LENGTHENING OF THE ALKYL CHAIN IN STEROID *O*-(ω-CARBOXYALKYL)OXIMES BY WITTIG REACTION*

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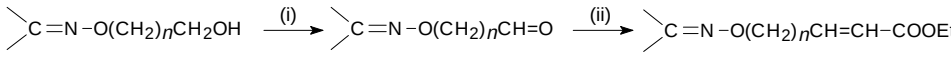
Dedicated to Dr Jan Fajkos on the occasion of his 75th birthday.

The steroid *O*-alkyloximes with various alkyl length (2–4 carbons) and with terminal hydroxyl groups were oxidized to aldehydes and their Wittig reaction with triethyl phosphonoacetate was studied. Oximes derived from 17-oxoandrost-5-en-3β-yl acetate and from 7-oxo and 19-oxocholest-5-en-3β-yl acetate were used. Except of 7- and 19-[*O*-(2-hydroxyethyl)]oximes, all the hydroxyalkyloximes gave successively aldehydes and corresponding unsaturated esters. The method is useful for the lengthening of the carbon chain in ω-substituted *O*-alkyloximes.
Key words: Steroids; *O*-Alkyloximes; Wittig reaction; Horner–Emmons reaction; Swern oxidation.

In our preceding paper[2] we reported the synthesis of *O*-(ω-hydroxyalkyl)oxime steroid derivatives by reduction of corresponding *O*-(ω-carboxyalkyl)oximes. The terminal hydroxyl group can be subjected to a variety of chemical transformations. In this paper we describe its oxidation to the corresponding aldehyde and subsequent lengthening of the alkyl chain by Wittig reagents (Scheme 1). The substituted alkyloxime bridge is routinely used in the synthesis of immunoanalysis components. Methods of its modifica-



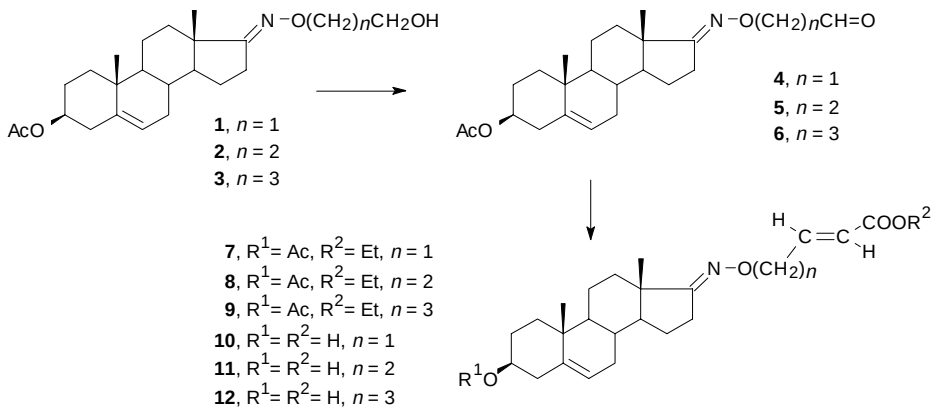
(i) $(COCl)_2$, CH_3SOCH_3, Et_3N/CH_2Cl_2, -78 °C, (ii) $(EtO)_2P(O)CH_2COOEt$, NaH/THF

SCHEME 1

* Part CD in the series On Steroids; Part CCCXCIX see ref.[1]

tion may support the broader study of the bridge structure impact on assay sensitivity and specificity.

Based on our preliminary experiments, the oxidation was done by the reagent formed *in situ* from dimethyl sulfoxide and oxalyl chloride (Swern oxidation[3]). Androstane derivatives **1**–**3** were chosen for the first experiments (Scheme 2). The corresponding aldehydes **4**–**6** were obtained in yields higher than 90%. In their ^{1}H NMR spectra, a characteristic triplet of aldehyde proton at about δ 9.8 ppm with the coupling constant ^3J = 1.3–2.3 Hz was present. The stability of these aldehydes is satisfactory to store them for several days in a refrigerator in the argon atmosphere. Note that aldehydes of this type cannot be prepared from ketones with correspondingly substituted hydroxylamines due to nonexistence of the reagents.



SCHEME 2

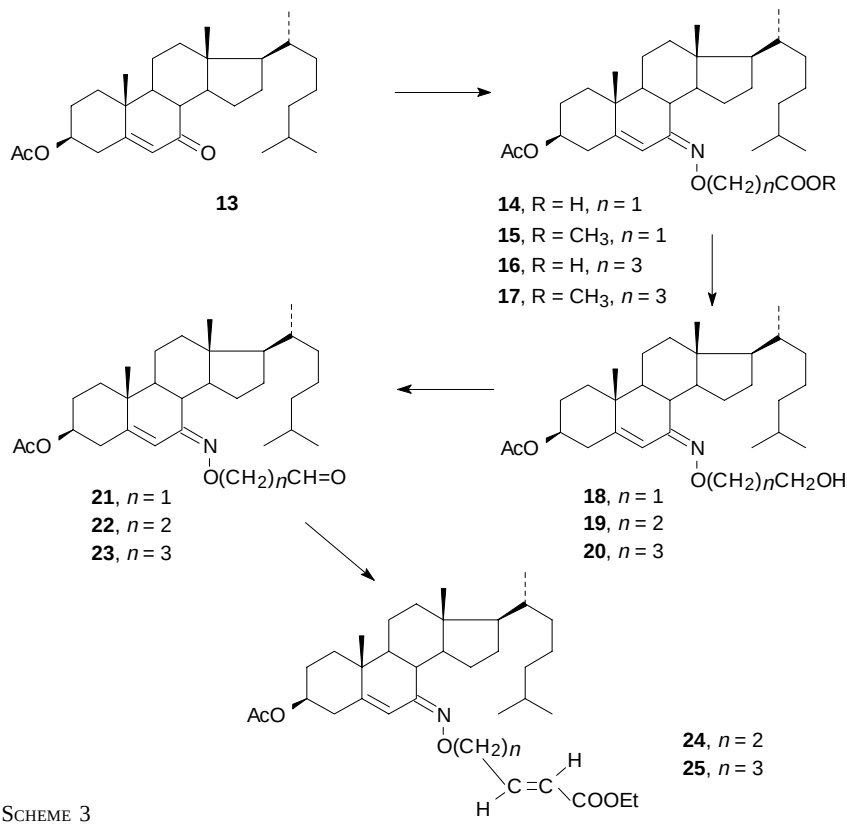
The Wittig reaction (Horner–Emmons variant) of aldehydes **4**–**6** with triethyl phosphonoacetate gave corresponding unsaturated esters **7**–**9**. The yield depended on the length of the alkyl chain in the substituted oxime; the longer-chain oximes were observed to give better yields (n = 1, 39%; n = 2, 51%, n = 3, 72%). *E*-Configuration of the prepared unsaturated esters followed from the analysis of ^{1}H NMR spectra, where the characteristic[4] coupling constant $^3J \approx 15.7$ Hz at the olefin proton signals was present.

The ethyl esters **7**–**9** were hydrolyzed in alkaline medium with simultaneous deacetylation to carboxylic acids **10**–**12**. During the whole reaction sequence, the oxime configuration 17*E* was conserved as follows from the ^{1}H NMR chemical shift of H-18 at δ 0.92 ppm (see refs[5,6])

For the future application of this method in preparing haptens for immunology, other more interesting positions of oxime at the steroid skeleton were to be evaluated. In this study we use the method for oximes in positions 7 (ref.[7]) and 19 (ref.[8]). The starting

compounds **18**–**20** and **33**–**35** were prepared by the method reported in our preceding paper[2] in the standard yields.

Compounds substituted at position 7 (configuration 7*Z*) gave the expected results except for the lowest homologue **18** (n = 1). Its oxidation led to aldehyde **21** in the >90% yield but the subsequent Wittig reaction did not afford the unsaturated ester (Scheme 3), only a mixture of polar phosphorus containing products. For compounds **19** and **20** (n = 2 and 3), the corresponding aldehydes **22** and **23** were prepared in yields about 90% and transformed by Wittig reaction to expected esters **24** and **25** in yields of ≈55%.

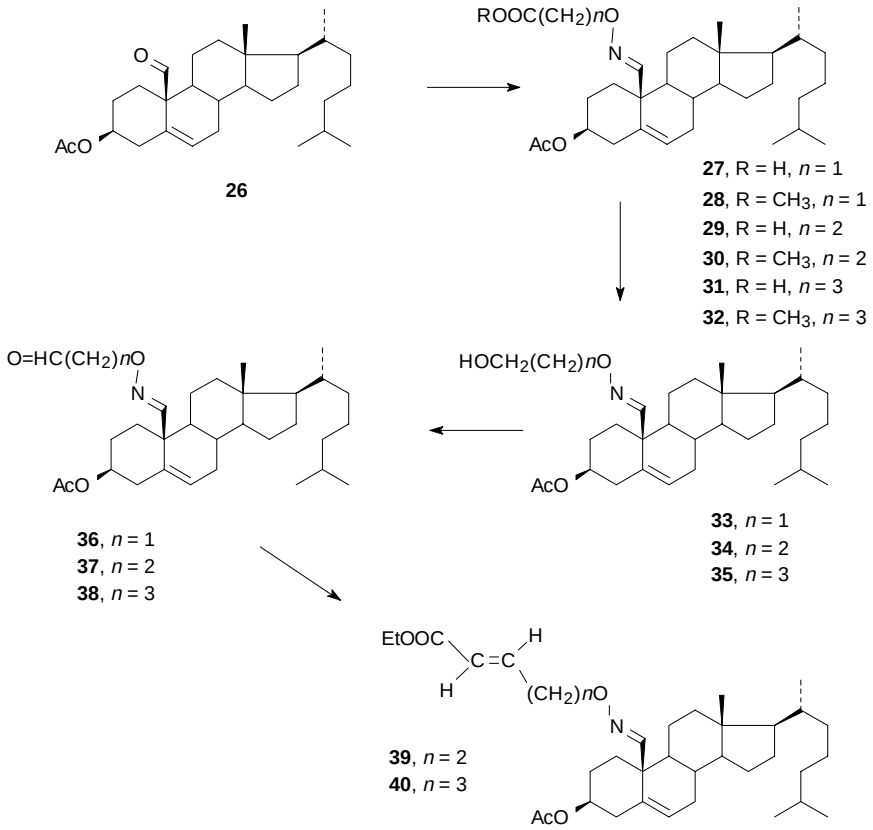


SCHEME 3

Again, the configuration of oxime (7*Z*) was retained and the newly formed unsaturated ester had *E*-configuration, as follows[9] from ^{1}H NMR chemical shifts of H-6 (δ 6.5 ppm, $J \approx 1.2$ Hz) and coupling constants of olefin protons[4] (^3J = 15.6 Hz).

Similar results were found in the 19-oxime series (Scheme 4). Moreover, the aldehyde **36**, derived from the lowest homologue **33** (n = 1), was isolated in 66% yield only and was less stable compared to the corresponding compounds from the other series.

No unsaturated ester was found among products from its Wittig reaction. The different behaviour may be caused by the fact that, unlike the aldehydes from the preceding series (7 and 17-oximes), derived from steroid ketoximes, the aldehyde **36** is more reactive aldoxime. Higher homologues **34** and **35** (n = 2 and 3) gave corresponding aldehydes (**37** and **38**) and unsaturated esters (**39** and **40**) in a usual way. The configurations of oxime[8,10] and unsaturated ester[4] were in the whole series both *E* (H-19: δ 7.3 ppm, olefin protons $^3J \approx 15.7$ Hz).



SCHEME 4

Summarizing, the method under study is suitable for the lengthening of *O*-alkyl chains in steroid oximes but in positions 7 and 19 a minimum of two methylenes have to be present between the oxygen atom of oxime group and the terminal aldehyde for a successful Wittig reaction.

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. ^{1}H 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. Mass spectra (FAB) were recorded on a VG Analytical ZAB-EQ spectrometer. 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.

(7*Z*)-7-Oxocholest-5-en-3β-yl Acetate *O*-(Carboxymethyl)oxime (**14**)

O-(Carboxymethyl)hydroxylamine hemihydrochloride (656 mg, 6.0 mmol) was added to a solution of 7-oxocholesterol acetate[11] **13** (1.33 g, 3.0 mmol) in pyridine (15 ml), and the mixture was stirred at 55 °C for 8 h. The solvent was evaporated, the residue was coevaporated with toluene (35 ml) and partitioned between ethyl acetate and water. The aqueous phase was extracted with ethyl acetate and the extract was washed successively with dilute hydrochloric acid (1 : 4) and water (3 ×). Evaporation of the solvent afforded 1.32 g (85%) of amorphous **14** which was used directly for preparation of compounds **15** and **18**. ^{1}H NMR spectrum: 6.51 d, 1 H, *J* = 1.2 (H-6); 4.68 m, 1 H, *W* = 32 (H-3α); 4.60 s, 2 H (=N–O–CH_2); 2.05 s, 3 H (CH_3COO); 1.14 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).

(7*Z*)-7-Oxocholest-5-en-3β-yl Acetate *O*-(3-Carboxypropyl)oxime (**16**)

O-(3-Carboxypropyl)hydroxylamine hydrochloride[12] (933 mg, 6.0 mmol) was added to a solution of 7-oxocholesterol acetate[11] **13** (1.33 g, 3.0 mmol) in pyridine (15 ml), and the mixture was stirred at 60 °C for 8 h. The solvent was evaporated, the residue was coevaporated with toluene (35 ml) and partitioned between ethyl acetate and water. Aqueous phase was extracted with ethyl acetate and the combined organic phase was washed successively with dilute hydrochloric acid (1 : 4) and water (3 ×). The solvent was evaporated and the chromatography of the residue on a column of silica gel (50 g) in a mixture of benzene–acetone (97 : 3) afforded 1.25 g (77%) of amorphous **16**, $[\alpha]_D$ –175 (*c* 1.6, chloroform). IR spectrum: 3 517 (O–H, COOH monomer); 2 718, 2 674 (O–H, COOH dimer); 1 752 shoulder (C=O, COOH monomer); 1 729 (C=O, acetate); 1 712 (C=O, COOH dimer); 1 640 (C=N); 1 252, 1 034 (C–O, acetate); 1 053 (C–O). ^{1}H NMR spectrum: 6.45 d, 1 H, *J* = 0.9 (H-6); 4.67 m, 1 H, *W* = 32 (H-3α); 4.08 t, 2 H, *J* = 6.1 (=N–O–CH_2); 2.46 t, 2 H, *J* = 7.2 (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); 0.86 d, 6 H, *J* = 6.5 (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: 72.63% C, 10.05% H, 2.67% N.

General Procedure for Preparation of *O*-(ω-Carboxyalkyl)oximes **27**, **29**, and **31**

O-(ω-Carboxyalkyl)hydroxylamine hydrochloride (9.0 mmol) was added to a solution of aldehyde[13] **26** (1.33 g, 3.0 mmol) in pyridine (15 ml), and the mixture was stirred at room temperature for 72 h. The solvent was evaporated, the residue was coevaporated with toluene (35 ml) and partitioned be-

tween ethyl acetate and water. Aqueous phase was extracted with ethyl acetate and the combined organic phase was washed successively with dilute hydrochloric acid (1 : 4) and water (3 ×). The solvent was evaporated and the residue was chromatographed on a column of silica gel (50 g) in a mixture of benzene–acetone (97 : 3).

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-(carboxymethyl)oxime* (**27**). Aldehyde **26** (1.33 g, 3.0 mmol) and *O*-(carboxymethyl)hydroxylamine hemihydrochloride (984 mg, 9.0 mmol) afforded 1.03 g (67%) of **27**, m.p. 125–127°C (methanol), $[\alpha]_D$ –106 (*c* 1.9, chloroform). IR spectrum: 3 507 (O–H, COOH monomer); 2 660, 2 565 (O–H, COOH dimer); 1 772 (C=O, COOH monomer); 1 727 (C=O, acetate and COOH dimer); 1 254, 1 034 (C–O, acetate). ^{1}H NMR spectrum: 7.42 bs, 1 H (H-19); 5.64 bd, 1 H, $J \approx 5$ (H-6); 4.67 s, 2 H (=N–O–CH_2); 4.62 m, 1 H, W = 32 (H-3α); 2.03 s, 3 H (CH_3COO); 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); 0.63 s, 3 H (3 x H-18). For $C_{31}H_{49}NO_5$ (515.7) calculated: 72.20% C, 9.58% H, 2.72% N; found: 72.34% C, 9.76% H, 2.56% N.

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-(2-carboxyethyl)oxime* (**29**). Aldehyde **26** (1.33 g, 3.0 mmol) and *O*-(2-carboxyethyl)hydroxylamine hydrochloride[14] (1.27 g, 9.0 mmol) afforded 967 mg (61%) of amorphous **29**, $[\alpha]_D$ –110 (*c* 1.6, chloroform). IR spectrum: 3 513 (O–H, COOH monomer); 2 718 (O–H, COOH dimer); 1 750 shoulder (C=O, COOH monomer); 1 716 (C=O, acetate and COOH dimer); 1 254, 1 032 (C–O, acetate). ^{1}H NMR spectrum: 7.28 bs, 1 H (H-19); 5.63 bd, 1 H, $J \approx 5$ (H-6); 4.63 m, 1 H, W = 32 (H-3α); 4.34 t, 2 H, J = 6.1 (=N–O–CH_2); 2.74 t, 2 H, J = 6.1 (CH_2COO); 2.03 s, 3 H (CH_3COO); 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); 0.62 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: 72.76% C, 9.86% H, 2.38% N.

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-(3-carboxypropyl)oxime* (**31**). Aldehyde **26** (1.33 g, 3.0 mmol) and *O*-(3-carboxypropyl)hydroxylamine hydrochloride[12] (1.40 g, 9.0 mmol) afforded 1.20 g (74%) of **31**, m.p. 133–135°C (methanol), $[\alpha]_D$ –107 (*c* 1.6, chloroform). IR spectrum: 3 518 (O–H, COOH monomer); 2 718, 2 670 (O–H, COOH dimer); 1 751 shoulder (C=O, COOH monomer); 1 727 shoulder (C=O, acetate); 1 713 (C=O, COOH dimer); 1 255, 1 032 (C–O, acetate). ^{1}H NMR spectrum: 7.27 bs, 1 H (H-19); 5.63 bd, 1 H, $J \approx 5$ (H-6); 4.63 m, 1 H, W = 32 (H-3α); 4.11 t, 2 H, J = 6.3 (=N–O–CH_2); 2.74 t, 2 H, J = 7.5 (CH_2COO); 2.03 s, 3 H (CH_3COO); 0.89 d, 3 H, J = 6.4 (3 × H-21); 0.86 d, 6 H, J = 6.4 (3 × H-26 and 3 × H-27); 0.62 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: 72.68% C, 9.73% H, 2.65% N.

General Procedure for the Preparation of Methyl Esters

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 chromatographed on two PLC plates.

*(7Z)-7-Oxocholest-5-en-3*β*-yl acetate O-[(methoxycarbonyl)methyl]oxime* (**15**). From acid **14** (155 mg), after chromatography on two PLC plates in a mixture of benzene–ether (95 : 5), 143 mg (90%) of methyl ester **15** was obtained, m.p. 128–130 °C (hexane), $[\alpha]_D$ –163 (*c* 1.7, chloroform); literature[9] gives m.p. 124–125 °C, $[\alpha]_D$ –175. IR spectrum: 1 754 (C=O, $COOCH_3$); 1 731 (C=O, acetate); 1 641 (C=N); 1 252, 1 033 (C–O, acetate). ^{1}H NMR spectrum: 6.55 bd, 1 H, J = 1.2 (H-6); 4.67 m, 1 H, W = 32 (H-3α); 4.60 and 4.57 AB system, 2 H, J(AB) = 16.2 (=N–O–CH_2); 3.76 s, 3 H ($COOCH_3$); 2.04 s, 3 H (CH_3COO); 1.11 s, 3 H (3 × H-19); 0.92 d, 3 H, J = 6.4 (3 × H-21); 0.86 d, 6 H, J = 6.6 (3 × H-26 and 3 × H-27); 0.68 s, 3 H (3 × H-18).

*(7Z)-7-Oxocholest-5-en-3*β*-yl acetate O-[3-(methoxycarbonyl)propyl]oxime* (**17**). From acid **16** (163 mg), after chromatography on two PLC plates in a mixture of benzene–ether (95 : 5), 148 mg (89%) of methyl ester **17** was obtained, m.p. 116–118 °C (hexane), $[\alpha]_D$ –174 (*c* 1.3, chloroform). IR spectrum: 1 730 (C=O); 1 639 (C=N); 1 252, 1 034 (C–O, acetate); 1 173 (C–O). ^{1}H NMR spectrum:

6.45 bd, 1 H, $J \approx 1$ (H-6); 4.67 m, 1 H, $W = 32$ (H-3α); 4.06 t, 2 H, $J = 6.3$ (=N–O–CH_2); 3.68 s, 3 H ($COOCH_3$); 2.41 t, 2 H, $J = 7.6$ (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, $J = 6.4$ (3 × H-26 and 3 × H-27); 0.69 s, 3 H (3 × H-18). For $C_{34}H_{55}NO_5$ (557.8) calculated: 73.21% C, 9.94% H, 2.51% N; found: 73.45% C, 9.73% H, 2.75% N.

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-[(methoxycarbonyl)methyl]oxime* (**28**). From acid **27** (155 mg), after chromatography on two PLC plates in a mixture of benzene–ether (95 : 5), 136 mg (85%) of methyl ester **28** was obtained, m.p. 84–86 °C (methanol), $[\alpha]_D$ –102 (*c* 1.6, chloroform). IR spectrum: 1 754 (C=O, OCH_2COOCH_3); 1 728 (C=O, acetate); 1 254, 1 033 (C–O, acetate); 1 097 (C–O). ^{1}H NMR spectrum: 7.39 s, 1 H (H-19); 5.63 bd, 1 H, $J \approx 5$ (H-6); 4.64 s, 2 H (=N–O–CH_2); 4.63 m, 1 H, $W = 32$ (H-3α); 3.77 s, 3 H ($COOCH_3$); 2.02 s, 3 H (CH_3COO); 0.89 d, 3 H, $J = 6.1$ (3 × H-21); 0.86 d, 6 H, $J = 6.5$ (3 × H-26 and 3 × H-27); 0.65 s, 3 H (3 × H-18). For $C_{32}H_{51}NO_5$ (529.8) calculated: 72.55% C, 9.70% H, 2.64% N; found: 72.74% C, 9.61% H, 2.85% N.

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-[2-(methoxycarbonyl)ethyl]oxime* (**30**). From acid **29** (159 mg), after chromatography on two PLC plates in a mixture of benzene–ether (95 : 5), 149 mg (91%) of oily methyl ester **30** was obtained, $[\alpha]_D$ –104 (*c* 1.4, chloroform). IR spectrum: 1 728 (C=O); 1 255, 1 032 (C–O, acetate); 1 178, 1 050 (C–O, $COOCH_3$). ^{1}H NMR spectrum: 7.26 s, 1 H (H-19); 5.62 bd, 1 H, $J \approx 5$ (H-6); 4.63 m, 1 H, $W = 32$ (H-3α); 4.34 t, 2 H, $J = 6.5$ (=N–O–CH_2); 3.70 s, 3 H ($COOCH_3$); 2.69 t, 2 H, $J = 6.5$ (CH_2COO); 2.02 s, 3 H (CH_3COO); 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); 0.62 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: 72.67% C, 10.05% H, 2.43% N.

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-[3-(methoxycarbonyl)propyl]oxime* (**32**). From acid **31** (163 mg), after chromatography on two PLC plates in a mixture of benzene–ether (95 : 5), 148 mg (89%) of oily methyl ester **32** was obtained, $[\alpha]_D$ –103 (*c* 1.6, chloroform). IR spectrum: 1 727 (C=O); 1 255, 1 032 (C–O, acetate); 1 173 1 062 (C–O, $COOCH_3$). ^{1}H NMR spectrum: 7.26 s, 1 H (H-19); 5.62 bd, 1 H, $J \approx 5$ (H-6); 4.63 m, 1 H, $W = 32$ (H-3α); 4.09 t, 2 H, $J = 6.3$ (=N–O–CH_2); 3.68 s, 3 H ($COOCH_3$); 2.42 t, 2 H, $J = 7.5$ (CH_2COO); 2.03 s, 3 H (CH_3COO); 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); 0.62 s, 3 H (3 × H-18). For $C_{34}H_{55}NO_5$ (557.8) calculated: 73.21% C, 9.94% H, 2.51% N; found: 73.43% C, 10.13% H, 2.27% N.

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

A 1 M solution of ethyl chloroformate in THF (2.4 ml, 2.4 mmol) was added dropwise at –5 °C to a solution of *O*-(ω-carboxyalkyl)oxime derivative (2.0 mmol) in THF (14 ml) and *N*,*N*-diisopropylethylamine (420 μl, 2.4 mmol). The reaction mixture was stirred at –5 °C for 30 min, then warmed to 0 °C and a solution of sodium borohydride (190 mg, 5.0 mmol) in water (4 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 × 200 ml). The combined extracts were washed successively with dilute hydrochloric acid (1 : 4, 3 ×) and water (3 ×). The solvent was evaporated and the residue was dissolved in methanol (20 ml) and ether (30 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 (50 g) in a mixture of benzene–ether (98 : 2–95 : 5).

*(7Z)-7-Oxocholest-5-en-3*β*-yl acetate O-(2-hydroxyethyl)oxime* (**18**). Reduction of acid **14** (1032 mg) afforded, besides 275 mg (26%) of methyl ester **15**, 620 mg (62%) of hydroxy derivative **18**, m.p. 144–147 °C (petroleum ether), $[\alpha]_D$ –184 (*c* 1.9, chloroform). IR spectrum: 3 604, 3 466 (O–H); 1 729 (C=O); 1 639 (C=N); 1 584 (C=C); 1 252, 1 036 (C–O, acetate); 1 084 (C–OH). ^{1}H NMR spectrum: 6.50 d, 1 H, $J = 1.2$ (H-6); 4.68 m, 1 H, $W = 32$ (H-3α); 4.16 t, 2 H, $J = 4.3$ (=N–O–CH_2); 3.87 bt, 2 H, $J \approx 4.5$ (C**H**$_2$OH); 2.04 s, 3 H (CH_3COO); 1.13 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 $C_{31}H_{51}NO_4$ (501.8) calculated: 74.21% C, 10.25% H, 2.79% N; found: 74.35% C, 10.32% H, 2.95% N.

*(7Z)-7-Oxocholest-5-en-3*β*-yl acetate O-(4-hydroxybutyl)oxime* (**20**). Reduction of acid **16** (1088 mg) afforded, besides 324 mg (29%) of methyl ester **17**, 615 mg (58%) of hydroxy derivative **20**, m.p. 156–158 °C (petroleum ether), $[\alpha]_D$ –181 (*c* 1.5, chloroform). IR spectrum: 3 623 (O–H); 1 729 (C=O); 1 639 (C=N); 1 252, 1 034 (C–O, acetate); 1 048 (C–OH). ^{1}H NMR spectrum: 6.46 bd, 1 H, *J* ≈ 1.5 (H-6); 4.67 m, 1 H, *W* = 32 (H-3α); 4.07 t, 2 H, *J* = 6.0 (=N–O–CH_2); 3.68 m, 2 H, *W* = 17 (C**H**$_2$OH); 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* = 6.4 (3 × H-26 and 3 × H-27); 0.69 s, 3 H (3 × H-18). For $C_{33}H_{55}NO_4$ (529.8) calculated: 74.81% C, 10.46% H, 2.64% N; found: 74.57% C, 10.32% H, 2.76% N.

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-(2-hydroxyethyl)oxime* (**33**). Reduction of acid **27** (1 031 mg) afforded, besides 371 mg (35%) of methyl ester **28**, 552 mg (55%) of hydroxy derivative **33**, m.p. 108–110 °C (petroleum ether), $[\alpha]_D$ –110 (*c* 1.6, chloroform). IR spectrum: 3 608, 3 487 (O–H); 1 727 (C=O); 1 254, 1 032 (C–O, acetate); 1 043 (C–OH). ^{1}H NMR spectrum: 7.33 bs, 1 H (H-19); 5.64 bd, 1 H, *J* ≈ 5 (H-6); 4.63 m, 1 H, *W* = 32 (H-3α); 4.18 m, 2 H, *W* = 9 (=N–O–CH_2); 3.88 m, 2 H, *W* = 15 (C**H**$_2$OH); 2.02 s, 3 H (CH_3COO); 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); 0.62 s, 3 H (3 × H-18). For $C_{31}H_{51}NO_4$ (501.8) calculated: 74.21% C, 10.25% H, 2.79% N; found: 74.35% C, 10.47% H, 2.54% N.

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-(3-hydroxypropyl)oxime* (**34**). Reduction of acid **29** (1.06 g) afforded, besides 257 mg (24%) of methyl ester **30**, 668 mg (65%) of hydroxy derivative **34**, m.p. 121–123 °C (petroleum ether), $[\alpha]_D$ –114 (*c* 1.4, chloroform). IR spectrum: 3 628 (O–H); 1 726 (C=O); 1 254, 1 033 (C–O, acetate); 1 061 (C–OH). ^{1}H NMR spectrum: 7.28 bs, 1 H (H-19); 5.64 bd, 1 H, *J* ≈ 5 (H-6); 4.63 m, 1 H, *W* = 32 (H-3α); 4.22 t, 2 H, *J* = 6.0 (=N–O–CH_2); 3.76 bt, 2 H, *J* ≈ 6 (C**H**$_2$OH); 2.03 s, 3 H (CH_3COO); 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); 0.62 s, 3 H (3 × H-18). For $C_{32}H_{53}NO_4$ (515.8) calculated: 74.52% C, 10.36% H, 2.72% N; found: 74.75% C, 10.22% H, 2.96% N.

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-(4-hydroxybutyl)oxime* (**35**). Reduction of acid **31** (1.09 g) afforded, besides 276 mg (25%) of methyl ester **32**, 631 mg (60%) of hydroxy derivative **35**, m.p. 111–113 °C (petroleum ether), $[\alpha]_D$ –110 (*c* 1.3, chloroform). IR spectrum: 3 624, 3 467 (O–H); 1 726 (C=O); 1 254, 1 032 (C–O, acetate); 1 049 (C–OH). ^{1}H NMR spectrum: 7.26 bs, 1 H (H-19); 5.63 bd, 1 H, *J* ≈ 5 (H-6); 4.64 m, 1 H, *W* = 32 (H-3α); 4.11 t, 2 H, *J* = 6.0 (=N–O–CH_2); 3.68 t, 2 H, *J* = 6.0 (C**H**$_2$OH); 2.02 s, 3 H (CH_3COO); 0.89 d, 3 H, *J* = 6.4 (3 × H-21); 0.86 d, 6 H, *J* = 6.4 (3 × H-26 and 3 × H-27); 0.62 s, 3 H (3 × H-18). For $C_{33}H_{55}NO_4$ (529.8) calculated: 74.81% C, 10.46% H, 2.64% N; found: 74.84% C, 10.55% H, 2.92% N.

General Procedure for Preparation of Aldehydes

To a stirred solution of oxalyl chloride (105 μl, 1.2 mmol) in dichloromethane (6 ml) cooled to –78 °C under argon was added 1 M solution of dimethyl sulfoxide in dichloromethane (2.4 ml). After 10 min a solution of hydroxy derivative (1.0 mmol) in dichloromethane (5 ml) was added, and the resulting reaction mixture was further stirred for 15 min at –78 C. Then triethylamine (670 μl, 4.8 mmol) was added dropwise, and after 10 min stirring at –78 °C, the reaction mixture was allowed to attain the room temperature and stirred for additional 10 min. The mixture was then poured into water (100 ml) and the product was extracted with dichloromethane (2 × 50 ml). Combined extract was washed with 5% aqueous citric acid solution (2 ×), water, saturated aqueous $KHCO_3$ solution and water (2 ×). Evaporation of the solvent *in vacuo* afforded the aldehyde which was used directly for the Wittig reaction.

*(17E)-17-Oxoandrost-5-en-3*β*-yl acetate O-(formylmethyl)oxime* (**4**). Oxidation of hydroxy derivative[2] **1** (390 mg) afforded 353 mg (91%) of aldehyde **4**. ^{1}H NMR spectrum: 9.80 t, 1 H, J = 1.3 (CH=O); 5.39 bd, 1 H, $J \approx 5$ (H-6); 4.61 m, 1 H, W = 32 (H-3α); 4.50 d, 2 H, J = 1.3 (C=N–O–CH_2); 2.04 s, 3 H (CH_3COO); 1.05 s, 3 H (3 × H-19); 0.93 s, 3 H (3 × H-18).

*(17E)-17-Oxoandrost-5-en-3*β*-yl Acetate O-(2-formylethyl)oxime* (**5**). Oxidation of hydroxy derivative[2] **2** (404 mg) afforded 374 mg (93%) of aldehyde **5**. ^{1}H NMR spectrum: 9.80 t, 1 H, J = 2.3 (CH=O); 5.38 bd, 1 H, J ≈ 5 (H-6); 4.60 m, 1 H, W = 32 (H-3α); 4.37 t, 2 H, J = 5.9 (C=N–O–CH_2); 2.69 dt, 2 H, J = 2.3, J' = 5.9 + 5.9 (C**H**$_2$CHO); 2.04 s, 3 H (CH_3COO); 1.05 s, 3 H (3 × H-19); 0.93 s, 3 H (3 × H-18).

*(17E)-17-Oxoandrost-5-en-3*β*-yl acetate O-(3-formylpropyl)oxime* (**6**). Oxidation of hydroxy derivative[2] **3** (418 mg) afforded 381 mg (92%) of aldehyde **6**. ^{1}H NMR spectrum: 9.77 t, 1 H, J = 1.8 (CH=O); 5.39 bd, 1 H, $J \approx 5$ (H-6); 4.60 m, 1 H, W = 32 (H-3α); 4.05 t, 2 H, J = 6.1 (C=N–O–CH_2); 2.51 dt, 2 H, J = 1.8, J' = 7.2 + 7.2 (C**H**$_2$CHO); 2.04 s, 3 H (CH_3COO); 1.04 s, 3 H (3 × H-19); 0.91 s, 3 H (3 × H-18).

*(7Z)-7-Oxocholest-5-en-3*β*-yl acetate O-(formylmethyl)oxime* (**21**). Oxidation of hydroxy derivative **18** (502 mg) afforded 460 mg (92%) of aldehyde **21**. ^{1}H NMR spectrum: 9.82 X part of ABX system, 1 H, J(AX) = J(BX) = 1.5 (CH=O); 6.55 d, 1 H, J = 1.5 (H-6); 4.66 m, 1 H, W = 32 (H-3α); 4.47 and 4.50 AB part of ABX system, 2 H, J(AB) = 17.1 (C=N–O–CH_2); 2.05 s, 3 H (CH_3COO); 1.14 s, 3 H (3 × H-19); 0.92 d, 3 H, J = 6.4 (3 × H-21); 0.87 d, 6 H, J = 6.5 (3 × H-26 and 3 × H-27); 0.68 s, 3 H (3 × H-18).

*(7Z)-7-Oxocholest-5-en-3*β*-yl acetate O-(2-formylethyl)oxime* (**22**). Oxidation of hydroxy derivative[2] **19** (516 mg) afforded 456 mg (89%) of aldehyde **22**. IR spectrum (chloroform): 2 735 (CHO); 1 727 (C=O); 1 252, 1 034 (C–O, acetate). ^{1}H NMR spectrum: 9.82 t, 1 H, J = 2.1 (CH=O); 6.41 d, 1 H, J = 1.2 (H-6); 4.66 m, 1 H, W = 32 (H-3α); 4.66 m, 2 H (C=N–O–CH_2); 2.76 m, 2 H (C**H**$_2$CHO); 2.02 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 = 6.5 (3 × H-26 and 3 × H-27); 0.69 s, 3 H (3 × H-18).

*(7Z)-7-Oxocholest-5-en-3*β*-yl acetate O-(3-formylpropyl)oxime* (**23**). Oxidation of hydroxy derivative **20** (530 mg) afforded 460 mg (87%) of aldehyde **23**. IR spectrum (chloroform): 2 728 (CHO); 1 725 (C=O); 1 252, 1 034 (C–O, acetate). ^{1}H NMR spectrum: 9.83 t, 1 H, J = 1.5 (CH=O); 6.41 d, 1 H, J = 1.1 (H-6); 4.68 m, 1 H, W = 32 (H-3α); 4.07 t, 2 H, J = 6.1 (C=N–O–CH_2); 2.54 dt, 2 H, J = 1.5, J' = 7.2 + 7.2 (C**H**$_2$CHO); 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).

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-(formylmethyl)oxime* (**36**). Oxidation of hydroxy derivative **33** (502 mg) afforded 330 mg (66%) of crude aldehyde **36**. ^{1}H NMR spectrum: 9.84 t, 1 H, J = 1.2 (CH=O); 7.45 s, 1 H (H-19); 5.69 bd, 1 H, $J \approx 5$ (H-6); 4.60 m, 1 H, W = 32 (H-3α); 4.57 d, 2 H, J = 1.2 (C=N–O–CH_2); 2.03 s, 3 H (CH_3COO); 0.90 d, 3 H, J = 6.5 (3 × H-21); 0.86 d, 6 H, J = 6.4 (3 × H-26 and 3 × H-27); 0.64 s, 3 H (3 × H-18).

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-(2-formylethyl)oxime* (**37**). Oxidation of hydroxy derivative **34** (516 mg) afforded 456 mg (88%) of aldehyde **37**. ^{1}H NMR spectrum: 9.82 t, 1 H, J = 2.1 (CH=O); 7.25 s, 1 H (H-19); 5.63 bd, 1 H, $J \approx 5$ (H-6); 4.63 m, 1 H, W = 32 (H-3α); 4.41 t, 2 H, J = 6.0 (C=N–O–CH_2); 2.75 dt, 2 H, J = 2.1, J' = 6.1 + 6.1 (C**H**$_2$CHO); 2.03 s, 3 H (CH_3COO); 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); 0.61 s, 3 H (3 × H-18).

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-(3-formylpropyl)oxime* (**38**). Oxidation of hydroxy derivative **35** (530 mg) afforded 470 mg (89%) of aldehyde **38**. ^{1}H NMR spectrum: 9.79 t, 1 H, J = 1.5 (CH=O); 7.26 s, 1 H (H-19); 5.63 bd, 1 H, $J \approx 5$ (H-6); 4.63 m, 1 H, W = 32 (H-3α); 4.10 t, 2 H, J = 6.3 (C=N–O–CH_2); 2.54 dt, 2 H, J = 1.5, J' = 7.2 + 7.2 (C**H**$_2$CHO); 2.03 s, 3 H (CH_3COO); 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); 0.62 s, 3 H (3 × H-18).

General Procedure for the Wittig Reaction

Triethyl phosphonoacetate (317 μl, 1.6 mmol) was added dropwise under argon to a suspension of sodium hydride (38 mg, 1.6 mmol) in tetrahydrofuran (3 ml). The mixture was stirred at room temperature for 20 min and then a solution of aldehyde (0.8 mmol) in tetrahydrofuran (3 ml) was added. The mixture was stirred at room temperature for 3 h, then poured into a saturated aqueous sodium chloride solution (150 ml), the product was extracted with ethyl acetate (2 × 100 ml). Combined extract was washed with water (2 ×). The solvents were evaporated *in vacuo* and the residue was chromatographed on a column of silica gel (20 g) in benzene–ether (95 : 5) mixture.

*(17E)-17-Oxoandrost-5-en-3*β*-yl acetate O-[(2E)-3-(ethoxycarbonyl)prop-2-en-1-yl]oxime* (**7**). Aldehyde **4** (310 mg) afforded 142 mg (39%) of ester **7**, m.p. 92–95 °C (petroleum ether), $[\alpha]_D$ –43 (*c* 2.3, chloroform). IR spectrum: 1 718 (C=O); 1 662 (C=C); 1 254, 1 032 (C–O, acetate); 1 183 (C–O, ester). ^{1}H NMR spectrum: 7.01 dt, 1 H, *J* = 15.9, *J*′ = 4.4 + 4.4 ($CH_2C\mathbf{H}$=CHCOO); 5.97 dt, 1 H, *J* = 15.9, *J*′ = 2.0 + 2.0 (CH_2CH=C**H**COO); 5.39 bd, 1 H, *J* ≈ 5 (H-6); 4.61 m, 1 H, *W* = 32 (H-3α); 4.20 q, 2 H, *J* = 7.2 ($COOC\mathbf{H}_2CH_3$); 4.69 dd, 2 H, *J* = 4.4, *J*′ = 2.0 (=N–O–CH_2); 2.04 s, 3 H (CH_3COO); 1.29 t, 3 H, *J* = 7.2 ($COOCH_2C\mathbf{H}_3$); 1.04 s, 3 H (3 × H-19); 0.92 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 458 (M + 1). For $C_{27}H_{39}NO_5$ (457.6) calculated: 70.87% C, 8.59% H, 3.06% N; found: 70.95% C, 8.73% H, 3.12% N.

*(17E)-17-Oxoandrost-5-en-3*β*-yl acetate O-[(3E)-4-(ethoxycarbonyl)but-3-en-1-yl]oxime* (**8**). Aldehyde **5** (321 mg) afforded 194 mg (51%) of ester **8**, m.p. 75–78 °C (petroleum ether), $[\alpha]_D$ –38 (*c* 1.5, chloroform). IR spectrum: 1 716 (C=O); 1 655 (C=C); 1 255, 1 034 (C–O, acetate); 1 180 (C–O). ^{1}H NMR spectrum: 6.98 dt, 1 H, *J* = 15.6, *J*′ = 7.0 + 7.0 ($CH_2C\mathbf{H}$=CHCOO); 5.87 dt, 1 H, *J* = 15.6, *J*′ = 1.5 + 1.5 (CH_2CH=C**H**COO); 5.39 bd, 1 H, *J* × 5 (H-6); 4.60 m, 1 H, *W* = 32 (H-3α); 4.19 q, 2 H, *J* = 7.1 ($COOC\mathbf{H}_2CH_3$); 4.13 t, 2 H, *J* ≈ 6.5 (=N–O–CH_2); 2.53 dq, 2 H, *J* = 1.5, *J*′ ≈ 7 + 7 + 7 ($C\mathbf{H}_2CH$=CHCOO); 2.04 s, 3 H (CH_3COO); 1.29 t, 3 H, *J* = 7.1 ($COOCH_2C\mathbf{H}_3$); 1.04 s, 3 H (3 × H-19); 0.91 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 472 (M + 1). For $C_{28}H_{41}NO_5$ (471.6) calculated: 71.31% C, 8.76% H, 2.97% N; found: 71.45% C, 8.87% H, 3.03% N.

*(17E)-17-Oxoandrost-5-en-3*β*-yl acetate O-[(4E)-5-(ethoxycarbonyl)pent-4-en-1-yl]oxime* (**9**). Aldehyde **6** (332 mg) afforded 280 mg (72%) of oily ester **9**, $[\alpha]_D$ –35 (*c* 1.7, chloroform). IR spectrum: 1 716 (C=O); 1 654 (C=C); 1 255, 1 034 (C–O, acetate); 1 176 (C–O). ^{1}H NMR spectrum: 6.99 dt, 1 H, *J* = 15.6, *J*′ = 6.8 + 6.8 ($CH_2C\mathbf{H}$=CHCOO); 5.83 dt, 1 H, *J* = 15.6, *J*′ = 1.5 + 1.5 (CH_2CH=C**H**COO); 5.39 bd, 1 H, *J* ≈ 5 (H-6); 4.60 m, 1 H, *W* = 32 (H-3α); 4.18 q, 2 H, *J* = 7.0 ($COOC\mathbf{H}_2CH_3$); 4.03 t, 2 H, *J* = 6.2 (=N–O–CH_2); 2.04 s, 3 H (CH_3COO); 1.28 t, 3 H, *J* = 7.0 ($COOCH_2C\mathbf{H}_3$); 1.04 s, 3 H (3 × H-19); 0.91 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 486 (M + 1). For $C_{29}H_{43}NO_5$ (485.7) calculated: 71.72% C, 8.92% H, 2.88% N; found: 71.57% C, 8.71% H, 2.61% N.

*(7Z)-7-Oxocholest-5-en-3*β*-yl acetate O-[(3E)-4-(ethoxycarbonyl)but-3-en-1-yl]oxime* (**24**). Aldehyde **22** (411 mg) afforded 268 mg (57%) of oily ester **24**, $[\alpha]_D$ –144 (*c* 1.2, chloroform). IR spectrum: 1 720 (C=O); 1 655 (C=C, CH=CHCOO); 1 642 (C=N); 1 253, 1 035 (C–O, acetate); 1 180 (C–O). ^{1}H NMR spectrum: 6.98 dt, 1 H, *J* = 15.6, *J*′ = 7.0 + 7.0 ($CH_2C\mathbf{H}$=CHCOO); 6.44 d, 1 H, *J* = 1.2 (H-6); 5.88 dt, 1 H, *J* = 15.6, *J*′ = 1.5 + 1.5 (CH_2CH=C**H**COO); 4.67 m, 1 H, *W* = 32 (H-3α); 4.19 q, 2 H, *J* = 7.1 ($COOC\mathbf{H}_2CH_3$); 4.13 t, 2 H, *J* = 6.7 (=N–O–CH_2); 2.04 s, 3 H (CH_3COO); 1.29 t, 3 H, *J* = 7.2 ($COOCH_2C\mathbf{H}_3$); 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). Mass spectrum, *m/z*: 584 (M + 1). For $C_{36}H_{57}NO_5$ (583.9) calculated: 74.06% C, 9.84% H, 2.40% N; found: 73.95% C, 9.63% H, 2.21% N.

*(7Z)-7-Oxocholest-5-en-3*β*-yl acetate O-[(4E)-5-(ethoxycarbonyl)pent-4-en-1-yl]oxime* (**25**). Aldehyde **23** (422 mg) afforded 279 mg (58%) of ester **25**, m.p. 74–76 °C (methanol), $[\alpha]_D$ –161 (*c* 0.9, chloroform). IR spectrum: 1 718 (C=O); 1 654 (C=C, CH=CHCOO); 1 641 (C=N); 1 252, 1 035 (C–O, acetate); 1 176 (C–O). ^{1}H NMR spectrum: 6.99 dt, 1 H, *J* = 15.6, *J*′ = 6.9 + 6.9

(CH_2CH=CHCOO); 6.46 d, 1 H, J = 0.9 (H-6); 5.84 dt, 1 H, J = 15.6, J' = 1.5 + 1.5 (CH_2CH=C**H**COO); 4.68 m, 1 H, W = 32 (H-3α); 4.18 q, 2 H, J = 7.2 (COOC**H**$_2$CH$_3$); 4.05 t, 2 H, J = 6.3 (=N–O–CH_2); 2.04 s, 3 H (CH_3COO); 1.29 t, 3 H, J = 7.2 (COOCH$_2$C**H**$_3$); 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). Mass spectrum, *m/z*: 598 (M + 1). For $C_{37}H_{59}NO_5$ (597.9) calculated: 74.33% C, 9.95% H, 2.34% N; found: 74.23% C, 10.07% H, 2.13% N.

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-[(3E)-4-(ethoxycarbonyl)but-3-en-1-yl]oxime* (**39**). Aldehyde **37** (411 mg) afforded 360 mg (77%) of oily ester **39,** $[\alpha]_D$ –98 (*c* 1.5, chloroform). IR spectrum: 1 718 (C=O); 1 655 (C=C, CH=CHCOO); 1 254, 1 034 (C–O, acetate); 1 180 (C–O). ^{1}H NMR spectrum: 7.27 s, 1 H (H-19); 6.98 dt, 1 H, J = 15.6, J' = 6.5 + 6.5 (CH_2C**H**=CHCOO); 5.90 dt, 1 H, J = 15.6, J' = 1.5 + 1.5 (CH_2CH=C**H**COO); 5.62 bd, 1 H, $J \approx 5$ (H-6); 4.63 m, 1 H, W = 32 (H-3α); 4.19 q, 2 H, J = 7.1 (COOC**H**$_2$CH$_3$); 4.17 t, 2 H, J = 6.5 (=N–O–CH_2); 2.57 dq, 1 H, J = 1.5, J' = 6.5 + 6.5 + 6.5 (C**H**$_2$CH=CHCOO); 2.03 s, 3 H (CH_3COO); 1.29 t, 3 H, J = 7.1 (COOCH$_2$C**H**$_3$); 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). Mass spectrum, *m/z*: 584 (M + 1). For $C_{36}H_{57}NO_5$ (583.9) calculated: 74.06% C, 9.84% H, 2.40% N; found: 73.87% C, 9.75% H, 2.56% N.

*(19E)-19-Oxocholest-5-en-3*β*-yl acetate O-[(4E)-5-(ethoxycarbonyl)pent-4-en-1-yl]oxime* (**40**). Aldehyde **38** (422 mg) afforded 382 mg (80%) of oily ester **40**, $[\alpha]_D$ –95 (*c* 1.8, chloroform). IR spectrum: 1 716 (C=O); 1 655 (C=C, CH=CHCOO); 1 255, 1 034 (C–O, acetate); 1 176 (C–O). ^{1}H NMR spectrum: 7.27 s, 1 H (H-19); 6.99 dt, 1 H, J = 15.8, J' = 6.9 + 6.9 (CH_2C**H**=CHCOO); 5.85 dt, 1 H, J = 15.8, J' = 1.5 + 1.5 (CH_2CH=C**H**COO); 5.63 bd, 1 H, $J \approx 5$ (H-6); 4.63 m, 1 H, W = 32 (H-3α); 4.18 q, 2 H, J = 7.2 (COOC**H**$_2$CH$_3$); 4.08 t, 2 H, J = 6.4 (=N–O–CH_2); 2.03 s, 3 H (CH_3COO); 1.29 t, 3 H, J = 7.2 (COOCH$_2$C**H**$_3$); 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); 0.62 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 598 (M + 1). For $C_{37}H_{59}NO_5$ (597.9) calculated: 74.33% C, 9.95% H, 2.34% N; found: 74.57% C, 9.88% H, 2.11% N.

General Procedure for Hydrolysis of Ethyl Esters

Ester (0.3 mmol) in tetrahydrofuran (8 ml) and methanol (4 ml) at room temperature was treated with 2 M aqueous KOH (4 ml) while stirring. After 6 h, the reaction mixture was neutralized with dilute hydrochloric acid (1 : 4), the solvents were evaporated *in vacuo*, and the residue was partitioned between ethyl acetate and water. The aqueous phase was extracted with ethyl acetate, and the combined organic phase was washed with water. The solvent was evaporated, and the residue was crystallized from dichloromethane–petroleum ether.

*(17E)-3*β*-Hydroxyandrost-5-en-17-one O-[(2E)-3-carboxyprop-2-en-1-yl]oxime* (**10**). Ester **7** (137 mg) afforded 96 mg (83%) of acid **10**, m.p. 205–215 °C (decomposition), $[\alpha]_D$ –39 (*c* 1.3, chloroform–methanol 1 : 1). IR spectrum (KBr): 3 350 (O–H); 2 674, 2 596 (O–H, COOH dimer); 1 685 (C=O); 1 663 (C=C); 1 050 (C–O). ^{1}H NMR spectrum: 7.02 dt, 1 H, J = 15.9, J' = 4.3 + 4.3 (CH_2C**H**=CHCOO); 5.96 dt, 1 H, J = 15.9, J' = 2.0 + 2.0 (CH_2CH=C**H**COO); 5.36 bd, 1 H, $J \approx 5$ (H-6); 4.70 dd, 2 H, J = 4.3, J' = 2.0 (=N–O–CH_2); 3.50 m, 1 H, W = 32 (H-3α); 1.03 s, 3 H (3 × H-19); 0.93 s, 3 H (3 × H-18). For $C_{23}H_{33}NO_4$ (387.5) calculated: 71.29% C, 8.58% H, 3.61% N; found: 71.12% C, 8.45% H, 3.78% N.

*(17E)-3*β*-Hydroxyandrost-5-en-17-oneO-[(3E)-4-carboxybut-3-en-1-yl]oxime* (**11**). Ester **8** (141 mg) afforded 79 mg (66%) of acid **11**, m.p. 185–195 °C (decomposition), $[\alpha]_D$ –38 (*c* 1.3, chloroform–methanol 1 : 1). IR spectrum (KBr): 3 291 (O–H); 2 635 (O–H, COOH dimer); 1 702 (C=O); 1 655 (C=C); 1 047 (C–O). ^{1}H NMR spectrum: 7.09 dt, 1 H, J = 15.6, J' = 7.0 + 7.0 (CH_2C**H**=CHCOO); 5.88 dt, 1 H, J = 15.6, J' = 1.5 + 1.5 (CH_2CH=C**H**COO); 5.36 bd, 1 H, $J \approx 5$ (H-6); 4.45 t, 2 H, J =

6.3 (=N–O–CH_2); 3.53 m, 1 H, *W* = 32 (H-3α); 1.03 s, 3 H (3 × H-19); 0.91 s, 3 H (3 × H-18). For $C_{24}H_{35}NO_4$ (401.6) calculated: 71.79% C, 8.79% H, 3.49% N; found: 72.05% C, 8.96% H, 3.23% N.

(17E)-3β-Hydroxyandrost-5-en-17-one O-[(4E)-5-carboxypent-4-en-1-yl]oxime (**12**). Ester **9** (146 mg) afforded 85 mg (68%) of acid **12**, m.p. 153–163 °C (decomposition), $[\alpha]_D$ –43 (*c* 1.1, chloroform). IR spectrum: 3 608 (O–H); 3 516 (O–H, COOH monomer); 2 679 (O–H, COOH dimer); 1 698 (C=O); 1 653 (C=C); 1 047 (C–O). ^{1}H NMR spectrum: 7.10 dt, 1 H, *J* = 15.6, *J*′ = 7.0 + 7.0 (CH_2C**H**=CHCOO); 5.84 dt, 1 H, *J* = 15.6, *J*′ = 1.4 + 1.4 (CH_2CH=C**H**COO); 5.36 bd, 1 H, *J* ≈ 5 (H-6); 4.04 t, 2 H, *J* = 6.3 (=N–O–CH_2); 3.54 m, 1 H, *W* = 32 (H-3α); 1.03 s, 3 H (3 × H-19); 0.92 s, 3 H (3 × H-18). For $C_{25}H_{37}NO_4$ (415.6) calculated: 72.26% C, 8.97% H, 3.37% N; found: 72.13% C, 9.16% H, 3.45% N.

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