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An efficient synthesis of enantiomerically pure unnatural aryl glycinols and aryl glycines

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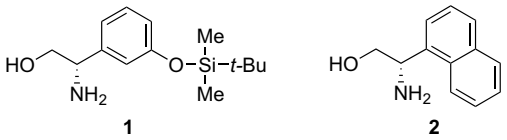
Abstract—A quick route to enantiomerically pure unnatural aryl glycinols and aryl glycines has been established based on an asymmetric azidation reaction using a chiral benzosultam auxiliary. The synthesis of aryl glycinols involves three steps starting from arylacetic acids, and the chiral auxiliary can be readily recovered.

1. Introduction

An efficient synthesis of enantiomerically pure α-amino acids has drawn a considerable research interest. A diversity of methodology[1] has been developed for the stereoselective construction of naturally occurring amino acids as well as optically active nonproteinogenic amino acids, of which aryl glycine derivatives constitute an important class.[2] Highly functionalized aryl glycines can be found in numerous peptide and glycopeptide antibiotics, such as the vancomycins.[3] Several substituted phenylglycine derivatives, including 3-hydroxyphenylglycine, have been described as potent and selective agonists or antagonists of glutamate receptors of the central nervous system (CNS).[4] Aryl glycinols constitute a class of β-amino alcohols, which are also valuable structural units in synthetic and natural compounds.[5] The enantiomerically pure aryl glycinols can be directly synthesized from the corresponding α-amino acids by reduction of the acid function.[6] This route is, however, only amenable to the case when an enantiopure amino acid is readily available, either from a natural source or by a short synthesis. Otherwise, other synthetic routes can be used. Over the course of our study on the development of oxazoline-based artificial receptors for the molecular recognition of organoammonium ions,[7] gram-quantities of (*m*-hydroxyphenyl)glycinol **1** and α-naphthylglycinol **2**[8] (Scheme 1) were required for the construction of new oxazoline receptors. We found that the corresponding enantiomerically pure amino acids were either not readily available or were very expensive.[9] Therefore, it was necessary for us to develop an efficient synthetic route. Herein, we report an efficient route to the aryl glycinols and the corresponding aryl glycines in gram quantities with high enantiomeric purities, which involves an asymmetric azidation reaction using a benzosultam chiral auxiliary[10] that can be readily recovered and reused. The established procedure can also be applied as an expeditious route to other enantiomerically pure β-amino alcohols and α-amino acids.



Scheme 1. Selected aryl glycinols.

2. Results and discussion

Among various plausible routes, we investigated two chemical synthesis routes to enantiomerically pure aryl glycinols:

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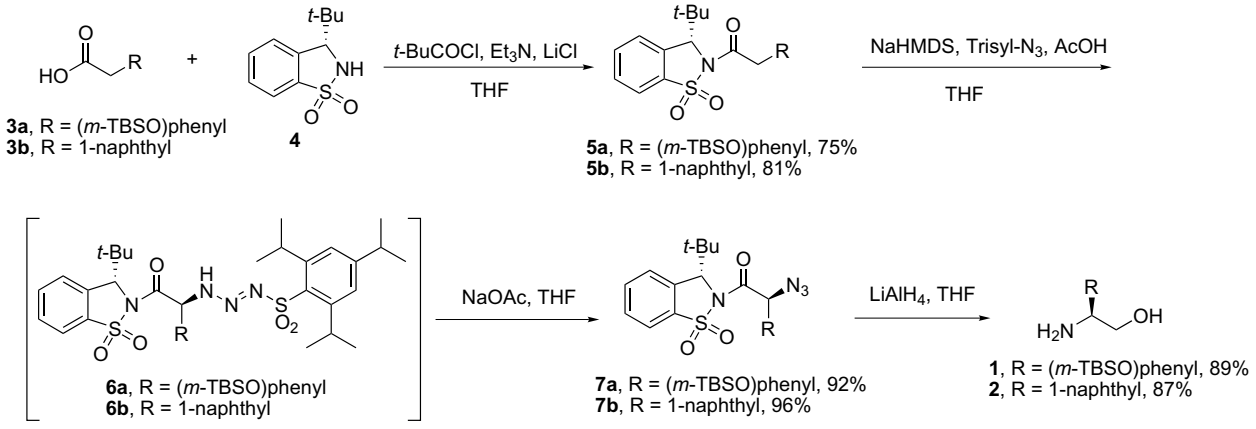
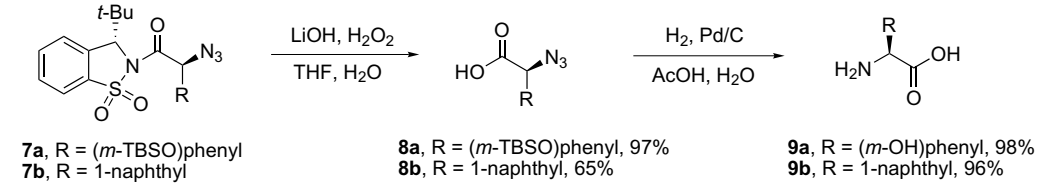
the Sharpless asymmetric aminohydroxylation (AA) of aryl olefins[11] and the chiral auxiliary-based asymmetric synthesis.[12] Although the Sharpless' AA route seemed to be concise, it has a drawback of low regioselectivity (about 7:3) in the case of most substituted styrene derivatives. Furthermore, the chromatographic separation of the regioisomers was problematic due to their similar R_f values. In addition to the regioselectivity problem, we had difficulty in reproducing the Sharpless AA reaction in cases where benzyl carbamate or *tert*-butyl carbamate was used as the amine source, even though we followed the reaction conditions described in the literature. When we used *N*-bromoacetamide as the amine source, this problem did not occur; however, this route was unsuitable for our purpose because an additional protection step raised a selectivity problem. Therefore, we turned our attention to the chiral auxiliary-based route, which involves readily available starting materials, gives high enantioselectivity, and, above all, the auxiliary can be recovered and reused.

To synthesize amino alcohol **1**, arylacetic acid **3a** was coupled with benzosultam **4**[13] using a mixed anhydride method (*t*-BuCOCl, LiCl, Et_3N)[14] to afford acyl sultam **5a** in 75% yield (Scheme 2). The next azidation reaction was carried out as following the Evans protocol:[15] enolization of acyl sultam **5a** with sodium hexamethyldisilazide (NaHMDS) in THF at −78 °C, and subsequent reaction with trisyl azide provided intermediate **6a**, which was then decomposed to azido compound **7a** by treatment with sodium acetate at 25 °C overnight. The azidation step proceeded in good yield (92%) and with near complete stereoselectivity, as judged by ^1H NMR spectrum analysis for the crude product (de > 98:2). Finally, treatment of azido compound **7a** with $LiAlH_4$ in THF at 0–25 °C, followed by quenching with water, afforded the desired amino alcohol **1**. This one-step reduction of the azido-sulfonamide to the amino alcohol is possible, because the chiral auxiliary is robust under the reaction conditions. After a standard extractive work-up and column chromatography on silica gel, amino alcohol **1** was then isolated in 89% yield as oil, together with recovered benzosultam **4** in quantitative yield. The enantiopurity of amino alcohol **1** was determined to be 91% ee by NMR analyses for its Mosher's amide, which in turn was synthesized from an unpurified sample. The value is a little lower than the diastereoselectivities observed in the cases of other azido compounds (>98:2). In previous cases,[10] acyl sultam intermediates were derived from 1-pentenoic acid and 3-phenylpropanoic acid, which are less prone to epimerization at the stereogenic center, compared to the present case of aryl acetic acid. We suspected that a certain degree of racemization occurred during the conversion of azido compound **7a** to the amino alcohol.[16] Following a similar route as above, (1-naphthyl)glycinol **2** can be synthesized, starting from commercially available (1-naphthyl)acetic acid. The whole sequence was efficiently carried out in 68% overall yield, while the enantiopurity was found to be 95% ee before recrystallization.

Aryl glycines **9a** and **9b** can be readily synthesized from azo compounds **7a** and **7b**. Hydrolysis of azido compound **7a** with lithium hydroxide and hydrogen peroxide, followed by catalytic hydrogenation provided amino acid **9a** in 95% overall yield (Scheme 3). Similarly, (1-naphthyl)glycine **9b** could also be obtained in 62% overall yield starting from azo compound **7b**.



Scheme 2. Asymmetric synthesis of aryl glycinols **1** and **2** using chiral auxiliary benzosultam **4**.



Scheme 3. Asymmetric synthesis of aryl glycine derivative **9a** and **9b**.

3. Conclusion

In conclusion, we have developed an efficient route for the synthesis of enantiomerically pure aryl glycinols **1** and **2**, as well as corresponding aryl glycines **9a** and **9b**. The procedure utilizes readily available starting materials and established reactions. Of particular note is that the chiral auxiliary can be readily recovered and reused. The established synthesis can be used as an expeditious route to other enantiomerically pure β-amino alcohols and α-amino acids.

4. Experimental

4.1. General methods

^{1}H NMR spectra are reported as follows: chemical shift in parts per million from internal tetramethylsilane on the delta scale, multiplicity (s = singlet, d = doublet, br s = broad singlet), integration, and coupling constant (in hertz). Elemental analyses were performed by Center for Integrated Molecular Systems. Melting points are uncorrected ones. Chromatography means flash column chromatography, which was carried out on Merck silica gel 60 (230–400 mesh). Analytical thin layer chromatography was carried out on Merck silica gel F_{254} plates. All reactions were run under an inert atmosphere of dry argon.

4.2. 3-(*tert*-Butyldimethylsilanyloxy)phenylacetic acid 3a

To a suspension of sodium hydride (60% dispersion in oil, 0.88 g, 22 mmol) in THF (30 mL) was added a solution of 3-hydroxyphenylacetic acid (1.52 g, 10.0 mmol) in THF (10 mL), dropwise at 0 °C, and the resulting mixture was stirred for 30 min. To this mixture was added *tert*-butyldimethylsilyl chloride (1.81 g, 12 mmol) in THF (10 mL) dropwise, and then stirred at room temperature for 18 h. The reaction mixture was quenched with 0.5 M aqueous HCl solution. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The crude residue was purified by flash column chromatography (20% EtOAc/hexane) to afford **3a** (2.21 g, 83%): $R_f = 0.53$ (EtOAc/hexanes = 2:3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.13 (s, 1H), 7.17 (dd, $J = 7.7$, 7.5, 1H), 6.65 (d, $J = 7.5$, 1H), 6.76 (s, 1H), 6.74 (d, $J = 7.7$, 1H), 3.58 (s, 2H), 0.97 (s, 9H), 0.21 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.3, 156.2, 135.1, 129.9, 122.7, 121.7, 119.4, 41.4, 26.1, 18.6, −3.4; MS (EI): *m*/*z* (rel intensity) 266 (M^+, 9), 209 (13), 181 (100), 107 (21).

4.3. 2-[3-(*tert*-Butyldimethylsilanyloxy)phenyl]-1-(3(*S*)-*tert*-butyl-1,1-dioxo-1,3-dihydro-1λ^6-benzo[*d*]isothiazol-2-yl)-ethanone 5a

To a solution of 3-(*tert*-butyldimethylsilanyloxy)phenylacetic acid **3a** (8.50 g, 31.9 mmol) and triethylamine (10.1 mL, 73.0 mmol) in THF (170 mL) was added pivaloyl chloride (4.5 mL, 36.5 mmol) at −20 °C. A white solid was formed instantaneously. The mixture was stirred at the same temperature for 2 h, and then treated with lithium chloride (1.42 g, 33.4 mmol), followed by 3-(*S*)-*tert*-butyl-1.2-benzisothiazoline 1,1-dioxide **4** (6.95 g, 30.4 mmol) dissolved in THF (30 mL). The reaction mixture was allowed to warm to room temperature and stirred for 1 h, and then treated with additional triethylamine (4.2 mL, 30.4 mmol). After being stirred for 12 h, the reaction mixture was quenched with water and THF was removed in vacuo. The residue was extracted with EtOAc, and the combined organic layers were washed with 1 M $NaHCO_3$ followed by brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography (5% EtOAc/hexane, then 10% EtOAc/hexane) to afford **5a** (10.7 g, 75%) and the sultam auxiliary (2.21 g): $R_f = 0.62$ (EtOAc/hexanes = 1:4, v/v); $[\alpha]_D^{27} = -12.1$ (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, $J = 7.7$, 1H), 7.57–7.65 (m, 2H), 7.50 (d, $J = 7.8$, 1H), 7.19 (dd, $J = 8.1$, 7.6, 1H), 6.92 (s, 1H), 6.75 (d, $J = 8.1$, 1H), 5.60 (s, 1H), 4.18 (dd, $J = 39.8$, 15.1, 2H), 0.96 (s, 9H), 0.88 (s, 9H), 0.17 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 156.1, 136.1, 135.5, 135.3, 133.4, 129.9, 129.8, 126.4, 123.4, 122.3, 122.1, 119.5, 66.4, 53.8, 44.6, 38.8, 27.4, 26.1, 18.6, −4.0; MS (EI): *m*/*z* (rel intensity) 473 (M^+, 3), 458 (5), 416 (100), 221 (35) 191 (36), 164 (78).

4.4. 1-(3(*S*)-*tert*-Butyl-1,1-dioxo-1,3-dihydro-1λ^6-benzo-[*d*]isothiazol-2-yl)-2-(naphthalen-1-yl)ethanone 5b

This material was prepared following the same procedure used for **5a**, starting from 1-naphthaleneacetic acid **3b** (3.65 g, 42.6 mmol). Purification by column chromatography (10–20% EtOAc/hexane) afforded **5b** (5.68 g, 81%) as a solid: $R_f = 0.56$ (EtOAc/hexanes = 3:7, v/v); mp 121–122 °C; $[\alpha]_D^{26} = -32.7$ (*c* 1.54, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25–7.87 (m, 11H), 5.63 (s, 1H), 4.72 (dd, $J = 41.6$, 16.6, 2H), 0.92 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 136.5, 135.7, 134.5, 133.8, 13.9, 130.9, 130.4, 129.4, 129.3, 129.0, 127.0, 126.7, 126.4, 126.1, 124.8, 122.6, 66.9, 42.4, 39.1, 27.8; MS (FAB): *m*/*z* (rel intensity) 394 (M+1, 100), 226 (40), 168 (29).

4.5. 2(*S*)-Azido-2-[3-(*tert*-butyl-dimethylsilanyloxy)phenyl]-1-(3(*S*)-*tert*-butyl-1,1-dioxo-1,3-dihydro-1λ^6-benzo[*d*]isothiazol-2-yl)ethanone 7a

To a solution of sodium bis(trimethylsilyl)amide (NaHMDS, 1.0 M in THF, 5.90 mL, 5.90 mmol) in THF (20 mL) at −78 °C was added a pre-cooled (−78 °C) solution of starting material **5a** (2.54 g, 5.36 mmol) in THF (15 mL) via a cannula, and the resulting solution was stirred for 30 min. This sodium enolate solution was treated with a pre-cooled (−78 °C) solution of trisyl azide (1.82 g, 6.97 mmol) in THF (7 mL) via a cannula, and then stirred for 2 min before being quenched with glacial acetic acid (1.47 mL, 25.7 mmol). After being stirred for 10 min, the cooling bath was removed, and the solution partitioned between EtOAc and water. The aqueous phase was extracted twice with EtOAc, and the combined organic phase was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo to afford crude compound **6a** as a light yellow solid, which was immediately used for the next reaction without further purification. To a solution of

crude compound **6a** in THF (54 mL) was added sodium acetate (880 mg, 10.7 mmol) at room temperature. After being stirred for 12 h, the solution was partitioned between EtOAc and water. The aqueous phase was extracted with EtOAc twice, and the combined organic phase was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (2–10% EtOAc/hexane) to afford **7a** (2.54 g, 92%) as a white solid. The diastereomeric ratio of the product (de > 98:2) was determined by ^{1}H NMR analysis. The diastereoselectivity increased to >99% de by recrystallizing the product from hexane–CH_2CH_2 (white crystals, 2.08 g, 78%). **7a**: $R_f = 0.65$ (EtOAc/hexanes = 1:4, v/v); mp 163–165 °C; $[\alpha]_D^{28} = +41.1$ (*c* 1.0, $CHCl_3$) before crystallization, $[\alpha]_D^{25} = +47.7$ (*c* 0.52, $CHCl_3$) after crystallization; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53–7.75 (m, 4H), 7.02–7.26 (m, 4H), 5.66 (s, 1H), 5.55 (s, 1H), 1.09 (s, 9H), 0.97 (s, 9H), 0.20 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 156.2, 135.4, 135.3, 133.9, 133.3, 130.3, 126.7, 122.5, 122.4, 121.6, 121.0, 67.1, 66.8, 39.0, 27.8, 26.3, 18.8, −3.8; MS (FAB): *m*/*z* (rel intensity) 514 (M+1, 10), 487 (50), 472 (100), 457 (43), 444 (55), 401 (63). Anal. Calcd for $C_{25}H_{34}N_4O_4SSi{\cdot}1/2H_2O$: C, 57.66; H, 6.71; N, 10.76. Found: C, 57.85; H, 6.82; N, 10.95.

4.6. 2(*S*)-Azido-1-(3(*S*)-*tert*-butyl-1,1-dioxo-1,3-dihydro-1λ^6-benzo[*d*]isothiazol-2-yl)-2(naphthalen-1-yl)ethanone 7b

This compound was prepared, as above, starting from **5b** (4.00 g, 10.2 mmol). Purification by column chromatography (10% EtOAc/hexane) afforded **7b** (4.48 g, 96%; de > 98:2) as a solid: $R_f = 0.33$ (EtOAc/hexanes = 1:4, v/v); mp 70–71 °C; $[\alpha]_D^{22} = -102.2$ (*c* 1.04, $CHCl_3$) before crystallization, $[\alpha]_D^{25} = -94.4$ (*c* 0.52, $CHCl_3$) after crystallization; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44–7.89 (m, 11H), 6.30 (s, 1H), 5.71 (s, 1H), 1.10 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 136.3, 135.4, 134.4, 134.8, 133.9, 131.8, 130.7, 130.3, 129.9, 129.6, 127.6, 126.9, 126.8, 126.7, 125.6, 124.2, 122.5, 67.2, 64.8, 39.1, 27.9; MS (FAB): *m*/*z* (rel intensity) 435 (M+1, 9), 407 (17), 392 (100), 226 (29), 165 (19). Anal. Calcd for $C_{23}H_{22}N_4O_3S$: C 63.58; H 5.10; N 12.89. Found: C, 63.82; H, 5.01; N, 12.82.

4.7. 2(*S*)-Amino-2-[3-(*tert*-butyldimethylsilanyloxy)-phenyl]ethanol 1

To a solution of $LiAlH_4$ (1.0 M in THF, 14.0 mL, 14.0 mmol) in THF (30 mL) was added a solution of compound **7a** (3.00 g, 5.83 mmol) in THF (10 mL) dropwise at 0 °C. The mixture was allowed to warm to room temperature and stirred for a further 1 h. The reaction mixture was cooled by using an ice-water bath, and then was quenched with water carefully. The mixture was diluted with EtOAc (8 mL) and treated with 20% aqueous Rochelle's salt (10 mL). After being vigorously stirred for 12 h at room temperature, the mixture was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The crude residue was purified by column chromatography (30% EtOAc in hexane; then 20% MeOH in EtOAc) to afford the desired compound **1** (1.39 g, 89%). The sultam auxiliary was also recovered (1.14 g, 87%). The enantiopurity of the resulting product was determined to be 91% ee by ^{19}F NMR analysis of the corresponding *N*-acylated derivative obtained by treatment with (*R*)-Mosher's chloride and triethylamine: $R_f = 0.31$ (MeOH/EtOAc = 1:9, v/v); $[\alpha]_D^{23} = +21.8$ (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.74–7.24 (m, 4H), 4.44 (br s, 1H), 3.81 (br s, 2H), 0.98 (s, 9H), 0.20 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.8, 136.9, 130.9, 121.4, 120.0, 64.8, 58.2, 26.3, 18.8, −3.7; MS (EI): *m*/*z* (rel intensity) 267 (M^+, 100). HRMS (EI) calcd for $C_{14}H_{25}NO_2Si$ 267.1655, found 267.1647.

4.8. 2(*S*)-Amino-2-(naphthalen-1-yl)ethanol 2

This compound was prepared, as above, starting from **7b** (0.40 g, 1.00 mmol) in 87% yield (0.16 g, 95% ee) as a white solid: $R_f = 0.17$ (MeOH/EtOAc = 1:9, v/v); mp 130–132 °C; $[\alpha]_D^{26} = +82.7$ (*c* 0.51, MeOH) [lit.[8b] $[\alpha]_D^{25} = +83$ (*c* 0.5, MeOH), lit.[8a] for (*R*)-**2** $[\alpha]_D = -85$ (*c* 0.5, MeOH)]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26–8.13 (m, 7H), 4.92 (dd, $J = 8.0, 3.9$, 1H), 3.95 (dd, $J = 10.8, 3.9$, 1H), 3.67 (dd, $J = 10.8, 8.0$, 1H), 2.03 (br s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7, 134.5, 131.5, 129.7, 128.6, 127.0, 126.4, 126.1, 123.5, 123.2, 67.9, 53.4; MS (EI): *m*/*z* (rel intensity) 187 (M^+, 28), 156 (100), 128 (38). Anal. Calcd for $C_{12}H_{12}NO$: C 76.98; H 7.00; N 7.48. Found: C, 77.32; H, 7.02; N, 7.40.

4.9. (*S*)-Azido[3-(*tert*-butyldimethylsilanyloxy)phenyl]-acetic acid 8a

To a solution of **7a** (770 mg, 1.5 mmol) in THF (24 mL) and H_2O (6 mL) at 0 °C was added H_2O_2 (35 wt %, 0.50 mL, 6.0 mmol) followed by LiOH (72 mg, 3.0 mmol). The mixture was allowed to warm to room temperature and stirred for a further 30 min, after which it was treated with 4 mL of 1 M Na_2SO_3 followed by 5 mL of 1 N NaOH. After being stirred for 30 min, most of the THF was removed in vacuo, and the residue diluted with water and extracted three times with CH_2Cl_2 to recover chiral auxiliary **4** after drying and concentration (315 mg). The aqueous layer was acidified to pH 1–2 with 4 M aqueous HCl and then extracted three times with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford nearly pure azido acid **8a** (280 mg, 97% yield) as a white solid: mp 142–143 °C; $[\alpha]_D^{22} = +122$ (*c* 0.5, acetone); ^{1}H NMR (300 MHz, CD_3COCD_3) δ 6.84–7.51 (m, 4H), 5.09 (s, 1H); ^{13}C NMR (75 MHz, CD_3COCD_3) δ 170.2, 158.2, 136.5, 130.4, 119.3, 116.4, 114.9, 64.9. HRMS (EI) calcd for $C_{14}H_{21}N_3O_3Si$ 307.1352, found 307.1354.

4.10. (*S*)-Azido(naphthalen-1-yl)acetic acid 8b

This compound was prepared, as above, starting from **7b** (625 mg, 1.5 mmol) in 65% yield (220 mg) as a white solid: mp 152–153 °C; $[\alpha]_D^{22} = +142$ (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.08 (br s, 1H), 7.41–8.09 (m, 7H), 5.69 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.4, 134.5,

131.2, 130.9, 129.5, 127.7, 127.1, 126.8, 125.5, 123.5, 63.5. MS (EI): *m*/*z* (rel intensity) 227 (M^+, 100).

4.11. (*S*)-Amino-(3-hydroxyphenyl)acetic acid 9a

A solution of compound **8a** (62 mg, 0.20 mmol) in H_2O (0.9 mL) and acetic acid (0.3 mL) was treated with Pd/C (10 wt %, 12 mg), and the mixture stirred for 18 h under a hydrogen atmosphere. The reaction mixture was filtered through Celite 545, and the filtrate was concentrated in vacuo to give a white solid. This amino acid was first dried by azeotropic removal of water and acetic acid with benzene, and then it was further dried over P_2O_5 under vacuum for 12 h to afford pure **9a** (34 mg, 98% yield). The enantiopurity of the resulting product was determined to be 99% ee by ^{19}F NMR analysis of the derived Mosher amide: mp 198–199 °C; $[\alpha]_D^{22} = +128$ (*c* 0.2, 1 M HCl); ^1H NMR (300 MHz, D_2O) δ 6.77–7.21 (m, 4H), 4.56 (s, 1H); ^{13}C NMR (75 MHz, D_2O) δ 173.4, 156.4, 136.0, 131.2, 120.3, 116.8, 115.0, 58.6. Anal. Calcd for $C_8H_9NO_3 \cdot 1/2H_2O$: C 54.54, H 5.72, N 7.95. Found: C 54.65, H 5.83, N 7.73.

4.12. (*S*)-Amino(naphthalen-1-yl)acetic acid 9b

Reduction of compound **8b** (52 mg, 0.22 mmol) afforded **9b** in 96% yield (42 mg, 99% ee) as a white solid: mp 167–168 °C (decomp.); $[\alpha]_D^{22} = +141$ (*c* 0.2, 1 M HCl) {lit.[17] $[\alpha]_D^{22} = +164.7$ (*c* 0.71 M HCl)}; ^1H NMR (300 MHz, D_2O) δ 7.39–8.01 (m, 4H), 5.31 (s, 1H); ^{13}C NMR (75 MHz, D_2O) δ 170.8, 132.2, 130.1, 129.2, 128.1, 127.5, 125.7, 125.0, 124.9, 124.2, 121.6, 53.3.

Acknowledgments

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