Novel Heterocycloaddition Reaction of Glycals

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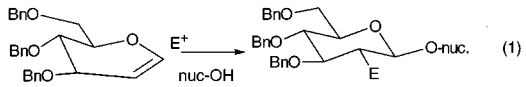
Diacyl thione species **1** has been generated and reacted in situ with both pyranoid and furanoid glycals to form novel [4 + 2] cycloadducts. Factors such as protecting groups and configuration of substituents in the glycals along with medium effects were varied to discover influences on face selectivity and reactivity. A qualitative correlation of reactivity with the HOMO−LUMO gap between the glycal (HOMO) and the heterodienic species (LUMO) is observed. In one example, the isolation of byproducts suggests that the cycloaddition may in fact be stepwise.

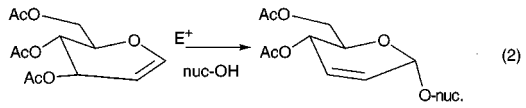
The attachment of ligands through heteroatom links to C-1 of carbohydrates, known as glycosidation or glycosyl transfer, is a field of both historic and current interest.[1] The chemistry is largely focused on creating and controlling the electrophilicity of C-1 of the carbohydrate. The concept of heterocycloaddition with glycals as a method to functionalize carbohydrates at C-1 (and C-2), as illustrated in Scheme 1, appeared to us as an attractive alternative to the "classical" methods.

Since their discovery by Fischer and Zach just before World War I,[2] glycals have evolved into significant starting materials for the simultaneous functionalization of the anomeric carbon and carbon 2 of sugars. Most glycal chemistry is initiated via electrophilic attack on its very nucleophilic enol ether double bond (eq 1).[3] A



(1)

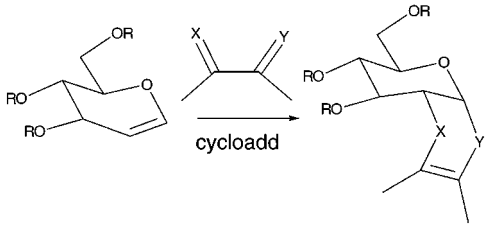
well-known electrophilic variation is induced by electrophilic attack at an allylic leaving group at C-3, followed by an SN2′-like attack of a nucleophile at C-1 (the Ferrier rearrangement, eq 2).[4] A less common and different



(2)

double bond chemistry of glycals is their participation as the allylic component in Claisen rearrangements.[5] Cycloaddition to the glycal double bond is an additional functionalization approach.[6] Examples include a [4 + 2]

Scheme 1



addition of an *o*-quinone methide (2 C−C bonds formed, eq 3),[7] a [4 + 2] addition of an isoquinolinium salt (2 C−C bonds formed, eq 4),[8] a [2 + 2] *β*-lactam synthesis (C−C at C-2 and C−N at C-1, eq 5),[9] a [4 + 2] addition of azodicarboxylate esters (C−O at C-1 and C−N at C-2 bond, eq 6),[10] a [2 + 2] addition of dichloroketene (eq 7),[11] and the work to be described below, a [4 + 2] addition of thionoketones (C−O at C-1 and C−S at C-2, eq 8).[12]

The genesis of our quest for a thionoketone reagent lay in the observation of the simplicity of carrying out the isoquinolinium salt cycloaddition (eq 4) and of its high yields of stereochemically homogeneous products.[8] This facile reaction was in marked contrast to our electrophilic method for 2-deoxy-*β*-glycosidation which required fairly sophisticated manipulation of corrosive reagents and which yielded mixtures of glycosides in most cases.[13] Thus, a search was undertaken for a diene with sulfur and oxygen at its termini so that glycals might be functionalized with heteroatoms under mild and facile cycloaddition conditions. The key diacylthione reagent **1**, generated in situ from phthalimidothiopentanedione precursor **2**, was first identified as a heterodienophile in

(1) (a) For a complete compilation of methods for preparation of *O*-disaccharides in the hexose series for1994, see: (a) Barresi, F.; Hindsgaul, O. *Modern Synthetic Methods, 1995*; Ernst, B., Leumann, C., Ed.; VCH: Basel, Switzerland, 1995; pp 281−330. (b) Barresi, F.; Hindsgaul, O. *J. Carbohydr. Chem.* **1995**, *14*, 1043−1087. (c) For a review of the widely used trichloroacetimidate method, see: Schmidt, R. R.; Kinzy, W. *Adv. Carbohydr. Chem. Biochem.* **1994**, 21−123.

(2) (a) Fischer, E.; Zach, K. *Sitzungsber. K. Preuss. Akad. Wiss.* **1913**, *16*, 311. (b) Fischer, E.; Zach, K. *Ber. Bunsen-Ges* **1914**, 311−317.

(3) For a recent review, see: Danishefsky, S. J.; Bilodeau, M. T. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1380−1419.

(4) (a) Ferrier, R. J.; Prasad, N. *J. Chem. Soc. C* **1969**, 581−586. (b) Ferrier, R. J. *Methods Carbohydr. Chem.* **1972**, *6*, 307−11.

(5) (a) Ireland, R. E.; Wilcox, C. S.; Thaisvirongs, S.; Varnier, N. R. *Can. J. Chem.* **1979**, *57*, 1743−1745. See the following reference for a complete listing of Ireland's Claisen work with carbohydrates: (b) Curran, D. P.; Suh, Y.-G. *Carbohydr. Res.* **1987**, *171*, 161−191.

(6) *Cycloaddition Reactions in Carbohydrate Chemistry*; Giuliano, R. M., Ed.; ACS Symposium Series 494; American Chemical Society: Washington, DC, 1992.

(7) (a) Franck, R. W.; John, T. V *J. Org. Chem.* **1983**, *48*, 3269. (b) Chew, S.; Ferrier, R. J.; Sinnwell, V. *Carbohydr. Res.* **1988**, *174*, 161−168.

(8) Gupta, R. B.; Franck, R. W. *J. Am. Chem. Soc.* **1989**, *111*, 7668.

(9) Chmielewski, M.; KaIuza, K.; Grodner, J.; Urbanski, R. Chapter 4 in ref 5.

(10) Leblanc, Y.; Labelle, M. Chapter 6 in ref 5.

(11) Oh, J. *Tetrahedron Lett.* **1997**, *38*, 3249−3250.

(12) For preliminary disclosures of aspects of this work, see: (a) Capozzi, G.; Franck, R. W.; Mattioli, M.; Menichetti, S.; Nativi, C.; Valle, G. *J. Org. Chem.* **1995**, *60*, 6416−6426. (b) Capozzi, G.; Dios, A.; Franck, R. W.; Geer, A.; Marzabadi, C.; Menichetti, S.; Nativi, C.; Tamarez, M. *Angew. Chemie, Int. Ed. Engl.* **1996**, *35*, 777−779.

(13) Grewal, G.; Kaila, N.; Franck, R. W.. *J. Org. Chem.* **1992**, *57*, 2084−2092.

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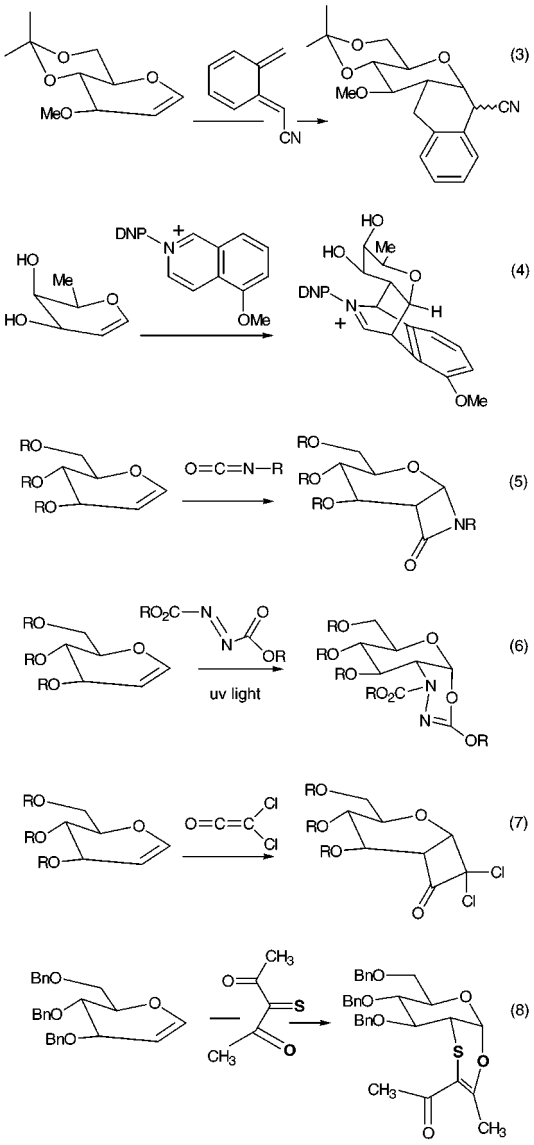
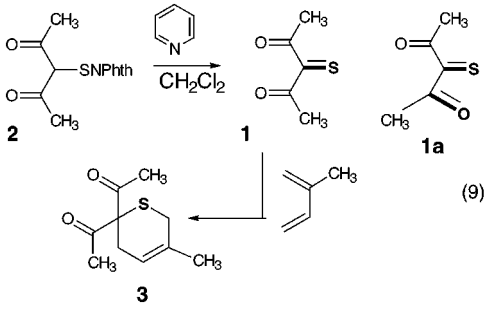


a high-yield trapping of isoprene to form thiapyran **3** (eq 9).[14] Simply by picturing diacylthione in a gauche (**1a**)



rather than anti conformation, we were able to conceive of it as our desired heterodiene. Its utility in cycloadditions to glycals is described below.

Results

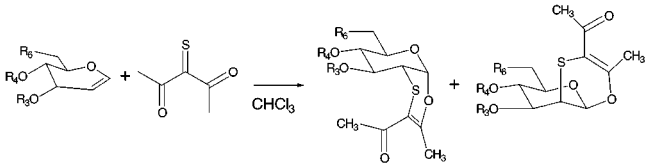
The cycloadditions are carried out by mixing glycal and thione precursor **2** in either chloroform or methylene chloride at room temperature, adding either pyridine or lutidine as an acid scavenger, and following the reaction progress by NMR and/or TLC. Product formation is slow, but the reaction mixtures are quite clean. Workup normally consists of a basic wash to remove phthalimide and an acid wash to removed the pyridine or lutidine, followed by flash chromatography to separate the cycloadducts from unreacted glycal and from residual impurities carried through from the preparation of precursor **2**. Table 1 shows the glycal reactant, the structures of the products, the approximate $t_{1/2}$ for the reaction, and the computed difference (in eV) between the HOMO of the glycal and the LUMO of thiono species **1**. The stereochemistry of the cycloadducts is easily deduced by identifying the protons at C-1, C-2, and C-3 along with their coupling constants. X-ray crystallography analysis of adducts **13**, **17**, and **23** (Table 2) served to reinforce the NMR assignments.

Table 1. Results of Cycloadditions of 3-Thionopentanedione 1 (LUMO, − 1.62 eV)

entry	dienophile	HOMO-LUMO gap apparent rate	adduct	yield
1	**10** (-9.53 ev)	7.91 ev slow t 1/2 3d	**11**	80%
2	**12** (-9.53 ev)	7.91 ev slow t 1/2 3d	**13**	54%
3	**14** (-9.17 ev)	7.55 ev moderate t 1/2 12h	**15**	73%
4	**16** (-9.50 ev)	7.88 ev slow t 1/2 3d	**17**	68%
5	**18** (-9.74 ev)	8.12 ev no rxn		
6	**19** (-9.39 ev)	7.77 ev moderate t 1/2 1d	**20**	74% 3.6α / 1 β
7	**21** (-9.35 ev)	7.73 ev moderate t 1/2 1 d	**22**	42% 1α / 3β

(14) Capozzi, G.; Nativi, C.; Menichetti, S.; Rosi, A.; Valle, G. *Tetrahedron* **1992**, *48*, 9023−9029.

Table 2. Results of Cycloadditions of 3-Thionopentanedione: Protecting Group Variables



entry				isolated yield (%)[a]
1	R_3,R_4 = Bn, R_6 = BnO **(10)**	95 **(11)**	05 **(23)**	83
2	R_3 = H, R_4 = Bn, R_6 = BnO **(24)**	68 **(25)**	32 **(26)**	87
3	R_3 = Bn, R_4 = H, R_6 = BnO **(27)**	83 **(28)**	17 **(29)**	41
4	R_3,R_4 = Bn, R_6 = HO **(30)**	86 **(31)**	14 **(32)**	48
5	R_3 = H, R_4,R_6 = isopropylidene **(12)**	88 **(13)**	12 **(33)**	58
6	R_3 = SEM, R_4 = Bn, R_6 = H **(34)**	75 **(35)**	25 **(36)**	75

[a] The remaining organic material is unreacted glycal.

Table 3. Results of Cycloadditions of 3-Thionopentanedione: Solvent Variables

entry					isolated yield
1	R_3,R_4 = Bn, R_6 = BnO **(10)**	$CHCl_3$	95 **(11)**	05 **(23)**	83[a]
2	**(10)**	DMSO	72 **(11)**	28 **(23)**	59[a]
3	**(10)**	DMF	68 **(11)**	32 **(23)**	*b*
4	**(10)**	THF	86 **(11)**	14 **(23)**	*b*
5	**(10)**	*t*-BuOH	77 **(11)**	23 **(23)**	*b*
6	**(10)**	MeOH	65 **(11)**	35 **(23)**	28[c]
7	R_3 = H, R_4 = Bn, R_6 = BnO **(24)**	$CHCl_3$	68 **(25)**	32 **(26)**	87[a]
8	**(24)**	DMF	67 **(25)**	33 **(26)**	60[a]

[a] The remaining material is unreacted glycal. [b] Not isolated, ratios determined by NMR. [c] 50% yield of methyl glycosides, see text.

Table 2 records the effect of protecting group variation on face selectivity of the cycloaddition of **1** and glucals where all substituents are equatorial. Table 3 records the face selectivity outcomes as a function of solvent. In both tables, only cycloadduct product ratios are recorded. With one exception, the other components in the reaction mixture are starting glycal and materials derived from the thionopentanedione. Notably, the reaction described in entry 6, Table 3, with methanol as solvent, afforded two other products, namely, methyl glycosides, the significance of which will be discussed below.

Discussion

In general, substituent and solvent effects on stereoselectivity are small. The results in Table 1 suggest that the obvious influence on the face selectivity of the cycloaddition is the steric effect of axial substituents on the glycal. In the ribal series, where the 3-substituent is not truly axial, the size of the blocking group on the oxygen has an effect. In the all-equatorial glucal series, below-plane selectivity is observed. This is the general rule for attacks on glucal. An apparent small effect of size variation of the C-3 group from benzyloxy to hydroxy might be invoked (entry 2, Table 2), but the data in entries 5 and 6 of Table 2 are not supportive. In Table 3, the solvent effects on face selectivity are small or nonexistent. The effect of solvent on rate is small, with the largest effect observed, about a factor of 2, with H-bond donor solvents, *t*-BuOH and MeOH. Somewhat larger solvent effects have been noted with other thionocarbonyl species that we have studied. It should be noted that the effect of solvent on the Diels−Alder reaction is a matter of intense study, with most of the focus dealing with overall rate acceleration.[15] There have also been studies where exo−endo selectivities have been an issue. However, the effect of solvent on diastereofacial selectivity has not been addressed. The number of data points, from this and related work, and the magnitude of the effect are too limited for us to offer any rationale. As a control, it has been ascertained that the isomer ratios are not due to reversibility of cycloaddition. We simply record that, for yield optimization purposes, solvent and blocking group effects should not be overlooked. It is also worth noting that carbohydrate hydroxyls need not be blocked at all.

The rate of cycloaddition appears to be a function of the HOMO−LUMO gap between the glycal and the diacylthione. In the one case (entry 5 Table 1) where the gap exceeded 8 eV, no reaction product was detected. On the other hand, entry 3 (Table 1), with reactants having the smallest gap, produces the fastest rate. Sustman has recently demonstrated an excellent correlation of rates versus the reciprocal of the HOMO−diene/LUMO−dienophile difference in a Diels−Alder reaction with normal polarity.[16] The energy gaps computed and the rates observed for our system are in qualitative agreement with those reported by Sustman. Our LUMO value for diacylthione is taken for its minimum energy conformation. This conformation has a dihedral angle between the thiocarbonyl and the carbonyl of 50°. One would guess that the optimum dihedral angle for cycloaddition would be 0°, where the LUMO is quite a bit lower. However, the conformational energy of this 0° conformation is so high that it would not be populated to a significant extent.

An attempt was made to model the transition state of the cycloaddition.[17] For three model reactions shown in Figure 1, we were able to locate structures, whose geometries are plotted in the figure, with single imaginary frequencies; structures we thus assign as transition states. It can be seen in the simplest case of the addition of ethylene to thionoglyoxal, the transition state has the appearance of a normal cycloaddition, with roughly equal lengths for the forming C−O and C−S bonds. In cases where the dienophile or the diene are substituted to resemble the experimental examples, the transition states are still cycloaddition-like, but the forming C−S bond is much shorter, really approaching the final bond length of the product. However, since starting materials are quite polarized, this unequal bond length is not unexpected. In the case where we examined the combination of both a polarized diene and a polarized dienophile, we were unable to locate a cycloaddition transition state. Our inital geometries usually collapsed to structures where the C−S bond was essentially fully

(15) van der Wel, G. K.; Wijnen, J. W.; Engberts, J. B. F. N. *J. Org. Chem.* **1996**, *61*, 9001−9005.
(16) Sustman, R.; Siangouri-Feulner, I. *Chem. Ber.* **1993**, *126*, 1241−1245.
(17) The AM1 semiempirical molecular orbital method implemented by the Spartan software package, version 3.1.3, was used for all calculations.

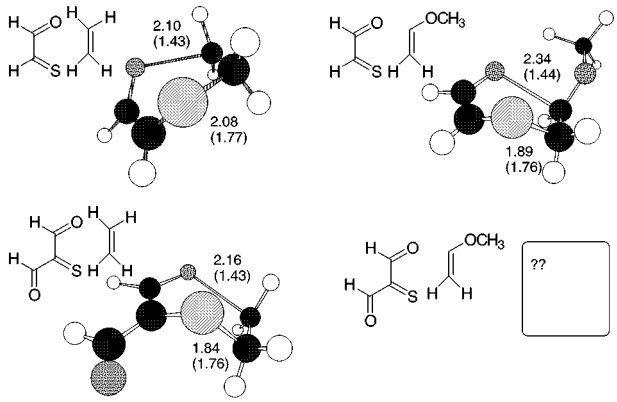
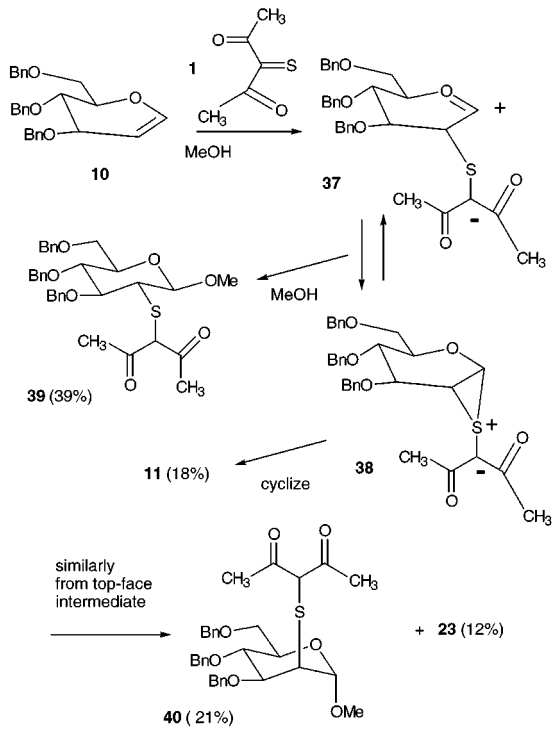


Figure 1. Chem3D$^+$ representations of computed transitions states for concerted cycloadditions for the reactants (shown in 2D) with TS bond lengths and product bond lengths (in parentheses).

Scheme 2



formed and the computed solution did not have a single imaginary frequency. Alternately, the two components of the cycloaddition simply moved away from each other to produce very unreasonable structures that were not transition states. This computational "discontinuity" from the simpler cases suggested to us that the mechanism might not be a true cycloaddition but might involve a charged intermediate.

Hence, the outcome of our cycloaddition reaction in methanol as solvent (Table 3, entry 6) is telling. Along with the bottom- (**11**) and top-face (**23**) cycloadducts shown in the tables, we also obtained methyl glycosides **39** and **40.** The ratio of adducts to glycosides before chromatography is 1/2.5 (Scheme 2). The ratio of bottom/top cycloadducts is 1.5/1 whereas the ratio of derived glycosides is 1.25/1. This result suggests that the cycloaddition (for the bottom-face) might proceed via the epithiosulfonium species **37** or its open oxonium ion isomer **38**.[18] Either could then rearrange to cycloadduct or be intercepted by methanol. The related intermediate top-face episulfonium species (not illustrated) and mechanism would hold for derived materials **23** and **40**. The slight difference in top/bottom ratios of cycloadducts and glycosides suggests slight differences between the diastereomers in rates of rearrangement versus methanol trapping. It is tempting to extrapolate from the methanol result that our cycloaddition is in fact a two-step process in every solvent; but at this time, there is no experiment which can support this generalization.

In summary, a novel cycloadditive functionalization of glycals by 3-thionopentanedione has been discovered. The virtue of the new reaction is its mildness and the fact that it is in a reactivity manifold orthogonal to most carbohydrate chemistry. The reaction is normally highly stereoselective. The ease of preparation of the novel heterodiene has led to the preparation of other thiono species with similar behavior.[19] The heterocycle formed from the cycloaddition also displays some interesting chemistry in its own right.[20] These newer developments coupled with the results described here serve to validate the original cycloaddition concept as presented in Scheme 1.

Experimental Section

General Information. ^{1}H and ^{13}C spectra were recorded in $CDCl_3$ solutions on a at 300 and 75 MHz, respectively. In some cases, 500 MHz ^{1}H spectra were obtained. The ^{1}H chemical shifts are reported in ppm downfield from Me_4Si. The ^{13}C chemical shifts are reported in ppm relative to the center line of $CDCl_3$ (77.0 ppm). Optical rotations were recorded on an automatic polarimeter under standard conditions. Infrared spectra were recorded on an FTIR. Melting points are uncorrected. Medium resolution mass spectra were obtained using a direct exposure probe and CI (NH_3) ionization methods on a quadropole instrument.

All reactions were performed under an inert atmosphere. Solvents were dried and distilled prior to use: THF from sodium/benzophenone ketyl, CH_2Cl_2 and $CHCl_3$ from P_2O_5, CH_3CN from CaH_2, and *t*-BuOH from Na. Anhydrous methanol, DMF, DMSO, 2,4-pentanedione, and 2,6-lutidine were purchased from Aldrich Chemical Co. (Milwaukee, WI). 3,4,6-Tri-*O*-benzyl-D-galactal,[21] 3,4,6-tri-*O*-benzyl-D-allal,[22] and 4,6-*O*-isopropylidene-D-glucal[23] were prepared using literature procedures. 3,4-Di-*O*-benzyl-D-glucal was prepared as described by Blackburne.[24] Thiophthalimide **2** was prepared as reported elsewhere.[25] Molecular sieves (3A) were purchased from Aldrich and were powdered and activated prior to use. Crude products were purified by flash column chromatography on silica gel (Merck, 230−400 mesh).

(18) It must be noted that semiempirical MO calculations suggest that in the pyranose series, the episulfonium species is somewhat less stable than the ring-opened thio-oxonium form: (a) Jones, D. K.; Liotta, D. C. *Tetrahedron Lett.* **1993**, *34*, 7209−7212. (b) Jones, D. K.; Liotta, D. *Adv. Mol. Model* **1995**, *3*, 67.

(19) (a) Capozzi, G.; Falciani, C.; Menichetti, S.; Nativi, C.; Franck, R. W. *Tetrahedron Lett.* **1995**, *36*, 6755−6758. (b) Win, W. W.; Franck, R. W. *J. Org. Chem.* **1997**, *62*, 4510−4512. (c) Capozzi, G.; Falciani, C.; Franck, R. W.; Menichetti, S.; Nativi, C.; Raffaelli, B. *Chem. Eur. J.*, in press.

(20) (a) Marzabadi, C. H.; Franck, R. W. *J. Chem. Soc., Chem. Commun.* **1996**, 2651−2652. (b) Marzabadi, C. H.; Franck, R. W. *J. Org. Chem.* **1998**, *63*, 2197−2208. (c) Capozzi, G.; Mannocci, F.; Menichetti, S.; Nativi, C.; Paoletti, S. *J. Chem. Soc., Chem. Commun.* **1997**, 2291−2292.

(21) Kozikowski, A. P.; Lee, J. *J. Org. Chem.* **1990**, *55*, 863.

(22) Witman, M. D.; Halcomb, R. L.; Danishefsky, S. J.; Golik, J.; Vyas, D. *J. Org. Chem.* **1990**, *55*, 1979.

(23) Fraser-Reid, B.; Walker, D. L.; Tam, S. Y.; Holder, N. L. *Can. J. Chem.* **1973**, *51*, 3950.

(24) Blackburne, I. D.; Fredericks, D. M.; Guthrie, R. D. *Aust. J. Chem.* **1976**, *29*, 381.

(25) (a) Capozzi, G.; Nativi, C.; Menichetti, S.; Rosi, A.; Valle, G. *Tetrahedron* **1992**, *48*, 9023. (b) Reference 19b.

General Procedure for Cycloaddition Reactions. 2,6-Lutidine (1.0 equiv) was added to a suspension of glycal (1.0 equiv), thiophthalimide **2** (1−2 equiv), and powdered, activated, 3A molecular sieves (typically, a portion equal in weight to the weight of the combined reactants) in dry solvent (0.5−1.0 mM). For ribal derivatives, it was necessary to add lutidine prior to addition of the thiophthalimide **2** in order to prevent formation of undesired furan derivatives. The mixture was stirred at room temperature, and the reaction progress was monitored at intervals by taking an aliquot from the suspension for analysis by ^{1}H NMR ($CDCl_3$). When the composition of the reaction mixture showed no additional change (3−7 days), the reaction mixture was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with CH_2Cl_2 (3×). The organics were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude mixtures were chromatographed (SiO_2) using gradients of ethyl acetate in petroleum ether. Removal of residual phthalimide impurities from the chromatographed fractions was accomplished by stirring with 0.1 M NaOH, followed by extraction with ethyl acetate.

Adduct 11 from 3,4,6-Tri-*O*-benzyl-D-glucal (10) with 3-(Phthalimidosulfenyl)-2,4-pentanedione (2). 3-(Phthalimidosulfenyl)-2,4-pentanedione (1.32 g, 4.8 mmol, 2.0 equiv) and tri-*O*-benzyl-D-glucal (1.01 g, 2.4 mmol, 1 equiv) in 10 mL of dry $CHCl_3$ under N_2 atmosphere with powdered 3A molecular sieves (activated, 0.5 g) plus dry 2,6 lutidine (0.28 mL, 2.4 mmol, 1 equiv) gave 1.10 g (83%) of 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-3,4,6-tri-*O*-benzyl-2-deoxy-2-thio-α-D-glucopyranoside (**11**) plus recovered starting material (tribenzyl-D-glucal 0.1555 g, 15.4%): mp 115−116 °C, identical to that reported in ref 12a; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 6H), 3.23 (dd, J = 3.1, and 10.5 Hz, 1H (H_2)), 3.59−3.97 (m, 5H), 4.51−4.92 (m, 6H), 5.62 (d, J = 3 Hz, 1H (H_1)), 7.10−7.40 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 22.5, 31.0, 42.5, 69.0, 73.9, 74.9, 76.5, 77.5, 78.6, 79.5, 97.3, 128−130 (18 C), 138.6, 138.7, 160.5; IR($CDCl_3$, cm^{-1}) 1678.

Isolation of Adduct 23 from 3,4,6-Tri-*O*-benzyl-D-glucal (10) with 3-(Phthalimidosulfenyl)-2,4-pentanedione (2)−DMSO as Solvent. 3-(Phthalimidosulfenyl)-2,4-pentanedione (2.02 g, 5.3 mmol, 2.0 equiv) and tri-*O*-benzyl-D-glucal (1.11 g, 2.7 mmol, 1 equiv) in 15 mL of dry DMSO under N_2 atmosphere with powdered 3A molecular sieves and dry 2,6-lutidine (0.32 mL, 2.7 mmol, 1 equiv) over a 7 day period afforded 241 mg of 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-3,4,6-tri-*O*-benzyl-2-deoxy-2-thio-β-D-mannopyranoside (**23**, 17% of total yield) and 611 mg of **11** (42% of total yield). The total yield, including top and bottom cycloadduct, was 59%. The amount of starting material (tri-benzyl-D-glucal) recovered was 0.279 g (25%). For **23**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.20 (s, 3H), 2.30 (s, 3H), 3.56 (m, J = 9.3, 3, 1H), 3.65 (dd, J = 1.2, 4.2, 1H (H_2)), 3.68 (m, J = 2.4, 1.8, 4.2, 2H), 3.89 (dd, J = 4.5, 8.4, 1H), 3.96 (dd, J = 9, 8.7, 1H), 4.4−4.7 (m, 4H), 4.7 (AB quartet, J = 10.8, 11.4, 2H), 5.1 (d, J = 0.9, 1H), 7.1−7.40 (m, 15H); ^{13}C NMR δ 21.4, 29.3, 41.2, 68.9, 71.0,73.5, 73.7, 75.2, 80.2, 92.3, 105.6, 127.5−128.5 (15 C), 137.2−138.2 (3 C), 155.6, 195.5; IR (cm^{-1}) 1679; M/S m/z 564.

Cycloadduct of 4,6-*O*-Isopropylidene-D-glucal and 3-(Phthalimidosulfenyl)-2,4-pentanedione (13). 4,6-Isopropylidene-D-glucal (**12**, 0.17 g, 0.9 mmol), thiophthalimide (**2,** 0.5 g, 1.8 mmol), and 2,6-lutidine (0.1 mL, 0.9 mmol) in $CHCl_3$ (3.8 mL) gave 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-4,6-*O*-isopropylidene-2-deoxy-2-thio-α-D-glucopyranoside (**13**) as a solid (0.15 g, 0.5 mmol, 54%, 5 days) following column chromatography (SiO_2, 33−50% EtOAc in petroleum ether): mp 142−144 °C (Et_2O/hexanes); $[\alpha]_D$ + 49.45° (c 0.64, $CHCl_3$); IR (thin film) 3446, 2994, 1683, 1558, 1374, 1234, 1130, 1038 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.60 (d, 1H, J = 3.3 Hz), 3.96−3.68 (m, 5H), 3.17−3.12 (m, 1H), 2.63 (s, 1H), 2.35 (s, 6H), 1.55 (s, 3H), 1.44 (s, 3H); ^{13}C NMR δ 195.3, 159.9, 101.8, 100.1, 95.9, 74.4, 67.0, 65.5, 61.8, 42.6, 30.3, 28.9, 19.1, 19.0; MS (DP/PCI) m/z (rel intensity) 334 (M + NH_4) (100), 317 (M + H) (82). Anal. Calcd for $C_{14}H_{20}O_6S$: C, 53.15; H, 6.37; S, 10.14. Found: C, 53.09; H, 6.57; S, 10.15.

Cycloadduct of 3,4,6-Tri-*O*-benzyl-D-galactal and 3-(Phthalimidosulfenyl)-2,4-pentanedione (15). 3,4,6-Tri-*O*-benzyl-D-galactal (**14**, 0.48 g, 1.2 mmol), **2** (0.64 g, 2.3 mmol), and 2,6-lutidine (0.14 mL, 1.2 mmol) in $CHCl_3$ (4.7 mL) afforded 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-3,4,6-tri-*O*-benzyl-2-deoxy-2-thio-α-D-galactopyranoside (**15**) as an oil (0.46 g, 0.8 mmol, 73%, 4 days) following column chromatography (SiO_2, 20% EtOAc/petroleum ether): $[\alpha]_D$ + 30.3° (c = 0.8; $CHCl_3$); IR (thin film) 1674 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.36−7.26 (m, 15H), 5.62 (d, 1H, J = 3.0 Hz), 4.89 (d, 1H, J = 13.8 Hz), 4.71−4.39 (m, 5H), 4.13−4.07 (m, 1H), 4.00 (d, 1 H, J = 1.2 Hz), 3.73 (dd, 1H, J = 10.8, 3.0 Hz), 3.60 (dd, 2 H, J = 6.9, 1.8 Hz), 3.53−3.44 (m, 1H), 2.29 (s, 3H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 195.4, 159.3, 138.2, 137.7, 137.5, 128.5, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 101.9, 96.7, 75.0, 73.7, 73.6, 73.3, 72.9, 71.8, 68.4, 38.0, 30.1, 29.7; MS m/z 564 (M + NH_4). Anal. Calcd for $C_{32}H_{34}O_6S$: C, 70.31; H, 6.52; S, 5.87. Found: C, 69.94; H, 6.64; S, 5.87.

Cycloadduct of 3,4,6-Tri-*O*-benzyl-D-allal and 3-(Phthalimidosulfenyl)-2,4-pentanedione (17). 3,4,6-Tri-*O*-benzyl-D-allal (**16**, 0.38 g, 0.9 mmol), **2** (0.5 g, 1.8 mmol), and 2,6-lutidine (0.1 mL, 0.9 mmol) in $CHCl_3$ (3.8 mL) gave 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-3,4,6-tri-*O*-benzyl-2-deoxy-2-thio-β-D-altropyranoside 17 (0.34 g, 0.6 mmol, 68%, 3 days) as a white solid following column chromatography (SiO_2, 33−50% EtOAc/petroleum ether): mp 68−71 °C (Et_2O/hexanes); $[\alpha]_D$ + 4.0° (c 0.02, $CHCl_3$); IR (thin film) 1678 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.30−7.25 (m, 15H), 5.65 (d, 1H, J = 1.8 Hz), 4.65−4.50 (m, 6H), 4.28 (m, 1H), 4.09 (dd, 1H, J = 7.2, 3.0 Hz), 3.82 (dd, 1H, J = 5.4, 3.0 Hz), 3.75−3.60 (m, 2H), 3.53 (dd, 1H, J = 5.7, 1.8 Hz), 2.30 (s, 3H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 195.1, 157.2, 138.1, 137.7, 137.5, 128.4, 127.9, 127.6, 93.3, 93.2, 76.1, 73.5, 72.8, 72.3, 72.2, 71.8, 69.5, 39.1, 29.6, 21.9; MS m/z 564 (M + NH_4). Anal. Calcd for $C_{32}H_{34}O_6S$: C, 70.31; H, 6.52; S, 5.87. Found: C, 70.23; H, 6.44; S, 6.11.

Preparation of 3,6- and 4,6-Di-*O*-benzyl-D-glucal. To a suspension of NaH (1.73 g, 4.3 mmol) in DMF (50 mL) was added D-glucal (3.16 g, 22 mmol) portionwise as a solution in DMF (25 mL). After 40 min of stirring at room temperature, the mixture was cooled to 5 °C and tetra-*N*-butylammonium iodide (0.31 g) and benzyl bromide (5.2 mL) were added. The mixture was slowly warmed to room temperature (2 h) and was stirred an additional 48 h. The reaction was quenched with water (10 mL), and the mixture was extracted with CH_2Cl_2 (3×, 75 mL). The combined organic fractions were extracted with additional water (5×, 100 mL) and with brine (100 mL) to afford after concentration in vacuo a mixture of glucals. Column chromatography (SiO_2; 15−40% ethyl acetate in petroleum ether) gave as the major products 3,4,6-tri-*O*-benzyl-D-glucal (**10**, 1.65 g) and 4,6-di-*O*-benzyl-D-glucal (**24**, 0.96 g): IR (thin film) 3409, 1647 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.29−7.19 (m, 10H), 6.33 (dd, 1H, J = 6.0, 0.9 Hz), 4.74−4.48 (m, 5H), 4.28−4.26 (m, 1H), 3.93−3.89 (m, 1H), 3.75−3.74 (m, 1H), 3.61 (dd, 1H, J = 8.9, 6.3 Hz); ^{13}C NMR δ 144.6, 128.5, 128.4, 127.9, 127.8, 127.7, 102.7, 97.4, 77.3, 76.8, 73.7, 73.6, 69.1, 68.9; MS m/z 344 (M + NH_4). Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.52; H, 6.94. 3,6-Di-*O*-benzyl-D-glucal[26] (**27**, 0.08 g) was also obtained.

Reaction of 4,6-Di-*O*-benzyl-D-glucal with 3-(Phthalimidosulfenyl)-2,4-pentanedione. $CHCl_3$ as solvent: Glucal **24** (0.087 g, 0.27 mmol), thiophthalimide (**2**, 0.35 mmol), and 2,6-lutidine (0.03 mL, 0.27 mmol) in $CHCl_3$ (1.8 mL) after 6 days at room temperature afforded following chromatography (SiO_2; 25−50% EtOAc in petroleum ether) the α-gluco cycloadduct 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-4,6-tri-*O*-benzyl-2-deoxy-2-thio-α-D-glucopyranoside (**25**) as an oil (0.08 g, 63%): ^{1}H NMR ($CDCl_3$) δ 7.54−7.21 (m, 10H), 5.21 (d, 1H, J = 3.3 Hz), 4.83 (d, 1H, J = 11.1 Hz), 4.67 (d, 1H, J = 12.3 Hz), 4.58 (d, 1H, J = 10.8 Hz), 4.55 (d, 1H, J = 12.3 Hz), 3.95 (dd, 1H, J = 6.9, 2.1 Hz), 3.81 (dd, 1H, J = 11.1, 3.3 Hz), 3.74−3.70 (m, 2H), 3.13 (dd, 1H, J = 10.2, 3.0 Hz), 2.69 (s, 1H), 2.27 (s, 3H), 2.05 (s, 3H); MS (DEP/CI) m/z 474 (M + NH_4) 344. The β-manno cycloadduct 1-*O*,2-*S*-(2-acetyl-1-

(26) Danishefsky, S. J.; Behar, V.; Randolph, J. T.; Lloyd, K. O. *J. Am. Chem. Soc.* **1995**, *117*, 5701.

methyl-1,2-ethenediyl)-4,6-tri-*O*-benzyl-2-deoxy-2-thio-*β*-D-mannopyranoside (**26**) was also obtained as a white powder (0.03 g, 24%): ^{1}H NMR ($CDCl_3$) δ 7.29−7.16 (m, 10H), 5.17 (d, 1H, J = 0.9 Hz), 4.66−4.49 (m, 4H), 3.99−3.97 (m, 2H), 3.78−3.75 (m, 2H), 3.56−3.53 (m, 2H), 2.27 (s, 3H), 2.24 (s, 3H); MS *m*/*z* 474 (M + NH_4).

DMF as solvent: Glucal **24** (0.05 g, 0.15 mmol), thiophthalimide (**2**, 0.15 mmol), and 2,6-lutidine (0.02 mL, 0.15 mmol) in DMF (0.9 mL) were stirred at room temperature for 5 days. Column chromatography on the crude reaction mixture using conditions described above afforded recovered glycal **24** (0.01 g), α-gluco cycloadduct **25** (0.03 g, 44%), and *β*-manno cycloadduct **26** (0.01 g, 16%).

The diastereomeric cycloadducts **25** and **26** were benzylated under standard conditions[27] and afforded derivatives with properties consistent with tri-*O*-benzylated adducts **11** and **23**.

Reaction of 3,6-Di-*O*-benzyl-D-glucal with 3-(Phthalimidosulfenyl)-2,4-pentanedione. Glucal **27** (0.07 g, 0.23 mmol), thiophthalimide (**2**, 0.15 mmol), and 2,6-lutidine (0.03 mL, 0.23 mmol) in $CHCl_3$ (1.2 mL) were stirred at room temperature for 4 days. Column chromatography on the crude reaction mixture (SiO_2; 20−30% EtOAc in petroleum ether) gave recovered glycal **27** (0.02 g, 19%), α-gluco cycloadduct 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-3,6-tri-*O*-benzyl-2-deoxy-2-thio-α-D-glucopyranoside (**28**, 0.02 g, 34%) as an oil, and *β*-manno cycloadduct 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-3,6-tri-*O*-benzyl-2-deoxy-2-thio-*β*-D-mannopyranoside (**29**, 0.005 g, 7%) as an oil. For **28**: ^{1}H NMR ($CDCl_3$) δ 7.31−7.19 (m, 10H), 5.52 (d, 1H, J = 3.0 Hz), 4.90 (d, 1H, J = 11.1 Hz), 4.70 (d, 1H, J = 11.1 Hz), 4.56 (d, 1H, J = 12.3 Hz), 4.54 (d, 1H, J = 12.0 Hz), 3.85 (dd, 1H, J = 9.0, 4.5 Hz), 3.75−3.63 (m, 3H), 3.40 (dd, 1H, J = 9.6, 9.3 Hz), 3.11 (dd, 1H, J = 10.8, 3.0 Hz), 2.26 (s, 6H); MS *m*/*z* 474 (M + NH_4). For **29**: ^{1}H NMR ($CDCl_3$) δ 7.40−7.26 (m, 10H), 5.22 (d, 1H, J = 1.2 Hz), 4.84 (d, 1H, J = 11.7 Hz), 4.65−4.55 (m, 3H), 4.14−4.11 (m, 1H), 3.82−3.77 (m, 2H), 3.70 (dd, 1H, J = 4.5, 1.2 Hz), 3.64 (dd, 1H, J = 9.6, 4.5 Hz), 2.78 (d, 1H, J = 2.1 Hz), 2.35 (s, 3H), 2.30 (s, 3H); MS *m*/*z* 474 (M + NH_4). The diastereomeric cycloadducts **28** and **29** were benzylated under standard conditions and afforded derivatives with properties consistent with tri-*O*-benzylated adducts **11** and **23**.

Reaction of 3,4-Di-*O*-benzyl-D-glucal with 3-(Phthalimidosulfenyl)-2,4-pentanedione. A mixture of glucal **30** (0.09 g, 0.28 mmol), thiophthalimide (**2**, 0.28 mmol), and 2,6-lutidine (0.033 mL, 0.28 mmol) in $CHCl_3$ (1.6 mL) was stirred for 3 days at room temperature. Column chromatography on the crude product mixture (20−40% EtOAc in petroleum ether) gave starting glycal **30** (0.02 g) and then α-gluco cycloadduct 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-3,4,-tri-*O*-benzyl-2-deoxy-2-thio-α-D-glucopyranoside (**31**, 0.054 g, 42%) as a clear oil: ^{1}H NMR ($CDCl_3$) δ 7.31−7.18 (m, 10H), 5.52 (d, 1H, J = 3.0 Hz), 4.86−4.76 (m, 3H), 4.63 (d, 1H, J = 10.8 Hz), 3.82−3.75 (m, 3H), 3.61 (ddd, 2H, J = 19.2, 9.6, 9.0 Hz), 3.11 (dd, 1H, J = 9.9, 3.0 Hz), 2.24 (s, 6H); MS *m*/*z* 474 (M + NH_4). The *β*-manno cycloadduct, 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-3,4-tri-*O*-benzyl-2-deoxy-2-thio-*β*-D-mannopyranoside (**32**, 0.01 g, 6%) was also obtained as an inseparable mixture with the major cycloadduct **31**: ^{1}H NMR ($CDCl_3$) δ 5.23 (d, 1H, $J_{1,2}$ = 1.2 Hz) (C1−H). The mixture of diastereomeric cycloadducts **31** and **32** was benzylated under standard conditions and afforded derivatives with properties consistent with tri-*O*-benzylated adducts **11** and **23**.

Reaction of 3-((((Trimethylsilyl)ethyl)oxy)methyl)-4-*O*-benzyl-D-rhamnal with 3-(Phthalimidosulfenyl)-2,4-pentanedione. 3-(Phthalimidosulfenyl)-2,4-pentanedione (0.3928 g, 0.88 mmol, 2.0 equiv) in 2.2 mL of dry $CHCL_3$ under N_2 atmosphere with powdered 4A molecular sieves (activated, 0.144 g) in a dry 25-mL flask plus rhamnal (**34**, 0.1516 g, 0.43 mmol, 1 equiv) and dry 2,6-lutidine (0.05 mL, 0.43 mmol, 1 equiv) gave, after 24 h, 0.1531 g (75%) of a mixture of 109.2 mg (56%) of 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-3-((((trimethylsilyl)ethyl)oxy)methyl)-4-*O*-benzyl-2,6-dideoxy-2-thio-α-D-glucopyranoside (**35**) and 43.6 mg (19%) of 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-3-((((trimethylsilyl)ethyl)oxy)-methyl)-4-*O*-benzyl-2,6-dideoxy-2-thio-*β*-D-mannopyranoside (**36**).

For **35** (bottom-face diastereomer): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.00 (s, 3H), 0.02 (s, 3H), 0.03 (s, 3H), 0.92 (m, 2H), 1.34 (d, J = 6.3 Hz, 3H), 2.32 (s, 3H), 2.35 (s, 3H), 3.14 (dd, J = 3, 10.5 Hz, 1H) 3.23 (dd, J = 9.3, 8.1 Hz, 1H), 3.65 (dd, J = 10.8, 10.5 Hz, 1H), 3.66−3.80 (m, 3H), 3.95 (q, J = 6.4 Hz, 1H), 4.7, 4.9 (AB quartet, J = 10.8, 11.1 Hz, 2H), 4.97 (s, 2H), 5.57 (dd, J = 3.3 Hz, 1H), 7.3−7.4 (m, 5H); ^{13}C NMR δ −1.2, 0.2, 18.1, 18.2, 21.8, 30.4, 42.3, 66.8, 69.7, 75.2, 75.6, 76.6, 77.95, 84.5, 96.0, 96.6, 102.5, 128.0, 128.2, 128.7, 137.95, 159.7, 195.4; IR (cm^{-1}) 3036, 2966, 2907, 1666, 1555, 1355, 1249, 1132, 1055, 932, 826, 749, 691; MS *m*/*z* 498; [α]$_D$ (*c* 0.11, $CHCl_3$) +120.2°. Anal. Calcd for $C_{24}H_{36}O_6SSi$: C, 60.0; H, 7.5; S, 6.7. Found: C, 59.32; H, 7.59; S, 6.43. For **36** (top-face diastereomer): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.00 (s, 6H), 0.04 (s, 3H), 0.96 (m, 2H), 1.4 (d, J = 6 Hz, 3H), 2.33 (s, 3H), 2.35 (s, 3H), 3.5−4.0 (m, 4H), 4.1 (dd, J = 4.5, 4.5 Hz, 1H), 4.64 (AB quartet, J = 10.8 Hz, 1H), 4.7−5.0 (m, 3H), 5.25 (dd, J = 1.2 Hz, 1H), 7.3−7.4 (m, 5H).

Reaction of 3,4,6-Tri-*O*-benzyl-D-glucal (10) with 3-(Phthalimidosulfenyl)-2,4-pentanedione (2). Methanol as the solvent: A sample of glucal **10** (0.41 g, 0.98 mmol), thiophthalimide (**2**, 1.2 mmol), and 2,6-lutidine (11 mL, 0.98 mmol) in dry MeOH (6 mL) after 3 days showed by ^{1}H NMR ($CDCl_3$) complete consumption of tri-*O*-benzyl-D-glucal and a mixture of α-gluco cycloadduct **11**, *β*-manno cycloadduct **23**, *β*-gluco methyl glycoside **39**, and α-manno methyl glycoside **40** (1.5:1:3.5:2.8).The reaction mixture was worked up as previously described and repeatedly chromatographed (SiO_2; 10% EtOAc/petroleum ether) to afford **11** and **39** in purified form, whereas **23** and **40** were present as components of mixtures: α-gluco cycloadduct **11** (0.11 g, 21%), *β*-manno cycloadduct **23** (0.04 g, 6.5%), *β*-gluco methyl glycoside **39** (0.16 g, 29%), and α-manno methyl glycoside **40** (0.12 g, 21%).

Methyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-thio-3-(pentane-2,4-dione)-*β*-D-glucopyranose (39): IR (thin film) 1574 cm^{-1}: ^{1}H NMR ($CDCl_3$) δ 7.41−7.16 (m, 15H), 4.91−4.78 (m, 3H), 4.64−4.52 (m, 3H), 4.34 (d, 1H, 8.3 Hz), 3.73−3.63 (m, 4H), 3.49−3.37 (m, 1H), 3.43 (s, 3H), 2.72 (dd, 1H, J = 8.4, 13.5 Hz), 2.40 (s, 6H); MS (DEP/CI) *m*/*z* 596 (M + NH_4).

Reaction of the Tri-*O*-benzylglucose α-Gluco Cycloadduct (11) with Thiophthalimide (2) and 2,6-Lutidine. Methanol as solvent. Cycloadduct **11** (0.05 g, 0.08 mmol), thiophthalimide (**2**, 0.08 mmol), and 2,6-lutidine (0.01 mL, 0.08 mmol) in MeOH (0.5 mL) gave only recovered **11** after being allowed to react for 3 days.

Reaction of 3-((*tert*-Butyldimethylsilyl)oxy)-4-methoxymethyl-D-ribal with 3-(Phthalimidosulfenyl)-2,4-pentanedione. Major adduct (top-face) 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-3-((*tert*-butyldimethylsilyl)oxy)-4-methoxymethyl-2-deoxy-2-thio-*β*-D-arabinofuranoside (**22*β***): ^{1}H NMR $CDCl_3$ δ 7.68−7.34 (m, 10H, Ph), 5.55 (d, J = 4.89 Hz, 1H, $C_{1'}$), 4.33 (d, J = 2.32, 2H, $-OCH_2O-$), 4.22−4.18 (m, 1H, $C_{4'}$), 4.08 (dd, J = 7.99, 2.05 Hz, 1H, $C_{3'}$), 3.69 (dd, J = 8.02, 3.16 Hz, 1H, $C_{2'}$), 3.29−3.03 (abq, J = 11.08, 6.27, 2.91 Hz, 2H, $C_{5'}$,$C_{5''}$), 3.18 (s, 3H, $-OCH_3$), 2.15 (s, 3H, $-CH_3$), 2.11 (s, 3H, $-CH_3$), 1.07 (s, 9H, *t*-Bu); ^{13}C NMR ($CDCl_3$) δ 195.02, 161.39, 135.95, 135.76, 132.91, 132.52, 130.07, 127.76, 127.68, 103.44, 100.62, 96.37, 85.45, 73.69, 67.46, 55.06, 48.20, 29.49, 26.84, 22.02, 19.19. Anal. Calcd: C, 63.60; H, 6.86; S, 6.06. Found: C, 63.38; H, 6.87; S, 6.17.

Minor adduct (bottom-face) 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-3-((*tert*-butyldimethylsilyl)oxy)-4-methoxymethyl-2-deoxy-2-thio-α-D-ribofuranoside (**22α**): ^{1}H NMR $CDCl_3$ δ 7.82−7.35 (m, 10H, Ph), 5.42 (d, J = 3.79 Hz, 1H, $C_{1'}$), 4.36−4.28 (m, 3H, $-OCH_2O-$, $C_{4'}$), 4.21 (bs, 1H, $C_{3'}$), 3.51 (dd, J = 5.78, 1.91 Hz, 1H, $C_{2'}$), 3.17−2.45 (AB quartet, J = 12.0, 5.68, 3.17 Hz, 2H, $C_{5'}$, $C_{5''}$), 3.13 (s, 3H, $-OCH_3$), 2.37 (s, 3H, CH_3), 2.35 (s, 3H, $-CH_3$), 1.03 (s, 9H, *t*-Bu); ^{13}C NMR ($CDCl_3$) δ 195.14, 159.61, 136.57, 136.37, 135.74, 135.43, 135.38, 134.01, 132.99, 130.59, 130.46, 130.03, 128.20, 127.94, 105.47, 98.58,

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96.92, 88.81, 73.83, 67.03, 55.57, 44.28, 30.26, 27.24, 23.12, 19.55. Anal. Calcd: C, 63.60; H, 6.86; S, 6.06. Found: C, 63.44; H, 6.95; S, 6.32.

Reaction of 4-Methoxymethyl-D-ribal with 3-(Phthalimidosulfenyl)-2,4-pentanedione. Major adduct (bottom-face) 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-4-methoxymethyl-2-deoxy-2-thio-*β*-D-ribofuranoside (**20α**): ^{1}H NMR $CDCl_3$ δ 5.48 (d, J = 3.78 Hz, 1H, $C_{1'}$), 4.63 (s, 2H, $-OCH_2O$), 4.48 (q, 2.23 Hz, 1H, $C_{4'}$), 4.28−4.23 (bdd, 1H, $C_{3'}$), 3.76 (d, J = 3.56 Hz, 2H, $C_{5'}$,$C_{5''}$), 3.73 (dd, J = 3.82, 0.92 Hz, 1H, $C_{2'}$), 3.36 (s, 3H, $-OCH_3$), 2.41 (s, 3H, CH_3), 2.23 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 194.63, 160.11, 106.01, 98.42, 96.79, 86.61, 71.78, 67.35, 55.41, 45.38, 30.16, 22.46.

Minor adduct (top-face) 1-*O*,2-*S*-(2-acetyl-1-methyl-1,2-ethenediyl)-4-methoxymethyl-2-deoxy-2-thio-*β*-D-arabinofuranoside (**20*β***): ^{1}H NMR $CDCl_3$ δ 5.54 (d, J = 4.85 Hz, 1H, $C_{1'}$), 4.66 (s, 2H, $-OCH_2O$), 3.69−3.68 (m, 2H, $C_{3'}$, $C_{4'}$), 3.61 (d, J = 4.39 Hz, 2H, $C_{5'}$, $C_{5''}$), 3.60 (dd, J = 8.81, 3.96 Hz, 1H, $C_{2'}$), 3.38 (s, 3H, $-OCH_3$), 2.98 (bd, 1H, $C_{3'}$-OH), 2.35 (s, 3H, CH_3), 2.32 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 195.65, 161.33, 103.86, 100.51, 96.86, 83.86, 72.98, 68.09, 55.41, 47.69, 29.87, 22.23.

To further establish their identity, both isomers of **20** were silylated under standard conditions to yield the corresponding isomers of **21**.

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