PREPARATION OF 3β-HYDROXY-21,26,27-TRINORCHOLESTA-5,23--DIEN-25→22-OLIDE AND 3β-HYDROXY-20-(2-FURYL)-21--NOR-5-PREGNENE DERIVATIVES*

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A mixture of 22*R*- and 22*S*-isomers of 3β-methoxymethoxy-21,26,27-trinorcholesta-5,23-dien-25→→22-olide (*IX*) was prepared from ester *I* by two synthetic pathways. Lactone *IX* was converted into hemisuccinate *XII via* the intermediates *X* and *XI*. The isomer ratio in compounds *IX*—*XII* was determined by ^{1}H NMR and CD spectra. Lactone *IX* was converted into 20-(2-furyl)-3β--methoxymethoxy-21-nor-5-pregnene (*XIII*) and further, *via* intermediates *XIV* and *XV*, to the β-D-glucoside *XVI*.

Recently we prepared[1] derivatives of 21,26,27-trinor-5α-cholestan-25→22-olide and determined their absolute configuration at $C_{(22)}$. The present communication concerns the synthesis of analogous derivatives containing double bond in position 5,6 and hydroxyl group in position 3.

We started from the methyl ester *I* which can be easily prepared[2,3] from condensation products of 3β-acetoxy-5-androsten-17-one with derivatives of cyanoacetic acid. The key intermediate, lactone *IX*, was synthesized from the ester *I* by two independent routes. In the first (already used[4,5] in the preparation of α,β-unsaturated γ-lactones) the ester *I* was reduced to alcohol *II* and this was oxidized with pyridinium chlorochromate to aldehyde *III*. Reaction of this aldehyde with lithium salt of 1-(2-tetrahydropyranyloxy)-2-propyne afforded a mixture of alcohols *IV*, differing in configuration at $C_{(22)}$, which was converted into a mixture of diols *V* by removal of the tetrahydropyranyl protective group. Partial hydrogenation of the acetylenic diols *V* on P-2 nickel gave unsaturated diols *VI* whose oxidation with silver carbonate on Celite afforded a mixture of lactones *IX*.

Although this mixture was unseparable by thin-layer as well as column chromatography, the population of the isomers was determined from intensities of the separated ^{1}H NMR signals of both isomers. The signals were assigned on the basis of comparison with the spectra of model lactones *XVII* and *XVIII* (see Table I). In this way, we found that the ratio of both isomers in *IX* amounted to about 1 : 1. In addition to lactone *IX* (56% yield), the oxidation of the diols *VI* gave as the side-product the

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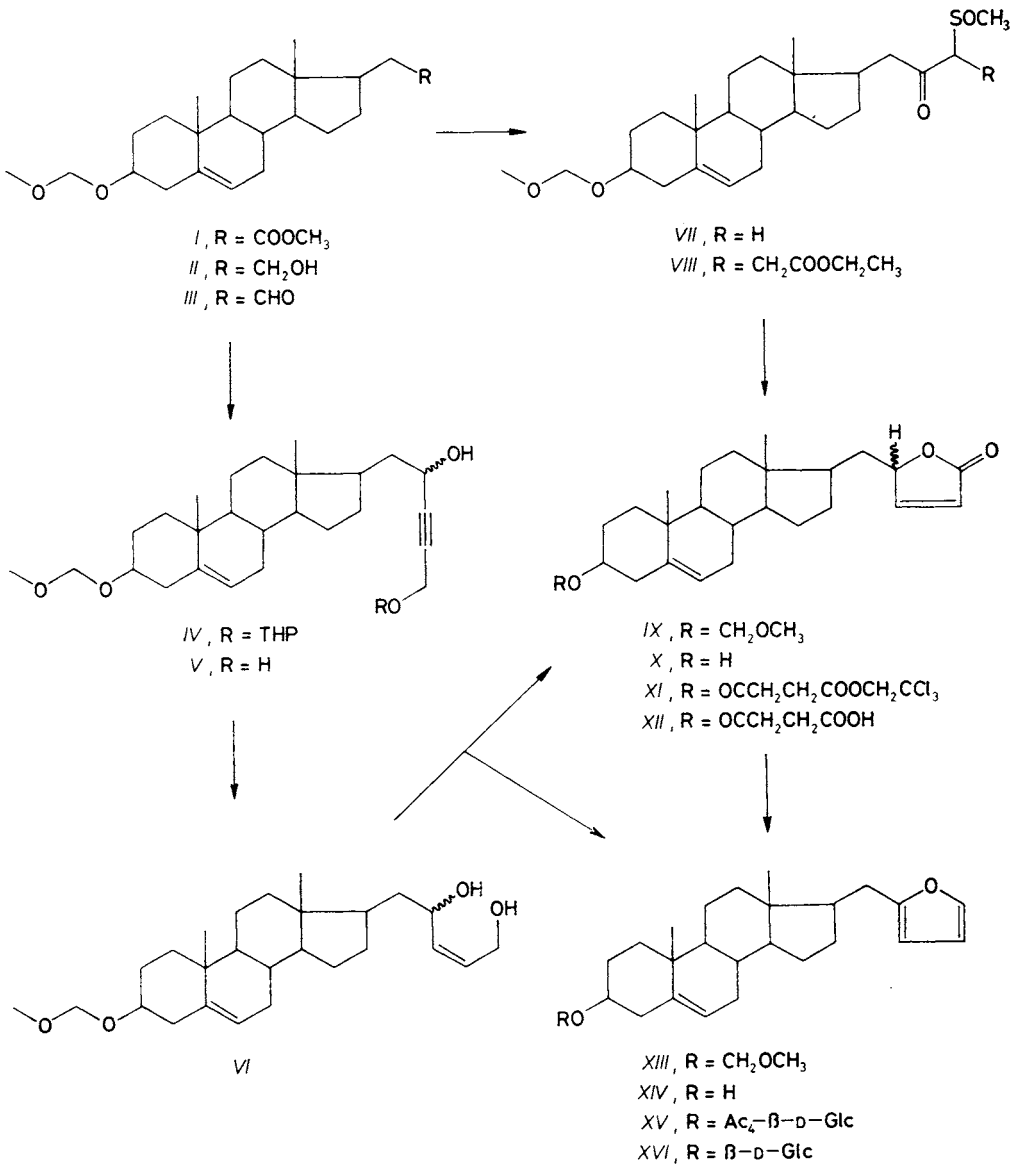
furyl derivative *XIII* (in 26% yield) whose formation could have been expected according to an analogy[5]. The structure of *XIII* follows from its IR spectrum which exhibits characteristic furan bands[6] at 1 594 and 1 506 cm^{-1}, and also from the H-3',



THP = 2-tetrahydropyranyl
Ac_4–β–D–Glc = 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl
β–D–Glc = β-D-glucopyranosyl

H-4′ and H-5′ ^{1}H NMR signals at δ 5·83, 6·11 and 7·15, respectively, ($J_{3',4'} = 3$, $J_{4',5'} = 1{\cdot}8$ and $J_{3',5'} = 0{\cdot}7$ Hz): these values agree well with those reported for 2-methylfuran[7]. The structure of *XIII* was further confirmed by its preparation by reduction of *IX* with diisobutylaluminium hydride[8].

The lactones *IX* were also prepared by the procedure[9] starting from the ketosulfoxide *VII*, accessible[3] from the ester *I*. Sodium salt of *VII*, obtained by treatment with sodium hydride, was alkylated with ethyl bromoacetate to give compound *VIII* which on reduction with sodium borohydride afforded lactones *IX* in the ratio 22*R* : : 22*S* ≈ 6 : 4 (^{1}H NMR spectrum). This second way proved to be more advantageous since the yield of the reaction sequence *I* → *VII* → *VIII* → *IX* was 54% whereas the pathway *I* → *II* → *III* → *VI* → *IX* gave the lactone *IX* in an only 37% yield.

The methoxymethyl protecting group in position 3 of *IX* was removed by treatment with hydrochloric acid in a benzene–methanol mixture and the obtained hydroxy derivative *X* was converted by an indirect method[10] *via* the intermediate *XI* into the hemisuccinate *XII*. The compounds *X*–*XII* were again mixtures of isomeric lactones

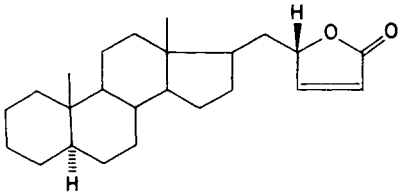
TABLE I

Characteristic ^{1}H NMR spectral parameters of 21,26,27-trinorcholestan-25→22-olide derivatives

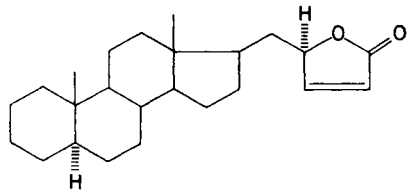
Compound[a]		$C_{(18)}$—H_3	$C_{(19)}$—H_3	$C_{(22)}$—H	$C_{(23)}$—H	$C_{(24)}$—H
IX[b]	22*R*	0·61 s	1·02 s	5·05 m[c]	7·44 dd[d]	6·10 dd[e]
IX[b]	22*S*	0·62 s	1·02 s	5·05 m[c]	7·48 dd[f]	6·11 dd[e]
X[g]	22*R*	0·61 s	1·01 s	5·06 m[c]	7·46 dd[d]	6·10 dd[e]
X[g]	22*S*	0·62 s	1·01 s	5·06 m[c]	7·48 dd[f]	6·11 dd[e]
XI[h]	22*R*	0·61 s	1·02 s	5·05 m[c]	7·46 dd[i]	6·10 dd[j]
XI[h]	22*S*	0·62 s	1·02 s	5·05 m[c]	7·48 dd[i]	6·11 dd[j]
XII[k]	22*R*	0·61 s	1·03 s	5·06 m[c]	7·46 dd[i]	6·10 dd[j]
XII[k]	22*S*	0·62 s	1·03 s	5·06 m[c]	7·49 dd[i]	6·11 dd[j]
XVII[l]	22*R*	0·57 s	0·77 s	5·03 m	7·44 dd[d]	6·08 dd[e]
XVIII[l]	22*S*	0·57 s	0·77 s	5·02 m	7·47 dd[f]	6·08 dd[m]

[a] Measured in deuteriochloroform with tetramethylsilane as internal standard on Varian XL-200 (200·058 MHz) spectrometer. All values were obtained by first order analysis. [b] Sample prepared by procedure *a*): ratio of distinguished signals of 22*R* and 22*S* isomers about 1 : 1, sample prepared by procedure *b*): ratio 6 : 4; other signals: 3·38 s and 4·70 s (OCH_2OCH_3); 5·35 bd, $J = 5$ ($C_{(6)}$—H). [c] $W \approx 22$. [d] $J_{22,23} = 1{\cdot}5$, $J_{23,24} = 5{\cdot}6$. [e] $J_{22,24} = 2{\cdot}0$, $J_{23,24} = 5{\cdot}6$. [f] $J_{22,23} = 1{\cdot}4$, $J_{23,24} = 5{\cdot}6$. [g] Ratio of signals of 22*R* and 22*S* isomers about 1 : 1; other signals: 3·52 m, $W = 30$ ($C_{(3)}$—H); 5·36 bd, $J = 5$ ($C_{(6)}$—H). [h] Ratio of signals of 22*R* and 22*S* isomers about 1 : 1; other signals: 2·68 m and 2·77 m ($OOCCH_2CH_2COO$); 4·63 m, $W = 30$ ($C_{(3)}$—H); 4·77 s ($COOCH_2CCl_3$); 5·38 bd, $J = 5$ ($C_{(6)}$—H). [i] $J_{22,23} = 1{\cdot}4$, $J_{23,24} = 5{\cdot}7$. [j] $J_{22,24} = 2{\cdot}0$, $J_{23,24} = 5{\cdot}7$. [k] Ratio of signals of 22*R* and 22*S* isomers about 3 : 7; other signals: 2·65 m ($OOCCH_2CH_2COO$); 4·62 m, $W = 30$ ($C_{(3)}$—H); 5·38 bd, $J = 4$ ($C_{(6)}$—H). [l] Values taken from ref.[1], 60 MHz spectrum. [m] $J_{22,24} = 1{\cdot}8$, $J_{23,24} = 5{\cdot}6$.

differing in configuration at $C_{(22)}$. As in the case of *IX*, the isomer ratio was determined by ^{1}H NMR spectroscopy and verified by CD spectra ($\Delta\varepsilon$ at 215 nm), both methods using the known[1] lactones *XVII* and *XVIII* as reference compounds. As seen from Table II, in the course of the reaction sequence *IX* → *X* → *XI* → *XII* the ratio of the isomers fluctuated, probably due to different isomer enrichment during crystallization of the samples.



XVII



XVIII

The furyl derivative *XIII* was deprotected to the hydroxy derivative *XIV* which was subjected to silver silicate-catalyzed glycosylation with tetra-O-acetyl-α-D-glucopyranosyl bromide. The structure of the peracetyl β-D-glucoside *XV* was confirmed by its ^{1}H NMR spectrum in which we identified signals of all β-D-glucopyranose protons; the found chemical shifts and coupling constants agreed well with the values found earlier for other peracetyl β-D-glucosides[11]. The peracetyl β-D-glucoside *XV* was converted into the free β-D-glucoside *XVI* by hydrolysis in a mixture of methanol, triethylamine and water.

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 on a Zeiss UR-20 spectrometer; wavenumbers are given in cm^{-1}. CD spectra were measured in dioxane on a Dichrographe II (Roussel–Jouan) instrument. ^{1}H NMR spectra were taken in deuteriochloroform with tetramethylsilane as internal standard on Tesla BS-467 (60 MHz) or on Varian XL-200 (200·058 MHz) instruments at 23°C. 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 (TLC) was carried out 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. The 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 determination.

3β-Methoxymethoxy-5-pregnen-21-ol (*II*)

Sodium bis(2-methoxyethoxy)aluminium hydride (13·5 ml; 70% solution in benzene; 48·3 mmol) was added to a solution of methyl ester *I* (ref.[3], 8·08 g; 20·7 mmol) in ether (350 ml). The stirred

mixture was refluxed for 1·5 h, decomposed with water and poured into dilute (1 : 4) hydrochloric acid. The product was extracted with ether and the extract washed with dilute hydrochloric acid, water, potassium hydrogen carbonate solution and water. The solvents were removed and the residue was crystallized from light petroleum–ether to afford 7·08 g (94%) of alcohol *II*, m.p. 98–100°C (remelting at 105–106°C), $[\alpha]_D$ −45° (*c* 0·4, chloroform). IR spectrum (tetrachloromethane): 3 635, 3 350 (OH), 3 030, 1 668 (C=C—H), 1 148, 1 104 1 045 (C—O—C). ^{1}H NMR spectrum: 5·35 m (1 H, $C_{(6)}$—H), 4·67 s (2 H, O—CH_2—O), 3·58 m (2 H, $C_{(21)}$—H), 3·33 s (3 H, OCH_3), 1·00 s (3 H, $C_{(19)}$—H), 0·59 s (3 H, $C_{(18)}$—H). For $C_{23}H_{38}O_3$ (362·6) calculated: 76·20% C, 10·56% H; found: 76·38% C, 10·84% H.

3β-Methoxymethoxy-5-pregnen-21-al (*III*)

Pyridinium chlorochromate (4 g; 18·6 mmol) was added to a solution of *II* (4·0 g; 11·0 mmol) in dichloromethane (100 ml). After stirring at room temperature for 1 h, the mixture was diluted with ether (200 ml) and filtered through a column of alumina (60 g). The column was washed with ether, the organic solutions were combined and evaporated *in vacuo* and the residue was crystallized from light petroleum; yield 3·9 g (98%) of aldehyde *III*, m.p. 85–88°C, $[\alpha]_D$ −54° (*c* 0·3, chloroform). IR spectrum (tetrachloromethane): 2 825, 2 715, 1 728 (CHO), 3 035, 1 669 (C=C—H), 1 150, 1 108, 1 048 (C—O—C). ^{1}H NMR spectrum: 9·77 t (1 H, $C_{(21)}$—H, $J_{20,21}$ = = 2), 5·36 m (1 H, $C_{(6)}$—H), 4·67 s (2 H, O—CH_2—O), 3·33 s (3 H, OCH_3), 1·02 s (3 H, $C_{(19)}$—H), 0·62 s (3 H, $C_{(18)}$—H). For $C_{23}H_{36}O_3$ (360·5) calculated: 76·62% C, 10·06% H; found: 76·95% C, 10·00% H.

(22*R*)+(22*S*)-3β-Methoxymethoxy-21,26,27-trinorcholest-5-en-23-yne-22,25-diol (*V*)

A solution of 1-butyllithium in hexane (14 ml; *c* 1·6 mol l^{-1}) was added at −78°C to a solution of 1-(2-tetrahydropyranyloxy)-2-propyne[4] (3·71 g; 26·46 mmol) in tetrahydrofuran (28 ml). The mixture was stirred at −20°C for 1 h, cooled to −78°C and a solution of aldehyde *III* (3·8 g; 10·5 mmol) in tetrahydrofuran (32 ml) was added. The mixture was left to attain the room temperature during 1 h, stirred for 1 h at this temperature and decomposed with saturated aqueous solution of ammonium sulfate. The product was extracted with ether and the extract washed with

TABLE II

CD spectral data for 21,26,27-trinorcholestan-25→22-olide derivatives

Compound	$\Delta\varepsilon/\lambda_{max}$ [a]	22*S* %	22*R* %
X [b]	−2·37/215	36	64
XI	−0·80/215	45	55
XII	−0·64/215	46	54
XIII	+2·62/215	66	34
XVII [c]	+8·97/215	100	0
XVIII [c]	−8·77/215	0	100

[a] CD spectra measured in dioxane on a Dichrographe II (Roussel–Jouan), λ_{max} in nm; [b] prepared by procedure *b*); [c] the value taken from ref.[1].

a solution of ammonium sulfate. The solvents were evaporated and the residue was chromatographed on a column of silica gel (200 g; pretreated with ammonia vapours for 24 h). Light petroleum–ether mixture (95 : 5) eluted nonpolar impurities; further elution with light petroleum–ether (70 : 30) gave 4·4 g (83%) of acetylene mixture *IV*. ^{1}H NMR spectrum: 5·35 m (1 H, $C_{(6)}$—H), 4·82 bs (1 H, O—CH—O), 4·68 s (2 H, O—CH_2—O), 4·30 bs (2 H, $C_{(25)}$—H), 3·60 m (2 H, OCH_2), 3·36 s (3 H, OCH_3), 1·00 s (3 H, $C_{(19)}$—H), 0·60 s (3 H, $C_{(18)}$—H). The mixture *IV* (4·4 g; 8·78 mmol) was dissolved in a mixture of benzene (28 ml) and methanol (110 ml) and *p*-toluenesulfonic acid monohydrate (2·5 g; 13·1 mmol) was added. After stirring at room temperature for 1 h the mixture was evaporated *in vacuo* and the residue was partitioned between an ethyl acetate–ether mixture (1 : 1; 400 ml) and water (200 ml). The aqueous layer was separated and extracted with ethyl acetate, the combined organic layers were washed with potassium hydrogen carbonate solution and water and the solvents were evaporated. The residue was chromatographed on a column of silica gel (200 g) in benzene–acetone (90 : 10), affording 3·13 g (85%) of mixture of diols *V*, m.p. 124—134°C, $[\alpha]_D$ −38° (*c* 2·1, chloroform). IR spectrum (chloroform): 3 605, 3 410 (OH), 1 669 (C=C), 1 148, 1 201, 1 042 (C—O—C). ^{1}H NMR spectrum: 5·33 m (1 H, $C_{(6)}$—H), 4·66 s (2 H, O—CH_2—O), 4·28 bs (2 H, $C_{(25)}$—H), 3·33 s (3 H, OCH_3), 0·99 s (3 H, $C_{(19)}$—H), 0·58 s (3 H, $C_{(18)}$—H). For $C_{26}H_{40}O_4$ (416·6) calculated: 74·96% C, 9·68% H; found: 74·72% C, 9·73% H.

(22*R*)+(22*S*)-3β-Methoxymethoxy-21,26,27-trinorcholesta-5,23-dien-25→22-olide (*IX*)

a) A solution of sodium borohydride in ethanol–sodium hydroxide mixture (ref.[12]; 0·8 ml *c* 1 mol l^{-1}) was added to a solution of nickel acetate tetrahydrate (200 mg) in ethanol (25 ml). After stirring for 30 s in a hydrogen atmosphere, 1,2-diaminoethane (0·11 ml) was added, followed by the diol mixture *V* (1 g; 2·40 mmol) in ethanol (100 ml). The mixture was stirred under hydrogen until 57·6 ml of hydrogen (100%) was consumed, diluted with chloroform (200 ml) and filtered through a column of silica gel (50 g) layered with Celite (25 g). The column was washed with chloroform and the combined fractions containing the product were taken down affording 1 g (99%) of the diol mixture *VI* free of the starting *V* (according to TLC in benzene–acetone 8 : 2). IR spectrum (KBr pellet): 3 400 (OH), 1 668, 1 630 (C=C), 1 148, 1 102, 1 030 (C—O—C). Silver carbonate on Celite[13] (18 g) was added to benzene (100 ml), a part of the benzene (20 ml) was distilled off under stirring and then a solution of *VI* (1 g; 2·39 mmol) in benzene (100 ml) was added. Another part of benzene (40 ml) was distilled off, the mixture was refluxed for 1·5 h with stirring, then cooled and filtered through a column of silica gel (30 g) layered with Celite (20 g). The products were eluted with a dichloromethane–ether (1 : 1) mixture and after evaporation chromatographed on a column of silica gel (50 g). Elution with benzene–ether (99 : 1) gave furyl derivative fraction (see *XIII*). Further elution with benzene–ether (96 : 1) yielded 554 mg (56%) of mixture of lactones *IX*, m.p. 123—140°C, $[\alpha]_D$ −33° (*c* 0·23, chloroform). IR spectrum (tetrachloromethane): 1 762 (γ-lactone), 1 149, 1 105, 1 044 (C—O—C). ^{1}H NMR spectrum: see Table I. Mass spectrum (*m/z*): 352 (M − $C_2H_6O_2$). For $C_{26}H_{38}O_4$ (414·6) calculated: 75·32% C, 9·24% H; found: 75·53% C, 9·58% H.

b) Ketosulfoxide *VII* (prepared from 2 g, 5·12 mmol of methyl ester *I* according to ref.[3]) in a mixture of tetrahydrofuran (36 ml) and benzene (10 ml) was added to a suspension of sodium hydride (270 mg; 11·3 mmol) in tetrahydrofuran (4 ml). After the evolution of hydrogen ceased, the mixture was cooled to −5°C and ethyl bromoacetate (0·93 ml; 8·39 mmol) was added. The mixture was stirred for 2 h at room temperature, decomposed with ammonium chloride solution, the product was taken up in ethyl acetate and the extract was washed with ammonium chloride solution. The solvent was evaporated and the residue (2·6 g) which represented practically pure

ester *VIII* (TLC in benzene–acetone 4 : 6) was dissolved in methanol (21 ml) and dichloromethane (4·2 ml) and cooled to 0°C. Sodium borohydride (212 mg; 5·6 mmol) was added, the mixture was stirred at 0°C for 20 min and another portion of sodium borohydride (212 mg; 5·6 mmol) was added. After stirring for 2 h at 0°C, the mixture was diluted with ethyl acetate (150 ml), washed with sodium hydroxide solution (*c* 2M) and a solution of ammonium chloride, the solvents were evaporated and the residue was chromatographed on a column of silica gel (200 g). Benzene–ether (97 : 3) eluted 1·15 g (54% based on *I*) of *IX*, m.p. 120—150°C, $[\alpha]_D$ −42° (*c* 0·3, chloroform). For ^{1}H NMR spectrum see Table I.

(22*R*)+(22*S*)-3β-Hydroxy-21,26,27-trinorcholesta-5,23-dien-25→22-olide (*X*)

Concentrated hydrochloric acid (0·26 ml) was added to a solution of the mixture of lactones *IX* (520 mg; 1·25 mmol) in benzene (26 ml) and methanol (26 ml). After heating to 42°C for 7 h, the mixture was taken down *in vacuo*, the residue was dissolved in ether, and the ethereal solution was washed with solution of potassium hydrogen carbonate and water. The ether was evaporated and the residue chromatographed on a column of silica gel (70 g). Elution with light petroleum–dichloromethane (2 : 1) afforded 350 mg (75%) of an amorphous mixture of hydroxy derivatives *X*, $[\alpha]_D$ −45° (*c* 0·14, chloroform). IR spectrum (tetrachloromethane): 1 776, 1 764 (γ-lactone); (chloroform): 1 754 (γ-lactone), 3 610, 3 480 (OH), 1 668, 1 630 (C=C). ^{1}H NMR spectrum: see Table I. For $C_{24}H_{34}O_3$ (370·5) calculated: 77·80% C, 9·25% H; found: 77·67% C, 9·36% H.

(22*R*)+(22*S*)-21,26,27-Trinorcholesta-5,23-dien-25→22-olide-3β-yl 2,2,2-Trichloroethyl Butanedioate (*XI*)

N,N′-Dicyclohexylcarbodiimide (185 mg; 0·90 mmol) and 4-dimethylaminopyridine (6 mg) were added to a solution of the hydroxy derivatives *X* (300 mg; 0·81 mmol) and 2,2,2-trichloroethyl hydrogen butanedioate[14] (377 mg; 1·51 mmol) in benzene (20 ml). After stirring at room temperature for 4 h, another portion of N,N′-dicyclohexylcarbodiimide (50 mg; 0·24 mmol) and 4-dimethylaminopyridine (2 mg) was added. The mixture was stirred for 4 h, poured into water (100 ml) and the product was extracted with dichloromethane (3 × 70 ml) and ether (3 × 70 ml). The combined organic extracts were dried over anhydrous magnesium sulfate, the solvents were taken off *in vacuo* and the residue was chromatographed on a column of silica gel (50 g). Elution with benzene and benzene–ether (4 : 1) afforded 580 mg of crude product which on crystallization from light petroleum–ether yielded 292 mg (60%) of mixture of succinates *XI*, m.p. 97—100°C. IR spectrum (tetrachloromethane): 1 763 (γ-lactone), 1 737 (COOR). ^{1}H NMR spectrum: see Table I. For $C_{30}H_{39}Cl_3O_6$ (602·0) calculated: 59·86% C, 6·53% H, 17·67% Cl; found: 59·75% C, 6·87% H, 17·35% Cl.

(22*R*)+(22*S*)-21,26,27-Trinorcholesta-5,23-dien-25→22-olide-3β-yl Hydrogen Butanedioate (*XII*)

A mixture of succinates *XI* (460 mg; 0·76 mmol), tetrahydrofuran (15 ml), acetic acid (10 ml) and water (2 ml) was stirred with powdered zinc (70 mg) in an ice bath for 7 h. During this time, 30 mg portions of zinc powder were added every 30 min. The mixture was filtered through Celite and taken down. The residue was coevaporated with toluene (3 × 25 ml) and then chromatographed on a column of silica gel (50 g). Dichloromethane–methanol (9 : 1) eluted 210 mg of crude product which was crystallized from dichloromethane–ether. Yield 110 mg (31%) of mixture of hemisuccinates *XII*, m.p. 195—199°C, $[\alpha]_D$ −11° (*c* 0·2 , chloroform). IR spectrum (chloroform): 3 500—2 500, 1 710 sh (COOH), 1 753 (γ-lactone), 1 723 (COOR). ^{1}H NMR spectrum: see Table I. For $C_{28}H_{38}O_6$ (470·6) calculated: 71·46% C, 8·14% H; found: 71·49% C, 7·95% H.

20-(2-Furyl)-3β-methoxymethoxy-21-nor-5-pregnene (*XIII*)

a) A solution of diisobutylaluminium hydride in toluene (1·7 ml, *c* 1 mol l^{-1}) was added at −20°C to a solution of lactone mixture *IX* (252 mg; 0·61 mmol) in tetrahydrofuran (5 ml). After stirring at −20°C for 3 h, the mixture was decomposed with 10% sulfuric acid (5 ml), allowed to attain room temperature and poured into dilute hydrochloric acid (1 : 4, 40 ml). The product was extracted with ether, the extract was washed with dilute hydrochloric acid, water, potassium hydrogen carbonate solution and water and the solvents were evaporated. Chromatography of the residue on a silica gel column (30 g) in benzene–ether (99 : 1) afforded 96 mg (40%) of *XIII*, m.p. 125–126°C (light petroleum), $[\alpha]_D$ −54°, (*c* 0·15, chloroform). IR spectrum (tetrachloromethane): 3 115, 3 025, 1 594, 1 506 (furyl), 1 149, 1 106, 1 041 (C—O—C). ^{1}H NMR spectrum (tetrachloromethane): 7·15 dd (1 H, $C_{(5')}$—H, $J_{3',5'}$ = 0·7, $J_{4',5'}$ = 1·8), 6·11 dd (1 H, $C_{(4')}$—H, $J_{3',4'}$ = 3, $J_{4',5'}$ = 1·8), 5·83 bd (1 H, $C_{(3')}$—H, $J_{3',4'}$ = 3), 5·25 m (1 H, $C_{(6)}$—H), 4·51 s (2 H, OCH_2O), 3·23 s (3 H, OCH_3), 0·98 s (3 H, $C_{(19)}$—H), 0·65 s (3 H, $C_{(18)}$—H). Mass spectrum (*m/z*): 398 M^+, 336 (M − 62), 317 (M − C_5H_5O), 81 (C_5H_5O). For $C_{26}H_{38}O_3$ (398·6) calculated: 78·35% C, 9·61% H; found: 78·64% C, 9·56% H.

b) Fractions containing *XIII* (from the preparation of *IX*, procedure *b*) were combined and evaporated *in vacuo*; yield 246 mg (26%) of *XIII*, m.p. 123–125°C (light petroleum), $[\alpha]_D$ −58° (*c* 0·22, chloroform).

20-(2-Furyl)-21-nor-5-pregnen-3β-ol (*XIV*)

Concentrated hydrochloric acid (0·14 ml) was added to a solution of *XIII* (280 mg; 0·70 mmol) in a mixture of benzene (14 ml) and methanol (14 ml). After warming to 40°C for 7 h, the mixture was evaporated *in vacuo*, the residue was dissolved in ether, and the ethereal solution was washed with a solution of potassium hydrogen carbonate and with water. Ether was evaporated and the residue crystallized from methanol to give 204 mg (82%) of *XIV*, m.p. 135–138°C, $[\alpha]_D$ −66° (*c* 0·22, chloroform). IR spectrum (chloroform): 3 610, 3 455 (OH), 1 668 (C=C), 1 594, 1 509 (furyl). ^{1}H NMR spectrum (tetrachloromethane + hexadeuteriodimethyl sulfoxide): 7·36 dd (1 H, $C_{(5')}$—H, $J_{3',5'}$ = 0·8, $J_{4',5'}$ = 2), 6·24 dd (1 H, $C_{(4')}$—H, $J_{3',4'}$ = 3, $J_{4',5'}$ = 2), 5·97 d (1 H, $C_{(3')}$—H, $J_{3',4'}$ = 3), 5·97 m (1 H, $C_{(6)}$—H), 0·94 s (3 H, $C_{(19)}$—H), 0·63 s (3 H, $C_{(18)}$—H). For $C_{24}H_{34}O_2$ (354·4) calculated: 81·31% C, 9·67% H; found: 81·19% C, 9·78% H.

20-(2-Furyl)-21-nor-5-pregnen-3β-yl 2,3,4,6-Tetra-O-acetyl-β-D-glucopyranoside (*XV*)

A solution of furyl derivative *XIV* (150 mg; 0·42 mmol) in 1,2-dichloroethane (2 ml) was stirred for 30 min with ground molecular sieve 4A (400 mg) and silver silicate[15] (200 mg) under argon. A solution of 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide (250 mg; 0·61 mmol) in 1,2-dichloroethane (2 ml) was added and the mixture was stirred at room temperature overnight. The solid material was filtered through a column of Celite which was then washed with dichloromethane, the combined filtrates were washed with potassium hydrogen carbonate solution, dried and the solvent was distilled off *in vacuo*. The residue was chromatographed on a column of silica gel (50 g) in benzene–ether (100 : 1 to 50 : 1) and the crude product was crystallized from methanol; yield 120 mg (42%) of glycoside *XV*, m.p. 184–186°C, $[\alpha]_D$ −26° (*c* 0·23, chloroform). IR spectrum (chloroform): 1 757, 1 745 (CH_3COO), 1 594, 1 508 (furyl). ^{1}H NMR spectrum (200 MHz): 7·28 dd (1 H, $C_{(5')}$—H, $J_{4',5'}$ = 1·8, $J_{3',5'}$ = 0·9), 6·26 dd (1 H, $C_{(4')}$—H, $J_{3',4'}$ = = 3·2, $J_{4',5'}$ = 1·8), 5·96 dd (1 H, $C_{(3')}$—H, $J_{3',4'}$ = 3·2, $J_{3',5'}$ = 0·9), 5·36 bd (1 H, $C_{(6)}$—H, $J_{6,7\beta}$ = 4·6, $J_{6,7\alpha} \neq 0$), 5·21 t (1 H, $C_{(3'')}$—H, $J_{2'',3''}$ = 9·4, $J_{3'',4''}$ = 9·4), 5·07 t (1 H, $C_{(4'')}$—H, $J_{3'',4''}$ = 9·4, $J_{4'',5''}$ = 9·2), 4·96 dd (1 H, $C_{(2'')}$—H, $J_{2'',1''}$ = 8·0, $J_{2'',3''}$ = 9·4), 4·59 d (1 H, $C_{(1'')}$—H, $J_{1'',2''}$ = 8·0), 3·68 ddd (1 H, $C_{(5'')}$—H, $J_{5'',4''}$ = 9·2, $J_{5'',6a''}$ = 4·8, $J_{5'',6b}$ = 2·6),

4·26 dd (1 H, $C_{(6a'')}$—H, $J_{6a'',6b''}$ = 12·3, $J_{6a'',5''}$ = 4·8), 4·11 dd (1 H, $C_{(6b'')}$—H, $J_{6b'',6a''}$ = = 12·3, $J_{6b'',5''}$ = 2·6), 3·48 m (1 H, $C_{(3)}$—H, W = 30), 2·70 dd (1 H, $C_{(20a)}$—H, $J_{20a,20b}$ = = 15·0, $J_{20a,17}$ = 4·8), 2·44 dd (1 H, $C_{(20b)}$—H, $J_{20b,20a}$ = 15·0, $J_{20b,17}$ = 8·5), 2·08 s (3 H, CH_3COO), 2·05 s (3 H, CH_3COO), 2·02 s (3 H, CH_3COO), 2·00 s (3 H, CH_3COO), 0·99 s (3 H, $C_{(19)}$—H), 0·67 s (3 H, $C_{(18)}$—H). For $C_{38}H_{52}O_{11}$ (684·8) calculated: 66·65% C, 7·65% H; found: 66·92% C, 7·66% H.

20-(2-Furyl)-21-nor-5-pregnen-3β-yl β-D-Glucopyranoside (*XVI*)

Acetyl derivative *XV* (70 mg; 0·10 mmol) was stirred in a mixture of methanol (10 ml), triethylamine (10 ml) and water (0·5 ml) until it dissolved. The solution was set aside for 72 h, and the solvents were evaporated. The residue was coevaporated with ethanol, dried and chromatographed on silica gel (40 g) in chloroform–methanol (50 : 1—10 : 1). Glycoside *XVI* was crystallized from methanol, yield 50 mg (95%), m.p. 240—245°C (decomposition), $[\alpha]_D$ −60° (*c* 0·23, methanol). IR spectrum (chloroform): 3 450 (OH), 1 597, 1 509 (furyl). ^{1}H NMR spectrum (200 MHz, deuteriochloroform–hexadeuteriodimethyl sulfoxide 75 : 25): 7·27 dd (1 H, $C_{(5')}$—H, $J_{5',4'}$ = 1·8, $J_{5',3'}$ = 0·8), 6·24 dd (1 H, $C_{(4')}$—H, $J_{4',5'}$ = 1·8, $J_{4',3'}$ = 3·2), 5·95 bdd (1 H, $C_{(3')}$—H, $J_{3',4'}$ = 3·2, $J_{3',5'}$ = 0·8), 5·33 bd (1 H, $C_{(6)}$—H, $J_{6,7} \sim$ 5·0), 4·66 d (1 H, OH, J = 3·3), 4·58 d (1 H, OH, J = 2·6), 4·36 d (1 H, $C_{(1'')}$—H, $J_{1'',2''} \sim$ 8·0), 4·33 d (1 H, OH, J = 3·7), 1·00 s, (3 H, $C_{(19)}$—H), 0·67 s (3 H, $C_{(18)}$—H). For $C_{30}H_{44}O_7$ (516·7) calculated: 69·74% C, 8·58% H; found: 70·01% C, 8·67% H.

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