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Note

Two approaches to the synthesis of 3-β-D-glucopyranosyl-D-glucitol

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Dedicated to the memory of Aleksander Zamojski who passed away February 23, 2004

Abstract—Glycosidation of 1,2:5,6-di-*O*-isopropylidene-D-glucose with tetra-*O*-acetyl-glucosyl bromide in 1:1 benzene–$MeNO_2$ afforded approximately equal amounts of the 3-*O*-β-D-glycoside and the rearranged 6-*O*-β-D-glycoside, while in MeCN only the latter was formed. When tetra-*O*-acetyl-β-thiophenylglucoside was used as donor in CH_2Cl_2 in the presence of NIS/TfOH as activator, the 6-*O*-β-D-glycoside and a 3-*O*-orthoester were formed in a 1:2 ratio at −20 °C, while at 20 °C only the former could be isolated. Glycosidation of 1-*O*-benzoyl-2,4-*O*-benzylidene-5,6-*O*-isopropylidene-D-glucitol with tetra-*O*-acetyl-glucosyl bromide in MeCN in the presence of $Hg(CN)_2$ afforded the corresponding 3-*O*-α- and 3-*O*-β-glycopyranoside in a 1:4 ratio in MeCN and 1:5 in 1:1 benzene–$MeNO_2$, respectively. When $Hg(CN)_2/HgBr_2$ was used as promoter, the corresponding orthoester was also formed. When tetra-*O*-acetyl-β-thiophenylglucoside was used as donor, the 3-*O*-β-anomer and the orthoester were obtained predominantly in a 3:2 ratio together with traces of the 3-*O*-α-glycoside. Both β-glycosides could be smoothly converted into 3-β-D-glucopyranosyl-D-glucitol.

Keywords: Glycosidation; Partially protected D-glucitol; Disaccharides

For our ongoing search on heparin degradation products and their analogs,[1,2] a larger amount of 3-β-D-glucopyranosyl-D-glucitol (**1**) was needed as starting material. This compound can be easily prepared by borohydride reduction of the corresponding disaccharide laminaribiose (3-β-D-glucopyranosyl-D-glucose **2**), but the latter is not commercially available and its preparation by hydrolysis of natural polysaccharides is a very tedious process.[3] In the last decades, many synthetic approaches were published[4–16] for **2** via **6**, using 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose **3** as acceptor and tetra-*O*-acetyl-α-D-glucopyranosyl bromide **4** as donor. All of these methods had the drawback that the yields of the glycosidation reaction affording **6** were very modest, due to the fact that under acidic conditions an isopropylidene migration takes place resulting in 1,2:3,5-di-*O*-isopropylidene-D-glucofuranose **7**, which reacts with **4** yielding the corresponding 6-*O*-glycosylated derivative **8**.[15] In 1990, a high yielding (83%) approach to **6** was published,[17] which used the thiophenylglycoside **5** as donor, *N*-iodosuccinimide as promoter and TfOH as catalyst.

1. Reinvestigation of the synthesis of 6

In a first attempt, we repeated the glycosylation reaction of **3** with **4** at 20 °C, using the conditions described by Lipták et al.[15] (1:1 benzene–$MeNO_2$, $Hg(CN)_2$) and could isolate the two isomeric glycosides **6** and **8** after repeated column chromatography in 25% and 28% yields, respectively. When acetonitrile was used as solvent, only the 6-*O*-glycoside **8** could be isolated in a very poor yield (15%). Thereafter, we applied the thioglycoside **5** as donor and used the conditions according to lit.[17] but, contrary to the published data, the following results were obtained. When the reaction was carried out at −40 °C, two compounds, the rearranged 6-*O*-glycoside **8** as well as the orthoester **9** were formed in a 1:2 ratio. The structure of the latter is evident from its NMR spectra as in the ^1H NMR spectrum the methyl

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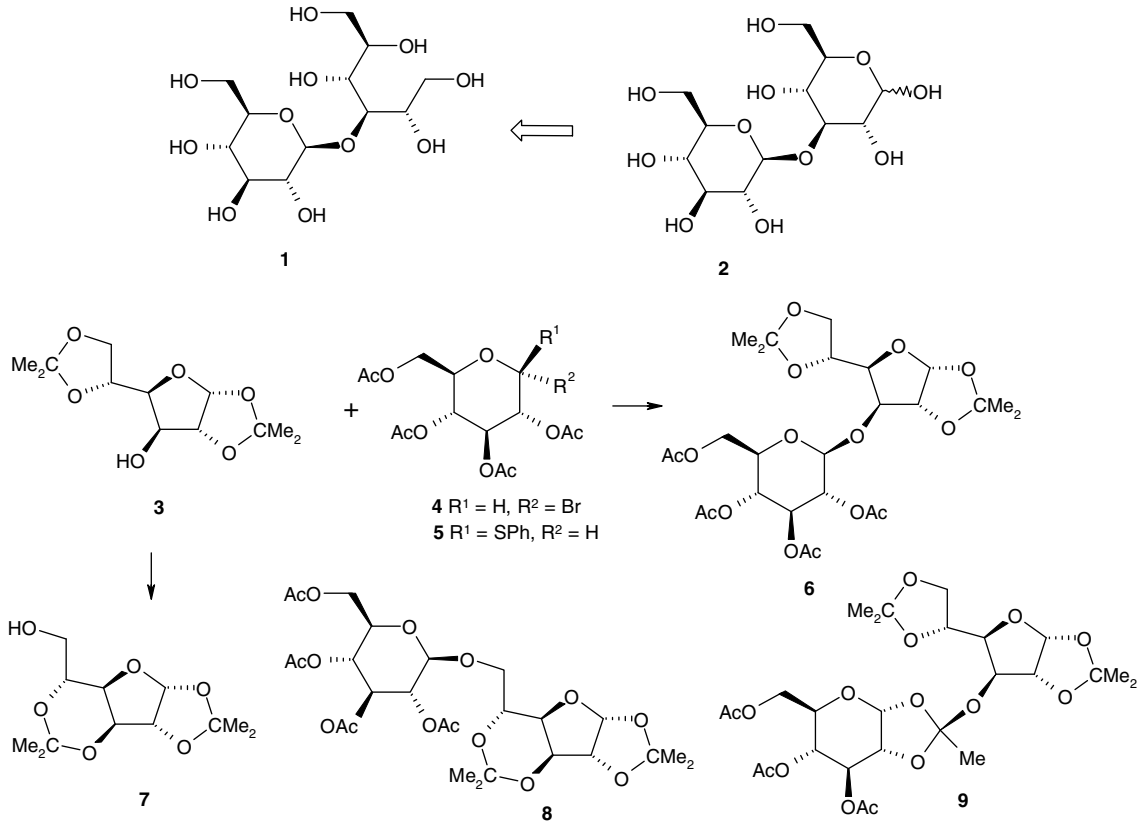


Scheme 1.

signal of the orthoester appears at δ 1.76 ppm, well separated from the three acetyl signals (δ 2.06, 2.06 and 2.07 ppm), and in the ^{13}C NMR spectrum the signal of the quaternary carbon atom can be detected at δ 121.4 ppm, while the three carbonyl atoms appear at δ 168.9, 169.5 and 170.0 ppm, respectively. The NOE effect observed between the methyl group of the orthoester, H-3′ and H-5′ proved the exo orientation of the aglycon that is the *S*-configuration of the orthoester carbon. When the temperature of the glycosidation reaction was raised to 20 °C for 5 min, only the 6-*O*-glycoside **8** could be isolated from the multicomponent mixture in a modest yield (24%) (Scheme 1).

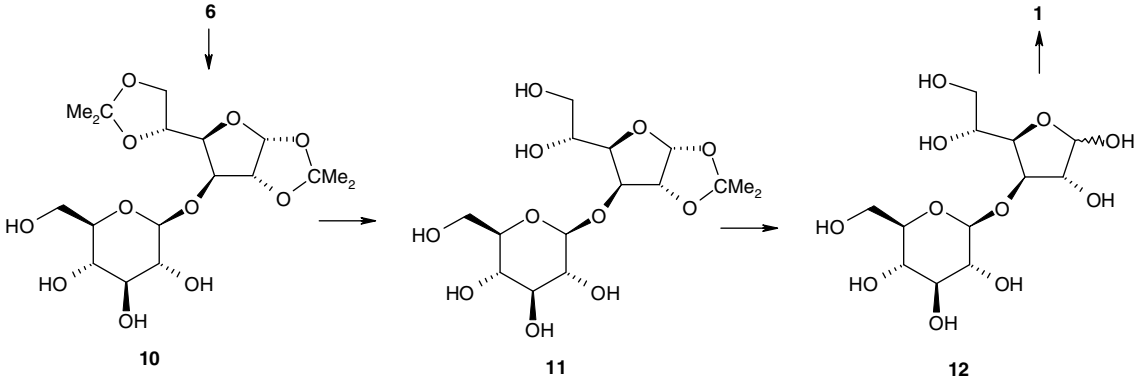
2. Conversion of 6 into 1

The disaccharide derivative **6** was first deacetylated according to Zemplén and thereafter the 5,6-*O*-isopropylidene group of the resulting glycoside **10** could be removed selectively with aqueous sulfuric acid at rt affording **11**. The remaining 1,2-*O*-isopropylidene group of the latter could be hydrolyzed with aqueous sulfuric acid at 60 °C and the resulting free disaccharide **12** afforded, on treatment with sodium borohydride, the required glucitol derivative **1** (Scheme 2). Because of the low yield and tedious preparation of **6**, an independent approach was taken into consideration, that is the glycosidation of an appropriately protected D-glucitol derivative.

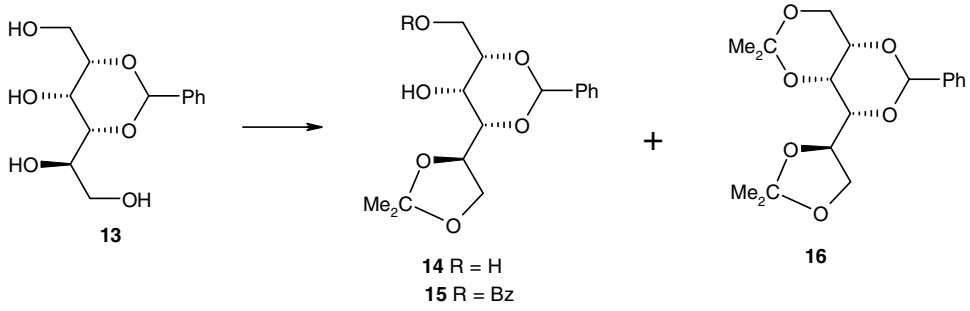
3. Synthesis of a partially protected D-glucitol derivative 15

D-Glucitol can be easily converted into its 2,4-*O*-benzylidene derivative **13**, which, on treatment with acetone in the presence of $CuSO_4$, afforded[18] the corresponding 5,6-*O*-isopropylidene derivative **14**. The relative low yield of this latter reaction (~25%) can be ascribed to the low solubility of **13** in acetone and the fact that the formed diacetal **14** reacts further with acetone affording triacetal **16** (Scheme 3). To overcome this problem, 2,2-dimethoxypropane was used as reagent in the presence of a catalytic amount of *p*-TsOH and different solvents, for example, DMF, Me_2SO, dioxane and methanol, but only DMF proved to be superior to acetone. The optimal reaction time as well as the optimal excess of the reagent was established by following the reaction by GLC (after acetylation of the withdrawn samples).

As can be seen from the Tables 1 and 2 the reaction rate increases with the ratio of the reagent, but simultaneously the amount of triacetal **16** increases too. As,



Scheme 2.



Scheme 3.

Table 1. Reaction of **13** with 1.6 equiv of 2,2-dimethoxypropane in DMF according to GLC data

Time (h)	**13** (%)	**14** (%)	**16** (%)	Yield[a] (%)
0.5	35.0	40.3	8.4	15
1	28.2	45.4	11.5	24
2	24.9	47.1	13.2	30
4	24.0	49.3	13.8	34
20	19.2	48.1	17.4	36

[a] Isolated yield of **14**.

Table 2. Reaction of **13** with 3 equiv of 2,2-dimethoxypropane in DMF according to GLC data

Time (h)	**13** (%)	**14** (%)	**16** (%)	Yield[a] (%)
0.5	15.7	47.0	17.6	
1	7.6	50.1	27.6	44
2	3.5	47.2	37.1	
3	1.7	44.4	45.2	
5	1.1	39.1	50.1	38

[a] Isolated yield of **14**.

during the work up process, it is difficult to remove the unchanged starting material **13**, the yield of the isolated product **14** is not proportional to its amount present in the reaction mixture as detected by GLC. For this reason, it is worthwhile to drive the conversion as far as possible, as triacetal **16**, which is formed as by-product, can be easily removed by a simple recrystallization of the crude product from benzene. On the other hand, formation of the triacetal **16** seems to be a slower process than the dissolution of the starting material, therefore the amount of solvent could be diminished without significantly lowering the yield. The diacetal **14** was treated in pyridine at low temperature (−20 °C) with 1.1 equiv of benzoyl chloride to afford the 1-*O*-benzoate **15**, which was contaminated with some 1,4-di-*O*-benzoate. The latter could be removed by column chromatography, but for the large scale glycosidation reaction the crude mixture could be used, as the diester remained unchanged during this reaction and the required glycoside had to be separated by column chromatography anyway.

4. Glycosidation of 15

When bromide **4** was used as donor, acetonitrile as solvent and $Hg(CN)_2$ as promoter for the glycosydation of **15**, the crude reaction product (formed at 20 °C; 20 h) contained besides several decomposition products two anomeric glycosides **17** and **18** in a 1:4 ratio. From this mixture, the needed crystalline β-glycoside **18** could be separated in a relatively modest yield (~20%) after repeated column chromatography only because of the similar R_f value of these isomers. This purification step could not be avoided, as the purity of the final product

Table 3. Influence of the reaction conditions on the glycosidation reaction

Donor	Promoter	Solvent[a]	Temp/time	**17**:**18**:**19**	Yield[b] (%)
4	$Hg(CN)_2$	A	20 °C; 20 h	1:4:Tr	20
4	$Hg(CN)_2$	A	20 °C; 5 h	1:3:Tr	10
4	$Hg(CN)_2$	A	20 °C; 48 h	1:4:Tr	20
4	$Hg(CN)_2/HgBr_2$	A	20 °C; 20 h	1:4:2	5
4	AgOTf	A	20 °C; 20 h	—	—
5	NIS/AgOTf	B	−30 °C; 1.5 h	Tr:3:2	30
4	$Hg(CN)_2$	C	20 °C; 15 h + 45 °C; 2 h	1:5:Tr	30
4	$Hg(CN)_2$	C	20 °C; 15 h + 45 °C; 3 h	1:5:Tr	35
4	$Hg(CN)_2$	C	50 °C; 5 h	1:3:Tr	25

[a] A: MeCN; B: CH_2Cl_2; C: 1:1 benzene:$MeNO_2$.
[b] Yield of isolated **18**.

1 depends on the purity of **18** because the further intermediates could not be separated from the accompanying by-products. For increasing the yield of **18** different reaction conditions (solvents, promoters, reaction temperature) were applied (Table 3), the formed glycosides were isolated and their structure was established by NMR spectroscopy (Tables 4–6). Depending on the reaction conditions, three main products were formed in different ratios the two anomers **17** and **18** as well as the orthoester **19** (Scheme 4). The chemical shifts of the anomeric protons of these products differed significantly (**17**: 5.39 ppm, $J_{1,2}$ 3.8 Hz; **18**: 4.78 ppm, $J_{1,2}$ 8 Hz; and **19**: 5.9 ppm, $J_{1,2}$ 5 Hz), consequently their ratio could be determined in the crude reaction mixtures by recording the NMR spectra. When the reaction time was shortened to 5 h, the reaction was incomplete, consequently the isolated yield of **18** dropped. A prolonged reaction time of 48 h had no influence on the yield. When $Hg(CN)_2/HgBr_2$ was used as promoter, a significant amount of the orthoester **19** was formed, diminishing the yield. In the presence of AgOTf no reaction took place. When the thioglycoside **5** was used as donor in the presence of NIS/AgOTf, the α-anomer **17** was only formed in traces, but the amount of the orthoester increased substantially. The best results were obtained using **4** as donor, $Hg(CN)_2$ as promoter and 1:1 benzene–nitromethane as solvent, but in this system the reaction was slower, therefore after 20 h at 20 °C the temperature had to be increased to 45 °C to complete the reaction. In this way the yield of **18** could be increased to 35%.

5. Conversion of 18 into 1

The ester groups of **18** were removed by the Zemplén method and the benzylidene group of the resulting pentahydroxy derivative **20** was removed by catalytic hydrogenation over Pd/C. Finally, the terminal 5,6-*O*-isopropylidene group of the formed **21** was hydrolyzed with aqueous sulfuric acid to yield, after freeze–drying, the target disaccharide **1** in excellent yield.

6. Experimental

6.1. General methods

Organic solns were dried over $MgSO_4$ and concentrated under diminished pressure at or below 40 °C. TLC: E. Merck precoated Silica Gel 60 F_{254} plates, with EtOAc–hexane mixtures (A, 1:1; B, 1:2; C, 2:1), EtOAc–MeOH mixtures (D, 3:1; E, 1:1); detection by spraying the plates with a 0.02 M soln of I_2 and a 0.3 M soln of KI in 10% aq H_2SO_4 soln followed by heating at ca. 200 °C. For column chromatography, Kieselgel 60 was used. Melting points are uncorrected. Optical rotations were determined on 1.0% solns in $CHCl_3$ at 20 °C unless stated otherwise. GLC were performed on a Chrompack CP9000 equipment using a RH-5ms column (30 m × 0.25 mm), N_2 as carrier gas at 25 kPa, temperature, 2 °C min^{-1} from 185 to 325 °C and a CP-Maitre data system. The NMR spectra were recorded on a Bruker Avance 500 spectrometer at 500 (^1H) and 125 (^{13}C) MHz, respectively, at ambient temperature. The chemical shifts were referenced to $\delta_{TMS} = 0$ ppm. The solvent is indicated at the ^1H NMR spectral data. For structure determination ^1H, ^1H-COSY, TOCSY, HMQC or HSQC, HMBC as well as selective 1D TOCSY and NOESY spectra were recorded. For data see Tables 4–6.

6.2. 3-*O*-(β-D-Glucopyranosyl)-D-glucitol (1)

(a) To a stirred soln of **12** (0.9 g, 2.6 mmol) in water (10 mL), $NaBH_4$ (0.2 g) was added at rt. After 2 h, sodium ions were removed with an ion exchange resin and the filtered soln was concentrated. The residue was reevaporated with MeOH (2 × 10 mL), the obtained syrup was dissolved in water and freeze–dried to give **1** (0.85 g, 94%) as an amorphous hygroscopic powder, $[\alpha]_D$ −17 (*c* 1, water). Anal. Calcd for $C_{12}H_{24}O_{11}$: C, 41.86; H, 7.03. Found: C, 41.64; H, 7.15.

(b) To a soln of **18** (4.46 g, 6 mmol) in dry MeOH (20 mL), 2 M NaOMe (0.2 mL) was added. After 1 h, when according to TLC the reaction was complete, the

Table 4. Characteristic ^{1}H NMR chemical shifts

No.	Solvent	Glucose/glucitol unit								Glucose unit							Others
		H_a-1	H_b-1	H-2	H-3	H-4	H-5	H_a-6	H_b-6	H-1′	H-2′	H-3′	H-4′	H-5′	H_a-6′	H_b-6′	
1	Me_2SO	3.41	3.54	3.74	3.83	3.41	3.64	3.41	3.58	4.30	3.07	3.16	2.97	3.14	3.34	3.72	
8	$CDCl_3$	5.94		4.53	4.15	4.18	3.72	3.64	3.97	4.59	4.97	5.15	5.04	3.67	4.11	4.22	
9	$CDCl_3$	5.82		4.46	4.29	4.05	4.17	3.92	4.08	5.76	4.37	5.14	4.85	3.88	4.16		1.76 (orthoacetate); 2 × 2.06, 2.07 (OAc)
10	Me_2SO	5.86		4.60	4.24	4.22	4.34	3.85	3.91	4.27	2.90	3.13	3.01	3.13	3.41	3.68	
11	Me_2SO	5.81		4.60	4.20	3.93	3.71	3.36	3.57	4.34	2.99	3.16	3.03	3.19	3.40	3.70	
14	Me_2SO	3.50–3.63		3.86	3.57	3.80	4.23	3.91	3.98								
15	$CDCl_3$	4.60	4.66	4.31	3.89	3.83	4.40	4.07	4.14								
17	$CDCl_3$	4.67		4.26	3.92	3.74	4.47	4.04–4.11			5.39	5.11	5.57	5.12	4.34	4.25	4.33
18	$CDCl_3$	4.47	4.59	4.27	3.94	3.84	4.51	4.06–4.15		4.79	5.13	5.21	5.15	3.65	4.18	4.24	
19	$CDCl_3$	4.46	4.72	4.23	3.82	3.71	4.44	4.03	4.12	5.88	4.62	5.19	4.91	4.00	4.15	4.24	1.88 (orthoacetate); 2.04, 2.07, 2.09 (OAc)

Table 5. Characteristic ^{1}H, ^{1}H coupling constants

No.	Glucose/glucitol unit									Glucose unit						
	^2J (1_a,1_b)	^3J (1_a,2)	^3J (1_b,2)	^3J (2,3)	^3J (3,4)	^3J (4,5)	^3J (5,6_a)	^3J (5,6_b)	^2J (6_a,6_b)	^3J (1′,2′)	^3J (2′,3′)	^3J (3′,4′)	^3J (4′,5′)	^3J(5′, $6'_a$)	^3J(5′, $6'_b$)	^2J($6'_a$, $6'_b$)
1	11.3		4.2	6.3	~2.5	8.5	~6.0	2.9	11.1	7.9	8.6	9.1	9.1	8.0	2.0	11.1
8		3.6		~0	~3.0	7.3	7.3	1.8	11.1	7.9	9.7	9.5	9.7	2.3	4.8	12.2
9		3.5		~0	3.2	7.7	5.8	7.0	8.6	5.1	2.8	1.9	9.5	(4.2)		
10		3.5		~0	~3.0	4.3	6.2	6.4	8.7	7.8	8.0	8.5	8.5	5.3	5.1	10.0
11		3.7		~0	2.9	9.0	5.9	3.5	11.2	7.9	8.5	9.0	9.1	7.0	45	10.8
14	11.3	6.1	6.1	~1	~1	7.2	5.5	6.4	8.4							
15	11.7	6.8	5.4	~1	~1	8.2	4.6	6.2	8.6							
17		(5.8)		~1	~1	9.2	(3.8)			3.8	9.9	9.9	9.5			
18	11.3	6.0	6.8	~1	~1	6.6	(6.1)			7.8	9.5	9.6	9.6	2.3	4.0	12.1
19	11.8	7.3	4.8	~1	~1	8.7	5.3	6.4	8.6	5.3	4.5	4.5	9.2	2.8	5.6	12.5

Table 6. Characteristic ^{13}C NMR chemical shifts

No.	Glucose/glucitol unit						Glucose unit						Others
	C-1	C-2	C-3	C-4	C-5	C-6	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′	
1	61.7	72.9	80.0	71.1	70.6	63.3	104.5	740	76.8	70.8	76.8	61.6	
8	106.3	83.9	74.9	79.0	71.5	69.9	101.0	71.2	72.7	68.4	71.7	61.9	112.1 (1,2-O-CMe_2); 100.8 (3,5-O-CMe_2)
9	105.0	84.1	75.9	81.1	72.1	67.6	97.0	73.3	69.8	68.2	66.9	63.1	111.8 (1,2-O-CMe_2); 109.1 (5,6-O-CMe_2); 121.4, 22.1 (orthoacetate)
10	104.5	82.4	79.6	79.7	73.0	64.9	101.3	73.3	76.6	70.2	77.0	61.3	110.8 (1,2-O-CMe_2); 107.4 (5,6-O-CMe_2)
11	104.6	82.8	80.4	79.4	68.3	63.2	102.4	72.7	76.5	70.2	77.0	61.2	110.7 (1,2-O-CMe_2)
14	60.7	80.4	62.0	80.1	73.4	65.8							108.0 (5,6-O-CMe_2); 100.0 (2,4-O-CHPh)
15	63.9	78.1	63.4	80.8	73.1	66.7							109.4 (5,6-O-CMe_2); 101.0 (2,4-O-CHPh)
17	65.0	78.1	73.0	80.8	72.4	67.0	98.0	70.3	70.0	68.4	68.5	61.8	101.5 (2,4-O-CHPh); 109.6 (5,6-O-CMe_2)
18	63.1	77.1	71.1	80.0	74.1	66.1	100.9	71.8	73.0	68.2	71.9	61.7	101.3 (2,4-O-CHPh); 108.8 (5,6-O-CMe_2)
19	64.8	77.5	64.9	80.6	72.9	66.7	97.6	75.1	71.1	67.6	68.2	62.7	101.0 (2,4-O-CHPh); 109.3 (5,6-O-CMe_2); 122.8, 25.0 (orthoacetate)

sodium ions were removed by an ion exchange resin and the filtered soln was concentrated. The residue, which contained besides **20** methyl benzoate, was dissolved in MeOH (50 mL), water (3 mL), AcOH (1 mL) and 5% Pd/C catalyst (2 g) were added and the mixture was hydrogenated at rt for 15 h. The filtered soln was concentrated, the residue partitioned between $CHCl_3$ and water, the aq soln was concentrated to a volume of 15 mL, 1.5 mL M sulfuric acid was added and the mixture was heated at 60 °C for 1 h. After neutralization with an ion exchange resin, the filtered soln was concentrated to a vol of 15 mL and was freeze–dried to give **1** (2 g, 97%) identical with that described above.

6.3. Glycosidation of 3 using phenyl 1-thioglucoside 5 as donor

A soln of **3** (2.6 g, 10 mmol) and **5**[19] (4.4 g, 10 mmol) in CH_2Cl_2 (50 mL) was stirred in the presence of molecular sieves (4 Å) (6 g) for 1 h. Thereafter the mixture was cooled to −40 °C and NIS (3.4 g, 15 mmol) as well as TfOH (0.2 mL) were added. Stirring was continued at −40 °C for 15 min and then the reaction was quenched with Et_3N (3 mL). The filtered soln was diluted with CH_2Cl_2 (50 mL) washed with 10% aq thiosulfate soln, 4% $NaHCO_3$ soln and water. The residue of the dried and concentrated soln was submitted to column chromatography (A). The fractions having R_f 0.65 afforded 3,4,6-tri-*O*-acetyl-1,2-(*S*)-*O*-[1′-*O*-(1,2:5,6-di-*O*-isopropylidene-D-glucofuranos-3-yl)-ethylidene]-α-D-glucopyranose **9** (1.0 g, 17%) as a syrup. Anal. Calcd for $C_{26}H_{38}O_{15}$: C, 52.88; H, 6.49. Found: C, 52.65; H, 6.72.

Concentration of the fractions having R_f 0.60 afforded **8** (0.5 g, 8.5%), mp 103–104 °C (ether–hexane); lit.[15] mp 104–105 °C.

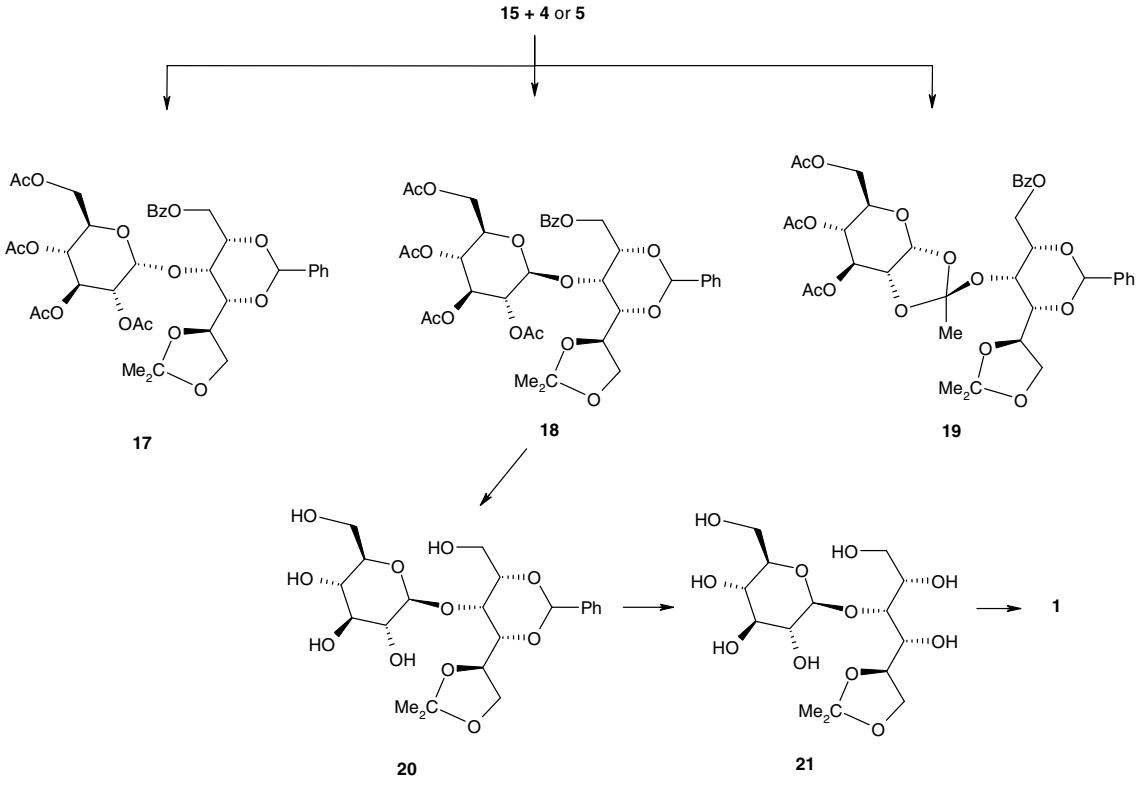
When the temperature of the reaction was raised for 5 min to 20 °C before quenching with Et_3N, only **8** (1.4 g, 24%) could be separated by column chromatography.

6.4. 1,2:5,6-Di-*O*-isopropylidene-3-*O*-(β-D-glucopyranosyl)-D-glucofuranose (10)

To a soln of **6**[15] (3.5 g, 5.9 mmol) in dry MeOH (60 mL) 2 M NaOMe (0.2 mL) was added. After 1 h, when according to TLC the reaction was complete, the sodium ions were removed by an ion exchange resin and the filtered soln was concentrated to give **10** (2.5 g, ~100%) as a syrup, $[\alpha]_D$ −33 (*c* 1, water). Anal. Calcd for $C_{18}H_{30}O_{11}$: C, 51.18; H, 7.16. Found: C, 51.02; H, 7.26.

6.5. 1,2-*O*-Isopropylidene-3-*O*-(β-D-glucopyranosyl)-D-glucofuranose (11)

A soln of **10** (2.4 g, 5.7 mmol) in 0.1 N H_2SO_4 (20 mL) was kept at rt for 24 h. The soln was neutralized with



Scheme 4.

an ion exchange resin, filtered and concentrated to give **11** (2.0 g, 92%). $[\alpha]_D$ −23 (*c* 1, water); R_f 0.4 (D). Anal. Calcd for $C_{15}H_{26}O_{11}$: C, 47.12; H, 6.85. Found: C, 46.88; H, 7.12.

6.6. 3-*O*-(β-D-Glucopyranosyl)-D-glucose (12)

A soln of the *O*-isopropylidene derivative **11** (1.2 g, 3.1 mmol) in 0.5 N sulfuric acid (10 mL) was heated at 60 °C for 90 min. The cooled soln was neutralized with an ion exchange resin, filtered and freeze–dried to give amorphous **12** (1 g, 93%): $[\alpha]_D$ +25 → +20 (24 h, *c* 1, water); R_f 0.4 (E); lit.[3] $[\alpha]_D$ +19 (*c* 0.6, water).

6.7. 2,4-*O*-Benzylidene-5,6-*O*-isopropylidene-D-glucitol (14)

To a stirred slurry of 2,4-O-benzylidene-D-glucitol (**13**, 27 g, 0.1 mol) in DMF (75 mL), 2,2-dimethoxypropane (22.5 mL, 0.3 mol) and *p*-TsOH (200 mg) were added at 20 °C. Stirring was continued until a clear solution was obtained (~50 min), and after further 30 min the reaction was quenched with Et_3N (1.5 mL). The residue of the concentrated mixture was boiled with $CHCl_3$ (200 mL) for 30 min. The undissolved **13** (~2 g) was filtered off without cooling and was washed with $CHCl_3$ (20 mL). The combined filtrate was washed with water, dried and concentrated. The solid residue was recrystallized from benzene (70 mL) to yield **14** (14.29 g, 46%), mp 175–179 °C, R_f 0.4 (C); lit.[18] mp 179 °C.

For checking the course of the reaction by GLC, samples (0.1 mL) were withdrawn at different intervals and acetylated with pyridine (0.5 mL)–Ac_2O (0.3 mL) before GLC investigation. The retention time of the three components was the following: **13** (14.77 min); **14** (13.77 min); **16** (12.32 min).

6.8. 1-*O*-Benzoyl-2,4-*O*-benzylidene-5,6-*O*-isopropylidene-D-glucitol (15)

To a stirred soln of **14** (3,1 g, 10 mmol) in pyridine (20 mL), benzoyl chloride (1.3 mL, 11 mmol) was added dropwise at −20 °C. The mixture was stirred at this temperature for 15 min and subsequently at rt for 30 min to give after usual processing a syrup (4.2 g, ~100%), which after purification by column chromatography (B) afforded **15** (2.9 g, 70%); R_f 0.6, $[\alpha]_D$ −24 (*c* 1, $CHCl_3$). Anal. Calcd for $C_{23}H_{26}O_7$: C, 66.65; H, 6.32. Found: C, 66.78; H, 6.55.

6.9. Glycosidation reactions of 15

(a) To a stirred soln of **15** (2.5 g, 6 mmol) in dry MeCN (20 mL) molecular sieves (4 Å) (5 g) were added. After 30 min, acetobromoglucose **4** (2.5 g, 6 mmol) and $Hg(CN)_2$ (1.6 g, 6.5 mmol) were added and the stirring

was continued at rt for 20 h. The filtered mixture was diluted with threefold $CHCl_3$, washed with 5% $NaHCO_3$ soln and an 10% aq soln of KBr, dried and concentrated. The residue was submitted to column chromatography (A). The fractions having R_f 0.5–0.7 were concentrated and the residue separated by a repeated column chromatography. Concentration of the fractions having R_f 0.65 gave 1-*O*-benzoyl-2,4-*O*-benzylidene-5,6-*O*-isopropylidene-3-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-D-glucitol (**17**) (125 mg, 7%): mp 177–179 °C; $[\alpha]_D$ +37 (*c* 1, $CHCl_3$). Anal. Calcd for $C_{37}H_{44}O_{16}$: C, 59.67; H, 5.96. Found: C, 59.55; H, 6.09.

Concentration of the fractions having R_f 0.55 gave 1-*O*-benzoyl-2,4-*O*-benzylidene-5,6-*O*-isopropylidene-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-D-glucitol (**18**) (900 mg, 20%); mp 170–171 °C (after two recrystallizations from EtOH), $[\alpha]_D$ −4 (*c* 1, $CHCl_3$). Anal. Calcd for $C_{37}H_{44}O_{16}$: C, 59.67; H, 5.96. Found: C, 59.63; H, 6.00.

(b) To a stirred soln of **15** (4.3 g, 10.4 mmol) in dry CH_2Cl_2 (65 mL), molecular sieves 4 Å (8 g) and phenyl thioglycoside **5** (4.4 g, 10 mmol) were added. After 30 min, the mixture was cooled to −30 °C, NIS (3.4 g, 15 mmol) and AgOTf (0.4 g, 1.5 mmol) were added, and stirring was continued −30 °C for 90 min. Thereafter the reaction was quenched with Et_3N (2 mL), the temperature was raised to 20 °C, the mixture was filtered, diluted with CH_2Cl_2 (60 mL), washed with 10% aq $Na_2S_2O_3$, 5% $NaHCO_3$ and water, dried and concentrated. The residue was separated by column chromatography (A). Concentration of the fractions having R_f 0.7 gave 3,4,6-tri-*O*-acetyl-1,2-(*S*)-*O*-[1′-*O*-(1-*O*-benzoyl-2,4-*O*-benzylidene-5,6-*O*-isopropylidene-D-glucitol-3-yl)-ethylidene]-α-D-glucopyranose (**19**) (1.4 g, 19%), $[\alpha]_D$ +14.5 (*c* 1, $CHCl_3$). Anal. Calcd for $C_{37}H_{44}O_{16}$: C, 59.67; H, 5.96. Found: C, 59.42; H, 6.17.

Concentration of the fractions having 0.55 gave **18** (2.2 g, 29%) identical with that described above.

(c) A soln of **15** (31 g, 75 mmol) in benzene (125 mL) and $MeNO_2$ (125 mL) was concentrated to a vol of 200 mL. Molecular sieves (4 Å) (24 g) were added, the mixture was stirred for 30 min at rt and thereafter **4** (34 g, 83 mmol) and $Hg(CN)_2$ (21 g) were added. Stirring was continued at 20 °C for 15 h, and at 45 °C for further 3 h. The filtered soln was concentrated, the residue dissolved in $CHCl_3$, washed with 10% KBr soln and water, dried and concentrated. The residue was submitted to column chromatography (A). The residue obtained on concentration of the fractions having R_f 0.55 was recrystallized from fivefold EtOH to give **18** (19.5 g, 35%) identical to that, described above.

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