

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

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Supporting Information 1 (Experimental):

Table of Contents

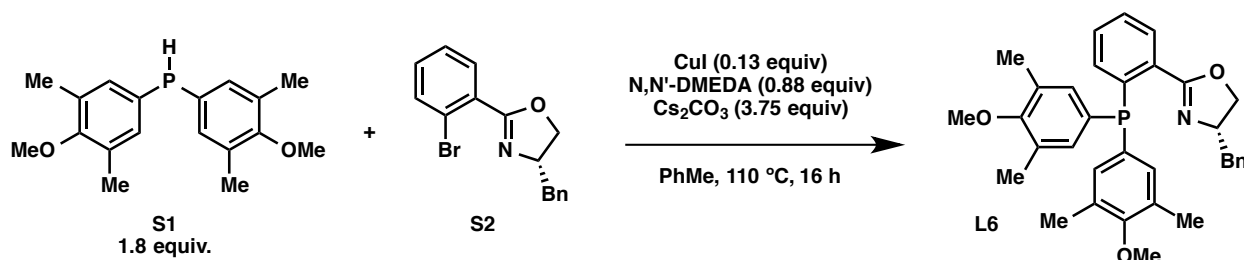
1.	Materials and Methods	S3
2.	Catalyst and Substrate Preparation	S4
3.	Cross-Coupling Reactions and Product Characterization	S8
4.	Synthesis of Enantioenriched Nitrile Derivatives	S22
5.	SFC traces for racemic and enantioenriched benzylic nitriles	S25
6.	X-ray crystallographic data for 3e	S50

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. NiCl₂(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. ¹H and ¹³C 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 (¹H, $\delta = 7.26$, ¹³C, $\delta = 77.0$). Data for ¹H 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 CO₂ 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 α radiation ($\lambda = 1.54178$ Å) from an I μ S micro-source.

Abbreviations used: IPA – isopropanol; Et₂O – 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)

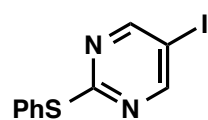


To a flame-dried flask was added CuI (0.13 equiv, 241 mg, 1.3 mmol), followed by anhydrous toluene (40 mL). To this solution was added $\text{N,N}'\text{-DMEDA}$ (0.88 equiv, 0.93 mL, 8.6 mmol) and diarylphosphine **S1** (1.8 equiv, 5.3 g, 17.5 mmol). These were stirred for 15 minutes at room temperature. 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 $110\text{ }^\circ\text{C}$ 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% $\text{Et}_2\text{O}/\text{Hexanes}$) to afford **L6** as a white foamy solid (1.62 g, 3.01 mmol, 31% yield). ^1H NMR (500 MHz, $\text{Chloroform-}d$) 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) 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} ; $[\alpha]_{\text{D}}^{25} = +37.355$ ($c = 1.285, \text{CHCl}_3$). HRMS (MM) calc'd for $[\text{M}+\text{H}_2\text{O}]^+$ 555.2533, found 555.2544.

b. General procedure 1 for preparation of heteroaryl iodides.

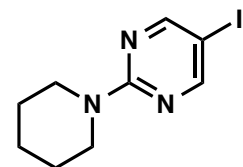
To a flame-dried flask was added copper(I) iodide (0.05 equiv), followed by 1,4-dioxane and N,N'-DMEDA (0.10 equiv), then aryl bromide (1.0 equiv) and sodium iodide (2.0 equiv). The reaction was heated to 110 °C for 24 h. Upon cooling to room temperature, the reaction was filtered over Celite and washed 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)



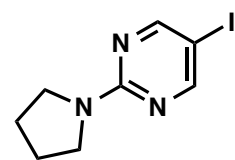
Prepared from 5-bromo-2-phenylthiopyrimidine (10.3 mmol, 2.75 g) following General Procedure 1 to yield 3.14 g (97% yield) of **6j** as a light tan solid. ¹H NMR (500 MHz, Chloroform-*d*) δ 8.62 (s, 2H), 7.65 – 7.56 (m, 2H), 7.48 – 7.40 (m, 3H); ¹³C NMR (126 MHz, cdcl₃) δ 171.40, 162.64, 135.25, 129.61, 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. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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)



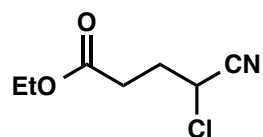
Prepared from 5-bromo-2-(pyrrolidin-1-yl)pyrimidine (10.3 mmol, 2.35 g) following General Procedure 1 to yield 2.75 g (97% yield) of **6l** as a very light pink solid. ¹H NMR (500 MHz, Chloroform-*d*) δ 8.37 (s, 2H), 3.57 – 3.47 (m, 4H), 2.18 – 1.77 (m, 4H); ¹³C NMR (126 MHz, cdcl₃) δ 162.34, 158.19, 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 $[\text{M}]^+$ 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.

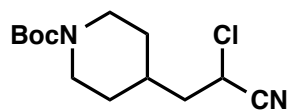
Ethyl 4-chloro-4-cyanobutyrate (1g)



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. ^1H NMR (500 MHz, $\text{Chloroform-}d$) 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):

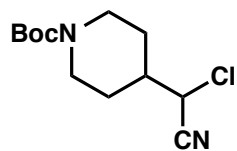
2983.27, 2249.74, 1734.19, 1608.59, 1564.56, 1419.07, 1378.34, 1193.90, 1096.48, 1024.20, 852.08, 795.42, 665.51 cm^{-1} ; HRMS (MM) calc'd for $[\text{M}]^+$ 175.0395, found 175.0380.

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



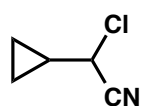
Prepared from 2-(1-Boc-4-piperidyl)acetaldehyde (1.0 g, 4.4 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (5:95 to 20:80 EtOAc:hexanes) to yield 837 mg (70% yield) of **XX** as a white solid. ^1H NMR (500 MHz, Chloroform-*d*) δ 4.49 (t, $J = 7.6$ Hz, 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 $[\text{M}+\text{H}]^+$ 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. ^1H 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 $[\text{M}+\text{H}]^+$ 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. ^1H 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,

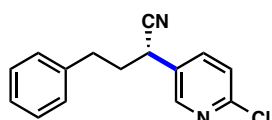
2H), 0.74 – 0.62 (m, 2H); ¹³C NMR (126 MHz, cdcl₃) δ 115.79, 46.91, 16.59, 6.09, 5.40; IR (NaCl/thin film): 3091.35, 3013.92, 2958.47, 2247.22, 1732.61, 1430.84, 1220.80, 1029.90, 991.98, 926.86, 832.41, 728.05 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 116.0262, found 116.0258.

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, Mn⁰ powder (3 equiv, 33 mg, 0.6 mmol), aryl iodide (*if solid*, 1 or 2 equiv, 0.2 or 0.4 mmol), NiCl₂(dme) (0.1 equiv, 4.4 mg, 0.02 mmol), **L6** (0.2 equiv, 21.6 mg, 0.04 mmol) and NaBF₄ 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.

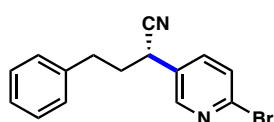
2-(6-chloropyridin-3-yl)-4-phenylbutanenitrile (**7a**)



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 CO₂, λ = 210 nm): *t*_R(minor) = 9.8 min, *t*_R(major) = 13.0 min. ¹H NMR (500 MHz,

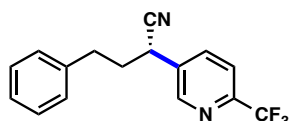
Chloroform-*d*) δ 8.31 (d, $J = 2.6$ Hz, 1H), 7.66 (dd, $J = 8.3, 2.7$ Hz, 1H), 7.40 – 7.28 (m, 3H), 7.28 – 7.22 (m, 1H), 7.22 – 7.17 (m, 2H), 3.77 (dd, $J = 9.2, 6.0$ Hz, 1H), 2.87 – 2.81 (m, 2H), 2.34 – 2.27 (m, 1H), 2.16 (dddd, $J = 13.7, 8.5, 7.6, 6.0$ Hz, 1H); ^{13}C NMR (126 MHz, cdCl_3) δ 151.54, 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} ; $[\alpha]_{\text{D}}^{25} = -12.081$ ($c = 1.410$, CHCl_3). HRMS (MM) calc'd for $[\text{M}+\text{Na}]^+$ 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 , $\lambda = 280$ nm): $t_{\text{R}}(\text{minor}) = 9.5$ min, $t_{\text{R}}(\text{major}) = 12.2$ min. ^1H 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} ; $[\alpha]_{\text{D}}^{25} = -4.695$ ($c = 1.180$, CHCl_3). HRMS (MM) calc'd for $[\text{M}+\text{H}]^+$ 301.0335, found 301.0341.

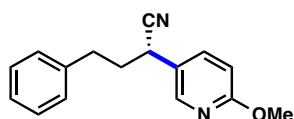
4-phenyl-2-(6-(trifluoromethyl)pyridin-3-yl)butanenitrile (7c)



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 , $\lambda = 254$ nm): $t_{\text{R}}(\text{minor}) = 3.0$ min, $t_{\text{R}}(\text{major}) = 4.7$

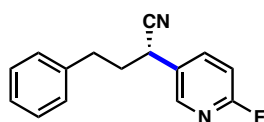
min. ^1H NMR (500 MHz, Chloroform-*d*) δ 8.64 (d, $J = 2.2$ Hz, 1H), 7.89 (dd, $J = 8.1, 2.3$ Hz, 1H), 7.73 (dd, $J = 8.2, 0.8$ Hz, 1H), 7.40 – 7.29 (m, 2H), 7.29 – 7.22 (m, 1H), 7.22 – 7.14 (m, 2H), 3.87 (dd, $J = 9.3, 5.9$ Hz, 1H), 2.93 – 2.82 (m, 2H), 2.39 – 2.28 (m, 1H), 2.21 (dddd, $J = 13.7, 8.5, 7.7, 5.9$ Hz, 1H); ^{13}C NMR (126 MHz, cdCl_3) δ 148.93, δ 148.18 (q, $J_{\text{C-F}} = 35.3$ Hz), 138.77, 136.28, 134.83, 128.92, 128.40, 128.38, 126.91, 126.89, 120.81 (q, $J_{\text{C-F}} = 2.7$ 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} ; $[\alpha]_{\text{D}}^{25} = -21.304$ ($c = 1.475$, CHCl_3). HRMS (MM) calc'd for $[\text{M}+\text{H}]^+$ 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 , $\lambda = 245$ nm): $t_{\text{R}}(\text{minor}) = 6.5$ min, $t_{\text{R}}(\text{major}) = 7.5$ min. ^1H 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} ; $[\alpha]_{\text{D}}^{25} = -9.806$ ($c = 0.790$, CHCl_3). HRMS (MM) calc'd for $[\text{M}+\text{Na}]^+$ 275.1155, found 275.1175.

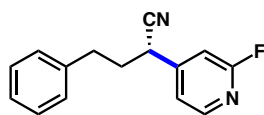
2-(6-fluoropyridin-3-yl)-4-phenylbutanenitrile (7e)



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

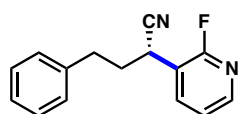
excess was determined to be 87% by chiral SFC analysis (AD, 2.5 mL/min, 8% IPA in CO₂, λ = 254 nm): *t*_R(minor) = 5.2 min, *t*_R(major) = 6.4 min. ¹H NMR (500 MHz, Chloroform-*d*) δ 8.18 – 8.10 (m, 1H), 7.79 (ddd, *J* = 8.5, 7.2, 2.7 Hz, 1H), 7.38 – 7.28 (m, 2H), 7.28 – 7.22 (m, 1H), 7.22 – 7.16 (m, 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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = -27.336 (*c* = 1.155, CHCl₃). 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 NaBF₄ (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 CO₂, λ = 210 nm): *t*_R(minor) = 4.7 min, *t*_R(major) = 5.5 min. ¹H 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).; ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = -22.036 (*c* = 0.45, CHCl₃). HRMS (MM) calc'd for [M+H]⁺ 241.1136, found 241.1134.

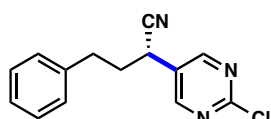
2-(2-fluoropyridin-3-yl)-4-phenylbutanenitrile (7g)



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

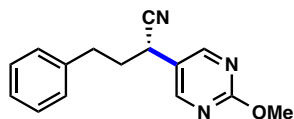
crude residue was purified by silica gel chromatography (0:100 to 10:90 EtOAc:hexanes) to yield 16.7 mg (35% yield) of **7g** as a clear oil. The enantiomeric excess was determined to be 83% by chiral SFC analysis (AD, 2.5 mL/min, 6% IPA in CO₂, λ = 245 nm): *t*_R(minor) = 4.9 min, *t*_R(major) = 5.8 min. ¹H 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); ¹³C NMR (126 MHz, cdCl₃) 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; [α]_D²⁵ = -29.296 (*c* = 0.635, CHCl₃). 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 CO₂, λ = 210 nm): *t*_R(minor) = 6.2 min, *t*_R(major) = 7.0 min. ¹H 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); ¹³C NMR (126 MHz, cdCl₃) 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; [α]_D²⁵ = -14.892 (*c* = 0.305, CHCl₃). HRMS (MM) calc'd for [M+H]⁺ 258.0793, found 258.0257.

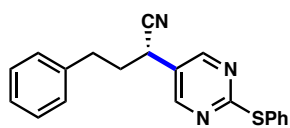
2-(2-methoxypyrimidin-5-yl)-4-phenylbutanenitrile (**7i**)



Prepared from 5-iodo-2-methoxypyrimidine (89.2 mg, 0.4 mmol) and 2-chloro-4-phenylbutanenitrile (36 mg, 0.2 mmol) with NaBF₄ (22 mg, 0.2 mmol) following General Procedure 3. The crude residue was

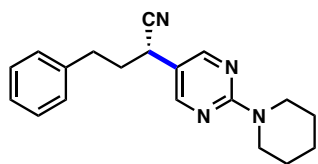
purified by florisil gel chromatography (0:100 to 40:60 EtOAc:hexanes) to yield 35.8 mg (71% yield) of **7i** as a clear oil. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AS, 2.5 mL/min, 10% IPA in CO₂, λ = 254 nm): *t*_R(minor) = 4.5 min, *t*_R(major) = 5.0 min. ¹H NMR (500 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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = -17.013 (*c* = 0.395, CHCl₃). 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 CO₂, λ = 280 nm): *t*_R(minor) = 11.3 min, *t*_R(major) = 12.7 min. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = +10.214 (*c* = 1.965, CHCl₃). HRMS (MM) calc'd for [M+H]⁺ 332.1216, found 332.1746.

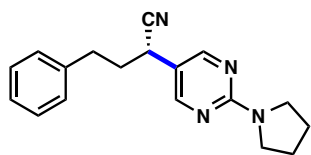
4-phenyl-2-(2-(piperidin-1-yl)pyrimidin-5-yl)butanenitrile (**7k**)



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%

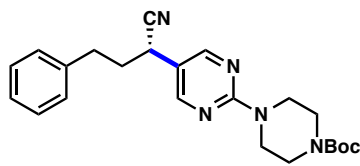
by chiral SFC analysis (AD, 2.5 mL/min, 15% IPA in CO₂, λ = 254 nm): *t*_R(minor) = 7.5 min, *t*_R(major) = 8.6 min. The product could be further enriched via recrystallization by vapor diffusion of pentane to a saturated solution of **7k** in DCM, affording 38.4 mg (89% recovery) of white needles. The enantiomeric excess of recrystallized **7k** was determined to be 95%. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = +13.073 (*c* = 1.595, CHCl₃). HRMS (MM) calc'd for [M+H]⁺ 307.1917, found 307.1848.

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



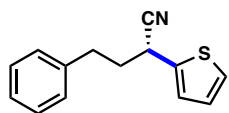
Prepared from 5-iodo-2-(pyrrolidin-1-yl)pyrimidine (55 mg, 0.2 mmol) and 2-chloro-4-phenylbutanenitrile (36.0 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 40:60 EtOAc:hexanes) to yield 35.0 mg (60% yield) of **7l** as a white solid. The enantiomeric excess was determined to be 85% by chiral SFC analysis (AD, 2.5 mL/min, 12% IPA in CO₂, 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%. ¹H 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).; ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = +12.942 (*c* = 1.130, CHCl₃). HRMS (MM) calc'd for [M+H₃O]⁺ 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 CO₂, 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%. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = +13.500 (*c* = 1.980, CHCl₃). HRMS (MM) calc'd for [M+Na]⁺ 430.2213, found 430.2294.

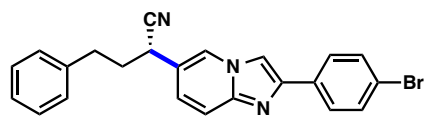
4-phenyl-2-(thiophen-2-yl)butanenitrile (**7n**)



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 CO₂, λ = 245 nm): *t_R*(minor) = 5.8 min, *t_R*(major) = 7.1 min. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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,

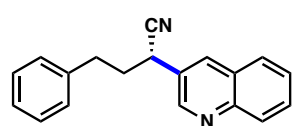
1029.74, 833.92, 750.39, 699.80 cm^{-1} ; $[\alpha]_{\text{D}}^{25} = -27.559$ ($c = 1.455$, CHCl_3). HRMS (MM) calc'd for $[\text{M}+\text{H}_3\text{O}]^+$ 246.0947, found 246.1107.

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 , $\lambda = 245$ nm): $t_{\text{R}}(\text{minor}) = 10.7$ min, $t_{\text{R}}(\text{major}) = 14.3$ 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 ($t_{\text{R}} = 8.6$ min) that was not observed in any other analysis. This peak was significantly diminished following recrystallization. ^1H 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} ; $[\alpha]_{\text{D}}^{25} = +28.004$ ($c = 0.275$, CHCl_3). HRMS (MM) calc'd for $[\text{M}+\text{H}]^+$ 416.0757, found 416.0698.

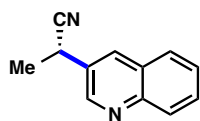
4-phenyl-2-(quinolin-3-yl)butanenitrile (3a)



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

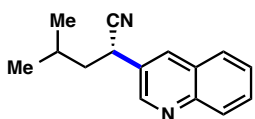
3a as a light yellow oil that solidified on standing. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AD, 2.5 mL/min, 20% IPA in CO₂, λ = 280 nm): *t*_R(major) = 6.1 min, *t*_R(minor) = 6.8 min. ¹H NMR (500 MHz, Chloroform-*d*) δ 8.81 (s, 1H), 8.18 (d, *J* = 2.3 Hz, 1H), 8.12 (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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = -1.617 (*c* = 0.952, CHCl₃). 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 CO₂, λ = 254 nm): *t*_R(major) = 7.8 min, *t*_R(minor) = 8.8 min. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = -20.200 (*c* = .355, CHCl₃). HRMS (MM) calc'd for [M+H₃O]⁺ 201.1022, found 201.1022.

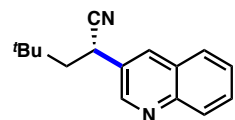
4-methyl-2-(quinolin-3-yl)pentanenitrile (**3c**)



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

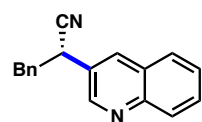
excess was determined to be 89% by chiral SFC analysis (OB-H, 2.5 mL/min, 5% IPA in CO₂, λ = 254 nm): *t_R*(minor) = 4.2 min, *t_R*(major) = 4.6 min. ¹H NMR (500 MHz, Chloroform-*d*) δ 8.83 (d, *J* = 2.4 Hz, 1H), 8.19 (d, *J* = 2.4 Hz, 1H), 8.13 (dq, *J* = 8.5, 0.9 Hz, 1H), 7.85 (ddd, *J* = 8.1, 1.3, 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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = -22.811 (*c* = 0.350, CHCl₃). HRMS (MM) calc'd for [M+H₃O]⁺ 243.1492, found 243.1194.

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



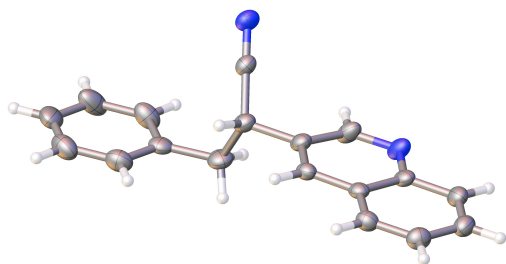
Prepared from 3-iodoquinoline (51.2 mg, 0.2 mmol) and 2-chloro-4,4-dimethylpentanenitrile (29.1 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 30:70 EtOAc:hexanes) to yield 21.4 mg (45% yield) of **3d** as a clear oil. The enantiomeric excess was determined to be 93% by chiral SFC analysis (AD, 2.5 mL/min, 12% IPA in CO₂, λ = 280 nm): *t_R*(major) = 5.5 min, *t_R*(minor) = 6.8 min. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = -55.546 (*c* = 0.515, CHCl₃). HRMS (MM) calc'd for [M+H]⁺ 239.1543, found 239.1530.

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

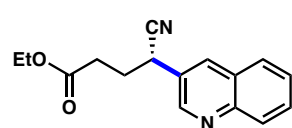


Prepared from 3-iodoquinoline (51.2 mg, 0.2 mmol) and 2-chloro-3-phenylpropanenitrile (33.1 mg, 0.2 mmol) with NaBF₄ (22 mg, 0.2 mmol) following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 30:70 EtOAc:hexanes) to yield 33.8 mg (65% yield) of **3e** as a light

yellow solid. The enantiomeric excess was determined to be 90% by chiral SFC analysis (AD, 2.5 mL/min, 20% IPA in CO₂, 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 SHELXS¹ and refined against *F*² on all data by full-matrix least squares with SHELXL-2014² 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 *P*2₁2₁2₁ and absolute configuration was determined by anomalous dispersion (Flack = -0.15(8)). ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = -1.218 (*c* = 0.870, CHCl₃). 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.

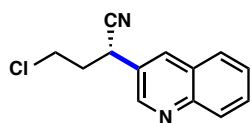
¹ Sheldrick, G. M. *Acta Cryst.* **1990**, *A46*, 467.

² Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112.

³ Müller, P. *Crystallography Reviews* **2009**, *15*, 57.

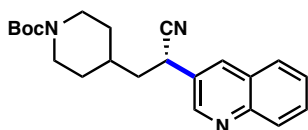
The crude residue was purified by silica gel chromatography (0:100 to 30:70 EtOAc:hexanes) to yield 34.0 mg (63% yield) of **3f** as a clear oil. The enantiomeric excess was determined to be 80% by chiral SFC analysis (AD, 2.5 mL/min, 12% IPA in CO₂, λ = 254 nm): *t*_R(major) = 7.2 min, *t*_R(minor) = 8.3 min. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = -9.319 (*c* = 0.860, CHCl₃). 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 CO₂, λ = 254 nm): *t*_R(major) = 7.1 min, *t*_R(minor) = 9.7 min. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = +9.150 (*c* = 0.665, CHCl₃). HRMS (MM) calc'd for [M+H₃O]⁺ 249.0789, found 249.0270.

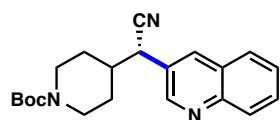
tert-butyl-4-(2-cyano-2-(quinolin-3-yl)ethyl)piperidine-1-carboxylate (**3h**)



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)

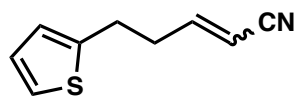
following General Procedure 3. The crude residue was purified by silica gel chromatography (0:100 to 40:60 EtOAc:hexanes) to yield 44.7 mg (61% yield) of **3h** as a clear oil. The enantiomeric excess was determined to be 89% by chiral SFC analysis (AD, 2.5 mL/min, 25% IPA in CO₂, $\lambda = 280$ nm): $t_R(\text{major}) = 4.8$ min, $t_R(\text{minor}) = 6.0$ min. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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; $[\alpha]_D^{25} = -4.158$ ($c = 1.900$, CHCl₃). 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 CO₂, $\lambda = 280$ nm): $t_R(\text{minor}) = 18.5$ min, $t_R(\text{major}) = 19.5$ min. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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; $[\alpha]_D^{25} = -21.275$ ($c = 0.640$, CHCl₃). HRMS (MM) calc'd for $[M+Mg]^+$ 377.1948, found 377.2042.

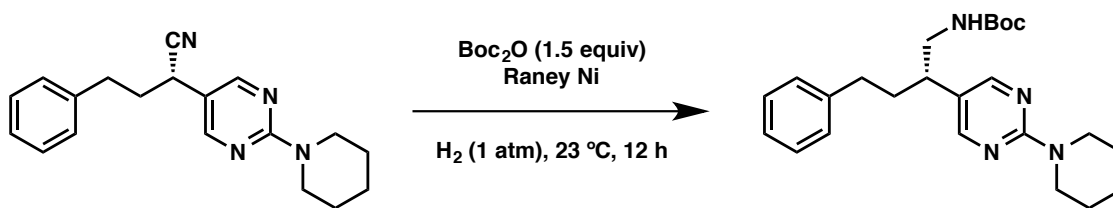
5-(thiophen-2-yl)pent-2-enitrile (1:1 cis/trans) (**12**)



Prepared from 2-iodothiophene (11 μ L, 0.1 mmol) and 2-chloro-2-cyclopropylacetonitrile (11.6 mg, 0.1 mmol) following General Procedure 3. The crude residue was purified by preparative 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. ¹H 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)[§]. ¹³C NMR (126 MHz, cdcl₃) 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.

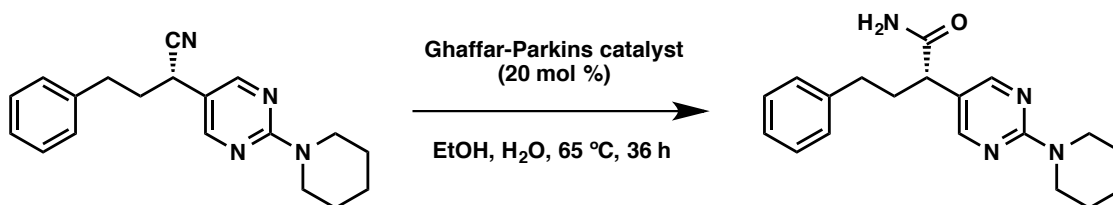
a. Hydrogenation of **7k** over Raney Ni to Boc-amine **8**.



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 N₂ for 15 min, then flushed with two balloons of H₂. The flask was equipped with a balloon of H₂ 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 CO₂, λ = 235 nm): *t_R*(major) = 10.5 min, *t_R*(minor) = 12.3 min. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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; [α]_D²⁵ = -15.883 (*c* = 2.365, CHCl₃). HRMS (MM) calc'd for [M]⁺ 410.2676, found 410.2101.

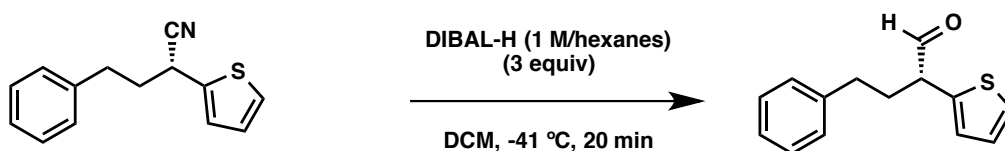
b. Hydrolysis of XX with Ghaffar-Parkins catalyst to carboxamide 9.



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 H₂O (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 °C for 36 h. After cooling to room temperature, the reaction was diluted with DCM and filtered through a short plug of silica gel and Na₂SO₄. 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 ¹H NMR using Europium(III) tris[3-(trifluoromethylhydroxymethylene)-*d*-camphorate] (30 mol %) as a chiral shift reagent. ¹H 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); ¹³C NMR (126 MHz, cdcl₃) 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} $[\alpha]_{\text{D}}^{25} = +35.005$ ($c = 2.455$, CHCl_3). HRMS (MM) calc'd for $[\text{M}]^+$ 324.1945, found 324.1904.

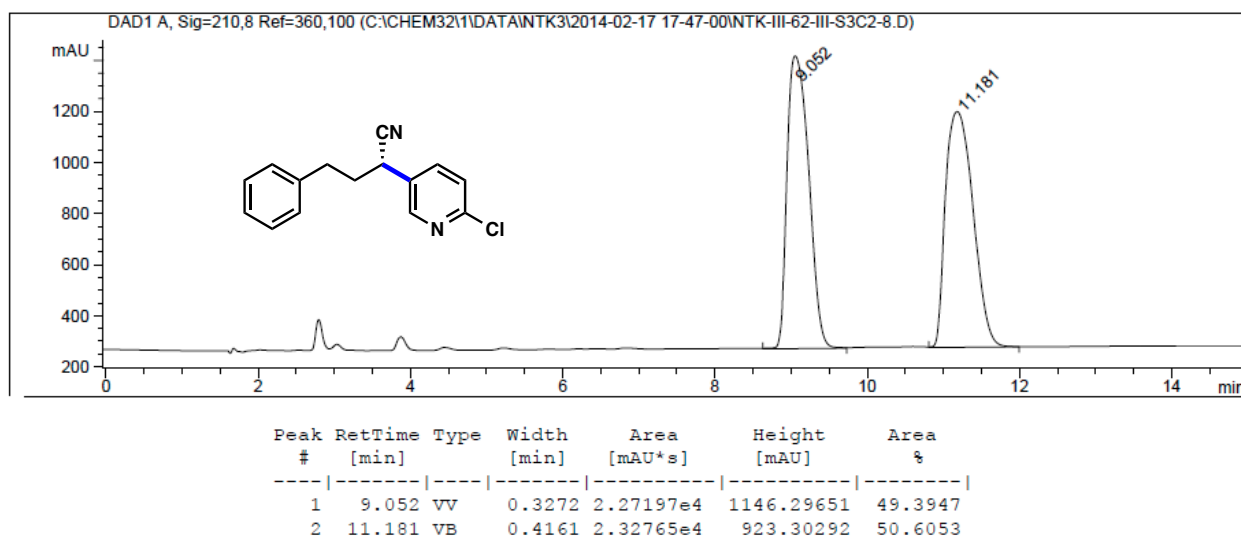
c. DIBAL-H reduction of **7n** to carboxaldehyde **10**.



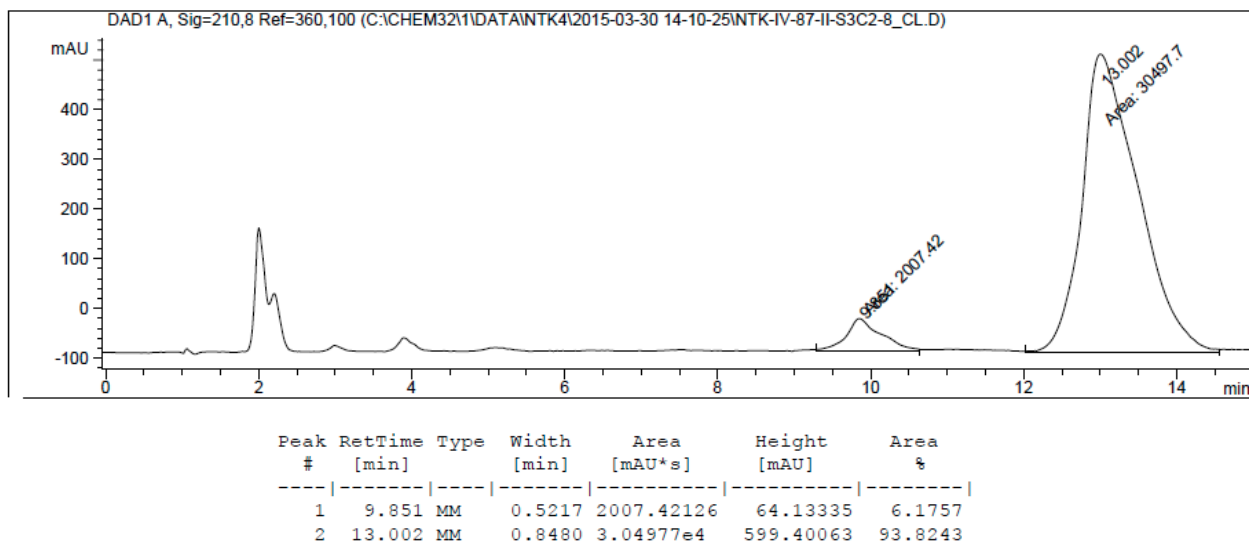
To a flame-dried flask was added 4-phenyl-2-(thiophen-2-yl)butanenitrile (**7n**, 46 mg, 0.2 mmol, 88% ee) and DCM (30 mL). The reaction was cooled to $-41\text{ }^{\circ}\text{C}$ and a 1 M solution of DIBAL-H in hexanes (3 equiv, 0.6 mL, 0.6 mmol) was added slowly via syringe. The reaction was complete 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 , $\lambda = 235\text{ nm}$): $t_{\text{R}}(\text{minor}) = 4.5\text{ min}$, $t_{\text{R}}(\text{major}) = 5.1\text{ min}$. $^1\text{H NMR}$ (500 MHz, Chloroform- d) δ 9.61 (d, $J = 2.1\text{ Hz}$, 1H), 7.34 – 7.28 (m, 3H), 7.25 – 7.20 (m, 1H), 7.18 (dq, $J = 7.6, 0.7\text{ Hz}$, 2H), 7.07 (dd, $J = 5.1, 3.5\text{ Hz}$, 1H), 6.95 (ddd, $J = 3.5, 1.2, 0.7\text{ Hz}$, 1H), 3.79 (ddd, $J = 8.4, 6.3, 2.1\text{ Hz}$, 1H), 2.73 (ddd, $J = 14.4, 9.0, 5.7\text{ Hz}$, 1H), 2.64 (ddd, $J = 13.8, 8.8, 7.0\text{ Hz}$, 1H), 2.43 (dddd, $J = 13.6, 9.0, 7.1, 6.3\text{ Hz}$, 1H), 2.17 – 2.07 (m, 1H); $^{13}\text{C NMR}$ (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} ; $[\alpha]_{\text{D}}^{25} = +4.156$ ($c = 0.70$, CHCl_3). HRMS (MM) calc'd for $[\text{M}]^+$ 410.2676, found 410.2101.

5. SFC traces for racemic and enantioenriched benzylic nitriles.

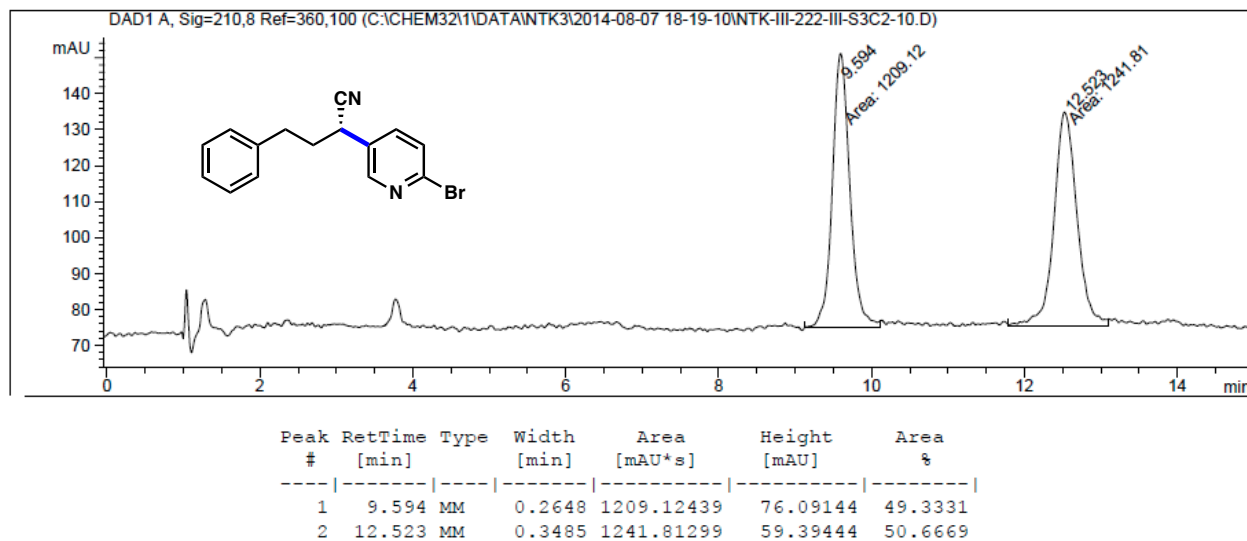
7a racemic



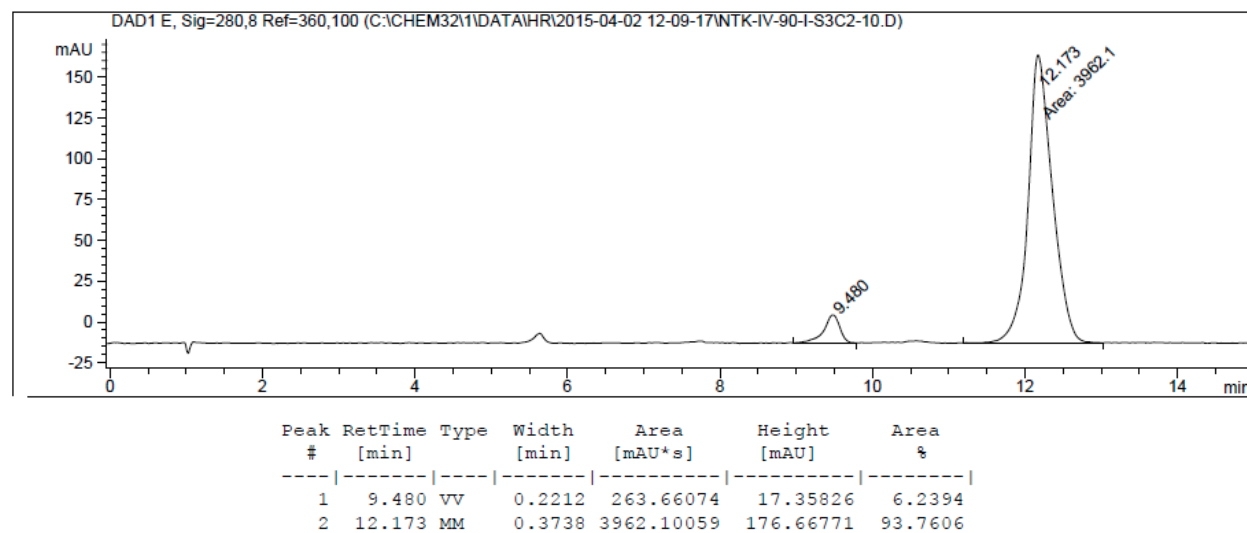
7a enantioenriched, 88% ee



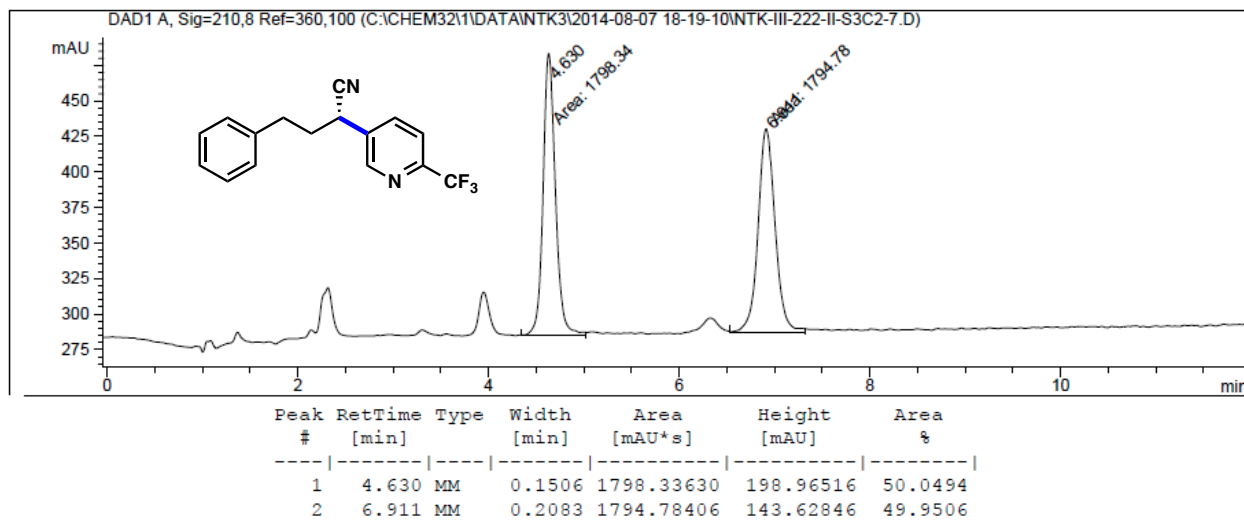
7b racemic



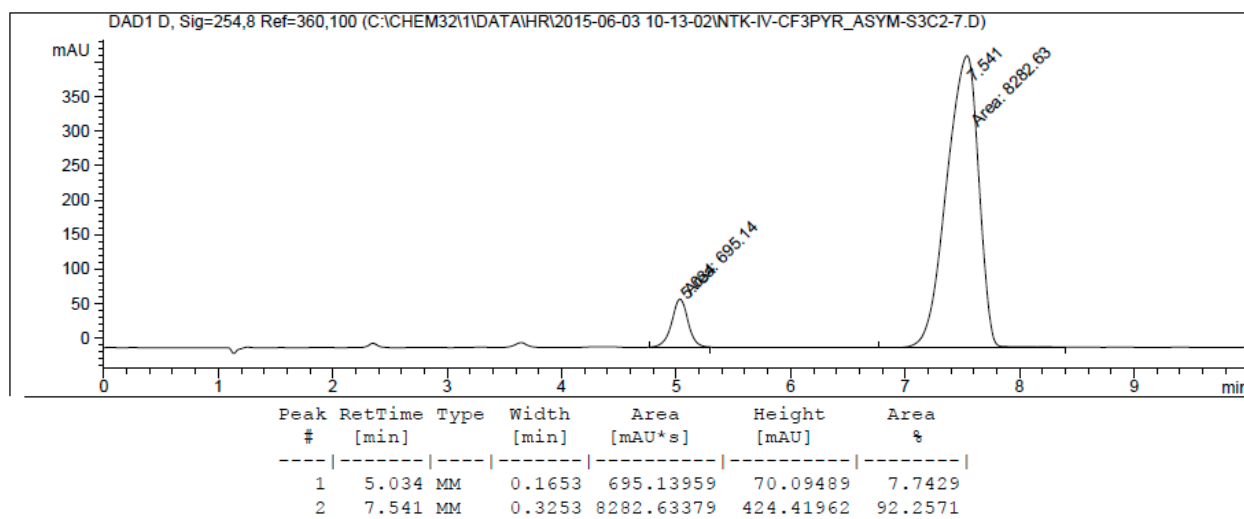
7b enantioenriched, 88% ee



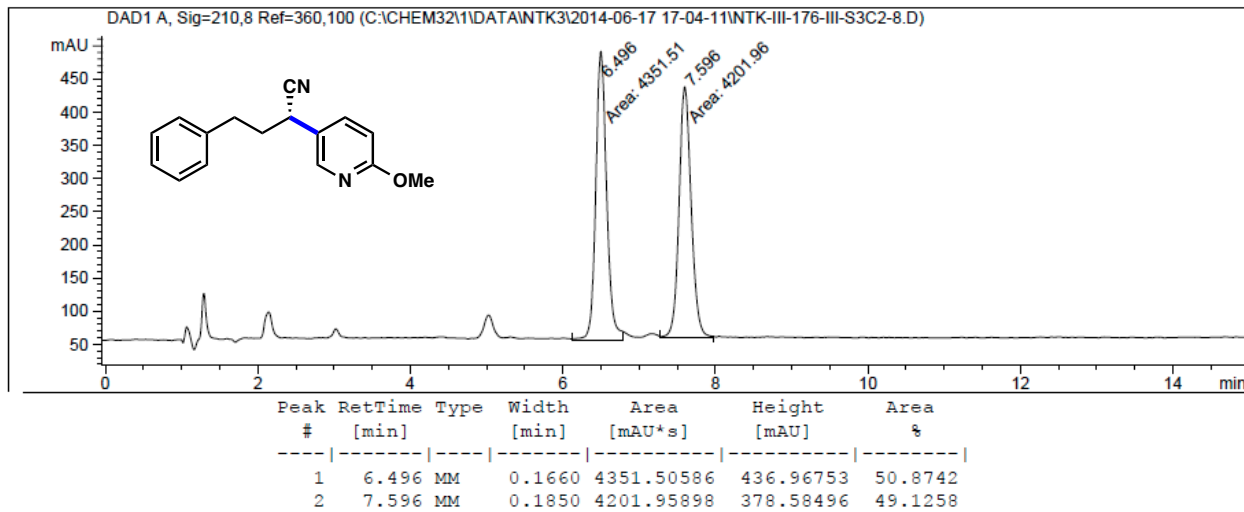
7c racemic



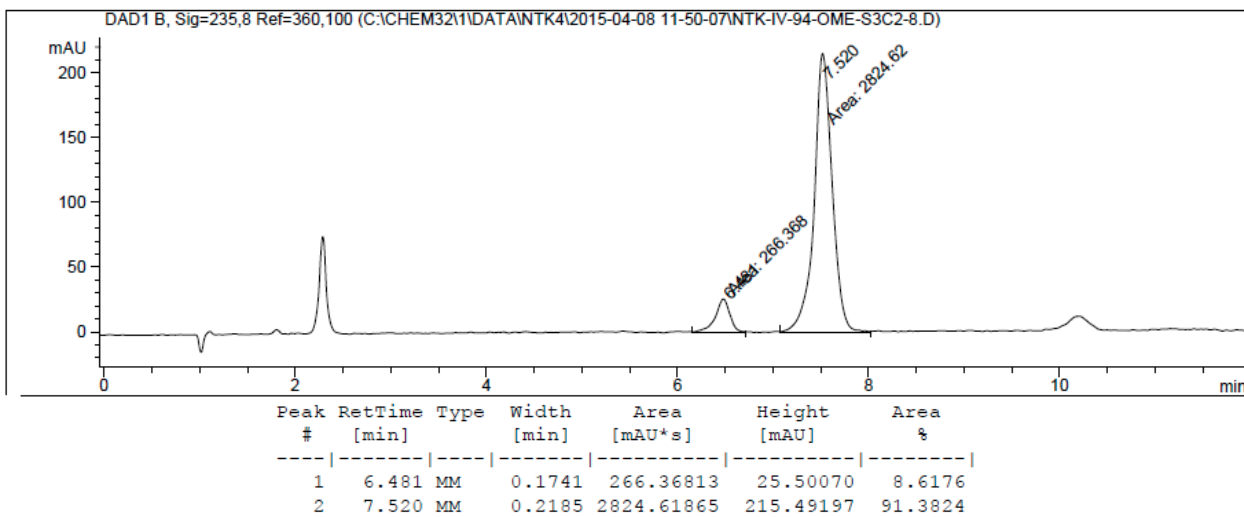
7c enantioenriched, 85% ee



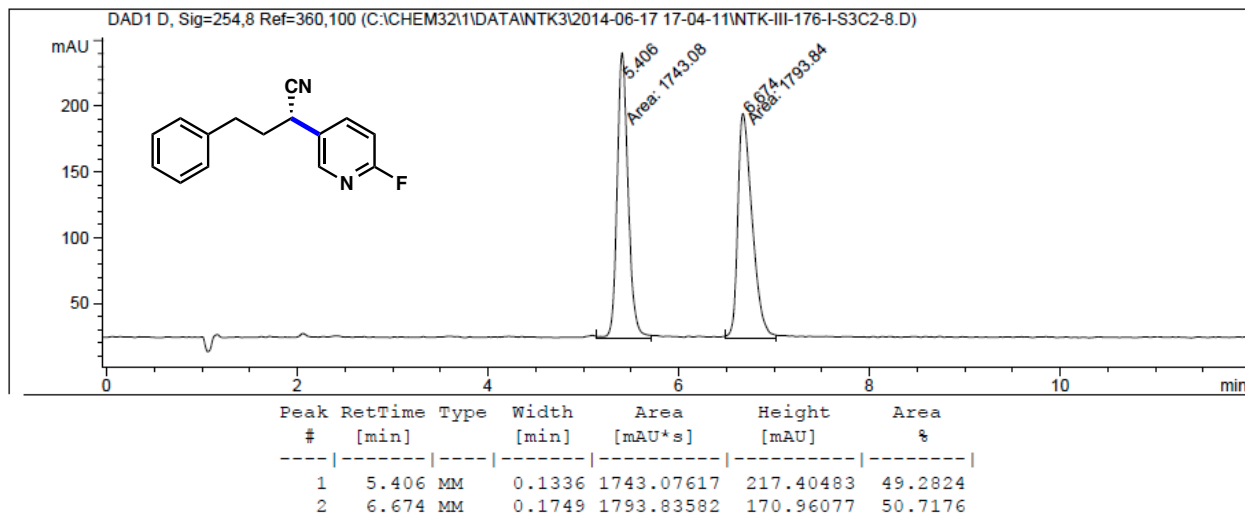
7d racemic



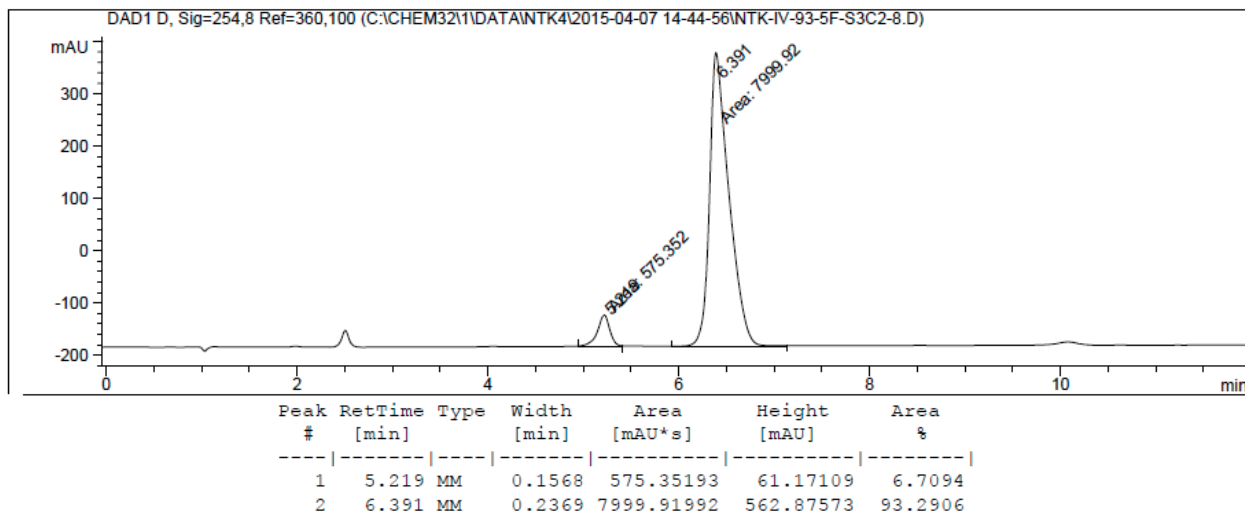
7d enantioenriched, 83% ee



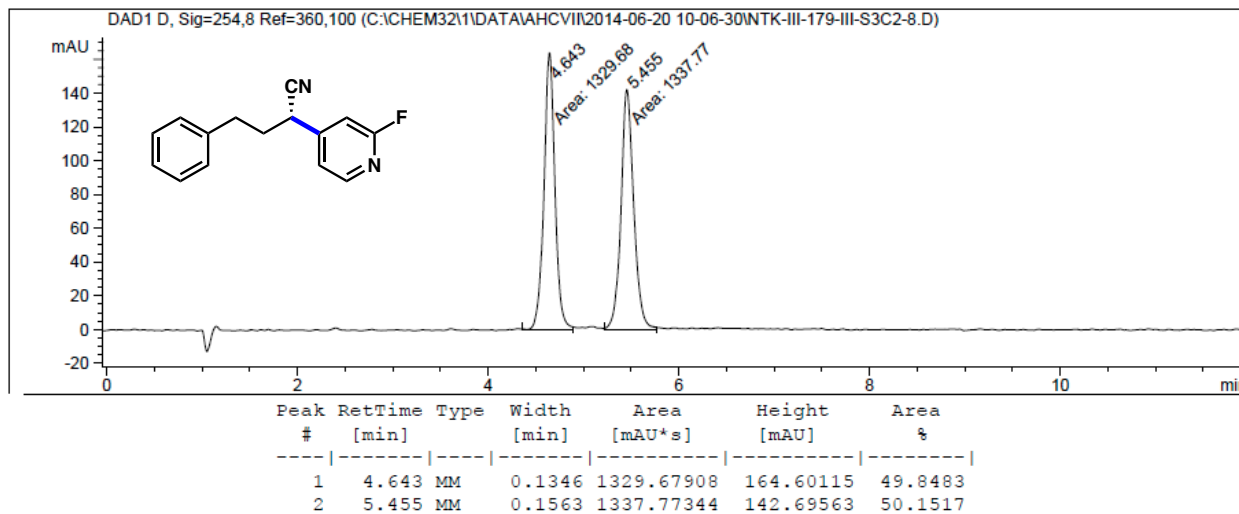
7e racemic



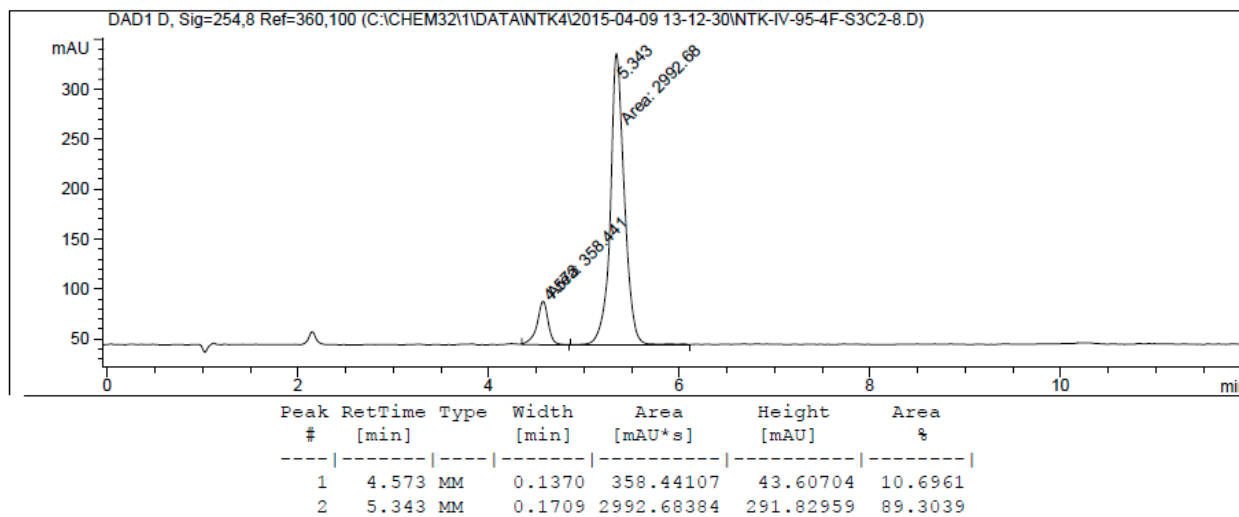
7e enantioenriched, 87% ee



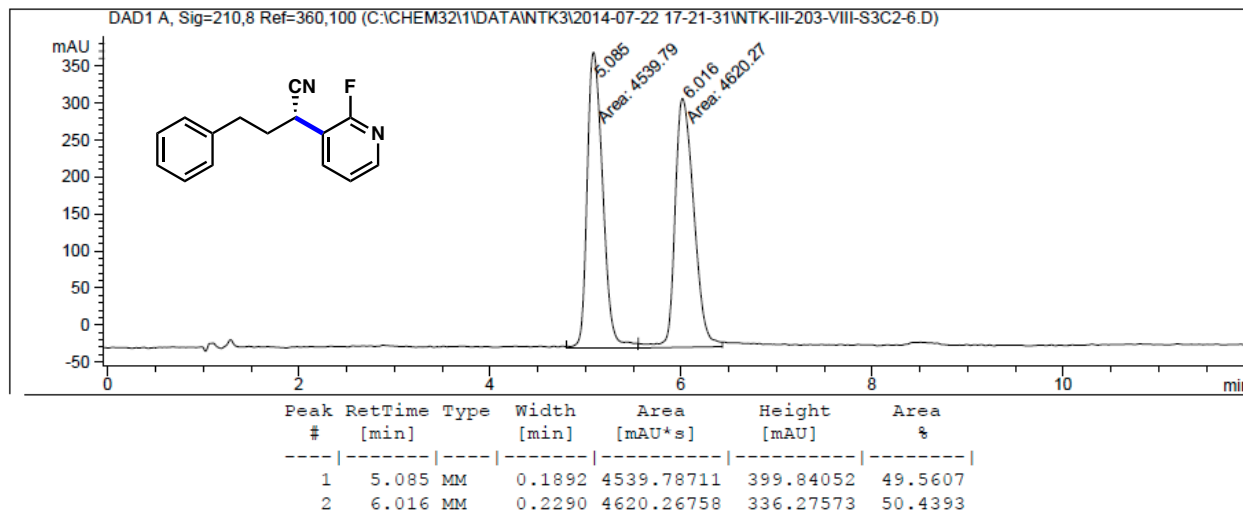
7f racemic



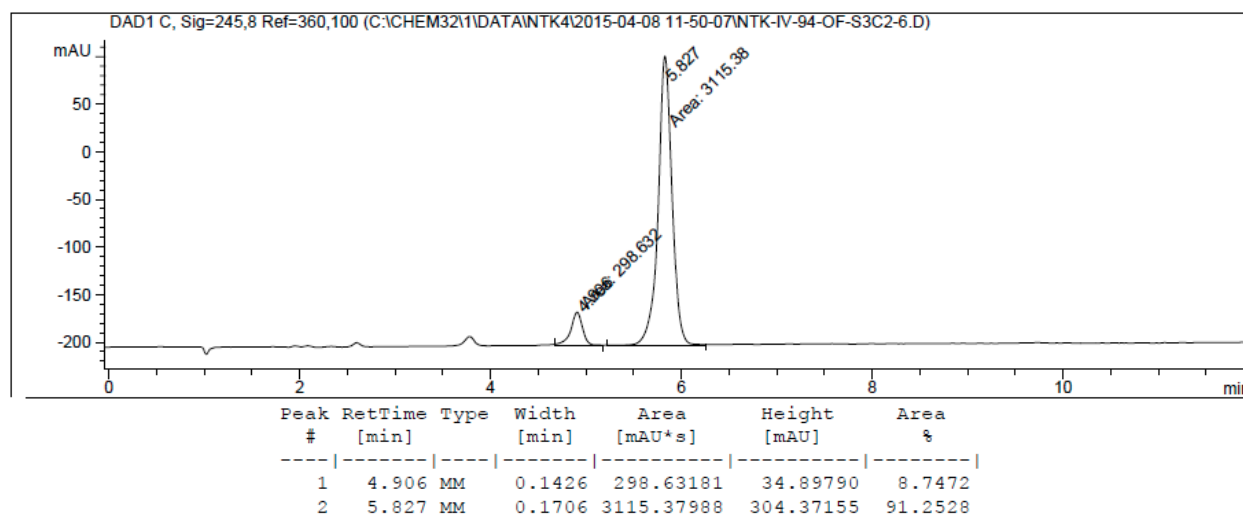
7f enantioenriched, 79% ee



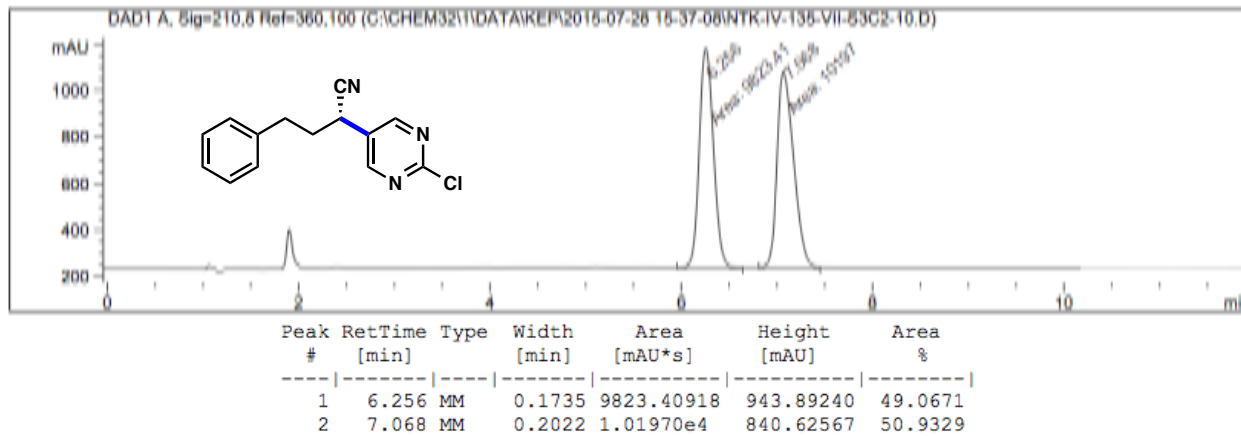
7g racemic



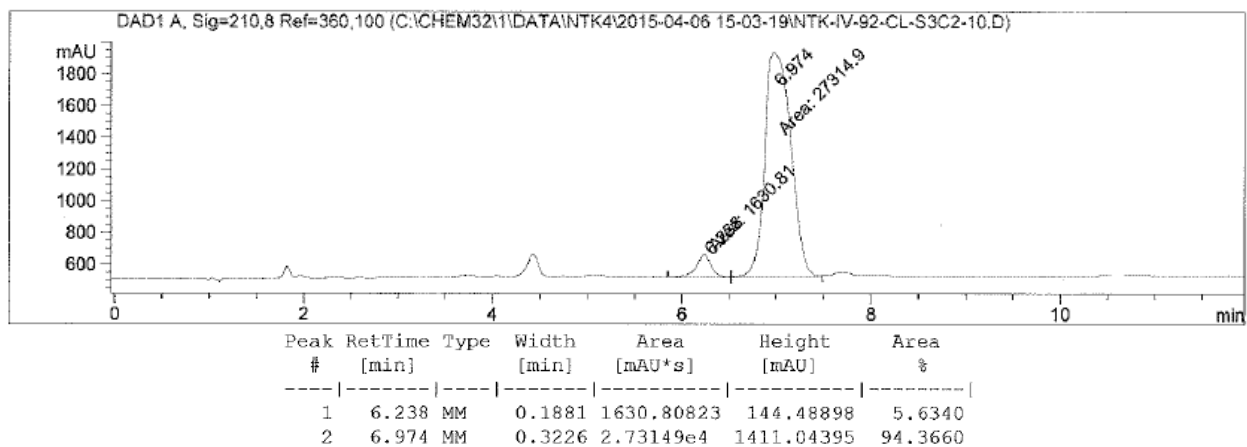
7g enantioenriched, 83% ee



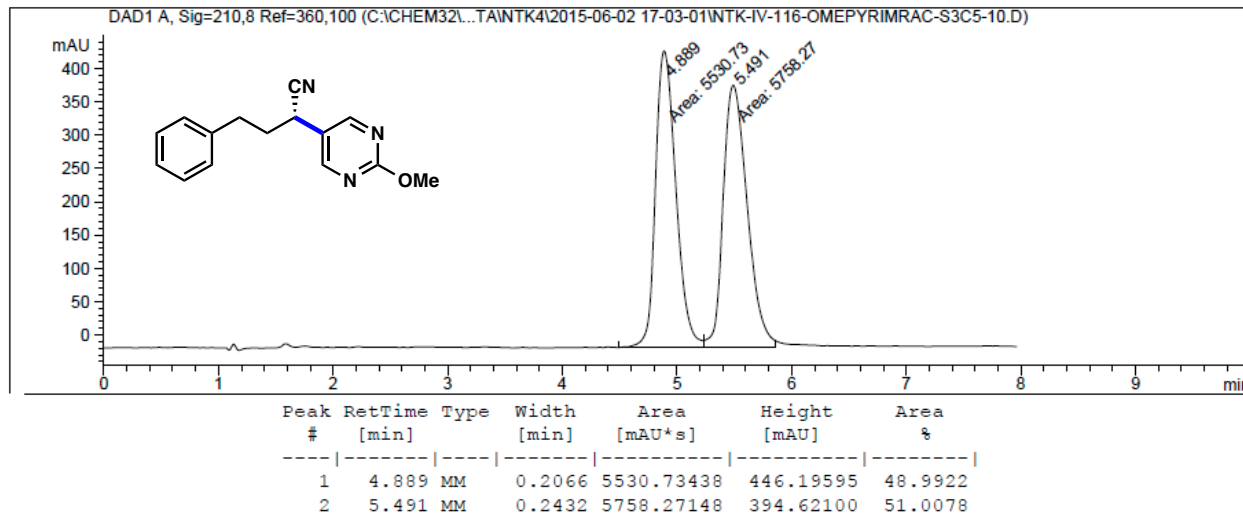
7h racemic



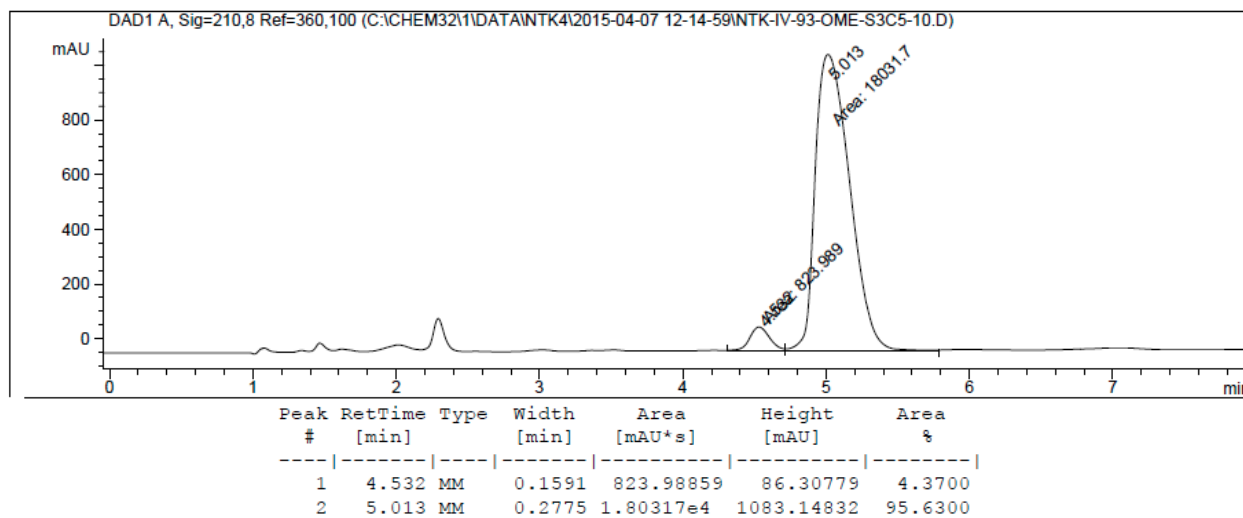
7h enantioenriched, 89% ee



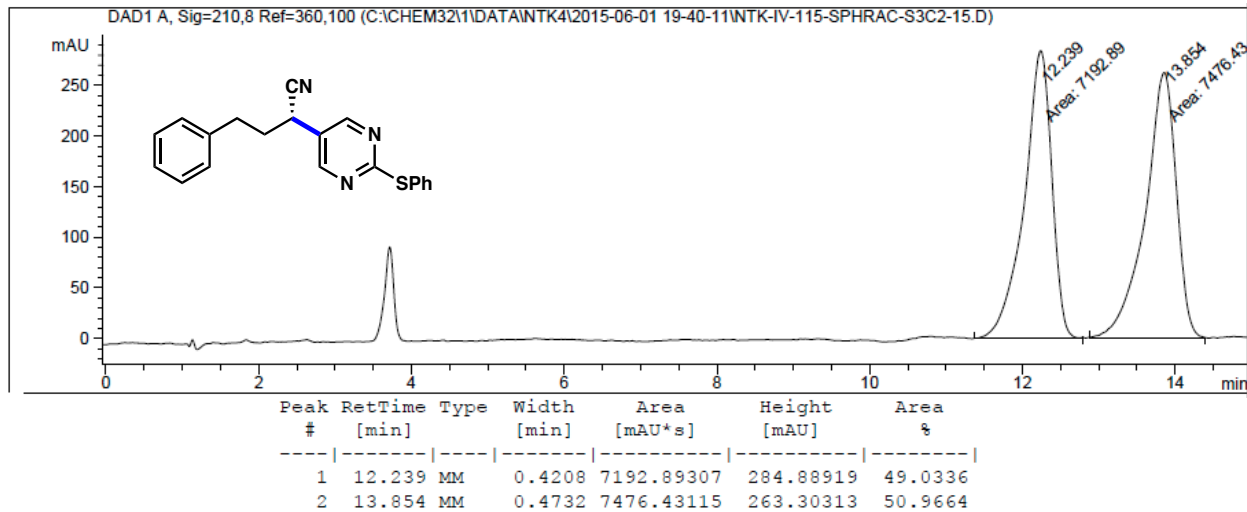
7i racemic



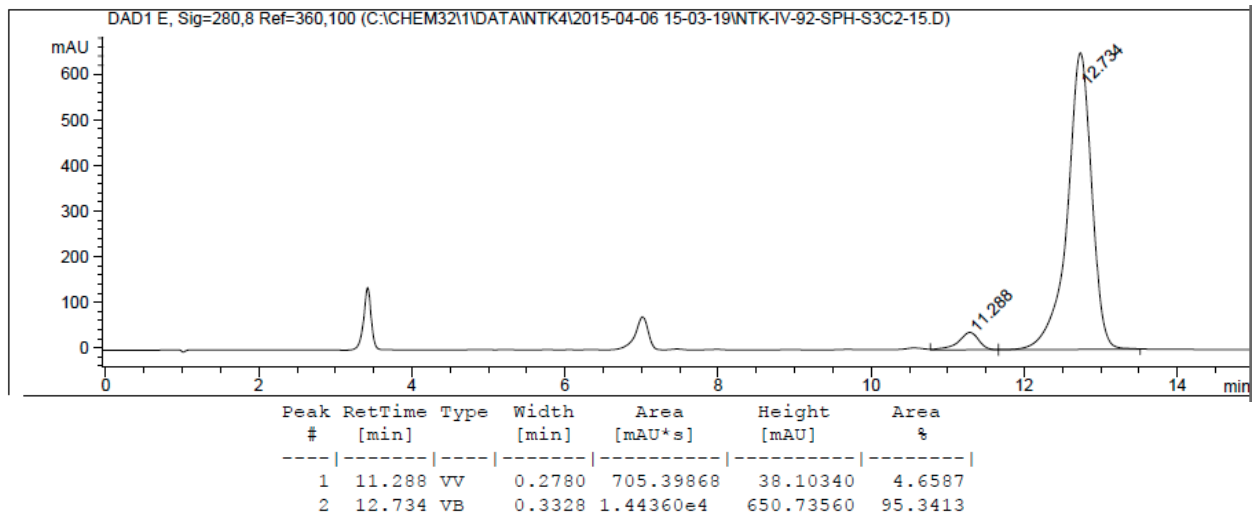
7i enantioenriched, 92% ee



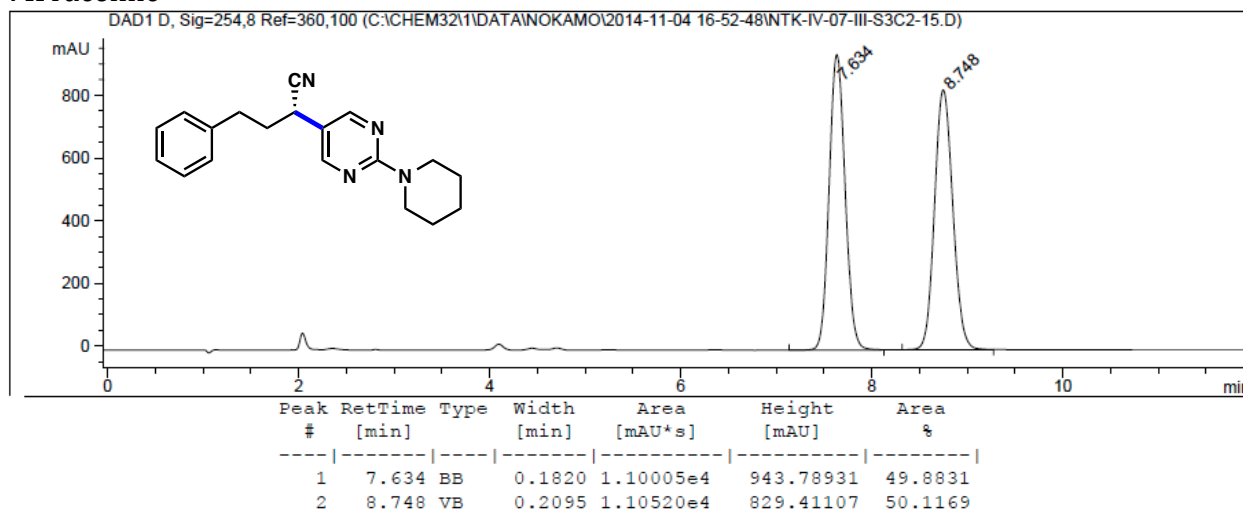
7j racemic



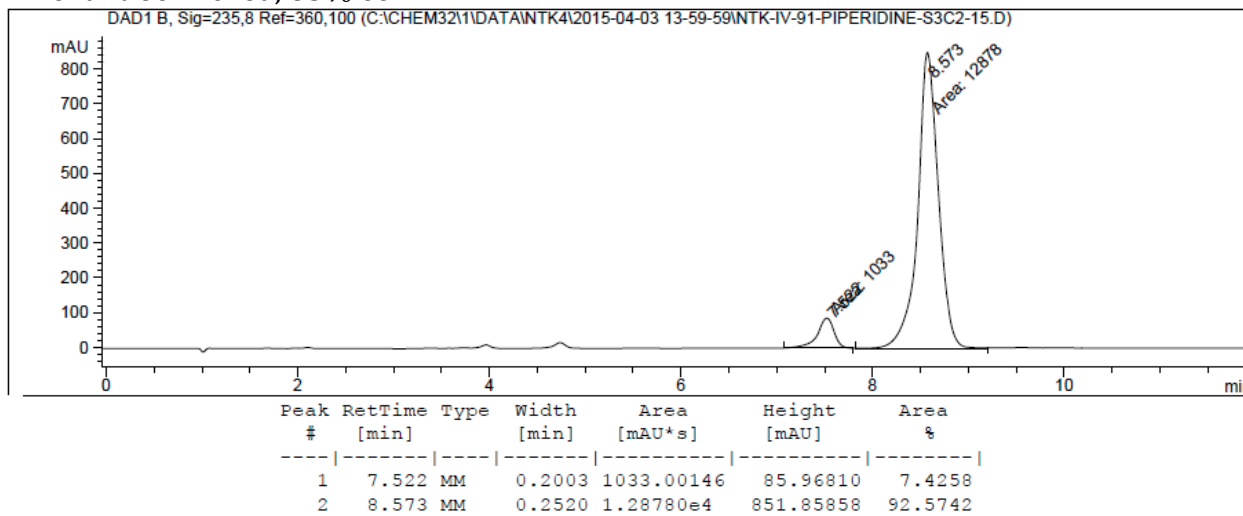
7j enantioenriched, 91% ee



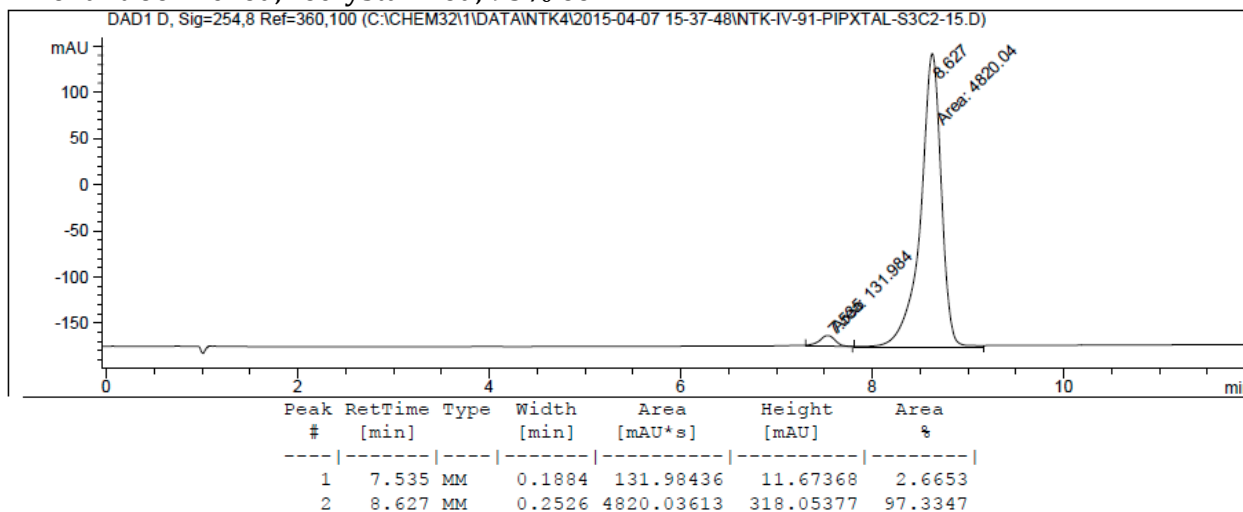
7k racemic



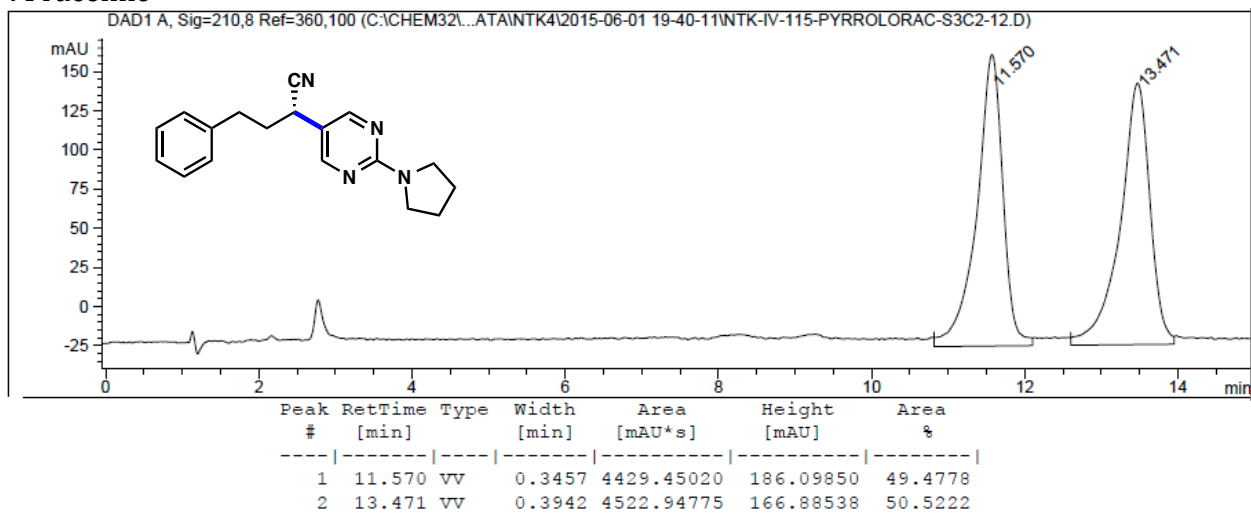
7k enantioenriched, 85% ee



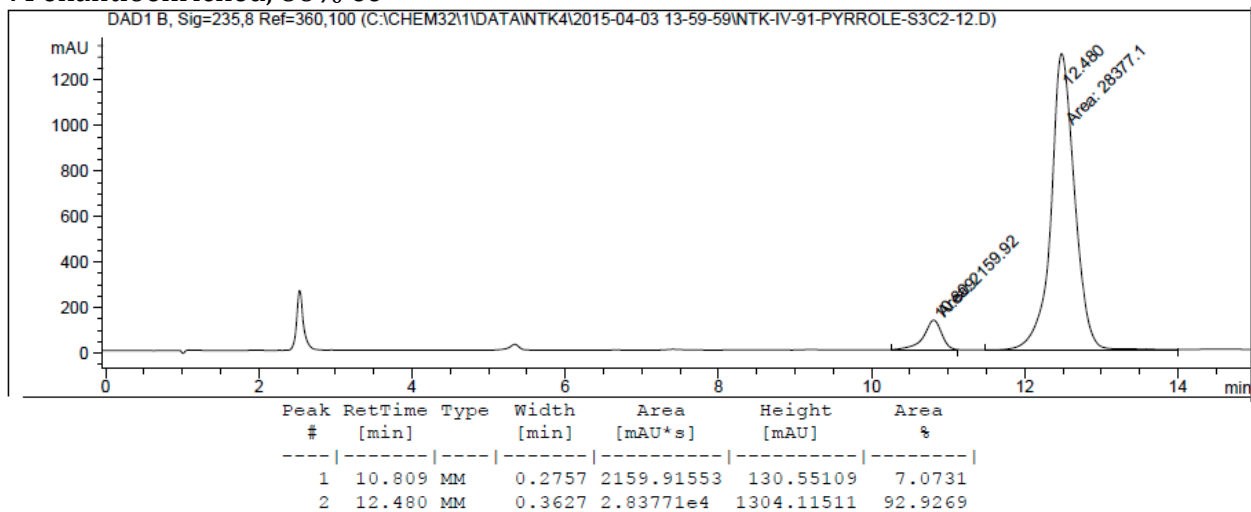
7k enantioenriched, recrystallized, 95% ee



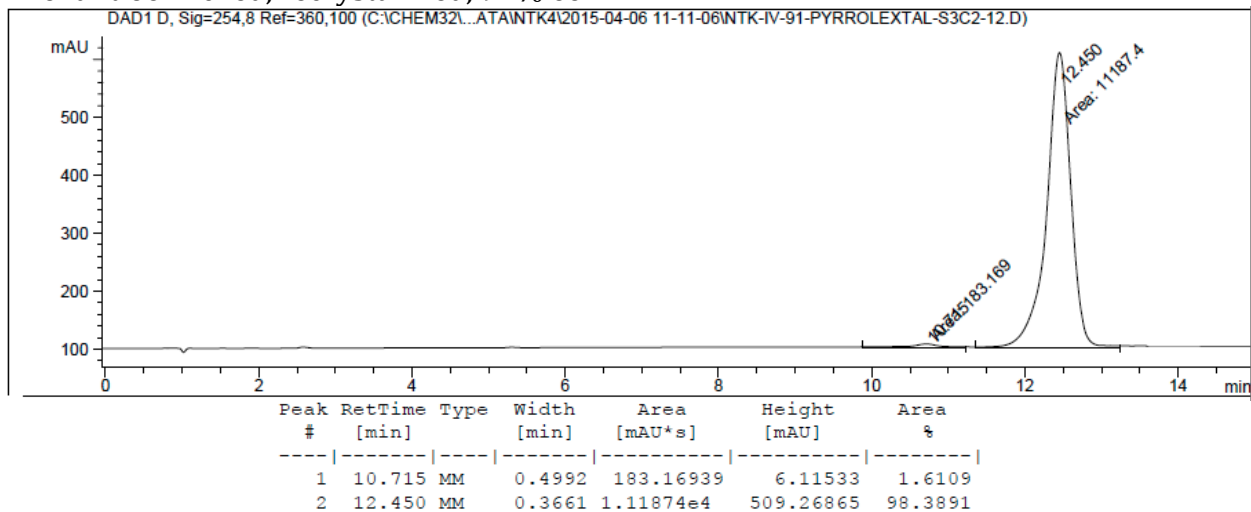
7l racemic



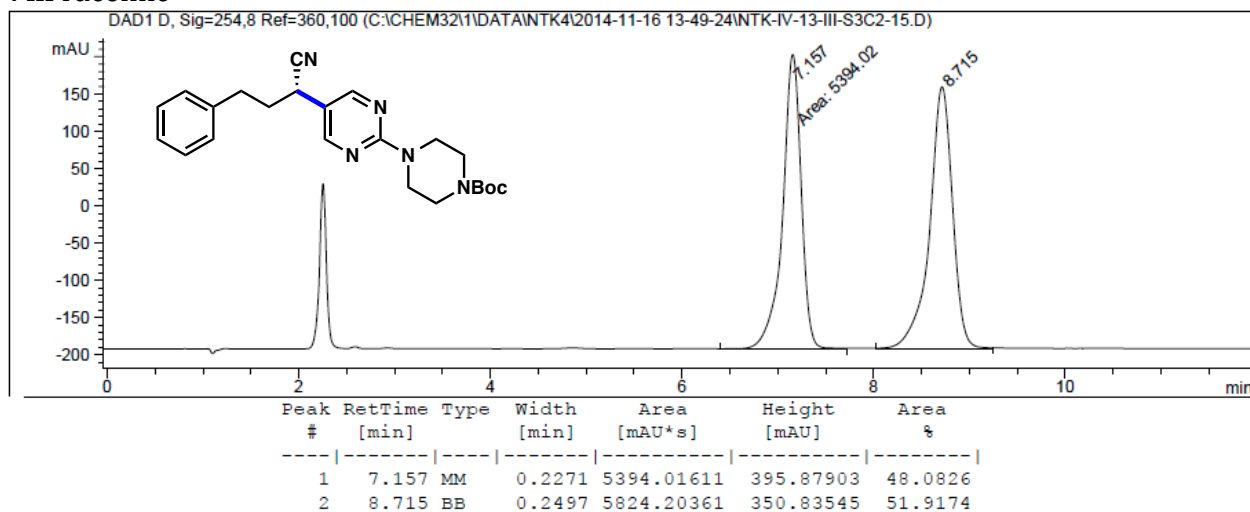
7l entioenriched, 86% ee



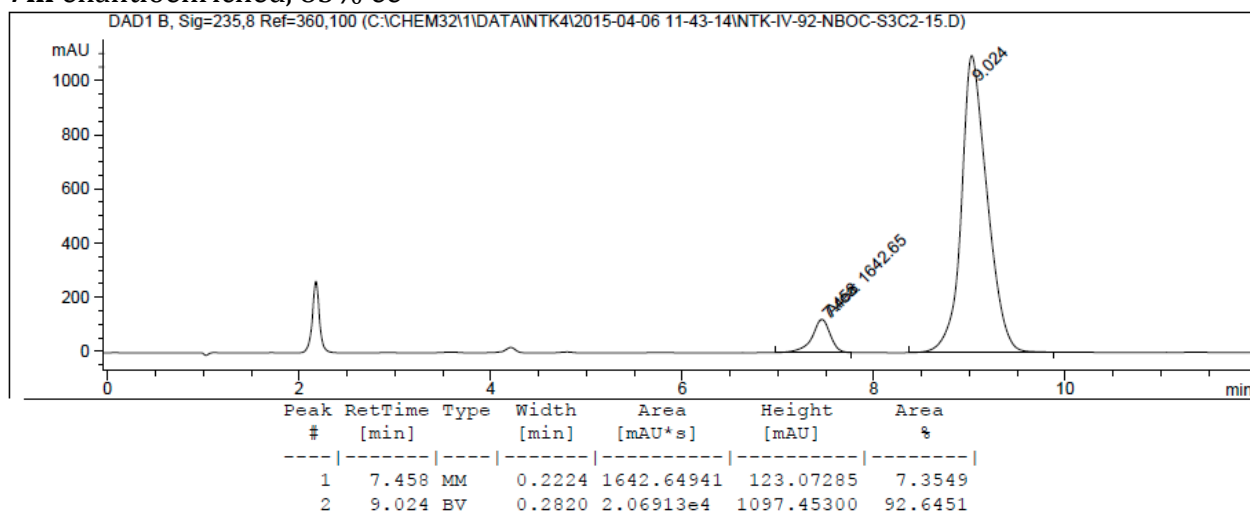
7l entioenriched, recrystallized, 97% ee



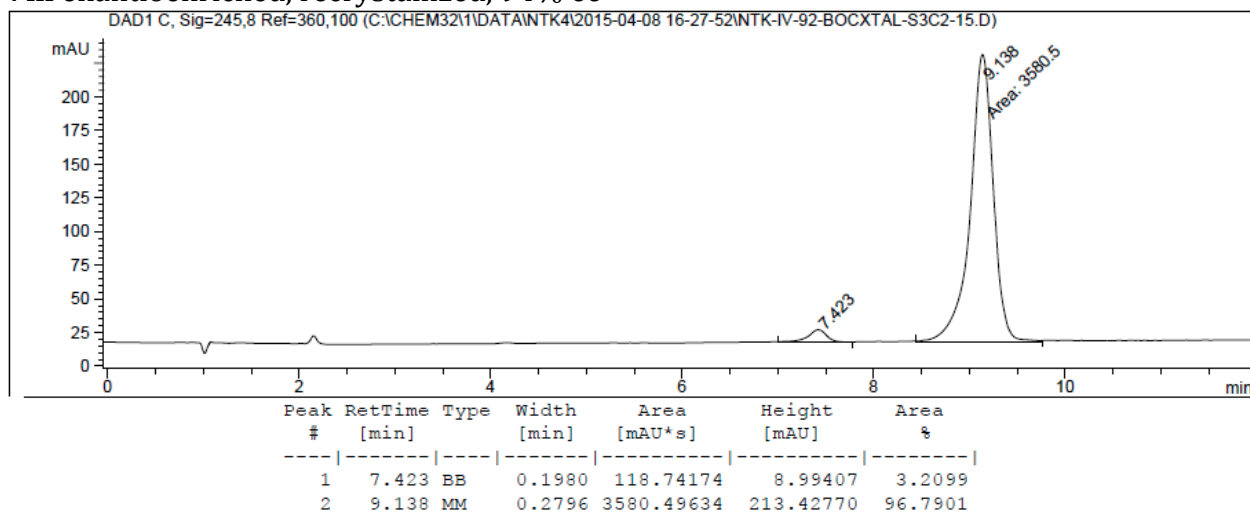
7m racemic



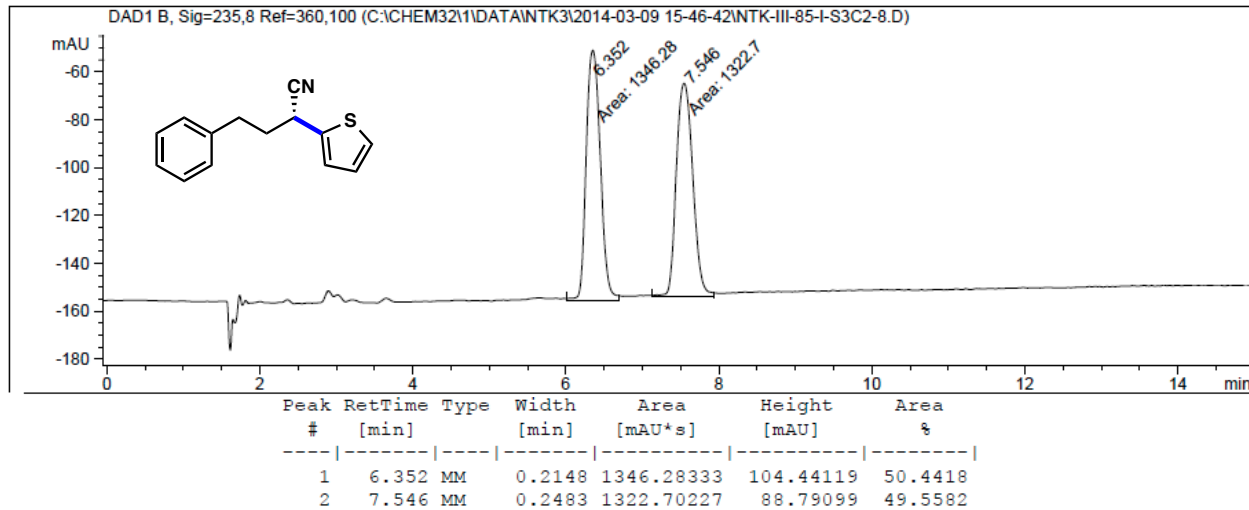
7m enantioenriched, 85% ee



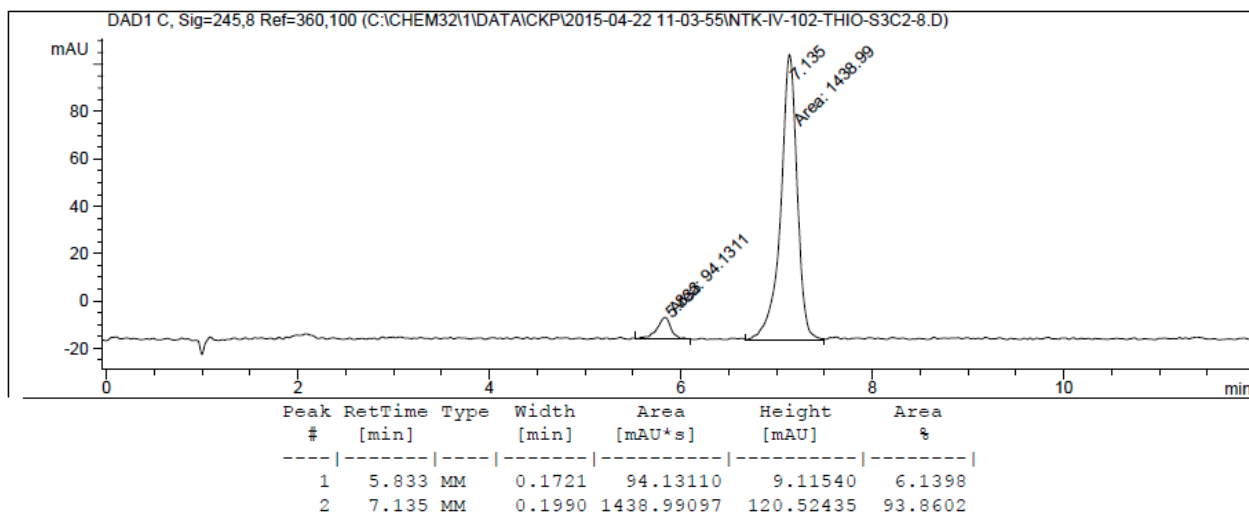
7m enantioenriched, recrystallized, 94% ee



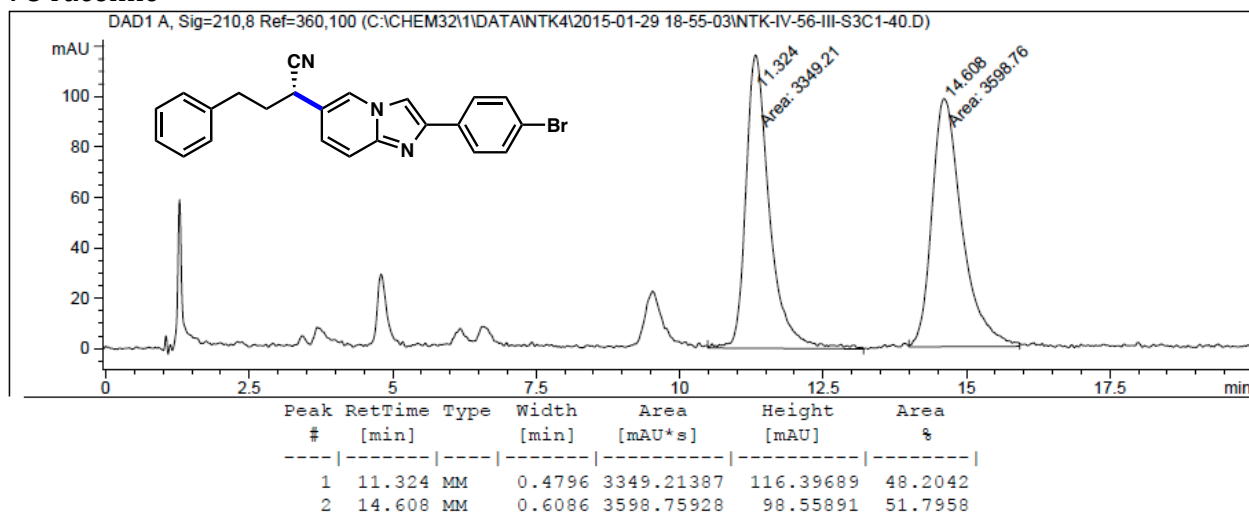
7n racemic



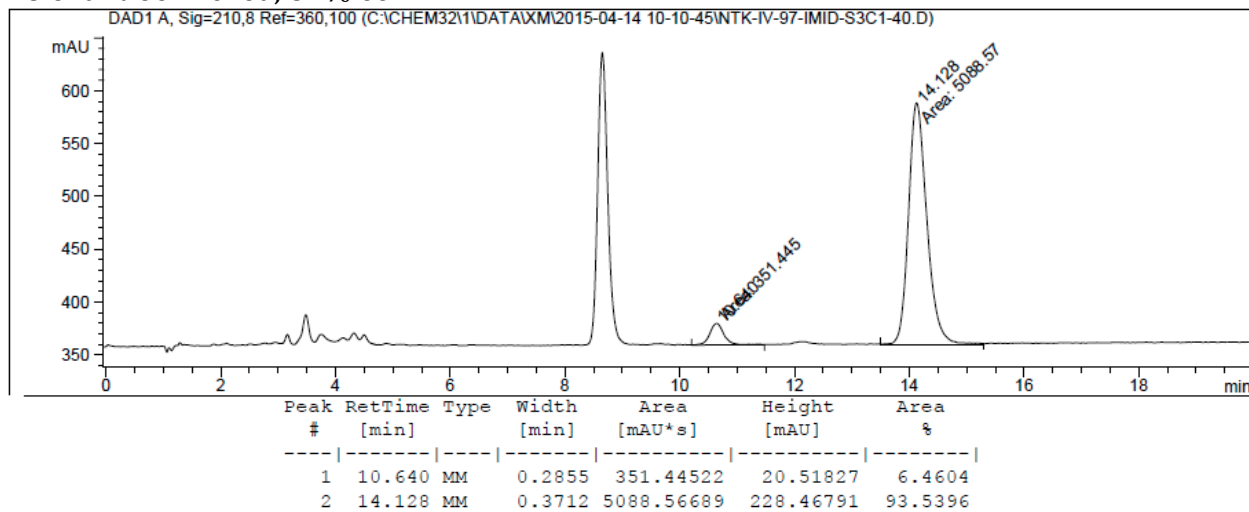
7n enantioenriched, 88% ee



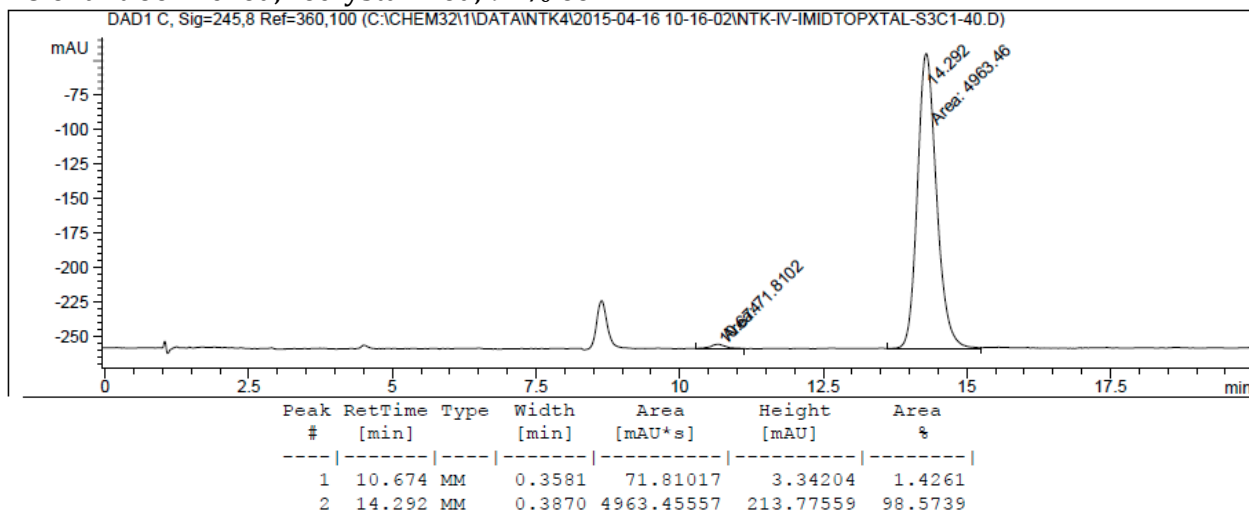
7o racemic



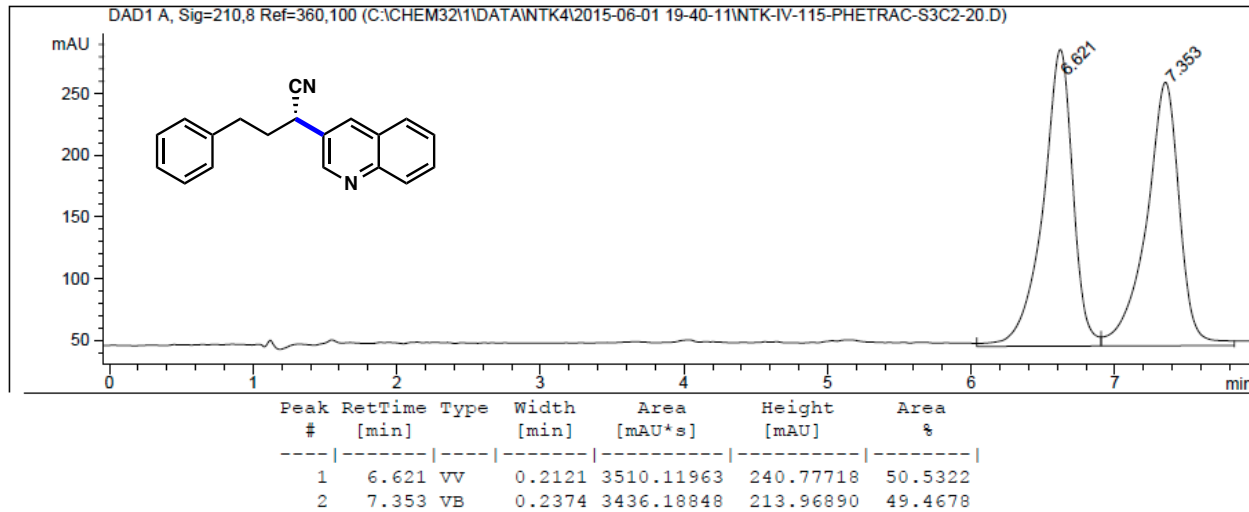
7o enantioenriched, 87% ee



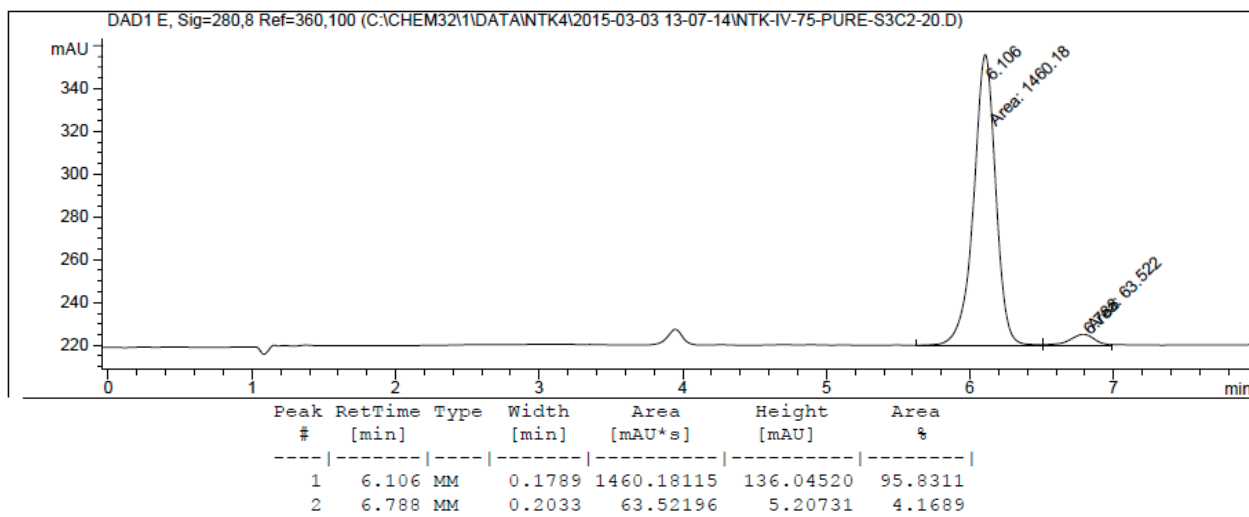
7o enantioenriched, recrystallized, 97% ee



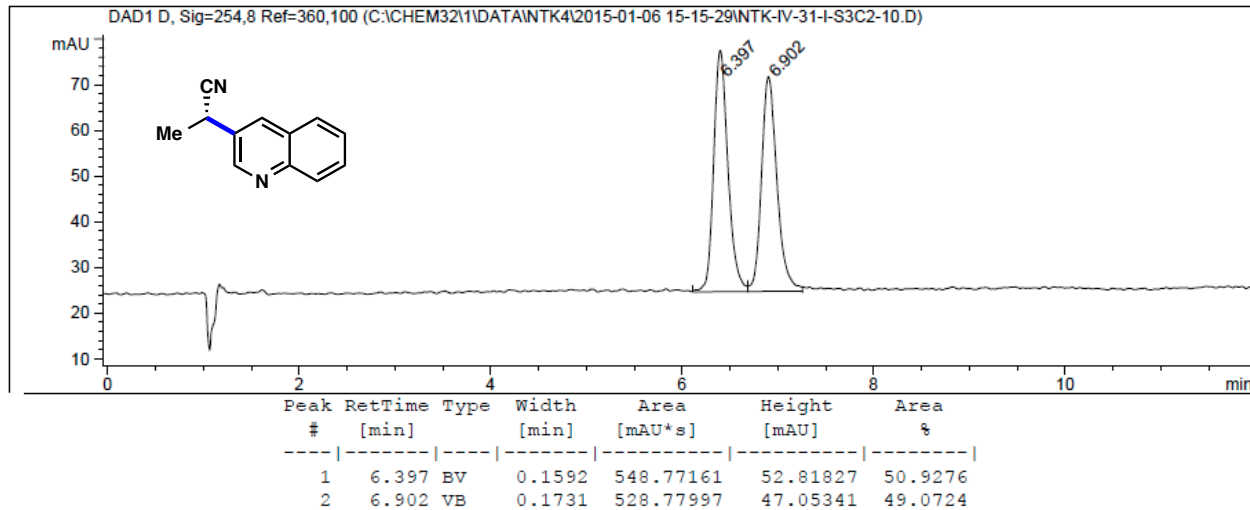
3a racemic



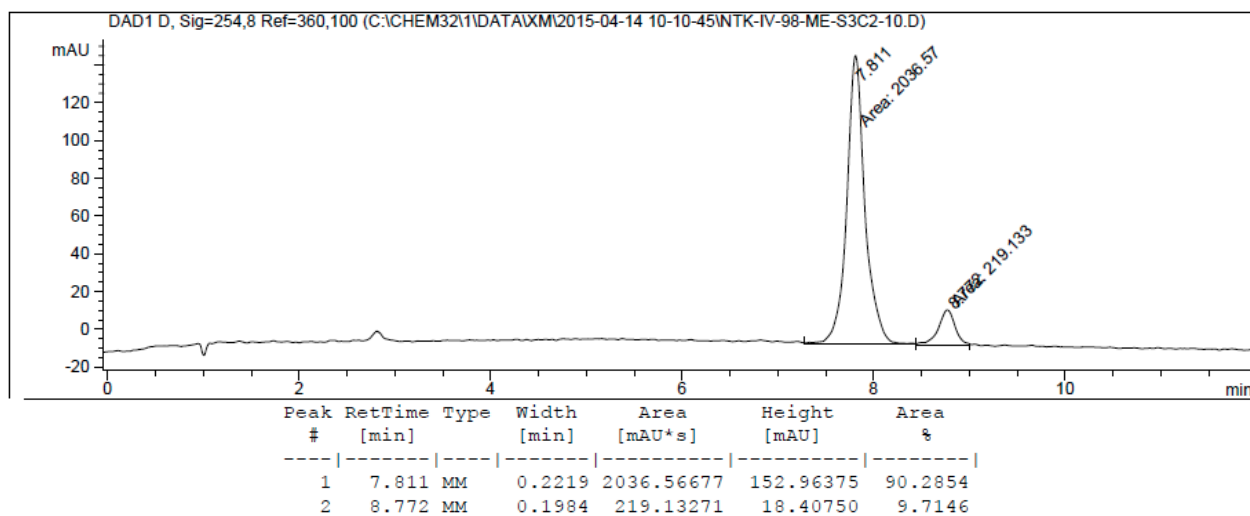
3a enantioenriched, 92% ee



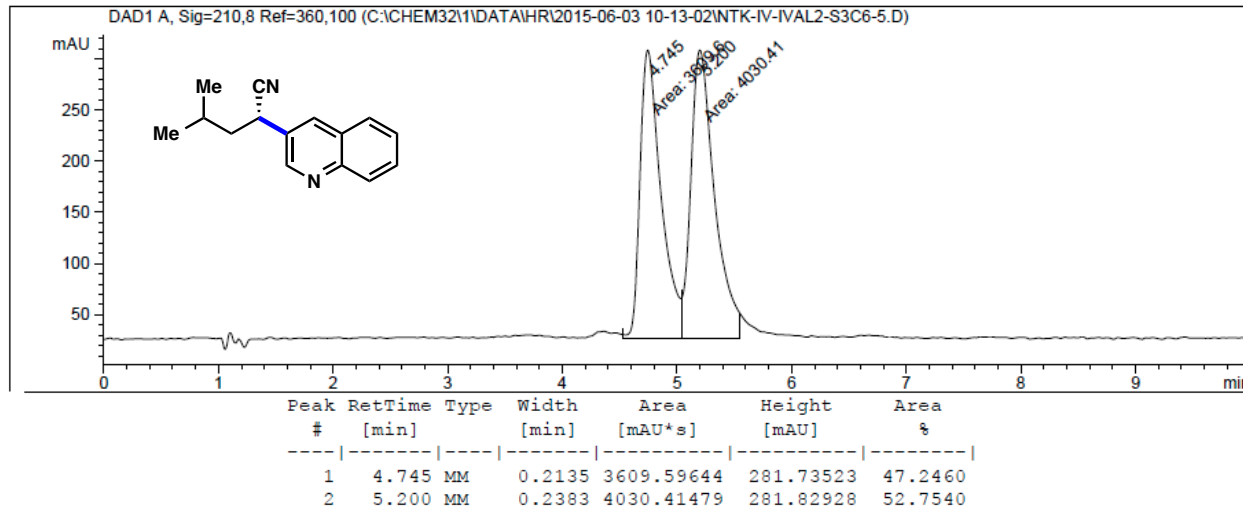
3b racemic



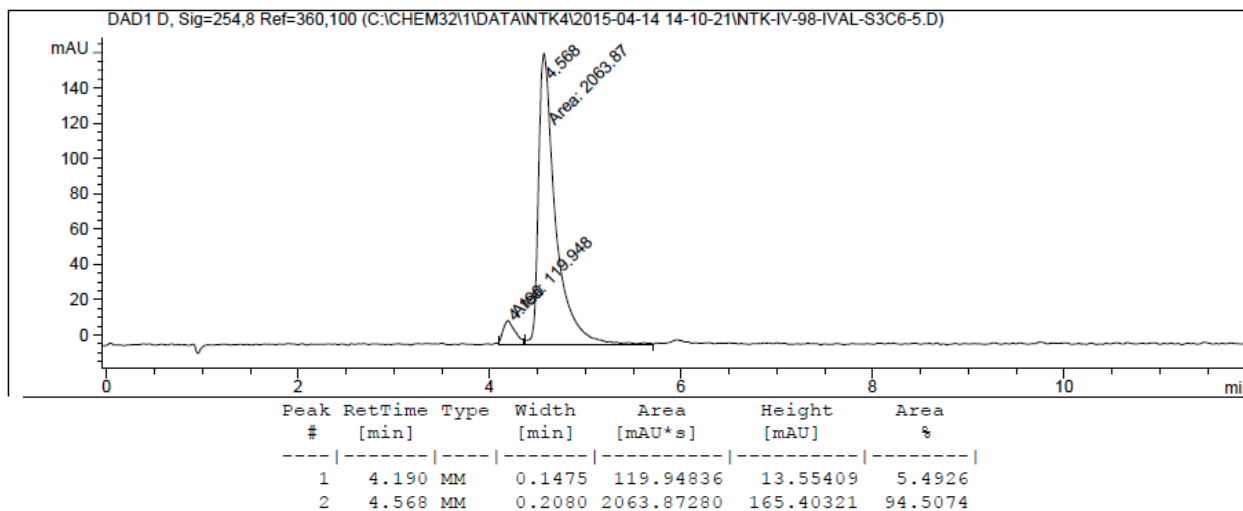
3b enantioenriched, 81% ee



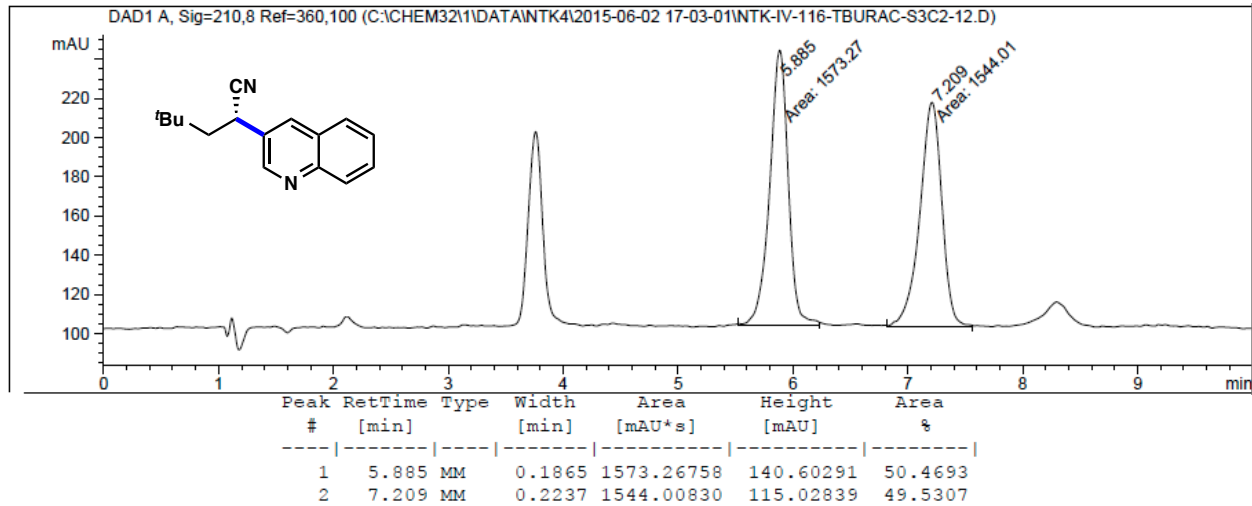
3c racemic



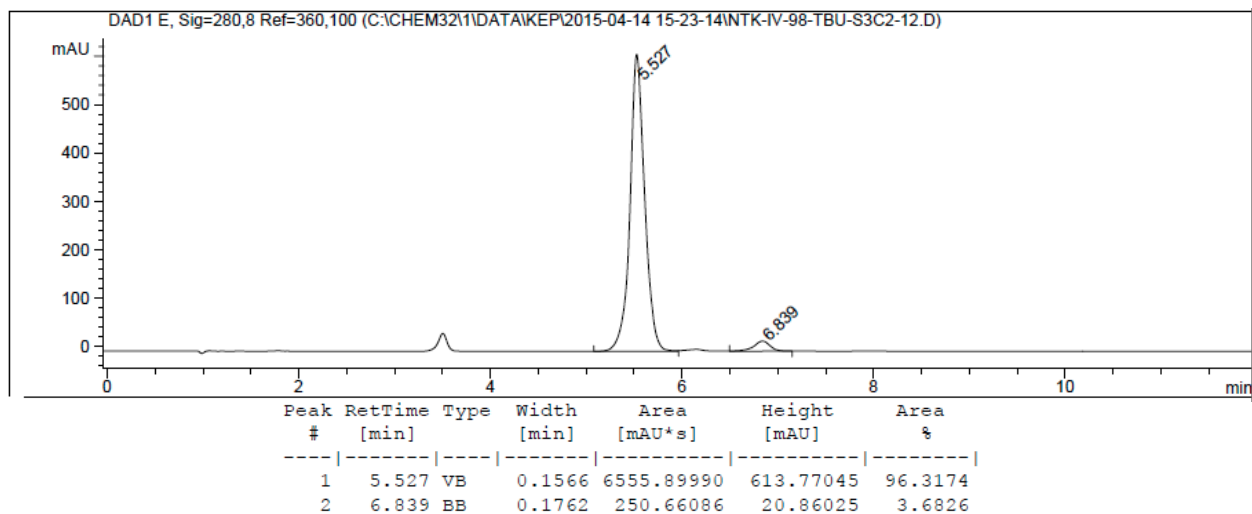
3c enantioenriched, 89% ee



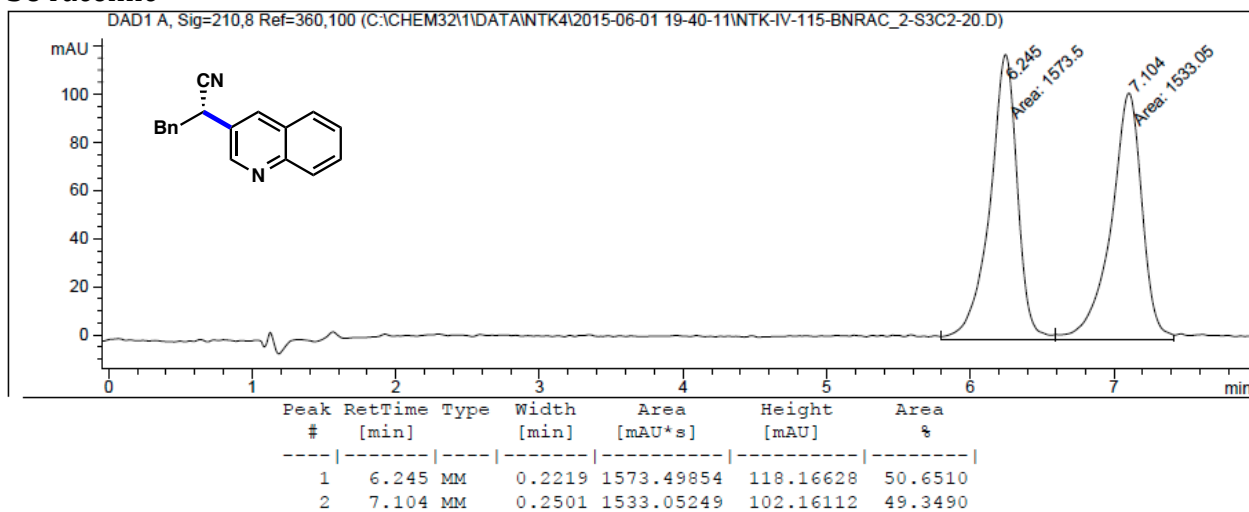
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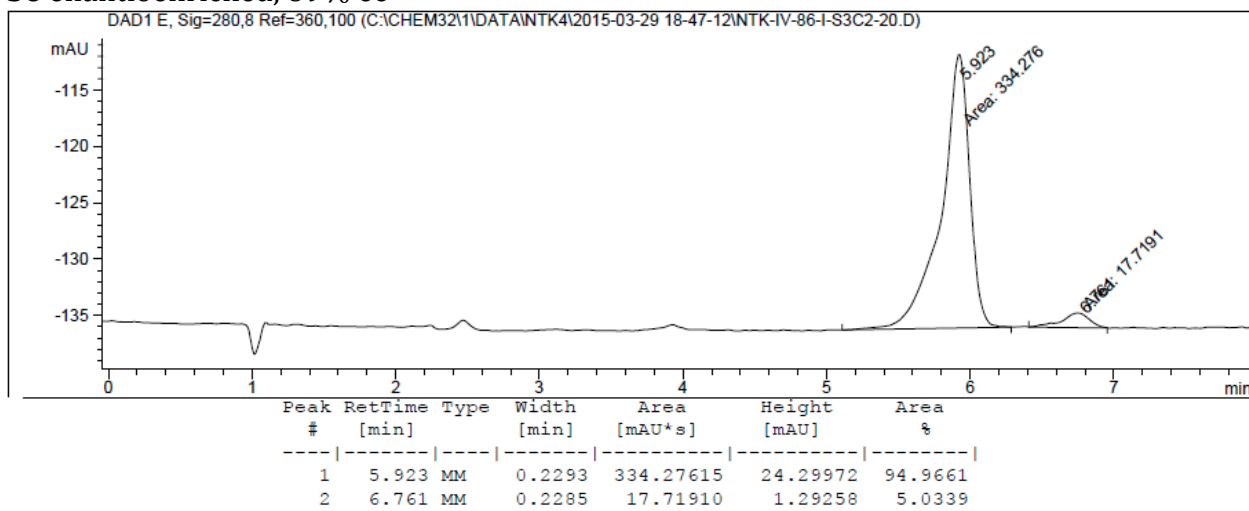
3d enantioenriched, 93% ee



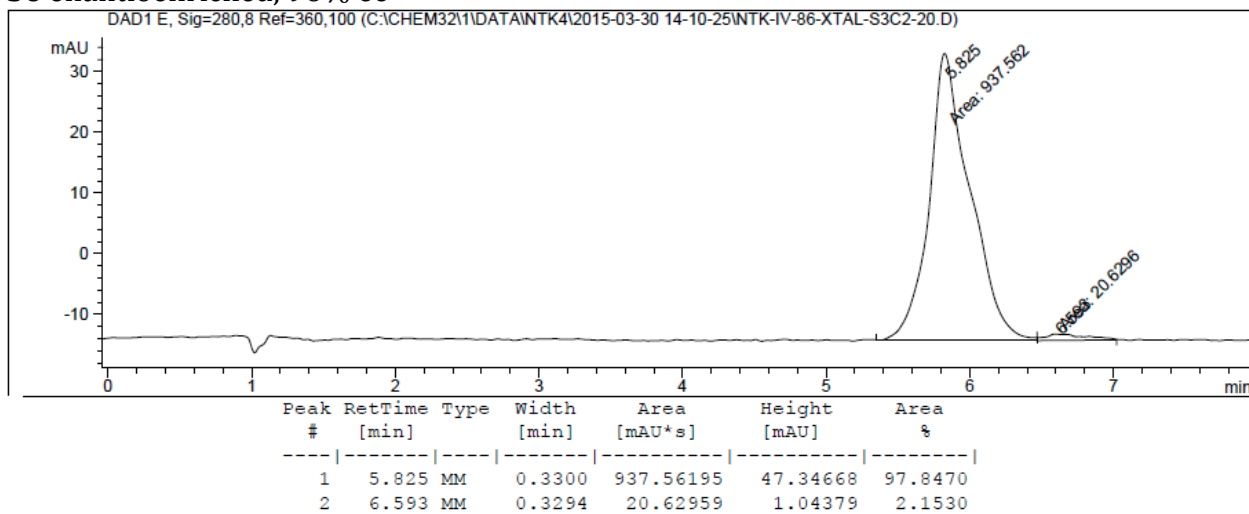
3e racemic



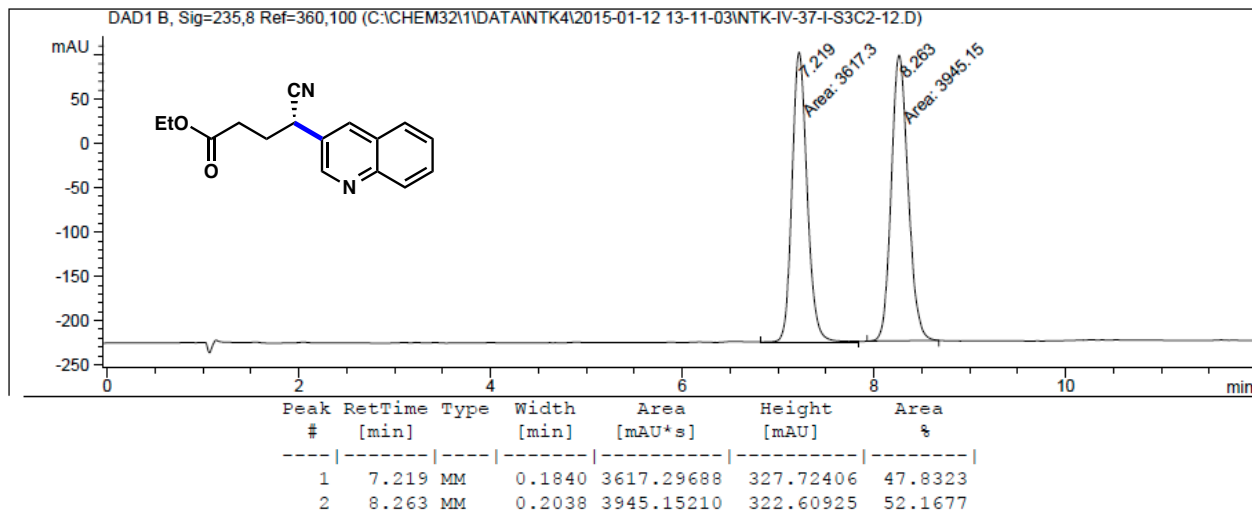
3e enantioenriched, 89% ee



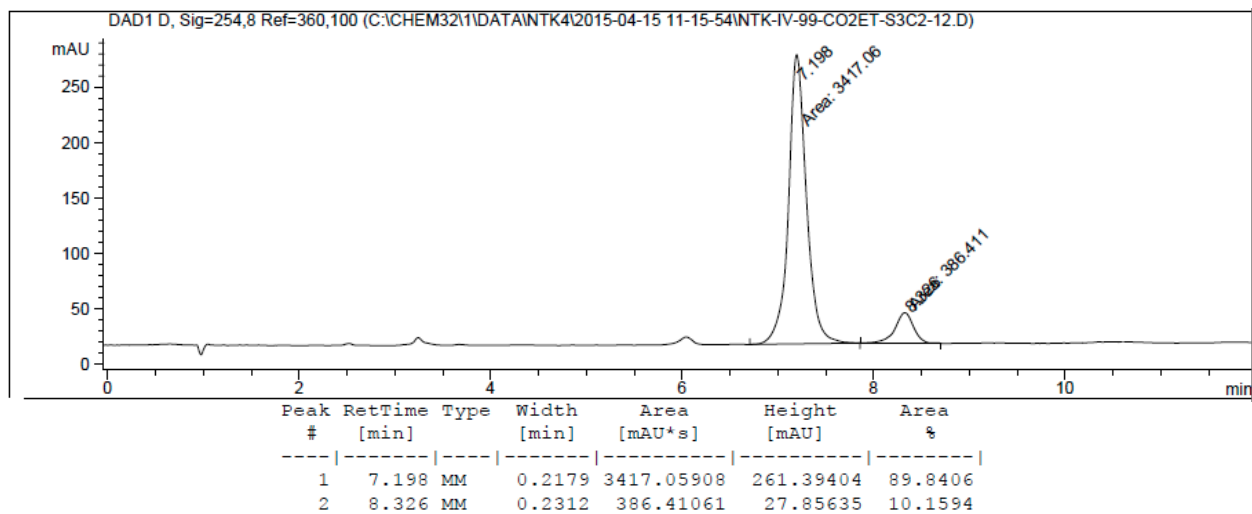
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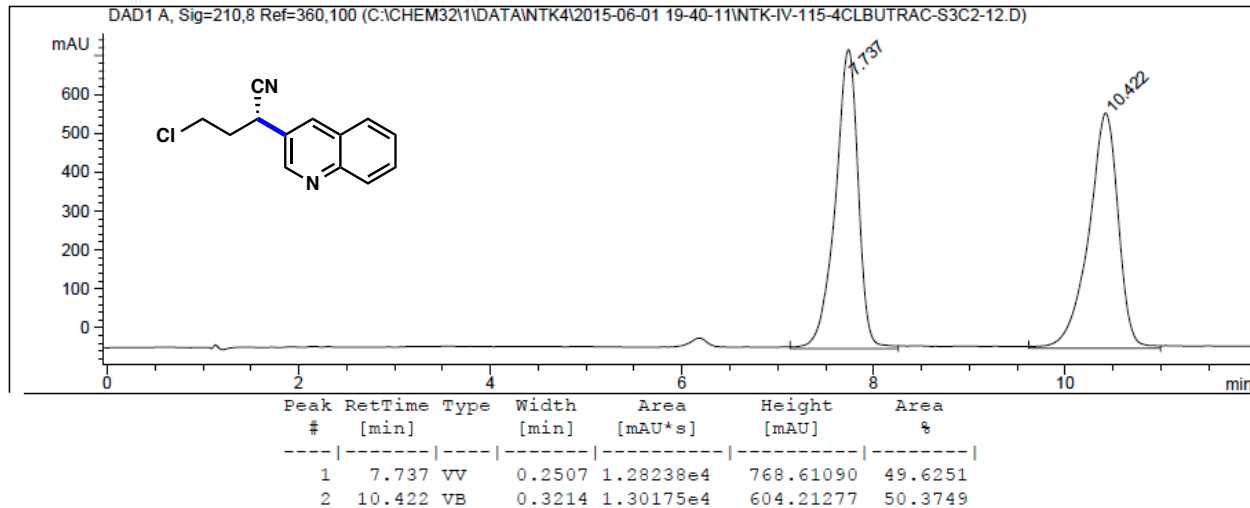
3f racemic



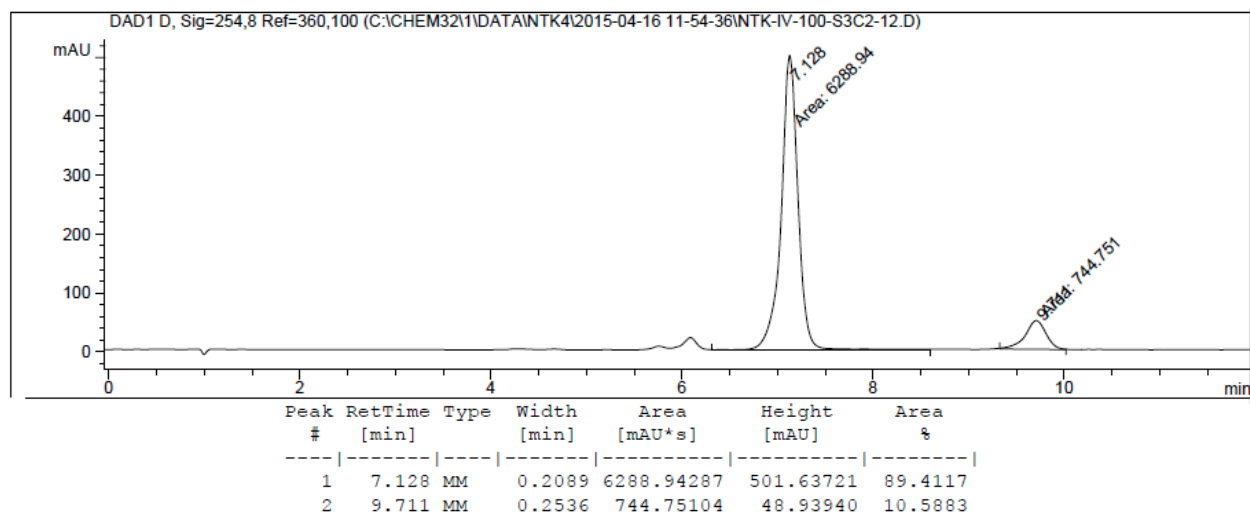
3f enantioenriched, 80% ee



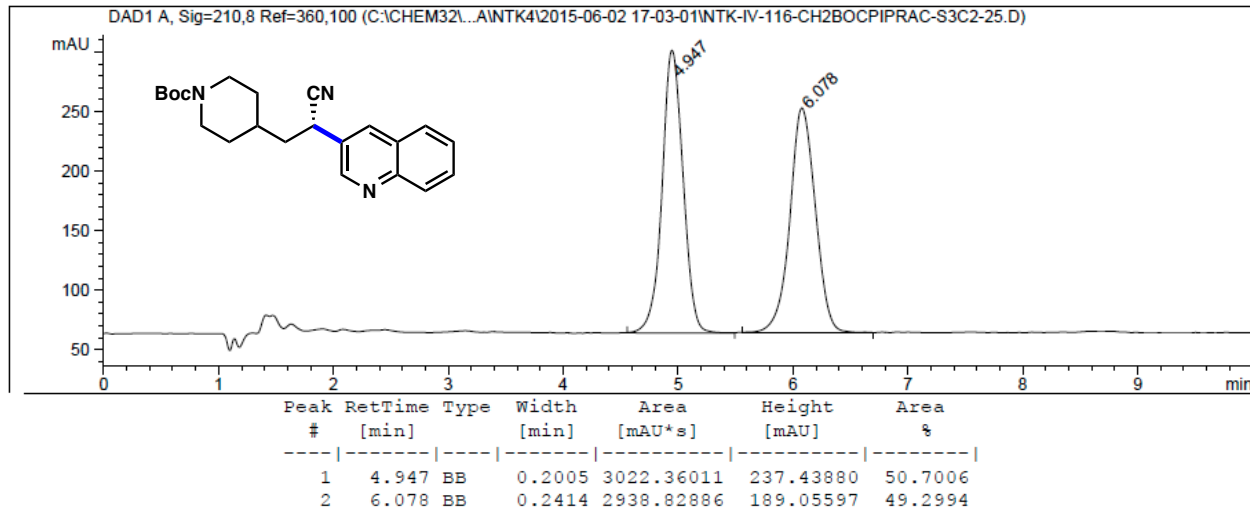
3g racemic



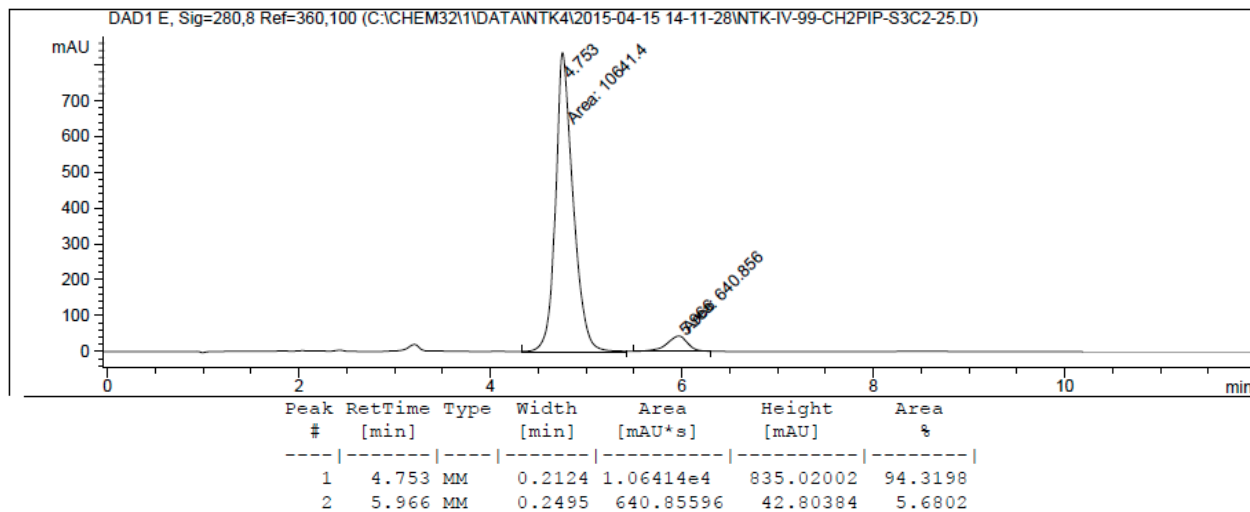
3g enantioenriched, 79% ee



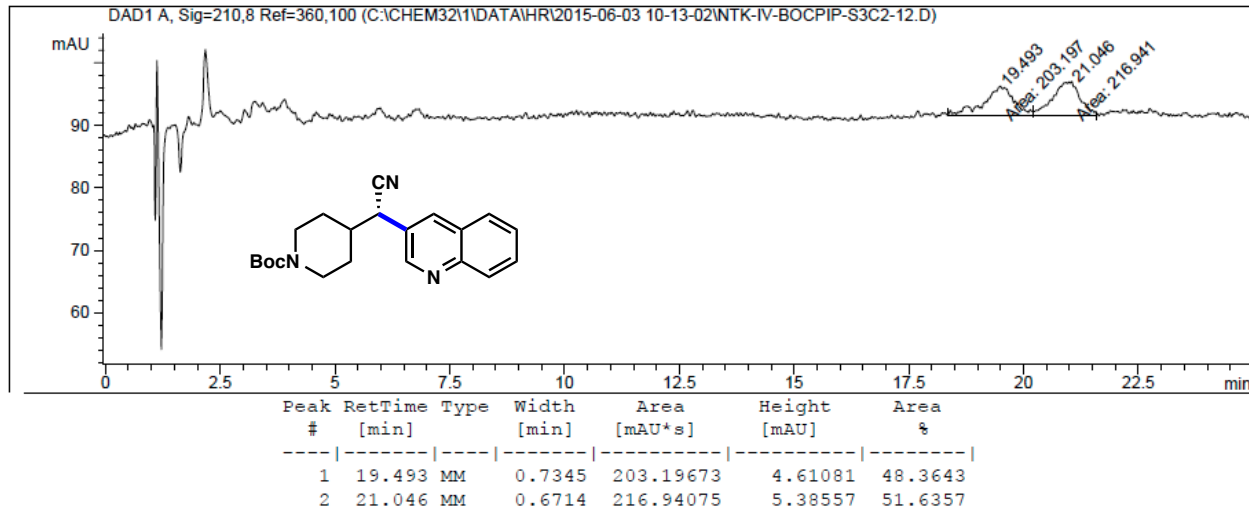
3h racemic



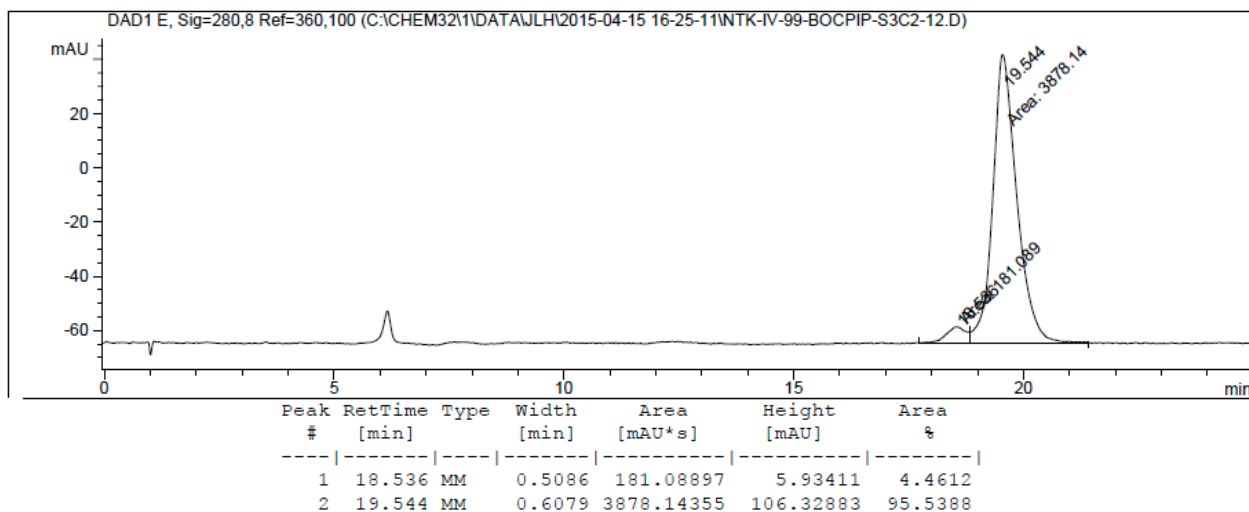
3h enantioenriched, 89% ee



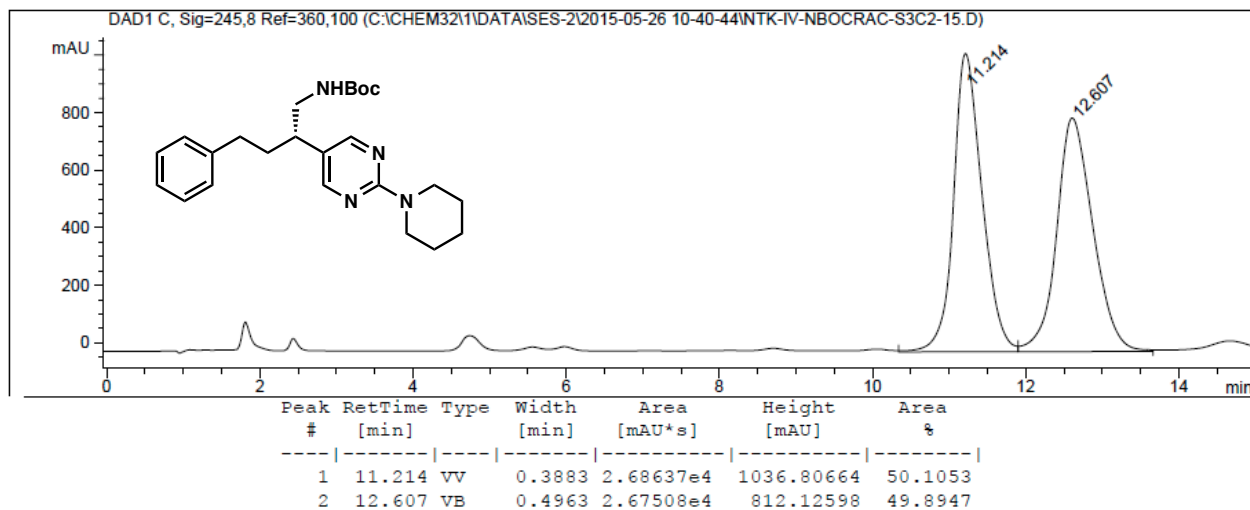
3i racemic



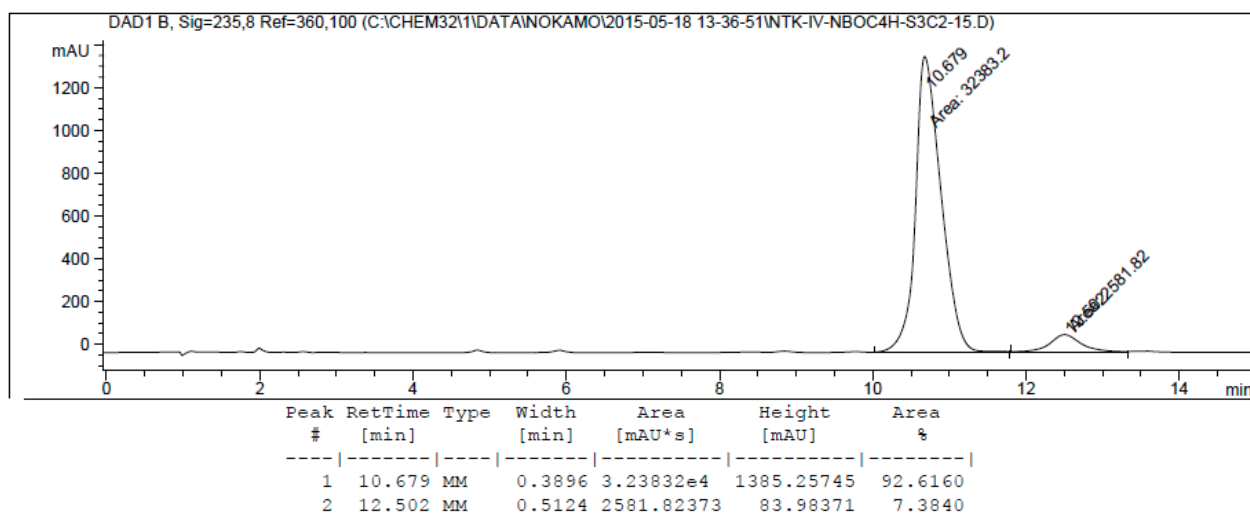
3i enantioenriched, 91% ee



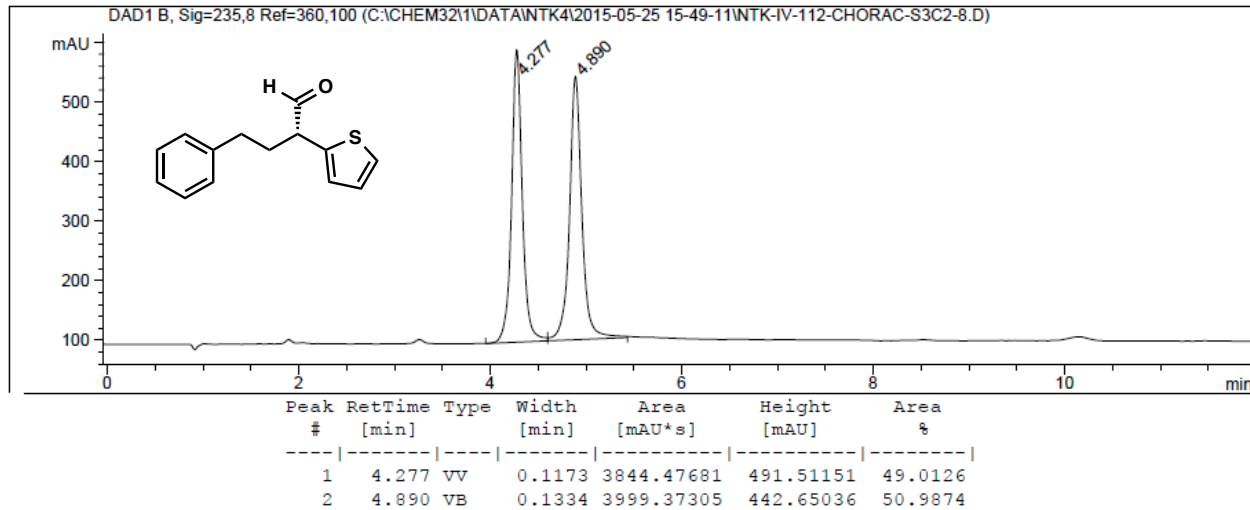
8 racemic



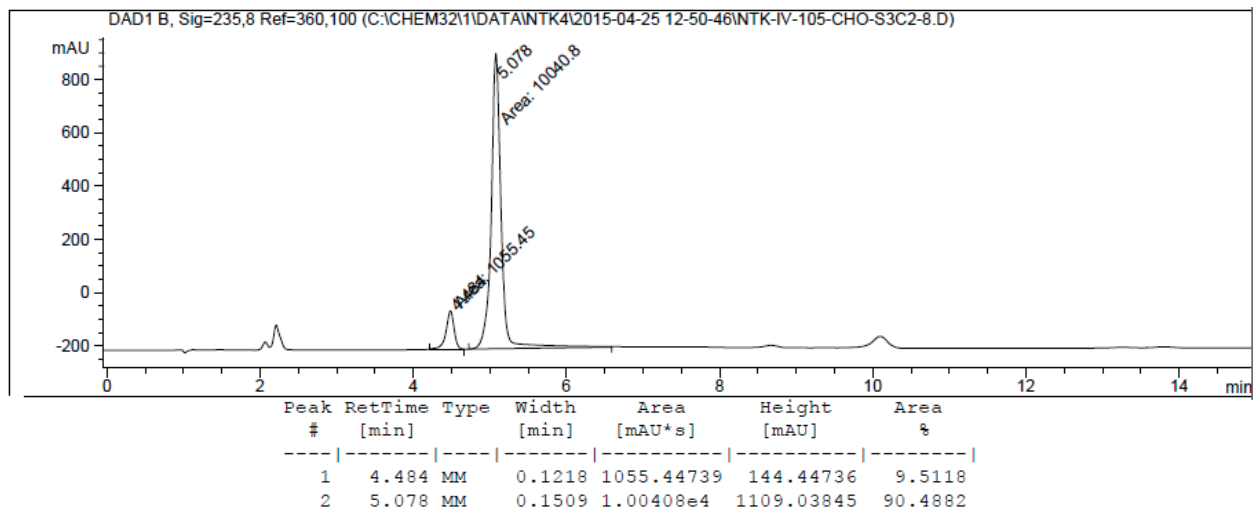
8 enantioenriched, 85% ee



10 racemic



10 enantioenriched, 81% ee



6. XRay crystallographic data for 3e.

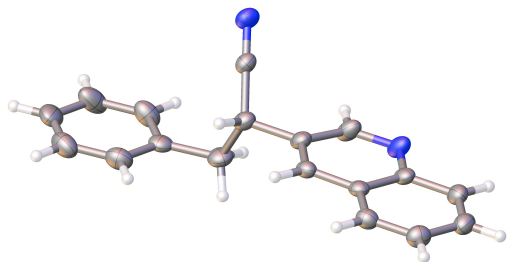


Table 1. Crystal data and structure refinement for final_p15159.

Identification code	p15159	
Empirical formula	C ₁₈ H ₁₄ N ₂	
Formula weight	258.31	
Temperature	100.01 K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2 ₁ 2 ₁ 2 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 ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for final_p15159. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
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 [\AA] and angles [$^\circ$] 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 ($\text{\AA}^2 \times 10^3$) for final_p15159. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^*2U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	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 ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) 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:

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

Nathaniel T. Kadunce and Sarah E. Reisman*

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Engineering
Division of Chemistry and Chemical Engineering, California Institute of Technology
Pasadena, California 91125
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Supporting Information 2 (Spectra):

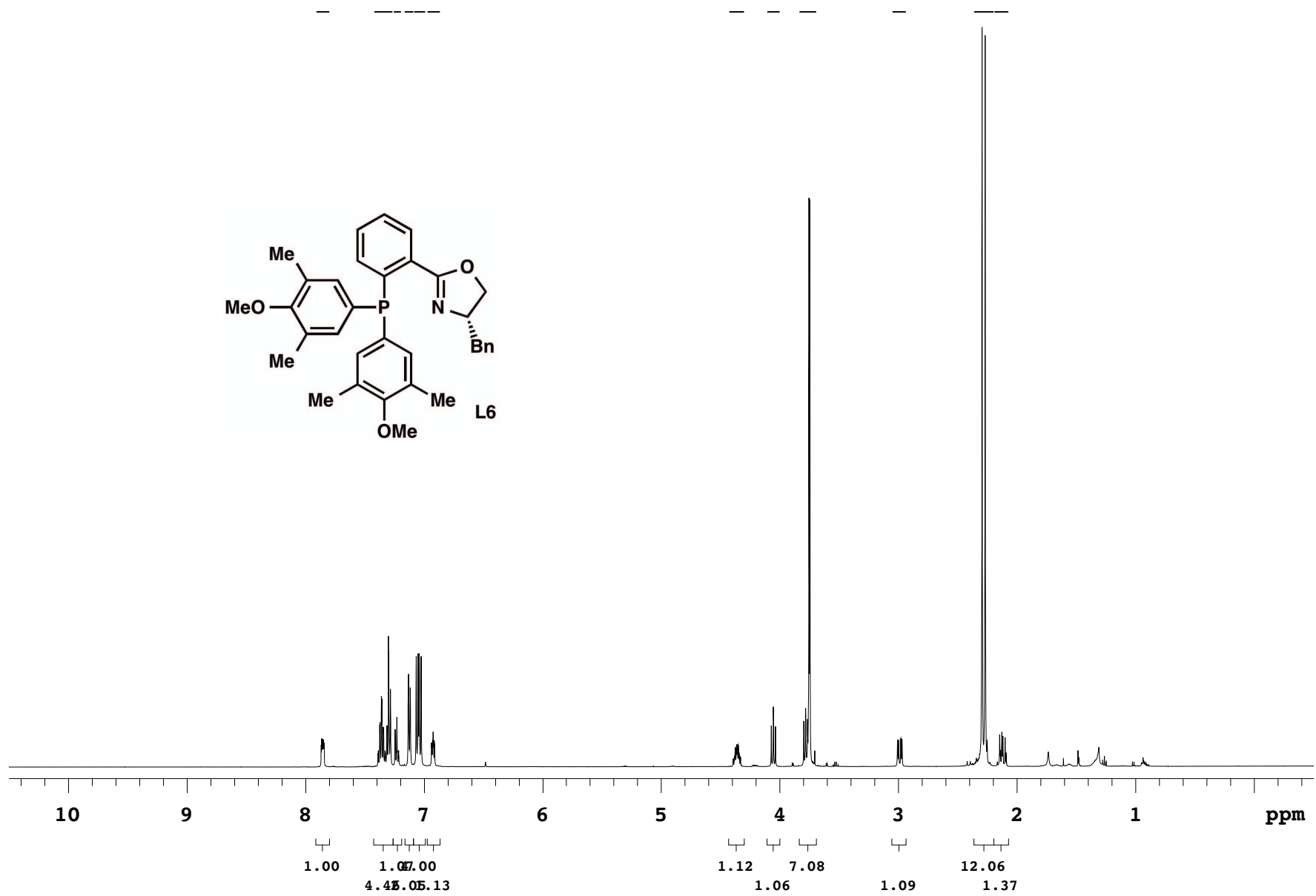
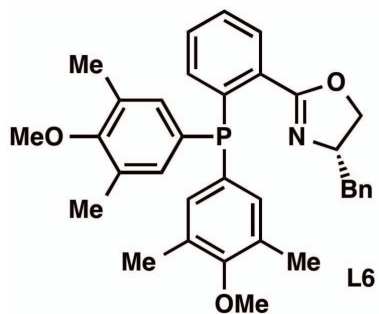
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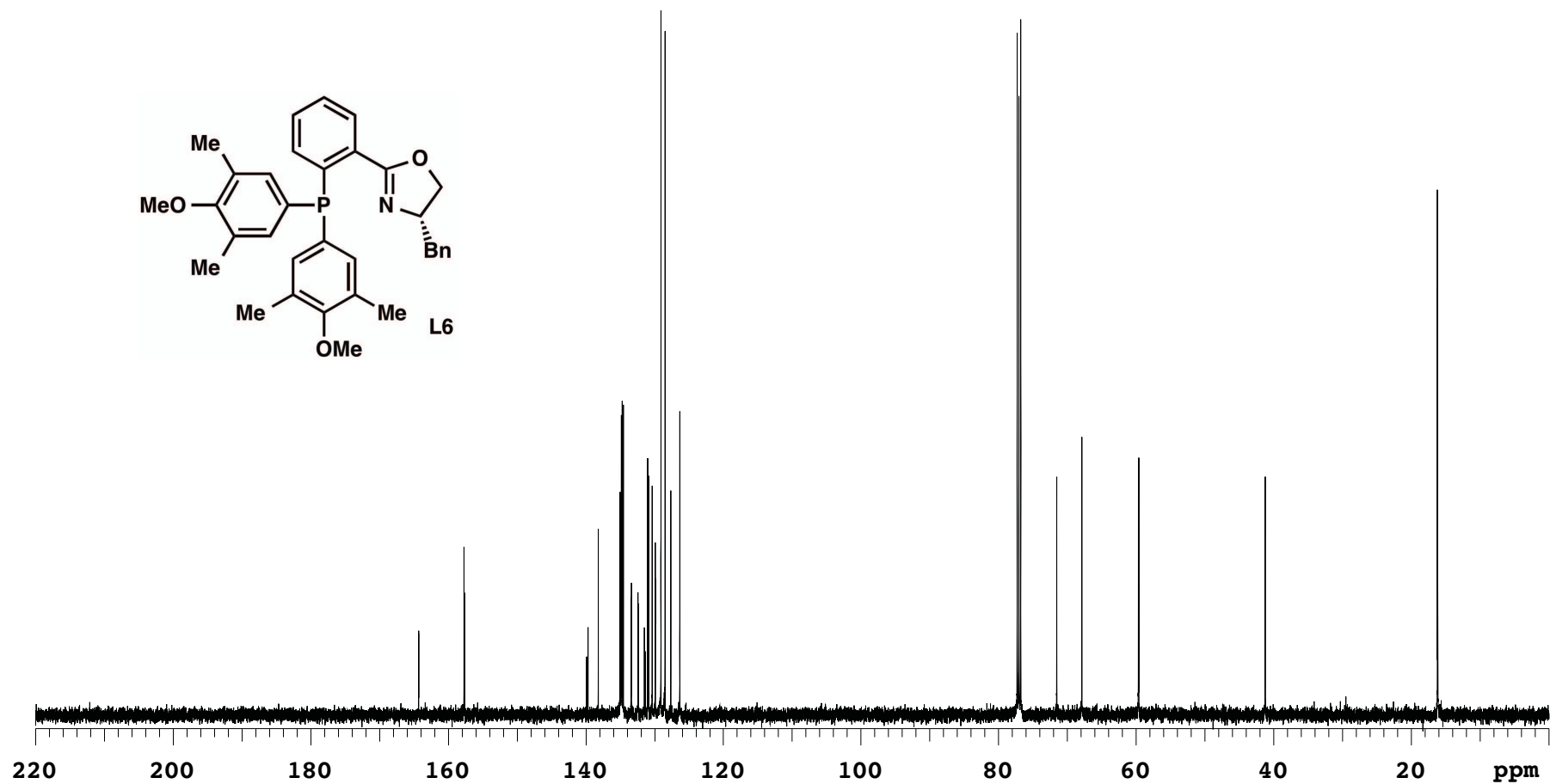
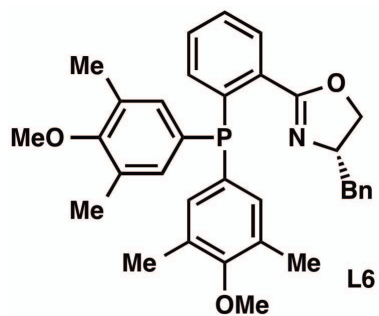
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Date collected 2015-05-19

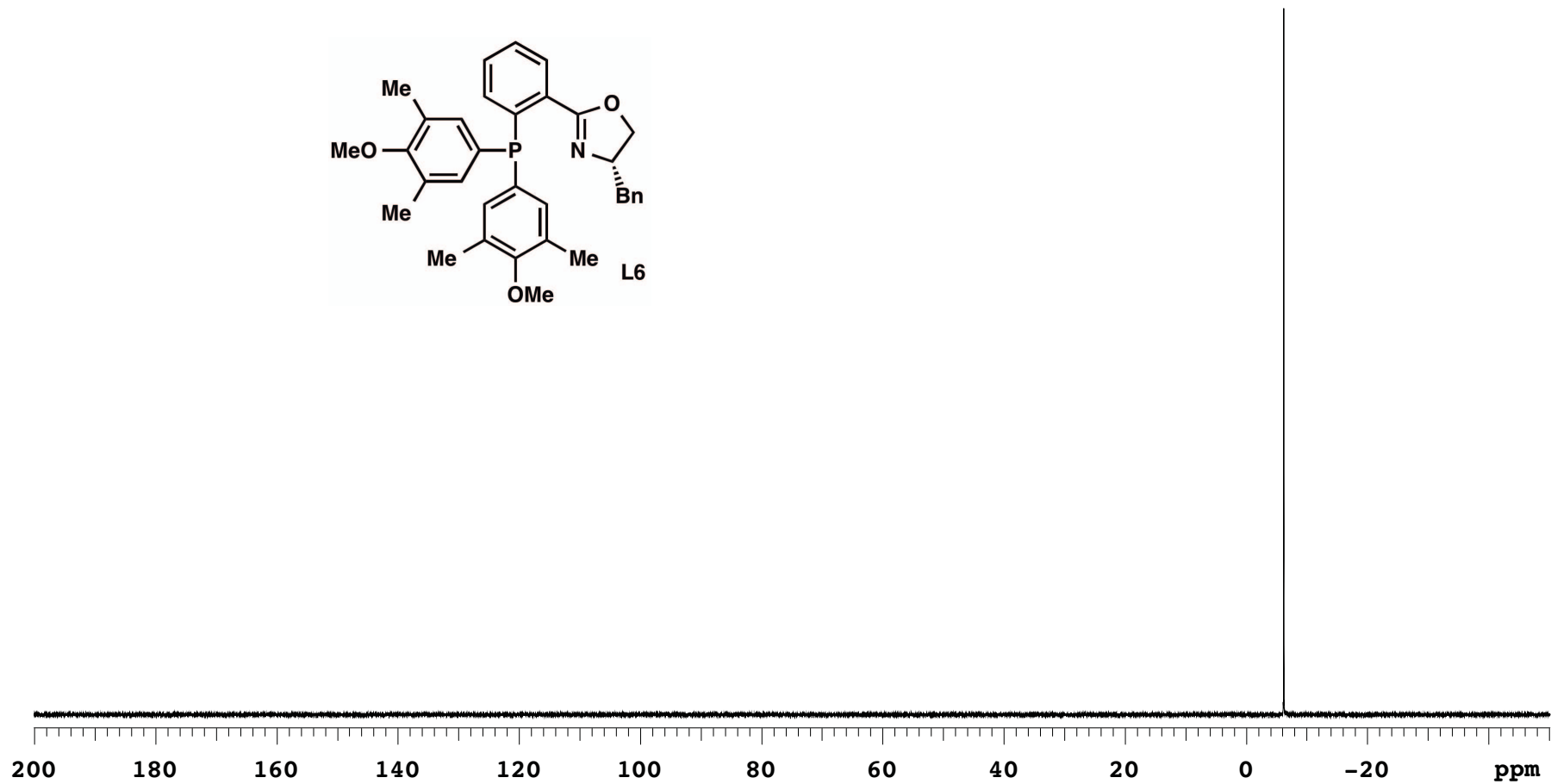
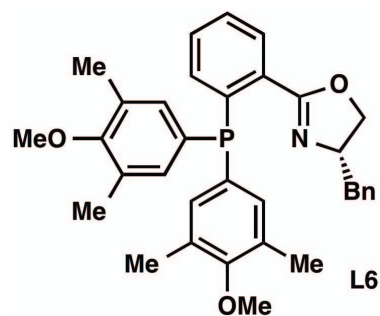
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Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser







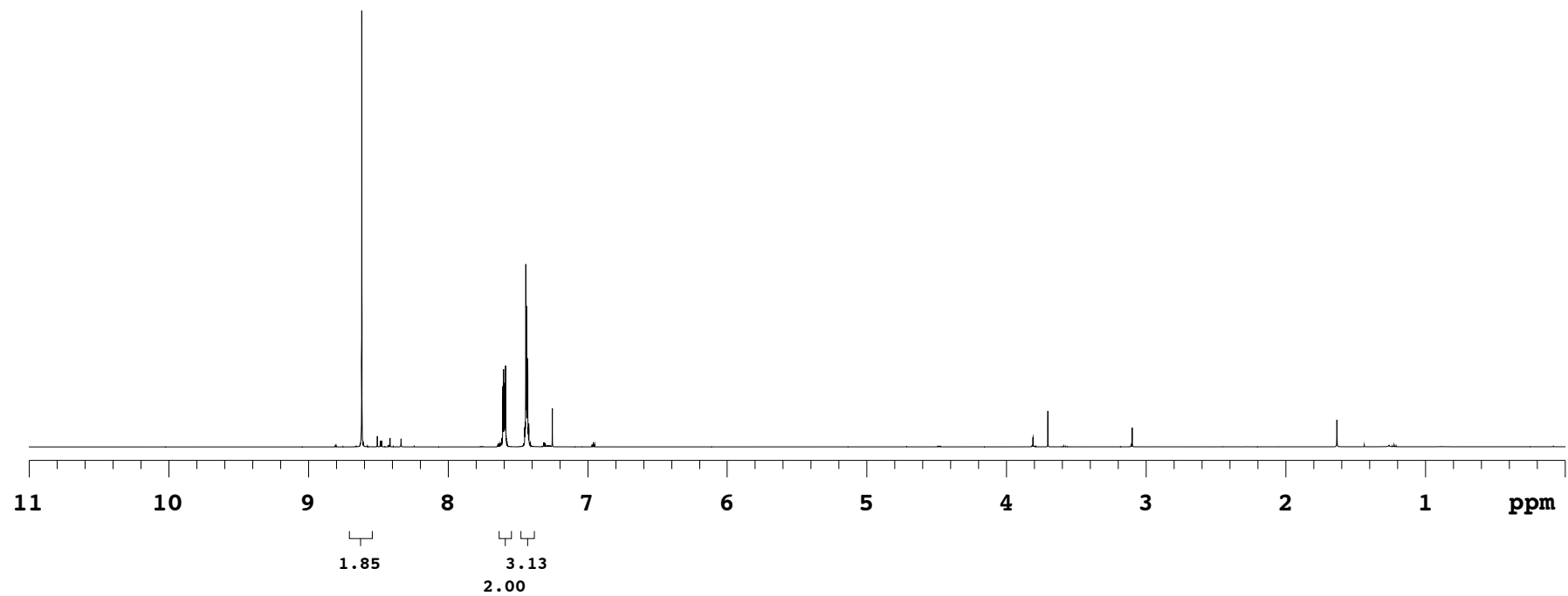
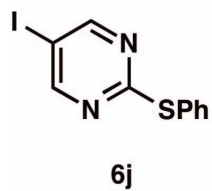
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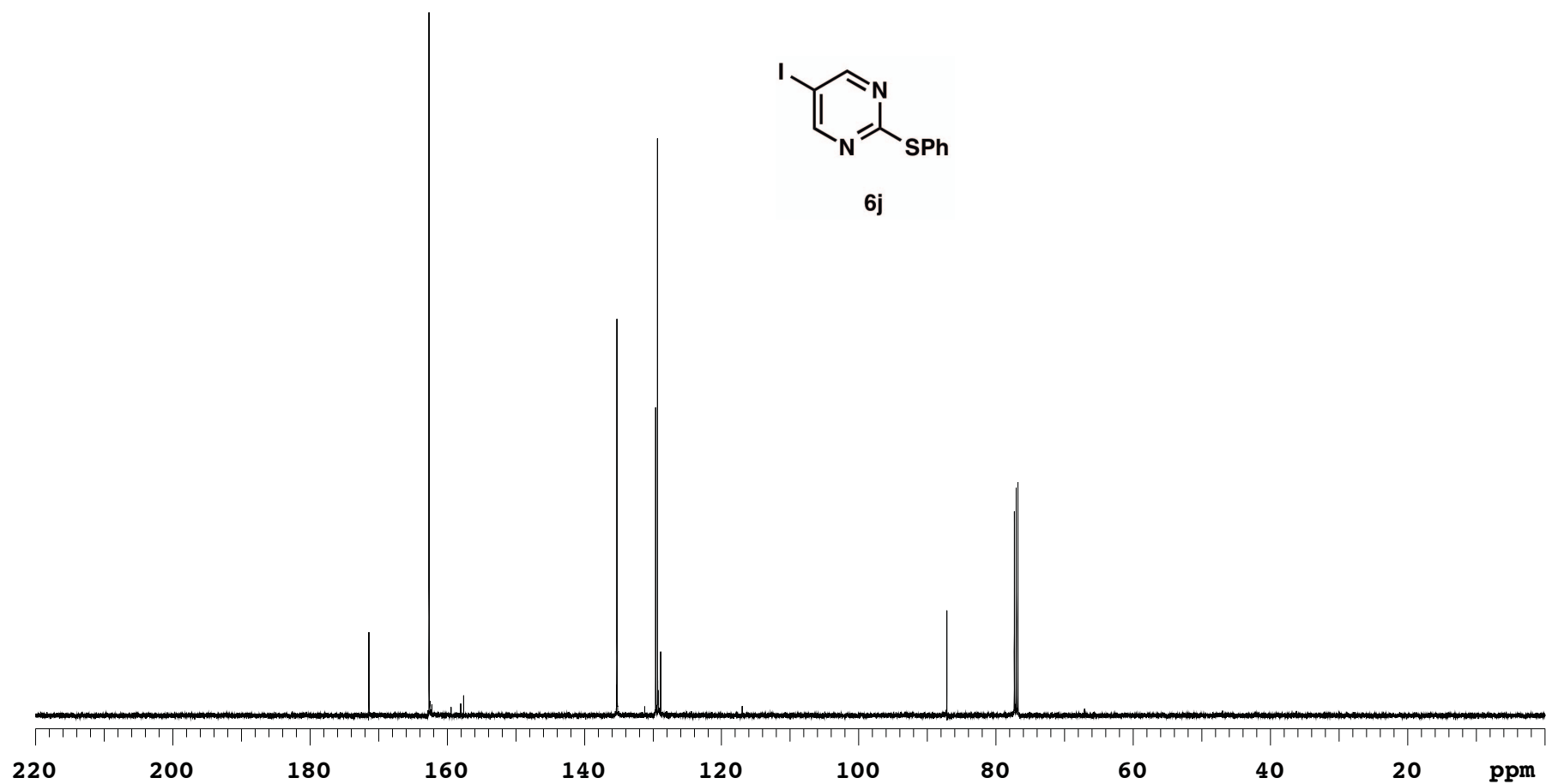
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Date collected 2015-05-19

Pulse sequence PROTON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser





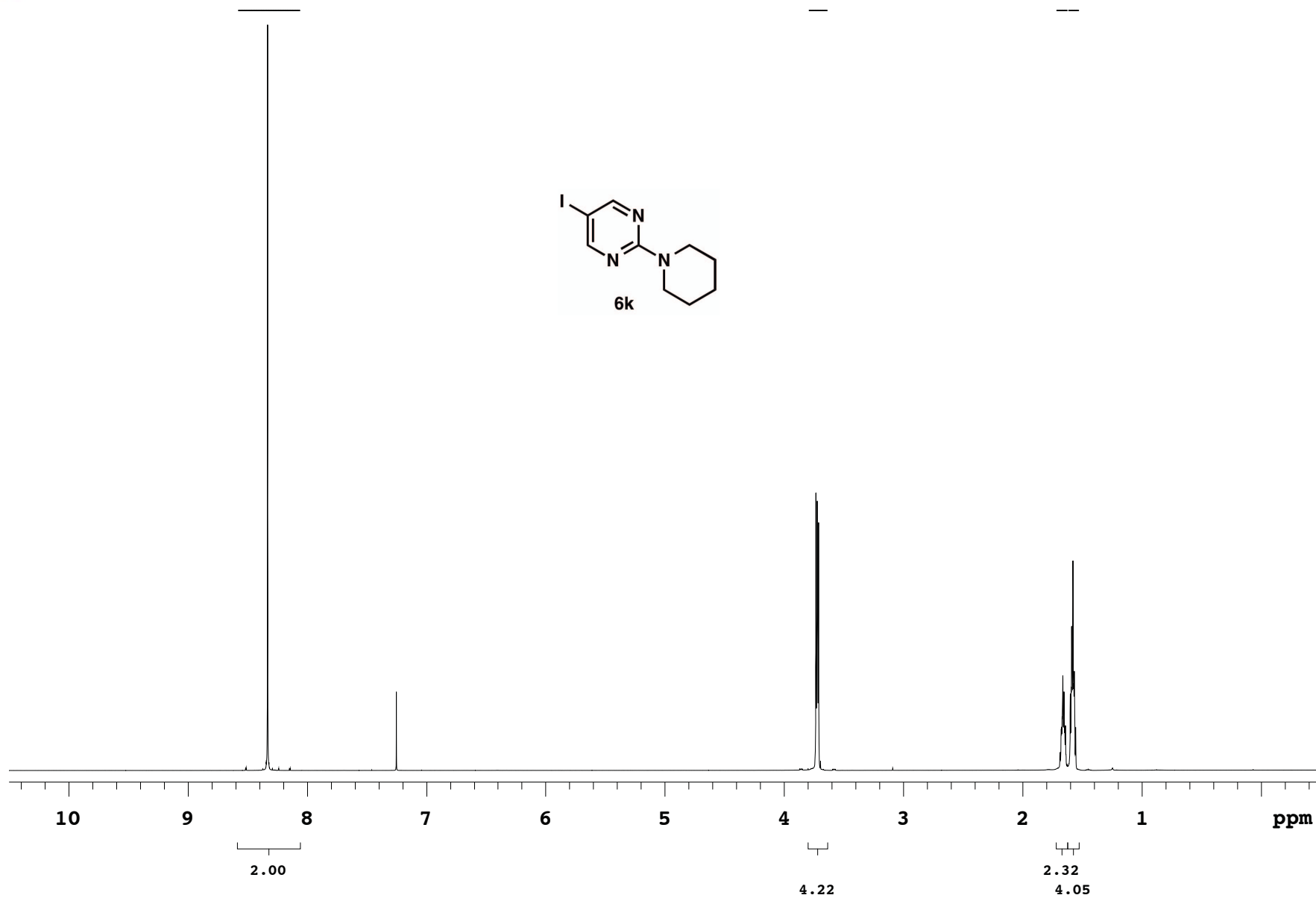
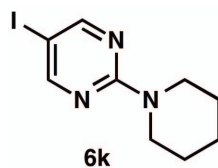
NTK-IV-piperidylArl

Sample Name NTK-IV-piperidylArl
Date collected 2015-05-19

Pulse sequence PROTON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser



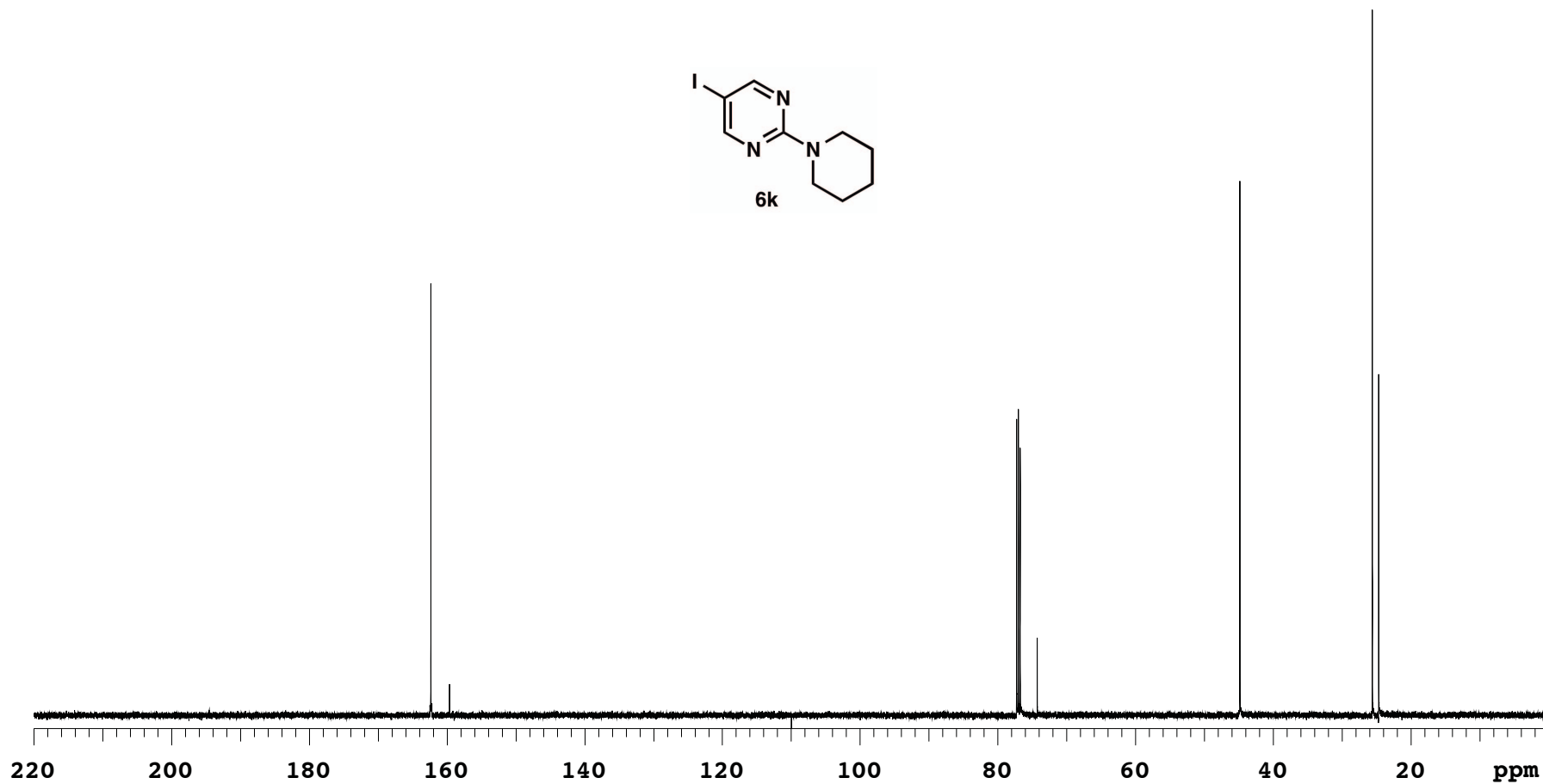
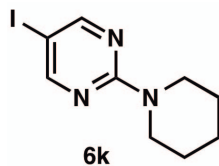
NTK-IV-piperidylArl

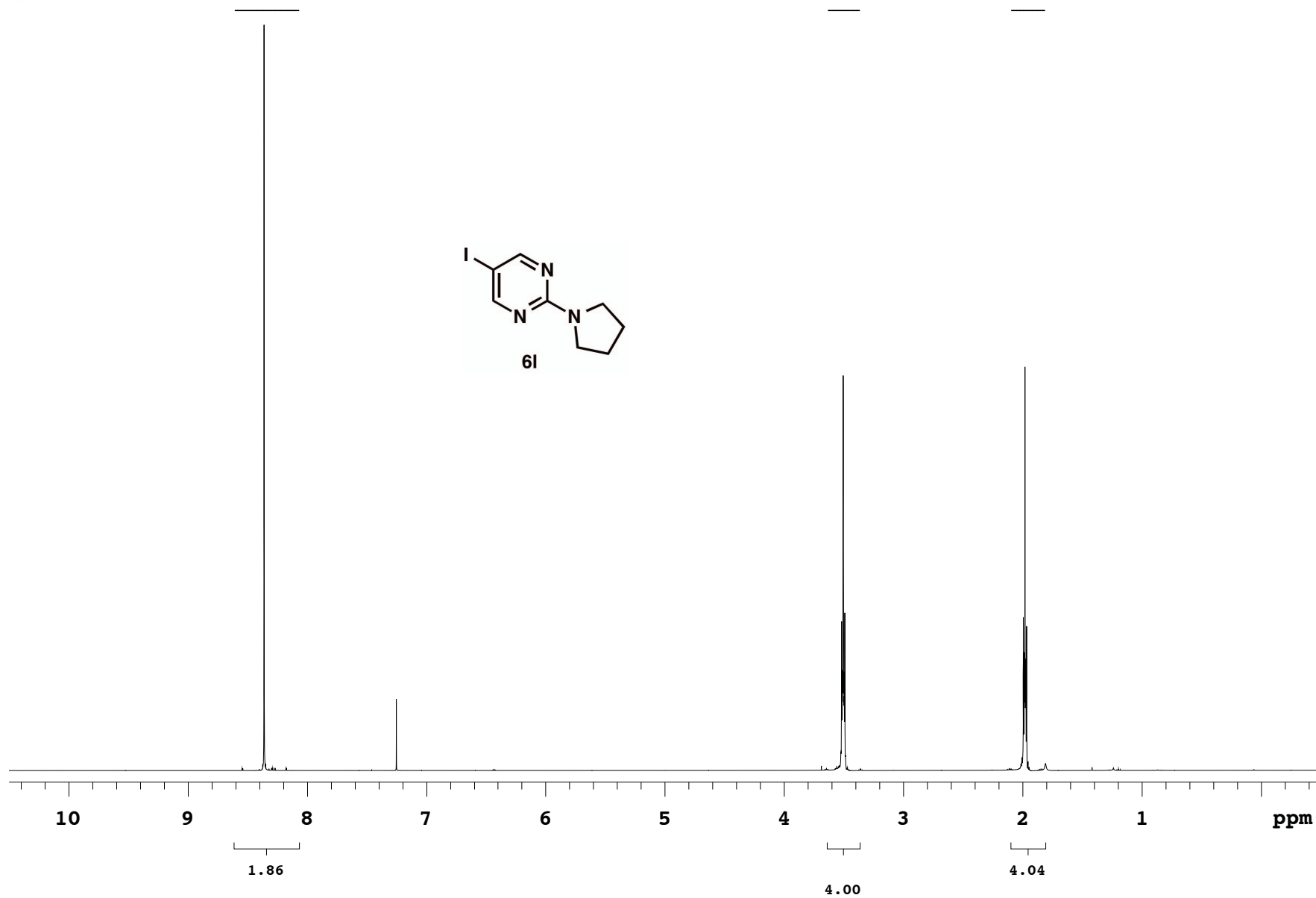
Sample Name NTK-IV-piperidylArl
Date collected 2015-05-19

Pulse sequence CARBON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser





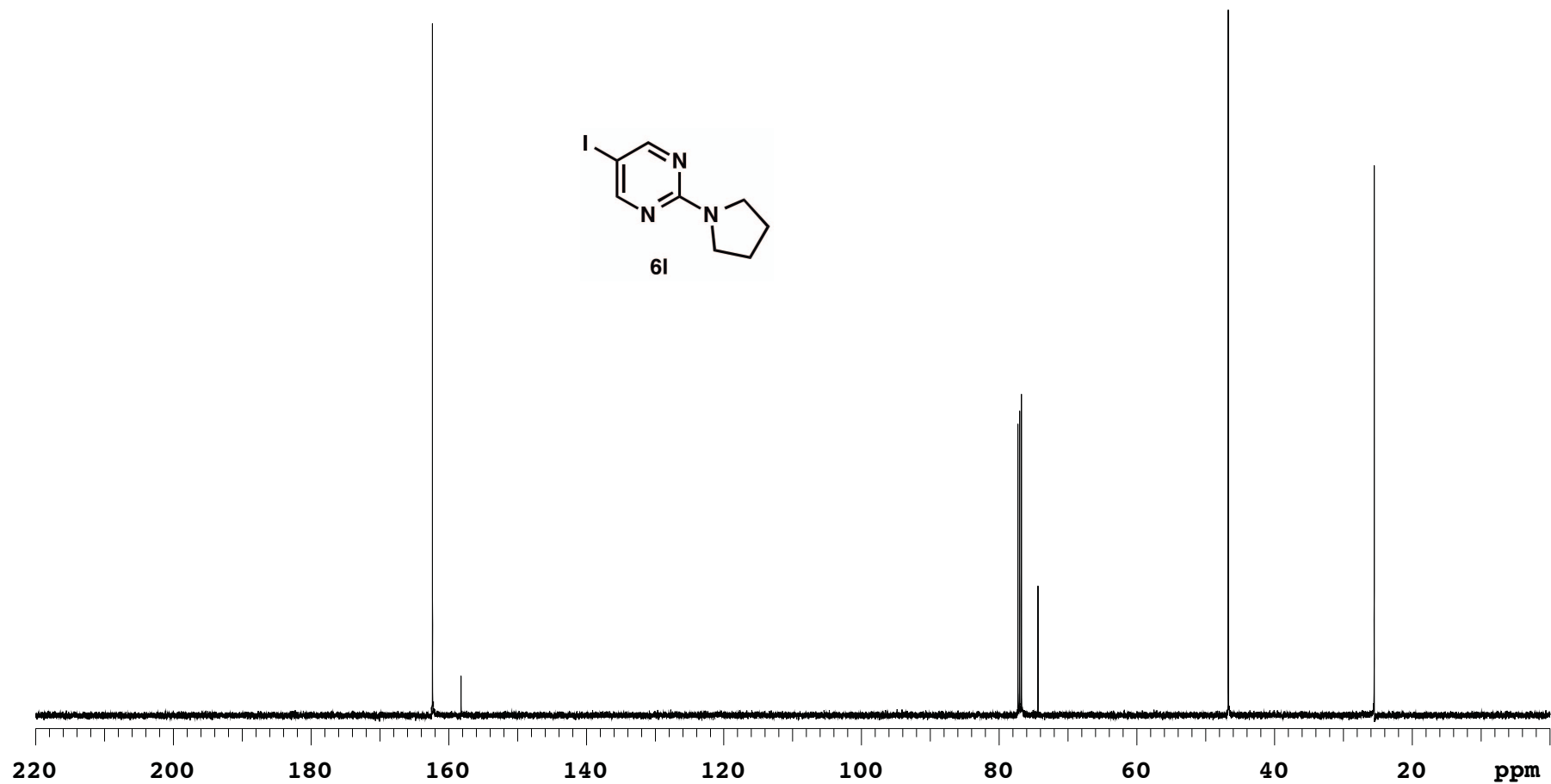
NTK-IV-pyrroloArl

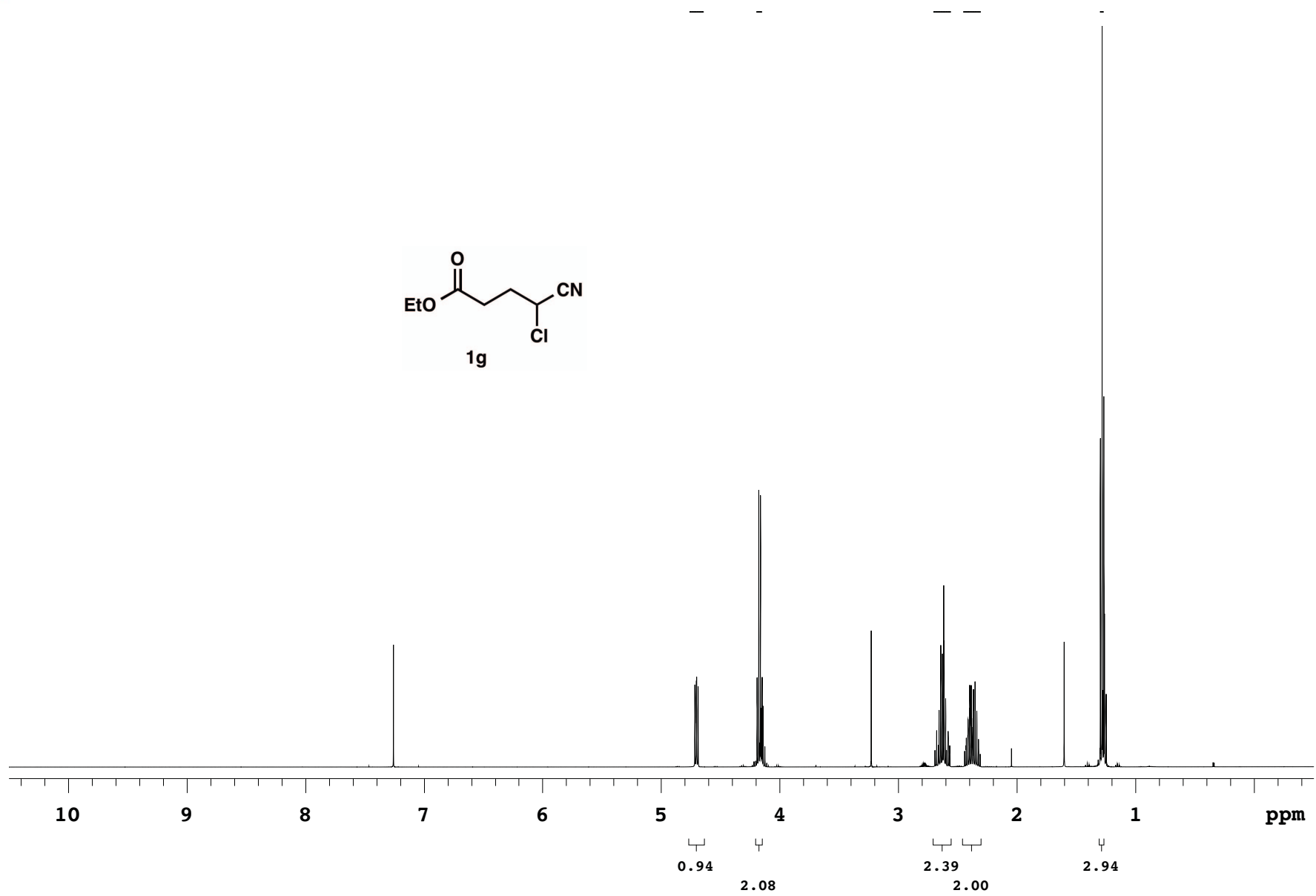
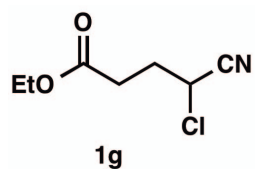
Sample Name NTK-IV-pyrroloArl
Date collected 2015-05-19

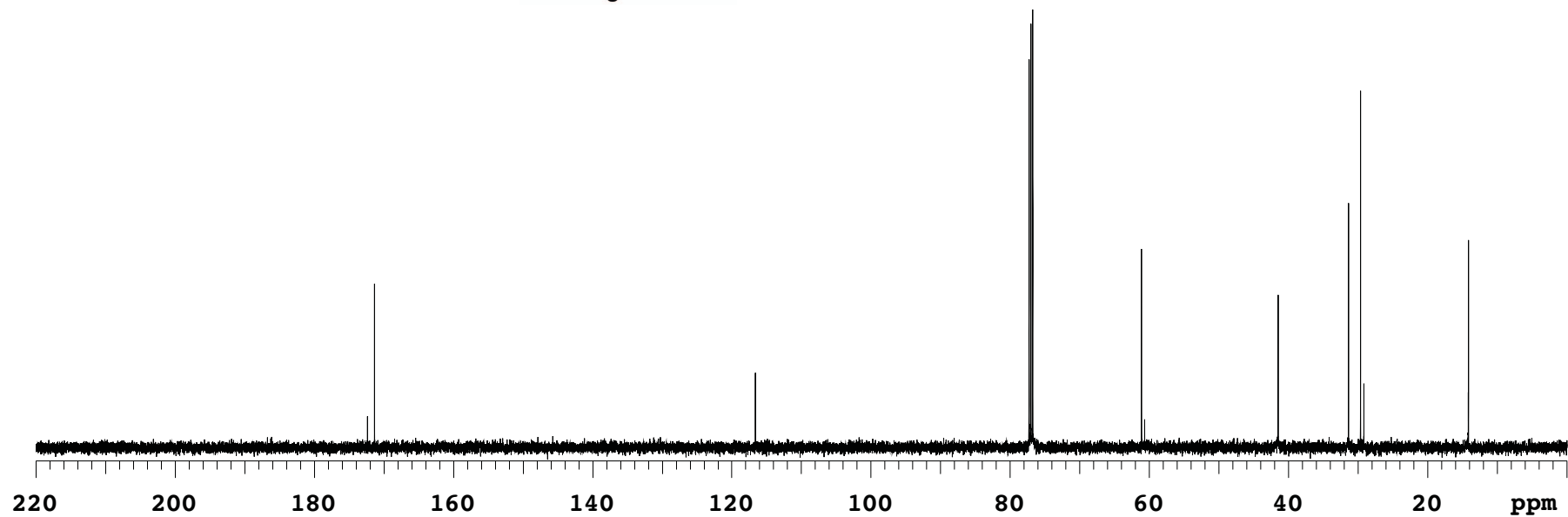
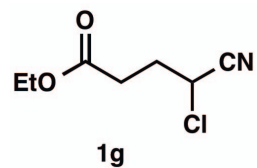
Pulse sequence CARBON
Solvent cdcl3

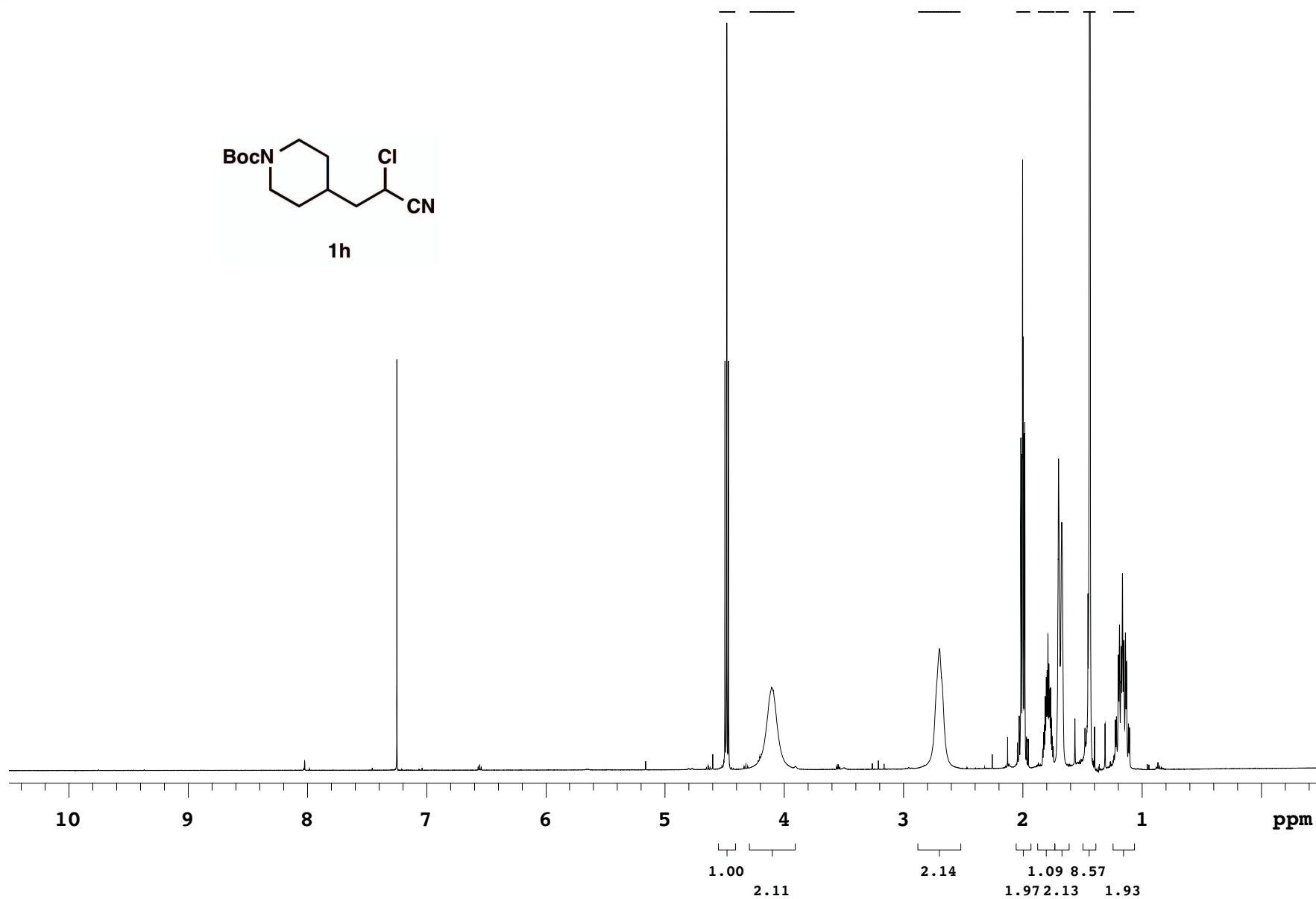
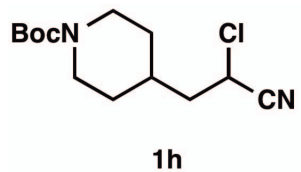
Temperature 25
Spectrometer -vnmrs400

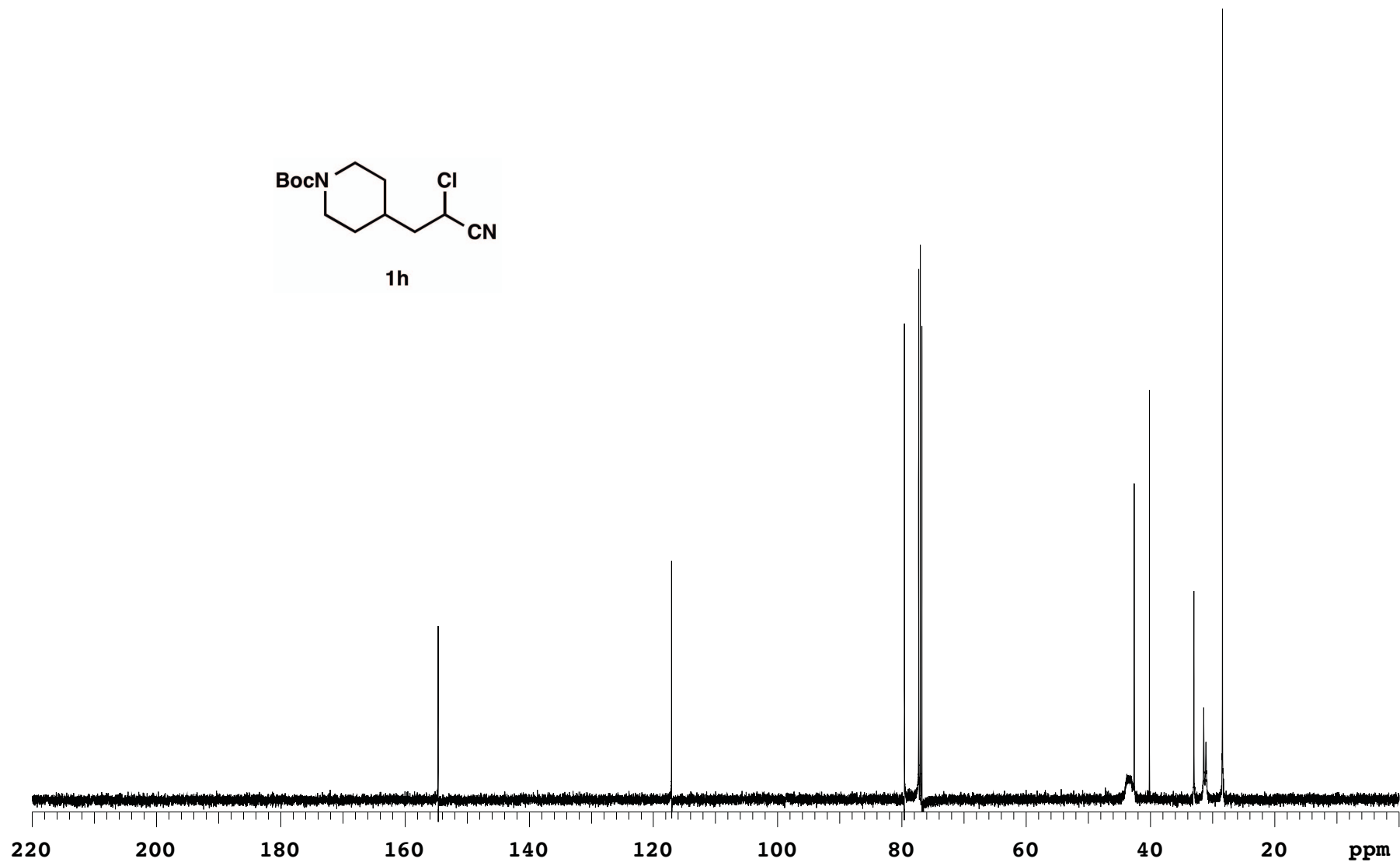
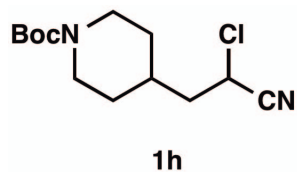
Study owner nkadunce
Operator autouser











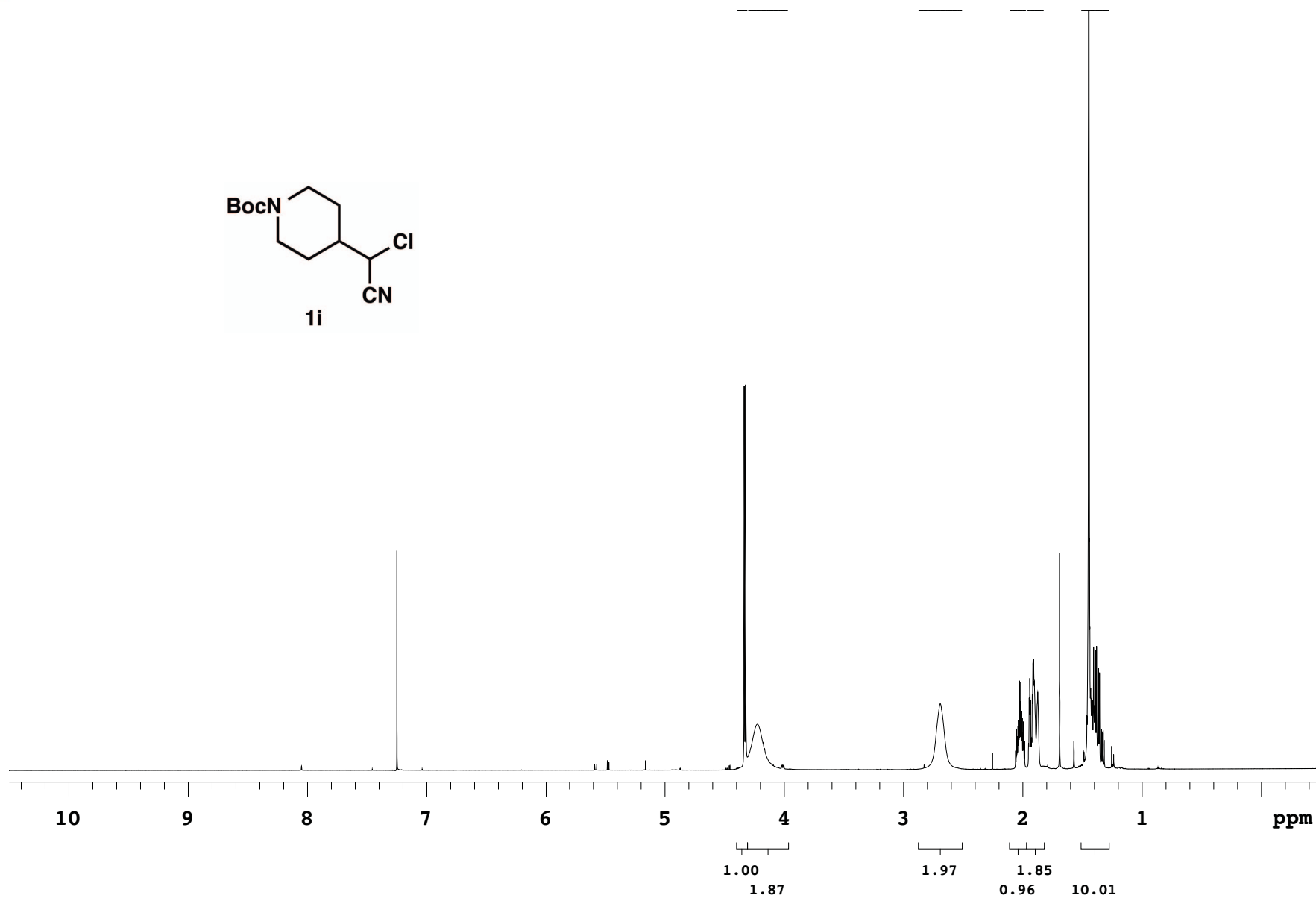
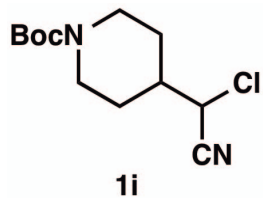
NTK-IV-BocPipClCN

Sample Name NTK-IV-BocPipClCN
Date collected 2015-05-20

Pulse sequence PROTON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser



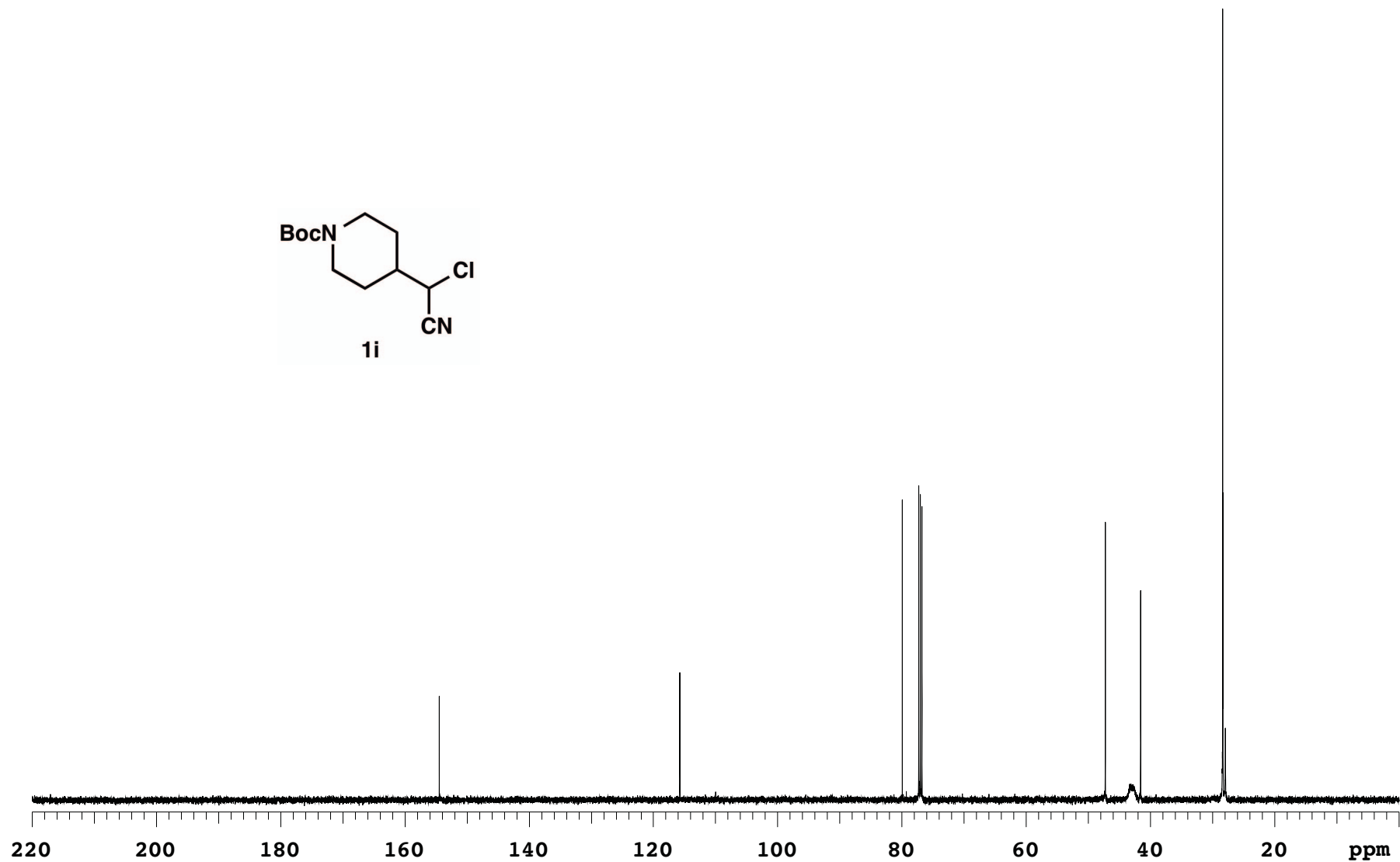
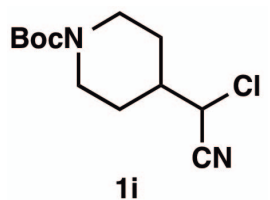
NTK-IV-BocPipClCN

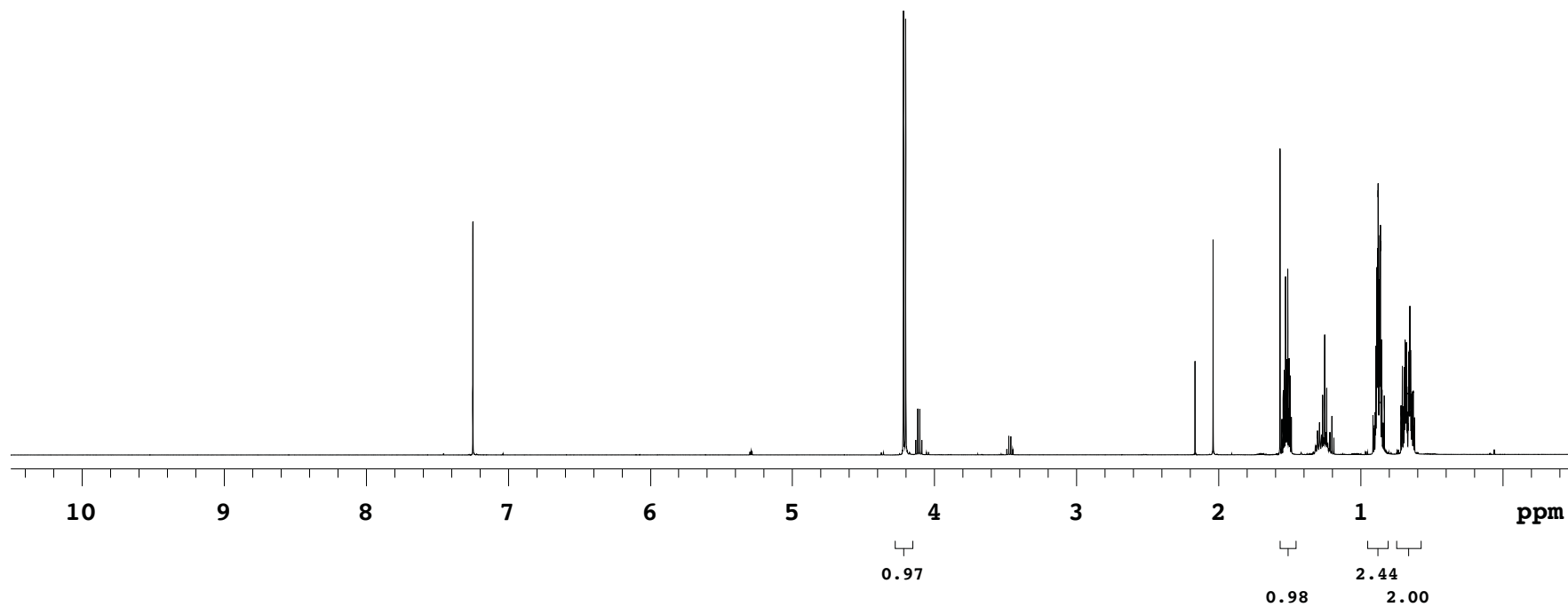
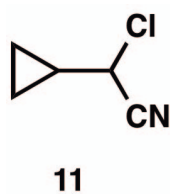
Sample Name NTK-IV-BocPipClCN
Date collected 2015-05-20

Pulse sequence CARBON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser





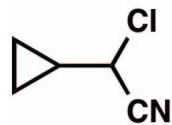
NTK-IV-cPrClCN

Sample Name NTK-IV-cPrClCN
Date collected 2015-05-20

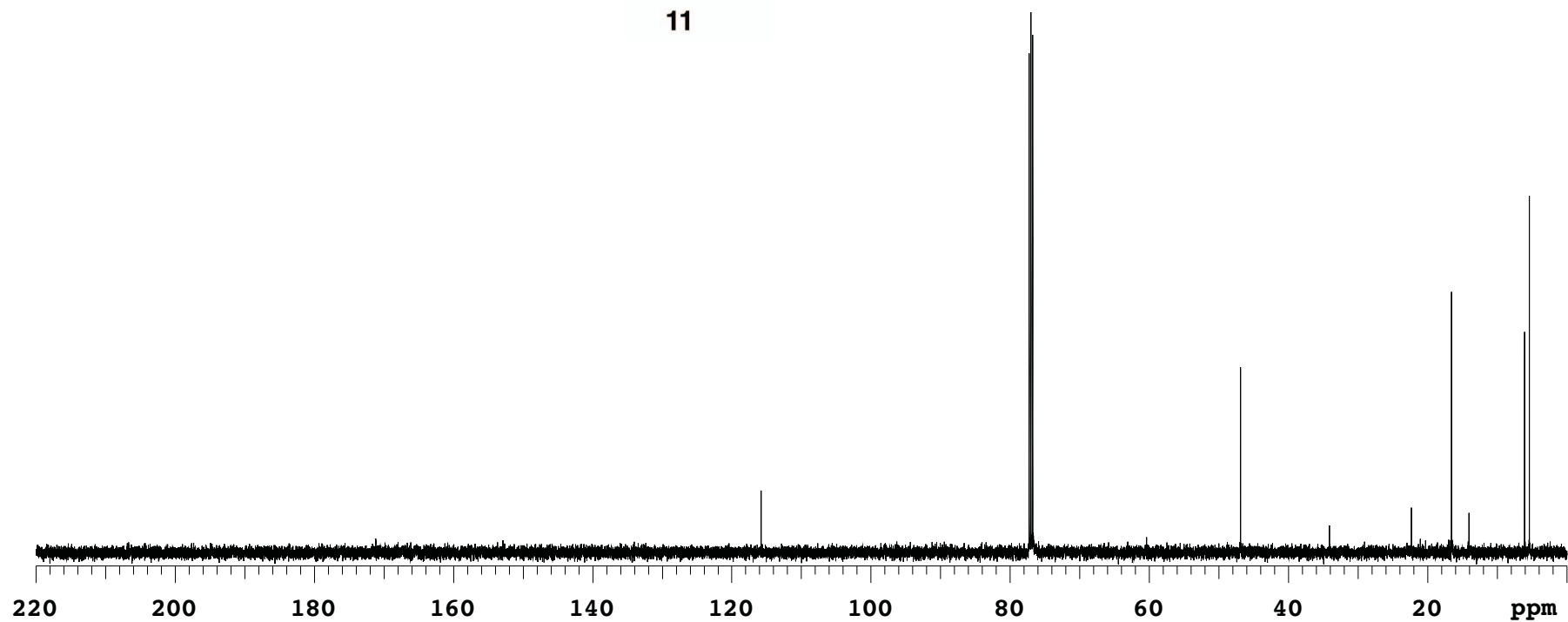
Pulse sequence CARBON
Solvent cdcl3

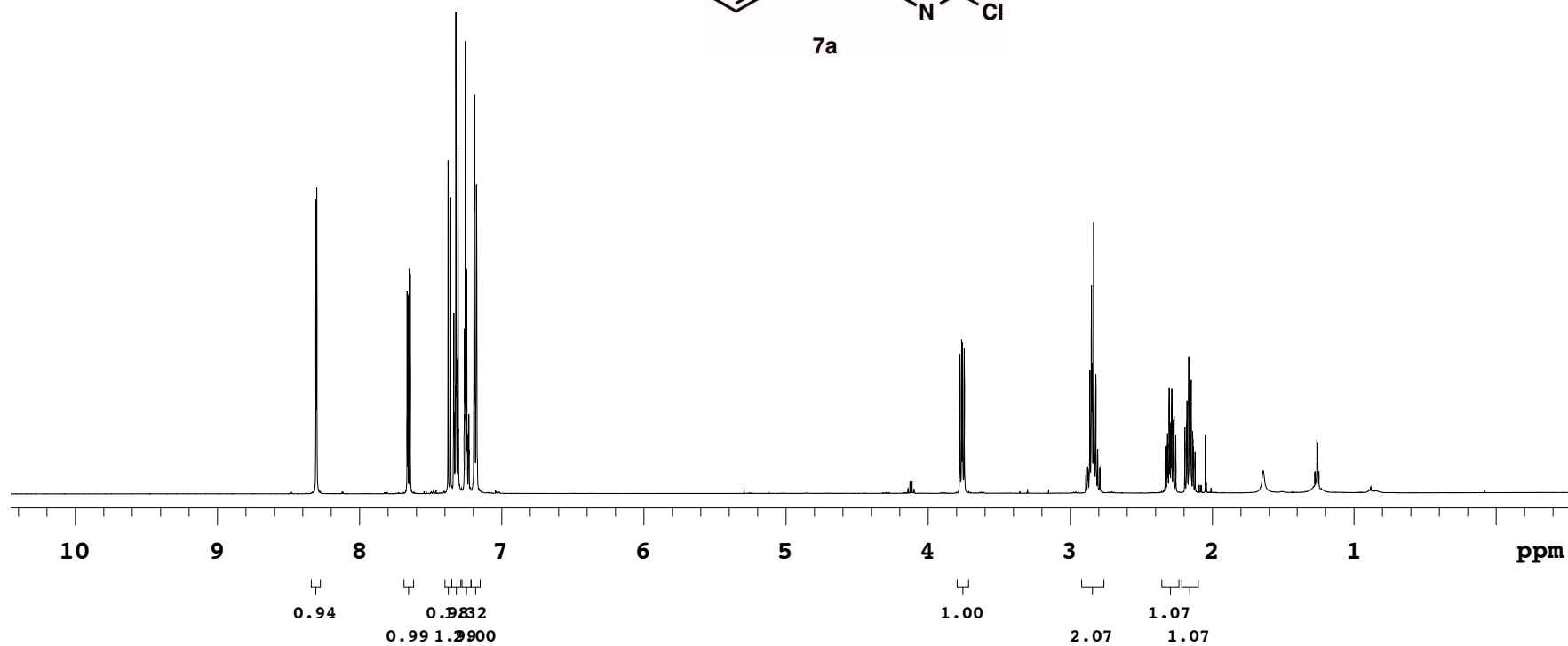
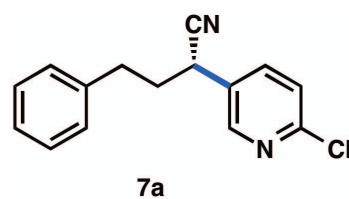
Temperature 25
Spectrometer -vnmrs400

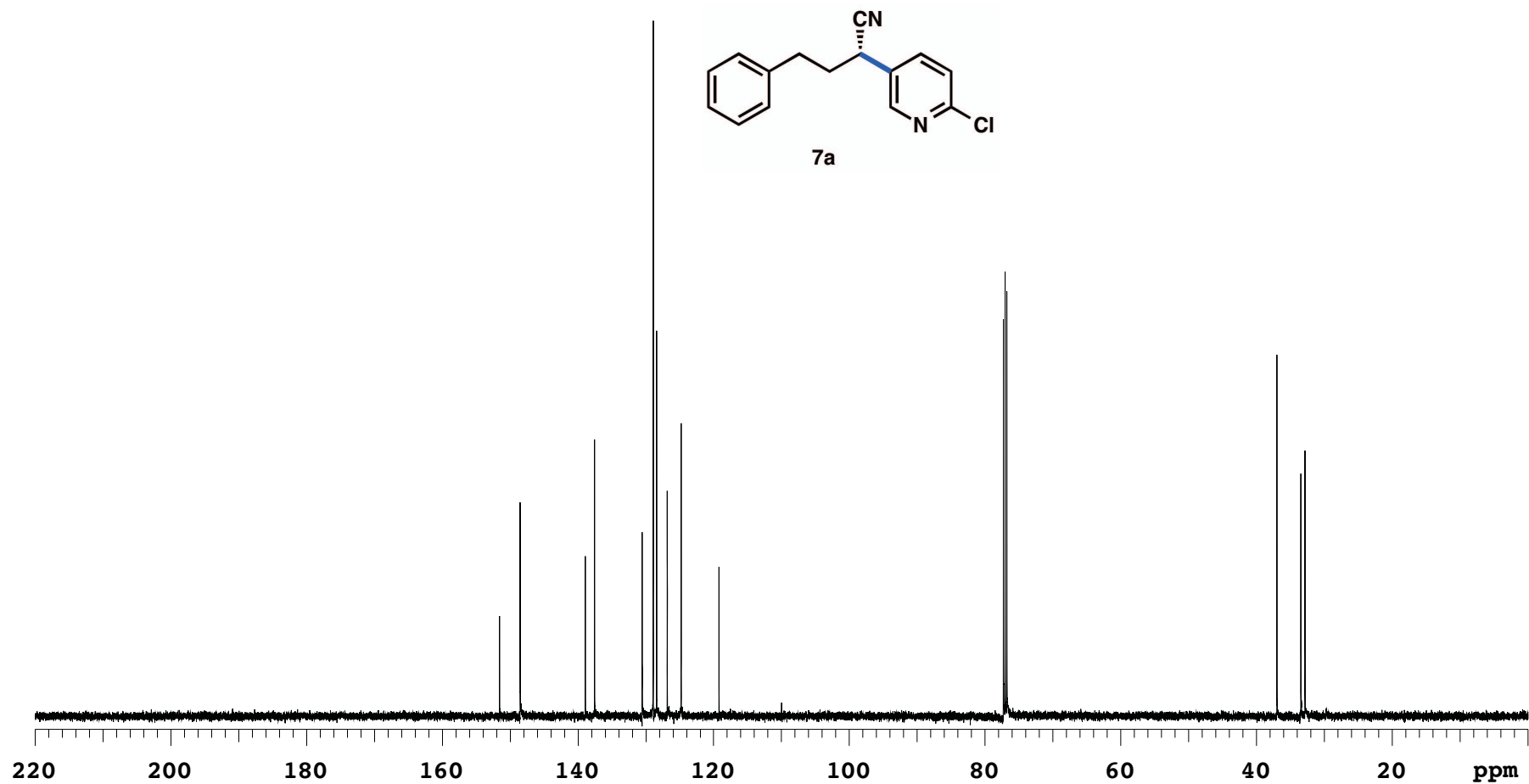
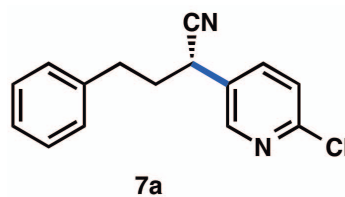
Study owner nkadunce
Operator autouser

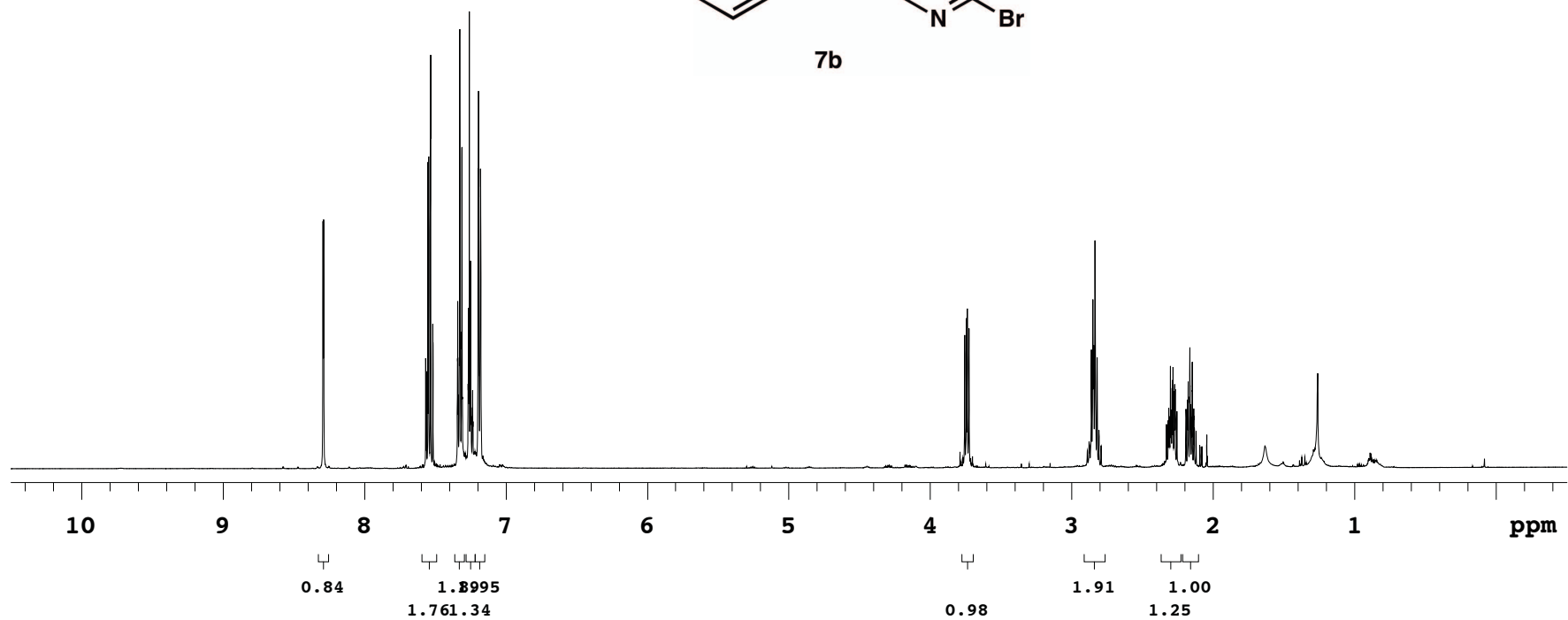
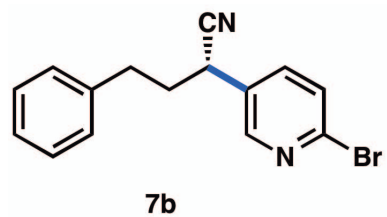


11









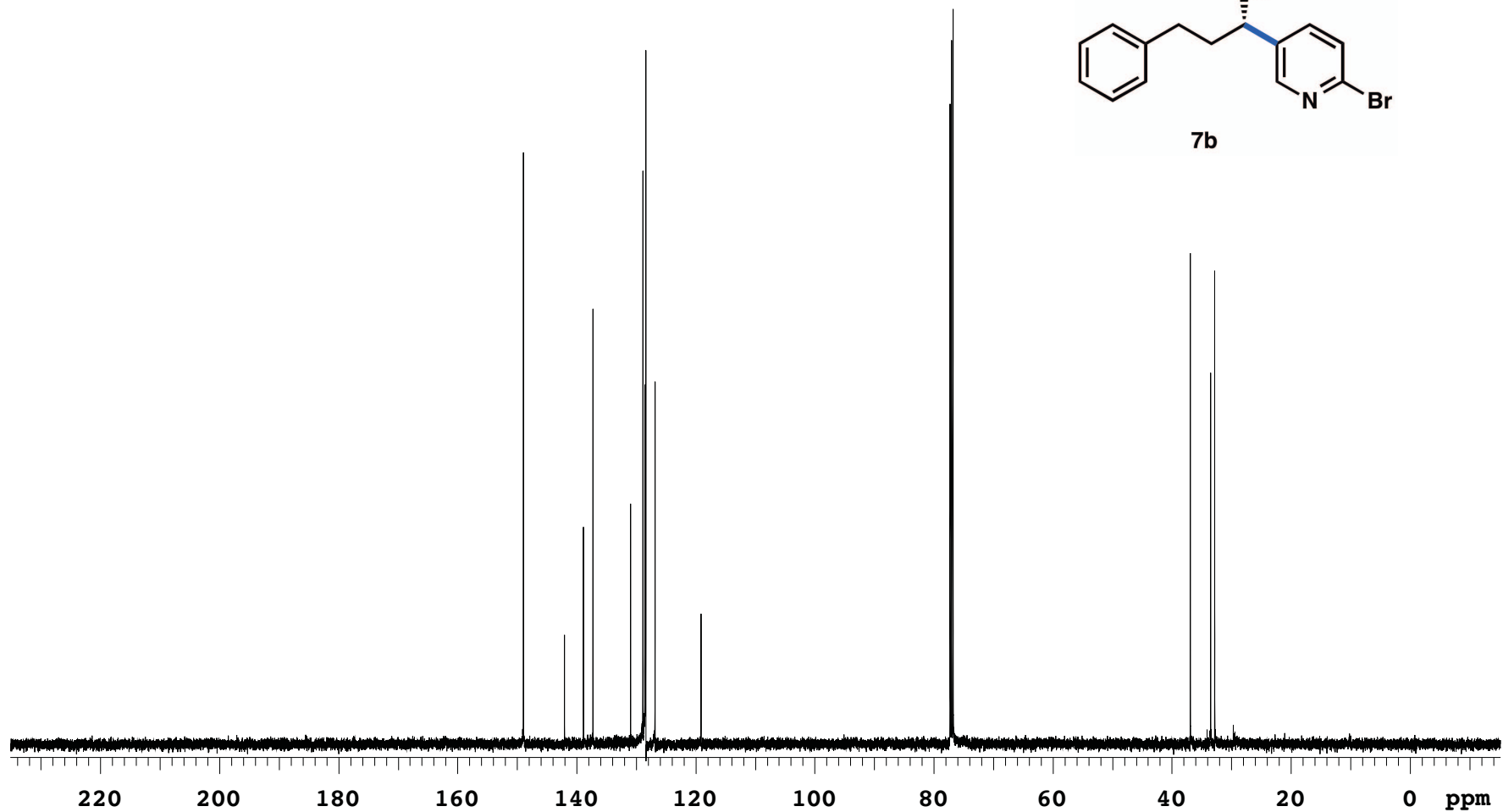
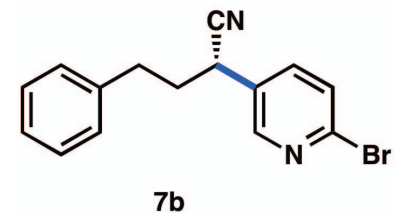
NTK-IV-90-BrPyr

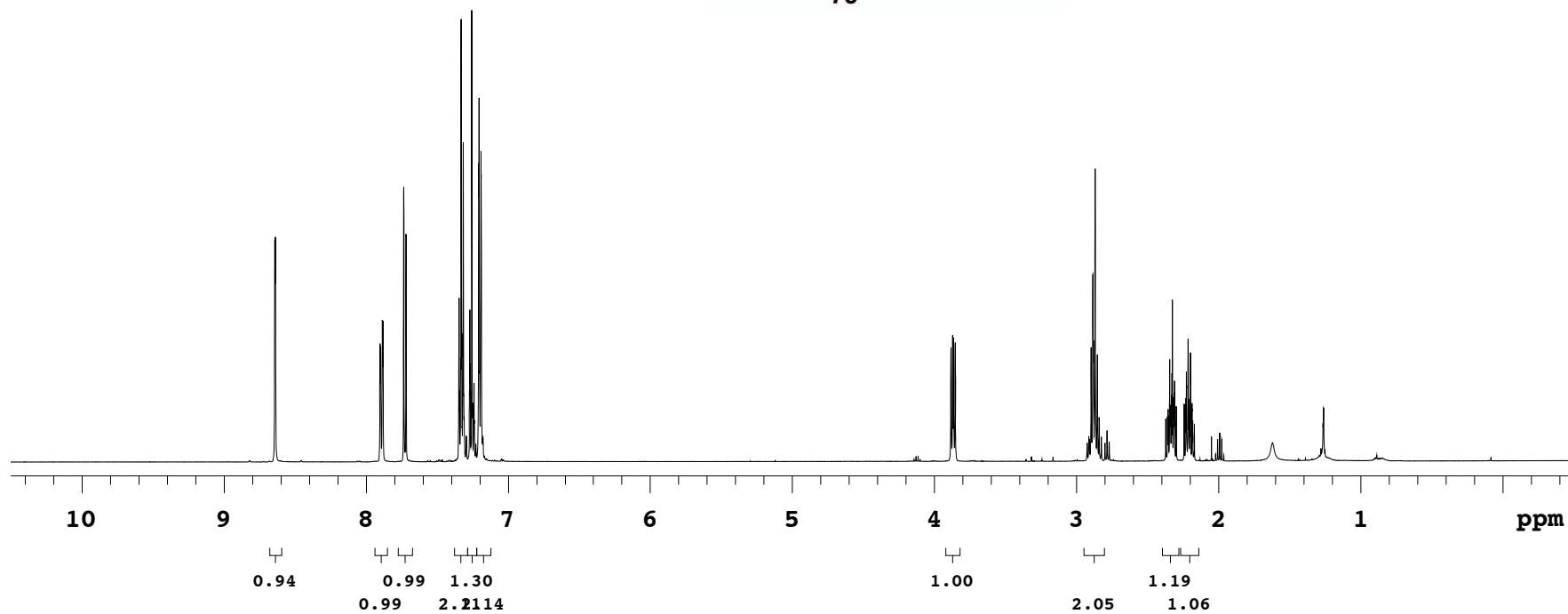
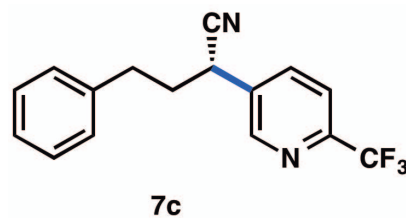
Sample Name NTK-IV-90-BrPyr
Date collected 2015-04-02

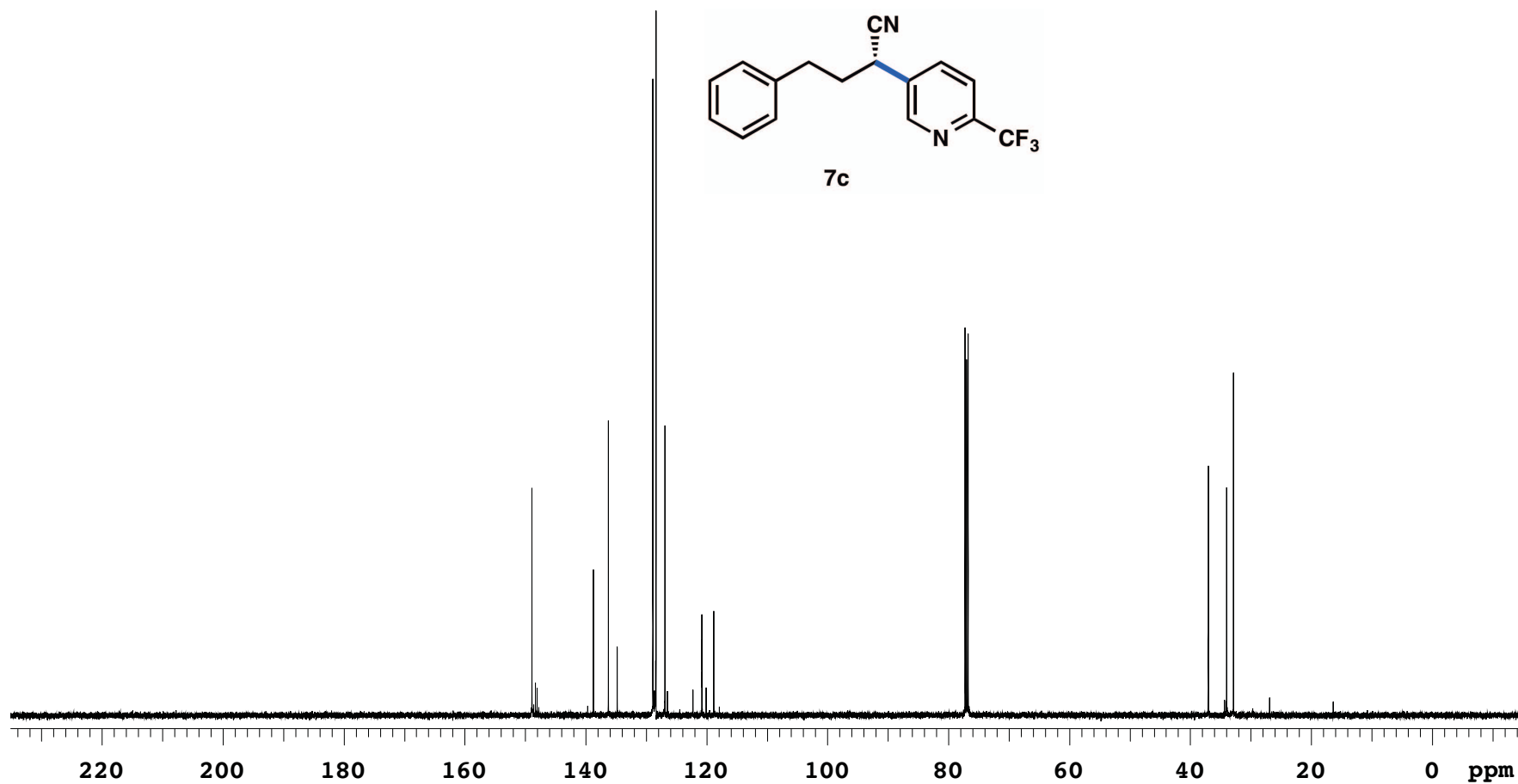
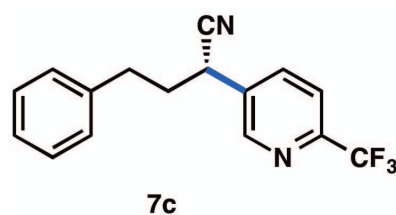
Pulse sequence CARBON
Solvent cdcl3

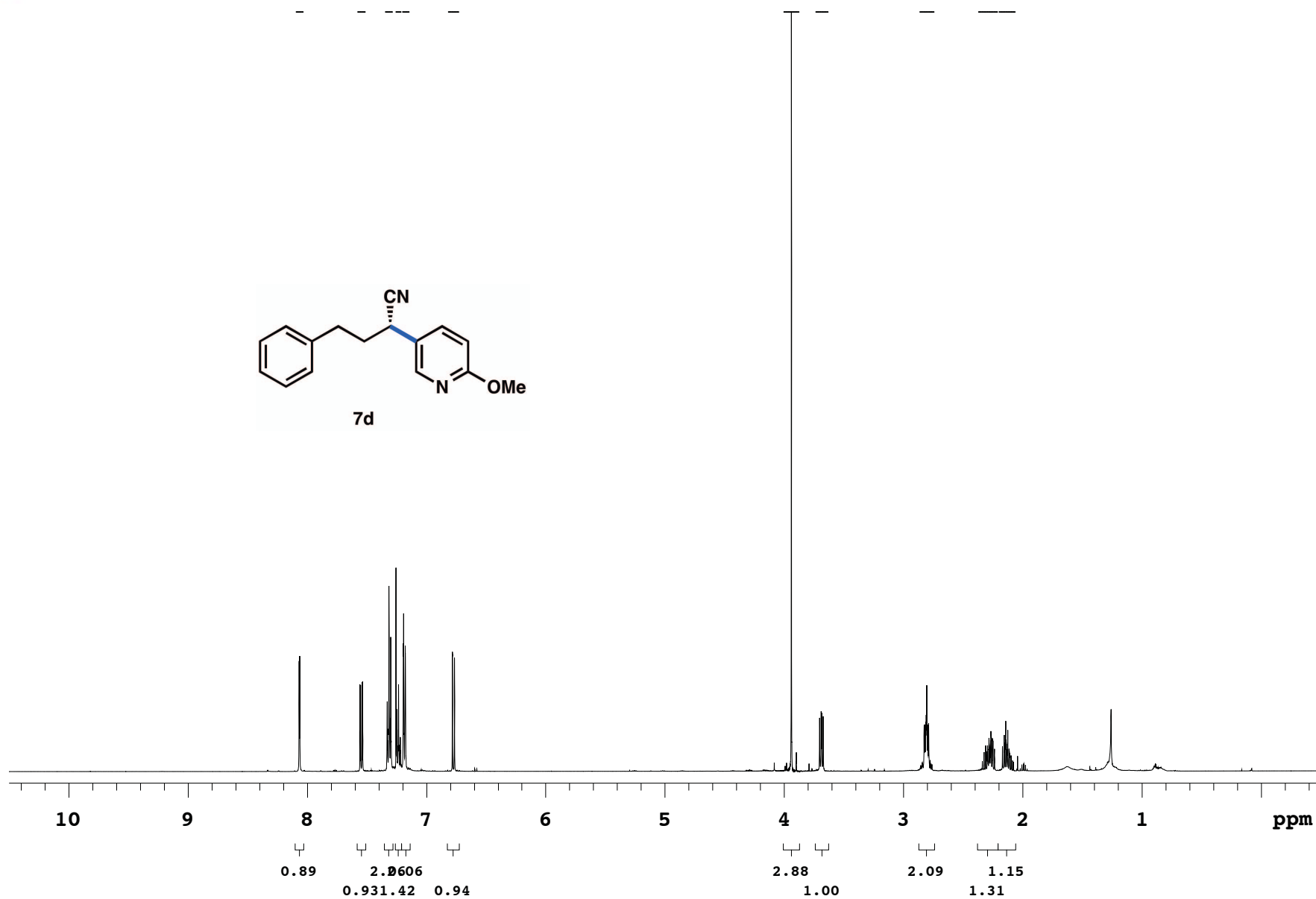
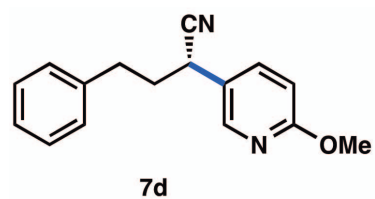
Temperature 25
Spectrometer -vnmrs400

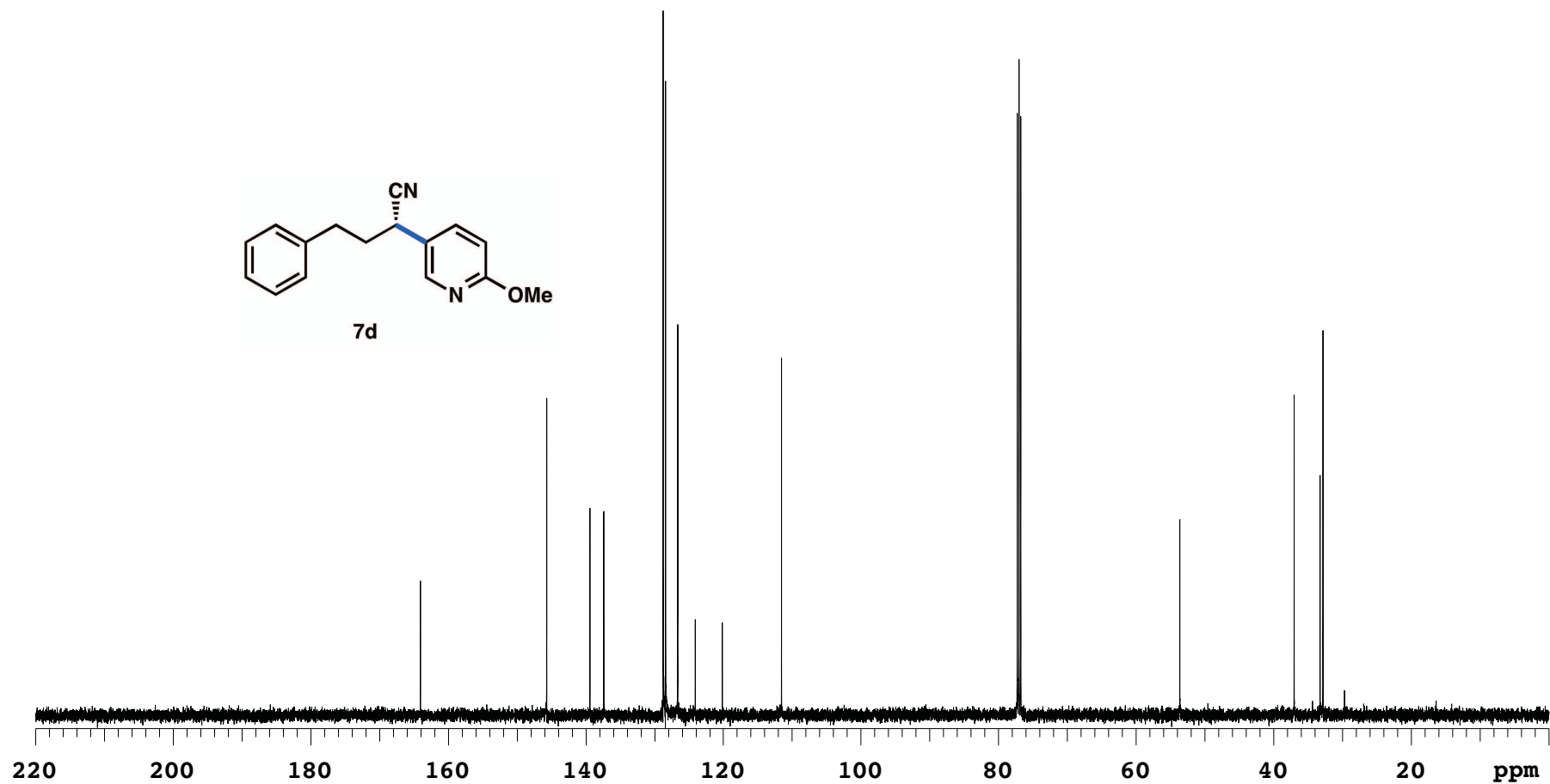
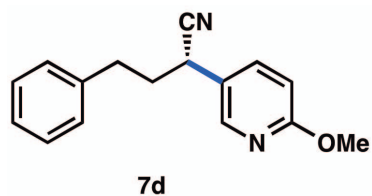
Study owner nkadunce
Operator autouser











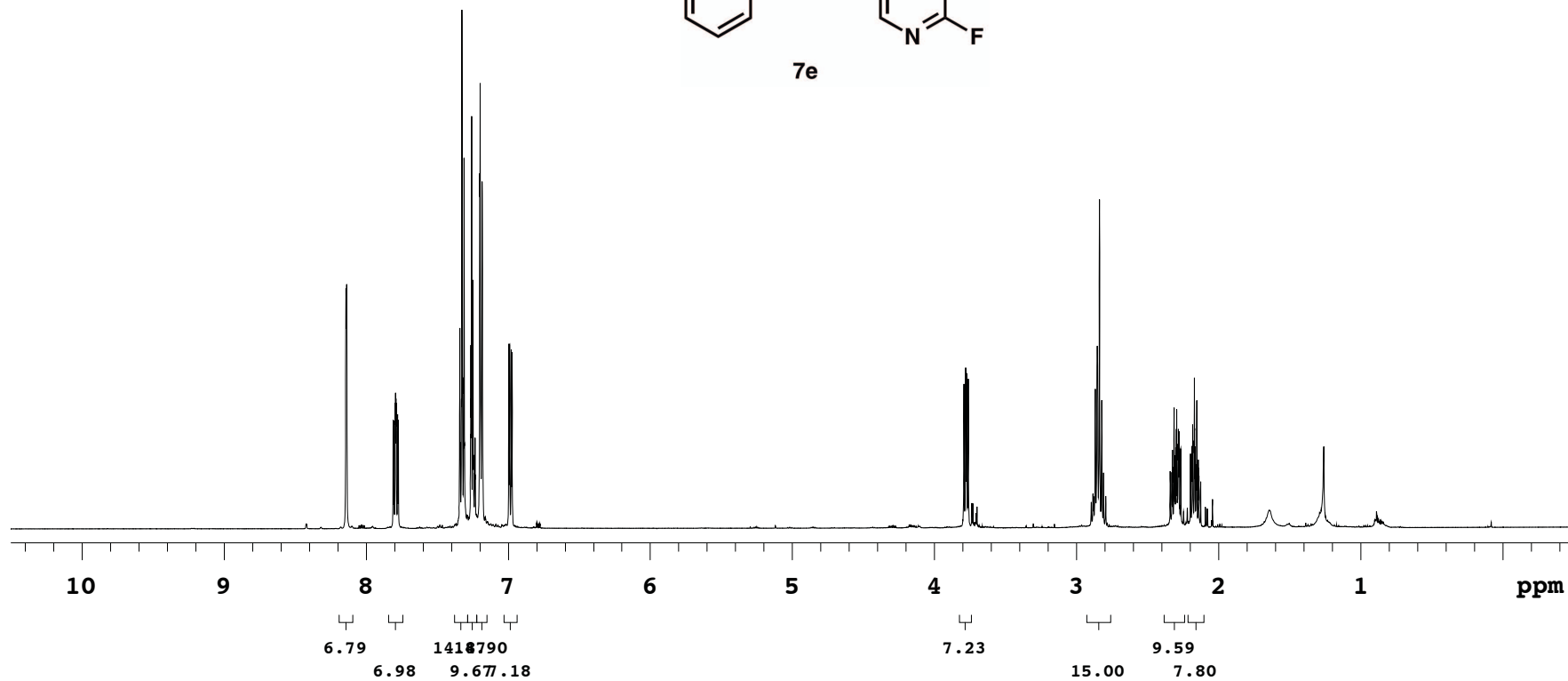
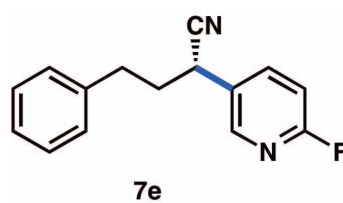
NTK-IV-93-5Fpyridine

Sample Name NTK-IV-93-5Fpyridine
Date collected 2015-04-07

Pulse sequence PROTON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser



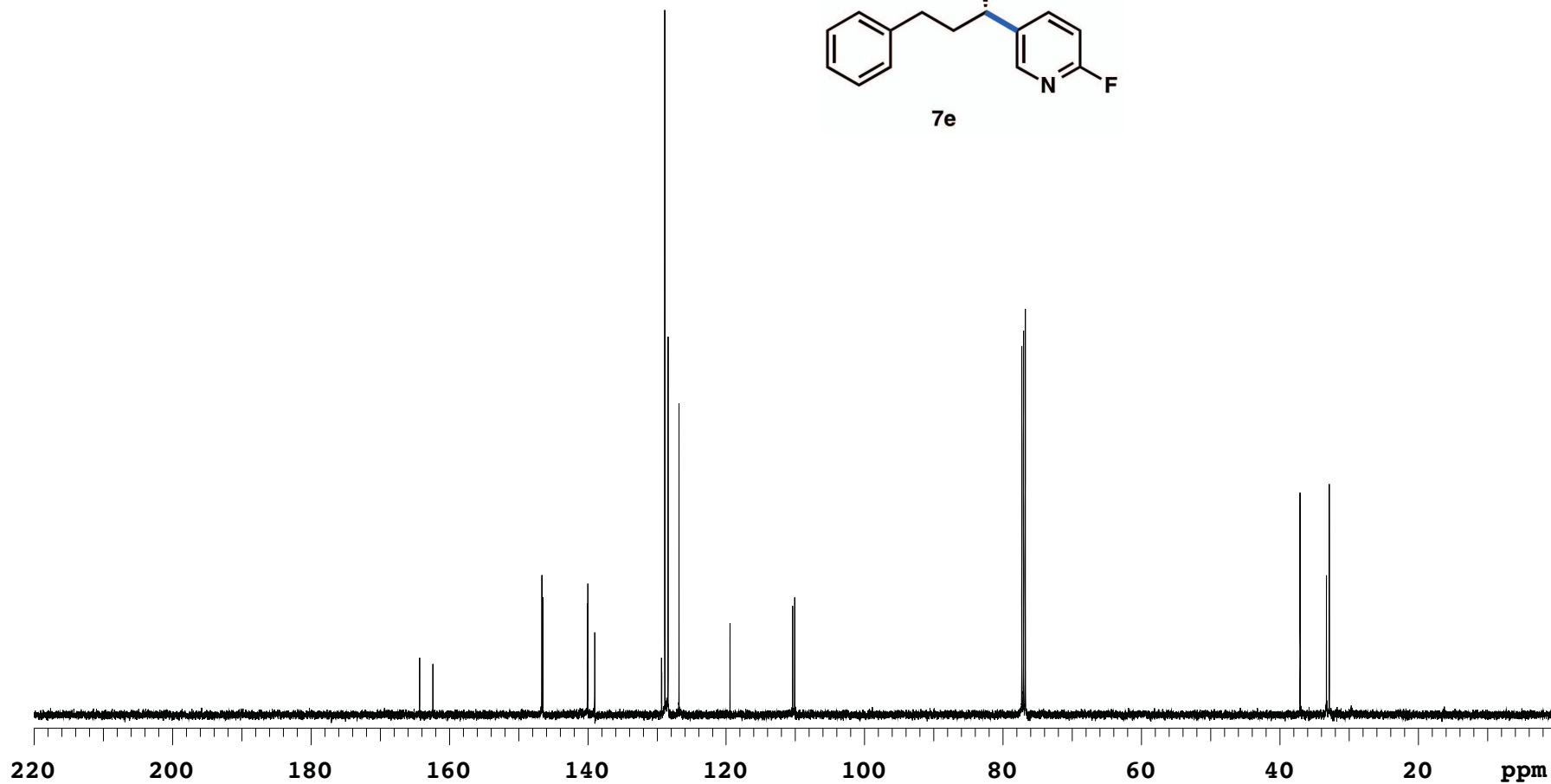
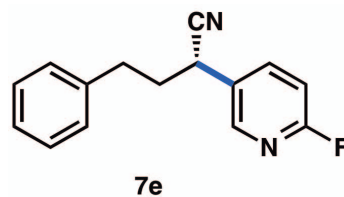
NTK-IV-93-5Fpyridine

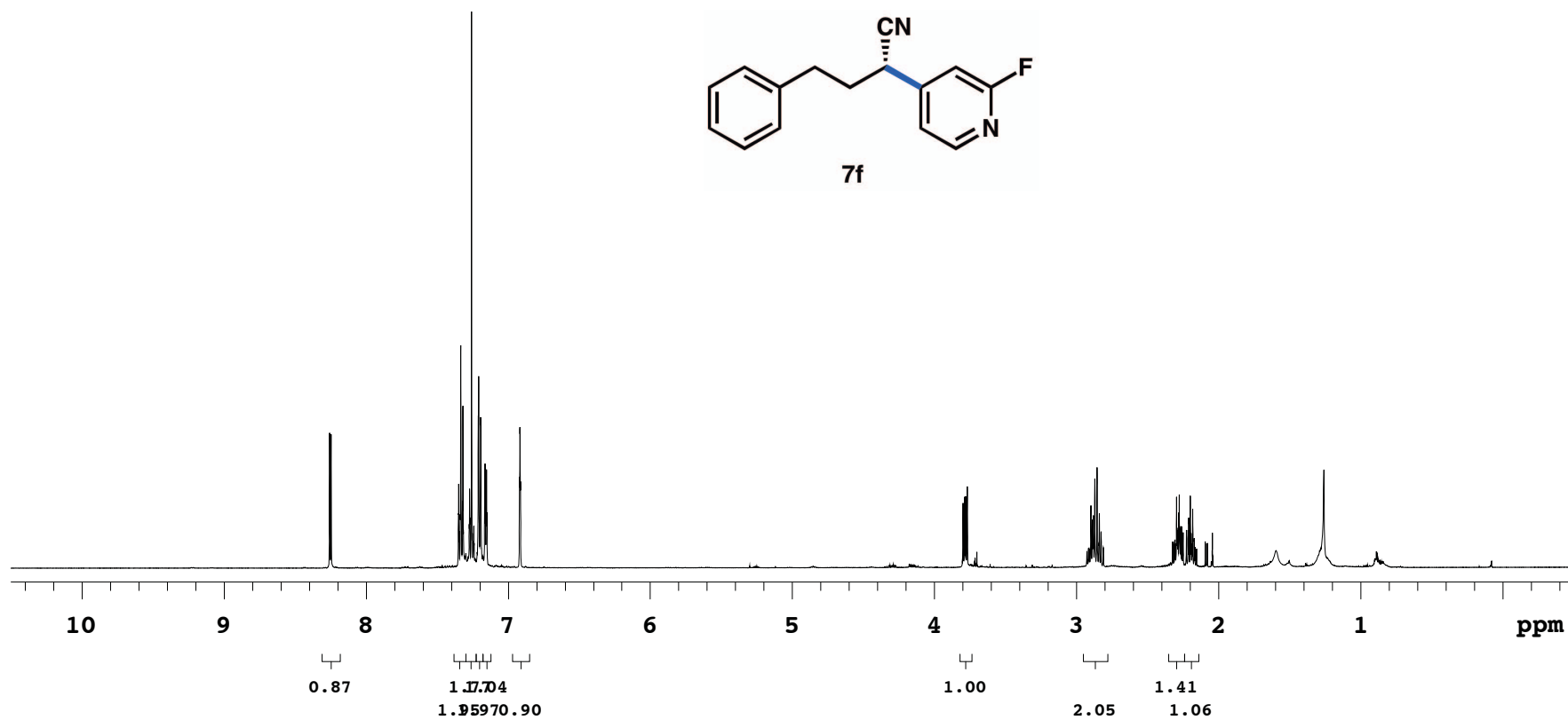
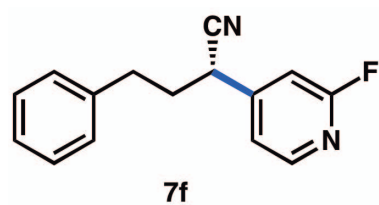
Sample Name NTK-IV-93-5Fpyridine
Date collected 2015-04-07

Pulse sequence CARBON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser





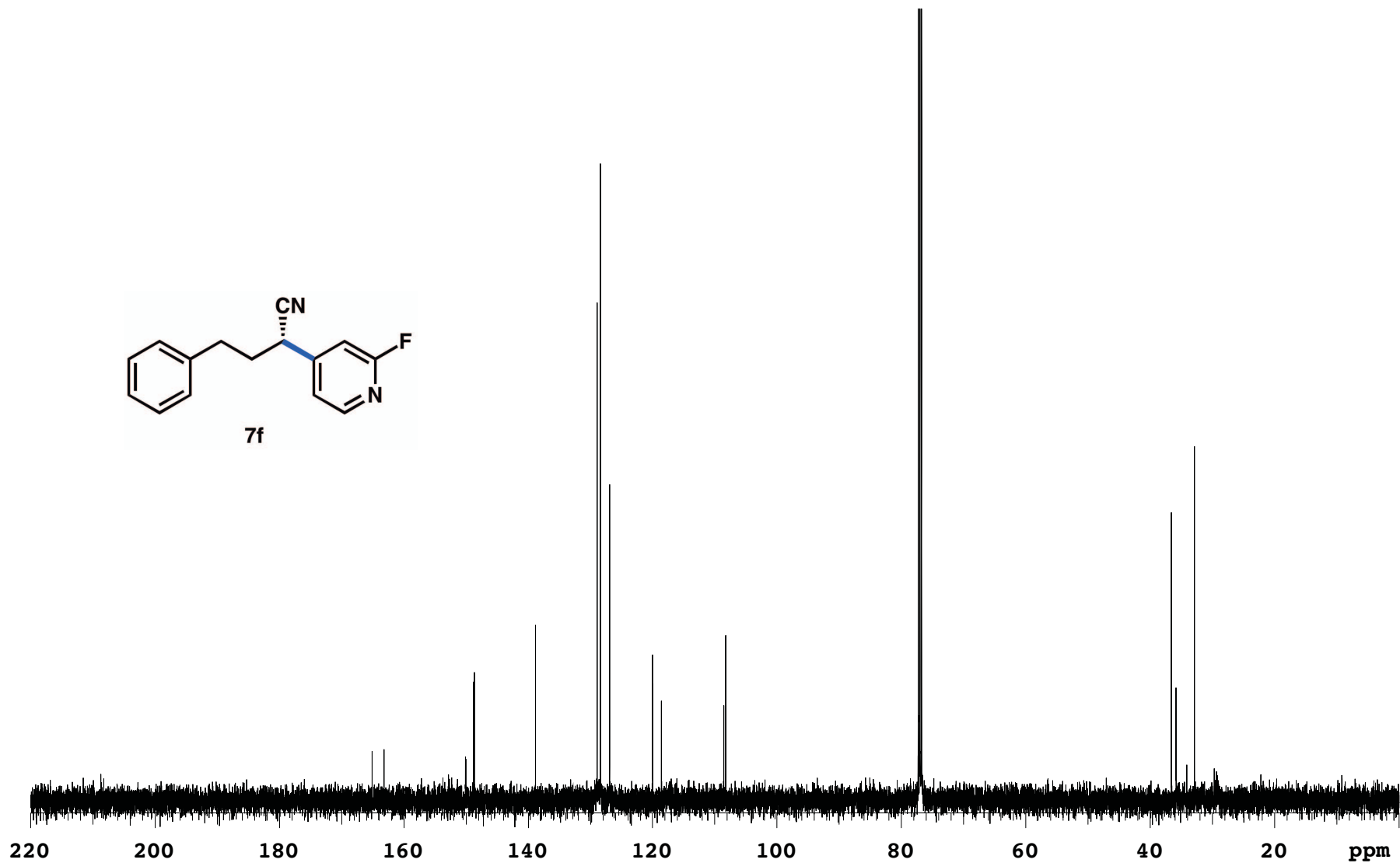
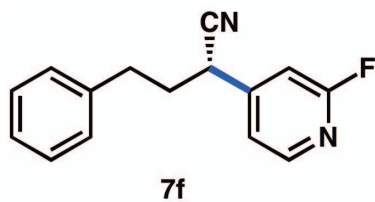
NTK-IV-93-4FPyridine

Sample Name NTK-IV-93-4FPyridine
Date collected 2015-04-07

Pulse sequence CARBON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser



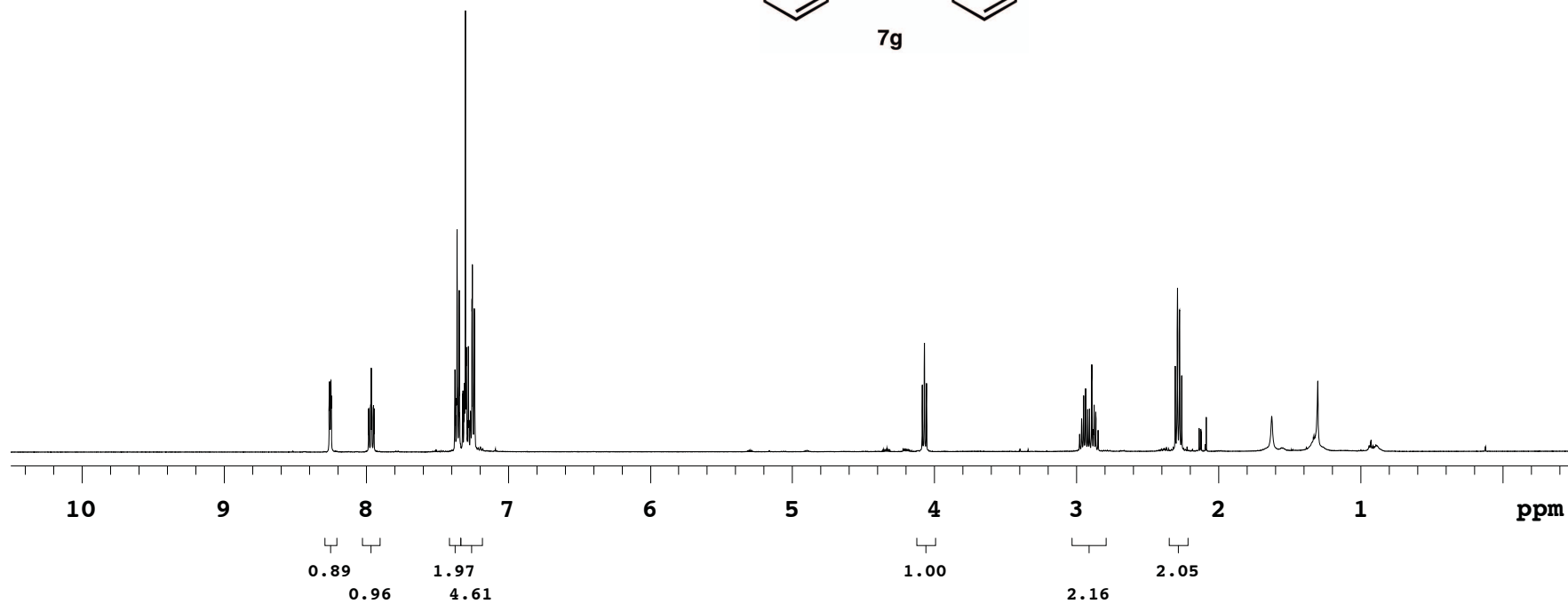
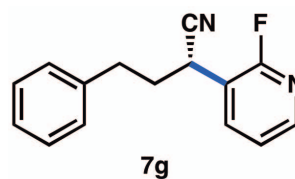
NTK-IV-94-orthoF

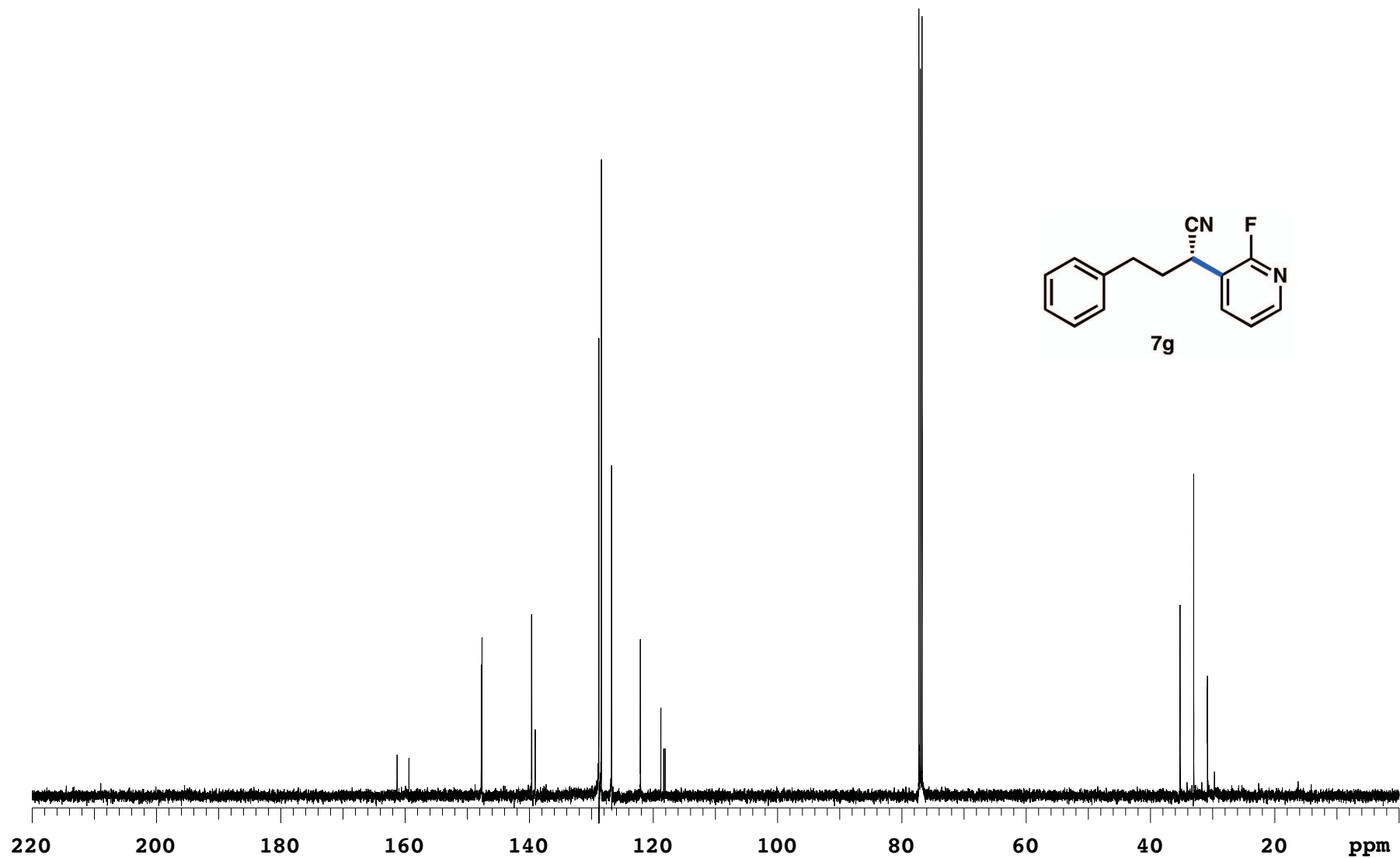
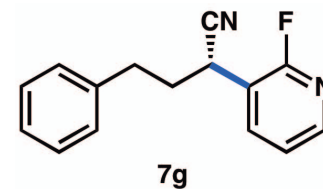
Sample Name NTK-IV-94-orthoF
Date collected 2015-04-12

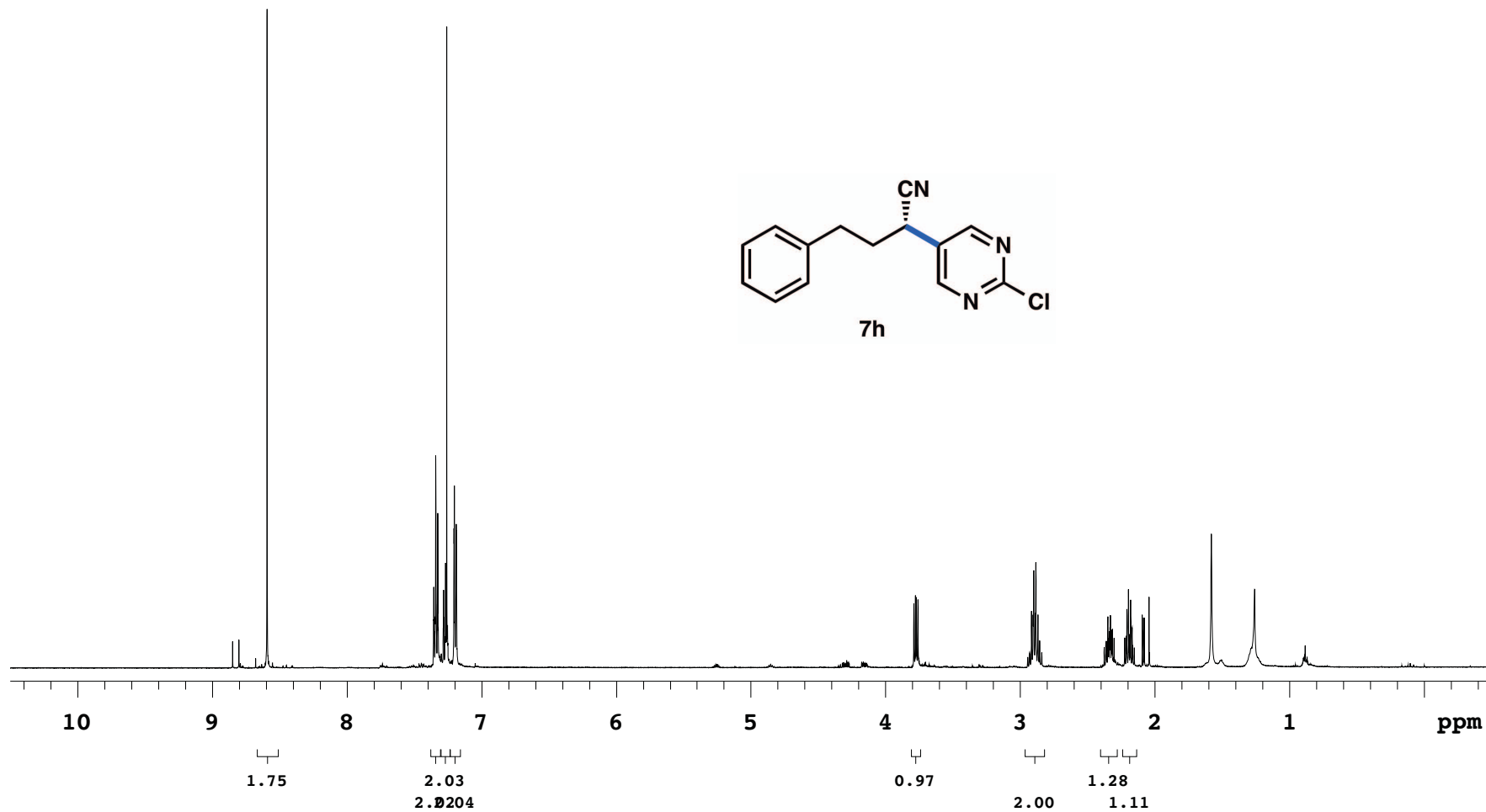
Pulse sequence PROTON
Solvent cdcl3

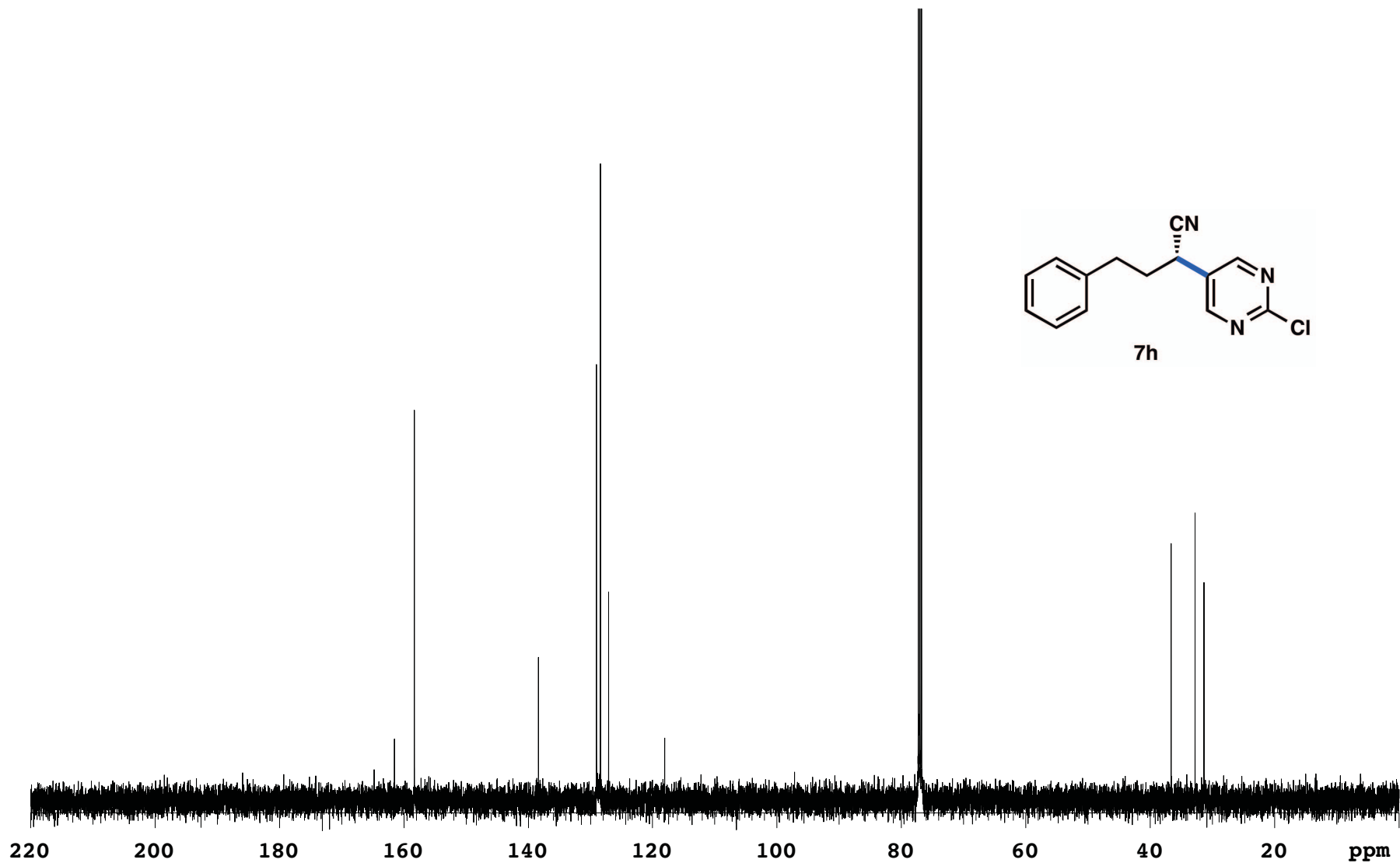
Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser







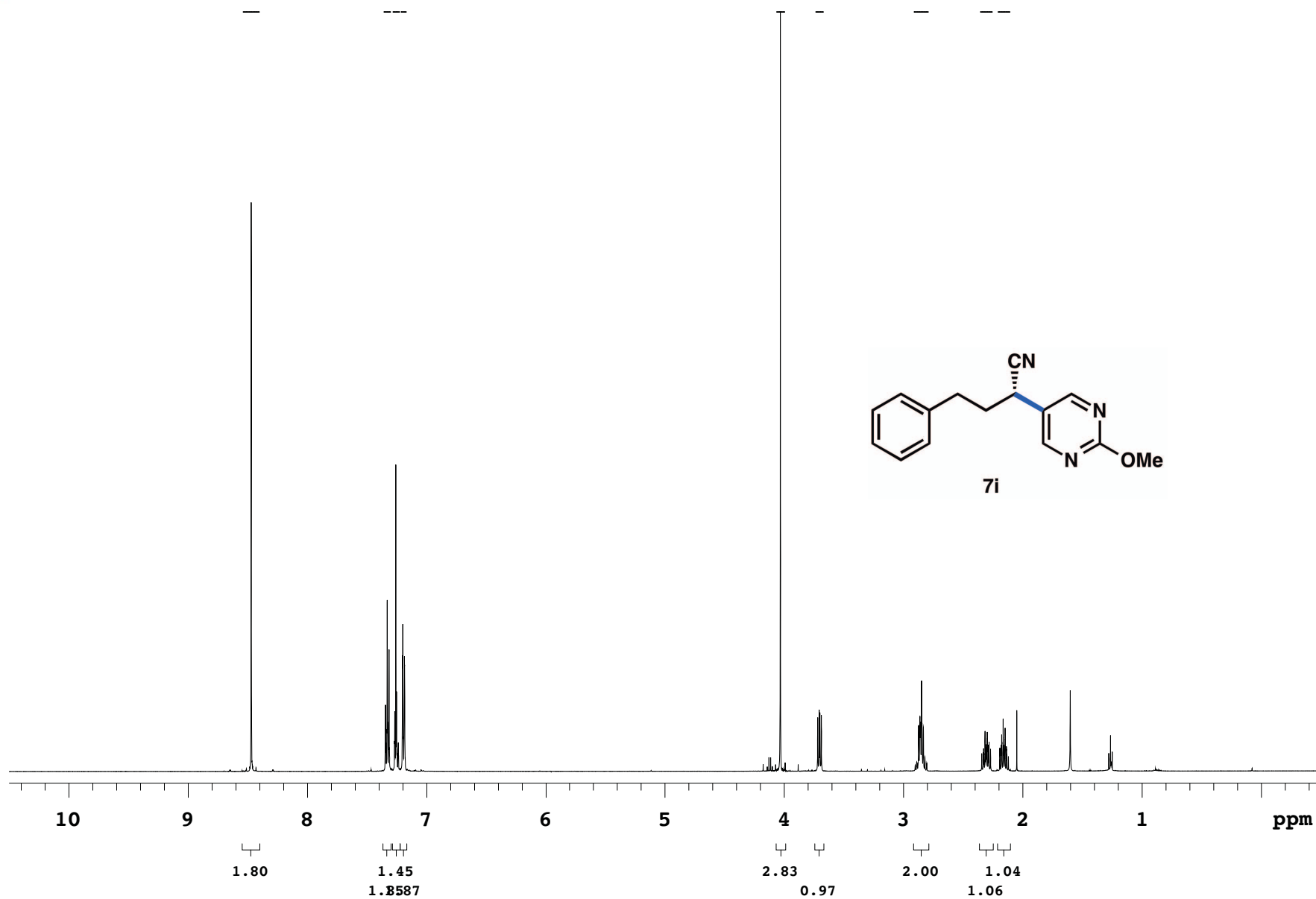


NTK-IV-96-OMePyrimidine

Sample Name NTK-IV-96-OMePyrimidine Pulse sequence PROTON
 Date collected 2015-04-12 Solvent cdcl3

Temperature 25
 Spectrometer -vnmrs400

Study owner nkadunce
 Operator autouser

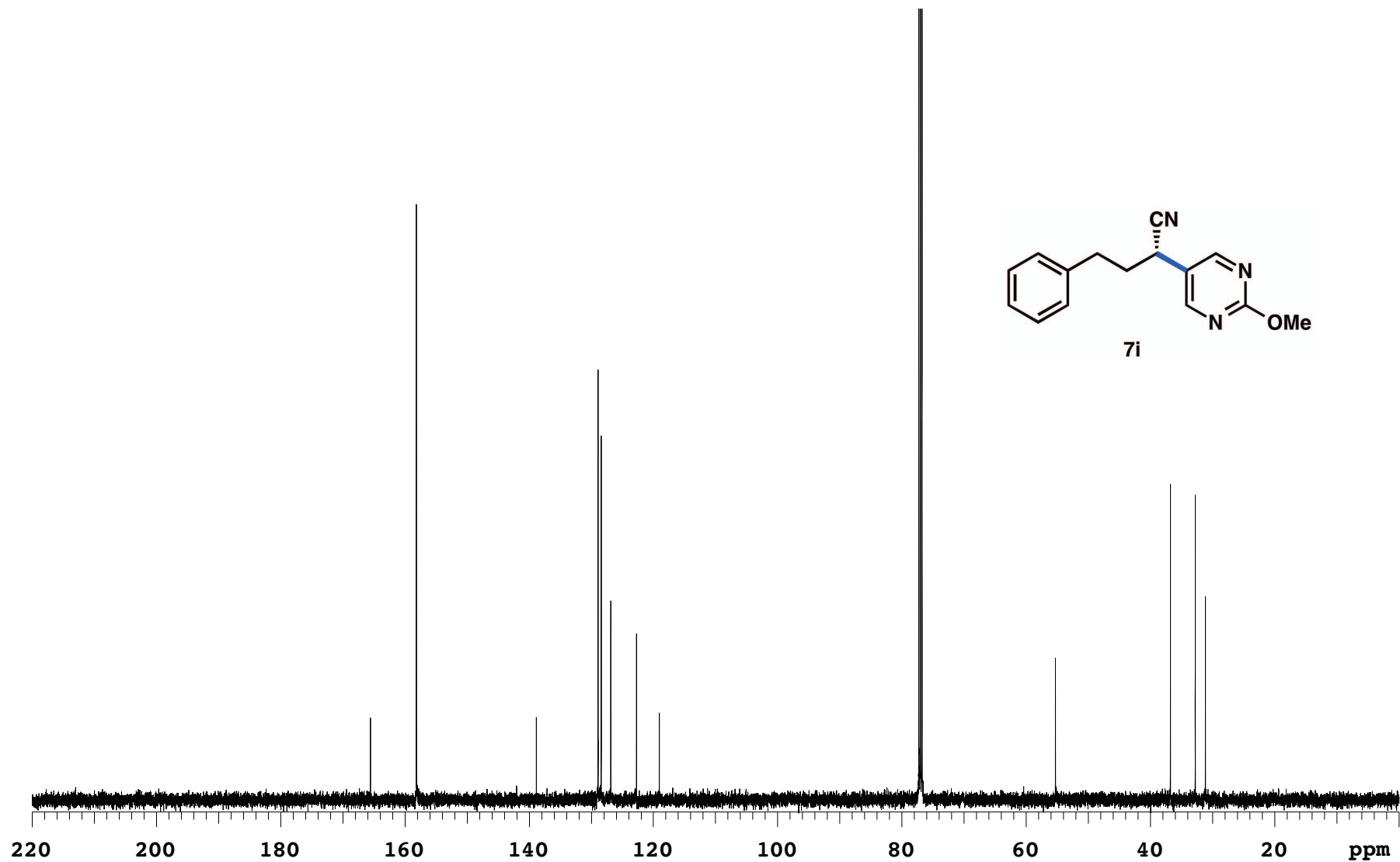


NTK-IV-96-OMePyrimidine

Sample Name NTK-IV-96-OMePyrimidine Pulse sequence CARBON
Date collected 2015-04-12 Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser

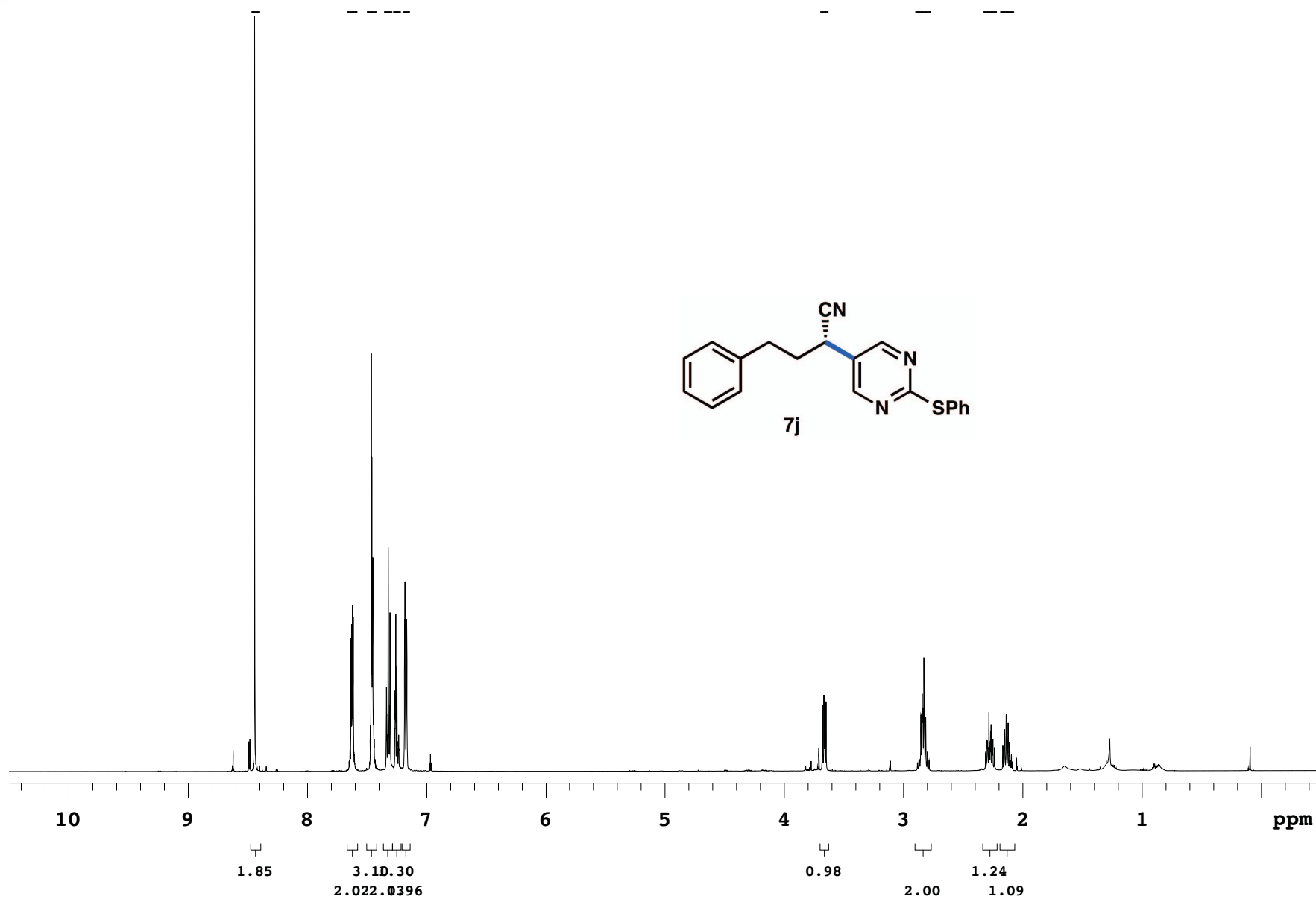


NTK-IV-92-SPhPyrimidine

Sample Name NTK-IV-92-SPhPyrimidine Pulse sequence PROTON
 Date collected 2015-04-06 Solvent cdcl3

Temperature 25
 Spectrometer -vnmrs400

Study owner nkadunce
 Operator autouser

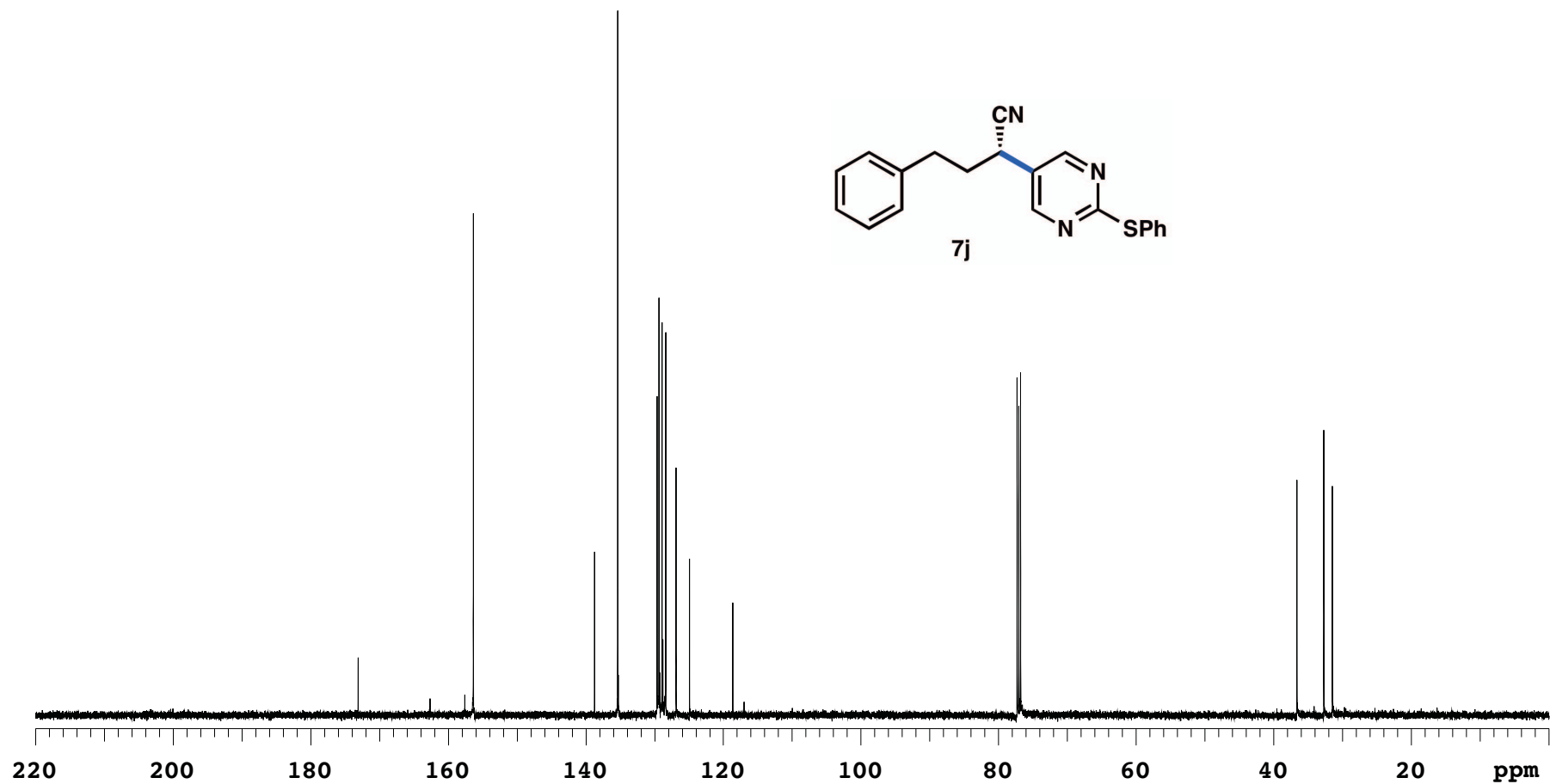


NTK-IV-92-SPhPyrimidine

Sample Name NTK-IV-92-SPhPyrimidine Pulse sequence CARBON
Date collected 2015-04-06 Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser



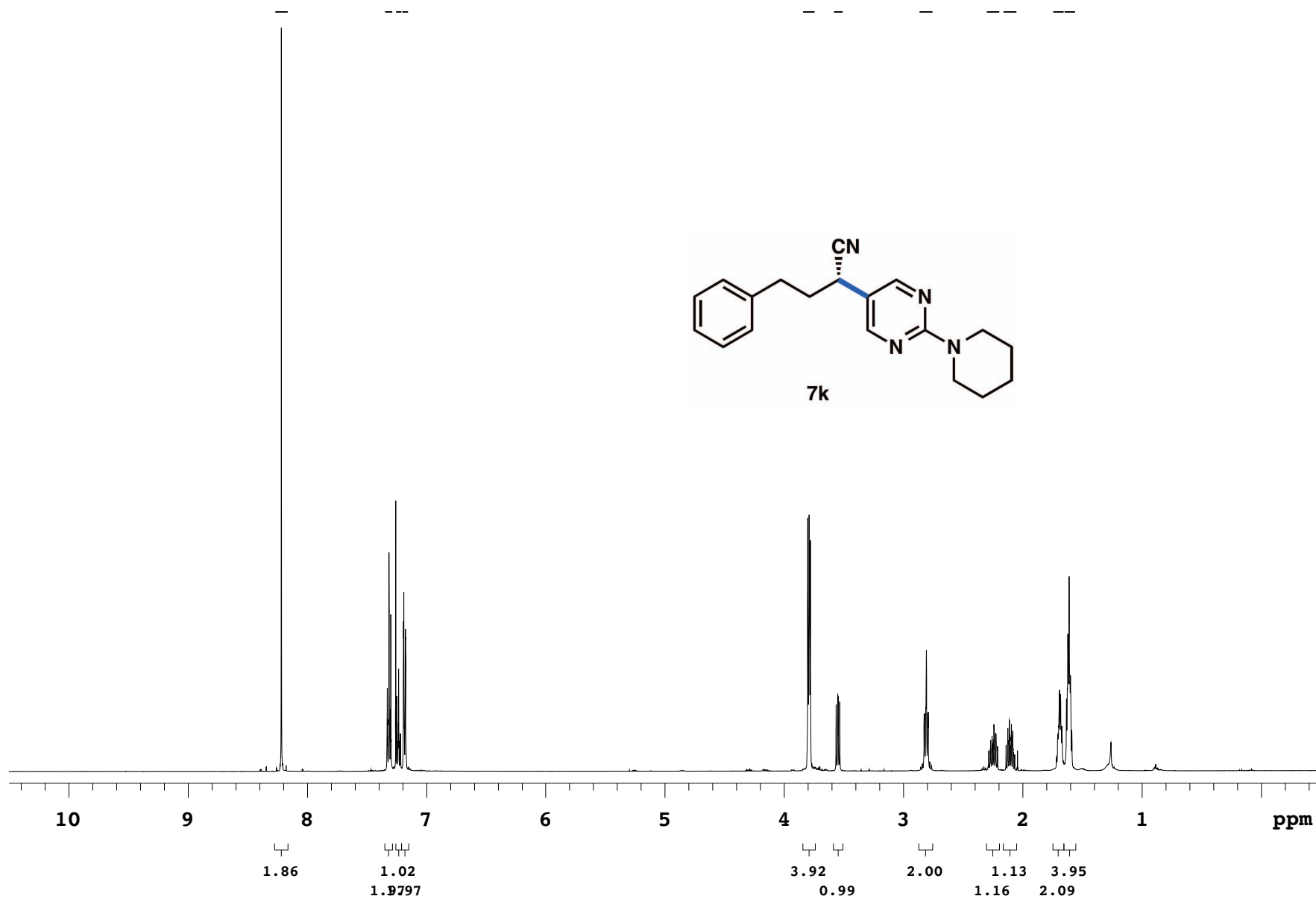
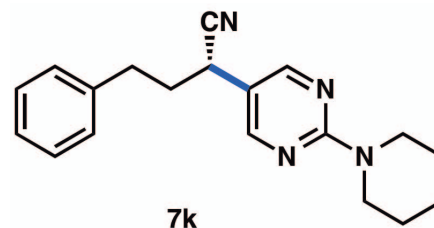
NTK-IV-91-piperidine

Sample Name NTK-IV-91-piperidine
Date collected 2015-04-03

Pulse sequence PROTON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser



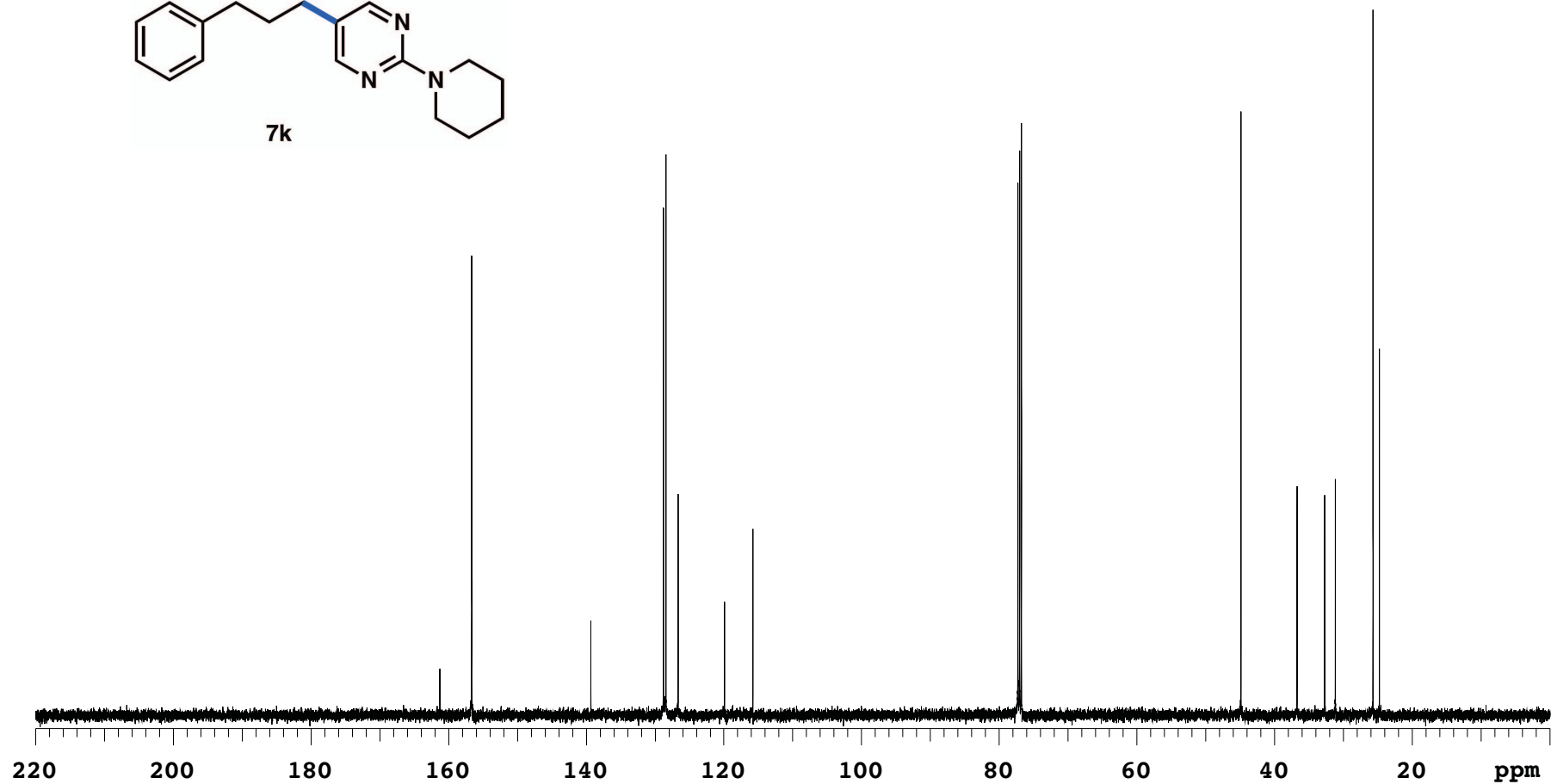
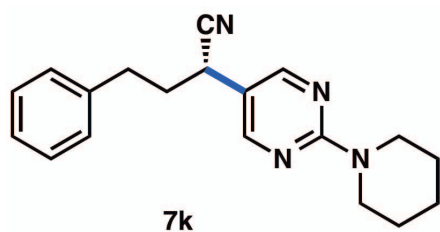
NTK-IV-91-piperidine

Sample Name NTK-IV-91-piperidine
Date collected 2015-04-03

Pulse sequence CARBON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser



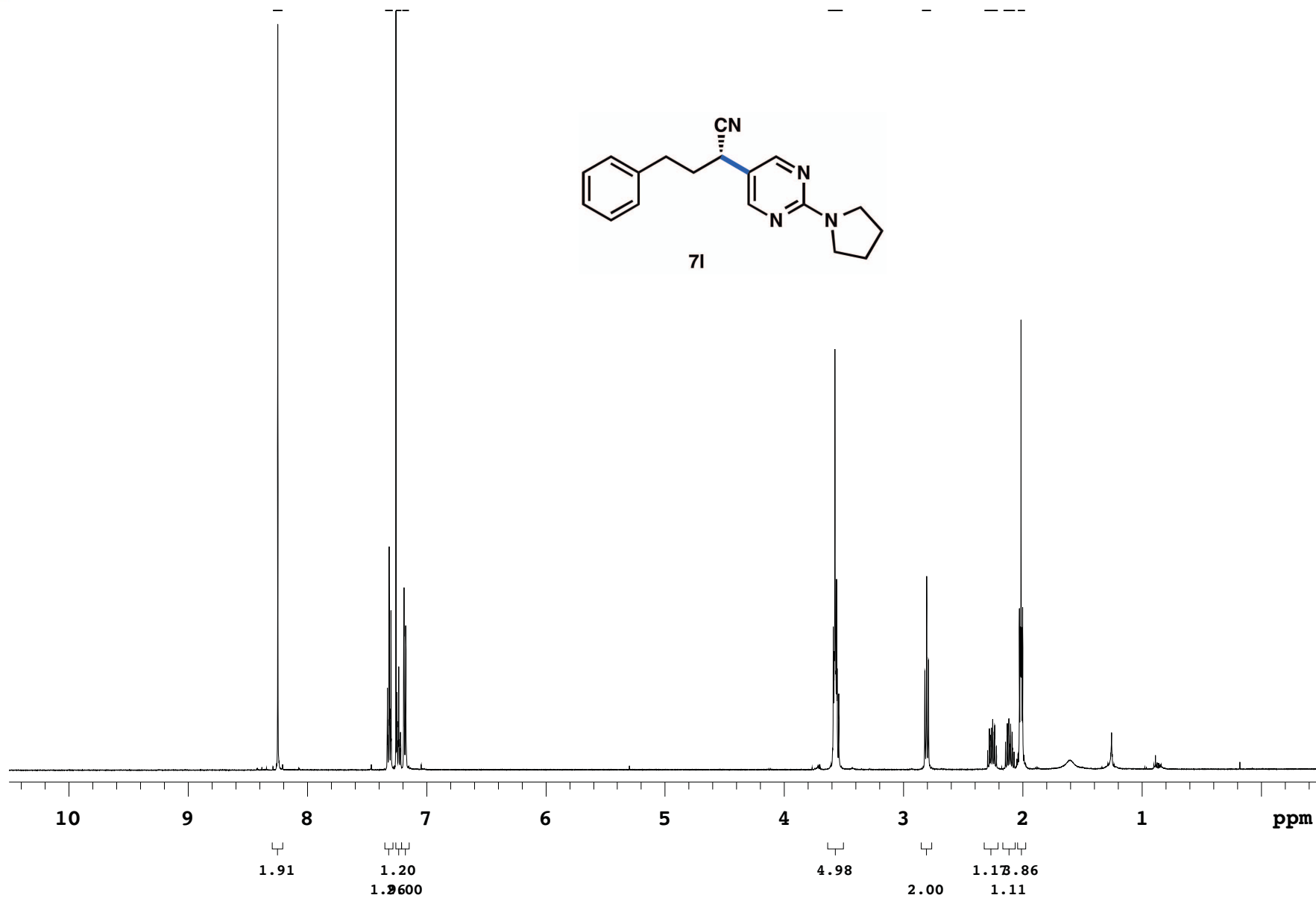
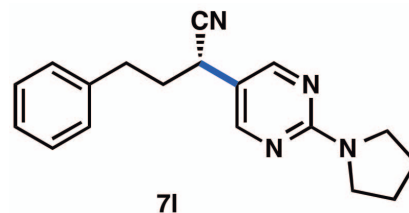
NTK-IV-91-pyrrole

Sample Name NTK-IV-91-pyrrole
Date collected 2015-04-03

Pulse sequence PROTON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser



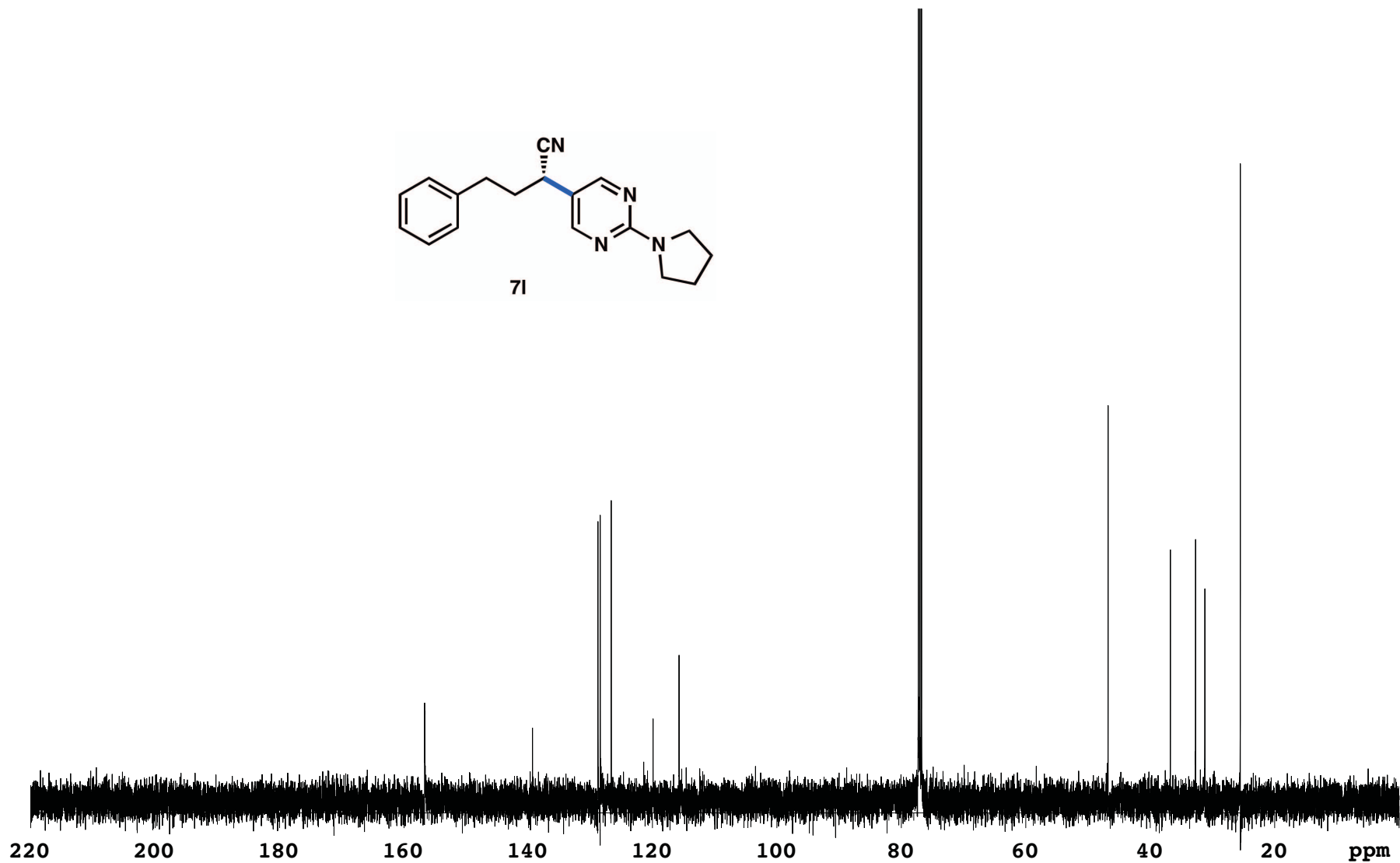
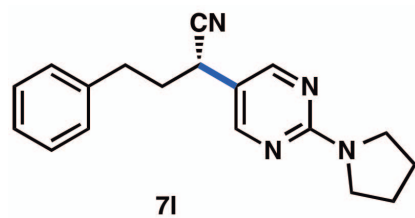
NTK-IV-91-pyrrole

Sample Name NTK-IV-91-pyrrole
Date collected 2015-04-03

Pulse sequence CARBON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser

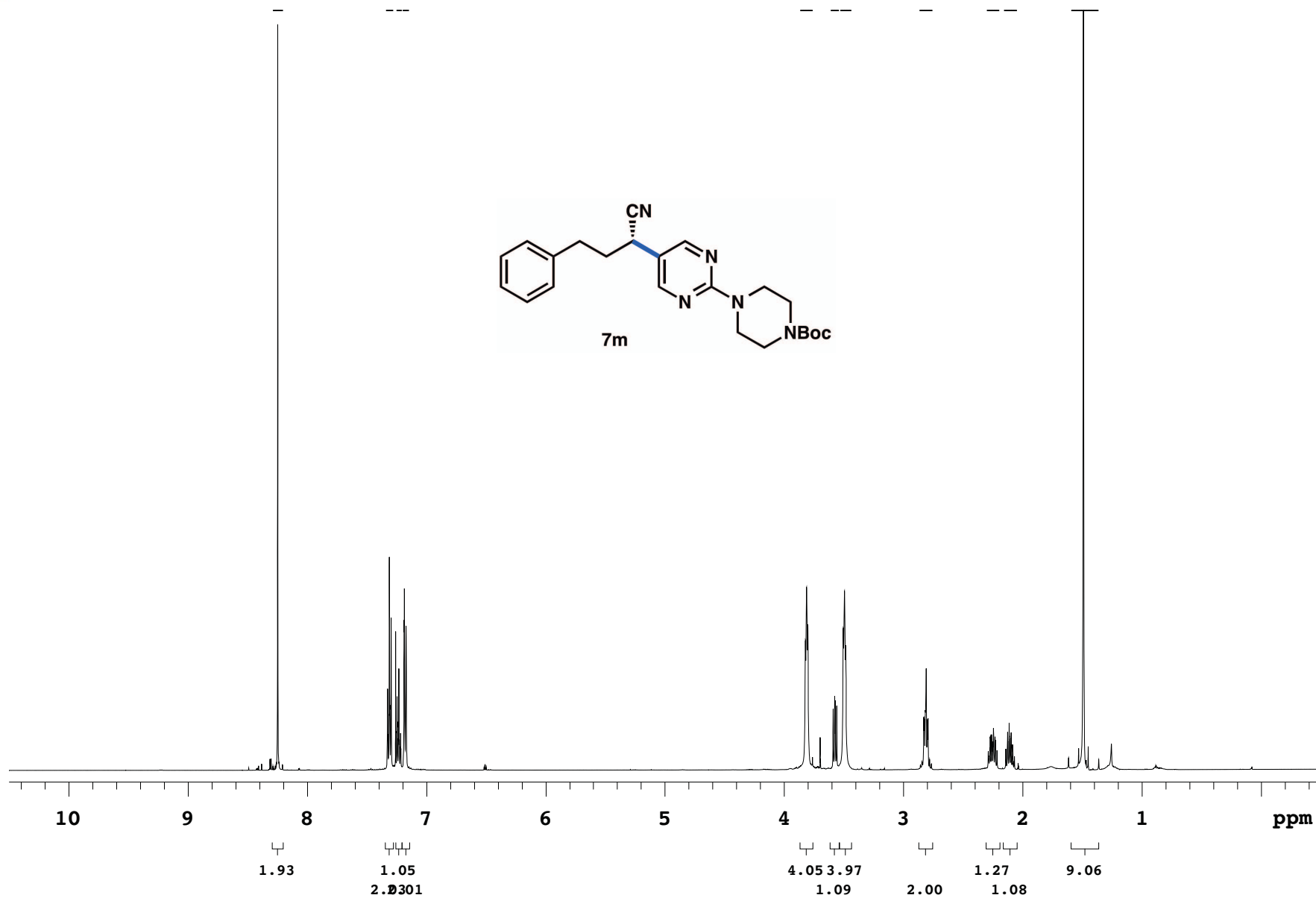
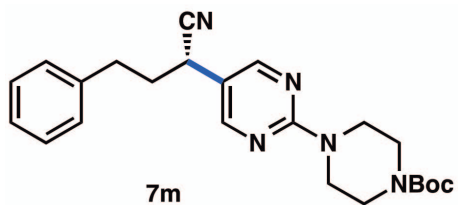


NTK-IV-92-NBocPiperazinyIPyrimidine

Sample Name NTK-IV-92-NBocPiperazinyIPyrimidine
 Date collected 2015-04-06
 Solvent cdcl3

Temperature 25
 Spectrometer -vnmrs400

Study owner nkadunce
 Operator autouser



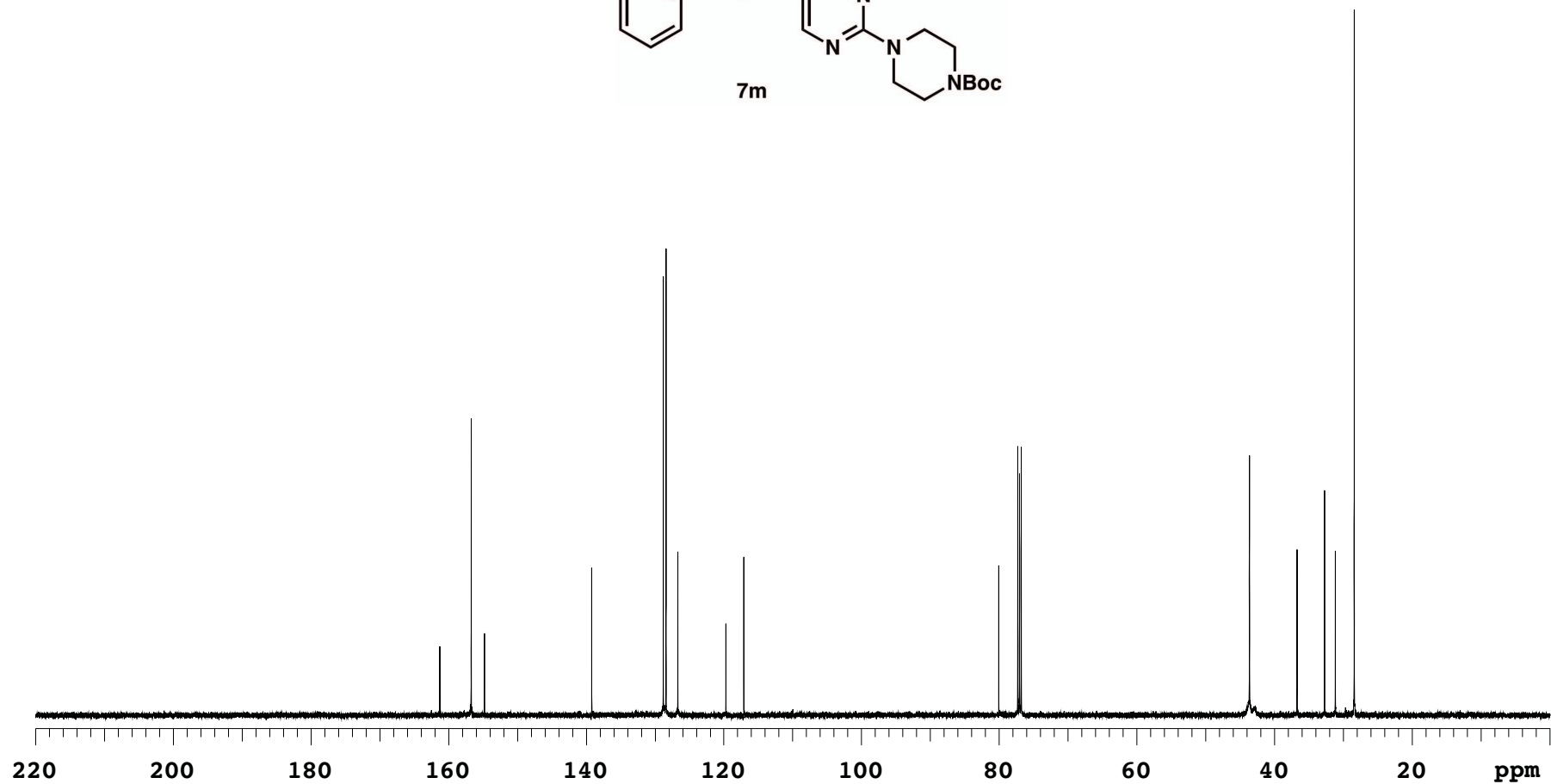
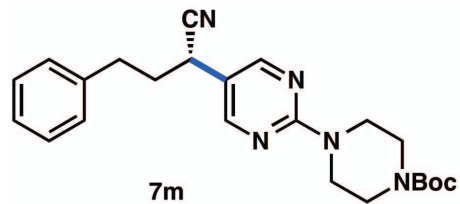
NTK-IV-92-NBocPiperazinyIPyrimidine

Sample Name NTK-IV-92-NBocPiperazinyIPyrimidine
Date collected 2015-04-06

Reference CARBON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser



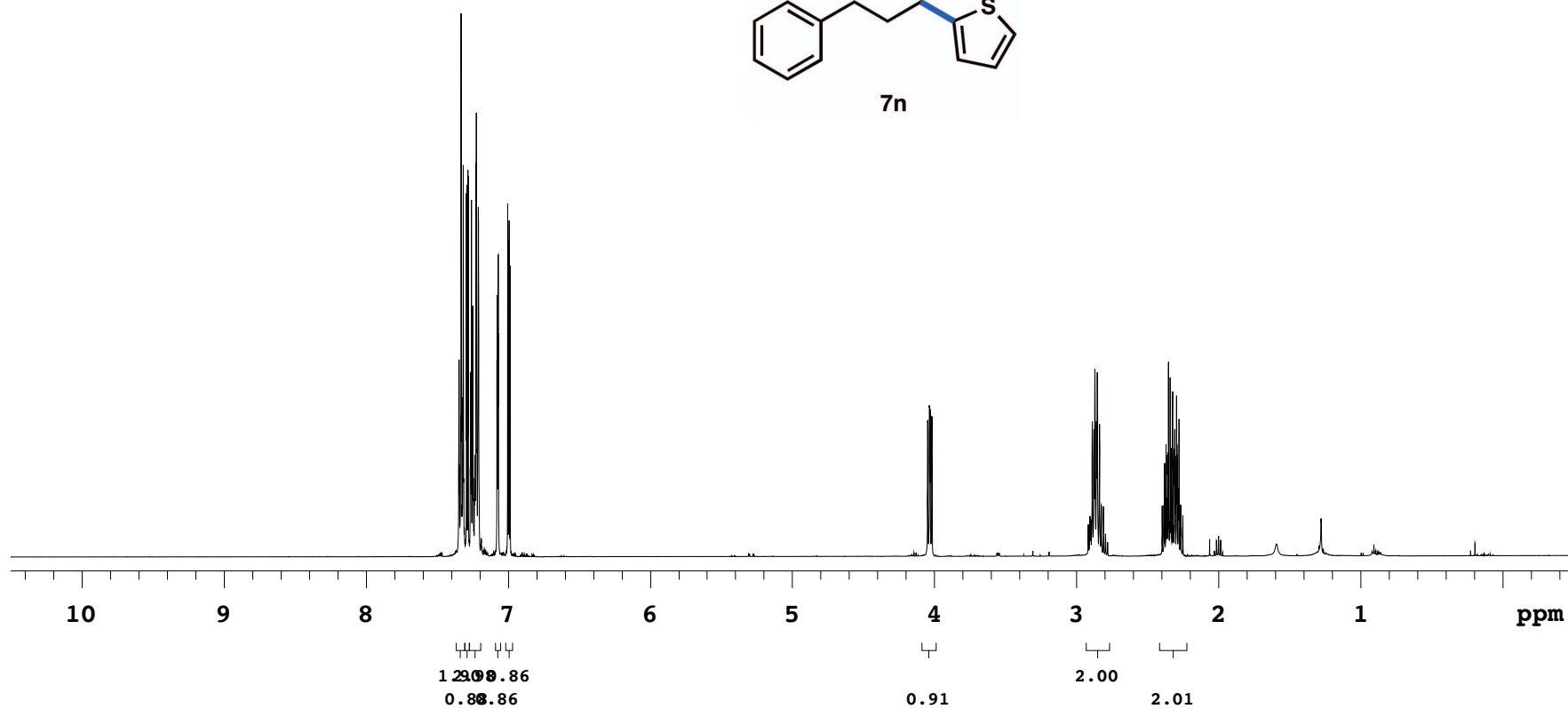
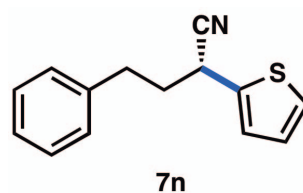
NTK-IV-90-thiophene

Sample Name NTK-IV-90-thiophene
Date collected 2015-04-02

Pulse sequence PROTON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser



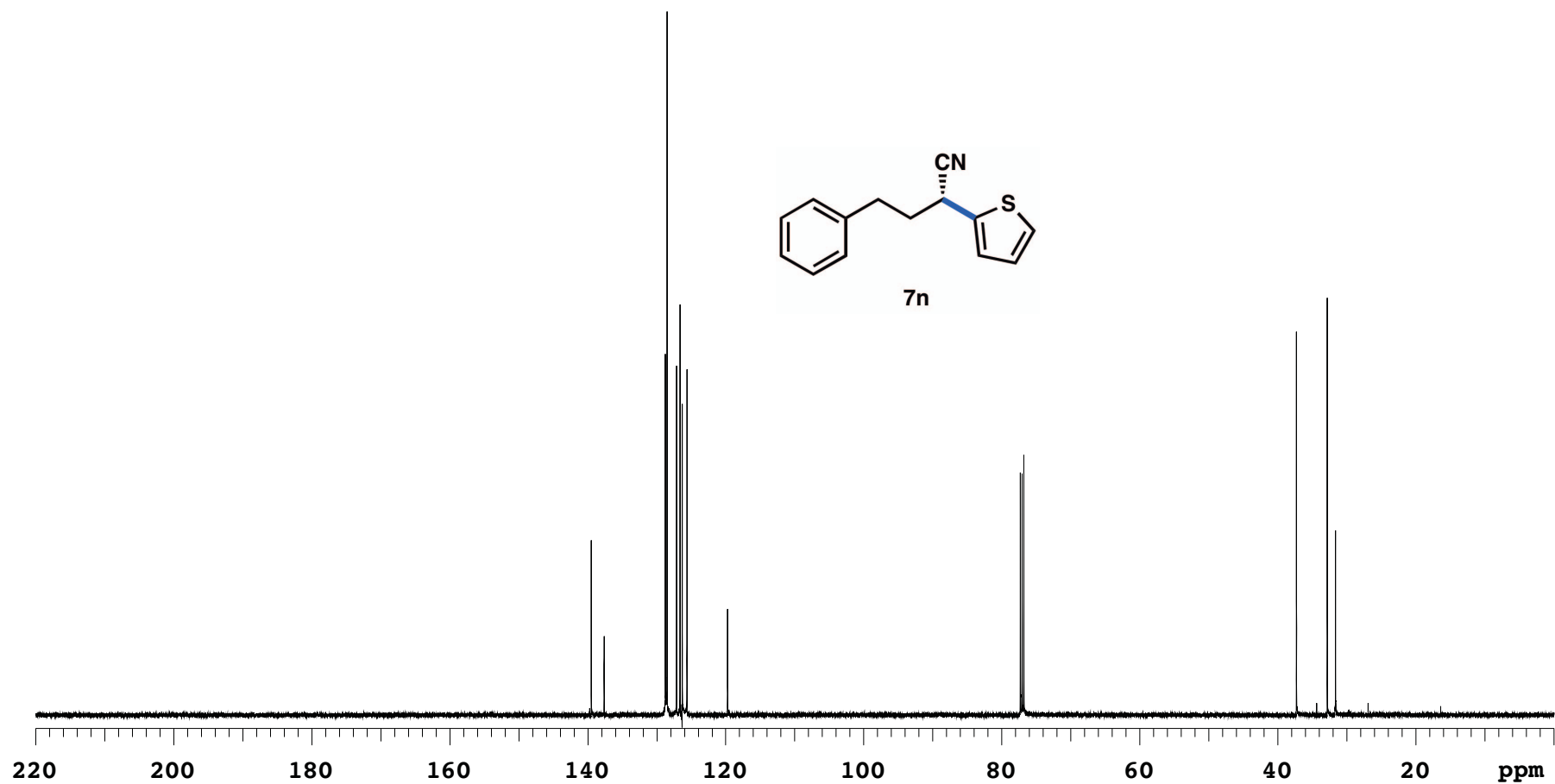
NTK-IV-90-thiophene

Sample Name NTK-IV-90-thiophene
Date collected 2015-04-02

Pulse sequence CARBON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser



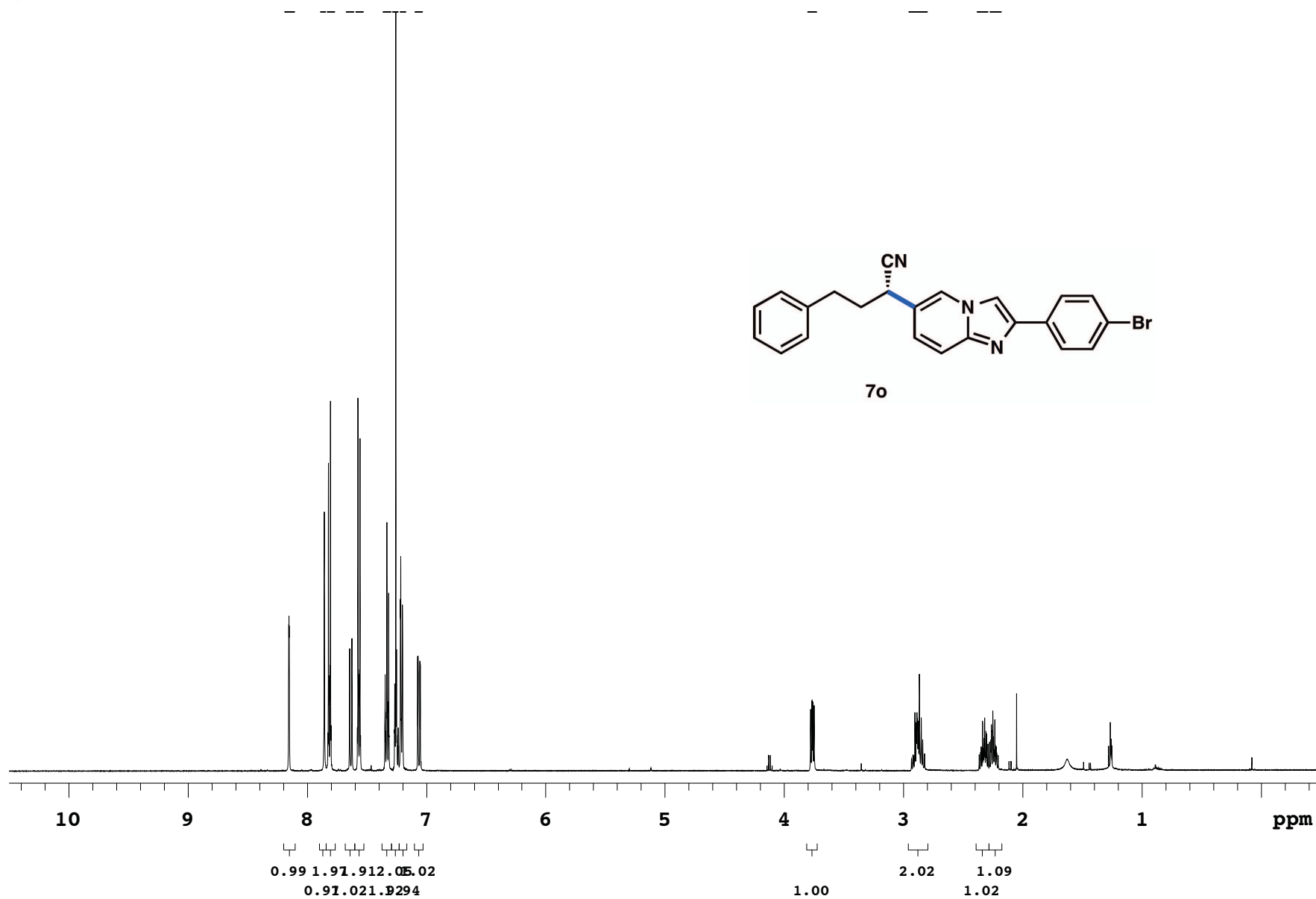
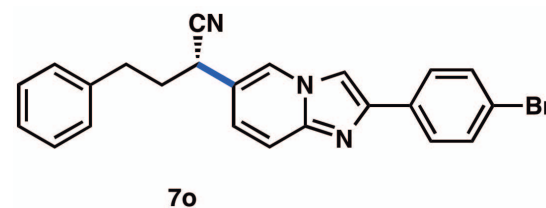
NTK-IV-94-imidprep

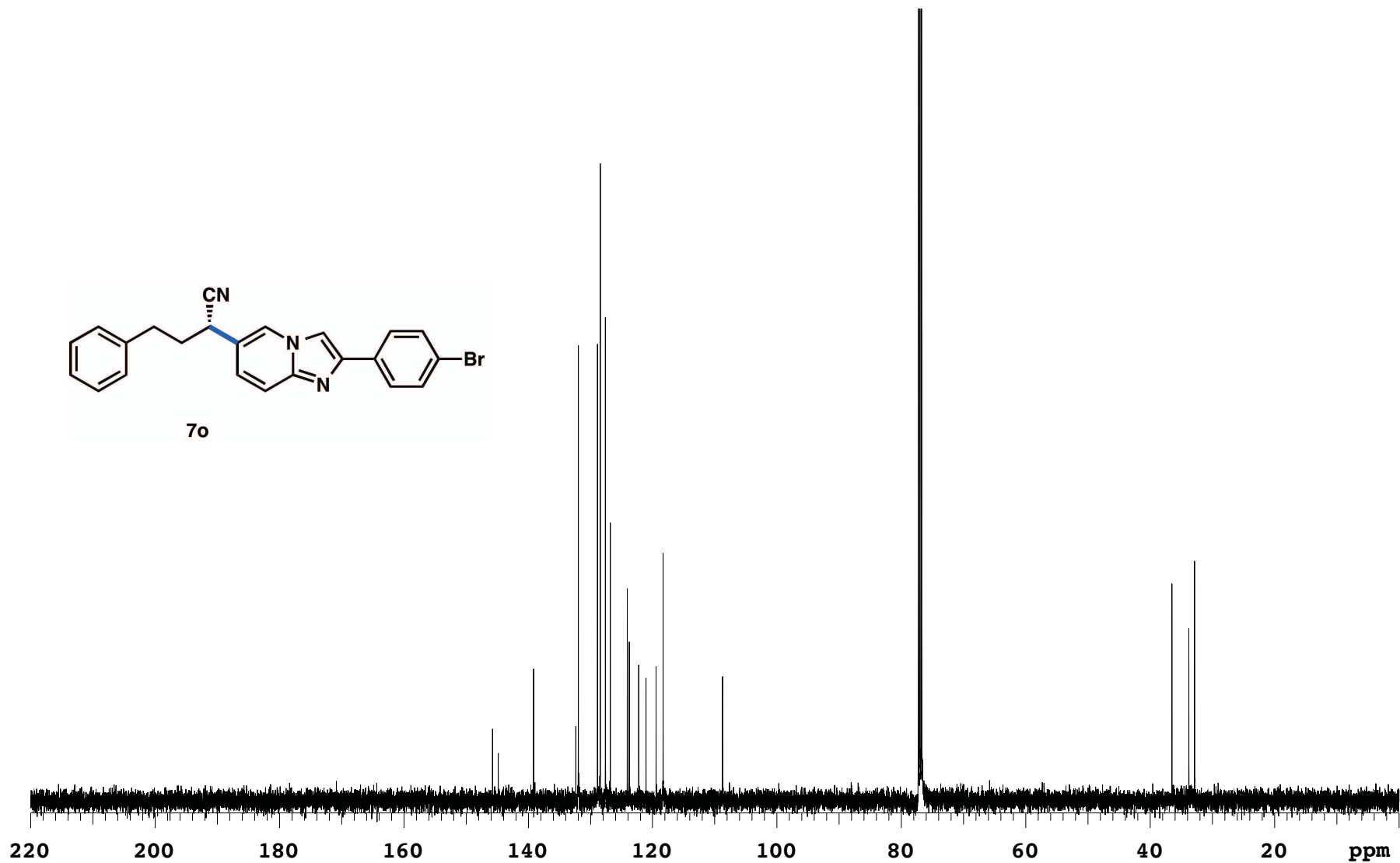
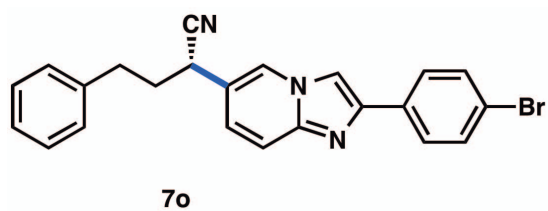
Sample Name NTK-IV-94-imidprep
Date collected 2015-04-16

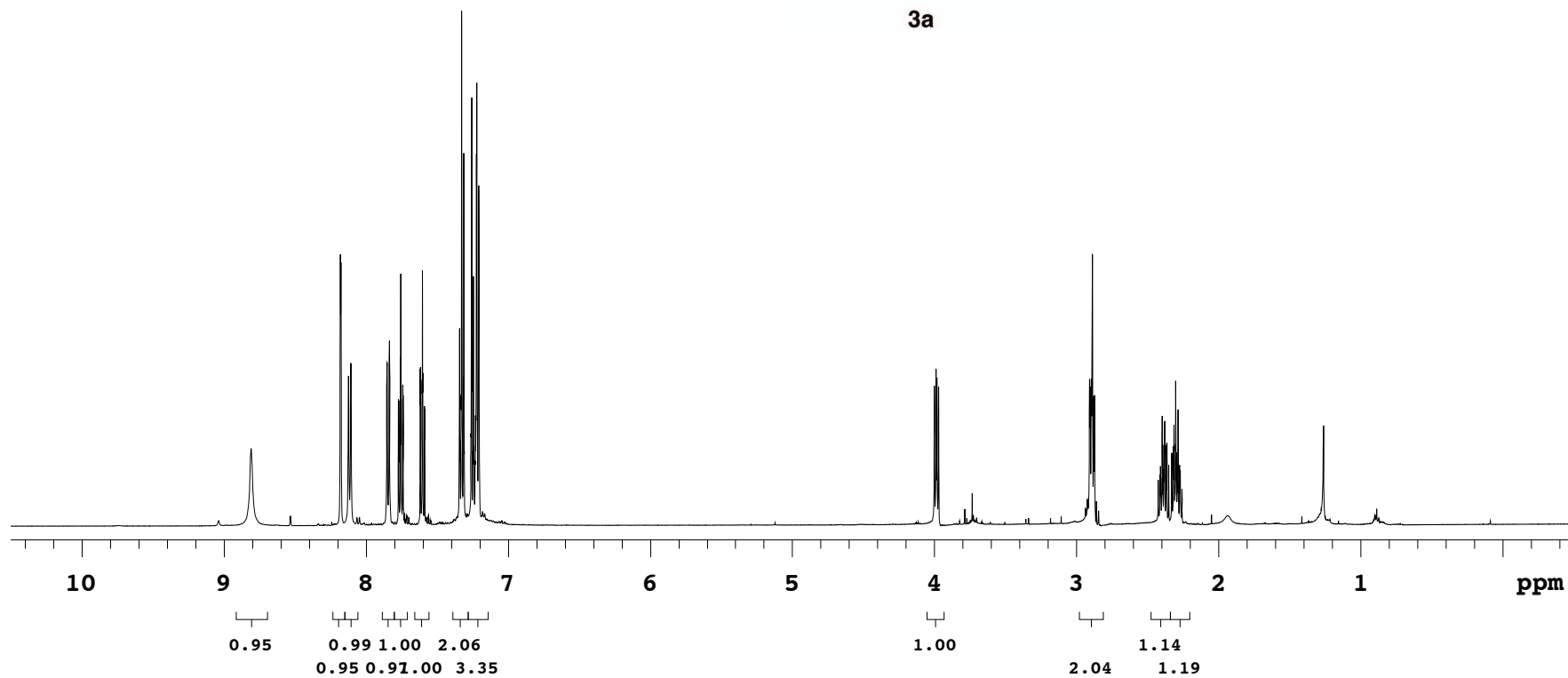
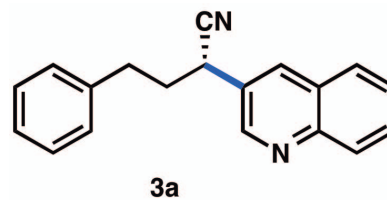
Pulse sequence PROTON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser







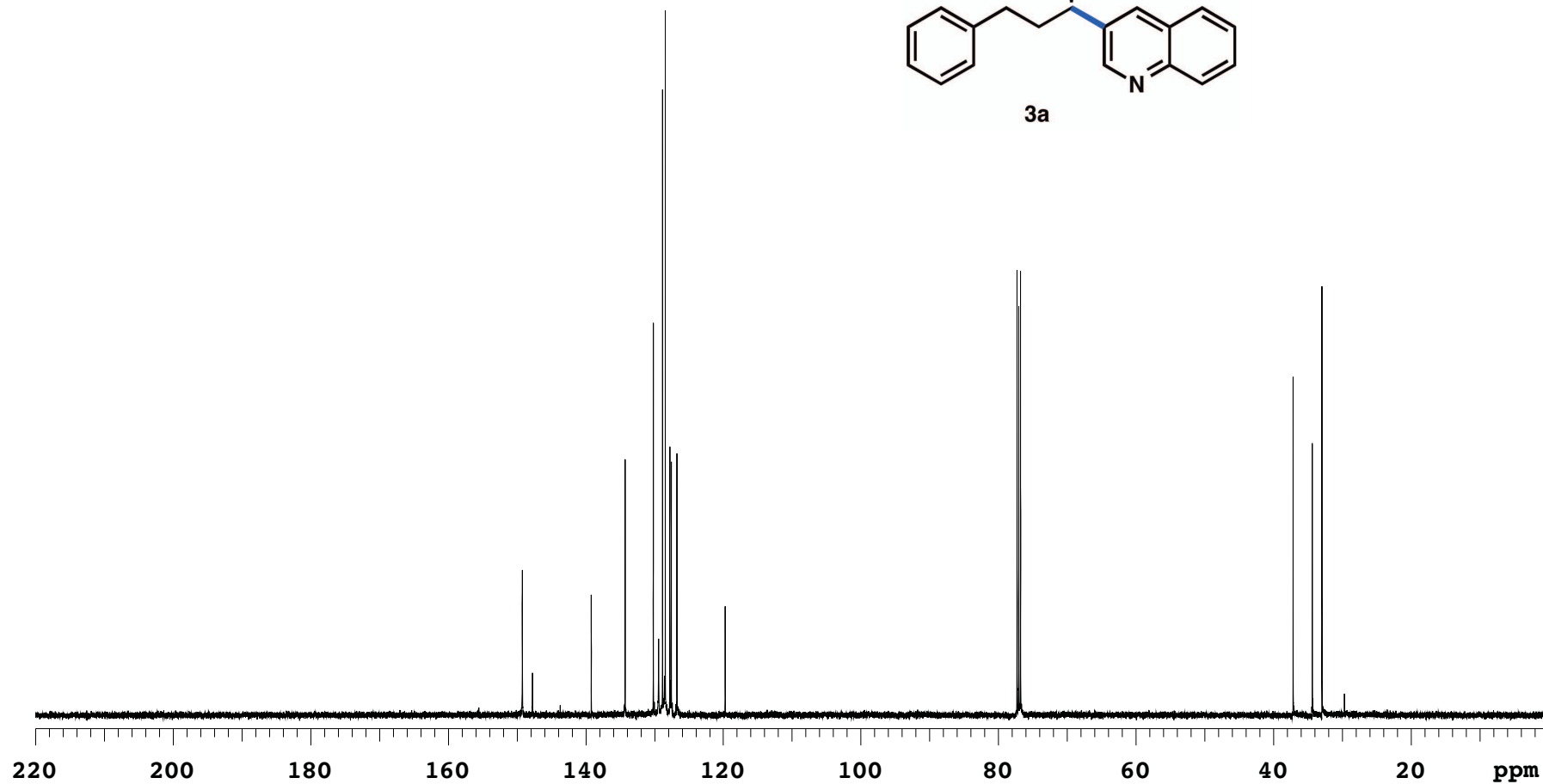
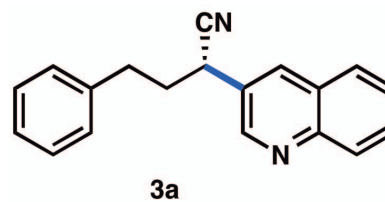
NTK-IV-75-pure

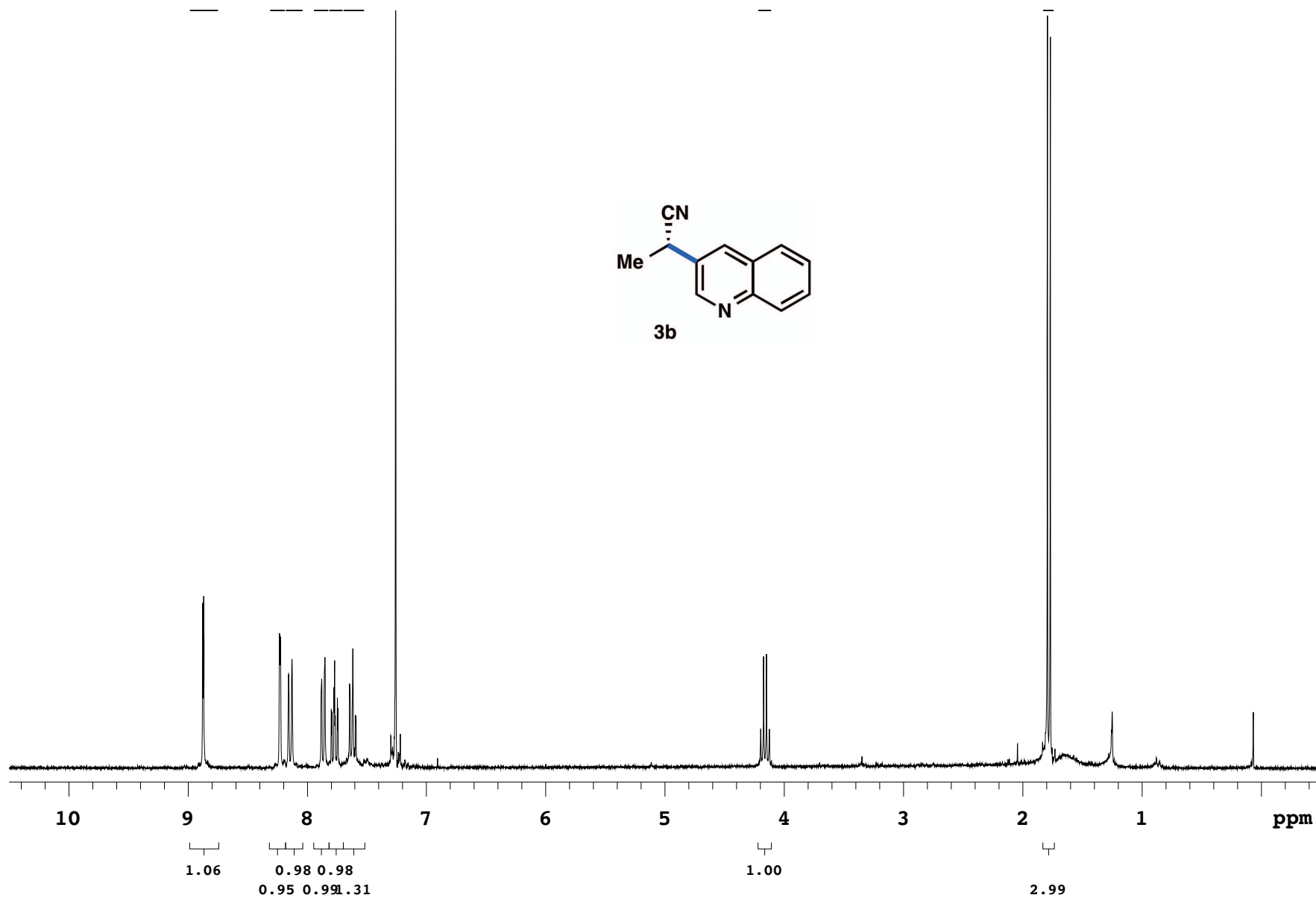
Sample Name NTK-IV-75-pure
Date collected 2015-03-03

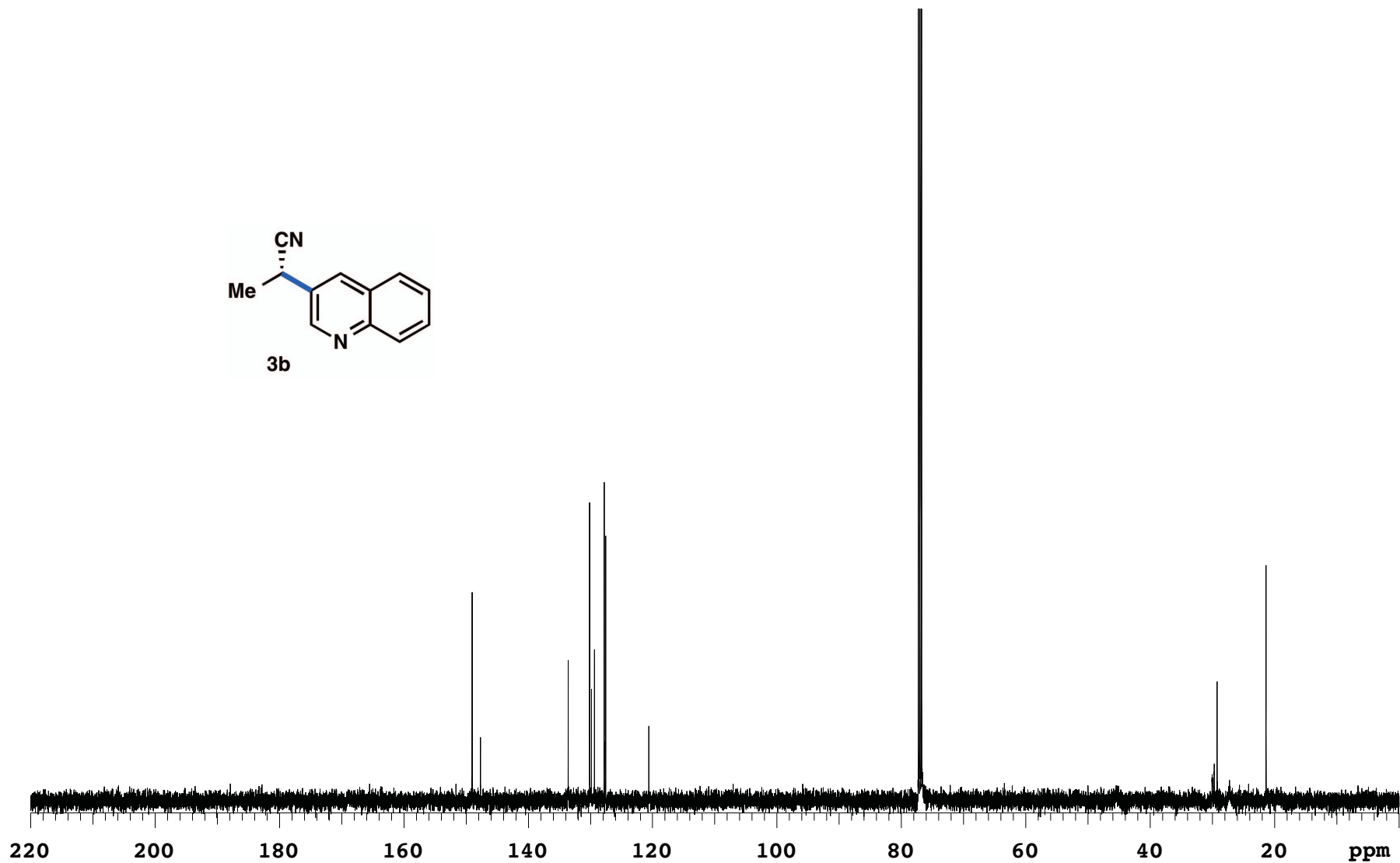
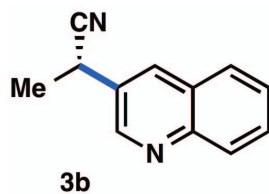
Pulse sequence CARBON
Solvent cdcl3

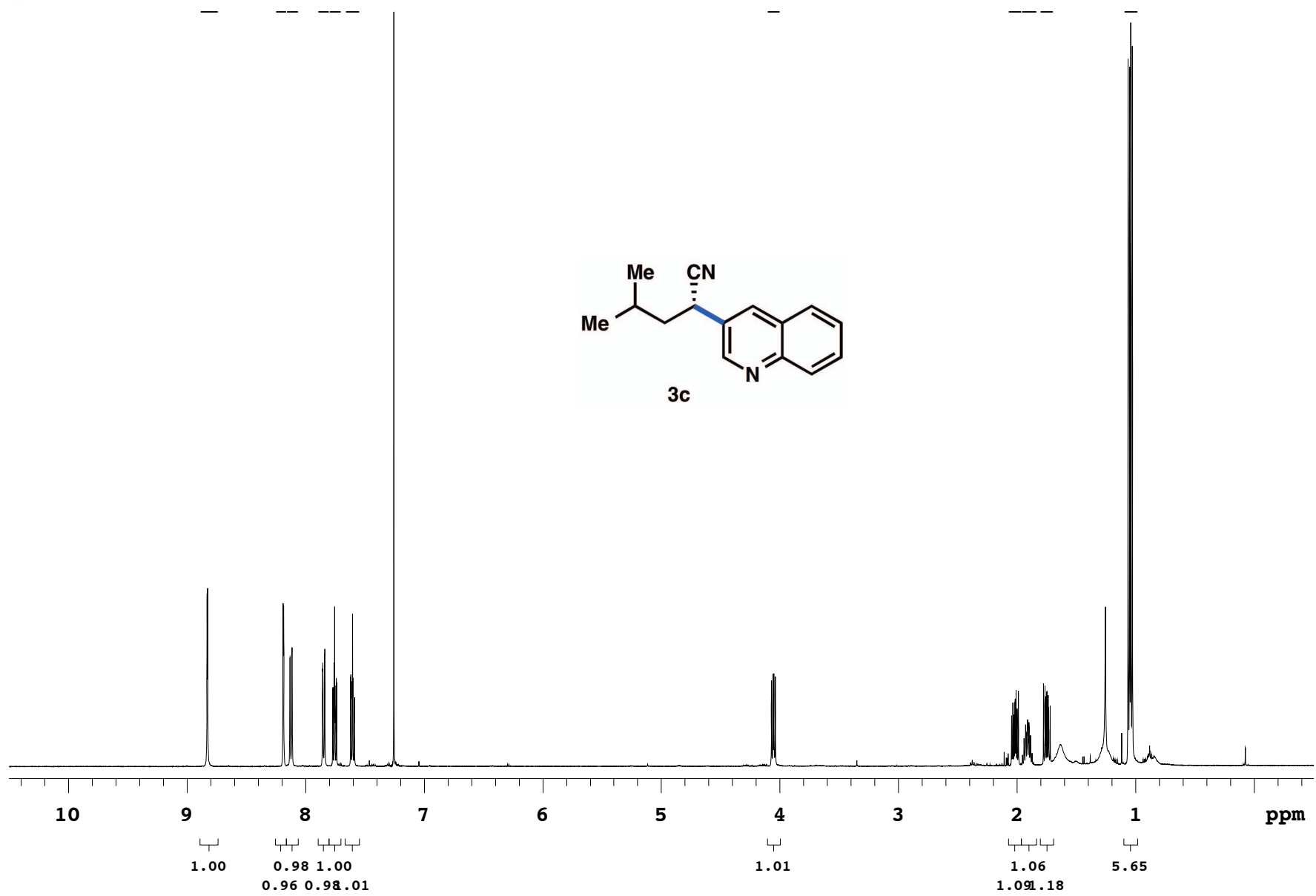
Temperature 25
Spectrometer -vnmrs400

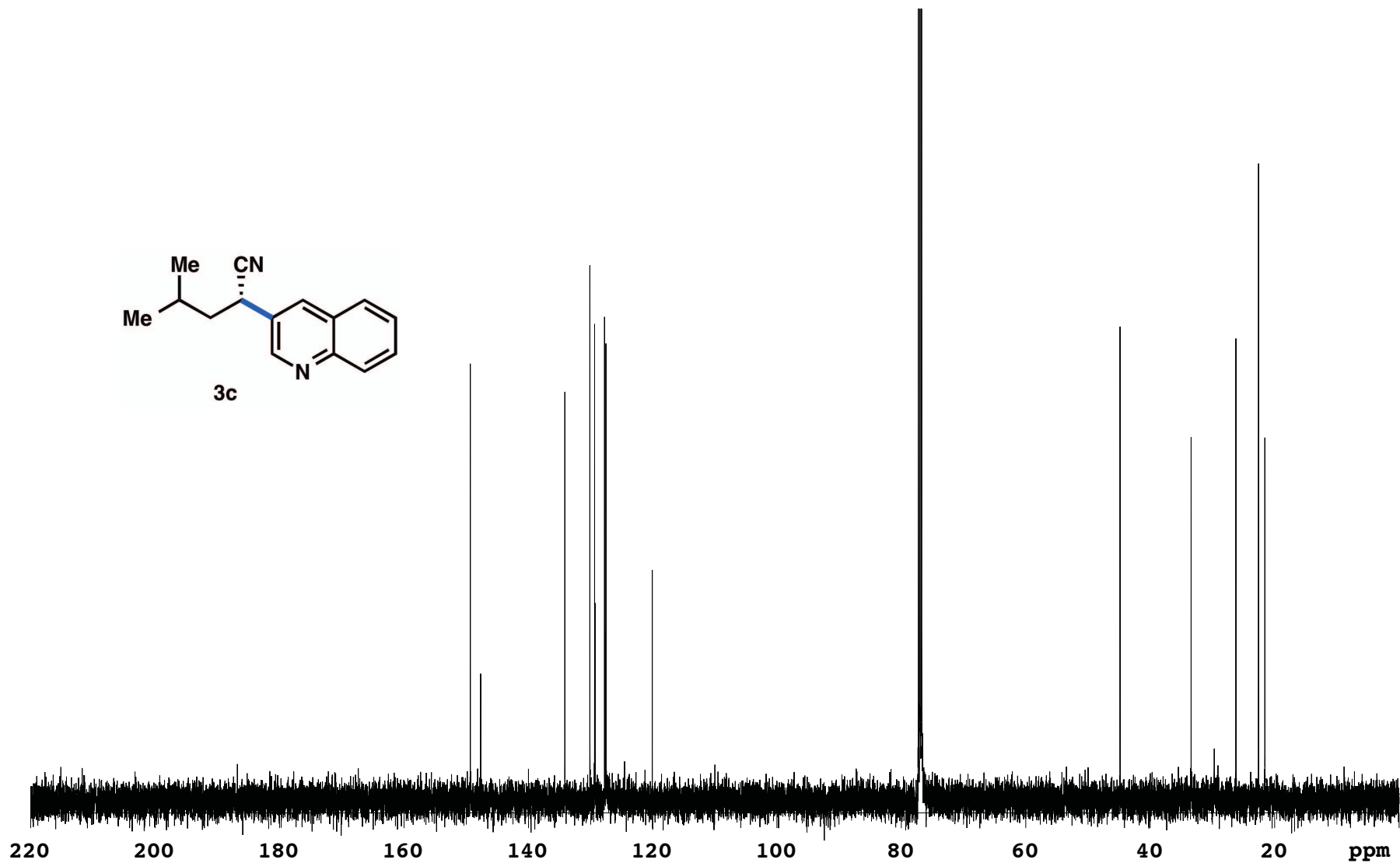
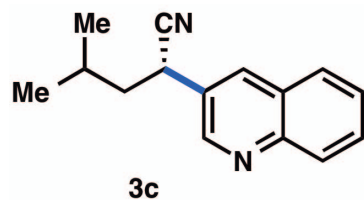
Study owner nkadunce
Operator autouser

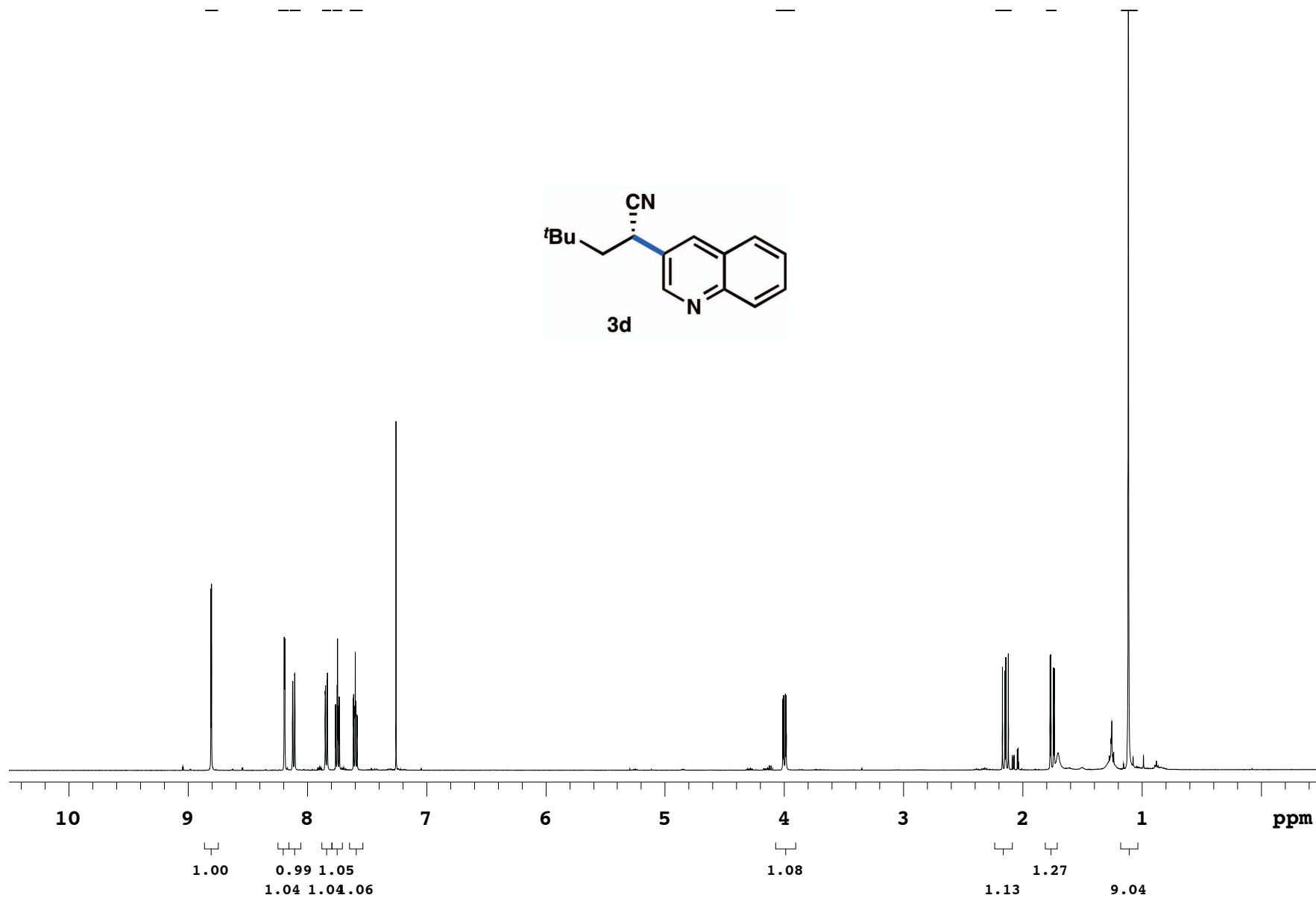
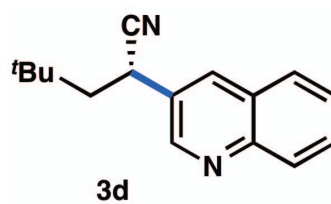


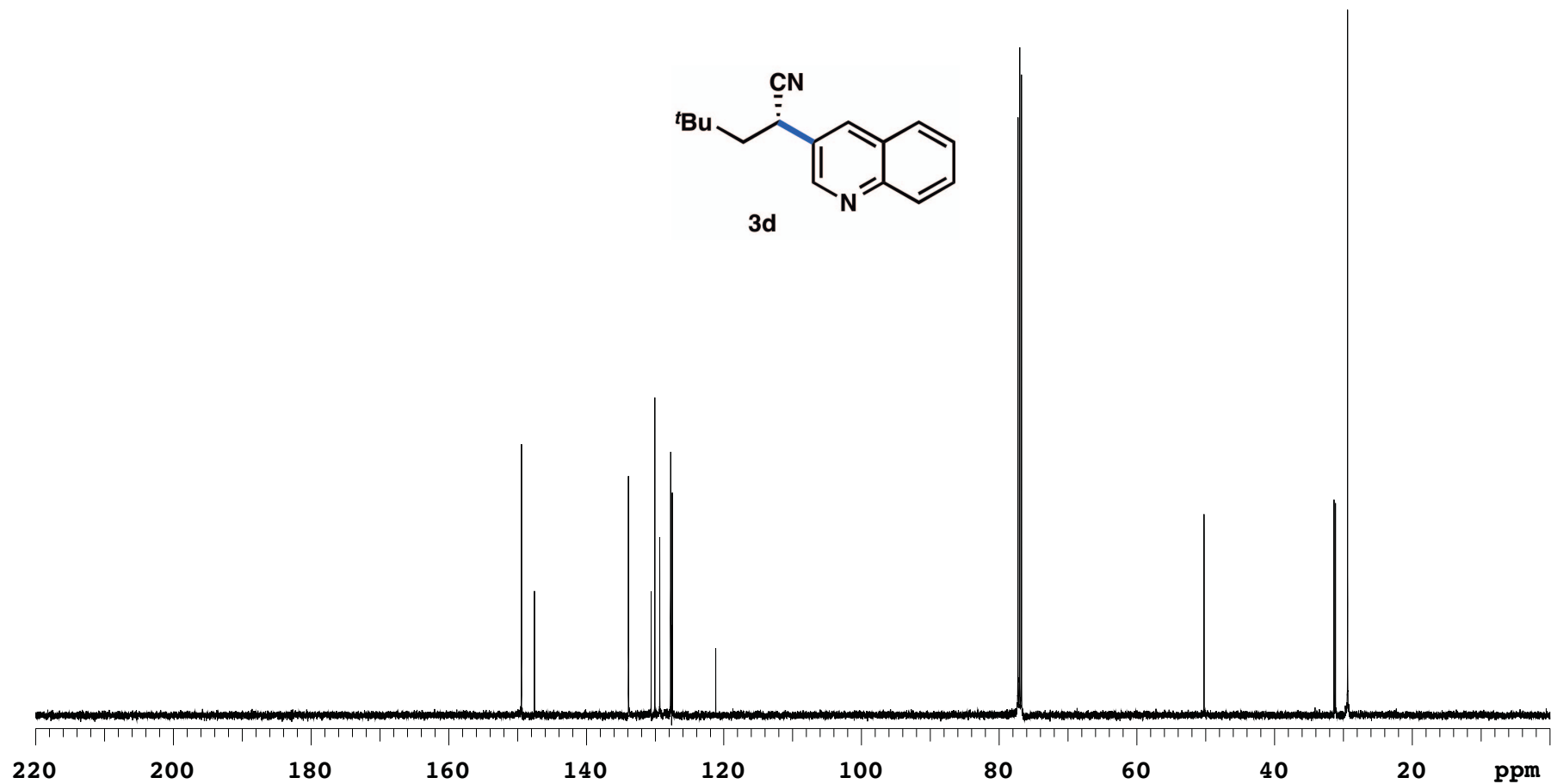
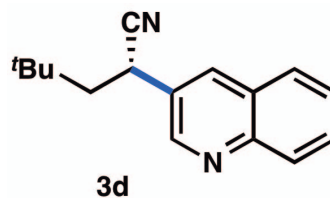


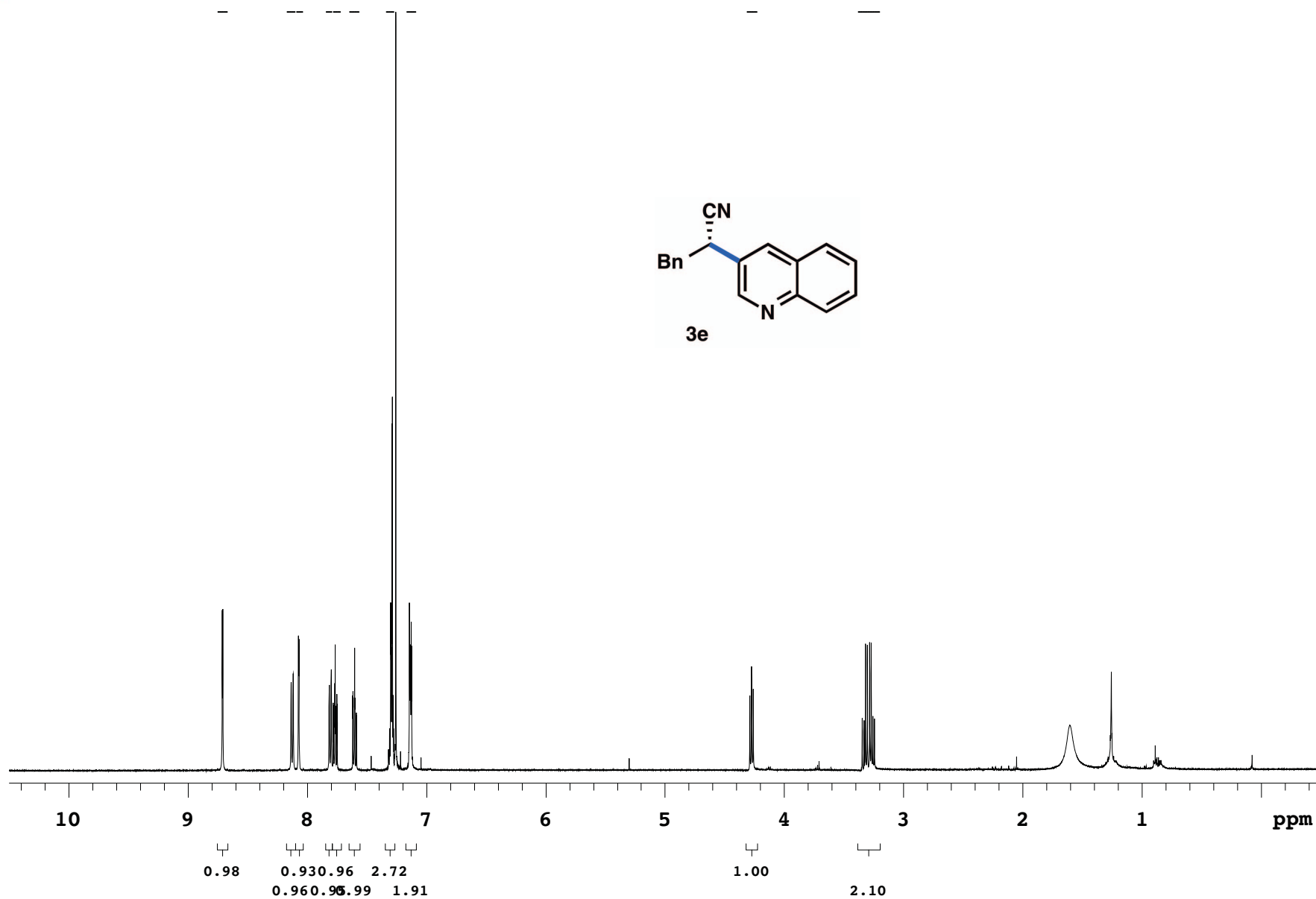
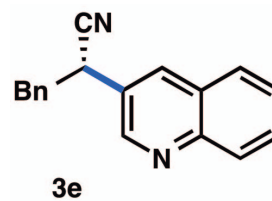


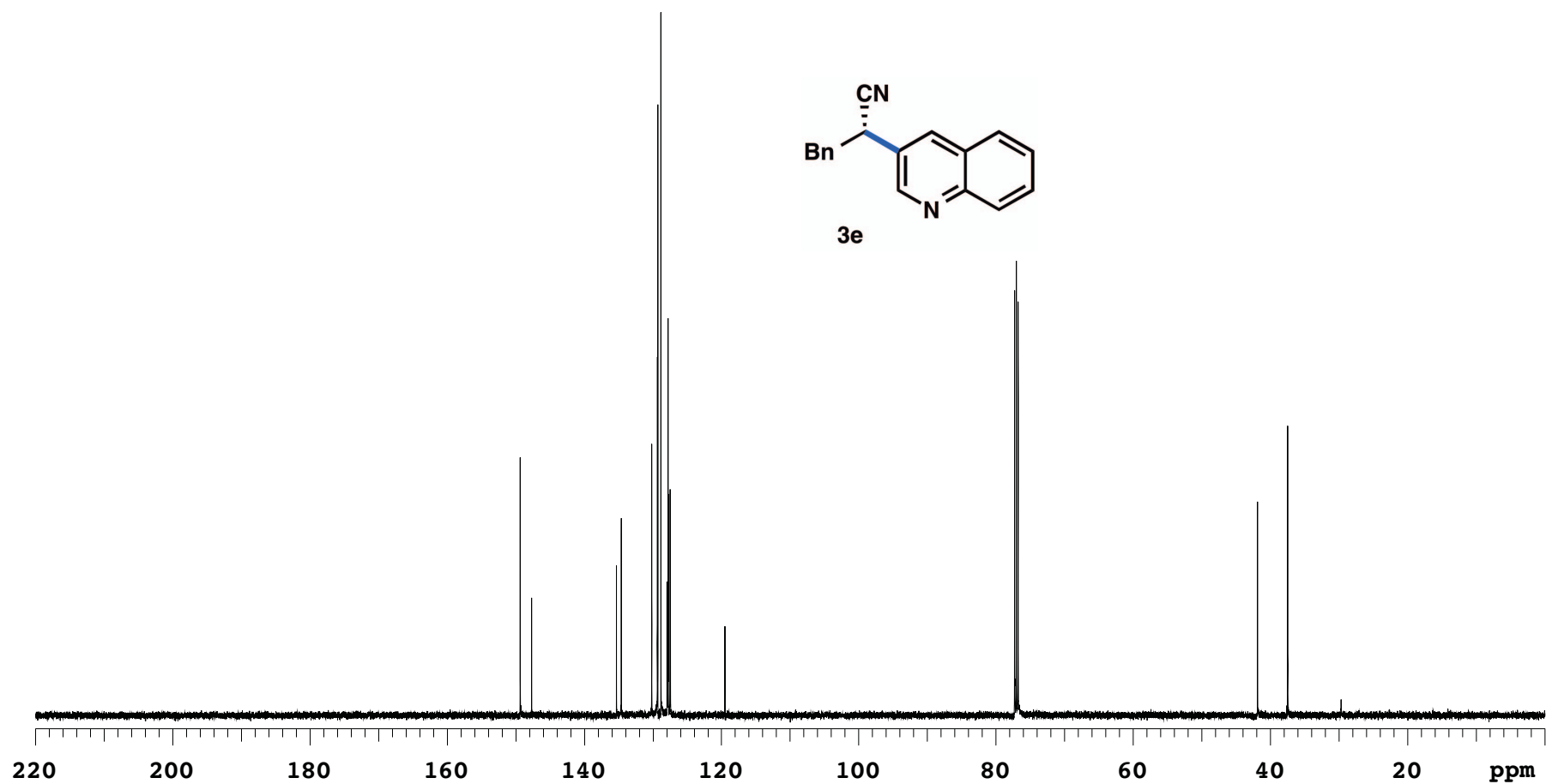


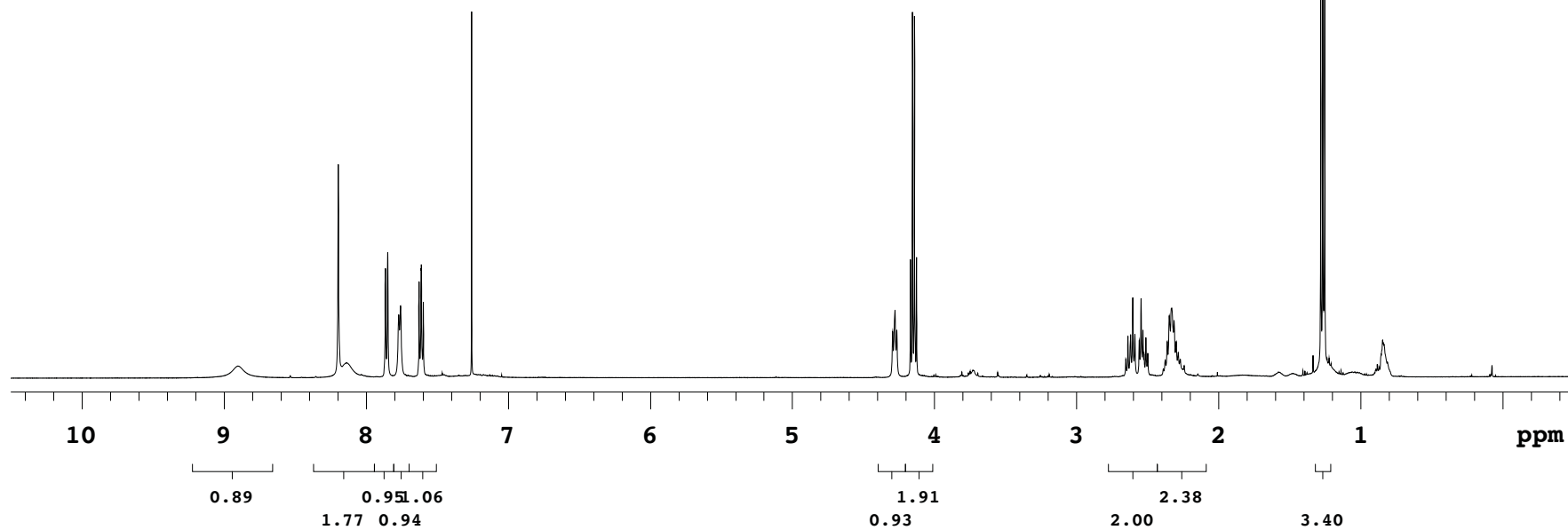
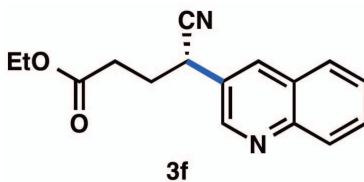


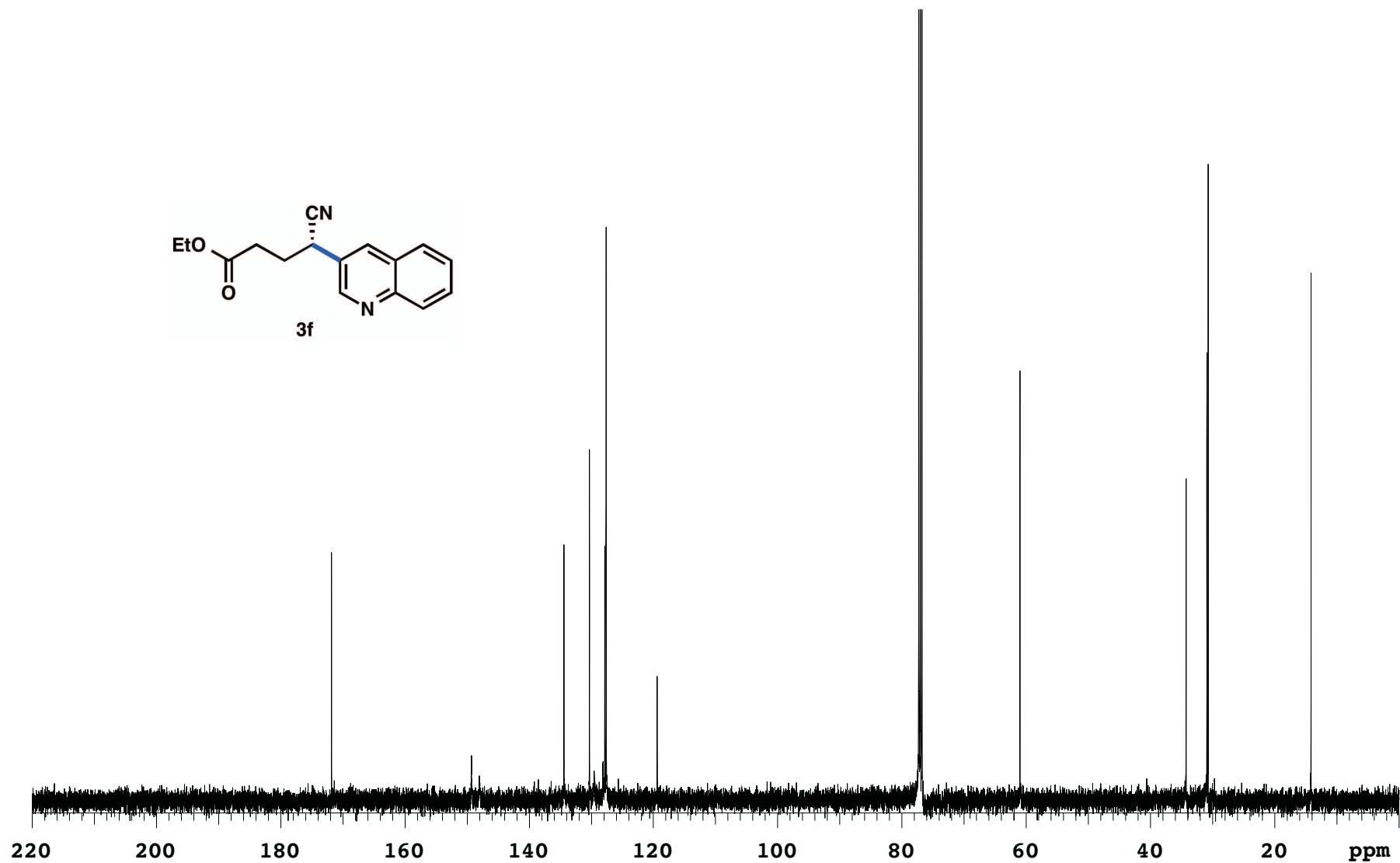
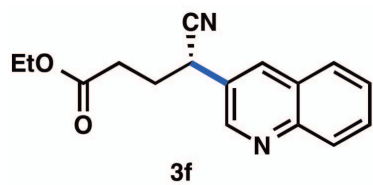


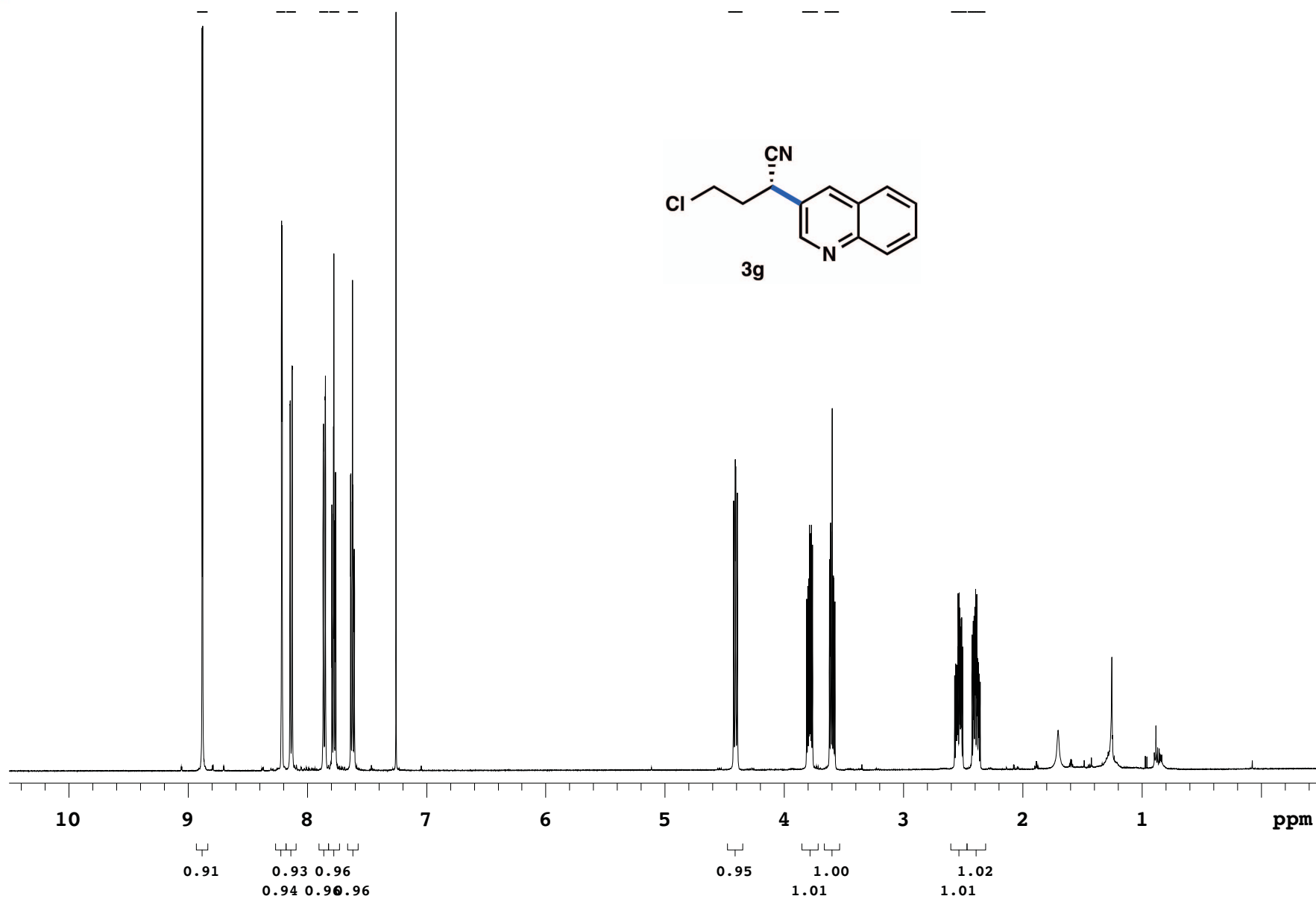
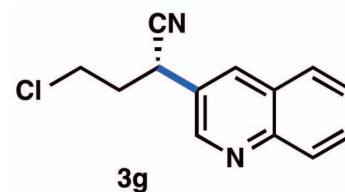


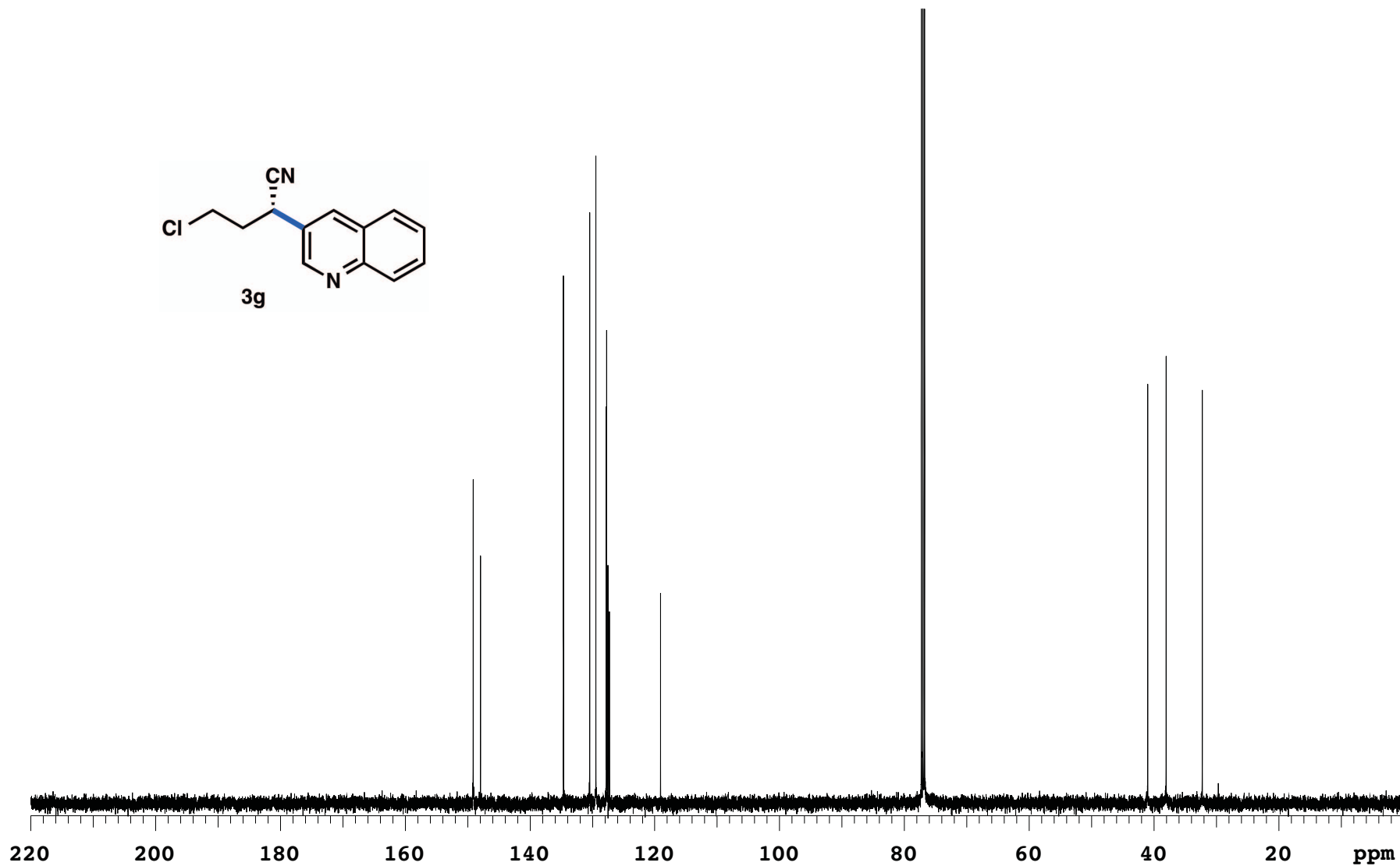
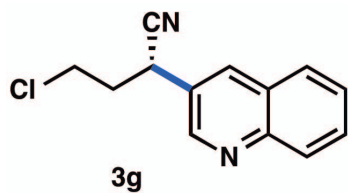


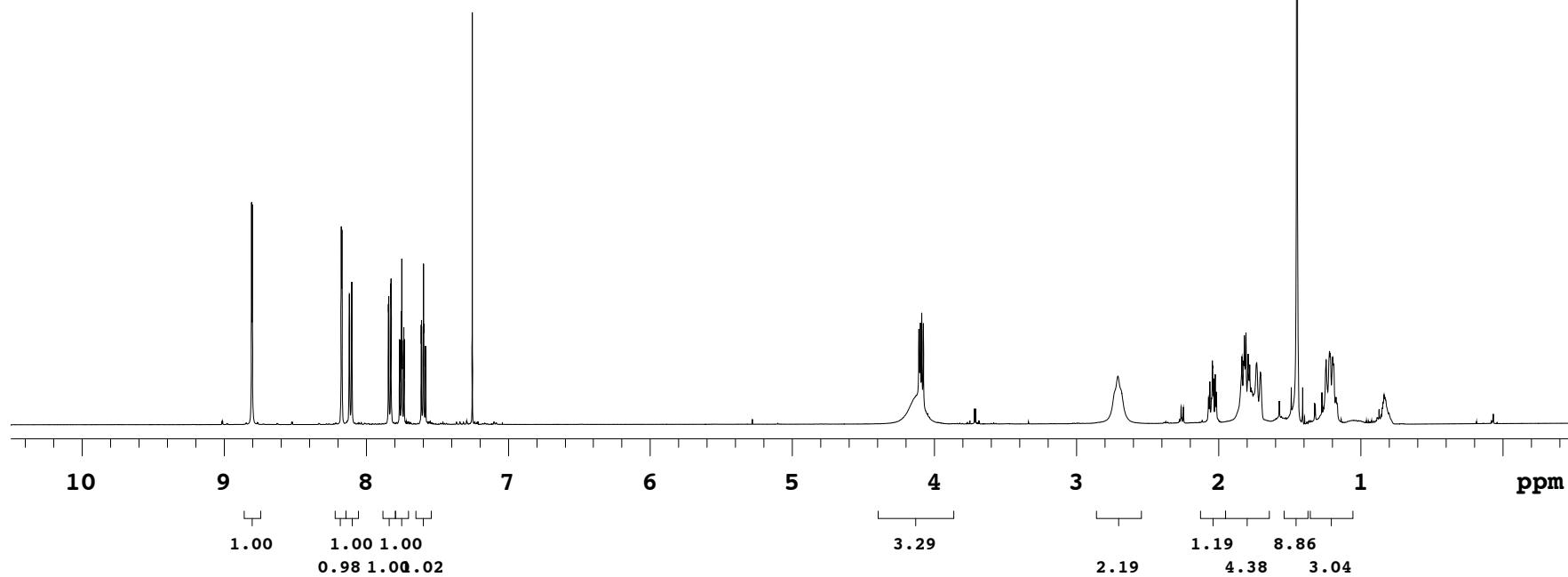
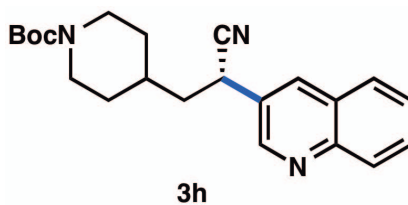


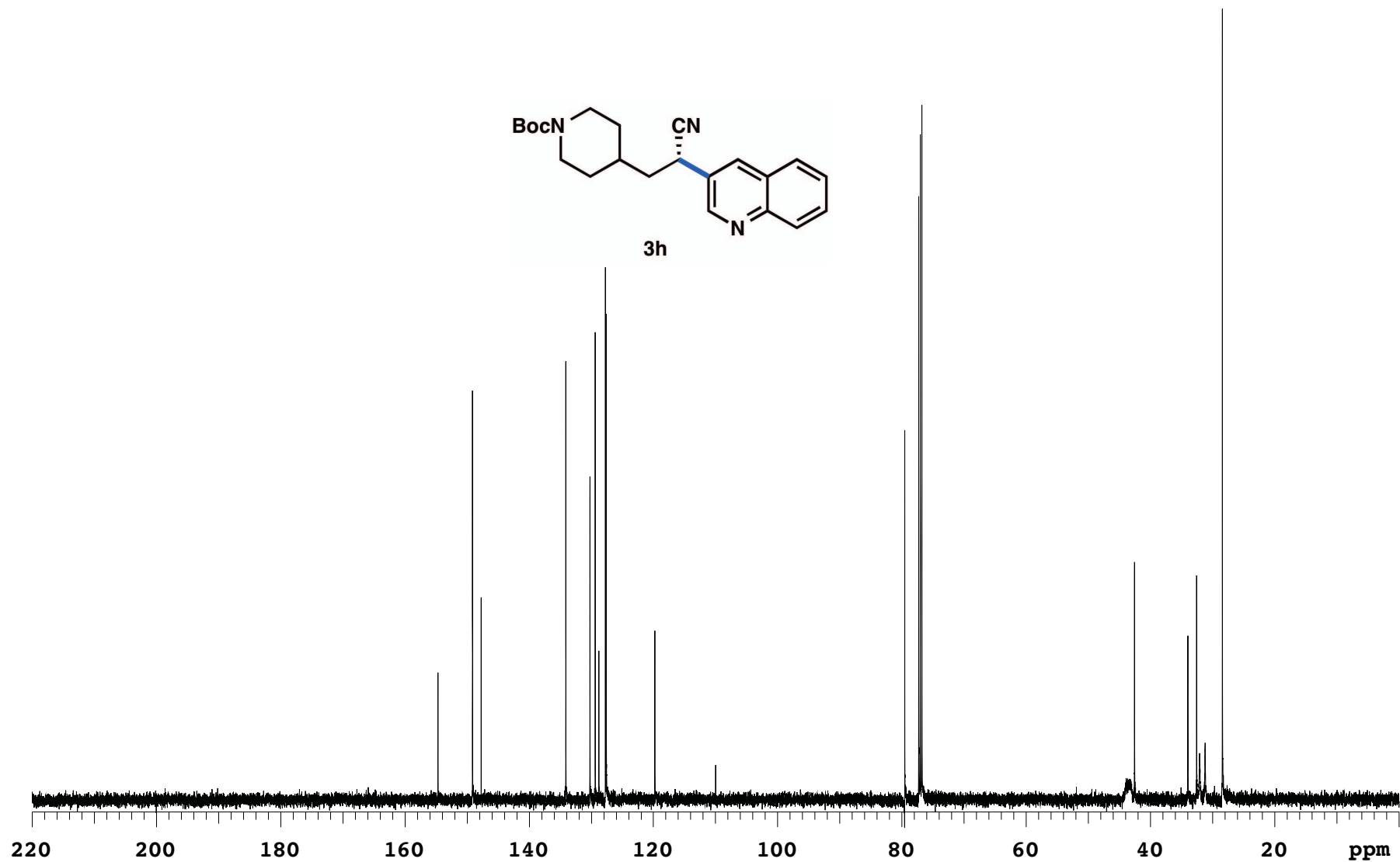


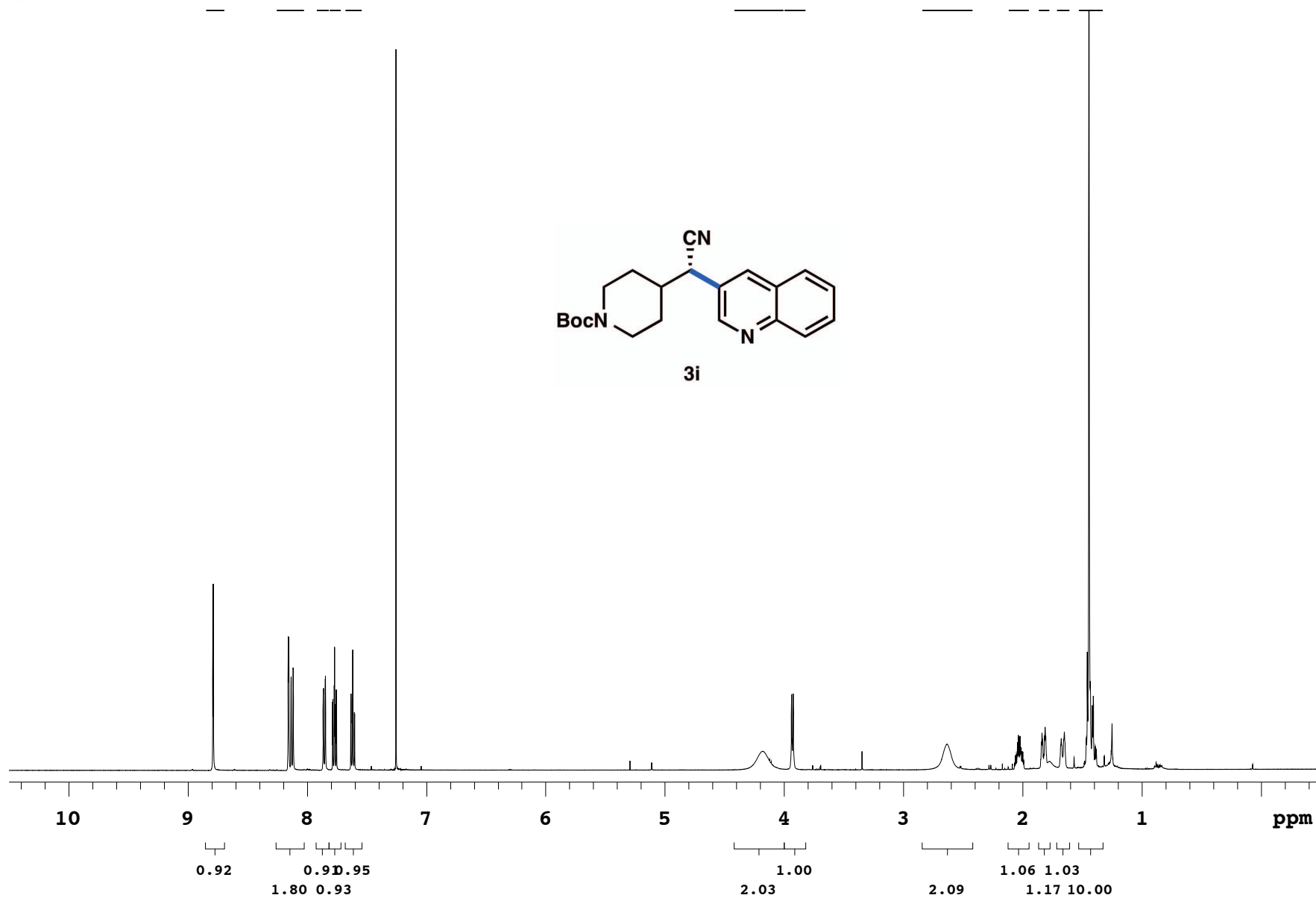
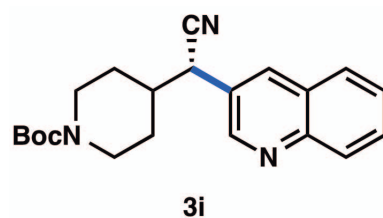












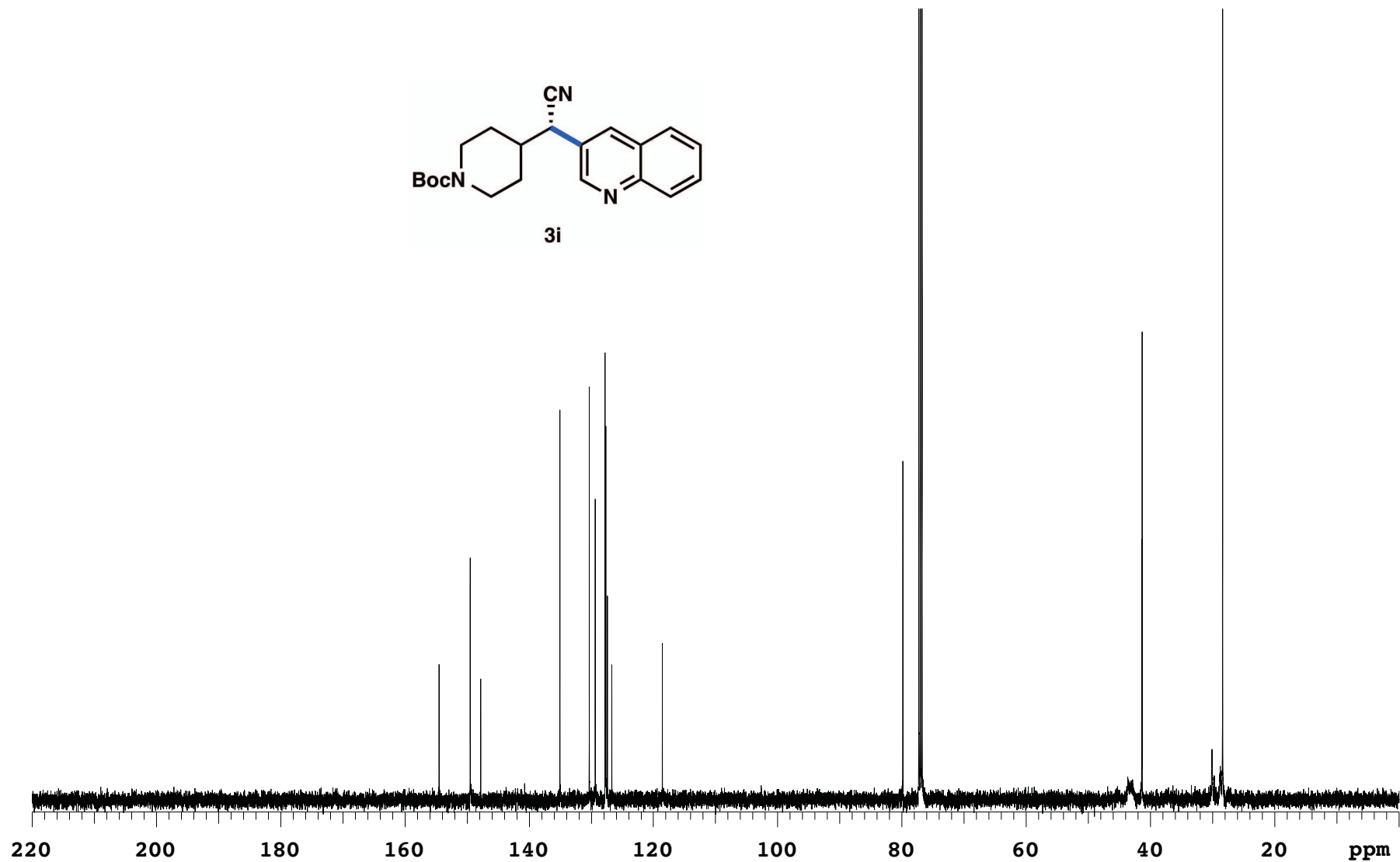
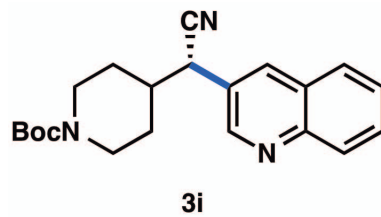
NTK-IV-99-BocPip

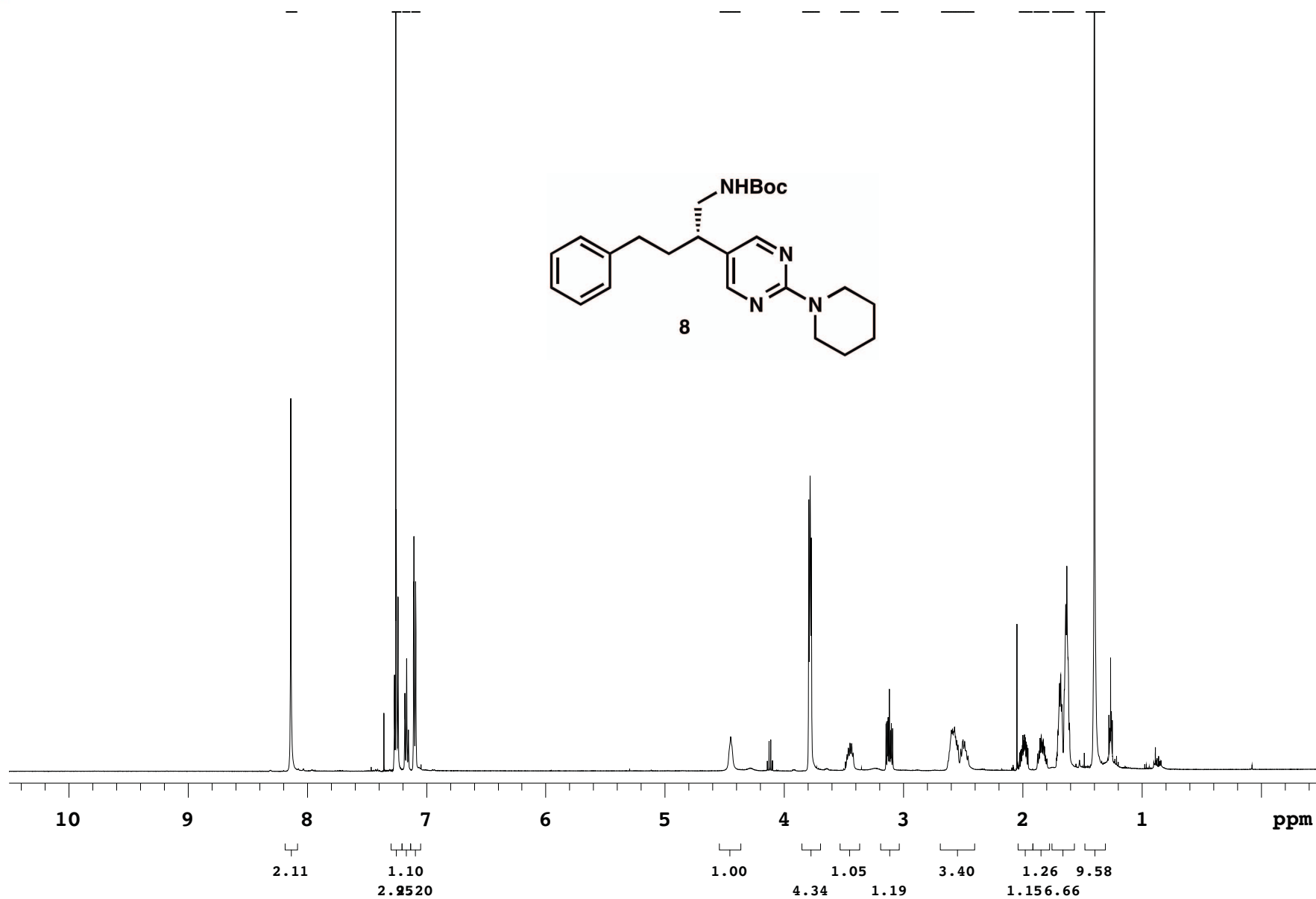
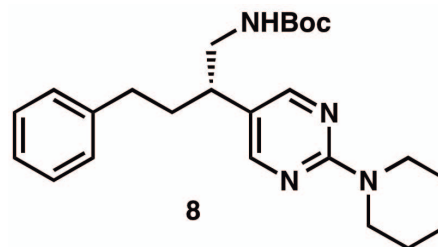
Sample Name NTK-IV-99-BocPip
Date collected 2015-04-15

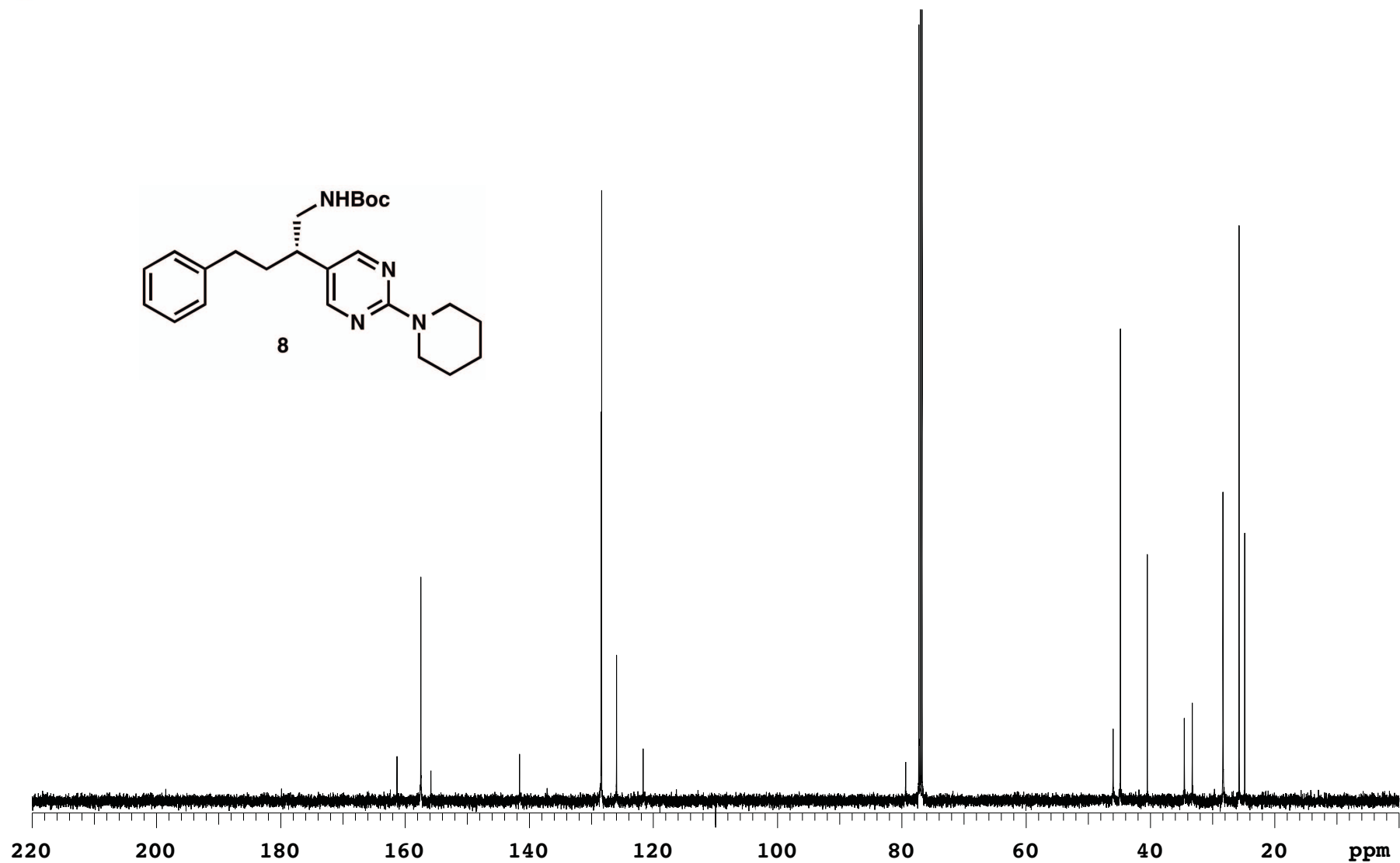
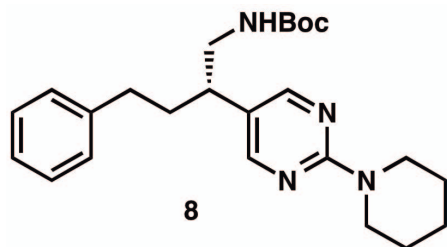
Pulse sequence CARBON
Solvent cdcl3

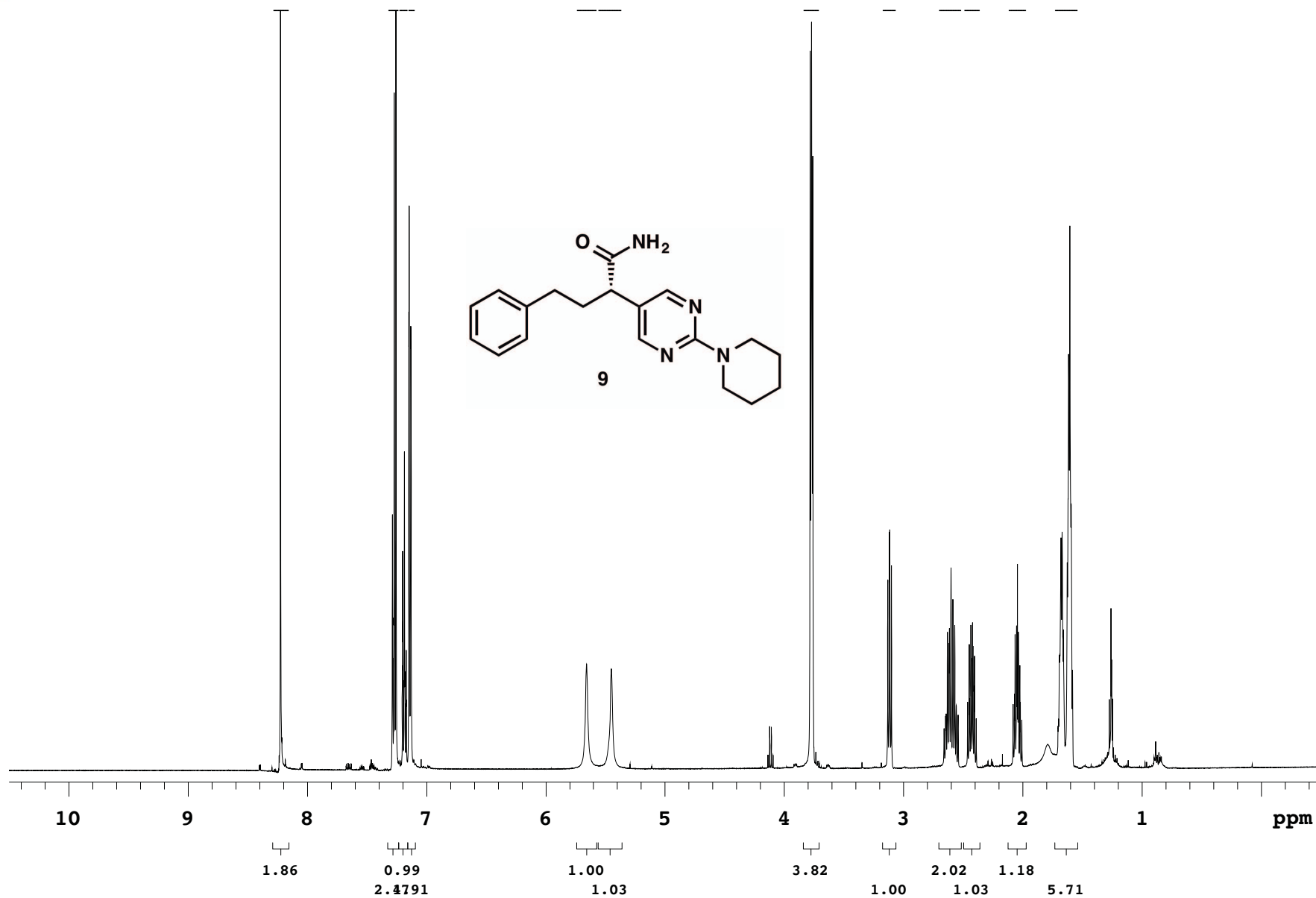
Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser









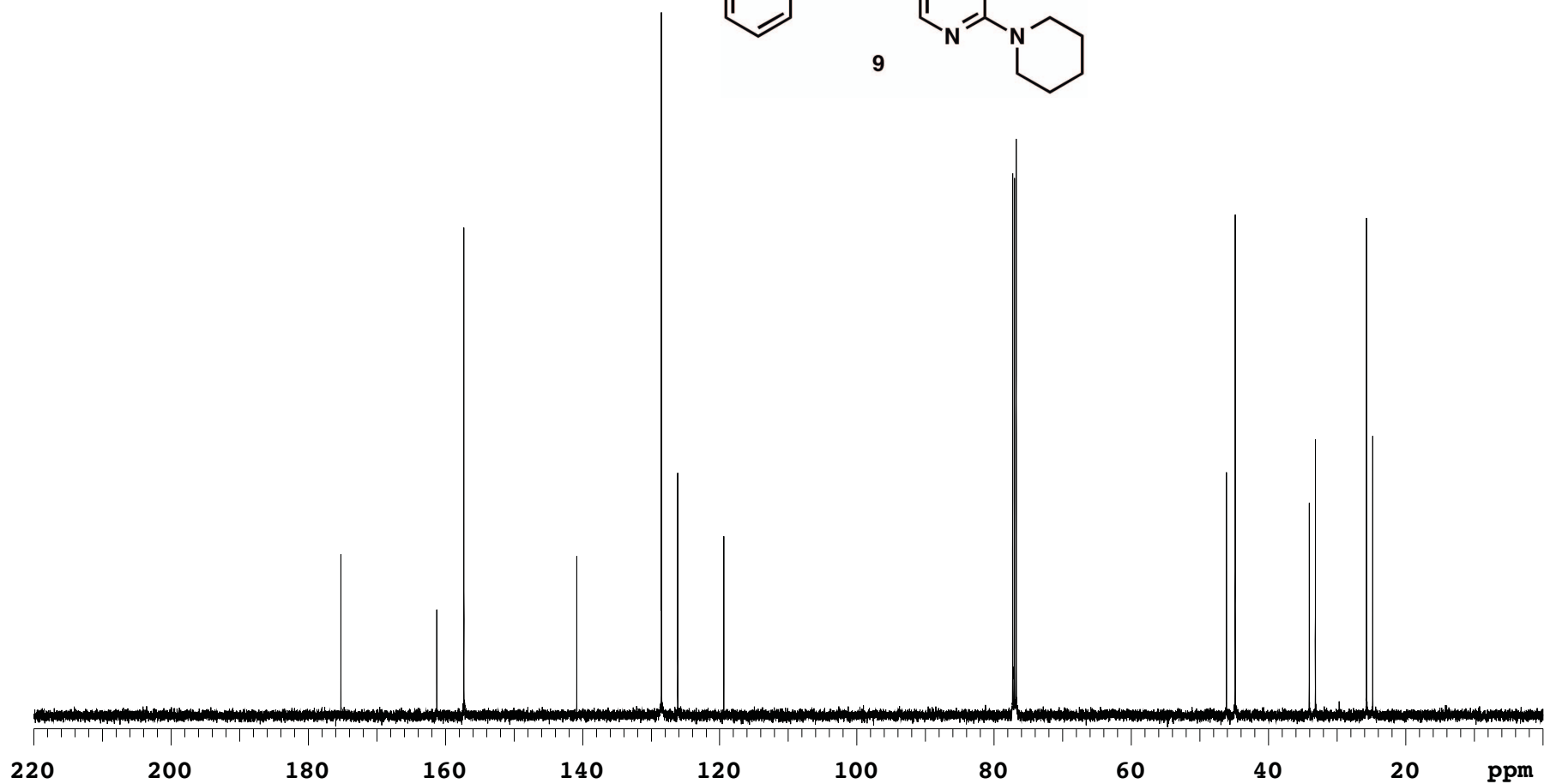
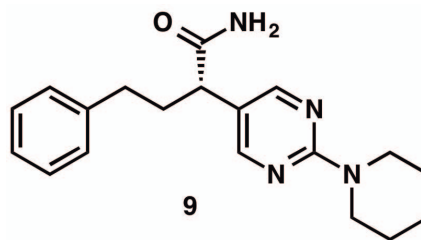
NTK-IV-CONH2-pure

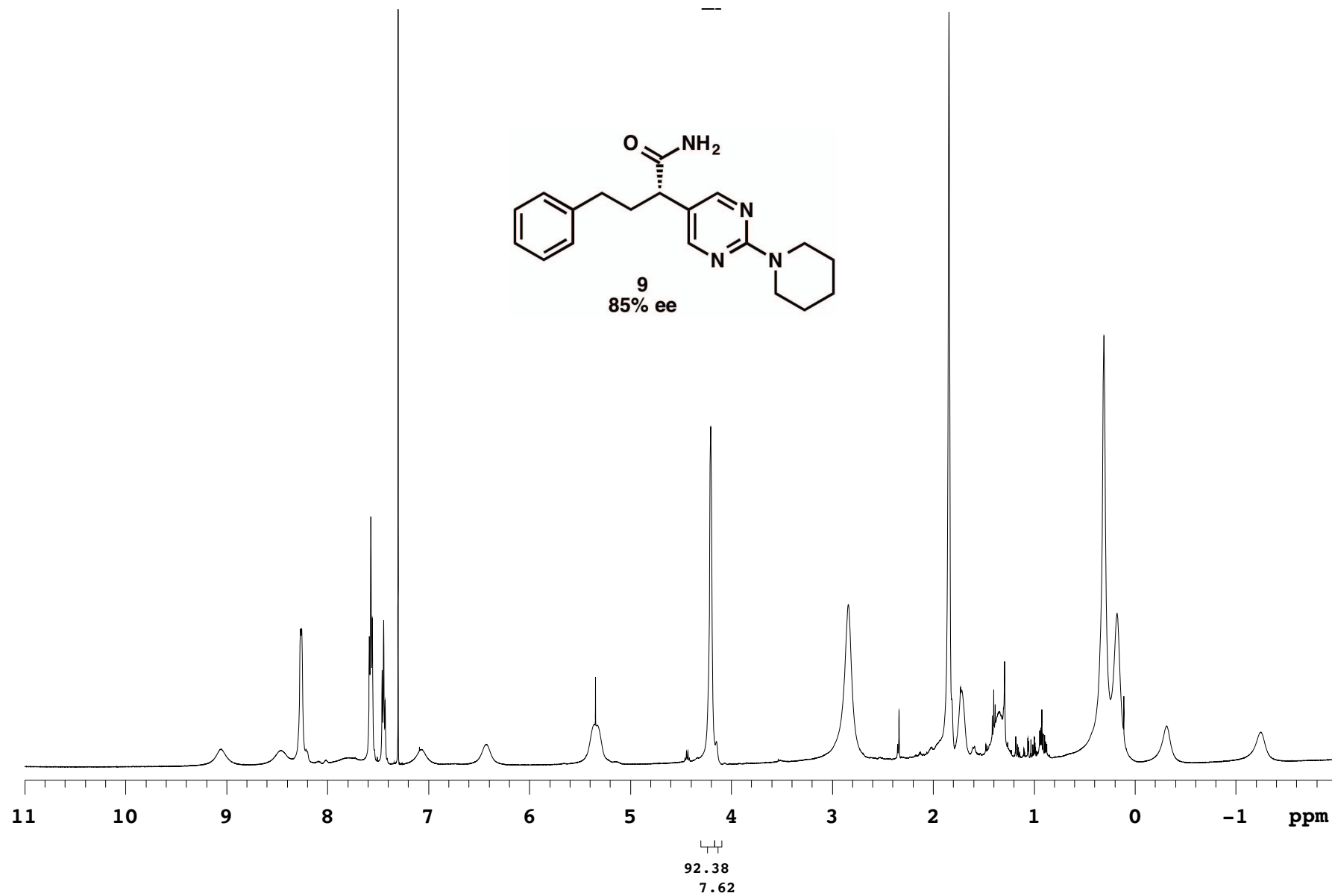
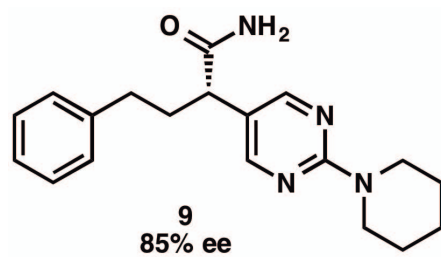
Sample Name NTK-IV-CONH2-pure
Date collected 2015-05-19

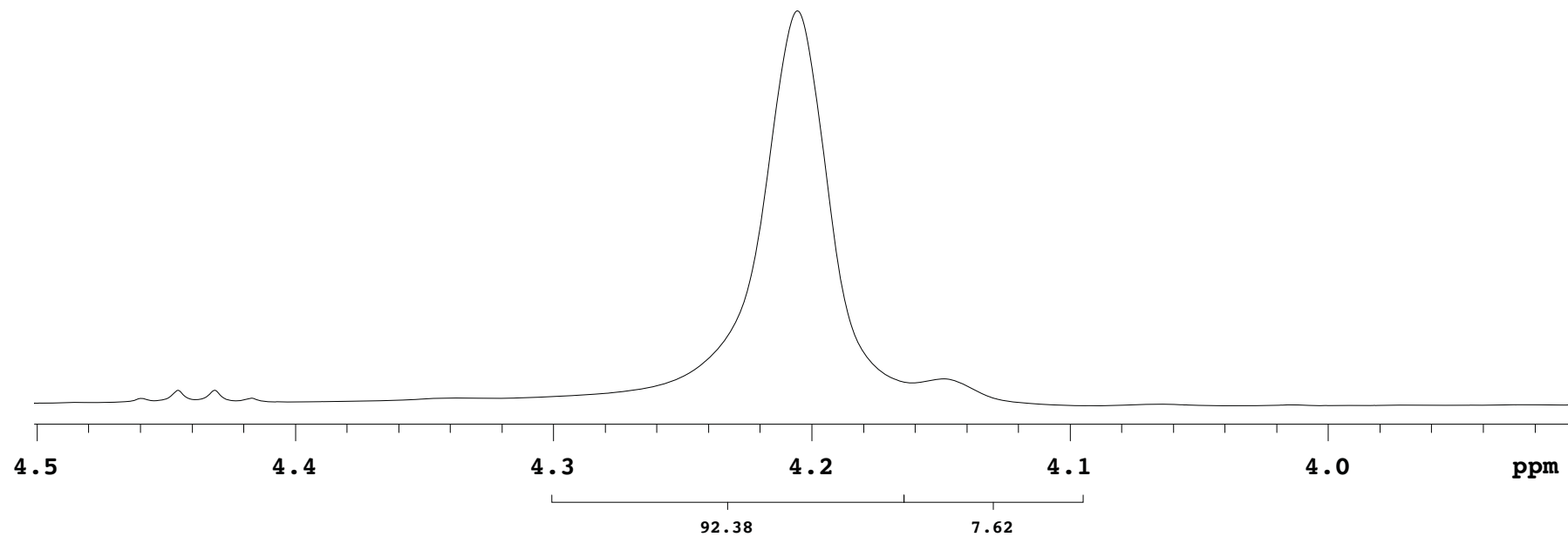
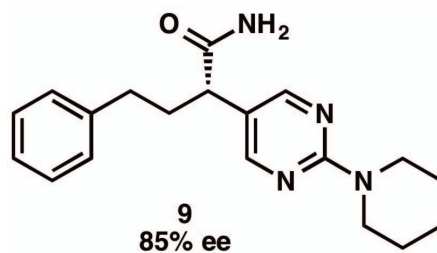
Pulse sequence CARBON
Solvent cdcl3

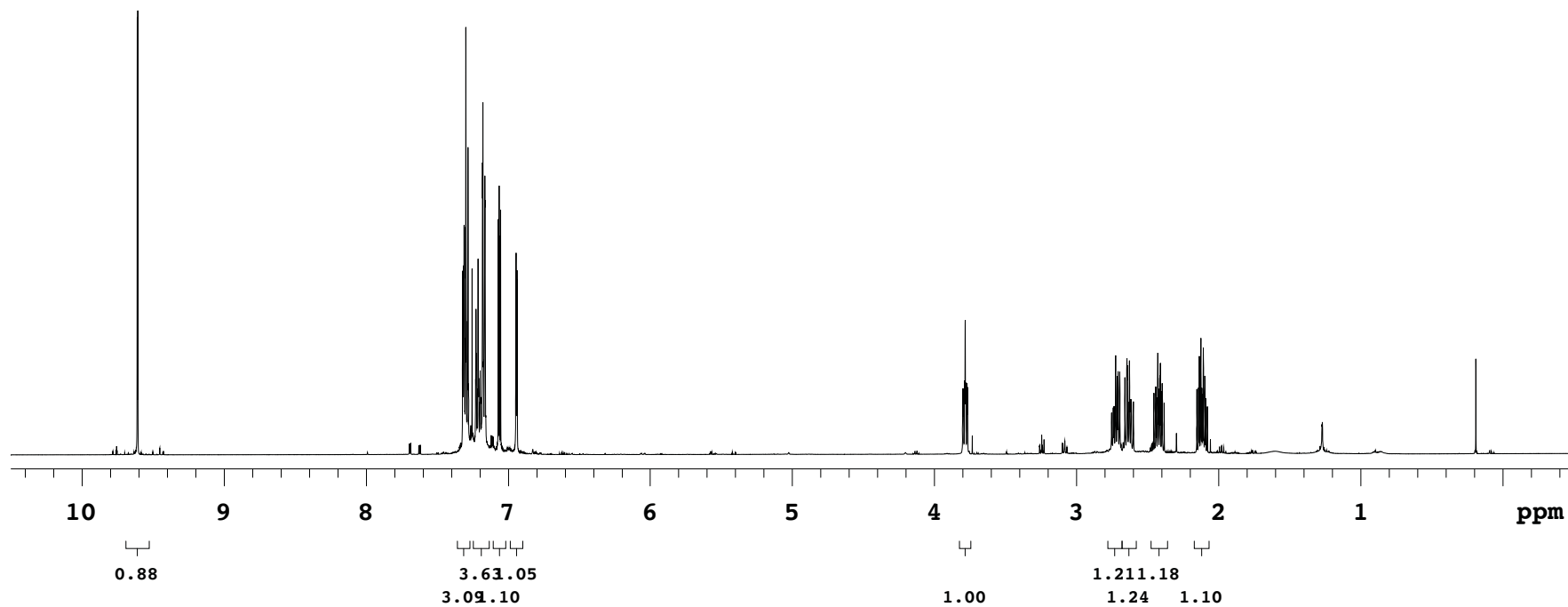
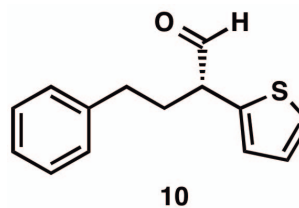
Temperature 25
Spectrometer -vnmrs400

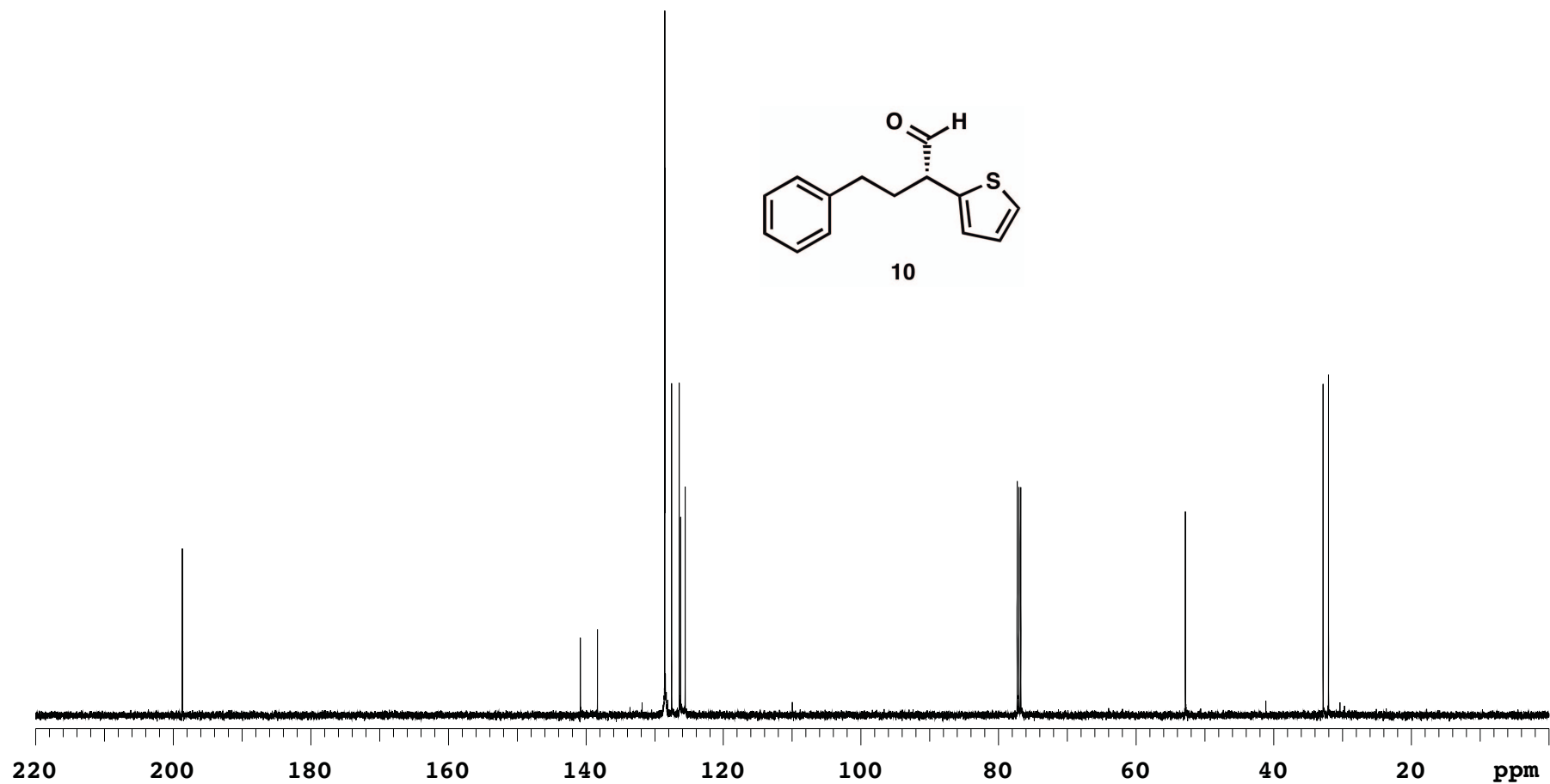
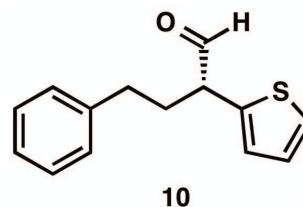
Study owner nkadunce
Operator autouser

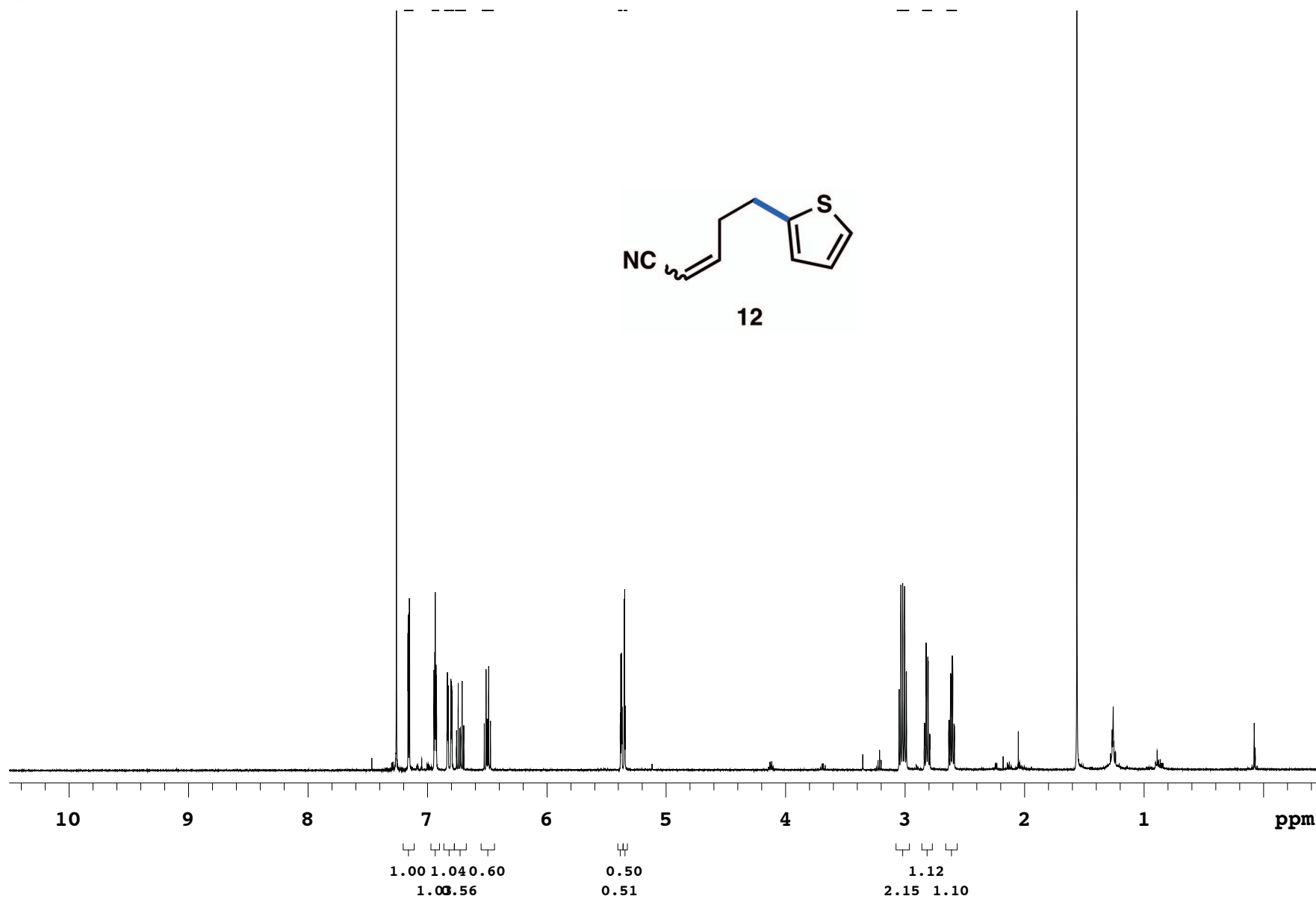
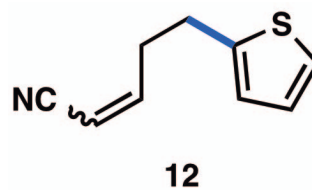












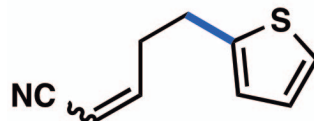
NTK-IV-110-Thiophene-Prep1

Sample Name NTK-IV-110-Thiophene-Prep1
Date collected 2015-05-14

Pulse sequence CARBON
Solvent cdcl3

Temperature 25
Spectrometer -vnmrs400

Study owner nkadunce
Operator autouser



12

