49. Photochemical Rearrangement of a Steroidal α,β-Epoxylactam[1])

Photochemical Reactions, XII [1]

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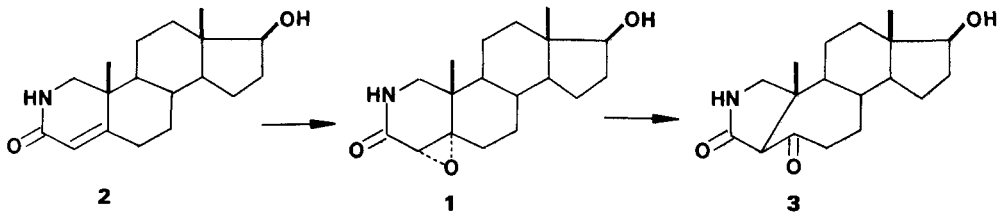
Summary

The UV. irradiation of 17β-hydroxy-4α,5α-epoxy-2-azaandrostan-3-one (**1**) yields 17β-hydroxy-2-aza-10(5→4-*abeo*)-4ξ(H)-androsta-3,5-dione (**3**).

Introduction. – We have reported that steroidal lactones behave photochemically in a similar way to their carbocyclic counterparts: α,β-unsaturated lactones, for example, undergo the 'type A' [2] and the di-π-methane [3] rearrangements, while α,β-epoxylactones suffer the 10(5→4) rearrangement to an *abeo* structure [1]. Therefore, as a part of a systematic study on the photochemical behaviour of heterocyclic steroids, we investigated the UV. irradiation of the α,β-epoxylactam **1** *(Scheme)*.

Scheme



2 **1** **3**

Synthesis and photolysis of 1. – Conversion of 17β-hydroxy-2-aza-4-androsten-3-one (**2**) [4] with *m*-chloroperbenzoic acid yielded the desired α,β-epoxylactam **1** in quantitative yield *(Scheme)*. The configuration of the oxirane ring was established on the basis of its CD. data ($\lambda_{max} = 233.2$ nm; $\Delta\varepsilon = -5.387$)[2]).

The UV. irradiation ($\lambda = 254$ nm) of a 0.0089 M solution of **1** in dioxane yielded a multicomponent mixture from which 18% **1**, 60% of the *abeo*-lactam **3** and 6% of an unstable compound which was not identified, were isolated, together with two minor impurities (10%). For the unidentified compound, a 3,4-*seco* structure

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with solvent incorporation could be perhaps postulated on the basis of its spectral data (see experimental part).

Conclusion. – The photochemical behaviour of the lactam **1** is similar to its lactone analogue and it is, to our knowledge, the first example of an α,β-epoxy-lactam undergoing the 10(5→4) rearrangement to an *abeo* structure. Moreover, this, together with the previously reported result [1], suggest that the outcome of the photo-rearrangement of ring A α,β-epoxycarbonyl steroids is not greatly influenced by the nature of the heteroatom in the α' position.

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Experimental Part

General remarks: [3].

17β-Hydroxy-4a,5a-epoxy-2-azaandrostan-3-one (**1**). A solution of 856 mg of **2** [4] in 250 ml of $CHCl_3$ and 1.511 g of *m*-chloroperbenzoic acid, was stirred at RT. for 24 h. The usual work-up, washing successively with aqueous solutions of $NaHCO_3$, Na_2SO_3 and NaCl, yielded 879 mg of **1**, m.p. 266–267° after 5 crystallizations; $[\alpha]_D^{20} = +84.5°$ (0.51). – CD. CH_3CN (*c* (mg/g) = 0.2616, path length = 0.2): 233.2 (−5.387); 194.8 (2.447). – UV.: 207 (4500), 270 (200). – IR.: 3550, 3330, 3210, 1675, 1635, 1070, 1050, 795. – ^{1}H-NMR. (CD_3OD): 0.70 (*s*, $H_3C(18)$); 1.12 (*s*, $H_3C(19)$); 2.88, 2.95 (*AB*-system, $J_{AB} = 12$, $H_2C(1)$); 3.10 (*s*, H–C(4)); 3.65 (*m*, H–C(17)). – MS.: 305 (M^+).

$C_{18}H_{27}NO_3$ (305.42) Calc. C 70.79 H 8.91 N 4.59% Found C 70.88 H 8.89 N 4.86%

Photolysis of **1**. A solution of 435 mg of **1** in 160 ml of dioxane (*Carlo Erba,* analytical purity) was irradiated during 48 h with a low-pressure Hg-lamp. Solvent evaporation *in vacuo* yielded 441 mg of an oil. Chromatography on silica gel *Merck* ('reinst') with cyclohexane/ethyl acetate 3:7 furnished in the first fraction 28 mg of a pure compound that could not be identified, m.p. 240–241° after 3 crystallizations. – UV.: 213 (4300). – IR.: 3400, 3200, 3080, 1745, 1730, 1710, 1660, 1175, 1120. – ^{1}H-NMR.: 0.82 (*s*, $H_3C(18)$); 1.13 (*s*, $H_3C(19)$); 2.73 (*d*×*d*, *J* = 9 and 6, H–C(1)); 3.02 (*d*, *J* = 9, H–C(1)); 3.13 (*s*, H–C(4)); 3.32–4.00 (*m*, 10 H); 4.22 (*m*, 1 H); 4.63 (*m*, 1 H); 6.65 (br., H–N(2)); 8.00 (*s*, H–C(3)); after D_2O addition, the signal at 6.65 disappeared, the *d*×*d* at 2.73 simplified to a *d* and the relative integral of the *m* at 3.32–4.00 diminished in 2 unities. – MS.: 409 (M^+).

The second fraction, 43 mg of a mixture of 2 components, was not further investigated. The third fraction consisted of 81 mg of starting material **3** (identification by mixed m.p., TLC. and IR. spectrum). The fourth and last fraction afforded 266 mg of *17β-hydroxy-10(5→4-*abeo*)-4ξH-2-azaandrosta-3,5-dione* (**3**), m.p. 217–219° after 3 crystallizations; $[\alpha]_D^{20} = -30.2°$ (0.26). – UV.: 212 (1.560); 260 (1.500); after addition of one drop of 1N NaOH: 293 (5400); Fe^{3+} complex (3.2 mg of **3** in 5 ml of $3.7 \cdot 10^{-3}$M solution of $FeCl_3$ in ethanol): 600 (730). – IR.: 3380, 1727, 1680. – ^{1}H-NMR. (CD_3OD): 0.75 (*s*, $H_3C(18)$); 1.25 (*s*, $H_3C(19)$); 3.00 (*s*, $H_2C(1)$); 3.55 (*m*, *s*, H–C(17) and H–C(4)). – MS.: 305 (M^+).

$C_{18}H_{27}NO_3$ (305.42) Calc. C 70.79 H 8.91 N 4.59% Found C 70.84 H 9.12 N 4.33%

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