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A new and expeditious asymmetric synthesis of (*R*)- and (*S*)-2-aminoalkanesulfonic acids from chiral amino alcohols

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Abstract—The mechanism for the transformation of β-amino alcohol methanesulfonate hydrochlorides into sodium β-amino alkanesulfonates using sodium sulfite was investigated. The results show that sodium sulfite initially neutralizes the β-amino alcohol methanesulfonate hydrochloride to give a free β-amino alcohol methanesulfonate, which then cyclizes to a 2-alkylaziridine. Attack by the previously formed sodium bisulfite at the less hindered carbon atom of the aziridine ring then yields a β-amino alkanesulfate sodium salt. Based on this mechanistic proposal, a new and rapid asymmetric synthesis of (*R*)- and (*S*)-2-aminoalkanesulfonic acids from chiral amino alcohols was developed. Chiral amino alcohols were converted to chiral aziridines through the Wenker method or Mitsunobu reaction and the resulting aziridines were reacted with sodium bisulfite to produce chiral β-amino alkanesulfonic acids.

1. Introduction

Several 2-aminoalkanesulfonic acids have been found in many mammalian tissues and are involved in various important physiological processes.[1] However, little attention has been paid to their syntheses either in racemic or enantiomerically pure form, which could allow the study of these physiological processes.[1] On the other hand, there has been increasing interest in the structural modification of natural peptides to overcome the limitations associated with their development as therapeutically useful agents, and to gain information on the nature and mechanism of the peptide–receptor interactions.[2–4] Phosphonamidate-, phosphonate- and sulfonamide-containing peptides are very important modified peptides and are recognized to be able to mimic transition-state analogues for ester and amide hydrolysis because of their tetrahedral structure.[5,6] Recently aminoalkylphosphonic acid and aminoalkanesulfonic acid derivatives, and phosphonopeptides and sulfonopeptides have been widely used as enzyme inhibitors and heptans in the development of catalytic antibodies.[5,6] Many methods for the synthesis of amino alkylphosphonic acids have been developed,[7,8] but few methods are available for the synthesis of aminoalkanesulfonic acids[9–15] and their derivatives.[16–23] To carry out these investigations, it is very important to develop effective routes to prepare chiral amino alkanesulfonic acids as research materials or building blocks for the synthesis of sulfonopeptides.

As part of a program directed towards the synthesis and study of phosphonopeptides and sulfonopeptides as enzyme inhibitors, we sought to prepare chiral 2-aminoalkanesulfonic acids as building blocks. Preparation of chiral 2-aminoalkanesulfonic acids from chiral amino alcohols is very useful method. Although both chiral β-amino primary alcohols and chiral β-amino secondary alcohols produce chiral 2-aminoalkanesulfonic acids,[10–13] chiral β-amino primary alcohols produce chiral 2-aminoalkanesulfonic acids with the same configuration;[10,12,13] however, chiral β-amino secondary alcohols produce chiral 2-aminoalkanesulfonic acids with inverted configuration.[11] The mechanism of the reaction is still unclear.[11,14] I herein report the study of the mechanism and a short preparative route to chiral 2-aminoalkanesulfonic acids from chiral β-amino alcohols.

2. Results and discussion

Chiral 2-aminoalkanesulfonic acids can be prepared effectively from chiral β-amino alcohols.[10–13] However, inversion of the configuration and rearrangement occurred when chiral β-amino secondary alcohols were

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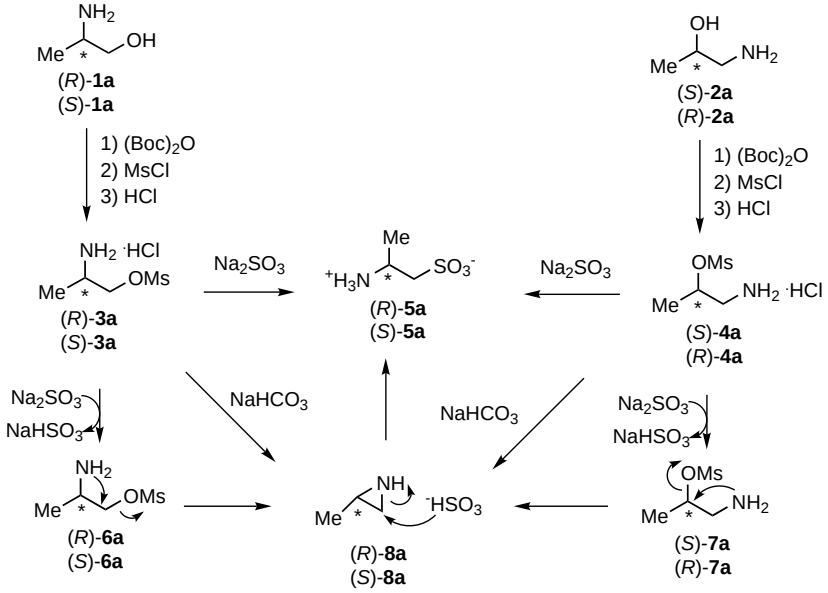
used in the preparation.[11,14] To understand the reaction and to use the method effectively, the mechanism and stereochemical outcome of the reaction were examined. Because the preparation of both (*R*)- and (*S*)-2-aminopropanesulfonic acids (*R*)-**5a** and (*S*)-**5a** from (*R*)- and (*S*)-2-aminopropanols (*R*)-**1a** and (*S*)-**1a** or (*S*)- and (*R*)-1-amino-2-propanols (*R*)-**2a** and (*S*)-**2a**, respectively, was reported and they were characterized fully,[10,11] these chiral amino alcohols are perfectly suited for use in model reactions for mechanistic investigations into the reaction. The amino alcohols (*R*)-**1a** and (*S*)-**1a**, and (*R*)-**2a** and (*S*)-**2a** were converted to the corresponding amino alcohol methanesulfonate hydrochlorides (*R*)-**3a** and (*S*)-**3a**, and (*R*)-**4a** and (*S*)-**4a**, respectively, according to literature procedures.[10,11] Based on the stereochemistry of the reactions,[10,11] it was rationalized that an aziridine could be a possible intermediate in the sodium sulfite substitution step. To verify this, the (*R*)- and (*S*)-2-aminopropanol methanesulfonate hydrochlorides (*R*)-**3a** and (*S*)-**3a** were neutralized carefully with the non-nucleophilic sodium bicarbonate to obtain the corresponding (*R*)- and (*S*)-2-methylaziridines (*R*)-**8a** and (*S*)-**8a**, respectively, without configurational inversion. However, the (*R*)- and (*S*)-1-amino-2-propanol methanesulfonate hydrochlorides (*R*)-**4a** and (*S*)-**4a** give (*S*)- and (*R*)-2-methylaziridines (*S*)-**8a** and (*R*)-**8a**, respectively, with inversion at the stereogenic center under the same reaction conditions. The (*R*)- and (*S*)-2-methylaziridines (*R*)-**8a** and (*S*)-**8a** were treated with sodium bisulfite to give (*R*)- and (*S*)-2-aminopropanesulfonic acids (*R*)-**5a** and (*S*)-**5a**, respectively, in good yields. The results indicate that aziridines are intermediates in the reaction of β-amino alcohol methanesulfonate hydrochlorides and sodium sulfites. The proposed mechanism is as follows: Sodium sulfite initially neutralizes the β-amino alcohol methanesulfonate hydrochloride (**3**, **4**) to give a free β-amino alcohol methanesulfonate (**6**, **7** respectively), and sodium bisulfite. The β-amino alcohol methanesulfonates **6** and **7** undergo neighboring-group assisted cyclization to form the 2-alkylaziridine **8**, which is further attacked by the previously generated sodium bisulfite at the less hindered carbon atom of the aziridine ring to yield the β-amino alkanesulfonate sodium salt **5**. In the aziridine formation step, the free amino groups attack sulfonate groups to form the aziridine rings. For the β-amino primary alcohol methanesulfonates **6**, secondary amines attack primary alcohol methanesulfonates to form aziridines **8** with the same configuration as amino alcohols **1**. However, for β-amino secondary alcohol methanesulfonates **7**, primary amines attack secondary alcohol methanesulfonates to form aziridines **8** with inverted configuration due to S_N2 substitution. In the nucleophilic aziridine ring-opening step, sodium bisulfite always attacks the less hindered atom of the aziridine ring to yield 2-aminoalkanesulfonic acids **5** without any configurational change. Thus, chiral β-amino primary alcohols **1** produce chiral 2-aminoalkanesulfonic acids **5** having the same configuration. However, chiral β-amino secondary alcohols **2** produce chiral 2-aminoalkanesulfonic acids **5** with inverted configuration (Scheme 1).

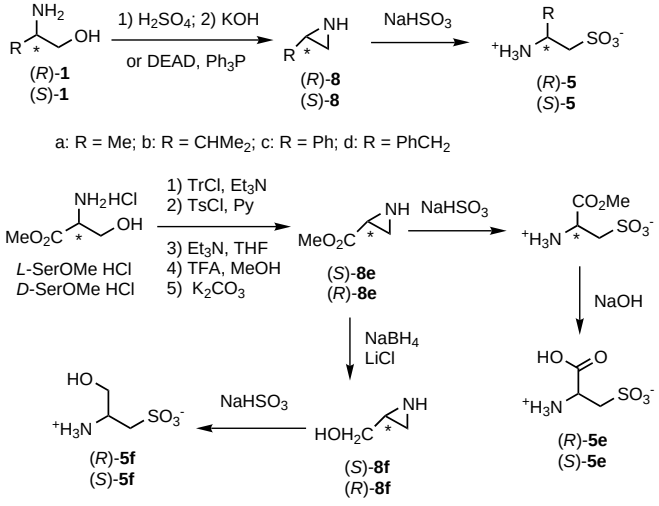
Based on this mechanism, aziridines should be useful starting materials for the preparation of 2-aminoalkanesulfonic acids. It has been found that preparation of racemic 2-aminoalkanesulfonic acids was claimed in patents,[24,25] but no report on the asymmetric synthesis of 2-aminoalkanesulfonic acids from aziridines was found. There is no available method for the direct preparation of enantiomerically pure *N*-unsubstituted aziridines from olefins, but they can be formed from chiral β-amino alcohols, which in turn can be readily prepared from chiral amino acids by reduction.[26] Chiral amino alcohols **1** were converted to chiral aziridines **8** through the Wenker method via their corresponding hydrogen sulfates.[27,28] The chiral amino alcohols were



Scheme 1.

neutralized with sulfuric acid and the resulting salts were dehydrated to yield the hydrogen sulfates. Addition of aqueous potassium hydroxide resulted in the formation of 2-substituted aziridines **8**. In the cyclization, amino groups attack activated hydroxy groups to produce the corresponding aziridines without configuration conversion. Chiral amino alcohols **1** were also converted to chiral aziridines **8** through Mitsunobu reaction using DEAD (diethyl azodicarboxylate) and triphenylphosphine as reagents in mild conditions.[29] The aziridines **8** were reacted with sodium bisulfite to produce chiral β-amino alkanesulfonic acids **5** with the same configurations as the corresponding β-amino primary alcohols **1** (Scheme 2).

To extend the application of this method, four functionalized chiral aziridines were prepared from L- or D-serines. Although L- and D-serine methyl esters can be converted to the corresponding methyl 2-aziridinecarboxylates directly via Mitsunobu reaction,[29] the yields are not satisfactory due to the volatile nature of these compounds.[30] Additionally, most of the methyl 2-aziridinecarboxylates degraded during work-up. L- and D-Serines were converted successfully to chiral methyl 2-aziridinecarboxylates according to the literature procedure.[30] L- and D-Serine methyl ester hydrochlorides were *N*-tritylated and *O*-tosylated, respectively. The resulting products were treated with triethylamine in refluxing THF to give the corresponding chiral methyl *N*-trityl 2-aziridinecarboxylates. Deprotection of the trityl group using excess trifluoroacetic acid and methanol at low temperature furnished the unstable methyl 2-aziridinecarboxylate trifluoroacete salts **8e**·TFA, which were basified and reacted with sodium bisulfite immediately to produce sodium 2-amino-2-methoxycarbonylethanesulfonates. After saponification and purification via ion-exchange chromatography, 2-amino-2-carboxyethanesulfonic acids **5e**, D- and L-cysteic acids, were obtained in good yields. While the methyl 2-aziridinecarboxylate trifluoroacete salts were basified and reduced with lithium borohydride to give rise to corresponding chiral 2-aziridinemethanols **8f**, which were reacted in situ with sodium bisulfite to yield chiral 2-amino-3-hydroxypropanesulfonic acids **5f**, D- and L-cysteinolic acids (Scheme 2). Both carboxy- and hydroxy-functionalized aziridines can be converted to the corresponding functionalized β-amino alkanesulfonic acids via nucleophilic substitution with sodium bisulfite.



Scheme 2.

3. Conclusion

In conclusion, the mechanism for the transformation of β-amino alcohol methanesulfonate hydrochlorides into sodium β-amino alkanesulfonates with sodium sulfite was investigated. The results show that sodium sulfite neutralizes the β-amino alcohol methanesulfonate hydrochloride to give sodium bisulfite and the free β-amino alcohol methanesulfonate, which undergoes a sequence involving neighboring-group assisted cyclization to a 2-alkylaziridine. The sodium bisulfite generated then attacks the aziridine at the less hindered carbon atom to yield a sodium β-amino alkanesulfonate. Based on this mechanism, a new and short asymmetric synthesis of chiral 2-aminoalkanesulfonic acids from chiral amino alcohols was developed through Wenker or Mitsunobu cyclization and nucleophilic ring-opening reaction with sodium bisulfite.

4. Experimental

4.1. General method

Melting points were measured on a Yanaco MP-500 melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian Mercury 200 (200 MHz) spectrometer in $CDCl_3$ with TMS as an internal standard or in D_2O. Mass spectra were obtained on a VG-ZAB-HS mass spectrometer. CHN analyses were recorded on an Elementar Vario EL analyzer. Optical rotations were measured on a Perkin–Elmer 341LC polarimeter with a thermally jacketed 10 cm cell (concentration c given as g/100 mL). IR spectra were taken on a Brucker Vector 22 FT-IR spectrophotometer in KBr pellet. The NMR data of all known compounds are identical to those earlier reported in the literature.[10,11,27,28,31–33]

(*R*)- and (*S*)-Amino alcohols were prepared from the corresponding chiral amino acids according to known method[26] or were purchased from Aldrich and Acros Chemical Co., Inc. Dichloromethane was heated under reflux over calcium hydride and distilled prior to use. Triethylamine was heated under reflux over sodium hydroxide and distilled prior to use.

4.2. General procedure for the synthesis of chiral amino alcohol methanesulfonate hydrochlorides (*R*)- and (*S*)-3a, and (*R*)- and (*S*)-4a

(*R*)- and (*S*)-amino alcohol methanesulfonate hydrochlorides **3a** and **4a** were synthesized from the corresponding (*R*)- and (*S*)-amino alcohols according to the literature method.[11]

4.2.1. (*R*)-2-Aminopropanol methanesulfonate hydrochlorides (*R*)-3a. Colorless crystal; mp 135–136°C; $[\alpha]_D^{25}=-10.4$ (*c*, 1.10, DMF). Lit.:[10] mp 135–136°C; $[\alpha]_D^{25}=-10.3$ (*c*, 1, DMF).

4.2.2. (*S*)-2-Aminopropanol methanesulfonate hydrochlorides (*S*)-3a. Colorless crystal; mp 133–134°C; $[\alpha]_D^{25}=+10.2$ (*c*, 1.08, DMF). Lit.:[10] mp 132–133°C; $[\alpha]_D^{25}=+10.3$ (*c*, 1, DMF).

4.2.3. (*R*)-1-Amino-2-propanol methanesulfonate hydrochlorides (*R*)-4a. Colorless crystal; mp 128–129°C; $[\alpha]_D^{25}=-18.5$ (*c*, 1.02, H_2O). Lit.:[11] mp. 128–129°C; $[\alpha]_D^{25}=-18.5$ (*c*, 1.0, H_2O).

4.2.4. (*S*)-1-Amino-2-propanol methanesulfonate hydrochlorides (*S*)-4a. Colorless crystal; mp 128–129°C; $[\alpha]_D^{25}=+18.4$ (*c*, 1.12, H_2O). Lit.:[11] mp 128–129°C. $[\alpha]_D^{25}=+18.5$ (*c*, 1.0, H_2O).

4.3. Neutralization of chiral amino alcohol methanesulfonate hydrochlorides (*R*)- and (*S*)-3a, and (*R*)- and (*S*)-4a with sodium bicarbonate, and synthesis of (*R*)- and (*S*)-2-methylaziridines (*R*)- and (*S*)-8a

To a solution of amino alcohol methanesulfonate hydrochlorides **3a** or **4a** (7.58 g, 40 mmol) in water (20 mL) was added portionwise sodium bicarbonate (5.04 g, 60 mmol) under stirring in an ice bath. The resulting mixture was stirred for 2 h and then distilled. The distillate was saturated with potassium hydroxide and the organic layer separated was dried over potassium hydroxide and finally with sodium metal to give chiral 2-methylaziridine.[28]

4.3.1. (*R*)-2-Methylaziridine (*R*)-8a. Colorless oil; yield: 65%; $[\alpha]_D^{20}=+12.4$ (*c*, 1.21, EtOH). Lit.:[28] bp 66–67°C; $[\alpha]_D=+12.6$ (*c*, 1.43, EtOH).

4.3.2. (*S*)-2-Methylaziridine (*S*)-8a. Colorless oil; yield: 63%; $[\alpha]_D^{20}=-12.4$ (*c*, 1.13, EtOH). Lit.:[28] bp 66–67°C; $[\alpha]_D=-12.5$ (*c*, 1.43, EtOH).

4.4. General procedure for synthesis of chiral 2-substituted aziridines 8 (Wenker method)

A cold mixture of sulfuric acid (98%, 4 g), and water (4 mL) was added to an amino-alcohol (40 mmol) in water (2.4 mL) at 0–5°C. The mixture was heated to 120°C and then water was carefully distilled off in vacuo. The solid sulfate residue was treated with 6.2 M potassium hydroxide, and steam-distilled. The distillate was saturated with potassium hydroxide pellets and the upper organic layer, which separated, was fractionally distilled from potassium hydroxide through a short column to give a colorless oil aziridine **8**.

4.4.1. (*R*)-2-Isopropylaziridine (*R*)-8b. Colorless oil; yield: 78%; bp 104–106°C; $[\alpha]_D^{20}=+21.7$ (*c*, 1.11, EtOH). IR (film): $\nu=3220$ (NH), 3030 (CH_2 in aziridine) cm^{-1}; ^1H NMR $\delta=2.91$ (1H, br, s, NH), 1.80–0.80 (10H, m, all aliphatic H); MS (EI) *m*/*z*: 84 (M^+-H), 70 (M^+-NH), 56 (M^+-NHCH_2), 43 ($C_3H_7^+$, base peak). Anal. calcd for $C_5H_{11}N$ (85.15): C, 70.53; H, 13.02; N, 16.45. Found: C, 70.31; H, 13.13; N, 16.56%.

4.4.2. (*R*)-2-Phenylaziridine (*R*)-8c. Colorless oil; yield: 86%; bp 72–73°C/4 mmHg; $[\alpha]_D^{20}=-43.2$ (*c*, 1.07, EtOH). Lit.:[30] bp 73°C/4 mmHg; $[\alpha]_D^{20}=-43.4$ (*c*, 1.0062, EtOH).

4.4.3. (*R*)-2-Benzylaziridine (*R*)-8d. Colorless oil; yield: 88%; bp 73–74°C/1 mmHg; $[\alpha]_D^{20}=+26.6$ (*c*, 1.07, EtOH). Lit.:[32] bp 73–74°C/1 mmHg; $[\alpha]_D^{24}=+26.7$ (*c*, 0.152, EtOH).

4.4.4. (*S*)-2-Isopropylaziridine (*S*)-8b. Colorless oil; yield: 80%; bp 104–106°C; $[\alpha]_D^{20}=-21.7$ (*c*, 1.11, EtOH). Lit.:[27] bp 100–101°C/690 mmHg; $[\alpha]_D^{20}=-21.8$ (*c*, 1.5, EtOH).

4.4.5. (*S*)-2-Phenylaziridine (*S*)-8c. Colorless oil yield: 85%; bp 72–73°C/4 mmHg; $[\alpha]_D^{20}=+43.6$ (*c*, 1.07, H_2O). Lit.:[33] $[\alpha]_D^{20}=+43.8$ (*c*, 0.26, EtOH).

4.4.6. (*S*)-2-Benzylaziridine (*S*)-8d. Colorless oil; yield: 87%; bp 73–74°C/1 mmHg; $[\alpha]_D^{20}=-26.7$ (*c*, 1.15, EtOH). Lit.:[32] bp 73–74°C/1 mmHg; $[\alpha]_D^{24}=-26.6$ (*c*, 0.186, EtOH).

4.5. General procedure for synthesis of chiral 2-substituted aziridines 8 (Mitsunobu reaction)

The amino alcohol (20 mmol) was dissolved in toluene (30 mL) and added to a solution of triphenylphosphine (5.5 g, 21 mmol) and DEAD (3.65 g, 21 mmol) in toluene (45 mL). After refluxing overnight, the mixture was poured into water (75 mL) and diluted with diethyl ether (75 mL). Drying over $MgSO_4$, filtration, and concentration gave a residue, which was diluted with diethyl ether (75 mL) and left in the freezer overnight. Precipitated triphenylphosphine oxide was filtered off, and the filtrate was concentrated and subjected to column chromatography to give aziridine as a colorless oil. Yield: (*R*)-**8b**, 73%; (*S*)-**8b**, 71%; (*R*)-**8c**, 83%; (*S*)-**8c**, 85%; (*R*)-**8d**, 85%; (*S*)-**8d**, 86%.

4.6. General procedure for synthesis of chiral 2-aminoalkanesulfonic acids 5

Sodium bisulfite (1.25 g, 12 mmol) was added to a solution of the appropriate 2-substituted aziridine **8** (10 mmol) in water or a mixture of water and ethanol (10 mL) and the mixture was stirred for 24 h. The resulting solution was passed through columns first of Amberlite IR-120 (H^+ form) then of Dowex 11 (acetate form). The eluate was evaporated to dryness under reduced pressure and the residue was crystallized from a mixture of water and ethanol to give **5**.

4.6.1. (*R*)-2-Aminopropanesulfonic acid (*R*)-5a. Colorless crystal; yield: 88%; mp >330°C; $[\alpha]_D^{20}=-18.5$ (*c*, 1.11, H_2O). Lit.:[10] mp >330°C; $[\alpha]_D^{20}=-18.3$ (*c*, 1, H_2O).

4.6.2. (*R*)-2-Amino-3-methylbutanesulfonic acid (*R*)-5b. Colorless crystal; yield: 90%; mp: 325–326°C; $[\alpha]_D^{20}=-29.6$ (*c*, 0.97, H_2O). Lit.:[10] mp: 325–326°C; $[\alpha]_D^{20}=-29.7$ (*c*, 1, H_2O).

4.6.3. (*R*)-2-Amino-2-phenylethanesulfonic acid (*R*)-5c. Colorless crystal; yield: 96%; mp 338–340°C; $[\alpha]_D^{20}=+1.4$ (*c*, 1.07, H_2O). Lit.:[10] mp >330°C; $[\alpha]_D^{20}=+1.3$ (*c*, 1, H_2O).

4.6.4. (*R*)-2-Amino-3-phenylpropanesulfonic acid (*R*)-5d. Colorless crystal; yield: 96%; mp >330°C; $[\alpha]_D^{20}=+3.7$ (*c*, 1.10, H_2O). Lit.:[10] mp >330°C; $[\alpha]_D^{20}=+3.6$ (*c*, 1, H_2O).

4.6.5. (*S*)-2-Aminopropanesulfonic acid (*S*)-5a. Colorless crystal; yield: 87%; mp >330°C; $[\alpha]_D^{20}=+18.4$ (*c*, 1.01, H_2O). Lit.:[10] mp >330°C; $[\alpha]_D^{20}=+18.5$ (*c*, 1, H_2O).

4.6.6. (*S*)-2-Amino-3-methylbutanesulfonic acid (*S*)-5b. Colorless crystal; yield: 89%; mp 325–326°C; $[\alpha]_D^{20}=+29.6$ (*c*, 0.96, H_2O). Lit.:[10] mp 325–326°C; $[\alpha]_D^{20}=+29.8$ (*c*, 1, H_2O).

4.6.7. (*S*)-2-Amino-2-phenylethanesulfonic acid (*S*)-5c. Colorless crystal; yield: 95%; mp 338–340°C. $[\alpha]_D^{20}=-1.4$ (*c*, 1.10, H_2O). IR (KBr): $\nu=3300$–2400 (NH_3^+), 1220 (SO_2), 1175 (SO_2) cm^{-1}; ^1H NMR $\delta=7.46$–7.40 (5H, m, ArH), 4.08 (1H, dd, $J=6$, 10 Hz), 3.43 (1H, dd, $J=6$, 13 Hz), 3.23 (1H, dd, $J=10$, 13 Hz); MS (FAB) m/z: 202 (MH^+). Anal. calcd for $C_8H_{11}NO_3S$ (201.24): C, 47.75; H, 5.51; N, 6.96. Found: C, 47.51; H, 5.33; N, 7.06%.

4.6.8. (*S*)-2-Amino-3-phenylpropanesulfonic acid (*S*)-5d. Colorless crystal; yield: 96%; mp >330°C; $[\alpha]_D^{20}=-3.6$ (*c*, 0.99, H_2O). Lit.:[10] mp >330°C; $[\alpha]_D^{20}=-3.5$ (*c*, 1, H_2O).

4.7. General procedure for synthesis of chiral cysteic acids 5e

To a solution of methyl *N*-trityl 2-aziridinecarboxylate (3.45 g, 10 mmol) (prepared as described in the literature[30]) in dichloromethane (10 mL) and methanol (12 mL) at −10°C was added trifluoroacetic acid (16 mL) dropwise under nitrogen. After stirring at this temperature for 10 h, water (40 mL) was added and the organic volatiles removed in vacuo to precipitate of a mixture of triphenylmethanol and methyl triphenylmethyl ether as a white solid which was filtered off. To the aqueous filtrate was added solid potassium carbonate (6.91 g, 50 mmol), and the solution stirred for 15 min prior to addition of solid sodium bisulfite (2.08 g, 2 mmol) portionwise. After the mixture was stirred for 24 h, sodium hydroxide (4.0 g, 100 mmol) was added portionwise under stirring. The resulting solution was stirred another 8 h and was passed through columns first of Amberlite IR-120 (H^+ form) then of Dowex 11 (acetate form). The eluate was evaporated to dryness under reduced pressure and the residue was crystallized from a mixture of water and ethanol to give **5e**.

4.7.1. (*R*)-2-Amino-2-carboxyethanesulfonic acid (*R*)-5. Colorless crystal; yield: 74%; monohydrate mp 271–273°C; $[\alpha]_D^{25}=+8.3$ (*c*, 7.2, H_2O). Lit.:[34] mp: 272–274°C; $[\alpha]_D^{25}=+8.5$ (*c*, 7.4, H_2O).

4.7.2. (*S*)-2-Amino-2-carboxyethanesulfonic acid (*S*)-5e. Colorless crystal; yield: 72%; monohydrate mp 271–273°C. $[\alpha]_D^{25}=-8.4$ (*c*, 7.3, H_2O). IR (KBr): $\nu=3300$–2400 (NH_3^+), 1221 (SO_2), 1176 (SO_2) cm^{-1}; ^1H NMR $\delta=3.38$ (1H, dd, $J=4$, 9 Hz), 3.08 (1H, dd, $J=4$, 14 Hz), 2.83 (1H, dd, $J=9$, 14 Hz); MS (FAB) m/z: 170 (MH^+). Anal. calcd for $C_3H_7NO_5S\cdot H_2O$ (187.17): C, 19.25; H, 4.85; N, 7.48. Found: C, 19.12; H, 5.03; N, 7.19%.

4.8. General procedure for synthesis of chiral cysteinolic acids 5f

To a solution of methyl *N*-trityl 2-aziridinecarboxylate (3.45 g, 10 mmol) (prepared as described in the literature[30]) in dichloromethane (10 mL) and methanol (12 mL) at −10°C was added trifluoroacetic acid (16 mL) dropwise under nitrogen. After stirring at this temperature for 10 h, water (40 mL) was added and the volatiles organic components removed in vacuo to precipitate of a mixture of triphenylmethanol and methyl triphenylmethyl ether as a white solid which was filtered off. To the aqueous filtrate was added solid potassium carbonate (6.91 g, 50 mmol) and the solution was stirred for 15 min prior to addition of solid lithium chloride (2.12 g, 50 mmol) and sodium borohydride (1.89 g, 50 mmol) portionwise. After the mixture was stirred overnight, sodium bisulfite (2.08 g, 2 mmol) was added portionwise under stirring. The resulting solution was stirred another 24 h and was passed through columns first of Amberlite IR-120 (H^+ form) then of Dowex 11 (acetate form). The eluate was evaporated to dryness under reduced pressure and the residue was crystallized from aqueous ethanol to give **5f**.

4.8.1. (*R*)-2-Amino-3-hydroxypropanesulfonic acid (*R*)-5f. Colorless crystal; yield: 78%; mp 279–281°C (dec.); $[\alpha]_D^{20}=+7.6$ (*c*, 1.00, H_2O). Lit.:[10] mp: 279–281°C (dec.); $[\alpha]_D^{20}=+7.5$ (*c*, 1, H_2O).

4.8.2. (*S*)-2-Amino-3-hydroxypropanesulfonic acid (*S*)-5f. Colorless crystal; yield: 76%; mp 279–281°C. $[\alpha]_D^{20}=-7.4$ (*c*, 1.10, H_2O). IR (KBr): $\nu=3300$–2400 (NH_3^+), 1222 (SO_2), 1177 (SO_2) cm^{-1}; ^1H NMR $\delta=3.52$ (1H, dd, $J=7$, 11 Hz), 3.58 (1H, dd, $J=6$, 11 Hz), 3.34–3.23 (1H, m), 3.07 (1H, dd, $J=4$, 14 Hz), 2.82 (1H, dd, $J=9$, 14 Hz); MS (FAB) m/z: 156 (MH^+). Anal. calcd for $C_3H_9NO_4S$ (155.17): C, 23.22; H, 5.85; N, 9.03. Found: C, 23.50; H, 5.79; N, 9.06%.

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