An Expeditious Synthesis of 1-Substituted and Cyclic Taurines

Jiaxing Huang, Fei Wang, Da-Ming Du, Jiaxi Xu*

Key Laboratory of Bioorganic Chemistry and Molecular Engineering of the Ministry of Education, Department of Chemical Biology, College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, P. R. China
Fax +86(10)62751708; E-mail: jxxu@pku.edu.cn

Received 20 January 2005; revised 7 April 2005

Abstract: A series of 1-substituted taurines, including optically active taurines, were synthesized expeditiously from epoxides via episulfidation with potassium sulfocyanate, ring-opening with dibenzylamine, followed by oxidation with performic acid, and hydrogenolysis in the presence of palladium hydroxide on carbon powder. This method was also used for the synthesis of *trans*-cyclic taurines.

Key words: amino acid, aminoalkanesulfonic acid, epoxide, episulfide, synthesis, taurine

During the last two decades aminoalkylphosphonic acid and aminoalkanesulfonic acid derivatives have been widely used as enzyme inhibitors and haptens in the development of catalytic antibodies because of their structural properties.[1–5] Several 2-aminoalkanesulfonic acids have also been found in many mammalian tissues and they are involved in various and important physiological processes.[6] It has been demonstrated clearly that taurine and its cyclic analogues show different effects on ATP-dependent calcium ion uptake and protein phosphorylation in rat retina.[7] Thus, it has become very important to develop efficient methods to synthesize structurally diverse aminoalkanesulfonic acids for the investigation of biological activities and structure-activity relationships. β-Aminoalkanesulfonic acids are very important sulfur analogues of naturally occurring amino acids because α-aminoalkanesulfonic acids and their derivatives are unstable.[5] There are three types of structural analogues of naturally occurring amino acids of β-aminoalkanesulfonic acids, which include 1-substituted taurines, 2-substituted taurines, and 1,2-disubstituted taurines (Figure 1).

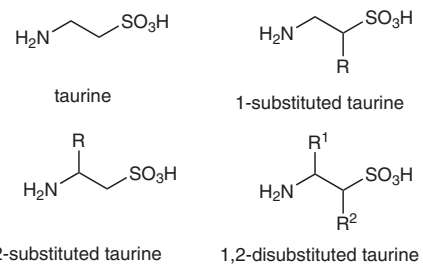


Figure 1 Taurine and substituted taurines

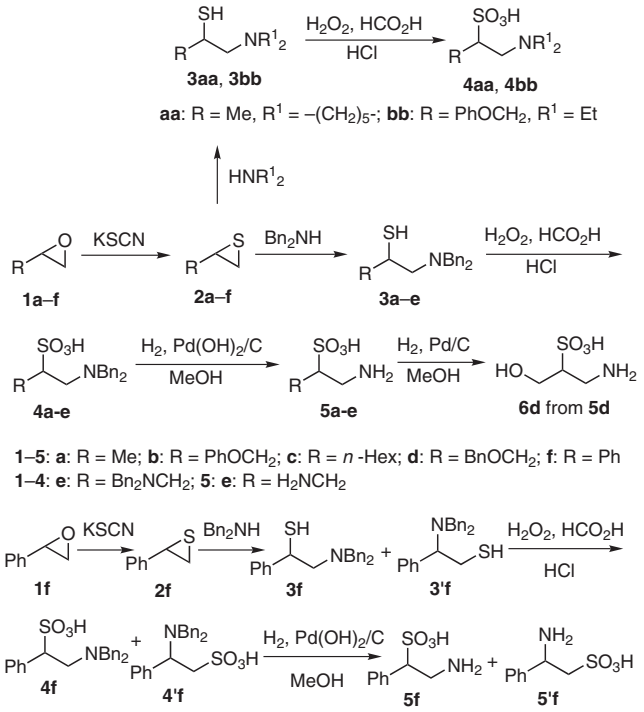
2-Substituted taurines have been synthesized effectively via sulfite displacement of the methanesulfonates of the vicinal amino alcohols,[8–13] the peroxy acid oxidation of the thioacetates of vicinal amino primary alcohols,[14–19] aminosulfonation of alkenes,[20] and sulfite ring-opening of aziridines.[21] However, there has been little attention paid to the synthesis of 1-substituted taurines.[16,19,22,23] Very recently, we reported an effective and general method for the preparation of N-protected 1-substituted and *cis*-1,2-disubstituted taurines.[23,24] Herein, we describe a short route to the synthesis of 1-substituted and cyclic taurines from olefins and epoxides.

In our on-going research concerning the synthesis of structurally diverse sulfur analogues of naturally occurring amino acids we attempted to prepare 1-substituted and cyclic taurines effectively. It is well known that vicinal amino primary alcohols have been used as important key intermediates for synthesizing 2-substituted taurines.[8,9,14–19] In most cases, their hydroxyl group was converted to a thiol or its ester, which after peroxy acid oxidation gave rise to 2-substituted taurines. Sulfite ring-opening of aziridines has been utilized as an expeditious method for the synthesis of 2-substituted taurines due to sulfite attack on the less bulky carbon atom of the aziridine rings.[21] Episulfides should be useful starting materials for the synthesis of 1-substituted taurines because they can be prepared from commercially available terminal olefins or 1,2-epoxyalkanes efficiently.[25,26] Ammonia or amine ring-opening of 1,2-episulfides would generate vicinal amino secondary thiols, subsequent peroxy acid oxidation would afford 1-substituted taurines.

Commercially available or self-prepared 1,2-alkanepoxides **1** were converted to the corresponding episulfides **2** with potassium sulfocyanate in the absence or presence of silica gel in acceptable and satisfactory yields according to the literature.[26] Firstly, ammonia and primary amines, including methylamine, benzylamine, and aniline, were subjected to the ring-opening reactions of 1,2-episulfides to generate vicinal amino secondary thiols.[27] The results indicated that complex mixtures were always obtained in the reactions. In most cases, polymerization occurred as described in the literature even when episulfides were added dropwise into a large excess of ammonia and primary amine.[25] However, the desired ring-opened products, vicinal amino secondary mercaptans **3aa** and **3bb**, were obtained in good yields for secondary amines, including linear diethylamine and cyclic piperidine.[27] After crude purification the mercaptans were directly subjected

SYNTHESIS 2005, No. 13, pp 2122–2128
Advanced online publication: 13.07.2005
DOI: 10.1055/s-2005-869994; Art ID: F01305SS

to further oxidation. It is not easy to afford very pure mercaptans because they were easily oxidized to disulfides in air. Both the mercaptans and the disulfide could be oxidized to N,N-disubstituted 1-substituted taurines with peroxy acid. After the peroxy acid oxidation of *N*,*N*-dialkylamino mercaptan hydrochlorides,[23] N,N-disubstituted 1-substituted taurines **4aa** and **4bb** were obtained in good yields (Scheme 1).

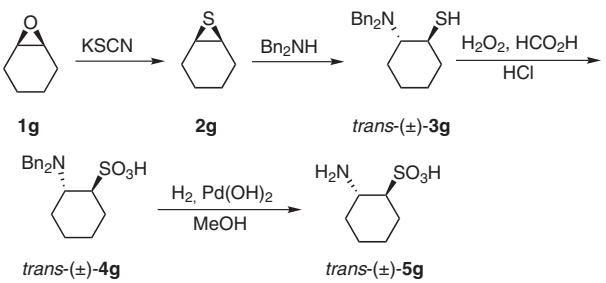


Scheme 1 Synthesis of 1-substituted taurines

If *N*,*N*-dialkylamino mercaptans were directly oxidized by peroxy acid, N,N-disubstituted 1-substituted taurines were obtained in low yields (around 40%) due to the formation of *N*-oxide derivatives of N,N-disubstituted 1-substituted taurines. In order to synthesize N-nonsubstituted 1-substituted taurines **5**, dibenzylamine was chosen and used as a secondary amine. After the dibenzylamine ring-opening of episulfides **2** the desired vicinal *N*,*N*-dibenzyl amino secondary thiols **3** were obtained in satisfactory yields. They were dissolved in formic acid and treated with concentrated hydrochloric acid to form their hydrochlorides; oxidation with performic acid afforded *N*,*N*-dibenzyl 1-substituted taurines **4**. Firstly, *N*,*N*-dibenzyl derivatives **4** were hydrogenolyzed in methanol under an atmosphere of hydrogen in the presence of palladium on carbon powder. The results indicated that the benzyl group on the nitrogen atom cannot be removed completely, a mixture of *N*,*N*-dibenzyl, *N*-monobenzyl, and *N*-nonbenzyl derivatives were obtained even after a reaction time of several days. Finally, they were hydrogenolyzed in methanol under an atmosphere of hydrogen in the presence of palladium hydroxide on carbon powder to yield the desired 1-substituted taurines **5** in good to excellent yields (Scheme 1). It is interesting to note that the benzyl group attached to the oxygen atom in 1-benzyloxymethyl taurine **5d** is not removed in the presence of palladium hydroxide on carbon powder. Compound **5d** was further treated under an atmosphere of hydrogen in the presence of palladium on carbon powder to yield the desired 1-hydroxymethyl taurine **6d** in good yield (Scheme 1). The results indicated that palladium hydroxide on carbon powder chemoselectively removes the benzyl group from nitrogen, but it cannot effect the removal of the benzyl group attached to an oxygen atom. However, palladium on carbon powder does not show such chemoselectivity. A series of 1-substituted taurines with a diverse range of functional groups were synthesized by this method.

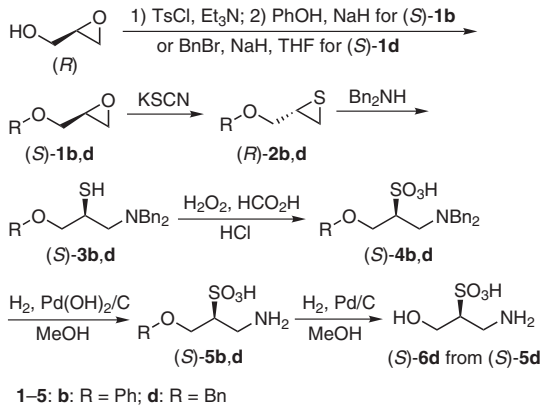
For styrene episulfide **2f**, an aromatic-substituted episulfide; its ring-opening reaction with dibenzylamine produced a mixture of vicinal amino secondary thiol **3f** and primary thiol **3′f** in a ratio near 1:1. No regioselectivity was observed although regiospecific ring-opened products were obtained for alkyl-substituted episulfides **2a**–**e**. It is similar to the ring-opening reactions of styrene oxide[28] and 2-phenylaziridine[29] with nucleophiles. Thus, a mixture of 1- and 2-phenyl taurines was obtained from styrene sulfide **2f**. This seems to indicate that 1-aryltaurines cannot be prepared by this method.

Previously, *cis*-2-(benzyloxycarbonyl)aminocycloalkanesulfonic acids were prepared from cycloalkene oxides.[23] After the deprotection of the benzyloxycarbonyl group, *cis*-2-aminocycloalkanesulfonic acids could be obtained. *cis*-2-Aminocyclohexanesulfonic acid was also prepared from the hydrogenation of aniline-2-sulfonic acid.[30] *trans*-2-Aminocyclohexanesulfonic acid was prepared by the amino-sulfonation of cyclohexene.[20,30] In a route similar to the synthesis of 1-substituted taurines, *trans*-cyclic aminoalkanesulfonic acids could also be prepared from cycloalkene oxides. Cyclohexene oxide **1g** was converted to cyclohexene sulfide **2g**, which underwent a ring-opening reaction with dibenzylamine to afford *trans*-2-*N*,*N*-dibenzylamino-1-cyclohexanethiol (**3g**). The thiol was converted to its hydrochloride and subsequenetly oxidized with performic acid to afford *trans*-2-*N*,*N*-dibenzylaminocyclohexanesulfonic acid (**4g**). It was hydrogenolyzed in methanol under an atmosphere of hydrogen in the presence of palladium hydroxide on carbon powder to afford *trans*-2-aminocyclohexanesulfonic acid (**5g**) in a good yield (Scheme 2).



Scheme 2 Synthesis of *trans*-cyclic taurine

The current synthetic method was also applied to the preparation of optically active 1-substituted taurines (Scheme 3). (*R*)-Glycidol (98%ee from Aldrich) was converted to (*S*)-benzyl glycidyl ether (*S*)-**1d** in 69% yield and 98% ee via benzylation,[31] and (*S*)-glycidyl phenyl ether (*S*)-**1b** in 58% total yield and 93% ee via tosylation and displacement with sodium phenolate.[32] (*S*)-Glycidyl phenyl ether (*S*)-**1b** was obtained in relatively low optical purity because the displacement of sodium phenolate with (*S*)-glycidyl tosylate could result in both S_N2 and S_N2' pathways (ratio 97:3 in DMF[32]). Both optically active glycidyl ethers (*S*)-**1b** and (*S*)-**1d** were further converted to episulfides (*R*)-**2b** in 49% yield and 91% ee, and (*R*)-**2d** in 64% yield and 96% ee, respectively, with potassium sulfocyanate. It was found that their optical purities decreased slightly, which is in agreement with a previous report that a complete Walden inversion occurred during the conversion.[33] Optically active *N*,*N*-dibenzylaminoalkylmercaptans (*S*)-**3b** and (*S*)-**3d** were obtained via the ring-opening reaction of episulfides (*R*)-**2b** and (*R*)-**2d** with dibenzylamine without loss of optical activity on the basis of HPLC analysis on a chiral column. After oxidation and hydrogenolysis, optically active 1-substituted taurines (*S*)-**5b**, (*S*)-**5d**, and (*S*)-**6d** were obtained in satisfactory yields. Optical activities should not decrease during oxidation and hydrogenolysis because the reactions do not affect the chiral centers. This indicated that the current method is an efficient synthesis of optically active 1-substituted taurines by using optically active epoxides as starting materials with only a slight loss of optical activity during the transformation of an epoxide to the corresponding episulfide.



Scheme 3 Synthesis of optically active 1-substituted taurines

In summary, 1-substituted and *trans*-cyclic taurines were synthesized expeditiously from epoxides via episulfidation with potassium sulfocyanate, ring-opening reaction with dibenzylamine, followed by the oxidation with peroxyformic acid, and hydrogenolysis in the presence of palladium hydroxide on carbon powder. This synthetic route can be used as a general method to synthesize racemic and optically active 1-substituted taurines and *trans*-cyclic 2-aminocycloalkanesulfonic acids, which are important sulfur analogues of naturally occurring amino acids. The current method can also be used to prepare N,N-disubstituted 1-substituted taurines.

Melting points were measured on a Yanaco MP-500 melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian Mercury 200 (200 MHz), Mercury Plus 300 (300 MHz), or Bruker ARX400 (400 MHz) spectrometer in $CDCl_3$ with TMS as an internal standard, in D_2O, in DMSO-d_6, or in formic acid. Mass spectra were obtained on a VG-ZAB-HS mass spectrometer or a Brucker ESQUIRE-LC™ ESI ion trap mass spectrometer. HRMS data was carried out on a Brucker APEX 47e Fourier transform ion cyclotron resonance (FTICR) mass spectrometer. IR spectra were determined on a Nicolet AVATAR 330 FT-IR spectrometer. CHN analyses were recorded on an Elementar Vario EL analyzer. Optical rotations were measured on a Perkin-Elmer Model 341LC polarimeter with a thermally jacketed 10 cm cell (concentration *c* given as g/100 mL). HPLC analyses were performed on an HP1100 HPLC equipment. The ee values were determined by HPLC analysis with chiralcel AD, OB, or OD-H columns (4.6 × 250 mm) using a mixture of hexane–*i*-PrOH as eluent at monitoring wave 220 nm. Petroleum ether used had a boiling range of 30–60 °C. Episulfides **2** were prepared from epoxides **1** with potassium sulfocyanate in the presence or absence of silica gel in acceptable and satisfactory yields according to the literature method.[26] The analytical data of all known compounds are identical to those reported.[20,22,32,34–36]

(*S*)-Glycidyl Phenyl Ether (*S*)-1b[32]

Prepared from (*R*)-glycidol by a known method.

Yield: 58%; colorless oil; R_f 0.39 (petroleum ether–EtOAc, 20:1).

93% ee; determined by HPLC with Chiralcel OD-H column (hexane–*i*-PrOH, 90:10), flow rate 0.8 mL/min; t_{Rminor} 9.10 min, t_{Rmajor} 13.51 min.

$[\alpha]_D^{20}$ +12.4 (*c* 1.58, EtOH) {Lit.[32] $[\alpha]_D^{25}$ +14.1 (*c* 2.36, MeOH)}.

(*S*)-Benzyl Glycidyl Ether (*S*)-1d[31]

Prepared from (*R*)-glycidol by a known method.

Yield: 69%; colorless oil; R_f 0.20 (petroleum ether–EtOAc, 20:1).

98% ee; determined by HPLC with Chiralcel OD-H column (hexane–*i*-PrOH, 90:10), flow rate 0.8 mL/min; t_{Rmajor} 8.78 min, t_{Rminor} 9.36 min.

$[\alpha]_D^{20}$ +6.78 (*c* 1.23, EtOH) {Lit.[34] $[\alpha]_D^{20}$ +7.82 (*c* 0.40, EtOH)}.

(*R*)-2-Phenoxymethylepisulfide (2b)[26]

Prepared from epoxide (*S*)-**1b** and potassium sulfocyanate by a known method.

Yield: 64%; colorless oil; R_f 0.45 (petroleum ether–EtOAc, 20:1).

91% ee; determined by HPLC with Chiralcel OD column (hexane–*i*-PrOH, 90:10), flow rate 0.8 mL/min; t_{Rmajor} 6.84 min, t_{Rminor} 8.29 min.

$[\alpha]_D^{20}$ –15.0 (*c* 1.25, $CHCl_3$) {Lit.[35] $[\alpha]^{23}_D$ +15.9 (*c* 1.0, $CHCl_3$)}; the configuration of **2b** in the literature is wrong, it should be *S* because a Walden inversion occurred during the transformation; based on the mechanism proposed in the literature[33] and our current results.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.34–6.89 (m, 5 H, Ph), 4.22 (dd, *J* = 5.6, 10.3 Hz, 1 H, OC*H*H), 3.90 (dd, *J* = 6.8, 10.3 Hz, 1 H, OCH*H*), 3.27 (dddd, *J* = 5.0, 5.2, 5.6, 6.8 Hz, 1 H, SCH), 2.61 (dd, *J* = 1.0, 5.0 Hz, 1 H, SC*H*H), 2.33 (dd, *J* = 1.0, 5.2 Hz, 1 H, SCH*H*).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 158.4, 129.6, 121.3, 114.6, 72.5, 31.3, 24.0.

(*R*)-2-Benzyloxymethylepisulfide (2d)
Prepared from epoxide (*S*)-**1d** and potassium sulfocyanate by a known method.

Yield: 49%; colorless oil; R_f 0.38 (petroleum ether–EtOAc, 20:1).

96% ee; determined by HPLC with Chiralcel OB column (hexane–*i*-PrOH, 95:5), flow rate 0.8 mL/min; t_{Rminor} 12.01 min, t_{Rmajor} 13.03 min.

$[\alpha]_D^{20}$ –9.05 (*c* 1.31, $CHCl_3$) {Lit.[36] $[\alpha]_D$ 11 (*c* 10, $CHCl_3$) for (*S*)-**2d**}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.37–7.28 (m, 5 H, Ph), 4.59 (s, 2 H, CH_2O), 3.70 (dd, *J* = 5.8, 10.6 Hz, 1 H, OC*H*H), 3.49 (dd, *J* = 6.8, 10.6 Hz, 1 H, OCH*H*), 3.11 (dddd, *J* = 5.6, 5.8, 6.2, 6.8, Hz, 1 H, SCH), 2.52 (dd, *J* = 1.4, 6.2 Hz, 1 H, SC*H*H), 2.21 (dd, *J* = 1.4, 5.6 Hz, 1 H, SCH*H*).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 137.8, 128.4, 127.77, 127.73, 76.6, 73.1, 32.1, 23.6.

Vicinal *N*,*N*-Dialkylaminoalkylmercaptans 3; General Procedure
To a rapidly stirred amine (6 mmol) in benzene–EtOH (6 mL, 9:1) was added dropwise (the flask was pressurized by a rubber capsule and the reagent was added by using an injector) to a solution of alkene sulfide (3 mmol) in the same solvent (3 mL) at 60 °C over 1 h. The reaction was then stirred at 60 °C for 24 h when TLC indicated the complete disappearance of thiirane. After removal of the solvent under reduced pressure, crude purification of the residue by column chromatography (silica gel; petroleum ether–EtOAc, 20:1) afforded amino alkylmercaptan.

1-Piperidino-2-propylmercaptan (3aa)
Yield: 69%; colorless oil; R_f 0.48 (petroleum ether–acetone, 5:1).

The product was oxidized directly without purification.

1-*N*,*N*-Diethylamino-3-phenoxy-2-propylmercaptan (3bb)
Yield: 82%; colorless oil; R_f 0.47 (petroleum ether–acetone, 10:1).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.80–6.88 (m, 5 H, Ph), 4.24–4.19 (m, 2 H, OCH_2), 3.18 (m, 1 H, SCH), 2.60 (br s, 1 H, SH), 2.50 (q, *J* = 6.8 Hz, 4 H, 2 × NCH_2), 0.97 (t, *J* = 6.8 Hz, 6 H, 2 × CH_3).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 158.5, 129.3, 120.8, 114.6, 67.5, 54.5, 50.2, 47.5, 11.8.

1-*N*,*N*-Dibenzylamino-2-propylmercaptan (3a)
Yield: 66%; colorless oil; R_f 0.53 (petroleum ether–EtOAc, 10:1).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.40–7.21 (m, 10 H, Ph), 3.64 (d, *J* = 13.2 Hz, 2 H, 2 × NC*H*H), 3.50 (d, *J* = 13.2 Hz, 2 H, 2 × NCHH), 3.14 (tq, *J* = 7.2, 6.8 Hz, 1 H, SCH), 2.48 (d, *J* = 7.2 Hz, 2 H, CH_2), 2.01 (br s,1 H, SH), 1.27 (d, *J* = 6.8 Hz, 3 H, CH_3).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 130.7, 130.4, 129.6, 129.3, 128.6, 128.2, 65.6, 59.6, 31.4, 21.5.

1-*N*,*N*-Dibenzylamino-3-phenoxy-2-propylmercaptan (3b)
Yield: 75%; colorless oil; R_f 0.43 (petroleum ether–EtOAc, 20:1).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.45–6.80 (m, 15 H, Ph), 4.08 (dd, *J* = 5.2, 9.5 Hz, 1 H, OC*H*H), 3.91 (dd, *J* = 6.2, 9.5 Hz, 1 H, OCH*H*), 3.62 (s, 4 H, 2 × NC*H*H), 3.45 (dddd, *J* = 5.2, 6.2, 7.2, 7.6 Hz, 1 H, SCH), 2.86 (dd, *J* = 7.6, 13.2 Hz, 1 H, NCH*H*), 2.60 (dd, *J* = 7.2, 13.2 Hz, 1 H, NCH*H*), 1.59 (br s, 1 H, SH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 158.5, 138.9, 129.5, 129.1, 128.3, 127.2, 121.0, 114.6, 70.8, 58.8, 57.6, 37.9.

(*S*)-1-*N*,*N*-Dibenzylamino-3-phenoxy-2-propylmercaptan [(*S*)-3b]
Colorless oil; yield: 78%; R_f 0.43 (petroleum ether–EtOAc, 20:1).

90% ee; determined by HPLC with Chiralcel AD column (hexane–*i*-PrOH, 99:1), flow rate 0.8 mL/min; t_{Rmajor} 8.17 min, t_{Rminor} 9.32 min.

$[\alpha]_D^{20}$ +4.2 (*c* 1.10, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.38–6.78 (m, 15 H, Ph), 4.07 (dd, *J* = 4.8, 9.2 Hz, 1 H, OC*H*H), 3.91 (dd, *J* = 3.2, 9.2 Hz, 1 H, OCH*H*), 3.61 (s, 4 H, 2 × NCH_2), 3.41 (dddd, *J* = 3.2, 4.8, 7.2, 7.6 Hz, 1 H, SCH), 2.85 (dd, *J* = 7.6, 13.0 Hz, 1 H, NC*H*H), 2.59 (dd, *J* = 7.2, 13.0 Hz, 1 H, NCH*H*), 2.02 (br s, 1 H, SH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 158.5, 138.9, 129.4, 129.0, 128.3, 127.2, 121.0, 114.6, 70.7, 58.8, 57.6, 37.9.

1-*N*,*N*-Dibenzylamino-2-octylmercaptan (3c)
Yield: 49%; colorless oil; R_f 0.51 (petroleum ether–EtOAc, 30:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37–7.24 (m, 10 H, Ph), 3.65 (d, *J* = 13.5 Hz, 2 H, 2 × NCH*H*), 3.46 (d, *J* = 13.5 Hz, 2 H, 2 × NC*H*H), 2.88 (quintet, *J* = 5.7 Hz, 1 H, SCH), 2.50 (dd, *J* = 0.9, 6.0 Hz, 1 H, NCH*H*), 2.15 (dd, *J* = 0.9, 5.4 Hz, 1 H, NCH*H*), 1.85–1.77 (m, 1 H, C*H*H), 1.56–1.42 (m, 3 H, CH_2CH_2), 1.40–1.22 (m, 6 H, 3 × CH_2), 0.89 (t, *J* = 6.6 Hz, 3 H, CH_3).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 130.1, 129.0, 128.2, 127.0, 58.6, 36.6, 36.0, 31.7, 29.3, 28.9, 25.6, 22.6, 14.0.

1-Benzyloxy-3-*N*,*N*-dibenzylamino-2-propylmercaptan (3d)
Yield: 82%; colorless oil; R_f 0.36 (petroleum ether–EtOAc, 20:1).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.29 (s, 15 H, Ph), 4.43 (s, 2 H, OCH_2), 3.60 (d, *J* = 13.6 Hz, 2 H, 2 × NC*H*H), 3.57 (dd, *J* = 4.8, 9.6 Hz, 1 H, OCH*H*), 3.49 (d, *J* = 13.6 Hz, 2 H, 2 × NCH*H*), 3.39 (dd, *J* = 6.6, 9.6 Hz, 1 H, OC*H*H), 3.24 (dddd, *J* = 4.8, 6.6, 12.8, 13.0 Hz, 1 H, SCH), 2.72 (dd, *J* = 7.7, 13.0 Hz, 1 H, NC*H*H), 2.49 (dd, *J* = 7.7, 12.8 Hz, 1 H, NC*H*H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.9, 138.1, 129.0, 128.3, 128.2, 127.6, 127.0, 73.1, 72.9, 58.5, 57.7, 38.5.

(*S*)-1-Benzyloxy-3-*N*,*N*-dibenzylamino-2-propylmercaptan [(*S*)-3d]
Yield: 78%; colorless oil; R_f 0.36 (petroleum ether–EtOAc, 20:1).

96% ee; determined by HPLC with Chiralcel OD column (hexane–*i*-PrOH, 99.7:0.3), flow rate 0.8 mL/min, t_{Rmajor} 29.6 min, t_{Rminor} 32.3 min.

$[\alpha]_D^{20}$ +13.1 (*c* 1.17, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37–7.20 (m, 15 H, Ph), 4.45 (s, 2 H, OCH_2), 3.60 (d, *J* = 13.6 Hz, 2 H, 2 × NC*H*H), 3.57 (dd, *J* = 4.8, 9.6 Hz, 1 H, OC*H*H), 3.49 (d, *J* = 13.6 Hz, 2 H, 2 × NCH*H*), 3.40 (dd, *J* = 6.3, 9.6 Hz, 1 H, OCH*H*), 3.26 (dddd, *J* = 4.8, 6.3, 6.9, 7.8 Hz, 1 H, SCH), 2.73 (dd, *J* = 6.9, 13.0 Hz, 1 H, NC*H*H), 2.50 (dd, *J* = 7.8, 13.0 Hz, 1 H, NCH*H*), 2.05 (br s, 1 H, SH).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 138.9, 138.0, 129.0, 128.3, 128.2, 127.61, 127.59, 127.0, 73.2, 73.0, 58.6, 57.8, 38.6.

1,3-Bis(*N*,*N*-dibenzylamino)-2-propylmercaptan (3e)
Yield: 75%; colorless oil; R_f 0.43 (petroleum ether–EtOAc, 20:1).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.41–7.10 (m, 20 H, Ph), 3.71 (d, *J* = 3.4 Hz, 1 H, SH), 3.59 (d, *J* = 13.8 Hz, 2 H, 2 × NCH*H*), 3.41 (d, *J* = 13.8 Hz, 2 H, 2 × NC*H*H), 3.00–2.78 (m, 1 H, SCH), 2.63 (dd, *J* = 5.0, 12.8 Hz, 2 H, 2 × NC*H*H), 2.34 (dd, *J* = 8.8, 12.8 Hz, 2 H, 2 × NCH*H*).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.9, 129.1, 128.7, 128.3, 128.2, 127.0, 59.2, 58.5, 58.4.

***trans*-2-*N*,*N*-Dibenzylaminocyclohexylmercaptan (3g)**
Yield: 18%; colorless oil; R_f 0.33 (petroleum ether–EtOAc, 20:1). The product was oxidized directly without further purification.

N,N-Disubstituted Aminoalkanesulfonic Acids 4; General Procedure

To a performic acid solution, prepared by mixing and stirring H_2O_2 (30%; 1.2 mL) and HCO_2H (88%; 12 mL) at r.t. for 1 h and cooled in an ice bath, was added amino mercaptan (2 mmol) in a mixture of HCl (36%; 1 mL) and HCO_2H (88%; 2.7 mL) dropwise, keeping the temperature at 0 °C. The resulting mixture was stirred at 0 °C for an additional 2 h and at r.t. for 2 d. After removal of the solvent, the residue was purified by column chromatography (CH_2Cl_2–MeOH, 20:1). Recrystallization (EtOH) gave 1-substituted 2-dialkylaminoethanesulfonic acid as colorless crystals.

1-Piperidinopropane-2-sulfonic Acid (4aa)

Yield: 88%; colorless crystals; mp 211–213 °C (from the episulfide); R_f 0.47 (CH_2Cl_2–MeOH, 5:1).

IR (KBr): 1239.8 (S=O), 1154.1 (S=O), 698.7 (SO) cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 9.18 (br s, 1 H, SO_3H), 3.91 (dd, *J* = 12.0, 14.0 Hz, 2 H, 2 × NCH*H*), 3.54–3.41 (m, 2 H, 2 × NCH*H*), 2.98–2.63 (m, 3 H, CH, NCH_2), 2.18–1.78 (m, 4 H, 2 × CH_2), 1.60–1.28 (m, 2 H, CH_2), 1.39 (d, *J* = 6.0 Hz, 3 H, CH_3).

^{13}C NMR (50 MHz, HCO_2H): δ = 57.6, 55.4, 52.4, 48.8, 22.3, 22.2, 20.3, 12.1.

MS (ESI): *m*/*z* = 208 $(MH)^+$.

Anal. Calcd for $C_8H_{17}NO_3S·0.75H_2O$ (220.81): C, 43.52; H, 8.45; N, 6.34. Found: C, 43.40; H, 8.39; N, 6.19.

1-*N*,*N*-Diethylamino-3-phenoxypropane-2-sulfonic Acid (4bb)

Yield: 93%; colorless crystals, mp 177–179 °C; R_f 0.57 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 1291.2 (S=O), 1144.4 (S=O), 726.0 (SO) cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 8.88 (br s, 1 H, SO_3H), 7.37–6.91 (m, 5 H, ArH), 4.70 (dd, *J* = 3.2, 9.2 Hz, 1 H, OC*H*H), 4.05 (t, *J* = 10.0 Hz, 1 H, OCH*H*), 3.71 (q, *J* = 7.2 Hz, 4 H, 2 × NCH_2), 3.92–3.20 (m, 3 H, $CHCH_2$), 1.46 (t, *J* = 7.2 Hz, 6 H, 2 × CH_3).

^{13}C NMR (75.5 MHz, HCO_2H): δ = 151.6, 129.3, 127.7, 126.0, 122.5, 114.2, 65.6, 54.0, 50.5, 49.5, 47.8, 8.1, 7.1.

MS (Negative-ESI): *m*/*z* = 286 $(M - H)^-$.

Anal. Calcd for $C_{13}H_{21}NO_4S$ (287.38): C, 54.33; H, 7.37; N, 4.87. Found: C, 54.25; H, 7.26; N, 4.87.

1-*N*,*N*-Dibenzylaminopropane-2-sulfonic Acid (4a)

Yield: 89%; colorless crystals, mp 253–255 °C; R_f 0.39 (CH_2Cl_2–MeOH, 5:1).

IR: 1233.4 (S=O), 1165.1 (S=O), 702.8 (SO) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 10.01 (br s, 1 H, SO_3H), 7.53–7.40 (m, 10 H, Ph), 4.72 (d, *J* = 12.2 Hz, 1 H, NC*H*H), 4.37 (d, *J* = 12.2 Hz, 1 H, NCH*H*), 3.28 (d, *J* = 11.0 Hz, 1 H, NC*H*H), 4.20 (d, *J* = 11.0 Hz, 1 H, NCH*H*), 3.26–3.20 (m, 2 H, NCH_2), 3.17–3.08 (m, 1 H, CH), 1.02 (d, *J* = 6.5 Hz, 3 H, CH_3).

^{13}C NMR (75.5 MHz, HCO_2H): δ = 130.2, 130.1, 129.4, 129.1, 128.3, 128.1, 58.6, 57.4, 53.6, 49.4, 11.9.

MS (Negative-ESI): *m*/*z* = 318 $(M - H)^-$.

Anal. Calcd for $C_{17}H_{21}NO_3S·0.5CH_3OH$ (335.44): C, 62.66; H, 6.91; N, 4.18. Found: C, 62.78; H, 6.82; N, 4.02.

1-*N*,*N*-Dibenzylamino-3-phenoxypropane-2-sulfonic Acid (4b)

Yield: 81%; colorless crystals; mp 199–201 °C; R_f 0.43 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 1244.7 (S=O), 1166.9 (S=O), 697.6 (SO) cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 10.34 (br s, 1 H, SO_3H), 7.62–6.71 (m, 15 H, Ph), 4.78–4.36 (m, 3 H, $CHCH_2$), 4.36–4.17 (m, 1 H, OC*H*H), 4.03–3.88 (m, 1 H, OCH*H*), 3.61 (s, 4 H, 2 × NCH_2).

^{13}C NMR (75.5 MHz, HCO_2H): δ =130.2, 130.1, 129.4, 129.1, 128.3, 128.1, 58.6, 57.4, 53.6, 49.4, 11.9.

MS (ESI): *m*/*z* = 412 $(MH)^+$.

Anal. Calcd for $C_{23}H_{25}NO_4S·1.25H_2O$ (434.03): C, 63.65; H, 6.39; N, 3.23. Found: C, 63.41; H, 6.12; N, 3.09.

(*S*)-1-*N*,*N*-Dibenzylamino-3-phenoxypropane-2-sulfonic Acid [(*S*)-4b]

Yield: 87%; colorless crystal; mp 210–212 °C; R_f 0.43 (CH_2Cl_2–MeOH, 10:1).

90% ee.

$[\alpha]_D^{20}$ +15.7 (*c* 1.05, 88% HCO_2H).

IR (KBr): 1244.7 (S=O), 1166.9 (S=O), 697.6 (SO) cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 10.32 (br s, 1 H, SO_3H), 7.62–6.71 (m, 15 H, Ph), 4.78–4.36 (m, 3 H, $CHCH_2$), 4.36–4.17 (m, 1 H, OC*H*H), 4.03–3.88 (m, 1 H, OCH*H*), 3.61 (s, 4 H, 2 × NCH_2).

^{13}C NMR (75.5 MHz, HCO_2H): δ = 130.2, 130.1, 129.4, 129.1, 128.3, 128.1, 58.6, 57.4, 53.6, 49.4, 11.9.

MS (ESI): *m*/*z* = 412 $(MH)^+$.

Anal. Calcd for $C_{23}H_{25}NO_4S·1.25H_2O$ (434.03): C, 63.65; H, 6.39; N, 3.23. Found: C, 63.41; H, 6.12; N, 3.09.

1-*N*,*N*-Dibenzylaminooctane-2-sulfonic Acid (4c)

Yield: 56%; colorless crystals; mp 230–232 °C; R_f 0.40 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 1291.9 (S=O), 1145.5 (S=O), 725.9 (SO) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 10.72 (br s, 1 H, SO_3H), 7.57–7.41 (m, 10 H, Ph), 4.60–4.43 (m, 3 H, NC*H*H, 2 × C*H*HN), 4.31 (dd, *J* = 5.1, 13.2 Hz, 1 H, CH*H*N), 3.60–3.45 (m, 2 H, 2 × CH*H*N), 2.64 (m, 1 H, CH), 2.04 (m, 1 H, C*H*H), 1.41–1.28 (m, 1 H, CH*H*), 1.28–1.10 (m, 8 H, 4 × CH_2), 0.84 (t, *J* = 6.9 Hz, 3 H, CH_3).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 130.6, 130.5, 130.2, 130.1, 129.6, 129.5, 129.2, 59.5, 56.5, 55.3, 54.4, 31.4, 29.1, 28.3, 26.6, 22.5, 14.0.

MS (Negative-ESI): *m*/*z* = 388 $(M - H)^-$.

Anal. Calcd for $C_{22}H_{31}NO_3S$ (389.55): C, 67.83; H, 8.02; N, 3.60. Found: C, 67.84; H, 7.96; N, 3.50.

1-Benzyloxy-3-*N*,*N*-dibenzylaminopropane-2-sulfonic Acid (4d)

Yield: 90%; colorless crystals, mp 164–166 °C; R_f 0.42 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 1246.7 (S=O), 1153.9 (S=O), 694.9 (SO) cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ =10.24 (br s, 1 H, SO_3H), 7.60–7.18 (m, 15 H, Ph), 4.51 (s, 2 H, OCH_2), 4.61–4.28 (m, 3 H, $CHCH_2$), 4.28–4.03 (m, 2 H, NCH_2), 3.55 (s, 4 H, 2 × NCH_2).

^{13}C NMR (50 MHz, HCO_2H): δ = 130.7, 130.4, 129.8, 129.4, 128.5, 128.3, 128.0, 127.1, 67.9, 58.7, 57.7, 53.9, 52.0.

MS (ESI): *m*/*z* = 426 $(MH)^+$.

Anal. Calcd for $C_{24}H_{27}NO_4S·1.5H_2O$ (452.56): C, 63.69; H, 6.68; N, 3.09. Found: C, 63.46; H, 6.17; N, 2.91.

(*S*)-1-Benzyloxy-3-*N*,*N*-dibenzylaminopropane-2-sulfonic Acid [(*S*)-4d]

Yield 84%; colorless crystals; mp 170–171.5 °C; R_f 0.42 (CH_2Cl_2–MeOH, 10:1).

96% ee.

$[\alpha]_D^{20}$ +26.5 (*c* 1.38, 88% HCO_2H).

IR (KBr): 1246.7 (S=O), 1153.9 (S=O), 694.9 (SO) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 10.26 (br s, 1 H, SO_3H), 7.60–7.18 (m, 15 H, Ph), 4.51 (s, 2 H, OCH_2), 4.61–4.28 (m, 3 H, $CHCH_2$), 4.28–4.03 (m, 2 H, NCH_2), 3.55 (s, 4 H, 2 × NCH_2).

^{13}C NMR (50 MHz, HCO_2H): δ = 130.7, 130.4, 129.8, 129.4, 128.5, 128.3, 128.0, 127.1, 67.9, 58.7, 57.7, 53.9, 52.0.

MS (ESI): *m*/*z* = 426 $(MH)^+$.

Anal. Calcd for $C_{24}H_{27}NO_4S·1.5H_2O$ (452.56): C, 63.69; H, 6.68; N, 3.09. Found: C, 63.46; H, 6.17; N, 2.91.

1,3-Bis(*N*,*N*-dibenzylamino)propane-2-sulfonic Acid (4e)
Yield: 90%; colorless crystals; mp 210–212 °C; R_f 0.33 (CH_2Cl_2–MeOH, 20:1).

IR (KBr): 1247.1 (S=O), 1168.2 (S=O), 695.6 (SO) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.14 (br s, 1 H, SO_3H), 7.60–7.40 (m, 20 H, ArH), 4.30 (br s, 8 H, 4 × NCH_2), 3.80–3.57 (m, 4 H, 2 × NCH_2), 3.44 (m, 1 H, CH).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 130.6, 130.5, 130.4, 130.0, 129.3, 128.6, 127.8, 59.0, 58.5, 50.6, 48.8.

MS (ESI): *m*/*z* = 515 $(MH)^+$.

Anal. Calcd for $C_{31}H_{34}N_2O_3S·2H_2O$ (550.71): C, 67.61; H, 6.95; N, 5.09. Found: C, 67.60; H, 6.69; N, 4.95.

***trans*-2-*N*,*N*-Dibenzylaminocyclohexanesulfonic Acid (4g)**
Yield: 77%; colorless crystals; mp 285–287 °C; R_f 0.61 (CH_2Cl_2–MeOH, 10:1).

IR (KBr): 1239.5 (S=O), 1214.5 (S=O), 699.2 (SO) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.02 (br s, 1 H, SO_3H), 7.64–7.12 (m, 10 H, Ph), 4.86 (d, *J* = 12.8 Hz, 1 H, CH*H*N), 4.40 (dd, *J* = 7.4, 14.0 Hz, 1 H, C*H*HN), 4.16 (dd, *J* = 2.9, 13.4 Hz, 1 H, CH*H*N), 4.11 (dd, *J* = 9.1, 12.8 Hz, 1 H, C*H*HN), 3.42 (dt, *J* = 3.3, 11.4 Hz, 1 H, CH), 3.30 (dd, *J* = 4.0, 11.1 Hz, 1 H, CH), 2.30 (dd, *J* = 2.56, 12.5 Hz, 1 H, C*H*H), 2.15 (m, 1 H, CH*H*), 1.87 (m, 1 H, C*H*H), 1.71–1.60 (m, 2 H, CH_2), 1.40–1.18 (m, 3 H, CH_2).

^{13}C NMR (75.5 MHz, HCO_2H): δ = 130.3, 129.9, 129.7, 129.6, 129.2, 129.0, 128.6, 61.1, 56.1, 53.2, 26.0, 23.2, 22.8, 22.5.

MS (Negative-ESI): *m*/*z* = 358 $(M – H)^-$.

Anal. Calcd for $C_{20}H_{25}NO_3S$ (359.48): C, 66.82; H, 7.01; N, 3.90. Found: C, 66.43; H, 7.10; N, 3.56.

1-Substituted 2-Aminoethanesulfonic Acids and 2-Aminocycloalkanesulfonic Acid (Hydrogenolysis); General Procedure
N,*N*-Dibenzylaminoalkanesulfonic acid (0.50 mmol) was dissolved in MeOH (10 mL), and $Pd(OH)_2$/C (20%; 30 mg) was added. The suspension was stirred under an atmosphere of hydrogen at 50 °C overnight. MeOH (20 mL) was added to dissolve the precipitate. The catalyst was removed by filtration through filter paper and was washed with MeOH (2 × 5 mL). After evaporation of the solvent the crude product was purified by recrystallization (MeOH) to afford colorless crystals.

1-Aminopropane-2-sulfonic Acid (5a)
Yield: 90%; colorless crystals; mp 286–288 °C (Lit.[22] 283–286 °C).

MS (ESI): *m*/*z* = 140 $(MH)^+$.

1-Amino-3-phenoxypropane-2-sulfonic Acid (5b)
Yield: 72%; colorless crystals; mp 307–309 °C.

IR (KBr): 3062 (br, NH, OH), 1248.9 (SO_2), 1170 (SO_2) cm^{-1}.

^{1}H NMR (300 MHz, D_2O): δ = 7.33–6.80 (m, 5 H, Ph), 4.39 (dd, *J* = 3.9, 10.5 Hz, 1 H, OC*H*H), 4.17 (dd, *J* = 3.3, 7.2 Hz, 1 H, NC*H*H), 3.56–3.39 (m, 3 H, OCH*H*, NCH*H*, CH).

^{13}C NMR (75.5 MHz, D_2O): δ = 157.1, 128.7, 120.1, 113.6, 64.7, 54.3, 37.3.

MS (Negative-ESI): *m*/*z* = 230 $(M – H)^-$.

Anal. Calcd for $C_9H_{13}NO_4S$ (231.27): C, 46.74; H, 5.67; N, 6.06. Found: C, 46.78; H, 5.76; N, 5.86.

(*S*)-1-Amino-3-phenoxypropane-2-sulfonic Acid [(*S*)-5b]
Yield: 93%; colorless crystals; mp 329–331 °C.

90% ee.

$[\alpha]_D^{20}$ +22.9 (*c* 0.85, 88% HCO_2H).

IR (KBr): 3062 (br, NH, OH), 1248.9 (SO_2), 1170 (SO_2) cm^{-1}.

^{1}H NMR (300 MHz, D_2O): δ = 7.33–6.80 (m, 5 H, Ph), 4.39 (dd, *J* = 3.9, 10.5 Hz, 1 H, OC*H*H), 4.17 (dd, *J* = 3.3, 7.2 Hz, 1 H, NC*H*H), 3.56–3.39 (m, 3 H, OCH*H,* NCH*H*, CH).

^{13}C NMR (75.5 MHz, D_2O): δ = 157.1, 128.7, 120.1, 113.6, 64.7, 54.3, 37.3.

MS (Negative-ESI): *m*/*z* = 230 $(M – H)^-$.

Anal. Calcd for $C_9H_{13}NO_4S$ (231.27): C, 46.74; H, 5.67; N, 6.06. Found: C, 46.78; H, 5.76; N, 5.86.

1-Aminooctane-2-sulfonic Acid (5c)
Yield: 89%; colorless crystals; mp >360 °C.

IR (KBr): 3174.3 (br, NH, SOH), 1228.8 (SO_2), 1167.5 (SO_2) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.70 (br s, 3 H, NH_3^+), 2.98 (dd, *J* = 2.9, 13.1 Hz, 1 H, NC*H*H), 2.86 (dd, *J* = 9.6, 13.1 Hz, 1 H, NCH*H*), 2.54 (m, 1 H, CH), 1.79–1.73 (m, 1 H, CH*H*), 1.43–1.30 (m, 1 H, C*H*H), 1.30–1.24 (m, 8 H, 4 × CH_2), 0.88 (t, *J* = 6.6 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 55.6, 39.5, 31.1, 28.6, 27.9, 26.2, 22.1, 14.0.

MS (ESI): *m*/*z* = 232 $(M + Na)^+$.

Anal. Calcd for $C_8H_{19}NO_3S$ (209.31): C, 45.91; H, 9.15; N, 6.69. Found: C, 45.96; H, 8.78; N, 6.70.

1-Amino-3-benzyloxypropane-2-sulfonic Acid (5d)
Yield: 83%; colorless crystals; mp 227–229 °C.

IR (KBr): 3376.4, 3217.6 (br, NH, OH), 1269.8 (SO_2), 1175 (SO_2) cm^{-1}.

^{1}H NMR (300 MHz, D_2O): δ = 7.30 (s, 5 H, Ph), 4.17 (d, *J* = 13.2 Hz, 1 H, C*H*HO), 4.19 (d, *J* = 13.2 Hz, 1 H, CH*H*O), 3.85 (dd, *J* = 4.2, 12.0 Hz, 1 H, C*H*HO), 3.56 (dd, *J* = 7.5, 12.0 Hz, 1 H, CH*H*O), 3.30–3.24 (m, 2 H, NCH_2), 3.24–3.12 (m, 1 H, CH).

^{13}C NMR (100 MHz, D_2O): δ = 130.6, 130.29, 130.28, 129.8, 59.7, 57.8, 51.8.

MS (Positive-ESI): *m*/*z* = 246 $(MH)^+$.

Anal. Calcd for $C_{10}H_{15}NO_4S$ (245.30): C, 48.96; H, 6.16; N, 5.71. Found: C, 48.96; H, 6.21; N, 5.64.

(*S*)-1-Amino-3-benzyloxypropane-2-sulfonic Acid [(*S*)-5d]
Yield 81%; colorless crystal; mp 239–241 °C.

96% ee.

$[\alpha]_D^{20}$ +28.9 (*c* 1.71, 88% HCO_2H).

IR (KBr): 3376.4, 3217.6 (br, NH, OH), 1269.8 (SO_2), 1175 (SO_2) cm^{-1}.

^{1}H NMR (300 MHz, D_2O): δ = 7.30 (s, 5 H, Ph), 4.17 (d, *J* = 13.2 Hz, 1 H, C*H*HO), 4.19 (d, *J* = 13.2 Hz, 1 H, CH*H*O), 3.85 (dd, *J* = 4.2, 12.0 Hz, 1 H, C*H*HO), 3.56 (dd, *J* = 7.5, 12.0 Hz, 1 H, CH*H*O), 3.30–3.24 (m, 2 H, NCH_2), 3.24–3.12 (m, 1 H, CH).

^{13}C NMR (100 MHz, D_2O): δ = 130.6, 130.29, 130.28, 129.8, 59.7, 57.8, 51.8.

MS (ESI, positive ion): *m*/*z* = 246 $(MH)^+$.

Anal. Calcd for $C_{10}H_{15}NO_4S$ (245.30): C, 48.96; H, 6.16; N, 5.71. Found: C, 48.96; H, 6.21; N, 5.64.

1,3-Diaminopropane-2-sulfonic Acid (5e)
Yield: 92%; colorless crystals, mp 251–253 °C.

IR (KBr): 3152.4 (br, NH, SOH), 1191.8 (SO_2), 1090.0 (SO_2), 715.2 (SO) cm^{-1}.

^1H NMR (300 MHz, D_2O): δ = 3.41–3.31 (m, 1 H, CH), 3.29–3.19 (m, 4 H, 2 × CH_2).

^{13}C NMR (75.5 MHz, D_2O): δ = 56.1, 40.4.

MS (Negative-ESI): *m*/*z* = 153 $(M - H)^-$.

Anal. Calcd for $C_3H_{10}N_2O_3S{\cdot}2H_2O$ (190.22): C, 18.94; H, 7.42; N, 14.73. Found: C, 18.92; H, 7.58; N, 14.79.

***trans*-2-Aminocyclohexanesulfonic Acid (5g)**
Yield: 75%; colorless crystals; mp >360 °C (Lit.[20] 408 °C).

MS (ESI): *m*/*z* = 180 $(MH)^+$.

1-Amino-3-hydroxypropane-2-sulfonic Acid (6d)
1-Amino-3-benzyloxypropane-2-sulfonic acid (**5d**; 0.20 g, 0.82 mmol) was dissolved in MeOH (15 mL), and Pd/C (20%, 20 mg) was added. The suspension was stirred under an atmosphere of hydrogen at 50 °C for 1 d. The catalyst was removed by filtration through filter paper and was washed with MeOH (2 × 5 mL). Recrystallization (MeOH–Et_2O) of the residue gave **6d**.

Yield: 72%; colorless crystals, mp 165–167 °C.

IR (KBr): 3396.4, 3087.6 (br, NH, OH), 1211.7 (SO_2), 1165.5 (SO_2) cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.70 (br s, NH_3^+), 4.80 (br s, 1 H, OH), 3.83 (dd, *J* = 4.2, 11.2 Hz, 1 H, OC*H*H), 3.35 (dd, *J* = 2.4, 11.2 Hz, 1 H, OCH*H*), 3.14 (dd, *J* = 3.7, 13.0 Hz, 1 H, NC*H*H), 2.97 (dd, *J* = 9.2, 13.0 Hz, 1 H, NCH*H*), 2.76 (dddd, *J* = 2.4, 3.7, 4.2, 9.2 Hz, 1 H, CH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 59.2, 58.2, 38.1.

MS (Positive-ESI): *m*/*z* = 156 $(MH)^+$.

HRMS (Negative-SIMS): *m*/*z* calcd for $C_3H_9NO_4S$, 154.0174 $[M - H]^-$; found, 154.0180.

(*S*)-1-Amino-3-hydroxypropane-2-sulfonic Acid [(*S*)-6d]
Yield: 77%; colorless crystals; mp 221–222 °C.

96% ee.

$[\alpha]_D^{20}$ +26.4 (*c* 1.32, 88% HCO_2H).

IR (KBr): 3396.4, 3087.6 (br, NH, OH), 1211.7 (SO_2), 1165.5 (SO_2) cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.69 (br s, NH_3^+), 4.80 (br s, 1 H, OH), 3.83 (dd, *J* = 4.2, 11.2 Hz, 1 H, OC*H*H), 3.35 (dd, *J* = 2.4, 11.2 Hz, 1 H, OCH*H*), 3.14 (dd, *J* = 3.7, 13.0 Hz, 1 H, NC*H*H), 2.97 (dd, *J* = 9.2, 13.0 Hz, 1 H, NC*H*H), 2.76 (dddd, *J* = 2.4, 3.7, 4.2, 9.2 Hz, 1 H, CH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 59.2, 58.2, 38.1.

MS (ESI, positive ion): *m*/*z* = 156 $(MH)^+$.

HRMS (Negative-SIMS): *m*/*z* calcd for $C_3H_9NO_4S$, 154.0174 $[M - H]^-$; found, 154.0179.

Acknowledgment

The project was supported partly by the National Natural Science Foundation of China (No. 20272002 and 20472005), Ministry of Education of P. R. China (SRF for ROCS and EYTP), and Peking University (President grant).

References

(1) Pollack, S. J.; Hsiun, P.; Schultz, P. G. *J. Am. Chem. Soc.* **1989**, *111*, 5961.
(2) Morgan, B. P.; Scholtz, J. M.; Ballinger, M. D.; Zipkin, I. D.; Bartlett, P. A. *J. Am. Chem. Soc.* **1991**, *113*, 297.
(3) Xu, J. X.; Yu, L. *Chin. J. Synth. Chem.* **1999**, *7*, 153.
(4) Xu, J. X.; Fu, N. Y. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1223; and references cited therein.
(5) Xu, J. X. *Chin. J. Org. Chem.* **2003**, *23*, 1.
(6) Huxtable, R. J. *Physiol. Rev.* **1992**, *72*, 101.
(7) Liebowitz, S. M.; Lombardini, J. B.; Salva, P. S. *Biochem. Pharmacol.* **1988**, *37*, 1303.
(8) Higashiura, H.; Morino, H.; Matsuura, H.; Toyomaki, Y.; Ienaga, K. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1479.
(9) Gude, M.; Piarulli, U.; Potenza, D.; Salom, B.; Gennari, C. *Tetrahedron Lett.* **1996**, *37*, 8589.
(10) Braghiroli, D.; Di Bella, M. *Tetrahedron: Asymmetry* **1996**, *7*, 2145.
(11) Braghiroli, D.; Avallone, R.; Di Bella, M. *Tetrahedron: Asymmetry* **1997**, *8*, 2209.
(12) Braghiroli, D.; Mussati, E.; Di Bella, M.; Saladini, M. *Tetrahedron: Asymmetry* **1996**, *7*, 831.
(13) Braghiroli, D.; Di Bella, M. *Tetrahedron Lett.* **1996**, *37*, 7319.
(14) Higashiura, K.; Ienaga, K. *J. Org. Chem.* **1992**, *57*, 764.
(15) Moree, W. J.; van der Marel, G. A.; Liskamp, R. M. J. *Tetrahedron Lett.* **1992**, *33*, 6389.
(16) Moree, W. J.; van der Marel, G. A.; Liskamp, R. M. J. *J. Org. Chem.* **1995**, *60*, 5157.
(17) Monnee, M. C. F.; Marijne, M. F.; Brouwer, A. J.; Liskamp, R. M. J. *Tetrahedron Lett.* **2000**, *41*, 7991.
(18) Brouwer, A. J.; Monnee, M. C. F.; Liskamp, R. M. J. *Synthesis* **2000**, 1579.
(19) Lowik, D. W. P. M.; Liskamp, R. M. J. *Eur. J. Org. Chem.* **2000**, 1219.
(20) Cordero, F. M.; Cacciarini, M.; Machetti, F.; De Sarlo, F. *Eur. J. Org. Chem.* **2002**, 1407.
(21) Xu, J. X. *Tetrahedron: Asymmetry* **2002**, *13*, 1129.
(22) Gold, M. H.; Skebelsky, M.; Lang, G. *J. Org. Chem.* **1951**, *16*, 1500.
(23) Xu, J. X.; Xu, S. *Synthesis* **2004**, 276.
(24) Xu, J. X.; Xu, S. *Heteroat. Chem.* **2005**, *16*, in press.
(25) Snyder, H. R.; Stewart, J. M.; Ziegler, J. B. *J. Am. Chem. Soc.* **1947**, *69*, 2672.
(26) Brimeyer, M. O.; Mehrota, A.; Quici, S.; Nigam, A.; Regen, S. L. *J. Org. Chem.* **1980**, *45*, 4254.
(27) Stewart, J. M. *J. Org. Chem.* **1963**, *28*, 596.
(28) Parker, R. E.; Isaacs, N. S. *Chem. Rev.* **1959**, *59*, 737.
(29) Ma, L. G.; Xu, J. X. *Prog. Chem.* **2004**, *16*, 220.
(30) Liebowitz, S. M.; Lombardini, J. B.; Salva, P. S. *Biochem. Pharmacol.* **1987**, *36*, 2109.
(31) Lai, M. T.; Oh, E.; Shih, Y.; Liu, H. W. *J. Org. Chem.* **1992**, *57*, 2471.
(32) Klunder, J. M.; Onami, T.; Sharpless, K. B. *J. Org. Chem.* **1989**, *54*, 1295.
(33) Price, C. C.; Kirk, P. F. *J. Am. Chem. Soc.* **1953**, *75*, 2396.
(34) Hansen, T. V.; Vaagen, V.; Partali, V.; Anthonsen, H. W.; Anthonsen, T. *Tetrahedron: Asymmetry* **1995**, *6*, 499.
(35) Imai, T.; Hayakawa, K.; Satoh, T.; Kaga, H.; Kakuchi, T. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 3443.
(36) Calvo-Flores, F. G.; Carcia-Mendoza, P.; Hernandez-Mateo, F.; Isac-Garcia, J.; Santoyo-Gonzalez, F. *J. Org. Chem.* **1997**, *62*, 3944.