ACRYLATE SIDE CHAIN DERIVATIVES OF 5β-STEROIDS*

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Steroids with 5β-configuration and acrylate 17β-side chain, namely, methyl (20*E*)-3β-hydroxy-5β-pregnane-21-carboxylate (*XVI*), its 3α-epimer *XXVI*, and homological ethyl ester *XVIII* were prepared from 3β-(2-tetrahydropyranyloxy)-21-norpregn-5-en-20-ol (*I*). The stereoselectivity of key steps was checked. Whereas hydrogenation of 4-en-3-one derivative *IV* gave exclusively 5β-derivative *VI*, the subsequent borohydride reduction yielded 3β- and 3α-hydroxy derivatives *VII* and *XI* in 1 : 4 ratio. The 3-hydroxy derivatives prepared (*XVI*, *XVIII*, and *XXVI*) were converted to the corresponding hemisuccinates (*XX* and *XXVIII*) and β-D-glucopyranosides (*XXII*, *XXIV*, and *XXX*) for latter use in biological studies.

Recently we described[1] the preparation of methyl and ethyl esters of (20*E*)-3-hydroxy-5α-pregn-20-en-21-carboxylic acid, their hemisuccinates and β-D-glucopyranosides. To extend the study to the analogical derivatives with cis-annulation of rings A and B less accessible starting compounds, i.e. derivatives of 21-nor-5β-pregnane, were needed. From derivatives of this type only (20*E*)-21-ethoxycarbonyl-5β-pregn-20-en-3β-yl hydrogen butanedioate has been prepared[2]. As a source of 5β-steroid skeleton served[2] 20-oxo-5β-pregnane-3β-yl acetate, minor by-product from pregnenolone acetate hydrogenation, separated by tedious chromatographic methods only in small quantities.

The aim of present work was to find the synthetic way affording sufficient amounts of suitable 21-nor-5β-pregnane derivatives and to prepare corresponding α,β-unsaturated esters, their hemisuccinates and β-D-glucopyranosides.

As the starting compound we used easily available[3] partially protected diol *I* with double bond in position 5. For conversion of 3β-hydroxy 5-unsaturated arrangement to corresponding 3-hydroxy derivative of 5β-series we adopted the procedure developed earlier[4] for similar transformation of androstane derivatives. First we changed the protection in positions 3 and 20 by preparing the 20-pivalate *III* via fully blocked diol *II* (Scheme 1). Free 3-hydroxy group was needed for the subsequent Oppenauer oxidation

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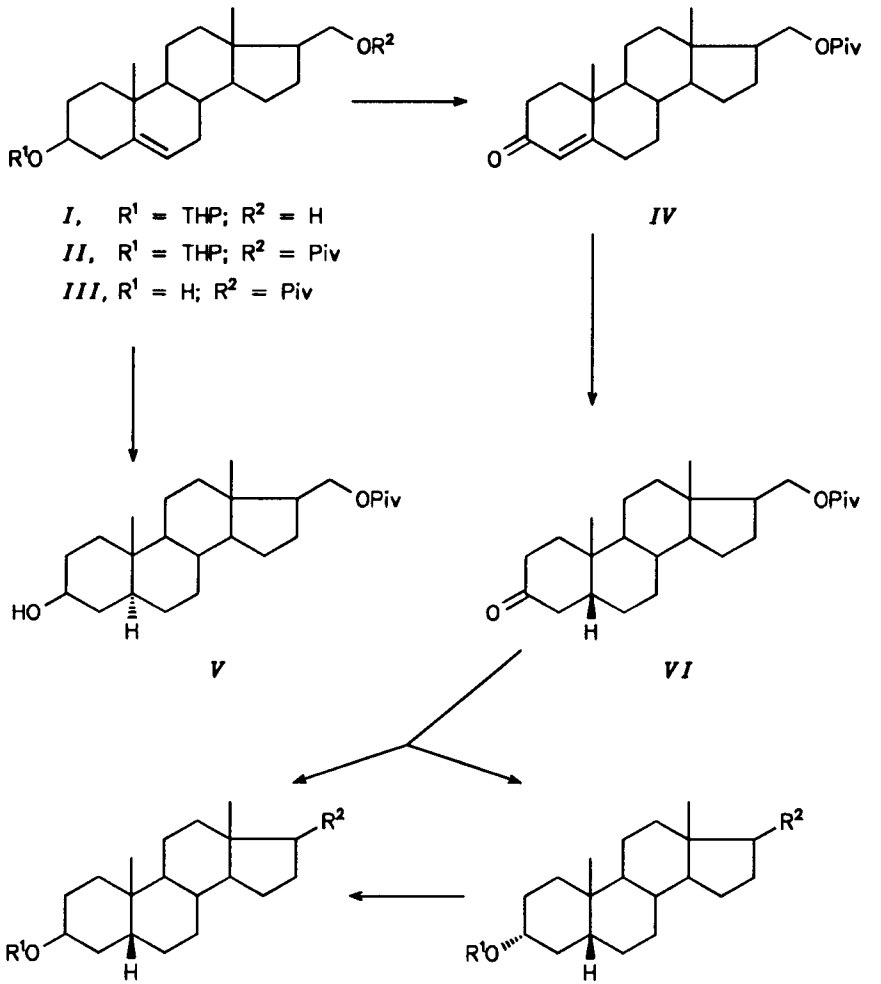


I, R^1 = THP; R^2 = H
II, R^1 = THP; R^2 = Piv
III, R^1 = H; R^2 = Piv

IV

V

VI

VII, R^1 = H; R^2 = CH_2OPiv
VIII, R^1 = THP; R^2 = CH_2OH
IX, R^1 = H; R^2 = COOH
X, R^1 = THP; R^2 = CHO

XI, R^1 = H; R^2 = CH_2OPiv
XII, R^1 = Ts; R^2 = CH_2OPiv
XIII, R^1 = THP; R^2 = CH_2OH
XIV, R^1 = THP; R^2 = CHO

Piv: pivaloyl

SCHEME 1

which afforded α,β-unsaturated ketone *IV*. This derivative was then hydrogenated on palladium on activated carbon in ethanol with addition of aqueous sodium hydroxide. Crude ketone *VI* with desired 5β-configuration was reduced with sodium borohydride yielding the mixture of 3β-hydroxy derivative *VII* and its 3α-epimer *XI* in about 1 : 4 ratio. Re-oxidation of both hydroxy derivatives *VII* and *XI* with pyridinium chlorochromate gave the same product, ketone *VI*.

We checked the above mentioned mixture for presence of 3β,5α-derivative *V* which could originate from the less favorable α-side attack of hydrogen in hydrogenation reaction. The authentic sample of derivative *V* was independently prepared by hydrogenation of unsaturated derivative *III* with palladium on activated carbon in ethyl acetate. By means of thin-layer chromatography we did not reveal the presence of derivative *V* and this may serve as a confirmation of the stereospecificity of hydrogen addition.

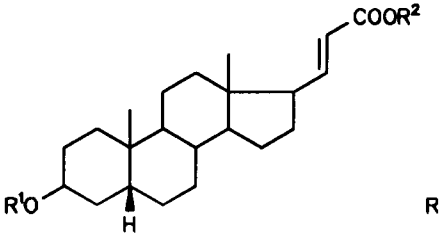
The configuration assignment for hydroxy derivatives *VII* and *XI* follows from analysis of their ^{1}H NMR spectra. The width of H-3 signal of in situ prepared[5] trichloroacetyl carbamate amounts of 14 Hz for derivative *VII* and confirms the axial orientation of hydroxyl group, i.e. the configuration of 3β. We used TAI derivatization for avoiding the overlap of this multiplet with signals of H-20. Epimeric 3α-hydroxy derivative *XI* exhibits much broader H-3 multiplet (36 Hz) in accord with equatorial hydroxyl orientation. Prevailing 3α-hydroxy derivative *XI* was in part converted via tosylate *XII* into the 3β-hydroxy derivative *VII*.

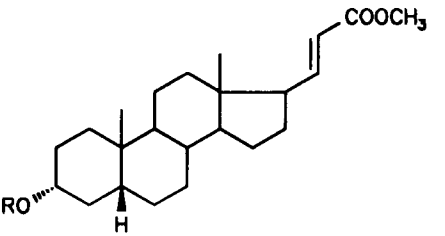
Both hydroxy derivatives *VII* and *XI* were reacted with dihydropyran to protect 3-hydroxy groups in form of THP-derivatives. Then the pivaloyl groups were split-off by sodium bis(2-methoxyethoxy)dihydroaluminate and 20-hydroxy derivatives *VIII* and *XIII*, respectively, were prepared. Additional structural proof for the derivative *VIII* was achieved by its independent synthesis from known[2] 3β,5β-etianic acid *IX*.

The rest of the synthesis of α,β-unsaturated esters *XVI*, *XVIII* and *XXVI* from hydroxy derivatives *VIII* and *XIII* was accomplished after the known procedure via aldehydes *X* and *XIV*. Purity of the target compounds was checked by HPLC. Table I gives the mobilities of these hydroxy derivatives with comparable derivatives *XXXI* – *XXXIII* prepared earlier. We were able to differentiate all possible isomers which could originate from different sterical courses both in hydrogenation and in borohydride reduction steps during the synthesis.

From hydroxy derivatives *XVI* and *XXVI* bearing methyl ester group the hemisuccinates *XX* and *XXVIII*, respectively, were prepared via 2-(trimethylsilyl)ethyl succinates *XIX* and *XXVII*. Hemisuccinate homological to *XX* with ethyl ester side chain was prepared by different procedure recently[2]. Hydroxy derivatives *XVI*, *XVIII* and *XXVI* were converted also to β-D-glucopyranosides *XXII*, *XXIV* and *XXX*, respectively. ^{1}H NMR spectra of their acetates *XXI*, *XXIII* and *XXIX* exhibit the patterns characteristic[6] for skeletal protons of β-D-glucopyranoside tetraacetates.

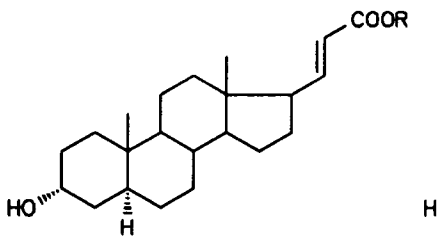
The polar steroid derivatives of α,β-unsaturated esters (hemisuccinates, D-glucosides) are designed for Na^+,K^+-ATPase inhibition studies and this work forms a part of broader project dealing with structural prerequisites for steroid–enzyme interactions.

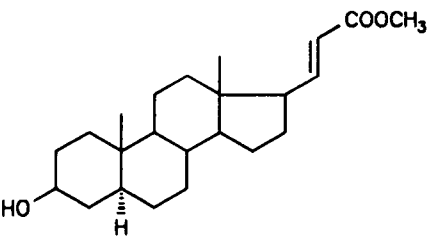




XV, R^1 = THP; R^2 = CH_3
XVI, R^1 = H; R^2 = CH_3
XVII, R^1 = THP; R^2 = C_2H_5
XVIII, R^1 = H; R^2 = C_2H_5
XIX, R^1 = $COCH_2CH_2COOTse$; R^2 = CH_3
XX, R^1 = $COCH_2CH_2COOH$; R^2 = CH_3
XXI, R^1 = Ac_4-β-D-Glc; R^2 = CH_3
XXII, R^1 = β-D-Glc; R^2 = CH_3
XXIII, R^1 = Ac_4-β-D-Glc; R^2 = C_2H_5
XXIV, R^1 = β-D-Glc; R^2 = C_2H_5

XXV, R = THP
XXVI, R = H
XXVII, R = $COCH_2CH_2COOTse$
XXVIII, R = $COCH_2CH_2COOH$
XXIX, R = Ac_4-β-D-Glc
XXX, R = β-D-Glc





XXXI, R = CH_3
XXXII, R = C_2H_5

XXXIII

Tse: $(CH_3)_3SiCH_2CH_2$
Ac_4-β-D-: tetra-*o*-acetyl-β-D-glucopyranosyl
β-D-Glc: β-D-glucopyranosyl

EXPERIMENTAL

Melting points were determined on a micro melting point apparatus Boetius (Germany). Optical rotations were measured on a Perkin–Elmer 141 MC polarimeter at 25 °C. IR spectra were taken on a Perkin–Elmer PE 580 spectrometer (wavenumbers in cm^{-1}). ^1H NMR spectra were obtained with a Tesla BS-467 (CW mode, 60 MHz) and Tesla BS-497 (FT mode, 100 MHz) instruments at 23 °C in deuteriochloroform with tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. All parameters were obtained by the first-order analysis. Mass spectra were recorded on a VG Analytical ZAB-EQ spectrometer (energy of ionizing electrons 70 eV, ion source temperature 170 – 200 °C). Column chromatography was performed on silica gel (60 – 120 μm) or on neutral alumina (Reanal, activity II), thin-layer chromatography on silica gel G according to Stahl (ICN Biochemicals). HPLC analysis was carried out on Spectra-Physics SP 8800, SP 4290, SP 8450 instruments (detection at 230 nm) and 250 × 4 mm column packed with Separon SGX C18 (Tessek, Prague). Samples were applied as 1 mg ml^{-1} solutions (10 μl) in methanol. Solutions in organic solvents were dried over anhydrous sodium sulfate and the solvents were evaporated in vacuo (about 2 kPa). Analytical samples were dried over phosphorus pentoxide at 40 °C/26 Pa for 12 h. The identity of samples prepared by different routes was checked by comparison of their IR and ^1H NMR spectra, thin-layer chromatography and mixture melting point determination.

3β-(2-Tetrahydropyranyloxy)-21-norpregn-5-en-20-yl Pivalate (*II*)

The solution of compound *I* (ref.[3], 13.4 g, 34.5 mmol) and 4-dimethylaminopyridine (428 mg, 3.5 mmol) in pyridine (130 ml) was cooled to 0 °C and pivaloyl chloride (8.5 ml, 70.0 mmol) was added dropwise. The reaction mixture was allowed to stay for 12 h at room temperature and then poured onto ice (500 g). The product was extracted with ether and the extract was washed with saturated aqueous solution of potassium hydrogen carbonate (3 ×) and water, dried and solvent was evaporated. The residue was chromatographed on a column of alumina (600 g). Elution with light petroleum–benzene–ether (50 : 49 : 1) gave 14.2 g (87%) of pivalate *II*, which was used directly in the next step. An analytical sample was obtained by crystallization from light petroleum, m.p. 115 – 119 °C; $[\alpha]_D$ −41° (*c* 0.3, chloroform). IR spectrum (tetrachloromethane): 1 726 (C=O); 1 668 (C=C). ^1H NMR spectrum (60 MHz): 5.34 bd, 1 H (H-6, J = 4.5); 4.71 bs, 1 H (H-2′ of tetrahydropyranyloxy

TABLE I
HPLC retention times (t_r) of isomeric α,β-unsaturated esters on Separon SGX C18 in methanol–water (9 : 1), flow rate 1 ml min^{-1}, pressure 10.69 MPa

Compound	Configuration	Ester	t_r, min
XXXIII[a]	3β,5α	$COOCH_3$	6.44
XXVI	3α,5β	$COOCH_3$	5.46
XXXI[a]	3α,5α	$COOCH_3$	6.10
XVI	3β,5β	$COOCH_3$	6.26
XXXII[a]	3α,5α	$COOC_2H_5$	6.31
XVIII	3β,5β	$COOC_2H_5$	6.57

[a] Ref.[1].

group); 4.03 m, 2 H (2 × H-20); 1.18 s, 9 H ($OOCC(CH_3)_3$); 1.00 s, 3 H (3 × H-19); 0.65 s, 3 H (3 × H-18). For $C_{30}H_{48}O_4$ (472.7) calculated: 76.23% C, 10.24% H; found: 76.60% C, 10.10% H.

3β-Hydroxy-21-norpregn-5-en-20-yl Pivalate (*III*)

To a solution of compound *II* (14.1 g, 29.8 mmol) in a mixture of benzene (150 ml) and methanol (360 ml) 10% hydrochloric acid (48 ml) was added . After stirring at room temperature for 1.5 h, the solvents were evaporated and the residue was partitioned between water and ether. The aqueous phase was extracted with ether and the combined ethereal phases were washed with saturated aqueous solution of potassium hydrogen carbonate (3 ×) and water, dried and solvent was evaporated. Crystallization of the residue from acetone–methanol–water gave 10.0 g (86%) of product *III*, m.p. 113 – 114 °C; $[\alpha]_D$ −54° (*c* 0.2, chloroform). IR spectrum (chloroform): 3 610, 3 490 (O–H); 1 717 (C=O); 1 670 sh (C=C). ^{1}H NMR spectrum (100 MHz): 5.35 bd, 1 H (H-6, *J* = 4.5); 4.04 m, 2 H (2 × H-20); 3.48 m, 1 H (H-3α, *W* = 36); 1.19 s, 9 H ($OOCC(CH_3)_3$); 1.02 s, 3 H (3 × H-19); 0.68 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 388 (M^+), 370 (M – 18). For $C_{25}H_{40}O_3$ (388.6) calculated: 77.27% C, 10.38% H; found: 77.24% C, 10.21% H.

3-Oxo-21-norpregn-4-en-20-yl Pivalate (*IV*)

1-Methyl-4-piperidone (21 ml, 171 mmol) was added under argon to a solution of hydroxy derivative *III* (12.0 g, 30.9 mmol) in toluene (415 ml). A part (50 ml) of toluene was distilled off and 1 M solution of aluminum isopropoxide in toluene (27 ml) was added. After refluxing under argon for 4 h, the reaction mixture was cooled, diluted with ether (500 ml) and washed with 10% hydrochloric acid (3 ×), water, saturated aqueous solution of potassium hydrogen carbonate, water and dried. The solvents were evaporated and the residue was chromatographed an a column of alumina (1 kg) in light petroleum–benzene–ether (50 : 45 : 5) to give 8.43 g (71%) of ketone *IV*, m.p. 93 – 95 °C (light petroleum); $[\alpha]_D$ +86° (*c* 0.4, chloroform). IR spectrum (tetrachloromethane): 1 726 (C=O, ester); 1 677 (C=O, ketone); 1619 (C=C); 1 156 (C–O). ^{1}H NMR spectrum (100 MHz): 5.73 bs, 1 H (H-4); 4.04 m, 2 H (2 × H-20); 1.19 s, 12 H ($OOCC(CH_3)_3$ and 3 × H-19); 0.72 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 386 (M^+). For $C_{25}H_{38}O_3$ (386.6) calculated: 77.68% C, 9.91% H; found: 77.40% C, 9.83% H.

3β-Hydroxy-21-nor-5α-pregnan-20-yl Pivalate (*V*)

Olefin *III* (505 mg, 1.3 mmol) was hydrogenated in ethyl acetate (30 ml) over 10% palladium on activated carbon (50 mg) at ambient temperature and pressure until corresponding amount of hydrogen was consumed (31 ml, 1.3 mmol). The catalyst was filtered off, washed with ethyl acetate and the filtrate was taken down in vacuo. Crystallization of the residue from methanol gave 265 mg (52%) of hydroxy derivative *V*, m.p. 66 – 69 °C; $[\alpha]_D$ +5° (*c* 0.1, chloroform). IR spectrum (chloroform): 3 610, 3 480 (O–H); 1 717 (C=O); 1 166 (C–O). ^{1}H NMR spectrum (100 MHz): 4.02 m, 2 H (2 × H-20); 3.58 m, 1 H (H-3α, *W* = 36); 1.18 s, 9 H ($OOCC(CH_3)_3$); 0.82 s, 3 H (3 × H-19); 0.65 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 390 (M^+), 372 (M – H_2O). For $C_{25}H_{42}O_3$ (390.6) calculated: 76.87% C, 10.84% H; found: 76.76% C, 10.99% H.

3-Oxo-21-nor-5β-pregnan-20-yl Pivalate (*VI*)

A) Pyridinium chlorochromate (216 mg, 1 mmol) was added to a solution of hydroxy derivative *VII* (117 mg, 0.3 mmol) in dichloromethane (3 ml). After 2 h stirring at room temperature the reaction mixture was diluted with ether (10 ml), filtered through a column of alumina (5 g) and the product was washed out with ether. The combined filtrates were concentrated in vacuo. Yield 110 mg (95%) of oily ketone *VI*; $[\alpha]_D$ +21° (*c* 0.3, chloroform). IR spectrum (tetrachloromethane): 1 722 (C=O); 1 158 (C–O). ^{1}H NMR spectrum (100 MHz): 4.04 bd, 1 H (2 × H-20, *J* = 7); 1.19 s, 9 H ($OOCC(CH_3)_3$); 1.03 s, 3 H (3 × H-19); 0.69 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 388 (M^+), 373 (M – CH_3), 355 (M – CH_3 – H_2O). For $C_{25}H_{40}O_3$ (388.6) calculated: 77.27% C, 10.38% H; found: 77.03% C, 10.11% H.

B) Hydroxy derivative *XI* (117 mg, 0.3 mmol) was oxidized in the same manner as described above. Yield 104 mg (89%) of ketone *VI* identical with the product prepared by procedure *A*).

C) Fractions containing ketone *VI* (see preparation of hydroxy derivative *VII*, procedure *B*)) were collected and solvents were evaporated affording 404 mg (19%) of ketone *VI* identical with the product prepared by procedure *A*).

3β-Hydroxy-21-nor-5β-pregnan-20-yl Pivalate (*VII*)

A) A solution of sodium hydroxide (16 g, 400 mmol) in water (80 ml) was added to a solution of unsaturated ketone *IV* (8.43 g, 21.8 mmol) in ethanol (500 ml). The mixture was stirred with 10% palladium on activated carbon (2.5 g) in atmosphere of hydrogen at ambient temperature and pressure until corresponding amount of hydrogen (1.05 l, 44 mmol) was consumed (about 30 min). After addition of acetic acid (23 ml), the catalyst was filtered off and washed with ethyl acetate (100 ml). The solvents were evaporated in vacuo and the residue (containing mainly the saturated ketone *VI*, according to TLC in light petroleum–ether 1 : 1) was dissolved in benzene (160 ml) and methanol (160 ml). Sodium borohydride (1.6 g, 42 mmol) was added to cold (0 °C) solution which was then stirred at 0 °C for 2 h. Acetic acid (4.6 ml) was added and the solvents were evaporated in vacuo. The residue was partitioned between water and ether and the aqueous phase was extracted with ether. The combined organic phases were washed with saturated aqueous solution of potassium hydrogen carbonate (2×), water, dried and the solvent was evaporated. The residue was chromatographed on a column of silica gel (700 g) in light petroleum–benzene–ether (50 : 45 : 5) affording 1.59 g (19%) of amorphous hydroxy derivative *VII*; $[\alpha]_D$ +8° (*c* 1.9, chloroform). IR spectrum (tetrachloromethane): 3 622, 3 440 (O–H); 1 726 (C=O); 1 160 (C–O). ^{1}H NMR spectrum (100 MHz, after addition of trichloroacetyl isocyanate): 8.35 bs, 1 H ($CCl_3CONHCOO$); 5.22 m, 1 H (H-3α, *W* = 14); 4.03 bd, 2 H (2 × H-20, *J* = 6.6); 1.18 s, 9 H ($OOCC(CH_3)_3$); 1.01 s, 3 H (3 × H-19); 0.66 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 372 (M – H_2O). For $C_{25}H_{42}O_3$ (390.6) calculated: 76.87% C, 10.84% H; found: 76.54% C, 10.72% H.

B) A mixture of tosylate *XII* (3.00 g, 5.5 mmol), sodium nitrite (8.63 g, 125 mmol) and hexamethylphosphoramide (65 ml) was stirred at 90 °C for 2 h. After cooling, the reaction mixture was poured into water and product was extracted with ethyl acetate. The extract was washed with 10% sulfuric acid (5 ×), water, saturated aqueous solution of potassium hydrogen carbonate, and water. After drying and evaporation of solvent the residue was chromatographed on a column of silica gel (100 g). Elution with light petroleum–benzene–ether (50 : 45 : 5) afforded ketone *VI*, further elution with light petroleum–benzene–ether (50 : 40 : 10) gave 1.25 g (58%) of hydroxy derivative *VII* identical with the product prepared by procedure *A*).

3β-(2-Tetrahydropyranyloxy)-21-nor-5β-pregnan-20-ol (*VIII*)

A) *p*-Toluenesulfonic acid monohydrate (10 mg, 52 μmol) and 3,4-dihydro-2*H*-pyran (1.20 ml, 13.1 mmol) were added to a solution of compound *VII* (1.45 g, 3.7 mmol) in benzene (30 ml). After stirring for 8 h at room temperature the mixture was mixed with 3.5 M solution of sodium bis(2-methoxyethoxy)dihydroaluminate in benzene (4.0 ml) and refluxed under argon for 2 h. After cooling to room temperature the excess of hydride was decomposed with moist ether and water and the mixture was extracted with ethyl acetate (2 ×). The combined extracts were washed with saturated sodium chloride solution (3 ×), dried and solvents were evaporated. The residue was chromatographed on a column of alumina (150 g) in light petroleum–benzene–ether (50 : 40 : 10) affording 1.02 g (70%) of product *VIII*; m.p. 111 – 113 °C; $[\alpha]_D$ +8° (*c* 0.3, chloroform). IR spectrum (tetrachloromethane): 3 635, 3 470 (O–H). ^{1}H NMR spectrum (100 MHz): 4.63 bs, 1 H (H-2′ of tetrahydropyranyloxy group); 3.96 m, 1 H (H-3, *W* = 14); 0.95 s, 3 H (3 × H-19); 0.64 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 390 (M^+), 372 (M – H_2O). For $C_{25}H_{42}O_3$ (390.6) calculated: 76.87% C, 10.84% H; found: 77.03% C, 10.89% H.

B) *p*-Toluenesulfonic acid monohydrate (10 mg, 52 μmol) and 3,4-dihydro-2*H*-pyran (2.1 ml, 23 mmol) were added to a solution of acid *IX* (ref.[2]; 2.15 g, 6.7 mmol) in benzene (40 ml). After stirring for 5 h at room temperature the mixture was refluxed with 3.5 M solution of sodium bis-(2-methoxyethoxy)dihydroaluminate in benzene (8.0 ml) under argon for 4 h. After cooling to room temperature the excess of hydride was decomposed with moist ether and water and the mixture was partitioned between ethyl acetate (200 ml) and water (100 ml). Aqueous phase was extracted with ethyl acetate and combined organic phases were washed with saturated sodium chloride solution (3 ×), dried and solvents were evaporated. The residue was chromatographed on a column of alumina (200 g), mixture light petroleum–benzene–ether (45 : 45 : 10) eluted non-polar impurities and the same solvent mixture 40 : 40 : 20 eluted 1.84 g (70%) hydroxy derivative *VIII* identical with the product prepared by procedure *A*).

3β-(2-Tetrahydropyranyloxy)-21-nor-5β-pregnan-20-al (*X*)

Anhydrous sodium acetate (328 mg, 4.0 mmol) and pyridinium chlorochromate (1.72 g, 8.0 mmol) were added to a solution of the hydroxy derivative *VIII* (975 mg, 2.5 mmol) in dichloromethane (20 ml). After stirring for 2 h at room temperature in an argon atmosphere, the reaction mixture was diluted with ether (50 ml), filtered through a column of alumina (25 g) and the product was eluted with ether. The combined filtrates were concentrated in vacuo yielding 930 mg (96%) of aldehyde *X*, which was used without further purification. ^{1}H NMR spectrum (100 MHz): 9.77 d, 1 H (H-20, $J \approx 2$); 4.64 bs, 1 H (H-2′ of tetrahydropyranyloxy group); 3.97 m, 1 H (H-3, *W* = 14); 0.96 s, 3 H (3 × H-19); 0.74 s, 3 H (3 × H-18).

3α-Hydroxy-21-nor-5β-pregnan-20-yl Pivalate (*XI*)

Crude α-hydroxy derivative *XI* isolated from the fractions following β-isomer *VII* (see preparation of compound *VII*, procedure *A*)) was purified by repeated chromatography on a column of alumina (500 g) in light petroleum–ether (90 : 10). Yield 6.72 g (79%) of amorphous compound *XI*; $[\alpha]_D$ +15° (*c* 2.7, chloroform). IR spectrum (chloroform): 3 610, 3 530, 3 420 (O–H); 1 717 (C=O); 1 166 (C–O). ^{1}H NMR spectrum (100 MHz): 4.03 m, 2 H (2 × H-20); 3.64 m, 1 H (H-3β, *W* = 36); 1.19 s, 9 H (OOCC(CH_3)$_3$); 0.93 s, 3 H (3 × H-19); 0.70 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 390 (M^+), 372 (M – H_2O). For $C_{25}H_{42}O_3$ (390.6) calculated: 76.87% C, 10.84% H; found: 76.63% C, 10.67% H.

21-Nor-5β-pregnane-3α,20-diyl 3-Tosylate 20-Pivalate (*XII*)

p-Toluenesulfonyl chloride (2.50 g, 13.1 mmol) was added to an ice-cooled solution of hydroxy derivative *XI* (2.38 g, 6.1 mmol) in pyridine (17 ml). After stirring for 24 h at room temperature, the mixture was poured on ice (400 g), the precipitated product was collected, washed with water and dissolved in ether–dichloromethane mixture (2 : 1). This solution was washed with 10% hydrochloric acid (3 ×), water, saturated aqueous solution of potassium hydrogen carbonate and dried. The solvents were evaporated and the residue was chromatographed on a column of silica gel (150 g) in light petroleum–benzene–ether (50 : 45 : 5). Yield 3.06 g (92%) of tosylate *XII*, m.p. 68 – 71 °C (methanol), $[\alpha]_D$ +28° (*c* 0.4, chloroform). IR spectrum (tetrachloromethane): 1 724 (C=O); 1 599 (arom. system); 1 370, 1 189, 1 178 (SO_2); 1 158 (C–O). ^{1}H NMR spectrum (100 MHz): 7.80 bd, 2 H and 7.32 bd, 2 H (H-arom.); 4.46 m, 1 H (H-3β, *W* = 36); 4.01 bd, 2 H (2 × H-20, *J* = 7); 2.44 s, 3 H (CH_3-arom.); 1.18 s, 9 H ($OOCC(CH_3)_3$); 0.89 s, 3 H (3 × H-19); 0.62 s, 3 H (3 × H-18). For $C_{32}H_{48}O_5S$ (544.8) calculated: 70.55% C, 8.88% H, 5.89% S; found: 70.81% C, 8.93% H, 5.83% S.

3α-(2-Tetrahydropyranyloxy)-21-nor-5β-pregnan-20-ol (*XIII*)

The title compound was prepared from the compound *XI* (1.45 g, 3.7 mmol) in the same manner as described for preparation of compound *VIII* from *VII*. Yield 1.30 g (90%) of hydroxy derivative *XIII*. An analytical sample was obtained by crystallization from acetone; m.p. 158 – 161 °C; $[\alpha]_D$ +8° (*c* 2.2, chloroform). IR spectrum (chloroform): 3 620, 3 460 (O–H); 1 132, 1 024 (C–O). ^{1}H NMR spectrum (100 MHz, after addition of trichloroacetyl isocyanate): 8.30 bs, 1 H ($CCl_3CONHCOO$); 4.71 bs, 1 H (H-2′ of tetrahydropyranyloxy group); 4.24 m, 2 H (2 × H-20, *W* = 16); 0.92 s, (3 × H-19); 0.66 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 390 (M^+), 372 (M – H_2O). For $C_{25}H_{42}O_3$ (390.6) calculated: 76.87% C, 10.84% H; found: 76.56% C, 10.71% H.

3α-(2-Tetrahydropyranyloxy)-21-nor-5β-pregnan-20-al (*XIV*)

The title aldehyde was prepared from the hydroxy derivative *XIII* (975 mg, 2.5 mmol) as described for preparation of aldehyde *X* from the hydroxy derivative *VIII*. The obtained aldehyde *XIV* 920 mg (95%) was used without further purification. ^{1}H NMR spectrum (100 MHz): 9.76 d, 1 H (H-20, *J* = 1.6); 4.71 bs, 1 H (H-2′ of tetrahydropyranyloxy group); 0.92 s, 3 H (3 × H-19); 0.72 s, 3 H (3 × H-18).

Methyl (20*E*)-3β-Hydroxy-5β-pregnane-21-carboxylate (*XVI*) via *XV*

Trimethyl phosphonoacetate (1.31 ml, 11.5 mmol) was added during 10 min under cooling (ice bath) in an argon atmosphere to a suspension of sodium hydride (276 mg, 11.5 mmol) in 1,2-dimethoxyethane (26 ml). The mixture was stirred at room temperature for 20 min and a solution of aldehyde *X* (895 mg, 2.3 mmol) in 1,2-dimethoxyethane (26 ml) was added. After stirring at room temperature under argon for 4 h, the solvent was evaporated in vacuo and the residue was partitioned between ether and water. The aqueous phase was extracted with ether, the combined organic phases were washed with water (3 ×), dried and the solvent was evaporated. The residue was chromatographed on a column of alumina (100 g). Light petroleum–ether (96 : 4) eluted non-polar impurities, the same solvent mixture 92 : 8 eluted protected ester *XV* (yield 785 mg, 77%. IR spectrum (tetrachloromethane): 1 723 (C=O); 1 650 (C=C); 1 272 (C–O, ester); 1 134, 1 028, 1 000 (C–O). ^{1}H NMR spectrum (100 MHz): 6.95 dd, 1 H (H-20, *J*(17,20) = 7.6, *J*(20,21) = 15.9); 5.77 dd, 1 H

(H-21, J(17,21) = 1.0, J(20,21) = 15.9); 4.63 bs, 1 H (H-2' of tetrahydropyranyloxy group); 3.97 m, 1 H (H-3α, W = 14); 3.73 s, 3 H ($COOCH_3$); 0.95 s, 3 H (3 × H-19); 0.63 s, 3 H (3 × H-18). Mass spectrum, m/z: 444 (M^+).

p-Toluenesulfonic acid monohydrate (875 mg, 4.6 mmol) was added to a solution of protected ester *XV* (721 mg, 1.62 mmol) in mixture of benzene (15 ml) and methanol (30 ml). After heating to 45 °C for 1 h, the solvents were evaporated in vacuo, the residue was partitioned between dichloromethane and water and the aqueous phase was extracted with ether. The combined organic phases were washed with water, saturated aqueous solution of potassium hydrogen carbonate, water, dried and solvent was evaporated. The residue was chromatographed on a column of silica gel (60 g) in light petroleum–benzene–ether (40 : 40 : 20) affording 534 mg (91% from *XV*) of compound *XVI*, m.p. 120 – 123 °C (hexane–benzene), $[\alpha]_D$ +29° (*c* 0.3, chloroform). IR spectrum (chloroform): 3 615, 3 500 (OH); 1 712 (C=O); 1 650 (C=C). ^{1}H NMR spectrum (100 MHz): 6.96 dd, 1 H (H-20, J(17,20) = 7.6, J(20,21) = 15.9); 5.77 dd, 1 H (H-21, J(17,21) = 1.2, J(20,21) = 15.9); 3.82 m, 1 H (H-3α, W = 12); 3.73 s, 3 H ($COOCH_3$); 0.97 s, 3 H (3 × H-19); 0.63 s, 3 H (3 × H-18). Mass spectrum, m/z: 360 (M^+), 342 (M – H_2O), 327 (M – H_2O – CH_3). For $C_{23}H_{36}O_3$ (360.5) calculated: 76.62% C, 10.06% H; found: 76.87% C, 10.23% H.

Ethyl (20*E*)-3β-Hydroxy-5β-pregnane-21-carboxylate (*XVIII*) via *XVII*

Triethyl phosphonoacetate (2.3 ml, 11.6 mmol) was added during 10 min under cooling (ice bath) in an argon atmosphere to a suspension of sodium hydride (278 mg, 11.6 mmol) in 1,2-dimethoxyethane (5 ml). The mixture was stirred at room temperature for 20 min and a solution of aldehyde *X* (900 mg, 2.3 mmol) in 1,2-dimethoxyethane (5 ml) was added. After stirring at room temperature under argon for 16 h, the solvent was evaporated in vacuo and the residue was partitioned between ether and water. The aqueous phase was extracted with ether, the combined organic phases were washed with saturated aqueous solution of sodium chloride, dried and the solvent was evaporated. The residue was chromatographed on a column of alumina (150 g), mixture light petroleum–ether (96 : 4) eluted non-polar impurities, the same solvent mixture 92 : 8 eluted 860 mg (81%) of product *XVII*. M.p. 78 – 82 °C (hexane), $[\alpha]_D$ +42° (*c* 0.1, chloroform). IR spectrum (tetrachloromethane): 1 718 (C=O); 1 650 (C=C). ^{1}H NMR spectrum (60 MHz): 6.92 dd, 1 H (H-20, J(17,20) = 7.5, J(20,21) = 15.5); 5.73 d, 1 H (H-21, J(20,21) = 15.5); 4.60 bs, 1 H (H-2' of tetrahydropyranyloxy group); 4.16 q, 2 H ($COOCH_2CH_3$, J = 7); 1.28 t, 3 H ($COOCH_2CH_3$, J = 7); 0.95 s, 3 H (3 × H-19); 0.62 s, 3 H (3 × H-18). Concentrated hydrochloric acid (0.5 ml, 6 mmol) was added to a solution of protected ester *XVII* (850 mg, 1.85 mmol) in mixture of benzene (50 ml) and ethanol (50 ml). After stirring at room temperature for 2 h, the solvents were evaporated in vacuo, the residue was dissolved in mixture ethanol–dichloromethane (1 : 3) and the solution was filtered through a column of alumina (50 g). The product was washed out with the same solvent mixture and the combined filtrates were concentrated in vacuo. The residue was chromatographed on a column of silica gel (70 g) in light petroleum–benzene–ether (10 : 10 : 2) affording 585 mg (84% from *XVII*) of product *XVIII*; m.p. 147 – 149 °C (ether), $[\alpha]_D$ +39° (*c* 0.2, chloroform). IR spectrum (chloroform): 3 615, 3 470 (OH); 1 704 (C=O); 1 648 (C=C). ^{1}H NMR spectrum (60 MHz): 6.95 dd, 1 H (H-20, J(17,20) = 7, J(20,21) = 15.5); 5.76 d, 1 H (H-21, J(20,21) = 15.5); 4.17 q, 2 H ($COOCH_2CH_3$, J = 7); 4.09 m, 1 H (H-3α, W = 15); 1.28 t, 3 H ($COOCH_2CH_3$, J = 7); 0.95 s, 3 H (3 × H-19); 0.62 s, 3 H (3 × H-18). Mass spectrum, m/z: 374 (M^+), 356 (M – H_2O), 341 (M – H_2O – CH_3). For $C_{24}H_{38}O_3$ (374.6) calculated: 76.96% C, 10.23% H; found: 76.98% C, 10.21% H.

(20*E*)-21-Methoxycarbonyl-5β-pregn-20-en-3β-yl Hydrogen Butanedioate (*XX*) via *XIX*

2-(Trimethylsilyl)ethyl hydrogen butanedioate[7] (218 mg, 1.0 mmol) and 4-dimethylaminopyridine (7 mg, 60 μmol) were added to a solution of the hydroxy derivative *XVI* (180 mg, 0.5 mmol) in tetrahydrofuran (4 ml). After addition of 0.5 M solution of *N,N'*-dicyclohexylcarbodiimide in benzene (1.3 ml), the reaction mixture was stirred at room temperature for 6 h, diluted with light petroleum (10 ml) and set aside 10 min. The separated *N,N'*-dicyclohexylurea was filtered off, washed with light petroleum, the filtrate was taken down in vacuo and the residue was chromatographed on a column of silica gel (25 g). Light petroleum–benzene–ether (50 : 48 : 2) eluted non-polar impurities, light petroleum–benzene–ether (50 : 46 : 4) washed out 272 mg of succinate *XIX*. IR spectrum (tetrachloromethane): 1 724 (C=O); 1 650 (C=C); 1 250, 852, 840 (Si–C); 1 274, 1 168, 1 152 (C–O). A solution of succinate *XIX* in tetrahydrofuran (4 ml) was stirred with 1 M solution of tetrabutylammonium fluoride in tetrahydrofuran (1 ml) for 8 h at room temperature. The mixture was diluted with benzene (150 ml) and washed with 10% sulfuric acid (2 ×), water (3 ×), dried and the solvents were evaporated. The residue was dissolved in dichloromethane triturated with light petroleum, yield 205 mg (89% from *XVI*) of amorphous hemisuccinate *XX*, $[\alpha]_D$ +2° (*c* 0.3, chloroform). IR spectrum (chloroform): 3 500 – 2 500 (COOH); 1 716 (C=O); 1 650 (C=C); 1 218, 1 180 (C–O). ^{1}H NMR spectrum (100 MHz): 6.96 dd, 1 H (H-20, *J*(17,20) = 7.6, *J*(20,21) = 15.6); 5.77 dd, 1 H (H-21, *J*(17,21) = 0.8, *J*(20,21) = 15.6); 5.12 m, 1 H (H-3α, *W* = 12); 3.72 s, 3 H ($COOCH_3$); 2.66 s, 4 H ($OOCCH_2CH_2COO$); 0.96 s, 3 H (3 × H-19); 0.63 s, 3 H (3 × H-18). For $C_{27}H_{40}O_6$ (460.6) calculated: 70.41% C, 8.75% H; found: 70.70% C, 9.04% H.

Methyl (20*E*)-3β-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyloxy)-5β-pregn-20-ene-21-carboxylate (*XXI*)

A solution of glucoside *XXII* (200 mg, 0.38 mmol) in a mixture of pyridine (5 ml) and acetic anhydride (0.5 ml, 5.3 mmol) was allowed to stand overnight at room temperature. The mixture was coevaporated with toluene under diminished pressure, residue was chromatographed on a column of silica gel (20 g) in benzene–acetone (10 : 1). Yield 257 mg (97%) of product *XXI*, m.p. 217 – 218 °C, $[\alpha]_D$ +7° (*c* 0.2, chloroform). IR spectrum (chloroform): 1 753 (C=O, acetate); 1 710 sh (C=O, ester); 1 650 (C=C); 1 042 (C–O, acetate). ^{1}H NMR spectrum (100 MHz): 6.94 dd, 1 H (H-20, *J*(17,20) = 8, *J*(20,21) = 16); 5.74 d, 1 H (H-21, *J*(20,21) = 16); 5.24 t, 1 H (H-3′, *J*(3′,2′) = *J*(3′,4′) = 9); 5.08 t, 1 H (H-4′, *J*(4′,3′) = *J*(4′,5′) = 9); 5.00 dd, 1 H (H-2′, *J*(2′,1′) = 7.5, *J*(2′,3′) = 9); 4.56 d, 1 H (H-1′, *J*(1′,2′) = 7.5); 4.28 dd, 1 H (H-6′a, *J*(6′a,6′b) = 12, *J*(6′a,5′) = 5); 4.10 dd, 1 H (H-6′b, *J*(6′b,6′a) = 12, *J*(6′b,5′) = 3); 4.00 m, 1 H (H-3α, *W* = 20); 3.73 s, 3 H ($COOCH_3$); 3.68 m, 1 H (H-5′, *W* = 40); 2.07 s, 3 H (CH_3COO); 2.02 s, 9 H (3 × CH_3COO); 0.91 s, 3 H (3 × H-19); 0.62 s, 3 H (3 × H-18). For $C_{37}H_{54}O_{12}$ (690.8) calculated: 64.33% C, 7.88% H; found: 64.62% C, 7.91% H.

Methyl (20*E*)-3β-(β-D-Glucopyranosyloxy)-5β-pregn-20-ene-21-carboxylate (*XXII*)

A dry mixture of hydroxy derivative *XVI* (279 mg, 0.77 mmol), silver silicate[8] (1.0 g) and ground molecular sieve 4Å (1.0 g) was stirred in vacuo (10 Pa) 4 h. The flask was then filled with argon under slight overpressure (about 5 kPa) and 1,2-dichloroethane (5 ml) was injected through a septum. The mixture was stirred at room temperature for 20 min and then a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (480 mg, 1.17 mmol) in 1,2-dichloroethane (3 ml) was added through the septum. After stirring at room temperature for 20 h, the catalyst was filtered through a column of silica gel (layered with Celite). The column was washed with chloroform, and the combined eluates

were washed with 5% aqueous sodium hydrogen carbonate solution, water, dried and the solvents were evaporated. Crude acetyl derivative *XXI* was deacetylated in methanol (10 ml) with 5% solution of sodium methoxide in methanol (5 drops). After 24 h standing at room temperature the mixture was neutralized with solid carbon dioxide (ca 300 mg). After evaporation of solvent in vacuo, the residue was chromatographed on a column of silica gel in chloroform–methanol (10 : 1 to 5 : 1). Yield 296 mg (73%) of glucoside *XXII*, m.p. 193 – 195 °C, $[\alpha]_D$ +24° (*c* 0.2, methanol). IR spectrum (KBr): 3 438 (OH); 1 725 (C=O); 1 652 (C=C); 1 172, 1 077, 1 025 (C–O). For $C_{29}H_{46}O_8$ (522.7) calculated: 66.64% C, 8.87% H; found: 66.79% C, 9.01% H.

Ethyl (20*E*)-3β-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyloxy)-5β-pregn-20-ene-21-carboxylate (*XXIII*)

Preparation of title compound was carried out from hydroxy derivative *XVIII* (360 mg, 0.96 mmol), 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (600 mg, 1.46 mmol) and corresponding amounts of other reagents as in preceding experiment, only the deacetylation step was omitted. The crude acetyl derivative was chromatographed on a column of silica gel (40 g) in light petroleum–ether (9 : 1). Yield 448 mg (66%) of product *XXIII*, m.p. 190 – 191 °C (ethanol), $[\alpha]_D$ +7° (*c* 0.2, chloroform). IR spectrum (chloroform): 1 753 (C=O, acetate); 1 708 (C=O, ester); 1 650 (C=C); 1 042 (C–O, acetate). ^{1}H NMR spectrum (100 MHz): 6.96 dd, 1 H (H-20, J(17,20) = 8, J(20,21) = 16); 5.76 d, 1 H (H-21, J(20,21) = 16); 5.23 t, 1 H (H-3′, J(3′,2′) = J(3′,4′) = 9); 5.06 t, 1 H (H-4′, J(4′,3′) = J(4′,5′) = 9); 4.97 dd, 1 H (H-2′, J(2′,1′) = 7.5, J(2′,3′) = 9); 4.54 d, 1 H (H-1′, J(1′,2′) = 7.5); 4.27 dd, 1 H (H-6′a, J(6′a,6′b) = 12, J(6′a,5′) = 5); 4.17 q, 2 H (OCH_2CH_3, J = 7); 4.11 dd, 1 H (H-6′b, J(6′b,6′a) = 12, J(6′b,5′) = 3); 3.99 m, 1 H (H-3α, W = 12); 3.66 m, 1 H (H-5′, W = 40); 2.07 s, 3 H (CH_3COO); 2.01 s, 9 H (3 × CH_3COO); 1.28 t, 3 H (OCH_2CH_3, J = 7); 0.91 s, 3 H (3 × H-19); 0.62 s, 3 H (3 × H-18). For $C_{38}H_{56}O_{12}$ (704.9) calculated: 64.75% C, 8.01% H; found: 64.93% C, 8.05% H.

Ethyl (20*E*)-3β-(β-D-Glucopyranosyloxy)-5β-pregn-20-ene-21-carboxylate (*XXIV*)

To the solution of acetate *XXIII* (300 mg, 0.43 mmol) in ethanol (10 ml) a 5% solution of sodium ethoxide in ethanol (5 drops) was added. After 24 h standing at room temperature the mixture was neutralized with solid carbon dioxide (ca 300 mg). After evaporation of solvent in vacuo, the residue was chromatographed on a column of silica gel (20 g) in chloroform–methanol (25 : 1 to 10 : 1). Yield 207 mg (91%) of glucoside *XXIV*, m.p. 222 – 224 °C, $[\alpha]_D$ +24° (*c* 0.2, methanol). IR spectrum (KBr): 3 400 (OH); 1 703 (C=O); 1 653 (C=C); 1 172, 1 071, 1 025 (C–O). For $C_{30}H_{48}O_8$ (536.7) calculated: 67.14% C, 9.01% H; found: 66.93% C, 8.88% H.

Methyl (20*E*)-3α-Hydroxy-5β-pregn-20-ene-21-carboxylate (*XXVI*) via *XXV*

Methyl ester *XXVI* was prepared from aldehyde *XIV* (895 mg, 2.3 mmol) according to the preparation of *XVI*, via intermediate *XXV*. Protected ester *XXV* (725 mg, 71%). IR spectrum (tetrachloromethane): 1 727 (C=O); 1 652 (C=C); 1 140, 1 031 (C–O). ^{1}H NMR spectrum (100 MHz): 6.95 dd, 1 H (H-20, J(17,20) = 7.6; J(20,21) = 15.8); 5.77 dd, 1 H (H-21, J(17,21) = 1.0; J(20,21) = 15.8); 4.71 bs, 1 H (H-2′ of tetrahydropyranyloxy group); 3.72 s, 3 H ($COOCH_3$); 0.92 s, 3 H (3 × H-19); 0.62 s, 3 H (3 × H-18). Mass spectrum, *m/z*: 444 (M^+). Title compound *XXVI* (577 mg, 99% from 721 mg, 1.62 mmol of *XXV*), m.p. 159 – 160 °C (hexane), $[\alpha]_D$ +29° (*c* 0.5, chloroform). IR spectrum (chloroform): 3 610, 3 460 (OH); 1 712 (C=O); 1 650 (C=C); 1 280, 1 035 (C–O). ^{1}H NMR spectrum

(100 MHz): 6.96 dd, 1 H (H-20, J(17,20) = 7.5, J(20,21) = 15.7); 5.78 dd, 1 H (H-21, J(17,21) = 1.1, J(20,21) = 15.7); 3.72 s, 3 H ($COOCH_3$); 3.63 m, 1 H (H-3β, W = 36); 0.92 s, 3 H (3 × H-19); 0.62 s, 3 H (3 × H-18). Mass spectrum, m/z: 360 (M^+), 342 (M – H_2O), 327 (M – H_2O – CH_3). For $C_{23}H_{36}O_3$ (360.5) calculated: 76.62% C, 10.06% H; found: 76.56% C, 9.97% H.

(20*E*)-21-Methoxycarbonyl-5β-pregn-20-en-3α-yl Hydrogen Butanedioate (*XXVIII*) via *XXVII*

Hydroxy derivative *XXVI* (180 mg, 0.5 mmol) was converted to succinate *XXVII* (258 mg) by above-described procedure (see preparation of *XX*). Succinate *XXVII*: IR spectrum (tetrachloromethane): 1 730 (C=O); 1 653 (C=C); 1 251, 862, 840 (Si–C); 1 162 (C–O). A solution of succinate *XXVII* in tetrahydrofuran (4 ml) was stirred with 1 M solution of tetrabutylammonium fluoride in tetrahydrofuran (1 ml) for 8 h at room temperature. The mixture was diluted with benzene (150 ml) and washed with 10% sulfuric acid (2 ×), water (3 ×), and dried. Evaporation of the solvents and crystallization of the residue from hexane–dichloromethane (–78 °C) afforded 178 mg (77%) of hemisuccinate *XXVIII*; m.p. 142 – 143 °C, $[\alpha]_D$ +68° (*c* 0.3, chloroform). IR spectrum (chloroform): 3 500 – 2 500 (COOH); 1 716 (C=O); 1 652 (C=C); 1 280, 1 177 (C–O). ^{1}H NMR spectrum (100 MHz): 6.96 dd, 1 H (H-20, J(17,20) = 7.6, J(20,21) = 15.8); 5.78 dd, 1 H (H-21, J(17,21) = 0.8, J(20,21) = 15.8); 4.76 m, 1 H (H-3β, W = 36); 3.73 s, 3 H ($COOCH_3$); 2.63 m, 4 H ($OOCCH_2CH_2COO$); 0.94 s, 3 H (3 × H-19); 0.63 s, 3 H (3 × H-18). For $C_{27}H_{40}O_6$ (460.6) calculated: 70.41% C, 8.75% H; found: 70.57% C, 8.59% H.

Methyl (20*E*)-3α-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyloxy)-5β-pregn-20-ene-21-carboxylate (*XXIX*)

Preparation of title compound was carried out as in preparation of compound *XXIII* from hydroxy derivative *XXVI* (180 mg, 0.50 mmol), 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (300 mg, 0.73 mmol), and corresponding amounts of other reagents. Yield 236 mg (68%) of product *XXIX*, m.p. 155 – 156 °C, $[\alpha]_D$ +2.5° (*c* 0.2, chloroform). IR spectrum (chloroform): 1 753 (C=O, acetate); 1 710 sh (C=O, ester); 1 650 (C=C); 1 042 (C–O, acetate). ^{1}H NMR spectrum (100 MHz): 6.93 dd, 1 H (H-20, J(17,20) = 8, J(20,21) = 16); 5.76 d, 1 H (H-21, J(20,21) = 16); 5.22 t, 1 H (H-3', J(3',2') = J(3',4') = 9); 5.04 t, 1 H (H-4', J(4',3') = J(4',5') = 9); 4.93 dd, 1 H (H-2', J(2',1') = 7.5, J(2',3') = 9); 4.58 d, 1 H (H-1', J(1',2') = 7.5); 4.26 dd, 1 H (H-6'a, J(6'a,6'b) = 12.5, J(6'a,5') = 5); 4.09 dd, 1 H (H-6'b, J(6'b,6'a) = 12.5, J(6'b,5') = 3); 3.72 s, 3 H ($COOCH_3$); 3.60 m, 2 H (H-5' and H-3β, W = 40); 2.04 s, 3 H (CH_3COO); 2.02 s, 3 H (CH_3COO); 2.01 s, 3 H (CH_3COO); 2.00 s, 3 H (CH_3COO); 0.92 s, 3 H (3 × H-19); 0.61 s, 3 H (3 × H-18). For $C_{37}H_{54}O_{12}$ (690.8) calculated: 64.33% C, 7.88% H; found: 64.57% C, 8.06% H.

Methyl (20*E*)-3α-(β-D-Glucopyranosyloxy)-5β-pregn-20-ene-21-carboxylate (*XXX*)

To the solution of acetate *XXIX* (200 mg, 0.29 mmol) in methanol (10 ml) a 5% methanolic sodium methoxide (5 drops) was added. After 24 h standing at room temperature the mixture was neutralized with solid carbon dioxide (ca 300 mg). After evaporation of solvent in vacuo, the residue was chromatographed on a column of silica gel (20 g) in chloroform–methanol (20 : 1 to 10 : 1). Yield 147 mg (97%) of glucoside *XXX*, m.p. 195 – 198 °C, $[\alpha]_D$ +51° (*c* 0.2, chloroform). IR spectrum (KBr): 3 446, 3 340 (OH); 1 727 (C=O); 1 653 (C=C); 1 160, 1 147, 1 075 (C–O). For $C_{29}H_{46}O_8$ (522.7) calculated: 66.64% C, 8.87% H; found: 66.77% C, 9.02% H.

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