

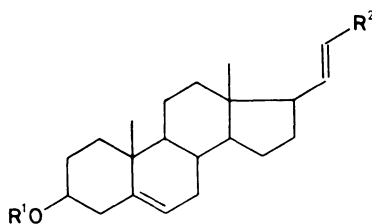
**PREPARATION OF 3-( $\beta$ -D-GALACTOPYRANOSYLOXY)ANDROSTANE  
DERIVATIVES WITH UNSATURATED SIDE CHAIN IN POSITION 17 $\beta$**

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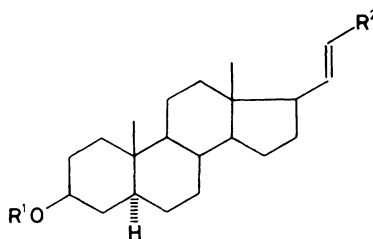
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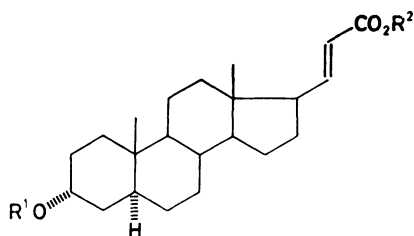
The 3-hydroxy derivatives *I–VIII* were transformed into the  $\beta$ -D-galactosides *IX–XVI* respectively, by the silver silicate promoted<sup>1</sup> glycosylation with 2,3,4,6-tetra-O-acetyl- $\alpha$ -D-galactopyranosyl bromide. Without further purification, the obtained acetylated galactosides (unseparable from by-products) were hydrolyzed to give free  $\beta$ -D-galactosides whose structure was confirmed by acetylation to the corresponding tetraacetates *XVII–XXIV*. The <sup>1</sup>H NMR signals correspond to reported data for steroid<sup>2,3</sup> and sugar<sup>4</sup> moieties.



- I*, R<sup>1</sup> = H ; R<sup>2</sup> = CO<sub>2</sub>CH<sub>3</sub>  
*II*, R<sup>1</sup> = H ; R<sup>2</sup> = CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>  
*III*, R<sup>1</sup> = H ; R<sup>2</sup> = CN  
*IX*, R<sup>1</sup> =  $\beta$ -D-Gal ; R<sup>2</sup> = CO<sub>2</sub>CH<sub>3</sub>  
*X*, R<sup>1</sup> =  $\beta$ -D-Gal ; R<sup>2</sup> = CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>  
*XI*, R<sup>1</sup> =  $\beta$ -D-Gal ; R<sup>2</sup> = CN  
*XVII*, R<sup>1</sup> = Ac<sub>4</sub>- $\beta$ -D-Gal ; R<sup>2</sup> = CO<sub>2</sub>CH<sub>3</sub>  
*XVIII*, R<sup>1</sup> = Ac<sub>4</sub>- $\beta$ -D-Gal ; R<sup>2</sup> = CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>  
*XIX*, R<sup>1</sup> = Ac<sub>4</sub>- $\beta$ -D-Gal ; R<sup>2</sup> = CN



- IV*, R<sup>1</sup> = H ; R<sup>2</sup> = CO<sub>2</sub>CH<sub>3</sub>  
*V*, R<sup>1</sup> = H ; R<sup>2</sup> = CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>  
*VI*, R<sup>1</sup> = H ; R<sup>2</sup> = CN  
*XII*, R<sup>1</sup> =  $\beta$ -D-Gal ; R<sup>2</sup> = CO<sub>2</sub>CH<sub>3</sub>  
*XIII*, R<sup>1</sup> =  $\beta$ -D-Gal ; R<sup>2</sup> = CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>  
*XIV*, R<sup>1</sup> =  $\beta$ -D-Gal ; R<sup>2</sup> = CN  
*XX*, R<sup>1</sup> = Ac<sub>4</sub>- $\beta$ -D-Gal ; R<sup>2</sup> = CO<sub>2</sub>CH<sub>3</sub>  
*XXI*, R<sup>1</sup> = Ac<sub>4</sub>- $\beta$ -D-Gal ; R<sup>2</sup> = CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>  
*XXII*, R<sup>1</sup> = Ac<sub>4</sub>- $\beta$ -D-Gal ; R<sup>2</sup> = CN



- VII,  $R^1 = H$  ;  $R^2 = CH_3$   
 VIII,  $R^1 = H$  ;  $R^2 = CH_2CH_3$   
 XV,  $R^1 = \beta\text{-D-Gal}$  ;  $R^2 = CH_3$   
 XVI,  $R^1 = \beta\text{-D-Gal}$  ;  $R^2 = CH_2CH_3$   
 XXIII,  $R^1 = \text{Ac}_4\text{-}\beta\text{-D-Gal}$  ;  $R^2 = CH_3$   
 XXIV,  $R^1 = \text{Ac}_4\text{-}\beta\text{-D-Gal}$  ;  $R^2 = CH_2CH_3$

$\beta\text{-D-Gal} = \beta\text{-D-galactopyranosyl}$

$\text{Ac}_4\text{-}\beta\text{-D-Gal} = 2,3,4,6\text{-tetra-O-acetyl-}\beta\text{-D-galactopyranosyl}$

TABLE I  
 Yields and physico-chemical data of  $\beta\text{-D-galactosides IX-XVI}$

$\beta\text{-D-Galactoside}$	Yield, % Solvent <sup>a</sup>	M.p. °C	$[\alpha]_D$ (c) <sup>b</sup>	Formula M.w.	Calculated/Found		
					% C	% H	% N
IX	61	224–226	–37° (2.2)	$C_{29}H_{44}O_8$ 520.7	66.90	8.52	—
	A + E				67.18	8.77	—
X	45	234–237	–36° (2.4)	$C_{30}H_{46}O_8$ 534.7	67.39	8.67	—
	A + E + C				67.25	8.55	—
XI	73	270–274	–32° (0.6)	$C_{28}H_{41}NO_6$ 487.6	68.97	8.47	2.87
	C + M				68.88	8.33	3.01
XII	65	214–217	+6° (2.5)	$C_{29}H_{46}O_8$ 522.7	66.64	8.87	—
	C + A + M				66.43	9.01	—
XIII	68	226–230	+8° (3.1)	$C_{30}H_{48}O_8$ 536.7	67.14	9.01	—
	A + E + C				66.98	8.75	—
XIV	57	255–275 decomp.	+14° (0.8)	$C_{28}H_{43}NO_6$ 489.7	68.68	8.85	2.86
	C + M				68.76	8.99	3.01
XV	75	214–218	+27° (2.5)	$C_{29}H_{46}O_8$ 522.7	66.64	8.87	—
	A + E				66.42	8.62	—
XVI	75	214–216	+32° (3.1)	$C_{30}H_{48}O_8$ 536.7	67.14	9.01	—
	T + A				66.95	8.88	—

<sup>a</sup> Solvents: A ether, E ethanol, C chloroform, M methanol, T toluene; <sup>b</sup> measured in chloroform.

## 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 Perkin-Elmer PE 580 spectrometer. <sup>1</sup>H NMR spectra were measured on spectrometer Varian XL-200 (FT mode, 200 MHz) in deuteriochloroform with tetramethylsilane as internal standard. Chemical shifts are given in ppm ( $\delta$ -scale), coupling constants ( $J$ ) and widths of multiplets ( $W$ ) are given in Hz. All parameters were obtained by first-order analyses. Column chromatography was performed on Silpearl (Kavalier, Votice), thin-layer chromatography on silica gel G according to Stahl (ICN Biochemicals). 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.

TABLE II  
IR spectra ( $\tilde{\nu}$ , cm<sup>-1</sup>; KBr pellet) of  $\beta$ -D-galactosides IX–XVI

Compound	O-H	C $\equiv$ N	C=O	C=C	C-O
IX	3 450	—	1 718	1 652	1 065
X	3 510 sh, 3 420, 3 330 sh, 3 110	—	1 718	1 653	1 092, 1 077, 1 047
XI	3 485, 3 420, 3 350, 3 120	2 225	—	1 631	1 153, 1 095, 1 077, 1 046
XII	3 540 sh, 3 420, 3 340 sh, 3 130 sh	—	1 724	1 653	1 093, 1 074, 1 044
XIII	3 500 sh, 3 415, 3 330 sh, 3 120 sh	—	1 713	1 656	1 093, 1 075, 1 044
XIV	3 520, 3 415, 3 350 sh, 3 120	2 225	—	1 631	1 148, 1 094, 1 078, 1 045
XV	3 475, 3 400, 3 160	—	1 713	1 649	1 104, 1 058, 1 040 sh
XVI	3 410	—	1 703	1 652	1 085 sh, 1 067, 1 040

## General Procedure for Preparation of Galactosides IX–XVI

A dry mixture of 3-hydroxy derivative<sup>2,3</sup> (1 mmol), silver silicate<sup>1</sup> (1.4 g) and ground molecular sieve 4A (2.0 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 (20 ml) was injected through a septum. The mixture was stirred at room temperature for 20 min and a solution of 2,3,4,6-tetra-O-acetyl- $\alpha$ -D-galactopyranosyl bromide (500 mg, 1.2 mmol) in 1,2-dichloroethane (3 ml) was added (through septum). After stirring at room temperature for 20 h, the catalyst was removed by filtration through a column of Celite. The column was washed with chloroform–ether (4 : 1) and combined filtrates were washed with 5% aqueous sodium hydrogen carbonate and water.

TABLE III  
Yields and physico-chemical data of  $\beta$ -D-galactosides tetraacetates XVII–XXIV

Acetate	Yield, % Solvent <sup>a</sup>	M.p. °C	[ $\alpha$ ] <sub>D</sub> (c) <sup>b</sup>	Formula M.w.	Calculated/Found		
					% C	% H	% N
XVII	65	222–223	–14° (5.0)	C <sub>37</sub> H <sub>52</sub> O <sub>12</sub> 688.8	64.52	7.61	–
	A + E				64.81	7.75	–
XVIII	61	204–205	–15° (2.3)	C <sub>38</sub> H <sub>54</sub> O <sub>12</sub> 702.8	64.94	7.74	–
	A + C				65.10	7.89	–
XIX	71	161–162	–11° (1.7)	C <sub>36</sub> H <sub>49</sub> NO <sub>10</sub> 655.8	65.94	7.53	2.14
	A + P				66.12	7.66	2.11
XX	76	231–233	+18° (3.9)	C <sub>37</sub> H <sub>54</sub> O <sub>12</sub> 690.8	64.33	7.88	–
	A + C				64.12	7.98	–
XXI	85	219–222	+17° (1.9)	C <sub>38</sub> H <sub>56</sub> O <sub>12</sub> 704.9	64.75	8.01	–
	A				65.02	7.87	–
XXII	72	164–165	+22° (1.7)	C <sub>36</sub> H <sub>51</sub> NO <sub>10</sub> 657.8	65.73	7.81	2.13
	E + P				65.89	7.66	2.01
XXIII	83	162–164	+4° (2.8)	C <sub>37</sub> H <sub>54</sub> O <sub>12</sub> 690.8	64.33	7.88	–
	A + P				64.31	8.02	–
XXIV	48	161–162	+4° (1.4)	C <sub>38</sub> H <sub>56</sub> O <sub>12</sub> 704.9	64.75	8.01	–
	A + P				64.88	8.22	–

<sup>a</sup> Solvents: A ether, E ethyl acetate, C chloroform, P light petroleum; <sup>b</sup> measured in chloroform

The solvents were evaporated and the residue was dissolved in methanol (30 ml; in the case of methyl esters *IX*, *XII*, and *XV* and nitriles *XI*, and *XIV*) or in ethanol (30 ml; in the case of ethyl esters *X*, *XIII*, and *XVI*). After addition of 20 drops of 5% solution of the corresponding sodium alkoxide, the mixture was stirred at room temperature for 3 h, neutralized with dry ice (about 300 mg) and the solvent was evaporated in vacuo. The residue was chromatographed on a column of Silpearl (40 g) in chloroform-methanol (9 : 1, for compounds *IX*, *XI*, *XII*, *XIV*, and *XV*) or in chloroform-ethanol (9 : 1, for compounds *X*, *XIII*, and *XVI*). The product was further purified by crystallization. Solvents used for crystallization, yields, melting points, optical rotations and elemental analyses are given in Table I. Infrared spectra are given in Table II.

#### General Procedure for Preparation of Tetraacetates *XVII*–*XXIV*

A solution of the galactoside (0.2 mmol) in a mixture of pyridine (1 ml) and acetic anhydride (1 ml) was allowed to stand overnight at room temperature. The mixture was coevaporated with toluene (3×), the residue was dissolved in ether, filtered through Celite and the solvent was evaporated in vacuo. The product was further purified by crystallization. Solvents used for crystallization, yields, melting points, optical rotations and elemental analyses are given in Table III. Infrared and  $^1\text{H}$  NMR spectra are given in Tables IV and V, respectively.

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TABLE IV

IR spectra ( $\tilde{\nu}$ ,  $\text{cm}^{-1}$ ; tetrachloromethane) of  $\beta$ -D-galactosides tetraacetates *XVII*–*XXIV*

Compound	$\text{C}\equiv\text{N}$	$\text{C}=\text{O}^a$	$\text{C}=\text{O}^b$	$\text{C}=\text{C}$	$\text{C}-\text{O}$
<i>XVII</i>	—	1 758	1 726	1 652	1 221, 1 058
<i>XVIII</i>	—	1 757	1 720	1 652	1 220, 1 055
<i>XIX</i>	2 225	1 757	—	1 631	1 222
<i>XX</i> <sup>c</sup>	—	1 750	1 715	1 650	
<i>XXI</i>	—	1 758	1 719	1 652	1 220
<i>XXII</i>	2 225	1 757	—	1 631	1 222
<i>XXIII</i>	—	1 758	1 726	1 652	1 220
<i>XXIV</i> <sup>c</sup>	—	1 750	1 707	1 650	

<sup>a</sup> Carbonyl of galactoside acetates; <sup>b</sup> carbonyl of unsaturated ester; <sup>c</sup> in chloroform solution.

TABLE V  
<sup>1</sup>H NMR spectral parameters (in deuteriochloroform) for galactoside tetraacetates XVII—XXIV<sup>a</sup>

Parameter	XVII <sup>b</sup>	XVIII <sup>c</sup>	XIX	XX <sup>b</sup>	XXI <sup>c</sup>	XXII	XXIII <sup>b</sup>	XXIV <sup>c</sup>
H-18 (s, 3 H)	0.66	0.66	0.66	0.63	0.63	0.63	0.62	0.62
H-19 (s, 3 H)	0.99	1.00	1.00	0.79	0.79	0.79	0.78	0.78
H-21 (dd, 1 H)	5.78	5.78	5.28	5.77	5.77	5.26	5.78	5.77
H-20 (dd, 1 H)	7.01	6.94	6.69	6.94	6.93	6.68	6.95	6.94
H-3 (m, 1 H)	3.49 <sup>d</sup>	3.49 <sup>d</sup>	3.36 <sup>d</sup>	3.55 <sup>d</sup>	3.56 <sup>d</sup>	3.55 <sup>d</sup>	3.92 <sup>e</sup>	3.92 <sup>e</sup>
H-6 (m, 1 H)	5.35	5.35	5.36	<i>f</i>	<i>f</i>	<i>f</i>	<i>f</i>	<i>f</i>
J(20, 21)	15.6	15.6	16.4	15.6	15.6	16.4	15.6	15.6
J(17, 20)	8.0	8.0	8.1	8.0	8.0	8.2	8.0	8.0
J(17, 21)	1.1	1.1	1.2	1.2	1.1	1.2	1.1	1.1

Steroid unit

	Sugar unit									
H-1 (d, 1 H)	4-55	4-54	4-55	4-54	4-55	4-54	4-55	4-54	4-55	4-49
H-2 (dd, 1 H)	5-19	5-18	5-19	5-18	5-19	5-18	5-19	5-18	5-19	5-22
H-3 (dd, 1 H)	5-02	5-01	5-01	5-01	5-02	5-01	5-02	5-01	5-02	5-02
H-4 (dd, 1 H)	5-38	5-38	5-38	5-38	5-38	5-38	5-37	5-37	5-38	5-38
H-5 (dt, 1 H)	3-89	3-88	3-89	3-88	3-89	3-88	3-88	3-88	3-87	3-87
H-6a (dd, 1 H)	4-10	4-10	4-10	4-10	4-10	4-10	4-12	4-09	4-10	4-10
H-6b (dd, 1 H)	4-19	4-19	4-19	4-19	4-19	4-19	4-20	4-18	4-18	4-17
J(1, 2)	7-7	7-8	7-7	7-8	7-7	7-8	7-8	7-7	7-8	7-7
J(2, 3)	10-5	10-6	10-5	10-6	10-5	10-6	10-4	10-5	10-5	10-6
J(3, 4)	3-4	3-4	3-4	3-4	3-4	3-4	3-4	3-4	3-4	3-4
J(4, 5)	1-1	1-2	1-1	1-1	1-1	1-1	1-1	1-0	1-1	1-1
J(5, 6a)	6-8	6-7	6-7	6-7	6-8	6-7	6-8	6-8	6-7	6-7
J(5, 6b)	6-8	7-0	7-0	7-0	6-8	7-0	6-8	6-8	6-8	6-8
J(6a, 6b)	11-1	11-3	11-0	11-3	11-1	11-3	11-1	11-1	11-2	11-1
OAc (s, 3 H)	2-14	2-14	2-15	2-14	2-14	2-14	2-14	2-14	2-15	2-15
OAc (s, 3 H)	2-06	2-06	2-06	2-06	2-06	2-06	2-05	2-05	2-05	2-05
OAc (s, 3 H)	2-04	2-04	2-04	2-04	2-04	2-04	2-04	2-04	2-04	2-04
OAc (s, 3 H)	1-98	1-98	1-98	1-98	1-98	1-98	1-98	1-98	1-98	2-00

<sup>a</sup> For other conditions see Experimental; <sup>b</sup> other signal 3-72 s, 3 H (COOCH<sub>3</sub>); <sup>c</sup> other signals 4-18 q, 2 H and 1-28 t, 3 H (COOCH<sub>2</sub>CH<sub>3</sub>, J = 7-2); <sup>d</sup> W = 32; <sup>e</sup> W = 16; <sup>f</sup> undeterminable value.

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