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Highly Diastereoselective Route to α-Glucosidase Inhibitors, Neosalacinol and Neoponkoranol

Genzoh Tanabe,[†] Youya Matsuda,[†] Misato Oka,[†] Yousuke Kunikata,[†] Nozomi Tsutsui,[†] Weija Xie,[§] Gorre Balakishan,[∥] Mumen F. A. Amer,[⊥] Shinsuke Marumoto,[‡] and Osamu Muraoka*[,†]

[†]Faculty of Pharmacy, [‡]Joint Research Center, Kindai University, 3-4-1 Kowakae, Higashi-osaka, Osaka 577-8502, Japan

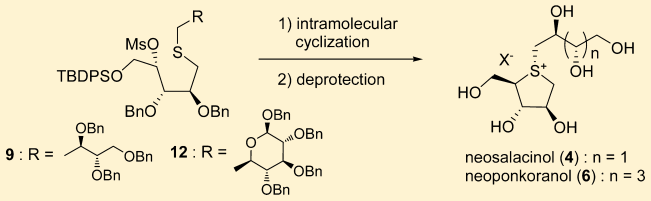
[§]State Key Laboratory of Natural Medicines and Department of Medicinal Chemistry, China Pharmaceutical University, Nanjing 210009, P. R. China

[∥]Department of Organic Chemistry, Telangana University, Nizamabad 503322, Telangana State, India

[⊥]Faculty of Pharmacy, Applied Science Private University, Al Arab St 21, Amman 11931, Jordan

Supporting Information

ABSTRACT: A facile and highly diastereoselective route to potent natural α-glucosidase inhibitors, i.e., neosalacinol (**4**) and neoponkoranol (**6**), isolated from the traditional Ayurvedic medicine "*Salacia*" was developed by intramolecular cyclization of appropriately substituted sulfides (**9** and **12**).



In the late 1990s, Muraoka et al. isolated a highly potent α-glucosidase inhibitor called salacinol (**1**) from *Salacia reticulata* roots and stems, which have traditionally been used in Ayurveda for the treatment of diabetes. The α-glucosidase inhibitory activity of **1** was revealed to be as potent as that of voglibose and acarbose, which are used clinically worldwide.[1] The structure of **1** revealed by X-ray analysis is unique; the sulfonium cation and sulfonate anion yield an inner salt to compose a spirobicyclic structure as shown in Figure 1.[1] After the isolation of **1**, the related sulfonium sulfonates, i.e., kotalanol[2] (**2**) and ponkoranol[3] (**3**), and their desulfonated analogues, i.e., neosalacinol[4] (**4**), neokotalanol[5] (**5**), and neoponkoranol[6] (**6**), were subsequently isolated from plants of the same genus and identified as compounds responsible for the antidiabetic activity, composing a new class of α-glucosidase inhibitors. Human clinical trials with the extract of *Salacia reticulata* on patients with type-2 diabetes have shown its effective treatment with minimal side effects.[7] These inhibitors (**1**–**6**) have attracted much attention owing to their high inhibitory activity and intriguing structure, and intensive structure–activity relationship (SAR) studies,[8] including their total syntheses,[9] have been conducted. In 2010, the crystal structure of a complex of salacinol (**1**) with the human *N*-terminal catalytic domain of maltase-glucoamylase was revealed by Pinto and co-workers,[8d] and thereafter, several inhibitors with measurably better activities have been developed with the aid of *in silico* drug design.[8c]

These SAR studies employed a common approach to construct the sulfonium structure: the intermolecular *S*-alkylation of thiosugar (**8**) with cyclic sulfates (**A**) for sulfonates (**1**, **2**, **3**) or with epoxides (**B**) for their desulfonates (**4**, **5**, **6**), respectively, as shown in Scheme 1.

Although these routes are general and applicable to the syntheses of a wide range of sulfoniums required for the SAR study, they suffer from disadvantages in some instances as follows: (1) *S*-alkylation with cyclic sulfates (**A**) often requires a long reaction period (~7 days or more) with low yield; (2) a coexisting acid HA as the catalyst in the process **B** causes partial decomposition of reactants epoxides or products; and (3) poor diastereoselectivity in both processes.[8,9] Thus, an alternative route leading to compounds that are inefficiently synthesized via the above route is required. In this paper, we have developed a facile and efficient alternative route to neosalacinol (**4**) by employing an intramolecular *S*-alkylation of an appropriate disulfide. The reaction proceeded with high diastereoselectivity to give the target sulfonium (**4**) in good overall yield. Application of the protocol to another neo-type inhibitor called neoponkoranol (**6**) successfully gave the desired inhibitor also in good yield.

The retrosynthetic routes to neosalacinol (**4**) and neoponkoranol (**6**) via intramolecular *S*-alkylation are provided in Scheme 2. The reactant (**9**) for the synthesis of **4** was prepared as follows. According to the literature,[8f] D-xylose was first converted to tosylate (**14**), which was treated with BnBr in the presence of NaH to give the corresponding benzyl ether (**15**) in 95% yield. After the replacement of the TsO moiety of **15** by AcSK, the resultant thioester (**16**) was reduced with $LiAlH_4$ to give the thiol (**10**) in good yield. The thiol (**10**) was then subjected to a coupling reaction with epoxide[10] (**11**), giving the corresponding sulfide (**17**) in 90% yield. Acidic hydrolysis of the acetal moiety of **17**, followed by the $NaBH_4$ reduction of the hemiacetal (**18**), gave a tetraol (**19**) in 52% yield from **17**.

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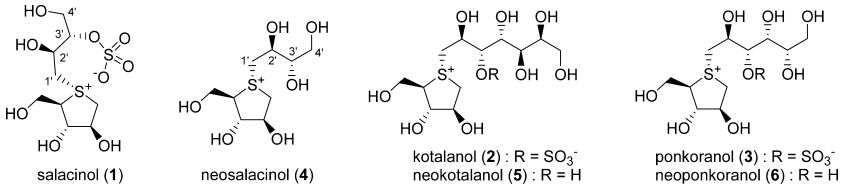
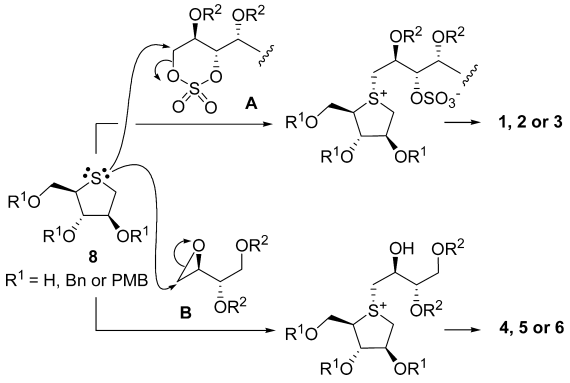


Figure 1. A new class of natural α-glucosidase inhibitors.

Scheme 1. Conventional Routes to Sulfonium Salts



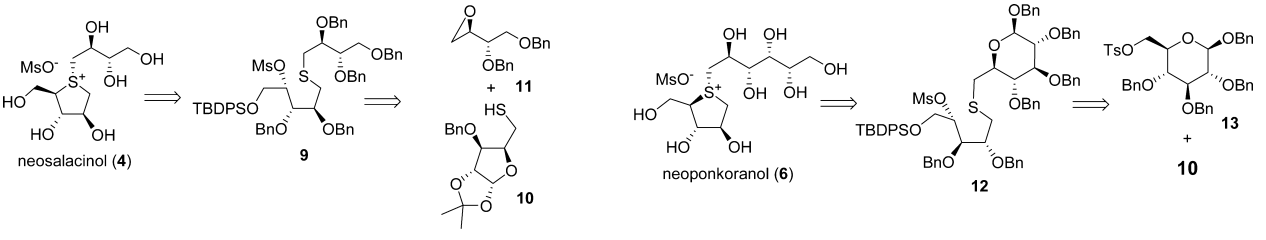
Selective protection of the 1,2-glycol moiety of the tetraol (**19**) with 2,2-DMP gave **20** in 62% yield. Protection of the remaining two secondary hydroxyls in **20** with BnBr led to the corresponding benzyl ether (**21**). Then, the 1,3-dioxolane moiety of **21** was removed by acid hydrolysis to give 1,2-glycol (**22**). Selective protection of the primary hydroxyl of **22** with TBDPSCl, followed by the mesylation of the resultant alcohol (**23**), furnished **9** in good yield. Gradual transformation of **9** into sulfonium salt (**24**) was observed; therefore, **9** was subjected to the next reaction immediately after purification. Finally, heating the sulfide (**9**) in EtOH under reflux for 3 h gave the desired sulfonium salt (**24**) in 90% yield with an excellent diastereo ratio (α/β = ~23/1). The ratio was determined on the basis of ^{1}H NMR specroscopic measurement with respect to the integration of the *tert*-butyl moiety of the TBDPS group of the products (***α*-24**: δ_H 1.00, ***β*-24**: δ_H 0.97). The major isomer ***α*-24** was successfully separated from the β-isomer ***β*-24** by silica gel column chromatography. The positive FAB-MS spectrum run in the negative mode showed peaks at m/z 943 corresponding to the sulfonium cation structure $[M - CH_3SO_3]^+$. The relative stereochemistry of the side chain of ***α*-24** was confirmed to be in an anti-relationship to the $TBDPSOCH_2$ moiety at C-4 by nuclear Overhauser effect spectroscopy. Finally, the simultaneous deprotection of Bn and TBDPS moieties of ***α*-24** under acidic hydrogenolysis conditions successfully gave the target neosalacinol (**4**, X = CH_3SO_3) in 90% yield. By the ion-exchange reaction of **4** (X = CH_3SO_3) with IRA-400J (Cl^- form), **4** (X = CH_3SO_3) was converted to the known sulfonium salt[8e,9h] (**4**, X = Cl) (Scheme 3), the physical and spectroscopic properties of which were consistent with those of an authentic specimen obtained via an alternative route[8e,9h] (Scheme 3).

The protocol was then applied to the synthesis of neoponkoranol (**6**) (Scheme 4). The sulfide (**12**) for cyclization was synthesized as follows. Tosylate (**25**), prepared starting from D-glucose according to the literature,[11] was coupled with **10** in the presence of NaOH to give the corresponding sulfide (**26**) in 97% yield. The acetal moiety of the sulfide (**26**) was selectively hydrolyzed with TFA, and the resultant hemiacetal was subsequently reduced with $NaBH_4$ to give the triol (**27**) in 87% overall yield from the sulfide (**26**). Selective protection of the 1,2-glycol moiety of **27** with 2,2-DMP, followed by the protection of the remaining secondary hydroxyl in **28** with BnBr, led to **29** in good yield. After the 1,3-dioxolane moiety of **29** was selectively hydrolyzed by TFA, the resultant 1,2-glycol (**30**) was treated with TBDPSCl to give the corresponding silyl ether (**31**) in 87% yield. Finally, the mesylation of **31** furnished the key sulfide (**12**) in 92% yield.

Compound **12** was then heated in EtOH under reflux. The reaction proceeded with high diastereoselectivity to give ***α*-32** in good yield (94%, dr, α/β = ~20/1). After the benzyl moieties of ***α*-32** were removed by hydrogenolysis on Pd–C at 60 °C in a mixture of aqueous TFA and 1,4-dioxane, MsO^- of the resultant sulfonium salt (**33**) was exchanged with Cl^- by IRA-400J (Cl^- form) to give an ~1:1 mixture of hemiacetal (**34**), which was finally reduced with $NaBH_4$ to give neoponkoranol (**6**) in 52% yield. Physical and spectroscopic properties of the product (**6**) were consistent with those of an authentic specimen obtained via an alternative route[6] (Scheme 4).

In summary, a new and highly diastereoselective route to neosalacinol (**4**), a potent α-glucosidase inhibitor isolated from the traditional Ayurvedic medicine "*Salacia*", has been developed. The process was successfully applied to the synthesis of neoponkoranol (**6**) and would be applicable to other "neo-types" of these characteristic cyclic sulfoniums. The present protocol consists of generally used practical transformations, avoiding disadvantages, i.e., poor diastereoselectivity or long reaction period, encountered in some instances via

Scheme 2. Retrosynthesis of 4 and 6 via Intramolecular Cyclization



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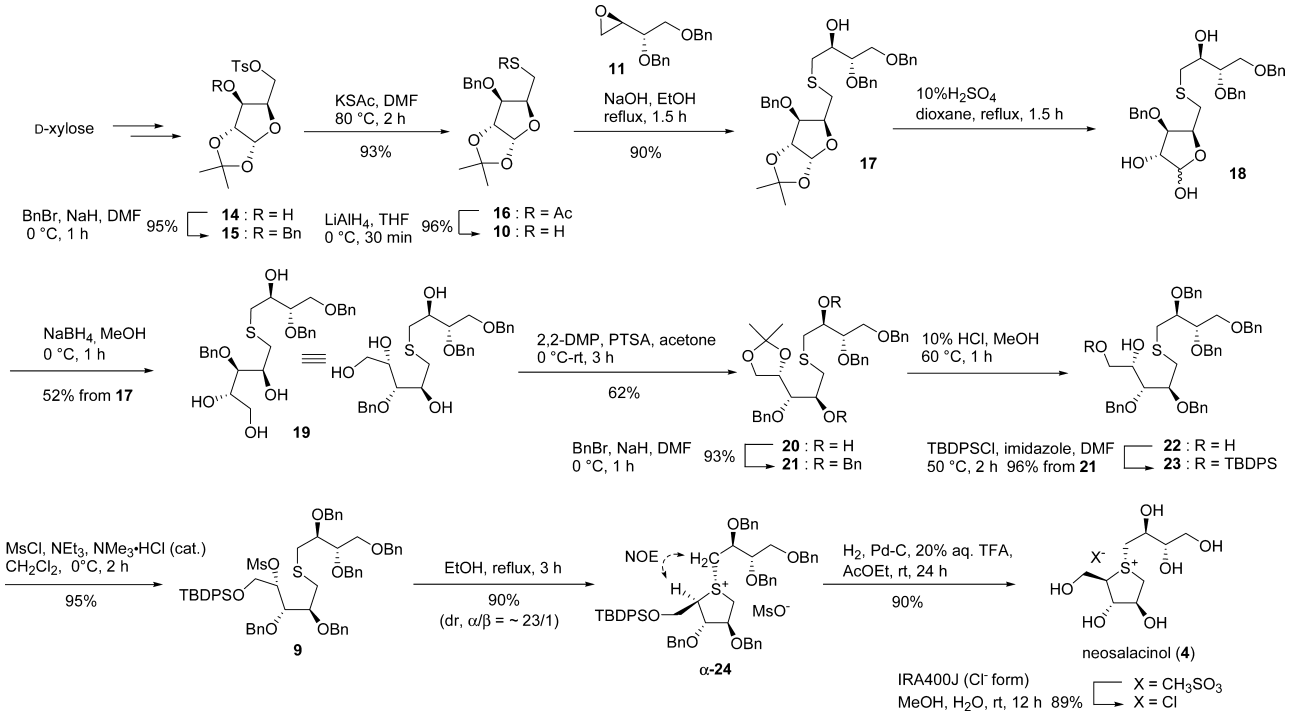
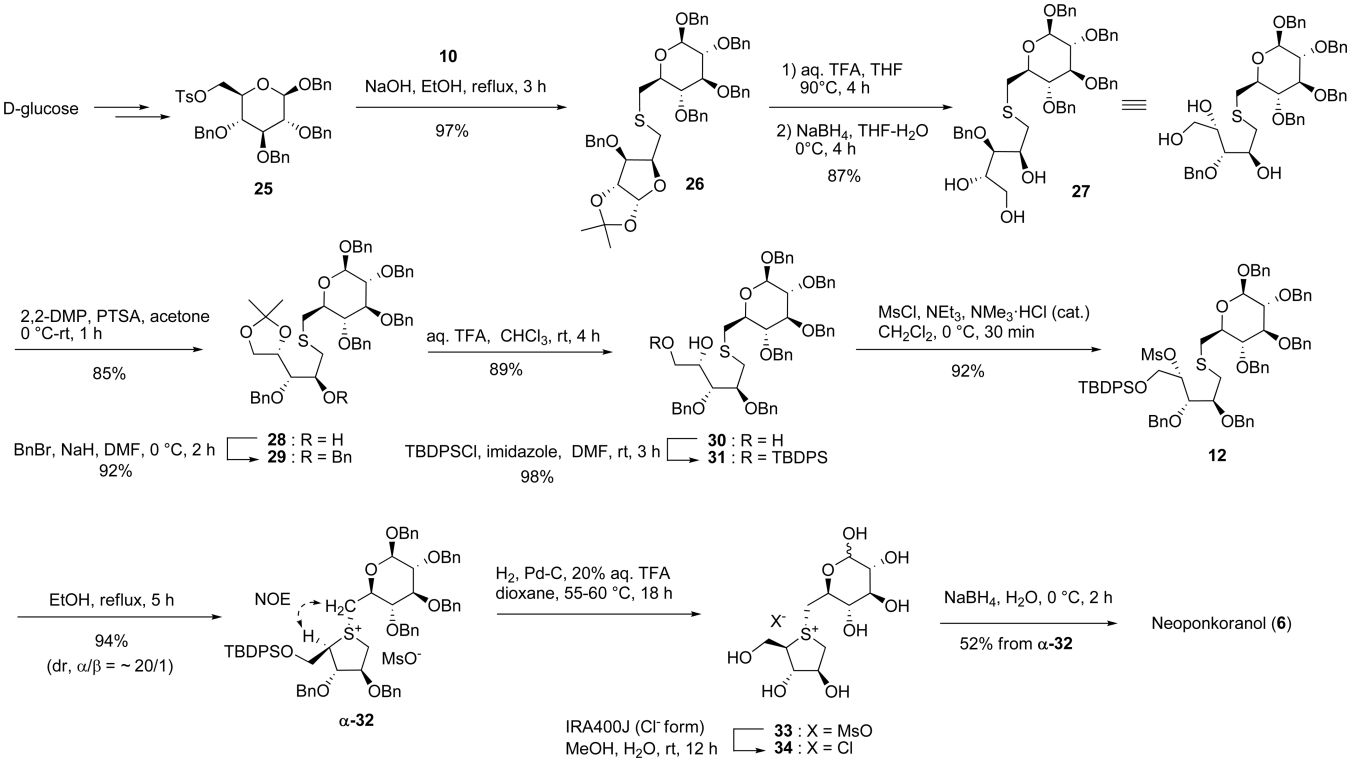
Scheme 3. Synthesis of Neosalacinol (4)



Scheme 4. Synthesis of Neoponkoranol (6)



the conventional methods, and provides an efficient alternative route for SAR studies on this class of α-glucosidase inhibitors.

EXPERIMENTAL SECTION

General Experimental Details. Melting points were determined on a hot-stage melting point apparatus and are uncorrected. IR spectra were measured on an FT-IR spectrophotometer. NMR spectra were recorded on an FT-NMR spectrometer (^{1}H, 500 or 800 MHz; ^{13}C, 125 or 200 MHz). Chemical shifts (δ) and coupling constants (J) are given in ppm and Hz, respectively. DSS was used as an internal standard in the measurement of NMR spectra in D_2O. Low-resolution and high-resolution mass spectra were recorded on a double-focusing mass spectrometer (FAB) or an orbitrap mass spectrometer (ESI). Optical rotations were determined with a digital polarimeter. Column chromatography was performed over silica gel (45−106 μM). HPLC was performed on a DAISOPAK-SP120-5-ODS-BP (20 × 250 mm)

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with a refractive index detector. All the organic extracts were dried over anhydrous Na_2SO_4 prior to evaporation.

3-*O*-Benzyl-1,2-*O*-isopropylidene-5-*O*-tosyl-thio-α-D-xylofuranose (15). A solution of 1,2-*O*-isopropylidene-5-*O*-tosyl-α-D-xylofuranose[8f] (**14**, 13.4 g, 39.0 mmol) in DMF (70 mL) was added dropwise to a mixture of NaH (3.25 g, 81.3 mmol, 60% in liquid paraffin), BnBr (5.3 mL, 44.3 mmol), and DMF (100 mL) at 0 °C. After being stirred at 0 °C for 1 h, the mixture was poured into cold water (900 mL) and extracted with Et_2O (3 × 200 mL). The extract was washed with brine and condensed to give a colorless oil (18.4 g), which on column chromatography (*n*-hexane−acetone, 10:1 → 5:1) gave the title compound **15** (16.1 g, 95%) as a colorless oil. The spectral properties of **15** agreed well with those reported.[8f]

3-*O*-Benzyl-1,2-*O*-isopropylidene-5-thio-α-D-xylofuranose Acetate (16). A mixture of **15** (15.8 g, 36.4 mmol), KSAc, (6.23 g, 54.6 mmol), and DMF (50 mL) was heated at 80 °C for 2 h. After being cooled, the reaction mixture was diluted with cold water (300 mL) and extracted with EtOAc (2 × 100 mL, 1 × 50 mL). The extract was washed with brine and condensed to give a brown oil (13.2 g), which on column chromatography (*n*-hexane−EtOAc, 10:1 → 3:1) gave the title compound **16** (11.4 g, 93%) as a pale yellow oil. $[\alpha]_D^{24}$ −14.4 (*c* 1.10, $CHCl_3$). IR (neat): 2986, 2936, 1693, 1454, 1373, 1354, 1256, 1215, 1165, 1134, 1076, 1026 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 1.30/1.47 [each 3H, s, $C(CH_3)_2$], 2.33 (3H, s, $COCH_3$), 3.15 (1H, dd, *J* = 13.4, 6.9, H-5a), 3.28 (1H, dd, *J* = 13.4, 7.4, H-5b), 3.91 (1H, d, *J* = 3.2, H-3), 4.27 (1H, ddd, *J* = 7.4, 6.9, 3.2, H-4), 4.52/4.68 (each 2H, d, *J* = 11.6, CH_2Ph), 4.61 (1H, d, *J* = 3.9, H-2), 5.91 (1H, d, *J* = 3.9, H-1), 7.29−7.38 (5H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 26.2/26.8 [$C(CH_3)_2$], 27.1 (C-5), 30.4 ($COCH_3$), 72.0 (CH_2Ph), 79.1 (C-4), 82.0 (C-3), 82.1 (C-1), 105.1 (C-1), 111.7 [$C(CH_3)$], 127.7/128.0/128.4 (d, arom.), 137.2 (s, arom.), 195.2 ($COCH_3$). LRMS (FAB) *m*/*z*: 339 $[M + H]^+$, 361 $[M + Na]^+$. HRMS (FAB) *m*/*z*: $[M + Na]^+$ Calcd for $C_{17}H_{22}O_5SNa$ 361.1085; Found 361.1059.

3-*O*-Benzyl-1,2-*O*-isopropylidene-5-thio-α-D-xylofuranose (10). A solution of the thioacetate **16** (11.3 g, 33.4 mmol) in THF (50 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (1.5 g, 39.4 mmol) in THF (50 mL) at 0 °C, and the mixture was stirred at 0 °C for 30 min. After cooling, the excess of hydride was decomposed successively with EtOAc and water. The resulting mixture was acidified with 10% hydrochloric acid (pH ca. 3) and extracted with EtOAc (2 × 100 mL, 1 × 50 mL). The extract was washed with brine and condensed to give a pale yellow solid (10.1 g), which on recrystallization from a mixture of *n*-hexane and EtOAc gave the title compound **10** (8.56 g, 87%) as colorless needles. Column chromatography (*n*-hexane−acetone, 20:1) of the mother liquid gave **10** (936 mg, 9%) as a pale yellow solid. mp 54−56 °C. $[\alpha]_D^{24}$ −84.5 (*c* 1.0, $CHCl_3$). IR (KBr): 2974, 2935, 2573 (S−H), 1454, 1373, 1319, 1254, 1215, 1162, 1138, 1099, 1072, 1049, 1010 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 1.32 (1H, t, *J* = 9.1, S*H*), 1.32/1.51 [each 3H, s, $C(CH_3)_2$], 2.76 (1H, ddd, *J* = 13.1, 9.1, 8.3, H-5a), 2.81 (1H, ddd, *J* = 13.1, 9.1, 6.0, H-5b), 4.02 (1H, d, *J* = 3.2, H-3), 4.26 (1H, ddd, *J* = 8.3, 6.0, 3.2, H-4), 4.50/4.72 (each 1H, d, *J* = 11.8, CH_2Ph), 4.63 (1H, d, *J* = 3.9, H-2), 5.91 (1H, d, *J* = 3.9, H-1), 7.29−7.38 (5H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 21.1 (C-5), 26.2/26.7 [$C(CH_3)_2$], 71.9 (CH_2Ph), 80.8 (C-3), 81.9 (C-2), 82.3 (C-4), 105.1 (C-1), 111.7 [$C(CH_3)_2$], 127.9/128.1/128.5 (d, arom.), 137.2 (s, arom.). HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{15}H_{20}O_4SNa$ 319.0975; Found 319.0968.

3-*O*-Benzyl-5-*S*-(3,4-di-*O*-benzyl-1-deoxy-L-erythritol-1-yl)-1,2-*O*-isopropylidene-5-thio-D-xylofuranose (17). Under an Ar atmosphere, a mixture of **10** (1.02 g, 3.45 mmol), 1,2-anhydro-3,4-di-*O*-benzyl-L-erythritol[10] (**11**, 1.17 g, 4.12 mmol), NaOH (190 mg, 4.8 mmol), and EtOH (40 mL) was heated under reflux for 1.5 h. After being cooled, the reaction mixture was concentrated *in vacuo* to give a pale yellow oil, which was dispersed with water (20 mL), and the resulting mixture was extracted with EtOAc (1 × 60 mL, 2 × 20 mL). The extract was washed with brine and condensed to give a pale yellow oil (2.28 g), which on column chromatography (*n*-hexane−acetone, 50:1 → 20:1) gave the title compound **17** (1.8 g, 90%) as a pale yellow oil. $[\alpha]_D^{25}$ −40.5 (*c* = 1.05, $CHCl_3$). IR (neat): 3471, 2928, 2866, 1454, 1373, 1215, 1165, 1076, 1026 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 1.31/1.48 [each 3H, s, $C(CH_3)_2$], 1.60 (1H, br s, OH), 2.73 (1H, dd, *J* = 14.0, 8.3, H-1′a), 2.85 (1H, dd, *J* = 13.2, 7.1, H-5a), 2.88 (1H, dd, *J* = 13.2, 6.6, H-5b), 2.90 (1H, dd, *J* = 14.0, 3.4, H-1′b), 3.62 (1H, ddd, *J* = 6.0, 4.9, 4.3, H-3′), 3.66 (1H, dd, *J* = 10.3, 4.9, H-4′a), 3.73 (1H, dd, *J* = 10.3, 4.3, H-4′b), 3.90 (1H, ddd, *J* = 8.3, 6.0, 3.4, H-2′), 3.94 (1H, d, *J* = 3.1, H-3), 4.33 (1H, ddd, *J* = 7.1, 6.6, 3.1, H-4), 4.51/4.67 (each 1H, d, *J* = 11.7, CH_2Ph), 4.54 (2H, s, CH_2Ph), 4.57/4.70 (each 1H, d, *J* = 11.4, CH_2Ph), 4.60 (1H, d, *J* = 4.0, H-2), 5.90 (1H, d, *J* = 4.0, H-1), 7.25−7.35 (15H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 26.2/26.8 [$C(CH_3)_2$], 30.5 (C-5), 37.0 (C-1′), 69.8 (C-4′), 70.8 (C-2′), 72.0/72.6/73.5 (CH_2Ph), 79.6 (C-3′), 80.3 (C-4), 81.8 (C-3), 82.0 (C-2), 105.0 (C-1), 111.6 [$C(CH_3)_2$], 127.67/127.71/127.91/127.94/128.36/128.41/128.5 (d, arom.), 137.3/138.0/138.2 (s, arom.). LRMS (FAB) *m*/*z*: 581 $[M + H]^+$, 603 $[M + Na]^+$. HRMS (FAB) *m*/*z*: $[M + H]^+$ Calcd for $C_{33}H_{41}O_7S$ 581.2573; Found 581.2593.

3-*O*-Benzyl-5-*S*-(3,4-di-*O*-benzyl-1-deoxy-L-erythritol-1-yl)-5-thio-D-xylitol (19). A mixture of **17** (1.7 g, 2.93 mmol), 1,4-dioxane (20 mL), and 10% H_2SO_4 (4 mL) was heated under reflux for 1.5 h. After being cooled, the reaction mixture was diluted with water (50 mL), and the resulting mixture was neutralized with $NaHCO_3$. The mixture was extracted with EtOAc (1 × 50 mL, 2 × 30 mL). The extract was washed with brine and evaporated to give 3-*O*-benzyl-5-*S*-(3,4-di-*O*-benzyl-1-deoxy-L-erythritol-1-yl)-5-thio-D-xylitol (**18**) as a pale yellow oil (1.64 g), which was then dissolved in methanol (30 mL) and treated with $NaBH_4$ (220 mg, 5.8 mmol) at 0 °C for 1 h. The reaction mixture was diluted with a mixture of acetone (1 mL) and water (5 mL) and condensed to give a pale yellow semisolid (1.92 g), which on column chromatography ($CHCl_3$−acetone, 50:1) gave the title compound **19** (821 mg, 52% from **17**) as a pale yellow oil. $[\alpha]_D^{23}$ +91.2 (*c* 0.91, $CHCl_3$). IR (neat): 3406, 2920, 2870, 1454, 1396, 1365, 1311, 1257, 1211, 1091, 1072, 1026 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 2.72 (2H, br t-like, *J* = 6.9, H-5a and H-5b), 2.74 (1H, br dd, *J* = 13.2, 6.9, H-1′a), 2.84 (1H, br d-like, *J* = 13.2, H-1′b), 3.58 (1H, dd, *J* = 4.6, 2.9, H-3), 3.60 (1H, dd, *J* = 11.8, 4.3, H-1a), 3.62 (1H, ddd, *J* = 6.9, 4.6, 4.6, H-3′), 3.68 (1H, dd, *J* = 10.3, 4.6, H-4′a), 3.71 (1H, dd, *J* = 10.3, 4.6, H-4′b), 3.74 (1H, dd, *J* = 11.8, 4.6, H-1b), 3.84 (1H, ddd, *J* = 4.6, 4.6, 4.3, H-2), 3.91 (1H, ddd, *J* = 6.9, 6.9, 3.2, H-2′), 3.94 (1H, ddd, *J* = 6.9, 6.9, 2.9, H-4), 4.53 (2H, s, CH_2Ph), 4.55/4.67 (each 1H, d, *J* = 11.7, CH_2Ph), 4.61/4.64 (each 1H, d, *J* = 11.4, CH_2 Ph), 7.25−7.35 (15H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 36.4 (C-1′), 36.8 (C-5), 62.6 (C-1), 69.7 (C-4′), 70.0 (C-4), 70.9 (C-2), 71.2 (C-2′), 72.6/73.5/74.4 (CH_2Ph), 79.2 (C-3′), 79.7 (C-3), 127.7/127.8/127.9/128.2/128.3/128.4/128.5/128.6 (d, arom.), 137.5/137.7/138.0 (s, arom). LRMS (FAB) *m*/*z*: 543 $[M + H]^+$, 565 $[M + Na]^+$. HRMS (FAB) *m*/*z*: $[M + H]^+$ Calcd for $C_{30}H_{39}O_7S$ 543.2417; Found 543.2403.

3-*O*-Benzyl-5-*S*-(3,4-di-*O*-benzyl-1-deoxy-L-erythritol-1-yl)-1,2-*O*-isopropylidene-5-thio-D-xylitol (20). To a mixture of **19** (582 mg, 0.93 mmol), 2,2-dimethoxypropane (2,2-DMP, 1.15 mL, 9.4 mmol), and acetone (7 mL) was added *p*-toluenesulfonic acid (PTSA, 40 mg) at 0 °C, and the mixture was stirred at room temperature for 3 h. The reaction mixture was poured into aqueous $NaHCO_3$ (30 mL) and extracted with EtOAc (1 × 30 mL, 2 × 10 mL). The extract was washed with brine and condensed to give a colorless oil (674 mg), which on column chromatography (*n*-hexane−EtOAc, 30:1 → 10:1) gave the title compound **20** (390 mg, 62%) as a colorless oil. $[\alpha]_D^{25}$ +1.13 (*c* 0.96, $CHCl_3$). IR (neat): 3445, 2916, 2870, 1454, 1369, 1254, 1211, 1076, 1029 cm^{-1}. ^1H NMR (800 MHz, $CDCl_3$) δ: 1.38/1.44 [each 3H, s, $C(CH_3)_2$], 2.67 (1H, dd, *J* = 13.6, 5.6, H-5a), 2.69 (1H, dd, *J* = 13.6, 7.2, H-5b), 2.70 (1H, dd, *J* = 13.6, 8.0, H-1′a), 2.83 (1H, dd, *J* = 13.6, 3.2, H-1′b), 2.96 (1H, d, *J* = 6.4, O*H*), 3.13 (1H, d, *J* = 4.0, O*H*), 3.52 (1H, dd, *J* = 6.4, 2.4, H-3), 3.61 (1H, ddd, *J* = 6.4, 4.0, 4.0, H-3′), 3.65 (1H, dddd-like, *J* = 7.2, 6.4, 5.6, 2.4, H-4), 3.69 (1H, dd, *J* = 10.4, 4.0, H-4′a), 3.72 (1H, dd, *J* = 10.4, 4.0, H-4′b), 3.74 (1H, dd, *J* = 8.0, 7.2, H-1a), 3.88 (1H, dddd-like, *J* = 8.0, 6.4, 4.0, 3.2, H-2′), 4.03 (1H, dd, *J* = 8.0, 6.4, H-1b), 4.37 (1H, ddd, *J* = 7.2, 6.4, 6.4, H-2), 4.54/4.55 (each 1H, d, *J* = 12.0, CH_2Ph), 4.56/4.69 (each 1H, d, *J* = 11.2, CH_2Ph), 4.65/4.85 (each 1H, d, *J* = 11.2, CH_2Ph), 7.27−7.35

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(15H, m, arom.). ^{13}C NMR (200 MHz, $CDCl_3$) δ: 25.5/26.6 [$C(CH_3)_2$], 36.6 (C-1′), 36.9 (C-5), 66.0 (C-1), 69.8 (C-4′), 71.0 (C-4), 71.2 (C-2′), 72.6/73.5/74.1 (CH_2Ph), 77.2 (C-2), 79.2 (C-3′), 79.6 (C-3), 109.3 [$C(CH_3)_2$], 127.7/127.8/127.89/127.90/128.3/126.39/128.44 (d, arom.), 137.8/138.00/138.04 (s, arom.). LRMS (FAB) m/z: 583 $[M + H]^+$, 605 $[M + Na]^+$. HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{33}H_{43}O_7S$ 583.2729; Found 583.2734.

3,4-Di-*O*-benzyl-5-*S*-(2,3,4-tri-*O*-benzyl-1-deoxy-L-erythritol-1-yl)-1,2-*O*-isopropylidene-5-thio-D-xylitol (21). A solution of **20** (276 mg, 0.47 mmol) in DMF (4 mL) was added dropwise to a mixture of NaH (40 mg, 1.0 mmol, 60% in liquid paraffin), benzyl bromide (125 μL, 1.1 mmol), and DMF (2 mL) at 0 °C. After being stirred at 0 °C for 1 h, the mixture was poured into cold water (30 mL) and extracted with EtOAc (1 × 30 mL, 2 × 10 mL). The extract was washed with brine and condensed to give a pale yellow oil (492 mg), which on column chromatography (*n*-hexane−EtOAc, 30:1 → 10:1) gave the title compound **21** (334 mg, 93%) as a colorless oil. $[\alpha]_D^{25}$ −21.6 (*c* 1.02, $CHCl_3$). IR (neat): 2866, 1496, 1454, 1369, 1253, 1211, 1091, 1072, 1026 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.35/1.39 [each 3H, s, $C(CH_3)_2$], 2.77 (1H, dd, *J* = 13.5, 6.6, H-5a), 2.81 (2H, d-like, *J* = ca. 4.0, H-1′a and H-1′b), 2.88 (2H, dd, *J* = 13.5, 6.0, H-5b), 3.49 (1H, ddd, *J* = 8.3, 6.3, 3.5, H-2), 3.53 (1H, dd, *J* = 8.3, 8.0, H-1a), 3.58 (1H, dd, *J* = 7.2, 3.5, H-3), 3.64 (1H, dd, *J* = 10.6, 4.6, H-4′a), 3.66 (1H, dd, *J* = 8.3, 6.3, H-1b), 3.70 (1H, dd, *J* = 10.6, 3.2, H-4′b), 3.77−3.83 (2H, m, H-2′ and H-3′), 4.27 (1H, ddd, *J* = 7.2, 6.6, 6.0, H-4), 4.33/4.55 (each 1H, d, *J* = 11.7, CH_2Ph), 4.51 (2H, s, CH_2Ph), 4.52/4.62 (each 1H, d, *J* = 11.4, CH_2Ph), 4.59/4.71 (each 1H, d, *J* = 11.4, CH_2Ph), 4.65/4.79 (each 1H, d, *J* = 11.7, CH_2Ph), 7.23−7.34 (30H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 25.7/26.6 [$C(CH_3)_2$], 33.1 (C-5), 34.2 (C-1′), 65.9 (C-1), 69.2 (C-4′), 72.1/72.5/72.7/73.3/74.0 (CH_2Ph), 77.1 (C-4), 78.77, 78.82, 78.9 (C-2′, C-3′ and C-2), 79.0 (C-3), 108.9 [$C(CH_3)_2$], 127.6/127.7/127.8/127.9/128.16/128.22/128.25/128.30/128.34 (d, arom.), 137.8/138.1/138.2/138.42/138.5 (s, arom.). LRMS (FAB) m/z: 763 $[M + H]^+$, 785 $[M + Na]^+$. HRMS (FAB) m/z: $[M + Na]^+$ Calcd for $C_{47}H_{54}O_7SNa$ 785.3489; Found 785.3488.

3,4-Di-*O*-benzyl-5-*S*-(2,3,4-tri-*O*-benzyl-1-deoxy-L-erythritol-1-yl)-5-thio-D-xylitol (22). A mixture of **21** (300 mg, 0.39 mmol), 10% hydrochloric acid (0.5 mL), and methanol (2.5 mL) was heated at 60° for 1 h. After being cooled, the reaction mixture was poured into cold water (25 mL). The resulting mixture was neutralized with $NaHCO_3$ and extracted with EtOAc (1 × 30 mL, 2 × 10 mL). The extract was washed with brine and condensed to give a pale yellow oil (285 mg), which was pure enough for the next reaction. For analytical purposes, a small portion was purified by means of column chromatography (*n*-hexane−EtOAc, 15:1) to give the title compound **22** as a colorless oil. $[\alpha]_D^{25}$ +62.5 (*c* 0.1, $CHCl_3$). IR (neat): 3441, 2920, 2870 1497, 1454, 1396, 1362, 1207, 1095, 1072, 1026 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.13 (1H, br s, OH), 2.54 (1H, d, *J* = 5.5 OH), 2.83 (1H, dd, *J* = 13.5, 6.6, H-5a), 2.88 (2H, d-like, *J* = ca. 5.5, H-1′a and H-1′b), 2.90 (1H, dd, *J* = 13.5, 5.2, H-5b), 3.49 (2H, br d-like, *J* = ca. 4.3, H-1a and H-1b), 3.64 (1H, dd, *J* = 5.2, 4.6, H-3), 3.65 (1H, dd, *J* = 10.3, 4.9, H-4′a), 3.71 (1H, dd, *J* = 10.3, 3.2, H-4′b), 3.71—3.75 (1H, m, H-2), 3.79 (1H, ddd, *J* = 6.6, 5.2, 5.2 Hz, H-4), 3.80−3.86 (2H, m, H-2′ and H-3′), 4.46−4.73 (10H, m, CH_2Ph), 7.23−7.34 (25H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 33.6 (C-5), 34.4 (C-1′), 64.0 (C-1), 69.2 (C-4′), 70.9 (C-2), 72.5/72.7/72.8/73.3/74.5 (CH_2Ph), 78.7, 78.8 (C2′, C3′), 79.1 (C-4), 79.2 (C-3), 127.56/127.60/127.63/127.66/127.79/127.84/127.88/128.0/128.23/128.30/128.34/128.4/128.5 (d, arom.), 137.7/137.8/138.1/138.4 (s, arom.). LRMS (FAB) m/z: 723 $[M + H]^+$, 745 $[M + Na]^+$. HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{44}H_{51}O_7S$ 723.3356; Found 723.3358.

3,4-Di-*O*-benzyl-5-*S*-(2,3,4-tri-*O*-benzyl-1-deoxy-L-erythritol-1-yl)-1-*O*-(*tert*-butyldiphenylsilyl)-5-thio-D-xylitol (23). A mixture of **22** (265 mg, 0.37 mmol), *tert*-butyldiphenylsilyl chloride (142 μL, 0.55 mmol), imidazole (75 mg, 1.1 mmol), and DMF (2 mL) was heated at 50 °C for 2 h. The reaction mixture was poured into cold water (10 mL) and extracted with EtOAc (1 × 30 mL, 2 × 10 mL). The extract was washed with brine and condensed to give a colorless oil (423 mg), which on column chromatography (*n*-hexane−acetone, 30:1 → 10:1) gave the title compound **23** (338 mg, 96% from **21**) as a colorless oil. $[\alpha]_D^{25}$ −2.74 (*c* = 1.21, $CHCl_3$). IR (neat): 3475, 2928, 2859, 1589, 1496, 1454, 1427, 1361, 1207, 1111, 1072, 1026 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.04 (9H, s, [$C(CH_3)_3$]), 2.40 (1H, d, *J* = 6.6, OH), 2.84 (1H, dd, *J* = 13.8, 6.6, H-5a), 2.87 (1H, dd, *J* = 13.7, 6.0, H-1′a), 2.89 (1H, dd, *J* = 13.8, 5.2, H-5b), 2.91 (1H, dd, *J* = 13.8, 4.0, H-1′b), 3.58 (1H, dd, *J* = 10.0, 6.9, H-1a), 3.64 (1H, dd, *J* = 10.0, 6.1, H-1b), 3.65 (1H, dd, *J* = 10.6, 4.9, H-4′a), 3.71 (1H, dd, *J* = 10.6, 3.2, H-4′b), 3.79 (1H, ddd-like, *J* = ca. 6.6, 5.4, 5.2, H-4), 3.80−3.85 (2H, m, H-2′ and H-3′), 3.86 (1H, dddd-like, *J* = ca. 6.9, 6.6, 6.1, 2.3, H-2), 3.89 (1H, dd, *J* = 5.4, 2.3, H-3), 4.47−4.72 (10H, m, CH_2Ph), 7.17−7.65 (35H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.2 [$SiC(CH_3)_3$], 26.9 [$SiC(CH_3)_3$], 34.1 (C-5), 34.4 (C-1′), 64.6 (C-1), 69.3 (C-4′), 71.0 (C-2), 72.5/72.7/72.9/73.3/74.6 (CH_2Ph), 77.8 (C-3), 78.6, 79.0 (C-2′, C-3′), 79.7 (C-2), 127.5/127.55/127.58/127.61/127.64/127.73/127.8/127.91/127.93/128.1/128.27/128.32/129.74/135.6 (d, arom.) 133.15/133.21/138.0/138.21/138.24/138.5 (s, arom.). LRMS (FAB) m/z: 961 $[M + H]^+$, 983 $[M + Na]^+$. HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{60}H_{69}O_7SSi$ 961.4533; Found 961.4503.

3,4-Di-*O*-benzyl-5-*S*-(2,3,4-tri-*O*-benzyl-1-deoxy-L-erythritol-1-yl)-1-*O*-(*tert*-butyldiphenylsilyl)-2-*O*-methanesulfonyl-5-thio-D-xylitol (9). To a mixture of **23** (254 mg, 0.26 mmol), Et_3N (150 μL, 1.08 mmol), Me_3N·HCl (10 mg, 0.10 mmol), and CH_2Cl_2 (2.5 mL) was added methanesulfonyl chloride (37 μL, 0.48 mmol) at 0 °C. After being stirred at 0 °C for 2 h, the reaction mixture was poured into cold water (10 mL) and extracted with EtOAc (1 × 30 mL, 2 × 10 mL). The extract was washed with brine and condensed *in vacuo* at below 20 °C to give a pale yellow oil (278 mg), which on column chromatography (*n*-hexane−acetone, 30:1 → 10:1) gave the title compound **9** as a colorless oil (269 mg, 95%). IR (neat): 2990, 2859, 1497, 1454, 1358, 1207, 1177, 1111, 1072 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.03 (9H, s,[$C(CH_3)_3$]), 2.78 (1H, dd, *J* = 13.8, 5.4, H-1′a), 2.79 (1H, dd, *J* = 13.5, 8.0, H-5a), 2.84 (1H, dd, *J* = 13.8, 3.8, H-1′b), 2.85 (3H, s, SO_2CH_3), 2.88 (1H, dd, *J* = 13.5, 5.2, H-5b), 3.64 (1H, dd, *J* = 12.0, 5.2, H-1a), 3.66 (1H, dd, *J* = 10.3, 5.0, H-4′a), 3.67 (1H, ddd-like, *J* = ca. 8.0, 5.2, 3.2, H-4), 3.70 (1H, dd, *J* = 10.3, 3.2, H-4′b), 3.78−3.85 (2H, m, H-2′ and H-3′), 3.92 (1H, dd, *J* = 12.0, 2.9, H-1b), 4.16/4.44 (each 1H, d, *J* = 11.5, CH_2Ph), 4.18 (1H, dd, *J* = 6.9, 3.2, H-3), 4.51 (2H, s-like, CH_2Ph), 4.54/4.62 (each 1H, d, *J* = 11.5, CH_2Ph), 4.56/4.70 (each 1H, d, *J* = 11.5, CH_2Ph), 4.65/4.66 (each 1H, d, *J* = 11.5, CH_2Ph), 4.78 (1H, ddd, *J* = 6.9, 5.2, 2.9, H-2), 7.08−7.65 (35H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.2 [$C(CH_3)_3$], 26.9 [$C(CH_3)_3$], 32.3 (C-5), 34.1 (C1′), 38.2 (SO_2CH_3), 63.1 (C-1), 69.3 (C4′), 71.8/72.6/72.8/73.3/75.1 (CH_2Ph), 76.9 (C-3), 77.1 (C-4), 78.9/79.0 (C2′ and C3′), 83.5 (C-2), 127.55/127.59/127.7/127.79/127.82/127.9/127.8/128.2/128.29/128.31/128.35/128.44/129.9/130.0/135.5/135.6 (d, arom.), 132.5/132.9/137.4/137.6/138.17/138.24/138.5 (s, arom.). LRMS (FAB) m/z: 1039 $[M + H]^+$. HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{61}H_{71}O_9S_2Si$ 1039.4309; Found 1039.4298.

Cyclization of Mesylate (9). A solution of **9** (244 mg, 0.24 mmol) in ethanol (8 mL) was heated under reflux for 3 h. Removal of the solvent *in vacuo* left a pale yellow oil (245 mg), which on column chromatography ($CHCl_3$ → $CHCl_3$−MeOH, 50:1 → 30:1 → 10:1) gave 2,3,-di-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-1,4-dideoxy-1,4-{(*R*)-[4-deoxy-1,2,3-tri-*O*-benzyl-D-erythritol-1-yl]episulfonium-ylidene}-D-arabinitol methanesulfonate (***α*-24**, 208 mg, 85%) and a ca. 1:3.5 mixture of ***α*-24** and its *β*-isomer ***β*-24** (11.7 mg, 5%).

*Major Isomer **α*-24*. Colorless oil. $[\alpha]_D^{24}$ +36.0 (*c* 0.92, $CHCl_3$). IR (neat): 2931, 2858, 1496, 1454, 1392, 1362, 1323, 1312, 1207, 1111, 1041 cm^{-1}. ^{1}H NMR (800 MHz, $CDCl_3$) δ: 1.00 (9H, s, [$C(CH_3)_3$]), 2.72 (3H, s, $^-OSO_2CH_3$), 3.63 (1H, dd, *J* = 13.6, 2.4, H-1a), 3.64 (1H, dd, *J* = 10.4, 4.8, H-4′a), 3.75 (1H, dd, *J* = 13.6, 4.0, H-1b), 3.78 (1H, dd, *J* = 10.4, 5.6, H-4′b), 3.87 (1H, dd, *J* = 10.4, 8.0, H-5a), 3.93 (1H, ddd, *J* = 5.6, 4.8, 3.2, H-3′), 4.01 (1H, dd, *J* = 10.2, 6.4, H-5b), 4.19 (1H, dd, *J* = 13.6, 6.4, H-1′a), 4.26 (1H, dd, *J* = 13.6, 4.0, H-1′b), 4.25/4.30 (each 1H, d, *J* = 12.0, CH_2Ph), 4.36 (1H, dd, *J* = 2.4, 1.6, H-3), 4.38 (1H, ddd, *J* = 6.4, 4.0, 3.2, H-2′) 4.44 (1H, ddd, *J* = 4.0, 2.4, 2.4, H-2), 4.48 (1H, br dd-like, *J* = ca. 8.0, 6.4, H-4), 4.49 (2H, s,

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CH_2Ph), 4.51/4.520 (each 1H, d-like, J = 12.0, CH_2Ph), 4.524/4.58 (each 1H, d, J = 12.0, CH_2Ph), 4.56/4.63 (each 1H, d, J = 12.0 Hz, CH_2Ph), 7.05−7.55 (35H, m, arom.). ^{13}C NMR (200 MHz, $CDCl_3$) δ: 19.2 [$C(CH_3)_3$], 26.8 [$C(CH_3)_3$], 39.6 ($^-OSO_2CH_3$), 48.1 (C-1′), 48.5 (C-1), 61.4 (C-5), 65.2 (C-4), 68.7 (C-4′), 71.7/71.9/72.4/72.6/73.4 (CH_2Ph), 76.0 (C-2′), 76.9 (C-3′), 82.7 (C-2), 82.8 (C-3), 127.7/127.79/127.83/127.88/127.93/127.97/128.0/128.1/128.2/128.3/128.36/128.39/128.54/128.58/128.64/130.07/130.11/135.50/135.53 (d, arom.), 132.1/132.2/136.2/136.4/137.1/137.7/137.9 (s, arom). LRMS (FAB$^+$) m/z: 943 [M − CH_3SO_3]$^+$. HRMS (FAB$^+$) m/z: [M − CH_3SO_3]$^+$ Calcd for $C_{60}H_{67}O_6SSi$ 943.4428; Found 943.4455.

NMR Data for Minor Isomer ***β*****-24** *Extracted from the Spectrum of a Mixture (α/β = ca. 1:3.5).* ^{1}H NMR (800 MHz, $CDCl_3$) δ: 0.97 [9H, s, $C(CH_3)_3$], 2.75 (3H, s, SO_2CH_3), 3.45 (1H, dd, J = 10.4, 4.8, H-4′a), 3.57 (1H, dd, J = 10.4, 5.6, H-4′b), 3.76 (1H, dd-like, J = ca. 9.6, 5.6, H-4), 3.81 (1H, dd, J = 13.6, 3.2, H-1′a), 3.85 (1H, ddd, J = 5.6, 4.8, 2.4, H-3′), 3.88 (1H, dd, J = 15.2, 4.0, H-1a), 3.93 (1H, dd, J = 10.4, 9.6, H-5a), 4.12 (1H, dd, J = 13.6, 4.0, H-1′b), 4.23 (1H, dd, J = 10.4, 5.6, H-5b), 4.27 (2H, s, CH_2Ph), 4.30/4.38 (each 1H, d, J = 12.0, CH_2Ph), 4.34 (1H, br s, H-3), 4.35/4.37 (each 1H, d-like, J = ca. 12.0, CH_2Ph), 4.36 (1H, br s-like, H-2), 4.45 (1H, br dd-like, J = ca. 15.2, 2.0, H-1b), 4.47 (1H, m, H-2′), 4.53/4.54 (each 1H, d-like, J = 12.0, CH_2Ph), 4.57/4.59 (each 1H, d, J = 12.0, CH_2 Ph), 7.26−7.51 (35H, m, arom.). ^{13}C NMR (200 MHz, $CDCl_3$) δ: 19.0 [$C(CH_3)_3$], 26.7 [$C(CH_3)_3$], 39.6 (SO_2CH_3), 41.3 (C-1′), 46.3 (C-1), 60.2 (C-5), 61.7 (C-4), 68.9 (C-4′), 71.3/71.7/72.4/73.1/73.4 (CH_2Ph), 76.2 (C-2′), 76.5 (C-3′), 82.0 (C-2), 84.3 (C-3), 127.57/127.6/127.9/128.20/128.23/128.24/128.3/128.4/128.61/128.64/128.7/130.2/135.4/135.5 (d, arom.), 131.9/132.1/136.17/136.22/137.2/137.87/137.90 (s, arom.).

Neosalacinol Methanesulfonate (4, X = OMs). A suspension of 10% palladium-on-carbon (200 mg) in 20% aqueous triflacetic acid (4 mL) was pre-equilibrated with hydrogen. To the suspension was added a solution of ***α*****-24** (191 mg, 0.18 mmol) in EtOAc (2 mL), and the mixture was hydrogenated at room temperature under atmospheric pressure until the uptake of hydrogen ceased. The catalyst was filtered off, and the catalyst was washed with methanol. The combined filtrate and washings were condensed *in vacuo*. The residue (64 mg) was purified by means of column chromatography ($CHCl_3$ → $CHCl_3$−MeOH → 10:1 → 3/1) to give the title compound **4** (52.5 mg, 90%) as a colorless oil. $[\alpha]_D^{22}$ +4.77 (c 1.50, CH_3OH). IR (neat): 3321, 1415, 1335, 1207, 1192, 1072, 1041 cm^{-1}. ^{1}H NMR (800 MHz, CD_3OD) δ: 2.70 (3H, s, $CH_3SO_3^-$), 3.60 (1H, ddd, J = 6.4, 4.8, 4.0, H-3′), 3.62 (1H, dd, J = 11.2, 4.8, H-4′a), 3.69 (1H, dd, J = 11.2, 4.0, H-4′b), 3.73 (1H, dd, J = 12.8, 8.8, H-1′a), 3.85 (1H, dd, J = 12.8, 3.2, H-1′b), 3.86 (2H, m, H-1a and H-1b), 3.92 (1H, dd, J = 11.2, 8.8, H-5a), 4.01 (1H, br dd, J = 8.8, 5.6, H-4), 4.05 (1H, dd, J = 11.2, 5.6, H-5b), 4.08 (1H, ddd, J = 8.8, 6.4, 3.2, H-2′), 4.37 (1H, dd, J = 2.4, 1.6, H-3), 4.62 (1H, ddd-like, J = 2.4, 2.4, 2.4, H-2). ^{13}C NMR (200 MHz, $CDCl_3$) δ: 39.5 ($CH_3SO_3^-$), 51.8 (C-1′), 52.0 (C-1), 61.1 (C-5), 64.0 (C-4′), 69.6 (C-2′), 73.7 (C-4), 75.3 (C-3′), 79.45 (C-2), 79.53 (C-3). LRMS (FAB) m/z: 255 [M − CH_3SO_3]$^+$, 95 [CH_3SO_3]$^-$. HRMS (FAB) m/z: [M − CH_3SO_3]$^+$ Calcd for $C_9H_{19}O_6S$ 255.0902; Found 255.0901.

Ion Exchange Reaction of 4 (X = OMs). A mixture of **4** (X = OMs, 16 mg, 0.046 mmol), ion-exchange resin IRA-400J (Cl^- form, 1 g), and methanol (3 mL) was stirred at room temperature for 12 h. The resin was filtered off, and the filtrate was evaporated to give a pale yellow oil (15 mg), which on column chromatography ($CHCl_3$ → $CHCl_3$−MeOH → 10:1 → 3/1) gave the corresponding chloride **4** (X = Cl, 11.7 mg, 89%). The spectral properties of **4** agreed well with those reported.[8e]

Benzyl 2,3,4-Tri-*O*-benzyl-6-*S*-(3-*O*-benzyl-1,2-di-*O*-isopropylidene-5-deoxy-α-D-xylofuranos-5-yl)-6-thio-β-D-glucopyranoside (26). A mixture of benzyl 2,3,4-tri-*O*-benzyl-6-*O*-(*p*-toluenesulfonyl)-β-D-glucopyranoside[11] (**25**, 4.54 g, 6.5 mmol), thiol **10** (2.03 g, 6.9 mmol), NaOH (533 mg, 13.3 mmol), and EtOH (60 mL) was heated under reflux for 3 h. After being cooled, the reaction mixture was condensed *in vacuo* and the residue was diluted with water (100 mL), and the resulting mixture was extracted with EtOAc (1 × 200 mL, 2 × 50 mL). The extract was washed with brine and condensed to give a pale brown solid (5.6 g), which on recrystallization from methanol gave the title compound **26** (4.61 g, 91%) as colorless needles. Column chromatography (*n*-hexane−EtOAc, 10/1 → 5/1) of the mother liquid gave **26** (310 mg, 6%) as a colorless solid. mp 120−121 °C. $[\alpha]_D^{24}$ −47.6 (c = 1.37, $CHCl_3$). IR (KBr): 3032, 2920, 2854, 1454, 1361, 1319, 1215, 1080 cm^{-1}. ^{1}H NMR (800 MHz, $CDCl_3$) δ: 1.31/1.49 [each 3H, s, $C(CH_3)_2$], 2.72 (1H, dd-like, J = ca. 13.6, 8.0, H-6′a), 2.96 (1H, dd, J = 13.6, 5.6, H-5a), 2.976 (1H, dd-like, J = ca. 13.6, 2.4, H-6′b), 2.982 (1H, dd, J = 13.6, 8.0, H-5b), 3.46 (1H, dd, J = 9.6, 9.6, H-4′), 3.45−3.48 (1H, m, H-5′), 3.50 (1H, dd, J = 9.6, 8.0, H-2′), 3.62 (1H, dd, J = 9.6, 9.6, H-3′), 4.00 (1H, d, J = 3.2, H-3), 4.40 (1H, ddd, J = 8.0, 5.6, 3.2 H-4), 4.48 (1H, d, J = 8.0, H-1), 4.54/4.66 (each 1H, d, J = 11.2, CH_2Ph), 4.590/4.86 (each 1H, d, J = 11.2, CH_2Ph), 4.596 (1H, d, J = 3.2, H-2), 4.63/4.914 (each 1H, d, J = 12.0, CH_2Ph), 4.70/4.94 (each 1H, d, J = 11.2, CH_2Ph), 4.76/4.918 (each 1H, d, J = 10.4, CH_2Ph), 4.00 (1H, d, J = 3.2, H-1), 7.24−7.38 (25H, m, arom.). ^{13}C NMR (200 MHz, $CDCl_3$) δ: 26.2/26.8 [$C(CH_3)_2$], 31.0 (C-5), 34.5 (C-6′), 71.0/72.2/74.8/75.1/75.7 (CH_2Ph), 75.8 (C-5′), 80.2 (C-4), 80.3 (C-4′), 81.9 (C-3), 82.1 (C-2), 82.5 (C-2′), 84.6 (C-3′), 102.2 (C-1′), 105.1 (C-1), 111.6 [$C(CH_3)_2$], 127.60/127.62/127.71/127.75/127.85/127.86/127.89/128.0/128.1/128.2/128.31/128.35/128.37/128.43/128.45 (d, arom.), 137.3/137.5/138.0/138.4/138.5 (s, arom.). LRMS (FAB) m/z: 841 [M + Na]$^+$. HRMS (FAB) m/z: [M + Na]$^+$ Calcd for $C_{49}H_{54}O_9SNa$ 841.3386; Found 841.3382.

Benzyl 2,3,4-Tri-*O*-benzyl-6-*S*-(3-*O*-benzyl-5-deoxy-α-D-xylitol-5-yl)-6-thio-β-D-glucopyranoside (27). A mixture of **26** (4.61 g, 5.6 mmol), trifluoroacetic acid (TFA, 18 mL), THF (36 mL), and water (9 mL) was heated at 90° for 4 h. After being cooled, the reaction mixture was diluted with water (100 mL), and the resulting mixture was extracted with $CHCl_3$ (1 × 100 mL, 2 × 50 mL). The extract was successively washed with aqueous $NaHCO_3$ and brine and condensed to give a pale yellow oil (4.54 g), which was then dissolved in a mixture of THF and water (150 mL, 2/1, v/v) and treated with $NaBH_4$ (1.04 g, 28 mmol) at 0 °C for 4 h. The reaction mixture was poured into water (150 mL), and the resulting mixture was extracted with EtOAc (1 × 100 mL, 2 × 50 mL). The extract was washed with brine and condensed to give a pale yellow viscous oil, (4.56 g), which on column chromatography (*n*-hexane−EtOAc, 10:1 → 3:1) gave the title compound **27** (3.81 g, 87%) as a colorless waxy solid. mp 96−97 °C. $[\alpha]_D^{23}$ +1.37 (c = 1.67, $CHCl_3$). IR (KBr): 3412, 3032, 2924, 2873, 1497, 1454, 1357, 1311, 1281, 1227, 1076, 1030 cm^{-1}. ^{1}H NMR (800 MHz, $CDCl_3$) δ: 2.74 (1H, dd-like, J = ca. 8.0, 4.0, OH), 2.75 (1H, d, J = 6.4, OH), 2.77 (1H, dd, J = 14.4, 8.0, H-5a), 2.82 (1H, dd-like, J = 14.4, 6.4, H-6′a), 2.86 (1H, dd, J = 14.4, 5.6, H-5b), 2.90 (1H, dd, J = 14.4, 2.4, H-6′b), 3.17 (1H, d, J = 5.6, OH), 3.49 (1H, ddd, J = 9.6, 6.4, 2.4, H-5′), 3.52 (1H, dd-like, J = 8.8, 8.0, H-2′), 3.57 (1H, dd, J = 8.8, 8.8, H-4′), 3.61 (1H, ddd-like, J = ca. 12.0, 8.0, 4.0, H-1a), 3.638 (1H, dd, J = 8.8, 8.8, H-3′), 3.640 (1H, dd, J = 4.0, 3.2, H-3), 3.77 (1H, ddd, J = 12.0, 4.0, 4.0, H-1b), 3.84 (1H, ddt, J = 6.4, 4.0, 4.0, H-2), 4.00 (1H, dddd, J = 8.0, 5.6, 5.6, 3.2, H-4), 4.52 (1H, d, J = 8.0, H-1′), 4.61/4.89 (each 1H, d, J = 10.4, CH_2Ph), 4.64/4.65 (each 1H, d, J = 12.0, CH_2Ph), 4.66/4.944 (each 1H, d, J = 12.0, CH_2Ph), 4.72/4.948 (each 1H, d, J = 11.2, CH_2Ph), 4.77/4.93 (each 1H, d, J = 11.2, CH_2Ph), 7.23−7.39 (25H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 34.1 (C-6′), 37.6 (C-5), 62.4 (C-1), 69.6 (C-4), 70.6 (C-2), 71.3/74.4/74.9/75.2/75.7 (CH_2Ph), 75.0 (C-5′), 79.6 (C-3), 79.7 (C-4′), 82.3 (C-2′), 84.4 (C-3′), 102.4 (C-1′), 127.7/127.86/127.90/128.0/128.1/128.2/128.3/128.39/128.45/128.50/128.6 (d, arom.), 137.1/137.5/137.9/138.2/138.4 (s, arom.). LRMS (FAB) m/z: 803 [M + Na]$^+$. HRMS (FAB) m/z: [M + Na]$^+$ Calcd for $C_{46}H_{52}O_9SNa$ 803.3230; Found 803.3256.

Benzyl 2,3,4-Tri-*O*-benzyl-6-*S*-(3-*O*-benzyl-1,2-*O*-isopropylidene-5-deoxy-α-D-xylitol-5-yl)-6-thio-β-D-glucopyranoside (28). To a mixture of **27** (3.48 g, 4.46 mmol), 2,2-dimethoxypropane (2,2-DMP, 1.1 mL, 9.0 mmol), and acetone (30 mL) was added *p*-toluenesulfonic acid (PTSA, 24 mg, 0.14 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. To the reaction mixture was added aqueous $NaHCO_3$, and the resulting mixture was

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extracted with EtOAc (1 × 50 mL, 2 × 20 mL). The extract was washed with brine and condensed to give a colorless viscous oil (3.67 g), which on column chromatography (*n*-hexane−EtOAc, 50:1 → 5:1) gave the title compound **28** (3.11 g, 85%) as a colorless viscous oil. $[\alpha]_D^{24}$ −14.8 (*c* = 1.55, $CHCl_3$). IR (neat): 3460, 3032, 2909, 2877, 1497, 1454, 1369, 1250, 1211, 1072, 1030 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) *δ*: 1.38/1.45 [each 3H, s, $C(CH_3)_2$], 2.74 (1H, dd, *J* = 14.0, 6.6, H-6′a), 2.76 (2H, d, *J* = 6.6, H-5a and H-5b), 2.85 (1H, d, *J* = 6.6, OH), 2.89 (1H, dd, *J* = 14.0, 2.3, H-6′b), 3.46 (1H, ddd, *J* = 9.7, 6.6, 2.3, H-5′), 3.498 (1H, dd, *J* = 9.2, 7.8, H-2′), 3.504 (1H, dd, *J* = 9.7, 9.7, H-4′), 3.55 (1H, dd, *J* = 6.9, 2.3, H-3), 3.63 (1H, dd, *J* = 9.7, 9.2, H-3′), 3.66 (1H, dtd, *J* = 6.6, 6.6, 2.3, H-4), 3.74 (1H, dd, *J* = 8.3, 8.1, H-1a), 4.04 (1H, dd, *J* = 8.3, 6.6, H-1b), 4.41 (1H, ddd-like, *J* = 8.1, 6.9, 6.6, H-2), 4.51 (1H, d, *J* = 7.8, H-1′), 4.59/4.88 (each 1H, d, *J* = 10.9, CH_2Ph), 4.64/4.926 (each 1H, d, *J* = 11.8, CH_2Ph), 4.66/4.86 (each 1H, d, *J* = 11.5, CH_2Ph), 4.71/4.95 (each 1H, d, *J* = 10.9, CH_2Ph), 4.77/4.928 (each 1H, d, *J* = 10.9, CH_2Ph), 7.23−7.39 (25H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 25.6/26.6 [$C(CH_3)_2$], 34.2 (C-6′), 37.5 (C-5), 66.1 (C-1), 70.9 (C-4), 71.2/74.5/74.9/75.2/75.7 (CH_2Ph), 75.3 (C-5′), 77.4 (C-2), 79.6 (C-3), 79.9 (C-4′), 82.4 (C-2′), 84.5 (C-3′), 102.4 (C-1′), 109.3 [$C(CH_3)_2$], 127.6/127.7/127.83/127.85/127.91/128.01/128.05/128.13/128.26/128.33/128.37/128.42/128.5 (d, arom.), 137.1/137.9/138.1/138.3/138.4 (s, arom.). LRMS (FAB) *m*/*z*: 843 $[M + Na]^+$. HRMS (FAB) *m*/*z*: $[M + Na]^+$ Calcd for $C_{49}H_{56}O_9SNa$ 843.3543; Found 843.3563.

Benzyl 2,3,4-Tri-*O*-benzyl-6-*S*-(3,4-di-*O*-benzyl-1,2-*O*-isopropylidene-5-deoxy-*α*-D-xylitol-5-yl)-6-thio-*β*-D-glucopyranoside (29). A solution of **28** (3.0 g, 3.7 mmol) in DMF (20 mL) was added dropwise to a mixture of NaH (310 mg, 7.8 mmol, 60% in liquid paraffin), benzyl bromide (0.7 mL, 5.9 mmol), and DMF (5 mL) at 0 °C, and the mixture was stirred at room temperature for 2 h. The reaction mixture was poured into cold water (150 mL) and extracted with EtOAc (2 × 50 mL, 1 × 30 mL). The extract was washed with brine and condensed to give a colorless oil (3.75 g), which on column chromatography (*n*-hexane−EtOAc, 50:1 → 10:1) gave the title compound **29** (3.05 g, 92%) as a colorless viscous oil. $[\alpha]_D^{23}$ −30.3 (*c* = 1.56, $CHCl_3$). IR (neat): 3032, 2873, 1496, 1454, 1365, 1250, 1211, 1069, 1030 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) *δ*: 1.35/1.41 [each 3H, s, $C(CH_3)_2$], 2.67 (1H, dd-like, *J* = 14.0, 7.2, H-6′a), 2.88 (1H, dd, *J* = 14.0, 2.1, H-6′b), 2.89 (1H, dd, *J* = 13.5, 6.3, H-5a), 3.01 (1H, dd, *J* = 13.5, 6.3, H-5b), 3.45 (1H, ddd, *J* = 9.7, 7.2, 2.1, H-5′), 3.47 (1H, dd-like, *J* = 9.7, 9.2, H-4′), 3.50 (1H, dd, *J* = 9.2, 7.8, H-2′), 3.53 (1H, td, *J* = 6.3, 3.5, H-4), 3.56 (1H, dd, *J* = 8.3, 8.1, H-1a), 3.61 (1H, dd, *J* = 6.9, 3.5, H-3), 3.62 (1H, dd, *J* = 9.2, 9.2, H-3′), 3.70 (1H, dd, *J* = 8.3, 6.3, H-1b), 4.33 (1H, ddd-like, *J* = 8.1, 6.9, 6.3, H-2), 4.43/4.63 (each 1H, d, *J* = 11.7, CH_2Ph), 4.49 (1H, d, *J* = 7.8, H-1′), 4.58/4.88 (each 1H, d, *J* = 10.9, CH_2Ph), 4.64/4.91(each 1H, d, *J* = 12.0, CH_2Ph), 4.68/4.81 (each 1H, d, *J* = 11.8, CH_2Ph), 4.71/4.96 (each 1H, d, *J* = 10.9, CH_2Ph), 4.77/4.93 (each 1H, d, *J* = 10.9, CH_2Ph), 7.22−7.38 (30H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 25.7/26.6 [$C(CH_3)_2$], 33.2 (C-5), 34.3 (C-6′), 65.9 (C-1), 71.1/72.1/74.1/74.9/75.1/75.7 (CH_2Ph), 76.0 (C-5′), 77.1 (C-2), 78.5 (C-4), 79.0 (C-3), 80.3 (C-4′), 82.4 (C-2′), 84.5 (C-3′), 102.3 (C-1′), 108.9 [$C(CH_3)_2$], 127.59/127.64/127.82/127.86/127.93/127.99/128.1/128.22/128.26/128.33/128.38/128.42/128.45/128.55 (d, arom.), 137.1/137.8/137.9/138.3/138.4/138.5 (s, arom.). FABMS *m*/*z*: 933 $[M + Na]^+$.

Benzyl 2,3,4-Tri-*O*-benzyl-6-*S*-(3,4-di-*O*-benzyl-5-deoxy-*α*-D-xylitol-5-yl)-6-thio-*β*-D-glucopyranoside (30). A mixture of **29** (2.83 g, 3.1 mmol), TFA (20 mL), chloroform (30 mL), and water (30 mL) was vigorously stirred at room temperature for 4 h. The reaction mixture was poured into cold water (200 mL) and extracted with $CHCl_3$ (3 × 50 mL). The extract was successively washed with aqueous $NaHCO_3$ and brine and condensed to give a colorless viscous oil (2.81 g), which on column chromatography (*n*-hexane−acetone, 10:1 → 3:1) gave the title compound **30** (2.41 g, 89%) as a colorless waxy solid. mp 82−83 °C. $[\alpha]_D^{23}$ −1.15 (*c* = 2.05, $CHCl_3$). IR (KBr): 3395, 3032, 2904, 2859, 1497, 1454, 1400, 1358, 1207, 1192, 1111, 1076, 1029 cm^{-1}. ^1H NMR (800 MHz, $CDCl_3$) *δ*: 2.11 (1H, dd, *J* = 6.4, 5.6, OH), 2.51 (1H, d, *J* = 5.6, OH), 2.78 (1H, dd, *J* = 14.4, 7.2, H-6′a), 2.945 (1H, dd, *J* = 13.6, 6.4, H-5a), 2.950 (1H, dd, *J* = 14.4, 2.4, H-6′b), 3.07 (1H, dd, *J* = 13.6, 5.6, H-5b), 3.50 (1H, ddd, *J* = 9.6, 7.2, 2.4, H-5′), 3.51 (1H, dd, *J* = 8.8, 8.0, H-2′), 3.528 (1H, ddd-like, *J* = ca. 11.2, 6.4, 4.8, H-1a), 3.534 (1H, dd-like, *J* = ca. 9.6, 8.8, H-4′), 3.55 (1H, ddd-like, *J* = ca. 11.2, 5.6, 5.2, H-1b), 3.63 (1H, dd, *J* = 8.8, 8.8, H-3′), 3.69 (1H, dd, *J* = 5.0, 4.0, H-3), 3.82 (1H, ddd-like, *J* = ca. 5.6, 5.2, 4.8, 4.0, H-2), 3.86 (1H, ddd-like, *J* = ca. 6.4, 5.6, 5.0, H-4), 4.50 (1H, d, *J* = 8.0, H-1′), 4.54/4.716 (each 1H, d, *J* = 11.2, CH_2Ph), 4.56/4.718 (each 1H, d, *J* = 11.2, CH_2Ph), 4.59/4.88 (each 1H, d, *J* = 10.4, CH_2Ph), 4.65/4.92 (each 1H, d, *J* = 12.0, CH_2Ph), 4.74/4.95 (each 1H, d, *J* = 11.2, CH_2Ph), 4.77/4.93 (each 1H, d, *J* = 10.4, CH_2Ph), 7.22−7.38 (30H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 33.9 (C-5), 34.3 (C-6′), 64.1 (C-1), 71.0 (C-2), 71.2/72.8/74.6/74.8/75.2/75.69 (CH_2Ph), 75.72 (C-5′), 79.1 (C-4), 79.3 (C-3), 80.1 (C-4′), 82.3 (C-2′), 84.5 (C-3′), 102.4 (C-1′), 108.9 [$C(CH_3)_2$], 127.6/127.88/127.97/128.08/128.13/128.26/128.34/128.38/128.46/128.54 (d, arom.), 137.1/137.7/137.8/138.0/138.3/138.4 (s, arom.). LRMS (FAB) *m*/*z*: 893 $[M + Na]^+$. HRMS (FAB) *m*/*z*: $[M + Na]^+$ Calcd for $C_{53}H_{58}O_9SNa$ 893.3699; Found 893.3701.

Benzyl 2,3,4-Tri-*O*-benzyl-6-*S*-[3,4-di-*O*-benzyl-1-(*tert*-butyldiphenylsilyl)-5-deoxy-*α*-D-xylitol-5-yl]-6-thio-*β*-D-glucopyranoside (31). A mixture of **30** (2.38 g, 2.74 mmol), *tert*-butyldiphenylsilyl chloride (1.0 mL, 3.85 mmol), imidazole (550 mg, 8.09 mmol), and DMF (12 mL) was stirred at room temperature for 3 h. The reaction mixture was poured into cold water (200 mL) and extracted with EtOAc (1 × 100 mL, 2 × 30 mL). The extract was washed with brine and condensed to give a colorless oil (3.53 g), which on column chromatography (*n*-hexane−EtOAc, 10:1 → 3:1) gave the title compound **31** (2.97 g, 98%) as a colorless viscous oil. $[\alpha]_D^{25}$ −1.07 (*c* = 0.95, $CHCl_3$). IR (neat): 3557, 3032, 2932, 1497, 1454, 1392, 1361, 1211, 1111, 1069, 1030 cm^{-1}. ^1H NMR (800 MHz, $CDCl_3$) *δ*: 1.04 (9H, s,[$C(CH_3)_3$]), 2.42 (1H, d, *J* = 7.2, OH), 2.75 (1H, dd-like, *J* = ca. 13.6, 8.0, H-6′a), 2.94 (1H, dd, *J* = 13.6, 6.4, H-5a), 2.98 (1H, dd, *J* = 13.6 1.6, H-6′b), 3.03 (1H, dd, *J* = 13.6, 4.8, H-5b), 3.47 (1H, m, H-4′), 3.48 (1H, m, H-5′), 3.51 (1H, dd, *J* = 8.8, 8.0, H-2′), 3.61 (1H, dd, *J* = 10.4, 7.0, H-1a), 3.62 (1H, dd, *J* = 8.8, 8.8, H-3′), 3.66 (1H, dd, *J* = 10.4, 6.4, H-1b), 3.83 (1H, ddd, *J* = 6.4, 4.8, 4.8, H-4), 3.90 (1H, ddd-like, *J* = ca. 7.2, 7.0, 6.4, 3.2, H-2), 3.91 (1H, dd, *J* = 4.8, 3.2, H-3), 4.48 (1H, d, *J* = 8.0, H-1′), 4.53/4.71 (each 1H, d, *J* = 11.2, CH_2Ph), 4.55/4.65 (each 1H, d, *J* = 11.2, CH_2Ph), 4.58/4.86 (each 1H, d, *J* = 11.2, CH_2Ph), 4.64/4.91 (each 1H, d, *J* = 12.0, CH_2Ph), 4.70/4.95 (each 1H, d, *J* = 10.4, CH_2Ph), 4.76/4.92 (each 1H, d, *J* = 10.4, CH_2Ph), 7.21−7.64 (40H, m, arom.). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 19.2 [$C(CH_3)_3$], 26.9 [$C(CH_3)_3$], 34.2 (C-5), 34.6 (C-6′), 64.6 (C-1), 71.0/72.8/74.7/74.8/75.1/75.7 (CH_2Ph), 71.1 (C-2), 75.8 (C-5′), 77.9 (C-3), 79.5 (C-4), 80.4 (C-4′), 82.4 (C-2′), 84.6 (C-3′), 102.3 (C-1′), 127.66/127.75/127.82/127.85/127.90/127.97/128.02/128.1/128.34/128.36/128.40/128.43/129.8/135.6 (d, arom.), 133.2/133.2/137.2/138.0/138.1/138.4/138.5 (s, arom.). LRMS (FAB) *m*/*z*: 1131 $[M + Na]^+$. HRMS (FAB) *m*/*z*: $[M + Na]^+$ Calcd for $C_{69}H_{76}O_9SSiNa$ 1131.4877; Found 1131.4878.

Benzyl 2,3,4-Tri-*O*-benzyl-6-*S*-[3,4-di-*O*-benzyl-1-(*tert*-butyldiphenylsilyl)-5-deoxy-2-*O*-methanesulfonyl-*α*-D-xylitol-5-yl]-6-thio-*β*-D-glucopyranoside (12). To a mixture of **31** (2.95 g, 2.66 mmol), triethylamine (2.4 mL, 17.3 mmol), trimethylamine hydrochloride (70 mg, 0.73 mmol), and CH_2Cl_2 (30 mL) was added methanesulfonyl chloride (0.42 mL, 5.42 mmol) at 0 °C. After being stirred at 0 °C for 30 min, the reaction mixture was poured into cold water (200 mL) and extracted with EtOAc (2 × 50 mL, 1 × 30 mL). The extract was washed with brine and condensed *in vacuo* to give a colorless oil (3.44 g), which on column chromatography (*n*-hexane−EtOAc, 10:1 → 3:1) gave the title compound **12** (2.90 g, 92%) as a colorless viscous oil. $[\alpha]_D^{25}$ −24.7 (*c* = 0.74, $CHCl_3$). IR (neat): 3032, 2943, 2859, 1497, 1454, 1357, 1177, 1111, 1069, 1029 cm^{-1}. ^1H NMR (800 MHz, $CDCl_3$) *δ*: 1.04 (9H, s,[$C(CH_3)_3$]), 2.67 (1H, dd, *J* = 13.6, 8.0, H-6′a), 2.86 (3H, s, SO_2CH_3), 2.89 (1H, dd, *J* = 13.6, 2.4, H-6′b), 2.91 (1H, dd, *J* = 13.6, 8.0, H-5a), 3.08 (1H, dd, *J* = 13.6, 4.8, H-5b), 3.44 (1H, dd-like, *J* = 9.6, 8.8, H-4′), 3.49 (1H, ddd-like, *J* = ca. 9.6, 8.0, 2.4, H-5′), 3.51 (1H, dd, *J* = 8.8, 8.0, H-2′), 3.64 (1H, dd, *J* = ca. 8.8, 8.8, H-3′), 3.66 (1H, dd, *J* = 12.8, 4.8, H-1a), 3.72 (1H, ddd, *J* =

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8.0, 4.8, 4.0, H-4), 3.94 (1H, dd, J = 12.8, 3.2, H-1b), 4.21 (1H, dd, J = 6.4, 4.0, H-3), 4.31/4.58 (each 1H, d, J = 11.2, CH_2Ph), 4.51 (1H, d, J = 8.0, H-1′), 4.53/4.86 (each 1H, d, J = 10.4, CH_2Ph), 4.64/4.91 (each 1H, d, J = 12.0, CH_2Ph), 4.67/4.69 (each 1H, d, J = 12.0, CH_2Ph), 4.72/4.95 (each 1H, d, J = 10.4, CH_2Ph), 4.77/4.93 (each 1H, d, J = 10.4, CH_2Ph), 4.82 (1H, ddd, J = 6.4, 4.8, 3.2, H-2), 7.15−7.65 (40H, m, arom.). ^{13}C NMR (200 MHz, $CDCl_3$) δ: 19.2 [C(CH_3)$_3$], 26.9 [C(CH_3)$_3$], 32.3 (C-5), 34.2 (C-6′), 38.2 (SO_2CH_3), 63.2 (C-1), 71.2/71.8/74.8/75.15/75.16/75.7 (CH_2Ph), 76.5 (C-5′), 76.86 (C-3), 76.90 (C-4), 80.7 (C-4′), 82.4 (C-2′), 83.4 (C-2), 84.5 (C-3′), 102.5 (C-1′), 127.62/127.65/127.81/127.83/128.85/127.92/128.0/128.1/128.26/128.33/128.37/128.40/128.43/128.5/129.88/129.92/135.5/135.6 (d, arom.), 132.6/132.9/137.2/137.4/137.6/138.0/138.4/138.5 (s, arom.). LRMS (FAB) m/z: 1187 [M + H]$^+$. HRMS (FAB) m/z: [M + H]$^+$ Calcd for $C_{70}H_{79}O_{11}S_2Si$ 1187.4833; Found 1187.4828.

Cyclization of Mesylate (12). A solution of **12** (1.5 g, 1.26 mmol) in EtOH (30 mL) was heated under reflux for 5 h. Removal of the solvent *in vacuo* left a colorless oil (1.53 g), which on column chromatography ($CHCl_3$ → $CHCl_3$−MeOH, 50:1 → 30:1 → 10:1) gave 2,3-di-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-1,4-dideoxy-1,4-{(*R*)-[benzyl 6-deoxy-2,3,4-tri-*O*-benzyl-*β*-D-glucopyranoside-6-yl]episulfoniumylidene}-D-arabinitol methanesulfonate (***α*-32**, 1.34 g, 89%) and a ca. 1:5 mixture of ***α*-32** and its *β*-isomer ***β*-32** (82 mg, 5%).

*Major Isomer **α**-32.* Colorless amorphous. $[\alpha]_D^{25}$ +9.3 (c = 1.18, $CHCl_3$). IR (neat): 3032, 2932, 2886, 1497, 1454, 1427, 1396, 1361, 1203, 1068, 1037 cm^{-1}. ^{1}H NMR (800 MHz, $CDCl_3$) δ: 1.02 (9H, s, [C(CH_3)$_3$]), 2.74 (3H, s, $^-$OSO$_2$CH_3), 3.32 (1H, dd, J = 9.6, 8.0, H-2′), 3.42 (1H, dd, J = 9.6, 8.8, H-4′), 3.65 (1H, dd-like, J = 9.6, 8.8, H-3′), 3.74 (1H, dd, J = 13.6, 4.0, H-1a), 3.85 (1H, ddd, J = 9.6, 6.4, 4.0, H-5′), 3.86 (1H, dd, J = 11.2, 6.4, H-5a), 3.90 (1H, dd, J = 11.2, 6.4, H-5b), 3.92 (1H, dd, J = 13.6, 6.4, H-6′a), 4.01 (1H, dd, J = 13.6, 4.8, H-1b), 4.11 (1H, td, J = 6.4, 3.2, H-4), 4.13 (1H, dd, J = 13.6, 3.2, H-6′b), 4.22 (1H, dd-like, J = 4.0, 3.2, H-3), 4.46/4.57 (each 1H, d, J = 11.2, CH_2Ph), 4.48 (1H, d, J = 8.0, H-1′), 4.49/4.61 (each 1H, d, J = 11.2, CH_2Ph), 4.55/4.71 (each 1H, d, J = 12.0, CH_2Ph), 4.59/4.81 (each 1H, d, J = 11.2, CH_2Ph), 4.68 (1H, ddd, J = 4.8, 4.0, 4.0, H-2), 4.75/4.86 (each 1H, d, J = 11.2, CH_2Ph), 4.77/4.92 (each 1H, d, J = 10.4, CH_2Ph), 7.16−7.55 (40H, m, arom.). ^{13}C NMR (200 MHz, $CDCl_3$) δ: 19.2 [C(CH_3)$_3$], 26.9 [C(CH_3)$_3$], 39.7 ($^-$OSO$_2$CH_3), 46.2 (C-1), 47.1 (C-6′), 60.9 (C-5), 66.9 (C-4), 71.1 (C-5′), 71.9/72.3/72.4/74.2/74.8/75.6 (CH_2Ph), 77.3 (C-4′), 81.8 (C-2′), 82.2 (C-2), 82.7 (C-3), 83.9 (C-3′), 102.9 (C-1′), 127.67/127.70/127.8/127.9/128.05/128.09/128.2/128.3/128.36/128.38/128.5/128.6/128.68/128.72/129.0/130.29/130.33/135.4/135.5 (d, arom.), 131.9/132.0/136.3/136.5/136.9/137.6/138.1/138.2 (s, arom.). LRMS (FAB) m/z: 1091 [M − CH_3SO_3]$^+$, 95 [CH_3SO_3]$^-$. HRMS (FAB) m/z: [M − CH_3SO_3]$^+$ Calcd for $C_{69}H_{75}O_8SSi$ 1091.4952; Found 1091.4957, [CH_3SO_3]$^-$ Calcd for CH_3O_3S 94.9803; Found 94.9804.

*NMR Data for Minor Isomer **β**-32 Extracted from the Spectrum of a Mixture (α/β = ca. 1:5).* 1.04 (9H, s,[C(CH_3)$_3$]), 2.74 (3H, s, $^-$OSO$_2$CH_3), 3.09 (1H, dd, J = 9.6, 8.8, H-4′), 3.13 (1H, dd, J = 12.8, 10.4, H-6′a), 3.37 (1H, dd, J = 9.6, 8.0 H-2′), 3.74 (1H, dd, J = 9.6, 8.8, H-3′), 3.86 (1H, dd-like, J = 11.2, 7.2, H-5a), 3.90 (1H, dd-like, J = 11.2, 6.4, H-5b), 3.93 (1H, ddd-like, J = ca. 7.2, 6.4, 2.4, H-4), 4.06 (1H, dd, J = 12.8, 3.2, H-6′b), 4.09 (1H, ddd-like, J = ca. 10.4, 9.6, 3.2, H-5′), 4.12 (1H, dd, J = 14.4, 4.8, H-1a), 4.18 (1H, br s-like, H-3), 4.30/4.35 (each 1H, d, J = 12.0, CH_2Ph), 4.416/4.46 (each 1H, d, J = 12.0, CH_2Ph), 4.420/4.68 (each 1H, d, J = 11.2, CH_2Ph), 4.45 (1H, br d-like, J = 14.4, H-1b), 4.68 (1H, m, H-2), 4.70/4.94 (each 1H, d, J = 10.4, CH_2Ph), 4.71/4.90 (each 1H, d, J = 10.4, CH_2Ph), 4.80/4.86 (each 1H, d, J = 12.0, CH_2Ph), 4.84 (1H, d, J = 8.0, H-1′), 7.06−7.59 (40H, m, arom.). ^{13}C NMR (200 MHz, $CDCl_3$) δ: 19.1 [C(CH_3)$_3$], 26.8 [C(CH_3)$_3$], 39.7 ($^-$OSO$_2$CH_3), 41.2 (C-6′), 46.2 (C-1), 59.9 (C-5), 62.9 (C-4), 69.1 (C-5′), 71.87/71.90/72.3/74.2/74.6/75.7 (CH_2Ph), 79.9 (C-4′), 82.1 (C-2′), 82.7 (C-2), 83.7 (C-3′), 84.4 (C-3), 103.1 (C-1′), 127.62/127.68/127.69/127.7/127.87/127.93/128.00/128.16/128.20/128.32/128.37/128.42/128.69/128.72/130.50/130.52/135.42/135.5 (d, arom.), 131.7/131.9/136.0/136.1/137.57/137.63/138.25/138.32 (s, arom.).

1,4-Dideoxy-1,4-[(*S*)-(6-deoxy-1-D-glucopyranos-6-yl)episulfoniumylidene]-2,3,5-tri-*O*-benzyl-D-arabinitol Methanesulfonate (33). A suspension of 10% Pd-C (800 mg) in a mixture of 20% aqueous TFA (25 mL) was pre-equilibrated with hydrogen. To the suspension was added a solution of ***α*-32** (820 mg, 0.69 mmol) in 1,4-dioxane (10 mL). The resulted mixture was hydrogenated at 55−60 °C under atmospheric pressure until uptake of hydrogen ceased. The catalyst was filtered off and washed with water. The combined filtrate and the washings were condensed *in vacuo* to give a colorless oil (290 mg), which was used for the subsequent reaction without further purification. For analytical purposes, a small portion was purified by column chromatography ($CHCl_3$/CH_3OH, 10/1 → 5/1 → 3/1) to give the title compound **33** as a ca. 1:1 amoneric mixture. ^{1}H NMR (800 MHz, D_2O) δ: 3.33 (0.5H, dd, J = 9.6, 8.0, H-2′*β*), 3.39 (3H, s, CH_3SO_3), 3.47 (0.5H. dd, J = 10.4, 9.6, H-4′*α*), 3.49 (0.5H, dd, J = 9.6, 9.6, H-4′*β*), 3.55 (0.5H, dd, J = 9.6, 9.6, H-3′*β*), 3.52 (0.5H, dd, J = 9.6, 3.2, H-2′*α*), 3.77 (0.5H, dd, J = 9.6, 9.6 Hz, H-3′*α*), 3.88 (0.5H, dd, J = 13.6, 1.6, H-6′*α*a), 3.89 (0.5H, d-like, J = 13.6 H-6′*β*a), 3.92−3.97 (1H, m, H-1*α*a and H-1*β*a), 3.96−3.99 (0.5H, m, H-5′*β*), 3.94−3.99 (1H, m, H-1*α*b and H-1*β*b), 3.99−4.02 (1H, m, H-5*α*a and H-5*β*a), 4.06/4.07 (each 0.5H, dd, J = 13.6, 3.2, H-1′*α*b and H-1′*β*b), 4.14−4.20 (2H, m, H-5*α*b, H-5*β*b, H-4*α* and H-4*β*), 4.31 (0.5H, ddd, J = 10.4, 8.8, 3.2, H-5′*α*), 4.51 (1H, m, H-3*α* and H-3*β*), 4.73 (0.5H, d, J = 8.0, H-1′ *β*), 4.80 (1H, m,, H-2*α* and H-2*β*), 5.31 (0.5H, d, J = 3.2, H-1′ *α*). ^{13}C NMR (200 MHz, D_2O) δ: 41.1 (CH_3SO_3), 49.6/49.9 (C-6′*α* and C6′*β*), 50.9 (C-1*α* and C1*β*), 61.9 (C-5*α* and C5*β*), 70.3 (C-5′*α*), 73.1/73.2 (C-4*α* and C4*β*), 73.9 (C-2′*α*), 74.2 (C-5′*β*), 74.9 (C-4′*β*), 74.98 (C-3′*α*), 75.02 (C-4′*α*), 76.6 (C-2′*β*), 77.9 (C-3′*β*), 79.8 (C-2*α* and C2*β*), 80.3/80.4 (C-3*α* and C3*β*), 95.0 (C-1′*α*), 98.9 (C-1′*β*). HRMS (ESI) m/z: [M − CH_3SO_3]$^+$ Calcd for $C_{11}H_{21}O_8S$ 313.0952; Found 313.0942; [CH_3SO_3]$^-$ Calcd for 94.9808, Found 94.9791.

1,4-Dideoxy-1,4-[(*S*)-(6-deoxy-1-D-glucopyranos-6-yl)episulfoniumylidene]-2,3,5-tri-*O*-benzyl-D-arabinitol Chloride (34). A mixture of **33** (240 mg), ion-exchange resin IRA-400J (Cl$^-$ form, 5 g), methanol (10 mL), and water (2 mL) was stirred at room temperature for 12 h. The resin was filtered off, and the filtrate was evaporated to give a pale yellow oil (203 mg), which was used for the subsequent reaction without further purification. For analytical purposes, a small portion was purified by column chromatography ($CHCl_3$/CH_3OH, 10/1 → 5/1 → 3/1) to give the title compound **34** as a ca. 1:1 amoneric mixture. ^{1}H NMR (800 MHz, D_2O) δ: 3.27 (0.5H, dd, J = 9.6, 8.0, H-2′*β*), 3.42 (0.5H. dd, J = 10.4, 9.6, H-4′*α*), 3.43 (0.5H, dd, J = 9.6, 9.6, H-4′*β*), 3.50 (0.5H, dd, J = 9.6, 9.6, H-3′*β*), 3.56 (0.5H, dd, J = 9.6, 3.2, H-2′*α*), 3.71 (0.5H, dd, J = 9.6, 9.6 Hz, H-3′*α*), 3.832/3.834 (each 0.5H, dd, J = 13.6, 8.8, H-6′*α*a and H-6′*β*a), 3.87−3.91 (1H, m, H-1*α*a and H-1*β*a), 3.90−3.92 (0.5H, m, H-5′*β*), 3.90−3.95 (1H, m, H-1*α*b and H-1*β*b), 3.93−3.96 (1H, m, H-5*α*a and H-5*β*a), 4.01/4.02 (each 0.5H, dd, J = 13.6, 3.2, H-1′*α*b and H-1′*β*b), 4.09−4.15 (2H, m, H-5*α*b, H-5*β*b, H-4*α* and H-4*β*), 4.25 (0.5H, ddd, J = 10.4, 8.8, 3.2, H-5′*α*), 4.45 (1H, m, H-3*α* and H-3*β*), 4.68 (0.5H, d, J = 8.0, H-1′*β*), 4.75 (1H, m, H-2*α* and H-2*β*), 5.26 (0.5H, d, J = 3.2, H-1′ *α*). ^{13}C NMR (200 MHz, D_2O) δ: 49.5/49.8 (C-6′*α* an d C6′*β*), 50.9 (C-1*α* and C1*β*), 61.82/61.83 (C-5*α* and C5*β*), 70.3 (C-5′*α*), 73.0/73.1 (C-4*α* and C4*β*), 73.9 (C-2′*α*), 74.2 (C-5′*β*), 74.8 (C-4′*β*), 74.9 (C-3′*α*), 75.0 (C-4′*α*), 76.5 (C-2′*β*), 77.8 (C-3′*β*), 79.7 (C-2*α* and C2*β*), 80.2/80.4 (C-3*α* and C3*β*), 95.0 (C-1′*α*), 98.8 (C-1′*β*). HRMS (ESI) m/z: [M − Cl]$^+$ Calcd for $C_{11}H_{21}O_8S$ 313.0952; Found 313.0944.

1,4-Dideoxy-1,4-{(*R*)-[(2*S*,3*S*,4*R*,5*S*)-2,3,4,5,6-pentahydroxyhexyl]episulfoniumylidene}-D-arabinitol Chloride (Neoponkoranol 6). To a solution of **34** (160 mg) in water (5 mL) was added $NaBH_4$ (60 mg, 1.57 mmol) at 0 °C, and the mixture was stirred at 0 °C for 5 h. The reaction mixture was acidified with 1 M HCl to pH 4 at 0 °C. After the reaction mixture was condensed *in vacuo*, the residue was triturated with methanol. The MeOH insoluble material was filtered off, and washed with methanol. The combined filtrate and washings were condensed *in vacuo*, to give a colorless solid (208 mg), which on column chromatography ($CHCl_3$/MeOH = 5/1 → 3/1 → 3/2) gave as colorless solid (172 mg). Repurification by HPLC (H_2O)

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gave the title compound **6** (82 mg, 52% from **α-32**) as a colorless solid. ^{1}H and ^{13}C NMR data of **6** agreed well with those reported.[6]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02894.

^{1}H and ^{13}C NMR spectra for all new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: muraoka@phar.kindai.ac.jp.

Notes

The authors declare no competing financial interest.

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