Chirality Transfer from Carbon to Nitrogen to Carbon via Cyclic Ammonium Ylides

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Supporting Information. Physical data for **2b**-**e** and **3b**,**d**,**e** and procedures for determining stereochemical ratios for **3a**,**b** (2 pages).

Ammonium salts **2b**-**e** were prepared in a manner analogous to that given in footnote 8 for **2a**, except that the initial counterion for **2d**,**e** was exchanged using NaPF6. Characterization data for **2b**-**e** are given below:

2b: white needles, mp 141-143 °C; $[\alpha]^{22}_{D}$ = -14.0 ° (c = 0.22, CH_2Cl_2); IR (KBr) 2968, 1761, 1448 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.70-7.67 (m, 2H), 7.52-7.41 (m, 3H), 5.37 (dd, 1H, *J* = 9.9, 9.9 Hz), 5.27 (dd, 1H, *J* = 7.8, 7.8 Hz), 5.24 (s, 2H), 4.46 (app. q, 1H, *J* = 9.3 Hz), 4.24 (dd, 1H, *J* = 14.1, 7.7 Hz), 4.10 (dd, 1H, *J* = 14.1, 7.8 Hz), 3.78 (s, 3H), 3.72 (ddd, 1H, *J* = 11.4, 8.4, 2.7 Hz), 2.77-2.66 (m, 1H), 2.43-2.25 (m, 2H), 2.11-1.96 (m, 1H), 1.84 (s, 3H), 1.75 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.6, 146.4, 138.6, 132.7, 129.1, 127.8, 113.3 70.4, 64.6, 61.0, 55.6, 53.2, 26.5, 25.6, 19.4; 18.7; Anal. Calcd for $C_{18}H_{26}BrNO_2$: C, 58.70; H, 7.11; N, 3.80. Found: C, 58.80; H, 7.16; N, 3.88.

2c: white prisms, mp 92-94 °C; $[\alpha]^{22}_{D}$ = +6.3 ° (c = 0.20, CH_3CN); IR (KBr) 2964, 1755 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.57-7.46 (m, 5H), 5.27 (d, 1H, J_{AB} = 5.4 Hz), 5.07 (dd, 1H, *J* = 9.9, 8.1 Hz), 4.96 (s, 2H), 4.77 (d, 1H, J_{AB} = 5.4 Hz J_{AB} = 5.4 Hz), 4.72 (dd, 1H, *J* = 9.9, 9.6 Hz), 4.45 (dd, 1H, *J* = 9.6, 8.1 Hz), 3.88 (s, 3H), 3.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.0, 132.2, 131.2, 129.7, 126.5, 93.2, 67.7, 67.5, 65.2, 54.3, 43.4; ^{19}F NMR ($CDCl_3$, 281 MHz) δ 26.7 (s); Anal. Calcd for $C_{13}H_{18}BF_4NO_3$: C, 48.33; H, 5.62; N, 4.34. Found: C, 48.25; H, 5.68; N, 4.36.

2d: Initially formed tetrafluoroborate salt was stirred in acetone with $NaPF_6$ (1 equiv) for 12 h, then the reaction was filtered, solvent was removed, and the residue was recrystallized from CH_2Cl_2/Et_2O to give white prisms, mp 110-112 °C; $[\alpha]^{22}_{D}$ = +8.6 ° (c = 0.20, CH_2Cl_2); IR (KBr) 2970, 1743 cm^{-1}; ^{1}H NMR (CD_3CN, 300 MHz) δ 7.58-7.51 (m, 5H), 5.12 (d, 1H, J_{AB} = 6.0 Hz), 4.83 (d, 1H, J_{AB} = 13.2 Hz), 4.76 (dq, 1H, *J* = 8.7, 6.0 Hz), 4.70 (d, 1H, J_{AB} = 6.0 Hz), 4.65 (d, 1H, J_{AB} = 13.2 Hz), 4.27 (d, 1H, *J* = 8.7 Hz), 3.85 (s, 3H), 3.10 (s, 3H), 1.50 (d, 3H, *J* = 6.0 Hz); ^{13}C NMR (CD_3CN, 75 MHz) δ 164.8, 133.8, 132.5, 130.9, 128.2, 93.2, 77.6, 75.4, 67.0, 55.3, 45.0, 19.3; Anal. Calcd for $C_{14}H_{20}F_6PNO_3$: C, 42.54; H, 5.10; N, 3.54. Found: C, 42.57; H, 5.18; N, 3.59.

2e: Initially formed tetrafluoroborate salt was stirred in THF with $NaPF_6$ (1 equiv) for 12 h, then the reaction was filtered, solvent was removed, and the residue was recrystallized from CH_2Cl_2/Et_2O to give a white solid (isolated as a 4.4:1 mixture of diastereomers); IR (KBr) 2972, 1747 cm^{-1}; ^{1}H NMR (CD_3CN, 300 MHz, major diastereomer) δ 5.40-5.31 (m, 1H), 5.09 (d, 1H, J_{AB} = 6.0 Hz), 4.83 (d, 1H, J_{AB} = 6.0 Hz), 4.67 (dq, 1H, *J* = 8.7, 6.0 Hz), 4.10 (d, 1H, *J* = 8.7 Hz), 4.38-4.16 (m, 2H), 3.92 (s, 3H), 3.18 (s, 3H), 1.85 (s, 3H), 1.83 (s, 3H), 1.54 (d, 3H, *J* = 6.0 Hz); ^{13}C NMR (CD_3CN, 75 MHz) δ 164.3, 150.2, 111.0, 92.6, 77.2, 73.8, 61.5, 54.5, 44.3, 26.2, 18.6, 18.2.

Rearrangement products **3b**,**d**,**e** were prepared from **2b**,**d**,**e** via the procedure given in footnote 12 for **3a**. Characterization data for **3b**,**d**,**e** are given below:

3b: colorless oil, $[\alpha]^{22}_{D}$ = -50.8 ° (c = 0.10, CH_2Cl_2); R_f 0.33 (1:8 EtOAc/hexanes); IR (neat) 2970, 1728 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.37-7.17 (m, 5H), 6.30 (dd, 1H, *J* = 17.7, 10.8 Hz), 5.02 (dd, 1H, *J* = 17.7, 1.5 Hz), 4.98 (dd, 1H, *J* = 10.8, 1.5 Hz), 4.29 (d, 1H, J_{AB} = 14.4 Hz), 3.74 (s, 3H), 3.49 (d, 1H, J_{AB} = 14.4 Hz), 3.04-2.97 (m, 1H), 2.46 (dd, 1H, *J* = 17.1, 8.7 Hz), 2.29 (dt, 1H, *J* = 12.9, 8.4 Hz), 2.01 (ddd, 1H, *J* = 13.5, 7.2, 7.2 Hz), 1.73-1.62 (m, 2H), 1.25 (s, 3H), 1.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.8, 146.0, 140.8, 128.1, 127.4, 126.3, 111.6 75.8, 56.1, 53.5, 50.7, 43.5, 34.2, 24.9, 23.0, 22.9; Anal. Calcd for $C_{18}H_{25}NO_2$: C, 75.22; H, 8.77; N, 4.87. Found: C, 75.09; H, 8.73; N, 4.86.

3d: colorless oil, 2.8:1 mixture of partially separable diastereomers; R_f 0.32 (1:3 EtOAc/hexanes); IR (neat) 2956, 1736 cm^{-1}; **major diastereomer:** ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.29-7.18 (m, 5H), 4.56 (d, 1H, *J* = 2.4 Hz), 4.41 (q, 1H, *J* = 6.6 Hz), 4.30 (d, 1H, *J* = 2.4 Hz), 3.70 (s, 3H), 3.11 (d, 1H, J_{AB} = 14.1 Hz), 3.04 (d, 1H, J_{AB} = 14.1 Hz), 2.22 (s, 3H), 1.34 (d, 3H, *J* = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.0, 137.0, 128.8, 128.1, 126.4, 85.9, 80.5, 71.9, 51.7, 37.2, 33.8, 16.6; **minor diastereomer:** ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.29-7.18 (m, 5H), 4.56 (s, 2H), 3.85 (q, 1H, *J* = 6.6 Hz), 3.78 (s, 3H), 3.08 (s, 2H), 2.38 (s, 3H), 1.12 (d, 3H, *J* = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.7, 136.2, 130.7, 127.8, 126.5, 86.2, 78.7, 72.9, 51.4, 36.0, 32.1, 15.2; Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.51; H, 7.63; N, 5.57.

3e: yellow oil, inseparable 4.1:1 mixture of diastereomers; R_f 0.35 (3:7 EtOAc/hexanes); IR (neat) 2938, 1730 cm^{-1}; **major diastereomer:** ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.26 (dd, 1H, *J* = 17.4, 10.8 Hz), 5.01 (dd, 1H, *J* = 17.4, 1.2 Hz), 4.98 (dd, 1H, *J* = 10.8, 1.2 Hz), 4.66 (d, 1H, *J* = 2.4 Hz), 4.43 (q, 1H, *J* = 6.3 Hz), 4.10 (d, 1H, *J* = 2.4 Hz), 3.70 (s, 3H), 2.63 (s, 3H), 1.33 (d, 3H, *J* = 6.3 Hz), 1.22 (s, 3H), 1.19 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.1, 145.1, 111.5, 85.0, 81.4, 70.6, 51.0, 40.8, 33.7, 26.5, 18.5, 18.0.

Enantiomeric analysis of 3a by conversion to MTPA ester. A solution of **3a** (280 mg, 1.20 mmol) in Et_2O (2 mL) was added dropwise to an ice-cooled suspension of $LiAlH_4$ (140 mg, 3.71 mmol) in Et_2O (10 mL). After stirring for 20 min, the reaction was quenched by slow addition of water (1.0 mL) and filtered through a Celite plug. The filter cake was washed with Et_2O (2 x 10 mL) and the filtrate was concentrated to give a yellow residue which was purified via flash chromatography silica gel, 2.5-cm x 4-cm column, 1:1 EtOAc/hexanes) to give 179 mg (73%) of N-methyl-2-benzylprolinol as a yellow oil: R_f 0.10 (1.1 EtOAc/hexanes); IR (neat) 3401, 2939 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.22-7.10 (m, 3H), 7.05-7.01 (m, 2H), 3.41 (d, 1H, J_{AB} = 9.9 Hz), 3.25-3.16 (br s, 1H), 3.22 (d, 1H, J_{AB} = 9.9 Hz), 3.08-3.02 (m, 1H), 2.61 (dd, 1H, *J* = 17.4, 8.1 Hz), 2.58 (d, 1H, J_{AB} = 12.9 Hz), 2.47 (d, 1H, J_{AB} = 12.9 Hz), 2.29 (s, 3H), 1.76-1.55 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.0, 130.1, 128.1, 126.1, 66.1, 63.1, 53.8, 35.9, 33.4, 30.1, 21.4.

(*R*)-(-)-α-Methoxy-α-(trifluoromethyl)phenylacetyl chloride (26 μL, 0.14 mmol) was added to a solution of the alcohol (15 mg, 0.07 mmol), Et_3N (29 μL, 0.21 mmol) and DMAP (ca. 1 mg) in CH_2Cl_2 (1.5 mL) and the reaction was stirred for 12 h. Excess acid chloride was quenched by addition of 1 drop sta. Aq. $NaHCO_3$, and the reaction mixture was filtered through a silica gel plug. Removal of solvent gave 20 mg (63%) of the ester product as a pale yellow oil: 3.3:1 mixture of diastereomers by NMR; ^{19}F NMR ($CFCl_3$, 281 MHz) δ 105.54 (s), 105.45 (s).

Enantiomeric analysis of 3b by conversion to MTPA ester. Rearrangement product **3b** (248 mg, 0.86 mmol) was subjected to the reduction procedure described above for **3a** to give 126 mg (57%) of N-benzyl-2-(1,1-dimethylallyl)prolinol as a colorless oil: $[\alpha]^{22}_{D}$ = +12.1 ° (c = 0.03, CH_2Cl_2); IR (neat) 3428, 2960 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38-7.22 (m, 5H), 6.14 (dd, 1H, *J* = 17.7, 10.8 Hz), 5.01 (dd, 1H, *J* = 17.7, 1.5 Hz), 4.98 (dd, 1H, *J* = 10.8, 1.5 Hz), 4.24 (d, 1H, J_{AB} = 14.4 Hz), 4.06 (d, 1H, J_{AB} = 11.1 Hz), 3.84 (d, 1H, J_{AB} = 14.4 Hz), 3.57 (d, 1H, J_{AB} = 11.1 Hz), 2.98-2.92 (m, 1H), 2.56 (dd, 1H, *J* = 15.6, 8.7 Hz), 2.03-1.84 (m, 2H), 1.80 (br s, 1H), 1.71-1.60 (m, 2H), 1.13 (s, 3H), 1.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 146.6, 141.4, 128.2, 127.6, 126.4, 111.7, 69.8, 64.7, 54.9, 54.4, 44.9, 31.7, 24.1, 23.9, 23.2; Anal. Calcd for $C_{17}H_{25}NO$: C, 78.72; H, 9.71; N, 5.40. Found: C, 78.52; H, 9.71; N, 5.34.

(*R*)-(-)-α-Methoxy-α-(trifluoromethyl)phenylacetyl chloride (18 μL, 0.09 mmol) was added to a solution of the alcohol (12 mg, 0.046 mmol), Et_3N (20 μL, 0.14 mmol) and DMAP (ca. 1 mg) in CH_2Cl_2 (1.5 mL) and the reaction was stirred for 12 h. Excess acid chloride was quenched by addition of 1 drop sta. Aq. $NaHCO_3$, and the reaction mixture was filtered through a silica gel plug. Removal of solvent gave 13 mg (62%) of the ester product as a colorless oil: single diastereomer by NMR; ^{19}F NMR ($CFCl_3$, 281 MHz) δ 106.05 (s).