0 °C and a 3 N NaOH solution (21 mL) was added. The aqueous phase was saturated with K_2CO_3, decanted, and extracted three times with diethyl ether. The combined organic phases collected were dried over Na_2SO_4 and concentrated under reduced pressure. The oily residue obtained was fractionally distilled (44–47 °C, 0.1 mmHg) to yield α-methylbenzyl alcohol (2.8 g, 72%). Preparative HPLC purification achieved a GC purity of 99%, $[\alpha]^{22}_D$ +2.96° (neat), 7% ee.[11]

Registry No. 3, 7785-70-8; 4, 6712-78-3; 5, 19894-97-4; 7, 84619-19-2; 8, 84525-73-5; 9, 125827-38-5; (+)-myrtenal, 23727-16-4; (−)-myrtenyl bromide, 55527-89-4; 1,3-dithiane, 505-23-7; 1-methylcyclohexene, 591-49-1; (1*S*,2*S*)-*trans*-2-methylcyclohexanol, 15963-37-8; (1*R*,2*R*)-*trans*-2-methylcyclohexanol, 19043-03-9; 2-methyl-2-butene, 513-35-9; (*R*)-3-methyl-2-butanol, 1572-93-6; (*S*)-3-methyl-2-butanol, 1517-66-4; 2-methylcyclohexanone, 583-60-8; *cis*-2-methylcyclohexanol, 7443-70-1; *trans*-2-methylcyclohexanol, 7443-52-9; 4-*tert*-butylcyclohexanone, 98-53-3; *cis*-4-*tert*-butylcyclohexanol, 937-05-3; *trans*-4-*tert*-butylcyclohexanol, 21862-63-5; acetophenone, 98-86-2; (+)-α-methylbenzyl alcohol, 1517-69-7; *cis*-2-butene, 590-18-1; (*R*)-2-butanol, 14898-79-4; 2,3-dimethyl-1-butene, 563-78-0; (*S*)-2,3-dimethyl-1-butanol, 15071-36-0; 1-methylcyclopentene, 693-89-0; (1*S*,2*S*)-*trans*-2-methylcyclopentanol, 39947-48-3.

The in Situ Activation of Thioglycosides with Bromine: An Improved Glycosylation Method†

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A one-step conversion of thioglycosides into 1,2-*trans*- or 1,2-*cis*-*O*-glycosides was accomplished, in situ, by treatment with bromine in the presence of a glycosyl acceptor and a promoter such as silver triflate or mercuric cyanide. This mild "one-pot" procedure gives *O*-glycosides in excellent yields with high stereochemical control, even with unreactive and hindered glycosyl acceptors. The reaction conditions are compatible with various protecting groups such as acetates, benzoates, benzyl ethers, *N*-phthalimido groups, and benzylidene acetals.

Introduction

Thioglycosides are stable and versatile derivatives that allow flexible strategies for the synthesis of complex oligosaccharides.[1] As glycosyl donors thioglycosides can be activated for glycosylations by conversion into glycosyl halides, usually under mild conditions that are compatible with sensitive protecting groups such as acetals. The glycosyl halides may then be employed in glycoside synthesis using "halophilic" reagents such as silver or mercury salts or tetraethylammonium bromide.[1] In some cases the preparation of glycosyl halides from thioglycosides, and their subsequent utilization in glycosylations, has been difficult due to low yields and side reactions.[1,2]

Alternatively, the *direct* glycosylation of alcohols with thioglycosides can be accomplished using various thiophilic reagents as promoters.[1] Promotion by methyl triflate[1,3] or dimethyl(methylthio)sulfonium triflate[1,4] (DMTST) is well documented and gives excellent results, but methyl triflate is a potential carcinogen and is also highly toxic, whereas DMTST is prepared using carcinogenic methylating agents. Benzeneselenyl triflate,[5] which should also be treated as toxic, suffers from a lack of stereoselectivity when used with glycosyl donors that have nonparticipating groups at O-2. Nitrosyl tetrafluoroborate,[6] a powerful activating agent, has been reported[7] to give irreproducible yields, especially in glycosylations of unreactive alcohols. More attractive methods for direct glycosylations with thioglycosides include promotion by methylsulfenyl triflate[7] (prepared in situ from methylsulfenyl bromide and silver triflate) and transformation of the thioglycosides into bromides using a copper(II) bromide/tetrabutylammonium bromide complex followed by in situ glycosylation using suitable promoters.[8]

As part of a study[9] to map the combining sites of antibodies against the *Brucella* A polysaccharide antigen using synthetic oligosaccharides,[10] the glycosylation of the alcohol **3** with the thioglycoside **1**[10] was envisaged as a route to the target trisaccharide **4** (Scheme I). Activation of the thioglycoside **1** with methylsulfenyl triflate (prepared in situ) was considered an attractive alternative to the hazardous methyl triflate[3] previously used[10] in similar syntheses. When the glycosylation of **3** was attempted using silver triflate and crude methylsulfenyl bromide (prepared as described[7] by reaction of dimethyl disulfide and bromine in 1,2-dichloroethane for 4 h) as promoters, the *bromide* **2** was isolated unexpectedly in 27–37% yields, in addition to the expected trisaccharide **4** (34–47%). Though an excess of silver triflate (1.5 equiv relative to **1**) was used[7] no further change in the product distribution was observed after ~30 min, as determined by TLC.[11] The formation of the bromide **2** was not detected in the

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(2) In one case preparation of a glycosyl bromide by treatment of a thioglycoside with bromine resulted in the formation of the corresponding *benzyl* glycoside as a byproduct in the subsequent glycosylation. The benzyl glycoside was presumed to derive from a reaction between the glycosyl bromide, moisture, and benzyl bromide (formed from toluene used for concentration of the glycosyl bromide). In another case, cleavage of a *p*-methoxybenzyl ether (Classon, B.; Garegg, P. J.; Samuelsson, B. *Acta Chem. Scand.* **1984**, *B38*, 419) upon treatment of a thioglycoside with bromine was assumed to account for the diversity of products obtained. Kihlberg, J.; Eichler, E.; Bundle, D. R., unpublished results.

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(11) This was probably due to deactivation of the silver triflate by sulfides, such as methyl ethyl disulfide, which are formed in the reaction. In fact, the silver triflate promoted reaction of **3** and the glycosyl bromide **2** was complete in less than 5 min (66% of **4** was isolated), whereas the addition of dimethyl disulfide (1 equiv relative to **2**) yielded a mixture of **4** (52%) and unreacted **2** (15%) at equilibrium (reached after ~30 min, TLC).

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Table I. Reaction Conditions and Products in the Glycosylations Performed by the in Situ Activation of Thioglycosides with Bromine

entry	donor (D)	acceptor (A)	promoter (P)	molar ratio D/A/P	reaction time	product	yield,[a,b] %
1	1	3	AgOTf[c]	0.8/1.0/3.0	30 min	4	68 (55–70[d])
						5	14 (10–15[d])
2	6	7	AgOTf + TMU[e,f]	1.2/1.0/3.0	75 min	8	88 (74–85[16,17])
3	9	10	AgOTf[c]	1.1/1.0/3.0	45 min	11	76 (62–80[18])
4	9	10	$Hg(CN)_2$[c]	1.1/1.0/2.0	24 h	11	46
5	12	13	AgOTf[c]	1.25/1.0/4.0	2 h	14	64 (5[20])
6	12	13	AgOTf + TMU[c,e]	1.25/1.0/4.0	3 h	15	32
7	16	17	AgOTf[c]	1.25/1.0/3.0	50 min	18	94 (70[22])

[a] Isolated yields based on the lesser of the two reactants. [b] The yields in parentheses were either obtained by us using an alternative method for glycosylation or were previously reported in the literature for similar syntheses. [c] In dichloromethane. [d] Obtained from 1 and 3 with promotion by methylsulfenyl triflate[7] or methyl triflate[3] or from 2 and 3 with silver triflate as promoter. [e] TMU: 2 equiv of 1,1,3,3-tetramethylurea was added before the addition of bromine. [f] In toluene.

reaction between 1 and 3 when the methylsulfenyl bromide was prepared overnight. This method of preparation for methylsulfenyl bromide also resulted in a slower conversion of 1 into 2 (~50% of 1 was consumed after 1 h using 3 equiv of methylsulfenyl bromide). We therefore concluded that the formation of methylsulfenyl bromide, from dimethyl disulfide and bromine, was incomplete after 4 h and that 2 was formed from 1 by reaction with remaining amounts of bromine.

Based upon these observations it occurred to us that addition of bromine to a solution of a thioglycoside, a glycosyl acceptor, and a suitable promoter should initially convert the thioglycoside into a glycosyl bromide that would subsequently react in situ with the glycosyl acceptor under influence of the promoter. This was indeed found to be the case, and this paper describes the successful application of the procedure to the synthesis of a variety of α- and β-linked oligosaccharides.

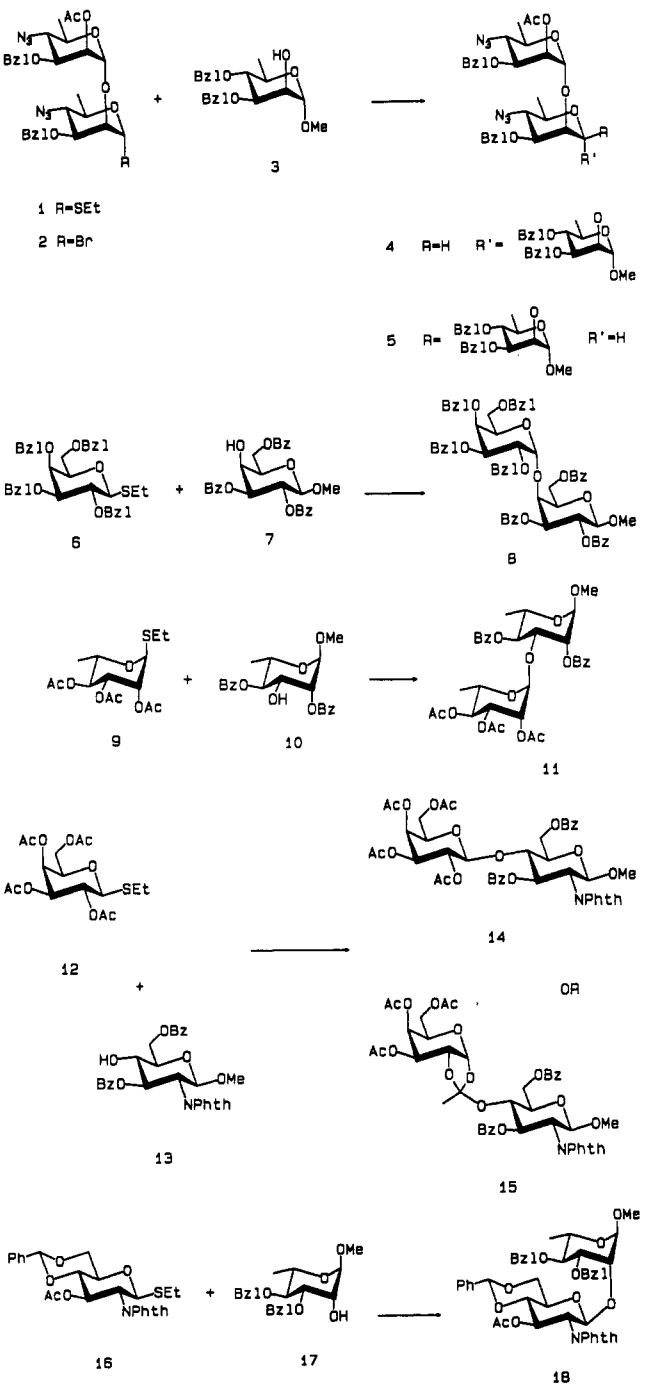
Results and Discussion

Activation of 1[10] with bromine and in situ glycosylation of 3 using silver triflate as promoter gave the α- and β-linked trisaccharides 4 and 5 in 68 and 14% yields, respectively (Scheme I and Table I). In comparison, almost identical yields of 4 (64–70%) and 5 (10–15%) were obtained when the reaction between 1 and 3 was promoted by methylsulfenyl triflate[7] (generated in situ or prepared separately) or when 2 and 3 were reacted using silver triflate as promoter. Promotion by methyl triflate[3] gave a lower yield of 4 (55%), and no formation of products was observed with dimethyl(methylthio)sulfonium tetrafluoroborate[4a,12] (DMTSB) as promoter.

The syntheses of the disaccharides 8, 11, 14, and 18 (Scheme I) provide further examples of the versatility of bromine as an activator of thioglycosides in the direct glycosylations of alcohols (Table I). The model compounds were chosen for their occurrence in glycoconjugates of biological importance: in glycolipids functioning as receptors for uropathogenic *E. coli* and bacterial toxins[13] (8), in the lipopolysaccharide *O*-antigens of *Shigella flexneri*[9,14] (11 and 18), and in N-linked glycoproteins[15] (14).

Initial attempts to prepare the galabioside 8[16] by α-galactosidation of the alcohol 7[16] with the per-*O*-benzylated thioglycoside 6, using silver triflate as promoter in dichloromethane, resulted in a mixture of α- and β-linked disaccharides (~5:1 as determined by ^{1}H NMR). Addition of 1,1,3,3-tetramethylurea to the reaction mixture, and substitution of toluene for dichloromethane as solvent,

Scheme I



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afforded the galabioside **8** stereoselectively in 88% yield. Lower yields (74–85%) were obtained by others in syntheses of galabiosides from galactosyl halides or imidates even though larger excesses of the galactosyl donors were often employed.[16,17]

The 3-*O*-α-L-rhamnopyranosyl-α-L-rhamnopyranoside **11**,[18] exhibiting a 1,2-trans glycosidic linkage, was prepared in 76% yield from **10**[18] and the per-*O*-acetylated thioglycoside **9** (1.1 equiv) using silver triflate as promoter. The use of mercuric cyanide as promoter produced **11** in 46% yield. In comparison, when 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl bromide was coupled with **10** using a donor:acceptor ratio of 1.4:1 62–80% yields of **11** were reported.[18]

The lactosamine derivative **14** was prepared in 64% yield from the galactosyl donor **12**[19] and the 3,6-di-O-benzoylated acceptor **13** with silver triflate as promoter. Interestingly, addition of 1,1,3,3-tetramethylurea (2 equiv, relative to **13**) before the addition of bromine resulted in the formation of the orthoester **15** (32% yield) as the only product. These results should be viewed in relation to the previously reported[15] low reactivity of HO-4 of glucosamine derivatives. When acyl groups were used to protect O-3 and O-6 of the glucosamine, glycosylations of HO-4 by 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide were accomplished in only 5% yield.[20] On the other hand, if alkyl groups were employed at O-3 and O-6 of the glucosamine acceptor, improved yields (60–85%) of the desired lactosamines resulted.[20,21]

The glycosylation of HO-2 of a 3,4-di-O-benzylated rhamnopyranoside with 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranosyl bromide using silver triflate as promoter has been reported[22] to proceed in 70% yield. In situ activation with bromine of the selectively protected thioglycoside **16**, carrying an acid labile 4,6-*O*-benzylidene group, enabled the coupling to HO-2 of **17**[23] to be performed in 94% yield using a silver triflate as promoter.

In conclusion, activation of thioglycosides with bromine and glycosylation, in situ, with silver triflate as promoter has been shown to provide a practical and convenient synthesis of *O*-glycosides in yields equivalent to, or greater than, those obtained with alternative methods. In the presence of a participating group (i.e. *O*-acetyl or *N*-phthalimido) at C-2 of the glycosyl donor 1,2-*trans*-glycosides were formed exclusively, whereas with a nonparticipating group (i.e. *O*-glycosyl or *O*-benzyl) the more stable axial (α) glycosides were obtained with high or complete stereoselectivity. Furthermore, the glycosylations were performed with low donor:acceptor ratios (1.1–1.25:1) and proceded rapidly at room temperature.

Experimental Section

General. Bruker AM 200 and AM 500 spectrometers were used to record ^1H and ^{13}C NMR spectra for solutions in $CDCl_3$, utilizing the residual $CHCl_3$ resonance (δ 7.24) as internal standard. First-order chemical shifts (expressed relative to Me_4Si) and coupling constants were obtained from one-dimensional spectra, and assignments of proton resonances were based on COSY and NOE experiments. Optical rotations were measured with a Perkin-Elmer 243 polarimeter. Melting points were determined with a Büchi 535 melting point apparatus and are uncorrected.

TLC was performed on silica gel 60 F_{254} (Merck) with detection by UV light and charring with sulfuric acid. Silica gel 60 (Merck, 230–400 mesh) and analytical reagent-grade solvents (BDH) were used for column chromatography. Organic solutions were dried over Na_2SO_4.

Ethyl 2-*O*-(2-*O*-acetyl-4-azido-3-*O*-benzyl-4,6-dideoxy-α-D-mannopyranosyl)-4-azido-3-*O*-benzyl-4,6-dideoxy-1-thio-α-D-mannopyranoside[10] (**1**), methyl 2,3,6-tri-*O*-benzoyl-β-D-galactopyranoside[16] (**7**), methyl 2,4-di-*O*-benzoyl-α-L-rhamnopyranoside[18] (**10**), ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside[19] (**12**), and methyl 3,4-di-*O*-benzyl-α-L-rhamnopyranoside[23] (**17**) were prepared according to literature methods. Methyl 3,4-di-*O*-benzyl-α-D-rhamnopyranoside (**3**) and methyl 3,6-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**13**) were prepared as described for compound **17**[23] and *tert*-butyl 3,6-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranoside,[24] respectively.

General Procedure for Glycosylations with Thioglycosides Activated in Situ by Bromine. A solution of the thioglycoside (120–190 μmol, cf. Table I) and the glycosyl acceptor (150 μmol) in an anhydrous solvent (3 mL) was stirred for 4 h in the presence of powdered molecular sieve (4 Å, 300 mg). The promoter (300 μmol, cf. Table I) and, in the preparation of **8**, 1,1,3,3-tetramethylurea (36 μL, 300 μmol), were added followed after 20 min by bromine (5.7 μL, 110 μmol). More promoter was added (cf. Table I) when necessary (TLC) to give complete consumption of the reactants. All operations were carried out at room temperature under a positive pressure of dry nitrogen and in the dark. The mixture was neutralized with triethylamine (63 μL, 450 μmol) and filtered through Celite, and the flask and Celite were washed with dichloromethane (10 mL). The solution was washed with saturated aqueous sodium hydrogencarbonate (5 mL), dried, and concentrated. The residue was subjected to column chromatography on silica gel.

2-*O*-(2-*O*-Acetyl-4-azido-3-*O*-benzyl-4,6-dideoxy-α-D-mannopyranosyl)-4-azido-3-*O*-benzyl-4,6-dideoxy-α-D-mannopyranosyl bromide (2): $[\alpha]^{25}_D$ +153° (*c* 0.76, $CHCl_3$); NMR δ_H (500.14 MHz) 6.27 (1 H, bs, H-1), 5.34 (1 H, dd, J = 3.0, 2.0 Hz, H-2′), 4.70 (1 H, d, J = 2.0 Hz, H-1′), 4.15 (1 H, dd, J = 10.2, 2.9 Hz, H-3), 3.89 (1 H, dd, J = 2.7, 1.9 Hz, H-2), 3.71 (1 H, dd, J = 9.9, 3.2 Hz, H-3′), 3.68 (1 H, dq, J = 10.2, 6.2 Hz, H-5), 3.52 (1 H, dq, J = 10.1, 6.2 Hz, H-5′), 3.39 (1 H, t, J = 10.0 Hz, H-4′), 3.36 (1 H, t, J = 10.2 Hz, H-4), 2.10 (3 H, s, OAc), 1.32 (3 H, d, J = 6.1 Hz, H-6), 1.29 (3 H, d, J = 6.0 Hz, H-6′); δ_C (125.76 MHz) 99.9 ($^1J_{C,H}$ = 172 Hz, C-1′), 87.1 ($^1J_{C,H}$ = 182 Hz, C-1). A satisfactory elemental analysis could not be obtained for **2**, but the compound was pure according to TLC (SiO_2, 1:4 EtOAc–hexane) and ^1H NMR analysis.

Methyl 2-*O*-[2-*O*-(2-*O*-Acetyl-4-azido-3-*O*-benzyl-4,6-dideoxy-α-D-mannopyranosyl)-4-azido-3-*O*-benzyl-4,6-dideoxy-α- and -β-D-mannopyranosyl]-3,4-di-*O*-benzyl-α-D-rhamnopyranoside (4 and 5). Compounds **4** and **5** were obtained after column chromatography with hexane–ethyl acetate (8:1 followed by 5:1) as eluant. Compound **4**: $[\alpha]^{25}_D$ +57° (*c* 0.59, $CHCl_3$); NMR δ_H (500.14 MHz) 5.40 (1 H, dd, J = 2.9, 1.7 Hz, H-2″), 5.06 (1 H, d, J = 1.6 Hz, H-1′), 4.85 (1 H, d, J = 1.7 Hz, H-1″), 4.53 (1 H, d, J = 1.5 Hz, H-1), 3.95 (1 H, bt, J = 2.4 Hz, H-2′), 3.90 (1 H, bt, J = 2.4 Hz, H-2), 3.81 (1 H, dd, J = 9.3, 2.8 Hz, H-3), 3.78 (1 H, dd, J = 9.8, 3.5 Hz, H-3″), 3.77 (1 H, J = 9.7, 3.1 Hz, H-3′), 3.63 (1 H, dq, J = 9.4, 6.1 Hz, H-5), 3.55, 3.54 (each 1 H, each dq, J = 10.0, 6.1 Hz and J = 10.3, 6.1 Hz, H-5′,5″), 3.36, 3.35 (each 1 H, each t, J = 10.0 Hz each, H-4′,4″), 3.30 (1 H, t, J = 9.3 Hz, H-4), 3.29 (3 H, s, MeO), 2.09 (3 H, s, AcO), 1.29 (3 H, d, J = 6.3 Hz, H-6), 1.28, 1.18 (each 3 H, each d, J = 6.0 and J = 6.1 Hz, H-6′,6″); δ_C (125.76 MHz) 100.1, 98.8, 99.2 ($^1J_{C,H}$ = 175, 169, 171 Hz, C-1,1′,1″). Anal. Calcd for $C_{49}H_{58}O_{12}N_6$: C, 63.8; H, 6.33; N, 9.10. Found: C, 64.1; H, 6.36; N, 8.91.

Compound **5**: $[\alpha]^{25}_D$ −14° (*c* 0.95, $CHCl_3$); NMR δ_H (500.14 MHz) 5.49 (1 H, dd, J = 2.9, 1.4 Hz, H-2″), 5.35 (1 H, d, J = 1.1 Hz, H-1″), 4.65 (1 H, bs, H-1), 4.45 (1 H, bs, H-1′), 4.29 (2 H, bd, J = 2.0 Hz, H-2,2′), 4.10 (1 H, dq, J = 10.1, 6.0 Hz, H-5″), 3.98

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(1 H, dd, J = 10.0, 3.3 Hz, H-3″), 3.83 (1 H, dd, J = 9.0, 3.8 Hz, H-3), 3.68 (1 H, dq, J = 9.4, 6.3 Hz, H-5), 3.57 (1 H, t, J = 9.2 Hz, H-4), 3.56 (1 H, t, J = 9.8 Hz, H-4′), 3.43 (1 H, t, J = 10.0 Hz, H-4″), 3.40 (1 H, dd, J = 9.7, 2.3 Hz, H-3′), 3.33 (3 H, s, MeO), 3.15 (1 H, dq, J = 9.7, 6.0 Hz, H-5′), 2.04 (3 H, s, AcO), 1.39 (3 H, d, J = 6.4 Hz, H-6″), 1.38 (3 H, d, J = 6.1 Hz, H-6), 1.31 (3 H, d, J = 6.0 Hz, H-6′); δ_C (125.76 MHz) 98.0, 97.0 ($^1J_{C,H}$ = 166, 178 Hz, C-1,1″), 97.1 ($^1J_{C,H}$ = 153 Hz, C-1′). Anal. Calcd for $C_{49}H_{58}O_{12}N_6$: C, 63.8; H, 6.33; N, 9.10. Found: C, 63.8; H, 6.35; N, 8.88.

Ethyl 2,3,4,6-Tetra-*O*-benzyl-1-thio-β-D-galactopyranoside (6). A solution of **12**[19] (580 mg, 1.48 mmol) in dichloromethane–methanolic 25 mM sodium methoxide (1:1, 15 mL) was stirred for 19 h at room temperature, neutralized with acetic acid (6.0 μL), and concentrated. Sodium hydride dispersion (50% in oil, 570 mg, 12 mmol) was slowly added to a solution of the residue and benzyl bromide (1.06 mL, 8.9 mmol) in dry *N*,*N*-dimethylformamide (10 mL) at 0 °C. The mixture was allowed to attain room temperature, and after 16 h methanol (5 mL) was added to destroy excess benzyl bromide. After 45 min the solution was neutralized with acetic acid, diluted with dichloromethane (50 mL), washed with water (2 × 50 mL), dried, and concentrated. Column chromatography (hexane–ethyl acetate, 10:1) of the residue gave **6** as a syrup (780 mg, 90%): $[\alpha]^{25}_D$ −5.3° (*c* 1.4, $CHCl_3$); NMR δ_H (200.13 MHz) 4.42 (1 H, d, J = 9.6 Hz, H-1), 3.94 (1 H, d, J = 2.8 Hz, H-4), 3.81 (1 H, t, J = 9.4 Hz, H-2), 1.28 (3 H, t, J = 7.4 Hz, SCH_2CH_3). Anal. Calcd for $C_{36}H_{40}O_5S$: C, 73.9; H, 6.89. Found: C, 73.9; H, 6.90.

Ethyl 2,3,4-Tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside (9). Ethanethiol (3.0 mL, 40.5 mmol) and boron trifluoride etherate (2.5 mL, 20.3 mmol) were added to a stirred solution of tetra-*O*-acetyl-L-rhamnopyranose[25] (5.0 g, 15.1 mmol) in dichloromethane (100 mL) at 0 °C containing molecular sieve (4 Å, 0.5 g). After 10 h triethylamine (5.0 mL, 35.8 mmol) was added dropwise, and the mixture was filtered and concentrated. Column chromatography (hexane–ethyl acetate, 3:1) of the residue gave **9** (4.7 g, 65%): mp 69–70 °C; $[\alpha]^{25}_D$ −115° (*c* 2.0, $CHCl_3$); NMR δ_H (200.13 MHz) 5.31 (1 H, dd, J = 3.4, 1.6 Hz, H-2), 5.20 (1 H, dd, J = 10.0, 3.4 Hz, H-3), 5.17 (1 H, bs, H-1), 5.06 (1 H, t, J = 9.7 Hz, H-4), 4.20 (1 H, dq, J = 9.4, 6.2 Hz, H-5), 2.13, 2.03, 1.96 (each 3 H, s, OAc), 1.26 (3 H, t, J = 7.4 Hz, SCH_2CH_3), 1.20 (3 H, d, J = 6.2 Hz, H-6). Anal. Calcd for $C_{14}H_{22}O_7S$: C, 50.3; H, 6.63. Found: C, 49.9; H, 6.74.

Methyl 4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-3,6-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (14). Compound **14** was obtained after column chromatography with toluene–ethyl acetate (4:1) as eluant: $[\alpha]^{25}_D$ +60° (*c* 1.1, $CHCl_3$); NMR δ_H (500.14 MHz) 6.06 (1 H, dd, J = 10.7, 8.7 Hz, H-3), 5.37 (1 H, d, J = 8.5 Hz, H-1), 5.07 (1 H, bd, J = 3.9 Hz, H-4′), 5.06 (1 H, dd, J = 10.4, 7.9 Hz, H-2′), 4.77 (1 H, dd, J = 11.3, 2.0 Hz, H-6), 4.77 (1 H, dd, J = 10.4, 3.5 Hz, H-3′), 4.56 (1 H, d, J = 7.9 Hz, H-1′), 4.42 (1 H, dd, J = 11.9, 4.9 Hz, H-6), 4.38 (1 H, dd, J = 10.7, 8.5 Hz, H-2), 4.11 (1 H, dd, J = 9.8, 8.8 Hz, H-4), 4.01 (1 H, ddd, J = 9.9, 4.8, 1.9 Hz, H-5), 3.48 (1 H, dd, J = 10.9, 8.2 Hz, H-6′), 3.43 (3 H, s, MeO), 3.38 (1 H, dd, J = 10.9, 5.5 Hz, H-6′), 3.33 (1 H, dd, J = 8.0, 5.6 Hz, H-5′), 1.98, 1.93, 1.89, 1.87 (each 3 H, s, AcO). Anal. Calcd for $C_{43}H_{43}O_{18}N$: C, 59.9; H, 5.03; N, 1.63. Found: C, 60.1; H, 5.15; N, 1.51.

3,4,6-Tri-*O*-acetyl-α-D-galactopyranose 1,2-(methyl 3,6-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranosid-4-yl orthoacetate) (15): $[\alpha]^{25}_D$ +108° (*c* 0.67, $CHCl_3$); NMR δ_H (500.14 MHz) 6.00 (1 H, dd, J = 11.0, 8.7 Hz, H-3), 5.61 (1 H, d, J = 4.6 Hz, H-1′), 5.35 (1 H, d, J = 8.6 Hz, H-1), 5.21 (1 H, t, J = 2.8 Hz, H-4′), 4.68 (1 H, dd, J = 11.8, 2.4 Hz, H-6), 4.66 (1 H, dd, J = 6.6, 3.0 Hz, H-3′), 4.57 (1 H, dd, J = 12.0, 4.9 Hz, H-6), 4.42 (1 H, dd, J = 10.9, 8.5 Hz, H-2), 4.08 (1 H, dd, J = 6.7, 4.6 Hz, H-2′), 4.04–4.00 (2 H, m, H-4,5′), 3.93 (1 H, ddd, J = 9.7, 4.9, 2.3 Hz, H-5), 3.89 (1 H, dd, AB-type, J = 11.4, 6.4 Hz, H-6′), 3.86 (1 H, dd, AB-type, J = 11.4, 6.9 Hz, H-6′), 3.41 (3 H, s, MeO), 1.99, 1.96, 1.78 (each 3 H, s, AcO), 1.56 (3 H, s, CH_3CO_3); δ_C (125.76 MHz) 122.3 (CH_3CO_3), 25.8 (CH_3CO_3). Anal. Calcd for $C_{43}H_{43}O_{18}N$: C, 59.9; H, 5.03; N, 1.63. Found: C, 59.9; H, 4.92; N, 1.92.

Ethyl 3-*O*-Acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (16). Treatment of ethyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside[26] (175 mg, 396 μmol) with acetic anhydride (2.5 mL) and pyridine (2.5 mL) for 18 h, concentration, and column chromatography (hexane–ethyl acetate, 3:1) of the residue gave **16** (169 mg, 88%): mp 166–167 °C; $[\alpha]^{25}_D$ −4.8° (*c* 1.1, $CHCl_3$); NMR δ_H (500.14 MHz) 5.90 (1 H, bt, J = 9.5 Hz, H-3), 5.56 (1 H, d, J = 10.4 Hz, H-1), 5.53 (1 H, s, PhC*H*), 4.35 (1 H, t, J = 10.3 Hz, H-2), 1.88 (3 H, s, OAc), 1.18 (3 H, t, J = 7.4 Hz, SCH_2CH_3). Anal. Calcd for $C_{25}H_{25}O_7NS$: C, 62.1; H, 5.21; N, 2.90. Found: C, 62.1; H, 5.11; N, 3.06.

Methyl 2-*O*-(3-*O*-Acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (18). Compound **18** was obtained after column chromatography with hexane–ethyl acetate (2.5:1) as eluant: $[\alpha]^{25}_D$ −12° (*c* 0.81, $CHCl_3$); NMR δ_H (500.14 MHz) 6.11 (1 H, bt, J = 9.6 Hz, H-3′), 5.52 (1 H, s, PhC*H*), 5.42 (1 H, d, J = 8.3 Hz, H-1′), 4.57 (1 H, d, J = 1.3 Hz, H-1), 4.41 (1 H, dd, J = 10.3, 8.7 Hz, H-2′), 4.36 (1 H, dd, J = 10.3, 4.2 Hz, H-6′), 3.80–3.69 (3 H, m, H-4′, 5′, 6′), 3.63 (1 H, bt, J = 2.1 Hz, H-2), 3.54 (1 H, dd, J = 9.5, 2.8 Hz, H-3), 3.46 (1 H, dq, J = 9.5, 6.2 Hz, H-5), 3.21 (3 H, s, MeO), 2.97 (1 H, t, J = 9.5 Hz, H-4), 1.92 (3 H, s, AcO), 1.18 (3 H, d, J = 6.3 Hz, H-6). Anal. Calcd for $C_{44}H_{45}O_{12}N$: C, 67.8; H, 5.82; N, 1.80. Found: C, 68.0; H, 5.80; N, 1.78.

Registry No. **1**, 115196-80-0; **2**, 125519-97-3; **3**, 125519-98-4; **4**, 125519-99-5; **5**, 125520-00-5; **6**, 125411-99-6; **7**, 34820-01-4; **8**, 117149-98-1; **9**, 125520-01-6; **10**, 88331-96-8; **11**, 88337-87-5; **12**, 55722-49-1; **13**, 86263-38-9; **14**, 125520-02-7; **15**, 125520-03-8; **16**, 125520-04-9; **16** deacetyl derivative, 99409-33-3; **17**, 69558-07-2; **18**, 125520-05-0; tetra-*O*-acetyl-L-rhamnopyranose, 30021-94-4.

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