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Two Straightforward Strategies for the Synthesis of Thiodisaccharides with a Furanose Unit as the Nonreducing End

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Thiodisaccharides having a 1-thiopentofuranose nonreducing end were synthesized by two routes starting from per-*O*-acylaldofuranoses with *arabino*, *ribo*, and *xylo* configurations. These glycosyl donors were converted into *S*-glycosyl isothiourea derivatives as precursors of 1-thiofuranose units, which were generated in situ and trapped by a sugar enone to produce, by Michael addition, the thioglycosidic linkage. Alternatively, the MoO_2Cl_2-promoted glycosylation of the thiol group of 6-thiosugar derivatives by per-*O*-acylfuranose led to thiodisaccharides with exclusive 1,2-*trans* diastereocontrol.

Introduction

The search for new glycosidase inhibitors and stable sugar mimetics has led to oligosaccharide analogues with the glycosidic oxygen atom substituted by sulfur or other heteroatoms. The *S*-glycosides are carbohydrate mimetics that are usually resistant to metabolic processes.[1,2] The interglycosidic sulfur atom in *S*-glycosides may act as a hydrogen-bond acceptor, which, as in the natural substrate, could play an important role in ligand binding and especially in the case of enzyme inhibitors and enzyme-resistant scaffolds.[3] Therefore, thiooligosaccharides have attracted considerable attention, and a number of approaches to their synthesis have been reported.[2,4,5] However, this large body of information refers mainly to thiooligosaccharides constituted by pyranose units, whereas just a very few examples were found of thiodisaccharides having a furanose moiety as a constituent. For instance, 1,2:5,6-di-*O*-isopropylidene-3-*O*-trifluoromethylsulfonyl-α-D-gulofuranose was converted into the *S*-α-sialyl(2→3)-3-thiogalactofuranose derivative, which on deprotection led to the galactopyranose isomer as the major product.[6] The synthesis of a glyconucleoside containing a ribofuranosyl residue linked to the thiol group of 3′-thiothymine, has recently been reported.[7] Heteroatom analogues of oligosaccharides of galactofuranose having the ring oxygen atom replaced by sulfur have been prepared.[8]

The interest in furanose sugars arises from the fact that they are widely distributed in nature. Ribofuranose occurs in nucleic acids and arabinofuranose is found in soil bacteria, fungi, and plants.[9] Arabinose and galactose in the furanose form are constituents of polysaccharides of mycobacteria. Inhibition of the enzymes that assemble these polyfuranosides prevents proliferation of pathogenic mycobacteria.[10] Recently, thioimidoyl α-L-arabinofuranosides have been described as the first potent inhibitors of an arabinofuranosidase.[11] In view of the previous considerations and in connection with our studies on the synthesis and inhibitory activity of *S*-linked saccharides,[12–14] we explored the construction of thiodisaccharides containing a pentofuranose unit as potential inhibitors of pentofuranosidases. We report here two successful approaches for the synthesis of such thiodisaccharides starting from readily available per-*O*-acylated pentofuranoses.

Results and Discussion

The Michael addition of thiosugars to carbohydrate-derived enones constitutes a direct procedure for the construction of an *S*-linkage to the β carbon of the α,β-unsaturated carbonyl group of the enone.[12,14] Witczak[15] and Thiem[16] employed this methodology for the synthesis of a number of thiodisaccharides starting from levoglucosenone, or other enones, and 1-thiopyranoses as *S*-glycosyl donors. To apply this procedure, we tried unsuccessfully to prepare tri-*O*-benzoyl-1-thio-D-arabinofuranose by the methods described for pyranoses,[17] as the disulfide was mainly produced. The tendency of thiofuranoses to undergo self-condensation and other side reactions has been reported.[6] However, we have described that 1-thiosugars generated in situ from *S*-glycosyl isothiourea derivatives can be trapped by a sugar enone to yield the corresponding thiodisaccharide.[12] Glycosyl isothiourea derivatives may be readily prepared start-

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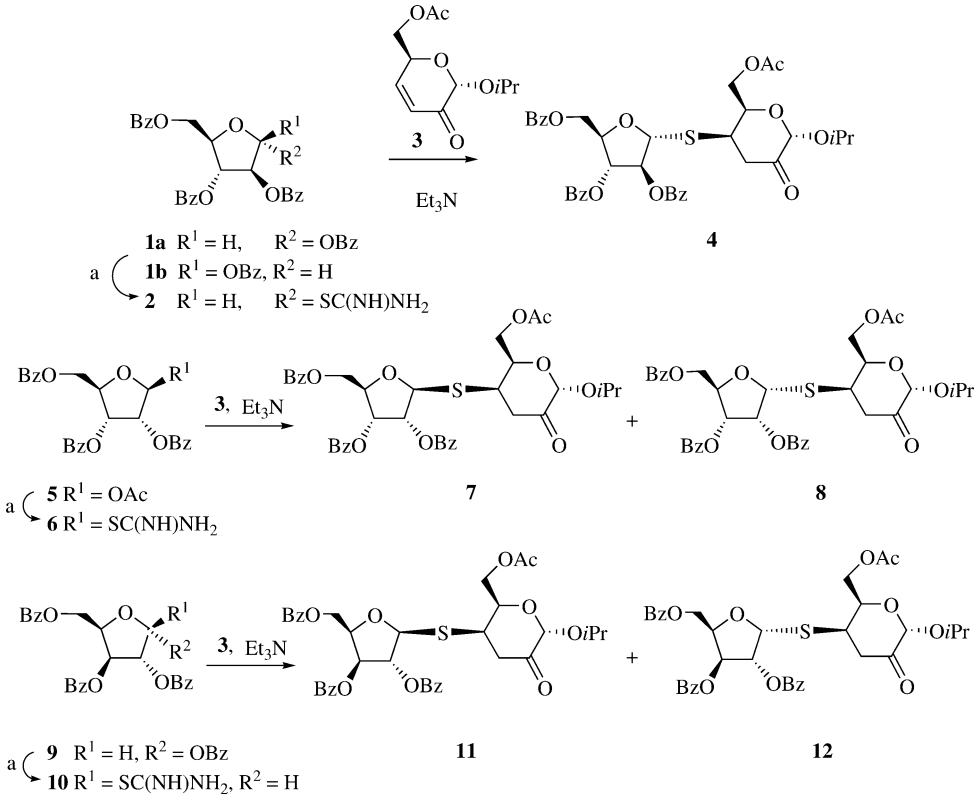
ing from 1,2-*trans*-glycopyranosyl acetates.[18] As 1,2,3,5-tetra-*O*-benzoyl-α-D-arabinofuranose (**1a**) is easily obtained by direct benzoylation of D-arabinose at high temperature,[19] we studied the glycosylation of this compound with thiourea by using $BF_3{\cdot}OEt_2$ as a catalyst. Thus, a solution of **1a** and thiourea in acetonitrile was heated under reflux in the presence of $BF_3{\cdot}OEt_2$ to afford α-*S*-glycosyl isothiourea **2** (Scheme 1). In the NMR spectra of **2**, the C-1 signal showed a strong upfield shift (relative to that of **1a**) as observed for thioglycosylation of per-*O*-acylated furanoses[11,13] and the $J_{1,2}$ value (<1 Hz) indicated the α configuration for the anomeric center (1,2-*trans* thioglycoside).[19,20] As benzoylation of arabinose also provides β anomer **1b**, the reaction of this compound with thiourea was conducted under the conditions employed for isomer **1a**; *S*-glycosyl isothiourea **2** was obtained in good yield. From these results we can conclude that the Ibatullin reaction can be applied to benzoylated furanoses, even when they possess the 1,2-*cis* configuration. Therefore, the mixture of anomers **1a**, **1b** may be employed for the synthesis of **2**.

Compound **2**, without isolation, was treated with triethylamine (Et_3N) to promote the formation of the 1-thioaldose derivative as the thioglycosyl donor.[18] Addition of 2-propyl 6-*O*-acetyl-2,3-dideoxy-α-D-*glycero*-hex-3-enopyranosid-2-ulose (**3**) to the reaction mixture led to the formation of thioulose **4**. The Michael addition of the nucleophilic 1-thioaldose, released from **2**, to enone **3** was highly diastereoselective and took place from the face of the pyranone opposite the axially oriented anomeric substituent. The configuration of the new stereocenter at C-4, which was generated during the conjugate addition, was established as *R* on the basis of the ^1H NMR spectrum of **4**. As 4-H is coupled with the adjacent methylene protons, the small coupling constant values ($J_{3ax,4}$ = 4.7 Hz, $J_{3eq,4}$ = 1.8 Hz) indicate that 4-H is equatorially oriented. Furthermore, the small value for the coupling between 1′-H and 2′-H ($J_{1',2'}$ < 1 Hz) is indicative of an 1′,2′-*trans* stereochemistry[11,13] (α anomeric configuration) for the furanose.

Michael addition to sugar enone **3** was studied for other per-*O*-acylated furanoses. Thus, commercially available 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**5**) was treated with thiourea in the presence of $BF_3{\cdot}OEt_2$ to give *S*-glycosyl isothiourea **6**. The ^1H NMR spectrum of **6** showed a $J_{1,2}$ value (3.7 Hz) that suggested the β configuration for the anomeric center. However, the Et_3N-promoted reaction of **6** with **3** led to two products, which were isolated by column chromatography. The ^1H NMR spectra of both **7** and **8** exhibited small values for $J_{3ax,4}$ and $J_{3eq,4}$, which is indicative of, as in the case of **4**, the α-D-*threo* configuration of the hexopyranosid-2-ulose moiety. The substantial differences observed for the signals of the anomeric protons of the 1-thiofuranose unit of **7** and **8** suggested that anomerization took place during the reaction. The anomeric configuration of ribofuranosides was tentatively assigned on the basis of the relative chemical shifts and coupling constants of the anomeric proton.[21] Thus, **7** showed the 1-H resonance ($J_{1',2'}$ = 3.7 Hz) at higher field than that of **8** ($J_{1',2'}$ = 6.0 Hz) and was assigned as the β anomer. These assign-



Scheme 1. Reaction conditions: (a) $(NH_2)_2CS$, $BF_3{\cdot}OEt_2$, CH_3CN, reflux.

ments were confirmed by NOE experiments performed on thiodisaccharides **17** and **19**, which are the respective products of carbonyl reduction from **7** and **8**, as discussed below.

β-*S*-Glycosyl isothiourea **10** was prepared from commercial per-*O*-benzoyl-D-xylofuranose (**9**). The corresponding 1-thiosugar derivative, released from **10** with Et_3N, was coupled to enone **3** to give (similar to the ribofuranose series) the anomeric mixture of thiodisaccharides **11** and **12**. The ratio **11/12** was about 1.4:1 according to the ^1H NMR spectrum, and this mixture could not be separated by column chromatography.

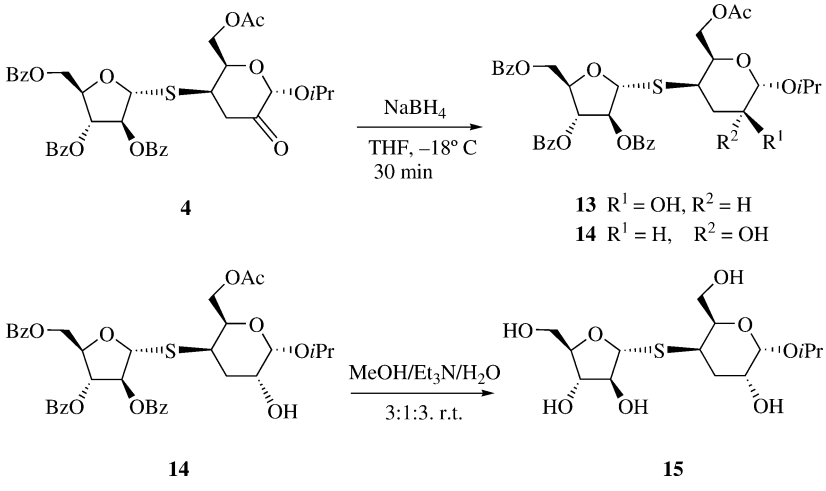
It is worthy to mention that the thiodisaccharides obtained by the methodology described above were difficult to isolate in pure form, as they were accompanied by enone **3**. During column chromatography, the silica gel seems to catalyze the retro-Michael reaction. In fact, the proportion of **3** increased when **4** was maintained in contact with the silica gel for longer periods.

The carbonyl functionality of the 4-*S*-Ara*f*-4-thio-α-D-*threo*-hexopyranosid-2-ulose derivative (**4**) was reduced with sodium borohydride to afford epimeric thiodisaccharides **13** and **14** (Scheme 2). The major diastereoisomer had the α-D-*xylo* configuration (**14**) for the hexopyranose moiety, as deduced from the NMR spectra. The proton bonded to the new stereocenter (2-H) showed small coupling constant values with 1-H ($J_{1,2}$ = 3.8 Hz) and 3-Heq ($J_{2,3eq}$ = 3.9 Hz) as expected for a *gauche* relationship of 2-H with these adjacent protons. Furthermore, the large coupling value between 2-H and 3-Hax ($J_{2,3ax}$ = 12.8 Hz) confirmed that the HO group at C-2 is equatorially disposed. In contrast, in the ^1H NMR of epimer **13**, the coupling of 2-H with 1-H, 3-Ha and 3-Hb were all small ($J_{1,2} < 1$ Hz, $J_{2,3a}$ = 3.0 Hz, $J_{2,3b}$ = 3.9 Hz) in agreement with an axial orientation for HO-2 (α-D-*lyxo* configuration).

Removal of the ester protecting groups of **14** was accomplished with MeOH/Et_3N/H_2O (3:1:3) to give the free isopropyl glycoside of thiodisaccharide **15**. This product was deionized by elution through a column filled with mixed-bed ion-exchange resin, followed by filtration through a reverse phase minicolumn. The first-order ^1H NMR spectrum of **15** was fully assigned by using 2D NMR techniques, and the previous structure assignments were confirmed.

The starting material for the carbonyl reduction–deprotection sequence was 4-*S*-(β-D-ribofuranosyl)-4-thiohex-2-ulose (**7**; Scheme 3). The reduction of the carbonyl group led to a mixture of diastereoisomers **16** and **17**, which were isolated by column chromatography. Isomer **17** possessed the 4-thio-α-D-*xylo* configuration of the hexopyranose, and it was the major product. Hydrolysis of the acetyl and benzoyl groups of **17** afforded free thiodisaccharide **18**. As for the analogues in the *arabino* series (**13**–**15**), the structures of **16**–**18** were established on the basis of the NMR spectroscopic data. In particular, the anomeric configuration was determined by ROESY experiments. A characteristic NOE contact[22] between 1′-H and 4′-H in **17** (not observed for **19**) indicated that these two protons are on the same face of the furanose ring (β configuration). Similarly, the NOE connection between 1′-H and 3′-H in **19** (not detected for **17**) established the α configuration for **19**. These results confirmed the previous assignments for the anomeric configuration of **7** and **8**, which are the respective precursors of **17** and **19**.

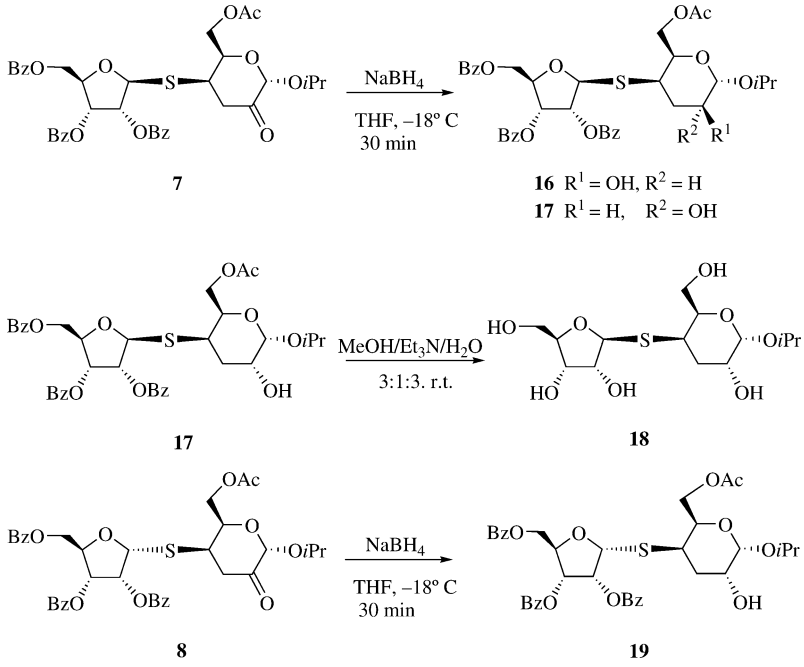
The reduction of the carbonyl group of **4**, **7**, and **8** was diastereoselective and led to the 4-*S*-glycofuranosyl-4-thio-α-D-*xylo*-hexopyranosides (**14**, **17**, and **19**, respectively) as the main products. The ratio for the *xylo*/*lyxo* isomers was ca. 4:1 (from **4** and **7**) and ca. 7:1 (from **8**). The selectivity observed suggests that the approach of the hydride to the C-2 carbonyl is controlled by the axial isopropyl group at the adjacent stereocenter (C-1). The diastereoselectivity in the reduction of **8** was somewhat higher than that determined for **4** and **7**. Thioulose **8** bears, in contrast to **4** and **7**, the 1,2-*cis* stereochemistry of the thiofuranose ring. Hence, the stereochemical course of the reduction seems to be influenced by the anomeric configuration of the thiofuranose. Conformational studies of the thiodisaccharides are in progress. The reduction of glycosylthioulosides with bulkier agents is also under study with the aim to increase the selectivity.



4 **13** R^1 = OH, R^2 = H; **14** R^1 = H, R^2 = OH

14 **15**

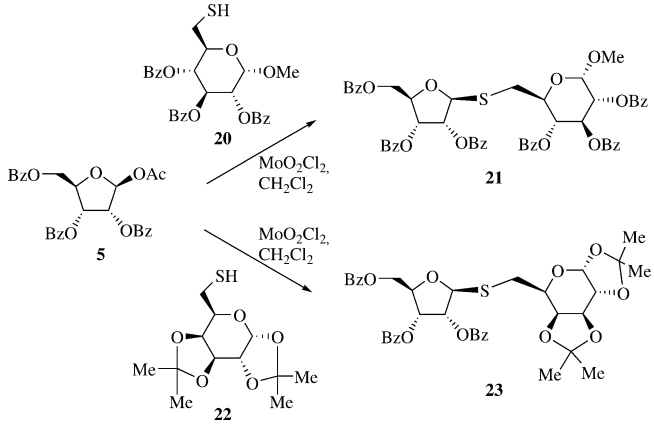
Scheme 2.



7 **16** R^1 = OH, R^2 = H; **17** R^1 = H, R^2 = OH; **17** **18** **8** **19**

Scheme 3.

Moreover, we studied an alternative route for the construction of the *S*-linkage of thiodisaccharides having a furanose unit as the nonreducing end. For this purpose, readily available per-*O*-acyl furanoses were selected as glycosylating agents of the thiol group of a thiosugar. Thus, the glycosylation of the 6-thiol functionality of **20**[23] by per-*O*-acyl-β-D-ribofuranose derivative **5** was conducted as a model reaction (Scheme 4). The glycosylation was unsuccessful when a Lewis acid ($SnCl_4$) was employed as the catalyst. However, MoO_2Cl_2 efficiently promoted the formation of an *S*-linkage between **5** and **20**. This catalyst has recently been reported[24] for the thioglycosylation of per-*O*-acetylated pyranoses. Similar to pyranoses, the thioglycosylation of **5** took place under exclusive diastereocontrol to give the 1,2-*trans*-thioglycoside. The reaction was also applied to thiosugar **22**[25] to afford diastereoselectively the β(1→6)-*S*-linked disaccharide **23**.



20 **21** **5** **22** **23**

Scheme 4.

Conclusions

We have achieved the first two successful routes for the synthesis of thiodisaccharides having a 1-thiopentofuranose as the nonreducing end. One of the strategies employed is based on the Michael addition of a 1-thiofuranose to a sugar enone. The intermediate 1-thiofuranose was produced in situ by treatment of *S*-glycosyl isothiourea derivatives with a base. The conjugate addition to the enone was diastereoselective, but anomerization occurred for ribo- and xylofuranoses. Alternatively, per-*O*-acylfuranoses were employed for glycosylation of the thiol group of 6-thiosugar derivatives. This reaction was successfully promoted by neutral MoO_2Cl_2 to give exclusive 1,2-*trans* diastereocontrol.

Experimental Section

General Information: Melting points were determined with a Fisher-Johns apparatus and are uncorrected. Analytical thin-layer chromatography (TLC) was performed on Silica Gel 60 F254 (Merck) aluminum-supported plates (layer thickness 0.2 mm) with solvent systems given in the text. Visualization of the spots was effected by exposure to UV light and charring with a solution of 5% (v/v) sulfuric acid in EtOH containing 0.5% *p*-anisaldehyde. Column chromatography was carried out with Silica Gel 60 (230–400 mesh, Merck). Optical rotations were measured with a Perkin–Elmer 343 digital polarimeter. Nuclear magnetic resonance (NMR) spectra were recorded with a Bruker AC 200 or with a Bruker AMX 500 instrument. Assignments of ^1H and ^{13}C resonances were assisted by 2D 1H-COSY and HSQC experiments.

2-Propyl 6-*O*-Acetyl-3-deoxy-4-*S*-(2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl)-4-thio-α-D-*threo*-hexopyranosid-2-ulose (4): To a solution of 1,2,3,5-tetra-*O*-benzoyl-β-D-arabinofuranose (**1b**; 140 mg, 0.25 mmol) in anhydrous acetonitrile (5 mL) was added thiourea (21 mg, 0.276 mmol) and $BF_3{\cdot}OEt_2$ (162 μL, 1.29 mmol). The mix-

ture was heated under reflux for 1 h at which point TLC (toluene/EtOAc, 3:1) showed disappearance of the starting material and a spot of $R_f = 0$. Evaporation of the solvent led to α-*S*-glycosyl isothiourea **2** as a syrup. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 9.29, 9.17 (2 s, each 2 H, 2 × NH$_2$), 8.06–7.35 (m, 20 H, Ar*H*), 6.67 (br. s, 1 H, 1-H), 5.74 (br. s, 1 H, 2-H), 5.72 (d, $J_{3,4}$ = 4.8 Hz, 1 H, 3-H), 4.88 (m, $J_{4,5}$ = 3.1 Hz, $J_{4,5'}$ = 4.4 Hz, 1 H, 4-H), 4.74 (dd, $J_{4,5}$ = 3.1 Hz, $J_{5,5'}$ = 12.3 Hz, 1 H, 5-H), 4.70 (dd, $J_{4,5'}$ = 4.4 Hz, $J_{5,5'}$ = 12.3 Hz, 1 H, 5′-H) ppm. ^{13}C NMR (125.7 MHz, [D$_6$]-DMSO): δ = 167.9 [S*C*(NH$_2$)$_2$], 167.1, 165.9, 165.4, 165.2 (Ph*C*O), 135–128 (C-aromatic), 87.8 (C-1), 82.8, 81.8 (C-2, 4), 77.3 (C-3), 63.1 (C-5) ppm.

The original mixture without any further treatment, was cooled to –18 °C and 2-propyl 6-*O*-acetyl-2,3-dideoxy-α-D-*glycero*-hex-3-enopyranosid-2-ulose (**3**; 47 mg, 0.21 mmol) was added. Upon addition of Et$_3$N (289 μL, 2.08 mmol) the mixture was stirred at –18 °C for 3 h. TLC (CH$_2$Cl$_2$/EtOAc, 15:1) revealed the presence of a major product (R_f = 0.75) and a faint spot of unreacted enone **3** (R_f = 0.54). The mixture was concentrated, and the residue was purified by flash chromatography (chloroform/EtOAc, 98:1) to give syrupy thiodisaccharide **4** (85 mg, 57.3%) slightly contaminated with **3**. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.10–7.73 (m, 15 H, Ar*H*), 5.64 (br. s, 1 H, 1′-H), 5.62 (d, $J_{2',3'} \approx 0$ Hz, $J_{3',4'}$ = 5.0 Hz, 1 H, 3′-H), 5.52 (br. s, 1 H, 2′-H), 4.84 (dd, $J_{4',5'a}$ = 3.0 Hz, $J_{5'a,5'b}$ = 11.6 Hz, 1 H, 5′a-H), 4.79–4.76 (m, 2 H, 4′-H, 5-H), 4.76 (br. s, 1 H, 1-H), 4.73 (dd, $J_{4',5'b}$ = 4.6 Hz, $J_{5'a,5'b}$ = 11.6 Hz, 1 H, 5′b-H), 4.39 (dd, $J_{5,6a}$ = 7.0 Hz, $J_{6a,6b}$ = 11.7 Hz, 1 H, 6a-H), 4.36 (dd, $J_{5,6b}$ = 5.2 Hz, $J_{6a,6b}$ = 11.7 Hz, 1 H, 6b-H), 4.01 [m, *J* = 6.2 Hz, 1 H, (CH$_3$)$_2$C*H*O], 3.76 (m, 1 H, 4-H), 3.22 (dd, $J_{3ax,3eq}$ = 14.9 Hz, $J_{3ax,4}$ = 4.7 Hz, 1 H, 3ax-H), 2.94 (dd, $J_{3eq,4}$ = 1.8 Hz, $J_{3ax,3eq}$ = 14.9 Hz, 1 H, 3eq-H), 2.07 (s, 3 H, C*H*$_3$CO), 1.28, 1.19 [2 d, *J* = 6.2 Hz, 6 H, (C*H*$_3$)$_2$CHO] ppm. ^{13}C NMR (125.7 MHz, CDCl$_3$): δ = 199.3 (C-2), 170.5 (CH$_3$*C*O), 166.1, 165.6, 165.4 (Ph*C*O), 133.7, 133.1, 130.0, 129.9, 129.8 (× 2), 128.6, 128.5, 128.4 (C-aromatic), 98.0 (C-1), 89.6 (C-1′), 83.3 (C-2′), 81.0 (C-4′), 77.7 (C-3′), 71.7 [(CH$_3$)$_2$*C*HO], 68.5 (C-5), 64.4 (C-6), 63.2 (C-5′), 48.5 (C-4), 44.2 (C-3), 23.3, 21.8 [(*C*H$_3$)$_2$CHO], 20.7 (*C*H$_3$CO) ppm.

The procedure described above was also applied to 1,2,3,5-tetra-*O*-benzoyl-α-D-arabinofuranose (**1a**) to afford **4** (93 mg, 62.7%).

2-Propyl 6-*O*-Acetyl-3-deoxy-4-*S*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-4-thio-α-D-*threo*-hexopyranosid-2-ulose (7) and α-D-Ribofuranosyl Analogue 8: A solution of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**5**; 300 mg, 0.595 mmol), thiourea (50 mg, 0.658 mmol) and BF$_3$·OEt$_2$ (78 μL, 0.625 mmol) in anhydrous acetonitrile (10 mL) was stirred under reflux for 1 h to afford *S*-glycosyl isothiourea derivative **6**. ^{1}H NMR (200 MHz, [D$_6$]DMSO): δ = 9.27, 9.22 (2 s, each 2 H, 2 × NH$_2$), 8.07–7.45 (m, 15 H, Ar*H*), 6.42 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 5.94 (m, 2 H, 2-H, 3-H), 4.91 (m, $J_{4,5}$ = 3.5 Hz, $J_{3,4}$ = $J_{4,5'}$ = 4.0 Hz, 1 H, 4-H), 4.69 (dd, $J_{4,5}$ = 3.5 Hz, $J_{5,5'}$ = 11.9 Hz, 1 H, 5-H), 4.59 (dd, $J_{4,5'}$ = 4.0 Hz, $J_{5,5'}$ = 11.9 Hz, 1 H, 5′-H) ppm. ^{13}C NMR (50 MHz, [D$_6$]DMSO): δ = 166.8 [S*C*(NH$_2$)$_2$], 165.6, 164.9, 164.6 (Ph*C*O), 134.4–128.2 (C-aromatic), 84.3 (C-1), 81.5, 74.3, 71.8 (C-2, C-3, C-4), 63.8 (C-5) ppm.

An acetonitrile solution containing **6** was cooled to –18 °C and enone **3** (100 mg, 0.439 mmol) and Et$_3$N (220 μL, 1.58 mmol) were added. After 2.5 h, the mixture showed by TLC (CH$_2$Cl$_2$/EtOAc, 15:1) two main spots with R_f = 0.60 and 0.49. Purification by flash chromatography (chloroform/EtOAc, 99:1) gave first less polar product **7** (110 mg, 35.5%). The following fractions from the column afforded compound **8** (140 mg, 45.2%). Compound **7**: ^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.08–7.32 (m, 15 H, Ar*H*), 5.89 (dd, $J_{2',3'}$ = 5.1 Hz, $J_{3',4'}$ = 6.0 Hz, 1 H, 3′-H), 5.69 (dd, $J_{1',2'}$ = 3.7 Hz, $J_{2',3'}$ = 5.1 Hz, 1 H, 2′-H), 5.52 (d, $J_{1',2'}$ = 3.7 Hz, 1 H, 1′-H), 4.77 (m, $J_{4,5}$ = 1.5 Hz, 1 H, 5-H), 4.74 (br. s, 1 H, 1-H), 4.71 (dd, $J_{4',5'a}$ = 3.7 Hz, $J_{5'a,5'b}$ = 11.6 Hz, 1 H, 5′a-H), 4.67 (m, 1 H, 4′-H), 4.58 (dd, $J_{4',5'b}$ = 4.5 Hz, $J_{5'a,5'b}$ = 11.6 Hz, 1 H, 5′b-H), 4.27 (dd, $J_{5,6a}$ = 6.8 Hz, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6a-H), 4.24 (dd, $J_{5,6b}$ = 5.3 Hz, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6b-H), 3.99 [m, *J* = 6.2 Hz, 1 H, (CH$_3$)$_2$-C*H*O], 3.81 (m, 1 H, 4-H), 3.16 (dd, $J_{3ax,4}$ = 4.7 Hz, $J_{3ax,3eq}$ = 15.2 Hz, 1 H, 3ax-H), 2.83 (dd, $J_{3eq,4}$ = 2.0 Hz, $J_{3ax,3eq}$ = 15.2 Hz, 1 H, 3eq-H), 2.08 (s, 3 H, C*H*$_3$CO), 1.17, 1.12 [2 d, *J* = 6.2 Hz, 6 H, (C*H*$_3$)$_2$CHO] ppm. ^{13}C NMR (125.7 MHz, CDCl$_3$): δ = 198.2 (C-2), 170.4 (CH$_3$*C*O), 166.0, 165.2 (2 C, Ph*C*O), 133.6, 133.5, 133.3, 129.8, 129.7, 128.5, 128.4 (C-aromatic), 97.9 (C-1), 84.2 (C-1′), 80.4 (C-4′), 75.5 (C-2′), 72.6, 71.6 [C-3′, (CH$_3$)$_2$*C*HO], 68.4 (C-5), 64.4, 64.3 (C-5′, 6), 44.8 (C-4), 42.7 (C-3), 23.2, 21.7 [(*C*H$_3$)$_2$-CHO], 20.7 (*C*H$_3$CO) ppm. Compound **8**: ^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.09–7.30 (m, 15 H, Ar*H*), 5.96 (d, $J_{1',2'}$ = 6.0 Hz, 1 H, 1′-H), 5.72 (dd, $J_{3',4'}$ = 4.6 Hz, $J_{2',3'}$ = 6.4 Hz, 1 H, 3′-H), 5.65 (dd, $J_{1',2'}$ = 6.0 Hz, $J_{2',3'}$ = 6.4 Hz, 1 H, 2′-H), 4.78–4.71 (m, 4 H, 1-H, 4′-H, 5-H, 5′a-H), 4.61 (dd, $J_{4',5'b}$ = 4.0 Hz, $J_{5'a,5'b}$ = 12.0 Hz, 1 H, 5′b-H), 4.22 (dd, $J_{5,6a}$ = 6.6 Hz, $J_{6a,6b}$ = 11.3 Hz, 1 H, 6a-H), 4.18 (dd, $J_{5,6b}$ = 5.7 Hz, 1 H, 6b-H), 3.98 [m, *J* = 6.2 Hz, 1 H, (CH$_3$)$_2$C*H*O], 3.63 (m, 1 H, 4-H), 3.23 (dd, $J_{3ax,4}$ = 3.8 Hz, $J_{3ax,3eq}$ = 14.8 Hz, 1 H, 3ax-H), 2.98 (dd, $J_{3eq,4}$ = 2.0 Hz, 1 H, 3eq-H), 2.05 (s, 3 H, C*H*$_3$CO), 1.26, 1.18, [2 d, *J* = 6.2 Hz, 6 H, (C*H*$_3$)$_2$CHO] ppm. ^{13}C NMR (125.7 MHz, CDCl$_3$): δ = 199.5 (C-2), 170.4 (CH$_3$*C*O), 166.1, 165.6, 165.1 (Ph*C*O), 133.5 (× 2), 133.3, 130.0, 129.9, 129.7, 128.6, 128.5, 128.4 (C-aromatic), 98.0 (C-1), 88.8 (C-1′), 79.0 (C-4′), 72.0 (C-2′), 71.7 [(CH$_3$)$_2$*C*HO], 70.9 (C-3′), 68.5 (C-5), 64.3 (C-6), 63.5, (C-5′), 48.6 (C-4), 44.9 (C-3), 23.2, 21.8 [(*C*H$_3$)$_2$CHO], 20.7 (*C*H$_3$CO) ppm.

Similar to **4**, thiodisaccharides **7** and **8** appeared slightly contaminated with **3** after the column chromatography.

2-Propyl 6-*O*-Acetyl-3-deoxy-4-*S*-(2,3,5-tri-*O*-benzoyl-β-D-xylofuranosyl)-4-thio-α-D-*threo*-hexopyranosid-2-ulose (11) and α-D-Xylofuranosyl Analogue 12: Commercially available 1,2,3,5-tetra-*O*-benzoyl-α-D-xylofuranose (**9**; 200 mg, 0.35 mmol), thiourea (30 mg, 0.395 mmol) and BF$_3$·OEt$_2$ (67 μL, 0.53 mmol) were combined in anhydrous acetonitrile (7 mL) to yield *S*-glycosyl isothiourea **10**. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 9.28–9.19 (2 s, each 2 H, 2 × NH$_2$), 8.10–7.48 (m, 20 H, Ar*H*), 6.44 (br. s, 1 H, 1-H), 6.02 (d, $J_{3,4}$ = 4.6 Hz, 1 H, 3-H), 5.78 (br. s, 1 H, 2-H), 5.12 (q, $J_{4,5} \approx J_{4,5'}$ = 5.0 Hz, 1 H, 4-H), 4.64 (m, 2 H, 5-H, 5′-H) ppm. ^{13}C NMR (50 MHz, [D$_6$]DMSO): δ = 167.7, 167.4, 165.7, 164.6 (2 C, Ph*C*O + S*C*(NH$_2$)$_2$], 134.6–128.5 (C-aromatic), 86.0 (C-1), 80.8, 80.6 (C-2, 4), 75.0 (C-3), 62.5 (C-5) ppm.

Compound **10** was treated with enone **3** (64 mg, 0.28 mmol) and Et$_3$N (350 μL, 2.52 mmol) at 0 °C to afford a 1.4:1 mixture of thiodisaccharides **11/12**. β-D-Xylofuranosyl isomer **11** was partially purified by column chromatography (CHCl$_3$/EtOAc, 85:1→70:1). Compound **11**: ^{1}H NMR (500 MHz, CDCl$_3$): δ = 5.47 (d, $J_{1',2'}$ = 1.4 Hz, 1 H, 1′β-H), 4.73 (br. s, 1 H, 1-H), 3.87 (m, 1 H, 4-H), 3.22 (dd, $J_{3ax,4}$ = 4.9 Hz, $J_{3ax,3eq}$ = 15.2 Hz, 1 H, 3ax-H), 2.86 (dd, $J_{3eq,4}$ = 1.8 Hz, $J_{3ax,3eq}$ = 15.2 Hz, 1 H, 3eq-H) ppm. ^{13}C NMR (125.7 MHz, CDCl$_3$): δ = 198.8 (C-2), 97.9 (C-1), 85.6 (C-1′), 81.6, 79.8 (C-2′, 4′), 75.2 (C-3′), 45.3 (C-4), 42.6 (C-3) ppm. Compound **12**: ^{1}H NMR (500 MHz, CDCl$_3$): δ = 6.00 (d, $J_{1',2'}$ = 6.0 Hz, 1 H, 1′α-H), 4.76 (br. s, 1 H, 1-H), 3.65 (m, 1 H, 4-H), 3.19 (dd, $J_{3ax,4}$ = 4.7 Hz, $J_{3ax,3eq}$ = 14.9 Hz, 1 H, 3ax-H), 2.97 (dd, $J_{3eq,4}$ = 1.8 Hz, $J_{3ax,3eq}$ = 14.9 Hz, 1 H, 3eq-H) ppm. ^{13}C NMR (125.7 MHz, CDCl$_3$): δ = 97.9 (C-1), 88.2 (C-1′), 78.5 (C-4′), 61.8 (C-5′), 48.1 (C-4), 44.6 (C-3) ppm.

2-Propyl 6-*O*-Acetyl-3-deoxy-4-*S*-(2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl)-4-thio-α-D-*lyxo*-hexopyranoside (13) and 4-Thio-α-D-*xylo* Analogue 14: To a solution of thiodisaccharide **4** (120 mg, 0.17 mmol) in THF (7 mL) was added $NaBH_4$ (64 mg, 1.7 mmol), and the mixture was stirred for 30 min at –18 °C. The solution was neutralized with Dowex 50W (H^+) resin, filtered, and concentrated. The residue was dissolved in MeOH, and the solvent was evaporated to remove boric acid. The procedure was repeated three times to afford a syrup that showed two spots by TLC (hexane/EtOAc, 1:1) having R_f = 0.56 and 0.50. Column chromatography (hexane/EtOAc, 70:30) of the mixture first afforded the less polar product. Further purification through a dry column of silica gel (hexane/EtOAc, 1:1) afforded syrupy thiodisaccharide **13** (12.0 mg, 10.0%) and foamy **14** (61.0 mg, 50.7%). Compound **13**: $[\alpha]_D^{20}$ = +80.7 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09–7.31 (m, 15 H, Ar*H*), 5.66 (s, 1 H, 1′-H), 5.64 (d, $J_{3',4'}$ = 4.4 Hz, 1 H, 3′-H), 5.56 (s, 1 H, 2′-H), 4.89 (br. s, 1 H, 1-H), 4.84 (dd, $J_{4',5'a}$ = 3.5 Hz, $J_{5'a,5'b}$ = 11.1 Hz, 1 H, 5′a-H), 4.81 (m, 1 H, 4′-H), 4.73 (dd, $J_{4',5'b}$ = 4.3 Hz, $J_{5'a,5'b}$ = 1.1 Hz, 1 H, 5′b-H), 4.41 (ddd, $J_{4,5}$ = 2.4 Hz, $J_{5,6b}$ = 4.6 Hz, $J_{5,6a}$ = 7.5 Hz, 1 H, 5-H), 4.37 (dd, $J_{5,6a}$ = 7.5 Hz, $J_{6a,6b}$ = 11.1 Hz, 1 H, 6a-H), 4.31 (dd, $J_{5,6b}$ = 4.6 Hz, $J_{6a,6b}$ = 11.1 Hz, 1 H, 6b-H), 3.92 [m, *J* = 6.3 Hz, 1 H, $(CH_3)_2CHO$], 3.62 (m, 1 H, 2-H), 3.48 (d, *J* = 9.6 Hz, 1 H, OH), 3.32 (br. s, 1 H, 4-H), 2.41 (ddd, $J_{2,3a} \approx J_{3a,4}$ = 3.0 Hz, $J_{3a,3b}$ = 15.0 Hz, 1 H, 3a-H), 2.35 (ddd, $J_{2,3b} \approx J_{3b,4}$ = 3.9 Hz, $J_{3a,3b}$ = 15.0 Hz, 1 H, 3b-H), 1.22, 1.16 [2 d, *J* = 6.3 Hz, 6 H, $(CH_3)_2CHO$] ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 170.6 (CH_3CO), 166.1, 165.6 (2 C, Ph*C*O), 133.8, 133.7, 133.1, 130.0, 129.9, 129.8, 128.8, 128.6, 128.4 (C-aromatic), 98.9 (C-1), 89.7 (C-1′), 83.2 (C-2′), 81.5 (C-4′), 77.8 (C-3′), 69.5 [$(CH_3)_2$ *C*HO], 68.0 (C-5), 67.7 (C-2), 65.0 (C-6), 63.3 (C-5′), 42.4 (C-4), 31.8 (C-3), 23.2, 21.5 [$(CH_3)_2CHO$], 20.8 (CH_3CO) ppm. $C_{37}H_{40}O_{12}S$ (708.78): calcd. C 62.70, H 5.69, S 4.52; found C 62.82, H 5.59, S 4.63. Compound **14**: $[\alpha]_D^{20}$ = +73.1 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.11–7.30 (m, 15 H, Ar*H*), 5.61 (d, $J_{3',4'}$ = 5.3 Hz, 1 H, 3′-H), 5.60 (s, 1 H, 1′-H), 5.55 (s, 1 H, 2′-H), 4.92 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 4.84 (dd, $J_{4',5'a}$ = 3.0 Hz, $J_{5'a,5'b}$ = 11.6 Hz, 1 H, 5′a-H), 4.77 (m, 1 H, 4′-H), 4.72 (dd, $J_{4',5'b}$ = 5.0 Hz, $J_{5'a,5'b}$ = 11.6 Hz, 1 H, 5′b-H), 4.32 (dd, $J_{5,6a}$ = 8.7 Hz, $J_{6a,6b}$ = 12.2 Hz, 1 H, 6a-H), 4.27 (m, 1 H, 5-H), 4.26 (dd, $J_{5,6b}$ = 4.8 Hz, $J_{6a,6b}$ = 12.2 Hz, 1 H, 6b-H), 4.02 (m, 1 H, 2-H), 3.95 [m, *J* = 6.2 Hz, $(CH_3)_2CHO$], 3.38 (br. s, 1 H, 4-H), 2.29 (ddd, $J_{2,3eq} \approx J_{3eq,4} \approx 3.9$ Hz, $J_{3ax,3eq}$ = 12.8 Hz, 1 H, 3eq-H), 2.09 (ddd, $J_{3ax,4}$ = 3.7 Hz, $J_{2,3ax} = J_{3ax,3eq}$ = 12.8 Hz, 1 H, 3ax-H), 2.02 (s, 3 H, CH_3CO), 1.26, 1.19 [2 d, 6 H, $(CH_3)_2CHO$] ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 170.6 (CH_3CO), 166.2, 165.4 (Ph*C*O), 133.7, 133.6, 133.1, 130.0, 129.9, 128.9, 128.6, 128.5, 128.4 (C-aromatic), 96.8 (C-1), 90.0 (C-1′), 83.2 (C-2′), 81.2 (C-4′), 78.0 (C-3′), 70.9 [$(CH_3)_2CHO$], 67.8 (C-5), 64.9 (C-6), 64.6 (C-2), 63.4 (C-5′), 45.7 (C-4), 35.7 (C-3), 23.2, 22.0 [$(CH_3)_2CHO$], 20.8 (CH_3CO) ppm. $C_{37}H_{40}O_{12}S$ (708.78): calcd. C 62.70, H 5.69, S 4.52; found C 62.64, H 5.60, S 4.62.

2-Propyl 3-Deoxy-4-*S*-(α-D-arabinofuranosyl)-4-thio-α-D-*xylo*-hexopyranoside (15): Thiodisaccharide **14** (60 mg, 0.085 mmol) was suspended in a solution of MeOH/Et_3N/H_2O (3:1:3; 8.5 mL) and stirred at room temperature. After 3 h, TLC (hexane/EtOAc, 1:1) showed a spot of R_f = 0.0 (UV inactive) and no starting **14** (R_f = 0.50). The mixture was concentrated, and the residue, dissolved in water (1 mL), was eluted through a column filled with Dowex MR-3C mixed-bed ion-exchange resin. The deionized solution was concentrated, and the free thiodisaccharide was purified by dissolution in water (1 mL) and filtered through an octadecyl C18 minicolumn (Amprep, Amersham Biosciences). Evaporation of the solvent afforded crystalline free thiodisaccharide **15** (21 mg, 70.6%). M.p. 176–177 °C. $[\alpha]_D^{20}$ = +195.9 (*c* = 0.9, H_2O). ^{1}H NMR (500 MHz, D_2O): δ = 5.09 (d, $J_{1',2'}$ = 4.7 Hz, 1 H, 1′-H), 4.88 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 4.12 (ddd, $J_{4,5}$ = 1.9 Hz, $J_{5,6a} \approx J_{5,6b} \approx 6.1$ Hz, 1 H, 5-H), 4.00–3.96 (m, 2 H, 2-H, 4′-H), 3.95 (dd, $J_{1',2'}$ = 4.7 Hz, $J_{2',3'}$ = 4.8 Hz, 1 H, 2′-H), 3.91 [m, *J* = 6.2 Hz, 1 H, $(CH_3)_2CHO$], 3.87 (dd, $J_{2',3'}$ = 4.8 Hz, $J_{3',4'}$ = 7.1 Hz, 1 H, 3′-H), 3.73 (dd, $J_{4',5'a}$ = 3.0 Hz, $J_{5'a,5'b}$ = 12.5 Hz, 1 H, 5′a-H), 3.64 (m, 2 H, 6a-H, 6b-H), 3.63 (dd, $J_{4',5'b}$ = 5.5 Hz, $J_{5'a,5'b}$ = 12.5 Hz, 1 H, 5′b-H), 3.33 (m, 1 H, 4-H), 2.13 (ddd, $J_{3ax,4}$ = 4.0 Hz, $J_{3ax,3eq}$ = 12.5 Hz, $J_{2,3ax}$ = 12.8 Hz, 1 H, 3ax-H), 2.02 (ddd, $J_{2,3eq} \approx J_{3eq,4} \approx 3.9$ Hz, $J_{3ax,3eq}$ = 12.5 Hz, 1 H, 3eq-H), 1.16, 1.08 [2 d, *J* = 6.2 Hz, 6 H, $(CH_3)_2CHO$] ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 96.0 (C-1), 89.7 (C-1′), 82.4 (C-4′), 81.6 (C-2′), 75.8 (C-3′), 70.6, 70.5 [C-5, $(CH_3)_2CHO$], 64.1 (C-2), 62.5 (C-6), 60.7 (C-5′), 44.7 (C-4), 33.8 (C-3), 22.3, 20.5 [$(CH_3)_2CHO$] ppm. $C_{14}H_{26}O_8S$ (354.41): calcd. C 47.44, H 7.39, S 9.06; found C 47.32, H 7.45, S 9.23.

2-Propyl 6-*O*-Acetyl-3-deoxy-4-*S*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-4-thio-α-D-*lyxo*-hexopyranoside (16) and 4-Thio-α-D-*xylo* Analogue 17: Compound **7** (95 mg, 0.135 mmol) was treated with $NaBH_4$ (70 mg, 1.85 mmol) as described for **4**. After 30 min, monitoring of the reaction mixture by TLC (hexane/EtOAc, 1:1) revealed two main spots having R_f = 0.61 and 0.54. The mixture was subjected to column chromatography (hexane/EtOAc, 70:30). The less polar compound was repurified through a dry column of silica gel (hexane/EtOAc, 1:1) to afford pure **16** (6 mg, 6.3%) and major thiodisaccharide **17** (36 mg, 37.7%). From intermediate fractions of the column, a mixture of **16** and **17** was obtained (33 mg, 83.6% overall yield). Compound **16**: $[\alpha]_D^{20}$ = +15.7 (*c* = 0.8, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09–7.33 (m, 15 H, Ar*H*), 5.89 (dd, $J_{2',3'}$ = 5.0 Hz, $J_{3',4'}$ = 5.9 Hz, 1 H, 3′-H), 5.73 (dd, $J_{1',2'}$ = 3.6 Hz, $J_{2',3'}$ = 5.0 Hz, 1 H, 2′-H), 5.64 (d, $J_{1',2'}$ = 3.6 Hz, 1 H, 1′-H), 4.88 (br. s, 1 H, 1-H), 4.73 (dd, $J_{4',5'a}$ = 3.9 Hz, $J_{5'a,5'b}$ = 11.2 Hz, 1 H, 5′a-H), 4.71 (m, 1 H, 4′-H), 4.58 (dd, $J_{4',5'b}$ = 4.0 Hz, $J_{5'a,5'b}$ = 11.2 Hz, 1 H, 5′b-H), 4.41 (m, 1 H, 5-H), 4.26 (dd, $J_{5,6a}$ = 7.9 Hz, $J_{6a,6b}$ = 11.6 Hz, 1 H, 6a-H), 4.16 (dd, $J_{5,6b}$ = 4.5 Hz, $J_{6a,6b}$ = 11.6 Hz, 1 H, 6b-H), 3.94 [m, *J* = 6.2 Hz, 1 H, $(CH_3)_2CHO$], 3.62 (m, 1 H, 2-H), 3.54 (d, *J* = 10.3 Hz, 1 H, 2-*H*O), 3.41 (m, 1 H, 4-H), 2.30 (m, 2 H, 3a-H, 3b-H), 2.05 (s, 3 H, CH_3CO), 1.23, 1.18 [2 d, *J* = 6.2 Hz, 6 H, $(CH_3)_2CHO$] ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 170.5 (CH_3CO), 166.1, 165.1 (×2, Ph*C*O), 133.6, 133.5, 129.9, 129.8, 128.5, 128.4 (C-aromatic), 98.9 (C-1), 84.5 (C-1′), 80.4 (C-4′), 75.6 (C-2′), 72.6 (C-3′), 69.4 [$(CH_3)_2CHO$], 67.9 (C-2), 67.6 (C-5), 64.9 (C-6), 64.3 (C-5′), 39.3 (C-4), 29.8 (C-3), 23.1, 21.5 [$(CH_3)_2CHO$], 20.7 (CH_3CO) ppm. $C_{37}H_{40}O_{12}S$ (708.78): calcd. C 62.70, H 5.69, S 4.52; found C 62.39, H 5.77, S 4.43. Compound **17**: $[\alpha]_D^{20}$ = +37.5 (*c* = 0.95, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09–7.33 (m, 15 H, Ar*H*), 5.87 (dd, $J_{2',3'}$ = 5.1 Hz, $J_{3',4'}$ = 5.8 Hz, 1 H, 3′-H), 5.69 (dd, $J_{1',2'}$ = 3.7 Hz, $J_{2',3'}$ = 5.1 Hz, 1 H, 2′-H), 5.51 (d, $J_{1',2'}$ = 3.7 Hz, 1 H, 1′-H), 4.89 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 4.71 (dd, $J_{4',5'a}$ = 4.0 Hz, $J_{5'a,5'b}$ = 11.2 Hz, 1 H, 5′a-H), 4.68 (ddd, $J_{4',5'a}$ = 4.0 Hz, $J_{4',5'b}$ = 4.2 Hz, $J_{3',4'}$ = 5.8 Hz, 1 H, 4′-H), 4.59 (dd, $J_{4',5'b}$ = 4.2 Hz, $J_{5'a,5'b}$ = 11.2 Hz, 1 H, 5′b-H), 4.25 (ddd, $J_{4,5}$ = 2.0 Hz, *J* = 5.0 Hz, *J* = 6.9 Hz, 1 H, 5-H), 4.18 (m, 2 H, 6a-H, 6b-H), 4.02 (ddd, $J_{1,2}$ = 3.8 Hz, $J_{2,3eq}$ = 4.3 Hz, $J_{2,3ax}$ = 11.5 Hz, 1 H, 2-H), 3.93 [m, *J* = 6.2 Hz, 1 H, $(CH_3)_2CHO$], 3.42 (br. s, 1 H, 4-H), 2.24 (ddd, $J_{3eq,4}$ = 3.5 Hz, $J_{2,3eq}$ = 4.3 Hz, $J_{3ax,3eq}$ = 13.0 Hz, 1 H, 3eq-H), 2.01 (m, 4 H, 3ax-H, CH_3CO), 1.21, 1.18, [2 d, *J* = 6.2 Hz, 6 H, $(CH_3)_2CHO$] ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 170.5 (CH_3CO), 166.1, 165.1 (Ph*C*O), 133.6, 133.5, 133.1, 129.8, 128.5, 128.4 (C-aromatic), 96.8 (C-1), 85.4 (C-1′), 80.2 (C-4′), 75.8 (C-2′), 72.8, 70.8 [C-3′, $(CH_3)_2CHO$], 67.8 (C-2), 65.1 (C-6), 64.5 (C-5), 64.2 (C-5′), 43.2 (C-4), 34.2 (C-3), 23.2, 22.0 [$(CH_3)_2CHO$], 20.8

(CH_3CO) ppm. $C_{37}H_{40}O_{12}S$ (708.78): calcd. C 62.70, H 5.69, S 4.52; found C 62.89, H 5.65, S 4.43.

2-Propyl 3-Deoxy-4-*S*-(β-D-ribofuranosyl)-4-thio-α-D-*xylo*-hexopyranoside (18): Compound **17** (65 mg, 0.092 mmol) was subjected to the same *O*-deacylation procedure as that described for **14** to afford crystalline **18** (22 mg, 65.2%). M.p. 149–151 °C. $[\alpha]_D^{20}$ = +3.5 (c = 0.9, H_2O). ^1H NMR (500 MHz, $CDCl_3$): δ = 5.04 (d, $J_{1',2'}$ = 4.8 Hz, 1 H, 1′-H), 4.88 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 4.16 (ddd, J = 2.0 Hz, J = 5.5 Hz, J = 6.8 Hz, 1 H, 5-H), 4.12 (dd, $J_{2',3'} \approx J_{3',4'} \approx$ 5.0 Hz, 1 H, 3′-H), 4.02 (ddd, $J_{2,3eq}$ = 4.3 Hz, $J_{2,3ax}$ = 12.0 Hz, $J_{1,2}$ = 3.7 Hz, 1 H, 2-H), 3.99 (dd, $J_{1',2'}$ = 4.8 Hz, $J_{2',3'}$ = 5.0 Hz, 1 H, 2′-H), 3.92 (ddd, $J_{4',5'a}$ = 3.6 Hz, $J_{3',4'}$ = 5.0 Hz, $J_{4',5'b}$ = 5.8 Hz, 1 H, 4′-H), 3.91 [m, J = 6.2 Hz, 1 H, $(CH_3)_2CHO$], 3.67 (dd, $J_{4',5'a}$ = 3.6 Hz, $J_{5'a,5'b}$ = 12.4 Hz, 1 H, 5′a-H), 3.63–3.60 (m, 2 H, 6a-H, 6b-H), 3.58 (dd, $J_{4',5'b}$ = 5.8 Hz, $J_{5'a,5'b}$ = 12.4 Hz, 1 H, 5′b-H), 3.34 (m, 1 H, 4-H), 2.08 (ddd, $J_{2,3ax}$ = 12.0 Hz, $J_{3ax,4}$ = 3.6 Hz, $J_{3ax,3eq}$ = 13.1 Hz, 1 H, 3ax-H), 2.00 (ddd, $J_{3eq,4}$ = 3.5 Hz, $J_{2,3eq}$ = 4.3 Hz, $J_{3ax,3eq}$ = 13.1 Hz, 1 H, 3eq-H), 1.16, 1.09 [2 d, J = 6.2 Hz, 6 H, $(CH_3)_2CHO$] ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 96.1 (C-1), 86.6 (C-1′), 84.5 (C-4′), 75.2 (C-2′), 71.1 (C-3′), 70.5 [$(CH_3)_2CHO$], 70.3 (C-5), 64.0 (C-2), 62.6 (C-6), 62.1 (C-5′), 42.9 (C-4), 32.2 (C-3), 22.4, 20.5 [$(CH_3)_2CHO$] ppm. $C_{14}H_{26}O_8S$ (354.41): calcd. C 47.44, H 7.39, S 9.06; found C 47.33, H 7.41, S 9.19.

2-Propyl 6-*O*-Acetyl-3-deoxy-4-*S*-(2,3,5-tri-*O*-benzoyl-α-D-ribofuranosyl)-4-thio-α-D-*xylo*-hexopyranoside (19): The reduction of **8** (45 mg, 0.064 mmol) with $NaBH_4$ was performed as described for analogue **7**. Purification of the reaction mixture by column chromatography (hexane/EtOAc, 70:30) gave **19** (29 mg, 64%) as the major product. $[\alpha]_D^{20}$ = +93.2 (c = 0.6, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 8.08–7.30 (m, 15 H, Ar*H*), 5.93 (d, $J_{1',2'}$ = 6.0 Hz, 1 H, 1′-H), 5.74 (dd, $J_{2',3'}$ = 6.6 Hz, $J_{3',4'}$ = 4.3 Hz, 1 H, 3′-H), 5.63 (t, $J_{1',2'}$ = 6.0 Hz, 1 H, 2′-H), 4.90 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 4.76 (br. s, 1 H, 4′-H), 4.75 (dd, $J_{5'a,5'b}$ = 12.8 Hz, $J_{4,5'a}$ = 3.1 Hz, 1 H, 5′a-H), 4.63 (dd, $J_{4,5'b}$ = 4.8 Hz, $J_{5'a,5'b}$ = 12.8 Hz, 1 H, 5′b-H), 4.22 (ddd, $J_{4,5}$ = 1.7 Hz, $J_{5,6b}$ = 5.5 Hz, $J_{5,6a}$ = 7.0 Hz, 1 H, 5-H), 4.13 (dd, $J_{6a,6b}$ = 11.4 Hz, 1 H, 6a-H), 4.08 (dd, $J_{5,6b}$ = 5.5 Hz, $J_{6a,6b}$ = 11.4 Hz, 1 H, 6b-H), 4.03 (m, 1 H, 2-H), 3.92 [m, J = 6.2 Hz, 1 H, $(CH_3)_2CHO$], 3.28 (br. s, 1 H, 4-H), 2.34 (ddd, $J_{2,3eq}$ = 3.8 Hz, $J_{3eq,4}$ = 3.8 Hz, $J_{3eq,3ax}$ = 12.5 Hz, 1 H, 3eq-H), 2.10 (ddd, $J_{3ax,4}$ = 3.6 Hz, $J_{2,3ax}$ = 12.0 Hz, $J_{3ax,3eq}$ = 12.5 Hz, 1 H, 3ax-H), 2.03 (s, 3 H, CH_3CO), 1.86 (d, $J_{2,OH}$ = 12.0 Hz, 1 H, HO), 1.24, 1.81 [2 d, J = 6.2 Hz, 6 H, $(CH_3)_2CHO$] ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 170.5 (CH_3CO), 166.1, 165.1, 165.2 (Ph*C*O), 151.0, 136.0, 133.5, 133.3, 129.9, 129.7, 129.5, 129.0, 128.8, 128.5, 128.4, 127.8 (C-aromatic), 96.8 (C-1), 89.2 (C-1′), 79.0 (C-4′), 72.2 (C-2′), 71.2 (C-3′), 70.9 [$(CH_3)_2CHO$], 67.8 (C-5), 64.7 (C-6), 63.6 (C-5′), 60.4 (C-2), 46.1 (C-4), 35.2 (C-3), 23.2, 21.9 [$(CH_3)_2CHO$], 20.7 (CH_3CO) ppm. $C_{37}H_{40}O_{12}S$ (708.78): calcd. C 62.70, H 5.69, S 4.52; found C 62.79, H 5.81, S 4.42.

Methyl 2,3,4-Tri-*O*-benzoyl-6-S-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6-thio-α-D-glucopyranose (21): To a solution of MoO_2Cl_2 (0.9 mg, 0.004 mmol) in anhydrous CH_2Cl_2 (0.1 mL) was added a solution of compound **5** (45 mg, 0.09 mmol) in CH_2Cl_2 (0.3 mL). The reaction mixture was flushed with Ar and stirred at room temperature for 10 min. Methyl 2,3,4-tri-*O*-benzoyl-6-thio-D-glucopyranoside[23] (**20**; 70 mg, 0.134 mmol) dissolved in CH_2Cl_2 (0.2 mL) was added. The solution immediately turned deep blue and gradually changed to yellowish brown. After 2 h, TLC (toluene/EtOAc, 9:1) showed a main spot of R_f = 0.56. The reaction was quenched with saturated aqueous $NaCO_3H$, and the organic layer was separated, washed with brine, dried, filtered, and concentrated. The residue was purified by column chromatography (toluene/EtOAc, 95:5) to afford syrupy **21** (45 mg, 51.7%). $[\alpha]_D^{20}$ = +22.6 (c = 0.8, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 8.09–7.28 (m, 15 H, Ar*H*), 6.11 (t, $J_{2,3} \approx J_{3,4}$ = 10 Hz, 1 H, 3-H), 5.87 (t, $J_{2',3'} \approx J_{3',4'}$ = 5.5 Hz, 1 H, 3′-H), 5.73 (dd, $J_{1',2'}$ = 3.3 Hz, $J_{2',3'}$ = 5.5 Hz, 1 H, 2′-H), 5.70 (d, $J_{1',2'}$ = 3.3 Hz, 1 H, 1′-H), 5.45 (t, $J_{4,5}$ = 9.8 Hz, 1 H, 4-H), 5.23 (dd, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H), 5.19 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 4.70 (m, 2 H, 4′-H, 5′a-H), 4.54 (dd, $J_{4',5'b}$ = 5.5 Hz, $J_{5'a,5'b}$ = 12.9 Hz, 1 H, 5′b-H), 4.26 (ddd, $J_{5,6b}$ = 2.2 Hz, $J_{5,6a}$ = 9.5 Hz, $J_{4,5}$ = 9.8 Hz, 1 H, 5-H), 3.45 (s, 3 H, CH_3O), 3.06 (dd, $J_{5,6a}$ = 9.5 Hz, $J_{6a,6b}$ = 14.4 Hz, 1 H, 6a-H), 2.91 (dd, $J_{5,6b}$ = 2.2 Hz, $J_{6a,6b}$ = 14.4 Hz, 1 H, 6b-H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 166.1, 165.8, 165.3 (Ph*C*O), 133.5, 133.3, 133.1, 133.0, 129.8, 129.7, 129.6, 128.4, 128.2 (C-aromatic), 96.8 (C-1), 87.0 (C-1′), 79.9 (C-4′), 75.7 (C-2′), 72.5 (C-3′), 72.2 (C-4), 72.1 (C-2), 70.8 (C-5), 70.3 (C-3), 65.0 (C-5′), 56.6 (CH_3O), 32.6 (C-6) ppm. $C_{54}H_{46}O_{15}S$ (967.01): calcd. C 67.07, H 4.79, S 3.31; found C 66.89, H 4.89, S 3.25.

1,2:3,4-Di-*O*-isopropylidene-6-*S*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6-thio-α-D-galactopyranose (23): The procedure described above was followed, starting from **5** (95 mg, 0.188 mmol) and 1,2:3,4-di-*O*-isopropylidene-4-thio-D-galactose[25] (**22**; 78 mg, 0.28 mmol). Purification by column chromatography (toluene/EtOAc, 97:3) gave compound **23** (53 mg, 39.1%). $[\alpha]_D^{20}$ = –48.5 (c = 0.9, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 8.10–7.16 (m, 15 H, Ar*H*), 5.90 (dd, $J_{2',3'} \approx J_{3',4'}$ = 5.3 Hz, 1 H, 3′-H), 5.71 (dd, $J_{1',2'}$ = 3.9 Hz, $J_{2',3'}$ = 5.3 Hz, 1 H, 2′-H), 5.61 (d, $J_{1',2'}$ = 3.9 Hz, 1 H, 1′-H), 5.52 (d, $J_{1,2}$ = 5.0 Hz, 1 H, 1-H), 4.69 (dd, $J_{4'5'a}$ = 3.8, $J_{5'a,5'b}$ = 11.1 Hz, 1 H, 5′a-H), 4.66 (ddd, $J_{4',5'a}$ = 3.8 Hz, $J_{4',5'b}$ = 4.1 Hz, $J_{3',4'}$ = 5.3 Hz, 1 H, 4′-H), 4.61 (dd, $J_{4',5'b}$ = 4.1 Hz, $J_{5'a,5'b}$ = 11.1 Hz, 1 H, 5′b-H), 4.58 (dd, $J_{2,3}$ = 2.5 Hz, $J_{3,4}$ = 7.8 Hz,1 H, 3-H), 4.31–4.38 (m, 2 H, 2-H, 4-H), 3.95 (ddd, $J_{4,5}$ = 1.4 Hz, $J_{5,6b}$ = 6.2 Hz, $J_{5,6a}$ = 7.3 Hz, 1 H, 5-H), 3.07 (dd, $J_{5,6a}$ = 7.3 Hz, $J_{6a,6b}$ = 13.7 Hz, 1 H, 6a-H), 2.90 (dd, $J_{5,6b}$ = 6.2 Hz, $J_{6a,6b}$ = 13.7 Hz, 1 H, 6b-H), 1.49, 1.43, 1.31, 1.30 [4 s, 12 H, 2×$(CH_3)_2C$] ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 165.2, 165.1 (×2, Ph*C*O), 133.4, 133.1, 129.8, 129.7, 128.4, 128.3 (C-aromatic), 109.3, 108.6 [$(CH_3)_2C$], 96.5 (C-1), 86.3 (C-1′), 80.0 (C-4′), 75.7 (C-2′), 72.6 (C-3′), 71.5, 70.5 (C-2, C-4), 70.8 (C-3), 68.4 (C-5), 64.5 (C-5′), 30.5 (C-6), 26.0, 25.9, 24.9, 24.4 [$(CH_3)_2C$] ppm. $C_{38}H_{40}O_{12}S$ (720.79): calcd. C 63.32, H 5.59, S 4.45; found C 63.15, H 5.66, S 4.37.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR spectra for precursors, intermediates, and thiodisaccharide final products.

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