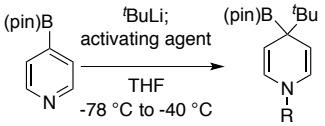
Table of Conents

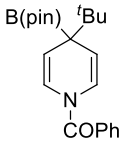
General Information: Unless otherwise stated, reactions were performed under argon using freshly purified solvents which were purified using solvent purification columns purchased from Glass Contour, Laguna Beach, CA. All reactions were monitored by thin-layer chromatography with E. Merck silica gel 60 F254 pre-coated plates (0.25 mm). Flash chromatography was performed with indicated solvents using silica gel (particle size 0.032-0.063m) purchased from Sorbent Technologies. 1 H and 13 C NMR spectra were recorded on Varian MR or Inova 400 MHz spectrometer. Data for 1H NMR are reported as follows: chemical shift (ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, dd = doublet of doublets, ddd = doublet of doublets of doublets and m = multiplet), and coupling constant (Hz). Mass spectra were acquired on an Agilent technologies 1200 series LC/MS using indicated ionization methods.

Materials: Chemicals were purchased from Aldrich, Fisher or Alfa Aesar and used without purification unless otherwise noted.

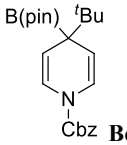
General Procedurefor the synthesis of dihydropyridine intermediate



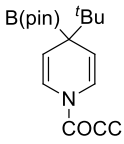
(4-(tert-butyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-1(4H)-yl)(phenyl)methanone: To a stirred solution of 4-pyridineboronic acid pinacol ester (62 mg, 0.3 mmol, recrystallized from $CHCl_3$ and hexanes) in dry THF (1.5 mL) at -78 ^oC was added ^{t}BuLi solution in pentane (193 µL, 0.33 mmol, 1.7 M in pentane) under an argon atmosphere. The reaction was stirred at -78 ^oC for 30 min then rt for 15 min. The reaction mixture was degassed by three freeze-pump-thaw cycles, andthen cooled to -78^oC.Adegassed solution of the desired activating agent (0.36 mmol) in THF (0.5 mL) was added dropwise with constant stirring. The reaction was stirred at -78 ^oC for 30 min then warmed to -40 ^oC and stirred overnight (15h). Water was added and the reaction was warmed to rt. 10 mL of brine was added to the reaction mixture and the product was extracted with EtOAc (3 × 10mL). The organic layer was collected, dried over $Na_2SO_4$and then concentrated in vaccuo. The crude product was purified by silicagel chromatography.



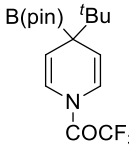
(4-(tert-butyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-1(4H)-yl)(phenyl)methanone(6): Synthesized using general procedure, purified by silica gel chromatography(10% EtOAc/hexane), white solid, yield 82%, mp 143-144 ^oC,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.55 – 7.11 (m, 6H), 6.44 (s, 1H), 5.26 (s, 1H), 4.90 (s, 1H), 1.21 (s, 12H), 0.95 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.6, 134.3, 130.5, 128.3, 128.2, 124.7, 121.9, 113.5, 110.7, 83.5, 37.5, 37.4 (quaternary carbon attached to boron weak broad peak), 26.5, 24.7. ^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 31.87. ESI MS m/z: $[M+H]^+$ 368.2.



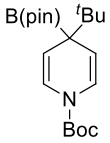
Benzyl 4-(tert-butyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-1(4H)-carboxylate (7): Synthesized using general procedure, purified by silica gel chromatography(10% EtOAc/hexane), white solid, yield 82%, mp 145-147 ^oC,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.45 – 7.24 (m, 5H), 6.83 (dd, *J* = 8.7, 1.7 Hz, 1H), 6.74 (dd, *J* = 8.6, 1.8 Hz, 1H), 5.18 (app q, *J* = 12.2 Hz, 2H), 5.03 (dd, *J* = 8.6, 2.5 Hz, 1H), 4.92 (dd, *J* = 8.7, 2.5 Hz, 1H), 1.22 (s, 12H), 0.92 (s, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 151.2, 135.9, 128.5, 128.3, 128.1, 122.3, 121.9, 110.4, 109.9, 83.4, 67.7, 37.1, 36.1 (quaternary carbon attached to boron; weak broad peak), 26.5, 24.7.^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 32.27. ESI MS m/z: $[M+H]^+$ 398.2.



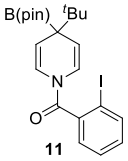
1-(4-(tert-butyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydropyridin-1(2H)-yl)-2,2,2-trichloroethanone (8): Synthesized using general procedure, purified by silica gel chromatography(10% EtOAc/hexane), yellow gum, yield 88%,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.24 – 7.03 (m, 2H), 5.51 – 5.15 (m, 2H), 1.31 – 1.17 (m, 12H), 0.95 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 155.5, 123.5, 122.9, 116.7, 113.4, 92.4, 83.8, 37.6, 30.3, 26.6, 24.7.^{11}B NMR (96 MHz, $CDCl_3$) 31.52 δ ppm. ESI MS m/z: $[M+H]^+$ 408.2.

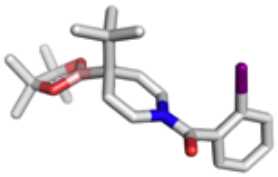


1-(4-(tert-butyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-1(4H)-yl)-2,2,2-trifluoroethanone (9): Synthesized using general procedure, purified by silica gel chromatography(10% EtOAc/hexane), white solid, yield 84%, mp 115-116 ^oC,^{1}H NMR (400 MHz, Acetone-d_6) δ ppm 7.03 (dd, *J* = 8.5, 1.8 Hz, 1H), 6.76 (dt, *J* = 8.4, 2.3 Hz, 1H), 5.51 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.34 (dd, *J* = 8.5, 2.5 Hz, 1H), 1.24 (s, 13H), 0.97 (s, 9H). ^{13}C NMR (101 MHz, Acetone-d_6) δ ppm 151.31 (q, *J* = 37.60 Hz, **CO**CF_3), 120.4, 120.2,117.4, 116.3 (q, *J* = 291.46, CF_3), 115.2, 83.8, 37.0, 25.9, 24.1, (quaternary carbon attached to boron not observed). ^{11}B NMR (96 MHz, Acetone-d_6) δ ppm 31.69. ESI MS m/z: $[M+H]^+$ 360.2.



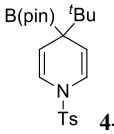
tert-butyl4-(tert-butyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-1(4H)-carboxylate (10): Synthesized using general procedure, purified by silica gel chromatography(10% EtOAc/hexane), white solid, yield 83%, mp 203-205 ^{o}C,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.77 (dd, *J* = 8.5, 1.9 Hz, 1H), 6.69 – 6.60 (m, 1H), 4.93 (dd, *J* = 8.7, 2.5 Hz, 1H), 4.83 (dd, *J* = 8.6, 2.6 Hz, 1H), 1.46 (s, 9H), 1.20 (s, 12H), 0.90 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 150.2, 122.5, 122.1, 109.4, 108.8, 83.3, 81.3, 37.1, 35.8 (quaternary carbon attached to boron weak broad peak), 28.2, 26.4, 24.7. ^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 32.82. ESI MS m/z: $[M+H]^+$ 364.2.





X-ray structure of **11**

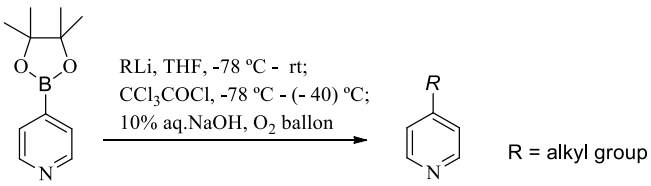
(4-(tertbutyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-1(4H)-yl)(2-iodophenyl)methanone (11):.Synthesized using general procedure, purified by silica gel chromatography (10% EtOAc/hexane), white solid, yield 84%,mp 165 – 167 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.79 (d, *J* = 7.9 Hz, 1H), 7.45 – 7.31 (m, 1H), 7.31 – 7.13 (m, 2H), 7.06 (td, *J* = 7.7, 1.7 Hz, 1H), 5.99 (dd, *J* = 8.6, 1.8 Hz, 1H), 5.31 (ddd, *J* = 8.6, 5.4, 2.4 Hz, 1H), 4.91 (ddd, *J* = 8.4, 5.1, 2.5 Hz, 1H), 1.19 (s, 12H), 0.92 (d, *J* = 10.4 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.7, 140.8, 139.3, 130.7, 128.3, 127.9, 123.2, 120.8, 114.5, 112.1, 92.8, 83.6, 37.2, 37.0, 26.8, 24.8.^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 31.64. ESI MS m/z: $[M+H]^+$ 494.8. A single crystal suitable forX-ray crystallography was grown by slow diffusion of pentane in ethyl acetate & pentane mixture at room temperature.



4-(tert-butyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-tosyl-1,4-dihydropyridine (12): Synthesized using general procedure, purified by silica gel chromatography(15% EtOAc/hexane), white solid, yield 69%, mp 195-197^{o}C,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.67 – 7.57 (m, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 6.50 – 6.34 (m, 2H), 4.99 – 4.87 (m, 2H), 2.37 (s, 3H), 1.11 (s, 12H), 0.70 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 143.7, 134.6, 129.6, 126.9, 121.6, 112.1, 83.4, 36.3, 36.2 (quaternary carbon attached to boron weak broad peak), 26.2, 24.5, 21.5. ^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 31.62. ESI MS m/z: $[M+H]^+$ 418.2.

Preparation of Substituted pyridines

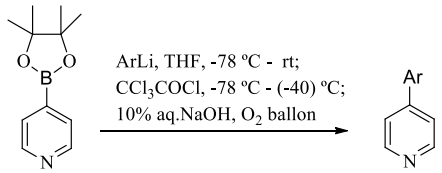
General procedure **A**:addition of alkyl lithium reagents to 4-pyridine boronic acid pinacol esters



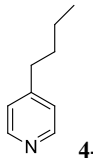
To a stirred solution of the 4-pyridine boronic acid pinacol ester(0.3 mmol, recrystallized from $CHCl_3$ and hexanes) in dry THF (1.5 mL) at -78 ^{o}C was added RLi (0.33 mmol) dropwise for 5 min under argon atmosphere. The reaction was stirred at -78 ^{o}C

for 30 min then rt for 15 min. The reaction was then cooled to -78 °C and trichloroacetyl chloride (65 µL, 0.6 mmol) was added dropwise with constant stirring. The reaction was stirred at -78 °C for 30 min then warmed to -40 °C and stirred overnight (15h). 10% aqueous NaOH solution was added and the reaction was warmed to rt. The reaction vessel was purged with oxygen and stirred under an oxygen balloon for 2h. An aqueous solution of Rochelles salt (sat. 1mL) was then added and the reaction continued to stir for 1 h. 10 mL of brine was added to the reaction mixture and the product was extracted with DCM (3 × 10mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo to afford the crude product(care was taken during evaporation of the solvent due to potential product volatility). This crude material was purified by silica gel chromatography.

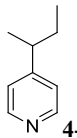
General procedure **B:** addition of ArLi to 4-pyridine boronic acid pinacol esters



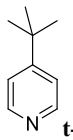
To a stirred solution of 4-pyridine boronic acid pinacol ester(0.3 mmol, recrystallized from $CHCl_3$ and hexanes) in dry THF (1.5 mL) at -78 °C was added ArLi (0.33 mmol) under argon atmosphere. The reaction was stirred at -78 °C for 30 min then rt for 5 min. The reaction was then cooled to -78 °C and trichloroacetyl chloride (65 µL, 0.6 mmol) was added dropwise with constant stirring. The reaction was stirred at -78 °C for 30 min then warmed to -40 °C and stirred overnight (15h). 10% NaOH solution was added and the reaction was warmed to rt. The reaction vessel was purged with oxygen and stirred under an oxygen balloon for 2h. An aqueous solution of Rochelles salt (sat. 1mL) was then added and the reaction continued to stir for 1 h. 10 mL of brine was added to the reaction mixture and the product was extracted with DCM (3 × 10mL). The organic layer was collected, dried over $Na_2SO_4$and then concentrated in vaccuo. The crude product was purified by silica gel chromatography.



4-butylpyridine (13)[1]: Synthesized using general procedure A, purified by silica gel chromatography(1% methanol/DCM), yellow oil, yield 82%,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.69 – 8.15 (m, 2H), 7.23 – 6.91 (m, 2H), 2.68 – 2.49 (t, *J* = 8.0 Hz, 2H), 1.73 – 1.51 (m, 2H), 1.35 (h, *J* = 7.6 Hz, 2H), 0.93 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 151.7, 149.6, 123.9, 34.9, 32.4, 22.2, 13.8. ESI MS m/z: $[M+H]^+$ 136.1

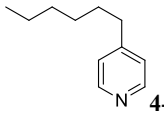


4-secbutylpyridine (14)[2]: Synthesized using general procedure A, purified by silica gel chromatography(1% methanol/DCM), yield 79%,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.58 – 8.35 (m, 2H), 7.16 – 6.93 (m, 2H), 2.53 (h, *J* = 6.9 Hz, 1H), 1.74 – 1.44 (m, 2H), 1.31 – 1.07 (m, 3H), 0.77 (td, *J* = 7.5, 1.0 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 156.4, 149.6, 122.6, 41.1, 30.4, 20.9, 11.9. ESI MS m/z: $[M+H]^+$ 136.1.

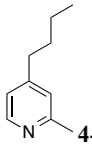


t-butylpyridine (15)[3]: Synthesized using general procedure A, purified by silica gel chromatography(1% methanol/DCM), yellow oil, yield 85%,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.58 – 8.34 (dd, *J* = 4.8, 1.2 Hz, 2H), 7.38 – 7.14 (dd, *J* = 4.4, 1.2 Hz, 2H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.9, 149.6, 120.7, 34.6, 30.5. ESI MS m/z: $[M+H]^+$ 136.1.

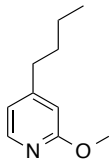
(1)Comins, Daniel L.; Killpack, Michael O. *Heterocycles*, **1990** , *31*, 2025 – 2028.
(2)Akiba, Kin-ya; Iseki, Yuji; Wada, Makoto.*Tetrahedron Lett*, **1982**, *23*, 429 – 432.
(3)Russell et al. *J. Am. Chem. Soc.*, **1993**, *115*, 23, 10596 – 10604.



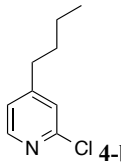
4-hexylpyridine (16)[4]: Synthesized using general procedure A, purified by silica gel chromatography(1% methanol/DCM), yellow oil, yield 83%,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.53 – 8.39 (m, 2H), 7.14 – 7.01 (m, 2H), 2.65 – 2.50 (m, 2H), 1.59 (tt, *J* = 9.1, 6.8 Hz, 2H), 1.39 – 1.16 (m, 6H), 0.92 – 0.77 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm ^{13}C NMR 151.7, 149.5, 123.9, 35.2, 31.6, 30.2, 28.8, 22.5, 14.0.ESI MS m/z: $[M+H]^+$ 164.1.



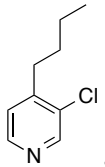
4-butyl-2-methylpyridine (17)[5]: Synthesized using general procedure A, purified by sillica gel chromatography (1:2 Et_2O/hexanes), yellow oil, yield 93%: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.35 (d, *J* = 5.16 Hz, 1H), 6.96 (s, 1H), 6.90 (d, *J* = 5.16 Hz, 1H), 2.55 (t, J = 7.67 Hz, 2H), 2.51 (s, 3H), 1.62-1.54 (m, 2H), 1.39-1.29 (m, 2H), 0.92 (t, *J* = 7.37, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.11, 151.96, 148.92, 123.38, 120.99, 34.95, 32.47, 24.35, 22.30, 13.86 ESI MS m/z: $[M+H]^+$150.2



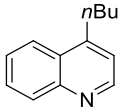
4-butyl-2-methoxypyridine (18): Synthesized using general procedure A, crude material was purified by silica gel chromatography (1:2 Et_2O/Hexanes),yellow oil, yield 80%:^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.01 (d, *J* = 5.27, 1H), 6.68 (dd, *J* = 5.30, *J* = 1.30, 1H), 6.53 (s, 1H), 3.90 (s, 3H) 2.53 (t, *J* = 7.52, 2H), 1.60-1.52 (m, 2H), 1.37-1.27 (m, 2H), 0.90 (t, *J* = 7.47, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 164.5, 154.6, 146.4, 117.6, 110.1, 53.2, 34.8, 32.2, 22.2, 13.9 ESI MS m/z: $[M+H]^+$ 166.2



4-butyl-2-chloropyridine 19: Synthesized using general procedure A, crude material was purified by silica gel Chromatography (1:2 Et_2O/Hexanes), yellow oil, yield 60%: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.25 (d, *J* = 5.05, 1H), 7.14 (s, 1H), 7.02 (d, *J* = 5.05, 1H), 2.59 (t, *J* = 7.75, 2H), 1.63-1.56 (m, 2H), 1.39-1.30 (m, 2H), 0.93 (t, *J* = 7.35, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 155.2, 151.1, 149.3, 129.1, 122.8, 34.7, 32.2, 22.2, 13.8 ESI MS m/z: $[M+H]^+$ 170.1

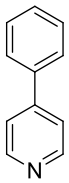


4-butyl-3-chloropyridine 20: Synthesized using general procedure A, crude material was purified by silica gel chromatography (1:2 Et_2O/Hexanes), yellow oil, yield 50%: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.50 (s, 1H), 8.36 (d, *J* = 4.97, 1H), 7.14 (d, *J* = 4.97, 1H), 2.72 (t, *J* = 7.85, 2H), 1.65-1.57 (m, 2H), 1.44-1.35 (m, 2H), 0.95 (t, *J* = 7.34, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 149.2, 149.1, 147.6, 132.1, 124.8, 35.2, 30.9, 22.4, 13.9 δ ppm ESI MS m/z: $[M+H]^+$ 170.1.

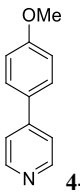


4-butylquinoline (21): Synthesized using general procedure A, purified by silica gel chromatography(1% methanol/DCM), yellow oil, yield 77%,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.78 (d, *J* = 4.4 Hz, 1H), 8.12 – 8.06 (m, 1H), 8.06 – 7.98 (m, 1H), 7.68 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H), 7.53 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 7.27 – 7.17 (m, 1H), 3.14 – 2.94 (m, 2H), 1.81 – 1.66 (m, 2H), 1.45 (h, *J* = 7.4 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 150.1, 148.7, 148.3, 130.2, 128.9, 127.6, 126.2, 123.6, 120.7, 32.2, 31.9, 22.7, 13.9. ESI MS m/z: $[M+H]^+$ 186.1.

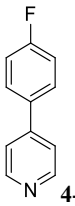
(4)Andou et al. *Angew. Chem. Int. Ed.,***2013**, *52*, 3213 – 3216.
(5) Kaiser et al. *J. Org. Chem.* **1973**,*38*, 77-74.



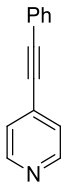
4-phenylpyridine (22)[6]: Synthesized using general procedure B, purified by silica gel chromatography(1% methanol/DCM), yellow solid, mp 67 – 72 °C, yield 84%, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.71 – 8.56 (m, 2H), 7.69 – 7.57 (m, 2H), 7.54 – 7.37 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 150.3, 148.3, 138.1, 129.1, 129.0, 126.9, 121.6. ESI MS m/z: $[M+H]^+$ 156.1.



4-(4-methoxyphenyl)pyridine (23)[7]: Synthesized using general procedure B, purified by silica gel chromatography(1% methanol/DCM), white solid, mp 92-93 °C, yield 82%, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm δ 8.59 (d, J = 4.0 Hz, 2H), 7.58 (d, J = 8.8 Hz, 2H), 7.47 – 7.43 (d, J = 4.0 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.84 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 160.5, 150.1, 147.9, 130.3, 128.1, 121.1, 114.8, 55.4. ESI MS m/z: $[M+H]^+$ 186.1.

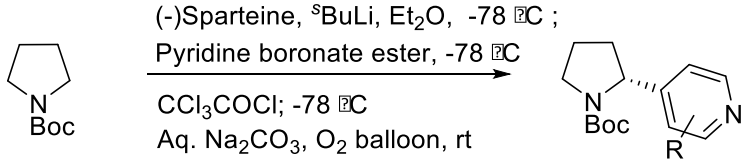


4-(4-fluorophenyl)pyridine (24)[8]: Synthesized using general procedure B, purified by silica gel chromatography(1% methanol/DCM), yield 85%, white solid, mp 116-118 °C,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.69 – 8.58 (m, 2H), 7.66 – 7.54 (m, 2H), 7.49 – 7.39 (m, 2H), 7.21 – 7.07 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 163.4 (d, J = 251.47,C-F coupling), 150.3, 147.2, 134.2, 128.7 (d, J = 8.61, *meta* C-F coupling), 121.4, 116.1 (d, J = 26.2, *ortho* C-F coupling). ESI MS m/z: $[M+H]^+$ 174.1.



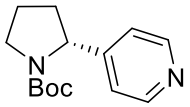
4-(phenylethynyl)pyridine (25)[9]: Synthesized using general procedure A, purified by silica gel chromatography(1% methanol/DCM), yellow oil, yield 87%, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.65 – 8.56 (m, 2H), 7.63 – 7.51 (m, 2H), 7.44 – 7.32 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) 149.7, 131.9, 131.5, 129.2, 128.5, 125.5, 122.1, 93.9, 86.6.ESI MS m/z: $[M+H]^+$ 180.1.

General procedure **C** for the Synthesis of Chiral Pyridines

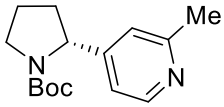


(6) Tanimoro, K.; Ueno, M.; Takeda, K.; Kirihata, M.; Tanimori, S., *J. Org. Chem.* **2012,***77* , 7844-7849.
(7)Rao, Maddali L.N.; Dhanorkar, Ritesh J. *Eur. J. Org. Chem.*, **2014** , 2014, 5214 - 5228
(8)Gall et al. *Tetrahedron*, **2001**, *57*, 1923-1927.
(9) Moulton, Benjamin E., *J. Org. Chem.* **2011,**76, 5320-5334.

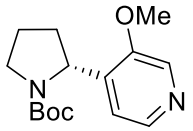
To a stirred solution of the (-) sparteine (76µL, 0.33 mmol) in Et_2O (1.5 mL) was added s-BuLi (0.25 mL, 0.39 mmol)slowly dropwise at -78 ^oC. The reaction was stirred for 30 minutes at -78 ^oC. A Et_2O (1mL) solution of N-Bocpyrrolidine (68 µL, 0.39 mmol) was added slowly dropwise into the reaction mixture at -78 ^oC. The reaction was stirred at -78 ^oC for 3h. A precooled Et_2O (2 mL)/THF (2mL) solution of Boronic ester (0.3 mol) was added dropwise to the reaction mixture at -78 ^oC. The reaction was stirred for another 3h at -78 ^oC. Trichloroacetyl chloride (120 µL, 1.05 mmol) was added to the reaction mixture dropwise with constant stirring. The reaction was stirred for another 2h. After 2h the reaction was quenched by aq. Na_2CO_3 solution (3 mL). The reaction vessel was purged with oxygen and stirred under an oxygen balloon for 2h. 10 mL of brine was added to the reaction mixture and the product was extracted with EtOAc (3 × 10mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo to afford the crude product. This crude material was purified by silica gel chromatography to afford the desired pyridines.



tert-butyl (R)-2-(pyridin-4-yl)pyrrolidine-1-carboxylate (26): Synthesized using general procedure C, purified by silica gel chromatography (60% EtOAc/hexane), gum, yield 70%, $[\alpha]_D^{20}$ +49 (c = 0.2, $CHCl_3$), NMR (400 MHz, $CDCl_3$, rotamers) δ ppm 8.50 (d, *J* = 5.1 Hz, 2H), 7.16 – 6.98 (m, 2H), 4.99 – 4.81 (m, 0.5H), 4.71 (m, 0.6H), 3.70 – 3.39 (m, 2H), 2.32 (m, 1H), 1.94 – 1.72 (m, 3H), 1.43 (s, 3H), 1.17 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, rotamers) δ ppm 154.2, 149.6, 120.7, 79.8, 60.5, 59.9, 47.3, 47.1, 35.5, 34.3, 28.4, 28.1, 23.6, 23.2. ESI MS m/z: $[M+H]^+$ 249.2; The ee was determined by HPLC analysis using Daicel Chiralpak AD-H column (25 cm 0.46 cm ID), conditions: n-hexane/EtOH = 90:10, 0.5 mL/min, 254 nm; t_R = 13.3 min (major) and 27.5 min (minor). e.r. = 98:2.

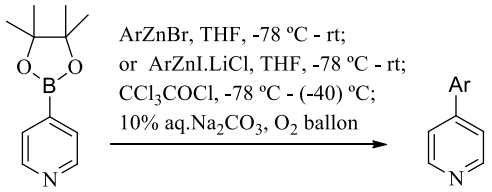


tert-butyl (R)-2-(2-methylpyridin-4-yl)pyrrolidine-1-carboxylate (27): Synthesized using general procedure C, purified by silica gel chromatography (60% EtOAc/hexane), gum, yield 76%, $[\alpha]_D^{20}$ +74 (c = 0.3, $CHCl_3$), NMR (400 MHz, $CDCl_3$, rotamers) δ ppm 8.37 (d, *J* = 5.1 Hz, 1H), 6.92 (d, *J* = 1.7 Hz, 1H), 6.87 (dd, *J* = 5.2, 1.7 Hz, 1H), 4.90 – 4.77 (m, 0.5H), 4.67 (m, 0.7H), 3.66 – 3.43 (m, 2H), 2.50 (s, 3H), 2.30 (m, 1H), 1.80 (m, 3H), 1.33 (s, 3H), 1.17 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, rotamers) δ ppm 158.3, 154.4, 153.4, 149.0, 120.1, 117.9, 117.7, 79.7, 60.4, 59.9, 47.3, 47.0, 35.4, 34.3, 24.4, 23.6, 23.2. ESI MS m/z: $[M+H]^+$ 263.2. The ee was determined by HPLC analysis using Daicel Chiralpak AD-H column (25 cm 0.46 cm ID), conditions: n-hexane/EtOH = 98:2, 1.0 mL/min, 245 nm; t_R = 15.3 min (major) and 41.3 min (minor). e.r. = 98:2.

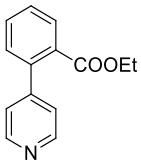


tert-butyl (R)-2-(3-methoxypyridin-4-yl)pyrrolidine-1-carboxylate (28): Synthesized using general procedure C, purified by silica gel chromatography (60% EtOAc/hexane), gum, yield 78%, $[\alpha]_D^{20}$ +85 (c = 0.3, $CHCl_3$), NMR (400 MHz, $CDCl_3$, rotamers) δ ppm 8.31 – 8.09 (m, 2H), 6.96 (m, 1H), 5.17 (m, 0.4H), 5.03 (dd, *J* = 8.5, 3.8 Hz, 0.6H), 3.91, 3.90 (s, 3H), 3.70 – 3.39 (m, 2H), 2.42 – 1.97 (m, 1H), 1.92 – 1.65 (m, 3H), 1.44 (s, 3H), 1.19 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, rotamers) δ ppm 154.3, 152.4, 142.6, 141.5, 140.4, 132.8, 120.3, 119.8, 79.4, 55.9, 55.9, 55.4, 47.2, 46.9, 33.4, 32.3, 28.5, 28.1, 23.5, 23.1. ESI MS m/z: $[M+H]^+$ 279.2. The ee was determined by HPLC analysis using Daicel Chiralpak AD-H column (25 cm 0.46 cm ID), conditions: n-hexane/EtOH = 98:2, 1.0 mL/min, 224 nm; t_R = 38.8 min (major) and 62.8 min (minor). e.r. = 99.5:0.5.

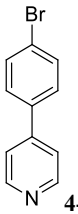
General procedure **D**:addition of aryl zinc to 4-pyridine boronic acid pinacol esters



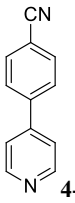
To a stirred solution of 4-pyridine boronic acid pinacol ester(0.3 mmol, recrystallized from $CHCl_3$ and hexanes) in dry THF (1.0 mL) at 0 ^oC was added an arylzinc bromide solution (0.33 mmol) dropwise over 5 min under argon atmosphere. In case of functionalized ArI, ArZnI.LiCl in THF was prepared by using Knochel method[10] and titrated[11] using iodine before addition. The reaction was stirred at 0 ^oC for 20 min then rt for 24 h under argon atmosphere. The reaction was cooled to -78 ^oC and trichloroacetyl chloride (65 µL, 0.6 mmol) was added dropwise with constant stirring. The reaction was stirred at -78 ^oC for 30 min then warmed to -40 ^oC and stirred for 20h. A saturated Na_2CO_3 solution was added and the reaction was warmed to rt. The reaction vessel was purged with oxygen and stirred under an oxygen atmosphere for 2h. An aqueous solution of Rochelles salt (sat. 1mL) was then added and the reaction was stirred for additional 1 h. 10 mL of brine was added to the reaction mixture and the product was extracted with DCM (3 × 10mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo to afford a crude product. The crude product was purified by silica gel chromatography.



ethyl 2-(pyridin-4-yl)benzoate (29)[12]: Synthesized using general procedure D, purified by silica gel chromatography (1% methanol/DCM), white solid, mp 67 – 69 ^oC , yield 83%, ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.66 – 8.56 (m, 2H), 7.90 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.55 (td, *J* = 7.5, 1.5 Hz, 1H), 7.47 (td, *J* = 7.6, 1.4 Hz, 1H), 7.30 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.24 – 7.18 (m, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 1.01 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 167.7, 149.6, 149.3, 139.9, 131.6, 130.6, 130.3, 130.1, 128.3, 123.4, 61.1, 13.6. ESI MS m/z: $[M+H]^+$ 228.1.

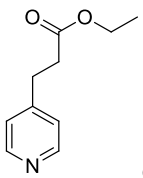


4-(4-bromophenyl)pyridine (30)[13]: Synthesized using general procedure D, purified by silica gel chromatography (1% methanol/DCM), white solid, mp 122 - 124 ^oC, yield 89%,^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.71 – 8.57 (dd, *J* = 5.6, 2.0 Hz, 2H), 7.64 – 7.54 (m, 2H), 7.54 – 7.36 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 150.3, 147.2, 137.0, 132.3, 128.5, 123.5, 121.3. ESI MS m/z: $[M+H]^+$ 236.0.



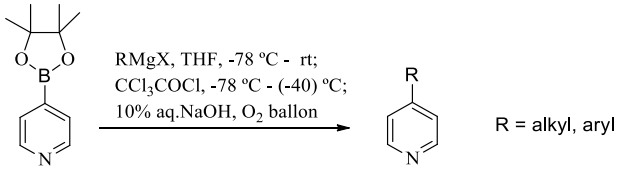
4-(pyridin-4-yl)benzonitrile (31)[14]: Synthesized using general procedure D, purified by silica gel chromatography (1% methanol/DCM), white solid, mp 76 – 77 ^oC, yield 88%, ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.76 – 8.66 (dd, *J* = 4.4, 1.6 Hz, 2H), 7.82 – 7.68 (m, 4H), 7.53 – 7.44 (dd, *J* = 4.8, 2.0Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 150.6, 146.3, 142.6, 132.9, 127.7, 121.6, 118.4, 112.8. ESI MS m/z: $[M+H]^+$ 181.1.

(10) Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P., *Angew. Chem. Int. Ed.* **2006,***45*, 6040-6044.
(11) Krasovskiy, A.; Knochel, P.*Synthesis*, **2006**, 890-891.
(12)Rebstock, A.-S.; Mongin, F.; Trécourt, F.; Quéguiner, G., *Tetrahedron* **2003,***59*, 4973-4977.
(13)Choi-Sledeski, Y. M *J. Med. Chem.* **1999,***42*, 3572-3587.
(14) Molander, G. A.; Canturk, B.; Kennedy, L. E., *J. Org. Chem.* **2009,***74*, 973-980.

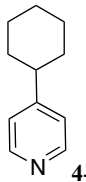


ethyl 3-(pyridin-4-yl)propanoate (32)[15]: To a stirred solution of 3-ethoxy-3-oxopropylzinc bromide (0.5 M solution in THF, 0.95 mL, 0.48 mmol) in dry THF (1.0 mL) at -50 ^{o}C was added ^{t}BuMgCl (1 M in THF, 0.48 mL, 0.48 mmol) dropwise for 5 min under argon atmosphere. The reaction was stirred at -50 ^{o}C for 5 min then transferred via cannula to a vial containing 4-pyridineboronic acid pinacol ester (50 mg, 0.24 mmol) in THF (0.25 mL). The reaction was stirred at -50 ^{o}C for 30 min then slowly warmed to room temperature and stirred for 16 h. The reaction was cooled to -78 ^{o}C and trichloroacetyl chloride (65 µL, 0.6 mmol) was added dropwise with constant stirring. The reaction was stirred at -78 ^{o}C for 30 min then warmed to -40 ^{o}C and stirred for 20h. A saturated Na_2CO_3 solution was added and the reaction was warmed to rt. The reaction vessel was purged with oxygen and stirred under oxygen atmosphere for 2h. Brine was added to the reaction mixture and the product was extracted with EtOAc (3 × 10mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo to afford crude oil, which was purified by silica gel chromatography (1% MeOH in DCM) to afford the product as yellow oil (36 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.59 – 8.40 (m, 2H), 7.18 – 7.06 (m, 2H), 4.13 (qd, *J* = 7.2, 1.7 Hz, 2H), 2.94 (dd, *J* = 8.5, 6.7 Hz, 2H), 2.64 (td, *J* = 7.6, 1.7 Hz, 2H), 1.36 – 1.09 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 172.2, 149.9, 149.4, 123.7, 60.7, 34.5, 30.1, 14.2. ESI MS m/z: $[M+H]^+$ 180.1.

General procedure **E:** addition of alkyl or aryl Grignards to 4-pyridine boronic acid pinacol esters

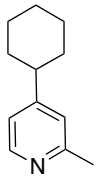


To a stirred solution of 4-pyridine boronic acid pinacol ester (0.3 mmol, recrystallized from $CHCl_3$ and hexanes) in dry THF (1.5 mL) at -78 ^{o}C was added alkyl/aryl magnesium halide solution (0.33 mmol) dropwise for 5 min under argon atmosphere. The reaction was stirred at -78 ^{o}C for 10 min then rt for 2 h. The reaction was then cooled to -78 ^{o}C and trichloroacetyl chloride (65 µL, 0.6 mmol) was added dropwise with constant stirring. The reaction was stirred at -78 ^{o}C for 30 min then warmed to -40 ^{o}C and stirred overnight (18h). 10% NaOH solution was added and the reaction was warmed to rt. The reaction vessel was purged with oxygen and stirred under oxygen balloon for 2h. An aqueous solution of Rochelles salt (sat. 1mL) was then added and the reaction continued to stir for 1 h. 10 mL of brine was added to the reaction mixture and the product was extracted with DCM (3 × 10mL). The organic layer was collected, dried over Na_2SO_4 then concentrated in vaccuo to afford the crude product (care was taken during evaporation of the solvent due to potential product volatility). The crude product was purified by silica gel chromatography.

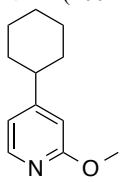


4-cyclohexylpyridine[16](33): Synthesized using general procedure E, purified by silica gel chromatography (1:8 ethyl acetate/hexanes), yellow oil, 81%: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.46 (d, *J* = 5.73, 2H), 7.09 (d, *J* = 5.90, 2H), 2.50-2.43 (m, 1H), 1.89-1.81 (m, 4H), 1.76-1.71 (m, 1H), 1.43-1.31 (m, 4H), 1.28-1.17 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 156.4, 149.7, 122.3, 43.8, 33.5, 26.5, 25.9. ESI MS m/z: $[M+H]^+$ 162.1.

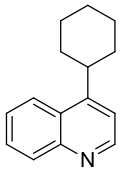
(15) Hunter, C. A.; Misuraca, M. C.; Turega, S. M., *J. Am. Chem. Soc.* **2011,***133*, 582-594.
(16) Branchaud, B. P.; Choi, Y. L., *J. Org. Chem.* **1988,***53*, 4638-4641.



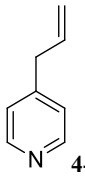
4-cyclohexyl-2-methylpyridine (34): Synthesized using general procedure E, purified by silica gel chromatography (1:2 ethyl acetate/hexanes), yellow oil, 80%: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.35 (d, *J* = 5.14, 1H), 6.96 (s, 1H), 6.90 (d, *J* = 5.14, 1H), 2.50 (s, 3H), 2.46-2.39 (m, 1H), 1.87-1.79 (m, 4H), 1.76-1.71 (m, 1H), 1.42-1.34 (m, 4H), 1.27-1.20 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.2, 156.8, 150.0, 121.8, 119.4, 43.8, 33.5, 26.5, 26.0, 24.4. ESI MS m/z: $[M+H]^+$ 176.2



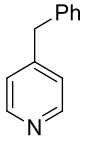
4-cyclohexyl-2-methoxypyridine (35): Synthesized using general procedure E, purified by silica gel chromatography (1:2 Et_2O/Hexanes),yellow oil, 73%:^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.02 (d, *J* = 5.21, 1H), 6.71 (dd, *J* = 5.35 *J* = 1.24, 1H), 6.55 (s, 1H), 3.90 (s, 3H), 2.45-2.40 (m, 1H), 1.86-1.78 (m, 4H), 1.75-1.70 (m, 1H), 1.41-1.29 (m, 4H), 1.27-1.17 (m, 1H) ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 164.5, 159.5, 146.4, 116.1, 108.6, 53.3, 43.7, 33.4, 26.5, 25.9 ESI MS m/z: $[M+H]^+$ 192.1



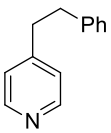
4-cyclohexylquinoline (36)[17]: Synthesized using general procedure E, purified by silica gel chromatography(25% EtOAc in Hexane), yellow gum, yield 70%, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.83 (d, *J* = 4.6 Hz, 1H), 8.10 (td, *J* = 9.2, 8.8, 1.6 Hz, 2H), 7.68 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 7.54 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H), 7.27 (d, *J* = 4.5 Hz, 1H), 3.39 – 3.25 (m, 1H), 2.06 – 1.79 (m, 5H), 1.62 – 1.26 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 153.7, 150.2, 148.1, 130.1, 128.9, 126.9, 126.2, 123.0, 117.5, 38.9, 33.5, 26.9, 26.2. ESI MS m/z: $[M+H]^+$ 212.1.



4-allylpyridine (37)[18]: Synthesized using general procedure E, purified by silica gel chromatography(1% methanol/DCM), yellow oil, yield 80%, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.52 (d, *J* = 4.8 Hz, 2H), 7.13 (d, *J* = 4.8 Hz, 2H), 5.94 (m, 1H), 5.15 (m, 2H), 3.40 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ ppm149.8, 148.9, 135.2, 123.9, 117.4, 39.4. ESI MS m/z: $[M+H]^+$ 120.1.



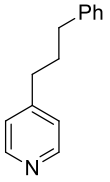
4-benzylpyridine (38)[19]: Synthesized using general procedure E, purified bysilica gel chromatography(1% methanol/DCM), yellow oil, yield 85%,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.61 – 8.36 (m, 2H), 7.39 – 7.08 (m, 7H), 3.99 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 151.1, 148.9, 138.5, 129.0, 128.8, 126.8, 124.4, 41.3. ESI MS m/z: $[M+H]^+$ 170.1.



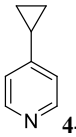
4-phenethylpyridine (39)[20]: Synthesized using general procedure E, purified by silica gel chromatography (1%

(17) Luo et al., *Org. Lett.***2007**, *22*, 4571-4574.
(18) Ishikura, Minoru.,*J. Heterocycl. Chem,* **1987**, *24*, 377-386.
(19)Katrizky et al., *Org. Lett.***2001**, *3*, 2807-2809.

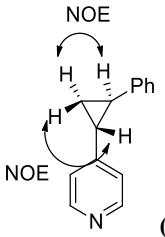
methanol/DCM), yellow gum, yield 84%, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.56 – 8.41 (m, 2H), 7.40 – 6.96 (m, 7H), 2.94 (s, 4H).^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 151.1, 149.1, 140.5, 128.5, 128.4, 126.3, 124.1, 37.1, 36.51. ESI MS m/z: $[M+H]^+$ 184.1.



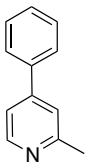
4-(3-phenylpropyl)pyridine (40)[21]: Synthesized using general procedure E, purified by silica gel chromatography(1% methanol/DCM), yellow gum, yield 85%,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.50 (d, *J* = 5.7 Hz, 2H), 7.41 – 7.06 (m, 7H), 2.66 (td, *J* = 7.8, 3.7 Hz, 4H), 2.08 – 1.86 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 151.8, 149.2, 141.5, 128.4, 128.4, 125.9, 124.0, 35.3, 34.7, 31.7. ESI MS m/z: $[M+H]^+$ 198.1.



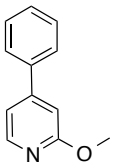
4-cyclopropylpyridine (41)[23]: Synthesized using general procedure E, purified bysilica gel chromatography(1% methanol/DCM), yellow oil, yield 80%, ^{1}H NMR (400 MHz, Acetone-d_6) δ ppm 8.43 – 8.29 (m, 2H), 7.04 (dt, *J* = 4.8, 1.4 Hz, 2H), 1.96-1.85 (1H, m), 1.14 – 0.99 (m, 2H), 0.86 – 0.70 (m, 2H). ^{13}C NMR (100 MHz, Acetone-d_6) δ ppm 153.4, 149.4, 120.5, 14.4, 9.9. ESI MS m/z: $[M+H]^+$ 120.1.



(±) 4-(2-phenylcyclopropyl)pyridine (42)[24]: The relative stereochemistry was confirmed by 1D-NOE of the corresponding protons.Synthesized using general procedure E, purified by silica gel chromatography(1% methanol/DCM), yellow oil, yield 72%, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm δ 8.50 (m, 2H), 7.55 – 6.85 (m, 7H), 2.27 (ddd, *J* = 8.7, 6.2, 4.3 Hz, 1H), 2.12 (ddd, *J* = 8.5, 5.8, 4.3 Hz, 1H), 1.59 (dt, *J* = 8.5, 5.8 Hz, 1H), 1.53 (dt, *J* = 8.9, 5.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 151.9, 149.5, 141.2, 128.5, 126.3, 125.8, 120.9, 29.1, 27.2, 18.9. ESI MS m/z: $[M+H]^+$ 196.1.



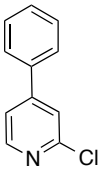
2-methyl-4-phenylpyridine(43)[25]: Synthesized using general procedure E, purified by silica gel chromatography (1% MeOH/DCM), yellow oil, yield 83%, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.54 (d, *J* = 5.18 Hz, 1H), 7.64 – 7.61 (m, 2H), 7.50-7.41 (m, 5H), 7.37 (brS, 1H), 7.31 (dd, *J* = 5.18 Hz, *J* = 1.37 Hz, 1H), 2.63 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.9, 149.6, 148.7, 138.5, 129.0, 128.8, 127.0, 121.2, 118.8, 24.6. ESI MS m/z: $[M+H]^+$ 170.1.



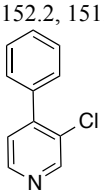
2-methoxy-4-phenylpyridine (44): Synthesized using general procedure E, purified by silica gel chromatography (0.5% MeOH/DCM), yellow oil, yield 77%: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.21 (d, *J* = 5.37 Hz, 1H), 7.63 – 7.61 (m, 2H),

(20)Lautens et al., *J. am. Chem. Soc.***2001**, *123*, 5358.
(21)Molander et al., Org. Lett.**2010**, *12*, 5783-5785.
(23) Lemhadri et al.,*Synth.Commun.***2006**, *36*, 121-128.
(24) Lavine et al.,*J. Org. Chem.***1973**, *38*, 3942-3943.
(25) Wei et al., *J. Am. Chem. Soc.* **2013,***135*, 3756-3759.

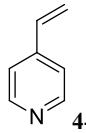
7.49-7.40 (m, 3H), 7.11 (dd, J = 5.37 Hz, J = 1.09 Hz, 1H) 3.99 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 164.9, 151.2, 147.2, 138.3, 129.0, 129.0, 127.0, 115.4, 108.5, 53.5. ESI MS m/z: $[M+H]^+$ 186.1



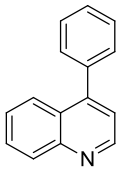
2-chloro-4-phenylpyridine(45)[26]: Synthesized using general procedure E, purified by silica gel chromatography (1:10 ethyl acetate/hexanes), yellow solid, yield 83%:^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.43 (d, J = 5.21 Hz, 1H), 7.63 – 7.60 (m, 2H), 7.55 (d, J = 1.08 Hz, 1H) 7.53-7.47 (m, 3H), 7.43 (dd, J = 5.19 Hz, J = 1.51 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 152.2, 151.6, 150.0, 136.9, 129.7, 129.3, 127.1, 122.0, 120.5. ESI MS m/z: $[M+H]^+$ 190.0.



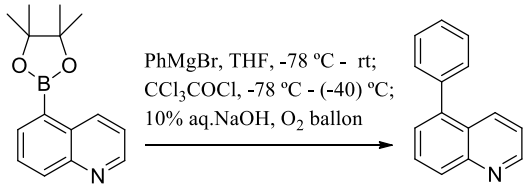
3-chloro-4-phenylpyridine(46)[27]: Synthesized using general procedure E, purified by silica gel chromatography (0.5% MeOH/DCM), yellow oil, yield 80%: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.68 (s, 1H), 8.53 (d, J = 4.96 Hz, 1H), 7.49 – 7.44 (m, 5H), 7.29 (d, J = 4.93 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 150.0, 147.8, 147.6, 136.5, 130.2, 128.9, 128.9, 128.4, 125.4. ESI MS m/z: $[M+H]^+$ 190.0.



4-vinylpyridine (47)[28]: Synthesized using general procedure E, purified bysilica gel chromatography(1% DCM/methanol), yellow oil, yield 76%, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (dd, J = 4.6, 1.0 Hz, 2H), 7.32 – 7.15 (m, 2H), 6.63 (dd, J = 17.6, 10.8 Hz, 1H), 5.94 (d, J = 17.6 Hz, 1H), 5.46 (d, J = 10.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 150.1, 144.7, 134.7, 120.7, 118.6. ESI MS m/z: $[M+H]^+$ 106.1.



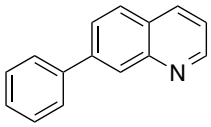
4-phenylquinoline (48)[29]: Synthesized using general procedure E, purified by silica gel chromatography(25% EtOAc in Hexane), light yellow solid, yield 78 %,mp62 – 64 ^{o}C,^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, J = 4.4 Hz, 1H), 8.23 – 8.10 (m, 1H), 7.97 – 7.85 (m, 1H), 7.72 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.57 – 7.43 (m, 6H), 7.33 (d, J = 4.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 148.6, 148.5, 137.9, 129.8, 129.5, 129.3, 128.6, 128.4, 126.7, 126.6, 125.9, 121.3. ESI MS m/z: $[M+H]^+$ 206.1.



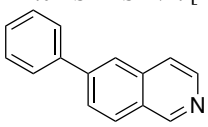
5-phenylquinoline (49)[30]: To a stirred solution of 5-quinolineboronic acid pinacol ester (76 mg, 0.3 mmol, recrystallized from $CHCl_3$ and hexanes) in dry THF (1.5 mL) at -78 ^{o}C was added 0.96 M phenylmagnesium bromide solution in THF (343 µL, 0.33 mmol) dropwise for 15 min under argon atmosphere. The reaction was stirred at -78 ^{o}C for 30 min then brought to 0 - 2 ^{o}C for 2 h, then rt for 20 min. The reaction was then cooled to -78 ^{o}C and trichloroacetyl chloride (65 µL, 0.6 mmol) was added dropwise with constant stirring. The reaction was stirred at -78 ^{o}C for 2 h then warmed to rt and stirred for 20 min. 10% NaOH solution was added and the reaction was stirred for 2 h under oxygen balloon. An aqueous solution of Rochelles salt (sat. 1mL) was then added and the reaction was stirred for 1 h. 10 mL of brine was added to the reaction mixture and the product was extracted with DCM (3 × 10mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo to afford a yellow gum.

(26) Gurung, S. K et al. *Org. Lett.***2014,***16*, 1264-1267.
(27)Guo, P et al. *J. Am. Chem. Soc.* **2011,***133*, 16338-16341.
(28)Battace. A et al. *J. Organomet. Chem.***2005**, *690*, 3790-3802.
(29)An, Xiao-De; Yu, Shouyun., *Org. Lett.* **2015**, *17*, 2692 – 2695.
(30) Gandhamsetty, N et al. *J. Am. Chem. Soc.* **2014**,*136*, 16780-16783.

The crude product was purified by silica gel chromatography (15% EtOAc in Hexane) to afford the product as yellow gum (25 mg, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.98 – 8.87 (m, 1H), 8.24 (dd, *J* = 8.5, 1.6, Hz, 1H), 8.13 (dd, *J* = 8.7, 1.4 Hz, 1H), 7.76 (m, 1H), 7.57 – 7.41 (m, 6H), 7.35 (dd, *J* = 8.6, 4.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 150.2, 148.5, 140.5, 139.3, 134.4, 130.0, 128.9, 128.5, 127.7, 127.3, 126.7, 121.1. ESI MS m/z: $[M+H]^+$ 206.1.

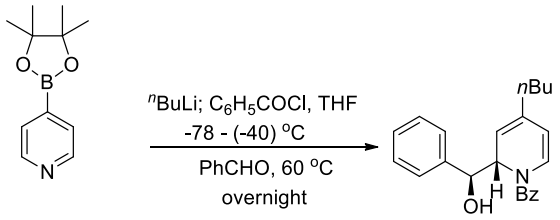


7-phenylquinoline (50)[32]: To a -78 °C stirred solution of 7-quinolineboronic acid pinacol ester (76 mg, 0.3 mmol) in THF (1.5 mL) was added phenyl magnesium bromide (351 µL, 0.33 mmol) (0.94 M in THF). The reaction was stirred at -78 °C and slowly allowed to warm to rt over 2 hours. After stirring at rt for 20 min the reaction was cooled to -78 °C and trichloroacetyl chloride (65 µL L, 0.6 mmol) was added dropwise. Upon complete addition of the acid chloride the reaction was warmed to 4 °C and stirred at temperature overnight (15h). 10% NaOH (1 mL) was then added and the reaction was warmed to rt. The reaction vessel was then purged with oxygen and the reaction was stirred under oxygen atmosphere for 2 hours. Rochelles salt (sat. 1 mL) was then added and the reaction was stirred for an additional 1 hour. 20 mL of Brine was added and DCM was then used to extract the product (3 x 10 mL).The organic layer was collected, dried over sodium sulfate and then concentrated in vaccuo to give the crude product. The crude material was purified by silica gel chromatography (1:10 ethyl acetate/hexanes) to give a clear oil, 18 mg, 30%: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.93 (dd, *J* = 4.30, *J* = 1.68, 1H), 8.32 (s, 1H), 8.17 (d, *J* = 8.40, 1H), 7.88 (d, J = 8.40, 1H), 7.82 (dd, *J* = 8.45, *J* = 1.85, 1H), 7.76-7.74 (m, 2H), 7.52-7.98 (m, 2H), 7.42-7.37 (m, 2H) ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.9, 148.6, 142.2, 140.2, 135.7, 129.0, 128.2, 127.9, 127.5, 127.1, 126.2, 121.0 ESI MS m/z: $[M+H]^+$ 206.1.



6-phenylisoquinoline (51)[33]:The title compound was prepared following a similar procedure as used for compound **50**. Thecrude material was purified by silica gel chromatography (1:10 ethyl acetate/hexanes) to give a clear oil, yield 34%.^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.26 (s, 1H), 8.54 (d, *J* = 6.17, 1H), 8.09 (d, *J* = 7.71, 1H), 7.99 (s, 1H), 7.86 (dd, *J* = 8.62, *J* = 2.15, 1H), 7.72-7.68 (m, 3H), 7.52-7.48 (m, 2H), 7.44-7.40 (m, 1H) ESI MS m/z: $[M+H]^+$ 206.1.

Procedure for trapping aldehyde with dihydropyridine intermediate

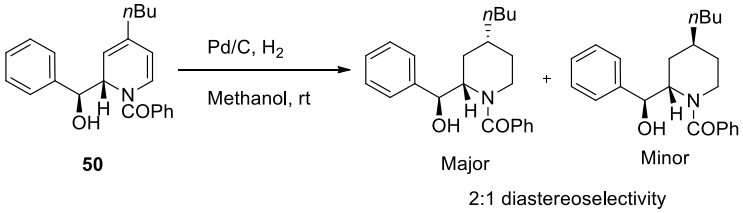


(±) (4-butyl-2-(hydroxy(phenyl)methyl)pyridin-1(2H)-yl)(phenyl)methanone (52): To a stirred solution of 4-pyridineboronic acid pinacol ester (62 mg, 0.3 mmol, recrystallized from $CHCl_3$ and hexanes) in dry THF (1.5 mL) at -78 °C was added 2.5 M ^{n}BuLi in hexane (132 µL, 0.26 mmol) dropwise for 5 min under argon atmosphere. The reaction was stirred at -78 °C for 30 min then rt for 15 min. The reaction was degassed by three freeze-pump-thaw cycles then recooled to -78 °C. In another vial a THF solution (0.2 mL) of PhCOCl (28.5 µL, 0.33 mmol) was degassed by three freeze-pump-thaw cycles and added slowly (10 minutes) into the reaction mixture. The reaction was stirred at -78 °C for 30 min then warmed to -40 °C and stirred for 6h under argon atmosphere. Dry and degassed benzaldehyde (122 µL, 1.2 mmol) was added into the reaction and the reaction was stirred overnight at 60 °Cunder argon atmosphere. The reaction was quenched with aq. NH_4Cl. Brine was added to the reaction mixture and the product was extracted with EtOAc (3 × 10 mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo to afford the crude product. The crude materialwas purified by silica gel chromatography (30% EtOAc in hexane) to afford the product as yellow oil (81 mg, 78%). ^{1}H NMR (400 MHz, benzene-d6) δ ppm 7.74 – 7.08 (m, 10H), 6.35 (m, 1H), 5.39 – 5.13 (m, 2H), 4.80 (dt, *J* = 6.0, 1.3 Hz, 1H), 4.73 (d, *J* = 9.2 Hz, 1H), 4.35 (m, 1H), 2.03 (td, *J* = 7.2, 4.0 Hz, 2H), 1.43 – 1.19 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, benzene-d6) δ ppm 172.8, 141.1, 135.3, 133.9, 131.4, 128.4,

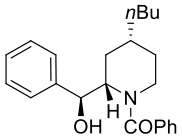
(32) Molander, G. A.; Canturk, B.; Kennedy, L. E., *J. Org. Chem.* **2009,***74*, 973-980
(33)Molander, G. A.; Iannazzo, L., *J. Org. Chem.* **2011,***76*, 9182-9187.

128.1, 127.8, 127.4, 126.2, 115.2, 110.5, 75.5, 58.1, 33.8, 30.2, 22.2, 13.8.ESI MS m/z: $[M+H]^+$ 348.2. The relative stereochemistry was determined by X-ray data obtained of the product isolated after reduction followed by ester formation (see compound **51**below).

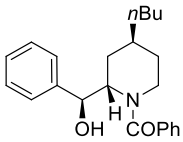
Reduction of the dihydropyridine using Pd/C, H_2



To a stirred solution of compound **52** (68 mg, 0.2 mmol) in dry methanol was added 10% Pd/C (60 mg) under argon atmosphere. The reaction vessel was charged with hydrogen gas (110 psi) using a bombapparatus and stirred for 48h. The reaction was filtered through Celite and washed with methanol (3 × 5mL). The filtrate was concentrated to afford yellow oil, which was purified by silica gel chromatography (35% EtOAc in hexane) to afford the product as gum (58 mg, 82%), dr 2:1.

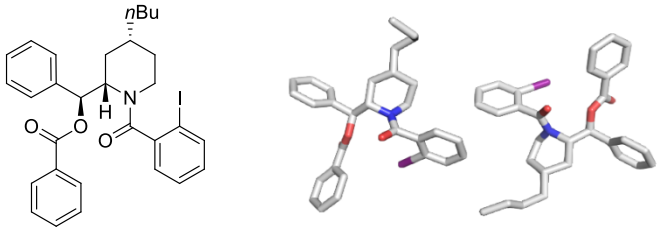


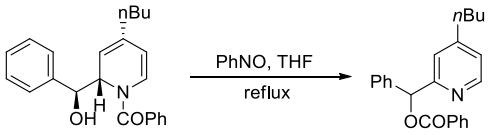
(±) 4-butyl-2-(hydroxy(phenyl)methyl)piperidin-1-yl)(phenyl)methanone (53): Separated by silica gel flash chromatography (30% EtOAc in hexane), gum, yield 52%, ^{1}H NMR (400 MHz, Benzene-d_6) δ ppm 7.55 – 6.99 (m, 10H), 4.86 (d, J = 8.0 Hz, 1H), 4.42 (d, J = 11.1 Hz, 1H), 3.17 – 2.80 (m, 2H), 1.55 – 0.49 (m, 14H). ^{13}C NMR (100 MHz, Benzene-d_6, mixture of rotamers) δ ppm 173.4, 165.3, 143.1, 138.7, 137.0, 132.5, 130.7, 129.6, 129.3, 128.2, 128.2, 128.0, 127.3, 127.1, 126.8, 80.6, 76.3, 61.3, 60.4, 46.3, 43.3, 36.9, 36.3, 35.9, 35.5, 32.6, 31.9, 31.4, 30.7, 28.7, 22.9, 22.8, 13.9, 13.9. ESI MS m/z: $[M+H]^+$ 352.2.



4-butyl-2-(hydroxy(phenyl)methyl)piperidin-1-yl)(phenyl)methanone: yield 25%, ^{1}H NMR (400 MHz, acetone-d_6, mixture of rotamers) δ ppm 8.08 (m, 0.3H), 7.68 – 7.05 (m, 9.7H), 5.09 (d, J = 10.0 Hz, 1H), 5.01 – 4.90 (m, 0.35H), 4.64 – 4.52 (m, 0.64H), 3.90 (dt, J = 11.1, 3.8 Hz, 0.6H), 3.64 (m, 0.4H), 3.43 (td, J = 13.5, 2.9 Hz, 0.4H), 3.16 – 2.96 (m, 2.6H), 2.02 – 1.79 (m, 2H), 1.54 – 0.90 (m, 8H), 0.85 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, acetone-d_6, mixture of rotamers) δ ppm 176.7, 176.2, 148.9, 148.5, 143.3, 142.4, 134.3, 134.1, 133.6, 133.3, 133.0, 132.9, 132.6, 132.4, 131.0, 131.9, 77.4, 75.9, 65.9, 60.5, 48.8, 42.09, 41.7, 41.6, 37.9, 37.3, 37.3, 37.1, 35.9, 35.8, 35.5, 34.8, 30.4, 28.5, 27.6, 18.5. ESI MS m/z: $[M+H]^+$ 352.2.

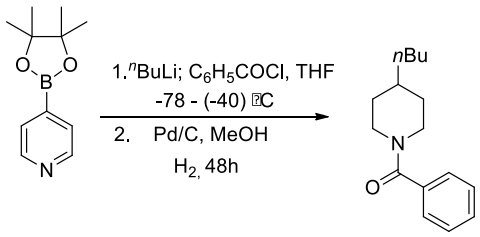
The relative stereochemistry of **53**was determined by converting it to an ester by using Et_3N, 2-I-PhCOCl, cat DMAP, in DCM. We observed migration of the benzoyl group during that reaction which was shown in the X-ray structure.A single crystal suitable forX-ray crystallography was grown by slow evaporation of ethyl acetate and pentane at room temperature.



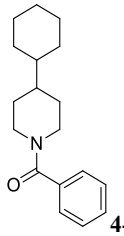


50

(4-butylpyridin-2-yl)(phenyl)methyl benzoate (54): To a stirred solution of **52** (27 mg, 0.08 mmol) in THF (1 mL) was added nitrosobenzene (25 mg, 0.24 mmol) this mixture was then heated to 70 ^{o}Cand stirred at temperature for 30h. At which point the reaction was quenched with water. Brine was added to the reaction mixture and the product was extracted with EtOAc (3 × 5mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo. The crude product was purified by silica gel chromatography (20% EtOAc in hexane) to afford the product as gum (19 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.46 (dd, *J* = 5.1, 0.8 Hz, 1H), 8.22 – 8.12 (m, 2H), 7.62 – 7.27 (m, 9H), 7.10 (s, 1H), 7.02 (dd, *J* = 5.1, 1.6 Hz, 1H), 2.66 – 2.54 (m, 2H), 1.70 – 1.54 (m, 2 H), 1.35 (dq, *J* = 14.7, 7.3 Hz, 2H), 0.91 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.5, 159.0, 152.8, 149.3, 139.2, 133.2, 129.9, 128.6, 128.4, 128.1, 127.3, 122.9, 120.9, 78.5, 35.1, 32.3, 22.3, 13.8. ESI MS m/z: $[M+H]^+$ 346.2.

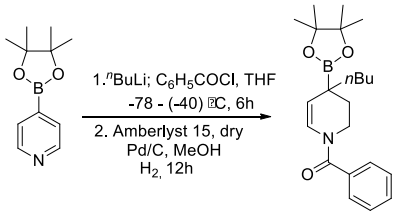


(4-butylpiperidin-1-yl)(phenyl)methanone (56)[42]: To a stirred solution of 4-pyridineboronic acid pinacol ester (50 mg, 0.24 mmol)(recrystallized from $CHCl_3$ and hexanes) in dry THF (1.0 mL) at -78 ^{o}C was added ^{n}BuLi(105 µL, 0.26 mmol, 2.5 M in hexane) dropwise for 5 min under argon atmosphere. The reaction was stirred at -78 ^{o}C for 30 min then rt for 15 min. The reaction was degassed by three freeze-pump-thaw cycles then recooled to -78 ^{o}C and a degassed THF solution (0.5 mL) of PhCOCl (31 µL, 0.26 mmol) was added slowly (10 minutes) into the reaction mixture. The reaction was stirred at -78 ^{o}C for 30 min then warmed to -40 ^{o}C and stirred for 6h under argon atmosphere. The reaction mixture was transferred to a flask contain Pd/C (10mol%) and methanol (4mL, dry & degassed). The reaction vial was charged with hydrogen gas(balloon) and stirred for 48h. The reaction was filtered through Celite and washed with methanol (3 × 5mL). The filtrate was concentrated to afford yellow oil, which was purified by silica gel chromatography (25% EtOAc in hexane) to afford the product as gum (41 mg, 70%). ^{1}H NMR (400 MHz, Benzene-d_6,) δ ppm 7.36 (td, *J* = 5.5, 4.9, 2.8 Hz, 2H), 7.07 – 6.96 (m, 3H), 4.79 (m, 1H), 3.71 – 3.23 (m, 1H), 2.50 – 2.20 (m, 2H), 1.43 – 0.53 (m, 14H). ^{13}C NMR (100 MHz, Benzene-d_6) δ ppm 169.2, 137.2, 128.9, 128.0, 127.2, 47.2, 42.3, 36.6, 35.9, 32.3, 29.3, 28.7, 22.8, 13.9. ESI MS m/z: $[M+H]^+$ 246.2.

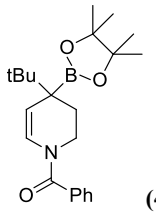


4-cyclohexylpiperidin-1-yl)(phenyl)methanone (57): Synthesized using similar procedure as **56**, cyclohexylmagnesium chloride was used in place of ^{n}BuLi, purified by silica gel chromatography (25% EtOAc in hexane), yellow gum, yield 72%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.36 (m, 5H), 4.87 – 4.50 (m, 1H), 3.88 – 3.58 (m, 1H), 2.90 (t, *J* = 12.7 Hz, 1H), 2.66 (m, 1H), 1.82 – 0.89 (m, 16H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 170.1, 149.6, 136.5, 129.3, 128.3, 126.8, 48.4, 42.8, 42.5, 41.9, 33.5, 30.1, 29.1, 26.6, 26.5. ESI MS m/z: $[M+H]^+$ 272.2.

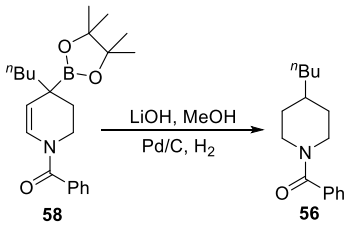
(42)Yu, X.; Yang, T.; Wang, S.; Xu, H.; Gong, H., *Org. Lett.***2011,***13*, 2138-2141.



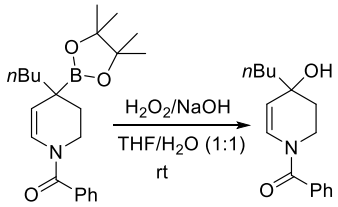
(4-butyl-4-(4,4,5,5-tetramethyl-1,2-oxaborolan-2-yl)-3,4-dihydropyridin-1(2H)-yl)(phenyl)methanone (58): To a stirred solution of 4-pyridineboronic acid pinacol ester (100 mg, 0.48 mmol)(recrystallized from $CHCl_3$ and hexanes) in dry THF (1 mL) at -78 ^oC was added ^{n}BuLi in hexane (0.21 mL, 0.53 mmol, 2.5 M in hexane) dropwise for 5 min under argon atmosphere. The reaction was stirred at -78 ^oC for 30 min then rt for 15 min. The reaction was degassed by three freeze-pump-thaw cycle. The reaction was recooled to -78 ^oC and a degassed THF solution (0.5 mL) of PhCOCl (55 µL, 0.48mmol) was added slowly (10 minutes) into the reaction mixture. The reaction was stirred at -78 ^oC for 30 min then warmed to -40 ^oC and stirred for 6h under argon atmosphere. The reaction mixture was transferred to another flask containing dry amberlyst 15 (145 mg) and stirred for 10 minutes under argon atmosphere. The reaction was settled down for another 10 minutes. In the meantime 10% Pd/C and degassed methanol (4mL)was transferred to another dry flask under argon atmosphere. At this point the reaction mixture was transferred to the flask contain Pd/C and methanol. The reaction flask was washed with dry degassed THF (0.5 mL) and transferred to the flask. Reaction was charged with hydrogen gas (balloon) and stirred at rt for 12h. The reaction was filtered through Celite and washed with methanol (3 × 5mL). The filtrate was concentrated to afford yellow oil, which was purified by silica gel chromatography (15% EtOAc in hexane) to afford the product as yellow oil (130 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers) δ 7.59 – 7.29 (m, 5H), minor rotamer 7.19 (d, J = 8.2 Hz, 0.21 H), major rotamer 6.37 (d, J = 8.2 Hz, 0.69H), minor rotamer 5.11 (d, J = 8.2 Hz, 0.34 H), major rotamer 4.74 (d, J = 8.2 Hz, 0.89H), major rotamer 4.17 (dt, J = 13.6, 4.4 Hz, 0.9H), major & minor rotamer 3.54 (m, 2H), major & minor rotamer 2.23 – 1.09 (m, 20H), major & minor rotamer 0.86 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, mixture of rotamers) δ 169.1, 168.3, 135.6, 135.1, 130.1, 129.9, 128.4, 127.4, 125.1, 122.5, 117.1, 114.1, 83.4, 45.1, 41.7, 39.9, 38.3, 30.1, 29.6, 28.2, 24.8, 24.6, 24.5, 23.3, 23.1, 14.1, 14.0. ^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 30.02, ESI MS m/z: $[M+H]^+$ 370.2.



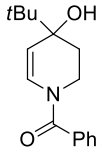
(4-(tert-butyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydropyridin-1(2H)-yl)(phenyl)methanone (59): Followedsame procedure as**56**, ^{t}BuLi was used instead of ^{n}BuLi, Purified by silica gel chromatography (15% EtOAc in hexane), gum, yield 69%, ^{1}H NMR (400 MHz, Benzene-d_6, mixture of rotamers) δ ppm minor rotamer 7.72 (m, 0.15 H), major rotamer 7.58 – 7.25 (m, 2H), minor rotamer 7.00 (m, 0.2H), major rotamer 6.95 (m, 3H), major rotamer 6.47 (d, J = 8.5 Hz, 1H), minor rotamer 5.29 (m, 0.2H), major rotamer 4.86 (d, J = 8.8 Hz, 0.79H), major rotamer 4.75 (d, J = 13.2 Hz, 1H), minor rotamer 3.65 (m, 0.19 H), major rotamer 3.36 (td, J = 13.2, 2.8 Hz, 1H), mixture of major and minor rotamer 2.25-1.23 (m, 2H), 0.97 (s, 9H), 0.91 (s, 12H). ^{13}C NMR (100 MHz, Benzene-d_6, mixture of rotamers) δ ppm 168.0, 135.8, 129.6, 128.5, 125.9, 123.7, 111.6, 82.9, 41.2034.3226.8, 26.6, 26.1, 24.7, 24.5, 24.2.^{11}B NMR (96 MHz, Benzene-d_6) δ ppm 32.99. ESI MS m/z: $[M+H]^+$ 370.2.



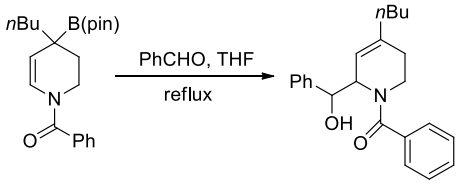
To a stirred solution of compound **58**(20mg, 0.08mmol) in methanol (0.5 mL) was added LiOH (1mg, 0.04) followed by 20 mol% Pd/C under argon atmosphere. The reaction was charged with hydrogen gas (balloon) and stirred overnight(15h). At this point the reaction was filtered through Celite and concentrated in vaccuo. The crude material was purified by silica gel column chromatography (25% EtOAc in hexane) to afford **56** (11 mg,56%).



(4-butyl-4-hydroxy-3,4-dihydropyridin-1(2H)-yl)(phenyl)methanone (60): To a stirred solution of compound **58** (43 mg, 0.12 mmol) in 1.0 mL of THF was added 30% aq. H_2O_2 (0.2 mL) and 3N aq. NaOH (0.1 mL) at 0 ^oC. The reaction was stirred for 24h at room temperature. At this point the reaction was quenched with aq. $Na_2S_2O_3$. Brine was added to the reaction mixture and extracted with EtOAc (3 × 5mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo, which was purified by silica gel chromatography (40% EtOAc in hexane) to afford the product as gum (25 mg, 78%). ^1H NMR (400 MHz, Benzene-d_6, mixture of rotamers) δ ppm major rotamer 7.34 (d, J = 8.4 Hz, 2H), major rotamer 7.09 – 6.84 (m, 3.3H), major rotamer 6.29 (m, 0.7H), major and minor rotamer 4.92-4.15 (m, 1.6H), major and minor rotamer 4.50-3.05 (m, 1.4H), major and minor rotamer 1.84 – 1.01 (m, 9H, including OH proton), major and minor diastereomer 0.91 – 0.66 (m, 3H). ^{13}C NMR (100 MHz, Benzene-d_6, mixture of rotamers) δ ppm 168.2, 136.6, 135.3, 129.9, 129.3, 111.7, 66.5, 41.8, 37.9, 36.3, 34.3, 29.2, 25.6, 23.2, 22.3, 13.9, 13.7. ESI MS m/z: $[M+H]^+$ 260.2

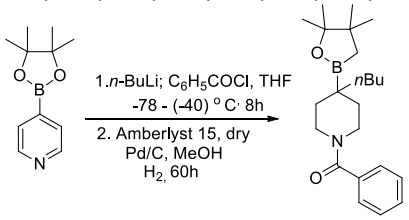


(4-(tert-butyl)-4-hydroxy-3,4-dihydropyridin-1(2H)-yl)(phenyl)methanone (61):followed same procedure as for **60**, Purified by silica gel chromatography (40% EtOAc in hexane), gum, yield 75%, ^1H NMR (400 MHz, Benzene-d_6, mixture of rotamers) δ ppm 7.57 – 7.18 (m, 2H), 7.05 – 6.92 (m, 3.3H), 6.29 (m, 0.7H), 4.50 (m, 1.6H), 4.85 (m, 0.34H), 3.16 (m, 1.4H), 1.42 (m, 2H), 1.25 (m, H, OH proton), 0.82 (s, 9H). ^{13}C NMR (100 MHz, Benzene-d_6, mixture of rotamers) δ ppm 168.3, 135.2, 129.9, 129.4, 128.4, 108.5, 70.5, 37.8, 36.4, 34.7, 29.6, 28.1, 24.6. ESI MS m/z: $[M+H]^+$ 260.2.



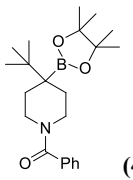
Yield 70%, dr 2:1

(4-butyl-2-(hydroxy(phenyl)methyl)-5,6-dihydropyridin-1(2H)-yl)(phenyl)methanone (62): To a stirred solution of compound **56** (20 mg, 0.05 mmol) in THF was added benzaldehyde (26 µL, 0.25 mmol). The reaction washeated to 70 $^oC$and stirred at temperature for 36h. Water was then added to the reaction mixture and the product was extracted with EtOAc (3 × 5mL). The organic layer was collected, dried over $Na_2SO_4$and then concentrated in vaccuo. The crude product was purified by silica gel chromatography (20% EtOAc in hexane) to afford the product as gum (19 mg, 70%). ^1H NMR (400 MHz, Acetone-d_6) major & minor diastereomer δ ppm 7.71 – 7.05 (m, 10H), major 5.40 (t, J = 2.9 Hz, 0.76H), 5.17 (m, 0.86H), 4.95 (dd, J = 6.9, 4.1 Hz, 0.75H), minor 4.88 (d, J = 3.8 Hz, 0.34H), major 4.83 (d, J = 4.2 Hz, 0.64H), minor 4.80 (d, J = 3.6 Hz, 0.26H), 4.70 (dd, J = 8.2, 3.6 Hz, 0.37H), 4.59 (dd, J = 13.0, 6.3 Hz, 0.38H), 4.22 (m, 0.38H), major 3.48 (dd, J = 13.5, 5.6 Hz, 0.81H), minor 2.99 (td, J = 12.5, 4.4 Hz, 0.44H), major 2.71 (td, J = 13.1, 3.8 Hz, 0.86H), minor 2.26 (m, 0.46H), 2.14 – 2.07 (m, 0.52H), major 2.01 – 1.90 (m, 3H), 1.71 (dd, J = 17.1, 3.8 Hz, 0.8H),) major & minor diastereomer 1.41 – 1.18 (m, 4H),) major & minor diastereomer 0.86 (t, J = 6.9 Hz, 3H).^{13}C NMR (100 MHz, Acetone-*d6*)) major & minor diastereomer δ ppm 170.9, 168.5, 142.4, 138.0, 137.2, 129.3, 128.7, 128.3, 127.9, 127.8, 127.7, 127.6, 127.4, 127.3, 127.2, 127.1, 126.7, 118.4, 117.9, 74.9, 74.8, 61.1, 60.9, 56.4, 56.3, 41.7, 36.6, 36.4, 35.2, 34.9, 28.1, 27.4, 21.9, 21.8, 13.3, 13.2. ESI MS m/z: $[M+H]^+$ 350.2.

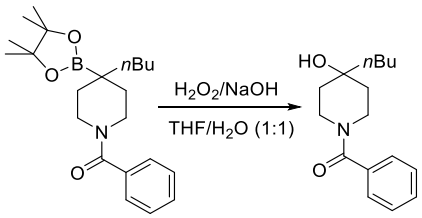


(4-butyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)piperidin-1-yl)(phenyl)methanone (63): To a stirred solution of 4-pyridineboronic acid pinacol ester (100 mg, 0.48 mmol)(recrystallized from $CHCl_3$ and hexanes) in dry THF (1 mL) at -78 $^oC$was

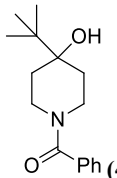
added ^{n}BuLi in hexane (0.21 mL, 0.53 mmol, 2.5 M in hexane) dropwise for 5 min under argon atmosphere. The reaction was stirred at -78 ^{o}C for 30 min then rt for 15 min. The reaction was degassed by three freeze-pump-thaw cyclesthenrecooled to -78 ^{o}C and a degassed THF solution (0.5 mL) of PhCOCl (55 µL, 0.48mmol) added slowly (10 minutes) into the reaction mixture. The reaction was stirred at -78 ^{o}C for 30 min then warmed to -40 ^{o}C and stirred for an additional 6h. The reaction mixture was then transferred to another flask containing dry amberlyst 15 (145 mg) and stirred for 10 minutes under argon atmosphere. The reaction was allowed to settle for10 minutes at which point the solvent was transferred into a flask containing 10% Pd/C and degassed methanol (4mL). The reaction flask was washed with dry degassed THF (0.5 mL) and transferred to the flask. The reaction vessel was then charged with hydrogen gas (balloon) and stirred at rt for 20h. Another 10 mol% of Pd/C was added to the reaction and stirred for 40h. The reaction was filtered through Celite and washed with methanol (3 × 5mL). The filtrate was concentrated to afford yellow oil, which was purified by silica gel chromatography (15% EtOAc in hexane) to afford the product as gum (122 mg, 69%). ^{1}H NMR ((400 MHz, $CDCl_3$) δ ppm 7.35 (s, 5H), 4.55 (d, J = 13.3 Hz, 1H), 3.62 (d, J = 13.5 Hz, 1H), 2.90 (dt, J = 77.6, 12.9 Hz, 2H), 2.12 – 1.75 (m, 2H), 1.41 – 1.00 (m, 20H), 0.85 (t, J = 6.9 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 170.2, 136.5, 129.3, 128.3, 126.8, 83.4, 47.3, 41.7, 39.9, 36.1, 35.1, 34.3, 28.8, 27.7, 23.5, 22.8, 14.1, 13.9. ^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 33.50, ESI MS m/z: $[M+H]^+$ 372.2.



(4-(tert-butyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)piperidin-1-yl)(phenyl)methanone (64): Purified by silica gel chromatography (25% EtOAc in hexane), gum, yield 74%, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.34 (m, 5H), 4.68 (d, J = 13.6 Hz, 1H), 3.67 (d, J = 12.9 Hz, 1H), 2.94 (t, J = 13.3 Hz, 1H), 2.79 – 2.56 (m, 1H), 1.90 (d, J = 13.0 Hz, 1H), 1.73 (d, J = 12.8 Hz, 1H), 1.48 – 1.31 (m, 1H), 1.29 – 1.11 (m, 13H), 0.86 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 170.0, 136.5, 129.2, 128.3, 126.8, 83.5, 47.6, 42.1, 34.2, 33.6, 29.4, 28.5, 27.2, 26.7, 25.1.^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 34.02, ESI MS m/z: $[M+H]^+$ 372.2.

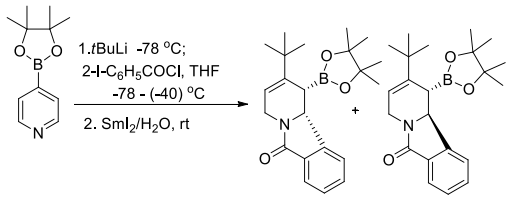


(4-butyl-4-hydroxypiperidin-1-yl)(phenyl)methanone (65): To a stirred solution of compound **63** (50 mg, 0.13 mmol) in 1.0 mL of THF/H_2O (1:1) was added 30% aq. H_2O_2 (0.2 mL) and 3N aq. NaOH (0.1 mL) at 0 ^{o}C. This mixture wasthen warmed to rt and stirred for 24h. The reaction was then cooled to 0 ^{o}C and an additional 30% aq. H_2O_2 (0.1 mL) and 3N aq. NaOH (0.1 mL) was added. The reaction was stirred for another 40h at rt at which point it was quenched with aq. $Na_2S_2O_3$. Brine was added to the reaction mixture and the product was extracted with EtOAc (3 × 5mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo giving the crude product which was purified by silica gel chromatography (40% EtOAc in hexane) to afford the product as gum (30 mg, 86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ ppm ^{1}H NMR (400 MHz,) δ 7.37 (m, 5H), 4.55 – 4.26 (m, 1H), 3.59 – 3.12 (m, 3H), 1.80 – 1.16 (m, 11H, including OH proton), 1.03 – 0.74 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 170.2, 136.2, 129.5, 128.4, 126.8, 69.9, 43.8, 43.0, 38.3, 37.3, 36.6, 24.9, 23.1, 14.0. ESI MS m/z: $[M+H]^+$ 262.2.

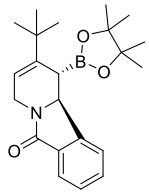


(4-(tert-butyl)-4-hydroxypiperidin-1-yl)(phenyl)methanone (66): purified by silica gel chromatography(40% EtOAc/hexane), gum, yield 88%,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.36 (m, 5H), 4.65 – 4.51 (m, 1H), 3.55 (d, J = 13.5 Hz, 1H), 3.34 (t, J = 13.0 Hz, 1H), 3.06 (t, J = 12.5 Hz, 1H), 1.94 – 1.46 (m, 5H, including OH proton), 0.91 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 170.1, 136.2, 129.4, 128.4, 126.8, 73.8, 43.8, 38.2, 37.4, 31.6, 30.8, 24.8. ESI MS m/z: $[M+H]^+$ 262.2.

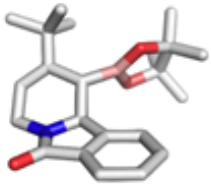
General procedure for SmI_2 mediated cyclization of dihydropyridine intermediate



To a stirred solution of 4-pyridineboronic acid pinacol ester (50 mg, 0.24 mmol)(recrystallized from $CHCl_3$ and hexanes) in dry THF (1 mL) at -78 °C was added a*t*BuLi solution in pentane (0.15 mL, 0.26 mmol). The reaction was stirred at -78 °C for 30 min then rt for 15 min at which point the reaction was degassed by three freeze-pump-thaw cycles. The reaction was then recooled to -78 °C. In another vial a THF (0.2 mL) solution of 2-I-PhCOCl (69 mg, 0.26 mmol) was degassed by three freeze-pump-thaw cycles and added slowly (10 minutes) into the reaction mixture. The reaction was stirred at -78 °C for 30 min then warmed to -40 °C and stirred for overnight (15h) at -40 °C.After that the reaction mixture was kept outside at room temperature for 10 minutes.. In the meantime SmI_2 solution in THF with water was prepared. In a dry reaction flask 0.1 M SmI_2 solution (7.2 mL, 0.72 mmol) in THF was transferred followed by addition of degassed water (0.1 mL, 5.52 mmol) and stirred for 5 minutes under an inert atmosphere of argon. The reaction mixture was then transferred into the SmI_2 mixture via cannula, dropwise with constant stirring. Extra 0.1 M SmI_2 solution (3- 4 equivalent) in THF was added to the reaction mixture to maintain the blue color. The reaction was stirred for an additional 30 minutes at which point it was quench with water. The reaction mixture was filtered through Celite. Brine was added to the filtrate and the product was extracted with EtOAc (3 × 15mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo to give a yellow gum.This crude material was purified by silica gel chromatography (30% EtOAc in hexane) to afford the product as white solid as a mixture of diastereomer (72 mg, 82%), dr*anti: syn* (2:1). The diastereomers are separated by preparative TLC (25% EtOAc in hexane).

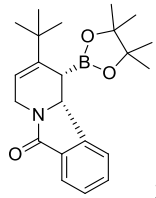


anti-**68**

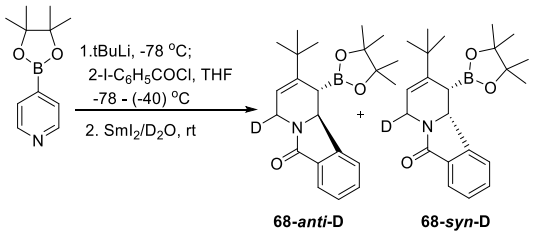


X-ray structure of *anti*-**68**

2-(tert-butyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*anti*-68):The relative stereochemistry was confirmed by X-ray crystallography.A single crystal suitable forX-ray crystallography was grown by slow evaporation of ethyl acetate and pentane at room temperature.Purified by preparative TLC (25% EtOAc in hexane), white solid, mp 190-192 ° C, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.82 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.69 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.51 (td, *J* = 7.5, 1.2 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 5.79 (dt, *J* = 5.8, 1.9 Hz, 1H), 4.68 – 4.54 (m, 2H), 3.75 (dt, *J* = 17.6, 2.4 Hz, 1H), 2.14 – 2.05 (m, 1H), 1.40 (s, 6H), 1.35 (s, 6H), 1.05 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.1, 146.8, 144.4, 132.2, 131.2, 127.9, 123.5, 122.3, 116.2, 84.2, 57.3, 38.5, 36.1, 30.4, 29.2 (carbon attach to boron), 25.6, 24.8. ^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 33.18. ESI MS m/z: $[M+H]^+$ 368.2.

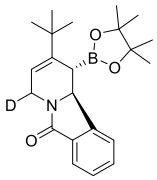


2-(tert-butyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*syn*-68): Purified by preparative TLC (25% EtOAc in hexane), white solid, mp 138 -140 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.83 (dt, *J* = 7.4, 1.0 Hz, 1H), 7.60 – 7.47 (m, 2H), 7.44 (td, *J* = 7.4, 1.2 Hz, 1H), 5.65 (dd, *J* = 4.0, 2.5 Hz, 1H), 4.58 (dd, *J* = 18.4, 2.5 Hz, 1H), 4.46 (d, *J* = 4.6 Hz, 1H), 3.94 (ddt, *J* = 18.4, 4.0, 1.2 Hz, 1H), 2.69 (d, *J* = 4.5 Hz, 1H), 1.12 (s, 9H), 0.75 (s, 6H), 0.71 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 167.5, 145.3, 144.7, 134.2, 130.7, 128.2, 123.2, 123.1, 113.4, 83.2, 57.8, 40.5, 35.9, 28.9, 27.4 (carbon attached to boron show weak broad peak), 24.4, 24.2.^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 32.32. ESI MS m/z: , $[M+H]^+$ 368.2.



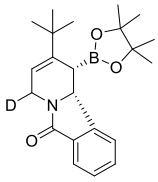
68-*anti*-D **68-*syn*-D**

Synthesized using same procedure as **68** except H_2O was replaced by D_2O. The crude material was purified by silica gel chromatography (30% EtOAc in hexane), yield 78%, dr*anti: syn* (2:1).



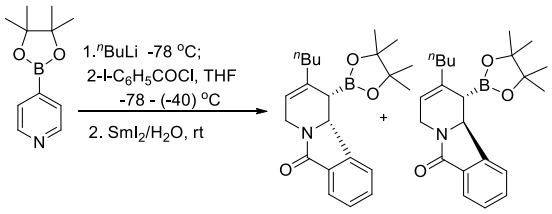
68-*anti*-D

Purified by preparative TLC (25% EtOAc in hexane), white solid, mp 195-197 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.82 (d, *J* = 7.6 Hz, 1H), 7.73 – 7.64 (m, 1H), 7.51 (td, *J* = 7.5, 1.3 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 5.78 (p, *J* = 1.9 Hz, 1H), 4.58 (d, *J* = 9.1 Hz, 1H), 4.60, 3.73 (m, 1H), 2.09 (dt, *J* = 9.2, 2.4 Hz, 1H), 1.40 (s, 6H), 1.35 (s, 6H) 1.04 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.1, 146.9, 144.5, 132.2, 131.2, 127.9, 123.5, 122.3, 116.1, 84.2, 57.2, 38.4, 38.2, 37.9, 36.0, 30.4, 28.9 (boron attached to the carbon broad peak), 25.6, 24.8.^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 33.33. ESI MS m/z: $[M+H]^+$ 369.3.

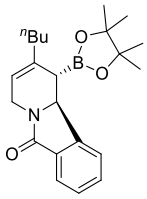


68-*syn*-D

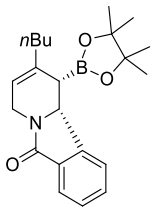
Purified by preparative TLC (25% EtOAc in hexane), white solid, mp 125-127 °C, ^{1}H NMR (400 MHz, Acetone-d6) δ ppm 7.70 – 7.64 (m, 2H), 7.57 – 7.52 (td, *J* = 7.2, 1.6 Hz), 7.49 – 7.44 (1H, m), 5.64 (m, 1H), 4.50 (d, *J* = 4.4 Hz, 1H), 4.41, 3.80 (m, 1H), 2.77 (dd, *J* = 4.4, 1.2 Hz, 1H), 1.10 (s, 9H), 0.72 (s, 6H), 0.69 (s, 6H). ^{13}C NMR (100 MHz, Acetone-d6) δ ppm 166.5, 145.5, 145.1, 134.5, 130.4, 128.0, 123.7, 122.4, 113.3, 82.7, 57.4, 40.0, 39.8, 39.6, 35.6, 28.5, 23.9, 23.7 (carbon attached to boron is not observed). ^{11}B NMR (96 MHz, Acetone-d6) δ ppm 31.88. ESI MS m/z: $[M+H]^+$ 369.3.



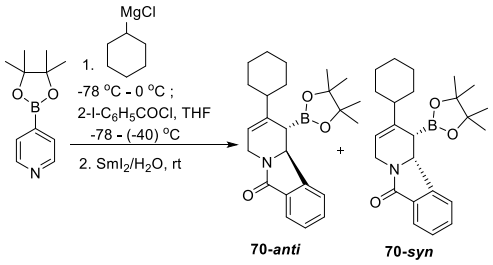
Synthesized using same procedure as **68**, The crude material was purified by silica gel chromatography (30% EtOAc in hexane), yield 76%, dr*anti: syn* (2:1).



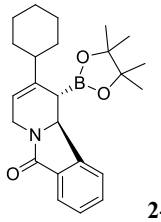
2-butyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*anti*-69): Purified by preparative TLC (25% EtOAc in hexane, gum, ^{1}H NMR (400 MHz, Acetone-d_6) δ ppm 7.72 (dd, J = 7.5, 1.2 Hz, 1H), 7.66 – 7.55 (m, 2H), 7.49 (td, J = 7.2, 1.5 Hz, 1H), 5.63 (m, 1H), 4.63 – 4.55 (d, J = 10.8 Hz, 1H), 4.55 – 4.45 (m, 1H), 3.72 (ddt, J = 18.0, 4.4, 2.1 Hz, 1H), 2.17 – 2.08 (m, 2H), 1.78 (dd, J = 10.9, 3.7 Hz, 1H), 1.58 – 1.14 (m, 16H), 0.85 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ ppm 165.0, 146.6, 135.3, 132.5, 131.0, 128.0, 122.9, 122.3, 116.9, 84.2, 56.3, 38.4, 36.8, 29.7, 23.9, 23.4, 13.3 (carbon attached to boron is not observed). ^{11}B NMR (96 MHz, Acetone-d_6) δ ppm 32.82. ESI MS m/z: $[M+H]^+$ 368.2.



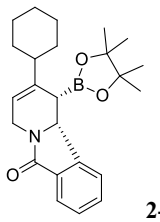
2-butyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*syn*-69): Purified by preparative TLC (25% EtOAc in hexane), gum, ^{1}H NMR (400 MHz, Acetone-d_6) δ ppm δ 7.68 (d, J = 7.4 Hz, 1H), 7.62 – 7.49 (m, 2H), 7.46 (td, J = 7.3, 1.1 Hz, 1H), 5.55 (td, J = 3.2, 1.5 Hz, 1H), 4.56 (d, J = 5.1 Hz, 1H), 4.44 (dt, J = 17.4, 3.0, 2.6, 1.3 Hz, 1H), 3.75 (ddt, J = 19.4, 4.5, 2.0 Hz, 1H), 2.53 (d, J = 5.5 Hz, 1H), 2.16 – 2.06 (m, 2H), 1.54 – 1.25 (m, 4H), 0.91 (t, J = 7.3 Hz, 3H), 0.78 (s, 6H), 0.69 (s, 6H). ^{13}C NMR (100 MHz, Acetone-d_6) δ ppm 166.2, 145.4, 136.6, 134.4, 130.4, 127.8, 123.1, 122.4, 115.6, 82.7, 56.1, 39.4, 36.9, 29.7, 23.9, 23.4, 22.2, 13.3 (carbon attached to boron is not observed). ^{11}B NMR (96 MHz, Acetone-d_6) δ ppm 30.90. ESI MS m/z: $[M+H]^+$ 368.2.



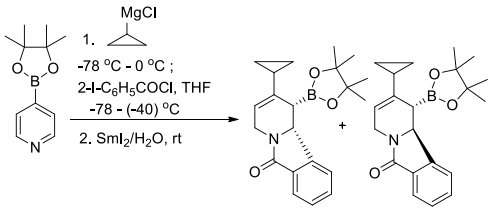
To a stirred solution of 4-pyridineboronic acid pinacol ester (50 mg, 0.24 mmol)(recrystallized from $CHCl_3$ and hexanes) in dry THF (1.0 mL) at -78 ^{o}C was added 1.8 M cyclohexylmagnesium chloride (145 µL, 0.26 mmol) dropwise for 5 min under an inert atmosphere of argon. The reaction was stirred at -78 ^{o}C for 10 min then rt for 2 h. The reaction was degassed by three freeze-thaw cycle. The reaction was recooled to -78 ^{o}C. In another vial a THF (0.2 mL) solution of 2-I-PhCOCl (69 mg, 0.26 mmol) was degassed by three freeze-thaw cycle and added slowly (10 minutes) into the reaction mixture. The reaction was stirred at -78 ^{o}C for 30 min then warmed to -40 ^{o}C and stirred for overnight (15h) under an inert atmosphere of argon. After that the reaction mixture was kept outside at room temperature for 10 minutes. In the meantime SmI_2 solution in THF with water was prepared. In a dry reaction flask 0.1 M SmI_2 solution (7.2 mL, 0.72 mmol) in THF was transferred followed by addition of degassed water (0.1 mL, 5.52 mmol) and stirred for 5 minutes under an inert atmosphere of argon. The reaction mixture was transferred into the SmI_2 mixture by cannula dropwise with constant stirring under an inert atmosphere of argon. Extra 0.1 M SmI_2 solution (3- 4 equivalent) in THF was added to the reaction mixture to persist the blue color. The reaction was stirred for another 30 minutes and then quench with water. The reaction mixture was filtered through Celite. Brine was added to the reaction mixture and extracted with EtOAc (3 × 15mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo to give yellow gum.The crude product was purified by Silica gel chromatography (30% EtOAc in hexane) to afford the product as gum as a mixture of diastereomer (75 mg, 80%, dr 2:1). The diastereomers are separated by preparative TLC (25% EtOAc in hexane).



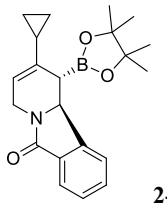
2-cyclohexyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*anti*-70): Purified by preparative TLC 25% EtOAc in hexane, mp 230-232 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.86 (dt, *J* = 7.4, 1.1 Hz, 1H), 7.54 – 7.34 (m, 3H), 5.56 (dt, *J* = 4.8, 2.5 Hz, 1H), 4.74 – 4.54 (m, 2H), 3.83 (ddt, *J* = 18.2, 3.0, 1.7 Hz, 1H), 2.01 (dd, *J* = 10.0, 3.1 Hz, 1H), 1.94 – 1.64 (m, 7H), 1.41 (s, 12H), 1.34 – 0.70 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.3, 146.5, 140.2, 132.4, 130.9, 128.0, 123.6, 121.9, 114.6, 84.2, 56.7, 44.1, 39.0, 33.5, 31.4, 26.8, 26.7, 26.3, 25.5, 25.3 (carbon attached to boron is not observed). ^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 32.46. ESI MS m/z: $[M+H]^+$ 394.3.



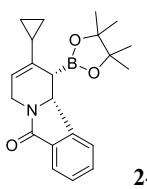
2-cyclohexyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*syn*-70): separated by preparative TLC 25% EtOAc in hexane, solid,mp 130-132 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.85 – 7.78 (m, 1H), 7.58 – 7.35 (m, 3H), 5.53 (t, *J* = 2.8 Hz, 1H), 4.56 (ddd, *J* = 18.4, 2.7, 1.3 Hz, 1H), 4.47 (d, *J* = 4.8 Hz, 1H), 3.93 – 3.82 (m, 1H), 2.50 (d, *J* = 4.8 Hz, 1H), 1.97 – 1.62 (m, 5H), 1.43 – 1.21 (m, 5H), 0.75 (s, 6H), 0.70 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 167.4, 144.9, 141.9, 134.2, 130.7, 128.1, 123.1, 122.7, 114.4, 83.1, 57.0, 45.6, 40.1, 31.9, 29.5 (carbon attached to boron show weak broad peak), 26.6, 26.2, 24.3, 24.0.^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 31.90. ESI MS m/z: $[M+H]^+$394.3.



Synthesized using same procedure as **71**, The crude material was purified by silica gel chromatography (30% EtOAc in hexane), yield 64%,dr*anti: syn* (2:1).

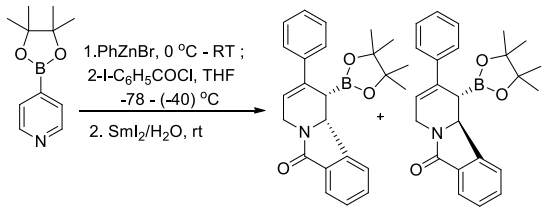


2-cyclopropyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*anti*-71): separated by preparative TLC 25% EtOAc in hexane, solid, mp 191-192 ^{o}C, ^{1}H NMR (400 MHz, Acetone-d_6) δ ppm 7.71 (dt, *J* = 7.5, 1.1 Hz, 1H), 7.68 – 7.56 (m, 2H), 7.53 – 7.45 (m, 1H), 5.53 (tt, *J* = 4.2, 1.8 Hz, 1H), 4.67 – 4.53 (m, 1H), 4.55 – 4.33 (m, 1H), 3.78 – 3.59 (m, 1H), 1.94 – 1.76 (m, 1H), 1.41 (s, 12H), 1.38 (m, 1H), 0.79 – 0.47 (m, 3H), 0.46 – 0.25 (m, 1H). ^{13}C NMR (100 MHz, Acetone-d_6) δ ppm 165.0, 146.6, 136.9, 132.5, 131.0, 128.0, 122.9, 122.4, 115.0, 84.1, 56.4, 38.3, 24.7, 24.3, 15.9, 6.4, 5.1 (carbon attached to boron is not observed). ^{11}B NMR (96 MHz, Acetone-d_6) δ ppm 32.64. ESI MS m/z: $[M+H]^+$ 352.2.

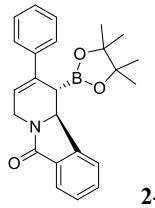


2-cyclopropyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*syn*-71): separated by preparative TLC 25% EtOAc in hexane, solid, mp 120-122^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.81 (dt, *J* = 7.4, 1.0 Hz, 1H), 7.55 – 7.33 (m, 3H), 5.54 – 5.48 (m, 1H), 4.63 – 4.47 (m, 2H), 3.85 (dt, *J* = 18.2, 2.0 Hz, 1H), 2.40 (d,

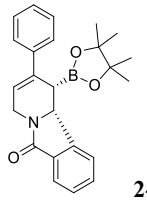
J= 4.5 Hz, 1H), 1.28 – 1.22 (m, 1H), 0.79 (s, 6H), 0.70 (s, 6H), 0.67 – 0.57 (m, 3H), 0.48 – 0.40 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 167.3, 144.8, 137.3, 134.0, 130.7, 128.2, 123.2, 122.7, 113.9, 83.2, 56.6, 39.9, 29.7 (carbon attached to boron show weak broad peak), 24.4, 23.9, 17.1, 5.9, 4.1.^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 31.28. ESI MS m/z: $[M+H]^+$ 352.2.



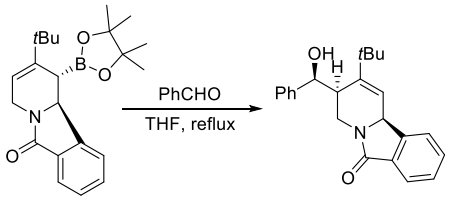
To a stirred solution of 4-pyridineboronic acid pinacol ester (50 mg, 0.24 mmol)(recrystallized from $CHCl_3$ and hexanes) in dry THF (0.5 mL) at 0 °C was added a solution of phenylzinc bromide in THF (650 µL, 0.26 mmol, 0.4M) dropwise for 5 min under argon atmosphere. The reaction was stirred at 0 °C for 20 min then rt for 24 h under argon atmosphere. The reaction was degassed by three freeze-pump-thaw cycles and then recooled to -78 °C. In another vial a THF (0.2 mL) solution of 2-I-PhCOCl (69 mg, 0.26 mmol) was degassed by three freeze-pump-thaw cycles and added slowly (10 minutes) into the reaction mixture. The reaction was stirred at -78 °C for 30 min then warmed to -40 °C and stirred for overnight (15h) under argon atmosphere. After that the reaction mixture was kept outside at room temperature for 5 minutes. In the meantime SmI_2 solution in THF with water was prepared. In a dry reaction flask 0.1 M SmI_2 solution (7.2 mL, 0.72 mmol) in THF was transferred followed by addition of degassed water (0.1 mL, 5.52 mmol) and stirred for 5 minutes under an inert atmosphere of argon. The reaction mixture was transferred into the SmI_2 mixture via cannula dropwise with constant stirring under argon atmosphere. Extra 0.1 M SmI_2solution (3 - 4 equivalents) in THF was added to the reaction mixture to maintainthe blue color. The reaction was stirred for another 30 minutes at which point it was quenched with water. The reaction mixture was filtered through Celite. Brine was added to the filtrate and the product was extracted with EtOAc (3 × 15mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo to give yellow gum, which was purified by silica gel chromatography (30% EtOAc in hexane) to afford the product as white solid as a mixture of diastereomer (52 mg, 56%, dr 1:1). The diastereomers are separated by preparative TLC (25% EtOAc in hexane).



2-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*anti*-72): Purified by preparative TLC (25% EtOAc in hexane), mp 200-202 °C, ^{1}H NMR (400 MHz, Acetone-d_6) δ ppm δ 7.74 – 7.47 (m, 6H), 7.39 – 7.24 (m, 3H), 6.26 (t, *J* = 3.3 Hz, 1H), 4.78 – 4.73 (m, 1H), 4.71 – 4.62 (m, 1H), 4.06 – 3.91 (m, 1H), 3.18 – 3.04 (m, 1H), 0.71 (s, 6H), 0.63 (s, 6H). ^{13}C NMR (100 MHz, Acetone-d_6) δ ppm 166.2, 145.2, 140.9, 136.0, 134.3, 130.6, 128.3, 128.1, 127.2, 125.5, 123.4, 122.6, 118.8, 82.9, 56.2, 39.9, 23.7, 23.3.^{11}B NMR (96 MHz, Acetone-d_6) δ ppm 31.40. ESI MS m/z: $[M+H]^+$ 388.2.

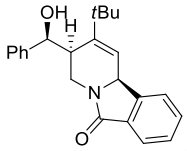


2-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*syn*-72): purified by preparative TLC (25% EtOAc in hexane), gum,^{1}H NMR (400 MHz, Acetone-d_6) δ ppm7.77 – 7.66 (m, 2H), 7.63 – 7.46 (m, 4H), 7.42 – 7.32 (m, 2H), 7.32 – 7.22 (m, 1H), 6.26 (t, *J* = 3.3 Hz, 1H), 4.76 (d, *J* = 4.9 Hz, 1H), 4.72 – 4.62 (m, 1H), 3.99 (dtd, *J* = 19.5, 2.7, 1.1 Hz, 1H), 3.18 – 3.08 (m, 1H), 0.71 (s, 6H), 0.63 (s, 6H). ^{13}C NMR (100 MHz, Acetone-d_6) δ ppm 166.2, 145.2, 140.9, 135.9, 134.3, 130.6, 128.3, 128.1, 127.2, 125.5, 123.4, 122.6, 118.8, 82.9, 56.2, 39.9, 23.7, 23.3(carbon attached to boron is not observed). ^{11}B NMR (96 MHz, $CDCl_3$) δ ppm 32.21. ESI MS m/z: $[M+H]^+$388.2.

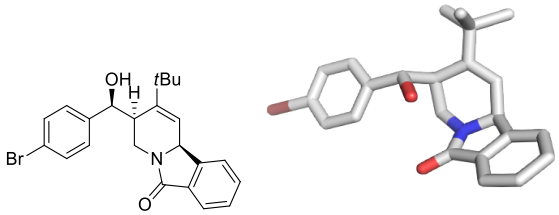


68 (*anti*)

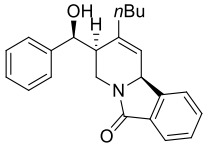
To a stirred solution of compound **68(*anti*)** (25 mg, 0.07 mmol) in dry THF (0.2 mL) was added degassed benzaldehyde (40 µL, 0.35 mmol) under argon atmosphere. The reaction was heated to 70 ^{o}Cand stirred at temperature for 24h. Upon completion the reaction was quenched with water. Brine was added to the reaction mixture and the product was extracted with EtOAc (3 × 10mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo giving the crude productwhich was purified by silica gel chromatography (25% EtOAc in hexane) to afford the product as white solid (20 mg, 84%).



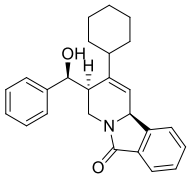
2-(tert-butyl)-3-hydroxy(phenyl)methyl)-3,4-dihydropyrido[2,1-a]isoindol-6(10bH)-one (74): Based on crude NMR dr 18:1, Purified by silica gel chromatography (25% EtOAc in hexane), white solid, yield 84%, mp 205-206 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.80 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.65 – 7.08 (m, 8H), 6.16 (d, *J* = 2.0 Hz, 1H), 5.52 – 5.36 (m, 1H), 5.32 (t, *J* = 3.1 Hz, 1H), 3.83 (dd, *J* = 13.6, 2.5 Hz, 1H), 3.58 (ddd, *J* = 13.5, 7.9, 0.9 Hz, 1H), 3.08 (dt, *J* = 8.0, 2.9 Hz, 1H), 2.41 (d, *J* = 3.0 Hz, 1H), 1.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 168.4, 149.0, 145.5, 142.8, 132.6, 131.4, 128.6, 128.0, 127.6, 125.7, 123.5, 122.9, 121.7, 75.2, 58.0, 41.7, 38.1, 36.4, 29.9. ESI MS m/z: [M-H_2O] 330.2.



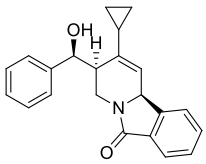
4-bromophenyl(hydroxy)methyl)-2-(tert-butyl)-3,4-dihydropyrido[2,1-a]isoindol-6(10bH)-one: The relative stereochemistry was determined by X-ray crystallography. A single crystal suitable forX-ray crystallography was grown by slow evaporation of ethyl acetate and pentane at room temperature.Based on crude NMR dr 16:1, Purified by silica gel chromatography (25% EtOAc in hexane), solid, mp 229-230 ^{o}C, yield 75%,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.77 (d, *J* = 7.5 Hz, 1H), 7.63 – 7.13 (m, 7H), 6.14 (d, *J* = 2.0 Hz, 1H), 5.34 (d, *J* = 2.2 Hz, 1H), 5.24 (t, *J* = 3.2 Hz, 1H), 3.75 (dd, *J* = 13.6, 2.7 Hz, 1H), 3.55 (dd, *J* = 13.5, 7.7 Hz, 1H), 3.01 (dt, *J* = 6.9, 3.0 Hz, 1H), 2.58 (d, *J* = 3.7 Hz, 1H), 1.07 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 168.3, 148.7, 145.3, 141.7, 132.5, 131.6, 131.5, 128.1, 127.5, 123.5, 123.1, 121.6, 121.4, 74.4, 57.9, 41.7, 38.0, 36.4, 29.7. ESI MS m/z: $[M+H]^+$ 426.1.



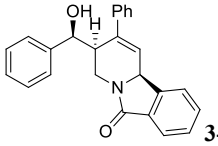
2-butyl-3-((S)-hydroxy(phenyl)methyl)-3,4-dihydropyrido[2,1-a]isoindol-6(10bH)-one (75) : Based on crude NMR dr 14:1, by silica gel chromatography (25% EtOAc in hexane), solid, mp 203-205 ^{o}C, yield 76%,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.77 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.57 – 7.24 (m, 8H), 5.98 (m, 1H), 5.30 (m, 1H), 4.99 (m, 1H), 3.99 (dd, *J* = 13.5, 7.0 Hz, 1H), 3.36 (dd, *J* = 13.5, 10.0 Hz, 1H), 2.75 (m, 1H), 2.39 – 2.09 (m, 2H), 1.85 (d, *J* = 2.5 Hz, 1H), 1.53 – 1.09 (m, 4H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 167.1, 144.4, 141.3, 138.8, 132.3, 131.4, 128.6, 128.1, 127.6, 125.3, 123.7, 122.9, 121.8, 71.1, 57.5, 43.4, 35.7, 34.1, 29.9, 22.5, 13.9. ESI MS m/z: $[M+H]^+$ 348.2.



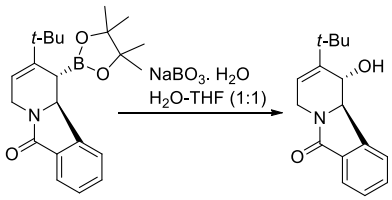
2-cyclohexyl-3-((S)-hydroxy(phenyl)methyl)-3,4-dihydropyrido[2,1-a]isoindol-6(10bH)-one (76) : Based on crude NMR dr 15:1, Purified by silica gel chromatography (25% EtOAc in hexane), solid, mp 190-193 ^{o}C, yield 77%,^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.65 – 7.18 (m, 8H), 5.95 (dd, *J* = 2.8, 1.2 Hz, 1H), 5.28 (d, *J* = 2.8 Hz, 1H), 5.01 (dd, *J* = 3.0, 1.7 Hz, 1H), 3.95 (dd, *J* = 13.5, 7.2 Hz, 1H), 3.39 (dd, *J* = 13.5, 9.3 Hz, 1H), 2.88 (m, 1H), 2.12 (m, 1H), 1.93 (d, *J* = 2.0 Hz, 1H), 1.90 – 1.65 (m, 4H), 1.43 – 0.65 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 167.1, 144.5, 143.8, 141.4, 132.4, 131.4, 128.6, 128.1, 127.6, 125.3, 123.7, 121.8, 121.1, 71.4, 57.5, 42.9, 40.2, 36.0, 33.7, 31.0, 26.8, 26.5, 26.3. ESI MS m/z: $[M+H]^+$ 374.2.



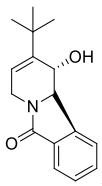
2-cyclopropyl-3-((R)-hydroxy(phenyl)methyl)-3,4-dihydropyrido[2,1-a]isoindol-6(10bH)-one (77) : Based on crude NMR dr 12:1, Purified by silica gel chromatography (25% EtOAc in hexane), solid, mp 228 -230 ^{o}C, yield 74%,^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.74 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.59 – 7.25 (m, 8H), 5.89 (t, *J* = 1.8 Hz, 1H), 5.58 (d, *J* = 2.7 Hz, 1H), 4.96 (dd, *J* = 3.4, 1.9 Hz, 1H), 4.00 (dd, *J* = 13.6, 7.0 Hz, 1H), 3.35 (dd, *J* = 13.5, 10.2 Hz, 1H), 2.74 (dd, *J* = 9.6, 2.7 Hz, 1H), 1.51 (m, 1H), 0.88 – 0.47 (m, 3H), 0.31 (dtd, *J* = 9.6, 5.7, 4.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 161.9, 139.0, 136.4, 134.9, 127.1, 126.2, 123.4, 122.9, 122.3, 120.2, 118.5, 116.6, 116.4, 66.4, 52.2, 39.9, 30.6, 9.2, 1.2, -0.9. ESI MS m/z: $[M]^+$ 330.2.



3-((R)-hydroxy(phenyl)methyl)-2-phenyl-3,4-dihydropyrido[2,1-a]isoindol-6(10bH)-one (78): Based on crude NMR dr 11:1, Purified by silica gel chromatography (25% EtOAc in hexane), solid, mp 208 -210 ^{o}C, yield 78%, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.79 (d, *J* = 7.5 Hz, 1H), 7.56 – 7.26 (m, 13H), 6.26 (m, 1H), 5.15 (m, 1H), 4.98 (t, *J* = 3.0 Hz, 1H), 4.16 (dd, *J* = 13.5, 7.0 Hz, 1H), 3.51 (dd, *J* = 13.6, 9.9 Hz, 1H), 3.33 (m, 1H), 1.66 (d, *J* = 3.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 167.3, 143.8, 141.1, 140.4, 140.1, 132.3, 131.5, 128.8, 128.5, 128.3, 127.8, 127.5, 126.6, 125.2, 123.8, 121.9, 71.2, 57.7, 43.5, 35.5. ESI MS m/z: $[M+H]^+$ 368.2.

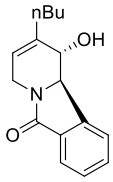


2-(tert-butyl)-1-hydroxy-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one: To a stirred solution of the boronic acid pinacole ester (30 mg, 0.08 mmol) in 1.0 mL of THF/water (1:1) was added $NaBO_3.H_2O$ (24 mg, 0.24 mmol) at 0 ^{o}C. This reaction was then warmed to rt and stirred for 24hUpon completion the reaction was quenched with water. Brine was added to the reaction mixture and the product was extracted with EtOAc (3 × 5mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo giving the crude product ,which was purified by silica gel chromatography (40% EtOAc in hexane) to afford the product as gum (17 mg, 82%).

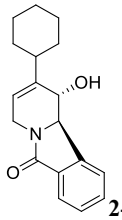


2-(tert-butyl)-1-hydroxy-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (79): Purified by silica gel chromatography (40% EtOAc in hexane), gum, yield 82%, ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.66 (ddt, *J* = 12.3, 7.6, 1.0 Hz, 2H), 7.60 – 7.32 (m, 2H), 5.79 (t, *J* = 3.2 Hz, 1H), 4.84 (dd, *J* = 8.7, 2.3 Hz, 1H), 4.71 – 4.42 (m, 2H), 3.80 (dd, *J* = 18.8, 3.3 Hz, 1H), 3.55 (d, *J* =

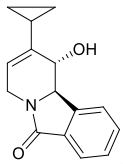
8.7 Hz, 1H), 2.83 (bs, 1H), 1.19 (s, 9H); ^{13}C NMR (100 MHz, Acetone-d_6) δ 167.1, 146.3, 143.9, 134.4, 130.6, 127.6, 122.9, 122.3, 117.8, 117.8, 63.7, 61.7, 39.8, 34.9, 28.8. ESI MS m/z: $[M+H]^+$ 258.2.



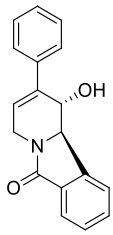
2-butyl-1-hydroxy-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (80): purified by silica gel chromatography (40% EtOAc in hexane), gum, yield 80%, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.87 (dt, J = 7.3, 1.1 Hz, 1H), 7.84 – 7.75 (m, 1H), 7.56 (td, J = 7.4, 1.3 Hz, 1H), 7.50 (td, J = 7.4, 1.1 Hz, 1H), 5.62 (m, 1H), 4.68 – 4.48 (m, 1H), 4.24 (dd, J = 8.9, 1.0 Hz, 1H), 4.04 – 3.86 (m, 1H), 3.88 – 3.67 (m, 1H), 2.45 – 2.23 (m, 2H), 2.23 – 2.07 (m, 1H), 1.53 – 1.18 (m, 4H), 0.89 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.9, 144.9, 138.9, 132.4, 131.4, 128.5, 123.6, 123.2, 119.0, 70.9, 60.6, 39.4, 31.4, 30.1, 22.5, 13.9. ESI MS m/z: $[M+H]^+$258.2.



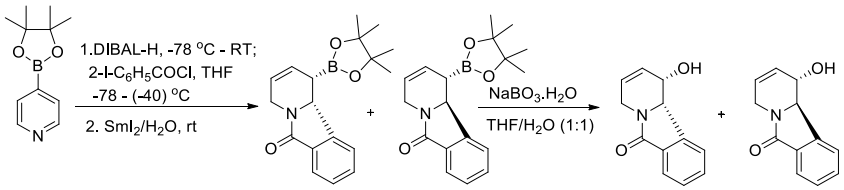
2-cyclohexyl-1-hydroxy-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (81): Purified by silica gel chromatography (40% EtOAc in hexane), yield 82%, ^{1}H NMR (400 MHz, Acetone-d_6) δ ppm δ 7.85 (dd, J = 7.6, 0.9 Hz, 1H), 7.72 (dt, J = 7.3, 0.9 Hz, 1H), 7.58 (td, J = 7.5, 1.3 Hz, 1H), 7.51 (td, J = 7.5, 1.0 Hz, 1H), 5.62 – 5.50 (m, 1H), 4.89 (d, J = 8.4 Hz, 1H), 4.50 – 4.34 (m, 1H), 4.24 (dd, J = 8.9, 0.9 Hz, 1H), 3.91 (m, 1H), 3.76 (dd, J = 18.2, 2.3 Hz, 1H), 2.49 (m, 1H), 1.96 – 1.55 (m, 5H), 1.45 – 0.79 (m, 5H). ^{13}C NMR (100 MHz, Acetone-d6) δ ppm 165.6, 145.8, 145.3, 132.7, 130.9, 128.0, 123.7, 122.6, 115.9, 69.7, 60.4, 39.0, 37.7, 33.1, 31.3, 26.7, 26.5, 26.3. ESI MS m/z: $[M+H]^+$ 284.2.



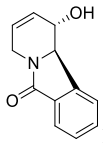
2-cyclopropyl-1-hydroxy-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (82): Purified by silica gel chromatography (40% EtOAc in hexane), yield 82%, ^{1}H NMR (400 MHz, Acetone-d_6) δ ppm 7.86 (dt, J = 7.5, 0.8 Hz, 1H), 7.71 (dt, J = 7.4, 1.0 Hz, 1H), 7.59 (td, J = 7.5, 1.2 Hz, 1H), 7.54 – 7.48 (m, 1H), 5.51 – 5.46 (m, 1H), 5.01 (dd, J = 7.7, 1.5 Hz, 1H), 4.43 – 4.33 (m, 1H), 4.28 (d, J = 8.9 Hz, 1H), 3.90 – 3.81 (m, 1H), 3.77 – 3.67 (m, 1H), 1.77 – 1.59 (m, 1H), 1.15 (m, 1H), 0.77 – 0.53 (m, 3H), 0.31 – 0.19 (m, 1H). ^{13}C NMR (100 MHz, Acetone-d_6) δ ppm 165.7, 145.7, 141.8, 132.6, 131.0, 128.1, 123.6, 122.6, 115.9, 70.9, 60.4, 38.7, 11.5, 5.6, 4.7. ESI MS m/z: $[M+H]^+$ 242.1.



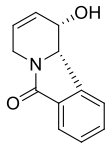
1-hydroxy-2-phenyl-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (83): Purified by silica gel chromatography (40% EtOAc in hexane), yield 79%, ^{1}H NMR (400 MHz, Acetone-d_6) δ ppm 7.89 (d, J = 7.5 Hz, 1H), 7.76 (dt, J = 7.4, 1.0 Hz, 1H), 7.62 (td, J = 7.5, 1.3 Hz, 1H), 7.54 (td, J = 7.4, 1.1 Hz, 1H), 7.47 – 7.36 (m, 2H), 7.36 – 7.18 (m, 3H), 6.08 (ddd, J = 3.9, 2.5, 1.4 Hz, 1H), 4.77 – 4.57 (m, 2H), 4.44 (m, 2H, including OH), 3.91 (dt, J = 19.2, 2.2 Hz, 1H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 165.6, 145.7, 141.2, 139.0, 132.6, 131.1, 128.2, 127.9, 127.4, 126.9, 123.7, 122.7, 122.6, 69.2, 60.4, 39.1. ESI MS m/z: $[M+H]^+$ 278.1.



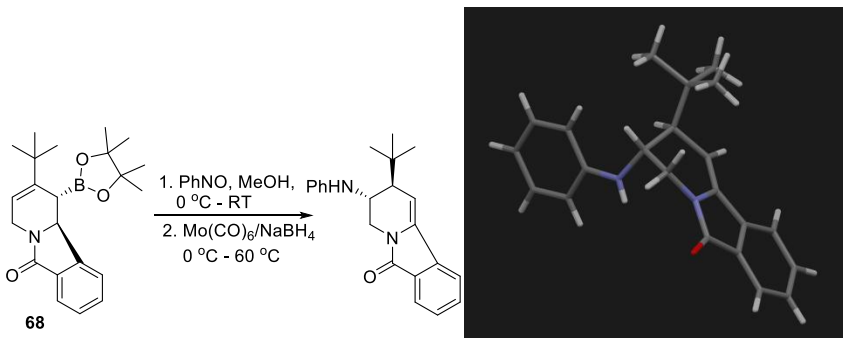
To a stirred solution of 4-pyridineboronic acid pinacol ester (100 mg, 0.48 mmol)(recrystallized from $CHCl_3$ and hexanes) in dry THF (1.5 mL) at -78 °C was added DIBAL-H (25% wt. in toluene, 0.4 mL, 0.72mmol). The reaction was stirred at -78 °C for 30 min then warmed tortand stirred for an additional 1.5 h. The reaction was then degassed by three freeze-pump-thaw cycles at which point it was recooled to -78 °C. In separate vial a THF (0.4 mL) solution of 2-I-PhCOCl (140 mg, 0.53 mmol) was degassed by three freeze-pump-thaw cycles and added slowly (10 minutes) into the reaction mixture. The reaction was stirred at -78 °C for 30 min then warmed to -40 °C and stirred at temperature overnight (15h). After that the reaction mixture was kept outside at room temperature for 10 minutes. In the meantime SmI_2 solution in THF with water was prepared. In a dry reaction flask 0.1 M SmI_2 solution (14.4 mL, 1.44 mmol) in THF was transferred followed by addition of H_2O (0.2 mL, 11.4 mmol) and stirred for 5 minutes under an inert atmosphere of argon. The reaction mixture was transferred into the SmI_2 mixture via cannula dropwise with constant stirring. Extra SmI_2 solution (3-4 equivalents) in THF was added to the reaction mixture to maintain the blue color. The reaction was stirred for an additional 30 minutes and then quenched with water. The reaction mixture was filtered through Celite. Brine was added to the filtrate and the product was extracted with EtOAc (3 × 15mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo to afford yellow gum, which was directly taken to the next step without further purification. The yellow gum was dissolved in THF (1mL) and water (1mL) followed by addition of $NaBO_3.H_2O$ (110 mg, 0.72 mmol) and stirred at rt for 20h. The reaction mixture was extracted withEtOAc (10 × 5mL), dried over $Na_2SO_4$and concentrated. The crude reaction mixture was was purified by silica gel chromatography (40% EtOAc in hexane) to afford the product as mixture of diastereomers (54 mg, 56%).



1-hydroxy-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (84-anti): Purified by silica gel chromatography (40% EtOAc in hexane), gum, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.96 – 7.72 (m, 2H), 7.54 (m, 2H), 5.99 – 5.81 (m, 2H), 4.67 – 4.50 (m, 1H), 4.20 (dd, *J* = 8.7, 1.0 Hz, 1H), 3.97 (d, *J* = 7.0 Hz, 1H), 3.80 (dt, *J* = 19.6, 2.6 Hz, 1H), 2.41 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 167.2, 144.7, 132.2, 131.6, 129.4, 128.5, 124.7, 123.6, 123.2, 69.7, 60.5, 39.3. ESI MS m/z: $[M+H]^+$ 202.1

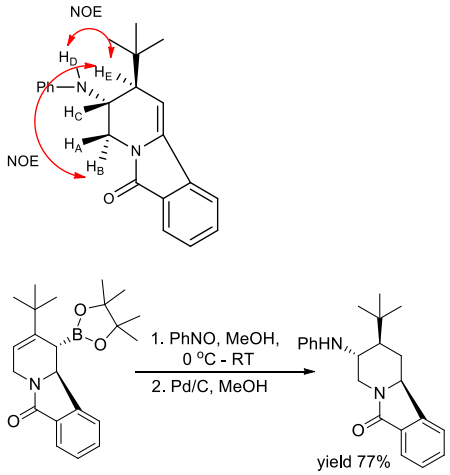


1-hydroxy-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (84-syn): Purified by silica gel chromatography (40% EtOAc in hexane), gum, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.60 – 7.48 (m, 3H), 7.31 (ddd, *J* = 8.0, 6.3, 2.0 Hz, 1H), 6.25 (ddt, *J* = 10.3, 5.3, 2.4 Hz, 1H), 6.09 (ddd, *J* = 10.0, 3.5, 2.5 Hz, 1H), 4.75 – 4.54 (m, 3H), 3.83 (dt, *J* = 19.4, 1.9 Hz, 1H), 2.83 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 168.1, 142.5, 133.0, 131.3, 128.3, 127.7, 126.2, 123.5, 122.5, 64.05, 60.8, 40.1. ESI MS m/z: $[M+H]^+$ 202.1

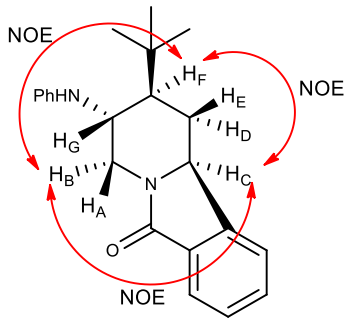


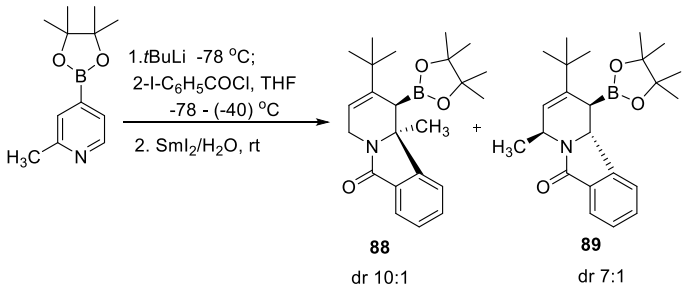
2-(tert-butyl)-3-(phenylamino)-3,4-dihydropyrido[2,1-a]isoindol-6(10bH)-one (85): To a stirred solution of compound **66** (25 mg, 0.067 mmol) and nitrosobenzene (25 mg, 0.237 mmol) under argon atmosphere at 0 °C was added ice cooled dry degassed methanol (1.2 mL). The reaction was stirred for 10 minutes at 0 °C then warmed to rt and stirred for one hour. The reaction was cooled to 0 °Cand transferred to an oven dried vial containing $NaBH_4$ (13 mg, 0.33 mmol) &$Mo(CO)_6$ (53 mg, 0.20 mmol). To

the reaction mixture was added 0.1 mL of water. The reaction was stirred at 0 °C for 10 min and then warmed to 60°C and stirred for 1.5 h. Upon completion the reaction was quenched with water and the product was extracted with EtOAc (3 × 5mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo to afford yellow gum, which was purified by silica gel chromatography to afford the product as white solid (16 mg, 69%), mp ^{1}H NMR (400 MHz, Acetone-d_6) δ ppm 7.90 (dt, J = 7.7, 0.9 Hz, 1H), 7.70 (dt, J = 7.6, 1.0 Hz, 1H), 7.63 (td, J = 7.5, 1.2 Hz, 1H), 7.52 (td, J = 7.5, 1.0 Hz, 1H), 7.12 – 7.03 (m, 2H), 6.69 (m, J = 7.0, 1.1 Hz, 2H), 6.56 (tt, J = 7.3, 1.1 Hz, 1H), 6.02 (dd, J = 5.7, 1.2 Hz, 1H), 5.07 (d, J = 9.4 Hz, 1H), 4.26 (ddt, J = 9.1, 3.2, 1.6 Hz, 1H), 4.15 (ddd, J = 13.5, 2.6, 1.5 Hz, 1H), 3.64 (dd, J = 13.5, 3.4 Hz, 1H), 2.44 (dt, J = 5.8, 1.7 Hz, 1H), 1.11 (s, 9H). ^{13}C NMR (100 MHz, Acetone-d_6) δ ppm 165.5, 146.9, 135.6, 134.5, 131.4, 130.3, 129.0, 128.7, 122.3, 120.0, 116.5, 113.0, 102.8, 49.6, 45.9, 40.8, 34.4, 28.0. ESI MS m/z: $[M+H]^+$ 333.2.The relative stereochemistry was assigned based on 2D-NOESY data.

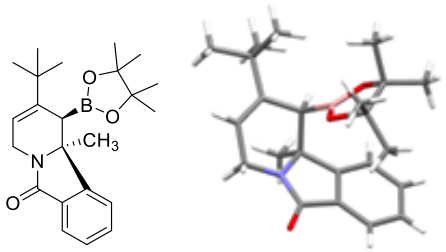


2-(tert-butyl)-3-(phenylamino)-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (86): To a 0°Cstirred solution of compound **66** (20 mg, 0.054 mmol) and nitrosobenzene (20 mg, 1.89 mmol) was added ice cooled dry degassed methanol (1.0 mL). The reaction was stirred for 10 minutes at 0 °C then warmed to room temperature and stirred for one hour. The reaction mixture was transferred to an oven dried vial containing palladium (30%) on carbon under argon atmosphere. The reaction vessel was then charged with hydrogen (ballon) and stirred at rt overnight (15h). The reaction mixture was filtered through Celite and concentrated in vaccuogiving a yellow oil, which was purified by silica gel chromatography (30% EtOAc in hexane) to afford the product as yellow oil (14 mg, 77%). ^{1}H NMR (400 MHz, Acetone-d_6) δ ppm 7.69 (dt, J = 7.6, 1.0 Hz, 1H), 7.66 – 7.54 (m, 2H), 7.52 – 7.43 (m, 1H), 7.18 – 7.06 (m, 2H), 6.78 – 6.67 (m, 2H), 6.58 (tt, J = 7.3, 1.0 Hz, 1H), 4.71 (d, J = 10.7 Hz, 1H), 4.52 – 4.34 (m, 2H), 3.46 (tt, J = 10.5, 5.2 Hz, 1H), 2.75 (dd, J = 13.5, 10.3 Hz, 1H), 2.63 (dt, J = 13.0, 3.6 Hz, 1H), 1.83 (ddd, J = 12.2, 10.4, 3.2 Hz, 1H), 1.05 (s, 10H). ^{13}C NMR (100 MHz, Acetone-d_6) δ ppm 164.5, 147.0, 146.1, 132.7, 131.1, 129.3, 127.9, 122.9, 122.4, 116.4, 112.3, 57.8, 52.2, 48.5, 43.6, 33.2, 32.8, 26.8. ESI MS m/z: $[M+H]^+$ 335.2. The relative stereochemistry was assignedbased on 2D-NOESY data.

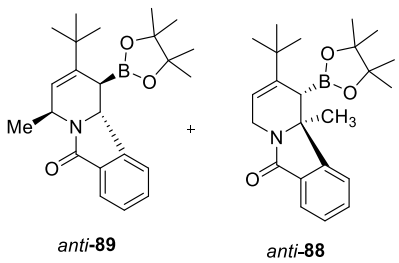




To a stirred solution of 2-methyl-4-pyridineboronic acid pinacol ester (50 mg, 0.23mmol)(recrystallized from $CHCl_3$ and hexanes) in dry THF (1 mL) at -78 ^oC was added ^{t}BuLi solution in pentane (145 µL, 0.25mmol). The reaction was stirred at -78 ^oC for 30 min then warmed to rtand stirred for 15 min. The reaction was degassed by three freeze-pump-thaw cycles at which point it was recooled to -78 ^oC. In another vial a THF (0.2 mL) solution of 2-I-PhCOCl (67 mg, 0.25mmol) was degassed by three freeze-pump-thaw cycles and added slowly (10 minutes) into the reaction mixture. The reaction was stirred at -78 ^oC for 30 min then warmed to -40 ^oC and stirred overnight (15h).After that the reaction mixture was kept outside at room temperature for 10 minutes. In the meantime SmI_2 solution in THF with water was prepared. In a dry reaction flask 0.1 M SmI_2 solution (6.9 mL, 0.69 mmol) in THF was transferred followed by addition of degassed water (0.1 mL, 5.52 mmol) and stirred for 5 minutes under an inert atmosphere of argon. The reaction mixture was transferred into the SmI_2 mixture via cannula dropwise with constant stirring under argon atmosphere. Extra 0.1 M SmI_2 solution (3- 4 equivalent) in THF was added to the reaction mixture to maintain the blue color. The reaction was stirred for an additional 30 minutes and then quenched with water. The reaction mixture was filtered through Celite. Brine was added to the filtrate and the product was extracted with EtOAc (3 × 15mL). The organic layer was collected, dried over Na_2SO_4 and then concentrated in vaccuo to give yellow gum mixture of regioisomer and diastereomers, which was purified by silica gel chromatography (30% EtOAc in hexane) to afford the product as gum(75 mg, 86%). The diastereomers are separated by preparative TLC (30% EtOAc in hexane).



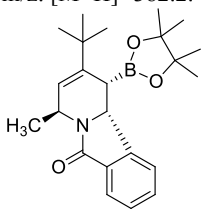
2-(tert-butyl)-10b-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one *(syn*-88): The relative stereochemistry was determinedby X-ray crystallography.A single crystal suitable forX-ray crystallography was grown by slow evaporation of ethyl acetate and pentane at room temperature.Purified by silica gel chromatography (30% EtOAc in hexane), white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.78 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.60 – 7.44 (m, 2H), 7.39 (ddd, *J* = 8.1, 6.4, 2.1 Hz, 1H), 5.61 – 5.50 (m, 1H), 4.65 (dd, *J* = 18.7, 2.8 Hz, 1H), 3.76 (ddd, *J* = 18.8, 3.6, 1.4 Hz, 1H), 2.46 (s, 1H), 1.38 (s, 3H), 1.07 (s, 9H), 0.71 (6H, s), 0.65 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.5, 150.3, 143.9, 132.9, 130.9, 128.0, 123.3, 122.1, 112.4, 83.1, 61.2, 38.8, 35.6, 33.3 (boron attach to carbon), 28.9, 24.6, 24.4. ESI MS m/z: $[M+H]^+$ 382.2.



Inseparable mixture of two compounds,

Combined NMR Data

2-(tert-butyl)-4-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*anti*-89): ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.82 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.51 (td, *J* = 7.5, 1.3 Hz, 1H), 7.46 – 7.40 (m, 1H), 5.76 (dd, *J* = 5.4, 2.1 Hz, 1H), 4.87 – 4.75 (m, 1H), 4.65 (d, *J* = 9.5 Hz, 1H), 2.03 (dt, *J* = 9.6, 2.1 Hz, 1H), 1.39 (s, 6H), 1.32 (d, *J* = 6.7 Hz,3H), 1.35 (s, 6H), 1.05 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.4, 146.9, 143.5, 131.0, 127.9, 123.5, 122.4, 121.4, 84.2, 54.2, 44.0, 30.5, 28.9 (carbon attach with boron), 25.6, 24.8, 20.6. ESI MS m/z: $[M+H]^+$ 382.2.
2-(tert-butyl)-10b-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*anti*-88): ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.78 (m, 1H), 7.68 (d, *J* = 1.0 Hz, 1H), 7.49 (d, *J* = 1.3 Hz, 1H), 7.40 (1H, m), 5.79 (s, 1H), 1.53 (d, *J* = 17.4 Hz, 3H), 1.34 (s, 6H), 1.32 (s, 6H), 0.98 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.4, 153.1, 146.1, 132.3, 131.3, 127.8, 123.5, 121.6, 117.3, 84.1, 61.7, 35.9, 33.8 (carbon attach with boron), 30.3, 25.8, 25.4, 24.2. ESI MS m/z: $[M+H]^+$ 382.2.

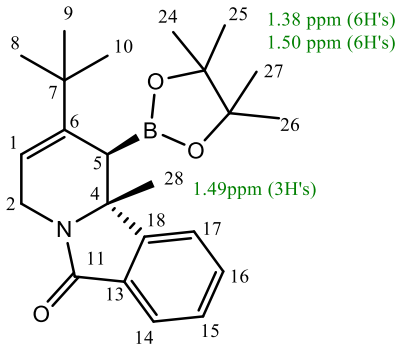


2-(tert-butyl)-4-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10b-dihydropyrido[2,1-a]isoindol-6(4H)-one (*syn*-89): ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.81 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.55 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.49 (td, *J* = 7.4, 1.2 Hz, 1H), 7.46 – 7.38 (m, 1H), 5.49 (d, *J* = 2.5 Hz, 1H), 4.71 (qd, *J* = 6.8, 2.4 Hz, 1H), 4.44 (d, *J* = 4.6 Hz, 1H), 2.62 (d, *J* = 4.6 Hz, 1H), 1.34 (d, *J* = 6.8 Hz, 3H), 1.10 (s, 9H), 0.74 (s, 6H), 0.69 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.9, 144.9, 144.7, 134.6, 130.6, 128.2, 123.2, 123.1, 120.1, 83.2, 55.9, 45.9, 35.8, 29.7 (boron attach to carbon), 29.0, 24.4, 24.2, 21.5. ESI MS m/z: $[M+H]^+$ 382.2.
The relative stereochemistry was determined based on following data

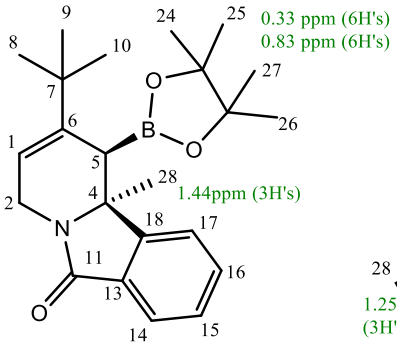
1. B(pin) and Ph are cis based on the 4.6 Hz coupling constant of the respective proton.
2. The relative stereochemistry of the CH_3 group was determined tentatively based on lack of 1,3 coupling which was obtained in the unsubstituted compound **68-syn**.

Computational Section:

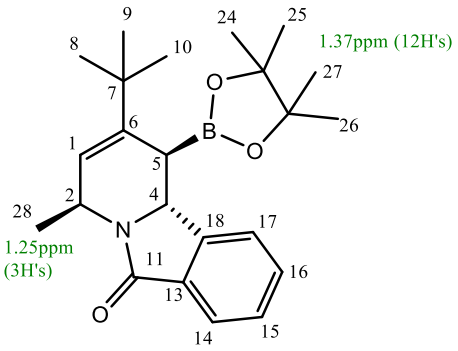
NMR calculations:



88-*anti*



88*syn*



89-*anti*

With the initial experimental ^{1}H-δ and ^{13}C-δ of the major product and ^{1}H-δ of the minor products, and based on the derived relative stereochemistry, we built and optimized (M06-2X/6-31+G(d,p))[43] these structures with Gaussian09,[44] then performed quantum mechanical ^{1}H-NMR and ^{13}C-NMR calculations (mPW1PW91/6-311+G(2d,p) in chloroform)[45],[463,4] (see supporting information for more details). With a smaller mean average deviation (MAD) from the experimental values of the major product (MAD = 0.08 ppm for ^{1}H-δ, and 1.33 ppm for ^{13}C-δ), **computed 88-*syn***(or its enantiomer) was predicted to be the major diastereomer/major regioisomer, which was later confirmed by X-Ray crystallography. The predicted ^{13}C-δ of **computed 88-*anti*** and **89-*anti***were also shown to be in good agreement with the latter experimental ^{13}C-NMR data of minor diastereomer/major regioisomer and major diastereomer/minor regioisomer, respectively. In addition, computed and experimental proton assignments also reveal the diagnostic peaks that would help distinguish between the pair of diastereomers of the major product, as shown in figure above.

All the calculations were done with *Gaussian09, Revision D*.

Geometry optimization method: M06-2X/6-31+G(d,p).

NMR calculation method: mPW1PW91/6-311+G(2d,p) in Chloroform (SMD solvation model).

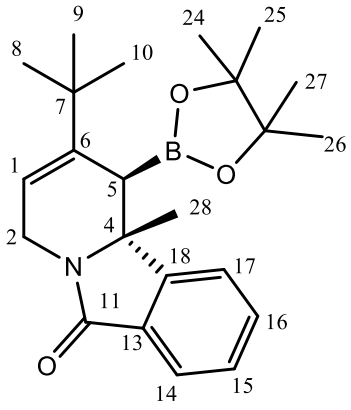
Scaling factor obtained from http://cheshirenmr.info/:

Slope = -1.0938 (for H) and -1.0446 (for C)

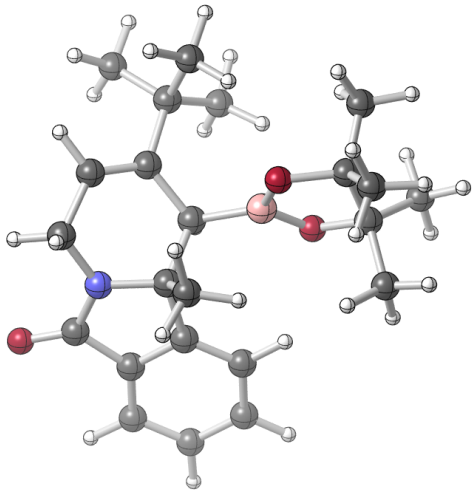
Intercept = 31.8723 (for H) and 186.7246 (for C)

Analysis for the diastereomer pair of the major regioisomers

Based on the comparison shown below: this structure (**88-*anti***) (or its enantiomer) was predicted to be the minor diastereomer/major regioisomer.



88-*anti*



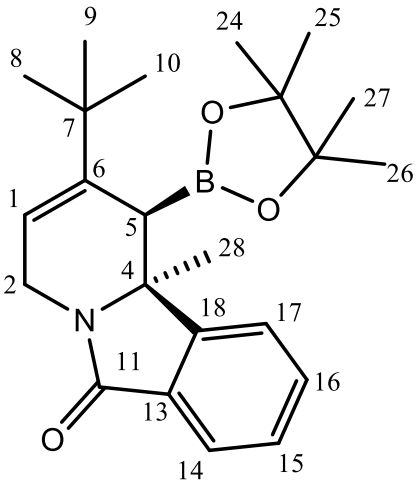
(43) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc*. **2008**, 120, 215-241.

(44)*Gaussian 09, Revision B.01*; Gaussian, Inc.: Wallingford, CT, 2004 (full reference in Supporting Information).
(45)Adamo, C.; Barone, V. *J. Chem. Phys.***1998**, 108, 664-675.
(46) For a review on the application of QM calculations in synthesis: Nguyen, Q. N. N.; Tantillo, D. J. *Chem. Asian. J.***2014**, 9, 674-680.

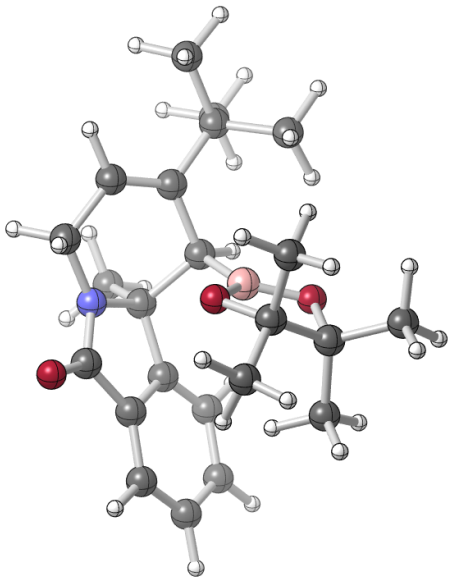
			Major Diastereomer/major regiomer			Minor Diastereomer/major regiomer	
Computed δ (ppm) [A]	Atom Labels		Exp δ (ppm) [1]	Δ b/w [A] and [1]		Exp δ (ppm) [2]	Δ b/t [A] and [2]
8.03	H17		7.5	0.53		7.68	0.35
7.64	H14		7.78	0.14		7.77	0.13
7.41	H16		7.4	0.01		7.4	0.01
7.35	H15		7.48	0.13		7.51	0.16
5.85	H1		5.55	0.30		5.81	0.04
4.53	H2		4.65	0.12		4.65	0.12
3.58	H2'		3.77	0.19		3.68	0.10
2.27	H5		2.47	0.20		2.32	0.05
1.50	H24,25 or H26,27		0.7	0.80		1.39	0.11
1.49	H28		1.39	0.10		1.55	0.06
1.38	H24,25 or H26,27		0.64	0.74		1.39	0.01
1.17	H8,9,10		1.1	0.07		1.00	0.17
			MAD =	0.28		MAD =	0.11

			Major Diastereomer/major regiomer			Minor Diastereomer/major regiomer	
Computed δ (ppm) [A]	Atom Labels		Exp δ (ppm) [1]	Δ b/w [A] and [1]		Exp δ (ppm) [2]	Δ b/t [A] and [2]
161.8	C11		166.62	4.77		166.42	4.57
152.9	C18		150.41	2.46		153.06	0.19
148.1	C6		144.13	3.96		146.24	1.85
131.0	C13		133.07	2.04		132.47	1.44
130.0	C16		131.07	1.08		131.48	1.49
126.8	C15		128.17	1.36		127.99	1.18
122.9	C17		123.47	0.58		123.69	0.80
122.3	C14		122.23	0.09		121.74	0.58
119.9	C1		112.43	7.44		117.46	2.41
83.3	C22 or C21		83.24	0.09		84.11	0.78
82.8	C22 or C21		83.24	0.47		84.11	1.34
60.1	C4		61.38	1.32		61.87	1.81
38.2	C7		35.63	2.61		36.12	2.12
36.5	C2		38.99	2.45		36.89	0.35
35.2	C5		33.12	2.13		28.96	6.29
29.9	C8, 9, or 10		29.11	0.82		30.51	0.58
26.1	C24, 25, 26, 27		24.6	1.55		25.99	0.16
24.3	C28		24.73	0.48		24.4	0.15
23.3	C24, 25, 26, 27		24.53	1.27		25.53	2.27
			MAD =	1.95		MAD =	1.60

Based on the comparison shown below: this structure (**88-*syn***) (or its enantiomer) was predicted to be the major diastereomer/major regioisomer.Confirmed by crystal structure.



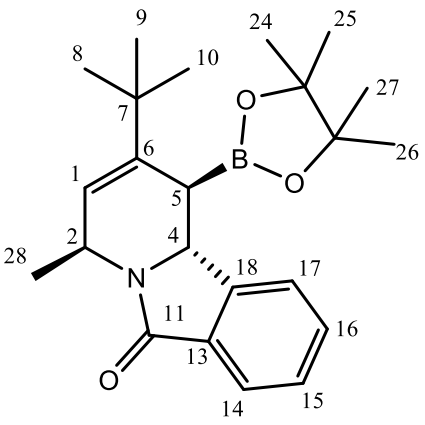
88-*anti*



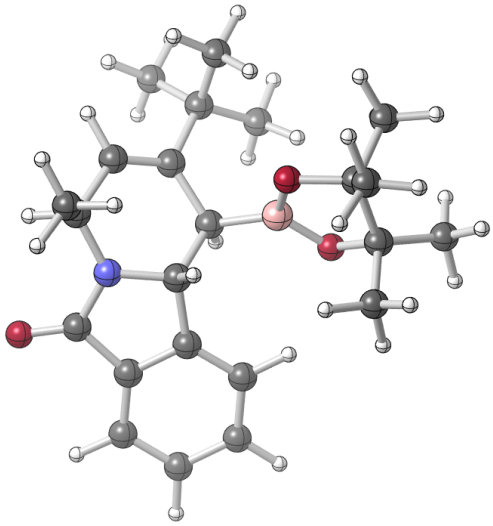
			Major Diastereomer/major regiomer			Minor Diastereomer/major regiomer	
Computed δ (ppm) [B]	Atom Labels		Exp δ (ppm) [1]	Δ b/w [B] and [1]		Exp δ (ppm) [2]	Δ b/t [B] and [2]
7.72	H14		7.78	0.06		7.77	0.05
7.47	H17		7.5	0.03		7.68	0.21
7.38	H16		7.4	0.02		7.4	0.02
7.32	H15		7.48	0.16		7.51	0.19
5.52	H1		5.55	0.03		5.81	0.29
4.55	H2		4.65	0.10		4.65	0.10
3.75	H2'		3.77	0.02		3.68	0.07
2.54	H5		2.47	0.07		2.32	0.22
1.44	H28		1.39	0.05		1.55	0.11
1.09	H8,9,10		1.1	0.01		1.00	0.09
0.83	H24,25 or H26,27		0.7	0.13		1.39	0.56
0.33	H24,25 or H26,27		0.64	0.31		1.39	1.06
			MAD =	0.08		MAD =	0.25

			Major Diastereomer/major regiomer			Minor Diastereomer/major regiomer	
Computed δ (ppm) [B]	Atom Labels		Exp δ (ppm) [1]	Δ b/w [B] and [1]		Exp δ (ppm) [2]	Δ b/t [B] and [2]
164.8	C11		166.62	1.79		166.42	1.59
150.5	C18		150.41	0.12		153.06	2.53
146.2	C6		144.13	2.02		146.24	0.09
134.3	C13		133.07	1.26		132.47	1.86
130.2	C16		131.07	0.83		131.48	1.24
126.8	C15		128.17	1.39		127.99	1.21
122.9	C17		123.47	0.61		123.69	0.83
121.8	C14		122.23	0.41		121.74	0.08
113.6	C1		112.43	1.17		117.46	3.86
82.3	C22 or C21		83.24	0.92		84.11	1.79
81.9	C22 or C21		83.24	1.31		84.11	2.18
61.8	C4		61.38	0.41		61.87	0.08
38.0	C7		35.63	2.34		36.12	1.85
39.7	C2		38.99	0.76		36.89	2.86
35.5	C5		33.12	2.39		28.96	6.55
27.1	C8, 9, or 10		29.11	2.01		30.51	3.41
24.7	C24, 25, 26, 27		24.6	0.08		25.99	1.31
22.2	C28		24.73	2.51		24.4	2.18
21.6	C24, 25, 26, 27		24.53	2.90		25.53	3.90
			MAD =	1.33		MAD =	2.07

Analysis for the major diastereomer/minor regioisomer



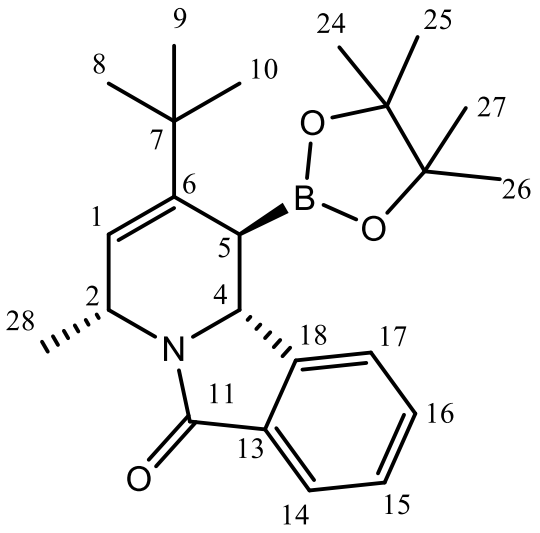
89 (*anti*)



Atom labels	Exp δ (ppm)	Computed δ (ppm)	Δ
C11	165.36	162.18	3.18
C18	146.86	147.51	0.65
C6	143.71	146.91	3.20
C13	131.02	131.82	0.80
C16	131.2	129.40	1.80
C15	128.11	126.30	1.81
C1	121.61	125.35	3.74
C17	123.45	123.67	0.22
C14	122.58	121.86	0.72
C21, 22	84.16	82.78	1.38
C4	54.38	53.52	0.86
C2	44.17	45.34	1.17
C7	36.17	38.61	2.44
C8, 9, or 10	30.45	29.98	0.47
C5	29.13	30.87	1.74
C24, 25, 26, or 27		26.21	
C24, 25, 26, or 27		24.78	
C24, 25, 26, or 27		22.52	
C24, 25, 26, or 27		22.04	
C28		19.41	
		MAD =	1.61

Atom labels	Exp δ (ppm)	Computed δ (ppm)	Δ
H14	7.82	7.59	0.23
H15	7.51	7.40	0.11
H16	7.4	7.48	0.08
H17	7.69	8.11	0.42
H8, 9, 10	1.06	1.14	0.08
H24, 25, 26, 27	1.38	1.37	0.01
H5	2.04	2.13	0.09
H4	4.65	4.51	0.14
H28	1.32	1.25	0.07
H1	5.77	5.81	0.04
H2	4.82	4.62	0.20
		MAD =	0.13

…changing the stereochemistry of C2 resulted in a worse MADs.

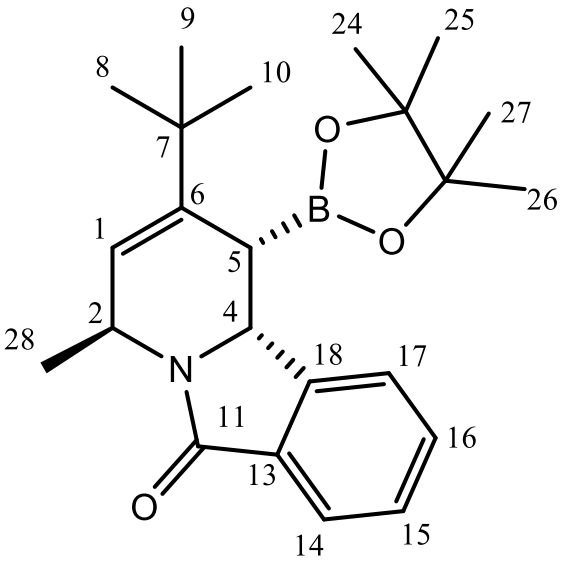


computed **89-*anti***
different stereocenter at C2

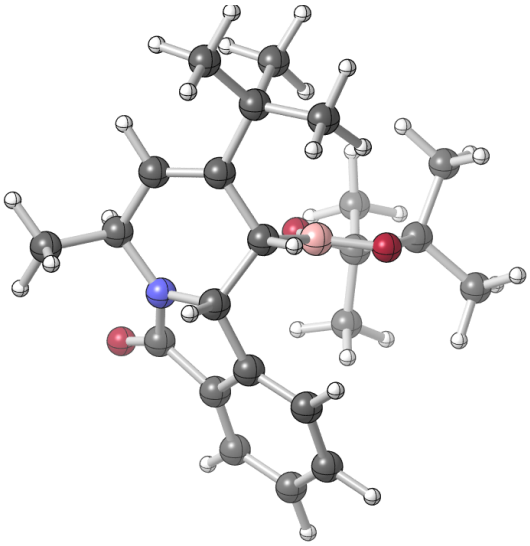
Atom Labels	Exp δ (ppm)	Computed δ (ppm)	Δ
C11	165.36	162.18	3.18
C18	146.86	147.51	0.65
C6	143.71	146.91	3.20
C13	131.02	131.82	0.80
C16	131.2	129.40	1.80
C15	128.11	126.30	1.81
C1	121.61	125.35	3.74
C17	123.45	123.67	0.22
C14	122.58	121.86	0.72
C21, 22	84.16	82.78	1.38
C4	54.38	53.52	0.86
C2	44.17	45.34	1.17
C7	36.17	38.61	2.44
C8, 9, or 10	30.45	29.98	0.47
C5	29.13	30.87	1.74
C24, 25, 26, or 27		26.21	
C24, 25, 26, or 27		24.78	
C24, 25, 26, or 27		22.52	
C24, 25, 26, or 27		22.04	
C28		19.41	
		MAD =	1.61

Atom Labels	Exp δ (ppm)	Computed δ (ppm)	Δ
H14	7.82	7.6	0.22
H15	7.51	7.4	0.14
H16	7.4	7.5	0.07
H17	7.69	8.1	0.41
H8, 9, 10	1.06	1.2	0.13
H24, 25, 26, 27	1.38	1.3	0.03
H5	2.04	2.2	0.21
H4	4.65	4.3	0.38
H28	1.32	1.8	0.45
H2	4.82	4.2	0.58
H1	5.77	5.5	0.23
		MAD =	0.26

Analysis for the minor diastereomer/minor regioisomer



89-*syn*



Atom Labels	Exp δ (ppm)	Computed δ (ppm)	Δ
C1	120.05	123.81	3.76
C11	166.97	163.85	3.12
C13	134.57	135.63	1.06
C14	123.19	123.67	0.48
C15	128.16	127.16	1.00
C16	130.67	129.86	0.81
C17	123.11	123.40	0.29
C18	144.67	144.95	0.28
C2	45.89	46.16	0.27
C21 or 22	83.15	81.96	1.19
C24, 25, 26, or 27		26.21	
C24, 25, 26, or 27		24.78	
C24, 25, 26, or 27		22.52	
C24, 25, 26, or 27		22.04	
C28		19.41	
C4	54.38	54.14	0.24
C5	29.13	29.43	0.30
C6	144.98	147.82	2.84
C7	36.17	38.13	1.96
C8, 9, or 10	29	29.60	0.60
		MAD =	1.22

Atom Labels	Exp δ (ppm)	Computed δ (ppm)	Δ
H1	5.49	5.66	0.17
H14	7.81	7.73	0.08
H15	7.49	7.38	0.11
H16	7.42	7.46	0.04
H17	7.55	7.53	0.02
H2	4.71	4.49	0.22
H24, 25, 26, 27	0.74	0.96	0.22
H24, 25, 26, 27	0.68	0.30	0.38
H28	1.33	1.29	0.04
H4	4.44	4.42	0.02
H5	2.62	2.75	0.13
H8, 9, 10	1.1	1.16	0.06
		MAD =	0.12

Full *Gaussian09* Citation:

Gaussian 09, Revision D.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, **2009**.

STRUCTURAL COORDINATES:

COMPUTED 88-*anti*

C	-0.05421800	2.13271300	-0.08932800
C	-0.88148500	2.84476200	0.68553100
C	-2.10833700	2.30174100	1.36050500
C	-1.33350300	0.02411500	0.66504300
C	-0.22529400	0.62286900	-0.26758100
H	-0.71995800	3.91147300	0.81506300
H	-2.97602400	2.93557800	1.15052700
C	-3.63247600	0.60595100	0.37580600
C	-3.42474900	-0.77401000	-0.14737400
C	-4.35344900	-1.63938600	-0.70951300
C	-3.90507100	-2.89378400	-1.11979300
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H	-4.59974800	-3.60086400	-1.56209200
H	-2.22897900	-4.22995700	-1.29774700
H	-0.59152300	-2.64925500	-0.30844500
N	-2.40905700	0.99488000	0.84550900
O	-4.65989400	1.26413700	0.39417500
H	-1.98500300	2.27407200	2.45489800
C	1.06673500	2.85725400	-0.86860500
C	1.55450800	2.03379000	-2.07251400
C	0.55464300	4.19290900	-1.43928000
C	2.25231400	3.15439600	0.06698300
H	2.00156800	1.07467200	-1.79654100
H	0.73963000	1.82960000	-2.77522100
H	2.32426700	2.59975800	-2.60736700
H	0.30097400	4.90879000	-0.65349700
H	1.33495500	4.65184600	-2.05634600
H	-0.33336700	4.03979400	-2.06070100
H	3.06250900	3.63818400	-0.49240600
H	1.93908100	3.82967800	0.86989100
H	2.63526400	2.24144500	0.52645500
C	-0.79124700	-0.38046300	2.04472900
H	-1.62606000	-0.65800500	2.69386400
H	-0.11556000	-1.23759900	1.96568200
H	-0.23008300	0.44344000	2.49746100
B	1.11343100	-0.21285900	-0.07675800
O	1.43631500	-1.29223700	-0.86176700
O	2.04118500	0.00939400	0.90768100
C	2.57559300	-1.96106500	-0.27492800
C	3.17103600	-0.86363200	0.68274200
C	3.50700400	-2.40044700	-1.39457000
C	2.04055300	-3.18534700	0.46584900

C	3.64822000	-1.38811700	2.02922500
C	4.27110600	-0.02206300	0.03701900
H	4.41570600	-2.85330600	-0.98427700
H	3.00077000	-3.14505400	-2.01421000
H	3.78759800	-1.56041500	-2.03240300
H	1.51511000	-3.82735300	-0.24690700
H	2.85119900	-3.76321800	0.91870600
H	1.33629400	-2.90142100	1.25393800
H	4.46407100	-2.10622900	1.89575900
H	4.01968800	-0.55354400	2.62938400
H	2.83935900	-1.87073700	2.58101200
H	4.52879600	0.79968600	0.71060300
H	5.17089900	-0.61736500	-0.14245300
H	3.94358400	0.41154400	-0.91230100
H	-0.55093900	0.44317900	-1.30246300

COMPUTED 88-*syn*

C	-2.37857700	-0.50007700	0.14170100
C	-2.41153300	-1.05183000	1.36034900
C	-1.25894400	-1.76120900	2.01755000
C	-0.26826600	-1.79883100	-0.31709000
C	-1.07708800	-0.51379200	-0.64893700
H	-3.32171700	-1.03475000	1.95176100
H	-1.59529900	-2.74917700	2.36588100
C	1.16643900	-1.76682500	1.58593600
C	2.01132600	-1.69813700	0.35898800
C	3.39351800	-1.62620800	0.24881200
C	3.93928500	-1.55740700	-1.03329300
C	3.10899000	-1.55544300	-2.16070800
C	1.71954000	-1.62688100	-2.03568500
C	1.18004500	-1.70211800	-0.75615500
H	4.01272500	-1.62587600	1.14087500
H	5.01556100	-1.50155500	-1.16303900
H	3.55357200	-1.49232700	-3.14932700
H	1.08530300	-1.61761500	-2.91816600
N	-0.12044700	-1.89729600	1.13638900
O	1.52517100	-1.71748500	2.75043000
H	-0.91569100	-1.21455600	2.90451000
C	-0.94338200	-3.04940500	-0.89075000
H	-1.96069200	-3.14706500	-0.50106000
H	-0.99655600	-2.98258700	-1.98214700
H	-0.37041200	-3.94032200	-0.62003000
C	-3.59038600	0.15702200	-0.51772200
C	-3.20483500	1.55002600	-1.04475800
C	-4.05797200	-0.72065900	-1.69375700
C	-4.76390500	0.31742900	0.45392200
H	-2.85329100	2.18921000	-0.22612900
H	-2.41547300	1.50637400	-1.80106200
H	-4.07707600	2.03232300	-1.49891400
H	-4.36109000	-1.71061300	-1.33683500
H	-4.91715000	-0.25601600	-2.19014300
H	-3.27440400	-0.85412400	-2.44604700
H	-5.59263700	0.82109600	-0.05380100
H	-5.13302000	-0.65052100	0.80757600
H	-4.48176400	0.91980700	1.32375900
B	-0.20777700	0.76409900	-0.30357700
O	0.29156700	0.98512600	0.95080300
O	0.15841500	1.72835100	-1.20567600
C	0.92263400	2.28451800	0.95100600
C	1.19063900	2.52770100	-0.57561600
C	2.17056900	2.20925700	1.81593400

C	-0.08663600	3.26334100	1.54680400
C	1.03947800	3.97057500	-1.02705700
C	2.52648400	1.95451700	-1.04109000
H	2.72784800	3.15117100	1.77255700
H	1.88079300	2.02177300	2.85308300
H	2.82108900	1.39140200	1.49884800
H	-0.36759000	2.91127600	2.54263400
H	0.33579500	4.26855000	1.63554400
H	-0.99162700	3.31516600	0.93341500
H	1.75224000	4.61254300	-0.49852500
H	1.24443500	4.04017000	-2.09871600
H	0.02897400	4.34114500	-0.84592900
H	2.55752900	1.97840400	-2.13393500
H	3.36810400	2.53562800	-0.65198700
H	2.63899600	0.91444600	-0.71987000
H	-1.28120700	-0.51413100	-1.72636300

COMPUTED 89-*anti*

C	0.03126100	2.01966000	-0.39947200
C	-0.75842300	2.73273100	0.41225000
C	-1.94478000	2.20608500	1.17512300
C	-1.21540000	-0.06833700	0.38917500
C	-0.13121800	0.51422700	-0.55708400
H	-0.57904300	3.79891600	0.53830600
H	-2.81858000	2.82795000	0.94513900
C	-3.53666500	0.43266000	0.45662800
C	-3.36380400	-0.93881400	-0.10293900
C	-4.33559000	-1.82903500	-0.53834200
C	-3.90921400	-3.04815100	-1.06306800
C	-2.54433900	-3.34381300	-1.15095700
C	-1.57428400	-2.44109200	-0.70837500
C	-2.00482500	-1.23284300	-0.17078500
H	-5.38659600	-1.56501400	-0.47176000
H	-4.63715400	-3.77121100	-1.41733200
H	-2.23181000	-4.29237900	-1.57757500
H	-0.51676700	-2.66684700	-0.80399000
N	-2.26771000	0.88597600	0.68952200
O	-4.57223400	1.04463000	0.66238500
C	1.13830600	2.73183500	-1.20739400
C	1.76803500	1.82231400	-2.27401500
C	0.54889900	3.94457900	-1.94958300
C	2.24406400	3.21358400	-0.25192900
H	2.29455400	0.96168500	-1.84952100
H	1.02328800	1.44582300	-2.98233200
H	2.50869200	2.39507700	-2.84149700
H	0.14632900	4.68985100	-1.25926400
H	1.32718100	4.43154700	-2.54795000
H	-0.25926000	3.63469400	-2.62014400
H	3.05588100	3.68633400	-0.81769200
H	1.84913800	3.94726700	0.45771600
H	2.65101300	2.37707200	0.32271600
B	1.18667500	-0.28573600	-0.19604200
O	1.58841300	-1.44338200	-0.81718200
O	1.97228400	0.03000700	0.88249000
C	2.56930800	-2.07870200	0.03831100
C	3.09874600	-0.87792700	0.89502600
C	3.61779300	-2.75233900	-0.83160800
C	1.82055400	-3.11794200	0.87044500
C	3.42865500	-1.22314200	2.33878800
C	4.27476600	-0.14908200	0.24816300

H	4.41675700	-3.17263700	-0.21159000
H	3.15498500	-3.56753100	-1.39388300
H	4.05476200	-2.05043800	-1.54375600
H	1.34910200	-3.83922600	0.19728000
H	2.49797300	-3.65992600	1.53623200
H	1.03562200	-2.64948400	1.47367800
H	4.22300100	-1.97587000	2.38071800
H	3.77843100	-0.32544400	2.85508000
H	2.55311800	-1.60283400	2.86839200
H	4.46900300	0.77177400	0.80437500
H	5.17936000	-0.76367400	0.26693300
H	4.05799300	0.11951900	-0.78991100
H	-0.41942600	0.28490900	-1.59163500
H	-0.74022600	-0.36614200	1.33951300
C	-1.72302200	2.21753300	2.69268100
H	-1.48732400	3.22927000	3.03632400
H	-2.62566300	1.87388100	3.20488300
H	-0.88438700	1.56596200	2.95832000

COMPUTED 89-*anti*; different stereochemistry at C2

C	0.06799800	2.01774100	0.25236300
C	0.93009100	2.60804800	-0.58257800
C	2.17011400	1.99824400	-1.19125000
C	1.19454800	-0.14842100	-0.37834300
C	0.12915600	0.52113800	0.51431400
H	0.81746400	3.66860700	-0.80074200
C	3.55177400	-0.02020900	-0.53718200
C	3.18409900	-1.35156300	0.02271100
C	4.02379500	-2.39092500	0.39798600
C	3.43651100	-3.53102500	0.94384500
C	2.04897600	-3.60179100	1.11073200
C	1.21376200	-2.55153900	0.72185100
C	1.80275400	-1.42496400	0.15750900
H	5.09808500	-2.29624600	0.27216600
H	4.05641500	-4.36606800	1.25454800
H	1.61207600	-4.48992700	1.55764400
H	0.14208000	-2.60724900	0.88059900
N	2.37365100	0.68671700	-0.59952400
O	4.66695100	0.35289400	-0.86122300
C	-1.01074700	2.86715000	0.95783700
C	-1.73437100	2.09136400	2.06998100
C	-0.35771500	4.09165400	1.62425400
C	-2.04845600	3.34757200	-0.07105000
H	-2.30808600	1.23692500	1.69845900
H	-1.03827000	1.72215600	2.83012400
H	-2.44708800	2.75807000	2.56628400
H	0.12140000	4.74770900	0.89327900
H	-1.11671600	4.67890400	2.15312600
H	0.40358800	3.77960200	2.34677100
H	-2.83695900	3.92600900	0.42535300
H	-1.57833800	3.98680100	-0.82497000
H	-2.50368700	2.49922600	-0.58847900
B	-1.23928700	-0.20095100	0.15818500
O	-1.80153500	-1.22576100	0.87924800
O	-1.93012000	0.06807500	-0.99480600
C	-2.81760500	-1.84146800	0.05035000
C	-3.15297600	-0.70418500	-0.97759200
C	-3.97884200	-2.26578000	0.93461600
C	-2.17772600	-3.06439600	-0.60412000
C	-3.44166300	-1.18638100	-2.39086800

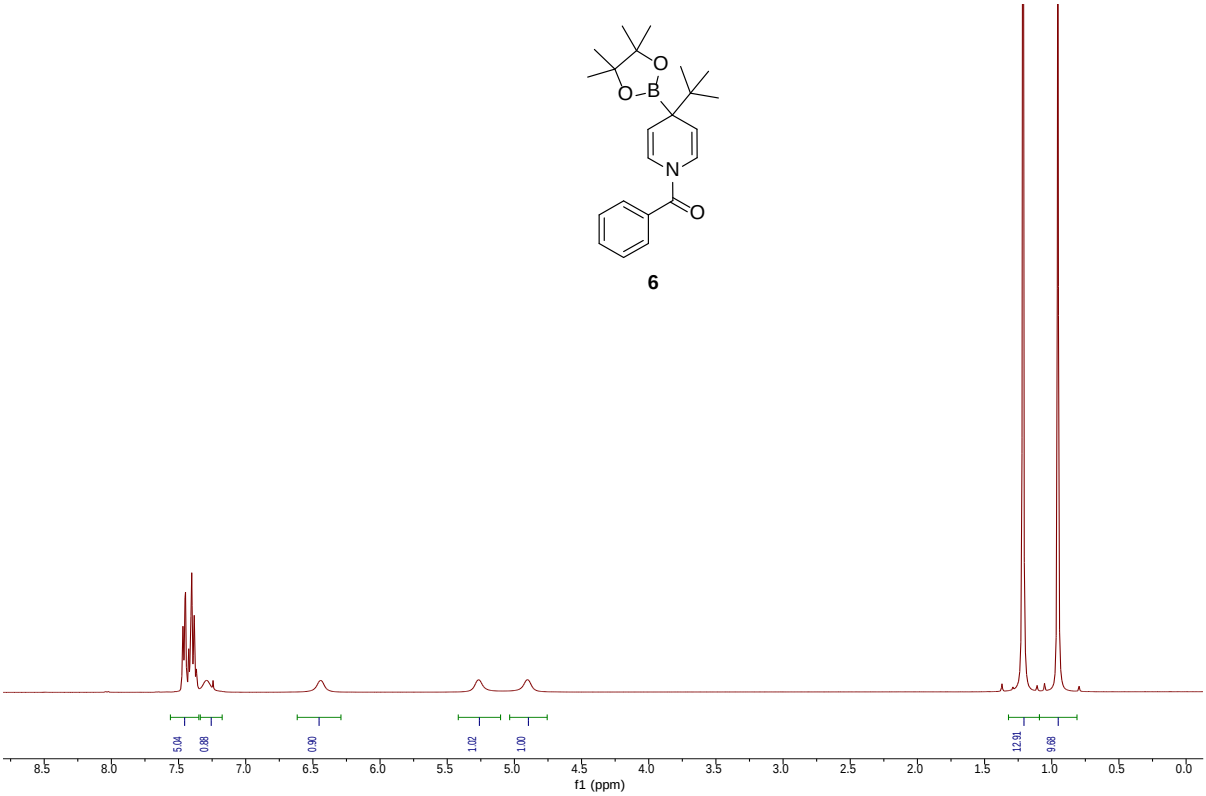
C	-4.27063200	0.22317200	-0.50596000
H	-4.79461000	-2.67152600	0.32689100
H	-3.64385700	-3.04529000	1.62392200
H	-4.35837500	-1.42908800	1.52369400
H	-1.82812700	-3.74431000	0.17790500
H	-2.89673600	-3.60123300	-1.22923200
H	-1.31820600	-2.78330000	-1.22154500
H	-4.32032700	-1.83994400	-2.40190400
H	-3.64728700	-0.32459200	-3.03105300
H	-2.59230800	-1.72800200	-2.81047000
H	-4.33418700	1.07521300	-1.18792300
H	-5.23547100	-0.29203400	-0.50448700
H	-4.07852500	0.60671400	0.50040400
H	0.38000300	0.32978200	1.56631200
H	0.74100100	-0.34527700	-1.36643300
C	3.35036000	2.94198000	-0.93917400
H	4.25970800	2.58657600	-1.41978400
H	3.53259300	3.02540700	0.13666900
H	3.09449600	3.93252200	-1.32688100
H	2.03753200	1.88744800	-2.28165500

COMPUTED 89-*syn*:

C	-2.31918200	0.51238700	-0.31363400
C	-2.48846000	1.52452200	0.54715500
C	-1.43004200	2.49185200	1.00783900
C	-0.13887800	1.56851500	-0.95833100
C	-0.96483800	0.26702000	-0.95798800
H	-3.45907800	1.68080700	1.01330800
C	1.04711900	2.43419800	0.90680300
C	2.03668300	1.92659700	-0.08829800
C	3.42280400	1.91404800	-0.01665100
C	4.12022000	1.32357600	-1.06972600
C	3.43304300	0.76146900	-2.15310900
C	2.03790800	0.79149100	-2.21983000
C	1.34738600	1.39358300	-1.17362100
H	3.92926800	2.34221900	0.84319300
H	5.20500500	1.28932000	-1.05032300
H	3.99490900	0.29462700	-2.95649100
H	1.51506300	0.34623900	-3.06178800
N	-0.17670200	2.21219300	0.34227000
O	1.25909100	2.93717700	1.99892200
C	-3.45036900	-0.50012100	-0.56898500
C	-3.18134600	-1.37689900	-1.80161600
C	-3.55277900	-1.41558400	0.66544500
C	-4.79660100	0.20911700	-0.78150100
H	-3.11322700	-0.77685200	-2.71592300
H	-2.25963200	-1.96064700	-1.70329800
H	-4.00862400	-2.08234200	-1.92993400
H	-3.84089000	-0.84040500	1.55036300
H	-4.29612300	-2.20426300	0.50105600
H	-2.58939600	-1.88959000	0.88266400
H	-5.57857300	-0.53206200	-0.98008300
H	-5.10463300	0.78246300	0.09660300
H	-4.74616100	0.89356900	-1.63430700
H	-0.56126500	2.24580100	-1.71657900
B	-0.16080900	-0.89989900	-0.25202100
O	0.29036700	-2.00771900	-0.92265100
O	0.18849800	-0.89163500	1.06985200
C	0.86475900	-2.90629900	0.05561400
C	1.16283900	-1.94732000	1.26106700

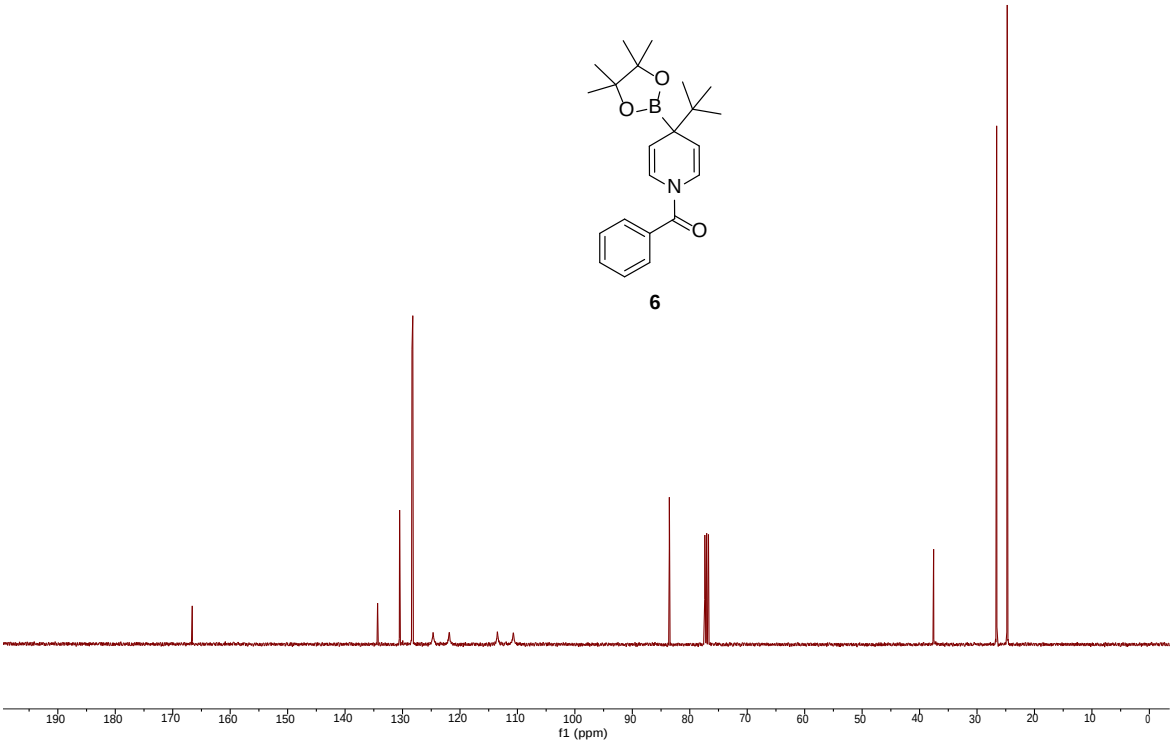
C	2.09449100	-3.56358800	-0.55107500
C	-0.19634400	-3.95935500	0.36659400
C	0.95104400	-2.56431600	2.63357300
C	2.53957200	-1.29416100	1.17356600
H	2.60822600	-4.17777000	0.19609100
H	1.78959400	-4.21132300	-1.37747000
H	2.79166100	-2.81819800	-0.93775400
H	-0.48797400	-4.44932300	-0.56633800
H	0.18554400	-4.71732400	1.05678300
H	-1.08862000	-3.50577700	0.80713200
H	1.61696900	-3.42266800	2.77271900
H	1.17994000	-1.82200700	3.40255000
H	-0.08171100	-2.89104200	2.76977300
H	2.59336000	-0.48786400	1.91075800
H	3.33529100	-2.01643100	1.38017300
H	2.70852800	-0.85723700	0.18376200
H	-1.10433600	-0.02072300	-2.00617000
H	-1.24822600	2.33074300	2.07927100
C	-1.85199000	3.95200700	0.80597000
H	-2.79248800	4.15513300	1.32747600
H	-1.08080900	4.61771500	1.20145400
H	-1.99653300	4.16034700	-0.25900700

Proton NMR



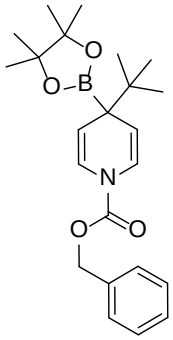
6

Carbon NMR

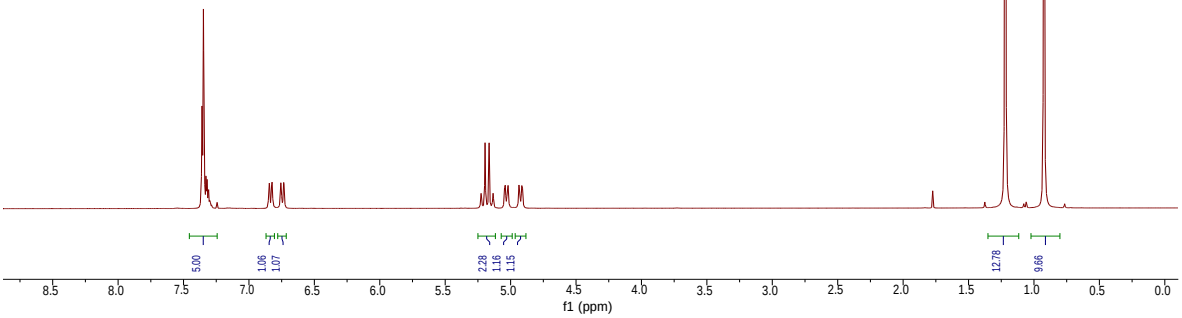


6

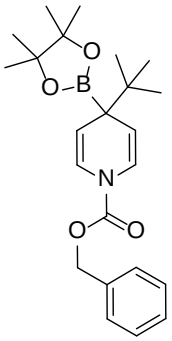
Proton NMR



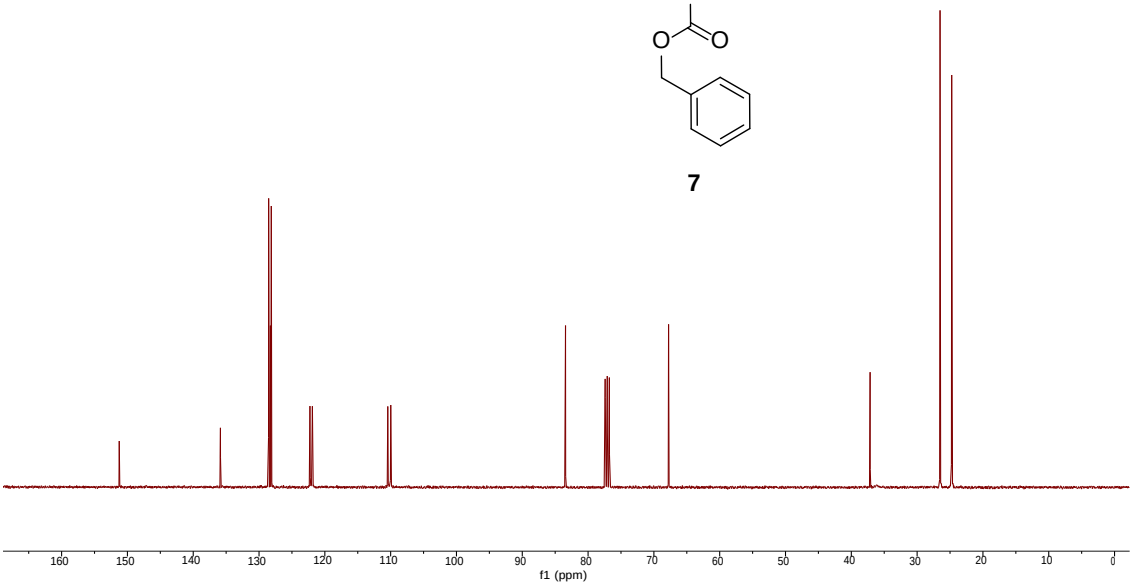
7



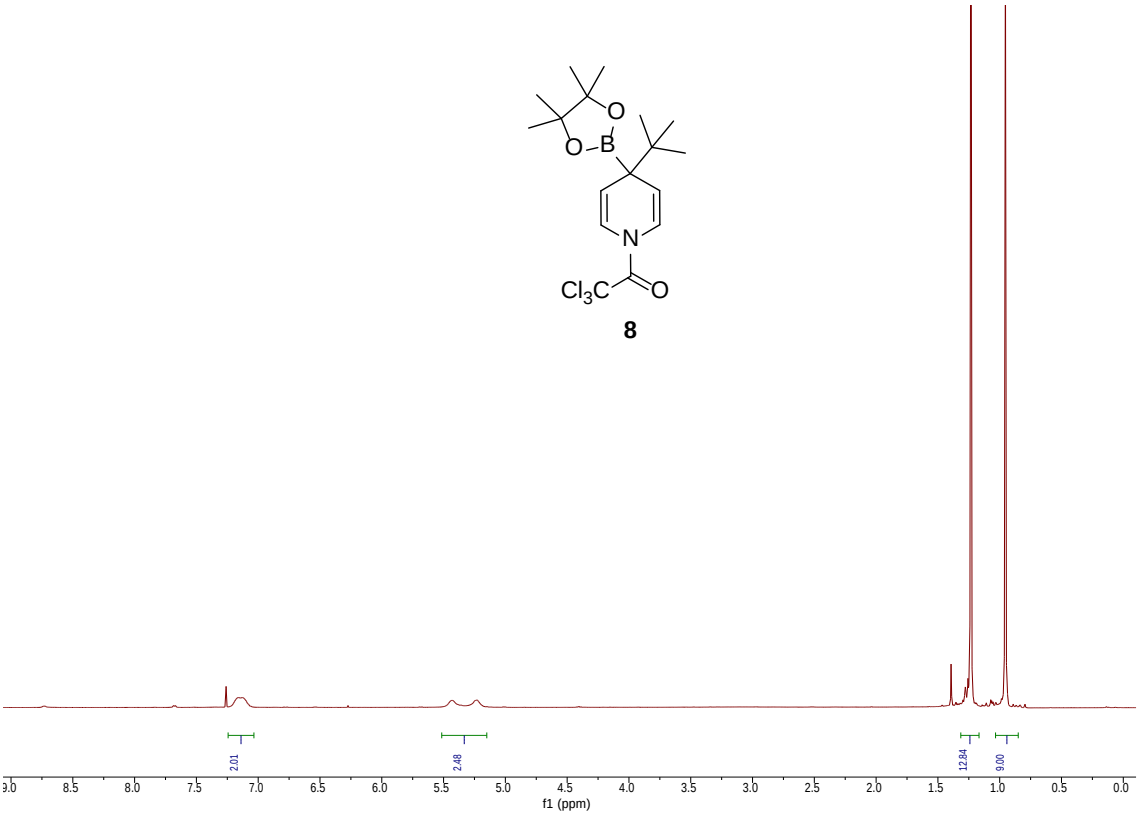
Carbon NMR



7

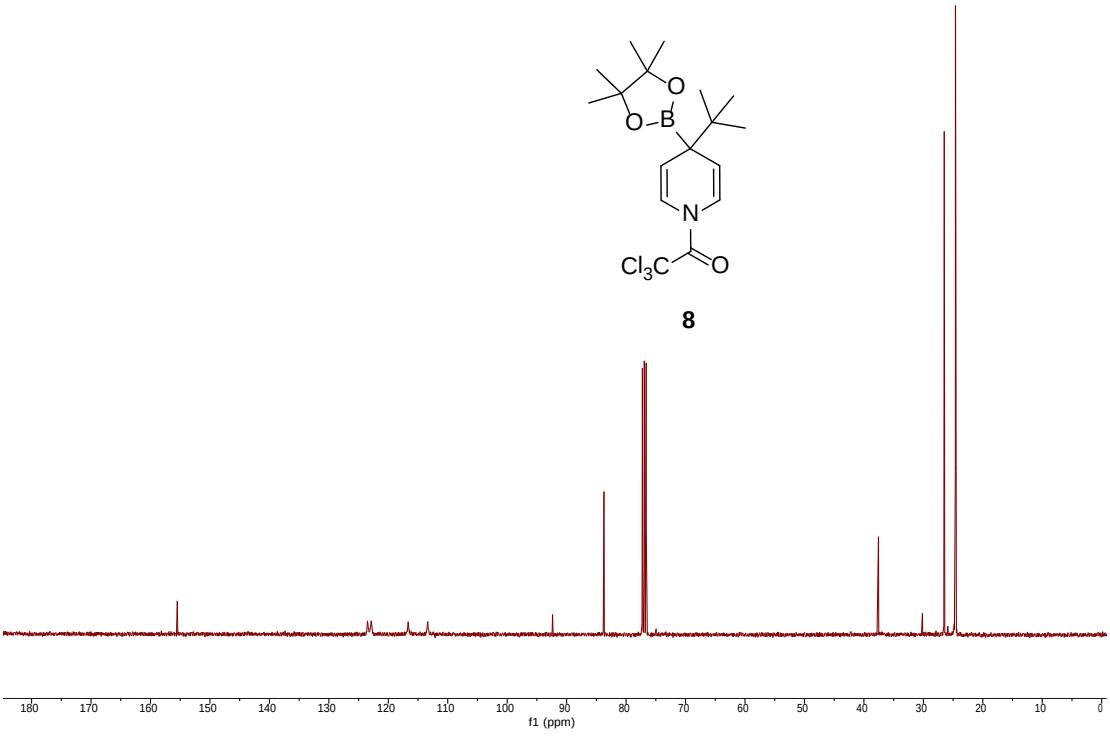


Proton NMR



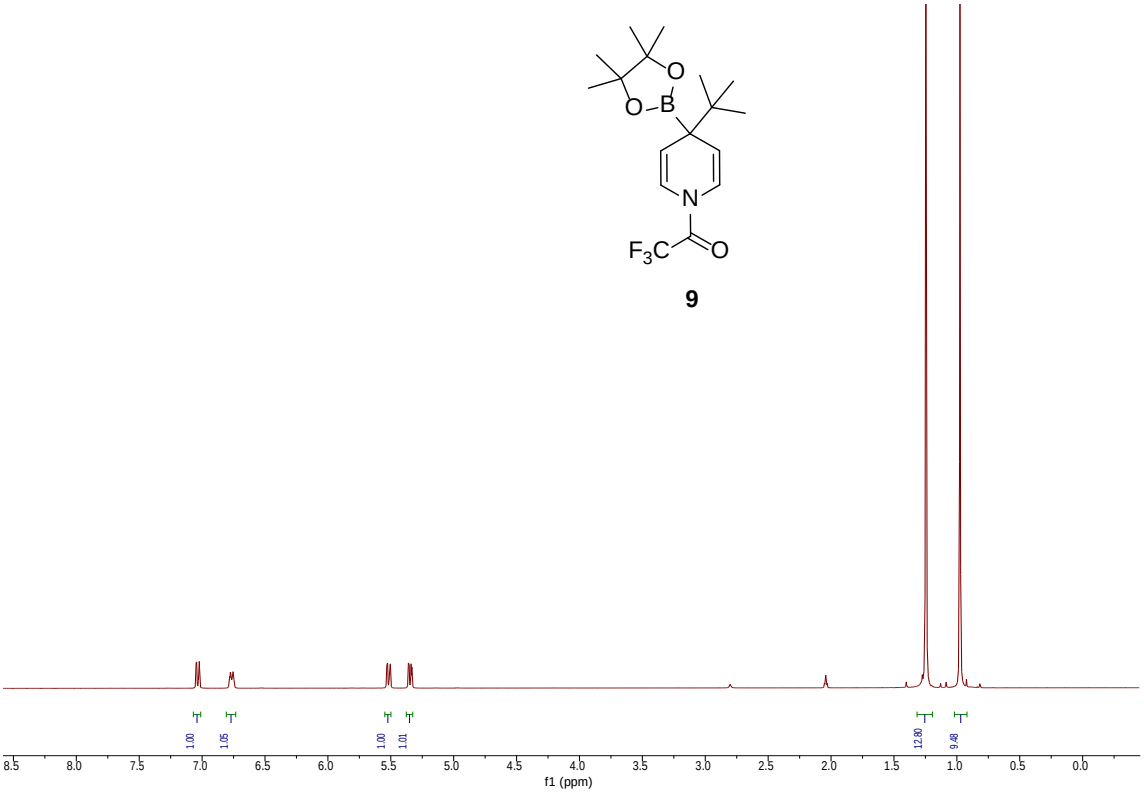
8

Carbon NMR

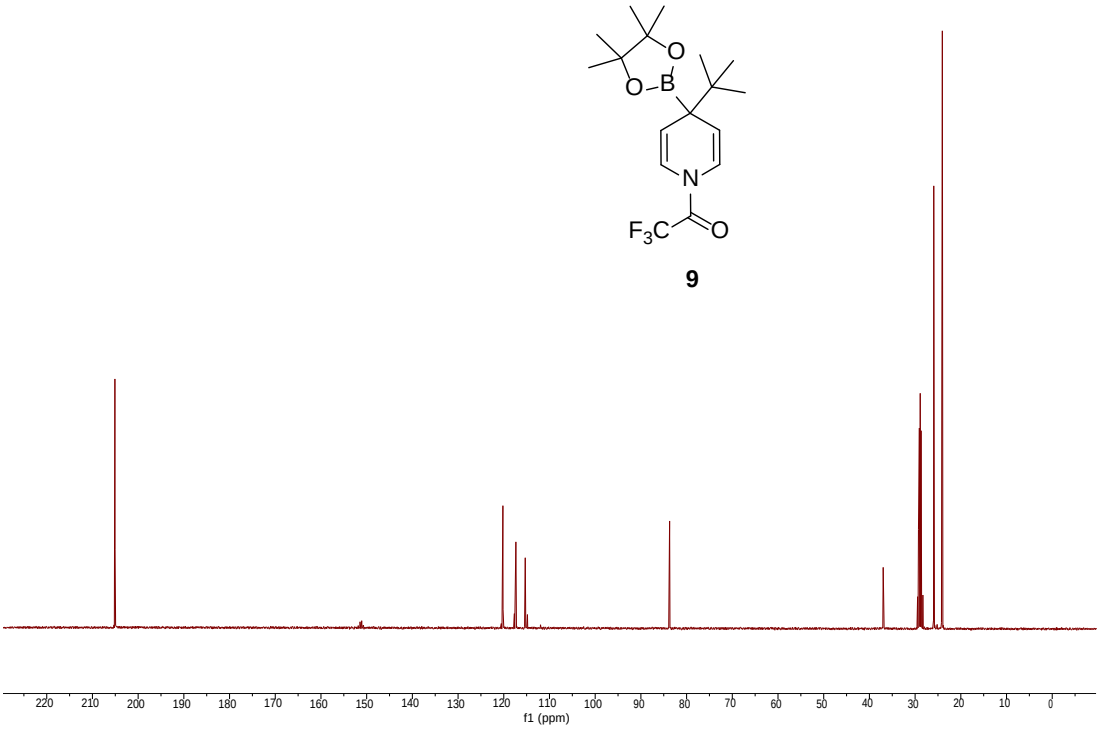


8

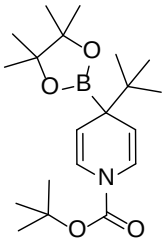
Proton NMR



Carbon NMR



Proton NMR



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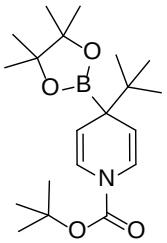

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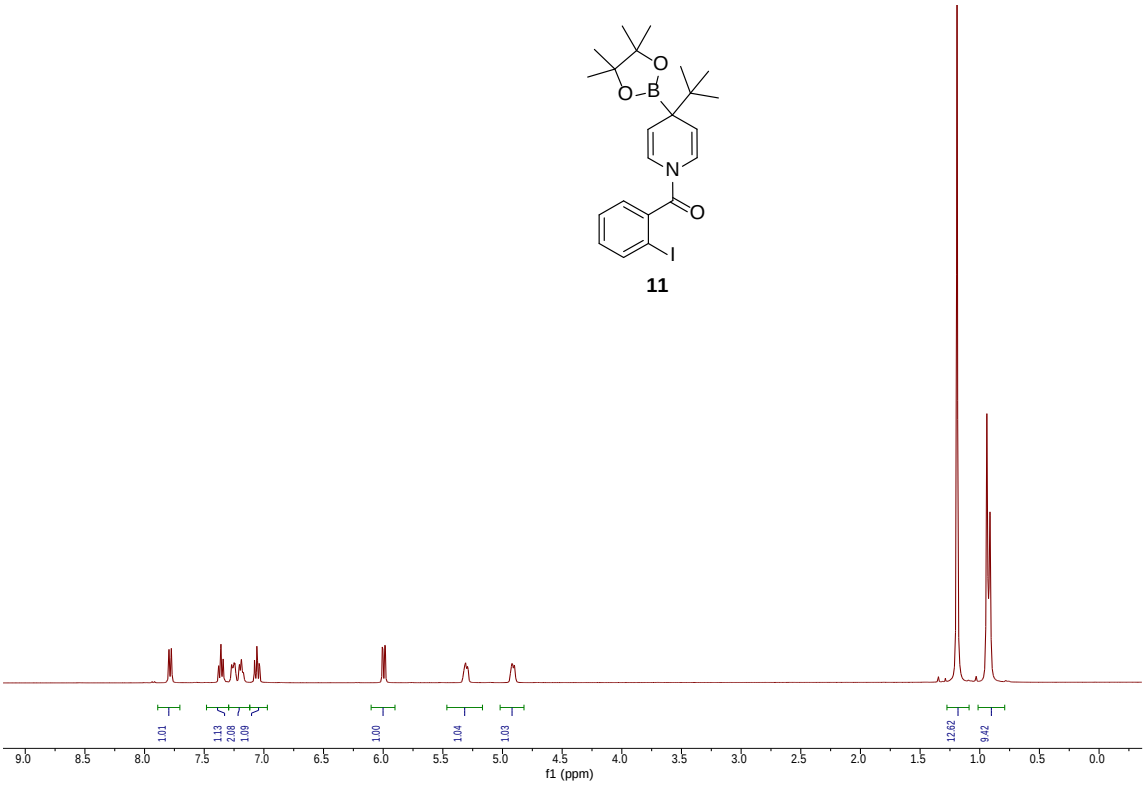

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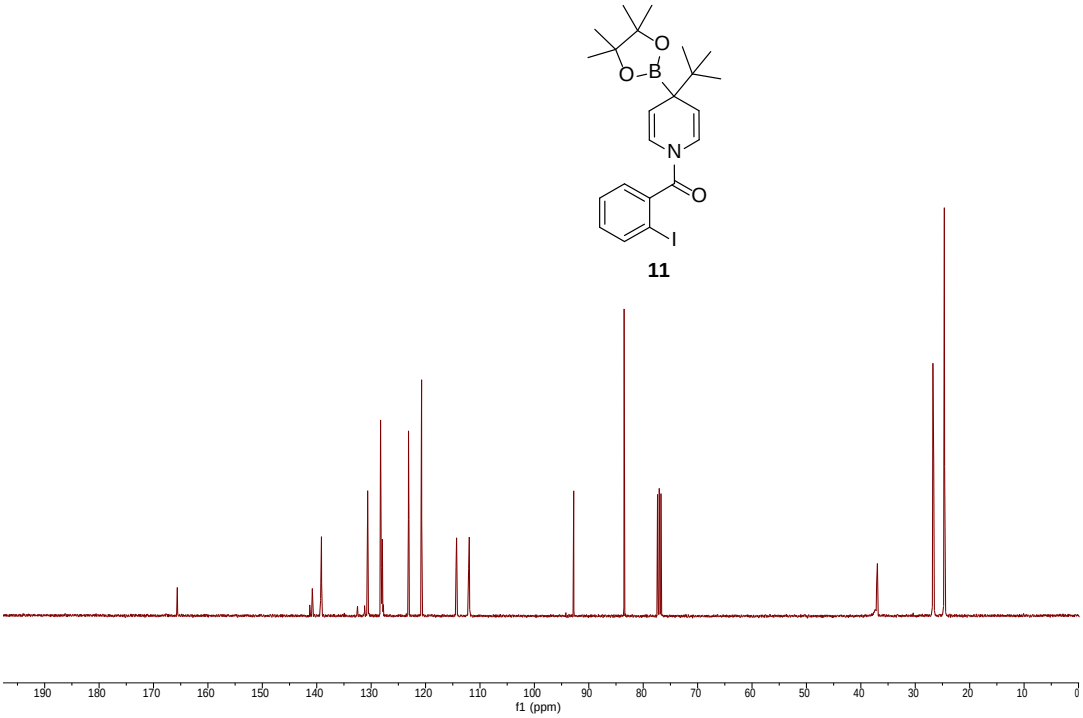

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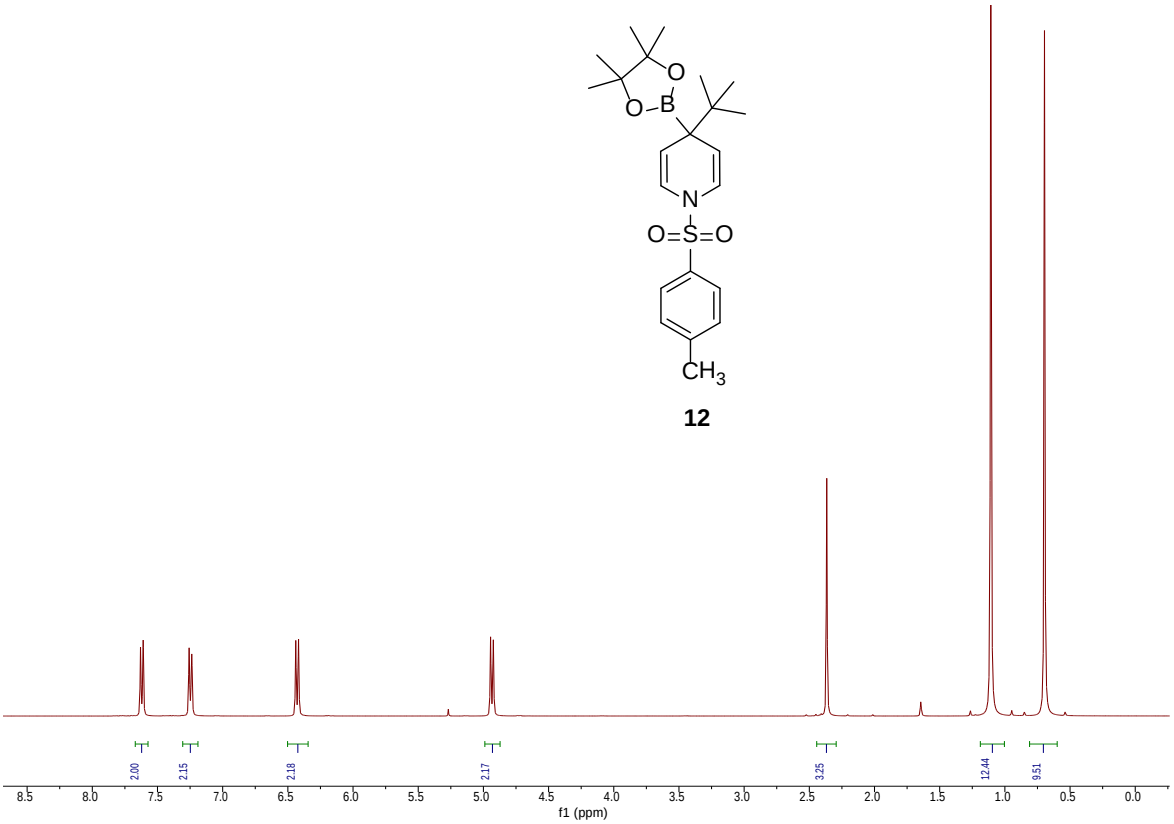

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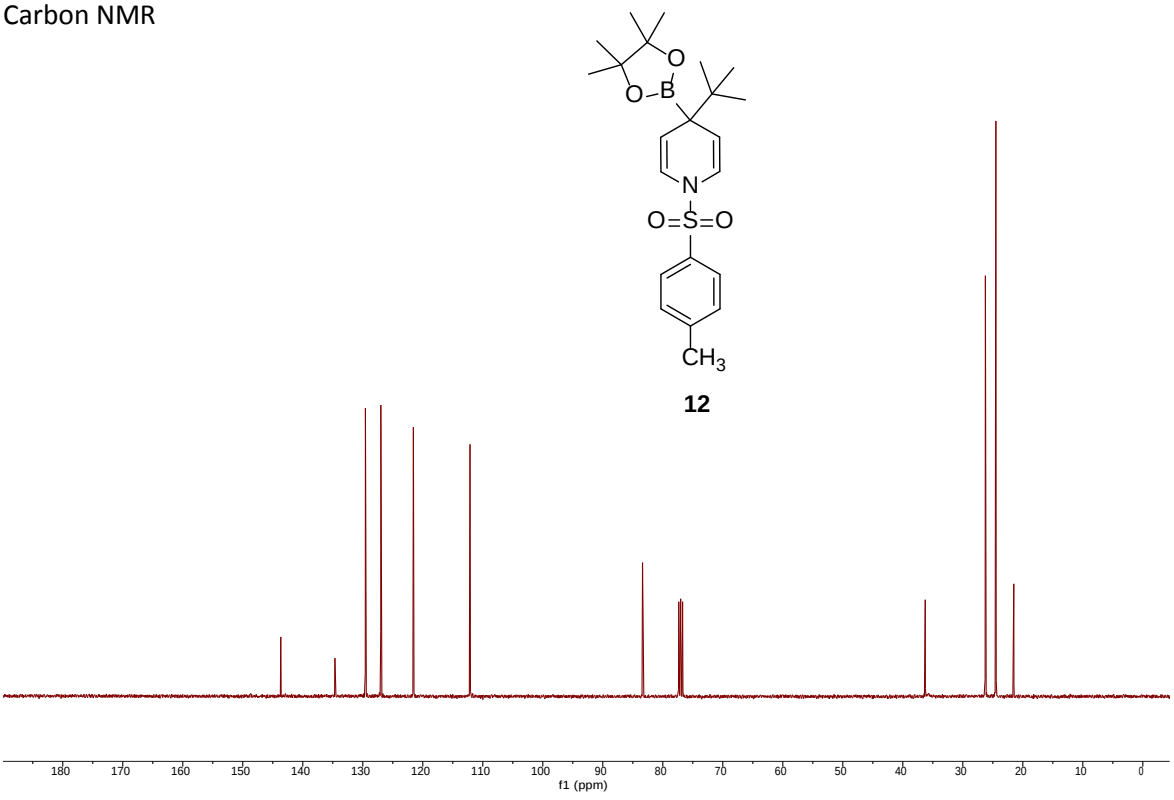

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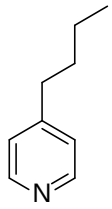

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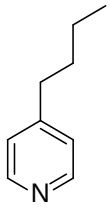

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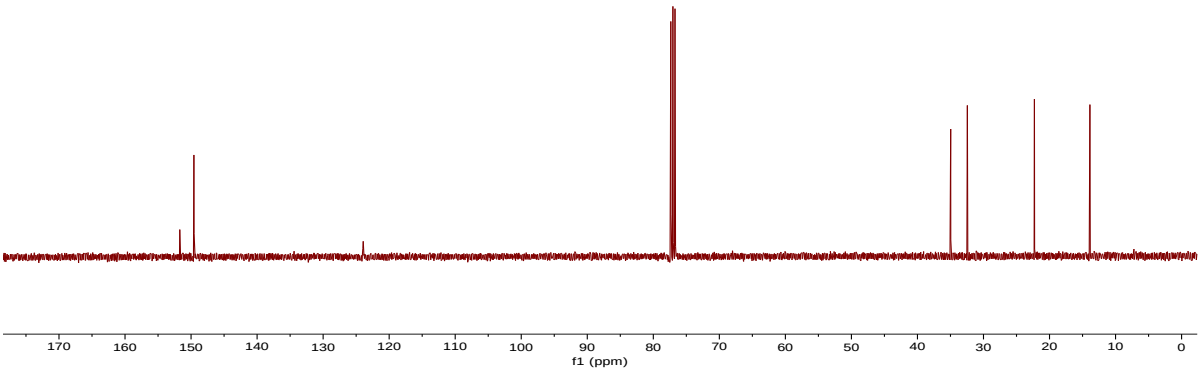

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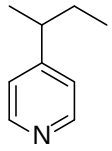

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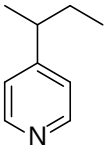

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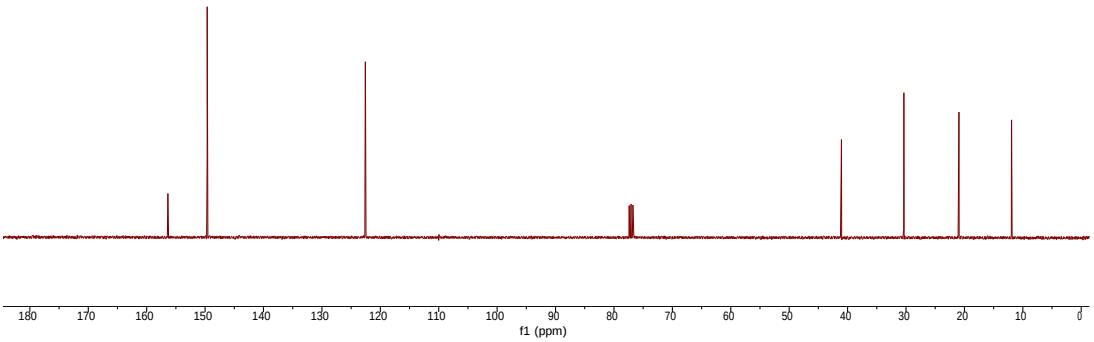

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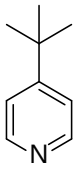

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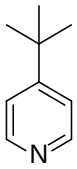

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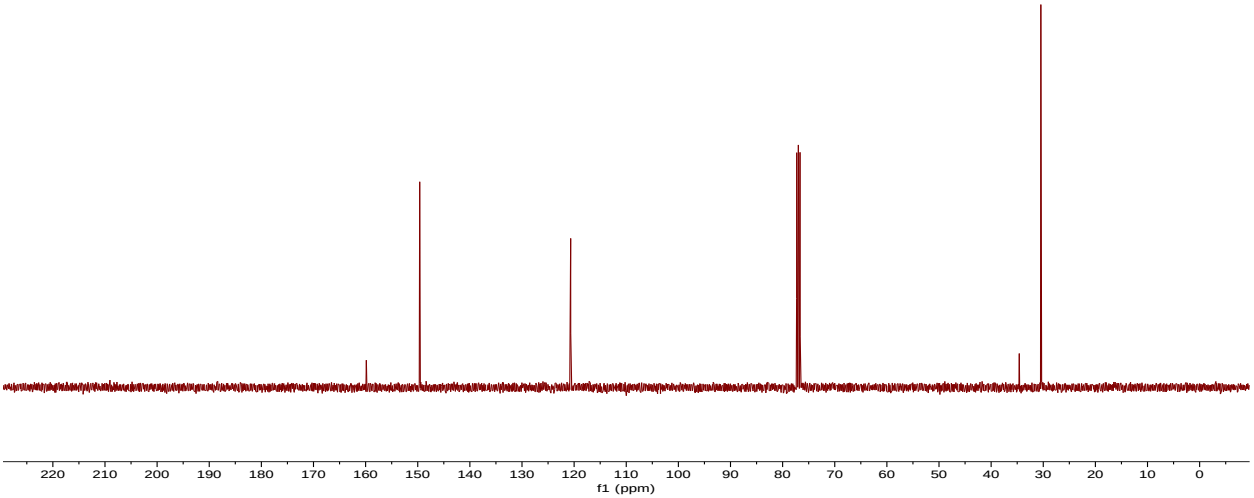

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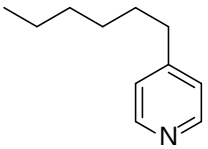

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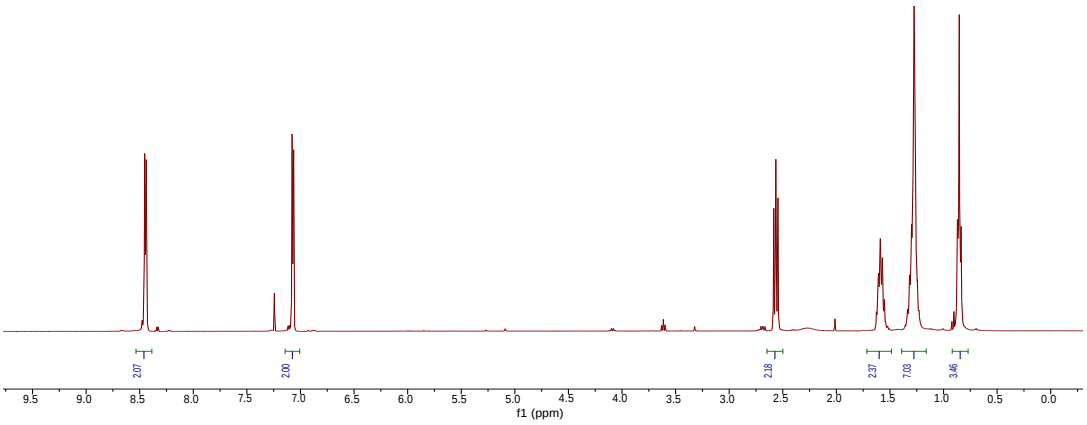

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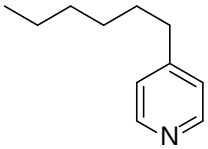

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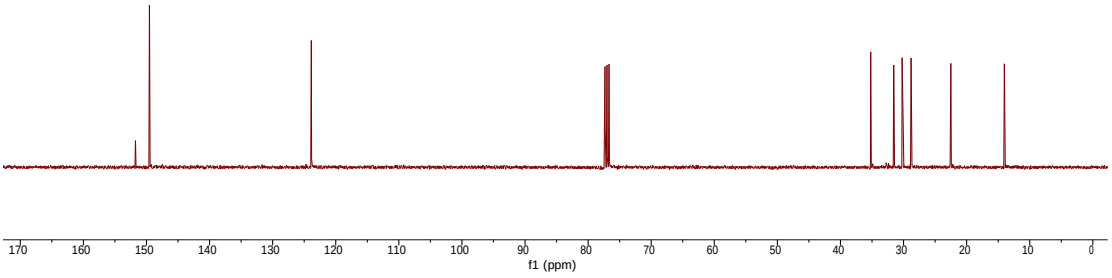

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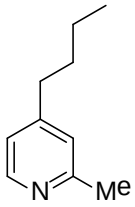

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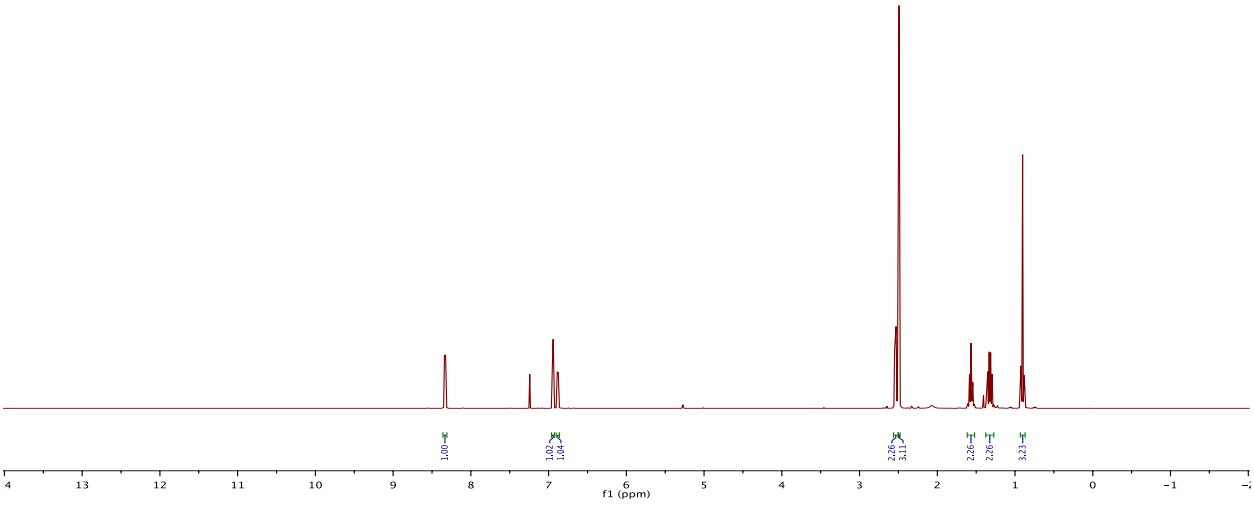
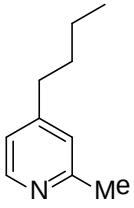


Carbon NMR



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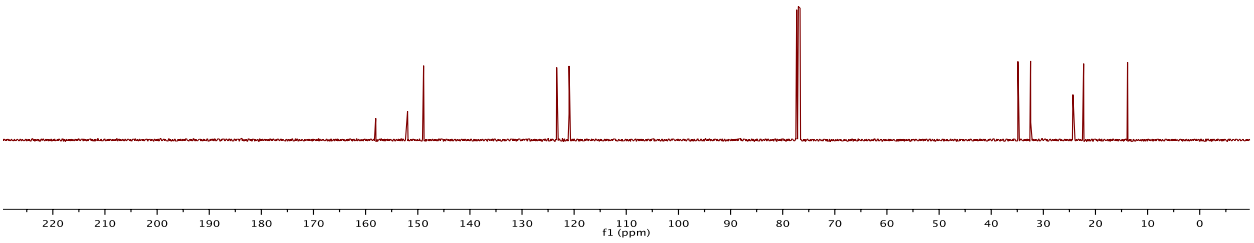

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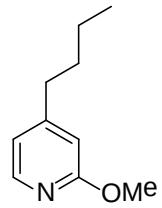

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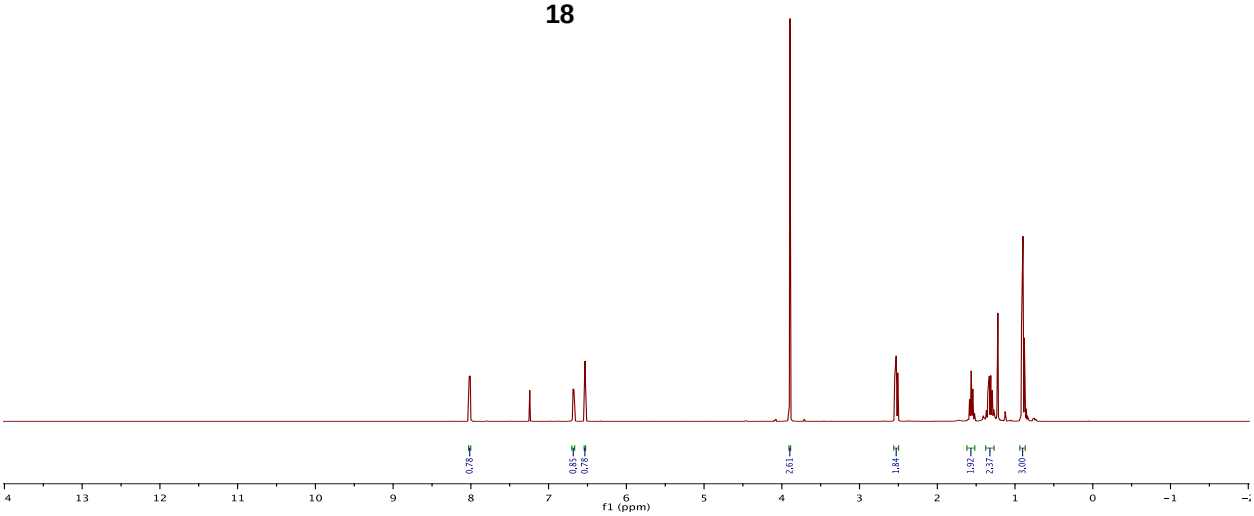

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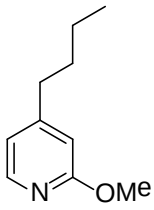

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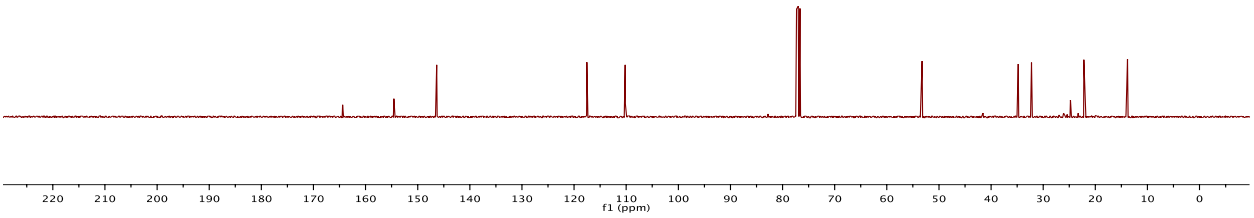

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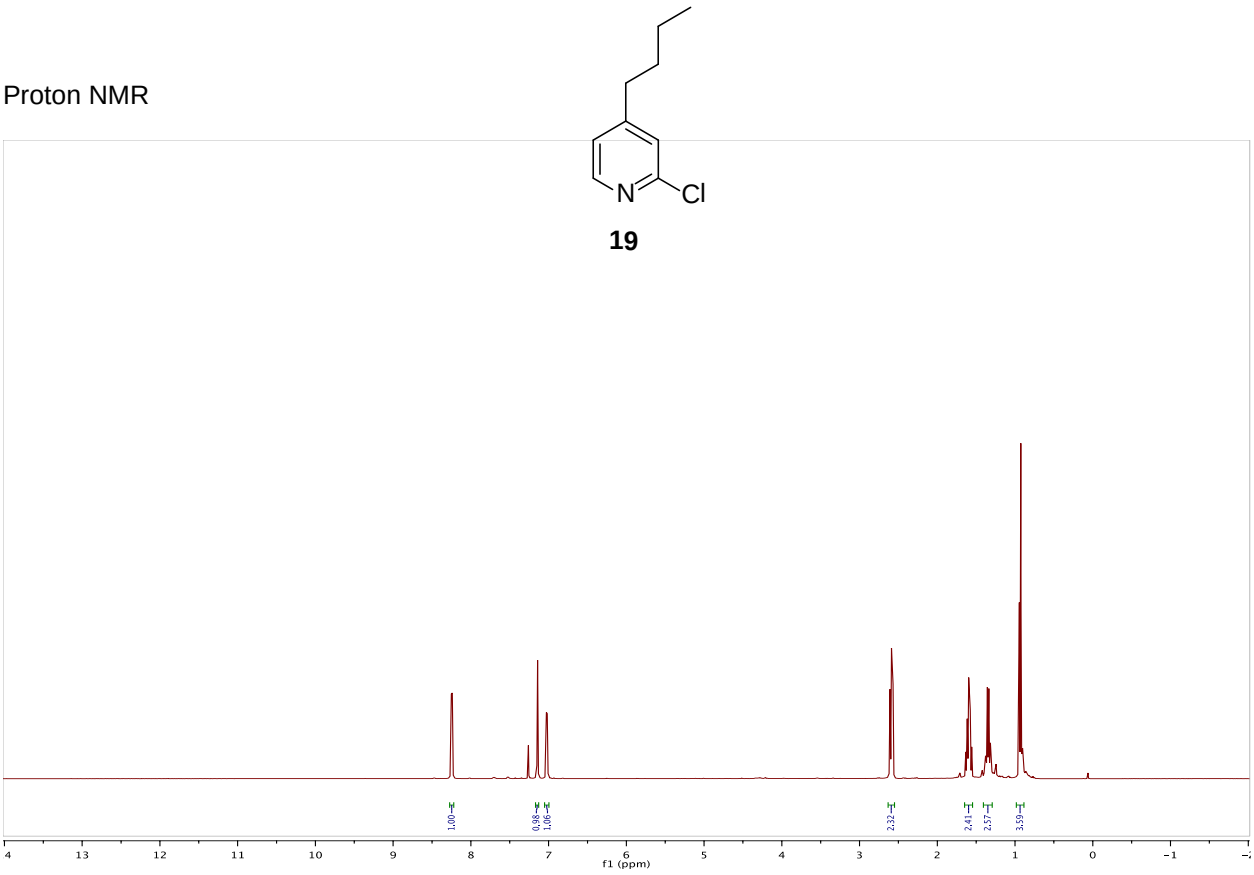

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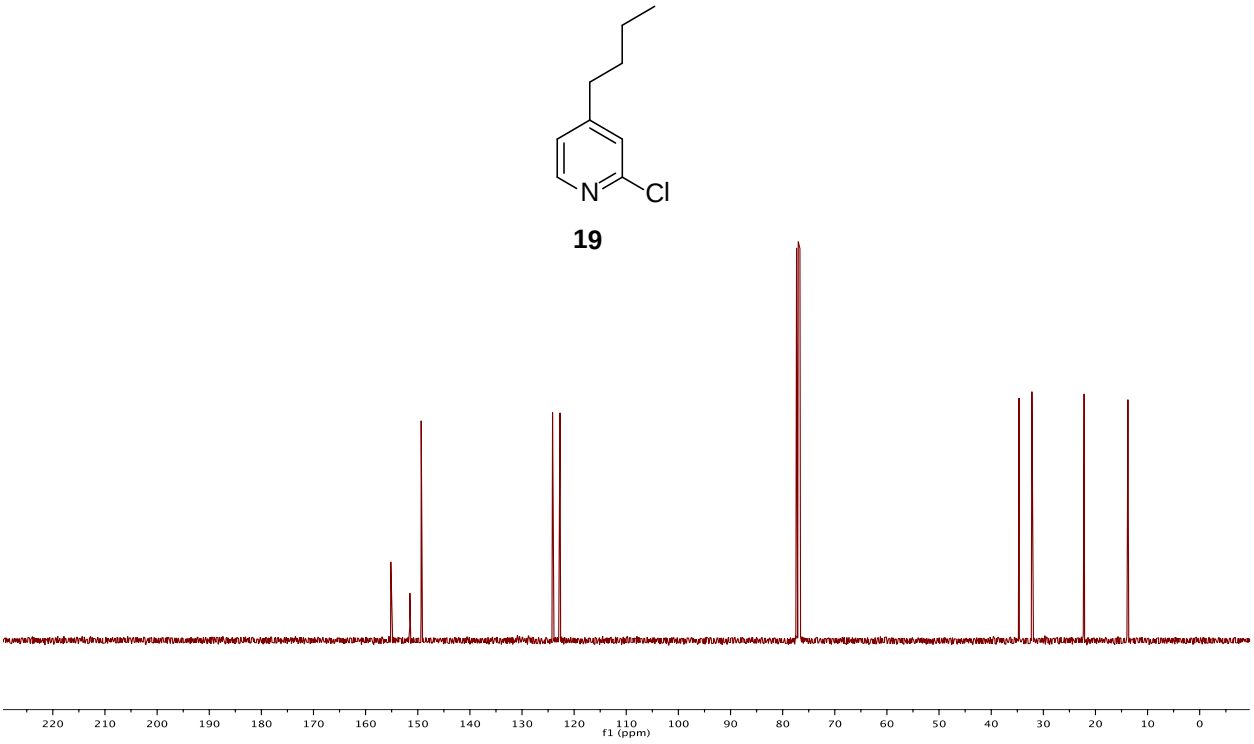

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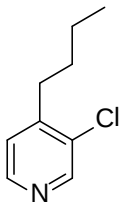

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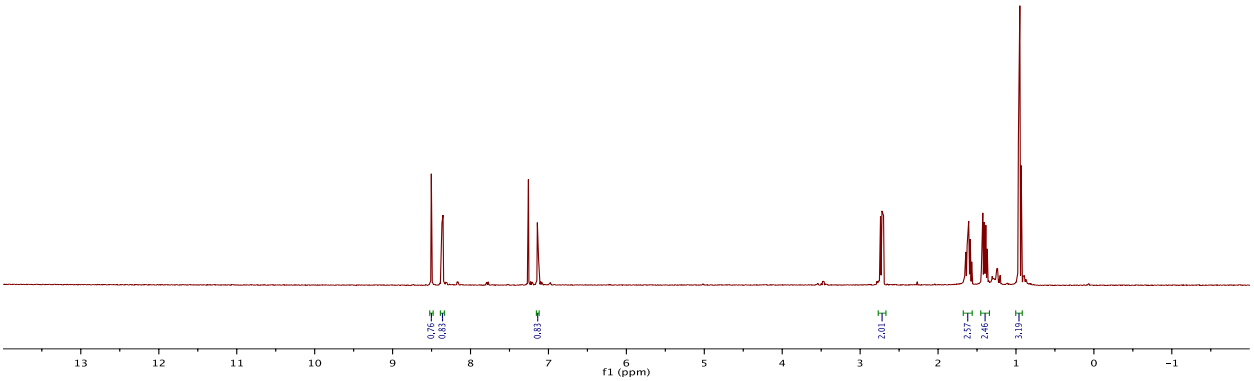
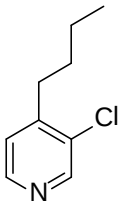


Carbon NMR



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Proton NMR

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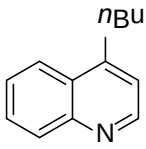

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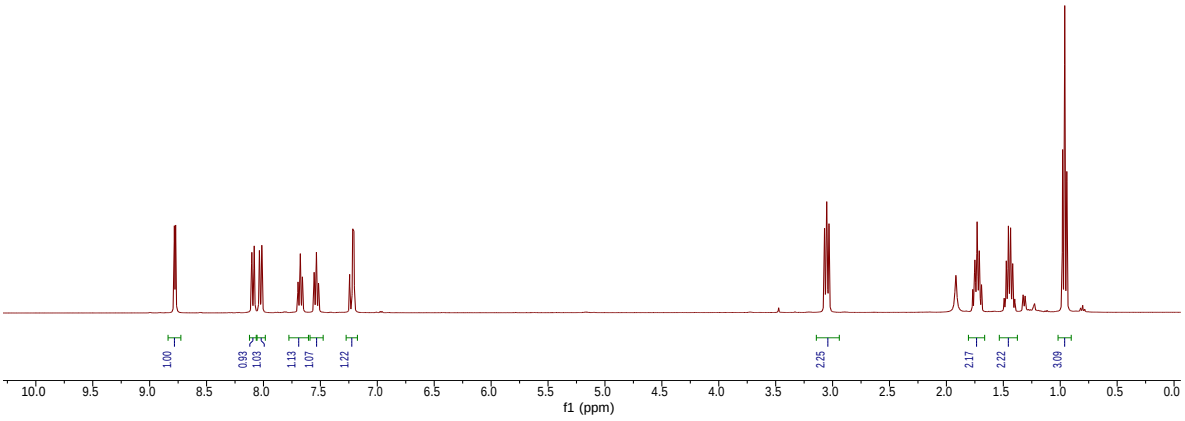
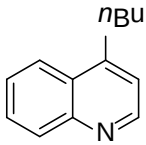


Carbon NMR

CARBON_01



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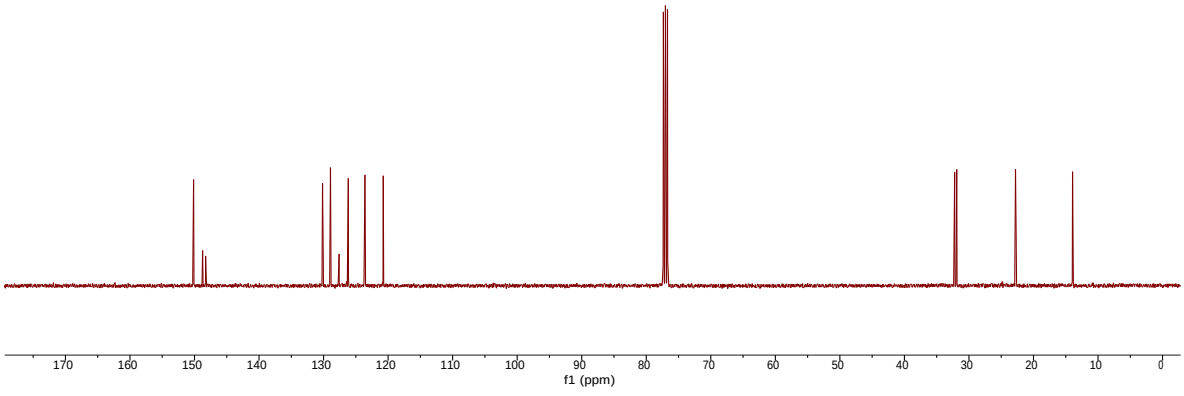

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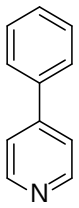

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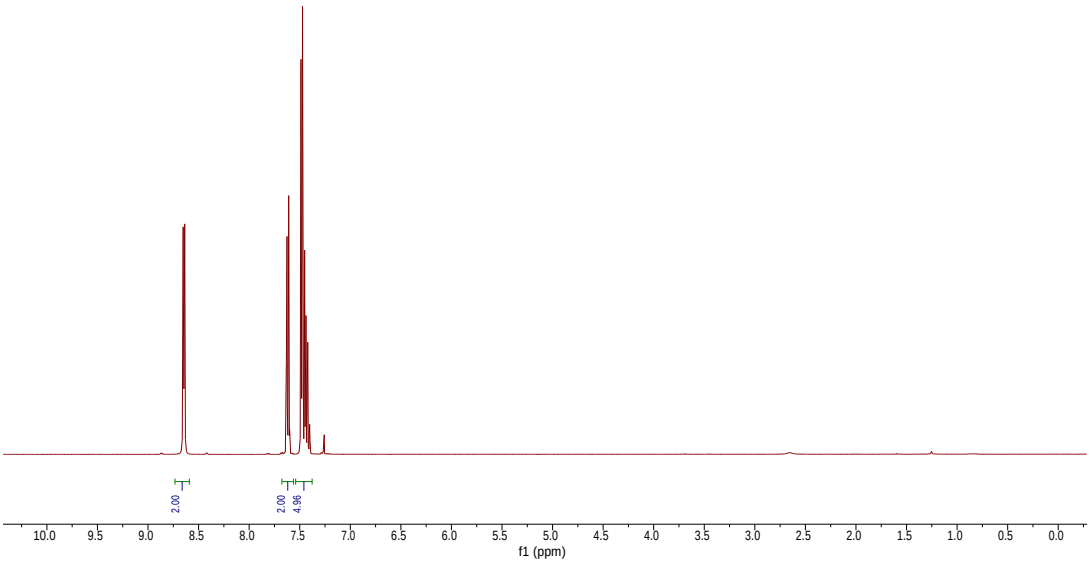

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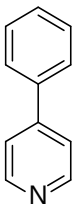

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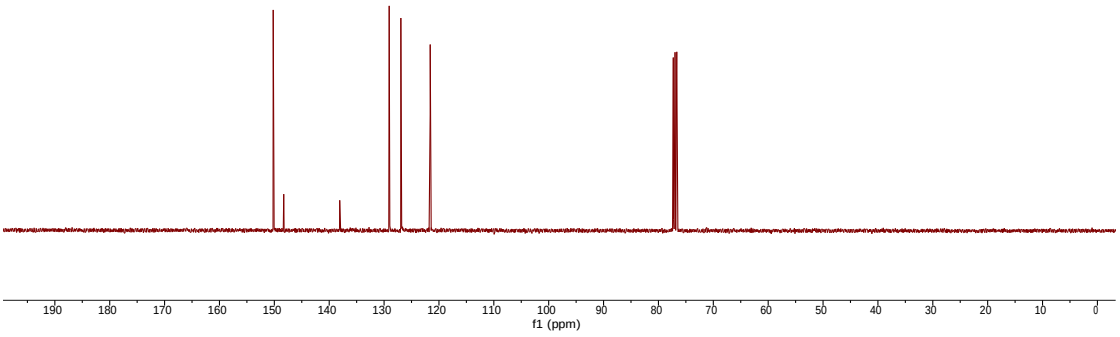

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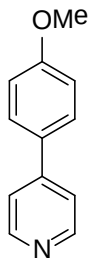

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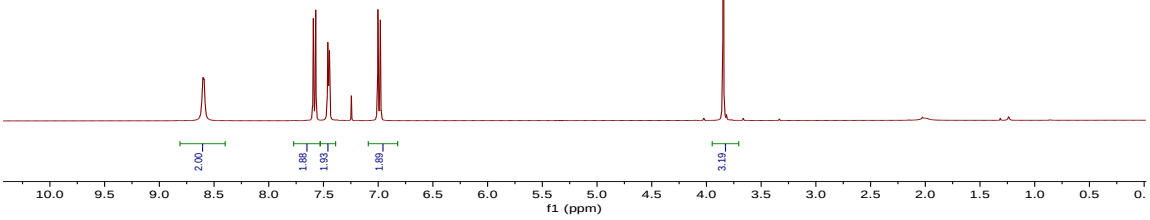

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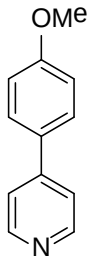

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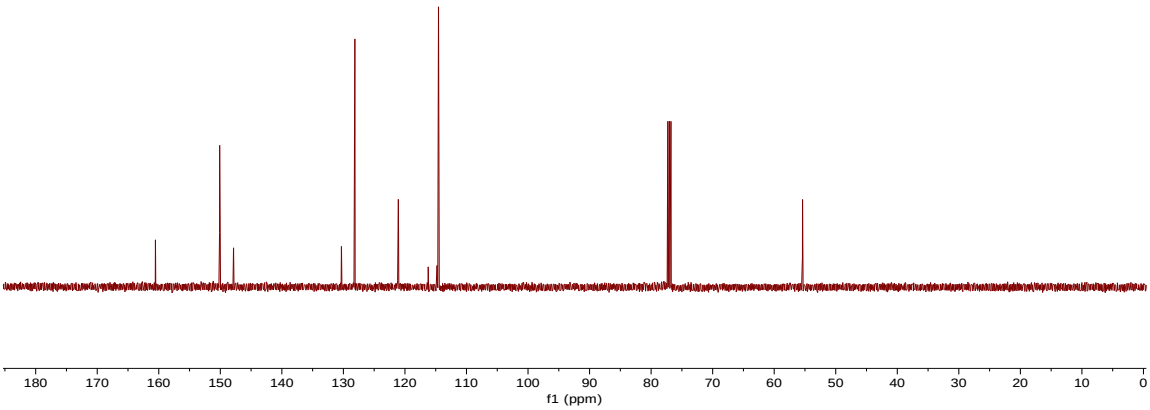

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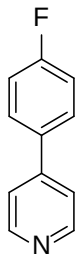

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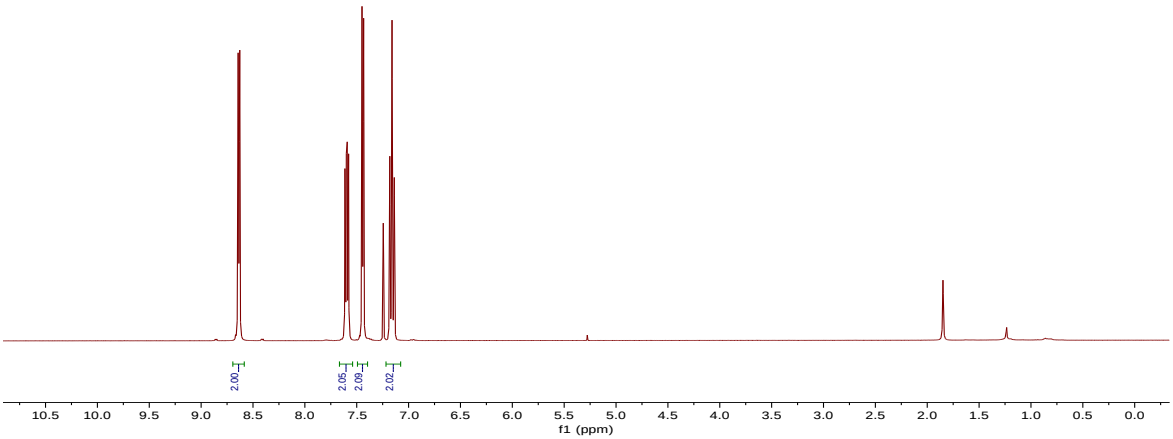

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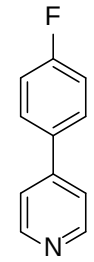

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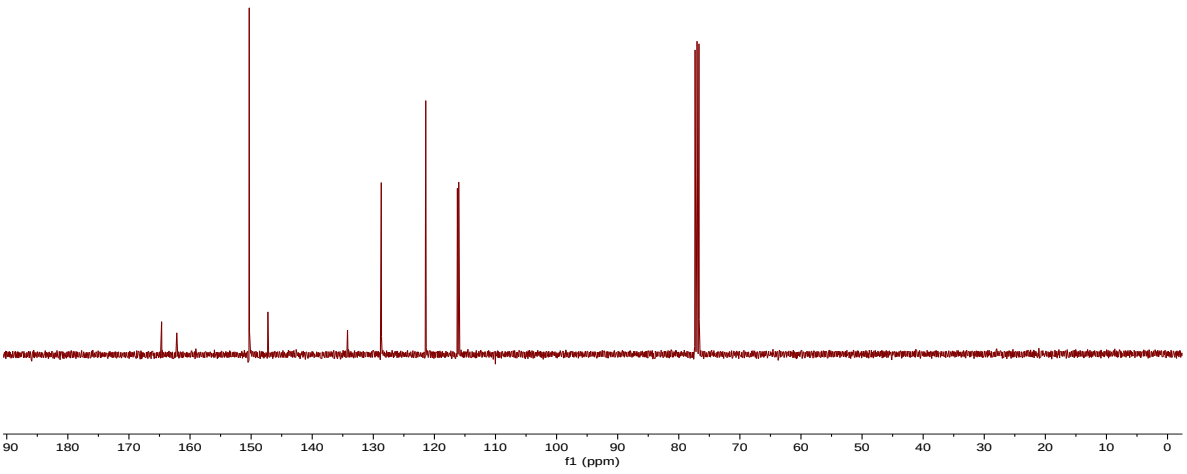

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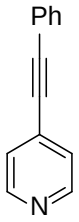

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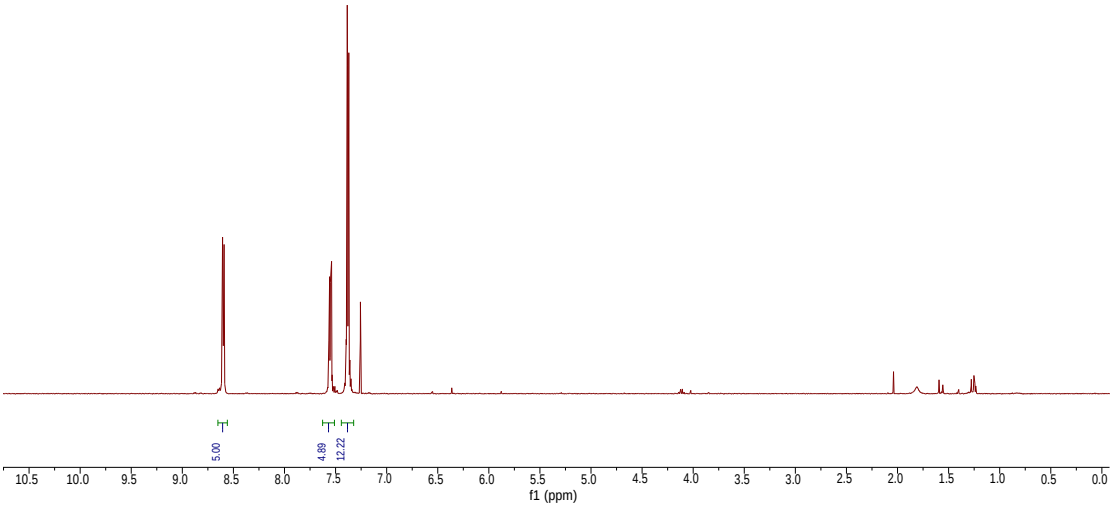

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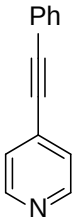

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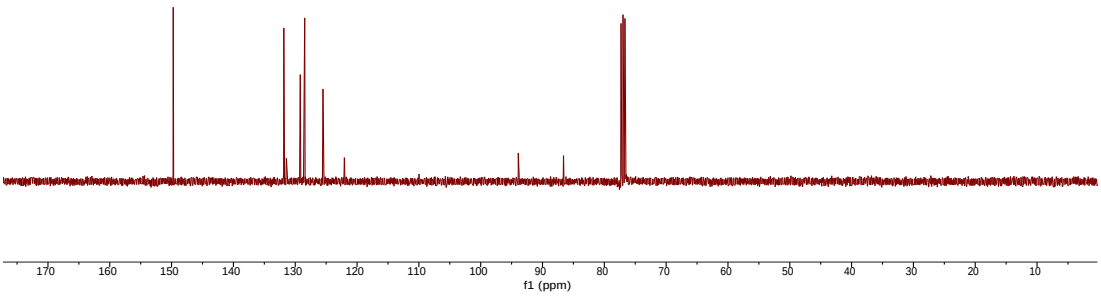
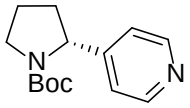


Proton NMR



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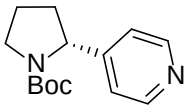
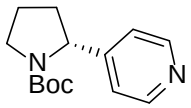
Carbon NMR



26

Chiral HPLC Trace



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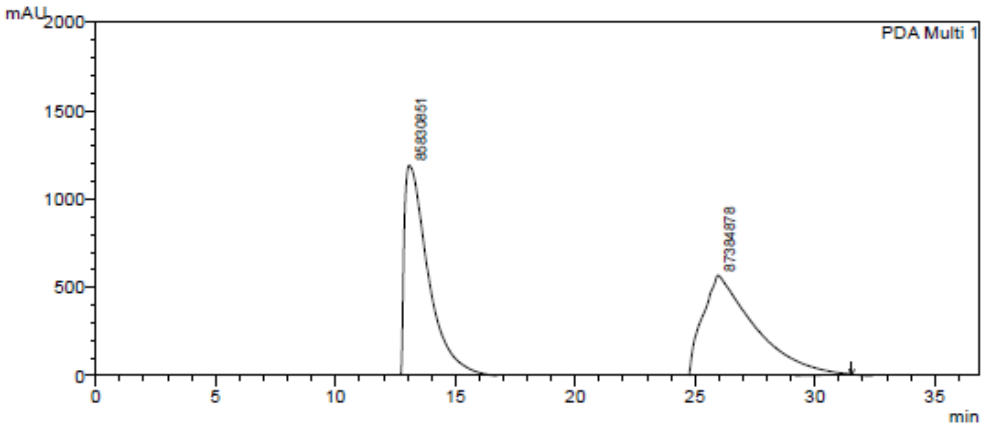

1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %
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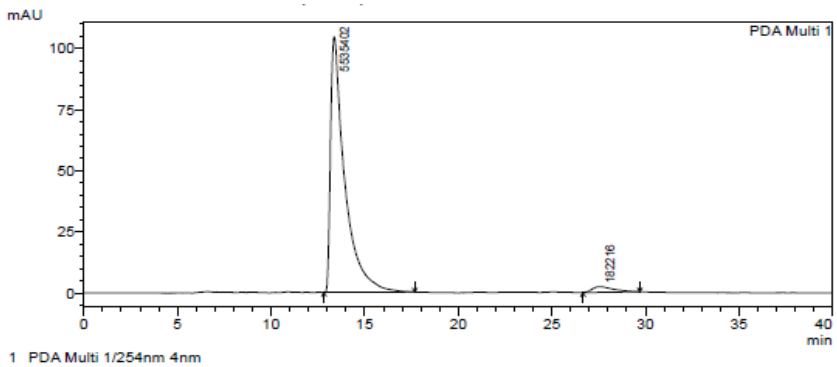
2	25.953	87384878	577943	50.449
Total		173215729	1780994	100.000

Height %
67.549
32.451
100.000



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
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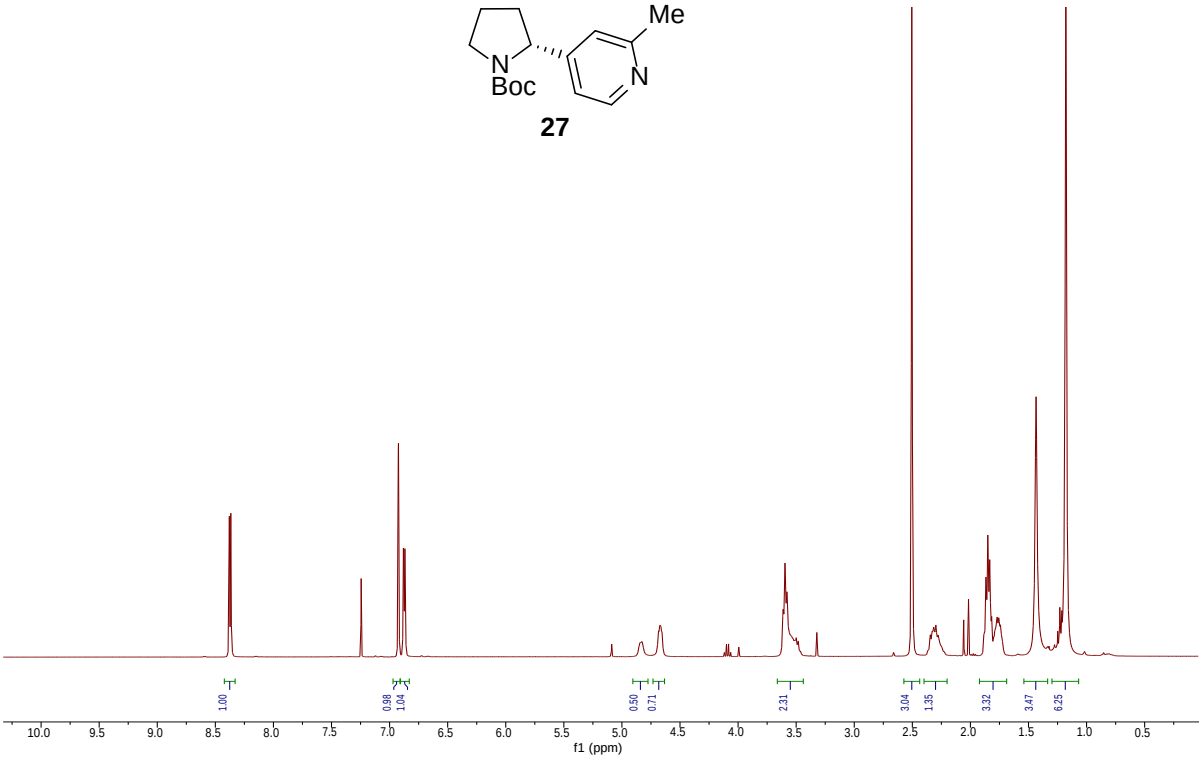
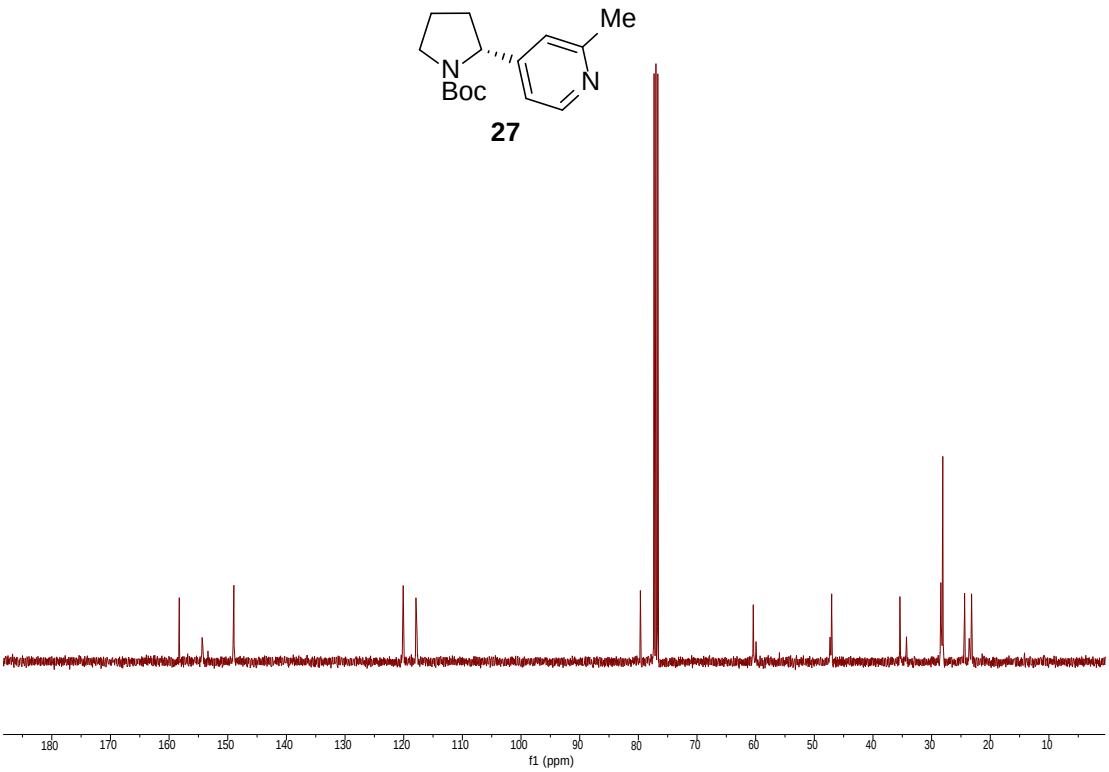
2	27.573	182216	2345	3.187	2.194
Total		5717619	106888	100.000	100.000

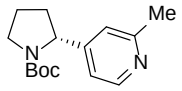
Proton NMR



Carbon NMR



Chiral HPLC Trace



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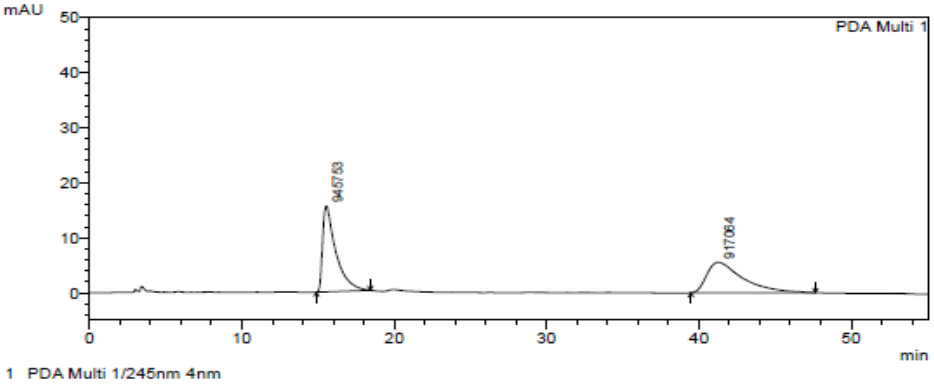
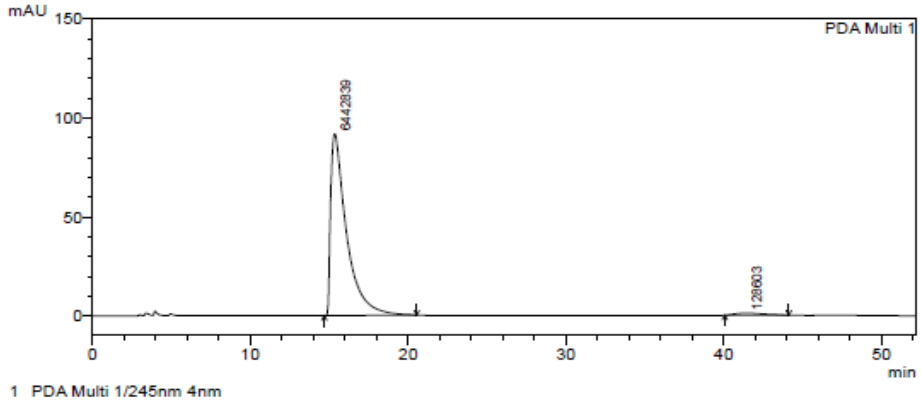


PeakTable

PDA Ch1 245nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.541	945753	15636	50.770	73.791
2	41.262	917064	5554	49.230	26.209
Total		1862817	21190	100.000	100.000



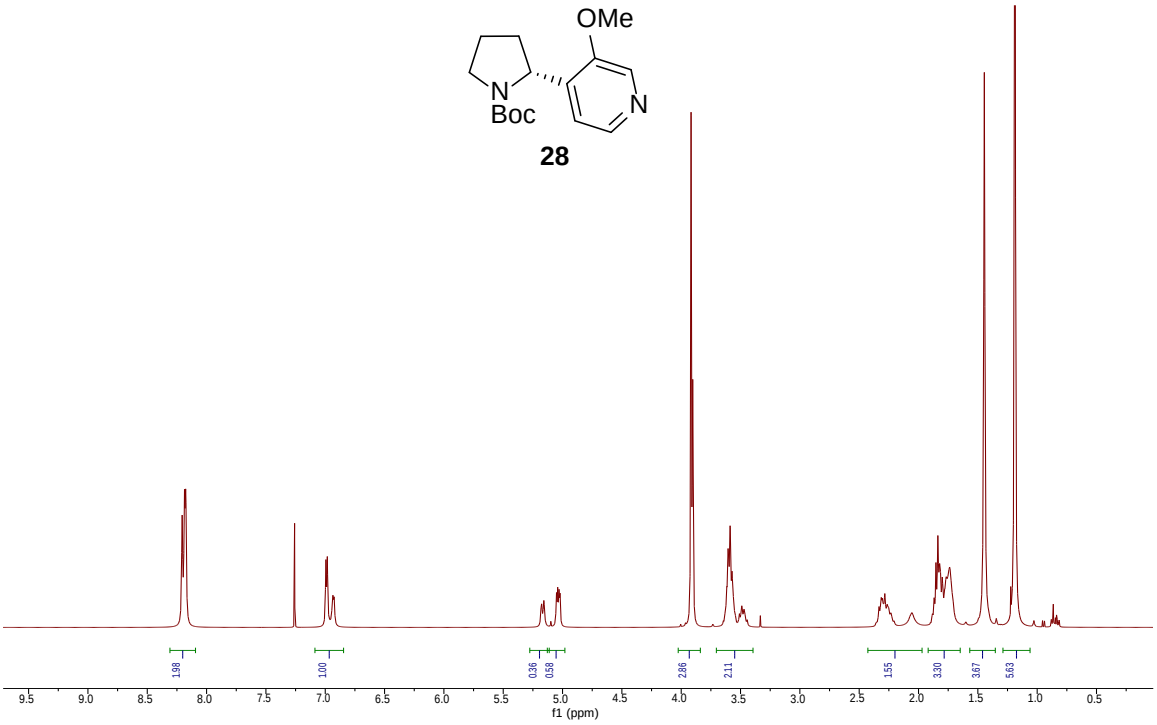
PeakTable

PDA Ch1 245nm 4nm

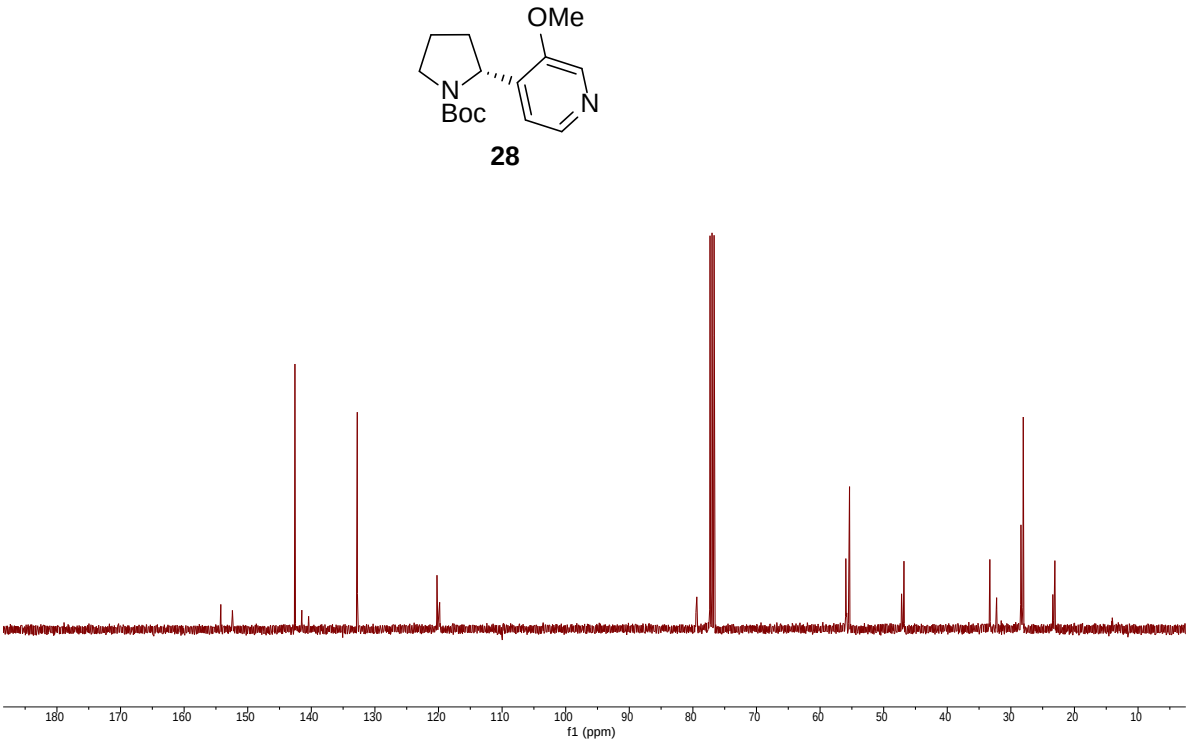
Peak#	Ret. Time	Area	Height	Area %
1	15.347	6442839	91886	98.043
2	41.394	128603	1053	1.957
Total		6571441	92938	100.000

Height %
98.867
1.133
100.000

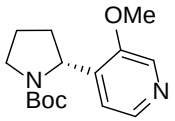
Proton NMR



Carbon NMR



Chiral HPLC Trace



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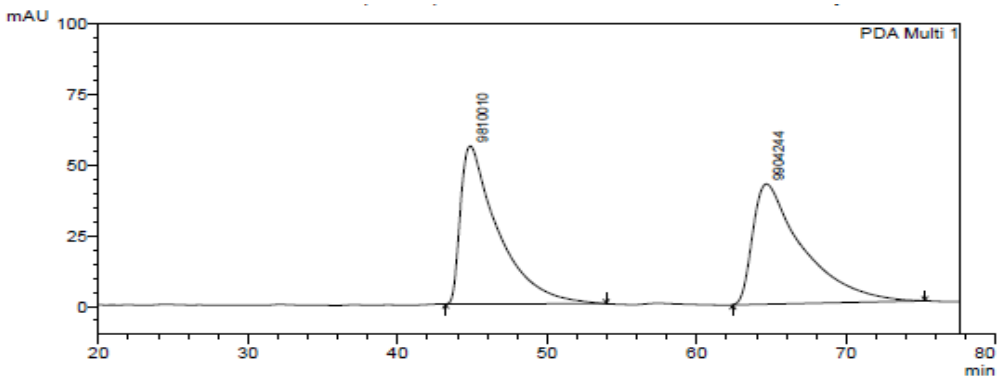


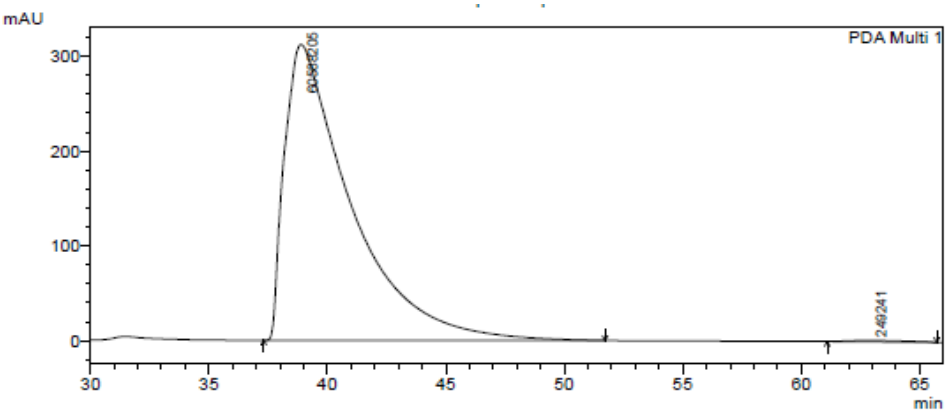
1 PDA Multi 1/224nm 4nm

PeakTable

PDA Ch1 224nm 4nm

Peak#	Ret. Time	Area	Height	Area %
1	44.855	9810010	55992	49.761
2	64.657	9904244	42543	50.239
Total		19714254	98536	100.000

Height %
56.824
43.176
100.000



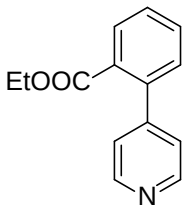
1 PDA Multi 1/224nm 4nm

PeakTable

PDA Ch1 224nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	38.881	60588205	312195	99.590	99.513
2	62.876	249241	1527	0.410	0.487
Total		60837447	313722	100.000	100.000

Proton NMR



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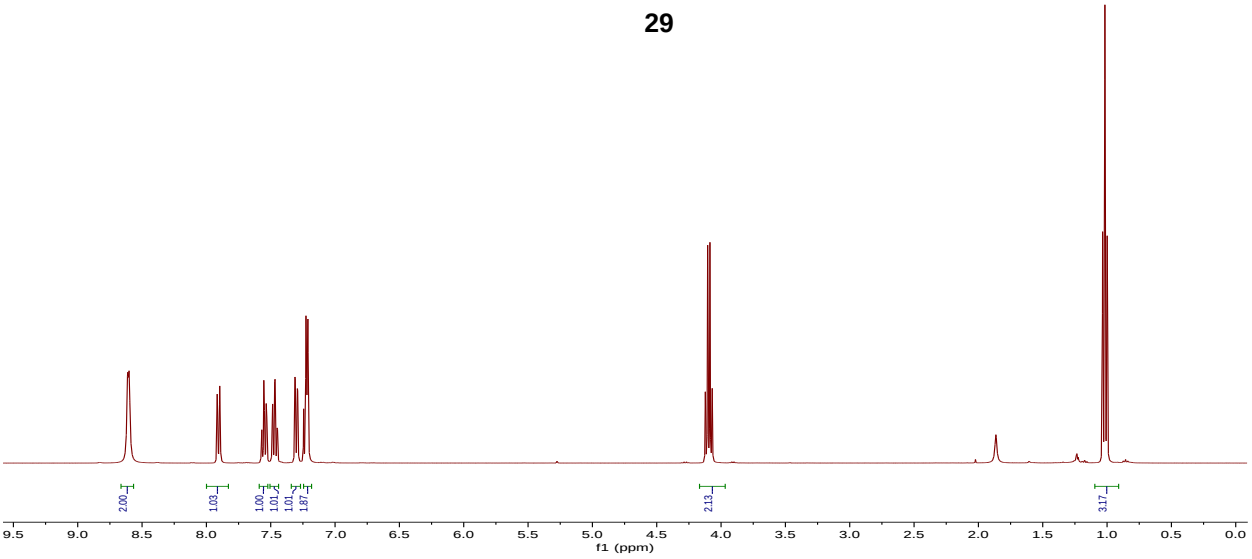
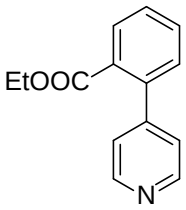


Carbon NMR



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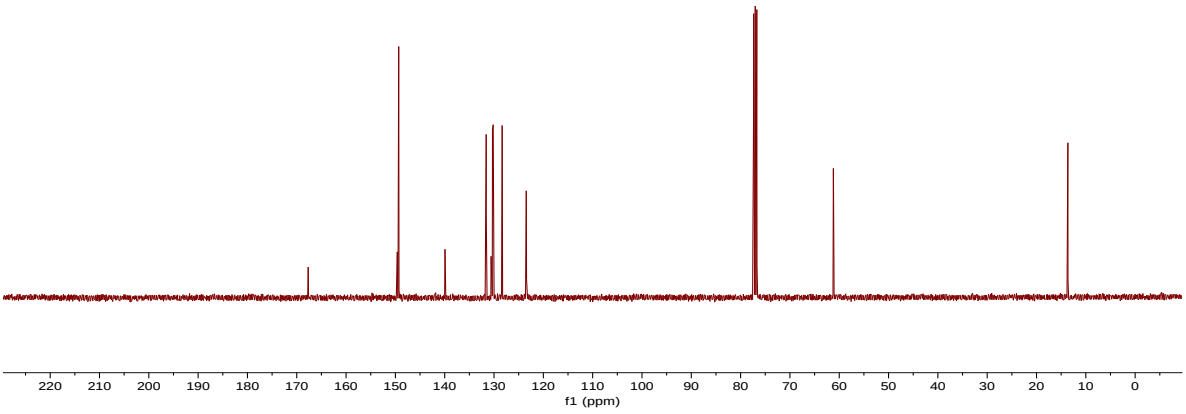
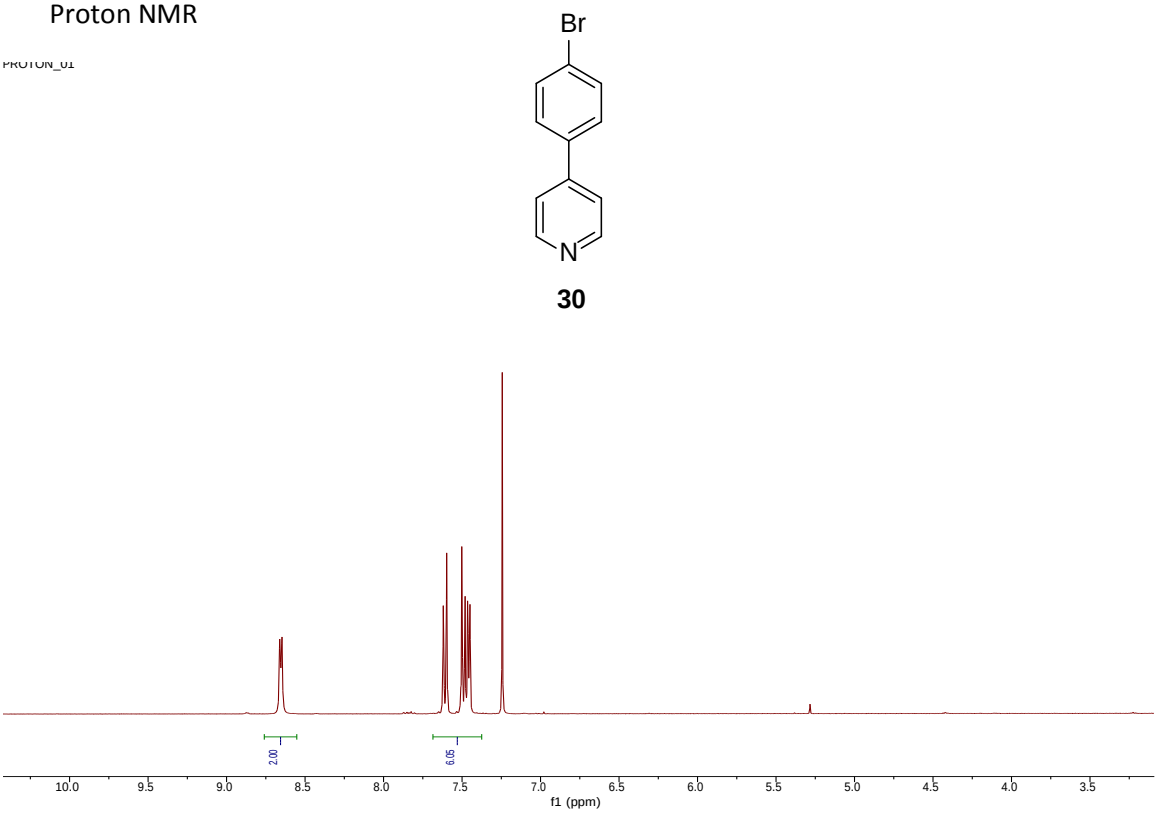
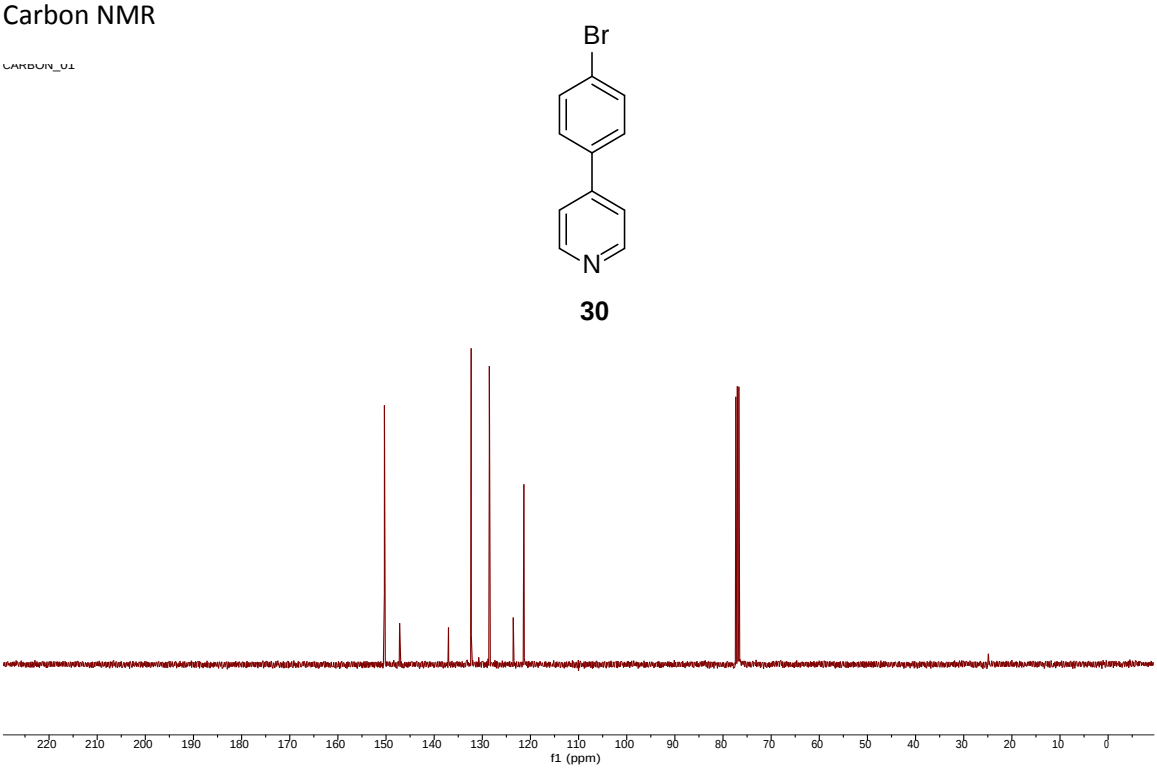


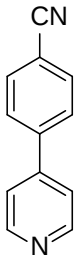
Proton NMR



Carbon NMR



Proton NMR



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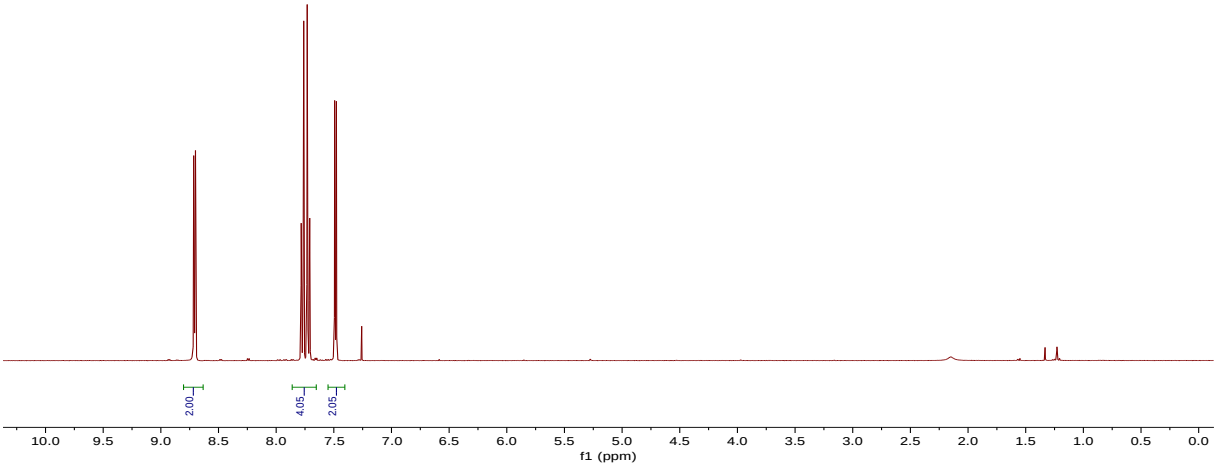
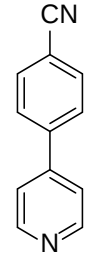


Carbon NMR



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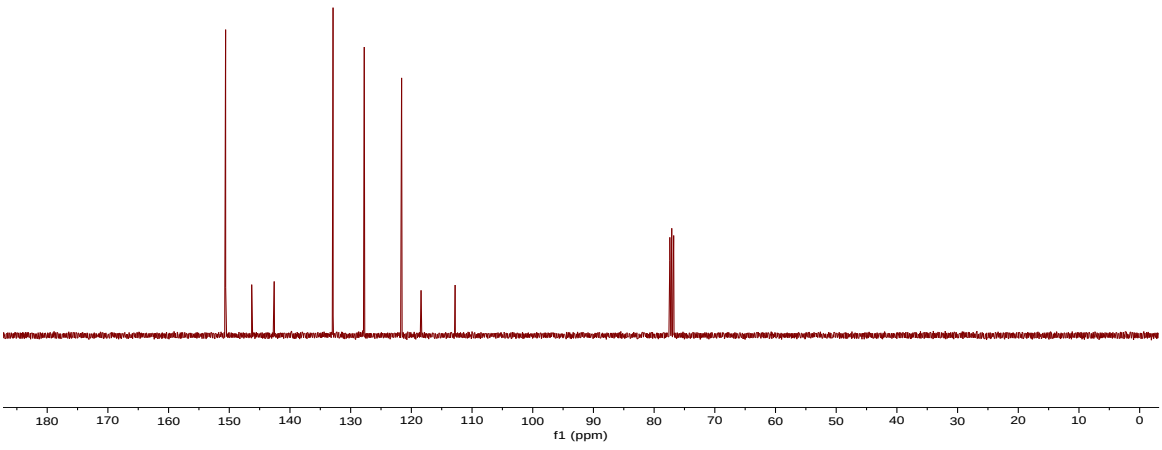
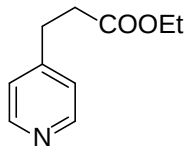


Proton NMR



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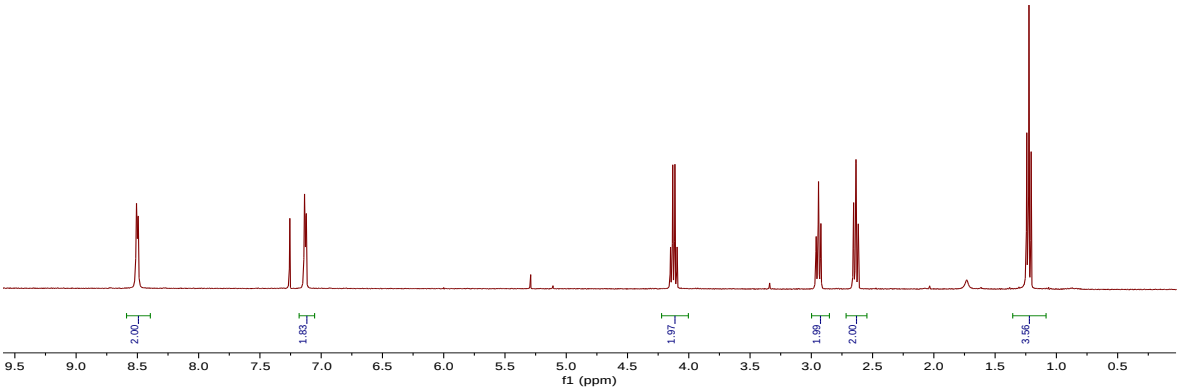
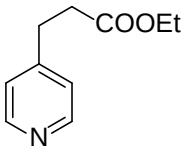


Carbon NMR



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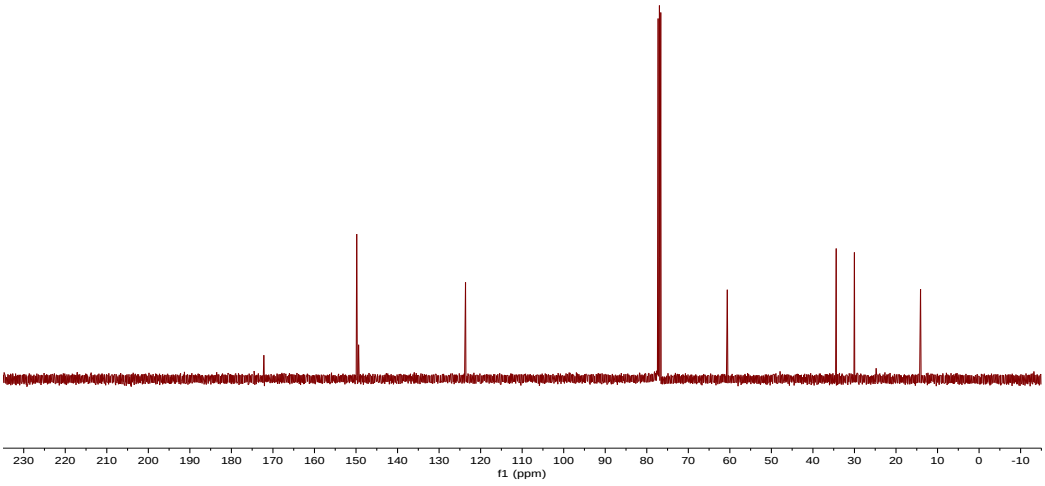
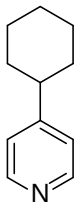


Proton NMR



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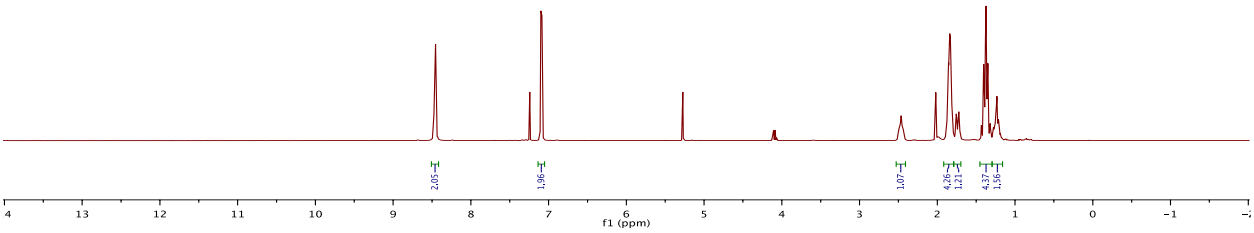
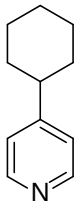


Carbon NMR



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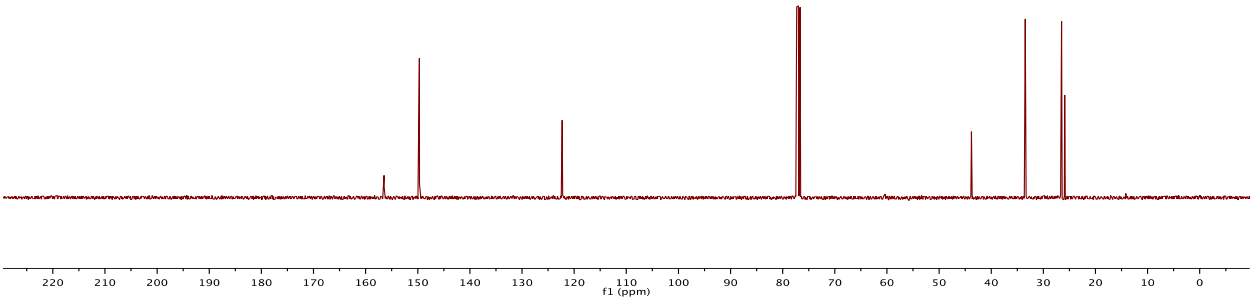
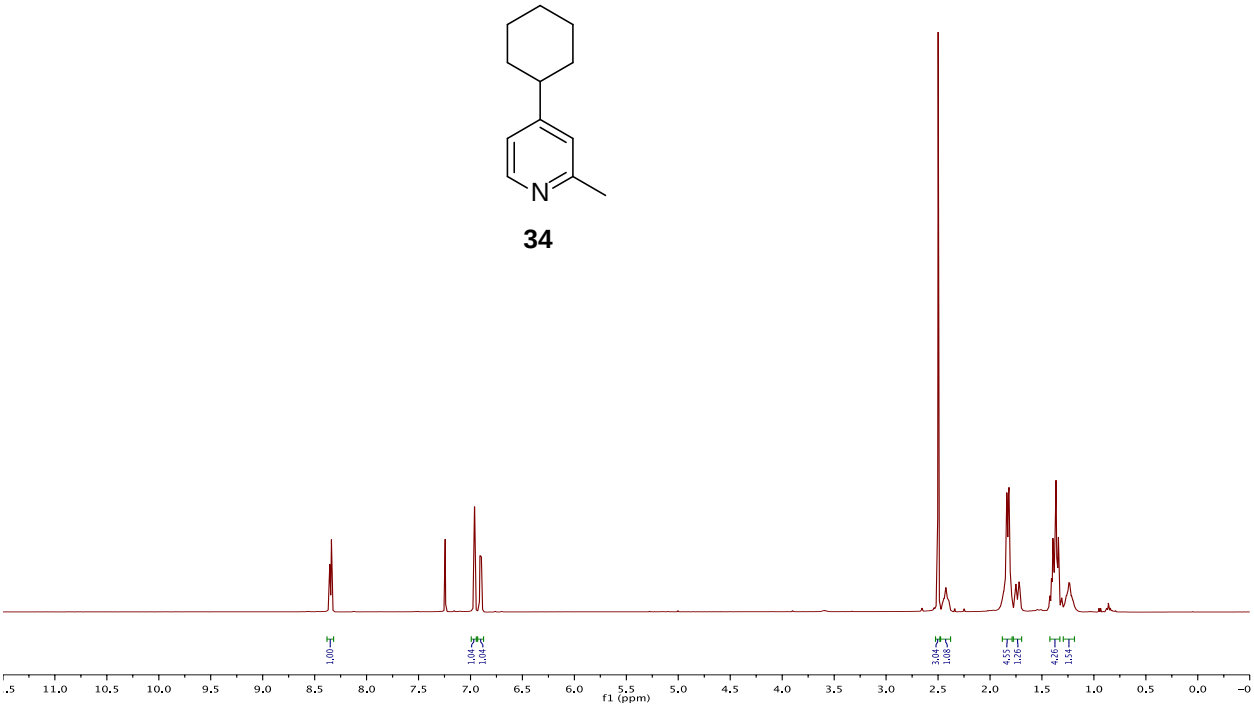
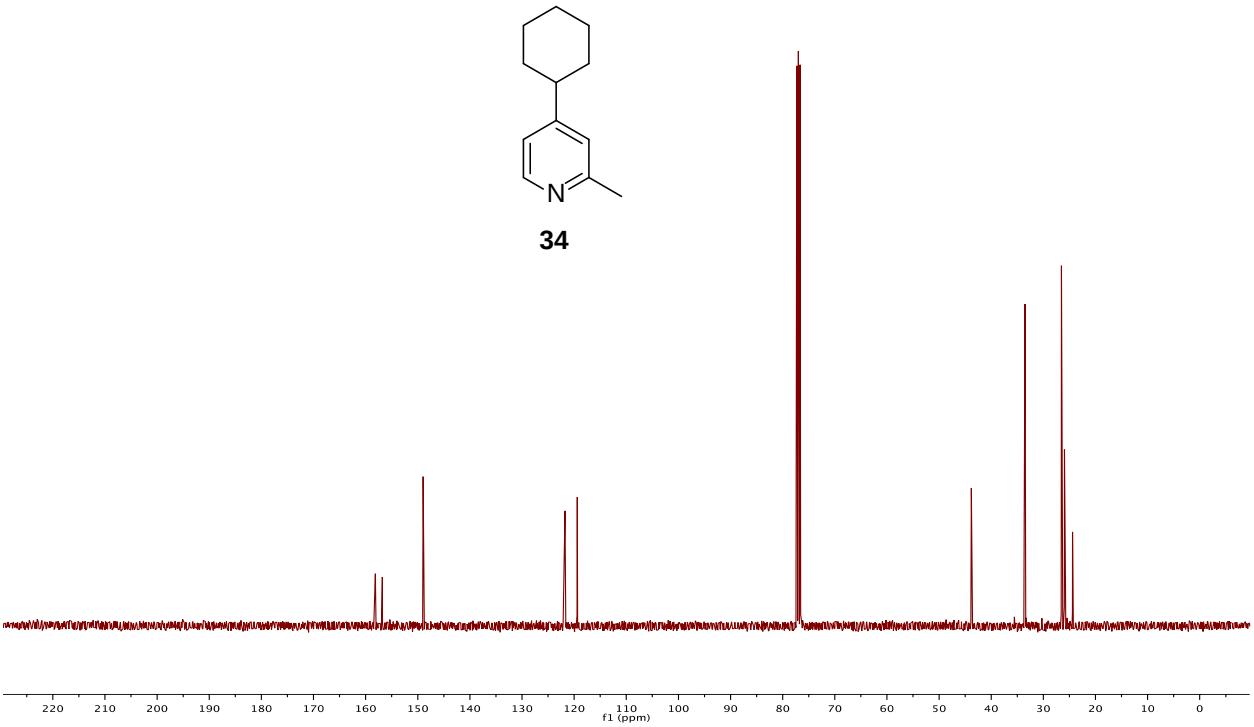


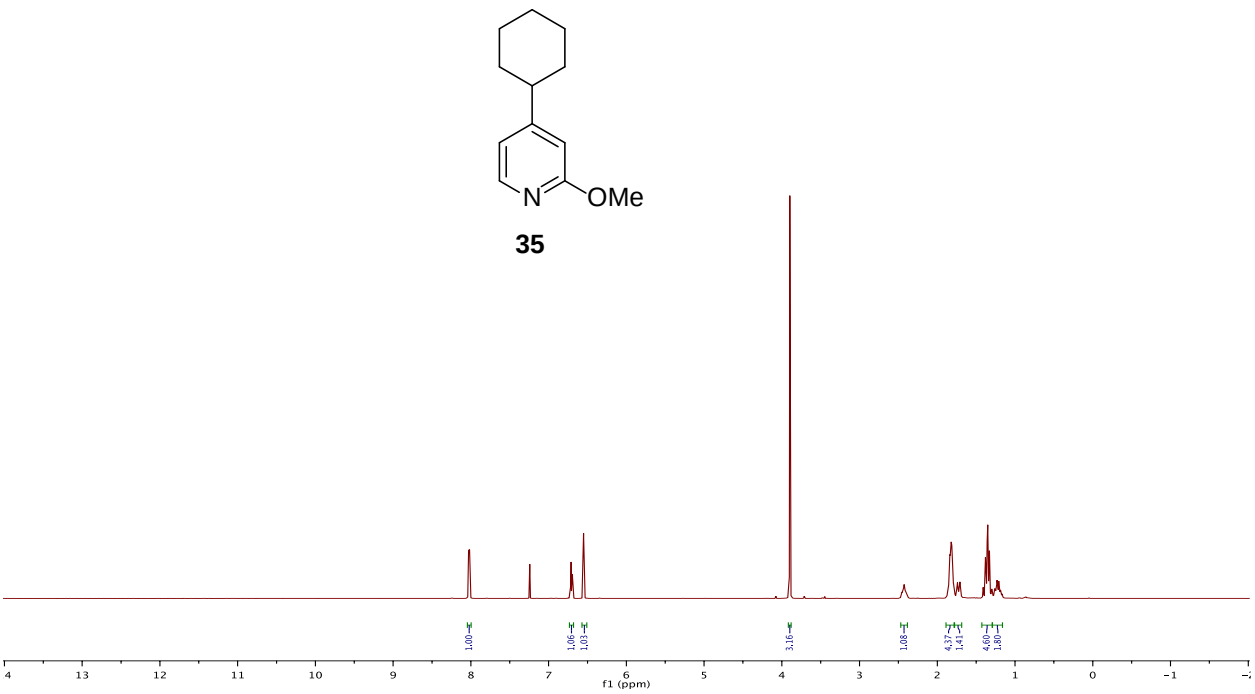
Proton NMR



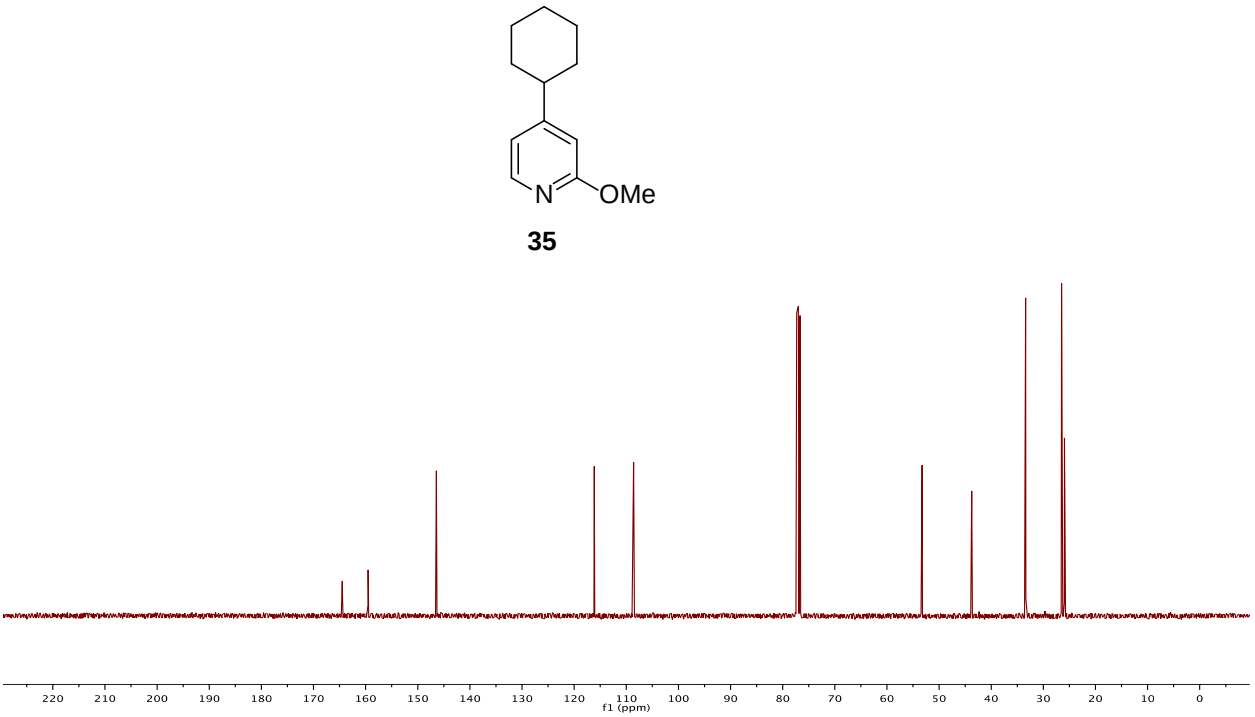
Carbon NMR



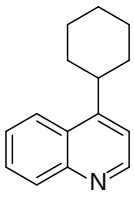
Proton NMR



Carbon NMR



Proton NMR



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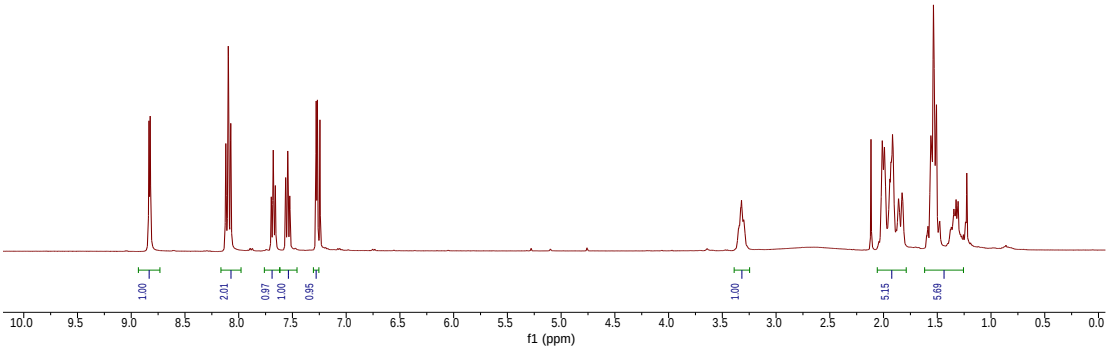
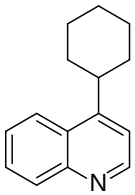


Carbon NMR



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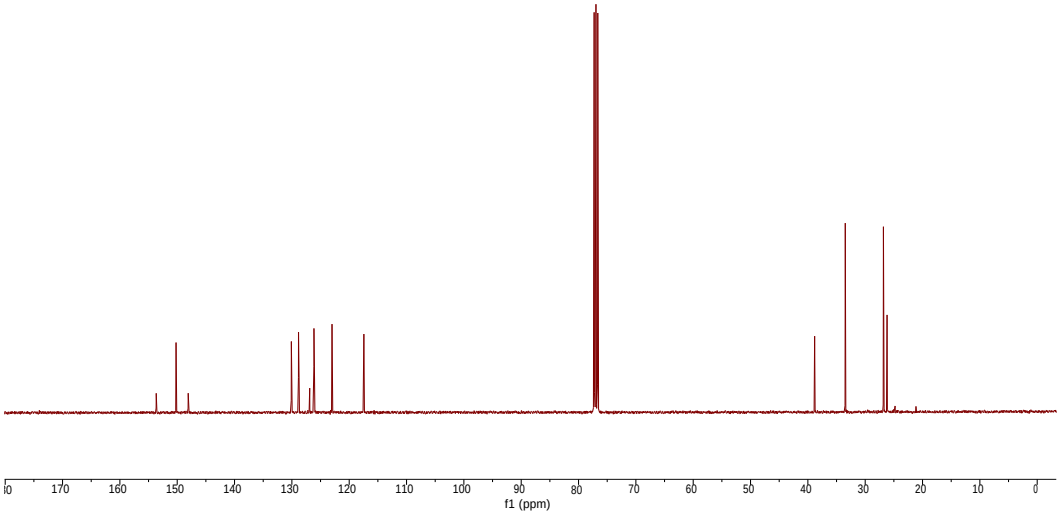
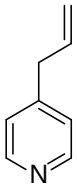


Proton NMR



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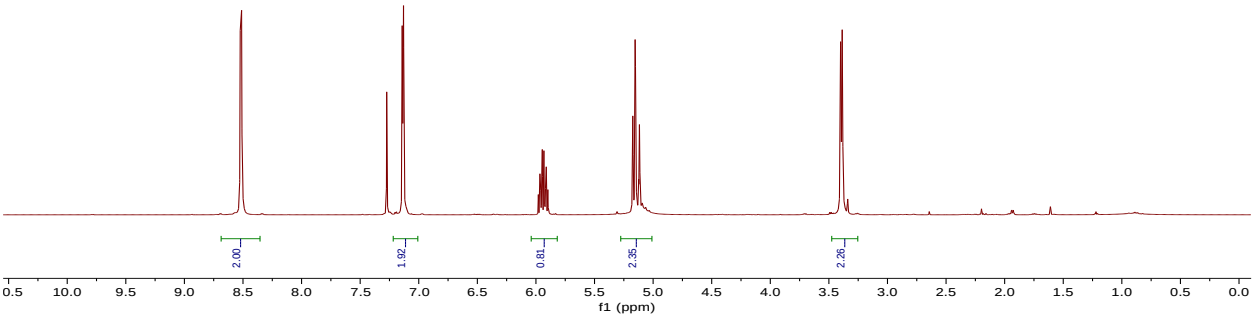
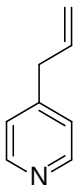


Carbon NMR



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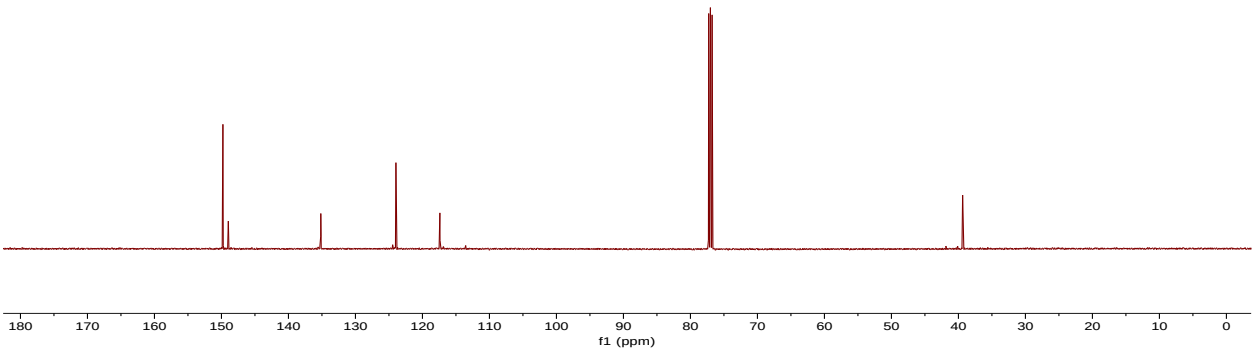
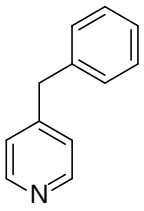


Proton NMR



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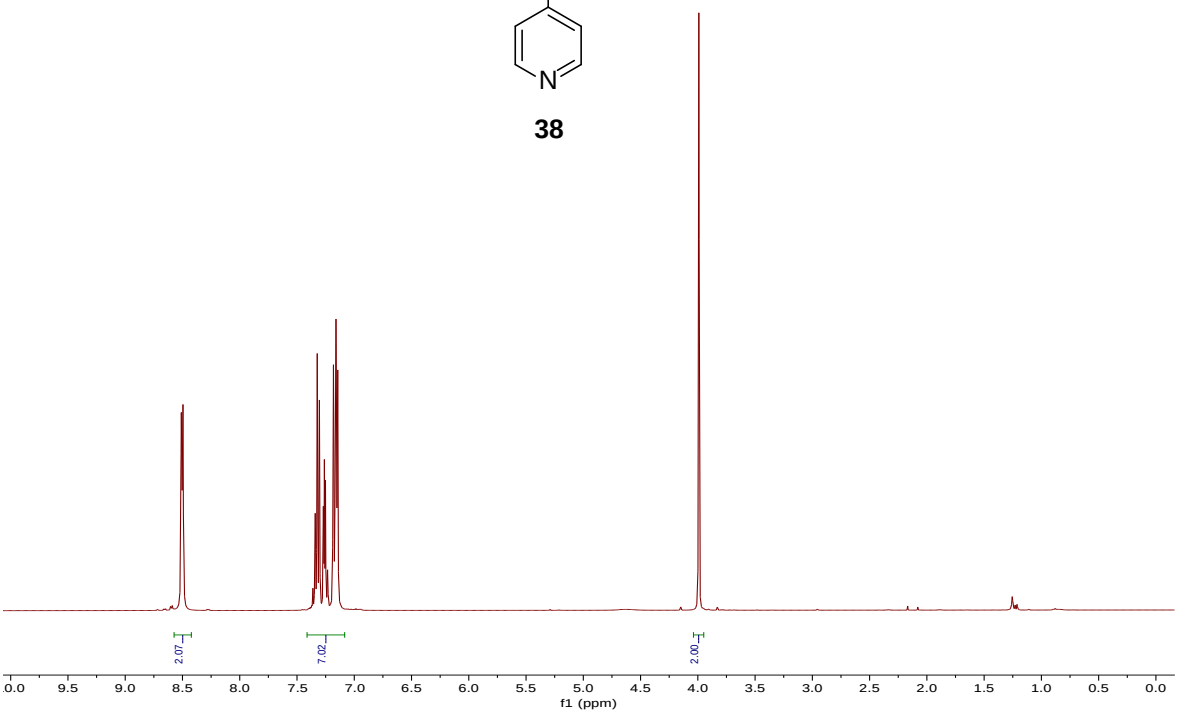
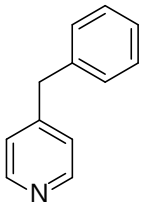


Carbon NMR



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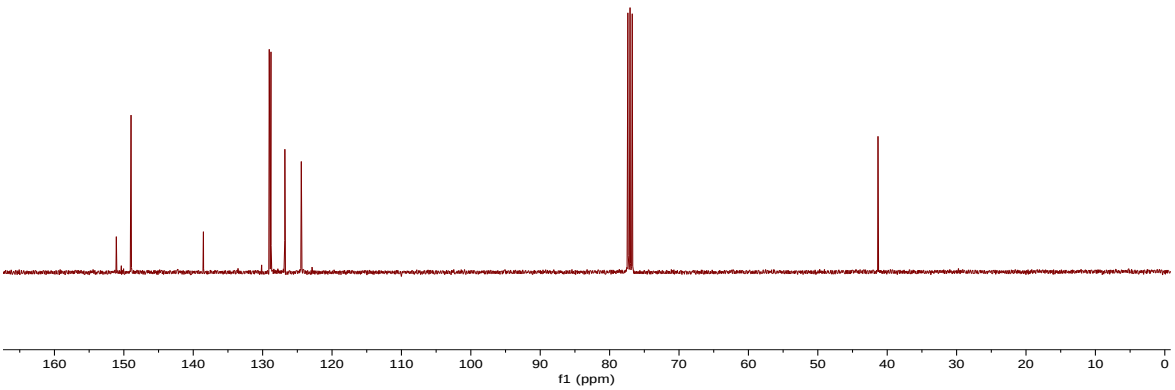
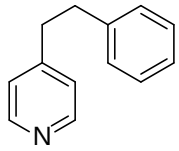


Proton NMR



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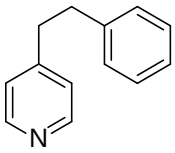
Carbon NMR



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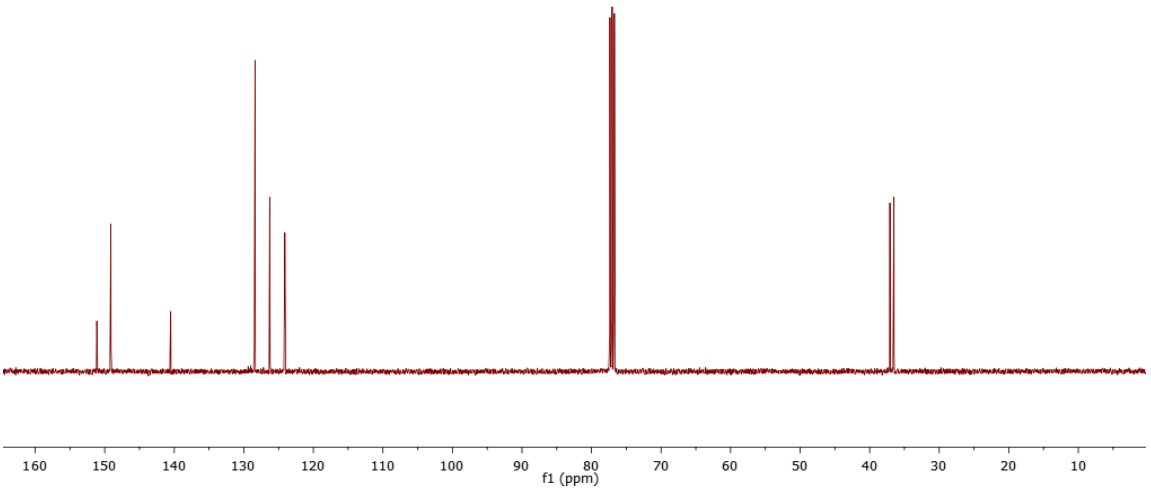
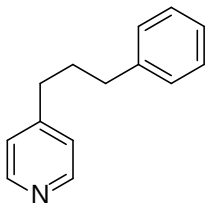


Proton NMR



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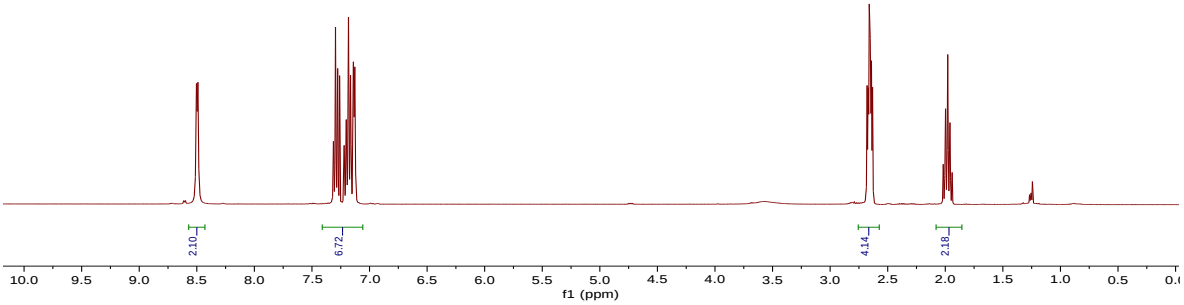
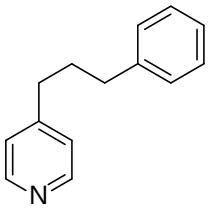


Carbon NMR



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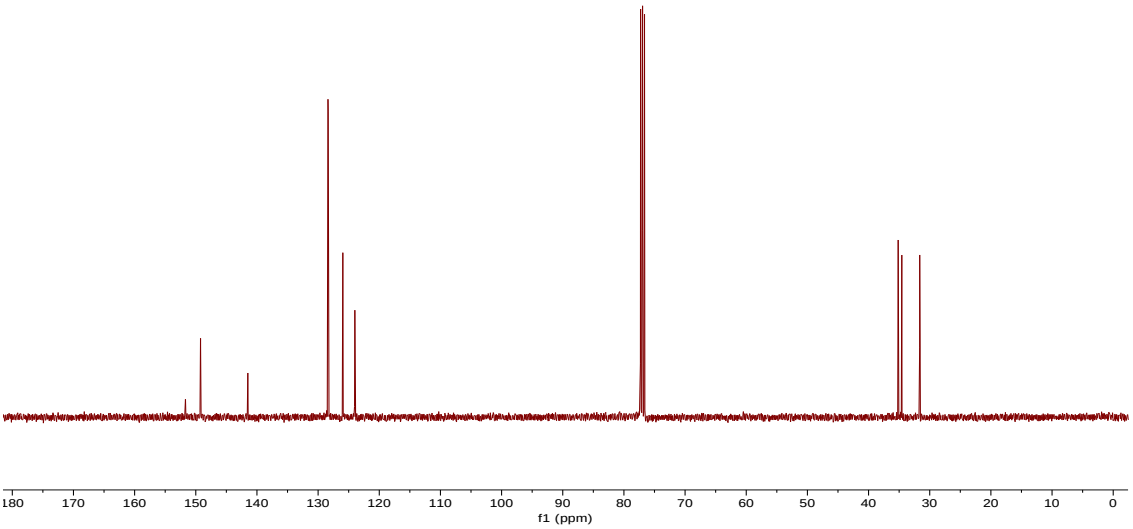
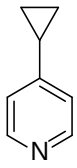
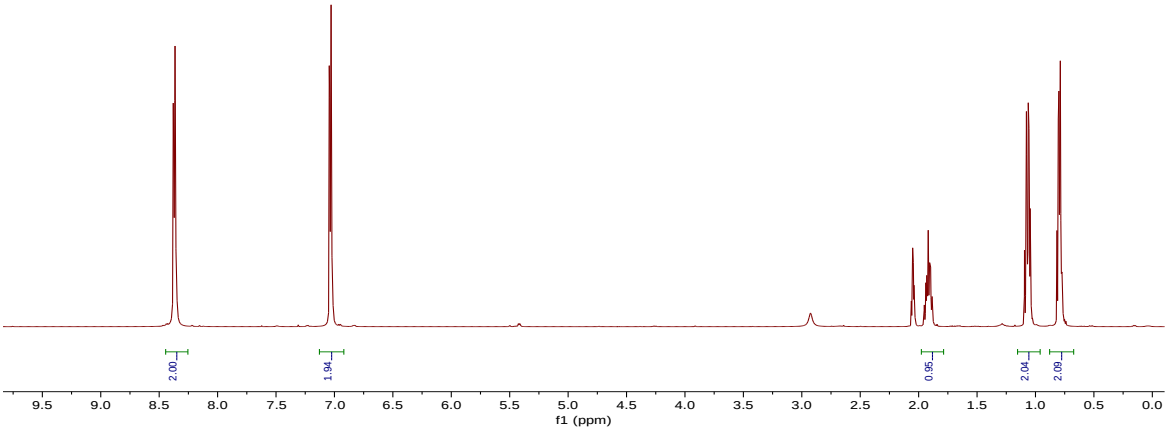


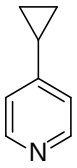
Proton NMR



41



Carbon NMR



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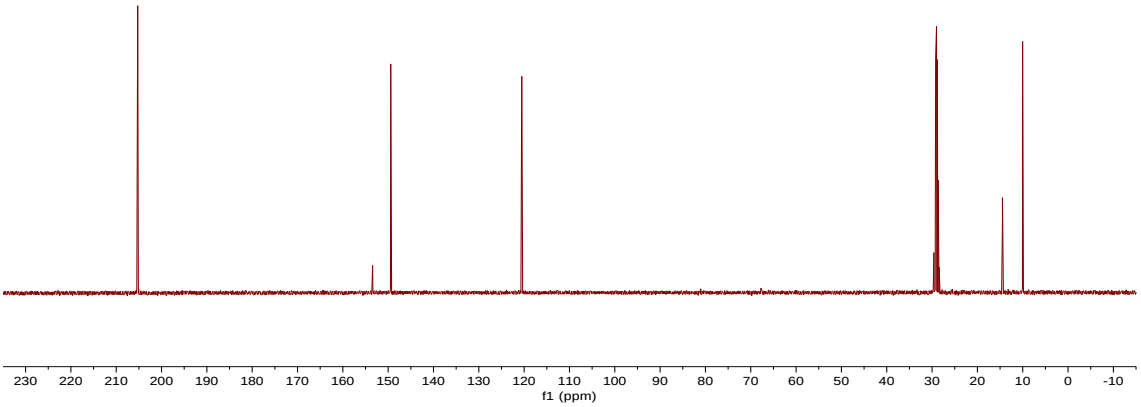
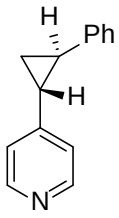


Proton NMR



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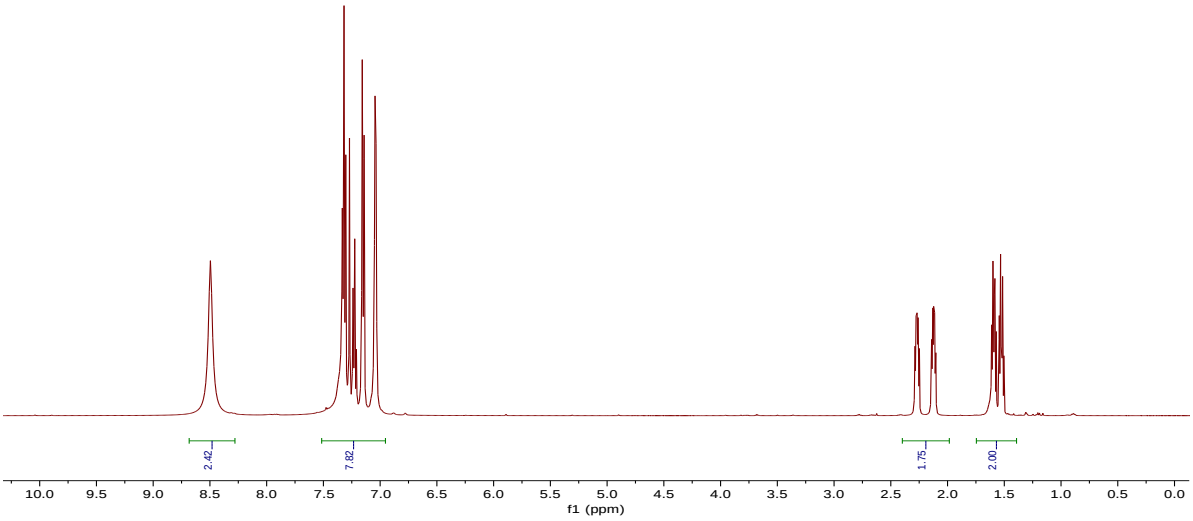
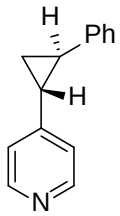


Carbon NMR



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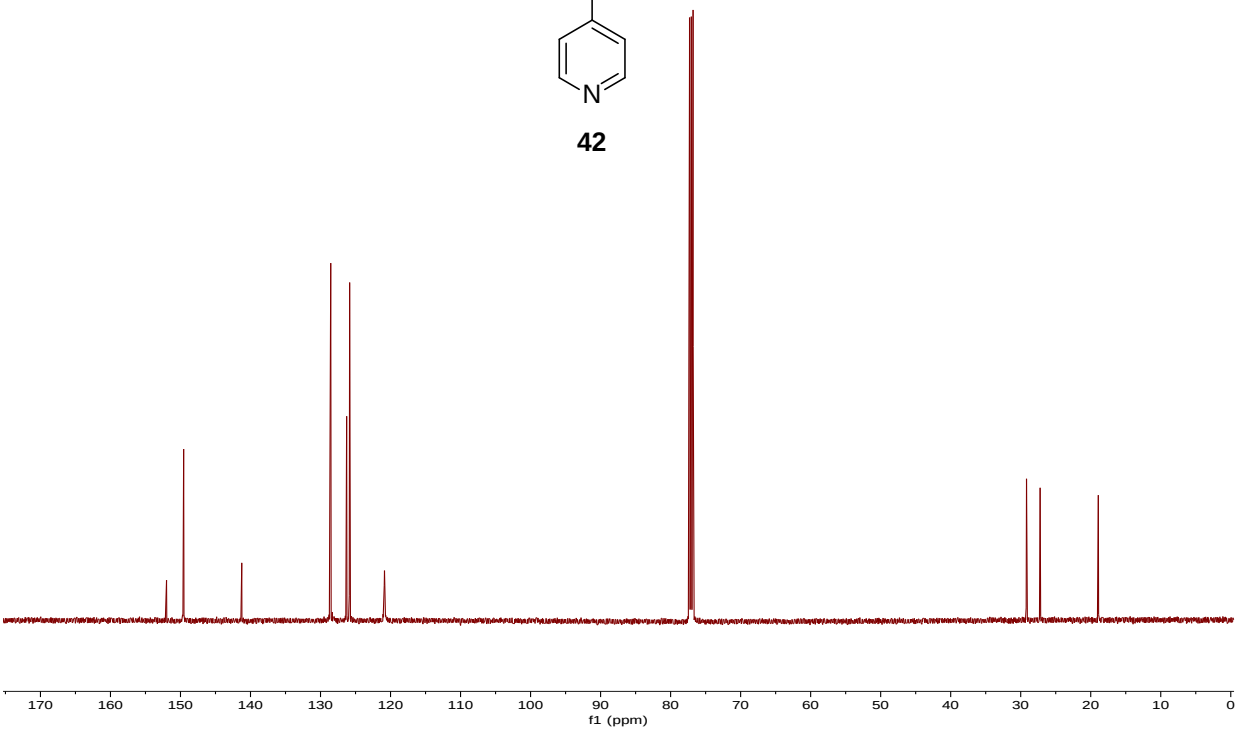

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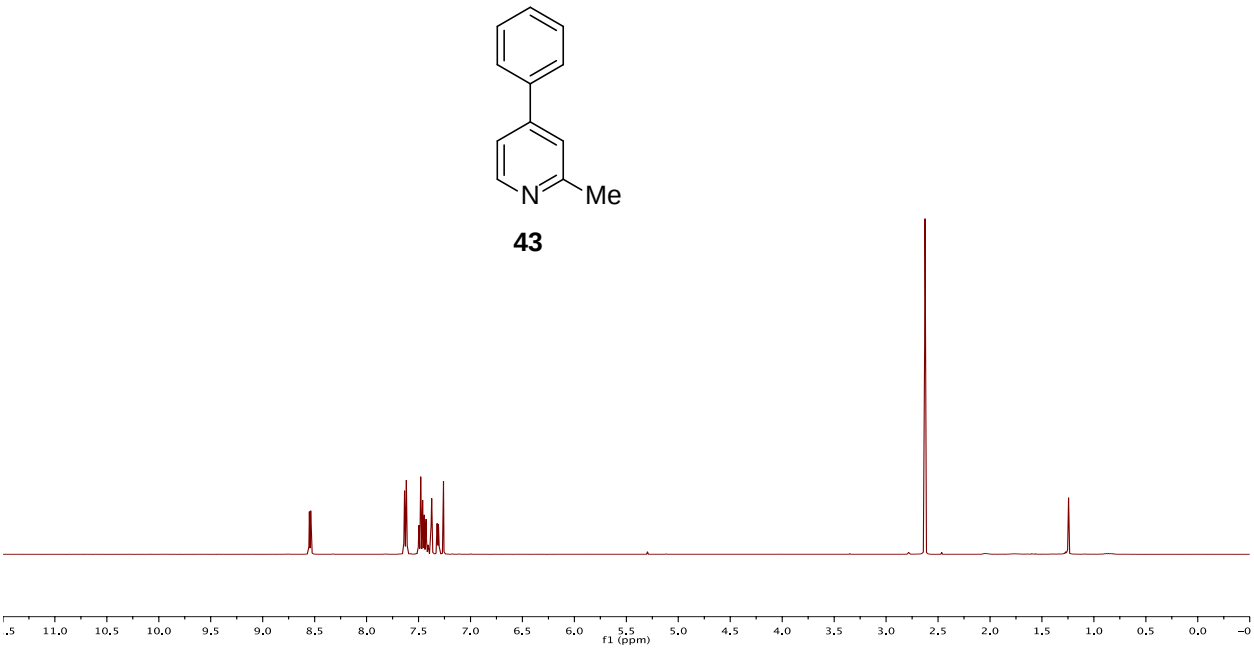

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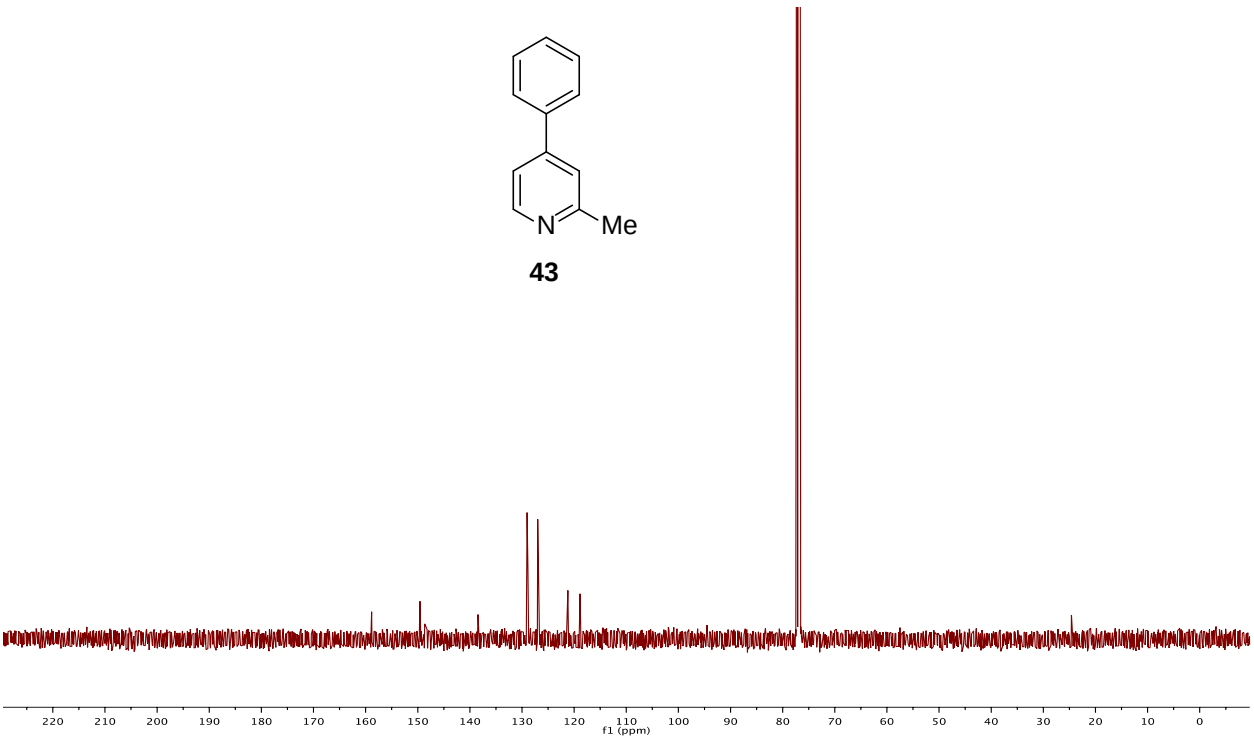

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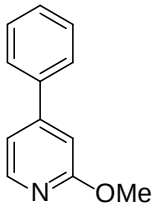

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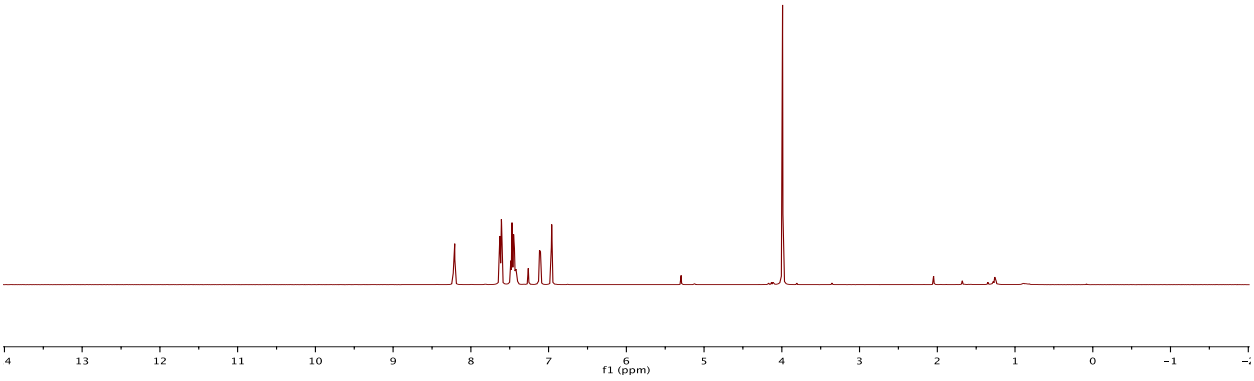

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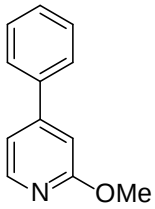

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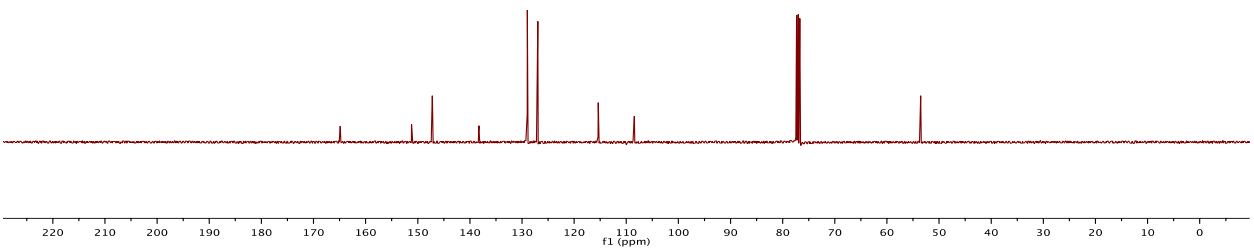

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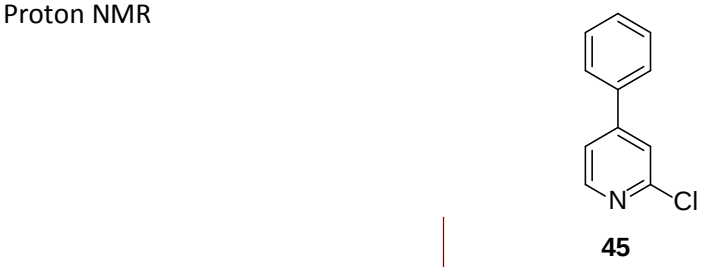

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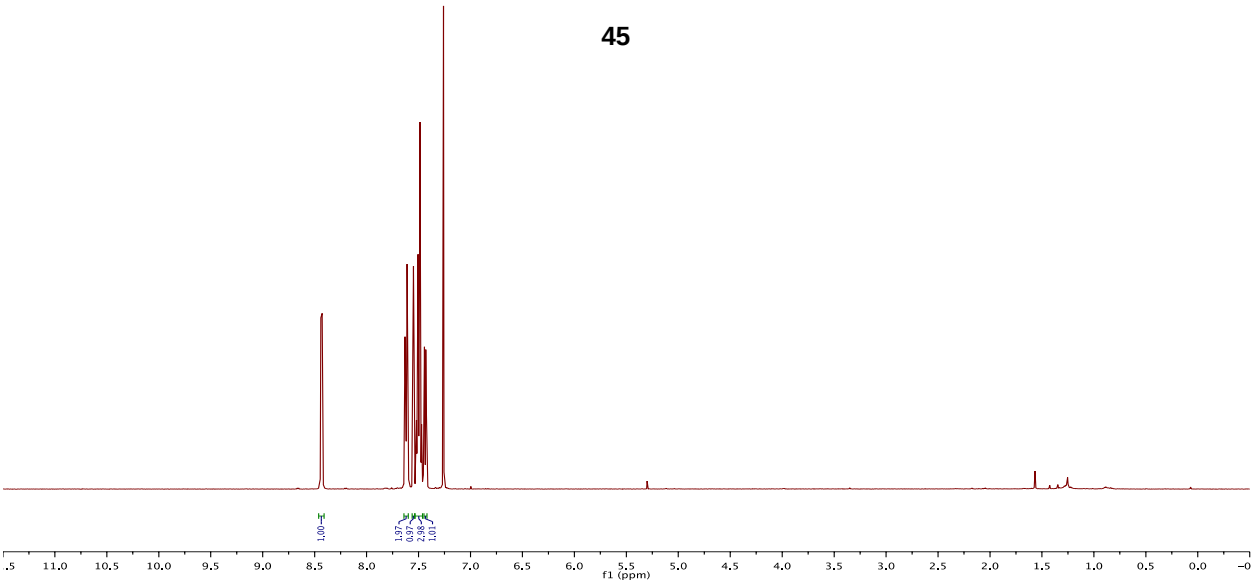

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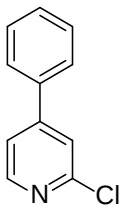

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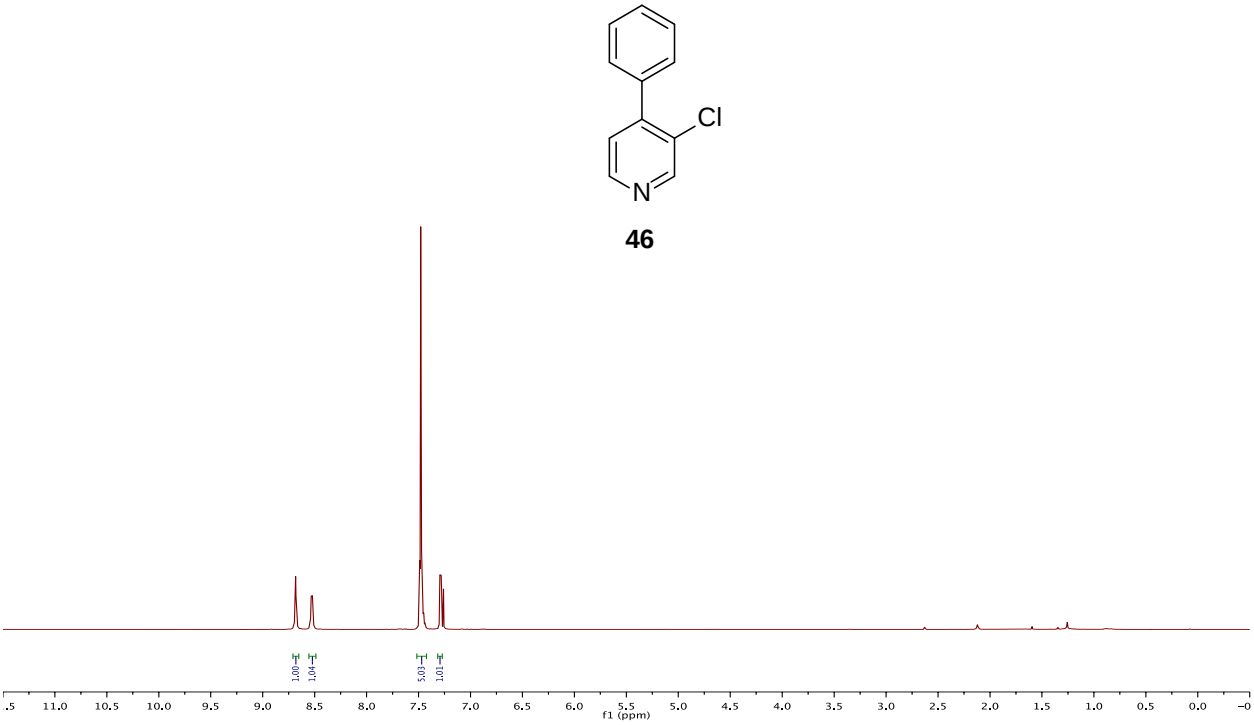

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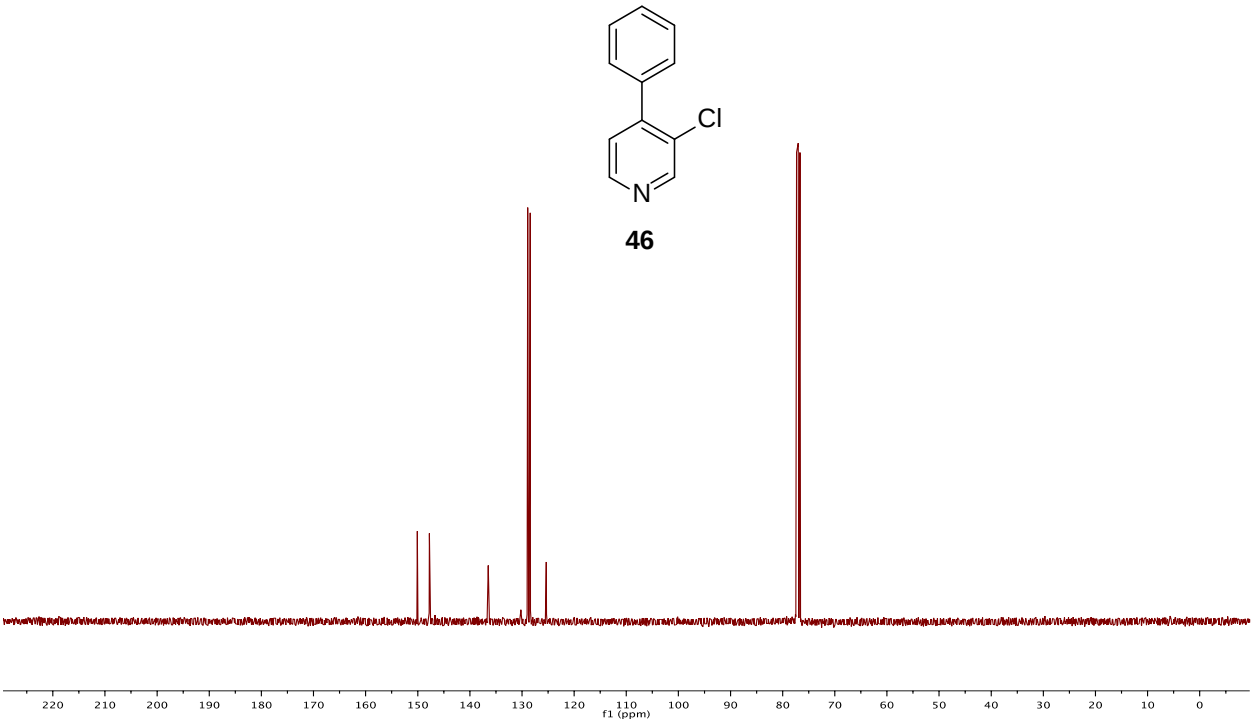

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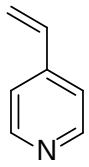

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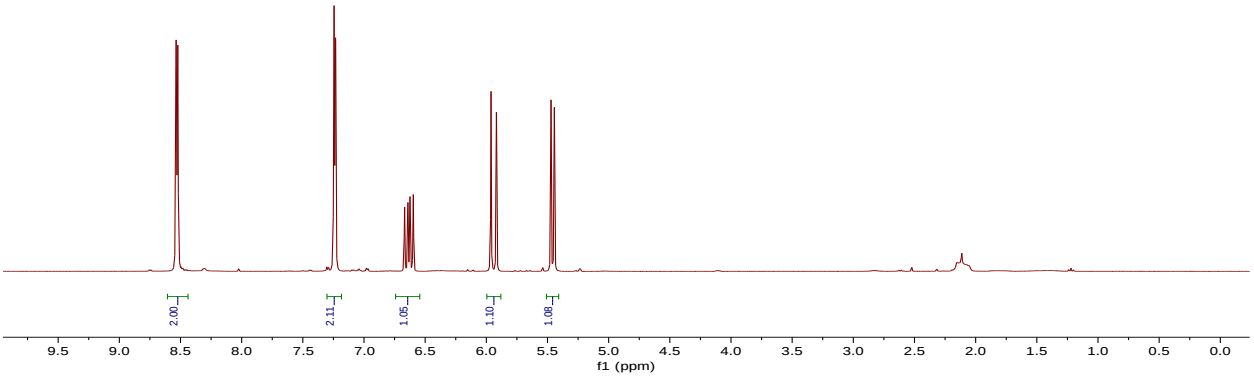

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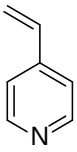

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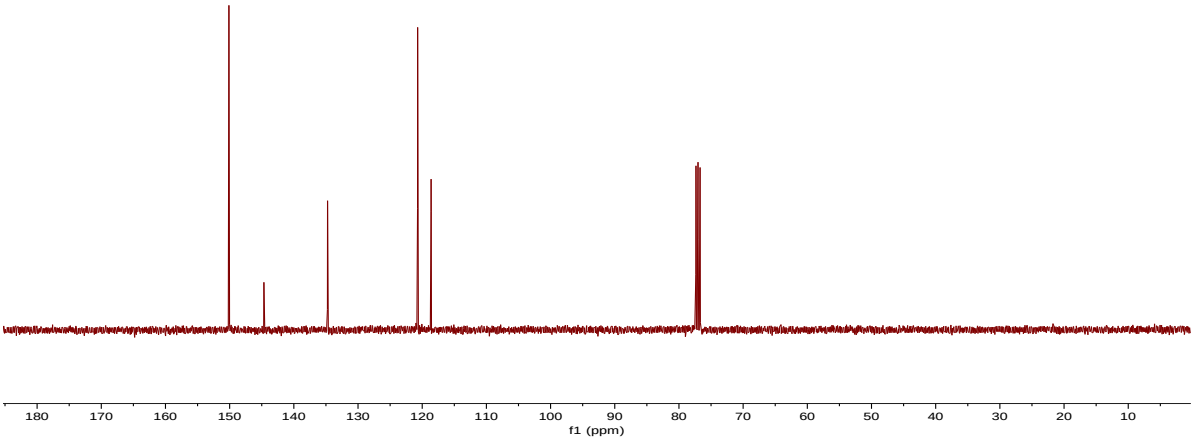

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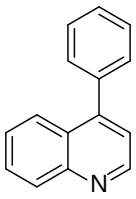

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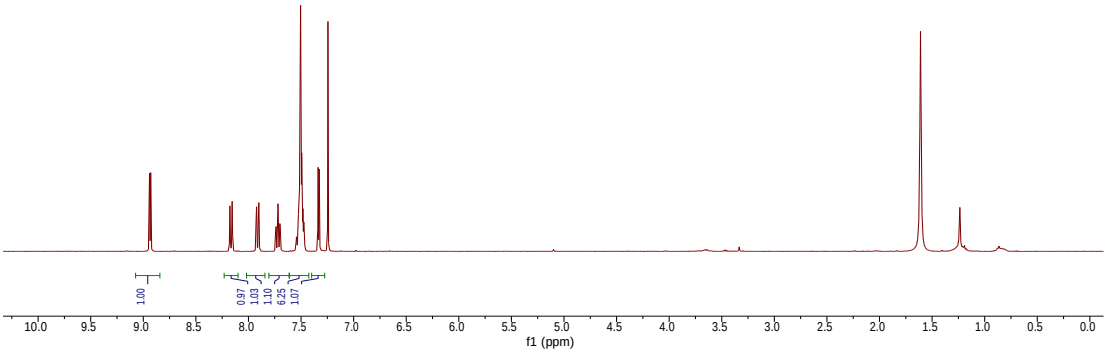

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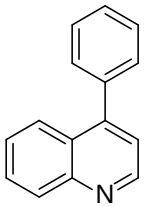

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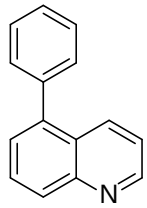

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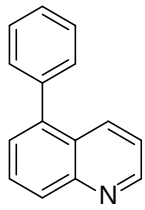

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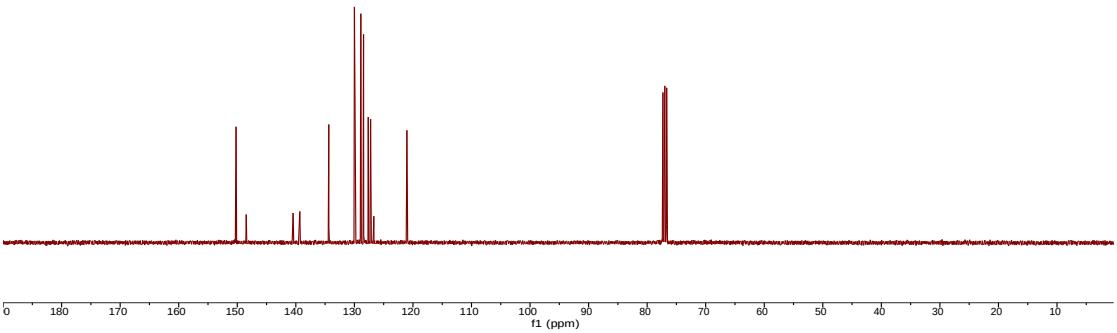

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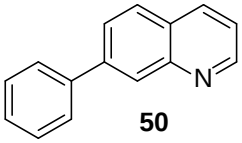

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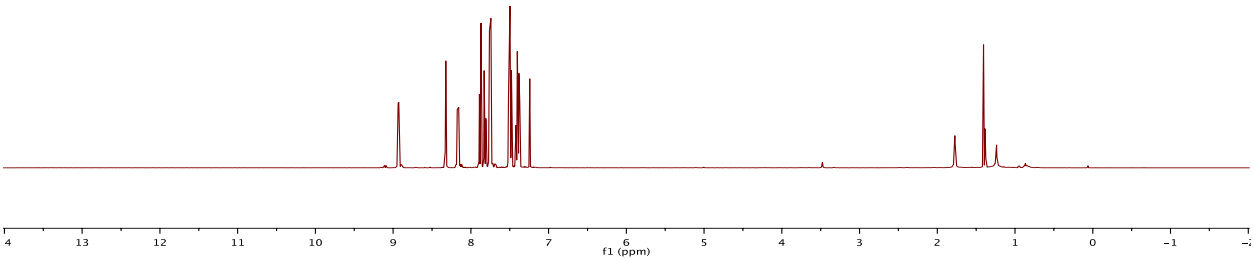

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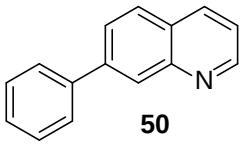

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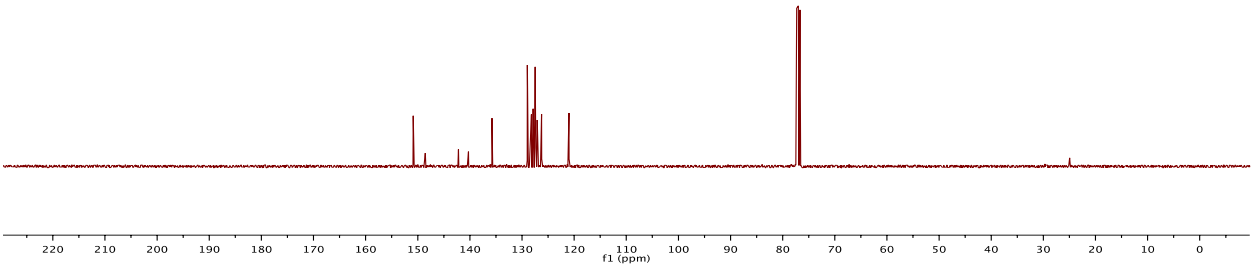

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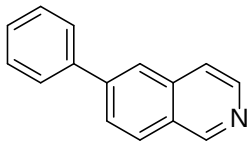

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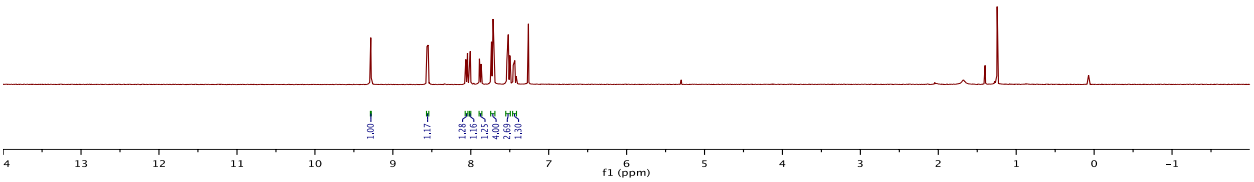

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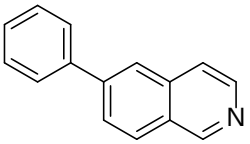

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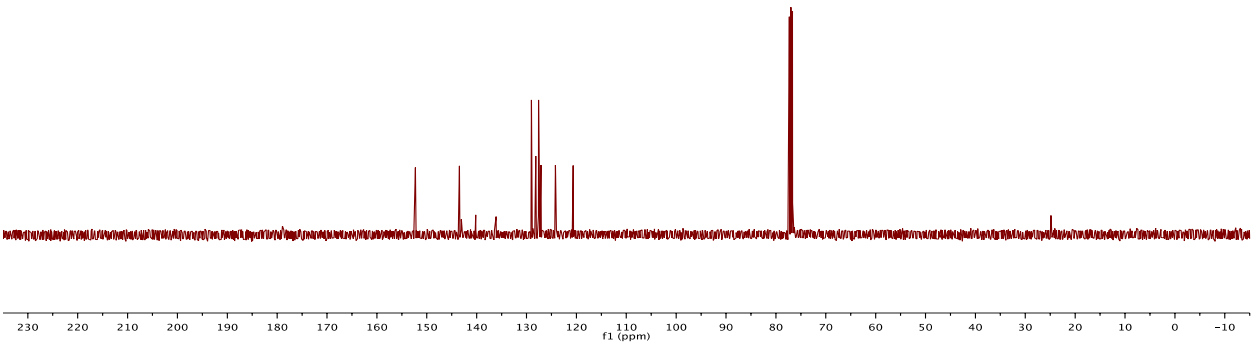

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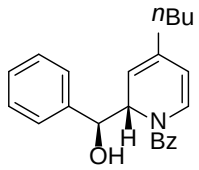

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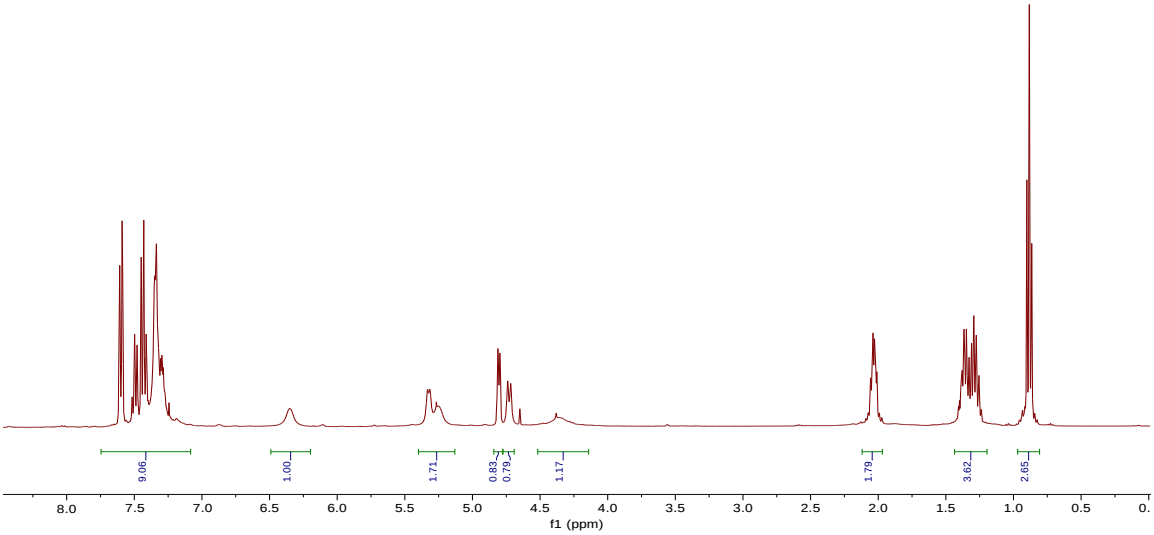
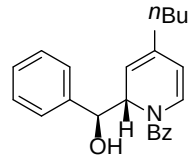


Carbon NMR



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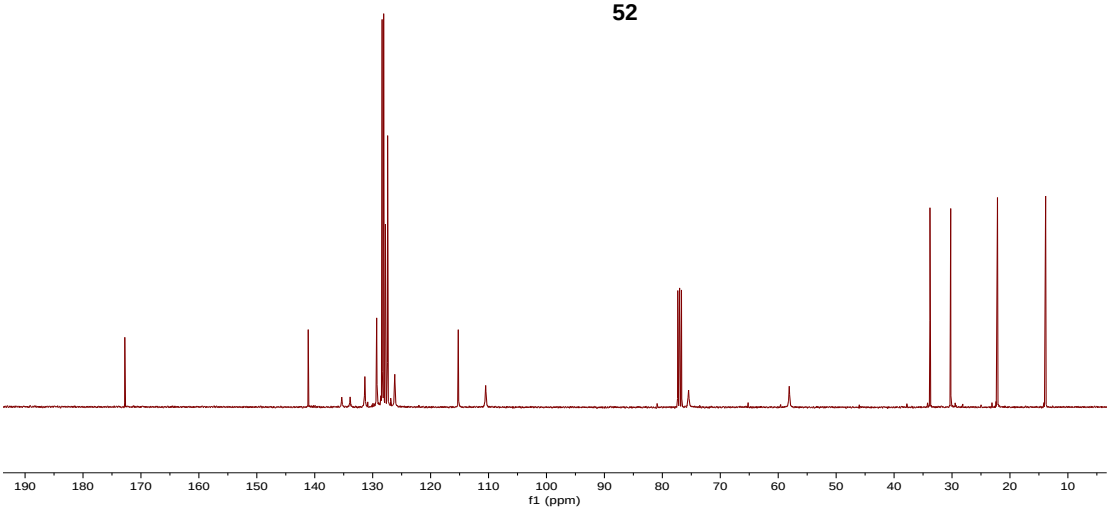

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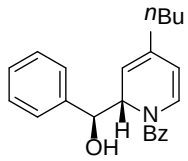

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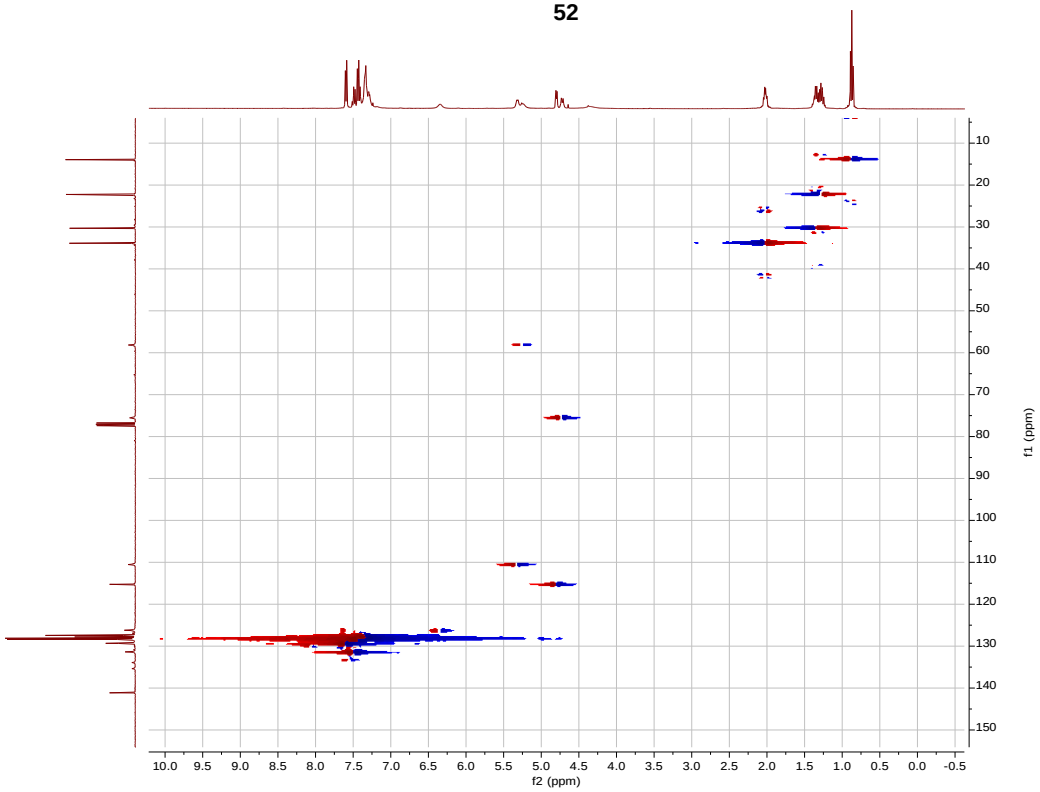

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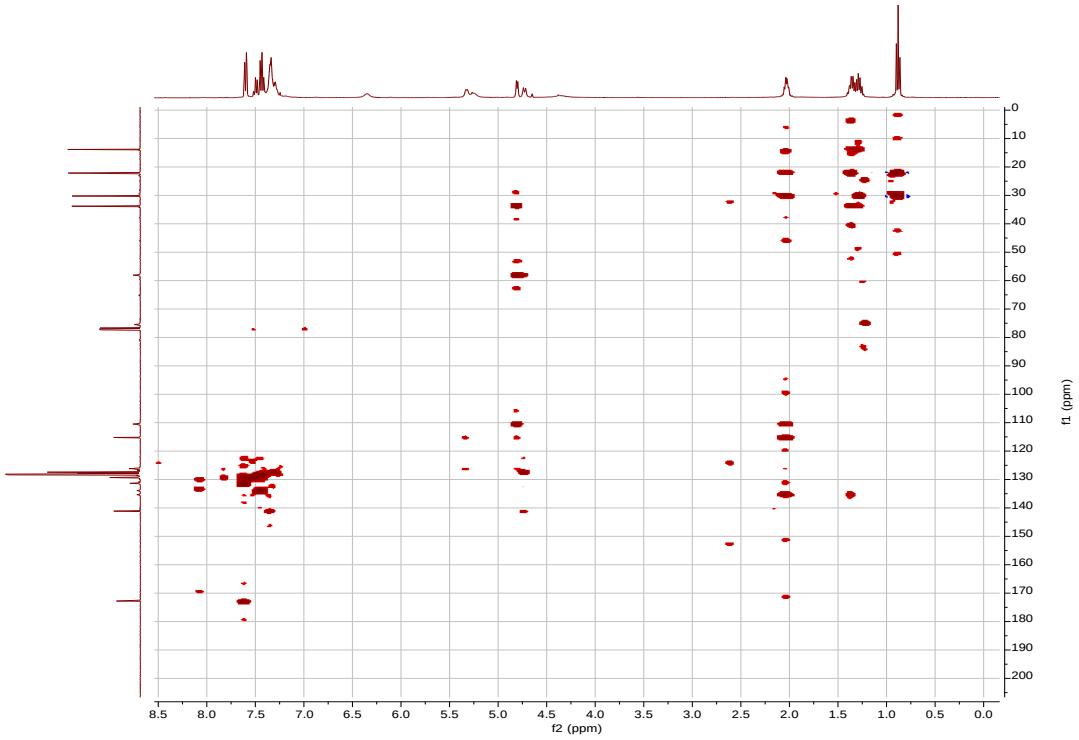

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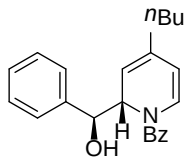

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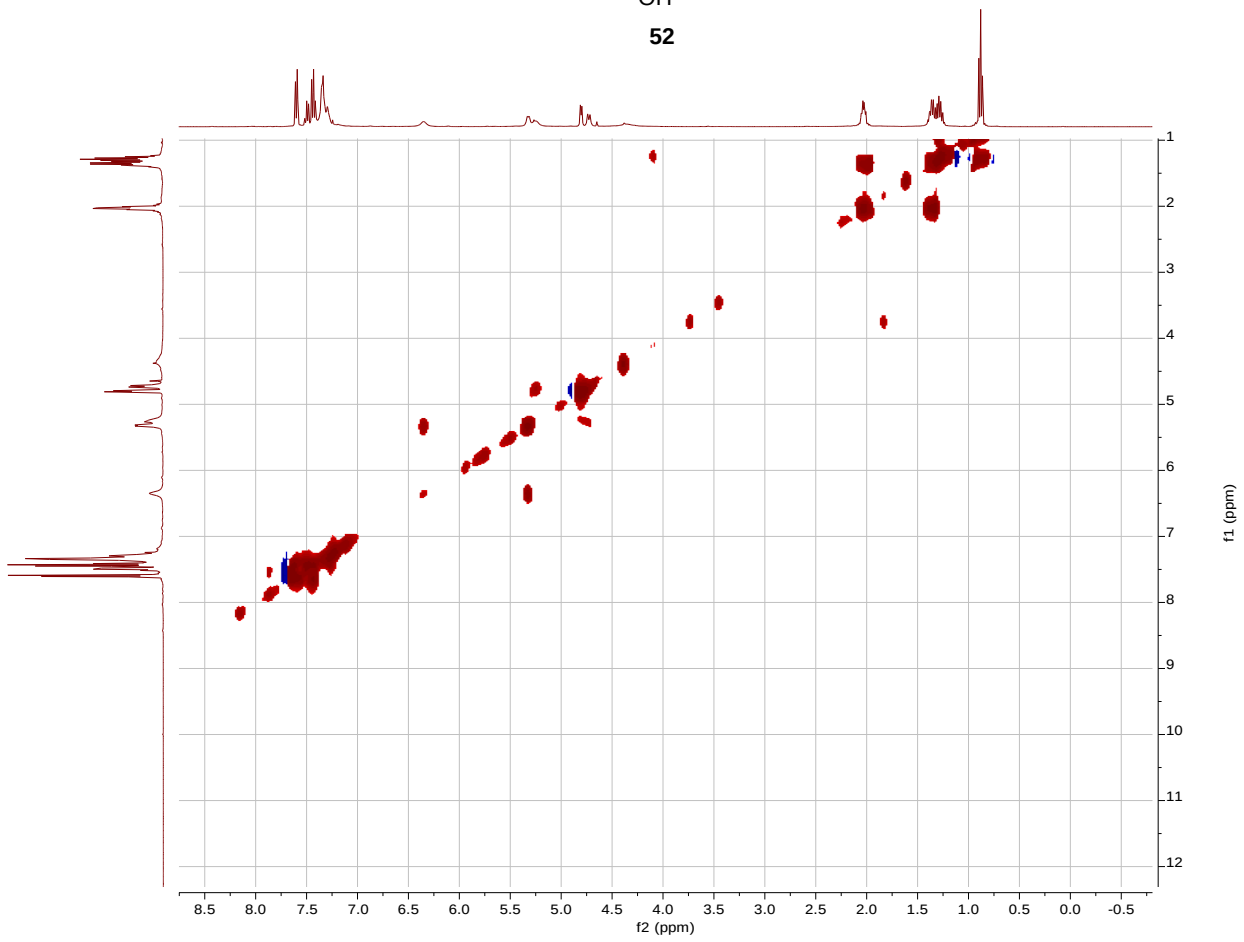
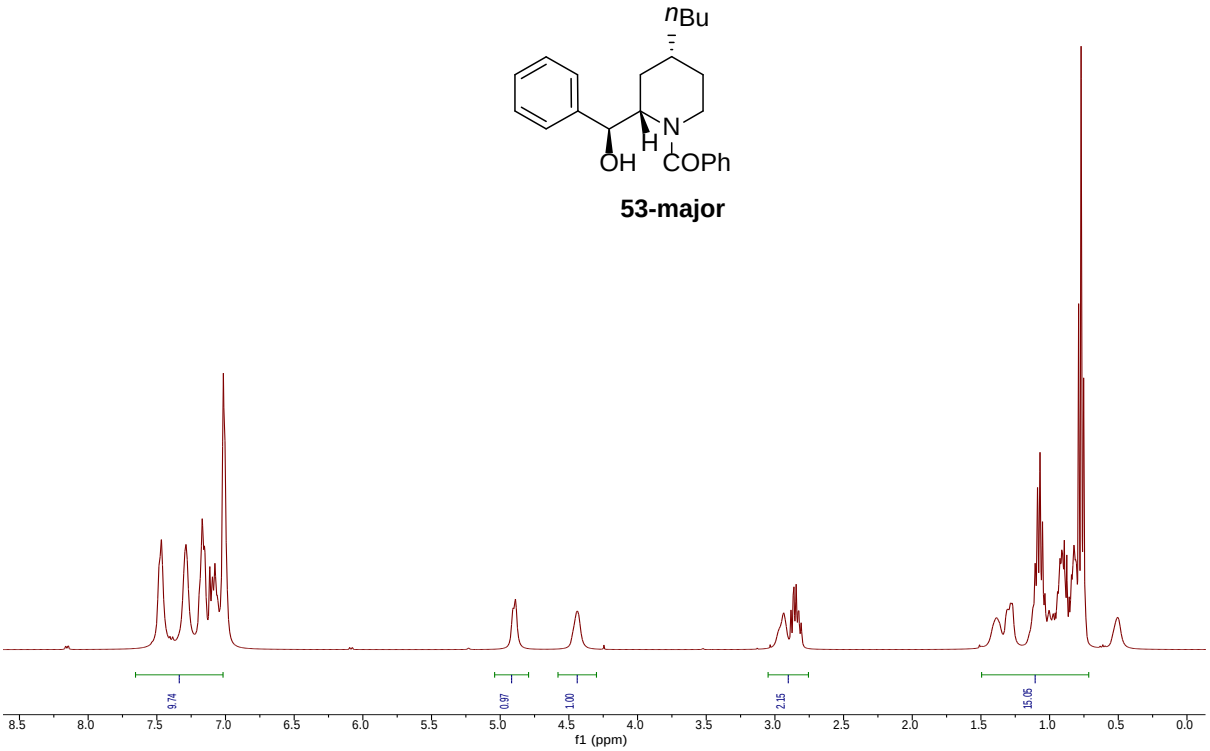
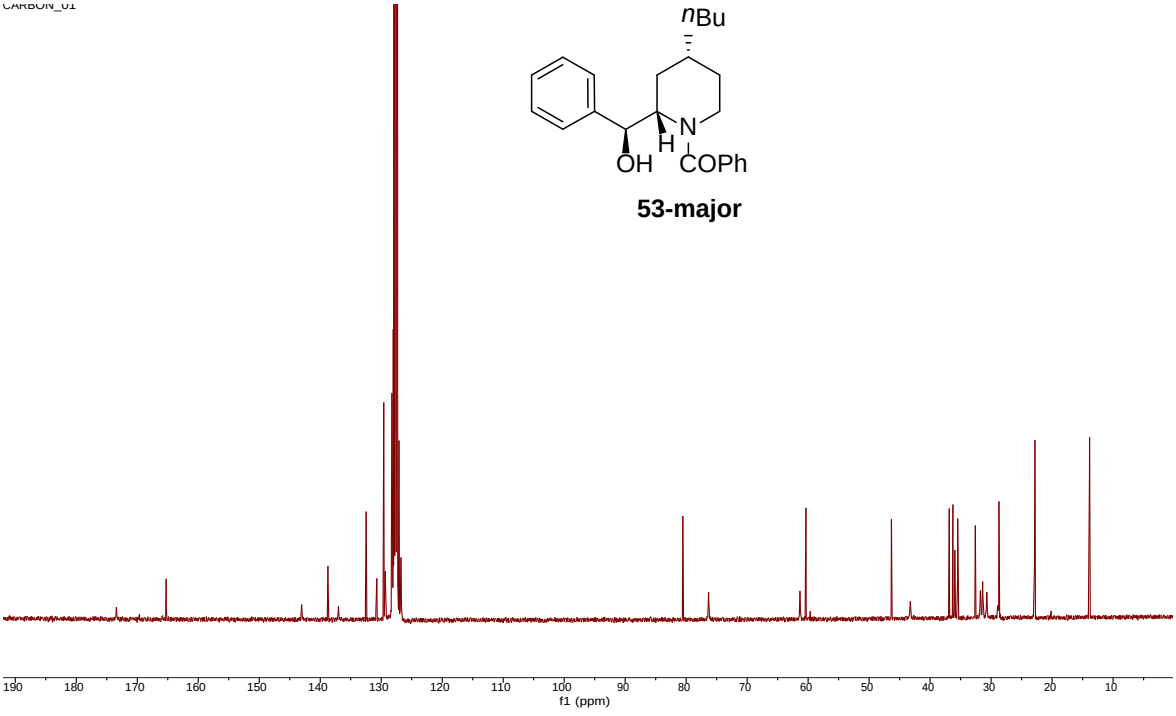


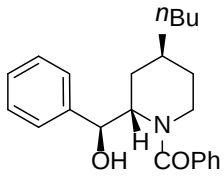
Proton NMR



Carbon NMR



Proton NMR



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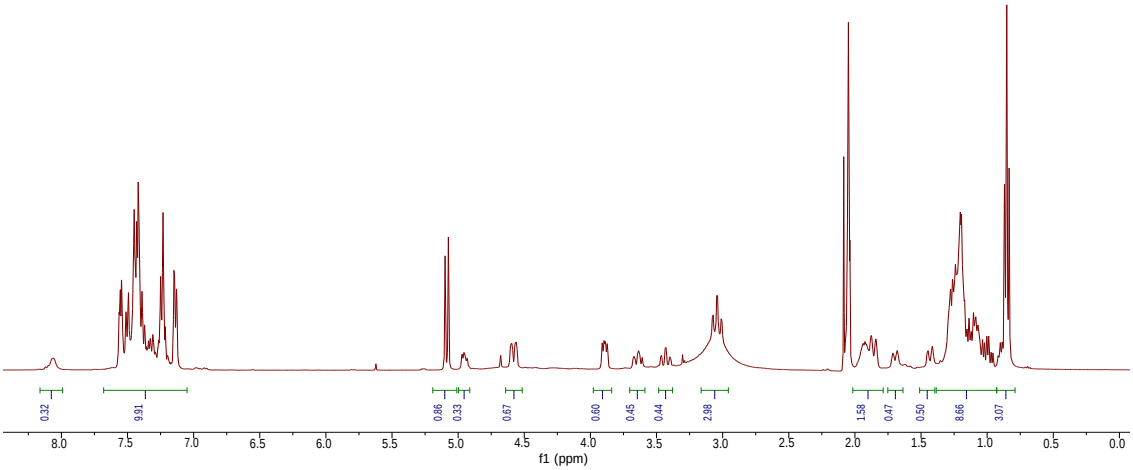
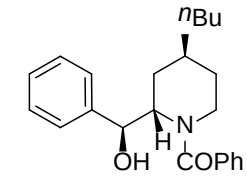
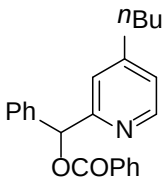


Carbon NMR



53-minor

Proton NMR



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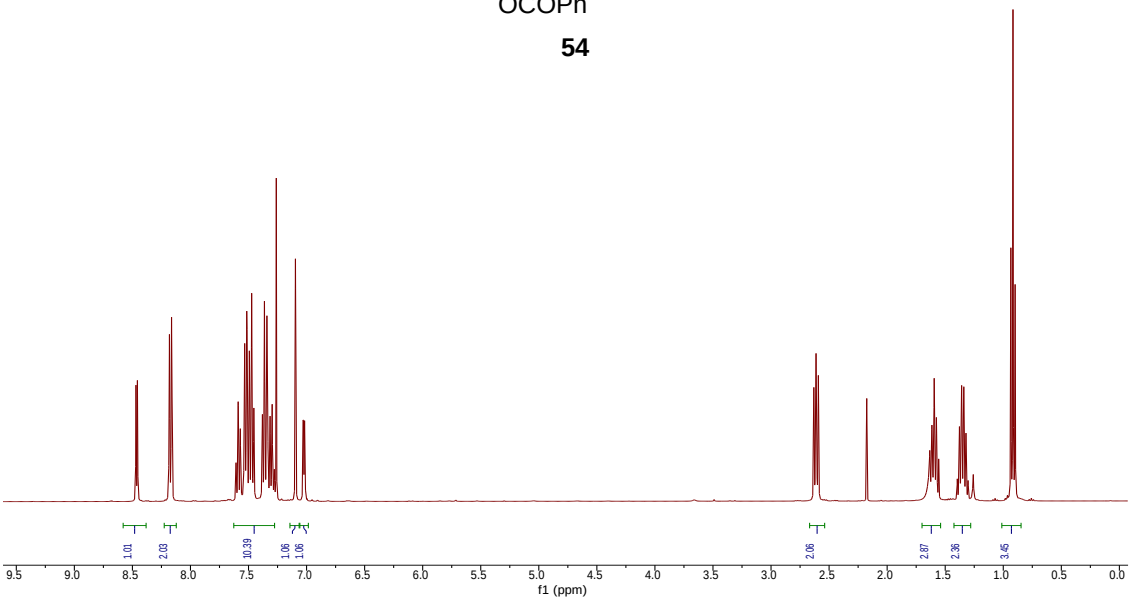
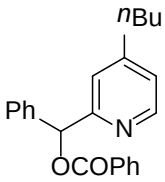


Carbon NMR



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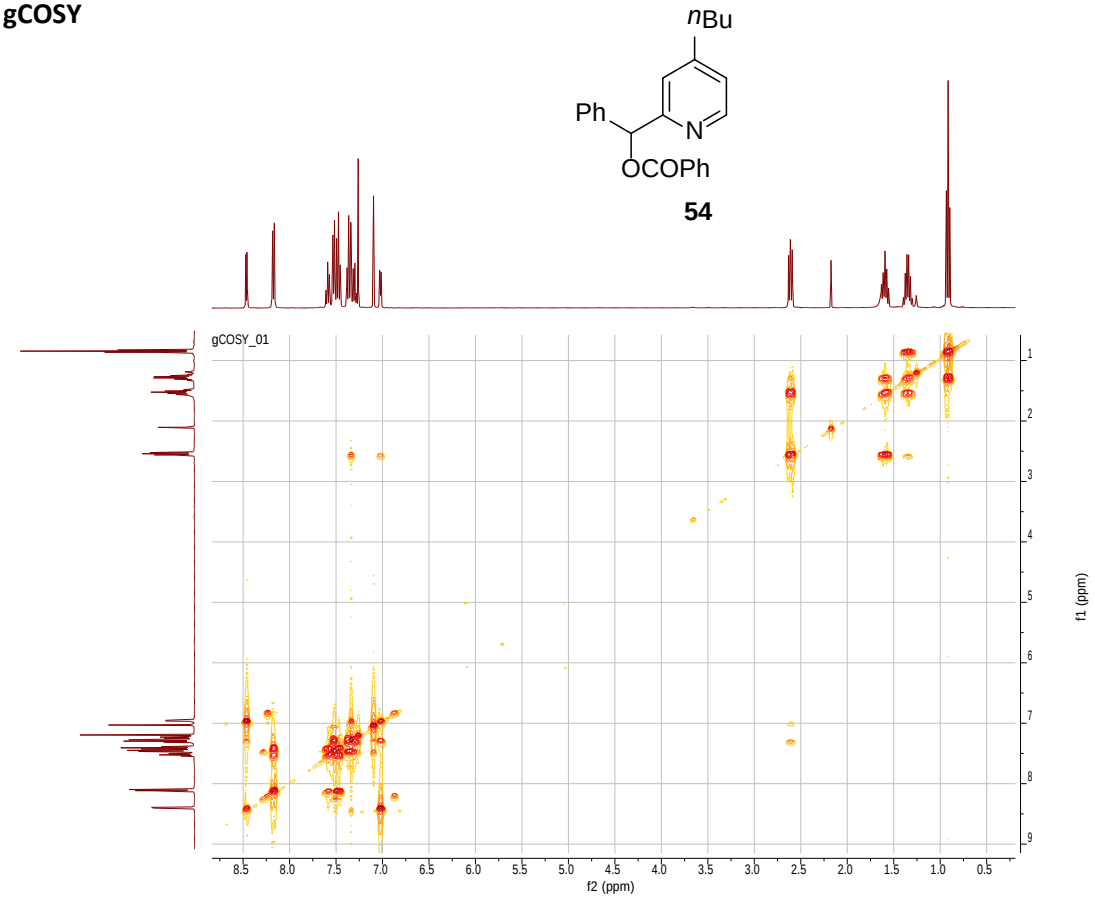
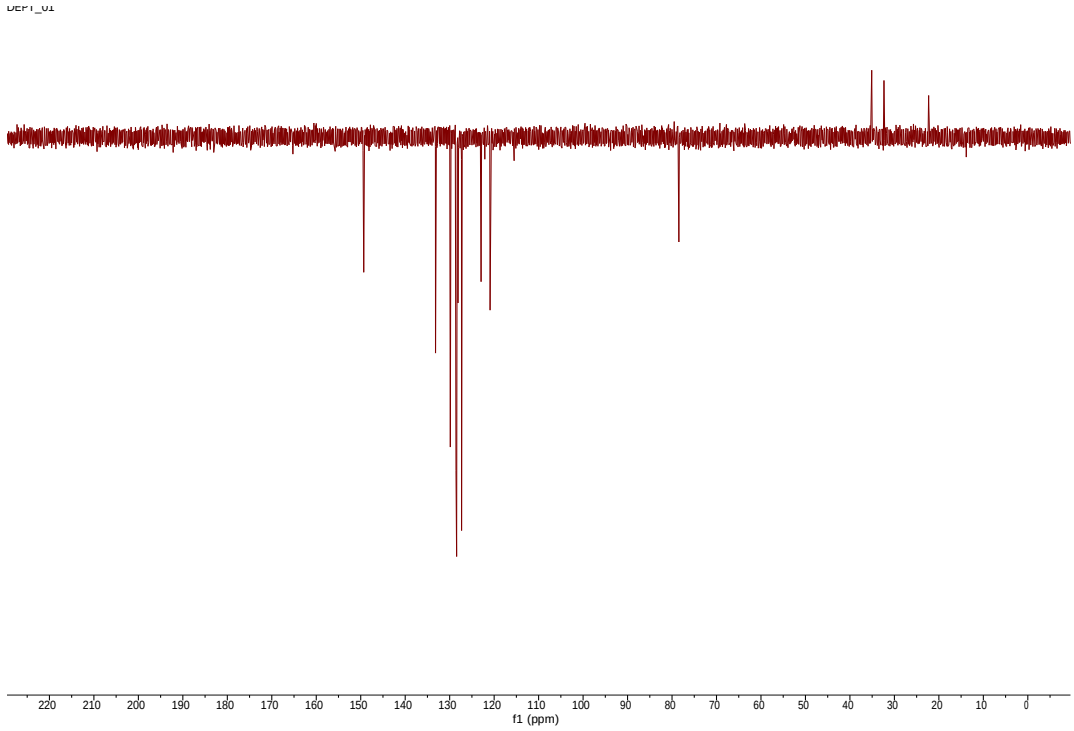
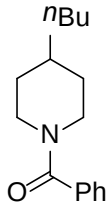
gCOSY



DEPT



Proton NMR



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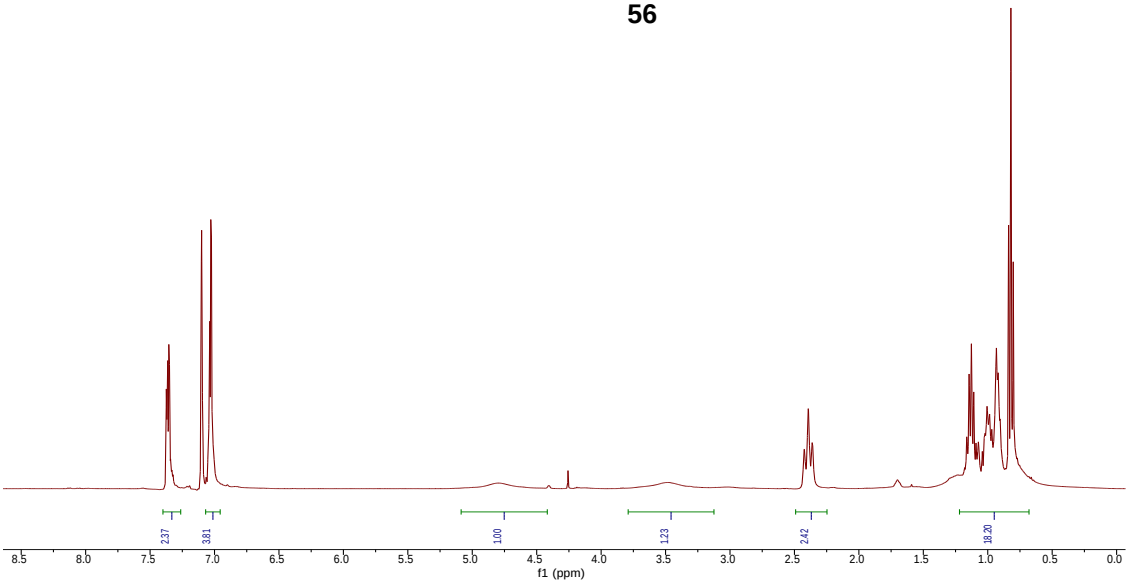
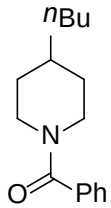


Carbon NMR



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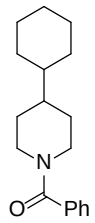

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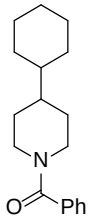

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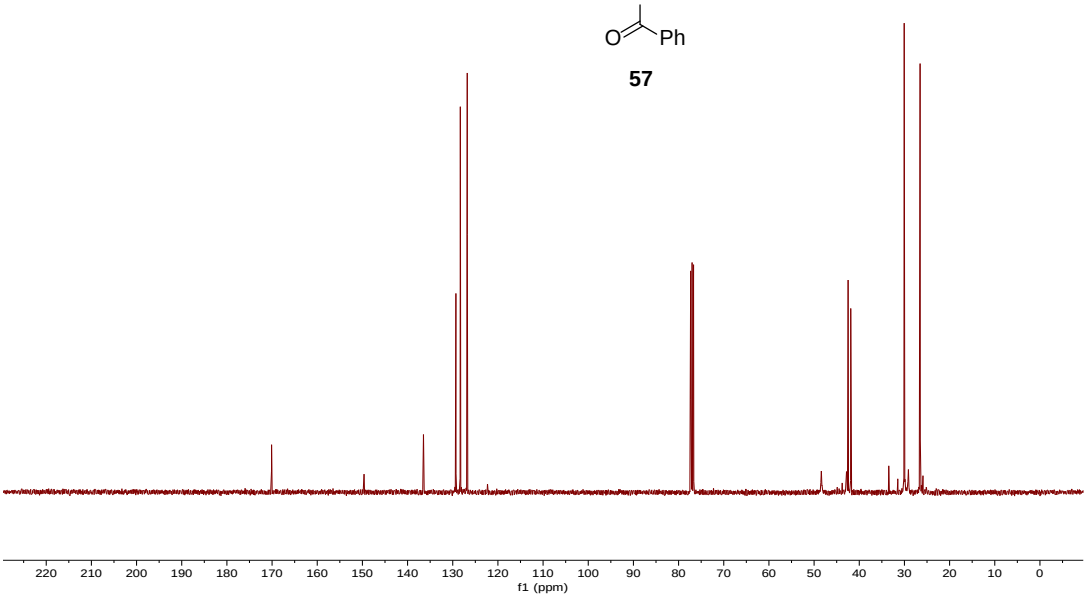

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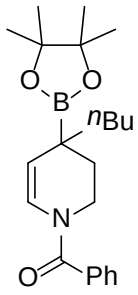

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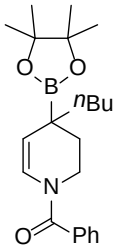

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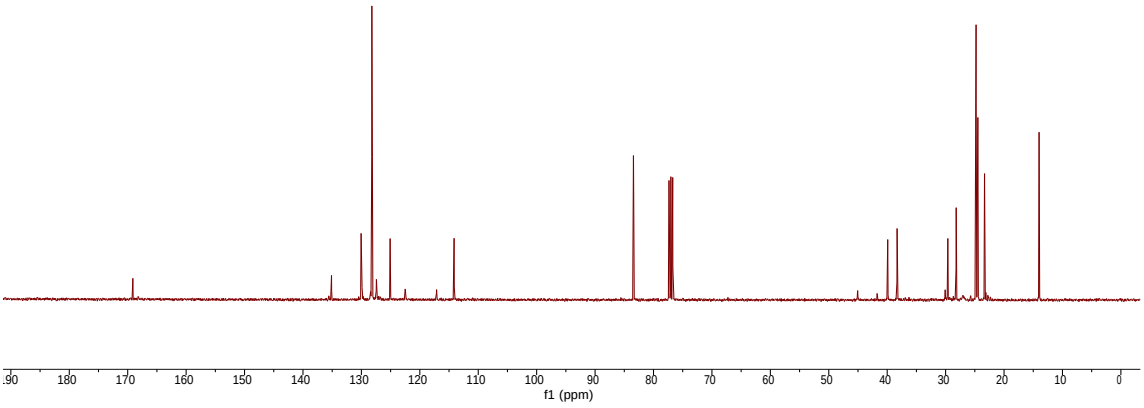
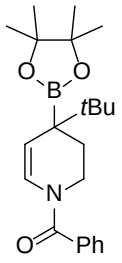
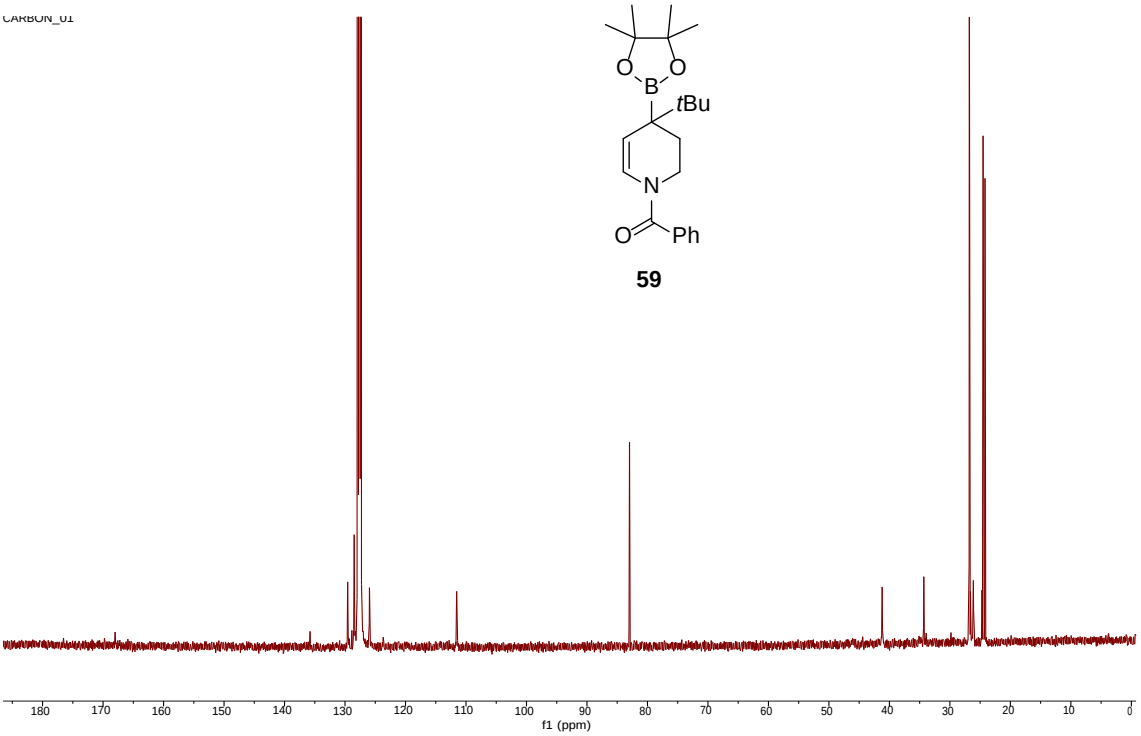


Proton NMR



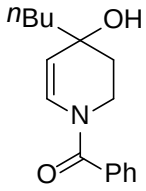
59

Carbon NMR

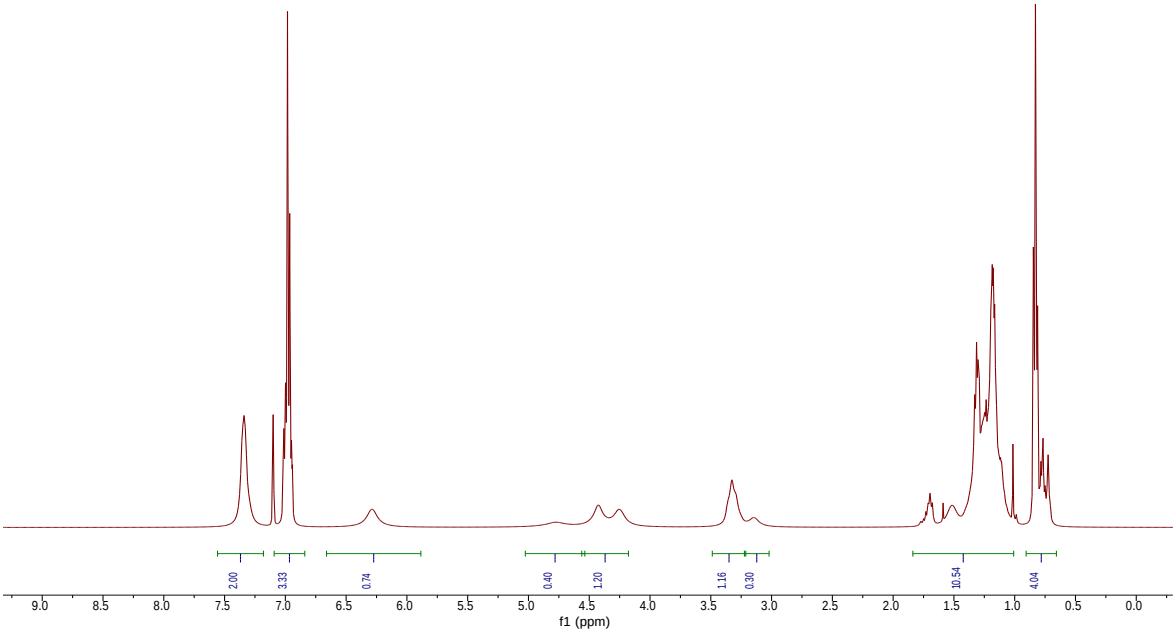


59

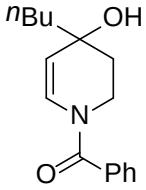
Proton NMR



60



Carbon NMR



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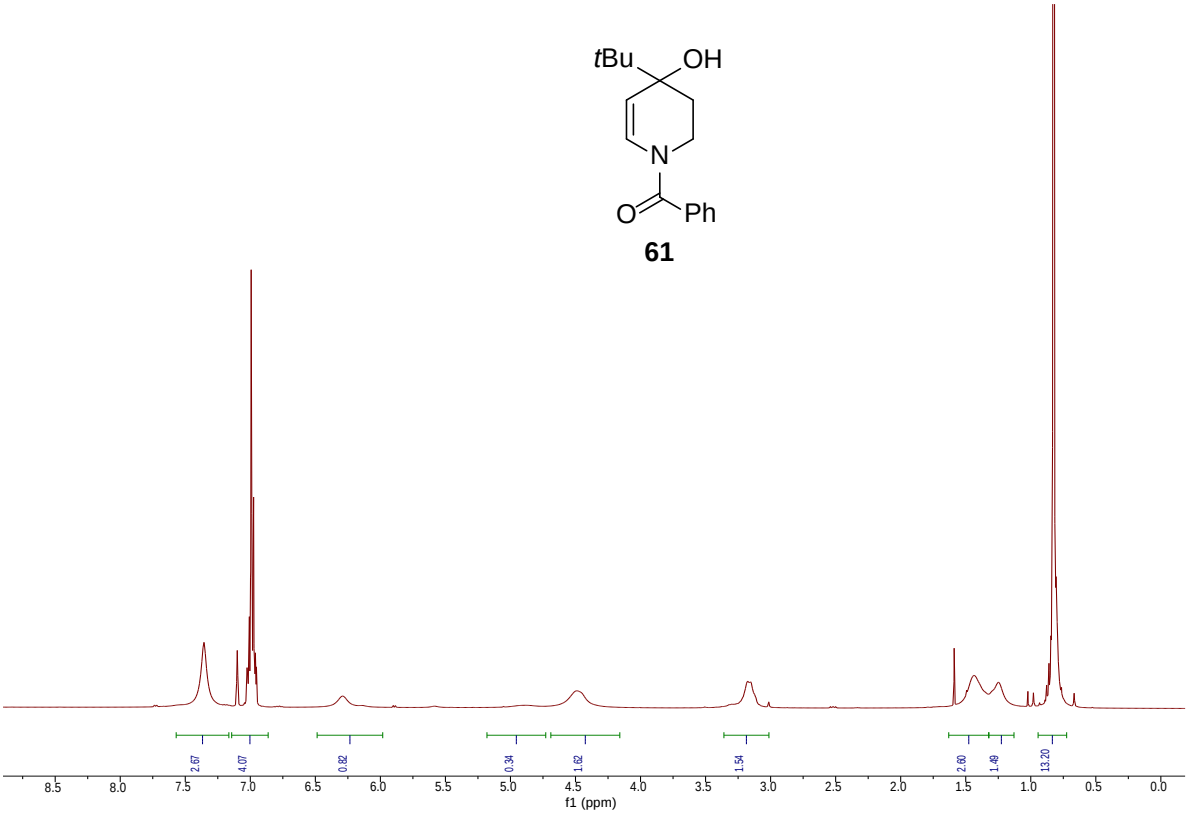
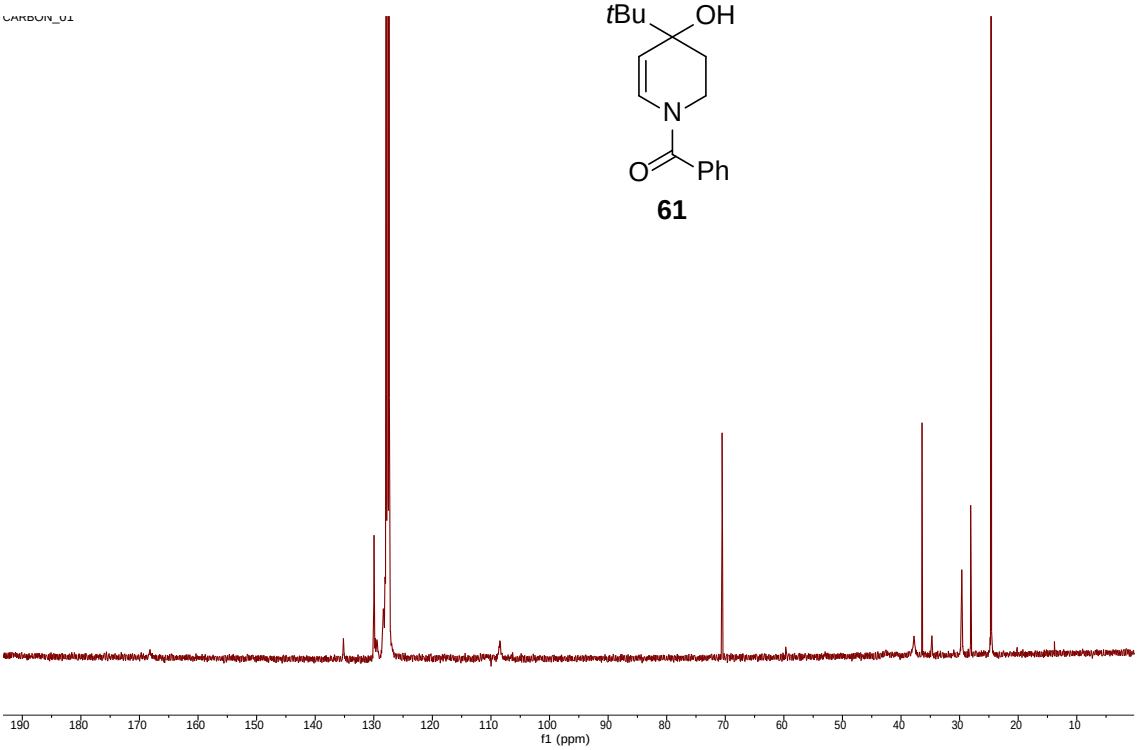
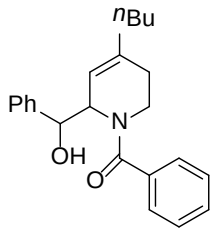
Proton NMR



Carbon NMR



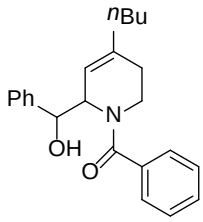
Proton NMR



dr 2:1

62

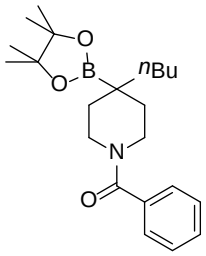
Carbon NMR



dr 2:1

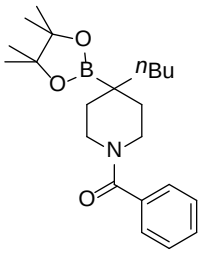
62

Proton NMR

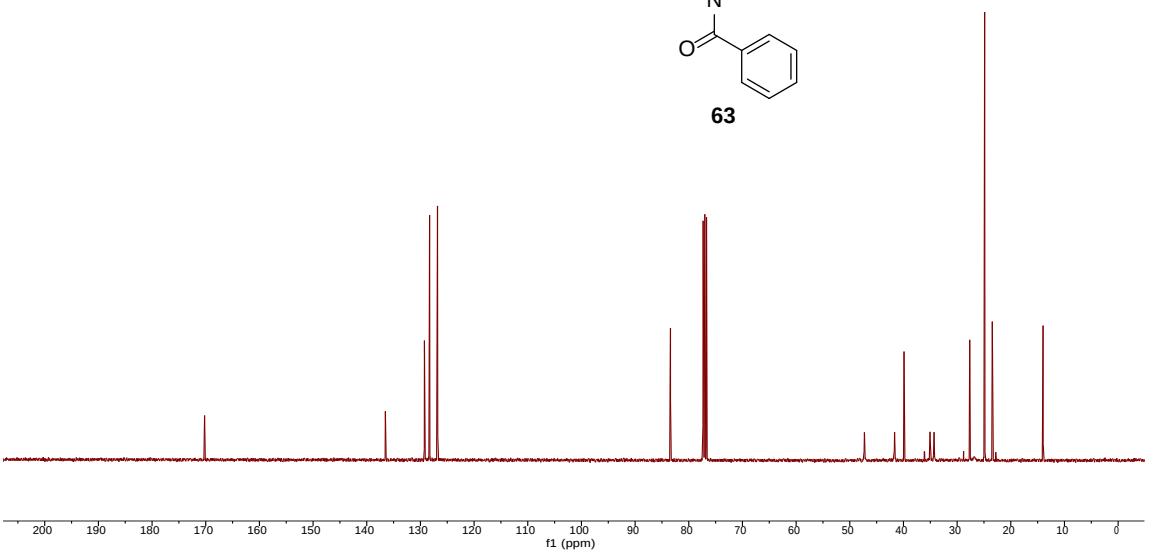


63

Carbon NMR



63



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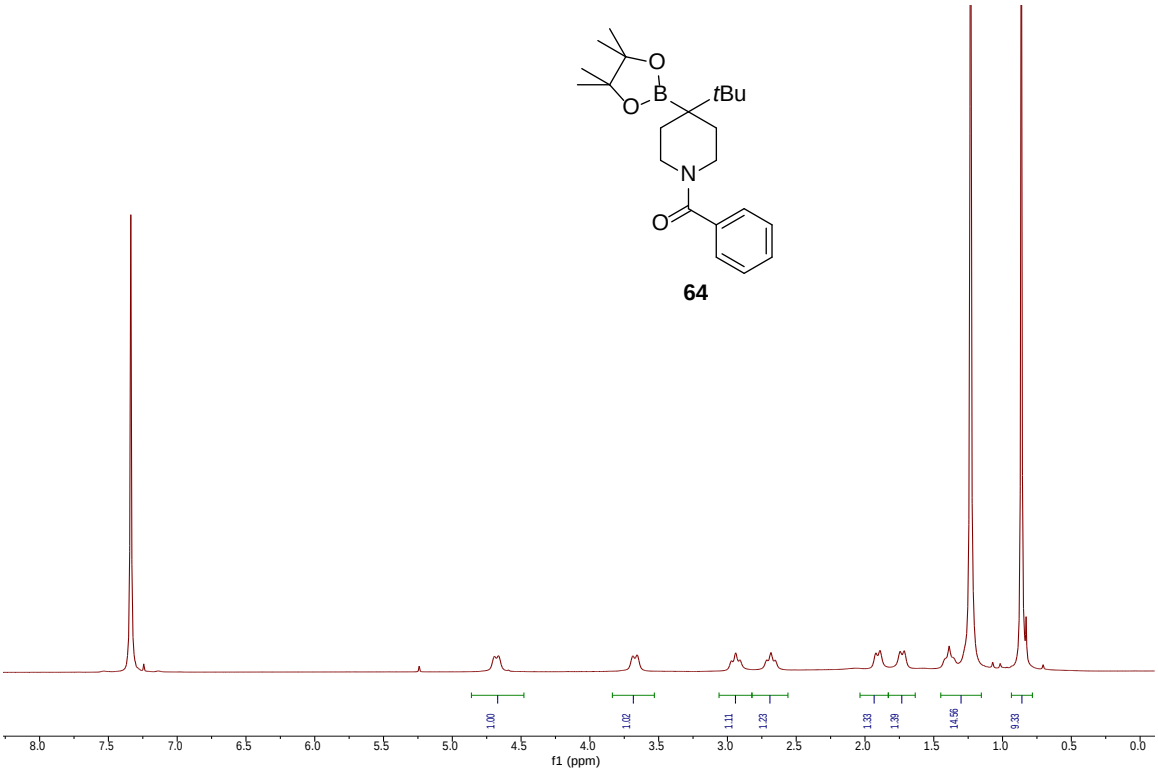
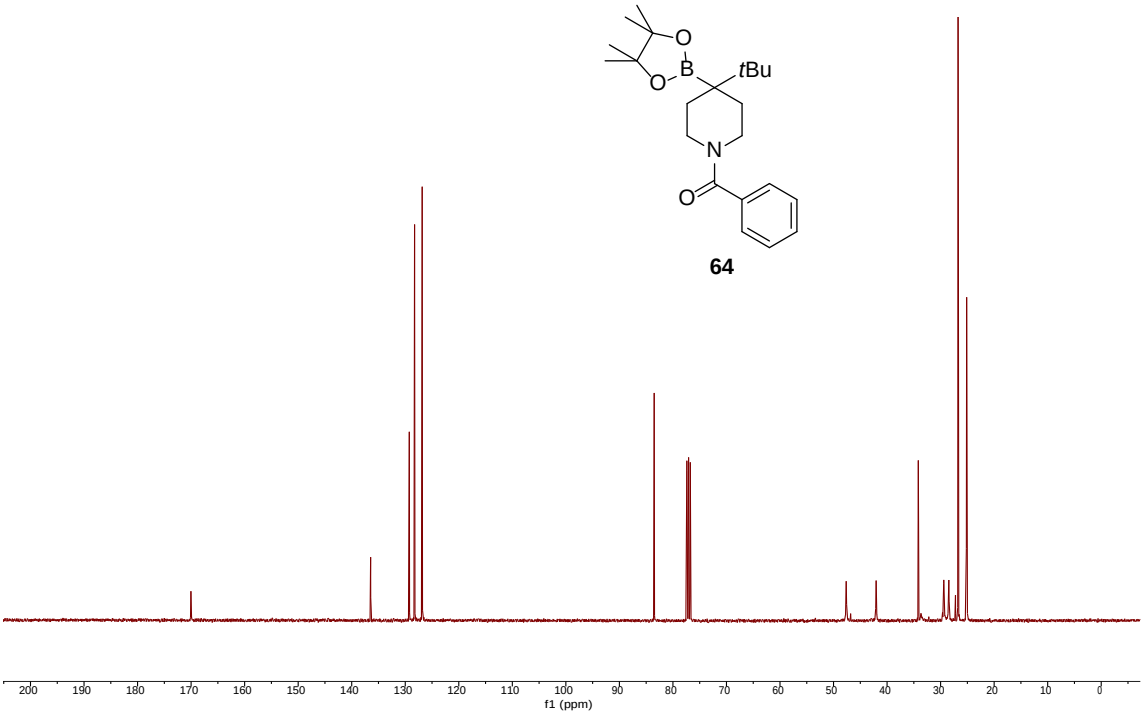
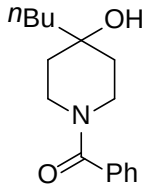


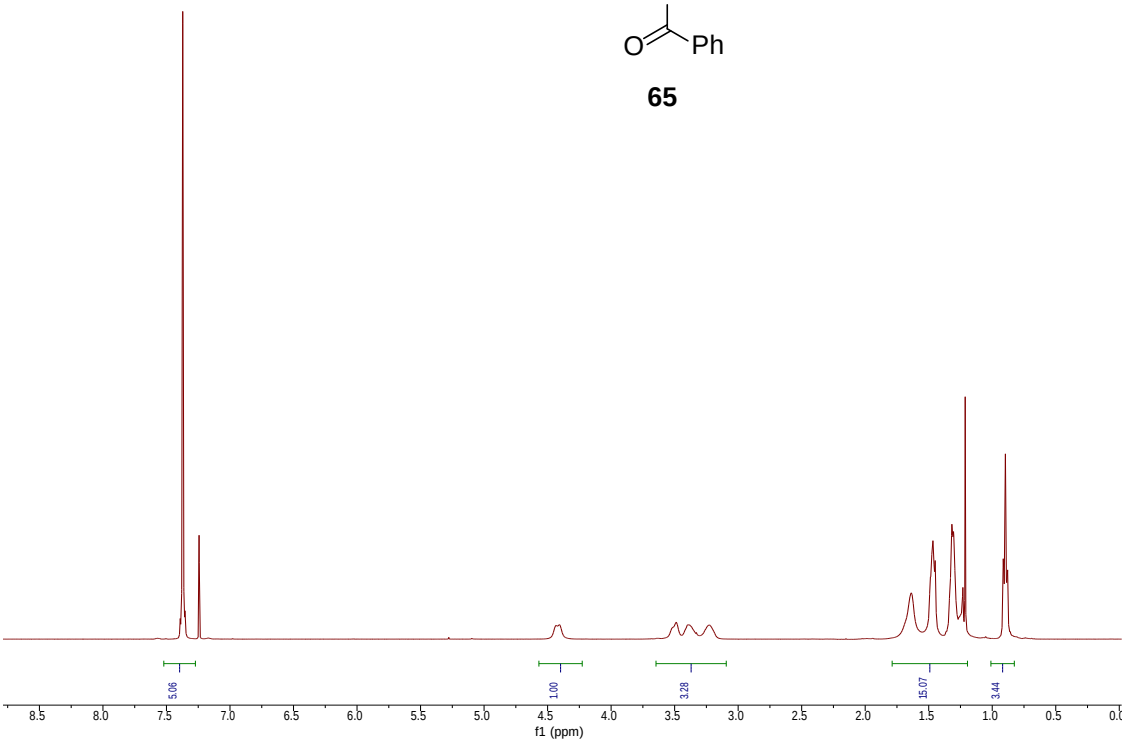
Carbon NMR



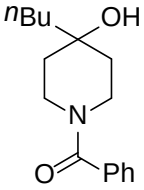
Proton NMR



65



Carbon NMR



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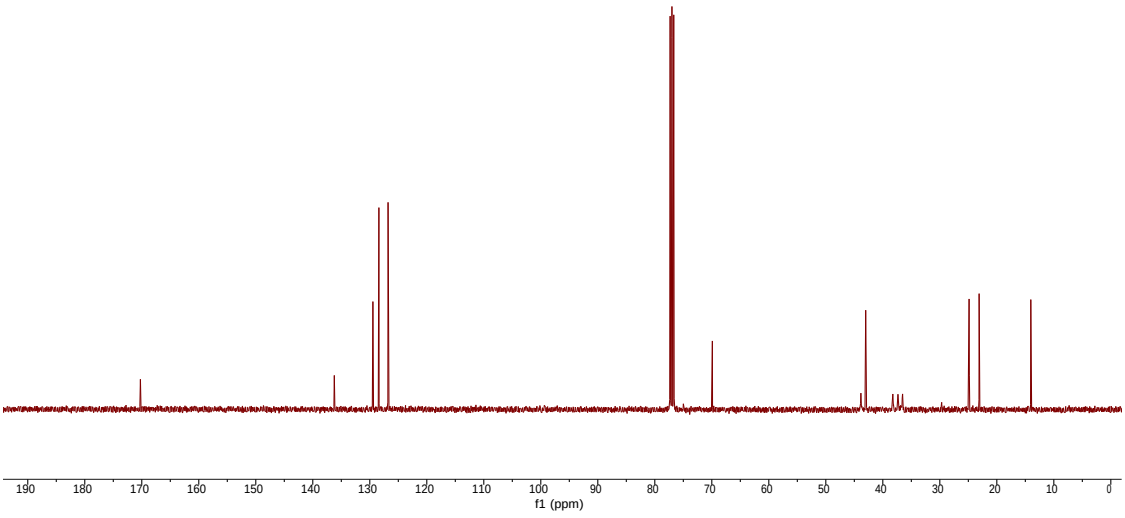
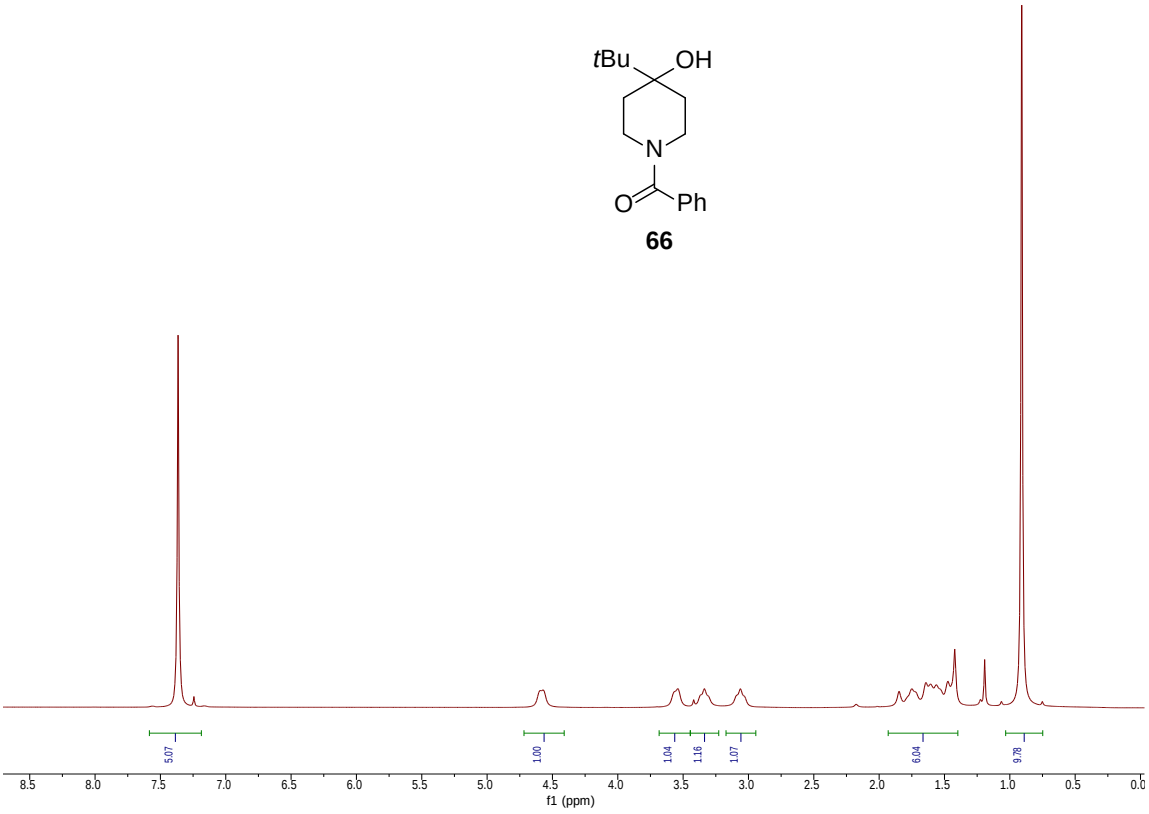
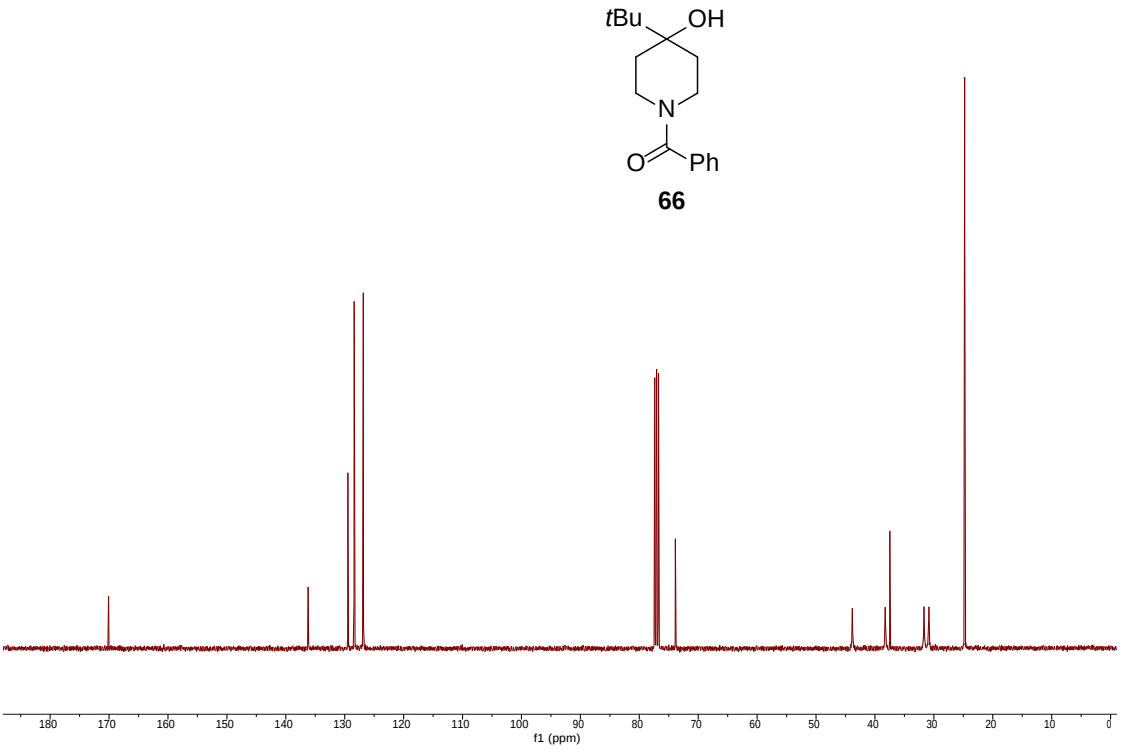


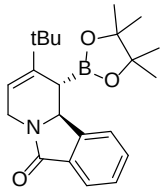
Proton NMR



Carbon NMR

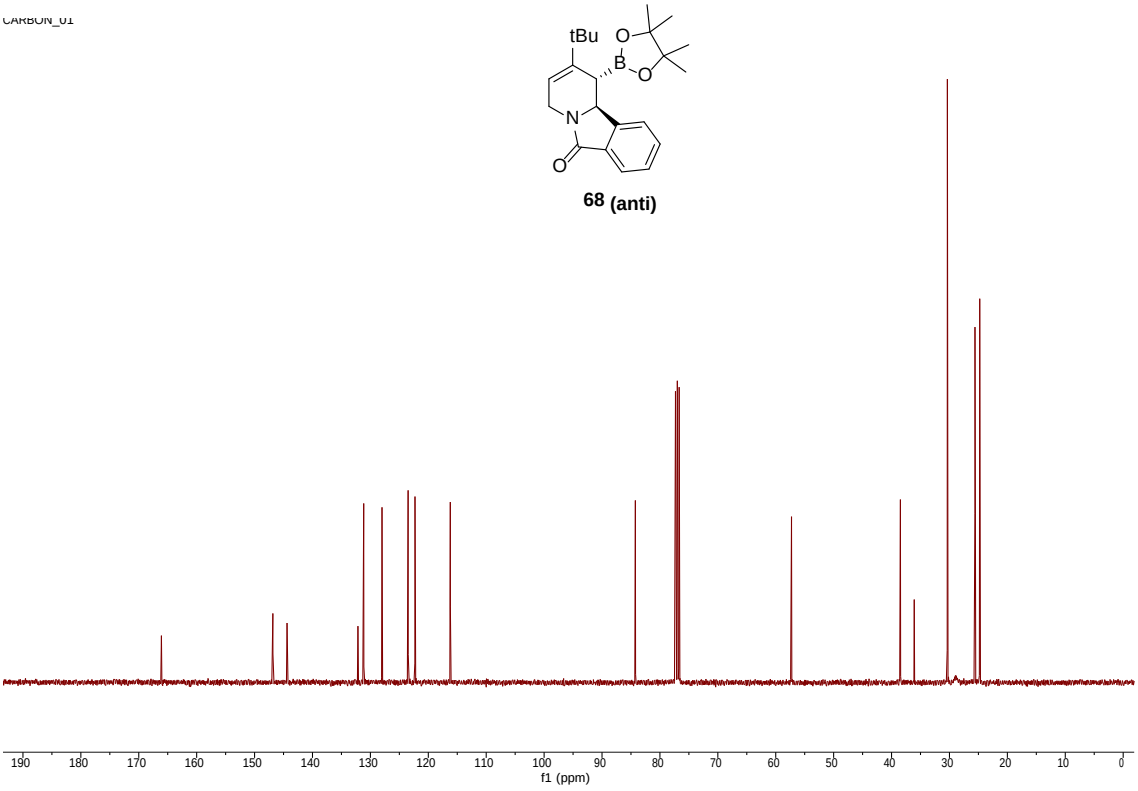


Proton NMR



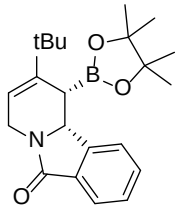
68 (anti)

Carbon NMR



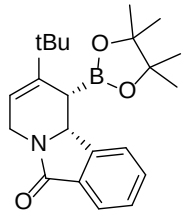
68 (anti)

Proton NMR

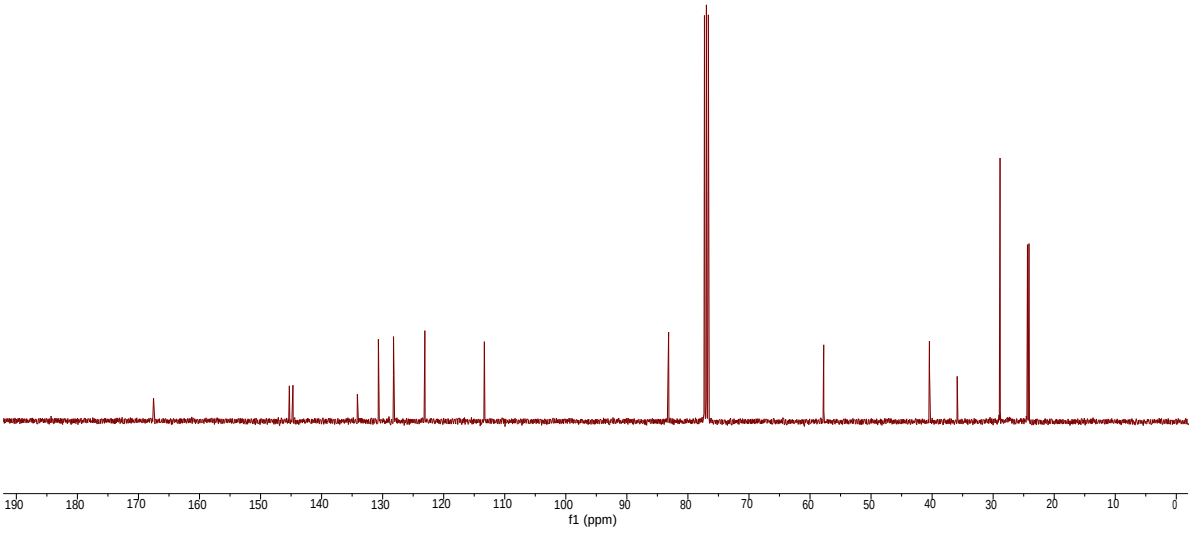


68 (syn)

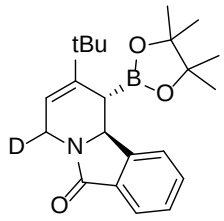
Carbon NMR



68 (syn)

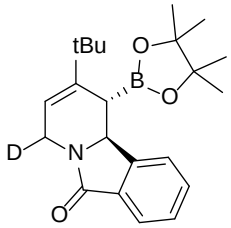


Proton NMR



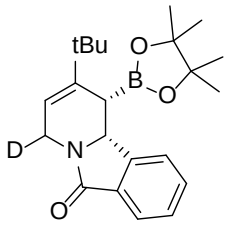
68-*anti*-D

Carbon NMR



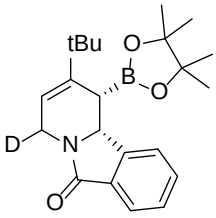
68-*anti*-D

Proton NMR



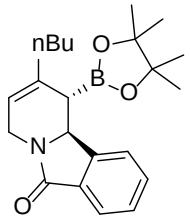
68-*syn*-D

Carbon NMR



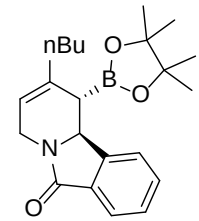
68-*syn*-D

Proton NMR



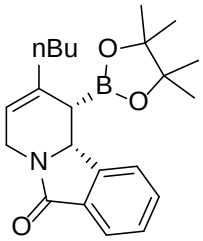
69 (anti)

Carbon NMR



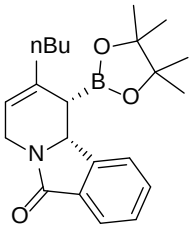
69 (anti)

Proton NMR



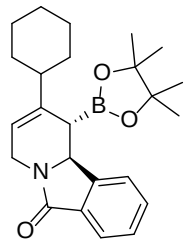
69 (syn)

Carbon NMR



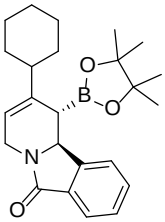
69-(syn)

Proton NMR



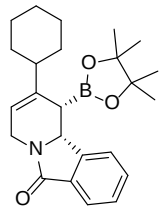
70 (anti)

Carbon NMR



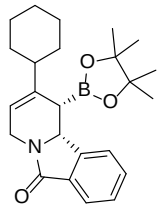
70 (anti)

Proton NMR

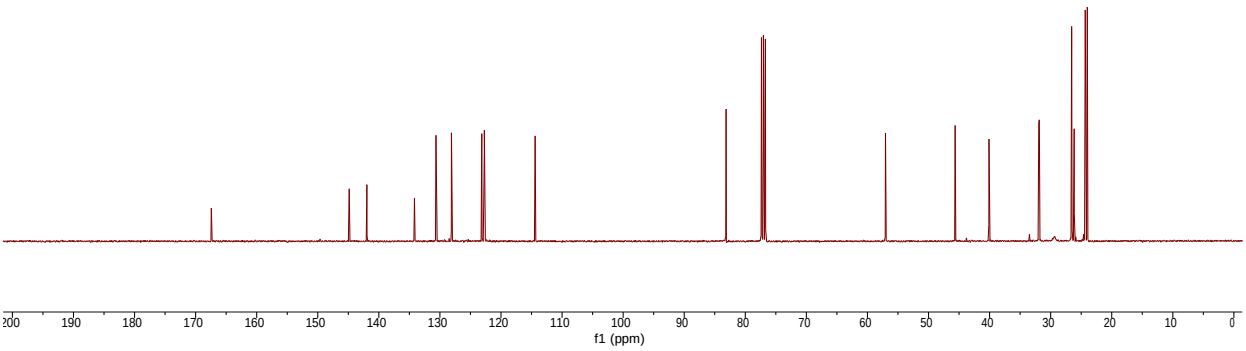


70 (syn)

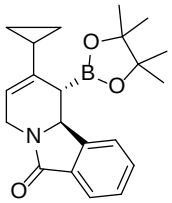
Carbon NMR



70 (syn)

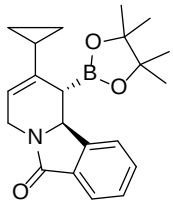


Proton NMR



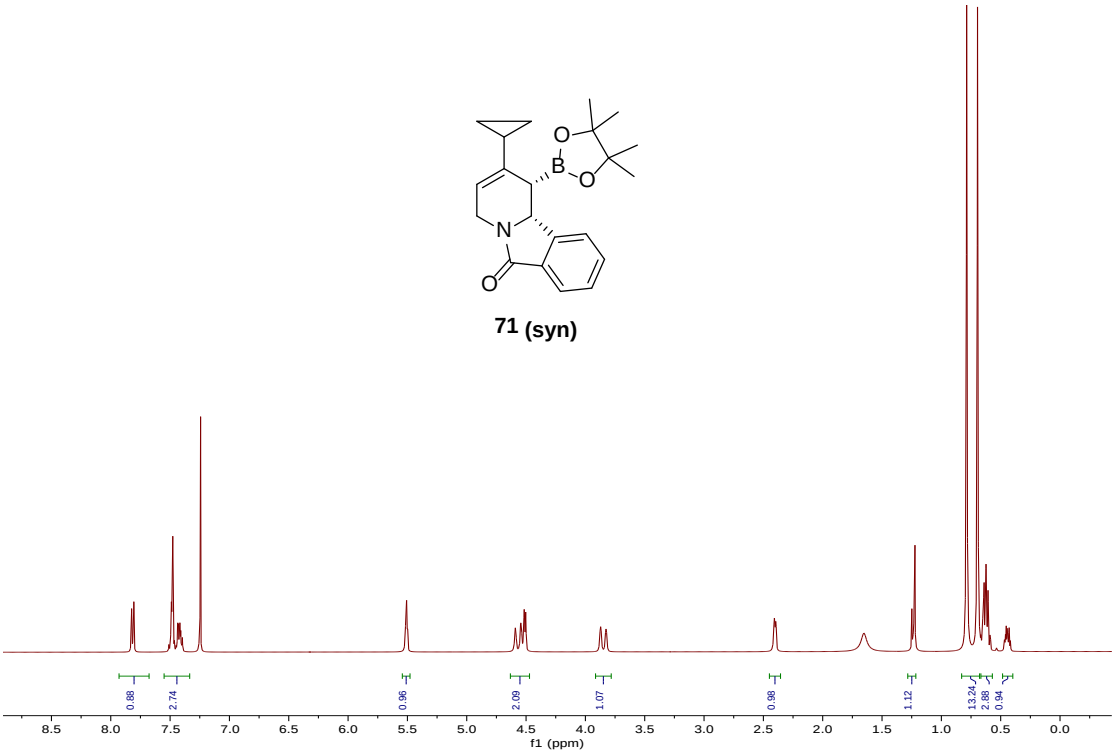
71 (anti)

Carbon NMR



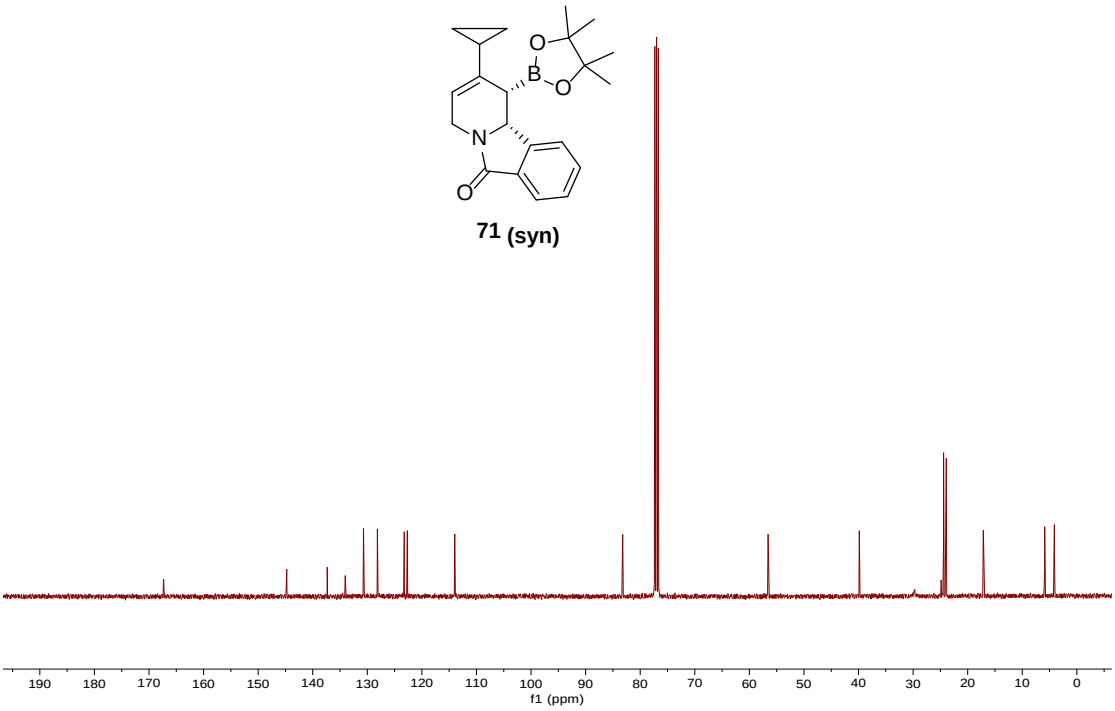
71 (anti)

Proton NMR



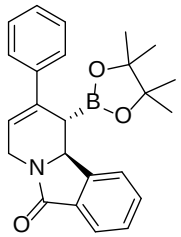
71 (syn)

Carbon NMR



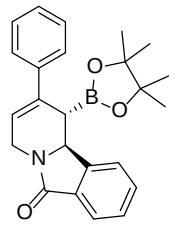
71 (syn)

Proton NMR



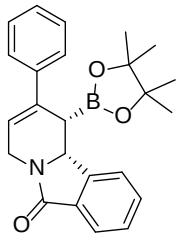
72 (anti)

Carbon NMR



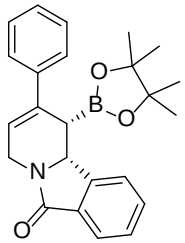
72 (anti)

Proton NMR



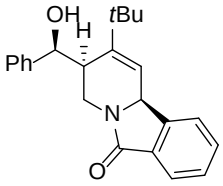
72 (syn)

Carbon NMR



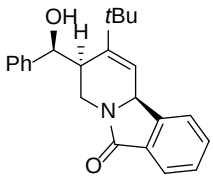
72 (syn)

Proton NMR



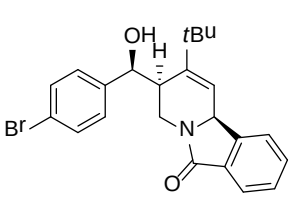
74

Carbon NMR

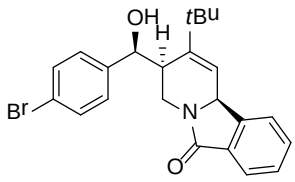


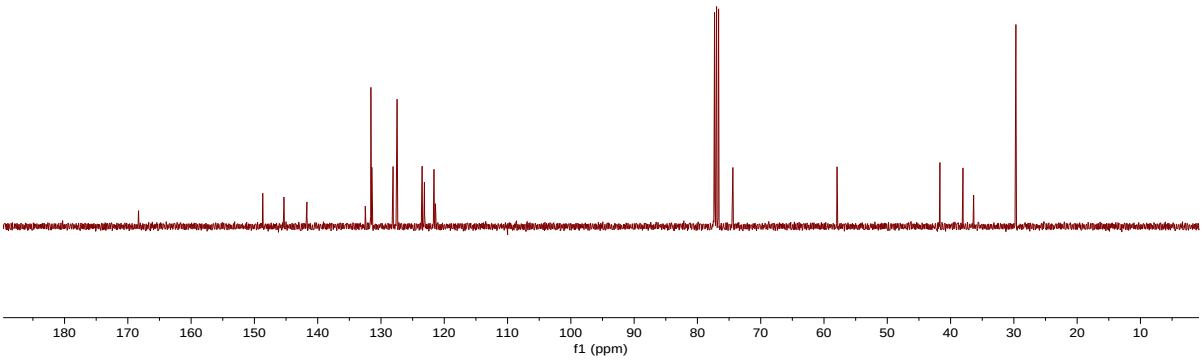
74

Proton NMR

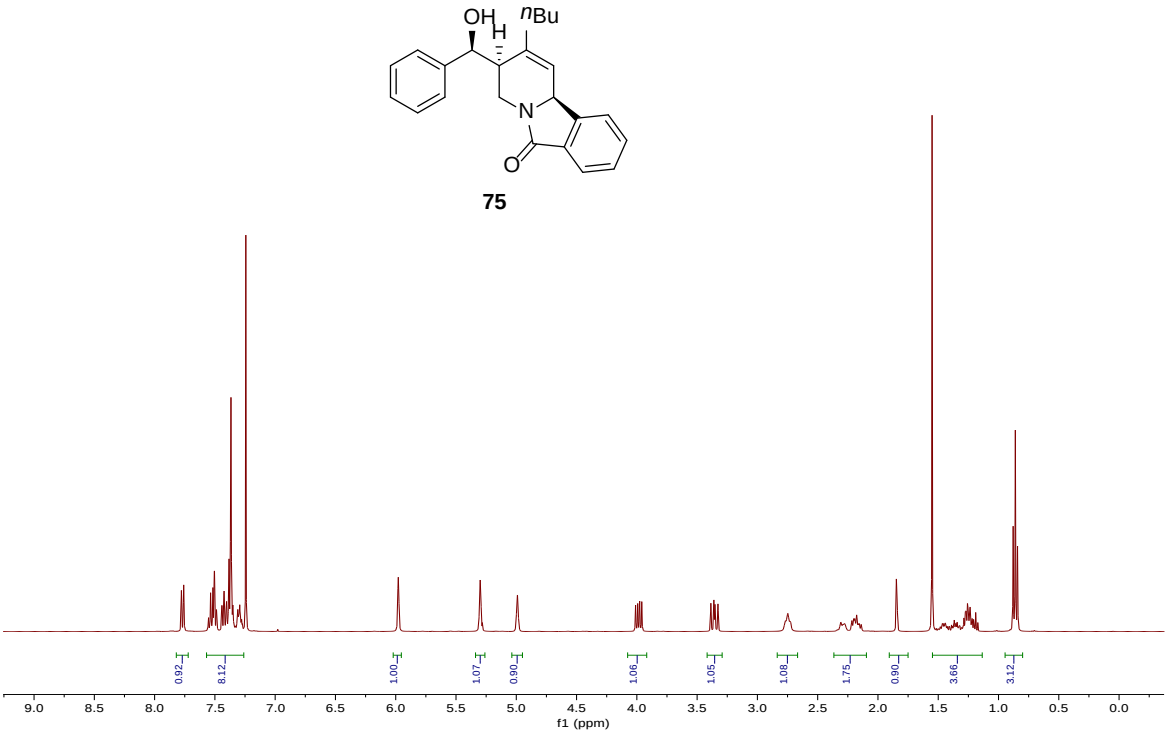


Carbon NMR

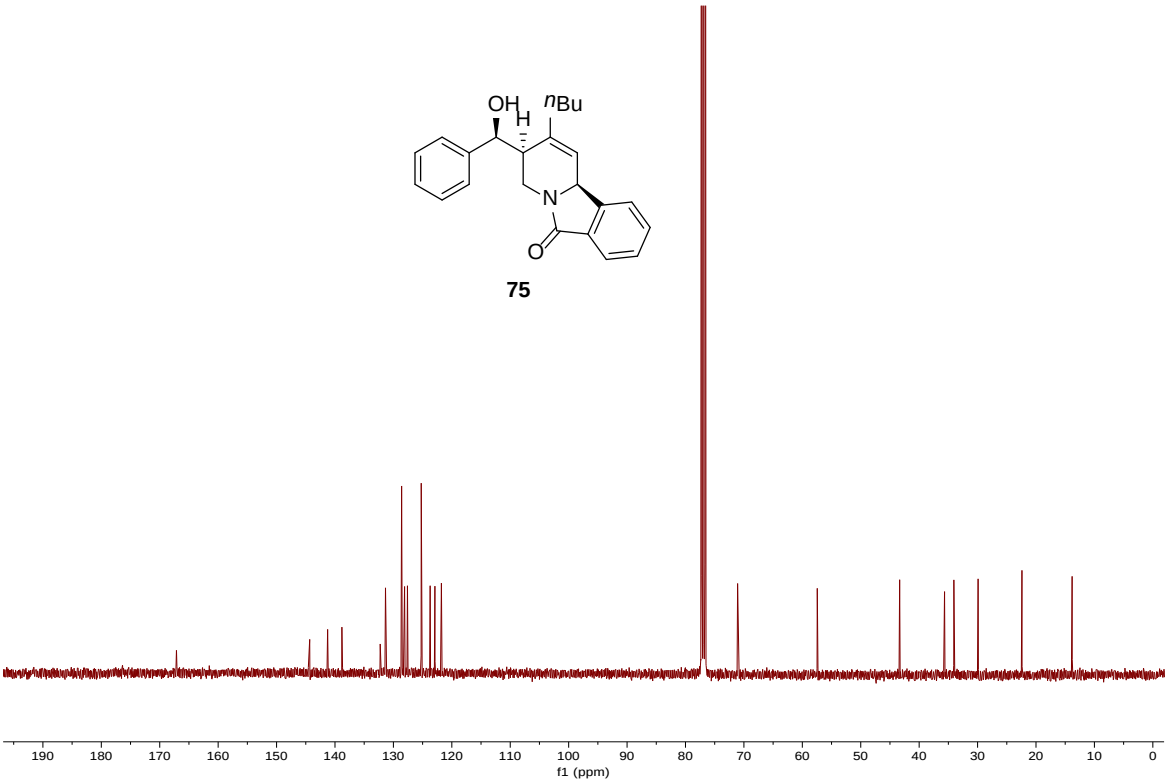




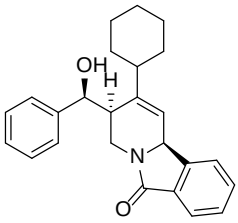
Proton NMR



Carbon NMR

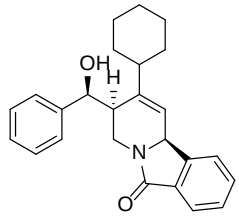


Proton NMR

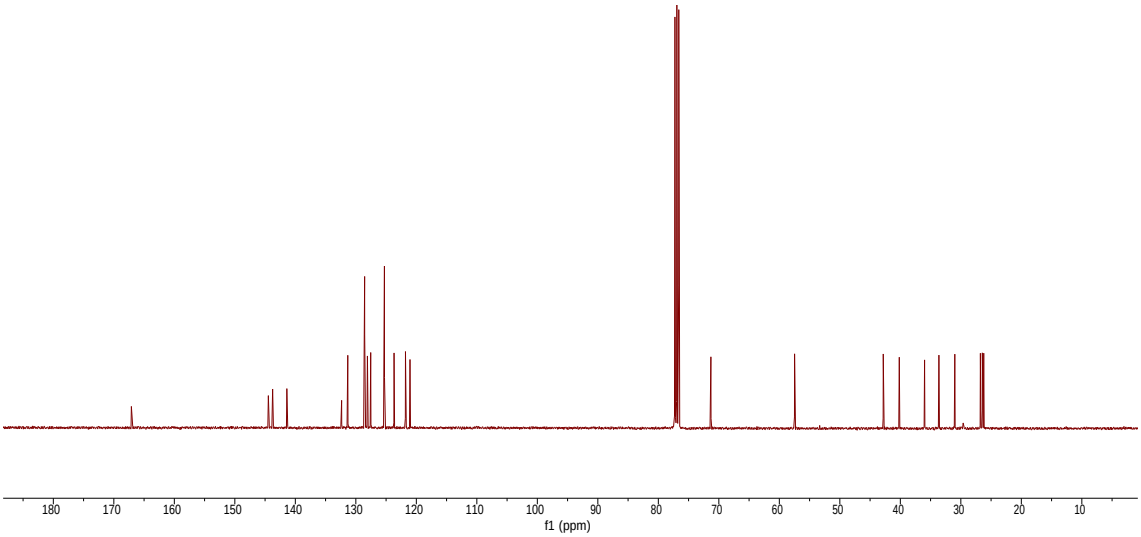


76

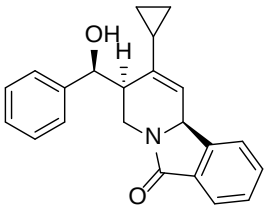
Carbon NMR



76



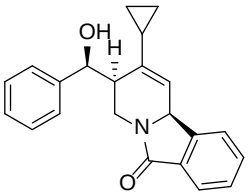
Proton NMR



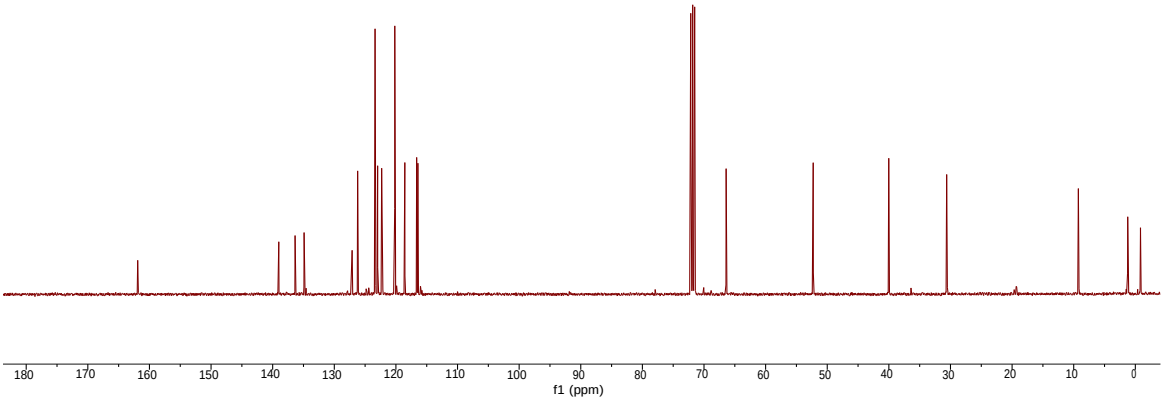
77

Carbon NMR

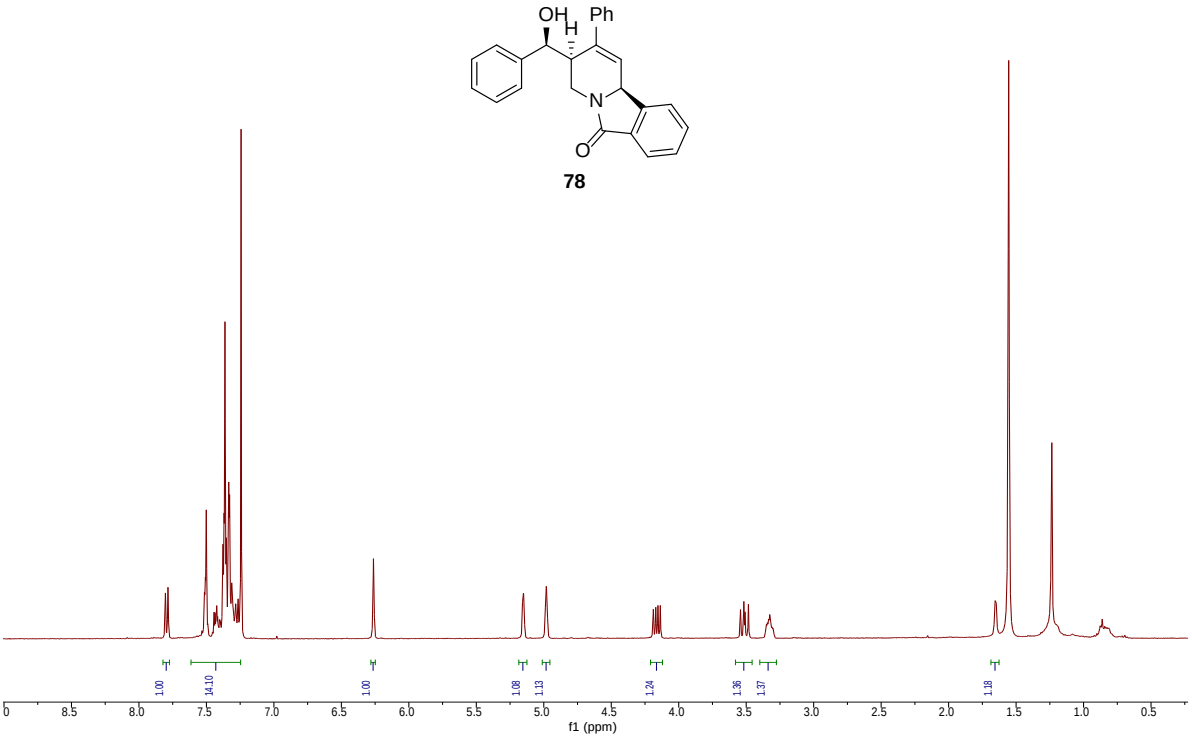
CARBON_01



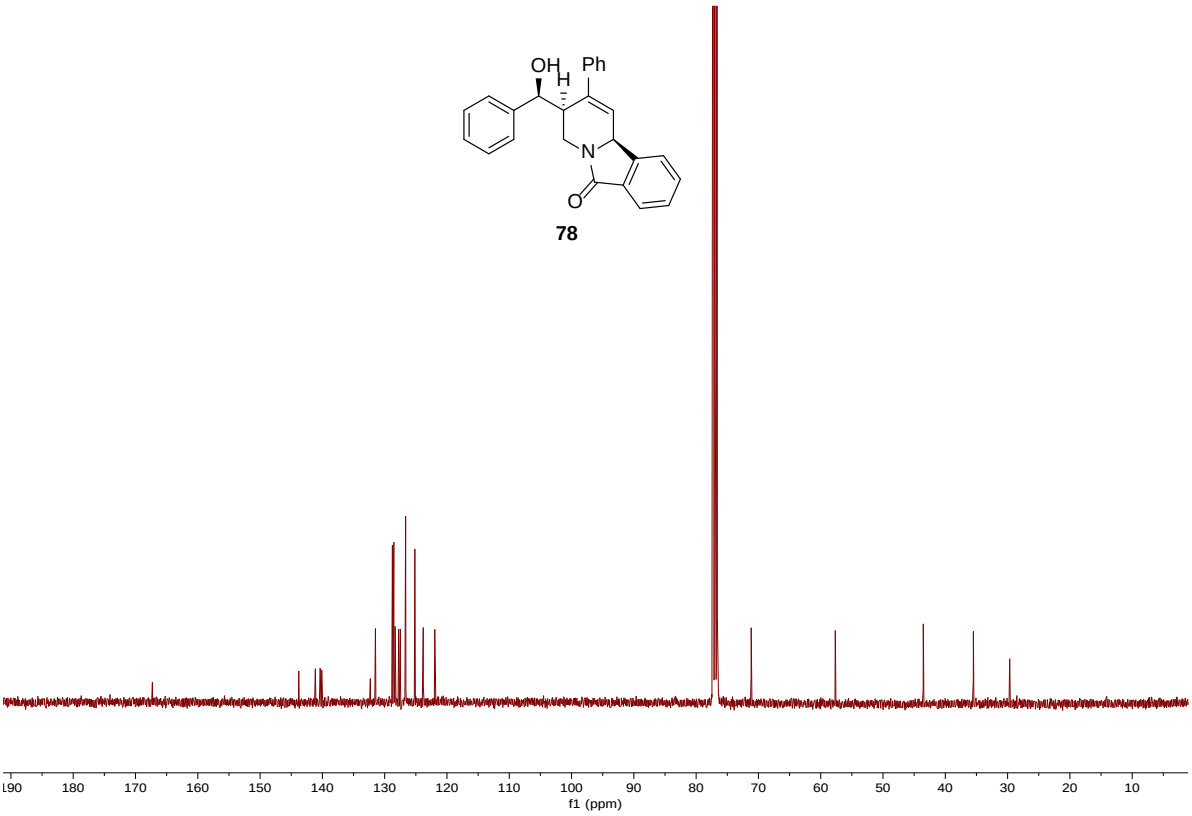
77



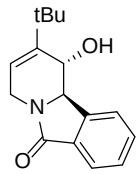
Proton NMR



Carbon NMR



Proton NMR



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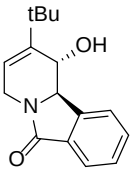
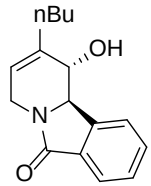
Carbon NMR

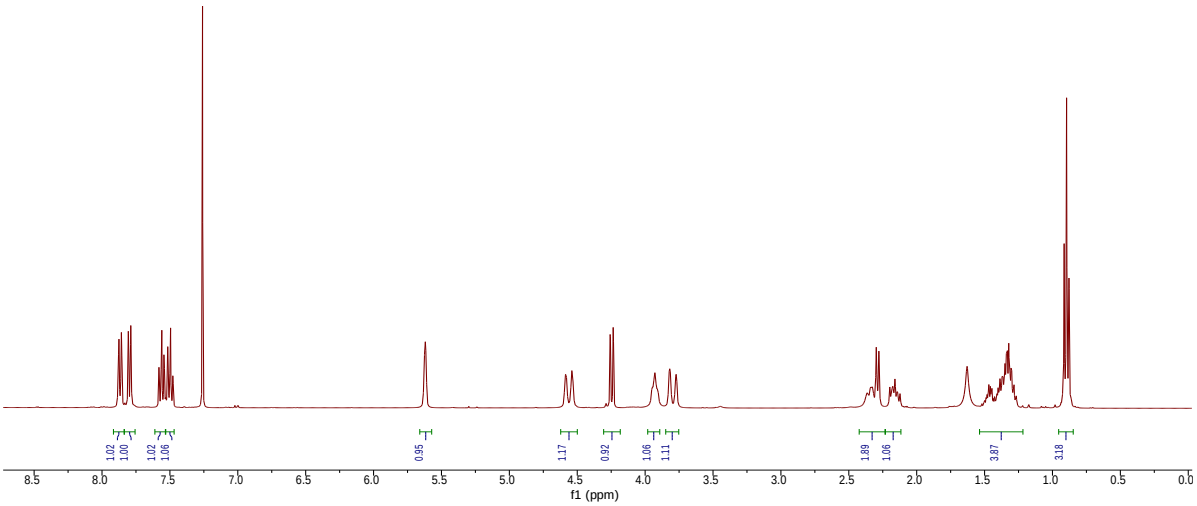


79

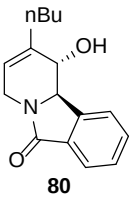
Proton NMR



80



Carbon NMR



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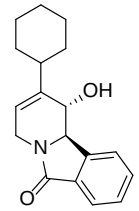
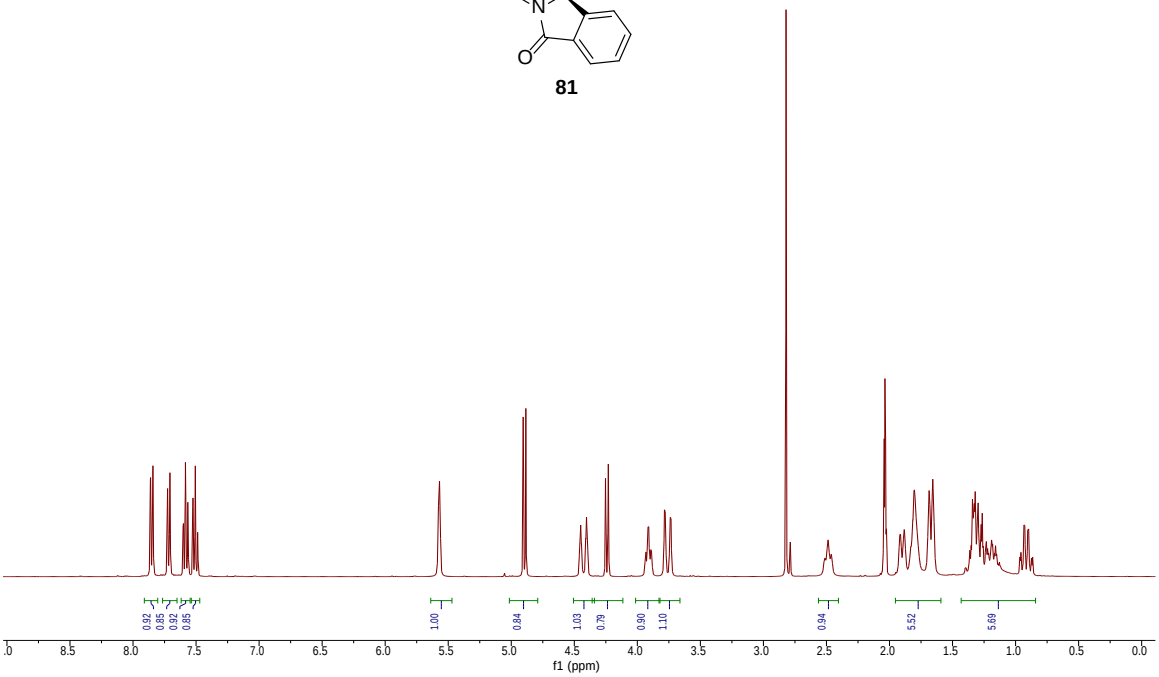
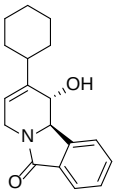
Proton NMR



81



Carbon NMR



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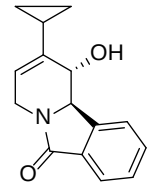
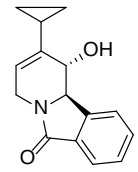
Proton NMR



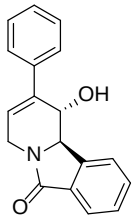
82

Carbon NMR



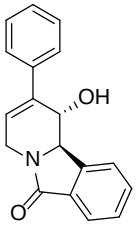
82

Proton NMR



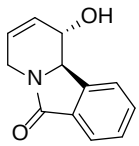
83

Carbon NMR

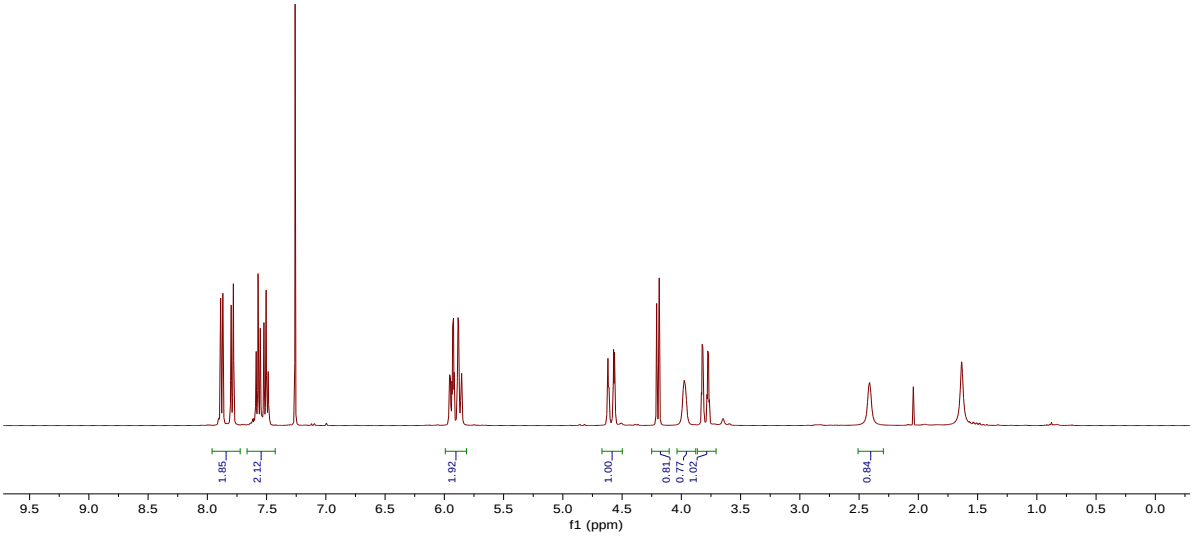


83

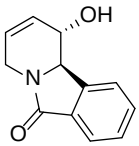
Proton NMR



84-anti

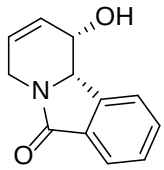


Carbon NMR

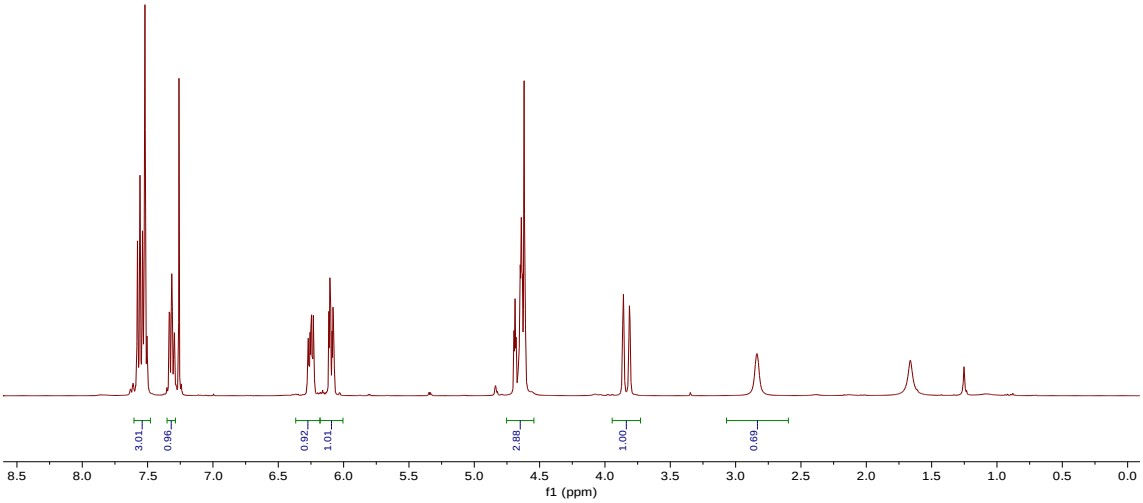


84-anti

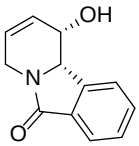
Proton NMR



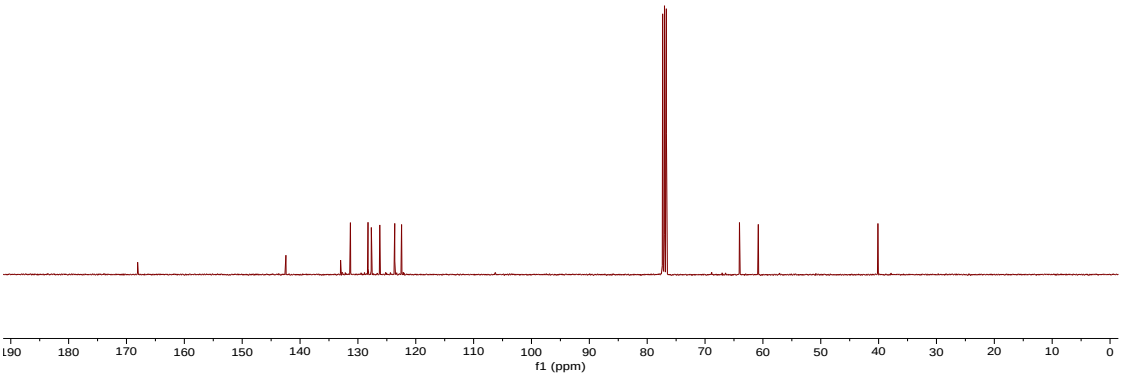
84-syn



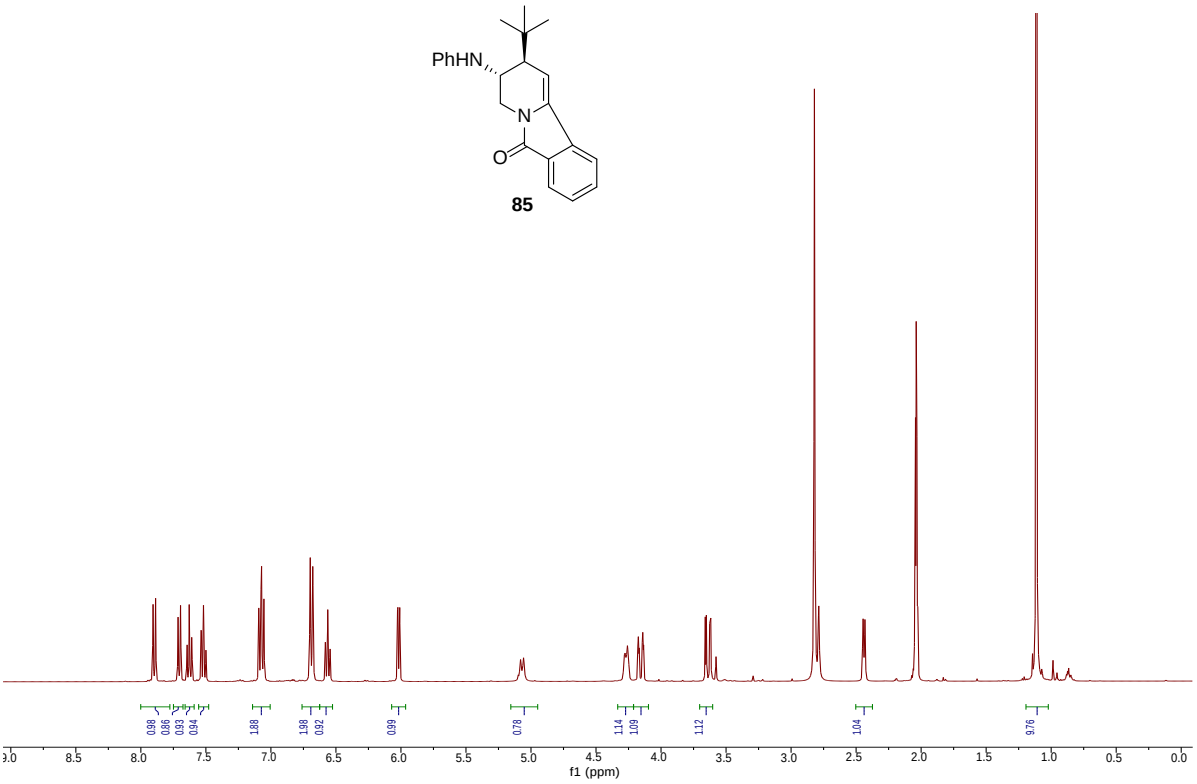
Carbon NMR



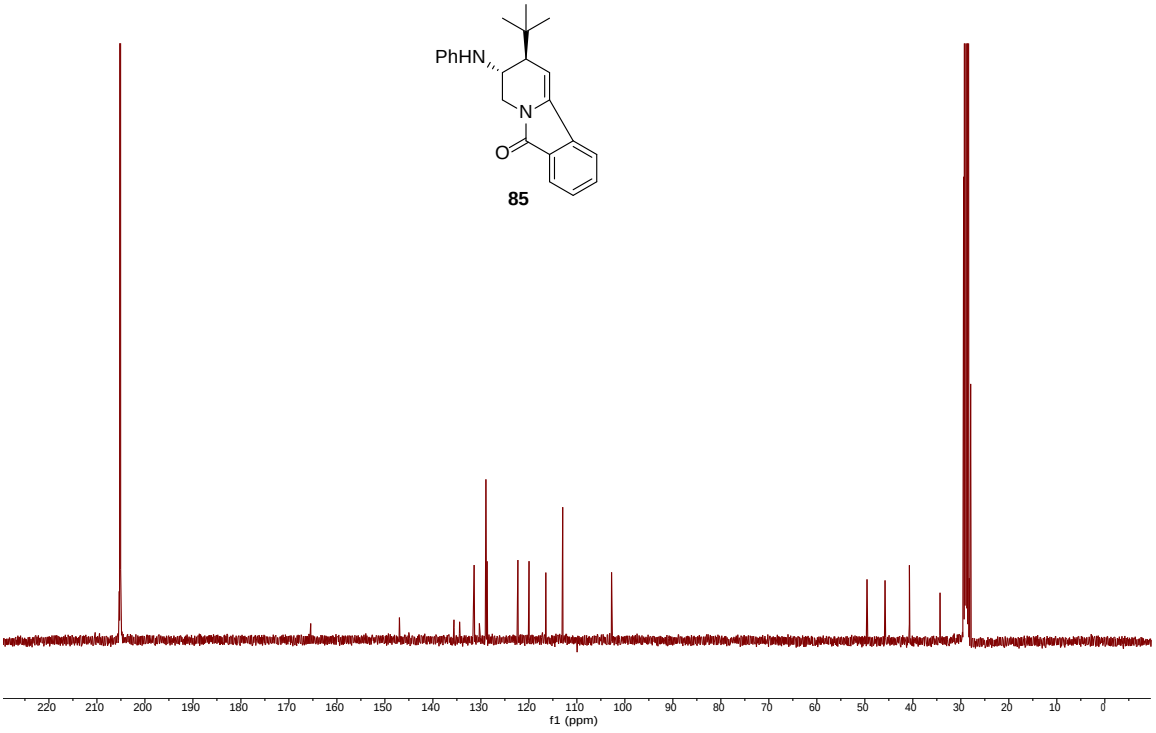
84-syn



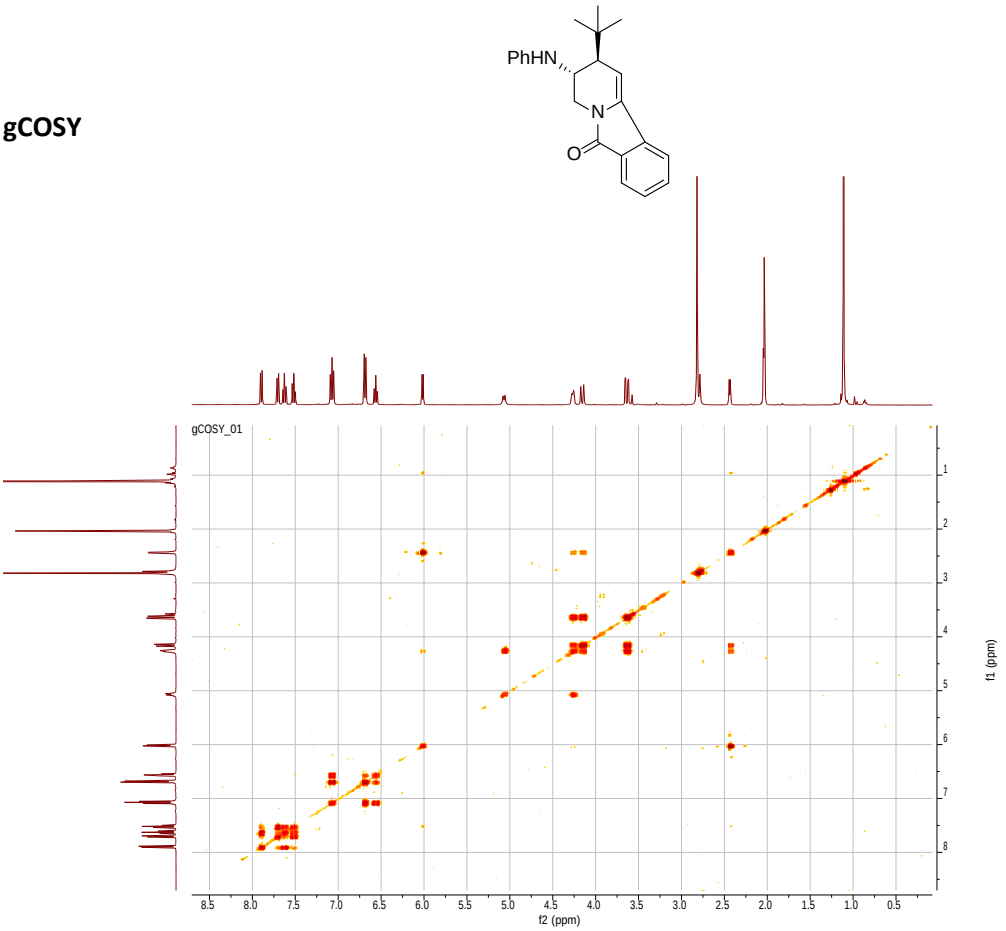
Proton NMR



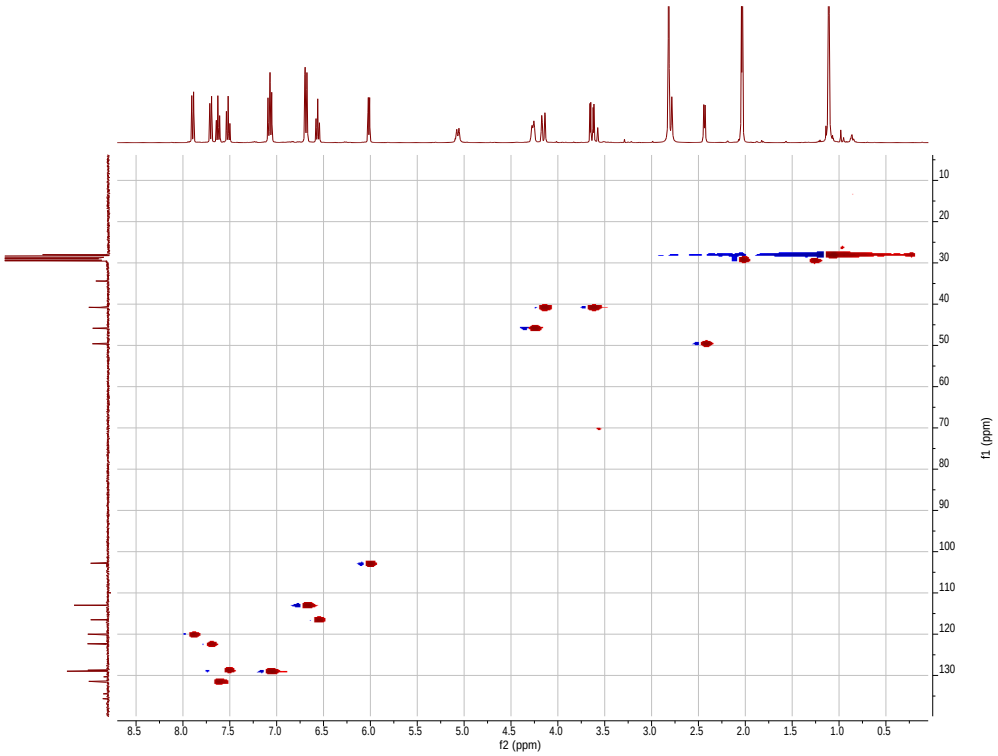
Carbon NMR



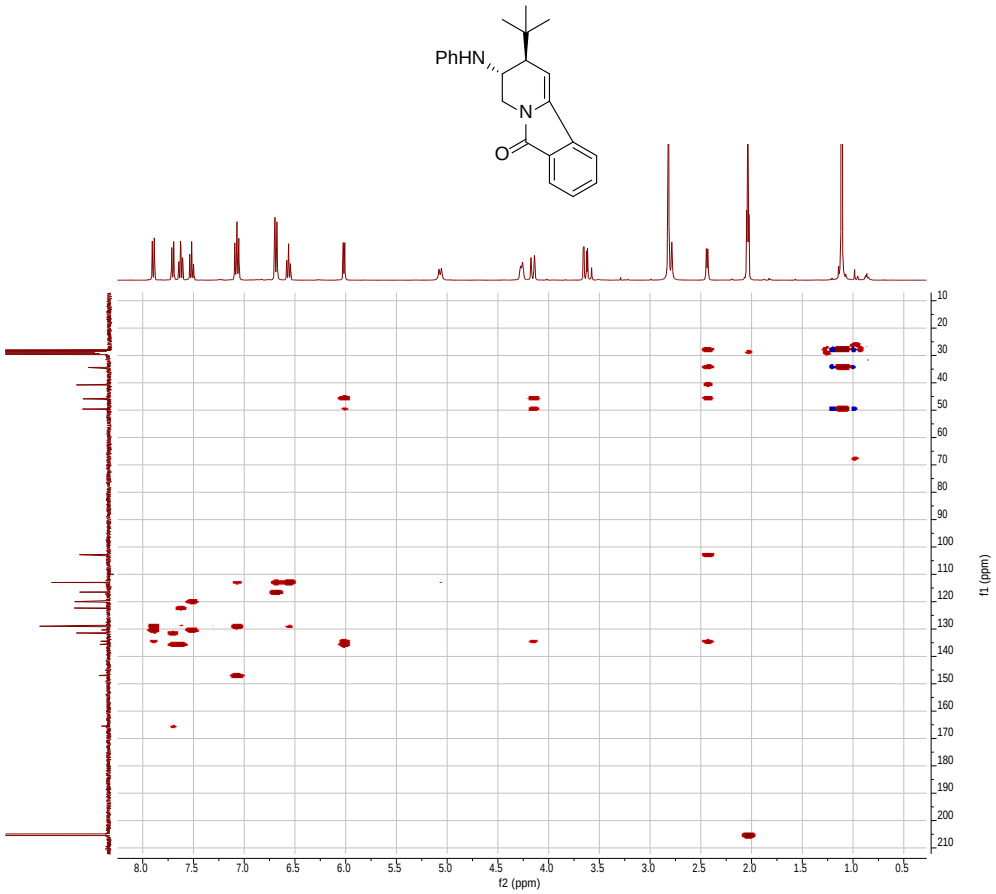
gCOSY



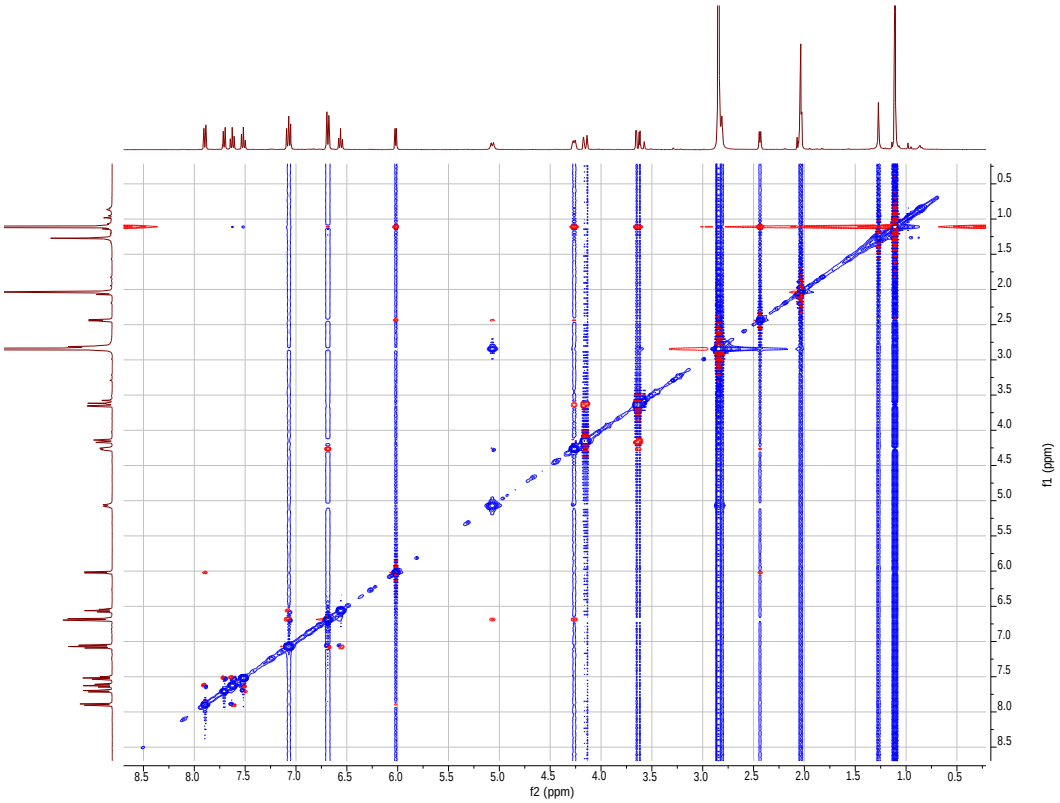
HSQC



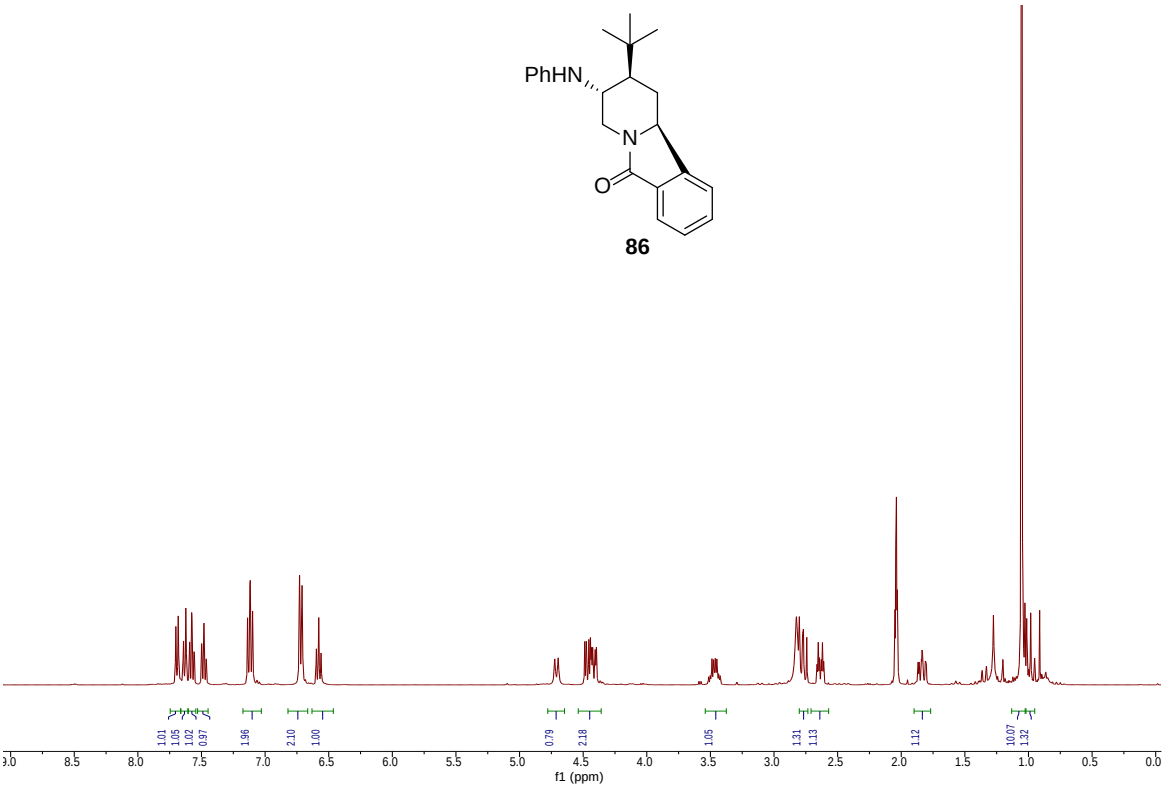
HMBC



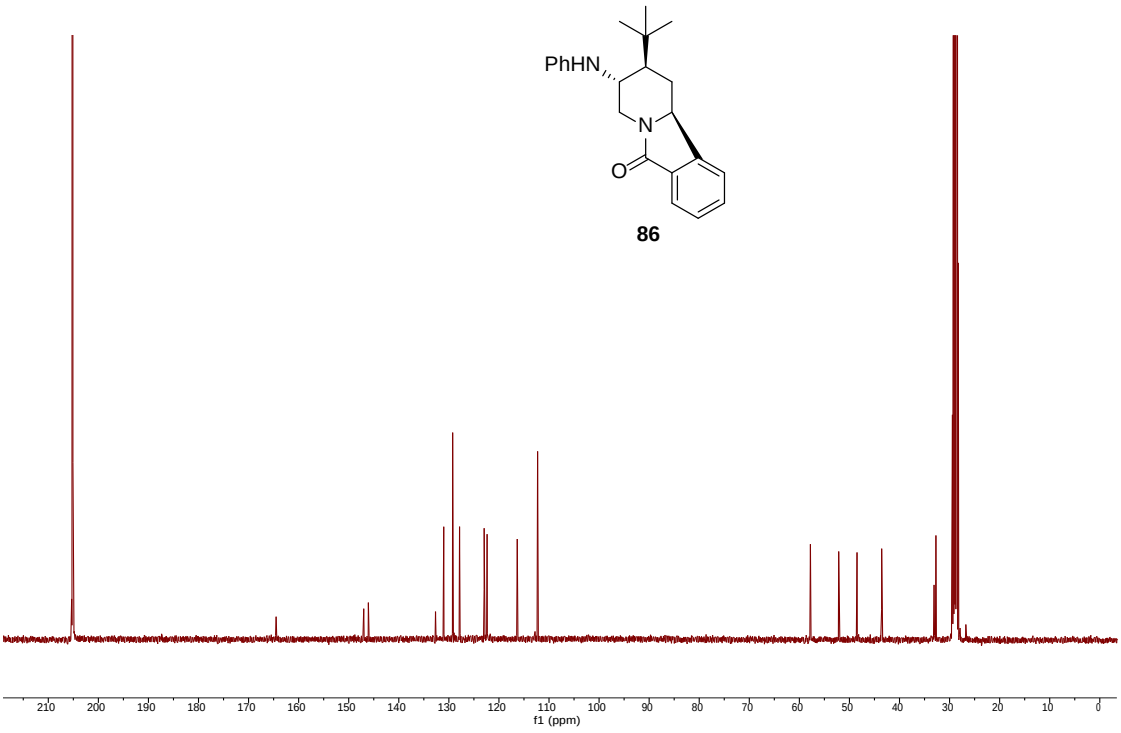
2D-NOESY



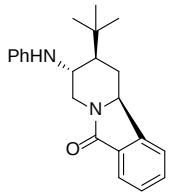
Proton NMR



Carbon NMR

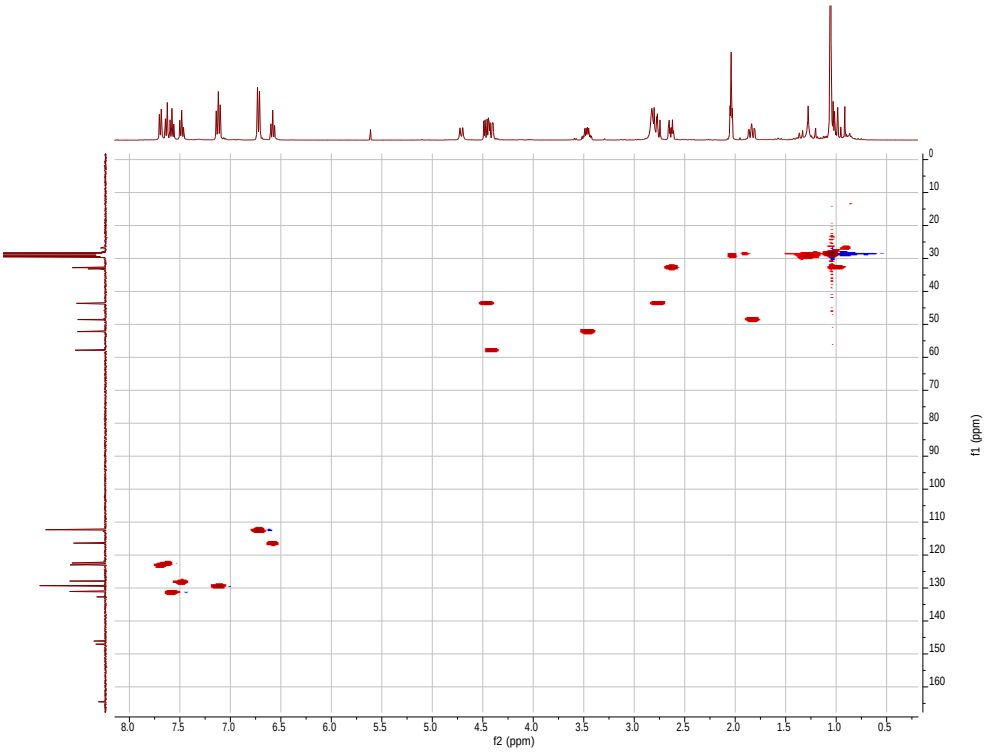


gCOSY

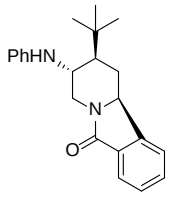


86

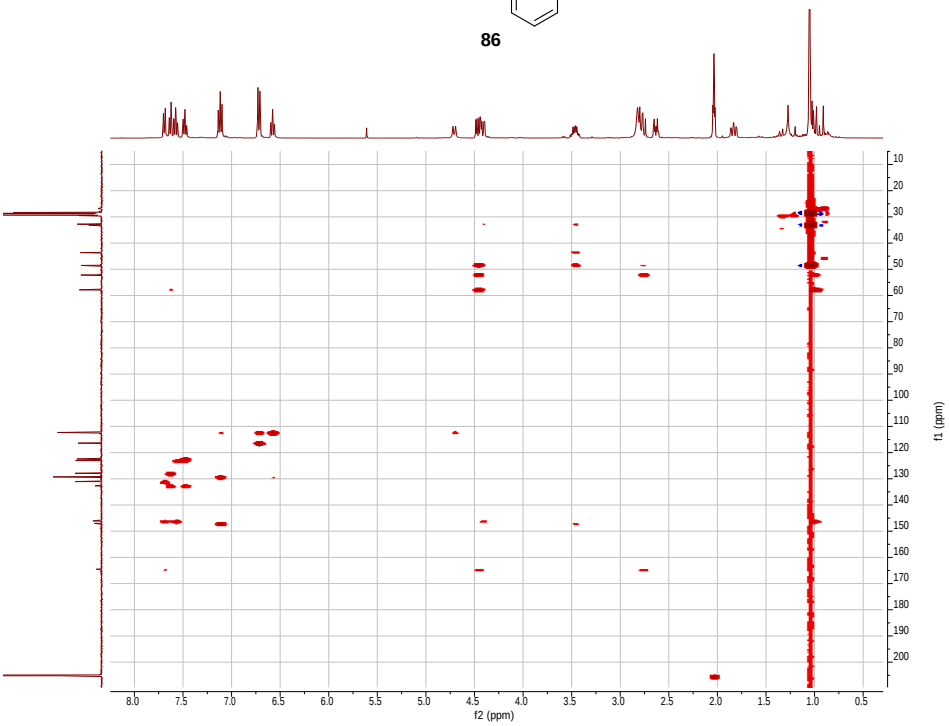
HSQC



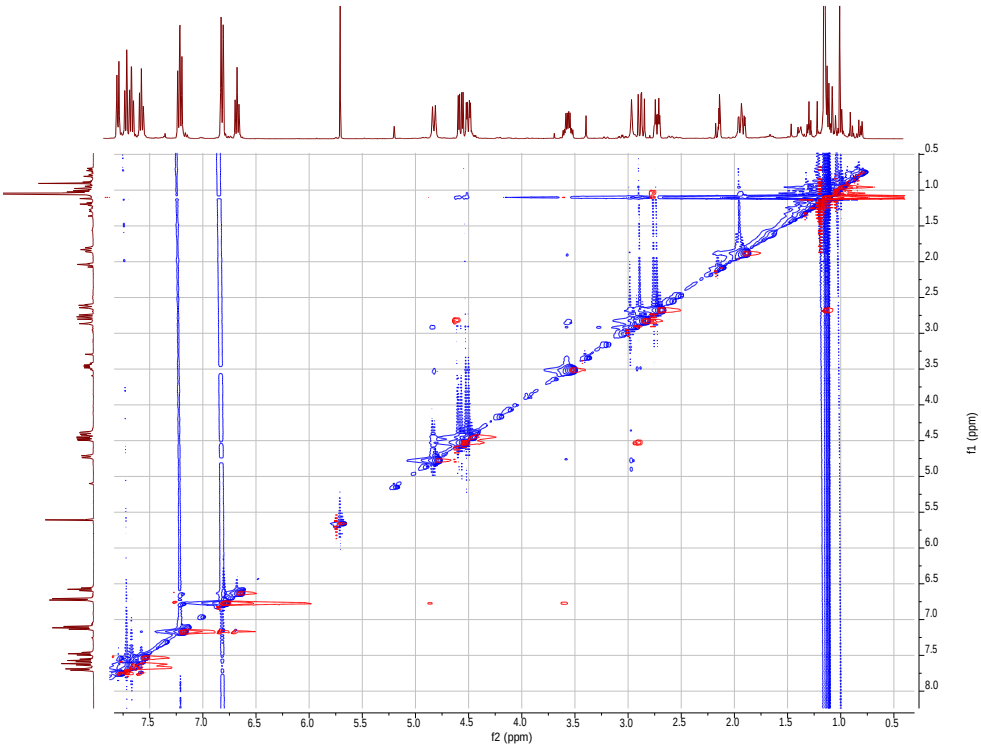
HMBC



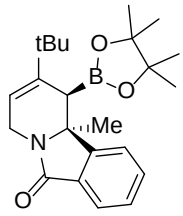
86



2D NOESY

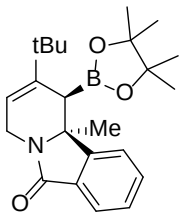


Proton NMR



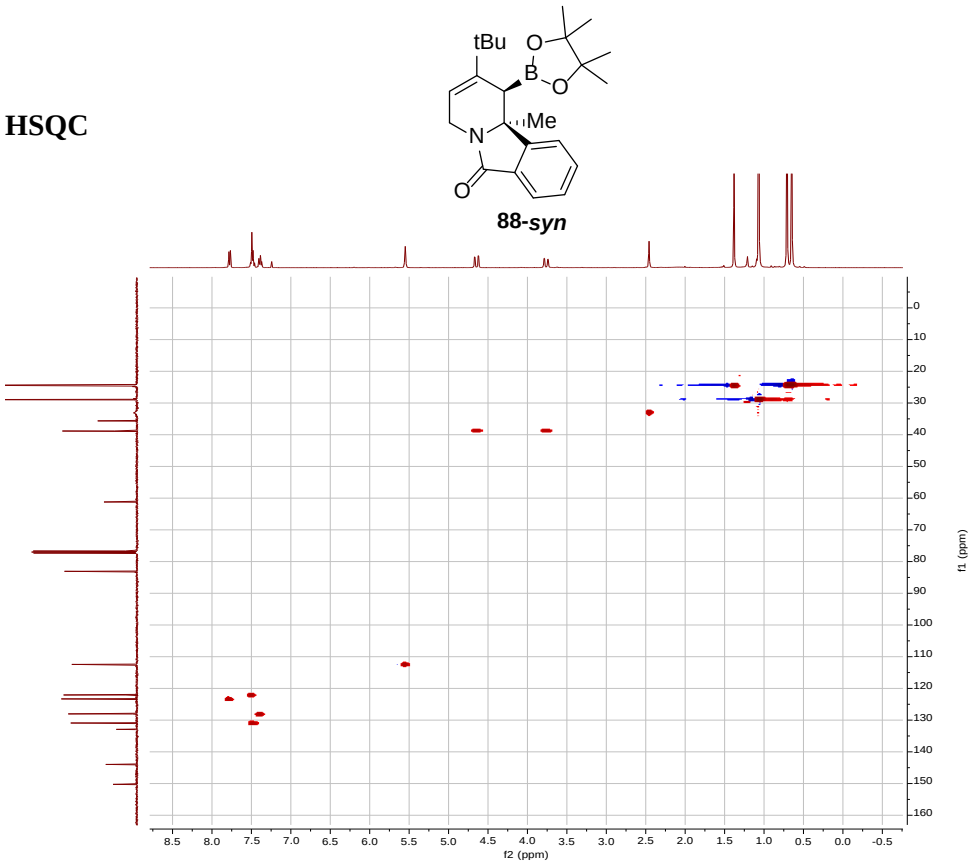
88 - *syn*

Carbon NMR

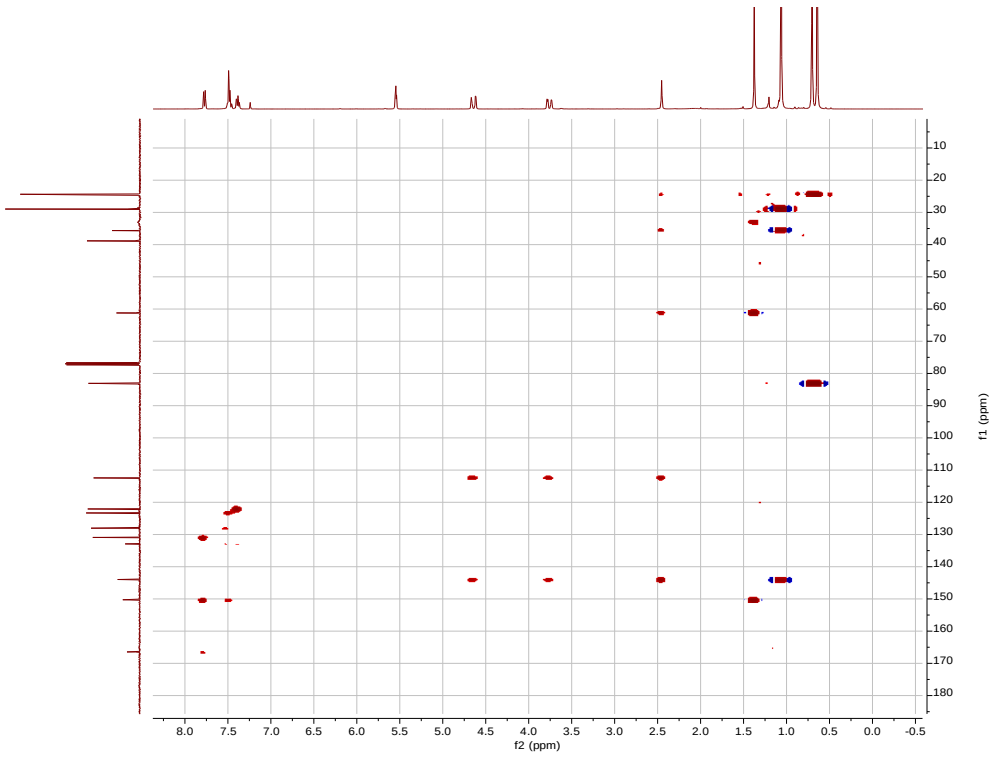


88-*syn*

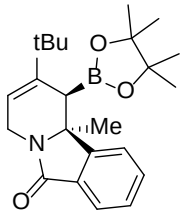
HSQC



HMBC



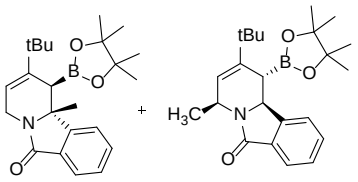
gCOSY


tBu
O
B
O
Me
N
O

88-*syn*

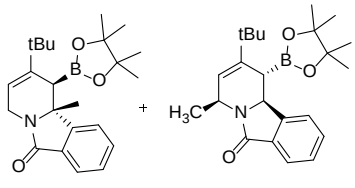
gCOSY_01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)
0
1
2
3
4
5
6
7
8
f1 (ppm)

Proton NMR



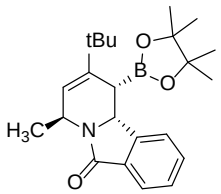
88-anti (1:2.5) **89-anti**

Carbon NMR



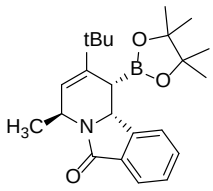
88-anti (1:2.5) **89-anti**

Proton NMR

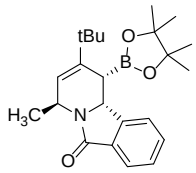


89-syn

Carbon NMR

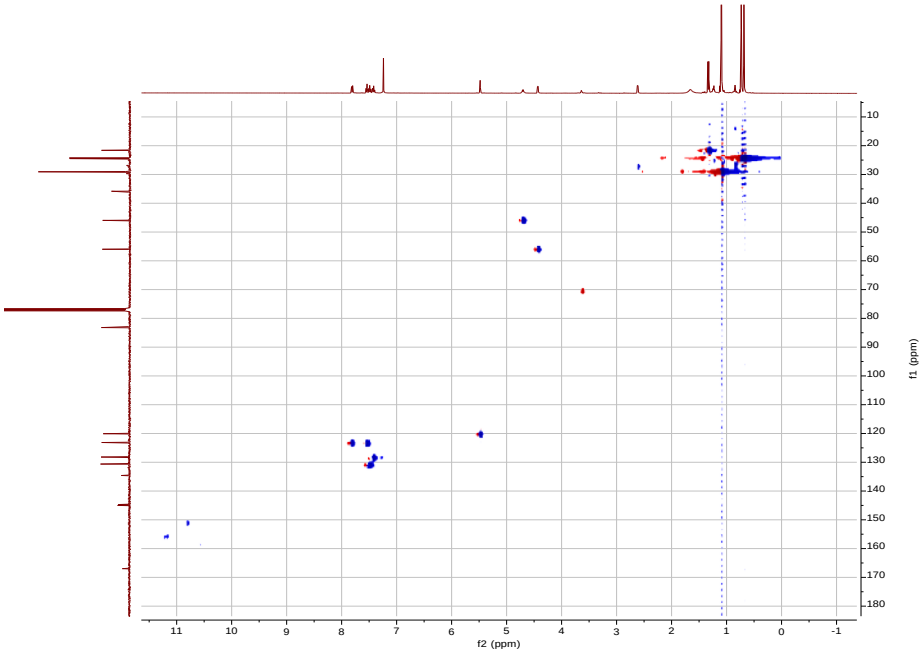


89-syn



89-syn

HSQC



HMBC