Supporting Information

for Asymmetric Synthesis of Functionalized Aza-Cyclic Amino Acids with Quaternary Stereocenters by a Phase–Transfer–Catalyzed Alkylation Strategy

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***N*-(*t*-Butoxycarbonyl)-3-oxoproline *t*-Butyl Ester (2).** To a mixture of *N*-*t*-butoxycarbonyl-*N*-(2-methoxylcarbonylethyl)glycine *t*-butyl ester[1] (6.22 g, 19.6 mmol) in dry toluene (200 mL) was added potassium *t*-butoxide (4.49 g, 40.0 mmol) at 0 ˚C under argon atmosphere and the mixture was stirred for 20 min at the same temperature. The resulting mixture was quenched with glacial acetic acid (6 mL), diluted with 1N HCl (150 mL) and extracted with Et_2O (3 times). The combined ethereal extracts were washed with water and brine, and then dried over Na_2SO_4. Evaporation of solvents and purification of the residual crude products by column chromatography on silica gel (hexane/AcOEt = 4:1 as eluent) gave **2** (3.98 g, 14.0 mmol, 71%): ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 4.43 (0.3H, s, NCHCO), 4.36 (0.7H, s, NCHCO), 4.00-3.80 (1H, m, CH_2N), 3.80-3.69 (1H, m, CH_2N), 2.65 (2H, t, *J* = 7.2 Hz, CH_2CO), 1.48 (9H, s, *t*-Bu), 1.46 (9H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 204.6, 204.2, 164.9, 153.7, 82.7, 80.8, 80.6, 66.3, 66.1, 42.2, 41.5, 37.0, 36.3, 28.2, 27.8, 27.6; IR (neat) 2978, 2932, 1771, 1734, 1703, 1477, 1393, 1368, 1242, 1153, 951, 914, 839, 772 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{14}H_{23}NO_5Na$ ($[M+Na]^+$): 308.1468, found: 308.1473.

***N*-(*t*-Butoxycarbonyl)-3-oxopipecoline *t*-Butyl Ester (3).** This compound was prepared from *N*-*t*-butoxycarbonyl-*N*-(3-methoxylcarbonylpropyl)glycine *t*-butyl ester (3.07 g, 9.27 mmol) in a similar manner to that for **2** (776 mg, 2.59 mmol, 28%): ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 5.14 (0.3H, s, NCHCO), 4.94 (0.7H, s, NCHCO), 4.08-3.96 (0.7H, m, CH_2N), 3.93-3.81 (0.3H, m, CH_2N), 3.45-3.23 (1H, m, CH_2N), 2.55-2.38 (2H, m, CH_2CO), 2.08-1.87 (2H, m, C*H*$_2$$CH_2N$), 1.52 (2.7H, s, *t*-Bu), 1.48 (9H, s, *t*-Bu), 1.45 (6.3H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 200.1, 199.8, 165.6, 154.7, 154.2, 83.1, 80.8, 67.7, 66.3, 41.4, 40.4, 37.7, 28.2, 27.9, 22.7, 22.5; IR (neat) 2978, 2934, 2876, 1730, 1699, 1456, 1393, 1368, 1248, 1159, 984, 908, 839, 772 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{15}H_{25}NO_5K$ ($[M+K]^+$): 338.1364, found: 338.1378.

General Procedure for Enantioselective Alkylation of *α*-Amino-*β*-keto Esters 2 and 3 under Liquid–Liquid Phase–Transfer Conditions. To a mixture of *α*-amino-*β*-keto ester **2** or **3** (0.30 mmol) and (*S*,*S*)-**1** (3.2 mg, 0.003 mmol, 1 mol% for **2** or 6.5 mg, 0.006 mmol, 2 mol% for **3**) in *o*-xylene (2 mL) was added alkyl bromide (0.36 mmol) and saturated aqueous K_2CO_3 (1.5 mL, 10 mmol) sequentially at 0 ˚C under argon atmosphere, and the mixture was stirred for several hours at the same temperature. The resulting mixture was diluted with aqueous NH_4Cl and extracted with Et_2O (3 times). The combined ethereal extracts were washed with brine and then dried over Na_2SO_4. Evaporation of solvents and purification of the residual crude products by column chromatography on silica gel (hexane/AcOEt as eluent) gave the corresponding alkylation product **4** or **5**.

Characterization of Alkylation Products.

(*R*)-*N*-(*t*-Butoxycarbonyl)-2-benzyl-3-oxoproline *t*-Butyl Ester (4a): $[\alpha]_D^{29}$ –68.2° (*c* 1.0, $CHCl_3$) (94% ee); ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 7.26-7.18 (3H, m, Ph), 7.07-7.00 (2H, m, Ph), 3.67 (0.4H, d, *J* = 13.6 Hz, CH_2Ph), 3.62 (0.6H, ddd, *J* = 10.0, 9.6, 6.8 Hz, CH_2N), 3.56 (0.4H, ddd, *J* = 10.0, 9.6, 6.8 Hz, CH_2N), 3.51 (0.6H, d, *J* = 13.6 Hz, CH_2Ph), 3.42 (1H, d, *J* = 13.6 Hz, CH_2Ph), 2.98 (0.6H, ddd, *J* = 10.0, 10.0, 6.0 Hz, CH_2N), 2.92 (0.4H, ddd, *J* = 10.0, 10.0, 6.0 Hz, CH_2N), 2.46 (0.4H, ddd, *J* = 18.8, 9.6, 6.0 Hz, CH_2CO), 2.45 (0.6H, ddd, *J* = 18.8, 9.6, 6.0 Hz, CH_2CO), 1.78 (0.4H, ddd, *J* = 18.8, 10.0, 6.8 Hz, CH_2CO), 1.72 (0.6H, ddd, *J* = 18.8, 10.0, 6.8 Hz, CH_2CO), 1.58 (5.4H, s, *t*-Bu), 1.54 (3.6H, s, *t*-Bu), 1.46 (5.4H, s, *t*-Bu), 1.45 (3.6H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 208.9, 208.5, 166.3, 153.8, 153.7, 135.9, 135.1, 130.0, 128.4, 128.2, 126.9, 126.7, 82.6, 82.4, 81.5, 80.4, 74.6, 74.4, 42.1, 41.7, 38.2, 37.6, 36.4, 35.5, 28.6, 28.4, 27.9, 27.8; IR (neat) 2976, 2932, 1767, 1740, 1701, 1454, 1387, 1368, 1252, 1136, 1080, 995, 841, 766, 704 cm^{-1}. HPLC conditions: DAICEL Chiralcel-OD, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 11.7 min (*S*), 13.4 min (*R*). HRMS (ESI-TOF) calcd for $C_{21}H_{29}NO_5Na$ ($[M+Na]^+$): 398.1938, found: 398.1933. The absolute configuration was determined after derivatization to **6** as described in page 7.

***N*-(*t*-Butoxycarbonyl)-2-(4-fluorophenyl)methyl-3-oxoproline *t*-Butyl Ester**: $[\alpha]_D^{30}$ –54.2° (*c* 1.1, $CHCl_3$) (95% ee); ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 7.03-6.88 (4H, m, Ar-H), 3.65 (0.6H, ddd, *J* = 10.0, 10.0, 7.2 Hz, CH_2N), 3.64 (0.4H, d, *J* = 13.6 Hz, CH_2Ar), 3.59 (0.4H, ddd, *J* = 10.0, 10.0, 7.2 Hz, CH_2N), 3.47 (0.6H, d, *J* = 13.6 Hz, CH_2Ar), 3.40 (1H, d, *J* = 13.6 Hz, CH_2Ar), 3.03 (0.6H,

ddd, *J* = 10.0, 10.0, 5.6 Hz, CH_2N), 3.00 (0.4H, ddd, *J* = 10.0, 10.0, 5.6 Hz, CH_2N), 2.50 (0.4H, ddd, *J* = 18.8, 10.0, 5.6 Hz, CH_2CO), 2.49 (0.6H, ddd, *J* = 18.8, 10.0, 5.6 Hz, CH_2CO), 1.82 (0.4H, ddd, *J* = 18.8, 10.0, 7.2 Hz, CH_2CO), 1.76 (0.6H, ddd, *J* = 18.8, 10.0, 7.2 Hz, CH_2CO), 1.58 (5.4H, s, *t*-Bu), 1.54 (3.6H, s, *t*-Bu), 1.46 (5.4H, s, *t*-Bu), 1.45 (3.6H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 208.7, 208.3, 166.1, 161.7 (d, $^1J_{C–F}$ = 246 Hz), 161.7 (d, $^1J_{C–F}$ = 246 Hz), 153.8, 153.6, 131.6 (d, $^4J_{C–F}$ = 3 Hz), 131.5 (d, $^3J_{C–F}$ = 8 Hz), 131.4 (d, $^3J_{C–F}$ = 8 Hz), 130.9 (d, $^4J_{C–F}$ = 3 Hz), 115.3 (d, $^2J_{C–F}$ = 21 Hz), 115.0 (d, $^2J_{C–F}$ = 21 Hz), 82.7, 82.5, 81.5, 80.5, 74.5, 74.3, 42.1, 41.7, 37.3, 36.7, 36.3, 35.4, 28.5, 28.4, 27.9, 27.8; IR (neat) 2978, 2934, 1769, 1740, 1699, 1510, 1456, 1387, 1368, 1250, 1223, 1136, 1098, 999, 843, 812, 772 cm^{-1}. HPLC conditions: DAICEL Chiralcel-OD, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 12.3 min (minor), 13.4 min (major). HRMS (ESI-TOF) calcd for $C_{21}H_{28}FNO_5Na$ ($[M+Na]^+$): 416.1844, found: 416.1842.

***N*-(*t*-Butoxycarbonyl)-2-(4-methoxyphenyl)methyl-3-oxoproline *t*-Butyl Ester:** $[\alpha]_D^{27}$ –74.5° (*c* 1.0, $CHCl_3$) (94% ee); ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 6.95 (0.8H, d, *J* = 8.8 Hz, Ar-H), 6.94 (1.2H, d, *J* = 8.8 Hz, Ar-H), 6.78 (1.2H, d, *J* = 8.8 Hz, Ar-H), 6.77 (0.8H, d, *J* = 8.8 Hz, Ar-H), 3.77 (1.2H, s, CH_3O), 3.76 (1.8H, s, CH_3O), 3.63 (0.6H, ddd, *J* = 10.0, 10.0, 6.8 Hz, CH_2N), 3.61 (0.4H, d, *J* = 13.6 Hz, CH_2Ar), 3.56 (0.4H, ddd, *J* = 10.0, 10.0, 6.8 Hz, CH_2N), 3.44 (0.6H, d, *J* = 13.6 Hz, CH_2Ar), 3.36 (1H, d, *J* = 13.6 Hz, CH_2Ar), 3.02 (0.6H, ddd, *J* = 10.0, 10.0, 6.0 Hz, CH_2N), 2.98 (0.4H, ddd, *J* = 10.0, 10.0, 6.0 Hz, CH_2N), 2.45 (0.4H, ddd, *J* = 18.8, 10.0, 6.0 Hz, CH_2CO), 2.44 (0.6H, ddd, *J* = 18.8, 10.0, 6.0 Hz, CH_2CO), 1.80 (0.4H, ddd, *J* = 18.8, 10.0, 6.8 Hz, CH_2CO), 1.75 (0.6H, ddd, *J* = 18.8, 10.0, 6.8 Hz, CH_2CO), 1.57 (5.4H, s, *t*-Bu), 1.54 (3.6H, s, *t*-Bu), 1.46 (5.4H, s, *t*-Bu), 1.44 (3.6H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 209.0, 208.6, 166.3, 158.4, 158.3, 153.7, 153.6, 130.9, 127.7, 126.9, 113.8, 113.6, 82.4, 82.3, 81.3, 80.3, 74.6, 74.4, 55.1, 42.1, 41.7, 37.3, 36.7, 36.4, 35.5, 28.5, 28.4, 27.9, 27.8; IR (neat) 2976, 2934, 1767, 1738, 1699, 1514, 1456, 1387, 1368, 1248, 1138, 1036, 997, 843, 772 cm^{-1}. HPLC conditions: DAICEL Chiralcel-OD, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 15.6 min (minor), 17.3 min (major). HRMS (ESI-TOF) calcd for $C_{22}H_{31}NO_6Na$ ($[M+Na]^+$): 428.2044, found: 428.2042.

***N*-(*t*-Butoxycarbonyl)-2-(*β*-naphthyl)methyl-3-oxoproline *t*-Butyl Ester**: $[\alpha]_D^{28}$ –98.4° (*c* 1.0, $CHCl_3$) (93% ee); ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 7.81-7.68 (3H, m, Ar-H), 7.51 (1H, d, *J* = 8.8 Hz, Ar-H), 7.47-7.39 (2H, m, Ar-H), 7.16 (1H, t, *J* = 8.0 Hz, Ar-H), 3.86 (0.5H, d, *J* = 14.0 Hz, CH_2Ar), 3.67 (0.5H, d, *J* = 14.0 Hz, CH_2Ar), 3.60 (0.5H, ddd, *J* = 10.8, 10.0, 7.2 Hz, CH_2N), 3.59

(1H, d, *J* = 14.0 Hz, CH_2Ar), 3.52 (0.5H, ddd, *J* = 10.8, 10.0, 7.2 Hz, CH_2N), 2.91 (0.5H, ddd, *J* = 10.8, 10.0, 5.6 Hz, CH_2N), 2.86 (0.5H, ddd, *J* = 10.8, 10.0, 5.6 Hz, CH_2N), 2.44 (0.5H, ddd, *J* = 18.8, 10.0, 5.6 Hz, CH_2CO), 2.42 (0.5H, ddd, *J* = 18.8, 10.0, 5.6 Hz, CH_2CO), 1.76 (0.5H, ddd, *J* = 18.8, 10.0, 7.2 Hz, CH_2CO), 1.69 (0.5H, ddd, *J* = 18.8, 10.0, 7.2 Hz, CH_2CO), 1.63 (4.5H, s, *t*-Bu), 1.56 (4.5H, s, *t*-Bu), 1.48 (4.5H, s, *t*-Bu), 1.47 (4.5H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 208.9, 208.5, 166.2, 153.8, 153.6, 133.5, 133.2, 133.1, 132.7, 132.2, 128.9, 128.8, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 127.4, 126.0, 125.8, 125.7, 125.5, 82.6, 82.4, 81.5, 80.3, 74.6, 74.5, 42.1, 41.7, 38.3, 37.7, 36.4, 35.5, 28.6, 28.4, 27.9, 27.8; IR (neat) 2976, 2932, 1767, 1740, 1699, 1456, 1387, 1368, 1250, 1134, 1074, 1005, 843, 820, 750 cm^{-1}. HPLC conditions: DAICEL Chiralcel-OD, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 14.8 min (minor), 17.2 min (major). HRMS (ESI-TOF) calcd for $C_{25}H_{31}NO_5K$ ($[M+K]^+$): 464.1834, found: 464.1849.

***N*-(*t*-Butoxycarbonyl)-2-(4-benzoylphenyl)methyl-3-oxoproline *t*-Butyl Ester**: $[\alpha]_D^{30}$ –67.6° (*c* 1.9, $CHCl_3$) (95% ee); ^1H NMR (400 MHz, $CDCl_3$, RT) δ 7.79-7.67 (4H, m, Ar-H), 7.61-7.55 (1H, m, Ar-H), 7.52-7.45 (2H, m, Ar-H), 7.20-7.13 (2H, m, Ar-H), 3.79 (0.5H, d, *J* = 13.6 Hz, CH_2Ar), 3.73-3.55 (1H, m, CH_2N), 3.60 (0.5H, d, *J* = 13.6 Hz, CH_2Ar), 3.52 (1H, d, *J* = 13.6 Hz, CH_2Ar), 3.07 (0.5H, ddd, *J* = 10.8, 10.8, 5.6 Hz, CH_2N), 3.03 (0.5H, ddd, *J* = 10.8, 10.8, 5.6 Hz, CH_2N), 2.53 (1H, ddd, *J* = 19.2, 9.6, 5.6 Hz, CH_2CO), 1.91-1.78 (1H, m, CH_2CO), 1.59 (4.5H, s, *t*-Bu), 1.54 (4.5H, s, *t*-Bu), 1.48 (4.5H, s, *t*-Bu), 1.46 (4.5H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 208.4, 208.0, 196.2, 195.8, 166.0, 166.0, 153.9, 153.6, 141.1, 140.3, 137.4, 137.3, 136.1, 136.0, 132.2, 130.1, 130.0, 129.9, 129.8, 129.7, 128.1, 128.1, 82.9, 82.7, 81.7, 80.6, 74.4, 74.3, 42.2, 41.8, 38.1, 37.5, 36.3, 35.5, 28.5, 28.4, 27.9, 27.8; IR (neat) 2976, 2932, 1767, 1738, 1699, 1659, 1454, 1387, 1368, 1275, 1252, 1136, 1001, 924, 847, 702 cm^{-1}. HPLC conditions: DAICEL Chiralcel-OD, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 38.7 min (major), 53.6 min (minor). HRMS (ESI-TOF) calcd for $C_{28}H_{33}NO_6Na$ ($[M+Na]^+$): 502.2200, found: 502.2203.

***N*-(*t*-Butoxycarbonyl)-2-allyl-3-oxoproline *t*-Butyl Ester:** $[\alpha]_D^{27}$ –4.3° (*c* 1.0, $CHCl_3$) (90% ee); ^1H NMR (400 MHz, $CDCl_3$, RT) δ 5.62-5.46 (1H, m, C*H*=CH_2), 5.13-5.04 (2H, m, CH=C*H*$_2$), 3.80 (1H, ddd, *J* = 10.8, 9.6, 7.2 Hz, CH_2N), 3.68 (1H, ddd, *J* = 10.8, 9.6, 5.6 Hz, CH_2N), 3.16 (0.3H, dd, *J* = 14.0, 7.2 Hz, C*H*$_2$CH=CH_2), 3.02 (0.7H, dd, *J* = 14.0, 7.2 Hz, C*H*$_2$CH=CH_2), 2.84 (1H, dd, *J* = 14.0, 8.0 Hz, C*H*$_2$CH=CH_2), 2.69 (1H, ddd, *J* = 19.2, 9.6, 5.6 Hz, CH_2CO), 2.44 (1H,

ddd, *J* = 19.2, 9.6, 7.2 Hz, CH_2CO), 1.50 (2.7H, s, *t*-Bu), 1.48 (6.3H, s, *t*-Bu), 1.43 (6.3H, s, *t*-Bu), 1.42 (2.7H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 208.4, 207.9, 166.2, 166.2, 153.8, 153.7, 131.8, 131.3, 119.9, 119.7, 82.5, 82.3, 81.1, 80.3, 73.6, 73.3, 42.5, 42.0, 37.3, 36.5, 36.4, 35.6, 28.4, 27.8, 27.8; IR (neat) 2978, 2932, 1769, 1740, 1701, 1456, 1381, 1368, 1246, 1155, 1078, 1003, 922, 843, 772 cm^{-1}. HPLC conditions: DAICEL Chiralpak-AD, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 14.6 min (major), 18.7 min (minor). HRMS (ESI-TOF) calcd for $C_{17}H_{27}NO_5K$ ($[M+K]^+$): 364.1521, found: 364.1520.

***N*-(*t*-Butoxycarbonyl)-2-cinnamyl-3-oxoproline *t*-Butyl Ester**: $[\alpha]_D^{28}$ –44.0° (*c* 1.0, $CHCl_3$) (89% ee); ^1H NMR (400 MHz, $CDCl_3$, RT) δ 7.35-7.24 (4H, m, Ph), 7.24-7.16 (1H, m, Ph), 6.40 (1H, d, *J* = 15.6 Hz, CH=C*H*Ph), 5.93 (0.3H, ddd, *J* = 15.6, 8.4, 7.2 Hz, C*H*=CHPh), 5.89 (0.7H, ddd, *J* = 15.6, 8.4, 7.2 Hz, C*H*=CHPh), 3.87-3.70 (1H, m, CH_2N), 3.70-3.57 (1H, m, CH_2N), 3.31 (0.3H, dd, *J* = 14.4, 7.2 Hz, CH_2CH=CH), 3.17 (0.7H, dd, *J* = 14.4, 7.2 Hz, CH_2CH=CH), 2.99 (1H, dd, *J* = 14.4, 8.4 Hz, CH_2CH=CH), 2.67 (1H, ddd, *J* = 18.8, 9.6, 5.6 Hz, CH_2CO), 2.40 (1H, ddd, *J* = 18.8, 10.0, 6.8 Hz, CH_2CO), 1.52 (9H, s, *t*-Bu), 1.45 (6.3H, s, *t*-Bu), 1.44 (2.7H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 208.4, 207.9, 166.2, 166.1, 153.8, 137.0, 136.6, 134.8, 134.6, 128.4, 128.3, 127.4, 127.2, 126.0, 123.0, 122.4, 82.6, 82.4, 81.2, 80.4, 73.8, 73.5, 42.5, 42.0, 36.5, 35.7, 35.6, 28.4, 27.9, 27.8; IR (neat) 2976, 2932, 1769, 1738, 1699, 1456, 1385, 1368, 1250, 1142, 1076, 1003, 966, 845, 748, 694 cm^{-1}. HPLC conditions: DAICEL Chiralcel-OD, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 16.4 min (minor), 17.9 min (major). HRMS (ESI-TOF) calcd for $C_{23}H_{31}NO_5Na$ ($[M+Na]^+$): 424.2095, found: 424.2098.

(*R*)-*N*-(*t*-Butoxycarbonyl)-2-benzyl-3-oxopipecolic Acid *t*-Butyl Ester (5a): $[\alpha]_D^{27}$ –74.5° (*c* 1.0, $CHCl_3$) (91% ee); ^1H NMR (400 MHz, $CDCl_3$, –20 ˚C) δ 7.30-7.20 (3H, m, Ph), 7.06-6.98 (2H, m, Ph), 3.82-3.72 (0.4H, m, CH_2N), 3.67 (0.6H, d, *J* = 13.6 Hz, CH_2Ph), 3.61 (0.6H, d, *J* = 13.6 Hz, CH_2Ph), 3.60 (0.4H, d, *J* = 14.0 Hz, CH_2Ph), 3.62-3.52 (0.6H, m, CH_2N), 3.54 (0.4H, d, *J* = 14.0 Hz, CH_2Ph), 2.67 (0.6H, ddd, *J* = 12.8, 8.4, 4.0 Hz, CH_2N), 2.57 (0.4H, ddd, *J* = 12.8, 9.6, 3.2 Hz, CH_2N), 2.52-2.38 (1H, m, CH_2CO), 2.01 (0.6H, ddd, *J* = 18.0, 8.4, 5.6 Hz, CH_2CO), 1.90 (0.4H, ddd, *J* = 18.0, 9.6, 5.6 Hz, CH_2CO), 1.82-1.65 (1H, m, CH_2CH_2N), 1.59 (3.6H, s, *t*-Bu), 1.56 (5.4H, s, *t*-Bu), 1.46 (3.6H, s, *t*-Bu), 1.44 (5.4H, s, *t*-Bu), 1.17-1.05 (0.4H, m, CH_2CH_2N), 0.98-0.86 (0.6H, m, CH_2CH_2N); ^{13}C NMR (100 MHz, $CDCl_3$, –20 ˚C) δ 204.4, 204.3, 166.8, 166.3, 153.9, 153.8, 136.3, 135.5, 130.1, 130.0, 128.3, 128.1, 126.8, 126.6, 82.1, 82.0, 81.7, 80.5, 76.8, 76.5, 43.2, 42.7,

39.9, 38.9, 38.1, 37.9, 28.3, 28.3, 27.6, 27.5, 19.4, 19.3; IR (neat) 2976, 2934, 2874, 1755, 1715, 1694, 1454, 1393, 1366, 1256, 1163, 1078, 989, 853, 760, 702 cm^{-1}. HPLC conditions: DAICEL Chiralcel-OD, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 12.4 min (*S*), 18.6 min (*R*). HRMS (ESI-TOF) calcd for $C_{22}H_{31}NO_5Na$ ($[M+Na]^+$): 412.2095, found: 412.2105. The absolute configuration was established after derivatization to known amino acid **11** as described in page 8.

***N*-(*t*-Butoxycarbonyl)-2-(4-fluorophenyl)methyl-3-oxopipecolic Acid *t*-Butyl Ester**: $[\alpha]_D^{28}$ –76.5° (*c* 1.0, $CHCl_3$) (93% ee); ^{1}H NMR (400 MHz, $CDCl_3$, –10 ˚C) δ 6.99-6.94 (4H, m, Ar-H), 3.85-3.76 (0.4H, m, CH_2N), 3.64 (0.6H, d, *J* = 13.6 Hz, CH_2Ar), 3.61 (0.6H, d, *J* = 13.6 Hz, CH_2Ar), 3.65-3.56 (0.6H, m, CH_2N), 3.60 (0.4H, d, *J* = 13.6 Hz, CH_2Ar), 3.50 (0.4H, d, *J* = 13.6 Hz, CH_2Ar), 2.71 (0.6H, ddd, *J* = 12.8, 7.6, 3.6 Hz, CH_2N), 2.60 (0.4H, ddd, *J* = 13.2, 9.2, 2.8 Hz, CH_2N), 2.55-2.40 (1H, m, CH_2CO), 2.05 (0.6H, ddd, *J* = 17.6, 7.6, 5.6 Hz, CH_2CO), 1.93 (0.4H, ddd, *J* = 17.6, 9.2, 5.6 Hz, CH_2CO), 1.87-1.70 (1H, m, C*H*$_2$$CH_2N$), 1.58 (3.6H, s, *t*-Bu), 1.56 (5.4H, s, *t*-Bu), 1.46 (3.6H, s, *t*-Bu), 1.44 (5.4H, s, *t*-Bu), 1.22-1.10 (0.4H, m, C*H*$_2$$CH_2N$), 1.05-0.92 (0.6H, m, C*H*$_2$$CH_2N$); ^{13}C NMR (100 MHz, $CDCl_3$, –10 ˚C) δ 204.1, 204.0, 166.5, 166.2, 161.6 (d, $^1J_{C–F}$ = 246 Hz), 161.5 (d, $^1J_{C–F}$ = 246 Hz), 153.9, 153.7, 132.1 (d, $^4J_{C–F}$ = 3 Hz), 131.5 (d, $^3J_{C–F}$ = 8 Hz), 131.3 (d, $^4J_{C–F}$ = 3 Hz), 115.2 (d, $^2J_{C–F}$ = 21 Hz), 115.0 (d, $^2J_{C–F}$ = 21 Hz), 82.2, 82.1, 81.9, 80.6, 76.8, 76.6, 43.3, 42.8, 38.9, 37.9, 37.7, 28.3, 28.3, 27.7, 27.5, 19.5, 19.5; IR (neat) 2976, 2934, 2874, 1755, 1694, 1510, 1456, 1393, 1366, 1254, 1221, 1157, 993, 845 cm^{-1}. HPLC conditions: DAICEL Chiralcel-OD, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 13.1 min (minor), 19.8 min (major). HRMS (ESI-TOF) calcd for $C_{22}H_{30}FNO_5Na$ ($[M+Na]^+$): 430.2000, found: 430.2009.

***N*-(*t*-Butoxycarbonyl)-2-allyl-3-oxopipecolic Acid *t*-Butyl Ester**: $[\alpha]_D^{29}$ –23.4° (*c* 1.1, $CHCl_3$) (87% ee); ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 5.73-5.59 (1H, m, C*H*=CH_2), 5.11-5.03 (2H, m, CH=C*H*$_2$), 4.10-3.75 (1H, br, CH_2N), 3.41-3.31 (1H, m, CH_2N), 3.16-2.98 (2H, m, C*H*$_2$CH=CH_2), 2.62 (1H, ddd, *J* = 17.6, 6.4, 6.4 Hz, CH_2CO), 2.38 (1H, ddd, *J* = 17.6, 8.4, 6.4 Hz, CH_2CO), 2.12-1.99 (1H, m, C*H*$_2$$CH_2N$), 1.97-1.85 (1H, m, C*H*$_2$$CH_2N$), 1.48 (9H, s, *t*-Bu), 1.43 (9H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, 50 ˚C) δ 203.4, 166.5, 153.9, 132.8, 119.1, 81.8, 80.9, 76.2, 43.5, 38.7, 37.5, 28.4, 27.8, 20.7; IR (neat) 2976, 2934, 2874, 1753, 1715, 1694, 1456, 1393, 1366, 1238, 1163, 1007, 920, 845, 773 cm^{-1}. HPLC conditions: DAICEL Chiralpak-AD-H, hexane/*i*-PrOH = 200:1,

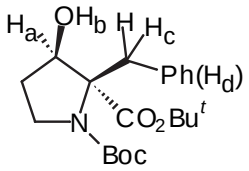
flow rate = 0.5 mL/min, retention time; 27.4 min (major), 33.5 min (minor). HRMS (ESI-TOF) calcd for $C_{18}H_{29}NO_5Na$ ([M+Na]$^+$): 362.1938, found: 362.1944.

***N*-(*t*-Butoxycarbonyl)-2-cinnamyl-3-oxopipecolic Acid *t*-Butyl Ester**: $[\alpha]_D^{28}$ –69.5° (*c* 1.0, $CHCl_3$) (90% ee); ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 7.33-7.18 (5H, m, Ph), 6.38 (1H, d, *J* = 15.6 Hz, CH=C*H*Ph), 6.03 (1H, dt, *J* = 15.6, 8.0 Hz, C*H*=CHPh), 4.05-3.75 (1H, br, NCH_2), 3.35 (1H, ddd, *J* = 13.2, 8.8, 3.6 Hz, NCH_2), 3.30-3.21 (1H, br, C*H*$_2$CH=CH), 3.17 (1H, dd, *J* = 14.0, 8.0 Hz, C*H*$_2$CH=CH), 2.61 (1H, ddd, *J* = 17.6, 6.8, 6.8 Hz, CH_2CO), 2.37 (1H, ddd, *J* = 17.6, 7.2, 7.2 Hz, CH_2CO), 2.10-1.97 (1H, m, C*H*$_2$CH$_2$N), 1.91-1.78 (1H, m, C*H*$_2$CH$_2$N), 1.50 (9H, s, *t*-Bu), 1.44 (9H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, 50 ˚C) δ 203.5, 166.4, 154.0, 137.1, 134.2, 128.4, 127.2, 126.0, 124.1, 81.9, 81.0, 76.4, 43.5, 37.8, 37.5, 28.4, 27.8, 20.8; IR (neat) 2976, 2934, 2872, 1753, 1713, 1694, 1456, 1393, 1366, 1254, 1163, 1078, 968, 847, 750, 694 cm^{-1}. HPLC conditions: DAICEL Chiralpak-AD, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 30.0 min (major), 36.2 min (minor). HRMS (ESI-TOF) calcd for $C_{24}H_{33}NO_5Na$ ([M+Na]$^+$): 438.2251, found: 438.2250.

Reduction of Benzylation Product 4a. *N*-(*t*-Butoxycarbonyl)-2-benzyl-3-hydroxyproline *t*-Butyl Ester (6). To a solution of **4a** (642 mg, 1.71 mmol) in MeOH (10 mL) was added $NaBH_4$ (128 mg, 3.38 mmol) at 0 ˚C under argon atmosphere and the mixture was stirred for 15 min at the same temperature. The reaction was quenched with 1N HCl and extractive workup was performed with Et_2O. The combined ethereal extracts were washed with brine and then dried over Na_2SO_4. Evaporation of solvents and purification of the residual crude products by column chromatography on silica gel (hexane/AcOEt = 2:1 as eluent) gave the corresponding 3-hydroxyproline derivative **6** (642 mg, 1.70 mmol, 99%) as a single diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 7.32-7.14 (5H, m, Ph), 4.40-4.27 (1H, m, C*H*OH), 3.53 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 3.41 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 3.37 (1H, d, *J* = 14.4 Hz, CH_2Ph), 3.25-3.08 (1.5H, m, CH_2N), 3.05-2.97 (0.5H, m, CH_2N), 2.85 (0.5H, dd, *J* = 6.0, 2.0 Hz, OH), 2.71 (0.5H, d, *J* = 6.0, 2.0 Hz, OH), 1.85-1.76 (1H, m, C*H*$_2$CH$_2$N), 1.54 (4.5H, s, *t*-Bu), 1.52 (9H, s, *t*-Bu), 1.48 (4.5H, s, *t*-Bu), 1.10-0.96 (0.5H, m, C*H*$_2$CH$_2$N), 0.92-0.79 (0.5H, m, C*H*$_2$CH$_2$N); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 173.0, 172.7, 153.6, 138.1, 137.7, 131.1, 130.8, 128.0, 127.6, 126.2, 125.9, 81.3, 81.1, 80.6, 79.3, 78.4, 77.0, 70.8, 70.7, 43.7, 43.5, 34.5, 33.7, 31.2, 30.3, 28.5, 28.5, 28.0, 27.9; IR (neat) 3435, 2976, 2932, 2880, 1732, 1695, 1674, 1454, 1391, 1366, 1256, 1157, 1072, 1005, 982, 845, 766, 702 cm^{-1}.

HRMS (ESI-TOF) calcd for $C_{21}H_{31}NO_5Na$ ([M+Na]$^+$): 400.2095, found: 400.2092. The minor diastereomer was not detected by ^{1}H NMR analysis. The relative configuration was determined by a NOE experiment (Table 1). Absolute configuration of the hydroxy–bearing carbon center of **6** was determined to be *R* by ^{1}H NMR analysis of the corresponding (*R*)- and (*S*)-MTPA esters.[2]

Table 1. Summary of the NOE Data for **6**

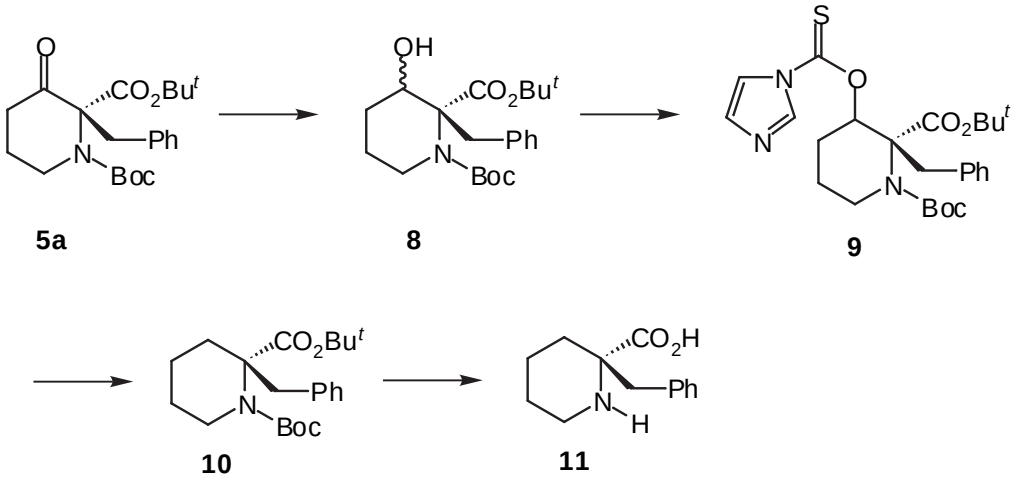


NOE (saturate/observe, %)						
H_a/H_c	H_a/H_d	H_b/H_c	H_b/H_d	H_c/H_a	H_c/H_b
0	0	2	5	0	4

(*R*)-MTPA Ester of 6: ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 7.61-7.52 (2H, m, Ph), 7.51-7.42 (3H, m, Ph), 7.03 (1H, t, *J* = 7.6 Hz, Ph), 6.89 (1H, t, *J* = 7.6 Hz, Ph), 6.82 (1H, d, *J* = 7.6 Hz, Ph), 6.77 (1H, d, *J* = 7.6 Hz, Ph), 5.53-5.41 (1H, m, OCH), 3.67 (3H, s, MeO), 3.50 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 3.37 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 3.28-3.14 (1.5H, m, CH_2N), 3.15 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 3.10 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 2.93 (0.5H, t, *J* = 10.0 Hz, CH_2N), 1.98-1.83 (1H, m, C*H*$_2$CH$_2$N), 1.54 (4.5H, s, *t*-Bu), 1.52 (4.5H, s, *t*-Bu), 1.51 (4.5H, s, *t*-Bu), 1.48 (4.5H, s, *t*-Bu), 0.85-0.71 (0.5H, m, C*H*$_2$CH$_2$N), 0.66-0.52 (0.5H, m, C*H*$_2$CH$_2$N).

(*S*)-MTPA Ester of 6: ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 7.62-7.44 (5H, m, Ph), 7.15-7.07 (3H, m, Ph), 6.90-6.82 (2H, m, Ph), 5.67-5.50 (1H, m, OCH), 3.55 (1.5H, s, MeO), 3.51 (1.5H, s, MeO), 3.40 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 3.26 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 3.30-3.16 (1.5H, m, CH_2N), 3.00 (0.5H, t, *J* = 10.0 Hz, CH_2N), 2.79 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 2.77 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 1.94-1.84 (1H, m, C*H*$_2$CH$_2$N), 1.53 (4.5H, s, *t*-Bu), 1.52 (4.5H, s, *t*-Bu), 1.51 (9H, s, *t*-Bu), 1.10-0.98 (0.5H, m, C*H*$_2$CH$_2$N), 0.90-0.77 (1H, m, C*H*$_2$CH$_2$N).

Assignment of the Absolute Configuration of *N*-(*t*-Butoxycarbonyl)-2-benzyl-3-oxopipecolic Acid *t*-Butyl Ester (5a). The absolute configuration of **5a** was determined to be *R* by comparison of the optical rotation with the literature value after derivatization to known amino acid **11** as shown below.



***N*-(*t*-Butoxycarbonyl)-2-benzyl-3-hydroxypipecolic Acid *t*-Butyl Ester (8)**. This compound was synthesized from **5a** in a similar manner to that for **6** (96% yield): ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 7.34-7.14 (5H, m, Ph), 4.13-4.05 (0.5H, m, C*H*OH), 3.93 (0.5H, dt, *J* = 11.2, 6.0 Hz, C*H*OH), 3.80-3.67 (0.5H, m, CH_2N), 3.71 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 3.70-3.55 (0.5H, br, CH_2N), 3.50 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 3.35 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 3.32 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 2.82 (0.5H, ddd, *J* = 14.0, 8.4, 5.6 Hz, CH_2N), 2.69-2.58 (0.5H, m, CH_2N), 2.25-2.15 (0.5H, m, OH), 2.09-2.00 (0.5H, m, OH), 1.90-1.61 (2.5H, m, CH_2), 1.61-1.35 (1.5H, m, CH_2), 1.54 (4.5H, s, *t*-Bu), 1.53 (4.5H, s, *t*-Bu), 1.42 (4.5H, s, *t*-Bu), 1.39 (4.5H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 172.5, 170.6, 155.2, 154.4, 137.6, 136.8, 131.3, 130.7, 127.9, 127.6, 126.3, 126.1, 81.7, 81.1, 80.1, 72.1, 67.6, 67.0, 65.8, 41.9, 39.6, 36.4, 33.0, 28.6, 28.3, 28.1, 27.8, 27.2, 25.3, 22.4, 20.2, 15.3; IR (neat) 3480, 2974, 2932, 2874, 1726, 1692, 1454, 1393, 1366, 1252, 1161, 1063, 980, 849, 766, 706 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{22}H_{33}NO_5Na$ ($[M+Na]^+$): 414.2251, found: 414.2252.

***N*-(*t*-Butoxycarbonyl)-2-benzyl-3-(imidazole-1-carbothioyloxy)pipecolic Acid *t*-Butyl Ester (9)**. To a solution of **8** (195.8 mg, 0.5 mmol) and DMAP (92.0 mg, 0.75 mmol) in CH_2Cl_2 (5 mL) was added 1,1'-thiocarbonyldiimidazole (267.2 mg, 1.50 mmol) at room temperature under argon atmosphere and the mixture was stirred overnight at the same temperature. Evaporation of solvent and purification of the residual crude products by column chromatography on silica gel (hexane/AcOEt = 4:1 as eluent) gave **9** (196.9 mg, 0.393 mmol, 79%): ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 8.42 (0.5H, s, Im-H), 8.26 (0.5H, s, Im-H), 7.71 (0.5H, s, Im-H), 7.56 (0.5H, s, Im-H), 7.33 (1H, d, *J* = 7.2 Hz, Ar-H), 7.29-7.15 (3H, m, Ar-H), 7.11 (1H, d, *J* = 7.2 Hz, Ar-H), 7.05 (1H, d, *J* = 8.8 Hz, Ar-H), 5.87 (0.5H, dd, *J* = 10.4, 4.8 Hz, CHO), 5.70-5.55 (0.5H, m, CHO), 3.80 (1H, d, *J* =

14.4 Hz, CH_2Ph), 3.80-3.56 (1.5H, m, CH_2N), 3.33 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 2.99 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 3.00-2.88 (0.5H, m, CH_2N), 2.40-2.08 (1.5H, m, CH_2), 1.98-1.63 (2.5H, m, CH_2), 1.56 (4.5H, s, *t*-Bu), 1.55 (4.5H, s, *t*-Bu), 1.38 (4.5H, s, *t*-Bu), 1.37 (4.5H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 182.7, 182.1, 169.6, 169.2, 154.2, 154.1, 137.3, 137.1, 136.5, 135.5, 131.3, 131.3, 131.0, 130.9, 128.1, 127.9, 126.8, 126.5, 118.0, 117.8, 84.1, 82.1, 81.9, 80.7, 78.3, 66.7, 66.1, 41.7, 39.7, 37.1, 34.9, 28.6, 28.3, 28.2, 27.8, 23.4, 21.5, 20.3, 19.8; IR (neat) 2976, 2932, 2880, 1732, 1694, 1472, 1389, 1366, 1329, 1285, 1231, 1161, 976, 912, 849, 731, 702, 654 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{26}H_{35}N_3O_5SNa$ ($[M+Na]^+$): 524.2190, found: 524.2188.

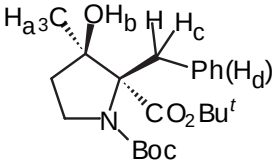
2-Benzylpipecolic Acid (11). A solution of **9** (129.2 mg, 0.258 mmol), tributyltinhydride (0.10 mL, 0.372 mmol) and AIBN (10.0 mg, 0.0609 mmol) in benzene (8 mL) was stirred for 3 h at 70 ˚C under argon atmosphere. After removal of solvent, the residual crude products were purified by column chromatography on silica gel (hexane/AcOEt = 10:1 as eluent) to furnish **10** (50.2 mg, 0.134 mmol, 52%). Then, a mixture of **10** (50.2 mg, 0.134 mmol) in 6N HCl (4 mL) was stirred for 4.5 h at 100 ˚C. The solution was washed with Et_2O and evaporated. Purification of the residual crude products by Dowex 50W-X8 afforded **11** (26.3 mg, 0.120 mmol, 90%)[3]: $[\alpha]_D^{30}$ +60.0° (*c* 0.1, 30 mM HCl); ^{1}H NMR (400 MHz, D_2O, RT) δ 7.30-7.24 (3H, m, Ph), 7.14-7.09 (2H, m, Ph), 3.19-3.11 (1H, m, CH_2N), 3.08 (1H, d, *J* = 14.4 Hz, CH_2Ph), 3.02 (1H, td, *J* = 12.8, 3.2 Hz, CH_2N), 2.90 (1H, d, *J* = 14.4 Hz, CH_2Ph), 2.25-2.21 (1H, m, CH_2), 1.74-1.64 (2H, m, CH_2), 1.64-1.43 (2H, m, CH_2), 1.35-1.21 (1H, m, CH_2). ^{13}C NMR (100 MHz, D_2O, RT) δ 173.4, 133.1, 129.8, 128.5, 127.5, 67.1, 43.3, 32.5, 31.5, 21.4, 19.4.

General Procedure for the Stereoselective Alkylation of 4a. To a solution of **4a** (0.2 mmol) in Et_2O (2 mL) was added a requisite Grignard reagent (0.40 mmol) at 0 ˚C under argon atmosphere and the mixture was stirred for 15 min at the same temperature. The reaction was quenched with saturated aqueous NH_4Cl and extractive workup was performed with Et_2O. The combined ethereal extracts were washed with brine and then dried over Na_2SO_4. Evaporation of solvents and purification of the residual crude products by column chromatography on silica gel (hexane/AcOEt = 4:1 as eluent) gave the corresponding alkylation product **7** as a single diastereomer. The minor diastereomer was not detected by ^{1}H NMR analysis.

***N*-(*t*-Butoxycarbonyl)-2-benzyl-3-hydroxy-3-methylproline *t*-Butyl Ester (7a)**: ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 7.40-7.13 (5H, m, Ph), 3.66 (0.5H, d, *J* = 14.4 Hz, CH_2Ph), 3.53 (0.5H, *J* =

14.4 Hz, CH_2Ph), 3.45 (1H, *J* = 14.4 Hz, CH_2Ph), 3.41-3.17 (1.5H, m, CH_2N), 3.10-2.95 (0.5H, m, CH_2N), 2.67-2.23 (1H, br, OH), 1.72-1.58 (1H, m, C*H*$_2$CH$_2$N), 1.55 (4.5H, s, *t*-Bu), 1.53 (4.5H, s, *t*-Bu), 1.52 (4.5H, s, *t*-Bu), 1.50 (4.5H, s, *t*-Bu), 1.40-1.31 (0.5H, m, C*H*$_2$CH$_2$N), 1.32 (1.5H, s, Me), 1.29 (1.5H, s, Me), 1.24-1.15 (0.5H, m, C*H*$_2$CH$_2$N); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 171.4, 170.7, 154.0, 153.9, 138.4, 138.2, 131.2, 130.6, 128.1, 127.6, 126.2, 125.9, 81.8, 81.6, 81.5, 80.6, 80.5, 79.2, 74.8, 44.6, 37.2, 36.7, 36.5, 35.9, 28.6, 28.5, 28.2, 27.9, 26.4, 26.3; IR (neat) 3447, 2976, 2932, 2882, 1730, 1695, 1674, 1454, 1389, 1366, 1256, 1157, 1063, 982, 845, 764, 702 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{22}H_{33}NO_5K$ ([M+K]$^+$): 430.1990, found: 430.1992. The relative configuration was determined by a NOE experiment (Table 2).

Table 2. Summary of the NOE Data for **7a**



NOE (saturate/observe, %)					
H_a/H_c	H_a/H_d	H_b/H_c	H_b/H_d	H_c/H_a	H_c/H_b
0	1	2	6	0	2

***N*-(*t*-Butoxycarbonyl)-2-benzyl-3-allyl-3-hydroxyproline *t*-Butyl Ester (7b)**: ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 7.42-7.12 (5H, m, Ph), 5.95-5.77 (1H, m, C*H*=CH$_2$), 5.25-5.03 (2H, m, CH=C*H*$_2$), 3.70 (0.6H, d, *J* = 14.8 Hz, CH_2Ph), 3.57 (0.4H, d, *J* = 14.8 Hz, CH_2Ph), 3.44 (1H, d, *J* = 14.8 Hz, CH_2Ph), 3.44-3.20 (1.4H, m, CH_2N), 3.11-3.01 (0.6H, m, CH_2N), 2.40-2.18 (2H, m, C*H*$_2$CH=CH$_2$), 2.23 (0.6H, s, OH), 2.10 (0.4H, s, OH), 1.90-1.77 (1H, m, C*H*$_2$CH$_2$N), 1.55 (3.6H, s, *t*-Bu), 1.52 (5.4H, s, *t*-Bu), 1.51 (5.4H, s, *t*-Bu), 1.49 (3.6H, s, *t*-Bu), 1.30-1.17 (0.6H, m, C*H*$_2$CH$_2$N), 1.15-1.04 (0.4H, m, C*H*$_2$CH$_2$N); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 171.2, 170.7, 153.9, 138.4, 138.3, 132.8, 132.6, 131.2, 130.5, 128.1, 127.6, 126.2, 125.9, 119.6, 119.5, 83.3, 82.3, 82.0, 81.7, 80.6, 79.3, 75.3, 75.2, 44.7, 44.7, 41.9, 41.7, 37.0, 36.2, 33.9, 32.8, 28.6, 28.5, 28.2, 28.0; IR (neat) 3447, 2976, 2930, 2884, 1732, 1695, 1674, 1454, 1387, 1366, 1254, 1155, 1057, 982, 916, 845, 764, 702 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{24}H_{35}NO_5Na$ ([M+Na]$^+$): 440.2408, found: 440.2410.

***N*-(*t*-Butoxycarbonyl)-2-benzyl-3-hydroxy-3-(phenylethynyl)proline *t*-Butyl Ester (7c)**: ^{1}H NMR (400 MHz, $CDCl_3$, RT) δ 7.46-7.15 (10H, m, Ph), 3.70 (0.5H, d, *J* = 14.8 Hz, CH_2Ph), 3.65 (0.5H, d, *J* = 14.8 Hz, CH_2Ph), 3.63 (0.5H, d, *J* = 15.2 Hz, CH_2Ph), 3.64-3.47 (1H, m, CH_2N), 3.53

(0.5H, d, J = 15.2 Hz, CH_2Ph), 3.39-3.30 (0.5H, m, CH_2N), 3.25-3.16 (0.5H, m, CH_2N), 2.95 (0.5H, s, OH), 2.81 (0.5H, s, OH), 2.20-2.07 (1H, m, CH_2CH_2N), 1.71-1.57 (1H, m, CH_2CH_2N), 1.54 (4.5H, s, *t*-Bu), 1.53 (4.5H, s, *t*-Bu), 1.50 (4.5H, s, *t*-Bu), 1.45 (4.5H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$, RT) δ 170.2, 169.3, 153.9, 153.8, 137.8, 137.5, 131.5, 131.4, 130.9, 128.5, 128.5, 128.1, 128.1, 127.7, 126.4, 126.1, 122.0, 121.8, 89.3, 89.1, 86.4, 86.1, 81.8, 81.6, 80.7, 79.5, 78.6, 77.8, 76.0, 45.1, 45.0, 38.1, 37.2, 37.1, 36.4, 28.6, 28.5, 28.2, 28.0; IR (neat) 3391, 2976, 2932, 2884, 1742, 1695, 1674, 1491, 1454, 1389, 1366, 1254, 1144, 1069, 980, 841, 756, 692 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{29}H_{35}NO_5Na$ ($[M+Na]^+$): 500.2408, found: 500.2408.

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