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Synthesis of New Nitrogen Analogues of Salacinol and Deoxynojirimycin and Their Evaluation as Glycosidase Inhibitors

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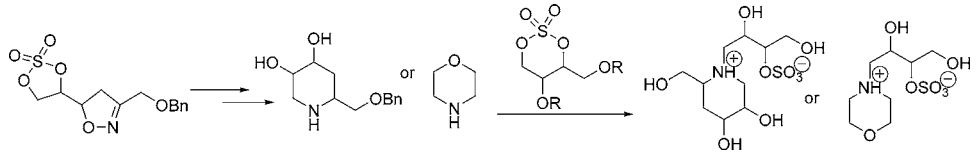

The synthesis of two enantiomerically pure iminosugars, analogues of 1-L-deoxynojirimycin (L-DNJ) and 1-D-deoxymannojirimycin (DMJ), was achieved using cyclic sulfate substituted isoxazoline derivatives. The piperidine ring was formed via the reduction of an isoxazoline into an amine which underwent a spontaneous intramolecular cyclization by reaction with the cyclic sulfate moiety. The nucleophilic attack of these two trisubstituted piperidines and morpholine on L- and D-erythritol-1,3-cyclic sulfates gave six new nitrogen analogues of salacinol. The inhibitory properties of the synthesized salacinol analogues were evaluated on several commercial glycosidases.

Introduction

Glycosidases are widely distributed in microorganisms, plants, and animals. They selectively hydrolyze glycosidic bonds and play important roles in crucial biological pathways, including polysaccharide and glycoconjugate anabolism and catabolism,[1] cellular recognition,[2] and eukaryotic glycoprotein processing.[3] Glycosidases are also involved in a variety of metabolic disorders and diseases such as diabetes, viral or bacterial infection, and cancer formation. Therefore, glycosidase inhibitors have many potential applications[4] as antidiabetic,[5] antiviral (HIV, influenza),[6] or anticancer[7] drugs.

The design and synthesis of glycosidase inhibitors are mainly focused on mimicking the transition state (TS) that occurs in enzymatic glycoside hydrolysis.[8] A partial positive charge develops at the anomeric carbon atom and the endocyclic oxygen atom (Figure 1). Natural and synthetic alkaloid sugar mimics with a nitrogen in the ring (iminosugars), such as 1-deoxynojirimycin (DNJ, **1**) and 1-deoxymannojirimycin (DMJ, **2**) (Figure 1), are of particular interest in inhibitor design.[8,9] They are supposed to be partially protonated in the active site at physiological pH, mimicking the TS where the positive charge is located at the endocyclic oxygen atom. As a consequence, a wide range of synthetic approaches including both chemical and enzymatic methods have been used to develop this class of compounds, employing a wide range of starting materials from sugars to aromatic compounds.[10]

Salacinol **3** (Figure 1) has recently been attracting a great deal of attention, due to the fact that the sulfonium cation ensures

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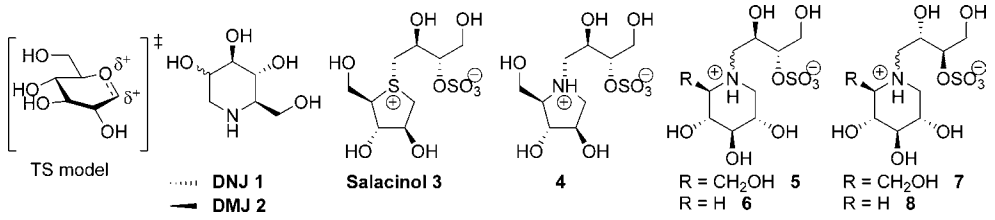
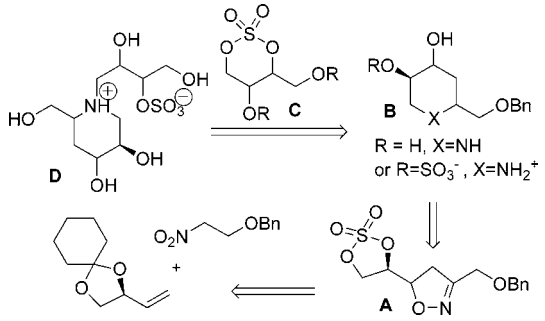


FIGURE 1. Transition-state model, DNJ and DMJ, salacinol, and its nitrogen analogues.

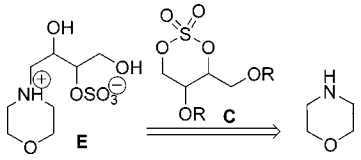
it a permanent positive charge. Salacinol is a naturally occurring α-glucosidase inhibitor found in *Salacia reticulata*.[11] The aqueous extracts of this plant are used in India and Sri Lanka in traditional medicine for the treatment of diabetes. This compound has a unique zwitterionic structure: a sulfonium cation stabilized by a sulfate anion. As for iminosugars, it was proposed that salacinol mimics the oxocarbenium-ion intermediate with the positive charge located on the endocyclic oxygen atom.[8] Salacinol can also be considered as a disaccharide-like substrate, with the acyclic part mimicking a second carbohydrate unit, and where the role of the sulfate group is not fully established. Several syntheses of salacinol[12] and analogues have been described including nitrogen (compounds **4**−**8**, Figure 1),[13] sulfur,[13c,d,14] and selenium analogues.[13d,15] Yuasa et al.[12a] initiated the major strategy employed for preparing such zwitterionic compounds, which is based on the nucleophilic attack of the heteroatom of a protected or unprotected polyhydroxylated heterocycle such as compound **B** at the least-hindered carbon atom of a protected L- or D-erythritol cyclic sulfate **C**, as illustrated in Scheme 1. Several nitrogen analogues of salacinol were synthesized, including **4** and several stereoisomers.[13a−c] Piperidine analogues **5**−**8** were also prepared, and **5** and **7** can be also considered as DNJ derivatives.[13d] Muraoka et al.[13b] showed that compound **4** inhibited intestinal α-glucosidases including maltase, sucrase, and isomaltase with IC_{50} values of 306, 44, and 136 μM, respectively. Almond β-glucosidase is not inhibited by **4**. Ghavami et al.[13a,c] showed that compound **4** and two other stereoisomers are not active against *Aspergillus niger* glucoamylase G2, barley α-amylase, and porcine pancreatic α-amylase. Compounds **5**−**8** are inactive against glucoamylase G2.[13d]

In a preliminary report, we described the synthesis of racemic trihydroxylated piperidines, which are analogues of DNJ and

SCHEME 1. Synthesis and Alkylation of the Piperidines



SCHEME 2. Morpholine Alkylation



DMJ, via a stereocontrolled reduction of an isoxazoline **A** by hydrogenolysis (Scheme 1).[16] Δ-2-Isoxazolines **A** are usually obtained by 1,3-dipolar cycloaddition reaction of nitrile oxides (generated in situ from primary nitro derivatives) with alkenes (Scheme 1). The key step of our isoxazoline route is the one-pot reduction of the isoxazoline moiety into an amine which attacks the sulfate ester in a highly stereoselective and regioselective intramolecular cyclization.

As part of a search for novel glycosidase inhibitors, we report here the synthesis of enantiomerically pure L-DNJ and D-DMJ analogues. Since the effect of substituting a sulfur atom of salacinol analogues by nitrogen has not been completely clarified, we also present the further transformation of morpholine and these iminosugars into their substituted ammonium derivatives (Schemes 1 and 2). To examine the influence of a side chain with different stereocenters, and of the permanent positive charge of the ammonium ion associated to the sulfate, we studied the activity of our zwitterionic piperidines **B** (where $R = SO_3^-$, $X = NH_2^+$) and alkylated zwitterionic piperidines **D** toward several glycosidases. We also studied compounds **E**, where the polyhydroxylated piperidine was replaced by morpholine.

Results and Discussion

1. Preparation of the Polyhydroxylated Piperidines. The first step of our synthesis (Scheme 3) starts with the 1,3-dipolar cycloaddition reaction of the nitrile oxide generated in situ from nitro compound **10**[17] with the optically pure alkene **9** prepared

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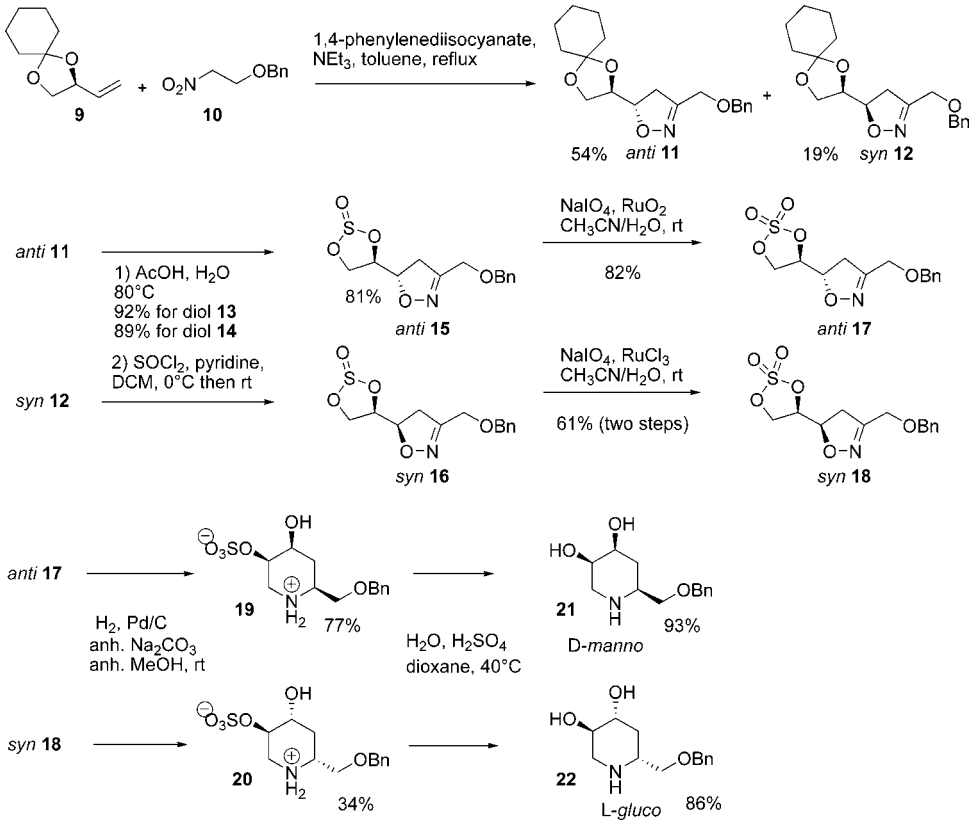
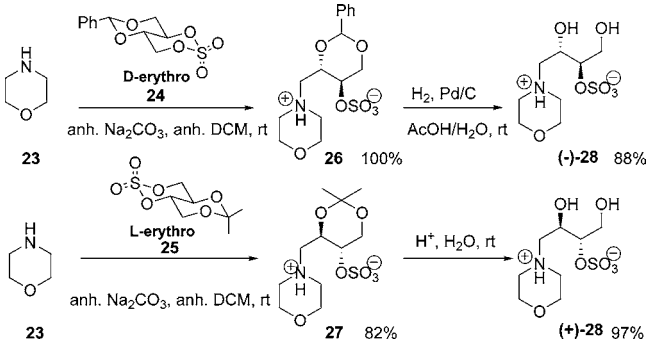
SCHEME 3. Synthesis of the Piperidines D-21 and L-22 via the Isoxazoline Sulfates 17 and 18



from D-mannitol.[18] The improved Mukaiyama procedure[19] was applied to afford the new isoxazolines *anti*-**11** and *syn*-**12** in 52% and 18% yield, respectively. The two diastereoisomers obtained in a 3:1 ratio were separated on silica gel. Removal of the cyclohexylidene moiety was performed in acetic acid and water,[20] and the diols **13** and **14** were isolated in 92% and 89% yield, respectively. During preparation of the cyclic sulfates **17** and **18** from cyclic sulfites **15** and **16**, we had previously observed a difference of the reactivity between the *anti* and *syn* stereoisomers.[16] Therefore, two different methods were needed to oxidize the sulfite group. Following a typical procedure,[21] cyclic sulfite *anti*-**15** was obtained in 81% yield. To prevent the partial oxidation of the benzyl ether into benzoate observed with $RuCl_3$,[16] the sulfite was then oxidized with catalytic RuO_2 in the presence of $NaIO_4$ in CH_3CN/H_2O. The cyclic sulfate *anti*-**17** was isolated in 82% yield. In the case of the syn configuration, the cyclic sulfite **16** was used without chromatographic purification and was oxidized with catalytic $RuCl_3$ in the presence of $NaIO_4$ in CH_3CN/H_2O. The cyclic sulfate **18** was thus isolated in 61% yield (two steps). The reduction of the isoxazolines **17** and **18** was performed by hydrogenolysis over 10% Pd/C in anhydrous methanol in the presence of sodium carbonate (Scheme 4). Anhydrous conditions were used to prevent competitive hydrolysis of the imine intermediate into ketone. Furthermore, without carbonate, strong acidification was observed due to sulfate decomposition resulting in the formation

SCHEME 4. Synthesis of Alkylated Morpholine (−)-28 and (+)-28



of byproducts. In basic conditions, the reduction of the isoxazoline was followed by the intermediate amine opening the cyclic sulfate ring, and the zwitterionic piperidines **19** and **20** were obtained in 77% and 34% yield, respectively, after purification by cation exchange chromatography (Dowex 50WX8, H^+ form). Compound **20** was analyzed in basic medium for solubility reasons. In both cases, the reaction was highly regioselective, giving only piperidine rings. From the isoxazoline *anti*-**17**, the reaction was also highly stereoselective, as only one compound was formed with high purity as evidenced by NMR analyses of the crude reaction mixture. In the case of the *syn* isomer **18**, the lower yield was due to the formation of several byproducts, which could not be clearly identified. In both cases, the benzyl group was not cleaved due to the basicity of the reaction medium. This was an advantage for the next steps. Indeed, this protective group may prevent the possible nucleophilicity-induced side reactions of a primary alcohol toward cyclic sulfates, and also simplify the purifications.

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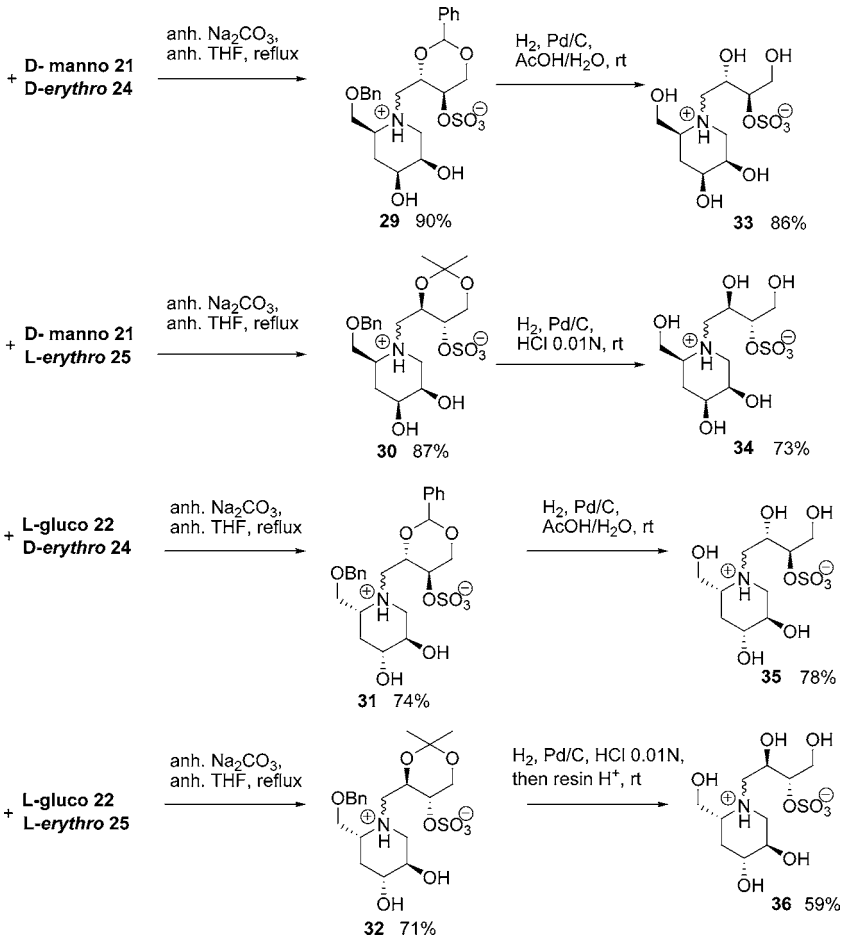
SCHEME 5. Synthesis of Alkylated Piperidines 33−36



The sulfate group of **19** and **20** was removed using concentrated H_2SO_4 and water in dioxane.[22] The new piperidines D-**21** and L-**22** were isolated in 93% and 86% yield, respectively, after purification by cation exchange chromatography (Dowex 50WX8, H^+ form). Compound D-**21** with D-manno configuration is a 1,4-D-dideoxymannojirimycin analogue, and L-**22** with L-gluco configuration is a 1,4-L-dideoxynojirimycin analogue.

2. Preparation of the Salacinol Analogues. Preparation of the zwitterionic compounds required the synthesis of the cyclic sulfates D-*erythro* **24** and L-*erythro* **25**. Both sulfates were obtained from D-glucose as previously described.[14b] Morpholine, first chosen as a model, was reacted with the two cyclic sulfates **24** and **25** in anhydrous dichloromethane in the presence of sodium carbonate at room temperature (Scheme 4). The protected zwitterionic compounds **26** and **27** were isolated in quantitative and 82% yield, respectively. This difference in the reactivity of these two cyclic sulfates was also observed with thio heterocycles. We suggested that the axial methyl group of the acetonide protection creates steric hindrances in the nucleophile approach.[14b] Nevertheless, the yields were excellent, and we have shown that such coupling reactions do not always require polar solvents such as DMF, methanol, acetone, or hexafluoro-2-propanol (HFIP).[12−15] Removal of the benzylidene protective group of **26** was performed by hydrogenolysis catalyzed by 10% Pd/C in aqueous acetic acid. The alkylated morpholine (−)-**28** was obtained in 88% yield as an amorphous solid. The acetonide protective group of **27** was hydrolyzed in the presence of acidic Dowex 50WX8 resin. Compound (+)-**28** was isolated in 97% yield as an amorphous solid.

In the case of the piperidines **21** and **22**, dichloromethane had to be replaced by another solvent. After several attempts with various more polar solvents (acetone, MeOH, etc.), anhydrous THF was found to be the best. In the presence of sodium carbonate and after several hours under reflux with either cyclic sulfate **24** or **25**, compounds **29** and **30** were isolated from piperidine D-manno **21** in 90% and 87% yield, respectively. Under the same conditions, the L-gluco stereoisomer **22** was reacted with D-erythro cyclic sulfate **24** and L-erythro **25**. Zwitterionic compounds **31** and **32** were isolated in 74% and 71% yield, respectively.

Benzyl ether and benzylidene protective groups were cleaved by hydrogenolysis over 10% Pd/C in aqueous acetic acid. From **29** and **31**, **33** and **35** were prepared in 86% and 78% yield, respectively. The acetonide protective group was cleaved during the hydrogenolysis by HCl-catalyzed hydrolysis. Zwitterions **34** and **36** were isolated in 73% and 59% nonoptimized yield, respectively (Scheme 5).

As observed by Pinto et al. with their compounds,[13d] the zwitterionic salts **27** to **36** gave dramatically broadened ^{1}H NMR spectra and nonobservable ^{13}C signals mainly for the heterocycle moiety at neutral pH. These observations were attributed to the equilibrium taking place at NMR time scale, between the *R* and *S* configurations of the conjugate acids through the free amines with their nitrogen inversion.[13d] The addition of sodium carbon-

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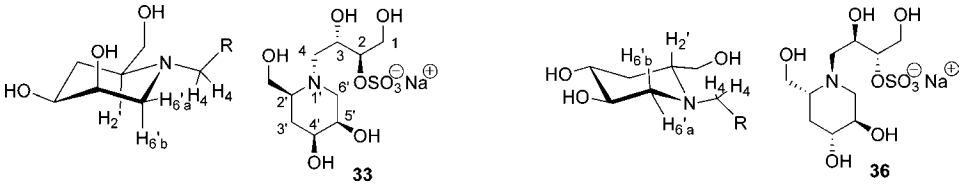

FIGURE 2. Conformation of **33** and **36** in basic medium.

ate to the NMR samples gave the deprotonated amine form and the sulfate with sodium as a counterion, with which standard signals were then observed. As a result, the carbonate neutralizing the ammonium, the NMR spectra of compounds **27** to **36** are described as amine and sodium sulfate salts. Compound **26** was an exception and could be studied in its zwitterionic form.

As determined by NMR analyses, the major conformation adopted by the piperidine rings was $^{6'}C_{3'}$ ($^{1}C_4$ as usually employed if those compounds are considered as carbohydrates analogues and using carbohydrate numbering) for D-manno configuration **33** and **34** and $^{3'}C_{6'}$ for L-gluco **35** and **36** ($^{4}C_1$ using carbohydrate numbering) (Figure 2). In every case, the amines were present in one major configuration at the nitrogen center. Determination of this configuration was performed on the sodium salt forms of **33** and **36** with a NOESY experiment. Correlations were found between the two H_4 with $H_{2'}$, $H_{6'b}$, and $H_{6'a}$. The bond $N-C_4$ is in the equatorial position, and the linear chain is *trans* relative to the hydroxymethyl (Figure 2). Such a conformation and configuration were also observed on other analogous compounds.[13c,d] By extension and based on NMR results for **34** and **35**, we can propose the same *trans* configuration between the hydroxymethyl and the side chain bonded to the nitrogen.

3. Glycosidase Inhibition Studies. The zwitterionic piperidines **19** and **20** and the alkylated heterocycles (−)-**28**, (+)-**28** and **33**−**36** were evaluated as inhibitors of six commercial glycosidases: baker's yeast α-glucosidase, rice α-glucosidase, almond β-glucosidase, green coffee bean α-galactosidase, *Aspergillus oryzae* β-galactosidase, and jack bean α-mannosidase. *p*-Nitro- or *o*-nitrophenylglycopyranosides were used as the corresponding substrates following a previously described procedure.[14b]

To our surprise, all of the zwitterionic compounds **19**, **20**, (−)-**28**, (+)-**28**, and **33**−**36** showed no activity against the tested glycosidases. Pinto et al. also found no activity toward glucoamylase with zwitterionic DNJ analogues **5**−**8** (Figure 1).[13d] Only (+)-**28** (morpholine with salacinol side chain) induced a slight inhibition ($K_i \approx 2$ mM, noncompetitive) of green coffee bean α-galactosidase. A few years ago, morpholines bearing an alkyl hydroxylated chain (CH_2CH_2OH, $CH_2CHOHCH_2OH$, $CH(CH_2OH)_2$) were shown to inhibit almond β-glucosidase (Ki 620, 640, and 730 μM, respectively).[23] The zwitterionic morpholine derivatives (+)- and (−)-**28** possessing both sulfate and permanent ammonium groups had lost their inhibitory potential.

Regarding the zwitterionic piperidines **19** and **20**, it should be noted that the interaction with the C(2)OH group in the active site has been proven to be fundamental to good inhibition.[24] As a result, the bulkier and negatively charged sulfate group in this position may have induced the loss of inhibition. Concerning all of the other zwitterionic compounds **33**−**36**, this ammonium sulfate association carried a negative effect. Somehow, this was surprising, since *N*,*N*-dimethyl-1-DNJ and *N*-methyl-1-DNJ *-N*-oxide, having a permanent positive charge (ammonium), have been previously described as inhibitors of α- and β-glucosidases.[25]

In conclusion, we have developed an original asymmetric synthesis of two polysubstituted piperidines with D-manno and L-gluco configurations. The one-pot reduction−cyclization key step on isoxazoline sulfate compounds was highly regio- and stereoselective for the D-manno series. Coupling the two piperidines and morpholine with two cyclic 1,3-sulfates allowed us to isolate new zwitterionic analogues of salacinol, in very high yields. The evaluation of inhibitory properties revealed that the zwitterionic compounds showed no activity against the tested enzymes. The association of an ammonium and a sulfate anion has an apparently negative effect on inhibition.

Experimental Section

(5*S*)-3-Benzyloxymethyl-5-[(1*R*)-1,2-*O*-cyclohexylidene-1,2-dihydroxyethyl]-2-isoxazoline 11 and (5*R*)-3-Benzyloxymethyl-5-[(1*R*)-1,2-*O*-cyclohexylidene-1,2-dihydroxyethyl]-2-isoxazoline 12. To a solution of benzyloxynitroethane **10** (3.87 g, 21.3 mmol, 1.2 equiv) in anhydrous toluene (160 mL) were added under argon (2*S*)-1,2-*O*-cyclohexylidenebut-3-ene-1,2-diol **9** (2.93 g, 17.4 mmol), 1,4-phenylenediisocyanate (10.43 g, 64.4 mmol, 3.7 equiv), and NEt_3 (320 μL, 2.3 mmol, 0.1 equiv). The mixture was refluxed for 42 h. Water (35 mL) was then added, and the mixture was refluxed for 6 h. The precipitate thus formed was filtered and washed with cyclohexane. The organic phase was dried over $MgSO_4$ and concentrated under vacuum. The crude product was purified by flash chromatography (cyclohexane/ether, 8:2 then 6:4) to give **11** (2.99 g, 52%) and **12** (1.03 g, 18%) as slightly yellow oils.

11: R_f 0.18 (cyclohexane/ether, 7:3); $[\alpha]_D$ +60 (*c* 1.3, $CHCl_3$); IR (film) ν 3030, 1626, 1099 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38−7.28 (m, 5H, H_{arom}), 4.58−4.49 (m, 1H, H_3), 4.53 (s, 2H, H_7), 4.29 (s, 2H, H_6), 4.10 (dd, 1H, H_{1a}, $J_{1a-2} = 6.2$, $J_{1a-1b} = 8.5$ Hz), 4.04−3.99 (m, 1H, H_2), 3.87 (dd, 1H, H_{1b}, $J_{1b-2} = 4.8$, $J_{1b-1a} = 8.5$ Hz), 3.15 (dd, 1H, H_{4a}, $J_{4a-3} = 9.8$, $J_{4a-4b} = 17.5$ Hz), 3.09 (dd, 1H, H_{4b}, $J_{4b-3} = 7.0$, $J_{4b-4a} = 17.5$ Hz), 1.63−1.52 (m, 10H, $5CH_2$); ^{13}C NMR ($CDCl_3$) δ 156.5 (C_5), 137.2, 128.4, 127.8, 127.7 (C_{arom}), 110.1 (C_8), 80.8 (C_3), 75.5 (C_2), 72.5 (C_7), 66.6 (C_1), 64.3 (C_6), 37.8 (C_4), 36.3, 34.5, 25.0, 23.8, 23.6 ($5CH_2$); MS (CI) *m*/*z* 332 [(M + H)$^+$]. Anal. Calcd for $C_{19}H_{25}NO_4$: C, 68.86; H, 7.60; N, 4.23. Found: C, 68.80; H, 7.50; N, 4.35.

12: R_f 0.11 (cyclohexane/ether, 7:3); $[\alpha]_D$ −85 (*c* 1.3, $CHCl_3$); IR (film) ν 3030, 1626, 1071 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.39−7.30 (m, 5H, H_{arom}), 4.66 (ddd, 1H, H_3, $J_{3-2} = 4.4$, $J_{3-4b} = 7.9$, $J_{3-4a} = 10.9$ Hz), 4.55 (d_{AB}, 1H, H_{7a}, $J_{AB} = 11.7$ Hz), 4.50 (d_{AB}, 1H, H_{7b}, $J_{AB} = 11.7$ Hz), 4.30 (s, 2H, H_6), 4.21 (td, 1H, H_2, $J_{2-3} = 4.4$, $J_{2-1b} = J_{2-1a} = 6.5$ Hz), 4.04 (dd, 1H, H_{1a}, $J_{1a-2} = 6.5$, $J_{1a-1b} = 8.4$ Hz), 3.84 (dd, 1H, H_{1b}, $J_{1b-2} = 6.5$, $J_{1b-1a} = 8.4$ Hz), 3.10 (dd, 1H, H_{4a}, $J_{4a-3} = 10.9$, $J_{4a-4b} = 17.4$ Hz), 3.00 (dd, 1H, H_{4b}, $J_{4b-3} = 7.9$, $J_{4b-4a} = 17.4$ Hz), 1.67−1.44 (m, 10H, $5CH_2$);

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^{13}C NMR ($CDCl_3$) δ 156.2 (C_5), 137.2, 128.3, 127.8 (C_{arom}), 110.3 (C_8), 79.7 (C_3), 76.1 (C_2), 72.3 (C_7), 64.8 (C_1), 64.2 (C_6), 37.0 (C_4), 35.7, 34.7, 25.0, 23.8, 23.6 ($5CH_2$); MS (CI) *m*/*z* 332 [$(M + H)^+$]. Anal. Calcd for $C_{19}H_{25}NO_4$: C, 68.86; H, 7.60; N, 4.23. Found: C, 69.01; H, 7.70; N, 4.25.

(5*S*)-3-Benzyloxymethyl-5-[(1*R*)-1,2-dihydroxyethyl]-2-isoxazoline 13. Following the procedure described by Gravestock et al.,[20] diol **13** (3.24 g, 12.3 mmol) was obtained in 92% yield after purification on silica gel (cyclohexane/ether, 6:4).

The spectral data are consistent with the data from the literature.[17]

(5*R*)-3-Benzyloxymethyl-5-[(1*R*)-1,2-dihydroxyethyl]-2-isoxazoline 14. Following the procedure described by Gravestock et al.,[20] diol **14** (693 mg, 2.76 mmol) was obtained in 89% yield after purification on silica gel (cyclohexane/ether, 6:4).

The spectral data are consistent with the data from the literature.[17]

(5*S*)-3-Benzyloxymethyl-5-[(4*R*)-2-oxo-1,3,2-dioxathiolan-4-yl]-2-isoxazoline 15. To a solution of diol **13** (3.05 g, 12.1 mmol) and anhydrous pyridine (3 mL, 36.8 mmol, 3 equiv) in anhydrous CH_2Cl_2 (110 mL) was added dropwise at 0 °C and under argon a solution of $SOCl_2$ (1 mL, 13.7 mmol, 1.1 equiv) in anhydrous CH_2Cl_2 (25 mL). Stirring was continued at room temperature for 2 h. The mixture was washed with water (2 × 40 mL) and then with brine (60 mL). The organic phase was dried over $MgSO_4$ and concentrated under vacuum. The crude product was purified by flash chromatography (cyclohexane/AcOEt, 6:4) to give a slightly yellow oil (2.94 g, 81%) as a mixture of two diastereoisomers (67:33): R_f 0.36 (cyclohexane/AcOEt, 6:4); $[\alpha]_D$ +44 (*c* 1.4, $CHCl_3$); IR (film) ν 1628, 1209, 1093 cm^{-1}. *Major isomer:* ^{1}H NMR ($CDCl_3$) δ 7.40−7.30 (m, 5H, H_{arom}), 4.78 (dd, 1H, H_{1a}, J_{1a-2} = 6.2, J_{1a-1b} = 9.0 Hz), 4.69 (ddd, 1H, H_2, J_{2-1b} = 3.8, J_{2-1a} = 6.2, J_{2-3} = 8.4 Hz), 4.55 (s, 2H, H_7), 4.51 (ddd, 1H, H_3, J_{3-4b} = 5.8, J_{3-2} = 8.4, J_{3-4a} = 10.4 Hz), 4.47 (dd, 1H, H_{1b}, J_{1b-2} = 3.8, J_{1b-1a} = 9.0 Hz), 4.30 (s, 2H, H_6), 3.32−3.19 (m, 1H, H_{4a}), 3.06 (dd, 1H, H_{4b}, J_{4b-3} = 5.8, J_{4b-4a} = 17.8 Hz); ^{13}C NMR ($CDCl_3$) δ 157.1 (C_5), 137.0, 128.6, 127.9 (C_{arom}), 80.2 (C_2), 77.1 (C_3), 73.0 (C_7), 69.1 (C_1), 64.2 (C_6), 38.6 (C_4). *Minor isomer:* ^{1}H NMR ($CDCl_3$) δ 7.40−7.30 (m, 5H, H_{arom}), 4.88 (ddd, 1H, H_2, *J* = 6.6, J_{2-3} = 7.5, *J* = 9.9 Hz), 4.65−4.57 (m, 2H, H_{1a} and H_{1b}), 4.55 (s, 2H, H_7), 4.41 (td, 1H, H_3, *J* = 7.5 Hz), 4.30 (s, 2H, H_6), 3.32−3.19 (m, 2H, H_{4b} and H_{4a}); ^{13}C NMR ($CDCl_3$) δ 157.2 (C_5), 137.1, 128.6, 127.9 (C_{arom}), 81.6 (C_2), 77.5 (C_3), 73.0 (C_7), 70.1 (C_1), 64.1 (C_6), 38.7 (C_4); MS (CI) *m*/*z* 298 [$(M + H)^+$]. Anal. Calcd for $C_{13}H_{15}NO_5S$: C, 52.52; H, 5.08; N, 4.71; S, 10.78. Found: C, 52.68; H, 5.13; N, 4.74; S, 10.76.

(5*R*)-3-Benzyloxymethyl-5-[(4*R*)-2-oxo-1,3,2-dioxathiolan-4-yl]-2-isoxazoline 16. Sulfite **16** was prepared as described above for compound **15** without the flash chromatography purification step. It was characterized as a slightly yellow oil obtained in 85% yield (1.81 g, 6 mmol) after flash chromatography (cyclohexane/AcOEt, 6:4). Mixture of two diastereoisomers (64:36): R_f 0.26 (cyclohexane/AcOEt, 6:4); $[\alpha]_D$ −158 (*c* 1.2, $CHCl_3$); IR (film) ν 1628, 1209, 1093 cm^{-1}. *Major isomer:* ^{1}H NMR ($CDCl_3$) δ 7.39−7.30 (m, 5H, H_{arom}), 5.03−4.94 (m, 1H, H_2), 4.79−4.73 (m, 2H, H_3 and H_{1a}), 4.58−4.48 (m, 2H, H_7), 4.40 (dd, 1H, H_{1b}, *J* = 5.7, *J* = 8.6 Hz), 4.30 (s, 2H, H_6), 3.29−3.12 (m, 1H, H_{4a}), 3.07 (dd, H, H_{4b}, *J* = 7.1, *J* = 17.6 Hz); ^{13}C NMR ($CDCl_3$) δ 156.6 (C_5), 128.6, 128.0 (C_{arom}), 79.9 (C_2), 77.6 (C_3), 72.8 (C_7), 68.5 (C_1), 64.1 (C_6), 37.5 (C_4). *Minor isomer:* ^{1}H NMR ($CDCl_3$) δ 7.39−7.30 (m, 5H, H_{arom}), 5.03−4.94 (m, 1H, H_2), 4.65−4.60 (m, 1H, H_3), 4.58−4.48 (m, 4H, $2H_7$, H_{1b} and H_{1a}), 4.30 (s, 2H, H_6), 3.29−3.12 (m, 2H, H_{4b} and H_{4a}); ^{13}C NMR ($CDCl_3$) δ 128.1, 128.0 (C_{arom}), 82.5 (C_2), 77.7 (C_3), 72.9 (C_7), 67.0 (C_1), 64.1 (C_6), 37.7 (C_4); MS (CI) *m*/*z* 298 [$(M + H)^+$]. Anal. Calcd for $C_{13}H_{15}NO_5S$: C, 52.52; H, 5.08; N, 4.71; S, 10.78. Found: C, 52.36; H, 5.29; N, 4.68; S, 10.73.

Note: absent δ for some carbons means that the signals were not detected.

(5*S*)-3-Benzyloxymethyl-5-[(4*R*)-2,2-dioxo-1,3,2-dioxathiolan-4-yl]-2-isoxazoline 17. To a solution of sulfite **15** (2.59 g, 8.7 mmol) in acetonitrile (95 mL) containing RuO_2 (170 mg, 1.27 mmol, 0.15 equiv) was added a solution of $NaIO_4$ (3.93 g, 17.5 mmol, 2 equiv) in water (20 mL). The mixture was stirred at room temperature for 32 h and then extracted with CH_2Cl_2 (3 × 30 mL). Organic phases were washed with brine (50 mL), dried over $MgSO_4$, and concentrated under vacuum. The crude product was purified by flash chromatography (cyclohexane/AcOEt, 6:4) to give **17** (2.24 g, 82%) as a slightly yellow oil: R_f 0.40 (cyclohexane/AcOEt, 5:5); $[\alpha]_D$ +49 (*c* 1.1, $CHCl_3$); IR (film) ν 1389, 1210, 1093 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.40−7.30 (m, 5H, H_{arom}), 4.82 (ddd, 1H, H_3, J_{3-4b} = 5.5, J_{3-2} = 8.1, J_{3-4a} = 10.5 Hz), 4.77 (dd, 1H, H_{1a}, *J* = 3.0, *J* = 8.1 Hz), 4.64−4.57 (m, 2H, H_2 and H_{1b}), 4.57 (d_{AB}, 1H, H_{7a}, J_{AB} = 11.9 Hz), 4.53 (d_{AB}, 1H, H_{7b}, J_{AB} = 11.9 Hz), 4.32 (d_{AB}, 1H, H_{6a}, J_{AB} = 12.8 Hz), 4.28 (d_{AB}, 1H, H_{6b}, J_{AB} = 12.8 Hz), 3.29 (dd, 1H, H_{4a}, J_{4a-3} = 10.5, J_{4a-4b} = 17.9 Hz), 3.09 (dd, 1H, H_{4b}, J_{4b-3} = 5.5, J_{4b-4a} = 17.9 Hz); ^{13}C NMR ($CDCl_3$) δ 157.1 (C_5), 137.0, 128.6, 128.2, 128.0 (C_{arom}), 79.3 (C_2), 77.6 (C_3), 73.3 (C_7), 70.4 (C_1), 64.0 (C_6), 38.7 (C_4); MS (EI) *m*/*z* 314 [$(M + H)^+$]. Anal. Calcd for $C_{13}H_{15}NO_6S$: C, 49.83; H, 4.83; N, 4.47; S, 10.23. Found: C, 48.72; H, 5.05; N, 4.33; S, 10.07.

(5*R*)-3-Benzyloxymethyl-5-[(4*R*)-2,2-dioxo-1,3,2-dioxathiolan-4-yl]-2-isoxazoline 18. To a solution of crude sulfite **16** (0.539 g, 1.8 mmol) in acetonitrile (20 mL) containing $RuCl_3$ (37 mg, 0.18 mmol, 0.1 equiv) was added a solution of $NaIO_4$ (0.582 g, 2.7 mmol, 1.5 equiv) in water (4.5 mL). The mixture was stirred at room temperature for 50 min and then extracted with CH_2Cl_2 (3 × 20 mL). Organic phases were washed with brine (20 mL), dried over $MgSO_4$, and concentrated under vacuum. The crude product was purified by flash chromatography (cyclohexane/AcOEt, 6:4) to give **18** (0.34 g, 61%, two steps) as a white solid: R_f 0.26 (cyclohexane/AcOEt, 5:5); $[\alpha]_D$ −129 (*c* 1.1, $CHCl_3$); mp 93 °C; IR (KBr) ν 1389, 1210, 1093 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.39−7.30 (m, 5H, H_{arom}), 4.98 (td, 1H, H_2, J_{2-3} = 3.3, J_{2-1b} = J_{2-1a} = 7.0 Hz), 4.83 (ddd, 1H, H_3, J_{3-2} = 3.3, J_{3-4b} = 6.9, J_{3-4a} = 11.4 Hz), 4.73−4.65 (m, 2H, H_1), 4.57 (d_{AB}, 1H, H_{7a}, J_{AB} = 11.9 Hz), 4.53 (d_{AB}, 1H, H_{7b}, J_{AB} = 11.9 Hz), 4.31 (s, 2H, H_6), 3.29 (dd, 1H, H_{4a}, J_{4a-3} = 11.4, J_{4a-4b} = 17.8 Hz), 3.12 (dd, 1H, H_{4b}, J_{4b-3} = 6.9, J_{4b-4a} = 17.8 Hz); ^{13}C NMR ($CDCl_3$) δ 156.7 (C_5), 137.1, 128.8, 128.3, 128.2 (C_{arom}), 80.6 (C_2), 76.6 (C_3), 73.1 (C_7), 68.8 (C_1), 64.0 (C_6), 37.3 (C_4); MS (IC) *m*/*z* 314 [$(M + H)^+$]. Anal. Calcd for $C_{13}H_{15}NO_6S$: C, 49.83; H, 4.83; N, 4.47; S,10.23. Found: C, 49.72; H, 4.89; N, 4.45; S, 10.13.

(2*S*,4*S*,5*R*)-2-Benzyloxymethyl-4-hydroxypiperidinium 5-Sulfate 19. A solution of sulfate **17** (1.43 g, 4.6 mmol) in anhydrous MeOH (82 mL) containing 10% Pd/C (786 mg) and anhydrous Na_2CO_3 (536 mg, 5.0 mmol, 1.1 equiv) was stirred at room temperature under an H_2 atmosphere for 5 h. The catalyst was filtered and washed with MeOH. The filtrate was concentrated under vacuum, and the crude product was purified by cation-exchange chromatography (Dowex 50WX8, 200−400 mesh, H^+ form) eluted with distilled water. A white solid was isolated (1.12 g, 77%): R_f 0.27 (CH_2Cl_2/MeOH, 85:15); $[\alpha]_D$ −11 (*c* 1.0, H_2O); mp 182 °C; IR (KBr) ν 3410, 2538, 1622, 1270, 1228, 1078, 1048 cm^{-1}; ^{1}H NMR (D_2O) δ 7.48−7.39 (m, 5H, H_{arom}), 4.77 (br s, 1H, H_5), 4.63 (s, 2H, H_8), 4.05 (ddd, 1H, H_4, J_{4-3a} = 3.4, J_{4-5} = 4.8, J_{4-3b} = 12.6 Hz), 3.84 (dd, 1H, H_{6a}, J_{6a-5} = 3.0, J_{6a-6b} = 14.1 Hz), 3.74 (dd, 1H, H_{7a}, J_{7a-2} = 3.7, J_{7a-7b} = 11.1 Hz), 3.65 (dd, 1H, H_{7b}, J_{7b-2} = 8.3, J_{7b-7a} = 11.1 Hz), 3.59−3.51 (m, 1H, H_2), 3.27 (dd, 1H, H_{6b}, J_{6b-5} = 1.3, J_{6b-6a} = 14.1 Hz), 1.99 (td, 1H, H_{3a}, J_{3a-4} = J_{3a-2} = 3.4, J_{3a-3b} = 12.6 Hz), 1.82 (td, 1H, H_{3b}, *J* = 12.6 Hz); ^{13}C NMR (D_2O) δ 136.9, 128.8, 128.5 (C_{arom}), 73.1 (C_8), 72.8 (C_5), 68.8 (C_7), 65.6 (C_4), 55.0 (C_2), 45.7 (C_6), 27.4 (C_3); HRMS (LSIMS+) calcd for $C_{13}H_{20}NO_6S$ [$(M + H)^+$] 318.1011, found 318.1014.

(2*R*,4*R*,5*R*)-2-Benzyloxymethyl-4-hydroxypiperidinium 5-Sulfate 20. Sulfate **18** (714 mg, 2.3 mmol) was reacted as described above for compound **17**. Compound **20** was isolated as a white solid (248 mg, 34%): R_f 0.38 (CH_2Cl_2/MeOH, 85:15); $[\alpha]_D$ −34 (*c* 1.0, NH_4OH 0.1 N); mp 241 °C; IR (KBr) ν 3315, 2547, 1640, 1263, 1216, 1104, 1040 cm^{-1}; ^{1}H NMR (D_2O + Na_2CO_3) δ 7.46−

7.36 (m, 5H, H_{arom}), 4.57 (s, 2H, H_8), 4.06 (ddd, 1H, H_5, J_{5-6a} = 5.2, J_{5-4} = 9.1, J_{5-6b} = 10.8 Hz), 3.68 (ddd, 1H, H_4, J_{4-3a} = 5.1, J_{4-5} = 9.1, J_{4-3b} = 12.1 Hz), 3.54 (dd, 1H, H_{7a}, J_{7a-2} = 4.4, J_{7a-7b} = 10.3 Hz), 3.43 (dd, 1H, H_{7b}, J_{7b-2} = 7.4, J_{7b-7a} = 10.3 Hz), 3.41 (dd, 1H, H_{6a}, J_{6a-5} = 5.2, J_{6a-6b} = 12.2 Hz), 2.92−2.85 (m, 1H, H_2), 2.53 (dd, 1H, H_{6b}, J_{6b-5} = 10.8, J_{6b-6a} = 12.2 Hz), 2.01 (ddd, 1H, H_{3a}, J_{3a-2} = 2.6, J_{3a-4} = 5.1, J_{3a-3b} = 12.1 Hz), 1.23 (td, 1H, H_{3b}, J = 12.1 Hz); ^{13}C NMR (D_2O + Na_2CO_3) δ 137.3, 128.7, 128.4, 128.3 (C_{arom}), 80.1 (C_5), 73.0 (C_8), 72.7 (C_7), 70.3 (C_4), 53.2 (C_2), 46.9 (C_6), 34.7 (C_3); HRMS (LSIMS+) calcd for $C_{13}H_{20}NO_6S$ [(M + H)$^+$] 318.1011, found 318.1012.

(2*S*,4*S*,5*R*)-2-Benzyloxymethyl-4,5-dihydroxypiperidine 21. A solution of **19** (999 mg, 3.1 mmol) in 1,4-dioxane (50 mL) was heated at 50 °C with water (500 μL) and concentrated H_2SO_4 (600 μL) for 36 h. The mixture was neutralized by NH_4OH (1 N) and concentrated under vacuum. The crude product was purified by cation-exchange chromatography (Dowex 50WX8, 200−400 mesh, H^+ form) eluted with distilled water and then 0.5 N NH_4OH to give **21** (697 mg, 93%) as a slightly yellow solid: R_f 0.21 (CH_2Cl_2/MeOH/H_2O, 55:40:5); $[\alpha]_D$ −22 (*c* 1.0, H_2O); mp 88 °C; IR (KBr) ν 3384, 3237, 1141, 1049 cm^{-1}; ^{1}H NMR (D_2O) δ 7.46−7.37 (m, 5H, H_{arom}), 4.58 (s, 2H, H_8), 3.83 (br s, 1H, H_5), 3.75 (ddd, 1H, H_4, J_{4-3a} = 3.1, J_{3-5} = 4.8, J_{4-3b} = 12.0 Hz), 3.56−3.48 (m, 2H, H_7), 3.02 (dd, 1H, H_{6a}, J_{6a-5} = 2.9, J_{6a-6b} = 14.1 Hz), 2.83−2.76 (m, 1H, H_2), 2.68 (dd, 1H, H_{6b}, J_{6b-5} = 1.5, J_{6b-6a} = 14.1 Hz), 1.69 (ddd, 1H, H_{3a}, J_{3a-4} = 3.1, J_{3a-2} = 4.0, J_{3a-3b} = 12.0 Hz), 1.45 (td, 1H, H_{3b}, J = 12.0 Hz); ^{13}C NMR (D_2O) δ 137.4, 128.7, 128.4, 128.3 (C_{arom}), 73.0 (C_8), 72.9 (C_7), 69.2 (C_4), 67.1 (C_5), 53.5 (C_2), 48.6 (C_6), 30.3 (C_3); HRMS (LSIMS+) calcd for $C_{13}H_{20}NO_3$ [(M + H)$^+$] 238.1443, found 238.1442.

(2*R*,4*R*,5*R*)-2-Benzyloxymethyl-4,5-dihydroxypiperidine 22. Compound **20** (147 mg, 0.46 mmol) was reacted as described above for **19**. Compound **22** was isolated as a slightly yellow solid (94.4 mg, 86%): R_f 0.43 (CH_2Cl_2/MeOH/H_2O, 55:40:5); $[\alpha]_D$ −29 (*c* 1.0, H_2O); mp 102 °C; IR (KBr) ν 3420, 3320, 1175, 1155, 1049 cm^{-1}; ^{1}H NMR (D_2O) δ 7.46−7.37 (m, 5H, H_{arom}), 4.58 (d_{AB}, 1H, H_{8a}, J_{AB} = 11.9 Hz), 4.55 (d_{AB}, 1H, H_{8b}, J_{AB} = 11.9 Hz), 3.54 (dd, 1H, H_{7a}, J = 4.3, J = 10.4 Hz), 3.51−3.46 (m, 1H, H_4), 3.44−3.37 (m, 2H, H_{7b} and H_5), 3.11 (dd, 1H, H_{6a}, J_{6a-5} = 5.1, J_{6a-6b} = 11.9 Hz), 2.91−2.84 (m, 1H, H_2), 2.41 (dd, 1H, H_{6b}, J_{6b-5} = 10.6, J_{6b-6a} = 11.9 Hz), 1.94 (ddd, 1H, H_{3a}, J = 2.5, J = 4.8, J_{3a-3b} = 12.1 Hz), 1.14 (td, 1H, H_{3b}, J = 12.1 Hz); ^{13}C NMR (D_2O) δ 137.3, 128.7, 128.4, 128.3 (C_{arom}) 73.0 (C_8), 72.9 (C_7), 72.7 (C_4), 72.2 (C_5), 53.5 (C_2), 49.1 (C_6), 34.8 (C_3); HRMS (LSIMS+) calcd for $C_{13}H_{20}NO_3$ [(M + H)$^+$] 238.1443, found 238.1441.

General Procedure for Morpholine Coupling Reaction. The cyclic sulfate **24** or **25** (1.2 mmol) was dissolved in anhydrous CH_2Cl_2 (5 mL) in the presence of anhydrous Na_2CO_3 (0.5 mmol) under argon. Morpholine **23** (1.0 mmol) was added, and the mixture was stirred at room temperature for several days and then concentrated under vacuum. The crude product was purified by flash chromatography (CH_2Cl_2/MeOH, 85:15) to give **26** or **27**.

(2*R*,3*S*)-1,3-*O*-Benzylidene-1,3-dihydroxy-4-(morpholin-4-ium-4-yl)butane-2-sulfate 26. Compound **26** was obtained as a white solid after 2 days of stirring (34.7 mg, quantitative): R_f 0.28 (CH_2Cl_2/MeOH, 85:15); $[\alpha]_D$ −37 (*c* 1.0, MeOH); mp 143 °C; IR (KBr) ν 2765, 1619, 1243, 1012 cm^{-1}; ^{1}H NMR (CD_3OD) δ 7.49−7.46 (m, 2H, H_{arom}), 7.37−7.33 (m, 3H, H_{arom}), 5.63 (s, 1H, H_5), 4.55 (dd, 1H, H_{1a}, J_{1a-2} = 5.3, J_{1a-1b} = 10.9 Hz), 4.25 (td, 1H, H_2, J_{2-1a} = 5.3, J = 9.8, J = 9.8 Hz), 4.16 (td, 1H, H_3, J = 1.2, J = 8.2, J = 8.2 Hz), 3.84−3.74 (m, 5H, $4H_{2'}$ and H_{1b}), 3.38 (br d, 1H, H_{4a}, J = 13.8 Hz), 3.06−2.96 (m, 5H, $4H_{3'}$ and H_{4b}); ^{13}C NMR (CD_3OD) δ 138.9, 130.1, 129.2, 127.5 (C_{arom}), 102.3 (C_5), 77.7 (C_3), 70.3 (C_1), 69.2 (C_2), 66.3 ($2C_{2'}$), 59.8 (C_4), 54.8 ($2C_{3'}$); HRMS (ESI+) calcd for $C_{15}H_{21}NO_7NaS$ [(M + Na)$^+$] 382.0936, found 382.0917.

(2*S*,3*R*)-1,3-Dihydroxy-1,3-*O*-isopropylidene-4-(morpholin-4-ium-4-yl)butane-2-sulfate 27. Compound **27** was obtained as a white solid after 4 days of stirring (295 mg, 82%): R_f 0.22 (CH_2Cl_2/MeOH, 85:15); $[\alpha]_D$ +33 (*c* 1.1, MeOH); mp 190 °C; IR (KBr) ν 2785, 1622, 1279, 1207, 1066, 1010 cm^{-1}; ^{1}H NMR (CD_3OD + D_2O + Na_2CO_3) δ 4.11 (dd, 1H, H_{1a}, J_{1a-2} = 4.3, J_{1a-1b} = 11.4 Hz), 4.09−4.01 (m, 2H, H_3 and H_2), 3.89 (dd, 1H, H_{1b}, J_{1b-2} = 6.4, J_{1b-1a} = 11.4 Hz), 3.76−3.68 (m, 4H, $4H_{2'}$), 2.90 (br d, 1H, H_{4a}, J_{4a-4b} = 13.9 Hz), 2.63−2.55 (m, 4H, $4H_{3'}$), 2.48 (dd, 1H, H_{4b}, J_{4b-3} = 8.1, J_{4b-4a} = 13.9 Hz), 1.51 (s, 3H, CH_3), 1.36 (s, 3H, CH_3); ^{13}C NMR (CD_3OD + D_2O + Na_2CO_3) δ 100.9 (C_5), 72.6 (C_2), 70.8 (C_3), 67.3 ($2C_{2'}$), 63.6 (C_1), 60.6 (C_4), 54.7 ($2C_{3'}$), 27.8 (CH_3), 20.4 (CH_3); HRMS (ESI+) calcd for $C_{11}H_{22}NO_7S$ [(M + H)$^+$] 312.1117, found 312.1132.

(2*R*,3*S*)-1,3-Dihydroxy-4-(morpholin-4-ium-4-yl)butane-2-sulfate (−)-28. The zwitterion **26** (256 mg, 0.712 mmol) was dissolved in a mixture of acetic acid and water 4:1 (20 mL). Pd/C 10% (117 mg) was added, and the mixture was stirred at room temperature under an H_2 atmosphere for 24 h. Catalyst was removed by filtration and washed with methanol. The mixture was concentrated under vacuum and the crude product was then purified by cation-exchange chromatography (Dowex 50WX8, 200−400 mesh, H^+ form) eluted with distilled water to give (−)-**28** (169 mg, 88%) as an amorphous solid: R_f 0.55 (CH_2Cl_2/MeOH/H_2O, 70:30:1); $[\alpha]_D$ −14 (*c* 1.95, H_2O); IR (KBr) ν 3430, 2750, 1636, 1255, 1234, 1060, 1016 cm^{-1}; ^{1}H NMR (CD_3OD + D_2O + Na_2CO_3) δ 4.25 (td, 1H, H_2, J_{2-1b} = J_{2-1a} = J_{2-3} = 4.6 Hz), 4.12 (ddd, 1H, H_3, J_{3-4a} = 3.2, J_{3-2} = 4.6, J_{3-4b} = 8.4 Hz), 3.89 (dd, 1H, H_{1a}, J_{1a-2} = 4.6, J_{1a-1b} = 12.4 Hz), 3.81 (dd, 1H, H_{1b}, J_{1b-2} = 4.6, J_{1b-1a} = 12.4 Hz), 3.78−3.71 (m, 4H, $4H_{2'}$), 2.74 (dd, 1H, H_{4a}, J_{4a-3} = 3.2, J_{4a-4b} = 13.4 Hz), 2.67−2.58 (m, 4H, $4H_{3'}$), 2.50 (dd, 1H, H_{4b}, J_{4b-3} = 8.4, J_{4b-4a} = 13.4 Hz); ^{13}C NMR (CD_3OD + D_2O + Na_2CO_3) δ 82.2 (C_2), 68.4 (C_3), 67.3 ($2C_{2'}$), 61.6 (C_4 or C_1), 61.1 (C_4 or C_1), 54.4 ($2C_{3'}$); HRMS (ESI+) calcd for $C_8H_{17}NNaO_7S$ [(M + Na)$^+$] 294.0623, found 294.0615.

(2*S*,3*R*)-1,3-Dihydroxy-4-(morpholin-4-ium-4-yl)butane-2-sulfate (+)-28. The zwitterion **27** (187 mg, 0.601 mmol) was dissolved in distilled water (18 mL). Then, 357 mg of cation-exchange resin (Dowex 50WX8, 16−40 mesh, H^+ form) were added and the mixture was stirred at room temperature for 5 days. The resin was removed by filtration and washed with methanol. The filtrate was concentrated under vacuum to give **(+)-28** (158 mg, 97%) as an amorphous solid: $[\alpha]_D$ +15 (*c* 2.8, H_2O).

The spectral data are consistent with the data from its enantiomer (−)-**28**.

General Procedure for the Piperidine Coupling Reaction. The piperidine **21** or **22** (1.0 mmol) and the cyclic sulfate **24** or **25** (1.2 mmol) were dissolved in anhydrous THF (3 mL) in the presence of anhydrous Na_2CO_3 (0.5 mmol) under argon. The mixture was refluxed for several hours.

(2*R*,3*S*)-1,3-*O*-Benzylidene-1,3-dihydroxy-4-[(2*S*,4*S*,5*R*)-2-benzyloxymethyl-4,5-dihydroxypiperidinium-1-yl]butane-2-sulfate 29. Compound **29** was isolated as a white solid after 20 h of refluxing and by filtration without further purification (283 mg, 90%): R_f 0.30 (CH_2Cl_2/MeOH, 85:15); $[\alpha]_D$ −53 (*c* 1.0, MeOH); mp 129 °C; IR (KBr) ν 3432, 2872, 1636, 1263, 1234, 1088, 1013 cm^{-1}; ^{1}H NMR (CD_3OD + D_2O + Na_2CO_3) δ 7.46−7.43 (m, 2H, H_{arom}), 7.38−7.27 (m, 8H, H_{arom}), 5.57 (s, 1H, H_5), 4.56 (d_{AB}, 1H, $H_{8'a}$, J_{AB} = 11.6 Hz), 4.56−4.53 (m, 1H, H_{1a}), 4.47 (d_{AB}, 1H, $H_{8'b}$, J_{AB} = 11.6 Hz), 4.14 (td, 1H, H_2, J = 5.2, J = 10.4, J_{2-1b} = 10.4 Hz), 4.01−3.96 (m, 1H, H_3), 3.80 (dd, 1H, H_{1b}, J_{1b-1a} = J_{1b-2} =10.4 Hz), 3.71 (br s, 1H, $H_{5'}$), 3.65 (dd, 1H, $H_{7'a}$, $J_{7'a-2'}$ = 4.2, $J_{7'a-7'b}$ = 10.2 Hz), 3.62−3.57 (m, 1H, $H_{4'}$), 3.57 (dd, 1H, $H_{7'b}$, $J_{7'b-2'}$ = 3.7, $J_{7'b-7'a}$ = 10.2 Hz), 3.23 (br d, 1H, H_{4a}, J_{4a-4b} = 15.1 Hz), 3.09 (dd, 1H, $H_{6'a}$, J = 3.8, J = 13.0 Hz), 2.98 (dd, 1H, H_{4b}, J_{4b-3} = 8.2, J_{4b-4a} = 15.1 Hz), 2.64−2.61 (m, 2H, $H_{2'}$ and $H_{6'b}$), 1.80−1.71 (m, 2H, $H_{3'b}$ and $H_{3'a}$); ^{13}C NMR (CD_3OD + D_2O + Na_2CO_3) δ 139.0, 138.8, 130.1, 129.5, 129.3, 128.9, 127.3 (C_{arom}), 102.1 (C_5), 77.9 (C_3), 74.2 ($C_{8'}$), 72.8 ($C_{7'}$), 70.7 ($C_{4'}$), 70.3 (C_1), 69.7 (C_2), 69.3 ($C_{5'}$), 58.8 ($C_{2'}$), 58.4 ($C_{6'}$), 54.8 (C_4), 33.1 ($C_{3'}$); HRMS (ESI+) calcd for $C_{24}H_{32}NO_9S$ [(M + H)$^+$] 510.1798, found 510.1815.

(2*S*,3*R*)-1,3-Dihydroxy-1,3-*O*-isopropylidene-4-[(2*S*,4*S*,5*R*)-2-benzyloxymethyl-4,5-dihydroxypiperidinium-1-yl]butane-2-sulfate 30. Compound **30** was isolated as a white solid after 14 h of refluxing and purification by flash chromatography (CH_2Cl_2/MeOH, 85:15) (255 mg, 87%): R_f 0.21 (CH_2Cl_2/MeOH, 85:15); $[\alpha]_D$ −1.7 (*c* 1.0, MeOH); mp 132 °C; IR (KBr) ν 3430, 2882, 1658, 1265, 1226, 1078, 1010 cm^{-1}; ^1H NMR (CD_3OD + D_2O + Na_2CO_3) δ 7.42−7.29 (m, 5H, H_{arom}), 4.54 (s, 2H, $2H_{8'}$), 4.07 (dd, 1H, H_{1a}, J_{1a-2} = 4.3, J_{1a-1b} = 11.6 Hz), 4.00−3.95 (m, 2H, H_3 and H_2), 3.86 (dd, 1H, H_{1b}, J_{1b-2} = 6.7, J_{1b-1a} = 11.6 Hz), 3.76−3.71 (m, 2H, $H_{7'a}$ and $H_{5'}$), 3.62−3.55 (m, 2H, $H_{4'}$ and $H_{7'b}$), 3.17 (br d, 1H, H_{4a}, *J* = 14.6 Hz), 3.04 (dd, 1H, $H_{6'a}$, *J* = 4.0, *J* = 12.6 Hz), 2.62−2.52 (m, 3H, $H_{6'b}$, $H_{2'}$ and H_{4b}), 1.84−1.70 (m, 2H, $H_{3'b}$ and $H_{3'a}$), 1.44 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (CD_3OD + D_2O + Na_2CO_3) δ 138.9, 129.5, 129.0 (C_{arom}), 100.7 (C_5), 74.3 ($C_{8'}$), 72.9 (C_2), 72.2 ($C_{7'}$), 71.0 ($C_{4'}$ or C_3), 70.7 ($C_{4'}$ or C_3), 69.3 ($C_{5'}$), 63.7 (C_1), 59.7 ($C_{2'}$), 57.7 ($C_{6'}$), 54.9 (C_4), 33.1 ($C_{3'}$), 27.7 (CH_3), 20.5 (CH_3); HRMS (ESI+) calcd for $C_{20}H_{32}NO_7S$ [(M + H)$^+$] 462.1798, found 462.1802.

(2*R*,3*S*)-1,3-*O*-Benzylidene-1,3-dihydroxy-4-[(2*R*,4*R*,5*R*)-2-benzyloxymethyl-4,5-dihydroxypiperidinium-1-yl]butane-2-sulfate 31. Compound **31** was isolated as a white solid after 24 h of refluxing by filtration without further purification (120 mg, 74%): R_f 0.23 (CH_2Cl_2/MeOH, 85:15); $[\alpha]_D$ −33 (*c* 0.48, MeOH); mp 208 °C; IR (KBr) ν 3456, 2872, 1636, 1255, 1213, 1090, 1068, 1005 cm^{-1}; ^1H NMR (CD_3OD + D_2O + Na_2CO_3) δ 7.43−7.40 (m, 2H, H_{arom}), 7.35−7.25 (m, 8H, H_{arom}), 5.57 (s, 1H, H_5), 4.54 (dd, 1H, H_{1a}, J_{1a-2} = 4.4, J_{1a-1b} = 10.6 Hz), 4.41 (d_{AB}, 1H, $H_{8'a}$, J_{AB} = 11.9 Hz), 4.34 (d_{AB}, 1H, $H_{8'b}$, J_{AB} = 11.9 Hz), 4.13−4.06 (m, 2H, H_3 and H_2), 3.80 (dd, 1H, H_{1b}, J_{1b-1a} = J_{1b-2} = 10.6 Hz), 3.64 (dd, 1H, $H_{7'a}$, $J_{7'a-2'}$ = 3.2, $J_{7'a-7'b}$ = 9.7 Hz), 3.56 (dd, 1H, $H_{7'b}$, $J_{7'b-2'}$ = 5.9, $J_{7'b-7'a}$ = 9.7 Hz), 3.52−3.48 (m, 1H, $H_{5'}$), 3.39−3.32 (m, 1H, $H_{4'}$), 3.28 (br d, 1H, H_{4a}, J_{4a-4b} = 15.5 Hz), 3.06 (dd, 1H, $H_{6'a}$, $J_{6'a-5'}$ = 4.8, $J_{6'a-6'b}$ = 11.2 Hz), 2.88 (dd, 1H, H_{4b}, J_{4b-3} = 7.2, J_{4b-4a} = 15.5 Hz), 2.75−2.70 (m, 1H, $H_{2'}$), 2.40 (dd, 1H, $H_{6'b}$, $J_{6'b-6'a}$ = $J_{6'b-5'}$ = 11.2 Hz), 2.01 (ddd, 1H, $H_{3'a}$, *J* = 2.4, *J* = 4.8, $J_{3'a-3'b}$ = 12.5 Hz), 1.45 (td, 1H, $H_{3'b}$, $J_{3'b-3'a}$ = 12.5 Hz); ^{13}C NMR (CD_3OD + D_2O + Na_2CO_3) δ 139.0, 138.4, 129.9, 129.2, 129.1, 128.9, 128.6, 127.0 (C_{arom}), 101.8 (C_5), 77.4 (C_3), 74.1 ($C_{4'}$), 74.0 ($C_{8'}$), 72.4 ($C_{5'}$), 71.7 ($C_{7'}$), 70.1 (C_1), 69.2 (C_2), 59.2 ($C_{2'}$), 58.5 ($C_{6'}$), 53.8 (C_4), 36.8 ($C_{3'}$); HRMS (ESI+) calcd for $C_{24}H_{32}NO_9S$ [(M + H)$^+$] 510.1798, found 510.1791.

(2*S*,3*R*)-1,3-Dihydroxy-1,3-*O*-isopropylidene-4-[(2*R*,4*R*,5*R*)-2-benzyloxymethyl-4,5-dihydroxypiperidinium-1-yl]butane-2-sulfate 32. Compound **32** was isolated as a white solid after 24 h of refluxing and purification by flash chromatography (CH_2Cl_2/MeOH, 85:15) (115 mg, 71%): R_f 0.16 (CH_2Cl_2/MeOH, 85:15); $[\alpha]_D$ +11 (*c* 1.1, MeOH); mp 112 °C; IR (KBr) ν 3429, 2863, 1636, 1269, 1226, 1082, 1011 cm^{-1}; ^1H NMR (CD_3OD + D_2O + Na_2CO_3) δ 7.42−7.31 (m, 5H, H_{arom}), 4.59 (d_{AB}, 1H, $H_{8'a}$, J_{AB} = 11.9 Hz), 4.51 (d_{AB}, 1H, $H_{8'b}$, J_{AB} = 11.9 Hz), 4.10 (dd, 1H, H_{1a}, J_{1a-2} = 4.0, J_{1a-1b} = 11.6 Hz), 4.04−3.98 (m, 2H, H_3 and H_2), 3.88 (dd, 1H, H_{1b}, J_{1b-2} = 6.5, J_{1b-1a} = 11.6 Hz), 3.62 (dd, 1H, $H_{7'a}$, $J_{7'a-2'}$ = 4.1, $J_{7'a-7'b}$ = 10.3 Hz), 3.52 (dd, 1H, $H_{7'b}$, $J_{7'b-2'}$ = 5.2, $J_{7'b-7'a}$ = 10.3 Hz), 3.45−3.34 (m, 2H, $H_{4'}$ and $H_{5'}$), 3.06 (br d, 1H, $H_{6'a}$, $J_{6'a-6'b}$ = 11.6 Hz), 3.04 (br d, 1H, H_{4a}, J_{4a-4b} = 14.7 Hz), 2.76 (dd, 1H, H_{4b}, J_{4b-3} = 8.0, J_{4b-4a} = 14.7 Hz), 2.62−2.59 (m, 1H, $H_{2'}$), 2.31 (dd, 1H, $H_{6'b}$, $J_{6'b-5'}$ = 10.6, $J_{6'b-6'a}$ = 11.6 Hz), 1.98 (ddd, 1H, $H_{3'a}$, *J* = 2.5, *J* = 4.4, $J_{3'a-3'b}$ = 12.5 Hz), 1.48 (s, 3H, CH_3), 1.45 (td, 1H, $H_{3'b}$, $J_{3'b-3'a}$ = 12.5 Hz), 1.36 (s, 3H, CH_3); ^{13}C NMR (CD_3OD + D_2O + Na_2CO_3) δ 139.4, 129.5, 128.9 (C_{arom}), (C_5), 74.4 (C_2), 74.2 ($C_{8'}$), 72.7 ($C_{4'}$ or C_3), 72.5 ($C_{4'}$ or C_3), 72.1 ($C_{7'}$), 69.3 ($C_{5'}$), 63.7 (C_1), 59.3 ($C_{2'}$), 59.2 ($C_{6'}$), 54.6 (C_4), 36.6 ($C_{3'}$), 27.8 (CH_3), 20.4 (CH_3); HRMS (ESI+) calcd for $C_{20}H_{31}NO_7NaS$ [(M + Na)$^+$] 484.1617, Found 484.1595.

General Procedure for Benzylidene Protective Group Removal. The zwitterion **29** or **31** (1.0 mmol) was dissolved in a mixture of acetic acid and water 4:1 (18 mL). Pd/C 10% (350 mg) was added, and the mixture was stirred at room temperature under an H_2 atmosphere for several hours. Catalyst was removed by filtration and washed with water. The mixture was concentrated under vacuum, and the crude product was purified by cation-exchange chromatography (Dowex 50WX8, 200−400 mesh, H^+ form) eluted with distilled water to give **33** or **35**.

(2*R*,3*S*)-1,3-Dihydroxy-4-[(2*S*,4*S*,5*R*)-4,5-dihydroxy-2-hydroxymethylpiperidinium-1-yl]butane-2-sulfate 33. Compound **33** was isolated as a white solid after 24 h of stirring (78.6 mg, 86%): R_f 0.28 (CH_2Cl_2/MeOH/H_2O, 55:40:5); $[\alpha]_D$ −42 (*c* 1.0, H_2O); mp 166 °C; IR (KBr) ν 3405, 1636, 1271, 1234, 1064, 1004 cm^{-1}; ^1H NMR (D_2O + Na_2CO_3) δ 4.26 (ddd, 1H, H_2, J_{2-1a} = 3.6, J_{2-1b} = 4.5, J_{2-3} = 5.8 Hz), 4.14 (ddd, 1H, H_3, J_{3-4b} = 2.5, J_{3-2} = 5.8, J_{3-4a} = 9.4 Hz), 3.91 (dd, 1H, H_{1a}, J_{1a-2} = 3.6, J_{1a-1b} = 12.6 Hz), 3.91−3.87 (m, 1H, $H_{5'}$), 3.84 (dd, 1H, H_{1b}, J_{1b-2} = 4.5, J_{1b-1a} = 12.6 Hz), 3.80 (ddd, 1H, $H_{4'}$, $J_{4'-3'a}$ = 3.5, $J_{4'-5'}$ = 5.1, $J_{4'-3'b}$ = 11.3 Hz), 3.73−3.66 (m, 2H, $H_{7'}$), 3.10 (dd, 1H, $H_{6'a}$, $J_{6'a-5'}$ = 4.0, $J_{6'a-6'b}$ = 13.0 Hz), 2.89 (dd, 1H, H_{4a}, J_{4a-3} = 9.4, J_{4a-4b} = 14.2 Hz), 2.68 (dd, 1H, H_{4b}, J_{4b-3} = 2.5, J_{4b-4a} = 14.2 Hz), 2.55 (dd, 1H, $H_{6'b}$, $J_{6'b-5'}$ = 1.6, $J_{6'b-6'a}$ = 13.0 Hz), 2.56−2.51 (m, 1H, $H_{2'}$), 1.82 (td, 1H, $H_{3'a}$, $J_{3'a-2'}$ = 3.5, $J_{3'a-4'}$ = 3.5, $J_{3'a-3'b}$ = 12.6 Hz), 1.73 (td, 1H, $H_{3'b}$, $J_{3'b-2'}$ = 11.3, $J_{3'b-4'}$ = 11.3, $J_{3'b-3'a}$ = 12.6 Hz); ^{13}C NMR (D_2O + Na_2CO_3) δ 81.4 (C_2), 69.0 ($C_{4'}$), 67.5 ($C_{5'}$), 66.6 (C_3), 62.7 ($C_{7'}$), 59.8 (C_1), 59.4 ($C_{2'}$), 55.6 ($C_{6'}$), 54.6 (C_4), 30.6 ($C_{3'}$); HRMS (ESI+) calcd for $C_{10}H_{21}NNaO_9S$ [(M + Na)$^+$] 354.0835, found 354.0835.

(2*R*,3*S*)-1,3-Dihydroxy-4-[(2*R*,4*R*,5*R*)-4,5-dihydroxy-2-hydroxymethylpiperidinium-1-yl]butane-2-sulfate 35. Compound **35** was isolated as an amorphous solid after 23 h of stirring (35.3 mg, 78%): R_f 0.18 (CH_2Cl_2/MeOH/H_2O, 55:40:5); $[\alpha]_D$ −16 (*c* 1.0, H_2O); IR (KBr) ν 3403, 1636, 1251, 1163, 1074 cm^{-1}; ^1H NMR (D_2O + Na_2CO_3) δ 4.25 (ddd, 1H, H_2, J_{2-1a} = 3.4, J_{2-1b} = 4.4, J_{2-3} = 5.8 Hz), 4.15 (ddd, 1H, H_3, J_{3-4a} = 2.9, J_{3-2} = 5.8, J_{3-4b} = 8.4 Hz), 3.90 (dd, 1H, H_{1a}, J_{1a-2} = 3.4, J_{1a-1b} = 12.6 Hz), 3.83 (dd, 1H, H_{1b}, J_{1b-2} = 4.4, J_{1b-1a} = 12.6 Hz), 3.74 (dd, 1H, $H_{7'a}$, $J_{7'a-2'}$ = 4.3, $J_{7'a-7'b}$ = 11.9 Hz), 3.64 (dd, 1H, $H_{7'b}$, $J_{7'b-2'}$ = 5.3, $J_{7'b-7'a}$ = 11.9 Hz), 3.57−3.47 (m, 2H, $H_{4'}$ and $H_{5'}$), 3.14 (dd, 1H, $H_{6'a}$, $J_{6'a-5'}$ = 4.2, $J_{6'a-6'b}$ = 11.7 Hz), 3.08 (dd, 1H, H_{4a}, J_{4a-3} = 2.9, J_{4a-4b} = 14.6 Hz), 2.69−2.63 (m, 1H, $H_{2'}$), 2.59 (dd, 1H, H_{4b}, J_{4b-3} = 8.4, J_{4b-4a} = 14.6 Hz), 2.32 (dd, 1H, $H_{6'b}$, $J_{6'b-5'}$ = 10.2, $J_{6'b-6'a}$ = 11.7 Hz), 2.01 (ddd, 1H, $H_{3'a}$, *J* = 2.6, *J* = 4.5, $J_{3'a-3'b}$ = 12.5 Hz), 1.38 (td, 1H, $H_{3'b}$, $J_{3'b-3'a}$ = 12.5 Hz); ^{13}C NMR (D_2O + Na_2CO_3) δ 81.4 (C_2), 72.6 ($C_{5'}$ or $C_{4'}$), 70.7 ($C_{5'}$ or $C_{4'}$), 68.0 (C_3), 62.3 ($C_{7'}$), 60.6 ($C_{2'}$), 59.7 (C_1), 57.0 ($C_{6'}$), 53.7 (C_4), 34.3 ($C_{3'}$); HRMS (ESI+) calcd for $C_{10}H_{21}NNaO_9S$ [(M + Na)$^+$] 354.0835, found 354.0846.

(2*S*,3*R*)-1,3-Dihydroxy-4-[(2*S*,4*S*,5*R*)-4,5-dihydroxy-2-hydroxymethylpiperidinium-1-yl]butane-2-sulfate 34. The zwitterion **30** (129 mg, 0.280 mmol) was dissolved in 0.01 N HCl (21 mL). Pd/C 10% (98 mg) was added, and the mixture was stirred at room temperature under an H_2 atmosphere for 7 days. Catalyst was removed by filtration and washed with water. The mixture was neutralized by 1 N NH_4OH and concentrated under vacuum, and the crude product was purified by cation exchange chromatography (Dowex 50WX8, 200−400 mesh, H^+ form) eluted with distilled water to give **34** (67.4 mg, 73%) as an amorphous solid: R_f 0.23 (CH_2Cl_2/MeOH/H_2O, 55:40:5); $[\alpha]_D$ −4.9 (*c* 1.1, H_2O); IR (KBr) ν 3402, 1636, 1251, 1165, 1061, 1013 cm^{-1}; ^1H NMR (D_2O + Na_2CO_3) δ 4.29 (td, 1H, H_2, J_{2-1a} = 3.6, J_{2-1b} = J_{2-3} = 5.0 Hz), 4.13 (ddd, 1H, H_3, J_{3-4a} = 3.9, J_{3-2} = 5.0, J_{3-4b} = 8.0 Hz), 3.91 (dd, 1H, H_{1a}, J_{1a-2} = 3.6, J_{1a-1b} = 12.7 Hz), 3.89−3.87 (m, 1H, $H_{5'}$), 3.82 (dd, 1H, H_{1b}, J_{1b-2} = 5.0, J_{1b-1a} = 12.7 Hz), 3.82−3.78 (m, 1H, $H_{4'}$), 3.77 (dd, 1H, $H_{7'a}$, $J_{7'a-2'}$ = 4.2, $J_{7'a-7'b}$ = 11.6 Hz), 3.68 (dd, 1H, $H_{7'b}$, $J_{7'b-2'}$ = 4.9, $J_{7'b-7'a}$ = 11.6 Hz), 3.10 (dd, 1H, H_{4a}, J_{4a-3} = 3.9, J_{4a-4b} = 14.6 Hz), 3.08 (dd, 1H, $H_{6'a}$, $J_{6'a-5'}$ = 4.5, $J_{6'a-6'b}$ = 13.0 Hz), 2.58 (dd, 1H, $H_{6'b}$, $J_{6'b-5'}$ = 1.8, $J_{6'b-6'a}$ = 13.0 Hz), 2.59−2.56 (m, 1H, $H_{2'}$), 2.54 (dd, 1H, H_{4b}, J_{4b-3} = 8.0, J_{4b-4a} = 14.6 Hz), 1.81 (td, 1H, $H_{3'a}$, *J* = 3.5, *J* = 3.5, $J_{3'a-3'b}$ = 12.9 Hz), 1.69 (td, 1H, $H_{3'b}$, *J* = 10.8, *J* = 10.8, $J_{3'b-3'a}$ = 12.9 Hz); ^{13}C NMR (D_2O + Na_2CO_3) δ 81.4 (C_2), 68.9 ($C_{4'}$), 68.3 ($C_{5'}$),

67.6 (C_3), 62.9 ($C_{7'}$), 60.3 ($C_{2'}$), 59.7 (C_1), 56.1 ($C_{6'}$), 54.8 (C_4), 30.4 ($C_{3'}$); HRMS (ESI+) calcd for $C_{10}H_{20}NNa_2O_9S$ [$(M - H + 2Na)^+$] 376.0654, found 376.0648.

(2*S*,3*R*)-1,3-Dihydroxy-4-[(2*R*,4*R*,5*R*)-4,5-dihydroxy-2-hydroxymethylpiperidinium-1-yl]butane-2-sulfate 36. The zwitterion **32** (28.0 mg, 0.061 mmol) was dissolved in 0.01 N HCl (2.6 mL). Pd/C 10% (21 mg) was added, and the mixture was stirred at room temperature under an H_2 atmosphere for 20 h. Catalyst was removed by filtration and washed with water. The mixture was neutralized by 1 N NH_4OH before concentration under vacuum. As the reaction was not completed, the crude product was dissolved in distilled water (2 mL) containing 75 mg of a cation-exchange resin (Dowex 50WX8, 16−40 mesh, H^+ form). The mixture was stirred at room temperature for 3 days. The resin was removed by filtration and washed with water. The filtrate was concentrated under vacuum, and the crude product was purified by flash chromatography (CH_2Cl_2/MeOH/H_2O, 55:44:1) to give **36** (12.0 mg, 59%) as an amorphous solid: R_f 0.30 (CH_2Cl_2/MeOH/H_2O, 55:40:5); $[\alpha]_D$ +20 (*c* 0.9, H_2O); IR (KBr) ν 3405, 1636, 1250, 1069, 1008 cm^{-1}. ^1H NMR (D_2O + Na_2CO_3) δ 4.24−4.20 (m, 1H, H_2), 4.20−4.15 (m, 1H, H_3), 3.89 (dd, 1H, H_{1a}, J_{1a-2} = 3.3, J_{1a-1b} = 12.6 Hz), 3.83 (dd, 1H, H_{1b}, J_{1b-2} = 4.4, J_{1b-1a} = 12.6 Hz), 3.68 (dd, 1H, $H_{7'a}$, $J_{7'a-2'}$ = 3.8, $J_{7'a-7'b}$ = 12.0 Hz), 3.62 (dd, 1H, $H_{7'b}$, $J_{7'b-2'}$ = 5.0, $J_{7'b-7'a}$ = 12.0 Hz), 3.54−3.45 (m, 2H, $H_{4'}$ and $H_{5'}$), 3.13 (dd, 1H, $H_{6'a}$, $J_{6'a-5'}$ = 3.9, $J_{6'a-6'b}$ = 11.5 Hz), 2.85−2.77 (m, 2H, H_{4b} and H_{4a}), 2.61−2.55 (m, 1H, $H_{2'}$), 2.38 (dd, 1H, $H_{6'b}$, $J_{6'b-5'}$ = 10.3, $J_{6'b-6'a}$ = 11.5 Hz), 2.04 (ddd, 1H, $H_{3'a}$, *J* = 2.8, *J* = 4.1, $J_{3'a-3'b}$ = 13.0 Hz), 1.44 (td, 1H, $H_{3'b}$, *J* = 13.0 Hz); ^{13}C NMR (D_2O + Na_2CO_3) δ 81.4 (C_2), 72.6 ($C_{5'}$ or $C_{4'}$), 71.1 ($C_{5'}$ or $C_{4'}$), 66.6 (C_3), 62.1 ($C_{7'}$), 59.7 (C_1), 59.6 ($C_{2'}$), 57.3 ($C_{6'}$), 54.3 (C_4), 34.5 ($C_{3'}$); HRMS (ESI+) calcd for $C_{10}H_{21}NNaO_9S$ [$(M + Na)^+$] 354.0835, found 354.0839.

Supporting Information Available: General experimental information and ^1H and ^{13}C NMR spectra of compounds **19**−**22**, **28**, and **33**−**36**. This material is available free of charge via the Internet at http://pubs.acs.org.

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