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Synthesis of Sulfonium Sulfate Analogues of Disaccharides and Their Conversion to Chain-Extended Homologues of Salacinol: New Glycosidase Inhibitors

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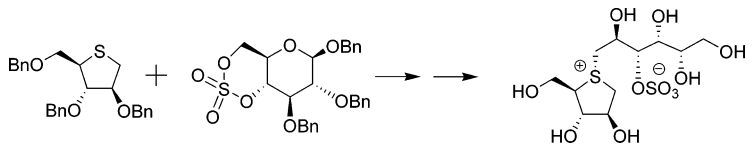
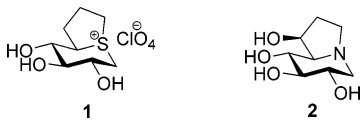


Four chain extended homologues of salacinol, a naturally occurring glycosidase inhibitor, were prepared for evaluation as inhibitors of glucosidase enzymes involved in the breakdown of carbohydrates. The syntheses involved the reactions of 1,4-anhydro-2,3,5-tri-*O*-benzyl-4-thio-D-arabinitol with cyclic sulfate derivatives of different monosaccharides. Debenzylation of the products afforded the novel sulfonium sulfate derivatives of D-glucose, D-galactose, D-arabinose, and D-xylose that are of interest in their own right as glycosidase inhibitors. Reduction to the corresponding alditols then afforded the homologues of salacinol containing polyhydroxylated, acyclic chains of 5- and 6-carbons, differing in stereochemistry at the stereogenic centers. Three of the chain-extended homologues inhibited recombinant human maltase glucoamylase, one of the key intestinal enzymes involved in the breakdown of glucose oligosaccharides in the small intestine, with K_i values in the low micromolar range, of approximately the same magnitude as salacinol, thus providing lead candidates for the treatment of Type 2 diabetes.

Introduction

Sulfonium salts are known to exhibit enhanced stability in comparison to their lighter congeners, the oxonium ions. Nevertheless, these salts are reactive species and simple sulfonium salts have found widespread use as photoinitiators for cationic polymerizations[1] or as precursors to the synthetically important sulfur ylides.[2] More highly functionalized sulfonium salts are generally only encountered as proposed intermediates in isomerization or rearrangement reactions.[3]

Sulfonium salts resemble tertiary amines yet bear permanent positive charges. Amines are ubiquitous in physiologically active compounds, and natural and synthetic sugar-mimetic amines are well-known as inhibitors of glycosidase enzymes.[4] It has often been hypothesized that such inhibitors are protonated by active site carboxylic acids and bind to enzymes as the ammonium salts.[4] We have proposed that sulfonium salts may mimic ammonium salts and could thus act as glycosidase inhibitors. Indeed, a sulfonium salt analogue **1**[5] of the well-known bicyclic azasugar castanospermine **2** was a weak (K_i, mM) inhibitor of



1 **2**

glucoamylase G2 and bound to the enzyme in a high-energy boat conformation, presumably resembling the oxacarbenium ion transition state in the glycosidase-mediated hydrolysis reaction.[6] Other groups have also taken up this theme and the synthesis of a sulfonium analogue of swainsonine[7] and sulfonium analogues of the 1-aza glycosidase inhibitor isofucofago-

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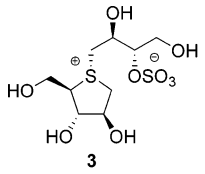
mine have appeared.[8] Most recently, Siriwardena et al.[9] have reported an inventive synthetic route for a sulfonium salt analogue of the bicyclic glycosidase inhibitor swainsonine. This compound was found to be a selective, potent inhibitor for certain α-mannosidase enzymes.

A naturally occurring, stable sulfonium salt, salacinol **3**, having an internal sulfate counterion was isolated as one of the physiologically active components of the medicinal plant *Salacia reticulata*.[10] This compound is the first of a new class of naturally occurring glycosidase inhibitors, and is responsible, at least in part, for the beneficial effects of the ingestion of *Salacia* extracts as a traditional treatment for diabetes.[11] It has been found to be a potent inhibitor of intestinal glycosidase enzymes,[10,12−14] and should thus attenuate the undesirable spike in blood glucose levels that is experienced by diabetics after consuming a meal rich in carbohydrates.[15] Another related sulfonium sulfate, kotalanol **4**,[12] was subsequently isolated from



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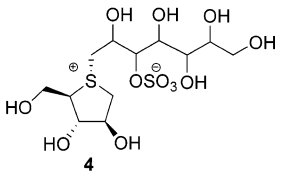

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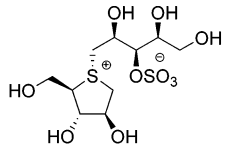
the *Salacia* extracts and was shown to possess even greater inhibitory power for certain glycosidase enzymes. A close relationship to the prototypical salacinol structure is obvious, with the alditol side chain being simply extended by three carbons. Although the absolute configuration of the stereogenic centers in the heptitol chain has not been reported, the 1,4-thioanhydro pentitol portion of kotalanol **4** has the identical D-arabinitol configuration as salacinol **3**.

We[16] and others[17] have reported the synthesis of salacinol **3** and some of its enantio- and diastereoisomers. In addition, we have undertaken a limited structure−activity study of related compounds. Thus far, we have reported the synthesis and glycosidase inhibitory activities of ammonium[18] and selenonium[19] analogues of salacinol, other stereoisomers of salacinol,[20] and six-membered-ring analogues of salacinol and its heteroanalogues.[21] Significantly, salacinol **3** and its selenium analogue, blintol, have been shown to be very effective in controlling blood glucose levels in rats after a carbohydrate meal, thus providing lead candidates for the treatment of Type 2 diabetes.[19c] These agents act by inhibiting the membrane-bound glucosidase enzymes in the small intestine that break down oligosaccharides to glucose.[19c] The structure−activity studies have revealed an interesting variation in the inhibitory power of these compounds against glycosidase enzymes of different origin. The molecular basis for this selectivity is being investigated through structural studies of the enzyme-bound inhibitors, using molecular modeling in conjunction with STD-NMR techniques[22] and X-ray crystallography.[23]

Initial findings with Golgi α-mannosidase II have indicated that the alditol side chain extends out of the substrate binding site,[23] and thus the length of the chain may not be of particular importance for binding specificity and inhibitor action with this particular enzyme. However, the reported greater inhibitory potency of kotalanol **4** than salacinol **3** with other glucosidase enzymes[12] suggests that this conclusion might not be general. To test this hypothesis, and to provide new candidates for the treatment of Type 2 diabetes, we now report the synthesis of four salacinol analogues **5**−**8** having either a five- or six-carbon alditol side chain.



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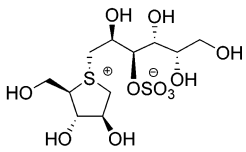

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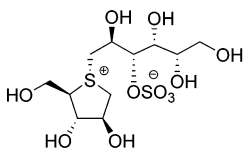

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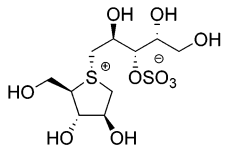

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In the course of these studies we had occasion to prepare and examine the stability of sulfonium−sulfate disaccharide analogues. These compounds **9**−**12** are representatives of a new class of carbohydrate derivatives since they are disaccharide analogues in which a permanent positive charge resides on the chain-linkage atom, which simultaneously acts as the ring heteroatom for an anhydroalditol unit. This feature may approximate the partial positive charges that are generated on analogous atoms in the transition states for enzyme-catalyzed disaccharide hydrolysis reactions. Electrostatic and hydrogen-bonding interactions of enzyme active-site functional groups with the charged atom could enhance binding and lead to the discovery of new glycosidase inhibitors.

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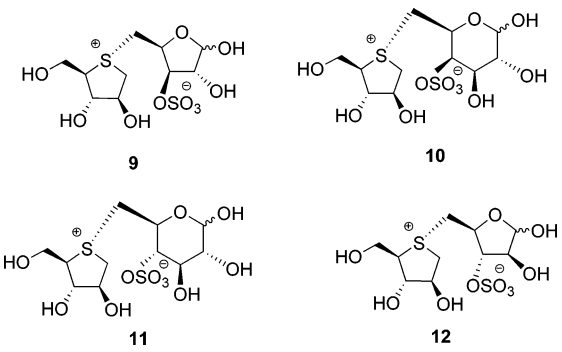
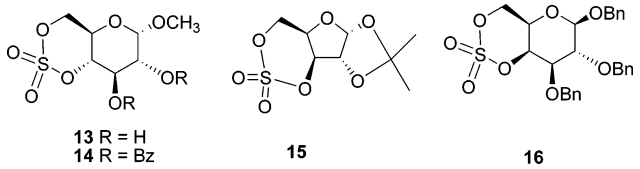


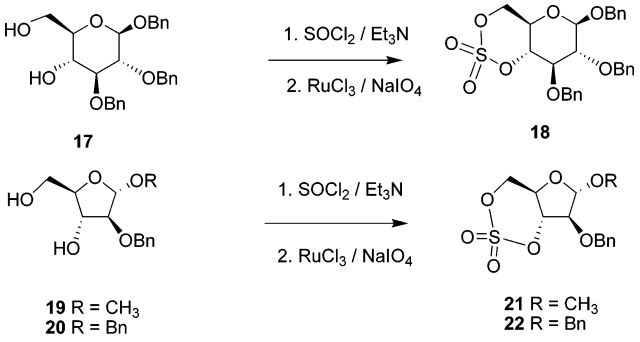
Results and Discussion

Our synthetic strategy was analogous to that used for the synthesis of salacinol **3** and related structures in that it involved the opening of a 1,3-cyclic sulfate ring by nucleophilic attack of a thioether.[16,17,20] A literature survey revealed the following 1,3-cyclic sulfates of carbohydrate derivatives as potential acceptors: D-glucopyranoside-4,6-*O*-cyclic sulfates **13**[24] and **14**[25] as well as the D-xylose derivative **15**[26] and the D-galactose derivative **16**.[27] These derivatives have been shown to react with oxygen, nitrogen, or sulfur nucleophiles selectively at the primary carbon. The methyl pyranosides **13** and **14** were rejected due to the probable harsh conditions necessary for hydrolysis of the glycoside bond during the deprotection of the proposed, and possibly sensitive, sulfonium-ion intermediates. Compounds **15** and **16** were deemed to be more suitable and were prepared

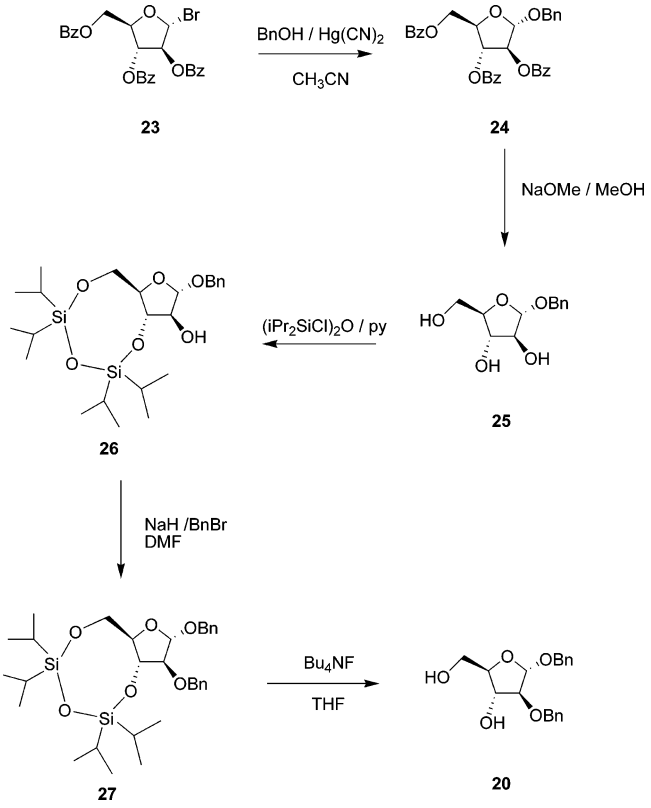


by the literature methods. Three other cyclic sulfates were prepared by new methods. Thus, benzyl D-glucopyranoside 4,6-cyclic sulfate **18** was prepared by the Sharpless method[28] from the known benzyl D-glucopyranoside **17**,[29] and similar treatment of the methyl or benzyl D-arabinofuranosides **19**[30] and **20** yielded the cyclic sulfates **21** and **22** (Scheme 1).

SCHEME 1



SCHEME 2



The cyclic sulfate derivatives **15** and **16** were prepared uneventfully. However, the trans fused [5.6] bicyclic systems in compounds **21** and **22** impart considerably more ring strain to these compounds than the cis fused [5.6] bicyclic compound **15** or the [6.6] cis or trans fused ring systems of compounds **16** or **18**. This resulted in the formation of substantial amounts of bridging sulfate dimers by intermolecular reactions during the synthesis of **21** and **22**. The careful control of reactant concentration and temperature gave modest yields of monomeric cyclic sulfates **21** and **22**, which were isolated as pure crystalline solids.

The required diol **20** was prepared by analogy to the methods already reported for **19**.[30] Thus, benzyl D-arabinofuranoside **24**[31] was prepared by glycosylation of benzyl alcohol with the glycosyl bromide **23**,[32] using the Helferich method. The benzoyl protecting groups were removed to give **25** and the 3- and 5-positions were then blocked as the tetraisopropyldisiloxane derivative **26**. The 2-hydroxyl group was protected as the benzyl ether **27** in a reaction that required careful monitoring to prevent premature silyl group cleavage and subsequent benzylation of the exposed hydroxyl groups. The silyl protecting group was finally removed by treatment of **27** with fluoride to give the diol **20** (Scheme 2).

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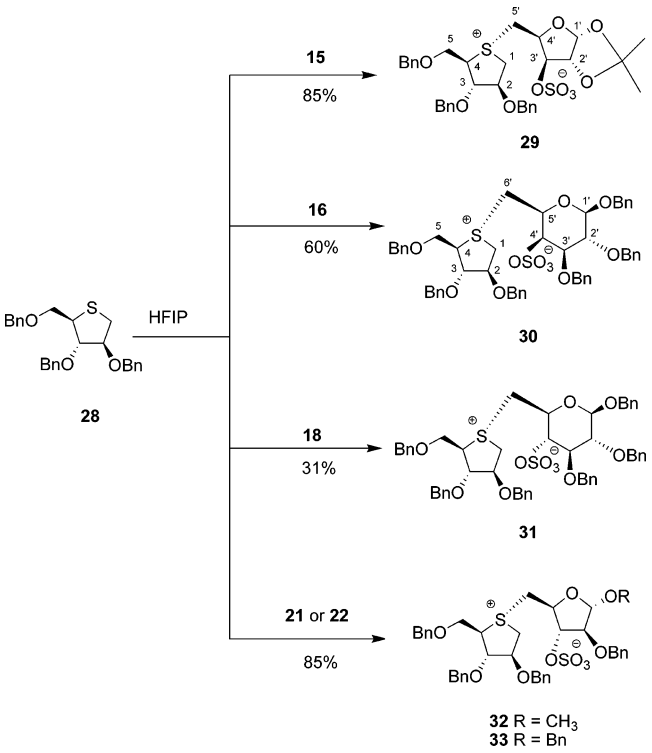
SCHEME 3



The thioether **28** was available from earlier work[16] and could be prepared more conveniently by a method analogous to that developed for the corresponding selenium derivative.[19] Compound **28** was reacted with each of the cyclic sulfates **15**, **16**, **18**, **21**, and **22** to give the protected sulfonium sulfate compounds **29**−**32** (Scheme 3). The solvent chosen for these reactions was 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), which we have found previously to offer significant advantages in reactions that yield sulfonium salts from neutral precursors.[33] Initial trials with the cyclic sulfate **15** showed that the addition of K_2CO_3, which we had previously routinely included to ensure that the reaction mixture did not become acidic through hydrolysis of the cyclic sulfate by traces of water, was not necessary. In the present case, the presence of base led to decomposition of **15** and inferior yields of the desired coupled product **29**. All subsequent reactions were therefore performed without base. In addition, use of the thioether **28** in slight excess over the cyclic sulfate gave superior yields in certain cases.

The reactivity of the cyclic sulfates varied widely, with the D-glucose derivative **18** being the least reactive and giving the desired product **31** in a yield of just 31% after 42 h at 70 °C. In contrast, the strained cyclic sulfate **22** was most reactive and yielded the coupled product **33** in 85% yield after only 2.5 h at 40 °C. The selectivity for attack of the thioether **28** at the primary over the secondary cyclic sulfate center was excellent, and in no case were isolable quantities of the regioisomeric products detected. There was evidence in the NMR spectra of the crude reaction mixtures for minor amounts of stereoisomers formed through electrophilic attack on the β-face of the thioether **28** to give products that were diastereomeric at the stereogenic sulfur center. In all cases, the minor β-isomer was removed by chromatography, albeit in most instances only by sacrificing

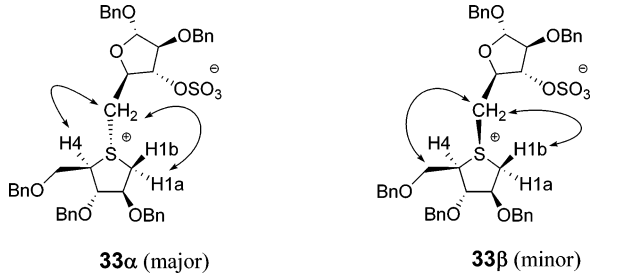


FIGURE 1. NOESY Correlations of Selected Protons in the Isomers of **33**.

part of the major α-isomer. The final yields of the coupled products **29**−**33** in Scheme 3 refer to the pure α-isomers isolated after one or two rounds of chromatography. The minor isomers were produced in variable proportion (up to 20% in the case of compound **31**) but, due to the similarity in chromatographic mobilities, they could not be obtained free of the major isomers in most instances. However, in the case of the coupled product **33**, almost pure fractions of the isomer **33**β were obtained and the product was characterized by NMR spectroscopy. The ^{1}H and ^{13}C NMR spectra of **33**β were very similar to those of the major isomer **33**α, but a NOESY spectrum showed clear H-5 to H-5′ and H-1b to H-5′ correlations, implying that these atoms are syn-facial on the sulfonium salt ring. In contrast, the major isomer **33**α exhibited H-1a to H-5′ and H-4 to H-5′correlations, as expected for the isomer of the opposite configuration at the sulfonium center (Figure 1).

We initially approached the deprotection steps with some apprehension of encountering problems in performing two or three successive reactions in the presence of a reactive sulfonium salt. This sense of unease was reinforced by our first attempts. Treatment of the sulfonium salt **29**, first with aqueous trifluoroacetic acid to remove the isopropylidene group, and then with $NaBH_4$ to reduce the hemiacetal led only to an intractable mixture. Similarly, although hydrogenolysis of the benzyl groups in compound **32** seemed to be successful, giving eventually a single product according to TLC analysis of the reaction mixture, removal of the catalyst by filtration and concentration led to decomposition of this initial product to give extremely polar material. We have been unable to develop an efficient deprotection protocol for compound **32**.

In contrast, the corresponding benzyl glycoside **33** gave, upon hydrogenolysis, a virtually quantitative yield of the hemiacetal product **12** as a 1:1 α:β mixture. The crude product was stable after removal of the solvent, and was even unchanged after storage in aqueous solution for several days at ambient temperature. Nevertheless, the crude product was generally immediately reduced with $NaBH_4$ to provide the desired alditol sulfonium sulfate **8**, in a yield of 66% for the two steps (Scheme 4). Analogous treatment of the protected compounds **30** and **31** gave the target compounds **6** and **7** via the intermediate hemiacetal derivatives **10** and **11**. The deprotection of compound **29** required a three-step procedure, which was eventually implemented as either of two possible sequences to give **5** (Scheme 4). Removal of the benzyl groups first (Procedure A) to yield the isopropylidene compound **34** was found to be advantageous since the alternative method (Procedure B), to give initially the 1,2-diol **35**, was found to lead to partial conversion to a methyl D-furanoside mixture **36** during the subsequent hydrogenolysis reaction in MeOH solvent. The methyl glycoside could be hydroyzed by re-treatment with

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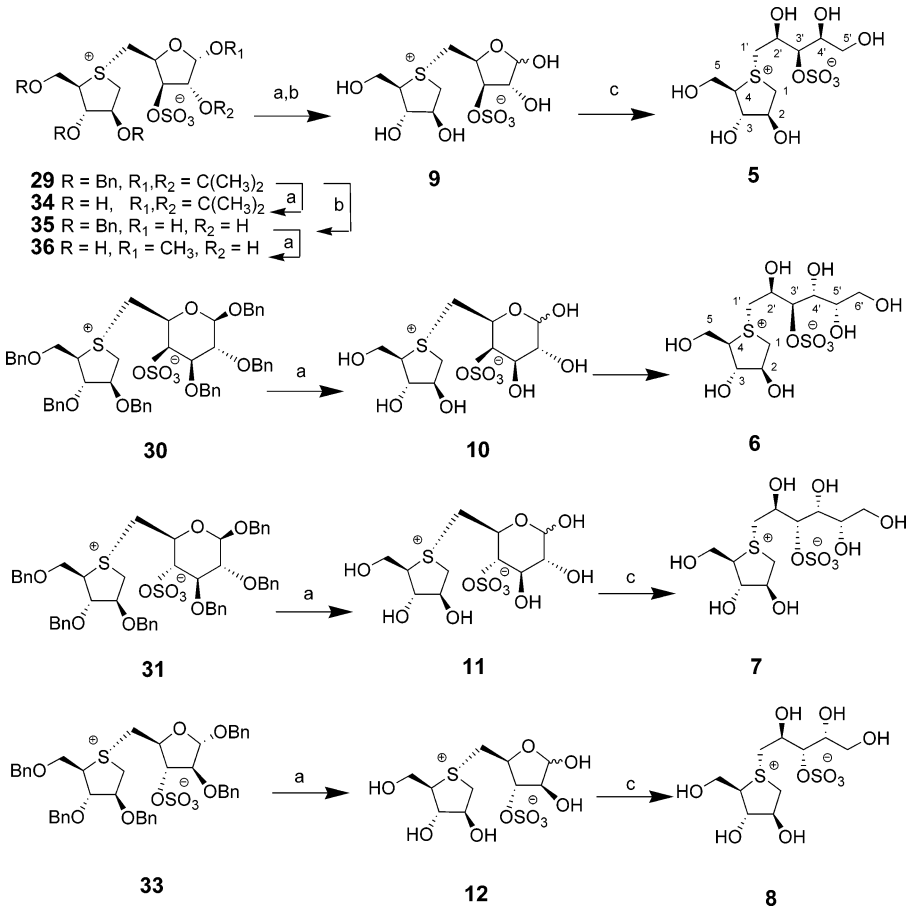
SCHEME 4[a]



[a] Reagents: (a) H_2, Pd(C)/MeOH, (b) TFA/H_2O, (c) $NaBH_4$/H_2O.

aqueous trifluoroacetic acid to give the intermediate hemiacetal **9** but this additional step resulted in a lower overall yield. Reduction of the hemiacetal with $NaBH_4$, as with the previous compounds, gave compound **5**. The sulfonium sulfates **5**−**12** were obtained as hygroscopic gums that were unsuitable for combustion analysis. Despite intensive efforts they could not be induced to crystallize. They were, however, extensively characterized by spectroscopic methods. MALDI-TOF mass spectrometry for compounds **5**−**8** in the positive-ion mode typically showed base peaks for masses attributable to sodium adduct ions (M + Na), and lower intensity peaks corresponding to M + H and M + H − SO_3H. The protected compounds **29**−**33** fragmented to give M + H − SO_3 base peaks and lower intensity M + H and M + Na peaks. This behavior seems general for this class of compound and is similar to that of sulfated carbohydrates which show loss of sulfate ion in their MALDI mass spectra.[34] Both the protected and the deprotected sulfonium compounds also exhibited variable intensity dimer or trimer cluster-ion peaks at higher masses. The compounds **5**−**12** were also characterized by high-resolution mass spectrometry. The NMR spectra for compounds **9**−**12** showed two sets of resonances corresponding to the mixture of α/*β* isomers at the hemiacetal center. In the ^1H NMR spectra, coupling constants between H-1 and H-2 allowed the assignment of these resonances to either the α- or the *β*-isomer and the assignment of the other resonances followed from analysis of the COSY spectra. The NMR spectra for compounds **5**−**8** were also in accord with the assigned structures, and were almost identical with those of salacinol **3** for those portions of the sulfonium salts having similar structure (see Tables 5 and 6). As was the case with salacinol **3**,[16] the stereochemical integrity at the stereogenic sulfur atom in each of **5**−**8** was maintained.

As a final point of interest, we comment on the glycosidase inhibitory properties of **5**−**12** against recombinant human maltase glucoamylase (MGA), a critical intestinal glucosidase involved in the processing of oligosaccharides of D-glucose into D-glucose itself, and of relevance to the control of Type 2 diabetes. Significantly, although compound **5** did not inhibit the activity of MGA, compounds **6**−**8** showed K_i values of 0.25, 0.26, and 0.17 *μ*M, respectively.[35] For purposes of comparison, salacinol inhibits MGA with a K_i value of 0.19 *μ*M.[35] It is clear that the stereochemistry of the C-4′ stereogenic center is critical for activity. The disaccharide analogues **9**−**12** were not active against MGA. Compounds **6**−**8**, together with others synthesized previously in our program, will serve as useful probes to map the enzyme-active sites of MGA and other related enzymes.

Experimental Section

Benzyl 2,3-Di-*O*-benzyl-*β*-D-glucopyranoside-4,6-cyclic Sulfate (18). Benzyl 2,3-di-*O*-benzyl-*β*-D-glucopyranoside[29] (1.63 g, 3.62

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mmol) and triethylamine (2.5 mL) were dissolved in CH_2Cl_2 (60 mL) and the mixture was stirred at room temperature. Thionyl chloride (0.60 mL, 8.2 mmol) was added dropwise and allowed to react for 20 min. The mixture was diluted with CH_2Cl_2 and washed with cold water (2 × 50 mL). The organic phase was dried over $MgSO_4$ and concentrated to a dark orange-brown syrup that was filtered through a short column of silica gel with hexanes:EtOAc, 3:1, and again concentrated to give a pale orange syrup (1.57 g). Analysis by TLC (hexanes:EtOAc, 3:1) showed that two products of approximately equal proportion had been formed. The mixture of cyclic sulfites was dissolved in CCl_4:CH_3CN (1:1, 60 mL) and the solution was stirred at room temperature. Sodium periodate (3.2 g, 15 mmol), $RuCl_3$:H_2O (56 mg, 0.25 mmol), and water (30 mL) were added sequentially. The dark-colored mixture was stirred for 15 min at room temperature and transferred to a separatory funnel with the aid of additional CH_2Cl_2 (50 mL). Without shaking, the organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (50 mL). The combined organic phase was treated with ethylene glycol (0.2 mL) and concentrated to a black syrup. This was dissolved in EtOAc (150 mL) and filtered through Celite to remove black RuO_2. The filtrate was washed with saturated aqueous $NaHCO_3$ (50 mL), dried over $MgSO_4$, and concentrated to give a yellow syrup. Purification by column chromatography on silica gel (hexanes:EtOAc,1:1) yielded the cylic sulfate **18** as a colorless syrup (1.48 g, 80%), which crystallized on standing, and was recrystallized from Et_2O/hexanes: mp 73−81°C, $[\alpha]_D$ −28 (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.4−7.2 (15H, m, Ar), 4.89, 4.64 (2H, 2d, $J_{A,B}$ = 11.7 Hz, C*H*$_2$Ph), 4.85, 4.71 (2H, 2d, $J_{A,B}$ = 10.8 Hz, C*H*$_2$Ph), 4.79, 4.73 (2H, 2d, $J_{A,B}$ = 11.1 Hz,C*H*$_2$Ph), 4.66 (1H, ddd, $J_{4,5}$ = 10.4 Hz, H-4), 4.65 (1H, dd, $J_{5,6a}$ = 10.5 Hz, $J_{6a,6b}$ = 10.7 Hz, H-6a), 4.63 (1H, d, $J_{1,2}$ = 7.7 Hz, H-1), 4.56 (1H, dd, $J_{5a,6b}$ = 5.2 Hz, H-6b), 3.75 (1H, ddd, H-5), 3.73 (1H, dd, $J_{2,3}$ = 8.7 Hz, $J_{3,4}$ = 9.2 Hz, H-3), 3.52 (1H, dd, H-2); ^{13}C NMR ($CDCl_3$) δ 137.7, 137.4 and 136.4 (3 × C═O, OBz), 128.6−127.9 (18C_{Ar}), 103.1 (C-1), 84.2 (C-4), 81.4 (C-2), 79.4 (C-3), 75.5, 75.4 and 71.9 (3 × *C*H$_2$Ph), 71.8 (C-6), 64.4 (C-5); MALDI MS *m*/*e* 551.13 (M^+ + K), 535.12 (M^+ + Na). Anal. Calcd for $C_{27}H_{28}O_8S$: C, 63.27; H, 5.51. Found: C, 63.58; H, 5.47.

Methyl 2-*O*-Benzyl-α-D-arabinofuranoside-3,5-cyclic Sulfate (21). Methyl 2-*O*-benzyl-α-D-arabinofurananoside **19**[30] (1.47 g, 5.78 mmol) and triethylamine (3.0 mL) were dissolved in CH_2Cl_2 (75 mL) and the mixture was stirred at room temperature. A solution of thionyl chloride (0.70 mL, 9.6 mmol) in CH_2Cl_2 (20 mL) was added dropwise over 15 min and allowed to react for 30 min. The mixture was diluted with CH_2Cl_2 (100 mL) and washed with ice−water (50 mL), cold saturated $NaHCO_3$ solution (50 mL), and cold water (20 mL). The organic phase was dried over $MgSO_4$ and concentrated to a dark orange-brown syrup that was filtered through a short column of silica gel with hexanes:EtOAc (1:2), and again concentrated to give a clear red oil (1.59 g). Analysis by TLC (hexanes:EtOAc, 3:1) showed that two products of approximately equal proportion had been formed. The mixture of cyclic sulfites was dissolved in CCl_4:CH_3CN (1:1, 40 mL), water (30 mL) was added, and the two-phase mixture was stirred rapidly at room temperature. $RuCl_3$:H_2O (18 mg, 0.08 mmol) was added followed by small portions of $NaIO_4$ (1.59 g, 7.43 mmol in total) added over 45 min, while monitoring the progress of the reaction by TLC. A slightly more-polar, major product was formed along with more polar byproducts. The dark-colored mixture was stirred for an additional 15 min at room temperature and then processed to give crude **21** by the same procedure described above for the preparation of compound **18**. Purification by column chromatography on silica gel (hexanes:EtOAc, 3:1 to 1:1) yielded the cyclic sulfate **21** as a colorless crystalline solid (1.01 g, 55%). Also isolated was a sample of the major byproduct as a colorless solid (216 mg). A sample of compound **21** was recrystallized from EtOAc/hexanes to give large leaflets: mp 97−98°C, $[\alpha]_D$ +12 (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.40−7.30 (5H, m, Ar), 4.97 (1H, d, $J_{1,2}$ = 2.8 Hz, H-1), 4.79 (1H, dd, $J_{2,3}$ = 7.6 Hz, $J_{3,4}$ = 10.2 Hz, H-3), 4.72 (1H, dd, $J_{4,5a}$ = 11.0 Hz, $J_{5a,5b}$ = 9.8 Hz, H-5a), 4.66 (1H, dd, $J_{4,5b}$ = 4.9 Hz, H-5b), 4.65 and 4.57 (2H, 2d, $J_{A,B}$ = 11.7 Hz, C*H*$_2$Ph), 4.26 (1H, ddd, H-4), 4.18 (1H, dd, H-2), 3.39 (3H, s, OC*H*$_3$); ^{13}C NMR ($CDCl_3$) δ 136.5 (C_{ipso}, Ar), 128.6 (2C), 128.3, and 128.0 (2C) (5C_{Ar}), 109.6 (C-1), 86.7 (C-3), 83.7 (C-2), 73.7 (C-5), 72.9 (*C*H$_2$Ph), 67.9 (C-4), 56.3 (O*C*H$_3$); MALDI MS *m*/*e* 355.08 (M^+ + K), 339.08 (M^+ + Na). Anal. Calcd for $C_{13}H_{16}O_7S$: C, 49.36; H, 5.10. Found: C, 49.56; H, 5.12.

Benzyl 2-*O*-Benzyl-α-D-arabinofuranoside-3,5-cyclic Sulfate (22). The diol **20** (1.37 g, 4.15 mmol) was converted to the cyclic sulfate **22** in two steps (via the intermediate cyclic sulfite), using the same procedure detailed above for the preparation of the cyclic sulfate **21** from diol **19**. The syrupy product (1.23 g) after column chromatography was found to contain approximately 15% of a sulfate-dimer impurity by ^{1}H NMR analysis. Crystallization from EtOAc:hexanes gave pure **22** (838 mg, 48%) as small colorless needles: mp 84−86°C, $[\alpha]_D$ +84 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.40−7.27 (10H, m, Ar), 5.18 (1H, d, $J_{1,2}$ = 2.8 Hz, H-1), 4.80 (1H, dd, $J_{2,3}$ = 7.6 Hz, $J_{3,4}$ = 10.2 Hz, H-3), 4.76 and 4.50 (2H, 2d, $J_{A,B}$ = 11.7 Hz, C*H*$_2$Ph), 4.74 (1H, dd, $J_{4,5a}$ = 11.0 Hz, $J_{5a,5b}$ = 9.8 Hz, H-5a), 4.67 (1H, dd, $J_{4,5b}$ = 4.9 Hz, H-5b), 4.62 and 4.53 (2H, 2d, $J_{A,B}$ = 11.7 Hz, C*H*$_2$Ph), 4.33 (1H, ddd, H-4), 4.28 (1H, dd, H-2); ^{13}C NMR ($CDCl_3$) δ 136.5 (2C, 2 × C_{ipso}, Ar), 128.6−127.9 (10 × C_{Ar}), 107.5 (C-1), 86.7 (C-3), 83.7 (C-2), 73.7 (C-5), 72.8 and 70.7 (2 × *C*H$_2$Ph), 68.1 (C-4); MALDI MS *m*/*e* 415.00 (M^+ + Na). Anal. Calcd for $C_{19}H_{120}O_7S$: C, 58.15; H, 5.14. Found: C, 58.06; H, 5.17.

Benzyl 2,3,5-Tri-*O*-benzoyl-α-D-arabinofuranoside (24).[31] To a stirred mixture of mercuric cyanide (5.20 g, 20.6 mmol) in CH_3-CN (50 mL) was added benzyl alcohol (2.0 mL, 19 mmol) and the glycosyl bromide **23**[32] (5.25 g, 10.0 mmol). The mixture was stirred for 0.5 h at room temperature and then concentrated by rotary evaporation to remove most of the solvent. The residue was partitioned between Et_2O (150 mL) and water (50 mL). The organic phase was washed with saturated $NaHCO_3$ (30 mL), water (30 mL), and brine (30 mL) and dried over $MgSO_4$. Solvent removal gave the crude product contaminated with mercury salts and excess benzyl alcohol. Purification by colmn chromatography on silica gel (hexanes:EtOAc, 3:1) yielded the benzyl glycoside **24** as a colorless syrup, which crystallized on standing. Recrystallization from EtOH gave the pure compound **24** (4.73 g, 86%): mp 92−93°C (lit.[31] mp 89−90°C); $[\alpha]_D$ +9.3 (*c* 1.1, $CHCl_3$)(lit.[31] $[\alpha]_D$ +10.1 (*c* 1.04, $CHCl_3$)); ^{1}H NMR data were identical with the literature data;[31] ^{13}C NMR ($CDCl_3$) δ 166.2, 165.8 and 165.3 (3 × C═O, 3 × OBz), 137.4−126.9 (24 × C_{Ar}), 105.1 (C-1), 82.0 (C-2), 81.4 (C-4), 77.9 (C-3), 68.9 (*C*H$_2$Ph), 63.9 (C-5).

Benzyl 3,5-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-α-D-arabinofuranoside (26). The tribenzoate **24** (4.48 g, 8.11 mmol) was added to MeOH (150 mL) and the heterogeneous mixture was placed under a nitrogen atmosphere. A solution of NaOMe in MeOH (1.0 M, 4.0 mL) was added and the mixture was stirred at room temperature for 3 h. The starting material slowly dissolved during the first hour. Upon completion of the reaction, as judged by TLC analysis, the NaOMe was neutralized by addition of excess Rexyn 101 H^+ ion-exchange resin, the resin was removed by filtration, and the solution was concentrated. The syrupy residue was shaken with hexanes (3 × 50 mL) to dissolve methyl benzoate, and the hexane extracts were decanted from the insoluble, crude, triol product **25** (2.02 g, after 3 h under high vacuum). The triol was dissolved in pyridine (30 mL) and a solution of 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (4.0 mL, 12 mmol) in CH_2Cl_2 (30 mL) was added dropwise at room temperature. The mixture was stirred for 2 h, diluted with CH_2Cl_2 (100 mL), and washed with saturated $NaHCO_3$ (50 mL). The aqueous phase was extracted with CH_2Cl_2 (50 mL) and the combined extracts were dried over $MgSO_4$ and concentrated by rotary evaporation, first at water aspirator pressure and then under high vacuum to remove pyridine. Purification by column chromatography on silica gel (hexanes:EtOAc, 5:1) yielded compound **26** as a colorless syrup (3.58 g, 91% for 2 steps):

$[\alpha]_D$ +47 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.44−7.25 (5H, m, Ar), 4.97 (1H, d, $J_{1,2}$ = 2.7 Hz, H-1), 4.78, 4.49 (2H, 2d, $J_{A,B}$ = 11.8 Hz, CH_2Ph), 4.25 (1H, dd, $J_{2,3}$ = 6.1 Hz, H-2), 4.19−4.15 (1H, 2nd order m, H-3), 4.02−3.91 (3H, m, H-4, H-5a, H-5b), 1.12−0.98 (24H, m, 4 × CH(CH_3)$_2$; ^{13}C NMR ($CDCl_3$) δ 137.8, (C_{ipso}, Ar), 128.4 (2C), 127.9 (2C) and 127.7 (5 × C_{Ar}), 106.3 (C-1), 82.9 (C-2), 81.1 (C-4), 77.6 (C-3), 69.6 (CH_2Ph), 61.8 (C-5), 17.5, 17.3 (3C), 17.2, 17.1, 17.05, 17.00, 13.5, 13.2, 12.9 and 12.6 (12C, 4 × CH(CH_3)$_2$); MALDI MS *m*/*e* 505.19 (M^+ + Na). Anal. Calcd for $C_{24}H_{42}O_6Si_2$: C, 59.71; H, 8.77. Found: C, 59.37; H, 8.99.

Benzyl 2-*O*-Benzyl-α-D-arabinofuranoside (20). The silyl protected compound **26** (3.50 g, 7.26 mmol) was dissolved in DMF (20 mL) and cooled by stirring in an ice bath under N_2. Benzyl bromide (2.0 mL, 17 mmol) was added in a single portion followed by 60% NaH/oil (0.37 g, 9.2 mmol), added carefully in small portions over 10 min. The reaction mixture was stirred at 0 °C for 1.5 h. Cold Et_2O (150 mL) and ice−water (50 mL) were added and the organic phase was separated. The aqueous phase was extracted with more Et_2O (100 mL) and the combined extracts were washed with water (2 × 50 mL), then brine (30 mL), and dried over $MgSO_4$. The solvents were evaporated and the residue was warmed under high vacuum to remove the excess benzyl bromide by distillation. The crude benzylated product **27** (4.12 g) was found to be approximately 90% pure as judged by analysis of the ^1H NMR spectrum, and was used directly in the following procedure.

The syrupy compound **27** was dissolved in dry THF (70 mL) and stirred while a 1.0 M solution of *n*-Bu_4NF in THF (16 mL, 16 mmol) was added. The reaction mixture was kept for 0.5 h at room temperature and concentrated to a brown residue. Nonpolar material was removed by shaking with hexanes (3 × 50 mL) and decanting the hexanes solution from the crude, insoluble diol product. The crude product was dissolved in EtOAc (150 mL), washed with brine (20 mL), dried over $MgSO_4$, and concentrated. The residue was purified by flash chromatography (hexanes:EtOAc, 1:3) to give diol **20** (1.50 g, 66%) as a colorless syrup, which crystallized on standing: mp 73−74 °C; $[\alpha]_D$ +99 (*c* 1.1, $CHCl_3$); MALDI MS *m*/*e* 353.02 (M^+ + Na). Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 68.90; H, 6.79.

NMR data for compound 20: ^1H NMR ($CDCl_3$) δ 7.4−7.2 (10H, m, Ar), 5.16 (1H, s, $J_{1,2} \approx 0$ Hz, H-1), 4.77 and 4.51 (2H, 2d, $J_{A,B}$ = 11.7 Hz, CH_2Ph), 4.61 and 4.54 (2H, 2d, $J_{A,B}$ = 11.7 Hz, CH_2Ph), 4.17 (1H, ddd, $J_{3,4}$ = 3.1 Hz, $J_{4,5a}$ = 3.1 Hz, $J_{4,5b}$ = 4.2 Hz, H-4), 4.15 (1H, ddd, $J_{3,OH}$ = 9.8 Hz, $J_{2,3}$ = 1.1 Hz, H-3), 3.96 (1H, d, H-2), 3.83 (1H, ddd, $J_{5a,5b}$ = 11.7 Hz, $J_{5a,OH}$ = 4.5 Hz, H-5a), 3.77 (1H,ddd, $J_{5b,OH}$ = 7.0 Hz, H-5b), 2.51 (1H, d, OH-3), 2.14 (1H, dd, OH-5); ^{13}C NMR ($CDCl_3$) δ 137.1 (2C, 2 × C_{ipso}, Ar), 128.6 (4C), 128.1 (3C) 128.0, and 127.9 (2C) (10 × C_{Ar}), 104.9 (C-1), 87.6 (C-2), 86.4 (C-4), 75.6 (C-3), 71.9 and 69.1 (2 × CH_2Ph), 62.6 (C-5).

NMR data for intermediate compound 27: ^1H NMR ($CDCl_3$) δ 7.4−7.2 (10H, m, Ar), 5.02 (1H, d, $J_{1,2}$ = 2.4 Hz, H-1), 4.76 and 4.49 (2H, 2d, $J_{A,B}$ = 11.9 Hz, CH_2Ph), 4.59 and 4.55 (2H, 2d, $J_{A,B}$ = 11.9 Hz, CH_2Ph), 4.30−4.27 (1H, 2nd order m, H-3), 4.04 (1H, dd, $J_{2,3}$ = 5.9 Hz, H-2), 4.02−3.91 (3H, m, H-4, H-5a, H-5b), 1.12−0.90 (24H, m, 4 × CH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$) δ 137.9 and 137.9, (2 × C_{ipso}, Ar), 128.4 (2C), 128.3 (2C), 127.9 (2C), 127.6 (2C), 127.6 and 127.6 (10 × C_{Ar}), 104.8 (C-1), 89.8 (C-2), 80.8 (C-4), 76.6 (C-3), 72.5 and 69.3 (2 × CH_2Ph), 61.8 (C-5), 17.5, 17.4 (3C), 17.1 (3C), 17.0, 13.5, 13.2, 12.9 and 12.6 (12C, 4 × CH(CH_3)$_2$).

General Procedure for the Preparation of Sulfonium Sulfates 29−33. A mixture of the thioether **28** (1.00−1.15 equiv) and the cyclic sulate **15**, **16**, **17**, **18**, or **19** (0.79−1.00 equiv) in HFIP (1.0−3.0 mL/mmol of **28**) was placed in a sealed reaction vessel and warmed with stirring for the indicated time at the temperatures given below. The progress of the reaction was followed by TLC analysis of aliquots (developing solvent $CHCl_3$:MeOH, 10:1). When the limiting starting compound had been essentially consumed, the mixture was cooled, then diluted with CH_2Cl_2 and evaporated to give a syrupy residue. Purification by column chromatography ($CHCl_3$ to $CHCl_3$:MeOH, 10:1) gave the purified sulfonium salts **29**−**33**.

5-Deoxy-5-[2,3,5-tri-*O*-benzyl-1,4-dideoxy-1,4-episufonium-ylidene-D-arabinitol]-1,2-*O*-isopropylidene-3-*O*-sulfoxy-α-D-xylofuranose Inner Salt (29). Reaction of the thioether **28** (833 mg, 2.03 mmol) with the cyclic sulfate **15** (649 mg, 2.57 mmol) in HFIP (2.5 mL) for 44 h at 70 °C gave compound **29** as a colorless crystalline solid (1.16 g, 85%). A sample was recrystallized from MeOH: mp 149−151°C; $[\alpha]_D$ −10 (*c* 1.0, $CHCl_3$). See Tables 1 and 2 for NMR data. MALDI MS *m*/*e* 695.18 (M^+ + Na), 673.13 (M^+ + H), 593.20 (M^+ + H − SO_3). Anal. Calcd for $C_{34}H_{40}O_{10}S_2$: C, 60.70; H, 5.99. Found: C, 60.81; H, 5.86.

Benzyl 2,3-Di-*O*-benzyl-6-deoxy-6-[2,3,5-tri-*O*-benzyl-1,4-dideoxy-1,4-episufoniumylidene-D-arabinitol]-4-*O*-sulfoxy-β-D-galactopyranose Inner Salt (30). Reaction of the thioether **28** (431 mg, 1.02 mmol) with the cyclic sulfate **16** (588 mg, 1.15 mmol) in HFIP (3.0 mL) for 42 h at 70 °C gave compound **30** as a colorless gummy solid (571 mg, 60%). $[\alpha]_D$ −7.6 (*c* 1.1, $CHCl_3$). See Tables 1 and 2 for NMR data. MALDI MS *m*/*e* 955.39 (M^+ + Na), 853.42 (M^+ + H − SO_3). Anal. Calcd for $C_{53}H_{56}O_{11}S_2$: C, 68.22; H, 6.05. Found: C, 68.48; H, 6.09.

Benzyl 2,3-Di-*O*-benzyl-6-deoxy-6-[2,3,5-tri-*O*-benzyl-1,4-dideoxy-1,4-episufoniumylidene-D-arabinitol]-4-*O*-sulfoxy-β-D-glucopyranose Inner Salt (31). Reaction of the thioether **28** (937 mg, 2.22 mmol) with the cyclic sulfate **18** (1.12 g, 2.17 mmol) in HFIP (4.0 mL) for 42 h at 70 °C gave, after chromatography, partially purified compound **31** as a colorless gummy solid (1.02 g, 50%), containing a minor amount of a more-polar isomer. Analysis of this material by ^1H NMR showed it to be ∼80% pure and that the minor isomer could be tentatively identified as the diastereomer at the sulfonium center. Repurification by chromatography ($CHCl_3$:MeOH, 20:1) keeping only those fractions which were pure by TLC yielded compound **31** (639 mg, 31%) as a gum: $[\alpha]_D$ −8.7 (*c* 1.2, $CHCl_3$). See Tables 1 and 2 for NMR data. MALDI MS *m*/*e* 955.53 (M^+ + Na), 933.60 (M^+ + H), 853.54 (M^+ + H − SO_3). Anal. Calcd for $C_{53}H_{56}O_{11}S_2$: C, 68.22; H, 6.05. Found: C, 68.34; H, 6.02.

Methyl 2-*O*-Benzyl-5-deoxy-5-[2,3,5-tri-*O*-benzyl-1,4-dideoxy-1,4-episufoniumylidene-D-arabinitol]-3-*O*-sulfoxy-α-D-arabino-furanose Inner Salt (32). Reaction of the thioether **28** (487 mg, 1.16 mmol) with the cyclic sulfate **21** (322 mg, 1.02 mmol) in HFIP (2.5 mL) for 3 h at 40 °C gave compound **32** as a colorless gummy solid (756 mg, quantitative). Analysis by NMR showed the presence of an 8:1 ratio of isomers at the sulfonium center. See Tables 1 and 2 for NMR data of the major isomer **32**. MALDI MS *m*/*e* 759.13 (M^+ + Na), 737.18 (M^+ + H), 657.16 (M^+ + H − SO_3). Anal. Calcd for $C_{39}H_{44}O_{10}S_2$: C, 63.57; H, 6.02. Found: C, 63.36; H, 6.01.

Benzyl 2-*O*-Benzyl-5-deoxy-5-[2,3,5-tri-*O*-benzyl-1,4-dideoxy-1,4-episufoniumylidene-D-arabinitol]-3-*O*-sulfoxy-α-D-arabino-furanose Inner Salt (33). Reaction of the thioether **28** (514 mg, 1.22 mmol) with the cyclic sulfate **22** (448 mg, 1.06 mmol) in HFIP (3.0 mL) for 2.5 h at 40 °C gave the major isomer **33α** as a pale-yellow amorphous, hard foam (763 mg, 85%). A sample of the minor isomer **33*β*** suitable for NMR analysis (see Tables 1 and 2) was obtained with a purity of >80% from the early chromatographic fractions. For the major isomer **33α**: $[\alpha]_D$ +40 (*c* 1.6, $CHCl_3$). See Tables 1 and 2 for NMR data. MALDI MS *m*/*e* 813.25 (M^+ + H), 733.24 (M^+ + H − SO_3). Anal. Calcd for $C_{45}H_{48}O_{10}S_2$: 66.48; H, 5.95. Found: C, 66.64; H, 5.88.

1,4-Dideoxy-1,4-[[2*S*,3*R*,4*S*-2,4,5-trihydroxy-3-(sulfooxy)pentyl]episufoniumylidene]-D-arabinitol (5). Procedure A: The protected sulfonium salt **29** (252 mg, 0.375 mmol) was dissolved in MeOH (20 mL) and stirred at room temperature with 10% Pd/C catalyst (227 mg) under 1 atm of H_2 for 17 h. Analysis by TLC ($CHCl_3$:MeOH, 7:3) showed the formation of a single product (R_f 0.3). The catalyst was removed by filtration through Celite with

additional MeOH and the filtrate was evaporated to give the crude isopropylidene compound **34** as a gummy residue (137 mg). The residue was dissolved in 50% aq trifluoroacetic acid (3.0 mL) and kept at room temperature for 4 h. Evaporation of the solvent gave the crude hemiacetal, 3-*O*-sulfoxy-5-deoxy-5-[1,4-dideoxy-1,4-episufoniumylidene-D-arabinitol]-α/*β*-D-xylofuranose inner salt (**9**, α:*β* = 5:4) as a pale-yellow glass (121 mg, 89%). See Tables 3 and 4 for NMR data of **9**. MALDI MS *m*/*e* 385.02 ($M^+ + Na$), 363.04 ($M^+ + H$), 283.08 ($M^+ + H - SO_3$).

NMR data for the intermediate compound 34: ^{1}H NMR (D_2O) δ 6.17 (1H, d, $J_{1,2} = 3.7$ Hz, H-1′), 5.05 (1H, d, $J_{2',3} \sim 0$ Hz, H-2′), 4.95 (1H, d, $J_{3',4'} = 2.9$ Hz, H-3′), 4.87 (1H, ddd, $J_{4',5'a} = 3.3$ Hz, $J_{4',5'b} = 7.8$ Hz, H-4′), 4.79 (1H, ddd, H-2), 447 (1H, dd, $J_{2,3} = 3.3$ Hz, $J_{3,4} = 2.9$ Hz, H-3), 4.17 (1H, ddd, H-4), 4.16 (1H, dd, $J_{4,5a} = 4.7$ Hz, $J_{5a,5b} = 14.0$ Hz, H-5a), 4.05 (1H, dd, $J_{5'a,5'b} = 13.8$ Hz, H-5′a), 3.98 (1H, dd, $J_{1a,1b} = 12.7$ Hz, H-1a), 3.97 (1H, dd, $J_{4,5b} = 11.0$ Hz, H-5b), 3.95 (1H, dd, $J_{1b,2} = 3.1$ Hz, H-1b), 3.94 (1H, dd, $J_{4',5'b} = 7.8$ Hz, H-5′b), 1.57 and 1.40 (6H, 2 × s, each 3H, $C(CH_3)_2$); ^{13}C NMR (D_2O) δ 114.2 ($C(CH_3)_2$), 105.4 (C-1′), 83.6 (C-2′), 81.3 (C-3′), 78.2 (C-3), 77.4 (C-2), 75.6 (C-4′), 71.3 (C-4), 59.8 (C-5), 48.3 (C-1), 44.8 (C-5′), 26.2 and 25.8 ($C(CH_3)_2$).

Procedure B: The protected sulfonium salt **29** (254 mg, 0.378 mmol) was dissolved in TFA (3.0 mL) and the mixture was stirred at room temperature until the solid dissolved. Water (3.0 mL) was added and the mixture was placed in a 45 °C bath for 2 h. Analysis by TLC ($CHCl_3$:MeOH, 7:3) showed formation of a single product (R_f 0.8). The solvents were evaporated to give the crude hemiacetal **35** as an anomeric mixture (α:*β* = 5:4) The mixture was dissolved in MeOH (20 mL) and hydrogenolyzed over 10% Pd/C catalyst (200 mg) at room temperature for 18 h. Filtration through Celite with additional MeOH and evaporation of the solvent gave a colorless foam that was shown by NMR analysis to consist of four compounds which were tentatively identified to be an anomeric mixture of the hemiacetal **9** together with an anomeric mixture of the corresponding methyl glycoside **35**. Re-treatment of the mixture with 50% aq TFA (6.0 mL, rt, 4 h) resulted in hydrolysis of most of the methyl glycoside. Filtration through silica gel (EtOAc:MeOH:H_2O) to remove polar impurities, followed by solvent removal gave the crude compound **9** (101 mg, 74%) that was identical by NMR with that obtained above by procedure A.

The hemiacetal **9** (101 mg, 0.279 mmol) was dissolved in water (8.0 mL). The solution was stirred at room temperature while $NaBH_4$ (44 mg, 1.2 mmol) was added in small portions over 30 min. Stirring was continued for another 20 min and the mixture was acidified to pH ≤4 by dropwise addition of 2 M HCl. The solution was evaporated to dryness and then coevaporated with anhydrous MeOH (3 × 30 mL). The semisolid residue was purified by column chromatograhy on silica gel (EtOAc:MeOH:H_2O, 6:3:1) to give the product **5** as a colorless gum (86 mg, 85%). $[\alpha]_D$ +19 (*c* 0.32, MeOH). See Tables 5 and 6 for NMR data of **5**. MALDI MS *m*/*e* 386.89 ($M^+ + Na$), 285.01 ($M^+ + H - SO_3$); HRMS. Calcd for $C_{10}H_{20}O_{10}S_2Na$ (M + Na): 387.0396. Found: 387.0382.

1,4-Dideoxy-1,4-[[2*S*,3*R*,4*R*,5*S*-2,4,5,6-tetrahydroxy-3-(sulfooxy)-hexyl]episufoniumylidene]-D-arabinitol (6). The protected sulfonium salt **30** (460 mg, 0.493 mmol) was dissolved in MeOH (50 mL) and the mixture was stirred at room temperature with 10% Pd/C catalyst (580 mg) under 1 atm of H_2 for 24 h. Analysis by TLC (EtOAc:MeOH:H_2O, 6:3:1) showed the formation of a single product (R_f 0.10). The catalyst was removed by filtration through Celite, using additional MeOH, and the filtrate was evaporated to give the crude hemiacetal, 4-*O*-sulfoxy-6-deoxy-6-[1,4-dideoxy-1,4-episufoniumylidene-D-arabinitol]-α/*β*-D-galactopyranose inner salt (**10**, α:*β* = 1:1) as a colorless foam (184 mg, 95%). See Tables 3 and 4 for NMR data of **10**. MALDI MS *m*/*e* 414.89 ($M^+ + Na$), 392.93 ($M^+ + H$), 312.93 ($M^+ + H - SO_3$).

Reduction of the hemiacetal **10** (430 mg, 1.10 mmol) with $NaBH_4$, as described above for compound **9**, gave the sulfonium sulfate **6** (232 mg, 54%) as a colorless glass. $[\alpha]_D$ +18 (*c* 0.72, MeOH). See Tables 5 and 6 for NMR data of **6**. MALDI MS *m*/*e* 416.94 ($M^+ + Na$), 315.03 ($M^+ + H - SO_3$); HRMS. Calcd for $C_{11}H_{22}O_{11}S_2Na$ (M + Na): 417.0501. Found: 417.0498.

1,4-Dideoxy-1,4-[[2*S*,3*S*,4*R*,5*S*-2,4,5,6-tetrahydroxy-3-(sulfooxy)-hexyl]episufoniumylidene]-D-arabinitol (7). The protected sulfonium salt **31** (602 mg, 0.645 mmol) was dissolved in HOAc (22 mL). Water (2.2 mL) was added and the mixture was stirred at room temperature with 10% Pd/C catalyst (520 mg) under 1 atm of H_2 for 22 h. Analysis by TLC (EtOAc:MeOH:H_2O, 6:3:1) showed the formation of a single product (R_f 0.15). The catalyst was removed by filtration through Celite with additional water and the filtrate was evaporated to a syrup. Water (3 × 30 mL) was added and evaporated to remove residual HOAc. The crude hemiacetal, 4-*O*-sulfoxy-6-deoxy-6-[1,4-dideoxy-1,4-episufoniumylidene-D-arabinitol]-α/*β*-D-glucopyranose inner salt (**11**, α:*β* = 1:1), was obtained as a colorless foam (263 mg, quantitative). See Tables 3 and 4 for NMR data of **11**. MALDI MS *m*/*e* 414.99 ($M^+ + Na$), 313.05 ($M^+ + H - SO_3$).

Reduction of the hemiacetal **11** (255 mg, 0.650 mmol) with $NaBH_4$, as described above for compound **9**, gave the sulfonium sulfate **7** (165 mg, 64%) as a colorless glass. $[\alpha]_D$ +13 (*c* 0.92, MeOH). See Tables 5 and 6 for NMR data of **7**. MALDI MS *m*/*e* 416.94 ($M^+ + Na$), 315.00 ($M^+ + H - SO_3$); HRMS. Calcd for $C_{11}H_{22}O_{11}S_2Na$ (M + Na): 417.0501. Found: 417.0499.

1,4-Dideoxy-1,4-[[2*S*,3*S*,4*R*-2,4,5-trihydroxy-3-(sulfooxy)pentyl]episufoniumylidene]-D-arabinitol (8). The protected sulfonium salt **33** (677 mg, 0.789 mmol) was dissolved in HOAc (20 mL). Water (2.0 mL) was added and the mixture was stirred at room temperature with 10% Pd/C catalyst (510 mg) under 1 atm of H_2 for 6 h. Analysis by TLC (EtOAc:MeOH:H_2O, 6:3:1) showed formation of a single product (R_f 0.25). The catalyst was removed by filtration through Celite with additional water and the filtrate was evaporated to a syrup. Water (3 × 20 mL) was added and evaporated to remove residual HOAc. The crude hemiacetal, 3-*O*-sulfoxy-5-deoxy-5-[1,4-dideoxy-1,4-episufoniumylidene-D-arabinitol]-α/*β*-D-arabinose inner salt (**12**, α:*β* = 1:1), was obtained as a colorless foam (294 mg, quantitative). See Tables 3 and 4 for NMR data of **12**. MALDI MS *m*/*e* 384.97 ($M^+ + Na$), 363.02 ($M^+ + H$), 283.07 ($M^+ + H - SO_3$).

Reduction of the hemiacetal **12** (283 mg, 0.781 mmol) with $NaBH_4$, as described above for compound **9**, gave the sulfonium sulfate **8** (194 mg, 66%) as a colorless glass. $[\alpha]_D$ −4.7 (*c* 1.0, MeOH). See Tables 5 and 6 for NMR data of **8**. MALDI MS *m*/*e* 386.95 ($M^+ + Na$), 364.97 ($M^+ + H$), 285.05 ($M^+ + H - SO_3$); HRMS. Calcd for $C_{10}H_{20}O_{10}S_2Na$ (M + Na): 387.0396. Found: 387.0386.

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Note Added after ASAP Publication. There was an error in structure **4** in the version published ASAP January 10, 2006; the corrected version was published ASAP January 11, 2006.

Supporting Information Available: Tables of ^{1}H and ^{13}C NMR data for the compounds synthesized in this study and copies of ^{1}H and ^{13}C NMR spectra for compounds **5**, **6**, **7**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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