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A novel diastereoselective α-functionalization of proline with benzaldehydes: synthesis of α-(α-hydroxybenzyl)prolines

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General Experimental Details

NMR spectra were recorded on Bruker DRX-400 (^{1}H – 400 MHz) and Bruker Avance III-500 (^{13}C – 126 MHz) spectrometers in D_2O with DSS as an internal standard (the methyl signal was set to 0 ppm in ^{1}H and –2.04 ppm in ^{13}C spectrum). Elemental analysis was performed on a PE 2400 automatic analyzer. Melting points were determined on Stuart Automatic Melting Point Apparatus SMP40.

Characterization Data of Products 4d–f

rac-*(*RS*)-2-[(*SR*)-Hydroxy(4-bromophenyl)methyl]pyrrolidine-2-carboxylic acid* **4d**. Yield 44%, white crystals, mp 259.3–259.6 °C. ^{1}H NMR (400 MHz, D_2O) δ: 1.67–1.86 (m, 2H, 4-CH_2), 2.03–2.24 (m, 2H, 3), 3.14 (dt, *J* 11.7, 7.8 Hz, 1H, 5-C*H*H), 3.32–3.42 (m, 5-CH*H*), 5.15 (s, 1H, CH), 7.35 (d, *J* 8.4 Hz, 2H, Ar), 7.61 (d, *J* 8.4 Hz, 2H, Ar). Found (%): C, 47.39; H, 4.70; N, 4.60. Calc. for $C_{12}H_{14}BrNO_3 \cdot 0.25H_2O$ (%): C, 47.31; H, 4.80; N, 4.60.

rac-*(*RS*)-2-[(*SR*)-Hydroxy(4-methoxyphenyl)methyl]pyrrolidine-2-carboxylic acid* **4e**. Yield 50%, white powder, mp 244.5–244.8 °C. ^{1}H NMR (400 MHz, D_2O) δ: 1.65–1.89 (m, 2H, 4-CH_2), 2.13 (dt, *J* 13.5, 8.4 Hz, 1H, 3-C*H*H), 2.23 (ddd, *J* 13.5, 7.5, 4.5 Hz, 1H, 3-CH*H*), 3.11 (dt, *J* 11.6, 7.8 Hz, 1H, 5-C*H*H), 3.38 (ddd, *J* 11.6, 8.0, 5.3 Hz, 1H, 5-CH*H*), 3.86 (s, 3H, CH_3O), 5.16 (s, 1H, CH), 7.05 (d, *J* 8.7 Hz, 2H, Ar), 7.41 (d, *J* 8.7 Hz, 2H, Ar). ^{13}C NMR (125 MHz, D_2O) δ: 23.5, 30.4, 46.9, 56.1, 73.9, 78.9, 114.9, 129.1, 131.0, 160.0, 174.7. IR (ν/cm^{-1}): 3387, 3046, 2959, 2839, 1611, 1514, 1446, 1379, 1276, 1253, 1178, 1059, 1025, 841, 582, 544. Found (%): C, 59.94; H, 6.86; N, 5.37. Calc. for $C_{13}H_{17}NO_4 \cdot 0.5H_2O$ (%): C, 59.99; H, 6.97; N, 5.38.

rac-*(*RS*)-2-[(*SR*)-(3,4-Dimethoxyphenyl)(hydroxy)methyl]pyrrolidine-2-carboxylic acid* **4f**. Yield 33%, light yellow powder, mp 229.6–230.1 °C. ^{1}H NMR (400 MHz, D_2O) δ: 1.67 (dtt, *J* 13.4, 7.8, 5.5 Hz, 1H, 4-C*H*H), 1.82 (dquin, *J* 13.4, 8.1 Hz, 1H, 4-CH*H*), 2.14 (dt, *J* 13.5, 8.3 Hz, 1H, 3-C*H*H), 2.22 (ddd, *J* 13.5, 7.6, 4.8 Hz, 1H, 3-CH*H*), 3.10 (dt, *J* 11.8, 7.8 Hz, 1H, 5-C*H*H), 3.37 (ddd, *J* 11.8, 8.1, 5.4 Hz, 1H, 5-CH*H*), 3.87 (s, 3H, CH_3O), 3.88 (s, 3H, CH_3O), 5.15 (s, 1H, CH), 7.05–7.11 (m, 3H, Ar). ^{13}C NMR (125 MHz, D_2O) δ: 23.6, 30.6, 46.9, 56.45, 56.51, 74.1, 78.9, 111.2, 112.5, 120.6, 131.7, 148.9, 149.2, 174.8. IR (ν/cm^{-1}): 3204, 2957, 2838, 1636, 1589, 1517, 1466, 1420, 1365, 1314, 1257, 1235, 1189, 1145, 1079, 1022, 965, 690, 657, 594. Found (%): C, 56.80; H, 6.62; N, 4.70. Calc. for $C_{14}H_{19}NO_5 \cdot 0.75H_2O$ (%): C, 57.04; H, 7.01; N, 4.75.