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A Stereospecific Approach towards the Synthesis of 2-Deoxy α- and β-Glycosides based on a 1,2-Ethyl (Phenyl) Thio Group Migration

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Abstract: Iodonium ion (NIS/TfOH)-assisted glycosylation of a sugar acceptor with properly protected ethyl (phenyl) 2-*O*-phenoxythiocarbonyl 1-thio-β-D-gluco- or 1-thio-α-D-mannopyranoside donors gives the respective 1,2-*trans* linked 2'-ethyl (phenyl) thio-2'-deoxy-α-D-manno- or β-D-glucopyranosides.

Introduction

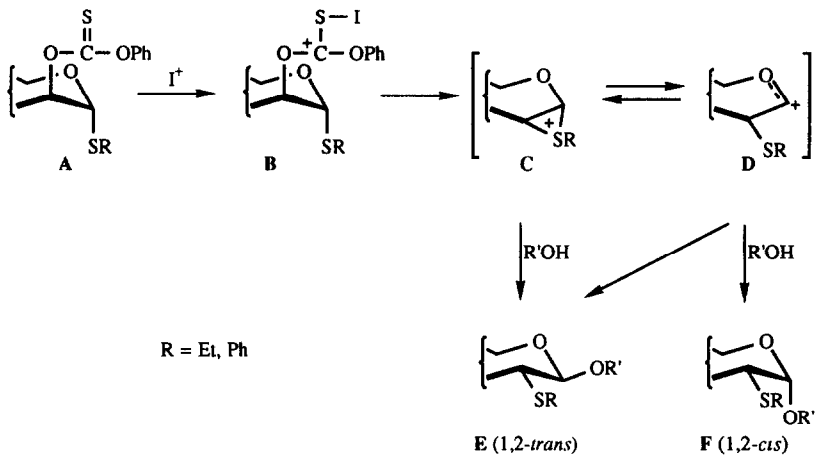
It is well-established now that the presence of a stereospecific (α or β) interglycosidic bond between a 2-deoxyoligosaccharide (glycon) and a heterocyclic moiety (aglycon) is a characteristic structural element of an interesting class of antitumor antibiotics (*e.g.* aureolic acids and chalicheamycin/esperamycin families). A successful synthetic route to this class of important antibiotics requires *inter alia* a reliable and general procedure for the stereocontrolled construction of 2-deoxyoligosaccharides having α- and (or) β-linkages. In order to achieve this goal a plethora of methods[1-5] for the stereocontrolled formation of α- or β-glycosidic 2-deoxyglycosides has been devised. For example, introduction of a 2-deoxy-α-glycosidic union can be accomplished[1,2] by electrophile-mediated addition of an acceptor molecule to the double bond of a glycal and subsequent removal of the resulting axially orientated substituent at C-2. A similar approach has also been adopted[3,4] for the synthesis of 2-deoxy-β-glycosides. However, the stereochemical outcome of the glycal approach strongly depends, especially so in the case of 2-deoxy-β-glycosidic bonds, on the nature of the electrophilic agent. In a recent report, Ikegami *et al* [6] showed that the latter drawback could be offset by using 2-deoxy-2-[(*p*-methoxyphenyl)thio]glycopyranosyl *N,N,N',N'*-tetramethylphosphoramidites as glycosyl donors in the formation of 2-deoxy-β-glycosides. On the other hand, a highly stereocontrolled glycosidation methodology for both 2,6-dideoxy α- and β-glycosides based on the combined application of "armed" 2,6-anhydro-2-thio glycosyl donors and "disarmed" 2,6-anhydro-2-sulfinyl glycosyl acceptors, both of which have the same type of leaving group at the anomeric center, was recently published by Toshima *et al* [7,2d]

We here report a stereospecific synthesis of 2-deoxy α- or β-glycosides by *N*-iodosuccinimide/trifluoromethanesulfonic acid (NIS/TfOH)-promoted glycosidation of ethyl (phenyl) 1-thioglycosides having at C-2 a *trans* orientated phenoxythiocarbonyl group

Results and discussion

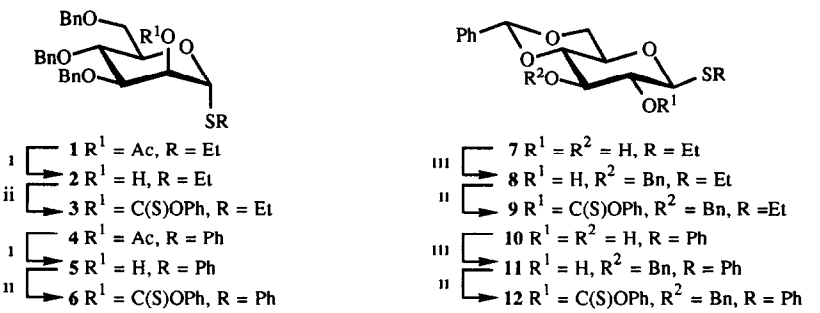
Preliminary studies[8] from this laboratory revealed that NIS/TfOH-promoted glycosidation of ethyl (phenyl) 2-*O*-phenoxythiocarbonyl (PTC) 1-thioglycosides with a glycosyl acceptor (R'OH), proceeded predominantly *via* the intermediate episulfonium ion **C** in Scheme 1. For instance, iodonium ion-mediated activation of an ethyl (phenyl) 2-*O*-PTC mannosyl derivative **A** in the presence of I^+-ions affords intermediate **B**. Intramolecular nucleophilic substitution of the activated thiocarbonyl species **B** by the anomeric ethyl (phenyl) thio group gives the episulfonium ion **C**, which is opened from the β-face by an incoming alcohol (R'OH), to furnish exclusively the *gluco* type β-linked saccharide **E**.

Scheme 1



In order to study in detail the scope of the new approach, the PTC-derivatives **3**, **6**, **9** and **12** were chosen as donors for the glycosylation of the known terminal galactosyl (*i.e.* compounds **13-14**) and glucosyl (*i.e.* compound **15**) acceptors. The respective mannosyl and glucosyl donors **3**, **6** and **9**, **12** were readily accessible by the sequence of reactions depicted in Scheme 2. Thus, saponification of the known[9] mannopyranosides **1** (**4**) followed by acylation of the individual secondary hydroxyl groups in **2** (**5**) with PTC-Cl[10] afforded the PTC-donors **3** (**6**) in 81% (82%) overall yield. On the other hand, regioselective benzylation[11] of the diol derivative

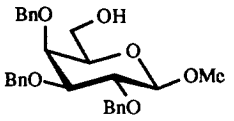
Scheme 2[a]



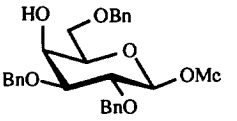
[a]**Key:** (i) NaOMe, MeOH (**2** and **5**, quant.); (ii) ClC(S)OPh, DMAP, CH_3CN (**3**, 81%; **6**, 82%; **9**, 80%; **12**, 82%), (iii) Bu_2SnO, MeOH, Δ, then BnBr, CsF, DMF (**8**, 65%; **11**, 66%)

7[12] (→**8**) and subsequent introduction of the PTC function, gave the glucopyranosyl donor **9** in 52% yield over the two steps. The corresponding phenyl 1-thioglucoside **12** was prepared from **10**[12] by the same procedure mentioned for the synthesis of **9**.

The outcome of the NIS/TfOH-assisted glycosidation of the known[13-15] terminal acceptors **13-15** with the above prepared PTC-donors are summarized in Table 1. Thus, condensation of the ethyl 2-*O*-PTC-1-thio-α-D-mannopyranosyl donor **3** with the primary hydroxyl function in acceptor **13** resulted in the exclusive formation of the β-linked disaccharide **16** (entry 1), the *gluco* configuration of which was unambiguously ascertained by ^{1}H- and ^{13}C NMR spectroscopy. The stereochemical outcome of the glycosylation indicates that the proposed oxycarbonium ion **D** (R = Et in Scheme 1), which may lead to 1,2-*trans*- and 1,2-*cis* linked dimers **16** (*i.e.* species **E** and **F** in Scheme 1), does not play a significant role in the glycosylation process. Similarly,



13



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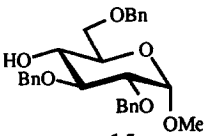

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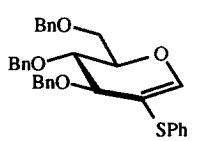
glycosylation of **13** with the corresponding glycopyranosyl donor **9** provided (entry 2) the α-linked *manno* type dimer **17** in a comparable yield. Interestingly, iodonium-promoted condensation of the phenyl-2-*O*-PTC-1-thioglycosyl donors **6** and **12** with the same acceptor **13** (entries 3-4) proceeded, in terms of yield and rate of activation, less satisfactory. The decrease in yield of the latter condensations is mainly due to the concomitant formation of a side product, the ^{1}H- and ^{13}C NMR data of which were in complete accordance with the glycal derivative **22**[16]. The identity of the byproduct was established independently by short (5 min) treatment of the mannopyranoside **6** with NIS/TfOH to give, after work-up and purification, a product which was in every aspect identical with **22**. The formation of the unexpected 2-thiophenyl glycal **22** may be ascribed to the occurrence of the intermediate oxycarbonium species **D** (R = Ph in Scheme 1), which, instead of reacting with an acceptor, undergoes a rapid elimination.

The results thus far obtained clearly show that ethyl 2-*O*-PTC-1-thioglycosyl donors are more effectively glycosylated than their thiophenyl counterparts. However, it is well known[3f] that thiophenyl functions are more readily desulfurised than thioalkyl groups. Indeed, desulfurisation of disaccharide **17** with Raney nickel was rather sluggish (5 days) to afford 2-deoxy compound **23** in 50% yield. As expected, desulfurisation of **19** went to completion within 2h to afford the 2-deoxy disaccharide **23** in 81% yield. The smooth and effective removal of the thiophenyl group in the final stage of the synthesis was the deciding factor to use phenyl 2-*O*-PTC-1-thioglycosides in glycosylations of secondary alcohols. In a first experiment, coupling of mannopyranosyl donor **6** with the axial hydroxyl group of galactopyranoside **14**, under the same conditions as



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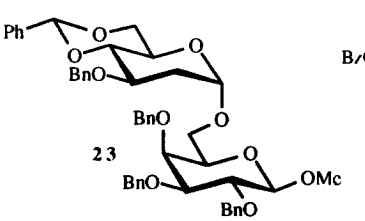

23

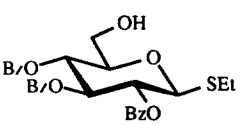

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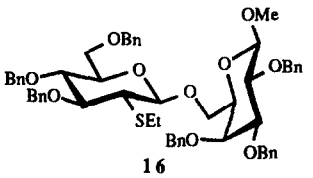
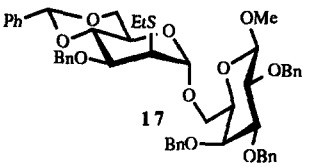
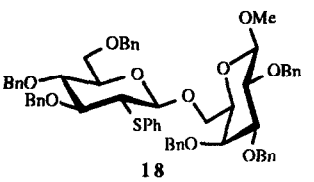
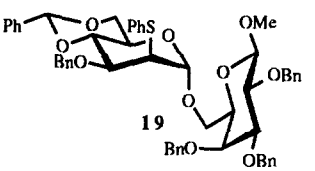
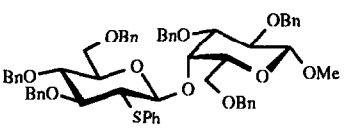
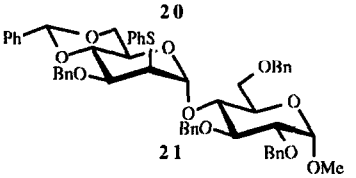
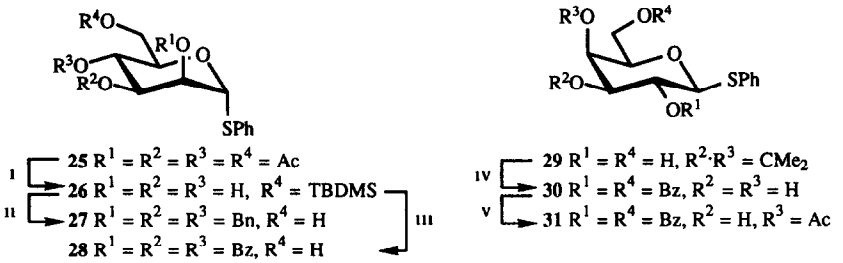
Table 1 Results of NIS/TfOH-promoted glycosidations of 2-*O*-PTC-thioglycosides **3**, **6**, **9** and **12**

Entry	Donor	Acceptor	Time (min)	Disaccharide	Yield(%)
1[a]	**3**	**13**	10	 **16**	85
2[a]	**9**	**13**	10	 **17**	85
3[a]	**6**	**13**	50	 **18**	75
4[a]	**12**	**13**	60	 **19**	71
5[b]	**6**	**14**	15	 **20**	61
6[b]	**12**	**15**	20	 **21**	67

[a] Donor (0 3 mmol) and acceptor (0.25 mmol) in $(CH_2Cl)_2$/ether, 1/1 (5 mL)
[b] Donor (0.3 mmol) and acceptor (0.25 mmol) in $(CH_2Cl)_2$/ether, 1/1 (1 mL)

mentioned before, yielded predominantly glycal **22**. Fortunately, it was established that execution of the reaction with a high concentration of reactants had a beneficial effect on the condensation. Thus, disaccharide **20** was now isolated in an acceptable yield (see entry 5) and the rate of the reaction was comparable with those observed for the ethyl 1-thioglycosides **3** and **9** (*cf.* entries 1-2 in Table 1). Likewise, glucopyranosyl donor **12** was

Scheme 3[a]

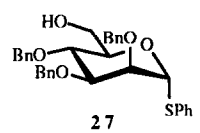
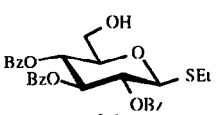
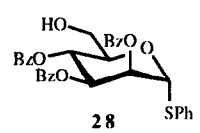
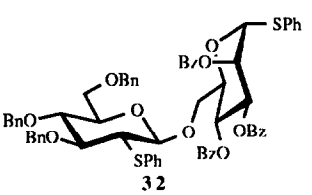
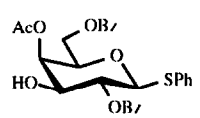
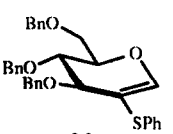


[a]**Key:** (i) NaOMe, MeOH, then TBDMSCl/C_5H_5N (72%); (ii) BzCl/C_5H_5N, then *p*-TsOH, CH_3CN, H_2O (92%); (iii) BnBr, NaH, DMF, *p*-TsOH, CH_3CN, H_2O (77%); BzCl/C_5H_5N, then HOAc/H_2O [4:1], 50°C (87%); (v) $(CH_3O)_3CCH_3$, *p*-TsOH, CH_3CN, then HOAc/H_2O [4:1], (85%).

readily glycosylated by the rather inreactive HO-4 of glucose acceptor **15** to furnish dimer **21** (see entry 6).

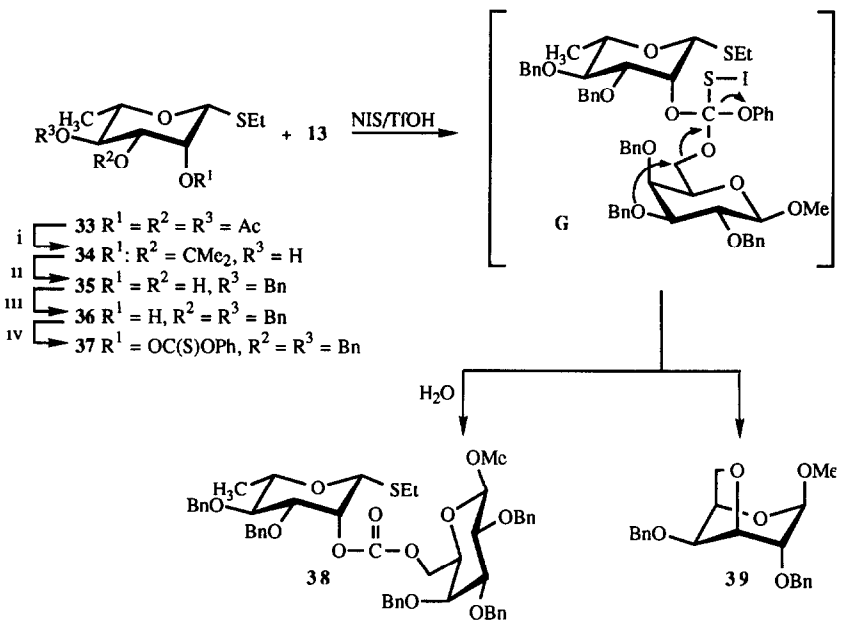
At this stage, we were anxious to find out whether the phenyl 2-*O*-PTC-1-thiomannopyranosyl donor **6** could be coupled with the non-terminal acceptors **24**, **27**, **28** and **31**. Interestingly (see entry 1 in Table 2), NIS/TfOH-promoted glycosidation of donor **6** with the phenyl 1-thiomannopyranosyl acceptor **27**, prepared in three steps (see Scheme 3) by regioselective silylation of **25**[17] (→**26**) with *t*-butyldimethylsilyl chloride (TBDMSCl) followed by benzylation and then acid-hydrolysis of the TBDMS group did not proceed as expected: fast disappearance of acceptor **27** was observed as gauged by TLC-analysis. A similar event took place in the

Table 2 Results of NIS/TfOH-promoted glycosidations of 2-*O*-PTC-thioglycoside **6** with non-terminal acceptors **24**, **27**, **28** and **31**

Entry	Donor	Acceptor	Time (min)	Product	Yield(%)
1	**6**	 **27**	5	-	
2	**6**	 **24**	5	-	
3	**6**	 **28**	15	 **32**	75
4	**6**	 **31**	5	 **22**	70

condensation of **6** with "disarmed" ethyl thioglucopyranosyl acceptor **24**[18] (entry 2). These rather disappointing results urged us to use phenyl 1-thio-α-D-mannopyranoside **28**, obtained by benzoylation of **26** followed by removal of the TBDMS group, as acceptor in the glycosylation. It can be seen in entry 3 that **28** was readily glycosidated by **6** to give the expected β-linked dimer **32**, which in turn is amenable to further elongation, in an acceptable yield. Unfortunately, NIS/TfOH-promoted glycosidation of mannosyl donor **6** with the secondary hydroxyl in the less reactive partially acylated acceptor **31**, prepared (see Scheme 3) by benzoylation of **29**[19] followed by acid-hydrolysis of the isopropylidene group (→**30**) and then regioselective acetylation[20], yielded predominantly the glycal derivative **22**.

Scheme 4[a]



[a]**Key:** (i) NaOMe, MeOH, then $(MeO)_2CMe_2$, acetone, *p*-TsOH (85%); (ii) BnBr, NaH, DMF, then $HOAc/H_2O$ [4:1], 50°C (89%); (iii) Bu_2SnO, MeOH, Δ, then BnBr, CsF, DMF (64%); (iv) ClC(S)OPh, DMAP, CH_3CN (77%)

The results thus far obtained, clearly show that alkyl (aryl) 2-*O*-PTC-1-thioglycosyl donors having a *trans* orientated PTC-group are promising synthons for the future assembly of both α- and β-glycosides. In order to explore the fate of an 1,2-*cis* alkyl 2-*O*-PTC-1-thio derivative, we prepared the L-rhamnosyl donor **37** by the sequence of reactions outlined in Scheme 4. Thus, Zemplén deacetylation of ethyl 2,3,4-tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside (**33**)[21] and subsequent acetonation yielded derivative **34**. Benzylation and acid-hydrolysis (→**35**) followed by regioselective benzylation[11], and then treatment with PTC-Cl, gave the requisite donor in 34% overall yield. NIS/TfOH-assisted condensation of **37** with the partially benzylated galactosyl acceptor **13** gave, after work-up (10 min) and purification, two main products, one of which was in every aspect identical with the known[22] 3,6-anhydro derivative **39** On the other hand, the structure of the other product was in complete accordance, as evidenced by NMR and LC-MS analysis, with the carbonate derivative **38**. The

formation of these products may be rationalized by the rapid glycosylation of **37** with **13** to give the putative intermediate **G** (see Scheme 4), which may either hydrolyse or decompose slowly *via* an intramolecular substitution (see arrows) to give **38** and **39**, respectively.

In conclusion, NIS/TfOH-mediated glycosidation of ethyl (phenyl) 1-thioglycosides with a *trans* orientated PTC group at C-2 presents a stereocontrolled route to both α- and β-linked 2-deoxyglycosides. However, this glycosidation procedure is most effective when reactive acceptors are used. At present, we are exploring the ethyl (phenyl) 2-*O*-PTC-1-thioglycosides-iodonium ion glycosidation approach towards the preparation of naturally occurring 2-deoxyoligosaccharides.

Experimental

General methods and materials -Acetonitrile was dried by boiling over CaH_2 (5 g/L) and then distilled. 1,2-Dichloroethane was distilled from P_2O_5. DMF was stirred with CaH_2 at room temperature and distilled under reduced pressure. Ether was distilled from $LiAlH_4$ Acetonitrile and DMF were stored over molecular sieves 4Å (Aldrich). Ether was stored over sodium wire and 1,2-dichloroethane over alumina. Schleicher and Schull DC Fertigfolien F 1500 LS 254 were used for TLC. Compounds were detected by charring with 20% sulfuric acid in methanol Optical rotations were recorded at 20°C with a Perkin-Elmer 241 polarimeter for solutions in $CHCl_3$, unless stated otherwise. Column chromatography was performed on silica gel 60 (230-400 mesh, Merck) Gel permeation chromatography was performed on Sephadex LH20 (Pharmacia). ^1H NMR spectra (300 and 400 MHz) were recorded at 25°C with a Bruker WM 300 or 400 MSL spectrometer ^{13}C NMR spectra (50 MHz) were recorded with a Jeol JNM-FX 200 spectrometer. ^1H and ^{13}C chemical shifts (δ) are given in ppm relative to that of Me_4Si ($CDCl_3$) The liquid chromatography mass-spectra (LC-MS) were recorded in the positive ion mode on a TSQ 70 triple quadrupole spectrometer equipped with a HP 59980A Particle Beam LC/MS interface using ammonia for chemical ionisation

Ethyl 3,4,6-tri-*O*-benzyl-2-*O*-phenoxythiocarbonyl-1-thio-α-D-mannopyranoside (3).-Sodium methoxide (80 mg) was added to a solution of **1**[9] (3 7 mmol, 1 8 g) in MeOH (30 mL) After 2h at room temperature, the mixture was neutralised with Dowex (H^+ form), filtered and concentrated A solution of the residue, DMAP (7.4 mmol, 904 mg) and phenoxythiocarbonyl chloride (4.4 mmol, 752 mg) was stirred for 16h at room temperature, when TLC (98:2 CH_2Cl_2-acetone) showed the reaction to be complete The reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with M NaH_2PO_4 (25 mL) and water (25 mL), dried ($MgSO_4$), and concentrated Column chromatography [1:0 to 2.1 light petroleum (bp 40-60°C)-ether] yielded **3** (1 9 g, 81% based on **1**), $[\alpha]_D$ +26° (*c* 1). ^1H NMR ($CDCl_3$) δ 1.27 (t, 3H, SCH_2CH_3, *J* 7 4 Hz), 2 65 (AB, 2H, SCH_2CH_3), 3 68 (dd, 1H, H-3, $J_{3,4}$ 9 4 Hz), 3 81 (dd, 1H, H-6, $J_{5,6}$ 4.4 Hz, $J_{6,6'}$ 10 8 Hz), 3 92 (t, 1H, H-4, $J_{4,5}$ 9 5 Hz), 4 01 (dd, 1H, H-6', $J_{5,6}$ 3.1 Hz), 4 20 (m, 1H, H-5), 4.44-4.88 (AB, 6H, OCH_2Ph), 5.61 (d, 1H, $J_{1,2}$ 1 6 Hz), 5 84 (dd, 1H, H-2, $J_{2,3}$ 3 2 Hz), 7 12-7 98 (m, 20H, H_{arom}). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 14 6 (SCH_2CH_3), 25 3 (SCH_2CH_3), 68 4 (C-6), 71 7, 73 0, 74 8 (OCH_2Ph), 71 8, 74.4, 78 1, 80.4 (C-2, C-3, C-4, C-5), 80 9 (C-1), 121 9-139 1 (CH_{arom}), 137 2, 137 7, 138 0, 153 0 (C_{arom}), 194 0 (C=S).

Phenyl 3,4,6-tri-*O*-benzyl-2-*O*-phenoxythiocarbonyl-1-thio-α-D-mannopyranoside (6).-Prepared from **4**[9] as described for **3**, **6** (82% based on **4**) had $[\alpha]_D$ +14° (*c* 1) $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 68.5 (C-6), 71.9, 73.1, 75.1 (OCH_2Ph), 72 4, 74.5, 78.1, 80 0 (C-2, C-3, C-4, C-5), 84 9 (C-1), 121 6-131.9 (CH_{arom}), 137.2-153 1 (C_{arom}), 194.0 (C=S).

Ethyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (8).-A mixture of compound **7**[12] (5 mmol, 1.6 g) and dibutyltin oxide (6 mmol, 1 5 g) in MeOH (30 mL) was refluxed After 4h at room temperature, the reaction mixture was concentrated *in vacuo* The residue was dissolved in DMF (30 mL) and benzyl bromide (6.0 mmol, 1 0 g) and CsF (6.5 mmol, 990 mg) were added After stirring for 16h at room temperature, the reaction mixture was

concentrated. The residue was dissolved in CH_2Cl_2 (50 mL), washed with M KF (25 mL), dried ($MgSO_4$), and concentrated. Column chromatography [1:0 to 1:3 light petroleum (bp 40-60°C)-ether] afforded **8** (1.3 g, 65%), $[\alpha]_D$ -41° (*c* 1). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 15.1 (SCH_2CH_3), 24.4 (SCH_2CH_3), 68.4 (C-6), 70.5, 72.8, 81.0, 81.4 (C-2, C-3, C-4, C-5), 74.5 (OCH_2Ph), 86.4 (C-1), 101.0 (CHPh), 125.8-128.8 (CH_{arom}), 137.1, 138.2 (C_{arom}).

Ethyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-phenoxythiocarbonyl-1-thio-β-D-glucopyranoside (9).-To a stirred solution of compound **8** (3.3 mmol, 1.3 g) and DMAP (6.6 mmol, 806 mg) in CH_3CN (25 mL) was added phenoxythiocarbonyl chloride (4.0 mmol, 684 mg). After 16h at room temperature, the reaction mixture was concentrated to dryness. The residue was dissolved in CH_2Cl_2 (50 mL), washed with M NaH_2PO_4 (25 mL), water (25 mL), dried ($MgSO_4$), and concentrated. Purification of the residue [1:0 to 1:1 light petroleum (bp 40-60°C)-ether] gave **9** (1.4 g, 80%), $[\alpha]_D$ -45° (*c* 1). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 14.7 (SCH_2CH_3), 24.8 (SCH_2CH_3), 68.4 (C-6), 74.5 (OCH_2Ph) 70.5, 80.0, 80.7, 81.1 (C-2, C-3, C-4, C-5), 83.9 (C-1), 101.1 (CHPh), 121.8-129.4 (CH_{arom}), 136 9, 137.9, 153.4 (C_{arom}), 194.5 (C=S).

Phenyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (11).-Prepared from **10**[12] as described for **8**, **11** (66%) had $[\alpha]_D$ -36° (*c* 1). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 68.5 (C-6), 70.5, 72.1, 80.9, 81.5 (C-2, C-3, C-4, C-5), 74.7 (OCH_2Ph), 88.3 (C-1), 101.1 (CHPh), 125.9-138.1 (CH_{arom}, C_{arom}).

Phenyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-phenoxythiocarbonyl-1-thio-β-D-glucopyranoside (12).-Prepared from **11** as described for **9**, **12** (82%) had $[\alpha]_D$ +15° (*c* 1). ^1H NMR ($CDCl_3$) δ 3.54 (m, 1H, H-5), 3.83 (t, 1H, H-4, $J_{4,5}$ 10.3 Hz), 3.85 (t, 1H, H-6, $J_{5,6'} \approx J_{6,6'}$ 9.3 Hz), 3.97 (t, 1H, H-3, $J_{3,4}$ 9.0 Hz), 4.40 (dd, 1H, H-6', $J_{5,6'}$ 5.0 Hz), 4.86 (AB, 2H, OCH_2Ph), 4.90 (d, 1H, H-1, $J_{1,2}$ 10.1 Hz), 5.70 (dd, 1H, H-2, $J_{2,3}$ 8.6 Hz), 7.00-7.57 (m, 20H, H_{arom}).$^{13}C\{^1H\}$NMR ($CDCl_3$) δ 68.0 (C-6), 70.0 79 7, 80.4, 80.5 (C-2, C-3, C-4, C-5), 74.2 (OCH_2Ph), 86.4 (C-1), 100.7 (CHPh), 121.5-131.9, 132.5-153.2 (CH_{arom}, C_{arom}), 194.1 (C=S).

Phenyl 6-*O*-*tert*-butyldimethylsilyl-1-thio-α-D-mannopyranoside (26).-To a solution of **25**[17] (4.9 mmol, 1.3 g) in MeOH (30 mL) was added sodium methoxide (20 mg). After 1h at room temperature, the mixture was neutralised with Dowex (H^+ form), filtered and concentrated. The residue was dissolved in pyridine (30 mL) and TBDMSCl (5.9 mmol, 886 mg) was added. After 2h at room temperature, the reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with water (25 mL), 0.9 M $NaHCO_3$ (25 mL), dried ($MgSO_4$), and concentrated. Column chromatography (95:5 CH_2Cl_2-MeOH) afforded **26** (1.4 g, 72%), $[\alpha]_D$ +147° (*c* 1) $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 14.1 (CH_3Si), 18.3 ($(CH_3)_3C$), 25.9 ($(CH_3)_3C$), 64.3 (C-6), 70.0, 72.0, 72.2, 72.3 (C-2, C-3, C-4, C-5), 87 9 (C-1), 127.2-131.4 (CH_{arom}), 134.1 (C_{arom}).

Phenyl 2,3,4-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (27).-To a stirred solution of compound **26** (2 mmol, 720 mg) in DMF (20 mL) was added sodium hydride (7.8 mmol, 312 mg 60% suspension) and benzyl bromide (7.2 mmol, 1.2 g). After 3h at room temperature, MeOH was added and the mixture diluted with CH_2Cl_2 (20 mL), washed with water (2x 10 mL), dried ($MgSO_4$), and concentrated The residue was redissolved in CH_3CN (4 mL) and water (1 mL). *p*-TsOH (10 mmol, 1.7 g) was added and the reaction mixture stirred for 1h at room temperature. The mixture was diluted with CH_2Cl_2 (20 mL), washed with 0.9 M $NaHCO_3$ (10 mL), water (10 mL), dried ($MgSO_4$), and concentrated. Column chromatography (97:3 CH_2Cl_2-acetone) gave **27** (835 mg, 77%), $[\alpha]_D$ +94° (*c* 1). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 61 7 (C-6), 71.9, 72.1, 75.0 (OCH_2Ph), 73.2, 74.4, 76.2, 79.8 (C-2, C-3, C-4, C-5), 85.8 (C-1), 127.3-131.5 (CH_{arom}), 137.5, 137.9, 138 1 (C_{arom}).

Phenyl 2,3,4-tri-*O*-benzoyl-1-thio-α-D-mannopyranoside (28).-A solution of compound **26** (3.5 mmol, 1.4 g) in pyridine (25 mL) and benzoyl chloride (13.7 mmol, 1.9 g), was stirred for 4h at room temperature, then water (1 mL) was added and the mixture concentrated. A solution of the residue in CH_2Cl_2 (40 mL) was washed with 0.9 M $NaHCO_3$ (20 mL), water (20 mL), dried ($MgSO_4$), and concentrated. To a solution of the residue in CH_3CN (4 mL) and water (1 mL) was added *p*-TsOH (18 mmol, 3.1 g). After 0.5h at room temperature, the mixture was diluted with CH_2Cl_2 (30 mL), washed with 0.9 M $NaHCO_3$ (15 mL), water (15 mL), dried ($MgSO_4$), and concentrated. Column chromatography (97:3 CH_2Cl_2-acetone) gave **28** (1.9 g, 92% based on **26**), $[\alpha]_D$ -26° (*c* 1). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 61.0 (C-6), 67.0, 70.0, 71.7, 72.0 (C-2, C-3, C-4, C-5), 85.7 (C-1), 127.9-133.3 (CH_{arom}), 128.6, 128.9, 132.4 (C_{arom}), 165.1, 166.0 (PhCOO)

Phenyl 2,6-di-benzoyl-1-thio-β-D-galactopyranoside (30).-A solution of compound **29**[19] (2.4 mmol, 750 mg) in pyridine (20 mL) and benzoyl chloride (5.2 mmol, 731 mg) was stirred for 3h at room temperature, then water (1 mL) was added and the mixture concentrated. A solution of the residue in CH_2Cl_2 (20 mL) was washed with 0.9 M $NaHCO_3$ (10 mL), water (10 mL), dried ($MgSO_4$), and concentrated. The residue was redissolved in 4:1 acetic acid-water (50 mL) and the mixture stirred for 5h at 50°C. The reaction mixture was concentrated and toluene (3 x 20 mL) was evaporated from the residue. Column chromatography (97:3 CH_2Cl_2-MeOH) afforded **30** (1.0 g, 87%), $[\alpha]_D$ +13° (*c* 1). ^1H NMR ($CDCl_3$) δ 3.89 (dd, 1H, H-3, $J_{3,4}$ 3.3 Hz), 3 96 (t, 1H, H-5, $J_{5,6}$ 6.2 Hz), 4.10 (d, 1H, H-4), 4.64 (m, 2H, H-6, H-6'), 4 84 (d, 1H, H-1, $J_{1,2}$ 10 0 Hz), 5.35 (t, 1H, H-2, $J_{2,3}$ 9.8 Hz), 7.05-8.09 (m, 15H, H_{arom}). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 64.6 (C-6), 69.5, 71.5, 73.1, 76.9 (C-2, C-3, C-4, C-5), 86.9 (C-1), 127.5-133.4 (CH_{arom}), 134.1 (C_{arom}), 166.6, 166.8 (PhCOO).

Phenyl 4-*O*-acetyl-2,6-di-*O*-benzoyl-1-thio-β-D-galactopyranoside (31).-To a solution of **30** (2.1 mmol, 1.0 g) in CH_3CN (15 mL) was added trimethyl orthoacetate (4.2 mmol, 505 mg) and *p*-TsOH (20 mg). After 1h, the reaction mixture was neutralised with triethyl amine and concentrated. The residue was dissolved in 4:1 acetic acid-water (25 mL) and stirred for 1h at room temperature then concentrated, and toluene (3 x 25 mL) was evaporated from the residue. Purification of the residue on silica gel (97:3 CH_2Cl_2-acetone) afforded **31** (932 mg, 85%), $[\alpha]_D$ +5° (*c* 1). ^1H NMR ($CDCl_3$) δ 2.21 (s, 3H, CH_3COO), 4.44 (dd, 1H, H-3, $J_{3,4}$ 3 6 Hz), 4.47 (m, 1H, H-5), 4.50 (m, 2H, H-6, H-6'), 4.85 (d, 1H, H-1, $J_{1,2}$ 10.0 Hz), 5.29 (t, 1H, H-2, $J_{2,3}$ 9.8 Hz), 5.52 (d, 1H, H-4), 7.14-8.10 (m, 15H, H_{arom}). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 20.8 (CH_3COO), 62.8 (C-6), 70.1, 71 5, 72 3, 75 0 (C-2, C-3, C-4, C-5), 86.5 (C-1), 127.9-133.4 (CH_{arom}), 129.3, 130.1, 132.9 (C_{arom}), 166.7 (PhCOO), 170.9 (CH_3COO).

Ethyl 2,3-*O*-isopropylidene-1-thio-β-L-rhamnopyranoside (34).-Compound **33**[21] (7.0 mmol, 1.4 g), was dissolved in MeOH (50 mL) and sodium methoxide (50 mg) was added. After stirring for 1h at room temperature, the reaction was neutralised with Dowex (H^+ form), filtered and concentrated The residue was redissolved in acetone and 2,2-dimethoxypropane (70 mmol, 7.3 g) and *p*-TsOH (50 mg) was added After 3h at room temperature, the reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with 0 9 M $NaHCO_3$ (25 mL), water (25 mL), dried ($MgSO_4$), and concentrated. Purification of the crude product (97.3 CH_2Cl_2-MeOH) yielded **34** (1 5 g, 85%), $[\alpha]_D$ +90° (*c* 1). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 14.1 (SCH_2CH_3), 16.9 (C-6), 24.9 (SCH_2CH_3), 25 4, 27 3 ($(CH_3)_3C$), 73 6, 74.1, 75.6, 79.3 (C-2, C-3, C-4, C-5), 83.0 (C-1), 109.2 ($(CH_3)_3C$).

Ethyl 4-*O*-benzyl-1-thio-β-L-rhamnopyranoside (35).-To a stirred solution of compound **34** (6.0 mmol, 1.5 g) in DMF (50 mL) was added sodium hydride (7.8 mmol, 316 mg 60% suspension) and benzyl bromide (7.2 mmol, 1.2 g). The mixture was stirred for 4h at room temperature, MeOH was added, and the mixture concentrated. A solution of the residue in CH_2Cl_2 (50 mL) was washed twice with water (25 mL), dried ($MgSO_4$), and concentrated. The residue was redissolved in 9:1 acetic acid-water (50 mL) and stirred for 17h at 50°C. The mixture was concentrated and toluene (3 x 50 mL) was evaporated from the residue. Column chromatography (99:1 to 97:3 CH_2Cl_2-MeOH) gave **35** (1.6 g, 89%), $[\alpha]_D$

+52° (*c* 1). ^{1}H NMR ($CDCl_3$) δ 1.29 (t, 3H, SCH_2CH_3, *J* 7.4 Hz), 1.34 (d, 1H, $J_{5,6}$ 5.9 Hz), 2.73 (AB, 2H, SCH_2CH_3), 3.33 (m, 2H, H-4, H-5), 3 72 (m, 1H, H-3), 3.98 (d, 1H, H-2, $J_{2,3}$ 3.1 Hz), 4.60 (s, 1H, H-1), 4.76 (AB, 2H, OCH_2Ph), 7.26-7.36 (m, 5H, H_{arom}). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 14.9 (SCH_2CH_3), 18.0 (C-6), 25.3 (SCH_2CH_3), 72.4, 74.9, 75.7, 80.9 (C-2, C-3, C-4, C-5), 75.0 (OCH_2Ph), 83.5 (C-1), 127.6-128.2 (CH_{arom}), 138.1 (C_{arom}).

Ethyl 3,4-di-*O*-benzyl-1-thio-β-L-rhamnopyranoside (36).-Prepared from **35** as described for **8**, **36** (70%) had $[\alpha]_D$ +37° (*c* 1). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 14.9 (SCH_2CH_3), 18.0 (C-6), 25.3 (SCH_2CH_3), 71.4, 75.3 (OCH_2Ph), 69.6, 75.8, 79.3, 82.3 (C-2, C-3, C-4, C-5), 83.0 (C-1), 126.7-135.7 (CH_{arom}), 137.4, 138.0 (C_{arom})

Ethyl 3,4-di-*O*-benzyl-2-*O*-phenoxythiocarbonyl-1-thio-β-L-rhamnopyranoside (37).-Prepared from **36** as described for **9**, **37** (77%) had $[\alpha]_D$ +97° (*c* 1). ^{1}H NMR ($CDCl_3$) δ 1 31 (t, 3H, SCH_2CH_3, *J* 7.5 Hz), 1.37 (d, 1H, H-6, $J_{5,6}$ 5.4 Hz), 2.77 (AB, 2H, SCH_2CH_3), 3.47 (m, 2H, H-4, H-5), 3.75 (m, 1H, H-3), 4.75 (s, 1H, H-1), 4.55-4.97 (AB, 4H, OCH_2Ph), 6.24 (d, 1H, H-2, $J_{2,3}$ 3.1 Hz), 7 09-7.43 (m, 15H, H_{arom}) $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 14.9 (SCH_2CH_3), 18.2 (C-6), 25.4 (SCH_2CH_3), 72.4, 75.4 (OCH_2Ph), 76.2, 79.8, 80.4 (C-2, C-3, C-4, C-5), 81.3 (C-1), 121.9-129.4 (CH_{arom}), 136.7, 138.3, 156.6 (C_{arom}), 195.5 (C=S)

General procedure for NIS/TfOH-promoted glycosidations.

Method A: A mixture of ethyl (phenyl) 2-*O*-phenoxythiocarbonyl 1-thioglycoside (0 3 mmol), acceptor (0.25 mmol) and powdered molecular sieves (4Å, 0 5 g) in 1:1 1,2-dichloroethane-ether (v/v, 5 mL) was stirred for 15 min at room temperature. A solution of NIS and TfOH, freshly prepared by ultrasonic pulverisation in 1:1 1,2-dichloroethane-ether (v/v, 3.3 mL) and subsequent addition of TfOH (0.33 μmol, 4 μL) was added. When TLC analysis (97:3 CH_2Cl_2-acetone) showed the reaction to be complete, the reaction mixture was filtered, diluted with CH_2Cl_2 (30 mL), washed successively with M $Na_2S_2O_3$ (15 mL) and 0.9 M $NaHCO_3$ (15 mL), dried ($MgSO_4$), and concentrated The residue was purified on Sephadex LH20 (eluens: 1:1 CH_2Cl_2-MeOH) or silica gel to give the glycosidation products.

Method B: A mixture of ethyl (phenyl) 2-*O*-phenoxythiocarbonyl 1-thioglycoside (0.3 mmol), acceptor (0.25 mmol) and powdered molecular sieves (4Å, 0.5 g) in 1:1 1,2-dichloroethane-ether (v/v, 1 mL) was stirred for 15 min at room temperature. For further processing: see method A.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-ethylthio-β-D-glucopyranosyl)-β-D-galactopyranoside (16).-Prepared as described above (method A), starting from donor **3** and acceptor **13** in a yield of 85%, $[\alpha]_D$ -4° (*c* 1). ^{1}H NMR ($CDCl_3$) δ 1.22 (t, 3H, SCH_2CH_3, *J* 7.4 Hz), 2 62-2.79 (m, 3H, SCH_2CH_3, H-2^{Gl}), 3 33 (dd, H-3^{Gl}, $J_{2,3}$ 11.0 Hz, $J_{3,4}$ 8 7 Hz), 3.40 (ddd, 1H, 1H, H-5^{Gl}, $J_{5,6}$ 2 2 Hz, $J_{5,6'}$ 3.9 Hz), 3.50 (dd, 1H, H-3^G, $J_{3,4}$ 2.8 Hz), 3.53-3.59 (m, 2H, H-5^G, H-6^G), 3 56 (s, 3H, OCH_3), 3.59-3.70 (m, 2H, H-$6'^{Gl}$, H-6^{Gl}), 3.68 (t, 1H, H-4^{Gl}, $J_{4,5}$ 8.7 Hz), 3.81 (dd, 1H, H-2^G, $J_{2,3}$ 9.7 Hz), 3 83-3.86 (m, 2H, H-4^G, H-$6'^G$), 4.28 (d, 1H, H-1^G, $J_{1,2}$ 7.7 Hz), 4.39 (d, 1H, H-1^{Gl}, $J_{1,2}$ 8 8 Hz), 4 44-4 98 (AB, 12H, OCH_2Ph), 7.09-7.41 (m, 30H, H_{arom}) $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 14 9 (SCH_2CH_3), 27.0 (SCH_2CH_3), 52 2 (C-2^{Gl}), 56 9 (OCH_3), 68.4 (C-6^{Gl}, C-6^G), 72.8, 73.2, 74 1, 74.7, 74.8, 76.1 (OCH_2Ph), 73.4, 73.7, 74.4, 78 7, 79 4, 81.7. 83 2 (C-3^{Gl}-C-5^{Gl}, C-2^G-C-5^G), 104 6 (C-1^{Gl}, $J_{C\text{-}1,H\text{-}1}$ 157 Hz), 104.7 (C-1^G), 127.3-128 1 (CH_{arom}), 137 8, 137 9, 138.2, 138 3 138.6 (C_{arom})

Anal Calc for $C_{57}H_{64}O_{10}S$ C, 72.77; H, 6 81 Found. C, 72 65, H, 6 84

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-ethylthio-α-D-mannopyranosyl)-β-D-galactopyranoside (17).-Prepared as described above (method A), starting from donor **9** and acceptor **13** in a yield of 85%, $[\alpha]_D$ +14° (*c* 1). ^{1}H NMR ($CDCl_3$) δ 1.25 (t, 3H, SCH_2CH_3, *J* 7.4 Hz), 2 68 (AB, 2H, SCH_2CH_3), 3 06 (dd, 1H, H-2^M, $J_{2,3}$ 3 7 Hz), 3 40-3 47 (m, 2H, H-5^G, H-6^G), 3 52 (s, 3H, OCH_3), 3.53 (dd, 1H, H-

3^G, $J_{3,4}$ 2.9 Hz), 3.71-3.92 (m, 3H, H-4^M, H-6^M, H-$6'^M$), 3.82 (dd, 1H, H-2^G, $J_{2,3}$ 9.8 Hz), 4.11 (m, 1H, H-3^M), 4.15-4.23 (m, 2H, H-$6'^M$, H-5^M), 4.26 (d, 1H, H-1^G, $J_{1,2}$ 7.7 Hz), 4.78 (d, 1H, H-1^M, $J_{1,2}$ 1.4 Hz), 4.55-4.98 (AB, 8H, OCH_2Ph), 5.60 (s, 1H, CHPh), 7.12-7.49 (m, 25H, H_{arom}). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 14.5 (SCH_2CH_3), 27.9 (SCH_2CH_3), 50.4 (C-2^M), 56.9 (OCH_3), 65.7, 68.9 (C-6^M, C-6^G), 72.6, 73.2, 74.2, 75.0 (OCH_2Ph), 64.3, 72.6, 73.1, 74.6, 79.5, 80.0, 82.1 (C-3^M-C-5^M, C-2^G-C-5^G), 101.3 (CHPh, C-1^M, $J_{C\text{-}1,H\text{-}1}$ 173 Hz), 104.8 (C-1^G), 125.9-129.3 (CH_{arom}), 137.4, 138.3, 138.5 (C_{arom}).

Anal Calc. for $C_{50}H_{56}O_{10}S$. C, 70.75; H, 6.60. Found: C, 70.86; H, 6.64.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-phenylthio-β-D-glucopyranosyl)-β-D-galactopyranoside (18).-Prepared as described above (method A), starting from donor **6** and acceptor **13** in a yield of 75%, $[\alpha]_D$ -10° (*c* 1). ^1H NMR ($CDCl_3$) δ 3.24 (dd, 1H, H-2^{Gl}, $J_{2,3}$ 10.9 Hz), 3.37 (m, 1H, H-5^G), 3.38 (dd, H-3^G, $J_{2,3}$ 9.8 Hz, $J_{3,4}$ 2.8 Hz), 3.45 (ddd, 1H, 1H, H-5^{Gl}, $J_{5,6}$ 9.7Hz, $J_{5,6'}$ 3.7 Hz), 3.51 (dd, 1H, H-3^{Gl}, $J_{3,4}$ 8.6 Hz), 3.53 (s, 3H, OCH_3), 3.66 (d, 1H, H-4^G), 3.67-3.83 (m, 4H, H-$6'^{Gl}$, H-6^{Gl}, H-2^G, H-$6'^G$), 3.72 (dd, 1H, H-4^{Gl}, $J_{4,5}$ 9.7 Hz), 3.94 (dd, 1H, H-6^G, $J_{5,6}$ 6 7 Hz, $J_{6,6'}$ 10.4 Hz), 4 23 (d, 1H, H-1^G, $J_{1,2}$ 7.6 Hz), 4.47 (d, 1H, H-1^{Gl}, $J_{1,2}$ 9.0 Hz), 4.46-5 02 (AB, 12H, OCH_2Ph), 7.08-7 48 (m, 35H, H_{arom}) $^{13}C\{^1H\}$NMR ($CDCl_3$) 55.9 (C-2^{Gl}), 57.0 (OCH_3), 67.8, 68.5 (C-6^{Gl}, C-6^G), 72.6, 73.4, 74.2, 74.8, 75.0, 76 1 (OCH_2Ph), 72.9, 73.1, 74.5, 79.0, 79.3, 81.3. 82.8 (C-3^{Gl}-C-5^{Gl}, C-2^G-C-5^G), 103.8 (C-1^{Gl}, $J_{C\text{-}1,H\text{-}1}$ 157 Hz), 104 7 (C-1^G), 126.3-130 7 (CH_{arom}), 135.9, 137.8, 138.0, 138.3, 138.5. 138.6 (C_{arom}).

Anal Calc. for $C_{61}H_{64}O_{10}S$· C, 74 09; H, 6.48 Found· C, 74.05; H, 6.51.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phenylthio-α-D-mannopyranosyl)-β-D-galactopyranoside (19).-Prepared as described above (method A), starting from donor **12** and acceptor **13** in a yield of 71%, $[\alpha]_D$ +17° (*c* 1). ^1H NMR ($CDCl_3$) δ 3 36-3 42 (m, 2H, H-5^G, H-6^G), 3.50 (dd, 1H, H-3^G, $J_{3,4}$ 2 6 Hz), 3.51 (s, 3H, OCH_3), 3.57 (dd, 1H, H-2^M, $J_{2,3}$ 4.8 Hz), 3.70 (d, 1H, H-4^G), 3.72 (dd, 1H, H-$6'^G$, $J_{5,6'}$ 3.8 Hz, $J_{6,6'}$ 7.1 Hz), 3 80 (dd, 1H, H-2^G, $J_{2,3}$ 9 8 Hz), 3 84-3.86 (m, 2H, H-6^M, H-4^M), 4 10 (m, 1H, H-$6'^M$, $J_{5,6'} \approx J_{6,6'}$ 7 1 Hz), 4 06-4.09 (m, 1H, H-5^M), 4 20 (dd, 1H, H-3^M, $J_{3,4}$ 9.8 Hz), 4 24 (d, 1H, H-1^G, $J_{1,2}$ 7.7 Hz), 4.83 (d, 1H, H-1^M, $J_{1,2}$ 1.3 Hz), 4 67-4.91 (AB, 8H, OCH_2Ph), 5 62 (s, 1H, CHPh), 7.10-7.50 (m, 30H, H_{arom}). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 54.4 (C-2^M), 56.9 (OCH_3), 65.7, 68 5 (C-6^M, C-6^G), 72.2, 73.1, 74 1, 75.0 (OCH_2Ph), 64.1, 72 4, 72 9, 74 0, 79.4, 79.7, 82 0 (C-3^M-C-5^M, C-2^G-C-5^G), 100.6 (C-1^M, $J_{C\text{-}1,H\text{-}1}$ 172 Hz), 101 3 (CHPh), 104.7 (C-1^G), 125 8-131 9 (CH_{arom}), 137.3, 138 1, 138 3, 138 5 (C_{arom}).

Anal Calc for $C_{54}H_{56}O_{10}S$ C, 72 32, H, 6.25 Found C, 72 27; H, 6 30.

Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-phenylthio-β-D-glucopyranosyl)-β-D-galactopyranoside (20).-Prepared as described above (method B), starting from donor **6** and acceptor **14** in a yield of 61%, $[\alpha]_D$ -15° (*c* 1). ^1H NMR ($CDCl_3$) δ 3 10 (dd, 1H, H-2^{Gl}, $J_{2,3}$ 10.9 Hz), 3 34 (dt, 1H, H-5^{Gl}, $J_{5,6}$ 9.7 Hz, $J_{5,6'}$ 3.2 Hz), 3 46 (dd, 1H, H-3^{Gl}, $J_{3,4}$ 8.6 Hz), 3.51 (dd, H-3^G, $J_{3,4}$ 2.5 Hz), 3.55 (s, 3H, OCH_3), 3.58 (m, 2H, H-$6'^{Gl}$, H-5^G) 3.63 (t, 1H, H-4^{Gl}, $J_{4,5}$ 9.9 Hz), 3.69 (m, 2H, H-6^{Gl}, H-6^G), 3 73 (dd, 1H, H-6^G, $J_{5,6}$ 5 1 Hz, $J_{6,6'}$ 10 0 Hz), 3.92 (dd, 1H, H-2^G, $J_{2,3}$ 9 8Hz), 4.27 (d, 1H, H-1^G, $J_{1,2}$ 7.6 Hz), 4.31 (d, 1H, H-4^G), 5.06 (d, 1H, H-1^{Gl}, $J_{1,2}$ 8.8 Hz), 4.46-5 02 (AB, 12H, OCH_2Ph), 7.08-7 48 (m, 35H, H_{arom}). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 56.6 (C-2^{Gl}, OCH_3), 69.0, 70.0 (C-6^{Gl}, C-6^G), 72.9, 73.3, 74.4, 74 8, 75 0, 75.5 (OCH_2Ph), 70 7, 73 7, 74.4, 78.9, 79 2, 82.4, 83.1 (C-3^{Gl}-C-5^{Gl}, C-2^G-C-5^G), 101 6 (C-1^{Gl}, $J_{C\text{-}1,H\text{-}1}$ 159 Hz), 104 7 (C-1^G), 126 4-132.9 (CH_{arom}), 135.7, 137 9, 138.1, 138 4, 138.5, 138.5 (C_{arom})

Anal Calc for $C_{61}H_{64}O_{10}S$ C, 74 09; H, 6 48. Found· C, 74 04, H, 6 44

Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phenylthio-α-D-mannopyranosyl)-α-D-glucopyranoside (21).-Prepared as described above (method B), starting from donor **12** and

acceptor **15** in a yield of 67%, $[\alpha]_D$ +17° (*c* 1). ^{1}H NMR ($CDCl_3$) 3.36 (s, 3H, OCH_3), 3.48 (t, 1H, H-4^{Gl}, $J_{3,4} \approx J_{4,5}$ 7.0 Hz), 3.50 (m, 1H, H-2^M), 3.64-3.75 (m, 3H, H-3^{Gl}, H-6^{Gl}, H-$6'^{Gl}$), 3.81-3.87 (m, 3H, H-2^{Gl}, H-5^{Gl}, H-3^M), 3.95 (dt, 1H, H-5^M, $J_{5,6} \approx J_{5,6'}$ 4.4 Hz), 4.14 (dd, 1H, H-6^M, $J_{6,6'}$ 9.8 Hz), 4.16 (t, 1H, H-4^M, $J_{3,4} \approx J_{4,5}$ 9.4 Hz), 4.25 (dd, 1H, H-$6'^M$), 4.37-4.73 (m, 8H, OCH_2Ph), 4.56 (d, 1H, H-1^M, $J_{1,2}$ 1.4 Hz), 5.50 (d, 1H, H-1^{Gl}, $J_{1,2}$ 1.4 Hz), 5.64 (s, 1H, CHPh), 7.05-7.54 (m, 30H, H_{arom}).^{13}C{^{1}H}NMR ($CDCl_3$) δ 54.8 (C-2^M), 55.2 (OCH_3), 65.1, 69.6, 74.3, 76.8, 79.9, 80.1, 80.9 (C-3^M-C-5^M, C-2^{Gl}-C-5^{Gl}), 68.6, 68.7 (C-6^M, C-6^{Gl}), 72.3, 73.1, 73.5, 74.8 (OCH_2Ph), 97.6 (C-1^M, $J_{C\text{-}1,H\text{-}1}$ 167 Hz), 101.4 (CHPh), 103.0 (C-1^G), 125.9-131.9 ($CH_{arom.}$), 137.5, 138.1, 138.4 (C_{arom}).

Anal. Calc. for $C_{54}H_{56}O_{10}S$: C, 72.32; H, 6.25. Found: C, 72.38, H, 6.31.

1,5-Anhydro-3,4,6-tri-*O*-benzyl-1,2-dideoxy-2-phenylthio-D-*arabino*-hex-1-enitol (22).-Prepared as described above (method A), starting from compound **6** in a yield of 70%, $[\alpha]_D$ +23° (*c* 1). ^{1}H NMR ($CDCl_3$) δ 3.70 (dd, 1H, H-6', $J_{5,6'}$ 4.4 Hz, $J_{6,6'}$ 10.6 Hz), 3.82 (dd, 1H, H-6, $J_{5,6}$ 6.7 Hz), 3.89 (t, 1H, H-4, $J_{4,5}$ 4.2 Hz), 3.93 (dd, 1H, H-3, $J_{3,4}$ 4.2 Hz, $J_{3,5}$ 1.6 Hz), 4.45-4.62 (m, 7H, OCH_2Ph, H-5), 6.95 (s, 1H, H-1), 7.05-7.40 (m, 20H, H_{arom}). ^{13}C{^{1}H}NMR ($CDCl_3$) δ 67.9 (C-6), 72.3, 72.3, 72.8, 73.3 (OCH_2Ph), 73.5, 73.7, 76.3 (C-3, C-4, C-5), 103.6 (C-2), 120.7-129.6 (CH_{arom}), 137.5, 137.8 (C_{arom}), 152.0 (C-1)

Anal. Calc. for $C_{33}H_{32}O_5S$: C, 75.57; H, 6.11. Found: C, 75.65; H, 6.14.

Phenyl 2,3,4-tri-*O*-benzoyl-6-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-phenylthio-β-D-glucopyranosyl)-1-thio-α-D-mannopyranose (32).-Prepared as described above (method B), starting from donor **6** and acceptor **28** in a yield of 75%, $[\alpha]_D$ -19° (*c* 1). ^{1}H NMR ($CDCl_3$) δ 3.06 (dd, 1H, H-2^{Gl}, $J_{2,3}$ 10.5 Hz), 3.32 (dt, 1H, H-5^{Gl}, $J_{5,6}$ 9.7 Hz, $J_{5,6'}$ 3.3 Hz), 3.50 (dd, 1H, H-3^{Gl}, $J_{3,4}$ 8.6 Hz), 3.58 (t, 1H, H-4^{Gl}, $J_{4,5}$ 9.4 Hz), 3.60 (s, 3H, OCH_3), 3.71 (m, 1H H-$6'^{Gl}$), 3.90 (dd, 1H, H-$6'^M$, $J_{5,6'}$ 7.0 Hz), 4.07 (dd, 1H, H-6^M, $J_{5,6}$ 2.3 Hz, $J_{6,6'}$ 11.2 Hz), 4.08 (m, 1H, H-6^{Gl}), 4.33 (d, 1H, H-1^{Gl}, $J_{1,2}$ 8.6 Hz), 4.35-5.05 (AB, 6H, OCH_2Ph), 4 95 (m,1H, H-5^M), 5.74 (d, 1H, H-1^M, $J_{1,2}$ 1.7 Hz), 5.83 (dd, 1H, H-3^M, $J_{3,4}$ 9.8 Hz), 5.89 (t, 1H, H-4^M, $J_{4,5}$ 9.7 Hz), 5 94 (dd, 1H, H-2^M, $J_{2,3}$ 3.4 Hz), 7.00-8.01 (m, 35H, H_{arom}). ^{13}C{^{1}H}NMR ($CDCl_3$) δ 55.7 (C-2^{Gl}), 68.7 (C-6^M, C-6^{Gl}), 67.8, 70.4, 71.6, 72.2, 74 8, 79.0, 83.0 (C-3^{Gl}-C-5^{Gl}, C-2^M-C-5^M), 73.4, 74.7, 75.6 (OCH_2Ph), 86.0 (C-1^M), 102.7 (C-$1^G J_{C\text{-}1,H\text{-}1}$ 159 Hz), 127 1-133.4 (CH_{arom}, C_{arom}), 165.3, 165.4 (PhCOO).

Anal. Calc. for $C_{66}H_{60}O_{12}S$: C, 71.48; H, 5.42. Found. C, 71.41; H, 5.45.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(2-*O*-(ethyl 3,4-di-*O*-benzyl-1-thio-β-L-rhamnopyranoside)carbonyl)-β-D-galactopyranoside (38) and methyl 3,6-anhydro-2,4-di-*O*-benzyl-β-D-galactopyranoside (39).-Prepared as described above (method A) from donor **37** and acceptor **13**. Purification of the reaction mixture on silica gel [1:0 to 0:1 light petroleum (bp 40-60°C)-ether] afforded compound **38** and **39**. Relevant data for **38**: $[\alpha]_D$ +3° (*c* 0.2). ^{1}H NMR ($CDCl_3$) δ 1.31 (t, 3H, SCH_2CH_3, *J* 7.3 Hz), 1.37 (d, 1H, H-6^R, $J_{5,6}$ 5.7 Hz) 2.75 (AB, 2H, SCH_2CH_3), 3.44 (t, 1H, H-4^R, $J_{4,5}$ 8.9 Hz), 3.45 (m, 1H, H-5^R), 3.49 (dd, 1H, H-3^G, $J_{3,4}$ 2.9 Hz), 3.56 (m, 1H, H-5^G), 3.64 (dd, 1H, H-3^R, $J_{3,4}$ 8.9 Hz), 3.79 (dd, 1H, H-2^G, $J_{2,3}$ 9.8Hz), 3.90 (d, 1H, H-4^G), 4.11 (dd, 1H, H-$6'^G$, $J_{5,6'}$ 6.2 Hz), 4.17 (d, 1H, H-1^G, $J_{1,2}$ 7 6 Hz), 4 47 (dd, 1H, H-6^G, $J_{5,6}$ 4.4 Hz, $J_{6,6'}$ 10 9 Hz), 4.66 (d, 1H, H-1^R, $J_{1,2}$ 1 1 Hz), 4.51-5.02 (m, 10H, OCH_2Ph), 5.50 (dd, 1H, H-2^R, $J_{2,3}$ 3 3 Hz), 7.13-7.39 (m, 25H, H_{arom}). ^{13}C{^{1}H}NMR ($CDCl_3$) δ 14.5 (SCH_2CH_3), 18.1 (C-6^R), 34 0 (SCH_2CH_3), 57.0 (OCH_3), 66.7 (C-6^G), 71.7, 73.1, 73.8, 76.7, 79.2, 79.3, 81.1, 81.8 (C-2^R-C-5^R, C-2^G-C-5^G), 72.4, 72.6, 72.9, 73.0 (OCH_2Ph), 89.9 (C-1^R), 104.8 (C-1^G), 127.6-128.4 (CH_{arom}), 154.6 (OC(O)O). LC-MS: *m/z* 869 (M^++1). Relevant data for **39**: $[\alpha]_D$ -35° (*c* 1). ^{1}H NMR ($CDCl_3$) : δ 3.35 (s, 3H, OCH_3), 3.77 (d, 1H, H-2, $J_{2,3}$ 4.8 Hz), 3.93 (dd, 1H, H-6, $J_{5,6}$ 3.1 Hz, $J_{6,6'}$ 9.4 Hz), 4.12 (d, 1H, H-6'), 4.23 (d, 1H, H-4, $J_{4,5}$ 2.3 Hz), 4.29 (m, 1H. H-5), 4.38 (d, 1H, H-3), 4.52 (s, 1H, H-1), 4.48-4.63 (AB, 4H, OCH_2Ph), 7.17-7.37 (m, 10H, H_{arom}) ^{13}C{^{1}H}NMR ($CDCl_3$) δ 55.7 (OCH_3), 70.7 (C-6), 71.0, 72 6 (OCH_2Ph), 75.9, 77 1, 77.6, 77.8 (C-2, C-3, C-4, C-5), 101 1 (C-1), 127.6-128.4 (CH_{arom}) LC-MS: *m/z* 357 (M^++1).

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-*arabino*-hexopyranosyl)-β-D-galactopyranoside (23).-To a solution of compound **17** (0.2 mmol, 170 mg) or **19** (0.2 mmol, 179 mg) in dry THF (12 mL) was added Raney nickel (W2, 1.6 g) at room temperature. When TLC analysis (97:3 CH_2Cl_2-acetone) showed the reaction to be complete (**17**: 5 days; **19**: 2h), the reaction mixture was filtered and the solid washed with THF (3 x 5 mL). The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography (97:3 CH_2Cl_2-acetone) to yield compound **23** (R = Et: 50%, R = Ph: 81%), $[\alpha]_D$ +10° (*c* 1). ^1H NMR ($CDCl_3$) δ 1.66 (ddd, 1H, H-2a^A, $J_{2a,2e}$ 12.0 Hz, $J_{2a,3}$ 11.0 Hz), 1.98 (dd, 1H, H-2e^A, $J_{2e,3}$ 5.1 Hz), 3.43 (m, 1H, H-5^A), 3.54 (OCH_3), 3.56 (dd, 1H, H-3^G, $J_{3,4}$ 2.7 Hz), 3.65 (t, 1H, H-4^A, $J_{4,5}$ 8.5 Hz), 3.67 (m, 1H, H-6'^{G}), 3.75 (m, 1H, H-5^G) 3.81 (d, 1H, H-4^G), 3.82 (dd, 1H, H-2^G, $J_{2,3}$ 9.8 Hz), 3.91 (ddd, 1H, H-3^A, $J_{3,4}$ 8.9 Hz), 4.24 (dd, 1H, H-6^G, $J_{5,6}$ 3.8 Hz, $J_{6,6'}$ 9.2 Hz), 4.28 (d, 1H, H-1^G, $J_{1,2}$ 7.7 Hz), 4.49 (d, 1H, H-1^A, $J_{1,2a}$ 3.4 Hz), 4.61-4.97 (AB, 8H, OCH_2Ph), 5.60 (s, 1H, PhCH), 7.20-7.52 (m, 25H, H_{arom}). $^{13}C\{^1H\}$NMR ($CDCl_3$) δ 36.2 (C-2^A), 57.0 (OCH_3), 65.4, 69.0 (C-6^A, C-6^G) 63.0, 72.7, 79 7, 82.4, 83.7 (C-3^A-C-5^A, C-2^G-C-5^G), 73.2, 74.2, 75.1 (OCH_2Ph), 97.8 (C-1^A), 101.3 (C-1^G), 120.8-133.1 (CH_{arom}, C_{arom}).

Anal. Calc. for $C_{48}H_{52}O_{10}S$. C, 70.24; H, 6.34. Found: C, 70.18, H, 6.41

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