and 890 (=CH_2); δ 0.70 (3 H, s, 18-H_3 of **33** and **34**), 1.00 and 1.01 (3 H, s, 19-H_3 of **33** and **34**), 2.80 ($\frac{1}{2}$ H, s, 2β-H of **33**), 3.01 ($\frac{1}{2}$ H, dd, *J* 3.4 and 16.6, 4α-H of **33**), 3.07 ($\frac{1}{2}$ H, s, 2β-H of **34**), 4.65 (1 H, d, *J* 4.4, 1′-H^a of **33** and **34**) and 4.84 (1 H, d, *J* 4.4, 1′-H^b of **33** and **34**); *m/z* 414 (M^+, 100%), 397 [(M − OH)$^+$, 75.2], 384 (6.4), 152 (54.6) and 139 (48.6).

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