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Synthesis of Glycosylthiols and Reactivity Studies

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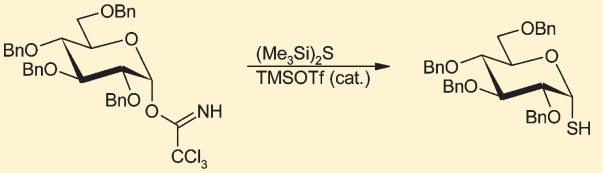
Supporting Information

ABSTRACT: The acid-catalyzed reaction of 1,2-anhydro-3,4,6-tri-*O*-benzyl-α-D-glucopyranose (**7**) as glycosyl donor with bis-trimethylsilyl sulfide as acceptor affords the α-thiol. Hence, this sterically hindered *S*-nucleophile as acceptor should provide with *O*-glycosyl trichloroacetimidates as glycosyl donors that have nonparticipating groups at C-2, glycosylthiols with the thiol group in axial position. This was confirmed for various donors (**4**, **16**−**19**) with the exception of the corresponding mannosyl donor (**20**). However, powerful participating groups at C-2 of the donor (**23**−**28**) governed the anomeric selectivity.



Glycoconjugates, particularly those containing lipid and/or protein moieties, play essential roles in many biological processes.[1] Hence, the development of readily available glycoconjugate mimetics as tools for model studies or even therapeutic intervention has gained great interest.[2] In this context glycosylthiols have been shown to be useful intermediates as they have been successfully employed, for instance, for high-yielding syntheses of sulfur-containing glycolipids, glycopeptides, and glycoprotein analogues.[3−12] The generally observed configurational stability of glycosylthiols and the high nucleophilicity of the derived glycosylthiolates (the intermediates in "base-promoted anomeric thiol group *S*-alkylations", Scheme 1, c) provide advantages in the synthesis of glycoconjugate mimetics.[3,13] Also worth mentioning is the radical-induced glycosylthiol−ene coupling that can be employed as a click process.[14] Furthermore, thioglycosidic linkages generally exhibit higher chemo- and enzymatic stability than their oxygen counterparts, and corresponding glycoconjugate mimetics are tolerated by most biological systems.[3,15]

For the construction of thioglycosides the acid-promoted *S*-glycosylation (Scheme 1, a) has similar drawbacks as *O*-glycosylation, as it is often not stereoselective.[3,13] Because of the high nucleophilicity of thiol groups under basic conditions, base-promoted *S*-glycosylation (Scheme 1, b) is often employed.[3,13] This way, the readily available glycosyl halides with the halide in axial position lead via an S_N2-substitution reaction stereoselectively to the corresponding inverted thioglycosides. However, glycosyl halides with the halide in the equatorial position are not readily available. As alternative the base-promoted anomeric thiol group *S*-alkylation (Scheme 1, c) is of interest.[3] However, the formation of the glycosylthiols that are required as α- and β-anomers, respectively, has the same limitations as discussed for thioglycoside generation. The most frequently employed method for glycosylthiol formation starts from glycosyl halides, with the halide in axial orientation, and thiourea or thioacetate as *S*-nucleophiles leading in the presence of base (Scheme 1, d) in an S_N2 reaction to glycosylthiols with the thiol group in equatorial position.[3,13,16] Glycosyl donor activation by acid catalysts/promoters in the presence of H_2S or equivalents (Scheme 1, e) often leads to anomeric glycosylthiol mixtures.[3,17] This is also found for the direct formation of glycosylthiols from 1-*O*-unprotected sugars and Lawesson's reagent.[6]

Hence, as glycosylthiols with the thiol group in axial position are not as readily available as their equatorial counterparts,[3,18] the recently reported stereospecific formation of α-glycosylthiols by opening of 1,6-anhydro sugars with bis(trimethylsilyl) sulfide (BTMSS) in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) as catalyst (Scheme 2) is a major advance.[11c,d] Thus, from levoglucosan **1** the corresponding α-thiol **2α** was obtained, as presumed in an S_N2-type fashion.[11c,d] The presence of two unprotected functional groups, the availability of other types of anhydro sugars and the required further investigation of the reaction mechanism were reason to continue our studies with BTMSS as *S*-nucleophile.

The reactivity studies with **2α** exhibited that alkylation under mild basic conditions leads to *S*-alkylation. For instance, benzylation of **2α** with benzyl bromide in a biphasic system in the presence of $NaHCO_3$ furnished the known benzyl 1-thio-glucopyransoside **3** (Scheme 2).[19] Surprisingly, acid-catalyzed glycosylation of **2α** with α-D-glucopyranosyl trichloroacetimidate **4**[20] as glycosyl donor led, presumably as a result of steric reasons, to β-selective 6-*O*-attack, thus providing gentiobiosylthiol **5** in good yield. The structural assignment was confirmed by 1-*S*-acetylation with acetic anhydride in pyridine furnishing disaccharide **6** (^{1}H NMR: 1a-H, δ 6.17, J = 5.3 Hz; 1b-H, δ 4.29, J = 7.8 Hz). Thus, it was proven that the thiol group was not oxidized to the

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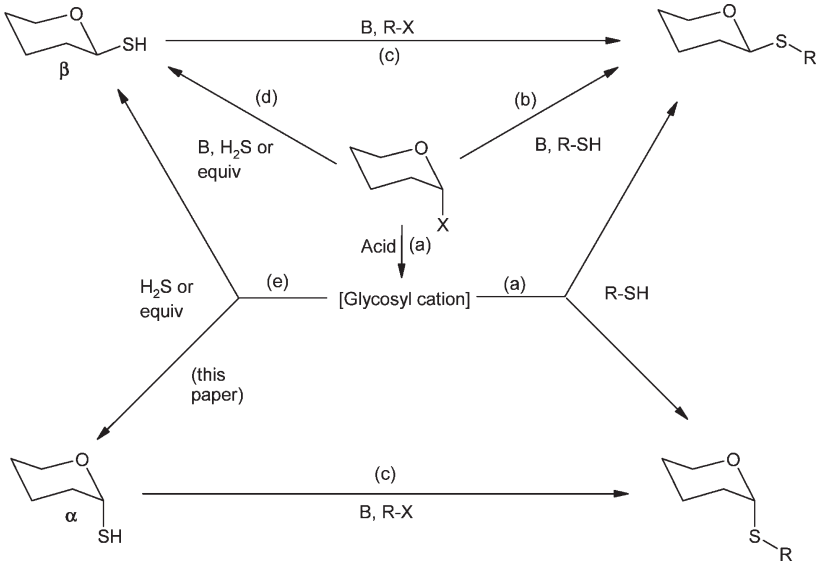
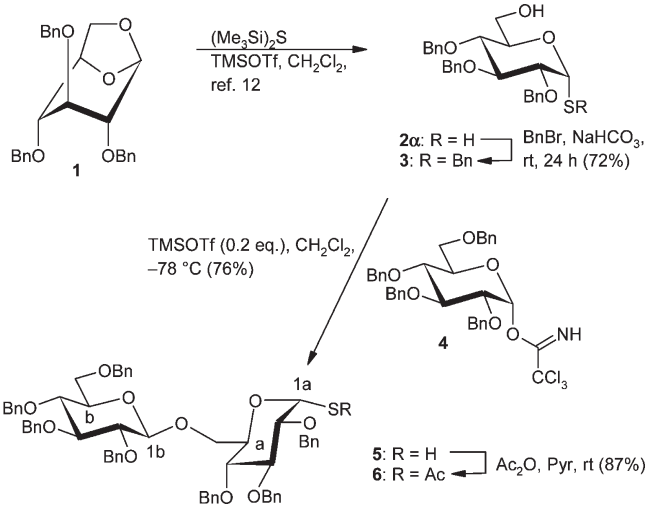
Scheme 1. Synthesis of Glycosylthiols and Thioglycosides[a]



[a] B = base, X = leaving group. (a) Acid-promoted *S*-glycosylation. (b) Base-promoted *S*-glycosylation. (c) Anomeric thiol group *S*-alkylation.

Scheme 2. *O*- versus *S*-Glycosylation of Acceptor 2α



disulfide stage in the transformations from starting material **1** to disaccharide **5**.

The convenient transformation of 1,6-anhydro sugars upon acid-catalyzed treatment with BTMSS into α-glycosylthiols[11c,d] led us to related studies with 1,2-anhydro sugars. Hence, readily available 1,2-anhydro-glucose derivative **7**[21] was treated with BTMSS in the presence of TMSOTf as catalyst (Scheme 3). Surprisingly, the major product was α-glycosyl thiol **8α** and not the expected *β*-glucosylthiol **8*β*** (α/*β* = 2:1), thus indicating that the reaction course is essentially or exclusively S_N1 type leading mainly to the stereoelectronically favored α-product. For the structural assignment, **8α** was fully acetylated, thus providing 1-*S*,2-*O*-diacetyl derivative **9** that showed the required ^{1}H NMR data (1-H: *δ* 6.23, $J_{1,2}$ = 5.3 Hz; 2-H: *δ* 5.24, $J_{2,3}$ = 9.9 Hz). **8α** underwent selective 1-*S*-benzylation under the biphasic conditions as described above providing benzylated product **10**. However, glycosylation of **8α** with **4** as glycosyl donor in the presence of TMSOTf as catalyst did not lead to 2-*O*-glycosylation; instead α-selective 1-*S*-glycosylation was observed furnishing thiotrehalose derivative **11**, which was transformed into the 2-*O*-acetyl derivative **12** in order to further confirm the structural assignment (^{1}H NMR: 1a-H: *δ* 5.75, $J_{1,2}$ = 5.7 Hz; 1b-H: *δ* 5.57, *J* = 4.9 Hz). **8α** was also reacted with dichloromethane in the presence of DBU as base, thus leading via 1-*S*-chloromethyl glucosyl-thiol **13** (which can be isolated) to oxothiolane derivative **14**. This compound seems to be an interesting glycosyl donor as the oxothiolane moiety, although opened upon activation with a thiophilic reagent, could serve as an anchimerically assisting group favoring *β*-product formation.[22] (Product **14A** formed with isopropanol; see Supporting Information)

The ring opening of 1,2-anhydro-glucose **7** with BTMSS indicates that glycosylthiols with axial thiol groups should be accessible directly from standard glycosyl donors with BTMSS as acceptor. Due presumably to its steric demand, the reaction leads first to a glycosyl cation, and then stereoelectronically favored axial attack takes place. Hence, glucosyl donor **4** was treated with BTMSS in the presence of TMSOTf as catalyst affording, as expected, only known α-glucosyl thiol **15α**[11a] in very good yield (Scheme 4, Table 1). The application of this procedure to other glycosyl donors is shown in Table 1. Thus, similar results were obtained for galactosyl, fucosyl, and 2-azido-2-deoxy-galactosyl and -lactosyl donors (entries 2−5, transformation of **16**,[23] **17**,[24] **18**, **19**[25] into **29α**, **30α**,[6] **31α**, **32α**). Unexpectedly, mannopyranosyl donor **20**[26] and *O*-acetyl protected glucopyranosyl and galactopyranosyl donors **21**[20] and **22**[27] afforded α/*β*-mixtures of the glycosylthiols **33α,*β***,[6] **34α,*β***,[28] **35α,*β***,[28] respectively (entries 6−8). Obviously, as supported by previous work, attack at the naked glycosyl cation intermediate is decisive for the anomeric stereocontrol.[29] For instance, the generated mannopyranosyl cation can adopt a twist-boat conformation that favors *β*-product formation. Hence, from 2-*O*-benzoyl or 2-*N*-dimethylmaleoyl (DMM) protected glycosyl donors (entries 9−14, transformation of donors **23**,[30] **24**, **25**,[31] **26**,[32] **27**,[33] **28**[34]

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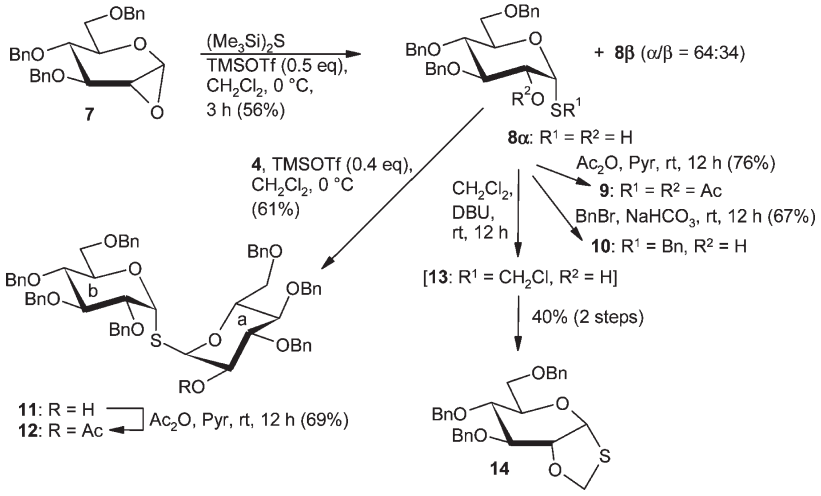
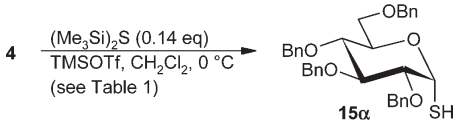
Scheme 3. Ring Opening of 1,2-Anhydro-glucose 7 and *O*- versus *S*-Alkylation and -Glycosylation of 8α[a]



[a] eq = equivalents.

Scheme 4. Synthesis of Glycosylthiol 15α



into thiols **36*β*−39*β***, **40α**, **41*β***) having more efficient anchimeric assistance only the 1,2-*trans* glycosylthiols were obtained. Thus, the simplicity and efficiency of this procedure to accessing various glycosyl thiols in either α- and/or *β*-configuration has been demonstrated.

As glycosyl thioacrylates are interesting intermediates, Michael-type addition of glucosylthiol **15α** to ethyl propiolate was studied (Scheme 5, Table 2).[35] Variation of solvent, base, and temperature exhibited that DABCO as base in acetonitrile or THF as solvent (entries 8 and 9) gave excellent product yields; mainly the (*E*)-isomer (*E*)-**42** was obtained. This way the availability of a nonoxidized thiol group is also confirmed. Accordingly, reaction of **30α** with ethyl propiolate furnished adduct **43** (*E*/*Z* = 94:6)

In conclusion, the acid-catalyzed ring opening of *O*-benzyl protected 1,6-anhydro- and 1,2-anhydro-glucopyranose, respectively, with BTMSS leads to exclusive or preferential formation of α-glucopyranosylthiols. Hence, for *O*-glycosyl trichloroacetimidate donors having no anchimeric assistance the sterically hindered BTMSS acceptor permits the generation of glycopyranosylthiols with the thiol group in the axial position (generally 1,2-*cis* orientation). The availability of the thiol groups in these products was proven by Michael-type additions leading to glycopyranosyl thioacrylates.

EXPERIMENTAL SECTION

General Methods. Solvents were purified by standard procedures. NMR spectra were recorded at 22 °C; tetramethylsilane (TMS) or the resonance of the undeuterated solvent was used as internal standards. Mass spectra were recorded with a ESI MS mass spectrometer. Thin-layer chromatography was performed on silica gel plastic plates; compounds were visualized by treatment with a solution of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (20 g) and $Ce(SO_4)_2$ (0.4 g) in sulfuric acid (10%, 400 mL) and then by heating to 120 °C. Flash chromatography was performed on silica gel (230−400 mesh) at a pressure of 0.2 bar. Optical rotations were measured at 22 °C using the sodium D line. Commercial grade BTMSS and ethyl propiolate were used.

Benzyl 2,3,4-Tri-*O*-benzyl-1-thio-α-D-glucopyranoside (3). A pH 8.5 solution of $NaHCO_3$ (3 mL) followed by TBAHS (274 mg, 0.80 mmol) was added to a solution of **2** (110 mg, 0.23 mmol) and benzyl bromide (45 mg, 0.25 mmol) in EtOAc (3 mL). The reaction mixture was vigorously stirred at room temperature for 24 h and then diluted with EtOAc and washed successively with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$ and concentrated in vacuo to give a crude product that was purified by flash column chromatography with petroleum ether/EtOAc (8:1) to afford **3** (94 mg, 72%) as a colorless oil. The physical properties found for **3** are in accordance with those reported previously.[19]

2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1−6)-2,3,4-tri-*O*-benzyl-1-thio-α-D-glucopyranose (5). To a solution of **2α** (200 mg, 0.42 mmol) and **4** (288 mg, 0.42 mmol) in dry CH_2Cl_2 (10 mL) was added TMSOTf (0.016 mL, 0.08 mmol) at −78 °C. The reaction mixture was then stirred at −78 °C until TLC indicated complete consumption of the starting material and then quenched by adding triethyl amine. The reaction mixture was diluted with CH_2Cl_2 (10 mL) washed with water. The organic layer was dried over $MgSO_4$ and concentrated in vacuo to give a residue that was purified by flash column chromatography with petroleum ether/EtOAc (8:1) to afford **5** (322 mg, 76%) as a white solid. $[\alpha]_D$ = +34.0 (*c* 0.35, $CHCl_3$). HRMS ($C_{61}H_{64}O_{10}S$): $[M + Na]^+$ *m*/*z* 1011.4118, found 1011.4110.

Acetylation of **5** under standard conditions afforded 2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl-(1−6)-1-*S*-acetyl-2,3,4-tri-*O*-benzyl-1-thio-α-D-glucopyranose (**6**) as a white solid (87%). $[\alpha]_D$ = +21.0 (*c* 0.31, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.24−7.21 (m, 16 H), 7.20−7.16 (m, 13 H), 7.12−7.07 (m, 6 H), 6.17 (d, *J* = 5.3 Hz, 1 H), 4.88−4.80 (m, 3 H), 4.73−4.68 (m, 2 H), 4.67−4.63 (m, 2 H), 4.60 (d, *J* = 6.8 Hz, 1 H), 4.56 (d, *J* = 11.0 Hz, 1 H), 4.50−4.48 (m, 2 H), 4.46 (s, 1 H), 4.44 (dd, *J* = 5.6, 3.5 Hz, 2 H), 4.29 (d, *J* = 7.8 Hz, 1 H), 4.09 (dd, *J* = 11.1, 1.6 Hz, 1 H), 3.80 (dd, *J* = 9.2, 5.3 Hz, 1 H), 3.75 (dd, *J* = 9.3, 3.0 Hz, 1 H), 3.64−3.59 (m, 3 H), 3.57−3.55 (m, 1 H), 3.51 (d, *J* = 4.2 Hz, 1 H), 3.48 (d, *J* = 3.8 Hz, 1 H), 3.46−3.44 (m, 1 H), 3.39 (d, *J* = 8.1 Hz, 1 H), 3.35−3.32 (m, 1 H), 2.21 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 192.8, 138.64, 138.61, 138.5, 138.3, 138.2, 138.1, 137.4, 128.5, 128.41,

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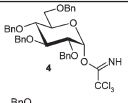
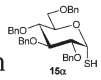
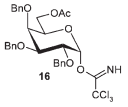
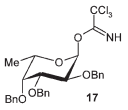
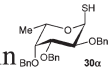
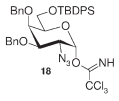
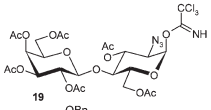
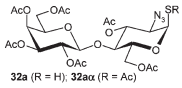
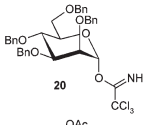
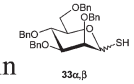
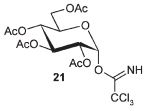
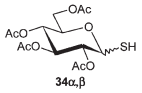
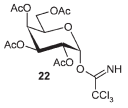
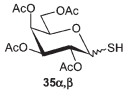
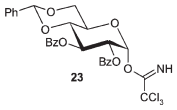
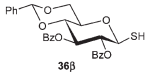
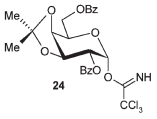
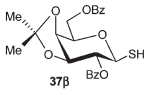
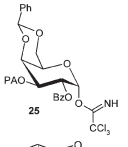
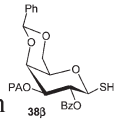
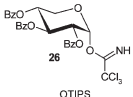
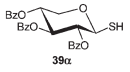
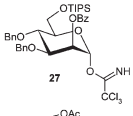
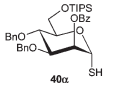
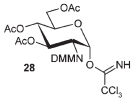
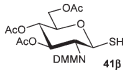
Table 1. Synthesis of Glycothiols 15 and 29−41[a]

Entry	Substrate	Time	Product	Yield (%)[b]	α/β ratio
1		30 min		86	α only
2		5 min		79	α only
3		30 min		55	α only
4		1 h		73	α only
5		3 h		76	α only
6		30 min		62	1:1
7		1 h		65	α + traces of β
8		2 h		77	1:1
9		1 h		61	β only
10		1 h		50	β only
11		30 min		58	β only
12		3 h		61	β only
13		1 h		81	α only
14		3 h		52	β only

[a] All reactions were carried out under the conditions shown in Scheme 4. [b] Isolated yields following chromatography. Abbreviations: DMM = dimethylmaleoyl; TBDPS = *tert*-butyldiphenylsilyl; TIPS = tri-isopropylsilyl; PA = phenoxyacetyl.

Scheme 5. Synthesis of β-(Glycosylthio)acrylate 42 and 43

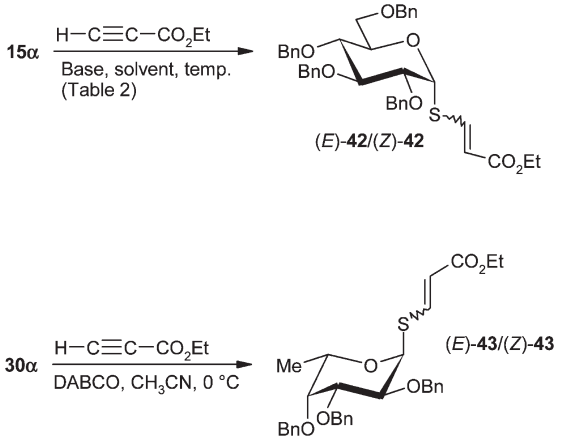


Table 2. Reaction Conditions for the Synthesis of 42

entry	base[a]	solvent	temp (°C)	time	yield (%)	E/Z
1	NMM	Et_2O	rt	12 h	90	68/32
2	NMM	Et_2O	−78	12 h	90	75/25
3	NMM	Et_2O	0	12h	87	73/27
4	Et_3N	Et_2O	0	12 h	88	78/22
5	Et_3N	Et_2O	0	12 h	81	78/22
6	Et_3N	CH_2Cl_2	0	12 h	86	76/24
7	DBU	Et_2O	0	12 h	85	66/44
8	DABCO	CH_3CN	0	30 min	92	93/07
9	DABCO	THF	0	30 min	89	94/06
10	Cs_2CO_3	Et_2O	0	12 h	81	72/28

[a] Abbreviations: NMM = *N*-methyl morpholine, DABCO = 1,4-diazabicyclo[2.2.2]octane.

128.40, 128.37, 128.34, 128.1, 128.0, 127.96, 127.90, 127.77, 127.75, 127.6, 127.59, 127.56, 127.50, 103.6, 84.8, 83.5, 81.9, 81.8, 78.5, 77.9, 77.2, 75.69, 75.65, 75.1, 74.9, 74.79, 74.71, 73.5, 72.7, 69.0, 68.1, 31.4. HRMS ($C_{63}H_{66}O_{11}S$): $[M + Na]^+$ m/z 1053.4224, found 1053.4233.

3,4,6-Tri-*O*-benzyl-1-thio-α,β-D-glucopyranose (8α,β). To a solution of **7** (200 mg, 0.46 mmol) and bis(trimethylsilyl) sulfide (146 μL, 0.69 mmol) in CH_2Cl_2 (10 mL) was added TMSOTf (0.042 mL, 0.23 mmol) at 0 °C. The reaction mixture was then stirred at 0 °C until TLC indicated complete consumption of the starting material (3 h), then poured into aqueous $NaHCO_3$, and extracted with EtOAc. The organic layer was washed successively with water and brine, dried over $MgSO_4$, and concentrated in vacuo to give a residue that was purified by flash column chromatography with petroleum ether/EtOAc (4:1) to afford **8** (120 mg, 56%) (α/β = 64:36) as a colorless oil. **8α,β** $[\alpha]_D$ = +29.0 (*c* 0.21, $CHCl_3$). HRMS ($C_{27}H_{30}O_5S$): $[M + Na]^+$ m/z 489.1712, found 489.1722.

Acetylation under standard conditions afforded 1,2-di-*S*,*O*-acetyl-3,4,6-tri-*O*-benzyl-1-thio-α-D-glucopyranose (**9α,β**) as a colorless oil (96%). $[\alpha]_D$ = +14.2 (*c* 0.23, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.47−7.05 (m, 24H), 6.25 (d, *J* = 5.4 Hz, 1H), 5.27−5.23 (dd, *J* = 10.0, 5.2 Hz, 1H), 5.17 (t, *J* = 8.4 Hz, 1H), 5.13 (dd, *J* = 10.0, 2.0 Hz, 1H), 4.86−4.80 (m, 4H), 4.76 (d, *J* = 12.8 Hz, 1H),4.70 (d, *J* = 12.0 Hz, 2H), 4.60 (dd, *J* = 12.2, 4.4 Hz, 2H), 4.53 (dd, *J* = 12.0, 3.9 Hz, 2H), 3.82−3.78 (m, 4H), 3.70 (t, *J* = 8.6 Hz, 2H), 3.65 (tt, *J* = 2.4 Hz, 1H) 2.44 (s, 3H), 2.41 (s, 1H), 2.01 (s, 3H), 1.97 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.2, 192.1, 169.6, 138.2, 137.94, 137.91, 128.45, 128.40, 128.0, 127.8, 127.75, 127.71, 127.6, 127.5, 84.4, 81.6, 81.0, 80.9, 79.7, 77.2, 75.4, 75.3, 75.2, 75. 0, 73.58, 73.51, 71.7, 71.1, 68.3, 68.2, 31.4,

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30.9, 20.87, 20.80. HRMS ($C_{31}H_{34}O_7S$): $[M + Na]^+$ m/z 573.1923, found 573.1916.

Benzyl 3,4,6-Tri-*O*-benzyl-1-thio-α-D-glucopyranoside (10). As described for **3**, **10** (40 mg, 67%) was obtained from **8** (50 mg, 0.10 mmol) as a colorless oil. $[\alpha]_D$ = +37.0 (c 0.45, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.28 (m, 18 H), 7.26−7.18 (m, 2 H), 5.35 (d, J = 5.4 Hz, 1 H), 4.85 (dd, J = 24.6, 11.2 Hz, 3 H), 4.67 (d, J = 12.1 Hz, 1 H), 4.56 (dd, J = 10.8, 7.9 Hz, 2 H), 4.19−4.17 (br. m, 1 H), 3.94 (dd, J = 8.9, 5.6 Hz, 1 H), 3.84 (d, J = 13.3 Hz, 1 H), 3.78−3.75 (m, 2 H), 3.68 (dd, J = 6.0, 3.5 Hz, 2 H), 3.56 (dd, J = 10.7, 1.9 Hz, 1 H), 2.14 (d, J = 5.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 138.0, 137.9, 137.8, 129.0, 128.56, 128.51, 128.42, 128.41, 127.9, 127.87, 127.85, 127.77, 127.74, 127.1, 85.0, 83.5, 75.3, 74.8, 73.5, 72.1, 71.5, 68.4, 34.5. HRMS ($C_{34}H_{36}O_5S$): $[M + Na]^+$ m/z 579.2181, found 579.2175.

***S*-(2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-glucopyranoside (11).** To a solution of **8** (35 mg, 0.07 mmol) and **4** (50 mg, 0.07 mmol) in dry CH_2Cl_2 (5 mL) was added TMSOTf (0.007 mL, 0.03 mmol) at 0 °C. The reaction mixture was then stirred at 0 °C until TLC indicated complete consumption of the starting material. The reaction was quenched by adding triethyl amine. The reaction mixture was diluted with CH_2Cl_2 (10 mL) washed with water. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography with petroleum ether/EtOAc (10:3) to afford **11** (45 mg, 61%) as a white solid. $[\alpha]_D$ = +25.0 (c 0.38, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.29 (m, 31 H), 7.23−7.17 (m, 4 H), 5.68 (d, J = 4.4 Hz, 1 H), 5.57 (d, J = 5.4 Hz, 1 H), 4.98 (d, J = 10.8 Hz, 1 H), 4.88 (d, J = 10.8 Hz, 4 H), 4.81 (d, J = 10.8 Hz, 1 H), 4.74 (d, J = 11.8 Hz, 1 H), 4.64−4.61(m, 3 H), 4.58−4.54 (m, 3 H), 4.51−4.48 (m, 2 H), 4.30 (d, J = 6.2 Hz, 2 H), 3.99 (dd, J = 5.4, 9.4 Hz, 1 H), 3.89−3.87 (m, 2 H), 3.78−3.73 (m, 2 H), 3.70 (s, 2 H), 3.68 (s, 2 H), 3.66 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 138.4, 138.2, 137.9, 137.8, 137.6, 128.5, 128.42, 128.41, 128.38, 128.35, 128.0, 127.99, 127.91, 127.89, 127.85, 127.7, 127.6, 83.7, 83.3, 82.6, 81.4, 78.9, 77.5, 75.7, 75.4, 75.0,74.8, 74.7, 73.5, 73.4, 72.4, 72.1, 71.9, 71.2, 68.6, 29.7. HRMS ($C_{61}H_{64}O_{10}S$): $[M + Na]^+$ m/z 1011.4118, found 1011.4128.

Acetylation of **11** under standard conditions afforded *S*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl) 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-1-thio-α-D-glucopyranoside (**12**) as a colorless oil (69%). $[\alpha]_D$ = +31.0 (c 0.32, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.19 (m, 31 H), 7.11 (dd, J = 7.8, 2.4 Hz, 2 H), 7.04 (dd, J = 7.5, 3.3 Hz, 2 H), 5.73 (d, J = 5.7 Hz, 1 H), 5.57 (d, J = 4.9 Hz, 1 H), 4.96 (dd, J = 10.0, 5.7 Hz, 1 H), 4.87 (d, J = 10.8 Hz, 1 H), 4.76−4.64 (m, 5 H), 4.60−4.55 (m, 2 H), 4.48 (s, 1 H), 4.45−4.43 (m, 2 H), 4.40−4.34 (m, 3 H), 4.25−4.20 (m, 1 H), 3.94 (d, J = 9.9 Hz, 1 H), 3.85 (t, J = 9.5 Hz, 1 H), 3.75−3.69 (m, 3 H), 3.64−3.58 (m, 3 H), 3.55−3.51 (m, 2 H), 1.89 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 138.7, 138.3, 138.1, 137.96, 137.93, 137.6, 128.4, 128.39, 128.38, 128.02, 128.00, 127.96, 127.93, 127.8, 127.74, 127.70, 82.7, 81.1, 80.6, 79.1, 78.7, 77.7, 77.1, 75.7, 75.5, 75.2, 74.9, 73.6, 73.5, 73.0, 72.1, 71.8, 71.4, 68.1, 29.7, 20.9. HRMS ($C_{63}H_{66}O_{11}S$): $[M + Na]^+$ m/z 1053.4224, found 1053.4232.

3,4,6-Tri-*O*-benzyl-1-*S*,2-*O*-methylidene-1-thio-α-D-glucopyranose (14). To a solution of **8** (50 mg, 0.10 mmol) in dry CH_2Cl_2 (5 mL) was added DBU (0.032 mL, 0.21 mmol) at room temperature. The reaction mixture was then stirred at room temperature until TLC indicated complete consumption of the starting material and then concentrated in vacuo. The residue was purified by flash column chromatography with petroleum ether/EtOAc (10:1) to afford **14** (21 mg, 40%) as a white solid. $[\alpha]_D$ = +41.0 (c 0.22, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.19 (m, 13 H), 7.12−7.10 (m, 2 H), 6.01 (d, J = 4.8 Hz, 1 H), 5.11 (d, J = 5.7 Hz, 1 H), 4.67 (d, J = 5.7 Hz, 1 H), 4.61 (d, J = 11.9 Hz, 1 H), 4.56−4.50 (m, 2 H), 4.48 (d, J = 12.1 Hz, 1 H), 4.41 (d, J = 12.1 Hz, 1 H), 4.31 (d, J = 11.4 Hz, 1 H), 4.00−3.95 (m, 2 H), 3.91 (t, J = 4.2 Hz, 1 H), 3.68−3.65 (m, 1 H), 3.52−3.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1, 137.8, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.89, 127.87, 127.6, 85.8, 82.5, 76.8, 75.7, 73.3, 73.0, 72.4, 71.3, 70.6, 69.3. HRMS ($C_{28}H_{30}O_5S$): $[M + Na]^+$ m/z 501.1712, found 501.1719. Addition of only 1 equiv of DBU permitted the isolation of chloromethyl 3,4,6-tri-*O*-benzyl-1-thio-α-D-glucopyranoside (**13**) intermediate. $[\alpha]_D$ = +5.1 (c 0.46, $CHCl_3$). HRMS ($C_{28}H_{31}ClO_5S$): $[M + Na]^+$ m/z 537.1478, found 537.1489.

***O*-(2-Azido-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-α-D-galactopyranosyl) Trichloroacetimidate (18).** General procedure for the synthesis of **18** and **24**. To a solution of the 1-*O*-unprotected sugar (1 mmol) in CH_2Cl_2 (5 mL) were added successively Cl_3C-CN (1 mL, 10 mmol) and DBU (35 μL, 0.25 mmol) at 0 °C. After stirring for 15 min, the mixture was directly chromatographed on SiO_2 (toluene/EtOAc) to give **18** and **24**, respectively, in practically quantitative yield. **18**: $[\alpha]_D$ = +4.62 (c 1.50, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.73−7.69 (m, 3H), 7.39−7.30 (m, 17H), 6.64 (d, J = 3.4 Hz, 1H), 4.98 (t, J = 10.0 Hz, 2H), 4.86 (dd, J = 12.2,11.0 Hz, 2H), 4.72 (dd, J = 13.7, 11.7 Hz, 2H), 4.19−4.09 (m, 1H), 3.99−3.85 (m, 3H), 3.80 (dd, J = 9.5, 3.5 Hz, 1H), 1.00 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3,138.5, 138.1, 135.8, 135.6, 133.5, 133.1, 129.66, 129.62,128.46, 128.42, 128.32, 128.2, 128.0, 127.8, 127.68, 127.63, 127.5, 94.3, 91.4, 81.5, 79.9, 75.8, 75.4, 74.3, 72.9, 62.4, 26.8, 19.3. HRMS ($C_{38}H_{41}Cl_3N4O_5Si$): $[M + Na]^+$ m/z 789.1809, found 789.1826.

***O*-(2,6-Di-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-galactopyranosyl) Trichloroacetimidate (24).** From 2,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-D-galactose,[36] **24** was obtained as described in the procedure for **18**. **24**: $[\alpha]_D$ = +55.6 (c 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1 H), 8.06−8.04 (m, 4 H), 7.60−7.56 (m, 2 H), 7.46 (td, J = 7.8, 2.6 Hz, 4 H), 6.61 (d, J = 3.7 Hz, 1 H), 5.55 (dd, J = 7.1, 3.8 Hz, 1 H), 4.74−4.68 (m, 3 H), 4.62−4.59 (m, 1 H), 4.53−4.51 (m, 1 H), 1.62 (s, 3 H), 1.41 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 165.5, 160.4, 133.4, 133.1, 129.89, 129.84, 129.7, 129.2, 128.43, 128.40, 110.7, 93.4, 90.8, 73.1, 72.9, 69.7, 68.8, 63.6, 27.6, 26.1. HRMS ($C_{25}H_{24}Cl_3NO_8$): $[M + Na]^+$ m/z 594.0465, found 594.0442.

General Procedure A for the Synthesis of Glycosylthiols 15 and 29−41. Synthesis of 2,3,4,6-tetra-*O*-benzyl-1-thio-α-D-glucopyranose (**15α**). To a solution of **4**[20] (100 mg, 0.14 mmol) and bis(trimethylsilyl) sulfide (0.031 mL, 0.14 mmol) in CH_2Cl_2 (5 mL) was added TMSOTf (0.005 mL, 0.02 mmol) at 0 °C. The mixture was stirred at 0 °C until TLC indicated complete consumption of the starting material, then poured into aqueous $NaHCO_3$, and extracted with EtOAc. The organic layer was washed successively with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography with petroleum ether/EtOAc (10:2) to afford **15α** (70 mg, 86%) as a colorless oil. The physical properties found for **15α** are in accordance with those reported previously.[11a]

6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-1-thio-α-D-galactopyranose (29α). By means of general procedure A **29α** was obtained from **16**[23] and BTMSS; see Table 1. $[\alpha]_D$ = +32.0 (c 0.46, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20−7.10 (m, 15 H), 5.63 (t, J = 4.3 Hz, 1 H), 4.77 (d, J = 11.4 Hz, 1 H), 4.68 (d, J = 11.7 Hz, 1 H), 4.57 (d, J = 4.9 Hz, 1 H), 4.54 (d, J = 4.6 Hz, 1 H), 4.50 (d, J = 11.5 Hz, 1 H), 4.44 (d, J = 11.4 Hz, 1 H), 4.14−4.10 (m, 1 H), 4.05 (dd, J = 9.4, 5.1 Hz, 1 H), 3.98 (dd, J = 11.4, 6.9 Hz, 1 H), 3.91 (dd, J = 11.4, 5.4 Hz, 1 H), 3.70−3.69 (m, 1 H), 3.63 (dd, J = 9.5, 2.6 Hz, 1 H), 1.81 (s, 3 H), 1.67 (d, J = 4.1 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 138.4, 138.0, 137.8, 128.47, 128.43, 128.42, 127.96, 127.91, 127.8, 127.7, 127.5, 79.1, 78.4, 75.9, 74.5, 74.3, 73.6, 72.7, 69.8, 63.0, 20.8. HRMS ($C_{29}H_{32}O_6S$): $[M + Na]^+$ m/z 531.1817, found 531.1833.

2-Azido-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-1-thio-α-D-galactopyranose (31α). By means of general procedure A **31α** was obtained from **18** and BTMSS; see

Table 1. $[\alpha]_D$ = +37.5 (*c* 0.59, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.55−7.51(m, 3H), 7.20−7.10 (m, 17 H), 5.65 (t, *J* = 4.9 Hz, 1 H), 4.78 (t, *J* = 10.0 Hz, 2H), 4,65 (dd, *J* = 13.8, 10.7 Hz, 2H),4,52 (dd, *J* = 10.7, 6.4 Hz, 2H), 3.99 (dd, *J* = 9.8, 1.7 Hz, 1H), 3.85 (dd, *J* = 11.5, 3.5 Hz, 1H), 3.79−3.61 (m, 2H), 1.71 (d, *J* = 4.5 Hz, 1H), 0.91 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.56, 138.30, 137.7, 135.85, 135.66, 134.81, 129.6, 129.60, 128.51, 128.45, 128.42, 128.0, 127.9, 127.8, 127.7, 127.5, 81.9, 79.7, 78.8, 75.9, 75.1, 72.5, 72.3,62.7, 26.8, 19.3.HRMS ($C_{36}H_{41}N_3O_4SSi$): $[M + Na]^+$ *m*/*z* 662.2485, found 662.2465.

2,3,4−6-Tetra-*O*-acetyl-β-D-glucopyranosyl-(1−4)-3,6-di-*O*-acetyl-2-azido-2-deoxy-1-thio-α-D-glucopyranose (32α). By means of general procedure A **32α** was obtained from **19**[25] and BTMSS; see Table 1. $[\alpha]_D$ = +22.1 (*c* 0.21, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 5.43 (t, *J* = 4.4 Hz, 1 H), 5.13 (d, *J* = 2.6 Hz, 1 H), 5.08 (t, *J* = 9.6 Hz, 1 H), 4.89 (dd, *J* = 10.3, 7.8 Hz, 1 H), 4.74 (dd, *J* = 10.4, 3.4 Hz, 1 H), 4.26−4.21 (m, 2 H), 4.09−4.05 (m, 1 H), 3.98−3.94 (m, 2 H), 3.92−3.87 (m, 1 H), 3.86−3.82 (m, 1 H), 3.67−3.63 (m, 2 H), 3.49 (t, *J* = 9.6 Hz, 1 H), 1.93 (s, 3 H), 1.89 (s, 6 H), 1.84 (s, 3 H), 1.82−1.81 (d, *J* = 4.3 Hz, 4 H), 1.74 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 170.3, 170.17. 170.12, 170.3, 169.3, 168.9, 100.9, 78.0, 76.0, 71.0, 70.79, 70.7, 69.7, 69.0, 66.6, 62.0, 61.6, 60.8, 20.8, 20.6, 20.5. HRMS ($C_{24}H_{33}N_3O_{15}S$): $[M + Na]^+$ *m*/*z* 658.1530, found 658.1504.

2,3-Di-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranose (36β). By means of general procedure A **36β** was obtained from **23**[30] and BTMSS; see Table 1. $[\alpha]_D$ = +31.1 (*c* 0.12, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.03−8.00 (m, 4 H), 7.57−7.52 (m, 4 H), 7.45−7.38 (m, 7 H), 5.86 (t, *J* = 9.8 Hz, 1 H), 5.60 (s, 1 H), 5.42 (dd, *J* = 10.0, 3.6 Hz, 1 H), 4.85 (t, *J* = 9.9 Hz, 1 H), 4.69 (d, *J* = 2.8 Hz, 1 H), 4.49 (dd, *J* = 12.5, 1.5 Hz, 1 H), 4.16 (dd, *J* = 12.5, 1.7 Hz, 1 H), 3.78 (d, *J* = 1.0 Hz, 1 H), 2.56 (d, *J* = 10.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 165.5, 133.4, 133.3, 129.9, 129.8, 129.0, 128.46, 128.42, 128.1, 126.2, 100.8, 79.2, 73.8, 73.5, 71.6, 70.6, 69.1. HRMS ($C_{27}H_{24}O_7S$): $[M + Na]^+$ *m*/*z* 515.1140, found 515.1129.

2,6-Di-*O*-benzoyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranose (37β). By means of general procedure A **37β** was obtained from **24** and BTMSS; see Table 1. $[\alpha]_D$ = +90.1 (*c* 1.21, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.02−7.97 (m, 4 H), 7.51 (t, *J* = 7.4 Hz, 2 H), 7.40−7.36 (m, 4 H), 5.26−5.22 (m, 1 H), 4.61 (dd, *J* = 11.8, 4.6 Hz, 1 H), 4.55−4.49 (m, 2 H), 4.32−4.30 (m, 2 H), 4.18−4.15 (m, 1 H), 2.39 (d, *J* = 9.9 Hz, 1 H), 1.56 (s, 3 H), 1.30 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 165.7, 133.4, 133.2, 129.9, 129.7, 129.5, 128.4, 111.0, 78.0, 77.3, 75.2, 74.7, 73.6, 63.9, 27.6, 26.2. HRMS ($C_{23}H_{24}O_7S$): $[M + Na]^+$ *m*/*z* 467.1140, found 467.1124.

2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-phenyloxyacetyl-1-thio-β-D-galactopyranose (38β). By means of general procedure A **38β** was obtained from **25**[31] and BTMSS; see Table 1. $[\alpha]_D$ = +10.1 (*c* 0.11, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.14−7.93 (d, *J* = 7.1 Hz, 2 H), 7.68−7.40 (m, 8 H), 7.04 (dd, *J* = 8.6, 7.5 Hz, 2 H), 6.87 (t, *J* = 7.5 Hz, 1 H), 6.72 (d, *J* = 8.6 Hz, 2 H), 5.64 (t, *J* = 9.8 Hz, 1 H), 5.54 (s, 1 H), 5.29 (dd, *J* = 10.0, 3.6 Hz, 2 H), 4.70 (t, *J* = 10.2 Hz, 1 H), 4.62 (d, *J* = 16.5 Hz, 1 H), 4.56−4.47 (m, 2 H), 4.38 (dd, *J* = 12.6, 1.4 Hz, 1 H), 4.07 (dd, *J* = 12.6, 1.7 Hz, 1 H), 3.66 (d, *J* = 1.0 Hz, 1 H), 2.50 (d, *J* = 10.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 165.4, 157.4, 137.2, 133.6, 129.9, 129.3, 129.2, 129.1, 128.6, 128.3, 126.3, 121.7, 114.3, 101.0, 79.1, 73.5, 73.4, 71.3, 70.3, 69.0, 64.7. HRMS ($C_{28}H_{26}O_8S$): $[M + Na]^+$ *m*/*z* 545.1246, found 545.1226.

2,3,4-Tri-*O*-benzyl-1-thio-β-D-xylopyranose (39β). By means of general procedure A **39β** was obtained from **26**[32] and BTMSS; see Table 1. $[\alpha]_D$ = +7.1 (*c* 0.11, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.04−7.87 (m, 6 H), 7.61−7.45 (m, 3 H), 7.40−7.29 (m, 6 H), 5.78 (t, *J* = 8.0 Hz, 1 H), 5.40 (t, *J* = 7.8 Hz, 1 H), 5.38−5.34 (m, 1 H), 5.00 (dd, *J* = 9.4, 7.7 Hz, 1 H), 4.54 (dd, *J* = 11.9, 4.8 Hz, 1 H), 3.69 (dd, *J* = 11.9, 8.4 Hz, 1 H), 2.44 (d, *J* = 9.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 165.4, 165.3, 133.4, 133.3 (2 C), 129.9−129.8 (3 C), 129.1, 128.9, 128.4 (2 C), 78.8, 73.2, 71.8, 69.2, 65.4. HRMS ($C_{26}H_{22}O_7S$): $[M + Na]^+$ *m*/*z* 501.0984, found 501.0965.

3,4-Di-*O*-benzyl-2-*O*-benzoyl-6-*O*-tri-isopropylsilyl-1-thio-α-D-mannopyranose (40α). By means of general procedure A **40α** was obtained from **27**[33] and BTMSS; see Table 1. $[\alpha]_D$ = +2.2 (*c* 0.08, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.04−8.01 (m, 2H), 7.53−7.48 (m, 1H), 7.38−7.34 (m, 2H), 7.27−7.17 (m, 10H), 5.60−5.57 (m, 2H), 4.81 (d, *J* = 10.6 Hz, 1H), 4.70 (d, *J* = 11.4 Hz, 1H), 4.65 (d, *J* = 10.6 Hz, 1H), 4.53 (d, *J* = 11.4 Hz, 1H), 4.12 (t, *J* = 9.5 Hz, 1H), 4.08 (dd, *J* = 11.2, 3.2 Hz, 1H), 4.02 (dd, *J* = 9.4, 3.0 Hz, 1H), 3.94 (m, 1H), 3.88 (dd, *J* = 11.2, 1.5 Hz, 1H), 2.08 (d, *J* = 7.2 Hz, 1H), 1.05 −1.00 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 138.5, 137.7, 133.2, 133.0, 129.8, 128.39, 128.34, 128.1, 128.0, 127.7, 127.6, 77.6, 77.2, 75.4, 74.0, 73.9, 72.1, 71.8, 62.3, 18.07, 18.03, 12.0. HRMS ($C_{36}H_{48}O_6SSi$): $[M + Na]^+$ *m*/*z* 659.2839, found 659.2820.

3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,3-dimethylmaleinimido)-2-deoxy-1-thio-β-D-glucopyranose (41β). By means of general procedure A **41β** was obtained from **28**[34] and BTMSS; see Table 1. $[\alpha]_D$ = +6.2 (*c* 0.10, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 5.57 (t, *J* = 10.0 Hz, 1H), 5.26 (t, *J* = 10.2 Hz, 1H), 5.08 (t, *J* = 10.0 Hz, 1H), 4.24 (dd, *J* = 12.4, 4.7 Hz, 1H), 4.08−4.05 (m. 1H), 3.97 (t, *J* = 10.3 Hz, 1H), 3.78−3.74 (m, 1H), 2.12 (d, *J* = 10.2 Hz, 1H), 2.04 (s, 3H), 1.95 s, 3H), 1.90 (s, 6), 1.85 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.74, 170.0, 169.79, 169.4, 132.6, 106.1 77.2, 76.49, 76.32, 71.3, 68.5, 62.0, 57.6, 20.8, 20.62, 20.53, 8.9. HRMS($C_{18}H_{23}NO_9S$): $[M + Na]^+$ *m*/*z* 452.0991, found 452.0981.

Ethyl (*E*/*Z*)-3-(2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyransoylthio)-acrylate [(*E*/*Z*)-42]. To a solution of **15α** (260 mg, 0.46 mmol) and ethyl propiolate (46 mg, 0.46 mmol) in dry THF (5 mL) was added DABCO (52 mg, 0.46 mmol) or NMM (47 mg, 0.46 mmol) at room temperature. The mixture was stirred at room temperature until TLC indicated complete consumption of the starting material. The organic layer was washed successively with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography with petroleum ether/EtOAc (10:1) to afford **42** (272 mg, 89%) as a colorless oil (*E*/*Z* mixture, see Table 2). *E* isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 15.4 Hz, 1 H), 7.38−7.30 (m, 18 H), 7.19−7.17 (m, 2 H), 6.13 (d, *J* = 15.4 Hz, 1 H), 5.75 (d, *J* = 5.3 Hz, 1 H), 4.98 (d, *J* = 10.8 Hz, 1 H), 4.87−4.81 (m, 2 H), 4.75 (d, *J* = 11.6 Hz, 1 H), 4.70−4.64 (m, 2 H), 4.55 (d, *J* = 10.8 Hz, 1 H), 4.51 (d, *J* = 12.0 Hz, 1 H), 4.27−4.19 (m, 2 H), 4.02 (d, *J* = 9.8 Hz, 1 H), 3.97 (dd, *J* = 9.3, 5.3 Hz, 1 H), 3.88 (d, *J* = 8.9 Hz, 1 H), 3.83−3.80 (m, 1 H), 3.77 (d, *J* = 9.3 Hz, 1 H), 3.67 (dd, *J* = 10.9, 1.8 Hz, 1 H), 1.33 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 143.2, 138.4, 138.0 137.7, 137.2, 128.5, 128.42, 128.40, 128.13, 128.10, 127.97, 127.95, 127.8, 127.77, 127.72, 117.4, 84.1, 82.4, 78.8, 76.8, 75.8, 75.1, 73.5, 72.8, 71.8, 68.0, 60.3, 14.3. *Z* isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 6.00 (d, *J* = 10.3 Hz, 1H), 5.66 (t, *J* = 5.8 Hz, 2H), 5.51 (d, *J* = 5.2 Hz, 1H), 5.42 (d, *J* = 3.8 Hz, 1H), 1.36 (d, *J* = 7.1 Hz, 3H). HRMS ($C_{39}H_{42}O_7S$): $[M + Na]^+$ *m*/*z* 677.2549, found 677.2527.

Ethyl (*E*/*Z*)-3-(2,3,4-Tri-*O*-benzyl-α-L-fucopyranosylthio)-acrylate [(*E*/*Z*)-43]. By means of the procedure for **42** (*E*/*Z*)-**43** was obtained from **30α** and ethyl propiolate; see Table 2. ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 15.5 Hz, 1 H), 7.35−7.24 (m, 15 H), 6.01 (d, *J* = 15.5 Hz, 1 H), 5.72 (d, *J* = 5.4 Hz, 1 H), 4.95 (d, *J* = 11.5 Hz, 1 H), 4.81 (d, *J* = 11.9 Hz, 1 H), 4.71−4.62 (m, 4 H), 4.43−4.29 (m, 2 H), 4.39−4.13 (m, 3 H), 3.98 (qt, *J* = 6.7 Hz, 1 H), 3.72 (dd, *J* = 9.9, 2.8 Hz, 1 H), 3.63 (d, *J* = 1.9 Hz, 1 H), 1.24 (t, *J* = 7.1 Hz, 3 H), 1.11 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 143.9, 138.5, 138.3, 137.7, 128.4−127.5 (9 C), 116.9, 84.7, 79.7, 75.6, 75.0, 73.4, 72.8, 68.3, 60.2, 16.5, 14.3. *Z* isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 12.2 Hz, 1 H), 6.78 (d, *J* = 16.0 Hz, 1 H), 6.46 (d, *J* = 16.0 Hz, 1 H), 5.65 (d, *J* = 12.2 Hz, 1 H). HRMS ($C_{32}H_{37}O_6S$): $[M + H]^+$ *m*/*z* 549.2311, found 549.2325.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H NMR and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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