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The Photochemistry of Steroidal 6-Membered Cyclic α-Nitro Enones[1)]

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Synopsis. The products of the photolysis of two steroidal cyclic α-nitro enones, newly synthesized, were compared with those of the cyclic α-nitro ketones and cyclic enones. Direct irradiation of 2α-nitrocholest-4-en-3-one in protic solvents resulted in an unexpected α-cleavage of the carbonyl group and gave 3-alkoxy-2-nitro-2,3-secocholest-4-en-3-one while irradiation of 4α-nitro-5α-cholest-1-en-3-one gave the parent cholest-1-en-3-one which arose from the removal of the nitro group.

In a previous paper,[2)] we have reported the results of the photolysis of several 6-membered cyclic α-nitro ketones in ethanol.

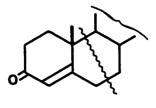
We have found that two versions of the products, the corresponding α-diketones and α-diketone monooximes, can be obtained when 6-membered cyclic α-nitro ketones which exist exclusively or predominantly in their enol forms in protic solvents, are irradiated in ethanol. We have also found that the corresponding α-diketone monooximes are products which do not accompany any corresponding α-diketones when the 6-membered cyclic α-nitro ketones, which exist in their keto forms, are irradiated in ethanol.

In this paper, we wish to report the results of a further investigation in this area: the photolysis of two steroidal cyclic α-nitro enones, 2α-nitrocholest-4-en-3-one (**2**) and 4α-nitro-5α-cholest-1-en-3-one (**6**). The study was carried out to help us to understand more fully the behavior of the excited nitro group in protic solvents.

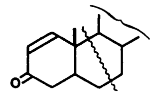
Preparation of α-Nitro Enones 2 and 6. The two steroidal α-nitro enones **2** and **6** chosen for the present investigation were prepared in a standard manner by nitration of the corresponding steroidal α,β-unsaturated ketones **1** and **5** with an alkyl nitrate and a base.[3—5)] The IR spectra of α-nitro enones **2** and **6** exhibited strong bands assignable to the α,β-unsaturated carbonyl and nonconjugated nitro groups. These α-nitro enones therefore exist almost exclusively as their keto form in the Nujol. An ^{1}H NMR spectra of both α-nitro enones also indicated that these α-nitro enones in $CHCl_3$ exist in their keto form.

The UV spectrum of α-nitro enone **2**, on the other hand, exhibited an absorption maximum with a medium intensity at 375 nm (ε; 1620), besides an intense absorption maximum at 244 nm (ε; 13200). The former is attributable to the presence of a small portion of α-nitro enone **2** in its enol form. The UV spectrum of α-nitro ketone **6** in ethanol exhibited a weak absorption maximum at 335 nm attributable to the $\pi \rightarrow \pi^*$ transition of the nitro group of the corresponding enol form[2)] besides a strong absorption maximum at 231 nm due to the $\pi \rightarrow \pi^*$ transition.

It has been reported that in the mass spectra of Δ^4- and Δ^1-androstan-3-ones, the base peaks occur at *m/z* 124 and 122 respectively. Both base peaks arise from a cleavage across ring B as indicated in the formulae **A** and **B**.[6)] On the basis of deuterium labelling studies

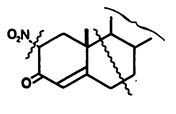


A *m/z* 124

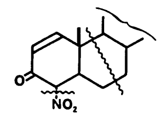


B *m/z* 122

Shapiro and Djerassi have suggested that the mechanism for the production of the base peak at *m/z* 124 involves the migration of hydrogen atoms from C-8 and C-11 of the steroid to the ring A fragment while the formation of the base peak at *m/z* 122 involves the reciprocal migration of hydrogen to the ring **A** fragment. It should be noted that in contrast to the simple enones studied by Shapiro and Djerassi, the mass spectra of both α-nitro enones **2** and **6** exhibited a base peak at *m/z* 121. Both ions seem to be formed as a result of the loss of NO_2 and a cleavage across the ring **B** as indicated in the formulae C and D.

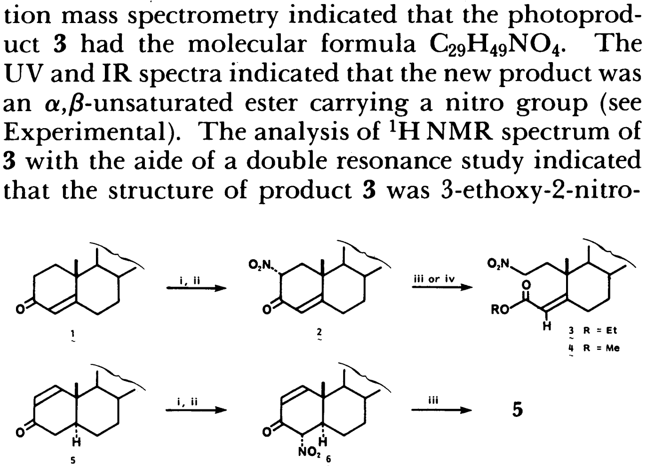


C *m/z* 121



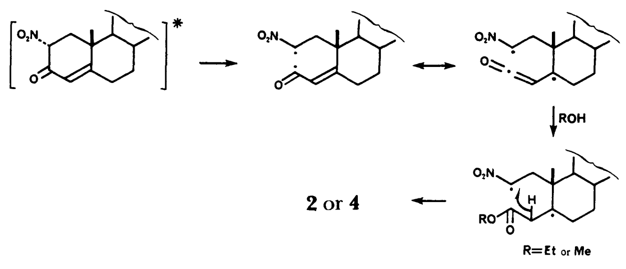
D *m/z* 121

Photochemistry of α-Nitro Enones 2 and 6. Photolysis of α-nitro enone **2** in ethanol with a 450-W high-pressure Hg arc through a Pyrex filter for 6 h gave a product mixture from which a product **3** (25%) was isolated by means of preparative TLC as the only indentifiable product (Scheme 1). The high-resolution mass spectrometry indicated that the photoproduct **3** had the molecular formula $C_{29}H_{49}NO_4$. The UV and IR spectra indicated that the new product was an α,β-unsaturated ester carrying a nitro group (see Experimental). The analysis of ^{1}H NMR spectrum of **3** with the aide of a double resonance study indicated that the structure of product **3** was 3-ethoxy-2-nitro-



i) $CH_3CH_2CH_2ONO_2$-$(CH_3)_3COK$ ii) CH_3COOH iii) EtOH-*hν* iv) MeOH-*hν*

Scheme 1.



Scheme 2.

2,3-secocholest-4-en-3-one (**3**) (See Experimental). The ^{13}C NMR spectrum exhibited five signals at δ 167.0, 165.5, 112.0, 71.5, and 59.6 in the downfield. On the basis of the results revealed by the INEPT technique and by considering the known structure-shift correlations, these signals were assigned respectively to the C=O of the ethoxycarbonyl, the trigonal α-carbon of the α,β-unsaturated ester, the trigonal β-carbon of the α,β-unsaturated ester, the methylene carbon carrying a nitro group, and the methylene carbon of the ethoxycarbonyl group of **3**.

The photolysis of **2** was also undertaken by using methanol as the solvent to give 3-methoxy-2-nitro-2,3-secocholest-4-en-3-one **4** in a 30% yield.

Photolysis of α-nitro enone **6** in ethanol under conditions similar to those described above gave the parent ketone **5** (37%) as the only identifiable product.

Although the photochemistry of nitro compounds has been extensively investigated,[7] the photochemistry of cyclic α-nitro enones has never been reported. The foregoing experiments have shown that the photoreaction of an α,β-unsaturated carbonyl group preceded the photoreaction of the nitro group in 2α-nitrocholest-4-en-3-one (**2**), while the photoreaction of nitro group preceded that of α,β-unsaturated carbonyl group in 4α-nitrocholest-1-en-3-one **6**. The probable pathway which led to the secosteroid **3** is outlined in Scheme 2.

Although the photoreactions of enones[8] have been extensively investigated only a few examples of the photochemical α-fission of α,β-unsaturated carbonyl group have so far been reported.[9] The general process of α,β-unsaturated ketones in hydrogen-donating solvents such as ethanol appears to be a photoreduction.[10] Thus, irradiation of testosterone acetate in ethanol has been reported to give a mixture of products from which only the corresponding saturated ketone have been isolated.[10] It is well-known that the irradiation of steroidal 4-en-3-ones in *t*-butyl alcohol leads to fascinating photorearrangements.[8,10,12,13]

The present α-cleavage of excited steroid-4-en-3-one therefore, is apparently due to the presence of the 2α-nitro group which directs the α-cleavage over other photochemical processes common to the excited α,β-unsaturated carbonyl group.

Experimental

For instruments and general procedure see Ref. 2.

Preparation of 2α-Nitrocholest-4-en-3-one (2). To THF (14 ml) containing potassium *t*-butoxide (0.5 g), cholest-4-en-3-one (1 g, 2.6 mmol) dissolved in THF (22 ml) was added over the course of 30 min at −30 °C. To this solution, propyl nitrate (0.6 g) in THF (5 ml) was added and the solution was stirred for 45 min during which period the temperature of the solution was raised to 0 °C. The solution was neutralized with glacial acetic acid. The solution was then poured into iced water (200 ml) and the aq solution was extracted twice with dichloromethane. The combined organic layers were dried over Na_2SO_4 and worked up in the usual way to give an oily product (1.173 g). This crude product was recrystallized from ethanol to yield yellow crystals (0.637 g, 57%), mp 140—142 °C. (Found: C, 75.44; H, 9.98; N, 3.28%. Calcd for $C_{27}H_{43}NO_3$: C, 75.48; H, 10.09; N, 3.26%): IR (Nujol) 1695 (C=O), 1605 (C=C), and 1544 cm^{-1} (NO_2); ^{1}H NMR (270 MHz) δ=0.71 (3H, s, 18-H), 1.3 (3H, s, 19-H), 2.06 (1H, dt, *J*=12.82, 3.3 and 3.3 Hz, 6α-H), 5.31 (1H, dd, *J*=13.19 and 5.86 Hz, 2β-H), 5.84 (1H, s, 4-H); MS *m/z* (rel intensity) 429 (M^+, 17) 413 [$(M-O)^+$, 12.4], 397 (14), 383 [$(M-NO_2)^+$, 27.5], 316 (20.3), 261 (16.7), 147 (36.7), 135 (40.3), 121 (100), 109 (27.1), 95 (42.3), 81 (33.7), 69 (35.5), 57 (44.2), and 43 (47.2); UV (C_2H_5OH) λ_{max} 375 nm (ε: 1620) and 2.44 (ε: 13240).

Preparation of 4α-Nitro-5α-cholest-1-en-3-one (6). To THF (28 ml) containing potassium *t*-butoxide (1 g), 5α-cholest-1-en-3-one (2 g, 5.21 mmol) dissolved in THF (44 ml) was added over the courses of 30 min at −30 °C. To this solution, propyl nitrate (1.2 g) in THF (10 ml) was added and the solution was stirred for 45 min during which time the temperature of the solution was raised to 0 °C. The solution was neutralized with glacial acetic acid until the pH of the solution became ca. 3. The solution was then poured into water (300 ml) and the aq solution was extracted with dichloromethane. The organic layers were combined and the solution was dried over Na_2SO_4 and worked up in the usual way to give an oily product (2.381 g). The crude product was subjected to column chromatrography (silica gel, 40 g). Elution with benzene gave a crude α-nitro ketone **5** (1.080 g, 48.3%) which was recrystallized from methanol. Mp 149—151 °C. (Found: C, 75.52; H, 9.97; N, 3.14%. Calcd for $C_{27}H_{43}NO_3$; C, 75.48; H, 10.09; N, 3.26%); IR (Nujol) 1694 (C=O), 1616 (C=C), and 1542 cm^{-1} (NO_2); ^{1}H NMR (270 MHz) δ=0.70 (3H, s, 18-H), 1.12 (3H, s, 19-H), 5.12 (1H, d, *J*=13.56 Hz, 4β-H), 6.01 (1H, d, *J*=10.25 Hz, 2-H), and 7.31 (1H, d, *J*=10.25 Hz, 1-H); MS *m/z* (rel intensity), 429 (M^+, 20.4 %), 383 [$(M-NO_2)^+$, 26.7], 229 (31), 173 (15.4), 147 (43.4), 121 (100), 109 (24.5), 95 (35.4), 81 (30), 69 (33.4), 55 (42.2), and 43 (42.9); UV (EtOH) λ_{max} 335 nm (ε: 60).

Photolysis of 2α-Nitrocholest-4-en-3-one (2). The nitro ketone **2** (400 mg, 0.93 mmol) in ethanol (400 ml) was flushed with nitrogen and irradiated for 6 h with a Hanovia 450-W high-pressure Hg arc through a Pyrex filter in an atmosphere of dry nitrogen. The solvent was then removed to give an oily product (455 mg). The product was subjected to preparative TLC with benzene to give product **3** (122 mg, 25.2%). (Found: *m/z* 475.3623; Calcd for $C_{29}H_{49}NO_4$: M, 475.3659); IR (Nujol) 1710 (COOEt), 1626 (C=C), 1548 (NO_2), 1191, 1183, and 1161 cm^{-1} (C-O-C); ^{1}H NMR (270 MHz) δ=0.70 (3H, s, 18-H), 1.14 (3H, s, 19-H), 1.29 (3H, t, *J*=7.14 Hz, $C\underline{H}_3$-CH_2O), 3.38 (1H, dt, *J*=14.29, 3.3 and 3.3 Hz, 6α-H), 4.15 (2H, q, *J*=7.14, $CH_3C\underline{H}_2$-O), 4.33 (1H, ddd, *J*=12.8, 12,8 and 6.2 Hz, 2-H), 4.49 (1H, ddd, *J*=12.8, 12.8 and 4.8 Hz, 2-H), and 5.67 (1H, s, 4-H); MS *m/z* (rel intensity) 475 (M^+, 3.4), 458 (27.7), 440 (11.2), 430 [$(M-OEt)^+$, 15.8], 402 [$(M-COOEt)^+$, 68.9], 372 (100), 147 (20.8), 133 (22.0), 121 (23.6), 107 (31.6), 95 (20.0), 82 (47.1), 69 (47.7), 55 (65.7), and 43 (74.6). UV(ethanol) λ_{max} 212 nm (ε; 13850).

The photoreaction of **2** (400 mg) in methanol (400 mg) for 8 h under the above conditions gave a product. The product was subjected to preparative TLC (3 : 1 dichloromethane-hexane) to yield a methoxy analogue **4** (180 mg, 47%, based on the converted nitro ketone) and the starting nitro ketone (41 mg). (Found: m/z 461.3457: Calcd for $C_{28}H_{47}NO_4$: M, 461.3505); IR (Nujol) 1710 (COOEt), 1630 (C=C), and 1577 cm^{-1} (NO_2); ^1H NMR (270 MHz) δ=0.70 (3H, s, 18-H), 1.14 (3H, s, 19-H), 3.70 (3H, s, OMe), 3.84 (1H, td, J=14.3 and 3.7 Hz, 6α-H), 4.33 (1H, ddd, J=12.8, 11.0 and 6.2 Hz, 2-H), 4.48 (1H, ddd, J=12.8, 11.4 and 4.8 Hz, 2-H), and 5.69 (1H, s, 4-H): ^{13}C NMR δ=56.1 (OMe), 71.5 (CH_2NO_2), 11.6 (the α-carbon of the α,β-unsaturated ester), 165.9 (the β-carbon of the α,β-unsaturated ester), and 167.3 (the C=O of the methoxycarbonyl); MS m/z (rel intensity) 461 (M^+, 9.2), 444 (38.9), 430 [$(M-OMe)^+$, 13.3], 426 (15.3), 402 [$(M-COOMe)^+$, 53.6], 386 (33.8), and 372 (100).

Photolysis of 4α-Nitro-5α-cholest-1-en-3-one (6). α-Nitro ketone **6** (300 mg, 0.7 mmol) in ethanol (350 ml) was flushed with nitrogen and irradiated for 3 h with a EIKOSHA 500-W high-pressure mercury arc through a Pyrex filter under an atmosphere of a nitrogen. The removal of the solvent left an oily residue (326 mg) which was subjected to preparative TLC with dichloromethane to yield two fractions. The most mobile fraction (26 mg, 8.7%) was starting nitro ketone. The next mobile fraction (91 mg, 36.8%) was 5α-cholest-1-en-3-one, **4** which was purified by recrystallization from methanol (55 mg), mp 149—151 °C.

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