SYNTHESIS OF (19*E*)-17β-HYDROXY-3-OXO-5α-ANDROSTAN-19-AL 19-(O-CARBOXYMETHYL)OXIME*

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The title compound *IX* was synthesized from triol diester *I*. Catalytic hydrogenation over Adams' catalyst afforded the 5α and 5β isomers *II* and *III* which were oxidized under mild conditions to the aldehydes *IV* and *XII*. Reaction with (O-carboxymethyl)hydroxylamine hemihydrochloride followed by methylation with diazomethane gave the oximes *VIII* and *XIV*. Partial hydrolysis to the alcohols *VI* and *XIII* and Jones' oxidation yielded the 3-oxo derivatives *XI* and *XVI*. Complete hydrolysis of the diester *XI* afforded the desired hapten *IX*.

In our preceding papers we dealt with the syntheses of a new type of immunogenes carrying the O-(carboxymethyl)oxime (CMO) grouping at C(19) and described the syntheses of the C(19)-CMO derivatives of testosterone (ref.[1]) and of progesterone (ref.[2]). In this paper we present the synthesis of an analogous hapten *IX* derived from dihydrotestosterone.

The starting unsaturated diester *I* was hydrogenated over Adams' catalyst in acetic acid to yield a mixture of the at C(5) isomeric alcohols *II* and *III* in which the 5α--isomer *II* predominated. Chromatographic separation over silica gel afforded both isomers in pure state. The configuration at C(5) was assigned on the basis of the ^{1}H NMR evidence: The C(3) proton in the main product *II* appears at 4·71 ppm as a broad multiplet (W = 38 Hz) typical for axial conformation, whereas in the epimeric compound *III* this proton exhibits a narrow multiplet (W = 15 Hz) at 5·07 ppm.

Analogous reactions have been carried out in both series: Jones' oxidation at mild conditions (+5°C) yielded the aldehydes *IV* and *XII* which on reaction with (O-carboxymethyl)hydroxylamine hemihydrochloride in pyridine followed by methylation with diazomethane afforded the corresponding methylated C(19)-CMO derivatives *VIII* and *XIV*. In the 5α-series the intermediate free acid *VII* was also characterized. Structure of the esters *VIII* and *XIV* are well documented by their

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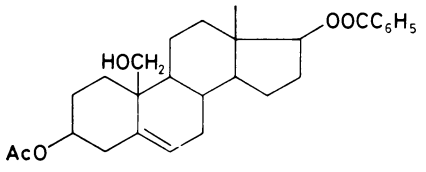
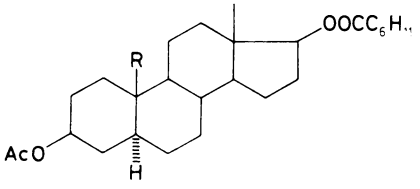
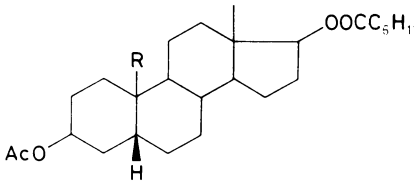
^{1}H NMR spectra (see Table I). The *E*-configuration of the oxime moiety follows from chemical shift of the H-19 proton[3]. Presence of the OCH_2COOCH_3 moiety proves the mass spectrum without any doubt (loss of *m/z* 89 fragment).



I



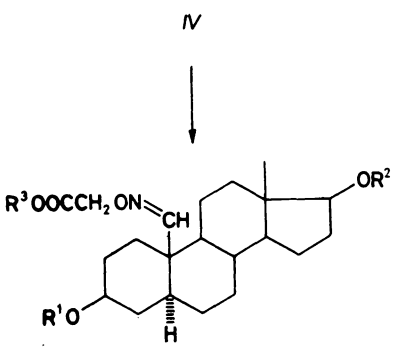
II, R = CH_2OH
IV, R = CHO



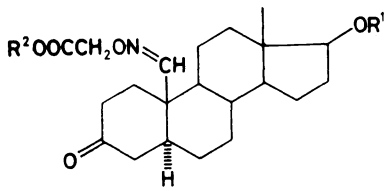
III, R = CH_2OH
XII, R = CHO

The esters *VIII* and *XIV* were submitted to partial hydrolysis with methanolic hydrochloric acid to afford the 3-hydroxy derivatives *VI* and *XIII*. In the 5α-series the diol *V* was also isolated. The alcohols *VI* and *XIII* were oxidized with Jones' reagent to yield the ketones *XI* and *XVI* which on acid hydrolysis in methanol gave the 17-hydroxy derivatives *X* and *XV*. Alkaline hydrolysis of the methyleser *X* then led to the desired C(19-)CMO derivative of dihydrotestosterone *IX*. Its structure follows from the IR spectrum showing characteristic bands of the carboxyl group, of an oxo group in a six-membered ring as well as of a hydroxyl group. In the ^{1}H NMR spectrum the characteristic singlets of the H-19 at 7·81 ppm and of the OCH_2COO grouping at 4·55 ppm are present.

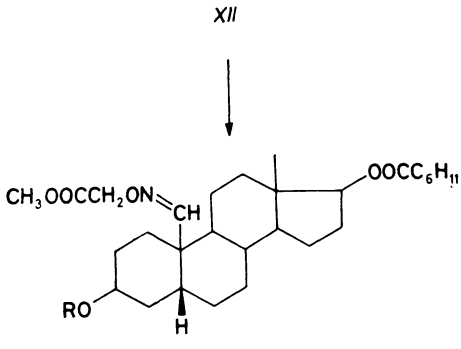
The antigenic properties of antibodies of this new hapten will be reported elsewhere.



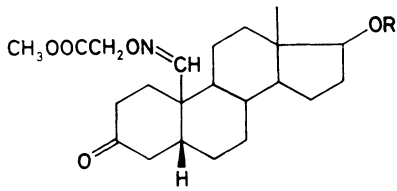
V, $R^1 = R^2 = H$; $R^3 = CH_3$
VI, $R^1 = H$; $R^2 = C_6H_{11}CO$; $R^3 = CH_3$
VII, $R^1 = Ac$; $R^2 = C_6H_{11}CO$; $R^3 = H$
VIII, $R^1 = Ac$; $R^2 = C_6H_{11}CO$; $R^3 = CH_3$



IX, $R^1 = R^2 = H$
X, $R^1 = H$; $R^2 = CH_3$
XI, $R^1 = C_6H_{11}CO$; $R^2 = CH_3$



XIII, R = H
XIV, R = Ac



XV, R = H
XVI, $R = C_6H_{11}CO$

EXPERIMENTAL

Melting points were determined on a Kofler block. Optical rotations were carried out in chloroform with an error of $\pm 2°$ at 23°C. The infrared spectra were recorded on the Zeiss UR 20 spectrometer; wavenumbers are given in cm^{-1}. ^1H NMR spectra were measured on a Tesla BS-476 instrument (100 MHz, FT mode) in deuteriochloroform with tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ-scale), coupling constants (J) and widths (W) in Hz. All data were obtained by first order analysis. Mass spectra were recorded on a VG Analytical ZAB-EQ spectrometer (energy of ionizing electrons 70 eV, ion source temperature 170—200°C). Thin-layer chromatography (TLC) was performed on silica gel G (Woelm). Prior evaporation in vacuo (about 2 kPa), solutions in organic solvents were dried over anhydrous magnesium sulfate. Analytical samples were dried over phosphorus pentoxide at 40°C/26 Pa for 12 h.

19-Hydroxy-5α-androstane-3β,17β-diyl 3-Acetate 17-Hexahydrobenzoate (*II*)

The unsaturated diester[1] *I* (10·0 g, 22·1 mmol) in glacial acetic acid (150 ml) was hydrogenated over Adams' catalyst (500 mg) until the theoretical amount of hydrogen was taken up (about 2·2 l). The catalyst was filtered off, washed with ether and the solvents were removed in vacuo. The residue was dissolved in ethyl acetate, washed with 5% sodium hydrogen carbonate solution, water and dried. The residue after evaporation of the solvent consisted of two components; the lipophilic 5α derivative *II* predominated. It was chromatographed over silica gel (300 g) in benzene–ether (19 : 1). Fractions with the lipophilic product were combined, solvents removed and the oily residue (5·1 g) was crystallized from methanol to afford 4·3 g (42%) of the saturated diester *II*, m.p. 77°C, $[\alpha]_D$ +9° (*c* 2·1). IR spectrum (chloroform): 3 631, 3 520 (OH); 1 721 (C=O); 1 250, 1 176, 1 027 (C—O). ^{1}H NMR spectrum: 4·71 m, 1 H (H-3, W = 38); 4·60 dd, 1 H (H-17, J = 7·0; J' = 8·8); 3·94 and 3·82 AB system, 2 H (2 × H-19, J(A, B) = 11·5); 2·02 s, 3 H (CH_3COO); 0·83 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 370 ($M^+ - CH_3COOH - CH_2O$), 242 ($M^+ - CH_3COOH - CH_2O - C_6H_{11}COOH$). For $C_{28}H_{44}O_5$ (460·7) calculated: 73·01% C, 9·63% H; found: 72·88% C, 9·57% H.

19-Hydroxy-5β-androstane-3β,17β-diyl 3-Acetate 17-Hexahydrobenzoate (*III*)

Fractions containing the polar component (see the preceding experiment) were worked up and the residue was crystallized from methanol to yield 3·2 g (32%) of the 5β isomer *III*, m.p. 76 to

TABLE I

^{1}H NMR spectral parameters of 19-O-carboxymethyloxime derivatives in deuteriochloroform for other conditions see Experimental

Compound	H-18 (3 H)	H-19 (1 H)	H-3α (1 H)	H-17α (1 H)	OCH_2CO (2 H)	$COOCH_3$ (3 H)	CH_3COO (3 H)
			5α-derivatives				
V	0·70 s	7·63 bs	3·63 m[a]	3·63 m[a]	4·64 s	3·76 s	—
VI	0·75 s	7·62 bs	3·64 m[b]	4·58 bt[c]	4·63 s	3·76 s	—
VII[d]	0·69 s	7·62 s	[e]	[e]	4·52 s	—	1·95 s
VIII	0·74 s	7·63 bs	[e]	[e]	4·65 s	3·78 s	2·00 s
IX[d]	0·60 s	7·81 s	—	[e]	4·55 s	—	—
X	0·74 s	7·81 bs	—	3·63 bt[c]	4·65 s	3·74 s	—
XI	0·79 s	7·80 bs	—	4·59 bt[c]	4·65 s	3·75 s	—
			5β-derivatives				
XIII	0·78 s	7·67 s	4·11 m[f]	4·59 bt[c]	4·60 s	3·76 s	—
XIV	0·78 s	7·70 s	5·04 m[f]	4·61 bt[c]	4·62 s	3·77 s	2·05 s
XV	0·77 s	7·77 s	—	3·67 bt[c]	4·61 s	3·76 s	—
XVI	0·82 s	7·75 s	—	4·61 bt[c]	4·60 s	3·76 s	—

[a] Overlapped signals; [b] $W \approx 36$; [c] $J \approx 8$; [d] measured in CD_3SOCD_3; [e] undeterminable value; [f] $W \approx 10$.

78°C, $[\alpha]_D$ +19° (*c* 2·3). IR spectrum (chloroform): 3 631, 3 516 (OH); 1 722 (C=O); 1 260, 1 176, 1 047 (C—O). ^{1}H NMR spectrum: 5·07 m, 1 H (H-3, W = 15); 4·60 dd, 1 H (H-17, J = 6·8; J' = 8·8); 3·92 and 3·56 AB system, 2 H (2 × H-19, J(A, B) = 11·5); 2·05 s, 3 H (CH_3COO); 0·78 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 369 (M^+ − 1 − CH_3COOH − CH_2O), 242 (M^+ − CH_3COOH − CH_2O − $C_6H_{11}COOH$). For $C_{28}H_{44}O_5$ (460·7) calculated: 73·01% C, 9·63% H; found: 72·83% C, 9·65% H.

19-Oxo-5α-androstane-3β,17β-diyl 3-Acetate 17-Hexahydrobenzoate (*IV*)

The alcohol *II* (4·0 g, 8·7 mmol) in acetone (100 ml) was treated at +5°C with excess Jones' reagent. After 15 min at the same temperature the excess reagent was removed with methanol, the reaction mixture was diluted with water (60 ml) and acetone was distilled off in vacuo. The crystalline product was collected by suction, dissolved in ethyl acetate. The solution was washed with 5% aqueous hydrochloric acid, water, 5% aqueous sodium hydrogen carbonate, water and dried. The residue after evaporation of the solvent was crystallized from methanol to give 3·1 g (78%) of the aldehyce *IV*, 142—144°C, $[\alpha]_D$ +13° (*c* 2·6). IR spectrum (tetrachloromethane): 1 730 (C=O); 1 245, 1 032 (C—O, acetate); 1 170 (C—O, hexahydrobenzoate). ^{1}H NMR spectrum: 10·03 s, 1 H (H-19); 4·67 m, 2 H (H-3 and H-17); 2·00 s, 3 H (CH_3COO); 0·72 s, 3 H (3 × H-18). For $C_{28}H_{42}O_5$ (458·6) calculated: 73·33% C, 9·23% H; found: 73·24% C, 9·25% H.

19-Oxo-5β-androstane-3β,17β-diyl 3-Acetate 17-Hexahydrobenzoate (*XII*)

The alcohol *III* (1·3 g, 2·8 mmol) was oxidized with Jones' reagent in acetone (40 ml) as described in the preceding experiment. Similar work-up gave an oily product which was purified by column chromatography over silica gel (60 g) in benzene–ether (98 : 2). Working up of the fractions and crystallization from hexane gave 800 mg (61%) of the aldehyde *XII*, m.p. 90—29°C, $[\alpha]_D$ −11° (*c* 2·5). IR spectrum (tetrachloromethane): 1 732 (C=O); 1 238, 1 023 (C—O, acetate); 1 172 (C—O, hexahydrobenzoate). ^{1}H NMR spectrum: 9·67 s, 1 H (H-19); 5·10 m, 1 H (H-3, $W \approx 14$); 4·61 bt, 1 H (H-17, $J \approx 8$); 2·06 s, 3 H (CH_3COO); 0·86 s, 3 H (3 × H-18). For $C_{28}H_{42}O_5$ (458·6) calculated: 73·33% C, 9·23% H; found: 73·37% C, 9·10% H.

(19*E*)-19-Oxo-5α-androstane-3β,17β-diyl 3-Acetate
17-Hexahydrobenzoate 19-(O-Carboxymethyl)oxime (*VII*)

The aldehyde *IV* (6·0 g, 13·1 mmol) in pyridine (50 ml) was treated with (O-carboxymethyl)-hydroxylamine hemihydrochloride (3·5 g, 32·0 mmol) and set aside for 20 h. The reaction mixture was poured onto ice and conc. hydrochloric acid (65 ml) and the product was taken into ethyl acetate. The solution was washed well with water, dried and solvent was distilled off under reduced pressure. Crystallization from ethyl acetate–ether afforded 6·2 g (89%) of the acid *VII*, m.p. 165—167°C, $[\alpha]_D$ +8° (*c* 2·6). IR spectrum (KBr): 3 500—2 500 (COOH); 1 765, 1 725 (C=O); 1 248, 1 095, 1 030 (C—O). For $C_{30}H_{45}NO_7$ (531·7) calculated: 67·77% C, 8·53% H, 2·63% N; found: 67·58% C, 8·29% H, 2·59% N.

(19*E*)-19-Oxo-5β-androstane-3β,17β-diyl 3-Acetate
17-Hexahydrobenzoate 19-(O-Carboxymethyl)oxime Methylester (*XIV*)

The aldehyde *XII* (2·8 g, 6·1 mmol) in pyridine (30 ml) was treated with (O-carboxymethyl)-hydroxylamine hemihydrochloride (2·0 g, 18·3 mmol) as described in the preceding experiment. Similar working up afforded the crude acid which was dissolved in methanol (10 ml) and treated

with ethereal solution of diazomethane. After 10 min at room temperature the excess diazomethane was removed with acetic acid, the reaction mixture was diluted with ethyl acetate, the solution was washed with a sodium hydrogen carbonate solution, water, dried, and the solvent was distilled off in vacuo. The residue was chromatographed on a silica gel column (50 g) in benzene–ether (19 : 1). Working up of the corresponding fractions and crystallization from methanol afforded 2·1 g (63%) of the methylester *XIV*, m.p. 87–88°C, $[\alpha]_D$ −10° (*c* 2·4). IR spectrum (tetrachloromethane): 1 765, 1 735 (C=O); 1 251, 1 237, 1 171, 1 021 (C–O). Mass spectrum, *m/z*: 545 (M^+), 485 ($M^+ - CH_3COOH$), 456 ($M^+ - OCH_2COOCH_3$), 396 ($M^+ - CH_3COOH - OCH_2COOCH_3$). For $C_{31}H_{47}NO_7$ (545·7) calculated: 68·23% C, 8·68% H, 2·57% N; found: 68·15% C, 8·59% H, 2·42% N.

(19*E*)-19-Oxo-5α-androstane-3β,17β-diyl 3-Acetate
17-Hexahydrobenzoate 19-(O-Carboxymethyl)oxime Methylester (*VIII*)

The acid *VII* (4·0 g, 7·5 mmol) in methanol (5 ml) and ether (50 ml) was treated with excess diazomethane in ether and allowed to stand at room temperature for 10 min. The excess diazomethane was destroyed with acetic acid and the reaction mixture was worked up similarly as described in the previous experiment. Evaporation of the solvents and crystallization from methanol yielded 3·2 g (78%) of the methylester *VIII*, m.p. 103–104°C, $[\alpha]_D$ −6° (*c* 1·9). IR spectrum (tetrachloromethane): 1 764, 1 732 (C=O); 1 246, 1 171, 1 030 (C–O). Mass spectrum, *m/z*: 545 (M^+), 485 ($M^+ - CH_3COOH$), 456 ($M^+ - OCH_2COOCH_3$), 396 ($M^+ - CH_3COOH - OCH_2COOCH_3$). For $C_{31}H_{47}NO_7$ (545·7) calculated: 68·23% C, 8·68% H, 2·57% N; found: 68·28% C, 8·51% H, 2·35% N.

(19*E*)-3β-Hydroxy-19-oxo-5α-androstan-17β-yl
Hexahydrobenzoate 19-(O-Carboxymethyl)oxime Methylester (*VI*)

The acetate *VIII* (3·8 g, 6·7 mmol) in chloroform (40 ml) was treated with 2% methanolic hydrochloric acid (150 ml) and allowed to stand at 30°C for 12 h. The reaction mixture was diluted with ethyl acetate, washed with a sodium hydrogen carbonate solution, water, dried, and the solvents were distiled off under reduced pressure. The residue contained according to the TLC about 20% of the diol *V*. It was chromatographed over silica gel (50 g) in benzene–ether (85 : 15). Fractions with more lipophilic component were combined and the solvents were distilled off to give 2·5 g (71%) of the alcohol *VI* which resisted all attempts at crystallization, $[\alpha]_D$ +7° (*c* 2·7). IR spectrum (chloroform): 3 604, 3 513 (OH); 1 753, 1 721 (C=O); 1 176, 1 135, 1 043 (C–O). Mass spectrum, *m/z*: 503 (M^+), 485 ($M^+ - H_2O$), 414 ($M^+ - OCH_2COOCH_3$), 396 ($M^+ - H_2O - OCH_2COOCH_3$). For $C_{29}H_{45}NO_6$ (503·7) calculated: 69·15% C, 9·01% H, 2·78% N; found: 68·92% C, 8·78% H, 2·51% N.

3β,17β-Dihydroxy-5α-androstane-19-al 19-(O-Carboxymethyl)oxime Methylester (*V*)

Fractions containing the diol *V* (see preceding experiment) were combined and the solvents removed under reduced pressure. The residue was crystallized from ethyl acetate–ether to afford 320 mg (9%) of the diol *V*, m.p. 92°C, $[\alpha]_D$ +27° (*c* 2·4). IR spectrum (KBr): 3 528, 3 490 (O–H); 1 752 (C=O); 1 232, 1 103 (C–O). Mass spectrum, *m/z*: 393 (M^+), 375 ($M^+ - H_2O$), 304 ($M^+ - OCH_2COOCH_3$), 286 ($M^+ - H_2O - OCH_2COOCH_3$). For $C_{22}H_{35}NO_5$ (393·5) calculated: 67·15% C, 8·96% H, 3·56% N; found 66·98% C, 8·85% H, 3·49% N.

(19*E*)-3β-Hydroxy-19-oxo-5β-androstan-17β-yl
Hexahydrobenzoate 19-(O-Carboxymethyl)oxime Methylester (*XIII*)

The acetate *XIV* (3·5 g, 6·4 mmol) in chloroform (40 ml) was treated with 2% methanolic hydrochloric acid (150 ml) and allowed to stand at 20°C for 16 h. The reaction mixture was diluted with ethyl acetate, washed with a sodium hydrogen carbonate solution, water, dried, and solvents were removed in vacuo. The oily residue contained only traces of the corresponding diol according to the TLC. It was chromatographed over silica gel (100 g) in benzene–ether (85 : 15) to afford after workig up of the corresponding fractions 2·8 g (86%) of the alcohol *XIII*, resisting all attempts at crystallization, $[\alpha]_D$ −12° (*c* 2·8). IR spectrum (chloroform): 3 613 (O—H); 1 754, 1 721 (C=O); 1 176, 1 135, 1 098, 1 022 (C—O). Mass spectrum, *m/z*: 503 (M^+), 485 ($M^+ - H_2O$), 414 ($M^+ - OCH_2COOCH_3$). For $C_{29}H_{45}NO_6$ (503·7) calculated: 69·15% C, 9·01% H, 2·78% N; found: 68·85% C, 8·92% H, 2·63% N.

(19*E*)-3,19-Dioxo-5α-androstan-17β-yl Hexahydrobenzoate
19-(O-Carboxymethyl)oxime Methylester (*XI*)

The alcohol *VI* (3·0 g, 6·0 mmol) in acetone (50 ml) was treated with excess Jones' reagent and allowed to stand at room temperature for 15 min. The excess reagent was removed with methanol the reaction mixture was diluted with water and acetone was distilled of in vacuo. The product was extracted with ethyl acetate. The extract was washed with sodium hydrogen carbonate solution, water, dried and solvent was removed in vacuo. The residue was chromatographed on a silica gel column (80 g) in benzene–ether (9 : 1) to yield 2·2 g (73%) of the ketone *XI* which resisted all attempts at crystallization, $[\alpha]_D$ +29° (*c* 2·8). IR spectrum (tetrachloromethane): 1 763, 1 728, 1 720 (C=O); 1 247, 1 207, 1 171, 1 024 (C—O). Mass spectrum, *m/z*: 501 (M^+), 473, 412 ($M^+ - OCH_2COOCH_3$). For $C_{29}H_{43}NO$ (501·7) calculated: 69·43% C, 8·64% H, 2·79% N; found: 69·22% C, 8·51% H, 2·67% N.

(19*E*)-3,19-Dioxo-5β-androstan-17β-yl Hexahydrobenzoate
19-(O-Carboxymethyl)oxime Methylester (*XVI*)

The alcohol *XIII* (800 mg, 1·6 mmol) was dissolved in acetone (12 ml) and oxidized with Jones' reagent as described in the preceding experiment. Similar working up and chromatography over silica gel (25 g) yielded 640 mg (80%) of the oily ketone *XVI*, $[\alpha]_D$ −6° (*c* 2·8). IR spectrum (tetrachloromethane): 1 755, 1 716 (C=O); 1 176, 1 135, 1 102, 1 024 (C—O). Mass spectrum, *m/z*: 501 (M^+), 470, 412 ($M^+ - OCH_2COOCH_3$). For $C_{29}H_{43}NO_6$ (501·7) calculated 69·43% C, 8·64% H, 2·79% N; found: 69·42% C, 8·58% H, 2·56% N.

(19*E*)-17β-Hydroxy-3-oxo-5α-androstan-19-al 19-(O-Carboxymethyl)oxime Methylester (*X*)

The hexahydrobenzoate *XI* (1·2 g, 2·4 mmol) in chloroform (10 ml) was treated with 6% methanolic hydrochloric acid (50 ml) and allowed to stand at 40°C for 72 h. The reaction mixture was diluted with ethyl acetate, washed with a sodium hydrogen carbonate solution, water, dried, and the solvents evaporated. The residue was chromatographed on a silica gel column (50 g) in benzene–ether (9 : 1) to afford 710 mg (76%) of the alcohol *X*, resisting all attempts at crystallization, $[\alpha]_D$ +56° (*c* 2·4). IR spectrum (chloroform): 3 614, 3 475 (OH); 1 754 (C=O, ester); 1 711 (C=O, ketone); 1 100 (C—O). Mass spectrum, *m/z*: 391 (M^+), 363, 302 ($M^+ - OCH_2.COOCH_3$). For $C_{22}H_{33}NO_5$ (391·5) calculated: 67·49% C, 8·50% H, 3·58% N; found: 67·34% C, 8·33% H, 3·47% N.

19-(O-Carboxymethyl)oxime Methylester (*XV*)

The hexahydrobenzoate *XVI* (450 mg, 0·9 mmol) was hydrolyzed with 6% methanolic hydrochloric acid as described in the preceding experiment for the 5α-epimer. Similar working up afforded 310 mg of a crude product which after chromatographic purification on a silica gel column (25 g) in benzene–esther (9 : 1) gave 245 mg (70%) of oily the alcohol *XV*, $[\alpha]_D$ +6° (*c* 2·5). IR spectrum (chloroform): 3 611, 3 497 (OH); 1 755 (C=O, ester); 1 712 (C=O, ketone); 1 099, 1 052, 1 023 (C—O). Mass spectrum, *m/z*: 391 (M^+), 360, 302 ($M^+ - OCH_2COOCH_3$). For $C_{22}H_{33}NO_5$ (391·5) calculated: 67·49% C, 8·50% H, 3·58% N; found: 67·28% C, 8·41% H, 3·33% N.

(19*E*)-17β-Hydroxy-3-oxo-5α-androstan-19-al 19-(O-Carboxymethyl)oxime (*IX*)

A solution of the methylester *X* (1·5 g, 3·8 mmol) in methanol (80 ml) was treated at 15°C with a solution of potassium hydroxide (250 mg) in water (10 ml). After 5 h at room temperature the excess alkali was neutralized with hydrochloric acid, methanol was distilled off in vacuo and the residue was acidified with hydrochloric acid. The product was extracted with ethyl acetate, the acid was taken into 7% sodium hydrogen carbonate solution and the solution of the sodium salt was washed thoroughly with ethyl acetate. The acid was then liberated with hydrochloric acid and extracted into ethyl acetate. The extract was washed with water to neutrality, dried. Evaporation of the solvent left 980 mg (67%) of the oily oxime *IX*, $[\alpha]_D$ +41° (*c* 2·3). IR spectrum (KBr): 3 500–2 500 (COOH); 3 434 (O—H); 1 739, 1 713 (C=O); 1 096 (C—O). For $C_{21}H_{31}NO_5$ (377·5) calculated: 66·82% C, 8·28% H, 3·71% N; found: 66·71% C, 8·15% H, 3·68% N.

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