PHOTOCHEMICAL 6β-HYDROXYLATION OF 11β-HYDROXY-4-ANDROSTENE-3,17-DIONE*

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The utilisability of the photochemical oxygenation of $\Delta^{3,5}$-enol ethers of the type *III* is limited in 11β-hydroxy derivatives which under the conditions of enol-etherification undergo dehydration to a considerable extent. A method for the protection of the 11β-hydroxy group in the form of a 11-keto group has been elaborated; after the enol-etherification the keto group can be reduced back to the 11β-hydroxy group.

The determination of the daily production of 11β-hydroxy-4-androstene-3,17-dione (*II*) in patients with pathological hyperandrogenesis is useful for detection whether the excess of the androgens is originated in gonads or adrenals. Quantitative radioimmunoassay of *II* has been described[1] with the use of 6β-semisuccinyloxy derivative of compound *II* (*XXII*) as hapten. The preparation of this compound started with cortisol (*I*) which was oxidized to 17-keto derivative *II* with sodium bismuthate. The preparation of enol ether *III* and its photochemical oxygenation to 6β-hydroxy derivative has been described with an overall yield of 7% (ref.[1]).

In an attempt at the reproduction of this procedure we obtained compound *IV* as the most polar product. In comparison with the starting compound *II* it contained an additional double bond. The signal of the $C_{(4)}$-proton occurred at a lower field (5·91 ppm) than usual for Δ^4-3-ketones unsubstituted in the position 6 (5·73 ppm) and on its oxidation triketone *VI* was formed in which two keto groups were constituents of a conjugated system (UV spectrum: ε_{251} 11 000). Therefore we assigned compound *IV* the structure of a 6β-hydroxy derivative (see Table I, compounds *IV* and *V*).

An alternative method of 6β-hydroxylation[2], based on the epoxidation of the corresponding ketal *VII* afforded another 6β-hydroxy derivative (compound *IX*, see Table I, downfield shift of the $C_{(4)}$-proton from 5·72 to 5·91 ppm), which, however, contained a 9α,11α-oxido group (triplet of the 11β-proton at 3·24 ppm) instead of the 11β-hydroxyl group; as a by-product the known 9α,11α-oxido-4-androstene-3,17-dione (*VIII*, ref.[3]) was obtained. The finding of these products suggested the

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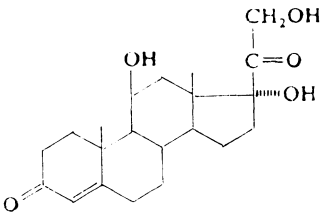
explanation of the low yields[1] of the photochemical oxygenation of the enol ethers in compounds with a 11β-hydroxy group in the molecule: under the conditions of acid catalysed etherification or ketalisation this group split off under formation of $\Delta^{9(11)}$-olefins of type *X* (a model experiment confirmed the credibility of this explanation).

TABLE I

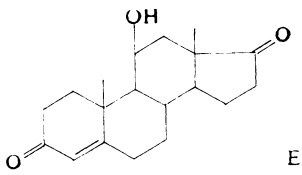
Characteristic parameters of the ^{1}H NMR spectra. The spectra were recorded on a Tesla 60 instrument in deuteriochloroform (concentrations between 0·25 and 0·50 mol/l) with tetramethylsilane as internal reference, chemical shifts are given in the δ-scale (ppm), the half-height width (*W*) is given in Hz

Compound	4-H[a]	6-H[b]	11-H[c]	18-H[d]	19-H[d]	Other signals
II	5·68[e]	—	4·43	1·17	1·48	—
IV	5·91	4·46	5·56[f]	0·92	1·56	—
V	5·98	5·53[g]	5·56[g]	0·91	1·45	2·08[h]
VI	6·21	—	5·47[f]	0·90	1·37	—
VIII	5·82[e,i]	—	3·24[j]	0·94	1·47	—
IX	5·91	4·47	3·22[j]	0·96	1·66	—
X	5·76[e]	—	5·57[f]	0·89	1·36	—
XI	5·73[e]	—	—	0·88	1·44	—
XII	5·08[k]	5·17[l]	—	0·82	1·15	3·55[m]
XIII	5·11[k]	5·20[l]	4·38	1·11	1·21	3·60[m]
XV	5·91	5·44	4·47	1·19	1·54	2·05[h]
XVI	6·21	—	—	0·88	1·36	—
XVIII	5·91[n]	5·76[o]	4·55	1·14	1·49	2·14[h]
XIX	—	—	4·44	1·15	1·23	—
XX	6·18	—	4·53	1·18	1·45	—
XXI	5·69[d]	6·21[p]	4·44	1·15	1·45	—
XXII	5·92	5·47	4·48	1·19	1·56	2·67[r,s]
XXIII	5·93	5·49	4·50	1·21	1·57	2·78[t,s], 4·76[u]
XXIV	5·92	5·47	4·48	1·19	1·55	2·61[r,s], 4·17[v]

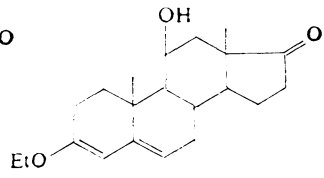
[a] Singlet (*W* = 1·6) unless otherwise stated; [b] dd (*J* = 3 and 3 Hz) unless otherwise stated: [c] dd (*J* = 6 and 2·5 Hz) unless otherwise stated; [d] singlet; [e] broad singlet (*W* = 3·3); [f] broad triplet (*J* = 3·5 and 3·5 Hz); [g] overlapping signals; [h] singlet of the acetoxy group; [i] a spectrum of the compound *VIII* was described[3] and this signal was mistakenly put further downfield; [j] broad triplet (*J* = 2·9 and 2·9 Hz) in agreement with ref.[3]. Previous authors[10] erroneously claimed this signal as a doublet; [k] mt (*W* = 4·5); [l] mt (*W* = *c.* 18); [m] quartets of CH_3CH_2O— groups, triplets of these groups appear at about 1·2 ppm; [n] d (*J* = 2 Hz); [o] ddd (*J* = 2 and 5·5 and 13 Hz); [p] singlet of protons in positions 6 and 7; [r] singlet; [s] the signal of hydrogen atoms of the succinic moiety; [t] multiplet (*W* = 13 Hz); [u] singlet of the 2,2,2-trichloroethanol moiety; [v] dd (*J* = 8 and 9 Hz) of the 2-trimethylsilylethanol moiety.



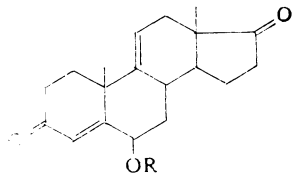
I



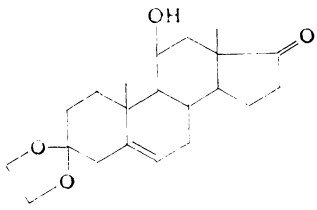
II



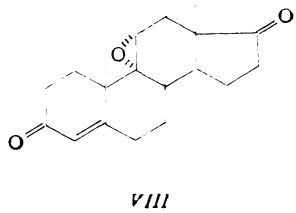
III



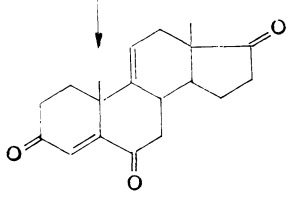
IV, R = H
V, R = Ac



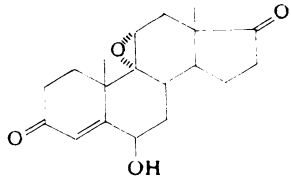
VII



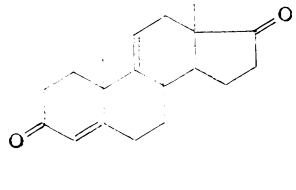
VIII



VI



IX



X

The protection of the 11β-hydroxyl group can be carried out in various ways (for example in the form of trimethylsilyl derivative[4]), but in this paper we described the advantageous protection of this group in the form of 11-keto group: low reactivity of the 11-keto group permits a shielding of the reactivity of other carbonyl groups, while the regeneration of the 11β-hydroxyl groups is given by the selective reduction course of this group. However, this method of protection also permits the use of cortisol as substrate, so that both oxidations (of the hydroxyl groups and of the side chain) are carried out simultaneously. For the enol-etherification of trione *XI* conditions were applied which also ensured the protection of the 17-keto group in the form of an acetal. Reduction of compound *XII* with lithium aluminum hydride afforded a substrate for photochemical oxygenation[5] (*XIII*).

Four modifications of the conditions of photochemical oxygenation were tested (Table II), differing in the characteristics of the active radiation and the efficiency of the contact of the substrate with oxygen. After the regeneration of the 17-oxo group from the acetal grouping more polar components than 11β-hydroxy-4-andro-

stene-3,17-dione (*II*) were sought in the product. The two most polar products (*XIV* and *XVII*) were oxidizable to the known[6] 4-androstene-3,6,11,17-tetraone (*XVI*), and the assignment of the configuration to the hydroxyl group at $C_{(6)}$ was carried out on the basis of the ^{1}H NMR spectra of corresponding acetates *XV* and *XVIII*: the required 6β,11β-dihydroxy-4-androstene-3,17-dione (*XIV*) was identified as the second most polar product. The third substance more polar than the hydroxy dione *II* was 11β-hydroxy-5α-androstane-3,6,17-trione[6] (*XIX*), the formation of which in photochemical oxygenation of enol ether *III* was observed earlier[1]. The main lipophilic product was identified with compound *II*, contaminated in some cases with 11β-hydroxy-4,6-androstadiene-3,17-dione (*XXI*) the presence of which was detected by the UV spectrum and the typical chemical shift of the vinylic protons in positions 4, 6 and 7 (two-proton singlet at 6·21 and one-proton singlet at 5·69 ppm). During the reaction in a quartz flask 11β-hydroxy-4-androstene-3,6,17-trione (*XX*) was also formed, which was oxidizable to the known tetraone *XVI*.

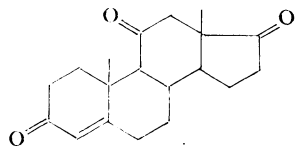
Table II shows that for the described 6β-hydroxylation the irradiation of a solution of enol ether *XIII* in a Pyrex flask under oxygen is the most suitable method when a medium-pressure discharge lamp is used as light source (method *A*). In the reaction in a quartz flask (method *B*) the yields of 6β-hydroxy product are decreased and those of the 6-oxo derivatives increased (formation of 6-oxo derivatives from

TABLE II

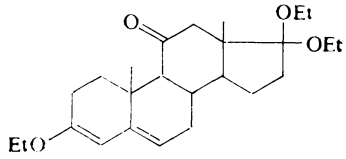
Photochemical oxygenation of some $\Delta^{3,5}$-enol ethers. Alcoholic solutions of enol ethers were shaken under oxygen (*A*, *B*, *D*) or bubbled through with oxygen (*C*) and irradiated with a medium pressure discharge mercury lamp (125 W). The irradiation was carried out either from outside of a Pyrex flask (*A*) or a quartz flask (*B*) or within a Pyrex reactor (*C*); solar irradiation was also used (*D*)

Starting compound[a]	Method	Time min	Reaction products, %		
			6β-ol	6α-ol	other products
II	*A*	180	*IV* (12)	[b]	*X* (35)
XI	*A*	60	*XIV* (31)	*XVII* (3)	*XIX* (7), *II* (4)
XI	*B*	18	*XIV* (9)	*XVII* (19)	*XIX* (13), *XX* (12), *II* (12), *XXI* (3)
XI	*C*	60	*XIV* (0)	*XVII* (0)	*II* (45)
XI	*D*	200	*XIV* (30)	*XVII* (4)	*XX* (17), *II* (18)

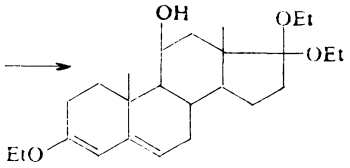
[a] The substrate proper for photochemical oxygenation was the enol ether prepared from the mentioned starting compound and used either directly (in compound *II*) or after reduction with lithium aluminium hydride (in compound *XI*). The mentioned yields correspond to the total yield of the isolated products, referred to the starting Δ^4-3-keto derivative; [b] the product was not isolated.



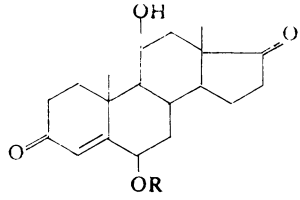
XI



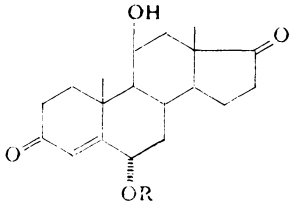
XII



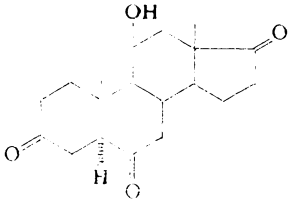
XIII



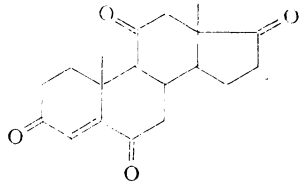
XIV, R = H
XV, R = $COCH_3$
XVII, R = $CO(CH_2)_2COOH$
XVIII, R = $CO(CH_2)_2COOCH_2CCl_3$
XVIV, R = $CO(CH_2)_2COO(CH_2)_2Si(CH_3)_3$



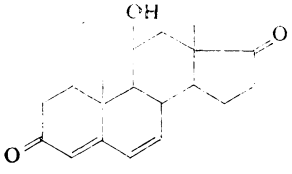
XVII, R = H
XVIII, R = $COCH_3$



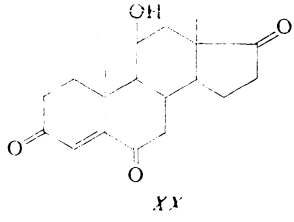
XIX



XVI



XXI



XX

Et = C_2H_5

6β-hydroxy and 6β-hydroxyperoxy derivatives is discussed in ref.[1]). The performance of the reaction in a submerged reactor (method *C*) is characterized by predominant formation of 6-deoxy products; the reactor does indeed ensure full utilization of the radiation energy, but the passage of oxygen through the mixture represents a lesser probability of an effective contact of the reactants than when the solution is intensively shaken under oxygen; hence, under the conditions of a relative insufficiency of oxygen in the mixture an alternative decomposition of the corresponding 3,6-diradical, derived from the enol ether *XIII*, takes place. The main disadvantage of method *D* is the long reaction time and the dependence on the non-standardized light source (the sun).

For the preparation of 6β-semisuccinate *XXII* we chose an indirect approach[7,8] which permitted the purification of the intermediary product: On reaction of semisuccinate of 2,2,2-trichloroethanol or 2-trimethylsilylethanol with compound *XIV* in the presence of dicyclohexylcarbodiimide and 4-dimethylaminopyridine we prepared the corresponding mixed succinates *XXIII* and *XXIV*. The ^{1}H NMR spectra of both succinates confirmed that under the conditions of succinylation no undesirable structural change in the substrate took place. The splitting off of 2,2,2-trichloroethanol from the molecule of succinate *XXIII* under the effect of zinc dust in a mixture of acetic acid and tetrahydrofuran was accompanied by reduction of the 3-keto group; the splitting off of the 2-trimethylsilylethanol from the molecule of compound *XXIV* under the effect of tetrabutylammonium fluoride in tetrahydrofuran took place quantitatively to the pure semisuccinate *XXII*, which was used for the immunisation experiments.

EXPERIMENTAL

The melting points were determined on a Kofler block and they are not corrected. Specific rotations and the infrared spectra were measured in chloroform, the ultraviolet spectra in ethanol. The mass spectra were recorded on an AEI MS 902 spectrometer. Thin-layer plates for preparative chromatography were made from silica gel MERCK, GF_{254}.

6β-Hydroxy-4,9(11)-androstadiene-3,17-dione (*IV*)

11β-Hydroxy-4-androstene-3,17-dione (*II*, 400 mg) was heated in a solution containing 100 mg of *p*-toluenesulfonic acid, 1 ml of ethanol and 3 ml of ethyl orthoformate in 100 ml benzene under a Dean-Stark adapter. After 1 h the solution was cooled and washed with a potassium carbonate solution (10%, 10 ml) and water, dried by filtration through a layer of anhydrous magnesium sulfate, and evaporated in a vacuum. The residue was dissoved in 20 ml of 96% ethanol in a Pyrex flask of 1 000 ml content. The flask was evacuated, filled with oxygen and shaken on a Tatlock shaker at a distance of 5–8 cm from the medium pressure discharge lamp (125 W). After 3 h the solution was evaporated under reduced pressure and the residue chromatographed on thin layers of silica gel, yielding the main product (52 mg) which was crystallized from acetone, m.p. 196–198°C, $[\alpha]_D^{20}$ +134° (*c* 1·0). IR spectrum: 3 605, 1 064, 1 049, 1 037 (OH), 1 735(CO), 1 678, 1 628 (=C—C=O) cm^{-1}. For $C_{19}H_{24}O_3$(300·4) calculated:75·97% C, 8·95% H; found: 76·03% C, 8·11% H.

6β-Hydroxy-9α,11α-oxido-4-androstene-3,17-dione (*IX*)

A solution of diketone *II* (875 mg) and *p*-toluenesulfonic acid (50 mg) in 2-ethyl-2-methyl-1,3-dioxolane (15 ml) was refluxed. After 90 min about 10 ml of distillate were collected. The mixture was diluted with 10 ml of an aqueous solution of potassium hydrogen carbonate, the product was extracted with chloroform and the extract was dried by filtration through magnesium sulfate. The volume of the solution was made up to 150 ml by addition of chloroform and *m*-chloroperoxybenzoic acid (770 mg) was added to the solution. After 3 days' standing at 20°C the mixture was washed with a potassium carbonate solution and water, then dried over sodium sulfate and concentrated in a vacuum. The residue was dissolved in 30ml of acetone to which dilute perchloric acid was added (24%, 2·25 ml). The mixture was alkalised with aqueous potassium carbonate, the product was extracted with ethyl acetate, washed with water, dried over sodium sulfate and chromatographed on a silica gel column (100 ml, ether–toluene 5 : 1). Gradually 210 mg of 9α,11α-epoxy-4-androstene-3,17-dione (*VIII*), 200 mg of unreacted *II* and 200 mg of the product *IX* were eluted. The product had m.p. 216–219°C (acetone), $[\alpha]_D^{20}$ +101° (*c* 1·1). IR spectrum: 1 740 (C=O), 1 680, 1 621 (C=C—C=O), 3 600 (OH), 882 (epoxide) cm^{-1}. For $C_{19}H_{24}O_4$ (316·4) calculated: 72·13% C, 7·65% H; found: 72·01% C, 7·86% H.

4-Androstene-3,11,17-trione (*XI*)

a) A solution of cortisol (*I*, 544 mg) in chloroform (10 ml) and acetone (40 ml) was bubbled through with nitrogen and an excess of Jones's reagent was added to it dropwise under stirring at 0°C. After 4 h the mixture was poured into a solution of potassium hydrogen carbonate, the product was extracted with ethyl acetate which was washed with water, dried over sodium sulfate and concentrated. The residue was crystallized from ether, m.p. 220–223°C (165 mg), undepressed in admixture with an authentic sample[8]. The mother liquors were purified by preparative thin-layer chromatography in 50% ether in benzene, affording another 160 mg of product. The total yield of trione *XI* was 72%.

b) A solution of cortisol (*I*, 380 mg) in 60 ml of acetic acid was bubbled through with nitrogen and a solution of chromium trioxide (680 mg) in water (0·5 ml) was added to it dropwise under stirring. After 4 h stirring at 20°C the solution was poured into 50 ml of ammonia and 20 ml of ice and the product was extracted with ethyl acetate. The solution was worked up as under *a*), affording 230 mg (73%) of trione *XI*.

c) 500 mg of dione *II* were dissolved in 5 ml of acetone at 20°C, the solution was blown through with nitrogen and mixed with the Jones reagent. After 5 min the solution was poured into a solution of potassium hydrogen carbonate, the product was extracted with chloroform, the extract washed with water, filtered through a layer of sodium sulfate and silica gel and concentrated in a vacuum. Crystallization of the residue and purification of the mother liquors afforded a total of 490 mg of trione *XI* (98%).

3,17,17-Triethoxy-3,5-androstadien-11-one (*XII*)

A suspension of 0·5 g of triketone *XI* in 5 ml of ethanol, 1 ml of ethyl orthoformate and 0·1 ml of a catalyst prepared from 1 ml of ethanol and 1 drop of sulfuric acid was refluxed for 1 h. Pyridine 0·5 ml was then added to the green solution and the mixture was cooled, diluted with 20 ml of aqueous potassium carbonate (10%) and the product was extracted with toluene (3 × 50 ml). The extract was washed with water, dried by filtration through a layer of magnesium sulfate and evaporated in a vacuum. IR spectrum: 1 709 (C=O), 1 656, 1 638 (C=C), 1 222, 1 178, 1 115 and 1 060 (C—O) cm^{-1}; $[\alpha]_D^{20}$ −46° (*c* 1·0). Mass spectrum: *m/z* 402 (M^+ for $C_{25}H_{38}O_4$).

11β-Hydroxy-3,17,17-triethoxy-3,5-androstadiene (*XIII*)

400 mg of ketone *XII* were reduced in tetrahydrofuran with about 100 mg of lithium aluminum hydride at room temperature. After 18 h the mixture was decomposed with moist ether and then with a few drops of a saturated magnesium sulfate solution. The mixture was saturated with anhydrous magnesium sulfate, the inorganic material was filtered off, washed with ether and the ethereal extract evaporated *in vacuo*. Yield, 380 mg (94·5%). IR spectrum (CCl_4): 3 625 (OH), 3 030 (C=C) cm^{-1}; $[\alpha]_D^{20}$ −40° (*c* 1·0); mass spectrum: *m/z* 404 (M^+ for $C_{25}H_{40}O_4$).

Photochemical Oxidation of Enol Ether *XIII*

a) 350 mg of enol ether *IX* were dissolved in 20 ml of 96% ethanol in a 1 l flask which was evacuated, filled with oxygen, evacuated again, refilled with oxygen and shaken intensively at a 5—10 cm distance from a medium pressure discharge lamp (125 W). After 1 h the solution was evaporated in a vacuum, the residue was dissolved in 5 ml of acetone and 15 drops of acetic acid. After 18 h standing the solution was evaporated under reduced pressure and the residue crystallized from acetone. Yield, 103 mg of a product, consisting of about 90% of 6β,11β-dihydroxy-4-androstene-3,18-dione (*XIV*) and about 10% of 6α-epimer *XVII*. Repeated crystallization from a mixture of methanol, acetone and heptane gave 57 mg of compound *XIV*, m.p. 261—266°C (literature[6] gives m.p. 257—284°C). Mass spectrum: *m/z* 318 (M^+). IR spectrum: 1 738 (C=O), 1 681, 1 669, 1 631 (C=C—C=O), 3 610, 1 056, 1 025 (OH) cm^{-1}. The combined mother liquors were dissolved in a chloroform–methanol (3 : 2) mixture and applied onto a thin layer of silica gel on a glass plate. The plate was developed twice with chloroform–ether–2-propanol 49·5 : 49·5 : 1, the zones of the substances were detected by inspection under the UV lamp and the elution of corresponding zones was carried out with a mixture of ether, chloroform and methanol 3 : 2 : 1. Another 30 mg of compound *XIV* were thus obtained (a total of 87 mg, 31%). Further substances were isolated chromatographically (in the order of increasing lipophility): 6α,11β-dihydroxy-4-androstene-3,17-dione (*XVII*, 10 mg), m.p. 263—272°C; 11β-hydroxy-5α-androstane-3,6,17-trione (*XIX*, 20 mg), IR spectrum: 1 738 and 1 718 (C=O), 3 615 (OH) cm^{-1}; mass spectrum: *m/z* 318 (M^+); m.p. 280—283°C (literature[6] gives 281—284°C); 11β-hydroxy-4-androstene-3,17-dione (*II*, 12 mg).

b) In an alternative working up of the product of photolysis the mixture was dissolved in ethyl acetate (4 ml) and acetic acid (0·3 ml) and shaken with a 10% potassium iodide solution in water (2 ml) for 4 min. The mixture was diluted with ethyl acetate, washed with a 5% sodium thiosulfate solution, 7% potassium hydrogen carbonate solution and water, and dried over sodium sulfate. In this reduction of possible peroxides the regeneration of the 17-oxo group from the corresponding acetal group also took place. The yields of the required products were not improved by this method of working up.

c) 210 mg of enol ether *XIII* were submitted to photo-oxidation under the same conditions as under *a*), *b*), with the difference that the reaction flask was made of quartz (content 250 ml) and the reaction time was shortened to 20 min. Thin-layer chromatography gave: 30 mg of 6α,11β-diol *XVII*, 15 mg of 6β,11β-diol *XIV*, 22 mg of 11β-hydroxy-3,6,17-trione *XIX*, 20 mg of unsaturated 11β-hydroxy-3,6,17-trione *XX*, 25 mg of a mixture of 11β-hydroxy diketone *II* and *XXI* (according to the UV spectrum in a 4 : 1 ratio).

6α-Acetoxy-11β-hydroxy-4-androstene-3,17-dione (*XVIII*)

30 mg of diol *XVII* were dissolved in 0·5 ml of pyridine and 0·2 ml of acetic anhydride. After 18h standing the mixture was decomposed by pouring it into water. The product was extracted

with chloroform, washed with dilute hydrochloric acid, water, an aqueous potassium hydrogen carbonate solution and water, dried over sodium sulfate and concentrated under reduced pressure. The product (22 mg) was crystallized from acetone, m.p. 236–240°C (lit.[6] gives 248–249°C).

6β-Acetoxy-11β-hydroxy-4-androstene-3,17-dione (*XV*)

Diol *XIV* (21 mg) was acetylated in the same manner. The product (16 mg) had m.p. 194–196°C (ethanol), lit.[6] gives 195–196°C.

Oxidation of Hydroxy Derivatives with Jones's Reagent

a) 6β-Hydroxy-4,9(11)-androstadiene-3,17-dione (*IV*, 15 mg) was dissolved in acetone (2 ml) and oxidized with Jones's reagent at 20°C under stirring. After 4 min the solution was poured into 20 ml of an aqueous potassium hydrogen carbonate solution, the product *VI* was extracted with ethyl acetate, the extract washed with water and dried over sodium sulfate and evaporated. The residue had in its ^{1}H NMR spectrum a singlet of the $C_{(4)}$-proton at 6·21 ppm and singlets of angular methyl groups at 0·90 and 1·37 ppm; UV spectrum (ethanol): ε_{251} 11 000.

b) Diol *XIV* (30 mg) was oxidized in a similar manner, affording 20 mg (68%) of 4-androstene-3,6,11,17-tetraone (*XVI*), m.p. 194–196°C (lit.[6] gives m.p. 191–197°C), IR spectrum: 1 745, 1 712, 1 692, 1 678 (sh), 1 606 cm^{-1}; mass spectrum: *m/z* 314 (M^+).

c) Diol *XVII* (37 mg) was oxidized in the same manner, affording tetraone (24 mg, 66%) identical with the sample described under *b*).

d) 11β-Hydroxy-4-androstene-3,6,17-trione (*XX*, 12 mg) was converted to tetraone *XVI* (4 mg, 34%) in a similar manner.

6β,11β-Dihydroxy-4-androstene-3,17-dione 6β-(3-Carboxypropanoate) (*XXII*)

a) 20 mg of diol *XIV* and 35 mg of ground succinic anhydride were dried in a test tube at 40°C in a vacuum (0·2 kPa) over phosphorus pentoxide. After 1 h pyridine (0·4 ml) was introduced into the tube, air was replaced by argon and the tube was sealed. The mixture was heated at 90°C for 20 h, the tube was opened and pyridine was evaporated at 70°C with a current of nitrogen. The residue was dissolved in chloroform and applied onto a thin layer of silica gel, the plate was developed in a mixture of ether, chloroform and isopropyl alcohol (49·5 : 49·5 : 1), detection was carried out by inspection in ultraviolet light. The product was eluted with a mixture of ether, chloroform and acetic acid (49 : 49 : 2) and applied onto another thin layer plate and developed with ether–chloroform–2-propanol–acetic acid (49 : 49 : 1 : 1). The product was eluted in a similar manner and pure semisuccinate *XXII* (20 mg) was obtained, free of the starting substance (in the 1st chromatography) and the polar impurities (in the 2nd chromatography). M.p. 156–163°C, after crystallization from acetone and ether m.p. 164–169°C (lit.[1] gives m.p. 174–178°C). IR spectrum: 1 712 (COOH), 1 683, 1 622 (C=C—C=O), 1 737 (COOR + + CO), 3 610 (OH) cm^{-1}; IR spectrum (KBr): 1 706 (COOH), 1 738 (COOR + CO), 1 694, 1 625 (C=C—C=O) cm^{-1}.

b) 20 mg of succinate *XXIV* were dissolved in 1 ml of tetrahydrofuran and 0·2 ml of a solution of tetrabutylammonium fluoride in tetrahydrofuran (1 mol l^{-1}) were added to it. After 70 min the solution was diluted with 20 ml of ethyl acetate, the solution was washed twice with 5 ml of water and dried over sodium sulfate. The residue (15 mg) had m.p. 169–160°C, after crystallization from acetone and ether it melted at 165–169°C. The IR spectrum was identical with the spectrum of the product prepared above.

6β,11β-Dihydroxy-4-androstene-3,17-dione 6β-[4-(2,2,2-Trichloroethyl)-4-oxobutanoate] (*XXIII*)

A suspension of 26 mg of 6β,11β-diol *XIV* in 8 ml of toluene was refluxed and concentrated at normal pressure to 1·5 ml volume. Semisuccinate of 1,1,1-trichloroethanol (45 mg), dicyclohexylcarbodiimide (33 mg) and 4-dimethylaminopyridine (1 mg) were added to the suspension. After 3 h standing the solution was diluted with toluene, washed with water (two 5 ml portions), dried and concentrated *in vacuo*. The residue was purified by thin-layer chromatography (developed with 50% ether in benzene), the main product was isolated with ether (27 mg) and crystallized from acetone, ether and heptane. M.p. 140–143°C, $[\alpha]_D^{20}$ +91° (*c* 1·0); IR spectrum: 1 680, 1 621 (C=C—C=O), 1 739, 1 152 (COOR), 1 739, 1 409 ($COCH_2$) cm^{-1}. For $C_{25}H_{31}.Cl_3O_7$ (549·9) calculated: 54·60% C, 5·68% H; found: 54·40% C, 6·52% H.

6β,11β-Dihydroxy-4-androstene-3,17-dione 6β-[4-(2-trimethylsilylethyl)-4-oxobutanoate] (*XXIV*)

A suspension of 23 mg of diol *XIV* in 1·5 ml of toluene was stirred at room temperature with semisuccinate of 2-trimethylsilylethanol (23 mg), dicyclohexylcarbodiimide (30 mg) and 4-dimethylaminopyridine (3 mg) for 2 h. The mixture was worked up in the same manner as in the preparation of compound *XXIII*. The main product (compound *XXIV*, 26 mg) would not crystallize from current solvents; IR spectrum: 3 610 (OH), 1 734 (CO), 1 682, 1 623 (C=C—C=O), 1 728 (sh), 1 161 (COO), 1 253, 862, 842 ($SiCH_3$) cm^{-1}; $[\alpha]_D^{20}$ +95° (*c* 0·7); mass spectrum: *m/z* 518 (M^+ for $C_{28}H_{40}O_7Si$), 318 (M^+ — ester group), 301 ($M^+ - C_{(6)}$-substituent), 173 ($CH_2CH_2COOCH_2CH_2Si(CH_3)_3$).

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