SYNTHESIS OF STEROID *O*-(ω-HYDROXYALKYL)OXIMES BY REDUCTION OF CORRESPONDING *O*-(ω-CARBOXYALKYL)OXIME DERIVATIVES*

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Received January 28, 1998
Accepted March 8, 1998

Steroid *O*-(ω-hydroxyalkyl)oximes with varying alkyl chain length were prepared from the corresponding carboxylic acids using the reduction of mixed anhydrides with sodium borohydride. An unexpected reaction course was observed with *O*-(2-carboxyethyl)oximes of 3-oxo-4-ene steroids, where a 4,5-dihydroisoxazol-3(2*H*)-one derivative was formed as a side product.
Key words: Steroids; *O*-Alkyl oximes; *E/Z* Isomers; 4,5-Dihydroisoxazol-3(2*H*)-ones.

Continuing our studies on steroid haptens of *O*-alkyloxime type, we have prepared compounds substituted in various positions of the steroid skeleton[2–6] and also of varying length of the alkyl chain and with various terminal substituents[7–11]. In the present study we are dealing with compounds bearing a hydroxy group at the end of an alkyl chain. These derivatives were prepared[10] by the reaction of steroid *O*-(carboxymethyl)oximes with amino alcohols. During the reaction, the alkyl chain was lengthened by one nitrogen and 2-4 carbon atoms and its flexibility was diminished by the newly created amide group. Mikola *et al.*[12] studied a reaction of steroid ketones with *O*-(ω-hydroxyalkyl)hydroxylamines, which could be transformed into corresponding substituted oximes with the terminal hydroxy group. Since preparation of starting hydroxylamines was difficult, we decided to evaluate the possibility of the synthesis of similar *O*-(ω-hydroxyalkyl)oxime derivatives from the easily available steroid *O*-(ω-carboxyalkyl)oximes (Scheme 1).

Such a transformation was described in the literature[13] only for a non-steroidal *O*-[(ethoxycarbonyl)methyl]oxime, which was reduced with sodium borohydride to give the corresponding *O*-(2-hydroxyethyl)oxime. The reduction of the ester group was

* Part CCCXCIV in the series On Steroids; Part CCCXCIII see ref.[1].

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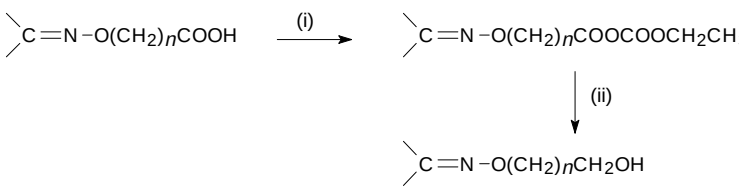
facilitated in this case by the presence of an electron-withdrawing substituent in the α-position to the carbonyl group[14]. The necessity for the presence of an activating group can be avoided by transformation of the carboxyl group to a suitable derivative, which is able to react under mild conditions. We chose a method based on the borohydride reduction of a mixed anhydride with carbonic acid[15], which we had previously used for the reduction of carboxyl group in amino acids conjugated with *O*-(carboxymethyl)oximes[10].

For the initial experiments we used *O*-(carboxymethyl)oxime (CMO), *O*-(2-carboxyethyl)oxime (CEO), and *O*-(3-carboxypropyl)oxime (CPO) derivatives of 17-oxoandrost-5-en-3β-yl acetate (**1**, **3**, and **5**, respectively). The transformation into mixed anhydrides was accomplished by reaction with ethyl chloroformate in the presence of *N*,*N*-diisopropylethylamine[7] and without isolation the resulting anhydride was reduced with sodium borohydride. The chromatographic separation after the reaction was made easier by prior methylation of the crude reaction product with diazomethane. This way the acid, formed as a by-product during the reduction, was transformed into a methyl ester. In all reductions, described below, each corresponding methyl ester was isolated and identified by comparison with the authentic methyl ester of the starting acid (see Experimental).

The hydroxy derivatives **7**, **9**, and **11** were isolated in the yield of 67, 67, and 59%, respectively. The structure of the prepared compounds were confirmed by IR spectra, in which characteristic bands of hydroxy group at *ca* 3 610 and 3 450 cm^{-1} were present. The ^1H NMR spectra contained extra multiplets arising from CH_2OH groups, when compared with the spectra of the corresponding starting acid. The (17*E*)-configuration of the C=N double bond was conserved in all resulting derivatives, as followed from the chemical shift of H-18 (δ 0.92 ppm, *cf.* refs[7,16]).

The starting acid **17** was to be prepared for a synthesis of *O*-(6-hydroxyhexyl)oxime derivative **13**. The oxime **15** was transformed into sodium salt[11], alkylated by ethyl 6-bromohexanoate, and the resulting ethyl ester **16** was hydrolyzed to acid **17**. Reduction of its mixed anhydride as above gave hydroxy derivative **13** in 64% yield.

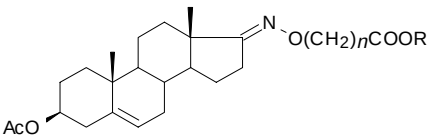
Additionally, the method was applied on the derivatives of testosterone (17β-hydroxyandrost-4-en-3-one). In this case during the oximation both possible isomers were



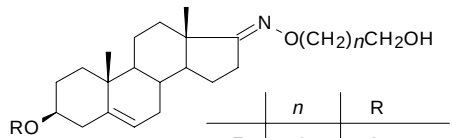
(i) $ClCOOCH_2CH_3$, *N*,*N*-diisopropylethylamine/THF; (ii) $NaBH_4/H_2O$

SCHEME 1

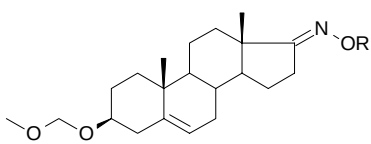
formed (3*E* and 3*Z*, *cf.* ref.[17]). In general, for 3-CMO derivatives the mutual isomerization took place[18] but 3-CEO and 3-CPO were more stable (*cf.* refs[9,11]). These derivatives were prepared by reaction of testosterone acetate (3-oxoandrost-4-en-17β-yl acetate) with appropriately substituted hydroxylamines in pyridine. CMO derivative **18** was prepared as a mixture of (3*E*)- and (3*Z*)-isomers in the ratio of 3 : 2. In the case of CEO and CPO derivatives both isomers were isolated by column chromatography on silica gel. The configuration at the C=N bond in the isomers was assigned using the ^{1}H NMR spectra, where the chemical shift of H-4 was influenced by the orientation of oxygen atom of the oxime group[19].



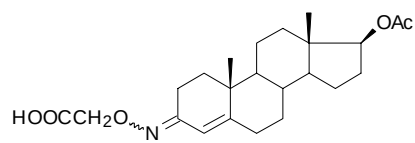
	n	R
1	1	H
2	1	CH_3
3	2	H
4	2	CH_3
5	3	H
6	3	CH_3



	n	R
7	1	Ac
8	1	H
9	2	Ac
10	2	H
11	3	Ac
12	3	H
13	5	CH_2OCH_3
14	5	H



15, R = H
16, R = $(CH_2)_5COOCH_2CH_3$
17, R = $(CH_2)_5COOH$



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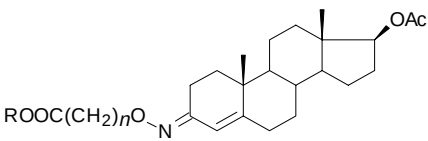
The reduction of testosterone CMO, CEO, and CPO derivatives was performed as above. From the mixture of (3*E*)-CMO and (3*Z*)-CMO derivatives **18**, hydroxy derivatives **29** (35%) and **35** (32%) were separated. The (3*E*)-CEO derivative **20** afforded the expected hydroxy derivative **31** in 75% yield. However, the reduction of the isomeric (3*Z*)-CEO derivative **25** gave, in addition to the hydroxy derivative **38** (43%), another product, **37**, in 15% yield.

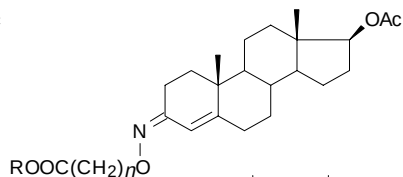
Its structure was elucidated using the spectral data. Its IR spectrum contained besides the bands of acetyl group, whilst another carbonyl band at 1 679 cm^{-1} and the absorption of an hydroxy group was missing. The ^{13}C NMR spectrum contained signals of 24 carbon atoms. After assigning the carbons of steroid skeleton and acetyl group, three

unidentified signals remained. Two of them were in the region characteristic of methylene carbons (δ 22.2 and 66.5 ppm) and the last corresponded to a carbon with sp^2 hybridization (δ 168.6 ppm). In the ^{1}H NMR spectrum, two methylene groups gave two triplets (δ 2.78 and 4.26 ppm) with coupling constants J = 8.2 Hz, corresponding to an isolated grouping CH_2–CH_2. With the data from mass spectrometry (molecular ion with *m/z* 401), the structure of 4,5-dihydroisoxazol-3(2*H*)-one **37** appeared probable. The literature has mentioned *N*-substituted isoxazolidin-3-one derivatives only rarely. French authors[20] published ^{1}H NMR data for *N*-methyl derivative, which were in accord with the data found for our compound and supported the structure **37** (triplets at δ 2.71 and 4.30 ppm, J = 8 Hz).

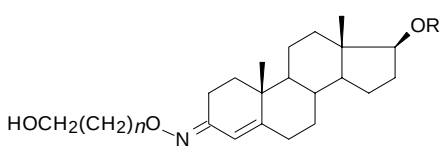
The reduction of isomeric CPO derivatives **22** and **27** proceeded in the expected manner to give the hydroxy derivatives **33** (55%) and **40** (65%).



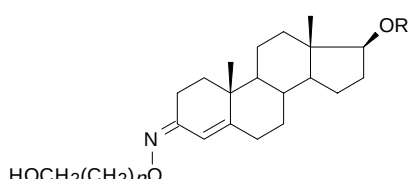
	n	R
19	1	CH_3
20	2	H
21	2	CH_3
22	3	H
23	3	CH_3



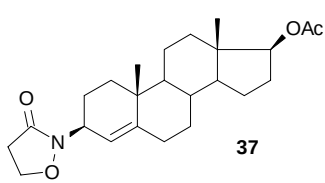
	n	R
24	1	CH_3
25	2	H
26	2	CH_3
27	3	H
28	3	CH_3



	n	R
29	1	Ac
30	1	H
31	2	Ac
32	2	H
33	3	Ac
34	3	H



	n	R
35	1	Ac
36	1	H
38	2	Ac
39	2	H
40	3	Ac
41	3	H



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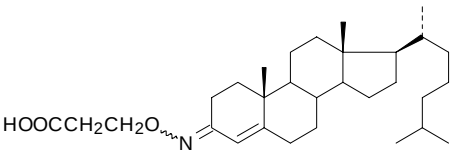
The acetyl protecting group in position 3β in compounds **7**, **9**, and **11** and in position 17β in compounds **29**, **31**, **33**, **35**, **38**, and **40** was removed by alkaline hydrolysis and the hydroxy derivatives **8**, **10**, **12**, **30**, **32**, **34**, **36**, **39**, and **41** were prepared. The methoxymethyl protecting group in position 3β in derivative **13** was split off under acidic conditions leaving hydroxy derivative **14**.

The isomeric *O*-(4-hydroxybutyl)oxime derivatives of testosterone, **34** and **41**, have been previously prepared by Mikola *et al.*[12], but only as an inseparable mixture after the reaction of testosterone with *O*-(4-hydroxybutyl)hydroxylamine. The published ^{1}H NMR data correspond to the data of pure isomers, prepared by us.

The unexpected formation of isoxazolidin-3-one derivative **37** led us to a more detailed study. All the fractions from the purification of products of the reduction of (3*E*)-CEO derivative **20** were analyzed for the presence of isoxazolidin-3-one derivative, but no detectable amounts was found.

In the next step, the reaction was performed on the cholestane skeleton. From cholest-4-en-3-one, a mixture of (3*E*)- and (3*Z*)-CEO derivatives **42** was prepared (ratio 3 : 2). Its reduction under standard conditions gave, besides the expected hydroxy derivatives **45** (35%) and **47** (22%), the isoxazolidin-3-one derivative **43** in 8% yield. Its IR spectrum contained an absorption band for a carbonyl group at 1 677 cm^{-1} and its ^{1}H NMR spectrum triplets at δ 4.29 and 2.78 ppm with J = 8 Hz.



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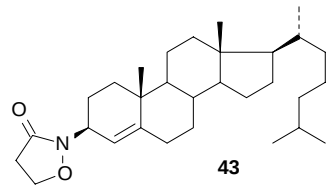

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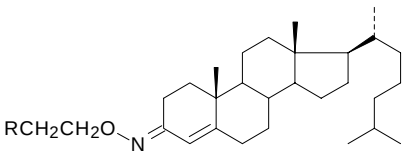
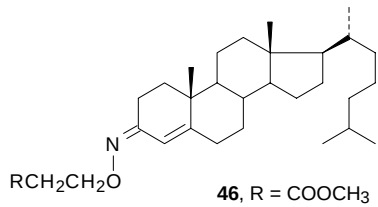


44, R = $COOCH_3$
45, R = CH_2OH



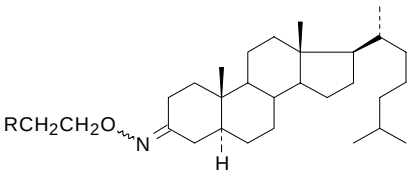
46, R = $COOCH_3$
47, R = CH_2OH

In another experiment, the 5α-cholestane derivative **48** was reduced. This derivative does not contain double bond and consists of a mixture of (3*E*)- and (3*Z*)-isomers in the ratio of 2 : 3. Only the hydroxy derivative **50** could be isolated after reduction, formed by a mixture of (3*E*)- and (3*Z*)-isomers in the same ratio (2 : 3). No isoxazolidin-3-one derivative was found.

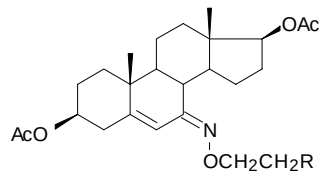
From the above observations it follows, that the occurrence of isoxazolidin-3-one derivatives during the reduction of steroid 3-CEO derivatives is limited to the conju-

gated unsaturated derivatives (with double bond in position 4) and with (3*Z*)-configuration, where the oxygen atom is oriented to the proximity of olefinic hydrogen (H-4).

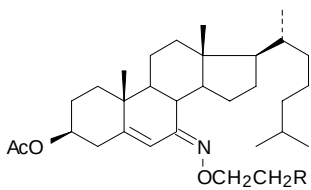
Other steroid derivatives, with a similar arrangement of the critical atoms, were represented by (7*Z*)-CEO derivatives **51** and **54**. However, their reduction under the same conditions gave only hydroxy derivatives **53** and **56**. The different course of the reaction was caused probably by the sterical shielding of the C=N double bond due to the proximity of carbon C-15 of steroid skeleton.



48, R = COOH
49, R = $COOCH_3$
50, R = CH_2OH



51, R = COOH
52, R = $COOCH_3$
53, R = CH_2OH



54, R = COOH
55, R = $COOCH_3$
56, R = CH_2OH

In conclusion, the presented method for preparation of steroid *O*-(ω-hydroxyalkyl)oximes gives good yields of pure geometrical isomers, the only limitation covers (3*Z*)-CEO derivatives of 3-oxo-4-ene steroids, where the concurrent formation of isoxazolidin-3-one occurs.

EXPERIMENTAL

Melting points were determined on a Boetius micro melting point apparatus (Germany). Optical rotations were measured 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 in chloroform unless stated otherwise. ^1H NMR spectra were taken on a Varian UNITY-200 (200 MHz, FT mode) 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. Thin-layer chromatography (TLC) was performed on silica gel G (ICN Biochemicals), with detection by spraying with concentrated sulfuric acid followed by heating. Preparative TLC (PLC) 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 Na_2SO_4.

(17*E*)-3β-(Methoxymethoxy)androst-5-en-17-one *O*-(6-Hydroxyhexyl)oxime (**13**)

A solution of ethyl chloroformate in THF (1 mol l^{-1}, 1.2 ml) was added dropwise at –5 °C to a solution of acid **17** (462 mg, 1.0 mmol) and *N*,*N*-diisopropylethylamine (210 μl, 1.2 mmol) in THF (7 ml). The reaction mixture was stirred at –5 °C for 30 min, then warmed to 0 °C and a solution of sodium borohydride (95 mg, 2.5 mmol) in water (2 ml) was added. After stirring at room temperature for 3 h, acetic acid (2 ml) was added and the products were extracted with ethyl acetate (2 × 150 ml). The combined extract was washed with water (3 ×), dried with anhydrous Na_2SO_4 and the solvent was evaporated. The residue was chromatographed on six PLC plates in benzene–ethyl acetate (60 : 40). Zones containing the product were collected and eluted with ethyl acetate. Evaporation of the solvent afforded 289 mg (64%) of hydroxy derivative **13**, m.p. 40–42 °C (ether), $[\alpha]_D^{23}$ –32° (*c* 1.3, chloroform). IR spectrum: 3 624, 3 476 (O–H); 1 655 (C=N); 1 148, 1 102, 1 037, 910 (O–CH_2–O–CH_3); 1 045 (C–O). ^{1}H NMR spectrum: 5.36 bd, 1 H, $J \approx 5$ (H-6); 4.69 s, 2 H (OCH_2O); 4.00 t, 2 H, J = 6.6 (=N–O–CH_2); 3.64 t, 2 H, J = 6.4 (C**H**$_2$OH); 3.43 m, 1 H, W = 32 (H-3α); 3.37 s, 3 H (OCH_3); 1.03 s, 3 H (3 × H-19); 0.91 s, 3 H (3 × H-18). For $C_{27}H_{45}NO_4$ (447.7) calculated: 72.44% C, 10.13% H, 3.13% N; found: 72.56% C, 9.98% H, 2.95% N.

(17*E*)-3β-Hydroxyandrost-5-en-17-one *O*-(6-Hydroxyhexyl)oxime (**14**)

Concentrated hydrochloric acid (40 μl) was added to a solution of methoxymethoxy derivative **13** (90 mg, 0.20 mmol) in benzene (3 ml) and methanol (3 ml), and the mixture was stirred at 40 °C for 9 h. The solvents were evaporated, the residue was dissolved in ethyl acetate (100 ml), and the solution was washed with saturated aqueous $KHCO_3$ and water. After drying, the solvent was evaporated and the residue was chromatographed on two PLC plates in a mixture of benzene–ethyl acetate (1 : 1). Crystallization from ether afforded 25 mg (31%) of hydroxy derivative **14**, m.p. 105–107 °C, $[\alpha]_D^{23}$ –40° (*c* 1.3, chloroform). IR spectrum: 3 615, 3 453 (O–H); 1 653 (C=N); 1 043 (C–O). ^{1}H NMR spectrum: 5.36 bd, 1 H, $J \approx 5$ (H-6); 4.01 t, 2 H, J = 6.4 (=N–O–CH_2); 3.65 t, 2 H, J = 6.4 (C**H**$_2$OH); 3.53 m, 1 H, W = 32 (H-3α); 1.03 s, 3 H (3 × H-19); 0.92 s, 3 H (3 × H-18). For $C_{25}H_{41}NO_3$ (403.6) calculated: 74.40% C, 10.24% H, 3.47% N; found: 74.67% C, 10.32% H, 3.58% N.

(17*E*)-3β-(Methoxymethoxy)androst-5-en-17-one *O*-(5-Carboxypentyl)oxime (**17**)

A solution of oxime[8] **15** (1.04 g, 3.0 mmol) in dioxane (20 ml) was added to sodium hydride (160 mg, 6.7 mmol) under argon and the reaction mixture was stirred at 70 °C for 2 h. Ethyl 6-bromohexanoate (1.10 ml, 6.2 mmol) was then added and the stirring continued at 90 °C for 20 h. The mixture was acidified with dilute hydrochloric acid (1 : 4) and the product was extracted with ether (2 × 200 ml). The combined organic phase was washed successively with dilute hydrochloric acid (1 : 4), water, saturated aqueous $KHCO_3$ solution and water. After drying, the solvent was evaporated and the residue was coevaporated with toluene (twice). Chromatography on a column of silica gel (50 g) in a mixture of petroleum ether–benzene–ether (45 : 45 : 10) afforded 510 mg (35%) of an oily ester **16** besides 320 mg (31%) of the starting oxime. ^{1}H NMR spectrum: 5.36 d, 1 H, $J \approx 5$ (H-6); 4.69 s, 2 H (OCH_2O); 4.12 q, 2 H, J = 7.2 (COOC**H**$_2$CH$_3$); 4.00 t, 2 H, J = 6.4 (=N–O–CH_2); 3.42 m, 1 H, W = 32 (H-3α); 3.37 s, 3 H (OCH_3); 2.30 t, 2 H, J = 7.3 (CH_2COO); 1.25 t, 3 H, J = 7.2 (COOCH$_2$C**H**$_3$); 1.03 s, 3 H (3 × H-19); 0.91 s, 3 H (3 × H-18).

Ester **16** (510 mg, 1.04 mmol) was dissolved in a mixture of tetrahydrofuran (10 ml) and methanol (20 ml), 2 M aqueous KOH (9 ml) was added, and the reaction mixture was stirred at room temperature for 10 h. The excess alkali was neutralized with dilute hydrochloric acid (1 : 4) and the solvents were evaporated. The residue was acidified with dilute hydrochloric acid (1 : 4) and the product was extracted with ethyl acetate (2 × 200 ml). The extract was washed with water (3 ×) and the solvent

was evaporated. Crystallization of the residue from a mixture of ether–hexane afforded 408 mg (85%) of acid **17** m.p. 99–102 °C, $[\alpha]_D^{23}$ –33° (*c* 1.3, chloroform). IR spectrum: 3 515, 3 092, 2 677 (O–H, COOH); 1 742 shoulder, 1 709 (C=O); 1 657 (C=N); 1 148, 1 102, 1 037 (O–CH_2–O–CH_3). ^{1}H NMR spectrum: 5.36 d, 1 H, $J \approx 5$ (H-6); 4.69 s, 2 H (OCH_2O); 4.00 t, 2 H, J = 6.4 (=N–O–CH_2); 3.42 m, 1 H, W = 32 (H-3α); 3.37 s, 3 H (OCH_3); 2.36 t, 2 H, J = 7.3 (CH_2COO); 1.03 s, 3 H (3 × H-19); 0.91 s, 3 H (3 × H-18). For $C_{27}H_{43}NO_5$ (461.6) calculated: 70.25% C, 9.39% H, 3.03% N; found: 70.11% C, 9.57% H, 2.97% N.

(3*E*+3*Z*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-(Carboxymethyl)oxime (**18**)

O-(Carboxymethyl)hydroxylamine hemihydrochloride (3.28 g, 30.0 mmol) was added to a solution of testosterone acetate (4.95 g, 15.0 mmol) in pyridine (45 ml). After stirring at 60 °C for 4 h, the solvent was evaporated, the residue was coevaporated with toluene (75 ml) and partitioned between ether and water. The aqueous phase was extracted with ether and the combined organic phase was washed successively with dilute hydrochloric acid (1 : 4) and water (3 ×). The solvent was evaporated and the crude product (5.84 g, 97%) was used further without purification. ^{1}H NMR spectrum: 6.43 d, 0.4 H, J = 1.2 (H-4, *Z*-isomer); 5.76 bs, 0.6 H (H-4, *E*-isomer); 4.61 s, 1.2 H (=N–O–CH_2, *E*-isomer); 4.60 s, 0.8 H (=N–O–CH_2, *Z*-isomer); 4.59 t, 1 H, J = 8.2 (H-17α); 3.04 ddd, 0.6 H, J(1β,2α) = 2.8, J(1α,2α) = 4.6, J(2α,2β) = 17.5 (H-2α, *E*-isomer); 2.05 s, 3 H (CH_3COO); 1.11 s, 1.2 H (3 × H-19, *Z*-isomer); 1.07 s, 1.8 H (3 × H-19, *E*-isomer); 0.82 s, 3 H (3 × H-18). For $C_{23}H_{33}NO_5$ (403.5) calculated: 68.46% C, 8.24% H, 3.47% N; found: 68.12% C, 8.56% H, 3.12% N.

(3*E*)-3-Oxoandrost-5-en-17β-yl Acetate *O*-(2-Carboxyethyl)oxime (**20**) and (3*Z*)-3-Oxoandrost-5-en-17β-yl Acetate *O*-(2-Carboxyethyl)oxime (**25**)

O-(2-Carboxyethyl)hydroxylamine hydrochloride[21] (2.82 g, 20.0 mmol) was added to a solution of testosterone acetate (3.30 g, 10.0 mmol) in pyridine (35 ml). After stirring at 60 °C for 4 h, the solvent was evaporated, and the residue was coevaporated with toluene (75 ml) and partitioned between ether and water. The aqueous phase was extracted with ether, the combined organic phase was washed successively with dilute hydrochloric acid (1 : 4) and water (3 ×), and the solvent was evaporated. Chromatography of the residue on a column of silica gel (125 g) in a mixture of petroleum ether–benzene–ether–acetic acid (50 : 44 : 5 : 1) afforded the following compounds.

Acid **20**, yield 1.65 g (40%), m.p. 138–141 °C (petroleum ether–ether), $[\alpha]_D^{23}$ +114° (*c* 1.2, chloroform). IR spectrum: 3 513 (O–H, COOH monomer); 2 669 broad (O–H, COOH dimer); 1 717 (C=O); 1 632 (C=N); 1 596 (C=C); 1 257, 1 042 (C–O, acetate). ^{1}H NMR spectrum: 5.75 bs, 1 H (H-4); 4.58 dd, 1 H, J = 9.0, J' = 7.5 (H-17α); 4.31 t, 2 H, J = 6.0 (=N–O–CH_2); 2.93 ddd, 1 H, J(1β,2α) = 2.9, J(1α,2α) = 4.7, J(2α,2β) = 17.4 (H-2α); 2.76 t, 2 H, J = 6.0 (CH_2COO); 2.04 s, 3 H (CH_3COO); 1.05 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{24}H_{35}NO_5$ (417.6) calculated: 69.04% C, 8.45% H, 3.35% N; found: 68.86% C, 8.26% H, 3.11% N.

Acid **25**, yield 1.32 g (32%), m.p. 158–161 °C (ether), $[\alpha]_D^{23}$ +178° (*c* 1.2, chloroform). IR spectrum: 3 518 (O–H, COOH monomer); 2 653 broad (O–H, COOH dimer); 1 717 (C=O); 1 626 (C=N); 1 257, 1 041 (C–O, acetate). ^{1}H NMR spectrum: 6.34 d, 1 H, J = 1.2 (H-4); 4.58 dd, 1 H, J = 9.0, J' = 7.5 (H-17α); 4.30 t, 2 H, J = 6.0 (=N–O–CH_2); 2.78 t, 2 H, J = 6.0 (CH_2COO); 2.04 s, 3 H (CH_3COO); 1.10 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{24}H_{35}NO_5$ (417.6) calculated: 69.04% C, 8.45% H, 3.35% N; found: 69.34% C, 8.49% H, 3.18% N.

(3*E*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-(3-Carboxypropyl)oxime (**22**) and (3*Z*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-(3-Carboxypropyl)oxime (**27**)

O-(3-Carboxypropyl)hydroxylamine hydrochloride[22] (3.11 g, 20.0 mmol) was added to a solution of testosterone acetate (3.30 g, 10.0 mmol) in pyridine (35 ml), and the mixture was stirred at 60 °C for 6 h. The solvent was evaporated, the residue was coevaporated with toluene (75 ml) and partitioned between ether and water. The aqueous phase was extracted with ether, the combined organic phase was washed successively with dilute hydrochloric acid (1 : 4) and water (3 ×), and the solvent was evaporated. Chromatography of the residue on a column of silica gel (100 g) in a mixture of petroleum ether–benzene–ether–acetic acid (50 : 44 : 5 : 1) afforded the following compounds.

Acid **22**, yield 1.78 g (41%), m.p. 92–95 °C (petroleum ether–ether), $[\alpha]_D^{23}$ +89° (*c* 1.1, chloroform). IR spectrum: 3 517 (O–H, COOH monomer); 2 668 broad (O–H, COOH dimer); 1 727 shoulder (C=O, acetate); 1 713 (C=O, COOH monomer); 1 633 (C=N); 1 594 (C=C); 1 257, 1 042 (C–O, acetate). ^{1}H NMR spectrum: 5.76 bs, 1 H (H-4); 4.59 dd, 1 H, J = 8.9, J' = 7.6 (H-17α); 4.10 t, 2 H, J = 6.0 (=N–O–CH_2); 2.94 ddd, 1 H, J(1β,2α) = 2.4, J(1α,2α) = 4.6, J(2α,2β) = 17.4 (H-2α); 2.47 t, 2 H, J = 7.3 (CH_2COO); 2.04 s, 3 H (CH_3COO); 1.05 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{25}H_{37}NO_5$ (431.6) calculated: 69.58% C, 8.64% H, 3.25% N; found: 69.35% C, 8.81% H, 3.32% N.

Acid **27**, yield 1.46 g (34%), m.p. 169–171 °C (ether), $[\alpha]_D^{23}$ +180° (*c* 1.2, chloroform). IR spectrum: 3 519 (O–H, COOH monomer); 2 668 broad (O–H, COOH dimer); 1 728 shoulder (C=O, acetate); 1 713 (C=O, COOH dimer); 1 626 (C=N); 1 257, 1 041 (C–O, acetate). ^{1}H NMR spectrum: 6.37 d, 1 H, J = 0.9 (H-4); 4.59 dd, 1 H, J = 9.1, J' = 7.6 (H-17α); 4.09 t, 2 H, J = 6.0 (=N–O–CH_2); 2.49 t, 2 H, J = 7.3 (CH_2COO); 2.04 s, 3 H (CH_3COO); 1.10 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{25}H_{37}NO_5$ (431.6) calculated: 69.58% C, 8.64% H, 3.25% N; found: 69.80% C, 8.80% H, 3.17% N.

(3*E*+3*Z*)-Cholest-4-en-3-one *O*-(2-Carboxyethyl)oxime (**42**)

O-(2-Carboxyethyl)hydroxylamine hydrochloride[21] (637 mg, 4.5 mmol) was added to a solution of cholest-4-en-3-one (1.15 g, 3.0 mmol) in pyridine (10 ml). After stirring at 60 °C for 4 h, the solvent was evaporated, the residue was coevaporated with toluene (75 ml) and partitioned between ethyl acetate and water. The aqueous phase was extracted with ethyl acetate, the combined organic phase was washed successively with dilute hydrochloric acid (1 : 4) and water (3 ×), and the solvent was evaporated. Chromatography of the residue on a column of silica gel (50 g) in a mixture of benzene–acetone (96 : 4) afforded 970 mg (69%) of acid **42**. ^{1}H NMR spectrum: 6.33 d, 0.4 H, J = 1.2 (H-4, *Z*-isomer); 5.75 s, 0.6 H (H-4, *E*-isomer); 4.32 t, 1.2 H, J = 6.0 (=N–O–CH_2, *E*-isomer); 4.30 t, 0.8 H, J = 5.9 (=N–O–CH_2, *Z*-isomer); 2.93 ddd, 0.6 H, J(1β,2α) = 2.4, J(1α,2α) = 4.6, J(2α,2β) = 17.4 (H-2α, *E*-isomer); 2.79 t, 0.8 H, J = 5.9 (CH_2COO, *Z*-isomer); 2.77 t, 1.2 H, J = 6.0 (CH_2COO, *E*-isomer); 1.09 s, 1.2 H (3 × H-19, *Z*-isomer); 1.05 s, 1.8 H (3 × H-19, *E*-isomer); 0.90 d, 3 H, J = 6.4 (3 × H-21); 0.86 d, 6 H, J = 6.5 (3 × H-26 and 3 × H-27); 0.69 s, 3 H (3 × H-18). For $C_{30}H_{49}NO_3$ (471.7) calculated: 76.39% C, 10.47% H, 2.97% N; found: 76.15% C, 10.73% H, 2.85% N.

(3*E*+3*Z*)-5α-Cholestan-3-one *O*-(2-Carboxyethyl)oxime (**48**)

O-(2-Carboxyethyl)hydroxylamine hydrochloride[21] (326 mg, 2.3 mmol) was added to a solution of 5α-cholestan-3-one (580 mg, 1.5 mmol) in pyridine (7 ml). After stirring at 60 °C for 4 h, the solvent was evaporated, the residue was coevaporated with toluene (50 ml) and partitioned between ethyl acetate and water. The aqueous phase was extracted with ethyl acetate, the combined organic

phase was washed successively with dilute hydrochloric acid (1 : 4) and water (3 ×), and the solvent was evaporated. Chromatography of the residue on a column of silica gel (30 g) in a mixture of benzene–acetone (96 : 4) afforded 505 mg (71%) of acid **48**. ^{1}H NMR spectrum: 4.27 t, 2 H, J = 5.8 (=N–O–CH_2); 3.10 dd, 0.4 H, J(1α,2α) = 4.5, J(2α,2β) = 19 (H-2α, *E*-isomer); 2.87 dd, 0.6 H, J(4α,4β) = 15, J(4α,5α) = 3 (H-4α, *Z*-isomer); 2.75 t, 2 H, J = 5.8 (CH_2COO); 0.89 d, 3 H, J = 6.4 (3 × H-21); 0.88 s, 3 H (3 × H-19); 0.86 d, 6 H, J = 6.5 (3 × H-26 and 3 × H-27); 0.65 s, 3 H (3 × H-18). For $C_{30}H_{51}NO_3$ (473.7) calculated: 76.06% C, 10.85% H, 2.96% N; found: 75.88% C, 10.98% H, 2.95% N.

(7*Z*)-7-Oxoandrost-5-ene-3β,17β-diyl Diacetate *O*-(2-Carboxyethyl)oxime (**51**)

O-(2-Carboxyethyl)hydroxylamine hydrochloride[21] (283 mg, 2.0 mmol) was added to a solution of 7-oxoandrost-5-ene-3β,17β-diyl diacetate[23] (388 mg, 1.0 mmol) in pyridine (6 ml). After stirring at 60 °C for 8 h, the solvent was evaporated, the residue was coevaporated with toluene (50 ml) and partitioned between ethyl acetate and water. The aqueous phase was extracted with ethyl acetate, the combined organic phase was washed successively with dilute hydrochloric acid (1 : 4) and water (3 ×), and the solvent was evaporated. Chromatography of the residue on a column of silica gel (20 g) in a mixture of benzene–acetone–acetic acid (98 : 2 : 0.2) afforded 330 mg (69%) of acid **51**, m.p. 243–244 °C (ether), $[\alpha]_D^{23}$ –176° (*c* 2.0, chloroform). IR spectrum: 3 513 (O–H, COOH monomer); 2 683 broad (O–H, COOH dimer); 1 721 (C=O); 1 640 (C=N); 1 590 (C=C); 1 255, 1 032 (C–O, acetate). ^{1}H NMR spectrum: 6.44 d, 1 H, J = 1.2 (H-6); 4.66 m, 1 H, W = 32 (H-3α); 4.62 dd, 1 H, J = 7.0, J' = 8.9 (H-17α); 4.30 t, 2 H, J = 6.4 (=N–O–CH_2); 2.73 t, 2 H, J = 6.4 (CH_2COO); 2.05 s, 3 H (CH_3COO); 2.04 s, 3 H (CH_3COO); 1.12 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{26}H_{37}NO_7$ (475.6) calculated: 65.66% C, 7.84% H, 2.95% N; found: 65.78% C, 8.05% H, 3.01% N.

(7*Z*)-7-Oxocholest-5-en-3β-yl Acetate *O*-(2-Carboxyethyl)oxime (**54**)

O-(2-Carboxyethyl)hydroxylamine hydrochloride[21] (566 mg, 4.0 mmol) was added to a solution of 7-oxocholest-5-en-3β-yl acetate (885 mg, 2.0 mmol) in pyridine (10 ml). After stirring at 60 °C for 8 h, the solvent was evaporated, the residue was coevaporated with toluene (50 ml) and partitioned between ethyl acetate and water. The aqueous phase was extracted with ethyl acetate, the combined organic phase was washed successively with dilute hydrochloric acid (1 : 4) and water (3 ×), and the solvent was evaporated. Chromatography of the residue on a column of silica gel (50 g) in a mixture of benzene–acetone (96 : 4) afforded 630 mg (59%) of acid **54**, m.p. 187–189 °C (ether), $[\alpha]_D^{23}$ –175° (*c* 1.8, chloroform). IR spectrum: 3 516 (O–H, COOH monomer); 2 685 broad (O–H, COOH dimer); 1 754 shoulder (C=O, COOH monomer); 1 727 shoulder (C=O, acetate); 1 716 (C=O, COOH dimer); 1 640 (C=N); 1 252, 1 035 (C–O, acetate). ^{1}H NMR spectrum: 6.44 bs, 1 H (H-6); 4.67 m, 1 H, W = 32 (H-3α); 4.31 t, 2 H, J = 6.3 (=N–O–CH_2); 2.27 t, 2 H, J = 6.3 (CH_2COO); 2.04 s, 3 H (CH_3COO); 1.12 s, 3 H (3 × H-19); 0.93 d, 3 H, J = 6.4 (3 × H-21); 0.87 d, 6 H, J = 6.5 (3 × H-26 and 3 × H-27); 0.69 s, 3 H (3 × H-18). For $C_{32}H_{51}NO_5$ (529.8) calculated: 72.55% C, 9.70% H, 2.64% N; found: 72.78% C, 9.54% H, 2.78% N.

General Procedure for the Preparation of Methyl Esters

The carboxylic acid (0.3 mmol) was dissolved in methanol (3 ml) and ether (5 ml). The solution was cooled with ice and then treated with a slight excess of an ethereal diazomethane solution for 5 min. The solvents were evaporated and the residue was crystallized from an appropriate solvent mixture or chromatographed on two PLC plates.

(17*E*)-17-Oxoandrost-5-en-3β-yl Acetate *O*-[(Methoxycarbonyl)methyl]oxime (**2**)

From acid[7] **1** (122 mg), after crystallization from a mixture of acetone–water, 75 mg (59%) of methyl ester **2** was obtained, m.p. 155–157 °C, $[\alpha]_D^{23}$ –36° (*c* 1.3, chloroform). IR spectrum: 1 757 (C=O, OCH_2COOCH_3); 1 727 (C=O, acetate); 1 255, 1 032 (C–O, acetate). ^{1}H NMR spectrum: 5.39 bd, 1 H, $J \approx 5$ (H-6); 4.60 m, 1 H, $W = 32$ (H-3α); 4.58 s, 2 H (=N–O–CH_2); 3.74 s, 3 H ($COOCH_3$); 2.04 s, 3 H (CH_3COO); 1.04 s, 3 H (3 × H-19); 0.93 s, 3 H (3 × H-18). For $C_{24}H_{35}NO_5$ (417.6) calculated: 69.04% C, 8.45% H, 3.35% N; found: 68.79% C, 8.17% H, 3.24% N.

(17*E*)-17-Oxoandrost-5-en-3β-yl Acetate *O*-[2-(Methoxycarbonyl)ethyl]oxime (**4**)

From acid[8] **3** (125 mg), after crystallization from a mixture of hexane–ether, 83 mg (64%) of methyl ester **4** was obtained, m.p. 79–82 °C, $[\alpha]_D^{23}$ –41° (*c* 1.6, chloroform). IR spectrum: 1 729 (C=O); 1 255, 1 034 (C–O, acetate); 1 178 (C–O). ^{1}H NMR spectrum: 5.38 bd, 1 H, $J \approx 4.5$ (H-6); 4.61 m, 1 H, $W = 32$ (H-3α); 4.28 t, 2 H, $J = 6.4$ (=N–O–CH_2); 3.69 s, 3 H ($COOCH_3$); 2.65 t, 2 H, $J = 6.4$ (CH_2COO); 2.04 s, 3 H (CH_3COO); 1.04 s, 3 H (3 × H-19); 0.90 s, 3 H (3 × H-18). For $C_{25}H_{37}NO_5$ (431.6) calculated: 69.58% C, 8.64% H, 3.25% N; found: 69.75% C, 8.72% H, 3.38% N.

(17*E*)-17-Oxoandrost-5-en-3β-yl Acetate *O*-[3-(Methoxycarbonyl)propyl]oxime (**6**)

From acid[11] **5** (129 mg), after the chromatography in a mixture of benzene–ether (90 : 10), 94 mg (71%) of oily methyl ester **6** was obtained, $[\alpha]_D^{23}$ –39° (*c* 1.4, chloroform). IR spectrum: 1 728 (C=O); 1 670 (C=C); 1 657 (C=N); 1 255, 1 032 (C–O, acetate); 1 174 (C–O). ^{1}H NMR spectrum: 5.38 d, 1 H, $J \approx 5$ (H-6); 4.61 m, 1 H, $W = 32$ (H-3α); 4.04 t, 2 H, $J = 6.2$ (=N–O–CH_2); 3.68 s, 3 H ($COOCH_3$); 2.04 s, 3 H (CH_3COO); 1.04 s, 3 H (3 × H-19); 0.91 s, 3 H (3 × H-18). For $C_{26}H_{39}NO_5$ (445.6) calculated: 70.08% C, 8.82% H, 3.14% N; found: 70.27% C, 8.95% H, 2.95% N.

(3*E*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-[(Methoxycarbonyl)methyl]oxime (**19**) and
(3*Z*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-[(Methoxycarbonyl)methyl]oxime (**24**)

From acid **18** (122 mg), a mixture of compounds **19** and **24** (125 mg) was obtained, which was separated by a chromatography on three PLC plates in a mixture of benzene–acetone (95 : 5).

From combined zones of the less polar compound, 69 mg (55%) of methyl ester **19** was obtained, m.p. 76–78 °C, $[\alpha]_D^{23}$ +114° (*c* 2.3, chloroform). Literature[19] gives m.p. 77–79 °C, $[\alpha]_D^{23}$ +117°. IR spectrum: 1 756 (C=O, OCH_2COOCH_3); 1 727 (C=O, acetate); 1 258, 1 042 (C–O, acetate); 1 102 (C–O). ^{1}H NMR spectrum: 5.75 bs, 1 H (H-4); 4.60 s, 2 H (=N–O–CH_2); 4.59 t, 1 H, $J = 8.2$ (H-17α); 3.76 s, 3 H ($COOCH_3$); 3.06 ddd, 1 H, $J(1\beta,2\alpha) = 2.8$, $J(1\alpha,2\alpha) = 4.6$, $J(2\alpha,2\beta) = 17.5$ (H-2α); 2.04 s, 3 H (CH_3COO); 1.06 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{24}H_{35}NO_5$ (417.6) calculated: 69.04% C, 8.45% H, 3.35% N; found: 68.83% C, 8.32% H, 3.55% N.

From combined zones of the more polar compound, 45 mg (36%) of methyl ester **24** was obtained, m.p. 85–87 °C, $[\alpha]_D^{23}$ +162° (*c* 1.5, chloroform). Literature[19] gives m.p. 102–104 °C, $[\alpha]_D^{23}$ +172°. IR spectrum: 1 756 (C=O, OCH_2COOCH_3); 1 727 (C=O, acetate); 1 257, 1 042 (C–O, acetate); 1 104 (C–O). ^{1}H NMR spectrum: 6.47 d, 1 H, $J = 0.9$ (H-4); 4.59 s, 2 H (=N–O–CH_2); 4.59 t, 1 H, $J = 8.4$ (H-17α); 3.76 s, 3 H ($COOCH_3$); 2.04 s, 3 H (CH_3COO); 1.10 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{24}H_{35}NO_5$ (417.6) calculated: 69.04% C, 8.45% H, 3.35% N; found: 68.84% C, 8.25% H, 3.17% N.

(3*E*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-[2-(Methoxycarbonyl)ethyl]oxime (**21**)

From acid **20** (125 mg), after the chromatography in a mixture of benzene–ether (90 : 10), 107 mg (83%) of methyl ester **21** was obtained, m.p. 86–88 °C (petroleum ether), $[\alpha]_D^{23}$ +107° (*c* 1.3, chloroform). IR spectrum: 1 731 (C=O); 1 634 (C=N); 1 591 (C=C); 1 258, 1 042 (C–O, acetate); 1 178 (C–O). ^{1}H NMR spectrum: 5.75 bs, 1 H (H-4); 4.59 dd, 1 H, J = 9.2, J' = 7.6 (H-17α); 4.31 t, 2 H, J = 6.4 (=N–O–CH_2); 3.70 s, 3 H ($COOCH_3$); 2.92 ddd, 1 H, J(1β,2α) = 2.7, J(1α,2α) = 4.5, J(2α,2β) = 17.3 (H-2α); 2.69 t, 2 H, J = 6.4 (CH_2COO); 2.04 s, 3 H (CH_3COO); 1.05 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{25}H_{37}NO_5$ (431.6) calculated: 69.58% C, 8.64% H, 3.25% N; found: 69.45% C, 8.37% H, 3.12% N.

(3*E*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-[3-(Methoxycarbonyl)propyl]oxime (**23**)

From acid **22** (129 mg), after the chromatography in a mixture of benzene–ether (85 : 15), 111 mg (83%) of oily methyl ester **23** was obtained, $[\alpha]_D^{23}$ +99° (*c* 1.7, chloroform). IR spectrum: 1 740 (C=O, acetate); 1 635 (C=N); 1 593 (C=C); 1 248, 1 043 (C–O, acetate); 1 171 (C–O). ^{1}H NMR spectrum: 5.76 s, 1 H (H-4); 4.59 t, 1 H, J = 8.4 (H-17α); 4.07 t, 2 H, J = 6.1 (=N–O–CH_2); 3.68 s, 3 H ($COOCH_3$); 2.96 ddd, 1 H, J(1β,2α) = 2.8, J(1α,2α) = 4.6, J(2α,2β) = 17.5 (H-2α); 2.42 t, 2 H, J = 7.5 (CH_2COO); 2.04 s, 3 H (CH_3COO); 1.05 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{26}H_{39}NO_5$ (445.6) calculated: 70.08% C, 8.82% H, 3.14% N; found: 69.79% C, 9.12% H, 3.26% N.

(3*Z*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-[2-(Methoxycarbonyl)ethyl]oxime (**26**)

From acid **25** (125 mg), after the chromatography in a mixture of benzene–ether (90 : 10), 103 mg (80%) of oily methyl ester **26** was obtained, $[\alpha]_D^{23}$ +170° (*c* 1.3, chloroform). IR spectrum: 1 730 (C=O); 1 626 (C=N); 1 593 (C=C); 1 255, 1 043 (C–O, acetate); 1 178 (C–O). ^{1}H NMR spectrum: 6.34 d, 1 H, J = 1.2 (H-4); 4.58 dd, 1 H, J = 9.0, J' = 7.5 (H-17α); 4.30 t, 2 H, J = 6.4 (=N–O–CH_2); 3.69 s, 3 H ($COOCH_3$); 2.70 t, 2 H, J = 6.4 (CH_2COO); 2.04 s, 3 H (CH_3COO); 1.09 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{25}H_{37}NO_5$ (431.6) calculated: 69.58% C, 8.64% H, 3.25% N; found: 69.29% C, 8.45% H, 3.17% N.

(3*Z*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-[3-(Methoxycarbonyl)propyl]oxime (**28**)

From acid **27** (129 mg), after the chromatography in a mixture of benzene–ether (85 : 15), 115 mg (86%) of oily methyl ester **28** was obtained, $[\alpha]_D^{23}$ +172° (*c* 1.3, chloroform). IR spectrum (tetrachloromethane): 1 739 (C=O); 1 628 (C=N); 1 247, 1 043 (C–O, acetate); 1 171 (C–O). ^{1}H NMR spectrum: 6.36 d, 1 H, J = 1.2 (H-4); 4.59 dd, 1 H, J = 9, J' = 7.5 (H-17α); 4.06 t, 2 H, J = 6.1 (=N–O–CH_2); 3.68 s, 3 H ($COOCH_3$); 2.44 t, 2 H, J = 7.5 (CH_2COO); 2.04 s, 3 H (CH_3COO); 1.10 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{26}H_{39}NO_5$ (445.6) calculated: 70.08% C, 8.82% H, 3.14% N; found: 70.32% C, 9.03% H, 3.29% N.

(3*E*)-Cholest-4-en-3-one *O*-[2-(Methoxycarbonyl)ethyl]oxime (**44**) and (3*Z*)-Cholest-4-en-3-one *O*-[2-(Methoxycarbonyl)ethyl]oxime (**46**)

From acid **42** (142 mg), a mixture of compounds **44** and **46** (145 mg) was obtained, which were chromatographed on three PLC plates in a mixture of petroleum ether–ether (90 : 10, double development).

From combined zones of the less polar compound, 84 mg (57%) of methyl ester **44** was obtained, m.p. 87–90 °C, $[\alpha]_D^{23}$ +101° (*c* 1.4 chloroform). IR spectrum (tetrachloromethane): 1 744 (C=O);

1 633 (C=N); 1 196, 1 176, 1 082, 1 045 (C–O). ^{1}H NMR spectrum: 5.74 bs, 1 H (H-4); 4.31 t, 2 H, J = 6.4 (=N–O–CH_2); 3.69 s, 3 H ($COOCH_3$); 2.92 ddd, 1 H, J(1β,2α) = 2.8, J(1α,2α) = 5.0, J(2α,2β) = 17.1 (H-2α); 2.69 t, 2 H, J = 6.4 (CH_2COO); 1.04 s, 3 H (3 × H-19); 0.90 d, 3 H, J = 6.4 (3 × H-21); 0.86 d, 6 H, J = 6.4 (3 × H-26 and 3 × H-27); 0.69 s, 3 H (3 × H-18). For $C_{31}H_{51}NO_3$ (485.8) calculated: 76.65% C, 10.58% H, 2.88% N; found: 76.92% C, 10.34% H, 3.01% N.

From combined zones of the more polar compound, 53 mg (36%) of oily methyl ester **46** was obtained, $[\alpha]_D^{23}$ +150° (*c* 1.3 chloroform). IR spectrum (tetrachloromethane): 1 743 (C=O); 1 628 (C=N); 1 196, 1 176, 1 085, 1 045 (C–O). ^{1}H NMR spectrum: 6.33 d, 1 H, J = 1.2 (H-4); 4.30 t, 2 H, J = 6.5 (=N–O–CH_2); 3.70 s, 3 H ($COOCH_3$); 2.70 t, 2 H, J = 6.5 (CH_2COO); 1.08 s, 3 H (3 × H-19); 0.90 d, 3 H, J = 6.5 (3 × H-21); 0.86 d, 6 H, J = 6.5 (3 × H-26 and 3 × H-27); 0.69 s, 3 H (3 × H-18). For $C_{31}H_{51}NO_3$ (485.8) calculated: 76.65% C, 10.58% H, 2.88% N; found: 76.78% C, 10.82% H, 3.05% N.

(3*E*+3*Z*)-5α-Cholestan-3-one *O*-[2-(Methoxycarbonyl)ethyl]oxime (**49**)

From acid **48** (142 mg), after the chromatography on three PLC plates in a mixture of petroleum ether–ether (90 : 20), 132 mg (90%) of oily methyl ester **49** was obtained. ^{1}H NMR spectrum: 4.27 t, 2 H, J = 6.4 (=N–O–CH_2); 3.69 s, 3 H ($COOCH_3$); 3.10 dd, 0.4 H, J(1α,2α) = 5, J(2α,2β) = 17 (H-2α, *E*-isomer); 2.87 dd, 0.6 H, J(4α,4β) = 15, J(4α,5α) = 3 (H-4α, *Z*-isomer); 2.66 t, 2 H, J = 6.4 (CH_2COO); 0.89 d, 3 H, J = 6.4 (3 × H-21); 0.88 s, 3 H (3 × H-19); 0.86 d, 6 H, J = 6.5 (3 × H-26 and 3 × H-27); 0.65 s, 3 H (3 × H-18). For $C_{31}H_{53}NO_3$ (487.8) calculated: 76.34% C, 10.95% H, 2.87% N; found: 76.56% C, 11.05% H, 3.02% N.

(7*Z*)-7-Oxoandrost-5-ene-3β,17β-diyl Diacetate *O*-[2-(Methoxycarbonyl)ethyl]oxime (**52**)

From acid **51** (143 mg), after the chromatography on two PLC plates in a mixture of benzene–ethyl acetate (90 : 10), 127 mg (86%) of methyl ester **52** was obtained, m.p. 129–130 °C (ether), $[\alpha]_D^{23}$ –180° (*c* 1.1, chloroform). IR spectrum: 1 729 (C=O); 1 639 (C=N); 1 588 (C=C); 1 254, 1 032 (C–O, acetate). ^{1}H NMR spectrum: 6.43 d, 1 H, J = 1.5 (H-6); 4.66 m, 1 H, W = 32 (H-3α); 4.63 dd, 1 H, J = 7.0, J' = 8.0 (H-17α); 4.29 t, 2 H, J = 6.4 (=N–O–CH_2); 3.70 s, 3 H ($COOCH_3$); 2.68 t, 2 H, J = 6.4 (CH_2COO); 2.05 s, 3 H (CH_3COO); 2.04 s, 3 H (CH_3COO); 1.12 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{27}H_{39}NO_7$ (489.6) calculated: 66.24% C, 8.03% H, 2.86% N; found: 66.53% C, 7.88% H, 3.06% N.

(7*Z*)-7-Oxocholest-5-en-3β-yl Acetate *O*-[2-(Methoxycarbonyl)ethyl]oxime (**55**)

From acid **54** (159 mg), after the chromatography on two PLC plates in a mixture of benzene–ether (80 : 20), 153 mg (94%) of methyl ester **55** was obtained, m.p. 125–127 °C (ether), $[\alpha]_D^{23}$ –178° (*c* 1.1, chloroform). IR spectrum: 1 731 (C=O); 1 640 (C=N); 1 252, 1 035 (C–O, acetate); 1 194 (C–O). ^{1}H NMR spectrum: 6.43 d, 1 H, J = 1 (H-6); 4.66 m, 1 H, W = 32 (H-3α); 4.30 t, 2 H, J = 6.6 (=N–O–CH_2); 3.70 s, 3 H ($COOCH_3$); 2.69 t, 2 H, J = 6.6 (CH_2COO); 2.04 s, 3 H (CH_3COO); 1.11 s, 3 H (3 × H-19); 0.93 d, 3 H, J = 6.4 (3 × H-21); 0.87 d, 6 H, J = 6.4 (3 × H-26 and 3 × H-27); 0.69 s, 3 H (3 × H-18). For $C_{33}H_{53}NO_5$ (543.8) calculated: 72.89% C, 9.82% H, 2.58% N; found: 73.06% C, 10.11% H, 2.76% N.

General Procedure for the Reduction of *O*-(ω-Carboxyalkyl)oximes

A solution of ethyl chloroformate in THF (1 mol l^{-1}, 1.2 ml) was added dropwise at –5 °C to a solution of an *O*-(ω-carboxyalkyl)oxime derivative (1.0 mmol) in THF (7 ml) and *N*,*N*-diisopropyl-

ethylamine (210 μl, 1.2 mmol). The reaction mixture was stirred at –5 °C for 30 min, then warmed to 0 °C and a solution of sodium borohydride (95 mg, 2.5 mmol) in water (2 ml) was added. After stirring at room temperature for 3 h, dilute hydrochloric acid (1 : 4, 20 ml) was added and the products were extracted with ethyl acetate (2 × 150 ml). The combined extracts were washed successively with dilute hydrochloric acid (1 : 4, 3 ×), water (3 ×), and then dried with anhydrous Na_2SO_4. The solvent was evaporated and the residue was dissolved in methanol (10 ml) and ether (15 ml). The solution was cooled with ice and then treated with a slight excess of an ethereal diazomethane solution for 5 min. The solvents were evaporated and the residue was chromatographed on a column of silica gel (20 g) in a mixture of benzene–acetone (98 : 2) (preparation of compounds **7**, **9**, **11**) or on five PLC plates in a mixture of benzene–acetone (9 : 1).

(17*E*)-17-Oxoandrost-5-en-3β-yl Acetate *O*-(2-Hydroxyethyl)oxime (**7**)

Reduction of acid[7] **1** (404 mg) afforded besides 130 mg (31%) of methyl ester **2**, identical with sample described above, 260 mg (67%) of hydroxy derivative **7**, m.p. 137–138 °C (ether–hexane), $[\alpha]_D^{23}$ –46° (*c* 1.3, chloroform). IR spectrum: 3 607, 3 450 (O–H); 1 726 (C=O); 1 659 (C=N); 1 255, 1 034 (C–O). ^{1}H NMR spectrum: 5.39 bd, 1 H, $J \approx 5$ (H-6); 4.60 m, 1 H, $W = 32$ (H-3α); 4.14 m, 2 H (=N–O–CH_2); 3.86 m, 2 H (C**H**$_2$OH); 2.93 t, 1 H, $J \approx 6$ (O–H); 2.04 s, 3 H (CH_3COO); 1.05 s, 3 H (3 × H-19); 0.92 s, 3 H (3 × H-18). For $C_{23}H_{35}NO_4$ (389.5) calculated: 70.92% C, 9.06% H, 3.60% N; found: 70.68% C, 9.31% H, 3.64% N.

(17*E*)-17-Oxoandrost-5-en-3β-yl Acetate *O*-(3-Hydroxypropyl)oxime (**9**)

Reduction of acid[8] **3** (418 mg) afforded besides 100 mg (23%) of methyl ester **4**, identical with sample described above, 271 mg (67%) of hydroxy derivative **9**, m.p. 143–146 °C (ether–hexane), $[\alpha]_D^{23}$ –41° (*c* 1.2, chloroform). IR spectrum: 3 625, 3 538, 3 429 (O–H); 1 726 (C=O); 1 659 (C=N); 1 255, 1 032 (C–O). ^{1}H NMR spectrum: 5.39 bd, 1 H, $J \approx 5$ (H-6); 4.60 m, 1 H, $W = 32$ (H-3α); 4.14 t, 2 H, $J = 6$ (=N–O–CH_2); 3.73 m, 2 H (C**H**$_2$OH); 2.76 bs, 1 H (O–H); 2.04 s, 3 H (CH_3COO); 1.04 s, 3 H (3 × H-19); 0.92 s, 3 H (3 × H-18). For $C_{24}H_{37}NO_4$ (403.6) calculated: 71.43% C, 9.24% H, 3.47% N; found: 71.03% C, 9.18% H, 3.29% N.

(17*E*)-17-Oxoandrost-5-en-3β-yl Acetate *O*-(4-Hydroxybutyl)oxime (**11**)

Reduction of acid **5** (432 mg) afforded besides 103 mg (23%) of methyl ester **6**, identical with sample described above, 240 mg (59%) of hydroxy derivative **11**, m.p. 105–107 °C (ether-hexane), $[\alpha]_D^{23}$ –42° (*c* 1.1, chloroform). IR spectrum: 3 624, 3 447 (O–H); 1 726 (C=O); 1 654 (C=N); 1 255, 1 032 (C–O). ^{1}H NMR spectrum: 5.38 bd, 1 H, $J \approx 5$ (H-6); 4.60 m, 1 H, $W = 32$ (H-3α); 4.06 t, 2 H, $J = 6$ (=N–O–CH_2); 3.67 m, 2 H (C**H**$_2$OH); 2.03 s, 3 H (CH_3COO); 1.04 s, 3 H (3 × H-19); 0.91 s, 3 H (3 × H-18). For $C_{25}H_{39}NO_4$ (417.6) calculated: 71.91% C, 9.41% H, 3.35% N; found: 71.90% C, 9.58% H, 3.32% N.

(3*E*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-(2-Hydroxyethyl)oxime (**29**) and
(3*Z*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-(2-Hydroxyethyl)oxime (**35**)

Reduction of acid **18** (404 mg) afforded besides 46 mg (11%) of methyl ester **19** and 30 mg (7%) of methyl ester **24**, identical with samples described above, the following compounds.

From combined zones of the less polar compound, 136 mg (35%) of hydroxy derivative **29** was obtained, m.p. 95–97 °C (petroleum ether–ether), $[\alpha]_D^{23}$ +125° (*c* 1.1 chloroform). IR spectrum: 3 604, 3 450 (O–H); 1 724 (C=O); 1 632 (C=N); 1 591 (C=C); 1 258, 1 041 (C–O, acetate); 1 083

(C–OH). ^{1}H NMR spectrum: 5.74 bs, 1 H (H-4); 4.59 dd, 1 H, J = 9.0, J' = 7.5 (H-17α); 4.16 m, 2 H, W = 9 (=N–O–CH_2); 3.87 m, 2 H, W = 12 (C**H**$_2$OH); 2.97 ddd, 1 H, J(1β,2α) = 2.8, J(1α,2α) = 4.6, J(2α,2β) = 17.4 (H-2α); 2.04 s, 3 H (CH_3COO); 1.06 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{23}H_{35}NO_4$ (389.5) calculated: 70.92% C, 9.06% H, 3.60% N; found: 70.92% C, 9.33% H, 3.46% N.

From combined zones of the more polar compound, 125 mg (32%) of hydroxy derivative **35** was obtained, m.p. 132–136 °C (petroleum ether–ether), $[\alpha]_D^{23}$ +185° (*c* 1.2 chloroform). IR spectrum: 3 604, 3 435 (O–H); 1 725 (C=O); 1 626 (C=N); 1 257, 1 041 (C–O, acetate); 1 083 (C–OH). ^{1}H NMR spectrum: 6.39 bd, 1 H, J = 1.2 (H-4); 4.58 dd, 1 H, J = 9.0, J' = 7.8 (H-17α); 4.15 m, 2 H, W = 9 (=N–O–CH_2); 3.87 m, 2 H, W = 10 (C**H**$_2$OH); 2.03 s, 3 H (CH_3COO); 1.10 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{23}H_{35}NO_4$ (389.5) calculated: 70.92% C, 9.06% H, 3.60% N; found: 70.78% C, 9.24% H, 3.64% N

(3*E*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-(3-Hydroxypropyl)oxime (**31**)

Reduction of acid **20** (418 mg) afforded besides 44 mg (10%) of methyl ester **21**, identical with sample described above, 305 mg (75%) of hydroxy derivative **31**, m.p. 93–96 °C (petroleum ether–ether), $[\alpha]_D^{23}$ +111° (*c* 1.1, chloroform). IR spectrum: 3 622, 3 546 (O–H); 1 723 (C=O); 1 633 (C=N); 1 596 (C=C); 1 258, 1 042 (C–O, acetate); 1 057 (C–OH). ^{1}H NMR spectrum: 5.78 bs, 1 H (H-4); 4.61 dd, 1 H, J = 9.1, J' = 7.6 (H-17α); 4.23 t, 2 H, J = 5.7 (=N–O–CH_2); 3.77 t, 2 H, J = 5.7 (C**H**$_2$OH); 2.97 ddd, 1 H, J(1β,2α) = 2.8, J(1α,2α) = 4.6, J(2α,2β) = 17.4 (H-2α); 2.06 s, 3 H (CH_3COO); 1.08 s, 3 H (3 × H-19); 0.84 s, 3 H (3 × H-18). For $C_{24}H_{37}NO_4$ (403.6) calculated: 71.43% C, 9.24% H, 3.47% N; found: 71.03% C, 9.18% H, 3.29% N.

(3*E*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-(4-Hydroxybutyl)oxime (**33**)

Reduction of acid **22** (432 mg) afforded besides 54 mg (12%) of methyl ester **23**, identical with sample described above, and 230 mg (55%) of oily hydroxy derivative **33**, $[\alpha]_D^{23}$ +115° (*c* 1.4, chloroform). IR spectrum: 3 624, 3 466 (O–H); 1 723 (C=O); 1 633 (C=N); 1 590 (C=C); 1 258, 1 043 (C–O, acetate). ^{1}H NMR spectrum: 5.76 bs, 1 H (H-4); 4.59 dd, 1 H, J = 9.2, J' = 7.6 (H-17α); 4.09 t, 2 H, J = 6.1 (=N–O–CH_2); 3.68 t, 2 H, J = 5.9 (C**H**$_2$OH); 2.97 ddd, 1 H, J(1β,2α) = 2.7, J(1α,2α) = 4.6, J(2α,2β) = 17.1 (H-2α); 2.04 s, 3 H (CH_3COO); 1.05 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{25}H_{39}NO_4$ (417.6) calculated: 71.91% C, 9.41% H, 3.35% N; found: 71.78% C, 9.35% H, 3.52% N.

3β-(3-Oxo-4,5-dihydroisoxazol-2-yl)-androst-4-en-17β-yl Acetate (**37**) and
(3*Z*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-(3-Hydroxypropyl)oxime (**38**)

Reduction of acid **25** (418 mg) afforded besides 48 mg (11%) of methyl ester **26**, identical with sample described above, the following compounds.

From combined zones of the less polar compound 60 mg (15%) of isoxazolidin-3-one **37** was obtained, m.p. 195–197 °C (petroleum ether–ether), $[\alpha]_D^{23}$ 0° (*c* 0.9, chloroform). IR spectrum: 1 721 (C=O, acetate); 1 679 (C=O, isoxazolidin-3-one); 1 257, 1 042 (C–O, acetate). ^{1}H NMR spectrum: 5.13 d, 1 H, J = 1.2 (H-4); 4.68 m, 1 H, W = 21 (H-3α); 4.58 dd, 1 H, J = 9.0, J' = 7.5 (H-17α); 4.29 t, 2 H, J = 8.2 (2 × H-5, isoxazolidin-3-one); 2.78 t, 2 H, J = 8.2 (2 × H-4, isoxazolidin-3-one); 2.04 s, 3 H (CH_3COO); 1.08 s, 3 H (3 × H-19); 0.81 s, 3 H (3 × H-18). ^{13}C NMR spectrum: 11.97 (C-18); 18.95 (C-19); 20.47 (C-11); 21.11 (CH_3, acetyl); 22.16 (C-4, isoxazolidin-3-one); 23.47 (C-15); 27.47 (C-16); 32.17 (C-7); 32.34 (C-6); 34.01 (C-2); 35.67 (C-8); 36.28 (C-1); 36.73 (C-10); 36.93 (C-12); 42.46 (C-13); 50.35 (C-14); 52.51 (C-3); 54.31 (C-9); 66.54 (C-5, isoxazolidin-3-one); 82.69 (C-17); 118.48 (C-4); 149.21 (C-5); 168.63 (C-3, isoxazolidin-3-one); 171.14 (C=O, acetyl). Mass

spectrum (FAB, *m/z*): 402 (M + 1). For $C_{24}H_{35}NO_4$ (401.6) calculated: 71.79% C, 8.79% H, 3.49% N; found: 72.03% C, 8.98% H, 3.51% N.

From combined zones of the more polar compound 175 mg (43%) of hydroxy derivative **38** was obtained, m.p. 111–113 °C (petroleum ether–ether), $[\alpha]_D^{23}$ +183° (*c* 1.5, chloroform). IR spectrum: 3 626, 3 547 (O–H); 1 725 (C=O); 1 626 (C=N); 1 257, 1 043 (C–O, acetate); 1 059 (C–OH). ^{1}H NMR spectrum: 6.35 d, 1 H, *J* = 1.5 (H-4); 4.58 dd, 1 H, *J* = 9.0, *J*′ = 7.5 (H-17α); 4.19 t, 2 H, *J* = 5.8 (=N–O–CH_2); 3.77 t, 2 H, *J* = 5.8 (C**H**$_2$OH); 2.04 s, 3 H (CH_3COO); 1.10 s, 3 H (3 × H-19); 0.82 s, 3 H (3 × H-18). For $C_{24}H_{37}NO_4$ (403.6) calculated: 71.43% C, 9.24% H, 3.47% N; found: 71.67% C, 9.31% H, 3.76% N.

(3*Z*)-3-Oxoandrost-4-en-17β-yl Acetate *O*-(4-Hydroxybutyl)oxime (**40**)

Reduction of acid **27** (432 mg) afforded besides 49 mg (11%) of methyl ester **28**, identical with sample described above, 272 mg (65%) of hydroxy derivative **40**, m.p. 106–109 °C (petroleum ether–ether), $[\alpha]_D^{23}$ +180° (*c* 1.3, chloroform). IR spectrum: 3 624, 3 444 (O–H); 1 724 (C=O); 1 625 (C=N); 1 257, 1 043 (C–O, acetate). ^{1}H NMR spectrum: 6.37 d, 1 H, *J* = 1.2 (H-4); 4.58 dd, 1 H, *J* = 9.2, *J*′ = 7.6 (H-17α); 4.07 t, 2 H, *J* = 6.0 (=N–O–CH_2); 3.68 t, 2 H, *J* = 5.9 (C**H**$_2$OH); 2.03 s, 3 H (CH_3COO); 1.09 s, 3 H (3 × H-19); 0.81 s, 3 H (3 × H-18). For $C_{25}H_{39}NO_4$ (417.6) calculated: 71.91% C, 9.41% H, 3.35% N; found: 72.09% C, 9.47% H, 3.08% N.

3β-(3-Oxo-4,5-dihydroisoxazol-2-yl)-cholest-4-ene (**43**), (3*E*)-Cholest-4-en-3-one *O*-(3-Hydroxypropyl)oxime (**45**), and (3*Z*)-Cholest-4-en-3-one *O*-(3-Hydroxypropyl)oxime (**47**)

Reduction of acid **42** (472 mg) afforded a mixture of products, from which after the chromatography on silica gel column (50 g) in a mixture of benzene–ether (99 : 1 to 95 : 5), the following compounds were separated.

Methyl ester **44** (49 mg, 10%) and methyl ester **46** (44 mg, 9%), both identical with samples described above.

Isoxazolidin-3-one **43** (36 mg, 8%), m.p. 121–124 °C (petroleum ether), $[\alpha]_D^{23}$ +14° (*c* 1.6, chloroform). IR spectrum: 1 677 (C=O, isoxazolidin-3-one). ^{1}H NMR spectrum: 5.12 bs, 1 H (H-4); 4.68 m, 1 H, *W* = 26 (H-3α); 4.29 t, 2 H, *J* = 8 (2 × H-5, isoxazolidin-3-one); 2.78 t, 2 H, *J* = 8 (2 × H-4, isoxazolidin-3-one); 1.07 s, 3 H (3 × H-19); 0.90 d, 3 H, *J* = 6.5 (3 × H-21); 0.87 d, 6 H, *J* = 6.5 (3 × H-26 and 3 × H-27); 0.68 s, 3 H (3 × H-18). For $C_{30}H_{49}NO_2$ (455.7) calculated: 79.07% C, 10.84% H, 3.07% N; found: 78.86% C, 11.09% H, 2.92% N.

Hydroxy derivative **45** (160 mg, 35%), m.p. 73–76 °C (ether), $[\alpha]_D^{23}$ +107° (*c* 1.4, chloroform). IR spectrum: 3 627, 3 533, 3 383 (O–H); 1 632 (C=N); 1 590 (C=C); 1 060 (C–OH). ^{1}H NMR spectrum: 5.76 bs, 1 H (H-4); 4.21 t, 2 H, *J* = 6.0 (=N–O–CH_2); 3.76 t, 2 H, *J* = 6.0 (C**H**$_2$OH); 2.93 ddd, 1 H, *J*(1β,2α) = 2.8, *J*(1α,2α) = 4.6, *J*(2α,2β) = 17.5 (H-2α); 1.05 s, 3 H (3 × H-19); 0.91 d, 3 H, *J* = 6.5 (3 × H-21); 0.87 d, 6 H, *J* = 6.5 (3 × H-26 and 3 × H-27); 0.70 s, 3 H (3 × H-18). For $C_{30}H_{51}NO_2$ (457.7) calculated: 78.72% C, 11.23% H, 3.06% N; found: 78.89% C, 11.34% H, 3.17% N.

Hydroxy derivative **47** (101 mg, 22%), m.p. 95–98 °C (petroleum ether), $[\alpha]_D^{23}$ +159° (*c* 1.0, chloroform). IR spectrum: 3 628, 3 552, 3 376 (O–H); 1 624 (C=N); 1 061 (C–OH). ^{1}H NMR spectrum: 6.35 bs, 1 H (H-4); 4.20 t, 2 H, *J* = 6.0 (=N–O–CH_2); 3.77 t, 2 H, *J* = 6.0 (C**H**$_2$OH); 1.09 s, 3 H (3 × H-19); 0.90 d, 3 H, *J* = 6.5 (3 × H-21); 0.88 d, 6 H, *J* = 6.5 (3 × H-26 and 3 × H-27); 0.69 s, 3 H (3 × H-18). For $C_{30}H_{51}NO_2$ (457.7) calculated: 78.72% C, 11.23% H, 3.06% N; found: 78.96% C, 11.51% H, 2.88% N.

(3*E*+3*Z*)-5α-Cholestan-3-one *O*-(3-Hydroxypropyl)oxime (**50**)

Reduction of acid **48** (474 mg) afforded besides 63 mg (13%) of methyl ester **49**, identical with sample described above, 377 mg (82%) of oily hydroxy derivative **50**. IR spectrum: 3 625 (O–H); 1 636 (C=N); 1 061 (C–OH). ^{1}H NMR spectrum: 4.16 t, 2 H, J = 5.8 (=N–O–C**H**$_2$); 3.75 bt, 2 H, $J \approx 6$ (C**H**$_2$OH); 3.10 dd, 0.4 H, J(1α,2α) = 4.5, J(2α,2β) = 14 (H-2α, *E*-isomer); 2.87 dd, 0.6 H, J(4α,4β) = 15, J(4α,5α) = 3 (H-4α, *Z*-isomer); 0.90 d, 3 H, J = 6.4 (3 × H-21); 0.88 s, 3 H (3 × H-19); 0.86 d, 6 H, J = 6.4 (3 × H-26 and 3 × H-27); 0.66 s, 3 H (3 × H-18). For $C_{30}H_{53}NO_2$ (459.8) calculated: 78.37% C, 11.62% H, 3.05% N; found: 78.09% C, 11.67% H, 3.26% N.

(7*Z*)-7-Oxoandrost-5-ene-3β,17β-diyl Diacetate *O*-(3-Hydroxypropyl)oxime (**53**)

Reduction of acid **51** (480 mg) afforded besides 173 mg (35%) of methyl ester **52**, identical with sample described above, 307 mg (66%) of hydroxy derivative **53**, m.p. 131–134 °C (ether), $[\alpha]_D^{23}$ –192° (*c* 1.3, chloroform). IR spectrum: 3 626, 3 549, 3 449 (O–H); 1 728 (C=O); 1 639 (C=N); 1 254, 1 032 (C–O, acetate); 1 047 (C–OH). ^{1}H NMR spectrum: 6.45 d, 1 H, J = 1.2 (H-6); 4.67 m, 1 H, W = 32 (H-3α); 4.63 dd, 1 H, J = 7, J' = 9 (H-17α); 4.18 t, 2 H, J = 5.9 (=N–O–C**H**$_2$); 3.78 t, 2 H, J = 5.8 (C**H**$_2$OH); 2.05 s, 3 H (CH$_3$COO); 2.04 s, 3 H (CH$_3$COO); 1.13 s, 3 H (3 × H-19); 0.83 s, 3 H (3 × H-18). For $C_{26}H_{39}NO_6$ (461.6) calculated: 67.65% C, 8.52% H, 3.03% N; found: 67.89% C, 8.76% H, 3.12% N.

(7*Z*)-7-Oxocholest-5-en-3β-yl Acetate *O*-(3-Hydroxypropyl)oxime (**56**)

Reduction of acid **54** (530 mg) afforded besides 190 mg (35%) of methyl ester **55**, identical with sample described above, 217 mg (42%) of hydroxy derivative **56**, m.p. 131–133 °C (petroleum ether), $[\alpha]_D^{23}$ –174° (*c* 1.5, chloroform). IR spectrum: 3 625, 3 531, 3 444 (O–H); 1 729 (C=O); 1 639 (C=N); 1 588 (C=C); 1 252, 1 034 (C–O, acetate); 1 057 (C–OH). ^{1}H NMR spectrum: 6.45 bs, 1 H (H-6); 4.67 m, 1 H, W = 32 (H-3α); 4.19 t, 2 H, J = 5.9 (=N–O–C**H**$_2$); 3.76 bt, 2 H, J = 6 (C**H**$_2$OH); 2.04 s, 3 H (CH$_3$COO); 1.12 s, 3 H (3 × H-19); 0.93 d, 3 H, J = 6.4 (3 × H-21); 0.87 d, 6 H, J = 6.4 (3 × H-26 and 3 × H-27); 0.69 s, 3 H (3 × H-18). From $C_{32}H_{53}NO_4$ (515.8) calculated: 74.52% C, 10.36% H, 2.72% N; found: 74.78% C, 10.64% H, 2.45% N.

General Procedure for the Hydrolysis of Acetate Protecting Group

Acetyl derivative (0.15 mmol) was dissolved in a tetrahydrofuran (1.5 ml) and methanol (0.3 ml) mixture, 2 M aqueous KOH (1.1 ml) was added, and the mixture was stirred at 40 °C for 3 h. The solvents were evaporated and the residue was partitioned between water and ethyl acetate. The aqueous layer was extracted with ethyl acetate and the combined extracts were washed successively with dilute hydrochloric acid (1 : 4), water, saturated aqueous $KHCO_3$ and water. After drying with anhydrous Na_2SO_4, the solvent was evaporated and the residue was crystallized from a mixture of ether–petroleum ether (compounds **8**, **10**, **12**), from a mixture of ethyl acetate–ether (compounds **30**, **32**, **36**), from ether (compound **39**), from a mixture of methanol–water (compound **34**), or from a mixture of petroleum ether–ether (compound **41**).

(17*E*)-3β-Hydroxyandrost-5-en-17-one *O*-(2-Hydroxyethyl)oxime (**8**)

Hydrolysis of acetate **7** (58 mg) afforded 37 mg (72%) of hydroxy derivative **8**, m.p. 167–169 °C, $[\alpha]_D^{23}$ –37° (*c* 1.1, chloroform). IR spectrum: 3 613, 3 449 (O–H); 1 655 (C=N); 1 047 (C–O). ^{1}H NMR spectrum: 5.36 bd, 1 H, $J \approx 5$ (H-6); 4.13 m, 2 H (=N–O–C**H**$_2$); 3.86 bs, 2 H (C**H**$_2$OH);

3.53 m, 1 H, *W* = 32 (H-3α); 1.05 s, 3 H (3 × H-19); 0.92 s, 3 H (3 × H-18). For $C_{21}H_{33}NO_3$ (347.5) calculated: 72.58% C, 9.57% H, 4.03% N; found: 72.68% C, 9.78% H, 3.97% N.

(17*E*)-3β-Hydroxyandrost-5-en-17-one *O*-(3-Hydroxypropyl)oxime (**10**)

Hydrolysis of acetate **9** (61 mg) afforded 42 mg (77%) of hydroxy derivative **10**, m.p. 156–157 °C, $[\alpha]_D^{23}$ –37° (*c* 1.1, chloroform). IR spectrum: 3 611, 3 540 shoulder, 3 426 (O–H); 1 659 (C=N); 1 050 (C–O). ^{1}H NMR spectrum: 5.36 bd, 1 H, *J* ≈ 5 (H-6); 4.19 t, 2 H, *J* = 5.8 (=N–O–CH_2); 3.73 bt, 2 H, *J* = 5.8 (C**H**$_2$OH); 3.53 m, 1 H, *W* = 32 (H-3α); 1.03 s, 3 H (3 × H-19); 0.92 s, 3 H (3 × H-18). For $C_{22}H_{35}NO_3$ (361.5) calculated: 73.09% C, 9.76% H, 3.87% N; found: 73.30.% C, 9.78% H, 3.88% N.

(17*E*)-3β-Hydroxyandrost-5-en-17-one *O*-(4-Hydroxybutyl)oxime (**12**)

Hydrolysis of acetate **11** (63 mg) afforded 39 mg (69%) of hydroxy derivative **12**, m.p. 139 °C, $[\alpha]_D^{23}$ –44° (*c* 1.1, chloroform). IR spectrum: 3 610, 3 449 (O–H); 1 664 (C=N); 1 050 (C–O). ^{1}H NMR spectrum: 5.36 bd, 1 H, *J* ≈ 5 (H-6); 4.06 t, 2 H, *J* = 6.0 (=N–O–CH_2); 3.67 t, 2 H, *J* = 6.1 (C**H**$_2$OH); 3.53 m, 1 H, *W* = 32 (H-3α); 1.03 s, 3 H (3 × H-19); 0.92 s, 3 H (3 × H-18). For $C_{23}H_{37}NO_3$ (375.6) calculated: 73.56% C, 9.93% H, 3.73% N; found: 73.28% C, 9.95% H, 3.77% N.

(3*E*)-17β-Hydroxyandrost-4-en-3-one *O*-(2-Hydroxyethyl)oxime (**30**)

Hydrolysis of acetate **29** (58 mg) afforded 39 mg (75%) of hydroxy derivative **30**, m.p. 125–126 °C, $[\alpha]_D^{23}$ +137° (*c* 1.2, chloroform). IR spectrum: 3 613, 3 455 (O–H); 1 633 (C=N); 1 083, 1 077, 1 041 (C–O). ^{1}H NMR spectrum: 5.75 bs, 1 H (H-4); 4.17 m, 2 H (=N–O–CH_2); 3.87 m, 2 H (C**H**$_2$OH); 3.64 t, 1 H, *J* = 8.2 (H-17α); 2.98 ddd, 1 H, *J*(1β,2α) = 2.7, *J*(1α,2α) = 4.6, *J*(2α,2β) = 17.4 (H-2α); 1.07 s, 3 H (3 × H-19); 0.78 s, 3 H (3 × H-18). For $C_{21}H_{33}NO_3$ (347.5) calculated: 72.58% C, 9.57% H, 4.03% N; found: 72.49% C, 9.61% H, 3.98% N.

(3*E*)-17β-Hydroxyandrost-4-en-3-one *O*-(3-Hydroxypropyl)oxime (**32**)

Hydrolysis of acetate **31** (61 mg) afforded 42 mg (77%) of hydroxy derivative **32**, m.p. 150–152 °C, $[\alpha]_D^{23}$ +101° (*c* 2.1, chloroform). IR spectrum: 3 615, 3 428 (O–H); 1 632 (C=N); 1 590 (C=C); 1 057 (C–O). ^{1}H NMR spectrum: 5.76 bs, 1 H (H-4); 4.21 t, 2 H, *J* = 5.8 (=N–O–CH_2); 3.75 t, 2 H, *J* = 5.8 (C**H**$_2$OH); 3.64 bt, 1 H, *J* = 8.5 (H-17α); 2.93 ddd, 1 H, *J*(1β,2α) = 2.7, *J*(1α,2α) = 4.6, *J*(2α,2β) = 17.4 (H-2α); 1.06 s, 3 H (3 × H-19); 0.77 s, 3 H (3 × H-18). For $C_{22}H_{35}NO_3$ (361.5) calculated: 73.09% C, 9.76% H, 3.87% N; found: 72.87% C, 10.03% H, 3.59% N.

(3*E*)-17β-Hydroxyandrost-4-en-3-one *O*-(4-Hydroxybutyl)oxime (**34**)

Hydrolysis of acetate **33** (63 mg) afforded 28 mg (49%) of hydroxy derivative **34**, m.p. 111–113 °C, $[\alpha]_D^{23}$ +112° (*c* 1.3, chloroform). IR spectrum: 3 616, 3 439 (O–H); 1 632 (C=N); 1 590 (C=C); 1 066, 1 050, 1 018 (C–O). ^{1}H NMR spectrum: 5.75 bs, 1 H (H-4); 4.08 t, 2 H, *J* = 6.1 (=N–O–CH_2); 3.63 m, 3 H (C**H**$_2$OH and H-17α); 2.94 ddd, 1 H, *J*(1β,2α) = 2.7, *J*(1α,2α) = 4.6, *J*(2α,2β) = 17.4 (H-2α); 1.05 s, 3 H (3 × H-19); 0.76 s, 3 H (3 × H-18). For $C_{23}H_{37}NO_3$ (375.6) calculated: 73.56% C, 9.93% H, 3.73% N; found: 73.85% C, 9.88% H, 3.67% N.

(3*Z*)-17β-Hydroxyandrost-4-en-3-one *O*-(2-Hydroxyethyl)oxime (**36**)

Hydrolysis of acetate **35** (58 mg) afforded 33 mg (64%) of hydroxy derivative **36**, m.p. 164–165 °C, $[\alpha]_D^{23}$ +194° (*c* 1.2, chloroform). IR spectrum: 3 613, 3 442 (O–H); 1 626 (C=N); 1 083, 1 066, 1 041 (C–O). ^{1}H NMR spectrum: 6.40 d, 1 H, *J* = 1.5 (H-4); 4.16 m, 2 H (=N–O–CH_2); 3.88 m, 2 H (C**H**$_2$OH); 3.64 bt, 1 H, *J* = 8 (H-17α); 1.11 s, 3 H (3 × H-19); 0.78 s, 3 H (3 × H-18). For $C_{21}H_{33}NO_3$ (347.5) calculated: 72.58% C, 9.57% H, 4.03% N; found: 72.76% C, 9.78% H, 3.91% N.

(3*Z*)-17β-Hydroxyandrost-4-en-3-one *O*-(3-Hydroxypropyl)oxime (**39**)

Hydrolysis of acetate **38** (61 mg) afforded 38 mg (70%) of hydroxy derivative **39**, m.p. 168–171 °C, $[\alpha]_D^{23}$ +194° (*c* 1.4, chloroform). IR spectrum: 3 615, 3 427 (O–H); 1 625 (C=N); 1 057 (C–O). ^{1}H NMR spectrum: 6.34 d, 1 H, *J* = 1.2 (H-4); 4.18 t, 2 H, *J* = 5.8 (=N–O–CH_2); 3.76 t, 2 H, *J* = 6 (C**H**$_2$OH); 3.63 bt, 1 H, *J* = 8.5 (H-17α); 1.10 s, 3 H (3 × H-19); 0.77 s, 3 H (3 × H-18). For $C_{22}H_{35}NO_3$ (361.5) calculated: 73.09% C, 9.76% H, 3.87% N; found: 73.26% C, 9.87% H, 3.97% N.

(3*Z*)-17β-Hydroxyandrost-4-en-3-one *O*-(4-Hydroxybutyl)oxime (**41**)

Hydrolysis of acetate **40** (63 mg) afforded 32 mg (57%) of hydroxy derivative **41**, m.p. 154–156/164 °C, $[\alpha]_D^{23}$ +200° (*c* 1.4, chloroform). IR spectrum: 3 617, 3 447 (O–H); 1 625 (C=N); 1 075, 1 050, 1 020 (C–O). ^{1}H NMR spectrum: 6.37 d, 1 H, *J* = 1.5 (H-4); 4.07 t, 2 H, *J* = 5.9 (=N–O–CH_2); 3.69 t, 2 H, *J* = 6.1 (C**H**$_2$OH); 3.64 t, 1 H, *J* = 8.1 (H-17α); 1.11 s, 3 H (3 × H-19); 0.78 s, 3 H (3 × H-18). For $C_{23}H_{37}NO_3$ (375.6) calculated: 73.56% C, 9.93% H, 3.73% N; found: 73.28% C, 9.97% H, 3.88% N.

The authors are indebted Dr P. Fiedler for taking and interpretation of IR spectra. Our thanks are due to Mrs M. Snopkova for measurements of 200 MHz ^{1}H NMR and to Dr D. Saman for measurements and interpretation of ^{13}C NMR spectra. The elemental analyses were carried out in the Analytical Laboratory (Dr V. Pechanec, Head). This work was supported by grant No. 203/96/0329 of the Grant Agency of the Czech Republic.

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