Heteroatom Chemistry
Volume 16, Number 6, 2005

The First Synthesis of Optically Active 1-Substituted Taurines

Jiaxi Xu, Shu Xu, and Qihan Zhang

Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, Department of Chemical Biology, College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, People's Republic of China

Received 16 November 2003; revised 22 July 2004 and 25 February 2005

ABSTRACT: *Optically active 1-substituted taurines, a type of important sulfur analogues of naturally occurring amino acids, and their N-benzyloxycarbonyl-protected derivatives were synthesized from the corresponding optically active β-amino secondary alcohols in three steps via N-protection with benzyl chloroformate, substitution with thiolacetic acid under Mitsunobu conditions, and oxidation with performic acid.* © 2005 Wiley Periodicals, Inc. Heteroatom Chem 16:466–471, 2005; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20133

INTRODUCTION

During the last decade, aminoalkylphosphonic acid and aminoalkanesulfonic acid derivatives have been widely used as enzyme inhibitors and heptans in the development of catalytic antibodies because of their tetrahedrally structural properties [1–3]. On the other hand, several 2-aminoalkanesulfonic acids have been found in many mammalian tissues till now and are involved in various and important physiological processes [4]. To date many methods for the synthesis of aminoalkylphosphonic acids and their derivatives have been developed [5,6]. For aminoalkanesulfonic acids, β-aminoalkanesulfonic acids are very important sulfur analogues of naturally occurring amino acids because α-aminoalkanesulfonic acids and their derivatives are unstable. 1-Substituted 2-aminoethanesulfonic acids (1-substituted taurines) and 2-substituted 2-aminoethanesulfonic acids (2-substituted taurines) are two types of structural analogues of naturally occurring amino acids for β-aminoalkanesulfonic acids. Optically active 2-substituted taurines have been synthesized effectively from optically active β-amino primary alcohols [3,7–16], which were easily obtained by reduction of natural amino acids, via sulfite displacement of their methanesulfonates [7–10], or peroxy acid oxidation of their thioacetates [11–15], and sulfite ring opening of optically active aziridines [16]. But little attention has been paid to synthesis of 1-substituted taurines [13,17–19]. Braghiroli and his coworkers attempted to synthesize optically active 1-substituted taurines from optically active β-amino secondary alcohols and failed to do so [20]. Liskamp's group prepared several 1-alkyltaurine-containing sulfonopeptides by the alkylation of taurine-containing sulfonopeptides [21,22] and by the acylation of 1-substituted 2-*N*-protected aminoethanesulfinyl chloride to amino acid esters and followed oxidation [18]. To our best knowledge, there is no report on the preparation of optically active 1-substituted taurines till now. We herein report the preparation of optically active 1-substituted taurines from optically active β-amino secondary alcohols.

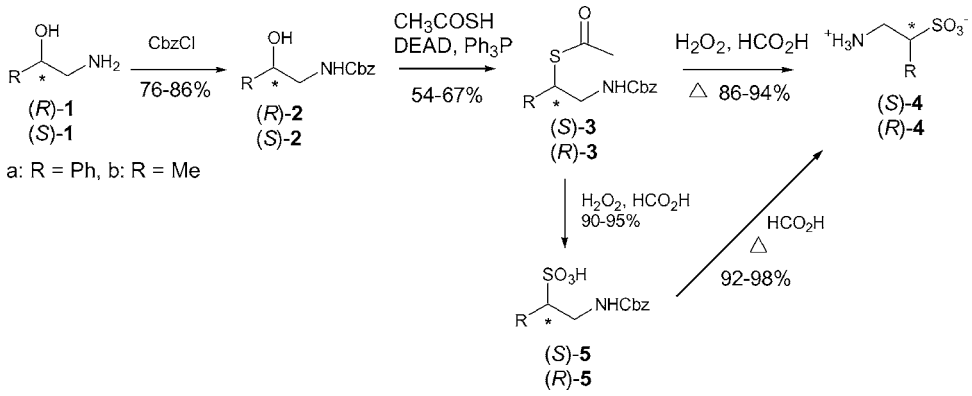
Correspondence to: J. Xu; e-mail: jxxu@pku.edu.cn.
Contract grant sponsor: National Natural Science Foundation of China, Ministry of Education of People's Republic of China.
Contract grant number: 20272002.
Contract grant sponsor: Peking University (President grant).

RESULTS AND DISCUSSION

As part of a program to synthesize structural analogs of naturally occurring amino acids, we sought to prepare optically active 1-substituted taurines. Optically active β-amino secondary alcohols are important key intermediates for synthesizing optically active 1-substituted taurines (see Scheme 1). First, optically active β-amino secondary alcohols **1** were protected with benzyl chloroformate to give 1-(benzyloxycarbonyl)amino-2-alkanols [benzyl *N*-(2-hydroxyalkyl) carbamates] **2**, which were converted to the corresponding thioacetates **3** in a Mitsunobu displacement reaction using DEAD (diethyl azodicarboxylate), triphenylphosphine, and thiolacetic acid [11–13], in which a Walden inversion occurs. HPLC analysis on a chiral column indicated that the benzyl *N*-(2-hydroxyalkyl) carbamates **2** occurred in a complete configurational inversion to yield the optically active corresponding thioacetates **3** in the Mitsunobu reaction except for some acetate by-products. Although vicinal *N*-acylamino alcohols yield oxazoline or oxazole derivatives as main by-products or desired products under the Mitsunobu conditions in most cases [23–26], no oxazoline derivative was found in the reaction mixture due to the hard enolization of the carbamates and the existence of a strong nucleophilic thioacetate anion in the reaction systems. The thioacetates **3** were subsequently oxidized with performic acid, in situ generated by mixing formic acid and hydrogen peroxide, under refluxing conditions to afford 1-substituted taurines **4** directly in good yields after removal of solvent and excess performic acid by evaporation under reduced pressure, washing with chloroform, and crystallization from ethanol. It has been found that the reaction mixture was mixed with silica gel, evaporated at room temperature, and separated on a silica gel column, 1-substituted *N*-benzyloxycarbonyl protected taurines **5** were obtained. In current reaction conditions, products **4** and **5** should not lose optical purities compared with compounds **3** because optically active amino acids can be obtained via hydrolysis of peptides and proteins in 6 mol/L HCl in a sealed tube at 110°C for 24 h. Substituted taurines are sulfur analogues of naturally occurring amino acids. They should show similar properties with amino acids. Thus, they should be stable in acidic conditions. On the other hand, both of enantiomers of substituted taurines with almost same specific rotation values and opposite sign were obtained. This supports our assumption. The free 1-substituted taurines **4** can also be obtained by treatment of 1-substituted *N*-benzyloxycarbonyl protected taurines **5** with formic acid under refluxing conditions. In general, the benzyloxycarbonyl group is removed with Pd/C under hydrogen atmosphere [11]. However, the current method can avoid hydrogenolytic cleavage on the benzylic position for products **5a**. It is an alternative method for the deprotection of a benzyloxycarbonyl group.

CONCLUSION

In summary, optically active 2-substituted taurines were prepared from optically active 2-amino-1-alkanols previously, herein optically active 1-substituted taurines were synthesized from corresponding optically active β-amino secondary alcohols by employing *N*-protected 1-amino-2-alkyl thioacetates as key intermediates. As another type of important sulfur analogues of naturally occurring amino acids, optically active 1-substituted taurines could be used as the structural analogues of naturally occurring 2-substituted 2-aminoethanesulfonic acids for studies of some physiological processes.



SCHEME 1 Synthesis of optically active 1-substituted taurines.

N-Protected optically active 1-substituted taurines are also very important building blocks for synthesis of α-substituted β-sulfonopeptides and other 1-substituted-2-aminoethanesulfonic acid containing compounds.

EXPERIMENTAL

General Method

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 a Varian Mercury 200 (200 MHz) or Mercury Plus 300 (300 MHz) spectrometer in $CDCl_3$ with TMS as an internal standard or in DMSO-d_6. Mass spectra were obtained on a VG-ZAB-HS mass spectrometer or a Bruker ESQUIRE∼LC™ ESI ion trap 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 analytical data of all known compounds are identical to those earlier reported in the literature [27–29].

(*R*)- And (*S*)-amino alcohols were purchased from Aldrich and Acros Chemical Co., Inc. THF was heated under reflux over sodium and distilled prior to use. Triethylamine was heated under reflux over sodium hydroxide and distilled prior to use.

*General Procedure for Synthesis of Optically Active Benzyl N-(2-hydroxyalkyl) Carbamate (R)- and (S)-***2**

To a solution of the amino alcohol **1** (50 mmol) in CH_2Cl_2 (50 mL) was added 50 mL of 1 N NaOH. The mixture was cooled in an ice bath and 50% benzyl chloroformate in toluene (17.06 g, 50 mmol) was added keeping the temperature at 0–5°C. After stirring overnight at room temperature, the organic layer was separated, washed with water (2 × 20 mL), dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give the *N*-Cbz protected amino alcohol [benzyl *N*-(2-hydroxyalkyl) carbamate] **2**. Benzyl *N*-(2-hydroxy-2-phenylethyl) carbamates **2a** were obtained as colorless crystals after crystallized from a mixture of petroleum ether and ethyl acetate.

*(R)-Benzyl N-(2-hydroxy-2-phenylethyl) Carbamate (R)-***2a**. Colorless crystal; yield: 76%; mp: 82–83°C. $R_f = 0.40$ (petroleum ether: AcOEt = 2:1, silica gel plate). $[\alpha]_D^{25} = -28.0$ (*c*, 1.02, $CHCl_3$). Lit [27]: $[\alpha]_D^{20} = -25.0$ (*c*, 2, $CHCl_3$), ee 83%.

*(S)-Benzyl N-(2-hydroxy-2-phenylethyl) Carbamate (S)-***2a**. Colorless crystal; yield: 86%; mp: 80–81°C. $R_f = 0.40$ (petroleum ether: AcOEt = 2:1, silica gel plate). $[\alpha]_D^{25} = +28.7$ (*c*, 1.10, $CHCl_3$). Lit [28]: mp 97–99°C; $[\alpha]_D^{25} = +27.16$ (*c*, 0.93, $CHCl_3$), 64% ee.

*(R)-Benzyl N-(2-hydroxypropyl) Carbamate (R)-***2b**. Colorless oil, yield 77%. $R_f = 0.35$ (petroleum ether: AcOEt = 2:1, silica gel plate). $[\alpha]_D^{25} = -9.66$ (*c*, 5.03, MeOH). Lit [29]: $[\alpha]_D^{25} = -9.47$ (*c*, 4.68, MeOH).

*(S)-Benzyl N-(2-hydroxypropyl) Carbamate (S)-***2b**. Colorless oil, yield 77%. $R_f = 0.35$ (petroleum ether: AcOEt = 2:1, silica gel plate). $[\alpha]_D^{25} = +9.85$ (*c*, 4.63, MeOH). +11.7 (*c*, 0.99, $CHCl_3$). IR (KBr): ν 3419, 3332 (NH, OH), 1707 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.407.22 (m, 5H, ArH), 5.22 (s, br, 1H, NH), 5.10 (s, 2H, OCH_2), 4.68 (s, br, 1H, OH), 3.90 (m, 1H, CH), 3.33 (m, 1H, H in CH_2), 3.05 (m, 1H, H in CH_2), 1.17 (d, $J = 6.3$ Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 157.01, 136.30, 128.33, 127.94, 127.86, 66.91, 66.65, 48.10, 20.33. MS (EI) *m/z*: 209 (M^+). Anal. Calcd for $C_{11}H_{15}NO_3$ (209.24): C, 63.14; H, 7.23; N, 6.69. Found: C, 63.41; H, 7.47; N, 6.46%.

*General Procedure for Synthesis of Optically Active 1-Substituted 2-(Benzyloxycarbonyl) aminoethyl Thioacetates (R)- and (S)-***3**

Diethyl azodicarboxylate (1.74 g, 10 mmol) in anhydrous tetrahydrofuran (6 mL) was added to an efficiently stirred solution of triphenylphosphine (2.62 g, 10 mmol) in 12 mL of anhydrous tetrahydrofuran at −10°C. The mixture was stirred at −10°C for 0.5 h. A white precipitate appeared. The benzyl *N*-(2-hydroxyalkyl) carbamate **2** (5 mmol) and thiolacetic acid (0.76 g, 10 mmol) in 12 mL of tetrahydrofuran were added dropwise over 30 min, and the mixture was stirred for 1 h at −10°C and at room temperature for 20 h. The resulting mixture was concentrated in reduced pressure. The triphenylphosphine oxide was crystallized upon addition of a mixture of ethyl acetate and petroleum ether. The combined filtrates were concentrated in vacuo and subject to silica gel column chromatographic separation with a mixture of petroleum ether and ethyl ether (8:1, v/v) as an eluent to give thioacetate **3**. Optical purity determination conditions: Chiralcel OD column 4.6 × 250 mm, eluent: hexane: 2-propanol (80:20, v/v) for the determination of 2-(benzyloxycarbonyl)amino-1-phenylethyl thioacetates with (*R*)-**3a** ($t = 17.75$ min) and (*S*)-**3a** ($t = 22.34$); hexane: 2-propanol (99:1, v/v) for

the determination of 2-(benzyloxycarbonyl)amino-1-methylethyl thioacetates with (*R*)-**3b** ($t = 33.79$ min), and (*S*)-**3b** ($t = 36.89$), flow rate: 0.6 mL/min.

(R)-2-(Benzyloxycarbonyl)amino-1-phenylethyl Thioacetate (R)-**3a**. Colorless crystal; yield 67%, mp 73–74°C, >99% ee. $R_f = 0.30$ (petroleum ether: ether = 3:1, silica gel plate). $[\alpha]_D^{25} = -126$ (*c*, 1.12, $CHCl_3$). IR (KBr): ν 3343 (NH), 1720 (C=O), 1695 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.29 (m, 10H, ArH), 5.08 (s, 2H, OCH_2), 4.96 (s, 1H, NH), 4.72 (t, $J = 7.5$ Hz, 1H, CH), 3.68 (dd, $J = 6.9$, 7.5 Hz, 2H, NCH_2), 2.30 (s, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 194.33, 156.09, 138.46, 136.38, 128.77, 128.64, 128.38, 127.98, 127.84, 127.79, 66.69, 47.81, 45.55, 30.34; MS (EI) *m/z*: 329 (M^+, 1.2), 286 (M^+-Ac, 14.9), 253 (M^+-AcSH, 1.1), 238 (M^+-$PhCH_2$, 19.8), 108 ($PhCH_2OH^+$, 5.9), 91 ($PhCH_2^+$, 100). Anal. Calcd for $C_{18}H_{19}NO_3S$ (329.41): C, 65.63; H, 5.81; N, 4.25. Found: C, 65.51; H, 5.71; N, 4.46%.

(S)-2-(Benzyloxycarbonyl)amino-1-phenylethyl Thioacetate (S)-**3a**. Colorless crystal; yield 63%, mp 72.5–73.5°C, >99% ee. $R_f = 0.30$ (petroleum ether: ether = 3:1, silica gel plate). $[\alpha]_D^{25} = +122$ (*c*, 0.72, $CHCl_3$). IR (KBr): ν 3342 (NH), 1718 (C=O), 1696 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.29 (m, 10H, ArH), 5.08 (s, 2H, OCH_2), 4.96 (s, 1H, NH), 4.72 (t, $J = 7.5$ Hz, 1H, CH), 3.68 (dd, $J = 6.9$, 7.5 Hz, 2H, NCH_2), 2.30 (s, 3H, CH_3);^{13}C NMR (75.5 MHz, $CDCl_3$) δ 194.27, 156.09, 138.46, 136.38, 128.77, 128.64, 128.38, 127.98, 127.84, 127.79, 66.69, 47.81, 45.55, 30.34; MS (EI) *m/z*: 329 (M^+, 1.2), 286 (M^+-Ac, 14.8), 253 (M^+-AcSH, 1.2), 238 (M^+-$PhCH_2$, 19.8), 108 ($PhCH_2OH^+$, 5.9), 91 ($PhCH_2^+$, 100). Anal. Calcd for $C_{18}H_{19}NO_3S$ (329.41): C, 65.63; H, 5.81; N, 4.25. Found: C, 65.51; H, 5.69; N, 4.05%.

(R)-2-(Benzyloxycarbonyl)amino-1-methylethyl Thioacetate (R)-**3b**. Colorless oil, yield 54%, >99% ee. $R_f = 0.25$ (petroleum ether: ether = 4:1, silica gel plate). $[\alpha]_D^{25} = +29.7$ (*c*, 1.22, $CHCl_3$). IR (KBr): ν 3344 (NH), 1721 (C=O), 1692 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H, Ph), 5.10 (s, 2H, OCH_2), 5.02 (s, br, 1H, NH), 3.66 (ddq, $J = 6.3$, 6.9, 6.9 Hz, 1H, CH), 3.43 (ddd, $J = 5.7$, 6.3, 13.9 Hz, 1H, H in NCH_2), 3.31 (ddd, $J = 6.9$, 6.9, 13.9 Hz, 1H, H in NCH_2), 2.30 (s, 3H, $COCH_3$), 1.30 (d, $J = 6.9$ Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 195.69, 156.41, 136.35, 128.45, 128.07, 127.98, 66.73, 46.08, 39.72, 30.68, 18.06; MS (EI) *m/z*: 267 (M^+, 1.2), 224 (M^+-Ac, 1.2), 191 (M^+-AcSH, 9.2), 108 ($PhCH_2OH^+$, 13.7), 107 ($PhCH_2O^+$, 8.2), 91 ($PhCH_2^+$, 100). Anal. Calcd for $C_{13}H_{17}NO_3S$ (267.35): C, 58.40; H, 6.41; N, 5.24. Found: C, 58.61; H, 6.29; N, 5.09%.

(S)-2-(Benzyloxycarbonyl)amino-1-methylethyl Thioacetate (S)-**3b**. Colorless oil, yield 67%, >99% ee. $R_f = 0.25$ (petroleum ether: ether = 4:1, silica gel plate). $[\alpha]_D^{25} = -29.5$ (*c*, 1.13, $CHCl_3$). IR (KBr): ν 3342 (NH), 1720 (C=O), 1693 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H, Ph), 5.10 (s, 2H, OCH_2), 5.02 (s, br, 1H, NH), 3.66 (ddq, $J = 6.3$, 6.9, 6.9 Hz, 1H, CH), 3.43 (ddd, $J = 5.7$, 6.3, 13.9 Hz, 1H in NCH_2), 3.31 (ddd, $J = 6.9$, 6.9, 13.9 Hz, 1H in NCH_2), 2.30 (s, 3H, $COCH_3$), 1.30 (d, $J = 6.9$ Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 195.69, 156.41, 136.35, 128.45, 128.07, 127.98, 66.73, 46.08, 39.72, 30.68, 18.06; MS (EI) *m/z*: 267 (M^+, 1.1), 224 (M^+-Ac, 1.2), 191 (M^+-AcSH, 9.3), 108 ($PhCH_2OH^+$, 13.7), 107 ($PhCH_2O^+$, 8.2), 91 ($PhCH_2^+$, 100). Anal. Calcd for $C_{13}H_{17}NO_3S$ (267.35): C, 58.40; H, 6.41; N, 5.24. Found: C, 58.51; H, 6.70; N, 5.09%.

General Procedure for Synthesis of Optically Active 1-Substituted Taurines (R)- and (S)-**4**

To a performic acid solution, prepared by mixing and stirring 30% H_2O_2 (1.2 mL) and 88% HCO_2H (12 mL) at room temperature for 1 h and cooled in an ice bath were added thioacetate derivatives **3** (2 mmol) in 88% HCO_2H (2.7 mL) dropwise, the resulting mixture was refluxed and stirred overnight. After removal of solvent and washing with chloroform, the residue was crystallized from methanol to give the pure 1-substituted taurines **4**.

(R)-2-Amino-1-phenylethanesulfonic Acid (R)-**4a**. Colorless crystal; yield: 96%; mp >360°C. $[\alpha]_D^{25} = -4.98$ (*c*, 0.91, H_2O). IR (KBr): ν 3424, 3217, 3061 (NH_3^+), 1212 (SO_2), 1170 (SO_2) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 7.78 (s, br, 3H, NH_3), 7.29 (s, 5H, ArH), 3.88 (dd, $J = 4.5$, 9.9 Hz, 1H, H in CH_2), 3.45 (d, $J = 4.5$ Hz, 1H, H in CH_2), 3.08 (d, $J = 9.9$ Hz, 1H, CH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 136.11, 129.06, 127.93, 127.21, 61.56, 40.88. MS (ESI, positive ion) *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, 47.60; H, 5.77; N, 7.14%.

(S)-2-Amino-1-phenylethanesulfonic Acid (S)- **4a**. Colorless crystal; yield: 92%; mp >360°C. $[\alpha]_D^{25} = +4.80$ (*c*, 0.77, H_2O). IR (KBr): ν 3421, 3215, 3058 (NH_3^+), 1214 (SO_2), 1170 (SO_2) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 7.82 (s, br, 3H, NH_3), 7.29 (s, 5H, ArH), 3.88 (dd, $J = 4.5$, 9.9 Hz, 1H, H in CH_2), 3.46 (m, 1H, H in CH_2), 3.09 (d, $J = 9.9$ Hz, 1H, CH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 136.09, 129.07, 127.95, 127.30, 61.59, 40.91. MS (ESI, positive ion) *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, 47.50; H, 5.79; N, 7.04%.

*(R)-2-Amino-1-methylethanesulfonic Acid (R)-***4b**. Colorless crystal; yield: 98%; mp: 236–238°C. $[\alpha]_D^{25} = -8.56$ (*c*, 1.10, H_2O). IR (KBr): ν 3140 (br, NH), 1219 (SO_2), 1171 (SO_2) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 3.87 (s, br, 3H, NH_3), 2.88 (m, 2H, CH_2), 2.68 (m, 1H, CH), 1.10 (d, $J = 6.6$ Hz, 3H, CH_3); ^{13}C NMR (75.5 Hz, DMSO-d_6) δ 51.12, 41.28, 13.94. MS (ESI, positive ion) *m/z*: 140 $(MH)^+$. Anal. Calcd for $C_3H_9NO_3S$ (139.17): C, 25.89; H, 6.52; N, 10.06. Found: C, 25.70; H, 6.78; N, 9.88%.

*(S)-2-Amino-1-methylethanesulfonic Acid (S)-***4b**. Colorless crystal; yield: 97%; mp 237–239°C. $[\alpha]_D^{25} = +8.70$ (*c*, 1.15, H_2O). IR (KBr): ν 3138 (br, NH), 1213 (SO_2), 1170 (SO_2) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 3.93 (s, br, 3H, NH_3), 2.89 (m, 2H, CH_2), 2.67 (m, 1H, CH), 1.10 (d, $J = 6.6$ Hz, 3H, CH_3); ^{13}C NMR (75.5 Hz, $CDCl_3$) δ 51.59, 41.22, 13.75. MS (ESI, positive ion) *m/z*: 140 $(MH)^+$. Anal. Calcd for $C_3H_9NO_3S$ (139.17): C, 25.89; H, 6.52; N, 10.06. Found: C, 26.00; H, 6.49; N, 9.89%.

*General Procedure for Synthesis of Optically Active 1-Substituted N- Benzyloxycarbonyl Taurines (R)- and (S)-***5**

To a performic acid solution, prepared by mixing and stirring 30% H_2O_2 (1.2 mL) and 88% HCO_2H (12 mL) at room temperature for 1 h and cooled in an ice bath, was added thioacetate derivative **3** (2 mmol) in 88% HCO_2H (2.7 mL) dropwise, keeping the temperature at 0°C. After the mixture was stirred at 0°C for an additional 2 h and at room temperature for 20 h, the resulting mixture was mixed with silica gel and evaporated to dry at room temperature. The residue was separated on a silica gel column with a mixture of chloroform and methanol in 20:1–10:1 (v/v), and methanol as eluents in order to give the pure 1-substituted *N*-benzyloxycarbonyl taurines **5**.

*(R)-2-(Benzyloxycarbonyl)amino-1-phenylethanesulfonic Acid (R)-***5a**. Colorless crystal; yield 95%, mp 190–192°C. $R_f = 0.60$ ($CHCl_3$: MeOH = 4:1, silica gel plate). $[\alpha]_D^{25} = +19.4$ (*c*, 1.14, MeOH). IR (KBr): ν 3411 (NH), 1699 (C=O), 1220 (SO_2), 1171 (SO_2) cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO) δ 7.36–7.22 (m, 10H, ArH), 7.00 (s, 1H, NH), 4.92 (s, 2H, OCH_2), 3.79 (dd, $J = 8.6$, 14.6 Hz, 1H, CH), 3.64 (m, 2H, NCH_2); ^{13}C NMR (50 MHz, d_6-DMSO) δ 155.79, 137.48, 137.22, 129.48, 128.33, 127.66, 127.45, 127.40, 126.47, 65.05, 64.42, 42.55; MS (ESI, negative ion) *m/z*: 334 $(M\text{-}H)^-$. Anal. Calcd for $C_{16}H_{17}NO_5S$ (335.38): C, 57.30; H, 5.11; N, 4.18. Found: C, 57.45; H, 5.19; N, 4.01%.

*(S)-2-(Benzyloxycarbonyl)amino-1-phenylethanesulfonic Acid (S)-***5a**. Colorless crystal; yield 93%, mp 190–192°C. $R_f = 0.60$ ($CHCl_3$: MeOH = 4:1, silica gel plate). $[\alpha]_D^{25} = -19.1$ (*c*, 0.94, MeOH). IR (KBr): ν 3413 (NH), 1698 (C=O), 1222 (SO_2), 1172 (SO_2) cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO) δ 7.36–7.22 (m, 10H, ArH), 6.99 (s, 1H, NH), 4.92 (s, 2H, OCH_2), 3.78 (dd, $J = 8.6$, 14.6 Hz, 1H, CH), 3.64 (m, 2H, NCH_2); ^{13}C NMR (50 MHz, d_6-DMSO) δ 155.79, 137.48, 137.22, 129.48, 128.33, 127.66, 127.45, 127.40, 126.47, 65.05, 64.42, 42.55; MS (ESI, negative ion) *m/z*: 334 $(M\text{-}H)^-$. Anal. Calcd for $C_{16}H_{17}NO_5S$ (335.38): C, 57.30; H, 5.11; N, 4.18. Found: C, 57.52; H, 5.29; N, 4.06%.

*(R)-2-(Benzyloxycarbonyl)amino-1-methylethanesulfonic Acid (R)-***5b**. Colorless crystal; yield 94%, mp >360°C. $R_f = 0.60$ ($CHCl_3$: MeOH = 4:1, silica gel plate). $[\alpha]_D^{25} = +3.96$ (*c*, 1.11, DMSO). IR (KBr): ν 3362 (NH), 1701 (C=O), 1215 (SO_2), 1170 (SO_2) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 7.33 (s, 5H, Ph), 7.04 (s, 1H, NH), 4.99 (s, 2H, OCH_2), 3.40–3.28 (m, 1H, H in NCH_2), 3.08 (ddd, $J = 7.5$, 7.5, 12.9 Hz, 1H, H in NCH_2), 2.57 (m, 1H, CH), 1.06 (d, $J = 6.9$ Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 156.11, 137.30, 128.47, 127.88, 127.80, 65.33, 53.66, 42.77, 13.80; MS (ESI, negative ion) *m/z*: 272 $(M\text{-}H)^-$. Anal. Calcd for $C_{11}H_{15}NO_5S$ (273.31): C, 48.34; H, 5.53; N, 5.12. Found: C, 49.50; H, 5.79; N, 5.00%.

*(S)-1-(Benzyloxycarbonyl)amino-2-propanesulfonic Acid (S)-***5b**. Colorless crystal; yield 90%, mp >360°C. $R_f = 0.60$ ($CHCl_3$: MeOH = 4:1, silica gel plate). $[\alpha]_D^{25} = -4.01$ (*c*, 1.19, DMSO). IR (KBr): ν 3360 (NH), 1700 (C=O), 1216 (SO_2), 1172 (SO_2) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 7.33 (m, 5H, Ph), 7.04 (s, 1H, NH), 4.99 (s, 2H, OCH_2), 3.34 (ddd, $J = 4.5$, 4.5, 12.9 Hz, 1H in NCH_2), 3.08 (ddd, $J = 7.5$, 7.5, 12.9 Hz, 1H in NCH_2), 2.57 (m, 1H, CH), 1.06 (d, $J = 6.9$ Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 156.11, 137.30, 128.47, 127.88, 127.80, 65.33, 53.66, 42.77, 13.80; MS (ESI, negative ion) *m/z*: 272 $(M\text{-}H)^-$. Anal. Calcd for $C_{11}H_{15}NO_5S$ (273.31): C, 48.34; H, 5.53; N, 5.12. Found: C, 48.55; H, 5.74; N, 4.96%.

*General Procedure for Synthesis of Optically Active 1-Substituted Taurines (R)- and (S)-4 from Optically Active 1-Substituted N-Protected Taurines (R)- and (S)-***5**

1-Substituted *N*-benzyloxycarbonyl taurine **5** (0.6 mmol) was dissolved in formic acid (5 mL). The resulting solution was stirred and refluxed overnight.

After removal of solvent, water was added and removed under reduced pressure three times for azeotropical removal of benzyl alcohol. The residue was refluxed in chloroform and cooled to room temperature. Crystallized optically active 1-substituted taurines **4** were obtained after filtration and washing with chloroform.

REFERENCES

[1] Pollack, S. J.; Hsiun, P.; Schultz, P. G. J Am Chem Soc 1989, 111, 5961–5962.
[2] Morgan, B. P.; Scholtz, J. M.; Ballinger, M. D.; Zipkin, I. D.; Bartlett, P. A. J Am Chem Soc 1991, 113, 297–307.
[3] Xu, J. X. Chin J Org Chem 2003, 23, 1–9.
[4] Huxtable, R. J. Physiol Rev 1992, 72, 101–163.
[5] Xu, J. X.; Yu, L. Chin J Synth Chem (Hecheng Huaxue) 1999, 7, 153–158.
[6] Xu, J. X.; Fu, N. Y. J Chem Soc, Perkin Trans 1 2001, 1223–1226 and cited there.
[7] Higashiura, H.; Morino, H.; Matsuura, H.; Toyomaki, Y.; Ienaga, K. J Chem Soc, Perkin Trans 1 1989, 1479–1481.
[8] Gude, M.; Piarulli, U.; Potenza, D.; Salom, B.; Gennari, C. Tetrahedron Lett 1996, 37, 8589–8592.
[9] Braghiroli, D.; Di Bella, M. Tetrahedron: Asymmetry 1996, 7, 2145–2150.
[10] Braghiroli, D.; Avallone, R.; Di Bella, M. Tetrahedron: Asymmetry 1997, 8, 2209–2213.
[11] Higashiura, K.; Ienaga, K. J Org Chem 1992, 57, 764–766.
[12] Moree, W. J.; van der Marel, G. A.; Liskamp, R. M. J. Tetrahedron Lett 1992, 33, 6389–6392.
[13] Moree, W. J.; van der Marel, G. A.; Liskamp, R. M. J. J Org Chem 1995, 60, 5157–5169.
[14] Monnee, M. C. F.; Marijne, M. F.; Brouwer, A. J.; Liskamp, R. M. J. Tetrahedron Lett 2000, 41, 7991–7995.
[15] Brouwer, A. J.; Monnee, M. C. F.; Liskamp, R. M. J. Synthesis 2000, 1579–1584.
[16] Xu, J. X. Tetrahedron: Asymmetry 2002, 13(11), 1129–1134.
[17] Gold, M. H.; Skebelsky, M.; Lang, G. J Org Chem 1951, 16, 1500–1502.
[18] Lowik, D. W. P. M.; Liskamp, R. M. J. Eur J Org Chem 2000, 1219–1228.
[19] Xu, J. X.; Xu, S. Synthesis 2004, 276–282.
[20] Braghiroli, D.; Mussati, E.; Di Bella, M.; Saladini, M. Tetrahedron: Asymmetry 1996, 7, 831–836.
[21] Moree, W. J.; van Gent, L. C.; van der Marel, G. A.; Liskamp, R. M. J. Tetrahedron 1993, 49, 1133–1150.
[22] Carson, K. G.; Schwender, C. F.; Shroff, H. N.; Cochran, N. A.; Gallant, D. L.; Briskin, M. J. Bioorg Med Chem Lett 1997, 7, 711–714.
[23] Roush, D. M.; Patel, M. M. Synth Commun 1985, 15, 675–679.
[24] Wipf, P.; Miller, C. P. Tetrahedron Lett 1992, 33, 6267–6270.
[25] Wang, F. J.; Hauske, J. R. Tetrahedron Lett 1997, 38, 6529–6532.
[26] Jiao, P.; Xu, J. X.; Zhang, Q. H.; Choi, M. C. K.; Chan, A. S. C. Tetrahedron: Asymmetry 2001, 12, 3081–3088.
[27] Kanerva, L. T.; Rahiala, K.; Vanttinen, E. J Chem Soc, Perkin Trans 1 1992, 1759–1762.
[28] Nesterenko, V.; Byers, J. T.; Hergenrother, P. J. Org Lett 2003, 5, 281–284.
[29] Friedrich, W.; Gross, G.; Bernhauer, K.; Zeller, P. Helv Chim Acta 1960, 43, 1759–1762.