A New Stereospecific Rearrangement of an Excited Steroidal α,β-Unsaturated Cyclic Ketone Oxime[1]

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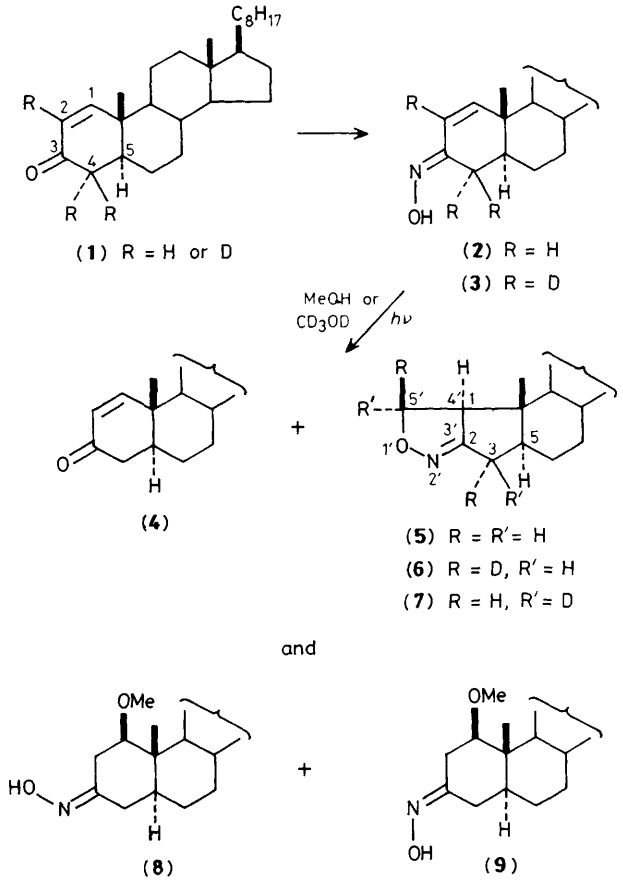
Irradiation of (*E*)-5α-cholest-1-en-3-one oxime in protic or aprotic solvent with a low pressure mercury arc gave 4α′,5′-dihydro-*A*-nor-5α-cholestano[2,1-*c*]isoxazole, the molecular structure of which was established by *X*-ray analysis, and a mechanism, which accommodates the stereospecificity of this new photo-rearrangement proved by deuterium labelling studies, is suggested.

The photoreactions of oximes are well documented.[2] The reported reactions of excited oximes are their rearrangement to lactams, α-fission, and the formation of the parent carbonyl compounds. We now report an unprecedented stereospecific rearrangement of an excited steroidal α,β-unsaturated cyclic ketone oxime. When (*E*)-5α-cholest-1-en-3-one oxime[3] (**2**) (100 mg) in methanol (60 ml) was irradiated with a low-pressure Hg arc in a Rayonet RPR photochemical reactor for 10 h under nitrogen, four products, cholest-1-en-3-one (**4**) (26%), (**5**), m.p. 111—112 °C (20%), (*Z*)-1β-methoxy-5α-cholestan-3-one oxime† (**8**) (5%), and its (*E*)-isomer† (**9**) (8%), were obtained (Scheme 1). None of the expected unsaturated lactams that arise from the photo-Beckmann rearrangement was formed. The molecular structure of the product (**5**), $C_{27}H_{45}NO$ (high resolution mass), was established as 4α′,5′-dihydro-*A*-nor-5α-cholestano[2,1-*c*]isoxazole (**5**) by *X*-ray crystallography (Figure 1).‡

Irradiation of [2,4,4-$^2H_3$]cholest-1-en-3-one oxime (**3**), prepared from [2,4,4-$^2H_3$]cholest-1-en-3-one (**1**),[4] under the above conditions resulted in the formation of the trideuterio-isoxazoline (**6**). The ^1H n.m.r. spectrum (500 MHz) of the isoxazoline (**5**) exhibited three 1H signals at δ 3.35 (dd, *J* 10.3 and 12.7 Hz), 3.84 (dd, *J* 8.3 and 12.7 Hz), and 4.33 (dd, *J* 8.3 and 10.3 Hz), assignable to 4α′-H, 5α′-H, and 5β′-H

† ^1H N.m.r. (270 MHz): (**8**) δ 0.80 (3H, s, 19-H), 2.93 (1H, dd, *J* 5.5 and 10.63 Hz, 1α-H), 3.31 (3H, s, OMe), and 3.66 (1H, dd, *J* 5.5 and 14.7 Hz, 2α-H); (**9**), δ 0.90 (3H, s, 19-H), 2.13 (1H, dd, *J* 9.53 and 14.7 Hz, 2β-H), 2.65 (1H, dd, *J* 5.5 and 14.7 Hz, 2α-H), 2.80 (1H, dd, *J* 3.8 and 15.4 Hz, 4α-H), 2.98 (1H, q, *J* 5.5 and 9.53 Hz, 1α-H), and 3.27 (3H, OMe); (**7**), δ 3.82 (1H, d, *J* 12.7 Hz, 4α′-H) and 3.34 (1H, d, *J* 12.7 Hz, 5′β-H).

‡ *Crystal data* for (**5**): $C_{27}H_{45}NO$, triclinic, space group *P*1, a = 11.673(6), b = 11.982(4), c = 11.102(6) Å, α = 100.86(4), β = 118.45(4), γ = 63.93(4)°, Z = 2, D_c = 1.083 g cm^{-3}. The intensities of 3651 independent reflections with $2\theta < 50°$ were measured on a Rigaku four-circle diffractometer with graphite-monochromated Mo-K_α radiation, using the ω–2θ scanning mode. The structure was solved by the Monte Carlo direct method on the basis of 878 $|E|$ values above 1.20, and was refined by block-diagonal least-squares with anisotropic thermal parameters. All the hydrogen atoms were located in a difference Fourier map, and further least-squares refinement included the hydrogen atoms. The final R value was 0.065. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.



Scheme 1

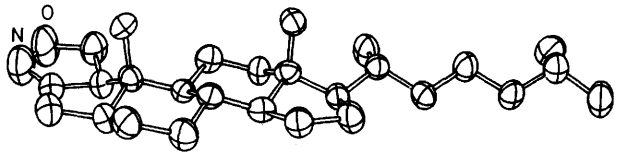
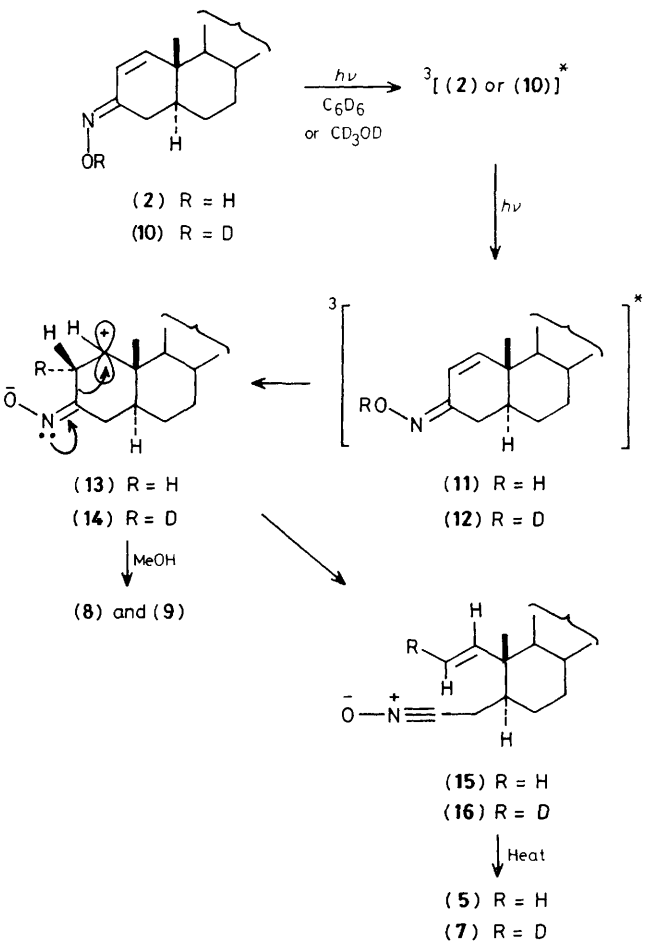


Figure 1. *X*-Ray crystal structure of the photoproduct (5).



Scheme 2

respectively on the basis of double resonance studies. In contrast, the ^{1}H n.m.r. spectrum of the trideuterio-isoxazoline (**6**) showed only two doublets at δ 3.35 (*J* 10.3 Hz) and 4.33 (*J* 10.3 Hz), assignable to the 4α′-H and 5α′-H. Thus, the two vicinal protons in the trideuterio-isoxazoline (**6**) are *cis*. The isoxazoline (**5**) is formed in 18% yield together with the parent ketone (**4**) when the oxime (**1**) is irradiated in C_6D_6. Thus 5α′-H of (**5**) is derived from the hydroxyimino proton and not from the solvent. Exchange of the hydroxyimino proton of the oxime (**2**) by deuterium by dissolving (**2**) in CD_3OD, followed by photolysis of the deuterio oxime (**10**) gave the monodeuterio-isoxazoline (**7**) in 12% yield. The ^{1}H n.m.r. spectrum of (**7**) showed that the deuterium was attached to C-5′ and α-oriented.† Thus 5α′-H of (**5**) is the hydroxyimino hydrogen of (**2**). No isoxazoline (**5**) is formed when (**2**) is irradiated in methanol saturated with oxygen.

A pathway which accommodates the foregoing results is outlined in Scheme 2. Irradiation of the (*E*)-oxime generates first triplet excited (*E*)- and (*Z*)-oximes from a singlet and/or a triplet manifold of (**2**) and then the hydroxyimino proton is transferred to C-2 of the twisted C=C bond of the relaxed unstable species from the α-face to generate the carbocation (**13**).[5] Cleavage of the C-2–C-3 bond to give the nitrile oxide intermediate (**15**), followed by intramolecular stereospecific 1,3-dipolar addition,[6] would give the isoxazoline (**5**). The involvement of the cationic intermediate (**13**) is supported by the formation of methoxy-containing derivatives (**8**) and (**9**).

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