131. Photochemical Reactions VII [1]. ¹) A 'Type A Rearrangement' in the Photolysis of a Steroidal α, β-unsaturated Lactone

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Summary

The irradiation of 17β-hydroxy-2-oxa-androst-4-en-3-one (**1**) yields a cyclopropane derivative **2**, which is the result of a rearrangement, formally analogous to the 'type A rearrangement' of the enones. Two other products, the dihydroxy compound **5** and the dimer **6**, have also been isolated (*Scheme 1*).

The photochemical behaviour of the unsaturated lactones has been less widely studied than that of the corresponding ketones. Usually, these lactones dimerise by a well known and documented process [2]. More recently, other reactions like deconjugation [3] or α-fragmentation to ketenes [4] have been described. The three reaction types are formally analogous to the situation described in the case of ketones. Nevertheless, to our knowledge, the rearrangement, well known in the case of cyclic enones [5] ('type A rearrangement', *i.e.* **3** → **4** [6]) has not been observed in the lactone series.

To study this possible photorearrangement of a lactone, compound **1** [7] was selected as model compound.

UV.-irradiation of **1** in *t*-butyl alcohol, in identical conditions as used in the case of testosterone, yields a mixture of the cyclopropane derivative **2**²) (10,3%), starting material **1** (36,1%), a dihydroxy compound **5**³) (3,2%) and dimeric material **6**³) (27,2%).

The structural relationship between **2** and **4** has been demonstrated by an independent synthesis of **2**. As starting material the cyclopropane derivative **8**, obtained

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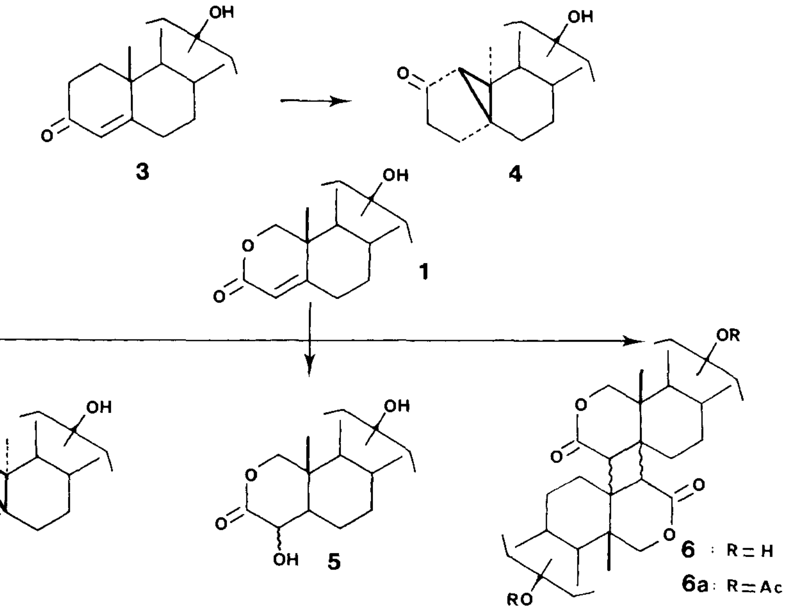
²) The UV.-, IR.-, NMR.-, and Mass Spectra of the new compounds are in good agreement with the proposed structures and will be reported only in the experimental part of this work.

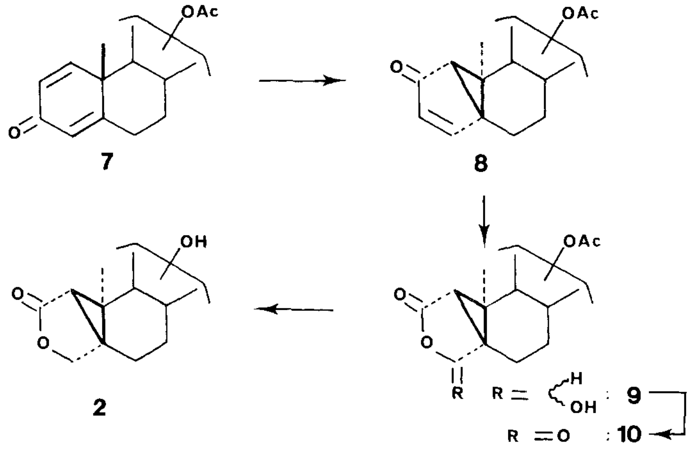
³) A head-to-tail structure is proposed on basis of the NMR.-spectrum of **6** (see exper. part.) It has been experimentally observed that at high dilutions (2×10^{-3} M) no dimers are formed. When water is added to this reaction medium, the yield of **5** slightly increases.

Scheme 1



by UV.-irradiation of Δ^1-dehydrotestosterone acetate (**7**) [8] (*Scheme 2*), was chosen[4]. The ozonolysis of **8** yields the pseudo-acid **9** and, to corroborate its structure, **9** was oxidized to **10**. Finally, the saponification and successive $NaBH_4$ reduction of **9** yielded a compound which was fully identified as **2** (see exper. part).

Scheme 2



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[4] Compounds **8**, **9** and **10** have been described by *Jeger et al.* [8] and its identification has taken place by comparison with independent samples. We acknowledge the kindness of PD Dr. *C. Ganter*, Laboratorium für Org. Chemie, Eidg. Techn. Hochschule, Zürich, in supplying samples and spectra of the mentioned compounds.

In conclusion, it can be said that the transformation **1** → **2**, is a new type of photochemical reaction of α,β-unsaturated lactones, to be catalogued in the group of the stereospecific 'type A rearrangements', as observed in the case of cyclic enones [5].

We are grateful to Dr. *U. Burger* (Univ. Geneva) for 100-MHz-^{1}H-NMR. spectra and to Dr. *J. Rivera* and Dr. *J. Camps* (Instituto de Quim. Org. Aplicada de Cataluna, C.S.I.C., Barcelona) for mass spectra and elemental analyses services.

Experimental part

General remarks. By extraction in the usual way is ment: dilution of the reaction mixture with ethyl acetate, washing of the organic phase with concentrated NaCl-solution till neutral, drying on anhydrous Na_2SO_4 and evaporation under reduced pressure with a rotatory evaporator.

Silica gel *Merck* 0,063–0,2 mm, was used for *column chromatography* (ratio to substance, 100:1). *Thin-layer chromatography* was performed using *Merck* Silica gel 60F–254 plates. Spots were detected by direct observation under UV. light (253,7 nm) or with 50% sulfuric acid spray followed by heating at 150° during 1 minute.

Melting points were determined in an open capillary (*Büchi-Tottoli* apparatus) and are uncorrected.

Infrared spectra (KBr) were recorded on a *Perkin-Elmer* 257 spectrophotometer; absorption is given in ν values (cm^{-1}). The *ultraviolet spectra* (in *Merck* Ethanol UVASOL solution) were recorded on a *Perkin-Elmer* 124 spectrophotometer; absorption is given in λ_{max} (nm) values, followed by the ε value in brackets. *Perkin-Elmer* R-24 or *Varian* XL-100 spectrometers were used to obtain the *^{1}H-NMR. spectra* (in $CDCl_3$ solution, unless otherwise specified). Chemical shifts (δ values) are reported relative to TMS. as an internal standard. Coupling constants (*J*) are given in Hz. Multiplicities are expressed as: singlet (*s*), doublet (*d*), triplet (*t*), quadruplet (*qa*), multiplet (*m*) and broad signal. (br.). *Mass spectra* were measured on a *Hitachi-Perkin-Elmer* RM-50-GC or *AEI* MS 902-S instruments.

The *irradiations* were carried out in an immersion unit using a medium pressure Hg lamp (Q81, *Quarzlampen GmbH*, Hanau).

Irradiation of **1** *with UV.-light.* A solution of 809 mg **1** in 160 ml *t*-butyl alcohol (*Merck*, analytical purity) was irradiated during 3 h 30 min, with a medium-pressure Hg lamp, without filter, under a nitrogen atmosphere. Solvent evaporation *in vacuo* yielded 829 mg of a yellowish oil mixture of several components. Chromatography with benzene/ethyl acetate 1:1, furnished 83 mg of lactone **2**, m.p. (three crystallisations) 195–6°. – IR.: 3470, 3060, 1745, 1190. – ^{1}H-NMR.: 0,75 (*s*, H_3C–C(18)); 1,17 (*s*, H_3C–C(19)); 1,60 (br. HO–C(17)); 1,89 (*s*, H–C(4)); 3,68 (*m*, H–C(17)); 4,08 + 4,22 (*AB* system, $J_{AB} = 10$, 2H–C(1); after D_2O addition, the signal at 1,60 disappeared). – MS.: $M^+ = 290$.

$C_{18}H_{26}O_3$ (290.39) Calc. C 74.45 H 9.02% Found C 74.38 H 9.39%

A second fraction consisted of 292 mg of starting material **1** [7] (identification through mixed m.p., TLC. and IR.-spectrum). The third fraction, 306 mg, was a mixture of **5** and **6** plus impurities, which could be separated into its components, after a new chromatography (*vide infra*).

The fourth and last fraction, furnished 75 mg of a highly polar complex mixture which was not further investigated.

As stated above, through a second chromatography of the third fraction, on Al_2O_3II N with benzene/ethyl acetate 1:1, the mixture of **5** and **6** was separated. First, 19 mg of a mixture in which starting material **1** was detected (TLC.) but not further investigated, were eluted. Then, 26 mg of 4ξ,17β-dihydroxy-2-oxa-5ξ-androstan-3-one (**5**), m.p. (two crystallisations) 155° (dec.). – IR.: 3400, 1710, 1040. – ^{1}H-NMR. (CD_3–CO–CD_3): 0.25 (*s*, H_3C–C(18)); 0.40 (*s*, H_3C–C(19)); (*s*, HO–C(4) and HO–C(17)); 3.1–3.4 (br., H–C(17) and H–C(4)); 3,4–3,9 (*AB* system, $J_{AB} = 10$, 2H–C(1)). – MS.: $M^+ = 308$. A third fraction consisted of 220 mg of the dimer **6**, m.p. (two crystallisations from benzene) > 350°. – IR.: 3520, 3430, 1725, 1200, 1050. – ^{1}H-NMR. (C_5D_5N): 0.92 and 1.12 (3*s*, angular methyl groups); 3,36 (*s*, H–C(4)); 3.6–3.8 (*m*, H–C(4′), H–C(17) and H–C (7′)); 4.2–4.8 (*m*, two overlapping *AB* systems, 2H–C(1) and 2H–C(1′)); 5,1 (br., HO–C(17) and HO–C(17′)); after D_2O addition, the signal at 5.1 disappeared). The ^1H-NMR.-spectrum, in $CDCl_3$, of **6a**, obtained by treatment of **6** with acetic anhydride/pyridine 1:1 at room temperature, presented two singlets at 3,00 and 3,15, attributed to the cyclobutane ring protons; as expected, part of the signal at 3.6–3.8 in the NMR. spectrum of **6** has shifted to 4.6 in **6a**. – MS.: 291 ($M^+/2+1$), 290 ($M^+/2$). After acetylation (**6a**), MS.: 604 (M^+-CH_3COOH).

$(C_{18}H_{26}O_3)_2$ (580.78) Calc. C 74.45 H 9.02% Found C 74.42 H 9.20%

At last, 31 mg of impure **6** were eluted and not further investigated.

Synthesis of **2** *from* **9**. A solution of 109 mg **9** in 7 ml 0.1 N NaOH, was refluxed during 2 h under nitrogen. After cooling, a suspension of 200 mg $NaBH_4$ in 6 ml H_2O was added and left at room temperature, under stirring, for 3 further hours. Acidification with 20% chlorhydric acid and extraction with ethyl acetate in the usual way, yielded 89 mg of a white solid which, after filtration through SiO_2 (adsorbent/substance 30:1) in methylene chloride/ethyl acetate 4:1, and two crystallisations, was identified as **2** (mixed m.p., TLC. and IR.-spectrum).

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