Nickel-Catalyzed Asymmetric Reductive Cross-Coupling between Heteroaryl Iodides and α-Chloronitriles

Nathaniel T. Kadunce and Sarah E. Reisman*

The Warren and Katharine Schlinger Laboratory of Chemistry and Chemical Engineering
Division of Chemistry and Chemical Engineering, California Institute of Technology
Pasadena, California 91125
reisman@caltech.edu

Supporting Information 1 (Experimental):

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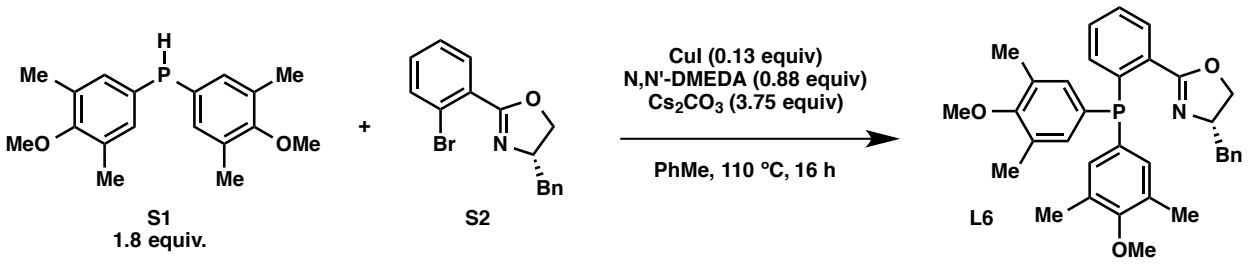
1. Materials and Methods. Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Methylene chloride, diethyl ether, tetrahydrofuran, and toluene were dried by passing through activated alumina. All other commercially obtained reagents were used as received unless specifically indicated. Aryl iodides were purchased from Sigma Aldrich, Combi-Blocks, or Astatech. Manganese powder (>99.9%) was purchased from Sigma Aldrich. $NiCl_2$(dme) was purchased from Strem. Ghaffar-Parkins catalyst was purchased from Strem. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm). Silica gel column chromatography was performed as described by Still et al. (W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem*. **1978**, *43*, 2923.) using silica gel (particle size 0.032-0.063) purchased from Silicycle. ^{1}H and ^{13}C NMR were recorded on a Varian Inova 500 (at 500 MHz and 125 MHz respectively) or a Varian Inova 600 (at 600 MHz and 150 MHz respectively, and are reported relative to internal chloroform (^{1}H, δ = 7.26, ^{13}C, δ = 77.0). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). Analytical SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system with Chiralcel AD-H, OD-H, AS-H, OB-H, and IA columns (4.6 mm x 25 cm). HRMS were acquired using either an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode. Low-temperature X-ray diffraction data (ϕ-and ω-scans) were collected on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON 100 CMOS detector with Cu-$K\alpha$ radiation (λ = 1.54178 Å) from an IμS micro-source.

Abbreviations used: IPA – isopropanol; Et_2O – diethyl ether; PhMe – toluene; EtOAc – ethyl acetate; DCM – dichloromethane; N,N'-DMEDA – N,N'-dimethylethylenediamine; ee – enantiomeric excess.

2. Catalyst and Substrate Preparation.

a. Preparation of (*S*)-4-benzyl-2-(2-(bis(4-methoxy-3,5-dimethylphenyl)phosphanyl)phenyl)-4,5-dihydrooxazole (L6, DMMBnPHOX)

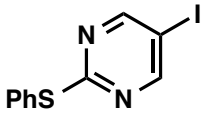


To a flame-dried flask was added CuI (0.13 equiv, 241 mg, 1.3 mmol), followed by anhydrous toluene (40 mL). To this solution was added N,N'-DMEDA (0.88 equiv, 0.93 mL, 8.6 mmol) and diarylphosphine **S1** (1.8 equiv, 5.3 g, 17.5 mmol). These were stirred for 15 minutes at room temperature. To the reaction was then added Cs_2CO_3 (3.75 equiv, 12.4 g, 36.7 mmol), followed by bromoarene **S2** (1 equiv, 3.1 g, 9.8 mmol) as a solution in toluene (40 mL). The reaction was heated to 110 ºC for 16 h. After cooling to room temperature, the reaction was filtered through a plug of Celite and washed with degassed anhydrous DCM. The solution was concentrated and quickly purified via column chromatography using a positive pressure of argon and degassed solvent (10-40% Et_2O/Hexanes) to afford **L6** as a white foamy solid (1.62 g, 3.01 mmol, 31% yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.90 – 7.82 (m, 1H), 7.40 – 7.32 (m, 2H), 7.32 – 7.27 (m, 2H), 7.26 – 7.20 (m, 1H), 7.15 – 7.10 (m, 2H), 7.05 (dd, *J* = 12.7, 7.9 Hz, 4H), 6.93 (ddd, *J* = 7.7, 4.5, 1.5 Hz, 1H), 4.44 – 4.29 (m, 1H), 4.06 (dd, *J* = 9.3, 8.3 Hz, 1H), 3.78 (dd, *J* = 8.4, 7.4 Hz, 1H), 3.75 (d, *J* = 4.0 Hz, 6H), 2.99 (dd, *J* = 13.7, 5.0 Hz, 1H), 2.28 (d, *J* = 13.0 Hz, 12H), 2.17 – 2.06 (m, 1H); ^{13}C NMR (126 MHz, cdcl$_3$) ^{13}C NMR (126 MHz, cdcl$_3$) δ 164.32, 164.30, 157.71, 157.63, 139.88, 139.68, 138.19, 135.02, 134.84, 134.72, 134.54, 133.40, 133.38, 132.43, 132.41, 132.36, 132.33, 131.49, 131.35, 131.01, 130.95, 130.90, 130.83, 130.36, 129.91, 129.89, 129.08, 128.48, 127.65, 126.34, 71.55, 67.90, 59.68, 59.62, 41.25, 16.22, 16.17; ^{31}P NMR (121 MHz, cdcl$_3$) δ -6.15; IR (NaCl/thin film): 3564.92, 2935.84, 1651.78, 1474.78, 1274.72, 1217.33, 1113.02, 1014.45, 909.83, 732.11, 700.48, 607.77 cm^{-1}; $[\alpha]_D^{25}$ = +37.355 (*c* = 1.285, $CHCl_3$). HRMS (MM) calc'd for $[M+H_2O]^+$ 555.2533, found 555.2544.

b. General procedure 1 for preparation of heteroaryl iodides.

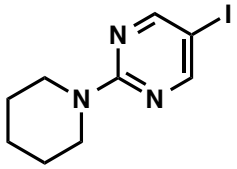
To a flame-dried flask was added copper(I) iodide (0.05 equiv), followed by 1,4-dioxane and N,N'-DMEDA (0.10 equiv), then aryl bromide (1.0 equiv) and sodium iodide (2.0 equiv). The reaction was heated to 110 ºC for 24 h. Upon cooling to room temperature, the reaction was filtered over Celite and washed with DCM. The solution was concentrated to afford the aryl iodide as a light solid. Purification by recrystallization was possible for all substrates but was generally unnecessary. Aryl iodides were employed in the coupling reactions as is.

5-iodo-2-phenylthiopyrimidine (6j)



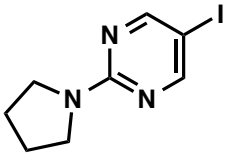
Prepared from 5-bromo-2-phenylthiopyrimidine (10.3 mmol, 2.75 g) following General Procedure 1 to yield 3.14 g (97% yield) of **6j** as a light tan solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.62 (s, 2H), 7.65 – 7.56 (m, 2H), 7.48 – 7.40 (m, 3H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 171.40, 162.64, 135.25, 129.61, 129.34, 128.88, 87.17; IR (NaCl/thin film): 3057.57, 1537.84, 1514.30, 1440.03, 1382.13, 1184.77, 994.96, 745.51, 687.91, 630.05 cm^{-1}; HRMS (MM) calc'd for [M]$^{+}$ 313.9369, found 313.9579.

5-iodo-2-(piperidin-1-yl)pyrimidine (6k)



Prepared from 5-bromo-2-(piperidin-1-yl)pyrimidine (10.3 mmol, 2.49 g) following General Procedure 1 to yield 2.86 g (96% yield) of **6k** as a light yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.34 (s, 2H), 3.78 – 3.69 (m, 4H), 1.71 – 1.63 (m, 2H), 1.59 (tt, *J* = 7.8, 4.5 Hz, 4H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 162.34, 159.63, 74.30, 44.87, 25.64, 24.71; IR (NaCl/thin film): 2929.42, 2849.82, 1558.04, 1505.31, 1360.11, 1266.59, 1253.66, 1023.84, 945.12, 851.36, 784.80, 642.34 cm^{-1}; HRMS (MM) calc'd for [M]$^{+}$ 289.0070, found 289.0033.

5-iodo-2-(pyrrolidin-1-yl)pyrimidine (6l)



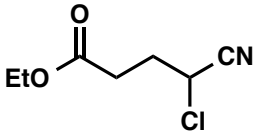
Prepared from 5-bromo-2-(pyrrolidin-1-yl)pyrimidine (10.3 mmol, 2.35 g) following General Procedure 1 to yield 2.75 g (97% yield) of **6l** as a very light pink solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.37 (s, 2H), 3.57 – 3.47 (m, 4H), 2.18 – 1.77 (m, 4H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 162.34, 158.19, 74.37, 46.74, 25.52; IR (NaCl/thin film): 2944.10, 2864.32, 1565.22, 1518.02, 1511.96,

1333.11, 1286.14, 1153.17, 940.39, 782.61, 639.66 cm^{-1}; HRMS (MM) calc'd for $[M]^+$ 274.9914, found 274.9874.

c. General Procedure 2 for preparation of α-chloronitriles.

To a flame-dried flask was added aldehyde starting material (1 equiv) followed by anhydrous Et_2O and K_2CO_3 (0.2 equiv). To this suspension was added TMSCN (1.02 equiv) (Warning: acutely toxic, handle with care). Reaction was stirred at room temperature overnight. Reaction was then quenched with saturated aqueous $NaHCO_3$ (1 mL/mmol). Layers were separated and the aqueous phase was extracted twice with Et_2O. Organic layers were combined and concentrated. The resulting oil was suspended in 1 N HCl and stirred at rt for 2 hours. The reaction was then washed twice with Et_2O and the organics were dried over Na_2SO_4 and concentrated to afford the crude cyanohydrin. A new flame-dried flask was charged with a large stirbar and cyanuric chloride (1.05 equiv). To this was added DMF (1.1 mL/gram cyanuric chloride) and the suspension was stirred vigorously until a white solid was obtained. The solid was then suspended by addition of DCM (0.5 M). The crude cyanohydrin was added to the reaction as a solution in DCM and stirred at room temperature for 24 hours. The reaction was quenched by addition of water and stirred for 10 minutes. Layers were separated and the aqueous layer was washed with DCM. Organic phases were combined and washed with saturated Na_2CO_3, then 1 N HCl, then brine. Organics were then dried over Na_2SO_4 and concentrated to afford the crude chloronitrile. Crude oils were purified by column chromatography to afford clear oils or white solids. Substrate preparations were unoptimized and the reported reactions were performed once.

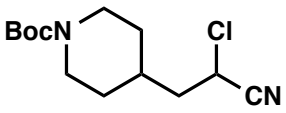
Ethyl 4-chloro-4-cyanobutyrate (1g)



Prepared from ethyl hemisuccinaldehyde (1.82 g, 14 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (5:95 to 20:80 EtOAc:hexanes) to yield 1.77 g (72% yield) of **8g** as a clear oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.70 (dd, *J* = 7.5, 6.2 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.73 – 2.53 (m, 2H), 2.49 – 2.28 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), ; ^{13}C NMR (126 MHz, cdcl$_3$) δ 171.34, 116.62, 61.14, 41.50, 31.39, 29.66, 14.15; IR (NaCl/thin film):

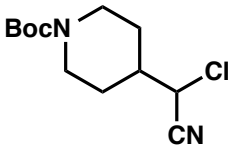
2983.27, 2249.74, 1734.19, 1608.59, 1564.56, 1419.07, 1378.34, 1193.90, 1096.48, 1024.20, 852.08, 795.42, 665.51 cm^{-1} ; HRMS (MM) calc'd for $[M]^+$ 175.0395, found 175.0380.

***tert*-Butyl-4-(2-chloro-2-cyanoethyl)piperidine-1-carboxylate (1h)**



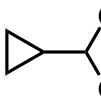
Prepared from 2-(1-Boc-4-piperidyl)acetaldehyde (1.0 g, 4.4 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (5:95 to 20:80 EtOAc:hexanes) to yield 837 mg (70% yield) of **XX** as a white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.49 (t, *J* = 7.6 Hz, 1H), 4.12 (bs, 2H), 2.71 (bs, 2H), 2.10 – 1.94 (m, 2H), 1.80 (ddd, *J* = 11.3, 7.6, 4.2 Hz, 1H), 1.72 – 1.67 (m, 2H), 1.45 (s, 9H), 1.28 – 1.06 (m, 2H); ^{13}C NMR (126 MHz, $cdcl_3$) δ 154.64, 117.08, 79.61, 43.72, 43.20, 42.63, 40.18, 33.02, 31.44, 31.08, 28.42; IR (NaCl/thin film): 2929.41, 1673.87, 1417.84, 1246.54, 1161.38, 1127.43, 966.65, 865.88, 769.18, 741.68, 677.80 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 273.1364, found 273.1352.

***tert*-Butyl-4-(chloro(cyano)methyl)piperidine-1-carboxylate (1i)**



Prepared from 1-Boc-piperidine-4-carboxaldehyde (2.0 g, 9.39 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (5:95 to 20:80 EtOAc:hexanes) to yield 570 mg (24% yield) of **XX** as a white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.34 (d, *J* = 6.1 Hz, 1H), 4.24 (bs, 2H), 2.70 (bs, 2H), 2.10 – 1.98 (m, 1H), 1.98 – 1.84 (m, 2H), 1.46 (s, m, 11H); ^{13}C NMR (126 MHz, $cdcl_3$) δ 154.47, 115.76, 79.95, 47.27, 43.17, 42.70, 41.59, 28.39, 28.35, 27.96; IR (NaCl/thin film): 1976.08, 1945.79, 2859.74, 1682.85, 1422.81, 1366.50, 1280.82, 1239.82, 1166.99, 1128.02, 973.46, 866.39, 760.71 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 259.1208, found 259.1256.

2-chloro-2-cyclopropylacetonitrile (11)



Prepared from cyclopropane carboxaldehyde (1 mL, 13.4 mmol) following General Procedure 2. The crude residue was purified by kugelrohr distillation followed by silica gel chromatography (100% pentanes) to yield 205 mg (13% yield) of **13** as a clear mobile liquid. The product was isolated with some residual pentane due to its volatility. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.22 (d, *J* = 7.7 Hz, 1H), 1.53 (qt, *J* = 7.9, 4.8 Hz, 1H), 0.94 – 0.84 (m,

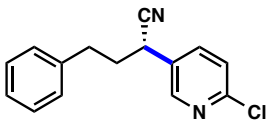
2H), 0.74 – 0.62 (m, 2H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 115.79, 46.91, 16.59, 6.09, 5.40; IR (NaCl/thin film): 3091.35, 3013.92, 2958.47, 2247.22, 1732.61, 1430.84, 1220.80, 1029.90, 991.98, 926.86, 832.41, 728.05 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 116.0262, found 116.0258.

3. Cross-Coupling Reactions and Product Characterization

General Procedure 3 for reductive cross-couplings.

A 20 mL scintillation vial was charged with a cross stirbar, Mn^0 powder (3 equiv, 33 mg, 0.6 mmol), aryl iodide (*if solid*, 1 or 2 equiv, 0.2 or 0.4 mmol), $NiCl_2$(dme) (0.1 equiv, 4.4 mg, 0.02 mmol), **L6** (0.2 equiv, 21.6 mg, 0.04 mmol) and $NaBF_4$ if applicable (1 equiv, 22 mg, 0.2 mmol). To this was added 1,4-dioxane (0.68 mL, 0.3M), aryl iodide (*if liquid*, 1 or 2 equiv, 0.2 or 0.4 mmol) and TMSCl (0.4 equiv, 33 μL, 0.08 mmol), followed by chloronitrile (1 equiv, 0.2 mmol). Reaction was sealed with a Teflon-lined cap and stirred on the benchtop at 500 RPM for 16 hours. Over this interval reactions turn from dark purple to cloudy red or yellow with significant white precipitate. Reactions were diluted with 1 mL of hexane, leading to additional salt precipitation. This slurry was loaded directly onto a silica gel or florisil column and eluted in a hexane/EtOAc gradient. Excess aryl iodide could be recovered in the first several fractions, with cross-coupled product being the most polar component. Reaction success is critically dependent on stirring. A stirbar too small for the reaction vessel will fail to suspend the Mn powder and lead to low conversions. The reaction vessel should be sufficiently large (solvent height should be sufficiently low) to allow even distribution of Mn powder with vigorous stirring. I think we should give more detail.

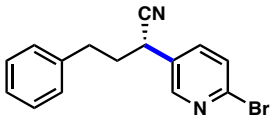
2-(6-chloropyridin-3-yl)-4-phenylbutanenitrile (7a)



Prepared from 2-chloro-5-iodopyridine (48.0 mg, 0.2 mmol) and 2-chloro-4-phenylbutanenitrile (36 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 10:90 EtOAc:hexanes) to yield 39.8 mg (78% yield) of **7a** as a clear oil. The enantiomeric excess was determined to be 85% by chiral SFC analysis (AD, 2.5 mL/min, 8% IPA in CO_2, λ = 210 nm): t_R(minor) = 9.8 min, t_R(major) = 13.0 min. ^{1}H NMR (500 MHz,

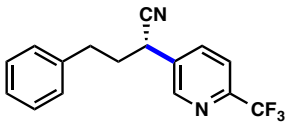
Chloroform-*d*) δ 8.31 (d, *J* = 2.6 Hz, 1H), 7.66 (dd, *J* = 8.3, 2.7 Hz, 1H), 7.40 – 7.28 (m, 3H), 7.28 – 7.22 (m, 1H), 7.22 – 7.17 (m, 2H), 3.77 (dd, *J* = 9.2, 6.0 Hz, 1H), 2.87 – 2.81 (m, 2H), 2.34 – 2.27 (m, 1H), 2.16 (dddd, *J* = 13.7, 8.5, 7.6, 6.0 Hz, 1H).; ^{13}C NMR (126 MHz, cdcl$_3$) δ 151.54, 148.52, 138.91, 137.56, 130.54, 128.89, 128.40, 126.84, 124.78, 119.22, 37.00, 33.47, 32.86.; IR (NaCl/thin film): 3027.23, 2926.09, 2242.46, 1586.64, 1566.17, 1496.29, 1460.14, 1389.42, 1141.53, 1108.27, 1022.71, 832.61, 741. 61, 700.19 cm^{-1}; $[\alpha]_D^{25}$ = -12.081 (*c* = 1.410, $CHCl_3$). HRMS (MM) calc'd for $[M+Na]^+$ 279.0659, found 279.0702.

2-(6-bromopyridin-3-yl)-4-phenylbutanenitrile (7b)



Prepared from 2-bromo-5-iodopyridine (56.8 mg, 0.2 mmol) and 2-chloro-4-phenylbutanenitrile (36 mg, 0.2 mmol) with $NaBF_4$ (22 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 10:90 EtOAc:hexanes) to yield 40.9 mg (68% yield) of **7b** as a clear oil. The enantiomeric excess was determined to be 88% by chiral SFC analysis (AD, 2.5 mL/min, 10% IPA in CO_2, λ = 280 nm): t_R(minor) = 9.5 min, t_R(major) = 12.2 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.29 (dt, *J* = 2.5, 0.6 Hz, 1H), 7.54 (qd, *J* = 8.3, 1.7 Hz, 2H), 7.42 – 7.29 (m, 2H), 7.29 – 7.22 (m, 1H), 7.22 – 7.14 (m, 2H), 3.74 (dd, *J* = 9.2, 6.0 Hz, 1H), 2.90 – 2.78 (m, 2H), 2.29 (dddd, *J* = 13.9, 9.3, 8.0, 6.0 Hz, 1H), 2.16 (dddd, *J* = 13.7, 8.5, 7.6, 6.0 Hz, 1H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 148.97, 142.08, 138.88, 137.29, 130.97, 128.89, 128.57, 128.40, 126.85, 119.13, 36.95, 33.53, 32.85; IR (NaCl/thin film): 3026.73, 2925.74, 2859.37, 2242.11, 1734.00, 1581.13, 1561.56, 1496.15, 1455.35, 1385.97, 1090.22, 1019.79, 830.73, 735.64, 699.99 cm^{-1}; $[\alpha]_D^{25}$ = -4.695 (*c* = 1.180, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 301.0335, found 301.0341.

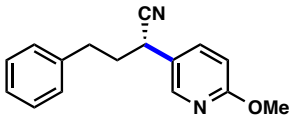
4-phenyl-2-(6-(trifluoromethyl)pyridin-3-yl)butanenitrile (7c)



Prepared from 5-iodo-2-trifluoromethylpyridine (54.6 mg, 0.2 mmol) and 2-chloro-4-phenylbutanenitrile (36 mg, 0.2 mmol) with $NaBF_4$ (22 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 10:90 EtOAc:hexanes) to yield 39.7 mg (68% yield) of **7c** as a clear oil. The enantiomeric excess was determined to be 85% by chiral SFC analysis (AD, 2.5 mL/min, 7% IPA in CO_2, λ = 254 nm): t_R(minor) = 3.0 min, t_R(major) = 4.7

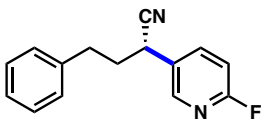
min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.64 (d, *J* = 2.2 Hz, 1H), 7.89 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.73 (dd, *J* = 8.2, 0.8 Hz, 1H), 7.40 – 7.29 (m, 2H), 7.29 – 7.22 (m, 1H), 7.22 – 7.14 (m, 2H), 3.87 (dd, *J* = 9.3, 5.9 Hz, 1H), 2.93 – 2.82 (m, 2H), 2.39 – 2.28 (m, 1H), 2.21 (dddd, *J* = 13.7, 8.5, 7.7, 5.9 Hz, 1H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 148.93, δ 148.18 (q, $J_{C\text{-}F}$ = 35.3 Hz), 138.77, 136.28, 134.83, 128.92, 128.40, 128.38, 126.91, 126.89, 120.81 (q, $J_{C\text{-}F}$ = 2.7 Hz), 118.87, 37.02, 34.03, 32.90.; IR (NaCl/thin film): 3028.51, 2928.97, 2862.95, 2243.85, 1735.25, 1602.71, 1496.75, 1454.95, 1403.90, 1339.65, 1178.34, 1137.96, 1088.63, 1027.88, 850.30, 751.10, 700.69 cm^{-1}; $[\alpha]_D^{25}$ = -21.304 (*c* = 1.475, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 291.1104, found 291.1181.

2-(6-methoxypyridin-3-yl)-4-phenylbutanenitrile (7d)



Prepared from 5-iodo-2-methoxypyridine (94.0 mg, 0.4 mmol) and 2-chloro-4-phenylbutanenitrile (36 mg, 0.2 mmol) with $NaBF_4$ (22 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 20:80 EtOAc:hexanes) to yield 22.8 mg (45% yield) of **7d** as a clear oil. The enantiomeric excess was determined to be 83% by chiral SFC analysis (AD, 2.5 mL/min, 8% IPA in CO_2, λ = 245 nm): t_R(minor) = 6.5 min, t_R(major) = 7.5 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.07 (dt, *J* = 2.6, 0.6 Hz, 1H), 7.55 (ddd, *J* = 8.6, 2.6, 0.4 Hz, 1H), 7.37 – 7.28 (m, 2H), 7.26 – 7.21 (m, 1H), 7.21 – 7.17 (m, 2H), 6.78 (dd, *J* = 8.6, 0.7 Hz, 1H), 3.94 (s, 3H), 3.69 (dd, *J* = 8.8, 6.3 Hz, 1H), 2.81 (td, *J* = 8.1, 3.5 Hz, 2H), 2.35 – 2.21 (m, 1H), 2.14 (dddd, *J* = 13.8, 8.5, 7.5, 6.4 Hz, 1H).; ^{13}C NMR (126 MHz, cdcl$_3$) δ 164.04, 145.68, 139.41, 137.39, 128.77, 128.42, 126.64, 124.09, 120.16, 111.56, 53.67, 37.04, 33.28, 32.85.; IR (NaCl/thin film): 2925.19, 1849.43, 2240.05, 1608.56, 1572.83, 1494.73, 1395.28, 1290.62, 1024.55, 831.08, 750.29, 699.95 cm^{-1}; $[\alpha]_D^{25}$ = -9.806 (*c* = 0.790, $CHCl_3$). HRMS (MM) calc'd for $[M+Na]^+$ 275.1155, found 275.1175.

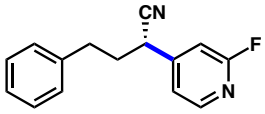
2-(6-fluoropyridin-3-yl)-4-phenylbutanenitrile (7e)



Prepared from 2-fluoro-5-iodopyridine (89.2 mg, 0.4 mmol) and 2-chloro-4-phenylbutanenitrile (36 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 10:90 EtOAc:hexanes) to yield 30.7 mg (64% yield) of **7e** as a clear oil. The enantiomeric

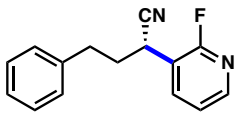
excess was determined to be 87% by chiral SFC analysis (AD, 2.5 mL/min, 8% IPA in CO_2, λ = 254 nm): t_R(minor) = 5.2 min, t_R(major) = 6.4 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.18 – 8.10 (m, 1H), 7.79 (ddd, *J* = 8.5, 7.2, 2.7 Hz, 1H), 7.38 – 7.28 (m, 2H), 7.28 – 7.22 (m, 1H), 7.22 – 7.16 (m, 2H), 6.99 (ddd, *J* = 8.5, 3.1, 0.6 Hz, 1H), 3.78 (dd, *J* = 9.2, 6.0 Hz, 1H), 2.93 – 2.77 (m, 2H), 2.31 (dddd, *J* = 14.0, 9.3, 8.1, 6.0 Hz, 1H), 2.17 (dddd, *J* = 13.7, 8.5, 7.6, 6.0 Hz, 1H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 163.33 (d, J_{C-F} = 241.3 Hz), 146.57 (d, J_{C-F} = 15.3 Hz), 140.02 (d, J_{C-F} = 8.2 Hz), 138.98, 129.33 (d, J_{C-F} = 4.7 Hz), 128.87, 128.40, 126.82, 119.45, 110.26 (d, J_{C-F} = 37.6 Hz), 37.11, 33.29 (d, J_{C-F} = 1.6 Hz), 32.88. ; IR (NaCl/thin film): 3027.76, 2926.65, 2859.25, 2242.02, 1599.81, 1484.95, 1399.59, 1256.76, 1127.35, 1025.00, 831.20, 748.87, 700.31 cm^{-1}; $[\alpha]_D^{25}$ = -27.336 (*c* = 1.155, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 241.1136, found 241.1210.

2-(2-fluoropyridin-4-yl)-4-phenylbutanenitrile (7f)



Prepared from 2-fluoro-4-iodopyridine (44.6 mg, 0.2 mmol) and 2-chloro-4-phenylbutanenitrile (36 mg, 0.2 mmol) with $NaBF_4$ (22 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 10:90 EtOAc:hexanes) to yield 28.8 mg (60% yield) of **7f** as a clear oil. The enantiomeric excess was determined to be 79% by chiral SFC analysis (AD, 2.5 mL/min, 8% IPA in CO_2, λ = 210 nm): t_R(minor) = 4.7 min, t_R(major) = 5.5 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.25 (d, *J* = 5.2 Hz, 1H), 7.36 – 7.31 (m, 2H), 7.29 – 7.23 (m, 1H), 7.22 – 7.18 (m, 2H), 7.17 – 7.14 (m, 1H), 6.92 (td, *J* = 1.5, 0.7 Hz, 1H), 3.79 (dd, *J* = 9.4, 5.6 Hz, 1H), 2.92 – 2.83 (m, 2H), 2.29 (dddd, *J* = 13.7, 9.5, 8.2, 5.5 Hz, 1H), 2.23 – 2.15 (m, 1H).; ^{13}C NMR (126 MHz, cdcl$_3$) δ 164.13 (d, J_{C-F} = 240.5 Hz), 163.17, 150.09, 148.71 (d, J_{C-F} = 15.3 Hz), 138.83, 128.91, 128.39, 126.90, 120.00 (d, J_{C-F} = 4.4 Hz), 118.59, 108.40 (d, J_{C-F} = 38.8 Hz), 36.61, 35.85 (d, J_{C-F} = 3.3 Hz), 32.90. ; IR (NaCl/thin film): 2923.87, 2851.17, 2244.02, 1734.43, 1611.28, 1569.24, 1454.61, 1414.02, 1277.86, 839.28, 751.37, 700.44 cm^{-1}; $[\alpha]_D^{25}$ = -22.036 (*c* = 0.45, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 241.1136, found 241.1134.

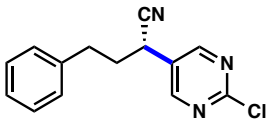
2-(2-fluoropyridin-3-yl)-4-phenylbutanenitrile (7g)



Prepared from 2-fluoro-3-iodopyridine (44.6 mg, 0.2 mmol) and 2-chloro-4-phenylbutanenitrile (36 mg, 0.2 mmol) following General Procedure 3. The

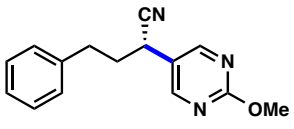
crude residue was purified by silica gel chromatography (0:100 to 10:90 EtOAc:hexanes) to yield 16.7 mg (35% yield) of **7g** as a clear oil. The enantiomeric excess was determined to be 83% by chiral SFC analysis (AD, 2.5 mL/min, 6% IPA in CO_2, λ = 245 nm): t_R(minor) = 4.9 min, t_R(major) = 5.8 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.21 (ddd, *J* = 4.9, 1.9, 1.2 Hz, 1H), 7.98 – 7.87 (m, 1H), 7.35 – 7.29 (m, 2H), 7.29 – 7.22 (m, 2H), 7.22 – 7.18 (m, 2H), 4.03 (t, *J* = 7.4 Hz, 1H), 2.94 – 2.80 (m, 2H), 2.30 – 2.18 (m, 2H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 160.30 (d, J_{C-F} = 239.3 Hz), 147.65 (d, J_{C-F} = 14.8 Hz), 139.59 (d, J_{C-F} = 4.3 Hz), 139.02, 128.78, 128.37, 126.74, 122.09 (d, J_{C-F} = 4.3 Hz), 118.80, 118.23 (d, J_{C-F} = 29.6 Hz), 35.26, 33.06, 30.83 (d, J_{C-F} = 2.5 Hz); IR (NaCl/thin film): 2925.09, 2853.97, 2244.15, 1734.36, 1606.84, 1577.55, 1441.07, 1248.36, 1101.26, 805.44, 750.96, 699.91 cm^{-1}; $[\alpha]_D^{25}$ = -29.296 (*c* = 0.635, CHCl$_3$). HRMS (MM) calc'd for $[M+H]^+$ 241.1136, found 241.1133.

2-(2-chloropyrimidin-5-yl)-4-phenylbutanenitrile (7h)



Prepared from 2-chloro-5-iodopyrimidine (48.1 mg, 0.2 mmol) and 2-chloro-4-phenylbutanenitrile (36 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by flash column chromatography using Florisil® stationary phase (0:100 to 15:85 EtOAc:hexanes) to yield 21.2 mg (41% yield) of **7h** as a clear oil. The enantiomeric excess was determined to be 89% by chiral SFC analysis (AD, 2.5 mL/min, 10% IPA in CO_2, λ = 210 nm): t_R(minor) = 6.2 min, t_R(major) = 7.0 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.59 (d, *J* = 0.5 Hz, 2H), 7.37 – 7.31 (m, 2H), 7.30 – 7.24 (m, 1H), 7.22 – 7.17 (m, 2H), 3.78 (dd, *J* = 9.4, 5.9 Hz, 1H), 2.95 – 2.84 (m, 2H), 2.34 (dddd, *J* = 13.6, 9.4, 7.7, 5.8 Hz, 1H), 2.19 (dtd, *J* = 13.8, 8.0, 5.9 Hz, 1H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 161.50, 158.30, 138.35, 129.03, 128.39, 128.36, 127.07, 118.06, 36.65, 32.80, 31.36; IR (NaCl/thin film): 2923.61, 2850.58, 2243.80, 1735.29, 1580.36, 1550.38, 1401.12, 1160.95, 772.57, 748.86, 700.55, 640.20 cm^{-1}; $[\alpha]_D^{25}$ = -14.892 (*c* = 0.305, CHCl$_3$). HRMS (MM) calc'd for $[M+H]^+$ 258.0793, found 258.0257.

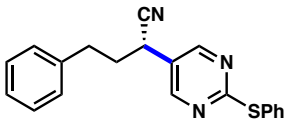
2-(2-methoxypyrimidin-5-yl)-4-phenylbutanenitrile (7i)



Prepared from 5-iodo-2-methoxypyrimidine (89.2 mg, 0.4 mmol) and 2-chloro-4-phenylbutanenitrile (36 mg, 0.2 mmol) with $NaBF_4$ (22 mg, 0.2 mmol) following General Procedure 3. The crude residue was

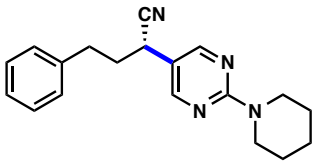
purified by florisil gel chromatography (0:100 to 40:60 EtOAc:hexanes) to yield 35.8 mg (71% yield) of **7i** as a clear oil. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AS, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(minor) = 4.5 min, t_R(major) = 5.0 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.47 (d, *J* = 0.4 Hz, 2H), 7.38 – 7.29 (m, 2H), 7.28 – 7.23 (m, 1H), 7.22 – 7.17 (m, 2H), 4.04 (s, 3H), 3.71 (dd, *J* = 9.1, 6.1 Hz, 1H), 2.89 – 2.82 (m, 2H), 2.31 (dddd, *J* = 13.9, 9.2, 7.9, 6.1 Hz, 1H), 2.16 (dddd, *J* = 13.7, 8.4, 7.6, 6.1 Hz, 1H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 165.54, 158.16, 138.84, 128.91, 128.40, 126.86, 122.72, 119.06, 55.30, 36.79, 32.79, 31.17; IR (NaCl/thin film): 3026.71, 2928.66, 2241.18, 1600.01, 1560.30, 1474.60, 1410.27, 1331.54, 1031.65, 803.93, 700.50 cm^{-1}; $[\alpha]_D^{25}$ = -17.013 (*c* = 0.395, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 254.1288, found 254.1310.

4-phenyl-2-(2-phenylthio)pyrimidin-5-yl)butanenitrile (7j)



Prepared from 5-iodo-2-phenylthiopyrimidine (62.8 mg, 0.2 mmol) and 2-chloro-4-phenylbutanenitrile (36 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 30:70 EtOAc:hexanes) to yield 50.3 mg (76% yield) of **7j** as a clear oil. The enantiomeric excess was determined to be 91% by chiral SFC analysis (AD, 2.5 mL/min, 15% IPA in CO_2, λ = 280 nm): t_R(minor) = 11.3 min, t_R(major) = 12.7 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.44 (s, 2H), 7.70 – 7.56 (m, 2H), 7.50 – 7.40 (m, 3H), 7.37 – 7.29 (m, 2H), 7.28 – 7.22 (m, 1H), 7.20 – 7.14 (m, 2H), 3.67 (dd, *J* = 9.0, 6.0 Hz, 1H), 2.89 – 2.79 (m, 2H), 2.28 (dddd, *J* = 13.9, 9.2, 7.9, 6.1 Hz, 1H), 2.13 (dddd, *J* = 13.7, 8.4, 7.7, 6.1 Hz, 1H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 173.10, 156.34, 138.73, 135.37, 129.65, 129.37, 128.92, 128.80, 128.38, 126.89, 124.93, 118.64, 36.64, 32.74, 31.50; IR (NaCl/thin film): 3025.13, 2926.01, 2242,07, 1734.06, 1580.58, 1539.37, 1399.77, 1170.57, 748.46, 701.21, 689.27 cm^{-1}; $[\alpha]_D^{25}$ = +10.214 (*c* = 1.965, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 332.1216, found 332.1746.

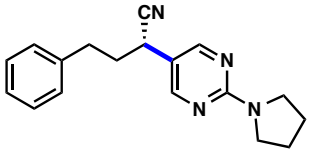
4-phenyl-2-(2-(piperidin-1-yl)pyrimidin-5-yl)butanenitrile (7k)



Prepared from 5-iodo-2-(piperidin-1-yl)pyrimidine (57.8 mg, 0.2 mmol) and 2-chloro-4-phenylbutanenitrile (36.0 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 40:60 EtOAc:hexanes) to yield 43.1 mg (70% yield) of **7k** as a white solid. The enantiomeric excess was determined to be 85%

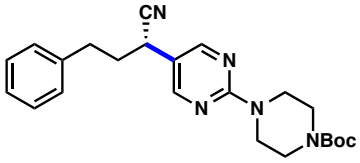
by chiral SFC analysis (AD, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm): t_R(minor) = 7.5 min, t_R(major) = 8.6 min. The product could be further enriched via recrystallization by vapor diffusion of pentane to a saturated solution of **7k** in DCM, affording 38.4 mg (89% recovery) of white needles. The enantiomeric excess of recrystallized **7k** was determined to be 95%. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.22 (s, 2H), 7.35 – 7.29 (m, 2H), 7.26 – 7.21 (m, 1H), 7.21 – 7.16 (m, 2H), 3.93 – 3.70 (m, 4H), 3.55 (dd, *J* = 8.6, 6.5 Hz, 1H), 2.81 (td, *J* = 8.0, 7.3, 2.1 Hz, 2H), 2.25 (dddd, *J* = 13.6, 8.6, 7.9, 6.5 Hz, 1H), 2.11 (dddd, *J* = 13.7, 8.3, 7.4, 6.5 Hz, 1H), 1.76 – 1.65 (m, 2H), 1.65 – 1.54 (m, 4H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 161.27, 156.64, 139.33, 128.78, 128.42, 126.64, 119.91, 115.78, 44.89, 36.74, 32.73, 31.18, 25.71, 24.78.; IR (NaCl/thin film): 2932.29, 2853.60, 2239.17, 1605.13, 1514.57, 1448.02, 1364.20, 1271.93, 1024.80, 947.51, 797.14, 700.19 cm^{-1}; $[\alpha]_D^{25}$ = +13.073 (*c* = 1.595, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 307.1917, found 307.1848.

4-phenyl-2-(2-(pyrrolidin-1-yl)pyrimidin-5-yl)butanenitrile (7l)



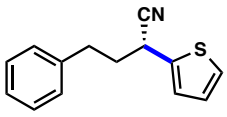
Prepared from 5-iodo-2-(pyrrolidin-1-yl)pyrimidine (55 mg, 0.2 mmol) and 2-chloro-4-phenylbutanenitrile (36.0 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 40:60 EtOAc:hexanes) to yield 35.0 mg (60% yield) of **7l** as a white solid. The enantiomeric excess was determined to be 85% by chiral SFC analysis (AD, 2.5 mL/min, 12% IPA in CO_2, λ = 235 nm): t_R(minor) = 10.8 min, t_R(major) = 12.5 min. The product could be further enriched via recrystallization by vapor diffusion of pentane to a saturated solution of **7l** in DCM, affording 31.8 mg (91% recovery) of white needles. The enantiomeric excess of recrystallized **7l** was determined to be 97%. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.25 (s, 2H), 7.34 – 7.29 (m, 2H), 7.26 – 7.21 (m, 1H), 7.21 – 7.16 (m, 2H), 3.66 – 3.49 (m, 5H), 2.81 (t, *J* = 7.6 Hz, 2H), 2.26 (ddt, *J* = 13.7, 8.5, 7.2 Hz, 1H), 2.11 (dtd, *J* = 13.6, 7.8, 6.6 Hz, 1H), 2.05 – 1.96 (m, 4H).; ^{13}C NMR (126 MHz, cdcl$_3$) δ 156.64, 139.30, 128.79, 128.42, 126.65, 121.43, 119.93, 115.75, 46.78, 36.76, 32.72, 31.22, 25.52; IR (NaCl/thin film): 2927.97, 2866.57, 2238.90, 1603.00, 1524.42, 1483.96, 1460.18, 1335.03, 798. 26, 699.99 cm^{-1}; $[\alpha]_D^{25}$ = +12.942 (*c* = 1.130, $CHCl_3$). HRMS (MM) calc'd for $[M+H_3O]^+$ 311.1826, found 311.1825.

***tert*-butyl-4-(5-(1-cyano-3-phenylpropyl)pyrimidin-2-yl)piperazine-1-carboxylate (7m)**



Prepared from 5-iodo-2-(4-Boc-piperazin-1-yl)pyrimidine (78.0 mg, 0.2 mmol) and 2-chloro-4-phenylbutanenitrile (36.0 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 40:60 EtOAc:hexanes) to yield 56.5 mg (69% yield) of **7m** as a white solid. The enantiomeric excess was determined to be 85% by chiral SFC analysis (AD, 2.5 mL/min, 15% IPA in CO_2, λ = 235 nm): t_R(minor) = 7.5 min, t_R(major) = 9.0 min. The product could be further enriched via recrystallization by vapor diffusion of pentane to a saturated solution of **7m** in benzene, affording 51.0 mg (90% recovery) of white needles. The enantiomeric excess of recrystallized **7m** was determined to be 94%. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.25 (s, 2H), 7.37 – 7.27 (m, 2H), 7.25 – 7.20 (m, 1H), 7.20 – 7.15 (m, 2H), 3.83 – 3.79 (m, 4H), 3.58 (dd, *J* = 8.7, 6.4 Hz, 1H), 3.50 (t, *J* = 5.3 Hz, 4H), 2.90 – 2.73 (m, 2H), 2.26 (dddd, *J* = 13.6, 8.7, 7.2, 4.1 Hz, 1H), 2.11 (dddd, *J* = 13.7, 8.4, 7.5, 6.4 Hz, 1H), 1.49 (s, 9H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 161.27, 156.70, 154.78, 139.21, 128.81, 128.40, 126.69, 119.71, 117.11, 80.07, 43.65, 42.86 (br), 36.74, 32.74, 31.18, 28.43; IR (NaCl/thin film): 2977.91, 2927.86, 2861.14, 2243.21, 1687.28, 1607.00, 1517.48, 1496.25, 1424.34, 1364.59, 1247.24, 1176.22, 1129.18, 999.26, 793.95, 696.53 cm^{-1}; $[\alpha]_D^{25}$ = +13.500 (*c* = 1.980, $CHCl_3$). HRMS (MM) calc'd for $[M+Na]^+$ 430.2213, found 430.2294.

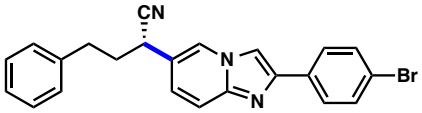
4-phenyl-2-(thiophen-2-yl)butanenitrile (7n)



Prepared from 2-iodothiophene (111 μL, 1.0 mmol) and 2-chloro-4-phenylbutanenitrile (180 mg, 1.0 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 10:90 EtOAc:hexanes) to yield 170 mg (75% yield) of **7n** as a clear oil. The enantiomeric excess was determined to be 88% by chiral SFC analysis (AD, 2.5 mL/min, 8% IPA in CO_2, λ = 245 nm): t_R(minor) = 5.8 min, t_R(major) = 7.1 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.36 – 7.31 (m, 2H), 7.29 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.27 – 7.23 (m, 1H), 7.22 (dq, *J* = 7.6, 0.7 Hz, 2H), 7.08 (dt, *J* = 3.5, 1.0 Hz, 1H), 7.00 (dd, *J* = 5.1, 3.5 Hz, 1H), 4.03 (ddd, *J* = 8.6, 6.3, 0.8 Hz, 1H), 2.94 – 2.82 (m, 2H), 2.41 – 2.24 (m, 2H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 139.49, 137.62, 128.76, 128.50, 127.13, 126.62, 126.31, 125.61, 119.74, 37.32, 32.85, 31.66; IR (NaCl/thin film): 3085.49, 3062.55, 3026.78, 2927.12, 2860.88, 2241.68, 1602.83, 1496.13, 1454.38, 1238.04, 1080.89,

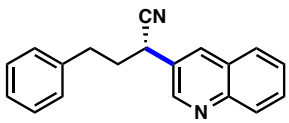
1029.74, 833.92, 750.39, 699.80 cm^{-1}; $[\alpha]_D^{25}$ = -27.559 (*c* = 1.455, $CHCl_3$). HRMS (MM) calc'd for $[M+H_3O]^+$ 246.0947, found 246.1107.

2-(2-(4-bromophenyl)imidazo[1,2-*a*]pyridin-6-yl)-4-phenylbutanenitrile (7o)



Prepared from 2-(4-bromophenyl)-6-iodoimidazo[1,2-*a*]pyridine (159.6 mg, 0.4 mmol) and 2-chloro-4-phenylbutanenitrile (36.0 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (5:95 to 20:80 acetone:hexanes) to yield 60.0 mg (72% yield) of **7o** as a white solid. The enantiomeric excess was determined to be 87% by chiral SFC analysis (IA, 2.5 mL/min, 40% IPA in CO_2, λ = 245 nm): t_R(minor) = 10.7 min, t_R(major) = 14.3 min. The product could be further enriched via recrystallization by vapor diffusion of pentane to a saturated solution of **7o** in DCM, affording 52.2 mg (87% recovery) of white needles. The enantiomeric excess of recrystallized **7o** was determined to be 97%. Following column chromatography, a UV active peak remained in the SFC trace (t_R = 8.6 min) that was not observed in any other analysis. This peak was significantly diminished following recrystallization. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.19 – 8.11 (m, 1H), 7.86 (d, *J* = 0.7 Hz, 1H), 7.85 – 7.78 (m, 2H), 7.64 (d, *J* = 9.4 Hz, 1H), 7.60 – 7.53 (m, 2H), 7.38 – 7.30 (m, 2H), 7.28 – 7.23 (m, 1H), 7.21 (dq, *J* = 7.7, 0.7 Hz, 2H), 7.07 (dd, *J* = 9.3, 1.9 Hz, 1H), 3.77 (dd, *J* = 9.0, 5.7 Hz, 1H), 2.93 – 2.83 (m, 2H), 2.33 (dddd, *J* = 13.8, 9.1, 8.2, 5.7 Hz, 1H), 2.25 (dddd, *J* = 13.7, 8.5, 7.7, 5.8 Hz, 1H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 145.73, 144.82, 139.13, 132.34, 131.93, 128.86, 128.41, 127.59, 126.80, 124.07, 123.75, 122.23, 121.06, 119.44, 118.31, 108.76, 36.51, 33.80, 32.88; IR (NaCl/thin film): 2924.20, 2854.07, 2240.70, 1472.83, 1435.81, 1354.99, 1208.78, 1067.55, 1009.04, 833.96, 806.47, 738.54, 700.04 cm^{-1}; $[\alpha]_D^{25}$ = +28.004 (*c* = 0.275, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 416.0757, found 416.0698.

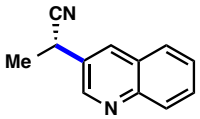
4-phenyl-2-(quinolin-3-yl)butanenitrile (3a)



Prepared from 3-iodoquinoline (51.2 mg, 0.2 mmol) and 2-chloro-4-phenylbutanenitrile (36.0 mg, 0.2 mmol) with $NaBF_4$ (22.0 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 40:60 EtOAc:hexanes) to yield 39.4 mg (72% yield) of

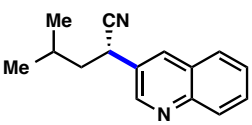
3a as a light yellow oil that solidified on standing. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AD, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R(major) = 6.1 min, t_R(minor) = 6.8 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.81 (s, 1H), 8.18 (d, *J* = 2.3 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.85 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.76 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.61 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H), 7.38 – 7.28 (m, 2H), 7.28 – 7.15 (m, 3H), 3.99 (dd, *J* = 9.0, 5.9 Hz, 1H), 2.95 – 2.82 (m, 2H), 2.39 (dddd, *J* = 14.0, 9.2, 7.9, 6.2 Hz, 1H), 2.30 (dddd, *J* = 13.7, 8.5, 7.7, 5.9 Hz, 1H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 149.22, 147.75, 139.21, 134.28, 130.18, 129.42, 128.85, 128.57, 128.45, 127.78, 127.62, 127.56, 126.76, 119.74, 37.18, 34.39, 32.99; IR (NaCl/thin film): 3026.11, 2926.11, 2241.03, 1603.40, 1571.03, 1495.05, 1454.48, 1125.63, 906.13, 787.96, 751.66, 700.17 cm^{-1}; $[\alpha]_D^{25}$ = -1.617 (*c* = 0.952, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 273.1386, found 273.1589.

2-(quinolin-3-yl)propanenitrile (3b)



Prepared from 3-iodoquinoline (51.2 mg, 0.2 mmol) and 2-chloropropanenitrile (17 µL, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 20:80 EtOAc:hexanes) to yield 28.7 mg (79% yield) of **3b** as a clear oil. The enantiomeric excess was determined to be 81% by chiral SFC analysis (AD, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(major) = 7.8 min, t_R(minor) = 8.8 min. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.87 (d, *J* = 2.4 Hz, 1H), 8.23 (d, *J* = 2.4 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.92 – 7.84 (m, 1H), 7.77 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.62 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 4.16 (q, *J* = 7.3 Hz, 1H), 1.78 (dd, *J* = 7.3, 0.5 Hz, 3H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 149.01, 147.67, 133.57, 130.13, 129.83, 129.34, 127.78, 127.58, 127.54, 120.60, 29.26, 21.39; IR (NaCl/thin film): 2924.03, 2850.94, 2241.83, 1570.25, 1496.55, 1457.22, 1378.86, 1126.13, 1082.83, 966.72, 907.45, 787.48, 752.77, 617.35 cm^{-1}; $[\alpha]_D^{25}$ = -20.200 (*c* = .355, $CHCl_3$). HRMS (MM) calc'd for $[M+H_3O]^+$ 201.1022, found 201.1022.

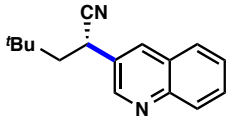
4-methyl-2-(quinolin-3-yl)pentanenitrile (3c)



Prepared from 3-iodoquinoline (51.2 mg, 0.2 mmol) and 2-chloro-4-methylpentanenitrile (26.2 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 30:70 EtOAc:hexanes) to yield 29.1 mg (65% yield) of **3c** as a clear oil. The enantiomeric

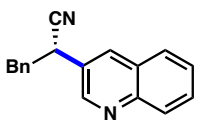
excess was determined to be 89% by chiral SFC analysis (OB-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R(minor) = 4.2 min, t_R(major) = 4.6 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.83 (d, *J* = 2.4 Hz, 1H), 8.19 (d, *J* = 2.4 Hz, 1H), 8.13 (dq, *J* = 8.5, 0.9 Hz, 1H), 7.85 (ddd, *J* = 8.1, 1.3, 0.7 Hz, 1H), 7.76 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.61 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 4.05 (dd, *J* = 9.8, 6.2 Hz, 1H), 2.06 – 1.97 (m, 1H), 1.96 – 1.86 (m, 1H), 1.75 (ddd, *J* = 13.5, 8.6, 6.2 Hz, 1H), 1.04 (dd, *J* = 11.3, 6.6 Hz, 6H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 149.31, 147.66, 134.09, 130.08, 129.34, 129.21, 127.73, 127.63, 127.50, 120.06, 44.85, 33.43, 26.23, 22.59, 21.58; IR (NaCl/thin film): 2957.60, 2928.61, 2238.86, 1653.55, 1570.26, 1494.77, 1467.80, 1369.63, 1280.03, 1116.26, 787.30, 752.79 cm^{-1}; $[\alpha]_D^{25}$ = -22.811 (*c* = 0.350, $CHCl_3$). HRMS (MM) calc'd for $[M+H_3O]^+$ 243.1492, found 243.1194.

4,4-dimethyl-2-(quinolin-3-yl)pentanenitrile (3d)



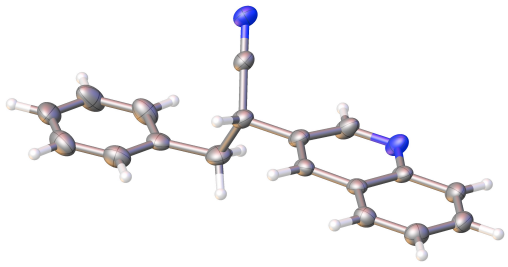
Prepared from 3-iodoquinoline (51.2 mg, 0.2 mmol) and 2-chloro-4,4-dimethylpentanenitrile (29.1 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 30:70 EtOAc:hexanes) to yield 21.4 mg (45% yield) of **3d** as a clear oil. The enantiomeric excess was determined to be 93% by chiral SFC analysis (AD, 2.5 mL/min, 12% IPA in CO_2, λ = 280 nm): t_R(major) = 5.5 min, t_R(minor) = 6.8 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.81 (d, *J* = 2.4 Hz, 1H), 8.20 (d, *J* = 2.4 Hz, 1H), 8.12 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.84 (ddt, *J* = 8.1, 1.3, 0.6 Hz, 1H), 7.75 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.60 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 4.00 (dd, *J* = 10.3, 3.4 Hz, 1H), 2.15 (dd, *J* = 14.2, 10.4 Hz, 1H), 1.76 (dd, *J* = 14.2, 3.4 Hz, 1H), 1.12 (s, 9H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 149.40, 147.52, 133.87, 130.57, 130.04, 129.32, 127.73, 127.61, 127.50, 121.19, 50.25, 31.37, 31.16, 29.40. IR (NaCl/thin film): 2956.95, 2239.66, 1734.18, 1495.05, 1477.11, 1280.54, 1116.30, 1012.66, 897.41, 788.79, 752.85, 619.63 cm^{-1}; $[\alpha]_D^{25}$ = -55.546 (*c* = 0.515, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 239.1543, found 239.1530.

3-phenyl-2-(quinolin-3-yl)propanenitrile (3e)

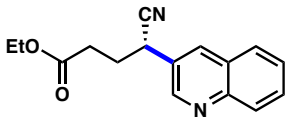


Prepared from 3-iodoquinoline (51.2 mg, 0.2 mmol) and 2-chloro-3-phenylpropanenitrile (33.1 mg, 0.2 mmol) with $NaBF_4$ (22 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 30:70 EtOAc:hexanes) to yield 33.8 mg (65% yield) of **3e** as a light

yellow solid. The enantiomeric excess was determined to be 90% by chiral SFC analysis (AD, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R(major) = 5.9 min, t_R(minor) = 6.8 min. The product could be further enriched via recrystallization by vapor diffusion of pentane to a saturated solution of **3e** in DCM, affording 29.7 mg (88% recovery) of clear pyramidal crystals suitable for X-Ray diffraction. The enantiomeric excess of recrystallized **3e** was determined to be 96%. The structure was solved by direct methods using SHELXS[1] and refined against F^2 on all data by full-matrix least squares with SHELXL-2014[2] using established refinement techniques and with an extinction coefficient of 0.0069(7).[3] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. Compound **3e** crystallizes in the orthorhombic space group $P2_12_12_1$ and absolute configuration was determined by anomalous dispersion (Flack = -0.15(8)).^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.71 (d, *J* = 2.4 Hz, 1H), 8.16 – 8.10 (m, 1H), 8.07 (d, *J* = 2.3 Hz, 1H), 7.81 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.77 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.61 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.33 – 7.27 (m, 3H), 7.17 – 7.11 (m, 2H), 4.32 – 4.25 (m, 1H), 3.36 – 3.23 (m, 2H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 149.35, 147.68, 135.32, 134.61, 130.18, 129.35, 129.29, 128.84, 127.96, 127.80, 127.76, 127.49, 127.45, 119.51, 41.90, 37.50; IR (NaCl/thin film): 3029.15, 2925.55, 2855.78, 2242.14, 1604.24, 1571.67, 1495.10, 1455.39, 1382.41, 1125.96, 908.49, 787.51, 752.04, 734.70, 699.30 cm^{-1}; $[\alpha]_D^{25}$ = -1.218 (*c* = 0.870, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 259.1230, found 259.1427.



Ethyl 4-cyano-4-(quinolin-3-yl)butanoate (3f)

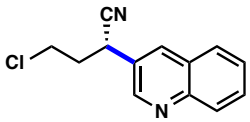


Prepared from 3-iodoquinoline (51.2 mg, 0.2 mmol) and ethyl 4-chloro-4-cyanobutyrate (35.1 mg, 0.2 mmol) following General Procedure 3.

[1] Sheldrick, G. M. *Acta Cryst.* **1990**, *A46*, 467.
[2] Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112.
[3] Müller, P. *Crystallography Reviews* **2009**, *15*, 57.

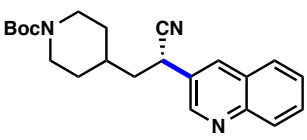
The crude residue was purified by silica gel chromatography (0:100 to 30:70 EtOAc:hexanes) to yield 34.0 mg (63% yield) of **3f** as a clear oil. The enantiomeric excess was determined to be 80% by chiral SFC analysis (AD, 2.5 mL/min, 12% IPA in CO_2, λ = 254 nm): t_R(major) = 7.2 min, t_R(minor) = 8.3 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.91 (s, 1H), 8.20 (s, 2H), 7.86 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.77 (d, *J* = 6.7 Hz, 1H), 7.61 (dd, *J* = 8.1, 6.8 Hz, 1H), 4.28 (dd, *J* = 8.7, 6.0 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.62 (dt, *J* = 16.9, 7.5 Hz, 1H), 2.53 (dt, *J* = 17.0, 6.5 Hz, 1H), 2.41 – 2.21 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 171.81, 149.29, 148.04, 134.40, 130.30, 129.54, 128.12, 127.83, 127.61, 127.59, 119.40, 61.01, 34.27, 30.92, 30.72, 14.17; IR (NaCl/thin film): 2979.77, 2926.59, 2242.45, 1731.81, 1495.27, 1377.67, 1312.77, 1189.37, 1024.39, 909.00, 788.82, 754.73 cm^{-1}; $[\alpha]_D^{25}$ = -9.319 (*c* = 0.860, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 269.1285, found 269.1313.

3-chloro-2-(quinolin-3-yl)propanenitrile (3g)



Prepared from 3-iodoquinoline (102.4 mg, 0.4 mmol) and 2,4-dichlorobutanenitrile (27.6 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 30:70 EtOAc:hexanes) to yield 35.8 mg (78% yield) of **3g** as a clear oil that slowly solidified on standing. The enantiomeric excess was determined to be 79% by chiral SFC analysis (AD, 2.5 mL/min, 12% IPA in CO_2, λ = 254 nm): t_R(major) = 7.1 min, t_R(minor) = 9.7 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.88 (d, *J* = 2.4 Hz, 1H), 8.22 (d, *J* = 2.4 Hz, 1H), 8.14 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.90 – 7.83 (m, 1H), 7.78 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.63 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 4.41 (dd, *J* = 8.6, 6.7 Hz, 1H), 3.79 (ddd, *J* = 11.5, 8.2, 4.6 Hz, 1H), 3.60 (ddd, *J* = 11.4, 6.4, 4.8 Hz, 1H), 2.54 (dddd, *J* = 14.4, 8.7, 6.5, 4.5 Hz, 1H), 2.40 (dddd, *J* = 14.4, 8.2, 6.7, 4.8 Hz, 1H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 149.09, 147.92, 134.63, 130.42, 129.44, 127.77, 127.71, 127.51, 127.27, 119.08, 41.02, 38.07, 32.28; IR (NaCl/thin film): 2960.74, 2922.28, 2242.62, 1571.06, 1495.00, 1443.08, 1382.69, 1125.91, 957.61, 906.20, 787.55, 753.85, 619.73 cm^{-1}; $[\alpha]_D^{25}$ = +9.150 (*c* = 0.665, $CHCl_3$). HRMS (MM) calc'd for $[M+H_3O]^+$ 249.0789, found 249.0270.

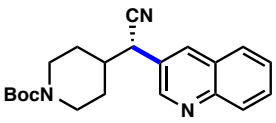
***tert*-butyl-4-(2-cyano-2-(quinolin-3-yl)ethyl)piperidine-1-carboxylate (3h)**



Prepared from 3-iodoquinoline (51.2 mg, 0.2 mmol) and *tert*-Butyl-4-(2-chloro-2-cyanoethyl)piperidine-1-carboxylate (54.6 mg, 0.2 mmol)

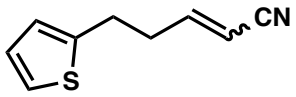
following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 40:60 EtOAc:hexanes) to yield 44.7 mg (61% yield) of **3h** as a clear oil. The enantiomeric excess was determined to be 89% by chiral SFC analysis (AD, 2.5 mL/min, 25% IPA in CO_2, λ = 280 nm): t_R(major) = 4.8 min, t_R(minor) = 6.0 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.81 (d, *J* = 2.3 Hz, 1H), 8.18 (d, *J* = 2.3 Hz, 1H), 8.12 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.84 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.76 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.60 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H), 4.10 (br, dd, *J* = 10.1, 5.6 Hz, 3H), 2.72 (br, 2H), 2.13 – 1.99 (m, 1H), 1.94 – 1.63 (m, 4H), 1.46 (s, 9H), 1.33 – 1.12 (m, 2H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 154.68, 149.12, 147.72, 134.10, 130.21, 129.37, 128.78, 127.73, 127.60, 127.58, 119.77, 79.55, 43.88 (br), 43.20 (br), 42.58, 33.99, 32.58, 32.10, 31.22, 28.44; IR (NaCl/thin film): 2974.27, 2926.66, 2852.75, 2239.98, 1685.09, 1495.27, 1424.19, 1365.34, 1278.99, 1244.13, 1163.05, 1125.17, 970.82, 865.20, 787.79, 755.04, 736.24, 620.45 cm^{-1}; $[\alpha]_D^{25}$ = -4.158 (*c* = 1.900, $CHCl_3$). HRMS (MM) calc'd for $[M+Mg]^+$ 389.1948, found 389.2091.

***tert*-butyl-4-(cyano(quinolin-3-yl)methyl)piperidine-1-carboxylate (3i)**



Prepared from 3-iodoquinoline (51.2 mg, 0.2 mmol) and *tert*-Butyl-4-(chloro(cyano)methyl)piperidine-1-carboxylate (51.8 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 40:60 EtOAc:hexanes) to yield 28.6 mg (41% yield) of **3i** as a clear oil. The enantiomeric excess was determined to be 91% by chiral SFC analysis (AD, 2.5 mL/min, 12% IPA in CO_2, λ = 280 nm): t_R(minor) = 18.5 min, t_R(major) = 19.5 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.79 (d, *J* = 2.4 Hz, 1H), 8.16 (d, *J* = 2.3 Hz, 1H), 8.13 (dq, *J* = 8.5, 0.8 Hz, 1H), 7.86 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.77 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.62 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 4.19 (s, 2H), 3.94 (d, *J* = 6.8 Hz, 1H), 2.64 (s, 2H), 2.03 (tdd, *J* = 12.0, 6.9, 3.5 Hz, 1H), 1.88 – 1.71 (m, 1H), 1.67 (dt, *J* = 12.9, 3.0 Hz, 1H), 1.45 (s, 11H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 154.49, 149.48, 147.80, 135.05, 130.33, 129.37, 127.79, 127.66, 127.41, 126.70, 118.57, 79.85, 43.53, 42.89, 41.41, 41.34, 30.11, 28.80, 28.40; IR (NaCl/thin film): 2975.09, 2929.55, 2853.85, 2240.07, 1688.65, 1424.27, 1365.82, 1248.34, 1165.15, 1121.49, 1059.13, 756.02 cm^{-1}; $[\alpha]_D^{25}$ = -21.275 (*c* = 0.640, $CHCl_3$). HRMS (MM) calc'd for $[M+Mg]^+$ 377.1948, found 377.2042.

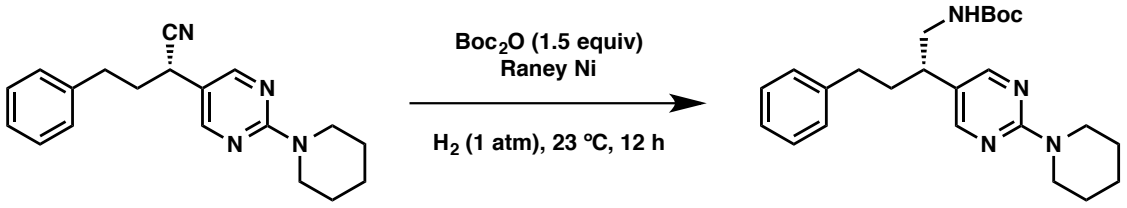
5-(thiophen-2-yl)pent-2-enenitrile (1:1 cis/trans) (12)



Prepared from 2-iodothiophene (11 μL, 0.1 mmol) and 2-chloro-2-cyclopropylacetonitrile (11.6 mg, 0.1 mmol) following General Procedure 3. The crude residue was purified by preperative thin layer chromatography (15:85 EtOAc:hexanes) to yield 3.5 mg (21% yield) of **12** as a clear oil as a 1:1 mixture of *cis*[*] and *trans*[§] isomers. Analysis of the crude NMR indicated no other conversion of the aryl iodide, with no cyclopropane-containing product detected. No unreacted chloronitrile was observed, presumably non-productive reaction pathways. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.16 (ddd, *J* = 5.1, 1.2, 0.7 Hz, 2H)[* §], 6.94 (ddd, *J* = 5.2, 3.4, 1.9 Hz, 2H)[* §], 6.86 – 6.77 (m, 2H)[* §], 6.73 (dt, *J* = 16.3, 6.9 Hz, 1H)[§], 6.50 (dt, *J* = 10.9, 7.5 Hz, 1H)[*], 5.45 – 5.27 (m, 2H)[* §], 3.02 (dtd, *J* = 15.6, 7.4, 0.8 Hz, 4H)[* §], 2.87 – 2.78 (m, 2H)[*], 2.62 (ddd, *J* = 7.7, 6.9, 1.7 Hz, 2H)[§]. ^{13}C NMR (126 MHz, cdcl$_3$) δ 153.94, 153.14, 142.38, 142.30, 126.95, 124.91, 123.78, 123.76, 100.98, 100.70, 35.11, 33.46, 28.43, 28.09; IR (NaCl/thin film): 2916.78, 2848.47, 2220.22, 1558.05, 1683.13, 848.26, 689.00, 668.02 cm^{-1}. HRMS (MM) calc'd for $[M]^+$ 163.0450, found 163.0765.

4. Synthesis of Enantioenriched Nitrile Derivatives.

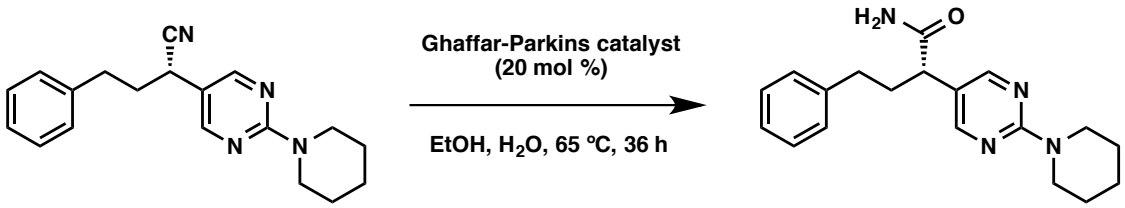
a. Hydrogenation of 7k over Raney Ni to Boc-amine 8.



Raney Ni (75 mg) was rinsed with dry MeOH 3 times to remove excess water and added to a flame-dried flask. To this was added dry MeOH (5 mL), 4-phenyl-2-(2-(piperidin-1-yl)pyrimidin-5-yl)butanenitrile (**7k**, 30 mg, 0.10 mmol, 85% ee), and Boc anhydride (33 mg, 0.15 mmol). The flask was purged with N_2 for 15 min, then flushed with two balloons of H_2. The flask was equipped with a balloon of H_2 and stirred for 3.5 hours. The reaction was then filtered over Celite with EtOAc to afford a viscous resinous clear oil. The crude residue was purified by silica gel chromatography (0:100 to 50:50 EtOAc:hexanes) to yield 39 mg (95% yield) of **8** as a clear oil that solidified slowly upon standing. The enantiomeric excess was determined to be

85% by chiral SFC analysis (AD, 2.5 mL/min, 15% IPA in CO_2, λ = 235 nm): t_R(major) = 10.5 min, t_R(minor) = 12.3 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.14 (s, 2H), 7.29 – 7.21 (m, 2H), 7.21 – 7.13 (m, 1H), 7.13 – 7.06 (m, 2H), 4.45 (s, 1H), 3.86 – 3.70 (m, 4H), 3.45 (dt, *J* = 13.1, 6.4 Hz, 1H), 3.12 (ddd, *J* = 13.9, 8.8, 5.4 Hz, 1H), 2.69 – 2.41 (m, 3H), 1.99 (dddd, *J* = 13.6, 9.8, 6.9, 4.8 Hz, 1H), 1.84 (dtd, *J* = 13.5, 9.8, 5.3 Hz, 1H), 1.74 – 1.55 (m, 6H), 1.40 (s, 9H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 161.26, 157.43, 155.82, 141.54, 128.42, 128.33, 125.93, 121.66, 79.40, 46.02, 44.85, 40.52, 34.57, 33.28, 28.34, 25.75, 24.84; IR (NaCl/thin film): 3337.97, 2930.35, 2853.42, 1712.79, 1602.18, 1504.75, 1449.34, 1364.47, 1271.22, 1255.54, 1169.92, 1028.05, 947.36, 798.75, 699.89 cm^{-1}; $[\alpha]_D^{25}$ = -15.883 (*c* = 2.365, $CHCl_3$). HRMS (MM) calc'd for $[M]^+$ 410.2676, found 410.2101.

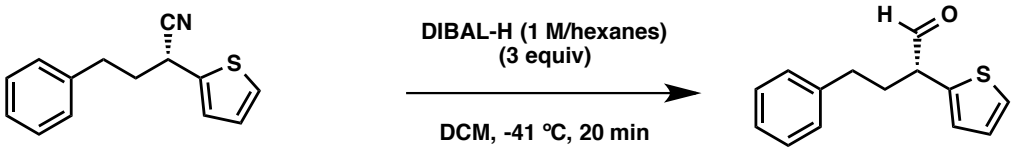
b. Hydrolysis of XX with Ghaffar-Parkins catalyst to carboxamide 9.



In a 1-dram vial, 4-phenyl-2-(2-(piperidin-1-yl)pyrimidin-5-yl)butanenitrile (**7k**, 30 mg, 0.10 mmol, 85% ee) was suspended in EtOH (0.4 mL) and H_2O (0.1 mL). To this was added hydrido(dimethylphosphinous acid-kP)[hydrogen bis(dimethylphosphinito-kP)]platinum(II) (9 mg, 20 μmol). The reaction was sealed with a Teflon-lined cap and heated to 65 ºC for 36 h. After cooling to room temperature, the reaction was diluted with DCM and filtered through a short plug of silica gel and Na_2SO_4. The plug was washed with additional DCM and the organics were concentrated to afford the carboxamide as a clear oil. The crude residue was purified by silica gel chromatography (30:70 to 60:40 EtOAc:hexanes) to yield 30.8 mg (95% yield) of **9** as a viscous clear oil. The enantiomeric excess was determined to be 85% by ^{1}H NMR using Europium(III) tris[3-(trifluoromethylhydroxymethylene)-*d*-camphorate] (30 mol %) as a chiral shift reagent. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.23 (s, 2H), 7.27 (d, *J* = 7.2 Hz, 2H), 7.22 – 7.16 (m, 1H), 7.16 – 7.11 (m, 2H), 5.66 (s, 1H), 5.45 (s, 1H), 3.92 – 3.61 (m, 4H), 3.12 (dd, *J* = 8.4, 6.8 Hz, 1H), 2.67 – 2.54 (m, 2H), 2.43 (ddt, *J* = 13.8, 8.7, 6.9 Hz, 1H), 2.12 – 1.97 (m, 1H), 1.68 (td, *J* = 6.7, 6.3, 4.7 Hz, 2H), 1.65 – 1.55 (m, 4H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 175.22,

161.24, 157.30, 140.84, 128.51, 126.13, 119.40, 46.14, 44.86, 34.06, 33.17, 25.72, 24.82; IR (NaCl/thin film): 3333.85, 3190.50, 2932.50, 2853.02, 1667.77, 1602.06, 1504.96, 1446.89, 1364.61, 1271.06, 1256.15, 1178.28, 1024.54, 947.10, 797.03, 733.36, 699.53 cm^{-1} $[\alpha]_D^{25}$ = +35.005 (*c* = 2.455, $CHCl_3$). HRMS (MM) calc'd for $[M]^+$ 324.1945, found 324.1904.

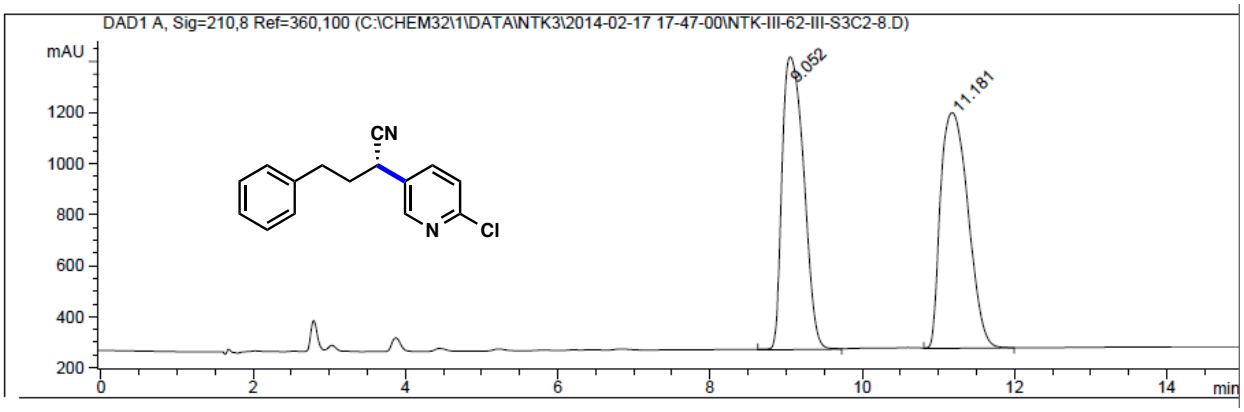
c. DIBAL-H reduction of 7n to carboxaldehyde 10.



To a flame-dried flask was added 4-phenyl-2-(thiophen-2-yl)butanenitrile (**7n**, 46 mg, 0.2 mmol, 88% ee) and DCM (30 mL). The reaction was cooled to -41 ºC and a 1 M solution of DIBAL-H in hexanes (3 equiv, 0.6 mL, 0.6 mmol) was added slowly via syringe. The reaction was complete by TLC after 20 min. A 5% AcOH/H_2O solution (12 mL) was added and the reaction was allowed to warm to room temperature. The reaction was stirred vigorously for 30 min and then the layers were separated. The organics were washed with dilute sodium bicarbonate, dried over sodium sulfate, and concentrated to afford light yellow oil. The crude residue was purified by silica gel chromatography (0:100 to 10:90 EtOAc:hexanes) to yield 44 mg (96% yield) of **10** as a yellow oil that was stored frozen in benzene. The enantiomeric excess was determined to be 81% by chiral SFC analysis (AD, 2.5 mL/min, 8% IPA in CO_2, λ = 235 nm): t_R(minor) = 4.5 min, t_R(major) = 5.1 min. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.61 (d, *J* = 2.1 Hz, 1H), 7.34 – 7.28 (m, 3H), 7.25 – 7.20 (m, 1H), 7.18 (dq, *J* = 7.6, 0.7 Hz, 2H), 7.07 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.95 (ddd, *J* = 3.5, 1.2, 0.7 Hz, 1H), 3.79 (ddd, *J* = 8.4, 6.3, 2.1 Hz, 1H), 2.73 (ddd, *J* = 14.4, 9.0, 5.7 Hz, 1H), 2.64 (ddd, *J* = 13.8, 8.8, 7.0 Hz, 1H), 2.43 (dddd, *J* = 13.6, 9.0, 7.1, 6.3 Hz, 1H), 2.17 – 2.07 (m, 1H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 198.65, 140.80, 138.31, 128.54, 128.52, 127.54, 126.43, 126.22, 125.56, 52.86, 32.84, 32.05; IR (NaCl/thin film): 3025.79, 2924.74, 1725.05, 1496.21, 1454.03, 750.13, 699.05 cm^{-1}; $[\alpha]_D^{25}$ = +4.156 (*c* = 0.70, $CHCl_3$). HRMS (MM) calc'd for $[M]^+$ 410.2676, found 410.2101.

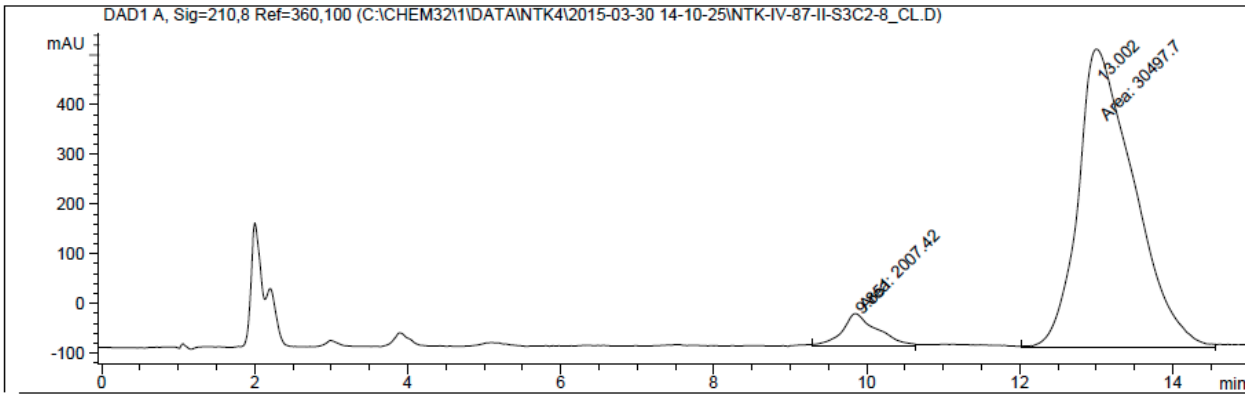
5. SFC traces for racemic and enantioenriched benzylic nitriles.

7a racemic



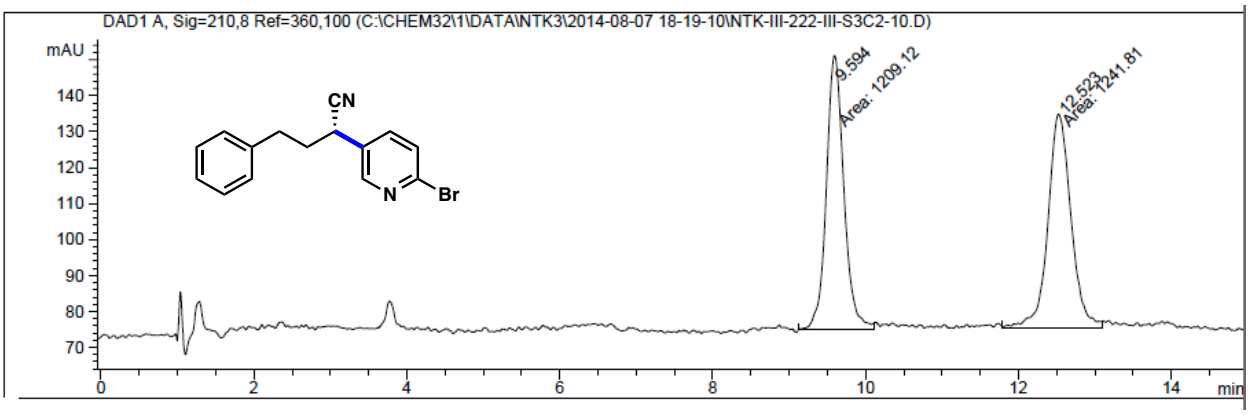
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.052	VV	0.3272	2.27197e4	1146.29651	49.3947
2	11.181	VB	0.4161	2.32765e4	923.30292	50.6053

7a enantioenriched, 88% ee



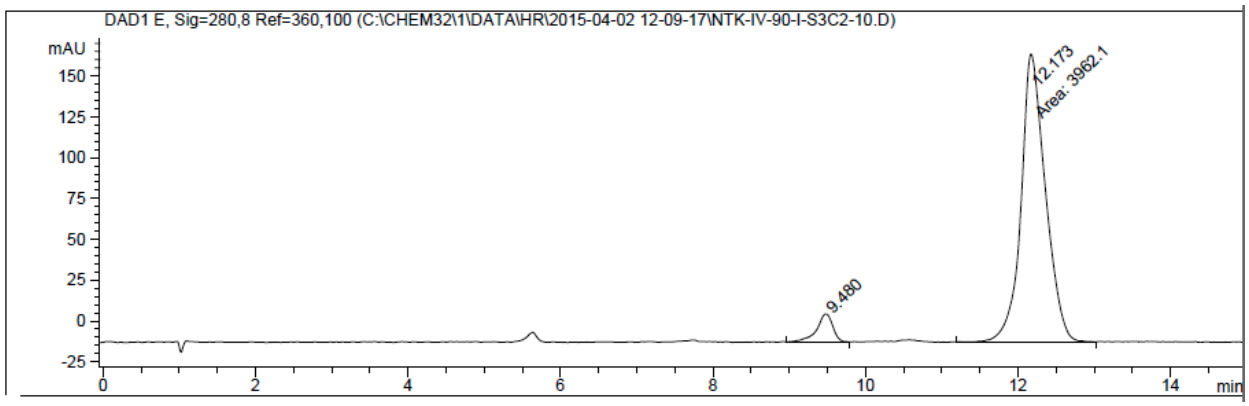
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.851	MM	0.5217	2007.42126	64.13335	6.1757
2	13.002	MM	0.8480	3.04977e4	599.40063	93.8243

7b racemic



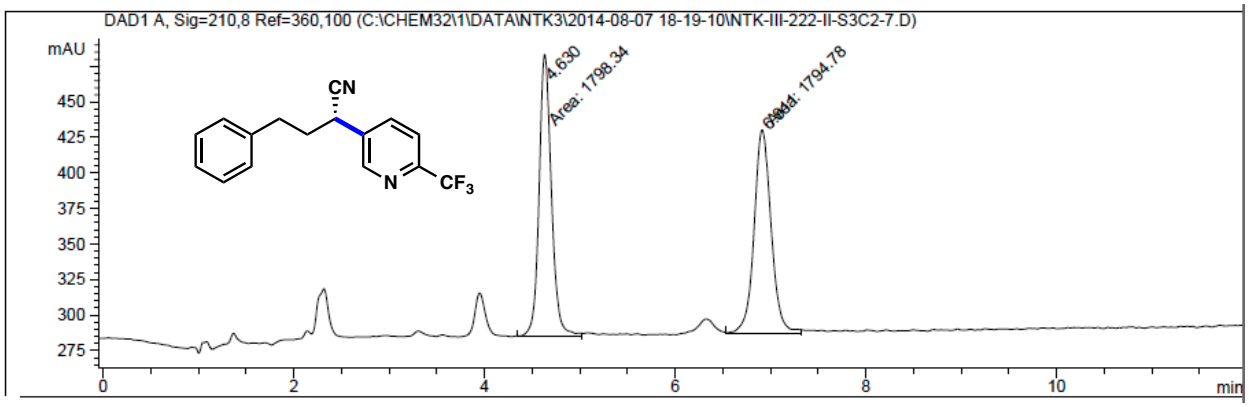
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.594	MM	0.2648	1209.12439	76.09144	49.3331
2	12.523	MM	0.3485	1241.81299	59.39444	50.6669

7b enantioenriched, 88% ee



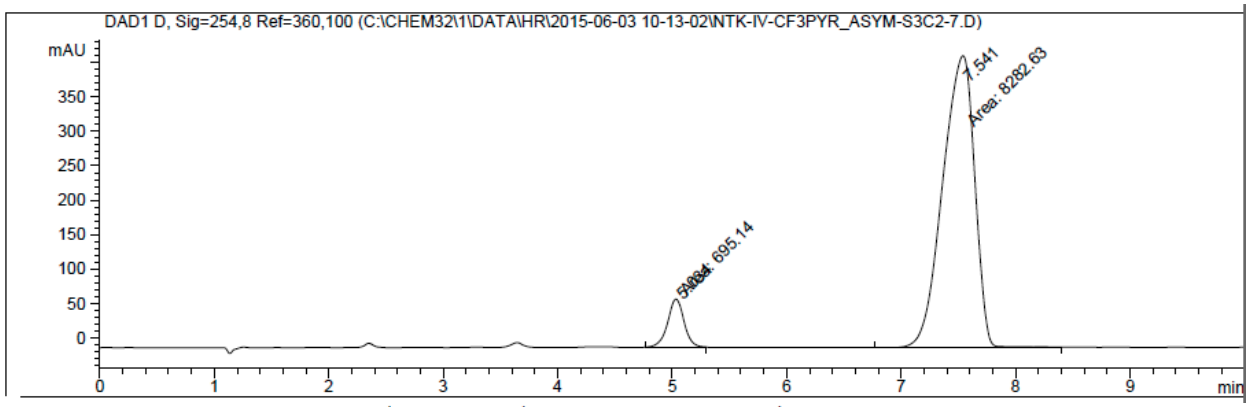
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.480	VV	0.2212	263.66074	17.35826	6.2394
2	12.173	MM	0.3738	3962.10059	176.66771	93.7606

7c racemic



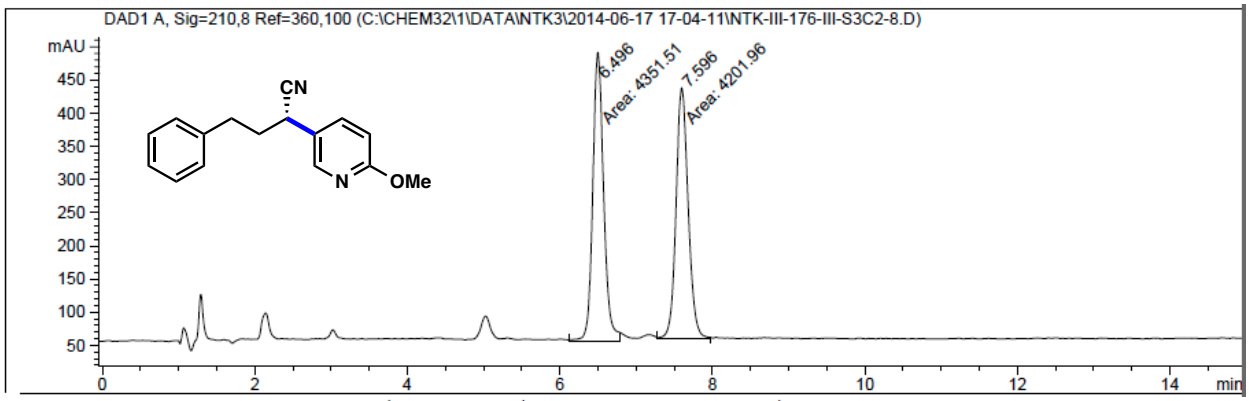
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.630	MM	0.1506	1798.33630	198.96516	50.0494
2	6.911	MM	0.2083	1794.78406	143.62846	49.9506

7c enantioenriched, 85% ee



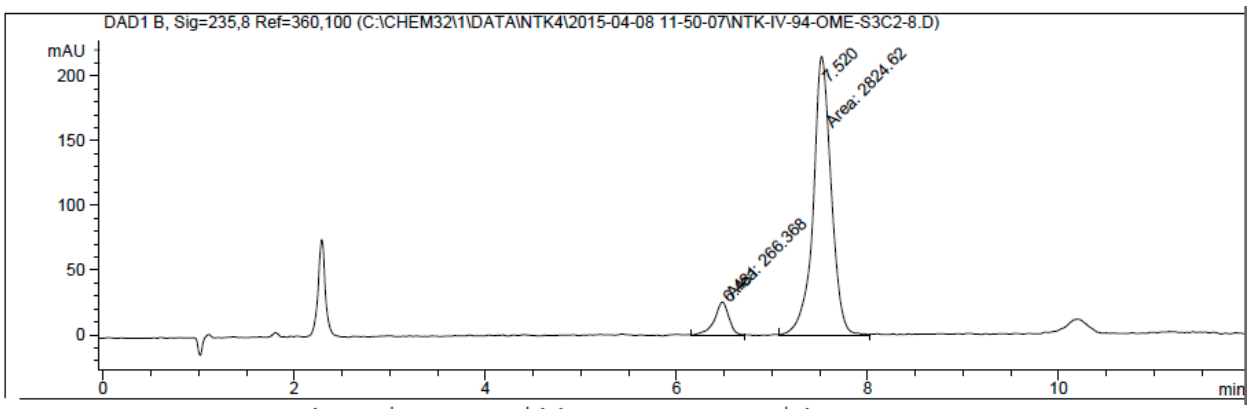
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.034	MM	0.1653	695.13959	70.09489	7.7429
2	7.541	MM	0.3253	8282.63379	424.41962	92.2571

7d racemic



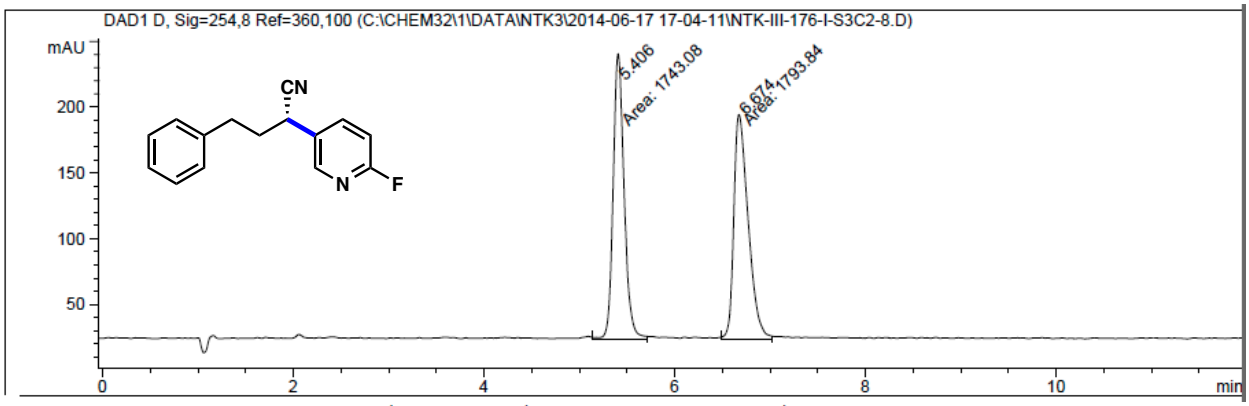
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.496	MM	0.1660	4351.50586	436.96753	50.8742
2	7.596	MM	0.1850	4201.95898	378.58496	49.1258

7d enantioenriched, 83% ee



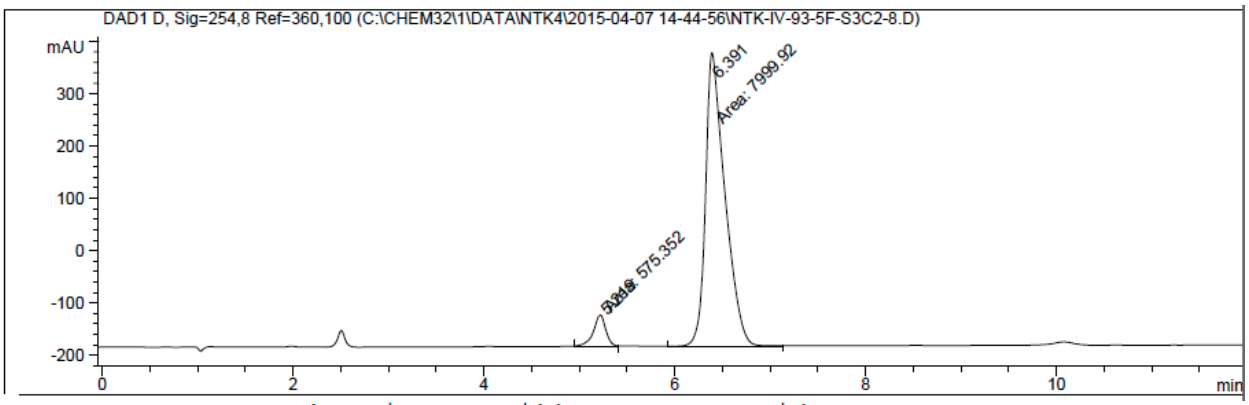
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.481	MM	0.1741	266.36813	25.50070	8.6176
2	7.520	MM	0.2185	2824.61865	215.49197	91.3824

7e racemic



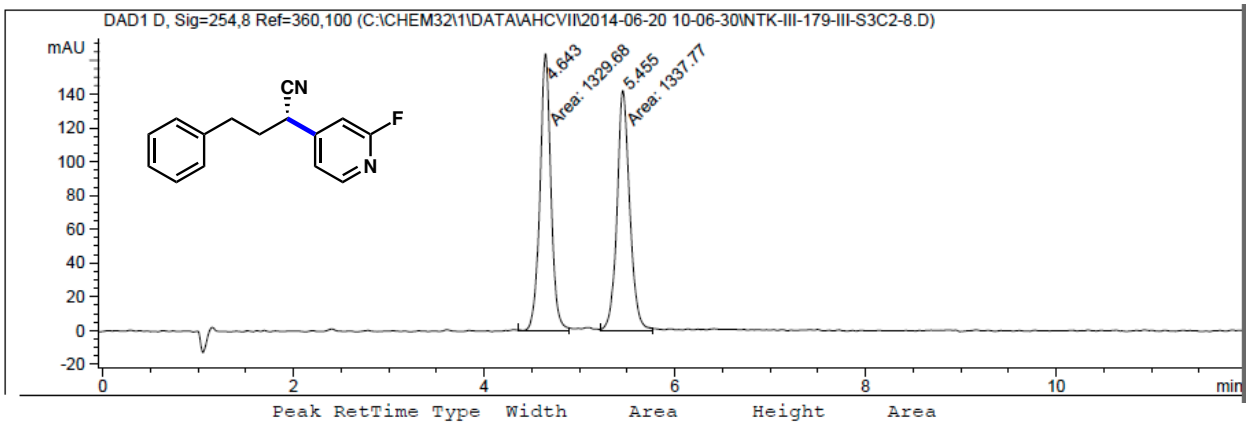
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.406	MM	0.1336	1743.07617	217.40483	49.2824
2	6.674	MM	0.1749	1793.83582	170.96077	50.7176

7e enantioenriched, 87% ee



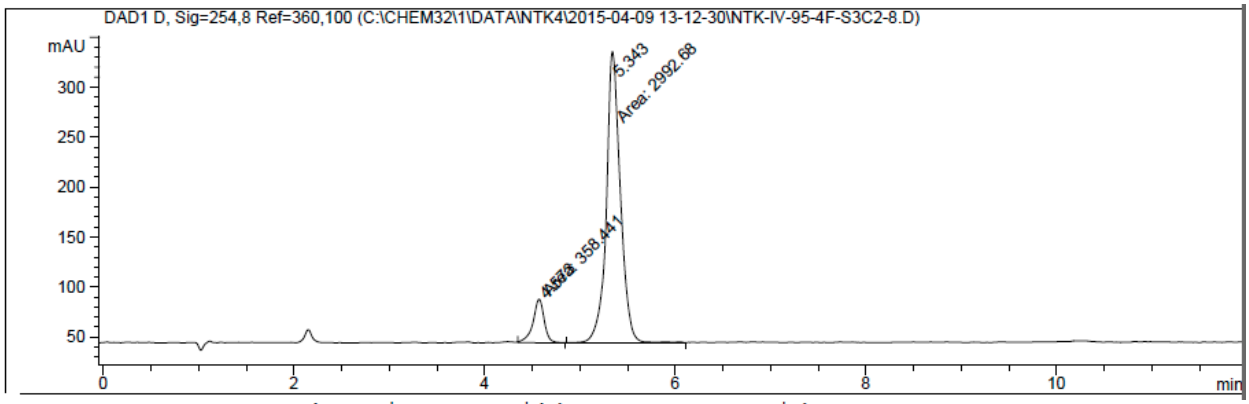
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.219	MM	0.1568	575.35193	61.17109	6.7094
2	6.391	MM	0.2369	7999.91992	562.87573	93.2906

7f racemic



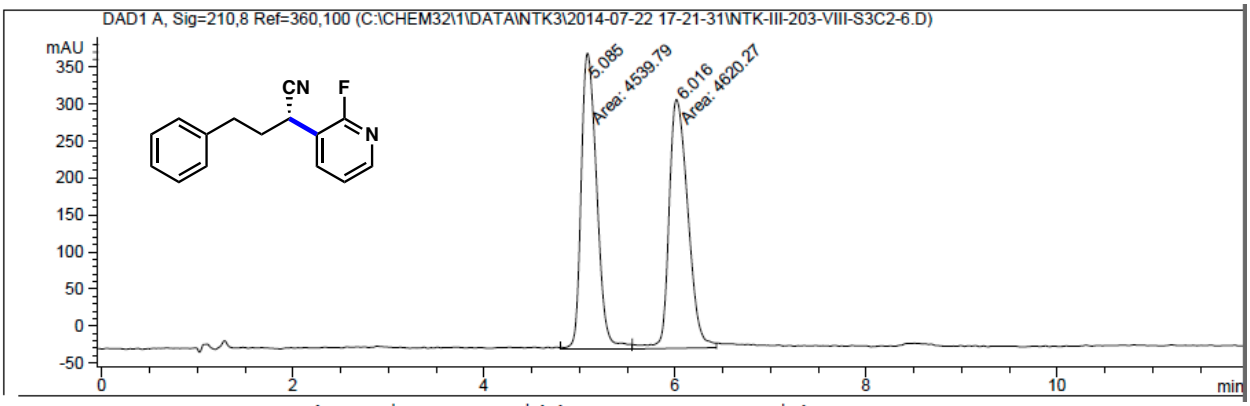
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.643	MM	0.1346	1329.67908	164.60115	49.8483
2	5.455	MM	0.1563	1337.77344	142.69563	50.1517

7f enantioenriched, 79% ee



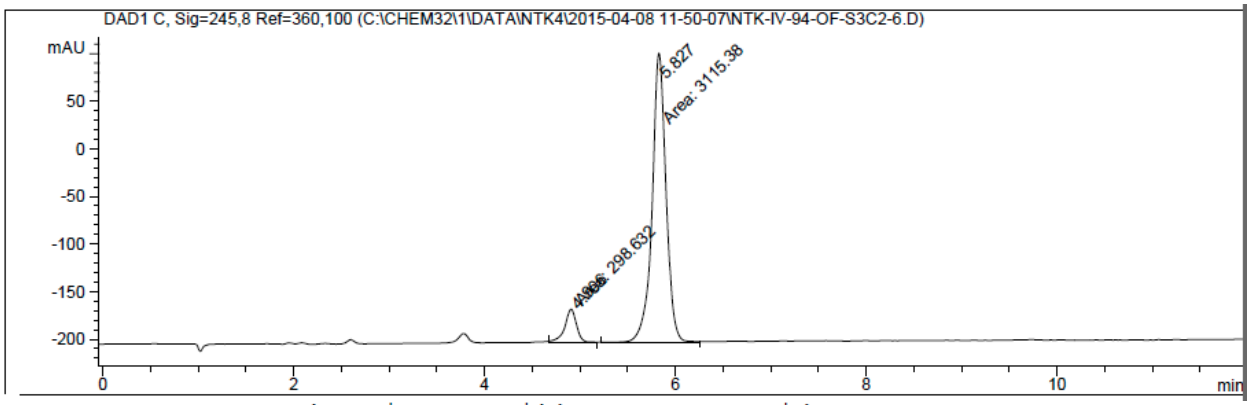
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.573	MM	0.1370	358.44107	43.60704	10.6961
2	5.343	MM	0.1709	2992.68384	291.82959	89.3039

7g racemic



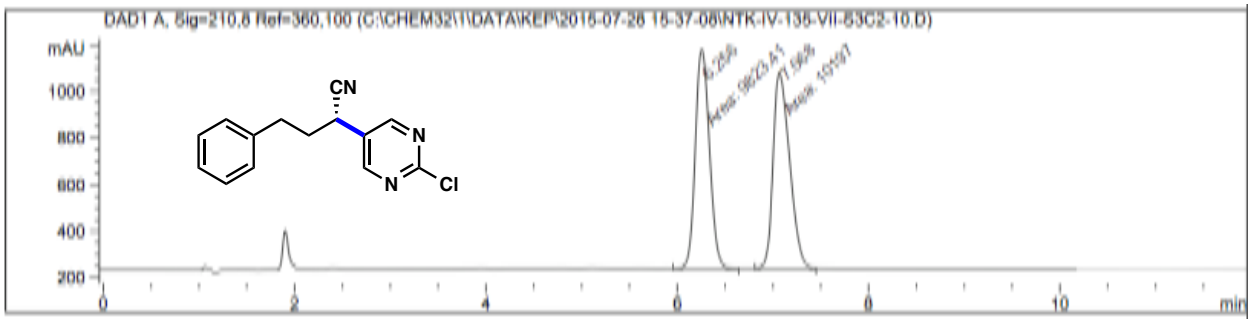
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.085	MM	0.1892	4539.78711	399.84052	49.5607
2	6.016	MM	0.2290	4620.26758	336.27573	50.4393

7g enantioenriched, 83% ee



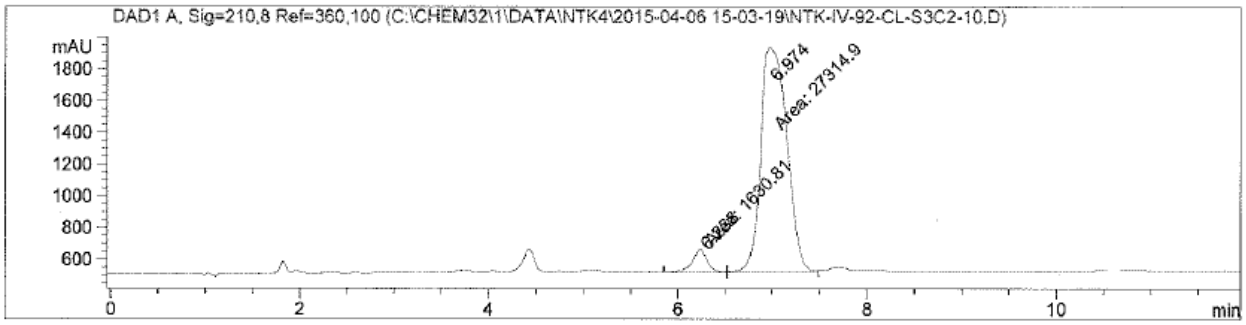
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.906	MM	0.1426	298.63181	34.89790	8.7472
2	5.827	MM	0.1706	3115.37988	304.37155	91.2528

7h racemic



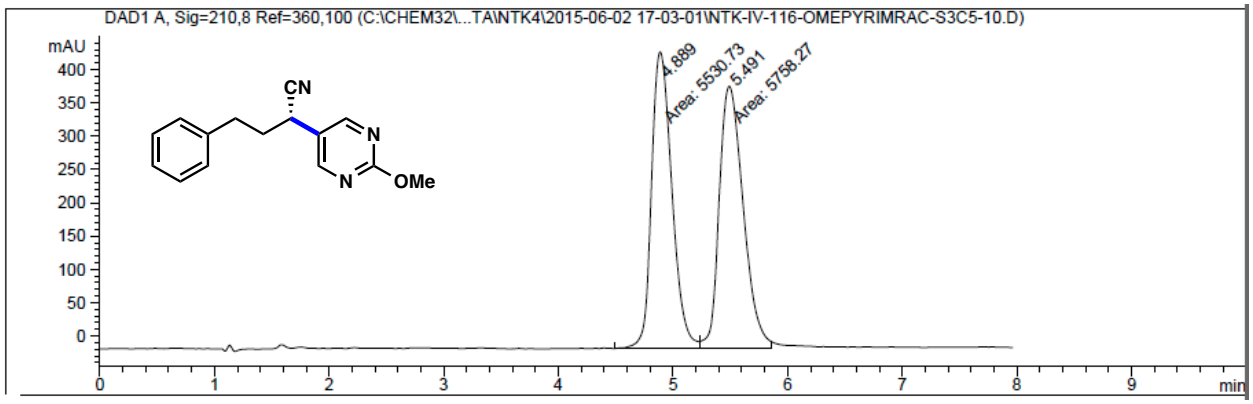
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.256	MM	0.1735	9823.40918	943.89240	49.0671
2	7.068	MM	0.2022	1.01970e4	840.62567	50.9329

7h enantioenriched, 89% ee



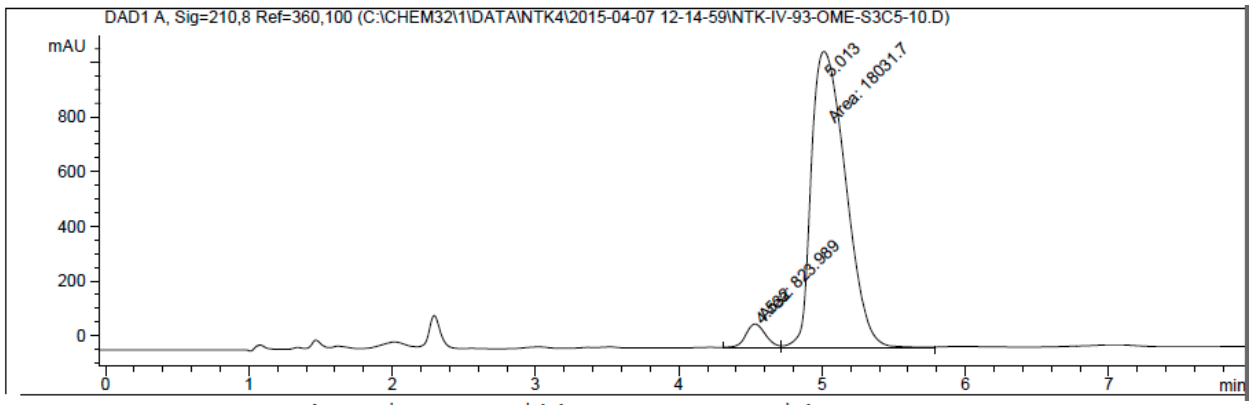
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.238	MM	0.1881	1630.80823	144.48898	5.6340
2	6.974	MM	0.3226	2.73149e4	1411.04395	94.3660

7i racemic



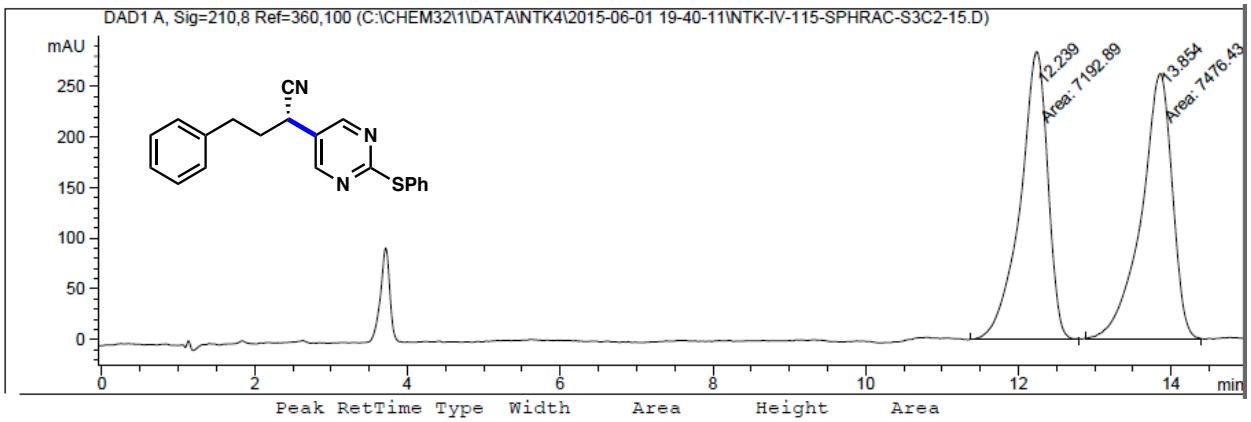
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.889	MM	0.2066	5530.73438	446.19595	48.9922
2	5.491	MM	0.2432	5758.27148	394.62100	51.0078

7i enantioenriched, 92% ee



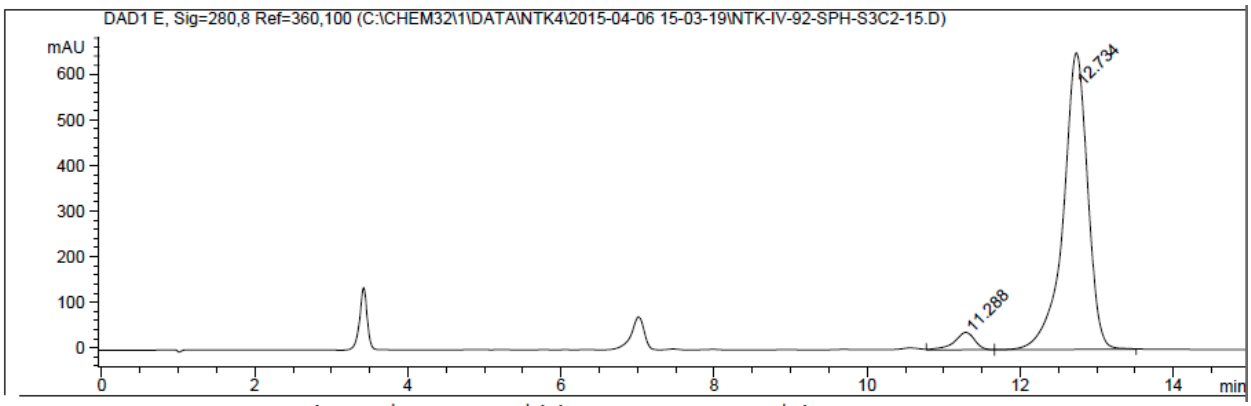
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.532	MM	0.1591	823.98859	86.30779	4.3700
2	5.013	MM	0.2775	1.80317e4	1083.14832	95.6300

7j racemic



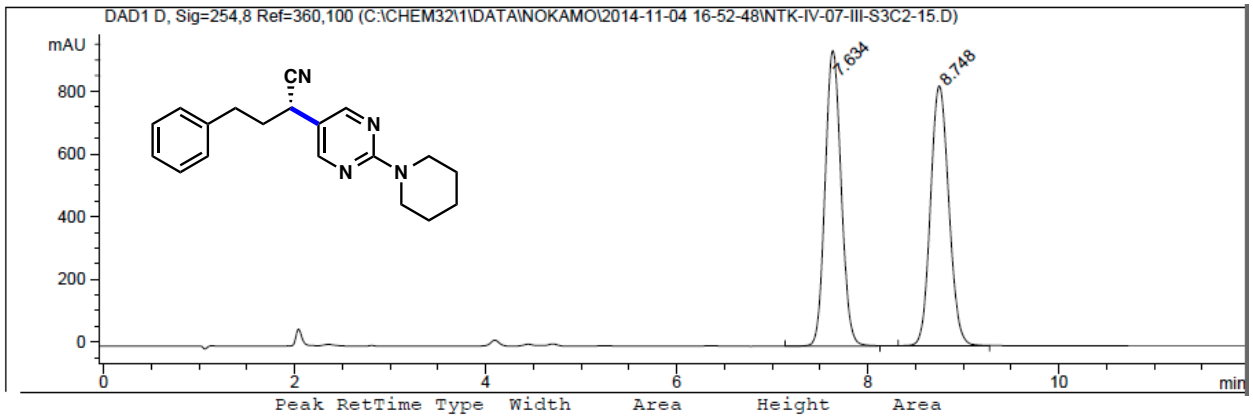
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.239	MM	0.4208	7192.89307	284.88919	49.0336
2	13.854	MM	0.4732	7476.43115	263.30313	50.9664

7j enantioenriched, 91% ee



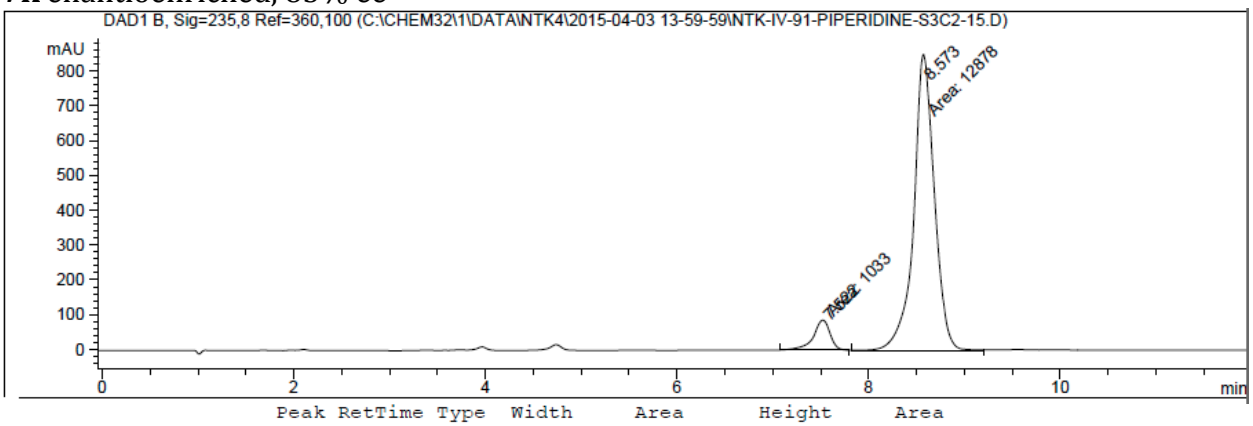
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.288	VV	0.2780	705.39868	38.10340	4.6587
2	12.734	VB	0.3328	1.44360e4	650.73560	95.3413

7k racemic



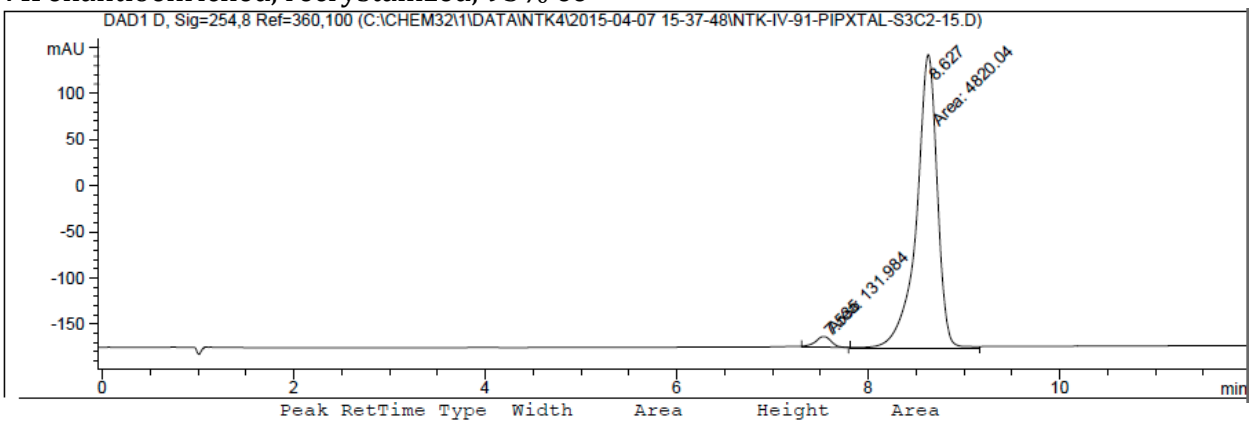
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.634	BB	0.1820	1.10005e4	943.78931	49.8831
2	8.748	VB	0.2095	1.10520e4	829.41107	50.1169

7k enantioenriched, 85% ee



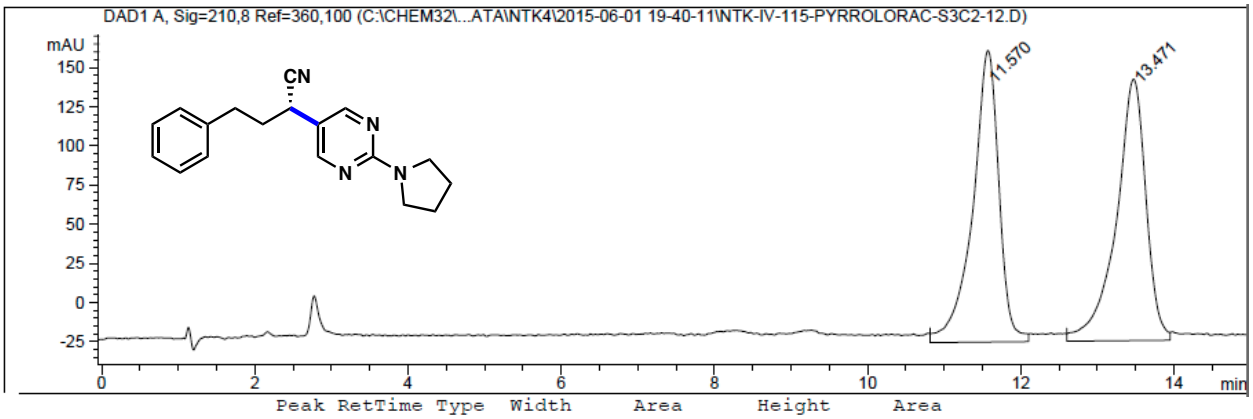
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.522	MM	0.2003	1033.00146	85.96810	7.4258
2	8.573	MM	0.2520	1.28780e4	851.85858	92.5742

7k enantioenriched, recrystallized, 95% ee



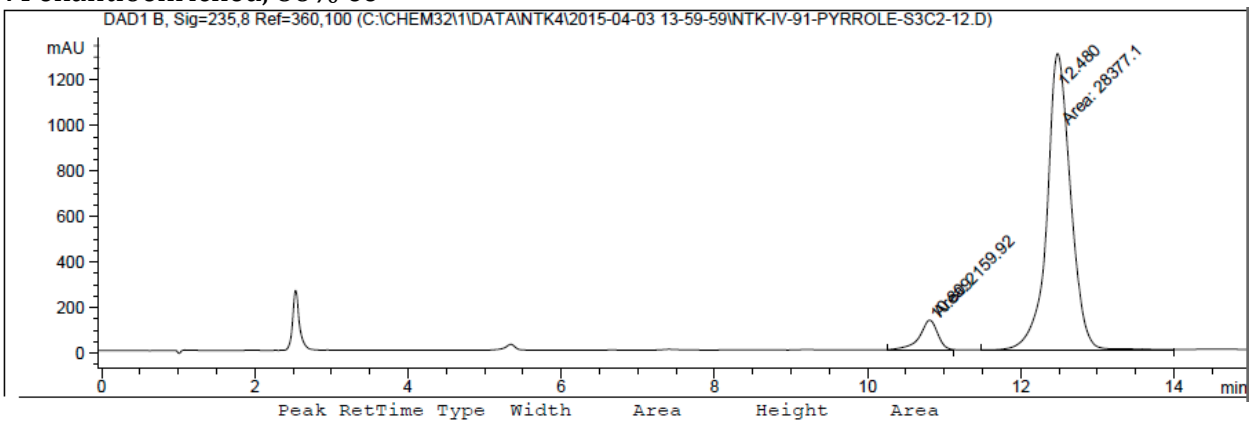
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.535	MM	0.1884	131.98436	11.67368	2.6653
2	8.627	MM	0.2526	4820.03613	318.05377	97.3347

7l racemic



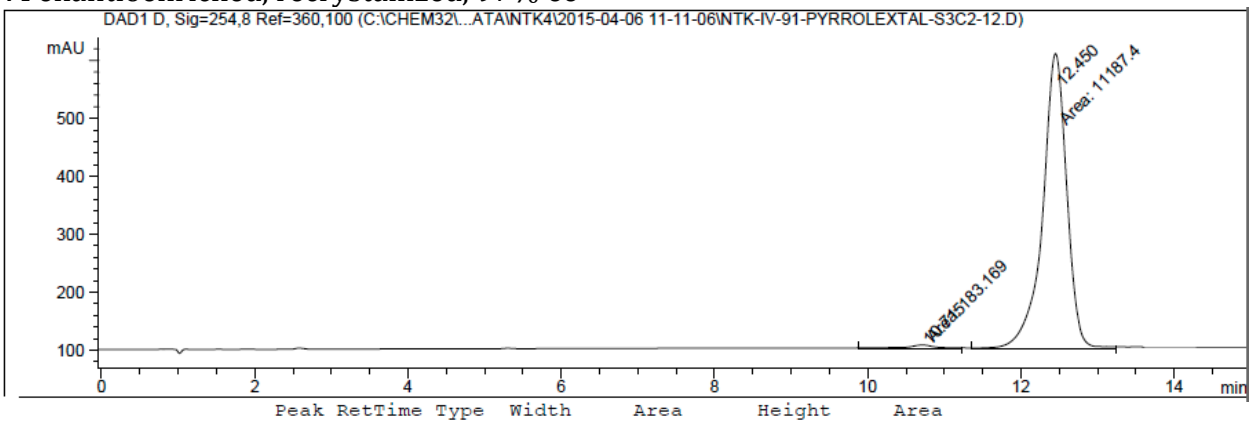
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.570	VV	0.3457	4429.45020	186.09850	49.4778
2	13.471	VV	0.3942	4522.94775	166.88538	50.5222

7l enantioenriched, 86% ee



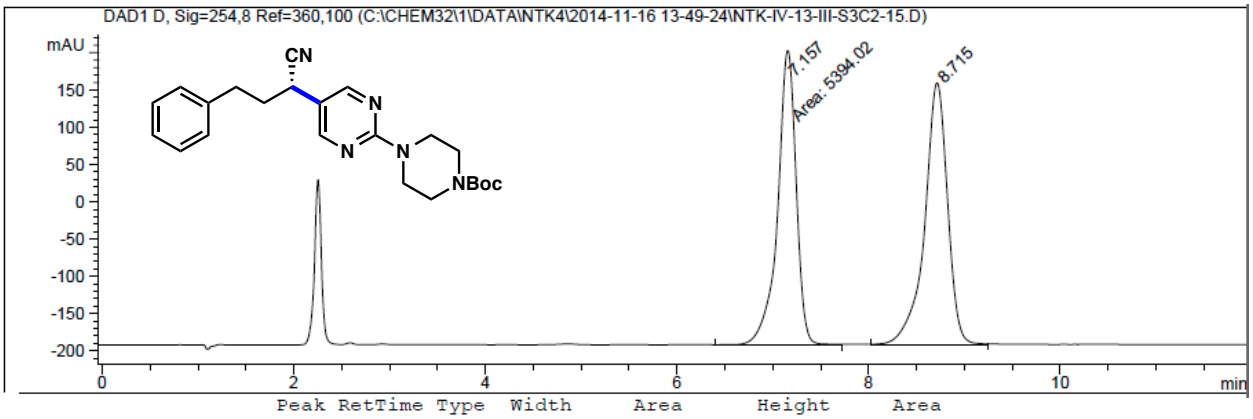
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.809	MM	0.2757	2159.91553	130.55109	7.0731
2	12.480	MM	0.3627	2.83771e4	1304.11511	92.9269

7l enantioenriched, recrystallized, 97% ee



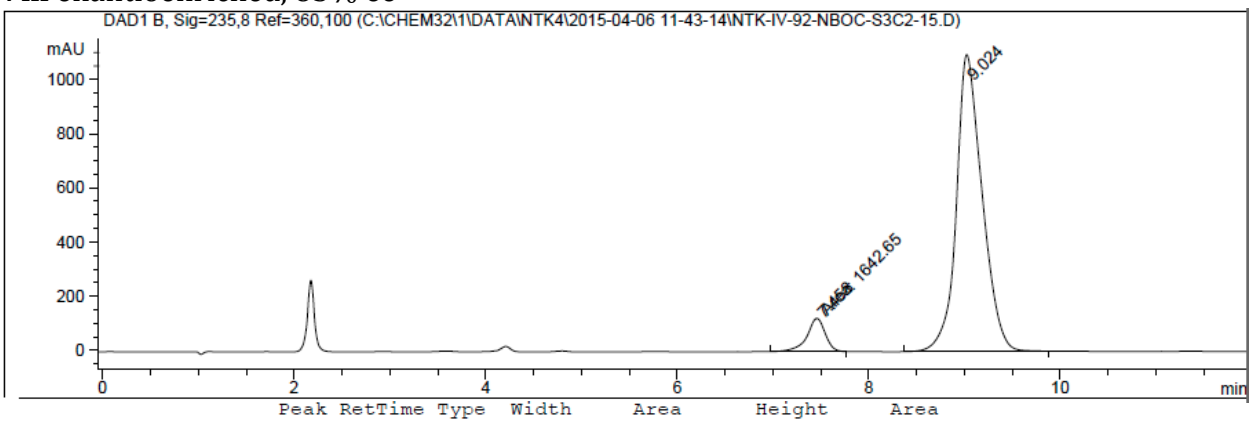
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.715	MM	0.4992	183.16939	6.11533	1.6109
2	12.450	MM	0.3661	1.11874e4	509.26865	98.3891

7m racemic



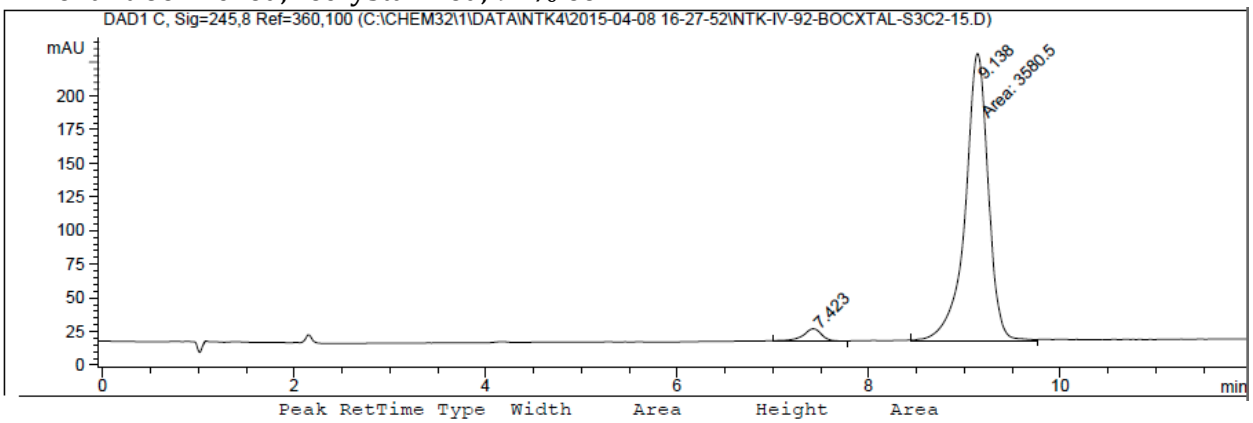
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.157	MM	0.2271	5394.01611	395.87903	48.0826
2	8.715	BB	0.2497	5824.20361	350.83545	51.9174

7m enantioenriched, 85% ee



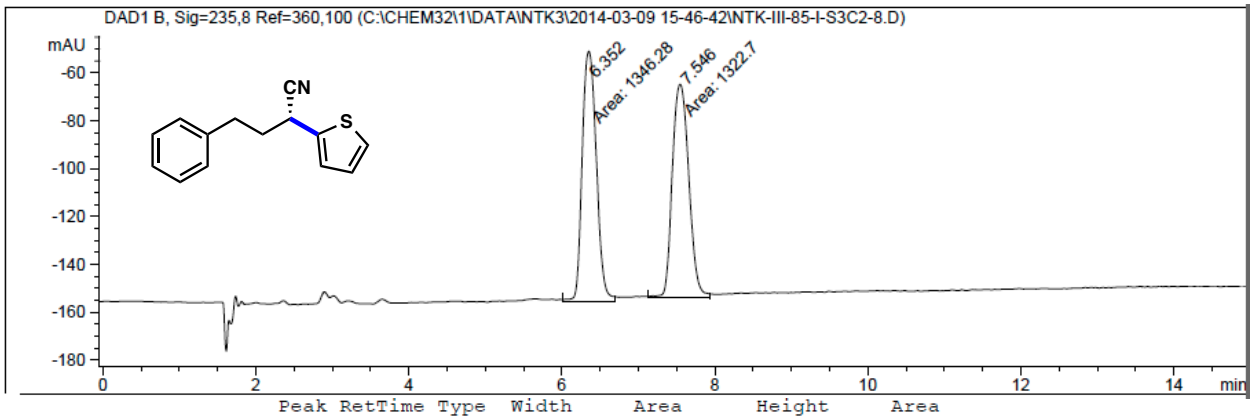
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.458	MM	0.2224	1642.64941	123.07285	7.3549
2	9.024	BV	0.2820	2.06913e4	1097.45300	92.6451

7m enantioenriched, recrystallized, 94% ee



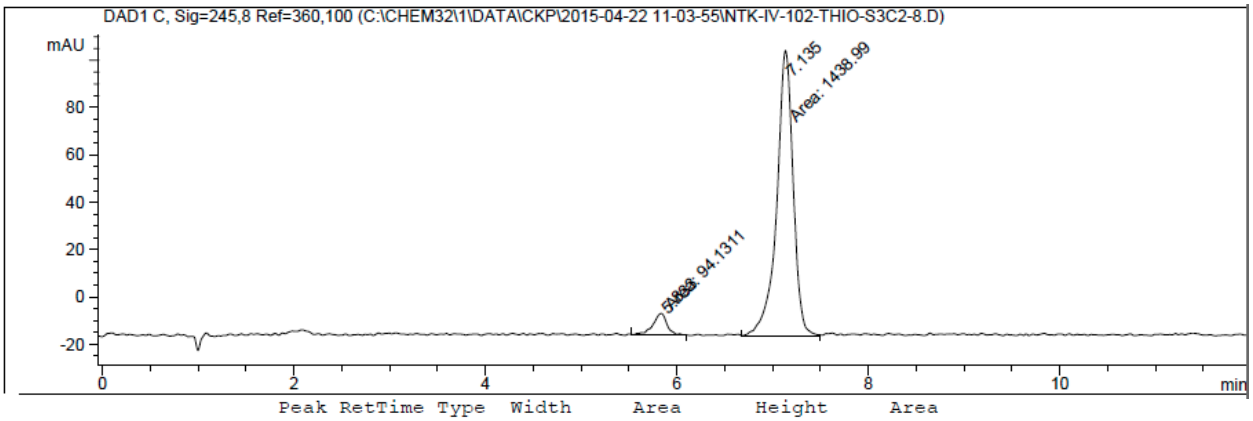
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.423	BB	0.1980	118.74174	8.99407	3.2099
2	9.138	MM	0.2796	3580.49634	213.42770	96.7901

7n racemic



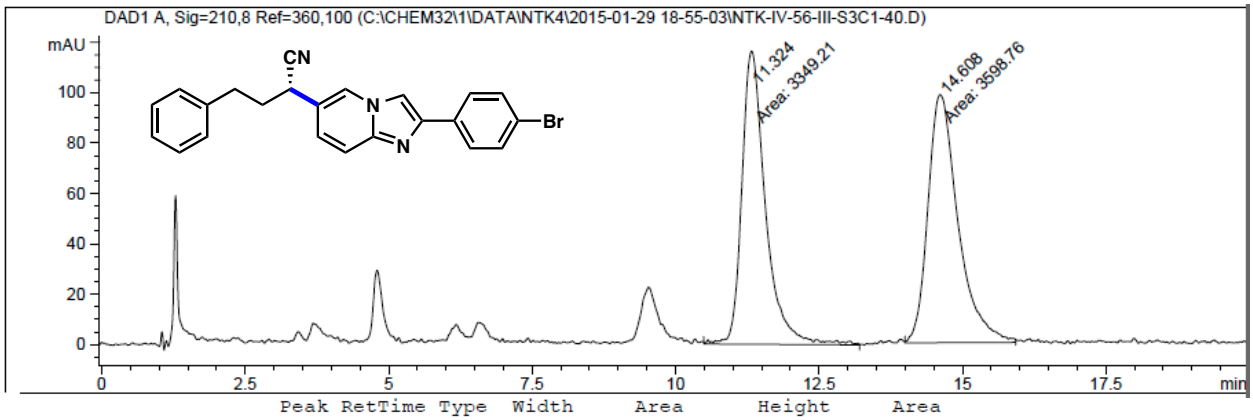
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.352	MM	0.2148	1346.28333	104.44119	50.4418
2	7.546	MM	0.2483	1322.70227	88.79099	49.5582

7n enantioenriched, 88% ee



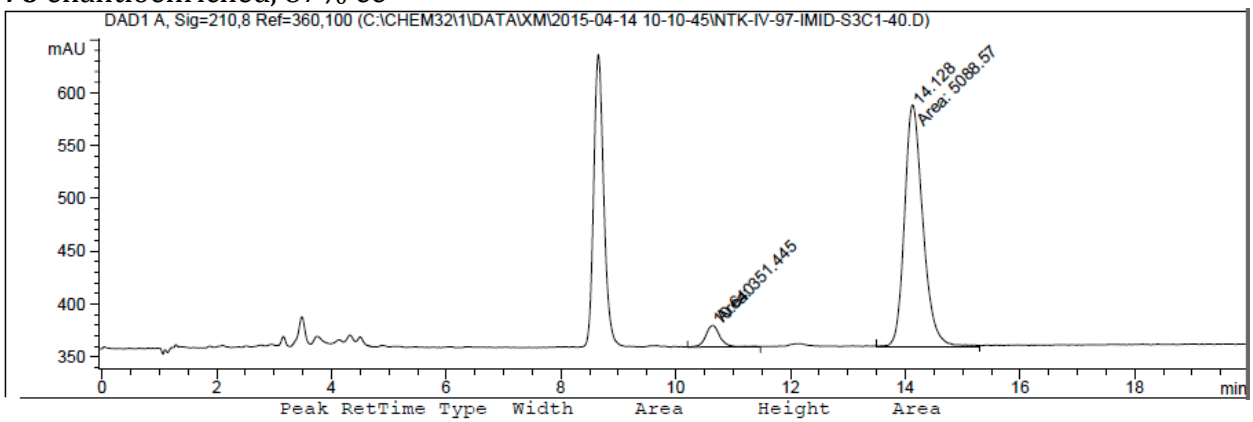
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.833	MM	0.1721	94.13110	9.11540	6.1398
2	7.135	MM	0.1990	1438.99097	120.52435	93.8602

7o racemic



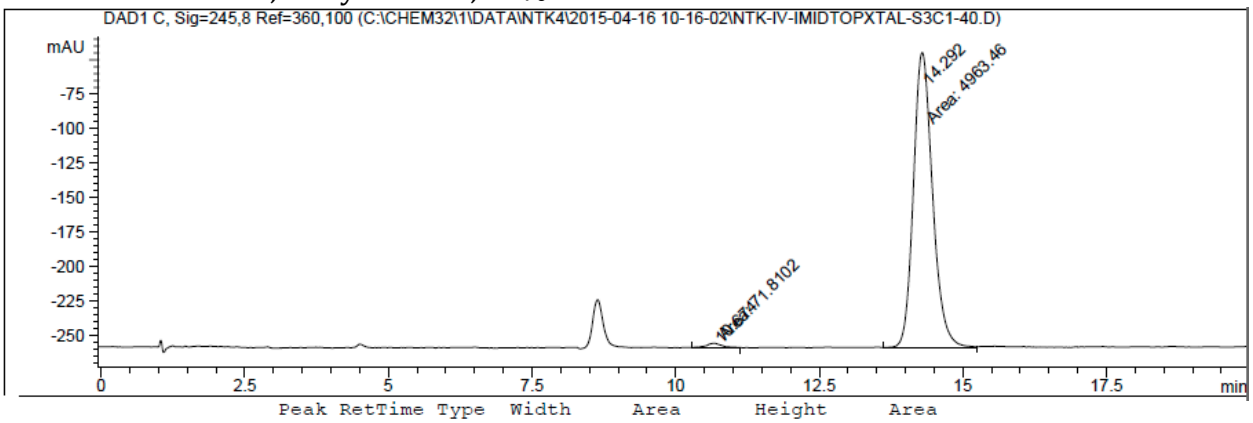
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.324	MM	0.4796	3349.21387	116.39689	48.2042
2	14.608	MM	0.6086	3598.75928	98.55891	51.7958

7o enantioenriched, 87% ee



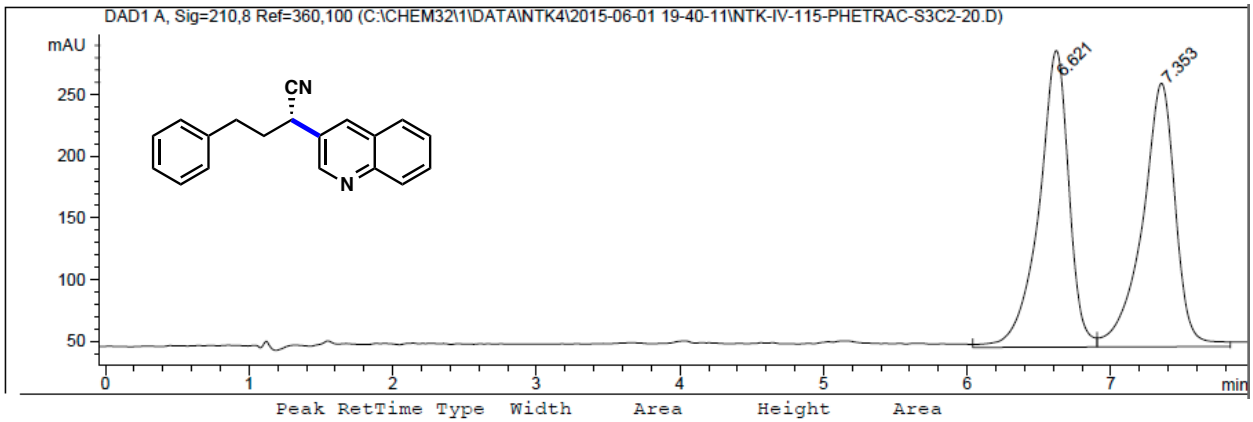
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.640	MM	0.2855	351.44522	20.51827	6.4604
2	14.128	MM	0.3712	5088.56689	228.46791	93.5396

7o enantioenriched, recrystallized, 97% ee



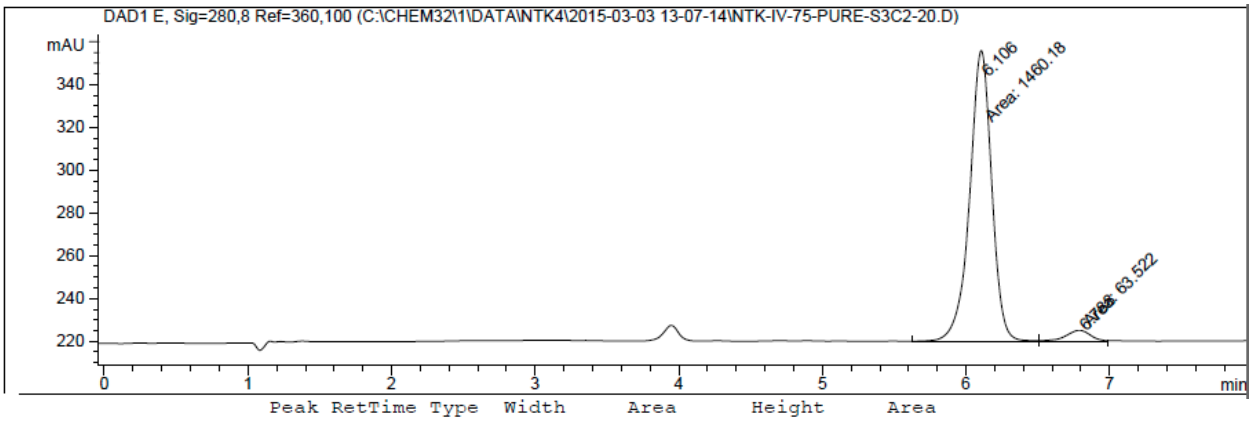
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.674	MM	0.3581	71.81017	3.34204	1.4261
2	14.292	MM	0.3870	4963.45557	213.77559	98.5739

3a racemic



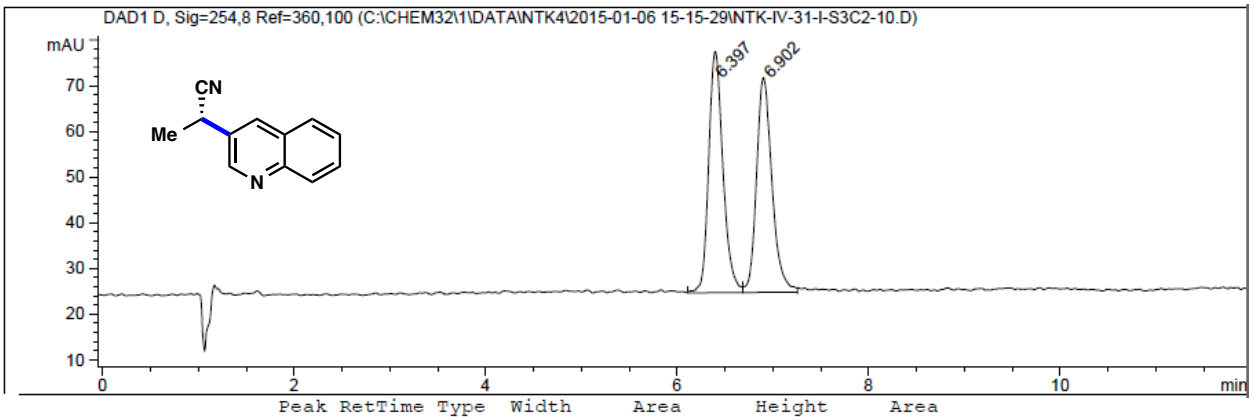
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.621	VV	0.2121	3510.11963	240.77718	50.5322
2	7.353	VB	0.2374	3436.18848	213.96890	49.4678

3a enantioenriched, 92% ee



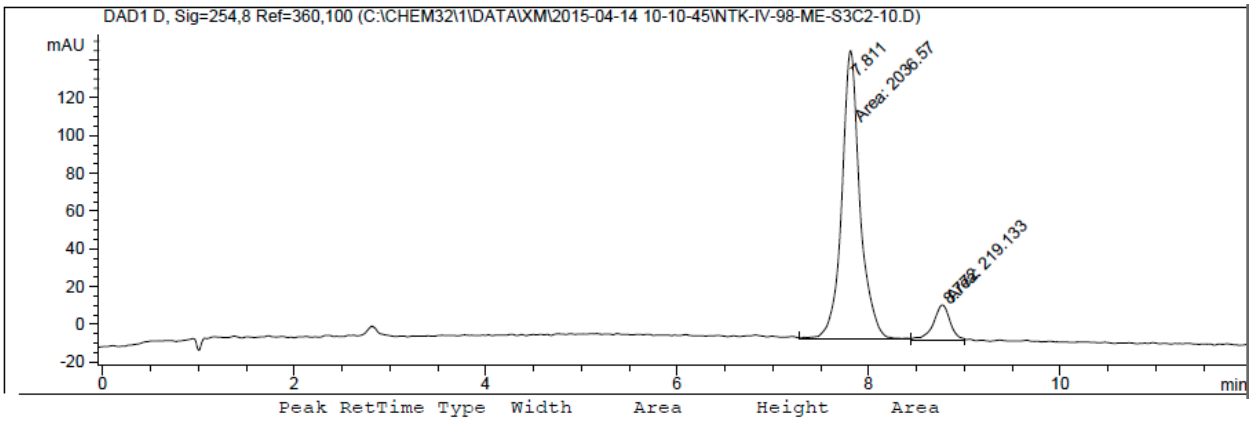
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.106	MM	0.1789	1460.18115	136.04520	95.8311
2	6.788	MM	0.2033	63.52196	5.20731	4.1689

3b racemic



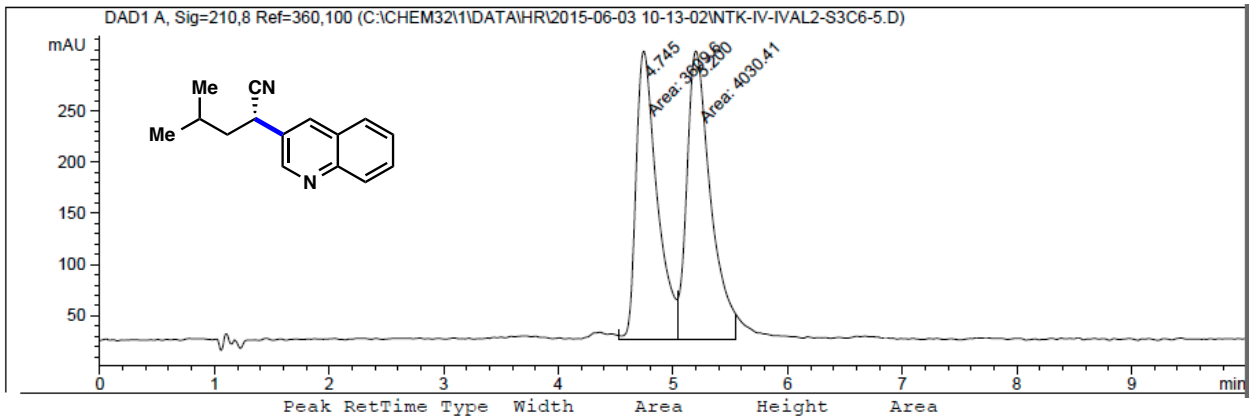
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.397	BV	0.1592	548.77161	52.81827	50.9276
2	6.902	VB	0.1731	528.77997	47.05341	49.0724

3b enantioenriched, 81% ee



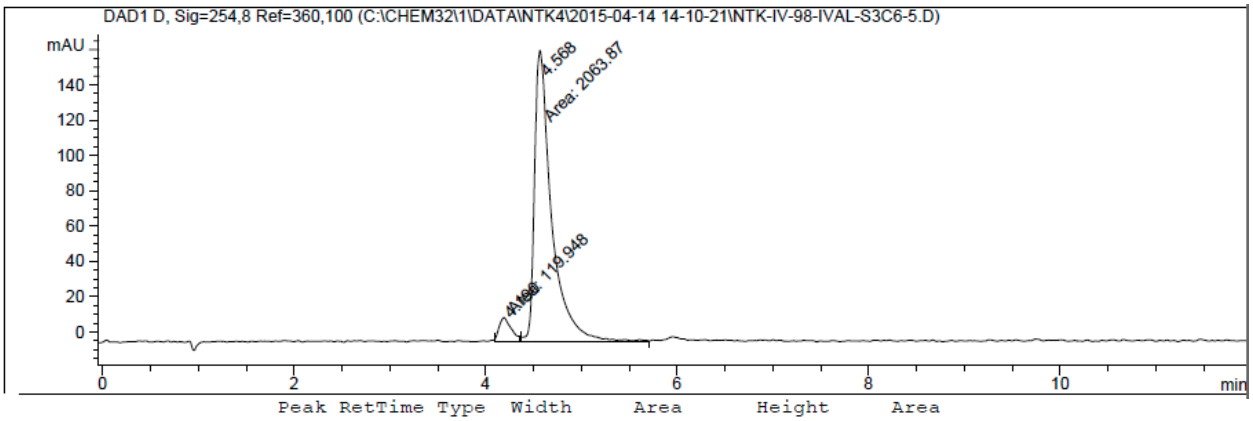
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.811	MM	0.2219	2036.56677	152.96375	90.2854
2	8.772	MM	0.1984	219.13271	18.40750	9.7146

3c racemic



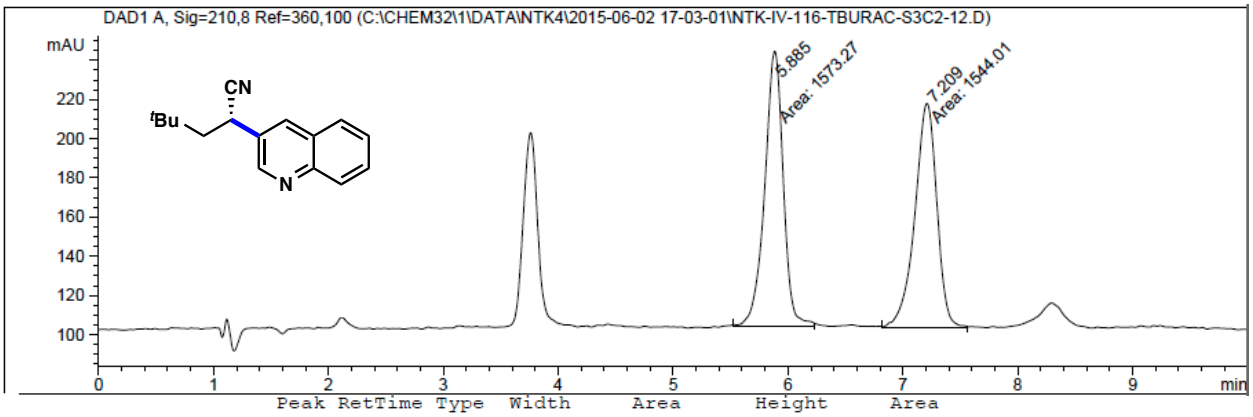
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.745	MM	0.2135	3609.59644	281.73523	47.2460
2	5.200	MM	0.2383	4030.41479	281.82928	52.7540

3c enantioenriched, 89% ee



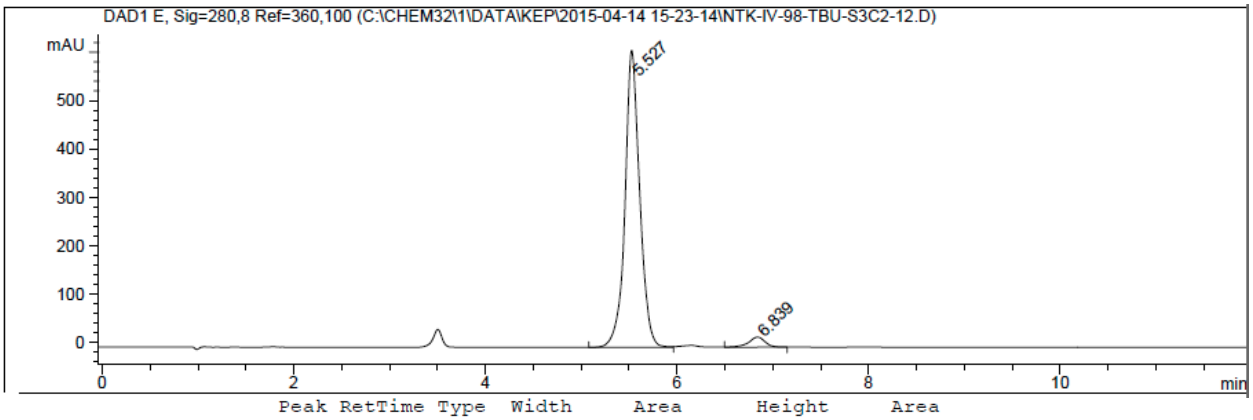
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.190	MM	0.1475	119.94836	13.55409	5.4926
2	4.568	MM	0.2080	2063.87280	165.40321	94.5074

3d racemic



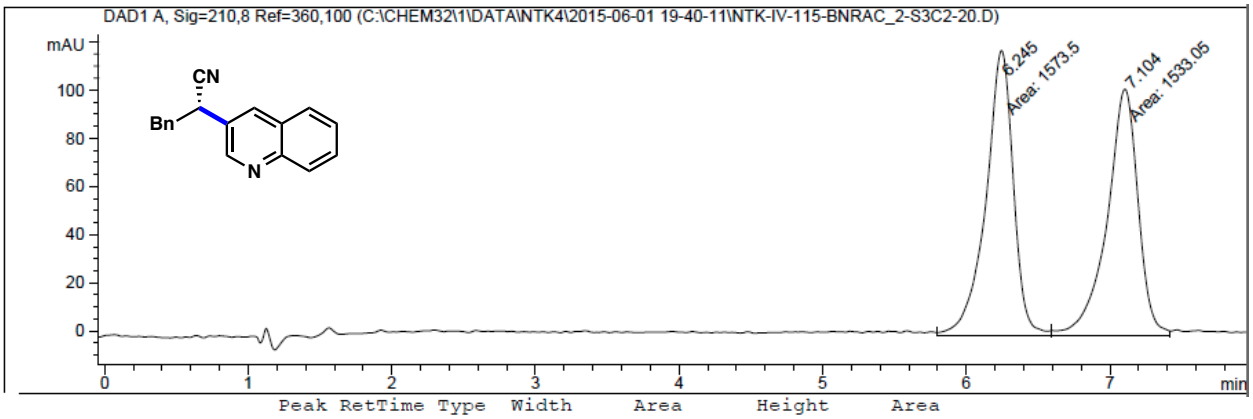
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.885	MM	0.1865	1573.26758	140.60291	50.4693
2	7.209	MM	0.2237	1544.00830	115.02839	49.5307

3d enantioenriched, 93% ee



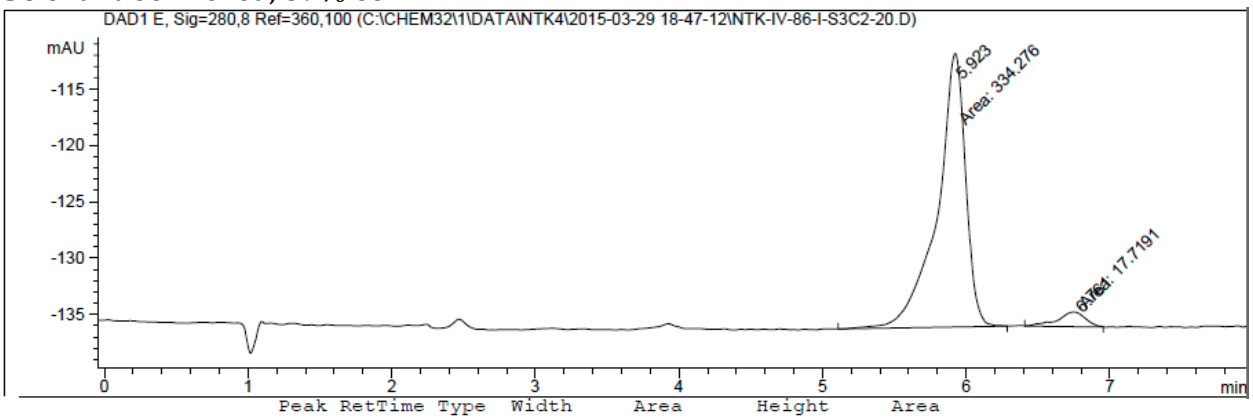
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.527	VB	0.1566	6555.89990	613.77045	96.3174
2	6.839	BB	0.1762	250.66086	20.86025	3.6826

3e racemic



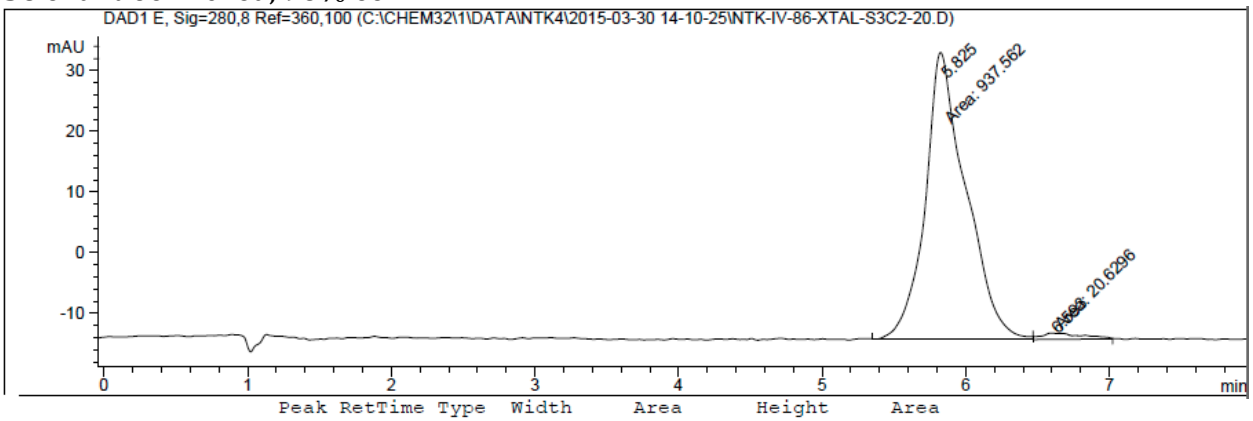
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.245	MM	0.2219	1573.49854	118.16628	50.6510
2	7.104	MM	0.2501	1533.05249	102.16112	49.3490

3e enantioenriched, 89% ee



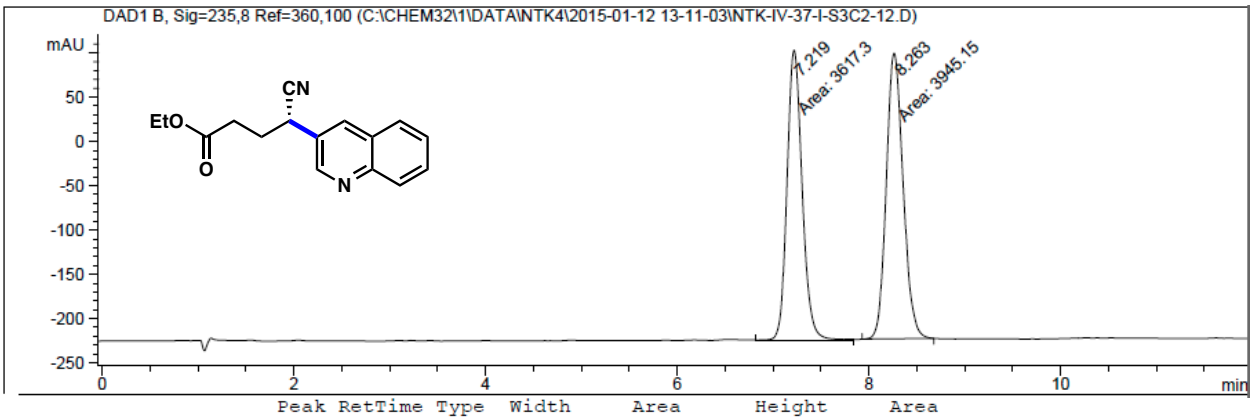
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.923	MM	0.2293	334.27615	24.29972	94.9661
2	6.761	MM	0.2285	17.71910	1.29258	5.0339

3e enantioenriched, 96% ee



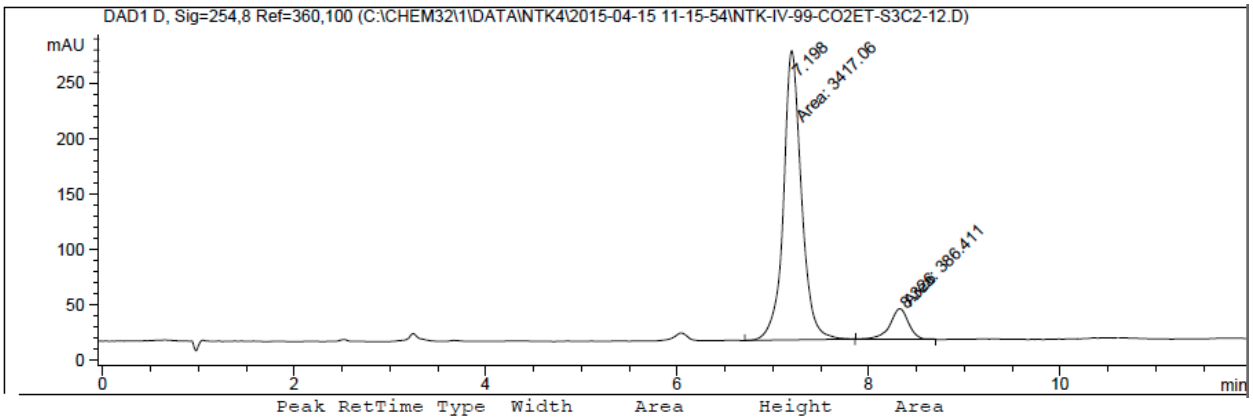
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.825	MM	0.3300	937.56195	47.34668	97.8470
2	6.593	MM	0.3294	20.62959	1.04379	2.1530

3f racemic



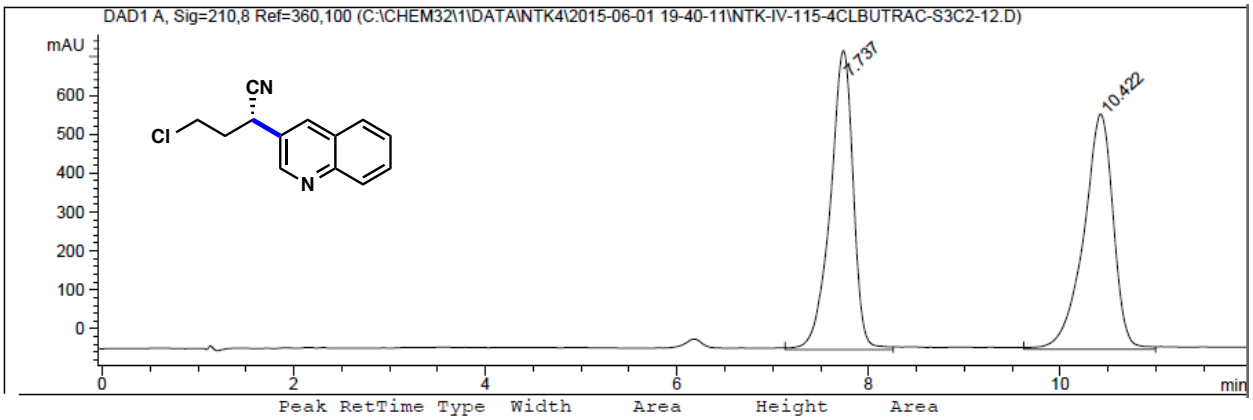
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.219	MM	0.1840	3617.29688	327.72406	47.8323
2	8.263	MM	0.2038	3945.15210	322.60925	52.1677

3f enantioenriched, 80% ee



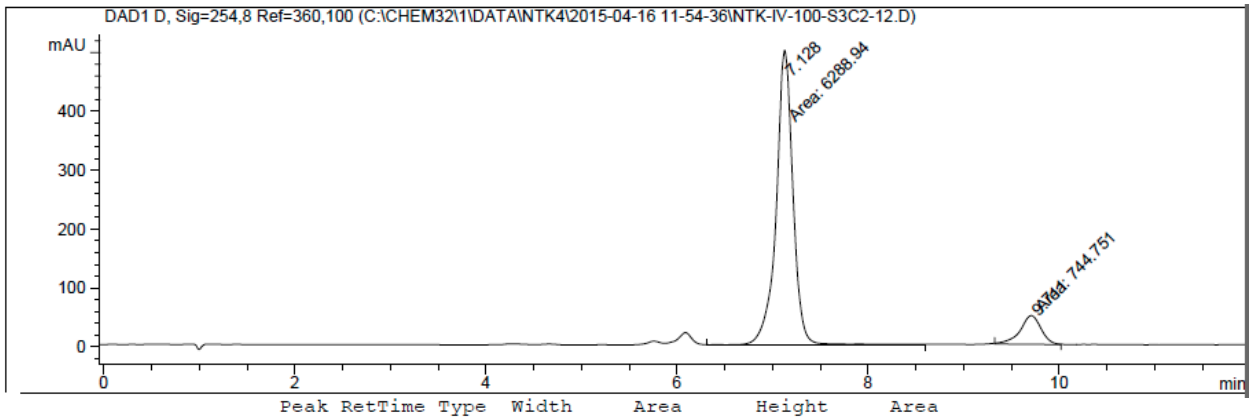
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.198	MM	0.2179	3417.05908	261.39404	89.8406
2	8.326	MM	0.2312	386.41061	27.85635	10.1594

3g racemic



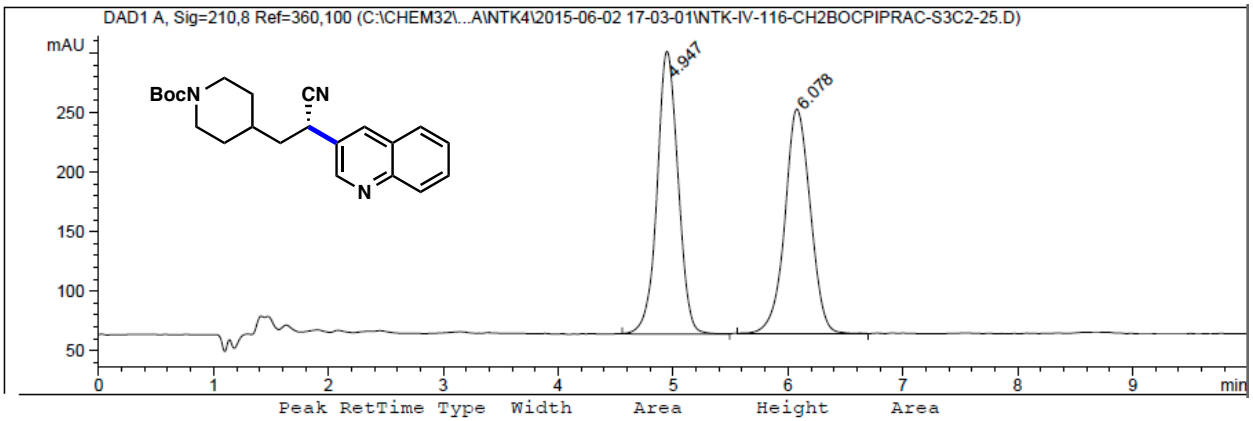
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.737	VV	0.2507	1.28238e4	768.61090	49.6251
2	10.422	VB	0.3214	1.30175e4	604.21277	50.3749

3g enantioenriched, 79% ee



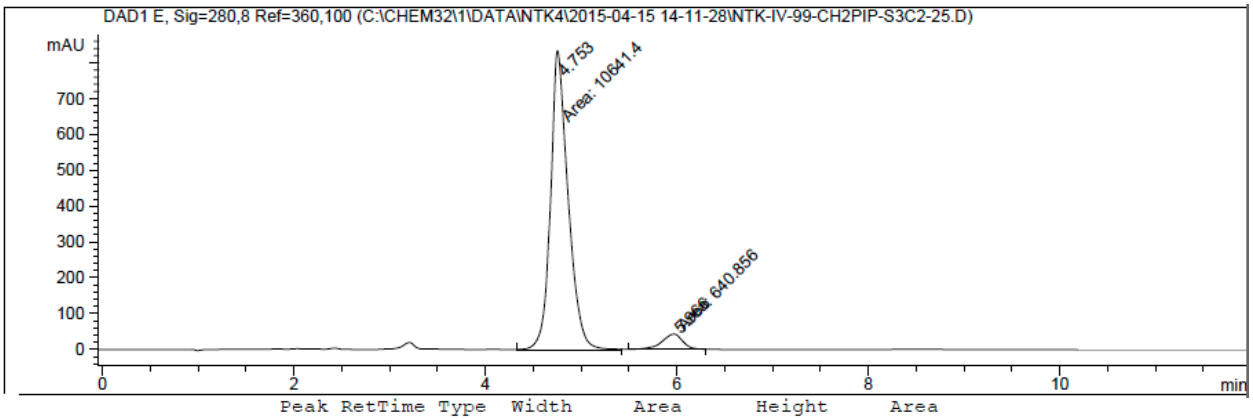
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.128	MM	0.2089	6288.94287	501.63721	89.4117
2	9.711	MM	0.2536	744.75104	48.93940	10.5883

3h racemic



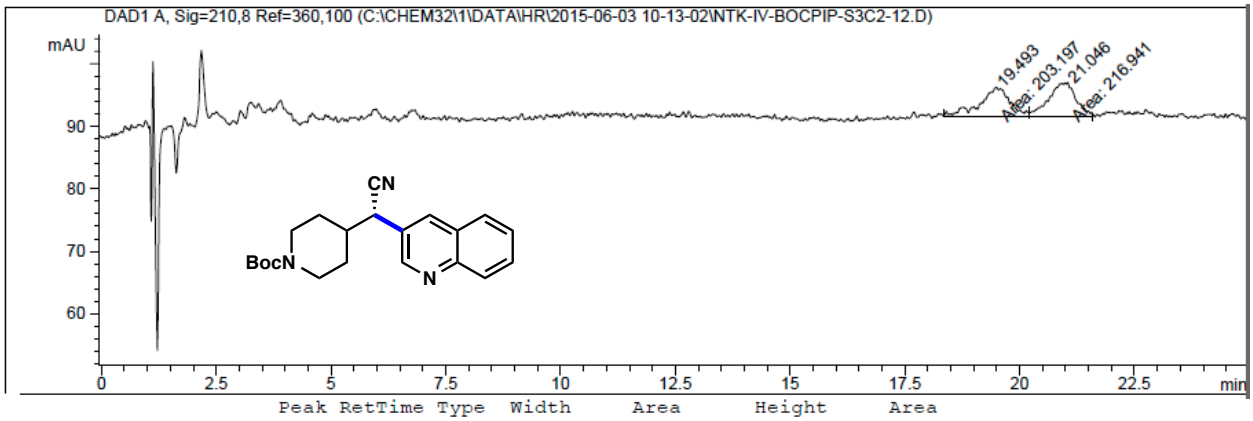
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.947	BB	0.2005	3022.36011	237.43880	50.7006
2	6.078	BB	0.2414	2938.82886	189.05597	49.2994

3h enantioenriched, 89% ee



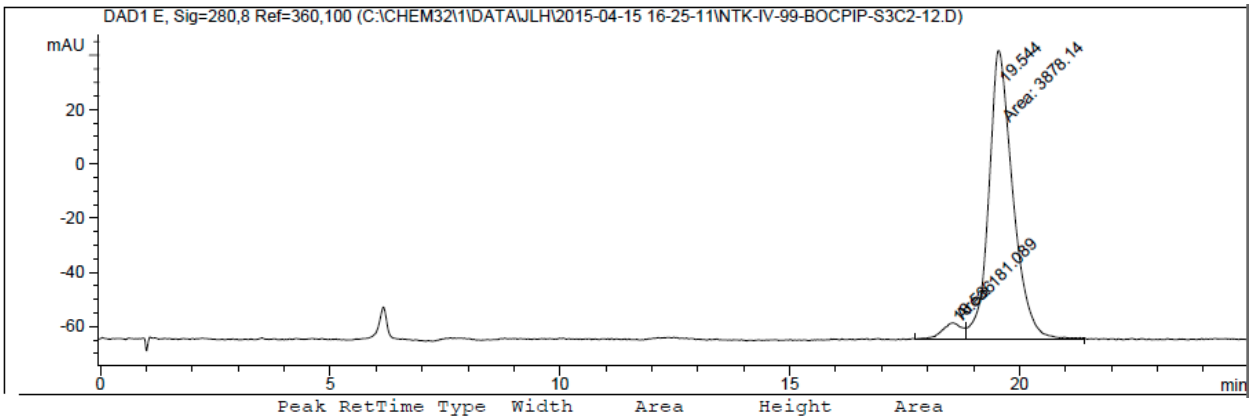
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.753	MM	0.2124	1.06414e4	835.02002	94.3198
2	5.966	MM	0.2495	640.85596	42.80384	5.6802

3i racemic



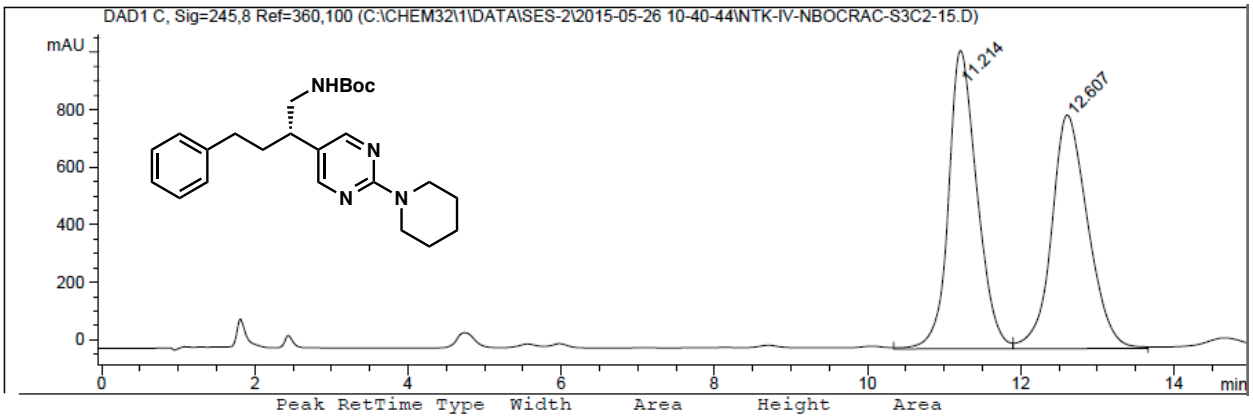
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.493	MM	0.7345	203.19673	4.61081	48.3643
2	21.046	MM	0.6714	216.94075	5.38557	51.6357

3i enantioenriched, 91% ee



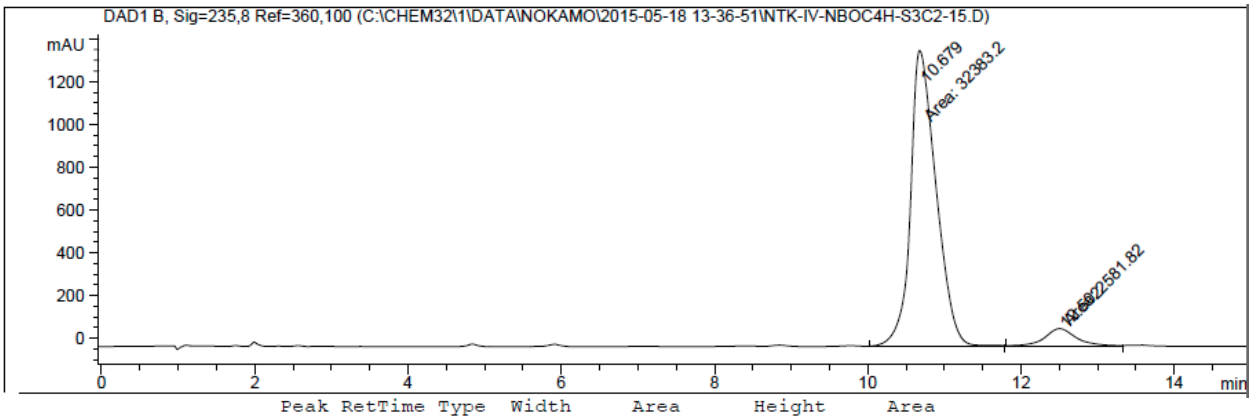
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.536	MM	0.5086	181.08897	5.93411	4.4612
2	19.544	MM	0.6079	3878.14355	106.32883	95.5388

8 racemic



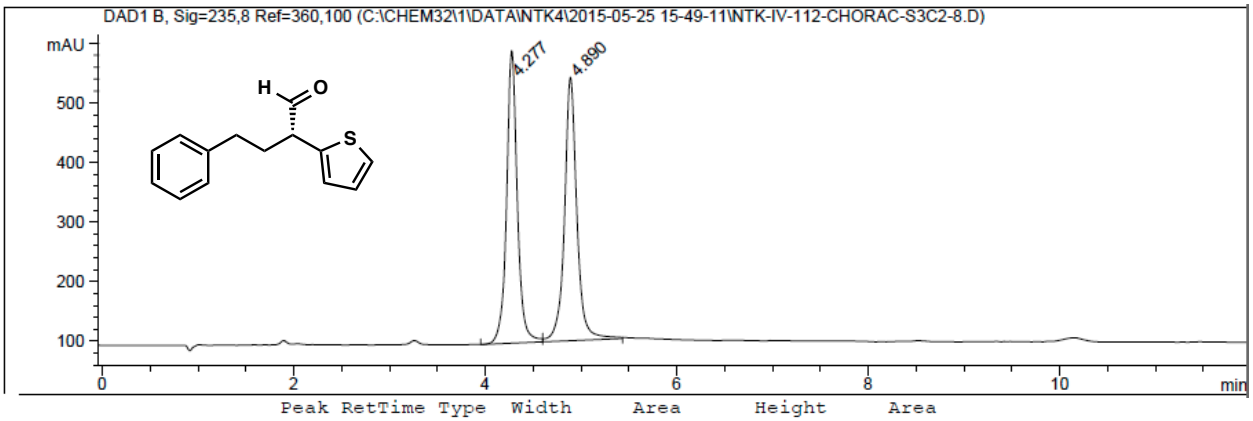
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.214	VV	0.3883	2.68637e4	1036.80664	50.1053
2	12.607	VB	0.4963	2.67508e4	812.12598	49.8947

8 enantioenriched, 85% ee



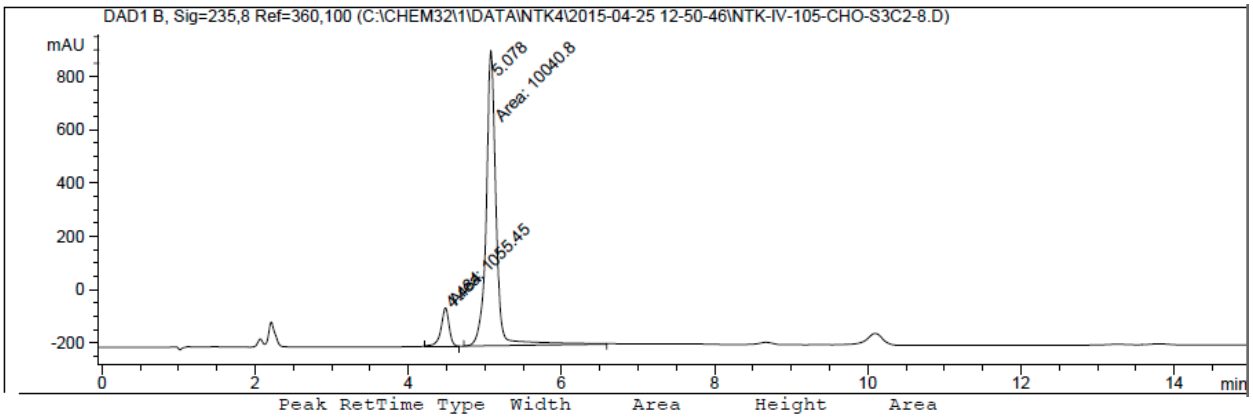
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.679	MM	0.3896	3.23832e4	1385.25745	92.6160
2	12.502	MM	0.5124	2581.82373	83.98371	7.3840

10 racemic



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.277	VV	0.1173	3844.47681	491.51151	49.0126
2	4.890	VB	0.1334	3999.37305	442.65036	50.9874

10 enantioenriched, 81% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.484	MM	0.1218	1055.44739	144.44736	9.5118
2	5.078	MM	0.1509	1.00408e4	1109.03845	90.4882

6. XRay crystallographic data for 3e.

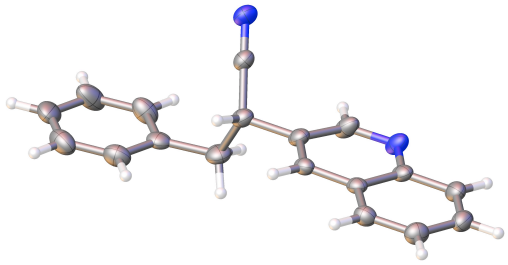


Table 1. Crystal data and structure refinement for final_p15159.

Identification code	p15159	
Empirical formula	C18 H14 N2	
Formula weight	258.31	
Temperature	100.01 K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.8946(6) Å	α= 90°.
	b = 12.0793(9) Å	β= 90°.
	c = 14.7171(11) Å	γ = 90°.
Volume	1403.44(18) $Å^3$	
Z	4	
Density (calculated)	1.223 Mg/m^3	
Absorption coefficient	0.562 mm^{-1}	
F(000)	544	
Crystal size	0.312 x 0.306 x 0.264 mm^3	
Theta range for data collection	4.736 to 74.595°.	
Index ranges	-9<=h<=9, -15<=k<=15, -17<=l<=18	
Reflections collected	33599	
Independent reflections	2860 [R(int) = 0.0298]	
Completeness to theta = 67.679°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7538 and 0.6982	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2860 / 0 / 182	
Goodness-of-fit on F^2	1.059	

Final R indices [I>2sigma(I)]	R1 = 0.0273, wR2 = 0.0712
R indices (all data)	R1 = 0.0277, wR2 = 0.0717
Absolute structure parameter	-0.15(8)
Extinction coefficient	0.0069(7)
Largest diff. peak and hole	0.163 and -0.104 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for final_p15159. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1)	8035(2)	6345(1)	4866(1)	35(1)
N(2)	5039(2)	7879(1)	7491(1)	34(1)
C(3)	7089(2)	4720(1)	6140(1)	26(1)
C(1)	6781(2)	6492(1)	5446(1)	36(1)
C(8)	10236(2)	5159(1)	4296(1)	33(1)
C(4)	8436(2)	4511(1)	5530(1)	26(1)
C(6)	10643(2)	3339(1)	4937(1)	35(1)
C(9)	8876(2)	5353(1)	4902(1)	28(1)
C(7)	11094(2)	4176(1)	4313(1)	34(1)
C(2)	6260(2)	5708(1)	6104(1)	29(1)
C(5)	9347(2)	3505(1)	5534(1)	31(1)
C(10)	4788(2)	5923(1)	6740(1)	29(1)
C(11)	4913(2)	7029(1)	7161(1)	28(1)
C(13)	1584(2)	5835(1)	6912(1)	31(1)
C(12)	3056(2)	5786(2)	6257(1)	38(1)
C(16)	-1090(2)	5948(2)	8156(1)	46(1)
C(14)	591(2)	6770(1)	6978(1)	41(1)
C(17)	-97(3)	5009(2)	8097(1)	47(1)
C(15)	-737(2)	6823(2)	7593(2)	50(1)
C(18)	1232(2)	4954(1)	7483(1)	40(1)

Table 3. Bond lengths [Å] and angles [°] for final_p15159.

N(1)-C(1)	1.319(2)
N(1)-C(9)	1.3710(19)
N(2)-C(11)	1.1394(19)
C(3)-H(3)	0.9500
C(3)-C(4)	1.414(2)
C(3)-C(2)	1.362(2)
C(1)-H(1)	0.9500
C(1)-C(2)	1.416(2)
C(8)-H(8)	0.9500
C(8)-C(9)	1.416(2)
C(8)-C(7)	1.368(2)
C(4)-C(9)	1.4172(19)
C(4)-C(5)	1.412(2)
C(6)-H(6)	0.9500
C(6)-C(7)	1.412(2)
C(6)-C(5)	1.364(2)
C(7)-H(7)	0.9500
C(2)-C(10)	1.515(2)
C(5)-H(5)	0.9500
C(10)-H(10)	1.0000
C(10)-C(11)	1.4761(19)
C(10)-C(12)	1.550(2)
C(13)-C(12)	1.511(2)
C(13)-C(14)	1.378(2)
C(13)-C(18)	1.383(2)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(16)-H(16)	0.9500
C(16)-C(17)	1.381(3)
C(16)-C(15)	1.372(3)
C(14)-H(14)	0.9500
C(14)-C(15)	1.387(3)
C(17)-H(17)	0.9500
C(17)-C(18)	1.386(3)

C(15)-H(15)	0.9500
C(18)-H(18)	0.9500

C(1)-N(1)-C(9)	117.15(13)
C(4)-C(3)-H(3)	120.2
C(2)-C(3)-H(3)	120.2
C(2)-C(3)-C(4)	119.57(13)
N(1)-C(1)-H(1)	117.6
N(1)-C(1)-C(2)	124.75(14)
C(2)-C(1)-H(1)	117.6
C(9)-C(8)-H(8)	119.7
C(7)-C(8)-H(8)	119.7
C(7)-C(8)-C(9)	120.50(13)
C(3)-C(4)-C(9)	118.01(13)
C(5)-C(4)-C(3)	122.30(13)
C(5)-C(4)-C(9)	119.69(13)
C(7)-C(6)-H(6)	119.9
C(5)-C(6)-H(6)	119.9
C(5)-C(6)-C(7)	120.17(14)
N(1)-C(9)-C(8)	119.14(13)
N(1)-C(9)-C(4)	122.28(13)
C(8)-C(9)-C(4)	118.57(13)
C(8)-C(7)-C(6)	120.61(14)
C(8)-C(7)-H(7)	119.7
C(6)-C(7)-H(7)	119.7
C(3)-C(2)-C(1)	118.23(14)
C(3)-C(2)-C(10)	119.68(13)
C(1)-C(2)-C(10)	122.06(13)
C(4)-C(5)-H(5)	119.8
C(6)-C(5)-C(4)	120.45(14)
C(6)-C(5)-H(5)	119.8
C(2)-C(10)-H(10)	107.7
C(2)-C(10)-C(12)	112.00(11)
C(11)-C(10)-C(2)	111.31(12)
C(11)-C(10)-H(10)	107.7
C(11)-C(10)-C(12)	110.35(13)

C(12)-C(10)-H(10)	107.7
N(2)-C(11)-C(10)	178.73(16)
C(14)-C(13)-C(12)	120.94(15)
C(14)-C(13)-C(18)	118.24(16)
C(18)-C(13)-C(12)	120.79(15)
C(10)-C(12)-H(12A)	109.1
C(10)-C(12)-H(12B)	109.1
C(13)-C(12)-C(10)	112.42(12)
C(13)-C(12)-H(12A)	109.1
C(13)-C(12)-H(12B)	109.1
H(12A)-C(12)-H(12B)	107.9
C(17)-C(16)-H(16)	120.7
C(15)-C(16)-H(16)	120.7
C(15)-C(16)-C(17)	118.68(17)
C(13)-C(14)-H(14)	119.5
C(13)-C(14)-C(15)	120.93(16)
C(15)-C(14)-H(14)	119.5
C(16)-C(17)-H(17)	119.7
C(16)-C(17)-C(18)	120.64(16)
C(18)-C(17)-H(17)	119.7
C(16)-C(15)-C(14)	120.77(17)
C(16)-C(15)-H(15)	119.6
C(14)-C(15)-H(15)	119.6
C(13)-C(18)-C(17)	120.73(16)
C(13)-C(18)-H(18)	119.6
C(17)-C(18)-H(18)	119.6

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for final_p15159. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	56(1)	27(1)	24(1)	1(1)	7(1)	1(1)
N(2)	38(1)	33(1)	33(1)	-6(1)	3(1)	4(1)
C(3)	34(1)	23(1)	22(1)	0(1)	-2(1)	-6(1)
C(1)	56(1)	26(1)	26(1)	-1(1)	5(1)	6(1)
C(8)	42(1)	34(1)	23(1)	-1(1)	3(1)	-7(1)
C(4)	32(1)	25(1)	21(1)	-3(1)	-4(1)	-6(1)
C(6)	34(1)	34(1)	37(1)	-3(1)	-2(1)	4(1)
C(9)	39(1)	26(1)	19(1)	-3(1)	-1(1)	-5(1)
C(7)	33(1)	41(1)	29(1)	-6(1)	2(1)	-2(1)
C(2)	39(1)	27(1)	21(1)	-4(1)	1(1)	-3(1)
C(5)	34(1)	27(1)	31(1)	1(1)	-4(1)	-2(1)
C(10)	38(1)	27(1)	23(1)	-2(1)	-1(1)	0(1)
C(11)	31(1)	30(1)	23(1)	-2(1)	1(1)	3(1)
C(13)	33(1)	31(1)	30(1)	-5(1)	-10(1)	-6(1)
C(12)	43(1)	42(1)	27(1)	-7(1)	-6(1)	-4(1)
C(16)	35(1)	55(1)	48(1)	-12(1)	2(1)	-18(1)
C(14)	35(1)	33(1)	56(1)	10(1)	-5(1)	-3(1)
C(17)	51(1)	44(1)	45(1)	8(1)	-6(1)	-17(1)
C(15)	32(1)	35(1)	83(1)	-6(1)	1(1)	-2(1)
C(18)	46(1)	30(1)	46(1)	0(1)	-6(1)	-3(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for final_p15159.

	x	y	z	U(eq)
H(3)	6765	4175	6571	32
H(1)	6184	7175	5420	43
H(8)	10554	5717	3874	39
H(6)	11244	2657	4941	42
H(7)	12002	4056	3901	41
H(5)	9054	2940	5955	37
H(10)	4844	5361	7239	35
H(12A)	2925	6379	5798	45
H(12B)	3035	5067	5935	45
H(16)	-1999	5986	8577	55
H(14)	819	7386	6597	50
H(17)	-327	4395	8480	56
H(15)	-1411	7474	7626	60
H(18)	1909	4305	7454	49

Table 6. Torsion angles [°] for final_p15159.

N(1)-C(1)-C(2)-C(3)	-0.9(2)
N(1)-C(1)-C(2)-C(10)	-179.01(15)
C(3)-C(4)-C(9)-N(1)	-0.5(2)
C(3)-C(4)-C(9)-C(8)	179.23(12)
C(3)-C(4)-C(5)-C(6)	-179.68(14)
C(3)-C(2)-C(10)-C(11)	134.26(14)
C(3)-C(2)-C(10)-C(12)	-101.68(16)
C(1)-N(1)-C(9)-C(8)	-179.75(14)
C(1)-N(1)-C(9)-C(4)	0.0(2)
C(1)-C(2)-C(10)-C(11)	-47.67(18)
C(1)-C(2)-C(10)-C(12)	76.39(18)
C(4)-C(3)-C(2)-C(1)	0.3(2)
C(4)-C(3)-C(2)-C(10)	178.47(12)
C(9)-N(1)-C(1)-C(2)	0.7(2)
C(9)-C(8)-C(7)-C(6)	-0.2(2)
C(9)-C(4)-C(5)-C(6)	-0.1(2)
C(7)-C(8)-C(9)-N(1)	-179.73(14)
C(7)-C(8)-C(9)-C(4)	0.5(2)
C(7)-C(6)-C(5)-C(4)	0.4(2)
C(2)-C(3)-C(4)-C(9)	0.33(19)
C(2)-C(3)-C(4)-C(5)	179.90(13)
C(2)-C(10)-C(12)-C(13)	171.71(14)
C(5)-C(4)-C(9)-N(1)	179.88(13)
C(5)-C(4)-C(9)-C(8)	-0.35(19)
C(5)-C(6)-C(7)-C(8)	-0.3(2)
C(11)-C(10)-C(12)-C(13)	-63.69(17)
C(13)-C(14)-C(15)-C(16)	0.4(3)
C(12)-C(13)-C(14)-C(15)	-178.60(15)
C(12)-C(13)-C(18)-C(17)	178.66(15)
C(16)-C(17)-C(18)-C(13)	-0.5(3)
C(14)-C(13)-C(12)-C(10)	103.57(17)
C(14)-C(13)-C(18)-C(17)	0.7(2)
C(17)-C(16)-C(15)-C(14)	-0.1(3)
C(15)-C(16)-C(17)-C(18)	0.2(3)

C(18)-C(13)-C(12)-C(10)	-74.31(19)
C(18)-C(13)-C(14)-C(15)	-0.7(2)

Symmetry transformations used to generate equivalent atoms: