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Synthesis of S-alkylated sulfonium-ions and their glucosidase inhibitory activities against recombinant human maltase glucoamylase

Sankar Mohan,[a] Lyann Sim,[b] David R. Rose[b] and B. Mario Pinto[a,*]

[a]*Department of Chemistry, Simon Fraser University, Burnaby, BC, Canada V5A 1S6*
[b]*Department of Medical Biophysics, University of Toronto and Division of Cancer Genomics and Proteomics, Ontario Cancer Institute, Toronto, Ont., Canada M5G 1L7*

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Abstract—The syntheses of nine S-alkylated, cyclic sulfonium-ions with varying alkyl chain lengths, as mimics of N-alkylated imino sugars, and their glucosidase inhibitory activities are described. The target compounds were synthesized by alkylation of 2,3,5-tri-*O*-benzyl-1,4-anhydro-4-thio-D-arabinitol at the ring sulfur atom using various alkyl halides, followed by deprotection using boron trichloride. Enzyme inhibitory assays against recombinant human maltase glucoamylase (MGA), a critical enzyme in the small intestine involved in the breakdown of glucose oligosaccharides into glucose itself, shows that they are effective inhibitors of MGA with K_i values ranging from 6 to 75 μM.

Keywords: Glucosidase inhibitors; Maltase glucoamylase; S-Alkylated sulfonium-ions; N-Alkylated imino sugars

1. Introduction

Over the past few decades, much research has focused on understanding the functions of glycosidase and glycosyltransferase enzymes due to their vital roles in living systems. Such functions can be revealed by modifying or blocking biological processes using specific inhibitors. Inhibitors of these two major classes of enzymes have many therapeutic applications as both the enzyme-catalyzed biosynthesis and hydrolysis of complex carbohydrates are biologically widespread processes in living systems.[1]

N-Alkylated imino sugars have been extensively studied in recent years due to their potential use as glycosidase inhibitors. A general observation is that N-alkylation increases the glycosidase inhibitory activity of the parent imino sugar.[2–4] For example, *N*-methyl- (**2**), *N*-butyl- (**3**), *N*-decyl- (**4**), and *N*-(7-oxadecyl)-1-deoxynojirimycin (**5**) are more potent inhibitors of porcine liver α-glucosidase I than the parent compound, 1-deoxynojirimycin (DNJ, **1**).[5] Although the exact role of the alkyl chain in increasing inhibition is not well understood, biochemical characterization of N-alkylated imino sugars indicated that the lipophilic alkyl chains play a role in the cellular uptake of the inhibitor.[6] In a recent study of the molecular requirements of these compounds for glycosidase inhibition, it was reported that the protonated imino sugar mimics the charge on the proposed oxacarbenium-ion transition state formed during hydrolysis of the natural substrate.[7] In addition, it has been proposed that the deprotonation of the imino sugars in the slightly basic pH (7.1) of the ER, resulting in a loss of cationic properties, could be one of the possible reasons for the much lower in vivo glycosidase activity exhibited by the *N*-butyl compound **3** than in the in vitro studies.[7] Hence, it would be of interest to design inhibitors that incorporate a permanent positive charge at a suitable position as possible substitutes for the N-alkylated imino sugars.

* Corresponding author. Tel.: +1 604 291 4152; fax: +1 604 291 4860; e-mail: bpinto@sfu.ca

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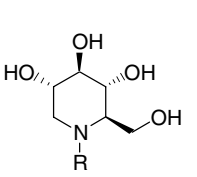
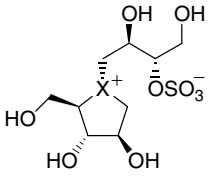
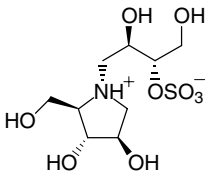


1 R=H
2 R=methyl
3 R=n-butyl
4 R=n-decyl
5 R=7-oxadecyl



6 X=S
7 X=Se



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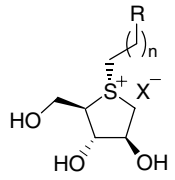
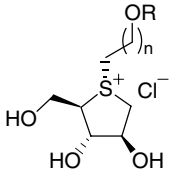
Our working hypothesis is to synthesize sulfonium-ions in order to increase the required electrostatic interactions between the inhibitor and an active-site carboxylate residue. Of relevance here, we[8,9] and others[10] have reported the synthesis of salacinol (**6**), a naturally occurring glucosidase inhibitor isolated from the roots of *Salacia reticulata*. Other structure–activity relationship studies of salacinol such as the syntheses and glycosidase inhibitory activities of selenium (**7**)[11–13] and nitrogen (**8**)[14] analogues of salacinol, and D-lyxitol and D-ribitol analogues of salacinol,[15] indicated that the D-arabinitol configuration in the heterocyclic ring displayed by salacinol (**6**) is critical for its activity. Hence, we have chosen the 1,4-anhydro-4-thio-D-arabinitol moiety as the sugar-based head group in the compounds of interest in the present study and now report the syntheses and glycosidase inhibitory properties of a series of S-alkylated sulfonium ions (**9**–**17**).



9 R=CH_3; X=OTf; n=12
10 R=CH_3; X=Cl; n=2
11 R=CH_3; X=Cl; n=4
12 R=CH_3; X=Cl; n=6
13 R=CH_3; X=Cl; n=12
14 R=CH_3; X=Cl; n=16
15 R=$CH(CH_3)_2$; X=Cl; n=1



16 R=CH_2CH_3; n=5
17 R=CH_3; n=8

It is worthy of note that the target compounds could also act as glucosyltransferase inhibitors by analogy with their N-alkylated imino sugar counterparts. Thus, *N*-butyl-1-deoxynojirimycin (**3**) was found to be not only an α-glucosidase I inhibitor but also a potent inhibitor of ceramide-specific glucosyltransferase, a key enzyme involved in the biosynthesis of glycosphingolipids.[7] Increases in alkyl chain lengths have led to increases in transferase inhibitory activities of these N-alkylated imino sugars, suggesting that a hydrophobic environment is part of substrate recognition. Since the glycosyl transfer is also believed to proceed through a transition-state with substantial oxacarbenium-ion character, by simple analogy with the well-studied mechanism of glycosidases,[16] our target compounds bearing a permanent positive charge on the sulfur atom could provide the necessary electrostatic interactions in the enzyme active site together with the attached lipophilic alkyl chains required for substrate recognition.

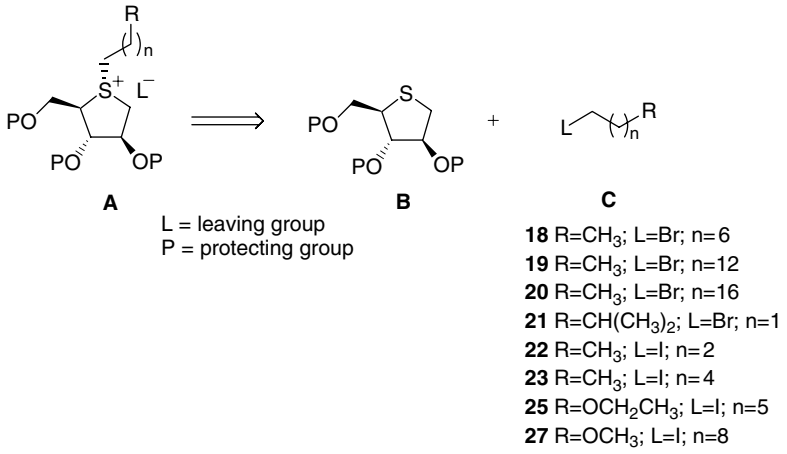
2. Results and discussion

Sulfonium ions **A** could be synthesized by alkylation of an appropriately protected anhydrothio-D-arabinitol **B** at the ring sulfur atom using alkylating agents (**18**–**23**, **25**, and **27**), corresponding to **C** (Scheme 1).

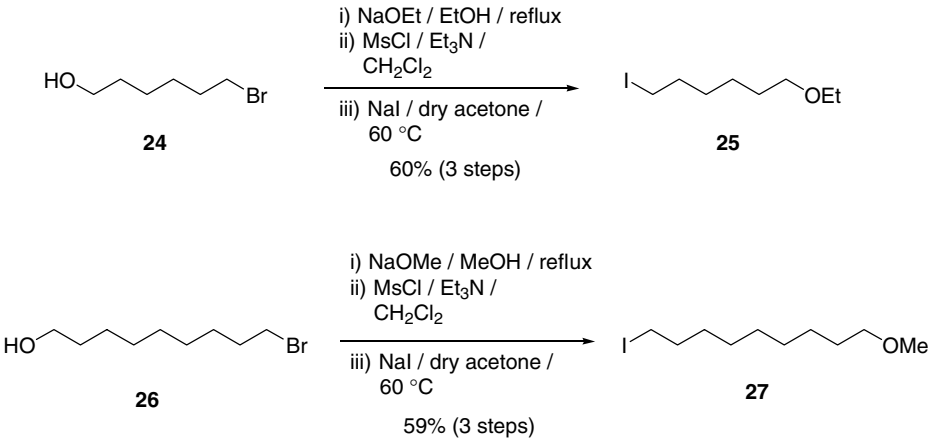
The required alkyl bromides **18**–**21** and alkyl iodides **22** and **23** were commercially available. Alkyl iodides **25** and **27** were synthesized in three steps starting from commercially available 6-bromohexan-1-ol (**24**) and 9-bromononan-1-ol (**26**), respectively, as shown in Scheme 2. Bromo alcohol **24** was treated with NaOEt in refluxing EtOH for 5 h to produce the ethoxy alcohol that was subsequently converted into the corresponding mesylate. The crude mesylate was then treated with NaI in dry acetone to produce the corresponding iodide **25** that was purified by chromatography and used immediately in the alkylation reaction. Similarly, iodide **27** was prepared from bromo alcohol **26**, except that NaOMe in refluxing MeOH was used in the first step (Scheme 2). The required 1,4-anhydro-2,3,5-tri-*O*-benzyl-4-thio-D-arabinitol (**28**), corresponding to **B**, was prepared from L-xylose, as described by Satoh et al.[17] for the synthesis of its enantiomer.

Initially, the S-alkylation of compound **28** with *n*-tetradecyl bromide **19** was examined in order to optimize the reaction conditions for the alkylation reaction. At first, the reaction was carried out at room temperature in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP), with **28** and **19** present in a 1:1 ratio. After 24 h of continuous stirring in a sealed tube at room temperature, there was no product formation observed, as indicated by TLC. Increasing the reaction temperature to 90 °C and stirring the reaction mixture for 24 h in a sealed tube resulted in 30% of the desired product **29** that was purified by column chromatography. As S-alkylated sulfonium ion **29** formed in this reaction was deemed to be unstable due to the ring opening reaction by the bromide counterion, after column chromatographic purification, product **29** was treated immediately with AgOTf (1 equiv) in CH_2Cl_2 to exchange the bromide counterion with triflate, resulting in the stable S-alkylated sulfonium ion **30** (Scheme 3).

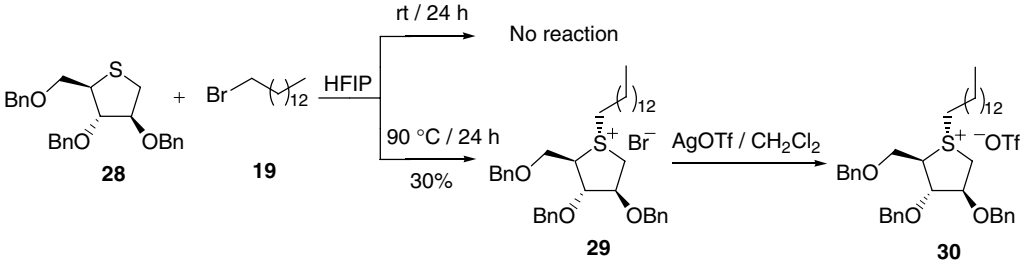
Attempts were made to improve the yield of this reaction by the addition of AgOTf (1 equiv with respect to alkyl bromide) initially to the reaction mixture in HFIP. Surprisingly, there was no product formation, and



Scheme 1.



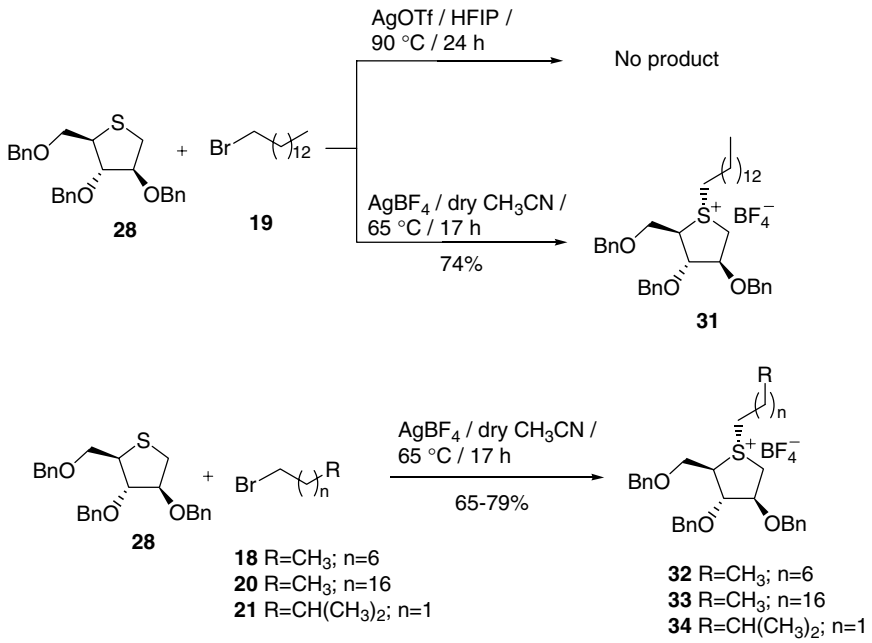
Scheme 2.



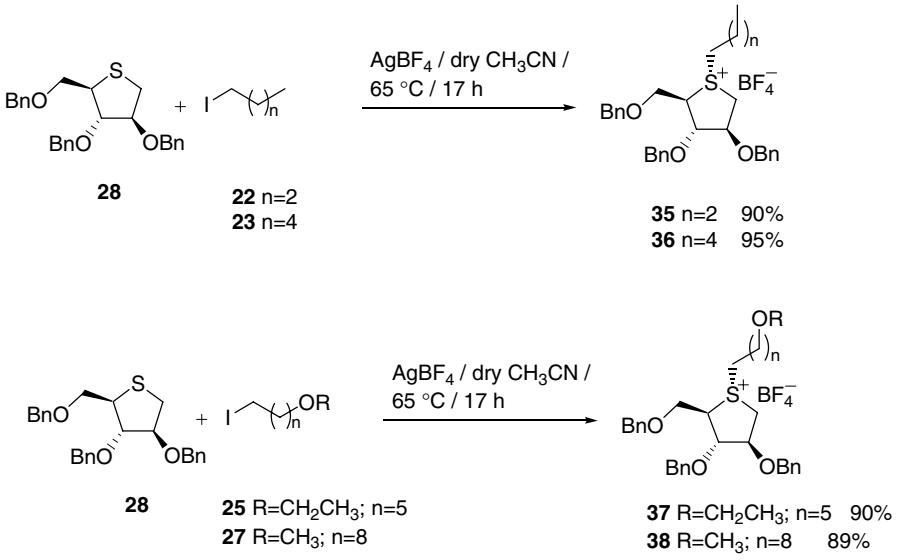
Scheme 3.

decomposition of the starting material **28** was observed after stirring at 90 °C for 24 h, as indicated by TLC. Based on a literature precedent,[18] the reaction was repeated with $AgBF_4$ (1 equiv with respect to alkyl bromide), instead of AgOTf, in refluxing CH_3CN; alkylated product **31** was obtained in 74% yield, with 15% of the unreacted starting material **28** being recovered. After optimizing the reaction conditions with compound **28** and bromide **19**, a series of S-alkylated sulfonium ions (**32**–**34**) were synthesized analogously in 65–79% yield using alkyl bromides **18**, **20**, and **21** (Scheme 4).

It was also observed that alkyl iodides **22** and **23** reacted with compound **28** smoothly to produce the corresponding S-alkylated sulfonium ions **35** and **36** in 90% and 95% yield, respectively. Similarly, sulfonium ions **37** and **38** with alkoxy substitutions at the end of the alkyl chain were synthesized in 90% and 89% yield, respectively, using the corresponding iodides **25** and **27** as the alkylating agents (Scheme 5).



Scheme 4.



Scheme 5.

The alkylation reactions proceeded stereoselectively and we did not observe (by TLC) the formation of the diastereomers at the stereogenic sulfur atom in any detectable amounts; the purified products were found to be only one isomer, as indicated by ^{1}H NMR spectroscopy. The absolute stereochemistry at the stereogenic sulfur center in **36** and **38** was established by means of 1D-NOESY experiments (Fig. 1). Correlation between H-1′ and H-4 and also a correlation between H-2′ and H-4 confirmed the *anti* relationship between the alkyl side chain and the C-4 substituent on the anhydroarabinitol moiety in both of these compounds (Fig. 1). The stereochemistry at the stereogenic sulfonium center in sulfonium ions **30**–**35** and **37** was also assigned to have an *anti* relationship between the alkyl side chain and the C-4 substituent on the anhydroarabinitol moiety, by analogy with compounds **36** and **38**, and based on our previous, extensive work with alkylation of anhydrothio-D-arabinitol derivatives.

Initial attempts to remove the benzyl protecting groups on the S-alkylated sulfonium ions using 10% Pd/C in MeOH and also in a 1:1 mixture of AcOH/MeOH were not successful. The benzyl groups of 2,3,5-tri-*O*-benzylsulfonium-ions (**30**–**38**) were therefore

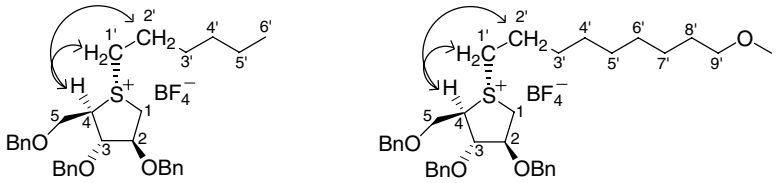
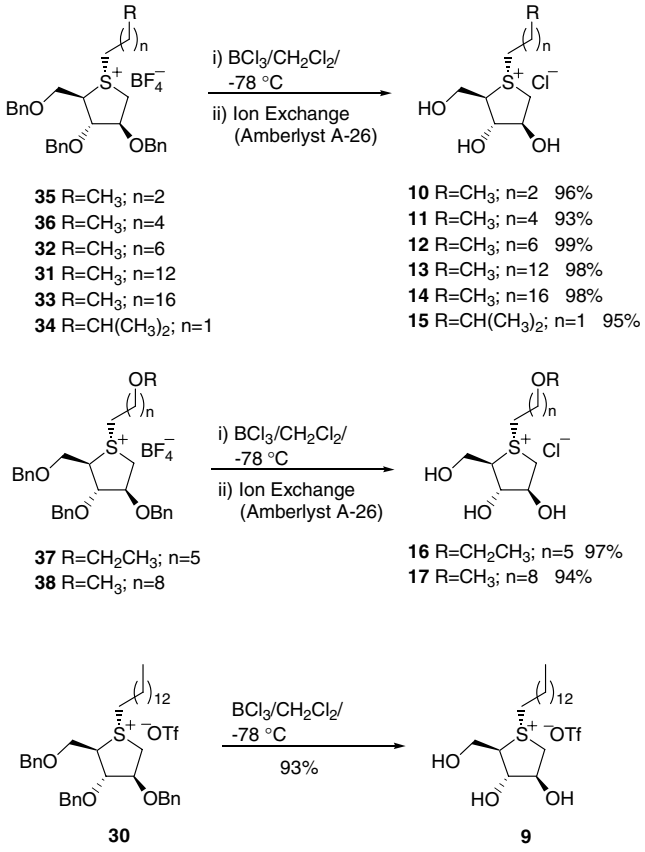


Figure 1. NOE correlations observed in the 1D-NOESY spectra of compounds **36** and **38**.

removed by treatment with boron trichloride at −78 °C in CH_2Cl_2. During the course of deprotection, some of the tetrafluoroborate counterion was exchanged with chloride ion. Similar results were also observed in previous work from our laboratory.[19] Hence, in the cases of sulfonium ions **31**–**38**, after removal of the benzyl groups, the products were subsequently treated with Amberlyst A-26 resin (chloride form) to completely exchange the tetrafluoroborate counterion with chloride ion to give compounds **10**–**17**, respectively (Scheme 6). In the case of compound **30**, the deprotected sulfonium ion **9** was obtained without any counterion exchange, probably due to the shorter reaction time.



Scheme 6.

Finally, we comment on the inhibitory properties of **9**–**17** against recombinant human maltase glucoamylase (MGA), a critical intestinal glucosidase involved in the breakdown of oligosaccharides of D-glucose into D-glucose itself. All of the synthesized compounds were inhibitors of MGA with K_i values ranging from 6 to 75 μM (Table 1). However, these compounds are less active

Table 1. Experimentally determined K_i values[a]

Inhibitor	Alkyl chain	K_i (μM)
9	Tetradecyl	10 ± 2
10	Butyl	32 ± 4
11	Hexyl	75 ± 13
12	Octyl	51 ± 8
13	Tetradecyl	6 ± 1
14	Octadecyl	19 ± 4
15	2-Methylbutyl	67 ± 11
16	1-Ethoxyhexyl	52 ± 9
17	1-Methoxynonyl	33 ± 2
Salacinol (**6**)	—	0.19 ± 0.02[b]

[a] Analysis of MGA inhibition was performed using *p*-nitrophenyl α-D-glucopyranoside as the substrate.
[b] Ref. 13.

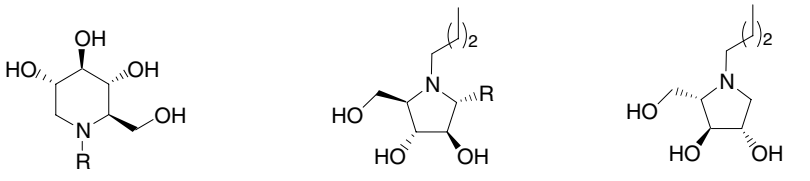


Figure 2. IC_{50} Values for various N-alkylated imino sugars against porcine liver α-glucosidase I.[7]

than salacinol which was previously shown to have a K_i value of 0.19 ± 0.02 μM against MGA.[13]

We also note that the K_i values for the sulfonium ions **9**–**17** against MGA are lower than the IC_{50} values previously reported for N-alkylated imino sugars **40**–**42** (Fig. 2) against porcine liver α-glucosidase I, but are greater than those for imino sugars **1**, **3**–**5**.[7]

3. Experimental

3.1. General methods

Optical rotations were measured at 23 °C and reported in deg dm^{-1} g^{-1} cm^3. ^1H and ^{13}C NMR spectra were recorded at frequencies of 500 and 125 MHz, respectively. All assignments were confirmed with the aid of two-dimensional ^1H, ^1H (gCOSY) and ^1H, ^{13}C (gHMQC) experiments using standard Varian pulse programs. Processing of the spectra was performed with MestRec software. 1D-NOESY experiments were recorded at 295 K on a 500 MHz spectrometer. For each 1D-NOESY spectrum, 512 or 256 scans were acquired with a Q3 Gaussian Cascade pulse. A mixing time of 500 ms or 800 ms was used in the 1D-NOESY experiments. Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectra were obtained on a PerSeptive Biosystems Voyager-DE spectrometer, using 2,5-dihydroxybenzoic acid as a matrix. The high-resolution mass spectrum was recorded in positive-mode with turbo-ion spray ionization on a Hybrid Quadrupole-TOF LC/MS/MS mass spectrometer. Analytical thin-layer chromatography (TLC) was performed on aluminum plates precoated with silica gel 60F-254 as the adsorbent. The developed plates were air-dried, exposed to UV light and/or sprayed with a solution containing 1% $Ce(SO_4)_2$ and 1.5% molybdic acid in 10% aqueous H_2SO_4, and heated. Column chromatography was performed with silica gel 60 (230–400 mesh).

3.1.1. Enzyme activity assay and enzyme kinetics. Kinetic parameters of MGA with compounds **9**–**17** were determined using the *p*-nitrophenyl-D-glucopyranoside (*p*NP-glucose, Sigma) 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, inhibitor (at three different concentrations), and *p*NP-glucose as substrate (2.5, 3.5, 5, 7.5, 15, and 30 mM), with a final volume of 50 μL. Reactions were incubated at 37 °C for 35 min and terminated by addition of 50 μL 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.

3.2. 1-Ethoxy-6-iodohexane (25)

A solution of 6-bromohexan-1-ol (**24**) (1 g, 5.5 mmol) was dissolved in EtOH (20 mL) and NaOEt (3.76 g, 55.2 mmol) was added. The reaction mixture was refluxed with vigorous stirring for 12 h. The reaction was monitored by TLC analysis of aliquots (30% EtOAc/hexanes). When the limiting reagents had been essentially consumed, the mixture was cooled and the solvent was evaporated to give a syrupy residue that was passed through a pad of silica to give the corresponding ethoxy alcohol (800 mg, crude) that was subsequently treated with MsCl (0.895 mL, 11.5 mmol) and Et_3N (1.98 mL, 14.3 mmol) in CH_2Cl_2 (30 mL) at 0 °C. After the consumption of starting material, as indicated by TLC after 7 h, the reaction mixture was diluted with CH_2Cl_2 (15 mL) and washed with water (2×10 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated to give the corresponding mesylate. The crude mesylate (800 mg) was dissolved in dry acetone (15 mL), and freshly fused NaI (1.6 g, 10.7 mmol) was added. The reaction mixture was heated at 55 °C for 6 h, cooled, and the solvents were removed by evaporation at atmospheric pressure (at 25 °C); the residue was then purified by chromatography to give the title compound as a colorless oil (850 mg, 60%); ^1H NMR ($CDCl_3$): δ 3.47 (q, 2H, $J = 7$ Hz, –OCH_2CH$_3$), 3.41 (t, 2H, $J_{1,2} = 7$ Hz, H-1), 3.19 (t, 2H, $J_{6,5} = 7$ Hz, H-6), 1.86–1.80 (m, 2H, H-5), 1.61–1.55 (m, 2H, H-2), 1.45–1.34 (m, 4H, H-3 and H-4), 1.20 (t, 3H, $J = 7$ Hz, –OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$): δ 70.4 (C-1), 66.1 (–O*C*H$_2$CH$_3$), 33.4 (C-5), 30.3, 29.6 (2C, C-2 and C-4), 25.2 (C-3), 15.2 (–OCH$_2$*C*H$_3$), 7.1 (C-6); Anal. Calcd for $C_8H_{17}IO$: C, 37.52; H, 6.69. Found: C, 37.75; H, 6.89.

3.3. 1-Iodo-9-methoxynonane (27)

A solution of 9-bromononan-1-ol (**26**) (1.1 g, 4.9 mmol) was dissolved in MeOH (20 mL) and NaOMe (2.66 g, 49.3 mmol) was added. The reaction mixture was refluxed with vigorous stirring for 12 h. The reaction was monitored by TLC analysis of aliquots (30% EtOAc/hexanes). When the limiting reagents had been essentially consumed, the mixture was cooled and the solvent was evaporated to give a syrupy residue that was passed through a pad of silica to give the corresponding methoxy alcohol (830 mg, crude) that was sub-

sequently treated with MsCl (0.775 mL, 10.0 mmol) and Et_3N (1.72 mL, 12.4 mmol) in CH_2Cl_2 (30 mL) at 0 °C. After the consumption of starting material, as indicated by TLC after 7 h, the reaction mixture was diluted with CH_2Cl_2 (15 mL) and washed with water (2 × 10 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated to give the corresponding mesylate. The crude mesylate (890 mg) was dissolved in dry acetone (15 mL), and freshly fused NaI (3.2 g, 21.2 mmol) was added. The reaction mixture was heated at 55 °C for 5 h, cooled, and the solvents were removed by evaporation at atmospheric pressure (at 25 °C); the residue was then purified by chromatography to give the title compound as a colorless oil (820 mg, 59%). This material was identical in all respects to that reported previously.[20] ^{1}H NMR ($CDCl_3$): δ 3.36 (t, 2H, $J_{9,8} = 7$ Hz, H-9), 3.33 (s, 3H, –OCH_3), 3.18 (t, 2H, $J_{1,2} = 7$ Hz, H-1), 1.84–1.78 (m, 2H, H-2), 1.59–1.53 (m, 2H, H-8), 1.41–1.25 (m, 10H, H-3–H-7); ^{13}C NMR ($CDCl_3$): δ 72.7 (C-9), 58.3 (–OCH_3), 33.4 (C-2), 30.3, 29.4 (2C, C-3 and C-8), 29.2, 29.1, 28.3 (3C, C-4, C-5 and C-6), 26.0 (C-7), 7.0 (C-1).

3.4. 2,3,5-Tri-*O*-benzyl-1,4-dideoxy-1,4-[(1-tetradecyl)-(*R*)-episulfoniumylidene]-D-arabinitol triflate (30)

A mixture of thioarabinitol **28** (500 mg, 1.19 mmol) and bromide **19** (0.357 mL, 1.31 mmol) in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP, 1 mL) was stirred and heated in a sealed tube at 90 °C for 24 h. The progress of the reaction was monitored by TLC analysis of aliquots ($CHCl_3$/MeOH, 10:1) that showed a 30% conversion of product. Further heating did not improve the conversion rate. Hence, the mixture was cooled and concentrated to give a syrupy residue. Purification by column chromatography (gradient of $CHCl_3$/MeOH, 10:1) gave the purified sulfonium ion **29** (235 mg, 47%, based on the isolation of 40% unreacted starting material **28**); treatment with silver triflate (86.6 mg, 0.337 mmol) in CH_2Cl_2 at ambient temperature for 5 h gave sulfonium ion **30** as a colorless syrup (240 mg, 93%): $[\alpha]_D$ +4.44 (*c* 0.2, MeOH); ^{1}H NMR ($CDCl_3$): δ 7.36–7.32 (m, 9H, Ar), 7.25–7.18 (m, 6H, Ar), 4.62 and 4.52 (2d, each 1H, $J_{a,b} = 11.9$ Hz, CH_2Ph), 4.61 and 4.43 (2d, each 1H, $J_{a,b} = 11.8$ Hz, CH_2Ph), 4.53 and 4.45 (2d, each 1H, $J_{a,b} = 11.7$ Hz, CH_2Ph), 4.53 (br s, 1H, H-2), 4.41 (d, 1H, $J_{1a,1b} = 12.9$ Hz, H-1a), 4.17 (br s, 1H, H-3), 3.81–3.76 (m, 2H, H-4 and H-5a), 3.74 (ddd, 1H, $J_{1'a,1'b} = 12.7$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.1$ Hz, H-1′a), 3.64 (dd, 1H, $J_{5b,4} = J_{5b,5a} = 12.1$ Hz, H-5b), 3.64 (dd, 1H, $J_{1b,1a} = 12.9$ Hz, $J_{1b,2} = 2.1$ Hz, H-1b), 3.30–3.24 (m, 1H, H-1′b), 1.78–1.72 (m, 2H, H-2′), 1.50–1.20 (m, 22H, H-3′–H-13′), 0.88 (dd, 3H, $J_{14',13'a} = J_{14',13'b} = 7$ Hz, H-14′); ^{13}C NMR ($CDCl_3$): δ 136.5, 135.9, 135.7 (3C_{ipso}), 128.9–127.9 (15C_{Ar}), 120.7 (q, 1C, $J_{C,F} = 319$ Hz, OTf), 83.1 (C-3), 81.7 (C-2), 73.8, 72.7, 71.9 (3CH_2Ph), 66.9 (C-5), 66.3 (C-4), 47.1 (C-1), 45.7 (C-1′), 31.9–22.7 (11C, C-3′–C-13′), 25.7 (C-2′), 14.1 (C-14′); MALDI-TOF MS: *m*/*z* 617.54 [M−OTf]$^+$. Anal. Calcd for $C_{41}H_{57}F_3O_6S_2$: C, 64.20; H, 7.49. Found: C, 63.91; H, 7.58.

3.5. General procedure for the preparation of sulfonium ions 31–38

To a mixture of thioarabinitol **28** and the alkyl halide (**18**–**23**, **25** or **27**) in dry CH_3CN was added $AgBF_4$ (1 equiv with respect to alkyl halide), and the stirred reaction mixture was heated at 65 °C for 17 h. The progress of the reaction was monitored by TLC analysis of aliquots ($CHCl_3$/MeOH, 10:1). When the limiting reagent had been essentially consumed, the mixture was cooled and concentrated to give a syrupy residue. Purification by column chromatography (gradient of $CHCl_3$/MeOH, 10:1) gave the purified sulfonium ions **31**–**38**.

3.5.1. 2,3,5-Tri-*O*-benzyl-1,4-dideoxy-1,4-[(1-tetradecyl)-(*R*)-episulfoniumylidene]-D-arabinitol tetrafluoroborate (31). The reaction of thioarabinitol **28** (300 mg, 0.71 mmol) with bromide **19** (0.195 mL, 0.79 mmol) and $AgBF_4$ (154 mg, 0.79 mmol) in dry CH_3CN (8 mL) gave compound **31** as a colorless syrup (370 mg, 74%): $[\alpha]_D$ +8.11 (*c* 0.4, MeOH); ^{1}H NMR ($CDCl_3$): δ 7.37–7.32 (m, 9H, Ar), 7.25–7.18 (m, 6H, Ar), 4.62 and 4.50 (2d, each 1H, $J_{a,b} = 11.9$ Hz, CH_2Ph), 4.61 and 4.43 (2d, each 1H, $J_{a,b} = 11.8$ Hz, CH_2Ph), 4.54 and 4.48 (2d, each 1H, $J_{a,b} = 11.7$ Hz, CH_2Ph), 4.54 (br s, 1H, H-2), 4.37 (d, 1H, $J_{1a,1b} = 13.2$ Hz, H-1a), 4.15 (br s, 1H, H-3), 3.78–3.75 (m, 2H, H-4 and H-5a), 3.68 (ddd, 1H, $J_{1'a,1'b} = 13.1$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.2$ Hz, H-1′a), 3.64 (dd, 1H, $J_{5b,4} = J_{5b,5a} = 11.9$ Hz, H-5b), 3.64 (dd, 1H, $J_{1b,1a} = 13.2$ Hz, $J_{1b,2} = 3.1$ Hz, H-1b), 3.28–3.22 (m, 1H, H-1′b), 1.78–1.72 (m, 2H, H-2′), 1.50–1.20 (m, 22H, H-3′–H-13′), 0.88 (dd, 3H, $J_{14',13'a} = J_{14',13'b} = 6.8$ Hz, H-14′); ^{13}C NMR ($CDCl_3$): δ 136.6, 136, 135.8 (3C_{ipso}), 128.8–127.8 (15C_{Ar}), 82.8 (C-3), 81.8 (C-2), 73.7, 72.6, 71.9 (3CH_2Ph), 66.9 (C-5), 66.6 (C-4), 46.8 (C-1), 45.4 (C-1′), 31.9–22.7 (11C, C-3′–C-13′), 25.7 (C-2′), 14.1 (C-14′); MALDI-TOF MS: *m*/*z* 617.86 [M−BF_4]$^+$. Anal. Calcd for $C_{40}H_{57}BF_4O_3S$: C, 68.17; H, 8.15. Found: C, 68.14; H, 8.29.

3.5.2. 2,3,5-Tri-*O*-benzyl-1,4-dideoxy-1,4-[(1-octyl)-(*R*)-episulfoniumylidene]-D-arabinitol tetrafluoroborate (32). The reaction of thioarabinitol **28** (500 mg, 1.19 mmol) with bromide **18** (253 mg, 1.31 mmol) and $AgBF_4$ (255 mg, 1.31 mmol) in dry CH_3CN (12 mL) gave compound **32** as a colorless syrup (590 mg, 79%): $[\alpha]_D$ +8.16 (*c* 0.5, MeOH); ^{1}H NMR ($CDCl_3$): δ 7.36–7.31 (m, 9H, Ar), 7.25–7.18 (m, 6H, Ar), 4.64 and 4.52 (2d, each 1H,

$J_{a,b} = 11.9$ Hz, CH_2Ph), 4.60 and 4.45 (2d, each 1H, $J_{a,b} = 11.8$ Hz, CH_2Ph), 4.53 and 4.48 (2d, each 1H, $J_{a,b} = 11.7$ Hz, CH_2Ph), 4.58 (br s, 1H, H-2), 4.32 (d, 1H, $J_{1a,1b} = 13.2$ Hz, H-1a), 4.18 (br s, 1H, H-3), 3.82–3.77 (m, 2H, H-4 and H-5a), 3.65 (dd, 1H, $J_{5b,4} = J_{5b,5a} = 11.4$ Hz, H-5b), 3.64 (dd, 1H, $J_{1b,1a} = 13.2$ Hz, $J_{1b,2} = 3.7$ Hz, H-1b), 3.64 (ddd, 1H, $J_{1'a,1'b} = 13.1$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 7.5$ Hz, H-1′a), 3.28–3.21 (m, 1H, H-1′b), 1.78–1.71 (m, 2H, H-2′), 1.50–1.19 (m, 10H, H-3′–H-7′), 0.87 (dd, 3H, $J_{8',7'a} = J_{8',7'b} = 7$ Hz, H-8′); ^{13}C NMR ($CDCl_3$): δ 136.6, 136.1, 135.9 (3C_{ipso}), 128.8–127.9 (15C_{Ar}), 82.8 (C-3), 81.9 (C-2), 73.7, 72.6, 71.9 (3*C*H_2Ph), 66.9 (C-5), 66.7 (C-4), 46.8 (C-1), 45.4 (C-1′), 31.6–22.5 (5C, C-3′–C-7′), 25.6 (C-2′), 14.0 (C-8′); MALDI-TOF MS: *m*/*z* 532.95 $[M-BF_4]^+$. Anal. Calcd for $C_{34}H_{45}BF_4O_3S$: C, 65.80; H, 7.31. Found: C, 65.92; H, 7.26.

3.5.3. 2,3,5-Tri-*O*-benzyl-1,4-dideoxy-1,4-[(1-octadecyl)-(*R*)-episulfoniumylidene]-D-arabinitol tetrafluoroborate (33). The reaction of thioarabinitol **28** (500 mg, 1.19 mmol) with bromide **20** (436 mg, 1.31 mmol) and $AgBF_4$ (255 mg, 1.31 mmol) in dry CH_3CN (12 mL) gave compound **33** as a colorless syrup (465 mg, 73%, based on the isolation of 30% unreacted starting material **28**): $[\alpha]_D$ +6.67 (*c* 0.3, MeOH); ^{1}H NMR ($CDCl_3$): δ 7.37–7.29 (m, 9H, Ar), 7.25–7.18 (m, 6H, Ar), 4.63 and 4.52 (2d, each 1H, $J_{a,b} = 11.9$ Hz, CH_2Ph), 4.60 and 4.44 (2d, each 1H, $J_{a,b} = 11.8$ Hz, CH_2Ph), 4.58 (br s, 1H, H-2), 4.53 and 4.48 (2d, each 1H, $J_{a,b} = 11.7$ Hz, CH_2Ph), 4.32 (d, 1H, $J_{1a,1b} = 13.2$ Hz, H-1a), 4.18 (br s, 1H, H-3), 3.81–3.78 (m, 2H, H-4 and H-5a), 3.67–3.62 (m, 1H, H-1′a), 3.64 (dd, 1H, $J_{5b,5a} = J_{5b,4} = 11.0$ Hz, H-5b), 3.64 (dd, 1H, $J_{1b,1a} = 13.2$ Hz, $J_{1b,2} = 3.6$ Hz, H-1b), 3.28–3.20 (m, 1H, H-1′b), 1.77–1.71 (m, 2H, H-2′), 1.50–1.20 (m, 30H, H-3′–H-17′), 0.88 (dd, 3H, $J_{18',17'a} = J_{18',17'b} = 6.8$ Hz, H-18′); ^{13}C NMR (CD_3Cl_3): δ 136.6, 136.1, 135.9 (3C_{ipso}), 128.8–127.8 (15C_{Ar}), 82.8 (C-3), 82.0 (C-2), 73.6, 72.6, 71.8 (3*C*H_2Ph), 66.9 (C-5), 66.7 (C-4), 46.8 (C-1), 45.3 (C-1′), 31.9–22.6 (15C, C-3′–C-17′), 25.6 (C-2′), 14.1 (C-18′); MALDI-TOF MS: *m*/*z* 673.57 $[M-BF_4]^+$. Anal. Calcd for $C_{44}H_{65}BF_4O_3S$: C, 69.46; H, 8.61. Found: C, 69.64; H, 8.53.

3.5.4. 2,3,5-Tri-*O*-benzyl-1,4-dideoxy-1,4-[[1-(3-methyl)-butyl]-(*R*)-episulfoniumylidene]-D-arabinitol tetrafluoroborate (34). The reaction of thioarabinitol **28** (580 mg, 1.38 mmol) with bromide **21** (0.182 mL, 1.52 mmol) and $AgBF_4$ (296 mg, 1.52 mmol) in dry CH_3CN (14 mL) gave compound **34** as a colorless syrup (518 mg, 65%): $[\alpha]_D$ +6.67 (*c* 0.5, MeOH); ^{1}H NMR ($CDCl_3$): δ 7.37–7.29 (m, 9H, Ar), 7.25–7.18 (m, 6H, Ar), 4.62 and 4.50 (2d, each 1H, $J_{a,b} = 11.9$ Hz, CH_2Ph), 4.61 and 4.44 (2d, each 1H, $J_{a,b} = 11.8$ Hz, CH_2Ph), 4.54 and 4.49 (2d, each 1H, $J_{a,b} = 11.7$ Hz, CH_2Ph), 4.54 (br s, 1H, H-2), 4.38 (d, 1H, $J_{1a,1b} = 13.1$ Hz, H-1a), 4.15 (br s, 1H, H-3), 3.78 (dd, 1H, $J_{4,5a} = 5$ Hz, $J_{4,5b} = 11.5$ Hz, H-4), 3.78 (dd, 1H, $J_{5a,4} = 5$ Hz, $J_{5a,5b} = 11.5$ Hz, H-5a), 3.70 (ddd, 1H, $J_{1'a,1'b} = 12.5$ Hz, $J_{1'a,2'a} = 10.5$ Hz, $J_{1'a,2'b} = 6.5$ Hz, H-1′a), 3.64 (dd, 1H, $J_{5b,4} = J_{5b,5a} = 11.5$ Hz, H-5b), 3.64 (dd, 1H, $J_{1b,1a} = 13.2$ Hz, $J_{1b,2} = 3.5$ Hz, H-1b), 3.24 (ddd, 1H, $J_{1'b,1'a} = 12.5$ Hz, $J_{1'b,2'a} = 9.5$ Hz, $J_{1'b,2'b} = 5$ Hz, H-1′b), 1.75–1.55 (m, 3H, H-2′ and H-3′), 0.91 and 0.87 (2d, each 3H, $J_{4',3'} = J_{5',3'} = 6.5$ Hz, H-4′ and H-5′); ^{13}C NMR ($CDCl_3$): δ 136.6, 136.1, 135.9 (3C_{ipso}), 128.8–127.9 (15C_{Ar}), 82.8 (C-3), 82.0 (C-2), 73.6, 72.6, 71.8 (3*C*H_2Ph), 66.9 (C-5), 66.6 (C-4), 46.8 (C-1), 43.5 (C-1′), 33.9 (C-2′), 27.1 (C-3′), 21.9, 21.5 (2C, C-4′ and C-5′); MALDI-TOF MS: *m*/*z* 491.18 $[M-BF_4]^+$. Anal. Calcd for $C_{31}H_{39}BF_4O_3S$: C, 64.36; H, 6.79. Found: C, 64.39; H, 6.99.

3.5.5. 2,3,5-Tri-*O*-benzyl-1,4-dideoxy-1,4-[(1-butyl)-(*R*)-episulfoniumylidene]-D-arabinitol tetrafluoroborate (35). The reaction of thioarabinitol **28** (500 mg, 1.19 mmol) with iodide **22** (0.162 mL, 1.43 mmol) and $AgBF_4$ (276 mg, 1.43 mmol) in dry CH_3CN (14 mL) gave compound **35** as a colorless syrup (600 mg, 90%): $[\alpha]_D$ +4.12 (*c* 0.5, MeOH); ^{1}H NMR ($CDCl_3$): δ 7.35–7.30 (m, 9H, Ar), 7.25–7.18 (m, 6H, Ar), 4.64 and 4.55 (2d, each 1H, $J_{a,b} = 11.9$ Hz, CH_2Ph), 4.58 and 4.45 (2d, each 1H, $J_{a,b} = 11.8$ Hz, CH_2Ph), 4.52 and 4.49 (2d, each 1H, $J_{a,b} = 11.8$ Hz, CH_2Ph), 4.57 (d, 1H, $J_{2,1b} = 2.6$ Hz, H-2), 4.27 (d, 1H, $J_{1a,1b} = 13.1$ Hz, H-1a), 4.24 (br s, 1H, H-3), 3.83 (dd, 1H, $J_{4,5a} = 5$ Hz, $J_{4,5b} = 11.3$ Hz, H-4), 3.83 (dd, 1H, $J_{5a,4} = 5$ Hz, $J_{5a,5\,b} = 11.3$ Hz, H-5a), 3.65 (dd, 1H, $J_{5b,4} = J_{5b,5a} = 11.3$ Hz, H-5b), 3.62 (dd, 1H, $J_{1b,1a} = 13.1$ Hz, $J_{1b,2} = 2.7$ Hz, H-1b), 3.62 (ddd, 1H, $J_{1'a,1'b} = 13.0$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 7.5$ Hz, H-1′a), 3.27–3.21 (m, 1H, H-1′b), 1.78–1.70 (m, 2H, H-2′), 1.49–1.39 (m, 2H, H-3′), 0.85 (dd, 3H, $J_{4',3'a} = J_{4',3'b} = 7.5$ Hz, H-4′); ^{13}C NMR ($CDCl_3$): δ 136.7, 136.2, 135.9 (3C_{ipso}), 128.7–127.8 (15C_{Ar}), 82.7 (C-3), 82.1 (C-2), 73.6, 72.5, 71.8 (3*C*H_2Ph), 66.8 (C-5), 66.6 (C-4), 46.7 (C-1), 45.1 (C-1′), 27.4 (C-2′), 21.1 (C-3′), 13.1 (C-4′); MALDI-TOF MS: *m*/*z* 477.33 $[M-BF_4]^+$. Anal. Calcd for $C_{30}H_{37}BF_4O_3S$: C, 63.83; H, 6.61. Found: C, 63.50; H, 6.57.

3.5.6. 2,3,5-Tri-*O*-benzyl-1,4-dideoxy-1,4-[(1-hexyl)-(*R*)-episulfoniumylidene]-D-arabinitol tetrafluoroborate (36). The reaction of thioarabinitol **28** (610 mg, 1.45 mmol) with iodide **23** (0.211 mL, 1.43 mmol) and $AgBF_4$ (276 mg, 1.43 mmol) in dry CH_3CN (14 mL) gave compound **36** as a colorless syrup (810 mg, 95%): $[\alpha]_D$ +4.00 (*c* 0.8, MeOH); ^{1}H NMR (CD_3OD): δ 7.37–7.24 (m, 15H, Ar), 4.65 and 4.62 (2d, each 1H, $J_{a,b} = 11.7$ Hz, CH_2Ph), 4.64 (br s, 1H, H-2), 4.56 and 4.47 (2d, each 1H, $J_{a,b} = 11.6$ Hz, CH_2Ph), 4.54 and 4.50 (2d, each 1H, $J_{a,b} = 11.7$ Hz, CH_2Ph), 4.39 (br s, 1H, H-3), 4.13

(dd, 1H, $J_{4,5a} = 5$ Hz, $J_{4,5b} = 11.0$ Hz, H-4), 4.04 (d, 1H, $J_{1a,1b} = 12.5$ Hz, H-1a), 3.88 (dd, 1H, $J_{5a,4} = 5$ Hz, $J_{5a,5b} = 10.5$ Hz, H-5a), 3.67 (dd, 1H, $J_{1b,1a} = 12.5$ Hz, $J_{1b,2} = 3$ Hz, H-1b), 3.64 (dd, 1H, $J_{5b,5a} = 10.5$ Hz, $J_{5b,4} = 11.0$ Hz, H-5b), 3.41 (ddd, 1H, $J_{1'a,1'b} = 12.5$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.0$ Hz, H-1′a), 3.31 (ddd, 1H, $J_{1'b,1'a} = 12.5$ Hz, $J_{1'b,2'a} = 5.5$ Hz, $J_{1'b,2'b} = 8.5$ Hz, H-1′b), 1.82–1.68 (m, 2H, H-2′), 1.43–1.40 (m, 2H, H-3′), 1.21–1.18 (m, 4H, H-4′ and H-5′), 0.85 (dd, 3H, $J_{6',5'a} = J_{6',5'b} = 7.0$ Hz, H-6′); ^{13}C NMR (CD_3OD): δ 138.5, 138.3, 138.0 ($3C_{ipso}$), 129.8–129.2 ($15C_{Ar}$), 84.3 (C-3), 84.2 (C-2), 74.6, 73.6, 73.1 ($3CH_2Ph$), 68.2 (C-5), 67.7 (C-4), 47.9 (C-1), 46.7 (C-1′), 32.2, 23.4 (C-4′ and C-5′), 28.8 (C-3′), 26.7 (C-2′), 14.3 (C-6′); MALDI-TOF MS: m/z 505.34 $[M-BF_4]^+$. Anal. Calcd for $C_{32}H_{41}BF_4O_3S$: C, 64.86; H, 6.97. Found: C, 64.78; H, 7.10.

3.5.7. 2,3,5-Tri-*O*-benzyl-1,4-dideoxy-1,4-[[1-(6-ethoxy)-hexyl]-(*R*)-episulfoniumylidene]-D-arabinitol tetrafluoroborate (37). The reaction of thioarabinitol **28** (500 mg, 1.19 mmol) with iodide **25** (363 mg, 1.42 mmol) and $AgBF_4$ (276 mg, 1.43 mmol) in dry CH_3CN (14 mL) gave compound **37** as a colorless syrup (680 mg, 90%): $[\alpha]_D$ +8.1 (*c* 0.6, MeOH); ^{1}H NMR ($CDCl_3$): δ 7.38–7.33 (m, 9H, Ar), 7.25–7.18 (m, 6H, Ar), 4.61 and 4.50 (2d, each 1H, $J_{a,b} = 11.9$ Hz, CH_2Ph), 4.60 and 4.43 (2d, each 1H, $J_{a,b} = 11.8$ Hz, CH_2Ph), 4.54 and 4.48 (2d, each 1H, $J_{a,b} = 11.7$ Hz, CH_2Ph), 4.54 (br s, 1H, H-2), 4.37 (d, 1H, $J_{1a,1b} = 13.2$ Hz, H-1a), 4.14 (br s, 1H, H-3), 3.79–3.74 (m, 2H, H-4 and H-5a), 3.70 (ddd, 1H, $J_{1'a,1'b} = 12.5$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.0$ Hz, H-1′a), 3.63 (dd, 1H, $J_{5b,4} = J_{5b,5a} = 12.5$ Hz, H-5b), 3.63 (dd, 1H, $J_{1b,1a} = 13.2$ Hz, $J_{1b,2} = 3.0$ Hz, H-1b), 3.45 (q, 2H, $J = 7$ Hz, $-OCH_2CH_3$), 3.36 (dd, 2H, $J_{6',5'a} = J_{6',5'b} = 6.5$ Hz, H-6′), 3.29–3.23 (m, 1H, H-1′b), 1.80–1.74 (m, 2H, H-2′), 1.53–1.40 (m, 4H, H-3′ and H-5′), 1.39–1.27 (m, 2H, H-4′), 1.18 (t, 3H, $J = 7$ Hz, $-OCH_2CH_3$); ^{13}C NMR ($CDCl_3$): δ 136.6, 136.1, 135.9 ($3C_{ipso}$), 128.8–127.9 ($15C_{Ar}$), 82.7 (C-3), 82.0 (C-2), 73.6, 72.6, 71.8 ($3CH_2Ph$), 70.1 (C-6′), 66.8 (C-5), 66.7 (C-4), 66.0 ($-OCH_2CH_3$), 46.8 (C-1), 45.2 (C-1′), 29.2 (C-5′), 27.7 (C-3′), 25.5 (C-2′), 25.4 (C-4′), 15.2 ($-OCH_2CH_3$); MALDI-TOF MS: m/z 549.49 $[M-BF_4]^+$. Anal. Calcd for $C_{34}H_{45}BF_4O_4S$: C, 64.15; H, 7.13. Found: C, 64.36; H, 7.33.

3.5.8. 2,3,5-Tri-*O*-benzyl-1,4-dideoxy-1,4-[[1-(9-methoxy)-nonyl]-(*R*)-episulfoniumylidene]-D-arabinitol tetrafluoroborate (38). The reaction of thioarabinitol **28** (740 mg, 1.76 mmol) with iodide **27** (600 mg, 2.11 mmol) and $AgBF_4$ (411 mg, 2.11 mmol) in dry CH_3CN (12 mL) gave compound **38** as a colorless syrup (1.05 g, 89%): $[\alpha]_D$ +7.30 (*c* 0.3, MeOH); ^{1}H NMR ($CDCl_3$): δ 7.37–7.33 (m, 9H, Ar), 7.25–7.18 (m, 6H, Ar), 4.61 and 4.50 (2d, each 1H, $J_{a,b} = 12.0$ Hz, CH_2Ph), 4.60 and 4.43 (2d, each 1H, $J_{a,b} = 11.8$ Hz, CH_2Ph), 4.54 and 4.48 (2d, each 1H, $J_{a,b} = 11.5$ Hz, CH_2Ph), 4.54 (br s, 1H, H-2), 4.37 (d, 1H, $J_{1a,1b} = 13.0$ Hz, H-1a), 4.14 (br s, 1H, H-3), 3.80–3.75 (m, 2H, H-4 and H-5a), 3.68 (ddd, 1H, $J_{1'a,1'b} = 13.0$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.0$ Hz, H-1′a), 3.64 (dd, 1H, $J_{5b,4} = J_{5b,5a} = 12.0$ Hz, H-5b), 3.64 (dd, 1H, $J_{1b,1a} = 13.0$ Hz, $J_{1b,2} = 2.8$ Hz, H-1b), 3.36 (dd, 2H, $J_{9',8'a} = J_{9',8'b} = 6.8$ Hz, H-9′), 3.33 (s, 3H, $-OCH_3$), 3.28–3.23 (m, 1H, H-1′b), 1.78–1.72 (m, 2H, H-2′), 1.56–1.52 (m, 2H, H-8′), 1.49–1.37 (m, 2H, H-3′), 1.34–1.18 (m, 8H, H-4′, H-5′, H-6′ and H-7′); ^{13}C NMR ($CDCl_3$): δ 136.6, 136.1, 135.9 ($3C_{ipso}$), 128.8–127.9 ($15C_{Ar}$), 82.8 (C-3), 81.9 (C-2), 73.6, 72.6, 71.8 ($3CH_2Ph$), 72.8 (C-9′), 66.8 (C-5), 66.7 (C-4), 58.5 ($-OCH_3$), 46.7 (C-1), 45.3 (C-1′), 29.5 (C-8′), 29.2, 29.1, 28.7, 26.0 (4C, C-4′–C-7′), 27.9 (C-3′), 25.6 (C-2′); MALDI-TOF MS: m/z 577.04 $[M-BF_4]^+$. Anal. Calcd for $C_{36}H_{49}BF_4O_4S$: C, 65.06; H, 7.43. Found: C, 65.13; H, 7.53.

3.6. 1,4-Dideoxy-1,4-[(1-tetradecyl)-(*R*)-episulfoniumylidene]-D-arabinitol triflate (9)

BCl_3 gas was bubbled vigorously through a solution of sulfonium ion **30** (200 mg, 0.26 mmol) in CH_2Cl_2 (5 mL) at −78 °C under N_2 atmosphere for 5 min. The mixture was stirred at −78 °C for 1.5 h and a stream of dry air was blown vigorously over the solution to remove excess BCl_3. The reaction was quenched with MeOH (3 mL), and the solvents were removed. The residue was co-evaporated with MeOH (2 × 4 mL) to give final product **9**, as a colorless, amorphous solid (120 mg, 93%): mp 69–71 °C; $[\alpha]_D$ +19.5 (*c* 0.2, MeOH); ^{1}H NMR (CD_3OD): δ 4.60 (br s, 1H, H-2), 4.31 (d, 1H, $J_{3,2} = 1.5$ Hz, H-3), 4.03–4.0 (m, 1H, H-5a), 3.86–3.80 (m, 2H, H-4 and H-5b), 3.81 (d, 1H, $J_{1a,1b} = 12.5$ Hz, H-1a), 3.70 (dd, 1H, $J_{1b,1a} = 12.5$ Hz, $J_{1b,2} = 3$ Hz, H-1b), 3.50 (ddd, 1H, $J_{1'a,1'b} = 12.5$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.0$ Hz, H-1′a), 3.40 (ddd, 1H, $J_{1'b,1'a} = 12.5$ Hz, $J_{1'b,2'a} = 8.5$ Hz, $J_{1'b,2'b} = 5.5$ Hz, H-1′b), 1.91–1.80 (m, 2H, H-2′), 1.55–1.42 (m, 2H, H-3′), 1.41–1.22 (m, 20H, H-4′–H-13′), 0.87 (dd, 3H, $J_{14',13'a} = J_{14',13'b} = 7.0$ Hz, H-14′); ^{13}C NMR (CD_3OD): δ 121.8 (q, 1C, $J_{C,F} = 316.3$ Hz, OTf), 79.6 (C-3), 79.5 (C-2), 73.6 (C-4), 61.0 (C-5), 50.1 (C-1), 46.7 (C-1′), 33.1–23.8 (10C, C-4′–C-13′), 29.2 (C-3′), 26.8 (C-2′), 14.5 (C-14′); MALDI-TOF MS: m/z 347.25 $[M-OTf]^+$. Anal. Calcd for $C_{20}H_{39}F_3O_6S_2$: C, 48.37; H, 7.92. Found: C, 47.97; H, 7.77.

3.7. General procedure for the deprotection of the S-alkylated sulfonium ions (31–38)

BCl_3 gas was bubbled vigorously through a solution of sulfonium ion (**31**–**38**) in CH_2Cl_2 at −78 °C under N_2 atmosphere for 10 min. The mixture was stirred at

−78 °C for 2 h and a stream of dry air was blown vigorously over the solution to remove excess BCl_3. The reaction was quenched with MeOH (3–4 mL), and the solvents were removed. The residue was co-evaporated with MeOH (2 × 4 mL) to give the deprotected products, which were subsequently dissolved in MeOH and a freshly washed ion-exchange resin Amberlyst A-26 (chloride form) was added. The mixture was stirred at room temperature for 2 h and filtered. The filtrate was concentrated to give final products **10**–**17**.

3.7.1. 1,4-Dideoxy-1,4-[(1-butyl)-(*R*)-episulfoniumylidene]-D-arabinitol chloride (10). Treatment of sulfonium ion **35** (560 mg, 0.99 mmol) with BCl_3 in CH_2Cl_2 (12 mL), followed by treatment with Amberlyst A-26 resin (250 mg) gave final product **10** as a colorless syrup (230 mg, 96%): $[\alpha]_D$ +21.05 (*c* 0.2, MeOH); ^{1}H NMR (CD_3OD): δ 4.62 (br s, 1H, H-2), 4.33 (br s, 1H, H-3), 4.10–4.0 (m, 1H, H-5a), 3.90–3.83 (m, 2H, H-4 and H-5b), 3.84 (d, 1H, $J_{1a,1b} = 12.5$ Hz, H-1a), 3.71 (dd, 1H, $J_{1b,1a} = 12.5$ Hz, $J_{1b,2} = 3.0$ Hz, H-1b), 3.50 (ddd, 1H, $J_{1'a,1'b} = 12.5$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.0$ Hz, H-1′a), 3.42 (ddd, 1H, $J_{1'b,1'a} = 12.5$ Hz, $J_{1'b,2'a} = 8.5$ Hz, $J_{1'b,2'b} = 6.2$ Hz, H-1′b), 1.90–1.80 (m, 2H, H-2′), 1.60–1.48 (m, 2H, H-3′), 1.0 (dd, 3H, $J_{4',3'a} = J_{4',3'b} = 7.0$ Hz, H-4′); ^{13}C NMR (CD_3OD): δ 79.6 (C-3), 79.4 (C-2), 73.6 (C-4), 61.0 (C-5), 50.2 (C-1), 46.4 (C-1′), 28.7 (C-2′), 22.5 (C-3′), 13.7 (C-4′); MALDI-TOF MS: *m*/*z* 207.36 $[M-Cl]^+$. Anal. Calcd for $C_9H_{19}ClO_3S$: C, 44.53; H, 7.89. Found: C, 44.28; H, 8.11.

3.7.2. 1,4-Dideoxy-1,4-[(1-hexyl)-(*R*)-episulfoniumylidene]-D-arabinitol chloride (11). Treatment of sulfonium ion **36** (425 mg, 0.72 mmol) with BCl_3 in CH_2Cl_2 (9 mL), followed by treatment with Amberlyst A-26 resin (200 mg), gave final product **11** as a colorless syrup (180 mg, 93%): $[\alpha]_D$ +19.05 (*c* 0.3, MeOH); ^{1}H NMR (CD_3OD): δ 4.59 (br s, 1H, H-2), 4.31 (d, 1H, $J_{3,2} = 1.5$ Hz, H-3), 4.03–3.97 (m, 1H, H-5a), 3.86–3.80 (m, 2H, H-4 and H-5b), 3.82 (d, 1H, $J_{1a,1b} = 12.0$ Hz, H-1a), 3.68 (dd, 1H, $J_{1b,1a} = 12.0$ Hz, $J_{1b,2} = 3.5$ Hz, H-1b), 3.48 (ddd, 1H, $J_{1'a,1'b} = 12.5$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.0$ Hz, H-1′a), 3.40 (ddd, 1H, $J_{1'b,1'a} = 12.5$ Hz, $J_{1'b,2'a} = 8.5$ Hz, $J_{1'b,2'b} = 6.0$ Hz, H-1′b), 1.91–1.78 (m, 2H, H-2′), 1.55–1.42 (m, 2H, H-3′), 1.39–1.32 (m, 4H, H-4′ and H-5′), 0.90 (dd, 3H, $J_{6',5'a} = J_{6',5'b} = 7.5$ Hz, H-6′); ^{13}C NMR (CD_3OD): δ 79.6 (C-3), 79.4 (C-2), 73.6 (C-4), 61.0 (C-5), 50.2 (C-1), 46.7 (C-1′), 32.3 (1C, C-4′ or C-5′), 28.9 (C-3′), 26.8 (C-2′), 23.5 (1C, C-4′ or C-5′), 14.3 (C-6′); MALDI-TOF MS: *m*/*z* 235.21 $[M-Cl]^+$. Anal. Calcd for $C_{11}H_{23}ClO_3S$: C, 48.78; H, 8.56. Found: C, 48.50; H, 8.76.

3.7.3. 1,4-Dideoxy-1,4-[(1-octyl)-(*R*)-episulfoniumylidene]-D-arabinitol chloride (12). Treatment of sulfonium ion **32** (500 mg, 0.81 mmol) with BCl_3 in CH_2Cl_2 (10 mL), followed by treatment with Amberlyst A-26 resin (250 mg), gave final product **12** as a colorless syrup (238 mg, 99%): $[\alpha]_D$ +22.22 (*c* 0.3, MeOH); ^{1}H NMR (CD_3OD): δ 4.62 (br s, 1H, H-2), 4.34 (br s, 1H, H-3), 4.06–4.01 (m, 1H, H-5a), 3.89–3.83 (m, 2H, H-4 and H-5b), 3.85 (d, 1H, $J_{1a,1b} = 12.5$ Hz, H-1a), 3.71 (dd, 1H, $J_{1b,1a} = 12.5$ Hz, $J_{1b,2} = 2.5$ Hz, H-1b), 3.50 (ddd, 1H, $J_{1'a,1'b} = 12.5$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.0$ Hz, H-1′a), 3.43 (ddd, 1H, $J_{1'b,1'a} = 12.5$ Hz, $J_{1'b,2'a} = 8.0$ Hz, $J_{1'b,2'b} = 6.0$ Hz, H-1′b), 1.91–1.83 (m, 2H, H-2′), 1.56–1.49 (m, 2H, H-3′), 1.46–1.32 (m, 8H, H-4′ – H-7′) 0.90 (dd, 3H, $J_{8',7'a} = J_{8',7'b} = 6.0$ Hz, H-8′); ^{13}C NMR (CD_3OD): δ 79.6 (C-3), 79.4 (C-2), 73.6 (C-4), 61.0 (C-5), 50.1 (C-1), 46.7 (C-1′), 32.9, 30.1, 30.0 and 23.7 (4C, C-4′–C-7′), 29.2 (C-3′), 26.8 (C-2′), 14.5 (C-8′); MALDI-TOF MS: *m*/*z* 263.33 $[M-Cl]^+$. Anal. Calcd for $C_{13}H_{27}ClO_3S$: C, 52.24; H, 9.11. Found: C, 52.55; H, 8.89.

3.7.4. 1,4-Dideoxy-1,4-[(1-tetradecyl)-(*R*)-episulfoniumylidene]-D-arabinitol chloride (13). Treatment of sulfonium ion **31** (200 mg, 0.28 mmol) with BCl_3 in CH_2Cl_2 (5 mL), followed by treatment with Amberlyst A-26 resin (150 mg), gave final product **13** as a colorless, amorphous solid (120 mg, 98%): mp 86–88 °C; $[\alpha]_D$ +10.87 (*c* 0.2, MeOH); ^{1}H NMR (CD_3OD): δ 4.62 (br s, 1H, H-2), 4.34 (br s, 1H, H-3), 4.10–4.0 (m, 1H, H-5a), 3.90–3.83 (m, 2H, H-4 and H-5b), 3.84 (d, 1H, $J_{1a,1b} = 12.5$ Hz, H-1a), 3.71 (dd, 1H, $J_{1b,1a} = 12.5$ Hz, $J_{1b,2} = 3$ Hz, H-1b), 3.50 (ddd, 1H, $J_{1'a,1'b} = 12.5$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.0$ Hz, H-1′a), 3.42 (ddd, 1H, $J_{1'b,1'a} = 12.5$ Hz, $J_{1'b,2'a} = 8.5$ Hz, $J_{1'b,2'b} = 5.5$ Hz, H-1′b), 1.91–1.81 (m, 2H, H-2′), 1.58–1.45 (m, 2H, H-3′), 1.43–1.28 (m, 20H, H-4′–H-13′), 0.89 (dd, 3H, $J_{14',13'a} = J_{14',13'b} = 7.0$ Hz, H-14′); ^{13}C NMR (CD_3OD): δ 79.6 (C-3), 79.3 (C-2), 73.6 (C-4), 61.0 (C-5), 50.1 (C-1), 46.7 (C-1′), 33.1–23.8 (10C, C-4′–C-13′), 29.2 (C-3′), 26.8 (C-2′), 14.5 (C-14′); MALDI-TOF MS: *m*/*z* 347.12 $[M-Cl]^+$. Anal. Calcd for $C_{19}H_{39}ClO_3S$: C, 59.58; H, 10.26. Found: C, 59.26; H, 10.33.

3.7.5. 1,4-Dideoxy-1,4-[(1-octadecyl)-(*R*)-episulfoniumylidene]-D-arabinitol chloride (14). Treatment of sulfonium ion **33** (450 mg, 0.59 mmol) with BCl_3 in CH_2Cl_2 (10 mL), followed by treatment with Amberlyst A-26 resin (280 mg), gave final product **14** as a colorless amorphous solid (256 mg, 98%): mp 95–97 °C; $[\alpha]_D$ +12.92 (*c* 0.5, MeOH); ^{1}H NMR (CD_3OD): δ 4.61 (br s, 1H, H-2), 4.33 (br s, 1H, H-3), 4.05–3.99 (m, 1H, H-5a), 3.88–3.82 (m, 2H, H-4 and H-5b), 3.83 (d, 1H, $J_{1a,1b} = 12.5$ Hz, H-1a), 3.70 (dd, 1H, $J_{1b,1a} = 12.5$ Hz, $J_{1b,2} = 3.2$ Hz, H-1b), 3.49 (ddd, 1H, $J_{1'a,1'b} = 12.5$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.0$ Hz, H-1′a), 3.41 (ddd, 1H, $J_{1'b,1'a} = 12.5$ Hz, $J_{1'b,2'a} = 8.5$ Hz, $J_{1'b,2'b} = 6.0$ Hz, H-1′b), 1.92–1.81 (m, 2H, H-2′), 1.56–1.42 (m, 2H, H-3′), 1.41–1.27 (m, 28H, H-4′–H-17′), 0.88 (dd, 3H, $J_{18',17'a} = J_{18',17'b} =$

7.0 Hz, H-18′); ^{13}C NMR (CD_3OD): δ 79.6 (C-3), 79.4 (C-2), 73.6 (C-4), 61.0 (C-5), 50.2 (C-1), 46.7 (C-1′), 33.1-23.8 (14C, C-4′–C-17′), 29.3 (C-3′), 26.8 (C-2′), 14.5 (C-18′); MALDI-TOF MS: m/z 403.47 $[M-Cl]^+$. Anal. Calcd for $C_{23}H_{47}ClO_3S$: C, 62.91; H, 10.79. Found: C, 62.57; H, 10.41.

3.7.6. 1,4-Dideoxy-1,4-[[1-(3-methyl)-butyl]-(*R*)-episulfoniumylidene]-D-arabinitol chloride (15). Treatment of sulfonium ion **34** (340 mg, 0.59 mmol) with BCl_3 in CH_2Cl_2 (8 mL), followed by treatment with Amberlyst A-26 resin (160 mg), gave final product **15** as a colorless syrup (144 mg, 95%): $[\alpha]_D$ +21.15 (*c* 0.4, MeOH); ^{1}H NMR (CD_3OD): δ 4.59 (br s, 1H, H-2), 4.31 (d, 1H, $J_{3,2} = 2.0$ Hz, H-3), 4.03–3.97 (m, 1H, H-5a), 3.85–3.80 (m, 2H, H-4 and H-5b), 3.81 (d, 1H, $J_{1a,1b} = 12.0$ Hz, H-1a), 3.67 (dd, 1H, $J_{1b,1a} = 12.0$ Hz, $J_{1b,2} = 3.0$ Hz, H-1b), 3.49 (ddd, 1H, $J_{1'a,1'b} = 12.5$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.0$ Hz, H-1′a), 3.38 (ddd, 1H, $J_{1'b,1'a} = 12.5$ Hz, $J_{1'b,2'a} = J_{1'b,2'b} = 7.5$ Hz, H-1′b), 1.79–1.70 (m, 3H, H-2′ and H-3′), 0.96 (2d, each 3H, $J_{4',3'} = J_{5',3'} = 6.5$ Hz, H-4′ and H-5′); ^{13}C NMR (CD_3OD): δ 79.6 (C-3), 79.4 (C-2), 73.6 (C-4), 61.0 (C-5), 50.2 (C-1), 44.8 (C-1′), 35.3 (C-2′), 28.6 (C-3′), 22.5, 22.2 (2C, C-4′ and C-5′); MALDI-TOF MS: m/z 221.14 $[M-Cl]^+$. Anal. Calcd for $C_{10}H_{21}ClO_3S$: C, 46.77; H, 8.24. Found: C, 46.43; H, 8.09.

3.7.7. 1,4-Dideoxy-1,4-[[1-(6-ethoxy)-hexyl]-(*R*)-episulfoniumylidene]-D-arabinitol chloride (16). Treatment of sulfonium ion **37** (230 mg, 0.36 mmol) with BCl_3 in CH_2Cl_2 (7 mL), followed by treatment with Amberlyst A-26 resin (150 mg), gave final product **16** as a colorless syrup (110 mg, 97%): $[\alpha]_D$ +18.56 (*c* 0.3, MeOH); ^{1}H NMR (CD_3OD): δ 4.59 (br s, 1H, H-2), 4.30 (d, 1H, $J_{3,2} = 2.0$ Hz, H-3), 4.03–3.97 (m, 1H, H-5a), 3.85–3.80 (m, 2H, H-4 and H-5b), 3.81 (d, 1H, $J_{1a,1b} = 12.5$ Hz, H-1a), 3.68 (dd, 1H, $J_{1b,1a} = 12.5$ Hz, $J_{1b,2} = 3.2$ Hz, H-1b), 3.47 (ddd, 1H, $J_{1'a,1'b} = 12.5$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.0$ Hz, H-1′a), 3.44 (q, 2H, $J = 7.0$ Hz, –OCH_2CH$_3$), 3.41 (dd, 2H, $J_{6',5'a} = J_{6',5'b} = 6.5$ Hz, H-6′), 3.40 (ddd, 1H, $J_{1'b,1'a} = 12.5$ Hz, $J_{1'b,2'a} = 8.5$ Hz, $J_{1'b,2'b} = 6.0$ Hz, H-1′b), 1.91–1.79 (m, 2H, H-2′), 1.59–1.52 (m, 2H, H-5′), 1.52–1.47 (m, 2H, H-3′), 1.44–1.39 (m, 2H, H-4′), 1.14 (t, 3H, $J = 7.0$ Hz, –OCH$_2$CH_3); ^{13}C NMR (CD_3OD): δ 79.6 (C-3), 79.5 (C-2), 73.7 (C-4), 71.5 (C-6′), 67.3 (1C, –OCH$_2$CH$_3$), 61.0 (C-5), 50.1 (C-1), 46.6 (C-1′), 30.4 (C-5′), 29.0 (C-3′), 26.8 (C-2′), 26.7 (C-4′), 15.5 (1C, –OCH$_2$$CH_3$); MALDI-TOF MS: m/z 279.20 $[M-Cl]^+$. HRMS Calcd for $C_{13}H_{27}ClO_4S$: 279.1630 $[M-Cl]^+$. Found: 279.1629.

3.7.8. 1,4-Dideoxy-1,4-[[1-(9-methoxy)-nonyl]-(*R*)-episulfoniumylidene]-D-arabinitol chloride (17). Treatment of sulfonium ion **38** (248 mg, 0.37 mmol) with BCl_3 in CH_2Cl_2 (7 mL), followed by treatment with Amberlyst A-26 resin (150 mg), gave final product **17** as a colorless syrup (120 mg, 94%): $[\alpha]_D$ +20.34 (*c* 0.5, MeOH); ^{1}H NMR (CD_3OD): δ 4.59 (br s, 1H, H-2), 4.31 (d, 1H, $J_{3,2} = 2.0$ Hz, H-3), 4.03–3.97 (m, 1H, H-5a), 3.86–3.80 (m, 2H, H-4 and H-5b), 3.82 (d, 1H, $J_{1a,1b} = 12.5$ Hz, H-1a), 3.68 (dd, 1H, $J_{1b,1a} = 12.0$ Hz, $J_{1b,2} = 3.0$ Hz, H-1b), 3.48 (ddd, 1H, $J_{1'a,1'b} = 12.5$ Hz, $J_{1'a,2'a} = J_{1'a,2'b} = 8.0$ Hz, H-1′a), 3.40 (ddd, 1H, $J_{1'b,1'a} = 12.5$ Hz, $J_{1'b,2'a} = 8.5$ Hz, $J_{1'b,2'b} = 5.5$ Hz, H-1′b), 3.35 (dd, 2H, $J_{9',8'a} = J_{9',8'b} = 6.5$ Hz, H-9′), 3.33 (s, 3H, –OCH_3), 1.91–1.78 (m, 2H, H-2′), 1.53–1.47 (m, 4H, H3′ and H-8′), 1.37–1.31 (m, 8H, H-4′–H-7′); ^{13}C NMR (CD_3OD): δ 79.6 (C-3), 79.4 (C-2), 73.9 (C-9′), 73.5 (C-4), 61.0 (C-5), 58.8 (1C, –OCH$_3$), 50.2 (C-1), 46.7 (C-1′), 30.6, 30.4, 30.3, 30.0, 29.2, 27.1 (6C, C-3′–C-8′), 26.8 (C-2′); MALDI-TOF MS: m/z 307.30 $[M-Cl]^+$. Anal. Calcd for $C_{15}H_{31}ClO_4S$: C, 52.54; H, 9.11. Found: C, 52.75; H, 9.07.

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