Supporting Information

Novel Approach to 5-Substituted Proline Derivatives Using a Silver-Catalyzed Cyclization as the Key Step

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General procedure A for the Sonogashira cross-coupling reactions:

To a solution of the acetylene-containing amino acid, aryl halide (1.2 equiv) and Et₂NH (5 equiv) in Et₂O, CuI (10 mol%) and the Pd-catalyst (5 mol%) were added. The mixture was stirred at room temperature under N₂-atmosphere for the indicated time. The reaction mixture was poured into a saturated aqueous solution of NH₄Cl and after separation of the organic layer the aqueous layer was extracted with Et₂O (2 ×). The combined organic layers were washed with brine, dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by flash chromatography to afford the pure product.

Methyl (2S)-5-(2-aminophenyl)-2-[(*tert*-butoxycarbonyl)amino]-4-pentynoate (12).

According to general procedure A, to a solution of **9** (326 mg, 1.43 mmol), 2-iodoaniline (379 mg, 1.73 mmol) and Et₂NH (0.75 mL, 7.23 mmol) in Et₂O (18 mL), CuI (29 mg, 0.15 mmol) and PdCl₂(PPh₃)₂ (51 mg, 0.07 mmol) were added and the resulting mixture was stirred for 2 h. Work-up and purification by chromatography (EtOAc/heptane = 1:3) afforded **12** (421 mg, 1.32 mmol, 92%) as a light-brown oil. *R*_f 0.28 (EtOAc/heptane = 1:2); [α]_D = +82.2 (*c* 0.5, CH₂Cl₂); IR (neat) 3369, 2978, 1743, 1711, 1618, 1493; ¹H NMR (300 MHz, CDCl₃) δ 7.17 (dd, *J* = 1.5, 7.6 Hz, 1H), 7.04 (m, 1H), 6.59 (m, 2H), 5.57 (br d, *J* = 8.3 Hz, 1H), 4.56 (m, 1H), 4.31 (s, 2H), 3.73 (s, 3H), 2.95 (d, *J* = 5.2 Hz, 2H), 1.42 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 171.6, 155.1, 148.2, 131.9, 129.3, 117.3, 114.1, 107.3, 88.8, 80.4, 80.0, 52.5, 52.3, 28.1, 24.1; HRMS (EI) calcd for C₁₇H₂₂N₂O₄ 318.1580, found 318.1580.

Methyl (2S)-2-[(*tert*-butoxycarbonyl)amino]-5-(2-methoxyphenyl)-4-pentynoate (13).

According to general procedure A, to a solution of **9** (281 mg, 1.24 mmol), 2-iodoanisole (358 mg, 1.53 mmol) and Et₂NH (0.64 mL, 6.23 mmol) in Et₂O (18 mL), CuI (24 mg, 0.13 mmol) and PdCl₂(PPh₃)₂ (44 mg, 0.06 mmol) were added and the resulting mixture was stirred for 2

h. Work-up and purification by chromatography (EtOAc/heptane = 1:4) afforded **13** (330 mg, 0.99 mmol, 80%) as a yellow oil. R_f 0.56 (EtOAc/heptane = 1:1); $[\alpha]_D +53.9$ (c 0.5, CH_2Cl_2); IR (neat) 3379, 2970, 1745, 1712, 1493; ^1H NMR (300 MHz, CDCl_3) δ 7.29 (m, 2H), 6.86 (m, 2H), 5.62 (d, J = 8.4 Hz, 1H), 4.58 (m, 1H), 3.89 (s, 3H), 3.78 (s, 3H), 3.04 (dd, J = 4.2, 17.1 Hz, 1H), 2.95 (dd, J = 5.1, 16.8 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.5, 160.3, 155.4, 133.3, 129.6, 120.5, 112.3, 110.6, 88.3, 80.3, 80.2, 55.8, 52.7, 52.3, 28.5, 24.2; HRMS (EI) calcd for $\text{C}_{18}\text{H}_{23}\text{NO}_5$ 333.1576, found 333.1573.

Methyl (2S)-2-[(*tert*-butoxycarbonyl)amino]-5-(4-nitrophenyl)-4-pentynoate (14).

According to general procedure A, to a solution of **9** (267 mg, 1.18 mmol), 1-iodo-4-nitrobenzene (353 mg, 1.42 mmol) and Et_2NH (0.61 mL, 5.92 mmol) in Et_2O (18 mL), CuI (24 mg, 0.13 mmol) and $\text{PdCl}_2(\text{PPh}_3)_2$ (41 mg, 0.06 mmol) were added and the resulting mixture was stirred for 2 h. Work-up and purification by chromatography (EtOAc/heptane = 1:4) afforded **14** (330 mg, 0.95 mmol, 81%) as a light-yellow solid. R_f 0.15; $[\alpha]_D +85.1$ (c 0.5, CH_2Cl_2); mp 98.8 °C; IR (neat) 3352, 2978, 2245, 1736, 1672, 1592, 1523, 1508; ^1H NMR (300 MHz, CDCl_3) δ 8.16 (d, J = 9.0 Hz, 2H), 7.52 (d, J = 9.0 Hz, 2H), 5.38 (d, J = 3.3 Hz, 1H), 4.60 (m, 1H), 3.81 (s, 3H), 2.99 (d, J = 5.1 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.2, 155.1, 147.1, 132.6, 130.1, 123.6, 90.2, 82.0, 80.5, 52.9, 52.3, 28.4, 24.3; HRMS (CI) calcd for $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_6$ (MH^+) 349.1400, found 349.1406.

Methyl (2S)-2-[(*tert*-butoxycarbonyl)amino]-5-(2-methylphenyl)-4-pentynoate (15).

According to general procedure A, to a solution of **9** (320 mg, 1.41 mmol), 2-iodotoluene (374 mg, 1.72 mmol) and Et_2NH (0.74 mL, 7.11 mmol) in Et_2O (18 mL), CuI (30 mg, 0.16 mmol) and $\text{PdCl}_2(\text{PPh}_3)_2$ (53 mg, 0.08 mmol) were added and the resulting mixture was stirred for 2 h. Work-up and purification by chromatography (EtOAc/heptane = 1:6) afforded

15 (400 mg, 1.26 mmol, 89%) as a brown oil. R_f 0.15; $[\alpha]_D +79.2$ (c 0.3, CH_2Cl_2); IR (neat) 3373, 2976, 1744, 1709, 1493; ^1H NMR (300 MHz, CDCl_3) δ 7.32 (d, $J = 7.5$ Hz, 1H), 7.12 (m, 3H), 5.38 (d, $J = 8.1$ Hz, 1H), 4.54 (m, 1H), 3.78 (s, 3H), 2.99 (m, 2H), 2.38 (s, 3H) 1.45 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.1, 154.9, 140.0, 131.9, 129.3, 128.1, 125.4, 122.7, 87.8, 82.6, 80.3, 52.8, 52.6, 28.6, 24.3, 21.0; HRMS (EI) calcd for $\text{C}_{18}\text{H}_{23}\text{NO}_4$ 317.1627, found 317.1626.

Methyl (2S)-2-[(tert-butoxycarbonyl)amino]-5-(4-fluorophenyl)-4-pentynoate (16).

According to general procedure A, to a solution of **9** (336 mg, 1.48 mmol), 1-fluoro-4-iodobenzene (409 mg, 1.84 mmol) and Et_2NH (0.79 mL, 7.62 mmol) in Et_2O (18 mL), CuI (30 mg, 0.16 mmol) and $\text{PdCl}_2(\text{PPh}_3)_2$ (56 mg, 0.08 mmol) were added and the resulting mixture was stirred for 2 h. Work-up and purification by chromatography ($\text{EtOAc/heptane} = 1:5$) afforded **16** (448 mg, 1.39 mmol, 94%) as a light-yellow oil. R_f 0.15; $[\alpha]_D +67.2$ (c 0.5, CH_2Cl_2); IR (neat) 3378, 2976, 1748, 1714, 1597, 1502; ^1H NMR (300 MHz, CDCl_3) δ 7.33 (m, 2H), 6.95 (t, $J = 8.7$ Hz, 2H), 5.36 (d, $J = 7.8$ Hz, 1H), 4.54 (m, 1H), 3.78 (s, 3H), 2.92 (m, 2H), 1.45 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.1, 163.8, 161.6, 154.9, 133.5, 133.4, 115.6, 115.3, 83.7, 82.7, 80.3, 52.6, 52.5, 28.6, 24.2; HRMS (EI) calcd for $\text{C}_{17}\text{H}_{20}\text{NO}_4\text{F}$ 321.1376, found 321.1376.

Methyl (2S)-2-[(tert-butoxycarbonyl)amino]-5-(2-pyridyl)-4-pentynoate (22).

According to general procedure A, to a solution of **9** (358 mg, 1.57 mmol), 2-iodopyridine (387 mg, 1.27 mmol) and Et_2NH (0.81 mL, 7.86 mmol) in Et_2O (18 mL), CuI (30 mg, 0.15 mmol) and $\text{PdCl}_2(\text{PPh}_3)_2$ (57 mg, 0.08 mmol) were added and the resulting mixture was stirred for 2 h. Work-up and purification by chromatography ($\text{EtOAc/heptane} = 1:1$) afforded **22** (405 mg, 1.33 mmol, 85%) as a light-yellow oil. R_f 0.25; $[\alpha]_D +74.8$ (c 0.5, CH_2Cl_2); IR (neat) 2975,

1744, 1709, 1583, 1507, 1462; ^1H NMR (300 MHz, CDCl_3) δ 8.53 (m, 1H), 7.62 (dt, $J = 1.8$, 7.5 Hz, 1H), 7.37 (d, $J = 7.8$ Hz, 1H), 7.21 (m, 1H) 5.67 (d, $J = 8.1$ Hz, 1H), 4.58 (m, 1H), 3.79 (s, 3H), 3.01 (d, $J = 4.8$ Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.9, 154.9, 149.7, 142.9, 136.0, 127.2, 122.7, 84.6, 83.1, 80.3, 52.9, 52.3, 28.6, 24.1; HRMS (EI) calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_4$ 304.1423, found 304.1426.

Methyl (2S)-2-[(*tert*-butoxycarbonyl)amino]-5-(3-pyridyl)-4-pentynoate (23). According to general procedure A, to a solution of **9** (310 mg, 1.38 mmol), 3-iodopyridine (336 mg, 1.64 mmol) and Et_2NH (0.72 mL, 6.97 mmol) in Et_2O (18 mL), CuI (28 mg, 0.15 mmol) and $\text{PdCl}_2(\text{PPh}_3)_2$ (50 mg, 0.07 mmol) were added and the resulting mixture was stirred for 2 h. Work-up and purification by chromatography ($\text{EtOAc/heptane} = 1:1$) afforded **23** (384 mg, 1.26 mmol, 91%) as a yellow oil. R_f 0.22; $[\alpha]_D +74.7$ (c 0.5, CH_2Cl_2); IR (neat) 2976, 1748, 1709, 1506, 1472; ^1H NMR (300 MHz, CDCl_3) δ 8.59 (m, 1H), 8.49 (d, $J = 4.2$ Hz, 1H), 7.64 (m, 1H), 7.22 (m, 1H), 5.43 (d, $J = 7.5$ Hz, 1H) 4.57 (m, 1H), 3.79 (s, 3H), 2.97 (d, $J = 4.8$ Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.9, 154.9, 151.7, 148.1, 144.8, 138.8, 123.0, 88.0, 80.4, 80.3, 52.9, 52.4, 28.6, 24.3; HRMS (EI) calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_4$ 304.1423, found 304.1424.

Methyl (2S)-2-[(*tert*-butoxycarbonyl)amino]-6-phenyl-5-hexynoate (29). According to general procedure A, to a solution of **27** (348 mg, 1.44 mmol), iodobenzene (359 mg, 1.76 mmol) and Et_2NH (0.75 mL, 7.26 mmol) in Et_2O (18 mL), CuI (31 mg, 0.16 mmol) and $\text{PdCl}_2(\text{PPh}_3)_2$ (50 mg, 0.07 mmol) were added and the resulting mixture was stirred for 2 h. Work-up and purification by chromatography ($\text{EtOAc/heptane} = 1:6$) afforded **29** (389 mg, 1.23 mmol, 85%) as a brown oil. R_f 0.26 ($\text{EtOAc/heptane} = 1:4$); $[\alpha]_D +18.4$ (c 1.0, CH_2Cl_2); IR (neat) 3390, 2974, 1743, 1714, 1506, 1491; ^1H NMR (300 MHz, CDCl_3) δ 7.38 (m, 2H),

7.25 (m, 3H), 5.31 (d, $J = 7.7$ Hz, 1H), 4.42 (m, 1H), 3.71 (s, 3H), 2.48 (t, $J = 7.1$ Hz, 2H), 2.15 (m, 1H), 1.97 (m, 1H), 1.43 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 172.8, 155.4, 131.6, 128.2, 127.8, 123.6, 88.4, 81.6, 80.0, 53.0, 52.4, 31.4, 28.3, 15.9; HRMS (EI) calcd for $\text{C}_{18}\text{H}_{23}\text{NO}_4$ 317.1627, found 317.1631.

Methyl (2S)-2-[(*tert*-butoxycarbonyl)amino]-7-phenyl-6-heptynoate (30). According to general procedure A, to a solution of **28** (209 mg, 0.82 mmol), iodobenzene (200 mg, 0.98 mmol) and Et_2NH (0.43 mL, 4.17 mmol) in Et_2O (16 mL), CuI (17 mg, 0.09 mmol) and $\text{PdCl}_2(\text{PPh}_3)_2$ (29 mg, 0.04 mmol) were added and the resulting mixture was stirred for 4 h. Work-up and purification by chromatography ($\text{EtOAc/heptane} = 1:6$) afforded **30** (223 mg, 0.67 mmol, 82%) as a brown oil. R_f 0.23 ($\text{EtOAc/heptane} = 1:4$); $[\alpha]_D +10.6$ (c 1.0, CH_2Cl_2); IR (neat) 3359, 2976, 1741, 1711, 1511, 1491; ^1H NMR (300 MHz, CDCl_3) δ 7.39 (m, 2H), 7.27 (m, 3H), 5.04 (d, $J = 7.5$ Hz, 1H), 4.34 (m, 1H), 3.75 (s, 3H), 2.45 (t, $J = 6.9$ Hz, 2H), 2.00 (m, 1H), 1.86-1.61 (m, 3H), 1.45 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 173.3, 155.5, 131.7, 128.3, 127.8, 123.9, 89.2, 81.4, 80.0, 53.3, 52.4, 32.1, 28.4, 24.7, 19.2; HRMS (CI) calcd for $\text{C}_{19}\text{H}_{26}\text{NO}_4$ (MH^+) 332.1862, found 332.1849.

General procedure B for the preparation of the cyclic imines:

To a solution of the Boc-protected cyclization precursor in EtOAc (0.25 M), a solution of HCl in EtOAc (~ 3 M, 5 equiv) was added dropwise at room temperature. The mixture was stirred at room temperature and monitored with TLC. After complete conversion of the starting material, the mixture was concentrated *in vacuo* to afford the corresponding HCl -salt. A solution of the HCl -salt in dioxane/water (0.08 M, 1:1 v/v) was treated dropwise at room temperature with 25% aqueous NH_4OH until the mixture had reached pH 10. The aqueous solution was extracted with CH_2Cl_2 (3 $\times$) and the combined organic layers were dried over

MgSO₄ and concentrated *in vacuo*. The remaining crude amino ester was subsequently dissolved in MeCN (0.1M) and AgOTf (10 mol%) was added. The mixture was stirred at room or reflux temperature under N₂-atmosphere and monitored by TLC. Upon completion, the reaction mixture was concentrated *in vacuo* and purified by flash chromatography to afford the pure product. The enantiopurity of the product was determined via chiral HPLC analysis (Chiralcel OD, hexane/isopropanol 9:1).

Methyl (2S)-5-(2-aminophenyl)-3,4-dihydro-2H-2-pyrrolecarboxylate (17). According to general procedure **B**, precursor **12** (535 mg, 1.68 mmol) afforded **17** (240 mg, 1.10 mmol, 65%) as a white solid after purification by chromatography (EtOAc/heptane = 1:4). *R_f* 0.20; [α]_D -26.0 (*c* 0.5, CH₂Cl₂); mp 71.2 °C; IR (neat) 3417, 3284, 2954, 1726, 1612, 1554; ¹H NMR (300 MHz, CDCl₃) δ 7.38 (m, 1H), 7.17 (m, 1H), 6.68 (m, 2H), 6.49 (br s, 2H), 4.97 (m, 1H), 3.76 (s, 3H), 3.22 (m, 1H), 3.04 (m, 1H), 2.23 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 176.5, 172.8, 148.1, 130.6, 130.2, 115.2, 114.8, 114.2, 73.6, 51.3, 35.6, 24.5; HRMS (EI) calcd for C₁₂H₁₄N₂O₂ 218.1055, found 218.1057.

Methyl (2S)-5-(2-methoxyphenyl)-3,4-dihydro-2H-2-pyrrolecarboxylate (18). According to general procedure **B**, precursor **13** (479 mg, 1.44 mmol) afforded **18** (233 mg, 0.99 mmol, 69%) as a light-yellow oil after purification by chromatography (EtOAc/heptane = 1:1). *R_f* 0.29; [α]_D +65.7 (*c* 0.5, CH₂Cl₂); IR (neat) 2951, 2837, 1736, 1599, 1489; ¹H NMR (300 MHz, CDCl₃) δ 7.82 (dd, *J* = 1.8, 7.8 Hz, 1H), 7.35 (m, 1H), 6.91 (m, 2H), 4.79 (m, 1H), 3.83 (s, 3H), 3.76 (s, 3H), 3.21 (m, 1H), 3.05 (m, 1H), 2.22 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 176.5, 173.3, 158.1, 131.6, 130.3, 123.8, 120.5, 111.2, 73.4, 55.6, 52.3, 39.0, 27.3; HRMS (EI) calcd for C₁₃H₁₅NO₃ 233.1052, found 233.1047.

Methyl (2*S*)-5-(4-nitrophenyl)-3,4-dihydro-2*H*-2-pyrrolecarboxylate (19). According to general procedure **B**, precursor **14** (152 mg, 0.44 mmol) afforded **19** (87 mg, 0.35 mmol, 80%) as a yellow solid after purification by chromatography (EtOAc/heptane = 1:2). R_f 0.16; $[\alpha]_D +83.7$ (c 0.5, CH₂Cl₂); mp 87.9 °C; IR (neat) 2950, 1735, 1588, 1524, 1433; ¹H NMR (300 MHz, CDCl₃) δ 8.22 (d, J = 9.0 Hz, 2H), 8.02 (d, J = 9.0 Hz, 2H), 4.98 (m, 1H), 3.79 (s, 3H), 3.17 (m, 1H), 3.05 (m, 1H), 2.37 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 174.0, 172.4, 149.0, 139.2, 128.8, 123.5, 74.9, 52.5, 35.8, 26.6; HRMS (EI) calcd for C₁₂H₁₂N₂O₄ 248.0797, found 248.0793.

Methyl (2*S*)-5-(2-methylphenyl)-3,4-dihydro-2*H*-2-pyrrolecarboxylate (20). According to general procedure **B**, precursor **15** (400 mg, 1.26 mmol) afforded **20** (147 mg, 0.68 mmol, 54%) as a yellow oil after purification by chromatography (EtOAc/heptane = 1:3). R_f 0.22; $[\alpha]_D +76.4$ (c 0.5, CH₂Cl₂); IR (neat) 2954, 1735, 1614, 1558, 1437; ¹H NMR (300 MHz, CDCl₃) δ 7.40 (d, J = 7.8 Hz, 1H), 7.22 (m, 3H), 4.93 (m, 1H), 3.76 (s, 3H), 3.04 (m, 2H), 2.52 (s, 3H), 2.25 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.8, 173.2, 137.3, 134.1, 131.2, 129.4, 128.8, 125.4, 75.1, 52.4, 39.0, 26.7, 21.8; HRMS (EI) calcd for C₁₃H₁₅NO₂ 217.1103, found 217.1104.

Methyl (2*S*)-5-(4-fluorophenyl)-3,4-dihydro-2*H*-2-pyrrolecarboxylate (21). According to general procedure **B**, precursor **16** (400 mg, 1.24 mmol) afforded **21** (174 mg, 0.79 mmol, 64%) as a yellow oil after purification by chromatography (EtOAc/heptane = 1:3). R_f 0.18; $[\alpha]_D +97.7$ (c 0.5, CH₂Cl₂); IR (neat) 2946, 1735, 1619, 1601, 1506, 1433; ¹H NMR (300 MHz, CDCl₃) δ 7.85 (dd, J = 5.4, 8.7 Hz, 2H), 7.06 (t, J = 8.7 Hz, 2H), 4.89 (m, 1H), 3.77 (s, 3H), 3.10 (m, 1H), 2.97 (m, 1H), 2.31 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 174.6, 173.0,

165.9, 162.6, 130.1, 130.0, 115.6, 115.3, 74.6, 52.5, 35.7, 26.7; HRMS (EI) calcd for $C_{12}H_{12}N_2O_2F$ 221.0852, found 221.0851.

Methyl (2*S*)-5-benzyl-3,4-dihydro-2*H*-2-pyrrolecarboxylate (31). According to general procedure **B**, precursor **29** (389 mg, 1.23 mmol) afforded **31** (140 mg, 0.64 mmol, 52%) as a light-yellow oil after purification by chromatography (EtOAc/heptane = 1:1) The product showed decomposition after being stored at $-10\text{ }^{\circ}\text{C}$ for some days. R_f 0.17; IR (neat) 2946, 1735, 1653, 1593, 1433; ^1H NMR (300 MHz, C_6D_6) δ 7.10 (m, 5H), 4.69 (m, 1H), 3.60 (d, J = 14.1 Hz, 1H), 3.53 (d, J = 14.4 Hz, 1H), 3.43 (s, 3H), 2.23 (m, 1H), 1.92 (m, 2H), 1.64 (m, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 179.1, 173.1, 137.1, 129.4, 128.9, 126.9, 74.8, 51.8, 40.8, 37.3, 26.9; HRMS (EI) calcd for $C_{13}H_{15}NO_2$ 217.1103, found 217.1102.

Methyl 6-benzyl-2,3,4,5-tetrahydro-2-pyridinecarboxylate (32). According to general procedure **B**, precursor **30** (326 mg, 0.98 mmol) afforded **32** (108 mg, 0.47 mmol, 48%) as a light-yellow oil after purification by chromatography (EtOAc/heptane = 1:1). R_f 0.19; IR (neat) 2943, 1738, 1655, 1587, 1495, 1435; ^1H NMR (300 MHz, $CDCl_3$) δ 7.23 (m, 5H), 4.29 (m, 1H), 3.77 (s, 3H), 3.56 (s, 2H), 2.06 (m, 2H), 1.91 (m, 1H), 1.66 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.4, 172.1, 137.2, 128.9, 128.5, 126.5, 61.1, 52.4, 48.4, 28.0, 24.7, 18.3; HRMS (EI) calcd for $C_{14}H_{17}NO_2$ 231.1259, found 231.1265.

General procedure C for the preparation of the pyridyl-substituted pyrrolines. To a solution of the Boc-protected cyclization precursor in EtOAc (0.25M), a solution of HCl in EtOAc (~3M, 5 equiv) was added dropwise at room temperature. The mixture was stirred at room temperature and monitored with TLC. After complete conversion of the starting material, the mixture was concentrated *in vacuo* to afford the corresponding HCl-salt. A

suspension of the HCl-salt in CHCl_3 (0.12M) was treated dropwise at room temperature with Et_3N until a clear solution was obtained. This solution was concentrated *in vacuo* and the precipitate was extracted with Et_2O (4 $\times$). The combined organic layers were concentrated *in vacuo* and the remaining crude amino ester was subsequently dissolved in MeCN (0.1M) and AgOTf (10 mol%) was added. The mixture was stirred at room or reflux temperature under N_2 -atmosphere and monitored by TLC. Upon completion, the reaction mixture was concentrated *in vacuo* and purified by flash chromatography to afford the pure product.

Methyl (2S)-5-(2-pyridyl)-3,4-dihydro-2H-2-pyrrolecarboxylate (24). According to general procedure C, precursor **22** (313 mg, 1.03 mmol) in EtOAc (4 mL) afforded **24** (80 mg, 0.39 mmol, 38%) as a yellow oil after purification by chromatography (EtOAc/heptane = 1:1). R_f 0.17; $[\alpha]_D^{+91.0}$ (c 0.5, CH_2Cl_2); IR (neat) 2950, 1736, 1652, 1612, 1563, 1433; ^1H NMR (300 MHz, CDCl_3) δ 8.62 (dd, J = 1.1, 3.7 Hz, 1H), 8.18 (d, J = 7.4 Hz, 1H), 7.72 (m, 1H), 7.32 (m, 1H), 4.96 (m, 1H), 3.78 (s, 3H), 3.30 (m, 1H), 3.14 (m, 1H), 2.31 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 177.6, 172.8, 152.3, 148.9, 136.2, 125.0, 122.3, 75.1, 52.4, 35.6, 26.6; HRMS (EI) calcd for $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_2$ 204.0899, found 204.0893.

Methyl (2S)-5-(3-pyridyl)-3,4-dihydro-2H-2-pyrrolecarboxylate (26). According to general procedure C, precursor **23** (540 mg, 1.77 mmol) afforded **26** (250 mg, 1.22 mmol, 69%) as a light-yellow oil after purification by chromatography (5% Et_3N in EtOAc/heptane = 9:1). R_f 0.37; $[\alpha]_D^{+82.7}$ (c 0.5, CH_2Cl_2); IR (neat) 2950, 1735, 1619, 1593, 1437; ^1H NMR (300 MHz, CDCl_3) δ 9.03 (s, 1H), 8.65 (dd, J = 1.5, 4.8 Hz, 1H), 8.21 (dt, J = 1.8, 7.8 Hz, 1H), 7.33 (m, 1H), 4.93 (m, 1H), 3.78 (s, 3H), 3.18 (m, 1H), 3.00 (m, 1H), 2.32 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 173.6, 172.7, 151.6, 149.1, 135.0, 129.3, 123.3, 74.6, 52.5, 35.5, 26.5; HRMS (EI) calcd for $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_2$ 204.0899, found 204.0896.

Methyl (2*S*,5*R*)-5-(3-pyridyl)tetrahydro-1*H*-2-pyrrolecarboxylate (33). To a solution of **26** (120 mg, 0.59 mmol) in *i*-PrOH (3 mL), 10% Pd/C (12 mg, 0.01 mmol) was added. The black suspension was subjected to hydrogen (1 atm) and stirred for 20 h at room temperature. The reaction mixture was filtered over Hyflo and concentrated *in vacuo* to afford **33** (120 mg, 0.58 mmol, 98%) as a light-yellow oil. An analytically pure sample was obtained after chromatography (CH₂Cl₂/MeOH saturated with NH₃ = 95:5). *R_f* 0.31 (5% Et₃N in EtOAc/heptane = 9:1); [α]_D +29.1 (*c* 0.5, CH₂Cl₂); IR (neat) 3339, 2945, 2876, 1731, 1575, 1433; ¹H NMR (300 MHz, CDCl₃) δ 8.57 (s, 1H), 8.46 (dd, *J* = 1.8, 4.8 Hz, 1H), 7.83 (dt, *J* = 1.8, 7.8 Hz, 1H), 7.24 (m, 1H), 4.24 (dd, *J* = 5.7, 9.0 Hz, 1H), 3.95 (dd, *J* = 5.1, 8.1 Hz, 1H), 3.76 (s, 3H), 2.34 (s, 1H), 2.18 (m, 3H), 1.73 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 175.1, 148.6, 148.5, 138.9, 134.1, 123.4, 61.0, 60.0, 52.4, 34.5, 30.5; HRMS (CI) calcd for C₁₁H₁₅N₂O₂ (MH⁺) 207.1134, found 207.1133.

Methyl 6-benzyl-2-piperidinecarboxylate (34). To a solution of **32** (108 mg, 0.47 mmol) in MeOH (10 mL), 10% Pd/C (15 mg, 0.01 mmol) was added. The black suspension was subjected to hydrogen (1 atm) and stirred for 2 h at room temperature. The reaction mixture was filtered over Hyflo and concentrated *in vacuo*. Purification by chromatography (EtOAc/heptane = 1:1) afforded **34** (44 mg, 0.19 mmol, 40%) as a colorless oil. *R_f* 0.17; IR (neat) 3332, 2931, 2852, 2791, 1739, 1603, 1495, 1435; ¹H NMR (300 MHz, CDCl₃) δ 7.25 (m, 2H), 7.18 (m, 3H), 3.66 (s, 3H), 3.26 (dd, *J* = 2.7, 10.8 Hz, 1H), 2.70 (m, 3H), 2.03-1.84 (m, 3H), 1.64 (m, 1H), 1.48-1.14 (m, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 173.3, 138.7, 129.1, 128.4, 126.3, 59.5, 58.0, 52.1, 43.8, 32.1, 29.3, 24.7; HRMS (EI) calcd for C₁₄H₁₉NO₂ 233.1371, found 233.1374.

Methyl (2*S*,5*R*)-5-phenyltetrahydro-1*H*-2-pyrrolicarboxylate (1).

Methyl (2*S*)-5-phenyl-3,4-dihydro-2*H*-2-pyrrolecarboxylate (11).

Methyl (2*S*)-5-(2-pyridyl)-3,4-dihydro-2*H*-2-pyrrolecarboxylate (24).

Methyl (2*S*)-5-(3-pyridyl)-3,4-dihydro-2*H*-2-pyrrolecarboxylate (26).

Methyl (2*S*)-5-benzyl-3,4-dihydro-2*H*-pyrrolecarboxylate (31).

Methyl 6-benzyl-2,3,4,5-tetrahydro-2-pyridinecarboxylate (32).

Methyl (2*S*,5*R*)-5-(3-pyridyl)tetrahydro-1*H*-2-pyrrolecarboxylate (33).

Methyl 6-benzyl-2-piperidinecarboxylate (34).