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Protecting Group-Free Glycoligation by the Desulfurative Rearrangement of Allylic Disulfides as a Means of Assembly of Oligosaccharide Mimetics

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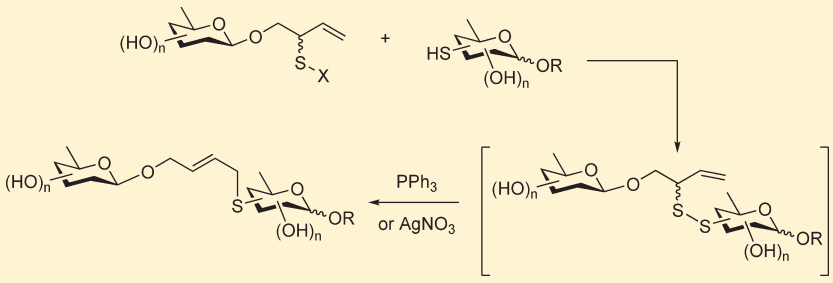
Supporting Information

ABSTRACT:



2-(2-Pyridyldithio-3-butenyl) glycosides react with carbohydrate-based thiols in a two-step process involving sulfenyl transfer followed by desulfurative 2,3-allylic rearrangement, promoted by either triphenylphosphine or silver nitrate, to give novel saccharide mimetics. In an alternative embodiment of the same chemistry anomeric thiols are coupled with carbohydrates derivatized in the form of 2-(2-pyridyldithio-3-butenyl) ethers. This new method of glycoligation does not require protection of hydroxyl groups and is compatible with the presence of acetamides, azides, trichloroethoxycarbamates, and thioglycosides. Variations on the general theme enable the preparation of mimetics of reducing and nonreducing oligosaccharides as well as of nonglycosidically linked systems.

INTRODUCTION

Peptide chemistry has benefitted enormously from the advent of chemical ligation techniques and native chemical ligation techniques enabling the assembly of larger peptides from two or more smaller segments using minimalist protecting group strategies;[1] the synthesis of complex oligosaccharides would similarly be considerably advanced by methods for the linking together of smaller preassembled oligosaccharides, preferably in an unprotected form. The need for the synthesis of such oligosaccharides, however, is increasing as it becomes apparent that for optimal binding certain carbohydrate−protein interactions require longer oligosaccharides. A case in point is the β-(1→3)-glucan interaction with the lectin dectin 1 for which the minimal binding motif is the decasaccharide.[2] While the synthesis of a β-(1→3)-glucodecaose has been reported,[2c] the assembly of even relatively short β-(1→3)-glucans[3] is challenging[4] and is frequently complicated by the unanticipated formation of α-glycosidic bonds depending on the substituent pattern in both the donor and the acceptor despite the reliance on neighboring group participation.[5] The established adoption of nonchair conformations by some pyranoside residues in the growing chain,[3,6] stereochemical matching and mismatching effects,[7] and the conformation of the polymer go some way toward explaining the origin of these problems but do not lessen the challenges to be faced in such syntheses. Other oligosaccharides of interest include the β-(1→6)-glucans, which are critical components of yeast cell walls,[8] and the mycobacterial polysaccharides 3-*O*-methyl-α-(1→4)-mannan and 6-*O*-methyl-α-(1→4)-glucan. These latter methylated glycans enhance the rate of fatty acid biosynthesis by the FA synthetase I from *Mycobacterium smegmatis* through association with the tetraenonic fatty acid products, for which at least a dodecasaccharide is required for optimal binding.[9] Another oligosaccharide of interest is the adhesin poly-β-(1→6)-*N*-acetyl-D-glucosamine from *Escherichia coli*[10] and *Staphylococcus aureus*[11] implicated in the growth of biofilms of these organisms and for which oligomers up the undecamer have been assembled by stepwise and block organic syntheses.[12] Yet another situation is presented by the glycan heparin of which a pentasaccharide motif suffices for association with antithrombin III, while an octadecasaccharide is the optimal chain length for the formation of a tertiary complex with both thrombin and antithrobin III.[13]

Ideally, large glycans can be constructed by the block assembly approach;[14] unfortunately, with certain exceptions,[15] such

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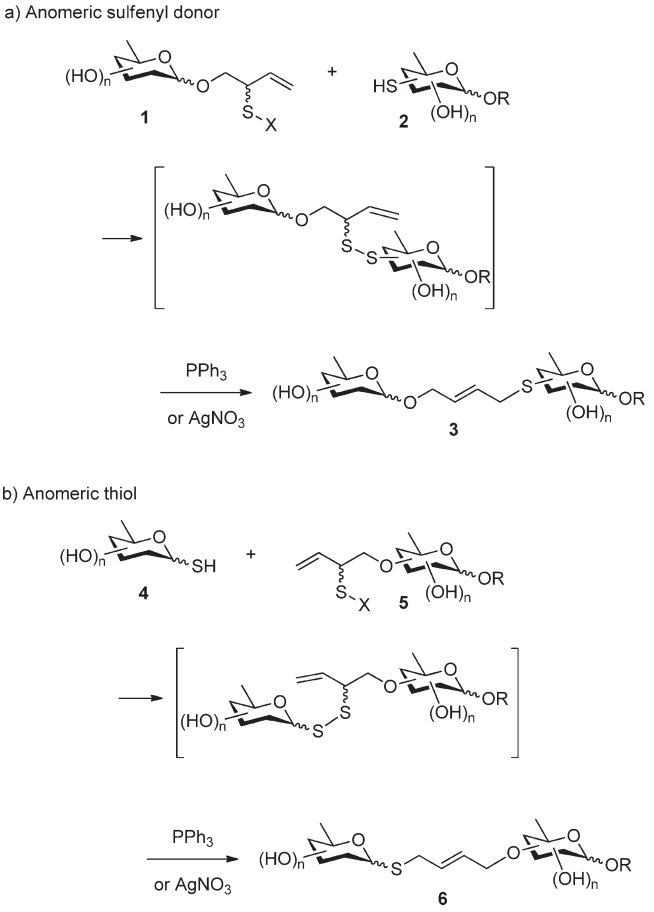
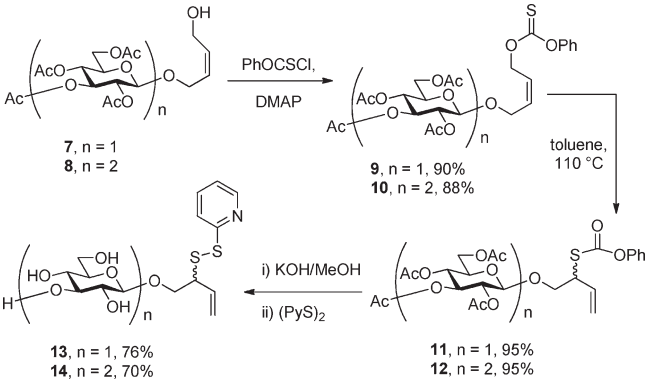
Scheme 1. Two Strategies for the Construction of Oligosaccharide Mimetics



Scheme 2. The Allylic Xanthate Rearrangement Pathway to Mono- and Disaccharyl Anomeric Sulfenyl Donors



methods have enjoyed only modest success owing to the complexities of the structures involved and especially the need for very high levels of stereocontrol. As such, chemists have turned to alternative methodologies that enable the ligation of preformed oligosaccharides into larger glycan-like structures. Among these methods the copper-catalyzed variant of the Huisgen 1,3-dipolar cycloaddition of alkynes and azides, known as Click chemistry,[16] because of the mildness of its reaction conditions and very broad functional group tolerance, has come to dominate the area of glycoconjugate and oligosaccharide mimetic chemistry.[17] The rigid nature of the triazole unit introduced in this process, however, leaves room for the development of alternative ligation techniques. For this reason, and because of their functional group tolerance, the so-called thiol−ene and thiol−yne click reactions[18] in which thiols undergo additions to alkenes or alkynes, respectively, resulting in thioether linkages have gained increased popularity in recent years albeit with most examples still involving the conjugation of sugars to peptides.[19] The thiol−ene and thiol−yne reactions differ from the copper-catalyzed Huisgen 1,3-dipolar cycloaddition click process not only in the nature of the fundamental chemistry and the functional groups required for ligation, but also in terms of the physical nature of the linkage unit introduced. Thus, the planar triazole moiety capable of imitating either a *trans*- or a *cis*-amide with its extensive hydrogen bonding capabilities[20] is replaced by the less-polar and more conformationally labile thioether unit, which may impact either positively or negatively on the binding of the construct to its biological target. In our laboratory we have been engaged in the development of the highly functional group respective dechalcogenative 2,3-sigmatropic rearrangement of allylic disulfides and selenosulfides as a means of the functionalization of thiols under mild protic conditions.[21] This method, which is somewhat related to the thiol−ene and thiol−yne reactions in that it requires derivatization of one of the substrates with a thiol and results in a thioether linkage, has been successfully applied to the formation of glycopeptides mimetics[22] and to the functionalization of proteins.[23] Here, we describe the extension of this method to the formation of oligosaccharide mimetics and, out of necessity, describe syntheses of carbohydrate-based thiols that may also find application in the thiol−ene and thiol−yne reactions and in other conjugation processes relying on thiolate alkylations.[24]

RESULTS AND DISCUSSION

Application of the desulfurative rearrangement of allylic disulfides to the problem of the formation of oligosaccharide mimetics can be envisaged as involving the coupling of an allylic sulfenyl donor **1** affixed to the anomeric position to a carbohydrate based thiol **2** (Scheme 1, strategy a) or, conversely, through the coupling of an anomeric thiol **4** with a sulfenyl donor located elsewhere in the second partner **5** (Scheme 1, strategy b). Ultimately, the two strategies give mimetics **3** and **6** that are close structural analogues differing only in the placement of the oxygen and sulfur atoms in the linker. Additionally, the rearrangement step can be executed with the aid of either triphenylphosphine or silver nitrate (Scheme 1). Both strategies and both reagents have been investigated as described below.

The anomeric sulfenyl donor strategy was targeted first, necessitating the synthesis of anomeric allylic sulfenyl donors and of deoxy sugar thiols. With the direct glycosylation of 2-(2-pyridyldisulfenyl)-3-buten-1-ol giving only moderate yields as previously described,[22b] attention was focused on approaches involving construction of the allylic sulfenyl donor moiety after formation of the glycosidic bond. As described previously,[21e,22b,25] the readily assembled glycoside **7** can be converted into thiocarbonate **9** and subjected to [3,3]-sigmatropic rearrangement to afford the secondary allylic thiol derivative **11**, which can be converted to the sulfenyl donor **13** by saponification and installation of the disulfide moiety (Scheme 2). While this method requires several steps it has the advantage of using only simple

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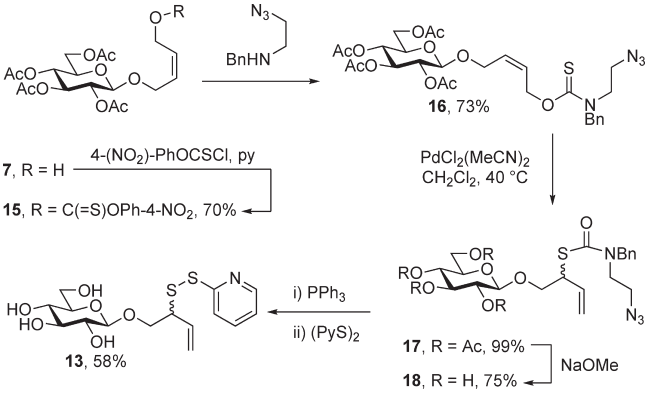
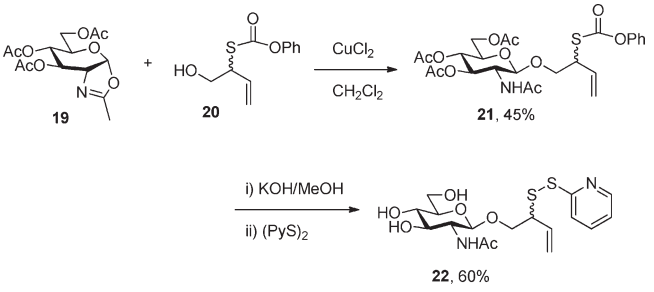
Scheme 3. Alternative Approach to an Anomeric Sulfenyl Donor



Scheme 4. A More Direct Preparation of an Anomeric Sulfenyl Donor



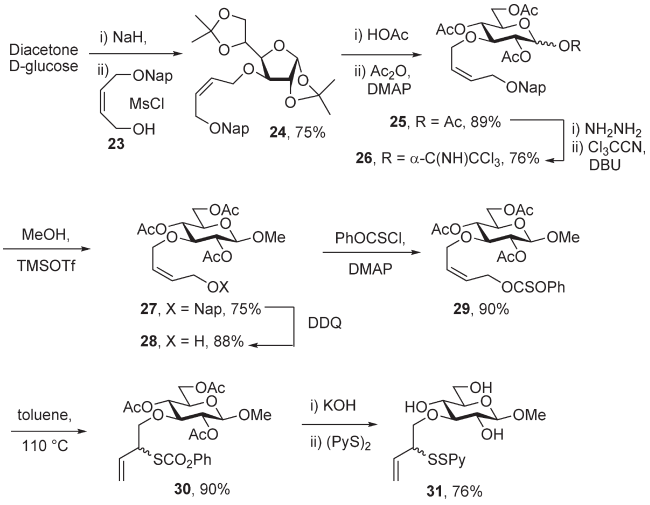
robust chemistry and can generally be conducted in high overall yield.

Seeking to lower the temperature of the sigmatropic rearrangement step and at the same time to dissociate saponification of the acetate protecting groups from the unmasking of the allylic thiol, we briefly investigated a variant on this approach (Scheme 3). This modification features the use of a thionocarbamate rather than a thiocarbonate, such that differential saponification can be affected, that of a palladium-catalyzed [3,3]-sigmatropic rearrangement of the allylic thiocarbonyl system related to ones developed earlier by ourselves[25] and by other laboratories,[26] and, recalling the work of Kahne on the release of esters under neutral conditions,[27] cleavage of the rearranged thiocarbamate by a reductive cyclization process (Scheme 3). Although certainly longer than the approach employing the thermal sigmatropic rearrangement, the chemistry described in Scheme 3 may be advantageous for more complex and thermally sensitive substrates.

A third more efficient approach is exemplified for the case of *N*-acetylglucosamine, which was converted to the oxazoline **19** by standard means[28] and coupled with the acceptor **20**[22b] in the presence of cupric chloride (Scheme 4). The subsequent steps of saponifcation and sulfenyl transfer took place under the standard conditions and led to the formation of the anomeric sulfenyl donor **22**.

With respect to the alternative strategy based on the use of anomeric thiols, a protocol for the synthesis of *O*-[2-(2-pyridyldisulfenyl)-3-butenyl] ethers was developed for the

Scheme 5. Synthesis of a 3-*O*-Sulfenyl Donor



3-position of the glucopyranosyl systems based on the allylic xanthate rearrangement. Thus, alkylation of diisopropylidene-D-glucofuranose with the mesylate derived from *cis*-2-butene-1,4-diol mono naphthylmethyl ether **23** gave a fully protected derivative **24** that was taken through a standard protocol to achieve rearrangement to the pyranose isomer **25** (Scheme 5). The anomeric acetate formed in this protocol was converted uneventfully to the corresponding methyl β-glycoside **27** by Schmidt's trichloroacetimidate chemistry[29] before the naphthylmethyl group was removed oxidatively, setting the stage for the application of the thiocarbonyl ester chemisty and conversion to an allylic sulfenyl donor (Scheme 5).

With respect to the synthesis of monosaccharyl thiols these were typically handled as their acetate esters to minimize problems of oxidation, with cleavage under Zemplen-like conditions immediately prior to use (Table 1, column 3). Depending on the synthetic route employed the hydroxyl groups of these thiol precursors were either free or protected in the form of acetate esters. In the latter case, the esters were cleaved concomitantly with the thioesters under Zemplen conditions prior to the ligation reaction. A 6-deoxyglucose-6-thiol **32** was prepared according to a literature route in the form of its derived thioacetate,[30] while an analogous *N*-acetyl glucosamine 6-thioacetate **33** was assembled by selective Mitunsobu reaction[31] at the 6-position without the need for protecting groups. A glucose-based 3-deoxy-3-mercapto sugar precursor **37** was prepared in a straightforward manner from peracetyl 3-thioglucopyranoside[32] via the trichloroacetimidate **36**, while the known phenylthio analogue **38** was obtained directly from the anomeric acetate (Scheme 6). The 1-deoxy-mercapto-β-D-glucopyranose perester **39** was a commercial compound.

With a series of monomeric sulfenyl donors and thiols in hand, attention was turned to the ligation protocol. This was typically conducted in methanolic solution by admixture of the two components, with monitoring of the sulfenyl transfer step either by TLC or electrospray mass spectrometry, followed by promotion of the desulfurative rearrangement by addition of triphenylphosphine or silver nitrate. As we have discussed previously,[21b,c] the use of trialkylphosphines in place of triarylphosphines generally results in the competing nucleophilic cleavage of the

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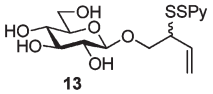
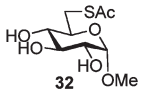
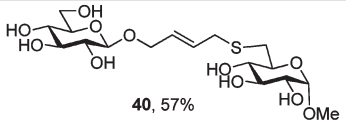
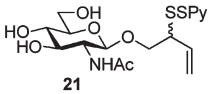
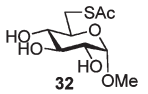
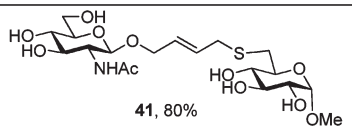
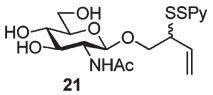
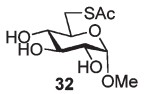
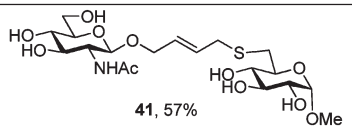
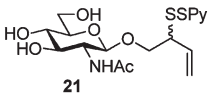
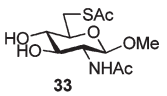
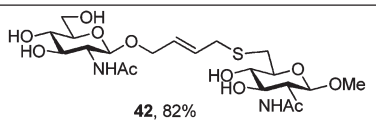
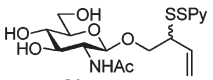
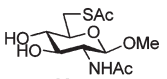
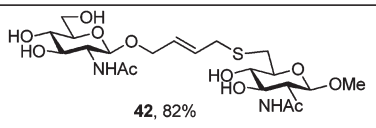
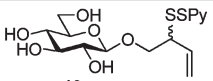
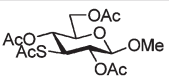
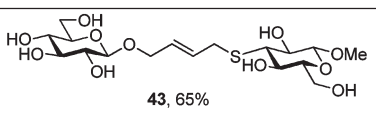
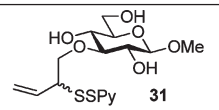
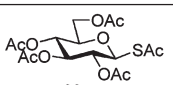
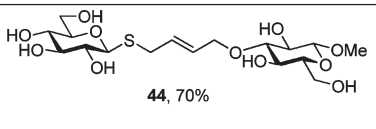
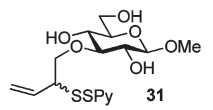
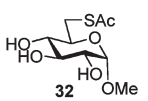
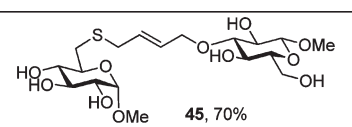
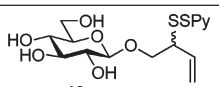
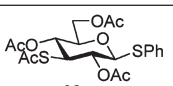
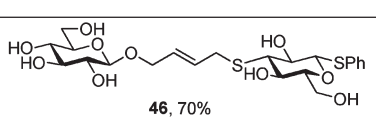
Table 1. Ligation of Monosaccharyl Sulfenyl Donors and Thiols

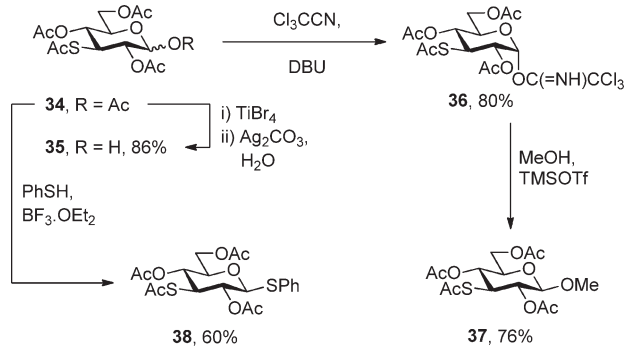
Entry	Sulfenyl Donor	Thiol Precursor	Reagent	Rearrangement Time (h)	Product, % yield
1	 **13**	 **32**	PPh_3	12	 **40**, 57%
2	 **21**	 **32**	PPh_3	30	 **41**, 80%
3	 **21**	 **32**	$AgNO_3$	40	 **41**, 57%
4	 **21**	 **33**	PPh_3	30	 **42**, 82%
5	 **21**	 **33**	$AgNO_3$	40	 **42**, 82%
6	 **13**	 **37**	$AgNO_3$	24	 **43**, 65%
7	 **31**	 **39**	$AgNO_3$	16	 **44**, 70%
8	 **31**	 **32**	$AgNO_3$	16	 **45**, 70%
9	 **13**	 **38**	$AgNO_3$	24	 **46**, 70%

disulfide intermediate and related processes. For this reason the use of highly water-soluble phosphines such as tris(carboxyethyl)phosphine, which are otherwise expected to increase the rearrangement rate, is precluded. The silver nitrate-based system is a later variant on the original phosphine-mediated rearrangement that was developed to circumvent the reliance on the insoluble phosphine.[25] Examples of both methods are presented in the reactions set out in Table 1.

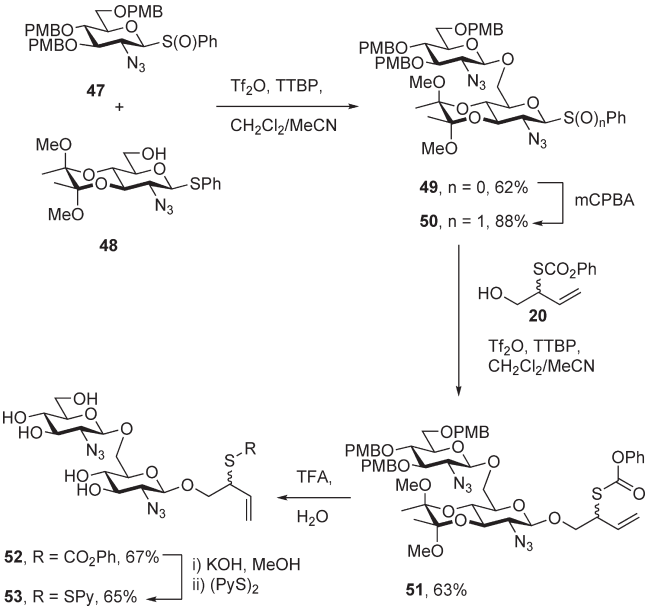
All of the couplings illustrated in Table 1 proceeded in moderate to good yield, whether promoted by triphenylphosphine or by silver nitrate, and gave excellent *trans*-selectivity for the 2-butenyl linker. The examples set out in Table 1 further demonstrate that this ligation protocol is compatible with acetamide groups and thioglycosidic units in addition to hydroxyl groups and *O*-glycosidic bonds. The reaction sequence can be used to assemble mimics of either classical "head-to-tail"-linked

dx.doi.org/10.1021/jo102411j |*J. Org. Chem.* 2011, 76, 3691–3709

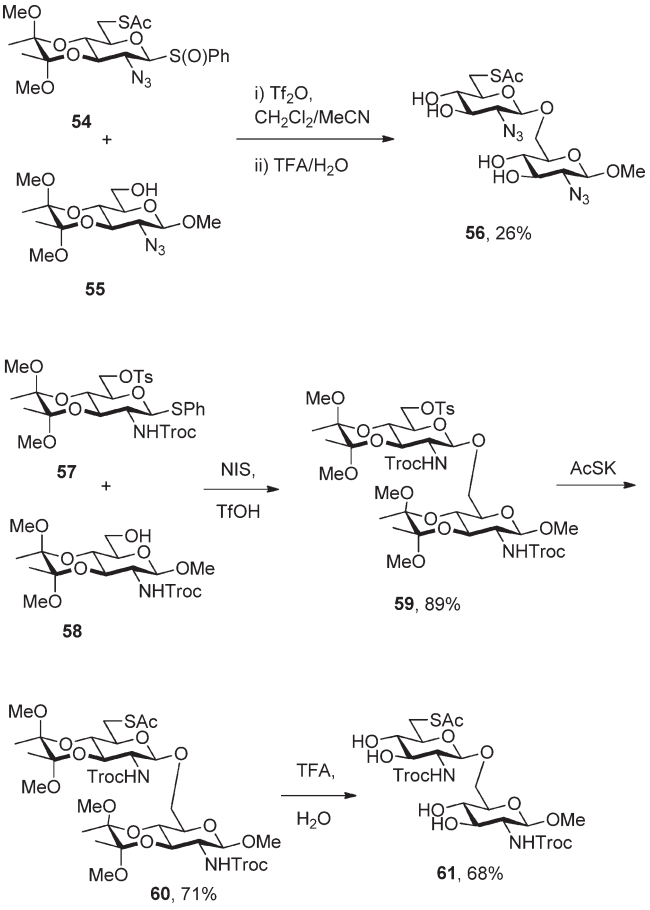
Scheme 6. Synthesis of 3-Deoxy-3-mercapto Sugar Precursors



Scheme 7. Synthesis of a Disaccharyl Sulfenyl Donor



Scheme 8. Synthesis of Two Primary Disaccharyl Thiol Precursors



oligosaccharides (Table 1, entries 1−7 and 9) or can be used to provide mimics of nonglycosidically linked disaccharides (Table 1, entry 8) which are of current interest.[33] For the mimics of the classical head-to-tail oligomers, the ligation can be conducted according to either of the two design principles set out in Scheme 1, but at least for the mimics of the β-(1→3)-glucans the employment of the anomeric thiol (Scheme 1b) results in a shorter reaction time than the use of an anomeric sulfenyl donor (Scheme 1a) as is seen from a comparison of entries 6 and 7 (Table 1). We believe that this difference in reactivity is due to the steric hindrance about the thiol derived from precursor **37** (Table 1, entry 6) which retards both sulfenyl transfer and especially the critical desulfurative 2,3-sigmatropic rearrangement step. This retarding effect of steric bulk around the thiol component on the sigmatropic rearrangement is in accord with predictions from computational studies.[21e]

With proof of principle established at the level of monosaccharyl sulfenyl donors and thiols, attention was turned to the synthesis of a set of disaccharyl allylic disulfides and thiols. As exemplified in Schemes 7 and 8, and as is described fully in the Experimental Section (Schemes 9−14), these units were assembled by the combination of standard coupling methods with variations on the themes set out in Schemes 2−5 for the introduction of the allylic disulfide and thiol moieties. These syntheses were generally uneventful and featured, inter alia, the use of acetonitrile to direct glycosylations to the β-stereochemistry in the 2-azido-2-deoxyglucose series,[34] the use of the sulfoxide glycosylation[35] method and the activation of glycosyl sulfoxides in the presence of thioglycosides as described originally by the van Boom group,[35b,36] the application of the Ley-type bisacetal protecting group for the 3- and 4-positions in the glucosamine series,[37] and the employment of both diisopropylidene glucofuranose and a 4,6-*O*-benzylidene protected glucopyranosyl-3-ol[3,38] as acceptors in the synthesis of laminaribiose derivatives. As in the monosaccharide series thiols were, with the exception of the laminaribiosyl thiol **65**, generated and handled as thioacetates which were cleaved immediately prior to use typically with concomitant removal of any residual acetate esters. The various disaccharyl sulfenyl donors and thiols synthesized in this manner were coupled in methanol at room temperature leading to the results set out in Table 2.

The results set out in Table 2 follow the pattern of moderate to good yield and excellent *trans*-selectivity established for the monosaccharides in Table 1. The results presented in Table 2 also bring the azide and trichloroethoxycarbamates into the range

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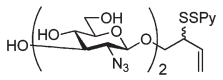
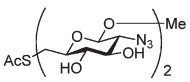
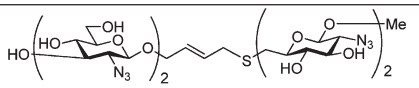
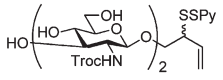
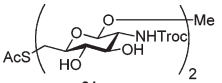
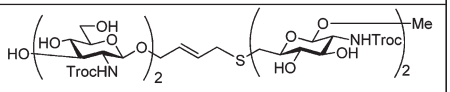
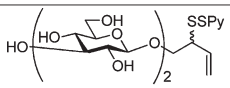
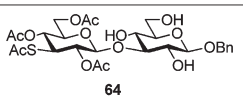
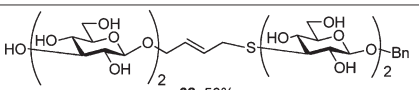
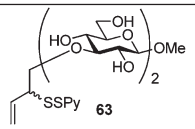
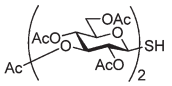
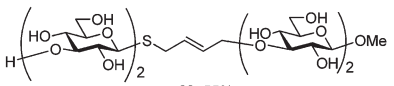
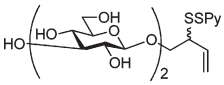
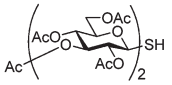
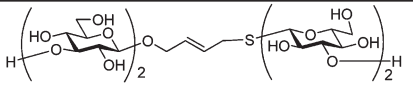
Table 2. Ligation of Disaccharyl Sulfenyl Donors and Thiols

Entry	Sulfenyl Donor	Thiol Precursor	Reagent	Rearrangement Time (h)	Product, % yield
1	 **53**	 **56**	$AgNO_3$	54	 **66**, 52%
2	 **62**	 **61**	PPh_3	60	 **67**, 54%
3	 **14**	 **64**	$AgNO_3$	24	 **68**, 50%
4	 **63**	 **65**	$AgNO_3$	16	 **69**, 55%
5	 **14**	 **65**	$AgNO_3$	16	 **70**, 55%

of functional groups tolerated by this ligation protocol and extend the type of linkages mimicked to include the head-to-head linkage of the nonreducing oligosaccharides (Table 2, entry 5) such as present in sucrose, trehalose, and the antibiotic everninomycin.[39] As was the case with the monosaccharyl examples (vide supra) application of the protocol to a thiol located at the 3-position of a glucopyranose ring resulted in longer reaction times, presumably for steric reasons (Table 2, entry 3) than the employment of the alternative mode of operation with an anomeric thiol and a 3-*O*-allylic sulfenyl donor (Table 2, entry 4).

Overall, the results presented in Tables 1 and 2 demonstrate sulfenyl transfer to give allyl disulfides followed by desulfurative rearrangement to provide a potentially useful means of combining short oligosaccharides into larger oligosaccharide mimetics. The ligation process takes place at room temperature in protic solvents and does not require the presence of protecting groups. It may be effectively promoted through the use of silver nitrate or triphenylphosphine, and tolerates the presence of various functional groups such as the azide, thioglycoside, and trichloroethoxycarbamate systems. Mimics of reducing and nonreducing oligosaccharides as well as of nonglycosidically linked systems can be produced by this facile ligation process.

EXPERIMENTAL SECTION

General Experimental. Unless otherwise stated ^1H and ^{13}C NMR spectra were carried out at 500 and 125 MHz, respectively, in deuteriochloroform solution, with chemical shifts downfield from tetramethylsilane. Specific rotations were measured in chloroform solution unless otherwise stated. Unless otherwise stated extracts were dried over sodium sulfate and concentrated at ambient temperature under water aspirator vacuum. Column chromatography was conducted over silica gel unless otherwise stated.

General Procedure 1 for the Preparation of Allylic Thionocarbonates. A solution of phenyl chlorothionocarbonate (2.0 mmol) in CH_2Cl_2 (2 mL) was added to a solution of the alcohol (1.0 mmol), pyridine (15.0 mmol), and DMAP (0.1 mmol) in CH_2Cl_2 (10.0 mL) and the resulting dark-yellow solution was stirred at room temperature for 4 h. The reaction mixture was poured into H_2O (20 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried, filtered, evaporated, and purified by column chromatography.

General Procedure 2 for the [3,3]-Sigmatropic Rearrangement of Allylic Thionocarbonates. A solution of allylic thionocarbonate (1 mmol) in toluene (10.0 mL) was heated at reflux for 12 h. Evaporation of the solvent and chromatographic purification of the crude products with EtOAc/hexanes as eluent afforded the products.

General Procedure 3 for Saponification of Phenoxycarbonylthioxybutenyl Groups and Installation of the Pyridyl Disulfide Moiety. To a solution of the glycosyl thiocarbonate (0.5 mmol) in MeOH (2.5 mL) was added, dropwise at 0 °C, a freshly prepared solution of 1 M KOH (2.3 mmol, 1.5 equiv per group to be saponified). The resulting mixture was stirred for 0.5 h then neutralized by careful addition of Amberlyst-15 resin and then filtered. The filtrate was added dropwise to a solution of 2,2′-dipyridyl disulfide (0.7 mmol) in MeOH at 0 °C. The resulting mixture was allowed to warm to room temperature and stirred for 4 h. The solvent was removed in vacuo and the residue was purified by silica gel column chromatography to give the desired products.

General Procedure 4 for the Preparation of Cyclic Bisacetals. Camphorsulfonic acid (0.34 mmol) was added to a stirred solution of the glycoside (3.4 mmol) in MeOH (32 mL) at room temperature. Then, trimethyl orthoformate (18.5 mmol) and butane-2,3-dione

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(4.0 mmol) were added and the mixture was heated at reflux for 14−16 h. The mixture was then basified to pH 8 by addition of triethylamine and the solvents were removed under reduced pressure. The residue was purified by silica gel column chromatography to give the desired bisacetals.

General Procedure 5 for the Preparation and Isolation of Tosylates. *p*-Toluenesulfonyl chloride (4.86 mmol) and tetramethylethylenediamine (4.86 mmol) were added sequentially to a stirred solution of the glycoside (0.24 mmol) in acetonitrile (25 mL) at room temperature. The mixture was stirred for 2−5 h, then poured into ice and extracted twice with CH_2Cl_2. The combined organic layers were dried, filtered, and concentrated in vacuo. The residue was purified by silica gel chromatography.

General Procedure 6 for the Introduction of the 6-Acetylthio Group from the Corresponding Tosylates. To a solution of tosylate (2.12 mmol) in DMF (28 mL) was added potassium thioacetate (4.24 mmol). The reaction mixture was heated to 80 °C (50 °C in the case of the disaccharide) for 18−36 h then concentrated in vacuo. The residue was taken up in CH_2Cl_2 and washed with water. The aqueous phase was extracted twice with CH_2Cl_2. The combined organic layers were dried, filtered, and concentrated and the 6-acetylthio derivatives were isolated by silica gel column chromatography.

General Procedure 7 for the Oxidation of Thioglycosides to Glycosyl Sulfoxides. To a stirred solution of thioglycoside (1.06 mmol) in CH_2Cl_2 (30 mL) was added dropwise at −80 °C a freshly prepared solution of *m*-chloroperoxybenzoic acid (1.04 mmol) in CH_2Cl_2 (3.8 mL). The resulting mixture was stirred at −80 °C for 0.5−1.5 h then quenched by addition of saturated aqueous $NaHCO_3$. The resulting mixture was allowed to warm to room temperature and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic layers were dried, filtered, concentrated, and purified by silica gel column chromatography to yield the desired glycosyl sulfoxides.

General Procedure 8 for Glycosylation under NIS/TfOH Conditions. The glycosyl donor (0.56 mmol) and glycosyl acceptor (0.73 mmol) were stirred in CH_2Cl_2 (4 mL) at room temperature in the presence of activated 4 Å powdered molecular sieves for 0.5 h before the reaction mixture was cooled to −35 °C. Then, *N*-iodosuccinimide (1.12 mmol) and trifluoromethanesulfonic acid (0.34 mmol) were added sequentially and the resulting mixture was stirred for 2 h. The reaction was quenched by addition of 20% $Na_2S_2O_3$ and allowed to warm to room temperature and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic layers were dried, filtered, concentrated, and purified by silica gel column chromatography to yield the desired product.

General Procedure 9 for Deprotection of 2-(Phenyloxycarbonylthioxy)-3-butenyl Disaccharides with Trifluoroacetic Acid. To a stirred solution of the disaccharide (0.14 mmol) and thioanisole (1.35 mmol) in CH_2Cl_2 (8 mL) was added an aqueous solution of trifluoroacetic acid, TFA/H_2O (19:1) (4 mL), at room temperature. The resulting mixture was stirred for 0.5 to 1 h at room temperature, taken up in toluene, and then evaporated. The deprotected disaccharide was isolated by silica gel column chromatography.

General Procedure 10 for Acetonide Removal from Derivatives of 1,2;5,6-Diisopropylideneglucofuranose Derivatives and the Subsequent Installation of Acetate Groups. The acetonide protected glucofuranoside (1.0 mmol) was dissolved in 80% acetic acid (10.0 mL) and heated with stirring to 95 °C for 8 h. After cooling the solvents were removed under reduced pressure, and the reaction mixture was azeotroped with toluene (2 × 30 mL). The crude product was dried under vacuum and dissolved in acetic anhydride (10.0 mmol), pyridine (10.0 mmol), and DMAP (0.1 mmol) and stirred at room temperature for 12 h. The solvents were evaporated under vacuum and the crude product was partitioned between EtOAc (30.0 mL) and water. The organic part was washed with brine (50 mL), dried, and evaporated to dryness.

General Procedure 11 for the Preparation of Glycosyl Trichloroacetimidates. To a stirred solution of the anomeric acetate (1.0 mmol) in DMF (10.0 mL) was added $NH_2NH_2 \cdot AcOH$ (1.5 mmol), after which the reaction mixture was stirred at room temperature for 3−4 h before it was diluted with EtOAc (100 mL) and washed with brine (50 mL). The organic portion was separated and dried to give the hemiacetal, which was dissolved in CH_2Cl_2 (100 mL) and treated with trichloroacetonitrile (10.0 mmol), followed by DBU (0.1 mmol). The reaction mixture was stirred at room temperature for 12 h before the solvents were evaporated and the crude product was purified by column chromatography with EtOAc/hexanes as eluent.

General Procedure 12 for Glycosylation with Trichloroacetaimidates. The trichloroacetimidate (1.2 mmol), alcohol (1.0 mmol), and activated 4 Å molecular sieves were mixed in CH_2Cl_2 (10 mL) and stirred at room temperature for 0.5 h before TMSOTf (0.125 mmol) was added. Stirring was continued at room temperature for 12 h before triethylamine (0.2 mmol) was added and the reaction mixture was filtered. The solvents were evaporated and the crude product was purified by column chromatography with EtOAc/hexanes as eluent.

General Procedure 13 for the Deprotection of Naphthylmethyl Groups. The protected pyranoside (1.0 mmol) was dissolved in a mixture of ~9:1 CH_2Cl_2 and water (10 mL) and DDQ (1.3 mmol) was added. The reaction mixture was stirred at room temperature for 3−4 h until TLC showed the starting material had been consumed. The reaction mixture was diluted with EtOAc (100 mL) and washed with saturated aqueous $NaHCO_3$ (50 mL). The combined organic part was dried and evaporated to dryness. The crude product was purified by column chromatography with ethyl acetate/hexanes as eluent.

General Procedure 14 for Triphenylphosphine-Promoted Rearrangement of Allylic Disulfides. A solution of acetylthio sugar (0.20 mmol) in MeOH (1.7 mL) was sparged with nitrogen before a freshly prepared solution of 1 M NaOMe in degassed MeOH (0.2 mL) was added. The resulting mixture was stirred for 0.5 h, quickly neutralized by addition of dry Amberlyst IR 120 resin, filtered, and then directly added to a stirred solution of the allylic sulfenyl donor (0.24 mmol) in MeOH (2 mL) at room temperature. The resulting mixture was stirred at room temperature until TLC showed complete consumption of the thiol (14 h). Then, triphenylphosphine (0.24 mmol) was added at room temperature and the resulting mixture was stirred for an additional 16 h. The mixture was evaporated in vacuo and subjected to chromatographic purification eluting with dichloromethane/methanol (15:1).

General Procedure 15 for Silver Nitrate Promoted Rearrangement of Allylic Disulfides. A stirred solution of protected thiol in degassed MeOH (1 mmol, 2.0 mL, 0.5 M) was treated with metallic sodium (2−3 equiv) and stirred under a N_2 atmosphere for 4−6 h until the saponification was complete (monitored by ESI mass spectrometry and TLC). The reaction mixture was acidified with Amberlyst 15 resin and filtered. The resin was washed with MeOH (3 × 5 mL). The combined washings and the filtrate were concentrated to a final volume of 1−2 mL and transferred to a stirred solution of disulfide (1.0 mmol, 20 mL, 0.05 M) in MeOH. The reaction mixture was stirred at room temperature under an atmosphere of nitrogen until complete disulfide exchange was visible on TLC (usually less than an hour). The reaction mixture was then treated with solid silver nitrate (2.0 equiv) and stirred in the dark for 16 h. After completion of the reaction (monitored by ESI mass spectrometry), NaCl (10 equiv) was added and the reaction mixture was stirred for 3−4 h. The reaction mixture was diluted with MeOH and centrifuged to remove the black

precipitate. The solvent was then concentrated to afford the crude product, which was purified by column chromatography

4-(Phenyloxythionocarbonyloxy)-2*Z*-butenyl Tetra-*O*-acetyl-β-D-glucopyranoside (9). The title compound was prepared in 90% yield from **7** by the literature procedure.[22b] It had spectral data identical with the literature values.[22b]

2-(Phenyloxycarbonylthioxy)-3-butenyl Tetra-*O*-acetyl-β-D-glucopyranoside (11). The title compound was prepared in 90% yield from **9** by the literature procedure.[22b] It had spectral data identical with the literature values.[22b]

2-(2-Pyridyldithio)-3-butenyl β-D-Glucopyranoside (13). The title compound was prepared in 76% yield as an approximately 1.1:1 mixture of isomers from **11** by general procedure 3 in the form of a white foam. ^{1}H NMR (CD_3OD) δ 8.35−8.36 (m, 1H), 7.92−7.94 (m, 1H), 7.19−7.36 (m, 1H), 5.79−5.88 (m, 1H), 5.23 (dd, J = 17.0, 9.0 Hz, 1H), 5.13−5.16 (m, 1H), 4.27 (dd, J = 14.5, 8.0 Hz, 1H), 4.10−4.18 (m, 1H), 3.75−3.86 (m, 3H), 3.62−3.66 (m, 1H), 3.17−3.32 (m, 8H); ^{13}C NMR δ 160.6, 148.8, 138.0, 134.22, 134.17, 121.1, 120.41, 120.38, 118.4, 118.2, 103.4, 103.3, 76,88, 76.86, 73.9, 70.42, 70.38, 70.10, 70.07, 61.6, 61.5, 54.3, 54.2; ESIHRMS calcd for $C_{15}H_{21}NO_6S_2Na$ $[M + Na]^+$ 398.0708, found 398.0717.

4-Hydroxy-2*Z*-butenyl Hepta-*O*-acetyl-β-D-laminaribioside (8). To a stirred solution of peracetyl laminaribiosyl bromide[38] (698 mg, 1.0 mmol) in CH_2Cl_2 (10.0 mL) was added *cis*-butene-1,4-diol (1.76 g, 20.0 mmol), Ag_2CO_3 (411 mg, 1.5 mmol), $CaSO_4$ (1.0 g), and a catalytic amount of I_2. The reaction mixture was shielded from light and stirred at room temperature for 12 h, then was diluted with CH_2Cl_2 (50.0 mL) and filtered through a pad of Celite. The filtrate was washed with saturated $NaHCO_3$ (50.0 mL), and the combined organic portion was dried over Na_2SO_4 and evaporated to dryness. The crude product was purified by column chromatography over silica gel (EtOAc/hexanes) to give the title compound as a colorless liquid in 80% yield. $[\alpha]^{23}_D$ −43.5 (*c* 1.5); ^{1}H NMR δ 5.84−5.79 (m, 1H), 5.60−5.55 (m, 1H), 5.11 (t, J = 9.5 Hz, 1H), 5.04 (t, J = 9.5 Hz, 1H), 4.98 (t, J = 8.0 Hz, 1H), 4.93 (t, J = 10.0 Hz, 1H), 4.87 (t, J = 8.5 Hz, 1H), 4.57 (d, J = 8.0 Hz, 1H), 4.41 (d, J = 8.0 Hz, 1H), 4.35 (dd, J = 12.5, 4.0 Hz, 1H), 4.31 (dd, J = 12.5, 5.5 Hz, 1H), 4.21 (dd, J = 13.0, 8.0 Hz, 1H), 4.17 (s, 2H), 4.16 (s, 2H), 4.02 (dd, J = 7.5, 2.5 Hz, 1H), 3.86 (t, J = 9.5 Hz, 1H), 3.67−3.64 (m, 2H), 2.12 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.01 (s, 3H), 1.98 (s, 3H × 2), 1.96 (s, 3H); ^{13}C NMR δ 171.1, 170.7, 170.6, 169.6, 169.5, 169.4, 169.2, 133.6, 126.9, 101.2, 99.3, 79.1, 73.2, 72.8, 72.1, 71.9, 71.2, 68.6, 68.3, 64.0, 62.5, 61.9, 58.7, 21.1, 20.9, 20.8, 20.7, 20.7, 20.6, 20.5; ESIHRMS calcd for $C_{30}H_{42}O_{19}Na^+$ $[M + Na]^+$ 729.2218, found 729.2210.

4-(Phenyloxythionocarbonyloxy)-2*Z*-butenyl Hepta-*O*-acetyl-β-D-laminaribioside (10). Following general procedure 1, and eluting with 75% EtOAc/hexanes the title compound was obtained in 88% yield. $[\alpha]^{23}_D$ −11.0 (*c* 1); ^{1}H NMR δ 7.43 (t, J = 8.0 Hz, 2H), 7.30 (t, J = 7.5 Hz, 1H), 7.11−7.09 (m, 2H), 5.88−5.84 (m, 1H), 5.82−5.77 (m, 1H), 5.15−5.11 (m, 2H), 5.09−5.06 (m, 2H), 5.04−4.99 (m, 1H), 4.96 (t, J = 10.0 Hz, 1H), 4.89 (t, J = 9.5 Hz, 1H), 4.58 (d, J = 8.5 Hz, 1H), 4.44 (d, J = 8.5 Hz, 1H), 4.38−4.33 (m, 3H), 4.19−4.18 (m, 2H), 4.03 (dd, J = 12.5, 2.0 Hz, 1H), 3.87 (t, J = 9.5 Hz, 1H), 3.68−3.66 (m, 2H), 2.14 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.98 (s, 3H); ^{13}C NMR δ 195.1, 170.9, 170.7, 170.6, 169.6, 169.5, 169.4, 169.1, 153.6, 130.9, 129.8, 126.9, 126.2, 122.1, 101.2, 99.6, 79.2, 73.2, 72.7, 72.2, 71.9, 71.3, 69.5, 68.4, 68.3, 64.4, 62.3, 61.9, 21.2, 21.0, 20.8, 20.8, 20.7, 20.7, 20.6; ESIHRMS calcd for $C_{37}H_{46}O_{20}SNa^+$ $[M + Na]^+$ 865.2201, found 865.2190.

2-(Phenyloxycarbonylthioxy)-3-butenyl Tetra-*O*-acetyl-β-D-laminaribioside (12). Following general procedure 2, and eluting with 75% EtOAc/hexanes the title compound was obtained as an approximately 1:1 mixture of stereoisomers in 95% yield. ^{1}H NMR δ 7.39−7.36 (m, 2H), 7.24−7.23 (m, 1H), 7.16−7.13 (m, 2H), 5.94−5.82 (m, 1H), 5.36 (dd, J = 17.0, 5.0 Hz, 1H), 5.22 (dd, J = 11.5, 10.5 Hz, 1H), 5.14−5.10 (m, 1H), 5.07−4.99 (m, 2H), 4.96−4.91 (m, 1H), 4.88 (t, J = 9.0 Hz, 1H), 4.58 (dd, J = 8.0, 6.0 Hz, 1H), 4.43 (t, J = 8.0 Hz, 1H), 4.35 (dd, J = 12.5, 4.5 Hz, 1H), 4.20−4.16 (m, 3H), 4.14−4.09 (m, 1H), 4.07−4.02 (m, 1H), 3.89−3.85 (m, 1H), 3.74 (dd, J = 10.5, 6.5 Hz, 1H), 3.68−3.65 (m, 2H), 2.14 (s, 3H), 2.12 (s, 3H), 2.07 (s, 3H × 2), 2.06 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H × 3), 1.97 (s, 3H), 1.96 (s, 3H); ^{13}C NMR δ 170.9, 170.7, 170.6, 169.6, 169.5, 169.4, 169.2, 169.0, 168.9, 151.3, 133.8, 133.5, 129.7, 126.5, 121.4, 119.1, 119.0, 101.5, 101.2 (2C), 100.7, 79.0, 78.9, 73.2, 72.7, 72.6, 72.2, 71.9, 71.7, 71.3, 70.3, 68.5, 68.4, 68.3, 62.3, 62.2, 61.9, 48.8, 48.0, 21.2, 21.1, 20.9, 20.8, 20.7, 20.7, 20.6, 20.5; ESIHRMS calcd for $C_{37}H_{46}O_{20}S$-Na^+ $[M + Na]^+$ 865.2201, found 865.2220.

2-(2-Pyridyldithio)-3-butenyl β-D-Laminaribioside (14). Following general procedure 3, and eluting with MeOH/CH_2Cl_2 the title compound was obtained as an approximately 1:1 mixture of stereoisomers in 70% yield. ^{1}H NMR (CD_3OD) δ 8.36 (d, J = 7.0 Hz, 1H), 7.95−7.92 (m, 1H), 7.79 (t, J = 9.0 Hz, 1H), 7.20 (dd, J = 9.0, 6.0 Hz, 1H), 5.88−5.78 (m, 1H), 5.27−5.20 (m, 1H), 5.16−5.13 (m, 1H), 4.55 (d, J = 10.0 Hz, 1 H), 4.33 (dd, J = 15.0, 10.0 Hz, 1H), 4.16−4.09 (m, 1H), 3.89−3.86 (m, 3H), 3.85−3.80 (m, 1H), 3.78−3.77 (m, 1H), 3.69−3.61 (m, 2H), 3.56−3.51 (m, 1H), 3.42−3.36 (m, 4H), 3.33−3.25 (m, 6H); ^{13}C NMR (CD_3OD) δ 160.6, 148.8, 137.9, 134.2, 134.1, 121.1, 120.4, 118.5, 118.3, 104.1, 102.9, 102.9, 86.7, 77.0, 76.6, 76.5, 74.3, 73.2, 70.4, 70.1, 68.8, 68.7, 61.4, 54.2, 54.1; ESIHRMS calcd for $C_{21}H_{31}NO_{11}S_2Na$ $[M + Na]^+$ 560.1236, found 560.1220.

4-(4-Nitrophenyloxythionocarbonyloxy)-2*Z*-butenyl Tetra-*O*-acetyl-β-D-glucopyranoside (15). Alcohol **7**[22b] (209.2 mg, 0.5 mmol), pyridine (687.5 μL, 8.5 mmol), and DMAP (12.2 mg, 0.01 mmol) were dissolved in dry CH_2Cl_2 (4.0 mL), and 4-nitrophenyl chlorothionoformate (119.7 mg, 0.55 mmol) in CH_2Cl_2 (1.0 mL) was added dropwise. The reaction mixture was stirred at room temperature for 5 h and then diluted with CH_2Cl_2 (10 mL) and washed with 2 N HCl and brine. The organic layer was dried and concentrated and purified by column chromatography over silica gel (eluent: EtOAc/hexanes = 1/2) to give the title compound (209.8 mg, 70%) as a colorless oil. $[\alpha]_D$ −12.2 (*c*, 2.0); ^{1}H NMR (400 Hz) δ 8.28−8.32 (m, 2H), 7.26−7.30 (m, 2H), 5.82−5.85 (m, 2H), 5.19 (t, J = 9.6 Hz, 1H), 5.06−5.12 (m, 3H), 4.97−5.02 (m, 1H), 4.56 (d, J = 7.2 Hz, 1H), 4.41−4.45 (m, 1H), 4.30−4.34 (m, 1H), 4.24 (dd, J = 12.0, 4.8 Hz, 1H), 4.13 (dd, J = 12.0, 2.4 Hz, 1H), 3.67−3.71 (m, 1H), 2.03 (s, 3H), 2.06 (s, 3H), 1.98 (s, 3H), 2.00 (s, 3H); ^{13}C NMR δ 193.7, 170.8, 170.5, 169.6, 169.5, 157.7, 146.2, 11.3, 125.6, 123.5, 99.8, 73.0, 72.1, 71.4, 70.0, 68.5, 64.9, 62.1, 21.0, 20.9, 20.8; ESIHRMS calcd for $C_{25}H_{29}NO_{14}SNa$ $[M + Na]^+$ 622.1206, found 622.1212.

4-[*N*-(2-Azidoethyl)-*N*-(benzyl)thionocarbamoyloxy]-2*Z*-butenyl 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranoside (16). The thionocarbonate **15** (196 g, 0.33 mmol), *N*-(2-azidoethyl)benzylamine[40] (86.3 mg, 0.49 mmol), and DMAP (80.0 mg, 0.65 mmol) were dissolved in dry CH_2Cl_2 (2 mL), and the reaction mixture was stirred at room temperature overnight. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and washed with 2 N HCl and brine. The organic layer was dried and concentrated and purified chromatographically (eluent: EtOAc/hexanes = 1/2) to give the title compound (152.1 mg, 73%) as a colorless oil. $[\alpha]_D$ −2.9 (*c*, 0.6); ^{1}H NMR ($CDCl_3$) δ 7.30−7.36 (m, 4H), 7.14 (d, J = 7.0 Hz, 1H), 5.65−5.83 (m, 2H), 5.16−5.20 (m, 3H), 5.04−5.12 (m, 2H), 4.97−5.03 (m, 2H), 4.81 (s, 1H), 4.51−4.59 (m, 1H), 4.32−4.33 (m, 1H), 4.24−4.29 (m, 1H), 4.12−4.17 (m, 1H), 3.90 (t, J = 6.5 Hz, 1H), 3.65−3.72 (m, 2H), 3.57 (t, J = 6.5 Hz, 1H), 3.37 (t, J = 6.0 Hz, 1H), 2.04 (s, 3H), 2.08 (s, 3H), 2.02 (s, 3H), 2.00 (s, 3H); ^{13}C NMR δ 189.6, 188.7, 170.9, 170.5, 169.62, 169.57, 136.2, 136.1, 129.9, 129.8, 129.1, 129.0, 128.2, 128.1, 128.0, 127.7, 127.6, 127.3, 126.4, 99.8, 99.7, 73.1, 72.10, 72..06, 71.5, 68.5, 67.5, 67.1, 65.0, 64.9, 62.1, 57.1, 53.7, 52.0, 49.4, 48.8, 46.9, 21.0, 20.9, 20.84, 20.83;

ESIHRMS calcd for $C_{28}H_{36}N_4O_{11}SNa$ $[M + Na]^+$ 659.1999, found 659.1979.

2-[*N*-(2-Azidoethyl)-*N*-(benzyl)carbamoylthioxy]-3-butenyl 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranoside (17). The thionocarbamate **16** (91.4 mg, 0.15 mmol) and $PdCl_2(CH_3CN)_2$ (3.9 mg, 0.015 mmol) were dissolved in CH_2Cl_2 (1.5 mL), and the reaction mixture was stirred at 40 °C for 20 h before it was concentrated and purified by column chromatography over silica gel (eluent: EtOAc/hexanes = 1/2) to give the title compound (90.4 mg, 99%) as a complex mixture of diastereomers and rotamers in the form of a colorless oil. ^{1}H NMR δ 7.22−7.37 (m, 5H), 5.85−5.95 (m, 1H), 5.36 (dd, *J* = 17.0, 6.0 Hz, 1H), 5.18−5.23 (m, 2H), 5.06−5.12 (m, 1H), 5.01 (t, *J* = 9.0 Hz, 1H), 4.64 (d, *J* = 7.5 Hz, 2.5H), 4.57 (d, *J* = 7.5 Hz, 0.5H), 4.35−4.39 (m, 0.5H), 4.24−4.31 (m, 1.5H), 4.12−4.16 (m, 1.5H), 4.01 (dd, *J* = 10.0, 8.0 Hz, 0.5 H), 3.84 (dd, *J* = 11.0, 4.0 Hz, 0.5 H), 3.70−3.76 (m, 1.5H), 3.44 (br s, 4H), 2.09 (s, 3H), 2.08 (s, 3H), 2.02 (s, 3H), 2.00 (s, 3H); ^{13}C NMR δ 170.9, 170.5, 169.6, 169.4, 134.8, 134.6, 129.1, 128.2, 127.5, 118.4, 118.3, 100.7, 100.5, 73.03, 72.95, 72.8, 72.1, 71.42, 71.37, 71.3, 68.7, 68.6, 62.2, 62.1, 52.8, 49.5, 47.9, 46.8, 46.5, 46.4, 21.0, 20.9, 20.85, 20.83; ESIHRMS calcd for $C_{28}H_{36}N_4O_{11}SNa$ $[M + Na]^+$ 659.1999, found 659.1969.

2-[*N*-(2-Azidoethyl)-*N*-(benzyl)carbamoylthioxy]-3-butenyl β-D-Glucopyranoside (18). Compound **17** (46.0 mg, 0.07 mmol) was dissolved in dry MeOH (1 mL), and NaOMe (1.5 μL, 25%, 0.007 mmol) was added. The reaction mixture was stirred at room temperature for 30 min, checked by TLC, and once the starting material had disappeared, was neutralized with Amberlyst-15 resin, filtered, concentrated, and purified by column chromatography over silica gel (eluent: CH_2Cl_2/MeOH = 5/1) to give the title compound (25.5 mg, 75%) as a complex mixture of diastereomers and rotamers in the form of a colorless oil. ^{1}H NMR (CD_3OD) δ 7.09−7.35 (m, 5H), 6.00−6.05 (m, 1H), 5.38 (d, *J* = 17.0 Hz, 1H), 5.16−5.19 (m, 1H), 4.68 (s, 2H), 4.38−4.43 (m, 1H), 4.34 (t, *J* = 8.5 Hz, 1H), 4.06−4.10 (m, 1H), 3.80−3.88 (m, 2H), 3.64−3.69 (m, 1H), 3.50 (t, *J* = 6.0 Hz, 2H), 3.43 (br s, 4H), 3.34−3.37 (m, 1H), 3.27−3.31 (m, 4H), 3.20 (t, *J* = 8.5 Hz, 1H); ^{13}C NMR δ 135.4, 135.2, 128.8, 128.7, 128.0, 127.65, 127.61, 117.0, 116.9, 103.8, 103.3, 76.93, 76.86, 76.8, 73.9, 73.8, 71.9, 71.3, 70.5, 70.4, 61.7, 61.6; ESIHRMS calcd for $C_{20}H_{28}N_4O_7SNa$ $[M + Na]^+$ 491.1576, found 491.1587.

2-(2-Pyridyldithio)-3-butenyl β-D-Glucopyranoside (13). Compound **18** (50.2 mg, 0.11 mmol) was dissolved in dry THF (1 mL), PPh_3 (28.1 mg, 0.11 mmol) was added, and the reaction mixture was heated to reflux for 30 min. Then H_2O (0.5 mL) was added and then the reaction mixture was dried over Na_2SO_4 and filtered. 2,2′-Dipyridyl disulfide (21.4 mg, 0.11 mmol) in $CHCl_3$ (1 mL) was added dropwise to this solution and the resulting reaction mixture was stirred at room temperature for 30 min before it was concentrated. The residue was purified by column chromatography over silica gel (eluent: CH_2Cl_2/MeOH = 5/1) to give the title compound (23.4 mg, 58%) as a white foam with identical characteristics to the sample described above.

2-(Phenyloxycarbonylthioxy)-3-butenyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (21). To a stirred solution of the oxazolinone[28] **19** (2.5 g, 7.6 mmol) and 2-(phenoxycarbonylthioxy)-3-butenol[25] **20** (425 mg, 1.9 mmol) in $CHCl_3$ (13 mL) was added, at room temperature, copper chloride (1.5 g, 11.4 mmol). The resulting mixture was heated at reflux for 14 h then allowed to cool to room temperature before saturated aqueous $NaHCO_3$ was added. The resulting mixture was filtered through Celite and washed twice with saturated aqueous $NaHCO_3$. The combined organic layers were dried, filtered, and concentrated. The glycoside was isolated chromatographically, eluting with hexanes/CH_2Cl_2/EtOAc (1:1:2) as a white foam as an approximately 1:1 mixture of diastereomers (473 mg, 45%). ^{1}H NMR (400 MHz) δ 7.35 (t, *J* = 8.0 Hz, 2 × 2H), 7.22 (t, *J* = 7.6 Hz, 2 × 1H), 7.12 (d, *J* = 6.4 Hz, 2 × 2H), 5.74−5.98 (m, 2 × 2H), 5.36 (dd, *J* = 3.2, 16.8 Hz, 2 × 1H), 5.28 (dd, *J* = 10.4, 11.6 Hz, 2 × 1H), 5.21 (dd, *J* = 4.4, 10.8 Hz, 2 × 1H), 5.04 (t, *J* = 9.6 Hz, 2 × 1H), 4.74 (t, *J* = 8.0 Hz, 2 × 1H), 4.02−4.28 (m, 2 × 4H), 3.86 (q, *J* = 8.8, 17.8 Hz, 2 × 1H), 3.82−3.66 (m, 2 × 2H), 2.04 (s, 2 × 3H), 2.00 (s, 2 × 6H), 1.92 (s, 2 × 3H); ^{13}C NMR (100 MHz) δ 171.1, 171.0, 170.6, 169.6, 151.2, 134.0, 133.8, 129.8, 126.5, 121.5, 119.1, 119.0, 101.4,100.7, 72.4, 72.1, 71.6, 70.4, 68.8, 62.2, 54.8, 54.6, 48.9, 48.2, 23.6, 23.5, 20,9, 20.8; ESIHRMS calcd for $C_{25}H_{31}NO_{11}SNa$ $[M + Na]^+$ 576.1516, found 576.1516.

2-(2-Pyridyldithio)-3-butenyl 2-Acetamido-2-deoxy-β-D-glucopyranoside (22). The title compound was prepared according to general procedure 3 as a white foam eluting from silica gel with CH_2Cl_2/MeOH (25:1) as an approximately 1:1 mixture of diastereomers in 60% yield over two steps. ^{1}H NMR (400 MHz, CD_3OD) δ 8.36 (s, 2 × 1H), 7.94−7.78 (m, 2 × 2H), 7.21 (t, *J* = 5.6 Hz, 2 × 1H), 5.87−5.67 (m, 2× 1H), 5.19 (dd, *J* = 4.8, 16.8 Hz, 2 × 1H), 5.11 (d, *J* = 10.4 Hz, 2 × 1H), 4.47−4.39 (m, 2 × 1H), 4.16−4.50 (m, 2 × 1H), 3.86 (dd, *J* = 5.6, 9.6, Hz, 2 × 1H), 3.82−3.75 (m, 2 × 1H), 3.74−3.63 (m, 2 × 4H), 3.50−3.42 (m, 2 × 1H), 3.36−3.23 (m, 2 × 4H), 1.98 (s, 2 × 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 172.5, 160.5, 148.9, 148.8, 138.1, 138.0, 134.2, 133,8, 121.1, 121,0, 120.2, 121.1, 118.4, 118.3, 116.9, 102.1, 101.7, 76.9, 76.7, 74.8, 74.7, 74.6, 71.4, 70.9, 69.9, 69.8, 61.6, 61.5, 56.1, 56.0, 54.4, 54.1, 22.1, 22.0; ESIHRMS calcd for $C_{17}H_{24}N_2O_6S_2Na$ $[M + Na]^+$ 439.0974, found 439.0978.

4-(2-Naphthylmethyloxy)-2*Z*-butene-1-ol (23). A stirred solution of *cis*-1,4-but-2-ene-diol (2.39 g, 27.1 mmol) in THF (10 mL) was treated under an atmosphere of N_2 with sodium hydride (0.38 g, 9.5 mmol) at 0 °C and stirring was continued at room temperature for 1 h. 2-(Bromomethyl)naphthalene (2.0 g, 9.0 mmol) was added and stirring was continued at room temperature for 2 h before the reaction mixture was heated to reflux for 6 h, then cooled to room temperature and diluted with saturated aqueous NH_4Cl (30 mL) and ethyl acetate (20 mL). The organic portion was separated, dried, and evaporated to dryness. The crude product was purified over silica gel with EtOAc/hexanes as eluent to give the title compound **23** as a thick oil (1.76 g, 85%). ^{1}H NMR δ 7.87−7.85 (m, 3H), 7.80 (s, 1H), 7.51−7.48 (m, 3H), 5.83 (dt, *J* = 11.0, 6.0 Hz, 1H), 5.78 (dt, *J* = 11.0, 6.0 Hz, 1H), 4.69 (s, 2H), 4.17 (d, *J* = 6.0 Hz, 2H), 4.13 (d, *J* = 6.5 Hz, 2H), 2.39 (br s, 1H); ^{13}C NMR δ 135.6, 133.5, 133.3, 132.8, 128.5, 128.3, 128.1, 127.9, 126.9, 126.4, 126.2, 126.1, 72.8, 65.9, 58.8; ESIHRMS calcd for $C_{15}H_{16}O_2Na$ $[M + Na]^+$ 251.1048, found 251.1055.

1,2:5,6-Di-*O*-isopropylidene-3-*O*-4-(2-naphthylmethyloxy)-2*Z*-butenyl-α-D-glucofuranose (24). To a stirred solution of 4-(2-naphthylmethyloxy)-2*Z*-butene-1-ol (**23**) (1.76 g, 7.7 mmol) in CH_2Cl_2 (20 mL) under an atmosphere of N_2 was added Et_3N (1.60 mL, 11.6 mmol) followed by DMAP (94 mg, 0.77 mmol) at 0 °C. A solution of methanesulfonyl chloride (0.75 mL, 9.64 mmol) in CH_2Cl_2 (2 mL) then was added dropwise and the reaction mixture was stirred for 2 h and then diluted with saturated NaCl solution (20 mL). The organic portion was separated and the aqueous part was again washed with CH_2Cl_2 (15 mL). The combined organic part was dried and evaporated to dryness. The crude mesylate (2.36 g, ∼100%) so obtained in DMF (50 mL) was added at 0 °C to a solution of diacetone-D-glucose (2.0 g, 7.7 mmol) and sodium hydride (338 mg, 8.5 mmol) in DMF (10.0 mL) that had been stirred for 1 h. The reaction mixture was heated to 60 °C and stirred for 12 h before it was cooled and diluted with water (100 mL) and ethyl acetate (100 mL). The organic layer was separated and washed with brine (100 mL), dried, and evaporated to dryness. The crude product was purified by column chromatography with 60% EtOAc/hexanes as eluent to give the title compound as a thick gum (2.65 g, 75%). $[\alpha]^{23}_D$ −2.0 (*c* 0.85); ^{1}H NMR δ 7.86−7.84 (m, 3H), 7.80 (s, 1H), 7.51−7.47 (m, 3H), 5.87 (d, *J* = 4.0 Hz, 1H), 5.85−5.83 (m, 1H), 5.79−5.74 (m, 1H), 4.69 (s, 2H), 4.52 (d, *J* = 4.0 Hz, 1H), 4.32−4.28 (m, 1H), 4.26−4.22 (dd, *J* = 13.0, 6.5 Hz, 1H), 4.19 (d, *J* = 6.0 Hz, 1H), 4.17−4.15 (m, 2H), 4.13−4.11(m, 1H), 4.09−4.07 (m, 1H), 4.03−3.99 (m, 1H), 3.92 (d, *J* = 3.0 Hz, 1H), 1.51 (s, 3H), 1.42 (s, 3H), 1.34 (s, 3H), 1.30 (s,

3H); ^{13}C NMR δ 135.8, 133.5, 133.3, 130.0, 129.3, 128.5, 128.1, 127.9, 126.7, 126.4, 126.2, 125.9, 112.0, 109.2, 105.5, 83.0, 81.8, 81.4, 72.7, 72.6, 67.6, 66.5, 66.0, 27.1, 27.0, 26.5, 25.6; ESIHRMS calcd for $C_{27}H_{34}O_7Na$ $[M + Na]^+$ 493.2202, found 493.2216.

1,2,4,6-Tetra-*O*-acetyl-3-*O*-[4-(2-naphthylmethyloxy)-2*Z*-butenyl]-D-α,β-glucopyranose (25). Following general procedure 10, and eluting with 50% EtOAc/hexanes the title compound was obtained as an approximately 1.4:1 mixture of stereoisomers in 89% yield. ^{1}H NMR δ 7.84−7.83 (m, 3H), 7.78 (s, 1H), 7.50−7.46 (m, 3H), 6.29 (d, J = 3.5 Hz, 1H), 5.81−5.77 (m, 1H), 5.67−5.58 (m, 2H), 5.09−5.03 (m, 2H), 4.99−4.97 (m, 1H), 4.67 (s, 2H, major), 4.66 (s, 2H, minor), 4.25−4.13 (m,3H), 4.12−4.04 (m, 3H), 4.00−3.97 (m, 1H), 3.81 (t, J = 9.5 Hz, 1H), 3.64−3.62 (m, 1H), 3.58−3.54 (m, 1H), 2.12−1.97 (s, 12H major + 12H minor); ^{13}C NMR δ 170.9, 169.7, 169.4, 169.2, 168.9, 135.7, 133.5, 133.2, 129.6, 129.4, 129.3, 129.2, 128.5, 128.5, 128.1, 128.0, 127.9, 126.7, 126.7, 126.4, 126.2, 125.9, 125.9, 92.1, 89.6, 79.7, 76.6, 73.2, 72.7, 71.6, 71.5, 70.4, 69.3, 69.1, 68.4, 67.8, 65.9, 65.8, 62.0, 61.9, 21.0, 20.9, 20.8, 20.7; ESIHRMS calcd for $C_{29}H_{34}O_{11}Na$ $[M + Na]^+$ 581.1999, found 581.1998.

2,4,6-Tri-*O*-acetyl-3-*O*-[4-(2-naphthylmethyloxy)-2*Z*-butenyl]-α-D-glucopyranosyl Trichloroacetimidate (26). Following general procedure 11, and eluting with 40% EtOAc/hexanes the title compound was obtained in 76% yield. $[\alpha]^{23}_D$ 63.8 (c 1); ^{1}H NMR δ 8.67 (s, 1H), 7.85−7.82 (m, 3H), 7.78 (s, 1H), 7.50−7.46 (m, 3H), 6.5 (d, J = 3.5 Hz, 1H), 5.83−5.78 (m, 1H), 5.68−5.64 (m, 1H), 5.12 (t, J = 10.0 Hz, 1H), 5.01 (dd, J = 10.0, 4.0 Hz, 1H), 4.68 (d, J = 4.5 Hz, 2H), 4.27−4.18 (m, 3H), 4.13−4.07 (m, 4H), 3.92 (t, J = 10.0 Hz, 1H), 2.07 (s, 3H), 2.02 (s, 3H), 1.94 (s, 3H); ^{13}C NMR δ 170.9, 169.9, 169.5, 160.8, 135.7, 133.5, 133.2, 129.6, 129.3, 128.5, 128.0, 127.9, 126.7, 126.4, 126.2, 125.9, 93.5, 91.1, 76.5, 72.7, 72.1, 70.7, 69.1, 68.5, 65.8, 61.9, 20.9, 20.9, 20.7; ESIHRMS calcd for $C_{29}H_{32}Cl_3NO_{10}Na$ $[M + Na]^+$ 682.0989, found 682.0999.

Methyl 2,4,6-Tri-*O*-acetyl-3-*O*-[4-(2-napthylmethyloxy)-2*Z*-butenyl]-β-D-glucopyranoside (27). Following general procedure 12, and eluting with 60% EtOAc/hexanes the title compound was obtained in 75% yield. $[\alpha]^{23}_D$ −14.5 (c 1); ^{1}H NMR δ 7.85−7.83 (m, 3H), 7.79 (s, 1H), 7.49−7.46 (m, 3H), 5.81−5.76 (m, 1H), 5.64−5.58 (m, 1H), 5.03 (t, J = 10.0 Hz, 1H), 4.94 (dd, J = 9.5, 8.0 Hz, 1H), 4.68 (s, 3H), 4.27 (d, J = 8.0 Hz, 1H), 4.20 (dd, J = 12.0, 5.0 Hz, 1H), 4.14 (d, J = 6.0 Hz, 1H), 4.11 (d, J = 3.0 Hz, 1H), 4.09−4.08 (m, 2H), 3.55−3.50 (m, 2H), 3.46 (s, 3H), 2.08 (s, 3H), 2.03 (s, 3H), 2.00 (s, 3H); ^{13}C NMR δ 171.0, 169.5, 169.4, 135.7, 133.5, 133.2, 129.4, 128.4, 128.1, 127.9, 126.7, 126.4, 126.2, 125.9, 101.9, 79.8, 72.7 (2C), 72.5, 72.2, 69.7, 67.3, 65.8, 62.5, 56.9, 21.1, 20.9 (2C); ESIHRMS calcd for $C_{28}H_{34}O_{10}Na$ $[M + Na]^+$ 553.2050, found 553.2064.

Methyl 2,4,6-Tri-*O*-acetyl-3-*O*-[4-hydroxy-2*Z*-butenyl]-β-D-glucopyranoside (28). Following general procedure 13, and eluting with 40% EtOAc/hexanes the title compound was obtained in 88% yield. $[\alpha]^{23}_D$ −25.4 (c 1); ^{1}H NMR δ 5.77−5.72 (m, 1H), 5.55−5.51 (m, 1H), 5.06 (t, J = 9.50 Hz, 1H), 4.98−4.95 (m, 1H), 4.34 (d, J = 8.0 Hz, 1H), 4.23 (dd, J = 12.0, 5.0 Hz, 1H), 4.15−4.11 (m, 5H), 3.62−3.58 (m, 2H), 3.48 (s, 3H), 2.11 (s, 3H), 2.09 (s, 3H), 2.08 (s, 3H); ^{13}C NMR δ 171.1, 169.8 (2C), 132.4, 127.9, 101.9, 79.8, 72.2 (2C), 69.3, 66.3, 62.5, 58.6, 57.1, 21.2, 21.1, 21.0; ESIHRMS calcd for $C_{17}H_{26}O_{10}Na$ $[M + Na]^+$ 413.1424, found 413.1425.

Methyl 2,4,6-Tri-*O*-acetyl-3-*O*-[4-(phenyloxythionocarbonyloxy)-2*Z*-butenyl]-β-D-glucopyranoside (29). Following general procedure 1, and eluting with 45% EtOAc/hexanes the title compound was obtained in 90% yield. $[\alpha]^{23}_D$ −11.5 (c 1); ^{1}H NMR δ 7.45−7.42 (m, 2H), 7.32−7.29 (m, 1H), 7.12−7.10 (m, 2H), 5.84−5.79 (m, 1H), 5.76−5.72 (m, 1H), 5.10−5.06 (m, 3H), 5.01−4.97 (m, 1H), 4.35 (d, J = 7.50 Hz, 1H), 4.26−4.24 (m, 2H), 4.22 (d, J = 5.0 Hz, 1H), 4.13 (dd, J = 12.5, 2.5 Hz, 1H), 3.65−3.59 (m, 2H), 3.48 (s. 3H), 2.13 (s, 3H), 2.11 (s, 3H), 2.08 (s, 3H); ^{13}C NMR δ 195.1, 171.0, 169.5, 169.5, 153.7, 131.9, 129.8, 126.9, 125.1, 122.1, 101.9, 80.0, 72.4, 72.2, 69.6, 69.5 (2C), 67.2 (2C), 62.4, 57.0, 21.2, 21.1, 21.0; ESIHRMS calcd for $C_{24}H_{30}O_{11}SNa$ $[M + Na]^+$ 549.1407, found 549.1398.

Methyl 2,4,6-Tri-*O*-acetyl-3-*O*-[(2-phenyloxycarbonylthioxy)-3-butenyl]-β-D-glucopyranoside (30). Following general procedure 2, and eluting with 45% EtOAc/hexanes the title compound was obtained in 90% yield as an approximately 1.25:1 mixture of stereoisomers. ^{1}H NMR δ 7.39−7.36 (m, 2H), 7.26−7.23 (m, 1H), 7.15−7.14 (m, 2H), 5.93−5.85 (m, 1H), 5.33 (d, J = 17.0 Hz, 1H), 5.19 (d, J = 10.5 Hz, 1H), 5.10 (t, J = 10.0 Hz, 1H), 5.03−4.99 (m, 1H), 4.33 (dd, J = 8.0, 3.0 Hz, 1H), 4.25−4.21 (m, 1H), 4.15−4.11 (m, 1H), 4.09−4.05 (m, 1H), 3.86−3.80 (m, 2H), 3.62−3.58 (m, 2H), 3.48 (s, 3H, major + minor), 2.12 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H), 2.08 (s, 3H × 3 minor); ^{13}C NMR δ 171.0, 169.6, 169.5, 169.4 (2 C), 151.3, 134.1, 134.0, 129.7, 126.5, 121.5, 118.7 (2 C), 102.0, 81.0, 73.9, 73.8, 72.2 (2 C), 69.6, 69.5, 62.4, 57.0, 48.9 (2 C), 21.3, 21.2 (2 C), 21.1, 21.0; ESIHRMS calcd for $C_{24}H_{30}O_{11}SNa$ $[M + Na]^+$ 549.1407, found 549.1385.

Methyl 3-*O*-[(2-Pyridyldithio)-3-butenyl]-β-D-glucopyranoside (31). Following general procedure 3, and eluting with 5% MeOH/CH_2Cl_2 the title compound was obtained in 76% yield as an approximately 1.5:1 mixture of stereoisomers. ^{1}H NMR (CD_3OD) δ 8.37−8.36 (m, 1H), 7.93−7.91 (m, 1H), 7.81−7.78 (m, 1H), 7.22−7.19 (m, 1H), 5.87−5.79 (m, 1H), 5.24−5.21 (m, 1H), 5.12 (d, J = 10.0 Hz, 1H), 4.17 (dd, J = 7.5, 1.5 Hz, 1H), 4.13−4.09 (m, 1H), 4.07−4.06 (m, 1H), 4.04−4.01 (m, 1H), 3.88−3.85 (m, 1H), 3.81−3.77 (m, 1H), 3.69−3.65 (m, 1H), 3.53 (s, 3H + 3H, two isomers), 3.32 (m, 5H), 3.28−3.19 (m, 3H); ^{13}C NMR (CD_3OD) δ 160.7, 148.8, 137.8, 134.6, 134.5, 121.0, 120.3, 118.1, 104.2, 85.9, 76.7, 73.8, 73.7 (2C), 70.1, 70.0, 61.4, 56.2, 54.9; ESIHRMS calcd for $C_{15}H_{21}NO_6S_2Na$ $[M + Na]^+$ 398.0708, found 398.0700.

Methyl 6-Acetylthio-α-D-glucopyranoside (32). The title compound was prepared by a literature method[30] and had data consistent with the literature.[30]

Methyl 2-Acetamido-6-acetylthio-2-deoxy-β-D-glucopyranoside (33). Diisopropyl azodicarboxylate (0.25 mL, 1.22 mmol) was added dropwise at 0 °C to a stirred solution of triphenylphosphine (326 mg, 1.24 mmol) in DMF (2 mL). The mixture was stirred at 0 °C for 1 h and gave a light yellow precipitate. A solution of methyl 2-acetamido-2-deoxy-β-D-glucopyranoside[41] (240 mg, 1.02 mmol) and thioacetic acid (0.09 mL, 1.22 mmol) in DMF (1.7 mL) then was added dropwise at 0 °C and the resulting mixture was stirred for 20 h at room temperature, resulting in a clear yellow solution. The mixture was concentrated in vacuo and the residue was purified by silica gel chromatography (eluting with CH_2Cl_2/MeOH = 15:1) to give the title compound as a white solid (176 mg, 59%). Mp 195 °C; $[\alpha]^{RT}_D$ +36.8 (c 1, MeOH); ^{1}H NMR (300 MHz, CD_3OD) δ 4.26 (d, J = 8.7 Hz, 1H), 3.66−3.55 (m, 2H), 3.48−3.38 (m, 4H), 3.38−3.26 (m, 4H), 3.20 (t, J = 9 Hz, 1H), 2.80 (dd, J = 8.1, 8.7 Hz, 1H), 2.32 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 195.8, 172.6, 102.2, 75.0, 74.6, 73.9, 56.0, 55.7, 30.9, 29.2, 21.8; ESIHRMS calcd for $C_{11}H_{19}NO_6S$ Na $[M + Na]^+$ 316.0831, found 316.0849.

2,4,6-Tri-*O*-acetyl-3-acetylthio-α,β-D-glucopyranose (35). A stirred solution of **34**[32] (406 mg, 1.0 mmol) in a mixture of EtOAc (20 mL) and CH_2Cl_2 (10.0 mL) was treated with $TiBr_4$ (908 mg, 2.5 mmol) and stirred at room temperature for 96 h before it was diluted with CH_2Cl_2 (30.0 mL) and filtered through a pad of Celite. The filtrate was washed with saturated aqueous $NaHCO_3$ (50.0 mL) and the organic portion was dried and evaporated to dryness. The so-obtained crude bromide was dissolved in an acetone/water mixture (20.0 mL, 2:1), treated with Ag_2CO_3 (411 mg, 1.5 mmol), and stirred at room temperature for 12 h. The reaction mixture was diluted with EtOAc (30.0 mL) and filtered through a short Celite pad and washed with saturated aqueous $NaHCO_3$ (50.0 mL). The organic portion was dried,

concentrated, and purified by column chromatography with 50% EtOAc/hexanes to give the title product in 86% yield as an approximately 2:1 mixture of stereoisomers in the form of an oil. ^{1}H NMR δ 5.39 (t, J = 4.0 Hz, 1H, major), 5.09−5.07 (m, 1H, major), 5.06−5.04 (m, 1H, minor), 4.95−4.92 (m, 1H, major), 4.84 (dd, J = 11.5, 8.0 Hz, 1H, minor), 4.73 (dd, J = 8.5, 8.0 Hz, 1H, minor), 4.28−4.25 (m, 1H, major), 4.23−4.15 (m, 2H, major), 4.12−4.11 (m, 1H, minor), 3.97−3.95 (m, 1H, minor), 3.85−3.83 (m, 1H, minor), 3.81−3.80 (m, 1H, major), 3.79−3.76 (m, 1H, minor), 2.32 (s, 3H, minor), 2.32 (s, 3H, major), 2.07 (s, 3H × 2), 2.06 (s, 3H × 2), 2.02 (s, 3H, major), 2.01 (s, 3H, minor); ^{13}C NMR δ 193.7 (2C), 171.2, 171.1 (minor), 170.8 (minor), 170.3, 169.7, 169.6 (minor), 97.1 (minor), 89.9, 75.0, 72.4 (minor), 70.3, 68.7 (minor), 67.6, 62.6 (minor), 47.7 (minor), 44.4, 30.9, 30.9 (minor), 21.1 (2C), 20.9, 20.8 (2C), 20.7 (2C), 20.7; ESIHRMS calcd for $C_{14}H_{20}O_9SNa$ $[M + Na]^+$ 387.0726, found 387.0724.

2,4,6-Tri-*O*-acetyl-3-acetylthio-α-D-glucopyranosyl Trichloroacetimidate (36). Following general procedure 11, and eluting with 45% EtOAc/hexanes the title compound was obtained in 80% yield. $[\alpha]^{23}_D$ 52.0 (c 1); ^{1}H NMR δ 8.66 (s, 1H), 6.48 (d, J = 3.0 Hz, 1H), 5.21−5.13 (m, 2H), 4.23−4.16 (m, 3H), 4.09−4.06 (m, 1H), 2.31 (s, 3H), 2.04 (s, 3H), 2.02 (s, 3H), 1.97 (s, 3H); ^{13}C NMR δ 193.2, 170.7, 169.8, 169.5, 161.0, 92.8, 91.0, 71.5, 68.9, 66.6, 61.9, 44.7, 30.9, 20.9, 20.7, 20.6; ESIHRMS calcd for $C_{16}H_{20}Cl_3NO_9SNa$ $[M + Na]^+$ 529.9822, found 529.9799.

Methyl 2,4,6-Tri-*O*-acetyl-3-acetylthio-β-D-glucopyranoside (37). Following general procedure 12, and eluting with 60% EtOAc/hexanes the title compound was obtained in 76% yield. $[\alpha]^{23}_D$ −8.7 (c 1); ^{1}H NMR δ 5.06 (dd, J = 11.0, 9.5 Hz, 1H), 4.95 (dd, J = 11.0, 7.5 Hz, 1H), 4.45 (d, J = 7.5 Hz, 1H), 4.26 (dd, J = 12.0, 4.5 Hz, 1H), 4.12 (dd, J = 12.0, 3.0 Hz, 1H), 3.85 (t, J = 11.0 Hz, 1H), 3.76−3.73 (m, 1H), 3.50 (s, 3H), 2.33 (s, 3H), 2.09 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H); ^{13}C NMR δ 193.7, 170.9, 169.5 (2C), 103.2, 74.7, 70.3, 67.8, 62.5, 57.1, 47.9, 30.8, 20.9, 20.9, 20.8; ESIHRMS calcd for $C_{15}H_{22}O_9SNa$ $[M + Na]^+$ 401.0882, found 401.0878.

Phenyl 2,4,6-Tri-*O*-acetyl-3-acetylthio-1-thio-β-D-glucopyranoside (38). The title compound was obtained by the literature procedure from **34** in 60% yield and had physical characteristics consistent with the literature.[32]

Methyl 6-[4-(β-D-Glucopyranosyloxy)-2*E*-butenyl]thio-α-D-glucopyranoside (40). General coupling procedure 14 gave the title compound (17.4 mg, 57%) as a white foam after purification by column chromatography over silica gel (eluent: CH_2Cl_2/MeOH = 1/1). (When using phosphate buffer solution as solvent, the yield is 93%.) $[\alpha]_D$ +31.3 (c 1.3, CH_3OH); ^{1}H NMR (CD_3OD) δ 5.68−5.79 (m, 2H), 4.63 (d, J = 4.0 Hz, 1H), 4.35 (dd, J = 12.0, 5.0 Hz, 1H), 4.31 (d, J = 8.0 Hz, 1H), 4.13−4.18 (m, 1H), 3.87 (d, J = 12.0 Hz, 1H), 3.60−3.68 (m, 2H), 3.57 (t, J = 9.5 Hz, 1H), 3.42 (s, 3H), 3.39 (dd, J = 10.0, 4.0 Hz, 1H), 3.33−3.36 (m, 2H), 3.30−3.31 (m, 6H), 3.17−3.28 (m, 6H), 2.91 (dd, J = 14.0, 2.0 Hz, 1H), 2.56 (dd, J = 14.0, 9.0 Hz, 1H); ^{13}C NMR δ 130.1, 128.9, 101.9, 99.9, 76.9, 76.8, 73.9, 73.8, 73.5, 72.5, 72.4, 70.5, 68.8, 61.6, 54.3, 33.9, 32.1; ESIHRMS calcd for $C_{17}H_{30}O_{11}SNa$ $[M + Na]^+$ 465.1407, found 465.1407.

Methyl 6-[4-(2-Acetamido-2-deoxy-β-D-glucopyranosyloxy)-2*E*-butenyl]thio-2-deoxy-β-D-glucopyranoside (41). The title compound was prepared according to general protocol 14 in 80% yield or in 57% yield according to protocol 15 as a white foam eluting from silica gel in CH_2Cl_2/MeOH (20:1). $[\alpha]^{RT}_D$ +74.0 (c 1.0, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 5.76−5.58 (m, 2H), 4.63 (d, J = 4.4 Hz, 1H), 4.44 (d, J = 8.0 Hz, 1H), 4.31 (dd, J = 4, 4.8 Hz, 1H), 4.09 (dd, J = 5.6, 6.0 Hz, 1H), 3.88 (d, J = 12.0 Hz, 1H), 3.74−3.54 (m, 4H), 3.47−3.16 (m, 11H), 2.90 (dd, J = 2.4, 14.0 Hz, 1H), 2.56 (dd, J = 8.8, 13.6 Hz, 1H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 172.6, 129.6, 128.7, 100.5, 99.9, 76.8, 74.9, 73.8, 73.6, 72.5, 72.4, 70.9, 68.5, 61.6, 56.2, 54.3, 34.0, 32.2, 21.9; ESIHRMS calcd for $C_{19}H_{33}NO_{11}SNa$ $[M + Na]^+$ 506.1672, found 506.1655.

Methyl 6-[4-(2-Acetamido-2-deoxy-β-D-glucopyranosyloxy)-2*E*-butenyl]thio-2-acetamido-2-deoxy-β-D-glucopyranoside (42). The title compound was prepared according to general protocol 14 in 82% yield or in 68% yield according to protocol 15 as a white foam eluting from silica gel with CH_2Cl_2/MeOH (20:1). $[\alpha]^{RT}_D$ +41.0 (c 0.5, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 5.80−5.60 (m, 2H), 4.40 (d, J = 8.0 Hz, 1H), 4.32 (d, J = 8.8 Hz, 1H), 4.27 (d, J = 8.8 Hz, 1H), 4.09 (dd, J = 5.2, 12.8 Hz, 1H), 3.88 (d, J = 12.0 Hz, 1H), 3.72−3.61 (m, 4H), 3.48−3.20 (m, 12H), 2.94 (d, J = 13.6 Hz, 1H), 2.62 (dd, J = 8.0, 14.4 Hz, 1H), 1.98 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 172.6, 129.6, 128.8, 102.4, 102.3, 100.6, 77.0, 76.8, 74.9, 74.8, 73.6, 70.9, 68.7, 61.6, 56.1, 56.0, 55.9, 34.0, 32.1, 21.9, 21.8; ESIHRMS calcd for $C_{21}H_{36}N_2O_{11}SNa$ $[M + Na]^+$ 547.1938, found 547.1942.

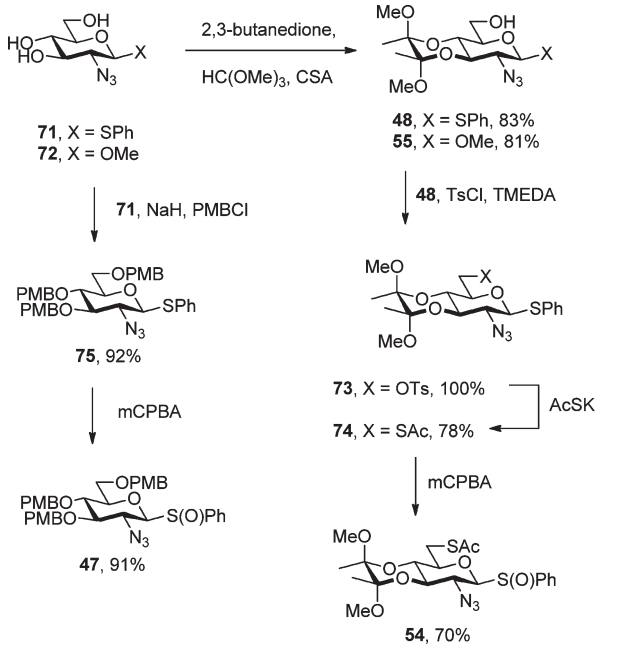
Methyl 3-Deoxy-3-[4-(β-D-glucopyranosyloxy)but-2*E*-enylthio]-β-D-glucopyranoside (43). Following general procedure 15, and eluting with 12% MeOH/CH_2Cl_2 the title compound was obtained in 65% yield. $[\alpha]^{23}_D$ −2.0 (c 0.85, MeOH); ^{1}H NMR (CD_3OD) δ 5.85 (dt, J = 15.0, 7.5 Hz, 1H), 5.75 (dt, J = 15.5, 6.5 Hz, 1H), 4.36 (d, J = 8.0 Hz, 1H), 4.32 (dd, J = 12.5, 5.0 Hz, 1H), 4.20 (d, J = 8.0 Hz, 1H), 4.17 (dd, J = 12.5, 6.5 Hz, 1H), 3.89−3.86 (m, 2H), 3.69 (dd, J = 12.0, 5.0 Hz, 1H), 3.66 (dd, J = 12.5, 5.5 Hz, 1H), 3.54 (s, 3H), 3.46−3.40 (m, 1H), 3.28−3.27 (m, 6H), 3.25−3.17 (m, 2H), 2.54 (t, J = 10.0 Hz, 1H); ^{13}C NMR (CD_3OD) δ 130.8, 128.7, 105.3, 101.5, 79.2, 76.8, 76.6, 73.9, 73.1, 70.5, 68.7, 68.6, 61.7, 61.6, 56.0, 54.6, 33.2; ESIHRMS calcd for $C_{17}H_{30}O_{11}SNa$ $[M + Na]^+$ 465.1401, found 465.1407.

Methyl 3-*O*-[4-(1-thio-β-D-glucopyranosyl)-2*E*-butenyl]-β-D-glucopyranoside (44). Following general procedure 15, and eluting with 12% MeOH/CH_2Cl_2 the title compound was obtained in 70% yield. $[\alpha]^{23}_D$ −45.1 (c 1, MeOH); ^{1}H NMR (CD_3OD) δ 5.79−5.77 (m, 2H), 4.38 (d, J = 9.5 Hz, 1H), 4.35−4.34 (m, 2H), 4.19−4.18 (m, 1H), 3.89−3.86 (m, 2H), 3.70−3.63 (m, 2H), 3.53 (s, 3H), 3.50−3.46 (m, 1H), 3.32−3.31 (m, 3H), 3.29−3.27 (m, 2H), 3.26−3.22 (m, 4H); ^{13}C NMR (CD_3OD) δ 130.3, 128.9, 104.2, 84.3, 83.9, 80.5, 78.5, 76.6, 73.9, 73.2, 72.7, 70.5, 70.1, 61.8, 61.5, 56.1, 30.9; ESIHRMS calcd for $C_{17}H_{30}O_{11}SNa$ $[M + Na]^+$ 465.1401, found 465.1407.

Methyl 3-*O*-[4-(Methyl α-D-glucopyranosid-6-thio)but-2*E*-enyl]-β-D-glucopyranoside (45). Following general procedure 15, and eluting with 10% MeOH/CH_2Cl_2 the title compound was obtained in 70% yield. $[\alpha]^{23}_D$ −26.0 (c 0.75, MeOH); ^{1}H NMR (CD_3OD) δ 5.78−5.69 (m, 2H), 4.65 (d, J = 3.5 Hz, 1H), 4.36−4.35 (m, 1H), 4.19−4.18 (m, 1H), 3.86 (dd, J = 12.0, 2.5 Hz, 1H), 3.69−3.54 (m, 3H), 3.44 (s, 3H), 3.43 (s, 3H), 3.44−3.37 (m, 1H), 3.32−3.31 (m, 2H), 3.29−3.19 (m, 6H), 2.94 (dd, J = 14.0, 2.0 Hz, 1H), 2.59 (dd, J = 14.6, 8.0 Hz, 1H); ^{13}C NMR (CD_3OD) δ 130.2, 129.3, 104.2, 99.8, 84.5, 76.6, 73.9, 73.8, 73.5, 72.8, 72.4, 70.1, 61.5, 56.2, 54.4, 34.1, 32.1; ESIHRMS calcd for $C_{18}H_{32}O_{11}SNa$ $[M + Na]^+$ 479.1563, found 479.1550.

Phenyl 3-Deoxy-3-[4-(β-D-glucopyranosyloxy)but-2*E*-enylthio]-1-thio-β-D-glucopyranoside (46). Following general procedure 15, phenyl 2,4,6-tri-*O*-acetyl-3-acetylthio-1-thio-β-D-glucopyranoside (**38**) was coupled with sulfenyl donor **13**. Chromatographic purification eluting with 8% MeOH/CH_2Cl_2 gave the title compound in 70% yield. $[\alpha]^{23}_D$ −36.0 (c 0.75, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 7.57−7.54 (m, 2H), 7.32−7.23 (m, 3H), 5.86−5.79 (m, 1H), 5.74−5.67 (m, 1H), 4.62 (d, J = 12.0 Hz, 1H), 4.34 (d, J = 10.0 Hz, 1H), 4.30 (dd, J = 16.5, 7.0 Hz, 1H), 4.14 (dd, J = 16.0, 9.0 Hz, 1H), 3.87 (dd, J = 15.0, 2.0 Hz, 2H), 3.69−3.62 (m, 2H), 3.46−3.26 (m, 8H), 3.18 (t, J = 11.0 Hz, 1H), 2.58 (t, J = 11.0 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 133.9, 131.6, 130.8, 128.7, 127.1, 101.5, 89.6, 82.7, 76.8, 76.6, 73.9, 72.4, 70.5, 68.6, 68.5, 61.8, 61.6, 56.7, 33.6; ESIHRMS calcd for $C_{22}H_{32}O_{10}S_2Na$ $[M + Na]^+$ 543.1335, found 543.1346.

Scheme 9. Preparation of 2-Azido-2-deoxyglucose-Based Monosaccharyl Units



Phenyl 2-Azido-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-1-thio-*β*-D-glucopyranoside (48). The title compound was prepared as a white solid from **71**[42] by general procedure 4 and eluted from silica gel with hexanes/EtOAc (2:1) in 83% yield (Scheme 9). Mp 110 °C; $[\alpha]^{RT}_D$ +47.3 (*c* 1.0); ^{1}H NMR (400 MHz) δ 7.55 (dd, *J* = 2.4, 5.6 Hz, 2H), 7.37−7.30 (m, 3H), 4.40 (d, *J* = 9.6 Hz, 1H), 3.92−3.83 (m, 1H), 3.77−3.68 (m, 2H), 3.63 (t, *J* = 9.6 Hz, 1H), 3.54−3.49 (m, 1H), 3.39 (t, *J* = 9.6 Hz, 1H), 3.33 (s, 3H), 3.28 (d, *J* = 5.6 Hz, 1H), 3.23 (s, 3H), 1.94 (dd, *J* = 5.6, 7.2 Hz, 1H), 1.33 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (100 MHz) δ:134.1, 129.4, 128.9, 100.4, 99.9, 86.3, 78.3, 73.2, 65.8, 61.7, 61.5, 48.3, 48.3, 17.8, 17.7; ESIHRMS calcd for $C_{18}H_{25}N_3O_6SNa$ $[M + Na]^+$ 434.1362, found 434.1354.

Methyl 2-Azido-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-*β*-D-glucopyranoside (55). The title compound was prepared as a white foam from **72**[42b,43] by the general procedure 4 and eluted from silica gel with hexanes/EtOAc (2:1) in 81% yield. $[\alpha]^{RT}_D$ +70.3 (*c* 1.0); ^{1}H NMR (400 MHz) δ 4.2 (d, *J* = 8 Hz, 1H), 3.88−3.80 (m, 1H), 3.76−3.66 (m, 2H), 3.60 (dd, *J* = 9.6, 10.8 Hz, 1H), 3.53 (s, 3H), 3.48−3.42 (m, 1H), 3.39 (dd, *J* = 7.2, 8.4 Hz, 1H), 3.28 (s, 3H), 3.23 (s, 3H), 2.50 (dd, *J* = 5.6, 8.0 Hz, 1H), 1.31 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz) δ 103.6, 100.3, 99.9, 76.9, 74.2, 71.0, 66.0, 62.9, 61.2, 57.6, 48.3, 17.8, 17.7; ESIHRMS calcd for $C_{13}H_{23}N_3O_7Na$ $[M + Na]^+$ 365.1434, found 365.1432.

Phenyl 2-Azido-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-1-thio-6-*O*-*p*-toluenesulfonyl-*β*-D-glucopyranoside (73). The title compound was prepared by general procedure 5 as a white solid eluted from silica gel with hexanes/EtOAc (3:1) in a quantitative yield. Mp 141 °C; $[\alpha]^{RT}_D$ +12.3 (*c* 1.0); ^{1}H NMR (400 MHz) δ 7.80 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.34−7.25 (m, 3H), 4.29 (t, *J* = 10.4 Hz, 2H), 4.21 (dd, *J* = 4.0, 10.8 Hz, 1H), 3.67−3.53 (m, 3H), 3.31 (d, *J* = 9.6 Hz, 1H), 3.28 (s, 3H), 3.23 (d, *J* = 7.6 Hz, 1H), 3.20 (s, 3H), 2.67 (s, 3H), 1.29 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz) δ 145.2, 134.4, 133.0, 130.3, 130.1, 129.3, 129.0, 128.2, 100.5, 100.1, 86.1, 77.6, 75.4, 73.0, 67.3, 65.3, 61.1, 48.6, 48.4, 21.9, 17.8, 17.7; ESIHRMS calcd for $C_{25}H_{31}N_3O_8S_2Na$ $[M + Na]^+$ 588.1450, found 588.1440.

Phenyl 2-Azido-2-deoxy-6-acetylthio-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-1-thio-*β*-D-glucopyranoside (74): The title compound was prepared by general procedure 6 and isolated as a light yellow foam eluted from silica gel with hexanes/EtOAc (6:1) in 78% yield. $[\alpha]^{RT}_D$ +132.1 (*c* 1.0); ^{1}H NMR (400 MHz) δ 7.57 (dd, *J* = 6.4, 7.2 Hz, 2H), 7.35−7.30 (m, 3H), 4.35 (d, *J* = 9.6 Hz, 1H), 3.67 (t, *J* = 9.6 Hz, 1H), 3.62−3.55 (m 1H), 3.51−3.45 (m, 2H), 3.44−3.30 (m, 2H), 3.30 (s, 3H), 3.22 (s, 3H), 3.07 (q, *J* = 7.2, 14.0 Hz, 1H), 2.35 (s, 3H), 1.31 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (100 MHz) δ 194.9, 134.5, 133.2, 130.7, 129.2, 129.1, 128.9, 100.4, 100.13, 86.2, 76.7, 73.0, 68.6, 61.5, 48.4, 48.3, 30.7, 30.1, 17.8, 17.7; ESIHRMS calcd for $C_{20}H_{27}N_3O_6S_2Na$ $[M + Na]^+$ 492.1239, found 492.1245.

Phenyl 6-Acetylthio-2-azido-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-1-thio-*β*-D-glucopyranoside *S*-Oxide (54). The title compound was prepared by general procedure 7 and isolated as a white solid eluting from silica gel in hexanes/EtOAc (4:1) in 70% yield. Mp 125 °C; $[\alpha]^{RT}_D$ −12.3 (*c* 1.0); ^{1}H NMR (400 MHz) δ 7.62−7.58 (m, 2H), 7.55−7.51 (m, 3H), 4.01 (dd, *J* = 9.6, 10.8 Hz, 1H), 3.83 (t, *J* = 9.6 Hz, 1H), 3.72 (d, *J* = 9.6 Hz, 1H), 3.54 (d, *J* = 9.6 Hz), 3.43−3.31 (m, 5H), 3.20 (s, 3H), 2.83 (dd, *J* = 8.0, 14.0 Hz, 1H), 2.19 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (100 MHz) δ 194.7, 139.1, 131.5, 129.2, 125.6, 100.5, 100.2, 91.9, 77.8, 73.3, 68.8, 57.6, 48.4, 48.3, 30.6, 29.8, 17.8, 17.7; ESIHRMS calcd for $C_{20}H_{27}N_3O_7S_2Na$ $[M + Na]^+$ 508.1188, found 508.1183.

Phenyl 2-Azido-2-deoxy-3,4,6-tri-*O*-(*p*-methoxybenzyl)-1-thio-*β*-D-glucopyranoside (75). To a stirred solution of **71**[42] (800 mg, 2.7 mmol) in DMF (6.4 mL) was added portionwise at 0 °C sodium hydride (542 mg, 16.1 mmol). The resulting mixture was stirred for 0.5 h at 0 °C before *p*-methoxybenzyl chloride (2.2 mL, 16.1 mmol) was added dropwise. The resulting mixture was allowed to warm to room temperature and stirred for 2 h. The reaction was quenched by addition of MeOH, concentrated, and purified by column chromatography eluting with 0.5% Et_3N in hexanes/EtOAc (4:1) to give the title compound (1.6 g, 92%) as a light yellow solid. Mp 72 °C; $[\alpha]^{RT}_D$ −45.8 (*c* 1.0); ^{1}H NMR (400 MHz) δ 7.60 (dd, *J* = 7.2, 8.0 Hz, 2H), 7.32−7.24 (m, 7H), 7.12 (d, *J* = 8.8 Hz, 2H), 6.92−6.82 (m, 6H), 4.78 (s, 2H), 4.72 (d, *J* = 10.4 Hz, 1H), 4.56 (d, *J* = 11.2 Hz, 1H), 4.52−4.46 (m, 2H), 4.40 (d, *J* = 9.6 Hz, 1H), 3.80 (s, 9H), 3.76−3.66 (m, 2H), 3.58−3.42 (m, 3H), 3.32 (t, *J* = 9.6 Hz, 1H); ^{13}C NMR (100 MHz) δ 159.7, 159.6, 159.4, 133.8, 131.5, 130.5, 130.3, 130.1, 130.0, 129.8, 129.6, 129.2, 128.5, 114.2, 114.1, 114.0, 86.1, 85.0, 79.6, 76.9, 75.7, 74.9, 73.3, 65.6, 65.3, 55.5; ESIHRMS calcd for $C_{36}H_{39}N_3O_7SNa$ $[M + Na]^+$ 680.2406, found 680.2404.

Phenyl 2-Azido-2-deoxy-3,4,6-tri-*O*-(*p*-methoxybenzyl)-1-thio-*β*-D-glucopyranoside *S*-Oxide (47). The title compound was prepared as a white solid by general procedure 7 and eluted from silica gel with 0.5% Et_3N in hexanes/EtOAc (4:1) as a mixture of diastereomers, in 92% yield. ^{1}H NMR (400 MHz) δ 7.71−7.63 (m, 2H), 7.51 (d, *J* = 4.8 Hz, 2H), 7.45 (dd, *J* = 2.4, 3.2 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.25 (t, *J* = 8.0 Hz, 3H), 7.18−6.79 (m, 3H), 6.92−6.81 (m, 7H), 4.83 (d, *J* = 1.6 Hz, 1H), 4.89−4.65 (m, 3H), 4.48 (dd, *J* = 7.2, 8.0 Hz, 3H), 4.31 (d, *J* = 11.6 Hz, 1H), 4.17 (dd, *J* = 9.6, 12.0 Hz, 1H), 3.86−3.3.77 (m, 13H), 3.74−3.67 (m, 2H), 3.66−3.57 (m, 1H), 3.56−3.45 (m, 4H); ^{13}C NMR (100 MHz) δ 159.7, 159.6, 140.3, 139.4, 131.6, 131.5, 130.1, 130.0, 129.9, 129.7, 129.6, 129.3, 129.2, 125.6, 124.9, 114.2, 114.1, 114.0, 113.9, 94.5, 91.8, 84.8, 84.7, 80.9, 80.4, 75.8, 75.7, 74.9, 73.5, 73.4, 68.4, 68.3, 61.0, 60.2, 55.5; ESIHRMS calcd for $C_{36}H_{39}N_3O_8SNa$ $[M + Na]^+$ 696.2356, found 696.2369.

Phenyl 3,4,6-Tri-*O*-acetyl-2-deoxy-1-thio-2-(2,2,2-trichloroethoxycarbonylamino)-*β*-D-glucopyranoside (77). To a stirred solution of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α,β-D-glucopyranose[44] (**76**) (10 g, 19.2 mmol) in CH_2Cl_2 (100 mL) was added, at room temperature, trimethylsilyl trifluoromethanesulfonate (4.2 mL, 23 mmol) and thiophenol (2.4 mL, 23 mmol).

The resulting mixture was stirred for 4 h, then neutralized by addition of triethylamine and concentrated. Chromatographic purification (hexanes/EtOAc = 3:1) afforded the title compound (9.2 g, 84%) as a light yellow solid (Scheme 10). Mp 87 °C; $[\alpha]^{RT}{}_D$ +18.5 (*c* 1.0); ^{1}H NMR (400 MHz) δ 7.49 (dd, *J* = 3.2, 4.0 Hz, 2H), 7.29 (dd, *J* = 2.0, 3.2 Hz, 3H), 4.95 (d, *J* = 9.6 Hz, 1H), 5.27 (t, *J* = 9.6 Hz, 1H), 5.01 (t, *J* = 9.6 Hz, 1H), 4.85 (d, *J* = 10.8 Hz, 1H), 4.74 (q, *J* = 12.0 Hz, 2H), 4.24−4.412 (m, 2H), 3.76−3.66 (m, 2H), 2.06 (s, 3H), 1.99 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (100 MHz) δ 170.9, 169.7, 154.2, 133.1, 132.3, 129.2, 128.5, 119.2, 86.8, 77.6, 75.9, 74.7, 73.4, 68.8, 62.6, 55.2, 21.0, 20.9, 20.8; ESIHRMS calcd for $C_{21}H_{24}Cl_3NO_9SNa$ $[M + Na]^+$ 594.0135, found 594.0112.

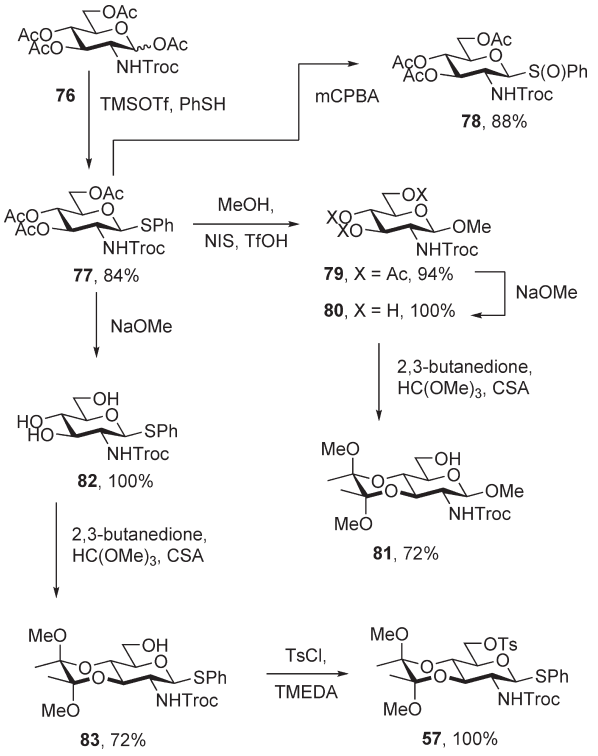
Methyl 3,4,6-Tri-*O*-acetyl-2-(2,2,2-trichloroethoxycarbonylamino)-2-deoxy-*β*-D-glucopyranoside (79). The title compound was prepared as a white solid by general NIS/TfOH protocol and eluted from silica gel with hexanes/EtOAc (2:1) in 94% yield. Mp 115 °C (lit.[45] mp 119−124 °C); $[\alpha]^{RT}{}_D$ +12.5 (*c* 1.0); ^{1}H NMR (400 MHz) δ 5.30 (dd, *J* = 9.2, 10.4 Hz, 1H), 5.20 (br s, 1H), 5.07 (dd, *J* = 8.8, 10.0 Hz, 1H), 4.80 (d, *J* = 11.2 Hz, 1H), 4.65 (d, *J* = 12 Hz, 1H), 4.54 (d, *J* = 7.6 Hz, 1H), 4.28 (dd, *J* = 4.0, 4.8 Hz, 1H), 4.15 (d, *J* = 10.0 Hz, 1H), 3.72 (d, *J* = 7.2 Hz, 1H), 3.64 (dd, *J* = 8.8, 17,6 Hz, 1H), 3.52 (s, 3H), 2.03 (s, 6H), 2.09 (s, 3H); ^{13}C NMR (100 MHz) δ 170.9, 169.7, 154.3, 119.2, 102.0, 74.7, 72.0, 68.9, 62.2, 57.4, 56.4, 55.1, 21.0, 20.8; ESIHRMS calcd for $C_{16}H_{22}Cl_3NO_{10}Na$ $[M + Na]^+$ 516.0207, found 516.0211.

Methyl 3,4-*O*-(2,3-Dimethoxybutane-2,3-diyl)-2-(2,2,2-trichloroethoxycarbonylamino)-2-deoxy-*β*-D-glucopyranoside (81). Compound **79** (600 mg, 1.66 mmol) was dissolved in MeOH (8.3 mL) at room temperature and a catalytic amount of 25% NaOMe in MeOH (0.16 mmol) was added. The resulting mixture was stirred for 1 h before the pH of the solution was adjusted to 7 by addition of dry Amberlyst IR 120 resin. The resulting mixture was filtered and concentrated to give methyl 2-(2,2,2-trichloroethoxycarbonylamino)-2-deoxy-*β*-D-glucopyranoside (**82**), which was immediately subjected to general procedure 4 and eluted from silica gel with hexanes/EtOAc (1:1) in 72% yield. White solid, mp 105 °C; $[\alpha]^{RT}$ α_D +123.0 (*c* 1.0); ^{1}H NMR (400 MHz) δ 5.20 (s, 1H), 4.72 (m 3H), 4.10 (dd, *J* = 7.2, 9.2 Hz, 1H), 3.92−3.84 (m, 1H), 3.80−3.74 (m, 1H), 3.69 (t, *J* = 10.0 Hz, 1H), 3.58−3.53 (m, 1H), 3.50 (s, 3H), 3.40−3.28 (m, 1H), 3.25 (s, 3H), 3.21 (s, 3H), 2.01 (dd, *J* = 4.8, 8.0 Hz, 1H), 1.28 (s, 6H); ^{13}C NMR (100 MHz) δ 119.2, 119.1, 102.2, 100.2, 99.8, 74.6, 74.1, 68.3, 67.2, 61.4, 57.2, 56.0, 48.2, 48.1, 17.9, 17.8; ESIHRMS calcd for $C_{16}H_{26}Cl_3NO_9Na$ $[M + Na]^+$ 504.0571, found 504.0572.

Phenyl 3,4,6-*O*-Acetyl-2-deoxy-1-thio-2-(2,2,2-trichloroethoxycarbonylamino)-*β*-D-glucopyranoside *S*-oxide (78). The title compound was prepared as a white foam by general procedure 7 and eluted from silica gel in hexanes/EtOAc (2:1) in 88% yield. Mp 134 °C; $[\alpha]^{RT}{}_D$ +31.0° (*c* 1.0); ^{1}H NMR (400 MHz) δ 7.71 (dd, *J* = 2.5, 3.2 Hz, 2H), 7.52 (dd, *J* = 2.4, 3.2 Hz, 3H), 5.68 (d, *J* = 8.8 Hz, 1H), 5.44 (t, *J* = 9.6 Hz, 1H), 4.92 (t, *J* = 9.6 Hz, 1H), 4.80 (d, *J* = 10.4 Hz, 1H), 4.62 (d, *J* = 12.4 Hz, 1H), 4.44 (d, *J* = 12.0 Hz, 1H), 4.16 (m, 2H), 3.86 (dd, *J* = 9.6, 10.8 Hz, 1H), 3.78 (m, 1H), 2.00 (s, 9H); ^{13}C NMR (100 MHz) δ 170.7, 170.6, 169.6, 153.9, 138.8, 131.6, 129.1, 125.9, 95.3, 93.3, 76.4, 74.6, 72.6, 68.1, 61.7, 51.7, 20.9, 20.8; ESIHRMS calcd for $C_{21}H_{24}Cl_3NO_{10}SNa$ $[M + Na]$ 610.0084, found 610.0067.

Phenyl 2-Deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-1-thio-2-(2,2,2-trichloroethoxycarbonylamino)-*β*-D-glucopyranoside (83). To a stirred solution of phenyl 3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-2-(2′,2′,2′-trichloroethoxycarbonylamino)-*β*-D-glucopyranoside[46] (**77**) (1 g, 1.75 mmol) in MeOH (8.8 mL) was added a catalytic amount of 25% sodium hydroxide in MeOH (0.18 mmol) at room temperature. The resulting mixture was stirred for 1 h, neutralized by addition of Amberlyst IR 120 resin, filtered, and concentrated to give phenyl 2-(2,2,2-trichloroethoxycarbonylamino)-1-thio-*β*-D-glucopyranoside (**82**),[47] which was subjected to general protocol 4 directly, giving the title compound as a white foam, eluted from silica gel with hexanes/EtOAc

Scheme 10. Preparation of 2-Deoxy-2-(trichloroethoxycarbonylamino)glucose-Based Monosaccharyl Units



(1.5:1) in 72% yield. $[\alpha]^{RT}{}_D$ +54.5 (*c* 1.0); ^{1}H NMR (400 MHz) δ 7.48 (dd, *J* = 2.4, 4.0 Hz, 2H), 7.31 (dd, *J* = 2.4, 4.4 Hz, 3H), 5.10 (d, *J* = 8.8 Hz, 2H), 4.75 (s, 2H), 4.10 (dd, *J* = 7.2, 9.6 Hz, 1H), 3.93−3.85 (m, 1H), 3.77−3.70 (m, 1H), 3.66 (t, *J* = 9.6 Hz, 1H), 3.62−3.56 (m, 1H), 3.41 (br s, 1H), 3.10 (dd, *J* = 4.4, 5.6 Hz, 1H), 3.24 (s, 3H), 3.21 (s, 3H), 1.91 (dd, *J* = 5.6, 7.6 Hz, 2H), 1.27 (s, 6H); ^{13}C NMR (100 MHz) δ 153.8, 133.0, 132.0, 129.4, 129.3, 128.4, 100.3, 99.8, 86.1, 78.1, 77.4, 74.7, 70.1, 67.0, 61.7, 54.7, 48.2, 48.1, 17.8, 17.8; ESIHRMS calcd for $C_{21}H_{28}Cl_3NO_8SNa$ $[M + Na]^+$ 582.0449, found 582.0494.

Phenyl 2-Deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-1-thio-6-*O*-*p*-toluenesulfonyl-2-(2,2,2-trichloroethoxycarbonylamino)-*β*-D-glucopyranoside (57). The title compound was prepared as a white solid by general procedure 5 and eluted from silica gel with hexanes/EtOAc (3:1) in a quantitative yield. Mp 144 °C; $[\alpha]^{RT}{}_D$ +84.2° (*c* 1.0); ^{1}H NMR (400 MHz) δ 7.81 (d, *J* = 7.2 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.34−7.21 (m, 5H), 5.03 (dd, *J* = 6.4, 10.0 Hz, 2H), 4.73 (s, 2H), 4.30 (d, *J* = 10.8 Hz, 1H), 4.23 (dd, *J* = 4.0 Hz, 10.8 Hz, 1H), 4.07 (dd, *J* = 10.0, 11.2 Hz, 1H), 3.67 (dd, *J* = 2.4, 3.2 Hz, 1H), 3.59 (t, *J* = 9.6 Hz, 1H), 3.31−3.23 (m, 1H), 3.29 (s, 3H), 3.18 (s, 3H), 2.40 (s, 3H), 1.25 (s, 6H); ^{13}C NMR (100 MHz) δ 145.1, 133.3, 130.1, 129.2, 128.5, 128.2, 100.4, 100.0, 85.6, 77.6, 75.4, 74.6, 69.7, 67.7, 66.5, 54.3, 48.5, 48.2, 21.9, 17.9, 17.7; ESIHRMS calcd for $C_{28}H_{34}Cl_3NO_{10}Na$ $[M + Na]^+$ 736.0587, found 736.0594.

Phenyl 2-Azido-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-1-thio-2′-azido-2′-deoxy-3′,4′,6′-tri-*O*-(*p*-methoxybenzyl)]-*β*-D-gentiobioside (49). Glycosyl sulfoxide **47** (1.2 g, 1.78 mmol) was premixed with acceptor **48** (880 mg, 2.14 mmol), 2,4,6-tri-*tert*-butylpyrimidine (886 mg, 3.57 mmol), and activated 4 Å powdered molecular sieves in CH_2Cl_2/acetonitrile (4:3) (3.6 mL) and the resulting mixture was stirred at room temperature for 0.5 h then cooled to −80 °C before trifluoromethanesulfonic anhydride (0.33 mL, 1.96 mmol) was added dropwise. The reaction mixture was stirred at −80 °C for

1.5 h, quenched by addition of aqueous saturated $NaHCO_3$, and then allowed to warm to room temperature. The aqueous phase was extracted twice with CH_2Cl_2. The organic layers were combined, dried, filtered, and concentrated in vacuo. Chromatographic purification eluting with 0.5% Et_3N in hexanes/EtOAc (4:1 to 2.5:1) gave the title compound (1.05 g, 62%) as a white foam. $[\alpha]^{RT}_D$ +29.6° (*c* 1.0); ^1H NMR (400 MHz) δ 7.61−7.53 (m, 2H), 7.36−7.27 (m, 5H), 7.27−7.22 (m, 3H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.83 (dd, *J* = 5.6, 8.8 Hz, 3H), 4.83−4.69 (m, 3H), 4.58−4.37 (m, 4H), 4.14 (d, *J* = 10.8 Hz, 1H), 3.90−3.46 (m, 16H), 3.44−3.19 (m, 11H), 1.32 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (100 MHz) δ 159.6, 159.5, 134.1, 133.8, 130.4, 130.0, 129.8, 129.3, 128.6, 114.1, 114.0, 102.4, 100.4, 100.0, 86.4, 83.1, 78.2, 75.9, 75.8, 75.5, 75.2, 74.9, 74.7, 73.4, 72.2, 71.2, 68.4, 68.1, 66.6, 66.3, 65.6, 61.7, 60.2, 55.5, 55.4, 48.3, 17.8, 17.7; ESIHRMS calcd for $C_{48}H_{58}N_6O_{13}SNa$ $[M + Na]^+$ 981.3680, found 981.3682.

Phenyl 2-Azido-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-1-thio-[2′-azido-2′-deoxy-3′,4′,6′-tri-*O*-(*p*-methoxybenzyl)]-β-D-gentiobioside *S*-Oxide (50). The title compound was prepared as a white foam by general procedure 7 and eluted from silica gel with 0.5% Et_3N in hexanes/EtOAc (3:1) in 88% yield, in an approximately 1:1 mixture of diastereomers. ^1H NMR (400 MHz) δ 7.68−7.60 (m, 2 × 2H), 7.55−7.45 (m, 2 × 3H), 7.33−7.20 (m, 2 × 4H), 7.12−7.02 (m, 2 × 2H), 6.91−6.79 (m, 2 × 6H), 4.80−4.66 (m, 2 × 3H), 4.54 (dd, *J* = 9.6, 10.8 Hz, 1 × 1H), 4.48−4.38 (m, 2 × 2H), 4.21 (dd, *J* = 5.6, 9.6 Hz, 1 × 1H), 4.02−3.84 (m, 2 × 3H), 3.83−3.73 (m, 2 × 10H), 3.73−3.44 (m, 2 × 6H), 3.43−3.14 (m, 2 × 9H), 1.34 (s, 2 × 3H), 1.26 (s, 2 × 3H); ^{13}C NMR (100 MHz) δ 159.6, 139.1, 131.7, 131.4, 130.3, 130.0, 129.9, 129.8, 129.7, 129.6, 129.4, 129.3, 125.4, 124.7, 114.2, 114.1, 114.0, 102.9, 102.1, 100.5, 100.1, 95.2, 91.7, 91.4, 82.7, 79.8, 78.8, 77.5, 75.4, 75.3, 75.0, 74.9, 74.8, 73.5, 73.4, 73.1, 68.5, 68.2, 67.7, 66.4, 66.1, 65.8, 57.7, 55.5, 55.4, 48.4, 48.3, 17.8, 17.7; ESIHRMS calcd for $C_{48}H_{58}N_6O_{14}SNa$ $[M + Na]^+$ 997.3629, found 997.3614.

2-(Phenyloxycarbonylthioxybut-3-enyl 2-Azido-2-deoxy-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-[2′-azido-2′deoxy-3′,4′,6′-tri-*O*-(*p*-methoxybenzyl)]-β-D-gentiobioside (51). The glycosyl sulfoxide **50** (560 mg, 0.57 mmol) was mixed with **20**[22b] (266 mg, 1.20 mmol), 2,4,6-tri-*tert*-butylpyrimidine (314 mg, 1.26 mmol), and activated 4 Å powdered molecular sieves in CH_2Cl_2/acetonitrile (4:3) (2 mL) and the resulting mixture was stirred at room temperature for 0.5 h then cooled to −60 °C before trifluoromethanesulfonic anhydride (0.15 mL, 0.86 mmol) was added dropwise. The reaction mixture was stirred at −60 °C for 8 h and was then cooled to −80 °C, quenched by addition of aqueous saturated $NaHCO_3$, and then allowed to warm to room temperature. The aqueous phase was extracted twice with CH_2Cl_2. The organic layers were combined, dried, filtered, and concentrated in vacuo. Chromatographic purification eluting with 0.5% Et_3N in hexanes/EtOAc (6:1 to 3:1) gave the title compound (390 mg, 63%) as a white foam as an approximately 1:1 mixture of diastereomers. ^1H NMR (400 MHz) δ 7.41−7.11 (m, 2 × 10H), 7.17−7.10 (m, 2 × 2H), 7.45 (d, *J* = 7.2 Hz, 2 × 2H), 6.90−6.79 (m, 2 × 7H), 6.03−5.92 (m, 2 × 1H), 5.43 (d, *J* = 16.8 Hz, 2 × 1H), 5.25 (d, *J* = 9.6 Hz, 2 × 1H), 4.80−4.67 (m, 2 × 4H), 4.55 (dd, *J* = 7.2, 11.6 Hz, 2 × 1H), 4.47−4.35 (m, 2 × 4H), 4.29−4.17 (m, 2 × 3H), 3.92−3.81 (m, 2 × 1H), 3.79 (s, 2 × 6H), 3.78 (s, 2 × 3H), 3.73−4.49 (m, 2 × 7H), 3.49−3.19 (m, 2 × 10H), 1.33 (s, 2 × 3H), 1.27 (s, 2 × 3H); ^{13}C NMR (100 MHz) δ 169.3, 169.2, 169.0, 159.6, 159.5, 159.4, 156.6, 151.4, 134.2, 134.1, 130.3, 130.2, 130.0, 130.0, 129.9, 129.8, 129.7, 126.4, 126.3, 124.7, 121.7, 121.6, 121.5, 120.3, 118.9, 115.7, 114.2, 114.1, 114.0, 103.0, 102.9, 102.8, 102.7, 100.2, 100.0, 83.2, 83.0, 75.4, 75.2, 74.9, 74.6, 73.4, 73.3, 71.4, 71.2, 70.8, 70.1, 70.0, 68.4, 67.1, 66.5, 63.2, 55.5, 55.4, 48.7, 48.3, 45.9, 18.0, 17.9, 17.8, 17.7; ESIHRMS calcd for $C_{53}H_{64}N_6O_{16}SNa$ $[M + Na]^+$ 1095.3997, found 1095.4004.

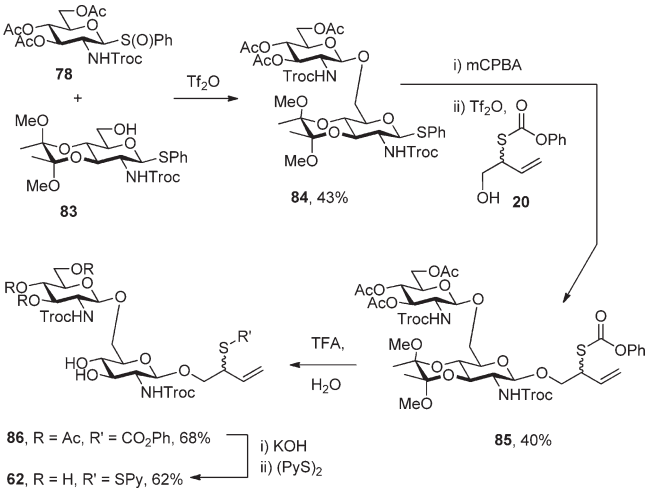
2-(Phenyloxycarbonylthioxy)but-3-enyl 2,2′-diazido-2,2′-dideoxy-β-D-gentiobioside (52). The title compound as a white foam was obtained by treatment of **51** with TFA according to general procedure 9 eluted from silica gel with CH_2Cl_2/MeOH (20:1) as an approximately 1:1 mixture of diastereomers in 67% yield. NMR (400 MHz) δ 7.40 (t, *J* = 7.3 Hz, 2 × 2H), 7.26 (t, *J* = 7.2 Hz, 2 × 1H), 7.15 (d, *J* = 9.2 Hz, 2 × 2H), 6.06−5.95 (m, 2 × 1H), 5.41 (d, *J* = 15.2 Hz, 2 × 1H), 5.23 (d, *J* = 10.8 Hz, 2 × 1H), 4.48 (dd, *J* = 7.3, 8.8 Hz, 2 × 1H), 4.41 (d, *J* = 8.0 Hz, 2 × 1H), 4.28−4.18 (m, 2 × 3H), 3.93−3.60 (m, 2 × 7H), 3.47 (dd, *J* = 6.4, 8.0 Hz, 2 × 1H), 3.34−3.06 (m, 2 × 9H); ^{13}C NMR (100 MHz) δ 164.0, 134.9, 129.5, 126.2, 121.3, 117.7, 117.6, 102.7, 102.3, 102.1, 101.9, 94.7, 76.8, 76.2, 75.1, 75.0, 70.7, 70.6, 70.3, 69.0, 67.1, 61.3, 48.6; ESIHRMS calcd for $C_{23}H_{30}N_6O_{11}SNa$ $[M + Na]^+$ 621.1591, found 621.1593.

2-(Pyridyldithio)but-3-enyl 2,2′-diazido-2,2′-dideoxy-β-D-gentiobioside (53). The title compound was prepared as a white foam by general procedure 3 and eluting from silica gel in CH_2Cl_2/MeOH (20:1) as an approximately 1:1 mixture of diastereomers in 65% yield over two steps. ^1H NMR (400 MHz, CD_3OD) δ 8.37 (d, *J* = 4.0 Hz, 2 × 1H), 8.75 (dd, *J* = 4.0, 8.4 Hz, 2 × 1H), 7.83−7.77 (m, 2 × 1H), 7.21 (dd, *J* = 4.8, 7.2 Hz, 2 × 1H), 5.90−5.78 (m, 2 × 1H), 5.30−5.21 (m, 2 × 1H), 5.15 (d, *J* = 10.8 Hz, 2 × 1H), 4.96−4.85 (m, 2 × 1H), 4.47−4.32 (m, 2 × 2H), 4.24−3.98 (m, 2 × 3H), 3.91−3.64 (m, 2 × 7H), 4.48−3.05 (m, 2 × 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 148.9, 137.9, 133.9, 121.1, 120.3, 120.2, 118.4, 102.7, 101.8, 76.8, 76.2, 75.1, 74.9, 70.6, 70.4, 69.8, 69.0, 67.0, 61.4, 53.8; ESIHRMS calcd for $C_{21}H_{29}N_7O_9S_2Na$ $[M + Na]^+$ 610.1366, found 610.1379.

Methyl 2,2′-Diazido-2,2′-dideoxy-6′-acetylthio-β-D-gentiobioside (56). Glycosyl sulfoxide (**54**) (340 mg, 0.70 mmol) was mixed with 2,4,6-tri-*tert*-butylpyrimidine (244 mg, 0.98 mmol) and activated 4 Å powdered molecular sieves in CH_2Cl_2/acetonitrile (3:1) (2.6 mL). The resulting mixture was stirred at room temperature for 0.5 h then cooled to −65 °C before trifluoromethanesulfonic anhydride (0.14 mL, 0.84 mmol) was added dropwise. The glycoside sulfoxide was preactivated for 10 min and a solution of **55** (466 mg, 1.4 mmol) in CH_2Cl_2 (0.8 mL) was added. The resulting mixture was stirred for 8 h at −65 °C quenched by addition of aqueous saturated $NaHCO_3$ and then allowed to warm to room temperature. The aqueous phase was extracted twice with CH_2Cl_2. The organic layers were combined, dried, filtered, and concentrated in vacuo. The crude protected disaccharide was subjected directly to the standard acid hydrolysis step after which the title compound was obtained as a white foam eluted from silica gel with CH_2Cl_2/MeOH (20:1) in 26% overall yield. $[\alpha]^{RT}_D$ +18.5 (*c* 1.0, MeOH); NMR (400 MHz) δ 4.42 (d, *J* = 7.8 Hz, 1H), 4.24 (d, *J* = 7.8 Hz, 1H), 4.16 (dd, *J* = 1.8, 11.4 Hz, 1H), 3.70 (dd, *J* = 6.9 11.7 Hz, 1H), 3.60−3.51 (m, 5H), 3.46 (dd, *J* = 7.2, 8.1 Hz, 1H), 3.35 (s, 1H), 3.32−3.24 (m 8H), 3.23−3.08 (m, 4H), 2.98 (dd, *J* = 8.1, 14.1 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz) δ 195.7, 102.9, 102.6, 75.9, 75.2, 75.0, 74.7, 73.4, 70.6, 69.1, 67.0, 48.7, 47.0, 30.6, 29.2; ESIHRMS calcd for $C_{15}H_{24}N_6O_9SNa$ $[M + Na]^+$ 487.1223, found 487.1232.

Phenyl 3′,4′,6′-Tri-*O*-acetyl-2,2′-dideoxy-3,4-*O*-(2,3-dimethoxybutan-2,3-diyl)-1-thio-2,2′-bis(2,2,2-trichloroethoxycarbonylamino)-β-D-gentiobioside (84). Glycosyl sulfoxide **78** (310 mg, 0.53 mmol) was stirred in CH_2Cl_2 (1.6 mL) with activated 4 Å powdered molecular sieves at room temperature for 0.5 h. The resulting mixture was cooled to −65 °C before trifluoromethanesulfonic anhydride (0.10 mL, 0.58 mmol) was added dropwise. After the mixture was stirred for 10 min a solution of **83** (350 mg, 0.62 mmol) in CH_2Cl_2 (0.4 mL) was added. The resulting mixture was stirred for 7 h at −65 °C, quenched by addition of aqueous saturated $NaHCO_3$, and then allowed to warm to room temperature. The aqueous phase was extracted twice with CH_2Cl_2. The organic layers were combined, dried, filtered, and concentrated in vacuo. Chromatographic purification eluting with hexanes/EtOAc (5:1 to 2:1) gave the title disaccharide as a white foam (230 mg, 43%) (Scheme 11): $[\alpha]^{RT}_D$ +44.2 (*c* 1.0); ^1H NMR δ 7.52 (d, *J* = 7.2 Hz, 2H), 7.43−7.33 (m, 3H), 5.36−5.06 (m, 2H), 5.00 (d, *J* = 7.6 Hz, 2H), 4.81−4.69 (m, 3H), 4.64 (dd, *J* = 8.8, 12.0 Hz, 1H), 4.52 (d,

Scheme 11. Preparation of the *N*-Troc Glucosamine-Based Disaccharyl Sulfenyl Donor 62



J = 8.0 Hz, 1H), 4.28−4.21 (m, 2H), 4.15−4.02 (m, 3H), 3.75−3.52 (m, 4H), 3.39 (t, J = 9.6 Hz, 2H), 3.20 (s, 3H), 3.17 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H), 1.26, (s, 3H), 1.24 (s, 3H); ^{13}C NMR δ 169.7, 169.3, 168.4, 153.1, 152.5, 132.2, 128.5, 127.7, 100.2, 99.0, 98.7, 94.5, 84.9, 78.1, 75.7, 73.5, 71.2, 70.5, 67.7, 67.3, 66.6, 66.3, 60.9, 54.9, 53.4, 47.0, 46.9, 19.7, 19.6, 16.6, 16.5; ESIHRMS calcd for $C_{36}H_{46}Cl_6N_2O_{17}$SNa $[M + Na]^+$ 1043.0549, found 1043.0546.

2-(Phenyloxycarbonylthioxy)but-3-enyl 3′,4′,6′-Tri-*O*-acetyl-2,2′-dideoxy-3,4-*O*-(2,3-dimethoxybutan-2,3-diyl)-2,2′-bis-(2,2,2-trichloroethoxycarbonylamino)-β-D-gentiobioside (85). The thioglycoside **84** was converted to the corresponding glycosyl sulfoxide according to general procedure 7 and 280 mg of this sulfoxide (0.27 mmol) was mixed with **20**[22b] (120 mg, 0.54 mmol) and activated 4 Å powdered molecular sieves in CH_2Cl_2 (1.2 mL) then the mixture was stirred at room temperature for 0.5 h and cooled to −60 °C before trifluoromethanesulfonic anhydride (0.07 mL, 0.40 mmol) was added dropwise. The reaction mixture was stirred at −60 °C for 12 h, then was cooled to −75 °C, quenched by addition of aqueous saturated $NaHCO_3$, and allowed to warm to room temperature. The aqueous phase was extracted twice with CH_2Cl_2. The organic layers were combined, dried, filtered, and concentrated in vacuo. Purification by column chromatography eluting with hexanes/EtOAc (4:1 to 2:1) gave the title compound as a white foam as an approximately 1:1 mixture of diastereomers (202 mg, 40% over two steps): ^{1}H NMR (400 MHz) δ 7.36 (t, J = 7.2 Hz, 2 × 2H), 7.25−7.13 (m, 2 × 3H), 6.1−5.85 (m, 2 × 1H), 5.40 (d, J = 16.8 Hz, 2 × 1H), 5.35−5.20 (m, 2 × 3H), 5.05 (dd, J = 8.8, 9.6 Hz, 2 × 2H), 4.85−4.65 (m, 2 × 6H), 4.30−3.95 (m, 2 × 6H), 3.90−3.80 (m, 2 × 1H), 3.75−3.50 (m, 2 × 5H), 3.45 (dd, J = 8.0, 10.0 Hz, 2 × 1H), 3.25 (s, 2 × 3H), 3.15 (s, 2 × 3H), 2.08 (s, 2 × 3H), 1.98 (s, 2 × 6H), 1.28 (s, 2 × 3H), 1.24 (s, 2 × 3H); ^{13}C NMR (100 MHz) δ 170.9, 170.6, 169.7, 154.2, 151.3, 134.1, 133.8, 129.7, 126.4, 121.6, 121.5, 119.2, 119.1, 101.1, 100.1, 99.9, 95.7, 76.9, 74.7, 72.2, 71.9, 71.6, 70.2, 68.8, 68.6, 68.3, 67.7, 62.2, 62.1, 56.5. 55.7, 55.4, 49.0, 48.6, 48.2, 48.1, 29.9, 21.0, 20.8, 17.9, 17.8; ESIHRMS calcd for $C_{41}H_{52}Cl_6N_2O_{20}$SNa $[M + Na]^+$ 1157.0885, found 1157.0890.

2-(Phenyloxycarbonylthioxy)but-3-enyl 3′,4′,6′-Tri-*O*-acetyl-2,2′-dideoxy-2,2′-bis(2,2,2-trichloroethoxycarbonylamino)-β-D-gentiobioside (86). Cleavage of the bis(acetal) groups from **85** according to general procedure 9 gave the title compound as a white foam that eluted from silica gel with hexanes/EtOAc (1:1 to 1:3) as an approximately 1:1 mixture of diastereomers in 68% yield. NMR (400 MHz) δ 7.38 (dd, J = 7.2, 8.4 Hz, 2 × 2H), 7.28−7.21 (m, 2 × 1H), 7.16 (dd, J = 4.0, 8.4 Hz, 2 × 2H), 6.00−6.57 (m, 2 × 1H), 5.55−5.45 (d, J = 16.8 Hz, 2 × 1H), 5.40 (d, J = 16.8 Hz, 2 × 1H), 5.25 (d, J = 10.4 Hz, 2 × 1H), 5.25−5.20 (m, 2 × 1H), 5.05 (t, J = 9.6 Hz, 2 × 1H), 4.80−4.65 (m, 2 × 4H), 4.55 (br s, 2 × 1H), 4.30−4.05 (m, 2 × 5H), 3.90−3.60 (m, 2 × 6H), 3.60−3.30 (m, 2 × 4H), 2.10 (s, 2 × 3H), 2.03 (s, 2 × 6H); ^{13}C NMR (100 MHz) δ 171.1, 171.0, 169.7, 155.3, 154.6, 151.3, 134.1, 133.8, 129.8, 126.5, 121.6, 121.5, 119.4, 119.3, 101.5, 95.5, 77.0, 75.1, 75.0, 74.8, 74.7, 74.3, 72.2, 71.5, 69.3, 68.7, 62.1, 58.3, 58.1, 56.4, 48.8, 48.4, 29.9, 21.1, 20.8; ESIHRMS calcd for $C_{35}H_{42}Cl_6N_2O_{18}$SNa $[M + Na]^+$ 1043.0182, found 1043.0209.

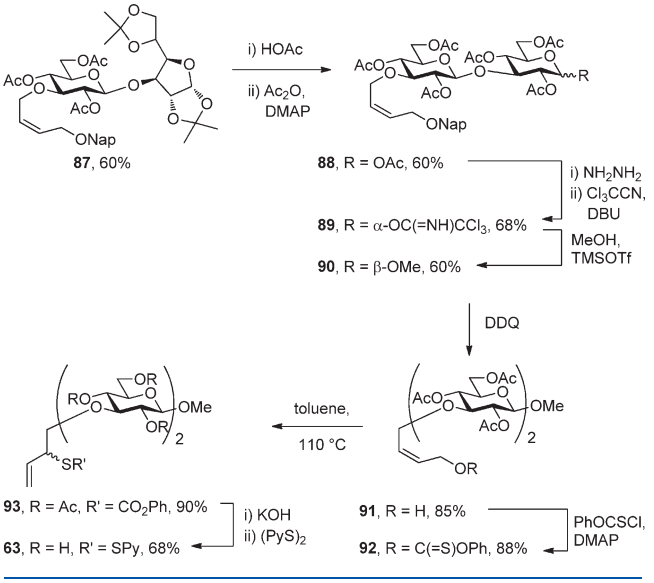
2-(2-Pyridyldithio)but-3-enyl 2,2′-Dideoxy-2,2′-bis(2,2,2-trichloroethoxycarbonylamino)-β-D-gentiobioside (62). Installation of the disulfide moiety on **86** by standard procedure 3 gave the title compound as a white foam eluting from silica gel with CH_2Cl_2/MeOH (20:1) as an approximately 1:1 mixture of diastereomers in 62% yield over two steps. ^{1}H NMR (400 MHz, CD_3OD) δ 8.36 (d, J = 4.8 Hz, 2 × 1H), 7.91 (dd, J = 7.2, 8.4 Hz, 2 × 1H), 7.87−7.79 (m, 2 × 1H), 7.20 (dd, J = 4.8, 7.2 Hz, 2 × 1H), 5.90−5.74 (m, 2 × 1H), 5.15 (dd, J = 9.6, 16.8 Hz, 2 × 2H), 4.85−4.64 (m, 2 × 10H), 4.53−4.33 (m, 2 × 2H), 4.21−4.00 (m, 2 × 2H), 3.88 (d, J = 12.0 Hz, 2 × 1H), 3.82−3.59 (m, 2 × 4H), 3.50−3.21 (m, 2 × 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 155.8, 149.1, 148.8, 138.1, 134.1, 133.8, 122.2, 121.0, 120.3, 118.6, 118.3, 102.1, 101.8, 101.7, 76.8, 75.8, 74.6, 74.5, 74.4, 71.1, 70.9, 70.0, 69.8, 69.0, 61.6, 58.0, 57.8, 54.4, 54.3, 29.6; ESIHRMS calcd for $C_{27}H_{35}Cl_6N_3O_{13}S_2$Na $[M + Na]^+$ 905.9637, found 905.9640.

Methyl 2,2′-Dideoxy-3,4;3′,4′-di-*O*-(2,3-dimethoxybutan-2,3-diyl)-2,2′-bis(2,2,2-trichloroethoxycarbonylamino)-6′-*O*-*p*-toluenesulfonyl-β-D-gentiobioside (59). The title compound was prepared as a white foam by general procedure 8 from **57** and **58** and eluted from silica gel with hexanes/EtOAc (5:1 to 3:1) in 89% yield. $[\alpha]^{23}_D$ +72.7 (c 1.0); ^{1}H NMR (400 MHz) δ 7.82 (d, J = 8.0 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 5.10 (br s, 2H), 4.88 (br s, 1H), 4.80−4.62 (m, 5H), 4.31 (d, J = 10.8 Hz, 1H), 4.16 (dd, J = 5.6, 10.8 Hz, 1H), 4.12−3.97 (m, 3H), 3.68 (dd, J = 6.4, 8.8 Hz, 3H), 3.59−3.45 (m, 5H), 3.40−3.12 (m, 14H), 2.45 (s, 3H), 1.28 (s, 6H), 1.25 (s, 6H); ^{13}C NMR (100 MHz) δ 154.6, 154.1, 145.2, 132.9, 130.1, 128.4, 128.2, 101.9, 101.6, 100.2, 99.8, 95.8, 95.7, 74.8, 74.5, 73.8, 73.6, 72.3, 71.7, 69.7, 69.2, 68.5, 67.7, 67.0, 57.3, 57.2, 56.5, 55.7, 55.6, 48.5, 48.4, 48.2, 48.1, 29.9, 21.9, 18.9, 17.8; ESIHRMS calcd for $C_{38}H_{54}Cl_6N_2O_{19}$SNa $[M + Na]^+$ 1107.1070, found 1107.1086.

Methyl 6′-Acetylthio-2,2′-dideoxy-3,4;3′,4′-di-*O*-(2,3-dimethoxybutan-2,3-diyl)-2,2′-bis(2,2,2-trichloroethoxycarbonylamino)-β-D-gentiobioside (60). The title compound was prepared as a light yellow foam by displacement of the tosylate from **59** according to general procedure 6 and eluted from silica gel with hexanes/EtOAc (6:1) in 71% yield. $[\alpha]^{RT}_D$ +82.3 (c 1.0); ^{1}H NMR (400 MHz) δ 5.16−5.0 (m, 1H), 4.92−4.83 (m, 1H), 4.78−4.63 (m, 5H), 4.12−3.99 (m, 3H), 3.74−3.65 (m, 2H), 3.64−3.56 (m, 1H), 3.53−3.42 (m, 6H), 3.33 (dd, 5.2, J = 7.2 Hz, 3H), 3.23 (s, 3H), 3.21 (s, 3H), 3.20 (s, 3H), 3.18 (s, 3H), 3.04 (q, J = 10.0, 18.8 Hz, 1H), 2.33 (s, 3H), 1.29 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (100 MHz) δ 195.1, 154.6 154.0, 129.2, 128.8, 101.8, 101.6, 100.1, 100.0, 99.8, 95.8, 77.6, 75.9, 74.8, 74.6, 74.2, 74.1, 72.7, 72.5, 70.1, 68.4, 67.8, 57.6, 57.3, 55.9, 48.5, 48.3, 48.1, 30.7, 30.2, 19.0, 17.9, 17.8; ESIHRMS calcd for $C_{33}H_{50}Cl_6N_2O_{17}$SNa $[M + Na]^+$ 1011.0859, found 1011.0869.

Methyl 2,2′-Dideoxy-2,2′-bis(2,2,2-trichloroethoxycarbonylamino)-6′-acetylthio-β-D-gentiobioside (61). Removal of the bisacetal groups from **60** according to general procedure 9 gave the title compound as a white foam eluted from silica gel with CH_2Cl_2/MeOH (20:1) in 68% yield. $[\alpha]^{RT}_D$ −6.0 (c 1.0); NMR (400 MHz) δ 4.84−4.69 (m, 6H), 4.60 (s, 1H), 4.45 (d, J = 7.6 Hz, 1H), 4.29 (d, J = 8.8 Hz, 1H), 4.11 (d, J = 10.4 Hz, 1H), 3.72−3.56 (m, 2H), 3.45−3.29 (m, 7H), 3.21 (dd, J = 8.8, 9.4 Hz, 3H), 2.90 (dd, J = 7.2, 13.6 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz) δ 196.0, 155.9, 102.4, 102.1, 91.5, 75.6, 75.0, 74.6, 74.4, 74.2, 74.1, 74.0, 72.1, 71.4, 69.5, 48.5, 47.4, 30.8, 29.3,

Scheme 12. Preparation of the Laminaribiosyl 3′-Sulfenyl Donor 63



25.6, 19.8; ESIHRMS calcd for $C_{21}H_{30}Cl_6N_2O_{13}SNa$ $[M + Na]^+$ 782.9497, found 782.9501.

3-*O*-{2,4,6-Tri-*O*-acetyl-3-*O*-[4-(2-naphthylmethyloxy)but-2*Z*-enyl]-β-D-glycopyranosyl}-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (87). Following general procedure 12, diacetone-D-glucose was glycosylated with trichloroacetimidate **26** and after eluting with 70% EtOAc/hexanes from silica gel the title compound was obtained in 60% yield (Scheme 12). $[\alpha]^{23}_D$ −15.7 (*c* 1); ^{1}H NMR δ 7.86−7.83 (m, 3H), 7.79 (s, 1H), 7.51−7.46 (m, 3H), 5.84 (d, *J* = 3.5 Hz, 1H), 5.81−5.76 (m, 1H), 5.62−5.57 (m, 1H), 5.03 (t, *J* = 10.0 Hz, 1H), 4.92 (dd, *J* = 9.5, 7.5 Hz, 1H), 4.68 (s, 2H), 4.50 (d, *J* = 8.0 Hz, 1H), 4.42 (d, *J* = 4.0 Hz, 1H), 4.35 (dd, *J* = 12.0, 6.0 Hz, 1H), 4.27 (dd, *J* = 5.5, 3.0 Hz, 1H), 4.25−4.24 (m, 1H), 4.18−4.11 (m, 3H), 4.08−4.03 (m, 3H), 3.97 (dd, *J* = 9.0, 6.0 Hz, 1H), 3.53−3.49 (m, 2H), 2.08 (s, 3H), 2.02 (s, 3H), 2.00 (s, 3H), 1.50 (s, 3H), 1.43 (s, 3H), 1.35 (s, 3H), 1.32 (s, 3H); ^{13}C NMR δ 170.9, 169.4, 168.9, 135.7, 133.5, 133.2, 129.5, 129.3, 128.5, 128.1, 127.9, 126.7, 126.5, 126.2, 125.9, 112.3, 108.8, 105.3, 99.6, 83.0, 81.2, 80.8, 79.7, 73.3, 72.7, 72.6, 69.5, 67.3, 66.4, 65.8, 62.4, 27.1, 26.8, 26.6, 25.5, 20.9; ESIHRMS calcd for $C_{35}H_{47}NO_{17}Na$ $[M + Na]^+$ 776.2742, found 776.2740.

2,2′,4,4′,6,6′-Hexa-*O*-acetyl-3′-*O*-[4-(2-naphthylmethyloxy)-but-2*Z*-enyl]-α-D-laminaribiosyl Trichloroacetimidate (89). Following general procedure 10, the acetonide groups were cleaved and the acetate groups were reinstalled to give the peracetate **88** in 60% yield as a mixture of stereoisomers that was applied directly to general procedure 11, after which elution from silica gel with 70% EtOAc/hexanes gave the title compound in 68% yield as yellow oil. $[\alpha]^{23}_D$ +28.0 (*c* 1); ^{1}H NMR δ 8.70 (s, 1H), 7.85−7.82 (m, 3H), 7.77 (s, 1H), 7.50−7.45 (m, 3H), 6.46 (d, *J* = 4.0 Hz, 1H), 5.79−5.74 (m, 1H), 5.59−5.54 (m, 1H), 5.12−5.06 (m, 2H), 4.99 (t, *J* = 9.5 Hz, 1H), 4.89−4.85 (m, 1H), 4.66 (s, 2H), 4.54 (d, *J* = 8.5 Hz, 1H), 4.23 (dd, *J* = 12.0, 5.0 Hz, 1H), 4.19 (dd, *J* = 12.5, 4.5 Hz, 1H), 4.16−4.03 (m, 8H), 3.55−3.49 (m, 2H), 2.08 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H), 1.98 (s, 3H), 1.97 (s, 3H); ^{13}C NMR δ 170.9, 170.8, 169.7, 169.4, 169.3, 169.1, 160.8, 135.7, 133.5, 133.2, 129.5, 129.2, 128.5, 128.1, 127.9, 126.7, 126.5, 125.9, 101.4, 93.4, 79.8, 76.3, 72.7, 72.3, 72.1, 72.0, 70.5, 69.4, 67.5, 66.8, 65.9, 62.3, 61.8, 20.9, 20.9, 20.9, 20.9, 20.8, 20.8, 20.7; ESIHRMS calcd for $C_{41}H_{48}Cl_3NO_{18}Na$ $[M + Na]^+$ 970.1835, found 970.1845.

Methyl 2,2′,4,4′,6,6′-Hexa-*O*-acetyl-3′-*O*-[4-(2-naphthylmethyloxy)but-2*Z*-enyl]-β-D-laminaribioside (90). Following general procedure 12, and eluting with 75% EtOAc/hexanes the title compound was obtained in 60% yield. $[\alpha]^{23}_D$ −17.0 (*c* 1); ^{1}H NMR δ 7.85−7.83 (m, 3H), 7.78 (s, 1H), 7.49−7.45 (m, 3H), 5.79−5.74 (m, 1H), 5.59−5.55 (m, 1H), 5.03−4.91 (m, 3H), 4.86 (t, *J* = 9.0 Hz, 1H), 4.66 (s, 2H), 4.46 (d, *J* = 8.5 Hz, 1H), 4.30−4.25 (m, 2H), 4.19−4.18 (m, 2H), 4.11 (d, *J* = 6.5 Hz, 2H), 4.07 (d, *J* = 6.0 Hz, 2H), 4.00 (dd, *J* = 12.0, 2.5 Hz, 1H), 3.85 (t, *J* = 9.0 Hz, 1H), 3.69−3.67 (m, 1H), 3.51−3.49 (m, 2H), 3.47 (s, 3H), 2.11 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 2.02 (s, 3H), 2.02 (s, 3H), 1.98 (s, 3H); ^{13}C NMR δ 171.1, 170.9, 169.5, 169.4, 169.4, 169.0, 135.7, 133.5, 133.2, 129.5, 129.2, 128.5, 128.1, 127.9, 126.7, 126.4, 126.2, 125.9, 101.7, 101.4, 79.8, 78.8, 72.9, 72.7, 72.1, 72.1, 72.0, 69.3, 68.7, 66.8, 65.9, 62.4, 62.3, 56.8, 21.2, 21.0, 20.9, 20.9, 20.8, 20.7; ESIHRMS calcd for $C_{40}H_{50}O_{18}Na$ $[M + Na]^+$ 841.2895, found 841.2870.

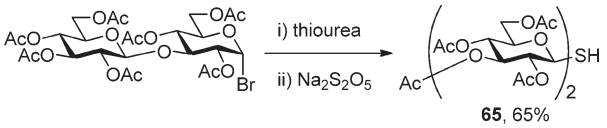
Methyl 2,2′,4,4′,6,6′-Hexa-*O*-acetyl-3′-*O*-[4-hydroxybut-2*Z*-enyl]-β-D-laminaribioside (91). Following general procedure 13, and eluting with 90% EtOAc/hexanes the title product was obtained in 85% yield. $[\alpha]^{23}_D$ −37.0 (*c* 1); ^{1}H NMR δ 5.75−5.69 (m, 1H), 5.50−5.45 (m, 1H), 5.02 (t, *J* = 9.5 Hz, 1H), 4.97−4.90 (m, 2H), 4.86 (dd, *J* = 9.5, 8.5 Hz, 1H), 4.49 (d, *J* = 8.0 Hz, 1H), 4.31−4.28 (m, 2H), 4.20−4.16 (m, 2H), 4.14−4.09 (m, 4H), 4.02 (dd, *J* = 12.0, 2.5 Hz, 1H), 3.85 (t, *J* = 9.5 Hz, 1H), 3.67−3.64 (m, 1H), 3.59−3.52 (m, 2H), 3.45 (s, 3H), 2.13 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.06 (s, 3H), 2.06 (s, 3H), 2.01 (s, 3H); ^{13}C NMR δ 171.0, 170.8, 169.7, 169.6, 169.5, 169.1, 132.3, 127.7, 101.7, 101.4, 79.8, 78.9, 72.9, 72.1, 72.0, 71.7, 68.8, 68.6, 65.9, 62.4, 62.3, 58.5, 56.8, 21.2, 21.0, 21.0, 20.9, 20.9, 20.7; ESIHRMS calcd for $C_{29}H_{42}O_{18}Na$ $[M + Na]^+$ 701.2269, found 701.2289.

Methyl 2,2′,4,4′,6,6′-Hexa-*O*-acetyl-3′-*O*-[4-(phenyloxy-thionocarbonyloxy)but-2*Z*-enyl]-β-D-laminaribioside (92). Following general procedure 1, and eluting with 70% EtOAc/hexanes the title product was obtained in 88% yield. $[\alpha]^{23}_D$ −32.0 (*c* 1); ^{1}H NMR δ 7.43−7.40 (m, 2H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.09−7.07 (m, 2H), 5.80−5.75 (m, 1H), 5.71−5.66 (m, 1H), 5.05−5.02 (m, 3H), 4.97−4.87 (m, 3H), 4.48 (d, *J* = 8.0 Hz, 1H), 4.31−4.28 (m, 2H), 4.21−4.17 (m, 4H), 4.02 (dd, *J* = 12.5, 2.5 Hz, 1H), 3.86 (t, *J* = 9.5 Hz, 1H), 3.68−3.65 (m,1H), 2.12 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.02 (s, 3H); ^{13}C NMR δ 195.1, 171.0, 170.8, 169.5, 169.4, 169.1, 153.6, 131.8, 129.8 (2C), 126.9, 125.1, 122.1 (2C), 101.7, 101.4, 80.4, 78.8, 77.0, 72.9, 72.1, 72.0, 71.9, 69.5, 69.2, 68.6, 66.8, 62.4, 62.2, 56.8, 21.1, 21.1, 21.0, 20.9 (2C), 20.7; ESIHRMS calcd for $C_{36}H_{46}O_{19}S$-Na $[M + Na]^+$ 837.2252, found 837.2239.

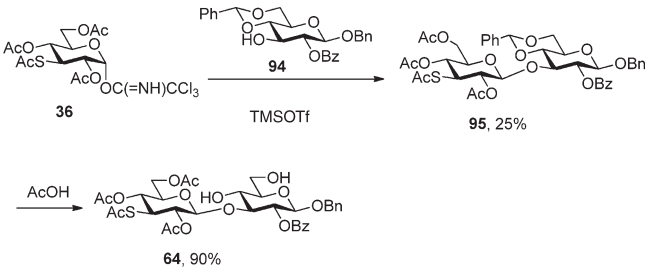
Methyl 2,2′,4,4′,6,6′-Hexa-*O*-acetyl-3′-*O*-[2-phenyloxycarbonylthioxy]but-3-enyl]-β-D-laminaribioside (93). Following general procedure 2, and eluting with 70% EtOAc/hexanes the title product was obtained as an approximately 1:1 mixture of stereoisomers in 90% yield. ^{1}H NMR δ 7.39−7.36 (m, 2H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.16−7.15 (m, 1H), 7.14−7.13 (m, 1H), 5.19 (dd, *J* = 10.0, 3.5 Hz, 1H), 4.10−5.05 (m, 1H), 4.99−4.91 (m, 3H), 4.49 (d, *J* = 8.5 Hz, 1H), 4.33−4.29 (m, 2H), 4.19−4.18 (m, 2H), 4.05−4.01 (m, 2H), 3.86 (t, *J* = 9.5 Hz, 1H), 3.82−3.77 (m, 2H), 3.47 (s, 3H), 2.13 (s, 3H), 2.11 (s, 3H), 2.09 (s, 3H × 3), 2.08 (s, 3H × 2), 2.08 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H); ^{13}C NMR δ 171.0, 171.9, 169.5, 169.4 (2C), 169.1, 151.3, 133.9, 133.8, 129.7, 126.5, 121.5, 118.8, 118.7, 101.7, 101.4, 81.0, 80.8, 78.8, 73.5, 73.4, 72.9, 72.1, 72.1, 71.9, 71.7, 69.1, 68.9, 68.6, 62.4, 62.2, 56.8, 48.9, 48.7, 21.2, 21.1, 21.0 (2C), 20.9, 20.9, 20.9 (2C), 20.7 (2C); ESIHRMS calcd for $C_{36}H_{46}O_{19}SNa$ $[M + Na]^+$ 837.2252, found 837.2224.

Methyl 3′-*O*-(2-Pyridin-2-yldithio)but-3-enyl-β-D-laminaribioside (63). Following general procedure 3, and eluting with 10% MeOH/CH_2Cl_2 the title product was obtained in 68% yield as an approximately 1.1:1 mixture of stereoisomers. ^{1}H NMR δ 8.37−8.36 (m, 1H), 7.94−7.90 (m, 2H), 7.82−7.78 (m, 1H), 7.22−7.19 (m, 1H), 5.87−5.79 (m, 1H), 5.25−5.21 (m, 1H), 5.14−5.12 (m, 1H), 4.55 (dd, *J* = 7.5, 4.5 Hz, 1H), 4.23 (dd, *J* = 7.5, 1.5 Hz, 1H), 4.12 (dd, *J* = 10.5,

Scheme 13. Preparation of the 1-Deoxymercaptolaminaribiose Precursor 65



Scheme 14. Preparation of the Laminaribiosyl-3′-thiol Precursor 64



6.0 Hz, 1H, minor), 4.08−4.07 (m, 1H), 4.03 (dd, J = 10.0, 6.0 Hz, 1H, minor), 3.90−3.86 (m, 2H), 3.80 (dd, J = 15.0, 6.5 Hz, 1H), 3.70 (dd, J = 11.5, 5.5 Hz, 1H), 3.65−3.61 (m, 1H), 3.54 (s, 3H major + 3H minor), 3.43−3.33 (m, 7H), 3.23 (t, J = 8.5 Hz, 1H); ^{13}C NMR δ 160.7, 148.8, 137.8, 134.6, 134.5, 121.0, 120.3, 118.1, 104.1, 103.7, 86.9, 85.7, 85.6, 76.8, 76.4, 74.4, 74.3, 73.7, 73.2, 69.9, 69.8, 68.8, 61.4, 61.3, 56.2, 54.9, 54.8; ESIHRMS calcd for $C_{22}H_{33}NO_{11}S_2Na$ $[M + Na]^+$ 574.1393, found 574.1385.

1-Thiohepta-*O*-acetyl-β-D-laminaribiose (65). A stirred solution of peracetyl laminaribiosyl bromide[38] (698 mg, 1.0 mmol) in acetone/water (5.0 mL) was treated with thiourea (114 mg, 1.5 mmol) and heated to reflux for 4−6 h. After cooling to room temperature the solvents were evaporated and a stirred solution of the residue in CH_2Cl_2/water (10.0 mL) was treated with sodium metabisulfite (2.0 mmol) and heated to reflux under an atmosphere of N_2 for 2−4 h. The reaction mixture was diluted with CH_2Cl_2 (10.0 mL) and washed with saturated aqueous $NaHCO_3$ (10.0 mL). The combined organic portion was dried over Na_2SO_4 and evaporated to dryness. The crude product was purified by column chromatography over silica gel 70% (EtOAc/hexanes) to give the title product as colorless oil in 65% yield (Scheme 13). $[\alpha]^{23}_D$ −18.2 (c 1); ^{1}H NMR δ 5.13 (t, J = 9.5 Hz, 1H), 5.06 (t, J = 9.5 Hz, 1H), 4.99−4.94 (m, 2H), 4.91−4.88 (m, 1H), 4.60 (d, J = 7.5 Hz, 1H), 4.42−4.36 (m, 2H), 4.19−4.12 (m, 2H), 4.03 (dd, J = 10.5, 2.0 Hz, 1H), 3.85 (t, J = 9.5 Hz, 1H), 3.70−3.66 (m, 2H), 2.29 (d, J = 10.5 Hz, 1H), 2.17 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.97 (s, 3H); ^{13}C NMR δ 170.9, 170.7, 170.6, 169.6, 169.5, 169.5, 169.4, 101.1, 80.1, 79.0, 76.6, 75.3, 73.2, 71.9, 71.3, 68.2, 68.1, 62.5, 61.8, 21.3, 21.0, 20.8, 20.7, 20.7, 20.6, 20.5; ESIHRMS calcd for $C_{26}H_{36}O_{17}SNa$ $[M + Na]^+$ 675.1571, found 675.1541.

Benzyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-2′,4′,6′-tri-*O*-acetyl-3′-acetylthio-β-D-laminaribioside (95). Following general procedure 12, benzyl 2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (**94**) was glycosylated with the trichloroacetimidate **36**. Purification was achieved by eluting from silica gel with 70% EtOAc/hexanes. The title product was obtained in 25% yield. $[\alpha]^{23}_D$ −47.7 (c 1); ^{1}H NMR (400 MHz) δ 7.99−7.97 (m, 2H), 7.64−7.60 (m, 1H), 7.51−7.45 (m, 4H), 7.35−7.33 (m, 3H), 7.21−7.16 (m, 1H), 7.14−7.12 (m, 4H), 5.57 (s, 1H), 5.35 (t, J = 10.0 Hz, 1H), 4.97 (t, J = 9.6 Hz, 1H), 4.90 (dd, J = 11.2, 7.2 Hz, 1H), 4.84 (d, J = 8.4 Hz, 1H), 4.64−4.58 (m, 3H), 4.38 (dd, J = 10.8, 4.8 Hz, 1H), 4.11−4.04 (m, 2H), 3.91−3.79 (m, 3H), 3.59 (t, J = 11.2 Hz, 1H), 3.52−3.46 (m, 2H), 2.21 (s, 3H), 1.94 (s, 3H), 1.92 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (100 MHz) δ 193.7, 169.4, 165.6, 137.4, 136.8, 133.5, 130.2, 130.0, 129.9, 129.3, 128.7, 128.6, 128.4, 128.1, 128.0, 126.3, 119.2, 102.1, 101.5, 99.8, 79.3, 79.1, 77.6, 77.3, 76.9, 74.4, 73.6, 70.6, 69.9, 68.8, 67.8, 66.8, 62.3, 47.9, 30.7, 20.9, 20.7, 20.2; ESIHRMS calcd for $C_{41}H_{44}O_{15}SNa$ $[M + Na]^+$ 831.2299, found 831.2259.

Benzyl 2-*O*-Benzoyl-2′,4′,6′-tri-*O*-acetyl-3′-acetylthio-β-D-laminaribioside (64). Compound **95** (41 mg, 0.05 mmol) was stirred in 50% aqueous AcOH (1.0 mL) at 50 °C for 4−6 h. After the solvents were evaporated the residue was purified for column chromatography over silica gel eluting with 90% EtOAc/hexanes to afford the title product in 90% yield (Scheme 14). $[\alpha]^{23}_D$ −38.7 (c 1); ^{1}H NMR (400 MHz) δ 7.99−7.97 (m, 2H), 7.64−7.61 (m, 1H), 7.51−7.47 (m, 2H), 7.19−7.14 (m, 1H), 7.12−7.11 (m, 4H), 5.25 (t, J = 11.0 Hz, 1H), 4.99−4.92 (m, 2H), 4.82−4.79 (m, 1H), 4.63−4.59 (m, 1H), 4.53 (d, J = 10.5 Hz, 2H), 4.17−4.08 (m, 2H), 3.99−3.94 (m, 1H), 3.83−3.75 (m, 4H), 3.73−3.71 (m, 1H), 3.67−3.62 (m, 2H), 3.41−3.36 (m, 1H), 2.23 (s, 3H), 2.07 (s, 3H × 2), 1.97 (s, 3H); ^{13}C NMR δ 193.4, 170.7, 169.4, 169.3, 165.1, 137.0, 133.6, 130.0, 129.8, 128.7, 128.5, 128.0, 127.9, 102.7, 99.7, 85.7, 75.8, 74.8, 72.5, 70.7, 69.9, 69.5, 67.8, 63.1, 62.3, 47.9, 30.7, 20.8, 20.6, 20.1; ESIHRMS calcd for $C_{34}H_{40}O_{15}SNa$ $[M + Na]^+$ 743.1986, found 743.1971.

Methyl 6-[4-*O*-(2,2′-Azido-2,2′-dideoxy-β-D-gentiobiosyloxy)but-2*E*-enyl]thio-2,2′-azido-2,2′-dideoxy-α-D-gentiobioside (66). Thiol precursor **56** (40 mg, 0.09 mmol) was dissolved in DMF (0.8 mL) at room temperature and hydrazine acetate (12 mg, 0.13 mmol) was added. The resulting mixture was stirred for 0.75 h and then directly transferred to a stirred solution of sulfenyl donor **53** (56 mg, 0.1 mmol) in MeOH (1 mL) at room temperature. The resulting mixture was stirred until TLC showed complete consumption of the thiol (18 h). Silver nitrate (26 mg, 0.20 mmol) was then added and the resulting mixture was stirred at room temperature, with exclusion of light, for an additional 36 h. The resulting mixture was filtered through a pad of Celite and silica gel and concentrated. Chromatographic purification eluting with CH_2Cl_2/MeOH (15:1) afforded the title compound as a white foam in 52% yield. $[\alpha]^{RT}_D$ +65.8 (c 1.0, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 5.84−5.67 (m, 2H), 4.62 (s, 2H), 5.52−4.36 (m, 5H), 4.23 (dd, J = 9.5, 12.0 Hz, 5H), 3.87 (d, J = 12.0 Hz, 2H), 3.83−3.62 (m, 5H), 3.56 (s, 3H), 3.54−3.43 (m, 5H), 3.42−3.05 (m, 15H), 2.95 (d, J = 15.0 Hz, 1H), 2.63 (q, J = 7.0 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 130.4, 128.6, 102.9, 102.6, 100.6, 77.2, 76.8, 76.1, 75.9, 75.2, 75.1, 74.8, 72.9, 70.6, 70.5, 70.3, 69.1, 69.0, 68.9, 67.0, 66.9, 61.3, 56.2, 33.9, 31.4; ESIHRMS calcd for $C_{29}H_{46}N_{12}O_{17}SNa$ $[M + Na]^+$ 889.2722, found 889.2736.

Methyl 6-[4-*O*-(2,2′-Dideoxy-2,2′-(2,2,2-trichloroethoxycarbonylamino)-β-D-gentiobiosyloxy)but-2*E*-enyl]thio-2,2′-dideoxy-(2,2,2-trichloroethoxycarbonylamino)-α-D-gentiobioside (67). Thiol precursor **61** (30 mg, 0.04 mmol) was dissolved in DMF (0.5 mL) at room temperature and hydrazine acetate (12 mg, 0.13 mmol) was added. The resulting mixture was stirred for 1.25 h and directly transferred to a stirred solution of sulfenyl donor **62** (42 mg, 0.05 mmol) in MeOH (0.8 mL). The resulting mixture was stirred until TLC showed complete consumption of the thiol compound (20 h). Triphenylphosphine (13 mg, 0.05 mmol) was then added and the resulting mixture was stirred at room temperature for an additional 40 h before it was concentrated. Purification by silica gel chromatography CH_2Cl_2/MeOH (15:1) afforded the title compound as a white foam in 54% yield. $[\alpha]^{RT}_D$ +72.6 (c 1.0, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 5.85−5.58 (m, 2H), 4.92 (d, J = 4.1 Hz, 3H), 4.93−4.86 (m, 12H), 4.85 (d, J = 4.0 Hz, 2H), 4.80 (d, J = 12.1 Hz, 2H), 4.73 (dd, J = 9.7, 12.2, 3 Hz), 4.62 (dd, J = 8.9, 11.3, 2 Hz), 4.54−4.37 (m, 2H), 4.36−4.24 (m, 2H), 4.19 (d, J = 4.0 Hz, 2H), 4.13−4.01 (m, 1H), 3.89 (d, J = 11.3, 1H), 3.77−3.59 (m, 4H),

3.53−3.18 (m, 18H), 2.96 (d, J = 13.0 Hz, 1H), 2.63 (dd, J = 5.7, 8.1 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 153.8, 153.6, 130.4,128.7, 102.8, 102.5, 100.7, 78.2, 77.7, 76.2, 75.9, 75.8, 75.3, 75.2, 74.9, 72.5, 72.3, 70.7, 70.6, 70.4, 69.2, 69.0, 68.6, 67.5, 67.3, 61.5, 56.3, 33.9, 32.2; ESIHRMS calcd for $C_{41}H_{58}Cl_{12}N_4O_{25}SNa$ $[M + Na]^+$ 1480.9271, found 1480.9316.

Benzyl 3-Deoxy-3-[4-(β-D-laminaribiosyloxy)but-2*E*-enyl-thio]-β-D-laminaribioside (68). Following general procedure 15, the title compound was obtained in 50% yield. $[\alpha]^{23}_D$ −16.0 (c 0.75, MeOH); ^{1}H NMR (CD_3OD) δ 7.44−7.42 (m, 2H), 7.36−7.32 (m, 2H), 7.29−7.27 (m, 1H), 5.88−5.83 (m, 1H), 5.76−5.71 (m, 1H), 4.94 (d, J = 12.0 Hz, 1H), 4.69 (d, J = 8.5 Hz, 1H), 4.58 (t, J = 8.0 Hz, 1H), 4.47−4.41 (m, 2H), 4.31 (dd, J = 13.0, 5.0 Hz, 1H), 4.20 (dd, J = 13.0, 7.5 Hz, 1H), 3.93−3.87 (m, 14H), 3.74−3.26 (m, 12H), 2.59 (t, J = 10.0 Hz, 1H); ^{13}C NMR (CD_3OD) δ 137.7, 131.2, 128.6, 128.2, 128.1, 127.6, 105.3, 104.2, 101.6, 100.7, 86.9, 86.8, 79.4, 76.9, 76.5, 76.4, 76.2, 74.4, 73.8, 73.4, 73.3, 72.6, 70.6, 70.4, 69.0, 68.9, 68.7, 68.4, 63.2, 61.7, 61.5, 61.4, 53.9, 33.3; ESIHRMS calcd for $C_{35}H_{54}O_{21}SNa$ $[M + Na]^+$ 865.2776, found 865.2768.

Methyl 3-*O*-[4-(1-thio-β-D-laminaribiosyl)but-2*E*-enyl]-β-D-laminaribioside (69). Following general procedure 15, the title compound was obtained in 55% yield. $[\alpha]^{23}_D$ −15.0 (c 0.75, MeOH); ^{1}H NMR (CD_3OD) δ 5.79−5.77 (m, 2H), 4.57 (d, J = 7.5, 4.0 Hz, 2H), 4.46 (d, J = 9.5 Hz, 1H), 4.36−4.35 (m, 2H), 4.24 (d, J = 7.5 Hz, 1H), 3.89 (dd, J = 7.0, 2.0 Hz, 4H), 3.72−3.67 (m, 2H), 3.66−3.62 (m, 3H), 3.58−3.53 (m, 2H), 3.54 (s, 3H), 3.52−3.47 (m, 2H), 3.45−3.21 (m, 13H); ^{13}C NMR (CD_3OD) δ 130.3, 129.1, 104.1, 104.0, 103.7, 88.3, 86.9, 83.6, 83.3, 80.2, 76.9, 76.8, 76.6, 76.4, 74.6, 74.4, 73.2, 72.5, 72.4, 70.4, 70.0, 69.0, 68.9, 61.7, 61.4, 56.1, 30.8; ESIHRMS calcd for $C_{29}H_{50}O_{21}SNa$ $[M + Na]^+$ 789.2463, found 789.2451.

4-(1-Thio-β-D-laminaribiosyl)but-2*E*-enyl β-D-laminaribioside (70). Following general procedure 15, the title compound was obtained in 55% yield. $[\alpha]^{23}_D$ −11.0 (c 0.75, MeOH); ^{1}H NMR (CD_3OD) δ 5.86−5.80 (m, 1H), 5.77−5.71 (m, 1H), 4.59 (d, J = 11.0, 7.5 Hz, 2H), 4.44−4.41 (m, 2H), 4.33 (dd, J = 12.5, 4.5 Hz, 1H), 4.20 (dd, J = 12.0, 7.5 Hz, 1H), 3.91−3.89 (m, 4H), 3.75−3.62 (m, 5H), 3.59−3.55 (m, 2H), 3.53−3.18 (m, 15H); ^{13}C NMR (CD_3OD) δ 130.2, 128.8, 104.1 (2C), 103.9, 100.9, 88.6, 87.3, 83.1, 80.2, 76.9, 76.8, 76.5, 76.4, 74.4, 74.4, 73.2, 72.4, 70.4, 69.0, 68.9, 66.5, 61.7, 61.5, 30.6; ESIHRMS calcd for $C_{28}H_{48}O_{21}SNa$ $[M + Na]^+$ 775.2306, found 775.2328.

■ ASSOCIATED CONTENT

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

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