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Sulfenic Acids in the Carbohydrate Field. Synthesis of Transient Glycosulfenic Acids and Their Addition to Unsaturated Acceptors

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A new method is described for building up anomeric glycosyl sulfoxides, via the formation of transient glycosulfenic acids and their addition to unsaturated acceptors. Thermolysis of α- and *β*-3-[(2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl)sulfinyl]propanenitriles affords 1-glucosulfenic acids, which are reacted in situ with common substituted alkynes. The obtained (R_S,*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]-2-butendioates are involved as enantiopure sulfinyl dienophiles in Diels−Alder reactions with 2,3-dimethyl-1,3-butadiene to evaluate the role that the sugar moiety plays in the steric control of the cycloaddition. This chemistry provides a direct synthetic strategy for the stereocontrolled connection between thioglycon and aglycon moieties, thus offering the basis for an easy elaboration of new molecules incorporating thiosugar residues.

Introduction

There is no need to demonstrate the great interest that the scientific community has reserved for the synthesis of saccharides in which at least one glycosidic oxygen is replaced with a sulfur atom.[1] Those are reported to be competitive inhibitors of various glycoside hydrolases,[2] to show antiinflammatory effect as copper complexes,[3] but principally to represent the most popular families of glycosyl donors.[4] Kahne's glycosyl sulfoxide reaction[5] has proven quite effective in glycosylating even very unreactive substrates. Consequently, investigation on methodologies for easy production of anomeric glycosyl sulfoxides represents a stimulating research topic. The conventional synthetic approach is based on the preparation of 1-thioglycosides following standard procedures;[6] subsequent oxidation of 1-thioglycosides leads to the anomeric glycosyl sulfoxides.[7]

In this paper we describe a new method for the building up of anomeric glycosyl sulfoxides, via the formation of transient glycosulfenic acids GlySOH, and their addition to unsaturated acceptors. It has been previously demonstrated[8] that the addition of enantiopure sulfenic acids to alkenes or alkynes is a concerted reaction that allows an easy and stereocontrolled introduction of a sulfinyl group into a suitable substrate. The generation of a transient glycosulfenic acid and its addition reaction provide in principle a direct synthetic strategy for the connection between thioglycon and aglycon moieties, thus offering the basis for an easy elaboration of new molecules incorporating thiosugar residues, which have been designed in view of their biological activity.

The D-glucose series was selected to provide the substrates for synthesizing (Schemes 1−3) precursors **2** and **12** of 1-glucosulfenic acids (**9** in Scheme 2 and **13** in Scheme 3, respectively), which have been generated by thermolysis and reacted in situ with common substituted alkynes **3**, **4**, and **14** to verify the easy and stereocontrolled formation of various D-glucopyranosyl sulfoxides through the envisaged methodology. Finally, (R_S,*E*)-2-[(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]-2-butendioates $\mathbf{17}_{R}$ and $\mathbf{18}_{R}$ were used as enantiopure sulfinyl dienophiles in Diels−Alder reactions with 2,3-dimethyl-1,3-butadiene (**19**) (Scheme 4) to fulfill our interest in evaluating the role that the sugar moiety can play in the steric control of the cycloaddition.[9] Because of coexistent polyfunctionality, enantiopurity, and conformational ri-

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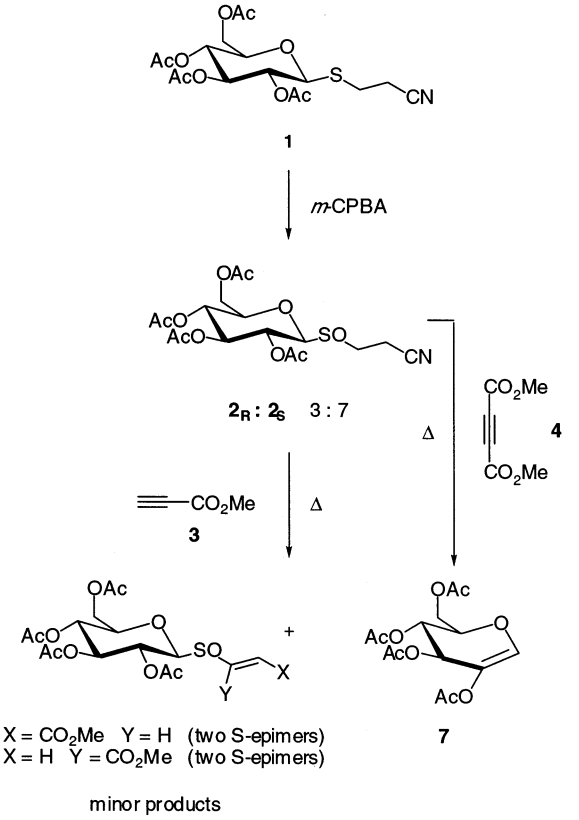
SCHEME 1



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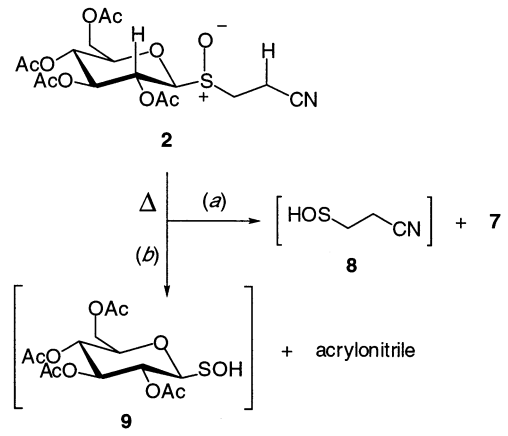
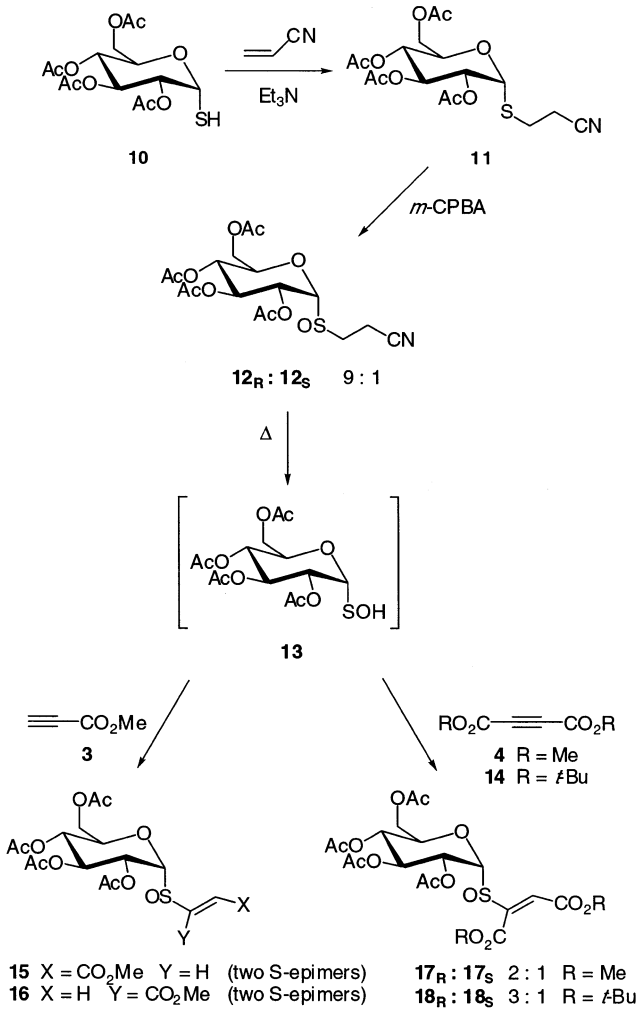


gidity in carbohydrates, the saccharidic part of the substrates would be expected to heavily affect the reaction course.

Results and Discussion

The synthesis of 2-cyanoethyl 2,3,4,6-tetra-*O*-acetyl-*β*-D-1-thioglucopyranoside (**1**) (Scheme 1) was performed by following a previously described procedure.[10] The thioglycoside **1** was then reacted with *m*-CPBA to obtain the epimeric mixture of sulfoxides **2**, which can undergo thermolysis without purification. In one experiment, overoxidation of **1** led to a small amount of the related

SCHEME 3



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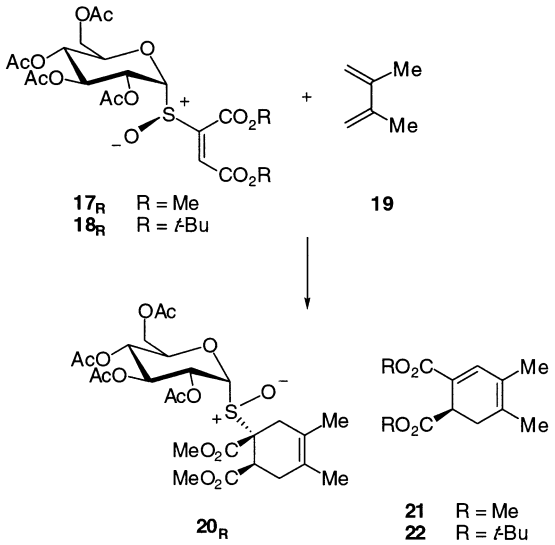

sulfone **23**, which was isolated and fully characterized. The attempted separation of the 7:3 epimeric mixture **2** was performed by column chromatography. In the adopted conditions, it allowed the isolation of the major, more mobile sulfoxide $\mathbf{2}_S$, whose (S_S) configuration was as-

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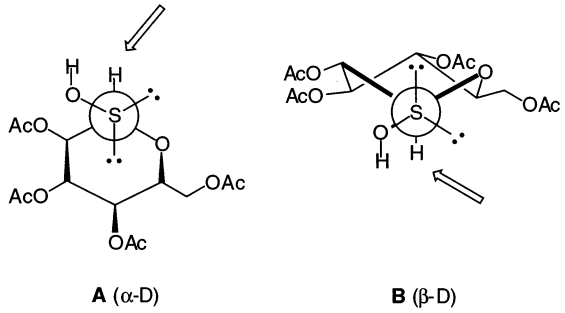
signed by taking into account the role of the exo-anomeric effect.[11]

Thermolysis of glucosulfinyl propanenitriles **2** was performed in benzene, toluene, or neat methyl propiolate (**3**) as reaction solvents and in the presence of **3** or dimethyl acetylenedicarboxylate (**4**) as trappers of the transient glucosulfenic acid (Scheme 2). The obtained results are reported in Table 1, entries 1−4. The products resulting from the **3**/**9** addition, which are the sulfur epimeric mixtures of 3-glucosylsulfinyl-2-propenoates **5** and 2-glucosylsulfinyl-2-propenoates **6**, were obtained in the experiment of thermolysis in benzene (entry 1) together with glucal **7**,[12] which represented the unique isolated product in the remaining experiments (entries 2−4). *β*-Sulfinyl and α-sulfinyl α,*β*-unsaturated esters **5** and **6** were obtained in 6:4 ratio respectively, and the observed regioselectivity was the one expected on the basis of the electronic nature of the reacting unsaturated carbons in the acceptor **3**.[8] Rather unexpected was the formation of glucal **7** resulting from the endo-cyclic elimination of sulfenic acid **8** (pathway a in Scheme 2), which competes with the exo-cyclic elimination of **9** (pathway b) in the thermolysis of sulfoxides **2**. The thermal *β*-elimination of sulfoxides is well-documented,[13] and its Ei mechanism predicts exclusive syn-elimination via a five-membered transition state where the five atoms making up the ring must be coplanar. Sulfoxides **2** show two different proton *β*-positions to the sulfinyl group (Scheme 2), but formation of the sulfenic acid **9** (pathway b) was predictable, as favored by the presence in **2** of the cyano group whose electron-withdrawing character increases the acidity of its α-protons. Moreover, the difficulty of the sugar ring of **2** in flattening out to achieve the required geometry in the transition state toward sulfenic acid **8** would represent a further point in favor of the elimination pathway b. However, the collected experimental data contradicted these expectations in that the formation of glucal **7** by endo-cyclic elimination of sulfenic acid **8** always represented the favored pathway a of the thermolysis of sulfoxides **2**. This behavior can be rationalized by taking into account that the electronic control of the regioselectivity in the elimination is in principle provided not only by the acidity of the *β*-protons but also by the basicity of the sulfinyl oxygen. This oxygen atom acts as internal base and thus the electronic nature of the unreactive side of the sulfoxide can influence the direction of elimination by increasing or decreasing oxygen basicity.[14] In our case the electronic nature of the glucosyl residue and its influence on the sulfoxide oxygen basicity appears to be the determining factor for the preferred formation of sulfenic acid **8** via the elimination pathway a.

2,3,4,6-Tetra-*O*-acetyl-α-D-1-thioglucopyranose (**10**)[15] was reacted with acrylonitrile in triethylamine to produce 2-cyanoethyl 2,3,4,6-tetra-*O*-acetyl-α-D-1-thioglucopyranoside (**11**) in 84% yield (Scheme 3). Oxidation with *m*-CPBA of sulfide **11** led to the epimeric mixture of sulfoxides **12**, which were used as precursors to the corresponding glucosulfenic acid **13**. α-D-Glucosulfinylpropanenitriles **12** were obtained in 9:1 ratio, separated by crystallization, and fully characterized. Their sulfur configurations were assigned as stated above for sulfoxides **2**. The high stereoselectivity observed in the oxidation of **11** was expected on the basis of previous experimental work.[11,16] 3-[(2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl)sulfonyl]propanenitrile (**24**) was occasionally obtained, isolated, and fully characterized.

Conditions and results of the thermolyses of sulfoxides **12**, performed in the presence of alkynes **3**, **4**, and **14**, are reported in Table 1 (entries 5−7). The axial sulfoxides **12** can undergo only exo-cyclic elimination toward α-D-glucosulfenic acid **13**. The products of all additions of **13** to alkynes were obtained in very good yields, thus demonstrating the effectiveness of the glucosyl template in preventing self-condensation of **13** to the corresponding thiosulfinate. The good diastereoselectivities observed in the formation of **15**−**18** can be explained in terms of preferred addition of carbon−carbon triple bond to the unhindered side of the sulfenic acid **13**, which is constrained in a conformation such as **A** by the exo-anomeric



A (α-D) **B** (β-D)

effect. The same effect imposes the preferred conformation **B** to the *β*-D-glucosulfenic acid **9**, where the two sulfenic sides are less sterically differentiated, and therefore, formation of compounds **5** and **6** occurs with very low diastereoselection (see above).

The major (R_S) epimers $\mathbf{17}_{\boldsymbol{R}}$ and $\mathbf{18}_{\boldsymbol{R}}$ were isolated and fully characterized, and the nature of vinyl sulfoxides possessing an electron-deficient carbon−carbon double bond prompted us to involve them as enantiopure sulfinyl dienophiles in asymmetric Diels−Alder cycloadditions with 2,3-dimethyl-1,3-butadiene (**19**) (Scheme 4). The reactivity of $\mathbf{17}_{\boldsymbol{R}}$ and $\mathbf{18}_{\boldsymbol{R}}$ was low (about half a month was required for the cycloadditions to be completed) and conjugated cyclohexadienes **21** and **22** were obtained respectively by spontaneous and completely regioselective elimination of sulfenic acid **13** from the initially formed cycloadducts. Again two different proton positions *β* to the sulfinyl group are available in $\mathbf{20}_{\boldsymbol{R}}$. The clear preference for elimination of **13** from $\mathbf{20}_{\boldsymbol{R}}$ by H-6 involvement is indicative of steric characteristics, which favor the transition state leading to 1,3-cyclohexadiene **21** instead of the one leading to the 1,4-cyclohexadiene derivative.

When the reaction of $\mathbf{17}_{\boldsymbol{R}}$ with **19** was stopped before the complete consumption of the dienophile, we could

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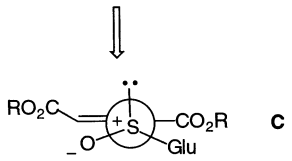
detect, isolate, and fully characterize enantiopure $\mathbf{20}_R$ as the unique product of the cycloaddition, so attesting to the complete π-facial selectivity previously observed in similar reactions.[17] The stereochemistry of adduct $\mathbf{20}_R$ and cyclohexadienes **21** and **22** has been proposed in agreement with the results obtained by the Spanish group:[17] the approach of the diene **19** takes place from the less hindered face (*Si*) of the dienophile in conformation **C**, with the sulfinyl oxygen in the nearly s-cis arrangement and the glucosyl moiety located as far as possible from the reaction site.



C

Conclusion

In this paper we have described an easy methodology for generating in situ glucosulfenic acids, which can be regarded as effective precursors of anomeric glucosyl sulfoxides. This chemistry presents good perspectives of modulation of the structures of glycosulfenic acids and aglycon moieties, thus laying the groundwork for subsequent investigations of the role of different anomeric glycosulfenic acids in the chemistry of thioglycosides. Formation of glucal **7** represents a limitation in the synthetic use of β-D-glucopyranosylsulfenic acid **9**, even though the utility of the β-elimination reaction of glycosulfoxides in the preparation of 2-substituted glycals has recently been pointed out.[18]

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively (unless otherwise specified), in $CDCl_3$ solutions with TMS as internal standard. *J* values are given in Hz. The assignments are supported by an attached proton test (APT) and homodecoupling experiments. Protons and carbon nuclei, marked with (′), pertain to glucopyranosyl moieties in compounds **2**, **12**, **15**−**18**, **20**, **23**, and **24**. Mass spectra were measured by FAB (*m*-nitrobenzyl alcohol as matrix). Optical rotations were measured in $CHCl_3$ solutions whose concentrations are expressed in g/100 mL. 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.

2-Cyanoethyl 2,3,4,6-tetra-*O*-acetyl-β-D-1-thioglucopyranoside (1) was prepared according to the method of Cerny and Pacák:[10] mp 110 °C; $[\alpha]^{25}_D$ −36.0 (*c* 0.70); lit.[10] mp 111 °C; $[\alpha]^{25}_D$ −33.3 (*c* 1.14); ^{1}H NMR (250 MHz) δ 5.23 (t, $J_{2,3} = J_{3,4}$ 9.5, H-3), 5.06 (t, $J_{4,5}$ 9.5, H-4), 5.03 (dd, $J_{1,2}$ 9.8, H-2), 4.57 (d, H-1), 4.24 (AB dd, $J_{5,6A}$ 4.7, $J_{6A,6B}$ 12.6, H_A-6), 4.17 (AB dd, $J_{5,6B}$ 2.5, H_B-6), 3.75 (ddd, H-5), 3.1−3.0 (m, CH_AS), 2.9−2.8 (m, CH_BS), 2.8−2.7 (m, CH_2CN), 2.10, 2.06, 2.03, and 2.01 (s, Me); ^{13}C NMR δ 170.54, 170.04, 169.45, and 169.39 (CO), 118.17 (CN), 83.33 (C-1), 76.04 (C-5), 73.47 (C-3), 69.39 (C-2), 68.08 (C-4), 61.91 (C-6), 25.75 (CH_2S), 20.71, 20.63, 20.55, and 20.54 (Me), 19.63 (CH_2CN).

***m*-CPBA Oxidation of Sulfide 1.** This reaction was performed according to the protocol previously described.[9a] It gave a mixture of sulfoxides **2** (89% yield, sulfur epimeric ratio 7:3) usable in the next synthetic step without purification. However, column chromatography of the product mixture, eluted with petrol containing 30−70% EtOAc, allowed the isolation of the major, more mobile epimer **(S_S)-3-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]propanenitrile (2*S*)** as a solid: mp 117−118 °C; $[\alpha]^{25}_D$ −27.5 (*c* 0.35); ^{1}H NMR δ 5.33 (t, $J_{2',3'} = J_{3',4'}$ 9.4, H-3′), 5.19 (t, $J_{1',2'}$ 9.7, H-2′), 5.11 (t, $J_{4',5'}$ 9.8, H-4′), 4.43 (d, H-1′), 4.29 (AB dd, $J_{5',6'A}$ 4.3, $J_{6'A,6'B}$ 12.8, H_A-6′), 4.23 (AB dd, $J_{5',6'B}$ 2.3, H_B-6′), 3.87 (ddd, H-5′), 3.30 (AB dt, $J_{2,3}$ 7.1, $J_{3A,3B}$ 13.7, H_A-3), 3.16 (AB dt, H_B-3), 2.99 (AB dt, $J_{2A,2B}$ 17.5, H_A-2), 2.80 (AB dt, H_B-2), 2.11, 2.08, 2.05, and 2.03 (s, Me); ^{13}C NMR δ 170.48, 169.91, 169.89, and 169.30 (CO), 117.56 (C-1), 89.91 (C-1′), 76.99 (C-5′), 72.74 (C-2′), 68.51 (C-3′), 67.40 (C-4′), 61.12 (C-6′), 41.12 (C-3), 20.69 and 20.51 (Me), 9.48 (C-2); MS *m*/*z* 331 [M + 1 − $NC(CH_2)_2$-SOH, 20], 169 (37), 117 (39), 95 (56), 81 (60), 69 (81), 55 (100). Anal. Calcd for $C_{17}H_{23}NO_{10}S$: C 47.11, H 5.35, N 3.23. Found: C 46.94, H 5.25, N 3.23. The minor epimer **(R_S)-3-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]propanenitrile (2*R*)** was always eluted in admixture with $\mathbf{2}_S$ and identified by ^{13}C NMR [δ 170.43, 169.85, 169.12, and 168.79 (CO), 117.36 (C-1), 87.95 (C-1′), 73.42, 67.47, and 66.56 (C-2′-5′), 61.66 (C-6′), 42.28 (C-3), 20.67 and 20.54 (Me), 11.12 (C-2)]. Incidental overoxidation of **1** afforded **3-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfonyl]propanenitrile (23)** (10% yield): mp 203−204 °C; $[\alpha]^{25}_D$ −8.4 (*c* 0.16); ^{1}H NMR δ 5.51 (dd, $J_{2',3'}$ 9.3, $J_{3',4'}$ 9.8, H-3′), 5.33 (t, $J_{1',2'}$ 9.5, H-2′), 5.14 (t, $J_{4',5'}$ 9.9, H-4′), 4.61 (d, H-1′), 4.31 (AB dd, $J_{5',6'A}$ 2.4, $J_{6'A,6'B}$ 12.7, H_A-6′), 4.25 (AB dd, $J_{5',6'B}$ 4.6, H_B-6′), 3.89 (ddd, H-5′), 3.62 (AB dt, $J_{2,3}$ 7.0, $J_{3A,3B}$ 14.7, H_A-3), 3.29 (AB dt, H_B-3), 2.93 (m, H_2-2), 2.12, 2.07, 2.05, and 2.03 (s, Me); ^{13}C NMR δ 170.51, 170.01, and 169.18 (CO), 116.40 (C-1), 88.22 (C-1′), 77.00 (C-5′), 72.79 (C-3′), 67.06 (C-4′), 66.18 (C-2′), 61.01 (C-6′), 45.38 (C-3), 20.79, 20.60 and 20.41 (Me), 11.64 (C-2). Anal. Calcd for $C_{17}H_{23}NO_{11}S$: C 45.43, H 5.16, N 3.12. Found: C 45.53, H 5.39, N 2.92.

2-Cyanoethyl 2,3,4,6-Tetra-*O*-acetyl-α-D-1-thioglucopyranoside (11). 2,3,4,6-Tetra-*O*-acetyl-α-D-1-thioglucopyranose (**10**)[15] (401 mg, 1.10 mmol) was dissolved in dry Et_3N (5.5 mL), and acrylonitrile (664 μL, 10.09 mmol) was added. After 1 h of standing at room temperature, the mixture was concentrated in vacuo and the crude residue purified by column chromatography (EtOAc/hexanes 1:1) to afford crystalline **11** (385 mg, 0.92 mmol, 84% yield): mp 118 °C; $[\alpha]^{25}_D$ +173.8 (*c* 0.22); ^{1}H NMR (250 MHz) δ 5.74 (d, $J_{1,2}$ 5.9, H-1), 5.34 (dd, $J_{2,3}$ 10.4, $J_{3,4}$ 9.5, H-3), 5.04 (t, $J_{4,5}$ 9.9, H-4), 5.02 (dd, H-2), 4.44 (ddd, $J_{5,6A}$ 5.1, $J_{5,6B}$ 2.2, H-5), 4.27 (AB dd, $J_{6A,6B}$ 12.4, H_A-6), 4.14 (AB dd, H_B-6), 3.0−2.8 (m, CH_2S), 2.8−2.7 (m, CH_2CN), 2.11, 2.09, 2.05, and 2.03 (s, Me); ^{13}C NMR δ 170.69, 170.16, 170.07, and 169.81 (CO), 117.99 (CN), 83.00 (C-1), 70.57 (C-2), 70.44 (C-3), 68.49 (C-4), 68.38 (C-5), 62.18 (C-6), 26.70 (CH_2S), 20.98, 20.86, and 20.78 (Me), 19.08 (CH_2CN). Anal. Calcd for $C_{17}H_{23}NO_9S$: C 48.91, H 5.55, N 3.36. Found: C 48.60, H 5.58, N 3.18.

***m*-CPBA Oxidation of Sulfide 11.** This reaction was performed according to the protocol previously described[9a] and gave a mixture of sulfoxides **12** (91% yield, sulfur epimeric ratio 9:1), usable in the next synthetic step without purification. Alternatively, **(R_S)-3-[(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]propanenitrile ($\mathbf{12}_R$)** could be isolated by crystallization from CH_2Cl_2/petrol as white solid: mp 165−167 °C; $[\alpha]^{25}_D$ +114.4 (*c* 0.04); ^{1}H NMR δ 5.53 (t, $J_{2',3'}$ 7.6, $J_{3',4'}$ 7.3, H-3′), 5.37 (dd, $J_{1',2'}$ 5.0, H-2′), 5.00 (dd, $J_{4',5'}$ 9.2, H-4′), 4.89 (d, H-1′), 4.21 (AB dd, $J_{5',6'A}$ 6.5, $J_{6'A,6'B}$ 12.5, H_A-6′), 4.13 (AB dd, $J_{5',6'B}$ 2.5, H_B-6′), 3.92 (ddd, H-5′), 3.25 (AB ddd, $J_{2,3}$ 8.6, 7.6, 7.4, and 5.9, $J_{3A,3B}$ 13.4, H_A-3), 3.10 (AB ddd, H_B-3), 2.95 (AB dt, $J_{2A,2B}$ 17.1, H_A-2), 2.88 (AB ddd, H_B-2), 2.13, 2.10, and 2.08 (s, Me); ^{13}C NMR δ 170.28, 169.66, 169.25, and 169.23 (CO), 117.20 (C-1), 88.06 (C-1′), 74.20, 69.45, 68.19, and 67.69

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TABLE 1. Thermolysis of 3-Sulfinylpropanenitriles 2 and 12 in the Presence of Alkynes 3, 4, and 14 at Reflux Temperature

entry	starting sulfoxides	alkyne	solvent	reaction time (h)	products (ratio[a])
1	**2**	**3**	benzene	6	**5_S/5_R/6_S/6_R/7** (12.4:11.2:8.8:7.6:60)
2	**2**	**3**	toluene	1	**7**
3	**2**	**3**	neat **3**	3	**7**
4	**2**	**4**	toluene	2	**7**[b]
5	**12**	**3**	neat **3**	6	**15_R/15_S/16_R/16_S** (52:26:15:7)
6	**12**	**4**	toluene	2.5	**17_R/17_S** (67:33)
7	**12**	**14**	toluene	4.5	**18_R/18_S** (75:25)

[a] Established from the relative intensities of significant ^{1}H NMR signals. [b] 71% yield of isolated glucal.

(C-2′-5′), 61.98 (C-6′), 43.50 (C-3), 20.65, 20.61, and 20.55 (Me), 10.11 (C-2); MS *m*/*z* 434 (M + 1, 34), 391 (30), 374 (15), 331 (66), 211 (4), 169 (100), 109 (49), 107 (18), 89 (16), 43 (63). Anal. Calcd for $C_{17}H_{23}NO_{10}S$: C 47.11, H 5.35, N 3.23. Found: C 47.30, H 5.41, N 2.93. **(*S*$_S$)-3-[(2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]propanenitrile (12$_S$)** was obtained by evaporating the mother liquors as a low-melting solid: $[\alpha]^{25}_D$ +69.8 (*c* 0.05); ^{1}H NMR δ 6.00 (m, H-3′), 5.39 (dd, $J_{1',2'}$ 6.9, $J_{2',3'}$ 9.9, H-2′), 5.13 (m, H-4′), 4.66 (d, H-1′), 4.17 (m, H_2-6′), 3.6−2.8 (m, H_2-2,3,5′), 2.18, 2.13, 2.05, and 2.04 (s, Me). Incidental overoxidation of **11** afforded **3-[(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)sulfonyl]propanenitrile (24)** (7% yield): mp 187−188 °C; $[\alpha]^{25}_D$ +128.8 (*c* 0.38); ^{1}H NMR δ 5.87 (split t, $J_{2',3'}$ 9.0, $J_{3',4'}$ 8.9, H-3′), 5.30 (m, H-1′,2′), 5.05 (dd, $J_{4',5'}$ 10.1, H-4′), 4.64 (ddd, $J_{5',6'A}$ 5.6, $J_{5',6'B}$ 2.8, H-5′), 4.22 (AB dd, $J_{6'A,6'B}$ 12.6, H_A-6′), 4.18 (AB dd, H_B-6′), 3.46 (AB ddd, $J_{2A,3A}$ 8.5, $J_{2B,3A}$ 7.6, $J_{3A,3B}$ 14.3, H_A-3), 3.40 (AB ddd, $J_{2A,3B}$ 6.7, $J_{2B,3B}$ 8.5, H_B-3), 2.94 (AB ddd, $J_{2A,2B}$ 17.6, H_A-2), 2.89 (AB ddd, H_B-2), 2.13, 2.07, and 2.06 (s, Me); ^{13}C NMR δ 170.46, 170.22, 169.45, and 169.31 (CO), 115.95 (C-1), 84.87 (C-1′), 72.58, 68.81, 68.49, and 67.49 (C-2′-5′), 62.11 (C-6′), 46.53 (C-3), 20.62, and 20.48 (Me), 10.92 (C-2). Anal. Calcd for $C_{17}H_{23}NO_{11}S$: C 45.43, H 5.16, N 3.12. Found: C 45.44, H 5.32, N 2.85.

Thermolysis of Sulfoxides 2 and 12 in the Presence of Alkyne Derivatives 3, 4, and 14. General Procedure. A solution of sulfoxides **2** or **12** (100 mg, 0.23 mmol) and alkyne **3**, **4**, or **14** (0.69 mmol) in benzene or toluene (3 mL) was maintained at reflux temperature. The thermolysis was also performed in neat **3** by reacting sulfoxides **2** or **12** (100 mg, 0.23 mmol) with 3 mL (33.72 mmol) of **3** at reflux temperature. When the reaction appeared complete by TLC (disappearance of **2** or **12**), the solvent was removed under reduced pressure and the crude mixture of products separated by column chromatography. Conditions and results of the performed experiments of thermolysis are depicted in Table 1.

Thermolysis of 3-[(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]propanenitriles 2 in the Presence of Methyl Propiolate (3). When the reaction was performed in benzene (entry 1 in Table 1) the column chromatography of the crude product mixture, eluted with petrol containing 20−40% EtOAc, afforded, in order of elution from the column, **2-acetoxy-3,4,6-tri-*O*-acetyl-D-glucal (7)**[12] as major product of the reaction (30% yield) and the sulfur epimeric mixtures (20% yield) of **methyl (*E*)-3-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]-2-propenoates 5** and **2-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]-2-propenoates 6.** The following are typical ^{1}H NMR signals of **5** and **6**: δ 7.72 (d, $J_{2,3}$ 15.2, H-3) and 6.66 (d, H-2) for 5_S; 7.52 (d, $J_{2,3}$ 15.2, H-3) and 6.72 (d, H-2) for 5_R; 6.85 and 6.52 (two s, H_2-3) for 6_S; 7.04 and 6.63 (two s, H_2-3) for **6_R**.

Thermolysis of 3-[(2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]propanenitriles 12 in the Presence of Methyl Propiolate (3). When the reaction was performed in neat **3** (entry 5 in Table 1) the column chromatography of the crude product mixture, eluted with petrol/EtOAc 8:2, afforded the epimeric mixtures (85% yield) of **methyl (*E*)-3-[(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]-2-propenoate 15** and **2-[(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-sulfinyl]-2-propenoate 16.** The following are typical ^{1}H NMR signals of **15** and **16**: δ 7.63 (d, $J_{2,3}$ 14.9, H-3), 6.83 (d, H-2), 6.04 (t, $J_{2',3'} = J_{3',4'}$ 9.8, H-3′), 5.42 (dd, $J_{1',2'}$ 6.8, H-2′), 5.11 (dd, $J_{4',5'}$ 9.2, H-4′), 4.88 (d, H-1′), 4.95 (m, H-5′), 4.13 (AB dd, $J_{5',6'A}$ 5.0, $J_{6'A,6'B}$ 12.5, H_A-6′), 4.01 (AB dd, $J_{5',6'B}$ 2.2, H_B-6′), 3.84 (s, OMe), 2.19, 2.08, 2.05, and 2.03 [s, C(O)Me] for 15_R; 7.82 (d, $J_{2,3}$ 15.2, H-3), 6.72 (d, H-2), 5.71 (t, $J_{2',3'} = J_{3',4'}$ 8.0, H-3′) for 15_S; 7.16 and 6.77 (two s, H_2-3), 6.12 (t, $J_{2',3'} = J_{3',4'}$ 9.8, H-3′) for 16_R; 7.01 and 6.73 (two s, H_2-3), 5.92 (t, $J_{2',3'} = J_{3',4'}$ 9.0, H-3′) for 16_S.

Thermolysis of 3-[(2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]propanenitriles 12 in the Presence of Dimethyl Acetylenedicarboxylate (4). When the reaction was performed in toluene (entry 6 in Table 1) the column chromatography of the crude product mixture, eluted with petrol/EtOAc 7:3, afforded the epimeric sulfoxides **17** (85% total yield). First eluted was the major epimer **dimethyl (*R*$_S$,E)-2-[(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]-2-butendioate (17$_R$)**, isolated as an oil: $[\alpha]^{25}_D$ + 232.9 (*c* 0.35); ^{1}H NMR δ 7.12 (s, H-3), 6.04 (t, $J_{2',3'}$ 9.9, $J_{3',4'}$ 9.6, H-3′), 5.42 (dd, $J_{1',2'}$ 6.9, H-2′), 5.13 (d, H-1′), 5.08 (dd, $J_{4',5'}$ 10.4, H-4′), 4.88 (ddd, $J_{5',6'A}$ 4.4, $J_{5',6'B}$ 2.1, H-5′), 4.19 (AB dd, $J_{6'A,6'B}$ 12.7, H_A-6′), 3.96 (AB dd, H_B-6′), 3.86 and 3.82 (s, OMe), 2.18, 2.04, 2.02, and 2.00 [s, C(O)Me]; ^{13}C NMR δ 170.51, 169.84, 169.56, and 169.49 [*C*(O)Me], 164.62 and 161.27 (C-1,4), 141.97 (C-2), 134.04 (C-3), 87.43 (C-1′), 73.98, 70.03, 69.78, and 67.52 (C-2′-5′), 61.55 (C-6′), 53.36 and 52.86 (OMe), 20.59 and 20.50 [C(O)*Me*]. Anal. Calcd for $C_{20}H_{26}O_{14}S$: C 45.98, H 5.02. Found: C 46.18, H 5.16. The minor epimer **dimethyl (*S*$_S$,E)-2-[(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]-2-butendioate (17$_S$)** was always eluted in mixture with **17$_R$** and identified by ^{1}H NMR {δ 6.96 (s, H-3), 5.86 (dd, $J_{2',3'}$ 9.0, $J_{3',4'}$ 7.8, H-3′), 5.41 (dd, $J_{1',2'}$ 5.6, H-2′), 5.14 (d, H-1′), 5.12 (dd, $J_{4',5'}$ 10.0, H-4′), 4.51 (ddd, $J_{5',6'A}$ 3.8, $J_{5',6'B}$ 2.5, H-5′), 4.23 (AB dd, $J_{6'A,6'B}$ 12.5, H_A-6′), 4.14 (AB dd, H_B-6′), 3.85 and 3.84 (s, OMe), 2.10, 2.07, 2.05, and 2.03 [s, C(O)Me]}.

Thermolysis of 3-[(2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]propanenitriles 12 in the Presence of Di-*tert*-butyl Acetylenedicarboxylate (14). The reaction performed in toluene (entry 7 in Table 1) afforded the sulfur epimeric mixture **18** (95% yield). **Di-*tert*-butyl (*R*$_S$,E)-2-[(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]-2-butendioate (18$_R$)** was isolated by crystallization from petrol as a solid: mp 120−121 °C; $[\alpha]^{20}_D$ +221.6 (*c* 0.15); ^{1}H NMR δ 6.96 (s, H-3), 6.10 (t, $J_{2',3'}$ 9.9, $J_{3',4'}$ 9.6, H-3′), 5.40 (dd, $J_{1',2'}$ 6.9, H-2′), 5.14 (d, H-1′), 5.11 (dd, $J_{4',5'}$ 10.3, H-4′), 4.86 (ddd, $J_{5',6'A}$ 3.9, $J_{5',6'B}$ 2.0, H-5′), 4.21 (AB dd, $J_{6'A,6'B}$ 12.7, H_A-6′), 3.98 (AB dd, H_B-6′), 2.18, 2.07, 2.03, and 2.00 [s, C(O)Me], 1.54 and 1.48 (s, CMe_3); ^{13}C NMR δ 170.59, 170.03, 169.59, and 169.54 [*C*(O)Me], 163.29 and 159.52 (C-1,4), 140.89 (C-2), 134.96 (C-3), 86.89 (C-1′), 84.98 and 83.61 (*C*Me$_3$), 73.59, 70.34, 69.70, and 67.54 (C-2′-5′), 61.22 (C-6′), 28.04 and 27.82 (C*Me*$_3$), 20.64, 20.63, 20.58, and 20.54 [C(O)*Me*]. Anal. Calcd for $C_{26}H_{38}O_{14}S$: C 51.48, H 6.31. Found: C 51.69, H 6.40. **Di-*tert*-butyl (*S*$_S$,E)-2-[(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]-2-butendioate (18$_S$)** was obtained by evaporating the mother liquors as an oil: $[\alpha]^{20}_D$ + 35.0 (*c* 0.12); ^{1}H NMR δ 6.81 (s, H-3), 6.09 (dd, $J_{2',3'}$ 9.9, $J_{3',4'}$ 8.7, H-3′), 5.40 (dd, $J_{1',2'}$ 5.9, H-2′), 5.20 (d, H-1′), 5.14 (dd, $J_{4',5'}$ 10.0, H-4′), 4.70 (ddd, $J_{5',6'A}$ 4.0, $J_{5',6'B}$ 2.2, H-5′), 4.32 (AB dd, $J_{6'A,6'B}$ 12.6, H_A-6′), 4.17 (AB dd, H_B-6′), 2.10, 2.06, 2.04, and 2.01 [s, C(O)Me], 1.55, 1.54, 1.52, and 1.51 (s, CMe_3); ^{13}C NMR δ 170.54, 170.20, and 169.61 [*C*(O)Me], 162.96 and 160.30 (C-1,4), 144.37 (C-2), 131.82 (C-3), 89.38 (C-1′), 85.39 and 83.43 (*C*Me$_3$), 73.59, 70.59, 69.21, and 68.04 (C-2′-5′), 61.50 (C-6′), 28.02, 27.93, and 27.81 (C*Me*$_3$), 20.68, 20.64, 20.60, and 20.41 [C(O)*Me*]. Anal. Calcd for $C_{26}H_{38}O_{14}S$: C 51.48, H 6.31. Found: C 51.66, H 6.29.

Cycloadditions of 2,3-Dimethyl-1,3-butadiene (19) with Dienophiles 17_R and 18_R. General Procedure. The reactions were performed in CH_2Cl_2 [2 mL for 1 mL (8.84 mmol) of **19** and 0.15 mmol of dienophile] under argon atmosphere. The reaction mixtures were stirred at room temperature and the crude products purified by column chromatography eluting with petrol containing up to 20% EtOAc.

Cycloaddition 17_R + 19. Experiment 1. The reaction was stopped after 24 h and, together with the starting product $\mathbf{17_R}$, **dimethyl (1*R*,2*S*,R_S)-4,5-dimethyl-1-[(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)sulfinyl]cyclohexene-1,2-dicarboxylate ($\mathbf{20_R}$)** was isolated as an oil (40% yield): $[\alpha]^{25}_D$ + 175.1 (*c* 0.19); ^{1}H NMR δ 5.81 (split t, $J_{2',3'}$ 9.6, $J_{3',4'}$ 9.5, H-3′), 5.33 (dt, $J_{4',5'}$ 10.4, $J_{5',6'}$ 2.7, H-5′), 5.20 (m, H-2′), 5.18 (d, $J_{1',2'}$ 6.8, H-1′), 5.12 (dd, H-4′), 4.15 (d, H_2-6′), 3.78 and 3.69 (s, OMe), 3.75 (m, H-2), 2.72 and 2.53 (split AB system, $J_{3A,3B}$ 19.0, H_2-3), 3.03 and 2.08 (broad AB system, $J_{6A,6B}$ 19.7, H_2-6), 2.09, 2.05, 2.03, and 2.01 [s, C(O)Me], 1.63 and 1.57 (s, 4,5-Me); ^{13}C NMR δ 172.92, 170.60, 169.89, 169.54, 169.51, and 169.05 (CO), 124.01 and 121.23 (C-4,5), 81.62 (C-1′), 74.02, 70.60, 70.07, and 67.27 (C-2′-5′), 63.59 and 61.02 (C-1,6′), 53.15 and 52.32 (OMe), 40.40 (C-2), 30.81 and 30.73 (C-3,6), 20.68, 20.62, 20.53, and 20.37 [C(O)*Me*], 18.68 and 18.61(4,5-Me). Anal. Calcd for $C_{26}H_{36}O_{14}S$: C 51.65, H 6.00. Found: C 51.26, H 6.17.

Cycloaddition 17_R + 19. Experiment 2. Dienophile $\mathbf{17_R}$ and diene **19** were reacted until the dienophile totally disappeared (15 days were required, as verified by TLC monitoring). **Dimethyl (*R*)-4,5-dimethyl-2,4-cyclohexadiene-1,2-dicarboxylate (21)**[19] was isolated as an oil (86% yield): ^{1}H NMR δ 7.02 (s, H-3), 3.77 and 3.65 (s, OMe), 3.62 (dd, $J_{1,6A}$ 3.2, $J_{1,6B}$ 9.5, H-1), 2.70 (AB dd, $J_{6A,6B}$ 17.3, H_A-6), 2.50 (AB dd, H_B-6), 1.82 and 1.79 (4,5-Me). Only traces of cycloadduct $\mathbf{20_R}$ were detected.

Cycloaddition 18_R + 19. The reaction needed 13 days to be completed and **di-*tert*-butyl (*R*)-4,5-dimethyl-2,4-cyclohexadiene-1,2-dicarboxylate (22)** was isolated (66% yield) as an oil: ^{1}H NMR δ 6.87 (s, H-3), 3.46 (dd, $J_{1,6A}$ 3.3, $J_{1,6B}$ 9.1, H-1), 2.61 (split AB dd, $J_{6A,6B}$ 17.5, H_A-6), 2.45 (split AB dd, H_B-6), 1.80 and 1.78 (4,5-Me), 1.50 and 1.39 (s, CMe_3).

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