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Sulfenic Acids in the Carbohydrate Field. An Example of Straightforward Access to Novel Multivalent Thiosaccharides

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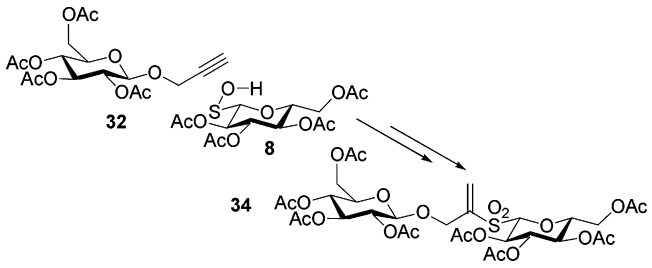

Both anomers of *O*-protected 1-thio-D-gluco- and -D-mannopyranoses were selected to provide the substrates for developing a smooth and general methodology that gives access to anomeric glycosulfoxides. The behavior of the corresponding β-D-galactopyran derivatives was also investigated. 2-{1-[(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl](1-methyl)ethyl}malonic acid diethyl esters **4** were thermolyzed in refluxing dichloromethane for generating 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose-1-sulfenic acid (**8**), in the presence of 2-propynyl β-D-glucopyranoside tetraacetate (**32**). The *syn*-addition of transient **8** onto the triple bond of **32** furnished 2-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfonyl]-2-propenyl β-D-glucopyranoside tetraacetate (**34**), after *m*-CPBA oxidation of the corresponding sulfinyl epimeric mixture **33**. This synthetic pathway appears particularly attractive since it represents an example of a mild and versatile approach to thiodisaccharides of foreseeably significant biological behavior. Various carbohydrate-derived sulfenic acids, different in glycosyl moiety and sulfenic function positioning, and various alkynylated carbohydrates can be adopted as combining units in the synthesis of alkene-linked multivalent thiosaccharides.

Introduction

Carbohydrates are among the most eclectic compounds in living systems. Their characteristics range from energy-store molecules to structural constituents of cells and tissues. Carbohydrates play a key role in several biological processes, such as signaling,[1] cell−cell communication,[2] recognition events,[2,3] etc. For accurate knowledge of carbohydrate behavior in some of these biological events, a great number of glycomimetics have been synthesized. They have received considerable attention not only as fundamental tools for biological research but also for their potentiality as agents in therapeutic intervention.[4] In this last field, carbohydrate mimetics often show a number of advantages over their parent structures: they are more resistant toward enzymatic hydrolysis and have improved availability and higher affinity and selectivity for receptors.[5] Thioglycosides are especially valuable as stable glycoside analogues and potential therapeutic compounds in the treatment of various pathologies, including cancer and infectious diseases.[6]

Recently, we described an easy methodology, starting from 1-thio-D-glucose, for generating in situ transient 1-glucosulfenic acids, which can be regarded as effective

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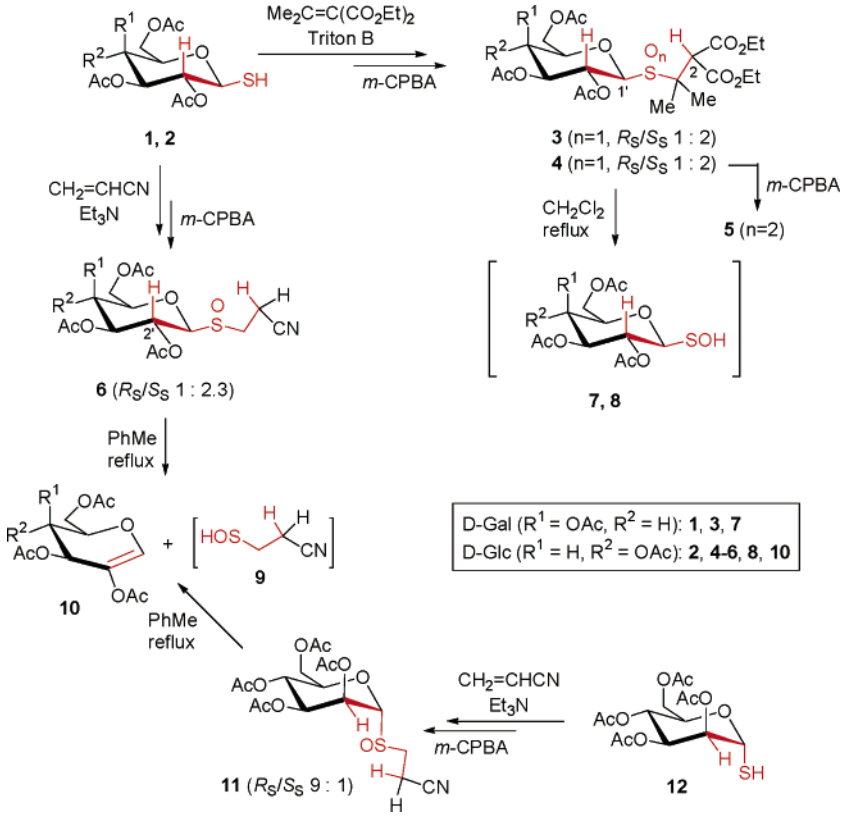
SCHEME 1. Generation of Glycosulfenic Acids 7 and 8



precursors of anomeric glucosyl sulfoxides.[7] This chemistry provides a direct synthetic strategy for the stereocontrolled connection among thioglycons and aglycons or further saccharidic moieties, thus offering the basis for an easy elaboration of new molecules incorporating thiosugar residues. 1-Glucopyranosyl sulfoxides were obtained in good yields from precursors prepared starting from 1-thio-α-D-glucopyranose, while the undesired but prevailing formation of a glucal in the thermal generation of β-D-1-glucosulfenic acid, attempted from 3-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]propanenitriles, pointed out a limitation of this synthetic strategy.

In this paper we present a significant improvement of the synthetic methodology summarized above. 1-α- and 1-β-glycosulfenic acids, to be captured by suitable acceptors, are now easily obtainable in good yields. We demonstrate the good modulation prospects of glycosulfenic acid structure offered by the methodology, through successful application to substrates different from 1-thio-D-glucose. The overall synthetic approach is applied to the preparation of a novel ethylene-linked thiodisaccharide, starting from 2-{1-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl](1-methyl)ethyl}-malonic acid diethyl esters, synthesized as suitable precursors of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose-1-sulfenic acid. At the center of this pathway there is the in situ generation of the transient sulfenic species and its *syn*-addition onto the triple bond of 2-propynyl β-D-glucopyranoside tetraacetate.[8]

Results and Discussion

Schemes 1 and 2 show the synthetic procedures adopted for preparing glycosyl sulfoxides **3**, **4**, **6**, **11**, **13**, and **16** and results obtained in their thermolysis, usually performed in toluene or dichloromethane, for the in situ generation of sulfenic acids. Glycosulfenic acids **7**, **8**, **14**, and **17** were generated in the presence of dimethyl or di-*tert*-butyl acetylenedicarboxylate (ADC), and their *syn*-addition products, prepared as models of more complex glycoconjugates, are reported in Table 1. In the same table the results of the already described reaction between 1-α-D-glucosulfenic acid **18** and ADC are also shown.[7] Both anomers of 1-thio-D-gluco- and -D-mannopyranose tetraacetates have been selected to provide the substrates for developing a general methodology that gives access to anomeric glycosyl sulfoxides. The behavior of the corresponding β-D-galactopyranose derivatives has also been investigated.

Glycosyl sulfoxides **3**, **4, 11**, and **13** were prepared in 59−85% yields (Schemes 1 and 2) through base-catalyzed Michael addition of the corresponding 1-thio-D-glycopyranoses to either acrylonitrile or diethyl isopropyl-

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SCHEME 2. Generation of Mannosulfenic Acids 14 and 17

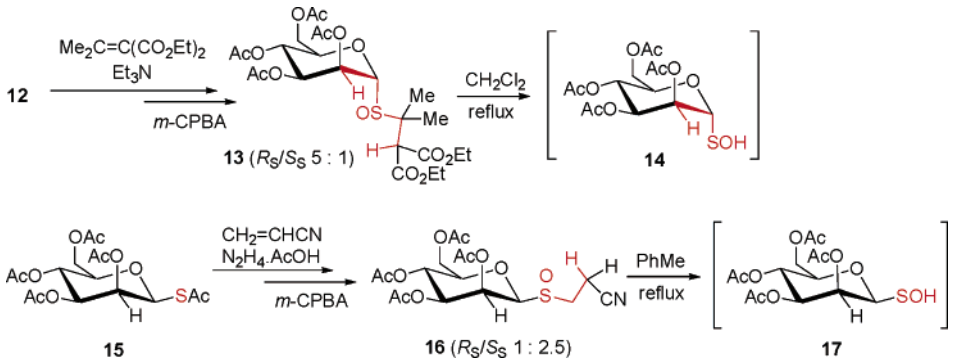
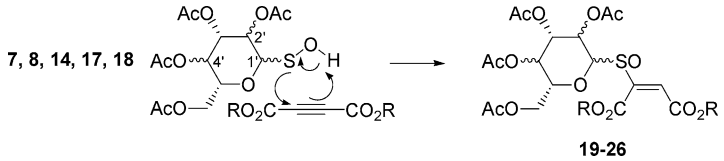


TABLE 1. Glycosulfenic Acids 7, 8, 14, 17, and 18, Thermally Generated in the Presence of ADC, and Their *syn*-Addition Products 19–26



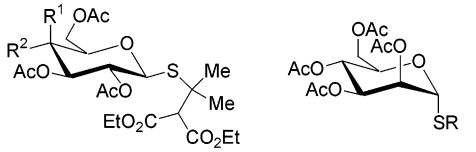
compd	sugar family	C-1	C-2	C-4	R	R_S:S_S
7	D-Gal	b	*R*	*S*		
19	D-Gal	b	*R*	*S*	*t*-Bu	1:1.5
18[7]	D-Glc	a	*R*	*R*		
20[7]	D-Glc	a	*R*	*R*	Me	2:1
21[7]	D-Glc	a	*R*	*R*	*t*-Bu	3:1
8	D-Glc	b	*R*	*R*		
22	D-Glc	b	*R*	*R*	Me	1:4.2
23	D-Glc	b	*R*	*R*	*t*-Bu	1:3.8
14	D-Man	a	*S*	*R*		
24	D-Man	a	*S*	*R*	Me	1.5:1
25	D-Man	a	*S*	*R*	*t*-Bu	1.2:1
17	D-Man	b	*S*	*R*		
26	D-Man	b	*S*	*R*	Me	1:1.4

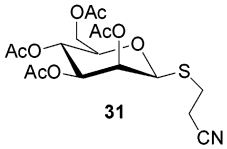
idenemalonate, followed by *m*-CPBA oxidation of the resulting thioglycosides **27**–**30**, respectively.[9] 3-[(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)thio]propanenitrile, the previously described[7,10] precursor of **6** (Scheme 1), can be easily obtained from the corresponding thiol, following the protocol reported in the Experimental Section for the preparation of 3-[(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)thio]propanenitrile (**29**), the precursor of **11** (Scheme 1). 3-[(2,3,4,6-Tetra-*O*-acetyl-*β*-D-mannopyranosyl)thio]propanenitrile (**31**),[9] the precursor of **16** (Scheme 2), was synthesized from 1-thio-*β*-D-mannopyranose pentaacetate (**15**).[11] The latter starting material was preferred to 1-thio-*β*-D-mannopyranose 2,3,4,6-tetraacetate, because this last thiol was only described as a minor product in an anomeric mixture of thiols obtained from the corresponding α-mannosyl bromide.[12] Alternatively, Szilágyi reported the preparation of 1-thio-*β*-D-mannopyranose 2,3,4,6-tetraacetate by chemoselective *S*-deacetylation of **15**.[13]

The diastereomeric ratios of the obtained *S*-epimeric mixtures of glycosyl sulfoxides **3**, **4**, **11**, **13**, and **16** were established from ^{1}H NMR parameters of the crude reaction products, while the *S*-configurations were assigned on the basis of previous results.[14]

As shown in Scheme 1, not all the thermolyses of glycosyl sulfoxides led to the desired 1-glycosulfenic acids.

(9) Formulas of sulfides **27**–**31**, precursors of sulfoxides **3**, **4**, **11**, **13**, and **16**, respectively, are omitted for simplicity in Schemes 1 and 2, but their complete characterization is reported in the Experimental Section.





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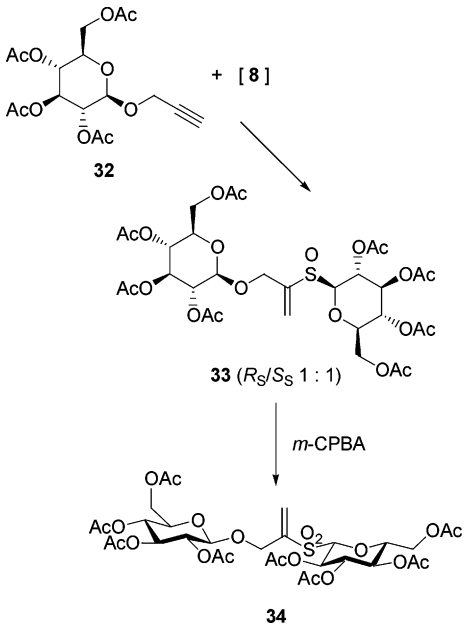
When (β-D-glucopyranosylsulfinyl)- and (α-D-mannopyranosylsulfinyl)propanenitriles **6** and **11**, both showing a *cis*-relationship between the anomeric sulfur and hydrogen atom at C-2′, were heated in the presence of ADC, the formation of 2-cyanoethanesulfenic acid (**9**) was always indirectly observed and glucal **10** was produced (Scheme 1).[15] The presence of a highly and suitably substituted alkyl group such as the 1,1-diethoxycarbonyl-2-methylprop-2-yl residue[15b] in the glycosyl derivatives **3** and **4** (Scheme 1) and **13** (Scheme 2) enabled the generation of sulfenic acids **7**, **8**, and **14** (Table 1), which retain the corresponding glycosyl residues.

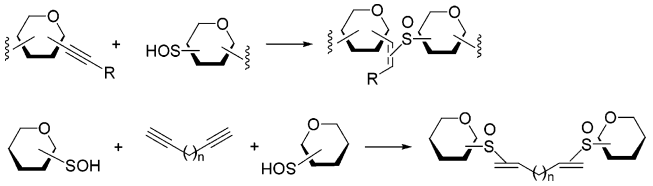
The synthetic pathways in Scheme 2, starting from D-mannopyranosyl derivatives **12** and **15**, can be regarded as illustrative of the rationale for generating both 1-α- and 1-β-glycosulfenic acids. A mutual *cis*-arrangement of the anomeric sulfur and the vicinal endocyclic hydrogen atom, as appearing in thiol **12**, requires the use of diester sulfoxide mixture **13** for generating the corresponding sulfenic acid **14** at low temperature (40 °C, reflux, CH_2Cl_2), while a *trans*-disposition of sulfur/β-hydrogen, as observed in **15**, allows the use of the cyanoethyl sulfoxide mixture **16**, which undergoes thermolysis in refluxing toluene. In our experience the presence of a 1,1-diethoxycarbonyl-2-methylprop-2-yl residue appears essential whenever the glycosyl sulfoxides show an evident problem of chemoselection in the sulfenic acid generation, due to the presence of two different *syn*-β-hydrogens with respect to the SO group. The sulfoxide thermolysis occurs at 40 °C when two β electron-withdrawing groups and two α-methyl substituents are present as in **13**, and complete chemoselectivity in favor of glycosulfenic acid generation is observed. An analogous behavior was previously reported and discussed in detail.[15b] On the other hand, the glycosylsulfinyl diesters such as **3**, **4**, and **13** must be handled with caution: they cannot be kept on the bench or even stored in the ice box for a long time, since they easily undergo spontaneous elimination, ultimately leading to undesirable mixtures of thiosulfinates and disulfides. (Glycosylsulfinyl)propanenitriles, such as **6**, **11**, and **16**, are more stable, and their use must be preferred on those occasions when only one pathway of sulfenic acid *syn*-elimination is possible. For clarity of presentation in Schemes 1 and 2, atom labels and bonds of the structural moieties that can be involved in *syn*-eliminations are drawn in red.

Many naturally occurring important molecules involve two sugar units, connected to each other by more than one atom.[4a] We envisaged that the reaction shown in Scheme 3 could represent an example of a multivalent approach (Scheme 4) to thiooligosaccharides of foreseeably significant biological behavior. 2-Propynyl β-D-glucopyranoside tetraacetate (**32**)[8] was used as an acceptor of glucosulfenic acid **8**, generated in situ from **4** in refluxing dichloromethane. The 1:1 epimeric mixture of pseudodisaccharidic sulfoxides **33** was obtained in 45% yield and quantitatively oxidized to the corresponding sulfone **34**. The NMR data of disaccharide **34** were fully assigned mainly on the basis of homodecoupling proton

SCHEME 3. Synthesis of Pseudo-Disaccharide 34



SCHEME 4. Schematic Representation of Some Possibilities of Multivalent Thiosaccharide Synthesis via Transient Glycosulfenic Acids



experiments and some typical spectral characteristics such as, for instance, the $J_{1,2}$ of the monosaccharide moiety, greater in the 1-thio-β-D-saccharide residue. The comparison with the NMR data of sulfone **5** (Scheme 1) and alkynyl glucoside **32** (Scheme 3) was also taken into account (see the Experimental Section).

Conclusion

In this paper we have shown, for the first time, how 1-glycosulfenic acids, such as transient species **8**, can be easily used as building blocks in the synthesis of thiooligosaccharides. In particular, we have reported the synthesis of the ethylene-linked thiodisaccharide **34**. The generation of glycosulfenic acids by a simple thermolysis, at temperatures depending on the chosen sulfoxide precursors, and their in situ *syn*-addition to propynyl glycosides do not imply acidic or basic conditions and thus allow the use of any protecting group or the presence of any reactive functional residue in the sugar rings. The sulfoxide moiety, resulting from sulfenic acid addition, can be easily reduced to a sulfide or oxidized to a sulfone group, as shown in the formation of thiodisaccharide **34**, or even transformed into other functional groups. The different oxidation states of the sulfur atom in thiosugars have been related to their biological activity.[6c] Finally, we have demonstrated the effectiveness of a synthetic strategy which appears particularly attractive since several glycosulfenic acids and alkynyl glycosides[16] can be adopted as combining units. Even dialkynyl linkers

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of different lengths and flexibilities can be involved in the synthesis of alkene-linked thiosaccharides as designed in Scheme 4, affording the possibility of developing a library of multivalent thiocarbohydrates. The availability of transient glycosulfenic acids is not restricted to the anomeric ones. A suitably designed alkylsulfinyl group, placed in any position of the pyranose or furanose ring, can undergo thermolysis to the required glycosulfenic acid provided that at least one mobile enough hydrogen atom is available *β-syn* with respect to the sulfoxide function.

Experimental Section

General Methods. Melting points were determined on a microscopic apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$ solutions. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively (unless otherwise stated), in $CDCl_3$ solutions with TMS as internal standard. *J* values are given in hertz. The NMR assignments are supported by the attached proton test (APT), homodecoupling, and homo- and heterocorrelation experiments: protons and carbon nuclei marked with a slanted prime pertain to thiomonosaccharide moieties. IR spectra were taken for neat oils with an FT spectrophotometer. Mass spectra were measured by FAB (*m*-nitrobenzyl alcohol as matrix) or IS (MeOH/H_2O as solvent). All reactions were monitored by TLC on commercially available precoated plates (silica gel 60 F 254), and the products were visualized with acidic vanillin solution. Silica gel 60, 230−400 mesh, was used for column chromatography. Petrol refers to light petroleum, bp 30−40 °C. Thiol **2** is commercially available. Compounds **1**,[17] **6**, **10**, **18**, **20**, and **21**,[7] **12**,[17,18] **15**,[11] and **32**[8] were previously described.

General Procedure for the Conversion of D-Glycopyranosyl Thiols 1, 2, and 12 into 2-[(1-D-Glycopyranosylthio)(1-methyl)ethyl]malonic Acid Diethyl Esters 27, 28, and 30, Precursors of Sulfoxides 3, 4, and 13, Respectively. Benzyltrimethylammonium hydroxide (Triton B; 0.0152 mL, 40 wt % solution in MeOH, 0.03 mmol) was added to a stirred solution of the thiol (1.37 mmol) in dry THF (5 mL) at −78 °C. After 10 min diethyl isopropylidenemalonate (1.37 g, 6.85 mmol) was added, and the reaction mixture was allowed to warm spontaneously to room temperature and maintained at room temperature overnight under stirring. The solvent was then removed in vacuo and the crude residue purified by column chromatography using petrol/EtOAc (4:1) as eluant.

General Procedure for the *m*-CPBA Oxidation of Thioglycosides 27−31 to the Corresponding Sulfoxides 3, 4, 11, 13, and 16. This reaction was performed according to the previously described protocol,[19] to convert the enantiopure thioglycoside into an *S*-epimeric mixture of sulfoxides in almost quantitative total yield.

General Procedure for the Thermolysis of 2-[(1-D-Glycopyranosylsulfinyl)(1-methyl)ethyl]malonic Acid Diethyl Esters 3, 4, and 13 in the Presence of Dimethyl or Di-*tert*-butyl Acetylenedicarboxylate. A solution of sulfoxides (*S*-epimeric mixture, 0.15 mmol) and ADC (0.80 mmol) in CH_2Cl_2 (3 mL) was refluxed overnight. The solvent was then removed under reduced pressure and the crude mixture of products separated by column chromatography.

General Procedure for the Thermolysis of 3-[(2,3,4,6-Tetra-*O*-acetyl-D-mannopyranosyl)sulfinyl]propanenitriles 11 and 16 in the Presence of Dimethyl Acetylenedicarboxylate. A solution of sulfoxides (*S*-epimeric mixture, 0.16 mmol) and dimethyl-ADC (0.06 mL, 0.49 mmol) in toluene (3 mL) was refluxed for about 2 h. The solvent was then removed under reduced pressure and the crude mixture of products separated by column chromatography.

***β*-D-Galactopyranose Derivatives. 2-{1-[(2,3,4,6-Tetra-*O*-acetyl-*β*-D-galactopyranosyl)thio]-(1-methyl)ethyl}-malonic Acid Diethyl Ester (27), the Precursor of Sulfoxides 3.** The thiogalactoside **27** was obtained (80%) from 1-thio-*β*-D-galactopyranose 2,3,4,6-tetraacetate (**1**)[17] as a pale yellow oil: $[\alpha]^{20}_D$ +2.1 (*c* 18.93); ^1H NMR *δ* 5.44 (dd, $J_{3',4'}$ = 3.3, $J_{4',5'}$ = 1.2, H-4′), 5.17 (t, $J_{1',2'} = J_{2',3'}$ = 9.7, H-2′), 5.08 (dd, H-3′), 4.88 (d, H-1′), 4.3−4.0 (m, H_2-6′, 2 × OCH_2), 3.96 (ddd, $J_{5',6'}$ = 7.2 and 5.8, H-5′), 3.76 (s, H-2), 2.16, 2.05, and 1.99 [3 s, 4 × C(O)Me], 1.64 and 1.59 (2 s, CMe_2), 1.29 (t, J_{vic} = 7.1, 2 × CH_2*Me*); ^{13}C NMR *δ* 170.3, 170.2, 169.9, and 169.3 [4 × *C*(O)Me], 166.8 and 166.7 (C-1,3), 82.2 (C-1′), 74.1, 71.9, 66.9, and 67.2 (C-2′,3′,4′,5′), 61.8, 61.3, and 61.2 (C-6′, 2 × OCH_2), 61.3 (C-2), 47.0 (*C*Me_2), 27.8 and 26.7 (C*Me*$_2$), 20.7, 20.6, 20.50, and 20.46 [4 × C(O)*Me*], 13.9 (2 × CH_2*Me*); MS/FAB *m/z* (rel intens) 565 (M + 1, 21), 331 (100), 201 (17), 169 (43). Anal. Calcd for $C_{24}H_{36}O_{13}S$: C, 51.05; H, 6.43. Found: C, 50.98; H, 6.49.

***m*-CPBA Oxidation of 2-{1-[(2,3,4,6-Tetra-*O*-acetyl-*β*-D-galactopyranosyl)thio](1-methyl)ethyl}malonic Acid Diethyl Ester (27).** An oily mixture of 2-{1-[(2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl)sulfinyl]-(1-methyl)ethyl}-malonic acid diethyl esters **3** (R_S:S_S = 1:2) was obtained: ^1H NMR *δ* 5.78 [t, $J_{1',2'} = J_{2',3'}$ = 9.9, H-2′ of major (S_S) epimer], 5.65 [t, $J_{1',2'} = J_{2',3'}$ = 10.1, H-2′ of minor (R_S) epimer], 5.45 (m, H-4′), 5.16 [dd, $J_{3',4'}$ = 3.5, H-3′ of minor (R_S) epimer], 5.10 [dd, $J_{3',4'}$ = 3.4, H-3′ of major (S_S) epimer], 4.49 [d, H-1′ of minor (R_S) epimer], 4.39 [d, H-1′ of major (S_S) epimer], 4.3−4.0 (m, H-5′, H_2-6′, 2 × OCH_2), 3.96 [s, H-2 of major (S_S) epimer], 3.89 [s, H-2 of minor (R_S) epimer], 2.18, 2.07, and 1.996 [3 s, 4 × C(O)Me of minor (R_S) epimer], 2.17, 2.05, 2.04, and 1.998 [4 s, 4 × C(O)Me of major (S_S) epimer], 1.61, 1.55, 1.53, and 1.51 (4 s, CMe_2 of both epimers), 1.28 (m, 2 × CH_2*Me*). The mixture **3** was used in the next synthetic step without further purification.

Thermolysis of 2-{1-[(2,3,4,6-Tetra-*O*-acetyl-*β*-D-galactopyranosyl)sulfinyl](1-methyl)ethyl}malonic Acid Diethyl Esters 3 in the Presence of Di-*tert*-butyl Acetylenedicarboxylate. An oily mixture of sulfoxides **19** (65% total yield, R_S:S_S = 1:1.5) was obtained. By column chromatography (petrol/EtOAc (4:1) as eluant) the minor epimer (R_S,*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl)sulfinyl]but-2-enedioic acid di-*tert*-butyl ester ((R_S)-**19**) [^1H NMR *δ* 6.65 (s, H-3), 5.62 (t, $J_{1',2'} = J_{2',3'}$ = 9.7, H-2′), 5.38 (dd, $J_{3',4'}$ = 3.4, $J_{4',5'}$ = 1.0, H-4′), 5.13 (dd, H-3′), 4.66 (d, H-1′), 4.2−4.0 (m, H-5′, H_2-6′), 2.15, 2.03, 1.98, and 1.96 [4 s, 4 × C(O)Me], 1.52 and 1.48 (2 s, 2 × CMe_3)] was always obtained in an admixture with the major, less mobile (S_S,*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl)sulfinyl]but-2-enedioic acid di-*tert*-butyl ester ((S_S)-**19**), the latter isolated as an oil: $[\alpha]^{21}_D$ −32.2 (*c* 10.97); ^1H NMR *δ* 6.77 (s, H-3), 5.59 (t, $J_{1',2'} = J_{2',3'}$ = 10.0, H-2′), 5.40 (dd, $J_{3',4'}$ = 3.4, $J_{4',5'}$ = 1.1, H-4′), 5.17 (dd, H-3′), 4.46 (d, H-1′), 4.11 (AB dd, $J_{5',6'A}$ = 7.3, $J_{6'A,6'B}$ = 11.4, H_A-6′), 4.07 (AB dd, $J_{5',6'B}$ = 5.8, H_B-6′), 3.95 (ddd, H-5′), 2.15, 2.09, 2.01, and 1.98 [4 s, 4 × C(O)Me], 1.51 and 1.50 (2 s, 2 × CMe_3); ^{13}C NMR *δ* 170.3, 170.2, 170.0, and 168.6 [4 × *C*(O)Me], 162.8 and 160.2 (C-1,4), 141.4 (C-2), 134.0 (C-3), 88.2 (C-1′), 84.5 and 83.0 (2 × *C*Me_3), 75.7, 72.0, 66.8, and 64.3 (C-2′,3′,4′,5′), 61.0 (C-6′), 28.0 and 27.9 (2 × C*Me*$_3$), 20.6, 20.54, and 20.47 [4 × C(O)*Me*]; IR ν_{max} 1725 (CO), 1371, 1315, 1220, 1146, 1059, 759 cm^{-1}; MS/FAB *m/z* (rel intens) 607 (M + 1, <1), 331 (100),

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169 (45), 57 (58), 43 (47). Anal. Calcd for $C_{26}H_{38}O_{14}S$: C, 51.48; H, 6.31. Found: C, 51.37; H, 6.32.

β-D-Glucopyranose Derivatives. 2-{1-[(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)thio](1-methyl)ethyl}-malonic Acid Diethyl Ester (28), the Precursor of Sulfoxides 4. From commercial 1-thio-β-D-glucopyranose 2,3,4,6-tetraacetate (**2**) the thioglucoside **28** was obtained (85%) as a pale yellow oil: $[\alpha]^{24}_D$ −8.5 (*c* 12.45); ^{1}H NMR δ 5.20 (dd, $J_{2',3'}$ = 9.0, $J_{3',4'}$ = 9.1, H-3′), 4.96 (dd, $J_{4',5'}$ = 9.7, H-4′), 4.88 (dd, $J_{1',2'}$ = 9.7, H-2′), 4.83 (d, H-1′), 4.2−4.0 (m, H_2-6′, 2 × OCH_2), 3.71 (s, H-2), 3.70 (m, H-5′), 2.02, 1.982, 1.978, and 1.95 [4 s, 4 × C(O)Me], 1.57 and 1.52 (2 s, CMe_2), 1.223 and 1.216 (2 t, J_{vic} = 7.1, 2 × CH_2*Me*); ^{13}C NMR δ 170.7, 170.3, 169.5, and 169.4 [4 × *C*(O)Me], 167.02 and 166.96 (C-1,3), 81.7 (C-1′), 75.4, 73.9, 69.9, and 68.5 (C-2′,3′,4′,5′), 62.5, 61.3, and 61.2 (C-6′, 2 × OCH_2), 61.4 (C-2), 47.0 (C-1′), 27.8 and 26.6 (CMe_2), 20.53 and 20.46 [4 × C(O)*Me*], 13.9 (2 × CH_2*Me*). Anal. Calcd for $C_{24}H_{36}O_{13}S$: C, 51.05; H, 6.43. Found: C, 50.88; H, 6.33.

***m*-CPBA Oxidation of 2-{1-[(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)thio](1-methyl)ethyl}malonic Acid Diethyl Ester (28).** An oily mixture of 2-{1-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl](1-methyl)ethyl}malonic acid diethyl esters **4** (R_S:S_S = 1:2) was obtained: ^{1}H NMR δ 5.6−5.0 (m, H-2′,3′,4′), 4.58 [d, $J_{1',2'}$ = 9.9, H-1′ of minor (R_S) epimer], 4.43 [d, $J_{1',2'}$ = 9.7, H-1′ of major (S_S) epimer], 4.3−4.1 (m, H_2-6′, 2 × OCH_2), 3.96 [s, H-2 of major (S_S) epimer], 3.90 [s, H-2 of minor (R_S) epimer], 3.79 (m, H-5′), 2.1−2.0 [m, 4 × C(O)Me], 1.6−1.5 (m, CMe_2), 1.29 (m, 2 × CH_2*Me*). The mixture **4** was used in the next synthetic step without further purification.

2-{1-[(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)sulfonyl]-(1-methyl)ethyl}malonic Acid Diethyl Ester (5). The conversion of sulfoxides **4** into sulfone **5** was performed according to the protocol previously described[19] for the oxidation of sulfides to sulfoxides. Sulfone **5** was obtained in almost quantitative yield as a low-melting-point solid not needing purification: ^{1}H NMR δ 5.57 (dd, $J_{1',2'}$ = 9.5, $J_{2',3'}$ = 9.3, H-2′), 5.31 (dd, $J_{3',4'}$ = 9.5, H-3′), 5.12 (d, H-1′), 5.02 (dd, $J_{4',5'}$ = 9.9, H-4′), 4.3−4.1 (m, H_A-6′, 2 × OCH_2), 4.10 (AB dd, $J_{5',6'B}$ = 6.4, $J_{6'A,6'B}$ = 12.6, H_B-6′), 4.04 (s, H-2), 3.85 (ddd, $J_{5',6'A}$ = 2.3, H-5′), 2.05, 2.03, 2.00, and 1.99 [4 s, 4 × C(O)Me], 1.71 and 1.64 (2 s, CMe_2), 1.27 and 1.26 (2 t, J_{vic} 7.2, 2 × CH_2*Me*); ^{13}C NMR δ 170.3, 170.1, 169.2, and 168.8 [4 × *C*(O)Me], 166.1 and 166.0 (C-1,3), 87.5 (C-1′), 76.2, 73.3, 67.5, and 66.5 (C-2′,3′,4′,5′), 67.6, 62.2, and 62.0 (C-6′, 2 × OCH_2), 55.1 (C-2), 20.53, 20.49, 20.0, and 19.7 [C*Me*$_2$ and 4 × C(O)*Me*], 20.4 (CMe_2), 13.9 and 13.8 (2 × CH_2*Me*). Anal. Calcd for $C_{24}H_{36}O_{15}S$: C, 48.32; H, 6.08. Found: C, 48.41; H, 6.06.

Thermolysis of 2-{1-[(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl](1-methyl)ethyl}malonic Acid Diethyl Esters 4 in the Presence of Dimethyl Acetylenedicarboxylate. By column chromatography, eluting with petrol/EtOAc (2.3:1), (R_S,*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]but-2-enedioic acid dimethyl ester ((R_S)-**22**) was first isolated as an oil (9%): ^{1}H NMR δ 6.87 (s, H-3), 5.45 (dd, $J_{2',3'}$ = 9.7, $J_{3',4'}$ = 9.3, H-3′), 5.29 (dd, $J_{4',5'}$ = 9.2, H-4′), 5.10 (t, $J_{1',2'}$ = 9.7, H-2′), 4.66 (d, H-1′), 4.3−4.1 (m, H_2-6′), 3.89 and 3.83 (2 s, 2 × OMe), 3.80 (m, H-5′), 2.10, 2.03, 2.01, and 1.99 [4 s, 4 × C(O)Me]. Anal. Calcd for $C_{20}H_{26}O_{14}S$: C, 45.98; H, 5.02. Found: C, 45.81; H, 5.04. The major epimer (S_S,*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]but-2-enedioic acid dimethyl ester ((S_S)-**22**) was then eluted as an oil (38%): ^{1}H NMR δ 6.89 (s, H-3), 5.39 (dd, $J_{3',4'}$ = 9.2, $J_{4',5'}$ = 9.3, H-4′), 5.32 (t, $J_{2',3'}$ = 9.2, H-3′), 5.04 (dd, $J_{1',2'}$ = 9.4, H-2′), 4.55 (d, H-1′), 4.15 (AB dd, $J_{5',6'A}$ = 6.0, $J_{6'A,6'B}$ = 12.7, H_A-6′), 4.07 (AB dd, $J_{5',6'B}$ = 2.4, H_B-6′), 3.85 and 3.83 (2 s, 2 × OMe), 3.73 (m, H-5′), 2.08, 2.03, and 2.01 [3 s, 4 × C(O)Me]; ^{13}C NMR δ 170.7, 170.5, 169.2, and 168.8 [4 × *C*(O)Me], 164.3 and 162.0 (C-1,4), 142.5 (C-2), 132.9 (C-3), 87.8 (C-1′), 76.9, 73.7, 67.7, and 66.9 (C-2′,3′,4′,5′), 61.8 (C-6′), 53.2 and 52.6 (2 × OMe), 20.41 and 20.37 [4 × C(O)*Me*]. Anal. Calcd for $C_{20}H_{26}O_{14}S$: C, 45.98; H, 5.02. Found: C, 46.08; H, 5.25.

Thermolysis of 2-{1-[(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]-(1-methyl)ethyl}malonic Acid Diethyl Esters 4 in the Presence of Di-*tert*-butyl Acetylenedicarboxylate. By column chromatography, eluting with petrol/EtOAc (4:1), (R_S,*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]but-2-enedioic acid di-*tert*-butyl ester ((R_S)-**23**) was first isolated as an oil (17%): $[\alpha]^{26}_D$ −11.2 (*c* 5.47); ^{1}H NMR δ 6.68 (s, H-3), 5.46 (dd, $J_{2',3'}$ = 9.5, $J_{3',4'}$ = 9.2, H-3′), 5.31 (dd, $J_{4',5'}$ = 9.4, H-4′), 5.11 (dd, $J_{1',2'}$ = 9.6, H-2′), 4.78 (d, H-1′), 4.26 (AB dd, $J_{5',6'A}$ = 5.0, $J_{6'A,6'B}$ = 12.5, H_A-6′), 4.16 (AB dd, $J_{5',6'B}$ = 2.2, H_B-6′), 3.80 (ddd, H-5′), 2.09, 2.03, 2.01, and 1.99 [4 s, 4 × C(O)Me], 1.55 and 1.51 (2 s, 2 × CMe_3); ^{13}C NMR δ 170.7, 170.5, 169.2, and 169.0 [4 × *C*(O)Me], 163.0 and 160.1 (C-1,4), 142.7 (C-2), 132.7 (C-3), 91.1 (C-1′), 85.0 and 83.5 (2 × *C*Me$_3$), 76.8, 74.1, 67.1, and 65.1 (C-2′,3′,4′,5′), 61.7 (C-6′), 27.90 and 27.88 (2 × C*Me*$_3$), 20.6, 20.5, 20.4, and 20.3 [4 × C(O)*Me*]. Anal. Calcd for $C_{26}H_{38}O_{14}S$: C, 51.48; H, 6.31. Found: C 51.17, H 6.34. Then the major epimer (S_S,*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]but-2-enedioic acid di-*tert*-butyl ester ((S_S)-**23**) was eluted as an oil (64%): $[\alpha]^{27}_D$ −34.9 (*c* 6.88); ^{1}H NMR δ 6.77 (s, H-3), 5.39 (dd, $J_{3',4'}$ = 9.1, $J_{4',5'}$ = 9.5, H-4′), 5.35 (dd, $J_{2',3'}$ = 9.3, H-3′), 5.08 (dd, $J_{1',2'}$ = 9.7, H-2′), 4.56 (br d, H-1′), 4.19 (AB dd, $J_{5',6'A}$ = 6.0, $J_{6'A,6'B}$ = 12.4, H_A-6′), 4.09 (AB dd, $J_{5',6'B}$ = 2.5, H_B-6′), 3.73 (ddd, H-5′), 2.10, 2.07, 2.032, and 2.029 [4 s, 4 × C(O)Me], 1.53 and 1.52 (2 s, 2 × CMe_3); ^{13}C NMR δ 170.5, 170.3, 169.0, and 168.6 [4 × *C*(O)Me], 162.7 and 159.9 (C-1,4), 140.9 (C-2), 134.1 (C-3), 87.6 (C-1′), 84.5 and 82.9 (2 × *C*Me$_3$), 76.7, 73.7, 67.8, and 66.9 (C-2′,3′,4′,5′), 61.8 (C-6′), 27.90 and 27.86 (2 × C*Me*$_3$), 20.5, 20.42, and 20.38 [4 × C(O)*Me*]. Anal. Calcd for $C_{26}H_{38}O_{14}S$: C, 51.48; H, 6.31. Found: C, 51.67; H, 6.37.

2-[(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)sulfonyl]-2-propenyl β-D-Glucopyranoside Tetraacetate (34). A solution of sulfoxides **4** (*S*-epimeric mixture, 87 mg, 0.15 mmol) and 2-propynyl β-D-glucopyranoside tetraacetate (**32**)[8,20] (309 mg, 0.80 mmol) in CH_2Cl_2 (3 mL) was refluxed overnight. After removal of the solvent under reduced pressure, the crude mixture was purified by column chromatography eluting with petrol/EtOAc (1:4). The total yield of 2-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]-2-propenyl β-D-glucopyranoside tetraacetates **33** was 45%, R_S:S_S = 1:1, isolated as a low-melting-point solid. This sulfoxide mixture, not separable by further column chromatography, was oxidized with *m*-CPBA, according to the previously described protocol.[19] The sulfone **34** was obtained in quantitative yield as a low-melting-point solid not needing purification: $[\alpha]^{24}_D$ −14.3 (*c* 13.10); ^{1}H NMR δ 6.36 and 6.24 (2 s, C=CH_2), 5.47 (dd, $J_{1',2'}$ = 9.5, $J_{2',3'}$ = 9.4, H-2′), 5.37 (dd, $J_{3',4'}$ = 9.3, H-3′), 5.21 (t, $J_{2,3}$ = $J_{3,4}$ = 9.5, H-3), 5.1−5.0 (m, H-2,4,4′), 4.60 and 4.39 (AB system, J_{gem} = 12.5, CH_2C=CH_2), 4.57 (d, $J_{1,2}$ = 7.7, H-1), 4.44 (d, H-1′), 4.28 (AB dd, $J_{5,6A}$ = 4.5, $J_{6A,6B}$ = 12.4, H_A-6), 4.19 (AB dd, $J_{5',6'A}$ = 4.8, $J_{6'A,6'B}$ = 12.5, H_A-6′), 4.14 (AB dd, $J_{5',6'B}$ = 2.6, H_B-6′), 4.10 (AB dd, $J_{5,6B}$ = 2.3, H_B-6), 3.82 (ddd, $J_{4',5'}$ = 10.0, H-5′), 3.71 (ddd, $J_{4,5}$ = 9.9, H-5), 2.13, 2.06, 2.04, 2.012, 2.009, 2.00, 1.99, and 1.98 [8 s, 8 × C(O)Me]; ^{13}C NMR δ 170.4, 170.2, 170.02, 169.96, 169.3, 169.2, and 168.8 [8 × *C*(O)Me], 142.0 (O_2SC=CH_2), 133.2 (O_2SC=CH_2), 100.1 (C-1), 88.1 (C-1′), 76.0, 73.1, 72.5, 71.9, 71.1, 68.1, 67.5, and 66.4 (C-2,2′,3,3′,4,4′,5,5′), 67.3 (CH_2C=CH_2), 61.6 and 61.2 (C-6,6′), 20.7, 20.6, 20.55, 20.47, and 20.4 [8 × C(O)*Me*]. Anal. Calcd for $C_{31}H_{42}O_{21}S$: C, 47.57; H, 5.41. Found: C, 47.87; H, 5.58.

D-Mannopyranose Derivatives. 2-{1-[(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)thio](1-methyl)ethyl}-malonic Acid Diethyl Ester (30), the Precursor of Sulfoxides 13. From 1-thio-α-D-mannopyranose 2,3,4,6-tetraacetate (**12**)[17,18] the thiomannoside **30** was obtained (75%) as

(20) ^{13}C NMR of **32**: δ 170.6, 170.2, and 169.4 [4 × *C*(O)Me], 98.1 (C-1), 78.1 (*C*≡CH), 75.4 (C≡*C*H), 72.7, 71.9, 70.9, and 68.3 (C-2,3,4,5), 61.7 (C-6), 55.9 (*C*H_2C≡CH), 20.7 and 20.6 [4 × C(O)*Me*].

a pale yellow oil: $[\alpha]^{21}_D$ +53.7 (*c* 9.16); ^{1}H NMR δ 5.53 (br s, H-1′), 5.3−5.1 (m, H-2′,3′,4′), 4.40 (m, H-5′), 4.3−4.0 (m, H_2-6′, 2 × OCH_2), 3.72 (s, H-2), 2.13, 2.04, 2.00, and 1.93 [4 s, 4 × C(O)Me], 1.59 and 1.57 (2 s, CMe_2), 1.23 (m, 2 × CH_2*Me*); ^{13}C NMR δ 170.4, 169.7, and 169.5 [4 × *C*(O)Me], 166.6 and 166.5 (C-1,3), 80.4 (C-1′), 71.4, 69.5, 69.1, and 66.0 (C-2′,3′,4′,5′), 62.2, 61.4, and 61.3 (C-6′, 2 × OCH_2), 60.4 (C-2), 48.1 (*C*Me_2), 26.8 and 26.7 (C*Me*$_2$), 20.7, 20.5, and 20.4 [4 × C(O)*Me*], 13.9 and 13.8 (2 × CH_2*Me*); IR ν_{max} 1739 (CO), 1368, 1252, 1143, 1048, 757 cm^{-1}; MS/FAB *m/z* (rel intens) 331 [M + 1 − SC(Me_2)CH(CO_2Et)$_2$, 100], 201 (25), 169 (86), 109 (40). Anal. Calcd for $C_{24}H_{36}O_{13}S$: C, 51.05; H, 6.43. Found: C, 51.44; H, 6.04.

***m*-CPBA Oxidation of 2-{1-[(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)thio](1-methyl)ethyl}malonic Acid Diethyl Ester (30).** An oily mixture of 2-{1-[(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)sulfinyl]-(1-methyl)ethyl}-malonic acid diethyl esters **13** (R_S:S_S = 5:1) was obtained: ^{1}H NMR δ 5.69 [dd, $J_{1',2'}$ = 1.7, $J_{2',3'}$ = 3.5, H-2′ of major (R_S) epimer], 5.54 [dd, $J_{3',4'}$ = 10.2, H-3′ of major (R_S) epimer], 5.36 [dd, $J_{4',5'}$ = 9.6, H-4′ of major (R_S) epimer], 5.07 [d, H-1′ of major (R_S) epimer], 4.3−4.0 (m, H-5′, H_2-6′, 2 × OCH_2), 3.89 [s, H-2 of major (R_S) epimer], 3.75 [s, H-2 of minor (S_S) epimer], 2.18, 2.08, 2.04, and 2.00 [4 s, 4 × C(O)Me of major (R_S) epimer], 1.52 and 1.50 [2 s, CMe_2 of major (R_S) epimer], 1.3−1.2 (m, 2 × CH_2*Me*). The mixture **13** was used in the next synthetic step without further purification.

Thermolysis of 2-{1-[(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)sulfinyl](1-methyl)ethyl}malonic Acid Diethyl Esters 13 in the Presence of Dimethyl Acetylenedicarboxylate. By column chromatography, eluting with petrol/EtOAc (2.3:1), an oily epimeric mixture of (*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)sulfinyl]but-2-enedioic acid dimethyl esters **24** was obtained (35%, R_S:S_S = 1.5:1): ^{1}H NMR δ 7.07 [s, H-3 of major (R_S) epimer], 7.00 [s, H-3 of minor (S_S) epimer], 5.9−5.2 (m, H-2′,3′,4′), 5.06 [d, $J_{1',2'}$ = 3.2, H-1′ of minor (S_S) epimer], 4.90 [d, $J_{1',2'}$ = 2.4, H-1′ of major (R_S) epimer], 4.59 [ddd, $J_{4',5'}$ = 9.6, $J_{5',6'A}$ = 5.6, $J_{5',6'B}$ = 2.0, H-5′ of major (R_S) epimer], 4.47 [ddd, $J_{4',5'}$ = 9.7, $J_{5',6'A}$ = 4.4, $J_{5',6'B}$ = 2.6, H-5′ of minor (S_S) epimer], 3.80 and 3.79 [2 s, 2 × OMe of major (R_S) epimer], 2.02, 2.01, and 1.99 [3 s, 4 × C(O)Me of major (R_S) epimer]. Anal. Calcd for $C_{20}H_{26}O_{14}S$: C, 45.98; H, 5.02. Found: C, 45.78; H, 5.10.

Thermolysis of 2-{1-[(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)sulfinyl](1-methyl)ethyl}malonic Acid Diethyl Esters 13 in the Presence of Di-*tert*-butyl Acetylenedicarboxylate. By column chromatography, eluting with petrol/EtOAc (4:1), (S_S,*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)sulfinyl]but-2-enedioic acid di-*tert*-butyl ester ((S_S)-**25**) was first isolated as an oil (29%): ^{1}H NMR δ 6.88 (s, H-3), 5.62 (dd, $J_{1',2'}$ = 3.8, $J_{2',3'}$ = 3.7, H-2′), 5.56 (dd, $J_{3',4'}$ = 7.1, H-3′), 5.22 (dd, $J_{4',5'}$ = 9.4, H-4′), 5.11 (d, H-1′), 4.56 (ddd, $J_{5',6'A}$ = 4.8, $J_{5',6'B}$ = 2.5, H-5′), 4.29 (AB dd, $J_{6'A,6'B}$ = 12.5, H_A-6′), 4.18 (AB dd, H_B-6′), 2.11, 2.08, 2.07, and 2.04, [4 s, 4 × C(O)Me], 1.53 and 1.51 (2 s, 2 × CMe_3). Anal. Calcd for $C_{26}H_{38}O_{14}S$: C, 51.48; H, 6.31. Found: C, 51.37; H, 6.50. The major epimer (R_S,*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)sulfinyl]-but-2-enedioic acid di-*tert*-butyl ester ((R_S)-**25**) was then eluted as an oil (36%): ^{1}H NMR δ 6.95 (s, H-3), 5.92 (dd, $J_{1',2'}$ = 2.6, $J_{2',3'}$ = 3.7, H-2′), 5.75 (dd, $J_{3',4'}$ = 8.9, H-3′), 5.29 (dd, $J_{4',5'}$ = 9.5, H-4′), 4.95 (d, H-1′), 4.66 (ddd, $J_{5',6'A}$ = 5.4, $J_{5',6'B}$ = 2.4, H-5′), 4.23 (AB dd, $J_{6'A,6'B}$ = 12.5, H_A-6′), 4.01 (AB dd, H_B-6′), 2.17, 2.09, and 2.04 [3 s, 4 × C(O)Me], 1.54 and 1.50 (2 s, 2 × CMe_3). Anal. Calcd for $C_{26}H_{38}O_{14}S$: C, 51.48; H, 6.31. Found: C, 51.67; H, 6.30.

3-[(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)thio]-propanenitrile (29), the Precursor of Sulfoxides 11. 1-Thio-α-D-mannopyranose 2,3,4,6-tetraacetate (**12**)[17,18] (0.88 g, 2.42 mmol) was dissolved in anhydrous Et_3N (12 μL, 0.09 mmol), and acrylonitrile (0.5 mL, 7.60 mmol) was added. After 1 h of stirring at room temperature, the reaction mixture was concentrated in vacuo and the crude product purified by column chromatography (petrol/EtOAc (1:1) as eluant) to give sulfide **29** (0.92 g, 2.20 mmol, 91%) as an oil: $[\alpha]^{25}_D$ +56.7 (*c* 1.93); ^{1}H NMR (250 MHz) δ 5.4−5.3 (m, H-1′,2′), 5.29 (dd, $J_{3',4'}$ = 9.8, $J_{4',5'}$ = 9.4, H-4′), 5.18 (dd, $J_{2',3'}$ = 3.0, H-3′), 4.41 (ddd, $J_{5',6'A}$ = 5.9, $J_{5',6'B}$ = 2.1, H-5′), 4.28 (AB dd, $J_{6'A,6'B}$ = 12.1, H_A-6′), 4.14 (AB dd, H_B-6′), 3.0−2.8 (m, H_2-2,3), 2.17, 2.10, 2.07, and 2.00 [4 s, 4 × C(O)Me]; ^{13}C NMR (63 MHz) δ 170.4, 169.8, 169.71, and 169.66 [4 × *C*(O)Me], 118.0 (C-1), 83.1 (C-1′), 70.5, 69.5, 69.2, and 66.0 (C-2′,3′,4′,5′), 62.4 (C-6′), 27.5 (C-3), 20.8, 20.7, 20.6, and 20.5 [4 × C(O)*Me*], 18.8 (C-2); MS/IS *m/z* (rel intens) 456 (M + K, 7), 440 (M + Na, 100), 331 (11), 169 (6). Anal. Calcd for $C_{17}H_{23}NO_9S$: C, 48.91; H, 5.55; N, 3.36. Found: C, 48.97; H, 5.60; N, 3.50.

***m*-CPBA Oxidation of 3-[(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)thio]propanenitrile (29).** This reaction gave an oily mixture of sulfoxides **11** (87%, R_S:S_S = 9:1) usable in the next synthetic step without purification. Moreover, the major epimer (R_S)-3-[(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)sulfinyl]propanenitrile ((R_S)-**11**) could be isolated by petrol/EtOAc crystallization as a white solid, mp 108 °C: ^{1}H NMR (250 MHz) δ 5.79 (dd, $J_{1',2'}$ = 2.1, $J_{2',3'}$ = 3.5, H-2′), 5.50 (dd, $J_{3',4'}$ = 9.4, H-3′), 5.33 (dd, $J_{4',5'}$ = 9.3, H-4′), 4.78 (d, H-1′), 4.29 (AB dd, $J_{5',6'A}$ = 6.0, $J_{6'A,6'B}$ = 12.6, H_A-6′), 4.2−4.1 (m, H-5′, H_B-6′), 3.3−2.9 (m, H_2-2,3), 2.18, 2.12, 2.08, and 2.04 [4 s, 4 × C(O)Me]; ^{13}C NMR (63 MHz) δ 170.6, 169.8, 169.71, and 169.67 [4 × *C*(O)Me], 117.5 (C-1), 91.0 (C-1′), 75.1, 68.7, 66.6, and 65.6 (C-2′,3′,4′,5′), 62.2 (C-6′), 45.1 (C-3), 20.9, 20.85, 20.80, and 20.7 [4 × C(O)*Me*], 10.9 (C-2); MS/ IS *m/z* (rel intens) 456 (M + Na, 100), 403 (17), 353 (57), 331 (33), 169 (17). Anal. Calcd for $C_{17}H_{23}NO_{10}S$: C, 47.11; H, 5.35; N, 3.23. Found: C, 47.42; H, 5.36; N, 3.24. By column chromatography of the mother liquors [petrol containing EtOAc (40−70%) as eluant] the minor, more mobile epimer (S_S)-3-[(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)sulfinyl]propanenitrile ((S_S)-**11**) was obtained as an oil: ^{1}H NMR δ 5.77 (dd, $J_{1',2'}$ = 3.7, $J_{2',3'}$ = 3.5, H-2′), 5.62 (dd, $J_{3',4'}$ = 8.1, H-3′), 5.26 (dd, $J_{4',5'}$ = 8.2, H-4′), 4.77 (m, H-5′), 4.50 (d, H-1′), 4.38 (AB dd, $J_{5',6'A}$ = 6.8, $J_{6'A,6'B}$ = 12.4, H_A-6′), 4.13 (dd, $J_{5',6'B}$ = 2.2, H_B-6′), 3.3−2.9 (m, H_2-2,3), 2.2−2.0 [4 s, 4 × C(O)Me]. Anal. Calcd for $C_{17}H_{23}NO_{10}S$: C, 47.11; H, 5.35; N, 3.23. Found: C, 47.21; H, 5.30; N, 3.27.

Thermolysis of 3-[(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)sulfinyl]propanenitriles 11 in the Presence of Dimethyl Acetylenedicarboxylate. By column chromatography, eluting with petrol/EtOAc (4:1), 2-acetoxy-3,4,6-tri-*O*-acetyl-D-glucal (10)[7,21] was isolated in 85% yield.

3-[(2,3,4,6-Tetra-*O*-acetyl-β-D-mannopyranosyl)thio]-propanenitrile (31), the Precursor of Sulfoxides 16. 1-Thio-β-D-mannopyranose pentaacetate (**15**)[11] (0.63 g, 1.55 mmol) was dissolved in dry acrylonitrile (2.1 mL, 31.90 mmol), and hydrazine acetate (0.16 g, 1.68 mmol) was added to the solution. After 1 h of stirring at room temperature, the reaction mixture was concentrated in vacuo and the crude product purified by column chromatography (petrol/EtOAc (1:1) as eluant) to give mannonitrile **31** (0.38 g, 0.91 mmol, 59%) as a solid, mp 131 °C: $[\alpha]^{25}_D$ −29.0 (*c* 1.00); ^{1}H NMR (250 MHz) δ 5.52 (dd, $J_{1',2'}$ = 0.8, $J_{2',3'}$ = 3.3, H-2′), 5.24 (dd, $J_{3',4'}$ = 10.1, $J_{4',5'}$ = 9.9, H-4′), 5.09 (dd, H-3′), 4.97 (d, H-1′), 4.21 (m, H_2-6′), 3.78 (ddd, $J_{5',6'}$ = 5.5 and 3.6, H-5′), 3.0−2.7 (m, H_2-2,3), 2.18, 2.11, 2.06, and 1.99 [4 s, 4 × C(O)Me]; ^{13}C NMR (63 MHz) δ 170.2, 170.1, 170.0, and 169.7 [4 × *C*(O)Me], 118.5 (C-1), 82.9 (C-1′), 76.6, 71.8, 70.7, and 65.7 (C-2′,3′,4′,5′), 62.8 (C-6′), 27.7 (C-3), 21.0, 20.9, 20.8, and 19.7 [4 × C(O)*Me*], 19.0 (C-2); MS/IS *m/z* (rel intens) 440 (M + Na, 100), 435 (M + NH_4, 15), 418 (M + 1, 7), 331 (35), 169 (17); HRMS *m/z* calcd for $C_{17}H_{23}NO_9S$ (M) 417.1093, found 417.1099. Anal. Calcd for $C_{17}H_{23}NO_9S$: C, 48.91; H, 5.55; N, 3.36. Found: C, 49.29; H, 5.17; N, 3.73.

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***m*-CPBA Oxidation of 3-[(2,3,4,6-Tetra-*O*-acetyl-*β*-D-mannopyranosyl)thio]propanenitrile (31).** This reaction gave an oily mixture of sulfoxides **16** (R_S:S_S = 1:2.5), usable in the next synthetic step without purification. Moreover, by column chromatography [petrol containing EtOAc (20−40%) as eluant], the minor epimer (R_S)-3-[(2,3,4,6-tetra-*O*-acetyl-*β*-D-mannopyranosyl)sulfinyl]propanenitrile ((R_S)-**16**) [^{1}H NMR δ 5.99 (m, H-2′)] was obtained always in a mixture with the major, less mobile (S_S)-3-[(2,3,4,6-tetra-*O*-acetyl-*β*-D-mannopyranosyl)sulfinyl]propanenitrile ((S_S)-**16**), the latter isolated as an oil: $[\alpha]^{21}_D$ +3.0 (*c* 12.35); ^{1}H NMR δ 5.78 (dd, $J_{1',2'}$ = 1.0, $J_{2',3'}$ = 3.3, H-2′), 5.25 (dd, $J_{3',4'}$ = 10.1, $J_{4',5'}$ = 10.0, H-4′), 5.12 (dd, H-3′), 4.60 (d, H-1′), 4.17 (m, H_2-6′), 3.84 (ddd, $J_{5',6'}$ = 4.6 and 3.2, H-5′), 3.3−2.7 (m, H_2-2,3), 2.17, 2.07, 2.03, and 1.96 [4 s, 4 × C(O)Me]; ^{13}C NMR δ 170.6, 170.0, 169.64, and 169.61 [4 × C(O)Me], 117.8 (C-1), 89.4 (C-1′), 77.4, 71.3, 65.6, and 65.2 (C-2′,3′,4′,5′), 61.9 (C-6′), 43.2 (C-3), 20.7, 20.6, 20.5, and 20.4 [4 × C(O)Me], 9.1 (C-2). Anal. Calcd for $C_{17}H_{23}NO_{10}S$: C, 47.11; H, 5.35; N, 3.23. Found: C, 46.74; H, 5.71; N, 2.87.

Thermolysis of 3-[(2,3,4,6-Tetra-*O*-acetyl-*β*-D-mannopyranosyl)sulfinyl]propanenitriles 16 in the Presence of Dimethyl Acetylenedicarboxylate. By column chromatography, eluting with petrol/EtOAc (1.5:1), (R_S,*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-*β*-D-mannopyranosyl)sulfinyl]but-2-enedioic acid dimethyl ester ((R_S)-**26**) was first isolated as an oil (31%): ^{1}H NMR δ 6.80 (s, H-3), 5.89 (dd, $J_{1',2'}$ = 0.9, $J_{2',3'}$ = 3.3, H-2′), 5.28 (t, $J_{3',4'} = J_{4',5'}$ = 10.0, H-4′), 5.06 (m, H-3′), 4.63 (d, H-1′), 4.2−4.1 (m, H_2-6′), 3.85 and 3.81 (2 s, 2 × OMe), 3.70 (m, H-5′), 2.05, 2.04, 2.03, and 1.99 [4 s, 4 × C(O)Me]. Anal. Calcd for $C_{20}H_{26}O_{14}S$: C, 45.98; H, 5.02. Found: C, 46.33; H, 4.67. Then the major epimer (S_S,*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-*β*-D-mannopyranosyl)sulfinyl]but-2-enedioic acid dimethyl ester ((S_S)-**26**) was eluted as an oil (44%): $[\alpha]^{21}_D$ −12.2 (*c* 5.08); ^{1}H NMR δ 6.77 (s, H-3), 5.82 (dd, $J_{1',2'}$ = 1.3, $J_{2',3'}$ = 3.3, H-2′), 5.29 (t, $J_{3',4'} = J_{4',5'}$ = 10.1, H-4′), 5.07 (dd, H-3′), 4.55 (d, H-1′), 4.17 (AB dd, $J_{5',6'A}$ = 5.4, $J_{6'A,6'B}$ = 12.6, H_A-6′), 4.12 (AB dd, $J_{5',6'B}$ = 2.7, H_B-6′), 3.87 and 3.83 (2 s, 2 × OMe), 3.70 (ddd, H-5′), 2.24, 2.11, 2.06, and 2.00 [4 s, 4 × C(O)Me]; ^{13}C NMR δ 170.5, 169.7, 169.5, and 169.3 [4 × *C*(O)Me], 163.6 and 161.8 (C-1,4), 150.0 (C-2), 127.7 (C-3), 93.1 (C-1′), 77.7, 71.0, 65.9, and 65.1 (C-2′,3′,4′,5′), 61.9 (C-6′), 53.1 and 52.8 (2 × OMe), 20.7, 20.6, 20.52, and 20.48 [4 × C(O)*Me*]. Anal. Calcd for $C_{20}H_{26}O_{14}S$: C, 45.98; H, 5.02. Found: C, 46.32; H, 4.68.

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