252. Photochemical Reactivity of α,β-Unsaturated δ-Lactams: Synthesis of Seco-steroids[1])

Photochemical Reactions. XIII [1]

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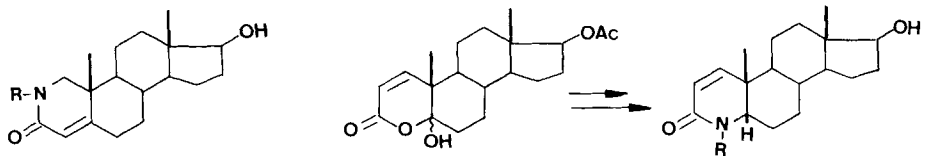
Summary

The UV. irradiation of 17β-hydroxy-2-aza-4-androsten-3-one (**1**), *N*-methyl-17β-hydroxy-2-aza-4-androsten-3-one (**3**), 17β-hydroxy-4-aza-5β-androst-1-en-3-one (**2**) and *N*-methyl-17β-hydroxy-4-aza-5β-androst-1-en-3-one (**4**), gives rise to 1,10-*seco* (from **1** and **3**) and 5,10-*seco* (from **2** and **4**) steroids.

Introduction. – Although in photochemical studies, lactams have received less attention than lactones and ketones, several examples can be found. Monocyclic [2] and bicyclic [3] compounds yield mainly fragmentation and sometimes [2b] dimerization products and the di-π-methane rearrangement of a lactam has been observed [4]. In the steroid field, several unsaturated lactams have been investigated. Enamidic lactams undergo photooxidation [5] or photoisomerization [6], and A-homolactams yield mainly dimers [7]. Owing to the little work done on α,β-unsaturated δ-lactams, we decided to investigate the photolytic behaviour of lactams **1**, **2**, **3** and **4** *(Scheme 1)*.

Scheme 1



1 R=H **3** R=Me — **5** — **2** R=H **4** R=Me

[1]) Communicated in part at the VIII. IUPAC-Symposium on Photochemistry, 13–19 July, 1980, Seefeld (Austria). Part of the doctoral thesis of *A. Cánovas*, I.Q.S., Barcelona, 1980.

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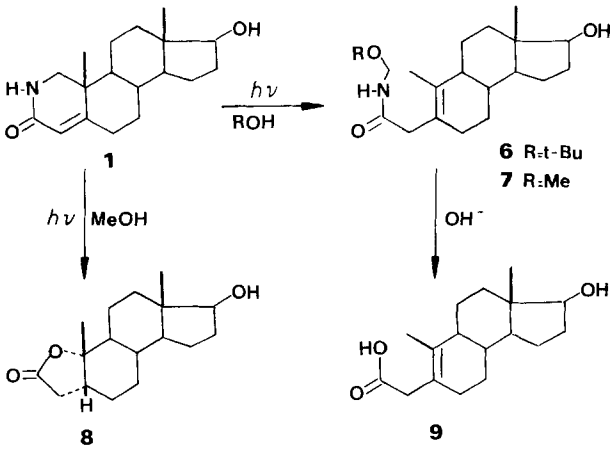
Synthesis and photolysis of *1–4*. – The synthesis of **2** has been described [8]. A *Leuckart* reaction on lactol **5** [9] followed by saponification, furnished lactam **2**, giving rise selectively to the 5β-isomer *(Scheme 1)*. Treatment of the 17-tetrahydropyranyl ethers of **1** and **2** with methyl iodide, and subsequent ether hydrolysis, yielded the corresponding *N*-methylated lactams, **3** and **4**, in high yield.

UV. irradiation ($\lambda = 254$ nm) of **1** in *t*-butyl alcohol, yielded the 1,10-*seco*-steroid **6** (75%) *(Scheme 2)*, together with mixtures of impurities of lower (8%) and higher polarity (14%). When the irradiation was carried out in methanol, the analogous 1,10-*seco*-steroid **7** (71%) was formed, accompanied by the lactone **8** (15%). The structures of these and the following photoproducts were deduced from their spectral data. Furthermore, basic hydrolysis of **6** and **7**, furnished the *seco*-acid **9**. An X-ray analysis confirmed the structure **8**.

Scheme 2



1 **8** **9**

Crystal data of **8**, *structure solution and refinement.* Crystals of **8** ($C_{17}H_{26}O_3$) were obtained by slow evaporation of an acetone solution. Preliminary *Weissenberg* photographs indicated the probable space group to be $P2_12_12_1$ (Z = 4) orthorombic. A needle shaped crystal was mounted on a glass fiber and used for all subsequent measurements. Three dimensional data were collected on a *Philips* single-crystal difractometer. Cell parameters: $a = 21{,}31$ Å; $b = 11{,}26$ Å; $c = 6{,}28$ Å; V = 1507 Å^3.

The 1260 reflections with $I \geq 2\sigma$ were considered reliable and used in the crystal structure analysis. After the *Lorentz*-polarization corrections had been applied, normalized structure factors amplitudes were computed and the structure was solved by direct methods (MULTAN program [10]). The atomic parameters were refined by full matrix least-squares calculations using AFFINE program [11]. After four isotropic and four anisotropic cycles the R value was 0.120 for all reflections. Atomic coordinates and anisotropic thermal factors are listed in *Table 1*, bond distances and angles in *Tables 2* and *3* respectively. They allow the determination of the structure of **8** as shown in *Figure 1*. Distances from least-squares plane defined by the atoms O(1), C(10) and C(5) are given in *Table 4*.

UV. irradiation ($\lambda = 254$ nm) of **2** in *t*-butyl alcohol, yielded a mixture of the isocyanate **10** (22%) conserving the β-configuration at C(5), and starting material **2** (69%) *(Scheme 3)*, together with several impurities (2%). When the irradiation was carried out in methanol, the 5,10-*seco*-steroid **12** (43%) was obtained as the major component, together with starting material **2** (5%), the isocyanate **10** (3%) and its corresponding carbamate **11** (9%).

Table 1. *Atomic coordinates* ($\times 10^4$) *and anisotropic thermal factors* ($\times 10^4$) (standard deviations in parentheses)

Atom	*X*	*Y*	*Z*	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
O(1)	2164 (5)	3295 (14)	2392 (18)	12 (3)	183 (18)	148 (33)	−28 (6)	−10 (9)	−31 (24)
C(2)	2502 (9)	2251 (18)	2983 (46)	22 (6)	73 (20)	805 (100)	7 (8)	120 (25)	62 (47)
C(3)	2261 (10)	1394 (17)	914 (34)	31 (6)	80 (20)	342 (71)	10 (9)	−8 (20)	91 (37)
C(5)	2035 (8)	2284 (17)	−876 (33)	18 (5)	83 (20)	294 (69)	−4 (8)	−21 (16)	−65 (36)
C(6)	1537 (9)	1741 (19)	−2489 (29)	27 (5)	138 (23)	99 (50)	−18 (10)	9 (15)	−32 (34)
C(7)	863 (7)	1469 (16)	−1476 (30)	7 (3)	100 (19)	244 (64)	7 (7)	10 (13)	−81 (34)
C(8)	576 (7)	2674 (14)	−406 (27)	10 (3)	53 (15)	204 (53)	−16 (6)	−15 (13)	5 (27)
C(9)	1050 (8)	3072 (16)	1437 (30)	18 (4)	94 (18)	88 (52)	−4 (7)	−19 (13)	9 (28)
C(10)	1730 (7)	3353 (17)	521 (27)	17 (4)	93 (20)	139 (50)	−25 (8)	9 (13)	18 (30)
C(11)	788 (7)	4085 (14)	2833 (30)	14 (4)	68 (16)	185 (58)	11 (6)	−23 (14)	−67 (28)
C(12)	96 (8)	3771 (16)	3740 (27)	26 (5)	61 (17)	106 (51)	1 (8)	18 (13)	−5 (26)
C(13)	−345 (7)	3375 (16)	1854 (25)	18 (4)	64 (16)	154 (50)	33 (7)	−13 (13)	−14 (27)
C(14)	−82 (7)	2388 (14)	571 (27)	14 (4)	68 (17)	92 (44)	5 (7)	2 (12)	24 (27)
C(15)	−582 (7)	1978 (15)	−909 (30)	5 (3)	83 (18)	246 (56)	−10 (6)	−1 (13)	−28 (30)
C(16)	−1185 (8)	2277 (16)	467 (38)	14 (4)	86 (19)	418 (79)	−11 (7)	13 (17)	−104 (40)
C(17)	−969 (7)	2878 (14)	2501 (33)	14 (4)	65 (16)	285 (66)	−3 (7)	66 (15)	−30 (30)
C(18)	−430 (7)	4504 (16)	342 (33)	19 (4)	57 (17)	336 (74)	10 (7)	49 (16)	52 (32)
C(19)	1761 (8)	4643 (16)	−572 (36)	25 (5)	94 (18)	305 (67)	−13 (8)	13 (18)	69 (33)
O(20)	2826 (7)	2118 (19)	4152 (24)	25 (4)	362 (34)	356 (58)	56 (10)	−60 (14)	111 (39)
O(21)	−1370 (6)	3766 (10)	3212 (24)	22 (3)	71 (11)	432 (55)	11 (5)	52 (12)	32 (24)

Table 2. *Bond distances* (Å) (standard deviations in parentheses)

O(1)-C(2)	1.427 (45)	C(9)-C(11)	1.543 (42)
O(1)-C(10)	1.497 (36)	C(10)-C(19)	1.607 (45)
C(2)-C(3)	1.697 (52)	C(11)-C(12)	1.618 (41)
C(2)-O(20)	1.019 (49)	C(12)-C(13)	1.576 (40)
C(3)-C(5)	1.580 (47)	C(13)-C(14)	1.482 (39)
C(5)-C(6)	1.590 (47)	C(13)-C(17)	1.499 (41)
C(5)-C(10)	1.625 (44)	C(13)-C(18)	1.596 (42)
C(6)-C(7)	1.601 (45)	C(14)-C(15)	1.487 (39)
C(7)-C(8)	1.632 (40)	C(15)-C(16)	1.585 (44)
C(8)-C(9)	1.600 (42)	C(16)-C(17)	1.517 (45)
C(8)-C(14)	1.563 (38)	C(17)-O(21)	1.389 (37)
C(9)-C(10)	1.591 (43)		

Table 3. *Bond angles (degrees)* (standard deviations in parentheses)

C(2)-O(1)-C(10)	123.5 (5.3)	C(5)-C(10)-C(9)	114.4 (4.8)
O(1)-C(2)-C(3)	96.7 (4.5)	C(5)-C(10)-C(19)	115.0 (4.9)
O(1)-C(2)-O(20)	130.5 (9.0)	C(9)-C(10)-C(19)	111.8 (4.7)
C(3)-C(2)-O(20)	132.3 (8.9)	C(9)-C(11)-C(12)	111.6 (4.6)
C(2)-C(3)-C(5)	106.0 (4.9)	C(11)-C(12)-C(13)	109.9 (4.4)
C(3)-C(5)-C(6)	114.4 (5.3)	C(12)-C(13)-C(14)	113.2 (4.7)
C(3)-C(5)-C(10)	102.0 (4.4)	C(12)-C(13)-C(17)	115.5 (4.9)
C(6)-C(5)-C(10)	111.1 (4.9)	C(12)-C(13)-C(18)	106.8 (4.3)
C(5)-C(6)-C(7)	114.8 (5.2)	C(14)-C(13)-C(17)	101.7 (4.1)
C(6)-C(7)-C(8)	109.9 (4.5)	C(14)-C(13)-C(18)	108.4 (4.4)
C(7)-C(8)-C(9)	107.1 (4.1)	C(17)-C(13)-C(18)	111.0 (4.6)
C(7)-C(8)-C(14)	109.1 (4.1)	C(8)-C(14)-C(13)	113.5 (4.5)
C(9)-C(8)-C(14)	109.9 (4.3)	C(8)-C(14)-C(15)	117.5 (4.8)
C(8)-C(9)-C(10)	111.7 (4.6)	C(13)-C(14)-C(15)	107.5 (4.4)
C(8)-C(9)-C(11)	112.9 (4.8)	C(14)-C(15)-C(16)	100.1 (4.0)
C(10)-C(9)-C(11)	112.8 (4.8)	C(15)-C(16)-C(17)	107.9 (4.8)
O(1)-C(10)-C(5)	98.2 (3.7)	C(13)-C(17)-C(16)	102.0 (4.4)
O(1)-C(10)-C(9)	105.7 (4.2)	C(13)-C(17)-O(21)	111.4 (4.8)
O(1)-C(10)-C(19)	110.4 (4.5)	C(16)-C(17)-O(21)	113.8 (5.1)

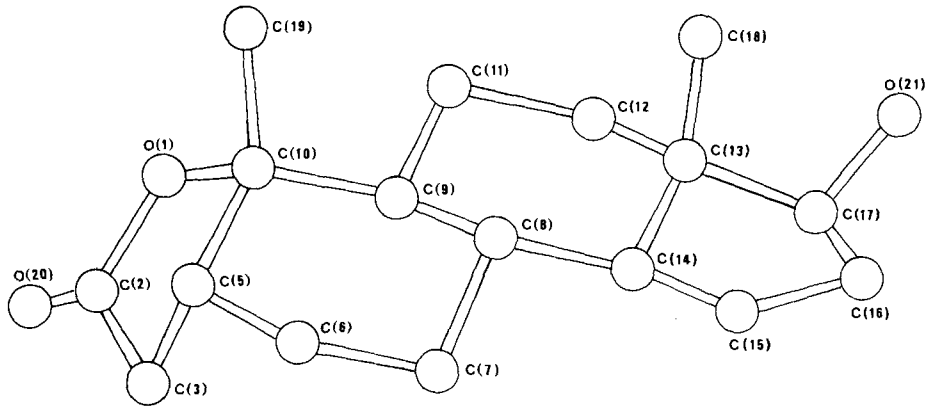
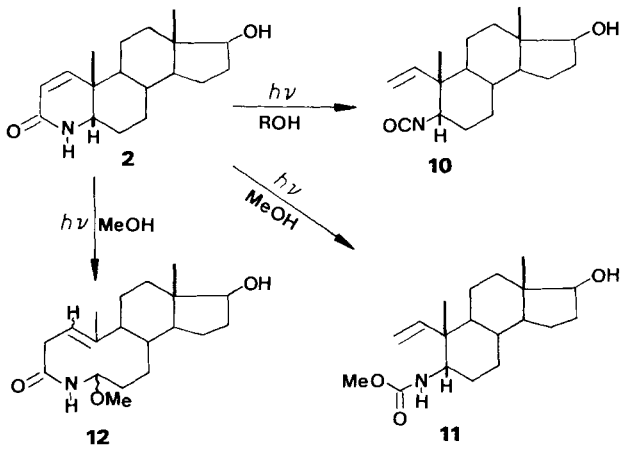


Figure. *The molecular structure of* **8**

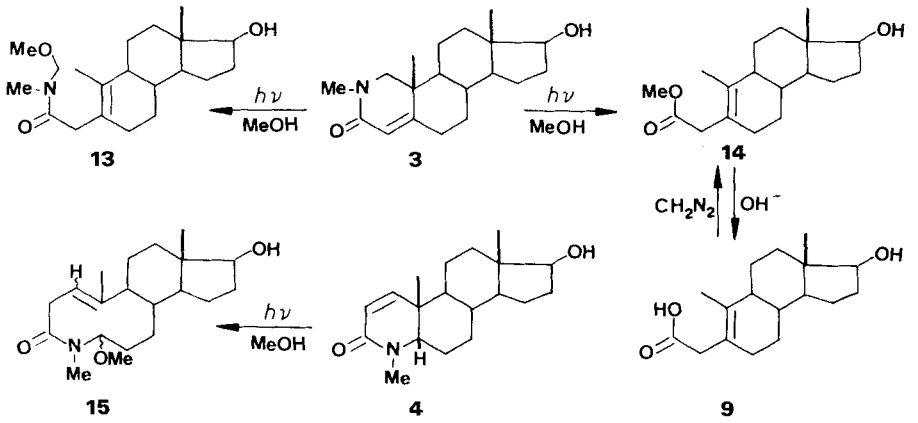
Table 4. *Distances from the least-squares plane defined by the atoms* O(1), C(10) and C(5)

Atom	C(9)	C(6)	C(19)	C(3)
Distance (Å)	−1.3482	−0.5976	1.2970	−0.8635

Scheme 3



Scheme 4

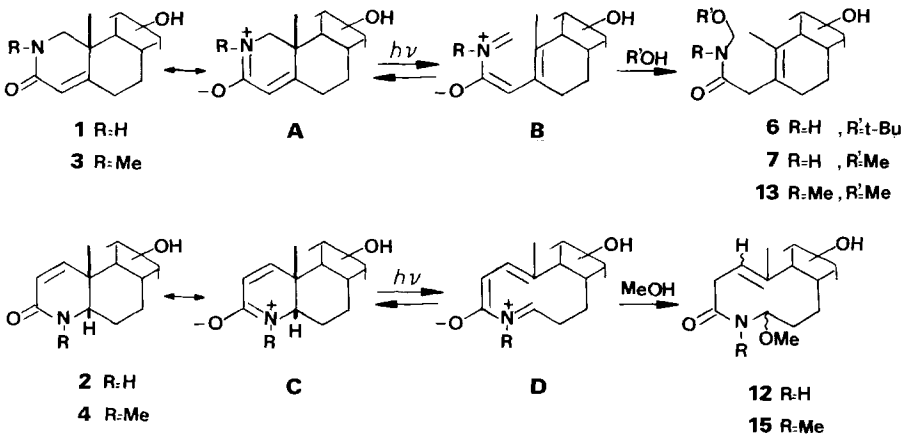


Concerning the *N*-methylated lactams, the irradiation ($\lambda = 254$ nm) of **3** and **4** in *t*-butyl alcohol yielded only mixtures of minor compounds that could not be separated from the starting material, the latter being recovered in about 70% in both cases. However, by irradiation in methanol, **4** afforded the *seco*-steroid **15** (68%) and **3** gave **13** (20%) and the *seco*-ester **14** (33%), identical to the product obtained by treatment of **9** with diazomethane. Saponification of **14** gave **9** *(Scheme 4)*.

Discussion. – The common feature explaining the formation of most, if not all, of these photoproducts, is the cleavage of the C,C-bond in the α-position to the N-atom of the lactam function, to yield 1,10- or 5,10-*seco*-steroids[3]) *(Scheme 5)*.

[3]) This phenomenon has already been observed in one monocyclic *N*-unsubstituted lactam [2c].

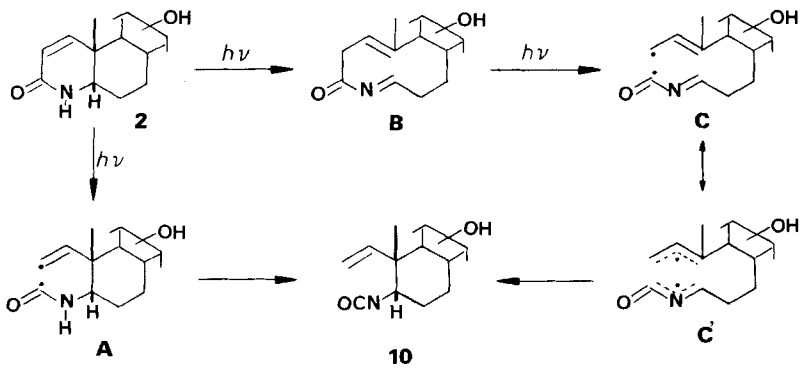
Scheme 5



It is assumed that the α,β-unsaturated lactam is partially diene in character, leading to ring opening by an electrocyclic process on irradiation. This mechanism is the aza-analogy to the cyclohexadiene photoisomerization and is related to that proposed for the photocyclization of α,β-unsaturated enamides in the synthesis of alkaloids [12]. The results of the irradiations of **2**, **3** and **4** in *t*-butyl alcohol can be explained by steric hindrance in the solvent addition to the azahexatriene, which then cyclizes back to starting material.

In order to explain the formation of the isocyanate **10** from **2**, a *Norrish* type I mechanism, is proposed *(Scheme 6)*. One possibility is *via* intermediate **A** and would be to our knowledge, the first exampple of an α-cleavage leading to a vinyl diradical[4]). An alternative is the above mentioned ring opening reaction (**2**→**B**) which would produce an allylic diradical (**C**↔**C'**), which could collapse to **10**. The fact that the configuration at C(5) is maintained in the photoproduct is in agree-

Scheme 6



[4]) No intramolecular migration of the amide H-atom to the vinyl group is proposed, since in the irradiation of the *N*-*D*-derivative of the tetrahydropyranyl ether of **2** in acetonitrile, incorporation of D in the vinyl group was not observed.

ment with the pathway **2**→**A**→**10**. On the other hand, the second mechanism implies short-lived intermediates or strong interaction between the delocalized π-allylic diradicals (**C'**).

No specific mechanism is proposed to explain the formation of **8**. However, it could arise from **1** *via* acid attack[5]) on a photolytic intermediate different from **9**[6]). Similarly, no detailed mechanism is formulated to explain the formation of the ester **14** in the photolysis of **3**. It may originate by solvent attack (methanol) on the carbonyl function of a 1,10-*seco*-intermediate, which cannot be **13**, since **13** is stable in the irradiation conditions.

Conclusion. – Our results and others [2] suggest that electrocyclic ring opening is a general reaction for α,β-unsaturated δ-lactams. Irradiation of enamides yields photocyclization products also derived *via* an electrocyclic reaction [12]. Therefore, the participation of the CO,N-bond of conjugated lactams and amides in photochemical reactions appears to be general.

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Experimental Part

General remarks: [9].

17β-Hydroxy-4-aza-5β-androst-1-en-3-one (**2**). To a solution of 22 g of ammonium formate in 25 ml of HCOOH, 980 mg of **5** [9] were added. The mixture was refluxed for 24 h. The usual work-up with $CHCl_3$ yielded an oil that was dissolved in 50 ml of MeOH, treated with 50 ml of 4N aq. NaOH, refulxed for 1 h and then cooled. The addition of 400 ml of water resulted in the formation of a precipitate of 667 mg of **2** pure, m.p. 282–283° after 3 crystallizations; $[\alpha]_D^{20} = +180.5°$ ($c = 0.25$). – UV.: 210 (10,500), 255 (2,600). – IR.: 3360, 3240, 1660, 1600. – ^{1}H-NMR.: 0.70 (*s*, $H_3C(18)$); 1.08 (*s*, $H_3C(19)$); 2.50 (br., HO), disappeared on D_2O addition); 3.40 (*m*, H–C(5)); 3.56 (*m*, H–C(17)); 5.73, 6.35 (*AB*-system, $J_{AB} = 11$, H–C(2), H–C(1)); 6.00 (br., HN, disappeared on D_2O addition). – MS.: 289 (M^+).

$C_{18}H_{27}NO_2$ (289.40) Calc. C 74.70 H 9.40 N 4.84% Found C 74.59 H 9.37 N 4.77%

N-Methyl-17β-hydroxy-2-aza-4-androsten-3-one (**3**). The same procedure described for the synthesis of **4** from **2** (see below), was applied to 317 mg of **1** [8], to obtain 302 mg of **3**, m.p. 130–132° after 4 crystallizations; $[\alpha]_D^{20} = +156°$ ($c = 0.21$). – UV.: 217 (6,850), 250 (1,450). – IR.: 3400, 1670, 1620. – ^{1}H-NMR.: 0.79 (*s*, $H_3C(18)$); 1.10 (*s*, $H_3C(19)$); 2.91 (*s*, H_3C–N); 3.05 (br., HO, disappeared

[5]) Formic acid produced in the irradiation of methanol in the presence of air [13].

[6]) Compound **9** is photostable when irradiated in MeOH containing Na_2CO_3. Treatment of **9** with chlorhydric acid gives a lactone different from **8**. The acid **9** reacts only slowly in MeOH/HCOOH and, on the other hand, **9** is not observed in the irradiation of **1**.

on D_2O addition); 3.07, 3.11 (*AB*-system, $J_{AB}=12$, $H_2C(1)$); 3.60 (*m*, H–C(17)); 5.50 (*s*, H–C(4)). – MS.: 303 (M^+).

$C_{19}H_{29}NO_2$ (303.45) Calc. C 75.21 H 9.63 N 4.62% Found C 75.04 H 9.87 N 4.58%

N-*Methyl-17β-hydroxy-4-aza-5β-androst-1-en-3-one* (**4**). To a solution of 380 mg of **2** in dry $CHCl_3$, 10 mg of *p*-toluenesulfonic acid and 2 ml dihydropyran were added. The mixture was stirred overnight at RT. The usual work-up with $CHCl_3$, washing with aqueous $NaHCO_3$-solution and water, yielded 450 mg of the tetrahydropyran derivative of **2**, m.p. 254–256° after one crystallization. – IR.: 3200, 3120, 3070, 3020, 1680, 1660, 1610, 1130, 1120, 1030, 1015. – ^{1}H-NMR.: 0.78 (*s*, $H_3C(18)$); 1.15 (*s*, $H_3C(19)$); 3.20–4.00 (br. *m*, H–C(5), H–C(17) and 4 H from the tetrahydropyran ring); 4.57 (br. *s*, H–C(R)–O–C(17)); 5.80 ($d\times d$, $J=11$ and 2, H–C(2)); 6.35 (br., H–N); 6.40 (*d*, $J=11$, H–C(1)); after D_2O addition the signal at 6.35 disappeared and the $d\times d$ at 5.80 simplified to a *d*. – MS.: 373 (M^+).

To the solution of 410 mg of the tetrahydropyran derivative in 50 ml of dry benzene, 40 mg of sodium hydride were added, and the mixture was refluxed for 1 h. After cooling, 1 ml of methyl iodide was added and the mixture refluxed for 1 h. Once cool, it was washed twice with water, dried (Na_2SO_4) and evaporated *in vacuo* to yield 422 mg of the 17-tetrahydropyranyl derivative of **4**, m.p. 131–133° after one crystallization. – IR.: 3020, 1675, 1620, 1610, 1130, 1120, 1030, 1015. – ^{1}H-NMR.: 0.82 (*s*, $H_3C(18)$); 1.20 (*s*, $H_3C(19)$); 3.00 (*s*, H_3C–N); 3.25–4.15 (br. *m*, H–C(5), H–C(17) and 4 H from the tetrahydropyran ring); 4.58 (br., H–C(R)–O–C(17)); 5.88, 6.40 (*AB*-system, $J_{AB}=11$, H–C(2), H–C(1)). – MS.: 387 (M^+).

Finally, 390 mg of this last derivative were dissolved in 15 ml of MeOH with 2 drops conc. hydrochloric acid and left at RT. for 1 h. After concentrating *in vacuo*, 50 ml of water were added, to give a white precipitate that was filtered off and washed with water, to yield 315 mg of pure **4**, m.p. 238–240° after 3 crystallizations; $[\alpha]_D^{20}=+99.0$ ($c=0.30$). – UV.: 210 (7,100), 255 (1,200). – IR.: 3430, 3340, 3210, 1665, 1605. – ^{1}H-NMR.: 0.76 (*s*, $H_3C(18)$); 1.18 (*s*, $H_3C(19)$); 2.55 (*s*, HO, disappeared on D_2O addition); 2.91 (*s*, H_3C–N); 3.29 (*m*, H–C(5)); 3.57 (*m*, H–C(17)); 5.79, 6.31 (*AB*-system, $J_{AB}=11$, H–C(2), H–C(1)). – MS.: 303 (M^+).

$C_{19}H_{29}NO_2$ (303.45) Calc. C 75.21 H 9.63 N 4.62% Found C 75.11 H 9.81 N 4.40%

Irradiation of 1. – a) *In t-butyl alcohol.* A solution of 150 mg of **1** in 160 ml of *t*-butyl alcohol *Merck* (analytical purity) was irradiated during 3 h with a low-pressure Hg-lamp. Solvent evaporation *in vacuo* yielded 166 mg of a crude containing a major component, which was purified by chromatography in ethyl acetate. The first fraction consisted of 13 mg of a mixture of several components, not further investigated. The second fraction yielded 125 mg of *1-t-butoxy-17β-hydroxy-2-aza-1,10-seco-androst-5(10)-en-3-one* (**6**), m.p. 139.5–140°; $[\alpha]_D^{20}=+65.0°$ ($c=0.25$). – UV.: 217 (6,700). – IR.: 3260, 3180, 3060, 1660, 1650, 1060. – ^{1}H-NMR.: 0.80 (*s*, $H_3C(18)$); 1.26 (*s*, $(CH_3)_3C$–O); 1.68 (br. *s*, $H_3C(19)$); 2.25 (br., HO); 2.95 (br., $H_2C(4)$); 3.70 (*m*, H–C(17)); 4.70, 4.80 (2 *s*, H_2–C(1)); 6.30 (br., H–N); after D_2O addition the signals at 2.25 and 6.30 disappeared. – MS.: 363 (M^+).

$C_{22}H_{37}NO_3$ (363.55) Calc. C 72.69 H 10.26 N 3.85% Found C 72.61 H 10.61 N 3.64%

The third fraction afforded 23 mg of a mixture which was not further investigated.

b) *In methanol.* A solution of 197 mg of **1** in 160 ml of MeOH was irradiated for 10 h with a low-pressure Hg-lamp. Solvent evaporation *in vacuo* afforded 215 mg of an oil. Chromatography on silica gel in ethyl acetate gave first 33 mg of *17β-hydroxy-1-oxa-A-nor-5β-androstan-2-one* (**8**), m.p. 238–240° after 3 crystallizations. – UV.: 203 (2,900). – IR.: 3490, 1740, 1245. – ^{1}H-NMR.: 0.78 (*s*, $H_3C(18)$); 1.45 (*s*, $H_3C(19)$); 2.50 (br., HO, $H_2C(4)$); 3.70 (*m*, H–C(17)); after D_2O addition the signal at 2.50 simplified. – MS.: 278 (M^+).

$C_{17}H_{26}O_3$ (278.39) Calc. C 73.35 H 9.41% Found C 73.31 H 9.75%

The second fraction consisted of 153 mg of *17β-hydroxy-1-methoxy-2-aza-1,10-seco-5(10)-androsten-3-one* (**7**), m.p. 120–120.5° after 2 crystallizations. – UV.: 205 (5,800), 270 (1,040). – IR.: 3580, 3350, 3240, 3040, 2830, 1660, 1640, 1600. – ^{1}H-NMR.: 0.72 (*s*, $H_3C(18)$); 1.61 (*s*, $H_3C(19)$); 2.40 (br., HO); 3.00 (*AB*-system, $J_{AB}=14$, $H_2C(4)$); 3.23 (*s*, H_3CO); 3.60 (*m*, H–C(17)); 4.52, 4.63 (2 *s*, $H_2C(1)$); 6.30 (br., H–N); after D_2O addition the signals at 2.40 and 6.30 disappeared. – MS.: 321 (M^+).

The third fraction afforded 12 mg of starting material **1** (mixed m.p., TLC. and IR. spectrum). The fourth and last fraction consisted of 8 mg of a mixture and was not further investigated.

Irradiation of 2. – a) *In t-butyl alcohol.* A solution of 720 mg of **2** in 160 ml of *t*-butyl alcohol *Merck* (analytical purity) was irradiated during 17 h with a low-pressure Hg-lamp. Solvent evaporation *in vacuo* yielded 732 mg of a mixture of 2 components which was chromatographed with ethyl acetate. The first fraction yielded 165 mg of *17β-hydroxy-4-aza-2,3-*seco*-5β-androsta-1,3-dien-3-one* (**10**), m.p. 110–111° after 3 crystallizations; $[\alpha]_D^{20} = +18.6°$ ($c = 0.35$). – UV.: 203 (980). – IR.: 3310, 3090, 3010, 2270, 1640, 915. – ^{1}H-NMR.: 0.70 (*s*, $H_3C(18)$); 1.05 (*s*, $H_3C(19)$); 1.70 (br., HO, disappeared on D_2O addition); 3.40 (*d*×*d*, $J = 2$ and 3, H–C(5)); 3.62 (*m*, H–C(17)); 5.00 (*d*×*d*, $J = 17$ and 1, H–C(2)); 5.07 (*d*×*d*, $J = 11$ and 1, H–C(2)); 5.70 (*d*×*d*, $J = 17$ and 11, H–C(1)). – MS.: 289 (M^+).

$C_{18}H_{27}NO_2$ (289.40) Calc. C 74.70 H 9.40 N 4.84% Found C 74.76 H 9.59 N 4.57%

The second fraction consisted of 17 mg of a mixture of several components. The third fraction yielded 512 mg of **2** (mixed m.p., TLC., and IR.).

b) *In methanol.* A solution of 575 mg of **2** in 160 ml of MeOH was irradiated during 36 h with a low-pressure Hg-lamp. Solvent evaporation *in vacuo* yielded 593 mg of an oil that was chromatographed on silica gel. With cyclohexane/ethyl acetate 7:3, 18 mg of **10** (mixed m.p., TLC., and IR.) were eluted. The second fraction consisted of 22 mg of a mixture of **10** and **11**. The third fraction yielded 57 mg of *methyl 17β-hydroxy-4-aza-2,3-*seco*-5β-androst-1-en-3-oate* (**11**), m.p. 118–120° after 3 crystallizations; $[\alpha]_D^{20} = +22°$ ($c = 0.30$). – UV.: end absorption. – IR.: 3350, 3090, 3010, 1715, 1640. – ^{1}H-NMR.: 0.77 (*s*, $H_3C(18)$); 1.12 (*s*, $H_3C(19)$); 1.80 (br., HO); 3.55 (*m*, H–C(17)); 3.60 (*s*, $COOCH_3$); 5.00 (*d*×*d*, $J = 17$ and 1, H–C(2)); 5.07 (*d*×*d*, $J = 11$ and 1, H–C(2)); 5.10 (br., H–N); 5.60 (*d*×*d*, $J = 17$ and 11, H–C(1)); after D_2O addition the signals at 1.80 and 5.10 disappeared. – MS.: 321 (M^+).

$C_{19}H_{31}NO_3$ (321.46) Calc. C 70.99 H 9.72 N 4.36% Found C 70.88 H 9.98 N 4.24%

With cyclohexane/ethyl acetate 1:1 133 mg of a mixture was eluted. The fifth fraction afforded 255 mg of *17β-hydroxy-5ξ-methoxy-4-aza-5,10-*seco*-1(10)-androsten-3-one* (**12**), m.p. 166–167° after 3 crystallizations; $[\alpha]_D^{20} = +48°$ ($c = 0.10$). – UV.: 207 (3,800). – IR.: 3500, 3200, 3100, 1720, 1680, 1620. – ^{1}H-NMR.: 0.80 (*s*, $H_3C(18)$); 1.80 (*s*, $H_3C(19)$, HO); 2.90 (*d*, $J = 7$, $H_2C(2)$); 3.33 (*s*, CH_3O); 3.60 (*m*, H–C(17)); 5.07 (*d*×*t*, $J = 8$ and 3, H–C(5)); 5.60 (*t*, $J = 7$, H–C(1)); 6.50 (*d*, $J = 8$, H–N). – MS.: 321 (M^+).

$C_{19}H_{31}NO_3$ (321.46) Calc. C 70.99 H 9.72 N 4.36% Found C 70.97 H 9.66 N 4.04%

With ethyl acetate 32 mg of **2** were eluted (mixed m.p., TLC., and IR.). The last fraction consisted of 53 mg of a mixture of polar components.

Irradiation of 3. – A solution of 260 mg of **3** in 160 ml of MeOH was irradiated during 48 h with a low-pressure Hg-lamp. Solvent evaporation *in vacuo* yielded 271 mg of an oil that was chromatographed in ethyl acetate. The first fraction yielded 89 mg of *methyl 17β-hydroxy-A-dinor-1,10-*seco*-5(10)-androsten-1-oate* (**14**) as an oil. – UV.: end absorption. – IR. (film): 3400, 1740. – ^{1}H-NMR.: 0.75 (*s*, $H_3C(18)$); 1.63 (br. *s*, $H_3C(19)$); 2.95, 3.10 (*AB*-system, $J_{AB} = 14$, $H_2C(2)$); 3.65 (*s*, *m*, $COOCH_3$, H–C(17)). – MS.: 292 (M^+).

The second fraction consisted of 55 mg of N-*methyl-17β-hydroxy-1-methoxy-2-aza-1,10-*seco*-5(10)-androsten-3-one* (**13**), as an oil. – UV.: end absorption. – IR. (film): 3380, 1640. – ^{1}H-NMR.: 0.70 (*s*, $H_3C(18)$); 1.55 (br. *s*, $H_3C(19)$); 2.95 (*s*, $H_3C–N$); 3.10 (br., $H_2C(4)$); 3.25 (*s*, H_3CO); 3.65 (*m*, H–C(17)); 4.60, 4,75 (2 *s*, $H_2C(1)$); 5.10 (br., HO, disappeared on D_2O addition). – MS.: 335 (M^+).

The third fraction afforded 39 mg of a mixture. The fourth fraction consisted of 69 mg of starting material **3** (mixed m.p., TLC., and IR.). The last fraction yielded 16 mg of a mixture of polar compounds.

Irradiation of 4. – A solution of 280 mg of **4** in 160 ml MeOH was irradiated during 16 h with a low-pressure Hg-lamp. Solvent evaporation *in vacuo* afforded 308 mg of a mixture containing a major component. Chromatography in ethyl acetate yielded, first, 47 mg of a mixture of several components which was not further investigated. The second fraction consisted of 210 mg of

N-methyl-17β-hydroxy-5ξ-methoxy-4-aza-5,10-seco-1(10)-androsten-3-one (**15**), m.p. 177–178° after 3 crystallizations; $[\alpha]_D^{20} = -44°$ ($c = 0.22$). – UV.: end absorption. – IR.: 3425, 3050, 1630. – ^{1}H-NMR.: 0.77 (*s*, $H_3C(18)$); 1.68 (br. *s*, $H_3C(19)$); 2.80 (*s*, H_3C-N); 3.20 (br. *s*, CH_3O, $H_2C(2)$); 3.70 (*m*, H–C(17)); 4.80 (*m*, H–C(5)); 5.20 (*m*, H–C(1)). – MS.: 335 (M^+).

$C_{20}H_{33}NO_3$ (335.49) Calc. C 71.60 H 9.91 N 4.17% Found C 72.02 H 10.13 N 4.14%

The last fraction consisted of 13 mg of a mixture.

Non-photochemical transformations. – *Hydrolysis of* **6**. A solution of 98 mg of **6** in 10 ml of dioxane and 15 ml of 4N NaOH, was refluxed for 12 h. After cooling, the mixture was extracted with ether. The aqueous layer was acidified and worked up in the usual way to yield 51 mg of *17β-hydroxy-A-dinor-1,10-seco-5(10)-androsten-1-oic acid* (**9**), pure, m.p. 159–160° after 3 crystallizations; $[\alpha]_D^{20} = +64°$ ($c = 0.05$). – UV.: end absorption. – IR.: 3300, 1685, 1655. – ^{1}H-NMR. (CD_3COCD_3): 0.75 (*s*, $H_3C(18)$); 1.65 (br. *s*, $H_3C(19)$); 2.90, 3.05 (*AB*-system, $J_{AB} = 15$, $H_2C(4)$); 3.65 (*m*, H–C(17)); 4.70 (br., HO, HOOC, disappeared on D_2O addition). – MS.: 278 (M^+).

$C_{17}H_{26}O_3$ (278.39) Calc. C 73.35 H 9.41 Found C 73.28 H 9.56%

Hydrolysis of **7**. The same procedure described above for **6**, when applied to 40 mg of **7**, yielded 19 mg of **9** (mixed m.p., TLC., and IR.).

Saponification of **14**. A solution of 13 mg of **14** in 5 ml of MeOH and 3 ml of 4N aqueous NaOH was left for 2 h at RT. After solvent concentration *in vacuo* and acidification, the usual work-up yielded 10 mg of pure **9** (mixed m.p., TLC., and IR.).

Treatment of **9** *with diazomethane.* A solution of 20 mg of **9** in 20 ml of ether was treated with an ethereal solution of diazomethane. Solvent elimination *in vacuo* yielded 22 mg of pure **14** (mixed TLC. and IR.).

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