JOC Article

Studies Directed toward the Stereochemical Structure Determination of the Naturally Occurring Glucosidase Inhibitor, Kotalanol: Synthesis and Inhibitory Activities against Human Maltase Glucoamylase of Seven-Carbon, Chain-Extended Homologues of Salacinol

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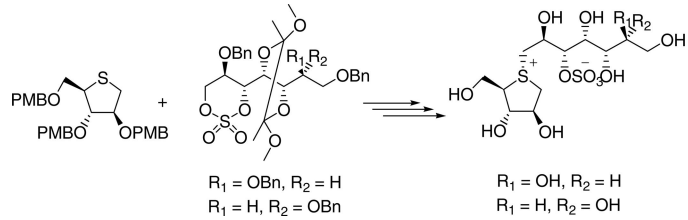

The synthesis of new seven-carbon, chain-extended sulfonium salts of 1,4-anhydro-4-thio-D-arabinitol, analogues of the naturally occurring glycosidase inhibitor salacinol, are described. These compounds were designed on the basis of the structure activity data of chain-extended analogues of salacinol, with the intention of determining the hitherto unknown stereochemical structure of kotalanol, the naturally occurring seven-carbon chain-extended analogue of salacinol. The target zwitterionic compounds were synthesized by means of nucleophilic attack of the PMB-protected 1,4-anhydro-4-thio-D-arabinitols at the least hindered carbon atom of two 1,3-cyclic sulfates differing in stereochemistry at only one stereogenic center. The desired cyclic sulfates were synthesized starting from D-glucose via Wittig olefination and Sharpless asymmetric dihydroxylation. Deprotection of the coupled products by using a two-step sequence afforded two sulfonium sulfates. Optical rotation data for one of our compounds indicated a correspondence with that reported for kotalanol. However, comparison of ^{1}H and ^{13}C NMR spectral data of the synthetic compounds with those of kotalanol indicated discrepancies. The collective data from this and published work were used to propose a tentative structure for the naturally occurring compound, kotalanol. Comparison of physical data of previously synthesized analogues with those for the recently isolated six-carbon chain analogue, ponkoranol or reticulanol, also led to elucidation of this structure. Interestingly, both our compounds inhibited recombinant human maltase glucoamylase (MGA), as expected from our previous structure activity studies of lower homologues, with K_i values of 0.13 ± 0.02 and 0.10 ± 0.02 μM.

Introduction

Glycosidases are responsible for the processing of complex carbohydrates which are essential in numerous biological recognition processes.[1] Inhibition of these glycosidases can have profound effects on quality control, maturation, transport, and secretion of glycoproteins, and can alter cell−cell or cell−virus recognition processes. This principle is the basis for the potential use of glycosidase inhibitors for the treatment of various

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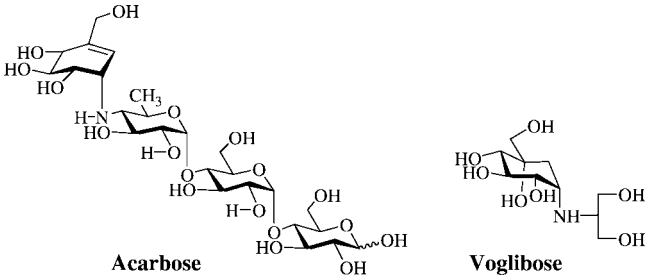
CHART 1

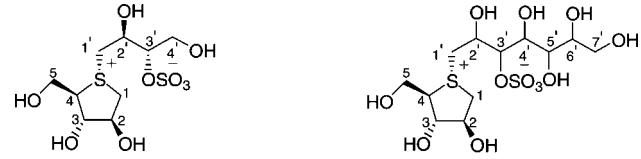


disorders and diseases such as diabetes, cancer, and other viral diseases;[2,3] for example, acarbose, a pseudotetrasaccharide, and voglibose, an aminocyclitol, are inhibitors of α-glucosidases and have been approved for the clinical treatment of diabetes (Chart 1).[4,5] Glycosidase inhibitors have also proved useful in the investigation of disorders such as Gaucher's disease.[6] An attractive approach to potent glucosidase inhibitors is to create compounds that mimic the oxacarbenium ion-like transition state of the enzyme-catalyzed reaction.[7,8]

Many of the natural and synthetic azasugars are believed to mimic the transition state in either charge or shape, thus making them good glycosidase inhibitors.[9] They are presumed to be partially protonated in the active site at physiological pH, thus providing the stabilizing electrostatic interactions between the inhibitor and the carboxylate residues in the enzyme active site. An alternative approach to carbohydrate mimics is to replace the ring oxygen atom of carbohydrates with other heteroatoms such as sulfur and selenium. Indeed, sulfonium salts are known to be quite stable, and have been proposed as mimics of the oxacarbenium ion-like transition state.[10]

It is noteworthy that sulfonium ions with glucosidase inhibitory properties occur naturally. Thus, in the course of studies on antidiabetic principles of natural medicines, Yoshikawa et al.[11] discovered that a water-soluble fraction (25−100 mg/kg) prepared from the roots and stems of *Salacia reticulata* strongly inhibited elevations in rats' serum glucose levels after the administration of sucrose or maltose, but not glucose. To confirm this activity, they conducted an additional study, a bioassay-guided chromatography separation, in which a water-soluble

CHART 2



fraction prepared from the dried roots of *S. reticulata* yielded a new class of glycosidase inhibitor, namely salacinol (**1**).[11] The structure of salacinol is unique, a ring sulfonium ion (1,4-dideoxy-1,4-thio-D-arabinitol cation) stabilized by an internal sulfate counterion (1-deoxy-L-erythrosyl-3-sulfate anion). Salacinol has been shown to be a potent inhibitor of intestinal glucosidase enzymes,[11–13] and thus capable of attenuating the spike in blood glucose levels experienced by diabetics after consuming a meal rich in carbohydrates.[14] It is noteworthy that a double-blind study of the effects of the extract from *S. reticulata* on human patients with type-2 diabetes mellitus has indeed shown that the extract is an effective treatment, with side effects comparable to those of the placebo control group.[15] The α-glucosidase inhibitory activities of salacinol were shown to be as strong as those of voglibose and acarbose.[16]

Another bioassay-guided separation by the same group resulted in the isolation of a second component, kotalanol (**2**), which was reported to exhibit stronger inhibitory activities against certain glycosidase enzymes. For example, kotalanol showed more potent inhibitory activity against isomaltase than either salacinol or acarbose.[17] On the basis of NMR spectroscopic data, Yoshikawa et al. proposed a partial structure of kotalanol (**2**),[17] very similar to that of salacinol but with an alditol side chain being extended by three carbons (Chart 2). However, to date, the absolute configurations of the stereogenic centers in the heptitol chain have not been determined. The 1-deoxy-4-thiopentofuranosyl portion of kotalanol was assigned the identical D-arabinitol configuration as salacinol, based on chemical degradation studies.[17]

As part of our ongoing program aimed at the synthesis of zwitterionic glycosidase inhibitors,[10] we have focused recently on the synthesis of chain-extended analogues of salacinol (**1**), as well as the corresponding nitrogen and selenium analogues.[18–22] Since the exact stereochemistry of kotalanol was not known, it

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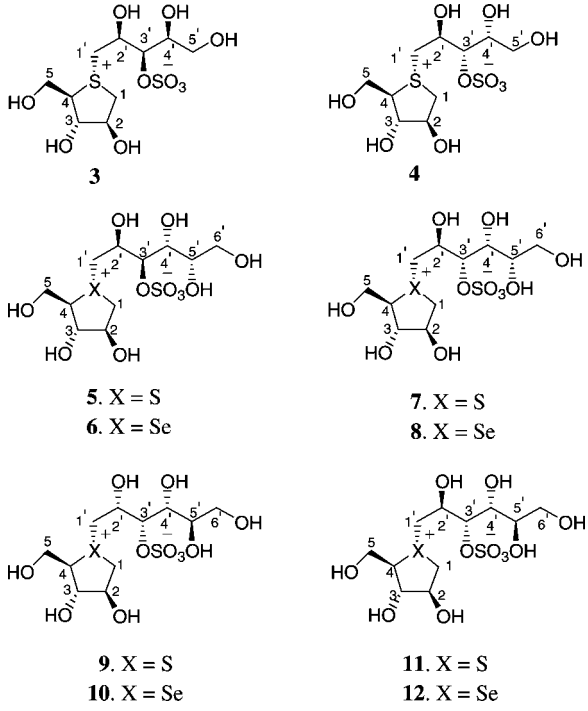
CHART 3



was deemed necessary to study the structure−activity relationships systematically by attaching side chains of different chain length and different stereochemistry at the stereogenic centers to the heteroanhydroalditols. In this regard, we have synthesized several 5-carbon- and 6-carbon-chain analogues (Chart 3), and some of these compounds have shown inhibitory activities in the low micromolar range against recombinant human maltase glucoamylase (MGA), a critical intestinal glucosidase involved in the breakdown of glucose oligomers into glucose itself.[18–22] The stereochemistries at the different stereogenic centers on the side chain play significant roles, and structure−activity studies revealed an interesting variation in the inhibitory power of these compounds (Table 1).

In summary, the structure−activity relationships predict that the common motif for inhibitory activity of the chain-extended analogues of salacinol contains the *S*-configuration at C-2′, the *R*-configuration at C-4′, and the *S*-configuration at C-5′, the configuration of the stereogenic center C-3′ bearing the sulfate group being unimportant. The choice of *S*-configuration at C-5′ is based on the lower K_i value for **7** vs **11**.

The inhibitory activities of the selenium compounds **6**, **8**, and **10** also corroborate the hypothesis. It is noteworthy that a recent report from Yoshikawa et al. describes the isolation from *Salacia prinoides* of a six-carbon chain analogue of salacinol, ponkoranol, that shows IC_{50} values against maltase, sucrase, and isomaltase in the low micromolar range.[23] Comparison of physical data to those of our synthetic derivatives[18,20,21] confirms that ponkoranol is indeed compound **7**. A U.S. patent also describes a six-carbon-chain analogue isolated from *Salacia reticulata* named reticulanol.[24] Comparison of the physical data indicate once again that this compound is also compound **7** above.

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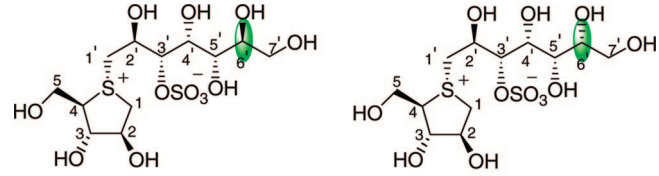
TABLE 1. Experimentally Determined K_i Values[a]

Inhibitor	Stereochemistry at the stereogenic centers in the acyclic side-chain				K_i (μM)	Ref.
	C-2′	C-3′	C-4′	C-5′		
3	*S*	*R*	*S*	-	NA[b]	18
4	*S*	*S*	*R*	-	0.26 ± 0.02	18
5	*S*	*R*	*R*	*S*	0.25 ± 0.02	18
6	*S*	*R*	*R*	*S*	0.10 ± 0.02	22
7	*S*	*S*	*R*	*S*	0.17 ± 0.03	18
8	*S*	*S*	*R*	*S*	0.10 ± 0.02	22
9	*R*	*S*	*R*	*R*	NA[b]	20
10	*R*	*S*	*R*	*R*	41.0 ± 7.0	20
11	*S*	*S*	*R*	*R*	0.65 ± 0.10	21
12	*S*	*S*	*R*	*R*	0.14 ± 0.03	21
Salacinol	*S*	*S*	-	-	0.19 ± 0.02	19
Blintol	*S*	*S*	-	-	0.49 ± 0.05	19

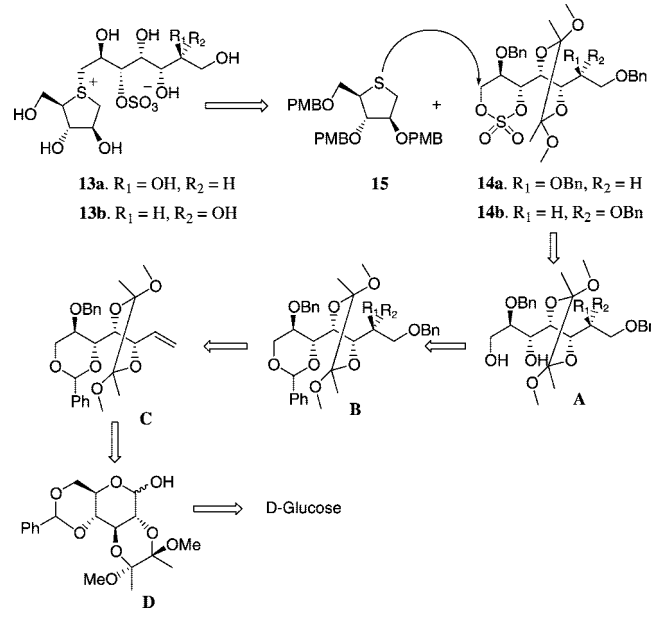
[a] Analysis of MGA inhibition was performed with maltose as the substrate, and measuring the release of glucose. Absorbance measurements were averaged to give a final result. [b] NA: not active.

CHART 4

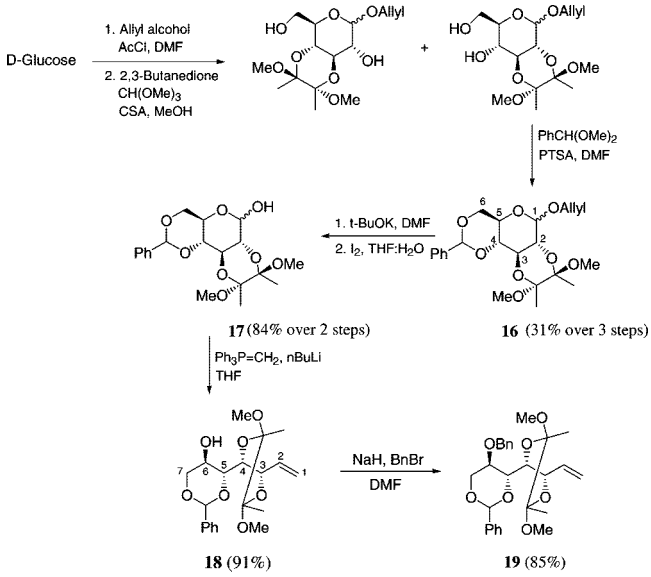


The data presented above suggest that the most logical structure for kotalanol (**2**) is **13a** or **13b** (Chart 4), in which the configuration at C-6′ cannot yet be specified. We have chosen the *S*-configuration at C-3′ to reflect a presumed common biosynthetic pathway for salacinol and kotalanol. We therefore describe herein the synthesis of these two candidates, together with a comparison of their physical data with those of the natural product in order to elucidate the structure of kotalanol. The inhibitory activities of both compounds against human maltase glucoamylase are also described.

SCHEME 1. Retrosynthetic Analysis



SCHEME 2. Synthesis of Compound 19



Results and Discussion

The proposed strategy to synthesize compounds **13a** and **13b** involves alkylation of the anhydrothioalditol **15**[10] at the heteroatom by a cyclic sulfate derivative, specifically, the tri-*O*-benzyl-butane-2,3-diacetal-heptyl-1,3-cyclic sulfates **14a** and **14b** (Scheme 1). Our previous experience suggests that selective attack of the heteroatom at the least hindered primary center will occur. The butane-2,3-diacetal (BDA) unit as a protecting group has been used extensively in the total synthesis of natural products,[25] and we have used it in the synthesis of lower homologues.[22] Relatively strong acidic conditions are required for its removal, thus permitting the selective removal of the benzylidene group in **B** prior to installation of the 1,3-cyclic sulfate in **A**. Intermediate B could be obtained from **C** via asymmetric dihydroxylation, which could, in turn, be obtained from the D-glucose derivative **D** by a Wittig reaction (Scheme 1).

The preparation of **16** was achieved from D-glucose via a three-step sequence (Scheme 2). Thus, allyl D-glucopyranoside was treated with 2,3-butanedione and trimethylorthoformate in the presence of camphorsulfonic acid (CSA) in boiling methanol to give an inseparable mixture of 2,3- and 3,4-BDA-protected intermediates. This mixture was reacted directly with benzaldehyde dimethylacetal in the presence of a catalytic amount of PTSA to yield the fully protected, and separable derivative **16** in 31% overall yield. Isomerization of the allyl glucoside **16** was effected with *t*-BuOK in DMF, and subsequent cleavage of the resulting enol ether with I_2 in THF:H_2O gave the 2,3-BDA-4, 6-*O*-benzylidene-D-glucopyranose (**17**). Treatment of this hemiacetal with methyltriphenylphosphonium bromide provided the olefinic product **18** (83%), which was benzylated to afford compound **19**.

With compound **19** in hand, our next goal was to introduce the two hydroxyl groups. The OsO_4-catalyzed dihydroxylation of **19** proceeded smoothly in an acetone−water mixture with *N*-methylmorpholine *N*-oxide (NMO) as reoxidant. The diastereoisomer **20** was obtained as a major isomer. (Scheme 3, Table 2). The stereochemical outcome of this dihydroxylation follows Kishi's empirical rule, which predicts that in the *syn*-hydroxylation of acyclic allylic alcohols the relative stereochemistry between the preexisting hydroxyl group and the adjacent newly introduced hydroxyl group in the major product is *erythro*.[26] The *syn*-hydroxylation from the same side of the allylalkoxy group, which is sterically more hindered, affords the minor product.[27]Kishi's rule has previously been shown to apply in the dihydroxylation of a variety of carbohydrate allylic systems.[27]

SCHEME 3. Dihydroxylation Reactions of Compound 19

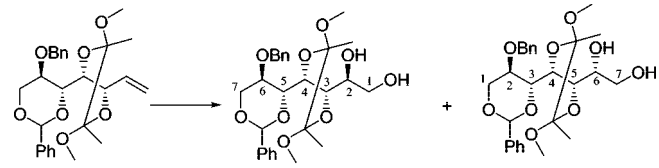


TABLE 2

entry	compd	conditions	product	yield (%)	dr[a]
1	**19**	OSO_4, NMO	20	93	20:1
2	**19**	AD-mix β	20:21	90	7:3
3	**19**	AD-mix α	20	91	20:1

[a] Determined by 500 MHz ^{1}H NMR.

Compound **20** was benzylated under standard conditions to give **22**, which was then subjected to mild methanolysis by using catalytic PTSA in methanol to effect selective removal of the benzylidene group (Scheme 4) and give the corresponding diol **23** in 73% yield. The cyclic sulfate **14a** was then obtained by treatment of **23** with thionyl chloride and triethylamine followed by oxidation with sodium periodate and ruthenium(III) chloride as a catalyst (Scheme 4).

We next examined the asymmetric dihydroxylation reaction using commercially available AD-mix β under the reported standard conditions (AD-mix β in a 1:1 mixture of *tert*-BuOH−H_2O). However, a separable 7:3 diastereomeric mixture (**20** and **21**) was obtained in which compound **20** was still the predominant isomer (Table 2). The corresponding asymmetric dihydroxylation of **19**, using AD-mix-α with the intention of obtaining the diastereoisomer of compound **20**, was examined next. Surprisingly, the AD-mix-α afforded compound **20** exclusively (Scheme 3). The unsatisfactory selectivity in the dihydroxylation reaction can probably be attributed to unfavorable steric interactions between the bulky dihydroxylating reagent and the BDA protecting group, situated next to the olefinic reactive site. The stereochemistry at the C-6 position in compound **20** was therefore inverted by the Mitsunobu protocol to obtain the desired diol **21**.

Accordingly, selective protection of the primary hydroxyl group by using *tert*-butyldimethylsilyl chloride gave **24** in 91% yield, which when treated under standard Mitsunobu conditions afforded the ester **25** (Scheme 4). Removal of the *p*- nitrobenzoyl and *tert*-butyldimethylsilyl groups with sodium methoxide and tetrabutylammonium fluoride, respectively, gave the diol **21**. Compound **21** was obtained as a colorless crystalline solid,

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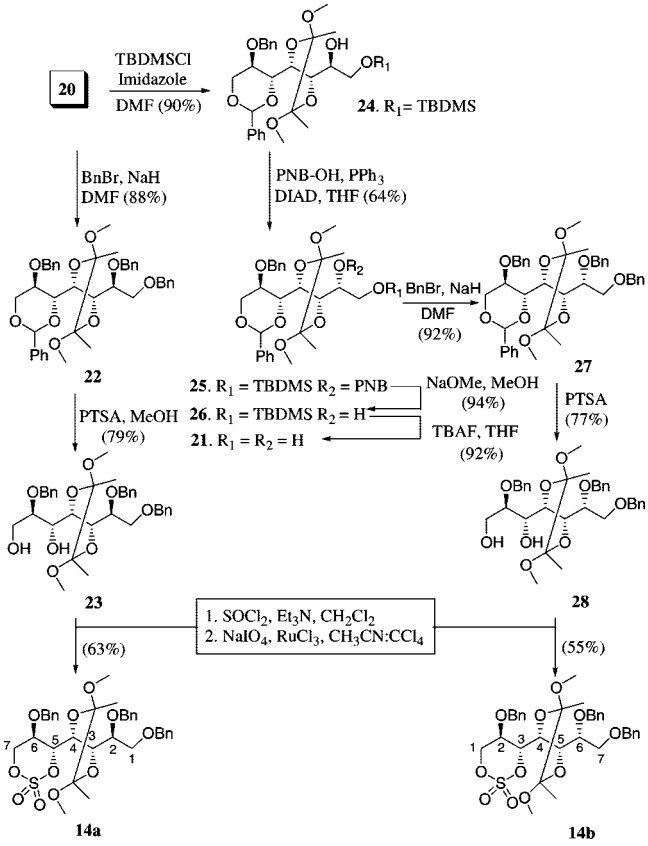
SCHEME 4. Synthesis of the Cyclic Sulfates 14a and 14b



suitable for single-crystal X-ray analysis (see the Supporting Information), that established conclusively the absolute configurations at the newly generated stereogenic center. With the diol in hand, the cyclic sulfate **14b** was synthesized following the same reaction sequence as discussed above for the synthesis of **14a**. The structure of the cyclic sulfate **14b** was also confirmed by single-crystal X-ray analysis (Figure 1, Supporting Information). The cyclic sulfates **14a** and **14b** were thus assigned the structures 1,2,6-tri-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-D-gulitol-5,7-cyclic sulfate and 2,6,7-tri-*O*-benzyl-4,5-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-L-gulitol-1,3-cyclic sulfate, respectively.[28]

The coupling reactions of the cyclic sulfate **14a** with the protected thioarabinitol were investigated next. 2,3,5-Tri-*O*-*p*-methoxybenzyl-1,4-anhydro-4-thio-D-arabinitol (**15**)[29] was prepared by a method analogous to that developed for the synthesis of the corresponding selenium derivative.[30] The reaction of the thioarabinitol **15** with the cyclic sulfate **14a** was found to proceed very slowly at 72 °C. We also observed that longer reaction time led to decomposition of the coupling product. The coupling reaction was therefore terminated before complete consumption of the starting materials. The protected sulfonium sulfate **29** was obtained as the sole product in 55% yield with use of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) as solvent. The observed slow reactivity of the cyclic sulfate may be attributed to the lack of release of torsional strain, in contrast to our earlier studies with cyclic sulfates with fused six-membered rings.[10] Alternatively, the opening of the cyclic sulfate might be impeded by the steric hindrance provided by the protecting groups. Deprotection of the coupled product **29** was performed with two successive reactions. The sulfonium salt **29** was first treated with Pd/C/H_2 in aqueous acetic acid to effect hydrogenolytic

SCHEME 5

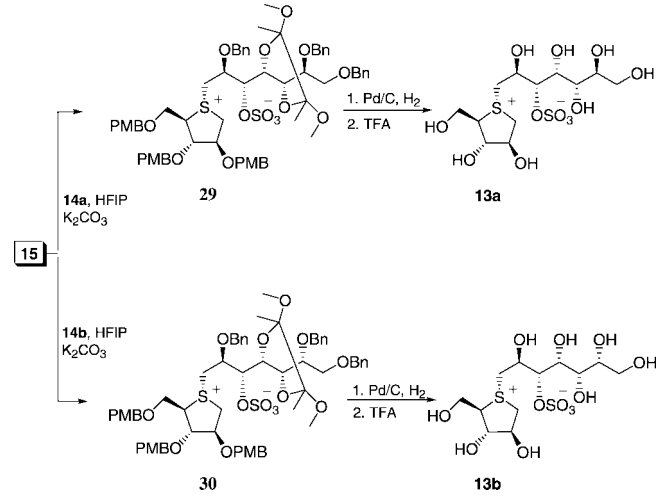


TABLE 3. Comparison of ^{13}C NMR Data[a] and Discrepancies[b] of the Chemical Shifts of Compounds 13a and 13b Relative to Those Reported for Kotalanol 2

position	**13a**	kotalanol	**13b**
1′	53.4 (−0.3)	53.7	53.3 (−0.4)
2′	68.0 (−1.4)	67.4	68.3 (+0.9)
3′	**81.8 (+3.9)**	**77.9**	**80.5 (+2.5)**
4′	68.1 (−2.4)	70.5	70.4 (−0.1)
5′	**72.8 (+1.5)**	**71.3**	**73.5 (+1.8)**
6′	**75.5 (+3.0)**	**72.5**	**73.9 (+1.4)**
7′	65.6 (+0.2)	65.3	64.6 (−0.7)
1	50.3 (+0.1)	50.2	50.5 (+0.3)
2	78.4 (+0.3)	78.1	78.4 (+ 0.3)
3	79.3 (−0.1)	79.4	79.3 (−0.1)
4	72.5 (+0.3)	72.2	72.5 (+0.3)
5	60.0 (0)	60.0	60.2 (+0.2)

[a] In pyridine-d_5. [b] Values in bold.

cleavage, followed by treatment with trifluoroacetic acid to yield the desired zwitterionic compound **13a**. Compound **13a** was then fully characterized by spectroscopic methods. The proton and carbon signals in the ^{1}H and ^{13}C NMR spectra of **13a** in D_2O were assigned unambiguously with the aid of ^{1}H−^{1}H COSY, HMQC, and HMBC experiments. The stereochemistry at the stereogenic sulfonium ion center was assigned by means of a NOESY experiment, which showed an H-4 to H-1′ correlation, implying that isomer **13a** has an *anti* relationship between C-5 and C-1′. MALDI-TOF mass spectrometry in the positive mode showed base peaks for masses attributable to M + Na and lower intensity peaks corresponding to M + H and M + H − SO_3H. The compounds were also characterized by high-resolution mass spectrometry and compound **13a** exhibited a dimer cluster ion peak at lower intensity.

Analogously, the cyclic sulfate **14b** was reacted with the thioether **15** at 72 °C for 48 h in HFIP to give **30** in 61% yield. Compound **30** was then deprotected, as above, to afford the desired zwitterionic compound **13b** (Scheme 5).

NMR analysis of **13a** and **13b** was carried out in both D_2O and pyridine-d_5 solution (Figure 2, Supporting Information). These studies revealed that the ^{1}H NMR spectra in pyridine-d_5 gave downfield shifts compared to those in D_2O, together with differential spectral patterns (Table 3). A careful comparison indicated the most downfield resonances were those of H-2, H-3, and H-2′ in D_2O. In contrast, the NMR studies in pyridine-d_5 showed the most downfield resonances (δ 5.34 for **13a** and δ

TABLE 4. Comparison of ^{1}H NMR Data[a] and Discrepancies[b] of the Chemical Shifts of Compounds 13a and 13b Relative to Those Reported for Kotalanol 2

position	**13a**	kotalanol (**2**)	**13b**
1′	4.84 (dd), 4.66 (dd)	4.93 (dd), 4.65 (dd)	4.91 (dd), 4.67 (dd)
2′	5.09 (m)	5.24 (m)	5.16 (ddd)
3′	**5.34 (d)**	**5.64 (dd)**	**5.47 (m)**
4′	5.31 (br s)	5.12 (br s)	5.05 (dd)
5′	**4.65 (m)**	**5.86 (dd-like)**	**4.94 (dd)**
6′	4.57 (m)	4.88 (ddd-like)	4.76 (ddd)
7′	4.49 (dd), 4.31 (dd)	4.50 (dd), 4.25 (dd)	4.41 (dd), 4.39 (dd)
1	4.30 (d)	4.31 (br s)	4.36 (dd), 4.32 (dd)
2	5.09 (m)	5.08 (dd-like)	5.09 (m)
3	5.16 (br s)	5.16 (br s)	5.16 (br s)
4	4.65 (m)	4.64 (t-like)	4.65 (m)
5	4.54 (d)	4.54 (dd-like)	4.55 (d)

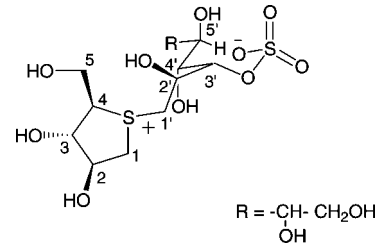
[a] In pyridine-d_5. [b] Values in bold.

5.47 for **13b**) for H-3′. The integrity of the compounds in this solvent was confirmed by TLC and by TOCSY and HMBC experiments.

Next, we turned to the comparison of the physical data of compounds **13a** and **13b** with those reported for kotalanol **2** (Table 4).[17] The specific rotation and melting point of **13b** ($[\alpha]_D^{25}$ + 12.0 (c 0.1, MeOH) and mp 169−171 °C, respectively) were found to be in agreement with the reported values ($[\alpha]_D^{27}$ +11.5 (MeOH); mp 175−177 °C) for kotalanol **2**. The optical rotation and melting point of **13a** were found to be $[\alpha]_D^{25}$ + 16.0 (*c* 0.1, MeOH) and mp 164−166 °C, respectively. Comparison of the ^{1}H and ^{13}C NMR spectroscopic data of **13b** with those reported[17] for kotalanol **2** revealed that the sets of data in pyridine-d_5 are not identical. A careful check of ^{1}H NMR data of kotalanol **2** and compound **13b** indicated that there was a difference in chemical shifts ($\pm\delta$ 0−0.17) (Table 4). However, the most notable difference was the chemical shift of H-5′, reported at δ 5.86 ppm in kotalanol **2**. In contrast, no signal below δ 5.47 ppm was observed in the spectrum of compound **13b**. The H-5′ signals of **13a** and **13b** appeared at δ 4.65 and δ 4.91, respectively. The ^{13}C NMR data also revealed discrepancies between those of **13b** and those reported for kotalanol **2**, especially for C-3′; specifically, C-3′ is shielded in kotalanol. Comparison of accumulated data to date for related analogues indicates that C-3′ exhibits an upfield shift when the sulfate moiety at C-3′ and the hydroxyl group at C-5′ are anti to one another. Thus, in kotalanol **2**, C-3′ resonates at 77.9 ppm; the corresponding shifts in **5**, **9**, and **11** are 78.9,[18] 77.6,[20b] and 78.3 ppm,[21] respectively. This shielding can be attributed to the γ-gauche effect of the axially oriented hydroxyl group (Chart 5) acting on C-3′. The proximity of the negatively charged sulfate moiety to H-5′ would also account for the unusual deshielding of this hydrogen. This leads us to speculate that kotalanol **2** has the opposite configuration at C-5′ to **13a** and **13b**, with an anti relationship between the substituents at C-3′ and C-5′. This still leaves the configuration at C-6′ unspecified.

Finally, we comment on the inhibitory activities of the compounds synthesized in this study against recombinant human maltase glucoamylase (MGA), a critical intestinal glucosidase involved in the processing of oligosaccharides of glucose into glucose itself. The seven-carbon-chain analogues of salacinol,

CHART 5



13a and **13b**, inhibited MGA with K_i values of 0.13 ± 0.02 and 0.10 ± 0.02 μM, respectively. The observed inhibition data are consistent with the structure activity relationships established previously for the lower homologues (Table 1). We note that **13a** and **13b** constitute the most active chain-extended analogues of salacinol to date. However, we note also that extension of the polyhydroxylated side chain does not confer any particular advantage over salacinol, presumably because no additional favorable contacts are formed with the enzyme-active site.

Experimental Section

Enzyme Kinetics. Kinetic parameters of MGA with compounds **13a** and **13b** were determined by using the pNP-glucose assay to follow the production of *p*-nitrophenol upon addition of enzyme (500 nM). The assays were carried out in 96-well microtiter plates containing 100 mM MES buffer pH 6.5 as inhibitor (at three different concentrations), and *p*-nitrophenyl-D-glucopyranoside (pNP-glucose, Sigma) as substrate (2.5, 3.5, 5, 7.5, 15, and 30 mM) with a final volume of 50 uL. Reactions were incubated at 37 °C for 35 min and terminated by addition of 50 uL of 0.5 M sodium carbonate. The absorbance of the reaction product was measured at 405 nm in a microtiter plate reader. All reactions were performed in triplicate and absorbance measurements were averaged to give a final result. Reactions were linear within this time frame. The program GraFit 4.0.14 was used to fit the data to the Michaelis−Menten equation and estimate the kinetic parameters, K_m, K_{mobs} (K_m in the presence of inhibitor), and V_{max}, of the enzyme. K_i values for each inhibitor were determined by the equation $K_i = [I]/[(K_{mobs}/K_m) + 1]$. The K_i reported for each inhibitor was determined by averaging the K_i values obtained from three different inhibitor concentrations.

Allyl 4,6-*O*-Benzylidene-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α,β-D-glucopyranoside (16). To a suspension of D-glucose (30 g, 0.16 mol) in allyl alcohol (100 mL) was added AcCl (1 mL) and the reaction mixture was refluxed for 12 h. The reaction mixture was cooled to room temperature and the reaction was quenched by addition of excess triethylamine (5 mL). The solvent was removed under reduced pressure and dried on high vacuum for 12 h. To the residue in dry MeOH (200 mL) were added 2,3-butanedione (17.2 mL, 0.2 mol), trimethyl orthoformate (70 mL, 0.6 mol), and CSA (500 mg) and the reaction mixture was refluxed for 24 h. When TLC analysis of aliquots (hexanes:EtOAc, 1:1) showed total consumption of the starting material, the reaction mixture was cooled to room temperature and excess triethylamine (4 mL) was added. The solvents were evaporated; the residue was dissolved in EtOAc (200 mL), washed with brine, and dried over Na_2SO_4, then concentrated to give brownish oil. The latter was dissolved in DMF (100 mL) then benzaldehyde dimethylacetal (35 g, 0.16 mol) and *p*-toluenesulfonic acid (300 mg) were added. The reaction mixture was stirred at 60 °C on a rotary evaporator under vacuum for 2 h. The reaction was then quenched by adding triethylamine, the solvent was removed, and the residue was dissolved in EtOAc (150 mL), washed with saturated aqueous NaCl (50 mL), dried over Na_2SO_4, and concentrated to give brown syrup. Purification by column chromatography on silica gel (hexanes:EtOAc, 1:1) yielded compound **16** as a white solid (22 g, 31%). Data for the β-isomer: ^{1}H

(28) See: tentative rules for carbohydrate nomenclature: *Biochemistry*, **1971**, *10*, 3983−4004.

(29) Ghavami, A.; Sadalapure, K. S.; Johnston, B. D.; Lobera, M.; Snider, B. B.; Pinto, B. M. *Synlett* **2003**, 1259–1262.

(30) Liu, H.; Pinto, B. M. *J. Org. Chem.* **2005**, *70*, 753–755.

NMR ($CDCl_3$) δ 7.36−7.26 (Ar), 5.93 (1H, dddd, allyl), 5.53 (1H, s, Ph-CH), 5.35 (1H, d, allyl), 5.19 (1H, d, allyl), 4.64 (1H, d, $J_{1,2}$ = 7.8 Hz, H-1), 4.36 (1H, dd, allyl), 4.30 (1H, dd, $J_{6a,6b}$ = 10.4 Hz, $J_{6a,5}$ = 4.8 Hz, H-6a), 4.16 (1H, dd, allyl), 3.99 (1H, dd, $J_{3,2}$ = 9.6 Hz, H-3), 3.82 (1H, dd, $J_{6b,5}$ = 10.2 Hz, H-6b), 3.72 (1H, dd, $J_{4,5}$ = 9.0 Hz, H-4), 3.69 (1H, dd, H-2), 3.45 (1H, ddd, H-5), 3.30, 3.28 (2 × −OMe), 1.33, 1.33 (2 × −Me). ^{13}C NMR δ 137.4−117.2 (Ar, allyl), 101.4 (Ph-CH), 100.6 (C-1), 99.9, 99.6 (BDA), 78.0 (C-4), 70.5 (C-2, allyl), 69.7 (C-3), 68.9 (C-6), 67.6 (C-5), 48.2, 48.1 (2 × −OMe), 17.8, 17.8 (2 × −Me). Anal. Calcd for $C_{22}H_{30}O_8$: C, 62.55; H, 7.16. Found: C, 62.78; H, 6.89.

4,6-*O*-Benzylidene-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α,β-D-glucopyranose (17). *t*-BuOK (0.07 mol, 7.8 g) was added to a solution of allyl-5,7-*O*-benzylidene-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α,β-D-glucopyranoside (**16**) (16.2 g, 0.038 mol) in DMF (200 mL), and the mixture was stirred for 2 h at 80 °C. The reaction mixture was cooled to room temperature and extracted with EtOAc (3 × 150 mL). The organic layer was washed with 1 M aqueous HCl and dried over Na_2SO_4. The solvent was removed under reduced pressure to give the enol ether as a brown syrup. The residue was redissolved in a mixture of THF and water (4:1, 150 mL) and treated with iodine (0.07 mol) for 1.5 h. The reaction was then quenched by addition of a saturated solution of $Na_2S_2O_3$. The organic layer was separated and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine solution, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography to give **17** as a white amorphous solid (12.2 g, 84%). Data for the β-isomer: ^{1}H NMR ($CDCl_3$) δ 7.53−7.35 (5H, Ar), 5.54 (1H, Ph-CH), 5.29 (1H, dd, $J_{1,2}$ = 3.5 Hz, $J_{1,\text{-OH}}$ = 3.0 Hz, H-1), 4.70 (1H, dd, $J_{3,2}$ = 10.8 Hz, $J_{3,4}$ = 9.6 Hz, H-3), 4.22 (1H, dd, $J_{6a,6b}$ = 10.2 Hz, $J_{6a,5}$ = 4.8 Hz, H-6a), 4.17 (1H, dd, H-2), 4.06 (1H, ddd, $J_{5,4}$ = 9.4 Hz, $J_{5,6b}$ = 10.4, H-5), 3.76 (1H, dd, H-6b), 3.54 (1H, dd, H-4), 3.42, 3.39 (2 × −OMe), 3.01 (1H, br s, −OH), 1.39 (2 × −Me). ^{13}C NMR δ 137.4−126.7 (Ar), 102.2 (Ph-CH), 101.8, 101.7 (BDA), 92.4 (C-1), 81.1 (C-4), 72.0 (C-2), 69.1 (C-3), 68.9 (C-6), 63.4 (C-5), 48.5, 48.4 (2 × −OMe), 19.1, 19.1 (2 × −Me). Anal. Calcd for $C_{19}H_{26}O_8$: C, 59.68; H, 6.85. Found: C, 59.82; H, 6.49.

5,7-*O*-Benzylidene-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-gluco-hept-1-enitol (18). *n*-BuLi (*n*-hexane solution, 0.058 mol, 2.90 equiv) was added dropwise to a solution of methyltriphenylphosphonium bromide (21.4, 0.06 mmol, 3.0 equiv) in dry THF (80 mL) at −78 °C under N_2. The mixture was stirred for 1 h at the same temperature. A solution of **17** (7.8 g, 0.02 mol) in dry THF (10 mL) was introduced into the solution at −78 °C, and the resulting solution was stirred for an additional 30 min. The reaction was allowed to warm to room temperature and stirred for another 3 h. The reaction mixture was quenched by adding acetone, and extracted with ether. The organic layer was washed with brine and dried over Na_2SO_4, then concentrated in vacuo. Purification by column chromatography on silica gel, (hexanes/EtOAc, 4:1) gave **18** as a colorless oil (7.12 g, 91% yield). $[\alpha]_D^{23}$ −139.0 (*c* 1.0, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 7.45−7.26 (5H, Ar), 5.90 (1H, ddd, $J_{2,3}$ = 7.4 Hz, $J_{2,1a}$ = 16.8 Hz, $J_{2,1b}$ = 10.4 Hz, H-2), 5.47 (1H, dd, $J_{1a,1b}$ = 1.5 Hz, H-1a), 5.39 (1H, s, Ph-CH), 5.30 (1H, dd, H-1b), 4.50 (1H, dd, $J_{3,4}$ = 9.8 Hz, H-3), 4.34 (1H, dd, $J_{7a,7b}$ = 10.4 Hz, $J_{7a,6}$ = 5.3 Hz, H-7a), 4.19 (1H, dddd, $J_{6,7b}$ = 10.3 Hz, $J_{6,5}$ = 9.4 Hz, $J_{6,\text{-OH}}$ = 4.5 Hz, H-6), 4.03 (1H, dd, $J_{4,5}$ = 2.7 Hz, H-4), 3.68 (1H, dd, H-5), 3.58 (1H, dd, H-7b), 3.30, 3.26 (6H, 2 × −OMe), 2.13 (1H, d, OH-6), 1.33, 1.31 (6H, 2 × −Me). ^{13}C NMR δ 137.7−126.4 (6C, Ar), 134.0 (C-2), 119.4 (C-1), 101.6 (Ph-CH), 99.4, 98.8, 80.4 (C-5), 71.6 (C-7), 70.1 (C-3), 69.4 (C-4), 61.4 (C-6), 48.3, 48.1 (2 × −OMe), 17.9, 17.8 (2 × −Me). Anal. Calcd for $C_{20}H_{28}O_7$: C, 63.14; H, 7.42. Found: C, 63.39; H, 7.37.

6-*O*-Benzyl-5,7-*O*-benzylidene-3,4-*O*-(2′, 3′-dimethoxybutane-2′,3′-diyl)-D-gluco-hept-1-enitol (19). A mixture of compound **18** (6.89 g, 0.018 mol) and 60% NaH (1.5 equiv) in DMF (100 mL) was stirred in an ice bath for 20 min. A solution of benzyl bromide (2.56 mL, 0.02 mol) in DMF (10 mL) was added, and the mixture was stirred at room temperature for 2 h. The reaction was quenched with ice water (50 mL) and the mixture was diluted with Et_2O (100 mL). The organic layer was washed with H_2O (50 mL) and brine (50 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude product was purified by flash chromatography [hexanes/EtOAc, 5:1] to give compound **19** as colorless oil (7.31 g, 85%). $[\alpha]_D^{23}$ −79.0 (*c* 1.0, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 7.48−7.26 (10H, Ar), 5.87 (1H, ddd, $J_{2,3}$ = 8.0 Hz, $J_{2,1a}$ = 17.2 Hz, $J_{2,1b}$ = 10.4 Hz, H-2), 5.43 (1H, dd, $J_{1a,1b}$ = 1.8 Hz, H-1a), 5.38 (1H, s, Ph-CH), 5.30 (1H, dd, H-1b), 4.60 (2H, dd, Ph-CH_2), 4.53 (1H, dd, $J_{3,4}$ = 9.8 Hz, H-3), 4.47 (1H, dd, $J_{7a,7b}$ = 10.7 Hz, $J_{7a,6}$ = 5.0 Hz, H-7a), 4.10 (1H, ddd, $J_{6,7b}$ = 10.4 Hz, $J_{6,5}$ = 9.3, Hz, H-6), 4.08 (1H, dd, $J_{4,5}$ = 1.9 Hz, H-4), 3.77 (1H, dd, H-5), 3.61 (1H, dd, H-7b), 3.24, 3.19 (6H, 2 × −OMe), 1.34, 1.31 (6H, 2 × −Me). ^{13}C NMR δ 138.1−126.3 (12C, Ar), 134.1 (C-2), 119.9 (C-1), 101.2 (Ph-CH), 99.5, 98.8, 78.9 (C-5), 71.7 (Ph-CH_2), 70.3 (C-3), 69.9 (C-7), 67.9 (C-4), 67.5 (C-6), 48.2, 48.0 (2 × −OMe), 18.1, 18.0 (2 × −Me). Anal. Calcd for $C_{27}H_{34}O_7$: C, 68.92; H, 7.28. Found: C, 69.13; H, 7.57.

6-*O*-Benzyl-5,7-*O*-benzylidene-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-D-gulo-heptitol (20). To a solution of **19** (3.2 g, 6.80 mmol) in acetone:water (9:1, 50 mL) at 0 °C were added NMO (820 mg, 5.10 mmol) and OsO_4 (340 mg, 0.034 mmol, 2.5 wt % solution in 2-methyl-2-propanol). The reaction mixture was stirred at room temperature for 4 h before it was quenched with a saturated solution of $NaHSO_3$. After being stirred for an additional 15 min the reaction mixture was extracted with ethyl acetate and the organic layer was washed with water and brine, dried, and concentrated. Chromatographic purification of the residue (hexanes/EtOAc, 2:1) afforded **20** (3.02 g, 88%) as a colorless oil. $[\alpha]_D^{23}$ −116.0 (*c* 0.1, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 7.40−7.23 (10H, Ar), 5.44 (1H, s, Ph-CH), 4.63 (2H, dd, Ph-CH_2), 4.43 (1H, dd, $J_{7a,7b}$ = 10.5 Hz, $J_{7a,6}$ = 5.1 Hz, H-7a), 4.25 (1H, dd, $J_{3,4}$ = 10.0 Hz, $J_{3,2}$ = 5.1 Hz, H-3), 4.16 (1H, dd, $J_{4,5}$ = 2.5 Hz, H-4), 4.11 (1H, ddd, $J_{6,5}$ = 9.2 Hz, $J_{6,7b}$ = 10.4, H-6), 3.97 (1H, dd, H-5), 3.87 (1H, m, H-1a), 3.79 (2H, m, H-2, H-1b), 3.63 (1H, dd, H-7b), 3.25, 3.18 (6H, 2 × −OMe), 2.86 (1H, OH-2), 2.33 (1H, OH-1), 1.32, 1.28 (6H, 2 × −Me). ^{13}C NMR δ 138.1−126.3 (12C, Ar), 101.4 (Ph-CH), 99.3, 98.9, 79.3 (C-5), 71.8 (Ph-CH_2), 70.6 (C-2), 70.1 (C-3), 69.9 (C-7), 67.7 (C-6), 67.7 (C-4), 63.8 (C-1), 48.3, 48.2 (2 × −OMe), 17.8, 17.7 (2 × −Me). Anal. Calcd for $C_{27}H_{36}O_9$: C, 64.27; H, 7.19. Found: C, 64.01; H, 7.44.

1,2,6-Tri-*O*-benzyl-5,7-*O*-benzylidene-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-D-gulo-heptitol (22). A mixture of compound **20** (2.90 g, 5.74 mmol) and 60% NaH (2.5 equiv) in DMF (100 mL) was stirred in an ice bath for 1 h. A solution of benzyl bromide (1.53 mL, 12.6 mmol) in DMF (10 mL) was added, and the mixture was stirred at room temperature for 3 h. The reaction was quenched with ice water and the mixture was diluted with Et_2O (100 mL). The organic layer was washed with H_2O and brine. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude product was purified by flash chromatography [hexanes/EtOAc, 5:1] to give compound **22** as a colorless oil (3.48 g, 88%). $[\alpha]_D^{23}$ −102.4 (*c* 1.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 7.43−7.21 (20H, Ar), 5.20 (1H, s, Ph-CH), 4.66−4.54 (6H, 3 × Ph-CH_2), 4.40 (2H, m, H-3, H-7a), 4.29 (1H, dd, $J_{4,5}$ = 2.4 Hz, $J_{4,3}$ = 9.9 Hz, H-4), 4.08 (1H, ddd, $J_{6,7a}$ = 5.0 Hz, $J_{6,7b}$ = 10.2 Hz, $J_{6,5}$ = 9.5 Hz, H-6), 3.96 (1H, dd, H-5), 3.84 (1H, dd, $J_{1a,2}$ = 3.3 Hz, $J_{1a,1b}$ = 8.9 Hz, H-1a), 3.81 (1H, ddd, $J_{2,3}$ = 5.6 Hz, $J_{2,1b}$ = 5.9 Hz, H-2), 3.78 (1H, dd, H-1b), 3.53 (1H, dd, H-7b), 3.24, 3.16 (6H, 2 × −OMe), 1.30, 1.28 (6H, 2 × −Me). ^{13}C NMR δ 138.7−126.4 (24C, Ar), 101.2 (Ph-CH), 99.3, 98.9, 79.1 (C-5), 78.5 (C-2), 73.6, 72.5, 71.5 (Ph-CH_2), 70.3 (C-1), 69.9 (C-7), 67.8 (C-6), 66.6 (C-4), 48.1, 47.9 (2 × −OMe), 17.9 (2 × −Me). Anal. Calcd for $C_{41}H_{48}O_9$: C, 71.91; H, 7.06. Found: C, 72.02; H, 7.24.

1,2,6-Tri-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-D-gulo-heptitol (23). To a solution of 1,2,6-tri-*O*-benzyl-5,7-*O*-benzylidene-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-D-gulo-heptitol (**22**) (3.12 g, 4.55 mmol) in MeOH (150 mL) was

added *p*-toluenesulfonic acid (200 mg) and the reaction mixture was stirred for 4 h at rt. The reaction was then quenched by addition of excess Et_3N, and the solvents were removed under vacuum to give a pale yellow syrup that was purified by flash column chromatography to give **23** (2.18 g, 79%). $[\alpha]_D^{23}$ −86.4 (*c* 1.0, CH_2Cl_2). ^1H NMR ($CDCl_3$) δ 7.33−7.26 (15H, Ar), 4.74−4.46 (6H, 3 × Ph-CH_2), 4.18 (1H, dd, $J_{3,4}$ = 10.0 Hz, $J_{3,2}$ = 5.6 Hz, H-3), 4.09 (1H, dd, $J_{4,5}$ = 1.0 Hz, H-4), 4.02 (1H, dd, $J_{5,6}$ = 8.0 Hz, $J_{5,5\text{-OH}}$ = 7.9 Hz, H-5), 3.84 (3H, m, H_2-7, H-1a), 3.73 (3H, m, H-6, H-2, H-1b), 3.23, 3.15 (2 × −OMe), 2.76 (1H, d, 5-OH), 2.29 (1H, dd, 7-OH), 1.29, 1.26 (2 × −Me). ^{13}C NMR δ 138.5−127.4 (Ar), 98.9, 98.6, 79.0 (C-2), 78.0 (C-6), 73.6, 72.6, 71.4 (3 × Ph-CH_2), 70.9 (C-5), 69.4 (C-4), 69.2 (C-1), 67.1 (C-3), 61.7 (C-7), 48.4, 48.2 (2 × −OMe), 17.8, 17.7 (2 × −Me). Anal. Calcd for $C_{34}H_{44}O_9$: C, 68.44; H, 7.43. Found: C, 68.39; H, 7.23.

1,2,6-Tri-*O*-benzyl-3,4-di-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-D-gulo-heptitol-5,7-cyclic Sulfate (14a). A mixture of **23** (2.0 g, 3.35 mmol) and Et_3N (1.5 mL, 15.0 mmol) in CH_2Cl_2 (100 mL) was stirred in an ice bath. Thionyl chloride (0.36 mL, 5.0 mmol) in CH_2Cl_2 (10 mL) was then added dropwise over 15 min, and the mixture was stirred for an additional 30 min. The mixture was poured into ice-cold water and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (8:1, 5:1, 3:1 hexanes:EtOAc) to gave the diastereomeric mixture of cyclic sulfites. To a solution of the cyclic sulfites in a mixture of CH_3CN:CCl_4 (100 mL) were added sodium periodate (1.48 g, 6.95 mmol) and $RuCl_3$ (100 mg), followed by H_2O (20 mL). The mixture was then stirred for 2 h at rt. The reaction mixture was filtered through a silica bed and washed repeatedly with EtOAc. The volatile solvents were removed, and the aqueous solution was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with saturated NaCl, dried over Na_2SO_4, and evaporated under diminished pressure. The residue was purified by flash column chromatography to give **14a** as a white amorphous solid (1.41 g, 63%). $[\alpha]_D^{23}$ −57.3 (*c* 0.7, CH_2Cl_2). ^1H NMR ($CDCl_3$) δ 7.34−7.26 (15H, Ar), 5.11 (1H, m, H-5), 4.68−4.51 (6H, 3 × Ph-CH_2), 4.39 (3H, m, H_2-7, H-6), 4.35 (1H, dd, $J_{4,5}$ = 1.9 Hz, $J_{4,3}$ = 9.8 Hz, H-4), 4.20 (1H, dd, $J_{3,2}$ = 3.6 Hz, H-3), 3.80 (1H, dd, $J_{1a,1b}$ = 9.7 Hz, $J_{1a,2}$ = 5.8 Hz, H-1a), 3.75 (1H, ddd, H-2), 3.67 (1H, dd, $J_{1b,2}$ = 5.0 Hz, H-1b), 3.22, 3.12 (6H, 2 × −OMe), 1.32, 1.26 (6H, 2 × −Me). ^{13}C NMR δ 138.4−127.3 (18C, Ar), 99.6, 98.9, 84.0 (C-5), 77.5 (C-2), 73.6, 72.7, 72.5 (Ph-CH_2), 72.0 (C-6), 69.2 (C-1), 67.1 (C-7), 68.8 (C-3), 65.9 (C-4), 48.4, 48.2 (2 × −OMe), 17.8, 17.6 (2 × −Me). Anal. Calcd for $C_{34}H_{42}O_{11}S$: C, 61.99; H, 6.43. Found: C, 61.76; H, 6.44.

6-*O*-Benzyl-5,7-*O*-benzylidene-1-*O*-(*tert*-butyldimethylsilyl)-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-D-gulo-heptitol (24). A mixture of **20** (3.6 g, 7.13 mmol), imidazole (1.42 g, 21.0 mmol), and TBDMSCl (1.18 g, 7.85 mmol) in dry DMF (80 mL) was stirred at 0 °C under N_2 for 2 h. The reaction was quenched by the addition of ice-cold water, and the reaction mixture was partitioned between Et_2O (200 mL) and H_2O (100 mL). The separated organic phase was washed with H_2O (50 mL) and brine (50 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc, 3:1) to give **24** as a colorless oil (3.98 g, 90%). $[\alpha]_D^{23}$ −73.0 (*c* 1.5, CH_2Cl_2). ^1H NMR ($CDCl_3$) δ 7.41−7.21 (10H, Ar), 5.39 (1H, s, Ph-CH), 4.55 (2H, dd, Ph-CH_2), 4.40 (1H, dd, $J_{7a,7b}$ = 10.6 Hz, $J_{7a,6}$ = 5.0 Hz, H-7a), 4.25 (1H, dd, $J_{5,4}$ = 2.3 Hz, $J_{5,6}$ = 9.4 Hz, H-6), 4.15 (1H, dd, $J_{4,3}$ = 9.7 Hz, H-4), 4.09 (2H, m, H-3, H-6), 3.83 (1H, dd, $J_{1a,1b}$ = 9.5, $J_{1a,2}$ = 4.4 Hz, H-1a), 3.70 (1H, dd, $J_{1b,2}$ = 3.8 Hz, H-1b), 3.65 (1H, ddd, $J_{2,\text{-OH}}$ = 7.5 Hz, H-2), 3.59 (1H, dd, $J_{7b,6}$ = 10.3 Hz, H-7b), 3.17, 3.11 (6H, 2 × −OMe), 2.50 (1H, d, OH-2), 1.26, 1.21 (6H, 2 × −Me). 0.80 (9H, s, TBDMS), 0.00 (6H, s, TBDMS). ^{13}C NMR δ 143.6−131.5 (12C, Ar), 101.3 (Ph-CH), 99.3, 98.8 (BDA), 79.6 (C-5), 71.9 (Ph-CH_2), 71.7 (C-2), 70.2 (C-7), 68.6 (C-4), 68.1 (C-6), 67.5 (C-3), 63.3 (C-1), 48.5, 48.3 (2 × −OMe), 26.2 (TBDMS), 16.6 (TBDMS), 18.1, 18.0 (2 × −Me), −5.0, −5.5 (TBDMS). Anal. Calcd for $C_{33}H_{50}O_9Si$: C, 64.05; H, 8.14. Found: C, 64.17; H, 8.38.

2-*O*-Benzyl-1,3-*O*-benzylidene-7-*O*-(*tert*-butyldimethylsilyl)-4,5-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-6-*O*-(4-nitrobenzoyl)-D-glycero-L-gulo-heptitol (25). A solution of **24** (3.72 g, 6.01 mmol) in THF (60 mL) containing *p*-nitrobenzoic acid (3.0 g, 18.0 mmol) and triphenylphosphine (4.7 g, 18.0 mmol) was cooled to 0 °C. A solution of diisopropyl azodicarboxylate (3.64 mL, 18.0 mmol) in THF (30 mL) was added to the mixture over 2 h. After being stirred for 20 h at ambient temperature, the reaction mixture was concentrated and then partitioned between Et_2O (200 mL) and H_2O (100 mL). The organic phase was washed with saturated aqueous $NaHCO_3$ (3 × 50 mL), followed by brine (50 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was purified by flash chromatography (hexanes/EtOAc, 3:1) to give **25** as a colorless oil (2.96 g, 64%). $[\alpha]_D^{23}$ −53.1 (*c* 1.5, CH_2Cl_2). ^1H NMR ($CDCl_3$) δ 8.18−6.99 (14H, Ar), 5.41 (1H, s, Ph-CH), 5.33 (1H, ddd, $J_{6,5}$ = 1.9 Hz, $J_{6,7a}$ = 6.8 Hz, $J_{6,7b}$ = 6.6 Hz, H-6), 4.52 (1H, d, Ph-CH_2), 4.49 (1H, dd, $J_{5,4}$ = 10.0 Hz, H-5), 4.44 (1H, $J_{1a,1b}$ = 10.4 Hz, $J_{1a,2}$ = 5.0 Hz, H-1a), 4.42 (1H, d, Ph-CH_2), 4.26 (1H, dd, $J_{4,3}$ = 2.0 Hz, H-4), 4.05 (1H, ddd, $J_{2,3}$ = 9.2 Hz, $J_{2,1b}$ = 10.4 Hz, H-2), 4.00 (1H, dd, $J_{7a,7b}$ = 10.0 Hz, $J_{7a,6}$ = 6.8 Hz, H-7a), 3.91 (1H, dd, $J_{7b,6}$ = 6.6 Hz, H-7b), 3.82 (1H, dd, H-3), 3.62 (1H, dd, H-1b), 3.27, 3.09 (6H, 2 × −OMe), 1.33, 1.32 (6H, 2 × −Me). 0.79 (9H, s, TBDMS), 0.03, 0.00 (6H, s, TBDMS). ^{13}C NMR δ 164.6 (C═O), 150.4−123.4 (18C, Ar), 101.1 (Ph-CH), 99.1, 98.8, 78.1 (C-3), 73.7 (C-6), 70.9 (Ph-CH_2), 69.6 (C-1), 66.8 (C-2), 65.2 (C-5), 64.9 (C-4), 59.9 (C-7), 47.9 (2 × −OMe), 25.6 (TBDMS), 18.0 (TBDMS), 17.6 (2 × −Me), −5.4, −5.5 (TBDMS). Anal. Calcd for $C_{39}H_{53}NO_{11}Si$: C, 63.31; H, 7.22. Found: C, 63.26; H, 7.12.

2-*O*-Benzyl-1,3-*O*-benzylidine-7-*O*-(*tert*-butyldimethylsilyl)-4,5-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-L-gulo-heptitol (26). Compound **25** (2.70 g, 3.51 mmol) was dissolved in MeOH (50 mL) and 1 N NaOMe/MeOH (1.0 mL) was added. The mixture was stirred at rt for 1 h and then Rexyn 101 (H^+) was added to adjust the pH to 7. The solvent was removed and the residue was partitioned between Et_2O (150 mL) and H_2O (100 mL). The organic layer was washed with brine (50 mL), dried over anhydrous Na_2SO_4, and concentrated. The residue was purified to give **26** as a white foam (2.05 g, 94%). $[\alpha]_D^{23}$ −66.4 (*c* 1.6, CH_2Cl_2). ^1H NMR ($CDCl_3$) δ 7.46−31 (Ar), 5.43 (1H, s, Ph-CH), 4.61 (2H, s, Ph-CH_2), 4.46 (1H, dd, $J_{4,3}$ = 2.4 Hz, $J_{4,5}$ = 10.0 Hz, H-4), 4.42 (1H, dd, $J_{1b,1a}$ = 10.5 Hz, $J_{1b,2}$ = 5.0 Hz, H-1b), 4.22 (1H, dd, $J_{5,6}$ = 1.3 Hz, H-5), 4.11 (1H, ddd, $J_{2,1b}$ = 10.4 Hz, $J_{2,3}$ = 9.2 Hz, H-2), 3.96 (1H, dd, H-3), 3.77 (1H, m, H-6), 3.71 (2H, m, H_2-7), 3.66 (1H, dd, H-1a), 3.20, 3.15 (2 × −OMe), 2.35 (1H, d, $J_{\text{-OH},6}$ = 7.0 Hz, OH-6), 1.31, 1.27 (2 × −Me), 0.80 (9H, TBDMS), 0.016, 0.00 (TBDMS). ^{13}C NMR δ 138.9−126.9 (12C, Ar), 101.1 (Ph-CH), 99.9, 99.5, 79.2 (C-2), 72.2 (Ph-CH_2), 70.8 (C-1), 70.5 (C-6), 68.2 (C-2), 67.1 (C-5), 66.0 (C-4), 64.1 (C-7), 48.7, 48.5 (2 × −OMe), 26.5 (TBDMS), 18.9 (TBDMS), 18.5, 18.4 (2 × −Me), −4.57, −4.65 (TBDMS). Anal. Calc. for $C_{33}H_{50}O_9Si$: C, 64.05; H, 8.14. Found: C, 64.02; H, 8.31.

2-*O*-Benzyl-1,3-*O*-benzylidene-4,5-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-L-gulo-heptitol (21). TBAF (1.0 M solution in THF, 3.90 mL, 3.9 mmol) was added dropwise to a stirred solution of the TBDMS-protected alcohol **26** (1.96 g, 3.25 mmol) in THF (30 mL) at rt. After 2 h at rt, the reaction mixture was concentrated and the residue was purified by flash chromatography (EtOAc:hexanes = 3: 7) to yield **21** as a white crystalline solid (1.48 g, 92%). Mp 118−120 °C; $[\alpha]_D^{23}$ −128.4 (*c* 1.3, CH_2Cl_2). ^1H NMR ($CDCl_3$) δ 7.43−7.26 (10H, Ar), 5.43 (1H, s, Ph-CH), 4.62 (2H, dd, Ph-CH_2), 4.46 (1H, dd, $J_{4,3}$ = 2.7 Hz, $J_{4,5}$ = 9.7 Hz, H-4), 4.44 (1H, dd, $J_{1a,1b}$ = 10.4 Hz, $J_{1a,2}$ = 5.0 Hz, H-1a), 4.17 (1H, dd, $J_{5,6}$ = 1.8 Hz, H-5), 4.12 (1H, ddd, $J_{2,3}$

= 9.2 Hz, $J_{2,1b}$ = 10.4, H-2), 3.99 (1H, dd, H-3), 3.85 (1H, ddd, $J_{7a,7b}$ = 11.0 Hz, $J_{7a,6}$ = 5.6, $J_{7a,-OH}$ = 2.0, H-7a), 3.80 (1H, m, H-6), 3.68 (1H, ddd, $J_{7b,6}$ = 10.0 Hz, $J_{7b,-OH}$ = 9.8 Hz, H-7b), 3.64 (1H, dd, H-1b), 3.21, 3.16 (6H, 2 × −OMe), 2.63 (1H, d, OH-6), 2.37 (1H, dd, OH-7), 1.31, 1.29 (6H, 2 × −Me). ^{13}C NMR δ 138.2−126.3 (12C, Ar), 101.3 (Ph-CH), 99.4, 99.3, 78.7 (C-3), 71.7 (Ph-CH_2), 70.2 (C-1), 69.9 (C-5), 69.3 (C-6), 67.6 (C-2), 65.5 (C-7), 65.3 (C-4), 48.2, 48.1 (2 × −OMe), 17.9 (2 × −Me). Anal. Calcd for $C_{27}H_{36}O_9$: C, 64.27; H, 7.19. Found: C, 64.63; H, 7.44.

2,6,7-Tri-*O*-benzyl-1,3-*O*-benzylidene-4,5-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-L-gulo-heptitol (27). A mixture of compound **21** (1.40 g, 2.77 mmol) and 60% NaH (1.5 equiv) in DMF (100 mL) was stirred at 0 °C for 1 h. A solution of benzyl bromide (0.74 mL, 6.01 mmol) in DMF (5 mL) was added, and the mixture was stirred at room temperature for 2 h. The reaction was quenched by addition of ice-cold water (50 mL) and the mixture was diluted with Et_2O (150 mL). The organic layer was washed with H_2O (50 mL) and brine (50 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude product was purified by flash chromatography [hexanes/EtOAc, 5:1] to give compound **27** as a white crystalline solid (1.76 g, 92%). Mp 104−106 °C; $[\alpha]_D^{23}$ −90.6 (*c* 0.7, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 7.38−7.23 (20H, Ar), 4.88 (1H, s, Ph-CH), 4.84−4.55 (6H, 3 × Ph-CH_2), 4.42 (1H, dd, $J_{4,3}$ = 2.7 Hz, $J_{4,5}$ = 9.7 Hz, H-4), 4.37 (1H, dd, $J_{1a,1b}$ = 10.5 Hz, $J_{1a,2}$ = 5.0 Hz, H-1a), 4.23 (1H, dd, $J_{5,6}$ = 2.2 Hz, H-5), 3.98 (1H, dd, $J_{2,1b}$ = 10.4 Hz, H-2), 3.90 (2H, d, $J_{7,6}$ = 5.6 Hz, H_2-7), 3.79 (1H, dt, H-6), 3.33 (1H, dd, H-1b), 3.13 (1H, m, H-3), 3.13 (6H, 2 × −OMe), 1.30, 1.28 (6H, 2 × −Me). ^{13}C NMR δ 138.6−126.4 (24C, Ar), 100.9 (Ph-CH), 99.3, 99.3, 78.1 (C-3), 73.3, 71.3, 71.2 (Ph-CH_2), 73.3 (C-6), 69.6 (C-1), 69.5 (C-7), 67.7 (C-5), 67.4 (C-2), 65.4 (C-4), 48.0, 47.9 (2 × −OMe), 18.0, 17.9 (2 × −Me). Anal. Calcd for $C_{41}H_{48}O_9$: C, 71.91; H, 7.06. Found: C, 71.99; H, 7.19.

2,6,7-Tri-*O*-benzyl-4,5-di-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-L-gulo-heptitol (28). To a solution of **27** (1.60 g, 9.6 mmol) in MeOH (100 mL) was added *p*-toluenesulfonic acid (200 mg), and the reaction mixture was stirred for 6 h at rt. The reaction was then quenched by addition of excess Et_3N, the solvents were removed, and the yellow syrup was purified by flash column chromatography to give **28** as a white amorphous solid (1.08 g, 77%). $[\alpha]_D^{23}$ −91.6 (*c* 0.6, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 7.33−7.21 (15H, Ar), 4.70−4.48 (6H, 3 × Ph-CH_2), 4.35 (1H, d, $J_{4,5}$ = 10.2 Hz, H-4), 4.14 (1H, dd, $J_{5,6}$ = 2.0 Hz, H-5), 3.90 (2H, m, H_2-1), 3.76 (3H, m, H-2, H-6, H-7a), 3.65 (2H, m, H-3, H-7b), 3.19, 3.16 (2 × −OMe), 2.65 (1H, *J* = 8.9 3-OH), 2.25 (1H, dd, *J* = 5.1, 7.6 Hz, 1-OH), 1.30, 1.29 (2 × −Me). ^{13}C NMR δ 137.9−126.8 (Ar), 99.1, 99.0, 78.3 (C-6), 75.3 (C-6), 73.4, 72.5, 71.7 (3 × Ph-CH_2), 69.9 (C-2), 69.8 (C-7), 67.8 (C-5), 66.9 (C-4), 61.4 (C-1), 48.4, 48.1 (2 × −OMe), 17.8, 17.7 (2 × −Me). Anal. Calcd for $C_{34}H_{44}O_9$: C, 68.44; H, 7.43. Found: C, 68.59; H, 7.39.

2,6,7-Tri-*O*-benzyl-4,5-di-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-L-gulo-heptitol-1,3-cyclic Sulfate (14b). A mixture of **22** (1.0 g, 1.68 mmol) and Et_3N (0.90 mL, 8.9 mmol) in CH_2Cl_2 (50 mL) was stirred at 0 °C. Thionyl chloride (0.2 mL, 2.7 mmol) in CH_2Cl_2 (5 mL) was then added dropwise over 20 min, and the mixture was stirred for an additional 30 min. The mixture was poured into ice-cold water and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. Column chromatography (hexanes:EtOAc, 8:1, 5:1, 3:1) gave the diastereomeric mixture of cyclic sulfites. To a solution of the cyclic sulfites in a mixture of CH_3CN:CCl_4 (1:1, 60 mL) were added sodium periodate (0.70 g, 3.35 mmol) and $RuCl_3$ (60 mg), followed by H_2O (10 mL). The mixture was then stirred for 2 h at room temperature. The reaction mixture was filtered through a silica bed and washed repeatedly with EtOAc. The volatile solvents were removed, and the aqueous solution was extracted with EtOAc (2 × 100 mL). The combined organic layer was washed with saturated NaCl, dried over Na_2SO_4, and evaporated under diminished pressure. The residue was purified by flash column chromatography to give **14b** as a white solid (620 mg, 55%). Mp 124−126 °C; $[\alpha]_D^{23}$ −128.0 (*c* 1.0, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 7.36−7.25 (15H, Ar), 4.80−4.52 (6H, 3 × Ph-CH_2), 4.47 (1H, dd, $J_{4,3}$ = 1.8 Hz, $J_{4,5}$ = 10.2 Hz, H-4), 4.45 (1H, dd, $J_{3,2}$ = 9.8, Hz, H-3), 4.41 (1H, dd, $J_{1a,1b}$ = 10.4 Hz, $J_{1a,2}$ = 4.6 Hz, H-1a), 4.32 (1H, ddd, $J_{2,1b}$ = 9.7 Hz, H-2), 4.24 (1H, dd, H-1b), 4.07 (1H, dd, $J_{5,6}$ = 2.6 Hz, H-5), 3.87 (1H, dd, $J_{7a,7b}$ = 10.0 Hz, $J_{7a,6}$ = 6.0 Hz, H-7a), 3.80 (1H, dd, $J_{7b,6}$ = 4.7 Hz, H-7b), 3.76 (1H, m, H-6), 3.15, 3.13 (2 × −OMe), 1.30, 1.28 (2 × −Me). ^{13}C NMR δ 138.3−127.4 (18C, Ar), 99.7, 99.3, 83.2 (C-3), 73.9 (C-6), 73.6, 72.7, 72.5 (Ph-CH_2), 71.8 (C-1), 69.6 (C-7), 66.9 (C-2), 66.8 (C-5), 64.8 (C-4), 48.4, 48.2 (2 × −-OMe), 17.8, 17.7 (2 × −Me). Anal. Calcd for $C_{34}H_{42}O_{11}S$: C, 61.99; H, 6.43. Found: C, 61.76; H, 6.44.

2,3,5-Tri-*O*-*p*-methoxybenzyl-1,4-dideoxy-1,4-[[2*S*,3*S*,4*R*,5*S*,6*S*]-2,6,7-tri-*O*-benzyl-4,5-di-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-3-(sulfooxy)heptyl]-(*R*)-*epi*-sulfoniumylidine]-D-arabinitol Inner Salt (29). The thioarabinitol **15** (210 mg, 0.42 mmol) and the cyclic sulfate **14a** (308 mg, 0.46 mmol) were added to 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) (3 mL) containing anhydrous K_2CO_3 (40 mg). The mixture was stirred in a sealed tube at 72 °C for 48 h. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (3:1 hexanes/EtOAc and then 20:1, 15:1 EtOAc/MeOH). The coupled product, **29**, was obtained as a white amorphous solid (258 mg, 52%). $[\alpha]_D^{23}$ −82.0 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (acetone-d_6) δ 7.44−6.84 (27H, Ar), 4.93 (1H, $J_{3',4'}$ = 1.7 Hz, $J_{3',2'}$ = 5.1 Hz, H-3′), 4.85−4.22 (12H, 3 × Ph-CH_2, 3 × Ph-CH_2), 4.68 (1H, m, H-2), 4.57 (1H, m, H-5′), 4.45 (1H, m, H-3), 4.37 (1H, dd, $J_{1a',1b'}$ = 13.5 Hz, $J_{1a',2'}$ = 3.9 Hz, H-1a′), 4.35 (1H, m, H-6′), 4.30 (1H, dd, $J_{4'5'}$ = 10.0 Hz, H-4′), 4.23 (1H, m, H-2′), 4.20 (1H, dd, $J_{1a,1b}$ = 13.5 Hz, $J_{1a,2}$ = 2.6 Hz, H-1a), 4.15 (1H, dd, $J_{1b',2'}$ = 4.4 Hz, H-1b′), 4.06 (1H, dd, H-4), 4.00 (1H, dd, $J_{1b,2}$ = 3.9 Hz, H-1b), 3.94 (1H, dd, $J_{7a',7b'}$ = 9.9 Hz, $J_{7a',6'}$ = 6.5 Hz, H-7a′), 3.80, 3.79 (3 × −OMe), 3.70 (1H, dd, $J_{5a,5b}$ = 10.0 Hz, $J_{5a,4}$ = 6.9 Hz, H-5a), 3.61 (1H, dd, $J_{7b',6'}$ = 5.4 Hz, H-7b′), 3.54 (1H, dd, $J_{5b,4}$ = 8.5, H-5b), 3.20, 3.09 (2 × −OMe), 1.19, 1.18 (2 × −Me). ^{13}C NMR δ 159.9−113.8 (32C, Ar), 99.2, 98.4, 83.3 (C-3), 82.2 (C-2), 76.2 (C-6′), 75.6 (C-2′), 73.4 (C-3′), 72.9, 72.6, 72.0, 71.7, 71.3, 71.3 (3 × Ph-CH_2, 3 × Ph-CH_2), 69.8 (C-7′), 68.9 (C-4′), 68.8 (C-5′), 66.8 (C-5), 65.7 (C-4), 54.9, 54.8 (3 × −OMe), 49.4 (C-1′), 49.2 (C-1), 47.9, 47.1 (2 × −OMe), 17.4, 17.3 (2 × −Me). Anal. Calcd for $C_{63}H_{76}O_{17}S_2$: C, 64.71; H, 6.55. Found: C, 64.38; H, 6.52.

2,3,5-Tri-*O*-*p*-methoxybenzyl-1,4-dideoxy-1,4-[[2*S*,3*S*,4*R*,5*S*,6*R*]-2,6,7-tri-*O*-benzyl-4,5-di-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-3-(sulfooxy)heptyl]-(*R*)-*epi*-sulfoniumylidine]-D-arabinitol Inner Salt (30). To HFIP (3 mL) were added the thioarabinitol **15** (238 mg, 0.46 mmol), the cyclic sulfate **14b** (324 mg, 0.49 mmol), and anhydrous K_2CO_3 (40 mg). The mixture was stirred in a sealed tube at 72 °C for 48 h. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (3:1 hexanes:EtOAc and then 15:1 EtOAc:MeOH) to give **30** as a white amorphous solids (265 mg, 49%). $[\alpha]_D^{23}$ −54.0 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (acetone-d_6) δ 7.42−6.84 (27H, Ar), 4.96−4.12 (12H, 3 × Ph-CH_2, 3 × Ph-CH_2), 4.90 (1H, $J_{3',4'}$ = 1.7 Hz, $J_{3',2'}$ = 6.4 Hz, H-3′), 4.74 (1H, m, H-6′), 4.69 (1H, m, H-2), 4.52 (1H, dd, $J_{4'5'}$ = 9.6 Hz, H-4′), 4.46 (1H, m, H-3), 4.39 (3H, m, H_2-1′, H-2′), 4.35 (1H, m, H-5′), 4.18 (1H, m, H-1a), 4.01 (2H, m, H-4, H-1b), 3.95 (1H, dd, $J_{7a',6'}$ = 7.7 Hz, $J_{7a',7b'}$ = 10.6 Hz, H-7a′), 3.81 (1H, dd, $J_{7b',6'}$ = 3.8 Hz, H-7b′), 3.80, 3.78, 3.77 (3 × −OMe), 3.63 (1H, dd, $J_{5a,5b}$ = 10.0 Hz, $J_{5a,4}$ = 4.7 Hz, H-5a), 3.50 (1H, dd, $J_{5b,4}$ = 8.0 Hz, H-5b), 3.14, 3.06 (2 × −OMe), 1.82 (2 × −Me). ^{13}C NMR δ 159.9−113.8 (32C, Ar), 99.1, 98.6, 83.4 (C-3), 82.1 (C-2), 75.9

(C-6′), 75.1 (C-2′), 73.3 (C-3′), 73.1, 72.6, 72.4, 71.7, 71.7, 71.4 (3 × Ph-CH_2, 3 × Ph-CH_2), 71.3 (C-7′), 69.1 (C-5′), 67.9 (C-4′), 66.7 (C-5), 65.3 (C-4), 54.8, 54.8 (3 × −OMe), 49.2 (C-1′), 48.9 (C-1), 47.9, 47.3 (2 × −OMe), 17.5, 17.4 (2 × −Me). Anal. Calcd for $C_{63}H_{76}O_{17}S_2$: C, 64.71; H, 6.55. Found: C, 64.93; H, 6.65.

1,4-Dideoxy-1,4-[[2*S*,3*S*,4*R*,5*S*,6*S*]-2,4,5,6-pentahydroxy-3-(sulfooxy)heptyl]-(*R*)-*epi*-sulfoniumylidine]-D-arabinitol Inner Salt (13a). Compound **29** (78 mg, 0.075 mmol) was dissolved in a mixture of CH_3COOH:H_2O (20 mL, 4:1) and the solution was stirred with 10% Pd/C (100 mg) under 100 psi of H_2 for 48 h. The catalyst was removed by filtration through a bed of silica, then washed with water (25 mL). The solvents were removed under reduced pressure and 80% aqueous TFA (10 mL) was added. The mixture was stirred at room temperature for 2 h. The solvents were then evaporated under diminished pressure and the residue was purified by flash column chromatography to give **13a** as a white crystalline solid. Mp 164−166. $[\alpha]_D^{23}$ +18.3 (*c* 0.6, MeOH). ^{1}H NMR (D_2O) δ 4.60 (1H, dd, $J_{2,1}$ = 3.4 Hz, $J_{2,3}$ = 3.2 Hz, H-2), 4.36 (1H, dd, $J_{3',2'}$ = 7.1 Hz, $J_{3',4'}$ = 2.7 Hz, H-3′), 4.32 (1H, ddd, $J_{2',1a'}$ = 3.2 Hz, $J_{2'b'}$ = 7.6 Hz, H-2′), 4.30 (1H, dd, $J_{3,4}$ = 3.1 Hz, H-3), 4.02 (1H, t, $J_{4'5'}$ = 2.7 Hz, H-4′), 3.95 (1H, dd, $J_{5a,5b}$ = 11.1, $J_{5a,4}$ = 4.9 Hz, H-5a), 3.93 (1H, ddd, H-4), 3.88 (1H, dd, $J_{1a',1b'}$ = 13.5 Hz, H-1a′), 3.81 (1H, dd, $J_{5b,4}$ = 7.6 Hz, H-5b), 3.72 (1H, dd, H-1b′), 3.71 (2H, d, H_2-1), 3.68 (1H, dd, $J_{5',6'}$ = 7.4 Hz, H-5′), 3.65 (1H, dd, $J_{7a',6'}$ = 3.2 Hz, $J_{7a',7b'}$ = 11.2 Hz, H-7a′), 3.61 (1H, ddd, H-6′), 3.50 (1H, dd, $J_{7b',6'}$ = 5.6 Hz, H-7b′). ^{13}C NMR δ 81.1 (C-3′), 77.8 (C-3), 76.8 (C-2), 71.4 (C-5′), 71.0 (C-6′), 70.0 (C-4), 67.7 (C-4′), 66.7 (C-2′), 62.6 (C-7′), 59.1 (C-5), 50.2 (C-1′), 47.8 (C-1). HRMS Calcd for $C_{12}H_{24}O_{12}NaS_2$ (M + Na) 447.0601, found 447.0601.

1,4-Dideoxy-1,4-[[2*S*,3*S*,4*R*,5*S*,6*R*]-2,4,5,6-pentahydroxy-3-(sulfooxy)heptyl]-(*R*)-*epi*-sulfoniumylidine]-D-arabinitol Inner Salt (13b). The sulfonium salt **30** (240 mg, 0.212 mmol) was deprotected following the same procedure that was used for compound **29**, to give compound **13b** as a crystalline solid. Mp 169−171; $[\alpha]_D^{23}$ +12.0 (*c* 0.5, MeOH). ^{1}H NMR (D_2O) δ 4.61 (1H, dd, $J_{2,1}$ = 3.4 Hz, $J_{2,3}$ = 3.2 Hz, H-2), 4.35 (2H, m, H-2′, H-3′), 4.32 (1H, dd, $J_{3,4}$ = 3.0 Hz, H-3), 3.98 (1H, dd, $J_{5a,5b}$ = 10.4 Hz, $J_{5a,4}$ = 4.9 Hz, H-5a), 3.95 (3H, m, H-4, H-4′, H-1a′), 3.85−3.76 (3H, m, H-5b, H-6′, H-1b′), 3.74 (2H, d, H_2-1), 3.69 (1H, dd, $J_{5',6'}$ = 7.8 Hz, $J_{5',4'}$ = 2.2 Hz, H-5′), 3.52 (2H, d, $J_{7',6'}$ = 5.4, H-7′). ^{13}C NMR δ 78.9 (C-3′), 77.8 (C-3), 76.8 (C-2), 70.8 (C-5′), 71.7 (C-6′), 70.1 (C-4), 69.2 (C-4′), 66.6 (C-2′), 63.6 (C-7′), 59.2 (C-5), 50.4 (C-1′), 47.9 (C-1). HRMS Calcd for $C_{12}H_{24}O_{12}NaS_2$ (M + Na) 447.0601, found 447.0589.

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Supporting Information Available: General experimental details, copies of ^{1}H and ^{13}C NMR spectra for all new compounds, and X-ray crystallographic (CIF) files for compounds **14b**, **21**, and **27**. This material is available free of charge via the Internet at http://pubs.acs.org.

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