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REACTIONS OF STEROIDAL 1,3-DIKETONES WITH SULFUR TETRAFLUORIDE†

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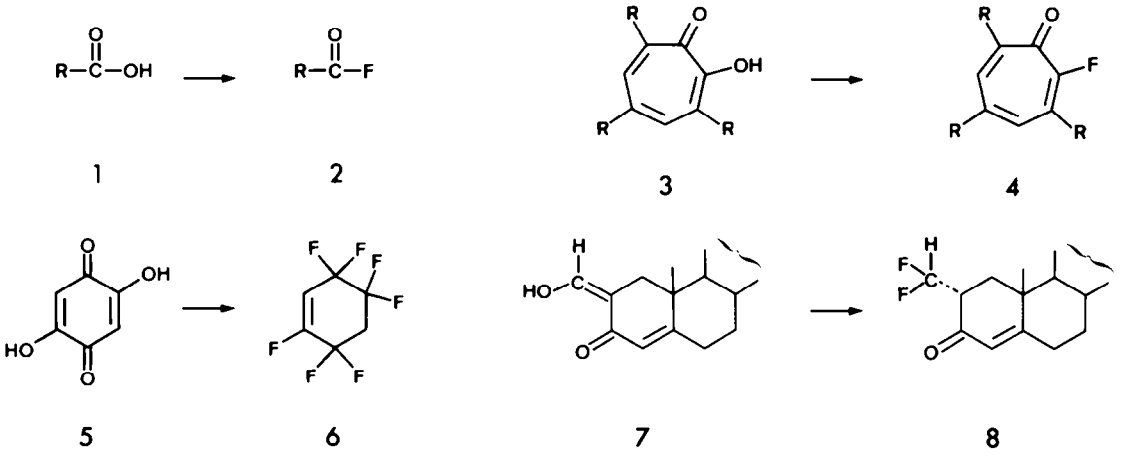
Abstract Steroidal 1,3-diketones of type **9** and **15** have been used as substrates in the study of the reaction of enolizable β-diketones with sulfur tetrafluoride in benzene. In a smooth reaction β-fluoro-(**10**; **17**) and β-phenyl-(**11**; **18**) enones are generated. In the case of the ring-A-dione **15** in addition, the alkynyl acyl fluoride **16** is formed in 35% yield. The different products formally derive from the corresponding activated tautomeric enols. A unifying mechanism involving vinyl cation-type species **B** and **G** is discussed.

The pioneering observation of Fried *et al.*[2] concerning the enhancing effect of a 9α-F substituent on the anti-inflammatory activity of corticoids, has stimulated a world-wide search for further fluorinated analogues. Sulfur tetrafluoride[3] and its derivatives[4] hereby were often shown to be the reagents of choice for the synthesis of many novel classes of compounds in this field.[5]

Apart from the best-known reaction of sulfur tetrafluoride with CO groups, used for the generation of geminal difluoro compounds, the smooth conversion of carboxylic acids to acyl fluorides (**1** → **2**) and subsequently to trifluoromethyl derivatives, is of great preparative value. The readiness of OH groups in general to be substituted by F is believed to be dependent on their acidity. The completely enolized tropolones (**3**)[2], e.g. behave like carboxylic acids, their OH group being substituted by F (*cf* **4**),[2h] and some dihydroxy quinones of type **5** react with sulfur tetrafluoride in a similar way (→**6**).[2h] The enolized aldehyde group in **7**, on the other hand, has been converted into a difluoromethyl group (→**8**).[6]

Since steroidal β-fluoro-α,β-unsaturated ketones would constitute a class of compounds of potential biological interest, we have decided to study the reaction of the corresponding enolizable β-diketones with sulfur tetrafluoride.

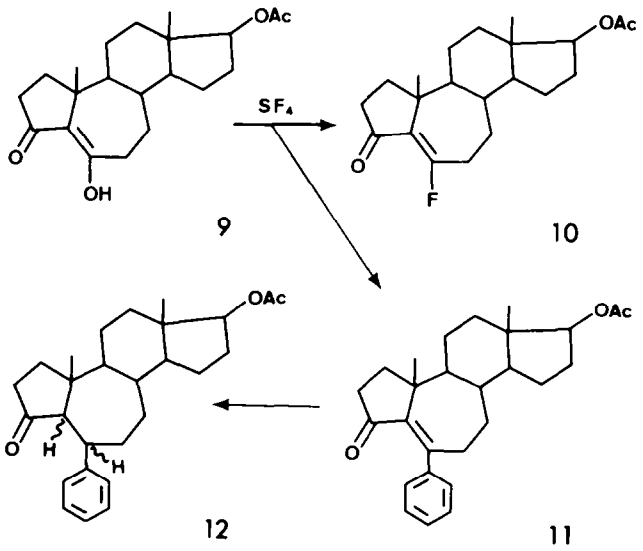
As a first substrate for the planned reactions the 10-*abeo*-steroid **9**[7] with a fixed *Z*-configuration at the enolic double bond‡ was chosen. By treating a solution



Scheme 1

†Presented in part (H.K.) at the Autumn Meeting of the Swiss Chemical Society, 9 October, 1976 in Geneva.

‡According to ^1H and ^{13}C NMR spectra (*cf* Table 1) the compound appears to be completely enolized, only one (=**9**) of the two possible tautomers being present in either $CDCl_3$ or DMSO solns.



Scheme 2

of compound **9** in anhydrous benzene† at room temperature for 210 min with sulfur tetrafluoride‡, two products were generated. The mixture was separated by chromatography and the structures of the individual compounds determined primarily on the basis of spectral data.

The more polar, main component of the mixture, formed in a yield of 65–70%, is an α,β-unsaturated ketone carrying a F atom in β-position to the CO group. ^{1}H-NMR, MS and UV data did not allow an unequivocal differentiation between the two possible isomeric formulas with the CO group in 3 or 5 position

Table 1. Characteristic chemical shifts in the ^{13}C-NMR spectra† of 5-substituted 17β-acetoxy-10(5 → 4)-*abeo*androst-4-en-3-ones. (Tentative assignment)

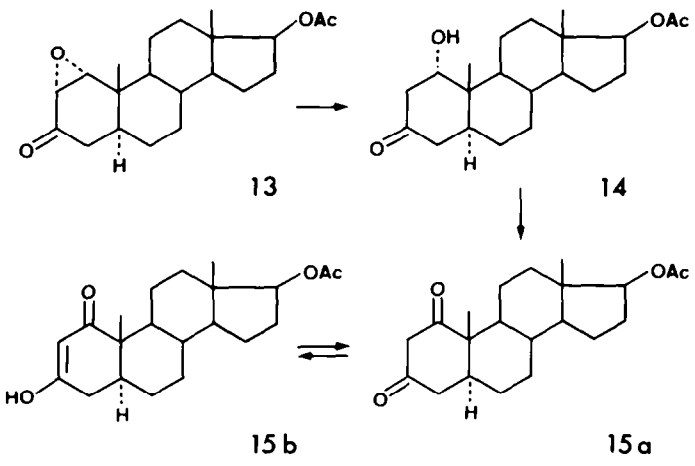
Compd / ^{13}C	9	11	10
1	36.7	36.2	36.4
2	35.0	35.9	36.2
3	204.1	206.4	204.0
4	119.6	143.5	126.1 (J_{CF} = 2.8)
5	183.8	153.8	167.0 (J_{CF} = 288.8)
6	34.1	35.7	29.3 (J_{CF} = 26.6)
7	29.3	30.0	27.5 §
8	37.3	37.0	36.8
9	53.7	51.6	51.8
10	45.1	47.1	44.3 §
19	18.7	18.0	18.5 §

† δ in p.p.m. vs. TMS measured in $CDCl_3$; J_{CF} in Hz

§ long-range coupling

†On addition of various amounts of water-saturated benzene to the reaction mixture **11** was no longer formed while **10** was isolated in a significantly lower yield.

‡The reaction was performed at atmospheric pressure by an unconventional procedure (glassware, SF_4 bubbled through the soln).

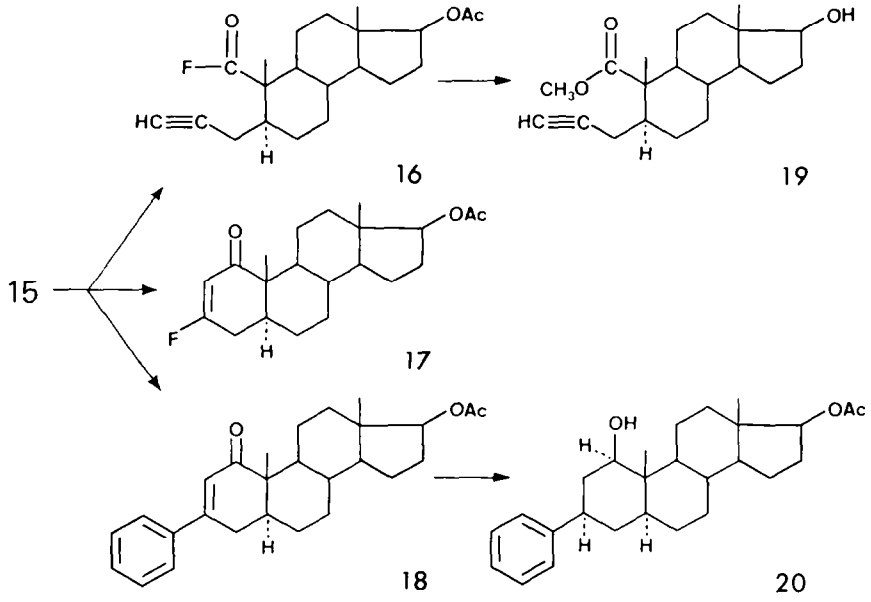


Scheme 3

respectively. The decisive arguments in favour of the desired 5-fluoro-10(5 → 4)-*abeo*androst-4-en-3-one structure **10**, were furnished by the ^{13}C-NMR spectrum (*cf* Table 1).

In the minor product (25%), a halogen-free unsaturated ketone, the OH function of **9** is formally substituted by a phenyl group. From the ^{1}H-NMR spectrum (360 MHz), in which the signal-pattern of the two C(2)-protons can be analyzed, structure **11** was deduced. This is confirmed by the ^{13}C-NMR data (Table 1), as well as by the IR spectrum of the hydrogenation product **12**, showing a single stretching band at 1730 cm^{-1}, corresponding to the overlapping absorptions of the 17-acetate and of a saturated cyclopentanone.

The high yields in the conversion of **9**→**10**, and the isolation of the interesting phenylated compound **11** stimulated the following experiments with an enolizable β-diketone containing a fixed *E*-configuration at the enolic double bond. The 17-acetoxy diketone **15**,[8]† easily available from the epoxy ketone **13** by hydrogenation to **14** and subsequent oxidation (Scheme 3), served as substrate for this second series of reactions. When compound **15** was treated with sulfur tetrafluoride under the same conditions, as described above for the keto-enol **9**, a mixture of *three* products was formed in a yield of approximately 70%. Using two different solvent-systems the mixture was separated by preparative tlc (*cf*. Scheme 4).



Scheme 4

†According to ^{1}H- and ^{13}C-NMR spectra the compound is completely enolized (*cf* structure **15b**) in DMSO, whereas in $CDCl_3$ only the diketo tautomer **15a** is observed

Table 2. Characteristic chemical shifts in the ^{13}C-NMR spectra[+] of **15** and its reaction products. (Tentative assignment)

Compd. / ^{13}C	15 a	15 b	18	17	16
1	206.3	204.0	206.2	204.6	167.0 (J_{CF}=373.8)
2	56.2	102.4	129.7	108.2 (J_{CF}=10.3)	70.4
3	203.2	173.0	153.8	175.2 (J_{CF}=288.4)	81.7
4	30.3	29.8	30.3	31.4 (J_{CF}=18.3)	23.1
5	44.2	41.5	43.0	41.1 (J_{CF}=4.2)	42.7
6	27.6	27.1	28.3	27.7 (J_{CF}=9.2)	26.0
7	35.7	33.2	32.9	30.0	30.4
8	36.9	36.1	36.5	36.4	34.1
9	47.0	47.8	47.6	47.5	48.7
10	50.3	44.8	46.3	46.7	50.9 (J_{CF}=38.8)
19	11.2	11.3	10.7	10.9	9.9

[+] measured in $CDCl_3$ (15 b in DMSO); δ in p.p.m. vs. TMS; J_{CF} in Hz

The most lipophilic component, obtained in 30–35% yield, contains one F atom and one acetylenic group, but no unsaturated ketone. From spectral data (coupling of F with the C (10) carbon, a broad signal for the ethynylic hydrogen, a CO-band in the IR spectrum at 1820 cm^{-1}, corresponding to an acyl fluoride etc) structure **16** was deduced for the compound. In accord with this proposal, acid-catalyzed methanolysis of **16** furnished the expected methyl ester **19**.

The second product (20%) is a β-fluorinated α,β-unsaturated ketone. On account of the ^{13}C-NMR spectrum (*cf* Table 2) structure **17** is proposed for this compound. The isomer with the CO function in position 3 and the F at C(1) was not found.

The most stable tautomer being substituted by F (**10**, **17**). Under the specific reaction conditions used, no further fluorination of the second CO group takes place.

In this respect, the reaction of enolized β-diketones with SF_4 represents a short way to β-fluoro-enones. Another interesting aspect of both described cases, which might cast some light on the more detailed mechanism of the reaction of SF_4 with β-diketones is the generation of the β-phenylated ketones **11** and **18**, and of the fragmentation product **16**.

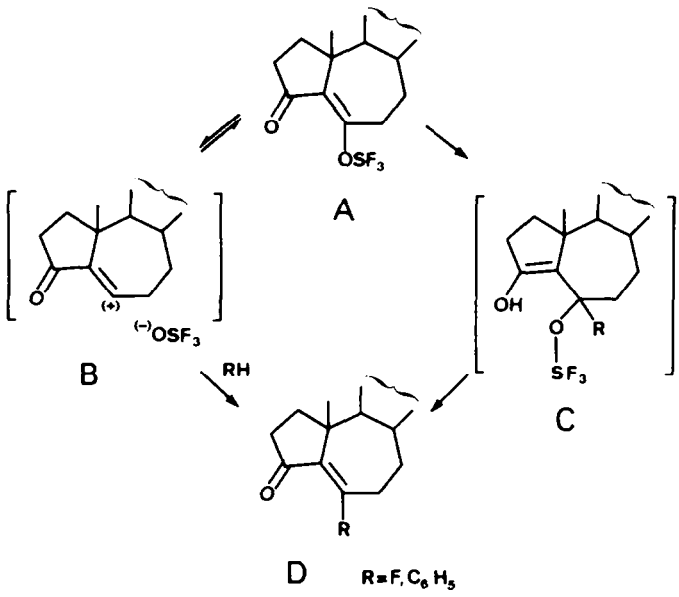
It is generally accepted[2] that the first step in the reaction of sulfur tetrafluoride with alcohols consists in the formation of an alkoxysulfur trifluoride intermediate (**a**), according to the following Scheme:

$$\geq C-OH + SF_4 \xrightarrow{-HF} \underset{\mathbf{a}}{\geq C-O-SF_3} \longrightarrow \geq C-F + SOF_2$$

Structure **18** was deduced for the last component of the original reaction mixture, a F-free phenylated compound on the ground of the spectral data and of its conversion to the tetrahydro derivative **20**. The position of the OH group in **20** was determined unambiguously by using the simple coupling pattern due to the geminal proton in the ^1H-NMR spectrum.

The results obtained in the reactions of sulfur tetrafluoride with compounds **9** and **15** have demonstrated that both types of β-diketones behave formally like vinylogous acids; the enolic OH group of S_N2- or S_Ni-type reactions have been postulated for the subsequent substitution of the OSF_3-group by F. But, as stated by Boswell *et al.*,[2a] there is most likely a continuum of mechanisms operative from S_Ni to S_N2.

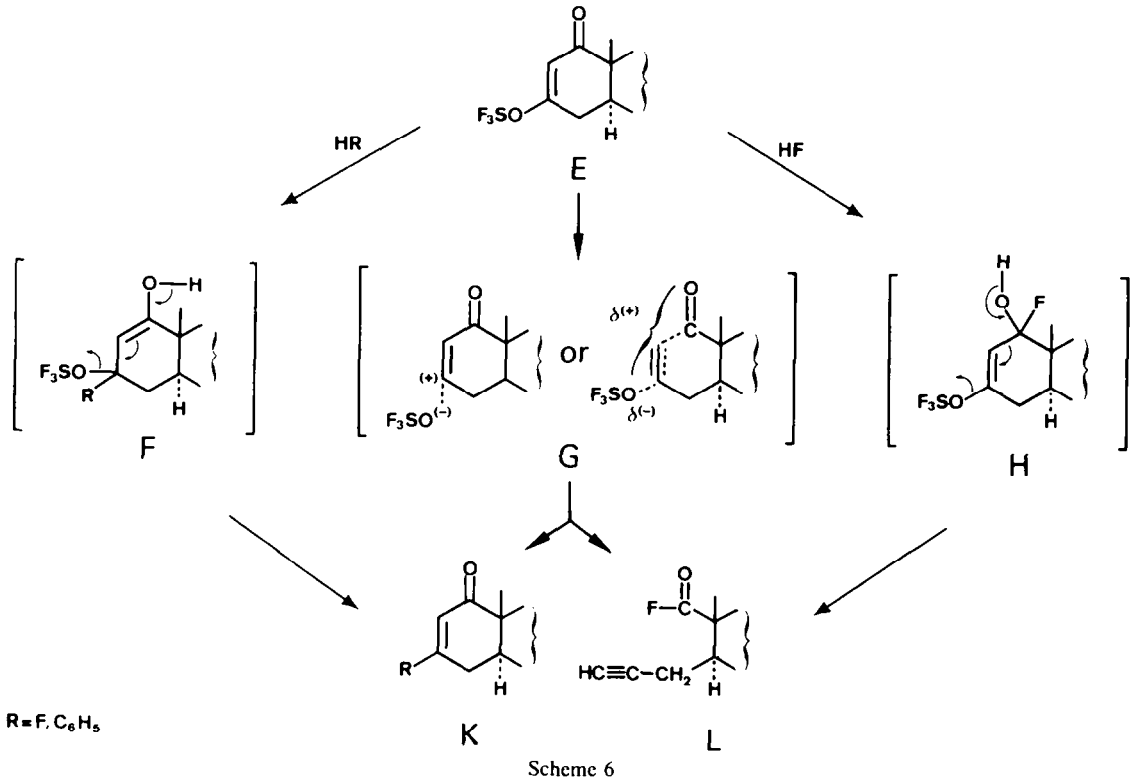
In the case of the alkoxysulfur trifluoride of type **A** (*cf* Scheme 5), most probably formed from the enol **9** in the first stage of the reaction, various "classical" mechanisms can be postulated for its transformation into 5-fluoro- and 5-phenyl-compounds **D** (*cf* **10** and **11**). A 1,4-addition of hydrofluoric acid across the α,β-unsaturated system, e.g. would generate the highly



Scheme 5

unstable enolic intermediate **C**, which would easily eliminate the elements of "hydroxysulfur trifluoride" (or one equivalent each of hydrofluoric acid and thionyl fluoride) to form the β-fluoro ketone **D** (R=F). It would be rather problematic to postulate a (HF-catalyzed) electrophilic attack on the benzene molecule by C(5) of **A**, to form the intermediate **C** ($R = C_6H_5$). Similar difficulties could arise, if one should postulate a primary interaction of sulfur tetrafluoride with the O of the CO function, followed by addition of the ate-complex to benzene.

Formally, a Friedel–Crafts-type reaction of a *vinyl cation* like **B**, would pose less problems. The F_3SO-anion should be an excellent leaving group and promote formation of such a highly reactive species. "Hot" vinyl cations[9] of this type have been postulated by Martin,[10] Schegolev,[11] Martens[12] *et al.*, as intermediates in the acyl chloride–$AlCl_3$ or acyl triflate-mediated acylations of alkynes. If these reactions were carried out in the presence of aromatic solvents, the corresponding β-aryl-α,β-unsaturated ketones have been also isolated.[11d]



Scheme 6

It would therefore seem reasonable to expect that similar vinyl cationic species, preferably as ion-pairs **B** or **G**† respectively are involved in the reactions of β-diketones described above. They could not only explain the generation of compounds of type **D** and **K**, but would also help to rationalize the fragmentation of **E** to the acyl fluoride **L**, which alternatively could be formed via the α-fluorohydrine **H** (cf. Scheme 6).

EXPERIMENTAL‡

(In collaboration with **O. Kopp**)

All the m.ps are uncorrected. Optical rotations were measured in $CHCl_3$ soln. ^{1}H-NMR spectra were obtained at 100 and/or 360 MHz with a Varian XL-100-15 and Bruker HX-360 spectrometer respectively in $CDCl_3$ soln, using TMS as internal standard; chemical shifts are reported in δ values (abbreviations: s singlet, d doublet, q quartet,§ m multiplet, **AB** AB-type signal pattern), coupling constants J in Hz. IR spectra were determined in CH_2Cl_2 on a Perkin–Elmer 540 E instrument. Mass spectra were taken on a Varian CH 7 mass spectrometer, and the UV spectra (in EtOH) on a Cary 118 Varian Spectrophotometer.

Reaction of 17β-acetoxy-5-hydroxy-10(5→4)-abeoandrost-4-en-3-one **9** *with* SF_4. A soln of **9**[7] (1,00 g) in anhyd. benzene (150 ml) was placed in a glass hydrogenation vessel connected on one side to a SF_4 cylinder, on the other side, via a reduction valve, to an aspirator (in a thoroughly ventilated hood). A gentle stream of pure SF_4 was bubbled through the soln and the progress of the reaction monitored by tlc [system: toluene–EtOAc (4:1)]. After about 180 min the gas supply was stopped and the closed vessel shaken for another 30 min. The mixture was flushed with N_2, diluted with ether-benzene, washed with ice-cold sat $NaHCO_3$aq and H_2O, dried over Na_2SO_4 and evaporated under vacuum. The crude amorphous product (1,10 g) was chromatographed on silica gel (50 g). The first fractions eluted with toluene-EtOAc (95:5) afforded 300 mg of *17β-acetoxy-5-phenyl-10(5→4)-abeoandrost-4-en-3-one* **11**, which was twice recrystallized from CH_2Cl_2–ether (211 mg)§§, m.p. 148–149°. $[\alpha]_D^{20} = -59°$ (c = 0.399); IR: 1730, 1710, 1620, 1380, 1120, 1040 cm^{-1}; NMR: 0.87 (3 H, s, CH_3-18), 1.29 (3 H, s, CH_2-19), 2.05 (3 H, s, CH_3–acetate), 2.45 + 2.64 (2 H, **AB**, CH_2–2; $J_{\alpha\beta}$ = 16.7, $J_{\alpha z} \simeq J_{\beta y} \simeq 11$, $J_{\alpha y} \simeq J_{\beta y} \simeq 1.9$), 4.62 (1 H, q, H-17α; $J_{\alpha\beta'}$ = 8.5, $J_{\alpha\alpha'}$ = 10.5), 7.0 + 7.25 (2 H + 3 H, m, aromatic protons); UV: λ_{max} 240 (ε 5000), 253 (ε 5000), 272 (ε 5000), 360 (ε 280); MS (*m/e*): 406 (M), 391 (M–Me), 388 (M H_2O; MI 370), 364 (M–C_2H_2O), 346 (M–AcOH), 198 (ring A + C(6) + C(7) + Ø). (Found: C, 79.80; H, 8.45%. $C_{27}H_{34}O_3$ Requires: C, 79.76; H, 8.43%).

From later fractions eluted with the same solvent crude crystalline *17α-acetoxy-5-fluoro-10(5→4)-abeoandrost-4-en-3-one* **10** (790 mg) was obtained. It was twice recrystallized from CH_2Cl_2–ether (579 mg), m.p. 156–157°. $[\alpha]_D^{20} = -47°$ (c = 1.125); IR: 1720, 1645, 1032, 868 cm^{-1}; UV: λ_{max} 245 (ε 9100), 290 (sh); NMR: 0.84 (3 H, s, CH_3-18), 1.18 (3 H, s, CH_3-19), 2.03 (3 H, s, CH_3 acetate), 2.13–2.55 (5 H, m, CH_2–2 + CH_2–6 + ?); 4.16 (1 H, q, H-17α; $J_{\alpha\alpha'}$ = 10.5, $J_{\alpha\beta'}$ = 8.5). MS (*m/e*): 349 (M + H), 348 (M), 328 (M–HF, MI 309.5), 306 (M–C_2H_2O), 288 (M–AcOH), 268 (328–AcOH, MI 219), 253 (268–Me, MI 239). (Found: C, 72.28; H, 8.48; F, 5.40%. $C_{21}H_{29}O_3F$ Requires: C, 72.39; H, 8.39; F, 5.45%).

Hydrogenation of 17β-acetoxy-5-phenyl-10(5→4)-abeoandrost-4-en-3-one **11**. Compound **11** (100 mg) was dissolved in EtOH (25 ml) and hydrogenated in the usual way, using 10% Pd/C (30 mg) as catalyst. Absorbed: 5.71 ml; calculated: 5.52 ml H_2. The mixture was filtered, the solvent evaporated and the isomeric *17β-acetoxy-5ξ-phenyl-10(5→4)-abeo-4ξ-androstan-3-ones* **12** recrystalized twice from CH_2Cl_2 ether–light petroleum to yield a single compound (16 mg), m.p. 148–150°. IR: 1730, 1601, 13781, 1125, 940 cm^{-1}; MS (*m/e*) 408 (M), 393 (M–Me), 390 (M–H_2O), 348 (M–AcOH); MI 297), 330 (348–H_2O).

17β-Acetoxy-1α-hydroxy-5α-androstan-3-one **14**. 17β-Acetoxy-1α,2-epoxy-5α-androstan-3-one[8] (1.00 g) was dissolved in a mixture of THF (20 ml) and EtOH (10 ml) and hydrogenated in the presence of a 5% Pd/C-catalyst (1.00 g!). Absorbed: 70.5 ml; calculated: 64.8 ml H_2. The filtered soln was evaporated under vacuum and the crude product recrystallized from $CHCl_3$–MeOH–ether, yielding 842 mg of pure **14**, m.p. 237–241° (lit.[8]: 231–234°). $[\alpha]_D^{20} = +25$ (c = 1,534). IR: 3600, 1730, 1715, 1230, 1110, 1030 cm^{-1}; NMR (d_5-pyridine): 0.85 (3 H, s, CH_3 18 or CH_3-19), 1.01 (3 H, s, CH_3-19 or CH_3-18), 2.01 (3 H, s, Me-acetate), 2.32 + 2.73 (2 + 2 H, m, CH_2–2 + CH_2–4), 4.21 (1 H, m, H-1β), 4.72 (1 H, q, H-17α), 6.45 (1 H, d, OH). (Found: C, 72.56; H, 9.31%. $C_{21}H_{32}O_4$ Requires: C, 72.38; H, 9.26%).

17β-Acetoxy-5α-androstane-1,3-dione[8] **15**. To a cooled (0–4°) stirred soln of hydroxy ketone 14 (500 mg) in acetone (50 ml) a small excess (0.5 ml) of Kiliani's chromic acid soln[13] was added. After 20 min the residual reagent was reduced by MeOH, ice-cold H_2O was added and the resulting suspension extracted into CH_2Cl_2–ether. The organic layer was washed with sat $NaHCO_3$aq and H_2O, dried over Na_2SO_4 and evaporated under vacuum. The crude product (290 mg) was recrystallized from CH_2Cl_2–ether to give **15** (189 mg), m.p. 212–213° (lit.[8]: 210–212°). $[\alpha]_D^{20} = +93°$ (c = 0.774): IR: 1727, 1703, 1245, 1060, 1043, 1030, 1017 cm^{-1}, UV (EtOH): λ_{max} 253 (ε 13 450); (EtOH + NaOH): λ_{max} 283 (ε 24 800); NMR: 0.82 (3 H, s, CH_3 18), 1.32 (3 H, s, CH_3 19), 2.04 (3 H, s, CH_3 acetate), 2.17 (1 H, m, H 11α ?), 2.42 (α) + 2.54 (β) (2 H, AB, CH_2 4; $J_{\alpha\beta}$ = 18, $J_{\alpha\alpha'}$ = 4.5, $J_{\alpha\alpha'}$ = 1.8, $J_{\beta\alpha'}$ = 13, 3.23(α) + 3.68 (β) (2 H, AB, CH_2 2; $J_{\alpha\beta}$ = 17, $J_{\alpha\alpha'}$ = 1.8), 4.59 (1 H, q, H 17α; $J_{\alpha\alpha'}$ = 11.5, $J_{\alpha\beta'}$ = 9); NMR (DMSO): 0.75 (3 H, s, CH_3-18), 0.92 (3 H, s, CH_3-19), 1.98 (1 H, s, CH_3 acetate), 4.50 (1 H, q, H 17α; $J_{\alpha\alpha'}$ = 10, $J_{\alpha\beta'}$ = 7), 4.96 (1 H, br. s, H-2), (Found: C, 72.90; H, 8.62%. $C_{21}H_{30}O_4$ Requires: C, 72.80; H, 8.73%).

Reaction of 17α-acetoxy-5α-androstane-1,3-dione **15** *with* SF_4. Under the same conditions as described for **9**, a soln of **15** (1.00 g) in anhyd benzene (200 ml) was treated with SF_4 for 210 min. The progress of the reaction was monitored by tlc [system: toluene–EtOAc (4:1)]. The mixture was flushed with N_2, diluted with ether-benzene, washed with ice-cold $NaHCO_3$aq and H_2O, dried over Na_2SO_4 and evaporated under vacuum. The crude product (920 mg) was separated on six TL-plates (100 cm; silicagel PF 254; 1,5 mm thick; system: toluene–EtOAc (90:10)] into two zones.

The less polar zone was eluted with toluene–EtOAc mixtures to give *17β-acetoxy-1,2-seco-5α-androst-2-yn-1-oic acid fluoride* **16** (400 mg), which was crystallized from ether–light petroleum (300 mg), m.p. 93–95°. $[\alpha]_D^{20} = -11°$ (c = 1.061); IR: 3300, 2120, 1820, 1727, 1242, 1050, 1040, 1030 cm^{-1}; NMR: 0.78 (3 H, s, CH_3 18), 1.09 (3 H, s, CH_3 19), 2.01 (3 H, s, CH_3–acetate), 2.07 (1 H, m, H–C≡C), 4.58 (1 H, q, H-17α; $J_{\alpha\alpha'}$ = 11, $J_{\alpha\beta'}$ = 8); MS (*m/e*): 348 (M), 333 (M–Me), 328 (M–HF), 313 (328–Me), 300 (328–CO?), 288 (M–AcOH), 273 (288–Me; MI 259), 268 (288–HF). (Found: C, 72.69; H, 8.54%. $C_{21}H_{29}FO_3$ Requires: C, 72.39; H, 8.39%).

The second zone afforded a mixture of two compounds (320 mg) which was separated by a second preparative tlc [system: light petroleum–MeOH (95:5)–4x" to top"].

†The optimal stereo-electronic arrangement in **G** should favour participation of the lone electron-pairs on the CO oxygen in the stabilization of the vinyl cation.

‡The elemental analyses were carried out in our Analytical Laboratories (direction of Dr. W. Padowetz). Special determinations were performed in the Spectroscopy Laboratories (Dr. H. Hürzeler, S. Moss).

§Doublet of doublets.

§§From other fractions and from the mother liquors additional amounts of less pure product were obtained.

The slightly less polar component (242 mg) was recrystallized from CH_2Cl_2–ether–light petroleum, yielding 17α-acetoxy-3-fluoro-5α-androst-2-en-1-one **17** (185 mg) m.p. 155–156°. $[\alpha]_D^{20} = +98°$ ($c = 1.394$). IR: 1725, 1680 (sh), 1670, 1375, 1358, 1158, 1042, 1032, 1020 cm^{-1}; UV: λ_{max} 224 (ε 8900), 282 (ε 25); NMR: 0.81 (3 H, s, CH_3 18), 1.06 (3 H, s, CH_3 19), 2.03 (3 H, s, CH_3–acetate), 2.49 (2 H, m, CH_2 4), 4.58 (1 H, q, H–17α; $J_{xx'} = 10$, $J_{x\beta'} = 8$), 5.50 (1 H, q, H 2; $J_{HF} = 14$, $J_{ww} = 2$); MS (*m/e*): 348 (M), 333 (M Me), 305 (M MeCO), 288 (M–AcOH; MI 238), 273 (288 Me; MI 259). (Found: C, 72.47, H, 8.42%. $C_{21}H_{29}FO_3$ Requires: C, 72.39; H, 8.39%).

The most polar compound (116 mg) was recrystallized from CH_2Cl_2 ether–light petroleum and gave the pure 17β-*acetoxy-3-phenyl-5α-androst-2-en-1-one* **18** (80 mg), m.p. 205–206°. $[\alpha]_D^{20} = +130°$ ($c = 0.496$); IR: 1725, 1615, 575, 1495, 1240, 1070, 1040, 1030, 1020 cm^{-1}; UV: λ_{max} 219 (ε 9250), 280 (ε 18900); NMR: 0.82 (3 H, s, CH_3 18), 1.09 (3 H, s, CH_3 19), 2.02 (3 H, s, CH_3 acetate), 2.54 (3 H, m, CH_2–4 + ?), 4.59 (1 H, s, H–17α; $J_{xx'} = 10$, $J_{x\beta'} = 8$), 6.25 (1 H, br. s, H 2), 7.37 + 7.51 (5 H, m, aromatic protons); MS (*m/e*): 406 (M), 391 (M–Me), 388 (M–H_2O), 378 (M 28), 363 (M MeCO), 346 (M–AcOH), 198, 185, 184. (Found: C, 79.80; H, 8.36%. $C_{27}H_{34}O_3$ Requires: C, 79.76; H, 8.43%).

Methyl 17β-hydroxy-1,2-seco-5α-androst-2-yn-1-oate **19**. A soln of **16** (100 mg) and *p*-toluenesulfonic acid (10 mg) in MeOH (10 ml) was heated under reflux for 66 hr†, the cool mixture poured into stirred ice-cold $NaHCO_3$aq and extracted twice with $CHCl_3$. The organic layers were washed with water, dried and evaporated under vacuum, yielding a mixture of three products (80 mg). This was chromatographed on silica gel (10 g) in toluene and toluene EtOAc (90:10) The combined more polar fractions afforded after recrystallization from CH_2Cl_2 ether **19** (36 mg), m.p. 146–148°. $[\alpha]_D^{20} = +2$ ($c = 0{,}500$); IR: 3600, 3300, 2120, 1720, 1170, 1135, 1100, 1078, 1055, 1026 cm^{-1}; NMR: 0.74 (3 H, s, CH_3–18), 1.05 (3 H, s, CH_3–19), 2.02 (1 H, m, H–C≡C–), 3.68 (1 H, q, H–17α), 3.70 (3 H, s, MeO); MS (*m/e*): 318 (M), 303 (M–Me), 300 (M–H_2O), 286 (M–MeOH), 259 (M $COOCH_3$), 241 (259 H_2O). (Found: C, 75.20; H, 9.52%. $C_{20}H_{30}O_3$ Requires: C, 75.43; H, 9.49%).

3β-Phenyl-5α-androstane-1β,17β-diol 17-acetate **20**. Compound **18** (200 mg) was dissolved in EtOH (50 ml) and hydrogenated in the presence of 10% Pd/C-cytalyst (60 mg!). The hydrogenation was stopped after 1.5 equiv of H_2 were absorbed. The filtrated soln was evaporated in vacuum, affording a mixture of three products, which was subsequently chromatographed [20 g silicagel; eluant: toluene and toluene–EtOAc (95:5)]. After separation of the residual crude **18** (about 10%) **20** (157 mg) was obtained, and purified by crystallization from CH_2Cl_2–ether (97 mg), m.p. 206–208°. $[\alpha]_D^{20} = -3$ (0,346); IR: 3590, 1725, 1602, 1220, 1155, 1030, 1000 cm^{-1}; NMR: 0.81 (3 H, s, CH_3 18), 0.94 (3 H, s, CH_3 19), 2.04 (3 H, s, CH_3 acetate), 2.7 (1 H, m, H 3α), 3.62 (1 H, m, H 1α), 4.52 (1 H, q, H–17α; $J_{xx'} = 10$, $J_{x\beta'} = 8$), 7.28 (5 H, m, aromatic protons). NMR (after addition of TAI): 4.92 (1 H, q, H–1α; $J_{xx'} = 5$, $J_{x\beta} = 12$). (Found: C, 78.91; H, 9.23%. $C_{27}H_{38}O_3$ Requires: C, 78.98; H, 9.33%).

†The reaction was monitored by tlc [toluene-ethyl acetate (4:1)] and by IR spectroscopy. The first step consists in saponification of the 17-acetoxy group, followed by hydrolysis of the acyl fluoride

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