GLYCOSYLATION OF STEROIDS WITH SILVER SILICATE AND 2-DEOXY-2-FLUORO-α-D-GLUCOPYRANOSYL BROMIDE TRIACETATE*

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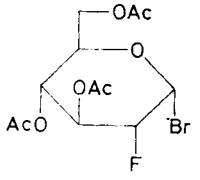
Glycosylation with the title glycosyl bromide *I* in 1,2-dichloroethane in the presence of silver silicate and a molecular sieves afforded mixtures of 3,4,6-tri-O-acetyl-2-deoxy-2-fluoro-α- and β-D--glucopyranosides (*V*—*X*), derived from ethyl (20*E*)-3β-hydroxy-24-nor-5,20(22)-choladien-23--oate (*II*), (20*E*)-3β-hydroxy-5β-pregn-20-ene-21-carboxylate (*III*) and 3β,14-dihydroxy-5β,14β--card-20(22)-enolide (*IV*, digitoxigenin), in which the β-anomers predominated. Separation and deacetylation furnished the corresponding 2-deoxy-2-fluoroglucosides *XI*—*XVI*.

Glycosylation, promoted by insoluble silver catalysts, represents a frequently used approach to β-glycosides[1]. Moreover, the method can be used even in the absence of a participating group on the C-2 carbon atom in the glycosylation reagent[1,2] (usually the corresponding glycosyl halide) and is utilized mainly for the synthesis of β-D-mannosides. One of the most effective catalysts of the mentioned glycosylations is silver silicate[3] which in our hands has been successfully used in the preparation of several steroidal β-D-glucopyranosides[4]. The availability of 3,4,6-tri-O-acetyl-2--deoxy-2-fluoro-α-D-glucopyranosyl bromide[5] (*I*) enabled us to extend our knowledge of this catalyst also to glycosylations in the D-*gluco* series without participating group. The described steroidal glucosides were prepared primarily for tests of



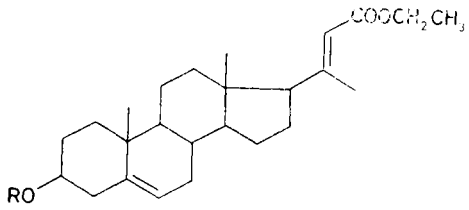
I

Ac = acetyl

* Part CCCXLVI in the series On Steroids; Part CCCXLV: Collect. Czech. Chem. Commun. *54*, 2218 (1989).

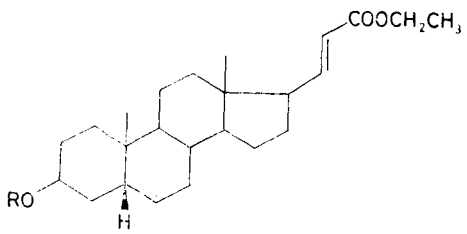
cardiotonic activity; from the viewpoint of pharmacological effect, the fact that 2-deoxy-2-fluoro-D-glucopyranosides are less readily hydrolyzed than the corresponding D-glucopyranosides might be of interest[5].

The steroidal aglycones were selected so as to represent various structural types with respect of reactivity of the 3-hydroxyl group. In the derivative *II* this group is equatorial and homoallylic to the double bond in position 5, in compound *III* it is axial with *cis*-fusion of rings A and B, in digitoxigenin (*IV*) it is also axial but the rings C and D are *cis*-fused too, the overall reactivity being moreover influenced by the presence of another hydroxyl on C-14.



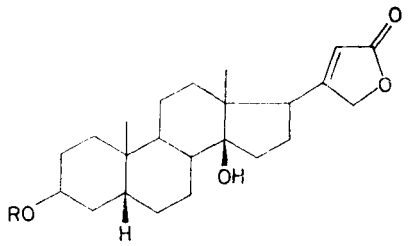
II, R = H
V, R = α-FglcAc$_3$
VI, R = β-FglcAc$_3$

XI, R = α-Fglc
XII, R = β-Fglc



III, R = H
VII, R = α-FglcAc$_3$
VIII, R = β-FglcAc$_3$

XIII, R = α-Fglc
XIV, R = β-Fglc



IV, R = H
IX, R = α-FglcAc$_3$
X, R = β-FglcAc$_3$

XV, R = α-Fglc
XVI, R = β-Fglc

α-FglcAc$_3$ = 3,4,6-tri-O-acetyl-2-fluoro-α-D-glucopyranosyl
β-FglcAc$_3$ = 3,4,6-tri-O-acetyl-2-fluoro-β-D-glucopyranosyl
α-Fglc = 2-deoxy-2-fluoro-α-D-glucopyranosyl
β-Fglc = 2-deoxy-2-fluoro-β-D-glucopyranosyl

So far, the halogenose *I* was utilized for glycosylations in the preparation of estrone glycosides[5] and disaccharides[6]. In the former study[5] the catalyst used was silver salicylate and the procedure afforded the β-glycoside, the latter preparation[6] used

silver triflate and led to the α-glycoside. In general, because of the absence of participating group on C-2 in this halogenose, the glycosylation may be expected to give a mixture of α- and β-glycosides.

As seen from Table I that summarizes the preparative yields, our results are in accord with this general consideration. The pairs of derivatives *V* and *VI*, or *VII* and *VIII*, were separated into the individual anomers by HPLC on silica gel; in the case of digitoxigenin glycosides *IX* and *X* where this method failed, we separated the anomers by crystallization. In the first two cases, the ratio of the α- and β-anomers was calculated from the net yields of the individual anomers. Since for digitoxigenin we used a different isolation method, the population of both isomers was determined from the ^{1}H NMR spectrum of the reaction mixture after deacetylation.

The structural proof is based on the evaluation of the ^{1}H NMR spectra which for the compounds *V*–*X* exhibit well separated signals of H-1′ to H-4′ protons in the region δ 4·26–6·04, for the β-anomers (*VI*, *VIII* and *X*) also analysable signals of H-5′ to H-6b′ in the region δ 3·68–4·26 (Table II). Fluorine atom on C-2′ splits markedly the H-2′ signal into a doublet with coupling constant J(F, H) amounting to 49·3–50·2 Hz, which is further split by coupling with H-1′ and H-3′ protons. Also the H-3′ proton interacts with the fluorine atom, the respective vicinal coupling constants being 11·7–12·0 Hz for the α-anomers and 14·4–14·5 Hz for the β-anomers.

For determination of configuration at the C-1′ atom the H-1′ proton doublet is of crucial importance: in the spectra of α-anomers the coupling constant J(1′, 2′) is 3·9–4·2 Hz and the signal is shifted 0·34–0·53 ppm upfield compared with the β-anomers. The coupling constant for the β-anomers amounts to 7·6–7·8 Hz and the signal is moreover split by the vicinal fluorine atom to give a doublet of doublets (J(F, H) = 2·8–3·0 Hz). The configuration of the anomeric center has less effect

TABLE I
Yields of glycosidations of steroids *II*–*IV*

Steroid	Total yield (%)	Anomers (%)[a] α	Anomers (%)[a] β	α : β
II	96	8 (*V*)	67 (*VI*)	1 : 8
III	71	13 (*VII*)[b]	37 (*VIII*)[b]	1 : 3
IV	73	13 (*IX*)	42 (*X*)	1 : 4[c]

[a] Preparative yields after separation, see text. [b] The yields include the deacetylation and reacetylation of the glycoside mixture, see Experimental. [c] Determined by ^{1}H NMR spectrum, see Experimental.

on the shifts of H-2′ signals ($\Delta\delta$ = 0·19–0·20) as well as on the system H-5′, H-6a′ and H-6b′ in which for the β-isomers the signals of individual protons can be separated.

The acetyl protecting groups in derivatives *V* to *VIII* were removed with ethanolic sodium ethoxide, for digitoxigenin glycosides we used a milder cleavage with a mixture of triethylamine, methanol and water[7]. The yields of both procedures were 62–86%, depending on the crystallization ability of the individual products. The ^{1}H NMR spectra of digitoxigenin glycosides *XV* and *XVI* in deuteriopyridine confirmed the preservation of the lactone ring as well as the sugar moiety.

Preliminary cardiotonic activity screening by measuring the inhibition of ^{86}Rb transport into erythrocytes has shown that for the digitoxigenin fluoroglucosides *XV* and *XVI* the 50% inhibition was achieved at concentrations similar to those for ouabain and digoxin. The α-anomer *XV* was approximately one order of magnitude less active than the β-anomer *XVI*.

More detailed biological activity data will be published elsewhere.

TABLE II

Proton NMR spectral data for steroidal 2-deoxy-2-fluoroglucosides *V*–*X*

Parameter	*V*	*VI*	*VII*	*VIII*	*IX*	*X*
H-18	0·60 s	0·60 s	0·63 s	0·62 s	0·88 s	0·87 s
H-19	1·02 s	1·01 s	0·97 s	0·95 s	0·96 s	0·93 s
H-1′	5·19 d	4·66 dd	5·11 d	4·61 dd	5·13 d	4·61 dd
H-2′	4·46 ddd	4·26 ddd	4·48 ddd	4·29 dd	4·49 ddd	4·30 ddd
H-3′	5·54 dt	5·31 dt	5·54 dt	6·04 ddd	5·53 dt	5·31 dt
H-4′	4·99 t	5·01 t	5·00 t	5·01 t	5·00 t	5·02 t
H-5′	[a]	3·69 ddd	[a]	3·68 ddd	[a]	3·68 ddd
H-6a′	[a]	4·26 dd	[a]	4·25 dd	[a]	4·25 dd
H-6b′	[a]	4·12 dd	[a]	4·08 dd	[a]	4·09 dd
J(1′, 2′)	3·9	7·8	4·0	7·6	4·2	7·7
J(H-1′, F)	≈0	2·8	≈0	3·0	≈0	3·0
J(2′, 3′)	9·6	9·0	9·5	9·0	9·5	8·9
J(H-2′, F)	49·6	50·4	49·3	50·2	49·4	50·2
J(3′, 4′)	9·6	9·4	9·5	9·5	9·5	9·6
J(H-3′, F)	12·0	14·4	12·0	14·4	11·7	14·5
J(4′, 5′)	9·8	9·6	9·8	10·0	9·5	10·0
J(5′, 6a′)	1·8	2·5	[a]	2·5	[a]	2·6
J(5′, 6b′)	[a]	4·7	[a]	5·0	[a]	5·0
J(6a′, 6b′)	7·2	10·0	[a]	12·3	[a]	12·3

[a] Value cannot be determined due to overlapped signals.

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 Perkin–Elmer PE 580 spectrometer (wavenumbers in cm^{-1}). ^1H NMR spectra were taken on a Varian XL-200 instrument (FT mode, 200·058 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. Flash column chromatography was performed on silica gel (according to Pitra, 60—120 μm), preparative HPLC on Lichrosorb SI 100 (Merck) using stainless steel column (12·6 × 500 mm), thin-layer chromatography on silica gel G according to Stahl (ICN Biochemicals). Spots were detected by spraying with sulfuric acid followed by heating. Prior to evaporation, solutions in organic solvents were dried over anhydrous sodium sulfate.

General Procedure for Glycosylation of Derivatives *II*—*IV*

A mixture of the steroidal hydroxy derivative, molecular sieves 4A (ground and activated by heating on a steel dish to about 300—400°C for 2 h) and silver silicate[3] was stirred under protection from light in a flask equipped with a septum, in vacuum of an oil pump (<0·1 kPa) for 1 h. The flask was filled with argon (slight overpressure) and 1,2-dichloroethane was introduced through the septum. After 30 min the mixture was cooled in an ice-bath, a solution of the halogenose[5] *I* in 1,2-dichloroethane was added through the septum and the stirring was continued at room temperature for 24 h. The solid material was filtered on Celite which was then washed with chloroform (in the case of glycosylation of *IV* with chloroform–methanol (10 : 1)). After dilution with chloroform, the organic phase was washed with a solution of potassium hydrogen carbonate and water, dried and the solvents were evaporated. The residue was flash-chromatographed on silica gel, fractions containing the glycoside mixture were combined, evaporated and subjected to further separation, unless stated otherwise.

Ethyl (20*E*)-3β-(3,4,6-Tri-O-acetyl-2-deoxy-2-fluoro-α-D--glucopyranosyloxy)-24-nor-5,20(22)-choladien-23-oate (*V*)

1,2-Dichloroethane (7 ml), followed by a solution of halogenose *I* (840 mg; 2·3 mmol) in the same solvent (3 ml), was added to a mixture of hydroxy derivative[8] *II* (0·8 g, 2·1 mmol), molecular sieves (1 g) and silver silicate (2 g) according to the above-described procedure. Flash chromatography in benzene–acetone (100 : 1) afforded 1·35 g (96%) of a mixture of glycosides *V* and *VI* which was separated by repeated HPLC in benzene–ethyl acetate (200 : 1). The less polar product consisted of the α-glycoside *V* (112 mg; 8%), which was crystallized from ethanol; yield 87 mg, m.p. 161—162°C, $[\alpha]_D$ +79° (*c* 0·8, chloroform). IR spectrum (chloroform): 1 753 (OAc); 1 707, 1 637 (C=C—COOR). ^1H NMR spectrum see Table II; further data: 5·69 bs, 1 H (H-22); 5·36 bd, 1 H (H-6, J = 4·8); 4·27—4·05 cm, 3 H, (H-5′, H-6′*a*, and H-6′b); 4·14 q, 2 H (O—CH_2—CH_3, J = 7·2); 3·50 m, 1 H (H-3); 2·18 d, 1 H (H-21, J = 0·9); 2·08, 2·06, and 2·04 s, 3 × 3 H (3 × $OCOCH_3$); 1·28 t, 3 H (O—CH_2—CH_3, J = 7·2). For $C_{37}H_{53}FO_{10}$ (676·8) calculated: 65·66% C, 7·89% H; found: 65·92% C, 8·04% H.

Ethyl (20*E*)-3β-(3,4,6,-Tri-O-acetyl-2-deoxy-2-fluoro-β-D--glucopyranosyloxy)-24-nor-5,20(22)-choladien-23-oate (*VI*)

The title compound *VI* represented the more polar product from the preceding experiment; yield 932 mg (67%), after crystallization from dichloromethane–ether 702 mg (50%); m.p. 209 to

212°C, $[\alpha]_D$ −30° (*c* 1·0, chloroform). IR spectrum (chloroform): 1 754 (OAc); 1 707, 1 636 (C=C—COOR). ^{1}H NMR spectrum see Table II, further data: 5·69 bs, 1 H (H-22); 5·37 bd, 1 H (H-6, J = 4·8); 4·14 q, 2 H (O-CH_2—CH_3, J = 7·1); 3·58 m, 1 H (H-3); 2·18 d, 1 H (H-21, J = 1·0); 2·08, 2·07, and 2·03 s, 3 × 3 H (3 × $OCOCH_3$); 1·28 t, 3 H (O—CH_2—CH_3, J = 7·1 For $C_{37}H_{53}FO_{10}$ (676·8) calculated: 65·66% C, 7·89% H; found: 65·87% C, 8·01% H.

Ethyl (20*E*)-3β-(3,4,6-Tri-O-acetyl-2-deoxy-2-fluoro-α-D-glucopyranosyloxy)-5β-pregn-20-en-21-carboxylate (*VII*)

A mixture of hydroxy derivative[9] *III* (445 mg; 1·2 mmol), molecular sieves (1·3 g), silver silicate (1·1 g) and 1,2-dichloroethane (5 ml) was treated with the halogenose *I* (450 mg; 1·2 mmol) in 1,2-dichloroethane (3 ml) as described in the above described general procedure, except that after filtration of the solid material the mixture was evaporated to dryness and deacetylated by standing with a mixture of triethylamine, methanol, and water (20 : 20 : 1; 20 ml) for 72 h. After evaporation to dryness, the mixture was flash-chromatographed on silica gel (25 g) in chloroform–methanol (20 : 1) to give a mixture of deacetylated glycosides (455 mg; 71%). A part of the product (400 mg; 0·74 mmol) was reacetylated by standing overnight with acetic anhydride (2 ml; 21 mmol) in pyridine (45 ml). The usual work-up procedure gave 430 mg (87%) of a mixture of glycosides *VII* and *VIII* which was separated by repeated HPLC in benzene–ethyl acetate (200 : 1). The less polar fraction consisted of α-glycoside *VII* (90 mg; 18%), m.p. 173–176°C (ethanol); $[\alpha]_D$ +114° (*c* 0·18. chloroform). IR spectrum (chloroform): 1 753 (OAc); 1 707, 1 650 (C=C—COOR). ^{1}H NMR spectrum see Table II, further data: 6·94 dd, 1 H (H-20, J(20, 21) = 15·7, J(17, 20) = 7·9); 5·77 dd, 1 H (H-21, J(20, 21) = 15·7, J(17, 21) = 1·2); 4·30–4·00 cm, 3 H, (H-5′, H-6a′, and H-6b′); 4·18 q, 2 H (O—CH_2—CH_3), J = 7·1); 3·98 m, 1 H (H-3); 2·08, 2·07, and 2·05 s, 3 × 3 H (3 × $OCOCH_3$); 1·29 t, 3 H (O—CH_2—CH_3, J = 7·1). For $C_{36}H_{53}FO_{10}$ (664·8) calculated: 65·04% C, 8·04% H; found: 65·21% C, 8·41% H.

Ethyl (20*E*)-3β-(3,4,6-Tri-O-acetyl-2-deoxy-2-fluoro-β-D-glucopyranosyloxy)-5β-pregn-20-en-21-carboxylate (*VIII*)

The title compound *VIII* was obtained as the more polar product from the preceding experiment, yield 260 mg (53%), m.p. 141–144°C (ethanol); $[\alpha]_D$ +36° (*c* 0·17, chloroform). IR spectrum (chloroform): 1 753 (OAc); 1 707, 1 650 (C=C—COOR). ^{1}H NMR spectrum see Table II, further data: 6·93 dd, 1 H (H-20, J(20,21) = 15·7, J(17, 20) = 7·9); 5·76 dd, 1 H (H-21, J(20, 21) = 15·7, J(17, 21) = 1·2); 4·17 q, 2 H (O—CH_2—CH_3, J = 7·1); 4·03 m, 1 H (H-3); 2·07, 2·06, and 2·02 s, 3 × 3 H (3 × $OCOCH_3$); 1·28 t, 3 H (O—CH_2—CH_3, J = 7·1). For $C_{36}H_{53}FO_{10}$ (664·8) calculated: 65·04% C, 8·04% H; found: 64·92% C, 8·30% H.

3β-(3,4,6-Tri-O-acetyl-2-deoxy-2-fluoro-α-D-glucopyranosyloxy)-14-hydroxy-5β,14β-card-20(22)-enolide (*IX*)

A mixture of digitoxigenin *IV* (1 g; 2·67 mmol), molecular sieves (1·2 g), silver silicate (2·2 g), 1,2-dichloroethane (10 ml) and a solution of halogenose *I* (900 mg; 2·42 mmol) in 1,2-dichloroethane (4 ml) was reacted as described in the general procedure. Flash chromatography on silica gel in chloroform–ethyl acetate (10 : 1) afforded 1·18 g (73% based on *I*) of a mixture of glycosides *IX* and *X*, together with 110 mg (11%) of the starting digitoxigenin *IV*. A sample of the glycoside mixture was deacetylated with a triethylamine–methanol–water mixture (20 : 20 : 1) and the anomer population was determined from the integrated H-19 signals in the ^{1}H NMR spectrum

(deuteriopyridine) (0·83 and 0·89 for the α- and β-anomer, respectively) to be 20% of α-anomer. The mixture (1 g) was crudely separated by repeated crystallization (dissolving in a minimum amount of chloroform–methanol (10 : 1) and adding ether) which removed the crystalline β-anomer *X*. The oily product *IX* was finally purified by HPLC in benzene–ethyl acetate (20 : 1), yield 180 mg (18% of the separated mixture), m.p. 122 – 123°C (ether), $[\alpha]_D$ +97° (*c* 0·18, chloroform). IR spectrum (chloroform): 3 610, 3 480 (OH); 1 747 (OAc); 1 623, 1 630 sh (butenolide). ^{1}H NMR spectrum see Table II, further data: 5·87 t, 1 H (H-22, *J* = 1·7); 4·99 dd, 1 H (H-21a, *J*(21a, 22) = 1·8, *J*(21a, 21b) = 18·1); 4·79 dd, 1 H (H-21b, *J*(21b, 22) = 1·7, *J*(21a, 21b) = = 18·1); 4·30–3·99 cm, 3 H (H-5′, H-6′a, and H-6′b); 3·90 m, 1 H (H-3); 2·78 m, 1 H (H-17); 2·08, 2·07, and 2·05 s, 3 × 3 H (3 × $OCOCH_3$). For $C_{35}H_{49}FO_{11}$ (664·8) calculated: 63·24% C, 7·43% H; found: 63·45% C, 7·15% H.

3β-(3,4,6-Tri-O-acetyl-2-deoxy-2-fluoro-β-D-glucopyranosyloxy)-14-hydroxy-5β,14β-card-20(22)-enolide (*X*)

The crystalline fractions from the above experiment, containing the β-anomer *X*, were combined and recrystallized; yield 577 mg (58% of the separated mixture); m.p. 250–258°C (partial decomposition), $[\alpha]_D$ +13° (*c* 0·22, chloroform). IR spectrum (chloroform): 3 610, 3 475 (OH); 1 747, 1 780 sh (OAc); 1 624, 1 634 (butenolide). ^{1}H NMR spectrum see Table II; further data: 5·87 t, 1 H (H-22, *J* = 1·8); 4·99 dd, 1 H (H-21a, *J*(21a, 22) = 1·8, *J*(21a, 21b) = 18·1); 4·79 dd, 1 H (H-21b, *J*(21b, 22) = 1·8, *J*(21a, 21b) = 18·1); 4·05 m, 1 H (H-3); 2·78 m, 1 H (H-17); 2·08, 2·07, and 2·05 s, 3 × 3 H (3 × $OCOCH_3$). For $C_{35}H_{49}FO_{11}$ (664·8) calculated: 63·24% C, 7·43% H; found: 63·17% C, 7·47% H.

General Procedure for Deacetylation of Derivatives *V*– *VIII*

The acetyl derivative was dissolved in absolute ethanol (10 ml) and mixed with 1M ethanolic sodium ethoxide (0·5 ml). The mixture was stirred at room temperature for 1–2 days and the reaction was monitored by TLC in chloroform–methanol (20 : 1). After all the starting compound had reacted, acetic acid (0·1 ml) was aded and the solvent was evaporated. The dry product was coevaporated with toluene and flash-chromatographed on silica gel (25 g) in chloroform–ethanol (10 : 1) to afford the free glycoside which was purified by crystallization from ethanol.

Ethyl (20*E*)-3β-(2-Deoxy-2-fluoro-α-D-glucopyranosyloxy)-24-nor-5,20(22)-choladien-23-oate (*XI*)

The acetyl derivative *V* (95 mg; 0·14 mmol) was deacetylated as described above and recrystallized from ethanol to yield 60 mg (78%) of glycoside *XI*, m.p. 225–227°C, $[\alpha]_D$ +74° (*c* 0·10, methanol). IR spectrum (KBr pellet): 3 400 (OH); 1 716, 1 642 (C=C–COOR); 1 068, 1 049 (C–O). For $C_{31}H_{47}FO_7$ (550·7) calculated: 67·61% C, 8·60% H; found: 68·00% C, 8·52% H.

Ethyl (20*E*)-3β-(2-Deoxy-2-fluoro-β-D-glucopyranosyloxy)-24-nor-5,20(22)-choladien-23-oate (*XII*)

Acetyl derivative *VI* (250 mg, 0·37 mmol) was deacetylated as described in the general procedure. Recrystallization from ethanol afforded 164 mg (81%) of glycoside *XII*, m.p. 220–230°C, $[\alpha]_D$ –43° (*c* 0·10, methanol). IR spectrum (KBr pellet): 3 505, 3 430, 3 355 (OH); 1 716, 1 642 (C=C–COOR); 1 046, 1 095 (C–O). For $C_{31}H_{47}FO_7$ (550·7) calculated: 67·61% C, 8·60% H; found: 68·82% C, 8·58% H.

Ethyl (20*E*)-3β-(2-Deoxy-2-fluoro-α-D-glucopyranosyloxy)-
-5β-pregn-20-ene-21-carboxylate (*XIII*)

The acetyl derivative *VII* (70 mg; 0·09 mmol) was deacetylated according to the above-described general procedure. Recrystallization from ethanol furnished 40 mg (70%) of glycoside *XIII*, m.p. 197–210°C, $[\alpha]_D$ +102° (*c* 0·19, methanol). IR spectrum (KBr pellet): 3 515, 3 350 (OH); 1 725, 1 651 (C=C—COOR); 1 053, 1 029, 1 012 (C—O). For $C_{30}H_{47}FO_7$ (538·7) calculated: 66·89% C, 8·79% H; found: 66·91% C, 8·87% H.

Ethyl (20*E*)-3β-(2-Deoxy-2-fluoro-β-D-glucopyranosyloxy)-
-5β-pregn-20-ene-21-carboxylate (*XIV*)

The acetyl derivative *VIII* (240 mg; 0·30 mmol) was deacetylated as described above and the obtained glycoside *XIV* was recrystallized from ethanol. Yield 121 mg (62%), m.p. 158–171°C. $[\alpha]_D$ +27° (*c* 0·17, methanol). IR spectrum (KBr pellet): 3 520, 3 390 sh, 3 320 (OH); 1 724, 1 650 (C=C—COOR). For $C_{30}H_{47}FO_7$ (538·7) calculated: 66·89% C, 8·79% H; found: 66·58% C, 8·78% H.

3β-(2-Deoxy-2-fluoro-α-D-glucopyranosyloxy)-14-hydroxy-5β,14β-card-20(22)-enolide (*XV*)

The acetyl derivative *IX* (120 mg; 0·18 mmol) was stirred with a mixture of triethylamine, methanol and water (20 : 20 : 1, 10 ml) for 72 h. After evaporation, the product was purified by flash chromatography on silica gel (25 g) in chloroform–methanol (10 : 1) and crystallized from methanol; yield 84 mg (86%) of glycoside *XV*, m.p. 278–281°C, $[\alpha]_D$ +85° (*c* 0·15, methanol). IR spectrum (KBr pellet): 3 500, 3 400, 3 320 sh (OH); 1 810, 1 724, 1 616 (butenolide); 1 004, 1 026, 1 051 (C—O). ^{1}H NMR spectrum (deuteriopyridine): 6·10 t, 1 H (H-22, J = 1·8); 5·43 d, 1 H (H-1′, J(1′, 2′) = 3·5); 5·30 dd, 1 H (H-21a, J(21a, 22) = 1·8, J(21a, 21b) = 18·2); 5·00 dd, 1 H (H-21b, J(21b, 22) = 1·8, J(21a, 21b) = 18·2); 4·75 ddd, 1 H (H-2′, J(1′, 2′) = 3·5, J(2′, 3′) = = 9·5, J(2′, F) = 52·2); 4·75 dt, 1 H (H-3′, J(2′, 3′) = J(3′, 4′) = 9·5, J(3′, F) = 11·5); 4·48 dd, 1 H (H-6a′, J(5′, 6a′) = 4·2, J(6a′, 6b′) = 13·8); 4·35 ddd, 1 H (H-5′, J(4′, 5′) = 9·5, J(5′, 6a′) = = 4·2, J(5′, 6′b) = 5·0); 4·34 dd, 1 H (H-6b′, J(5′, 6b′) = 5·0, J(6a′, 6b′) = 13·8); 4·21 bs, 1 H (H-3); 4·14 t, 1 H (H-4′, J(3′, 4′) = J(4′, 5′) = 8·5); 2·79 m, 1 H (H-17); 1·00 s, 3 H (3 × H-18); 0·83 s, 3 H (3 × H-19). For $C_{29}H_{43}FO_8$ (538·7) calculated: 64·66% C, 8·05% H; found: 64·52% C, 8·10% H.

3β-(2-Deoxy-2-fluoro-β-D-glucopyranosyloxy)-14-hydroxy-
-5β,14β-card-20(22)-enolide (*XVI*)

Acetyl derivative *X* (250 mg; 0·37 mmol) was deacetylated as described for preparation of *XV*; yield after crystallization from ethanol 158 mg of glycoside *XVI*, m.p. 240–252°C, $[\alpha]_D$ −8° (*c* 0·12, methanol). IR spectrum (KBr pellet): 3 440 (OH); 1 780, 1 744, 1 622 (butenolide); 1 078, 1 025 (C—O). ^{1}H NMR spectrum (deuteriopyridine): 6·11 t, 1 H (H-22, J = 1·7); 5·31 dd, 1 H (H-21a, J(21a, 22) = 1·7, J(21a, 21b) = 18·3); 5·09 dd, 1 H (H-1′, J(1′, 2′) = 7·6, J(1′, F) = = 2·4); 5·02 dd, 1 H (H-21b, J(21b, 22) = 1·7, J(21a, 21b) = 18·3; 4·73 dt, 1 H (H-2′, J(1′, 2′) = = 7·6, J(2′, 3′) = 9·0, J(2′, F) = 51·1); 4·53 dd, 1 H (H-6′a, J(5′, 6′a) = 2·4, J(6′a, 6′b) = 11·8); 4·37 m, 1 H (H-3); 4·36 dt, 1 H (H-3′, J(2′, 3′) = J(3′, 4′) = 9·0, J(3′, F) = 16·0); 4·35 dd, 1 H (H-6b′, J(5′, 6b′) = 5·2, J(6a′, 6b′) = 11·8); 4·24 t, 1 H (H-4′, J(3′, 4′) = J(4′, 5′) = 9·0); 3·93 ddd, 1 H (H-5′, J(4′, 5′) = 9·0, J(5′, 6a′) = 2·4, J(5′, 6′b) = 5·2); 2·79 m, 1 H (H-17); 1·00 s, 3 H (3 × H-18); 0·89 s, 3 H (3 × H-19). For $C_{29}H_{43}FO_8$ (538·7) calculated: 64·66% C, 8·05% H; found: 64·84% C, 8·01% H.

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