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From glycoside hydrolases to thioglycoligases: the synthesis of thioglycosides

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This paper is dedicated to the memory of Jacques van Boom

Abstract—The treatment of various glycosyl acceptors, each containing a reactive thiol group, with the appropriate glycosyl donor and a glycoside hydrolase or glycosynthase, failed to yield any thioglycosides—only the products of *O*-glycosylation were formed. However, thioglycosides were formed when a thioglycoligase was used to mediate the reaction between acceptor and donor. In fact, pyranose acceptors possessing a thiol group at C3, C4 or C6 (but not C2) were all capable of conversion into thioglycosides. Some comment is given regarding the mechanism of the various processes.

1. Introduction

The replacement of one of the oxygen atoms at the anomeric carbon of a glycoside by a sulfur atom leads to two distinctly different thio sugars, namely a 5-thio glycoside **1** and a 1-thio glycoside **2** (Fig. 1). Molecules with the structural elements of **1** are rarely found as natural products but synthetic molecules are not uncommon.[1,2] In stark contrast, molecules based on **2** are not uncommon natural products[3] and constitute one of the most frequently synthesised glycosyl donors for the construction of the glycosidic linkage.[4]

We became interested in thioglycosides with the revelation by Driguez et al. of the ability of sulfur-linked disaccharides, such as **3**, to act as potent, nonhydrolysable inhibitors of β-glucosidases and cellulases.[5] The synthesis of such disaccharides has generally involved either the alkylation of a 1-thio sugar with a sugar triflate[6] or the glycosylation of a 4-thio sugar with a glycosyl bromide (Scheme 1).[7] Indeed, in our hands, treatment of the hemithioacetal **4** with the triflate **5** gave the thioglycoside **6**, a direct precursor of the sulfur-linked disaccharide derivative **7** (Scheme 2). We required such 'double' thioglycosides to act as stable glycosyl acceptors in some other *trans*-glycosylation experiments (not described here) with wild-type enzymes.

It occurred to us, as it must have to countless others, that an enzyme-assisted approach should be able to construct the thioglycosidic linkage. In fact, there are very few reports of a glycoside hydrolase being used to cause a reactive glycosyl donor to glycosylate a simple thiol acceptor, let alone the thiol group of a thio sugar.[8–10]

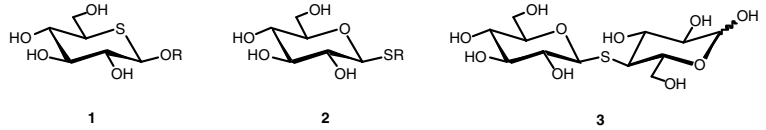

Figure 1.

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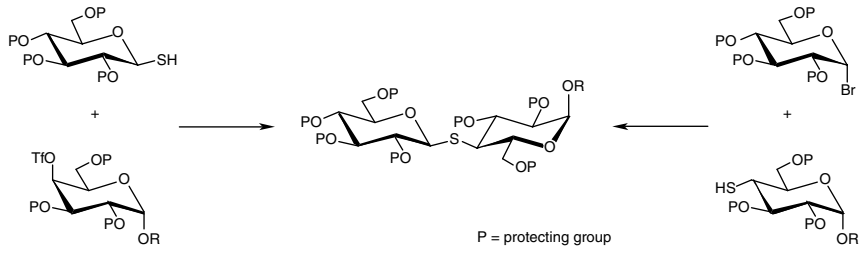
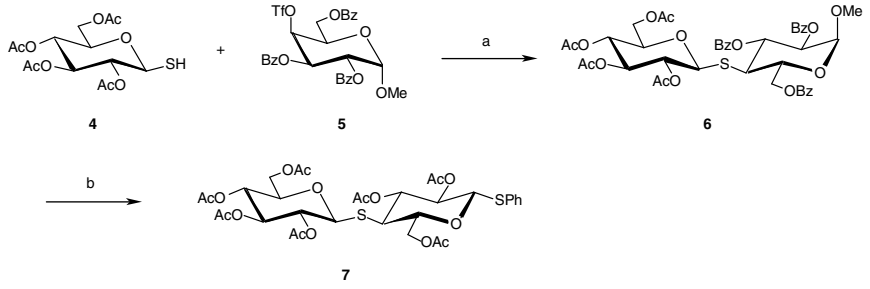
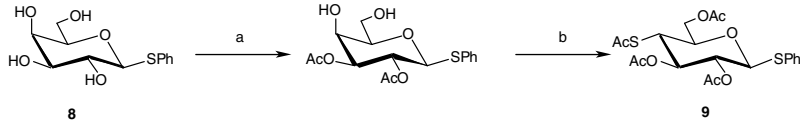


Scheme 1.



Scheme 2. Reagents and conditions: (a) DBU, PhMe; (b) (i) Na, MeOH; (ii) Ac_2O, pyr.; (iii) 18 M H_2SO_4, Ac_2O; (iv) 30% HBr, AcOH; (v) PhSH, Et_3N, CH_2Cl_2.

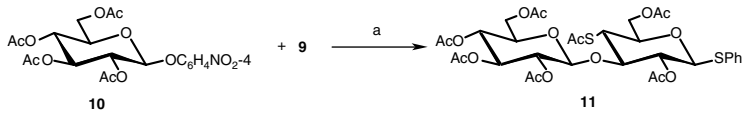


Scheme 3. Reagents and conditions: (a) (i) $PhCH(OEt)_2$, CSA, $CHCl_3$; (ii) Ac_2O, pyr.; (iii) AcOH/H_2O (4:1); (b) (i) AcCl, pyr., CH_2Cl_2; (ii) Tf_2O, pyr., CH_2Cl_2; (iii) KSAc, THF.

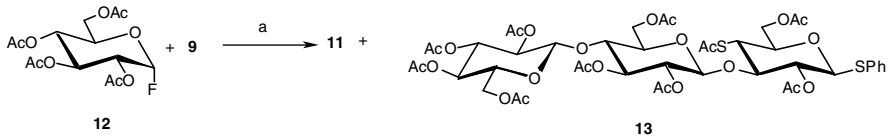
2. Results and discussion

In order to explore such a process more fully, we prepared the 1,4-dithio-D-glucoside **9** (Scheme 3) and then mixed it with 4-nitrophenyl tetra-*O*-acetyl-β-D-glucopyranoside **10** in the presence of sodium methoxide in methanol. A subsequent treatment of the presumed thiol and donor with Abg (a retaining *exo*-β-glucosidase from *Agrobacterium* sp.; Scheme 4) gave none of the expected thioglycoside; eventually isolated was the 1,3-β-linked disaccharide **11**. The same result was obtained when the D-glucoside **9** was treated with tetra-*O*-acetyl-α-D-glucopyranosyl fluoride **12**, first with sodium methoxide in methanol, then with the glycosynthase, Abg E358S;[11] also formed was an amount of the trisaccharide **13**, the product expected from the further glycosylation of the intermediate disaccharide (Scheme 5).

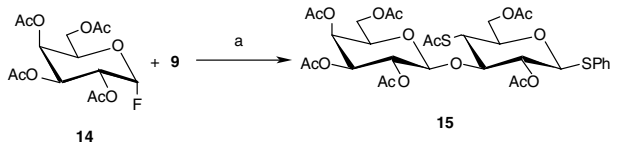
Out of interest we also subjected the D-glucoside **9** and tetra-*O*-acetyl-α-D-galactopyranosyl fluoride **14** to the normal deacetylation protocol, and then Abg E358S—a 1,3-β-linked disaccharide **15** was again formed, and at a higher rate than the comparable glycosylation with the fluoride **12** (Scheme 6). We even tried to vary the pH



Scheme 4. Reagents and conditions: (a) (i) Na, MeOH; (ii) Abg wild-type, phosphate buffer, pH 7.0; (iii) Ac_2O, pyr.



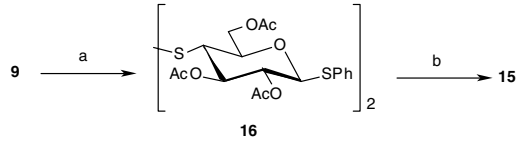
Scheme 5. Reagents and conditions: (a) (i) Na, MeOH; (ii) Abg E358S, 150 mM NH_4HCO_3; (iii) Ac_2O, pyr.



Scheme 6. Reagents and conditions: (a) (i) Na, MeOH; (ii) Abg E358S, 150 mM NH_4HCO_3 or 100 mM citrate buffer, pH 5.5; (iii) Ac_2O, pyr.

(5.5–8.4) of the media for the glycosynthase-mediated reactions described so far, in the hope of changing the ionisation state of the thiol group in the acceptor, but to no avail—the 1,3-β-linked product was always formed.

There was a concern that the thiol acceptor had been somehow converted during the various reactions into the disulfide **16** (Scheme 7). We therefore prepared **16** by the oxidation of the thiol with iodine, and subjected the product to a glycosynthase-mediated reaction with **14**. After no initial reaction, the addition of 1,4-dithioerythritol (DTE) caused the formation again of the 1,3-β-linked disaccharide **15**. Also of a confirmatory nature was the glycosylation, under glycosynthase control, of the thioglycoside **17** by the donor derived from **14**, giving the 1,4-β-linked disaccharide **18** (Scheme 8).



Scheme 7. Reagents and conditions: (a) (i) Na, MeOH; (ii) I_2, Et_3N, $CHCl_3$; (iii) Ac_2O, pyr.; (b) (i) **14**, Na, MeOH; (ii) Abg E358S, 150 mM NH_4HCO_3, 1,4-DTE; (iii) Ac_2O, pyr.

In light of the inability of a hydrolase or glycosynthase to cause the glycosylation of the thiol derived from **9**, at sulfur, we decided to check the potential of the 3-deoxy-1,4-dithio sugar **19** (Fig. 2)—surely the absence of the hydroxyl group at C3 would force the molecule to undergo glycosylation at sulfur (at C4) of the derived thiol. A useful preliminary check to see if a thiol was having any other effect on the process would be to attempt the glycosylation of the triol derived from the 4-deoxy sugar **20** (Scheme 9).

Treatment of the 4-deoxy sugar **20** with tetra-*O*-acetyl-α-D-glucopyranosyl fluoride **12** according to the normal deacetylation/glycosynthase protocol gave, in a very slow process, a mixture of the tri- and tetrasaccharides **21** and **22** (Scheme 10). It is obvious, from the absence of any disaccharide product **23** (Fig. 3) in the final

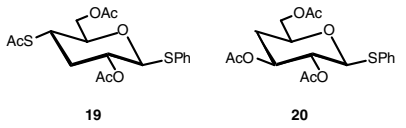
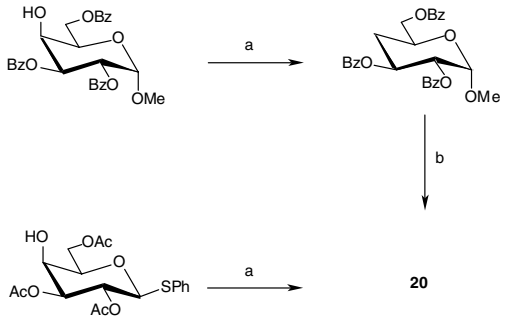


Figure 2.

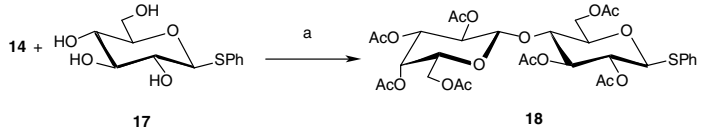


Scheme 9. Reagents and conditions: (a) (i) PhOC(S)Cl, pyr., CH_2Cl_2; (ii) Bu_3SnH, AIBN, PhMe; (b) (i) Na, MeOH; (ii) Ac_2O, pyr.; (iii) 18 M H_2SO_4, Ac_2O; (iv) PhSH, Et_2OBF_3, CH_2Cl_2.

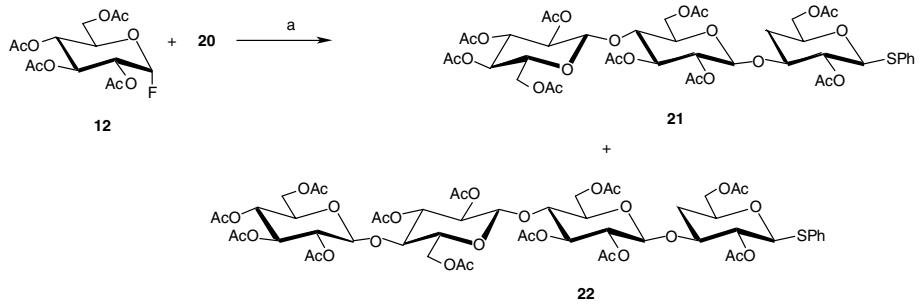
mixture, that the initial glycosylation is a slow process, followed by the more rapid glycosylation of the intermediate disaccharide to form the observed mixture of products. We also investigated the treatment of **20** with tetra-*O*-acetyl-α-D-galactopyranosyl fluoride **14** in the presence of the glycosynthase Abg E358S—the expected disaccharide **24** was formed in good yield (Scheme 11).

Having established that the triol derived from the deoxy sugar **20** was a viable, if slow, acceptor for glycosynthase-mediated reactions, we continued towards our synthesis of **19** (Fig. 2; Scheme 12). Although the thioglycoside **8** could be easily converted into the alcohol **25** and the 3-deoxy alcohol **26**, the subsequent attempt to introduce sulfur at C4 of the unstable triflate **27** yielded only the alkene **28**; the mesylate derived from **26** fared no better. A Mitsunobu reaction on **26** with thioacetic acid again produced only the alkene **28**. This result was in direct contrast to the successful Mitsunobu reaction on **26** with chloroacetic acid, followed by selective hydrolysis of the product **29** and another successful Mitsunobu reaction on the alcohol **30**, this time with thioacetic acid (Scheme 13).

Although the synthesis of **19** had eluded us, we were heartened by the appearance of a paper by Withers and co-workers that announced the use of an acid–base mutant of a glycoside hydrolase (E171A from the same retaining β-glucosidase from *Agrobacterium* sp.) for the



Scheme 8. Reagents and conditions: (a) (i) Na, MeOH; (ii) Abg E358S, 150 mM NH_4HCO_3; (iii) Ac_2O, pyr.



Scheme 10. Reagents and conditions: (a) (i) Na, MeOH; (ii) Abg E358S, 150 mM NH_4HCO_3; (iii) Ac_2O, pyr.

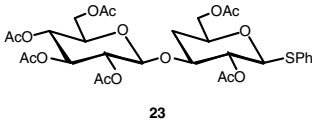
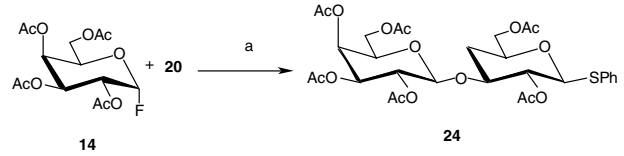


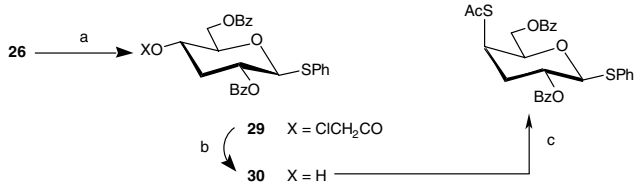
Figure 3.



Scheme 11. Reagents and conditions: (a) (i) Na, MeOH; (ii) Abg E358S, 150 mM NH_4HCO_3; (iii) Ac_2O, pyr.

synthesis of thioglycosides.[12] These 'thioglycoligases' were capable of transferring a reactive donor, such as **31**, via a glycosyl–enzyme intermediate **32**, onto the thiol group of a suitable acceptor (Scheme 14).

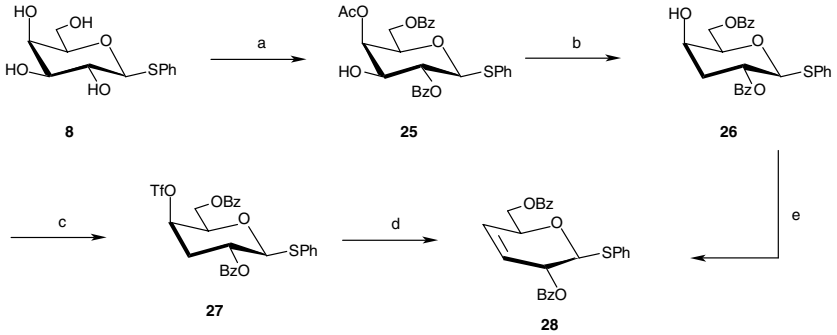
With this new methodology at hand, we treated the thiol derived from **9** with the donor **31** in the presence of the thioglycoligase—the 1,4-β-linked disaccharide **7** was formed in good yield (Scheme 15). Would such a ligation be possible on a thiol located at another position of the pyranose ring, a proposal investigated somewhat by Jahn and Withers?[13] We therefore prepared the thioacetate **33** (Scheme 16) and treated the derived thiol with the donor **31** in the presence of the thioglycoligase—the



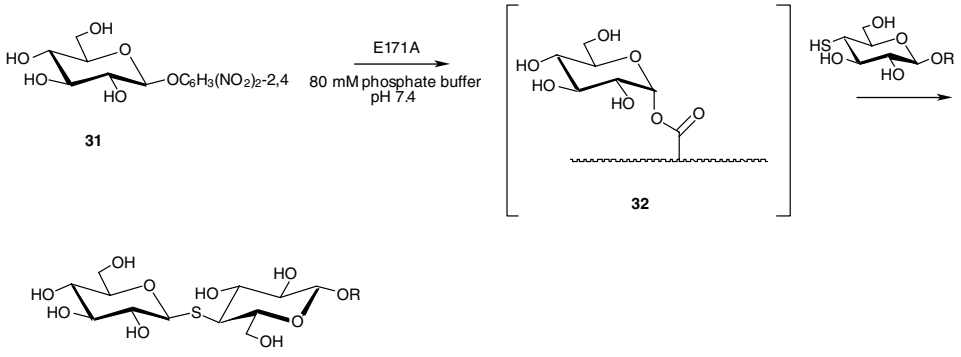
Scheme 13. Reagents and conditions: (a) $ClCH_2CO_2H$, Ph_3P, DEAD, CH_2Cl_2; (b) NH_2CSNH_2, 2,6-lutidine, MeOH/CH_2Cl_2 (1:1); (c) $CH_3C(O)SH$, Ph_3P, DEAD, CH_2Cl_2.

1,3-β-linked disaccharide **34** was virtually the sole product (Scheme 17). A similar result was obtained on the 4-nitrophenyl β-D-glucoside **35**, to produce the disaccharide **36**. Also readily available was the thioacetate **37** (Scheme 18), the derived thiol shown to be a reasonable acceptor in the thioglycoligase-mediated reaction with the donor **31** (Scheme 19). We reached the limit of the process with the thiol derived from the thioacetate **38** (Scheme 20)—there was no evidence for a successful glycosylation at sulfur in the presence of **31** and the thioglycoligase.

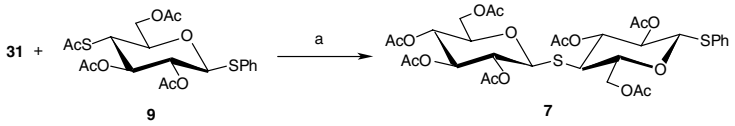
Our final foray into thioglycoside formation drew on some related results with glycosynthases—the glycosylation of 6-*O*-benzyl-D-glucopyranose **39** with α-D-galactopyranosyl fluoride in the presence of Abg E358S had given, somewhat surprisingly, a mixture of 1,2-β- and 1,3-β-linked disaccharides **41** and **42** (Scheme 21).[14] Would, then, the thiol derived from a thioacetate such



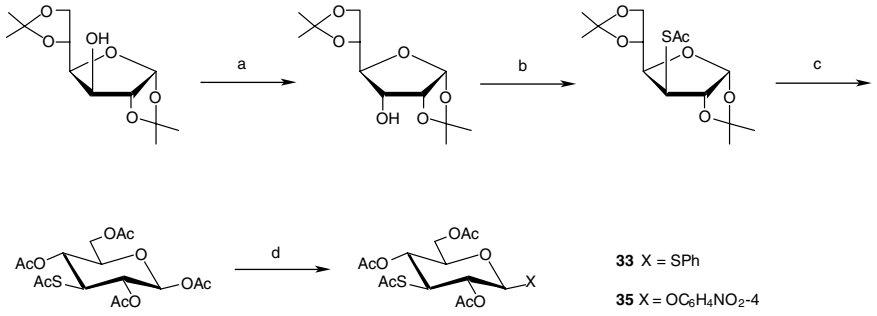
Scheme 12. Reagents and conditions: (a) (i) 2,2-dimethoxypropane, CSA; (ii) BzCl, pyr., CH_2Cl_2; (iii) AcOH/H_2O (4:1); (iv) $CH_3C(OEt)_3$, CF_3COOH, $CHCl_3$; (v) MeCN, H_2O; (b) (i) PhOC(S)Cl, pyr., CH_2Cl_2; (ii) Bu_3SnH, AIBN, PhMe; (iii) HCl, MeOH; (c) Tf_2O, pyr., CH_2Cl_2; (d) KSAc, DMF; (e) $CH_3C(O)SH$, Ph_3P, DEAD, CH_2Cl_2.



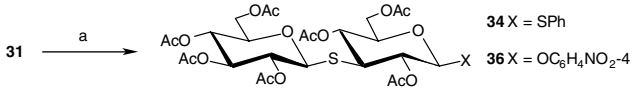
Scheme 14.



Scheme 15. Reagents and conditions: (a) (i) Na, MeOH; (ii) E171A, 80 mM phosphate buffer, pH 7.4; (iii) Ac_2O, pyr.



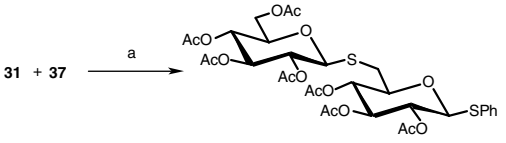
Scheme 16. Reagents and conditions: (a) (i) PDC, Ac_2O, CH_2Cl_2; (ii) $NaBH_4$, EtOH/H_2O (3:7); (b) (i) Tf_2O, pyr., CH_2Cl_2; (ii) KSAc, DMF; (c) (i) CF_3COOH/H_2O (4:1); (ii) NaOAc, Ac_2O; (d) (i) PhSH or 4-nitrophenol, Et_2OBF_3, CH_2Cl_2.



Scheme 17. Reagents and conditions: (a) (i) Na, MeOH; (ii) **33** or **35**, E171A, 80 mM phosphate buffer, pH 7.4; (iii) Ac_2O, pyr.

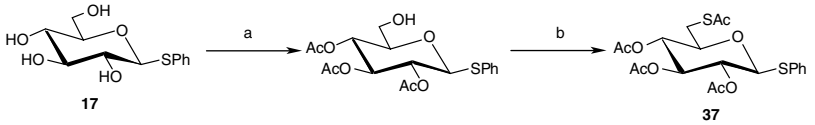
as **43** (Fig. 4) shows the same pattern of glycosylation under the control of the thioglycoligase?

Our approach to the synthesis of **43** is outlined in Scheme 22. Methyl α-D-mannopyranoside was easily converted into the alcohol **44** (characterised as its acetate **45**) that allowed for the introduction of a sulfur atom at C2 (the thioacetate **46**). Protecting group manipulations

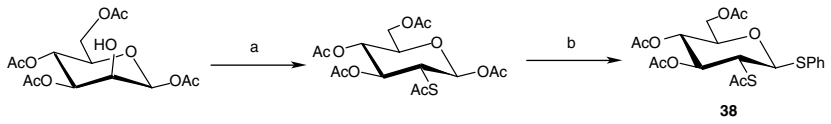


Scheme 19. Reagents and conditions: (a) (i) Na, MeOH; (ii) E171A, 80 mM phosphate buffer, pH 7.4; (iii) Ac_2O, pyr.

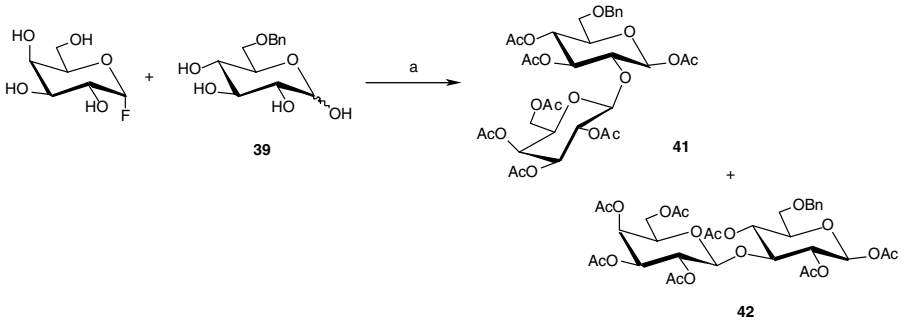
then gave the triacetate **47**, which, to our surprise, gave only the tetraacetate **48** upon standard acetolysis. More successful was a parallel sequence on methyl α-D-mannopyranoside that used 4-nitrobenzyl bromide as the alkylating agent and proceeded through the intermediates **49**–**52**—an acetolysis on **52**, with a less basic residue at C6, smoothly gave the tetraacetate **53**.



Scheme 18. Reagents and conditions: (a) (i) TrCl, Et_3N, DMAP, DMF; (ii) Ac_2O, pyr.; (iii) AcOH/H_2O (4:1); (b) (i) MsCl, Et_3N, CH_2Cl_2; (ii) KSAc, DMF.



Scheme 20. Reagents and conditions: (a) (i) Tf_2O, pyr., CH_2Cl_2; (ii) KSAc, DMF; (b) (i) PhSH, Et_2OBF_3, CH_2Cl_2.



Scheme 21. Reagents and conditions: (a) (i) Abg E358S, 150 mM NH_4HCO_3; (ii) Ac_2O, NaOAc.

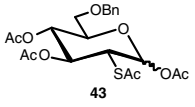
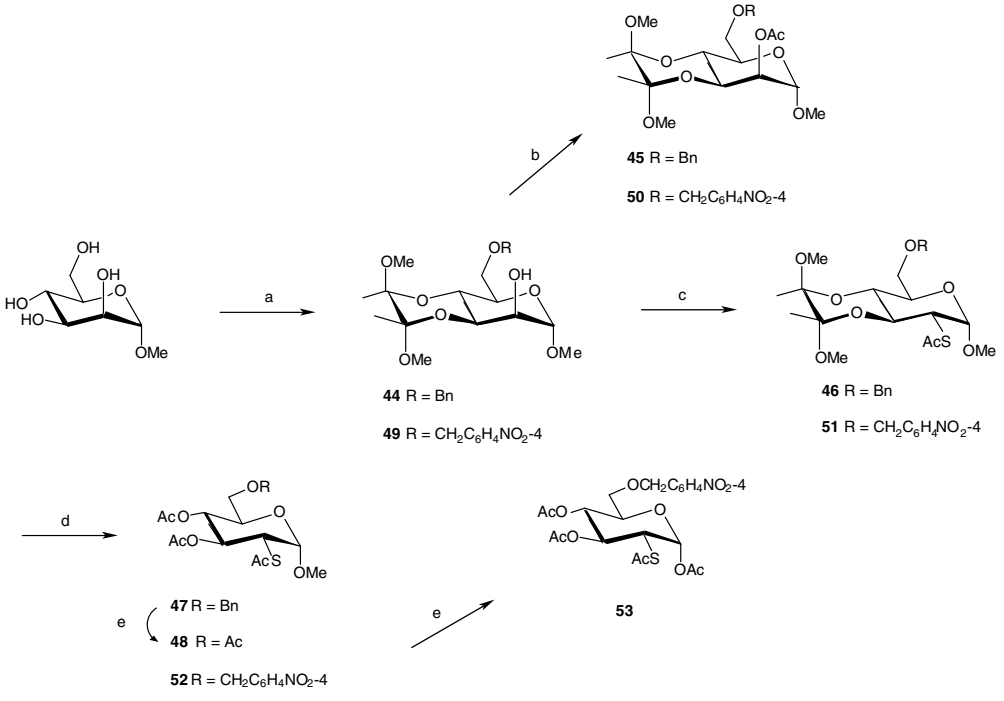


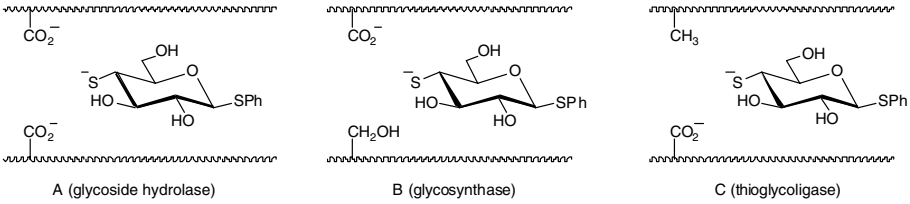
Figure 4.

Unfortunately, treatment of the thioacetate **53**, under the normal deacetylation conditions, with the donor **31** in the presence of the thioglycoligase gave no evidence for the formation of a disaccharide.

It is interesting to reflect on some of the chemistry underlying the various transformations reported in this paper. First, the measured pK_a (8.5) of phenyl 1,4-dithio-β-D-glucopyranoside (the thiol derived from the deacetylation of **9**) is commensurate with a molecule containing a slightly more acidic (than normal) thiol residue. Second, in light of this information and the fact that the thiol does not act as an acceptor in either glycoside hydrolase or glycosynthase-mediated process, the thiol must not be able to bind in its neutral form in the active site of either enzyme—the amino acid residues in this site must be capable of causing ionisation of the



Scheme 22. Reagents and conditions: (a) (i) 2,3-butanedione, $HC(OMe)_3$, MeOH, CSA; (ii) $(Bu_3Sn)_2O$, PhMe; (ii) BnBr or 4-$NO_2C_6H_4CH_2Br$; (b) Ac_2O, pyr.; (c) (i) Tf_2O, pyr., CH_2Cl_2; (ii) KSAc, DMF; (d) (i) CF_3COOH/H_2O (19:1); (ii) Ac_2O, pyr.; (e) 18 M H_2SO_4, Ac_2O.



Scheme 23.

thiol, so generating a thiolate ion that is repulsed by the general acid/base (carboxylate) of the enzyme (Scheme 23 A and B). Only when this residue is mutated to a benign methyl group (of alanine) is the thiolate able to bind in the active site of the enzyme (thioglycoligase) (Scheme 23C). Similar comments have been made by Jahn and Withers in their most recent publication on thioglycoligases.[13]

It goes almost without saying that, with thioglycoligases, which lack the general acid/base residue, *O*-alkylation, and hence oligomerisation of the initially formed disaccharide, is not possible.

3. Experimental

General experimental procedures have been given previously.[15]

3.1. Synthesis of the disaccharide 7

(a) (i) *Tetra-O-acetyl-β-D-glucopyranosyl-(1→4)-tri-O-acetyl-4-thio-β-D-glucosyl bromide*: HBr (30%) in AcOH (3 mL) was added to tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-tetra-*O*-acetyl-4-thio-D-glucose[16] (200 mg) in CH_2Cl_2 (5 mL) and the solution stirred (rt, 30 min). Standard workup (CH_2Cl_2) gave a colourless oil (200 mg), presumably the title bromide, which was used without purification.

(ii) *Phenyl tetra-O-acetyl-β-D-glucopyranosyl-(1→4)-tri-O-acetyl-1,4-dithio-β-D-glucoside* **7**: Thiophenol (64 mg, 0.60 mmol) and K_2CO_3 (81 mg, 0.60 mmol) were added to the above bromide (200 mg) in acetone (5 mL) and the resulting mixture stirred (rt, 30 min). Concentration of the mixture, followed by flash chromatography (EtOAc/petrol 3:7), gave the thioglycoside **7** as a colourless oil (170 mg, 81%), $[\alpha]_D = -42.6$ (*c* 1, $CHCl_3$). ^{1}H NMR (500 MHz): δ 1.82, 1.95, 1.98, 1.99, 2.01, 2.05, 2.08 (7 × s, 21H, CH_3), 2.91 (dd, $J_{3,4} \approx J_{4,5}$ 11.0, H4), 3.69 (ddd, $J_{4',5'}$ 9.8, $J_{5',6'}$ 2.3, 6.4, H5′), 3.83 (ddd, $J_{5,6}$ 1.9, 5.3, H5), 4.03 (dd, $J_{6',6'}$ 12.3, H6′), 4.12 (dd, H6′), 4.34 (dd, $J_{6,6}$ 12.1, H6), 4.61 (dd, H6), 4.63 (d, $J_{1,2}$ 10.1, H1), 4.71 (d, $J_{1',2'}$ 10.0, H1′), 4.88 (dd, $J_{2,3}$ 9.1, H2), 4.91 (dd, $J_{2',3'}$ 9.3, H2′), 4.94 (dd, $J_{3',4'}$ 9.3, H4′), 5.14 (dd, H3), 5.17 (dd, H3′), 7.25–7.29, 7.46–7.49 (2 × m, Ph). ^{13}C NMR (125.7 MHz): δ 20.25, 20.36, 20.42, 20.44, 20.45, 20.69, 20.72 (7 × C, CH_3), 46.21 (C4), 62.37 (C6′), 63.59 (C6), 68.23 (C4′), 70.05 (C2′), 71.11 (C3), 71.35 (C2), 73.55 (C3′), 75.63 (C5′), 77.88 (C5), 81.46 (C1′), 85.86 (C1), 128.50, 128.85, 131.55, 133.67 (Ph), 169.12, 169.31, 169.33, 169.87, 169.92, 170.24, 170.25 (7 × C, C=O). HR-MS (FAB) *m/z* 745.1825 [$C_{32}H_{41}O_{16}S_2$ $(M+H)^+$ requires 745.1836].

(b) NaOMe (10%) in MeOH (5 mL) was added to thioacetate **9** (50 mg, 0.11 mmol) in MeOH (5 mL) and the solution stirred (rt, 10 min). The mixture was quenched with resin (Amberlite IR-120, H^+), filtered and concentrated. The residue was taken up in 80 mM phosphate buffer (pH 6.8, 5 mL) and the D-glucoside **31** (76 mg, 0.22 mmol) and Abg E171A (2 mg) added and the solution kept at 25 °C for 24 h. The solution was concentrated and the residue dissolved in pyridine (5 mL), then Ac_2O (5 mL) was added and the solution stirred (rt, 12 h). The mixture was quenched by the addition of MeOH (5 mL) and concentrated. Standard work-up (CH_2Cl_2) and flash chromatography (EtOAc/petrol 1:4–1:1) gave disaccharide **7** as a colourless oil (68 mg, 84%). The ^{1}H and ^{13}C NMR spectra were consistent with those reported in (a).

3.2. Synthesis of the 1,4-dithio-D-glucoside 9

(i) *Phenyl 2,3,6-tri-O-acetyl-1-thio-β-D-galactopyranoside*: Acetyl chloride (0.27 mL, 1.6 mmol) in CH_2Cl_2 (5 mL) was added dropwise to phenyl 2,3-di-*O*-acetyl-1-thio-β-D-galactopyranoside[17] (500 mg, 1.4 mmol) and pyridine (0.20 mL, 2.2 mmol) in CH_2Cl_2 (15 mL) at −30 °C and the solution stirred (30 min). Methanol (10 mL) was added, followed by a standard work-up (CH_2Cl_2). Flash chromatography (EtOAc/petrol 1:4) then gave the title triacetate as colourless plates (520 mg, 80%), mp 126–129 °C (EtOH), $[\alpha]_D = +26.2$ (*c* 1, $CHCl_3$). Found: C, 54.2; H, 5.6. $C_{18}H_{22}O_8S$ requires C, 54.3; H, 5.6. ^{1}H NMR (300 MHz): δ 2.05, 2.08, 2.09 (3 × s, 9H, CH_3), 3.80 (ddd, $J_{4,5}$ 1.0, $J_{5,6}$ 5.5, 5.8, H5), 4.08 (dd, $J_{3,4}$ 3.2, H4), 4.27–4.35 (m, H6,6), 4.70 (d, $J_{1,2}$ 10.1, H1), 4.97 (dd, $J_{2,3}$ 9.8, H3), 5.27 (dd, H2), 7.28–7.31, 7.49–7.53 (2 × m, Ph). ^{13}C NMR (75.5 MHz): δ 20.71, 20.73, 20.76 (3 × C, CH_3), 62.69 (C6), 67.14, 67.43, 74.18 (C2,3,4), 75.86 (C5), 86.27 (C1), 127.90, 128.81, 132.21, 132.58 (Ph), 166.57, 170.13, 170.82 (3 × C, C=O). HR-MS (FAB) *m/z* 399.2066 [$C_{18}H_{23}O_8S$ $(M+H)^+$ requires 399.2052].

(ii) *Phenyl 2,3,6-tri-O-acetyl-1-thio-4-O-trifluoromethanesulfonyl-β-D-galactoside*: Trifluoromethanesulfonic anhydride (0.13 mL, 0.75 mmol) was added to the above triacetate (310 mg, 0.69 mmol) in CH_2Cl_2 (10 mL) and pyridine (200 μL, 2.0 mmol) at −30 °C and the solution stirred (30 min). Saturated $NaHCO_3$ solution (5 mL) was added and a standard work-up (CH_2Cl_2) gave a colourless oil (350 mg), presumably the title triflate, which was used without purification.

(iii) *Phenyl 2,3,6-tri-O-acetyl-4-S-acetyl-1,4-dithio-β-D-glucoside* **9**: Potassium thioacetate (190 mg, 1.7 mmol) was added to the above triflate (350 mg) in dry THF (10 mL) and the mixture stirred (rt, 16 h). Filtration and concentration of the mixture, followed by a standard work-up (CH_2Cl_2) and flash chromatography (EtOAc/petrol 1:4), gave the thioacetate **9** as a colourless oil (250 mg, 88%), $[\alpha]_D = -23.5$ (*c* 1, $CHCl_3$). Found: C, 52.6; H, 5.6. $C_{20}H_{24}O_8S_2$ requires C, 52.5; H, 5.5. ^{1}H NMR (300 MHz): δ 2.00, 2.09 (2 × s, 9H, CH_3CO), 2.32 (s, CH_3COS), 3.65 (dd, $J_{3,4}$ 11.2, $J_{4,5}$ 11.1, H4), 3.85 (ddd, $J_{5,6}$ 2.3, 5.9, H5), 4.29–4.34 (m, H6,6), 4.73 (d, $J_{1,2}$ 10.1, H1), 4.95 (dd, $J_{2,3}$ 8.9, H2), 5.24 (dd, H3), 7.31–7.34, 7.47–7.50 (2 × m, Ph). ^{13}C NMR (125.7 MHz): δ 20.52, 20.73, 20.75 (3 × C, CH_3CO), 30.71 (CH_3COS), 44.00 (C4), 63.35 (C6), 71.12, 72.18, 76.68 (C2,3,5), 85.71 (C1), 128.22, 128.88, 131.99, 132.84 (Ph), 166.37, 170.01, 170.61 (3 × C, C=O), 192.63 (SC=O). HR-MS (FAB) *m/z* 457.0973 $[C_{20}H_{25}O_8S_2\ (M+H)^+$ requires 457.0990].

3.3. Phenyl tetra-*O*-acetyl-β-D-glucopyranosyl-(1→3)-2,6-di-*O*-acetyl-4-*S*-acetyl-1,4-dithio-β-D-glucoside 11

(a) NaOMe (10%) in MeOH (2 mL) was added to 4-nitrophenyl β-D-glucoside **10**[18] (80 mg, 0.17 mmol) and the thioacetate **9** (75 mg, 0.14 mmol) in MeOH (3 mL) and the solution stirred (rt, 30 min). The mixture was quenched with resin (Amberlite IR-120, H^+), filtered and concentrated. The residue was dissolved in a phosphate buffer (pH 7, 2 mL), and Abg (2 mg) added and the solution kept at 25 °C for 2 h. The solution was concentrated and the residue dissolved in pyridine (5 mL), then Ac_2O (5 mL) was added and the solution stirred (rt, 12 h). The mixture was quenched by the addition of MeOH (5 mL), concentrated and subjected to a standard work-up (CH_2Cl_2). Flash chromatography (EtOAc/petrol 1:4–1:1) gave the disaccharide **11** as a colourless oil (20 mg, 18%), $[\alpha]_D = -34.1$ (*c* 1, $CHCl_3$). Found: C, 51.9; H, 5.2. $C_{32}H_{40}O_{16}S_2$ requires C, 51.6; H, 5.4. ^{1}H NMR (500 MHz): δ 1.98, 2.01, 2.04, 2.08, 2.10, 2.20 (6 × s, 18H, CH_3CO), 2.26 (s, CH_3COS), 3.18 (dd, $J_{3,4} \approx J_{4,5}$ 10.7, H4), 3.64 (ddd, $J_{4',5'}$ 8.8, $J_{5',6'}$ 2.3, 4.8, H5′), 4.04 (dd, $J_{6',6'}$ 12.4, H6′), 4.13 (dd, $J_{2,3}$ 7.8, H3), 4.23–4.27 (m, H6,6′), 4.34 (ddd, $J_{5,6}$ 1.9, 4.2, H5), 4.40 (dd, $J_{6,6}$ 12.0, H6), 4.68 (d, $J_{1',2'}$ 8.0, H1′), 4.69 (d, $J_{1,2}$ 10.2, H1), 4.96 (dd, $J_{2',3'}$ 7.9, H2′), 4.99 (dd, H2), 5.06 (dd, $J_{3',4'}$ 10.3, H4′), 5.12 (dd, H3′), 7.27–7.31, 7.41–7.45 (2 × m, Ph). ^{13}C NMR (125.7 MHz): δ 20.43, 20.55, 20.76, 20.84, 21.15 (CH_3CO), 30.66 (CH_3COS), 45.77 (C4), 61.92 (C6′), 63.99 (C6), 68.21 (C4′), 70.84 (C2′), 71.85 (C5′), 72.97 (C3′), 73.47 (C2), 75.38 (C3), 76.07 (C5), 86.40 (C1), 100.51 (C1′), 127.89, 128.87, 132.01, 133.19 (Ph), 169.19, 169.41, 169.64, 170.33, 170.62, 170.70 (6 × C, C=O), 194.2 (SC=O). HR-MS (FAB) *m/z* 745.1862 $[C_{32}H_{41}O_{16}S_2\ (M+H)^+$ requires 745.1836].

(b) NaOMe (10%) in MeOH (2 mL) was added to the D-glucosyl fluoride **12** (60 mg, 0.17 mmol) and the thioacetate **9** (75 mg, 0.14 mmol) in MeOH (3 mL) and the solution stirred (rt, 30 min). The mixture was quenched with resin (Amberlite IR-120, H^+), filtered and concentrated. The residue was dissolved in NH_4HCO_3 solution (2 mL of 150 mM), and Abg E358S (2 mg) was added and the solution kept at 25 °C for 2 h). The solution was concentrated and the residue dissolved in pyridine (5 mL), then Ac_2O (5 mL) was added and the solution stirred (rt, 12 h). The mixture was quenched by the addition of MeOH (5 mL), concentrated and subjected to a standard work-up (CH_2Cl_2). Flash chromatography (EtOAc/petrol 1:4–1:1) gave disaccharide **11** as a colourless oil (28 mg, 26%). The ^{1}H and ^{13}C NMR spectra were consistent with those reported in (a).

Next to elute was phenyl tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucosyl-(1→3)-2,6-di-*O*-acetyl-4-*S*-acetyl-1,4-dithio-β-D-glucoside **13**, obtained as colourless needles (47 mg, 52%), mp 100–103 °C (EtOH), $[\alpha]_D = -44.8$ (*c* 1, $CHCl_3$). Found: C, 51.5; H, 5.4. $C_{44}H_{56}O_{24}S_2$ requires C, 51.2; H, 5.5. ^{1}H NMR (500 MHz): δ 1.97, 1.99, 2.00, 2.02, 2.06, 2.07, 2.14, 2.18 (8 × s, 27H, CH_3CO), 2.25 (s, CH_3COS), 3.21 (dd, $J_{3,4}$ 10.3, $J_{4,5}$ 10.5, H4), 3.54 (ddd, $J_{4',5'}$ 10.3, $J_{5',6'}$ 1.9, 5.5, H5′), 3.63 (ddd, $J_{4'',5''}$ 10.4, $J_{5'',6''}$ 2.3, 4.4, H5″), 3.75 (dd, $J_{3',4'}$ 9.4, H4′), 4.01 (dd, $J_{6'',6''}$ 12.5, H6″), 4.05 (m, $J_{6',6'}$ 11.5, H5,6′), 4.23 (m, $J_{2,3}$ 9.8, $J_{5,6}$ 5.5, $J_{6,6}$ 12.8, H3,6), 4.33 (dd, H6″), 4.37 (dd, $J_{5,6}$ 3.7, H6), 4.44 (dd, H6′), 4.47 (d, $J_{1'',2''}$ 7.9, H1″), 4.64 (d, $J_{1',2'}$ 8.1, H1′), 4.66 (d, $J_{1,2}$ 10.1, H1), 4.87 (dd, $J_{2',3'}$ 7.8, H2′), 4.91 (dd, $J_{2'',3''}$ 8.0, H2″), 4.97 (dd, H2), 5.04 (dd, $J_{3',4''}$ 9.7, H4″), 5.07 (dd, H3′), 5.12 (dd, H3″), 7.25–7.30, 7.43–7.47 (2 × m, Ph). ^{13}C NMR (125.7 MHz): δ 20.35, 20.40, 20.43, 20.56, 20.73, 20.80, 21.07 (CH_3CO), 30.53 (CH_3COS), 45.51 (C4), 61.51 (C6″), 61.93 (C6′), 63.91 (C6), 67.74 (C4′), 70.96 (C2′), 71.53 (C2″), 71.97 (C5″), 72.75, 72.76, 72.78 (C3′,5′, 3″), 73.39 (C2), 75.65 (C5), 76.33 (C4″), 76.51 (C3), 86.38 (C1), 100.38 (C1′), 100.80 (C1″), 127.80, 127.83, 131.95, 133.24 (Ph), 168.98, 169.17, 169.21, 169.58, 169.79, 170.11, 170.18, 170.32, 170.57 (9 × C, C=O), 194.43 (SC=O). HR-MS (FAB) *m/z* 1033.2633 $[C_{44}H_{57}O_{24}S_2\ (M+H)^+$ requires 1033.2681].

3.4. Phenyl tetra-*O*-acetyl-β-D-galactopyranosyl-(1→3)-2,6-di-*O*-acetyl-4-*S*-acetyl-1,4-dithio-β-D-glucoside 15

(a) NaOMe (10%) in MeOH (5 mL) was added to the D-galactosyl fluoride **14** (60 mg, 0.17 mmol) and the thioglycoside **9** (75 mg, 0.14 mmol) in MeOH (3 mL) and the mixture treated as for the preparation of **11** (b). Flash chromatography (EtOAc/petrol 1:4–1:1) gave disaccharide **15** as a colourless oil (105 mg, 80%), $[\alpha]_D = -37.7$ (*c* 1, $CHCl_3$). Found: C, 51.8; H, 5.5. $C_{32}H_{40}O_{16}S_2$ requires C, 51.6; H, 5.4. ^{1}H NMR (600 MHz): δ 1.98, 2.01, 2.04, 2.08, 2.14, 2.22 (6 × s, 21H, CH_3CO), 2.29 (s, CH_3COS), 3.21 (dd, $J_{3,4}$ 10.1, $J_{4,5}$ 10.3, H4), 3.85 (ddd, $J_{4',5'}$ 1.1, $J_{5',6'}$ 6.7, H5′), 4.05 (dd, $J_{6',6'}$ 11.3, H6′), 4.09 (dd, H6′), 4.12 (dd, $J_{2,3}$ 9.9, H3), 4.25 (dd, $J_{5,6}$ 5.6, $J_{6,6}$ 12.1, H6), 4.32 (ddd, $J_{5,6}$ 2.0, H5), 4.40 (dd, H6), 4.64 (d, $J_{1',2'}$ 8.1, H1′), 4.69 (d, $J_{1,2}$ 10.1, H1), 4.92 (dd, $J_{2',3'}$ 10.5, $J_{3',4'}$ 3.5, H3′), 5.00 (dd, H2), 5.14 (d, H2′), 5.36 (dd, H4′), 7.28–7.31, 7.45–7.48 (2 × m, Ph). ^{13}C NMR (150.8 MHz): δ 20.51, 20.53, 20.64, 20.68, 20.80, 21.13 (CH_3CO), 30.7 (CH_3COS), 46.33 (C4), 61.19 (C6′), 64.03 (C6), 66.89

(C4′), 68.38 (C2′), 70.64 (C5′), 71.05 (C3′), 73.49 (C2), 75.45 (C3), 76.28 (C5), 86.41 (C1), 100.88 (C1′), 127.84, 128.85, 131.97, 133.24 (Ph), 169.16, 169.65, 170.19, 170.48, 170.65, 170.87 (C=O), 194.3 (SC=O). HR-MS (FAB) *m/z* 745.1858 [$C_{32}H_{41}O_{16}S_2$ $(M+H)^+$ requires 745.1836].

(b) (i) *Phenyl 2,3,6-tri-O-acetyl-1,4-dithio-β-D-glucoside, disulfide* **16**: NaOMe (10%) in MeOH (2 mL) was added to thioacetate **9** (75 mg, 0.14 mmol) in MeOH (2 mL) and the solution stirred (rt, 1 h). The mixture was quenched with resin (Amberlite IR-120, H^+), filtered and concentrated. The residue was dissolved in $CHCl_3$ (5 mL). Triethylamine (15 mg, 0.14 mmol) and I_2 (20 mg, 0.07 mmol) were added and the solution stirred (rt, 45 min). Pyridine (5 mL) and Ac_2O (5 mL) were then added and the solution stirred (rt, 1 h). The reaction was quenched with MeOH (5 mL) and the solution concentrated and subjected to a standard work-up ($CHCl_3$). Flash chromatography (EtOAc/petrol 3:7) gave the disulfide **16** as colourless needles (46 mg, 81%), mp 126–128 °C (Et_2O), $[\alpha]_D = -133.6$ (*c* 1, $CHCl_3$). Found: C, 52.0; H, 5.0. $C_{36}H_{42}O_{14}S_4$ requires C, 52.3; H, 5.1. ^1H NMR (300 MHz): δ 1.91, 2.07 (2 × s, 9H, CH_3), 2.91 (dd, $J_{3,4}$ 10.8, $J_{4,5}$ 10.5, H4), 3.72 (ddd, $J_{5,6}$ 1.9, 5.3, H5), 4.25 (dd, $J_{6,6}$ 12.1, H6), 4.64 (dd, H6), 4.68 (d, $J_{1,2}$ 10.1, H1), 4.85 (dd, $J_{2,3}$ 8.8, H2), 5.17 (dd, H3), 7.27–7.33, 7.46–7.51 (2 × m, Ph). ^{13}C NMR (125.7 MHz): δ 20.51, 20.70, 20.72 (3 × C, CH_3), 51.78 (C4), 63.15 (C6), 70.99 (C2), 72.67 (C5), 76.75 (C3), 85.18 (C1), 128.36, 128.81, 131.51, 133.32 (Ph), 169.46, 169.63, 170.39 (3 × C, C=O). HR-MS (FAB) *m/z* 827.1518 [$C_{36}H_{43}O_{14}S_4$ $(M+H)^+$ requires 827.1522].

(ii) NaOMe (10%) in MeOH (5 mL) was added to D-galactosyl fluoride **14** (42 mg, 0.12 mmol) and the disulfide **16** (40 mg, 0.05 mmol) in MeOH (3 mL) and the solution stirred (rt, 30 min). The mixture was quenched with resin (Amberlite IR-120, H^+), filtered and concentrated. The residue was dissolved in NH_4HCO_3 solution (2 mL of 150 mM), and Abg E358S (2 mg) was added and the solution kept at 25 °C for 2 h. This was followed by the addition of 1,4-dithioerythritol (10 mg, 0.06 mmol) and the solution kept (25 °C, 2 h). The solution was then concentrated and the residue dissolved in pyridine (5 mL), then Ac_2O (5 mL) was added and the solution stirred (rt, 12 h). The mixture was quenched by the addition of MeOH (5 mL), concentrated and subjected to a standard work-up (CH_2Cl_2). Flash chromatography (EtOAc/petrol 1:4–1:1) gave the disaccharide **15** as a colourless oil (21 mg, 30%). The ^1H and ^{13}C NMR spectra were consistent with those reported in (a).

3.5. Phenyl tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-1-thio-β-D-glucoside 18

NaOMe (10%) in MeOH (5 mL) was added to D-galactosyl fluoride **14** (60 mg, 0.17 mmol) and thioglycoside **17** (62 mg, 0.14 mmol) in MeOH (3 mL) and the mixture treated as for the preparation of **11** (b). Flash chromatography (EtOAc/petrol 1:4–1:1) gave disaccharide **18** as a colourless oil (92 mg, 74%). The ^1H and ^{13}C NMR spectra were consistent with those reported.[19]

3.6. Phenyl 2,3,6-tri-*O*-acetyl-4-deoxy-1-thio-β-D-*xylo*-hexoside 20

(a) Boron trifluoride diethyl etherate (10 μL) was added to tetra-*O*-acetyl-4-deoxy-α-D-*xylo*-hexopyranose[20] (160 mg, 0.48 mmol) and PhSH (0.15 μL, 1.4 mmol) in CH_2Cl_2 (5 mL) and the solution stirred (rt, 2 h). Standard work-up (CH_2Cl_2) and flash chromatography (EtOAc/petrol 1:4) gave triacetate **20** as colourless needles (150 mg, 83%), mp 53–57 °C (Et_2O), $[\alpha]_D = +4.6$ (*c* 1, $CHCl_3$). Found: C, 56.4; H, 5.7. $C_{18}H_{22}O_7S$ requires C, 56.5; H, 5.8. ^1H NMR (500 MHz): δ 2.02, 2.08, 2.10 (3 × s, 9H, CH_3), 2.09 (m, H4), 2.16 (m, $J_{3,4}$ 9.3, $J_{4,5}$ 9.1, H4), 3.79 (ddd, $J_{4,5}$ 2.0, $J_{5,6}$ 4.1, 6.3, H5), 4.13 (dd, $J_{6,6}$ 11.7, H6), 4.17 (dd, H6), 4.66 (d, $J_{1,2}$ 9.9, H1), 4.92 (dd, $J_{2,3}$ 10.0, H2), 5.03 (ddd, $J_{3,4}$ 5.3, H3), 7.28–7.32, 7.48–7.53 (2 × m, Ph). ^{13}C NMR (125.7 MHz): δ 20.76, 20.86, 20.91 (3 × C, CH_3), 32.57 (C4), 65.38 (C6), 70.53 (C2), 71.69 (C3), 73.34 (C5), 86.08 (C1), 127.99, 128.83, 132.56, 132.65 (Ph), 169.66, 170.26, 170.61 (3 × C, C=O). HR-MS (FAB) *m/z* 383.1174 [$C_{18}H_{23}O_7S$ $(M+H)^+$ requires 383.1164].

(b) (i) *Phenyl tri-O-acetyl-4-O-phenoxythiocarbonyl-1-thio-β-D-galactoside*: *O*-Phenyl chlorothioformate (0.30 mL, 2.2 mmol) and pyridine (0.36 μL, 4.4 mmol) were added to phenyl 2,3,6-tri-*O*-acetyl-1-thio-β-D-galactopyranoside (200 mg, 0.40 mmol) in CH_2Cl_2 (20 mL) and the solution stirred (rt, 24 h). The mixture was quenched with MeOH (5 mL), then concentrated, followed by a standard work-up (CH_2Cl_2) and flash chromatography (EtOAc/petrol 1:4) to give the title thiocarbonate as a colourless oil (153 mg, 59%), $[\alpha]_D = -16.0$ (*c* 1, $CHCl_3$). ^1H NMR (300 MHz): δ 2.08, 2.13, 2.15 (3 × s, 9H, CH_3), 4.21 (ddd, $J_{4,5}$ 1.0, $J_{5,6}$ 6.1, 6.1, H5), 4.51 (dd, $J_{6,6}$ 11.5, H6), 4.61 (dd, H6), 4.83 (d, $J_{1,2}$ 7.2, H1), 5.28 (dd, $J_{2,3}$ 9.9, $J_{3,4}$ 3.3, H3), 5.39 (dd, H2), 6.20 (dd, H4), 7.12–7.21, 8.05–8.12 (2 × m, Ph). ^{13}C NMR (75.5 MHz): δ 20.74, 20.81, 20.83 (3 × C, CH_3), 61.86 (C6), 67.37 (C2), 71.66 (C3), 74.52 (C5), 77.11 (C4), 87.04 (C1), 121.58, 128.01, 128.94, 129.25, 129.60, 132.71, 133.34, 153.38 (Ph), 165.91, 169.37, 170.01 (3 × C, C=O), 195.41 (C=S). HR-MS (FAB) *m/z* 535.2964 [$C_{25}H_{27}O_9S_2$ $(M+H)^+$ requires 535.2975].

(ii) Tributylstannane (0.28 mL, 1.1 mmol) was added to the above thiocarbonate (160 mg, 0.27 mmol) and AIBN (20 mg) in dry PhMe (15 mL) and the mixture stirred (60 °C, 4 h). Concentration of the mixture and flash chromatography (EtOAc/petrol 17:83) of the residue gave the triacetate **20** as colourless needles (85 mg, 73%). The ^1H NMR spectrum was consistent with that reported in (a).

3.7. Phenyl tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-tri-*O*-acetyl-β-D-glucopyranosyl-(1→3)-2,6-di-*O*-acetyl-4-deoxy-1-thio-β-D-*xylo*-hexoside 21 and phenyl tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-tri-*O*-acetyl-β-D-glucopyranosyl-(1→4)-tri-*O*-acetyl-β-D-glucopyranosyl-(1→3)-2,6-di-*O*-acetyl-4-deoxy-1-thio-β-D-*xylo*-hexoside 22

According to the procedure described for **11** (b) but leaving the reaction for 48 h, **12** (60 mg, 0.17 mmol)

and **20** (75 mg, 0.20 mmol) gave the trisaccharide **21** as colourless plates (49 mg, 26%), mp 89–91 °C (EtOH), $[\alpha]_D = -21.3$ (*c* 1, $CHCl_3$). Found: C, 52.4; H, 5.7. $C_{42}H_{54}O_{23}S$ requires C, 52.6; H, 5.7. ^{1}H NMR (500 MHz): δ 1.97, 1.99, 2.00, 2.01, 2.02, 2.07, 2.09, 2.10, 2.12 (9 × s, 27H, CH_3), 2.10–2.19 (m, 2H, H4), 3.53 (ddd, $J_{4',5'}$ 9.9, $J_{5',6'}$ 2.2, 4.6, H5′), 3.65 (ddd, $J_{4'',5''}$ 9.9, $J_{5'',6''}$ 2.3, 4.4, H5″), 3.68–3.77 (m, H3,5,4′), 4.03 (dd, $J_{6'',6''}$ 12.5, H6″), 4.06 (dd, $J_{6',6'}$ 12.1, H6′), 4.11 (dd, $J_{5,6}$ 6.2, $J_{6,6}$ 11.8, H6), 4.15 (dd, $J_{5,6}$ 3.9, H6), 4.35 (dd, H6″), 4.50 (d, $J_{1'',2''}$ 7.9, H1″), 4.54 (d, $J_{1,2}$ 10.0, H1), 4.55 (m, H6′), 4.58 (d, $J_{1',2'}$ 8.0, H1′), 4.82 (dd, $J_{2',3'}$ 9.1, H2′), 4.84 (dd, $J_{2,3}$ 9.5, H2), 4.91 (dd, $J_{2'',3''}$ 9.4, H2″), 5.05 (dd, $J_{3'',4''}$ 9.7, H4″), 5.11 (dd, H3″), 5.14 (dd, $J_{3',4'}$ 9.7, H3′), 7.26–7.31, 7.45–7.48 (2 × m, Ph). ^{13}C NMR (125.7 MHz): δ 20.37, 20.48, 20.59, 20.74, 20.80, 21.00 (CH_3), 34.45 (C4), 61.23 (C6′), 61.48 (C6″), 65.55 (C6), 67.73 (C4″), 71.16 (C2′), 71.58 (C2″), 71.95 (C5″), 72.10 (C2), 72.43 (C3″), 72.71 (C5′), 72.83 (C3′), 73.60 (C5), 76.21, 77.92 (C3,4′), 86.21 (C1), 100.76 (C1″), 101.12 (C1′), 127.74, 128.76, 132.12, 133.14 (Ph), 168.96, 169.19, 169.26, 169.60, 169.77, 170.07, 170.17, 170.43, 170.67 (9 × C, C=O). HR-MS (FAB) *m*/*z* 959.2928 [$C_{42}H_{55}O_{23}S$ $(M+H)^+$ requires 959.2855].

Next to elute was tetrasaccharide **22** as colourless plates (27 mg, 11%), mp 109–111 °C (EtOH), $[\alpha]_D = +2.7$ (*c* 1, $CHCl_3$). ^{1}H NMR (600 MHz): δ 1.96, 1.97, 1.99, 2.00, 2.01, 2.03, 2.07, 2.08, 2.11, 2.12, 2.13 (11 × s, 36H, CH_3), 2.00–2.08 (m, 2H, H4), 3.52 (ddd, $J_{4',5'}$ 9.9, $J_{5',6'}$ 2.2, 4.4, H5′), 3.57 (ddd, $J_{4'',5''}$ 9.8, $J_{5'',6''}$ 2.1, 5.1, H5″), 3.62 (ddd, $J_{4''',5'''}$ 9.9, $J_{5''',6'''}$ 2.4, 4.4, H5‴), 3.70–3.77 (m, H3,5,4′, 4″), 4.02 (dd, $J_{6''',6'''}$ 11.0, H6‴), 4.04 (dd, $J_{6',6'}$ 10.3, H6′), 4.11 (dd, $J_{6'',6''}$ 12.1, H6″), 4.13–4.17 (m, 2H, H6), 4.34 (dd, H6‴), 4.39 (dd, H6″), 4.46 (d, $J_{1''',2'''}$ 7.9, H1‴), 4.47 (d, $J_{1',2'}$ 7.9, H1′), 4.54 (d, $J_{1,2}$ 10.0, H1), 4.57 (d, $J_{1'',2''}$ 8.0, H1″), 4.58 (dd, H6′), 4.82 (dd, $J_{2,3}$ 9.6, H2), 4.83 (dd, $J_{2',3'}$ 9.2, H2′), 4.84 (dd, $J_{2'',3''}$ 9.2, H2″), 4.89 (dd, $J_{2''',3'''}$ 9.3, H2‴), 5.04 (dd, $J_{3''',4'''}$ 9.4, H4‴), 5.09 (dd, $J_{3',4'}$ 9.4, H3′), 5.12 (dd, $J_{3'',4''}$ 9.2, H3″), 5.13 (dd, $J_{3''',4'''}$ 9.5, H3‴), 7.25–7.30, 7.45–7.47 (2 × m, Ph). ^{13}C NMR (150.8 MHz): δ 20.40, 20.45, 20.49, 20.51, 20.53, 20.56, 20.60, 20.75, 20.77, 20.84, 21.02 (CH_3), 34.44 (C4), 61.08 (C6′), 61.45 (C6‴), 62.06 (C6″), 65.54 (C6), 67.67 (C4‴), 71.20 (C2), 71.51 (C2‴), 71.72, 71.98 (C2′, 2″), 72.09 (C5‴), 72.35 (C3′), 72.58 (C3″), 72.73 (C5′,5″), 72.82 (C3‴), 73.59 (C4′), 76.07, 77.89 (C3,5), 76.21 (C4″), 86.19 (C1), 100.57, 100.76 (C1′, 1‴), 101.09 (C1″), 127.74, 128.76, 132.09, 133.15 (Ph), 169.08, 169.22, 169.24, 169.28, 169.59, 169.76, 169.80, 170.10, 170.17, 170.18, 170.47, 170.72 (12 × C, C=O). HR-MS (FAB) *m*/*z* 1247.3717 [$C_{54}H_{71}O_{31}S$ $(M+H)^+$ requires 1247.3700].

3.8. Phenyl tetra-*O*-acetyl-β-D-galactopyranosyl-(1→3)-2,6-di-*O*-acetyl-4-deoxy-1-thio-β-D-*xylo*-hexoside 24

According to the procedure described for **11** (b), **14** (60 mg, 0.17 mmol) and **20** (53 mg, 0.14 mmol) gave disaccharide **24** as a colourless oil (79 mg, 85%), $[\alpha]_D = -20.8$ (*c* 1, $CHCl_3$). ^{1}H NMR (600 MHz): δ 1.97, 2.00, 2.01, 2.09, 2.12 (5 × s, 18H, CH_3), 2.10–2.16 (m, 2H, H4), 3.73 (m, H5), 3.83 (ddd, $J_{4',5'}$ 1.0, $J_{5',6'}$ 6.3, 7.0, H5′), 3.88 (m, $J_{2,3}$ 9.3, H3), 4.08 (dd, $J_{6',6'}$ 11.3, H6′), 4.14 (dd, $J_{5,6}$ 6.5, $J_{6,6}$ 11.7, H6), 4.16 (dd, $J_{5,6}$ 3.7, H6), 4.20 (dd, H6′), 4.56 (d, $J_{1,2}$ 10.0, H1), 4.60 (d, $J_{1',2'}$ 8.1, H1′), 4.88 (dd, H2), 4.95 (dd, $J_{2',3'}$ 10.5, $J_{3',4'}$ 3.4, H3′), 5.15 (dd, H2′), 5.37 (dd, H4′), 7.28–7.30, 7.46–7.49 (2 × m, Ph). ^{13}C NMR (150.8 MHz): δ 20.51, 20.55, 20.65, 20.79, 21.60 (CH_3), 34.57 (C4), 61.05 (C6′), 65.56 (C6), 66.83 (C4′), 68.41 (C2′), 70.62, 70.81 (C2,5′), 72.30 (C3′), 73.63 (C5), 77.56 (C3), 86.28 (C1), 101.73 (C1′), 127.75, 128.78, 132.08, 133.21 (Ph), 169.22, 169.47, 170.24, 170.26, 170.38, 170.71 (6 × C, C=O). HR-MS (FAB) *m*/*z* 671.1970 [$C_{30}H_{39}O_{15}S$ $(M+H)^+$ requires 671.2010].

3.9. Attempted synthesis of the 3-deoxy sugar 19

(i) *Phenyl 4-O-acetyl-2,6-di-O-benzoyl-1-thio-β-D-galactoside* **25**: Trifluoroacetic acid (one drop) was added to phenyl 2,6-di-*O*-benzoyl-1-thio-β-D-galactopyranoside[21] (500 mg, 1.0 mmol) and $CH_3C(OEt)_3$ (510 mg, 3.1 mmol) in $CHCl_3$ (5 mL) and the solution stirred (rt, 5 min). Acetonitrile (5 mL) and H_2O (1 mL) were then added and the mixture stirred vigourously (rt, 30 min). Concentration of the mixture, followed by flash chromatography (EtOAc/petrol 3:7), gave acetate **25** as needles (510 mg, 95%), mp 177–179 °C (EtOH), $[\alpha]_D = +0.1$ (*c* 1, $CHCl_3$). ^{1}H NMR (500 MHz): δ 2.21 (s, CH_3), 2.71 (s, OH), 4.06 (dd, $J_{5,6}$ 5.2, 7.6, H5), 4.11 (dd, $J_{2,3}$ 9.8, $J_{3,4}$ 3.5, H3), 4.44 (dd, $J_{6,6}$ 11.5, H6), 4.50 (dd, H6), 4.90 (d, $J_{1,2}$ 10.0, H1), 5.30 (dd, H2), 5.52 (d, H4), 7.12–7.21, 7.45–7.60, 8.05–8.08 (3 × m, 15H, Ph). ^{13}C NMR (125.7 MHz): δ 20.73 (CH_3), 62.69 (C6), 69.99 (C3), 71.59, 72.62 (C2,5), 74.95 (C4), 86.43 (C1), 127.96–133.54 (Ph), 166.03, 166.70, 170.82 (3 × C, C=O). HR-MS (FAB) *m*/*z* 523.1407 [$C_{28}H_{27}O_8S$ $(M+H)^+$ requires 523.1426].

(ii) *Phenyl 4-O-acetyl-2,6-di-O-benzoyl-3-O-phenoxythiocarbonyl-1-thio-β-D-galactoside*: *O*-Phenyl chlorothioformate (0.15 mL, 1.1 mmol) and pyridine (0.70 μL, 0.90 mmol) were added to acetate **25** (150 mg, 0.30 mmol) in CH_2Cl_2 (20 mL) and the solution stirred (rt, 24 h). The mixture was quenched with MeOH (5 mL), then concentrated, followed by a standard workup (CH_2Cl_2) and flash chromatography (EtOAc/petrol 1:4) to give the title thiocarbonate as a colourless oil (150 mg, 79%), $[\alpha]_D = +57.3$ (*c* 1, $CHCl_3$). ^{1}H NMR (500 MHz): δ 2.02 (s, CH_3), 4.23 (ddd, $J_{4,5}$ 1.0, $J_{5,6}$ 4.2, 5.2, H5), 4.43 (dd, $J_{6,6}$ 11.5, H6), 4.55 (dd, H6), 5.00 (d, $J_{1,2}$ 10.0, H1), 5.73 (dd, $J_{2,3}$ 10.0, H2), 5.85 (dd, $J_{3,4}$ 3.4, H4), 5.90 (dd, H3), 6.90–7.60, 8.00–8.10 (2 × m, 20H, Ph). ^{13}C NMR (125.7 MHz): δ 20.58 (CH_3), 62.43 (C6), 66.70, 67.98 (C2,4), 74.73 (C5), 80.94 (C3), 87.05 (C1), 121.48–133.59 (Ph), 165.06, 165.93, 169.98 (3 × C, C=O), 193.16 (C=S). HR-MS (FAB) *m*/*z* 659.1411 [$C_{35}H_{31}O_9S_2$ $(M+H)^+$ requires 659.1409].

(iii) *Phenyl 4-O-acetyl-2,6-di-O-benzoyl-3-deoxy-1-thio-β-D-xylo-hexoside*: Tributylstannane (0.2 mL, 0.8 mmol) was added to the above thiocarbonate (140 mg, 0.21 mmol) and AIBN (20 mg) in dry PhMe (15 mL) and the mixture stirred (60 °C, 3 h). Concentration of

the mixture, followed by flash chromatography (EtOAc/petrol 17:83), gave the title D-*xylo*-hexoside as colourless plates (80 mg, 75%), mp 118–121 °C (EtOH), $[\alpha]_D = -12.6$ (*c* 1, $CHCl_3$). ^1H NMR (500 MHz): δ 1.95 (ddd, $J_{2,3}$ 11.2, $J_{3,3}$ 14.0, $J_{3,4}$ 3.1, H3), 2.03 (s, CH_3), 2.64 (ddd, $J_{2,3}$ 3.3, $J_{3,4}$ 5.1, H3), 4.11 (ddd, $J_{4,5}$ 1.4, $J_{5,6}$ 5.1, 7.6, H5), 4.45 (dd, $J_{6,6}$ 11.5, H6), 4.50 (dd, H6), 4.98 (d, $J_{1,2}$ 10.0, H1), 5.30–5.33 (m, H2,4), 7.11–7.41, 7.52–7.64, 8.03–8.06 (3 × m, 15H, Ph). ^{13}C NMR (125.7 MHz): δ 20.89 (CH_3), 34.53 (C3), 63.10 (C6), 66.42, 67.32 (C2,4), 76.74 (C5), 88.22 (C1), 127.62–133.24 (Ph), 165.04, 166.04, 170.15 (3 × C, C=O). HR-MS (FAB) *m*/*z* 506.1399 [$C_{28}H_{26}O_7S$ $(M)^+$ requires 506.1399].

(iv) *Phenyl 2,6-di-O-benzoyl-3-deoxy-1-thio-β-D-xylo-hexopyranoside* **26**: Acetyl chloride (0.44 mL, 6.1 mmol) was added to the above D-*xylo*-hexoside (1.1 g, 2.3 mmol) in MeOH (60 mL) and the solution stirred (rt, 24 h). The solution was neutralised with resin (Amberlite IRA 400, OH^-), filtered and concentrated. Flash chromatography (EtOAc/petrol 1:4) gave dibenzoate **26** as colourless needles (751 mg, 74%), mp 165–168 °C (EtOH), $[\alpha]_D = -5.4$. Found: C, 67.3; H, 5.3. $C_{26}H_{24}O_6S$ requires C, 67.2; H, 5.2. ^1H NMR (500 MHz): δ 1.90 (ddd, $J_{2,3}$ 11.3, $J_{3,3}$ 13.6, $J_{3,4}$ 3.0, H3), 2.45 (s, OH), 2.65 (ddd, $J_{2,3}$ 5.1, $J_{3,4}$ 3.2, H3), 4.00 (ddd, $J_{4,5}$ 1.2, $J_{5,6}$ 5.1, 7.4, H5), 4.03 (ddd, H4), 4.53 (dd, $J_{6,6}$ 11.7, H6), 4.69 (dd, H6), 4.95 (d, $J_{1,2}$ 10.0, H1), 5.38 (ddd, H2), 7.10–7.20, 7.41–7.59, 8.04–8.09 (3 × m, 15H, Ph). ^{13}C NMR (125.7 MHz): δ 37.36 (C3), 63.86 (C6), 66.00 (C2), 66.55 (C4), 78.49 (C5), 88.42 (C1), 127.57–133.34 (Ph), 165.3, 166.5 (2 × C, C=O). HR-MS (FAB) *m*/*z* 465.1380 [$C_{26}H_{25}O_6S$ $(M+H)^+$ requires 465.1372].

(v) Trifluoromethanesulfonic anhydride (0.13 mL, 0.75 mmol) was added to dibenzoate **26** (310 mg, 0.67 mmol) in CH_2Cl_2 (10 mL) and pyridine (200 μL, 2.0 mmol) at −30 °C and the solution stirred (30 min). Saturated $NaHCO_3$ solution (5 mL) was added and, after a standard work-up (CH_2Cl_2), potassium thioacetate (190 mg, 1.7 mmol) was added to the residue, presumably triflate **27**, in dry THF (10 mL) and the mixture stirred (rt, 16 h). Filtration and concentration of the mixture, followed by a standard workup (CH_2Cl_2) and flash chromatography (EtOAc/petrol 1:4), gave alkene **28** as a colourless oil (175 mg, 59%). ^1H NMR (600 MHz): δ 4.48 (dd, $J_{5,6}$ 6.3, $J_{6,6}$ 11.5, H6), 4.53 (dd, $J_{5,6}$ 4.2, H6), 4.74 (m, $J_{3,5}$ 2.1, $J_{4,5}$ 1.3, H5), 5.13 (d, $J_{1,2}$ 8.2, H1), 5.58 (m, $J_{2,3}$ 2.1, $J_{2,4}$ 1.3, H2), 5.98 (ddd, $J_{3,4}$ 10.3, H4), 6.03 (ddd, H3), 7.20–7.26, 7.44–7.60, 8.02–8.08 (3 × m, 15H, Ph). ^{13}C NMR (150.8 MHz): δ 65.73 (C6), 67.19 (C2), 73.96 (C5), 84.30 (C1), 127.39, 127.87, 128.40, 128.45, 128.81, 129.71, 129.72, 129.77, 129.81, 132.57, 132.66, 133.17, 133.28 (C3,4, Ph), 165.60, 166.24 (2 × C, C=O). HR-MS (FAB) *m*/*z* 447.1244 [$C_{26}H_{33}O_5S$ $(M+H)^+$ requires 447.1266].

(vi) Methanesulfonyl chloride (0.060 mL, 0.75 mmol) was added to dibenzoate **26** (300 mg, 0.64 mmol) in CH_2Cl_2 (10 mL) and Et_3N (0.28 mL, 2.0 mmol) at 0 °C and the solution stirred (30 min). Saturated $NaHCO_3$ solution (5 mL) was added and, after a standard work-up (CH_2Cl_2), potassium thioacetate (190 mg, 1.7 mmol) was added to the residue in dry THF (10 mL) and the mixture stirred (rt, 16 h). Filtration and concentration of the mixture, followed by a standard work-up (CH_2Cl_2) and flash chromatography (EtOAc/petrol 1:4), gave alkene **28** as a colourless oil (184 mg, 64%). The ^1H NMR spectrum was consistent with that reported above.

(vii) Diethyl azodicarboxylate (0.15 mL, 0.70 mmol) was added to dibenzoate **26** (150 mg, 0.33 mmol), Ph_3P (170 mg, 0.70 mmol) and $CH_3C(O)SH$ (50 mg, 0.10 mmol) in PhMe (5 mL) and the mixture stirred (50 °C, 6 h). Another set of the three reagents was added to the solution after 6 h and again after 24 h, with subsequent stirring for 6 h. Concentration of the mixture, followed by flash chromatography (EtOAc/petrol 17:83), gave alkene **28** as a colourless oil (70 mg, 49%). The ^1H NMR spectrum was consistent with that reported in (v).

3.10. Phenyl 2,6-di-*O*-benzoyl-4-*O*-chloroacetyl-3-deoxy-1-thio-β-D-*ribo*-hexoside 29

Diethyl azodicarboxylate (0.1 mL, 0.4 mmol) was added to dibenzoate **26** (100 mg, 0.20 mmol), Ph_3P (114 mg, 0.44 mmol) and $ClCH_2CO_2H$ (40 mg, 0.40 mmol) in PhMe (5 mL) and the mixture stirred (rt, 3 h). Concentration of the mixture, followed by flash chromatography (EtOAc/petrol 17:83), gave chloroacetate **29** as a colourless oil (81 mg, 72%), $[\alpha]_D = -10.5$ (*c* 1, $CHCl_3$). ^1H NMR (500 MHz): δ 1.86 (ddd, $J_{2,3}$ 10.9, $J_{3,3}$ 11.8, $J_{3,4}$ 10.8, H3), 2.86 (ddd, $J_{2,3}$ 5.0, $J_{3,4}$ 4.9, H3), 3.96 (ddd, $J_{4,5}$ 9.8, $J_{5,6}$ 2.5, 5.7, H5), 4.03, 4.04 (2 × s, CH_2), 4.43 (dd, $J_{6,6}$ 12.1, H6), 4.64 (dd, H6), 4.89 (d, $J_{1,2}$ 9.9, H1), 5.01–5.04 (m, H2,4), 7.13–7.15, 7.21–7.24, 7.45–7.51, 7.58–7.64, 8.05–8.07 (5 × m, 15H, Ph). ^{13}C NMR (125.7 MHz): δ 34.98 (C3), 40.49 (CH_2), 62.99 (C6), 67.54, 67.71 (C2,4), 77.77 (C5), 87.19 (C1), 128.11–133.36 (Ph), 164.88, 165.96, 166.12 (3 × C, C=O). HR-MS (FAB) *m*/*z* 543.1030 [$C_{28}H_{26}ClO_7S$ $(M+H)^+$ requires 543.1058].

3.11. Phenyl 2,6-di-*O*-benzoyl-3-deoxy-1-thio-β-D-*ribo*-hexopyranoside 30

Chloroacetate **29** (80 mg, 0.15 mmol) was added to H_2NCSNH_2 (110 mg, 1.5 mmol) and 2,6-lutidine (0.02 mL, 0.15 mmol) in MeOH/CH_2Cl_2 (10 mL, 1:1) and the mixture stirred (35 °C, 12 h). Concentration of the mixture, followed by flash chromatography (EtOAc/petrol 1:4), gave alcohol **30** as colourless plates (63 mg, 87%), mp 142–143 °C (EtOH), $[\alpha]_D = -73.7$ (*c* 1, $CHCl_3$). ^1H NMR (600 MHz): δ 1.78 (ddd, $J_{2,3}$ 11.0, $J_{3,3}$ 12.1, $J_{3,4}$ 11.0, H3), 2.70 (ddd, $J_{2,3} \approx J_{3,4}$ 4.9, H3), 3.05 (s, OH), 3.64 (ddd, $J_{4,5}$ 9.4, $J_{5,6}$ 2.2, 4.6, H5), 3.70–3.72 (m, H4), 4.63 (dd, $J_{6,6}$ 12.1, H6), 4.78 (dd, H6), 4.85 (d, $J_{1,2}$ 9.8, H1), 4.92 (ddd, H2), 7.15–7.18, 7.22–7.25, 7.46–7.50, 7.58–7.63, 8.05–8.09 (5 × m, Ph). ^{13}C NMR (150.8 MHz): δ 38.12 (C3), 63.79 (C6), 64.46, 68.29 (C2,4), 81.19 (C5), 87.11 (C1), 127.88–133.43

(Ph), 165.18, 167.34 (2 × C, C=O). HR-MS (FAB) *m/z* 465.1378 [$C_{26}H_{25}O_6S$ $(M+H)^+$ requires 465.1372].

3.12. Phenyl 4-*S*-acetyl-2,6-di-*O*-benzoyl-3-deoxy-1,4-dithio-β-D-*xylo*-hexoside

Diethyl azodicarboxylate (0.30 mL, 0.26 mmol) was added to alcohol **30** (60 mg, 0.13 mmol), Ph_3P (67 mg, 0.26 mmol) and $CH_3C(O)SH$ (19 mg, 0.26 mmol) in PhMe (5 mL) and the mixture stirred (rt, 4 h). Concentration of the mixture, followed by flash chromatography (EtOAc/petrol 1:9), gave the title thioacetate as a colourless oil (53 mg, 79%), $[\alpha]_D = -14.0$ (*c* 1, $CHCl_3$). Found: C, 64.4; H, 5.1. $C_{28}H_{26}O_6S_2$ requires C, 64.3; H, 5.0. ^{1}H NMR (600 MHz): δ 2.24 (ddd, $J_{2,3}$ 10.4, $J_{3,3}$ 13.5, $J_{3,4}$ 4.9, H3), 2.39 (s, CH_3), 2.54 (ddd, $J_{2,3}$ 4.9, $J_{3,4}$ 2.1, H3), 4.19 (ddd, $J_{4,5}$ 1.5, H4), 4.26 (ddd, $J_{5,6}$ 4.4, 7.7, H5), 4.38 (dd, $J_{6,6}$ 11.7, H6), 4.49 (dd, H6), 4.94 (d, $J_{1,2}$ 9.9, H1), 5.11 (ddd, H2), 7.11–7.14, 7.18–7.23, 7.44–7.48, 7.57–7.61, 8.01–8.04 (5 × m, 15H, Ph). ^{13}C NMR (150.8 MHz): δ 30.87 (CH_3), 37.23 (C3), 41.80 (C4), 64.87 (C6), 67.51 (C2), 77.97 (C5), 88.58 (C1), 127.69–133.38 (Ph), 165.18, 166.13 (2 × C, C=O), 193.94 (SC=O). HR-MS (FAB) *m/z* 523.1249 [$C_{28}H_{27}O_6S_2$ $(M+H)^+$ requires 523.1249].

3.13. Synthesis of the thioacetates 33 and 35

(i) *Tetra-O-acetyl-3-S-acetyl-3-thio-β-D-glucopyranose*: 3-*S*-Acetyl-1,2:5,6-di-*O*-isopropylidene-3-thio-α-D-glucose[22] (3.5 g) was added to CF_3COOH/H_2O (4:1, 15 mL) and the solution stirred (rt, 30 min). Concentration of the mixture gave a brown residue, which was dissolved in Ac_2O (20 mL) containing NaOAc (500 mg). This mixture was heated at reflux (10 min) before being poured into ice/water. Standard work-up (EtOAc) gave the title thioacetate as a colourless oil (4.0 g, 90%), $[\alpha]_D = +1.2$ (*c* 1, $CHCl_3$). ^{1}H NMR (600 MHz): δ 2.03, 2.08, 2.10 (3 × s, 12H, CH_3CO), 2.34 (s, CH_3COS), 3.85 (m, $J_{2,3}$ 10.9, $J_{3,4}$ 10.5, H3,5), 4.06 (dd, $J_{5,6}$ 2.3, $J_{6,6}$ 12.5, H6), 4.26 (dd, $J_{5,6}$ 4.7, H6) 5.10 (m, H2,4), 5.72 (d, $J_{1,2}$ 8.0, H1). ^{13}C NMR (150.8 MHz): δ 20.38, 20.47, 20.71, 20.82 (4 × C, CH_3CO), 30.73 (CH_3COS), 47.70 (C3), 61.76 (C6), 66.76, 69.09, 75.35 (C2,4,5), 93.06 (C1), 168.85, 169.15, 169.26, 170.64 (4 × C, C=O), 193.06 (SC=O). HR-MS (FAB) *m/z* 407.1038 [$C_{16}H_{23}O_{10}S$ $(M+H)^+$ requires 407.1011].

(ii) *Phenyl 2,4,6-tri-O-acetyl-3-S-acetyl-1,3-dithio-β-D-glucoside* **33**: Boron trifluoride diethyl etherate (10 μL) was added to the above thioacetate (470 mg, 1.2 mmol) and PhSH (0.17 mL, 1.6 mmol) in CH_2Cl_2 (5 mL) and the solution stirred (rt, 24 h). The mixture was quenched with Et_3N (5 mL) and subsequent concentration and flash chromatography (EtOAc/petrol 1:9) yielded thioacetate **33** as a colourless oil (470 mg, 89%), $[\alpha]_D = -11.0$ (*c* 1, $CHCl_3$). Found: C, 52.4; H, 5.5. $C_{20}H_{24}O_8S_2$ requires C, 52.6; H, 5.3. ^{1}H NMR (600 MHz): δ 2.01, 2.07, 2.08 (3 × s, 9H, CH_3CO), 2.33 (s, CH_3COS), 3.74 (ddd, $J_{4,5}$ 9.9, $J_{5,6}$ 2.6, 5.0, H5), 3.86 (dd, $J_{2,3}$ 9.9, $J_{3,4}$ 10.0, H3), 4.16 (dd, $J_{6,6}$ 12.3, H6), 4.19 (dd, H6), 4.73 (d, $J_{1,2}$ 9.7, H1), 4.99–5.03 (m, H2,4), 7.27–7.34, 7.47–7.51 (2 × m, Ph). ^{13}C NMR (150.8 MHz): δ 20.53, 20.71, 20.75 (3 × C, CH_3CO), 30.66 (CH_3COS), 49.42 (C3), 62.43 (C6), 67.23, 69.12, 78.00 (C2,4,5), 87.64 (C1), 128.18, 128.87, 132.12, 132.74 (Ph), 170.64, 169.31, 170.64 (3 × C, C=O), 193.36 (SC=O). HR-MS (FAB) *m/z* 457.0986 [$C_{20}H_{25}O_8S_2$ $(M+H)^+$ requires 457.0990].

(iii) 4-*Nitrophenyl 2,4,6-tri-O-acetyl-3-S-acetyl-3-thio-β-D-glucoside* **35**: Boron trifluoride diethyl etherate (10 μL) was added to the above thioacetate (160 mg, 0.48 mmol) and 4-nitrophenol (72 mg, 0.52 mmol) in CH_2Cl_2 (5 mL) and the solution stirred (rt, 96 h). The mixture was quenched with Et_3N (5 mL) and subsequent concentration and flash chromatography (EtOAc/toluene 1:9) yielded thioacetate **35** as a colourless oil (136 mg, 71%), $[\alpha]_D = -8.1$ (*c* 1, $CHCl_3$). ^{1}H NMR (500 MHz): δ 2.04, 2.05, 2.08 (3 × s, 9H, CH_3CO), 2.37 (s, CH_3COS), 3.97 (dd, $J_{2,3}$ 10.0, $J_{3,4}$ 9.9, H3), 3.99 (ddd, $J_{4,5}$ 10.9, $J_{5,6}$ 2.5, 5.5, H5), 4.16 (dd, $J_{6,6}$ 12.4, H6), 4.25 (dd, H6), 5.15 (dd, H4), 5.22 (d, $J_{1,2}$ 7.3, H1), 5.30 (dd, H2), 7.16, 8.20 (AA′BB′, 4H, Ar). ^{13}C NMR (125.7 MHz): δ 20.51, 20.55, 20.67 (3 × C, CH_3CO), 30.63 (CH_3COS), 47.39 (C3), 62.11 (C6), 67.09, 69.80, 75.05 (C2,4,5), 99.27 (C1), 116.58, 125.77, 134.46, 161.18 (Ar), 169.08, 169.26, 170.47 (3 × C, C=O), 193.19 (SC=O). HR-MS (FAB) *m/z* 487.2083 [$C_{20}H_{24}NO_{11}S$ $(M+H)^+$ requires 487.2087].

3.14. Phenyl tetra-*O*-acetyl-β-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-acetyl-1,3-dithio-β-D-glucoside 34

NaOMe (10%) in MeOH (5 mL) was added to thioacetate **33** (50 mg, 0.11 mmol) in MeOH (5 mL) and the solution stirred (rt, 10 min). The mixture was quenched with resin (Amberlite IR-120, H^+), filtered and concentrated. The residue was taken up in 80 mM phosphate buffer (pH 6.8, 5 mL) and the D-glucoside **31** (76 mg, 0.22 mmol) and Abg E171A (2 mg) added and the solution kept at 25 °C for 24 h. The solution was concentrated and the residue dissolved in pyridine (5 mL), then Ac_2O (5 mL) was added and the solution stirred (rt, 12 h). The mixture was quenched by the addition of MeOH (5 mL) and concentrated. Standard work-up (CH_2Cl_2) and flash chromatography (EtOAc/petrol 1:4–1:1) gave the disaccharide **34** as a colourless oil (66 mg, 81%), $[\alpha]_D = -11.1$ (*c* 1, $CHCl_3$). Found: C, 51.5; H, 5.7. $C_{32}H_{40}O_{16}S_2$ requires C, 51.5; H, 5.5. ^{1}H NMR (500 MHz): δ 1.98, 2.01, 2.02, 2.06, 2.07, 2.09, 2.16 (7 × s, 21H, CH_3), 2.99 (dd, $J_{2,3}$ 9.8, $J_{3,4}$ 9.9, H3), 3.69–3.71 (m, H5,5′), 4.13, 4.17, 4.25 (3 × m, 4H, H6,6′), 4.61 (d, $J_{1,2}$ 9.8, H1), 4.64 (d, $J_{1',2'}$ 10.3, H1′), 4.85 (dd, $J_{4,5}$ 10.8, H4), 4.89 (dd, $J_{2',3'}$ 9.3, H2′), 5.03–5.07 (m, H2,4′), 5.17 (dd, $J_{3',4'}$ 9.3, H3), 7.28–7.32, 7.46–7.48 (2 × m, Ph). ^{13}C NMR (125.7 MHz): δ 20.40, 20.53, 20.72, 20.95 (CH_3), 52.29 (C3), 61.93, 62.62 (C6,6′), 66.73 (C4), 68.16, 71.73 (C2,4′), 70.03 (C2′), 73.67 (C3′), 75.64, 77.99 (C5,5′), 84.32 (C1′), 87.91 (C1), 128.08, 128.87, 132.44, 132.63 (Ph), 168.67, 169.12, 169.29, 169.44, 170.91, 170.57 (C=O). HR-MS (FAB) *m/z* 745.1832 [$C_{32}H_{41}O_{16}S_2$ $(M+H)^+$ requires 745.1836].

3.15. 4-Nitrophenyl tetra-*O*-acetyl-β-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-acetyl-3-thio-β-D-glucoside 36

According to the procedure described for **34**, **31** (76 mg, 0.22 mmol) and **35** (53 mg, 0.11 mmol) gave the disaccharide **36** as a colourless oil (46 mg, 58%), $[\alpha]_D = -13.1$ (*c* 1, $CHCl_3$). ^1H NMR (600 MHz): δ 1.99, 2.02, 2.03, 2.06, 2.08, 2.11, 2.14 (7 × s, 21H, CH_3), 3.11 (dd, $J_{2,3}$ 10.5, $J_{3,4}$ 10.4, H3), 3.73 (ddd, $J_{4',5'}$ 10.0, $J_{5',6'}$ 2.5, 5.0, H5′), 3.94 (ddd, $J_{4,5}$ 10.7, $J_{5,6}$ 2.4, 5.4, H5), 4.10–4.20, 4.23–4.29 (2 × m, 4H, H6,6′), 4.73 (d, $J_{1',2'}$ 10.2, H1′), 4.93 (dd, $J_{2',3'}$ 10.1, H2′), 4.98 (dd, $J_{3,4}$ 10.7, H4), 5.07 (dd, $J_{3',4'}$ 9.6, H4′), 5.10 (d, $J_{1,2}$ 7.4, H1), 5.20 (dd, H3′), 5.37 (dd, H2), 7.15, 8.20 (AA′BB′, 4H, Ar). ^{13}C NMR (150.8 MHz): δ 20.42, 20.54, 20.64, 20.75 (CH_3), 49.64 (C3), 62.01, 62.29 (C6,6′), 66.42 (C4), 68.17 (C4′), 70.10 (C2′), 72.04 (C2), 73.61 (C3′), 74.90 (C5), 75.69 (C5′), 83.70 (C1′), 99.29 (C1), 116.51, 125.76, 143.16, 161.17 (Ar), 168.44, 169.14, 169.29, 169.38, 170.16, 170.40, 170.55 (C=O). HR-MS (FAB) *m/z* 758.2915 [$C_{32}H_{40}NO_{18}S$ $(M+H)^+$ requires 758.2905].

3.16. Synthesis of the thioacetate 37

(i) *Phenyl 2,3,4-tri-O-acetyl-6-O-methanesulfonyl-1-thio-β-D-glucoside*: Triethylamine (1.0 mL, 7.0 mmol) and MsCl (0.33 mL, 4.2 mmol) were added to phenyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-glucoside[23] (1.4 g, 3.5 mmol) in CH_2Cl_2 (20 mL) and the solution stirred (rt, 1 h). Standard work-up (CH_2Cl_2) and flash chromatography (EtOAc/petrol 1:4) gave the title mesylate as a colourless oil (1.7 g, 93%), $[\alpha]_D = -10.9$ (*c* 1, $CHCl_3$). ^1H NMR (500 MHz): δ 2.03, 2.06, 2.11 (3 × s, 9H, CH_3), 3.03 (s, CH_3SO_2), 3.81 (ddd, $J_{4,5}$ 10.1, $J_{5,6}$ 3.0, 5.0, H5), 4.31 (dd, $J_{6,6}$ 11.5, H6), 4.36 (dd, H6), 4.79 (d, $J_{3,4}$ 10.1, H1), 5.01–5.04 (m, H2,4), 5.27 (dd, $J_{2,3}$ 9.4, $J_{3,4}$ 9.7, H3), 7.27–7.32, 7.47–7.49 (2 × m, Ph). ^{13}C NMR (125.7 MHz): δ 20.46, 20.62 (CH_3), 37.67 (CH_3SO_2), 66.88 (C6), 67.95, 69.74, 73.60, 75.46 (C2,3,4,5), 85.76 (C1), 128.47, 129.06, 131.31, 132.86 (Ph), 169.15, 169.41, 169.99 (3 × C, C=O). HR-MS (FAB) *m/z* 477.0862 [$C_{19}H_{25}O_{10}S_2$ $(M+H)^+$ requires 477.0899].

(ii) *Phenyl 2,3,4-tri-O-acetyl-6-S-acetyl-1,6-dithio-β-D-glucoside* **37**: Potassium thioacetate (800 mg, 7.0 mmol) was added to the above mesylate (1.6 g, 3.4 mmol) in DMF (15 mL) and the solution stirred (50 °C, 18 h). Concentration of the mixture, followed by a standard work-up (EtOAc) and flash chromatography (EtOAc/petrol 1:4), gave the thioacetate **37** as a colourless oil (1.4 g, 91%), $[\alpha]_D = -6.0$ (*c* 1, $CHCl_3$). Found: C, 52.4; H, 5.6. $C_{20}H_{24}O_8S_2$ requires C, 52.5; H, 5.5. ^1H NMR (300 MHz): δ 1.98, 2.06, 2.09 (3 × s, 9H, CH_3CO), 2.35 (s, CH_3COS), 3.09 (dd, $J_{5,6}$ 6.8, $J_{6,6}$ 14.4, H6), 3.25 (dd, $J_{5,6}$ 3.0, H6), 3.64 (ddd, $J_{4,5}$ 9.8, H5), 4.65 (d, $J_{1,2}$ 10.0, H1), 4.89–4.95 (m, H2,4), 5.17 (dd, $J_{2,3}$ 9.3, $J_{3,4}$ 9.5, H3), 7.31–7.35, 7.46–7.49 (2 × m, Ph). ^{13}C NMR (75.5 MHz): δ 20.63, 20.69 (CH_3CO), 30.19 (C6), 30.37 (CH_3COS), 69.85, 70.19, 73.83, 76.91 (C2,3,4,5), 85.46 (C1), 128.41, 128.89, 131.41, 133.27 (Ph), 169.24, 169.70, 170.15 (3 × C, C=O), 194.66 (SC=O). HR-MS (FAB) *m/z* 457.0989 [$C_{20}H_{25}O_8S_2$ $(M+H)^+$ requires 457.0990].

3.17. Phenyl tetra-*O*-acetyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-acetyl-1,6-dithio-β-D-glucoside

According to the procedure described for **34**, **31** (76 mg, 0.22 mmol) and **37** (50 mg, 0.11 mmol) gave the title disaccharide as a colourless oil (12 mg, 15%), $[\alpha]_D = -8.4$ (*c* 1, $CHCl_3$). ^1H NMR (600 MHz): δ 1.98, 2.00, 2.01, 2.03, 2.05, 2.08, 2.09 (7 × s, 21H, CH_3), 2.80 (dd, $J_{5,6}$ 2.9, $J_{6,6}$ 14.0, H6), 2.87 (dd, $J_{5,6}$ 8.6, H6), 3.66 (ddd, $J_{4',5'}$ 10.0, $J_{5',6'}$ 3.5, 4.3, H5′), 3.74 (ddd, $J_{4,5}$ 9.7, H5), 4.13–4.15 (m, 2H, H6′), 4.61, 4.76 (2d, H1,1′), 4.90 (dd, $J_{3,4}$ 9.7, H4), 4.95–4.99 (m, 2H, H2,2′), 5.05 (dd, $J_{3',4'}$ 10.0, H4′), 5.16 (dd, H3′), 5.21 (dd, H3), 7.29–7.35, 7.51–7.54 (2 × m, Ph). ^{13}C NMR (150.8 MHz): δ 20.56, 20.58, 20.65, 20.67, 20.73, 20.75 (CH_3), 31.24 (C6), 62.01 (C6′), 68.25, (C4′), 70.01, 70.16 (C2,2′), 71.45 (C4), 73.76, 73.77 (C3,3′), 75.94 (C5′), 78.21 (C5), 83.26, 85.83 (C1,1′), 128.30, 129.11, 131.98, 132.53 (Ph), 169.29, 169.36, 169.43, 169.58, 170.10, 170.13, 170.59 (C=O). HR-MS (FAB) *m/z* 745.1840 [$C_{32}H_{41}O_{16}S_2$ $(M+H)^+$ requires 745.1836].

3.18. Phenyl 3,4,6-tri-*O*-acetyl-2-*S*-acetyl-1,2-dithio-β-D-glucoside 38

Boron trifluoride diethyl etherate (10 μL) was added to tetra-*O*-acetyl-2-*S*-acetyl-2-thio-β-D-glucopyranose[24] (220 mg, 0.54 mmol) and PhSH (0.10 mL, 0.76 mmol) in CH_2Cl_2 (10 mL) and the solution stirred (rt, 24 h). Triethylamine (5 mL) was added and subsequent concentration of the mixture and flash chromatography (EtOAc/petrol 1:9) yielded the thioacetate **38** as a colourless oil (217 mg, 88%), $[\alpha]_D = +1.1$ (*c* 1, $CHCl_3$). ^1H NMR (500 MHz): δ 1.98, 1.99, 2.06 (3 × s, 9H, CH_3CO), 2.33 (s, CH_3COS), 3.55 (dd, $J_{2,3} \approx J_{3,4}$ 11.0, H2), 3.78 (dd, $J_{4,5}$ 9.3, $J_{5,6}$ 2.4, 5.5, H5), 4.14 (dd, $J_{6,6}$ 12.0, H6), 4.23 (dd, H6), 4.95 (d, $J_{1,2}$ 10.9, H1), 4.99 (dd, $J_{3,4}$ 9.1, H4), 5.30 (dd, H3), 7.28–7.31, 7.48–7.50 (2 × m, Ph). ^{13}C NMR (75.5 MHz): δ 20.51, 20.54, 20.67 (3 × C, CH_3CO), 30.66 (CH_3COS), 47.92 (C2), 62.27 (C6), 69.38, 72.22, 75.56 (C3,4,5), 86.36 (C1), 128.14, 128.87, 132.18, 132.75 (Ph), 169.45, 169.96, 170.53 (3 × C, C=O), 192.82 (SC=O). HR-MS (FAB) *m/z* 457.0969 [$C_{20}H_{25}O_8S_2$ $(M+H)^+$ requires 457.0990].

3.19. Attempted synthesis of the thioacetate 43

(i) *Methyl (2′S,3′S)-2-O-acetyl-6-O-benzyl-3,4-O-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-mannoside* **45**: Bis(tributyltin) oxide (4.8 mL, 9.3 mmol) was added to methyl (2′*S*,3′*S*)-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-mannoside[25] (2.4 g, 7.8 mmol) in PhMe (150 mL) and the solution heated at reflux to azeotropically remove H_2O (24 h). Benzyl bromide (1.30 mL, 10.9 mmol) was then added and the solution refluxed (6 h). Concentration of the mixture and flash chromatography (EtOAc/petrol 1:4) gave alcohol **44** (2.1 g, 74%) as an oil. A small portion in pyridine (5 mL) was treated with Ac_2O (5 mL) and the solution stirred (rt, 3 h). The mixture was quenched with MeOH (5 mL) and subsequent concentration, followed by a standard work-up (EtOAc) and flash chromatography (EtOAc/petrol

1:9), to furnish acetate **45** as a colourless oil, $[\alpha]_D = +106$ (*c* 1, $CHCl_3$). ^1H NMR (500 MHz): δ 1.24, 1.26 (2 × s, 6H, CH_3), 2.13 (s, CH_3CO), 3.17, 3.25, 3.37 (3 × s, 9H, OCH_3), 3.75 (m, 2H, H6), 3.89 (ddd, $J_{4,5}$ 9.9, $J_{5,6}$ 2.7, 3.7, H5), 4.06 (dd, $J_{3,4}$ 10.2, H4), 4.13 (dd, $J_{2,3}$ 3.3, H3), 4.57, 4.65 (AB, *J* 12.0, CH_2Ph), 4.73 (d, $J_{1,2}$ 1.5, H1), 5.03 (dd, H2), 7.24–7.28, 7.30–7.35 (2 × m, Ph). ^{13}C NMR (125.7 MHz): δ 17.61, 17.74 (2 × C, CH_3), 21.12 (*C*H_3CO), 47.78, 47.99, 54.89 (3 × C, OCH_3), 63.45, 66.04, 70.18, 70.54 (C2,3,4,5), 68.43 (C6), 73.41 (*C*H_2Ph), 98.93 (C1), 99.72, 100.14 (C2′,3′), 127.40, 128.19, 138.30 (Ph), 170.65 (C═O). HR-MS (FAB) *m*/*z* 441.2120 $[C_{22}H_{33}O_9\ (M+H)^+$ requires 441.2124].

(ii) *Methyl (2′S,3′S)-6-O-benzyl-3,4-O-(2′,3′-dimethoxybutane-2′,3′-diyl)-2-O-trifluoromethanesulfonyl-α-D-mannoside*: Trifluoromethanesulfonic anhydride (0.76 mL, 4.5 mmol) was added to alcohol **44** (1.6 g, 4.1 mmol) and pyridine (0.67 mL, 8.2 mmol) in CH_2Cl_2 at −30 °C and the solution stirred and allowed to warm to room temperature (30 min). The mixture was quenched by the addition of saturated $NaHCO_3$ solution (5 mL) and a standard work-up (CH_2Cl_2) to give a yellow oil, presumably the title triflate (2.2 g), which was used without purification.

(iii) *Methyl (2′S,3′S)-2-S-acetyl-6-O-benzyl-3,4-O-(2′,3′-dimethoxybutane-2′,3′-diyl)-2-thio-α-D-glucoside* **46**: Potassium thioacetate (1.4 g, 12 mmol) was added to the above triflate (2.2 g) in DMF (30 mL) and the solution stirred (40 °C, 4 d). Concentration of the mixture, followed by a standard work-up (EtOAc) and flash chromatography (EtOAc/petrol 1:9), furnished thioacetate **46** as a colourless oil (1.7 g, 88%), $[\alpha]_D = +186$ (*c* 1, $CHCl_3$). ^1H NMR (600 MHz): δ 1.25, 1.27 (2 × s, 6H, CH_3), 2.34 (s, CH_3CO), 3.18, 3.24, 3.34 (3 × s, 9H, OCH_3), 3.73 (m, 2H, H6), 3.83 (dd, $J_{3,4}$ 9.2,$J_{4,5}$ 10.3, H4), 3.86 (dd, $J_{1,2}$ 3.3, $J_{2,3}$ 11.6, H2), 3.90 (ddd, $J_{5,6}$ 1.9, 5.1, H5), 3.94 (dd, H3), 4.59 (AB, *J* 12.1, CH_2Ph), 4.78 (d, H1), 7.27–7.29, 7.31–7.35 (2 × m, Ph). ^{13}C NMR (150.8 MHz): δ 17.58, 17.66 (2 × C, CH_3), 30.47 (*C*H_3CO), 46.04 (C2), 47.89, 47.94, 55.24 (3 × C, OCH_3), 66.36 (C3), 68.09 (C4), 68.19 (C6), 69.46 (C5), 73.52 (*C*H_2Ph), 99.58 (C1), 99.80, 100.14 (C2′,3′), 127.46, 127.48, 128.25, 138.16 (Ph), 194.35 (SC═O). HR-MS (FAB) *m*/*z* 455.1724 $[C_{22}H_{31}O_8S\ (M-H)^+$ requires 455.1739].

(iv) *Methyl 3,4-di-O-acetyl-2-S-acetyl-6-O-benzyl-2-thio-α-D-glucoside* **47**: Thioacetate **46** (700 mg) in CF_3COOH/H_2O (1:19, 5 mL) was stirred (rt, 10 min). Concentration of the solution left a brown residue that was dissolved in pyridine (10 mL); Ac_2O (5 mL) was added and the solution stirred (rt, 2 h). The mixture was quenched with MeOH (5 mL) and subsequent concentration, followed by a standard work-up (EtOAc) and flash chromatography (EtOAc/petrol 1:4), to give the triacetate **47** as a colourless oil (590 mg, 90%), $[\alpha]_D = +66.9$ (*c* 1, $CHCl_3$). ^1H NMR (600 MHz): δ 1.89, 1.97 (2 × s, 6H, CH_3CO), 2.31 (s, CH_3COS), 3.38 (s, OCH_3), 3.53 (dd, $J_{5,6}$ 4.4, $J_{6,6}$ 10.3, H6), 3.56 (dd, $J_{5,6}$ 3.0, H6), 3.94 (m, H2,5), 4.50, 4.59 (AB, *J* 12.0, CH_2Ph), 4.76 (d, $J_{1,2}$ 3.3, H1), 5.14 (dd, $J_{2,3}$ 9.2, $J_{3,4}$ 9.7, H3), 5.30 (dd, $J_{4,5}$ 9.4, H4), 7.27–7.30, 7.31–7.34 (2 × m, Ph). ^{13}C NMR (150.8 MHz): δ 20.60, 20.63 (2 × C, *C*H_3CO), 30.33 (*C*H_3COS), 46.42 (C2), 55.51 (OCH_3), 68.42 (C6), 68.83, 70.18, 70.23 (C3,4,5), 73.54 (*C*H_2Ph), 99.41 (C1), 127.71, 127.87, 128.35, 137.68 (Ph), 169.55, 170.30 (2 × C, C═O), 193.62 (SC═O). HR-MS (FAB) *m*/*z* 427.1408 $[C_{20}H_{27}O_8S\ (M-H)^+$ requires 427.1426].

(v) *Methyl 3,4,6-tri-O-acetyl-2-S-acetyl-2-thio-α-D-glucoside* **48**: Concd H_2SO_4 (one drop) was added to the triacetate **47** (550 mg) in Ac_2O (10 mL) at 0 °C and the mixture allowed to warm to room temperature (20 min). The mixture was poured onto ice/water and standard work-up (CH_2Cl_2) and flash chromatography (EtOAc/petrol 1:4) gave the tetraacetate **48** as a colourless oil (430 mg, 73%). The ^1H NMR spectrum was consistent with that reported.[26]

3.20. Synthesis of thioacetate 53

(i) *Methyl (2′S,3′S)-2-O-acetyl-3,4-O-(2′,3′-dimethoxybutane-2′,3′-diyl)-6-O-(4-nitrobenzyl)-α-D-mannoside* **50**: According to the procedure described for **45** but using 4-nitrobenzyl bromide (2.40 g, 10.9 mmol) instead of benzyl bromide, alcohol **49** (2.4 g, 77%) was obtained as a colourless oil. A small portion of this was converted into acetate **50**, $[\alpha]_D = +107$ (*c* 1, $CHCl_3$): ^1H NMR (600 MHz): δ 1.24 (s, 6H, CH_3), 2.11 (s, CH_3CO), 3.17, 3.24, 3.35 (3 × s, 9H, OCH_3), 3.79 (m, 2H, H6), 3.91 (ddd, $J_{4,5}$ 10.1, $J_{5,6}$ 3.7, H5), 4.04 (dd, $J_{3,4}$ 10.1, H4), 4.14 (dd, $J_{2,3}$ 3.4, H3), 4.67, 4.74 (AB, *J* 13.5, CH_2Ar), 4.71 (d, $J_{1,2}$ 1.4, H1), 5.03 (dd, H2), 7.50, 8.18 (AA′BB′, 4H, Ar). ^{13}C NMR (150.8 MHz): δ 17.57, 17.71 (2 × C, CH_3), 21.11 (*C*H_3CO), 47.78, 47.99, 54.99 (3 × C, OCH_3), 63.41, 65.90, 70.11, 70.42 (C2,3,4,5), 69.09 (C6), 72.08 (*C*H_2Ar), 98.97 (C1), 99.77, 100.14 (C2′,3′), 123.46, 127.26, 145.99, 147.21 (Ar), 170.47 (C═O). HR-MS (FAB) *m*/*z* 484.1822 $[C_{22}H_{30}NO_{11}\ (M-H)^+$ requires 484.1819].

(ii) *Methyl (2′S,3′S)-3,4-O-(2′,3′-dimethoxybutane-2′,3′-diyl)-6-O-(4-nitrobenzyl)-2-O-trifluoromethanesulfonyl-α-D-mannoside*: According to the procedure for alcohol **44**, alcohol **49** (1.8 g, 4.0 mmol) was converted into the title triflate (2.3 g), obtained as a yellow oil, which was used without purification.

(iii) *Methyl (2′S,3′S)-2-S-acetyl-3,4-O-(2′,3′-dimethoxybutane-2′,3′-diyl)-6-O-(4-nitrobenzyl)-2-thio-α-D-glucoside* **51**: According to the procedure described for **46** but using the above triflate (2.3 g), the thioacetate **51** was obtained as a colourless oil (1.8 g, 88%), $[\alpha]_D = +152$ (*c* 1, $CHCl_3$). ^1H NMR (500 MHz): δ 1.27 (s, 6H, CH_3), 2.33 (s, CH_3CO), 3.18, 3.24, 3.34 (3 × s, 9H, OCH_3), 3.75 (dd, $J_{5,6}$ 2.0, $J_{6,6}$ 10.9, H6), 3.80 (dd, $J_{5,6}$ 4.6, H6), 3.84 (dd, $J_{3,4}$ 9.9, $J_{4,5}$ 10.0, H4), 3.86 (dd, $J_{1,2}$ 3.3, $J_{2,3}$ 9.2, H2), 3.92 (ddd, H5), 3.95 (dd, H3), 4.68, 4.72 (AB, *J* 13.5, CH_2Ar), 4.77 (d, H1), 7.50, 8.19 (AA′BB′, 4H, Ar). ^{13}C NMR (125.7 MHz): δ 17.55, 17.62 (2 × C, CH_3), 30.46 (*C*H_3CO), 45.96 (C2), 47.84, 47.95, 55.28 (3 × C, OCH_3), 66.21 (C3), 68.01 (C4), 68.81 (C6), 69.43 (C5), 72.22 (*C*H_2Ar), 99.62 (C1), 99.86, 100.14 (C2′,3′), 123.53, 127.32, 145.86,

147.24 (Ar), 194.38 (C=O). HR-MS (FAB) *m/z* 500.1556 [$C_{22}H_{30}NO_{11}S$ $(M-H)^+$ requires 500.1590].

(iv) *Methyl 3,4-di-O-acetyl-2-S-acetyl-6-O-(4-nitrobenzyl)-2-thio-α-D-glucoside* **52**: According to the procedure described for the preparation of **47** but using **51** (700 mg), triacetate **52** was obtained as a colourless oil (580 mg, 89%), $[\alpha]_D = +91.4$. ^{1}H NMR (600 MHz): δ 1.96, 1.98 (2 × s, 6H, CH_3CO), 2.33 (s, CH_3COS), 3.39 (s, OCH_3), 3.59 (dd, $J_{5,6}$ 4.6, $J_{6,6}$ 10.9, H6), 3.65 (dd, $J_{5,6}$ 2.5, H6), 3.94 (dd, $J_{1,2}$ 3.4, $J_{2,3}$ 11.6, H2), 3.97 (ddd, $J_{4,5}$ 9.2, H5), 4.60, 4.69 (AB, J 13.1, CH_2Ar), 4.76 (d, H1), 5.19 (dd, $J_{3,4}$ 9.4, H3), 5.34 (dd, H4), 7.51, 8.21 (AA′BB′, 4H, Ar). ^{13}C NMR (150.8 MHz): δ 20.61, 20.67 (2 × C, CH_3CO), 30.35 (CH_3COS), 46.41 (C2), 55.60 (OCH_3), 68.87, 70.01, 70.05 (C3,4,5), 69.25 (C6), 72.40 (CH_2Ar), 99.49 (C1), 123.61, 127.78, 145.38, 147.43 (Ar), 169.58, 170.23 (2 × C, C=O), 193.65 (SC=O). HR-MS (FAB) *m/z* 472.1253 [$C_{20}H_{26}NO_{10}S$ $(M+H)^+$ requires 472.1277].

(v) *1,3,4-Tri-O-acetyl-2-S-acetyl-6-O-(4-nitrobenzyl)-2-thio-α-D-glucose* **53**: Concd H_2SO_4 (one drop) was added to triacetate **52** (580 mg) in Ac_2O (1 mL) and AcOH (2 mL) at 0 °C and the solution allowed to warm to room temperature (2 h). The solution was poured onto ice. Standard work-up (EtOAc) and flash chromatography (EtOAc/petrol 3:7) furnished the tetraacetate **53** as a colourless oil (480 mg, 78%), $[\alpha]_D = +95.7$ (*c* 1, $CHCl_3$). Found: C, 52.4; H, 4.7. $C_{21}H_{23}NO_{10}S$ requires C, 52.4; H, 4.8. ^{1}H NMR (600 MHz): δ 1.94, 1.97, 2.10 (3 × s, 9H, CH_3CO), 2.29 (s, CH_3COS), 3.55 (dd, $J_{5,6}$ 4.0, $J_{6,6}$ 11.1, H6), 3.60 (dd, $J_{5,6}$ 2.6, H6), 3.94 (dd, $J_{1,2}$ 3.5, $J_{2,3}$ 11.6, H2), 3.97 (ddd, $J_{4,5}$ 9.3, H5), 4.54, 4.62 (AB, J 16.7, CH_2Ar 5.24 (dd, $J_{3,4}$ 9.2, H3), 5.30 (dd, H4), 6.15 (d, H1), 7.45, 8.15 (AA′BB′, 4H, Ar). ^{13}C NMR (150.8 MHz): δ 20.44, 20.47, 20.57 (3 × C, CH_3CO), 30.24 (CH_3COS), 45.29 (C2), 68.71 (C6), 69.14, 69.35, 71.09 (C3,4,5), 72.30 (CH_2Ar), 91.20 (C1), 123.41, 127.74, 145.20, 147.26 (Ar), 168.45, 169.25, 170.12 (3 × C, C=O), 192.58 (SC=O). HR-MS (FAB) *m/z* 498.1064 [$C_{21}H_{24}NO_{10}S$ $(M+H)^+$ requires 498.1070].

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