SYNTHESIS OF (19*E*)-3β,7β-DIHYDROXY-17-OXOANDROST-5-EN-19-AL 19-(*O*-CARBOXYMETHYL)OXIME, NEW HAPTEN FOR 7β-HYDROXY-DEHYDROEPIANDROSTERONE (3β,7β-DIHYDROXYANDROST-5-EN-17-ONE)*

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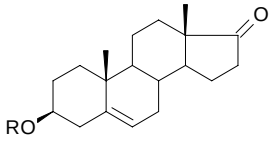
(19*E*)-3β,7β-Dihydroxy-17-oxoandrost-5-en-19-al 19-(*O*-carboxymethyl)oxime (**26**) was prepared in 15 steps from 17-oxoandrost-5-en-3β-yl benzoate (**2**, DHEA benzoate). Protection of position 17 by a borohydride reduction and acetylation, subsequent functionalization of position 19 by hypoiodite reaction, oxidation to 19-aldehyde and oximation gave successively (19*E*)-19-oxoandrost-5-ene-3β,17β-diyl 17-acetate 3-benzoate 19-(*O*-carboxymethyl)oxime methyl ester (**10**). Then 7-keto group was introduced by allylic oxidation with chromium(VI) oxide–3,5-dimethylpyrazole complex and stereoselectively reduced by borohydride in the presence of cerium(III) ions into 7β-hydroxy group. After protection as 7-isobutyrate the acetate at position 17 was removed and oxidation recovered 17-ketone. Final deprotection revealed both hydroxyl and carboxyl groups, giving desired 19-CMO 7β-hydroxy DHEA designed as hapten for immunassays.

Key words: 7β-Hydroxy DHEA; Hapten; Oxime.

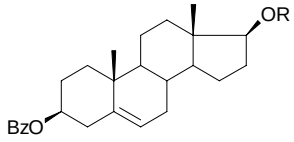
Recently, the natural metabolites of dehydroepiandrosterone **1** (DHEA) hydroxylated at position 7 were found to be involved in a process which may participate in the physiological regulation of the body's immune response[2]. Our work was subjected to the synthesis of an hapten, suitable for the immunoassay of one of both 7-hydroxy isomers, *i.e.* (19*E*)-3β,7β-dihydroxy-17-oxoandrost-5-en-19-al 19-(*O*-carboxymethyl)oxime (**26**). Two problems had to be solved for its preparation from the DHEA benzoate **2**: the introduction of the (*O*-carboxymethyl)oxime group into position 19 and the hydroxylation to the position 7β. The necessary compatible reaction pathways were firstly checked on the synthesis of derivatives with only one from the above mentioned functional groups. In both cases the preparation of partially substituted compounds was described in the literature, but the ways were different from ours.

* Part CCCLXXXVII in the series On Steroids; Part CCCLXXXVI see ref.[1].

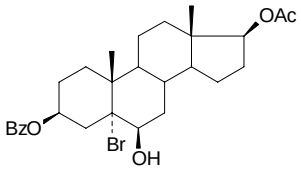
Reduction of starting DHEA benzoate **2** with sodium borohydride gave 17β-hydroxy derivative **3**. The hydroxyl group was protected as an acetate and the position 19 of acetate benzoate **4** was functionalized by radical hypoiodite reaction[3]. Unsaturated derivative **4** was transformed by addition of hypobromous acid into bromohydrine **5**, which



1, R = H
2, R = Bz



3, R = H
4, R = Ac



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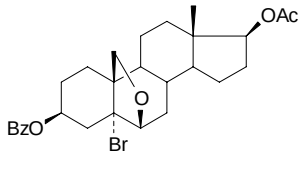

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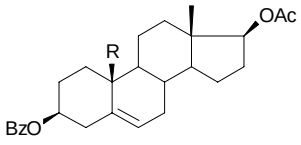
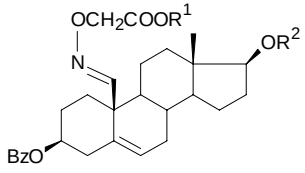
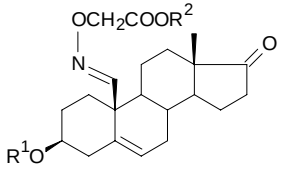


7, R = CH_2OH
8, R = CHO



9, R^1 = H; R^2 = Ac
10, R^1 = CH_3; R^2 = Ac
11, R^1 = CH_3; R^2 = H

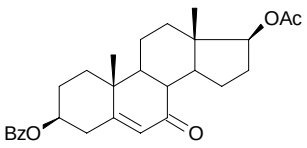


12, R^1 = Bz; R^2 = CH_3
13, R^1 = R^2 = H

was then submitted to a radical reaction with lead(IV) acetate in presence of iodine and calcium carbonate to yield bromoepoxide **6**. By the treatment of zinc in aqueous 2-methyl-2-propanol the 19-hydroxy derivative **7** with regenerated double bond at position 5(6) was prepared. Oxidation by Jones reagent gave aldehyde **8**, which was transformed by reaction with (*O*-carboxymethyl)hydroxylamine and subsequent diazomethane esterifi-

cation into 19-(*O*-carboxymethyl)oxime derivative **10**. Acetyl protecting group at position 17 was selectively removed by concentrated hydrochloric acid in a chloroform–methanol mixture, giving the compound **11** in a 87% yield. Hydroxyl group at position 17 was oxidized by Jones reagent and the resulted 17-keto derivative **12** was submitted to the alkaline hydrolysis to remove the rest of protecting groups. Prepared 19-(*O*-carboxymethyl)oximino derivative **13** melted in accord with literal data[4]. Its IR spectrum displayed bands at 3 602 cm^{-1} (hydroxyl group), 1 750 cm^{-1} (carboxylic acid monomer), and 1 734 cm^{-1} (carboxylic acid dimmer and ketone). The ^1H NMR spectrum showed signals characteristic[5] for 19-(*O*-carboxymethyl)oximino derivatives at δ 4.58 (s, OCH_2COO) and at δ 7.37 (s, H-19), and further signals at δ 3.52 (m, W = 32 Hz, H-3α) and at δ 5.60 (bd, $J \approx 5$ Hz, H-6).

The problem of an introduction of a hydroxyl group into position 7 and search for a suitable protecting group at this position was solved on the derivative **4**, without substitution at position 19. Its allylic oxidation by chromium(VI) oxide–3,5-dimethylpyrazole complex in dichloromethane[6] gave 7-keto derivative **14**, which was then stereoselectively reduced into 7β-hydroxy derivative **15** by sodium borohydride in the presence of cerium(III) chloride heptahydrate in a methanol–tetrahydrofuran mixture[7]. New hydroxyl group at position 7 was protected in the form of isobutyrate and resulted triester **16** was submitted to the selective removal of acetate at position 17 by concentrated hydrochloric acid in a chloroform–methanol mixture. Desired 17β-hydroxy derivative **17** was prepared in a 36% yield. Oxidation by Jones reagent gave 17-keto derivative **18**, which after removal of remaining protecting groups by alkaline hydrolysis gave 7β-hydroxy DHEA **19** with physical constants corresponding with literal data[8].



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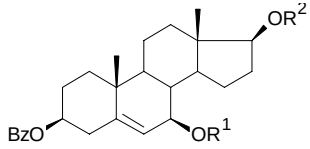
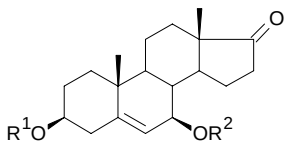


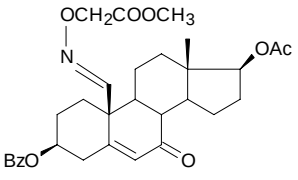
15, R^1 = H; R^2 = Ac
16, R^1 = iBu; R^2 = Ac
17, R^1 = iBu; R^2 = H



18, R^1 = Bz; R^2 = iBu
19, R^1 = R^2 = H

iBu = 2-methylpropionate

Before mentioned procedures were used for the synthesis of needed (19*E*)-3β,7β-dihydroxy-17-oxoandrost-5-en-19-al 19-(*O*-carboxymethyl)oxime (**26**). The reactions sequence leading to a 7β-hydroxy derivative was applied to the protected 19-(*O*-carboxymethyl)oximino derivative **10**. Its oxidation with chromium(VI) oxide–3,5-dimethylpyrazole complex in dichloromethane[6] gave 7-keto derivative **20**, which was stereoselectively reduced with sodium borohydride in the presence cerium(III) chloride heptahydrate in a methanol–tetrahydrofuran mixture[7]. After protection of hydroxyl at position 7β in the form of isobutyrate, the 17-acetate in triester **22** was selectively removed by concentrated hydrochloric acid in a chloroform–methanol mixture. The 17β-hydroxy derivative **23**, prepared in a 78% yield, was oxidized by Jones reagent into 17-keto derivative **24**. The structure of this "fully protected" derivative of final compound **26** was studied by ^{1}H NMR spectroscopy. The spectrum contained besides signals of protecting groups the signals characteristic for 19-(*O*-carboxymethyl)-oximino derivatives[5] at δ 4.69 (s, OCH_2COO) and at δ 7.51 (s, H-19). From other signals, those characteristic for acylated 3β,7β-dihydroxy derivatives at δ 5.23 (dt, J = 8.7 Hz, J' = 1.7 Hz, H-7α) and at δ 4.90 (m, W = 32 Hz, H-3α), and signal of C=C double bond proton at δ 5.50 (bs, H-6) could be mentioned.



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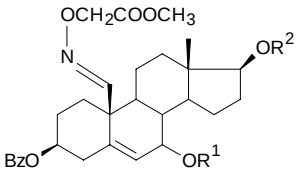
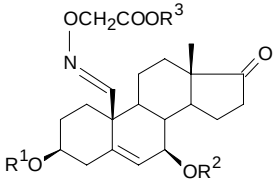


21, R^1 = H; R^2 = Ac
22, R^1 = iBu; R^2 = Ac
23, R^1 = iBu; R^2 = H



24, R^1 = Bz; R^2 = iBu; R^3 = CH_3
25, R^1 = H; R^2 = iBu; R^3 = H
26, R^1 = R^2 = R^3 = H
27, R^1 = H; R^2 = iBu; R^3 = CH_3
28, R^1 = R^2 = H; R^3 = CH_3

The ^{13}C NMR spectrum of derivative **24**, together with spectra of starting DHEA benzoate **2** and partially substituted intermediates **12** and **18**, were given in Table I. Differences in chemical shifts corresponding to introduction of protected 7β-hydroxyl

TABLE I
^{13}C NMR spectral parameters of 17-oxo-5-androstene derivatives

Carbon	Chemical shifts[a], δ, ppm				Substituent effects, ppm		
	2	**12**	**18**	**24**	**12 – 2**	**18 – 2**	**24 – 2**
C-1	36.94	31.30	36.72	32.71	–5.64	–0.22	–4.23
C-2	27.76	28.33	27.66	28.20	0.57	–0.10	0.44
C-3	74.29	73.76	73.61	73.10	–0.53	–0.68	–1.19
C-4	38.13	38.65	37.66	38.17	0.52	–0.47	0.04
C-5	139.94	135.06	144.15	138.96	–4.88	4.21	–0.98
C-6	122.00	125.10	122.20	125.17	3.10	0.20	3.17
C-7	31.37	33.17	74.54	73.78	1.80	43.17	42.41
C-8	31.44	31.81	36.20	36.44	0.37	4.76	5.00
C-9	50.13	51.28	34.25	34.22	1.15	–15.88	–15.91
C-10	36.75	43.75	36.57	43.52	7.00	–0.18	6.77
C-11	20.29	21.21	20.42	21.12	0.92	0.13	0.83
C-12	30.75	30.43	31.10	31.02	–0.32	0.35	0.27
C-13	47.49	47.38	47.65	47.56	–0.11	0.16	0.07
C-14	51.67	49.83	48.27	48.01	–1.84	–3.40	–3.66
C-15	21.83	21.71	23.41	23.37	–0.12	1.58	1.54
C-16	35.79	35.71	35.75	35.67	–0.09	–0.04	–0.12
C-17	221.06	220.59	220.34	219.97	–0.47	–0.72	–1.09
C-18	13.50	13.49	13.54	13.52	–0.01	0.04	0.02
C-19	19.35	155.25	19.06	153.84	135.90	–0.29	134.49
Bz-1′	130.75	130.64	130.61	130.49			
Bz-2′	129.53	129.52	129.55	129.53			
Bz-3′	128.28	128.29	128.30	128.30			
Bz-4′	132.77	132.82	132.83	132.89			
Bz-5′	128.28	128.29	128.30	128.30			
Bz-6′	129.53	129.52	129.55	129.53			
Bz-CO	165.99	165.97	165.83	165.80			
CMO CH_3	–	51.79	–	51.80			
CMO CH_2	–	70.42	–	70.50			
CMO CO	–	170.44	–	170.30			
iBu CH_3	–	–	18.80	18.75			
iBu CH_3	–	–	18.96	18.93			
iBu CH	–	–	50.71	50.58			
iBu CO	–	–	176.93	176.85			

[a] In $CDCl_3$.

group in **18** or protected 19-(*O*-carboxymethyl)oxime group in **12** into parent benzoate **2** were in good agreement with differences resulted from introduction of both these structural features in **24** compared with the same benzoate **2**. Good additivity of contributions of particular groups confirmed the structural assignments for all compounds discussed.

Alkaline hydrolysis of "fully protected" derivative **24** by aqueous sodium hydroxide in a methanol–tetrahydrofuran mixture gave two products, which were separated by preparative TLC on silica gel. The less polar product was identified as isobutyrate **25**. Its ^{1}H NMR spectrum contained signals of isobutyryl group (two doublets at δ 1.19 and 1.20 and a heptet at δ 2.55 with J = 7.0 Hz). Even chemical shifts of H-3α (δ 3.60) and H-7α (δ 5.18) confirmed exclusive splitting of benzoate at position 3 only. The conservation of 19-(*O*-carboxymethyl)oxime group was apparent from the presence of singlets at δ 4.65 (OCH_2COO) and at δ 7.34 (H-19). The more polar product was the desired (19*E*)-3β,7β-dihydroxy-17-oxoandrost-5-en-19-al 19-(*O*-carboxymethyl)oxime (**26**, 19-CMO 7β-OH-DHEA). The ^{1}H NMR spectrum did not contain any signals of protecting groups and the chemical shift of H-7α (δ 3.97) corresponded to free hydroxy group at position 7. Other signals were comparable with those for preceding derivative. The additional structural proofs were obtained from IR and ^{1}H NMR spectra of corresponding methyl esters **27** and **28**, prepared by diazomethane treatment of **25** and **26**, respectively.

Immunological properties of 19-(*O*-carboxymethyl)oxime derivatives **13** and **26** will be published separately.

EXPERIMENTAL

Melting points were determined on a Boetius micro melting point apparatus (Germany). Optical rotations were measured at 25 °C on a Perkin–Elmer 141 MC polarimeter and $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Infrared spectra (wavenumbers in cm^{-1}) were recorded on a Bruker IFS 88 spectrometer. ^{1}H NMR spectra were taken on a Varian UNITY-200 (200 MHz, FT mode) and ^{13}C NMR spectra on a Varian UNITY-500 (125.7 MHz, FT mode) spectrometer at 23 °C in deuteriochloroform with tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ-scale), coupling constants (J) and width of multiplets (W) in Hz. For ^{13}C NMR spectra the number of directly bonded hydrogen atoms was determined from the proton decoupled "attached proton test". Thin-layer chromatography was performed on silica gel G (ICN Biochemicals), with detection by spraying with concentrated sulfuric acid followed by heating. Preparative TLC was done on plates 200 × 200 mm, layer thickness 0.4 mm. For column chromatography silica gel 60–120 μm was used. Prior to evaporation on rotary evaporator *in vacuo* (bath temperature 50 °C), solutions in organic solvents were dried over anhydrous sodium sulfate.

17β-Hydroxyandrost-5-en-3β-yl Benzoate (**3**)

The solution of dehydroepiandrosterone benzoate **2** (9.81 g, 25.0 mmol) in dichloromethane (250 ml) and methanol (50 ml) was cooled to 8 °C. To this solution sodium borohydride (1.51 g, 40.0 mmol) was added during 5 min, the reaction mixture was stirred for 2 h at 10 °C, then acetic acid (12 ml)

was added dropwise. The solvents were distilled off *in vacuo* and the residue was dissolved in ether (700 ml) and water (100 ml). Ethereal phase was washed with water, saturated aqueous potassium hydrogen carbonate solution (two times) and water. The solvent was distilled off *in vacuo* and the residue was crystallized from an acetone–water mixture. Yield of compound **3** was 9.02 g (91%), m.p. 214–217 °C, $[\alpha]_D$ –27° (*c* 1.4, chloroform). IR spectrum (chloroform): 3 614, 3 503 (OH); 1 711 (C=O); 1 670 (C=C); 1 277 (C-O, benzoate). ^{1}H NMR spectrum: 0.78 s, 3 H (3 × H-18); 1.09 s, 3 H (3 × H-19); 3.67 dd, 1 H, J = 5.5, J' = 8 (H-17α); 4.86 m, 1 H, W = 32 (H-3α); 5.42 bd, 1 H, $J \approx 4.5$ (H-6); 7.50 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 8.04 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{26}H_{34}O_3$ (394.6) calculated: 79.15% C, 8.69% H; found: 79.32% C, 8.54% H.

Androst-5-ene-3β,17β-diyl 17-Acetate 3-Benzoate (**4**)

The hydroxy derivative **3** (9.08 g, 23.0 mmol) was acetylated with acetic anhydride (17.4 ml, 184 mmol) in pyridine (80 ml). After 48 h at room temperature, the reaction mixture was poured on ice. Crystalline product was filtered off and dissolved in dichloromethane (700 ml). This solution was washed with dilute hydrochloric acid (1 : 4), water, saturated aqueous potassium hydrogen carbonate solution and water. The solvent was distilled off *in vacuo* and the residue was crystallized from an acetone–water mixture. Yield of acetate **4** was 8.14 g (81%), m.p. 183–185 °C, $[\alpha]_D$ –35° (*c* 1.6, chloroform). IR spectrum (chloroform): 1 714 (C=O); 1 276 (C–O, benzoate); 1 256 (C–O, acetate). ^{1}H NMR spectrum: 0.82 s, 3 H (3 × H-18); 1.09 s, 3 H (3 × H-19); 2.05 s, 3 H (CH_3COO); 4.62 dd, 1 H, J = 7.6, J' = 9.2 (H-17α); 4.87 m, 1 H, W = 32 (H-3α); 5.44 bd, 1 H, $J \approx 4.5$ (H-6); 7.50 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 8.05 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{28}H_{36}O_4$ (436.6) calculated: 77.03% C, 8.31% H; found: 77.30% C, 8.39% H.

5-Bromo-6β,19-epoxy-5α-androstane-3β,17β-diyl 17-Acetate 3-Benzoate (**6**)

Olefin **4** (14.84 g, 34.0 mmol) was dissolved in a mixture of dichloromethane (100 ml) and ether (170 ml). To this solution water (11.3 ml) and *N*-bromoacetamide (5.52 g, 40.0 mmol) were added. After dissolution of all *N*-bromoacetamide, 70% perchloric acid (2.23 ml, 26.0 mmol) was added in one portion. The reaction mixture was stirred for 1 h at room temperature, then diluted with ether (200 ml), and washed with 5% aqueous sodium thiosulfate solution, saturated aqueous sodium hydrogen carbonate solution, and water. The solvents were distilled off *in vacuo* and the residue was crystallized from methanol. Yield of crude bromohydrine **5** was 9.79 g. ^{1}H NMR spectrum: 0.82 s, 3 H (3 × H-18); 1.39 s, 3 H (3 × H-19); 2.04 s, 3 H (CH_3COO); 4.23 m, 1 H, (H-6α); 4.62 dd, 1 H, J = 7.5, J' = 9 (H-17α); 5.74 m, 1 H, W = 32 (H-3α); 7.38–7.59 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 8.02 m, 2 H (H-2, H-6 of C_6H_5COO).

Calcium carbonate (7.83 g, 78.2 mmol) was suspended in benzene (700 ml). A part (70 ml) of benzene was distilled off and lead(IV) acetate (15.66 g, 35.3 mmol) was added. The mixture was refluxed for 2 h, cooled to 70 °C and bromohydrine **5** (9.79 g, 18.4 mmol) and iodine (7.83 g, 61.7 mmol) were added. After refluxing for 3 h, the reaction mixture was cooled to 50 °C, the solids were filtered off and the benzene solution was washed with 5% aqueous sodium thiosulfate solution (3 times), saturated aqueous sodium hydrogen carbonate solution and water. The solvent was distilled off *in vacuo* and the residue was chromatographed on column of silica gel (400 g) in a light petroleum–ether (95 : 5) mixture. Yield of bromoepoxide **6** was 8.54 g (47% based on olefin **4**), m.p. 199–202 °C (ether), $[\alpha]_D$ –2° (*c* 1.7, chloroform). IR spectrum (chloroform): 1 733 (C=O, acetate); 1 723 (C=O, benzoate); 1 273 (C–O, benzoate); 1 246 (C–O, acetate). ^{1}H NMR spectrum: 0.84 s, 3 H (3 × H-18); 2.04 s, 3 H (CH_3COO); 3.78 and 4.02 AB system, 2 H, J(AB) = 8.5 (2 × H-19); 4.11 d, 1 H, J = 4.3 (H-6α); 4.64 dd, 1 H, J = 7.3, J' = 9.2 (H-17α); 5.46 m, 1 H, W = 32 (H-3α); 7.39–7.61 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 8.03 m, 2 H (H-2, H-6 of C_6H_5COO). For

$C_{28}H_{35}BrO_5$ (531.5) calculated: 63.28% C, 6.64% H, 15.03% Br; found: 63.60% C, 6.83% H, 15.14% Br.

19-Hydroxyandrost-5-ene-3β,17β-diyl 17-Acetate 3-Benzoate (**7**)

The epoxide **6** (9.04 g, 17 mmol) was suspended in 2-methyl-2-propanol (235 ml) and water (155 ml), zinc dust (65.4 g, 1.0 mol) was added and the reaction mixture was refluxed under efficient stirring for 1 h. After cooling, the solid was removed by filtration, washed with ethanol and the filtrate was evaporated *in vacuo* to dryness. The residue was dissolved in ethyl acetate (500 ml) and the solution was washed with dilute hydrochloric acid (1 : 4), water, saturated aqueous potassium hydrogen carbonate solution and water. The solvent was distilled off *in vacuo* and the residue was crystallized from a chloroform–hexane mixture. Yield of hydroxy derivative **7** was 4.17 g (54%), m.p. 163–165 °C, $[\alpha]_D$ –22° (*c* 1.7, chloroform). IR spectrum (chloroform): 3 621, 3 573 (OH); 1 714 (C=O); 1 670 (C=C); 1 276 (C–O, benzoate); 1 260 (C–O, acetate); 1 046, 1 033 (C–O). ^{1}H NMR spectrum: 0.87 s, 3 H (3 × H-18); 2.04 s, 3 H (CH_3COO); 3.71 and 3.94 AB system, 2 H, J(AB) = 11.6 (2 × H-19); 4.61 dd, 1 H, J = 7.3, J' = 8.8 (H-17α); 4.90 m, 1 H, W = 32 (H-3α); 5.83 bd, 1 H, $J \approx 4.5$ (H-6); 7.38–7.60 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 8.03 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{28}H_{36}O_5$ (452.6) calculated: 74.31% C, 8.02% H; found: 75.54% C, 8.15% H.

19-Oxoandrost-5-ene-3β,17β-diyl 17-Acetate 3-Benzoate (**8**)

The hydroxy derivative **7** (4.53 g, 10 mmol) in acetone (70 ml) was treated with Jones reagent (3 ml) and then allowed to stand at room temperature for 4 min. Methanol (10 ml) was added and the reaction mixture was allowed to stand at room temperature for 10 min to remove the excess oxidizing agent. The product was precipitated with water (200 ml), collected by filtration with suction and dissolved in ethyl acetate (250 ml). The solution was washed with water, saturated aqueous potassium hydrogen carbonate solution and water. The solvent was distilled off *in vacuo* and the residue was crystallized from methanol. Yield of aldehyde **8** was 3.18 g (71%). This product was directly used in the next step. ^{1}H NMR spectrum: 0.76 s, 3 H (3 × H-18); 2.04 s, 3 H (CH_3COO); 4.61 dd, 1 H, J = 7.5, J' = 9 (H-17α); 4.87 m, 1 H, W = 32 (H-3α); 5.93 bd, 1 H, $J \approx 5$ (H-6); 7.38–7.58 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 8.01 m, 2 H (H-2, H-6 of C_6H_5COO); 9.72 s, 1 H (H-19).

(19*E*)-19-Oxoandrost-5-ene-3β,17β-diyl 17-Acetate 3-Benzoate 19-(*O*-Carboxymethyl)oxime Methyl Ester (**10**)

A mixture of aldehyde **8** (6.31 g, 14.0 mmol), (*O*-carboxymethyl)hydroxylamine hemihydrochloride (4.59 g, 42.0 mmol) and pyridine (75 ml) was stirred for 36 h at room temperature. Toluene (80 ml) was added and the solvents were evaporated *in vacuo*. The residue was dissolved in ether (500 ml) and 5% hydrochloric acid (250 ml), the aqueous phase was extracted with ether (250 ml) and the combined organic phases were washed with 5% hydrochloric acid and water. Evaporation of the solvent *in vacuo* afforded 5.6 g of crude acid **9**. ^{1}H NMR spectrum: 0.77 s, 3 H (3 × H-18); 2.05 s, 3 H (CH_3COO); 4.61 bt, 1 H, $J \approx 8$ (H-17α); 4.65 s, 2 H (OCH_2COO); 4.88 m, 1 H, W = 32 (H-3α); 5.68 bd, 1 H, $J \approx 4.5$ (H-6); 7.38–7.55 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 7.43 s, 1 H (H-19); 8.04 m, 2 H (H-2, H-6 of C_6H_5COO). The crude acid **9** (5.6 g) was dissolved in ether (150 ml) and methanol (50 ml) and treated with an ethereal solution of diazomethane for 5 min at 0 °C. The excess diazomethane and the solvents were evaporated *in vacuo* and the residue was chromatographed on a column of silica gel (200 g) in a benzene–ether (95 : 5) mixture. Yield of methyl ester **10** was 5.58 g (74% calculated on aldehyde **8**), m.p. 135–137 °C (ether), $[\alpha]_D$ –112° (*c* 1.6, chloroform). IR spectrum (chloroform): 1 755 (C=O, $COOCH_3$); 1 727 sh (C=O, acetate); 1 714 (C=O, benzoate);

1 275 (C–O, benzoate); 1 258 (C–O, acetate). ^{1}H NMR spectrum: 0.79 s, 3 H (3 × H-18); 2.04 s, 3 H (CH_3COO); 3.77 s, 3 H ($COOCH_3$); 4.61 dd, 1 H, J = 9, J' = 7.5 (H-17α); 4.67 s, 2 H (OCH_2COO); 4.88 m, 1 H, W = 32 (H-3α); 5.68 bd, 1 H, $J \approx 4.5$ (H-6); 7.38–7.60 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 7.44 s, 1 H (H-19); 8.02 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{31}H_{39}NO_7$ (537.6) calculated: 69.25% C, 7.31% H, 2.61% N; found: 69.07% C, 7.03% H, 2.78% N.

(19*E*)-17β-Hydroxy-19-oxoandrost-5-en-3β-yl 3-Benzoate 19-(*O*-Carboxymethyl)oxime Methyl Ester (**11**)

To the solution of diester **10** (700 mg, 1.3 mmol) in chloroform (5.5 ml) and methanol (5.5 ml) was added concentrated hydrochloric acid (540 μl). The mixture was stirred for 68 h at room temperature and then diluted with ether (350 ml). The solution was washed with water, saturated aqueous potassium hydrogen carbonate solution and water (3 times). The solvent was distilled off *in vacuo* and the residue was crystallized from dichloromethane. Yield of hydroxy derivative **11** was 560 mg (87%), m.p. 139–141 °C, $[\alpha]_D$ –93° (*c* 1.3, chloroform). IR spectrum (chloroform): 3 612, 3 522 (OH); 1 755 (C=O, $COOCH_3$); 1 710 (C=O, COOR); 1 277 (C–O, benzoate). ^{1}H NMR spectrum: 0.75 s, 3 H (3 × H-18); 3.66 t, 1 H, J = 8.4 (H-17α); 3.77 s, 3 H ($COOCH_3$); 4.67 s, 2 H (OCH_2COO); 4.89 m, 1 H, W = 32 (H-3α); 5.68 bd, 1 H, $J \approx 5$ (H-6); 7.38–7.60 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 7.45 s, 1 H (H-19); 8.02 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{29}H_{37}NO_6$ (495.6) calculated: 70.28% C, 7.52% H, 2.83% N; found: 70.01% C, 7.51% H, 2.74% N.

(19*E*)-17,19-Dioxoandrost-5-en-3β-yl 3-Benzoate 19-(*O*-Carboxymethyl)oxime Methyl Ester (**12**)

Jones reagent (0.6 ml) was added to a solution of hydroxy derivative **11** (510 mg, 1.0 mmol) in acetone (22 ml). After stirring for 5 min at room temperature, the excess reagent was decomposed by methanol (1.5 ml). The mixture was diluted with water (40 ml) and the acetone was evaporated *in vacuo*. The residue was partitioned between dichloromethane and water, the aqueous layer was extracted with dichloromethane. Combined dichloromethane extracts were washed with water, saturated aqueous potassium hydrogen carbonate solution (2 times) and water. Evaporation of the solvent *in vacuo* afforded 500 mg (98%) of ketone **12**. Analytical sample was obtained by crystallization from a light petroleum–ether mixture, m.p. 132–135 °C, $[\alpha]_D$ –58° (*c* 1.2, chloroform). IR spectrum (chloroform): 1 754 (C=O, $COOCH_3$); 1 712 (C=O, COOR); 1 277 (C–O, benzoate). ^{1}H NMR spectrum: 0.88 s, 3 H (3 × H-18); 3.76 s, 3 H ($COOCH_3$); 4.66 s, 2 H (OCH_2COO); 4.90 m, 1 H, W = 32 (H-3α); 5.71 bd, 1 H, $J \approx 5$ (H-6); 7.38-7.60 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 7.46 s, 1 H (H-19); 8.02 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{29}H_{35}NO_6$ (493.6) calculated 70.57% C, 7.15% H, 2.84% N; found 70.53% C, 7.19% H, 2.69% N.

(19*E*)-3β-Hydroxy-17-oxoandrost-5-en-19-al 19-(*O*-Carboxymethyl)oxime (**13**)

Compound **12** (420 mg, 0.85 mmol) was dissolved in tetrahydrofuran (8 ml) and methanol (8 ml). After addition of 0.4 M aqueous sodium hydroxide (6.65 ml) the mixture was stirred for 2 h at room temperature. The excess alkali was neutralized with 5% hydrochloric acid and the solvents were evaporated *in vacuo*. The residue was partitioned between ethyl acetate and water, the aqueous layer was extracted with ethyl acetate. Combined ethyl acetate extracts were washed with water (3 times). The solvent was distilled off *in vacuo* and the residue was crystallized from ethyl acetate. Yield of **13** was 150 mg (38%), m.p 171–174 °C, $[\alpha]_D$ –112° (*c* 1.2, chloroform). Literature[4] gives m.p. 166–168 °C. IR spectrum (chloroform): 3 602 (OH); 1 750, 1 734 (C=O, COOH); 1 652 (C=C). ^{1}H NMR spectrum: 0.82 s, 3 H (3 × H-18); 3.52 m, 1 H, W = 32 (H-3α); 4.58 s, 2 H (OCH_2COO); 5.60 bd,

1 H, $J \approx 5$ (H-6); 7.37 s, 1 H (H-19). For $C_{21}H_{29}NO_5$ (375.5) calculated 67.18% C, 7.79% H, 3.73% N; found: 66.97% C, 7.85% H, 3.61% N.

7-Oxoandrost-5-ene-3β,17β-diyl 17-Acetate 3-Benzoate (**14**)

To a suspension of chromium(VI) oxide (5.55 g, 55.5 mmol) in dichloromethane (30 ml) was added 3,5-dimethylpyrazole (5.50 g, 57.2 mmol) at –25 °C. The mixture was stirred at the same temperature for 15 min, then a solution of olefin **4** (1.39 g, 3.2 mmol) in dichloromethane (6 ml) was added dropwise. The reaction mixture was stirred for 3 h at –20 °C, diluted with a benzene–ethyl acetate mixture (30 ml, 7 : 3) and filtered through a short column of silica gel (25 g) layered with Celite. The column was washed with the same solvent mixture, and the solvents were evaporated *in vacuo*. The residue was chromatographed on a column of silica gel (60 g) in a benzene–ether (98 : 2) mixture. Yield of ketone **14** was 968 mg (68%), m.p. 171–173/191–192 °C (acetone–water), $[\alpha]_D$ –72° (*c* 1.5, chloroform). IR spectrum (chloroform): 1 716 (C=O); 1 669 (C=O, ketone); 1 635 (C=C); 1 274 (C–O, benzoate); 1 258 (C–O, acetate). ^{1}H NMR spectrum: 0.82 s, 3 H (3 × H-18); 1.27 s, 3 H (3 × H-19); 2.05 s, 3 H (CH_3COO); 4.64 dd, 1 H, J = 7.2, J' = 9.0 (H-17α); 4.98 m, 1 H, W = 32 (H-3α); 5.76 bd, 1 H, $J \approx 1.5$ (H-6); 7.50 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 8.05 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{28}H_{34}O_5$ (450.6) calculated: 74.64% C, 7.61% H; found: 74.75% C, 7.62% H.

7β-Hydroxyandrost-5-ene-3β,17β-diyl 17-Acetate 3-Benzoate (**15**)

To a solution of ketone **14** (2.70 g, 6.0 mmol) in tetrahydrofuran (32 ml) 0.4 M solution of cerium(III) chloride heptahydrate in methanol (15 ml) was added. To this mixture sodium borohydride (229 mg, 6.05 mmol) was added in small portions during 2 min. The reaction mixture was stirred for 5 min and then poured into 1 M HCl (100 ml). The product was extracted with dichloromethane (3 × 75 ml). The combined extracts were washed with water, saturated aqueous potassium hydrogen carbonate solution and water. The solvent was distilled off *in vacuo* and the residue was crystallized from a dichloromethane–hexane mixture. Yield of hydroxy derivative **15** was 2.25 g (83%), m.p. 218–221 °C, $[\alpha]_D$ 0° (*c* 1.9, chloroform). IR spectrum (chloroform): 3 627, 3 595 (OH); 1 720 (C=O, acetate); 1 715 (C=O, benzoate); 1 634 (C=C); 1 275 (C–O, benzoate); 1 258 (C–O, acetate). ^{1}H NMR spectrum: 0.88 s, 3 H (3 × H-18); 1.17 s, 3 H (3 × H-19); 2.10 s, 3 H (CH_3COO); 3.94 bd, 1 H, $J \approx 7$ (H-7α); 4.66 dd, 1 H, J = 7.5, J' = 9.5 (H-17α); 4.92 m, 1 H, W = 32 (H-3α); 5.76 bd, 1 H, $J \approx 1.5$ (H-6); 7.53 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 8.09 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{28}H_{36}O_5$ (452.6) calculated: 74.31% C, 8.02% H; found: 74.23% C, 7.86% H.

Androst-5-ene-3β,7β,17β-triyl 17-Acetate 3-Benzoate 7-(2-Methyl)propionate (**16**)

Isobutyryl chloride (472 μl, 4.5 mmol) was added dropwise to a solution of hydroxy derivative **15** (1.00 g, 2.2 mmol) in pyridine (10 ml), precooled to 0 °C. After stirring for 1 h at 0 °C, the mixture was poured on ice, the product was collected on filter and washed with water. The crude product was dissolved in dichloromethane (250 ml), the solution was washed with dilute hydrochloric acid (1 : 4), water, saturated aqueous potassium hydrogen carbonate solution and water. The solvent was distilled off *in vacuo* and the residue was crystallized from an acetone–water mixture. Yield of triester **16** was 1.04 g (90%), m.p. 185–188 °C (acetone–water), $[\alpha]_D$ +65° (*c* 1.3, chloroform). IR spectrum (chloroform): 1 718 (C=O); 1 274 (C–O, benzoate); 1 257 (C–O, acetate). ^{1}H NMR spectrum: 0.83 s, 3 H (3 × H-18); 1.15 s, 3 H (3 × H-19); 1.19 d, 6 H, J = 7.0 ($(C\mathbf{H}_3)_2CHCOO$); 2.05 s, 3 H (CH_3COO); 4.59 dd, 1 H, J = 8.5, J' = 7.0 (H-17α); 4.88 m, 1 H, W = 32 (H-3α); 5.10 bd, 1 H, $J \approx 8.5$ (H-7α); 5.24 bs, 1 H (H-6); 7.36–7.60 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 8.02 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{32}H_{42}O_6$ (522.7) calculated: 73.53% C, 8.10% H; found: 73.61% C, 8.27% H.

17β-Hydroxyandrost-5-ene-3β,7β-diyl 3-Benzoate 7-(2-Methyl)propionate (**17**)

To the solution of triester **16** (1.04 g, 2.0 mmol) in chloroform (8.4 ml) and methanol (8.4 ml) was added concentrated hydrochloric acid (830 μl). The mixture was stirred for 25 h at room temperature and then diluted with ether (200 ml). The solution was washed with water, saturated aqueous potassium hydrogen carbonate solution (2 times) and water. The solvent was distilled off *in vacuo* and the residue was chromatographed on a column of silica gel (80 g) in a benzene–ether (98 : 2) mixture. The crude product (540 mg) was chromatographed on seven silica gel plates in a benzene–ethyl acetate (8 : 2) mixture. Yield of hydroxy derivative **17** was 340 mg (36%), m.p. 177–179 °C (ether), $[\alpha]_D$ +75° (*c* 1.2, chloroform). IR spectrum (chloroform): 3 609 (O–H); 1 714 (C=O); 1 274 (C–O, benzoate). ^{1}H NMR spectrum: 0.97 s, 3 H (3 × H-18); 1.16 s, 3 H (3 × H-19); 1.16 d, 6 H, *J* = 7.0 ((C**H**$_3$)$_2$CHCOO); 3.64 bt, 1 H, *J* ≈ 8 (H-17α); 4.86 m, 1 H, *W* = 32 (H-3α); 5.09 bd, 1 H, *J* ≈ 9 (H-7α); 5.23 bs, 1 H (H-6); 7.39–7.58 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 8.03 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{30}H_{40}O_5$ (480.7) calculated: 74.97% C, 8.39% H; found: 75.26% C, 8.47% H.

17-Oxoandrost-5-ene-3β,7β-diyl 3-Benzoate 7-(2-Methyl)propionate (**18**)

Jones reagent (0.3 ml) was added to a solution of hydroxy derivative **17** (240 mg, 0.5 mmol) in acetone (10 ml). After stirring for 5 min at room temperature, the excess reagent was decomposed by methanol (1.1 ml). The mixture was diluted with water (10 ml) and the acetone was evaporated *in vacuo*. The residue was partitioned between ether and water, the aqueous layer was extracted with ether. Combined ethereal extracts were washed with water, saturated aqueous potassium hydrogen carbonate solution (twice) and water. Evaporation of the solvent *in vacuo* afforded 230 mg (93%) of ketone **18**. Analytical sample was obtained by crystallization from ether, m.p. 210–211.5 °C, $[\alpha]_D$ +126° (*c* 1.1, chloroform). IR spectrum (chloroform): 1 732 (C=O, ketone); 1 717 (C=O, ester); 1 274 (C–O, benzoate). ^{1}H NMR spectrum: 0.92 s, 3 H (3 × H-18); 1.17 s, 3 H (3 × H-19); 1.18 d, 6 H, *J* = 7.0 ((C**H**$_3$)$_2$CHCOO); 4.87 m, 1 H, *W* = 32 (H-3α); 5.21 bd, 1 H, *J* ≈ 9 (H-7α); 5.28 bs, 1 H (H-6); 7.39–7.58 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 8.04 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{30}H_{38}O_5$ (478.6) calculated: 75.28% C, 8.00% H; found: 75.37% C, 8.05% H.

3β,7β-Dihydroxyandrost-5-en-17-one (**19**)

Diester **18** (400 mg, 0.8 mmol) was dissolved in tetrahydrofuran (8 ml) and methanol (8 ml). After addition of 0.4 M aqueous sodium hydroxide (6.65 ml) the mixture was stirred for 29 h at 60 °C. The excess alkali was neutralized with 5% aqueous citric acid and the solvents were evaporated *in vacuo*. The product was extracted with ethyl acetate. The extract was washed with water (2 times) and the solvent was evaporated *in vacuo*. The residue was chromatographed on eight preparative silica gel plates in a benzene–acetone (7 : 3) mixture. Zones containing more polar compound were collected and the product was eluted with ethyl acetate. Evaporating of solvent and crystallization from acetone afforded 65 mg (26%) of diol **19**, m.p. 209–212 °C, $[\alpha]_D$ +63° (*c* 1.3, chloroform). Literature[8] gives 214–215 °C, $[\alpha]_D$ +71° (*c* 0.4, chloroform). IR spectrum (chloroform): 3 604, 3 444 (O–H); 1 732 (C=O). ^{1}H NMR spectrum: 0.91 s, 3 H (3 × H-18); 1.08 s, 3 H (3 × H-19); 3.57 m, 1 H, *W* = 32 (H-3α); 3.96 bd, 1 H, *J* ≈ 7.5 (H-7α); 5.32 bt, 1 H, *J* ≈ 1.7 (H-6).

(19*E*)-7,19-Dioxoandrost-5-ene-3β,17β-diyl 17-Acetate 3-Benzoate 19-(*O*-Carboxymethyl)oxime Methyl Ester (**20**)

To a suspension of chromium(VI) oxide (9.26 g, 92.6 mmol) in dichloromethane (50 ml) was added 3,5-dimethylpyrazole (9.17 g, 95.4 mmol) at –25 °C. The mixture was stirred at the same temperature for 15 min, then a solution of olefin **10** (2.85 g, 5.3 mmol) in dichloromethane (15 ml) was

added dropwise. The reaction mixture was stirred for 3 h at –20 °C, diluted with a benzene–ethyl acetate mixture (50 ml, 7 : 3) and filtered through a short column of silica gel (50 g) layered with Celite. The column was washed with the same solvent mixture, and the solvents were evaporated *in vacuo*. The residue was chromatographed on a column of silica gel (200 g) in a benzene–ether (95 : 5) mixture. Yield of ketone **20** was 1.50 g (51%), m.p. 152–153 °C (ether), $[\alpha]_D$ –131° (*c* 1.5, chloroform). IR spectrum (chloroform): 1 754 (C=O, $COOCH_3$); 1 727 (C=O, acetate); 1 718 (C=O, benzoate); 1 674 (C=O, ketone); 1 640 (C=C); 1 275 (C–O, benzoate); 1 256 (C–O, acetate). ^{1}H NMR spectrum: 0.80 s, 3 H (3 × H-18); 2.05 s, 3 H (CH_3COO); 3.76 s, 3 H ($COOCH_3$); 4.63 dd, 1 H, J = 9.2, J' = 7.3 (H-17α); 4.66 s, 2 H (OCH_2COO); 5.01 m, 1 H, W = 32 (H-3α); 5.92 d, 1 H, J = 1.6 (H-6); 7.42–7.62 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 7.59 s, 1 H (H-19); 8.03 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{31}H_{37}NO_8$ (551.6) calculated: 67.50% C, 6.76% H, 2.54% N; found: 67.71% C, 6.79% H, 2.62% N.

(19*E*)-7β-Hydroxy-19-oxoandrost-5-ene-3β,17β-diyl 17-Acetate 3-Benzoate 19-(*O*-Carboxymethyl)oxime Methyl Ester (**21**)

To the solution of ketone **20** (1 380 mg, 2.5 mmol) in tetrahydrofuran (15 ml), 0.4 M solution of cerium(III) chloride heptahydrate in methanol (6.4 ml) was added. To this mixture sodium borohydride (98 mg, 2.6 mmol) was added in small portions during 2 min. The reaction mixture was stirred for 7 min and then poured into 1 M HCl (100 ml). The product was extracted with dichloromethane (3 × 100 ml). The combined extracts were washed with water, saturated aqueous potassium hydrogen carbonate solution and water. The solvent was distilled off *in vacuo*. The residue was chromatographed on column of silica gel (70 g) in a benzene–ether (9 : 1) mixture. Yield of hydroxy derivative **21** was 1 150 mg (83%), m.p. 146–147 °C (ether), $[\alpha]_D$ –70° (*c* 1.6, chloroform). IR spectrum (chloroform): 3 615, 3 596 (OH); 1 754 (C=O, $COOCH_3$); 1 720 (C=O, acetate); 1 715 (C=O, benzoate). ^{1}H NMR spectrum: 0.81 s, 3 H (3 × H-18); 2.05 s, 3 H (CH_3COO); 3.77 s, 3 H ($COOCH_3$); 3.90 bt, 1 H, $J \approx 8$ (H-7α); 4.61 dd, 1 H, J = 9, J' = 7.5 (H-17α); 4.66 s, 2 H (OCH_2COO); 4.91 m, 1 H, W = 32 (H-3α); 5.60 bt, 1 H, J = 1.8 (H-6); 7.38–7.60 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 7.48 s, 1 H (H-19); 8.02 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{31}H_{39}NO_8$ (553.7) calculated: 67.25% C, 7.10% H, 2.53% N; found: 67.38% C, 7.07% H, 2.49% N.

(19*E*)-19-Oxoandrost-5-ene-3β,7β,17β-triyl 17-Acetate 3-Benzoate 7-(2-Methyl)propionate 19-(*O*-Carboxymethyl)oxime Methyl Ester (**22**)

Isobutyryl chloride (472 μl, 4.5 mmol) was added dropwise to a solution of hydroxy derivative **21** (830 mg, 1.5 mmol) in pyridine (10 ml), precooled to 0 °C. After stirring for 3 h at 0 °C, the mixture was poured on ice, the product was extracted with ether (2 × 100 ml), the extract was washed with dilute hydrochloric acid (1 : 4), water, saturated aqueous potassium hydrogen carbonate solution and water. The solvent was distilled off *in vacuo* and the residue was crystallized from ether. Yield of **22** was 875 mg (94%), m.p. 140–142 °C, $[\alpha]_D$ –11° (*c* 1.9, chloroform). IR spectrum (chloroform): 1 754 (C=O, $COOCH_3$); 1 722 (C=O, COOR); 1 274 (C–O, benzoate); 1 270 (C–O); 1 259 (C–O, acetate). ^{1}H NMR spectrum: 0.74 s, 3 H (3 × H-18); 1.09 d and 1.10 d, 3 H and 3 H, J = 7.0 (($CH_3)_2$CHCOO); 1.97 s, 3 H (CH_3COO); 3.71 s, 3 H ($COOCH_3$); 4.51 bt, 1 H, $J \approx 8$ (H-17α); 4.61 s, 2 H (OCH_2COO); 4.82 m, 1 H, W = 32 (H-3α); 5.05 dt, 1 H, J = 8.8, J' = 2 (H-7α); 5.39 bt, 1 H, J = 1.8 (H-6); 7.31–7.52 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 7.42 s, 1 H (H-19); 7.95 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{35}H_{45}NO_9$ (623.8) calculated: 67.40% C, 7.27% H, 2.25% N; found: 67.44% C, 7.31% H, 2.17% N.

(19*E*)-17β-Hydroxy-19-oxoandrost-5-ene-3β,7β-diyl 3-Benzoate 7-(2-Methyl)propionate 19-(*O*-Carboxymethyl)oxime Methyl Ester (**23**)

To the solution of triester **22** (873 mg, 1.4 mmol) in chloroform (8 ml) and methanol (8 ml) was added concentrated hydrochloric acid (620 μl). The mixture was stirred for 21 h at room temperature and then diluted with ether (500 ml). The solution was washed with water, saturated aqueous potassium hydrogen carbonate solution (2 times) and water. The solvent was distilled off *in vacuo* and the residue was chromatographed on a column of silica gel (60 g) in a benzene–ether (8 : 2) mixture. Yield of amorphous hydroxy derivative **23** was 632 mg (78%), $[\alpha]_D$ +1° (*c* 1.5, chloroform). IR spectrum (chloroform): 3 612, 3 532 (OH); 1 754 (C=O, $COOCH_3$); 1 716 (C=O, COOR); 1 276 (C–O, benzoate). ^{1}H NMR spectrum: 0.77 s, 3 H (3 × H-18); 1.16 d and 1.17 d, 3 H and 3 H, J = 7.0 ((CH_3)$_2$CHCOO); 3.62 bt, 1 H, $J \approx 8$ (H-17α); 3.78 s, 3 H ($COOCH_3$); 4.68 s, 2 H (OCH_2COO); 4.88 m, 1 H, W = 32 (H-3α); 5.11 dt, 1 H, J = 8.8, J' = 2 (H-7α); 5.45 bt, 1 H, J = 1.8 (H-6); 7.38–7.60 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 7.50 s, 1 H (H-19); 8.02 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{33}H_{43}NO_8$ (581.7) calculated: 68.14% C, 7.45% H, 2.41% N; found: 68.21% C, 7.45% H, 2.33% N.

(19*E*)-17,19-Dioxoandrost-5-ene-3β,7β-diyl 3-Benzoate 7-(2-Methyl)propionate 19-(*O*-Carboxymethyl)oxime Methyl Ester (**24**)

Jones reagent (1 ml) was added to a solution of hydroxy derivative **23** (465 mg, 0.8 mmol) in acetone (40 ml). After stirring for 5 min at room temperature, the excess reagent was decomposed by methanol (2.5 ml). The mixture was diluted with water (40 ml) and the acetone was evaporated *in vacuo*. The residue was partitioned between dichloromethane and water, the aqueous layer was extracted with dichloromethane. Combined dichloromethane extracts were washed with water, saturated aqueous potassium hydrogen carbonate solution (2 times) and water. The solvent was distilled off *in vacuo* and the residue was crystallized from an ether–hexane mixture. Yield of **24** was 310 mg (67%), m.p. 137–139 °C, $[\alpha]_D$ +43° (*c* 1.6, chloroform). IR spectrum (chloroform): 1 750 (C=O, $COOCH_3$); 1 734 (C=O, ketone); 1 725 (C=O, COOR); 1 271 (C–O, benzoate). ^{1}H NMR spectrum: 0.91 s, 3 H (3 × H-18); 1.19 d, 6 H, J = 7.0 ((CH_3)$_2$CHCOO); 3.77 s, 3 H ($COOCH_3$); 4.69 s, 2 H (OCH_2COO); 4.90 m, 1 H, W = 32 (H-3α); 5.23 dt, 1 H, J = 8.7, J' = 1.7 (H-7α); 5.50 bs, 1 H (H-6); 7.39–7.59 m, 3 H (H-3, H-4, H-5 of C_6H_5COO); 7.51 s, 1 H (H-19); 8.02 m, 2 H (H-2, H-6 of C_6H_5COO). For $C_{33}H_{41}NO_8$ (579.7) calculated: 68.38% C, 7.13% H, 2.42% N; found: 68.41% C, 7.10% H, 2.41% N.

(19*E*)-17,19-Dioxo-3β-hydroxyandrost-5-en-7β-yl 7-(2-Methyl)propionate 19-(*O*-Carboxymethyl)oxime (**25**) and (19*E*)-3β,7β-Dihydroxy-17-oxoandrost-5-en-19-al 19-(*O*-Carboxymethyl)oxime (**26**)

Compound **24** (290 mg, 0.5 mmol) was dissolved in tetrahydrofuran (6 ml) and methanol (1.2 ml). After addition of 0.4 M aqueous sodium hydroxide (3.37 ml) the mixture was stirred for 24 h at 60 °C. The excess alkali was neutralized with 5% hydrochloric acid and the solvents were evaporated *in vacuo*. The residue was acidified with 5% hydrochloric acid and the products were extracted with ethyl acetate. The extract was washed with water (2 times) and the solvent was evaporated *in vacuo*. The residue was chromatographed on four preparative silica gel plates in a mixture of chloroform–ether–methanol–acetic acid (60 : 40 : 8 : 2). Zones containing less polar compound were collected and the product was eluted with dichloromethane–acetone (1 : 1). Evaporating of solvents afforded 93 mg (40%) of amorphous compound **25**, $[\alpha]_D$ +15° (*c* 1.2, chloroform). ^{1}H NMR spectrum: 0.86 s, 3 H (3 × H-18); 1.19 d and 1.20 d, 3 H and 3 H, J = 7.0 ((CH_3)$_2$CHCOO); 2.55 h, 1 H, J = 7.0 ((CH_3)$_2$C**H**COO);

3.60 m, 1 H, *W* = 32 (H-3α); 4.65 s, 2 H (OCH_2COO); 5.18 bd, 1 H, *J* ≈ 9 (H-7α); 5.42 bs, 1 H (H-6); 7.34 s, 1 H (H-19). For $C_{25}H_{35}NO_7$ (461.6) calculated: 65.06% C, 7.64% H, 3.03% N; found: 65.11% C, 7.63% H, 3.01% N.

Zones containing more polar compound were collected and the product was eluted with dichloromethane–acetone (1 : 1). Evaporating of solvents afforded 67 mg (34%) of amorphous compound **26**, $[\alpha]_D$ –24° (*c* 1.1, chloroform–methanol 1 : 1). ^{1}H NMR spectrum: 0.85 s, 3 H (3 × H-18); 3.61 m, 1 H, *W* = 32 (H-3α); 3.97 bd, 1 H, *J* ≈ 8 (H-7α); 4.62 s, 2 H (OCH_2COO); 5.56 bs, 1 H (H-6); 7.46 s, 1 H (H-19). For $C_{21}H_{29}NO_6$ (391.5) calculated: 64.43% C, 7.47% H, 3.58% N; found: 64.48% C, 7.51% H, 3.49% N.

(19*E*)-17,19-Dioxo-3β-hydroxyandrost-5-en-7β-yl 7-(2-Methyl)propionate 19-(*O*-Carboxymethyl)oxime Methyl Ester (**27**)

Acid **25** (18 mg, 0.04 mmol) was dissolved in ether (1 ml) and methanol (1 ml) and treated with an ethereal solution of diazomethane for 5 min at 0 °C. The excess diazomethane and the solvents were evaporated *in vacuo* and the residue was chromatographed on a preparative silica gel plate in a benzene–acetone (70 : 30) mixture. Yield of amorphous methyl ester **27** was 17 mg (92%), $[\alpha]_D$ +32° (*c* 1.2, chloroform). IR spectrum (chloroform): 3 610, 3 530 (O–H); 1 754 (C=O, $COOCH_3$); 1 734 (C=O, ketone and COOR). ^{1}H NMR spectrum: 0.89 s, 3 H (3 × H-18); 1.19 d and 1.20 d, 3 H and 3 H, *J* = 7.0 ($(C\mathbf{H}_3)_2CHCOO$); 2.55 h, 1 H, *J* = 7.0 ($(CH_3)_2C\mathbf{H}COO$); 3.59 m, 1 H, *W* = 32 (H-3α); 3.77 s, 3 H ($COOCH_3$); 4.65 s, 2 H (OCH_2COO); 5.18 dt, 1 H, *J* = 8.8, *J′* = 1.2 (H-7α); 5.42 bt, 1 H, *J* ≈ 2 (H-6); 7.45 s, 1 H (H-19). For $C_{26}H_{37}NO_7$ (475.6) calculated: 65.66% C, 7.84% H, 2.95% N; found: 65.81% C, 7.88% H, 3.00% N.

(19*E*)-3β,7β-Dihydroxy-17-oxoandrost-5-en-19-al 19-(*O*-Carboxymethyl)oxime Methyl Ester (**28**)

Acid **26** (16 mg, 0.04 mmol) was dissolved in ether (1 ml) and methanol (1 ml) and treated with an ethereal solution of diazomethane for 5 min at 0 °C. The excess diazomethane and the solvents were evaporated *in vacuo* and the residue was chromatographed on a preparative silica gel plate in a benzene–acetone (60 : 40) mixture. Yield of amorphous methyl ester **28** was 15 mg (91%), $[\alpha]_D$ –35° (*c* 1.2, chloroform). IR spectrum (chloroform): 3 600, 3 520 (O–H); 1 754 (C=O, $COOCH_3$); 1 734 (C=O, ketone and COOR). ^{1}H NMR spectrum: 0.88 s, 3 H (3 × H-18); 3.59 m, 1 H, *W* = 32 (H-3α); 3.76 s, 3 H ($COOCH_3$); 3.95 bd, 1 H, *J* ≈ 7.5 (H-7α); 4.63 s, 2 H (OCH_2COO); 5.55 bs, 1 H (H-6); 7.44 s, 1 H (H-19). For $C_{22}H_{31}NO_6$ (405.5) calculated: 65.17% C, 7.71% H, 3.45% N; found: 65.27% C, 7.80% H, 3.44% N.

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