110. A Di-π-Methane Rearrangement in the Photolysis of a 4-Oxa-steroidal α,β-Unsaturated Enol-lactone[1])

Photochemical Reactions VIII [1]

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Dedicated to Professor *Oskar Jeger* on his 60th anniversary

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Summary

The irradiation of 17β-acetoxy-4-oxa-1,5-androstadien-3-one (**12**) yielded the two stereoisomeric spiro-lactones **13** and **14**, which result from a di-π-methane photorearrangement. A third product, the oxa-anthrasteroid **15**, was also isolated *(Scheme 3).*

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1. Introduction. - Di-π-methane photorearrangements have proven to be especially general and have received considerable attention in recent time [2]. A variant of this reaction is found in the photochemistry of cyclohexenones having double bonds in δ-position; such an example is the rearrangement of 3-oxo-$\Delta^{1,5}$-steroids, which has extensively been studied by *Jeger et al.* [3]: thus, the UV. irradiation of the two epimeric ketones **1** and **2** *(Scheme 1)* gave in each case and regardless of their configuration at C(10) the four cyclopentenones **3**–**6** and its photoisomer **7**.

In our efforts to study the influence of the modification of the chromophor on the course of this reaction, we investigated some years ago the photochemical behaviour of the oxime **8** *(Scheme 1)* [4]. Apart from other solvent dependent photoproducts, again the four cyclopentenones **3**–**6** were isolated. Nevertheless, given the easy photofragmentation of oximes to the corresponding ketones [5] it was not possible to establish weather the di-π-methane rearrangement had taken place in oxime **8** or in ketone **1**. However, the observed remarkable stability of the hydroxyimino derivate of **6** towards photofragmentation to ketone **6** [6], seems to indicate that di-π-methane rearrangement of the oxime **8** does not occur.

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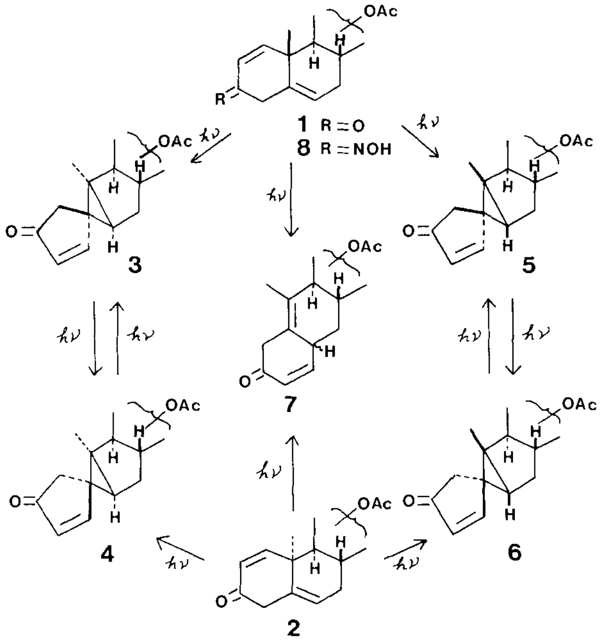
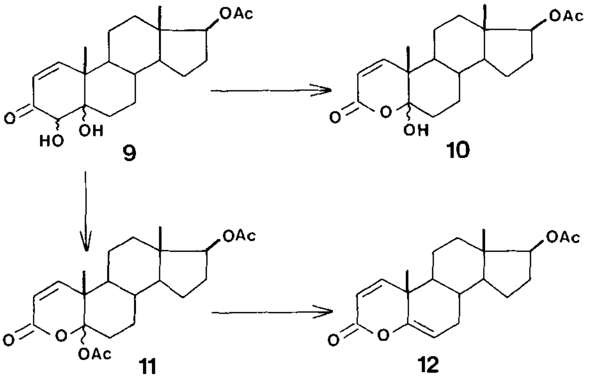
Scheme 1



Scheme 2



Pursuing this study we investigated the photoreactivity of the α,β-unsaturated enol-lactone **12** *(Scheme 2)*, the 4-oxa-analogue of ketone **1**.

2. Synthesis and photolysis of 12. - On treatment with lead tetraacetate in benzene 17β-acetoxy-4ξ,5ξ-dihydroxy-1-androsten-3-one (**9**) [7] [8] was converted to the hydroxy-compound **10** (24%) and the diacetate **11** (58%). Thermolysis of **11** gave the desired lactone **12** in quantitative yield[4]).

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[4]) The UV., IR., NMR. and mass spectra of **10-12** are in good agreement with the proposed structures (s. Exper. Part).

UV. irradiation ($\lambda = 254$ nm) of a 0,0047 M benzene solution of **12** yielded a mixture of **12** (45%), the spiro-lactones **13** (8%) and **14**[5] (10%), the oxa-anthrasteroid **15** (2%) and mixtures of unidentified products of very low polarity (14%) (*Scheme 3*). The structures of all photoproducts were deduced from their spectral data[4]. An X-ray analysis confirmed the structure of **13**.

Scheme 3

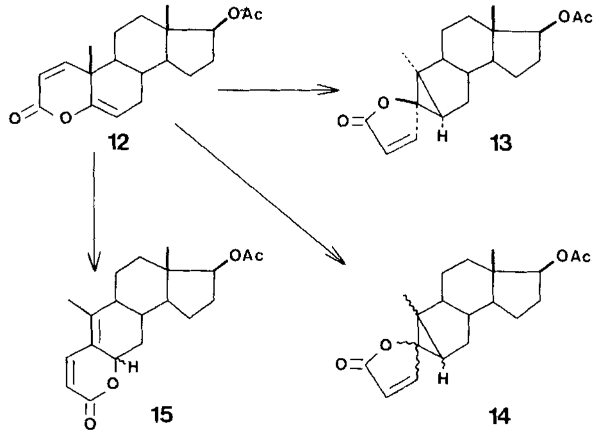

Table 1. *Atomic coordinates* (× 10^4) *and anisotropic thermal factors* (× 10^4) (standard deviations in parentheses)

Atom	X	Y	Z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
C(1)	1982 (9)	2943 (22)	6611 (8)	80 (10)	206 (33)	69 (8)	7 (17)	− 8 (7)	1 (15)
C(2)	1936 (11)	1287 (24)	7140 (9)	124 (14)	251 (37)	73 (9)	21 (22)	− 14 (9)	19 (17)
C(3)	2335 (10)	− 454 (27)	6523 (8)	67 (11)	570 (63)	52 (8)	31 (22)	− 2 (7)	− 45 (20)
O(4)	2647 (7)	350 (0)	5564 (6)	58 (8)	16 (17)	31 (6)	28 (11)	3 (5)	− 12 (9)
C(5)	2470 (9)	2457 (22)	5558 (8)	66 (10)	246 (34)	55 (7)	8 (16)	0 (7)	− 2 (14)
C(6)	3280 (10)	3879 (22)	5011 (8)	82 (11)	215 (35)	74 (9)	− 10 (18)	− 9 (8)	− 15 (15)
C(7)	4235 (9)	3154 (21)	4203 (9)	74 (10)	209 (34)	80 (8)	− 22 (16)	14 (7)	− 29 (15)
C(8)	3470 (9)	1533 (22)	3566 (8)	77 (10)	209 (32)	54 (7)	33 (16)	− 2 (7)	− 1 (14)
C(9)	2130 (9)	2408 (21)	3512 (7)	73 (9)	172 (28)	58 (7)	− 14 (14)	− 5 (6)	− 3 (12)
C(10)	1969 (9)	3469 (21)	4564 (8)	83 (10)	192 (29)	67 (8)	13 (15)	8 (7)	− 14 (13)
C(11)	1168 (10)	899 (21)	3115 (8)	83 (11)	250 (36)	63 (8)	− 19 (17)	13 (7)	− 5 (14)
C(12)	1506 (9)	294 (25)	1975 (8)	67 (10)	295 (35)	63 (7)	− 35 (18)	4 (7)	− 21 (16)
C(13)	2871 (9)	− 453 (21)	1960 (8)	84 (11)	200 (31)	57 (7)	− 19 (16)	4 (7)	− 2 (14)
C(14)	3797 (8)	1161 (22)	2430 (8)	56 (9)	246 (33)	66 (7)	− 2 (17)	5 (7)	− 33 (15)
C(15)	5104 (10)	321 (29)	2148 (9)	70 (10)	475 (49)	87 (9)	− 8 (21)	8 (8)	− 110 (21)
C(16)	4871 (10)	− 581 (26)	1054 (9)	83 (11)	381 (44)	89 (10)	− 39 (21)	19 (9)	− 58 (20)
C(17)	3356 (9)	− 558 (39)	823 (12)	53 (11)	641 (74)	88 (11)	− 40 (24)	10 (8)	− 64 (25)
C(18)	3008 (14)	− 2469 (22)	2481 (10)	170 (17)	136 (31)	75 (9)	3 (20)	9 (10)	11 (15)
C(19)	893 (10)	4963 (22)	4615 (9)	78 (10)	208 (35)	80 (9)	35 (17)	20 (7)	9 (15)
O(20)	2405 (9)	− 2187 (18)	6701 (7)	101 (12)	10 (20)	55 (7)	14 (13)	0 (7)	28 (11)
O(21)	3024 (21)	− 2171 (64)	282 (18)	102 (13)	282 (32)	35 (7)	0 (16)	− 9 (7)	− 23 (13)
C(22)	1962 (12)	− 2100 (33)	− 338 (8)	128 (15)	633 (76)	47 (8)	− 138 (32)	14 (8)	− 51 (23)
O(23)	1432 (10)	− 691 (26)	− 495 (8)	90 (12)	388 (45)	58 (8)	132 (20)	− 21 (8)	13 (18)
C(24)	1689 (15)	− 4266 (37)	− 730 (12)	140 (18)	699 (88)	101 (12)	− 78 (36)	22 (12)	− 78 (30)

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[5] In contrast to **13**, **14** could not be obtained as crystals suitable for X-ray analysis. Since no photoequilibrium between **13** and **14** was observed, they might be epimeric at C(5) [3].

Crystal data of **13**, *structure solution and refinement.* Crystals of **13** ($C_{20}H_{25}O_4$) were obtained by slow evaporation of an acetone solution. Preliminary *Weissenberg* photographs indicated the probable space group to be $P2_1$ (Z = 2), monoclinic. A prismatic crystal (0,3 × 0,1 × 0,1 mm) was mounted on a glass fiber and used for all subsequent measurements. Three-dimensional data were collected on a computer-controlled single-crystal diffractometer (a = 10,72 Å, b = 6,72 Å, c = 12,83 Å, β = 92,04°). The 1340 reflections with $I \geqslant 2{,}5$ were considered reliable and used in the crystal structure analysis. After the *Lorentz*-polarization corrections had been applied, normalized structure factor amplitudes were computed and the structure was solved by direct methods (MULTAN program [9]). The atomic parameters were refined by full-matrix least-squares calculations, using AFFINE program [10]. After four isotropic and four anisotropic cycles the R value was 0,117 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 **13** as shown in *Figure 1.* Distances from least-squares plane defined by the atoms C(5), C(10) and C(6), are given in *Table 4.*

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

C(22)–C(24)	1.584 (43)	C(8)–C(14)	1.531 (28)
C(22)–O(23)	1.118 (36)	C(8)–C(7)	1.574 (28)
C(22)–O(21)	1.367 (60)	C(7)–C(6)	1.561 (29)
O(21)–C(17)	1.328 (62)	C(6)–C(10)	1.524 (29)
C(17)–C(16)	1.641 (40)	C(10)–C(19)	1.532 (29)
C(16)–C(15)	1.541 (34)	C(10)–C(9)	1.541 (27)
C(15)–C(14)	1.565 (32)	C(5)–C(10)	1.526 (28)
C(14)–C(13)	1.576 (28)	C(5)–C(6)	1.484 (29)
C(13)–C(20)	1.515 (31)	C(5)–O(4)	1.428 (22)
C(13)–C(17)	1.567 (37)	C(5)–C(1)	1.503 (28)
C(13)–C(12)	1.548 (29)	O(4)–C(3)	1.395 (25)
C(12)–C(11)	1.572 (29)	C(3)–O(20)	1.189 (29)
C(11)–C(9)	1.521 (28)	C(3)–C(2)	1.484 (32)
C(9)–C(8)	1.551 (27)	C(2)–C(1)	1.305 (31)

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

O(23)–C(22)–C(24)	129.9 (6.3)	C(9)–C(8)–C(7)	103.0 (2.8)
C(24)–C(22)–O(21)	107.3 (5.8)	C(14)–C(8)–C(7)	118.3 (3.4)
O(23)–C(22)–O(21)	122.8 (7.3)	C(8)–C(7)–C(6)	102.7 (2.8)
C(22)–O(21)–C(17)	118.6 (9.0)	C(10)–C(6)–C(7)	108.1 (3.1)
O(21)–C(17)–C(13)	115.6 (6.6)	C(7)–C(6)–C(5)	121.5 (3.7)
O(21)–C(17)–C(16)	109.4 (6.1)	C(10)–C(6)–C(5)	60.9 (1.4)
C(13)–C(17)–C(16)	101.0 (3.7)	C(9)–C(10)–C(6)	106.4 (3.0)
C(17)–C(16)–C(15)	106.7 (3.7)	C(9)–C(10)–C(19)	116.6 (3.4)
C(16)–C(15)–C(14)	103.6 (3.4)	C(9)–C(10)–C(5)	118.6 (3.4)
C(15)–C(14)–C(13)	102.7 (2.9)	C(19)–C(10)–C(6)	123.5 (3.7)
C(8)–C(14)–C(13)	108.3 (3.0)	C(19)–C(10)–C(5)	120.0 (3.5)
C(15)–C(14)–C(8)	121.1 (3.7)	C(5)–C(10)–C(6)	58.2 (1.3)
C(18)–C(13)–C(17)	109.9 (3.7)	C(6)–C(5)–C(1)	120.9 (3.7)
C(18)–C(13)–C(14)	103.3 (3.4)	C(6)–C(5)–C(4)	124.1 (3.6)
C(17)–C(13)–C(12)	111.8 (3.6)	C(6)–C(5)–C(10)	60.8 (1.4)
C(12)–C(13)–C(14)	110.8 (3.1)	C(10)–C(5)–C(4)	119.3 (3.3)
C(17)–C(13)–C(14)	99.3 (3.1)	C(10)–C(5)–C(1)	122.1 (3.6)
C(18)–C(13)–C(12)	111.2 (3.4)	C(1)–C(5)–O(4)	105.1 (2.8)
C(13)–C(12)–C(11)	110.2 (3.2)	C(5)–O(4)–C(3)	110.6 (2.8)
C(9)–C(11)–C(12)	107.9 (3.1)	O(4)–C(3)–O(20)	122.2 (4.4)
C(11)–C(9)–C(8)	112.2 (3.1)	O(20)–C(3)–C(2)	133.4 (5.2)
C(8)–C(9)–C(10)	105.6 (2.8)	O(4)–C(3)–C(2)	104.3 (3.2)
C(11)–C(9)–C(10)	120.4 (3.5)	C(3)–C(2)–C(1)	112.2 (4.0)
C(17)–C(8)–C(9)	95.7 (2.0)	C(2)–C(1)–C(5)	107.6 (3.5)

Table 4. *Distances from the least-squares plane defined by the atoms* C(5), C(10) *and* C(6)

Atom	Distance (Å)	Atom	Distance (Å)
O(4)	1.1208	C(1)	− 1.1996
C(3)	0.7078	C(19)	− 1.2245
C(2)	− 0.7643		

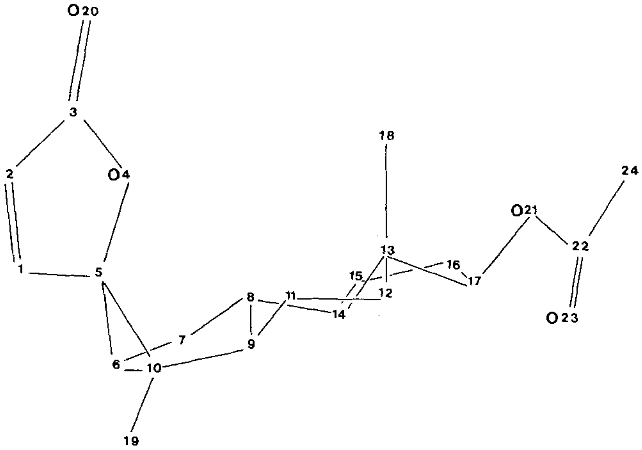
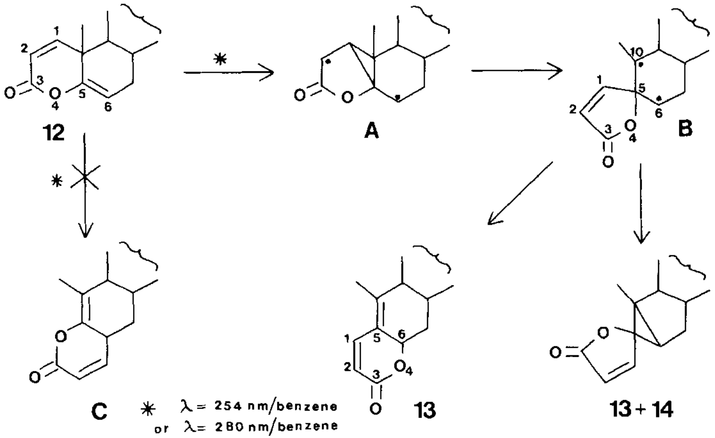


Fig. *Structure of 17β-acetoxy-4-oxa-6β,10-cyclo-1(10→5)*abeo-5(R),*10α-1-androsten-3-one* (**13**) *with numbering of atoms.*

3. Discussion. - The formation of **13**-**15** can formally be rationalized by the mechanism shown in *Scheme 4*. Irradiation of **12** would yield the typical [2] di-π-methane intermediate **A** by a benzene sensitized process⁶). Subsequently, **A** evolves towards **B**, which can be considered a hypothetical precursor common to the three

Scheme 4



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⁶) When ethanol, methanol or dioxane was used as solvent, no reaction was observed after the same irradiation times as with benzene, despite the UV. absorption of **12**.

isomeric photoproducts. Compound **15** would be the result of the migration of the lactone oxygen atom from C(5) to C(6). The spiro-derivatives **13** and **14** would arise from **B** by ring closure between C(10) and C(6). The fact that no product such as **C** resulting from a 1,3-shift of C(1) to C(6) is formed (the analogous carbocyclic structure is **7**, *Scheme 1*) is a point which at the present time can not be explained.

In conclusion, it can be said that to our knowledge the transformation **12**→**13** +**14** is the first example of a di-π-methane rearrangement of a lactone, or more precisely, of an α,β-unsaturated enol-lactone, and it further supports the general character of this type of photo-rearrangement [2][7].

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Experimental Part

General remarks. S. [1]. Crystallisations, unless otherwise specified, were carried out in acetone/petroleum ether (b.p. 50-70°). Optical rotations (in $CHCl_3$) were determined on a *Perkin Elmer* 141 polarimeter using a 1 dm cell; the concentration (g/100 ml) is given in brackets. The irradiations were carried out at room temp. (RT.) under N_2 with a low-pressure Hg lamp (NK 6/20, *Quarzlampen GmbH*, Hanau) in a typical immersion unit.

1. Preparation of 12. - 1.1. *Conversion of* **9** *by* $Pb(OAc)_4$. To a solution of 384 mg of **9** [7] in 80 ml of dry benzene, 1,231 g of $CaCO_3$ and 1,219 g of lead tetraacetate were added. The mixture was heated under reflux for 90 min and then let cool down to RT. After addition of 100 ml of H_2O and filtration the mixture was worked up in the usual way yielding 420 mg of a mixture of two components. Chromatography with benzene/ethyl acetate 7:3 furnished 102 mg (24%) of **10** and 246 mg (58%) of **11**. *17β-Acetoxy-5ξ-hydroxy-4-oxa-1-androsten-3-one* (**10**), m.p. 186-189° after three crystallizations. - UV.: 223 (7020). - IR.: 3550, 3360, 1735, 1730, 1250. - ^{1}H-NMR.: 0,87 (*s*, $H_3C(18)$); 1,30 (*s*, $H_3C(19)$); 2,07 (*s*, $CH_3COO-C(17)$); 4,18 (br. *s*, HO-C(5), disappeared on addition of D_2O); 4,60 (*m*, H-C(17)); 5,97, 6,68 (*AB*-system, J_{AB}= 10, H-C(2), H-C(1)). - MS.: 348 (M^+).

$C_{20}H_{28}O_5$ (348,44) Calc. C 68,94 H 8,10% Found C 68,92 H 8,06%

5ξ,17β-Diacetoxy-4-oxa-1-androsten-3-one (**11**), m.p. 155-156° after three crystallizations, $[\alpha]_D^{20}$= +167° (0,5). - UV.: 223 (7220). - IR.: 1750, 1730, 1250. - ^{1}H-NMR.: 0,86 (*s*, $H_3C(18)$); 1,28 (*s*, $H_3C(19)$); 1,95 (*s*, $CH_3COO-C(5)$); 2,04 (*s*, $CH_3COO-C(17)$); 4,62 (*m*, H-C(17)); 5,90, 6,68 (*AB*-system, J_{AB}=9,5, H-C(2), H-C(1)). - MS.: 390 (M^+).

$C_{22}H_{30}O_6$ (390,48) Calc. C 67,67 H 7,74% Found C 67,74 H 7,75%

1.2. *Pyrolysis of* **11**. 4,478 g of **11** were heated 1 h to 170-180° (oil bath) under a nitrogen current. After cooling and filtration through Al_2O_3 (neutral, activity II) in benzene, 4,143 g of *17β-acetoxy-4-oxa-1,5-androstadien-3-one* (**12**) were obtained: m.p. 182-184° after three crystallizations, $[\alpha]_D^{20}$= -133° (0,65). - UV.: 210 (9000), 270 (700). - IR.: 1775, 1740, 1690, 1250. - ^{1}H-NMR.: 0,88 (*s*, $H_3C(18)$); 1,27 (*s*, $H_3C(19)$); 2,09 (*s*, $CH_3COO-C(17)$); 4,66 (*d*×*d*, *J*=9, *J'*=7, H-C(17)); 5,37 (*d*×*d*, *J*=6, *J'*=2, H-C(6)); 5,91, 6,91 (*AB*-system, J_{AB}= 10, H-C(2), H-C(1)). - MS.: 330 (M^+).

$C_{20}H_{26}O_4$ (330,41) Calc. C 72,70 H 7,93% Found C 72,58 H 7,96%

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[7] Very recently the di-π-methane reaction of 4-benzyl-5,5-dimethyl-2(5*H*)-furanone has been published [11].

2. Photolysis of 12. - A solution of 1,552 g of **12** in 1 l of dry benzene (*Merck*, analytical purity) was irradiated during 35 h. Solvent evaporation *in vacuo* yielded 1,865 g of a mixture of several components. Chromatography with benzene/ethyl acetate 9:1 furnished first 258 mg of a complex mixture of compounds of very low polarity, followed by 841 mg of starting material **12** (identified by mixed m.p., TLC. and IR. spectrum). The third fraction contained 154 mg of *17β-acetoxy-4-oxa-6β,10-cyclo-1(10→5)abeo-5*(R)*,10α-1-androsten-3-one* (**13**), m.p. 178-179° after three crystallizations. - UV.: 245 (18800). - IR.: 3090, 1730, 1680, 1580, 1245, 1040. - ^{1}H-NMR.: 0,38 (*s*, $H_3C(18)$); 1,33 (*s*, $H_3C(19)$); 2,07 (*s*, $CH_3COO-C(17)$); 4,63 (br. *m*, H-C(17)); 6,10, 7,30 (*AB*-system, $J_{AB}=6$, H-C(2), H-C(1)). - MS.: 330 (M^+).

$C_{20}H_{26}O_4$ (330,41) Calc. C 72,70 H 7,93% Found C 72,51 H 7,93%

The fourth fraction yielded 182 mg of isomer **14** with traces of an impurity, m.p. 168-169°, after fractional crystallization from methanol. - UV.: 252 (12000). - IR.: 3090, 1760, 1745, 1722, 1680, 1570, 1245, 1040. - ^{1}H-NMR.: 0,84 (*s*, $H_3C(18)$); 1,36 (*s*, $H_3C(19)$); 2,05 (*s*, $CH_3COO-C(17)$); 4,64 (br. *m*, H-C(17)); 6,20, 7,76 (*AB*-system, $J_{AB}=6$, H-C(2), H-C(1)). - MS.: 330 (M^+).

$C_{20}H_{26}O_4$ (330,41) Calc. C 72,70 H 7,93% Found C 72,39 H 7,94%

The fifth fraction consisted of 43 mg of *17β-acetoxy-1(10→5)abeo-4(5→6)abeo-6ξ*(H)*-4-oxa-1,5(10)-androstadien-3-one* (**15**), m.p. 154° after two crystallizations. - UV.: 283 (18500). - IR.: 3100, 1750, 1730, 1695, 1645, 1250, 1040. - ^{1}H-NMR.: 0,84 (*s*, $H_3C(18)$); 1,92 (br. *s*, $CH_3(19)$); 2,08 (*s*, $CH_3COO-C(17)$); 4,60-4,80 (br. *m*, H-C(17), H-C(6)); 5,90, 6,46 (*AB*-system, $J_{AB}=10$, H-C(2), H-C(1)). - MS.: 330 (M^+).

$C_{20}H_{26}O_4$ (330,41) Calc. C 72,70 H 7,93% Found C 72,49 H 7,89%

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