PREPARATION OF (20*E*)-21-METHOXYCARBONYL-5,14,20--PREGNATRIEN-3β-OL DERIVATIVES*

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Received November 11th, 1986

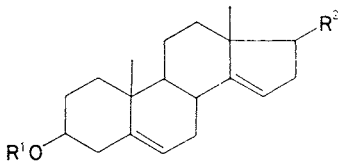
(20*E*)-21-Methoxycarbonyl-5,14,20-pregnatrien-3β-yl hydrogen butanedioate (*XII*) and (20*E*)--21-ethoxycarbonyl-5,14,20-pregnatrien-3β-yl hydrogen butanedioate (*XIV*) were prepared in nine steps from 3β-acetoxy-5,14-pregnadien-20-one (*I*). In the key intermediate, 20-(bis(4-methoxyphenyl)phenylmethoxy)-21-nor-5,14-pregnadien-3β-yl 2-(trimethylsilyl)ethyl butanedioate (*VIII*), the hydroxyl in position 20 was protected with 4,4′-dimethoxytrityl group and the succinate moiety with 2-(trimethylsilyl)ethyl group.

Our present communication concerns the preparation of (20*E*)-21-alkoxycarbonyl--5,14,20-pregnatrien-3β-ols as models for structure–activity studies of steroidal cardiotonics. This synthesis represents a close continuation of our previous approach to the analogous 5,20-dienes[1]. We used blocked succinate moiety as the 3β-hydroxyl--protecting group and at the same time as a source of the final hemisuccinate. We started from ketone *I* (refs[2,3]) which was converted into acid *II* by hypobromite degradation. Its methyl ester *III*, prepared by treatment with dimethyl sulfate and potassium carbonate in acetone, was reduced with sodium bis(2-methoxyethoxy)-dihydroaluminate to give the diol *IV*. Esterification of its monotrityl derivative *V* with 2-(trimethylsilyl)ethyl hydrogen butanedioate afforded the intermediate *VII*. The attempted removal of the trityl protecting group by standing on a silica gel column[1] was accompanied by formation of side-products, in contrast to the reaction of an analogous derivative[1] without the double bond in position 14. Also cleavage with a tetrahydrofuran–acetic acid–water mixture afforded the desired product *IX* in a low yield (32%).

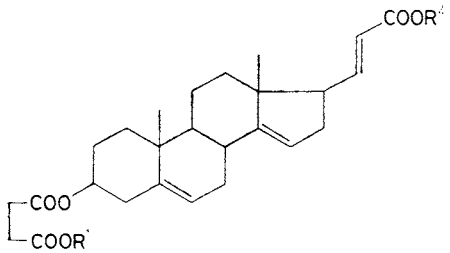
We tried therefore the more readily cleavable 4,4′-dimethoxytrityl group; this required modifications of several reaction steps. These modifications were first checked on the better accessible 21-nor-5-pregnene derivatives[1]. Reaction of diol *XV* with 1·1 equivalent of 4,4′-dimethoxytrityl chloride in pyridine afforded the monotrityl derivative *XVI* in high yield (80%). The compound *XVI* was esterified

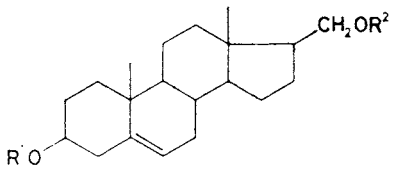
* Part CCCXXXII in the series On Steroids; Part CCCXXXI: Collect. Czech. Chem. Commun. *52*, 1043 (1987).

with 2-(trimethylsilyl)ethyl hydrogen butanedioate and N,N'-dicyclohexylcarbodiimide in pyridine with 4-dimethylaminopyridine as catalyst and the obtained intermediate *XVII* was converted in high yield (88% from *XVI*) into the desired product *XVIII* by treatment with silica gel in benzene at 70°C in an argon atmosphere. The total yield of *XVIII* from the diol *XV* was thus 70%, whereas the use of the trityl protecting group afforded[1] only 49% yield. This higher yield may be ascribed to a more facile removal of the 4,4'-dimethoxytrityl group.



I, R^1 = Ac; R^2 = $COCH_3$
II, R^1 = H; R^2 = COOH
III, R^1 = H; R^2 = $COOCH_3$
IV, R^1 = H; R^2 = CH_2OH
V, R^1 = H; R^2 = CH_2OTr
VI, R^1 = H; R^2 = CH_2ODMTr
VII, R^1 = $OCCH_2CH_2COOCH_2CH_2Si(CH_3)_3$; R^2 = CH_2OTr
VIII, R^1 = $OCCH_2CH_2COOCH_2CH_2Si(CH_3)_3$; R^2 = CH_2ODMTr
IX, R^1 = $OCCH_2CH_2COOCH_2CH_2Si(CH_3)_3$; R^2 = CH_2OH
X, R^1 = $OCCH_2CH_2COOCH_2CH_2Si(CH_3)_3$; R^2 = CHO





XI, R^1 = $CH_2CH_2Si(CH_3)_3$; R^2 = CH_3
XII, R^1 = H; R^2 = CH_3
XIII, R^1 = $CH_2CH_2Si(CH_3)_3$; R^2 = CH_2CH_3
XIV, R^1 = H; R^2 = CH_2CH_3
XV, R^1 = R^2 = H
XVI, R^1 = H; R^2 = DMTr
XVII, R^1 = $OCCH_2CH_2COOCH_2CH_2Si(CH_3)_3$; R^2 = DMTr
XVIII, R^1 = $OCCH_2CH_2COOCH_2CH_2Si(CH_3)_3$; R^2 = H

Tr = trityl
DMTr = 4,4'-dimethoxytrityl

This modified procedure was then applied to the synthesis of the intermediate *IX* according to the sequence *IV* → *VI* → *VIII* → *IX* which afforded the intermediate *IX* in 55% yield. Oxidation of the hydroxy derivative *IX* in position 20 with pyridi-

nium chlorochromate gave aldehyde *X*. The Wittig–Horner reaction with diethyl methoxycarbonylmethylphosphonate converted *X* into the unsaturated methyl ester *XI* which after removal of the 2-(trimethylsilyl)ethyl protecting group yielded the desired hemisuccinate *XII* (overall yield 9·3% from *I*). Analogously we prepared the hemisuccinate *XIV* in 7·5% yield using diethyl ethoxycarbonylmethylphosphonate.

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. Infrared spectra were recorded on a Zeiss UR-20 spectrometer (wavenumbers in cm^{-1}). Proton NMR spectra were taken on a Tesla BS-476 instrument (60 MHz) 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). Prior to evaporation, solutions in organic solvents were dried over anhydrous sodium sulfate. Solvents were evaporated *in vacuo* (about 2 kPa). Analytical samples were dried over phosphorus pentoxide at 40°C/26 Pa for 12 h. Identity of samples prepared by different routes was checked by comparison of their IR and ^{1}H NMR spectra, thin-layer chromatography, and mixture melting point determinations.

3β-Hydroxy-21-nor-5,14-pregnadien-20-oic Acid (*II*)

A solution of sodium hypobromite (prepared[4] from 2·9 g of sodium hydroxide, 25 ml of water, 3 g of bromine, and 17 ml of dioxane) was added during 5 min to a solution of ketone *I* (refs[2,3]; 2 g; 5·6 mmol) in a mixture of dioxane (70 ml) and water (23 ml), precooled to 8°C. After stirring for 4 h at room temperature, a solution of sodium sulfite (0·7 g) in water (5 ml) was added, the mixture was refluxed for 15 min without stirring and then acidified with concentrated hydrochloric acid (3·5 ml), diluted with water (60 ml) and set aside in a refrigerator overnight. The product was collected on filter, washed with water and dried over phosphorus pentoxide *in vacuo* (26 Pa), affording 1·36 g (77%) of the acid *II*, m.p. 275—280°C (decomp.); $[\alpha]_D$ −11° (*c* 0·2, pyridine). IR spectrum (KBr): 3 500—2 500, 1 704 (COOH), 3 430, 1 048 (OH). Mass spectrum (*m/z*): M^+ 316, 301, 298, 283. For $C_{20}H_{28}O_3$ (316·4) calculated: 75·91% C, 8·92% H; found: 76·07% C, 9·15% H.

Methyl 3β-Hydroxy-21-nor-5,14-pregnadien-20-oate (*III*)

A stirred mixture of acid *II* (1·3 g; 4·1 mmol), anhydrous potassium carbonate (1·8 g; 13·0 mmol), acetone (15 ml), and dimethyl sulfate (0·8 ml; 8·5 mmol) was refluxed for 4 h. After cooling, the mixture was diluted with dichloromethane–ether (200 ml, 1 : 1) and passed through a column of alumina (30 g) which was then washed with the same solvent mixture. Evaporation of the solvents and crystallization of the residue from dichloromethane–light petroleum yielded 1·22 g (90%) of the title ester *III*, m.p. 180—182°C; $[\alpha]_D$ −18° (*c* 0·3, chloroform). IR spectrum (chloroform): 3 610, 3 490 (OH), 1 738, 1 162 (COOR). ^{1}H NMR spectrum: 5·40 bd (1 H, $C_{(6)}$—H, J = 3·5), 5·15 bs (1 H, $C_{(15)}$—H), 3·67 s (3 H, $COOCH_3$), 3·52 m (1 H, $C_{(3)}$—H), 1·02 s (3 H, $C_{(19)}$—H), 0·90 s (3 H, $C_{(18)}$—H). For $C_{21}H_{30}O_3$ (330·5) calculated: 76·33% C, 9·15% H; found: 76·15% C, 8·95% H.

21-Nor-5,14-pregnadiene-3β,20-diol (*IV*)

Sodium bis(2-methoxyethoxy)dihydroaluminate in benzene (70% solution; 3·0 ml) was added to methyl ester *III* (1 g; 3·0 mmol) in tetrahydrofuran (30 ml). The stirred mixture was refluxed under argon for 5 h, cooled to room temperature and decomposed with water. The formed precipitate was partitioned between 1 : 1 chloroform–ethyl acetate mixture and dilute (1 : 4) hydrochloric acid. The aqueous layer was extracted with chloroform–ethyl acetate mixture and the combined organic phases were washed with dilute hydrochloric acid, water, potassium hydrogen carbonate solution, and water. After removal of the solvent, the residue was crystallized from chloroform–ethyl acetate to give 0·62 g (68%) of diol *IV*, m.p. 190—193°C; $[\alpha]_D$ −19° (*c* 0·4, chloroform). IR spectrum (KBr): 3 370 (OH). For $C_{20}H_{30}O_2$ (302·5) calculated: 79·42% C, 10·00% H; found: 79·27% C, 10·07% H.

20-Triphenylmethoxy-21-nor-5,14-pregnadien-3β-ol (*V*)

Triethylamine (0·87 ml; 6·2 mmol), 4-dimethylaminopyridine (40 mg), and a solution of triphenylmethyl chloride (1·36 g; 4·9 mmol) in dichloromethane (9·5 ml) were successively added to a solution of diol *IV* (620 mg; 2·05 mmol) in 1,2-dimethoxyethane (6·5 ml). The mixture was stirred at room temperature for 6 h, diluted with benzene (200 ml) and washed with water (3 x). After removal of the solvents, the residue was chromatographed on a silica gel column (120 g; pretreated with ammonia vapours for 24 h). Light petroleum–benzene–ether (48 : 48 : 4) washed out non-polar impurities; the amorphous trityl derivative *V* (908 mg; 81%) was eluted with light petroleum–benzene–ether (45 : 45 : 10); $[\alpha]_D$ −6° (*c* 0·2, chloroform). IR spectrum (chloroform): 3 610 (OH), 1 600, 1 595 (arom. system). ^{1}H NMR spectrum: 7·29 m (15 H, arom. H), 5·40 m (1 H, $C_{(6)}$—H), 5·13 bs (1 H, $C_{(15)}$—H), 3·50 m (1 H, $C_{(3)}$—H), 3·14 m (2 H, $C_{(20)}$—H), 1·01 s (3 H, $C_{(19)}$—H), 0·70 s (3 H, $C_{(18)}$—H). For $C_{39}H_{44}O_2$ (544·8) calculated: 85·99% C, 8·14% H; found: 86·30% C, 8·27% H.

20-(Bis(4-methoxyphenyl)phenylmethoxy)-21-nor-5,14-pregnadien-3β-ol (*VI*)

4,4′-Dimethoxytrityl chloride (559 mg; 1·65 mmol) was added at 0°C to a solution of diol *IV* (454 mg; 1·5 mmol) in pyridine (7·5 ml). After stirring at room temperature for 24 h, the mixture was diluted with benzene (200 ml), washed with a potassium hydrogen carbonate solution (2×), water (2×), dried over anhydrous potassium carbonate and taken down. The residue was coevaporated with toluene to remove most of the pyridine and chromatographed on a column of silica gel (70 g; pre-treated with ammonia vapours for 24 h). Light petroleum–benzene–triethylamine–ether (100 : 100 : 1 : 2) washed out non-polar impurities, and elution with light petroleum–benzene–triethylamine–ether (100 : 100 : 1 : 5) afforded 711 mg (78%) of the amorphous trityl derivative *VI*; $[\alpha]_D$ −7° (*c* 1·4, dioxane). IR spectrum (tetrachloromethane): 3 620, 3 360 (OH), 2 840, 1 252 (OCH_3), 1 610, 1 513 (aromatic system). ^{1}H NMR spectrum (tetrachloromethane): 7·22 m (9 H, arom. H), 6·70 bd (4 H, J = 9, arom. H), 5·31 bd (1 H, J = 4·5, $C_{(6)}$—H), 5·07 bs (1 H, $C_{(15)}$—H), 3·72 s (6 H, OCH_3), 3·08 m (2 H, $C_{(20)}$—H), 0·98 s (3 H, $C_{(19)}$—H), 0·70 s (3 H, $C_{(18)}$—H). For $C_{41}H_{48}O_4$ (604·8) calculated: 81·42% C, 8·00% H; found: 81·36% C, 7·82% H.

20-Triphenylmethoxy-21-nor-5,14-pregnadien-3β-yl
2-(Trimethylsilyl)ethyl Butanedioate (*VII*)

2-(Trimethylsilyl)ethyl hydrogen butanedioate[5] (685 mg; 3·1 mmol), N,N′-dicyclohexylcarbodiimide (365 mg; 1·8 mmol), and 4-dimethylaminopyridine (20 mg) were added to a solution

of hydroxy derivative *V* (860 mg; 1·6 mmol) in benzene (18 ml). After stirring at room temperature for 5 h, the mixture was diluted with light petroleum (20 ml), the precipitated N,N'-dicyclohexylurea was removed by filtration and the solvents were evaporated *in vacuo*. Chromatography of the residue on a silica gel column (50 g, Silpearl, Kavalier) in light petroleum–ether (4 : 1) afforded 1·01 g (86%) of the amorphous ester *VII*; $[\alpha]_D$ −6° (*c* 0·3, chloroform). IR spectrum (tetrachloromethane): 1 737, 1 136 (COOR), 1 600, 1 593 (aromatic system), 1 250, 859, 849 ($Si(CH_3)_3$). ^{1}H NMR spectrum (external lock): 7·42 m (15 H, arom. H), 5·42 m (1 H, $C_{(6)}$—H), 5·17 bs (1 H, $C_{(15)}$—H), 4·57 m (1 H, $C_{(3)}$—H), 4·19 m (1 H, *W* = 17, $COOCH_2CH_2Si$), 3·17 m (2 H, $C_{(20)}$—H), 2·61 s (4 H, $OOCCH_2CH_2COO$), 1·06 s (3 H, $C_{(19)}$—H), 0·72 s (3 H, $C_{(18)}$—H), 0·07 s (9 H, $Si(CH_3)_3$). For $C_{48}H_{60}O_5Si$ (745·1) calculated: 77·38% C, 8·12% H; found: 77·56% C, 7·97% H.

20-Hydroxy-21-nor-5,14-pregnadien-3β-yl 2-(Trimethylsilyl)ethyl Butanedioate (*IX*)

A) Acetic acid (5·5 ml) and water (3·5 ml) were added to a solution of trityl derivative *VII* (917 mg; 1·2 mmol) in tetrahydrofuran (18 ml). After heating to 70°C for 40 h, the mixture was coevaporated with toluene *in vacuo* (2×), the residue was dissolved in toluene–ether (1 : 1) and washed twice with water. After evaporation, the residue was chromatographed on a column of silica gel (90 g). Light petroleum–benzene–ether (10 : 10 : 1) washed out non-polar impurities, light petroleum–benzene–ether (10 : 10 : 2) eluted 200 mg (32%) of the oily alcohol *IX*; $[\alpha]_D$ −21° (*c* 1·2, chloroform). IR spectrum (chloroform): 3 623, 3 525 (OH), 1 728 (COOR), 1 252, 860, 841 ($Si(CH_3)_3$). ^{1}H NMR spectrum (external lock): 5·41 m (1 H, $C_{(6)}$—H), 5·17 bs (1 H, $C_{(15)}$—H), 4·62 m (1 H, $C_{(3)}$—H), 4·19 m (2 H, *W* = 17, $COOCH_2CH_2Si$), 3·78 m (2 H, $C_{(20)}$—H), 2·60 s (4 H, $OOCCH_2CH_2COO$), 1·05 s (3 H, $C_{(19)}$—H), 0·97 s (3 H, $C_{(18)}$—H), 0·08 s (9 H, $Si(CH_3)_3$). For $C_{29}H_{46}O_5Si$ (502·8) calculated: 69·28% C, 9·22% H; found: 69·57% C, 8·97% H.

B) A solution of hydroxy derivative *VI* (650 mg; 1·1 mmol) in benzene (5 ml) was added to 2-(trimethylsilyl)ethyl hydrogen butanedioate[5] (666 mg; 3·05 mmol) and 4-dimethylaminopyridine (13 mg) in pyridine (5 ml). N,N'-Dicyclohexylcarbodiimide (373 mg; 1·8 mmol) in benzene (3 ml) was added, the mixture was stirred at room temperature for 24 h, diluted with benzene (200 ml), washed twice with water, dried over anhydrous sodium sulfate and filtered through an alumina column (60 g). The column was washed with benzene, the solvents were evaporated *in vacuo* and the residue was coevaporated with toluene *in vacuo*. Yield 1·1 g of crude *VIII*. ^{1}H NMR spectrum (tetrachloromethane, external lock): 7·18 m (9 H, arom. H), 6·67 d (4 H, *J* = 9, arom. H), 5·36 m (1 H, $C_{(6)}$—H), 5·03 bs (1 H, $C_{(15)}$—H), 4·44 m (1 H, $C_{(3)}$—H), 4·07 m (2 H, *W* = 17, $COOCH_2CH_2Si$), 3·68 s (6 H, OCH_3), 3·03 m (2 H, $C_{(20)}$—H), 2·51 bs (4 H, $OOCCH_2CH_2COO$), 0·95 s (3 H, $C_{(19)}$—H), 0·65 s (3 H, $C_{(18)}$—H), −0·02 s (9 H, $Si(CH_3)_3$). The crude *VIII* (1·1 g) was dissolved in benzene (90 ml) and heated to 65°C with silica gel (30 g) under argon for 3 h. The content of the flask was washed with ether on a layer of silica gel and the product was eluted with ether. After evaporation of ether, the residue was subjected to column chromatography on silica gel (60 g). Light petroleum–benzene–ether (10 : 10 : 1) eluted non-polar impurities; the product was obtained on elution with light petroleum–benzene–ether (10 : 10 : 2); yield 376 mg (70% from *VI*) of oily *IX*, identical with the product prepared by procedure *A*.

(20*E*)-21-Methoxycarbonyl-5,14,20-pregnatrien-3β-yl
2-(Trimethylsilyl)ethyl Butanedioate (*XI*)

Pyridinium chlorochromate (345 mg; 1·6 mmol) was added to a solution of hydroxy derivative *IX* (300 mg; 0·6 mmol) in dichloromethane (16 ml). After stirring at room temperature under

argon for 2 h, the mixture was diluted with ether (30 ml) and filtered through an alumina column (10 g) which was then washed with ether. The combined filtrates were taken down *in vacuo* and the residue was coevaporated with toluene *in vacuo* to remove pyridine. Yield 285 mg (95%) of aldehyde *X*. ^{1}H NMR spectrum (external lock): 9·89 d (1 H, J = 1·5, $C_{(20)}$—H), 5·37 bd (1 H, J = 4·5, $C_{(6)}$—H), 5·13 bs (1 H, $C_{(15)}$—H), 4·55 m (1 H, $C_{(3)}$—H), 4·08 m (2 H, W = 17, $COOCH_2CH_2Si$), 2·47 s (4 H, $OOCCH_2CH_2COO$), 0·90 s (6 H, $C_{(18)}$—H and $C_{(19)}$—H), −0·08 s (9 H, $Si(CH_3)_3$). Diethyl methoxycarbonylmethylphosphonate (0·53 ml; 2·9 mmol) was added under argon during 10 min to a suspension of sodium hydride (68 mg; 2·8 mmol) in 1,2-dimethoxyethane (3·5 ml). The mixture was stirred at room temperature for 20 min and then a solution of the aldehyde *X* (270 mg; 0·54 mmol) in 1,2-dimethoxyethane (3 ml) was added. The mixture was stirred at room temperature in an argon atmosphere for 4 h and the solvent was removed *in vacuo*. The residue was partitioned between ether and water, the aqueous layer was extracted with ether and the combined organic phases were washed twice with water, dried and evaporated. The residue was chromatographed on a column of silica gel (25 g) in light petroleum–ether (9 : 1) to give 170 mg (54% from *IX*) of the product *XI*, m.p. 123–125°C (ether–light petroleum), $[\alpha]_D$ −16° (*c* 1·6, chloroform). IR spectrum (tetrachloromethane): 1 733 (COOR), 1 733, 1 655 (C=C—C=O), 860, 840 ($Si(CH_3)_3$). ^{1}H NMR spectrum (external lock): 7·09 dd (1 H, $J_{17,20}$ = 7·3, $J_{20,21}$ = 16, $C_{(20)}$—H), 5·83 d (1 H, $J_{20,21}$ = 16, $C_{(21)}$—H), 5·43 m (1 H, $C_{(6)}$—H), 5·23 bs (1 H, $C_{(15)}$—H), 4·20 m (2 H, W = 17, $COOCH_2CH_2Si$), 3·76 s (3 H, $COOCH_3$), 2·63 s (4 H, $OOCCH_2CH_2COO$), 1·07 s (3 H, $C_{(19)}$—H), 0·94 s (3 H, $C_{(18)}$—H), 0·08 s (9 H, $Si(CH_3)_3$). For $C_{32}H_{48}O_6Si$ (556·8) calculated: 69·03% C, 8·69% H; found: 69·32% C, 8·88% H.

(20*E*)-21-Methoxycarbonyl-5,14,20-pregnatrien-3β-yl Hydrogen Butanedioate (*XII*)

A solution of tetrabutylammonium fluoride in tetrahydrofuran (0·5 ml; *c* 1 mol l^{-1}) was added to ester *XI* (135 mg; 0·24 mmol) in tetrahydrofuran (3 ml). After stirring for 5 h at room temperature, the mixture was diluted with benzene (200 ml), washed with dilute sulfuric acid (10%), twice with water, and the solvents were evaporated. Crystallization from light petroleum–dichloromethane afforded 75 mg (68%) of hemisuccinate *XII*, m.p. 192–195°C, $[\alpha]_D$ −17° (*c* 1·3, chloroform). IR spectrum (chloroform): 3 500–2 500, 1 708 shoulder (COOH), 1 724 (COOR), 1 724, 1 654 (C=C—C=O). ^{1}H NMR spectrum: 7·09 dd (1 H, $J_{17,20}$ = 7, $J_{20,21}$ = 16, $C_{(20)}$—H), 5·81 d (1 H, $J_{20,21}$ = 16, $C_{(21)}$—H), 5·41 m (1 H, $C_{(6)}$—H), 5·20 bs (1 H, $C_{(15)}$—H), 4·61 m (1 H, W = 36, $C_{(3)}$—H), 3·72 s (3 H, $COOCH_3$), 2·63 bs (4 H, $OOCCH_2CH_2COO$), 1·03 s (3 H, $C_{(19)}$—H), 0·88 s (3 H, $C_{(18)}$—H). For $C_{27}H_{36}O_6$ (456·6) calculated: 71·03% C, 7·95% H; found: 70·85% C, 8·17% H.

(20*E*)-21-Ethoxycarbonyl-5,14,20-pregnatrien-3β-yl
2-(Trimethylsilyl)ethyl Butanedioate (*XIII*)

The title compound was prepared from hydroxy derivative *IX* (300 mg; 0·6 mmol) in the same manner as described for *XI*, except that the Wittig–Horner reaction was carried out with diethyl ethoxycarbonylmethyl phosphonate (0·57 ml; 2·9 mmol). The ethyl ester *XIII* (167 mg; 49%) was obtained by chromatography on a column of silica gel (30 g) in benzene–ether (98 : 2); m.p. 103–105°C (ether–light petroleum); $[\alpha]_D$ −13° (*c* 1·6, chloroform). IR spectrum (tetrachloromethane): 1 728 (COOR), 1 728, 1 650 (C=C—C=O), 1 252, 861, 840 ($Si(CH_3)_3$). ^{1}H NMR spectrum (external lock): 7·09 dd (1 H, $J_{17,20}$ = 7, $J_{20,21}$ = 16, $C_{(20)}$—H), 5·80 d (1 H, $J_{20,21}$ = 16, $C_{(21)}$—H), 5·41 m (1 H, $C_{(6)}$—H), 5·18 bs (1 H, $C_{(15)}$ —H), 4·54 m (1 H, $C_{(3)}$—H), 4·18 q (2 H, J = 7, $COOCH_2CH_3$), 4·16 m (2 H, W = 17, $COOCH_2CH_2Si$), 2·57 s (4 H,

$OOCCH_2CH_2COO$), 1·26 t (3 H, $J = 7$, $COOCH_2CH_3$), 0·99 s (3 H, $C_{(19)}$—H), 0·86 s (3 H, $C_{(18)}$—H), 0·01 s (9 H, $Si(CH_3)_3$). For $C_{33}H_{50}O_6Si$ (570·8) calculated: 69·43% C, 8·83% H; found: 69·55% C, 9·07% H.

(20*E*)-21-Ethoxycarbonyl-5,14,20-pregnatrien-3β-yl Hydrogen Butanedioate (*XIV*)

A solution of tetrabutylammonium fluoride in tetrahydrofuran (0·6 ml; 1 mol l^{-1}) was added to ester *XIII* (160 mg; 0·28 mmol) in tetrahydrofuran (4 ml). After stirring at room temperature for 4 h, the mixture was diluted with benzene (200 ml), washed twice with dilute (10%) sulfuric acid and twice with water. Evaporation and crystallization from hexane–dichloromethane yielded 74 mg (56%) of hemisuccinate *XIV*, m.p. 185–188°C, $[\alpha]_D$ −28° (*c* 1·0, pyridine). IR spectrum (chloroform): 3 300–2 500, 1 715 (COOH), 1 715 (COOR), 1 715, 1 650 (C=C—C=O). ^{1}H NMR spectrum: 7·08 dd (1 H, $J_{17,20} = 7$, $J_{20,21} = 16$, $C_{(20)}$—H), 5·80 d (1 H, $J_{20,21} = 16$, $C_{(21)}$—H), 5·42 m (1 H, $C_{(6)}$—H), 5·23 bs (1 H, $C_{(15)}$—H), 4·62 m (1 H, $C_{(3)}$—H), 4·18 q (2 H, $J = 7$, $COOCH_2CH_3$), 2·62 bs (4 H, $OOCCH_2CH_2COO$), 1·27 t (3 H, $J = 7$, $COOCH_2CH_3$), 1·01 s (3 H, $C_{(19)}$—H), 0·86 s (3 H, $C_{(18)}$—H). For $C_{28}H_{38}O_6$ (470·6) calculated: 71·46% C, 8·14% H; found: 71·67% C, 7·92% H.

20-(Bis(4-methoxyphenyl)phenylmethoxy)-21-nor-5-pregnen-3β-ol (*XVI*)

To a solution of diol *XV* (ref.[6]; 609 mg; 2·0 mmol) in pyridine (10 ml), precooled to 0°C, was added 4,4′-dimethoxytrityl chloride (745 mg; 2·2 mmol). The mixture was stirred for 24 h at room temperature, diluted with benzene (250 ml), washed with potassium hydrogen carbonate solution (3×), water (2×) and dried over anhydrous potassium carbonate. After evaporation of the solvents, the residue was coevaporated with toluene *in vacuo* to remove most of the pyridine and then chromatographed on a silica gel column (90 g; pretreated with ammonia vapours for 12 h). Light petroleum–benzene–triethylamine–ether (100 : 100 : 1 : 3) eluted non-polar impurities, further elution with the same solvents in different ratio (100 : 100 : 1 : 10) afforded 967 mg (80%) of amorphous trityl derivative *XVI*; $[\alpha]_D$ −26° (*c* 2·1, dioxane). IR spectrum (tetrachloromethane): 3 625, 3 360 (OH), 2 835, 1 245 (OCH_3), 1 610, 1 585, 1 509 (aromatic system). ^{1}H NMR spectrum (tetrachloromethane): 7·23 m (9 H, arom. H), 6·68 d (4 H, $J = 9$, arom. H), 5·25 m (1 H, $C_{(6)}$—H), 3·70 s (6 H, OCH_3), 2·92 m (2 H, $C_{(20)}$—H), 0·95 s (3 H, $C_{(19)}$—H), 0·43 s (3 H, $C_{(18)}$—H). For $C_{41}H_{50}O_4$ (606·9) calculated: 81·15% C, 8·30% H; found: 80·92% C, 8·02% H.

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

A solution of hydroxy derivative *XVI* (610 mg; 1·0 mmol) in benzene (4 ml) was added to a solution of 2-(trimethylsilyl)ethyl hydrogen butanedioate[5] (625 mg; 2·9 mmol) and 4-dimethylaminopyridine (12 mg) in pyridine (5 ml). After addition of N,N′-dicyclohexylcarbodiimide (350 mg; 1·7 mmol) in benzene (3 ml), the mixture was stirred at room temperature for 48 h, diluted with benzene (200 ml), washed twice with water, dried over anhydrous sodium sulfate and filtered through a column of alumina (60 g). The column was washed with benzene, the solvents were removed *in vacuo* and the residue was coevaporated with toluene *in vacuo*. Yield 1·1 g of crude *XVII*. ^{1}H NMR spectrum (tetrachloromethane, external lock): 7·12 m (9 H, arom. H), 6·64 bd (4 H, $J = 9$, arom. H), 5·25 m (1 H, $C_{(6)}$—H), 4·05 m (2 H, $W = 17$, $COO.CH_2CH_2Si$), 3·65 s (6 H, OCH_3), 2·85 m (2 H, $C_{(20)}$—H), 2·38 bs (4 H, $OOCCH_2CH_2COO$), 0·93 s (3 H, $C_{(19)}$—H), 0·38 s (3 H, $C_{(18)}$—H), 0·00 s (9 H, $Si(CH_3)_3$). The crude *XVII* (1·1 g) was dissolved in benzene (90 ml), mixed with silica gel (30 g) and heated under argon to 70°C

for 3 h. The content of the flask was washed out with ether onto a layer of silica gel and the product was eluted with ether. After evaporation of the solvents, the residue was chromatographed on a silica gel column (60 g). Non-polar impurities were eluted with light petroleum–benzene–ether (50 : 45 : 5), the product was obtained with light petroleum–benzene–ether (45 : 45 : 10); yield 445 mg (88% from *XVI*) of succinate *XVIII*, identical with an authentic sample[1].

The authors are indebted to Dr I. Roseberg for the kind gift of 4,4'-*dimethoxytrityl chloride and for valuable advice. The authors' thanks are due also to Mrs Z. Ledvinová for determination of optical rotations, to Mrs K. Matoušková for taking the* IR *spectra and to Dr S. Vašíčková for their interpretation, and to Mrs J. Jelínková and Mrs M. Snopková for the* ^{1}H NMR *spectral measurements. The elemental analyses were carried out in the Analytical Laboratory of our Institute (Dr V. Pechanec, Head).*

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Translated by M. Tichý.