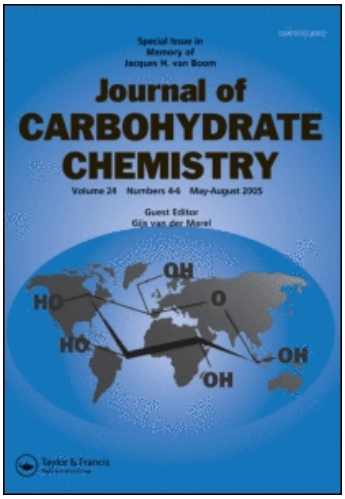

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PARTIAL SUBSTITUTION OF THIOGLYCOSIDES BY PHASE TRANSFER CATALYZED BENZOYLATION AND BENZYLATION.

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ABSTRACT

Partial substitution by phase transfer catalysis giving monobenzoylated and monobenzylated products from 2,3- and from 4,6-diols in ethyl 1-thio-D-hexopyranosides with the β-*gluco*-, β-*galacto*- and α-*manno*-configurations are described. Two disaccharide thioglucoside diols with either the 2',3'-hydroxyl groups or the 4',6'-hydroxyl groups free were included in the study. Good yields of monosubstitution products are obtained after chromatographic separations, making this a useful method for obtaining protected thioglycosides with a single hydroxyl group for further manipulations.

INTRODUCTION

In early studies on phase transfer catalyzed (PTC)[1-4] alkylation and esterification of carbohydrate diols we found, that by contradistinction to partial substitution obtained either by use of limited reaction time or reagent, the PTC method gave high yields of monosubstituted products in addition to some starting material.[5,6] Since unwanted disubstitutions proceeded at a much slower rate than monosubstitution, their products could largely be avoided. This has subsequently been confirmed by numerous workers.[7,8] The compounds thus easily obtained by PTC, with a single free hydroxyl

group, are useful intermediates for further synthesis. In block synthesis of oligosaccharides making use of thioglycosides as intermediates,[9] benzoyl and benzyl groups have been found to be useful intermediates. It was therefore of interest to see if PTC benzoylation and benzylation would yield the same advantageous results on thioglycosides as in *O*-glycosides.

RESULTS AND DISCUSSION

The PTC systems investigated were benzoyl chloride- tetrabutylammonium hydrogensulphate-sodium hydroxide in dichloromethane-water at 0-5 °C and benzyl bromide-tetrabutylammonium hydrogensulphate-sodium hydroxide in dichloromethane-water at reflux temperature. The monosaccharide diols investigated were the following: ethyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside, ethyl 2,3-di-*O*-benzyl-1-thio-β-D-glucopyranoside, the corresponding two β-D-galactopyranosides, and the two corresponding α-D-mannopyranosides. The 4,6-*O*-benzylidene compounds were made starting with thioglycosidation[10] of the penta-*O*-acetylpyranosides, followed by Zemplén deacetylation and acetalization.[11] The 2,3-di-*O*-benzyl ethers were then obtained by benzylation followed by removal of the benzylidene groups with trifluoroacetic or acetic acid.

Results of the partial PTC benzylations and benzoylations are shown in Table 1. With notable exception of the results obtained in the galactopyranose series, the 2-substituted products predominate over the 3-substituted ones, in partial substitution of the 4,6-*O*-benzylidene acetals. In previous work, which did not include galactopyranosides,[5,6] preferential 2-substitution of the corresponding *O*-glycosides was ascribed to the greater acidity of the 2-OH over the 3-OH. In the corresponding partial PTC substitutions of the 2,3-di-*O*-benzyl ethers, the primary position was preferentially substituted.

Two disaccharide derivatives were chosen as models for investigation: ethyl 4-*O*-(4,6-*O*-benzylidene-β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (**30**) and ethyl 4-*O*-(2,3-di-*O*-benzyl-β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (**31**), i.e., with the 2', 3'- and 4',6'-hydroxyls free, respectively. The two models **30** and **31** were constructed as follows: ethyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside was benzylated to give the 2,3-di-*O*-benzyl ether which was then treated with sodium cyanoborohydride-HCl in tetrahydrofuran[12] yielding **6**, identical to the product obtained by the PTC route. Silver triflate promoted glycosidation[13,14] of **6** with the glycosyl bromide **28** gave the key disaccharide **29**.

TABLE 1

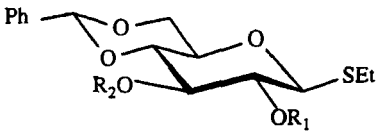
	Partial benzylations			Partial benzoylations		
Starting material	***Product***		***Yield (%)***	***Product***		***Yield (%)***
1	2-*O*-benzyl	**3**	49	2-*O*-benzoyl	**7**	56
	3-*O*-benzyl	**4**	28	3-*O*-benzoyl	**8**	29
2	4-*O*-benzyl	**5**	26			
	6-*O*-benzyl	**6**	46	6-*O*-benzoyl	**9**	87
10	2-*O*-benzyl	**12**	30	2-*O*-benzoyl	**16**	11
	3-*O*-benzyl	**13**	42	3-*O*-benzoyl	**17**	74
11	4-*O*-benzyl	**14**	7			
	6-*O*-benzyl	**15**	79	6-*O*-benzoyl	**18**	93
19	2-*O*-benzyl	**21**	62	2-*O*-benzoyl	**25**	75
	3-*O*-benzyl	**22**	20			
20	4-*O*-benzyl	**23**	34			
	6-*O*-benzyl	**24**	56	6-*O*-benzoyl	**26**	80

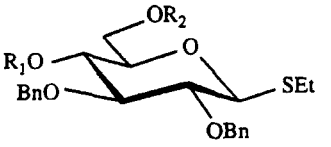
TABLE 2

	Partial benzylations			Partial benzoylations		
Starting material	***Product***		***Yield (%)***	***Product***		***Yield (%)***
30	2-*O*-benzyl	**32**	43	2-*O*-benzoyl	**36**	21
	3-*O*-benzyl	**33**	34	3-*O*-benzoyl	**37**	49
31	4-*O*-benzyl	**34**	26	4-*O*-benzoyl	**38**	14
	6-*O*-benzyl	**35**	36	6-*O*-benzoyl	**39**	78

Debenzoylation of **29** afforded the first target compound **30**, with free 2', 3'-OH groups. Benzylation at these two positions, followed by removal of the 4', 6'-*O*-benzylidene group resulted in the second target compound **31**.

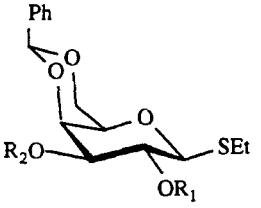
The disaccharides **30** and **31** were subjected to partial benzoylation and benzylation using PTC technique.[1-4] The results are shown in Table 2. Preponderance

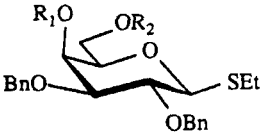




1. R_1=H R_2=H
3. R_1=Bn R_2=H
4. R_1=H R_2=Bn
7. R_1=Bz R_2=H
8. R_1=H R_2=Bz

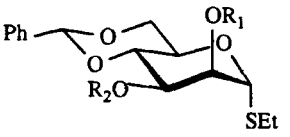
2. R_1=H R_2=H
5. R_1=Bn R_2=H
6. R_1=H R_2=Bn
9. R_1=H R_2=Bz

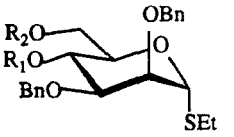




10. R_1=H R_2=H
12. R_1=Bn R_2=H
13. R_1=H R_2=Bn
16. R_1=Bz R_2=H
17. R_1=H R_2=Bz

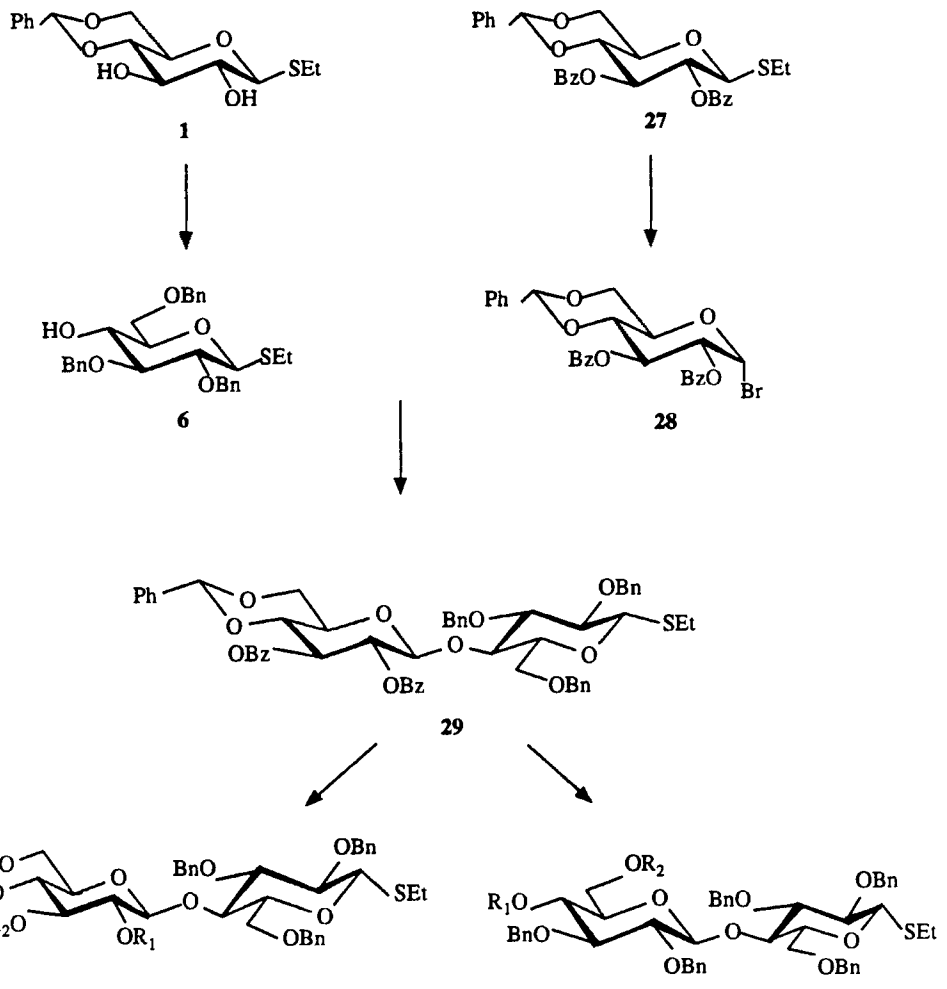
11. R_1=H R_2=H
14. R_1=Bn R_2=H
15. R_1=H R_2=Bn
18. R_1=H R_2=Bz





19. R_1=H R_2=H
21. R_1=Bn R_2=H
22. R_1=H R_2=Bn
25. R_1=Bz R_2=H

20. R_1=H R_2=H
23. R_1=Bn R_2=H
24. R_1=H R_2=Bn
26. R_1=H R_2=Bz



30.	R_1=H	R_2=H	**31.**	R_1=H	R_2=H
32.	R_1=Bn	R_2=H	**34.**	R_1=Bn	R_2=H
33.	R_1=H	R_2=Bn	**35.**	R_1=H	R_2=Bn
36.	R_1=Bz	R_2=H	**38.**	R_1=Bz	R_2=H
37.	R_1=H	R_2=Bz	**39.**	R_1=H	R_2=Bz

for 2-substitution in the 2,3-diols in the *O*-β-D-glucopyranoside series[5,6] is no longer observed. Indeed, the partial benzoylation now gives appreciable more 3'- than 2'-substitution. This must be due to the bulky 1'-position and indicates that caution is needed in extrapolating PTC results from mono- to oligosaccharides. As expected, 6-substitution dominates in the PTC substitution of the 4', 6'-diol.

The position of the substituents introduced in the various products was obvious from the NMR data reported in the experimental part. All new compounds gave satisfactory elemental analyses.

The ease of preparation and the good yields of monosubstitution products obtained shows that PTC is useful for obtaining protected thioglycosides with one free hydroxyl group, useful as building blocks for oligosaccharide synthesis.

EXPERIMENTAL

General procedures. Optical rotations were determined using a Perkin-Elmer 141 polarimeter. NMR spectra were recorded using either a JEOL JNM FX-100 or where indicated a GX-270 instrument. Chemical shifts are given in ppm relative to tetramethylsilane. TLC was performed using silica gel plates (F_{254}, Merck) and the spots were detected with UV light and/or by charring with sulfuric acid/ethanol (1:1). Column chromatography was performed on silica gel 60 (0.040-0.063 mm, Merck).

Ethyl 2,3-Di-*O*-benzyl-1-thio-β-D-glucopyranoside (2). Ethyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside **1**[11] (0.80 g, 2.56 mmol) in dry *N,N*-dimethylformamide (DMF) (16 mL) was stirred with sodium hydride (0.24 g, 10.0 mmol) for 1 h at room temperature. Benzyl bromide (1.2 mL, 10.1 mmol) was added dropwise and the reaction mixture was stirred for 4 h at room temperature. Methanol was added in order to decompose the excess of hydride and the solvent was evaporated. The residue was dissolved in CH_2Cl_2, washed with water, dried ($MgSO_4$), filtered and concentrated. The crude product was purified by column chromatography on silica gel (toluene-ethyl acetate, 15:1) to give ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside 1.0 g (79 %); mp 129-130 °C, $[\alpha]_D$-35.3° (*c* 1.24, chloroform).

Ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (0.87 g, 1.77 mmol) was dissolved in CH_2Cl_2 (5.0 mL) and treated with aqueous trifluoroacetic acid (TFA) (70 %, 5.0 mL) at room temperature. After 30 min the reaction mixture was diluted with CH_2Cl_2 and water and then neutralized with aqueous sodium hydroxide. The organic layer was separated, washed with water, dried ($MgSO_4$), filtered and concentrated. Purification by flash column chromatography on silica gel (toluene-ethyl acetate, 1:5) gave compound **2** (0.56 g, 78 %); mp 72-73 °C (from diethyl ether-light petroleum), $[\alpha]_D$ -36.7° (*c* 1.02, chloroform). ^{1}H-NMR data ($CDCl_3$, 270 MHz): δ 1.34 (t, 3H, SCH_2CH_3), 2.13 (s, 1H, OH), 2.37 (s, 1H, OH), 2.69-2.81 (m, 2H, SCH_2CH_3), 3.30-3.85 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.51 (d, 1H, H-1, $J_{1,2}$ = 9.5Hz), 4.69-4.99 (m, 4H, OCH_2Ph), 7.26-7.42 (m, 10H, aromatic). ^{13}C-NMR

data ($CDCl_3$): δ 15.1 (SCH_2CH_3), 25.1 (SCH_2CH_3), 62.3 (C-6), 70.1, 75.2, 75.2, 78.9, 81.2, 85.0 (C-2, C-3, C-4, C-5, 2 OCH_2Ph), 85.7 (C-1), 127.6-128.3 (aromatic C), 137.5, 138.1 (aromatic C-1 of $PhCH_2$ at *O*-2 and *O*-3).

Anal. Calcd for $C_{22}H_{28}O_5S$: C, 65.3; H, 7.0. Found: C, 65.4; H, 7.0.

Ethyl 2-*O*-and 3-*O*-Benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (3 and 4). Compound **1** (0.30 g, 0.96 mmol), tetrabutylammonium hydrogensulphate (66 mg, 0.19 mmol), and benzyl bromide (0.20 mL, 1.68 mmol) were dissolved in CH_2Cl_2 (16 mL). Aqueous sodium hydroxide (1.38 mL of a 5 % solution) was added and the mixture was stirred under reflux for 68 h. The reaction mixture was cooled and the organic layer was separated, washed with water, dried ($MgSO_4$), filtered and concentrated.[5] Purification by column chromatography on silica gel (toluene-ethyl acetate, 6:1) gave the 2-*O*-benzyl derivative **3** (0.19 g, 49 %) and the 3-*O*-benzyl derivative **4** (0.11 g, 28 %). Compound **3** had mp 116-117 °C (from diethyl ether-light petroleum), $[\alpha]_D$ -42.8°(*c* 0.96, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.31 (t, 3H, SCH_2CH_3), 2.64-2.85 (m, 3H, SCH_2CH_3, OH), 3.25-3.97, 4.24-4.39 (two m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.52 (d, 1H, H-1, $J_{1,2}$ = 9.8 Hz), 4.75, 4.94 (two d, 2H, OCH_2Ph), 5,48 (s, 1H, PhCH), 7.22-7.43 (m, 10H, aromatic). After acetylation of **3** only H-3 (t, 5.36) of the ring protons appeared in the shift region expected for protons geminal to acyloxy groups, thus confirming benzyl substitution in the 2-position. Futhermore, in acetylated **3** the line in the H-1 doublet at lower chemical shift showed higher intensity. ^{13}C-NMR data ($CDCl_3$): δ 15.0 (SCH_2CH_3), 24.5 (SCH_2CH_3), 68.5, 69.9, 75.0, 75.3, 80.2, 81.3 (C-2, C-3, C-4, C-5, C-6, OCH_2Ph), 85.3 (C-1), 101.5 (PhCH), 126.0, 127.8-128.9 (aromatic C), 136.7, 137.6 (aromatic C-1 of PhCH and of $PhCH_2$ at *O*-2). The upfield shift of C-1 from the value of 86.0 ppm in ethyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside **1** confirms the site of substitution in **3**.

Anal. Calcd for $C_{22}H_{26}O_5S$: C, 65.6; H, 6.5. Found: C, 65.4; H, 6.5.

Compound **4** had mp 145-146 °C (from diethyl ether-light petroleum), $[\alpha]_D$ -57.0°(*c* 0.87, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.30 (t, 3H, SCH_2CH_3), 2.63 (broad s, 1H, OH), 2.74 (q, 2H, SCH_2CH_3), 3.38-3.87, 4.28-4.43 (two m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.45 (d, 1H, H-1, $J_{1,2}$ = 9.8 Hz), 4.79, 4.98 (two d, 2H, OCH_2Ph), 5.56 (s, 1H, PhCH), 7.23-7.44 (m, 10H, aromatic). After acetylation of **4** only H-2 (t, 5.05) of the ring protons appeared in the shift region expected for protons geminal to acyloxy groups, thus confirming benzyl substitution in the 3-position. ^{13}C-NMR data ($CDCl_3$): δ 15.2 (SCH_2CH_3), 24.4 (SCH_2CH_3), 68.5, 70.6, 72.9, 74.6, 81.1, 81.4 (C-2, C-3, C-4, C-5, C-6, OCH_2Ph), 86.4 (C-1), 101.1 (PhCH), 125.8, 127.6-128.7 (aromatic C), 136.9, 138.0 (aromatic C-1 of PhCH and of $PhCH_2$

at *O*-3). The upfield shift of PhCH from the value of 101.5 ppm in compound **1** confirms the position of substitution in **4**.

Anal. Calcd for $C_{22}H_{26}O_5S$: C, 65.6; H, 6.5. Found: C, 65.8; H, 6.6.

Ethyl 2,3,4-Tri-*O*-benzyl- and 2,3,6-Tri-*O*-benzyl-1-thio-β-D-glucopyranoside (5 and 6). Partial benzylation of compound **2** was performed as described for compound **1**. The reaction mixture was refluxed for 80 h. Separation of the products by column chromatography on silica gel (toluene-ethyl acetate, 6:1) gave the 6-*O*-benzyl derivative **6** in 46 % yield and the 4-*O*-benzyl derivative **5** in 26 % yield. Compound **5** had mp 112.5-113.5 °C (from diethyl ether-light petroleum), $[\alpha]_D$ +0.64° (*c* 1.25, chloroform); lit.[15] mp 79 °C (from ethanol), $[\alpha]_D$ -1° (*c* 2,chloroform). ^{1}H -NMR data ($CDCl_3$): δ 1.31 (t, 3H, SCH_2CH_3), 2.06 (broad t, 1H, OH), 2.75 (q, 2H, SCH_2CH_3), 2.86-3.80 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.50 (d, 1H, H-1, $J_{1,2}$ = 9.6 Hz), 4.58-4.97 (m, 6H, OCH_2Ph), 7.22-7.31 (m, 15H, aromatic). Acetylation of compound **5** showed the downfield shift of two protons from the multiplet at 2.86-3.80 ppm to a multiplet at 4.09-4.42 ppm, thus confirming the site of benzylation in **5**. ^{13}C-NMR data ($CDCl_3$): δ 15.1 (SCH_2CH_3), 25.1 (SCH_2CH_3), 62.0 (C-6), 74.9, 75.3, 75.6, 77.5, 79.1, 81.6, 85.0 (C-2, C-3, C-4, C-5, 3 OCH_2Ph), 86.2 (C-1), 127.4-128.1 (aromatic C), 137.6, 137.6, 138.1 (aromatic C-1 of $PhCH_2$ at *O*-2, *O*-3 and *O*-4). The value of C-6 at 62.0 ppm, compared to C-6 in compound **2** (62.3ppm), confirms the position of substitution in **5**.

Anal. Calcd for $C_{29}H_{34}O_5S$: C, 70.4; H, 6.9. Found: C, 70.4; H, 7.0.

Compound **6** had mp 67-68 °C (from diethyl ether-light petroleum), $[\alpha]_D$ -31.8° (*c* 1.01, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.31 (t, 3H, SCH_2CH_3), 2.64-2.89 (m, 3H, SCH_2CH_3, OH), 3.38-3.74 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.48 (d, 1H, H-1, $J_{1,2}$ = 9.1 Hz), 4.56-4.99 (m, 6H, OCH_2Ph), 7.21-7.41 (m, 15H, aromatic). Acetylation of compound **6** gave a downfield shift for one proton from the multiplet at 3.38-3.74 ppm to a multiplet at 4.44-4.96 ppm (8H, OCH_2Ph, H-1, H-4), thus confirming the site of benzylation in **6**. ^{13}C-NMR data ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.9 (SCH_2CH_3), 70.4, 71.8, 73.4, 75.2, 75.2, 77.7, 81.0, 84.9 (C-2, C-3, C-4, C-5, C-6, 3 OCH_2Ph), 85.7 (C-1), 127.4-128.2 (aromatic C), 137.5, 137.6, 138.2 (aromatic C-1 of $PhCH_2$ at *O*-2, *O*-3 and *O*-6). The disapperance of C-6 from the value of 62.3 ppm in compound **2** confirms the site of substitution in **6**.

Anal. Calcd for $C_{29}H_{34}O_5S$: C, 70.4; H, 6.9. Found: C, 70.5; H, 7.0.

Ethyl 2-*O*- and 3-*O*-Benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (7 and 8). Compound **1** (0.20 g, 0.64 mmol), tetrabutylammonium hydrogensulphate (43 mg, 0.13 mmol) and benzoyl chloride (0.11 mL, 0.95 mmol) were dissolved in CH_2Cl_2 (18 mL). The reaction mixture was cooled to -5 to 0 °C and aqueous sodium hydroxide

(1.4 mL of a 5 % solution) was added. The mixture was stirred for 15 min at -5 to 0 °C. The organic layer was separated, washed with water, dried ($MgSO_4$), filtered and concentrated.[16] Purification of the crude product by column chromatography on silica gel (toluene-ethyl acetate, 6:1) gave the 2-*O*-benzoyl derivative **7** (0.15 g, 56 %) and the 3-*O*-benzoyl derivative **8** (78 mg, 29 %). Compound **7** had mp 114-116 °C (from diethyl ether-light petroleum), $[\alpha]_D$ -36.4° (*c* 1.12, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.23 (t, 3H, SCH_2CH_3), 2.72 (q, 2H, SCH_2CH_3), 2.92 (d, 1H, OH), 3.46-4.44 (m, 5H, H-3, H-4, H-5, H-6, H-6'), 4.63 (d, 1H, H-1, $J_{1,2}$ = 10.0 Hz), 5.22 (dd, 1H, H-2, $J_{1,2}$ = 10.0 Hz, $J_{2,3}$ = 8.6 Hz), 5.52 (s, 1H, PhCH), 7.24-7.56 (m, 8H, aromatic), 8.01-8.11 (m, 2H, *o*-H in benzoyl). ^{13}C-NMR data ($CDCl_3$): δ 14.8 (SCH_2CH_3), 24.0 (SCH_2CH_3), 68.4, 70.4, 72.9, 73.2, 80.6 (C-2, C-3, C-4, C-5, C-6), 83.8 (C-1), 101.6 (PhCH), 126.0, 128.1-129.7, 133.0, 136.6 (aromatic C), 165.4 (C=O). The upfield shift of C-1 from the value of 86.0 ppm in compound **1** confirms the position of substitution in **7**.

Anal. Calcd for $C_{22}H_{24}O_6S$: C, 63.4; H, 5.8. Found: C, 63.4; H, 5.8.

Compound **8** had mp 133-134.5 °C (from diethyl ether-light petroleum), $[\alpha]_D$ -122.9°(*c* 0.77, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.31 (t, 3H, SCH_2CH_3), 2.76 (q, 2H, SCH_2CH_3), 2.96 (d, 1H, OH), 2.87-4.44 (m, 5H, H-2, H-4, H-5, H-6, H-6'), 4.59 (d, 1H, H-1, $J_{1,2}$ = 9.8 Hz), 5.51 (s, t, 2H, PhCH, H-3, $J_{2,3}$ = $J_{3,4}$ = 7.3 Hz), 7.16-7.95 (m, 8H, aromatic), 8.01-8.10 (m, 2H, *o*-H in benzoyl). ^{13}C-NMR data ($CDCl_3$): δ 15.2 (SCH_2CH_3), 25.0 (SCH_2CH_3), 68.4, 70.7, 72.2, 75.3, 78.3 (C-2, C-3, C-4, C-5, C-6), 87.1 (C-1), 101.2 (PhCH), 125.8, 127.9-129.6, 133.0, 136.5 (aromatic C), 166.2 (C=O). The upfield shift of PhCH from the value of 101.5 ppm in compound **1** corresponds to the site of substitution in **8**.

Anal. Calcd for $C_{22}H_{24}O_6S$: C, 63.4; H, 5.8. Found: C, 63.6; H, 5.9.

The 2,3-di-*O*-benzoyl derivative of compound **1** was also isolated in 12 % yield; mp 187-189 °C, $[\alpha]_D$ +15.4° (*c* 0.76, chloroform); lit.[11] mp 186-187 °C, $[\alpha]_D$ +16° (*c* 1, chloroform).

Ethyl 6-*O*-Benzoyl-2,3-di-*O*-benzyl-1-thio-β-D-glucopyranoside (9). Partial benzoylation of compound **2** was performed as described for compound **1**. The reaction time was 1 h at -5 to 0 °C. Purification of the crude product by column chromatography on silica gel (toluene-ethyl acetate, 4:1) gave the 6-*O*-benzoyl derivative **9** in 87 % yield; mp 99 - 100 °C (from diethyl ether- light petroleum), $[\alpha]_D$ -28.7° (*c* 0.98, chloroform). ^{1}H-NMR data ($CDCl_3$, 270 MHz): δ 1.30 (t, 3H, SCH_2CH_3), 2.62 (s, 1H, OH), 2.69-2.77 (m, 2H, SCH_2CH_3), 3.43-3.56 (m, 4H, H-2, H-3, H-4, H-5), 4.51-4.97 (m, 6H, H-6, H-6', OCH_2Ph), 4.52 (d, 1H, H-1, $J_{1,2}$ = 9.5Hz), 7.25-7.59 (m, 13H, aromatic), 8.03-8.06 (m, 2H, *o*-H in benzoyl). ^{13}C-NMR

data ($CDCl_3$): δ 15.1 (SCH_2CH_3), 25.0 (SCH_2CH_3), 63.9 (C-6), 70.1, 75.4, 75.6, 77.5, 81.2, 85.0 (C-2, C-3, C-4, C-5, 2 OCH_2Ph), 85.5 (C-1), 127.7-129.5, 132.9, 137.4, 138.0 (aromatic C), 166.4 (C=O). The downfield shift of C-6 from the value of 62.3 ppm in compound **2** confirms the site of substitution in **9**.

Anal. Calcd for $C_{29}H_{32}O_6S$: C, 68.5; H, 6.3. Found: C, 68.3; H, 6.2.

Ethyl 2,3-Di-*O*-benzyl-1-thio-β-D-galactopyranoside (11). Benzylation of ethyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside **10**[17] was performed as described for compound **1** with a reaction time of 22 h. Ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside was obtained in 62 % yield; mp 154-156 °C (from dichloromethane-light petroleum), $[\alpha]_D$ +3.5° (*c* 1.30, chloroform).

Ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (1.65 g, 3.35 mmol) was treated with 80 % acetic acid at 100 °C for 30 min. The solvent was evaporated and the residue was co-distilled several times with toluene. Column chromatography on silica gel (toluene-ethyl acetate, 1:5) gave compound **11** (1.2 g, 89 %); mp 99-100 °C (from diethyl ether-light petroleum), $[\alpha]_D$ -6.1° (*c* 1.0, chloroform). ^{1}H-NMR data ($CDCl_3$, 270 MHz): δ 1.31 (t, 3H, SCH_2CH_3), 2.42 (broad s, 1H, OH), 2.68-2.83 (m, 3H, SCH_2CH_3, OH), 3.45-4.05 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.43 (d, 1H, H-1, $J_{1,2}$ = 9.5Hz), 4.72-4.90 (m, 4H, OCH_2Ph), 7.25-7.42 (m, 10H, aromatic). ^{13}C-NMR data ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.8 (SCH_2CH_3), 62.3 (C-6), 67.1, 72.0, 75.6, 77.6, 77.7, 82.0 (C-2, C-3, C-4, C-5, 2 OCH_2Ph), 85.0 (C-1), 127.6-128.2 (aromatic C), 137.3, 137.8 (aromatic C-1 of $PhCH_2$ at *O*-2 and *O*-3).

Anal. Calcd for $C_{22}H_{28}O_5S$: C, 65.3; H, 7.0. Found: C, 65.2; H, 6.9.

Ethyl 2-*O*-and 3-*O*-Benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (12 and 13). Partial benzylation of compound **10** was performed as described for compound **1**. The reaction time was 88 h. Column chromatography on silica gel (toluene-ethyl acetate, 2:1) gave the 3-O-benzyl derivative **13** in 42 % and the 2-O-benzyl derivative **12** in 30 % yield.

[The 2,3-di-O-benzyl derivative of compound **10** was also isolated in 3.9 % yield; mp 154-156 °C (from diethyl ether- light petroleum)]. Compound **12** had mp 108-110°C (from diethyl ether-light petroleum), $[\alpha]_D$ -24.5° (c 0.88, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.33 (t, 3H, SCH_2CH_3), 2.62-2.92 (m, 3H, SCH_2CH_3, OH), 3,35-4.24 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.42 (d, 1H, H-1, $J_{1,2}$ = 9.3 Hz), 4.74, 4.93 (two d, 2H, OCH_2Ph), 5.50 (s, 1H, PhCH), 7.23-7.56 (m, 10H, aromatic). ^{13}C-NMR data ($CDCl_3$): δ 14.9 (SCH_2CH_3), 24.1 (SCH_2CH_3), 69.1, 69.6, 74.0, 75.3, 75.7, 78.4 (C-2, C-3, C-4, C-5, C-6, OCH_2Ph), 84.0 (C-1), 101.3 (PhCH), 126.2-129.0 (aromatic C), 137.3, 137.8 (aromatic C-1 of PhCH and of $PhCH_2$ at O-2).

The upfield shift of C-1 from the value of 85.0 ppm in compound **10** confirms the site of substitution in **12.**

Anal. Calcd for $C_{22}H_{26}O_5S$: C, 65.6; H, 6.5. Found: C, 65.4; H, 6.4.

Compound **13** had mp 159-160 °C (from dichloromethane-diethyl ether-light petroleum), $[\alpha]_D$ +7.7° (*c* 0.99, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.31 (t, 3H, SCH_2CH_3), 2.63-2.90 (m, 3H, SCH_2CH_3, OH), 3.35-4.36 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.33 (d, 1H, H-1, $J_{1,2}$ = 9.5 Hz), 4.75 (s, 2H, OCH_2Ph), 5.42 (s, 1H, PhCH), 7.23-7.55 (m, 10H, aromatic). The ^{1}H-NMR spectrum of acetylated **13** showed a downfield shift of H-2 (t, 5.45 ppm). This confirms the position of acetylation and thus the site of benzylation in **13**. ^{13}C-NMR data ($CDCl_3$): δ 15.3 (SCH_2CH_3), 22.9 (SCH_2CH_3), 67.9, 69.3, 69.4, 71.3, 73.3, 80.1 (C-2, C-3, C-4, C-5, C-6, OCH_2Ph), 85.1 (C-1), 101.0 (PhCH), 126.1-128.7 (aromatic C), 137.5, 137.8 (aromatic C-1 of PhCH and of $PhCH_2$ at *O*-3).

Anal. Calcd for $C_{22}H_{26}O_5S$: C, 65.6; H, 6.5. Found: C, 65.5; H, 6.5.

Ethyl 2,3,4-Tri-*O*-benzyl and 2,3,6-Tri-*O*-benzyl-1-thio-β-D-galactopyranoside (14 and 15). Partial benzylation of compound **11** was performed as described for compound **1**. Separation of the products by column chromatography on silica gel (toluene-ethyl acetate, 4:1) gave the 6-*O*-benzyl derivative **15** in 79 % yield and the 4-*O*-benzyl derivative **14** in 6.5 % yield. Compound **14** had mp 102.5-104 °C (from diethyl ether-light pertoleum), $[\alpha]_D$ -13.8° (*c* 0.80, chloroform).

Anal. Calcd for $C_{29}H_{34}O_5S$: C, 70.4; H, 6.9. Found: C, 70.2; H, 6.8.

Compound **15** had $[\alpha]_D$ -1.8° (c 1.59, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.30 (t, 3H, SCH_2CH_3), 2.53 (broad d, 1H, OH), 2.74 (q, 2H, SCH_2CH_3), 3.55-3.79, 4.04-4.11 (two m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.42 (d, 1H, H-1, $J_{1,2}$ = 9.1 Hz), 4.56-4.94 (m, 6H, OCH_2Ph), 7.18-7.35 (m, 15H, aromatic). The ^{1}H-NMR spectrum of acetylated **15** showed a downfield shift of H-4 (broad doublet at 5.62 ppm). This confirms the site of benzylation in **15**. ^{13}C-NMR data ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.7 (SCH_2CH_3), 69.2 (C-6), 66.4, 71.9, 73.5, 75.6, 76.7, 77.7, 82.2 (C-2, C-3, C-4, C-5, 3 OCH_2Ph), 84.8 (C-1), 127.5-128.2 (aromatic C), 137.4, 137.6, 137.8 (aromatic C-1 of $PhCH_2$ at *O*-2, *O*-3 and *O*-6). The downfield shift of C-6 from the value of 62.3 ppm in compound **11** confirms the site of substitution in **15**.

Anal. Calcd for $C_{29}H_{34}O_5S$: C, 70.4; H, 6.9. Found: C, 70.5; H, 6.8.

Ethyl 2-*O*-and 3-*O*-Benzoyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (16 and 17). Partial benzoylation of compound **10** was performed as described for compound **1**. The reaction time was prolonged to 2 h and the temperature was raised from -20 to 0 °C. Separation of the products by column chromatography on silica gel

(toluene-ethyl acetate, 2:1) gave the 3-*O*-benzoyl derivative **17** in 74 % yield and the 2-*O*-benzoyl derivative **16** in 11 % yield. Compound **16** had mp 145-146 °C (from diethyl ether-light petroleum), $[\alpha]_D$ -13.2° (*c* 0.90, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.26 (t, 3H, SCH_2CH_3), 2.53-3.00 (m, 3H, SCH_2CH_3, OH), 3.54-4.44 (m, 5H, H-3, H-4, H-5, H-6, H-6'), 4.57 (d, 1H, H-1, $J_{1,2}$ = 10.0 Hz), 5.45 (t, 1H, H-2, $J_{1,2}$ = $J_{2,3}$ = 10.0 Hz), 5.54 (s, 1H, PhCH), 7.34-7.52 (m, 8H, aromatic), 8.00-8.10 (m, 2H, *o*-H in benzoyl). ^{13}C-NMR data ($CDCl_3$): δ 14.9 (SCH_2CH_3), 23.0 (SCH_2CH_3), 69.0, 69.9, 70.6, 72.5, 75.7 (C-2, C-3, C-4, C-5, C-6), 82.4 (C-1), 101.3 (PhCH), 126.1-129.6, 132.9, 137.0 (aromatic C), 165.7 (C=O). The upfield shift of C-1 from the value of 85.0 ppm in compound **10** confirms the position of substitution in **16**.

Anal. Calcd for $C_{22}H_{24}O_6S$: C, 63.4; H, 5.8. Found: C, 63.2; H, 5.9.

Compound **17** had mp 129.5-130.5 °C (from dichloromethane-diethyl ether-light petroleum), $[\alpha]_D$ +57.9° (*c* 1.20, chloroform); lit.[18] mp 123.5-125 °C, $[\alpha]_D$ +55.4°. ^{1}H-NMR data ($CDCl_3$): δ 1.32 (t, 3H, SCH_2CH_3), 2.62-2.92 (m, 3H, SCH_2CH_3, OH), 3.58-4.53 (m, 5H, H-2, H-4, H-5, H-6, H-6'), 4.48 (d, 1H, H-1, $J_{1,2}$ = 10.0 Hz), 5.16 (dd, 1H, H-3, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 4.0 Hz), 5.48 (s, 1H, PhCH), 7.18-7.54 (m, 8H, aromatic), 8.02-8.12 (m, 2H, *o*-H in benzoyl). ^{13}C-NMR data ($CDCl_3$): δ 16.3 (SCH_2CH_3), 21.3 (SCH_2CH_3), 66.5, 69.1, 69.8, 73.8, 75.2 (C-2, C-3, C-4, C-5, C-6), 85.7 (C-1), 100.6 (PhCH), 125.9-129.6, 133.0, 137.5 (aromatic C), 166.0 (C=O). The upfield shift of PhCH from the value of 101.1 ppm in compound **10** corresponds to the site of substitution in **17**.

The 2,3-di-*O*-benzoyl derivative of compound **10** was also isolated in 5 % yield; mp 148-150 °C (from dichloromethane-diethyl ether-light petroleum); lit.[17] mp 148-150 °C.

Ethyl 6-*O*-Benzoyl-2,3-di-*O*-benzyl-1-thio-β-D-galactopyranoside (18). Partial benzoylation of compound **11** was performed as described for compound **1**. The reaction time was 1.5 h. Column chromatography on silica gel (toluene-ethyl acetate, 4:1) of the crude product gave the 6-*O*-benzoyl derivative **18** in 93 % yield; mp 149-150 °C (from dichloromethane-diethyl ether-light petroleum), $[\alpha]_D$ -0.85° (*c* 1.29, chloroform). ^{1}H-NMR data ($CDCl_3$, 270 MHz): δ 1.27 (t, 3H, SCH_2CH_3), 2.51 (d, 1H, OH), 2.66-2.82 (m, 2H, SCH_2CH_3), 3.56-4.03 (m, 4H, H-2, H-3, H-4, H-5), 4.46 (d, 1H, H-1, $J_{1,2}$ = 9.5Hz), 4.51-4.68 (m, 2H, H-6, H-6'), 4.72-4.90 (m, 4H, OCH_2Ph), 7.25-7.60 (m, 13H, aromatic), 8.01-8.04 (m, 2H, *o*-H in benzoyl). ^{13}C-NMR data ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.9 (SCH_2CH_3), 63.6 (C-6), 66.7, 72.3, 75.6, 77.7, 82.0 (C-2, C-3, C-4, C-5, 2 OCH_2Ph), 84.9 (C-1), 127.6-129.6,

132.9, 137.3, 137.7 (aromatic C), 165.9 (C=O). The downfield shift of C-6 from the value of 62.3 ppm in compound **11** confirms the site of substitution in **18**.

Anal. Calcd for $C_{29}H_{32}O_6S$: C, 68.5; H, 6.3. Found: C, 68.4; H, 6.3.

Ethyl 4,6-*O*-Benzylidene-1-thio-α-D-mannopyranoside (19). Thioglycosidation of D-mannopyranose pentaacetate gave ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-manno-pyranoside in 54 % yield; mp 105-106 °C (from ethanol), $[\alpha]_D$ +103.0°(*c* 0.97, chloroform); lit.[19] mp 107-108 °C, $[\alpha]_D$ +104°(*c* 0.8, chloroform). The ^{13}C-NMR data of C-1 was not in agreement with that reported by Contour *et* al.[19] who stated a shift of C-1 at 88.9 ppm while we found C-1 at 82.0 ppm. Deacetylation with methanolic sodium methoxide gave ethyl 1-thio-α-D-mannopyranoside in 99% yield, mp 126.5-128.5 °C. Ethyl 1-thio-α-D-mannopyranoside (2.42 g, 10.8 mmol) was dissolved as rapidly as possible in 98-100 % formic acid (10.5 mL) and freshly distilled benzaldehyde (10.5 mL) was immediately added to the solution. After 5 min the mixture was poured with stirring into light petroleum (bp 60-80 °C, 85 mL) and water (85 mL) containing potassium carbonate (29 g). The upper layer was filtered and the residue was washed with light petrolum.[20] Column chromatography on silica gel(toluene-ethyl acetate, 1:3, containing 0.25 % triethylamine) gave compound **19** (1.64 g, 49 %); mp 174-175 °C (crystallized from chloroform-light petroleum), $[\alpha]_D$ +167.5° (*c* 1.22, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.30 (t, 3H, SCH_2CH_3), 2.51-2.75 (m, 2H, SCH_2CH_3), 2.97-3.02 (m, 2H, OH), 3.71-4.31 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 5.33 (s, 1H, H-1), 5.55 (s, 1H, PhCH), 7.25-7.45 (m, 5H, aromatic). ^{13}C-NMR data ($CDCl_3$): δ 14.8 (SCH_2CH_3), 25.0 (SCH_2CH_3), 63.4, 68.5, 68.9, 72.2, 79.0 (C-2, C-3, C-4, C-5, C-6), 84.2 (C-1), 102.1 (PhCH), 126.1, 128.1, 129,1 (aromatic C), 136.9 (aromatic C-1 of PhCH).

Anal. Calcd for $C_{15}H_{20}O_5S$: C, 57.7; H, 6.4. Found: C, 57.8; H, 6.4.

Ethyl 2,3-Di-*O*-benzyl-1-thio-α-D-mannopyranoside (20). Sodium hydride (0.45 g, 18.8 mmol) was added gradually to a solution of compound **19** (0.81g, 2.6 mmol) in dry *N,N*-dimethylformamide (DMF) (24 mL) and the suspension was stirred for 30 min at room temperature. The mixture was then cooled to 0 °C and benzyl bromide (4.86 mL, 40.9 mmol) was added . After 24 h at room temperature dry methanol was added in order to decompose the excess of hydride and the solution was concentrated to dryness. The residue was dissolved in dichloromethane, washed with water, dried ($MgSO_4$), filtered and concentrated.[21] Purification by column chromatography on silica gel (gradient elution- toluene to toluene-ethyl acetate, 20:1) gave ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (0.96 g, 75 %).

Deacetalisation of ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-α-D-manno-pyranoside was performed as described for ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside and gave compound **20** in 90 % yield; $[\alpha]_D$ +65.9° (*c* 1.38, chloroform). ^{1}H-NMR data ($CDCl_3$, 270 MHz): δ 1.26 (t, 3H, SCH_2CH_3), 2.19 (broad s, 1H, OH), 2.52-2.66 (m, 3H, SCH_2CH_3, OH), 3.63-4.10 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.41-4.69 (m, 4H, OCH_2Ph), 5.35 (d, 1H, H-1, $J_{1,2}$ = 1.1Hz), 7.25-7.37 (m, 10H, aromatic). ^{13}C-NMR data ($CDCl_3$): δ 14.7 (SCH_2CH_3), 25.1 (SCH_2CH_3), 62.2 (C-6), 66.9, 71.6, 72.0, 72.4, 75.6, 79.5 (C-2, C-3, C-4, C-5, 2 OCH_2Ph), 81.8 (C-1), 127.4-128.1 (aromatic C), 137.4, 137.4 (aromatic C-1 of $PhCH_2$ at *O*-2 and *O*-3)

Anal. Calcd for $C_{22}H_{28}O_5S$: C, 65.3; H, 7.0. Found: C, 65.2; H, 7.0.

Ethyl 2-*O*-and 3-*O*-Benzyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (21 and 22). Partial benzylation of compound **19** was performed as described for compound **1**. The reaction time was 58 h. Purification by column chromatography on silica gel (toluene-ethyl acetate, 6:1) gave the 2-*O*-benzyl derivative **21** in 62 % yield and the 3-*O*-benzyl derivative **22** in 20 % yield. Compound **21** had mp 66-68 °C (from diethyl ether-light petroleum), $[\alpha]_D$ +102.8° (*c* 1.30, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.25 (t, 3H, SCH_2CH_3), 2.52-2.71 (m, 3H, SCH_2CH_3, OH), 3.70-4.34 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.62, 4.75 (two d, 2H, OCH_2Ph), 5.36 (s, 1H, H-1), 5.54 (s, 1H, PhCH), 7.35-7.58 (m, 10H, aromatic). The position of alkylation was confirmed by acetylation of **21** which gave a double doublet of H-3 at 5.22 ppm. ^{13}C-NMR data ($CDCl_3$): δ 14.9 (SCH_2CH_3), 25.2 (SCH_2CH_3), 63.8, 68.4, 68.9, 73.0, 79.6, 80.0 (C-2, C-3, C-4, C-5, C-6, OCH_2Ph), 82.3 (C-1), 101.9 (PhCH), 126.0-128.0 (aromatic C), 137.0, 137.1 (aromatic C-1 of PhCH and of $PhCH_2$ at *O*-2). The upfield shift of C-1 from the value of 84.2 ppm in compound **19** confirms the site of substitution in **21**.

Anal. Calcd for $C_{22}H_{26}O_5S$: C, 65.6; H, 6.5. Found: C,65.8; H, 6.5.

Compound **22** had $[\alpha]_D$ +195.1° (*c* 0.82, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.27 (t, 3H, SCH_2CH_3), 2.58, 2.61 (dq, 2H, SCH_2CH_3), 2.96 (d, 1H, OH), 3.73-4.36 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.66, 4.85 (two d, 2H, OCH_2Ph), 5.35 (d, 1H, H-1, $J_{1,2}$ = 0.99 Hz), 5.60 (s, 1H, PhCH), 7.17-7.56 (m, 10H, aromatic). The position of alkylation was confirmed by acetylation of **22** which gave a double doublet of H-2 at 5.45 ppm. ^{13}C-NMR data ($CDCl_3$): δ 14.8 (SCH_2CH_3), 24.9 (SCH_2CH_3), 63.7, 68.5, 71.2, 73.0, 75.7, 79.0 (C-2, C-3, C-4, C-5, C-6, OCH_2Ph), 84.0 (C-1), 101.4 (PhCH), 125.8-128.6 (aromatic C), 137.2, 137.5 (aromatic C-1 of PhCH and of $PhCH_2$ at *O*-3). The upfield shift of PhCH from the value of 102.1 ppm in compound **19** confirms the site of substitution in **22**.

Anal. Calcd for $C_{22}H_{26}O_5S$: C, 65.6; H, 6.5. Found: C, 65.5; H, 6.4.

Ethyl 2,3,4-Tri-*O*-benzyl and 2,3,6-Tri-*O*-benzyl-1-thio-α-D-mannopyranoside (23 and 24). Partial benzylation of compound **20** was performed as described for compound **1**. The reaction time was 75 h. Column chromatography on silica gel(toluene-ethyl acetate, 4:1) gave the 6-*O*-benzyl derivative **24** in 56 % yield and the 4-*O*-benzyl derivative **23** in 34 % yield. Compound **23** had $[\alpha]_D$ +65.3° (*c* 1.46, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.21 (t, 3H, SCH_2CH_3), 2.11 (broad t, 1H, OH), 2.54 (q, 2H, SCH_2CH_3), 3.78-4.04 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.58-5.00 (m, 6H, OCH_2Ph), 5.28 (d, 1H, H-1, $J_{1,2}$ = 0.80 Hz), 7.18-7.31 (m, 15H, aromatic). In the ^{1}H-NMR spectrum of acetylated **23** two protons moved downfield from the multiplet at 3.78-4.04 to a new multiplet at 4.18-4.98 ppm (8H, 3 OCH_2Ph, H-6, H-6'). This confirms the position of benzylation in **23**. ^{13}C-NMR data ($CDCl_3$): δ 14.8 (SCH_2CH_3), 25.2 (SCH_2CH_3), 62.2 (C-6), 72.0, 72.2, 74.7, 75.0, 76.4, 77.0, 80.0 (C-2, C-3, C-4, C-5, 3 OCH_2Ph), 82.0 (C-1), 127.4-128.1 (aromatic C), 137.7, 137.8, 138.0 (aromatic C-1 of $PhCH_2$ at *O*-2, *O*-3 and *O*-4). The remaining shift of C-6 at the value of 62.2 ppm confirms the site of substitution in **23**.

Anal. Calcd for $C_{29}H_{34}O_5S$: C, 70.4; H, 6.9. Found: C, 70.6; H, 7.0.

Compound **24** had $[\alpha]_D$ +35.1° (*c* 1.46, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.25 (t, 3H, SCH_2CH_3), 2.49-2.73 (m, 3H, SCH_2CH_3 , OH), 3.58-3.85, 4.06-4.13 (two m, 6H, H-2, H-3, H-4, H-5, H-6, H-6'), 4.36-4.78 (m, 6H, OCH_2Ph), 5.41 (d, 1H, H-1, $J_{1,2}$ = 1.3 Hz), 7.18-7.39 (m, 15H, aromatic). In the ^{1}H-NMR spectrum of acetylated **24**, H-4 appeared as a triplet at 5.39 ppm. This confirms the site of benzylation in **24**. ^{13}C-NMR data ($CDCl_3$): δ 14.8 (SCH_2CH_3), 25.1 (SCH_2CH_3), 67.5, 69.8, 71.4, 71.4, 71.7, 73.1, 75.4, 79.5 (C-2, C-3, C-4, C-5, C-6, 3 OCH_2Ph), 81.6 (C-1), 127.1-128.1 (aromatic C), 137.5, 137.5, 137.9 (aromatic C-1 of $PhCH_2$ at *O*-2, *O*-3 and *O*-6). The downfield shift of C-6 from the value of 62.2 ppm confirms the site of substitution in **24**.

Anal. Calcd for $C_{29}H_{34}O_5S$: C, 70.4; H, 6.9. Found: C, 70.5; H, 7.1.

Ethyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (25). Partial benzoylation of compound **19** was performed as described for compound **1**. The reaction time was 30 min. Column chromatography on silica gel (toluene-ethyl acetate, 6:1) gave the 2-*O*-benzoyl derivative **25** in 75 % yield; $[\alpha]_D$ +49.5° (*c* 0.84, chloroform). ^{1}H-NMR data ($CDCl_3$): δ 1.28 (t, 3H, SCH_2CH_3), 2.71 (q, 2H, SCH_2CH_3), 2.74 (broad s, 1H, OH), 3.85-4.29 (m, 5H, H-3, H-4, H-5, H-6, H-6'), 5.39 (s, 1H, H-1), 5.48 (m, 1H, H-2), 5.62 (s, 1H, PhCH), 7.21-7.58 (m, 8H, aromatic), 8.04-8.13 (m, 2H, *o*-H in benzoyl). ^{13}C-NMR data ($CDCl_3$): δ 14.9 (SCH_2CH_3), 25.6 (SCH_2CH_3), 64.0, 67.6, 68.4, 74.3, 79.4 (C-2, C-3, C-4, C-5, C-6), 83.2 (C-1), 102.0 (PhCH), 126.0, 128.1-129.6, 133.1, 136.7 (aromatic C), 165.5

(C=O). The upfield shift of C-1 from the value of 84.2 ppm in compound **19** confirms the position of substitution in **25**.

Anal. Calcd for $C_{22}H_{24}O_6S$: C, 63.4; H, 5.8. Found: C, 63.7; H, 5.9.

The 2,3-di-*O*-benzoyl derivative of compound **19** was isolated in 13 % yield.

Ethyl 6-*O*-Benzoyl-2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside (26). Partial benzoylation of compound **20** was performed as described for compound **1** but with a reaction time of 1 h. Column chromatography on silica gel (toluene-ethyl acetate, 4:1), gave the 6-*O*-benzoyl derivative **26** in 80 % yield, $[\alpha]_D$ +22.2° (*c* 1.33, chloroform). ^{1}H-NMR data ($CDCl_3$, 270 MHz): δ 1.26 (t, 3H, SCH_2CH_3), 2.54-2.70 (m, 3H, SCH_2CH_3, OH), 3.68-4.28 (m, 4H, H-2, H-3, H-4, H-5), 4.47-4.71 (m, 6H, H-6, H-6', OCH_2Ph), 5.44 (s, 1H, H-1), 7.26-7.56 (m, 13H, aromatic), 8.02-8.05 (m, 2H, *o*-H in benzoyl). ^{13}C-NMR data ($CDCl_3$): δ 14.9 (SCH_2CH_3), 25.4 (SCH_2CH_3), 63.8 (C-6), 66.6, 70.8, 71.6, 71.8, 79.5 (C-2, C-3, C-4, C-5, 2 OCH_2Ph), 81.8 (C-1), 127.4-129.7, 132.6, 134.4, 137.6 (aromatic C), 166.3 (C=O). The downfield shift of C-6 from the value of 62.2 ppm in compound **20** confirms the position of substitution in **26**.

Anal. Calcd for $C_{29}H_{32}O_6S$: C, 68.5; H, 6.3. Found: C, 68.3; H, 6.4.

Ethyl 2,3,6-Tri-*O*-benzyl-1-thio-β-D-glucopyranoside (6). Ethyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside[11](**1**, 0.8 g, 2.56 mmol) was dissolved in dry *N,N*-dimethylformamide (16 mL) and sodium hydride (0.24 g, 10 mmol) was added in small portions. The reaction mixture was stirred at room temperature for 1 h and benzyl bromide (1.2 mL, 10 mmol) was added dropwise. Stirring was continued for 4 h and methanol was added in order to decompose the excess of hydride. Most of the solvent was evaporated and the residue was dissolved in dichloromethane. The organic layer was washed with water, dried ($MgSO_4$), filtered and concentrated to give a crude product, which was purified by column chromatography on silica gel (toluene:ethyl acetate, 15-1) to give ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-gluco-pyranoside (1.0 g, 79 %).

Ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (0.5 g, 1.02 mmol) was dissolved in dry tetrahydrofuran (15 mL) under nitrogen atmosphere. Powdered molecular sieves (3 Å) and sodium cyanoborohydride (0.8 g, 12.7 mmol) were added with stirring at room temperature.[12] Hydrogen chloride in diethyl ether was added until the evolution of gas ceased. The reaction was completed within 10 min. The mixture was diluted with dichloromethane and water and filtered. The filtrate was washed with water and then with saturated aqueous sodium hydrogencarbonate, dried (Na_2SO_4), filtered and concentrated. The crude product was purified by column chromatography on silica gel (toluene-ethyl acetate, 6:1) to give

compound **6** (0.36 g, 72 %); mp 67-68 °C, $[\alpha]_D$ -32.3° (*c* 0.85, chloroform). ^{13}C-NMR ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.9 (SCH_2CH_3), 85.1 (C-1).

Anal. Calcd for $C_{29}H_{34}O_5S$: C, 70.4; H, 6.9. Found: C, 70.5; H, 7.0.

Ethyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (29). A bromine solution (13.5 mL, prepared from 0.17 mL Br_2 in 28 mL dry dichloromethane) was added to a stirred mixture of ethyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside[16] (**27**, 0.75 g, 1.44 mmol) and powdered molecular sives (4 Å, 0.6 g) in dry dichloromethane (15 mL) under nitrogen atmosphere. After stirring at room temperature for 20 min tetraethylammonium bromide (0.705 g, 3.35 mmol) was added and the mixture was stirred for an additional 3 h. The reaction mixture was diluted with dichloromethane and filtered through Celite, washed with water, saturated $NaHCO_3$ solution and water, dried ($MgSO_4$), filtered and concentrated to give 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranosyl bromide (**28**, 0.75 g, 97 %). The bromide was used directly in the next step. Compound **6** (0.45 g, 0.91 mmol), 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranosyl bromide (**28**, 0.75 g, 1.39 mmol) and powdered molecular sieves (4 Å, 1.3 g) in dry dichloromethane (7 mL) was stirred under nitrogen atmosphere at -40 °C for 30 min. Silver triflate (0.364 g, 1.42 mmol) in dry toluene (4 mL) and sym-collidine (90 μL) were added. After 5 h at -40 °C, pyridine was added and the mixture was filtered through a bed of Celite. The solids were washed with dichloromethane and the combined organic layers were washed with water, aqueous thiosulfate solution, water, M sulfuric acid, $NaHCO_3$ solution and water, dried ($MgSO_4$), filtered and concentrated to give compound **29**, which was purified by column chromatography on silica gel (toluene-ethyl acetate, 15:1). Recrystallization from dichloromethane-light petroleum gave pure **29** (0.78 g, 90 %); mp 209-211 °C, $[\alpha]_D$ -14.5° (*c* 1.26, chloroform). ^{13}C-NMR ($CDCl_3$): δ 15.0 (SCH_2CH_3), 24.7 (SCH_2CH_3), 66.2 (C-5'), 67.6, 68.3 (C-6', C-6), 100.5 (C-1'), 101.1 (PhCH), 164.6, 165.1 (*C*=O).

Anal. Calcd for $C_{56}H_{56}O_{12}S$: C, 70.6; H, 5.9. Found: C, 70.7; H, 6.0.

Ethyl 2,3,6-Tri-*O*-benzyl-4-*O*-(4,6-*O*-benzylidene-β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (30). Compound **29** (0.4 g, 0.42 mmol) was dissolved in methanol:toluene (16 mL, 1:1) and methanolic sodium methoxide (0.32 mL, 1 M) was added and the reaction mixture was stirred at room temperature for 16 h. The mixture was neutralized with cation exchange resin (Dowex 50 WX8), filtered and concentrated. The crude product was purified by column chromatography on silica gel (toluene-ethyl acetate, 1:1). Recrystallization from dichloromethane-light petroleum gave **30** (0.25 g, 81 %); mp 152-154 °C, $[\alpha]_D$ 4.9° (*c* 0.77, chloroform). ^{13}C-NMR

($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.7 (SCH_2CH_3), 66.2 (C-5), 68.3 (C-6, C-6'), 101.5 (PhCH), 103.4 (C-1').

Anal. Calcd for $C_{42}H_{48}O_{10}S$: C, 67.7; H, 6.5. Found: C, 67.6; H, 6.6.

Ethyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (31). Compound **30** (0.245 g, 0.33 mmol) in dry *N,N*-dimethylformamide (2 mL) was treated with sodium hydride (32 mg, 1.32 mmol). After stirring at room temperature, benzyl bromide (0.16 mL, 1.32 mmol) was added and the reaction mixture was stirred for 16 h. Methanol was added in order to decompose the excess of hydride and most of the solvent was evaporated and the residue was dissolved in dichloromethane, washed with water, dried ($MgSO_4$), filtered and concentrated. The crude product was purified by column chromatography on silica gel (toluene-ethyl acetate, 15:1) to give ethyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (0.28 g, 92 %).

Ethyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)1-thio-β-D-glucopyranoside (0.28 g, 0.30 mmol) was treated with 80 % acetic acid and heated at 100 °C for 1 h. The reaction mixture was concentrated and co-distilled several times with toluene and the residue was purified by column chromatography on silica gel (toluene-ethyl acetate, 2:1) to give **31** (0.16 g, 73 %); mp 154-157 °C, $[\alpha]_D$ 15.9° (*c* 0.73, chloroform). ^{13}C-NMR ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.7 (SCH_2CH_3), 62.1 (C-6'), 68.0 (C-6),102.2 (C-1').

Anal. Calcd for $C_{49}H_{56}O_{10}S \cdot 0.5\,H_2O$: C, 69.6; H, 6.8. Found: C, 69.6; H, 6.3.

Ethyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2-*O*- and 3-*O*-benzyl 4,6-*O*-benzylidene-β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (32 and 33). Compound **30** (0.156 g, 0.21 mmol), tetrabutylammonium hydrogen sulfate (14 mg, 0.04 mmol) and benzyl bromide (44 μL, 0.37 mmol) were dissolved in dichloromethane (3.5 mL). Aqueous sodium hydroxide[5] (0.30 mL of a 5 % solution) was added and the mixture was refluxed for 72 h. The mixture was cooled and the organic layer was washed with water, dried ($MgSO_4$), filtered and concentrated. The residue was purified by column chromatography on silica gel (toluene-ethyl acetate, 4:1) to give the 2-*O*-benzyl derivative **32** (75 mg, 43 %) and the 3-*O*-benzyl derivative **33** (60 mg, 34%). Compound **32** had mp 143-145 °C, $[\alpha]_D$ -2.9° (*c* 0.7, chloroform). ^{13}C-NMR ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.7 (SCH_2CH_3), 65.8 (C-5'), 68.0, 68.5 (C-6, C-6'), 101.5 (PhCH), 102.4 (C-1'). The upfield shift for C-1' compared with compound **30** confirms substitution at the C-2' position.

Anal. Calcd for $C_{49}H_{54}O_{10}S$: C, 70.5; H, 6.5. Found: C, 70.2; H, 6.4.

Compound **33** had mp 119-120 °C, $[\alpha]_D$ 4.4° (*c* 0.82, chloroform). ^{13}C-NMR ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.7 (SCH_2CH_3),66.2 (C-5), 68.4 (C-6', C-6), 100.9

(PhCH), 103.4 (C-1'). Compared with compound **30** PhCH is moved upfield while C-1' remains at the same shift, thus confirming substitution at the 3'-position.

Anal. Calcd for $C_{49}H_{54}O_{10}S$: C, 70.5; H, 6.5. Found: C, 70.3; H, 6.5.

Ethyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4- and 2,3,6-Tri-*O*-benzyl-β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (34 and 35). Partial benzylation of compound **31** (132 mg, 0.16 mmol) was performed as described for compound **30**. The residue was purified by column chromatography on silica gel (toluene-ethyl acetate, 4:1) to give the 6-*O*-benzyl derivative **35** (56 mg, 38%) and the 4-*O*-benzyl derivative **34** (38 mg, 26 %). Compound **34** had mp 126-128 °C, $[\alpha]_D$ 13.4° (*c* 0.71, chloroform). ^{13}C-NMR ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.7 (SCH_2CH_3), 61.7 (C-6'), 67.9 (C-6), 102.2 (C-1'). The shift for C-6' remains at the same value as in compound **31**, thus confirming substitution at the 4'-position.

Anal. Calcd for $C_{56}H_{62}O_{10}S$: C, 72.6; H, 6.7. Found: C, 72.8; H,6.8.

Compound **35** had $[\alpha]_D$ -2.2° (*c* 0.64, chloroform). ^{13}C-NMR ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.7 (SCH_2CH_3), 68.0 (C-6), 71.0 (C-6'), 102.1 (C-1'). The downfield shift for C-6' compared with compound **31** confirms substitution at the 6'-position.

Anal. Calcd for $C_{56}H_{62}O_{10}S$: C, 72.6; H, 6.7. Found: C, 72.4; H, 6.7.

Ethyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2-*O*- and 3-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (36 and 37). Compound **30** (325 mg, 0.44 mmol), tetrabutylammonium hydrogen sulfate (29.6 mg, 0.09 mmol) and benzoyl chloride (76 μL, 0.65 mmol) were dissolved in dichloromethane (13 mL) and cooled to -20 °C.[16] Aqueous sodium hydroxide (0.99 mL of a 5 % solution) was added and the mixture was stirred at -20 to -10 °C for 20 min. The reaction temperature was allowed to rise to 0 °C over 60 min. The dichloromethane layer was washed with water, dried ($MgSO_4$), filtered and concentrated. The residue was purified by column chromatography on silica gel (toluene-ethyl acetate, 6:1) to give the 2-*O*-benzoyl derivative **36** (80 mg, 21 %) and the 3-*O*-benzoyl derivative **37** (181 mg, 49 %). (The 2,3-di-*O*-benzoyl derivative was also isolated in 6 % yield). Compound **36** had mp 171-173 °C, $[\alpha]_D$ -18.4° (*c* 0.57, chloroform). ^{13}C-NMR ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.7 (SCH_2CH_3), 65.8 (C-5'), 67.8, 68.4 (C-6, C-6'), 100.3 (C-1'), 101.6 (PhCH), 165.1 (C=O). The upfield shift for C-1' compared with compound **30** confirms 2-*O*-acylation.

Anal. Calcd for $C_{49}H_{52}O_{11}S$: C, 69.3; H, 6.2. Found: C, 69.4; H, 6.2.

Compound **37** had mp 120-122 °C, $[\alpha]_D$ -28.4° (*c* 1.21, chloroform). ^{13}C-NMR ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.7 (SCH_2CH_3), 66.2 (C-5'), 68.3 (C-6, C-6'), 101.1 (PhCH), 103.7 (C-1'), 166.2 (C=O). The C-1' shift remains at the same value as in

compound **30** and the shift for the PhCH moves upfield, thus indicating substitution at the 3'-position.

Anal. Calcd for $C_{49}H_{52}O_{11}S$: C, 69.3; H, 6.2. Found: C, 69.4; H, 6.1.

Ethyl 2,3,6-Tri-*O*-benzyl-4-*O*-(4-*O*- and 6-*O*-benzoyl-2,3-di-*O*-benzyl-β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (38 and 39). Partial benzoylation of compound **31** (0.114 g, 0.14 mmol) was performed as described for compound **30**. Reaction times and temperatures were 30 min at 0 °C and 60 min at +5 to +10 °C. The residue was purified by column chromatography on silica gel (toluene-ethyl acetate, 6:1) to give the 6-*O*-benzoyl derivative **39** (0.10 g, 78 %) and the 4-*O*-benzoyl derivative **38** (0.018 g, 14 %). Compound **38** had mp 127-129 °C, $[\alpha]_D$ -17.1° (*c* 0.51, chloroform). Compound **39** had $[\alpha]_D$ -23.4 (*c* 0.90, chloroform). ^{13}C-NMR ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.7 (SCH_2CH_3), 63.5 (C-6'), 68.0 (C-6), 70.1 (C-4'), 102.4 (C-1'), 166.7 (C=O). The C-6' shift has moved downfield compared with compound **31**, thus confirming substitution at the 6'-position.

Anal. Calcd for $C_{56}H_{60}O_{11}S$: C, 71.5; H, 6.4. Found: C, 71.2; H, 6.4

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