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New Glycomimetics: Anomeric Sulfonates, Sulfenamides, and Sulfonamides

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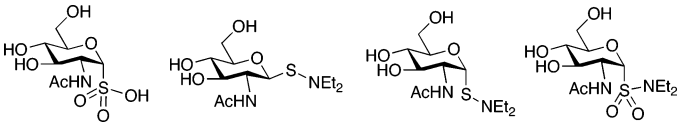

The synthesis of a variety of new 1-thio-D-glucopyranose derivatives oxidized at the sulfur atom is described, including seven 1-*C*-sulfonic acids, three sulfonate esters, three sulfinate esters, an *S*,*S*′-diglycosyl thiolsulfonate and thiolsulfinate, four *S*-glycosyl sulfenamides, an *S*-glycosyl sulfinamide, and two *S*-glycosyl sulfonamides. These compounds possess unusual anomeric functionality that might be resistant or even inhibitory to normal enzymatic carbohydrate processing, and therefore, they may be of future use in studies of enzyme inhibition, structure, mechanism, and function.

Introduction

Enzymes that recognize carbohydrates can be fooled by biomimetics that bind but are not processed to product in the usual way. Because understanding and manipulating the "normal" action of enzymes and other proteins is crucial to virtually all aspects of biology and medicine, the need continually arises to develop new structures with the potential to interact "abnormally" with them. As an example, thioglycosides,[1] in which a sulfur atom replaces an oxygen atom at the anomeric carbon of a normal substrate, have structures and properties similar to those of *O*-glycosides, yet resist enzymatic action. Consequently, these unnatural compounds can serve a variety of purposes in bioorganic and medicinal chemistry investigations. Chart 1 lists some representative thioglycoside mimetics, in particular those for which assay results are available.[2] A much larger list of examples might also be identified from among *C*-glycosides,[3] oximes,[4] triazoles,[5] disulfides,[6] cross-metathesis products,[7] and many other mimetics. One factor that distinguishes thioglycosides from most other neoglycoconjugates, however, is the capacity of the divalent (sulfenyl) sulfur atom to be converted to more highly oxidized forms (sulfinyl and sulfonyl), potentially extending the range of interactions with proteins.

We recently reported[8] the inadvertent synthesis of the glycosyl 1-*C*-sulfonate esters **5** and **6** and 1-*C*-sulfinate esters **3** and **4** by oxidation of respective thiazolines **1** and **2** with *m*-chloroperoxybenzoic acid (*m*-CPBA) in the presence of ethanol (Scheme 1). Further transformation of **5** to sulfonates **8** and **9** was also carried out. In this paper, we report the details of those transformations, a generalization of the glycosyl 1-*C*-sulfonate preparation, our unsuccessful attempts to transform the sulfonates into *S*-glycosyl sulfonamides, and finally a route to the sulfonamide through the corresponding *S*-glycosyl sulfenamide and sulfinamide.

(1) (a) Knapp, S.; Myers, D. S. *J. Org. Chem.* **2002**, *67*, 2995−2999. (b) Driguez, H. *ChemBioChem* **2001**, *2*, 311−318. (c) Driguez, H. *Top. Curr. Chem.* **1997**, *187*, 85−116. (d) Horton, D.; Wander, J. D. In *The Carbohydrates. Chemistry and Biochemistry*; Pigman, W., Horton, D., Eds.; Academic Press: New York, 1980; Vol. IB, pp 799−842.

(2) Respective citations for Chart 1: (a) Knapp, S.; Vocadlo, D.; Gao, Z.; Kirk, B.; Lou, J.; Withers, S. G. *J. Am. Chem. Soc.* **1996**, *118*, 6804−6805. (b) MacDougall, J. M.; Zhang, X.-D.; Polgar, W. E.; Khroyan, T. V.; Toll, L.; Cashman, J. R. *J. Med. Chem.* **2004**, *47*, 5809−5815. (c) Bousquet, E.; Spadaro, A.; Pappalardo, M. S.; Bernardini, R.; Romeo, R.; Panza, L.; Ronsisvalle, G. *J. Carbohydr. Chem.* **2000**, *19*, 527−541. (d) Ciccotosto, S.; Kiefel, M. J.; Abo, S.; Stewart, W.; Quelch, K.; von Itzstein, M. *Glycoconjugate J.* **1998**, *15*, 663−669. (e) Mizuma, T.; Hagi, K.; Awazu, S. *J. Pharm. Pharmacol.* **2000**, *52*, 303−310. (f) Kiefel, M. J.; Beisner, B.; Bennett, S.; Holmes, I. D.; von Itzstein, M. *J. Med. Chem.* **1996**, *39*, 1314−1320. (g) Schnabelrauch, M.; Vasella, A.; Withers, S. G. *Helv. Chim. Acta* **1994**, *77*, 778−799. (h) Michael, K.; Wittmann, V.; Konig, W.; Sandow, J.; Kessler, H. *Int. J. Peptide Protein Res.* **1996**, *48*, 59−70.

(3) Recent leading reference: Postema, M. H. D.; Piper, J. L.; Betts, R. L. *Synlett* **2005**, 1345−1358.

(4) Recent leading reference: Renaudet, O.; Dumy, P. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3619−3622.

(5) Recent leading reference: Périon, R.; Ferrières, V.; García-Moreno, M. I.; Ortiz Mellet, C.; Duval, R.; García Fernández, J. M.; Plusquellec, D. *Tetrahedron* **2005**, *61*, 9118−9128.

(6) Recent leading reference: Gamblin, D. P.; Garnier, P.; Ward, S. J.; Oldham, N. J.; Fairbanks, A. J.; Davis, B. G. *Org. Biomol. Chem.* **2003**, *1*, 3642−3644.

(7) Recent leading reference: Wan, Q.; Cho, Y. S.; Lambert, T. H.; Danishefsky, S. J. *J. Carbohydr. Chem.* **2005**, *24*, 425−440.

(8) Knapp, S.; Darout, E. *Tetrahedron Lett.* **2002**, *43*, 6075−6078.

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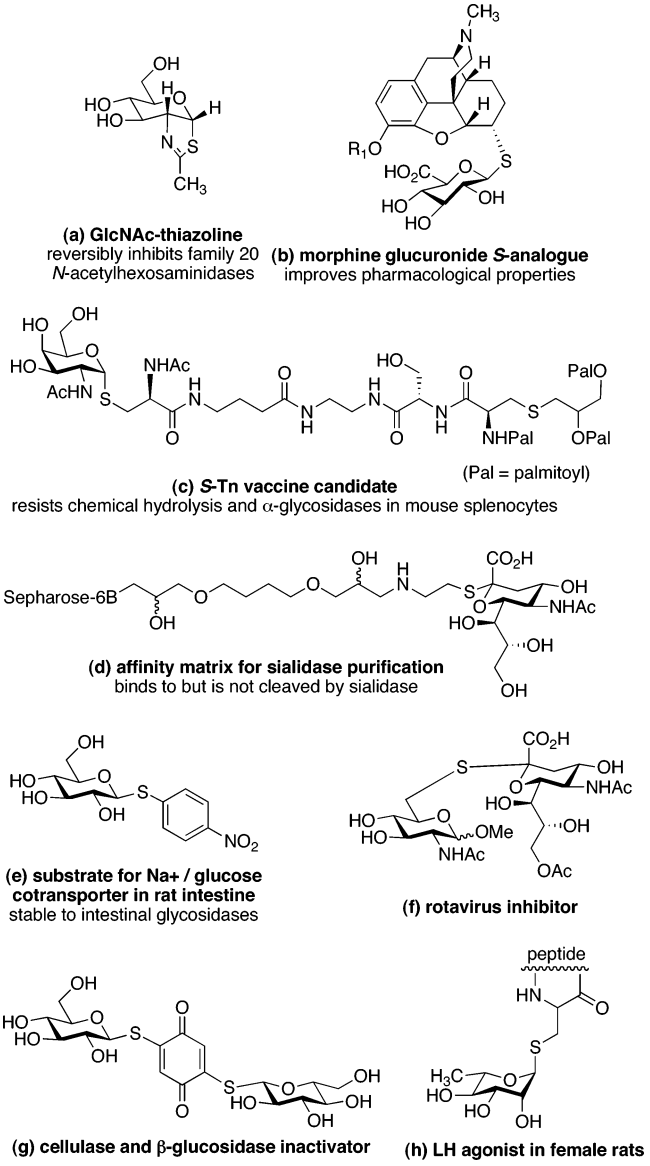
CHART 1. Some Enzyme-Resistant Thioglycosides with Interesting Activities

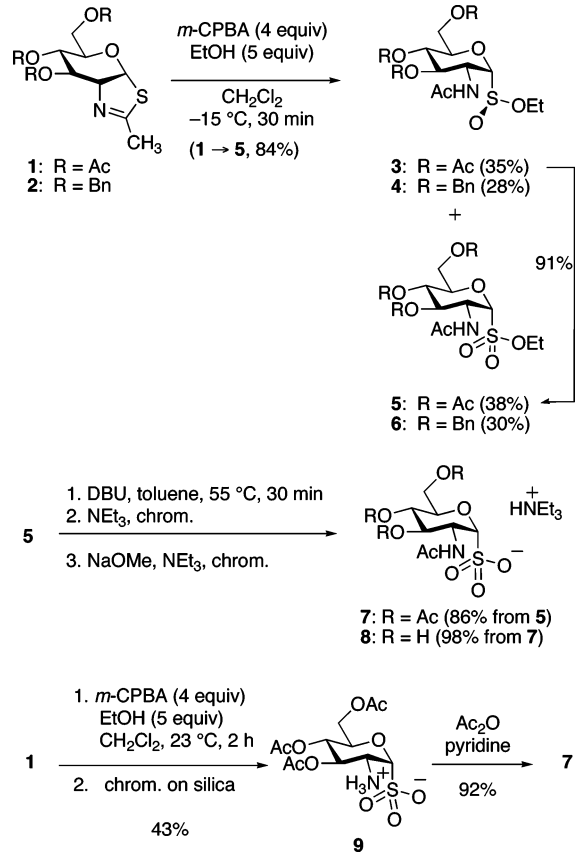


Results and Discussion

α-GlcNAc 1-*C*-Sulfonates. Treatment of the GlcNAc-thiazoline **1** with 4 equiv of buffer-washed *m*-CPBA at −15 °C (bath temperature) in the presence of several equiv of ethanol gave rise to a mixture of 2-acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-*β*-D-glucopyranosyl-1-*C*-sulfonic acid ethyl ester **5** and the corresponding sulfinate ester **3** (one diastereomer only). The structures of **5** and **3** (except for the configuration at sulfur) were established by their mass and NMR spectra, which resemble those of other 2-acetamido-2-deoxy-1-thio-α-D-glucopyranosides, and by the independent *m*-CPBA oxidation of **3** to **5**. Oxidation of the analogous tri-*O*-benzyl GlcNAc-thiazoline **2**, which was prepared from **1** by deacetylation followed by *O*-benzylation, likewise gave the corresponding *O*-benzyl-protected esters **4** and **6**.

The sulfonic acid triethylammonium salt **7** was prepared from **5** by DBU-promoted elimination of ethylene, followed by chromatography with triethylamine in the eluant (Scheme 1). Deacetylation with catalytic methoxide gave **8**, which was

SCHEME 1

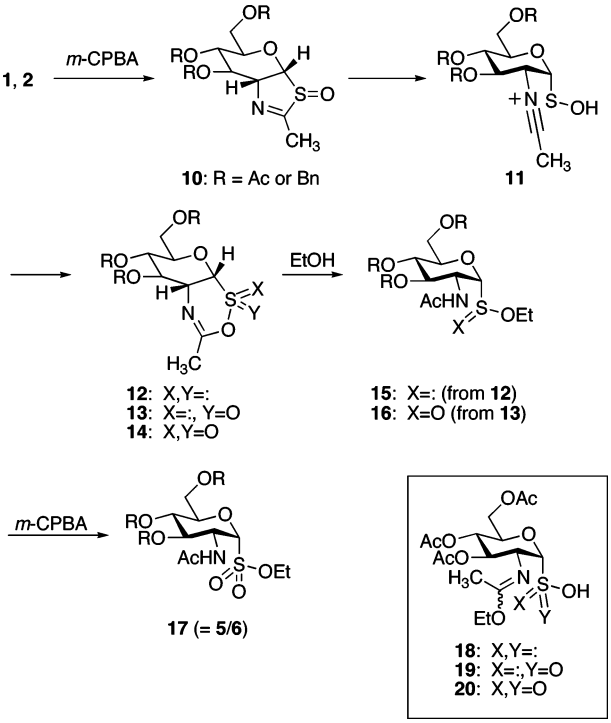


purified as the free sulfonic acid by Sephadex chromatography. When the oxidation of **1** with *m*-CPBA was carried out entirely at room temperature, a considerable amount of low R_f material was apparent by TLC analysis. Chromatography on silica with 9:1 dichloromethane/methanol as the eluant gave the amino sulfonate zwitterion **9** in 43% yield, in addition to 23% of **5**. The structure of **9** was secured by its *N*-acetylation to give **7**, which matched the material prepared previously.

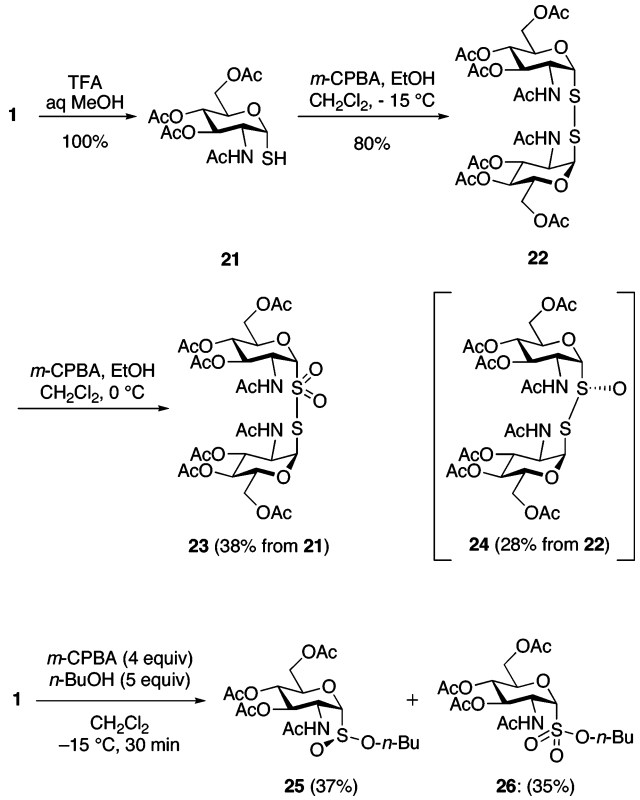
A mechanistic framework to account for these observations is proposed in Scheme 2. The first oxidation evidently takes place at the sulfur atom[9] of **1** and **2** (in contrast, the corresponding GlcNAc *oxazoline* reacts on nitrogen[10]) to give an *S*-oxide **10**. This intermediate may open to the nitrilium ion **11**, closure of which would lead to the thioxazine **12**. Acid-promoted ethanolysis of **12** would give an *O*-ethylsulfenate **15**, which could be oxidized further by *m*-CPBA[11,12] to the corresponding sulfinate **16** and sulfonate **17**. Alternatively, oxidation of thioxazine **12** at sulfur could give activated sulfinate or sulfonate intermediates (**13** or **14**), and then ethanolysis at sulfur would provide **16** and **17**, respectively. What can be ascertained about the order of the oxidation and ethanolysis steps? Oxidation of sulfinate to sulfonate (**3** to **5**) under these conditions (−15 °C) is indeed slow, as reported previously, but does occur to some extent in the presence of ethanol, according to a control experiment. An oxidation carried out with only 2 equiv of *m*-CPBA in dichloromethane/ethanol (quenched with

(9) Bonini, B. F.; Maccagnani, G.; Mazzanti, G.; Zwanenburg, Z. *Gazz. Chim. Ital.* **1977**, *107*, 289−292.
(10) Clark, M. A.; Wang, Q.; Ganem, B. *Tetrahedron Lett.* **2002**, *43*, 347−349.
(11) Netscher, T.; Prinzbach, H. *Synthesis* **1987**, 683−688.
(12) Braverman, S.; Duar, Y. *Tetrahedron* **1990**, *46*, 2975−2990.

SCHEME 2



SCHEME 3



bisulfite at −15 °C after 30 min) gave a product mixture that consisted primarily of starting thiazoline **1** and the same sulfinate ester **3** (one diastereomer only), but no more than a trace of **5**, and no other prominent carbohydrate products according to NMR analysis in the anomeric C−H region. A separate oxidation of **1** conducted with 4 equiv of *m*-CBPA and taken through a temperature gradient of −10 °C (2 h) and then 23 °C (1 h) produced sulfonate **5** only (84% yield from **1**, Scheme 1). These experiments suggest that **3** is the source of **5**, although the conversion is incomplete at the lower temperature. But what is the source of **3**, and why is it formed as a single diastereomer? Oxidation of bicyclic thioxazine **12** from the (less hindered) convex face ought to give **13** with predominantly the *S* configuration at sulfur. Ethanolysis of **13** with inversion of configuration at sulfur would then give the *R* (at sulfur) diastereomer of **16**. However, α-1-thioglucopyranosides are known to oxidize to sulfoxides with high stereoselectivity at sulfur attributable to conformational control by the *exo*-anomeric effect (the less hindered sulfur lone pair oxidizes),[13,14] and comparable oxidation of the sulfenate ester **15** is thus predicted to lead selectively to the *R* diastereomer of **16** directly. Therefore, either route from **12** (oxidation then ethanolysis, or ethanolysis then oxidation) could give **16** of the *R* configuration at sulfur, but neither **13** nor **15**, if formed, accumulates as an intermediate, and **14** is not formed. One possible route to sulfonate **5** can be ruled out: kinetically selective oxidation of the *S* diastereomer of **3** (in the presence of the *R* diastereomer, which would be left behind) cannot be operating because only the *R* diastereomer of **3** is formed initially.

The deacetylated product **9** might arise at the higher reaction temperature by interception of the nitrilium ion **11** by ethanol to give an imino ether derivative **18**. Further *m*-CPBA oxidation of the sulfenic acid,[15] analogous to previous observations,[16] would lead to **19** and then to **20**. Hydrolysis of imino ethers under acidic conditions to give D-glucosamine products similar to **9** has also been reported.[17] Alternatively, **20** could form at the higher temperature by ring opening of **13** to a nitrilium ion in the presence of ethanol, followed by oxidation of the sulfinic acid **19** to sulfonate **20**.

Thiazoline **1** is known to hydrolyze to the α-GlcNAc mercaptan **21** in acidic methanol solution (Scheme 3).[18] To check whether some **21** might form by hydrolysis during the reaction of **1** with *m*-CPBA, and thereby serve as an intermediate, the *m*-CPBA/ethanol reaction was repeated, but with added activated 3 Å molecular sieves. However, **3** and **5** were isolated just as before. When the ethanol was replaced by 5 equiv of freshly distilled *n*-butanol (which can be dried more effectively than ethanol), the corresponding *n*-butyl sulfinate and sulfonate **25** and **26** were isolated in yields similar to those of the respective ethyl esters **3** and **5** (Scheme 3), suggesting that no prior hydrolysis of **1** by adventitious water is occurring. Furthermore, **21**, prepared independently,[18] gave no **3** or **5**, but rather the corresponding disulfide **22** (80%) upon exposure to *m*-CPBA in dichloromethane/ethanol at −15 °C. Disulfide **22** was also prepared independently and quantitatively (see the

(13) Khiar, N. *Tetrahedron Lett.* **2000**, *41*, 9059−9063.

(14) (a) Aucagne, V.; Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Gianneto, P.; Rollin, P.; Tatibouët, A. *J. Org. Chem.* **2002**, *67*, 6925−6930. (b) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Bruno, G.; Giannetto, P.; Rollin, P. *Lett. Org. Chem.* **2004**, *1*, 376−380.

(15) For a leading reference to *S*-glycosylsulfenic acids, see: Aversa, M. C.; Barattucci, A.; Bilardo, M. C.; Bonaccorsi, P.; Giannetto, P.; Rollin, P.; Tatibouët, A. *J. Org. Chem.* **2005**, *70*, 7389−7396.

(16) (a) Gu, D.; Harpp, D. N. *Tetrahedron Lett.* **1993**, *34*, 67−70. (b) Hartwig, U.; Rall, K.; Sundermeyer, W. *Chem. Ber.* **1990**, *123*, 595−598. (c) Filby, W. G.; Günther, K.; Penzhorn, R. D. *J. Org. Chem.* **1973**, *38*, 4070−4071.

(17) (a) Jha, R.; Davis, J. T. *Carbohydr. Res.* **1995**, *277*, 125−134. (b) Kusumoto, S.; Yamamoto, M.; Shiba, T. *Tetrahedron Lett.* **1984**, *25*, 3727−3730. (c) Hanessian, S. *Tetrahedron Lett.* **1967**, 1549−1552.

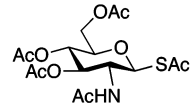
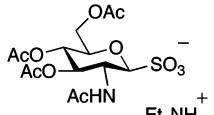
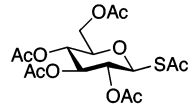
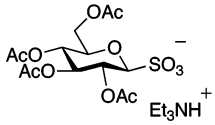
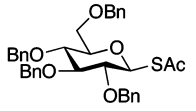
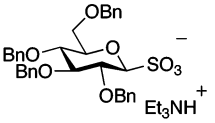
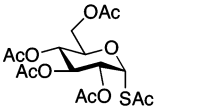
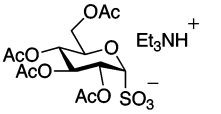
(18) Knapp, S.; Myers, D. S. *J. Org. Chem.* **2001**, *66*, 3636−3638.

Experimental Section) by treatment of **21** with iodine/pyridine, and TLC comparisons of this material with the reaction products of **1** with *m*-CPBA indicated that **22** was not formed, even as a minor product. Interestingly, treatment of **21** under slightly more forcing conditions (4 equiv of *m*-CPBA, −15 to 0 °C) led to the isolation of substantial amounts of an additional (over-oxidation) product, the unsymmetric anomeric thiolsulfonate ester **23**, in addition to 33% of **22**. Independent *m*-CPBA oxidation of **22** also produced **23**. The NMR spectra of **23** feature signals from each of the two distinct α-GlcNAc units, including respective anomeric C's and H's at 90.6/96.5 and 6.14/5.39 ppm. While comparable *m*-CPBA oxidations have been carried out on other symmetric dialkyl disulfides,[19] thiolsulfonate **23** is, according to a Beilstein structure search, the first example of a carbohydrate *thiolsulfonate* derivative with two anomeric C−S bonds, and the dissimilar reactivity expected of these bonds will be interesting to explore.

A report in the literature indicates that, in contrast to the oxidation of **22**, *m*-CPBA oxidation of *S*,*S*′-bis(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl) disulfide gives the *thiolsulfinate* product (i.e., the mono-*S*-oxide) only.[20] The formation of **23** from **21** or **22** ought to proceed through a thiosulfinate as well. Treatment of **22** with 1.2 equiv of *m*-CPBA for 1 h at −10 °C and then 5 h at 0 °C (reagent, time, and temperature must be carefully limited) gave a mixture of three products (in order of chromatographic elution): thiolsulfonate **23** (11%), starting disulfide **22** (46%), and a new, low R_f product that proved to be thiolsulfinate **24** (single diastereomer, 28%). The structure of **24** was established by its mass spectrum, its NMR spectra, which reveal the two distinct α-GlcNAc units with respective anomeric C's and H's at 88.4/96.8 and 6.08/5.56 ppm, and its independent *m*-CPBA oxidation at 23 °C to thiolsulfonate **23**. The apparent stereoselectivity of oxidation of **22** to **24** may again be attributed to the *exo*-anomeric effect operating as for thioglycosides,[13,14] and so **24** can be analogously assigned the *R* configuration at sulfur as shown (Scheme 3). Subjecting mixtures containing both **22** and **24** to further *m*-CPBA oxidation (more equiv and/or higher temperature) depletes **24** faster than **22**. This implies that the second oxidation of the disulfide (to give **23**) is faster than the first, which is opposite to the usual situation.[21,22]

Generalization of Anomeric Sulfonate Preparation. While carbohydrate C-sulfonates at C-2, C-3, C-4, and C-6 of the pyranose ring have been previously reported,[23] the sulfinates and sulfonates of Scheme 1 are, to our knowledge, the first examples with this functionality at C-1. The anomeric carbon is the most important linking position for natural glycoconjugates of various types. Carbohydrate 1-*C*-sulfonates, thioglycosides of a sort, may be thought of as potential enzyme-stable mimics[24] of naturally occurring negatively charged carbohydrate substructures such as *O*-phosphates, *O*-sulfates, neuraminidates, and glycuronates. The potential of using sulfonates to mimic these groups, or to otherwise interact with an electropositive group in an active site, or to use for linking to other moieties, makes them worthy of further exploration. Given also the specialized nature of the reactions leading to sulfonates **7**, **8**, and, **9**, it was of some interest to see whether the preparation of anomeric C-sulfonic acids could be extended to 1-thio-D-glucopyranosyl systems more generally.

TABLE 1. Synthesis of 1-*C*-Sulfonates from *S*-Acetyl-1-thiopyranoses[a]

starting material	product	yield
 **27**	 **31**	82%
 **28**	 **32**	87%
 **29**	 **33**	82%
 **30**	 **34**	86%

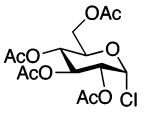
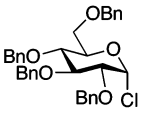
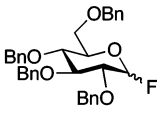
[a] Conditions: (1) DMDO, 0 °C, 12 h; (2) SiO_2 chromatography with CH_2Cl_2/MeOH/Et_3N as the eluant.

We find that anomeric thioacetates (*S*-acetyl-1-thio-D-glucopyranoses), which are conveniently prepared by known methods and can be stored without oxidation or decomposition, are transformed directly to the anomeric sulfonic acids by the action of dimethyldioxirane (DMDO). Each of the four anomeric thioacetate substrates investigated (**27**−**30**, Table 1) was dis-

(19) Bass, S. W.; Evans, S. A., Jr. *J. Org. Chem.* **1980**, *45*, 710−715.
(20) (a) Bell, R. H.; Horton, D. *Carbohydr. Res.* **1969**, *9*, 187−199. (b) Hürzeler, M.; Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1993**, *76*, 995−1012.
(21) Cogan, D. A.; Liu, G.; Kim, K.; Backes, B. J.; Ellman, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 8011−8019.
(22) Freeman, F.; Lee, C. *J. Org. Chem.* **1988**, *53*, 1263−1266.

(23) (a) Sajtos, F.; Lázár, L.; Borbás, A.; Bajza, I.; Lipták, A. *Tetrahedron Lett.* **2005**, *46*, 5191−5194. (b) Lipták, A.; Balla, E.; Jánossy, L.; Sajtos, F.; Szilágyi, L. *Tetrahedron Lett.* **2004**, *45*, 839−842. (c) Lipták, A.; Sajtos, F.; Jánossy, L.; Gehle, D.; Szilágyi, L. *Org. Lett.* **2003**, *5*, 3671−3674. (d) Fernández-Bolaños, J. G.; García, S.; Fernández-Bolaños, J.; Diánez, M. J.; Estrada, D.; López-Castro, A.; Pérez-Garrido, S. *Tetrahedron: Asymmetry* **2003**, *14*, 3761−3768. (e) Fernández-Bolaños, J. G.; Ulgar, V.; Maya, I.; Fuentes, J.; Diánez, M. J.; Estrada, M. D.; López-Castro, A.; Pérez-Garrido, S. *Tetrahedron: Asymmetry* **2003**, *14*, 1009−1018. (f) Hanashima, S.; Mizushina, Y.; Yamazaki, T.; Ohta, K.; Takahashi, S.; Sahara, H.; Sakaguchi, K.; Sugawara, F. *Bioorg. Med. Chem.* **2001**, *9*, 367−376. (g) Hanashima, S.; Mizushina, Y.; Yamazaki, T.; Ohta, K.; Takahashi, S.; Koshino, H.; Sahara, H.; Sakaguchi, K.; Sugawara, F. *Tetrahedron Lett.* **2000**, *41*, 4403−4407. (h) Robina, I.; Gómez-Bujedo, S.; Fernández-Bolaños, J. G.; Fuentes, J. *Synth. Commun.* **1998**, *28*, 2379−2398. (i) Roy, A. B.; Hewlins, M. J. E. *Carbohydr. Res.* **1997**, *302*, 113−117. (j) Fernández-Bolaños, J. G.; García, S.; Fernández-Bolaños, J.; Dianez, M. J.; Estrada, M. D.; López-Castro, A.; Pérez, S. *Carbohydr. Res.* **1996**, *282*, 137−147. (k) Fernández-Bolaños, J. G.; Morales, J.; García, S.; Diánez, M. J.; Estrada, M. D.; López-Castro, A.; Pérez, S. *Carbohydr. Res.* **1993**, *248*, 1−14. (l) Gordon, D. M.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1992**, *114*, 659−663. (m) Musicki, B.; Widlanski, T. S. *Tetrahedron Lett.* **1991**, *32*, 1267−1270. (n) Reddie, R. N. *Synth. Commun.* **1987**, *17*, 1129−1139. (o) Fernández-Bolaños, J.; Maya Castilla, I.; Fernández-Bolaños Guzman, J. *Carbohydr. Res.* **1988**, *173*, 33−40. (p) Fernández-Bolaños, J.; Castilla, I. M.; Guzman, J. F.-B. *Carbohydr. Res.* **1986**, *147*, 325−329. (q) Gigg, R.; Penglis, A. A. E.; Conant, R. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2490−2493.
(24) Musicki, B.; Widlanski, T. S. *J. Org. Chem.* **1990**, *55*, 4231−4233.

TABLE 2. Attempted Synthesis of Anomeric Sulfonyl Halides[a]

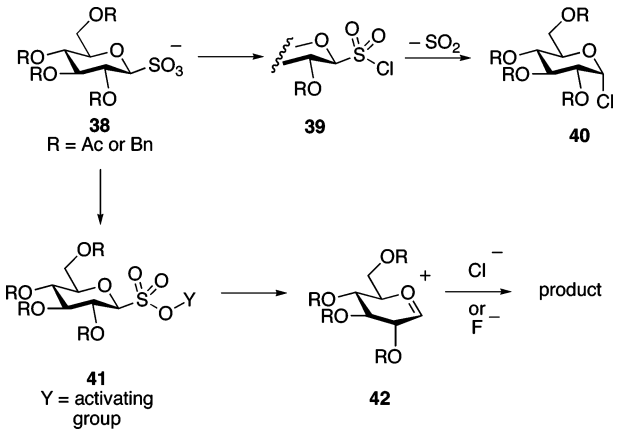
sulfonate	conditions	product
32	PCl_5	 **35**
33	$POCl_3$	 **36**
33	DAST	 **37** (α/β = 1:1)
32	PPh_3, SO_2Cl_2	**35**
32	ClCOCOCl	**35**

[a] Reactions were run in CH_2Cl_2 solution at 0−23 °C for 2 h.

solved in a solution of DMDO[25] in acetone at 0 °C and allowed to react for a 12 h period.[26] The solution was simply concentrated and chromatographed with an eluant containing triethylamine to afford the sulfonic acid as the triethylammonium salt. The ^1H and ^{13}C NMR spectra as well as the negative ion mass spectrum of each product confirm its identity.

Attempted Synthesis of Anomeric Sulfonyl Chlorides and Sulfonamides. An unusual enzyme-resistant replacement for the glycosidic linkage in neoglycoconjugates would be the *sulfonamide*[27,28] corresponding to the union of an anomeric sulfonic acid (e.g., **7**, **31**−**34**) and an amine.[29] We therefore invested some effort (see Table 2) in trying to activate anomeric sulfonates as the corresponding sulfonyl halide, either chloride or fluoride. For example, treatment of an anomeric sulfonate as its triethylamine salt (**32** or **33**) with PCl_5 or $POCl_3$, standard reagents for the formation of sulfonic acid chlorides, led only to the corresponding known α-anomeric chlorides (**35** and **36**, respectively, Table 2). Attempted conversion of **32** to the sulfonic acid fluoride with diethylaminosulfur trifluoride (DAST)[30,31] gave instead the known anomeric fluorides **37**. Reaction of **32** with oxalyl chloride or with triphenylphosphine and sulfuryl chloride[32] likewise gave only **35**. Evidently, the anomeric C-sulfonyl chloride **39**, if formed, is unstable toward loss of SO_2, or else halide anion intercepts an activated sulfonic mixed anhydride **41** at the anomeric carbon, possibly by way

SCHEME 4



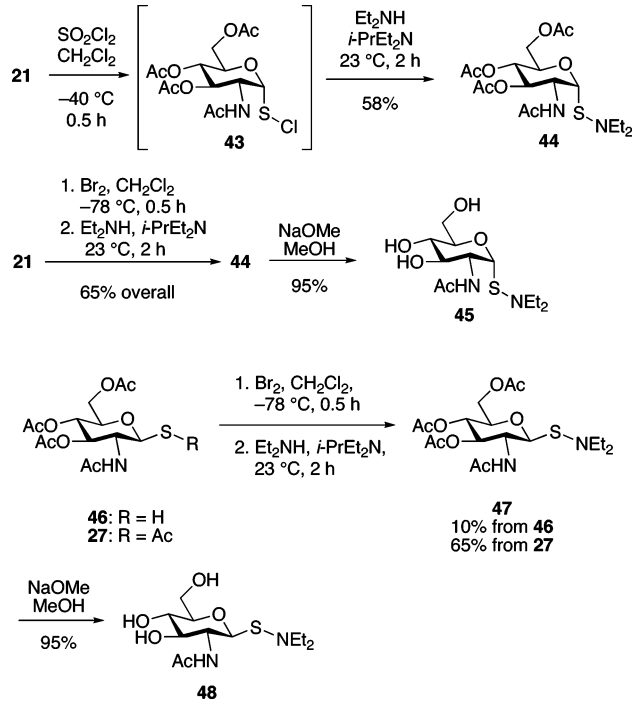
of an oxocarbenium ion **42** (Scheme 4). Kinetic addition of fluoride ion to the α- and β-face of **42**, without subsequent equilibration, could account for formation of the product **37** of the DAST reaction as the mixture of anomeric fluorides.[33] In contrast, equilibration of possible anomeric chloride kinetic mixtures derived from **42** to the more stable respective α-anomers **35** and **36** might be expected to occur under these conditions.[34]

Sulfonic acids **32** and **33** were also treated with various peptide coupling reagents, including *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide, 2-chloro-4,6-dimethoxy-1,3,5-triazine, and DCC/1-hydroxybenzotriazole, to activate the sulfonyl group. Attempted couplings in DMF solution with benzylamine present as the nucleophile, however, led only to the recovery of starting sulfonic acid.

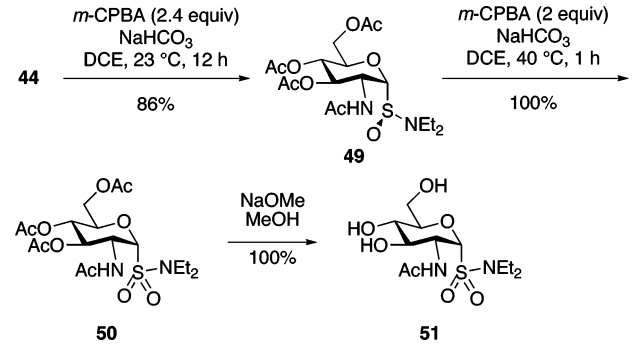
Synthesis of α- and β-GlcNAc Sulfenamides. Sulfenamides[35] can serve, through oxidation at sulfur, as precursors to sulfonamides. The α-GlcNAc mercaptan **21** was therefore treated with sulfuryl chloride[36] to generate a presumed intermediate sulfenyl chloride **43** (Scheme 5), and then 1 equiv of diethylamine, as a prototypical nucleophilic amine, was added along with Hünig's base in order to neutralize the acid formed. The desired *N*,*N*-diethylsulfenamide **44** was isolated in 58% yield.[37] Somewhat better efficiency was obtained by bromination[38] of **21** at −78 °C, presumably by way of the corresponding sulfenyl bromide. Deprotection of **44** to the α-GlcNAc sulfenamide triol **45** was achieved under Zemplén conditions. Analogous treatment of the β-GlcNAc mercaptan[39] **46** gave the corresponding *N*,*N*-diethylsulfenamide **47**, but the yield was low. However, bromination[40] of the β-GlcNAc *thioacetate* **27** proceeded more efficiently, and analogous deprotection to the β-GlcNAc sulfenamide triol **48** was also successful.

(25) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847−2853.
(26) Oxidation of thioacetates with H_2O_2 and acetic acid has been reported: Ulgar, V.; Maya, I.; Fuentes, J.; Fernández-Bolaños, J. *Tetrahedron* **2002**, *58*, 7967−7973 and references therein.
(27) Johnson, D. C., II; Widlanski, T. S. *Tetrahedron Lett.* **2004**, *45*, 8483−8487 and references therein.
(28) Caddick, S.; Wilden, J. D.; Bush, H. D.; Wadman, S. N.; Judd, D. B. *Org. Lett.* **2002**, *4*, 2549−2551.
(29) *N*-Glycosyl sulfonamides have also been reported: Colinas, P. A.; Bravo, R. D. *Tetrahedron Lett.* **2005**, *46*, 1687−1689.
(30) Singh, R. P.; Shreeve, J. M. *Synthesis* **2002**, 2561−2578.
(31) Segall, Y.; Quistad, G. B.; Casida, J. E. *Synth. Commun.* **2003**, *33*, 2151−2159.
(32) Huang, J.; Widlanski, T. S. *Tetrahedron Lett.* **1992**, *33*, 2657−2660.
(33) Griffith, M. H. E.; Hindsgaul, O. *Carbohydr. Res.* **1991**, *211*, 163−166.
(34) Ernst, B.; Winkler, T. *Tetrahedron Lett.* **1989**, *30*, 3081−3084.
(35) (a) Koval, I. V. *Russ. Chem. Rev.* **1996**, *65*, 421−440. (b) Capozzi, G.; Modena, G.; Pasquato, L. In *The Chemistry of Sulfenic Acids and Their Derivatives*; Patai, S., Ed.; Wiley: New York, 1990; pp 403−516. (c) Craine, L.; Raban, M. *Chem. Rev.* **1989**, *89*, 689−712.
(36) Barrett, A. G. M.; Braddock, D. C.; Christian, P. W. N.; Pilipauskas, D.; White, A. J. P.; Williams, D. J. *J. Org. Chem.* **1998**, *63*, 5818−5823.
(37) Other *S*-glycosyl sulfenamides: (a) Illyés, T.-Z.; Molnár-Gábor, D.; Szilágyi, L. *Carbohydr. Res.* **2004**, *339*, 1561−1564. (b) Owen, D. J.; von Itzstein, M. *Carbohydr. Res.* **2000**, *328*, 287−292. (c) Hürzeler, M.; Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1992**, *75*, 557−588. (d) Bell, R. H.; Horton, D.; Miller, M. J. *Carbohydr. Res.* **1969**, *9*, 201−214.
(38) Kharasch, N.; Bruice, T. C. *J. Am. Chem. Soc.* **1951**, *73*, 3240−3244.
(39) Meyer zu Reckendorf, W.; Bonner, W. A. *J. Org. Chem.* **1961**, *26*, 4596−4599.

SCHEME 5



SCHEME 6



Oxidation of sulfenamide **44** with 2.4 equiv of *m*-CPBA[41] at 23 °C did not give the corresponding sulfonamide, but rather the (mono-oxidized[42]) sulfinamide **49** as a single isomer in good yield (Scheme 6). Again, the stereoselectivity of the 1-thio-α-D-glucopyranoside oxidation may reflect the *exo*-anomeric effect[13,14] on sulfenamide conformation, presumably leading to the *S* stereoisomer at sulfur (shown). Resubjecting the **49** to 2 equiv of *m*-CPBA, but at 40 °C instead, gave the sulfonamide **50** quantitatively. Deacetylation as before provided the sulfonamide triol **51**.

The α-GlcNAc sulfonate **8**, sulfenamides **45** and **48**, and sulfonamide **51** possess atypical functionality at the pyranose anomeric center, where they might interact with active sites of carbohydrate processing enzymes such as *N*-acetylhexosaminidases or glucosyl transferases. The unnatural functionality ought to make them nonprocessable as substrates, so they and related compounds may ultimately have value as enzyme inhibitors, or as enzyme resistant components of vaccines, biomimetic probes, and other neoglycoconjugates.

Experimental Section

(3a*R*,5*R*,6*S*,7*R*,7a*R*)-5-Phenylmethoxymethyl-6,7-bis(phenylmethoxy)-2-methyl-5,6,7,7a-tetrahydro-3a*H*-pyrano[3,2-*d*]thiazole (2). A mixture of 212 μL (1.78 mmol) of benzyl bromide, 66 mg (1.66 mmol of a 60% dispersion in mineral oil) of sodium hydride, and 6 mL of DMF was treated at 0 °C (bath temperature) with 110 mg (0.502 mmol) of GlcNAc-thiazoline triol (prepared from **1** by methanolysis[18]) in 4 mL of DMF. The reaction was allowed to warm to 23 °C over 4 h and then was concentrated and chromatographed on silica with 1:3 ethyl acetate/hexanes as the eluant to provide 218 mg (98%) of **2** as a colorless oil, R_f 0.37 (3:7 ethyl acetate/hexanes): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23−7.42 (m, 13 H), 7.15−7.21 (m, 2 H), 6.35 (d, 1 H, J = 9.2 Hz), 4.72 and 4.64 (ABq, 2 H, J = 12.0 Hz), 4.53 and 4.24 (ABq, 2 H, J = 11.6), 4.46−4.58 (obscured m, 1 H), 4.51 and 4.46 (ABq, 2 H, J = 12.3), 4.34 (br t, 1 H, J = 1.8 Hz), 3.68 (br d, 1 H, J = 8.7 Hz), 3.40−3.58 (m, 3 H), 2.28 (d, 3 H, J = 2.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 138.3, 138.1, 137.9, 128.7, 128.49, 128.47, 128.3, 128.2, 128.1, 128.0, 127.97, 127.7, 89.6, 78.1, 76.4, 76.2, 73.4, 71.9 (2 C), 71.5, 70.0, 21.0; FAB-MS *m*/*z* 490 MH^+.

(2*R*,3*S*,4*R*,5*R*,6*R*)-5-Acetamido-2-(acetoxymethyl)-6-(ethoxysulfinyl)tetrahydro-2*H*-pyran-3,4-diylDiacetate(3)and(2*R*,3*S*,4*R*,5*R*,6*R*)-5-Acetamido-2-(acetoxymethyl)-6-(ethoxysulfonyl)tetrahydro-2*H*-pyran-3,4-diyl Diacetate (5). A solution of 46.2 mg (0.134 mmol) of **1** in 3 mL of dichloromethane was cooled to −17 °C (bath temperature) and maintained between −15 and −20 °C. Ethanol (39 μL, 0.670 mmol) was added, followed by 92 mg (0.536 mmol) of buffer-washed *m*-CPBA. The reaction was stirred at −15 to −20 °C for 0.5 h, and then the reaction mixture was quenched by addition of aqueous sodium sulfite and sodium bicarbonate. The organic layer was dried over anhydrous magnesium sulfate and then concentrated to a residue. Chromatography on silica with 3:7 ethyl acetate/dichloromethane as the eluant afforded 22 mg (38%) of sulfonate ester **5** as a colorless oil, R_f 0.47 (3:7 ethyl acetate/dichloromethane), and 20 mg (35%) of sulfinate ester **3** as a colorless oil, R_f 0.26 (3:7 ethyl acetate/dichloromethane). Data for **5**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.18 (d, 1 H, J = 7.6 Hz), 5.65 (dd, 1 H, J = 11.2, 9.2 Hz), 5.35 (d, 1 H, J = 6.3 Hz), 5.17 (t, 1 H, J = 9.6 Hz), 4.58 (ddd, 1 H, J = 9.2, 7.6, 6.0 Hz), 4.34 (q, 2 H, J = 7.2 Hz), 4.29−4.39 (partially obscured 1 H), 4.21 (dd, 1 H, J = 12.8, 4.4 Hz), 4.13 (dd, 1 H, J = 12.8, 2.4 Hz), 2.08, 2.05, 2.04, 1.98 (4 s, 3 H each), 1.41 (t, 3 H, J = 9.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 170.9, 170.2, 169.0, 86.1, 72.7, 69.5, 69.1, 67.1, 61.6, 50.6, 23.0, 20.7, 20.7, 20.6, 15.1; FAB-MS *m*/*z* 446 MLi^+. Data for **3**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.43 (d, 1 H, J = 8.4 Hz), 5.58 (dd, 1 H, J = 10.5, 9.0 Hz), 5.11 (t, 1 H, J = 9.3 Hz), 4.74 (d, 1 H, J = 5.7 Hz), 4.66−4.74 (obscd ddd, 1 H), 4.04−4.19 (m, 5 H), 2.04, 1.99, 1.98, 1.91 (4 s, 3 H each), 1.34 (t, 3 H, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 170.7, 170.6, 169.4, 92.6, 73.9, 70.6, 68.2, 66.9, 61.9, 51.2, 23.3, 20.9, 20.85, 20.76, 16.1; FAB-MS *m*/*z* 430 MLi^+, 424 MH^+.

The ethyl sulfonate **5** was also obtained by independent oxidation of sulfinate **3** as follows. A solution of 18 mg (0.043 mmol) of **3** in 0.8 mL in dichloromethane was cooled to 0 °C bath temperature and treated with 18 mg (0.106 mmol) of *m*-CPBA. The reaction mixture was allowed to warm to room temperature and stir for 1 h. The reaction was quenched with a 5% sodium bicarbonate/saturated aqueous sodium sulfite solution at 0 °C and allowed to warm to room temperature. The organic layer was separated, dried, concentrated, and then chromatographed on silica with 3:1 dichlo-

(40) Boehme, H.; Steudel, H. P. *Justus Liebigs Ann. Chem.* **1969**, *730*, 121−132.

(41) (a) García Martínez, A.; Teso Villar, E.; Moreno Jiménez, F.; García Amo, M. *Tetrahedron: Asymmetry* **2000**, *11*, 1709. (b) Refvik, M. D.; Schwan, A. L. *J. Org. Chem.* **1996**, *61*, 4232−4239. (c) Schwan, A. L.; Refvik, M. D. *J. Chem. Soc., Chem. Commun.* **1995**, 1949−1950. (d) Glass, R. S.; Swedo, R. J. *Synthesis* **1977**, 798−800.

(42) (a) Merricks, D.; Sammes, P. G.; Walker, E. R. H.; Henrick, K.; McPartlin, M. M. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2169−2176. (b) Harpp, D. N.; Mullins, D. F.; Steliou, K.; Triassi, I. *J. Org. Chem.* **1979**, *44*, 4196−4197.

romethane/ethyl acetate as the eluant to give 17.1 mg (91%) of **5** as a colorless oil, R_f 0.47 (7:3 dichloromethane/ethyl acetate). The ^{1}H NMR and FAB mass spectra matched those obtained previously for **5**.

A high-yield preparation of **5** from **1** was also carried out, as follows. A solution of 115 mg (0.333 mmol) of **1** in 6.0 mL of dichloromethane was cooled to −15 °C bath temperature and treated with 97.0 μL (1.67 mmol) of ethanol. *m*-CPBA (229 mg, 1.33 mmol) was added and the reaction mixture was stirred at −10 °C for 2 h and then allowed to warm to room temperature and stir for 1 h. The reaction was quenched with a 5% sodium bicarbonate/saturated aqueous sodium sulfite solution at 0 °C and allowed to warm to room temperature. The organic layer was separated, dried, concentrated, and then chromatographed on silica with 3:1 dichloromethane/ethyl acetate as the eluant to give 123 mg (84%) of **5** as a colorless oil, R_f 0.47 (7:3 dichloromethane/ethyl acetate). The ^{1}H NMR and FAB mass spectra matched those obtained previously for **5**.

Ethyl (2*R*,3*R*,4*R*,5*S*,6*R*)-3-Acetamido-4,5-bis(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2*H*-pyran-2-sulfinate (4) and Ethyl (2*R*,3*R*,4*R*,5*S*,6*R*)-3-Acetamido-4,5-bis(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2*H*-pyran-2-sulfonate (6). Ethanol (140 μL, 2.40 mmol) and 330 mg (1.91 mmol) of *m*-CPBA were added to a cooled solution of 231.2 mg (0.479 mmol) of **2** in 2 mL of dichloromethane, maintained between −15 and −20 °C bath temperature. The reaction mixture was stirred at that temperature for 0.5 h and then was quenched by addition of aqueous sodium sulfite and sodium bicarbonate. The organic layer was dried with anhydrous magnesium sulfate, concentrated, and then chromatographed on silica with 1:4 ethyl acetate/dichloromethane as the eluant to afford 84 mg (30%) of **6** as a colorless oil, R_f 0.4 (3:7 ethyl acetate/hexanes), and 76 mg (28%) of **4** as a colorless oil, R_f 0.27 (3:7 ethyl acetate/hexanes). Data for **6**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20−7.25 (m, 15 H), 5.32 (d, 1 H, J = 7.8 Hz), 5.27 (d, 1 H, J = 5.7 Hz), 4.83 (d, 1 H, J = 12.0 Hz), 4.78 (d, 1 H, J = 11.1 Hz), 4.64 (d, 1 H, J = 12.0 Hz), 4.59 (d, 1 H, J = 12.3 Hz), 4.58 (d, 1 H, J = 11.1 Hz), 4.49 (d, 1 H, J = 12.3 Hz), 4.42−4.50 (partially obscured ddd, 1 H), 4.30 (q, 2 H, J = 7.2 Hz), 4.21 (ddd, 1 H, J = 8.4, 4.8, 2.7 Hz), 3.77 (dd, 1 H, J = 11.1, 4.8 Hz), 3.71 (t, 1 H, J = 8.4 Hz), 3.69 (dd, 1 H, J = 11.1, 2.7), 1.75 (s, 3 H), 1.32 (t, 3 H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 137.9, 137.7, 128.9, 128.7, 128.6, 128.5, 128.4, 128.1, 127.9, 87.3, 77.4, 76.5, 74.9, 73.7, 69.3, 68.2, 50.4, 23.3, 15.4; FAB-MS *m*/*z* 590 MLi^+. Data for **4**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19−7.25 (m, 15 H), 5.33 (d, 1 H, J = 7.9 Hz), 4.69 (d, 1 H, J = 5.5 Hz), 4.46−4.82 (m, 7 H), 4.01−4.27 (m, 3 H), 4.05 (dd, 1 H, J = 9.8, 8.5 Hz), 3.58−3.66 (m, 3 H), 1.77 (s, 3 H), 1.33 (t, 3 H, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 170.7, 170.6, 169.4, 92.6, 73.9, 70.6, 68.2, 66.9, 61.9, 51.2, 23.3, 20.9, 20.85, 20.76, 16.1; FAB-MS *m*/*z* 574 MLi^+, 568 MH^+.

Triethylammonium (2*R*,3*R*,4*R*,5*S*,6*R*)-3-Acetamido-4,5-diacetoxy-6-(acetoxymethyl)tetrahydro-2*H*-pyran-2-sulfonate (7). A solution of 42.2 mg (0.096 mmol) of **5** and 16 μL (0.107 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene in 1 mL of toluene was heated at 55 °C for 0.5 h. The solution was concentrated and chromatographed on silica with 96:2:2 dichloromethane/methanol/triethylamine as the eluant to give 42.3 mg (86%) of **7** as a light brown oil, R_f 0.2 (96:2:2 dichloromethane/methanol/triethylamine): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.82 (br s, 1 H), 6.63 (d, 1 H, J = 9.6 Hz), 5.76 (dd, 1 H, J = 10.8, 9.2 Hz), 5.11 (t, 1 H, J = 9.2 Hz), 4.64 (d, 1 H, J = 6.0 Hz), 4.60−4.67 (m, 1 H), 4.54 (ddd, 1 H, J = 10.8, 9.6, 6.0 Hz), 4.12 (dd, 1 H, J = 12.8, 3.6 Hz), 4.06 (dd, 1 H, J = 12.8, 2.4 Hz), 3.07 (q, 6 H, J = 7.2 Hz), 1.99, 1.91, 1.90, 1.85 (4 s, 3 H each), 1.29 (t, 9 H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 170.8, 170.4, 169.4, 85.6, 71.3, 71.1, 68.6, 62.3, 50.1, 46.6 (3 C), 23.7, 21.1, 21.1, 20.9, 9.9 (3 C); NI-FAB-MS *m*/*z* 410 M^-.

Sulfonate **7** was also prepared by acetylating **9** as follows. A solution of 24 mg (0.065 mmol) of **9** (see below) and 7.4 μL (0.078 mmol) of acetic anhydride in 1 mL of pyridine was stirred for 16 h. The solution was concentrated and then chromatographed on silica with 96:2:2 dichloromethane/methanol/triethylamine as the eluant to give 42.3 mg (86%) of **7** as a light brown oil, R_f 0.2 (96:2:2 dichloromethane/methanol/triethylamine). The ^{1}H NMR spectrum and TLC behavior matched that of **7** as prepared above.

(2*R*,3*R*,4*R*,5*S*,6*R*)-3-Acetamido-4,5-dihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-sulfonic Acid (8). Sodium methoxide (10 μL of a 1 M methanol solution, 0.01 mmol) was added to a solution of 42 mg (0.082 mmol) of **7** in 1 mL of methanol at 0 °C. The reaction was allowed to stir for 1 h, concentrated, and then chromatographed with methanol through a Sephadex G-25 plug to give 23 mg (98%) of **8** as a colorless oil: ^{1}H NMR (300 MHz, D_2O) δ 4.71 (d, 1 H, J = 6.3 Hz), 4.10 (dd, 1 H, J = 10.8, 8.4 Hz), 4.02 (dd, 1 H, J = 10.8, 6.3 Hz), 3.89 (ddd, 1 H, J = 10.2, 3.9, 2.1 Hz), 3.72 (dd, 1 H, J = 12.3, 2.1 Hz), 3.64 (dd, 1 H, J = 12.6, 4.2 Hz), 3.39 (t, 1 H, J = 10 Hz), 1.89 (s, 3 H); ^{13}C NMR (75 MHz, D_2O) δ 174.9, 85.2, 75.8, 70.0, 69.9, 60.0, 52.1, 22.2; NI-FAB-MS *m*/*z* 274 M^-.

(2*R*,3*R*,4*R*,5*S*,6*R*)-4,5-Diacetoxy-6-(acetoxymethyl)-3-aminotetrahydro-2*H*-pyran-2-sulfonic Acid (9). Ethanol (88 μL, 1.51 mmol) and 208 mg (1.21 mmol) of *m*-CPBA were sequentially added to a solution of 104.2 mg (0.302 mmol) of **1** in 2 mL of dichloromethane at 23 °C. After 30 min, the reaction mixture was concentrated and then chromatographed on silica with 1:19 methanol/dichloromethane as the eluant to give 30 mg (23%) of **5** and then 48 mg (43%) of the amino sulfonic acid **9** as a colorless oil, R_f 0.2 (1:19 methanol dichloromethane): ^{1}H NMR (300 MHz, D_2O) δ 5.82 (dd, 1 H, J = 9.9, 8.1 Hz), 5.49 (dd, 1 H, J = 9.3, 8.1 Hz), 5.07 (d, 1 H, J = 5.4 Hz), 4.65−4.72 (m, 1 H), 4.42 (dd, 1 H, J = 12.8, 3.6 Hz), 4.24 (dd, 1 H, J = 12.6, 2.1 Hz), 4.01 (dd, 1 H, J = 9.0, 5.4 Hz), 2.15, 2.12, 2.10 (3 s, 3 H each); ^{13}C NMR (75 MHz, D_2O) δ 173.7, 172.9, 172.7, 82.8, 72.0, 69.7, 68.5, 61.9, 49.6, 20.5, 20.4, 20.4; FAB-MS *m*/*z* 370 MH^+.

***S*,*S*′-Bis(2-Acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl) Disulfide (22).** Iodine (66 μL of a 0.79 M solution in THF, 0.052 mmol) was added in aliquots over a 15 min period to a solution of 32 mg (0.088 mmol) of **21** in 0.75 mL of THF and 14 μL (0.176 mmol) of pyridine at 0 °C, whereupon a white precipitate formed and an orange color persisted. The reaction mixture was concentrated and then chromatographed on silica with ethyl acetate as the eluant to afford 32 mg (100%) of **22** as a white solid, mp (sealed capillary) 110−112 °C (change in crystal morphology), then 176−178 °C (melt), R_f 0.30 (ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (d, 2 H, J = 8.4 Hz), 5.41 (d, 2 H, J = 5.2 Hz), 5.14 (t, 2 H, J = 9.6 Hz), 5.04 (dd, 2 H, J = 9.6, 11.6 Hz), 4.47 (ddd, 2 H, J = 5.2, 8.6, 11.2 Hz), 4.25 (dd, 2 H, J = 4.0, 12.0 Hz), 4.19−4.09 (m, 4 H), 2.09 (s, 6 H), 2.04 (s, 6 H), 2.03 (s, 6 H), 1.97 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 170.8, 170.3, 169.3, 91.7, 71.0, 70.2, 67.7, 61.5, 53.2, 23.2, 20.85, 20.81, 20.7; FAB-MS *m*/*z* 747 MNa^+.

***S*-(2-Acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl) 2-Acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl-1-*C*-thiosulfonate (23).** A solution of 63.7 mg (0.175 mmol) of 2-acetamido-2-deoxy-1-thio-3,4,6-tri-*O*-acetyl-α-D-glucopyranose **21** in 3.5 mL of dichloromethane was cooled to −15 °C bath temperature and treated with 51.0 μL (0.875 mmol) of ethanol. *m*-CPBA (120 mg, 0.700 mmol) was added, and the reaction mixture was stirred at 0 °C for 0.5 h. The reaction was quenched with a 5% sodium bicarbonate/saturated aqueous sodium sulfite solution at 0 °C and allowed to warm to room temperature. The organic layer was separated, dried, and concentrated, and then the crude product was chromatographed on silica with 4:1 ethyl acetate/dichloromethane as the eluant to give 24.9 mg (38%) of **23** as a colorless oil, R_f 0.38 (ethyl acetate), and also 20.8 mg (33%) of the previously described disulfide **22**. Data for **23**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (δ, 1 H, J = 7.6 Hz), 6.14 (d, 1 H, J = 5.2 Hz), 5.80 (d, 1 H, J = 7.8 Hz), 5.62 (dd, 1 H, J = 9.3, 10.8 Hz), 5.39 (d, 1 H, J = 6.0 Hz), 5.20 and 5.17 (overlapping t's, 2 H, J

= 9.6 and 9.3 Hz respectively), 4.82 (dd, 1 H, *J* = 9.3, 11.7 Hz), 4.70−4.56 (m, 2 H), 4.38−4.02 (m, 6 H), 2.12 (s, 3 H), 2.11 (s, 3 H), 2.07 (s, 3 H), 2.06 (s, 6 H), 2.05 (s, 3 H), 2.02 (s, 3 H), 1.99 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 171.8, 171.1, 170.72, 170.68, 170.4, 169.3, 169.2, 96.5, 90.6, 74.1, 72.2, 71.3, 69.8, 67.1, 66.8, 61.5, 61.2, 52.9, 52.1, 23.4, 23.2, 20.9, 20.85, 20.84, 20.83, 20.74, 20.72; FAB-MS *m*/*z* 779 MNa^+.

An otherwise identical oxidation reaction of **21** run instead with 2.5 equiv of *m*-CPBA at −15 °C for 30 min gave no **23**, but rather the disulfide **22** in 80% yield, as determined by comparison to authentic material.

Thiosulfonate**23** was also prepared from the thiosulfinate **24** (see below) as proof of structure. *m*-CPBA (1.5 mg, 8.72 μmol) was added to a solution of 2.9 mg (3.92 μmol) of thiosulfinate **24** in 0.75 mL of dichloromethane at 0 °C. The mixture was stirred at 23 °C for 4 h, whereupon TLC indicated the complete consumption of the starting material and the appearance of a single new product with higher R_f. The TLC behavior, ^{1}H NMR spectrum, and FAB-MS of the product matched those of **23**.

***S*-(2-Acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl) 2-Acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl-1-*C*-thiosulfinate (24).** *m*-CPBA (11 mg, 0.066 mmol) was added to a solution of 40 mg (0.055 mmol) of disulfide **22** in 1.5 mL of dichloromethane at −15 °C bath temperature. The mixture was stirred at −10 °C for 1 h and then allowed to warm to 0 °C and to stir for 5 h. The reaction was quenched with a 5% sodium bicarbonate/saturated aqueous sodium sulfite solution at 0 °C and allowed to warm to room temperature. The organic layer was separated, dried, concentrated, and then chromatographed on silica with 4:1 dichloromethane/tetrahydrofuran as the eluant to give in order of elution 4.6 mg (11%) of the previously described thiosulfonate **23**, 18.3 mg (46%) of the disulfide **21**, and 11.4 mg (28%) of the thiosulfinate **24** as a single diastereomer, R_f 0.26 (ethyl acetate). Data for **24**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58 (d, 1 H, *J* = 8.4 Hz), 6.08 (d, 1 H, *J* = 4.8 Hz), 5.87 (d, 1 H, *J* = 7.6 Hz), 5.72 (app t, 1 H, *J* = 9.2 Hz), 5.56 (d, 1 H, *J* = 6.0 Hz), 5.21 and 5.19 (overlapping t's, 2 H, *J* = 9.6 Hz), 5.00 (dd, 1 H, *J* = 9.6, 11.2 Hz), 4.85 (ddd, 1 H, *J* = 6.4, 8.4, 10.8 Hz) 4.60 (ddd, 1 H, *J* = 4.8, 7.6, 11.6 Hz), 4.30−3.94 (m, 6 H), 2.10 (s, 6 H), 2.08 (s, 6 H), 2.06 (s, 6 H), 2.05 (s, 3 H), 2.00 (s, 3 H); ^{13}C NMR δ 172.1, 171.3, 171.0, 170.7, 170.6 (2 C's), 169.4, 169.2, 96.8, 88.4, 73.6, 71.7, 71.0, 70.3, 67.8, 67.4, 61.7, 61.6, 53.4, 52.2, 23.5, 23.4, 20.9 (2 C's), 20.85 (2 C's), 20.7 (2 C's); FAB-MS *m*/*z* 763 MNa^+.

***n*-Butyl 2-Acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl-1-*C*-sulfinate (25) and *n*-Butyl 2-Acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl-1-*C*-sulfonate (26).** *n*-Butanol (70 μL, 0.761 mmol) and 105 mg (0.609 mmol) of *m*-CPBA were added to a cooled solution of 52.5 mg (0.152 mmol) of **1** in 2 mL of dichloromethane, maintained between −15 and −20 °C bath temperature. The reaction mixture was stirred at that temperature for 0.5 h, then was quenched by addition of aqueous sodium sulfite and sodium bicarbonate. The organic layer was dried with anhydrous magnesium sulfate, concentrated, and then chromatographed on silica with 15:85 ethyl acetate/dichloromethane as the eluant to give 31 mg (43%) of **26** as a colorless oil, R_f 0.62 (3:7 ethyl acetate/dichloromethane), and 23 mg (34%) of **25** as a colorless oil, R_f 0.34 (3:7 ethyl acetate/dichloromethane). Data for **26**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.16 (d, 1 H, *J* = 8.0 Hz), 5.66 (dd, 1 H, *J* = 11.2, 9.2 Hz), 5.36 (d, 1 H, *J* = 6.4 Hz), 5.18 (t, 1 H, *J* = 9.6 Hz), 4.59 (ddd, 1 H, *J* = 11.2, 8.0, 6.4 Hz), 4.38 (ddd, 1 H, *J* = 8.0, 4.0, 2.0 Hz), 4.29 (t, 2 H, *J* = 6.4 Hz), 4.24 (dd, 1 H, *J* = 12.8, 4.0 Hz), 4.13 (d, 1 H, *J* = 12.8 Hz), 2.10, 2.06, 2.05, 1.99 (4 s, 3 H each), 1.72 (quint, 2 H, *J* = 7.2 Hz), 1.42 (sext, 2 H, *J* = 6.8 Hz), 0.98 (t, 3 H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 171.1, 170.4, 169.2, 86.2, 72.8, 72.7, 69.6, 67.1, 61.5, 50.6, 31.1, 23.0, 20.7, 20.6, 20.5, 18.5, 13.4; FAB-MS *m*/*z* 490 MNa^+, 468 MH^+. Data for **25**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.14 (d, 1 H, *J* = 8.8 Hz), 5.64 (dd, 1 H, *J* = 10.8, 9.6 Hz), 5.18 (t, 1 H, *J* = 9.6 Hz), 4.83 (d, 1 H, *J* = 5.6 Hz), 4.76 (ddd, 1 H, *J* = 10.8, 9.2, 6.0 Hz), 4.06−4.31 (m, 5 H), 2.11, 2.05, 2.05, 1.97 (4 s, 3 H each), 1.72 (quint, 2 H, *J* = 7.2 Hz), 1.42 (sext, 2 H, *J* = 7.4 Hz), 0.98 (t, 3 H, *J* = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 170.5, 170.4, 169.2, 92.4, 73.6, 70.6, 68.0, 62.2, 61.8, 54.9, 51.9, 32.0, 23.1, 20.7, 20.6, 18.7, 13.6; FAB-MS *m*/*z* 474 MNa^+, 452 MH^+.

Triethylammonium (2*S*,3*R*,4*R*,5*S*,6*R*)-3-Acetamido-4,5-diacetoxy-6-(acetoxymethyl)-tetrahydro-2*H*-pyran-2-sulfonate (31). Dimethyldioxirane (3.7 mL of a 0.079 M solution in acetone) was added to a flask containing a solution of 30 mg (0.740 mmol) of thioacetate **27**[43] in 1 mL of acetone at 0 °C. The solution was stirred at 0 °C for 12 h, then concentrated and chromatographed on silica with 97:2:1 dichloromethane/methanol/triethylamine as the eluant to give 31 mg (82%) of **31**, R_f 0.2 (97:2:1 dichloromethane/methanol/triethylamine): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.47 (d, 1 H, *J* = 8.4 Hz), 5.36 (d, 1 H, *J* = 9.6 Hz), 5.09 (t, 1 H, *J* = 9.9 Hz), 4.51 (d, 1 H, *J* = 10.2 Hz), 4.23−4.34 (m, 2 H), 4.09 (dd, 1 H, *J* = 12.6, 2.1 Hz), 3.81 (ddd, 1 H, *J* = 9.9, 4.2, 2.1 Hz), 3.06 (q, 1 H, *J* = 7.5 Hz), 2.02, 1.99, 1.98, 1.90 (4 s, 3 H each), 1.31, (t, 1 H, *J* = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 170.8, 170.7, 169.7, 86.3, 76.1, 74., 68.8, 62.6, 52.2, 46.4, 23.8, 21.3, 21.0, 9.3; NI-FAB-MS *m*/*z* 410 M^-.

Triethylammonium (2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Triacetoxy-6-(acetoxymethyl)tetrahydro-2*H*-pyran-2-sulfonate (32). Dimethyldioxirane (8 mL of a 0.070 M solution in acetone) was added to a flask containing a solution of 66 mg (0.16 mmol) of thioacetate **28**[44] in 1 mL of acetone at 0 °C. The solution was stirred at 0 °C for 12 h, concentrated, and then chromatographed on silica with 98:1:1 dichloromethane/methanol/triethylamine as the eluant to give 73 mg (87%) of **32**, R_f 0.2 (98:1:1 dichloromethane/methanol/triethylamine): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.40 (t, 1 H, *J* = 9.6 Hz), 5.22 (t, 1 H, *J* = 9.6 Hz), 5.08 (t, 1 H, *J* = 9.9 Hz), 4.30 (dd, 1 H, *J* = 12.6, 4.8 Hz), 4.24 (d, 1 H, *J* = 9.9 Hz), 4.08 (dd, 1 H, *J* = 12.6, 2.1 Hz), 3.74 (ddd, 1 H, *J* = 9.9, 4.8, 2.1 Hz), 2.86 (q, 6 H, *J* = 7.5 Hz), 1.99, 1.98, 1.96, 1.94 (4 s, 3 H each), 1.18 (t, 9 H, *J* = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 170.6, 170.5, 169.2, 92.6, 73.9, 70.6, 68.2, 66.9, 62.0, 51.3, 23.4, 21.0, 20.9, 16.3; NI-FAB-MS *m*/*z* 411 M^-.

Triethylammonium (2*S*,3*R*,4*S*,5*S*,6*R*)-3,4,5-Tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2*H*-pyran-2-sulfonate (33). Dimethyldioxirane (18 mL of a 0.079 M solution in acetone) was added to a flask containing a solution of 249 mg (0.415 mmol) of thioacetate **29**[45] in 1 mL of acetone at 0 °C. The solution was stirred at 0 °C for 12 h, concentrated, and then chromatographed on silica with 198:1:1 dichloromethane/methanol/triethylamine as the eluant to give 242 mg (82%) of **33**, R_f 0.4 (98:1:1 dichloromethane/methanol/triethylamine): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15−7.50 (m, 15 H), 5.24 (d, 1 H, *J* = 9.9 Hz), 5.00 (d, 1 H, *J* = 11.1 Hz), 4.85 (app dd, 2 H, *J* = 11.1, 11.4 Hz), 4.70 (d, 1 H, *J* = 9.6 Hz), 4.57 (d, 1 H, *J* = 10.8 Hz), 4.48, (s, 2 H), 4.22 (d, 1 H, *J* = 9.3 Hz), 3.94 (t, 1 H, *J* = 8.7 Hz), 3.68−3.82 (m, 4 H), 3.50−3.68 (m, 1 H), 3.01 (q, 6 H, *J* = 7.2 Hz), 1.24 (t, 9 H, *J* = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 138.4, 138.2, 138.1, 128.9, 128.4, 128.1, 127.9, 127.8, 127.7, 127.7, 127.5, 127.4, 88.2, 86.7, 80.5, 78.6, 77.5, 75.8, 75.1, 75.0, 73.3, 69.1, 46.0, 8.5; NI-FAB-MS *m*/*z* 604 M^-.

Triethylammonium (2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Triacetoxy-6-(acetoxymethyl)tetrahydro-2*H*-pyran-2-sulfonate (34). Dimethyldioxirane (5 mL of a 0.079 M solution in acetone) was added to a flask containing a solution of 46 mg (0.113 mmol) of thioacetate **30**[46] in 1 mL of acetone at 0 °C. The solution was stirred at 0 °C

(43) Zanini, D.; Park, W. K. C.; Roy, R. *Tetrahedron Lett.* **1995**, *36*, 7383−7386.
(44) Bonner, W. A. *J. Am. Chem. Soc.* **1951**, *73*, 2659−2666.
(45) Scheffler, G.; Behrendt, M. E.; Schmidt, R. R. *Eur. J. Org. Chem.* **2000**, 3527−3539.
(46) Blanc-Muesser, M.; Defaye, J.; Driguez, H. *J. Chem. Soc., Perkin Trans. 1* **1982**, 15−18.

for 16 h, concentrated, and then chromatographed on silica with 98:1:1 dichloromethane/methanol/triethylamine as the eluant to give 50 mg (86%) of sulfonate **34**, R_f 0.2 (98:1:1 dichloromethane/methanol/triethylamine): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.12 (dd, 1 H, J = 9.3, 9.9 Hz), 4.86−5.14 (m, 3 H), 4.73 (ddd, 1 H, J = 10.2, 3.6, 2.4 Hz), 4.26 (dd, 1 H, J = 12.9, 3.9 Hz), 4.12 (dd, 1 H, J = 12.9, 2.4 Hz), 2.92 (q, 6 H, J = 7.5 Hz), 2.07, 2.05, 2.00, 1.98 (4 s, 3 H each), 1.24, (t, 9 H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 170.7, 170.2, 169.8, 82.9, 70.9, 70.3, 70.3, 68.7, 62.3, 46.4, 21.4, 21.2, 21.2, 20.0, 10.0; NI-FAB-MS *m*/*z* 411 M^-.

Attempted Synthesis of Anomeric Sulfonyl Chlorides (Table 2). A solution of 43 mg (0.164 mmol) of triphenylphosphine in 500 μL of dichloromethane was stirred at −20 °C bath temperature. Sulfuryl chloride (15 μL, 0.180 mmol) was added dropwise, followed by slow addition of a solution of 42 mg (0.082 mmol) of **32** in 500 μL of dichloromethane, with the temperature maintained at −20 °C. The reaction was allowed to warm to 23 °C and was stirred at that temperature for 2 h. The solution was concentrated and then chromatographed on silica with 1:3 ethyl acetate/hexanes as the eluant to give 21 mg (70%) of tetra-*O*-acetyl-α-D-glucopyranosyl chloride **35** as an off-white solid, mp 70−72 °C, R_f 0.25 (1:3 ethyl acetate/hexanes). The mp and ^{1}H NMR spectrum of **35** matched the literature data.[47]

Treatment of **32** with phosphorus pentachloride or oxalyl chloride in the same fashion gave tetra-*O*-acetyl-α-D-glucopyranosyl chloride **35** as the only carbohydrate product identifiable by TLC and ^{1}H NMR analysis.

Similar treatment of sulfonate **33** with 1.75 equiv of phosphoryl chloride gave 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride **36** as the only identifiable carbohydrate product. The ^{1}H NMR spectrum matched the literature values.[48]

2,3,4,6-Tetra-*O*-benzyl-α/β-D-glucopyranosyl Fluoride (37). (Diethylamino)sulfur trifluoride (15 μL, 0.115 mmol) was added to a solution of 75.8 mg (0.108 mmol) of **33** in 2 mL of dichloromethane at 0 °C. The reaction was allowed to stir at 23 °C for 2 h, by which time TLC analysis indicated the consumption of starting material. ^{1}H NMR analysis of the crude concentrated reaction product and comparison with the literature spectra[49] showed two carbohydrate products, the anomeric fluorides **35**, as a 1:1 mixture.

(2*R*,3*S*,4*R*,5*R*,6*R*)-5-Acetamido-2-(acetoxymethyl)-6-(*N*,*N*-diethylaminothio)tetrahydro-2*H*-pyran-3,4-diyl Diacetate (44). A solution of 108.8 mg (0.299 mmol) of mercaptan **21** in 2 mL of dichloromethane was stirred at −78 °C bath temperature. Bromine (330 μL, 0.300 mmol) was added, and the reaction was maintained at −78 °C. After 0.5 h, 31 μL (0.300 mmol) of diethylamine was added, followed by 156 μL (8.98 mmol) of diisopropylethylamine. At this point, the dry ice bath was removed and the reaction was allowed to stir for 2 h. The solution was concentrated and then chromatographed on silica gel with 1:4 ethyl acetate/dichloromethane as the eluant to give 84.5 mg (65%) of **44** as a colorless oil, R_f 0.6 (7:3 ethyl acetate/dichloromethane): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76 (d, 1 H, J = 8.8 Hz), 5.50 (d, 1 H, J = 5.6 Hz), 5.01 (t, 1 H, J = 9.6 Hz), 4.81 (dd, 1 H, J = 11.2, 9.6 Hz), 4.48 (ddd, 1 H, J = 11.2, 8.8, 5.6 Hz), 3.38 (ddd, 1 H, J = 10.0, 4.8, 2.4 Hz), 4.26 (dd, 1 H, J = 12.0, 4.8 Hz), 4.10 (dd, 1 H, J = 12.0, 2.4 Hz), 2.81−2.99 (m, 4 H) 2.08, 2.03, 2.02, 1.97 (4 s, 3 H each), 1.14 (t, 6 H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 170.7, 169.7, 169.3, 87.1, 71.5, 69.3, 68.2, 62.3, 52.2, 52.0, 23.2, 20.7, 20.6, 13.7; FAB-MS *m*/*z* 457 MNa^+.

The preparation of **44** from **21** using sulfuryl chloride was also successful. A solution of 129.3 mg (0.356 mmol) of **21** in 5 mL of dichloromethane was stirred at −40 °C (bath temperature). Sulfuryl chloride (33 μL, 0.414 mmol) was added, and the reaction was maintained at −40 °C. After 0.5 h, 48 μL (0.465 mmol) of diethylamine was added, followed by 186 μL (1.08 mmol) of diisopropylethylamine. The dry ice bath was removed and the reaction was allowed to come to 23 °C and to stir for 2 h. The solution was concentrated and then chromatographed on silica gel with 1:4 ethyl acetate/dichloromethane as the eluant to give 90 mg (58%) of sulfenamide **44** as a colorless oil, R_f 0.6 (7:3 ethyl acetate/dichloromethane), with ^{1}H NMR spectrum and TLC behavior identical to that described above.

***N*-[(2*R*,3*R*,4*R*,5*S*,6*R*)-2-(Diethylaminothio)-4,5-dihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3-yl]acetamide (45).** Sulfenamide triacetate **44** (57 mg, 0.131 mmol) was dissolved in 2 mL of methanol at 0 °C bath temperature. Sodium methoxide (13 μL of a 1 M solution in methanol) was added at 0 °C. The reaction was stirred for 2 h, concentrated, and then chromatographed on silica gel with 1:19 methanol/dichloromethane as the eluant to give 38 mg (95%) of triol **45** as a white solid, mp 185 °C, R_f 0.4 (1:9 methanol/dichloromethane): ^{1}H NMR (300 MHz, D_2O) δ 5.58 (d, 1 H, J = 5.6 Hz), 3.92−4.00 (m, 2 H), 3.82 (dd, 1 H, J = 12.0, 2.8 Hz), 3.75 (dd, 1 H, J = 12.0, 4.8 Hz), 3.28−3.40 (m, 2 H), 2.80−2.99 (m, 4 H), 2.00 (s, 3 H), 1.14 (t, 6 H, J = 7.2 Hz); ^{13}C NMR (100 MHz, D_2O) δ 173.6, 87.5, 75.5, 73.0, 72.7, 62.7, 55.8, 53.4, 22.7, 14.2; FAB-MS *m*/*z* 331 MNa^+.

(2*R*,3*S*,4*R*,5*R*,6*S*)-5-Acetamido-2-(acetoxymethyl)-6-(diethylaminothio)tetrahydro-2*H*-pyran-3,4-diyl Diacetate (47). A 25 mL flask containing a solution of 94.3 mg (0.233 mmol) of thioacetate **27** in 2 mL of dichloromethane was cooled to −78 °C bath temperature. Bromine (256 μL, 0.256 mmol) was added, and the reaction mixture was maintained at −78 °C. After 0.5 h, 29 μL (0.279 mmol) of diethylamine was added, followed by 122 μL (0.699 mmol) of diisopropylethylamine. At this point, the dry ice bath was removed and the reaction was allowed to stir for 2 h. The solution was concentrated and then chromatographed on silica gel with 1:4 ethyl acetate/dichloromethane as the eluant to give 84.5 mg (65%) of sulfenamide **47** as a colorless oil, R_f 0.6 (7:3 ethyl acetate/dichloromethane): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.43 (d, 1 H, J = 8.7 Hz), 5.22 (t, 1 H, J = 9.3 Hz), 5.04 (t, 1 H, J = 9.09 Hz), 4.68 (d, 1 H, J = 10.8 Hz), 4.11−4.26 (m, 2 H), 3.95 (q, 1 H, J = 10.2 Hz), 3.67 (ddd, 1 H, J = 9.9, 5.4, 2.4 Hz), 2.84−3.02 (m, 4 H) 2.07, 2.04, 2.03, 1.96 (4 s, 3 H each), 1.13 (t, 6 H, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 170.7, 169.7, 169.3, 87.1, 71.5, 69.3, 68.2, 62.3, 52.2, 52.0, 23.2, 20.7, 20.6, 13.7; FAB-MS *m*/*z* 457 MNa^+. An earlier literature description of **47** records a different ^{1}H NMR ($CDCl_3$) spectrum.[37b]

***N*-((2*S*,3*R*,4*R*,5*S*,6*R*)-2-(Diethylaminothio)-4,5-dihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3-yl)acetamide (48).** A solution of 30 mg (0.069 mmol) of **47** in 1 mL of methanol at 0 °C bath temperature was treated with 6 μL of a 1 M solution of methanol sodium methoxide. After 2 h at 0 °C, the reaction mixture was concentrated and then chromatographed on silica gel with 1:19 methanol/dichloromethane as the eluant to give 38 mg (95%) of **48** as a colorless oil, R_f 0.4 (1:9 methanol/dichloromethane): ^{1}H NMR (300 MHz, D_2O) δ 4.58 (d, 1 H, J = 10.2 Hz), 3.87 (dd, 1 H, J = 12.0, 2.4 Hz), 3.79 (t, 1 H, J = 9.9 Hz), 3.70 (dd, 1 H, J = 12.0, 5.4 Hz), 3.47 (dd, 1 H, J = 9.6, 8.7 Hz), 3.26−3.42 (m, 2 H), 2.90 (q, 4 H, J = 7.2 Hz), 1.95 (s, 3 H), 1.16 (t, 6 H, J = 7.2 Hz); ^{13}C NMR (75 MHz, D_2O) δ 173.3, 91.3, 82.7, 77.4, 71.9, 62.9, 56.8, 52.6, 23.1, 14.0; FAB-MS *m*/*z* 331 MNa^+.

(2*R*,3*S*,4*R*,5*R*,6*R*)-5-Acetamido-2-(acetoxymethyl)-6-[(*S*)-*N*,*N*-diethylsulfinamoyl]tetrahydro-2*H*-pyran-3,4-diyl Diacetate (49). *m*-CPBA (40 mg, 0.232 mmol) was added to a mixture of 41.7 mg (0.096 mmol) of **44**, 24.2 mg (0.288 mmol) of sodium hydrogencarbonate, and 2 mL of 1,2-dichloroethane at 23 °C. The reaction was stirred for 12 h at 23 °C. Dichloromethane (2 mL) was added, and the resulting mixture was washed three times with aqueous sodium bicarbonate. Concentration of the organic layer and then chromatography on silica with 7:3 ethyl acetate/dichloromethane as the eluant gave 37 mg (86%) of **49** as a colorless oil, R_f 0.2 (7:3 ethyl acetate/dichloromethane): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04

(47) Jansson, K.; Noori, G.; Magnusson, G. *J. Org. Chem.* **1990**, *55*, 3181−3185.
(48) Cicchillo, R. M.; Norris, P. *Carbohydr. Res.* **2000**, *328*, 431−434.
(49) Drew, K. N.; Gross, P. H. *J. Org. Chem.* **1991**, *56*, 509−513.

(d, 1 H, J = 9.6 Hz), 5.41 (dd, 1 H, J = 11.1, 9.3 Hz), 5.2 (t, 1 H, J = 9.6 Hz), 4.82 (ddd, 1 H, J = 11.1, 9.6, 5.1 Hz), 4.49 (d, 1 H, J = 5.1 Hz), 4.16 (dd, 1 H, J = 12.6, 4.8 Hz), 4.00−4.12 (m, 2 H), 3.33 (quintet, 2 H, J = 7.5 Hz), 3.21 (quintet, 2 H, J = 7.5 Hz), 2.08, 2.04, 2.03, 1.96 (4 s, 3 H each), 1.24 (t, 6 H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 170.3, 170.1, 169.0, 87.4, 73.3, 71.5, 68.5, 62.1, 50.3, 41.8, 23.4, 20.8, 20.7, 20.7, 14.7; FAB-MS m/z 473 MNa^+.

(2*R*,3*S*,4*R*,5*R*,6*R*)-5-Acetamido-2-(acetoxymethyl)-6-(*N*,*N*-diethylsulfamoyl)tetrahydro-2*H*-pyran-3,4-diyl Diacetate (50). *m*-CPBA (15 mg, 0.058 mmol) was added to a mixture of 13 mg (0.029 mmol) of **49**, 7.3 mg (0.087 mmol) of sodium bicarbonate, and 1 mL of 1,2-dichloroethane at 23 °C. The reaction was heated for 1 h at 40 °C and then cooled and diluted with 1.5 mL of dichloromethane. The organic solution was washed three times with aqueous sodium bicarbonate and then concentrated and chromatographed on silica with 1:4 ethyl acetate/dichloromethane as the eluant to give 13.4 mg (100%) of **50** as a colorless oil, R_f 0.6 (7:3 ethyl acetate/dichloromethane): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.18 (d, 1 H, J = 9.0 Hz), 5.63 (dd, 1 H, J = 11.4, 9.3 Hz), 5.16 (dd, 1 H, J = 10.2, 9.6 Hz), 4.91 (d, 1 H, J = 6.3 Hz), 4.52−4.70 (m, 2 H), 4.17 (dd, 1 H, J = 12.6, 4.2 Hz), 4.09 (dd, 1 H, J = 12.6, 2.4 Hz), 3.42 (quintet, 2 H, J = 7.5 Hz), 3.28 (quintet, 2 H, J = 7.5 Hz), 2.09, 2.04, 2.04, 2.00 (4 s, 3 H each), 1.22 (t, 1 H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 170.7, 170.3, 169.1, 85.6, 72.4, 69.7, 67.7, 62.0, 50.3, 41.8, 23.3, 20.8, 20.7, 14.5; FAB-MS m/z 489 MNa^+.

***N*-((2*R*,3*R*,4*R*,5*S*,6*R*)-2-(*N*,*N*-Diethylsulfamoyl)-4,5-dihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3-yl)acetamide (51).** Sulfonamide **50** (15 mg, 0.032 mmol) was dissolved in 1 mL of methanol at 0 °C bath temperature. Sodium methoxide (3 μL of a 1 M solution in methanol) was added at 0 °C. The reaction mixture was stirred for 2 h at 23 °C, concentrated, and then chromatographed on silica with 1:19 methanol/dichloromethane as the eluant to give 11 mg (100%) of **51** as a colorless oil, R_f 0.4 (1:9 methanol/dichloromethane): ^{1}H NMR (300 MHz, D_2O) δ 5.12 (d, 1 H, J = 5.4 Hz), 4.02−4.14 (m, 3 H), 3.82 (dd, 1 H, J = 12.3, 2.4 Hz), 3.00 (dd, 1 H, J = 12.3, 4.8 Hz), 3.22−3.52 (m, 5 H), 1.99 (s, 3 H), 1.20 (t, 6 H, J = 7.2 Hz); ^{13}C NMR (75 MHz, D_2O) δ 174.4, 87.2, 78.8, 71.8, 71.1, 62.6, 54.0, 43.4, 22.8, 15.4; FAB-MS m/z 363 MNa^+.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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