PREPARATION OF 3-(6-DEOXY-β-D-GLUCOPYRANOSYLOXY) AND 3-(6-DEOXY-α-L-MANNOPYRANOSYLOXY)ANDROSTANE DERIVATIVES WITH UNSATURATED SIDE CHAIN IN POSITION 17β*

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In our previous papers[1 - 4] we described the preparation of 3-(β-D-glucopyranosyloxy) and 3-(β-D-galactopyranosyloxy) derivatives of steroids with an α,β-unsaturated ester chain in position 17β of androstane skeleton. In connection with this project we have studied silver silicate promoted[5] glycosylation of some of above mentioned steroidal derivatives with 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranosyl bromide and 2,3,4-tri-*O*-acetyl-6-deoxy-α-L-mannopyranosyl bromide. Glycosylation with the former gave corresponding β-D-quinovosides triacetates *I – III*, *V*, *VI*, and *IX* (see Table I). β-Configuration on anomeric centers in these compounds follow from $J(1,2)$ of sugar moieties in proton NMR spectra; values in the region 7.5 – 8.0 Hz (cf. Table II) agree with those found in spectra of analogous β-D-glucopyranosides tetraacetates[1 - 3].

The glycosylation with the latter reagent gave α-L-rhamnosides triacetates *IV*, *VII*, and *VIII*. In this case the value of $J(1,2)$ of sugar moiety could not be used for the determination of configuration on anomeric center; according to the literature[6] $J(1,2)$ of both α- and β-methyl L-rhamnosides *XIX* and *XX* are identical. Thus, we used the substantial differences of chemical shifts of H-2, H-3, and H-5 (cf. Table III) and C-2, C-3, and C-5 (cf. Table IV). Both these criteria proved that our compounds have α-configuration on anomeric center.

Hydrolysis of triacetates *I – IX* gave corresponding free β-D-quinovosides *X – XII*, *XIV*, *XV*, and *XVIII* and α-L-rhamnosides *XIII*, *XVI*, and *XVII* (Table V).

EXPERIMENTAL

Melting points were determined on a micro melting point apparatus Boetius (Germany). Optical rotations were measured in chloroform at 25 °C. IR spectra (Tables VI and VII) were taken on a

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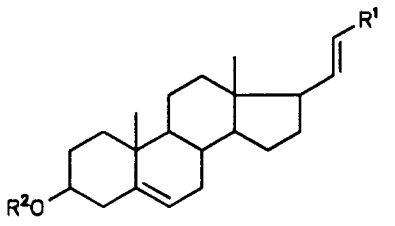
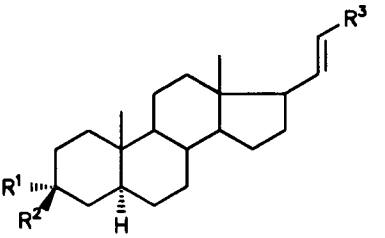
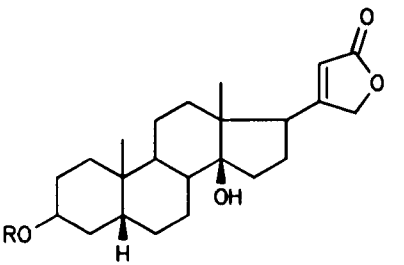




	R^1	R^2
I	$COOCH_3$	Ac_3-β-D-Qui
II	$COOC_2H_5$	Ac_3-β-D-Qui
III	C≡N	Ac_3-β-D-Qui
IV	$COOC_2H_5$	Ac_3-α-L-Rha
X	$COOCH_3$	β-D-Qui
XI	$COOC_2H_5$	β-D-Qui
XII	C≡N	β-D-Qui
XIII	$COOC_2H_5$	α-L-Rha

	R^1	R^2	R^3
V	Ac_3-β-D-Qui	H	CH_3
VI	H	Ac_3-β-D-Qui	CH_3
VII	Ac_3-α-L-Rha	H	C_2H_5
VIII	H	Ac_3-α-L-Rha	C_2H_5
XIV	β-D-Qui	H	CH_3
XV	H	β-D-Qui	CH_3
XVI	α-L-Rha	H	C_2H_5
XVII	H	α-L-Rha	C_2H_5



IX, R = Ac_3-β-D-Qui
XVIII, R = β-D-Qui

β-D-Qui = 6-deoxy-β-D-glucopyranosyl
α-L-Rha = 6-deoxy-α-L-mannopyranosyl
Ac_3-β-D-Qui = 2, 3, 4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranosyl
Ac_3-α-L-Rha = 2, 3, 4-tri-*O*-acetyl-6-deoxy-α-L-mannopyranosyl

Perkin–Elmer PE 580 spectrometer (wavenumbers in cm^{-1}). Proton and carbon-13 NMR spectra were measured on Varian XL-200 instrument (FT mode, 200.06 and 50.31 MHz for ^1H and ^{13}C, respectively) at 23 °C in deuteriochloroform. For ^1H NMR spectra tetramethylsilane was used as internal standard. Carbon-13 chemical shifts were referenced to the signal of solvent and recalculated to tetramethylsilane with relation $\delta(CDCl_3) = 77.0$ ppm. The number of directly bonded hydrogen atoms was determined from the proton decoupled "attached proton test" spectra (APT, refs[7,8]). Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. All parameters were obtained by the first-order analysis. Column chromatography was performed on Silpearl (Kavalier, Votice, The Czech Republic) and thin-layer chromatography on silica gel G according to Stahl (ICN Biochemicals). Solutions in organic solvents were dried over anhydrous magnesium sulfate and the solvents were evaporated in vacuo (about 2 kPa). Analytical samples were dried over phosphorus pentoxide at 40 °C/26 Pa for 12 h. 2,3,4-Tri-*O*-acetyl-6-deoxy-β-D-glucopyranosyl and 2,3,4-tri-*O*-acetyl-6-deoxy-α-L-mannopyranosyl bromides were prepared by passing dry hydrogen bromide into a solution of corresponding 6-deoxyhexose peracetate in dichloromethane. The preparations of starting hydroxy derivatives is described in refs[3,9].

TABLE I

Yields and physico-chemical data of β-D-quinovosides triacetates *I* – *III*, *V*, *VI*, and *IX* and α-L-rhamnosides triacetates *IV*, *VII*, and *VIII*

Compound	Yield, % solvent[a]	M.p., °C	$[\alpha]_D$, ° (*c*)[b]	Formula M.w.	Calculated/Found	
					% C	% H
I	65	154 – 156	−10	$C_{35}H_{50}O_{10}$	66.65	7.99
	E		(2.7)	630.8	66.45	8.23
II	51	154 – 155	−13	$C_{36}H_{52}O_{10}$	67.06	8.13
	E		(2.7)	644.8	66.87	7.95
III	45	195 – 196	−11	$C_{34}H_{47}NO_8$	68.32	7.93[c]
	E + C		(1.5)	597.8	68.56	8.12
IV	32	154 – 156	−73	$C_{35}H_{52}O_{10}$	67.06	8.13
	E + H		(1.1)	644.8	66.85	7.89
V	57	201 – 204	+6	$C_{35}H_{52}O_{10}$	66.43	8.28
	E		(1.6)	632.8	66.68	7.97
VI	60	159 – 162	+5	$C_{35}H_{52}O_{10}$	66.43	8.28
	H + E		(1.6)	632.8	66.72	8.56
VII	52	163 – 165	−4	$C_{35}H_{54}O_{10}$	66.85	8.41
	E + M		(1.9)	646.8	67.09	8.67
VIII	51	140 – 142	−30	$C_{35}H_{54}O_{10}$	66.85	8.41
	E + H		(1.5)	646.8	66.54	8.24
IX	30	248 – 250	0	$C_{35}H_{50}O_{11}$	65.00	7.79
	E		(1.7)	646.8	65.08	8.05

[a] Solvents: C chloroform, E ether, H hexane, M methanol. [b] Measured in chloroform. [c] Calculated: 2.34% N; found: 2.45% N.

TABLE II
^{1}H NMR spectral parameters (in $CDCl_3$) of quinovoside triacetates *I* – *III*, *V*, *VI*, and *IX*. For other conditions see Experimental

Parameter	*I*[a]	*II*[b]	*III*	*V*[a]	*VI*[a]	*IX*[c]
			Steroid unit			
H-18 (s, 3 H)	0.66	0.66	0.66	0.63	0.63	0.88
H-19 (s, 3 H)	0.99	0.99	0.99	0.77	0.78	0.96
H-21 (dd, 1 H)	5.79	5.77	5.28	5.78	5.78	4.88[d]
H-20 (dd, 1 H)	6.96	6.94	6.70	6.94	6.95	–
H-3 (m, 1 H)	3.48[e]	3.49[e]	3.48[e]	3.90[f]	3.55[g]	4.02[f]
H-6 (1 H)	5.36[h]	5.36[h]	5.36[h]	*i*	*i*	*i*
J(20,21)	15.6	16.0	16.5	16.0	16.0	–
J(17,20)	8.1	8.0	8.0	8.0	8.0	–
J(17,21)	1.2	1.2	1.0	1.2	1.0	≈0
			Sugar unit			
H-1 (d, 1 H)	4.56	4.54	4.64	4.51	4.56	4.51
H-2 (dd, 1 H)	4.93	4.92	4.92	4.96	4.92	4.94
H-3 (t, 1 H)	5.16	5.17	5.16	5.17	5.15	5.17
H-4 (t, 1 H)	4.81	4.79	4.81	4.82	4.80	4.82
H-5 (dq, 1 H)	3.54	3.53	3.54	3.54	3.55[g]	3.52
H-6 (d, 3 H)	1.23	1.23	1.23	1.23	1.23	1.23
J(1,2)	8.0	8.0	8.0	7.5	8.0	8.0
J(2,3)	9.5	9.5	9.5	9.5	9.5	9.5
J(3,4)	9.5	9.5	9.5	9.5	9.5	9.5
J(4,5)	9.5	9.5	9.0	9.5	9.5	9.5
J(5,6)	6.2	6.5	6.0	6.0	6.2	6.5
OAc (s, 3 H)	2.00	1.99	2.00	2.00	2.00	2.00
OAc (s, 3 H)	2.03	2.03	2.03	2.03	2.03	2.03
OAc (s, 3 H)	2.04	2.04	2.03	2.04	2.03	2.03

[a] Other signal: 3.72 s, 3 H ($COOCH_3$). [b] Other signals: 4.18 q, 2 H and 1.29 t, 3 H ($COOCH_2CH_3$, J = 7.2). [c] Other signals: 2.75 m, 1 H (H-17); 5.87 X part of ABX system (H-22, J(A,X) ≈ J(B,X) ≈ 2). [d] AB part of ABX system, J(A,B) = 18. [e] W = 32. [f] W = 14. [g] Multiplet of overlapped signals. [h] bd, J ≈ 4.5. [i] Undeterminable value.

TABLE III
^{1}H NMR spectral parameters (in $CDCl_3$) of rhamnoside triacetates *IV*, *VII*, and *VIII*. For other conditions see Experimental

Parameter	*IV*	*VII*	*VIII*	*XIX*[a]	*XX*[a]
		Steroid unit			
H-18 (s, 3 H)	0.66	0.63	0.63		
H-19 (s, 3 H)	1.01	0.78	0.81		
H-21 (dd, 1 H)	5.78	5.78	5.77		
H-20 (dd,1 H)	6.94	6.94	6.94		
H-3 (m, 1 H)	3.49[b]	3.87[c]	3.53[b]		
H-6 (1 H)	5.34[d]	[e]	[e]		
J(20,21)	15.6	15.6	15.6		
J(17,20)	7.9	7.9	7.9		
J(17,21)	1.1	1.1	1.1		
$COOCH_2CH_3$ (t, 3 H)	1.29[f]	1.29[g]	1.29[g]		
$COOCH_2CH_3$ (q, 2 H)	4.18[f]	4.18[g]	4.18[g]		
		Sugar unit			
H-1 (d, 1 H)	4.88	4.81	4.87	4.63	4.51
H-2 (dd, 1 H)	5.18	5.20	5.16	5.22	5.46
H-3 (dd, 1 H)	5.33	5.35	5.32	5.40	5.10
H-4 (bt, 1 H)	5.05	5.07	5.04	5.03	5.00
H-5 (dq, 1 H)	3.95	3.92	3.95	3.86	3.50
H-6 (d, 3 H)	1.20	1.20	1.20	1.21	1.30
J(1,2)	1.8	1.8	1.8	1.0	1.0
J(2,3)	3.4	3.5	3.4		
J(3,4)	10.1	10.1	10.2		
J(4,5)	9.9	9.7	9.7		
J(5,6)	6.2	6.2	6.3		
OAc (s, 3 H)	1.99	2.00	1.98		
OAc (s, 3 H)	2.04	2.06	2.04		
OAc (s, 3 H)	2.15	2.15	2.14		

[a] *XIX*, Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-L-mannopyranoside; *XX*, methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-L-mannopyranoside; values taken from literature[6]. [b] $W \approx 32$. [c] $W \approx 10$. [d] bd, $J \approx 4.5$. [e] Undeterminable value. [f] $J = 7.1$. [g] $J = 7.2$.

TABLE IV
^{13}C NMR spectral parameters (in $CDCl_3$) of α-L-rhamnoside triacetates *IV*, *VII*, and *VIII*. For other conditions see Experimental

Carbon	*IV*	*VII*	*VIII*	*XIX*[a]	*XX*[a]
		Steroid unit			
1	37.24	31.91	33.91		
2	29.25	24.69	28.61		
3	74.45	72.34	76.89		
4	38.25	34.13	36.98		
5	140.12	39.72	44.64		
6	121.28	28.42	29.04		
7	31.61	32.45	32.06		
8	31.61	35.49	35.47		
9	50.20	54.12	54.43		
10	36.71	35.90	35.64		
11	20.53	20.25	20.70		
12	37.19	37.40	37.48		
13	44.56	44.85	44.84		
14	55.99	55.75	55.78		
15	24.92	24.84	24.86		
16	26.96	27.00	26.99		
17	53.77	53.90	53.90		
18	12.96	13.22	13.20		
19	19.28	11.35	12.23		
20	150.41	150.75	150.62		
21	121.74	121.17	121.20		
C=O	166.54	166.66	166.60		
OCH_2CH_3	14.21	14.24	14.24		
OCH_2CH_3	60.01	60.00	60.03		
		Sugar unit			
1	95.59	95.37	95.39	98.1	98.7
2	71.27[b]	71.37[b]	71.34[b]	69.3	86.6
3	69.08[b]	69.29[b]	69.13[b]	69.0	70.7
4	70.39[b]	70.58[b]	70.58[b]	70.4	70.5
5	66.20	66.35	66.17	66.0	69.6
6	17.30	17.32	17.34	17.3	17.3
$OOCCH_3$	170.09	170.20	170.15	169.6	169.8
$OOCCH_3$	169.89[c]	170.05	169.94	169.6	169.4
$OOCCH_3$	169.89[c]	169.95	169.91	169.6	169.4
$OOCCH_3$	20.87	20.93	20.91	20.5	20.6
$OOCCH_3$	20.72	20.78	20.76	20.5	20.6
$OOCCH_3$	20.66	20.73	20.70	20.5	20.4

[a] *XIX*, Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-L-mannopyranoside; *XX*, methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-L-mannopyranoside (values taken from literature[10]). [b] Signals are assigned tentatively and can be mutually interchanged. [c] Overlapped signals.

General Procedure for Preparation of Quinovosides Triacetates *I* – *III*, *V*, *VI*, and *IX* and Rhamnosides Triacetates *IV*, *VII*, and *VIII*

A dry mixture of a hydroxy derivative (0.5 mmol), silver silicate[5] (0.7 g) and ground molecular sieve 4 Å (1 g) was stirred in vacuo (10 Pa) for 4 h. The flask was then filled with argon under slight overpressure (about 5 kPa) and 1,2-dichloroethane (10 ml) was injected through a septum. The mixture was stirred at room temperature for 10 min and a solution of corresponding halogenose (494 mg, 1.4 mmol) in 1,2-dichloroethane (3 ml) was added. After stirring at room temperature for 20 h, the catalyst was removed by filtration through a column of silica gel layered with Celite. The column was washed with dichloromethane–ether (4 : 1) and the combined filtrates were evaporated in vacuo. The residue was chromatographed on a column of Silpearl (30 g) in mixture toluene–ether (9 : 1). Obtained product was further purified by crystallization. For yield, solvent used for crystallization, melting points, optical rotations, and elemental analyses see Table I.

TABLE V

Yields and physico-chemical data of β-D-quinovosides *X* – *XII*, *XIV*, *XV*, and *XVIII* and α-L-rhamnosides *XIII*, *XVI*, and *XVII*

Compound	Yield, % solvent[a]	M.p., °C	$[\alpha]_D$, ° (*c*)[b]	Formula M.w.	Calculated/Found	
					% C	% H
X	88	205 – 207	–32	$C_{29}H_{44}O_7$	69.02	8.79
	E		(0.8)	504.7	68.88	9.02
XI	87	188 – 192	–40	$C_{30}H_{46}O_7$	69.47	8.94
	M + W		(0.7)	518.7	69.23	9.09
XII	85	254 – 259	–34	$C_{28}H_{41}NO_5$	71.31	8.76[c]
	C + M		(0.6)	471.6	71.05	8.53
XIII	84	207 – 211	–72	$C_{30}H_{46}O_7$	69.47	8.94
	E + A		(1.1)	518.7	69.35	9.06
XIV	77	120	+16	$C_{29}H_{46}O_7$	68.75	9.15
	H		(1.6)	506.7	68.46	8.92
XV	86	205 – 207	+24	$C_{29}H_{46}O_7$	68.75	9.15
	E + H		(1.7)	506.7	68.56	8.87
XVI	88	212 – 215	–12	$C_{30}H_{48}O_7$	69.20	9.29
	E + A		(1.0)	520.7	69.16	9.01
XVII	86	198 – 200	–26	$C_{30}H_{48}O_7$	69.20	9.29
	A		(1.1)	520.7	69.89	8.97
XVIII	37	298 – 299	–7	$C_{29}H_{44}O_8$	66.90	8.52
	E		(2.2)	520.7	67.05	8.75

[a] Solvents: A acetone, C chloroform, E ether, H hexane, M methanol, W water. [b] Measured in chloroform. [c] Calculated: 2.97% N; found: 2.68% N.

TABLE VI
IR spectra ($\tilde{\nu}$, cm^{-1}; in CCl_4) of β-D-quinovosides triacetates *I* – *III*, *V*, *VI*, and *IX* and α-L-rhamnosides triacetates *IV*, *VII*, and *VIII*. For other conditions see Experimental

Compound	C=O[a]	C=O[b]	C=C[c]	C–O
I	1 752	1 713	1 650	1 257, 1 080, 1 058, 1 038
II	1 760	1 719	1 652	1 247, 1 218, 1 035
III[d]	1 756	–	1 628	1 254, 1 078, 1 037
IV[e]	1 750	1 719	1 650	1 224
V	1 753	1 718	1 652	1 254, 1 078, 1 037
VI	1 754	1 714	1 650	1 252, 1 077, 1 036
VII[e]	1 753	1 719	1 652	1 225
VIII[e]	1 752	1 719	1 651	1 225
IX[f]	1 748	1 748	1 621	1 252, 1 232, 1 075, 1 035

[a] Carbonyl of glycoside acetates. [b] Carbonyl of unsaturated ester. [c] Conjugated double bond. [d] Other band 2 228 (C≡N). [e] Measured in chloroform solution. [f] Other bands 3 604, 3 408 (OH).

TABLE VII
IR spectra ($\tilde{\nu}$, cm^{-1}; KBr pellet) of β-D-quinovosides *X* – *XII*, *XIV*, *XV*, and *XVIII* and α-L-rhamnosides *XIII*, *XVI*, and *XVII*. For other conditions see Experimental

Compound	O–H	C=O	C=C[a]	C–O
X	3 440	1 723, 1 705	1 652	1 072
XI	3 439	1 725	1 658	1 055, 1 018
XII[b]	3 403	–	1 628	1 066, 1 012
XIII	3 405	1 733	1 655	1 061, 1 031
XIV	3 445	1 723	1 650	1 170, 1 070
XV	3 433	1 727	1 653	1 066, 1 012
XVI	3 405	1 733	1 655	1 055, 1 034
XVII	3 420	1 725	1 653	1 067, 1 023
XVIII	3 456	1 757, 1 742	1 621	1 093, 1 023

[a] Conjugated double bond. [b] Other band 2 222 (C≡N).

General Procedure for Preparation of Quinovosides *X – XII*, *XIV*, *XV*, and *XVIII* and Rhamnosides *XIII*, *XVI*, and *XVII*

To a solution of a glycoside triacetate (0.1 mmol) in methanol (5 ml) a solution of sodium methoxide in methanol (5%, 5 drops) was added. After stirring for 2 h at room temperature solid carbon dioxide (about 100 mg) was added and the solvent was evaporated in vacuo. The residue was chromatographed on a column of Silpearl (30 g) in chloroform–methanol (9 : 1). Obtained product was purified by crystallization. For yield, solvent used for crystallization, melting points, optical rotations, and elemental analyses see Table V.

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