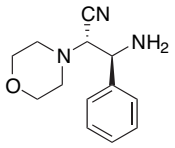
Supporting Information

Sample Experimental Procedures:

Cyanohydrin Formation from *N*-(9-Fluorenylmethoxycarbonyl)phenylglycinal: A solution of potassium cyanide (122 mg, 1.88 mmol, 1.25 equiv) and acetic acid (118 μL, 2.05 mmol, 1.37 equiv) in methanol (1.0 mL) was added via syringe to a suspension of *N*-(9-fluorenylmethoxycarbonyl)phenylglycinal (536 mg, 1.50 mmol, 1 equiv) in dichloromethane (5.0 mL) at 0 °C under an argon atmosphere. After 50 min, additional methanolic hydrogen cyanide [potassium cyanide (122 mg, 1.88 mmol, 1.25 equiv), acetic acid (118 μL, 2.05 mmol, 1.37 equiv), methanol (1.0 mL)] was added via syringe. After 2 h, the reaction mixture was partitioned between ether (10 mL) and a 4:1 mixture of brine and saturated aqueous sodium bicarbonate solution (10 mL). The aqueous layer was extracted with ether (10 mL) and the combined organic layers were washed with a 4:1 mixture of brine and saturated aqueous sodium bicarbonate solution (2 × 10 mL). The organic layer was dried over sodium sulfate and concentrated. The residue was concentrated from benzene (2 × 10 mL) to afford the *N*-(9-fluorenylmethoxy-carbonyl)phenylglycinal cyanohydrins as a white foam (577 mg, 98.5 %, unpurified).

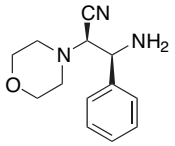
Synthesis of Morpholino Nitriles 4 from Cyanohydrins 2: Morpholine (300 μL, 3.44 mmol, 7.02 equiv) was added to a solution of the cyanohydrins prepared above (120-mg portion, 490 μmol, 1 equiv) in DMF (300 μL) at 0 °C under an atmosphere of argon. After 2 h, additional morpholine was added (350 μL, 4.00 mmol, 8.19 equiv) and the reaction solution was cooled to –20 °C whereupon TFE was added (1.0 mL, mild exotherm) followed by warming to 22 °C. After stirring for 10 h at 22 °C, volatiles were removed in vacuo, affording a yellow residue. The residue was purified by flash column chromatography (0.5→1→2% methanol–dichloromethane), furnishing separately the (*S*,*S*)-diastereomer (major, 76.4 mg, 67.4%, 93% ee) and the (*R*,*S*)-diastereomer (minor, 13.5 mg, 12.8%, 89% ee).

Spectroscopic and Analytical Data for Morpholino Nitrile-Protected α-Amino Aldehydes:



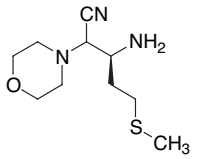
major, less polar (*S*,*S*)-diastereomer:

^{1}H NMR (400 MHz, $CDCl_3$), δ 7.38–7.26 (m, 5 H, Ar**H**), 4.23 (d, 1 H, *J* = 7.9 Hz, C**H**NH_2), 3.84–3.73 (m, 4 H, C$\mathbf{H}_2$OC$\mathbf{H}_2$), 3.55 (d, 1 H, *J* = 7.9 Hz, C**H**CN), 2.75–2.70 (m, 2 H, C$\mathbf{H}_2$NC$\mathbf{H}_2$), 2.52–2.47 (m, 2 H, C$\mathbf{H}_2$NC$\mathbf{H}_2$), 1.73 (s, br, 2 H, N$\mathbf{H}_2$). ^{13}C NMR (100 MHz, $CDCl_3$), δ 141.2, 128.7, 128.2, 126.6, 116.1, 66.7, 66.6, 55.3, 51.0. FTIR (neat film), cm^{-1} 3374 (m, br, NH), 2226 (w, CN). HRMS (CI^+) calcd for $C_{14}H_{20}N_3O$ $(M+H)^+$: 246.1606, found: 246.1604. TLC (2.5% MeOH in CH_2Cl_2) R_f 0.14.



minor, more polar (*R*,*S*)-diastereomer:

^{1}H NMR (400 MHz, $CDCl_3$), δ 7.47–7.35 (m, 5 H, Ar**H**), 4.20 (d, 1 H, *J* = 10.4 Hz, C**H**NH_2), 3.87–3.75 (m, 4 H, C$\mathbf{H}_2$OC$\mathbf{H}_2$), 3.45 (d, 1 H, *J* = 10.4 Hz, C**H**CN), 2.81–2.76 (m, 2 H, C$\mathbf{H}_2$NC$\mathbf{H}_2$), 2.63–2.58 (m, 2 H, C$\mathbf{H}_2$NC$\mathbf{H}_2$), 1.91 (s, br, 2 H, N$\mathbf{H}_2$). ^{13}C NMR (100 MHz, $CDCl_3$), δ 139.7, 128.9, 128.9, 127.7, 114.7, 66.8, 66.3, 54.6, 50.2. FTIR (neat film), cm^{-1} 3282 (m, br, NH), 2226 (w, CN). HRMS (CI^+) calcd for $C_{14}H_{20}N_3O$ $(M+H)^+$: 246.1606, found: 246.1596. TLC (2.5% MeOH in CH_2Cl_2) R_f 0.03.

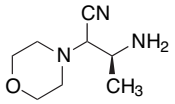


major, less polar diastereomer:

^{1}H NMR (600 MHz, $CDCl_3$), δ 3.75–3.67 (m, 4 H, C$\mathbf{H}_2$OC$\mathbf{H}_2$), 3.33 (d, 1 H, *J* = 8.8 Hz, C**H**CN), 3.31 (m, 1 H, C**H**NH_2), 2.71–2.62 (m, 4 H, C$\mathbf{H}_2$NC$\mathbf{H}_2$ and SC$\mathbf{H}_2$), 2.62–2.51 (m, 2 H, C$\mathbf{H}_2$NC$\mathbf{H}_2$), 2.14 (m, 1 H, C$\mathbf{H}_2$$CH_2$S), 2.09 (s, 3 H, SC$\mathbf{H}_3$), 2.18 (s, br, 2 H, N$\mathbf{H}_2$), 1.59 (m, 1 H, C$\mathbf{H}_2$$CH_2$S). ^{13}C NMR (125 MHz, $CDCl_3$), δ 116.3, 66.8, 66.7, 51.0, 49.4, 33.1, 30.8, 15.7. FTIR (neat film), cm^{-1} 3378 (m, br, NH), 2224 (w, CN), 1117 (s). HRMS (ESI^+) calcd for $C_{10}H_{20}N_3OS$ $(M+H)^+$: 230.1327, found: 230.1319. TLC (2.5% MeOH in CH_2Cl_2) R_f 0.10.

minor, more polar diastereomer:

^{1}H NMR (600 MHz, $CDCl_3$), δ 3.78–3.70 (m, 4 H, C**H**$_2$OC**H**$_2$), 3.25 (m, 1 H, C**H**NH$_2$), 3.22 (d, 1 H, *J* = 10.3 Hz, C**H**CN), 2.74–2.64 (m, 4 H, C**H**$_2$NC**H**$_2$ and SC**H**$_2$), 2.52–2.49 (m, 2 H, C**H**$_2$NC**H**$_2$), 2.24 (s, br, 2 H, N**H**$_2$), 2.10 (s, 3 H, SC**H**$_3$), 2.07 (m, 1 H, C**H**$_2$CH$_2$S), 1.61 (m, 1 H, C**H**$_2$CH$_2$S). ^{13}C NMR (125 MHz, $CDCl_3$), δ 115.4, 66.8, 64.9, 50.4, 48.6, 33.2, 30.6, 15.5. FTIR (neat film), cm^{-1} 3368 (m, br, NH), 2224 (w, CN), 1117 (s). HRMS (ESI$^+$) calcd for $C_{10}H_{20}N_3OS$ (M+H)$^+$: 230.1327, found: 230.1335. TLC (2.5% MeOH in CH_2Cl_2) R_f 0.08.

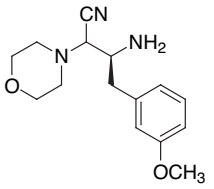


major, less polar diastereomer:

^{1}H NMR (400 MHz, $CDCl_3$), δ 3.82–3.71 (m, 4 H, C**H**$_2$OC**H**$_2$), 3.22–3.17 (m, 1 H, C**H**CH$_3$), 3.05 (d, 1 H, *J* = 10.1 Hz, C**H**CN), 2.73–2.68 (m, 2 H, C**H**$_2$NC**H**$_2$), 2.55–2.50 (m, 2 H, C**H**$_2$NC**H**$_2$), 1.57 (s, br, 2 H, N**H**$_2$), 1.26 (d, 3 H, *J* = 6.2 Hz C**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$), δ 116.3, 67.7, 66.8, 51.0, 46.5, 20.9. FTIR (neat film), cm^{-1} 3365 (m, br, NH), 2238 (w, CN), 1115 (s). HRMS (CI$^+$) calcd for $C_8H_{16}N_3O$ (M+H)$^+$: 170.1293, found: 170.1293. TLC (10% MeOH in CH_2Cl_2) R_f 0.40.

minor, more polar diastereomer:

^{1}H NMR (400 MHz, $CDCl_3$), δ 3.78–3.72 (m, 4 H, C**H**$_2$OC**H**$_2$), 3.22–3.17 (m, 1 H, C**H**CH$_3$), 3.06 (d, 1 H, *J* = 8.6 Hz, C**H**CN), 2.69–2.64 (m, 2 H, C**H**$_2$NC**H**$_2$), 2.56–2.49 (m, 2 H, C**H**$_2$NC**H**$_2$), 1.40 (s, br, 2 H, N**H**$_2$), 1.22 (d, 3 H, *J* = 6.3 Hz, C**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$), δ 115.6, 66.7, 66.5, 66.4, 53.5, 50.4, 45.4, 20.3. FTIR (neat film), cm^{-1} 3368 (m, br, NH), 2241 (w, CN), 1115 (s). HRMS (CI$^+$) calcd for $C_8H_{16}N_3O$ (M+H)$^+$: 170.1293, found: 170.1301. TLC (10% MeOH in CH_2Cl_2) R_f 0.24.



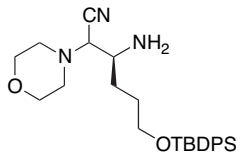
major, less polar diastereomer:

^{1}H NMR (400 MHz, $CDCl_3$), δ 7.26–7.22 (m, 1 H, Ar**H**), 6.81–6.74 (m, 3 H, Ar**H**), 3.79 (s, 3 H, OC**H**$_3$), 3.83–3.73 (m, 4 H, C**H**$_2$OC**H**$_2$), 3.33 (ddd, 1 H, *J* = 10.2, 7.5, 4.0 Hz, C**H**NH$_2$), 3.17 (d, 1

H, *J* = 9.0 Hz, C**H**CN), 3.04 (dd, 1 H, *J* = 13.6, 4.0 Hz, ArC**H**$_2$), 2.74–2.70 (m, 2 H, C**H**$_2$NC**H**$_2$), 2.66 (dd, 1 H, *J* = 13.6, 7.5 Hz, ArC**H**$_2$), 2.58–2.53 (m, 2 H, C**H**$_2$NC**H**$_2$), 1.42 (s, br, 2 H, N**H**$_2$). ^{13}C NMR (125 MHz, $CDCl_3$), δ 159.8, 138.4, 129.7, 121.8, 116.1, 115.6, 111.9, 66.6, 65.0, 55.1, 51.2, 50.7, 39.7. FTIR (neat film), cm^{-1} 3379 (m, br, NH), 2222 (w, CN), 1261 (s). HRMS (EI$^+$) calcd for $C_{15}H_{22}N_3O_2$ (M+H)$^+$: 276.1651, found: 276.1725. TLC (3% MeOH in CH_2Cl_2) R_f 0.31.

minor, more polar diastereomer:

^{1}H NMR (400 MHz, $CDCl_3$), δ 7.27–7.23 (m, 1 H, Ar**H**), 6.85–6.80 (m, 3 H, Ar**H**), 3.81 (s, 3 H, OC**H**$_3$), 3.79–3.69 (m, 4 H, C**H**$_2$OC**H**$_2$), 3.33 (ddd, 1 H, *J* = 10.2, 8.9, 3.0 Hz, C**H**NH$_2$), 3.22 (d, 1 H, *J* = 10.2 Hz, C**H**CN), 3.14 (dd, 1 H, *J* = 13.3, 2.9 Hz, ArC**H**$_2$), 2.75–2.70 (m, 2 H, C**H**$_2$NC**H**$_2$), 2.58–2.51 (m, 3 H, C**H**$_2$NC**H**$_2$ and ArC**H**$_2$), 1.61 (s, br, 2 H, N**H**$_2$). ^{13}C NMR (100 MHz, $CDCl_3$), δ 159.8, 138.5, 129.8, 121.7, 115.3, 115.0, 112.3, 66.6, 64.0, 55.2, 50.6, 50.3, 40.2. FTIR (neat film), cm^{-1} 3378 (m, br, NH), 2226 (w, CN), 1262 (s). HRMS (EI$^+$) calcd for $C_{15}H_{22}N_3O_2$ (M+H)$^+$: 276.1651, found: 276.1725. TLC (3% MeOH in CH_2Cl_2) R_f 0.18.



major, less polar diastereomer:

^{1}H NMR (500 MHz, $CDCl_3$), δ 7.66 (dd, 4 H, *J* = 7.9, 1.3 Hz, *o*–Ar**H**), 7.45–7.37 (m, 6 H, *m,p*–Ar**H**), 3.74–3.66 (m, 6 H, C**H**$_2$OTDS and C**H**$_2$OC**H**$_2$), 3.13 (d, 1 H, *J* = 8.7 Hz, C**H**CN), 3.04 (dt, 1 H, *J* = 8.7, 3.2 Hz, C**H**NH$_2$), 2.66–2.62 (m, 2 H, C**H**$_2$NC**H**$_2$), 2.52–2.48 (m, 2 H, C**H**$_2$NC**H**$_2$), 1.96–1.93 (m, 1 H, C**H**$_2$CHNH$_2$), 1.73–1.68 (m, 1 H, C**H**$_2$CH$_2$OTDS), 1.62–1.54 (m, 1 H, C**H**$_2$CH$_2$OTDS), 1.34–1.26 (m, 1 H, C**H**$_2$CHNH$_2$), 1.05 (s, 9 H, C(C**H**$_3$)$_3$). ^{13}C NMR (125 MHz, $CDCl_3$), δ 135.5, 133.8, 129.7, 127.7, 116.3, 66.6, 66.5, 63.6, 50.8, 50.3, 30.5, 28.5, 26.9, 19.2. FTIR (neat film), cm^{-1} 3385 (m, br, NH), 2228 (w, CN), 1111 (s). HRMS (ESI$^+$) calcd for $C_{26}H_{38}N_3O_2Si$ (M+H)$^+$: 452.2733, found: 452.2720. TLC (2% MeOH in CH_2Cl_2 saturated with NH_3) R_f 0.57.

minor, more polar diastereomer:

^{1}H NMR (500 MHz, $CDCl_3$), δ 7.67 (dd, 4 H, J = 7.9, 1.4 Hz, *o*–Ar**H**), 7.44–7.37 (m, 6 H, *m*,*p*–Ar**H**), 3.80–3.69 (m, 6 H, C**H**$_2$OTDS and C**H**$_2$OC**H**$_2$), 3.12 (d, 1 H, J = 10.0 Hz, C**H**CN), 3.08 (ddd, 1 H, J = 10.0, 8.5, 2.6 Hz, C**H**NH_2), 2.70–2.66 (m, 2 H, C**H**$_2$NC**H**$_2$), 2.53–2.49 (m, 2 H, C**H**$_2$NC**H**$_2$), 1.94–1.87 (m, 1 H, C**H**$_2$C**H**NH_2), 1.81–1.73 (m, 1 H, C**H**$_2$C**H**$_2$OTDS), 1.69–1.50 (m, 1 H, C**H**$_2$C**H**$_2$OTDS), 1.57 (s, br, 2 H, NH_2), 1.41–1.34 (m, 1 H, C**H**$_2$C**H**NH_2), 1.01 (s, 9 H, C(C**H**$_3$)$_3$). ^{13}C NMR (125 MHz, $CDCl_3$), δ 135.6, 133.8, 129.6, 127.7, 115.3, 66.7, 65.0, 63.6, 50.2, 49.2, 30.9, 28.6, 26.9, 19.2. FTIR (neat film), cm^{-1} 3374 (m, br, NH), 2228 (w, CN), 1111 (s). HRMS (ESI$^+$) calcd for $C_{26}H_{38}N_3O_2Si$ $(M+H)^+$: 452.2733, found: 452.2751. TLC (2% MeOH in CH_2Cl_2 saturated with NH_3) R_f 0.28.