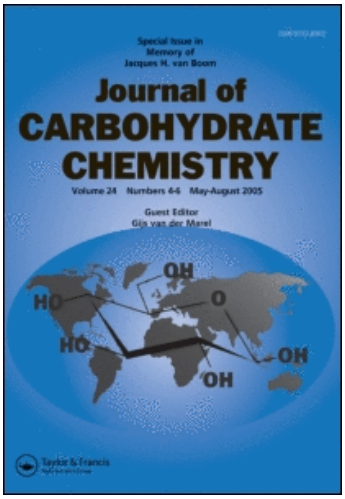

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PREPARATION OF SOME AMYGDALIN-DERIVED GENTIOBIOSYL DONORS AND ACCEPTORS FOR OLIGOSACCHARIDE SYNTHESES

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ABSTRACT

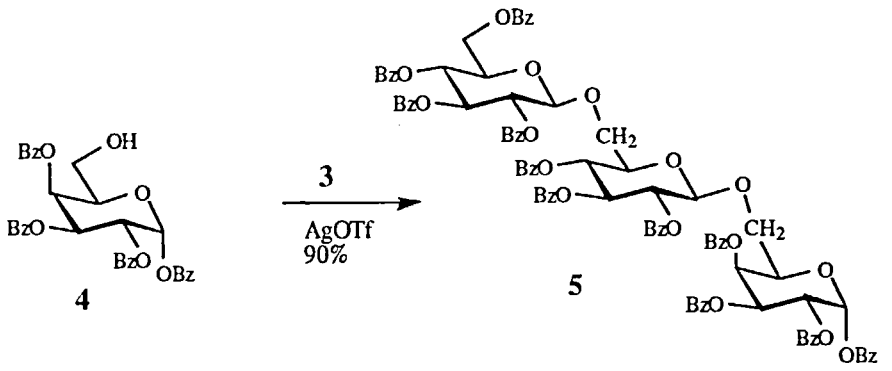
Amygdalin (**1**) was used as the starting material for the preparation of building blocks for oligosaccharide syntheses. Benzoylation of **1** followed by treatment of the fully benzoylated Amygdalin **2** with Cl_2CHOMe, $ZnCl_2$ gave α-D-gentiobiosylchloride **3** (83%) which was coupled to 1,2,3,4-tetra-*O*-benzoyl-α-D-galactopyranose (**4**), to give the corresponding β-(1→6)-linked trisaccharide **5** in 90% yield. Hydrogenolysis of **2** followed by treatment of thus obtained hepta-*O*-benzoyl gentiobiose **6** with Cl_3CCN, gave fully benzoylated α-D-gentiobiose trichloroacetimidate **7** which was converted to methyl hepta-*O*-benzoyl-β-D-gentiobioside **8**. Selective protection of O6(2) in **1** using dimethylthexyl- and *tert.*-butyldiphenylchlorosilane, respectively and subsequent benzoylation resulted in intermediates **12** and **11** which were converted to several gentiobiosyl acceptors and donors. Thus, 2,3,4-tri-*O*-benzoyl-6-*O*-bromoacetyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranosyl chloride (**19**) was prepared from **12** in 3 steps. Glycosylation of **11** and **12**, respectively using 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl fluoride (**18**) and 2 equivalents BF_3 gave the corresponding β-linked trisaccharide **19** in both cases, whereas 0.1 equivalents BF_3 only catalyzed the glycosylation of **12** effectively. Benzylidenation of **1** was achieved in 65% yield using DMF-dimethylsulfate-adduct/benzaldehyde, to give 4(2),6(2)-*O*-benzylidene acetal **21**. Benzoylation of the latter followed by treatment with $NaBH_3CN$ under acidic conditions, gave (*R*)-α-[(2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (**23**).

INTRODUCTION

Binding studies of β-(1→6)-D-galactan-specific antibodies required the synthesis of a series of β-(1→6)-linked galactooligosaccharides flanked by gentiobiosyl units. Since we chose a blockwise approach for the construction of the desired oligosaccharides we needed suitably protected gentiobiosyl-donors and acceptors, respectively. Furthermore, we also needed some gentiobiose derivatives for the synthesis of oligosaccharides related to bacterial polysaccharides. Gentiobiose (β-D-Glc$_p$-(1→6)-D-Glc$_p$) is a common structure which is widespread in naturally occuring glycosides and found as a partial sequence in many oligo- and polysaccharides; for example glycoglycerolipids,[1] phytoalexin-elicitor active glucans,[2,3] and a nephritogenic glycopeptide.[4] The chemical syntheses of gentiobiose structures are usually performed by β-selective coupling of two suitably protected D-glucose derivatives,[5,6,7] requiring multistep procedures. Therefore, direct access to protected gentiobiose-derivatives would open a convenient way for the preparation of useful building blocks. Our recent work on the enzyme-catalyzed cyanohydrin formation necessitated the isolation of the enzyme Oxynitrilase from almond flour and thus, prompted us to turn our attention to Amygdalin {(*R*)-α-[(6-*O*-β-D-glucopyranosyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile} which is a major glycoside constituent of bitter almonds.[8] Amygdalin can be isolated from defatted almonds in large amounts by simple extraction procedures[9] and thus, may serve as a convenient source for the preparation of gentiobiose blocks. Here we now describe simple syntheses of some useful β-(1→6)-linked D-glucobiose derivatives, starting from Amygdalin.

RESULTS AND DISCUSSION

Amygdalin heptaacetate has been shown to react with 1,1-dichloromethyl methyl ether (DCMME), to give hepta-*O*-acetyl-gentiobiosyl chloride in good yield.[10] Although the latter and the corresponding gentiobiosyl bromide were successfully used as glycosyl donors in silver salt promoted glycosylation-reactions,[11,12] some problems may arise when acetyl groups are present in the donor and silver trifluoromethansulfonate (silver triflate) is used as the promotor. In these cases transesterification of an acetyl group, present at position 2 of the donor, occurs and may significantly reduce the yield of glycosylation product. This complication is avoided by using benzoyl protective groups for glycosyl halides. Therefore, we prepared hepta-*O*-benzoyl-gentiobiosyl chloride **3** in 83% yield by treating fully benzoylated Amygdalin **2** with DCMME and a catalytic amount of $ZnCl_2$. Chloride **3** proved to be an excellent gentiobiose donor for silver

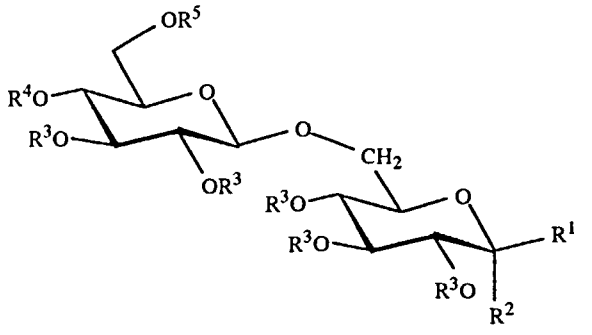


Scheme I

triflate-promoted glycosylations, as was demonstrated by the coupling of **3** and 1,2,3,4-tetra-*O*-benzoyl-α-D-galactopyranose (**4**, ref. 13), to give trisaccharide **5** in 90% yield. The use of triose derivative **5** for the preparation of the aforementioned galactooligosaccharides will be described elsewhere.[14]

Since glycosyl trichloroacetimidates have some advantages over glycosyl chlorides (*i.e.* significant higher reactivity), we also converted benzoylated Amygdalin **2** into the corresponding trichloroacetimidate **7**. This required first hydrogenolysis of the aglycon moiety in **2**, followed by reaction of the intermediate with trichloroacetonitrile. Hydrogenolysis of hepta-*O*-acetylated Amygdalin in acetic acid was previously described to give only moderate yields of the corresponding hepta-*O*-acetyl-D-gentiobiose.[15] As expected, we found that $Pd(OH)_2$ (10% on charcoal),[16] which is effective for difficult hydrogenolytic cleavages,[17] catalyzed smoothly the hydrogenolysis of **2** in toluene-acetone mixture. No reaction was observed with Pd on charcoal in the same solvent. Thus, we obtained a 87% yield of an anomeric mixture of partially benzoylated gentiobiose **6** (α:β = 4:1, determined from its ^{1}H-NMR-spectrum). Treatment of **6** with trichloroacetonitrile and a catalytic amount of NaH gave exclusively the α-imidate **7** (54%). The latter was a highly reactive intermediate which was converted directly to the fully benzoylated methyl β-D-gentiobioside **8** (52%) by BF_3-catalyzed methanolysis. TLC of the crude reaction mixture revealed that no methyl α-D-gentiobioside was formed during methanolysis of **7**. The occurrence of a slower moving spot on TLC, having the same mobility as compound **6**, was due to some hydrolysis and may count for the moderate yield of **8**. Alternatively, methyl β-D-gentiobioside **8** was prepared in 92% yield *via* nucleophilic substitution of methyl trifluoromethanesulfonate by *in situ* generated sodium salt of **6**.

Table I



N°	R^1	R^2	R^3	R^4	R^5
1	(*R*)-PhCH(CN)O	H	H	H	H
2	(*R*)-PhCH(CN)O	H	Bz	Bz	Bz
3	H	Cl	Bz	Bz	Bz
6α	H	OH	Bz	Bz	Bz
6β	OH	H	Bz	Bz	Bz
7	H	$Cl_3C(NH)O$	Bz	Bz	Bz
8	OMe	H	Bz	Bz	Bz
9	(*R*)-PhCH(CN)O	H	H	H	Si^tBuPh_2
10	(*R*)-PhCH(CN)O	H	H	H	$SiThex(Me)_2$
11	(*R*)-PhCH(CN)O	H	Bz	Bz	Si^tBuPh_2
12	(*R*)-PhCH(CN)O	H	Bz	Bz	$SiThex(Me)_2$
13	(*R*)-PhCH(CN)O	H	Bz	Bz	H
14	(*R*)-PhCH(CN)O	H	Bz	Bz	CHO
15	H	Cl	Bz	Bz	CHO
16	OMe	H	Bz	Bz	CHO
17	OMe	H	Bz	Bz	H
18	(*R*)-PhCH(CN)O	H	Bz	Bz	Ac
21	(*R*)-PhCH(CN)O	H	Bz	Bz	$BrCH_2CO$
22	H	Cl	Bz	Bz	$BrCH_2CO$
23	OMe	H	Bz	Bz	$BrCH_2CO$
24	(*R*)-PhCH(CN)O	H	H	——PhCH——	
25	(*R*)-PhCH(CN)O	H	Bz	——PhCH——	
26	(*R*)-PhCH(CN)O	H	Bz	H	Bn

For the desired extension of the sugar chain at position O6(2) of the β-(1→6)-linked D-glucobiose part it was necessary to introduce a temporary protecting group at that position of Amygdalin. For that purpose we chose the dimethylthexylsilyl[18] and the *tert.*-butyldiphenylsilyl[19,20] group since both provide different stabilities towards protodesilylation or nucleophilic catalyzed detachment[21] of the silyl-group. Treatment of Amygdalin with *tert.*-butyldiphenyl- and dimethylthexylchlorosilane, respectively, gave the corresponding silylated derivatives **9** (74%) and **10** (81%) which were benzoylated, to give compound **11** (93%) and crystalline **12** (90%). Subsequently, thexyldimethylsilyl-protected derivative **12** was easily deblocked under acidic conditions (BF_3/methanol, room temperature, 6 h), resulting in nucleophile **13** in 93% yield. In contrast, the corresponding conversion **11**→**13** was incomplete under similar conditions. In order to prepare a glucobiosyl donor having position O6(2) temporarily protected we attempted to convert either **11** or **12** to its corresponding chloride. Reaction of the *tert.*-butyldiphenylsilylated Amygdalin derivative **11** with DCMME/$ZnCl_2$ resulted in the formation of several slower moving products (TLC) which could not be separated by chromatography (no details given in the Experimental). When **12** was treated with the DCMME reagent at 40 °C TLC revealed rapid formation of a slower moving product which was further converted to (*R*)-α-[(2,3,4-tri-*O*-benzoyl-6-*O*-formyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)oxyl-phenylacetonitrile (**14**), isolated in 63% yield. Since the initially formed intermediate had the same mobility on TLC as nucleophile **13** it is most likely that the conversion **12**→**14** proceeds *via* desilylation of the starting material under acidic conditions followed by formylation with DCMME/$ZnCl_2$. DCMME is known to formylate alcohols.[22] When the reaction was performed at 65 °C, intermediate **14** was further converted to the corresponding formylated chloride **15** (62%). The assigned structures of compounds **14** and **15** were confirmed by their ^{13}C-NMR spectra which both showed additional carbonyl signals at 160.2 and 160.4 ppm, respectively. In addition, structure **15** was proven by silver-triflate-promoted methanolysis, to give methyl 6-*O*-formyl-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranoside (**16**, 69%) together with the deformylated compound **17** (22%).

The significant differences of the protodesilylation rates of compounds **11** and **12** also prompted us to attempt a direct glycosylation of these Amygdalin derivatives using 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl fluoride (**18**) in the presence of Lewis acid. This glycosylation protocol has been shown to be effective with various silyl protected alcohols.[23,24,25] Treatment of **11** and **12**, respectively with fluoride **18** and 2 equivalents BF_3-etherate resulted in both cases in an almost equally fast formation of trisaccharide **19** (0.5 h, room temperature), isolated in 63% and 69% yield, respectively.

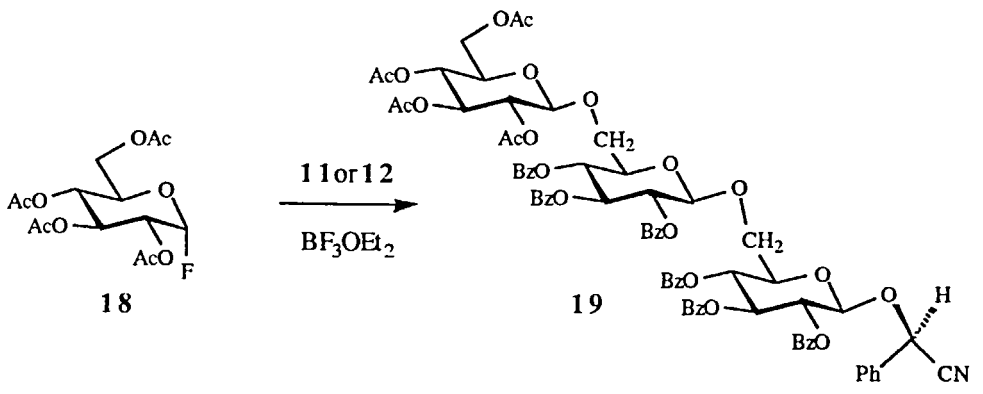
TABLE II. ^{1}H-NMR data in $CDCl_3$: chemical shifts δ [ppm]; (J [Hz])

	(residue)	H1 ($J_{1,2}$)	H2 ($J_{2,3}$)	H3 ($J_{3,4}$)	H4 ($J_{4,5}$)	H5 ($J_{5,61}$)	H61 ($J_{5,62}$)	H62 ($J_{61,62}$)	substituents (see footnotes)
2	(1)	4.48d	5.47dd	6.02t	5.67t	3.97-3.87m	4.11-4.06m	3.97-3.87m	5.18s[a], 1H
		(7.9)	(9.7)	(9.7)	(9.5)	(-)	(-)	(-)	
	(2)	5.13d	5.58dd	5.69t	5.32t	4.19ddd	4.60dd	4.42dd	
		(7.8)	(9.8)	(9.7)	(9.5)	(3.0)	(5.0)	(12.2)	
3	(1)	6.33d	5.25dd	6.13t	5.93t	4.58-4.52m	4.16-4.12m	3.84dd	
		(3.9)	(9.9)	(9.8)	(9.6)	(-)	(5.8)	(12.0)	
	(2)	4.97d	5.56dd	5.66t	5.47t	4.16-4.12m	4.61dd	4.47dd	
		(7.8)	(9.6)	(9.7)	(9.8)	(3.3)	(5.0)	(12.2)	
5	(1)	6.79d	5.87dd	6.04dd	6.09bd	4.61bt	3.62dd	3.32dd	
		(3.6)	(10.6)	(3.3)	(<1.0)	(6.4)	(6.6)	(11.2)	
	(2)	4.71d	5.31dd	5.84t	5.56t	4.01-3.85m	4.01-3.85m	4.01-3.85m	
		(7.8)	(9.6)	(9.6)	(9.6)	(-)	(-)	(-)	
	(3)	4.51d	5.42dd	5.73t	5.22t	4.01-3.85m	4.57dd	4.40dd	
		(7.9)	(9.7)	(9.6)	(9.6)	(7.4)	(5.4)	(12.3)	
6α	(1)	5.43bt	5.13dd	6.13t	5.71t	4.19-4.13m	4.05dd	3.84dd	3.16d, OH
		(3.3)	(9.8)	(9.6)	(9.6)	(1.7)	(7.9)	(11.8)	
	(2)	4.98d	5.52dd	5.93t	5.32t	4.19-4.13m	4.73dd	4.42dd	
		(7.6)	(9.6)	(9.6)	(9.6)	(2.9)	(4.6)	(12.2)	
6β	(1)	4.60d	5.24dd	5.91t	5.37t	4.54-4.48m	4.07dd	3.96-3.89m	3.69d, OH
		(7.8)	(9.8)	(9.3)	(9.7)	(1.8)	(-)	(11.4)	
	(2)	5.04d	5.51dd	5.82t	5.71t	4.54-4.48m	4.68dd	3.85dd	
		(7.5)	(9.3)	(9.6)	(9.6)	(2.1)	(7.9)	(12.0)	
7	(1)	6.67d	5.36dd	6.16t	4.48t	4.17-4.10m	4.45dd	3.85dd	8.38bs, NH
		(3.6)	(10.1)	(9.8)	(9.9)	(5.2)	(6.1)	(12.0)	
	(2)	5.00d	5.51dd	5.88t	5.61t	4.17-4.10m	4.59dd	4.45dd	
		(7.8)	(9.6)	(9.6)	(9.6)	(3.1)	(5.2)	(12.2)	
11	(1)	4.47d	5.55dd	5.93t	5.32t	3.99-3.80m	3.99-3.80m	3.99-3.80m	5.14s[a], 1H
		(7.8)	(9.7)	(9.7)	(9.6)	(-)	(-)	(-)	
	(2)	5.06d	5.47dd	5.67t	5.66t	3.99-3.80m	4.14bd	3.99-3.80m	0.94s[b], 9H
		(7.8)	(9.6)	(9.5)	(9.6)	(-)	(-)	(-)	
12	(1)	4.44d	5.46dd	5.92t	5.32t	3.96-3.73m	3.96-3.73m	3.96-3.73m	4.13s[a], 1H
		(7.9)	(9.7)	(9.7)	(9.6)	(-)	(-)	(-)	-0.09s[b], 3H
	(2)	5.00d	5.52dd	5.65t	5.53t	3.96-3.73m	4.10bd	3.96-3.73m	-1.30s[b], 3H
		(7.8)	(9.7)	(9.6)	(9.7)	(-)	(-)	(-)	0.75mc[b],12H
13	(1)	4.53d	5.48dd	6.00t	5.43t	3.94-3.90m	4.13-4.10m	3.94-3.90m	5.21s[a], 1H
		(7.8)	(9.6)	(9.7)	(9.7)	(-)	(-)	(-)	
	(2)	5.04d	5.51dd	5.69t	5.39t	3.69-3.62m	3.88-3.77m	3.88-3.77m	
		(7.9)	(9.7)	(9.6)	(9.6)	(-)	(-)	(-)	
14	(1)	4.50d	5.49dd	5.99t	5.35t	4.11-4.05m	4.11-4.05m	3.97-3.90m	5.22s[a], 1H
		(7.8)	(9.7)	(9.7)	(9.5)	(-)	(-)	(-)	
	(2)	5.08d	5.55dd	5.56t	5.68t	3.97-3.90m	4.36dd	4.30dd	
		(7.8)	(9.8)	(9.8)	(9.5)	(5.4)	(2.6)	(12.4)	

TABLE II. continued

15	(1)	6.35d	5.28dd	6.13t	5.89t	4.41-4.36m	4.14dd	3.68dd	
		(4.0)	(10.0)	(9.8)	(9.6)	(1.9)	(5.7)	(11.9)	
	(2)	4.95d	5.52dd	5.54t	5.50t	4.41-4.36m	4.39dd	4.32dd	
		(7.8)	(9.7)	(9.8)	(9.8)	(2.5)	(5.2)	(12.2)	
16	(1)	4.53d	5.38dd	5.52t	5.81t	4.02-3.96m	4.07dd	3.85dd	3.20s[b], 3H
		(7.9)	(9.8)	(9.7)	(9.6)	(2.0)	(7.7)	(11.1)	
	(2)	4.69d	5.50dd	5.33t	5.86t	4.02-3.96m	4.33mc	4.33mc	
		(7.9)	(9.8)	(9.7)	(9.6)	(-)	(-)	(-)	
17	(1)	4.55d	5.43dd[c]	5.89t	5.40t[c]	3.99ddd	4.12dd	3.86dd	3.20s[b], 3H
		(8.0)	(9.8)	(9.7)	(9.8)	(2.6)	(7.2)	(10.8)	
	(2)	4.94d	5.38dd[c]	5.81t	5.36t[c]	3.78-3.73m	3.78-3.73m	3.63bdd	
		(8.0)	(9.8)	(9.6)	(9.8)	(-)	(5.3)	(12.7)	
19	(1)	4.57d	5.52dd	5.96t	5.29t	4.06-3.89m	3.81-3.72m	3.81-3.72m	5.25s[a], 1H
		(7.7)	(9.5)	(9.7)	(9.6)	(-)	(-)	(-)	2.10s[b], 3H
	(2)	5.08d	5.46dd	5.73t	5.39t	4.21-4.18m	4.06-3.89m	4.06-3.89m	2.03s[b], 3H
		(7.8)	(9.6)	(9.5)	(9.6)	(-)	(-)	(-)	2.02s[b], 3H
	(3)	4.66d	4.98dd	5.38t	5.04t	4.06-3.89m	4.21dd	4.07dd	2.00s[b], 3H
		(8.0)	(9.5)	(9.7)	(9.7)	(5.0)	(2.2)	(12.4)	
20	(1)	4.40d	5.48dd	5.91t	5.25t	4.02-3.94m	3.90-3.79m	3.90-3.79m	5.12s[a], 1H
		(7.8)	(9.7)	(9.6)	(9.4)	(-)	(-)	(-)	
	(2)	4.99d	5.40dd	5.60t	5.50t	4.02-3.94m	4.22dd	4.09dd	1.83s[a], 3H
		(7.9)	(9.7)	(9.5)	(9.7)	(5.5)	(2.7)	(12.3)	
21	(1)	4.49d	5.55dd	5.99t	5.33t	4.14-4.05m	3.97-3.87m	3.97-3.87m	5.19s[a], 1H
		(7.8)	(9.6)	(9.6)	(9.6)	(-)	(-)	(-)	
	(2)	5.08d	4.47dd	5.68t	5.54t	4.14-4.05m	4.37dd	4.29dd	3.71s[d], 2H
		(7.9)	(9.7)	(9.6)	(9.6)	(5.6)	(2.7)	(12.2)	
22	(1)	6.34d	5.28dd	6.14t	5.90t	4.55ddd	4.17dd	3.87dd	
		(4.0)	(10.0)	(9.9)	(9.6)	(2.0)	(5.7)	(11.9)	
	(2)	4.94d	5.52dd	5.53t	5.48t	4.03ddd	4.39dd	4.33dd	3.83s[d], 2H
		(7.9)	(9.8)	(9.7)	(9.8)	(5.1)	(3.2)	(12.4)	
23	(1)	4.54d	5.38dd	5.88t	5.51t	4.05-3.90m	4.09dd	3.85dd	3.17s[b], 3H
		(7.9)	(9.8)	(9.7)	(9.7)	(1.6)	(8.0)	(11.1)	
	(2)	4.96d	5.50dd	5.82t	5.32t	4.05-3.90m	4.38dd	4.30dd	3.77s[d], 2H
		(7.8)	(9.8)	(9.7)	(9.7)	(3.4)	(2.8)	(12.2)	
25	(1)	4.48d	5.53[c]dd	5.67t	5.34t	3.93-3.68m	3.93-3.68m	3.93-3.68m	5.19s[a], 1H
		(7.8)	(9.4)	(9.5)	(9.5)	(-)	(-)	(-)	
	(2)	5.33d	5.46[c]dd	5.86t	4.37dd	3.93-3.68m	4.06bd	3.93-3.68m	5.52s[e], 1H
		(7.8)	(9.6)	(9.5)	(9.9)	(4.2)	(-)	(-)	
26	(1)	4.44d	5.44dd	5.65t	5.31t	3.78mc	3.78mc	3.70mc	5.13s[a], 1H
		(7.9)	(9.6)	(9.5)	(9.5)	(-)	(-)	(-)	3.22s, OH
	(2)	4.89d	5.50bt	5.53t	3.97bt	3.70mc	4.07bd	3.86dd	4.55d[f], 1H
		(7.4)	(9.1)	(9.0)	(9.0)	(-)	(9.5)	(12.7)	4.49d[f], 1H

[a]PhCH(CN)O; [b]CH_3; [c]row may be reversed; [d]$BrCH_2CO$; [e]PhCH; [f]$PhCH_2$, J=12.1Hz



Scheme II

(*R*)-α-[(6-*O*-acetyl-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (**20**) was formed as a side-product starting from **11** and **12** (TLC) and was isolated from the conversion **12**→**19** in 8% yield. However, performing the reaction with a catalytic amount of BF_3-etherate (0.1 equivalents) under otherwise identical conditions revealed the different stabilities of **11** and **12**. Only traces of trisaccharide **19** could be detected on TLC when the *tert.*-butyldiphenylsilyl protected derivative **11** was used (24 h, room temperature), whereas the thexyldimethylsilyl protected derivative **12** was almost completely converted to **19** (72%). Thus, making use of the different stabilities of silyl protected saccharides may serve as a useful extension of the Lewis acid catalyzed glycosylation procedures with glycosyl fluorides, and applications of this methodology are now under further investigation.

Attempts to hydrogenolyze silylated compounds **11** and **12** which would have resulted in suitable intermediates for the trichloroacetimidate activation method failed. Neither Pd or $Pd(OH)_2$ catalyst (10% on charcoal) in toluene-acetone mixtures under neutral conditions or with added acetic acid nor the application of more drastic conditions (80 °C, 8000 kPa, 3d) resulted in hydrogenolysis. Obviously, substitution of position O6(2) of β-(1→6)-linked D-glucobiosides by the bulky dimethylthexylsilyl or *tert.*-butyldiphenylsilyl group prevents hydrogenolytic cleavage of the aglycon. Therefore, we chose the easily accessible nucleophile **13** (see above) as starting material for the preparation of a complex disaccharide donor. Compound **13** allows the selective introduction of virtually any temporary protective group at the desired

position. For example, bromoacetylation of **13** gave the corresponding Amygdalin derivative **21** in 82% yield. Subsequent treatment of the latter with DCMME resulted in 82% yield. Subsequent treatment of the latter with DCMME resulted in 2,3,4-tri-*O*-benzoyl-6-*O*-bromoacetyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranosyl chloride (**22**, 75%). Chloride **22**, thus prepared from **13** in two high yielding steps is a useful gentiobiosyl donor. That was demonstrated by its silver triflate-promoted reaction with methanol, to give first **23** (88%), followed by subsequent removal of the bromoacetyl group in **23** with thiourea, to give **17** in 82% yield.

4,6-*O*-Benzylidene acetals of saccharides are extremely useful compounds for the preparation of a wide variety of synthetically important carbohydrate derivatives. Therefore, we also attempted to prepare (*R*)-α-[(4,6-*O*-benzylidene-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl)oxy]-phenylacetonitrile (**24**). Treatment of an appropriate glycose derivative with benzaldehyde and $ZnCl_2$ is among the most widely used procedures for the benzylidenation of monosaccharides. In our hands, however, this method could not be applied to Amygdalin due to the complexation of $ZnCl_2$ by the nitrile function of the aglycon of compound **1**. In contrast, smooth benzylidenation of Amygdalin (**1**) occured when the DMF-dimethylsulfate-adduct[26] was used as the condensation reagent. Thus, **1** gave the crystalline benzylidene derivative **24** in 65% yield. Recently, DMF-dimethylsulfate-adduct was also used for the preparation of benzylidene derivatives of some monosaccharides and disaccharides.[27] Compound **24** was benzoylated, to give the corresponding protected Amygdalin **25** (82%). Using Garegg's reductive ring opening procedure for benzylidene acetals of monosaccharides,[28] **25** reacted highly regioselective with $NaBH_3CN$ under acidic conditions, to give (*R*)-α-[(2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (**26**) in 71% yield. Nucleophile **26** may also serve as a useful gentiobiose block for oligosaccharide syntheses since it allows the selective extension of the sugar chain at position O4(2).

EXPERIMENTAL

General Methods. NMR data were extracted from spectra measured in solutions of $CDCl_3$ (with TMS as an internal standard) at 25 °C with a Bruker CXP 300 spectrometer. Proton-signal assignments presented in table II were made by first order analysis of the spectra. Of the two magnetically non-equivalent geminal protons, the one resonating at lower field is donated H61 and the one resonating at higher field is donated H62. Carbon-signal assignments found in the Experimental were made by mutual comparison of the spectra and by comparison with spectra of related compounds. Optical

rotations were measured at 25 °C with a Perkin-Elmer automatic polarimeter, Model 241. Melting points were measured with a Büchi apparatus, Model SMP-20. Thin-layer chromatography (TLC) was performed on precoated plastic sheets, Polygram SIL UV_{254}, 40 x 80 mm (Macherey-Nagel) using appropriately adjusted mixtures of carbon tetrachloride-acetone for the developing. Detection was effected by charring with 5% sulfuric acid in ethanol and with UV light. Preparative chromatography was performed by elution from columns of Silica Gel 60 (Merck) using solvent mixture *A*, carbon tetrachloride-acetone; *B*, toluene-acetone; *C*, dichloromethane-methanol; *D*, ethyl acetate-petroleum ether. Solutions in organic solvents were dried with anhydrous sodium sulfate, and concentrated at 2 kPa, ≤40 °C. Amydgalin (**1**) was isolated from bitter almonds as described in ref. 9. In a typical run, 10 g of **1** were obtained from 300 g of carefully defatted almond flour.

(*R*)-α-[(2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (2). Benzoyl-chloride (13 mL, 112 mmol) was added with stirring at 0 °C to a solution of **1** (5.0 g, 10.9 mmol) and a catalytic amount of 4-dimethylaminopyridine in pyridine (40 mL), and the mixture was stirred at room temperature for 3 h. Water and dichloromethane was added, and the organic layer was washed with 10% aqueous HCl and saturated aqueous sodium hydrogenecarbonate solution. After concentration, the residue was crystallized from ethanol, to give 10.4 g (80%); mp 235 °C; $[\alpha]_D$ = -10.7° (*c* = 1, chloroform); ref. 29: mp 218 °C, $[\alpha]_D$ = -10.5°; ^{13}C-NMR: δ 117.1 (CN); 101.2 (C1(2)); 97.9 (C1(1)); 74.5 (C2(2)); 72.8, 72.6 (C3(1),3(2)); 72.4, 72.3 (C5(1),5(2)); 71.3 (C2(1)); 69.6, 69.5 (C4(1),PhCH); 68.4 (C4(2)); 67.8 (C6(1)); 63.0 (C6(2)).

2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-α-D-glucopyranosyl Chloride (3). A mixture of **2** (1.5 g, 1.25 mmol), DCMME (6 mL) and a catalytic amount of $ZnCl_2$ (~120 mg) in chloroform (15 mL) was stirred at 65 °C, until TLC indicated complete conversion of **2** into a faster moving product (45 min.). After concentration and coevaporation of toluene, the residue was chromatographed (solvent *A*: 10:1) to give 1.13 g (83%) of colorless foam; $[\alpha]_D$ = +40.5° (*c* = 1.2, chloroform); ^{13}C-NMR: δ 101.5 (C1(2)); 90.2 (C1(1)); 72.8 (C2(2)); 72.4, 72.2 (C2(1),3(2)); 71.7, 71.6 (C3(1),5(2)); 69.8, 69.7 (C4(1),4(2)); 68.3 (C5(1)); 67.3 (C6(1)); 63.1 (C6(2)).

Anal. Calcd for $C_{61}H_{49}ClO_{17}$: C, 67.25; H, 4.53; Cl, 3.25. Found: C, 66.83; H, 4.55; Cl, 4.17.

2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl-(1→6)-1,2,3,4-tetra-O-benzoyl-α-D-galacto-pyranose (5). A solution of **3** (1.12 g, 1.03 mmol) and 2,4,6-trimethylpyridine (124.8

mg, 1.03 mmol) in dichloromethane (7 mL) was added with stirring at 0 °C to a suspension of 1,2,3,4-tetra-*O*-benzoyl-α-D-galactopyranose[13] (**4**, 676.5 mg, 1.13 mmol) and silver triflate (550.0 mg, 2.14 mmol) in dichloromethane (4 mL) and the mixture was stirred until TLC indicated complete conversion of the starting materials (15 min.). The mixture was diluted with dichloromethane, washed successively with aqueous sodium thiosulfate solution and water. After concentration, the residue was chromatographed (solvent *A*: 10:1) to give 1.52 g (90%) of a colorless foam; $[\alpha]_D$ = +60.9° (*c* = 1, chloroform); ^{13}C-NMR: δ 101.2 (C1(3)); 100.5 (C1(2)); 90.6 (C1(1)); 73.5 (C2(3)); 72.9, 72.8 (C3(2),3(3)); 72.3, 72.0, 71.8, 70.7 (C2(2),5(1),5(2),5(3)); 70.0, 69.8 (C4(2),4(3)); 68.7 (3 x C, C3(1),4(1),6(2)); 68.1 (C2(1)); 66.4 (C6(1)); 63.1 (C6(3)).

Anal. Calcd for $C_{95}H_{76}O_{27}$: C, 69.17; H, 4.64. Found: C, 69.15; H, 4.64.

2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-D-glucopyranose (6). A suspension of **2** (2.37 g, 2.0 mmol) and 10% Pd on charcoal (~1 g) in toluene-acetone (5:4, 90 mL) was hydrogenolyzed at room temperature and atmospheric pressure. TLC indicated no conversion of **2**. After addition of 10% $Pd(OH)_2$ on charcoal (~1 g) hydrogenolysis was continued until TLC indicated complete conversion of the starting material into a single slower moving product (20 h). After filtration of the mixture and concentration, the residue was chromatographed (solvent *B*: 5:1) to give 1.86 g (87%) of a colorless foam. Anomeric mixture (^{1}H-NMR): **6α:6β** = 4:1; $[\alpha]_D$ = +38.3° (*c* = 1, chloroform); ^{13}C-NMR (significant signals); **6α**: δ 102.3 (C1(2)); 90.2 (C1(1)); **6β**: δ 101.6 (C1(2)); 95.8 (C1(1)).

Anal. Calcd for $C_{54}H_{50}O_{18}$: C, 68.41; H, 4.71. Found: C, 68.43; H, 4.67.

2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-α-D-glucopyranose Trichloroacetimidate (7). A catalytic amount of NaH (~10 mg) was added to a solution of **6** (1.0 g, 0.93 mmol) and trichloroacetonitrile (0.5 mL) in dichloromethane (3 mL) and the brown mixture was stirred at room temperature until TLC indicated complete conversion of the starting material (15 min.). Concentration and chromatography of the residue gave 0.59 g (52%) of a colorless foam which was used immediately for the next step; $[\alpha]_D$ = +37.5° (*c* = 1, chloroform); ^{13}C-NMR: δ 160.3 (C=NH); 100.9 (C1(2)); 93.0 (C1(1)); 90.7 (CCl_3); 73.0 (C2(2)); 72.3, 72.1, 71.8 (C2(1),3(2),5(2)); 70.7 (C3(1)); 70.1, 69.8, 68.9 (C4(1),4(2),5(1)); 67.3 (C6(1)); 63.1 (C6(2)). Elemental analysis was not performed due to the instability of compound **7**.

Methyl 2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranoside (8). A: a solution of BF_3-etherate in diethyl ether (1M, 2 mL) was added at room temperature to a solution of **7** (0.40 g, 0.33 mmol)

and methanol (0.1 mL) in dichloromethane (10 mL). After stirring for 2 h additional BF_3 solution was added and stirring was continued for 0.5 h. After addition of sodium hydrogen carbonate (0.3 g), the mixture was washed with water, concentrated and the residue was chromatographed (solvent *A*: 5:1) to give 0.23 g (64%), mp 202 °C (methanol); $[\alpha]_D = +3.1°$ (*c* = 1, chloroform); ref. 30: mp 203 °C, $[\alpha]_D = +2.0°$.

B: NaH (24.0 mg, 1.0 mmol) was added to a solution of **6** (0.41 g, 0.38 mmol) and methyl trifluoromethanesulfonate (0.16 g, 1.0 mmol) in dichloromethane (20 mL) and the mixture was stirred until TLC indicated complete conversion of the starting material into a single faster moving product. The mixture was hydrolyzed by addition of water, washed with aqueous sodium hydrogenecarbonate solution and concentrated. The residue was crystallized from acetone-petroleum ether (1:1) to give 0.38 g (92%); mp 203 °C.

(*R*)-α-[(6-O-*tert.*-Butyldiphenylsilyl-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl)oxy]-phenylacetonitrile (9). *Tert* -butyldiphenylchlorosilane (1.72 mL, 6.6 mmol) was added to a solution of **1** (2.76 g, 6.0 mmol) and imidazole (0.90 g, 13.2 mmol) in DMF (20 mL) and the mixture was stirred at room temperature until TLC (solvent *C*: 5:1) indicated complete conversion of the starting material into a single faster moving product (3 h). The mixture was poured into water, extracted with dichloromethane (5 x) and the combined organic layers were washed with aqueous sodium chloride solution (1M). After concentration and coevaporation of xylene the residue was chromatographed (solvent *C*: 10:1) to give 3.09 g (74%) of a colorless foam; $[\alpha]_D$ = -14.3° (*c* = 0.7, chloroform); ^{13}C-NMR: δ 119.7 (CN); 105.0 (C1(2)); 102.8 (C1(1)); 78.2 (2C, C3(1),3(2)); 78.0, 77.9 (C5(1),5(2)); 75.4, 74.7 (C2(1),2(2)); 71.7, 71.6 (C4(1),4(2)); 69.9 (PhCH); 69.0 (C6(1)); 64.9 (C6(2)).

Anal. Calcd for $C_{36}H_{44}NO_{11}Si$ (monohydrate): C, 60.66; H, 6.50. Found: C, 60.51; H, 6.49.

(*R*)-α-[(6-O-Dimethylthexylsilyl-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl)oxy]-phenylacetonitrile (10). A mixture of dimethylthexylchlorosilane (2.9 mL, 17.8 mmol), **1** (4.58 g, 10.0 mmol) and imidazole (1.52 g, 22.3 mmol) in DMF (20 mL) was treated as described for the preparation of compound **9**. TLC (solvent *C*: 5:1) showed complete conversion of the starting material after 17h at room temperature. The mixture was poured into water and the precipitate was collected by filtration to give 4.88 g (81%); mp 106 °C; $[\alpha]_D$ = -42.9° (*c* = 1, acetone); ^{1}H-NMR (CD_3OD), significant signals: δ 5.88 (s, 1H, PhC*H*CN); 4.53 (d, 1H, H1(1), $J_{1(1),2(1)}$ = 7.8 Hz); 4.44 (dd, 1H, H-61(2), $J_{5(2),61(2)}$ = 1.8 Hz, $J_{61(2),62(2)}$ = 11.8 Hz); 3.96 (dd, 1H, H-61(1), $J_{5(1),61(1)}$ = 1.5 Hz, $J_{61(2),62(1)}$ = 11.6 Hz); 0.11 (s, 6H, Si(CH_3)$_2$); 0.93-0.88 (m, 13H, H^{thex}); ^{13}C-NMR (CD_3OD): δ 119.6 (CN); 104.9

(C1(2)); 102.8 (C1(1)); 78.1 (2 x C, C3(1),3(2)); 77.9, 77.8 (C5(1),5(2)); 75.4, 74.8 (C2(1),2(2)); 71.7 (2 x C, C4(1),4(2)); 69.9 (PhCH); 69.0 (C6(1)); 63.9 (C6(2)).

Anal. Calcd for $C_{28}H_{45}NO_{11}Si$ (monohydrate): C, 54.44; H, 7.67; N, 2.27. Found: C, 54.44; H, 7.57; N, 2.26.

(*R*)-α-[(2,3,4-Tri-O-benzoyl-6-O-*tert.*-butyldiphenylsilyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (11). Benzoyl chloride (3.37 g, 24.0 mmol) was added to a solution of **9** (2.09 g, 3.0 mmol) in pyridine (20 mL) and the mixture was stirred for 24 h at room temperature. After work-up as described for the preparation of **2**, the residue was chromatographed (solvent *A*: 10:1) to give 3.70 g (93%) of a colorless foam; $[\alpha]_D$ = -38.6° (*c* = 0.4, chloroform); ^{13}C-NMR: δ 117.0 (CN); 101.2 (C1(2)); 97.7 (C1(1)); 75.2 (C5(2)); 74.4 (C2(2)); 73.2 (C3(2)); 72.7 (C3(1)); 72.5 (C5(1)); 71.3 (C2(1)); 69.6 (PhCH); 69.1 (C4(2)); 68.4 (C4(1)); 67.7 (C6(1)); 62.7 (C6(2)).

Anal. Calcd for $C_{78}H_{69}NO_{17}Si$: C, 70.95; H, 5.27; N, 1.06. Found: C, 70.88; H, 5.25; N, 1.00.

(*R*)-α-[(2,3,4-Tri-O-benzoyl-6-O-dimethylthexylsilyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (12). A mixture of benzoyl chloride (4.84 g, 34.4 mmol) and **10** (2.0 g, 3.24 mmol) in pyridine (20 mL) was treated as described for the preparation of **11**. Chromatography (solvent *B*: 10:1) gave material which was crystallized from ethanol, to give 3.58 g (90%); mp 161-162 °C; $[\alpha]_D$ = -25.4° (*c* = 1, chloroform); ^{13}C-NMR: δ 117.0 (CN); 100.9 (C1(2)); 97.2 (C1(1)); 75.3 (C5(2)); 74.3 (C2(2)); 73.2 (C3(2)); 72.7, 72.4 (C3(1),5(1)); 71.2 (C2(1)); 69.5 (PhCH); 69.3 (C4(2)); 68.4 (C4(1)); 67.4 (C6(1)); 62.0 (C6(2)); -3.6 (2 x C, $Si(CH_3)_2$).

Anal. Calcd for $C_{70}H_{69}NO_{17}Si$: C, 68.67; H, 5.68; N, 1.14. Found: C, 68.68; H, 5.69; N, 1.12.

(*R*)-α-[(2,3,4-Tri-O-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (13). A: a solution of **12** (1.22 g, 1.0 mmol) and BF_3-etherate (1.0 mL) in dichloromethane-methanol (2:1, 100 mL) was stirred at room temperature until TLC indicated complete conversion of the starting material into a single slower moving product (6 h). Concentration and chromatography (solvent *A*: 5:1) gave material which was crystallized from acetone-n-hexane to give 1.01 g (93%); mp 188-190 °C; $[\alpha]_D$ = -34.3° (*c* = 0.5, chloroform); ^{13}C-NMR: δ 117.0 (CN); 100.8 (C1(2)); 98.0 (C1(1)); 74.7, 74.2 (C2(2),5(2)); 72.7, 72.5 (C3(1),3(2)); 72.0 (C5(1)); 71.3 (C2(1)); 69.7 (PhCH); 69.4 (C4(1)); 68.1 (C4(2)); 67.9 (C6(1)); 61.0 (C6(2)).

Anal. Calcd for $C_{62}H_{51}NO_{17}$: C, 68.82; H, 4.75; N, 1.29. Found: C, 69.10; H, 4.59; N, 1.19.

B: a mixture of **11** (1.32 g, 1.0 mmol) and BF_3-etherate (1.0 mL) in dichloromethane-methanol (2:1, 100 mL) was treated as described above. TLC indicated incomplete conversion of the starting material after 5 d. Work-up as described above gave 0.65 g (60%); mp 188-189 °C.

(*R*)-α-[(2,3,4-Tri-O-benzoyl-6-O-formyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (14). A mixture of **12** (1.13 g, 0.92 mmol), DCMME (1.4 mL) and a catalytic amount $ZnCl_2$ in chloroform (10 mL) was treated at 40 °C as described for the preparation of compound **3**. TLC revealed initial formation of a slower moving product having the same mobility as compound **13** and which was transformed during 1 h into a faster moving product. Work-up as described above and chromatography (solvent *A*: 10:1) gave 0.62 g (62%) of a colorless foam; $[\alpha]_D$ = -23.2° (*c* = 1, chloroform); ^{13}C-NMR: δ 160.2 (CHO); 117.1 (CN); 101.0 (C1(2)); 98.0 (C1(1)); 74.6 (C2(2)); 72.6, 72.5 (C3(1),3(2)); 72.1 (2 x C, C5(1),5(2)); 71.3 (C2(1)); 69.4, 69.3 (PhCH, C4(1)); 68.3 (C4(2)); 67.9 (C6(1)); 61.7 (C6(2)).

Anal. Calcd for $C_{63}H_{51}NO_{18}$: C, 68.16; H, 4.63; N, 1.27. Found: C, 67.83; H, 4.69; N, 1.17.

2,3,4-Tri-O-benzoyl-6-O-formyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-α-D-glucopyranosyl Chloride (15). A mixture of **12** (1.31 g, 1.07 mmol), DCMME (3 mL) and a catalytic amount $ZnCl_2$ in chloroform (10 mL) was treated at 65 °C as described for the preparation of compound **3**. TLC showed complete formation of a slower moving product (15 min.). Work-up as described above and chromatography (gradient solvent *A*: 20:1 to 10:1) gave 0.68 g (63%) of a colorless foam; $[\alpha]_D$ = -27.8° (*c* = 1, chloroform); ^{13}C-NMR: δ 160.3 (CHO); 101.4 (C1(2)); 90.2 (C1(1)); 72.8 (C2(2)); 72.3, 72.2 (C2(1),3(2)); 71.63, 71.59 (C3(1),5(2)); 69.8 (C4(1)); 69.4 (C4(2)); 68.4 (C5(1)); 67.4 (C6(1)); 61.9 (C6(2)).

Anal. Calcd for $C_{55}H_{45}ClO_{17}$: C, 65.19; H, 4.48; Cl, 3.50. Found: C, 64.74; H, 4.47; Cl, 4.05.

Methyl 2,3,4-Tri-O-benzoyl-6-O-formyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranoside (16) and Methyl 2,3,4-Tri-O-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranoside (17). A: a solution of **15** (423.4 mg, 0.42 mmol) and 2,4,6-trimethylpyridine (45.8 mg, 0.38 mmol) in dichloromethane (3 mL) was added to a suspension of methanol (0.1 mL) and silver triflate (200 mg, 0.78 mmol) in dichloromethane (4 mL) as described for the preparation of compound **5**. TLC showed almost complete conversion of the starting material into a slower moving product (15 min) which was further converted to another product after additional 15 min. Work-up as

described above and chromatography (solvent *A*: 10:1) gave first compound **16** (0.29 g, 69%) as a colorless foam; $[\alpha]_D = -11.8°$ ($c = 1$, chloroform); ^{13}C-NMR: δ 160.3 (CHO); 101.8 (C1(1)); 101.4 (C1(2)); 74.0 (C2(2)); 72.9, 72.8 (C3(1),3(2)); 72.1, 71.83, 71.78 (C2(1),5(1),5(2)); 69.9, 69.3 (C4(1),4(2)); 68.8 (C6(1)); 61.8 (C6(2)); 56.8 (OCH_3).

Anal. Calcd for $C_{56}H_{48}O_{18}$: C, 66.66; H, 4.79. Found: C, 66.83; H, 4.82.

Eluted next was **17** (0.09 g, 22%); mp 233 °C (acetone-n-hexane); $[\alpha]_D = -11.7$ ($c = 0.2$, chloroform); ^{13}C-NMR: δ 101.8 (C1(1)); 101.3 (C1(2)); 74.7 (C5(2)); 73.6 (C2(2)); 72.9, 72.8 (C3(1),3(2)); 71.9, 71.8 (C2(1),5(1)); 70.2 (C4(1)); 69.4 (C4(2)); 68.6 (C6(1)); 61.2 (C6(2)); 56.8 (OCH_3).

Anal. Calcd for $C_{55}H_{48}O_{17}$: C, 67.34; H, 4.93. Found: C, 67.34; H, 4.95.

B: a solution of **23** (see below, 2.0 g, 1.8 mmol) and thiourea (0.23 g, 3.0 mmol) in dichloromethane-methanol (1:1, 15 mL) was stirred at room temperature for 3 h, diluted with dichloromethane and washed with aqueous HCl and sodium hydrogenecarbonate solution. After concentration, the residue was chromatographed (solvent *A*: 5:1) to give **17**, 1.44 g (82%); mp 233 °C (acetone-n-hexane).

(*R*)-α-[(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (19) and (*R*)-α-[(6-O-Acetyl-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (20). A: BF_3-etherate (0.12 mL, 1.0 mmol) was added at room temperature to a solution of **11** (0.51 g, 0.39 mmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl fluoride (**18**, 0.18 g, 0.50 mmol) in dichloromethane (3 mL) and the mixture was stirred until TLC showed complete conversion of the starting material (0.5 h). The solution was washed with aqueous sodium hydrogenecarbonate solution concentrated and chromatographed (solvent *A*, 10:1) to give **19** (0.35 g, 63%), as a colorless foam; $[\alpha]_D = -72.9°$ ($c = 0.5$, chloroform); ^{13}C-NMR: δ 117.3 (CN); 101.0 (C1(3)); 100.8 (C1(2)); 98.7 (C1(1)); 74.5 (C5(2)); 73.8 (C2(2)); 72.9, 72.8 (C3(1),3(2)); 72.4, 72.3 (C3(3),5(1)); 71.9 (C5(3)); 71.3, 71.2 (C2(1),2(3)); 69.8 (C4(2)); 69.5 (CH); 68.5, 68.3, 68.2, 67.9 (C4(1),4(3),6(1),6(2)); 61.9 (C6(3)).

Anal. Calcd for $C_{76}H_{69}NO_{26}$: C, 64.63; H, 4.92; N, 0.99. Found: C, 64.54; H, 4.98; N, 0.92.

B: A solution of **12** (0.48 g, 0.39 mmol) and **18** (0.18 g, 0.50 mmol) in dichloromethane (3 mL) was treated with BF_3-etherate (0.12 mL, 1.0 mmol) as described above. Work-up and chromatography gave first **20** (0.03 g, 7.7 %); mp 179-180 °C (acetone-n-hexane, 1:3); $[\alpha]_D = -39.8°$ ($c = 0.7$, chloroform); ^{13}C-NMR: δ 117.1 (CN); 101.1 (C1(2)); 97.8 (C1(1)); 74.4 (C2(2)); 72.7, 72.5 (C3(1),3(2)); 72.2 (2 x C,

C5(1),5(2)); 71.2 (C2(1)); 69.5 (CH); 69.3 (C4(1)); 68.4 (C4(2)); 67.7 (C6(1)); 62.5 (C6(2)); 20.6 (CH_3).

Anal. Calcd for $C_{64}H_{53}NO_{18}$: C, 68.38; H, 4.75; N, 1.25. Found: C, 68.16; H, 4.77; N, 1.19.

Eluted next was **19** (0.38 g, 69%). ^{1}H- and ^{13}C-NMR spectra were identical to those reported in table II and above, respectively.

C: a solution of **11** (0.51 g, 0.39 mmol) and **18** (0.18 g, 0.50 mmol) in dichloromethane (3 mL) was treated with BF_3-etherate (6 µL, 0.05 mmol) for 24 h at room temperature. TLC revealed unchanged starting materials and the formation of traces of **19**.

D: a solution of **12** (0.48 g, 0.39 mmol) and **18** (0.18 g, 0.50 mmol) in dichloromethane (3 mL) was treated with BF_3-etherate (6 µL, 0.05 mmol) as described above until TLC (solvent *A*: 5:1) showed almost complete conversion of the starting material (24 h). Work-up and chromatography gave **19** (0.40 g, 72%). ^{1}H-NMR spectrum was identical to that reported in table II.

(*R*)-α-[(2,3,4-Tri-O-benzoyl-6-O-bromoacetyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (21). Bromoacetyl bromide (0.28 g, 1.4 mmol) was added with stirring at room temperature to a solution of **13** (1.08 g, 1.0 mmol) and 2,4,6-trimethylpyridine (0.18 g, 1.5 mmol) in dichloromethane (20 mL). After stirring for 1h, the mixture was washed with aqueous sodium hydrogenecarbonate solution and concentrated. The residue was chromatographed (solvent *A*: 5:1) to give 0.99 g (82%) of a colorless foam; $[\alpha]_D \simeq$ -26.8° (*c* = 0.5, chloroform); ^{13}C-NMR: δ 117.9 (CN); 101.0 (C1(2)); 97.9 (C1(1)); 74.4 (C2(2)); 72.55, 72.50 (C3(1),3(2)); 72.10, 72.05 (C5(1),5(2)); 71.3 (C2(1)); 69.5 (PhCH); 69.2 (C4(1)); 68.4 (C4(2)); 67.8 (C6(1)); 64.0 (C6(2)); 25.4 ($BrCH_2$).

Anal. Calcd for $C_{64}H_{52}BrNO_{18}$: C, 64.00; H, 4.36; N, 1.16; Br, 6.64. Found: C, 63.41; H, 4.45; N, 1.06; Br, 6.61.

2,3,4-Tri-O-benzoyl-6-O-bromoacetyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-α-D-glucopyranosyl Chloride (22). A mixture of **21** (0.89 g, 0.7 mmol), DCMME (4 mL) and a catalytic amount $ZnCl_2$ in chloroform (4 mL) was treated at 65-70 °C as described for the preparation of **3**. TLC showed complete formation of a faster moving product after 3 h. Work-up as described above and chromatography (solvent *A*: 10:1) gave 0.58 g (75%) of a colorless foam; $[\alpha]_D$ = +29.3° (*c* = 0.4, chloroform); ^{13}C-NMR: δ 101.4 (C1(2)); 90.2 (C1(1)); 72.6 (C2(2)); 72.2, 72.1 (C2(1),3(2)); 71.6, 71.5 (C3(1),5(2)); 69.7 (C4(1)); 69.3 (C4(2)); 68.4 (C5(1)); 67.4 (C6(1)); 64.0 (C6(2)); 25.5 ($BrCH_2$).

Anal. Calcd for $C_{56}H_{50}BrClO_{17}$: C, 60.58; H, 4.54; Br, 7.20; Cl, 3.19. Found: C, 60.57; H, 4.19; Br, 7.53; Cl, 3.34.

Methyl 2,3,4-Tri-O-benzoyl-6-O-bromoacetyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranoside (23). A solution of 22 (0.4 g, 0.36 mmol) in dichloromethane (2.5 mL) was added to a suspension of methanol (0.5 mL) and silver triflate (128.5 mg, 0.5 mmol) in dichloromethane (2.5 mL) as described for the preparation of compound 5. Work-up as described above and chromatography (solvent *A*: 10:1) gave 0.35 g (88%) of a colorless foam; $[\alpha]_D$ = -15.7° (*c* = 0.2, chloroform); ^{13}C-NMR: δ 101.7 (C1(1)); 101.3 (C1(2)); 73.7 (C2(2)); 72.8, 72.7 (C3(1),3(2)); 72.0, 71.8, 71.7 (C2(1),5(1),5(2)); 69.9 (C4(1)); 69.3 (C4(2)); 68.3 (C6(1)); 64.0 (C6(2)); 58.8 (OCH_3); 25.4 ($BrCH_2$).

Anal. Calcd for $C_{57}H_{49}BrO_{18}$: C, 62.13; H, 4.48; Br, 7.25. Found: C, 62.25; H, 4.48; Br, 7.24.

(*R*)-α-[(4,6-O-Benzylidene-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl)oxy]-phenylacetonitrile (24). A solution of dimethyl sulfate (0.76 g, 6.0 mmol) in DMF (30 mL) was heated to 60-65 °C for 2 h. After cooling to room temperature 1 (2.29 g, 5.0 mmol) and benzaldehyde (0.64 g, 6.0 mmol) was added and the mixture was stirred until TLC (solvent *C*: 10:1) indicated almost complete conversion of the starting material (3 d). The mixture was neutralized by addition of ion-exchange-resin (OH^--form), filtered and concentrated. The residue was chromatographed (solvent *C*: 10:1) to give material which was recrystallized from ethanol to give 1.78 g (65%); mp 242 °C; $[\alpha]_D$ = -66.7° (*c* = 2.3, methanol); ^{1}H-NMR (D_3COD) characteristic signals: δ 7.62-7.35 (m, 10H, H^{arom}); 5.93 (s, 1H, PhC*H*$(O)_2$); 5.58 (s, 1H, PhC*H*CN); 4.71 (d, 1H, H1(1), $J_{1(1),2(1)}$ = 7.8 Hz); 3.78 (d, 1H, H1(2), $J_{1(2),2(2)}$ = 7.7 Hz); ^{13}C-NMR (D_3COD): δ 119.8 (CN); 105.4 (C1(2)); 103.1 (C1(1)); 102.5 (PhCH$(O)_2$); 82.1 (C4(2)); 77.7, 77.6 (C3(1),5(1)); 75.9 (C2(2)); 74.5 (C3(2)); 74.1 (C2(1)); 71.2 (C4(1)); 70.0 (C6(1)); 69.4 (Ph*C*HCN); 68.8 (C6(2)); 67.3 (C5(2)).

Anal. Calcd for $C_{27}H_{31}NO_{11}$ (monohydrate): C, 57.54; H, 5.90; N, 2.48. Found: C, 57.66; H, 5.62; N, 2.52.

(*R*)-α-[(2,3-di-O-Benzoyl-4,6-O-benzylidene-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (25). A solution of 24 (0.25 g, 0.46 mmol) in pyridine (15 mL) was treated with benzoyl chloride (0.57 g, 4.0 mmol) as described for the preparation of compound 2. Crystallization from ethanol gave 0.4 g (82%); mp 219 °C; $[\alpha]_D$ = -18.4° (*c* = 1.1, chloroform); ^{13}C-NMR: δ 116.9 (CN); 101.53, 101.45 (C1(2), PhC*H*$(O)_2$); 97.5 (C1(1)); 78.8 (C5(2)); 74.2 (C2(2)); 72.7, 72.5 (C3(1),3(2)); 72.0 (C5(1)); 71.2 (C2(1)); 69.5, 68.5 (1 x C, 2 x C, C4(1),5(2), Ph*C*HCN); 67.6 (C6(1)); 66.5 (C6(2)).

Anal. Calcd for $C_{62}H_{51}NO_{16}$: C, 69.85; H, 4.82; N, 1.31. Found: C, 69.60; H, 4.81; N, 1.25.

(*R*)-α-[(2,3-di-O-Benzoyl-6-O-benzyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-β-D-glucopyranosyl)oxy]-phenylacetonitrile (26). A solution of HCl in diethyl ether (saturated at room temperature) was added in small portions at 0 °C to a stirred mixture of **25** (0.76 g, 0.71 mmol), $NaBH_3CN$ (0.4 g, 6.3 mmol) and molecular sieves (3 Å, 1 g) in THF (30 mL) at such a rate that the pH was maintained at 5.0-5.5. When TLC showed complete formation of a single slower moving product (4 h), the mixture was poured into water and the resulted solution was made acidic by addition of aqueous HCl solution (1 M). After extraction with dichloromethane, washing of the organic layers with aqueous sodium hydrogenecarbonate and concentration, chromatography (solvent *D*: 5:3) of the residue gave 0.53 g (71%) of a colorless foam; $[\alpha]_D$ = -3.5° (*c* = 0.4, chloroform); ^{13}C-NMR: δ 116.9 (CN); 100.9 (C1(2)); 97.4 (C1(1)); 74.7 (C5(2)); 74.3 (C2(2)); 73.8 (C3(2)); 72.6 (C3(1)); 71.7 (C5(1)); 71.2 (C2(1)); 70.8 (C6(2)); 69.5 (3 x C, C4(1), Ph*C*HCN, $PhCH_2$); 68.3 (C6(1)); 67.5 (C4(2)).

Anal. Calcd for $C_{62}H_{53}NO_{16}$: C, 69.72; H, 5.00; N, 1.31. Found: C, 69.99; H, 5.04; N, 1.29.

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