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Synthesis of α-Glycosyl Thiols by Stereospecific Ring-Opening of 1,6-Anhydrosugars

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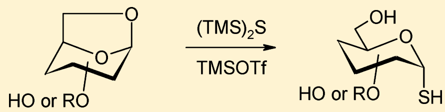
Supporting Information

ABSTRACT: Treatment of 1,6-anhydrosugars with commercially available bis(trimethylsilyl) sulfide in the presence of trimethylsilyl triflate led to the formation of α-glycosyl thiols. All the reactions were highly stereoselective and afforded the α-glycosyl thiols in good to excellent yields. By this procedure, a variety of 1,6-anhydrosugars, differing in their sugar units, glycosidic linkages, and protecting group pattern, were converted smoothly into the corresponding α-glycosyl thiols, which could be of great utility in thioglycoside chemistry. It is noteworthy that 1,6-anhydrosugars carrying the 2-*O*-acyl group and 1,6-anhydrosugar-containing oligosaccharides could also be ring-opened stereospecifically under the same conditions to give rise to the corresponding 1-thiosugars in high yields. Thus, a very concise and efficient access to α-glycosyl thiols of great value was established.



INTRODUCTION

Among glycomimetics, thioglycosides have been the subject of significant interest as they often exhibit higher stability against chemical and enzymatic hydrolysis and similar solution conformation compared to the corresponding *O*-glycosides.[1] The higher stability of thioglycosides could be ascribed to the lower proton affinity of sulfur in comparison to *O*-glycosides. According to the hard−soft acid−base (HSAB) theory, sulfur behaves more like soft base while oxygen is a hard base; a hard acid like proton is thus prone to attack the hard base *O*-glycosides, not the soft base thioglycosides. A similar solution conformation of thioglycosides may result from the relatively small difference between the positions of the atoms along the glycosidic linkage compared to *O*-glycosides. The C−S bond is longer than the C−O bond, but the C−S−C bond angle is smaller than the C−O−C angle, which renders thioglycoside sharing a similar overall conformation with the corresponding *O*-glycosides. Moreover, thioglycosides usually possess similar or even more potent bioactivities compared to *O*-glycosides. Owing to these properties, thioglycosides, including thiooligosaccharides and *S*-glycoconjugates, have frequently been the synthetic targets in carbohydrate chemistry in the past few decades.[2,3]

Glycosyl thiols[4] (sometimes called 1-thiosugars) or their precursors, such as anomeric thioacetates,[5] which can be *S*-deacetylated *in situ* to generate the desired glycosyl thiols, are becoming the key building blocks for the construction of various thiooligosaccharides and *S*-glycoconjugates.[2,6] Unlike the normal sugar hemiacetals, which could mutarotate easily under most conditions, glycosyl thiols are quite stable in terms of configuration, and their mutarotation does not occur readily. In contrast, it is highly restricted, and even blocked under basic conditions,[7] as such, the anomeric configuration of glycosyl thiols can be maintained during the glycosylation process.

In addition to their wide application in *S*-glycoside synthesis, glycosyl thiols are also useful in the synthesis of many other carbohydrate contexts, such as methylene *exo*-glycal[8] and *C*-glycoside synthesis,[9] glycosyl sulfenamide and glycosyl sulfonamide synthesis,[10] and glycosyl disulfide synthesis.[11] Also, glycosyl thiol was a key intermediate in the construction of a structurally challenging α-SO_2-galacturonylsphingolipid mimetic,[12] which otherwise would be troublesome to get by conventional glycosidation procedure due to the low reactivity of glycuronide donors. Glycosyl thiols have also been employed to prepare carbohydrate thionolactones,[13] which could be useful in the construction of spiro-*C*/*O*-glycoside-containing natural products. Recently, glycosyl thiols were converted into a new class of glycoslating agents, glycosyl *N*-phenyl-trifluorothioacetimidates,[14] which could be activated effectively with catalytic amounts of Lewis acid. In addition, novel sugar species have been developed from glycosyl thiols, such as GTM-Cl,[15] which could be applied in the synthesis of various neoglycoconjugates. Recently, glycosyl thiol was also used to generate the transient species, glycosylsulfenic acid.[16]

The great utility and potential that glycosyl thiols have exhibited in contemporary carbohydrate chemistry brought great impetus to develop procedures for the stereoselective preparation of both α- and β-glycosyl thiols. Of them, β-glycosyl thiols, such as β-glucosyl thiol and β-galactosyl thiol, could be readily obtained by treatment of the corresponding α-glycosyl halides with thiourea followed by hydrolysis with alkali metal disulfite.[17] However, prior to our work,[18,19] in the literature no direct procedure for the stereoselective preparation of normal α-glycosyl thiols has been reported,[20] although α-GlcNAc- and α-GalNAc-derived anomeric thiols could be readily prepared

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from the corresponding *per*-acetylated sugars by virtue of their neighboring acetamide groups.[21] So far, only β-glycosyl chlorides have been used occasionally to prepare α-glycosyl thiols in a multistep procedure;[20a] nevertheless, the reproducibility of this procedure is very low due to the highly reactive β-chlorides. Recently, Davis et al. reported an efficient procedure for the preparation of glycosyl thiols in which the Lawesson reagent was found capable of directly converting reducing sugars or unprotected sugars into the corresponding glycosyl thiols.[22] However, in this procedure configurationally unpure glycosyl thiols were often produced.

Therefore, the development of a direct and stereoselective procedure for the synthesis of α-glycosyl thiols seems to be of great importance. Such a procedure would not only facilitate the synthesis of α-*S*-linked saccharides and glycoconjugates but also expand greatly other applications of glycosyl thiols, eventually expediting the development of thioglycoside chemistry. In a previous communication,[18] we reported a stereospecific method for the synthesis of α-glycosyl thiols by ring-opening of 1,6-anhydrosugars with bis(trimethylsilyl) sulfide. We describe here a full account of the method and its applicability to a wide range of substrates including 2-*O*-acyl group-protected 1,6-anhydrosugars and oligosaccharides.

■ RESULTS AND DISCUSSION

The major challenge associated with the synthesis of α-glycosyl thiols lies in the stereoselectivity, i.e., how to α-selectively introduce a sulfhydryl group onto an anomeric center. In principle, this can be implemented by activating a glycosyl donor without neighboring participating group in the presence of a proper sulfur nucleophile; however, such a normal glycosidation procedure did not always lead to the predominant formation of α-thiosugars. On the contrary, sometimes significant amounts of β-products were also produced in the glycosidation reactions,[5a] and the subsequent isolation of α-glycosyl thiols from the resulting α/β-mixture could be very tedious and difficult. Furthermore, in this way two or even more steps are usually required in order to obtain the thiols.

Seeing that most glycosidation reactions involving a donor without neighboring participating group generate a mixture of α- and β-glycosides, a procedure precluding such a normal glycosyl donor would be desirable in order to obtain α-glycosyl thiols in a highly stereoselective way. We envisioned that 1,6-anhydrosugars could serve perfectly as glycosylating agents for the synthesis of α-glycosyl thiols because they differ from normal glycosyl donors in structure and may thus undergo unusual glycosidation pathway (Figure 1). Conceivably, if

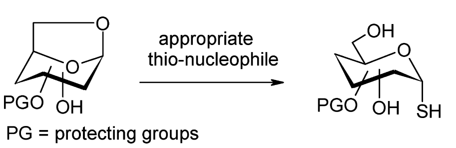


Figure 1. Proposed procedure for the synthesis of α-glycosyl thiols.

1,6-anhydrosugars are attacked by a nucleophile in an S_N2-type mode, it would give glycosides in α-only selectivity because β-face of 1,6-anhydrosugars is blocked by the intramolecular dioxolane ring.

Synthesis of 1,6-Anhydrosugars. To accomplish the chemistry outlined in Figure 1, we prepared a series of 1,6-anhydrosugars with different protecting group patterns and structural complexity. Known benzyl group-protected 1,6-anhydrosugars **1**[23] and **2**[24] (Figure 2) were first prepared

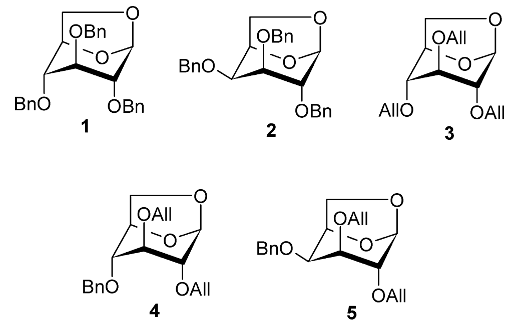
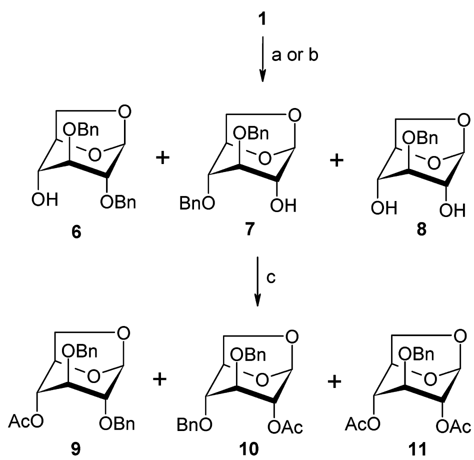


Figure 2. Prepared 1,6-anhydrosugars **1**−**5**.

from methyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranoside and methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside, respectively, according to the literature procedures.[24] 1,6-Anhydrosugars **3**,[25] **4**, and **5** were also prepared readily from the corresponding methyl glycosides following the same procedure. Here it should be mentioned that 1,6-anhydrosugars can also be easily prepared by other different procedures,[26] and many 1,6-anhydrosugars are commercially available as well.

In order to investigate the effect of electron-withdrawing acyl groups on the above proposed ring-opening reactions, we also synthesized a number of partially acylated 1,6-anhydrosugars. As shown in Scheme 1, compound **1** was first treated with one

Scheme 1. Synthesis of 1,6-Anhydrosugars 6−11[a]

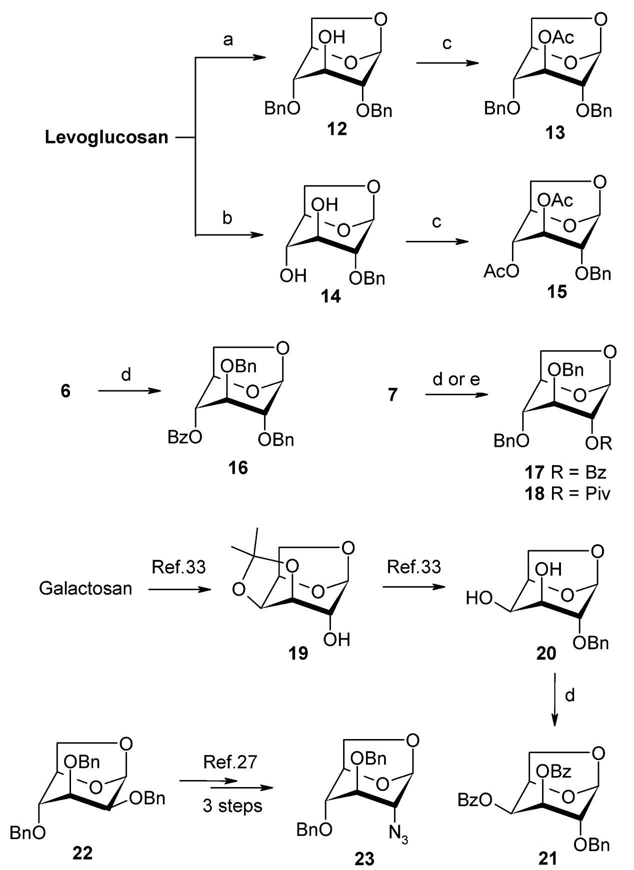


[a]Reagents: (a) 1.0 equiv of $SnCl_4$, CH_2Cl_2, **6** (46%), **7** (34%); (b) 1.3 equiv of $SnCl_4$, CH_2Cl_2, **6** (14%), **7** (9%), **8** (63%); (c) Ac_2O, Py, **9** (82%), **10** (86%), **11** (77%).

equivalent of $SnCl_4$ to produce the intermediates **6**[27] and **7**[27] in 46% and 34% yields, respectively, which could be separated by flash column chromatography. This regioselective debenzylation reaction could also give **8**[28] (63%) as the major product and **6** (14%) and **7** (9%) as the minor products when **1** was exposed to an excess of $SnCl_4$ for a prolonged time. Subsequently, **6**, **7**, and **8** were acetylated to give the corresponding 1,6-anhydrosugars **9**,[29] **10**, and **11** in 82%, 86%, and 77% yields, respectively.

Meanwhile, regioselective protection of commercially available levoglucosan with BnBr in the presence of BaO could generate smoothly the intermediate **12**,[30] which was acetylated subsequently to give 1,6-anhydrosugars 13[31] in 89% yield, as shown in Scheme 2. Also, levoglucosan could be monobenzylated regioselectively with BnBr under the action of $(Bu_3Sn)_2O$ to afford the intermediates 14,[32] which was again subjected to normal acetylation to furnish the fully protected levoglucosan 15.[32] Thus, two groups of 1,6-anhydrosugars, i.e., 9, 10, and 13 carrying one acetyl group at 4-O, 2-O, and 3-O positions, respectively, and 11 and 15 carrying two acetyl groups at 2,4-O and 3,4-O positions, respectively, are ready for testing the ring-opening reaction with appropriate thionucleophiles.

Scheme 2. Synthesis of 1,6-Anhydrosugars 12−23[a]

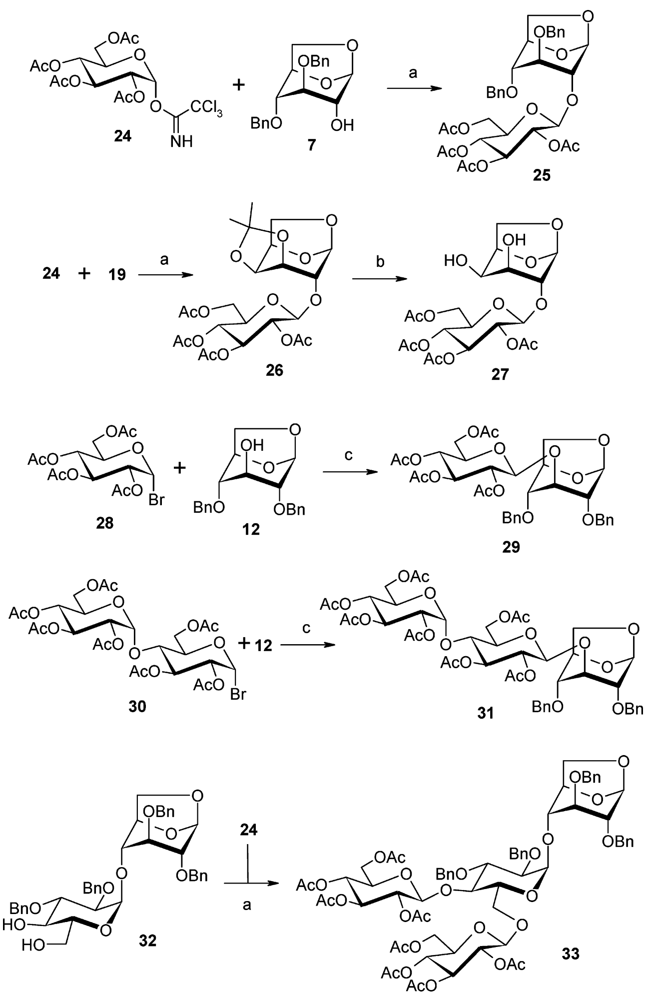


[a]Reagents and conditions: (a) BnBr, BaO, DMF, 60 °C, 96%; (b) BnBr, $(Bu_3Sn)_2O$, *N*-methylimidazole, toluene, 120 °C, 30%; (c) Ac_2O, Py, 13 (89%), 15 (72%); (d) BzCl, Py, 16 (81%), 17 (85%), 21 (79%); (e) PivCl, Py, 91%.

To extend the range and nature of the substituents on the sugar ring, benzoyl and pivaloyl groups were also introduced onto anhydrosugars, as depicted in Scheme 2. Compounds 6 and 7 were both benzoylated with BzCl to give the corresponding levoglucosan derivatives 16[27] and 17[27] in 81% and 85% yields, respectively. 7 was also acylated with pivaloyl chloride to provide the pivaloate 18 in 91% yield. Following literature procedure,[33] commercially available galactosan was also converted into the partially benzoylated derivative 21 via the intermediates 19[33] and 20[33] in very good overall yield. As azido group is the most common precursor to amino group and plays often an irreplaceable role in aminoglycoside synthesis, it would also be important to introduce azido group onto 6-anhydrosugars to trial the ring-opening reactions. Thus, we synthesized the azide derivative of levoglucosan 23 as well from commercially available mannosan 22 following the literature procedures.[27]

To examine if the ring-opening procedure is applicable to more complex structures, we also synthesized a group of anhydrosugar-containing oligosaccharides, as shown in Scheme 3.

Scheme 3. Synthesis of Anhydrosugar-Containing Oligosaccharides[a]



[a]Reagents and conditions: (a) TMSOTf, 4 Å MS, CH_2Cl_2, −50 to 0 °C, 25 (85%), 26 (89%), 33 (65%); (b) HCl−dioxane, 78%; (c) AgOTf, CH_2Cl_2, 29 (70%), 31 (72%).

Of them, 2-*O*-glucosylated levoglucosan 25 and galactosan 26 were synthesized readily in 85% and 89% yields, respectively, by glycosylation of the corresponding acceptors 7 and 19 with glucosyl trichloroacetimidate 24.[34] Considering that the acid-labile isopropylidene protecting group may not survive under the ring-opening conditions, 26 was treated subsequently with HCl in dioxane to remove the isopropylidene group to provide the disaccharide 27 in 78% yield. Two 3-*O*-glycosylated levoglucosans 29 and 31 were also synthesized by glycosylation of 12 with glucosyl bromide 28[35] and maltosyl bromide 30,[36] respectively, in order to further explore the ring-opening procedure. Both were produced in very good yields. Finally, to ensure that 4-*O*-glycosylated anhydrosugars could also be transformed effectively to 1-thiosugars, the known maltose-derived disaccharide 32[37] was prepared and subsequently subjected to Schmidt glycosidation conditions[38] with donor 24 furnished the tetrasaccharide 33 in very good yield.

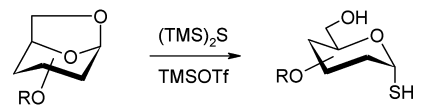
Synthesis of α-Glycosyl Thiols. Having the 1,6-anhydrosugar substrates in hand, attention was then focused on their transformation into α-glycosyl thiols, i.e., the development of appropriate ring-opening conditions to stereoselectively open the 1,3-dioxolane rings with thionucleophiles. Undoubtedly, it would be crucial to identify an appropriate nucleophile equivalent to a sulfhydryl group in order to achieve one-step direct synthesis of α-glycosyl thiols from these 1,6-anhydrosugars. We anticipated that commercially available bis(trimethylsilyl) sulfide could act as the required sulfur nucleophile to directly introduce the sulfhydryl group in view of the acid lability of the trimethylsilyl group which could be cleaved *in situ* under most glycosidation conditions.

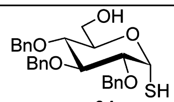
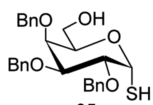
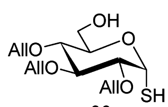
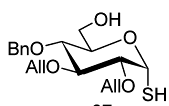
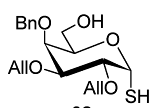
To verify this hypothesis, the per-benzylated 1,6-anhydrosugars **1** and **2** were first chosen as the substrates as the ether-type protecting groups are thought to be arming groups and can usually enhance the reactivity of glycosyl donors, thereby could compensate for the low reactivity of 1,6-anhydrosugars.[39] Hence, **1** and **2** were both treated with a small excess of bis(trimethylsilyl) sulfide $(TMS)_2S$ in the presence of catalytic amounts of TMSOTf (0.4 equiv), but unfortunately, no reaction took place at room temperature. Some attempts, such as increase of the amount of TMSOTf, change of promoter, and extension of reaction time, failed to bring about the expected ring-opening reactions. Fortunately, when the reactions were heated at 50 °C, the reactions occurred, and to our delight, the desired glycosyl thiols **34** and **35** were isolated from the reaction mixtures in 88% and 90% yields, respectively. More importantly, both thiols were produced as exclusively the α-anomers (Table 1, entries 1 and 2); i.e., no trace of β-isomers was produced in both reactions, which made the purification very simple and straightforward. The α-anomeric configuration of thiols **34** and **35** was readily determined by the coupling constant $^3J_{H1-H2}$ value, which is about 5.0 Hz, whereas analogous β-glycosyl thiols usually have $^3J_{H1-H2}$ value of 7–10 Hz.[15] The ready formation of **34** and **35** offered a preliminary suggestion that the present procedure may provide a convenient means to α-glycosyl thiols. Indeed, the yields and stereoselectivities with most investigated substrates were invariably high, as shown in Tables 1–4, and the one-step mode as well as the simplicity of the reaction conditions makes this approach a very attractive way of synthesizing α-glycosyl thiols.

Subsequently, the per-allylated levoglucosan **3** was subjected to the same conditions, and as expected, the reaction took place smoothly and gave rise to α-thiol **36** in 78% yield (Table 1, entry 3). Similarly, treatment of armed 1,6-anhydrosugars **4** and **5** with $(TMS)_2S$ under the same conditions also led to the desired α-thiols **37** and **38** in very high yields (Table 1, entries 4 and 5). It is important to note that all the reactions were stereospecific, and no trace of β-glycosyl thiol was produced. We speculated that the ring-opening reactions underwent very possibly a concerted S_N2-type process, which was also evidenced by the ring-opening of 2-*O*-acylated anhydrosugars (vide infra), but the precise mechanistic details remain to be investigated.

To obtain more information on the ring-opening reaction, we then turned to investigating partially unprotected substrates. The results are summarized in Table 2. Levoglucosan **7** with 2-OH unprotected was first treated with $(TMS)_2S$ under the above conditions, as expected, glucosyl thiol **39** was generated in very high yield and α-only selectivity. Exposure of anhydrosugar **12** carrying one free OH group at the 3-position

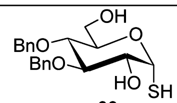
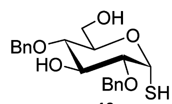
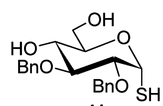
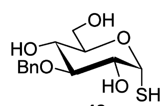
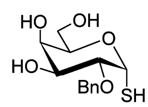
Table 1. Synthesis of α-Glycosyl Thiols 34–38[a]



Entry	Substrate	Product	Yield (%)[b]	α/β Ratio
1	**1**	 **34**	88	α only
2	**2**	 **35**	90	α only
4	**3**	 **36**	78	α only
5	**4**	 **37**	85	α only
6	**5**	 **38**	92	α only

[a]See the Experimental Section for details. [b]Isolated yield following chromatography.

Table 2. Synthesis of α-Glycosyl Thiols 39–43[a]

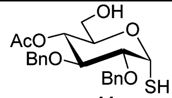
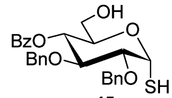
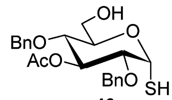
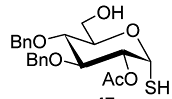
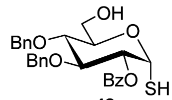
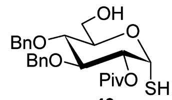
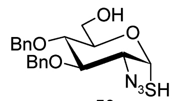
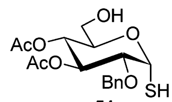
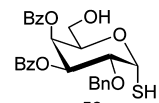
Entry	Substrate	Product	Yield (%)[b]	α/β Ratio
1	**7**	 **39**	86	α only
2	**12**	 **40**	90	α only
3	**6**	 **41**	83	α only
4	**8**	 **42**	76	α only
5	**20**	 **43**	83	α only

[a]See the Experimental Section for details. [b]Isolated yield following chromatography.

to $(TMS)_2S$ under the same conditions led also to thiol **40** in very high yield and α-selectivity (Table 2, entry 2). Similarly, ring-opening of 4-OH-free anhydrosugar **6** with $(TMS)_2S$ in the presence of catalytic amounts of TMSOTf also proceeded smoothly to give thiol **41** in 83% yield and α-only selectivity. At this point, we reasoned that anhydrosugars **8** and **20** with two free OH groups could also work under the ring-opening conditions, and indeed, as shown in entries 4 and 5 in Table 2, when **8** and **20** were treated with $(TMS)_2S$ according to the same procedure, thiols **42** and **43** were isolated in 76% and 83% yields, respectively, and TLC indicated no trace of their β-isomers were produced as well. These results further demonstrate the efficiency of the methodology for the preparation of α-thiols; moreover, conceivably these partially unprotected thiols **39**−**43** could be used for further protecting group manipulation, thereby providing a convenient and effective access to α-thiols with other different protecting groups.

To further demonstrate the power of this method in the synthesis of α-glycosyl thiols, 1,6-anhydrosugars carrying acyl protecting groups were subjected to the ring-opening reaction under the above conditions. In carbohydrate chemistry, the use of protecting groups goes far beyond the simple blocking of hydroxyl groups. Protecting groups often play important roles in modulating the reactivity of glycosyl donors and acceptors and directing the stereochemistry of glycosidation reactions.[40] On the basis of the results in Tables 1 and 2, we anticipated that one or two acyl protecting groups on a substrate would not ruin the ring-opening reactions, although they could deteriorate the reactivity of 1,6-anhydrosugars and even intervene the stereocontrol of the reactions. To verify this, the monoacylated levoglucosans **9**, **16**, **13**, and **10** were chosen as the substrates for the first set of experiments. As anticipated, 4-*O*-acetylated levoglucosan **9** could be converted smoothly into thiol **44** under similar conditions in very high yield (84%) and α-only selectivity (Table 3, entry 1). Notably, in comparison with the above non-acylated substrates, compound **9** (and all other partially acylated anhydrosugars in Table 3, see Experimental Section) required more Lewis acid (0.8 equiv) and a prolonged reaction time (10−15 h) to be converted into the corresponding α-thiol, presumably due to its reduced reactivity. Similarly, the dioxolane ring of 4-*O*-benzoylated levoglucosan **16** could also be opened stereospecifically to give rise to α-thiol **45** in 66% yield (Table 3, entry 2). The reaction of 3-*O*-acetylated levoglucosan **13** with $(TMS)_2S$ proceeded also very cleanly as indicated by TLC to produce stereospecifically α-thiol **46** in 89% yield. Thus, introducing one acyl group onto the sugar seems not to do much harm to the ring-opening process, and importantly, these results forebode the feasibility of performing the ring-opening reaction on even less reactive anhydrosugars (vide infra). More interestingly, the 2-*O*-acetyl group did not impair the α-selectivity as the substrate **10** could also undergo the ring-opening reaction under the above conditions to give solely the desired α-thiol **47** in high yield (Table 3, entry 4). This is a very interesting result as the conventional neighboring group participation did not occur in spite of the presence of neighboring acetyl group. We speculated that the possible S_N2-type ring-opening pathway and the $^1C_4$ conformation of the substrate might both restrain the neighboring group participation, thereby favoring the formation of α-product. To confirm the absence of neighboring group participation, 2-*O*-benzoylated and pivaloylated levoglucosan **17** and **18** were also treated with $(TMS)_2S$ in the presence of TMSOTf; as expected, the reactions proceeded well, and the corresponding α-thiols **48** and **49** were both produced stereospecifically and in very good yields (Table 3, entries 5 and 6).

Table 3. Synthesis of α-Glycosyl Thiols 44−52[a]

Entry	Substrate	Product	Yield (%)[b]	α/β Ratio
1	**9**	 **44**	84	α only
2	**16**	 **45**	66	α only
3	**13**	 **46**	89	α only
4	**10**	 **47**	78	α only
5	**17**	 **48**	77	α only
6	**18**	 **49**	83	α only
7	**23**	 **50**	86	α only
8	**11**	No Reaction	n.a.	n.a.
9	**15**	 **51**	30	α only
10	**21**	 **52**	69	α only

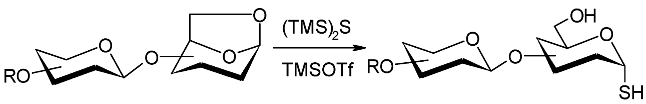
[a]See the Experimental Section for details. [b]Isolated yield following chromatography.

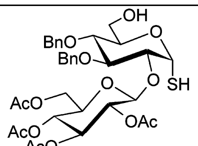
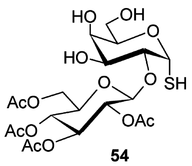
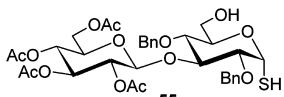
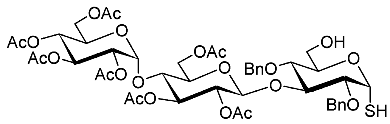
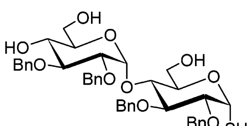
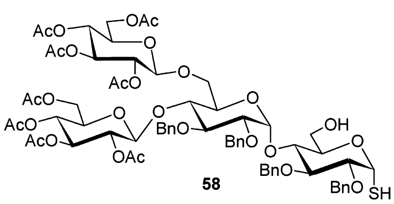
In this context, 2-azido-anhydrosugar **23** was also subjected to the ring-opening reaction with $(TMS)_2S$ under the above conditions; as expected, thiol **50** was generated in very high yield (Table 3, entry 7). Apparently, **50** could be used as a building block for the construction of α-*S*-linked aminoglycosides.

To further explore the scope of this procedure, we proceeded to use the less reactive 1,6-anhydrosugars **11**, **15**, and **21** with two electron-withdrawing groups as the substrates for the ring-opening reaction. We feared that the substrates might not be reactive enough to undergo the ring-opening process; indeed, reaction of **11** with $(TMS)_2S$ under the above conditions failed to gave any product and **11** was not affected even after a prolonged reaction time. Attempts to convert **11** to the corresponding thiol by increasing the amount of TMSOTf and/or the reaction temperature led to the loss of α-stereospecificity. Similarly, under the same conditions, ring-opening of **15** with $(TMS)_2S$ occurred very slowly and led to the desired α-thiol **51** in relatively low yield with most starting material recovered (Table 3, entry 9). These results indicate that protecting groups on a sugar ring have great impact on the ring-opening process. Subsequently, galactosan **21** was also treated with $(TMS)_2S$ according to the same procedure, and fortunately, α-thiol **52** was isolated in reasonably good yield (Table 3, entry 10). It should be noted that α-thiols carrying two acyl groups, such as the ring-opening product of **11** and **51**, could also be prepared from the products in Table 2 through protecting group manipulation.

The scope and utility of the ring-opening procedure in the synthesis of α-glycosyl thiols is further illustrated in Table 4.

Table 4. Synthesis of α-Glycosyl Thiols 53−58[a]



Entry	Substrate	Product	Yield (%)[b]	α/β Ratio
1	**25**	 **53**	58	α only
2	**27**	 **54**	67	α only
3	**29**	 **55**	72	α only
4	**31**	 **56**	65	α only
5	**32**	 **57**	74	α only
6	**33**	 **58**	81	α only

[a]See the Experimental Section for details. [b]Isolated yield following chromatography.

Treatment of 1,2-linked disaccharides **25** with $(TMS)_2S$ in the presence of 0.6 equiv of TMSOTf afforded the desired α-thiol **53** in 58% yield and α-only selectivity. 2-*O*-Glucosylated galactosan **27** could also be converted into thiol **54** in a stereospecific manner and 67% yield under the same conditions (Table 4, entry 2). Again, ring-opening of 3-*O*-glycosylated anhydrosugars **29** and **31** with $(TMS)_2S$ under the action of TMSOTf also led to the corresponding α-thiols **55** and **56** in very good yields, and TLC indicated no β-isomers were produced in both reactions (Table 4, entries 3 and 4). It is worth noting that these smooth reactions, together with the following reactions, provided a convenient access to α-oligosaccharidyl thiols, which can be used for chemical ligation with various electrophilic aglycones to synthesize biologically important α-*S*-glycoconjugates. Similarly, when 4-*O*-glycosylated anhydrosugars **32** and **33** were treated with $(TMS)_2S$ in the presence of catalytic amounts of TMSOTf, the corresponding α-thiols **57** and **58** were also produced readily in 74% and 81% yields, respectively, without observable contamination of β-isomers.

■ CONCLUSION

In this report, a series of α-glycosyl thiols were synthesized directly from the readily available 1,6-anhydosugars in a stereospecific way. To the best of our knowledge, this is the first direct stereospecific procedure for the synthesis of α-glycosyl thiols. A great advantage of this procedure is that most α-glycosyl thiols were isolated in good to excellent yields as exclusively the α-anomer. No trace of β-isomers was produced in all the reactions. Notably, by this procedure 1,6-anhydrosugars carrying a 2-*O*-acyl group could also be ring-opened stereospecifically to give rise to α-glycosyl thiols in high yields. Thus, this one-step procedure provided a convenient and efficient access to α-glycosyl thiols, which could be used to synthesize various α-*S*-glycoconjugates.

■ EXPERIMENTAL SECTION

General Remarks. All chemicals used were reagent grade and used as supplied except where noted. Reactions were performed in oven-dried glassware under a nitrogen atmosphere using dry solvents. Solvents were evaporated under reduced pressure while maintaining the water bath temperature below 40 °C. All reactions were monitored by thin-layer chromatography (TLC) using silica gel 60 F_{254} coated on an aluminum sheet, and the compounds were visualized by UV or by treatment with 8% H_2SO_4 in methanol followed by heating. Flash chromatography was performed with the appropriate solvent system using 40−60 μm silica gel. Optical rotations were measured at 20 °C with a Perkin-Elmer 343 polarimeter (1 dm cell). ^{1}H NMR spectra were obtained on a 300, 400, and 500 MHz and reported in parts per million (δ) relative to the response of the solvent or to TMS (0.00 ppm). Coupling constants (J) are reported in hertz (Hz). ^{13}C NMR spectra were recorded at 75, 100, or 125 MHz by using $CDCl_3$ as solvent and are reported in δ relative to the response of the solvent. Yields refer to chromatographically pure compounds and are calculated based on reagents consumed.

1,6-Anhydro-2,3-di-*O*-allyl-4-*O*-benzyl-β-D-glucopyranose (4). To a stirred solution of methyl 2,3-di-*O*-allyl-4-*O*-benzyl-α-D-glucopyranoside[41] (0.20 g, 0.59 mmol) in CH_3CN (10 mL) was added $Fe(ClO_4)_3{\cdot}(H_2O)_6$ (21 mg, 0.06 mmol). The mixture was refluxed for 6 h and was then diluted with CH_2Cl_2 and filtered through a short pad of silica gel. The filtrates were concentrated in vacuo to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc, 5:1) to afford the anhydrosugar **4** (135 mg, 74%) as a colorless syrup: $[\alpha]_D$ = +52.6 (c 1.0 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.28 (m, 5H), 5.92−5.80 (m, 2H), 5.43 (br s, 1H), 5.32 (d, J = 1.5 Hz, 1H), 5.27 (dd, J = 6.4, 1.5 Hz, 2H), 5.19 (dd, J = 12.0, 1.2 Hz, 2H), 4.67 (br s, 2H), 4.56 (d, J = 5.6 Hz, 1H), 4.10 (d, J = 5.4 Hz, 1H), 3.84 (d, J = 7.1 Hz, 1H), 3.65 (t, J = 6.8 Hz, 1H), 3.53

(d, J = 1.0 Hz, 1H), 3.27 (d, J = 15.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.0, 134.6, 134.5, 128.4, 127.8, 117.4, 117.1, 100.7, 77.5, 77.4, 77.1, 76.9, 76.8, 74.5, 71.3, 71.2, 65.6. ESI-MS m/z 355.4 [M + Na]$^+$. ESI-HRMS calcd for $C_{19}H_{24}O_5Na$ [M + Na]$^+$ 355.1521; found 355.1528.

1,6-Anhydro-2,3-di-*O*-allyl-4-*O*-benzyl-*β*-D-galactopyranose (5). Methyl 2,3-di-*O*-allyl-*α*-D-galactopyranoside[42] was smoothly transformed into methyl 2,3-di-*O*-allyl-4-*O*-benzyl-*α*-D-galactopyranoside by successive tritylation, benzylation, and detritylation, which was then treated with $Fe(ClO_4)_3{\cdot}(H_2O)_6$ following the procedure described for the synthesis of **4**. The anhydrosugar **5** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 5:1), as colorless syrup in 67% yield: $[\alpha]_D$ = +37.9 (c 1.0 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.27 (m, 5H), 5.95−5.81 (m, 2H), 5.37−5.24 (m, 3H), 5.18 (dd, J = 9.1, 5.4 Hz, 2H), 4.64 and 4.58 (AB peak, J = 11.8 Hz, 2H), 4.45 (d, J = 6.8 Hz, 1H), 4.39 (d, J = 3.7 Hz, 1H), 4.11 (m, 2H), 4.06−3.99 (m, 2H), 3.83 (d, J = 3.8 Hz, 1H), 3.75 (d, J = 3.7 Hz, 1H), 3.58 (t, J = 5.6 Hz, 1H), 3.51 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.3, 134.9, 134.4, 128.4, 127.8, 127.6, 100.1, 77.6, 76.9, 76.6, 74.4, 73.1, 72.7, 72.3, 71.3, 71.1, 64.3. ESI-MS m/z 355.5 [M + Na]$^+$. ESI-HRMS calcd for $C_{19}H_{24}O_5Na$ [M + Na]$^+$ 355.1521; found 355.1532.

1,6-Anhydro-2-*O*-acetyl-3,4-di-*O*-benzyl-*β*-D-glucopyranose (10). To a stirred solution of **7** (0.25 g, 0.73 mmol) in Py (4 mL) was added Ac_2O (0.1 mL, 0.9 mmol). The mixture was stirred overnight at room temperature and was then diluted with EtOAc, washed successively with 5% HCl, saturated aqueous $NaHCO_3$, and brine, dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 5:1) to afford the anhydrosugar **10** (243 mg, 86%) as colorless syrup: $[\alpha]_D$ −28.0 (c 2.5 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.27 (m, 10H), 5.45 (s, 1H), 4.75−4.72 (m, 2H), 4.61 (d, J = 5.2 Hz, 1H), 4.54 (dd, J = 12.4, 7.2 Hz, 2H), 4.45 (d, J = 12.4 Hz, 1H), 4.06 (d, J = 7.2 Hz, 1H), 3.72 (t, J = 6.4 Hz, 1H), 3.53 (d, J = 1.2 Hz, 1H), 3.34 (br s, 1H), 2.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 137.7, 137.6, 128.5, 128.4, 127.9, 127.78, 127.77, 99.4, 75.9, 74.8, 74.2, 71.8, 71.1, 69.1, 65.0, 21.1. ESI-MS m/z 407.4 [M + Na]$^+$. ESI-HRMS calcd for $C_{22}H_{25}O_6$ [M + H]$^+$ 385.1651; found 385.1639.

1,6-Anhydro-2,4-di-*O*-acetyl-3-*O*-benzyl-*β*-D-glucopyranose (11). The reaction procedure was identical to that described for **10**. The anhydrosugar **11** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 3:1), as a colorless syrup in 77% yield: $[\alpha]_D$ −64.4 (c 0.35 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.27 (m, 5H), 5.47 (s, 1H), 4.78−4.75 (m, 3H), 4.69 (d, J = 12.4 Hz, 1H), 4.61 (d, J = 5.2 Hz, 1H), 4.22 (d, J = 7.6 Hz, 1H), 3.78 (dd, J = 7.2, 6.0 Hz, 1H), 3.48 (d, J = 1.6 Hz, 1H), 2.13 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 169.9, 137.4, 128.3, 127.7, 127.5, 99.5, 75.5, 73.7, 72.2, 70.9, 69.1, 65.1, 21.0, 20.9. ESI-MS m/z 359.3 [M + Na]$^+$. ESI-HRMS calcd for $C_{17}H_{20}O_7Na$ [M + Na]$^+$ 359.1107; found 359.1109.

1,6-Anhydro-3,4-di-*O*-benzyl-2-*O*-pivaloyl-*β*-D-glucopyranose (18). Compound **7** (290 mg, 0.85 mmol) was dissolved in Py (10 mL), and PivCl (0.13 mL, 1.06 mmol) was added to this mixture at 0 °C. The resulting mixture was stirred at room temperature overnight and was then diluted with EtOAc, washed successively with 5% HCl, saturated aqueous $NaHCO_3$, and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 6:1) to afford the anhydrosugar **18** (329 mg, 91%) as a colorless syrup: $[\alpha]_D$ = −22.6 (c 1.0 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.25 (m, 10H), 5.47 (s, 1H), 4.69 (d, J = 2.9 Hz, 1H), 4.67 (s, 1H), 4.61 and 4.40 (AB peak, J = 11.8 Hz, 2H), 4.50 (m, 1H), 4.45 (s, 1H), 4.09 (d, J = 7.3 Hz, 1H), 3.72 (dd, J = 7.2, 6.0 Hz, 1H), 3.52 (br s, 1H), 3.35 (br s, 1H); 1.23 (s, 6H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.9, 137.7, 128.4, 128.3, 127.9, 127.8, 127.7, 100.8, 77.3. 77.1, 77.0, 76.7, 75.6, 74.4, 72.4, 72.1, 71.7, 65.8, 38.8, 27.0. ESI-MS m/z 449.5 [M + Na]$^+$. ESI-HRMS calcd for $C_{25}H_{30}O_6Na$ [M + Na]$^+$ 449.1940; found 449.1946.

1,6-Anhydro-3,4-di-*O*-benzoyl-2-*O*-benzyl-*β*-D-galactopyranose (21). To a stirred solution of **20** (225 mg, 0.89 mmol) in Py (5 mL) was added BzCl (0.25 mL, 2.14 mmol) at 0 °C. The mixture was stirred at room temperature for 5 h and was then diluted with EtOAc, washed successively with 5% HCl, saturated aqueous $NaHCO_3$, and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 3:1) to give the anhydrosugar **21** (317 mg, 79%) as an amorphous solid: $[\alpha]_D$ −27.0 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (d, J = 7.2 Hz, 2H), 8.04 (d, J = 7.2 Hz, 2H), 7.86 (d, J = 7.2 Hz, 2H), 7.61 (q, J = 7.5 Hz, 2H), 7.49 (m, 3H), 7.43−7.28 (m, 4H), 5.77 (d, J = 4.5 Hz, 1H), 5.64 (t, J = 4.6 Hz, 1H), 5.48 (br s, 1H), 4.73−4.68 (m, 2H), 4.93 (d, J = 12.0 Hz, 1H), 4.57 (d, J = 7.5 Hz, 1H), 3.84 (t, J = 6.1 Hz, 1H), 3.67 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.4, 165.6, 137.2, 133.7, 133.3, 130.1, 129.6, 128.6, 128.5, 128.4, 128.3, 128.0, 100.6, 72.3, 72.0, 67.7, 66.1, 64.5. ESI-MS m/z 483.3 [M + Na]$^+$. ESI-HRMS calcd for $C_{27}H_{24}O_7$ [M + H]$^+$ 461.1600; found 461.1605.

***O*-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-(1→2)-1,6-anhydro-3,4-di-*O*-benzyl-*β*-D-glucopyranose (25).** A suspension of imidate **24** (0.8 g, 1.62 mmol), acceptor **7** (450 mg, 1.31 mmol), and activated powdered molecular sieves (4 Å, 400 mg) in CH_2Cl_2 (20 mL) was stirred at room temperature for 15 min and then cooled to −50 °C, and a solution of TMSOTf (3.2 mL, 0.05 M) in CH_2Cl_2 was slowly added. After stirring for 30 min, the reaction mixture was quenched with Et_3N and filtered. The filtrates were concentrated in vacuo to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc, 3:1) to yield the title compound **25** (749 mg, 85%) as a white foam: $[\alpha]_D$ = −63.5 (c 1.0 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.29 (m, 10H), 5.43 (s, 1H), 5.19 (t, J = 9.4 Hz, 1H), 5.09 (t, J = 9.5 Hz, 1H), 4.99 (t, J = 9.0 Hz, 1H), 4.81 (d, J = 8.0 Hz, 1H), 4.62−4.53 (m, 4H), 4.43 (d, J = 12.1 Hz, 1H), 4.19 (dd, J = 12.4, 4.6 Hz, 1H), 4.06 (dd, J = 10.4, 1.9 Hz, 1H), 3.96 (d, J = 7.2 Hz, 1H), 3.76 (s, 1H), 3.73 (d, J = 6.5 Hz, 1H), 3.68 (s, 1H), 3.64−3.60 (m, 1H), 3.34 (s, 1H), 2.04(s, 3H), 2.03 (s, 6H), 1.97 (s. 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 170.3, 169.4, 169.2, 137.8, 137.7, 128.5, 127.9, 127.8, 127.6, 100.8, 99.3, 77.6, 77.3, 77.2, 76.7, 76.5, 75.8, 73.9, 72.8, 71.9, 71.4, 71.3, 68.2, 65.4, 61.8, 20.7, 20.6. ESI-MS m/z 695.7 [M + Na]$^+$. ESI-HRMS calcd for $C_{34}H_{40}O_{14}Na$ [M + Na]$^+$ 695.2316; found 695.2326.

***O*-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-(1→2)-1,6-anhydro-*β*-D-galactopyranose (27).** The reaction procedure for the synthesis of disaccharide **26** was identical to that described for **25**, except that acceptor **19** was used instead of **7**. The crude product was purified by flash column chromatography (petroleum ether/EtOAc, 2:1) to give **26** as a white foam in 89% yield, which was then treated with 4 M HCl/dioxane solution to cleave the isopropylidene protecting group to provide the title compound **27** as an amorphous solid in 78% yield: $[\alpha]_D$ +28.1 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.51 (s, 1H), 5.19 (t, J = 9.4 Hz, 1H), 5.10−4.97 (m, 2H), 4.67 (d, J = 7.8 Hz, 1H), 4.43 (t, J = 4.5 Hz, 1H), 4.22−4.17 (m, 3H), 3.93−3.82 (m, 3H), 3.74−3.69 (m, 1H), 3.63 (dd, J = 7.8, 5.1 Hz, 1H), 2.88 (d, J = 8.2 Hz, 1H), 2.72 (d, J = 6.9 Hz, 1H), 2.09 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 170.2, 169.3, 169.0, 108.6, 100.8, 100.1, 78.4, 74.6, 72.7, 72.0, 71.8, 71.3, 69.1, 68.2, 63.0, 61.8, 25.7, 24.2, 20.6, 20.5. ESI-MS m/z 515.4 [M + Na]$^+$. ESI-HRMS calcd for $C_{20}H_{28}O_{14}Na$ [M + Na]$^+$ 515.1377; found 515.1386.

***O*-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-(1→3)-1,6-anhydro-2,4-di-*O*-benzyl-*β*-D-glucopyranose (29).** To a stirred solution of **28** (198 mg, 0.48 mmol) and **13** (150 mg, 0.43 mmol) in CH_2Cl_2 (5 mL) was added 4 Å molecular sieves. AgOTf (123 mg, 0.48 mmol) was then added to the above mixture at 0 °C. After being stirred overnight at room temperature, the reaction was quenched with Et_3N and filtered through a pad of Celite. The filtrates were diluted with EtOAc, washed successively with water and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 3:1) to give the title compound **29** (189 mg, 70%) as an amorphous solid: $[\alpha]_D$ −1.2 (c 0.5 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.29 (m, 10H), 5.45 (s, 1H), 5.33 (d, J = 3.2 Hz, 1H), 5.08 (dd, J = 10.0, 8.4 Hz, 1H), 4.85 (dd, J = 10.8, 3.2 Hz, 1H), 4.77 (dd, J = 17.6, 12.8 Hz, 2H), 4.64 (d, J = 12.8 Hz, 1H), 4.55 (d, J = 12.0 Hz, 2H), 4.09 (d, J = 6.8 Hz, 2H), 3.95 (d, J = 8.4 Hz, 1H), 3.85 (br s, 1H), 3.79 (d, J = 7.2 Hz, 1H), 3.65−3.59 (m, 2H), 3.41 (br s, 1H), 3.13 (br s, 1H), 2.13 (s, 3H), 2.01 (s, 3H), 1.99 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 170.1, 170.0, 169.4, 137.9, 137.7, 128.7, 128.5, 128.4, 128.3, 127.8, 127.7, 99.7, 77.2, 76.2, 74.7, 74.3, 74.1, 72.3, 71.2, 70.7, 70.5, 68.1, 66.9, 64.8, 61.2, 20.7, 20.64, 20.61, 20.5. ESI-MS m/z 695.6 [M + Na]$^+$. ESI-HRMS calcd for $C_{34}H_{40}O_{14}Na$ [M + Na]$^+$ 695.2316; found 695.2329.

***O*-(2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→3)-1,6-anhydro-2,4-di-*O*-benzyl-β-D-glucopyranose (31).** The reaction procedure was identical to that described for **29**, except that bromide **30** was used instead of **28**. The crude product was purified by flash column chromatography (petroleum ether/EtOAc, 1:1) to give **31** as an amorphous solid in 72% yield: $[\alpha]_D$ +32.1 (c 0.8 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41−7.25 (m, 10H), 5.42 (s, 1H), 5.40−5.35 (m, 2H), 5.12 (t, J = 9.2 Hz, 1H), 5.05 (t, J = 9.8 Hz, 1H), 4.87 (dd, J = 10.4, 4.0 Hz, 1H), 4.74−4.68 (m, 3H), 4.62−4.56 (m, 2H), 4.53−4.50 (m, 1H), 4.44 (dd, J = 12.0, 2.4, 1H), 4.26 (dd, J = 12.8, 4.0 Hz, 1H), 4.16−4.10 (m, 2H), 4.06 (d, J = 12.0, 1H), 3.96−3.92 (m, 1H), 3.90 (d, J = 9.2 Hz, 1H), 3.84 (br s, 1H), 3.72 (d, J = 7.2 Hz, 1H), 3.58 (t, J = 6.6 Hz, 1H), 3.41−3.39 (m, 1H), 3.35 (br s, 1H), 3.15 (br s, 1H), 2.09−2.06 (m, 9H), 2.03−2.01 (m, 6H), 1.98−1.95 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 170.2, 170.0, 169.9, 169.5, 169.3, 137.9, 137.6, 128.6, 128.4, 128.3, 128.2, 127.8, 127.7, 109.9, 99.8, 98.9, 95.5, 76.1, 75.08, 75.05, 74.8, 74.3, 72.6, 72.3, 72.2, 71.4, 71.1, 70.0, 69.3, 68.5, 68.0, 64.9, 62.5, 61.4, 60.3, 29.6, 20.8, 20.60, 20.57, 20.54, 20.52. ESI-MS m/z 983.7 [M + Na]$^+$. ESI-HRMS calcd for $C_{46}H_{56}O_{22}Na$ [M + Na]$^+$ 983.3161; found 983.3146.

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-(1→4)-*O*-[2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→6)]-*O*-(2,3-di-*O*-benzyl-α-D-glucopyranosyl)-(1→4)-1,6-anhydro-2,3-di-*O*-benzyl-β-D-glucopyranose (33).** The reaction procedure was identical to that described for **29**, except that acceptor **32** was used instead of **13**. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH, 10:1) to give **33** as an amorphous solid in 65% yield: $[\alpha]_D$ +8.9 (c 0.9 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.27 (m, 20H), 5.50 (d, J = 8.0 Hz, 1H), 5.32−5.16 (m, 1H), 5.13−5.04 (m, 2H), 5.04−4.88 (m, 4H), 4.72−4.65 (m, 2H), 4.59−4.47 (m, 5H), 4.26−4.20 (m, 2H), 4.14−4.02 (m, 4H), 4.00−3.95 (m, 2H), 3.89−3.80 (m, 2H), 3.78−3.70 (m, 5H), 3.60−3.47(m, 2H), 3.55−3.47 (m, 2H), 3.39 (br s, 2H), 2.08−1.99 (m, 24H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 170.70, 170.69, 170.64, 170.62, 169.61, 169.60, 169.5, 138.6, 138.0, 137.9, 137.87, 137.80, 137.71, 137.70, 128.60, 128.58, 128.49, 128.45, 128.42, 128.3, 128.0, 127.9, 127.80, 127.79, 127.76, 127.73, 127.71, 127.60, 127.58, 127.55, 127.4, 124.7, 100.7, 100.6, 97.2, 81.0, 79.4, 77.1, 75.2, 75.1, 73.2, 72.7, 72.5, 72.4, 72.1, 72.04, 71.98, 71.9, 71.6, 71.49, 71.46, 71.3, 71.0, 70.7, 70.6, 68.3, 67.9, 67.5, 65.7, 62.5, 31.9, 30.2, 29.7, 29.6, 29.3, 26.8, 22.6, 20.9, 20.80, 20.78, 20.72, 20.69, 20.66, 20.65, 20.62, 20.58, 20.56. ESI-MS m/z 1368.7 [M + Na]$^+$. ESI-HRMS calcd for $C_{68}H_{80}O_{28}Na$ [M + Na]$^+$ 1367.4734; found 1367.4751.

General Procedure for the Synthesis of Thiols 34−43. To a solution of the appropriate 1,6-anhydrosugars (1.0 mmol) and bis(trimethylsilyl) sulfide (1.4 mmol) in CH_2Cl_2 (10 mL) was added TMSOTf (0.4 mmol) at 0 °C. The mixture was then stirred at 50 °C until TLC indicated complete consumption of the starting material (typically 4−6 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 which was purified by flash column chromatography to afford the corresponding α-glycosyl thiol.

2,3,4-Tri-*O*-benzyl-1-thio-α-D-glucopyranose (34). Thiol **34** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 4:1), as a colorless syrup in 88% yield: $[\alpha]_D$ +95.1 (c 1.0 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.22 (m, 15H), 5.62 (t, J = 5.2, 4.8 Hz, 1H), 4.88 and 4.74 (AB peak, J = 10.8 Hz, 2H), 4.81 and 4.58 (AB peak, J = 11.0 Hz, 2H), 4.66 and 4.57 (AB peak, J = 11.8 Hz, 2H), 4.02 (m, 1H), 3.82 (t, J = 9.2, 8.8 Hz, 1H), 3.68 (m, 3H), 3.48 (t, J = 10.0, 9.2 Hz, 1H), 1.84 (d, J = 4.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.7, 138.2, 137.7, 128.66, 128.65, 128.6, 128.22, 128.20, 128.17, 128.13, 128.09, 127.8, 81.8, 79.5, 78.9, 77.1, 75.9, 75.2, 72.6, 72.0, 61.9. ESI-MS m/z 489.2 [M + Na]$^+$. ESI-HRMS calcd for $C_{27}H_{30}NaO_5S$ [M + Na]$^+$ 489.1712; found 489.1698.

2,3,4-Tri-*O*-benzyl-1-thio-α-D-galactopyranose (35). Thiol **35** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 4:1), as a colorless syrup in 90% yield: $[\alpha]_D$ +93.6 (c 0.8 $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38−7.24 (m, 15H), 5.84 (t, J = 5.0, 4.5 Hz, 1H), 4.93 and 4.65 (AB peak, J = 11.5 Hz, 2H), 4.84 and 4.69 (AB peak, J = 12.0 Hz, 2H), 4.72 and 4.69 (AB peak, J = 11.0 Hz, 2H), 4.25 (dd, J = 5.0, 9.5 Hz, 1H), 4.15 (t, J = 6.0, 5.5 Hz, 1H), 3.89 (br s, 1H), 3.81(dd, J = 2.5, 9.5 Hz, 1H), 3.72 (dd, J = 6.5, 11.5 Hz, 1H), 3.54−3.49 (m, 1 H), 1.83 (d, J = 4.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.4, 138.0, 137.8, 128.6, 128.5, 128.44, 128.39, 128.0, 127.9, 127.8, 127.7, 127.6, 79.4, 78.6, 75.9, 74.6, 74.4, 73.6, 72.6, 71.6, 62.0. ESI-MS m/z 489.2 [M + Na]$^+$. ESI-HRMS calcd for $C_{27}H_{30}NaO_5S$ [M + Na]$^+$ 489.1712; found 489.1712.

2,3,4-Tri-*O*-allyl-1-thio-α-D-glucopyranose (36). Thiol **36** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 3:1), as a colorless syrup in 78% yield: $[\alpha]_D$ +173.1 (c 2.0 $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.99−5.87 (m, 3H), 5.70 (t, J = 5.0 Hz, 1H), 5.29 (m, 3H), 5.18 (m, 3H), 4.37−4.08 (m, 6H), 4.01 (dt, J = 3.5, 10.0 Hz, 1H), 3.82 (dd, J = 2.0, 12.0 Hz, 1H), 3.75 (d, J = 11.5 Hz, 1H), 3.58 (overlapped m, 2H), 3.35 (t, J = 9.0, 9.5 Hz, 1H), 1.88 (d, J = 5.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.1, 134.6, 134.3, 117.5, 117.1, 116.6, 81.0, 78.96, 78.80, 77.0, 74.3, 73.8, 71.8, 71.5, 61.7. ESI-MS m/z 339.1 [M + Na]$^+$. ESI-HRMS calcd for $C_{15}H_{25}O_5S$ [M + H]$^+$ 317.1423; found 317.1436.

2,3-Di-*O*-allyl-4-*O*-benzyl-1-thio-α-D-glucopyranose (37). Thiol **37** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 3:1), as a colorless syrup in 85% yield: $[\alpha]_D$ +117 (c 0.2 $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35−7.25 (m, 5H), 6.00−5.88 (m, 2H), 5.71 (t, J = 5.5 Hz, 1H), 5.31 (m, 2H), 5.19 (m, 2H), 4.88 and 4.66 (AB peak, J = 10.5, 11.0 Hz, 2H), 4.40 (dd, J = 5.5, 12.0 Hz, 1H), 4.28 (dd, J = 5.5, 12.0 Hz, 1H), 4.17 (dd, J = 5.5, 12.5 Hz, 1H), 4.10 (dd, J = 5.5, 12.5 Hz, 1H), 4.05 (dt, J = 3.5, 10.0 Hz, 1H), 3.79−3.68 (overlapped m, 3H), 3.62 (dd, J = 5.5, 9.5 Hz, 1H), 3.49 (t, J = 9.5 Hz, 1H), 1.87 (d, J = 4.5 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 138.1, 135.1, 134.3, 128.50, 128.45, 128.1, 127.9, 127.8, 117.6, 116.7, 81.3, 79.1, 78.8, 77.0, 75.1, 74.4, 71.8, 71.5, 61.8; ESI-MS m/z 389.1 [M + Na]$^+$. ESI-HRMS calcd for $C_{19}H_{26}NaO_5S$ [M + Na]$^+$ 389.1399; found 389.1418.

2,3-Di-*O*-allyl-4-*O*-benzyl-1-thio-α-D-galactopyranose (38). Thiol **38** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 3:1), as a colorless syrup in 92% yield: $[\alpha]_D$ +76.2 (c 2.0 $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39−7.32 (m, 5H), 6.02−5.91 (m, 2H), 5.87 (t, J = 4.5 Hz, 1H), 5.36 (m, 2H), 5.22 (m, 2H), 4.98 and 4.96 (AB peak, J = 11.5 Hz, 2H), 4.33−4.17 (m, 4H), 4.20 (overlapped m, 1H), 4.12 (dd, J = 5.5, 10.0 Hz, 1H), 3.91 (br s, 1H), 3.76 (dd, J = 6.5, 11.5 Hz, 1H), 3.68 (dd, J = 2.5, 9.5 Hz, 1H), 3.56 (m, 1H), 1.83 (d, J = 4.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.1, 134.9, 134.5, 128.6, 128.5, 128.0, 117.3, 116.6, 79.5, 78.3, 75.6, 74.49, 74.45, 72.2, 71.7, 71.6, 62.1. ESI-MS m/z 389.1 [M + Na]$^+$. ESI-HRMS calcd for $C_{19}H_{27}O_5S$ [M + H]$^+$ 367.1579; found 367.1562.

3,4-Di-*O*-benzyl-1-thio-α-D-glucopyranose (39). Thiol **39** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 3:1), as an amorphous solid in 86% yield: $[\alpha]_D$ +34.5 (c 1.0 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.30 (m, 10H), 5.62 (t, J = 5.8 Hz, 1H), 4.91−4.80 (m, 3H), 4.69 (d, J = 10.8 Hz, 1H), 4.04 (dt, J = 9.2, 3.2 Hz, 1H), 3.88−3.83 (m, 1H), 3.80−3.78 (m, 2H), 3.70 (d, J = 9.0 Hz, 1H), 3.58 (t, J = 9.2 Hz, 1H), 2.35 (d, J = 6.0 Hz, 1H), 1.97 (d, J = 6.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 128.6, 128.5, 128.03, 128.0, 127.9, 82.0, 80.0, 76.9, 75.3, 74.8, 72.8, 71.6, 61.5. ESI-MS m/z 377.5 [M + H]$^+$. ESI-HRMS calcd for $C_{20}H_{24}NaO_5S$ [M + Na]$^+$ 399.1242; found 399.1252.

2,4-Di-*O*-benzyl-1-thio-α-D-glucopyranose (40). Thiol **40** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 3:2), as an amorphous solid in 90% yield: $[\alpha]_D$ +156.1 (c 1.2 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ

7.37−7.29 (m, 10H), 5.70 (t, J = 5.2 Hz, 1H), 4.91 (d, J = 11.2 Hz, 1H), 4.70 (dd, J = 11.6, 8.8 Hz, 2H), 4.52 (d, J = 11.6 Hz, 1H), 4.05 (dt, J = 9.6, 3.2 Hz, 1H), 3.98 (t, J = 9.2 Hz, 1H), 3.80−3.72 (m, 2H), 3.58 (dd, J = 9.6, 5.6 Hz, 1H), 3.48 (t, J = 9.4 Hz, 1H), 2.70 (br s, 1H), 1.89 (d, J = 5.2 Hz, 1H), 1.78 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.1, 137.1, 128.6, 128.5, 128.20, 128.18, 128.1, 127.9, 78.6, 78.0, 76.6, 74.6, 73.4, 72.0, 71.4, 61.7. ESI-MS m/z 399.2 [M + Na]$^+$. ESI-HRMS calcd for $C_{20}H_{24}NaO_5S$ [M + Na]$^+$ 399.1242; found 399.1250.

2,3-Di-*O*-benzyl-1-thio-α-D-glucopyranose (41). Thiol **41** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 3:2), as an amorphous solid in 83% yield: $[\alpha]_D$ +43.4 (c 0.6 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.31 (m, 10H), 5.74 (t, J = 4.8 Hz, 1H), 5.00 (d, J = 11.6 Hz, 1H), 4.74 (dd, J = 18.0, 11.6 Hz, 2H), 4.62 (d, J = 11.6 Hz, 1H), 4.10−4.05 (m, 1H), 3.81−3.79 (m, 2H), 3.75 (dd, J = 9.2, 5.2 Hz, 1H), 3.71 (t, J = 9.0 Hz, 1H), 3.55 (t, J = 9.2 Hz, 1H), 2.36 (br s, 1H), 1.93 (d, J = 4.8 Hz, 1H), 1.84 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.4, 137.3, 128.6, 128.5, 128.1, 128.04, 128.01, 127.98, 127.95, 127.91, 80.8, 78.9, 78.7, 75.3, 72.1, 71.8, 70.0, 62.3. ESI-MS m/z 399.4 [M + Na]$^+$. ESI-HRMS calcd for $C_{20}H_{24}NaO_5S$ [M + Na]$^+$ 399.1242; found 399.1249.

3-*O*-Benzyl-1-thio-α-D-glucopyranose (42). Thiol **42** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 2:3), as an amorphous solid in 76% yield: $[\alpha]_D$ +92.3 (c 0.5 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.30 (m, 5H), 5.64 (t, J = 5.8 Hz, 1H), 4.95 (d, J = 11.6 Hz, 1H), 4.82 (d, J = 11.6 Hz, 1H), 4.00−3.96 (m, 1H), 3.98−3.82 (m, 3H), 3.62 (t, J = 8.6 Hz, 1H), 3.51 (t, J = 9.2 Hz, 1H), 2.51 (br s, 1H), 2.37 (d, J = 6.4 Hz, 1H), 1.97 (d, J = 6.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 128.7, 128.1, 127.9, 82.1, 80.7, 75.1, 72.5, 71.6, 70.2, 62.2; ESI-MS m/z 309.3 [M + Na]$^+$. ESI-HRMS calcd for $C_{13}H_{18}NaO_5S$ [M + Na]$^+$ 309.0773; found 309.0782.

2-*O*-Benzyl-1-thio-α-D-glucopyranose (43). Thiol **43** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 2:3), as an amorphous solid in 83% yield: $[\alpha]_D$ +87.4 (c 0.5 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.32 (m, 5H), 5.92 (t, J = 4.6 Hz, 1H), 4.77 (d, J = 11.2 Hz, 1H), 4.52 (d, J = 11.2 Hz, 1H), 4.26 (t, J = 4.4 Hz, 1H), 4.12 (br s, 1H), 4.01−3.94 (m, 2H), 3.90−3.85 (m, 2H), 2.84 (s, 1H), 2.57 (br s, 1H), 2.22 (br s, 1H), 1.83 (d, J = 4.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.1, 128.6, 128.2, 128.2, 78.5, 75.3, 71.9, 70.1, 70.0, 69.2, 63.1. ESI-MS m/z 309.4 [M + Na]$^+$. ESI-HRMS calcd for $C_{13}H_{18}NaO_5S$ [M + Na]$^+$ 309.0773; found 309.0760.

General Procedure for the Synthesis of Thiols 44−51. To a solution of the appropriate 1,6-anhydrosugars (1.0 mmol) and bis(trimethylsilyl) sulfide (1.4 mmol) in CH_2Cl_2 (10 mL) was added TMSOTf (0.8 mmol) at 0 °C. The mixture was then stirred at 50 °C overnight (10−15 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 which was purified by flash column chromatography to afford the corresponding α-glycosyl thiol.

4-*O*-Acetyl-2,3-di-*O*-benzyl-1-thio-α-D-glucopyranose (44). Thiol **44** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 4:1), as a colorless syrup in 84% yield: $[\alpha]_D$ +29.0 (c 0.25 $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35−7.29 (m, 10H), 5.74 (t, J = 4.6 Hz, 1H), 4.92−4.86 (m, 2H), 4.74−4.62 (m, 3H), 4.10 (d, J = 10.8 Hz, 1H), 3.90−3.79 (m, 2H), 3.64−3.52 (m, 2H), 2.46 (dd, J = 9.3, 5.4 Hz, 1H), 1.99 (s, 3H), 1.92 (d, J = 4.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 138.3, 137.2, 128.5, 128.3, 128.09, 128.06, 127.7, 127.6, 78.82, 78.76, 78.4, 75.4, 72.6, 70.7, 70.3, 61.1, 20.8. ESI-MS m/z 441.3 [M + Na]$^+$. ESI-HRMS calcd for $C_{22}H_{26}NaO_6S$ [M + Na]$^+$ 441.1348; found 441.1369.

4-*O*-Benzoyl-2,3-di-*O*-benzyl-1-thio-α-D-glucopyranose (45). Thiol **45** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 3:1), as an amorphous solid in 66% yield: $[\alpha]_D$ +19.0 (c 1.0 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00−7.98 (m, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.38−7.31 (m, 5H), 7.16−7.11 (m, 5H), 5.79 (t, J = 5.0 Hz, 1H), 5.20−5.15 (m, 1H), 4.85 (d, J = 11.2 Hz, 1H), 4.75 (d, J = 11.6 Hz, 1H), 4.68 (dd, J = 11.2, 8.4 Hz, 2H), 4.24−4.20 (m, 1H), 4.04 (t, J = 9.2 Hz, 1H), 3.90 (dd, J = 9.2, 5.2 Hz, 1H), 3.71−3.60 (m, 2H), 2.63 (dd, J = 9.6, 6.0 Hz, 1H), 1.96 (d, J = 4.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 137.3, 136.9, 133.0, 129.9, 129.7, 128.38, 128.35, 128.34, 128.1, 127.9, 127.87, 127.86, 78.3, 76.1, 75.2, 74.4, 73.9, 71.8, 71.7, 61.4. ESI-MS m/z 503.5 [M + Na]$^+$. ESI-HRMS calcd for $C_{27}H_{28}NaO_6S$ [M + Na]$^+$ 503.1504; found 503.1485.

3-*O*-Acetyl-2,4-di-*O*-benzyl-1-thio-α-D-glucopyranose (46). Thiol **46** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 4:1), as a colorless syrup in 89% yield: $[\alpha]_D$ +60.2 (c 0.4 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.30 (m, 10H), 5.70 (t, J = 4.8 Hz, 1H), 5.45 (t, J = 9.4 Hz, 1H), 4.68 and 4.50 (AB peak, J = 12.0 Hz, 2H), 4.62 (s, 2H), 4.15 (d-like, J = 9.6, 1H), 3.80 (br s, 2H), 3.69−3.60 (m, 2H), 2.07 (d, J = 4.4 Hz, 1H), 1.98 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 137.7, 137.3, 128.59, 128.55, 128.13, 128.12, 128.10, 128.07, 78.4, 76.5, 75.4, 74.5, 73.2, 71.9, 71.7, 61.4, 21.0. MALDI-MS m/z 441.1 [M + Na]$^+$. MALDI-HRMS calcd for $C_{22}H_{26}NaO_6S$ [M + Na]$^+$ 441.1348; found 441.1352.

2-*O*-Acetyl-3,4-di-*O*-benzyl-1-thio-α-D-glucopyranose (47). Thiol **47** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 4:1), as a colorless syrup in 78% yield: $[\alpha]_D$ +69.7 (c 0.6 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.25 (m, 10H), 5.86 (t, J = 5.8 Hz, 1H), 4.96 (dd, J = 10.5, 6.1 Hz, 1H), 4.87 (d, J = 8.8 Hz, 1H), 4.84 (d, J = 9.2 Hz, 1H), 4.79 (d, J = 11.6 Hz, 1H), 4.68 (d, J = 10.8 Hz, 1H), 4.11 (td, J = 9.6, 3.2 Hz, 1H), 3.93 (t, J = 9.4 Hz, 1H), 3.81−3.79 (m, 1H), 3.78 (t, J = 4.0 Hz, 1H), 3.67−3.62 (m, 2H), 2.03 (s, 3H), 1.80 (d, J = 6.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 138.7, 137.7, 128.5, 128.4, 128.1, 128.0, 127.7, 127.6, 79.9, 77.1, 75.5, 75.2, 73.1, 72.0, 61.6, 20.9. ESI-MS m/z 441.4 [M + Na]$^+$. ESI-HRMS calcd for $C_{22}H_{26}NaO_6S$ [M + Na]$^+$ 441.1348; found 441.1361.

2-*O*-Benzoyl-3,4-di-*O*-benzyl-1-thio-α-D-glucopyranose (48). Thiol **48** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 5:1), as an amorphous solid in 77% yield: $[\alpha]_D$ +10.5 (c 0.9 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 8.4 Hz, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.43 (t, J = 8.0 Hz, 2H), 7.38−7.29 (m, 5H), 7.11 (m, 5H), 5.80 (t, J = 4.8 Hz, 1H), 5.19 (t, J = 9.6 Hz, 1H), 4.83 (d, J = 11.2 Hz, 1H), 4.74−4.63 (m, 3H), 4.24−4.21 (m, 1H), 4.04 (t, J = 9.4 Hz, 1H), 3.90 (dd, J = 9.2, 5.2 Hz, 1H), 3.69−3.59 (m, 2H), 1.97 (d, J = 4.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 138.0, 137.4, 123.7, 128.55, 130.0, 129.1, 128.6, 128.58, 128.55, 128.54, 128.3, 128.2, 128.1, 128.0, 127.7, 79.0, 78.9, 78.3, 75.4, 72.6, 71.0, 70.8, 61.1. MALDI-MS m/z 503.2 [M + Na]$^+$. MALDI-HRMS calcd for $C_{27}H_{28}NaO_6S$ [M + Na]$^+$ 503.1504; found 503.1513.

3,4-Di-*O*-benzyl-2-*O*-pivaloyl-1-thio-α-D-glucopyranose (49). Thiol **49** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 5:1), as a colorless syrup in 83% yield: $[\alpha]_D$ +78.9 (c 1.4 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.23 (m, 10H), 5.77 (t, J = 4.8 Hz, 1H), 4.94 (t, J = 9.6 Hz, 1H), 4.88 (d, J = 10.8 Hz, 1H), 4.66 (t, J = 12.4, 11.6 Hz, 2H), 4.57 (d, J = 11.6 Hz, 1H), 4.12 (d, J = 9.6 Hz, 1H), 3.90 (t, J = 9.0 Hz, 1H), 3.84 (dd, J = 9.2, 5.2 Hz, 1H), 3.62 (dd, J = 12.8, 1.2 Hz, 1H), 3.49 (dd, J = 12.8, 3.6 Hz, 1H), 1.95 (d, J = 4.4 Hz, 1H), 1.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.7, 138.3, 137.4, 128.5, 128.4, 128.2, 128.1, 127.6, 127.4, 79.0, 78.9, 78.7, 75.4, 72.5, 70.0, 61.1, 39.0, 27.2. MALDI-MS m/z 483.2 [M + Na]$^+$. MALDI-HRMS calcd for $C_{25}H_{32}NaO_6S$ [M + Na]$^+$ 483.1817; found 483.1822.

2-Azido-3,4-di-*O*-benzyl-1-thio-α-D-glucopyranose (50). Thiol **50** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 3:1), as a colorless syrup in 86% yield: $[\alpha]_D$ +87.1 (c 0.5 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.30 (m, 10H), 5.66 (t, J = 5.0 Hz, 1H), 4.89 (d, J = 4.4 Hz, 2H), 4.85 (d, J = 2.8 Hz, 1H), 4.69 (d, J = 11.2 Hz, 1H), 4.09 (dt, J = 10.0, 3.2 Hz, 1H), 3.84−3.81 (m, 2H), 3.79−3.76 (m, 2H), 3.68 (d, J = 8.4 Hz, 1H), 3.64−3.61 (m, 1H), 1.96 (d, J = 5.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.6, 137.4, 128.6, 128.5, 128.10, 128.07, 128.0, 127.9, 81.0, 78.5, 77.6, 75.7, 75.1, 72.6, 64.0, 61.4. ESI-MS m/z 400.2

[M-H]$^-$. ESI-HRMS calcd for $C_{20}H_{22}O_4N_3S$ [M-H]$^-$ 400.1331; found 400.1318.

3,4-Di-*O*-acetyl-2-*O*-benzyl-1-thio-*α*-D-glucopyranose (51). Thiol **51** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 4:1), as an amorphous solid in 30% yield: $[\alpha]_D$ +126.9 (*c* 0.3 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.23 (m, 5H), 5.74 (t, *J* = 4.9 Hz, 1H), 5.42 (t, *J* = 9.6 Hz, 1H), 4.93 (t, *J* = 9.8 Hz, 1H), 4.67 and 4.52 (AB peak, *J* = 12.0 Hz, 2H), 4.19 (d-like, *J* = 10.0 Hz, 1H), 3.77 (dd, *J* = 9.6, 5.2 Hz, 1H), 3.70–3.56 (m, 2H), 2.06 (s, 3H), 2.04 (d, *J* = 4.4 Hz, 1H), 2.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 170.0, 137.0, 128.6, 128.2, 127.9, 78.4, 76.0, 72.2, 71.1, 70.4, 68.8, 60.9, 20.8, 20.7. MALDI-MS *m/z* 393.1 [M + Na]$^+$. MALDI-HRMS calcd for $C_{17}H_{22}NaO_7S$ [M + Na]$^+$ 393.0984; found 393.0985.

3,4-Di-*O*-benzoyl-2-*O*-benzyl-1-thio-*α*-D-galactopyranose (52). Thiol **52** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 3:1), as an amorphous solid in 69% yield: $[\alpha]_D$ +50.0 (*c* 0.3 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03–8.01 (m, 1H), 7.92–7.91 (m, 2H), 7.86–7.82 (m, 2H), 7.64–7.59 (m, 1H), 7.52–7.43 (m, 3H), 7.34–7.27 (m, 6H), 5.97 (t, *J* = 4.6 Hz, 1H), 5.74 (d, *J* = 3.2 Hz, 1H), 5.67 (dd, *J* = 10.4, 3.2 Hz, 1H), 4.76 (d, *J* = 12.4 Hz, 1H), 4.65 (dd, *J* = 13.6, 6.8 Hz, 1H), 4.61 (d, *J* = 12.4 Hz, 1H), 4.36 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.69 (dd, *J* = 12.0, 5.2 Hz, 1H), 3.58 (dd, *J* = 13.2, 6.8 Hz, 1H), 2.36 (t, *J* = 6.8 Hz, 1H), 2.07 (d, *J* = 4.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 165.2, 137.0, 133.6, 133.3, 133.1, 129.9, 129.6, 129.4, 129.0, 128.59, 128.58, 128.40, 128.39, 128.3, 128.1, 128.0, 79.1, 77.2, 72.5, 72.1, 70.1, 69.9, 60.7. ESI-MS *m/z* 495.6 [M + H]$^+$. ESI-HRMS calcd for $C_{27}H_{26}NaO_7S$ [M + Na]$^+$ 517.1297; found 517.1306.

General Procedure for the Synthesis of Thiols 53–58. To a solution of the appropriate 1,6-anhydrosugars (1.0 mmol) and bis(trimethylsilyl) sulfide (1.4 mmol) in CH_2Cl_2 (10 mL) was added TMSOTf (0.6 mmol) at 0 °C. The mixture was then stirred at 50 °C overnight (>6 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 which was purified by flash column chromatography to afford the corresponding *α*-glycosyl thiol.

***O*-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-(1→2)-3,4-di-*O*-benzyl-1-thio-*α*-D-glucopyranose (53).** Thiol **53** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 2:1), as an amorphous solid in 58% yield: $[\alpha]_D$ +47.9 (*c* 0.7 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.26 (m, 10H), 5.65 (t, *J* = 5.1 Hz, 1H), 5.14 (ddd, *J* = 12.1, 9.4, 7.0 Hz, 2H), 5.02 (d, *J* = 10.2 Hz, 1H), 4.97 (d, *J* = 10.6 Hz, 1H), 4.88 (dd, *J* = 16.2, 7.7 Hz, 2H), 4.65 (d, *J* = 11.6 Hz, 1H), 4.57 (d, *J* = 11.6 Hz, 1H), 4.13 (dd, *J* = 12.4, 3.6 Hz, 1H), 4.03 (d, *J* = 9.2 Hz, 1H), 3.88–3.82 (m, 3H), 3.77 (s, 2H), 3.71 (dd, *J* = 8.2, 5.5 Hz, 1H), 3.45 (d, *J* = 9.2 Hz, 1H), 2.07 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H), 1.97 (s, 3H), 1.95 (d, *J* = 4.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 170.3, 169.5, 169.3, 139.0, 137.3, 128.4, 128.2, 128.1, 128.0, 127.3, 126.8, 100.8, 79.6, 78.7, 78.6, 76.7, 74.8, 73.1, 72.5, 72.1, 71.8, 71.3, 67.8, 61.5, 60.6, 20.72, 20.67, 20.60, 20.57. ESI-MS *m/z* 729.8 [M + Na]$^+$. ESI-HRMS calcd for $C_{34}H_{42}NaO_{14}S$ [M + Na]$^+$ 729.2193; found 729.2204.

***O*-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-(1→2)-1-thio-*α*-D-galactopyranose (54).** Thiol **54** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 1:1), as an amorphous solid in 67% yield: $[\alpha]_D$ +41.4 (*c* 0.5 $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.82 (t, *J* = 4.7 Hz, 1H), 5.21 (t, *J* = 7.5 Hz, 1H), 5.08 (t, *J* = 9.7 Hz, 1H), 5.03 (dd, *J* = 9.5, 8.0 Hz, 1H), 4.76 (d, *J* = 7.5 Hz, 1H), 4.25 (dd, *J* = 12.5, 2.5 Hz, 1H), 4.19–4.17 (m, 2H), 4.16–4.14 (m, 1H), 4.10 (dd, *J* = 9.5, 5.0 Hz, 1H), 3.97–3.90 (m, 3H), 3.74–3.69 (m, 1H), 3.16 (br s, 1H), 2.60 (br s, 1H), 2.28 (br s, 1H), 2.10 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H), 1.93 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6, 170.2, 169.7, 169.3, 102.1, 79.6, 77.7, 72.6, 71.6, 68.3, 61.8, 20.8, 20.7, 20.6, 20.5. ESI-MS *m/z* 549.5 [M + Na]$^+$. ESI-HRMS calcd for $C_{20}H_{30}NaO_{14}S$ [M + Na]$^+$ 549.1254; found 549.1255.

***O*-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzyl-1-thio-*α*-D-glucopyranose (55).** Thiol **55** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 3:1), as an amorphous solid in 72% yield: $[\alpha]_D$ +48.5 (*c* 0.7 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.28 (m, 10H), 5.65 (t, *J* = 5.2 Hz, 1H), 5.19–4.99 (m, 5H), 4.62–4.55 (m, 3H), 4.26 (dd, *J* = 12.4, 4.4 Hz, 1H), 4.17 (t, *J* = 9.0 Hz, 1H), 4.12 (dd, *J* = 14.4, 7.2 Hz, 1H), 4.05–4.00 (m, 2H), 3.75–3.66 (m, 3H), 3.63–3.59 (m, 1H), 3.50 (t, *J* = 9.6 Hz, 1H), 2.08 (s, 3H), 2.01 (s, 6H), 1.98 (s, 3H), 1.83 (d, *J* = 4.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 170.1, 169.3, 169.2, 138.2, 136.8, 128.7, 128.40, 128.39, 128.36, 128.1, 127.8, 100.3, 79.7, 78.7, 78.1, 75.1, 74.6, 73.0, 72.6, 72.0, 71.7, 71.5, 68.3, 61.8, 61.7, 20.8, 20.59, 20.57, 20.5. ESI-MS *m/z* 729.6 [M + Na]$^+$. ESI-HRMS calcd for $C_{34}H_{42}NaO_{14}S$ [M + Na]$^+$ 729.2193; found 729.2225.

***O*-(2,3,4,6-Tetra-*O*-acetyl-*α*-D-glucopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-*β*-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzyl-1-thio-*α*-D-glucopyranose (56).** Thiol **56** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 2:1), as an amorphous solid in 65% yield: $[\alpha]_D$ +22.0 (*c* 0.3 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (m, 4H), 7.37–7.29 (m, 6H), 5.64 (t, *J* = 5.2 Hz, 1H), 5.38 (d, *J* = 4.0 Hz, 1H), 5.34–5.29 (m, 1H), 5.22 (t, *J* = 9.2 Hz, 1H), 5.16 (d, *J* = 8.0 Hz, 1H), 5.04 (dd, *J* = 10.0, 9.8 Hz, 2H), 4.95 (d, *J* = 9.6 Hz, 1H), 4.90–4.89 (m, 1H), 4.87 (dd, *J* = 10.4, 4.0 Hz, 1H), 4.61–4.54 (m, 3H), 4.35 (dd, *J* = 12.0, 2.8 Hz, 1H), 4.24–4.18 (m, 2H), 4.17–4.11 (m, 2H), 4.06–4.05 (m, 1H), 4.00 (s, 1H), 3.96 (d, *J* = 8.8 Hz, 1H), 3.93–3.89 (m, 1H), 3.69–3.66 (m, 2H), 3.63–3.59 (m, 1H), 3.48 (t, *J* = 9.2 Hz, 1H), 2.08, 2.07, 2.06, 2.019, 2.016, 2.00, 1.99 (each s, each 3H), 1.84 (d, *J* = 4.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.44, 170.40, 170.1, 169.8, 169.6, 169.4, 138.3, 136.9 128.7, 128.5, 128.41, 128.37, 128.0, 127.8, 99.9, 95.6, 79.6, 78.9, 78.1, 77.1, 75.4, 75.1, 74.4, 72.8, 72.7, 72.1, 71.5, 70.0, 69.4, 68.5, 68.0, 63.0, 61.7, 61.5, 20.88, 20.81, 20.62, 20.61, 20.55, 20.54. ESI-MS *m/z* 1018.0 [M + Na]$^+$. ESI-HRMS calcd for $C_{46}H_{58}NaO_{22}S$ [M + Na]$^+$ 1017.3038; found 1017.3019.

***O*-(2,3-Di-*O*-benzyl-*α*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-1-thio-*α*-D-glucopyranose (57).** Thiol **57** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 2:3), as an amorphous solid in 74% yield: $[\alpha]_D$ +24.4 (*c* 2.9 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.25 (m, 12H), 7.23–7.22 (m, 4H), 7.17–7.15 (m, 4H), 5.72 (m, 2H), 5.03 (d, *J* = 12.0 Hz, 1H), 4.93 (d, *J* = 11.2 Hz, 1H), 4.71 (d, *J* = 12.0 Hz, 1H), 4.64 (d, *J* = 11.6 Hz, 2H), 4.51–4.49 (m, 3H), 4.21 (d, *J* = 10.0 Hz, 1H), 4.09 (t, *J* = 9.2 Hz, 1H), 3.98 (t, *J* = 8.6 Hz, 2H), 3.90 (d-like, *J* = 12.0 Hz, 1H), 3.81–3.79 (m, 2H), 3.75–3.71 (m, 3H), 3.46–3.39 (m, 3H), 2.41 (br s, 1H), 2.31 (br s, 1H), 1.95 (d, *J* = 4.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.0, 138.7, 137.9, 137.4, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.4, 126.6, 97.2, 81.8, 81.5, 79.6, 79.3, 78.8, 77.4, 75.5, 74.3, 73.4, 72.6, 71.6. ESI-MS *m/z* 741.5 [M + Na]$^+$. ESI-HRMS calcd for $C_{40}H_{46}NaO_{10}S$ [M + Na]$^+$ 741.2709; found 741.2740.

***O*-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-(1→4)-*O*-[2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl-(1→6)]-*O*-(2,3-di-*O*-benzyl-*α*-D-glucopyranosyl)-(1→4)-2,3-di-*O*-benzyl-1-thio-*α*-D-glucopyranose (58).** Thiol **58** was obtained, after purification by flash column chromatography (petroleum ether/EtOAc, 1:1), as an amorphous solid in 81% yield: $[\alpha]_D$ +19.4 (*c* 0.7 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.16 (m, 20H), 5.74 (t, *J* = 5.0 Hz, 1H), 5.62 (d, *J* = 3.2 Hz, 1H), 5.54 (t, *J* = 9.8 Hz, 1H), 5.47 (t, *J* = 3.4 Hz, 1H), 5.18 (t, *J* = 9.4 Hz, 1H), 5.08 (t, *J* = 9.8 Hz, 3H), 5.03–4.96 (m, 2H), 4.93–4.85 (m, 3H), 4.73 (dd, *J* = 12.8, 8.8 Hz, 1H), 4.66 (dd, *J* = 13.6, 12.0 Hz, 2H), 4.59 (d, *J* = 7.6 Hz, 1H), 4.53 (t, *J* = 5.6 Hz, 2H), 4.28–4.25 (m, 1H), 4.26–4.24 (m, 1H), 4.24–4.21 (m, 1H), 4.17–4.14 (m, 1H), 4.14 (m, 1H), 4.12–4.07 (m, 1H), 4.04 (dd, *J* = 10.4, 2.4 Hz, 1H), 3.99–3.94 (m, 2H), 3.86–3.83 (m, 1H), 3.82–3.75 (m, 2H), 3.77–3.75 (m, 1H), 3.74 (d, *J* = 4.4 Hz, 1H), 3.64–3.61 (m, 1H), 3.45–3.40 (m, 1H), 3.06 (d, *J* = 3.2 Hz, 1H), 2.41 (d, *J* = 2.8 Hz, 1H), 2.09, 2.08, 2.06, 2.03, 2.02, 2.01 (each s, each 3H), 1.99 (s, 6H), 1.95 (d, *J* = 4.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.71, 170.67, 170.2, 170.1, 170.0, 169.6, 169.5, 169.3, 138.7, 138.5, 137.7, 137.2, 128.5, 128.4, 128.3, 128.2, 128.0, 127.80, 127.77, 127.71, 127.68, 127.67, 127.2, 126.7, 100.8, 96.8, 95.6, 90.2, 81.3, 80.7, 79.4, 78.5, 77.2, 75.0, 74.1, 73.3, 73.1, 72.7, 72.3, 72.1, 71.9, 71.4, 71.2, 70.4, 68.9, 68.4, 67.3, 61.9, 20.71, 20.69, 20.66, 20.63, 20.57, 20.56, 20.53. ESI-MS m/z 1379.2 $[M]^+$. ESI-HRMS calcd for $C_{68}H_{82}O_{28}NaS$ $[M + Na]^+$ 1401.4611; found 1401.4659.

■ 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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