NEW APPROACH TO STEROIDAL HEMISUCCINATES AND GLYCOSIDES*

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New synthesis of hemisuccinate and β-D-glucopyranoside of (20*E*)-21-ethoxycarbonyl-5,20-pregnadien-3β-ol (*XVIII* and *XXVI*) is described, consisting in the preparation of a protected hemisuccinate (*XV*) or glucoside (*XXIII*) intermediate, into which the unsaturated ester grouping in the side-chain is incorporated only in the final stage of the synthesis. The primary hydroxyl at $C_{(20)}$ was protected by tert-butyldimethylsilyl, trityl or nitrate groups, the succinate was blocked with 2-(trimethylsilyl)ethyl or 2,2,2-trichloroethyl groups and the glucosides were used in the form of peracetyl derivatives.

Recently we described[1-3] indirect methods of preparation of hemisuccinates, using reaction of steroid alcohols with monoester of succinic acid, followed by selective cleavage of the obtained mixed esters. This method was utilized in the synthesis of hemisuccinates derived from 3-hydroxysteroids bearing in position 17β a heterocycle[1,4,5] or an α,β-unsaturated ester moiety[1-3,6]. In these syntheses, a 3-hydroxy derivative, protected as acetate or methoxymethoxy ether, was converted into the final 17-substituted product and the protecting group in position 3 was then removed. The above-mentioned indirect method was then employed for introduction of the hemisuccinate moiety into the position 3. Similar strategy was used in the preparation of 3-O-(β-D-glucopyranosyl) derivatives[4,7], the glycosylation step being performed in the end of the whole synthesis.

The aim of the present study was to verify the potentialities of the monosuccinate or peracetylglucose units both as protecting groups and masked polar moieties in the position 3. According to our reaction scheme, the 3-substituent is introduced at the beginning of the synthesis and only then follows the reaction sequence leading to substitution in position 17. The whole synthesis ends by liberation of the hemisuccinate or glycoside. As the final products we chose derivatives with an α,β-unsaturated ester grouping in position 17β, *i.e.* the hemisuccinate *XVIII* and glucoside *XXVI*.

Originally, we intended to prepare the hemisuccinate *XVIII* by the following reaction sequence. The 4-dimethylaminopyridine-catalyzed[9] reaction of mono-

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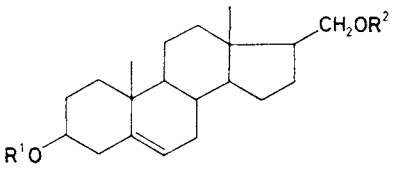
acetate *I* (ref.[8]) with tert-butylchlorodimethylsilane, followed by alkaline hydrolysis, afforded the hydroxy derivative *III* which on reaction with 2,2,2-trichloroethyl hydrogen butanedioate was converted into compound *IV*. Since it was not possible to remove selectively the tert-butyldimethylsilyl group in the presence of the 2,2,2-trichloroethyl group by treatment with tetrabutylammonium fluoride[10], the protecting group in position 20 was split off by acid hydrolysis[11]; however, the hydroxy derivative *V* was obtained in only 34% yield. We turned therefore our attention to the trityl protecting group. Reaction of the monoacetate *I* with trityl chloride, catalyzed by 4-dimethylaminopyridine[12], and subsequent alkaline hydrolysis afforded the monotrityl derivative *VIII*. This compound was prepared also by direct selective tritylation of diol *VII* in an 83% yield. Treatment of the 3-hydroxy derivative *VIII* with 2,2,2-trichloroethyl hydrogen butanedioate, followed by selective acid-catalyzed removal of the trityl group, gave the 20-hydroxy derivative *V* in 41% yield (based on the starting *VII*).

The alcohol *V* was oxidized with pyridinium chlorochromate to the aldehyde *X* which was condensed with diethyl ethoxycarbonylmethylphosphonate under conditions of Wittig–Horner reaction. Instead of the expected α,β-unsaturated ester with the 2,2,2-trichloroethyl succinate moiety in position 3 we isolated as the sole product a compound (*XI*) whose ^{1}H NMR spectrum had no singlet at δ 4·7, characteristic of 2,2,2-trichloroethyl esters. The ^{1}H NMR spectrum further displayed, in addition to α,β-unsaturated ethyl ester signals, a quartet and a triplet corresponding to another ethyl ester grouping. We may thus derive that the reaction of the aldehyde *X* with sodium salt of diethyl ethoxycarbonylmethyl phosphonate in the position 20 was accompanied by replacement of the 2,2,2-trichloroethyl protecting group with ethyl. This assumption was confirmed also by the IR spectrum in which the 2,2,2-trichloroethyl ester carbonyl band at 1 755 cm^{-1} was absent. No chlorine was detected by elemental analysis. We performed a model experiment with cholesterol derivative *XII*: under the same conditions the 2,2,2-trichloroethyl group was again replaced under formation of the product *XIII* as evidenced by the ^{1}H NMR spectrum (a quartet at δ 4·12 and a triplet at δ 1·25), IR spectrum (a single carbonyl band at 1 737 cm^{-1}), and elemental analysis (absence of chlorine).

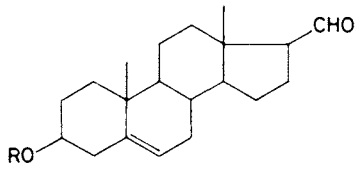
Because of the mentioned instability of the 2,2,2-trichloroethyl protecting group we used in further experiments the 2-(trimethylsilyl)ethyl group[2,3]. Reaction of the monotrityl derivative *VIII* with 2-(trimethylsilyl)ethyl hydrogen butanedioate furnished compound *XIV* which on selective acidic removal of the 20-trityl group was converted to the 20-hydroxy derivative *XV*. Oxidation of *XV* with pyridinium chlorochromate to the aldehyde *XVI*, followed by reaction with sodium salt of diethyl ethoxycarbonylmethylphosphonate, afforded the α,β-unsaturated ester *XVII*. In this case the protecting group had not been exchanged: the ^{1}H NMR spectrum displayed a multiplet at δ 4·15 and a singlet due to methyl groups bonded to the silicon atom at δ −0·02. Removal of the 2-(trimethylsilyl)ethyl group by treatment

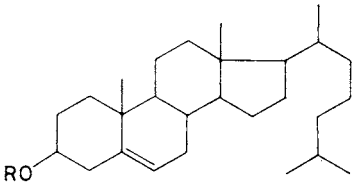
with tetrabutylammonium fluoride gave the hemisuccinate *XVIII*. The known[2,3] α,β-unsaturated methyl ester *XIX* was obtained by reaction of the aldehyde *XVI* with sodium salt of diethyl methoxycarbonylmethylphosphonate.



I, $R^1 = OCCH_3$; $R^2 = H$
II, $R^1 = OCCH_3$; $R^2 =$ TBDMS
III, $R^1 = H$; $R^2 =$ TBDMS
IV, $R^1 = OCCH_2CH_2COOTce$; $R^2 =$ TBDMS
V, $R^1 = OCCH_2CH_2COOTce$; $R^2 = H$
VI, $R^1 = OCCH_3$; $R^2 = C(C_6H_5)_3$
VII, $R^1 = R^2 = H$
VIII, $R^1 = H$; $R^2 = C(C_6H_5)_3$

IX, $R^1 = OCCH_2CH_2COOTce$; $R^2 = C(C_6H_5)_3$
XIV, $R^1 = OCCH_2CH_2COOTse$; $R^2 = C(C_6H_5)_3$
XV, $R^1 = OCCH_2CH_2COOTse$; $R^2 = H$
XX, $R^1 = OCCH_3$; $R^2 = NO_2$
XXI, $R^1 = H$; $R^2 = NO_2$
XXII, $R^1 = Ac_4\beta\text{—D—Glc}$; $R^2 = NO_2$
XXIII, $R^1 = Ac_4\beta\text{—D—Glc}$; $R^2 = H$





X, R = $OCCH_2CH_2COOTce$
XVI, R = $OCCH_2CH_2COOTse$
XXIV, R = $Ac_4\beta\text{—D—Glc}$

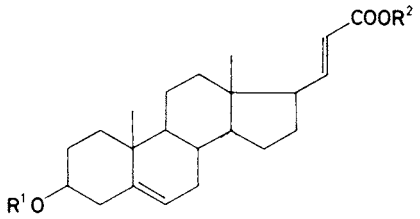
XII, R = $OCCH_2CH_2COOTce$
XIII, R = $OCCH_2CH_2COOCH_2CH_3$
XXIX, R = $Ac_4\beta\text{—D—Glc}$

TBDMS = $Si(CH_3)_2C(CH_3)_3$
Tce = CH_2CCl_3
Tse = $CH_2CH_2Si(CH_3)_3$
$Ac_4\beta$-D-Glc = 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl

Comparison of our new synthesis from etienic acid according to the reaction sequence *VII* → *VIII* → *XIV* → *XV* → *XVI* → *XIX* (total yield 24%) with the already published[2,3,7,8] synthesis, starting also from etienic acid (total yield of *XIX* 14%), shows that the former gives a twice as high yield of the desired product the number of steps being the same (seven).

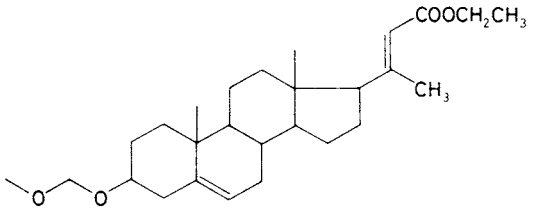
However, the method, in the form described, is not suitable for synthesis of glucosides because the trityl group, used successfully for protection of the $C_{(20)}$-hydroxyl in the case of succinates, is not stable under conditions of glucosylation[13]. We

therefore tried the nitrate group which proved to be both stable and easily removable by reduction. The starting acetyl derivative *I* was esterified with nitric acid in acetic anhydride at low temperature (−25°C) because at higher temperatures the Δ^5 double bond could be attacked. The obtained nitrate *XX* was deacetylated with sodium hydroxide in a mixture of dioxane, methanol, and water to give practically quantitatively the derivative *XXI* with free hydroxyl in position 3. It was glucosylated with tetra-O-acetyl-α-D-glucopyranosyl bromide in the presence of silver silicate as catalyst and afforded the easily crystallizing nitrate glucoside *XXII*. Its ^{1}H NMR spectrum displays signals of the starting nitro derivative as well as those of the attached glucopyranoside unit of β-configuration at $C_{(1')}$ ($C_{(1')}$—H: δ 4·59, $J_{1',2'}$ = = 7·9 Hz). The nitrate group in *XXII* was removed with zinc in acetic acid and the 20-hydroxy derivative *XXIII* was isolated in a 96% yield. This compound represents the crucial intermediate in the synthesis because it already contains the protected D-glucopyranosyl unit and at the same time enables construction of the side-chain in position 17. The overall yield of the whole reaction sequence *I* → *XX* → *XXI* → → *XXII* → *XXIII* is 52% and the reactions can be performed on a larger scale.



XI, R^1 = $OCCH_2CH_2COOCH_2CH_3$; R^2 = CH_2CH_3
XVII, R^1 = $OCCH_2CH_2COOTse$; R^2 = CH_2CH_3
XVIII, R^1 = $OCCH_2CH_2COOH$; R^2 = CH_2CH_3
XIX, R^1 = $OCCH_2CH_2COOTse$; R^2 = CH_3

XXV, R^1 = Ac_4β−D−Glc ; R^2 = CH_2CH_3
XXVI, R^1 = β−D−Glc ; R^2 = CH_2CH_3
XXVII, R^1 = H ; R^2 = CH_3



XXVIII

Tse = $CH_2CH_2Si(CH_3)_3$
Ac_4β−D−Glc = 2,3,4,6−tetra−O−acetyl−β−D−glucopyranosyl
β−D−Glc = β−D−glucopyranosyl

The further procedure was analogous to the previous case, *i.e.* the crude aldehyde *XXIV*, obtained by oxidation of the alcohol *XXIII* with pyridinium chlorochromate, reacted with sodium salt of diethyl ethoxycarbonylmethylphosphonate to give the ester *XXV*. Its ^{1}H NMR spectrum confirmed the presence of an α,β-unsaturated ester grouping ($C_{(20)}$—H, $C_{(22)}$—H: δ 6·94 and 5·78, respectively; $J_{17,20}$ = 8·0; $J_{17,22}$ = 1·0, $J_{20,22}$ = 15·6 Hz) as well as a tetra-O-acetyl-β-D-glucopyranose unit. In ^{13}C NMR spectrum this unit was manifested by shifts identical with those observed for the analogous cholesteryl β-D-glucoside (*XXIX*)[14] ($\Delta\delta \leqq 0{\cdot}4$ ppm). Individual carbon atoms of the steroid skeleton were assigned to the signals by comparison with the spectrum of (20*E*)-21-methoxycarbonyl-5,20-pregnadien-3β-ol (*XXVII*), ethyl (20*E*)-3β-methoxymethoxy-24-nor-5,20(22)-choladien-23-oate (*XXVIII*) and cholesteryl β-D-glucopyranoside (*XXIX*) (Table I).

Deacetylation of the ester *XXV* was done with sodium ethoxide in ethanol and afforded the free glucoside *XXVI* in a yield of 75%.

The advantage of the described procedure is that it makes accessible the glucoside intermediate *XXIII* which enables an aimed construction of the side-chain whose

TABLE I

^{13}C NMR parameters for derivatives *XXV* and *XXVII* and comparison with literature data

Carbon[a]	*XXV*	*XXVII*	Ref.[b]	Carbon	*XXV*	*XXVII*	Ref.[b]
1	37·3	37·3	37·3	15	25·0	25·1	24·3
2	29·4	31·6	29·5	16	27·0	27·1	25·0
3	79·1	71·7	80·0	17	53·8	53·9	60·4
4	38·9	42·3	39·0	18	13·0	13·1	13·0
5	140·4	140·9	140·9	19	19·3	19·4	—
6	121·8	121·4	122·0	20	150·4	151·0	—
7	31·9	31·9	—	21	121·4	121·0	—
8	31·9	32·0	—				
9	50·3	50·3	—	1′	99·6	—	99·7
10	36·8	36·6	—	2′	71·5	—	71·8
11	20·7	20·7	—	3′	72·9	—	73·1
12	37·2	37·4	38·6	4′	68·5	—	68·9
13	44·6	44·7	44·5	5′	71·7	—	71·8
14	56·1	56·2	56·7	6′	62·1	—	62·2

[a] Measured in $CDCl_3$, shifts based on tetramethylsilane as internal standard, interpretation based on proton-decoupled and APT (attached proton test)[17] spectra. [b] Literature data for comparison, values of $C_{(12)}$ to $C_{(18)}$ are taken from the spectrum of crotonate *XXVIII* in ref.[6], values of $C_{(1)}$ to $C_{(6)}$ and $C_{(1')}$ to $C_{(6')}$ taken from the spectrum of cholesteryl β-D-glucoside tetraacetate (*XXIX*) in ref.[14].

type depends on the phosphonate employed. However, since the nitrate protecting group cannot be introduced selectively into the diol *VII*, the yield of the whole reaction sequence *I* → *XXVI* is lower (18%) than in the previous[7] case (25%).

EXPERIMENTAL

Melting points were determined on a micro melting point apparatus Boetius (G.D.R.). Optical rotations were measured at 25°C on a Perkin–Elmer 141 MC polarimeter. IR spectra were recorded on a Zeiss UR-20 spectrometer (wavenumbers in cm^{-1}). NMR spectra were taken on Tesla BS-467 (60 MHz for ^1H) or Varian XL-200 (200·058 MHz for ^1H and 50·309 MHz for ^{13}C) instruments at 23°C, in deuteriochloroform with tetramethylsilane as internal standard, unless stated otherwise. Chemical shifts are given in ppm (δ-scale), coupling constants (J) and bandwidths (W) in Hz. All values were obtained by the first-order analysis. Column chromatography was performed on silica gel (according to Pitra, 60—120 μm) or on neutral alumina (Reanal, activity II), thin-layer chromatography on silica gel G according to Stahl (Woelm). 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 and 26 Pa for 12 h. 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.

20-Tert-butyldimethylsilyloxy-21-nor-5-pregnen-3β-yl Acetate (*II*)

Triethylamine (0·94 ml; 6·74 mmol), tert-butylchlorodimethylsilane (936 mg; 6·21 mmol) and 4-dimethylaminopyridine (25 mg; 0·2 mmol) were added to a solution of *I* (ref.[8], 1·96 g; 5·65 mmol) in dichloromethane (20 ml). After stirring at room temperature for 1 h, the mixture was diluted with ether (200 ml) and washed with water. The solvent was evaporated and the residue chromatographed on a column of silica gel (95 g). Elution with light petroleum–benzene (1 : 1) afforded 2·04 g (81%) of *II*, m.p. 104—106°C (hexane); $[\alpha]_D$ −72° (c 0·25, chloroform). IR spectrum (tetrachloromethane): 1 735, 1 250 (CH_3COO), 1 669 (C=C), 1 250, 849 (silane). ^1H NMR spectrum (deuteriochloroform, external lock): 5·34 bd (1 H, $C_{(6)}$—H, $J = 4$), 4·54 m (1 H, $C_{(3)}$—H, $W = 35$), 3·48 m (2 H, $C_{(20)}$—H), 1·99 s (3 H, CH_3COO), 0·99 s (3 H, $C_{(19)}$—H), 0·85 s (9 H, $SiC(CH_3)_3$), 0·60 s (3 H, $C_{(18)}$—H), −0·02 s (6 H, $Si(CH_3)_2$). For $C_{28}H_{48}O_3Si$ (460·8) calculated: 72·99% C, 10·50% H; found: 72·74% C, 10·86% H.

20-Tert-butyldimethylsilyloxy-21-nor-5-pregnen-3β-ol (*III*)

A solution of sodium hydroxide (1·4 g) in water (1·5 ml) and methanol (2 ml) was added to a solution of *II* (1 g; 2·17 mmol) in dioxane (10 ml) and methanol (10 ml). After reflux for 5 min, the mixture was diluted with ether (250 ml), washed successively with water, saturated aqueous solution of citric acid, water, potassium hydrogen carbonate solution, and again water. The solvent was evaporated and the residue chromatographed on a silica gel column (50 g). A mixture of light petroleum–ether (7 : 3) eluted 860 mg (95%) of *III*, m.p. 116—118°C (hexane); $[\alpha]_D$ −50° (*c* 0·3, chloroform). IR spectrum (chloroform): 3 620, 3 340 (OH), 1 670 (C=C), 1 256, 850, 840 (silane). ^1H NMR spectrum (deuteriochloroform, external lock): 5·34 bd (1 H, $C_{(6)}$—H, $J = 4$), 3·52 m (3 H, $C_{(3)}$—H and $C_{(20)}$—H_2), 1·00 s (3 H, $C_{(19)}$—H), 0·89 s (9 H, $SiC(CH_3)_3$), 0·64 s (3 H, $C_{(18)}$—H), 0·04 s (6 H, $Si(CH_3)_2$). For $C_{26}H_{46}O_2Si$ (418·7) calculated: 74·58% C, 11·07% H; found: 74·72% C, 11·27% H.

20-Tert-butyldimethylsilyloxy-21-nor-5-pregnen-3β-yl 2,2,2-Trichloroethyl Butanedioate (*IV*)

To a solution of *III* (810 mg; 1·93 mmol) in tetrahydrofuran (10 ml) and benzene (20 ml) was added 2,2,2-trichloroethyl hydrogen butanedioate[15] (934 mg; 3·74 mmol), followed by N,N'-dicyclohexylcarbodiimide (472 mg; 2·29 mmol) and 4-dimethylaminopyridine (10 mg). After stirring at room temperature for 4 h, the mixture was diluted with light petroleum (30 ml), the precipitated N,N'-dicyclohexylurea was filtered, the filtrate was diluted with ether (200 ml), washed with water and the solvent was evaporated. Column chromatography of the residue on silica gel (50 g) in light petroleum–ether (95 : 5) gave 1·05 g (83%) of succinate *IV*, m.p. 65–67°C, $[\alpha]_D$ −48° (*c* 0·25; chloroform). IR spectrum (tetrachloromethane): 1 765, 1 738 ($OOCCH_2CH_2$. .$COOCH_2CCl_3$), 1 672 (C=C), 1 258, 850, 840 (silane). ^{1}H NMR spectrum (deuteriochloroform, external lock): 5·35 m (1 H, $C_{(6)}$—H), 4·73 s (2 H, $COOCH_2CCl_3$), 4·63 m (1 H, $C_{(3)}$—H, $W = 35$), 3·52 m (2 H, $C_{(20)}$—H), 2·68 m (4 H, $OOCCH_2CH_2COO$), 1·00 s (3 H, $C_{(19)}$—H), 0·85 s (9 H, $SiC(CH_3)_3$), 0·62 s (3 H, $C_{(18)}$—H), 0·00 s (6 H, $Si(CH_3)_2$). For $C_{32}H_{51}Cl_3O_5Si$ (650·2) calculated: 59·11% C, 7·91% H, 16·36% Cl; found: 58·95% C, 7·91% H, 16·57% Cl.

20-Hydroxy-21-nor-5-pregnen-3β-yl 2,2,2-Trichloroethyl Butanedioate (*V*)

a) Acetic acid (5·1 ml) and water (3·4 ml) were added to a solution of silyl ether *IV* (860 mg; 1·32 mmol) in tetrahydrofuran (17 ml). After heating to 70°C for 24 h, the mixture was twice coevaporated *in vacuo* with toluene, the residue was dissolved in a mixture of ether and toluene and dried over anhydrous sodium sulfate. Chromatography on a column of silica gel (70 g) in light petroleum–ether (9 : 1) afforded 300 mg (35%) of the starting silyl ether *IV*, further elution with light petroleum–ether (7 : 3) gave 240 mg (34%) of amorphous *V*, $[\alpha]_D$ −45° (*c* 0·2, chloroform). IR spectrum (chloroform): 3 625, 3 530 (OH), 1 754, 1 730 ($OOCCH_2CH_2COOCH_2$. .CCl_3). ^{1}H NMR spectrum: 5·33 m (1 H, $C_{(6)}$—H), 4·73 s (2 H, $COOCH_2CCl_3$), 4·58 m (1 H, $C_{(3)}$—H, $W = 35$), 3·60 m (2 H, $C_{(20)}$—H), 2·70 m (4 H, $OOCCH_2CH_2COO$), 1·00 s (3 H, $C_{(19)}$—H), 0·64 s (3 H, $C_{(18)}$—H). For $C_{26}H_{37}Cl_3O_5$ (535·9) calculated: 58·27% C, 6·96% H, 19·85% Cl; found: 58·57% C, 6·92% H, 20·16% Cl.

b) A solution of *IX* (400 mg; 0·51 mmol) in benzene (20 ml) was applied on a column of silica gel (20 g). After standing for 5 days at room temperature, the product was eluted with an ether–dichloromethane (1 : 1) mixture and, after evaporation of the solvents, chromatographed on silica gel (50 g). Non-polar impurities were washed out by light petroleum–ether (4 : 1) and the amorphous hydroxy derivative *V* (195 mg; 71%) was then eluted with a 1 : 1 mixture of the same solvents. The product was identical with that obtained by procedure *a*).

20-Triphenylmethoxy-21-nor-5-pregnen-3β-ol (*VIII*)

a) A solution of *I* (ref.[8], 346 mg; 1 mmol) in dichloromethane (5 ml) was mixed with triethylamine (0·21 ml; 1·5 mmol), chlorotriphenylmethane (335 mg; 1·2 mmol) and 4-dimethylaminopyridine (10 mg). After stirring at room temperature for 48 h, the mixture was poured into water, the product taken up in benzene and the organic layer washed with water. The solvent was evaporated and the residue chromatographed on a column of alumina (50 g) in dichloromethane–benzene to give 430 mg (73%) of amorphous *VI*. ^{1}H NMR spectrum: 7·35 m (15 H, arom. H), 5·38 m (1 H, $C_{(6)}$—H), 4·66 m (1 H, $C_{(3)}$—H, $W = 35$), 3·02 m (2 H, $C_{(20)}$—H), 2·03 s (3 H, CH_3COO), 1·00 s (3 H, $C_{(19)}$—H), 0·42 s (3 H, $C_{(18)}$—H). The trityl derivative *VI* (430 mg; 0·73 mmol) was dissolved in a mixture of dioxane (4 ml) and methanol (4 ml) and refluxed with sodium hydroxide (350 mg) in water (0·5 ml) and methanol (0·5 ml) for 5 min. The mixture was

poured in a saturated aqueous sodium chloride solution (50 ml), the product extracted with ether and the extract washed with water. The residue after evaporation of the solvent was chromatographed on a column of alumina (35 g) in benzene–ether (1 : 1) to give 370 mg (93%) of amorphous *VIII*, $[\alpha]_D$ −37° (*c* 0·25, chloroform). IR spectrum (chloroform): 3 610, 3 500 (OH), 1 598, 1 494 (aromatic system). ^{1}H NMR spectrum: 7·36 m (15 H, arom. H), 5·33 bd (1 H, $J = 4$, $C_{(6)}$—H), 3·47 m (1 H, $C_{(3)}$—H, $W = 35$), 3·02 m (2 H, $C_{(20)}$—H), 0·96 s (3 H, $C_{(19)}$—H), 0·39 s (3 H, $C_{(18)}$—H). For $C_{39}H_{46}O_2$ (546·8) calculated: 85·67% C, 8·48% H; found: 85·47% C, 8·36% H.

b) To a suspension of diol *VII* (ref.[16]; 2 g; 6·6 mmol) in 1,2-dimethoxyethane (20 ml) were added in succession triethylamine (2·8 ml; 20·1 mmol), 4-dimethylaminopyridine (130 mg; 1·1 mmol) and a solution of chlorotriphenylmethane (4·4 g; 15·8 mmol) in dichloromethane (30 ml). After stirring for 20 h at room temperature, the mixture was diluted with benzene (300 ml) and washed with water. The solvents were evaporated and the residue was chromatographed on a column of silica gel (200 g; pre-treated with ammonia vapour for 12 h). Non-polar impurities (2·1 g) were washed out with a light petroleum–benzene–ether (50 : 45 : 5) mixture and then the product (2·97 g; 83%) was eluted with a 4 : 4 : 2 mixture of the same solvents. The amorphous *VIII* was identical with the product prepared by procedure *a*).

20-Triphenylmethoxy-21-nor-5-pregnen-3β-yl 2,2,2-Trichloroethyl Butanedioate (*IX*)

2,2,2-Trichloroethyl hydrogen butanedioate[15] (540 mg; 2·16 mmol), N,N′-dicyclohexylcarbodiimide (253 mg; 1·23 mmol), and 4-dimethylaminopyridine (6 mg) were added to a solution of *VIII* (625 mg; 1·14 mmol) in benzene (17 ml). After stirring for 4 h at room temperature, the mixture was diluted with light petroleum (30 ml), the precipitated N,N′-dicyclohexylurea filtered and the filtrate taken down *in vacuo*. Chromatography on silica gel (75 g; Silpearl, Kavalier, Votice) in light petroleum–benzene–ether (50 : 45 : 5) afforded 622 mg (70%) of amorphous succinate *IX*, $[\alpha]_D$ −24° (*c* 0·25, chloroform). IR spectrum (tetrachloromethane): 1 764, 1 738 ($OOCCH_2CH_2COOCH_2CCl_3$), 1 598, 1 494 (aromatic system). ^{1}H NMR spectrum: 7·32 m (15 H, arom. H), 5·35 bd (1 H, $C_{(6)}$—H, $J = 4$), 4·73 s (2 H, $COOCH_2CCl_3$), 4·61 m (1 H, $C_{(3)}$—H, $W = 35$), 3·00 m (2 H, $C_{(20)}$—H), 2·70 m (4 H, $OOCCH_2CH_2COO$), 0·98 s (3 H, $C_{(19)}$—H), 0·39 s (3 H, $C_{(18)}$—H). For $C_{45}H_{51}Cl_3O_5$ (778·3) calculated: 69·45% C, 6·61% H, 13·67% Cl; found: 69·63% C, 6·51% H, 13·48% Cl.

(20*E*)-21-Ethoxycarbonyl-5,20-pregnadien-3β-yl Ethyl Butanedioate (*XI*)

Pyridinium chlorochromate (430 mg; 1·99 mmol) was added to a solution of *V* (420 mg; 0·78 mmol) in dichloromethane (10 ml). After stirring for 1 h at room temperature in an argon atmosphere, the mixture was diluted with ether (10 ml) and filtered through a column of alumina (10 g). The column was washed with ether, the solvents were evaporated *in vacuo* and the residue was codistilled *in vacuo* with benzene (50 ml), affording 405 mg (97%) of aldehyde *X*. ^{1}H NMR spectrum: 9·79 d (1 H, $C_{(20)}$—H, $J = 1·5$), 5·35 m (1 H, $C_{(6)}$—H), 4·75 s (2 H, $COOCH_2CCl_3$), 4·60 m (1 H, $C_{(3)}$—H), 2·73 m (4 H, $OOCCH_2CH_2COO$), 1·02 s (3 H, $C_{(19)}$—H), 0·76 s (3 H, $C_{(18)}$—H). Diethyl ethoxycarbonylmethylphosphonate (0·8 ml; 4·03 mmol) was added dropwise to a suspension of sodium hydride (96 mg; 4 mmol) in 1,2-dimethoxyethane (4 ml), the mixture was stirred under argon for 20 min at room temperature and a solution of the aldehyde *X* (375 mg; 0·7 mmol) in 1,2-dimethoxyethane (4 ml) was added. After stirring under argon at room temperature for 4 h, the solvent was evaporated *in vacuo*, the residue partitioned between water and ether and the aqueous layer extracted with ether. The combined organic phases were washed with water and the residue was chromatographed on a column of silica gel (40 g) in light

petroleum–ether (85 : 15) to afford 250 mg (71%) of succinate *XI*, m.p. 94–97°C (hexane), $[\alpha]_D$ −29° (*c* 0·25, chloroform). IR spectrum (tetrachloromethane): 1 739 (COOR), 1 720 shoulder, 1 653 (C=C—COOR). ^{1}H NMR spectrum: 6·97 dd (1 H, $C_{(20)}$—H, $J_{17,20} = 7{\cdot}5$, $J_{20,21} = 16$), 5·76 d (1 H, $C_{(21)}$—H, $J_{20,21} = 16$), 5·35 bd (1 H, $J = 4{\cdot}5$, $C_{(6)}$—H), 4·18 q and 4·22 q (2× 2 H, 2× $COOCH_2CH_3$, $J = 7{\cdot}2$), 2·58 bs (4 H, $OOCCH_2CH_2COO$), 1·23 t and 1·26 t (2× 3 H, 2× $COOCH_2CH_3$, $J = 7{\cdot}2$), 1·00 s (3 H, $C_{(19)}$—H), 0·63 s (3 H, $C_{(18)}$—H). For $C_{30}H_{44}O_6$ (500·7) calculated: 71·97% C, 8·86% H; found: 71·85% C, 8·57% H.

5-Cholesten-3β-yl Ethyl Butanedioate (*XIII*)

Diethyl ethoxycarbonylmethylphosphonate (0·6 ml; 3·02 mmol) was added dropwise to a suspension of sodium hydride (60 mg; 2·5 mmol) in 1,2-dimethoxyethane (3 ml), the mixture was stirred under argon for 20 min at room temperature and a solution of succinate *XII* (ref.[1]; 320 mg; 0·52 mmol) in 1,2-dimethoxyethane (3 ml) was added. After stirring under argon for 4 h at room temperature, the solvent was evaporated *in vacuo* and the residue partitioned between ether and water. The aqueous layer was extracted with ether, the combined organic phases were washed with water and the ether was evaporated. The residue was chromatographed on a column of silica gel (20 g) in light petroleum–benzene–ether (50 : 45 : 5), affording 225 mg (84%) of succinate *XIII*, m.p. 77–80°C (hexane), $[\alpha]_D$ −36° (*c* 0·4, chloroform). IR spectrum (tetrachloromethane): 1 737 (COOR). ^{1}H NMR spectrum: 5·35 bd (1 H, $C_{(6)}$—H, $J = 4{\cdot}5$), 4·57 m (1 H, $C_{(3)}$—H, $W = 35$), 4·12 q (2 H, $COOCH_2CH_3$, $J = 7{\cdot}2$), 2·57 s (4 H, $OOCCH_2CH_2COO$), 1·25 t (3 H, $COOCH_2CH_3$, $J = 7{\cdot}2$), 1·02 s (3 H, $C_{(19)}$—H), 0·86 d (6 H, $C_{(26)}$—H and $C_{(27)}$—H, $J = 6$), 0·67 s (3 H, $C_{(18)}$—H). For $C_{33}H_{54}O_4$ (514·8) calculated: 77·00% C, 10·57% H; found: 77·26% C, 10·81% H.

20-Triphenylmethoxy-21-nor-5-pregnen-3β-yl 2-(Trimethylsilyl)ethyl Butanedioate (*XIV*)

2-(Trimethylsilyl)ethyl hydrogen butanedioate[2] (1·59 g; 7·28 mmol), N,N′-dicyclohexylcarbodiimide (0·85 g; 4·12 mmol), and 4-dimethylaminopyridine (46 mg) were added to a solution of *VIII* (2 g; 3·66 mmol) in benzene (40 ml). The mixture was stirred at room temperature for 5 h and diluted with light petroleum (50 ml). The precipitated N,N′-dicyclohexylurea was removed by filtration and the solvents were evaporated. The residue was chromatographed on a column of silica gel (110 g; Silpearl, Kavalier, Votice) in light petroleum–benzene–ether (50 : 45 : 5), affording 2·51 g (92%) of amorphous *XIV*, $[\alpha]_D$ −26° (*c* 0·25, chloroform). IR spectrum (tetrachloromethane): 1 738, 1 162 (COOR), 1 251, 860, 840 ($Si(CH_3)_3$), 1 598, 1 493 (aromatic system). ^{1}H NMR spectrum (deuteriochloroform, external lock): 7·34 m (15 H, arom. H), 5·35 m (1 H, $C_{(6)}$—H), 4·65 m (1 H, $C_{(3)}$—H), 4·18 m (2 H, $COOCH_2CH_2Si$, $W = 17$), 3·00 m (2 H, $C_{(20)}$—H), 2·59 s (4 H, $OOCCH_2CH_2COO$),0 ·98 s (3 H, $C_{(19)}$—H), 0·40 s (3 H, $C_{(18)}$—H), 0·01 s (9 H, $Si(CH_3)_3$). For $C_{48}H_{62}O_5Si$ (747·1) calculated: 77·17% C, 8·36% H; found: 77·26% C, 8·19% H.

20-Hydroxy-21-nor-5-pregnen-3β-yl 2-(Trimethylsilyl)ethyl Butanedioate (*XV*)

A solution of *XIV* (1·5 g; 2·01 mmol) in benzene (50 ml) was applied on a column of silica gel (50 g). After standing for 6 days at room temperature, the product was eluted with ether, the solvent evaporated and the residue subjected to column chromatography on silica gel (100 g). Non-polar impurities were eluted with light petroleum–ether (8 : 2) and the product was obtained by elution with a 6 : 4 mixture of the same solvents; yield 650 mg (64%) of *XV*, m.p. 76–78°C (hexane), $[\alpha]_D$ −45° (*c* 0·3, chloroform). IR spectrum (tetrachloromethane): 3 635, 3 555 (OH),

1 738, 1 163 (COOR), 1 252, 860, 841 ($Si(CH_3)_3$). ^1H NMR spectrum (200 MHz, deuteriochloroform, referenced to chloroform at signal 7·26 ppm): 5·35 bd (1 H, $C_{(6)}$—H, $J = 4$), 4·61 m (1 H, $C_{(3)}$—H), 4·16 m (2 H, $COOCH_2CH_2Si$, $W = 17$), 3·71 m and 3·54 m (1 H and 1 H, $C_{(20)}$—H), 2·59 m (4 H, $OOCCH_2CH_2COO$), 1·01 s (3 H, $C_{(19)}$—H), 0·65 s (3 H, $C_{(18)}$—H), 0·03 s (9 H, $Si(CH_3)_3$). For $C_{29}H_{48}O_5Si$ (504·8) calculated: 69·00% C, 9·58% H; found: 69·10% C, 9·58% H.

(20*E*)-21-Ethoxycarbonyl-5,20-pregnadien-3β-yl 2-(Trimethylsilyl)ethyl Butanedioate (*XVII*)

Pyridinium chlorochromate (600 mg; 2·78 mmol) was added to a solution of *XV* (510 mg; 1·01 mmol) in dichloromethane (10 ml). The mixture was stirred in an atmosphere of argon at room temperature for 2 h, diluted with ether (40 ml) and filtered through a column of alumina (15 g). The column was washed with ether, the solvents were evaporated *in vacuo* and the residue was coevaporated several times *in vacuo* with benzene. Yield 489 mg (96%) of the aldehyde *XVI*. ^1H NMR spectrum (deuteriochloroform, external lock): 9·81 d (1 H, $C_{(20)}$—H, $J = 1·5$), 5·35 bd (1 H, $C_{(6)}$—H, $J = 4$), 4·43 m (1 H, $C_{(3)}$—H, $W = 35$), 4·17 m (2 H, $COOCH_2CH_2Si$, $W = 17$), 2·55 s (4 H, $OOCCH_2CH_2COO$), 0·99 s (3 H, $C_{(19)}$—H), 0·74 s (3 H, $C_{(18)}$—H), 0·01 s (9 H, $Si(CH_3)_3$).

Diethyl ethoxycarbonylmethylphosphonate (1 ml; 5·04 mmol) was added during 10 min to a suspension of sodium hydride (120 mg; 5 mmol) in 1,2-dimethoxyethane (6 ml). The mixture was stirred under argon at room temperature for 20 min and a solution of the aldehyde *XVI* (474 mg; 0·94 mmol) in 1,2-dimethoxyethane (5 ml) was added. After stirring under argon at room temperature for 4 h, the solvent was evaporated *in vacuo* and the residue partitioned between ether and water. The aqueous layer was extracted with ether, the combined organic phases were washed with water, dried and taken down. Column chromatography of the residue on silica gel (50 g) in light petroleum–ether (85 : 15) yielded 350 mg (62%) of *XVII*, m.p. 86–87°C (light petroleum), $[\alpha]_D$ −24° (*c* 0·2, chloroform). IR spectrum (tetrachloromethane): 1 734, 1 650 (C=C—COOR), 1 734 (COOR), 1 252, 861, 841 ($Si(CH_3)_3$). ^1H NMR spectrum (deuteriochloroform, external lock): 6·96 dd (1 H, $C_{(20)}$—H, $J_{17,20} = 7$, $J_{20,21} = 16·5$), 5·76 d (1 H, $C_{(21)}$—H, $J_{20,21} = 16·5$), 5·33 bd (1 H, $C_{(6)}$—H, $J = 4$), 4·57 m (1 H, $C_{(3)}$—H), 4·14 m (2 H, $COOCH_2CH_2Si$, $W = 17$), 4·14 q (2 H, $COOCH_2CH_3$, $J = 7·2$), 2·55 s (4 H, $OOCCH_2CH_2$·.COO), 1·25 t (3 H, $COOCH_2CH_3$, $J = 7·2$), 0·99 s (3 H, $C_{(19)}$—H), 0·62 s (3 H, $C_{(18)}$—H), −0·02 (9 H, $Si(CH_3)_3$). For $C_{33}H_{52}O_6Si$ (572·9) calculated: 69·19% C, 9·15% H; found: 68·93% C, 8·90% H.

(20*E*)-21-Ethoxycarbonyl-5,20-pregnadien-3β-yl Hydrogen Butanedioate (*XVIII*)

A solution of tetrabutylammonium fluoride in tetrahydrofuran (1·1 ml, $c = 1$ mol l^{-1}) was added to a solution of *XVII* (303 mg; 0·54 mmol) in tetrahydrofuran (5 ml). After stirring at room temperature for 5 h, the mixture was diluted with benzene (70 ml), washed with dilute sulfuric acid (10%) and water, and the solvents were evaporated. Crystallization of the residue from hexane–dichloromethane afforded 223 mg (89%) of *XVIII*, m.p. 162–165°C, $[\alpha]_D$ −26° (*c* 0·3, chloroform). IR spectrum (chloroform): 3 500–2 500, 1 718 (COOH), 1 718 (COOR), 1 718, 1 650 (C=C—COOR). ^1H NMR spectrum: 6·95 dd (1 H, $C_{(20)}$—H, $J_{17,20} = 7$, $J_{20,21} = 16$), 5·76 d (1 H, $C_{(21)}$—H, $J_{20,21} = 16$), 5·33 m (1 H, $C_{(6)}$—H), 4·55 m (1 H, $C_{(3)}$—H, $W = 35$), 4·15 q (2 H, $COOCH_2CH_3$, $J = 7·3$), 2·59 bs (4 H, $OCCH_2CH_2COO$), 1·23 t (3 H, $COOCH_2CH_3$, $J = 7·3$), 0·97 s (3 H, $C_{(19)}$—H), 0·61 s (3 H, $C_{(18)}$—H). For $C_{28}H_{40}O_6$ (472·6) calculated: 71·16% C, 8·53% H; found: 71·30% C, 8·67% H.

(20*E*)-21-Methoxycarbonyl-5,20-pregnadien-3β-yl
2-(Trimethylsilyl)ethyl Butanedioate (*XIX*)

Diethyl methoxycarbonylmethylphosphonate (0·63 ml; 3·4 mmol) was added during 10 min to a suspension of sodium hydride (80 mg; 3·4 mmol) in 1,2-dimethoxyethane (4 ml) and the mixture was stirred under argon at room temperature for 20 min. A solution of *XVI* (326 mg; 0·65 mmol) in 1,2-dimethoxyethane (3·5 ml) was added and the stirring under argon at room temperature was continued for 4 h. The mixture was taken down *in vacuo* and the residue partitioned between ether and water. The aqueous layer was extracted with ether and the combined organic layers were washed with water. After evaporation of the solvent, the residue was chromatographed on a column of silica gel (33 g) in benzene–ether (95 : 5), affording 221 mg (61%) of *XIX*, m.p. 81—83°C (hexane), identical with an authentic sample[3].

21-Nor-5-pregnene-3β,20-diol 3-Acetate 20-Nitrate (*XX*)

Nitric acid (65%, 5 ml; 86 mmol) was added dropwise with stirring and cooling (—25°C) to acetic anhydride (24 ml). After stirring and cooling for 10 min, a solution of *I* (ref.[8], 4·2 g; 12·1 mmol) in dichloromethane (40 ml) was added dropwise at —25°C during 30 min. The mixture was stirred at —25°C for 3 h and poured into a mixture of ice (100 g) and aqueous ammonia (25%, 50 ml). The product was taken up in ether, the extract was washed with saturated aqueous solution of potassium hydrogen carbonate and water and the solvent was evaporated. Column chromatography of the residue on silica gel (200 g) in light petroleum–benzene (1 : 1) afforded 3·54 g (75%) of *XX*, m.p. 155—158°C, $[\alpha]_D$ —83° (*c* 0·15, chloroform). IR spectrum (tetrachloromethane): 1 736, 1 245 (CH_3COO), 1 633, 1 279 (ONO_2). ^{1}H NMR spectrum: 5·35 bd (1 H, $C_{(6)}$—H, J = 4·5), 4·52 m (1 H, $C_{(3)}$—H), 4·41 m (2 H, $C_{(20)}$—H), 2·03 s (3 H, CH_3COO), 1·02 s (3 H, $C_{(19)}$—H), 0·70 s (3 H, $C_{(18)}$—H). For $C_{22}H_{33}NO_5$ (391·5) calculated: 67·49% C, 8·50% H, 3·58% N; found: 67·22% C, 8·46% H, 3·76% N.

21-Nor-5-pregnene-3β,20-diol 20-Nitrate (*XXI*)

Acetate *XX* (2·3 g; 5·9 mmol) was dissolved in a boiling mixture of dioxane (23 ml) and methanol (23 ml). Sodium hydroxide (3·45 g) in water (3 ml) and methanol (4 ml) was added, the mixture was refluxed for 5 min and poured into saturated aqueous sodium chloride solution (250 ml). The product was extracted with ether–dichloromethane (4 : 1) and the extract washed with dilute (1 : 4) hydrochloric acid, water, saturated solution of potassium hydrogen carbonate, and water. Removal of the solvents *in vacuo* gave 1·9 g (93%) of *XXI*, m.p. 114—116°C (ether–hexane), $[\alpha]_D$ —43° (*c* 0·3, chloroform). IR spectrum (chloroform): 3 610, 3 455 (OH), 1 631, 1 282, 866 (ONO_2). ^{1}H NMR spectrum: 5·33 bd (1 H, $C_{(6)}$—H, J = 4·5), 4·43 m (2 H, $C_{(20)}$—H),3·48 m (1 H, $C_{(3)}$—H, W = 35), 1·01 s (3 H, $C_{(19)}$—H), 0·70 s (3 H, $C_{(18)}$—H). For $C_{20}H_{31}NO_4$ (349·5) calculated: 68·74% C, 8·94% H, 4·01% N; found: 69·14% C, 9·02% H, 4·02% N.

3β-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-21-nor-5-pregnen-20-yl Nitrate (*XXII*)

Hydroxy derivative *XXI* (785 mg; 2·25 mmol) was stirred with silver silicate (ref.[18]; 1·5 g) and ground molecular sieve (1 g) in the absence of solvent under reduced pressure (13 Pa) for 2 h. Then the flask was filled with argon and 1,2-dichloroethane (20 ml) was added through a septum. After stirring for 30 min, the mixture was cooled in an ice bath and 2,3,4,6-tetra-O-acetyl-α-D--glucopyranosyl bromide (1·4 g; 3·4 mmol) in 1,2-dichloromethane (4 ml) was added by means of a syringe. After attaining room temperature, the mixture was stirred in the dark for 24 h. The solid was removed by filtration through Celite which was then washed with dichloromethane

(100 ml). The filtrate was washed with aqueous potassium hydrogen carbonate, brine and dried over sodium sulfate. After removal of the solvent and repeated coevaporation with benzene, the residue was chromatographed on a column of silica gel in benzene–ether (20 : 1). Crystallization of the principal fraction from ethanol gave 1·2 g (78%) of glucoside *XXII*, m.p. 158–159°C, $[\alpha]_D$ −38° (*c* 0·2, chloroform). IR spectrum (chloroform): 1 757, 1 243 (CH_3COO), 1 631, 1 281 (ONO_2). ^{1}H NMR spectrum (200 MHz, deuteriochloroform): 5·36 bd (1 H, $C_{(6)}$—H, J = 5·2), 5·20 t (1 H, $C_{(3')}$—H, $J_{2',3'} = J_{3',4'}$ = 9·4), 5·07 t (1 H, $C_{(4')}$—H, $J_{3',4'} = J_{4',5'}$ = 9·4), 4·95dd (1 H, $C_{(2')}$—H, $J_{1',2'}$ = 7·9, $J_{2',3'}$ = 9·4), 4·59 d (1 H, $C_{(1')}$—H, $J_{1',2'}$ = 7·9), 4·43 higher order system (2 H, $C_{(20)}$—H, J_{gem} = 10·4, $J_{17,20}$ = 7·0), 4·26 dd (1 H, $C_{(6')}$—H_a, $J_{5',6'(a)}$ = 4·8, $J_{6'(a),6'(b)}$ = 12·3), 4·11 dd (1 H, $C_{(6')}$—H_b, $J_{5',6'(b)}$ = 2·6, $J_{6'(a),6'(b)}$ = 12·3), 3·68 ddd (1 H, $C_{(5')}$—H, $J_{4',5'}$ = 9·4, $J_{5',6'(a)}$ = 4·8, $J_{5',6'(b)}$ = 2·6), 3·48 m (1 H, $C_{(3)}$—H, W = 30), 2·08, 2·05, 2·02, 2·01 4× s (4× 3 H, 4× $OCOCH_3$), 1·00 s (3 H, $C_{(19)}$—H), 0·70 s (3 H, $C_{(18)}$—H). For $C_{34}H_{49}NO_{13}$ (679·8) calculated: 60·08% C, 7·27% H, 2·06% N; found: 60·16% C, 7·25% H, 1·84% N.

3β-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-21-nor-5-pregnen-20-ol (*XXIII*)

Acetic acid (10 ml) and water (2 ml) were added to glucoside *XXII* (1·1 g; 1·62 mmol) in tetrahydrofuran (40 ml). Powdered zinc (1·35 g) was added portionwise to the stirred solution during 1 h and the stirring was continued for 2 h. The solid was removed by filtration through Celite which was then washed with ether–dichloromethane (1 : 1). The filtrate was diluted with dichloromethane, washed with a sodium chloride solution, twice with a solution of potassium hydrogen carbonate and again with sodium chloride solution. After drying and evaporation of the solvents, the residue was coevaporated with toluene and subjected to flash chromatography on silica gel in chloroform; yield 988 mg (96%) of *XXIII*, m.p. 193–194°C (ethanol), $[\alpha]_D$ −36° (*c* 0·2, chloroform). IR spectrum (chloroform): 3 625 (OH); 1 756, 1 742, 1 254 (CH_3CO). For $C_{34}H_{50}O_{11}$ (634·8) calculated: 64·34% C, 7·94% H; found: 64·18% C, 8·08% H.

(20*E*)-3β-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)
-21-ethoxycarbonyl-5,20-pregnadiene (*XXV*)

A solution of *XXIII* (960 mg; 1·51 mmol) in dichloromethane (15 ml) was stirred with pyridinium chlorochromate (1 g, 4·6 mmol) at room temperature for 2 h under argon. The mixture was filtered through a column of alumina (20 g) which had been layered with Celite. The column was washed with ether, the filtrate taken down and the obtained aldehyde *XXIV* dissolved in dichloromethane (5 ml). A solution of the phosphonate salt, prepared from sodium hydride (180 mg; 7·5 mmol) and diethyl ethoxycarbonylmethylphosphonate (1·5 ml; 7·6 mmol) in 1,2-dimethoxyethane (10 ml) (stirring for 20 min under argon), was added dropwise under stirring in an argon atmosphere. After stirring at room temperature for 4 h, the solvents were evaporated, the residue was dissolved in dichloromethane, washed twice with a sodium chloride solution and dried over sodium sulfate. After removal of the solvent and drying *in vacuo*, the residue was allowed to stand overnight with pyridine (10 ml) and acetic anhydride (1·5 ml). Removal of solvents, coevaporation with toluene and flash chromatography on silica gel in benzene–ether (10 : 1) afforded 500 mg (47%) of *XXV*, m.p. 153–155°C (ethanol), $[\alpha]_D$ −21° (*c* 0·2, chloroform). IR spectrum (chloroform): 1 712, 1 650 (C=C—C=O), 1 756, 1 740, 1 253, 1 046 (CH_3CO). ^{1}H NMR spectrum (200 MHz): 6·94 dd (1 H, $C_{(20)}$—H, $J_{20,22}$ = 15·6, $J_{17,20}$ = 8·0), 5·78 dd (1 H, $C_{(22)}$—H, $J_{20,22}$ = 15·6, $J_{17,22}$ = 1·0), 5·36 bd (1 H, $C_{(6)}$—H, $J_{6,7}$ = 4·6), 5·21 t (1 H, $C_{(3')}$—H, $J_{2',3'} = J_{3',4'}$ = 9·3), 5·07 t (1 H, $C_{(4')}$—H, $J_{3',4'} = J_{4',5'}$ = 9·5), 4·95 dd (1 H, $C_{(2')}$—H, $J_{1',2'}$ = 7·9, $J_{2',3'}$ = 9·3), 4·59 d (1 H, $C_{(1')}$—H, $J_{1',2'}$ = 7·8), 4·26 dd (1 H, $C_{(6)}$—

—$H_{a'}$ $J_{5',6'(a)}$ = 4·8, $J_{6'(a),6'(b)}$ = 12·4), 4·18 q (2 H, $COOCH_2CH_3$, J = 7·0), 4·10 dd (1 H, $C_{(6')}$—$H_{b'}$ $J_{5',6'(b)}$ = 2·4, $J_{6'(a),6'(b)}$ = 12·3), 3·68 ddd (1 H, $C_{(5')}$—H, $J_{4',5'}$ = 9·6, $J_{5',6'(a)}$ = = 4·6, $J_{5',6'(b)}$ = 2·4), 3·49 bm (1 H, $C_{(3)}$—H, W = 40), 2·08, 2·05, 2·02, 2·00 4× s (4× 3 H, 4× CH_3CO), 1·28 t (3 H, $COOCH_2CH_3$, J = 7), 0·99 s (3 H, $C_{(19)}$—H), 0·66 s (3 H, $C_{(18)}$— —H). For $C_{38}H_{54}O_{12}$ (702·8) calculated: 64·94% C, 7·74% H; found: 64·78% C, 8·08% H.

(20*E*)-3β-(β-D-Glucopyranosyloxy)-21-ethoxycarbonyl-5,20-pregnadiene (*XXVI*)

A mixture of *XXV* (350 mg; 0·5 mmol), ethanol (20 ml), and sodium ethoxide (5 drops of a solution of 100 mg sodium in 5 ml ethanol) was stirred at room temperature for 2 h. Dry ice (about 0·5 cm^3) was added, ethanol evaporated, the residue mixed with chloroform–ethanol (10 : 1) and the suspension filtered through a column of silica gel layered with Celite. The column was washed with the same solvent mixture, the solvents were evaporated and the residue was crystallized from hot ethanol; yield 201 mg (75%) of *XXVI*, m.p. 215—220°C (dec.), $[\alpha]_D$ −45° (*c* 0·21, chloroform–ethanol 1 : 1). IR spectrum (KBr): 1 720, 1 650 (C=C—C=O), 1 630 (C=C), 1 170, 1 081, 1 030 (—O—). For $C_{30}H_{46}O_8$ (534·7) calculated: 67·39% C, 8·67% H; found: 67·53% C, 8·56% H.

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