(Supporting information)

Asymmetric Syntheses of 2-Substituted and 2,5-Disubstituted Pyrrolidines from (3*S*, 5*R*, 7*aR*)-5-(Benzotriazol-1-yl)-3-phenyl-[2,1-*b*] oxazolopyrrolidine

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Benzotriazole, 2,5-dimethoxytetrahydrofuran and (*S*)-phenylglycinol in one step gave 80% of (3*S*,5*R*,7*aR*)-5-(benzotriazol-1-yl)-3-phenyl-[2,1-a]oxazolopyrrolidine (**6**), whose crystal structure was confirmed by X-ray crystallography. Novel chiral pyrrolidine synthon **6** reacts with organosilicon (allyltrimethylsilanes and vinyloxytrimethylsilanes), organophosphorus, organozinc, and Grignard reagents to afford chiral 2-substituted and 2,5-disubstituted pyrrolidines.

(3*S*,5*S*,7*aR*)-5-(2-Methyl-2-propenyl)-3-phenylhexahydropyrrolo[2,1-b][1,3] oxazole (15). To a solution of **6** (1.5 g, 5 mmol) in CH_2Cl_2 (100 mL) was added

sequentially 2-methyl-propenyltrimethylsilane (1.2 g, 10 mmol) and $BF_3 \cdot Et_2O$ at 0°C. The reaction mixture was warmed to room temperature and stirred overnight. Then the reaction was quenched with 2 N NaOH, and the aqueous suspension extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried with Na_2SO_4, and evaporated in vacuo. Column chromatography on silica gel, eluting with hexane/ethyl acetate (10/1), yield 480 mg (40%) **15** as a colorless oil. $[\alpha]_D^{20}$ = +39.58 (c, 5.72, EtOH), ^{1}H NMR δ ppm: 1.47-1.70 (m, 1H), 1.62 (s, 3H), 1.78-2.02 (m, 3H), 2.10-2.26 (m, 2H), 3.00-3.04 (m, 1H), 3.54-3.59 (m, 1H), 4.11-4.15 (t, J = 6.9 Hz, 1H), 4.30-4.35 (t, J = 7.2 Hz, 1H), 4.60 (s, 1H), 4.64 (s, 1H), 4.94-4.97 (m, 1H), 7.14-7.32 (m, 5H); ^{13}C NMR δ ppm: 22.9, 29.8, 30.6, 44.6, 65.0, 67.9, 72.9, 96.8, 112.0, 118.0, 126.5, 126.8, 128.4, 143.2. HRMS Calcd for $C_{16}H_{21}NO$: 244.1701 (M+1). Found: 244.1696.

(2*S*)-2-Isobutylpyrrolidium chloride (18). Yield 95%. $[\alpha]_D^{20}$ = -4.10 (c, 2.56, EtOH), ^{1}H NMR δ ppm: 0.94 (d, J = 6.6 Hz, 3H), 0.97 (d, J = 6.3 Hz, 3H), 1.56-2.12 (m, 7H), 3.31-3.35 (m, 2H), 3.50-3.60 (m, 1H), 9.14 (br s, 1H), 9.80 (br s, 1H); ^{13}C NMR δ ppm: 22.2, 22.6, 23.5, 25.9, 30.6, 40.9, 44.5, 58.7. HRMS Calcd for $C_8H_{18}NCl$: 128.1439 (M-Cl). Found: 128.1394.

(2*S*)-2-[(2*S*,5*S*)-2-Allyl-5-pentyltetrahydro-1H-pyrrol-1-yl]-2-phenyl-1-ethanol (9b). Yield: 18%. $[\alpha]_D^{20}$ = +31.53 (c, 0.88, EtOH), ^{1}H NMR δ ppm: 0.90-0.95 (m, 3H), 1.14-1.43 (m, 10H), 1.72-1.80 (m, 2H), 2.04-2.10 (m, 1H), 2.20-2.28 (m, 1H), 3.00-3.10 (m, 2H), 3.66-3.68 (m, 1H), 3.86-3.96 (m, 2H), 5.00-5.06 (m, 2H), 5.70-5.79 (m, 1H), 7.21-7.35 (m, 5H); ^{13}C NMR δ ppm: 14.0, 22.7, 26.3, 29.4, 29.9, 32.2, 36.4, 42.7, 56.8, 61.6, 63.8, 64.7, 116.5, 127.7, 128.2, 128.8, 136.2, 137.2. MS *m/z* 302 (M^+), 270 (20), 260 (95),

140 (100), 131 (30), 103 (30). Anal. Calcd for $C_{20}H_{31}NO$: C, 79.67; H, 10.39; N, 4.65. Found: C, 79.29; H, 10.29; N, 4.83.

(2*S*)-2-[(2*S*,5*R*)-2-Allyl-5-pentyltetrahydro-1H-pyrrol-1-yl]-2-phenyl-1-ethanol (10b). Yield: 72%. $[\alpha]_D^{20}$ = -20.93 (c, 0.86, EtOH), ^{1}H NMR δ ppm: 0.85-0.90 (t, J = 6.9 Hz, 3H), 1.23-1.50 (m, 9H), 1.52-1.57 (m, 1H), 1.63-1.81 (m, 2H), 1.87-1.97 (m, 1H), 2.20-2.26 (m, 1H), 3.15-3.16 (m, 1H), 3.24-3.30 (m, 1H), 3.35-3.40 (m, 1H), 3.70-3.75 (m, 1H), 3.82-3.88 (m, 1H), 4.06-4.10 (m, 1H), 4.94-5.01 (m, 2H), 5.61-5.72 (m, 1H), 7.26-7.38 (m, 5H); ^{13}C NMR δ ppm: 14.0, 22.6, 26.6, 28.4, 28.9, 32.0, 33.1, 38.4, 60.0, 60.8, 62.2, 63.5, 116.5, 127.6, 128.3, 129.2, 136.1, 139.814.0, 22.6, 26.6, 28.4, 28.9, 32.0, 33.1, 38.4, 60.0, 60.8, 62.2, 63.5, 116.5, 127.6, 128.3, 129.2, 136.1, 139.8. MS *m/z* 302 (M^+), 260 (95), 140 (100), 131 (30), 103 (30). Anal. Calcd for $C_{20}H_{31}NO$: C, 79.67; H, 10.39; N, 4.65. Found: C, 79.02; H, 10.26; N, 4.98. HRMS Calcd for $C_{20}H_{31}NO$: 302.2484 (M+1). Found: 302.2479.

(2*S*)-2-[(2*S*,5*S*)-2-Allyl-5-phenethyltetrahydro-1H-pyrrol-1-yl]-2-phenyl-1-ethanol (9c). Yield: 14%. $[\alpha]_D^{20}$ = -56.39 (c, 2.08, EtOH), ^{1}H NMR δ ppm: 1.11-1.18 (m, 1H), 1.39-1.46 (m, 2H), 1.60-1.70 (m, 1H), 1.72-1.84 (m, 1H), 2.02-2.22 (m, 2H), 2.24-2.29 (m, 1H), 2.55-2.65 (m, 1H), 2.71-2.81 (m, 1H), 2.98-3.06 (m, 2H), 3.63-3.65 (m, 1H), 3.82-3.93 (m, 2H), 5.01-5.07 (m, 2H), 5.71-5.80 (m, 1H), 7.02-7.05 (m, 2H), 7.09-7.36 (m, 8H); ^{13}C NMR δ ppm: 29.5, 29.9, 33.0, 38.1, 42.8, 56.8, 61.6, 62.7, 64.7, 116.7, 125.8, 127.7, 128.2, 128.4, 128.8, 136.2, 142.2. MS *m/z* 335 (M^+), 292 (90), 228 (100), 155 (30), 91 (100). HRMS Calcd for $C_{23}H_{29}NO$: 336.2327 (M+1). Found: 336.2328.

(2*S*)-2-[(2*S*,5*R*)-2-Allyl-5-phenethyltetrahydro-1H-pyrrol-1-yl]-2-phenyl-1-ethanol (10c). Yield: 76%. $[\alpha]_D^{20}$ = -23.42 (c, 1.14, EtOH), ^{1}H NMR δ ppm: 1.44-1.55 (m,

3H), 1.70-1.95 (m 4H), 2.25-2.29 (m, 1H), 2.42-2.50 (m, 1H), 2.55-2.63 (m, 1H), 2.80 (br s, 1H), 3.14-3.16 (m, 1H), 3.26-3.27 (m, 1H), 3.67-3.72 (m, 1H), 3.78-3.84 (m, 1H), 4.04-4.08 (m, 1H), 4.95-5.02 (m, 2H), 5.64-5.74 (m, 1H), 7.10-7.29 (m, 10H); ^{13}C NMR δ ppm: 28.4, 28.9, 33.2, 35.6, 37.9, 59.5, 60.3, 62.2, 63.5, 116.5, 125.7, 127.6, 128.3, 129.2, 136.1, 139.8, 142.1. MS *m/z* 335 (M^+), 305 (20), 294 (100), 228 (30), 174 (65), 91 (70). HRMS Calcd for $C_{23}H_{29}NO$: 335.2249 (M). Found: 335.2249.

(2*R*, 5*R*)-2-Pentyl-5-propylpyrrolidium chloride (13b). From hydrogenation of **10b**. Yield: 95%. $[\alpha]_D^{20}$ = +1.13 (c, 1.41, EtOH), ^{1}H NMR δ ppm: 0.88 (t, J = 6.6 Hz, 3H), 0.97 (t, J = 7.2 Hz, 3H), 1.31-1.50 (m, 8H), 1.64-1.74 (m, 4H), 1.99-2.08 (m, 2H), 2.17-2.18 (m, 2H), 3.60-3.65 (m, 2H), 9.52 (br s, 2H); ^{13}C NMR δ ppm: 13.7, 13.9, 20.0, 22.4, 26.3, 30.3, 30.4, 31.4, 32.6, 34.6, 59.3, 59.5. HRMS Calcd for $C_{12}H_{26}NCl$: 184.2065 (M-Cl). Found: 184.2066.

(2*R*,5*R*)-2-Phenethyl-5-propylpyrrolidium chloride (13c). From hydrogenation of **10c**. Yield: 95%. $[\alpha]_D^{20}$ = -4.52 (c, 0.62, EtOH), ^{1}H NMR δ ppm: 0.87 (t, J = 7.2 Hz, 3H), 1.36-1.43 (m, 2H), 1.60-1.70 (m, 3H), 1.95-2.05 (m, 2H), 2.12-2.20 (m, 2H), 2.30-2.50 (m, 1H), 2.60-2.90 (m, 2H), 3.60-3.70 (m, 2H), 7.17-7.28 (m, 5H), 9.60-9.72 (m, 2H); ^{13}C NMR δ ppm: 13.6, 19.9, 30.4, 30.6, 32.9, 34.5, 34.6, 59.2, 59.5, 126.2, 128.4, 128.5, 140.2. Anal. Calcd for $C_{15}H_{24}NCl$: C, 70.98; H, 9.55; N, 5.52. Found: C, 70.95; H, 9.96; N, 5.53.

1-[(3*S*,5*S*,7*aR*)-3-Phenylhexahydropyrrolo[2,1-*b*][1,3]oxazol-5-yl]-3,3-dimethyl-2-butanone (19c). Yield 35%. $[\alpha]_D^{20}$ = +58.48 (c, 0.66, EtOH), ^{1}H NMR δ ppm: 1.01 (s, 9H), 1.44-1.50 (m, 1H), 1.91-1.96 (m, 1H), 2.13-2.22 (m, 2H), 2.52 (dd, J = 7.5 Hz, J = 17.5 Hz, 1H), 2.71 (dd, J = 5.4 Hz, J = 17.4 Hz, 1H), 3.47-3.50 (m, 1H), 3.60-3.65 (m, 1H),

4.24 (t, J = 6.6 Hz, 1H), 4.34 (t, J = 7.2 Hz, 1H), 5.01-5.03 (m, 1H), 7.20-7.32 (m, 5H); ^{13}C NMR δ ppm: 26.1, 30.1, 31.0, 43.4, 44.1, 62.2, 68.1, 73.1, 98.7, 126.6, 126.9, 128.4, 143.0, 214.7. MS *m/z* 287 (M^+, 20), 257 (30), 188 (35), 174 (40), 104 (100), 68 (80). Anal. Calcd for $C_{18}H_{25}NO_2$: C, 75.22; H, 8.79; N, 4.87. Found: C, 74.96; H, 8.92; N, 4.90.

(2*S*)-2-(2*R*,5*S*)-2,5-Dipropyltetrahydro-1*H*-1-pyrrolyl-2-phenylethan-1-ol (23c). Yield 55%. $[\alpha]_D^{20}$ = +20.34 (c, 1.48, EtOH), ^{1}H NMR δ ppm: 0.90 (t, J = 6.9 Hz, 3H), 0.96 (t, J = 6.9 Hz, 3H), 1.15-1.49 (m, 10H), 1.67-1.77 (m, 2H), 2.88-2.94 (m, 1H), 2.99-3.03 (m, 1H), 3.51 (br s, 1H), 3.63-3.68 (m, 1H), 3.85-3.98 (m, 2H), 7.20-7.36 (m, 5H); ^{13}C NMR δ ppm: 14.3, 14.5, 19.9, 20.1, 29.5, 29.9, 38.9, 40.7, 57.0, 61.6, 63.3, 64.6, 127.6, 128.2, 128.9, 137.3. Anal. Calcd for $C_{18}H_{29}NO$: C, 78.48; H, 10.62; N, 5.09. Found: C, 78.56; H, 10.91; N, 5.30.

(2*S*)-2-(2*R*,5*R*)-2,5-Dipropyltetrahydro-1*H*-1-pyrrolyl-2-phenylethan-1-ol (24c). Yield 22%. $[\alpha]_D^{20}$ = -36.73 (c, 0.82, EtOH), ^{1}H NMR δ ppm: 0.87 (t, J = 6.9 Hz, 6H), 1.20-1.34 (m, 8H), 1.48-1.54 (m, 2H), 1.62-1.68 (m, 2H), 3.10-3.20 (m, 3H), 3.64-3.71 (m, 1H), 3.77-3.84 (m, 1H), 4.04-4.08 (m, 1H), 7.26-7.34 (m, 5H); ^{13}C NMR δ ppm: 14.2, 20.2, 29.2, 36.1, 60.1, 61.6, 63.3, 127.4, 128.2, 129.2, 140.2. Anal. Calcd for $C_{18}H_{29}NO$: C, 78.48; H, 10.62; N, 5.09. Found: C, 78.53; H, 10.82; N, 5.28.

(2*S*)-2-(2*R*,5*S*)-2,5-Dipentyltetrahydro-1*H*-1-pyrrolyl-2-phenylethan-1-ol (23d). Yield 53%. $[\alpha]_D^{20}$ = +14.59 (c, 1.28, EtOH), ^{1}H NMR δ ppm: 0.89 (t, J = 6.9 Hz, 6H), 1.15-1.49 (m, 18H), 1.67-1.79 (m, 2H), 2.86-2.92 (m, 1H), 3.00-3.02 (m, 1H), 3.49 (br s, 1H), 3.63-3.68 (m, 1H), 3.84-3.94 (m, 2H), 7.20-7.36 (m, 5H); ^{13}C NMR δ ppm: 14.0, 22.7, 26.3, 26.6, 29.5, 29.8, 32.0, 32.2, 36.5, 38.3, 57.3, 61.6, 63.5, 64.5, 127.6, 128.2, 128.9, 137.3. Anal. Calcd for $C_{22}H_{37}NO$: C, 79.70; H, 11.25; N, 4.22. Found: C, 79.55; H, 11.45; N, 4.46.

(2*S*)-2-(2*R*,5*R*)-2,5-Dipentyltetrahydro-1*H*-1-pyrrolyl-2-phenylethan-1-ol (24d). Yield 17%. $[\alpha]_D^{20}$ = -42.88 (c, 0.62, EtOH), ^{1}H NMR δ ppm: 0.87 (t, J = 6.9 Hz, 6H), 1.23-1.35 (m, 16H), 1.40-1.60 (m, 2H), 1.60-1.80 (m, 2H), 3.10 (m, 2H), 3.60-3.69 (m, 2H), 3.76-3.82 (m, 1H), 4.02-4.07 (m, 1H), 7.24-7.32 (m, 5H); ^{13}C NMR δ ppm: 14.0, 22.6, 26.7, 29.2, 32.0, 33.8, 60.4, 61.7, 63.4, 127.4, 128.2, 129.2, 140.3. Anal. Calcd for $C_{22}H_{37}NO$: C, 79.70; H, 11.25; N, 4.22. Found: C, 79.82; H, 11.65; N, 4.54.

(2*S*)-2-(2*R*,5*S*)-2,5-Diphenylethantetrahydro-1*H*-1-pyrrolyl-2-phenylethan-1-ol (23e). Yield 60%. $[\alpha]_D^{20}$ = +8.20 (c, 4.51, EtOH), ^{1}H NMR δ ppm: 1.44-1.49 (m, 2H), 1.52-1.60 (m, 2H), 1.61-1.70 (m, 2H), 1.77-1.84 (m, 2H), 2.10-2.13 (m, 1H), 2.41-2.48 (m, 1H), 2.54-2.76 (m, 3H), 2.88-2.98 (m, 2H), 3.30 (br s, 1H), 3.50-3.55 (m, 1H), 3.68-3.84 (m, 2H), 6.76 (d, J = 6.6 Hz, 2H), 7.16-7.33 (m, 13H); ^{13}C NMR δ ppm: 29.2, 29.8, 32.9, 33.3, 37.8, 40.0, 56.0, 61.3, 62.3, 64.5, 125.8, 127.5, 128.1, 128.3, 128.4, 128.5, 128.9, 136.5, 142.0, 142.2. Anal. Calcd for $C_{28}H_{33}NO$: C, 84.17; H, 8.32; N, 3.51. Found: C, 83.93; H, 8.68; N, 3.70.

(2*S*)-2-(2*R*,5*R*)-2,5-Diphenylethantetrahydro-1*H*-1-pyrrolyl-2-phenylethan-1-ol (24e). Yield 30%. $[\alpha]_D^{20}$ = -25.50 (c, 1.37, $CHCl_3$), ^{1}H NMR δ ppm: 1.39-1.54 (m, 4H), 1.74-1.89 (m, 4H), 2.39-2.49 (m, 2H), 2.53-2.63 (m, 2H), 3.01 (br s, 1H), 3.15-3.18 (m, 2H), 3.61-3.66 (m, 1H), 3.71-3.77 (m, 1H), 3.99-4.10 (m, 1H), 7.09-7.27 (m, 15H); ^{13}C NMR δ ppm: 29.0, 33.2, 35.4, 59.8, 62.0, 63.3, 125.7, 127.4, 128.2, 129.1, 140.0, 142.0. Anal. Calcd for $C_{28}H_{33}NO$: C, 84.17; H, 8.32; N, 3.51. Found: C, 84.41; H, 8.69; N, 3.74.

(2*R*,5*S*)-2,5-Dipropyltetrahydro-1*H*-1-pyrrolidium chloride (25b). Yield 95%. m.p. 168-170°C. ^{1}H NMR δ ppm: 0.97 (t, J = 7.5 Hz, 6H), 1.38-1.50 (m, 4H), 1.76-1.90 (m, 4H), 2.04-2.18 (m, 4H), 3.47 (m, 2H), 9.00 (br s, 1H), 10.12 (br s, 1H); ^{13}C NMR δ ppm: 13.8,

20.2, 28.5, 34.2, 60.2. Anal. Calcd for $C_{10}H_{22}NCl$: C, 62.64; H, 11.56; N, 7.30. Found: C, 62.98; H, 11.94; N, 7.31.

(2*R*,5*R*)-2,5-Dipropyltetrahydro-1*H*-1-pyrrolidium chloride (26b). Yield 84%. m.p. 133-135°C. $[\alpha]_D^{20}$ = +0.32 (c, 0.94, EtOH). ^{1}H NMR δ ppm: 0.97 (t, J = 7.2 Hz, 6H), 1.40-1.50 (m, 4H), 1.61-1.73 (m, 4H), 1.96-2.07 (m, 2H), 2.14-2.20 (m, 2H), 3.62-3.66 (m, 2H), 9.48 (br s, 2H); ^{13}C NMR δ ppm: 13.8, 20.0, 30.4, 34.7, 59.4. Anal. Calcd for $C_{10}H_{22}NCl$: C, 62.64; H, 11.56; N, 7.30. Found: C, 62.90; H, 11.92; N, 7.33.

(2*R*,5*S*)-2,5-Dipentyltetrahydro-1*H*-1-pyrrolidium chloride (25c). Yield 92%. m.p. 148-150°C. ^{1}H NMR δ ppm: 0.88 (t, J = 6.9 Hz, 6H), 1.32-1.40 (m, 12H), 1.75-1.89 (m, 4H), 2.03-2.17 (m, 4H), 3.44-3.46 (m, 2H), 9.00 (br s, 1H), 10.15 (br s, 1H); ^{13}C NMR δ ppm: 13.9, 22.5, 26.5, 28.4, 31.4, 32.1, 60.3. Anal. Calcd for $C_{14}H_{30}NCl$: C, 67.84; H, 12.20; N, 5.65. Found: C, 67.72; H, 12.43; N, 5.70.

(2*R*,5*R*)-2,5-Dipentyltetrahydro-1*H*-1-pyrrolidium chloride (26c). Yield 80%. m.p. 123-125°C. $[\alpha]_D^{20}$ = +0.44 (c, 1.21, EtOH). ^{1}H NMR δ ppm: 0.88 (t, J = 6.6 Hz, 6H), 1.30-1.40 (m, 12H), 1.75-1.91 (m, 4H), 2.03-2.17 (m, 4H), 3.43-3.47 (m, 2H), 8.99 (br s, 2H); ^{13}C NMR δ ppm: 13.9, 22.5, 26.6, 28.5, 31.5, 32.2, 60.3. Anal. Calcd for $C_{14}H_{30}NCl$: C, 67.84; H, 12.20; N, 5.65. Found: C, 67.82; H, 12.12; N, 5.71.

(2*R*,5*S*)-2,5-Diphenylethyltetrahydro-1*H*-1-pyrrolidium chloride (25d). Yield 89%. m.p. 153-154°C. ^{1}H NMR δ ppm: 1.77-1.79 (m, 2H), 2.06-2.16 (m, 4H), 2.39-2.50 (m, 2H), 2.60-2.64 (m, 4H), 3.38-3.40 (m, 2H), 7.11-7.26 (m, 10H), 9.27 (br s, 1H), 10.30 (br s, 1H); ^{13}C NMR δ ppm: 28.6, 32.7, 33.7, 59.8, 126.2, 128.4, 128.5, 140.0. Anal. Calcd for $C_{20}H_{26}NCl$: C, 76.05; H, 8.30; N, 4.43. Found: C, 75.95; H, 8.49; N, 4.45.

(2*R*,5*R*)-2,5-Diphenylethyltetrahydro-1*H*-1-pyrrolidium chloride (26d). Yield 76%. m.p. 137-138°C. $[\alpha]_D^{20}$ = -7.70 (c, 0.61, EtOH). ^{1}H NMR δ ppm: 1.62-1.68 (m, 4H), 1.96-2.02 (m, 2H), 2.13-2.15 (m, 2H), 2.34-2.41 (m, 2H), 2.61-2.74 (m, 4H), 3.63-3.67 (m, 2H), 7.14-7.28 (m, 10H), 9.82 (br s, 2H); ^{13}C NMR δ ppm: 30.4, 32.7, 34.3, 59.2, 126.1, 128.3, 128.4, 140.0. Anal. Calcd for $C_{20}H_{26}NCl$: C, 76.05; H, 8.30; N, 4.43. Found: C, 76.18; H, 8.65; N, 4.50.