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Conversion of *p*-methoxyphenyl glycosides into the corresponding glycosyl chlorides and bromides, and into thiophenyl glycosides

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Abstract

p-Methoxyphenyl (pMP) β-D-glycopyranosides (Glc, Gal, GlcNPhth, GalNPhth, GlcNTroc, Galβ4Glc, Galα4Gal) were prepared from the corresponding 1-*O*-acetyl sugars in 79–90% yield, using boron trifluoride etherate as promoter. Treatment of the pMP glycosides with acyl chlorides or bromides in the presence of various Lewis acids gave the corresponding glycosyl chlorides and bromides in 81–98% yield. Treatment of the acyl-protected pMP glycosides with thiophenol and boron trifluoride etherate gave the corresponding thioglycosides in 80–100% yield and high (> 20:1) β/α selectivity. The stability of pMP glycosides was investigated against a series of reagents. © 1996 Elsevier Science Ltd.

Keywords: *p*-Methoxyphenyl glycosides, synthesis and transformations of; Glycosyl chlorides; Glycosyl bromides; Thiophenyl glycosides

1. Introduction

A judicious choice of anomeric blocking groups is often of decisive importance for the successful outcome of an oligosaccharide synthesis. Furthermore, conversion of the assembled saccharide into a functional derivative, such as a spacer glycoside, is a necessary prerequisite for the synthesis of neoglycoconjugates [1]. In addition to the self-evident requirement of stability towards the reaction conditions employed, it is

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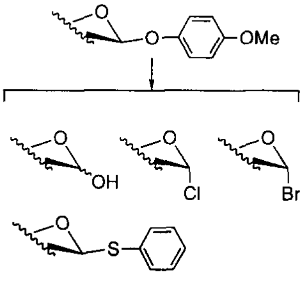


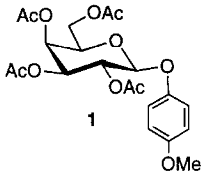
Scheme 1.

desirable that the anomeric blocking group can be removed selectively or that the glycoside can be transformed into an activated derivative for further glycosylation, for example of a spacer aglycon. Most of these conditions are satisfied by the 2-(trimethylsilyl)ethyl (Me_3SiEt) glycosides, which permit transformations into the corresponding hemiacetal, 1-*O*-acyl, and glycosyl chloride derivatives in high yields, even with large oligosaccharides that contain sensitive functionalities [2–5]. The Me_3SiEt glycosides have been utilized by us and others for the synthesis of numerous biologically significant oligosaccharide derivatives. Although anomeric Me_3SiEt protection is the preferred method for most oligosaccharide syntheses, cases exist where alternatives are needed. For example, Me_3SiEt deoxysaccharides are sometimes sensitive towards (Lewis) acidic reagents [6], and activation of their anomeric position in a single step to give glycosyl bromides or thioglycosides is not easy.

The *p*-methoxyphenyl (pMP) glycosides were introduced by Ogawa, who used them for temporary anomeric protection [7–11]. The pMP group was removed by treatment with ceric ammonium nitrate, to give the corresponding hemiacetals in 60–90% yield, followed by anomeric activation to yield 1-thio sugars, glycosyl chlorides and fluorides, as well as trichloroacetimidates. We have found that pMP glycosides (Scheme 1) can be converted in one step into the corresponding glycosyl halides and thiophenyl glycosides in high yields, thereby constituting a valuable alternative to Me_3SiEt glycosides in certain cases. However, it should be pointed out that the "standard" reactions of Me_3SiEt glycosides proceed in somewhat higher yields than the corresponding reactions of pMP glycosides.

2. Results and discussion

Preparation of p*-methoxyphenyl (pMP) glycosides.*—The pMP galactoside **1** was prepared by Ogawa in 88% yield, starting from D-galactose pentaacetate, with trimethylsilyl trifluoromethanesulfonate as promoter [10]. We obtained **1** in 81% yield after recrystallization, using boron trifluoride etherate ($BF_3 \cdot Et_2O$) as promoter. Similarly, compounds **2–8** were obtained in high yield by $BF_3 \cdot Et_2O$-promotion, as shown in Table 1 and described in detail in the Experimental section.



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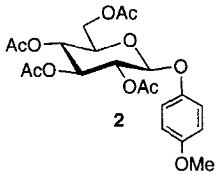

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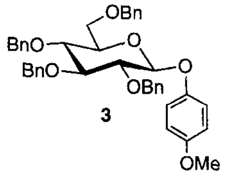

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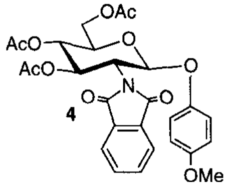

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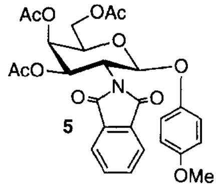

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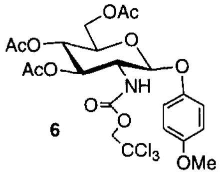

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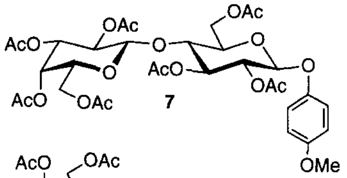

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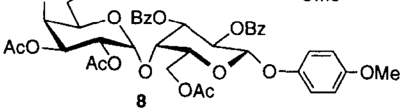

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Conversion of pMP glycosides into glycosyl chlorides and bromides.—Preparation of glycosyl halides is normally performed starting with hemiacetals or 1-*O*-acyl sugars, whereas direct conversion of glycosides other than Me_3SiEt glycosides [4,5] into glycosyl halides is quite uncommon. Inspired by the successful conversion of Me_3SiEt glycosides into glycosyl chlorides with $ZnCl_2$-promotion [4], we investigated the corresponding conversion of pMP glycosides, using various combinations of zinc halides and organic halides. The order of reactivity of these reagent combinations was found to be: (*i*) $ZnBr_2/AcBr > ZnBr_2/Me_3SiBr > ZnCl_2/AcCl$ and (*ii*) $ZnCl_2$/dichloromethyl methyl ether (DCMME) $> ZnCl_2/Me_3SiCl$. The zinc halide/Me_3Si halide combinations seem to cause a certain degree of anomerization of the starting pMP β-glycosides into the corresponding, virtually unreactive, α-glycosides. Therefore, we concentrated our attention on the remaining reagent combinations.

Treatment of the pMP galactoside **1** with $ZnCl_2/AcCl$ gave the acetochlorogalactose **9** (91%). Similarly, the pMP glucoside **2** was converted into the acetochloroglucose **12**

Table 1
Synthetic procedures and yields in the preparation of pMP glycosides, glycosyl chlorides and bromides, and thiophenyl glycosides

pMP Glycosides [a]			Glycosyl chloride [b]			Glycosyl bromide [b]			Thiophenyl glycoside [b]		
Method [c]	Product	Yield (%)	Method [c]	Product	Yield (%)	Method [c]	Product	Yield (%)	Method [c]	Product	Yield (%), (β/α)
A	**1**	81	B	**9**	91	G	**10**	98	J	**11**	97, (30:1)
A	**2**	89	C	**12**	90	G	**13**	97	J	**14**	80 [d], (20:1)
	3	[e]	D	**15**	81 [f]				J	**16**	87, (1:50)
A	**4**	90	E	**17**	99 [g]	H	**18**	96 [g]	J	**19**	96, (32:1)
A	**5**	79	E	**20**	90 [h]	I	**21**	98 [i]	J	**22**	100, (31:1)
A	**6**	87	E	**23**	97	H	**24**	98	J	**25**	98, (1:0)
A	**7**	90	F	**26**	91	G	**27**	82 [j]	J	**28**	80, (32:1)
	8					G	**29**	92	J	**30**	93, (50:1)

[a] The corresponding 1-*O*-acetyl sugar was used as starting material.

[b] The pMP glycosides **1–8** of the same row were used as starting materials.

[c] A: p-MeOC$_6$H$_4$OH, BF$_3$·Et$_2$O, CH$_2$Cl$_2$. B: AcCl, ZnCl$_2$, CH$_2$Cl$_2$, 30 °C. C: BzCl, ZnCl$_2$, CH$_2$Cl$_2$, 30 °C. D: AcCl, ZnCl$_2$, CHCl$_3$, 0 °C. E: AcCl, BF$_3$·Et$_2$O, ZnI$_2$, CHCl$_3$, 50 °C. F: MeOCHCl$_2$, ZnCl$_2$, CHCl$_3$, 22 °C. G: AcBr, ZnBr$_2$, CH$_2$Cl$_2$, 22 °C. H: AcBr, BF$_3$·Et$_2$O, ZnI$_2$, CHCl$_3$, 50 °C. I: AcBr, BF$_3$·Et$_2$O, CHCl$_3$, 55 °C. J: C$_6$H$_5$SH, BF$_3$·Et$_2$O, solvent.

[d] Compounds **14** (66%, β/α 13:1) and **2** (31%) were obtained from reaction of **2** in CHCl$_3$, 30 °C, 48 h.

[e] Deacetylation/benzylation of **2**.

[f] 2 h at 0 °C plus 4 h at 22 °C gave **31** (80%).

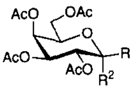
[g] α/β ~1:1.

[h] α/β 3:1.

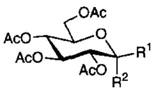
[i] α/β 6:1.

[j] A 1:1 mixture of **10** and **13** was also formed (18%).

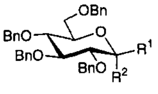
(90%) using $ZnCl_2$/BzCl. The benzyl-protected pMP glucoside **3** was more reactive than **2**. Low temperature (0 °C) permitted $ZnCl_2$/DCMME-induced formation of the glucosyl chloride **15** (81%), whereas with $ZnCl_2$/AcCl at room temperature, the 6-*O*-benzyl group was substituted by an acetyl group, giving **31** as the main product (80%). A similar observation was made with Me_3SiEt 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside [4]. It should be noted that **31** is a potentially valuable glycosyl donor, the synthesis of which by standard methods would require a number of steps.



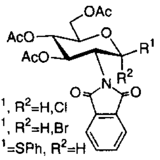
9: R^1=H, R^2=Cl
10: R^1=H, R^2=Br
11: R^1=SPh, R^2=H



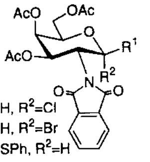
12: R^1=H, R^2=Cl
13: R^1=H, R^2=Br
14: R^1=SPh, R^2=H



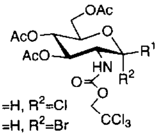
15: R^1=H, R^2=Cl
16: R^1=H, R^2=SPh



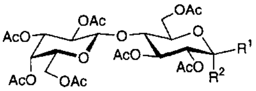
17: R^1, R^2=H,Cl
18: R^1, R^2=H,Br
19: R^1=SPh, R^2=H



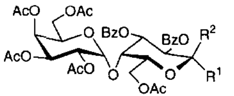
20: R^1=H, R^2=Cl
21: R^1=H, R^2=Br
22: R^1=SPh, R^2=H



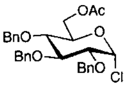
23: R^1=H, R^2=Cl
24: R^1=H, R^2=Br
25: R^1=SPh, R^2=H



26: R^1=H, R^2=Cl
27: R^1=H, R^2=Br
28: R^1=SPh, R^2=H



29: R^1=H, R^2=Br
30: R^1=SPh, R^2=H



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The amino sugars **4**–**6** required a stronger Lewis acid than $ZnCl_2$ in order to obtain the desired glycosyl chlorides in good yield and after reasonable reaction times. Treatment of **4**–**6** with AcCl in the presence of $BF_3 \cdot Et_2O$ and a catalytic amount of ZnI_2 gave the corresponding glycosyl chlorides **17**, **20**, and **23** in 90–97% yield.

The pMP lactoside **7** was smoothly converted into the acetochlorolactose **26** (91%) with $ZnCl_2$/DCMME, demonstrating that interglycosidic linkages are stable under these reaction conditions.

In addition to the synthesis of glycosyl chlorides described above, pMP glycosides can be transformed into the corresponding bromides, also in high yields. The pMP galactosides and glucosides **1** and **2** were converted into the bromides **10** and **13** in 98 and 97% yield, respectively, using a mixture of $ZnBr_2$ and AcBr. The amino sugars **4**–**6** were converted into the glycosyl bromides **18**, **21**, and **24** in 96–98% yield. The reactions of **4** and **6** (→ **18** and **24**) were performed in the presence of ZnI_2, which reduced the reaction time to 4 h, as compared to the reaction of **5** (→ **21**; no ZnI_2 added), which required 24 h for completion.

The pMP lactoside **7** was sensitive towards $ZnBr_2$/AcBr at room temperature, giving acetobromolactose **27** in only 82% yield. An equimolar mixture (18%) of **10** and **13** was also formed. When the reaction was run at 40 °C or when the reaction time at room temperature was increased to ca. 20 h, **10** and **13** were formed in almost quantitative yield. In contrast to **7**, the pMP galabioside **8** [18] was converted into the acetobromogalabioside **29** in 92% yield, without breakage of the interglycosidic bond.

Conversion of pMP glycosides into thiophenyl β-glycosides.—Thioglycosides have emerged as valuable glycosyl donors during the last few years [12]. Therefore, a high-yielding one-step conversion of *O*-glycosides into thioglycosides is highly desirable, especially with large oligosaccharides, as a prelude to the synthesis of (neo)glycoconjugates [1].

Thioglycosides are in general less basic than their *O*-glycoside counterparts, and thiolates are more nucleophilic than alcholates. Therefore, treatment of an *O*-glycoside with a Lewis acid, in the presence of a suitable thiol, should lead to an equilibrium where the thioglycoside is strongly preferred. The reaction rate should increase with highly electrophilic aglycons, such as the pMP glycosides. Preliminary experiments with the pMP glucoside **2** and thiophenol in the presence of $BF_3 \cdot Et_2O$ showed that in order to obtain a reasonable reaction time (< 20 h), 0.5–1.0 equiv of $BF_3 \cdot Et_2O$ and a reaction temperature of 40–60 °C were needed. As in the preparation of glycosyl halides above, the amino sugars **4–6** required a larger amount of $BF_3 \cdot Et_2O$ (5 equiv). The pMP glycosides **1–8** were treated under these conditions, which in most cases gave very high yields of the desired thioglycosides (Table 1).

The thiogalactoside **11** was thus obtained from **1** in 97% yield as a β/α mixture (30:1). The pMP glucosides **2** and **3** gave **14** and **16** in somewhat lower yields (80 and

Table 2

Comparison of the reactivity of *p*-methoxyphenyl (pMP) and 2-(trimethylsilyl)ethyl (Me_3SiEt) glycosides

Conditions [a]	Reactivity			
	pMP	ref.	Me_3SiEt	ref.
aq 80% AcOH, 70 °C	–		–	[3]
HCOOH, 60 °C	–		+	[3]
CF_3CO_2H/CH_2Cl_2, 20 °C	–	[34]	+	[3]
aq 90% CF_3CO_2H, 20 °C	–			
H_2SO_4/MeCN, 20 °C	+		+	[3]
$HClO_4$, aq 70%/MeCN	+		+	[3]
$CF_3SO_3Ag/CuBr_2/QBr/CHCl_3$	–	[9]	–	[6]
$AgClO_4/SnCl_2$/THF	–	[35]	–	[6]
$NIS/CF_3SO_3H/CHCl_3$,MS 4 Å	–		–	[18]
$CF_3SO_3SiMe_3$/MeCN, 20 °C	+		(+)	[3]
$BF_3 \cdot Et_2O/CH_2Cl_2$ or MeCN, 25 °C	(+)		(+)	[3]
$BF_3 \cdot Et_2O/CH_2Cl_2$, MS 4 Å, 25 °C	–	[36]		
$BF_3 \cdot Et_2O/Ac_2O$, 25 °C	+		+	[3]
DDQ/Me_3SiCl, MS 3 Å, 60 °C	–		–	[37]
DDQ/MeCN/H_2O	–	[9]	–	[37,38]
$Me_2SO/(ClCO)_2/CH_2Cl_2$, 20 °C	–	[36]	–	[3]
NBS/CF_3SO_3H/MeCN	–		–	
Me_3SiCl/imidazole/CH_2Cl_2	–		–	[38]
$BzCl/ZnI_2$, MS 3 Å, 20 °C	–			
H_2/PdC/AcOH	–	[18]	–	[3]
$MeC_6H_4CH(OMe)_2$ / $p CH_3C_6H_4SO_3H$	–	[18]	–	[3]
$NaCNBH_3$/HCl/THF	–	[18]	–	[3]
CF_3SO_3Me/DBMP [b]	–	[9]		
Ph_3SnH/AIBN	–	[34]		

[a] Compound **1** (10 mg) and reagent (1 equiv); analyzed by TLC: –, > 95% of **1** remained after 10 h; +, < 10% of **1** remained after 2 h; (+), > 50% but < 90% of **1** remained after 4 h.

[b] 2,6-Di-*tert*-butyl-4-methylpyridine.

87%, respectively); the benzyl-protected **16** was obtained mainly as the α anomer. The *N*-protected amino sugars **19**, **22**, and **25** were obtained in high yields and β selectivity. The pMP lactoside **7** underwent some degradation (as in the formation of glycosyl halides above) and the thiolactoside **28** was obtained in 80% yield. Finally, the thiogalabioside **30** was obtained in an excellent 93% yield and β/α ratio of 50:1.

Stability of pMP glycosides.—The pMP glycosides are stable under most of the conditions used in oligosaccharide synthesis. We conducted a number of reactivity tests with pMP glycosides and analyzed the resulting reaction mixtures by TLC (Table 2). For comparison, the corresponding reactivities of Me_3SiEt glycosides are included in Table 2. It was found that pMP and Me_3SiEt glycosides have similar reactivities, with one notable exception: while Me_3SiEt glycosides are transformed into the corresponding hemiacetals in high yield by treatment with trifluoroacetic acid in dichloromethane [3], pMP glycosides are stable under these conditions.

3. Conclusions

Treatment of 1-*O*-acyl sugars, carrying a participating group at the 2-position, with *p*-methoxyphenol and $BF_3 \cdot Et_2O$ gave the corresponding pMP β-glycosides **1–8** (79–90%). Treatment of the pMP glycosides with various chlorinating and brominating reagents gave the corresponding glycosyl chlorides and bromides in 81–98% yield. Treatment of the pMP glycosides with thiophenol and $BF_3 \cdot Et_2O$ gave the corresponding thiophenyl glycosides in 79–100% yield, with high β/α selectivity (> 20:1), except for the benzylated compound **16**, where the α-glycoside was the dominant product. It should also be noted that the *N*-Troc-protected glucoside **6** was synthesized and transformed into the anomerically activated compounds **23–25** in very high yields (> 96%), thereby further proving itself as a good substitute for the *N*-phthaloylated counterpart **4** (we recently reported [13] a comparative study of *N*-Troc- and *N*-Phth-protected glycosyl donors).

4. Experimental

NMR spectra were recorded in $CDCl_3$; chemical shifts are relative to Me_4Si. TLC was performed on Kieselgel 60 F_{254} (E. Merck). Synthetic products were chromatographed on Kieselgel 60 (E. Merck, 35–70 mesh). Melting points are uncorrected. Toluene and CH_2Cl_2 were distilled over drying agents under N_2 prior to use. 1,2-Dichloroethane and $CHCl_3$ were dried by passage through Al_2O_3 (activity I, E. Merck).

*4-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside* (**1**).—To a cold (0 °C) solution of 1,2,3,4,6-penta-*O*-acetyl-β-D-galactose (10.0 g, 25.6 mmol) and 4-methoxyphenol (3.38 g, 30.8 mmol) in dry CH_2Cl_2 (50 mL) was added $BF_3 \cdot Et_2O$ (3.85 mL, 30.6 mmol) under Ar. After 7 h, the mixture was diluted with CH_2Cl_2 (250 mL) and washed with water (200 mL), saturated aq $NaHCO_3$ (200 mL), and water (2 × 150 mL). The organic phase was dried, filtered, and concentrated. The residue was recrystallized (heptane/EtOAc, −20 °C) to give **1** (9.40 g, 81%); mp 109–110 °C;

$[\alpha]_D^{25}$ +3.2° (c 0.9, $CHCl_3$), lit. [10] +9.6° (c 0.54, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.96 (d, 2 H, J 9.2 Hz, Ar-H), 6.82 (d, 2 H, J 9.2 Hz, Ar-H), 5.49–5.42 (m, 2 H, H-2,4), 5.09 (dd, 1 H, J 10.5, 3.4 Hz, H-3), 4.92 (d, 1 H, J 8.0 Hz, H-1), 4.24 (dd, 1 H, J 11.3, 7.0 Hz, H-6), 4.16 (dd, 1 H, J 11.2, 6.4 Hz, H-6), 4.00 (dt, 1 H, 6.5, 1.0 Hz, H-5), 2.18, 2.09, 2.06, 2.01 (4 s, each 3 H, 4 × Ac).

4-Methoxyphenyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (**2**).—1,2,3,4,6-Penta-*O*-acetyl-β-D-glucose (10.0 g, 25.6 mmol) and 4-methoxyphenol (4.31 g, 38.4 mmol) in dry CH_2Cl_2 (100 mL) were treated with $BF_3 \cdot Et_2O$ (5.3 mL, 42.1 mmol) as described in the preparation of **1**. The crude product [14] was crystallized (heptane/EtOAc, −20 °C) to give **2** (7.80 g). The mother liquor was concentrated and crystallized to give a second crop of **2** (2.5 g; total yield 89%); mp 106–107 °C; $[\alpha]_D^{25}$ −8.4° (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.31–5.20 (m, 2 H, H-2,3), 5.16 (t, 1 H, J 9.8 Hz, H-4), 4.95 (d, 1 H, J 7.7 Hz, H-1), 4.29 (dd, 1 H, J 12.3, 4.2 Hz, H-6), 4.16 (dd, 1 H, J 12.3, 2.4 Hz, H-6), 3.81 (m, 1 H, H-5), 3.77 (s, 3 H, OMe), 2.08, 2.07, 2.04, 2.03 (s, each 3 H, 4 × Ac). HRMS: Calcd for $C_{21}H_{26}O_{11}$ (M^+): m/z 454.1475. Found: m/z 454.1490.

4-Methoxyphenyl 2,3,4,6-tetra-O-benzyl-β-D-glucopyranoside (**3**).—Compound **2** (7.0 g, 15.4 mmol) was dissolved in MeOH (20 mL) and methanolic NaOMe (1 M, 0.5 mL) was added. After 8 h, the mixture was neutralized with Duolite (H^+) resin, filtered, and concentrated to give deacetylated **2** (4.32 g, 98%). Part of the deacetylated material (1.00 g, 3.5 mmol) was dissolved in dry DMF (15 mL) and NaH (840 mg, 28.0 mmol) was added. The mixture was stirred for 30 min, benzyl bromide (3.3 mL, 28.0 mmol) was added, and the mixture was stirred at room temperature overnight. MeOH (5 mL) was added and the mixture was stirred for 15 min, then concentrated and co-concentrated with 10:1 $EtOH–H_2O$ (2 × 5 mL). The residue was diluted with CH_2Cl_2 (100 mL) and the mixture was washed with saturated aq NaCl (2 × 30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was dissolved in hot EtOH (10 mL) and the solution was left at room temperature for 1 h, at 4 °C for 1 h, and at −25 °C for 2 days. The crystalline mass was filtered off and washed with cold EtOH to give **3** (2.08 g, 92%); mp 95–96 °C, lit. [15] 94.5–95.5 °C; $[\alpha]_D^{25}$ −3.0° (c 1.0, $CHCl_3$), lit. [15] −4.0°; ^1H NMR ($CDCl_3$): δ 7.40–7.20 (m, 20 H, Ar-H), 7.06 (d, 2 H, J 9.2 Hz, Ar-H), 6.83 (d, 2 H, J 9.2 Hz, Ar-H), 3.79 (s, 3 H, OMe); ^{13}C NMR ($CDCl_3$): δ 155.3, 151.6, 138.6, 138.3, 138.2, 138.1, 118.5, 114.6, 102.8, 84.7, 82.1, 77.8, 75.8, 75.09, 75.05, 73.5, 68.9, 55.7.

4-Methoxyphenyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**4**).—1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranose (550 mg, 1.15 mmol) and 4-methoxyphenol (340 mg, 2.91 mmol) were dissolved in CH_2Cl_2 (8 mL), and $BF_3 \cdot Et_2O$ (0.29 mL, 2.31 mmol) was added. The mixture was treated as in the preparation of **1**. The crude product was crystallized (ether/heptane) to give **4** (344 mg, 55%). The mother liquor was concentrated and the residue was chromatographed (SiO_2, 2:1 → 1:1 heptane–EtOAc) to give additional **4** (216 mg, 35%); mp 132–134 °C; $[\alpha]_D^{25}$ +46.7° (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.90–6.70 (m, 8 H, Ar-H), 5.89–5.82 (m, 2 H, H-1,3), 5.25 (dd, 1 H, J 10.2, 9.1 Hz, H-4), 4.57 (dd, 1 H, J 10.7, 8.5 Hz, H-2), 4.36 (dd, 1 H, J 12.3, 5.0 Hz, H-6), 4.18 (dd, 1 H, J 12.2, 2.4 Hz, H-6), 3.96 (ddd, 1 H, J 10.1, 5.0, 2.4 Hz, H-5), 3.72 (s, 3 H, OMe), 2.11, 2.05, 1.89 (3 s, each 3 H, 3 × Ac). HRMS: Calcd for $C_{27}H_{27}NO_{11}$ (M^+): m/z 541.1584. Found: m/z 541.1614.

4-Methoxyphenyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-β-D-galactopyranoside (**5**).—1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-phthalimido-β-D-galactopyranose [16] (500 mg, 1.05 mmol) and 4-methoxyphenol (367 mg, 3.14 mmol) were dissolved in CH_2Cl_2 (10 mL), and $BF_3 \cdot Et_2O$ (0.2 mL, 2.10 mmol) was added. The mixture was treated as in the preparation of **1**. The residue was crystallized (ether/heptane) to give **5** (447 mg, 79%); mp ~ 150 °C (dec.); $[\alpha]_D^{25}$ +27.0° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.90–6.70 (8 H, Ar-H), 5.87 (dd, 1 H, *J* 11.4, 3.4 Hz, H-3), 5.80 (d, 1 H, *J* 8.5 Hz, H-1), 5.53 (d, 1 H, *J* 3.4 Hz, H-4), 4.80 (dd, 1 H, *J* 11.5, 8.5 Hz, H-2), 4.30–4.15 (m, 3 H, H-6,5), 3.72 (s, 3 H, OMe), 2.23, 2.06, 1.88 (3 s, each 3 H, 3 × Ac). Anal. Calcd for $C_{27}H_{27}NO_{11}$: C, 59.9; H, 5.0; N, 2.6. Found: C, 59.7; H, 4.9; N, 2.6.

4-Methoxyphenyl 3,4,6-tri-O-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (**6**).—1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranose [17] (400 mg, 0.96 mmol) and 4-methoxyphenol (164 mg, 1.46 mmol) were dissolved in CH_2Cl_2 (5 mL), and $BF_3 \cdot Et_2O$ (0.18 mL, 1.46 mmol) was added. The mixture was treated as in the preparation of **1**. The residue was chromatographed (SiO_2, 2:1 → 1:1 heptane–EtOAc) to give **6** (402 mg, 87%). Recrystallization (ether/heptane) gave an analytical sample; mp 61–64 °C; $[\alpha]_D^{25}$ +4.9° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.97, 6.80 (d, 2 H each, *J* 9.2 Hz, Ar-H), 5.41 (bt, 1 H, *J* 10.0 Hz, H-3), 5.29 (bd, 1 H, *J* 8.8 Hz, H-1), 5.17–5.09 (m, 2 H, H-4, NH), 4.77, 4.71 (ABq, 2 H, *J* 11.9 Hz, OCH_2CCl_3), 4.31 (dd, 1 H, *J* 12.3, 5.4 Hz, H-6), 4.16 (dd, 1 H, *J* 12.2, 2.4 Hz, H-6), 3.77 (s, 3 H, OMe), 2.09, 2.06, 2.04 (3 s, each 3 H, 3 × Ac). HRMS: Calcd for $C_{22}H_{26}Cl_3NNaO_{11}$: *m/z* 608.0469. Found: *m/z* 608.0479.

4-Methoxyphenyl 2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside (**7**) .—β-Lactose octaacetate (17.4 g, 25.6 mmol) and 4-methoxyphenol (4.31 g, 38.4 mmol) were dissolved in CH_2Cl_2 (100 mL), and $BF_3 \cdot Et_2O$ (6.4 mL, 51.2 mmol) was added. The mixture was treated as in the preparation of **1**. The crude product was crystallized (heptane/EtOAc, −20 °C) to give **7** (11.25 g, 59%). The mother liquor was concentrated and the residue was chromatographed (SiO_2, 2:1 heptane–EtOAc) to give additional **7** (5.90 g, total yield 90%); mp 118–120 °C; $[\alpha]_D^{25}$ −14.8° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.35 (d, 1 H, *J* 2.9 Hz, H-4′), 5.26 (t, 1 H, *J* 9.0 Hz, H-3), 5.16–5.08 (m, 2 H, H-2,2′), 4.96 (dd, 1 H, *J* 10.5, 3.4 Hz, H-3′), 4.98–4.90 (m, 2 H, H-1′,6), 4.53–4.48 (m, 2 H, H-1,1′), 3.76 (s, 3 H, OMe), 2.15, 2.09, 2.07, 2.07, 2.06, 2.04, 1.96 (7 s, each 3 H, 7 × Ac). Anal. Calcd for $C_{33}H_{62}O_{19}$: C, 53.4; H, 5.7. Found: C, 53.4; H, 5.6.

4-Methoxyphenyl 6-O-acetyl-2,3-di-O-benzoyl-4-O-(2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl)-β-D-galactopyranoside (**8**).—The synthesis has been reported [18].

2,3,4,6-Tetra-O-acetyl-α-D-galactopyranosyl chloride (**9**).—Compound **1** (150 mg, 0.33 mmol) was dissolved in dry CH_2Cl_2 (3 mL) under Ar, and AcCl (0.070 mL, 0.99 mmol) and $ZnCl_2$ (~ 5 mg, ~ 0.036 mmol) were added. The mixture was stirred at 30 °C for 8 h, then diluted with CH_2Cl_2 (50 mL) and washed with saturated aq $NaHCO_3$ (40 mL) and saturated aq NaCl (40 mL). The organic phase was dried (Na_2SO_4), filtered, and concentrated. The residue was chromatographed (SiO_2, 2:1 heptane–EtOAc) to give **9** (110 mg, 91%). Recrystallization (ether/heptane) gave an analytical sample; mp 61–62 °C, lit. [19] 78–79 °C (dec.); $[\alpha]_D^{25}$ +174.3° (*c* 0.7, $CHCl_3$), lit. [19] +177°; ^1H NMR ($CDCl_3$): δ 6.37 (d, 1 H, *J* 4.0 Hz, H-1), 5.52 (dd, 1 H, *J* 3.2, 1.2 Hz, H-4), 6.42 (dd, 1 H, *J* 10.8, 3.2 Hz, H-3), 5.25 (dd, 1 H, *J* 10.7, 3.9 Hz, H-2), 4.52 (bd, 1 H, *J* 6.3 Hz, H-5), 4.17, 4.10 (dd, each 1 H, *J* 6.4, 11.4, 6.8 Hz, H-6).

*2,3,4,6-Tetra-*O*-acetyl-α-*D*-galactopyranosyl bromide* (**10**).—Compound **1** (150 mg, 0.33 mmol) was dissolved in dry CH_2Cl_2 (3 mL) under Ar, and AcBr (0.072 mL, 0.99 mmol) and $ZnBr_2$ (~ 4 mg, ~ 0.018 mmol) were added. The mixture was stirred at 22 °C for 24 h, then diluted with CH_2Cl_2 (50 mL) and washed with saturated aq $NaHCO_3$ (40 mL) and saturated aq NaCl (40 mL). The organic phase was dried (Na_2SO_4), filtered, and concentrated. The residue was chromatographed (SiO_2, 5:1 → 2:1 heptane–EtOAc) to give **10** (134 mg, 98%). Recrystallization (ether/heptane) gave an analytical sample; mp 84–85 °C, lit. [24] 84–85 °C; $[\alpha]_D^{25}$ +210° (*c* 1.0, $CHCl_3$), lit. [24] +217°; ^1H NMR ($CDCl_3$): δ 6.69 (d, 1 H, *J* 3.9 Hz, H-1), 5.51 (dd, 1 H, *J* 3.2, 1.0 Hz, H-4), 5.40 (dd, 1 H, *J* 10.7, 3.3 Hz, H-3), 5.04 (dd, 1 H, *J* 10.6, 4.0 Hz, H-2), 4.48 (t, 1 H, *J* 6.8 Hz, H-5), 4.18 (dd, 1 H, *J* 11.4, 6.2 Hz, H-6), 4.10 (dd, 1 H, *J* 11.4, 6.8 Hz, H-6), 2.15, 2.11, 2.06, 2.03 (4 s, each 3 H, 4 × Ac).

*Phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-*D*-galactopyranoside* (**11**).—To a solution of **1** (250 mg, 0.55 mmol) and thiophenol (0.170 mL, 1.65 mmol) in toluene (5 mL) under Ar was added $BF_3 \cdot Et_2O$ (0.076 mL, 0.55 mmol) at room temperature, and the mixture was left at 60 °C for 16 h. The mixture was diluted with EtOAc (75 mL), washed with saturated aq $NaHCO_3$ (2 × 50 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was chromatographed (SiO_2, 5:1 → 3:2 heptane–EtOAc) to give **11** (234 mg, 97%, β/α ~ 30:1). Recrystallization (EtOAc/heptane) gave an analytical sample; mp 72–74 °C, lit. [30] 73–76 °C; $[\alpha]_D^{25}$ +4.9° (*c* 1.0, $CHCl_3$), lit. [30] +5°; ^1H NMR ($CDCl_3$): δ 5.40 (dd, 1 H, *J* 3.4, 1.0 Hz, H-4), 5.22 (t, 1 H, *J* 10.0 Hz, H-2), 5.04 (dd, 1 H, *J* 10.0, 3.4 Hz, H-3), 4.71 (d, 1 H, *J* 9.9 Hz, H-1), 4.21–4.06 (m, 2 H, H-6), 3.93 (m, 1 H, H-5), 2.10, 2.08, 2.02, 1.95 (4 s, each 3 H, 4 × Ac).

*2,3,4,6-Tetra-*O*-acetyl-α-*D*-glucopyranosyl chloride* (**12**).—Compound **2** (150 mg, 0.33 mmol) was treated with BzCl (0.19 mL, 1.65 mmol) and $ZnCl_2$ (~ 5 mg, ~ 0.036 mmol) in dry CH_2Cl_2 (3 mL), as described in the preparation of **9**. The crude product was chromatographed (SiO_2, 2:1 heptane–EtOAc) to give **12** (109 mg, 90%). Recrystallization (ether/heptane) gave an analytical sample; mp 72–73 °C, lit. [20] mp 75–76 °C; $[\alpha]_D^{25}$ + 163° (*c* 1.0, $CHCl_3$), lit. [20] + 166°; ^1H NMR ($CDCl_3$): δ 6.29 (d, 1 H, *J* 4.1 Hz, H-1), 5.56 (t, 1 H, *J* 9.8 Hz, H-3), 5.14 (t, 1 H, *J* 9.6 Hz, H-4), 5.01 (dd, 1 H, *J* 10.1, 4.0 Hz, H-2), 2.10, 2.05, 2.03 (3 s, 12 H, 4 × Ac).

*2,3,4,6-Tetra-*O*-acetyl-α-*D*-glucopyranosyl bromide* (**13**).—Compound **2** (150 mg, 0.33 mmol) was treated with AcBr (0.072 mL, 0.99 mmol) and $ZnBr_2$ (~ 4 mg, ~ 0.018 mmol) in dry CH_2Cl_2 (3 mL), as described in the preparation of **10**. The crude product was chromatographed (SiO_2, 5:1 → 3:2 heptane–EtOAc) to give **13** (131 mg, 97%). Recrystallization (EtOAc/heptane) gave an analytical sample; mp 89 °C, lit. [25] 88–89 °C; $[\alpha]_D^{25}$ + 197° (*c* 2, $CHCl_3$), lit. [25] 198°; ^1H NMR ($CDCl_3$): δ 6.61 (d, 1 H, *J* 4.2 Hz, H-1), 5.56 (t, 1 H, *J* 9.6 Hz, H-3), 5.16 (t, 1 H, *J* 9.8 Hz, H-4), 4.84 (dd, 1 H, *J* 10.0, 3.9 Hz, H-2), 2.10, 2.09, 2.05, 2.03 (4 s, each 3 H, 4 × Ac).

*Phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-*D*-glucopyranoside* (**14**).—Compound **2** (150 mg, 0.33 mmol) was treated with thiophenol (97%, 0.175 mL, 1.65 mmol) and $BF_3 \cdot Et_2O$ (0.045 mL, 0.33 mmol) in $ClCH_2CH_2Cl$ (5 mL) at 50 °C and worked up as described in the preparation of **11**. The residue was chromatographed (SiO_2, 5:1 → 3:2

heptane–EtOAc) to give **14** (116.3 mg, 80%, β/α ~ 20:1). Recrystallization (EtOAc/heptane) gave an analytical sample of the β anomer; mp 122–123 °C, lit. [30] mp 117–118 °C; $[\alpha]_D^{25}$ $-17.4°$ (*c* 1.0, $CHCl_3$), lit. [30] $-16°$; ^{1}H NMR ($CDCl_3$): δ 5.22 (t, 1 H, *J* 9.3 Hz, H-3), 5.03 (t, 1 H, *J* 10.0 Hz, H-2), 4.96 (dd, 1 H, *J* 10.0, 9.2 Hz, H-4), 4.70 (d, 1 H, *J* 10.1 Hz, H-1), 4.25–4.13 (m, 2 H, H-6), 3.72 (m, 1 H, H-5), 2.07, 2.06, 2.00, 1.97 (4 s, each 3 H, 4 × Ac).

2,3,4,6-Tetra-O-benzyl-α-D-glucopyranosyl chloride (**15**).—To a cold (ice–water bath) solution of **3** (100 mg, 0.155 mmol) in dry $CHCl_3$ (3 mL) under Ar were added AcCl (0.055 mL, 0.76 mmol) and $ZnCl_2$ (~ 3 mg, ~ 0.022 mmol). The reaction was monitored by TLC (4:1 heptane–EtOAc). When **3** had been consumed, the mixture was worked up as in the preparation of **9** and the crude product was chromatographed (SiO_2, 10:1 → 5:1 heptane–EtOAc) to give a mixture of **15** and 4-methoxyphenyl acetate (77 mg, ~ 2:1, calculated yield of **15**: 81%); $[\alpha]_D^{25}$ $+59.6°$ (*c* 1.0 of mixture, $CHCl_3$), lit. [21] $+62°$ (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.10 (d, 1 H, *J* 3.7 Hz, H-1), 5.02–4.45 (m, 8 H, $PhCH_2$), 4.11 (m, 1 H, H-5), 4.06 (t, 1 H, *J* 9.1 Hz, H-3), 3.67 (dd, 1 H, *J* 10.9, 2.0 Hz, H-6); ^{13}C NMR: δ 138.5, 138.0, 137.7, 137.5, 93.6, 81.4, 79.9, 76.4, 75.9, 75.3, 73.5, 73.4, 73.0, 67.8.

Phenyl 2,3,4,6-tetra-O-benzyl-1-thio-α-D-glucopyranoside (**16**).—Compound **3** (100 mg, 0.16 mmol) was treated with thiophenol (97%, 0.096 mL, 0.93 mmol) and $BF_3 \cdot Et_2O$ (0.011 mL, 0.078 mmol) in $CHCl_3$ (3 mL) at 22 °C and worked up as described in the preparation of **11**. The residue was chromatographed (SiO_2, 10:1 heptane–EtOAc) to give **16** (85 mg, 87%, α/β ~ 50:1). Recrystallization (ether/heptane) gave an analytical sample (containing a trace of the β isomer); mp 75 °C (dec.), lit. [30] 81–82 °C (MeOH); $[\alpha]_D^{25}$ $+128.2°$ (*c* 1.0, $CHCl_3$), lit. [30] $+154°$; ^{1}H NMR ($CDCl_3$): δ 5.65 (d, 1 H, *J* 4.5 Hz, H-1), 4.34 (ddd, 1 H, *J* 10.1, 3.8, 2.1 Hz, H-5), 3.78 (dd, 1 H, *J* 10.7, 3.8 Hz, H-6), 3.61 (dd, 1 H, *J* 10.8, 2.1 Hz, H-6).

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-α,β-D-glucopyranosyl chloride (**17**).—To a solution of **4** (50.0 mg, 0.092 mmol) in dry $CHCl_3$ (1.5 mL) under Ar were added AcCl (0.062 mL, 0.87 mmol), $BF_3 \cdot Et_2O$ (0.033 mL, 0.26 mmol), and ZnI_2 (~ 2 mg). The mixture was stirred at 50 °C overnight, then diluted with CH_2Cl_2 (50 mL) and washed with saturated aq $NaHCO_3$ containing ~ 5% $Na_2S_2O_3$ (30 mL), and water (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was chromatographed (SiO_2, 2:1 → 1:1 heptane–EtOAc) to give **17** [4,22,23] as an α/β mixture (41.3 mg, 99%, α/β 1:1); ^{1}H NMR: δ 6.22 (d, *J* 3.7 Hz, H-1α), 6.19 (d, *J* 9.4 Hz, H-1β), lit. [4] δ 6.19 (d, *J* 9.3 Hz, H-1β).

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-α,β-D-glucopyranosyl bromide (**18**).—To a solution of **4** (50.0 mg, 0.092 mmol) in dry $CHCl_3$ (1.5 mL) under Ar were added AcBr (0.062 mL, 0.87 mmol), $BF_3 \cdot Et_2O$ (0.033 mL, 0.26 mmol), and ZnI_2 (~ 2 mg). The mixture was stirred at 50 °C for 4 h, then diluted with CH_2Cl_2 (50 mL) and washed with saturated aq $NaHCO_3$ containing ~ 5% $Na_2S_2O_3$ (30 mL), and water (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was chromatographed (SiO_2, 2:1 → 1:1 heptane–EtOAc) to give **18** [26] as an α/β mixture (44.3 mg, 96%, α/β 1:1); ^{1}H NMR: δ 6.65 (dd, *J* 9.2, 11.5 Hz, H-3α), 6.57 (d, *J* 3.7 Hz, H-1α), 6.41 (d, *J* 9.6 Hz, H-1β), 5.76 (dd, *J* 9.2, 10.4 Hz, H-3β).

Phenyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**19**).—To a solution of **4** (50 mg, 0.092 mmol) in dry $CHCl_3$ (1.5 mL) under Ar were added thiophenol (0.046 mL, 0.44 mmol) and $BF_3 \cdot Et_2O$ (0.046 mL, 0.44 mmol). The mixture was stirred at 60 °C for 20 h, then diluted with CH_2Cl_2 (50 mL), washed with saturated aq $NaHCO_3$ (2 × 30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was crystallized from ether/heptane to give **19** (43 mg, 88%). The mother liquor was concentrated and the residue chromatographed (SiO_2, 2:1 → 1:1 heptane–EtOAc) to give **19** mixed with some α anomer (4.0 mg, 8%, α/β 1:2). Crystalline **19** had mp 148–149 °C, lit. [31] mp 145–146 °C; $[\alpha]_D^{25}$ +54.7° (*c* 1.0, $CDCl_3$), lit. [31] +53.0° ($CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.80 (dd, 1 H, *J* 10.2, 9.2 Hz, H-3), 5.72 (d, 1 H, *J* 10.6 Hz, H-1), 5.14 (dd, 1 H, *J* 10.1, 9.2 Hz, H-4), 5.35 (t, 1 H, *J* 10.4 Hz, H-2), 4.29, 4.21 (dd, 1 H each, *J* 12.3, 5.0, 2.4 Hz, H-6), 3.91 (ddd, 1 H, *J* 10.2, 5.1, 2.6 Hz, H-5), 2.11, 2.03, 1.84 (3 s, each 3 H, 3 × Ac).

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-α,β-D-galactopyranosyl chloride (**20**).—To a solution of **5** (40.0 mg, 0.074 mmol) in dry $CHCl_3$ (1.5 mL) under Ar were added AcCl (0.053 mL, 0.74 mmol), $BF_3 \cdot Et_2O$ (0.033 mL, 0.26 mmol), and ZnI_2 (~ 2 mg). The mixture was stirred at 50 °C for 10 h and an additional portion of AcCl (0.026 mL, 0.37 mmol) was added. The mixture was stirred for 14 h, then worked up as in the preparation of **17**, to give **20** together with some β anomer (30.2 mg, 90%, α/β 3:1); ^1H NMR: δ 6.34 (d, *J* 3.7 Hz, H-1α), 6.17 (d, *J* 9.3 Hz, H-1β), lit. [16] δ 6.34 (d, *J* 3.7 Hz, H-1α), 6.17 (d, *J* 9.3 Hz, H-1β).

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-α,β-D-galactopyranosyl bromide (**21**).—To a solution of **5** (40.0 mg, 0.074 mmol) in dry $CHCl_3$ (1.5 mL) under Ar were added AcBr (0.032 mL, 0.35 mmol) and $BF_3 \cdot Et_2O$ (0.027 mL, 0.22 mmol). The mixture was stirred at 55 °C for 14 h and an additional portion of AcBr (0.032 mL, 0.35 mmol) was added. The mixture was stirred for 10 h, then worked up as in the preparation of **18**, to give **21** mixed with some β anomer (36.0 mg, 98%, α/β 6:1); ^1H NMR: δ 6.69 (d, *J* 3.4 Hz, H-1α), 6.53 (dd, *J* 12.0, 3.0 Hz, H-3α), 6.39 (d, *J* 9.6 Hz, H-1β), 5.77 (dd, *J* 11.1, 3.4 Hz, H-3β), lit. [27,28] δ 6.69 (dd, *J* 3.4 Hz, H-1α), 6.53 (d, *J* 11.9, 3.1 Hz, H-3α), 6.36 (d, *J* 10 Hz, H-1β), 5.76 (dd, *J* 11.0, 3.5 Hz, H-3β).

Phenyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (**22**).—A solution of **5** (40.0 mg, 0.074 mmol) in dry $CHCl_3$ (1.5 mL) was treated with thiophenol (0.037 mL, 0.35 mmol) and $BF_3 \cdot Et_2O$ (0.037 mL, 0.35 mmol) at 60 °C overnight, and worked up as described in the preparation of **19**. The residue was chromatographed (SiO_2, 2:1 → 1:1 heptane–EtOAc) to give **22** (39.0 mg, 100%, β/α 31:1); mp 141–146 °C (dec.); $[\alpha]_D^{25}$ +90.6° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.82, (dd, 1 H, *J* 10.8, 3.4 Hz, H-3), 5.70 (d, 1 H, *J* 10.6 Hz, H-1), 5.50 (d, 1 H, *J* 3.4 Hz, H-4), 4.64 (t, 1 H, *J* 10.7 Hz, H-2), 4.27–4.08 (m, 3 H, H-5,6), 2.18, 2.05, 1.83 (3 s, each 3 H, 3 × Ac). HRMS: Calcd for $C_{26}H_{25}NNaO_9S$: *m/z* 550.1148. Found: *m/z* 550.1134.

3,4,6-Tri-O-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl chloride (**23**).—Compound **5** (50.0 mg, 0.10 mmol) was treated with AcCl (0.066 mL, 0.94 mmol), $BF_3 \cdot Et_2O$ (0.044 mL, 0.35 mmol), and ZnI_2 (~ 2 mg) at 50 °C, as described in the preparation of **17**. Workup and purification as described gave **23** (38.1 mg, 97%); $[\alpha]_D^{25}$ +83.5° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.20 (d, 1 H, *J*

3.7 Hz, H-1), 5.37 (t, 1 H, *J* 10.7 Hz, H-3), 5.21 (t, 1 H, *J* 9.5 Hz, H-4), 4.82, 4.65 (ABq, 2 H, *J* 12.2 Hz, OCH_2CCl_3), 2.11, 2.06, 2.04 (3 s, each 3 H, 3 × Ac). HRMS: Calcd for $C_{15}H_{18}Cl_3NNaO_9$ (M – HCl + Na): *m/z* 483.9945. Found: *m/z* 483.9951.

*3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-*D*-glucopyranosyl bromide* (**24**).—A solution of **5** (50.0 mg, 0.10 mmol) in dry $CHCl_3$ (1.5 mL) was treated with AcBr (0.046 mL, 0.63 mmol), $BF_3 \cdot Et_2O$ (0.021 mL, 0.17 mmol), and ZnI_2 (~ 2 mg), at 40 °C for 4 h. Workup and purification was performed as described in the preparation of **18**, to give **24** [29] as a syrup (43.0 mg, 98%); $[\alpha]_D^{25}$ +117.6° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.53 (d, 1 H, *J* 3.7 Hz, H-1), 5.40–5.30 (m, 2 H, H-3, NH), 5.24 (t, 1 H, *J* 9.7 Hz, H-4), 4.81–4.65 (ABq, 2 H, *J* 12.0 Hz, OCH_2CCl_3), 2.10, 2.06, 2.04 (3 s, each 3 H, 3 × Ac).

*Phenyl 3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-2-(2,2,2-trichloroethoxycarbonylamino)-β-*D*-glucopyranoside* (**25**).—A solution of **6** (50.0 mg, 0.10 mmol) in dry CH_2Cl_2 (1.5 mL) was treated with thiophenol (0.033 mL, 0.31 mmol) and $BF_3 \cdot Et_2O$ (0.063 mL, 0.50 mmol) at 40 °C overnight, and worked up as described in the preparation of **19**. The residue was chromatographed (3:2 heptane–EtOAc) to give **25** (47.5 mg, 98%, β/α 1:0). Recrystallization (ether/heptane) gave an analytical sample; mp 149–150 °C; $[\alpha]_D^{25}$ +0.5° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.32 (d, 1 H, *J* 9.0 Hz, NH), 5.28 (t, 1 H, *J* 9.8 Hz, H-3), 5.03 (t, 1 H, *J* 9.8 Hz, H-4), 4.87 (d, 1 H, *J* 10.3 Hz, H-1), 4.82–4.70 (ABq, 2 H, *J* 12.0 Hz, OCH_2CCl_3), 4.24, 4.17 (dd, each 1 H, *J* 12.3, 5.1, 2.7 Hz, H-6), 3.78–3.65 (m, 2 H, H-2,5), 2.08, 2.01 (2 s, 9 H, 3 × Ac). Anal. Calcd for $C_{21}H_{24}Cl_3NO_9$: C, 44.1; H, 4.2; N, 2.5. Found: C, 44.0; H, 4.0; N, 2.4.

*2,3,6-Tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-α-*D*-glucopyranosyl chloride* (**26**).—To a solution of **7** (200 mg, 0.270 mmol) in dry $CHCl_3$ (3 mL) were added dichloromethyl methyl ether (0.099 mL, 1.08 mmol) and $ZnCl_2$ (~ 5 mg, ~ 0.036 mmol), under Ar. The mixture was stirred at 22 °C for 20 h, then applied on an SiO_2 column. The column was eluted with 2:1 heptane–EtOAc to give **26** (161 mg, 91%). Recrystallization (ether/heptane) gave an analytical sample; mp 134–135 °C, lit. [20] mp 120–121 °C; $[\alpha]_D^{25}$ +78° (*c* 1.0, $CHCl_3$), lit. [20] +83.9°; ^1H NMR ($CDCl_3$): δ 6.19 (d, 1 H, *J* 3.9 Hz, H-1), 5.54 (t, 1 H, *J* 9.8 Hz, H-3), 5.34 (dd, 1 H, *J* 3.4, 1.0 Hz, H-4'), 5.11 (dd, 1 H, *J* 10.5, 7.8 Hz, H-2'), 4.95 (dd, 1 H, *J* 10.5, 3.4 Hz, H-3'), 4.92 (dd, 1 H, *J* 10.0, 4.1 Hz, H-2), 4.50 (d, 1 H, *J* 7.8 Hz, H-1'), 2.14, 2.12, 2.08, 2.05, 2.04, 2.03, 1.95 (7 s, each 3 H, 7 × Ac).

*2,3,6-Tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-α-*D*-glucopyranosyl bromide* (**27**).—A solution of **7** (200 mg, 0.27 mmol) in CH_2Cl_2 (4 mL) was treated with AcBr (0.075 mL, 1.01 mmol) and $ZnBr_2$ (~ 20 mg, ~ 0.090 mmol) at 22 °C. The reaction was carefully monitored by TLC (3:2 heptane–EtOAc). After 5 h, the mixture was diluted with CH_2Cl_2 (75 mL), then washed with saturated aq $NaHCO_3$ (40 mL) and water (40 mL). The organic phase was dried (Na_2SO_4), filtered, and concentrated. The residue was chromatographed (SiO_2, 2:1 → 1:2 heptane–EtOAc) to give a mixture of **10** and **13** (~ 1:1, 42 mg, 18%), and **27** (154 mg, 82%). Recrystallization (ether/heptane) of **27** gave an analytical sample; mp 147–148 °C; $[\alpha]_D^{25}$ + 102° (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.53 (d, 1 H, *J* 4.1 Hz, H-1), 5.56 (t, 1 H, *J* 9.7 Hz, H-3), 5.36 (dd, 1 H, *J* 3.4, 1.0 Hz, H-4'), 5.13 (dd, 1 H, *J* 10.5, 7.8 Hz, H-2'), 4.96 (dd, 1 H, *J* 10.4, 3.5 Hz, H-3′), 4.76 (dd, 1 H, *J* 10.0, 4.1 Hz, H-2), 4.51 (d, 1 H, *J* 7.8 Hz, H-1′), 2.16, 2.14, 2.10, 2.07, 2.066, 2.058, 1.97 (7 s, each 3 H, 7 × Ac).

*Phenyl 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-1-thio-β-*D*-glucopyranoside* (**28**).—A solution of **7** (250 mg, 0.34 mmol) in dry $CHCl_3$ (5 mL) was treated with thiophenol (97%, 0.155 mL, 1.69 mmol) and $BF_3 \cdot Et_2O$ (0.046 mL, 0.34 mmol) at 40 °C overnight, and worked up as described in the preparation of **19**. The residue was chromatographed (SiO_2, 5:1 → 3:2 heptane–EtOAc) to give **28** (197 mg, 80%, β/α 32:1). Recrystallization (EtOAc/heptane) gave an analytical sample; mp 169–170 °C, lit. [32] 165–166 °C; $[\alpha]_D^{25}$ −12.7° (*c* 1.0, $CHCl_3$), lit. [32] −18.2; ^1H NMR ($CDCl_3$): δ 5.32 (dd, 1 H, *J* 3.4, 1.0 Hz, H-4′), 5.20 (t, 1 H, *J* 9.1 Hz, H-3), 5.08 (dd, 1 H, *J* 10.4, 7.8 Hz, H-2′), 4.93 (dd, 1 H, *J* 10.4, 3.4 Hz, H-3′), 4.88 (dd, 1 H, *J* 10.0, 9.2 Hz, H-2), 4.66 (d, 1 H, *J* 10.1 Hz, H-1), 4.51 (dd, 1 H, *J* 12.0, 2.0 Hz, H-6), 4.46 (d, 1 H, *J* 7.8 Hz, H-1′), 3.85 (bt, *J* 6.9 Hz, H-5′), 3.62 (m, 1 H, H-5), 2.12, 2.08, 2.07, 2.02, 2.017, 2.01, 1.93 (7 s, each 3 H, 7 × Ac).

*6-*O*-Acetyl-2,3-di-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-*D*-galactopyranosyl)-α-*D*-galactopyranosyl bromide* (**29**).—A solution of **8** (100 mg, 0.12 mmol) in CH_2Cl_2 (2 mL) was treated with AcBr (0.026 mL, 0.35 mmol) and $ZnBr_2$ (~ 3 mg, ~ 0.013 mmol) as described in the preparation of **27**. The crude product was chromatographed (SiO_2, 5:1 → 3:2 heptane–EtOAc) to give **29** [18] (86.7 mg, 92%); $[\alpha]_D^{25}$ +201.8° (*c* 2.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.89 (d, 1 H, *J* 3.9 Hz, H-1), 5.73 (dd, 1 H, *J* 10.7, 2.7 Hz, H-3), 5.60 (dd, 1 H, *J* 10.8, 3.9 Hz, H-2), 5.48 (dd, 1 H, *J* 3.2, 1.4 Hz, H-4′), 5.43 (dd, 1 H, *J* 11.0, 3.2 Hz, H-3′), 5.25 (dd, 1 H, *J* 11.0, 3.6 Hz, H-2′), 5.11 (d, 1 H, *J* 3.7 Hz, H-1′), 3.82 (dd, 1 H, *J* 11.0, 7.5 Hz, H-6), 3.54 (dd, 1 H, *J* 11.0, 6.3 Hz, H-6), 2.15, 2.11, 1.99, 1.76 (4 s, 15 H, 5 × Ac).

*Phenyl 6-*O*-acetyl-2,3-di-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-*D*-galactopyranosyl)-1-thio-β-*D*-galactopyranoside* (**30**).—A solution of **8** (800 mg, 0.92 mmol) in 1:1 $ClCH_2CH_2Cl$–toluene (20 mL) was treated with thiophenol (97%, 0.379 mL, 3.70 mmol) and $BF_3 \cdot Et_2O$ (0.127 mL, 0.39 mmol) at 65 °C for 7 h, and worked up as described in the preparation of **19**. The residue was chromatographed (SiO_2, 4:3 heptane–EtOAc) to give **30** [18] (735 mg, 93%, β/α ~ 50:1).

*6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-α-*D*-glucopyranosyl chloride* (**31**).—To a cold (ice–water bath) solution of **3** (100 mg, 0.16 mmol) in dry $CHCl_3$ (3 mL) under Ar were added AcCl (0.066 mL, 0.93 mmol) and $ZnCl_2$ (~ 3 mg, ~ 0.022 mmol). The mixture was stirred at 0 °C for 2 h, and at 22 °C for 4 h. The mixture was chromatographed (SiO_2, 20:15:1 → 15:15:1 heptane–CH_2Cl_2–EtOAc) to give **31** (63.4 mg, 80%); $[\alpha]_D^{25}$ +85.7° (*c* 1.0, $CHCl_3$); lit. [33] $[\alpha]_D$ +90° ($CHCl_3$), mp 62–63 °C; ^1H NMR ($CDCl_3$): δ 6.03 (d, 1 H, *J* 3.7 Hz, H-1), 5.03–4.56 (m, 6 H, $PhCH_2$), 4.29 (d, 2 H, *J* 3.2 Hz, H-6), 4.16 (dt, 1 H, *J* 10.0, 3.0 Hz, H-5), 4.07 (t, 1 H, *J* 9.1 Hz, H-3), 3.72 (dd, 1 H, *J* 9.3, 3.8 Hz, H-2), 3.55 (dd, 1 H, *J* 10.1, 9.0 Hz, H-4), 2.03 (s, 3 H, Ac); ^{13}C NMR: δ 170.5, 138.3, 137.6, 137.3, 92.8, 81.3, 79.9, 76.1, 75.9, 75.2, 73.0, 71.8, 62.3, 20.8.

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