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PHOTOLYSIS OF 3-OXO-$\Delta^{5(10)}$-STEROIDS IN ALCOHOLIC SOLVENTS AND IN THE SOLID PHASE[1]

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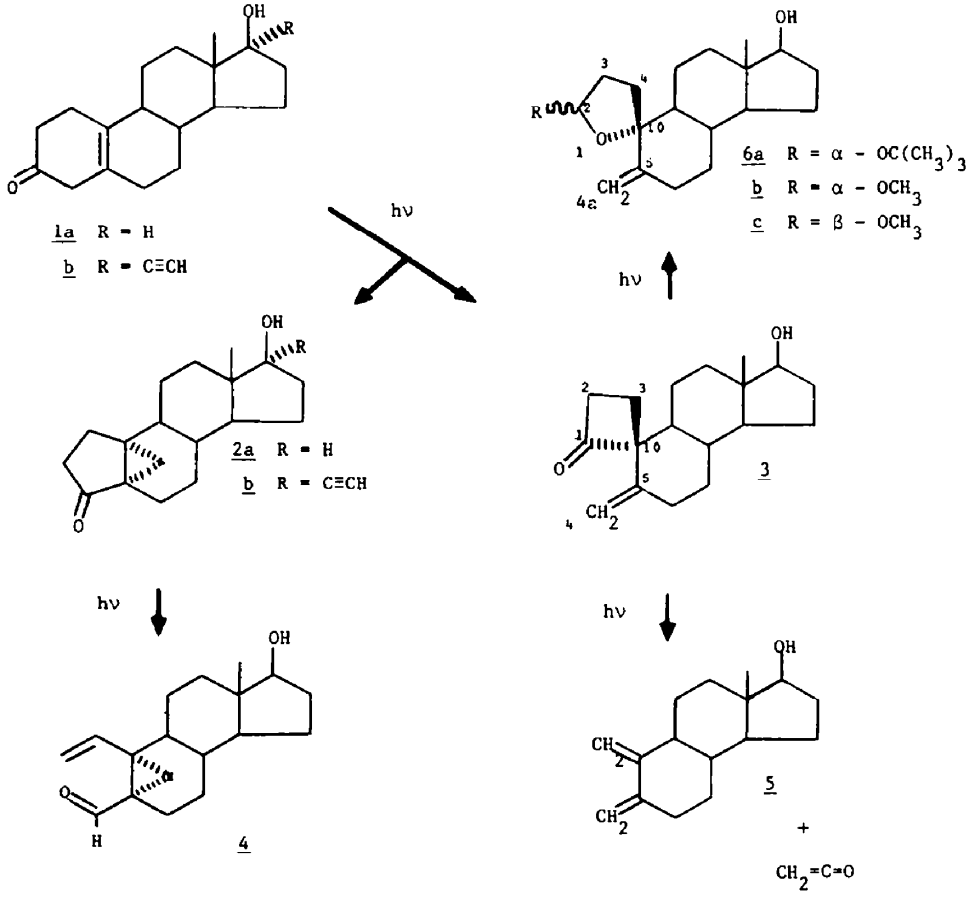
Abstract—Irradiation of the β, γ-unsaturated ketone **1a** in alcoholic solvents afforded the 1,2 and 1,3-acyl shift products **2a** and **3** respectively. The cyclobutanone **3** underwent further photochemistry incorporating a molecule of solvent and affording the ring expanded cyclic acetal **6**. Solid phase irradiation of **1a** yielded **2a** and **3** but **1b** was photostable.

Photolysis of β,γ-unsaturated ketones usually results in a 1,3-acyl shift to form a new β,γ-unsaturated ketone or a 1,2-acyl shift (oxadi-π-methane rearrangement ODPM) to give a conjugated cyclopropyl ketone.[2] Several years ago we reported the photolysis of the β,γ-unsaturated keto steroid **1a** in t-butanol to yield the conjugated cyclopropyl ketone **2a** together with at least two minor products.[3] Recently photolysis of **1a** in benzene resulted in a low yield of the 1,3-acyl shift product **3** together with two secondary photolysis products **4** and **5** formed from **2a** and **3** respectively.[4] We now wish to report further investigation of the photolysis of **1** in alcoholic solvents and in the solid phase.

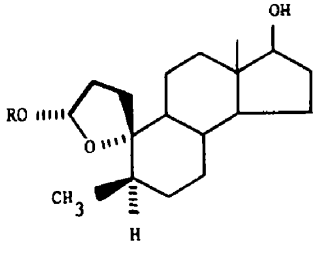
Photolysis of **1a** in t-butanol gave **2a** as the major product together with traces of **3** in variable yields. The other minor product, isolated in 11% yield, had incorporated a molecule of t-butanol and showed no CO absorption. The multiplet at δ 5.4 ppm in the NMR spectrum of the photoadduct **6a** was assigned to that of a cyclic acetal, since the absorptions of the exocyclic methylene at δ 5.27 and 4.65 ppm disappeared when **6a** was reduced to **7**. Furthermore, when the cyclobutanone **3** was irradiated in t-butanol, a molecule of solvent was incorporated yielding the previously obtained **6a**. The photochemical conversion of cyclic ketones in alcoholic solution to the ring expanded cyclic acetals is a general



reaction for cyclobutanones proceeding via an intermediate oxacarbene.[5]

Photolysis of **1a** in methanol gave **2a**, traces of **3** together with two epimers of the cyclic acetal **6b**.

The formation of one cyclic acetal in t-butanol and two in methanol can be explained based on the size of the solvent. In the case of t-butanol, the C-4 exocyclic methylene group sterically shields one face of the cyclopentyl oxacarbene intermediate, so that attack can only occur on the face opposite to that of the exocyclic methylene. Assuming that the C-1 oxo group is α at C-10 in **3**, based on the photoisomerisation of the closely analogous 17β-hydroxyestra-5(10), 9(11)-dien-3-one system[6] and secondly the steric shielding effect at C-2 due to the exocyclic methylene, the cyclic acetals have been assigned the structure **6**. In the case of the methanol adducts the 2α-methoxy derivative **6b** was assigned due to the close similarity of its NMR spectrum with that of the 2α-t-butoxy compound **6a**. Catalytic reduction of the exocyclic methylene, in **6a** and **b** should proceed from the less hindered side and yield the corresponding 5β-methyl compounds **7a** and **b**.



7a R = $C(CH_3)_3$

b R = CH_3

Photolysis of the oral contraceptive 17-hydroxy-19-nor-17α-pregn-5(10)-en-20-yn-3-one (Norethynodrel), **1b** in t-butanol has been found to yield the expected conjugated cyclopropyl ketone **2b** but no other products were reported.[7]

We next chose to look at the solid phase photochemistry of **1a** and **1b** and investigate the correlation of the ground-state structure with that of the photoproduct formed.[8] X-ray structure analysis of **1a**[9] and its iodoacetate derivative[10] showed that in both compounds ring A approximates to an envelope form with only C-2 displaced significantly in the α-direction from the C-1, C-10, C-5, C-4 plane as shown in Fig. 1. A recent single-crystal X-ray analysis of **1b**[11] showed that the two molecules comprising the asymmetric crystal unit approximate to different ring A envelope forms in which C-2 is displaced to the α-side in one molecule and to the β-side in the other. Thus, it was hoped that irradiation of **1b** should afford mixtures of stereoisomers of **2** and **3**.

Irradiation of solid **1a** afforded **2a** and **3** as the only isolable products. If one invokes the principle of ground-state control of photochemical reactions, then **3** is the expected product formed via a 1,3-acyl shift. Furthermore, **2a** is also that expected based on ground state control. This may be explained in that 1,2-acyl shifts of β,γ-unsaturated ketones are known[12] to proceed via initial C-3 to C-5 bonding which as can be seen in Fig. 1

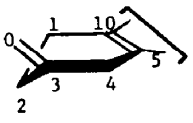


Fig. 1. Envelope conformation of ring A in **1a**.

should occur on the β-face of the molecule. α-Cleavage (C-3 to C-4) must then afford the observed α-cyclopropyl compound **2a**. In contrast irradiation of solid **1b** for as long as 70 hr resulted in only traces of an insoluble polymeric material being formed. The photostability of **1b** is probably due to an energy wasting step available only in the crystal structure of **1b**.

EXPERIMENTAL

The NMR spectra were obtained with a Varian XL-100 spectrometer, fitted with a Nicolet NTCFT 1180 pulse system, using $CDCl_3$ solns with TMS as an internal standard.

Photolysis of 17β-hydroxy-5(10)-estrene-3-one (**1a**) *in t-butanol.* A stirred soln of 1.5 g of **1a** in 800 ml t-BuOH was irradiated under N_2 with a 450 W Hanovia lamp through a Pyrex filter for 30 hr. Evaporation of the solvent *in vacuo* yielded a gum (1.5 g). The product mixture (3.0 g) was chromatographed over silica gel (activity III, ICN). Initial elution with 10% EtOAc/hexane afforded **6a** (330 mg; 11% yield), m.p. 166–8° (hexane); IR(KBr) 3210 cm^{-1} (OH), 1645, 875 cm^{-1} (C=CH_2); ^1H NMR($CDCl_3$) δ 5.4 ppm (m, 1, H-2), 5.27 (m, 1, H-4a), 4.65 (m, 1, H-4a), 3.62 (t, 1, H-17), 1.25 (s, 9, t-Bu), 0.76 (s, 3, H-18); ^{13}C NMR, δ 154.7 (C-5), 106.9 (C-4a), 100.05 (C-2), 82.2 (C-17) 74.3 (C-19), 29.2 (t-butyl CH_3), 11.3 (C-18): mass spectrum: *m/e* 348 (M+, <1%), 291 (P–C_4H_9, 100), 274 (P–$C_4H_{10}O$, 30), 246(30), 228(18), 190(57), 171(51). Found: C, 75.43; H, 10.34. Calc. for $C_{22}H_{36}O_3$: C, 75.81; H, 10.41%.

Further elution afforded **3** (95 mg, 3% yield) m.p. 150°, IR(KBr) 3300 (OH), 1775 (cyclobutanone C=O) 1645, 895 cm^{-1} (C=CH_2) NMR($CDCl_3$) 4.62 (m, 2, H-4), 3.64 (t, 1, H-17), 0.8 (s, 3, H-18) (lit.[4] m.p. 154°, IR 1775 cm^{-1}).

Further elution with 20% EtOAc/hexane yielded starting material **1a** (380 mg, 12.6%) followed by **2a** (1.47 g, 49%) m.p. 161–163° (lit.[3] m.p. 162–163.5°).

Photolysis of **1a** *in methanol.* A soln of 2.0 g of **1a** in 800 ml MeOH was irradiated for 30 hr and worked up as above. Chromatography of the product (3.5 g) over silica gel using 10% EtOAc/hexane afforded **5**[4] (80 mg; 2%), IR no CO. NMR δ 4.92 (m, 1, =CH_2), 4.83 (t, 1, =CH_2), 4.6 (m, 2, =CH_2), 3.65 (t, 1, H-17), 0.75 (s, 3, H-18).

Further elution afforded **6c** (190 mg, 6%); m.p. 136–7° (hexane) IR(KBr) 3430 (OH), 1635, 895 cm^{-1} (C=CH_2); NMR δ 5.01 (d, 1, H-2), 4.83 (m, 1, H-4a), 4.68 (m, 1, H-4a), 3.65 (t, 1, H-17), 3.37 (s, 3, OCH_3), 0.77 (s, 3, H-18); mass spectrum *m/e* 306 (M+, 100), 275 (P–CH_3O, 9), 274 (P–CH_4O, 13), 203(13), 190(48), 173(22), 115(91), 114(90); high resolution mass spectrum. Found: 306.2199. Calc. for $C_{19}H_{30}O_3$ = 306.21948.

Further elution afforded **6b** (370 mg, 11%) m.p. 167–9° (hexane) IR(KBr) 3250 (OH), 1645, 895 (C=CH_2); NMR δ 5.07 (m, 2, H-2 and 4a), 4.63 (m, 1, H-4a) 3.63 (t, 1, H-17) 3.45 (s, 3, OCH_3) 0.76 (s, 3, H-18); mass spectrum *m/e* 306 ($M^{\oplus}$, <1%), 274 (P–CH_4O, 100), 259(15), 256(22), 243(50), 241(18), 230(30), 215(30), 199(42). Found: C, 74.21; H, 9.78. Calc. for $C_{19}H_{30}O_3$: C, 74.4; H, 9.8.

Further elution with 15% EtOAc/hexane yielded **1a** (110 mg, 3%) and **2a** (1.75 g, 50%).

Reduction of **6a** *and* **b**. A soln of **6a** (200 mg) in t-BuOH (25 ml) and PtO_2 (200 mg) was hydrogenated at atmospheric pressure for 1.5 hr. Recrystallization of the evaporated filtrate from hexane gave **7a** (120 mg, 60%); m.p. 107–110°; IR(KBr), 3400 cm^{-1} (OH); NMR; δ 5.35 (m, 1, H-2) 3.62 (t, 1, H-17) 1.2 (s, 9, t-butyl) 1.02 (d, 3, H-4a), 0.75 (s, 3, H-18). Found: C, 75.39; H, 10.40. Calc. for $C_{22}H_{38}O_3$: C, 75.38; H, 10.93%.

Similarly reduction of 150 mg of **6b** afforded 88 mg of **7b**: m.p. 136–140°, IR(KBr) 3450 cm^{-1} (OH); NMR δ 4.95 (m, 1, H-2), 3.62 (t, 1, H-17), 3.34 (s, 3, OCH_3), 0.92 (d, 3, H-4a) 0.75 (s, 3, H-18); high resolution mass spectrum. Found: 308.2343. Calc. for $C_{19}H_{32}O_3$ = 308.23513.

Photolysis of **3** *in t-butanol.* A soln of **3** (40 mg) in t-BuOH (40 ml) was irradiated for 10 hr as above. Evaporation of the solvent afforded only **6a**.

Irradiation of **1a** *and* **b** *in the solid phase.* 500 mg of **1a** was dissolved in a mixture of ether–MeOH in a 1000 ml quartz tube. The solvent evaporated slowly while rotating the tube horizon-

tally to make a coat (film) of the crystalline solid material on the inner wall of the tube. The solid film was irradiated using a Rayonet reactor with 253.7 nm light for 8 hr.

The photolysis product mixture was chromatographed over silica gel (act. III, 30 g) using 15% EtOAc/hexane as initial eluent, to afford 12 mg of **3** followed by **1a** (280 mg) and **2a** (190 mg, 38% yield).

When **1b** was irradiated as above for 70 hr, only traces of an insoluble polymeric material were formed.

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