Supporting Information

Unified ionic and radical C-4 alkylation and arylation of pyridines

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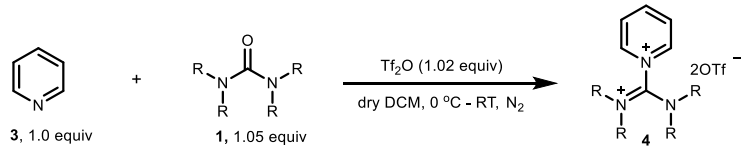
1. General information

Commercial reagents were purchased from Energy, TCI, J&K, Accela, Bide, Macklin or Adamas and used without further purification. The anhydrous solvents used in the experiments were all purchased from J&K and used directly. All reactions were carried out with oven-dried glassware or Schlenk tubes. Analytical thin layer chromatography (TLC) was performed on 0.20 mm silica gel HSGF-254 plates (Huanghai, China). Column chromatography was performed on 200-300 mesh silica gel or 300-400 mesh silica gel (General-Reagent, China).

^{1}H NMR (400 MHz or 600 MHz), ^{13}C NMR (101 MHz or 151 MHz) and ^{19}F NMR (377 MHz or 565 MHz) were recorded on an NMR spectrometer with $CDCl_3$, DMSO-d_6, D_2O, actone-d_6 or CD_3CN as the solvent. Chemical shifts of ^{1}H and ^{13}C NMR spectra are reported in parts per million (ppm). The residual solvent signals were used as references and the chemical shifts were converted to the TMS scale ($CDCl_3$: δ H = 7.26 ppm, δ C = 77.16 ppm. DMSO-d_6: δ H = 2.50 ppm, δ C = 39.52 ppm. D_2O: δ H = 4.79 ppm. CD_3CN: δ H = 1.94 ppm, δ C = 118.26 ppm.). Multiplicity (s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublet, dt = triplet of doublet, t = triplet, q = quartet, m = multiplet, br = broad). All coupling constants (*J* values) were reported in Hertz (Hz). High resolution mass spectrometry of products were recorded on an LTQ Orbitrap Elite LC/MS (ESI). GC-MS data were collected by an Agilent 5977B instrument. Single-crystal X-ray diffraction of **4a** and **4h**. A pale white block crystal was selected and on a SuperNova, AtlasS2 diffractometer (Rigaku Oxiford Diffraction). Single crystal data were collected at 223K on a Bruker D8 VENTURE diffractometer equipped with a PHOTON III detector and with a MetalJet Ga source. Data reduction, solution and refinement used the programs APEX3 and Olex2 respectively. The room temperature ranges from 18 to 35 ℃.

2. Synthesis of diiminium ditriflate pyridine salt

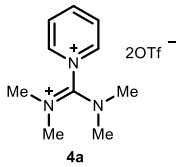
General Procedure I:



Under a nitrogen atmosphere, different ureas (2.1 mmol, 1.05 equiv) were added to an oven-dried 25 mL Schlenk tube with a magnetic bar. Anhydrous DCM (6.0 mL) was added and the solution was cooled to 0 ℃ in an ice-bath. Tf_2O (trifluoromethanesulfonic anhydride, 0.34 mL, 2.04 mmol, 1.02 equiv) was added dropwise via a 1.0 mL syringe within 5 minutes and the solution was stirred for 10 minutes at 0 ℃ (the reaction solution turned pale yellow during this period). Then pyridine (158.2 mg, 2.0 mmol, 1.0 equiv) was added dropwise via a 250 μL micro syringe within 1 minute. The cooling bath was removed, rapid crystallization was observed after circa 3 h and the reaction was stirred vigorously overnight. (Note: Due to the mild hygroscopic feature of the pyridine salt, we transfer the filtration to the glove

box for operation that can be referenced to the literature[1]). The reaction mixture was filtered with a buchner funnel with fritted disc and washed with anhydrous DCM (3 × 6.0 mL). The filtrate was removed, and the white solid was dried in vacuum and stored in the glove box to avoid contamination with water.

(4a)

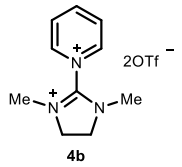


4a

Prepared via **General Procedure I** starting from pyridine (158.2 mg, 2.0 mmol, 1.0 equiv) and 1,1,3,3-tetramethylurea (243.8 mg, 2.1 mmol, 1.05 equiv) to give **4a** as a white solid.

R_f = 0.6 (eluent: DCM/MeOH = 10:1).
Yield 877.8 mg (92%).
NMR spectroscopy:
^{1}H NMR (CD_3CN, 400 MHz) δ 9.17 (d, *J* = 5.8 Hz, 2H), 9.06 (t, *J* = 7.9 Hz, 1H), 8.50 – 8.42 (m, 2H), 3.54 (s, 6H), 2.94 (s, 6H).
^{13}C NMR (CD_3CN, 101 MHz) δ 156.8, 155.5, 146.0, 131.3, 121.8 (q, *J* = 323.2 Hz), 44.7, 43.5.
^{19}F NMR (CD_3CN, 377 MHz) δ -79.2.
HRMS calcd for $(C_{10}H_{17}N_3)^{2+}$ $[m/z]^+$: 89.5706, found 89.5709.

(4b)

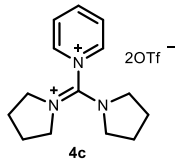


4b

Prepared via **General Procedure I** starting from pyridine (158.2 mg, 2.0 mmol, 1.0 equiv) and 1,3-dimethylimidazolidin-2-one (239.4 mg, 2.1 mmol, 1.05 equiv) to give **4b** as a white solid.

R_f = 0.6 (eluent: DCM/MeOH = 10:1).
Yield 807.8 mg (85%).
NMR spectroscopy:
^{1}H NMR (D_2O, 600 MHz) δ 8.63 (d, *J* = 5.3 Hz, 2H), 8.48 (tt, *J* = 7.9, 1.4 Hz, 1H), 7.94 (t, *J* = 6.9 Hz, 2H), 3.19 (s, 4H), 2.56 (s, 6H).
^{13}C NMR (D_2O, 151 MHz) δ 163.8, 147.2, 141.0, 127.4, 119.6 (q, *J* =318.6 Hz), 44.9, 30.7.
^{19}F NMR (D_2O, 565 MHz) δ -79.0.
HRMS calcd for $(C_{10}H_{15}N_3)^{2+}$ $[m/z]^+$: 88.5628, found 88.5632.

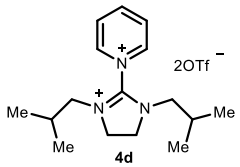
(4c)



Prepared via **General Procedure I** starting from pyridine (158.2 mg, 2.0 mmol, 1.0 equiv) and di(pyrrolidin-1-yl)methanone (352.8 mg, 2.1 mmol, 1.05 equiv) to give **4c** as a white solid.

R_f = 0.6 (eluent: DCM/MeOH = 10:1).
Yield 814.7 mg (77%).
NMR spectroscopy:
^{1}H NMR (CD_3CN, 400 MHz) δ 9.32 – 9.24 (m, 2H), 9.03 (t, *J* = 7.9 Hz, 1H), 8.50 (t, *J* = 7.0 Hz, 2H), 4.25 (t, *J* = 6.7 Hz, 4H), 3.33 (t, *J* = 6.9 Hz, 4H), 2.15 (p, *J* = 6.6 Hz, 4H), 1.96 (p, *J* = 6.7 Hz, 4H).
^{13}C NMR (CD_3CN, 101 MHz) δ 153.6, 149.6, 144.5, 131.8, 121.8 (q, *J* = 321.2 Hz), 55.1, 53.8, 26.7, 24.7.
^{19}F NMR (CD_3CN, 377 MHz) δ -79.2.
HRMS calcd for $(C_{14}H_{21}N_3)^{2+}$ $[m/z]^+$: 115.5863, found 115.5864.

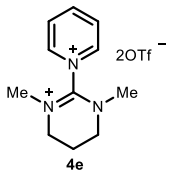
(4d)



Prepared via **General Procedure I** starting from pyridine (158.2 mg, 2.0 mmol, 1.0 equiv) and 1,3-diisobutylimidazolidin-2-one (416.2 mg, 2.1 mmol, 1.05 equiv) to give **4d** as a white solid.

R_f = 0.6 (eluent: DCM/MeOH = 10:1).
Yield 592.5 mg (53%).
NMR spectroscopy:
^{1}H NMR (CD_3CN, 400 MHz) δ 9.11 (t, *J* = 8.0 Hz, 1H), 9.07 (d, *J* = 6.1 Hz, 2H), 8.63 – 8.52 (m, 2H), 4.28 (s, 4H), 3.00 (d, *J* = 7.5 Hz, 4H), 2.05 – 1.95 (m, 2H), 0.87 (d, *J* = 6.7 Hz, 12H).
^{13}C NMR (CD_3CN, 101 MHz) δ 155.1, 154.8, 144.6, 132.4, 121.8 (q, *J* = 321.2 Hz), 55.9, 49.7, 26.4, 19.5.
^{19}F NMR (CD_3CN, 377 MHz) δ -79.2.
HRMS calcd for $(C_{16}H_{27}N_3)^{2+}$ $[m/z]^+$: 130.6097, found 137.6098.

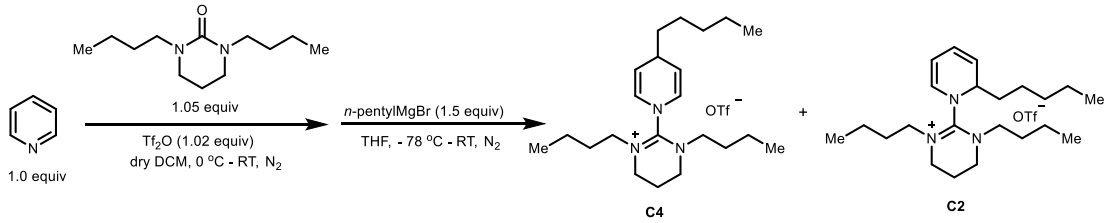
(4e)



Prepared via **General Procedure I** starting from pyridine (158.2 mg, 2.0 mmol, 1.0 equiv) and 1,3-dimethyltetrahydropyrimidin-2(1*H*)-one (269.0 mg, 2.1 mmol, 1.05 equiv) to give **4e** as a white solid.

R_f = 0.6 (eluent: DCM/MeOH = 10:1).
Yield 870.4 mg (89%).
NMR spectroscopy:
^{1}H NMR (CD_3CN, 600 MHz) δ 9.20 (d, *J* = 6.2 Hz, 2H), 9.05 (t, *J* = 7.9 Hz, 1H), 8.51 (t, *J* = 7.1 Hz, 2H), 3.83 (t, *J* = 5.9 Hz, 4H), 2.90 (s, 6H), 2.35 (p, *J* = 5.9 Hz, 2H).
^{13}C NMR (CD_3CN, 101 MHz) δ 154.1, 151.1, 144.7, 131.8, 121.7 (q, *J* = 321.2 Hz), 50.9, 41.6, 18.8.
^{19}F NMR (CD_3CN, 377 MHz) δ -79.2.
HRMS calcd for $(C_{11}H_{17}N_3)^{2+}$ $[m/z]^+$: 95.5706, found 95.5710.

(4f) Because 4f is oily, the 4f is not separated and used directly in one-pot



Under a nitrogen atmosphere, 1,3-dibutyltetrahydropyrimidin-2(1*H*)-one (66.8 mg, 0.315 mmol, 1.05 equiv) was added to an oven-dried 25 mL Schlenk tube with a magnetic bar. Anhydrous DCM (3.0 mL) was added and the solution was cooled to 0 ℃ in an ice-bath. Tf_2O (trifluoromethanesulfonic anhydride, 51.4 μL, 0.306 mmol, 1.02 equiv) was added dropwise via a 100 μL micro syringe within 2 minutes and the solution was stirred for 10 minutes at 0 ℃ (the reaction solution turned pale yellow during this period). Then pyridine (23.7 mg, 0.3 mmol, 1.0 equiv) was added dropwise within 1 minute. The cooling bath was removed, the reaction mixture was stirred vigorously for 16 h. Then the mixture was concentrated under reduced pressure. After three vacuum nitrogen cycles, anhydrous THF (3.0 mL) was added and the solution was cooled to -78 ℃ in a low-temperature reactor. A solution of the *n*-pentylMgBr (0.45 mmol, 1.5 equiv) was added dropwise via a 1.0 mL syringe within 2 minutes and the resulting suspension was stirred for 10 minutes. Water (3.0 mL) was added in one portion and the reaction mixture stirred for 5 minutes at room temperature, then DCM (5.0 mL) and 1,3,5-trimethoybenzene (5.3 mg) were added in one portion. The mixture was extracted with DCM (3 × 5.0 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The oil residue was dissolved by $CDCl_3$ and the selectivity of the reaction was

determined by crude NMR spectroscopy.

R_f = 0.4 (eluent: DCM/MeOH = 10:1).
Yield (NMR yield: 75%, C4/C2 = 12.6/1).

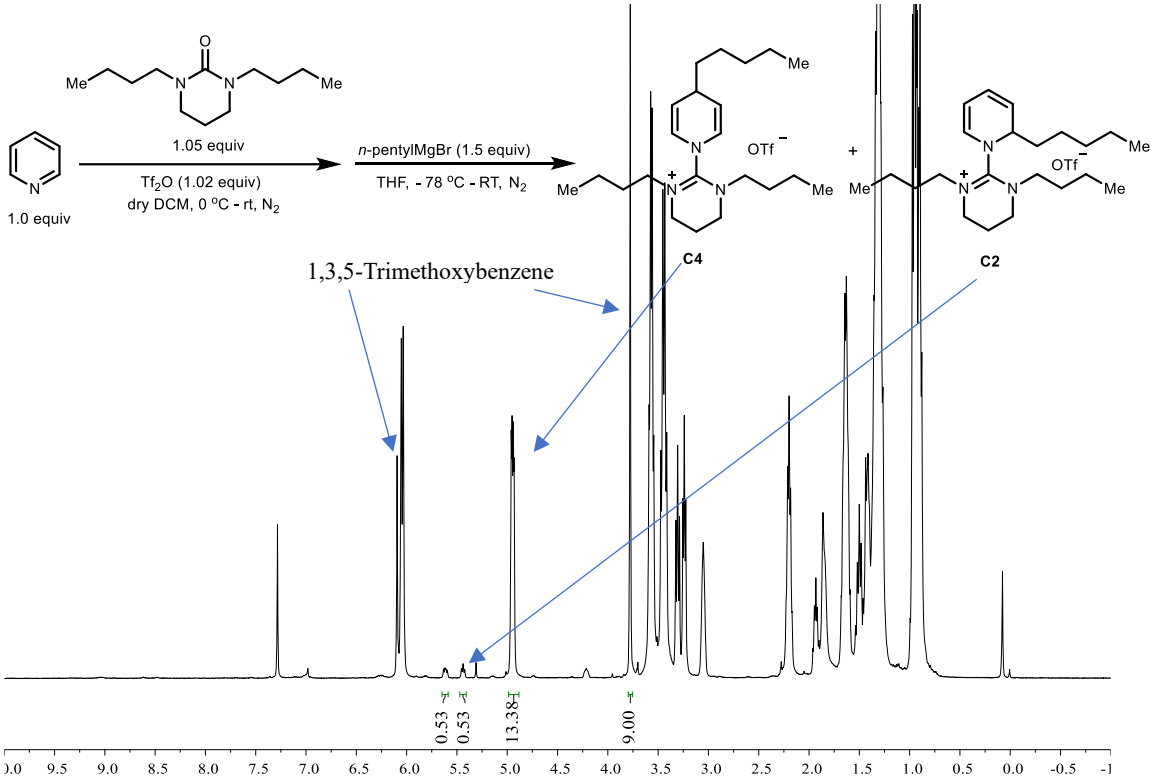
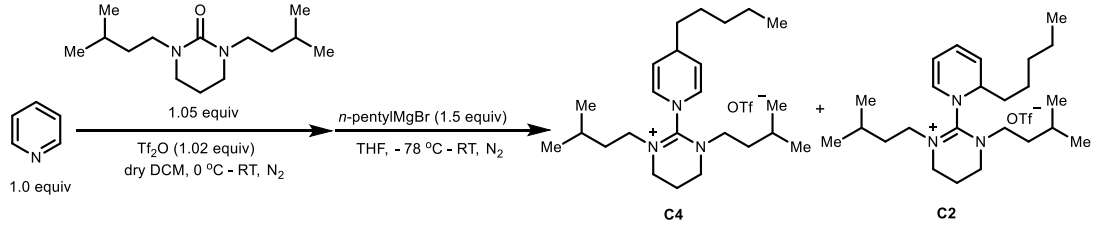


Figure S1. Crude ^{1}H NMR of **4f** ($CDCl_3$, 400 MHz)

(4g) Because 4g is oily, 4g is not separated and is used directly in one-pot



Under a nitrogen atmosphere, 1,3-diisopentyltetrahydropyrimidin-2(1*H*)-one (75.6 mg, 0.315 mmol, 1.05 equiv) was added to an oven-dried 25 mL Schlenk tube with a magnetic bar. Anhydrous DCM (3.0 mL) was added and the solution was cooled to 0 °C in an ice-bath. Tf_2O (trifluoromethanesulfonic anhydride, 51.4 μL, 0.306 mmol, 1.02 equiv) was added dropwise via a 250 μL micro syringe within 2 minutes and the solution was stirred for 10 minutes at 0 °C (the reaction solution turned pale yellow during this period). Then pyridine (23.7 mg, 0.3 mmol, 1.0 equiv) was added dropwise within 1 minute. The cooling bath was removed and the reaction was stirred vigorously for 16 h. Then the mixture was concentrated under reduced pressure. After three vacuum nitrogen cycle operations, anhydrous THF (3.0 mL) was added and the solution was cooled to -78 °C in a low-temperature reactor. A solution of the *n*-pentylMgBr (0.45

mmol, 1.5 equiv) was added dropwise via a 1.0 mL syringe within 2 minutes and the resulting suspension was stirred for 10 minutes. Water (3.0 mL) was added in one portion and the reaction mixture stirred for 5 minutes at room temperature, then DCM (5.0 mL) and 1,3,5-trimethoybenzene (5.3 mg) were added in one portion. The mixture was extracted with DCM (3 × 5.0 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The oil residue was dissolved by $CDCl_3$ and the selectivity of the reaction was determined by crude NMR spectroscopy.

R_f = 0.4 (eluent: DCM/MeOH = 10:1).
Yield (NMR yield: 74%, C4/C2 = 6.0/1).

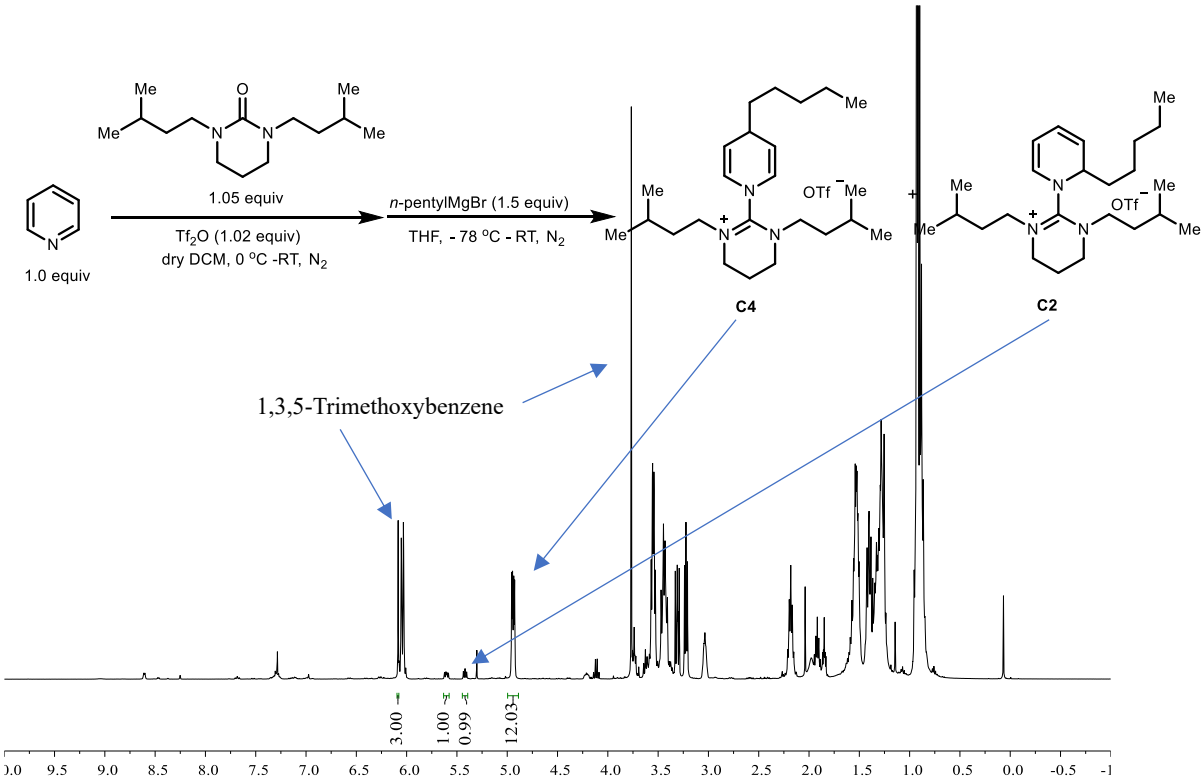
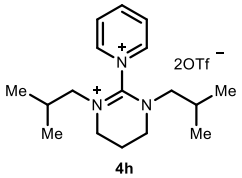


Figure S2. Crude ^{1}H NMR of **4g** ($CDCl_3$, 400 MHz)

(4h)

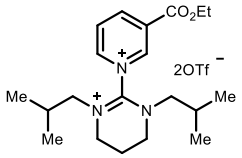


Prepared via **General Procedure I** starting from pyridine (158.2 mg, 2.0 mmol, 1.0 equiv) and 1,3-diisobutyltetrahydropyrimidin-2(1*H*)-one (445.2 mg, 2.1 mmol, 1.05 equiv) to give **4h** as a white solid.

R_f = 0.6 (eluent: DCM/MeOH = 10:1).

Yield 985.6 mg (86%).
NMR spectroscopy:
^{1}H NMR (CD_3CN, 400 MHz) δ 9.25 (d, *J* = 5.7 Hz, 2H), 9.11 (t, *J* = 8.0 Hz, 1H), 8.67 – 8.53 (m, 2H), 3.90 (t, *J* = 5.8 Hz, 4H), 2.89 (d, *J* = 7.6 Hz, 4H), 2.39 (p, *J* = 5.9 Hz, 2H), 2.13 – 1.83 (m, 2H), 0.82 (d, *J* = 6.7 Hz, 12H).
^{13}C NMR (CD_3CN, 101 MHz) δ 154.7, 151.1, 144.8, 132.1, 121.7 (q, *J* = 321.2 Hz), 61.6, 49.1, 26.9, 19.5, 18.6.
^{19}F NMR (CD_3CN, 565 MHz) δ -79.1.
HRMS calcd for $(C_{17}H_{29}N_3)^{2+}$ $[m/z]^+$: 137.6178, found 137.6175.

(S-4i)

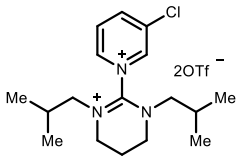


S-4i

Prepared via **General Procedure I** starting from ethyl nicotinate (302.0 mg, 2.0 mmol, 1.0 equiv), 1,3-diisobutyltetrahydropyrimidin-2(1*H*)-one (445.2 mg, 2.1 mmol, 1.05 equiv) and stirred at 50 °C for 48 h to give **S-4i** as a white solid.

R_f = 0.5 (eluent: DCM/MeOH = 10:1).
Yield 1.07 g (83%).
NMR spectroscopy:
^{1}H NMR (CD_3CN, 400 MHz) δ 9.77 (s, 1H), 9.46 (d, *J* = 8.2 Hz, 1H), 9.41 – 9.35 (m, 1H), 8.69 (dd, *J* = 8.1, 6.3 Hz, 1H), 4.52 (q, *J* = 7.1 Hz, 2H), 3.89 (t, *J* = 5.8 Hz, 4H), 2.95 – 2.83 (m, 4H), 2.38 (p, *J* = 5.9 Hz, 2H), 2.06 – 1.95 (m, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 0.81 (dd, *J* = 9.8, 6.7 Hz, 12H).
^{13}C NMR (CD_3CN, 101 MHz) δ 160.9, 154.1, 150.8, 147.3, 145.8, 134.9, 132.8, 121.8 (q, *J* = 322.2 Hz), 64.7, 61.7, 49.2, 26.9, 19.5, 19.4, 18.6, 14.1.
^{19}F NMR (CD_3CN, 377 MHz) δ -79.2.
HRMS calcd for $(C_{20}H_{33}N_3O_2)^{2+}$ $[m/z]^+$: 173.6281, found 173.6282.

(S-4j)



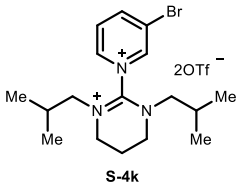
S-4j

Prepared via **General Procedure I** starting from 3-chloropyridine (226.0 mg, 2.0 mmol, 1.0 equiv), 1,3-diisobutyltetrahydropyrimidin-2(1*H*)-one (445.2 mg, 2.1 mmol, 1.05 equiv) and stirred at room temperature for 48 h to give **S-4j** as a white solid.

R_f = 0.5 (eluent: DCM/MeOH = 10:1).
Yield 995.8 mg (82%).

NMR spectroscopy:
^{1}H NMR (DMSO-d_6, 400 MHz) δ 9.92 (s, 1H), 9.55 (d, J = 6.0 Hz, 1H), 9.36 (d, J = 8.6 Hz, 1H), 8.69 (dd, J = 8.5, 6.2 Hz, 1H), 3.88 – 3.71 (m, 4H), 3.05 – 2.81 (m, 4H), 2.34 – 2.16 (m, 2H), 2.01 – 1.87 (m, 2H), 0.78 (t, J = 7.1 Hz, 12H).
^{13}C NMR (DMSO-d_6, 101 MHz) δ 153.2, 149.2, 143.1, 142.8, 137.8, 131.3, 120.7 (q, J = 323.2 Hz), 60.0, 48.1, 25.8, 19.19, 19.16, 17.9.
^{19}F NMR (DMSO-d_6, 377 MHz) δ -78.9.
HRMS calcd for $(C_{17}H_{28}ClN_3)^{2+}$ [m/z]$^+$: 154.5980, found 154.5978.

(S-4k)

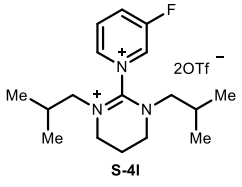


S-4k

Prepared via **General Procedure I** starting from 3-bromopyridine (314.0 mg, 2.0 mmol, 1.0 equiv), 1,3-diisobutyltetrahydropyrimidin-2(1*H*)-one (445.2 mg, 2.1 mmol, 1.05 equiv) and stirred at room temperature for 48 h to give **S-4k** as a white solid.

R_f = 0.5 (eluent: DCM/MeOH = 10:1).
Yield 989.5 mg (76%).
NMR spectroscopy:
^{1}H NMR (DMSO-d_6, 400 MHz) δ 9.96 (s, 1H), 9.56 (d, J = 6.0 Hz, 1H), 9.46 (d, J = 8.5 Hz, 1H), 8.65 – 8.58 (m, 1H), 3.83 – 3.72 (m, 4H), 2.99 – 2.90 (m, 2H), 2.89 – 2.79 (m, 2H), 2.33 – 2.17 (m, 2H), 2.07 – 1.86 (m, 2H), 0.84 – 0.72 (m, 12H).
^{13}C NMR (DMSO-d_6, 101 MHz) δ 155.7, 149.1, 144.4, 143.1, 131.2, 125.6, 120.7 (q, J = 323.2 Hz), 60.0, 48.0, 25.8, 19.19, 19.16, 17.9.
^{19}F NMR (DMSO-d_6, 377 MHz) δ -78.9.
HRMS calcd for $(C_{17}H_{28}BrN_3)^{2+}$ [m/z]$^+$: 176.5728, found 176.5727.

(S-4l)



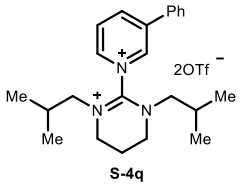
S-4l

Prepared via **General Procedure I** starting from 3-fluoropyridine (194.0 mg, 2.0 mmol, 1.0 equiv), 1,3-diisobutyltetrahydropyrimidin-2(1*H*)-one (445.2 mg, 2.1 mmol, 1.05 equiv) and stirred at room temperature for 48 h to give **S-4l** as a white solid.

R_f = 0.5 (eluent: DCM/MeOH = 10:1).
Yield 874.8 mg (74%).
NMR spectroscopy:
^{1}H NMR (DMSO-d_6, 400 MHz) δ 9.90 (s, 1H), 9.52 (d, J = 6.0 Hz, 1H), 9.22 (t, J =

7.2 Hz, 1H), 8.81 – 8.71 (m, 1H), 3.88 – 3.75 (m, 4H), 3.03 – 2.82 (m, 4H), 2.31 – 2.14 (m, 2H), 2.03 – 1.84 (m, 2H), 0.77 (dd, *J* = 14.6, 6.6 Hz, 12H).
^{13}C NMR (DMSO-d_6, 101 MHz) δ 161.5 (d, *J* = 259.6 Hz), 149.2, 141.7 (d, *J* = 3.0 Hz), 141.4 (d, *J* = 18.2 Hz), 134.2 (d, *J* = 40.4 Hz), 132.4 (d, *J* = 8.1 Hz), 120.7 (q, *J* = 323.2 Hz), 60.1, 48.1, 25.8, 19.20, 19.15, 17.9.
^{19}F NMR (DMSO-d_6, 377 MHz) δ -78.9, -106.4.
HRMS calcd for $(C_{17}H_{28}FN_3)^{2+}$ [m/z]$^+$: 146.6128, found 146.6127.

(S-4q)

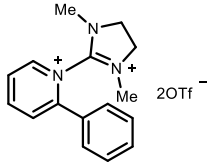


S-4q

Prepared via **General Procedure I** starting from 3-phenylpyridine (310.1 mg, 2.0 mmol, 1.0 equiv), 1,3-diisobutyltetrahydropyrimidin-2(1*H*)-one (445.2 mg, 2.1 mmol, 1.05 equiv) and stirred at room temperature for 48 h to give **S-4q** as a white solid.

R_f = 0.5 (eluent: DCM/MeOH = 10:1).
Yield 1.13 g (87%).
NMR spectroscopy:
^{1}H NMR (CD_3CN, 400 MHz) δ 9.58 (s, 1H), 9.33 (d, *J* = 8.4 Hz, 1H), 9.14 (d, *J* = 6.1 Hz, 1H), 8.61 (dd, *J* = 8.4, 6.1 Hz, 1H), 7.95 – 7.88 (m, 2H), 7.73 – 7.67 (m, 3H), 3.93 (t, *J* = 5.8 Hz, 4H), 3.07 – 2.91 (m, 4H), 2.51 – 2.35 (m, 2H), 2.14 – 2.01 (m, 2H), 0.89 – 0.82 (m, 12H).
^{13}C NMR (CD_3CN, 101 MHz) δ 151.0, 150.4, 144.0, 141.9, 140.9, 131.6, 131.5, 131.1, 130.0, 127.9, 121.1 (q, *J* = 321.6 Hz), 61.0, 48.3, 26.2, 18.74, 18.72, 17.9.
^{19}F NMR (CD_3CN, 565 MHz) δ -79.2.
HRMS calcd for $(C_{20}H_{33}N_3O_2)^{2+}$ [m/z]$^+$: 175.6332, found 175.6327.

(S-4s)



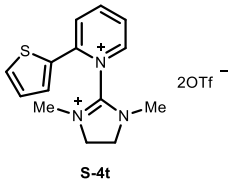
S-4s

Prepared via **General Procedure I** starting from 2-phenylpyridine (310.1 mg, 2.0 mmol, 1.0 equiv), 1,3-dimethylimidazolidin-2-one (239.4 mg, 2.1 mmol, 1.05 equiv) and stirred at room temperature for 48 h to give **S-4s** as a white solid.

R_f = 0.4 (eluent: DCM/MeOH = 10:1).
Yield 896.5 mg (81%).
NMR spectroscopy:
^{1}H NMR (CD_3CN, 400 MHz) δ 9.16 (d, *J* = 6.0 Hz, 1H), 9.08 (t, *J* = 8.0 Hz, 1H), 8.53

(d, *J* = 8.2 Hz, 1H), 8.47 (t, *J* = 7.0 Hz, 1H), 7.86 (t, *J* = 7.4 Hz, 1H), 7.77 (t, *J* = 7.5 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 2H), 4.20 – 4.07 (m, 2H), 4.05 – 3.90 (m, 2H), 2.91 (s, 6H).
^{13}C NMR (CD_3CN, 101 MHz) δ 155.6, 153.8, 153.1, 144.5, 134.0, 132.6, 130.5, 129.0, 128.8, 128.3, 121.0 (q, *J* = 321.2 Hz), 50.3, 34.3.
^{19}F NMR (CD_3CN, 565 MHz) δ -79.2.
HRMS calcd for $(C_{16}H_{19}N_3)^{2+}$ $[m/z]^+$: 126.5784, found 126.5785.

(S-4t)

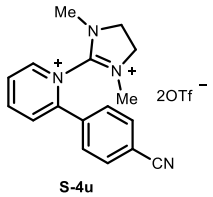


S-4t

Prepared via **General Procedure I** starting from 2-(thiophen-2-yl)pyridine (322.0 mg, 2.0 mmol, 1.0 equiv), 1,3-dimethylimidazolidin-2-one (239.4 mg, 2.1 mmol, 1.05 equiv) and stirred at room temperature for 48 h to give **S-4t** as a yellow solid.

R_f = 0.4 (eluent: DCM/MeOH = 10:1).
Yield 627.1 mg (56%).
NMR spectroscopy:
^{1}H NMR (CD_3CN, 600 MHz) δ 8.97 (d, *J* = 6.4 Hz, 1H), 8.93 (t, *J* = 8.1 Hz, 1H), 8.58 (d, *J* = 8.4 Hz, 1H), 8.32 (t, *J* = 6.5 Hz, 1H), 8.22 (d, *J* = 5.0 Hz, 1H), 7.90 (d, *J* = 3.9 Hz, 1H), 7.53 – 7.39 (m, 1H), 4.33 – 4.23 (m, 2H), 4.23 – 4.15 (m, 2H), 2.94 (s, 6H).
^{13}C NMR (CD_3CN, 151 MHz) δ 154.0, 153.5, 150.3, 144.6, 139.0, 137.2, 132.7, 131.7, 128.91, 128.86, 122.0 (q, *J* = 320.1 Hz), 51.3, 35.0.
^{19}F NMR (CD_3CN, 565 MHz) δ -79.2.
HRMS calcd for $(C_{14}H_{17}N_3S)^{2+}$ $[m/z]^+$: 129.5566, found 129.5567.

(S-4u)



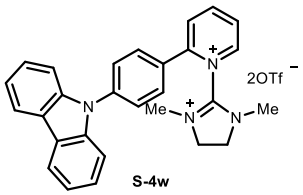
S-4u

Prepared via **General Procedure I** starting from 4-(pyridin-2-yl)benzonitrile (360.1 mg, 2.0 mmol, 1.0 equiv), 1,3-dimethylimidazolidin-2-one (239.4 mg, 2.1 mmol, 1.05 equiv) and stirred at 50 ℃ for 36 h to give **S-4u** as a white solid.

R_f = 0.4 (eluent: DCM/MeOH = 10:1).
Yield 780.0 mg (68%).
NMR spectroscopy:
^{1}H NMR (CD_3CN, 400 MHz) δ 9.22 (d, *J* = 6.2 Hz, 1H), 9.13 (t, *J* = 8.0 Hz, 1H), 8.77 – 8.49 (m, 2H), 8.10 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 4.20 – 4.08 (m, 2H),

4.02 – 3.94 (m, 2H), 2.92 (s, 6H).
^{13}C NMR (CD_3CN, 151 MHz) δ 153.0, 152.6, 150.9, 145.4, 133.5, 133.0, 130.5, 130.2, 129.9, 125.4, 124.6, 120.9 (q, J = 320.1 Hz), 50.4, 34.5.
^{19}F NMR (CD_3CN, 377 MHz) δ -79.2.
HRMS calcd for $(C_{17}H_{18}N_4)^{2+}$ $[m/z]^+$: 139.0760, found 139.0759.

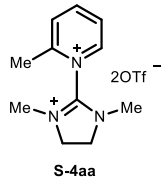
(S-4w)



Prepared via **General Procedure I** starting from 9-(4-(pyridin-2-yl)phenyl)-9*H*-carbazole (640.2 mg, 2.0 mmol, 1.0 equiv), 1,3-dimethylimidazolidin-2-one (239.4 mg, 2.1 mmol, 1.05 equiv) and stirred at room temperature for 48 h to give **S-4w** as an orange solid.

R_f = 0.4 (eluent: DCM/MeOH = 10:1).
Yield 1190.0 mg (83%).
NMR spectroscopy:
^{1}H NMR (CD_3CN, 400 MHz) δ 9.16 (d, J = 6.5 Hz, 1H), 9.11 (d, J = 8.0 Hz, 1H), 8.63 (d, J = 8.1 Hz, 1H), 8.51 (t, J = 7.0 Hz, 1H), 8.24 (d, J = 7.7 Hz, 2H), 8.07 (d, J = 8.5 Hz, 2H), 7.90 (d, J = 8.5 Hz, 2H), 7.67 (d, J = 8.3 Hz, 2H), 7.53 (t, J = 7.7 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 4.30 – 4.18 (m, 2H), 4.18 – 4.08 (m, 2H), 3.01 (s, 6H).
^{13}C NMR (CD_3CN, 151 MHz) δ 154.9, 153.7, 153.1, 144.7, 142.9, 139.8, 132.6, 130.8, 129.1, 128.0, 126.6, 126.1, 124.0, 121.3, 121.0 (q, J = 320.1 Hz), 120.6, 110.1, 50.5, 34.2.
^{19}F NMR (CD_3CN, 565 MHz) δ -79.2.
HRMS calcd for $(C_{28}H_{26}N_4)^{2+}$ $[m/z]^+$: 209.1073, found 209.1071.

(S-4aa)



Prepared via **General Procedure I** starting from 2-methylpyridine (186.1 mg, 2.0 mmol, 1.0 equiv), 1,3-dimethylimidazolidin-2-one (239.4 mg, 2.1 mmol, 1.05 equiv) and stirred at 50 °C for 48 h to give **S-4aa** as a brown solid.

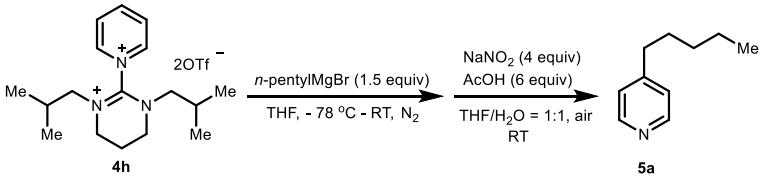
R_f = 0.4 (eluent: DCM/MeOH = 10:1).
Yield 680.6 mg (70%).
NMR spectroscopy:
^{1}H NMR (CD_3CN, 400 MHz) δ 9.02 (d, J = 6.2 Hz, 1H), 8.89 (t, J = 8.0 Hz, 1H), 8.35

(d, J = 8.2 Hz, 1H), 8.31 (t, J = 7.0 Hz, 1H), 4.44 – 4.34 (m, 2H), 4.32 – 4.23 (m, 2H), 2.95 (s, 6H), 2.89 (s, 3H).
^{13}C NMR (CD_3CN, 101 MHz) δ 157.2, 152.7, 152.5, 143.2, 132.6, 128.2, 121.0 (q, J = 321.2 Hz), 50.7, 33.9, 19.3.
^{19}F NMR (CD_3CN, 377 MHz) δ -79.2.
HRMS calcd for $(C_{11}H_{17}N_3)^{2+}$ [m/z]$^+$: 95.5706, found 95.5710.

3. C-4 alkylation and arylation with Grignard reagents as the nucleophile

General procedures II:
Under a nitrogen atmosphere, **4h** (171.9 mg, 0.3 mmol, 1.0 equiv) was added to an oven-dried 25 mL Schlenk tube with a magnetic bar at room temperature. Anhydrous THF (3.0 mL) was added and the suspension was cooled to -78 ℃ in a low-temperature reactor. (Note: If there is no low-temperature reactor in the laboratory, the reaction can also be carried out in an ice bath with a slight decrease in yield). A solution of the Grignard reagents (0.45 mmol, 1.5 equiv) was added dropwise via a 1.0 mL syringe within 2 minutes and the resulting suspension was stirred for 10 minutes to give a clear solution. Water (3.0 mL) was added in one portion and the reaction mixture was stirred for 5 minutes at room temperature, then $NaNO_2$ aqueous solution (100 mg/ mL, 0.83 mL, 4.0 equiv) and acetic acid (103 μL, 6.0 equiv) were added in one portion and the mixture were stirred for 12 hours at room temperature. The mixture was neutralized with a saturated sodium bicarbonate solution (2.0 mL), extracted with EtOAc (3 × 8.0 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford C-4 alkylation or arylation pyridine products.

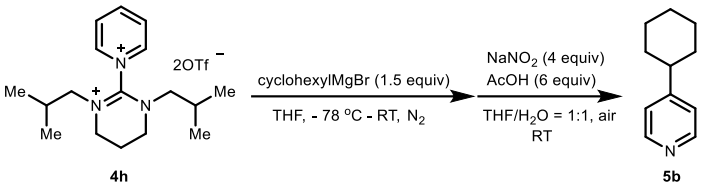
4-pentylpyridine (5a)



Prepared via **General Procedure II** starting from *n*-pentylMgBr (0.45 mmol, 1.5 equiv) to give 4-pentylpyridine (**5a**) as a pale-yellow oil.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 5:1).
Yield 35.4 mg (79%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.46 (d, J = 5.5 Hz, 2H), 7.09 (d, J = 5.7 Hz, 2H), 2.61 – 2.56 (m, 2H), 1.62 (p, J = 7.6 Hz, 2H), 1.37 – 1.27 (m, 4H), 0.88 (t, J = 7.0 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 151.8, 149.5, 123.9, 35.2, 31.3, 29.9, 22.4, 13.9.
HRMS calcd for $(C_{10}H_{16}N)^+$ [M + H]$^+$: 150.1277, found 150.1276.

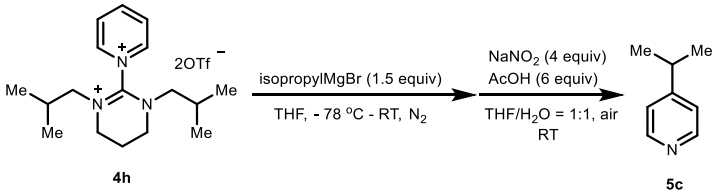
4-cyclohexylpyridine (5b)



Prepared via **General Procedure II** starting from cyclohexylMgBr (0.45 mmol, 1.5 equiv) to give 4-cyclohexylpyridine (**5b**) as a colorless oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 10:1).
Yield 44.0 mg (91%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.45 (d, *J* = 5.9 Hz, 2H), 7.09 (d, *J* = 5.9 Hz, 2H), 2.51 – 2.43 (m, 1H), 1.88 – 1.78 (m, 4H), 1.76 – 1.69 (m, 1H), 1.42 – 1.32 (m, 4H), 1.26 – 1.18 (m, 1H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 156.6, 149.6, 122.3, 43.8, 33.5, 26.5, 25.9.
HRMS calcd for $(C_{11}H_{16}N)^+$ $[M + H]^+$: 162.1277, found 162.1276.

4-isopropylpyridine (5c)



Prepared via **General Procedure II** starting from isopropylMgBr (0.45 mmol, 1.5 equiv) and 1,3,5-trimethoxybenzene (5.3 mg) as an internal standard to give 4-isopropylpyridine (**5c**) as a colorless oil. (Due to that the product is volatile, the yield of this substrate was determined by crude NMR)

R_f = 0.3 (eluent: petroleum ether/EtOAc = 10:1).
NMR yield: (72%).

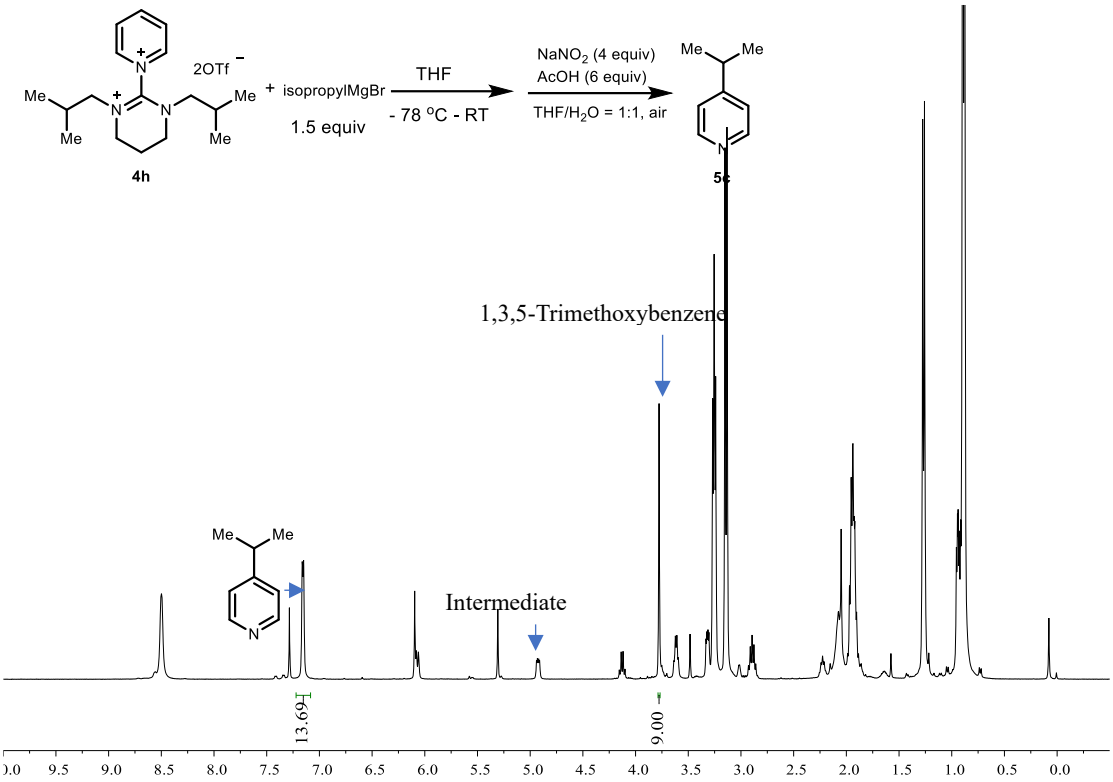
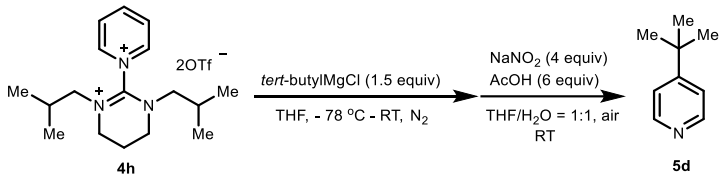


Figure S3. Crude ^{1}H NMR of **5c** ($CDCl_3$, 400 MHz)

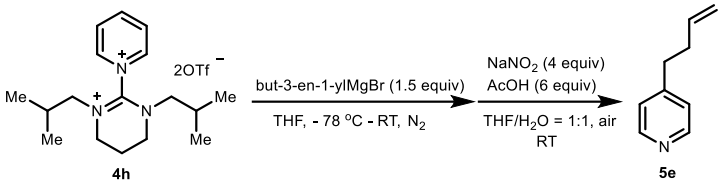
4-(*tert*-butyl)pyridine (5d)



Prepared via **General Procedure II** starting from *tert*-butylMgCl (0.45 mmol, 1.5 equiv) to give 4-(*tert*-butyl)pyridine (**5d**) as a colorless oil. (Note: the solvent concentration was carried out at room temperature)

R_f = 0.5 (eluent: petroleum ether/EtOAc = 5:1).
Yield 18.2 mg (45%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.41 (d, *J* = 6.0 Hz, 2H), 7.17 (d, *J* = 6.1 Hz, 2H), 1.21 (s, 9H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 159.8, 149.6, 120.6, 34.5, 30.4.
HRMS calcd for $(C_9H_{14}N)^+$ $[M + H]^+$: 136.1121, found 136.1120.

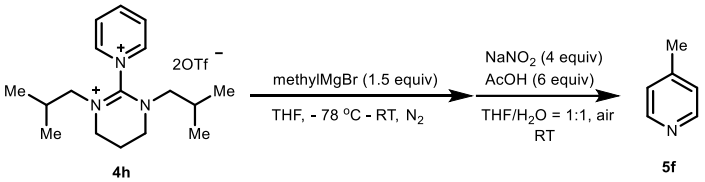
4-(but-3-en-1-yl)pyridine (5e)



Prepared via **General Procedure II** starting from but-3-en-1-ylMgBr (0.45 mmol, 1.5 equiv) to give 4-(but-3-en-1-yl)pyridine (**5e**) as a yellow oil.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 5:1).
Yield 23.1 mg (58%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.47 (d, *J* = 4.9 Hz, 2H), 7.10 (d, *J* = 5.1 Hz, 2H), 5.84 – 5.75 (m, 1H), 5.02 (d, *J* = 17.1 Hz, 1H), 4.99 (d, *J* = 10.2 Hz, 1H), 2.69 (t, *J* = 7.7 Hz, 2H), 2.37 (q, *J* = 7.2 Hz, 2H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 150.7, 149.6, 137.0, 123.9, 115.7, 34.5, 34.1.
HRMS calcd for $(C_9H_{12}N)^+$ $[M + H]^+$: 134.0964, found 134.0965.

4-methylpyridine (5f)



Prepared via **General Procedure II** starting from methylMgBr (0.45 mmol, 1.5 equiv) and 1,3,5-trimethoxybenzene (5.3 mg) as internal standard to give 4-methylpyridine (**5f**) as a colourless oil. (Due to that the product is volatile, the yield of this substrate was determined by crude NMR)

R_f = 0.5 (eluent: petroleum ether/EtOAc = 10:1).
NMR yield: (64%).

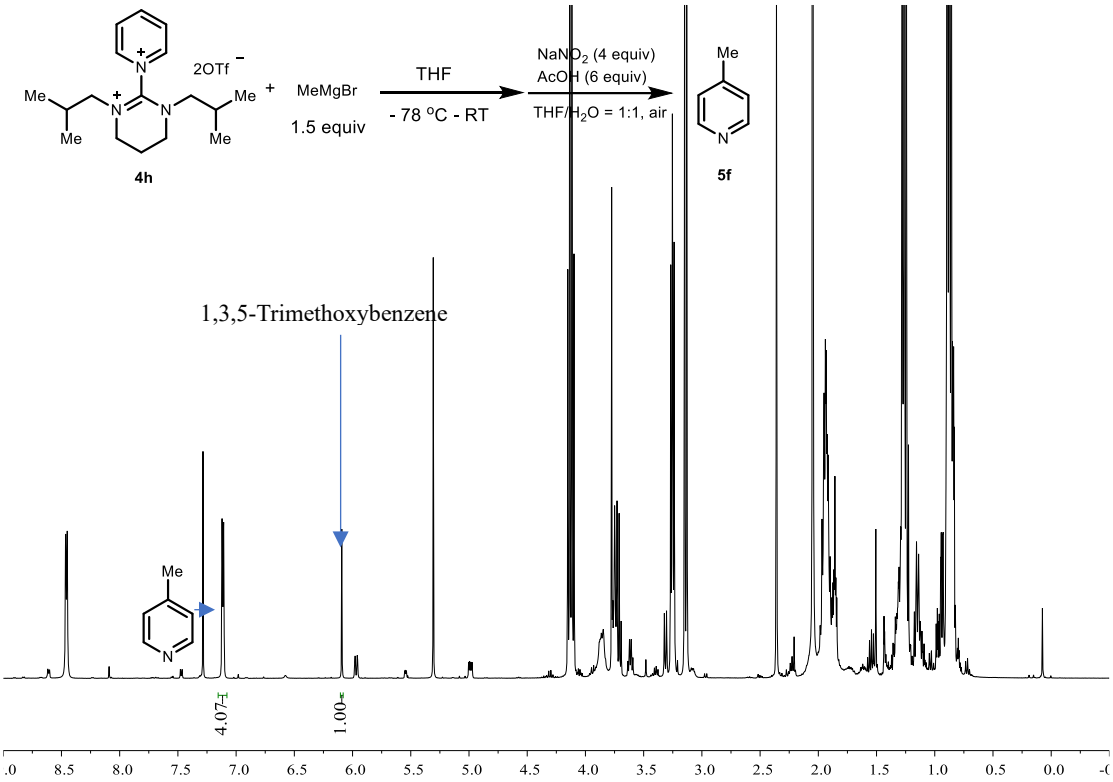
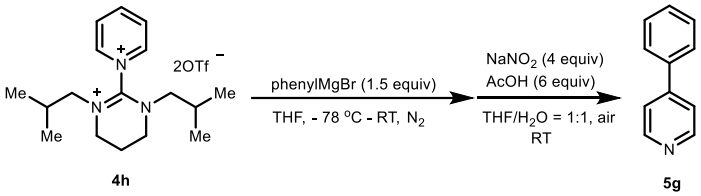


Figure S4. Crude ^{1}H NMR of **5f** ($CDCl_3$, 400 MHz)

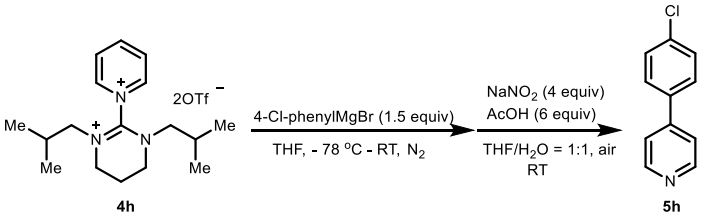
4-phenylpyridine (5g)



Prepared via **General Procedure II** starting from phenylMgBr (0.45 mmol, 1.5 equiv) to give 4-phenylpyridine (**5g**) as a white solid.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 5:1).
Yield 37.0 mg (80%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.67 – 8.61 (m, 2H), 7.63 – 7.56 (m, 2H), 7.50 – 7.43 (m, 4H), 7.45 – 7.38 (m, 1H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 150.3, 148.3, 138.1, 129.12, 129.07, 127.0, 121.6.
HRMS calcd for $(C_{11}H_{10}N)^+$ $[M + H]^+$: 156.0808, found 156.0807.

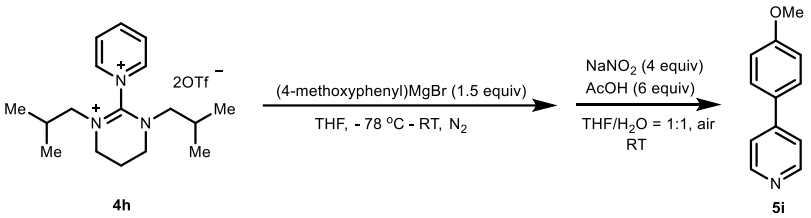
4-(4-chlorophenyl)pyridine (5h)



Prepared via **General Procedure II** starting from 4-chlorophenylMgBr (0.45 mmol, 1.5 equiv) to give 4-(4-chlorophenyl)pyridine (**5h**) as a white solid.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 4:1).
Yield 34.3 mg (60%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.65 (d, *J* = 5.2 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.47 – 7.42 (m, 4H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 150.3, 147.2, 136.6, 135.4, 129.4, 128.3, 121.4.
HRMS calcd for $C_{11}H_9ClN^+$ $[M + H]^+$: 190.0418, found 190.0417.

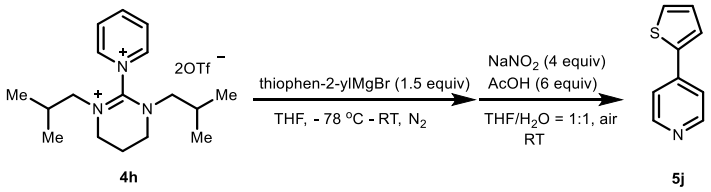
4-(4-methoxyphenyl)pyridine (5i)



Prepared via **General Procedure II** starting from 4-methoxyphenylMgBr (0.45 mmol, 1.5 equiv) to give 4-(4-methoxyphenyl)pyridine (**5i**) as a white solid.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 2:1).
Yield 39.4 mg (71%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.60 (d, *J* = 3.0 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 2H), 7.46 (d, *J* = 5.2 Hz, 2H), 7.00 (d, *J* = 8.6 Hz, 2H), 3.85 (s, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 160.6, 150.1, 147.9, 130.3, 128.2, 121.1, 114.6, 55.4.
HRMS calcd for $(C_{12}H_{12}NO)^+$ $[M + H]^+$: 186.0913, found 186.0912.

4-(thiophen-2-yl)pyridine (5j)



Prepared via **General Procedure II** starting from thiophen-2-ylMgBr (0.45 mmol, 1.5 equiv) to give 4-(thiophen-2-yl)pyridine (**5j**) as a brown solid.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 4:1).
Yield 31.1 mg (64%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.57 (dd, *J* = 4.7, 1.4 Hz, 2H), 7.50 – 7.47 (m, 1H), 7.46 (dd, *J* = 4.6, 1.6 Hz, 2H), 7.40 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.12 (dd, *J* = 5.0, 3.7 Hz, 1H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 150.3, 141.4, 141.2, 128.4, 127.2, 125.4, 119.9.

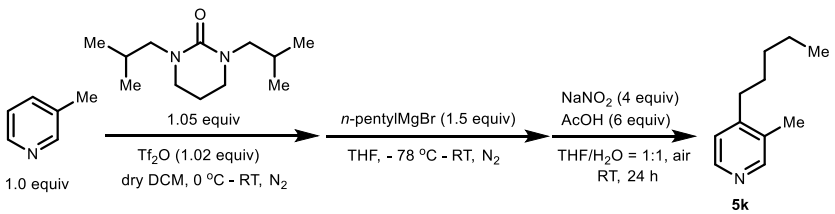
HRMS calcd for $(C_9H_8NS)^+$ $[M + H]^+$: 162.0372, found 162.0370.

4.: One-pot C-4 alkylation with Grignard reagents as the nucleophile

General procedures III:

Under a nitrogen atmosphere, 1,3-diisobutyltetrahydropyrimidin-2(1*H*)-one (222.6 mg, 1.05 mmol, 1.05 equiv) was added to an oven-dried 25 mL Schlenk tube with a magnetic bar. Anhydrous DCM (6.0 mL) was added and the solution was cooled to 0 ℃ in an ice-bath. Tf_2O (trifluoromethanesulfonic anhydride, 0.17 mL, 1.02 mmol, 1.02 equiv) was added dropwise via a 250 μL micro syringe within 2 minutes and the solution was stirred for 10 minutes at 0 ℃ (the reaction solution turned pale yellow during this period). Then different pyridines (1.0 mmol, 1.0 equiv) were added dropwise within 1 minute. The cooling bath was removed, and the reaction was stirred vigorously 12 ~ 48 h (Note: there are some substrates that we have heated, and the specific conditions have been written under each substrate). Then the mixture was concentrated under reduced pressure. After three vacuum nitrogen cycles, anhydrous THF (8.0 mL) was added and the suspension was cooled to -78 ℃ in a low-temperature reactor. (Note: If there is no low-temperature reactor in the laboratory, the reaction can also be carried out in an ice bath with a slight decrease in yield). A solution of the *n*-pentyl Grignard reagents (1.5 mmol, 1.5 equiv) was added dropwise via a 1.0 mL syringe within 2 minutes and the resulting suspension was stirred for 20 minutes to give a clear solution (Note: there are some substrates that we have reduced the amount of Grignard reagents, and the specific conditions have been written clearly under each substrate). Water (8.0 mL) was added in one portion and the reaction mixture stirred for 5 minutes at room temperature, then $NaNO_2$ aqueous solution (100 mg/ mL, 2.76 mL, 4.0 equiv) and acetic acid (346 μL, 6.0 equiv) were added in one portion and the mixture were stirred for 24 hours at different temperature. The mixture was neutralized with a saturated sodium bicarbonate solution (8.0 mL), extracted with EtOAc (3 × 10.0 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford C-4 alkylation pyridine products.

3-methyl-4-pentylpyridine (5k)

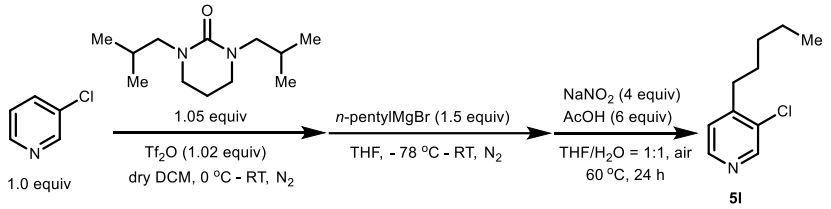


Prepared via **General Procedure III** starting from 3-methylpyridine (93.1 mg, 1.0 mmol, 1.0 equiv) and oxidized at room temperature for 24 h to give 3-methyl-4-pentylpyridine (**5k**) as a pale-yellow oil.

R_f = 0.5 (eluent: petroleum ether/EtOAc = 7:1).

Yield 94.7 mg (58%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.28 (s, 2H), 6.99 (d, *J* = 5.0 Hz, 1H), 2.54 – 2.47 (m, 2H), 2.22 (s, 3H), 1.57 – 1.49 (m, 2H), 1.35 – 1.28 (m, 4H), 0.87 (t, *J* = 6.9 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 150.5, 149.8, 147.4, 131.5, 123.4, 32.4, 31.7, 28.8, 22.5, 16.0, 13.9.
HRMS calcd for $(C_{11}H_{18}N)^+$ $[M + H]^+$: 164.1434, found 164.1433.

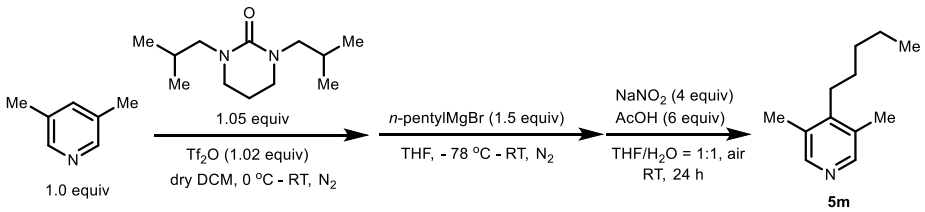
3-chloro-4-pentylpyridine (5l)



Prepared via **General Procedure III** starting from 3-chloropyridine (113.0 mg, 1.0 mmol, 1.0 equiv) and oxidized at 60 °C for 24 h to give 3-chloro-4-pentylpyridine (**5l**) as a pale-yellow oil.

R_f = 0.6 (eluent: petroleum ether/EtOAc = 5:1).
Yield 96.8 mg (53%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.51 (s, 1H), 8.36 (d, *J* = 4.9 Hz, 1H), 7.14 (d, *J* = 4.9 Hz, 1H), 2.74 – 2.66 (m, 2H), 1.67 – 1.57 (m, 2H), 1.37 – 1.30 (m, 4H), 0.91 (t, *J* = 6.9 Hz, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 149.3, 149.2, 147.5, 132.1, 124.8, 32.8, 31.4, 28.4, 22.4, 14.0.
HRMS calcd for $(C_{10}H_{15}ClN)^+$ $[M + H]^+$: 184.0888, found 184.0889.

3,5-dimethyl-4-pentylpyridine (5m)

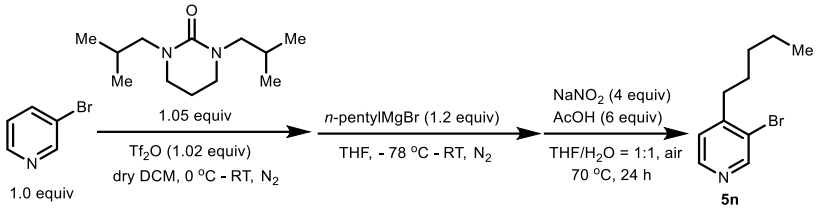


Prepared via **General Procedure III** starting from 3,5-dimethylpyridine (115.1 mg, 1.0 mmol, 1.0 equiv) and oxidized at room temperature for 24 h to give 3,5-dimethyl-4-pentylpyridine (**5m**) as a pale-yellow oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 5:1).
Yield 122.3 mg (69%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.12 (s, 2H), 2.55 – 2.49 (m, 2H), 2.20 (s, 6H), 1.43 –

1.29 (m, 6H), 0.86 (t, J = 7.1 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 148.7, 148.3, 130.8, 32.2, 29.2, 28.0, 22.4, 16.2, 14.0.
HRMS calcd for $(C_{12}H_{20}N)^+$ $[M + H]^+$: 178.1590, found 178.1589.

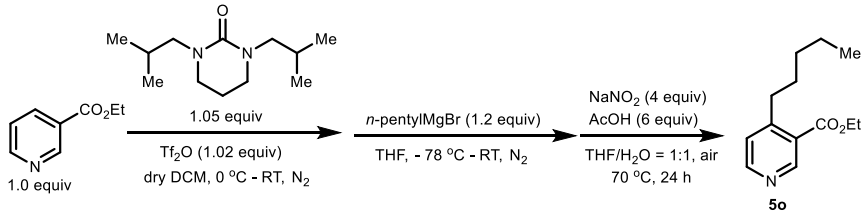
3-bromo-4-pentylpyridine (5n)



Prepared via **General Procedure III** starting from 3-bromopyridine (157.0 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 70 ℃ for 24 h to give 3-bromo-4-pentylpyridine (**5n**) as a pale-yellow oil.

R_f = 0.6 (eluent: petroleum ether/EtOAc = 10:1).
Yield 115.9 mg (51%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.64 (s, 1H), 8.39 (d, J = 4.9 Hz, 1H), 7.15 (d, J = 4.9 Hz, 1H), 2.75 – 2.67 (m, 2H), 1.66 – 1.56 (m, 2H), 1.42 – 1.31 (m, 4H), 0.91 (t, J = 7.0 Hz, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 151.7, 151.1, 148.0, 125.1, 123.2, 35.4, 31.4, 28.6, 22.4, 14.0.
HRMS calcd for $(C_{10}H_{15}BrN)^+$ $[M + H]^+$: 228.0382, found 228.0381.

ethyl 4-pentylnicotinate (5o)

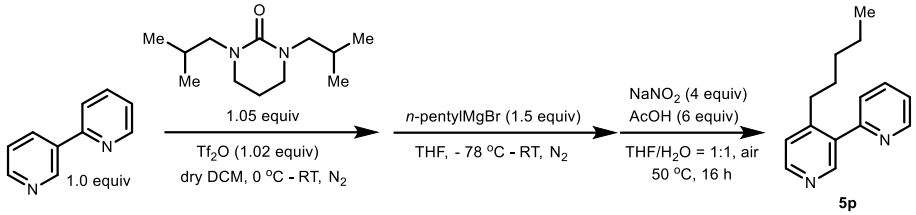


Prepared via **General Procedure III** starting from ethyl nicotinate (151.0 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 70 ℃ for 24 h to give ethyl 4-pentylnicotinate (**5o**) as a pale-yellow oil.

R_f = 0.6 (eluent: petroleum ether/EtOAc = 5:1).
Yield 127.1 mg (57%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.97 (s, 1H), 8.50 (d, J = 5.0 Hz, 1H), 7.12 (d, J = 5.0 Hz, 1H), 4.34 (q, J = 7.1 Hz, 2H), 2.95 – 2.86 (m, 2H), 1.61 – 1.48 (m, 2H), 1.35 (t, J = 7.1 Hz, 3H), 1.31 – 1.24 (m, 4H), 0.87 – 0.81 (m, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 166.1, 153.5, 151.9, 151.5, 125.9, 125.3, 61.1, 33.7, 31.7, 30.4, 22.4, 14.2, 13.9.

HRMS calcd for $(C_{13}H_{20}NO_2)^+$ $[M + H]^+$: 222.1489, found 222.1487.

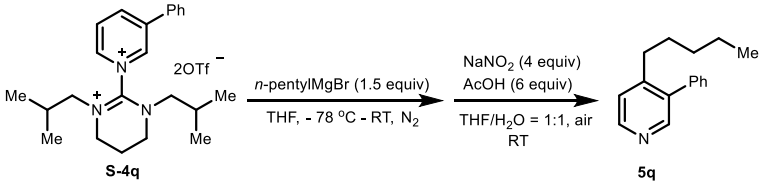
4'-pentyl-2,3'-bipyridine (5p)



Prepared via **General Procedure III** starting from 2,3'-bipyridine (156.0 mg, 1.0 mmol, 1.0 equiv) and oxidized at 50 ℃ for 16 h to give 4'-pentyl-2,3'-bipyridine (**5p**) as a yellow oil.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 1:1).
Yield 120.2 mg (53%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.72 (d, *J* = 4.8 Hz, 1H), 8.54 (s, 1H), 8.52 (d, *J* = 5.1 Hz, 1H), 7.80 (td, *J* = 7.7, 1.8 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.31 (ddd, *J* = 7.5, 4.9, 0.9 Hz, 1H), 7.24 (d, *J* = 5.1 Hz, 1H), 2.78 – 2.70 (m, 2H), 1.48 (p, *J* = 7.3 Hz, 2H), 1.24 – 1.15 (m, 4H), 0.80 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 156.9, 150.4, 149.8, 149.5, 148.9, 136.6, 136.2, 124.5, 124.2, 122.4, 32.3, 31.5, 29.8, 22.2, 13.9.
HRMS calcd for $(C_{15}H_{19}N_2)^+$ $[M + H]^+$: 227.1543, found 227.1541.

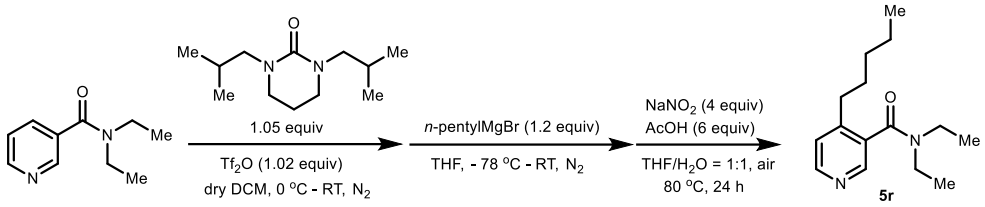
4-pentyl-3-phenylpyridine (5q)



Prepared via **General Procedure II** starting from **S-4q** (194.7 mg, 0.3 mmol, 1.0 equiv) and *n*-pentylMgBr (0.45 mmol, 1.5 equiv) to give 4-pentyl-3-phenylpyridine (**5q**) as a pale-yellow oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 10:1).
Yield 51.2 mg (76%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.47 (d, *J* = 5.1 Hz, 1H), 8.41 (s, 1H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.29 (d, *J* = 7.3 Hz, 2H), 7.20 (d, *J* = 5.1 Hz, 1H), 2.68 – 2.43 (m, 2H), 1.48 (p, *J* = 7.4 Hz, 2H), 1.28 – 1.09 (m, 4H), 0.80 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 150.2, 149.2, 148.4, 138.0, 137.6, 129.4, 128.4, 127.6, 123.9, 32.3, 31.5, 29.9, 22.3, 13.9.
HRMS calcd for $(C_{16}H_{20}N)^+$ $[M + H]^+$: 226.1590, found 226.1589.

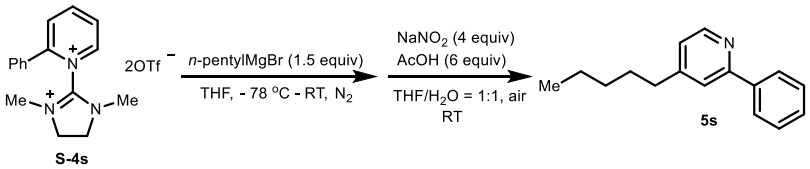
***N*,*N*-diethyl-4-pentylnicotinamide (5r)**



Prepared via **General Procedure III** starting from *N*,*N*-diethylnicotinamide (178.1 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 80 ℃ for 24 h to give *N*,*N*-diethyl-4-pentylnicotinamide (**5r**) as a pale yellow oil.

R_f = 0.2 (eluent: petroleum ether/EtOAc = 2:1).
Yield 71.2 mg (29%, 65.0 mg starting material, 45% b.r.s.m).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.48 (d, *J* = 5.1 Hz, 1H), 8.37 (s, 1H), 7.18 (d, *J* = 5.1 Hz, 1H), 3.96 – 3.22 (br, 2H), 3.11 (q, *J* = 7.1 Hz, 2H), 2.57 (t, *J* = 4.0 Hz, 2H), 1.72 – 1.48 (br, 2H), 1.33 – 1.28 (m, 4H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 168.1, 149.5, 148.8, 146.1, 133.0, 124.3, 43.0, 38.9, 32.5, 31.7, 29.5, 22.4, 14.1, 13.9, 12.7.
HRMS calcd for $(C_{15}H_{25}N_2O)^+$ $[M + H]^+$: 249.1962, found 249.1959.

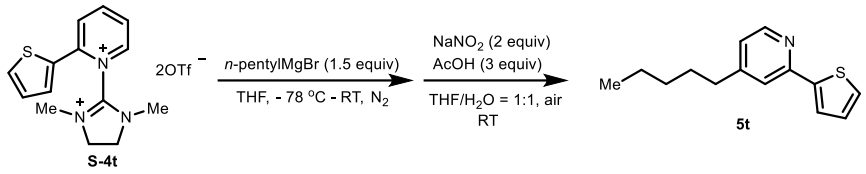
4-pentyl-2-phenylpyridine (5s)



Prepared via **General Procedure II** starting from **S-4s** (165.3 mg, 0.3 mmol, 1.0 equiv) and *n*-pentylMgBr (0.45 mmol, 1.5 equiv) to give 4-pentyl-2-phenylpyridine (**5s**) as a pale-yellow oil.

R_f = 0.5 (eluent: petroleum ether/EtOAc = 10:1).
Yield 53.2 mg (79%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.60 (d, *J* = 5.0 Hz, 1H), 8.01 (d, *J* = 7.4 Hz, 2H), 7.57 (s, 1H), 7.53 – 7.47 (m, 2H), 7.46 – 7.40 (m, 1H), 7.08 (d, *J* = 4.9 Hz, 1H), 2.73 – 2.63 (m, 2H), 1.70 (p, *J* = 7.3 Hz, 2H), 1.45 – 1.32 (m, 4H), 0.94 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 157.4, 152.6, 149.5, 139.6, 128.8, 128.7, 127.0, 122.5, 120.9, 35.5, 31.4, 30.1, 22.5, 14.0.
HRMS calcd for $(C_{16}H_{20}N)^+$ $[M + H]^+$: 226.1590, found 226.1588.

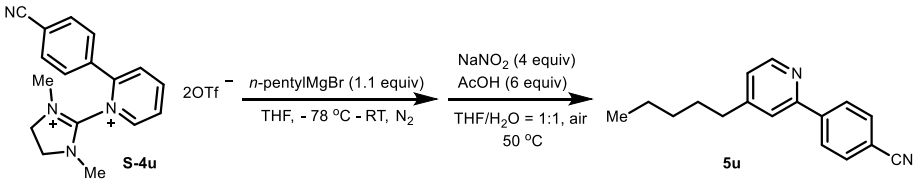
4-pentyl-2-(thiophen-2-yl)pyridine (5t)



Prepared via **General Procedure II** starting from **S-4t** (167.1 mg, 0.3 mmol, 1.0 equiv) and *n*-pentylMgBr (0.45 mmol, 1.5 equiv) and the $NaNO_2$ was reduced to 2.0 equiv to give 4-pentyl-2-(thiophen-2-yl)pyridine (**5t**) as a pale yellow oil.

R_f = 0.6 (eluent: petroleum ether/EtOAc = 10:1).
Yield 28.5 mg (41%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.44 (d, *J* = 5.1 Hz, 1H), 7.58 (d, *J* = 3.5 Hz, 1H), 7.47 (s, 1H), 7.37 (d, *J* = 5.0 Hz, 1H), 7.18 – 7.05 (m, 1H), 6.97 (d, *J* = 5.0 Hz, 1H), 2.62 (t, *J* = 7.7 Hz, 2H), 1.65 (p, *J* = 7.4 Hz, 2H), 1.41 – 1.28 (m, 4H), 0.90 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 152.6, 152.4, 149.3, 145.0, 128.0, 127.3, 124.3, 122.4, 119.0, 35.4, 31.4, 30.0, 22.5, 14.0.
HRMS calcd for $(C_{14}H_{18}NS)^+$ $[M + H]^+$: 232.1155, found 232.1153.

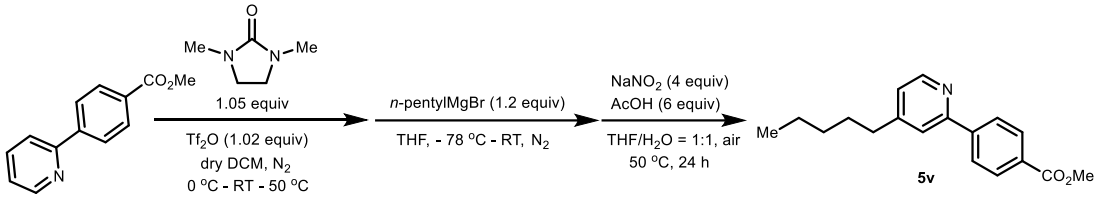
4-(4-pentylpyridin-2-yl)benzonitrile (5u)



Prepared via **General Procedure II** starting from **S-4u** (172.8 mg, 0.3 mmol, 1.0 equiv) and *n*-pentylMgBr (0.33 mmol, 1.1 equiv) and oxidized at 50 ℃ for 10 h to give 4-(4-pentylpyridin-2-yl)benzonitrile (**5u**) as a pale yellow oil.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 10:1).
Yield 45.2 mg (60%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.59 (d, *J* = 4.9 Hz, 1H), 8.10 (d, *J* = 8.3 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.57 (s, 1H), 7.14 (d, *J* = 4.5 Hz, 1H), 2.76 – 2.55 (m, 2H), 1.68 (p, *J* = 7.4 Hz, 2H), 1.42 – 1.30 (m, 4H), 0.90 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 155.1, 153.2, 149.8, 143.7, 132.5, 127.5, 123.6, 121.3, 118.9, 112.3, 35.5, 31.4, 30.1, 22.4, 14.0.
HRMS calcd for $(C_{17}H_{19}N_2)^+$ $[M + H]^+$: 251.1543, found 251.1540.

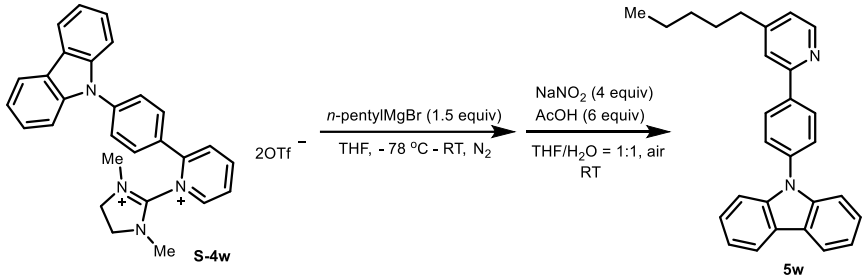
methyl 4-(4-pentylpyridin-2-yl)benzoate (5v)



Prepared via **General Procedure III** starting from methyl 4-(pyridin-2-yl)benzoate (213.1.0 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 50 °C for 24 h to give methyl 4-(4-pentylpyridin-2-yl)benzoate (**5v**) as a pale yellow oil.

R_f = 0.45 (eluent: petroleum ether/EtOAc = 10:1).
Yield 126.3 mg (45%, 86.1 mg starting material).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.57 (d, *J* = 5.0 Hz, 1H), 8.11 (d, *J* = 7.9 Hz, 2H), 8.05 (d, *J* = 8.5 Hz, 2H), 7.57 (s, 1H), 7.08 (d, *J* = 5.0 Hz, 1H), 3.92 (s, 3H), 2.68 – 2.58 (m, 2H), 1.65 (p, *J* = 7.4 Hz, 2H), 1.39 – 1.25 (m, 4H), 0.89 (t, *J* = 6.5 Hz, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 167.0, 156.1, 152.9, 149.7, 143.8, 130.3, 130.0, 126.9, 123.2, 121.3, 52.2, 35.5, 31.4, 30.2, 22.5, 14.0.
HRMS calcd for $(C_{18}H_{22}NO_2)^+$ $[M + H]^+$: 284.1645, found 284.1644.

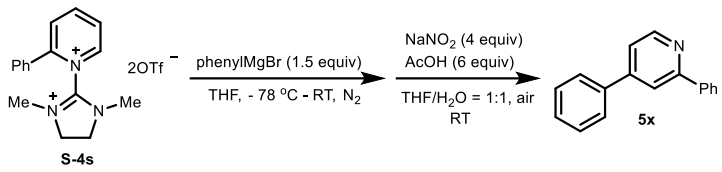
9-(4-(4-pentylpyridin-2-yl)phenyl)-9*H*-carbazole (5w)



Prepared via **General Procedure II** starting from **S-4w** (214.8 mg, 0.3 mmol, 1.0 equiv) and *n*-pentylMgBr (0.45 mmol, 1.5 equiv) to give 9-(4-(4-pentylpyridin-2-yl)phenyl)-9*H*-carbazole (**5w**) as a pale green oil.

R_f = 0.5 (eluent: petroleum ether/EtOAc = 10:1).
Yield 65.9 mg (56%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.66 (d, *J* = 5.0 Hz, 1H), 8.26 (d, *J* = 8.4 Hz, 2H), 8.19 (d, *J* = 7.7 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.67 (s, 1H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 2H), 7.14 (d, *J* = 4.7 Hz, 1H), 2.73 (t, *J* = 7.7 Hz, 2H), 1.75 (p, *J* = 7.2 Hz, 2H), 1.54 – 1.28 (m, 4H), 0.97 (t, *J* = 6.5 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 156.5, 152.9, 149.7, 140.8, 138.7, 138.3, 128.5, 127.2, 126.1, 123.6, 122.8, 120.9, 120.4, 120.1, 109.9, 35.6, 31.5, 30.2, 22.6, 14.1.
HRMS calcd for $(C_{28}H_{27}N_2)^+$ $[M + H]^+$: 391.2169, found 391.2164.

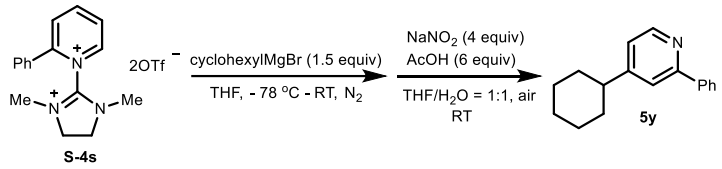
2,4-diphenylpyridine (5x)



Prepared via **General Procedure II** starting from **S-4s** (165.3 mg, 0.3 mmol, 1.0 equiv) and phenylMgBr (0.45 mmol, 1.5 equiv) to give 2,4-diphenylpyridine (**5x**) as a yellow oil.

R_f = 0.5 (eluent: petroleum ether/EtOAc = 10:1).
Yield 59.2 mg (85%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.76 (d, *J* = 5.0 Hz, 1H), 8.07 (d, *J* = 7.2 Hz, 2H), 7.94 (s, 1H), 7.70 (d, *J* = 7.1 Hz, 2H), 7.58 – 7.50 (m, 4H), 7.48 – 7.44 (m, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 158.1, 150.1, 149.4, 139.5, 138.5, 129.2, 129.1, 128.9, 127.14, 127.12, 127.11, 120.3, 118.8.
HRMS calcd for $(C_{17}H_{14}N)^+$ $[M + H]^+$: 232.1121, found 232.1119.

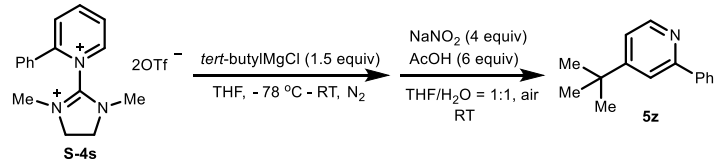
4-cyclohexyl-2-phenylpyridine (5y)



Prepared via **General Procedure II** starting from **S-4s** (165.3 mg, 0.3 mmol, 1.0 equiv) and cyclohexylMgBr (0.45 mmol, 1.5 equiv) to give 4-cyclohexyl-2-phenylpyridine (**5y**) as a yellow oil.

R_f = 0.5 (eluent: petroleum ether/EtOAc = 10:1).
Yield 53.5 mg (75%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.58 (d, *J* = 4.8 Hz, 1H), 7.99 (d, *J* = 7.4 Hz, 2H), 7.56 (s, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.07 (d, *J* = 4.3 Hz, 1H), 2.56 (t, *J* = 11.4 Hz, 1H), 1.92 (d, *J* = 12.2 Hz, 2H), 1.88 (d, *J* = 12.5 Hz, 2H), 1.78 (d, *J* = 13.1 Hz, 1H), 1.52 – 1.35 (m, 4H), 1.33 – 1.18 (m, 1H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 157.5, 157.4, 149.6, 139.8, 128.8, 128.7, 127.0, 120.9, 119.4, 44.1, 33.6, 26.6, 26.0.
HRMS calcd for $(C_{17}H_{20}N)^+$ $[M + H]^+$: 238.1590, found 238.1589.

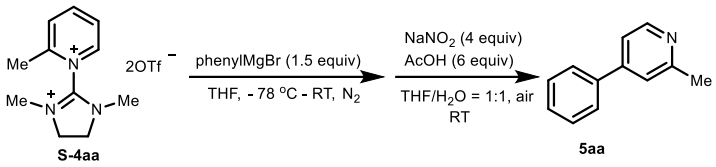
4-(*tert*-butyl)-2-phenylpyridine (5z)



Prepared via **General Procedure II** starting from **S-4s** (165.3 mg, 0.3 mmol, 1.0 equiv) and *tert*-butylMgCl (0.45 mmol, 1.5 equiv) to give 4-(*tert*-butyl)-2-phenylpyridine (**5z**) as a pale yellow oil.

R_f = 0.5 (eluent: petroleum ether/EtOAc = 10:1).
Yield 28.6 mg (45%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.61 (d, *J* = 5.2 Hz, 1H), 7.98 (d, *J* = 7.2 Hz, 2H), 7.71 (s, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.3 Hz, 1H), 7.24 (dd, *J* = 5.2, 1.8 Hz, 1H), 1.37 (s, 9H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 160.8, 157.5, 149.5, 140.0, 128.8, 128.7, 127.1, 119.4, 117.8, 34.9, 30.6.
HRMS calcd for $(C_{15}H_{18}N)^+$ $[M + H]^+$: 212.1434, found 212.1432.

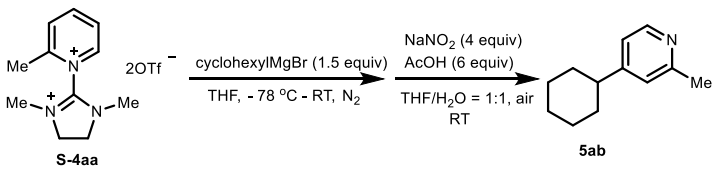
4-pentyl-3-phenylpyridine (5aa)



Prepared via **General Procedure II** starting from **S-4aa** (146.7 mg, 0.3 mmol, 1.0 equiv) and phenylMgBr (0.45 mmol, 1.5 equiv) to give 4-pentyl-3-phenylpyridine (**5aa**) as a pale-yellow oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 10:1).
Yield 21.7 mg (43%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.53 (d, *J* = 5.2 Hz, 1H), 7.62 (d, *J* = 7.3 Hz, 2H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.42 (t, *J* = 7.3 Hz, 1H), 7.37 (s, 1H), 7.31 (d, *J* = 4.7 Hz, 1H), 2.62 (s, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 158.8, 149.5, 148.8, 138.4, 129.1, 128.9, 127.0, 121.3, 118.9, 24.5.
HRMS calcd for $(C_{12}H_{12}N)^+$ $[M + H]^+$: 170.0964, found 170.0962.

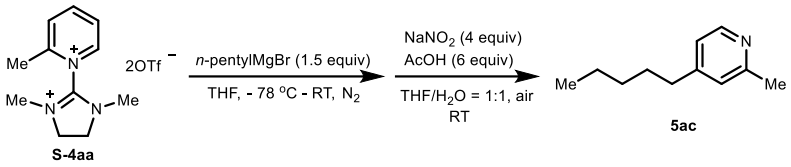
4-cyclohexyl-2-methylpyridine (5ab)



Prepared via **General Procedure II** starting from **S-4aa** (146.7 mg, 0.3 mmol, 1.0 equiv) and cyclohexylMgBr (0.45 mmol, 1.5 equiv) to give 4-cyclohexyl-2-methylpyridine (**5ab**) as a yellow oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 10:1).
Yield 17.7 mg (34%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.35 (d, *J* = 5.1 Hz, 1H), 6.97 (s, 1H), 6.91 (d, *J* = 4.8 Hz, 1H), 2.51 (s, 3H), 2.46 – 2.38 (m, 1H), 1.83 (d, *J* = 8.4 Hz, 4H), 1.74 (d, *J* = 12.8 Hz, 1H), 1.42 – 1.32 (m, 4H), 1.27 – 1.15 (m, 1H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 158.1, 157.0, 148.9, 121.9, 119.5, 43.9, 33.5, 26.6, 26.0, 24.4.
HRMS calcd for $(C_{12}H_{18}N)^+$ $[M + H]^+$: 176.1434, found 176.1432.

4-pentyl-2-methylpyridine (5ac)

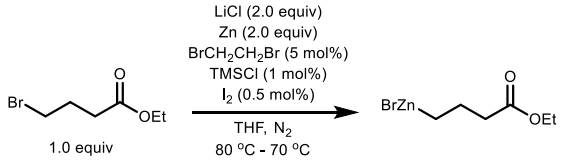


Prepared via **General Procedure II** starting from **S-4aa** (146.7 mg, 0.3 mmol, 1.0 equiv) and *n*-pentylMgBr (0.45 mmol, 1.5 equiv) to give 4-pentyl-2-methylpyridine (**5ac**) as a pale-yellow oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 10:1).
Yield 18.2 mg (37%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.35 (d, *J* = 5.1 Hz, 1H), 6.96 (s, 1H), 6.90 (d, *J* = 4.9 Hz, 1H), 2.56 – 2.52 (m, 2H), 2.51 (s, 3H), 1.59 (p, *J* = 7.6 Hz, 2H), 1.36 – 1.24 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 158.0, 152.2, 148.8, 123.5, 121.1, 35.2, 31.4, 30.0, 24.3, 22.5, 14.0.
HRMS calcd for $(C_{11}H_{18}N)^+$ $[M + H]^+$: 164.1434, found 164.1432.

6. C-4 alkylation with organozinc reagent as the nucleophile

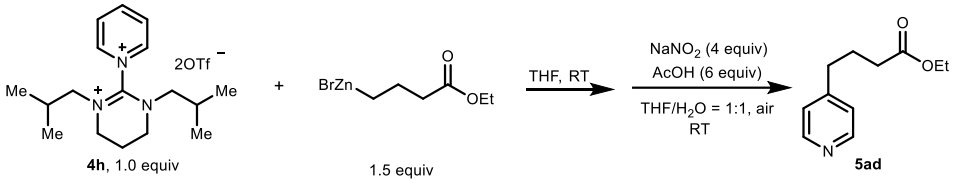
The preparation of organozinc reagent[2]



An oven-dried and N_2 flushed 25 mL Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the anhydrous LiCl (10 mmol, 2.0 equiv) and dried for 10 minutes under the vacuum with the heat gun. Zinc powder (10 mmol, 2.0 equiv) was added under N_2 and the heterogeneous mixture of Zn and LiCl was dried again for 10 minutes under the vacuum with the heat gun. The sealed tube was backfilled with N_2 (this process was repeated for three times). THF (5.0 mL) was added and the Zn was

activated with $BrCH_2CH_2Br$ (5 mol%) under 80 ℃ for 20 minutes. After cooling, Me_3SiCl (1 mol%) and I_2 (0.5 mol%) were added under N_2 atmosphere, then the mixture was refluxed for another 20 minutes. Ethyl 4-bromobutanoate (5.0 mmol) was then added neat at room temperature and the reaction mixture was stirred at 70 ℃ for 12 h. The concentration of organozinc reagents was titrated by iodine and the concentration is approximately 0.5 M. The resulting suspension (approx. 0.5 M) can be used directly by syringe and stored in the refrigerator for several days.

ethyl 4-(pyridin-4-yl)butanoate (5ad)



An oven-dried and N_2 flushed 25 mL Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the **4h** (171.9 mg, 0.3 mmol, 1.0 equiv) and dry THF (3.0 mL). Organozinc reagent (0.5 M in THF, 0.9 mL, 0.45 mmol, 1.5 equiv) was added dropwise within 1 minute and the reaction mixture was stirred at room temperature for 16 h to give a yellow suspension. Water (3.0 mL) was added in one portion and the reaction mixture was stirred for 5 minutes at room temperature, then $NaNO_2$ aqueous solution (100 mg/ mL, 0.83 mL, 4.0 equiv) and acetic acid (103 μL, 6.0 equiv) were added in one portion and the mixture were stirred for 10 hours at room temperature. The mixture was neutralized with a saturated sodium bicarbonate solution (2.0 mL), extracted with EtOAc (3 × 8.0 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford C-4 alkylation pyridine product (**5ad**) as a yellow oil.

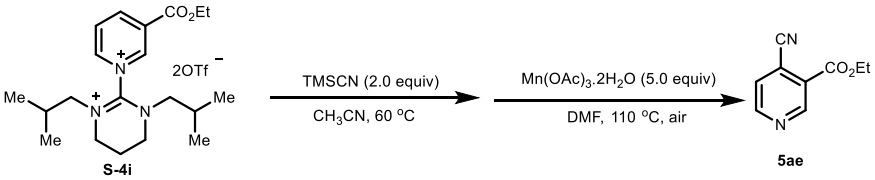
R_f = 0.4 (eluent: petroleum ether/EtOAc = 1:1).
Yield 30.1 mg (52%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.46 (d, *J* = 5.5 Hz, 2H), 7.09 (d, *J* = 5.5 Hz, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 2.65 – 2.53 (m, 2H), 2.30 (t, *J* = 7.4 Hz, 2H), 1.94 (p, *J* = 7.4 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 173.1, 150.5, 149.7, 123.9, 60.5, 34.4, 33.5, 25.4, 14.2.
HRMS calcd for $(C_{11}H_{16}NO_2)^+$ $[M + H]^+$: 194.1176, found 194.1170.

7. C-4 cyanation with TMSCN as the nucleophile

An oven-dried and N_2 flushed 25 mL Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding pyridine salt (0.1 mmol, 1.0 equiv), dry CH_3CN (1.0 mL) and TMSCN (25.0 μL, 0.2 mmol, 2.0 equiv). The resulting solution was heated to 60 ℃ and stirred vigorously overnight (Note: this reaction can be monitored by TLC, eluent: DCM/MeOH = 10:1). Then the mixture was concentrated

under reduced pressure and diluted by DMF (1.0 mL), and the oxidant $Mn(OAc)_3 \cdot 2H_2O$ (66.5 mg, 0.5 mmol, 5.0 equiv) was added in one portion. The reaction mixture was stirred at 110 ℃ for 18 h. The reaction mixture was diluted by EtOAc (5.0 mL), filtered with silica gel, extracted with water (5.0 mL) and EtOAc (3 × 5.0 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford C-4 cyanation pyridine products.

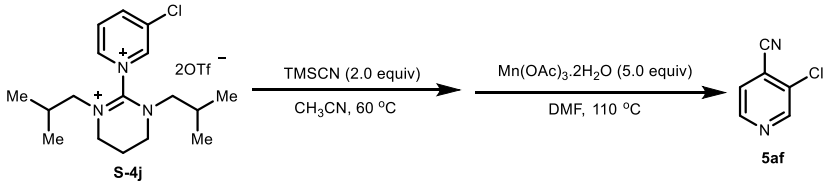
ethyl 4-cyanonicotinate (5ae)



Prepared via the above procedure starting from **S-4i** (64.5 mg, 0.1 mmol, 1.0 equiv) to give ethyl 4-cyanonicotinate (**5ae**) as a white solid.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 5:1).
Yield 12.8 mg (73%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 9.39 (s, 1H), 8.99 – 8.91 (br, 1H), 7.68 (d, *J* = 4.6 Hz, 1H), 4.52 (q, *J* = 7.1 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 162.7, 153.6, 152.3, 127.2, 126.3, 120.9, 115.3, 62.8, 14.1.
HRMS calcd for $(C_9H_9N_2O_2)^+$ $[M + H]^+$: 177.0659, found 177.0658.

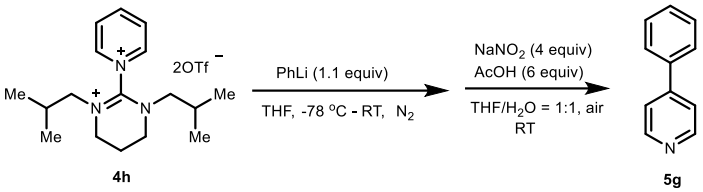
3-chloroisonicotinonitrile (5af)



Prepared via the above procedure starting from **S-4j** (60.7 mg, 0.1 mmol, 1.0 equiv) to give 3-chloroisonicotinonitrile (**5af**) as a white solid.

R_f = 0.5 (eluent: petroleum ether/EtOAc = 5:1).
Yield 5.5 mg (40%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.81 (s, 1H), 8.67 (d, *J* = 4.9 Hz, 1H), 7.56 (d, *J* = 4.9 Hz, 1H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 150.4, 148.1, 133.1, 126.3, 120.9, 113.7.
HRMS calcd for $(C_6H_4ClN_2)^+$ $[M + H]^+$: 139.0058, found 139.0055.

8. C-4 arylation with phenyl lithium as the nucleophile



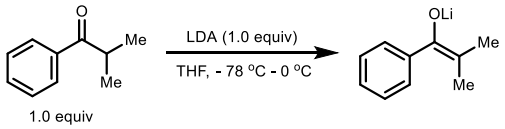
4h **5g**

An oven-dried and N_2 flushed 25 mL Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with **4h** (171.9 mg, 0.3 mmol, 1.0 equiv) and dry THF (3.0 mL). The resulting suspension was cooled to -78 ℃. PhLi (1.9 M in hexane, 0.17 mL, 0.33 mmol, 1.1 equiv) was added dropwise within 3 minutes and the reaction mixture was stirred at -78 ℃ for 3 minutes to give a red solution. Water (3.0 mL) was added in one portion and the reaction mixture was stirred for 5 minutes at room temperature, then $NaNO_2$ aqueous solution (100 mg/ mL, 0.83 mL, 4.0 equiv) and acetic acid (103 μL, 6.0 equiv) were added in one portion and the mixture were stirred for 10 hours at room temperature. The mixture was neutralized with a saturated sodium bicarbonate solution (2.0 mL), extracted with EtOAc (3 × 8.0 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford C-4 arylation pyridine products (**5g**) as a white solid.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 5:1).
Yield 19.5 mg (42%).
NMR spectroscopy:
The NMR spectroscopy and HRMS data of **5g** has already been written on page S18.

9. C-4 alkylation with the enolate as the nucleophile

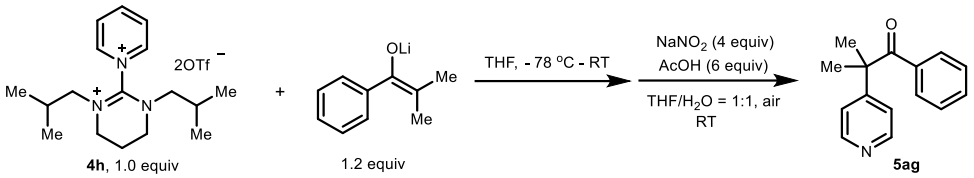
The preparation of lithium 2-methyl-1-phenylprop-1-en-1-olate



1.0 equiv

An oven-dried and N_2 flushed 25 mL Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding 2-methyl-1-phenylpropan-1-one (296.0 mg, 2.0 mmol, 1.0 equiv) and dry THF (3.7 mL). The resulting solution was cooled to -78 ℃. LDA (2.0 M in hexane, 1.0 mL, 2.0 mmol, 1.0 equiv) was added dropwise within 3 minutes and the reaction mixture was stirred at -78 ℃ for 1 h. Then the reaction tube was transferred to an ice bath and stirred for 30 min. The resulting brown solution (approx. 0.4 M) can be used directly by syringe and stored in the refrigerator for several days.

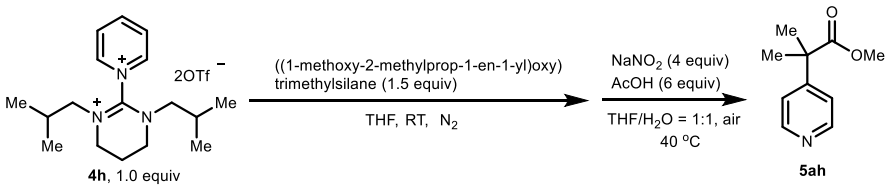
2-methyl-1-phenyl-2-(pyridin-4-yl)propan-1-one (5ag)



An oven-dried and N_2 flushed 25 mL Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with **4h** (171.9 mg, 0.3 mmol, 1.0 equiv) and dry THF (3.0 mL). The resulting suspension was cooled to -78 ℃. 2-Methyl-1-phenylprop-1-en-1-olate (0.4 M in THF, 0.9 mL, 0.36 mmol, 1.2 equiv) was added dropwise within 3 minutes and the reaction mixture was stirred at -78 ℃ for 20 minutes to give a clear solution. Water (3.0 mL) was added in one portion and the reaction mixture was stirred for 5 minutes at room temperature, then $NaNO_2$ aqueous solution (100 mg/ mL, 0.83 mL, 4.0 equiv) and acetic acid (103 μL, 6.0 equiv) were added in one portion and the mixture were stirred for 10 hours at room temperature. The mixture was neutralized with a saturated sodium bicarbonate solution (2.0 mL), extracted with EtOAc (3 × 8.0 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford C-4 alkylation pyridine product (**5ag**) as a yellow oil.

R_f = 0.15 (eluent: petroleum ether/EtOAc = 5:1).
Yield 34.4 mg (51%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.57 (d, *J* = 4.2 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.26 – 7.18 (m, 4H), 1.60 (s, 6H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 202.0, 154.7, 150.4, 135.4, 132.2, 129.6, 128.2, 121.0, 51.2, 27.4.
HRMS calcd for $(C_{15}H_{16}NO)^+$ $[M + H]^+$: 226.1226, found 226.1225.

10. C-4 alkylation with silyl ketene acetal as the nucleophile



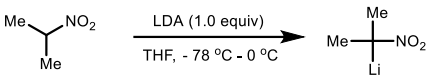
An oven-dried and N_2 flushed 25 mL Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with **4h** (114.6 mg, 0.2 mmol, 1.0 equiv), dry THF (2.0 mL) and ((1-methoxy-2-methylprop-1-en-1-yl)oxy)trimethylsilane (52.3 mg, 0.30 mmol, 1.5 equiv). The resulting suspension was stirred for 10 minutes at room temperature and the suspension changed to a clear solution. (Note: this reaction can be monitored by TLC, DCM/MeOH = 10:1). Water (2.0 mL) was added in one portion at room temperature, then $NaNO_2$ aqueous solution (100 mg/ mL, 0.55 mL, 4.0 equiv) and acetic acid (69 μL, 6.0 equiv) were added in one portion and the mixture were stirred for 10 hours at 40 ℃. The mixture was neutralized with a saturated sodium

bicarbonate solution (2.0 mL), extracted with EtOAc (3 × 6.0 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford C-4 alkylation pyridine products (**5ah**) as a pale-yellow oil.

R_f = 0.7 (eluent: petroleum ether/EtOAc = 5:1).
Yield 24.1 mg (67%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.53 (d, *J* = 4.6 Hz, 2H), 7.22 (d, *J* = 6.1 Hz, 2H), 3.65 (s, 3H), 1.55 (s, 6H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 175.9, 153.5, 149.8, 121.1, 52.4, 46.4, 25.8.
HRMS calcd for $(C_{10}H_{14}NO_2)^+$ $[M + H]^+$: 180.1019, found 180.1018.

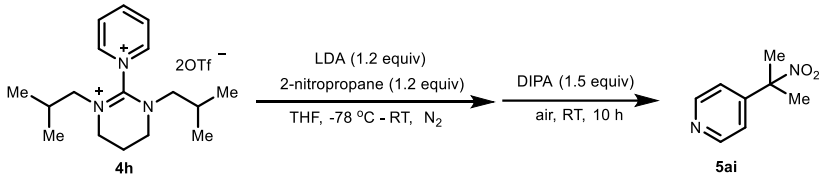
11. C-4 alkylation with nitronate as the nucleophile

The preparation of (2-nitropropan-2-yl)lithium



An oven-dried and N_2 flushed 25 mL Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding 2-nitropropane (178.0 mg, 2.0 mmol, 1.0 equiv) and dry THF (3.8 mL). The resulting solution was cooled to -78 ℃. LDA (2.0 M in hexane, 1.0 mL, 2.0 mmol, 1.0 equiv) was added dropwise within 3 minutes and the reaction mixture was stirred at -78 ℃ for 1 h. Then the reaction tube was transferred to an ice bath and stirred for 30 min. The resulting yellow solution (approx. 0.4 M) can be used directly by syringe and stored in the refrigerator for several days.

4-(2-nitropropan-2-yl)pyridine (5ai)



An oven-dried and N_2 flushed 25 mL Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding **4h** (114.6 mg, 0.2 mmol, 1.0 equiv) and dry THF (2.0 mL). The resulting suspension was cooled to -78 ℃. (2-nitropropan-2-yl)lithium (0.4 M in THF, 0.6 mL, 0.24 mmol, 1.2 equiv) was added dropwise within 3 minutes and the reaction mixture was stirred at -78 ℃ for 20 minutes to give a clear solution. Water (3.0 mL) was added in one portion and the reaction mixture stirred for 5 minutes at room temperature, then DCM (5.0 mL) was added and the mixture was extracted with DCM (3 × 5.0 mL) and the combined organic layers were concentrated under reduced pressure. The residue was dissolved by CH_3CN (2.0

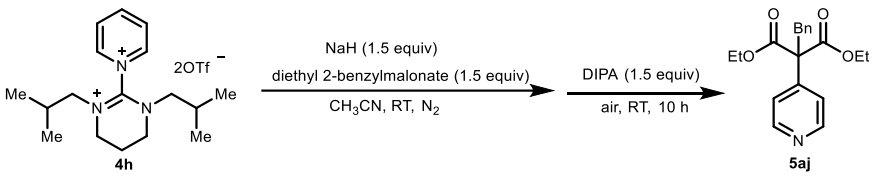
mL), the oxidant DIPA ((diacetoxyiodo)benzene, 96.6 mg, 0.3 mmol, 1.5 equiv) was added in one portion and stirred at room temperature for 10 h. The mixture was neutralized with a saturated sodium bicarbonate solution (2.0 mL), extracted with EtOAc (3 × 5.0 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford C-4 alkylation pyridine product (**5ai**) as a yellow oil.

R_f = 0.2 (eluent: petroleum ether/EtOAc = 2:1).
Yield 16.7 mg (50%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.66 (d, *J* = 6.2 Hz, 2H), 7.29 (d, *J* = 6.2 Hz, 2H), 1.98 (s, 6H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 150.4, 148.9, 120.0, 89.1, 26.9.
HRMS calcd for $(C_8H_{11}N_2O_2)^+$ $[M + H]^+$: 167.0815, found 167.0813.

12. C-4 alkylation with malonates as the nucleophile

An oven-dried and N_2 flushed 10 mL Schlenk-tube equipped with the screw cap and magnetic stirring bar, was charged with the corresponding malonate (0.15 mmol, 1.5 equiv), dry CH_3CN (1.0 mL) and NaH (0.15 mmol, 6.0 mg, 1.5 equiv). The reaction mixture was stirred at room temperature for 5 minutes. Then corresponding pyridine salt (0.1 mmol, 1.0 equiv) and dry CH_3CN (1.0 mL) were added in sequence. The resulting mixture was stirred at room temperature for 2 h and monitored by TLC (eluent: DCM/MeOH = 10:1). After the reaction was completed, DIPA (phenyliodine diacetate, 0.15 mmol, 48.3 mg, 1.5 equiv) was added to the tube under atmospheric conditions. The resulting mixture was stirred at room temperature for 10 h. Upon completion, the reaction was neutralized with saturated $NaHCO_3$ aqueous solution (2.0 mL) (pH >8). The crude mixture was diluted by DCM (5.0 mL) and the aqueous phase was extracted with DCM (3 × 5.0 mL). Then the combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was purified on silica gel chromatography to afford C-4 alkylation pyridine products.

diethyl 2-benzyl-2-(pyridin-4-yl)malonate (5aj)



Prepared via the above procedure starting from **4h** (0.1 mmol, 57.3 mg, 1.0 equiv) to give diethyl 2-benzyl-2-(pyridin-4-yl)malonate (**5aj**) as a yellow oil.

R_f = 0.5 (eluent: petroleum ether/EtOAc = 5:1).
Yield 16.1 mg (49%).

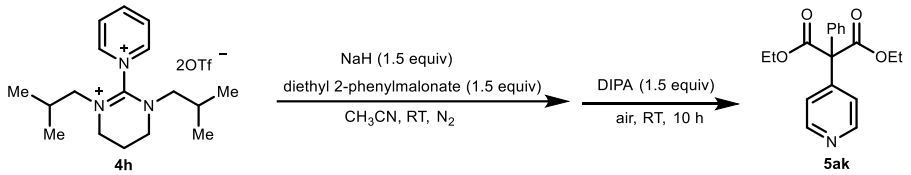
NMR spectroscopy:

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.60 – 8.38 (br, 2H), 7.21 – 7.10 (m, 5H), 6.82 (d, J = 7.0 Hz, 2H), 4.23 (q, J = 7.1 Hz, 4H), 3.57 (s, 2H), 1.23 (t, J = 7.1 Hz, 6H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ 169.0, 149.2, 145.8, 135.0, 130.3, 128.1, 127.2, 123.5, 63.8, 62.1, 42.7, 13.9.

HRMS calcd for $(C_{19}H_{22}NO_4)^+$ $[M + H]^+$: 328.1543, found 328.1542.

diethyl 2-phenyl-2-(pyridin-4-yl)malonate (5ak)



Prepared via the above procedure starting from **4h** (0.1 mmol, 57.3 mg, 1.0 equiv) to give diethyl 2-phenyl-2-(pyridin-4-yl)malonate (**5ak**) as a yellow oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 5:1).

Yield 14.0 mg (45%).

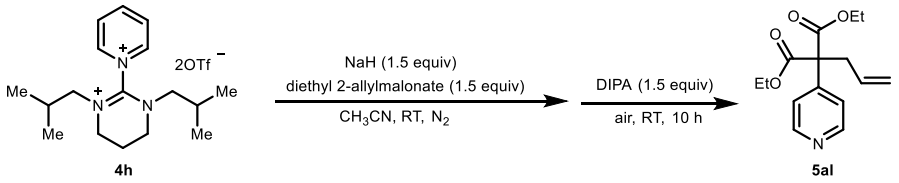
NMR spectroscopy:

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.57 (d, J = 6.4 Hz, 2H), 7.39 – 7.29 (m, 7H), 4.29 (q, J = 7.1 Hz, 4H), 1.24 (t, J = 7.1 Hz, 6H).

^{13}C NMR ($CDCl_3$, 151 MHz) δ 168.7, 149.4, 147.6, 137.1, 129.3, 128.2, 128.0, 124.4, 67.9, 62.3, 13.8.

HRMS calcd for $(C_{18}H_{20}NO_4)^+$ $[M + H]^+$: 314.1387, found 314.1385.

diethyl 2-allyl-2-(pyridin-4-yl)malonate (5al)



Prepared via the above procedure starting from **4h** (0.1 mmol, 57.3 mg, 1.0 equiv) to give diethyl 2-allyl-2-(pyridin-4-yl)malonate (**5al**) as a yellow oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 5:1).

Yield 16.0 mg (58%).

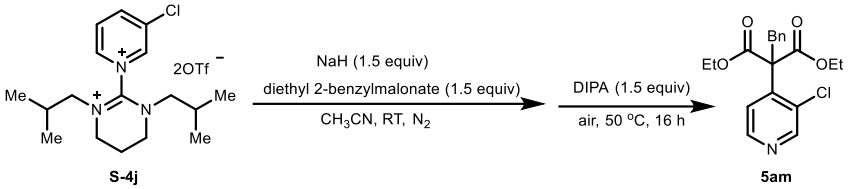
NMR spectroscopy:

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.61 – 8.56 (m, 2H), 7.40 – 7.35 (m, 2H), 5.75 – 5.61 (m, 1H), 5.08 (s, 1H), 5.06 – 5.02 (m, 1H), 4.30 – 4.16 (m, 4H), 3.03 (d, J = 7.1 Hz, 2H), 1.25 (t, J = 7.1 Hz, 6H).

^{13}C NMR ($CDCl_3$, 101 MHz) δ 169.1, 149.5, 149.4, 131.9, 123.3, 119.7, 62.3, 62.0, 40.0, 14.0.

HRMS calcd for $(C_{15}H_{20}NO_4)^+$ $[M + H]^+$: 278.1387, found 278.1386.

diethyl 2-benzyl-2-(3-chloropyridin-4-yl)malonate (5am)



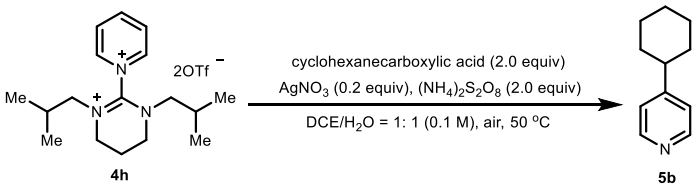
Prepared via the above procedure starting from **S-4j** (60.7 mg, 0.1 mmol, 1.0 equiv) and oxidized at 50 ℃ for 16 h to give diethyl 2-benzyl-2-(3-chloropyridin-4-yl)malonate (**5am**) as a colorless oil.

R_f = 0.5 (eluent: petroleum ether/EtOAc = 5:1).
Yield 20.0 mg (55%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.57 (s, 1H), 8.25 (d, *J* = 5.4 Hz, 1H), 7.17 – 7.04 (m, 4H), 6.91 – 6.84 (m, 2H), 4.35 – 4.20 (m, 4H), 3.75 (s, 2H), 1.26 (t, *J* = 7.2 Hz, 6H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 168.1, 150.2, 146.9, 144.3, 135.4, 130.5, 127.9, 127.0, 125.6, 64.3, 62.5, 39.2, 13.8.
HRMS calcd for $(C_{19}H_{21}ClNO_4)^+$ $[M + H]^+$: 362.1154, found 362.1164.

13. C-4 alkylation with carboxylic acids as the radical precursors [3]

To a 10 mL culture tube equipped with the Teflon septum screw cap and containing a stir bar, the corresponding pyridinium salt (0.2 mmol, 1.0 equiv), carboxylic acid (0.4 mmol, 2.0 equiv, in several substrates the carboxylic acid were used 4.0 equiv), $(NH_4)_2S_2O_8$ (91.3 mg, 0.4 mmol, 2.0 equiv), $AgNO_3$ (6.8 mg, 0.04 mmol, 20 mol%), dichloroethane (1.0 mL) and H_2O (1.0 mL) were added under atmospheric conditions and stirred at 50 ℃ for 10 h. Upon completion, the reaction was neutralized with saturated $NaHCO_3$ aqueous solution (2.0 mL) (pH >8). The crude mixture was diluted by DCM (3.0 mL) and the aqueous phase was extracted with DCM (3 × 3.0 mL). Then the combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. (The reaction mixture was analyzed by GC-MS and crude NMR dissolved in $CDCl_3$. 1, 3, 5-trimethoybenzene (2.7 mg) was used as an internal standard. The C-2 alkylated product was not observed in crude NMR spectroscopy and GC-MS.) The crude material was purified on silica gel chromatography to afford C-4 alkylation pyridine products **5**.

4-cyclohexylpyridine (5b)

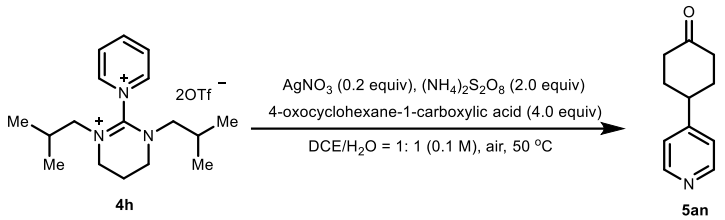


Prepared via the above procedure starting from **4h** (114.6 mg, 0.2 mmol, 1.0 equiv) and cyclohexanecarboxylic acid (51.4 mg, 0.4 mmol, 2.0 equiv) to give 4-

cyclohexylpyridine (**5b**) as a colorless oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 10:1).
Yield 22.6 mg (70%).
The NMR spectroscopy and HRMS data of **5b** has already been written on page S15.

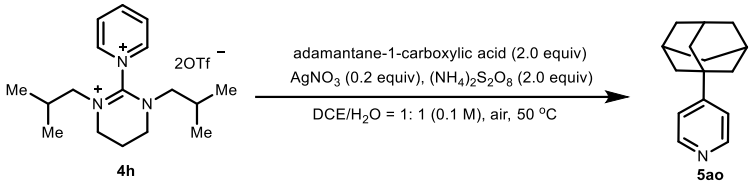
4-(pyridin-4-yl)cyclohexan-1-one (5an)



Prepared via the above procedure starting from **4h** (114.6 mg, 0.2 mmol, 1.0 equiv) and 4-oxocyclohexane-1-carboxylic acid (113.6 mg, 0.8 mmol, 4.0 equiv) to give 4-(pyridin-4-yl)cyclohexan-1-one (**5an**) as a pale yellow oil.

R_f = 0.25 (eluent: petroleum ether/EtOAc = 1:1).
Yield 12.2 mg (35%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.54 (d, *J* = 6.0 Hz, 2H), 7.18 (d, *J* = 6.0 Hz, 2H), 3.02 (tt, *J* = 12.1, 3.3 Hz, 1H), 2.56 – 2.48 (m, 4H), 2.28 – 2.18 (m, 2H), 2.01 – 1.85 (m, 2H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 210.0, 153.8, 149.8, 122.2, 42.0, 41.0, 33.0.
HRMS calcd for $(C_{11}H_{14}NO)^+$ $[M + H]^+$: 176.1070, found 176.1069.

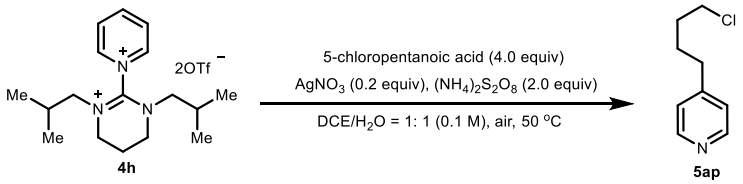
4-(adamantan-1-yl)pyridine (5ao)



Prepared via the above procedure starting from **4h** (114.6 mg, 0.2 mmol, 1.0 equiv) and adamantane-1-carboxylic acid (72.0 mg, 0.4 mmol, 2.0 equiv) to give 4-(adamantan-1-yl)pyridine (**5ao**) as a white solid.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 5:1).
Yield 19.8 mg (46%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.51 (d, *J* = 4.7 Hz, 2H), 7.24 (d, *J* = 6.0 Hz, 2H), 2.14 – 2.07 (br, 3H), 1.88 (d, *J* = 2.3 Hz, 6H), 1.83 – 1.70 (m, 6H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 160.0, 149.6, 120.4, 42.3, 36.6, 36.2, 28.6.
HRMS calcd for $(C_{15}H_{20}N)^+$ $[M + H]^+$: 214.1590, found 214.1589.

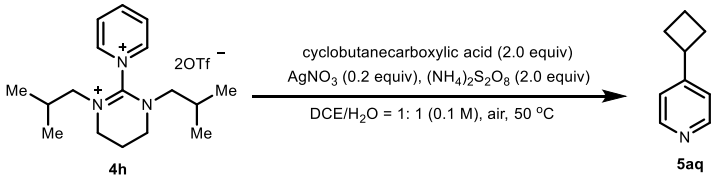
4-(4-chlorobutyl)pyridine (5ap)



Prepared via the above procedure starting from **4h** (114.6 mg, 0.2 mmol, 1.0 equiv) and 5-chloropentanoic acid (109.3 mg, 0.8 mmol, 4.0 equiv) to give 4-(4-chlorobutyl)pyridine (**5ap**) as a pale yellow oil.

R_f = 0.25 (eluent: petroleum ether/EtOAc = 5:1).
Yield 16.3 mg (48%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.49 (d, *J* = 4.9 Hz, 2H), 7.10 (d, *J* = 5.4 Hz, 2H), 3.59 – 3.48 (m, 2H), 2.63 (t, *J* = 7.0 Hz, 2H), 1.84 – 1.72 (m, 4H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 150.7, 149.7, 123.8, 44.6, 34.4, 31.9, 27.4.
HRMS calcd for $(C_9H_{13}ClN)^+$ $[M + H]^+$: 170.0731, found 170.0730.

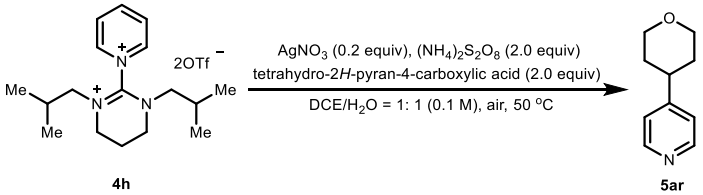
4-cyclobutylpyridine (5aq)



Prepared via the above procedure starting from **4h** (114.6 mg, 0.2 mmol, 1.0 equiv) and cyclobutanecarboxylic acid (40.0 mg, 0.4 mmol, 2.0 equiv) to give 4-cyclobutylpyridine (**5aq**) as a pale-yellow oil. (Due to the product is volatile, the yield of this substrate was determined by crude NMR, 1,3,5-trimethoxybenzene (2.7 mg) as the internal standard.)

R_f = 0.4 (eluent: petroleum ether/EtOAc = 5:1).
Yield 7.2 mg (NMR yield: 56%, isolate yield: 27%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.50 (d, *J* = 5.1 Hz, 2H), 7.16 (d, *J* = 5.8 Hz, 2H), 3.55 (p, *J* = 8.6 Hz, 1H), 2.44 – 2.35 (m, 2H), 2.21 – 2.13 (m, 2H), 2.11 – 2.02 (m, 1H), 1.95 – 1.86 (m, 1H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 155.2, 149.4, 121.8, 39.3, 28.9, 18.4.
HRMS calcd for $(C_9H_{12}N)^+$ $[M + H]^+$: 134.0964, found 134.0965.

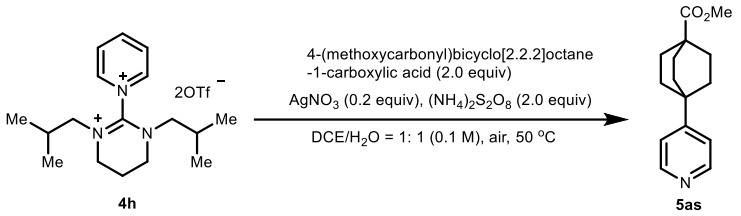
4-(tetrahydro-2*H*-pyran-4-yl)pyridine (5ar)



Prepared via the above procedure starting from **4h** (114.6 mg, 0.2 mmol, 1.0 equiv) and tetrahydro-2*H*-pyran-4-carboxylic acid (52.0 mg, 0.4 mmol, 2.0 equiv) to give 4-(tetrahydro-2*H*-pyran-4-yl)pyridine (**5ar**) as a colorless oil.

R_f = 0.5 (eluent: petroleum ether/EtOAc = 1:1).
Yield 20.0 mg (61%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.53 (d, J = 4.8 Hz, 2H), 7.16 (d, J = 5.6 Hz, 2H), 4.12 – 4.06 (m, 2H), 3.53 (td, J = 11.4, 3.2 Hz, 2H), 2.81 – 2.73 (m, 1H), 1.85 – 1.72 (m, 4H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 154.7, 149.7, 122.3, 68.0, 40.9, 32.9.
HRMS calcd for $(C_{10}H_{14}NO)^+$ $[M + H]^+$: 164.1070, found 164.1069.

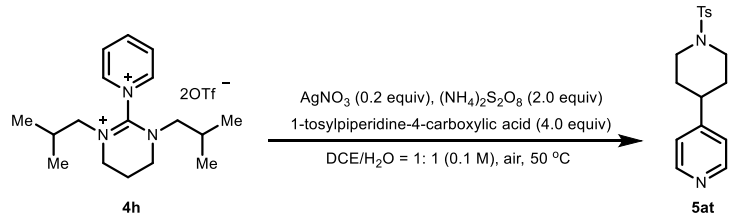
methyl 4-(pyridin-4-yl)bicyclo[2.2.2]octane-1-carboxylate (5as)



Prepared via the above procedure starting from **4h** (114.6 mg, 0.2 mmol, 1.0 equiv) and 4-(methoxycarbonyl)bicyclo[2.2.2]octane-1-carboxylic acid (84.8 mg, 0.4 mmol, 2.0 equiv) to give methyl 4-(pyridin-4-yl)bicyclo[2.2.2]octane-1-carboxylate (**5as**) as a white solid.

R_f = 0.6 (eluent: petroleum ether/EtOAc = 2:1).
Yield 31.2 mg (64%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.49 (d, J = 5.1 Hz, 2H), 7.20 (d, J = 5.7 Hz, 2H), 3.67 (s, 3H), 1.96 – 1.88 (m, 6H), 1.87 – 1.79 (m, 6H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 178.0, 158.2, 149.5, 121.0, 51.8, 39.0, 34.8, 31.1, 28.5.
HRMS calcd for $(C_{15}H_{20}NO_2)^+$ $[M + H]^+$: 246.1489, found 246.1487.

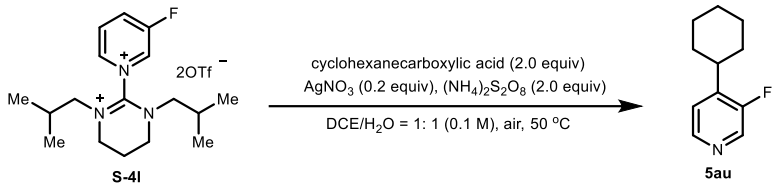
4-(1-tosylpiperidin-4-yl)pyridine (5at)



Prepared via the above procedure starting from **4h** (114.6 mg, 0.2 mmol, 1.0 equiv) and 1-tosylpiperidine-4-carboxylic acid (226.4 mg, 0.8 mmol, 4.0 equiv) to give 4-(1-tosylpiperidin-4-yl)pyridine (**5at**) as a white solid.

R_f = 0.6 (eluent: pure EtOAc).
Yield 21.1 mg (33%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.50 (d, *J* = 3.9 Hz, 2H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 5.4 Hz, 2H), 3.93 (d, *J* = 11.8 Hz, 2H), 2.44 (s, 3H), 2.34 (td, *J* = 12.0, 2.9 Hz, 2H), 1.95 – 1.75 (m, 5H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 153.5, 150.1, 143.6, 133.2, 129.7, 127.8, 122.1, 46.5, 41.1, 31.7, 21.5.
HRMS calcd for $(C_{17}H_{21}N_2O_2S)^+$ $[M + H]^+$: 317.1318, found 317.1319.

4-cyclohexyl-3-fluoropyridine (5au)

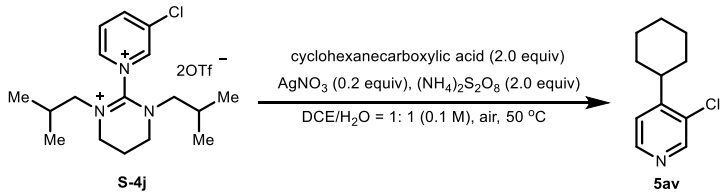


S-4l 5au

Prepared via the above procedure starting from **S-4l** (118.2 mg, 0.2 mmol, 1.0 equiv) and cyclohexanecarboxylic acid (51.4 mg, 0.4 mmol, 2.0 equiv) to give 4-cyclohexyl-3-fluoropyridine (**5au**) as a colorless oil.

R_f = 0.5 (eluent: petroleum ether/EtOAc = 10:1).
Yield 24.2 mg (68%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.34 (s, 1H), 8.31 (d, *J* = 5.5 Hz, 1H), 7.16 (t, *J* = 5.5 Hz, 1H), 2.86 (t, *J* = 8.7 Hz, 1H), 1.89 – 1.81 (m, 4H), 1.79 – 1.73 (m, 1H), 1.46 – 1.36 (m, 4H), 1.28 – 1.22 (m, 1H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 157.9 (d, *J* = 250.7 Hz), 145.7 (d, *J* = 4.5 Hz), 143.0 (d, *J* = 12.1 Hz), 137.6 (d, *J* = 25.7 Hz), 122.3, 36.8, 32.2, 26.4, 25.9.
^{19}F NMR ($CDCl_3$, 565 MHz) δ -133.7.
HRMS calcd for $(C_{11}H_{15}FN)^+$ $[M + H]^+$: 180.1183, found 180.1182.

3-chloro-4-cyclohexylpyridine (5av)



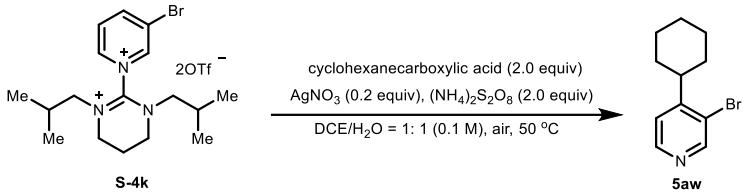
S-4j 5av

Prepared via the above procedure starting from **S-4j** (121.4 mg, 0.2 mmol, 1.0 equiv) and cyclohexanecarboxylic acid (51.4 mg, 0.4 mmol, 2.0 equiv) to give 3-chloro-4-cyclohexylpyridine (**5av**) as a pale-yellow oil.

R_f = 0.6 (eluent: petroleum ether/EtOAc = 10:1).
Yield 17.9 mg (46%).
NMR spectroscopy:

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.48 (s, 1H), 8.38 (d, *J* = 5.1 Hz, 1H), 7.15 (d, *J* = 5.1 Hz, 1H), 3.01 – 2.90 (m, 1H), 1.89 – 1.82 (m, 4H), 1.81 – 1.73 (m, 1H), 1.50 – 1.17 (m, 5H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 153.3, 149.3, 147.9, 131.6, 121.9, 40.1, 32.2, 26.5, 26.0.
HRMS calcd for $(C_{11}H_{15}ClN)^+$ $[M + H]^+$: 196.0888, found 196.0887.

3-bromo-4-cyclohexylpyridine (5aw)



S-4k 5aw

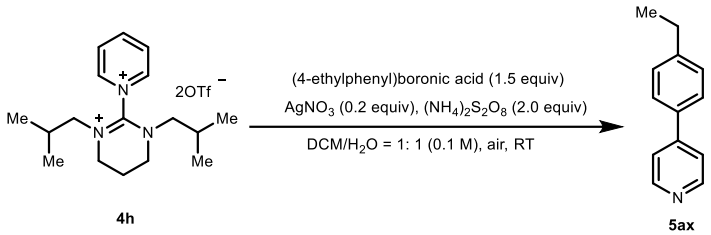
Prepared via the above procedure starting from **S-4k** (130.2 mg, 0.2 mmol, 1.0 equiv) and cyclohexanecarboxylic acid (51.4 mg, 0.4 mmol, 2.0 equiv) to give 3-bromo-4-cyclohexylpyridine (**5aw**) as a pale-yellow oil.

R_f = 0.6 (eluent: petroleum ether/EtOAc = 10:1).
Yield 23.6 mg (49%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.64 (s, 1H), 8.52 – 8.31 (br, 1H), 7.22 – 7.06 (br, 1H), 2.91 (tt, *J* = 11.3, 2.6 Hz, 1H), 1,92 – 1.82 (m, 4H), 1.81 – 1.72 (m, 1H), 1.50 – 1.18 (m, 5H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 154.9, 151.9, 148.5, 123.1 (low signal), 122.4, 42.9, 32.3, 26.5, 26.0.
HRMS calcd for $(C_{11}H_{15}BrN)^+$ $[M + H]^+$: 240.0383, found 240.0381.

14. C-4 arylation with aryl boronic acids as the radical precursors

Following the known literature procedure for borono-minisci reaction [4], to a 10 mL culture tube equipped with the screw cap and magnetic stir bar, the pyridinium salt **4h** (114.6 mg, 0.2 mmol, 1.0 equiv), 4-substituted aryl-boronic acid (0.3 mmol, 1.5 equiv), $(NH_4)_2S_2O_8$ (91.3 mg, 0.4 mmol, 2.0 equiv) and $AgNO_3$ (6.8 mg, 0.04 mmol, 20 mol%) were added, together with dichloromethane (1.0 mL) and H_2O (1.0 mL) under atmospheric conditions and stirred at room temperature for 10 h. Upon completion, the reaction was neutralized with saturated $NaHCO_3$ aqueous solution (2.0 mL) (pH >8). The crude mixture was diluted by DCM (3.0 mL) and the aqueous phase was extracted with DCM (3 × 3.0 mL). Then the combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was purified on silica gel chromatography to afford C-4 arylation pyridine products **5** as a white solid. 1, 3, 5-trimethoybenzene (2.7 mg) was used as an internal standard. The desired C-4 arylation product **5** was observed in GC-MS. The products of C-2 arylation can be observed in crude GC-MS at a ratio of less than 1:35 (C-2/C-4).

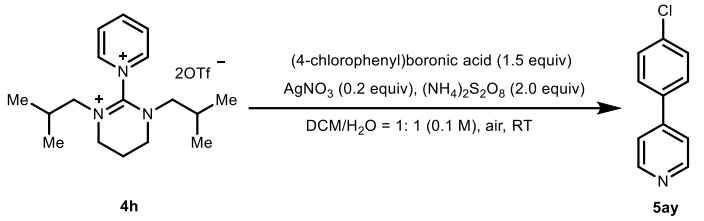
4-(4-ethylphenyl)pyridine (5ax)



Prepared via the above procedure starting from (4-ethylphenyl)boronic acid (45.0 mg, 0.3 mmol, 1.5 equiv) to give 4-(4-ethylphenyl)pyridine (**5ax**) as a white solid.

R_f = 0.6 (eluent: petroleum ether/EtOAc = 5:1).
Yield 23.1 mg (63%, GC-MS: C4/C2 = 61.8/1).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.63 (d, *J* = 5.5 Hz, 2H), 7.57 (d, *J* = 8.1 Hz, 2H), 7.49 (d, *J* = 5.8 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 2.71 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 7.6 Hz, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 150.1, 148.4, 145.6, 135.4, 128.7, 126.9, 121.5, 28.6, 15.5.
HRMS calcd for $(C_{13}H_{14}N)^+$ $[M + H]^+$: 184.1121, found 184.1120.

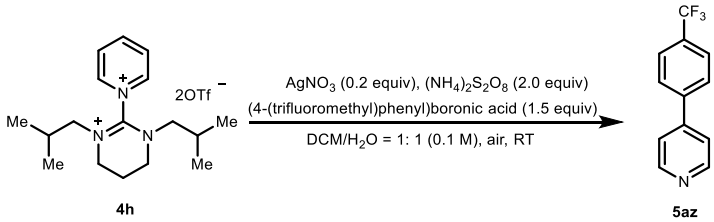
4-(4-chlorophenyl)pyridine (5ay)



Prepared via the above procedure starting from (4-chlorophenyl)boronic acid (46.8 mg, 0.3 mmol, 1.5 equiv) to give 4-(4-chlorophenyl)pyridine (**5ay**) as a white solid.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 4:1).
Yield 29.6 mg (78%, GC-MS: C4/C2 = 67.7/1).
The NMR spectroscopy and HRMS data of **5ay** are the same as **5**h

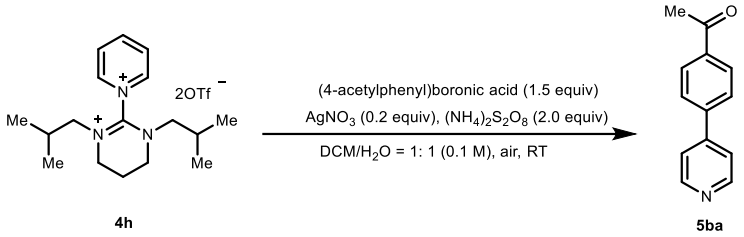
4-(4-(trifluoromethyl)phenyl)pyridine (5az)



Prepared via the above procedure starting from (4-(trifluoromethyl)phenyl)boronic acid (57.0 mg, 0.3 mmol, 1.0 equiv) to give 4-(4-(trifluoromethyl)phenyl)pyridine (**5az**) as a white solid.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 5:1).
Yield 34.0 mg (76%, GC-MS: C4/C2 = 35.7/1).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.70 (d, *J* = 6.1 Hz, 2H), 7.77 – 7.70 (m, 4H), 7.51 (d, *J* = 6.1 Hz, 2H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 150.4, 147.0, 141.7, 131.1 (q, *J* = 33.2 Hz), 127.5, 126.1 (q, *J* = 3.0 Hz), 124.0 (q, *J* = 271.8 Hz), 121.8.
^{19}F NMR ($CDCl_3$, 377 MHz) δ -62.7.
HRMS calcd for $(C_{12}H_9F_3N)^+$ $[M + H]^+$: 224.0682, found 224.0680.

1-(4-(pyridin-4-yl)phenyl)ethan-1-one (5ba)

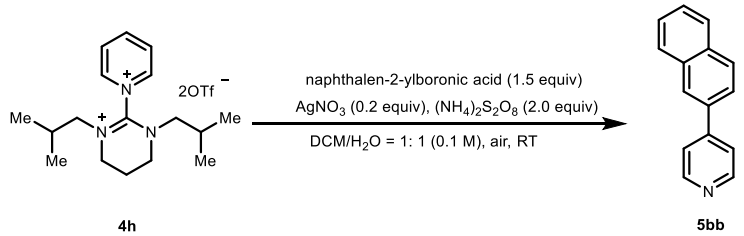


4h 5ba

Prepared via the above procedure starting from (4-acetylphenyl)boronic acid (49.2 mg, 0.3 mmol, 1.5 equiv) to give 1-(4-(pyridin-4-yl)phenyl)ethan-1-one (**5ba**) as a white solid.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 1:1).
Yield 25.4 mg (64%, GC-MS: C4/C2 > 99/1).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.70 (d, *J* = 5.2 Hz, 2H), 8.06 (d, *J* = 8.3 Hz, 2H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.53 (d, *J* = 5.7 Hz, 2H), 2.64 (s, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 197.5, 150.3, 147.2, 142.5, 137.3, 129.1, 127.3, 121.7, 26.7.
HRMS calcd for $(C_{13}H_{12}NO)^+$ $[M + H]^+$: 198.0913, found 198.0912.

4-(naphthalen-2-yl)pyridine (5bb)



4h 5bb

Prepared via the above procedure starting from naphthalen-2-ylboronic acid (51.6 mg, 0.3 mmol, 1.0 equiv) to give 4-(naphthalen-2-yl)pyridine (**5bb**) as a pale yellow solid.

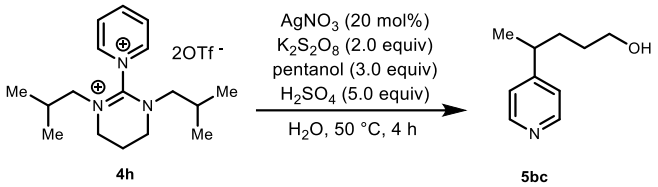
R_f = 0.5 (eluent: petroleum ether/EtOAc = 5:1).
Yield 24.6 mg (60%, GC-MS: C-4/C-2 > 99/1).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.70 (d, *J* = 6.0 Hz, 2H), 8.12 (s, 1H), 7.96 (d, *J* = 8.5

Hz, 1H), 7.94 – 7.90 (m, 1H), 7.90 – 7.85 (m, 1H), 7.74 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.64 (d, *J* = 6.1 Hz, 2H), 7.58 – 7.47 (m, 2H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 150.2, 148.4, 135.3, 133.5, 129.0, 128.5, 127.8, 126.9, 126.8, 126.5, 124.5, 121.9.
HRMS calcd for $(C_{15}H_{12}N)^+$ $[M + H]^+$: 206.0964, found 206.0963.

15. C-4 alkylation with functionalized alkanes as the radical precursors

A 25 mL Schlenk tube with the screw-cap was added silver nitrate (0.04 mmol, 0.2 equiv, 6.8 mg), $K_2S_2O_8$ (0.4 mmol, 2.0 equiv, 108.0 mg) and pyridine salt (0.2 mmol, 1.0 equiv, 114.6 mg). After sealing with a screw-cap, the tube was evacuated and back-filled with nitrogen three times. Then, water (1.0 mL), H_2SO_4 (18.4 mol/L, 1.0 mmol, 5.0 equiv, 54.0 μL) and alcohols (0.6 mmol, 3.0 equiv) were added consecutively. The resulting mixture was stirred at 50 ℃ using an oil bath for 4 h, after which saturated $NaHCO_3$ solution was added until the pH of the solution was above 8. Then, EtOAc (5.0 mL) was added and mixed to obtain a biphasic mixture. After that, the organic phase was separated and collected, while the aqueous phase was extracted three more times with EtOAc (3 × 5.0 mL). The organic phase was combined, dried over Na_2SO_4 and then concentrated under reduced pressure. The resulting crude mixture was purified by column chromatography on silica gel to afford C-4 alkylation pyridine products as a pale-yellow oil.

4-(pyridin-4-yl)pentan-1-ol (5bc)

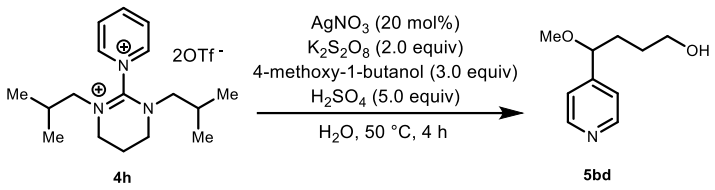


4h 5bc

Prepared via the above procedure starting from pentanol (52.8 mg, 0.6 mmol, 3.0 equiv) to give 4-(pyridin-4-yl)pentan-1-ol (**5bc**) as a pale yellow oil.

R_f = 0.3 (eluent: EtOAc)
Yeild 16.8 mg (51%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.46 (br, 2H), 7.11 (d, *J* = 5.1 Hz, 2H), 3.60 (t, *J* = 6.5 Hz, 2H), 2.76 – 2.64 (m, 1H), 2.23 (br, 1H), 1.69 – 1.62 (m, 2H), 1.57 – 1.46 (m, 1H), 1.46 – 1.35 (m, 1H), 1.25 (d, *J* = 6.9 Hz, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 156.6, 149.5, 123.0 (*low signal*), 62.5, 39.3, 33.7, 30.7, 21.5.
HRMS calcd for $(C_{10}H_{16}NO)^+$ $[M + H]^+$: 166.1226, found 166.1225.

4-methoxy-4-(pyridin-4-yl)butan-1-ol (5bd)

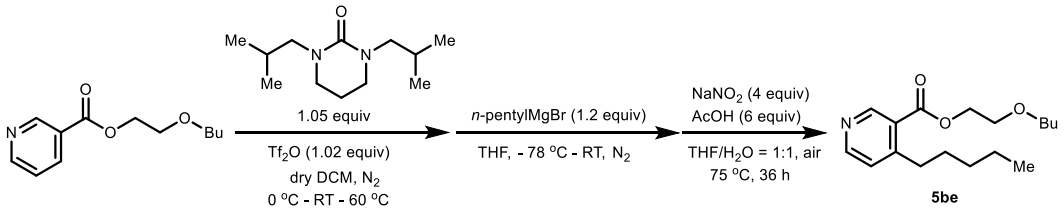


Prepared via the above procedure starting from 4-methoxy-1-butanol (62.4 mg, 0.6 mmol, 3.0 equiv) to give 4-methoxy-4-(pyridin-4-yl)butan-1-ol (**5bd**) as a pale yellow oil.

R_f = 0.2 (eluent: DCM/MeOH = 30:1)
Yeild 11.7 mg (32%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.56 (d, *J* = 5.9 Hz, 2H), 7.43 (d, *J* = 6.0 Hz, 2H), 4.29 (t, *J* = 6.2 Hz, 1H), 3.66 (t, *J* = 6.1 Hz, 2H), 3.29 (s, 3H), 1.83 – 1.75 (m, 2H), 1.66 – 1.63 (m, 2H). (*There is one less signal of active hydrogen on the hydroxyl group*)
^{13}C NMR ($CDCl_3$, 101 MHz) δ 151.7, 149.6, 121.7, 82.7, 62.5, 57.2, 34.4, 28.8.
HRMS calcd for $(C_{10}H_{16}NO_2)^+$ $[M + H]^+$: 182.1176, found 182.1175.

16. Late-stage functionalization of drug-like molecules.

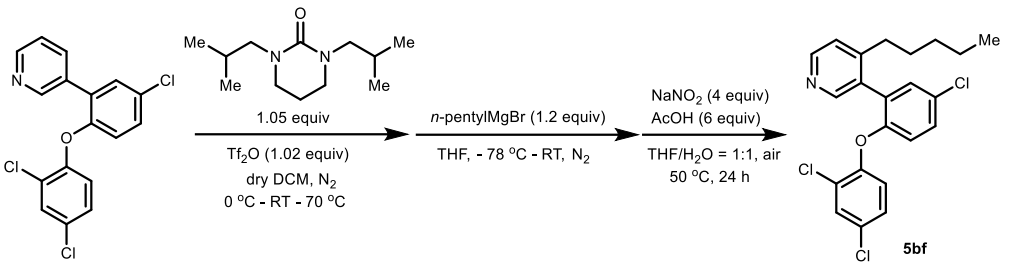
2-butoxyethyl 4-pentylnicotinate (5be)



Prepared via **General Procedure III** starting from 2-butoxyethyl nicotinate (223.1 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 75 ℃ for 36 h to give 2-butoxyethyl 4-pentylnicotinate (**5be**) as a yellow oil.

R_f = 0.2 (eluent: petroleum ether/EtOAc = 10:1).
Yield 109.3 mg (37%, 44.8 mg starting material, 47% b.r.s.m).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.04 (s, 1H), 8.55 (d, *J* = 4.5 Hz, 1H), 7.17 (d, *J* = 5.1 Hz, 1H), 4.51 – 4.42 (m, 2H), 3.78 – 3.68 (m, 2H), 3.49 (t, *J* = 6.6 Hz, 2H), 2.98 – 2.90 (m, 2H), 1.66 – 1.50 (m, 4H), 1.44 – 1.28 (m, 6H), 0.90 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 166.2, 153.9, 152.1, 151.7, 125.7, 125.4, 71.3, 68.5, 64.4, 33.7, 31.8, 31.7, 30.5, 22.5, 19.3, 14.0, 13.9.
HRMS calcd for $(C_{17}H_{28}NO_3)^+$ $[M + H]^+$: 294.2064, found 294.2062.

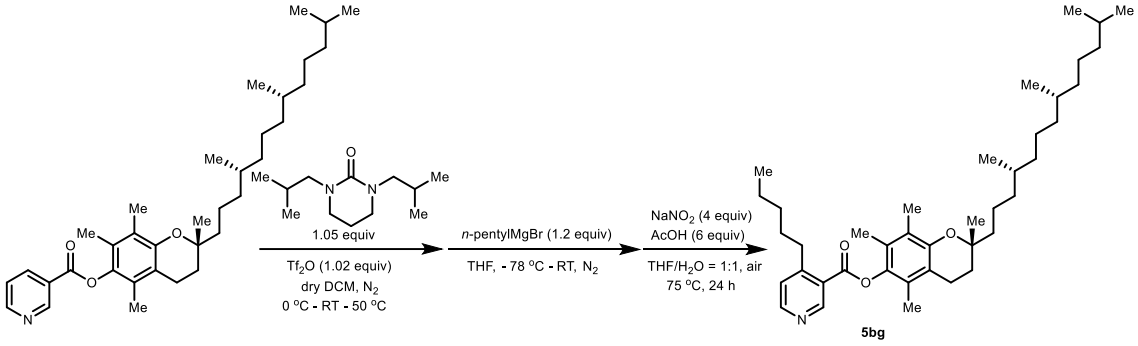
3-(5-chloro-2-(2,4-dichlorophenoxy)phenyl)-4-pentylpyridine (5bf)



Prepared via **General Procedure III** starting from 3-(5-chloro-2-(2,4-dichlorophenoxy)phenyl)pyridine (349.0 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 50 ℃ for 24 h to give 3-(5-chloro-2-(2,4-dichlorophenoxy)phenyl)-4-pentylpyridine (**5bf**) as a yellow oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 10:1).
Yield 194.4 mg (46%, 24.6 mg starting material, 49% b.r.s.m).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.46 (d, *J* = 5.0 Hz, 1H), 8.36 (s, 1H), 7.34 (s, 1H), 7.32 (d, *J* = 4.0 Hz, 1H), 7.28 (s, 1H), 7.20 (d, *J* = 5.1 Hz, 1H), 7.12 (d, *J* = 8.7 Hz, 1H), 6.81 – 6.74 (m, 2H), 2.60 (t, *J* = 8.2 Hz, 2H), 1.59 – 1.45 (m, 2H), 1.29 – 1.12 (m, 4H), 0.83 (t, *J* = 6.4 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 152.4, 150.7, 150.5, 150.0, 149.2, 131.9, 131.7, 130.7, 130.5, 129.48, 129.47, 129.0, 128.0, 126.2, 123.5, 120.7, 118.8, 32.6, 31.5, 29.3, 22.3, 13.9.
HRMS calcd for $(C_{22}H_{21}Cl_3NO)^+$ $[M + H]^+$: 420.0683, found 420.0678.

(*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl 4-pentylnicotinate (5bg)

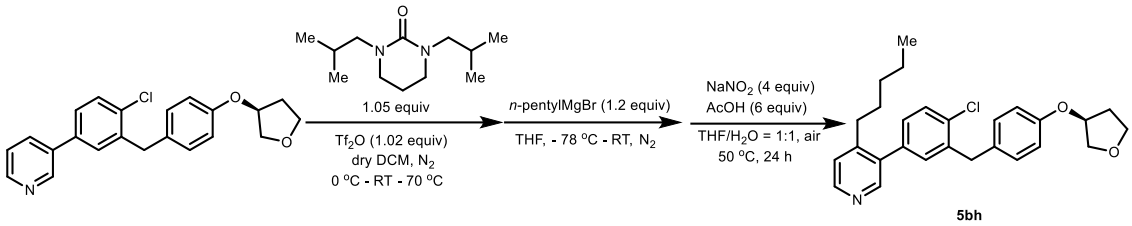


Prepared via **General Procedure III** starting from (*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl nicotinate (535.4 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 75 ℃ for 24 h to give (*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl 4-pentylnicotinate (**5bg**) as a pale yellow oil.

R_f = 0.5 (eluent: petroleum ether/EtOAc = 10:1).
Yield 208.3 mg (34%, 203.5 mg starting material, 55% b.r.s.m).
NMR spectroscopy:

^{1}H NMR (Actone-d_6, 600 MHz) δ 9.32 (s, 1H), 8.68 (d, J = 5.1 Hz, 1H), 7.43 (d, J = 5.1 Hz, 1H), 3.11 – 3.05 (m, 2H), 2.67 (t, J = 6.7 Hz, 2H), 2.13 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 1.91 – 1.76 (m, 2H), 1.69 – 1.50 (m, 7H), 1.48 – 1.30 (m, 14H), 1.28 (s, 3H), 1.20 – 1.08 (m, 6H), 0.95 – 0.83 (m, 15H).
^{13}C NMR (Actone-d_6, 151 MHz) δ 165.2, 155.3, 153.9, 152.7, 150.5, 141.8, 127.8, 126.9, 126.3, 126.0, 123.7, 118.8, 76.1, 40.4, 38.6, 38.5, 38.42, 38.35, 38.3, 34.4, 33.74, 33.66, 32.8, 32.1, 31.9, 28.9, 25.8, 25.4, 25.3, 23.4, 23.3, 23.2, 22.0, 21.4, 20.4, 20.3, 14.5, 13.6, 12.8, 12.3.
HRMS calcd for $(C_{40}H_{64}NO_3)^+$ $[M + H]^+$: 606.4881, found 606.4872.

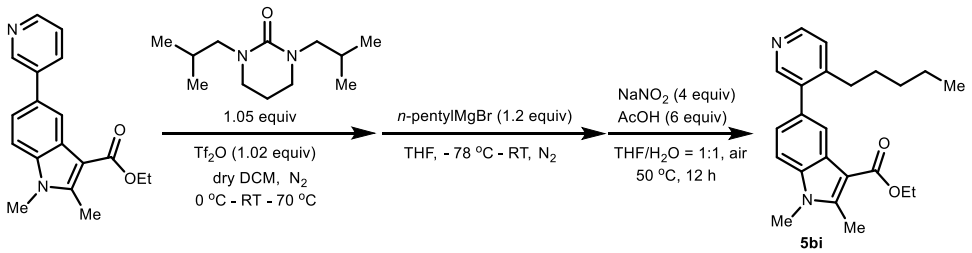
(*S*)-3-(4-chloro-3-(4-((tetrahydrofuran-3-yl)oxy)benzyl)phenyl)-4-pentylpyridine (5bh)



Prepared via **General Procedure III** starting from (*S*)-3-(4-chloro-3-(4-((tetrahydrofuran-3-yl)oxy)benzyl)phenyl)pyridine (365.1 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 50 °C for 24 h to give (*S*)-3-(4-chloro-3-(4-((tetrahydrofuran-3-yl)oxy)benzyl)phenyl)-4-pentylpyridine (**5bh**) as a pale yellow oil.

R_f = 0.6 (eluent: petroleum ether/EtOAc = 2:1).
Yield 245.9 mg (57%, 131.2 mg starting material, 89% b.r.s.m).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.46 (d, J = 4.3 Hz, 1H), 8.34 (s, 1H), 7.44 (d, J = 8.1 Hz, 1H), 7.17 (d, J = 4.8 Hz, 1H), 7.11 (d, J = 8.3 Hz, 2H), 7.09 (d, J = 9.2 Hz, 1H), 7.06 (s, 1H), 6.78 (d, J = 8.3 Hz, 2H), 4.90 – 4.86 (m, 1H), 4.08 (s, 2H), 4.03 – 3.93 (m, 3H), 3.91 – 3.70 (m, 1H), 2.55 – 2.42 (m, 2H), 2.22 – 2.09 (m, 2H), 1.43 (p, J = 7.5 Hz, 2H), 1.24 – 1.12 (m, 4H), 0.82 (t, J = 7.0 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 156.0, 150.0, 149.2, 148.6, 139.2, 136.7, 136.5, 133.7, 131.8, 131.5, 130.0, 129.5, 128.5, 124.0, 115.4, 77.3, 73.1, 67.2, 38.3, 33.0, 32.3, 31.5, 29.9, 22.3, 13.9.
HRMS calcd for $(C_{27}H_{31}ClNO_2)^+$ $[M + H]^+$: 436.2038, found 436.2034.

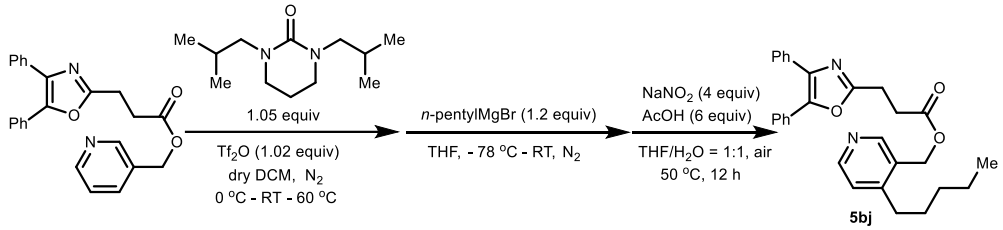
ethyl 1,2-dimethyl-5-(4-pentylpyridin-3-yl)-1*H*-indole-3-carboxylate (5bi)



Prepared via **General Procedure III** starting from ethyl 1,2-dimethyl-5-(pyridin-3-yl)-1*H*-indole-3-carboxylate (294.1 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 50 ℃ for 12 h to give ethyl 1,2-dimethyl-5-(4-pentylpyridin-3-yl)-1*H*-indole-3-carboxylate (**5bi**) as a white solid.

R_f = 0.6 (eluent: petroleum ether/EtOAc = 2:1).
Yield 171.3 mg (47%, 94.1 mg starting material, 69% b.r.s.m).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.48 (s, 1H), 8.47 (d, *J* = 5.2 Hz, 1H), 8.06 (s, 1H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.21 (d, *J* = 5.1 Hz, 1H), 7.15 (dd, *J* = 8.3, 1.5 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.73 (s, 3H), 2.79 (s, 3H), 2.73 – 2.51 (m, 2H), 1.52 (p, *J* = 7.4 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.23 – 1.06 (m, 4H), 0.78 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 166.0, 150.7, 149.5, 147.9, 146.0, 138.7, 135.9, 131.4, 126.6, 123.8, 123.5, 122.3, 108.9, 104.2, 59.4, 32.4, 31.5, 30.0, 29.7, 22.3, 14.7, 13.9, 11.9.
HRMS calcd for $(C_{23}H_{29}N_2O_2)^+$ $[M + H]^+$: 365.2224, found 365.2221.

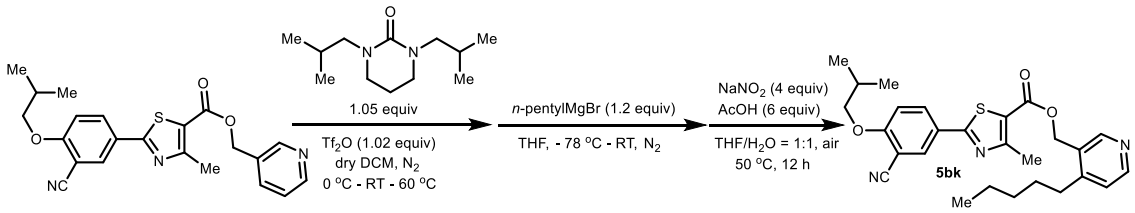
(4-pentylpyridin-3-yl)methyl 3-(4,5-diphenyloxazol-2-yl)propanoate (5bj)



Prepared via **General Procedure III** starting from pyridin-3-ylmethyl 3-(4,5-diphenyloxazol-2-yl)propanoate (384.1 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 50 ℃ for 12 h to give (4-pentylpyridin-3-yl)methyl 3-(4,5-diphenyloxazol-2-yl)propanoate (**5bj**) as a yellow oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 3:1).
Yield 123.8 mg (27%, 160.0 mg starting material, 47% b.r.s.m).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.53 (s, 1H), 8.46 (d, *J* = 5.0 Hz, 1H), 7.60 (d, *J* = 7.0 Hz, 2H), 7.54 (d, *J* = 6.9 Hz, 2H), 7.40 – 7.27 (m, 6H), 7.11 (d, *J* = 5.0 Hz, 1H), 5.21 (s, 2H), 3.19 (t, *J* = 7.5 Hz, 2H), 2.95 (t, *J* = 7.5 Hz, 2H), 2.65 – 2.51 (m, 2H), 1.66 – 1.54 (m, 2H), 1.34 – 1.28 (m, 4H), 0.88 (t, *J* = 6.6 Hz, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 171.7, 161.5, 151.2, 150.8, 150.0, 145.5, 135.2, 132.4, 129.3, 129.0, 128.7, 128.6, 128.5, 128.1, 127.9, 126.5, 124.1, 62.2, 31.8, 31.7, 31.1, 29.9, 23.5, 22.5, 14.0.
HRMS calcd for $(C_{29}H_{31}N_2O_3)^+$ $[M + H]^+$: 455.2329, found 455.2325.

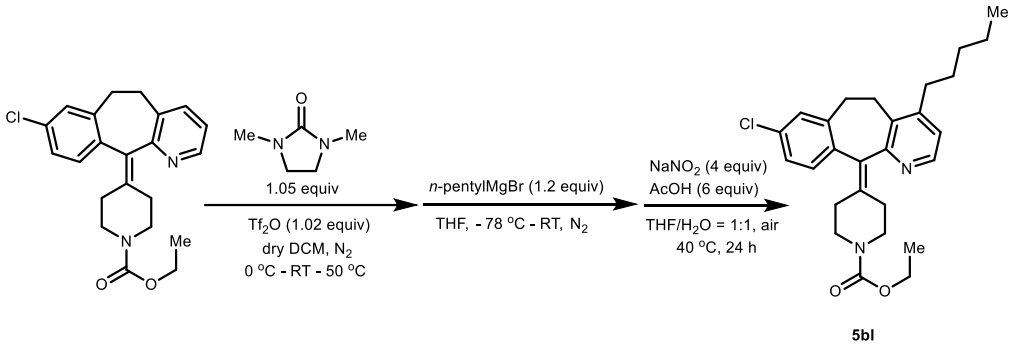
(4-pentylpyridin-3-yl)methyl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate (5bk)



Prepared via **General Procedure III** starting from pyridin-3-ylmethyl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate (407.1 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 50 ℃ for 12 h to give (4-pentylpyridin-3-yl) methyl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate (**5bk**) as a white solid.

R$_f$ = 0.3 (eluent: petroleum ether/EtOAc = 2:1).
Yield 120.7 mg (25%, 204.8 mg starting material, 50% b.r.s.m).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.62 (s, 1H), 8.51 (d, *J* = 4.9 Hz, 1H), 8.16 (d, *J* = 1.9 Hz, 1H), 8.06 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.19 (d, *J* = 4.9 Hz, 1H), 7.00 (d, *J* = 8.9 Hz, 1H), 5.38 (s, 2H), 3.89 (d, *J* = 6.4 Hz, 2H), 2.76 (s, 3H), 2.74 – 2.68 (m, 2H), 2.25 – 2.15 (m, 1H), 1.68 – 1.58 (m, 2H), 1.38 – 1.28 (m, 4H), 1.08 (d, *J* = 6.7 Hz, 6H), 0.89 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 167.6, 162.6, 162.1, 161.6, 151.5, 150.5, 149.8, 132.6, 132.1, 129.2, 125.9, 124.2, 120.9, 115.3, 112.7, 103.1, 75.7, 62.4, 31.9, 31.7, 29.9, 28.2, 22.5, 19.0, 17.6, 14.0.
HRMS calcd for $(C_{27}H_{32}N_3O_3S)^+$ $[M + H]^+$: 478.2159, found 478.2153.

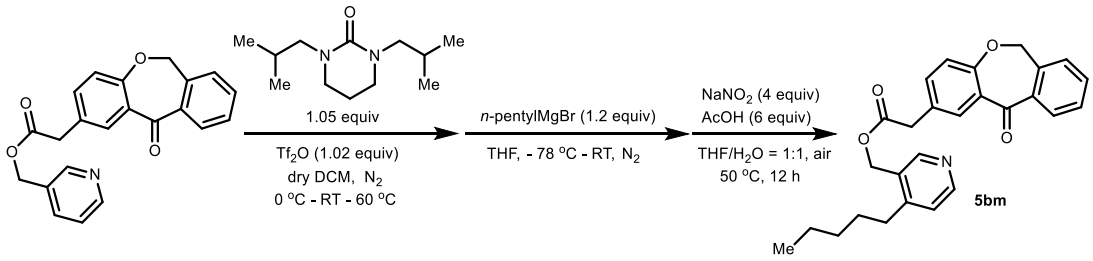
ethyl 4-(8-chloro-4-pentyl-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (5bl)



Prepared via **General Procedure III** starting from 1,3-dimethylimidazolidin-2-one (119.7 mg, 1.05 mmol, 1.05 equiv), ethyl 4-(8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (382.1 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 40 ℃ for 24 h to give ethyl 4-(8-chloro-4-pentyl-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (**5bl**) as a pale yellow oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 2:1).
Yield 261.4 mg (58%, 75.7 mg starting material, 72% b.r.s.m).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.24 (d, *J* = 5.0 Hz, 1H), 7.13 – 7.01 (m, 3H), 6.93 (d, *J* = 5.0 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.83 – 3.69 (br, 2H), 3.42 – 3.32 (m, 1H), 3.24 – 3.04 (m, 3H), 2.95 – 2.85 (m, 1H), 2.83 – 2.72 (m, 1H), 2.60 – 2.51 (m, 2H), 2.42 – 2.30 (m, 3H), 2.24 – 2.14 (m, 1H), 1.60 – 1.47 (m, 2H), 1.37 – 1.28 (m, 4H), 1.20 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 6.7 Hz, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 158.4, 155.5, 149.9, 146.5, 139.2, 136.7, 136.4, 134.8, 132.8, 131.5, 130.9, 129.4, 126.0, 123.0, 61.3, *44.8, 44.7 (both carbons in the nitrogen ortho position on the piperidine ring have signals),* 32.5, 31.9, 31.8, 30.6, 29.6, 26.5, 22.5, 14.7, 14.0.
HRMS calcd for $(C_{27}H_{34}ClN_2O_2)^+$ $[M + H]^+$: 453.2304, found 453.2302.

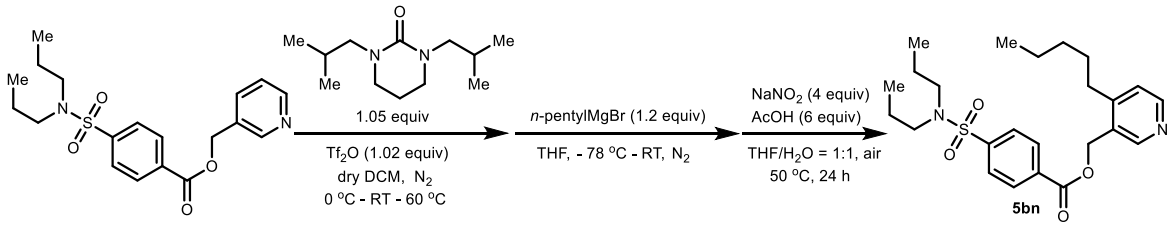
pyridin-3-ylmethyl 2-(11-oxo-6,11-dihydrodibenzo[*b*,*e*]oxepin-2-yl)acetate (5bm)



Prepared via **General Procedure III** starting from pyridin-3-ylmethyl 2-(11-oxo-6,11-dihydrodibenzo[*b*,*e*]oxepin-2-yl)acetate (359.1 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 50 °C for 12 h to give (4-pentylpyridin-3-yl)methyl 2-(11-oxo-6,11-dihydrodibenzo[*b*,*e*]oxepin-2-yl)acetate **(5bm)** as a pale yellow oil.

R_f = 0.4 (eluent: petroleum ether/EtOAc = 2:1).
Yield 120.1 mg (28%, 165.1 mg starting material, 52% b.r.s.m).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.49 (s, 1H), 8.45 (d, *J* = 5.0 Hz, 1H), 8.09 (d, *J* = 2.3 Hz, 1H), 7.89 – 7.83 (m, 1H), 7.54 (td, *J* = 7.4, 1.3 Hz, 1H), 7.45 (td, *J* = 7.6, 1.1 Hz, 1H), 7.39 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.34 (d, *J* = 7.4 Hz, 1H), 7.12 (d, *J* = 5.1 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 5.17 (s, 2H), 5.16 (s, 2H), 3.66 (s, 2H), 2.65 – 2.54 (m, 2H), 1.62 – 1.51 (m, 2H), 1.35 – 1.24 (m, 4H), 0.91 – 0.78 (m, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 190.7, 171.0, 160.6, 151.2, 150.5, 149.8, 140.4, 136.2, 135.5, 132.8, 132.5, 129.5, 129.30, 129.27, 127.8, 127.4, 125.2, 124.0, 121.2, 73.6, 62.3, 40.1, 31.7, 31.6, 29.7, 22.5, 13.9.
HRMS calcd for $(C_{27}H_{28}NO_4)^+$ $[M + H]^+$: 430.2013, found 430.2003.

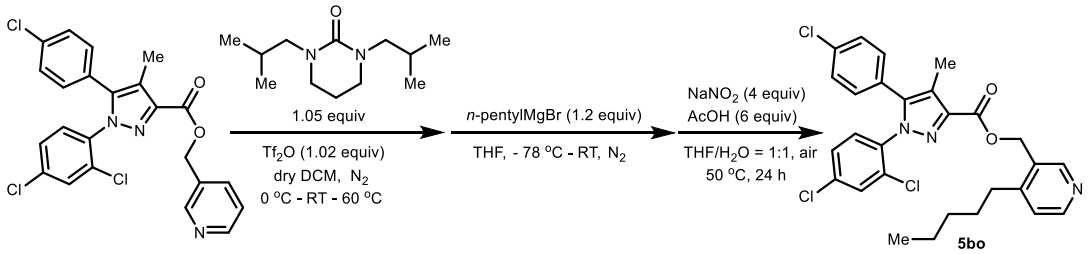
(4-pentylpyridin-3-yl)methyl 4-(*N*,*N*-dipropylsulfamoyl)benzoate (5bn)



Prepared via **General Procedure III** starting from pyridin-3-ylmethyl 4-(*N*,*N*-dipropylsulfamoyl)benzoate (376.1 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 50 ℃ for 12 h to give (4-pentylpyridin-3-yl)methyl 4-(*N*,*N*-dipropylsulfamoyl)benzoate (**5bn**) as a yellow oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 3:1).
Yield 177.1 mg (40%, 141.6 mg starting material, 64% b.r.s.m).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.62 (s, 1H), 8.50 (d, *J* = 5.0 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 2H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 5.1 Hz, 1H), 5.43 (s, 2H), 3.12 – 3.04 (m, 4H), 2.73 – 2.66 (m, 2H), 1.67 – 1.57 (m, 2H), 1.56 – 1.46 (m, 4H), 1.36 – 1.26 (m, 4H), 0.84 (t, *J* = 7.4 Hz, 9H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 165.0, 151.4, 150.9, 150.1, 144.7, 133.1, 130.4, 129.2, 127.2, 124.3, 62.9, 50.0, 32.0, 31.8, 30.1, 22.6, 22.0, 14.0, 11.2.
HRMS calcd for $(C_{24}H_{35}N_2O_4S)^+$ $[M + H]^+$: 447.2312, found 447.2309.

(4-pentylpyridin-3-yl)methyl 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1*H*-pyrazole-3-carboxylate (5bo)



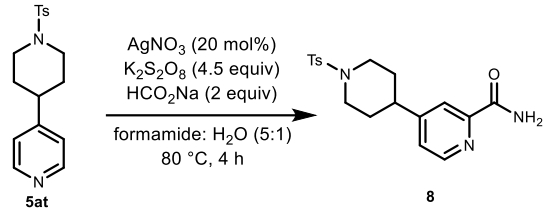
Prepared via **General Procedure III** starting from pyridin-3-ylmethyl 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1*H*-pyrazole-3-carboxylate (471.0 mg, 1.0 mmol, 1.0 equiv), *n*-pentyl Grignard reagents (1.2 mmol, 1.2 equiv) and oxidized at 50 ℃ for 12 h to give (4-pentylpyridin-3-yl)methyl 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1*H*-pyrazole-3-carboxylate (**5bo**) as a pale yellow oil.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 3:1).
Yield 245.1 mg (45%, 119.6 mg starting material, 60% b.r.s.m).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.67 (s, 1H), 8.48 (d, *J* = 5.1 Hz, 1H), 7.39 (d, *J* = 2.1 Hz, 1H), 7.34 – 7.26 (m, 4H), 7.15 (d, *J* = 5.1 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 5.48 (s, 2H), 2.81 – 2.69 (m, 2H), 2.31 (s, 3H), 1.65 (p, *J* = 7.6 Hz, 2H), 1.39 – 1.28 (m, 4H), 0.86 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR ($CDCl_3$, 151 MHz) δ 162.4, 151.1, 150.7, 149.7, 143.0, 142.4, 136.1, 135.8, 135.1, 133.0, 130.9, 130.6, 130.2, 129.5, 128.9, 127.8, 126.9, 124.1, 119.3, 62.0, 32.0, 31.7, 29.8, 22.5, 13.9, 9.7.
HRMS calcd for $(C_{28}H_{27}Cl_3N_3O_2)^+$ $[M + H]^+$: 542.1164, found 542.1159.

17. Synthesis of 4-(1-tosylpiperidin-4-yl)picolinamide

4-(1-tosylpiperidin-4-yl)picolinamide (8)

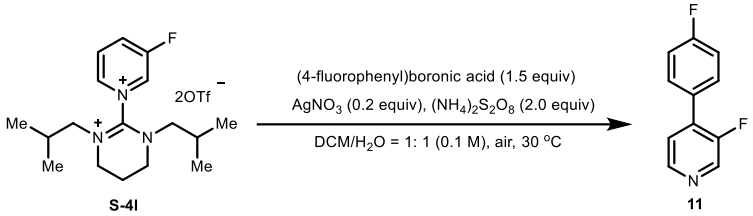


Follow the literature procedure [5].
To a 10 mL culture tube equipped with the screw cap and magnetic stir bar, $AgNO_3$ (7.2 mg, 0.04 mmol, 20 mol%), $K_2S_2O_8$ (81.1 mg, 0.3 mmol, 1.5 equiv), HCO_2Na (27.2 mg, 0.4 mmol, 2.0 equiv) and corresponding pyridine **5at** (63.2 mg, 0.2 mmol, 1,0 equiv) were added, together with formamide (1 mL), and H_2O (0.2 mL). While the resulting mixture was stirred at 80 °C other 2 portions of $K_2S_2O_8$ (2 × 81.1 mg, 0.3 mmol, 1.5 equiv) were added after 1 hour and 2 hours. The mixture was then stirred at the same temperature for another 2 hours. At the end of the reaction, the reaction mixture was cooled to room temperature, poured into a brine (7.0 mL) and extracted with EtOAc (3 × 7.0 mL). The organic phases were combined, evaporated in a rotary evaporator. The residue was purified by flash column chromatography on silica gel (EtOAc) to afford the corresponding product **8** as a white solid.

R_f = 0.6 (eluent: EtOAc).
Yield 48.9 mg (68%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.49 (d, *J* = 5.0 Hz, 1H), 8.02 (s, 1H), 7.92 – 7.82 (br, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.26 – 7.24 (m, 1H), 5.72 – 5.59 (br, 1H), 3.99 – 3.92 (m, 2H), 2.58 – 2.47 (m, 1H), 2.46 (s, 3H), 2.38 (td, *J* = 11.9, 3.0 Hz, 2H), 1.97 – 1.78 (m, 4H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 166.5, 155.4, 149.7, 148.6, 143.7, 133.2, 129.7, 127.7, 124.5, 121.3, 46.4, 41.2, 31.6, 21.6.
HRMS calcd for $(C_{18}H_{22}N_3O_3S)^+$ $[M + H]^+$: 360.1376, found 360.1375.

18. Synthesis of VU6001966

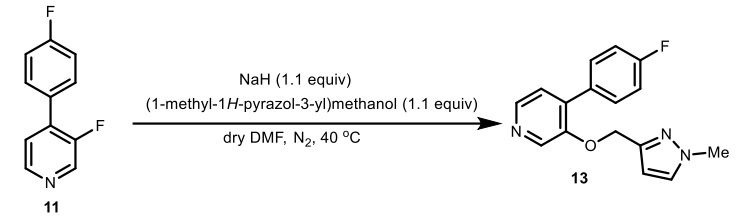
3-fluoro-4-(4-fluorophenyl)pyridine (11)



Prepared via the previous procedure starting from **S-4l** (295.5 mg, 0.5 mmol, 1.0 equiv) to give 3-fluoro-4-(4-fluorophenyl)pyridine (**11**) as a white solid.

R_f = 0.3 (eluent: petroleum ether/EtOAc = 5:1).
Yield 58.3 mg (61%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.54 (s, 1H), 8.47 (d, *J* = 4.7 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.38 (t, *J* = 5.8 Hz, 1H), 7.19 (t, *J* = 8.5 Hz, 2H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 163.4 (d, *J* = 250.7 Hz), 156.6 (d, *J* = 256.7 Hz), 145.9 (d, *J* = 4.5 Hz), 139.0 (d, *J* = 25.7 Hz), 135.2 (d, *J* = 10.6 Hz), 130.8 (dd, *J* = 9.1, 4.5 Hz), 128.9 (d, *J* = 3.0 Hz), 124.1, 116.0 (d, *J* = 21.1 Hz).
^{19}F NMR ($CDCl_3$, 377 MHz) δ -111.5, -132.9.
HRMS calcd for $(C_{11}H_8F_2N)^+$ $[M + H]^+$: 192.0619, found 192.0618.

4-(4-fluorophenyl)-3-((1-methyl-1*H*-pyrazol-3-yl)methoxy)pyridine (13)

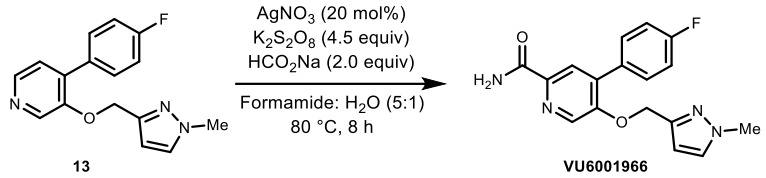


An oven-dried and N_2 flushed 10 mL Schlenk-tube equipped with the screw cap and magnetic stirring bar, was charged with the corresponding diethyl (1-methyl-1*H*-pyrazol-3-yl)methanol (0.22 mmol, 24.6 mg, 1.1 equiv), dry DMF (1.0 mL) and NaH (0.122 mmol, 8.8 mg, 1.1 equiv). The reaction mixture was stirred at room temperature for 10 minutes. Then **11** (0.2 mmol, 38.2 mg, 1.0 equiv) was dissolved in dry DMF (1.0 mL) and added to the mixture. The resulting mixture was stirred at 40 °C for 10 h and monitored by TLC. Water (6.0 mL) was added in one portion and the mixture was extracted with EtOAc (5 × 6.0 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford 4-(4-fluorophenyl)-3-((1-methyl-1*H*-pyrazol-3-yl)methoxy)pyridine (**13**) as a white solid.

R_f = 0.28 (eluent: Pure EtOAc, 1% Et_3N).
Yield 37.5 mg (66%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.50 (s, 1H), 8.30 (d, *J* = 4.7 Hz, 1H), 7.59 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.29 (d, *J* = 2.1 Hz, 1H), 7.24 (d, *J* = 4.8 Hz, 1H), 7.10 (t, *J* = 8.7 Hz, 2H),

6.19 (d, *J* = 2.1 Hz, 1H), 5.15 (s, 2H), 3.87 (s, 3H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 162.8 (d, *J* = 248.5 Hz), 151.8, 147.8, 143.1, 137.4, 136.6, 131.6 (d, *J* = 3.0 Hz), 131.13, 131.09 (d, *J* = 8.0 Hz), 124.3, 115.2 (d, *J* = 22.2 Hz), 105.2, 65.7, 38.9.
^{19}F NMR ($CDCl_3$, 377 MHz) δ -113.4.
HRMS calcd for $(C_{16}H_{15}FN_3O)^+$ $[M + H]^+$: 284.1194, found 284.1193.

4-(4-fluorophenyl)-5-((1-methyl-1*H*-pyrazol-3-yl)methoxy)picolinamide VU6001966

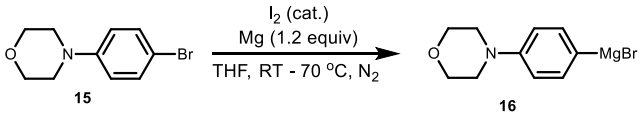


To a 10 mL culture tube equipped with the screw cap and magnetic stir bar, $AgNO_3$ (3.6 mg, 0.02 mmol, 20 mol%), $K_2S_2O_8$ (40.5 mg, 0.15 mmol, 1.5 equiv), HCO_2Na (13.6 mg, 0.2 mmol, 2 equiv) and corresponding pyridine **13** (28.3 mg, 0.1 mmol, 1.0 equiv) were added, together with formamide (1.0 mL) and H_2O (0.2 mL). While the resulting mixture was stirred at 80 °C other 2 portions of $K_2S_2O_8$ (40.5 mg, 0.15 mmol, 1.5 equiv) were added after 1 hour and 2 hours. The mixture was then stirred at the same temperature for another 6 hours. At the end of the reaction, the reaction mixture was cooled to room temperature, poured into a brine (4.0 mL), and extracted with EtOAc (3 × 5.0 mL). The organic phases were combined, evaporated in a rotary evaporator. The residue was purified by column chromatography on silica gel to afford the corresponding product 4-(4-fluorophenyl)-5-((1-methyl-1*H*-pyrazol-3-yl)methoxy)picolinamide (**VU6001966**) as a white solid.

R_f = 0.3 (eluent: Pure EtOAc, 1% Et_3N).
Yield 11.0 mg (34%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.44 (s, 1H), 8.19 (s, 1H), 7.78 – 7.72 (br, 1H), 7.66 – 7.60 (m, 2H), 7.32 (s, 1H), 7.11 (t, *J* = 8.5 Hz, 2H), 6.22 (s, 1H), 5.66 – 5.59 (br, 1H), 5.25 (s, 2H), 3.90 (s, 3H).
^{13}C NMR ($CDCl_3$, 151 MHz) δ 166.5, 162.9 (d, *J* = 249.2 Hz), 153.9, 147.3, 143.0, 137.8, 134.4, 131.3, 131.2 (d, *J* = 7.6 Hz), 131.0 (d, *J* = 3.0 Hz), 123.9, 115.3 (d, *J* = 21.1 Hz), 105.3, 65.6, 39.0.
^{19}F NMR ($CDCl_3$, 565 MHz) δ -112.8.
HRMS calcd for $(C_{17}H_{16}FN_4O_2)^+$ $[M + H]^+$: 327.1252, found 327.1250.

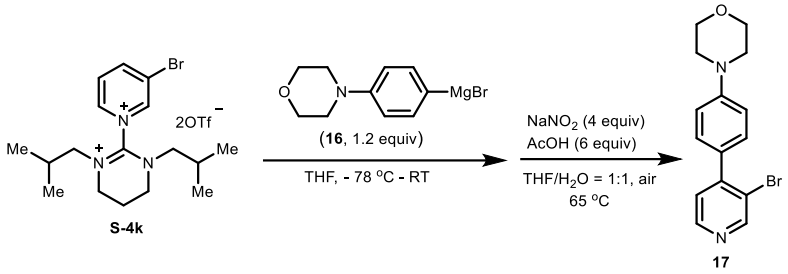
19. Synthesis of LJI308

The preparation of (4-morpholinophenyl)magnesium bromide (16)



An oven-dried and N_2 flushed 25 mL Schlenk-tube, equipped with a magnetic stirring bar and a septum, was charged with the corresponding 4-(4-bromophenyl)morpholine **15** (241.0 mg, 1.0 mmol, 1.0 equiv), magnesium chips (28.8 mg, 1.2 mmol, 1.2 equiv), I_2 (one crystals) and anhydrous THF (5.0 mL). The resulting solution was heated to 70 ℃ for 3 hours to obtain the product. The resulting brown clear solution (approx. 0.2 M) can be used directly by syringe and stored in the refrigerator for several days.

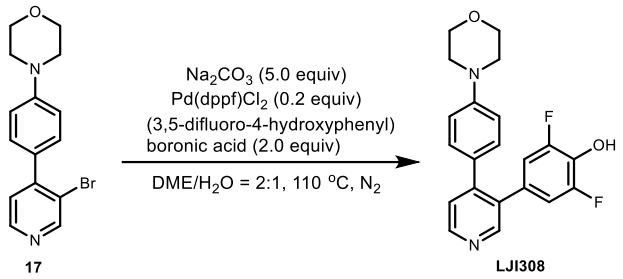
4-(4-(3-bromopyridin-4-yl)phenyl)morpholine (17)



Under a nitrogen atmosphere, **S-4k** (195.3 mg, 0.3 mmol, 1.0 equiv) was added to an oven-dried 25 mL Schlenk tube with a magnetic bar at room temperature. Anhydrous THF (3.0 mL) was added and the suspension was cooled to -78 ℃ in a low-temperature reactor. A solution of the (4-morpholinophenyl)magnesium bromide (1.8 mL, 0.36 mmol, 1.2 equiv) was added dropwise via a 2.5 mL syringe within 2 minutes and the resulting suspension was stirred for 10 minutes to give a clear solution. Water (3.0 mL) was added in one portion and the reaction mixture stirred for 5 minutes at room temperature, then $NaNO_2$ aqueous solution (100 mg/ mL, 0.83 mL, 4.0 equiv) and acetic acid (103 μL, 6.0 equiv) were added in one portion and the mixture were stirred for 16 hours at 65 ℃. The mixture was neutralized with a saturated sodium bicarbonate solution (2.0 mL), extracted with EtOAc (3 × 8.0 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford 4-(4-(3-bromopyridin-4-yl)phenyl)morpholine (**17**) as a white solid.

R_f = 0.3 (eluent: DCM/MeOH = 100:1).
Yield 20.9 mg (22%).
NMR spectroscopy:
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.78 (s, 1H), 8.50 (d, *J* = 4.8 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 2H), 7.27 (d, *J* = 5.0 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 3.92 – 3.85 (m, 4H), 3.29 – 3.23 (m, 4H).
^{13}C NMR ($CDCl_3$, 101 MHz) δ 152.3, 151.4, 149.6, 147.9, 130.0, 128.9, 125.6, 120.9 (low signal), 114.6, 66.8, 44.5.
HRMS calcd for $(C_{15}H_{16}BrN_2O)^+$ $[M + H]^+$: 319.0441, found 319.0440.

2,6-difluoro-4-(4-(4-morpholinophenyl)pyridin-3-yl)phenol (LJI308)



Under a nitrogen atmosphere, $Pd(dppf)Cl_2$ (7.3 mg, 20.0 mol%), Na_2CO_3 (26.5 mg, 5.0 equiv), (3,5-difluoro-4-hydroxyphenyl)boronic acid **18** (17.4 mg, 2.0 equiv) and **17** (0.05 mmol, 15.9 mg, 1.0 equiv) were added to an oven-dried 10 mL Schlenk tube with a magnetic bar at room temperature. To this tube were added a mixture solvent of DME and H_2O (ratio: 2:1, 0.9 mL) under a stream of nitrogen. The tube was heated at 110 ℃ for 10 h. The reaction mixture was filtered with silica gel and dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford 2,6-difluoro-4-(4-(4-morpholinophenyl)pyridin-3-yl)phenol (**LJI308**) as a white solid.

R_f = 0.15 (eluent: petroleum ether/EtOAc = 1:1).
Yield 12.6 mg (68%).
NMR spectroscopy:
^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.34 (s, 1H), 8.55 (d, J = 4.8 Hz, 1H), 8.50 (s, 1H), 7.37 (d, J = 4.9 Hz, 1H), 7.06 (d, J = 8.5 Hz, 2H), 6.90 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 7.9 Hz, 2H), 3.77 – 3.62 (m, 4H), 3.17 – 3.05 (m, 4H).
^{13}C NMR (DMSO-d_6, 151 MHz) δ 152.5 (dd, J = 241.6, 7.6 Hz), 151.0, 150.9, 149.3, 147.2, 133.5, 133.4 (t, J = 7.6 Hz), 130.3, 128.8 (t, J = 7.6 Hz), 128.1, 124.8, 114.8, 113.6 (dd, J = 16.6, 6.0 Hz), 66.5, 48.1.
^{19}F NMR (DMSO-d_6, 377 MHz) δ -132.2.
HRMS calcd for $(C_{21}H_{19}F_2N_2O_2)^+$ $[M + H]^+$: 369.1409, found 369.1408.

20. Comparison of two pyridine salt additions with methyl Grignard reagent

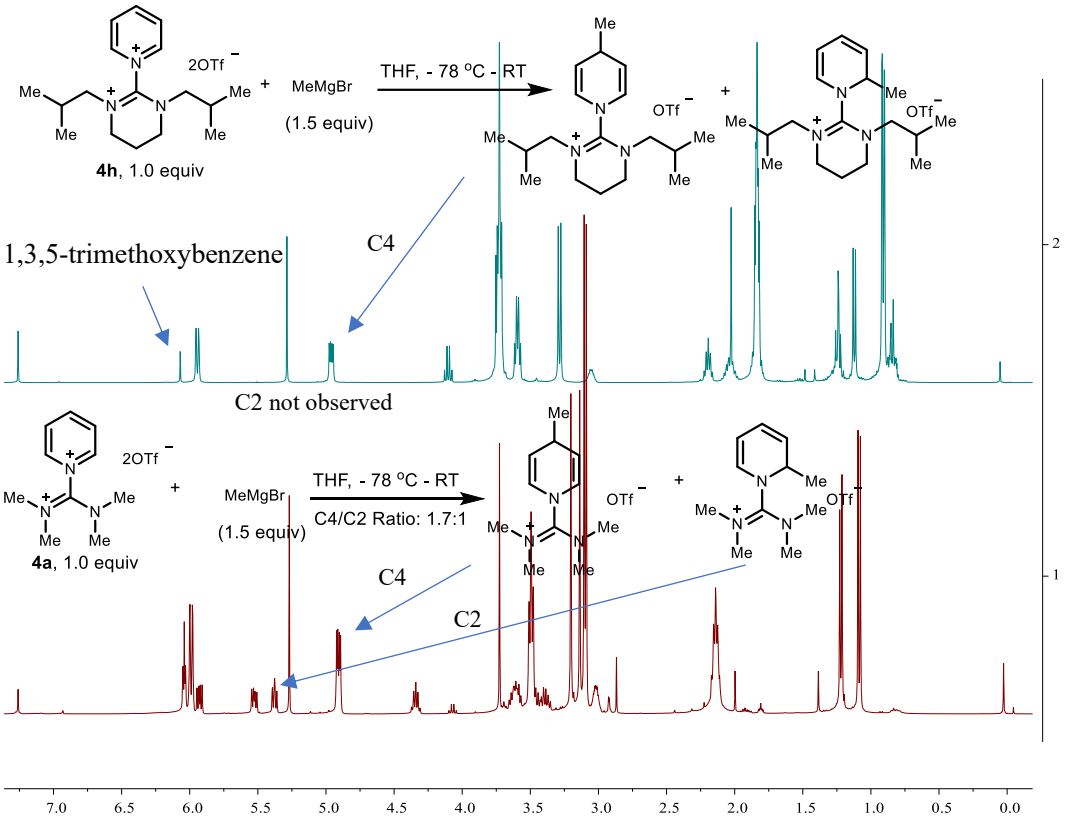


Figure S5. Crude ^{1}H NMR of **4h** and **4a** with methylMgBr

21. GC-MS data for the reaction of 5-chloropentanoic acid and 4h

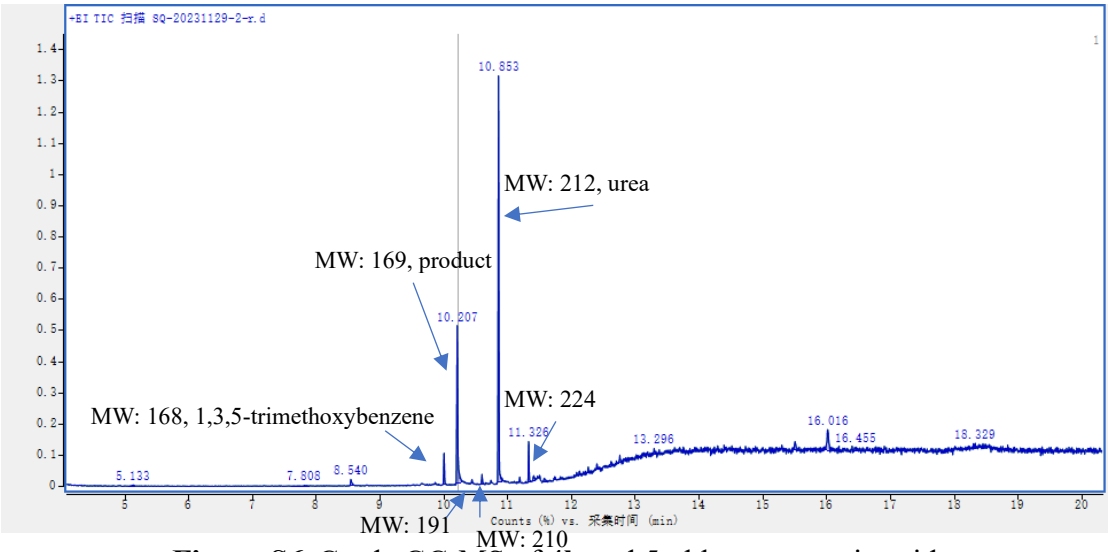
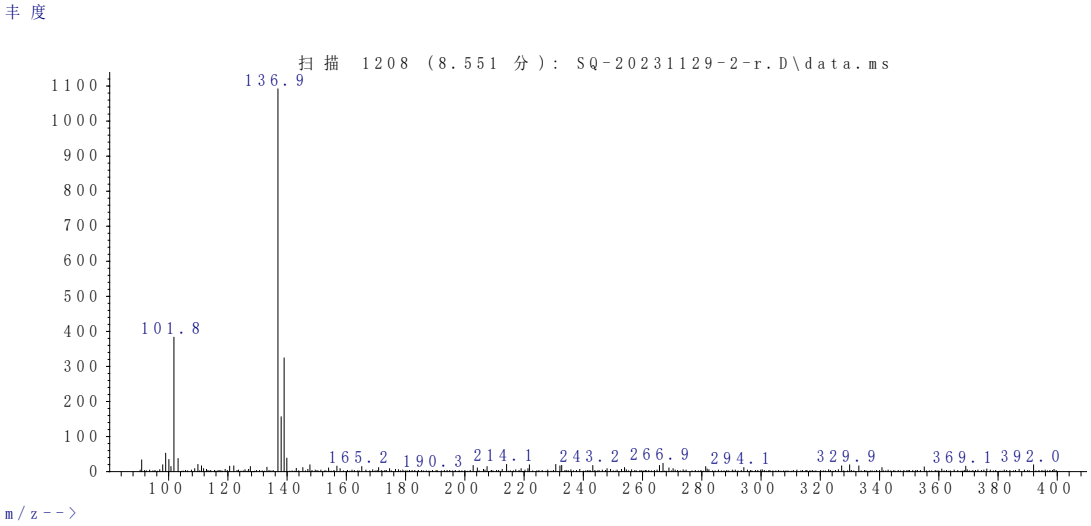
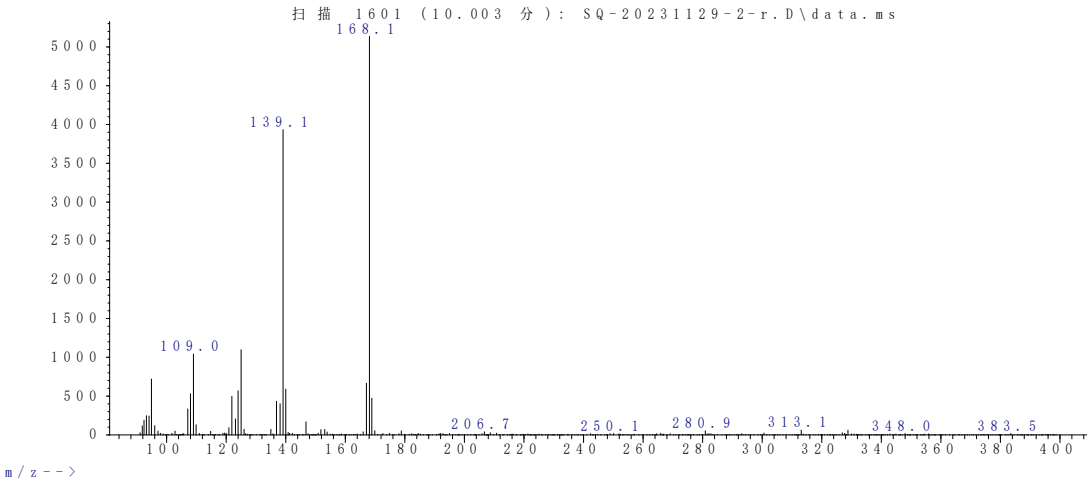
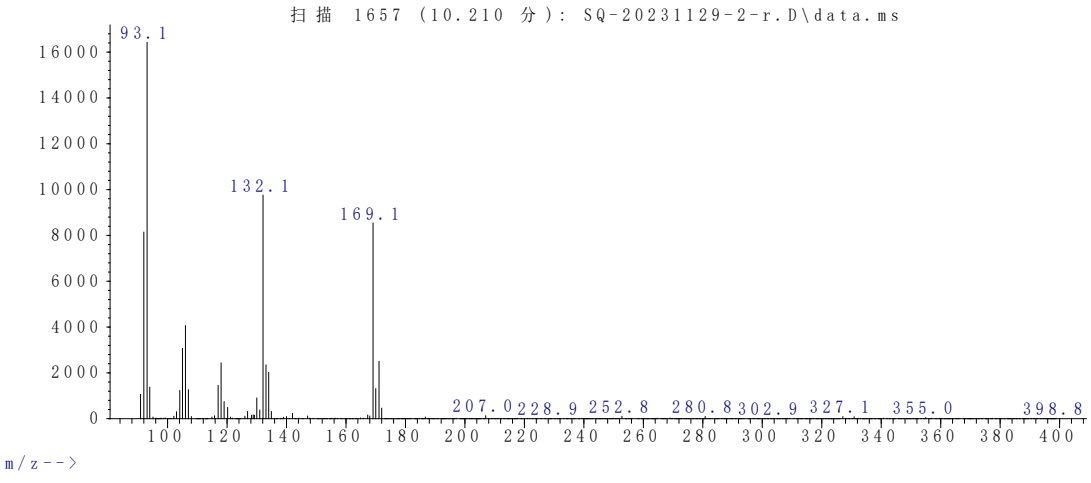


Figure S6. Crude GC-MS of **4h** and 5-chloropentanoic acid


丰 度
扫 描 1208 (8.551 分): SQ-20231129-2-r.D\data.ms
136.9
101.8
165.2
190.3
214.1
243.2
266.9
294.1
329.9
369.1
392.0
m/z-->
Figure S7. GC-MS detail (Time: 8.551 minutes)


丰 度
扫 描 1601 (10.003 分): SQ-20231129-2-r.D\data.ms
168.1
139.1
109.0
206.7
250.1
280.9
313.1
348.0
383.5
m/z-->
Figure S8. GC-MS detail (Time: 10.003 minutes)


丰 度
扫 描 1657 (10.210 分): SQ-20231129-2-r.D\data.ms
93.1
132.1
169.1
207.0
228.9
252.8
280.8
302.9
327.1
355.0
398.8
m/z-->
Figure S9. GC-MS detail (Time: 10.210 minutes)

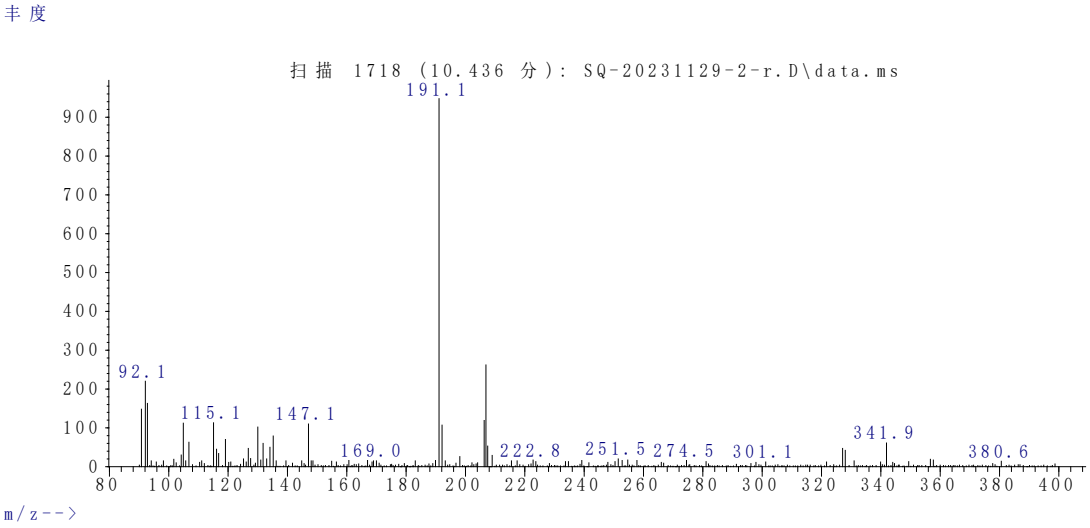


Figure S10. GC-MS detail (Time: 10.436 minutes)

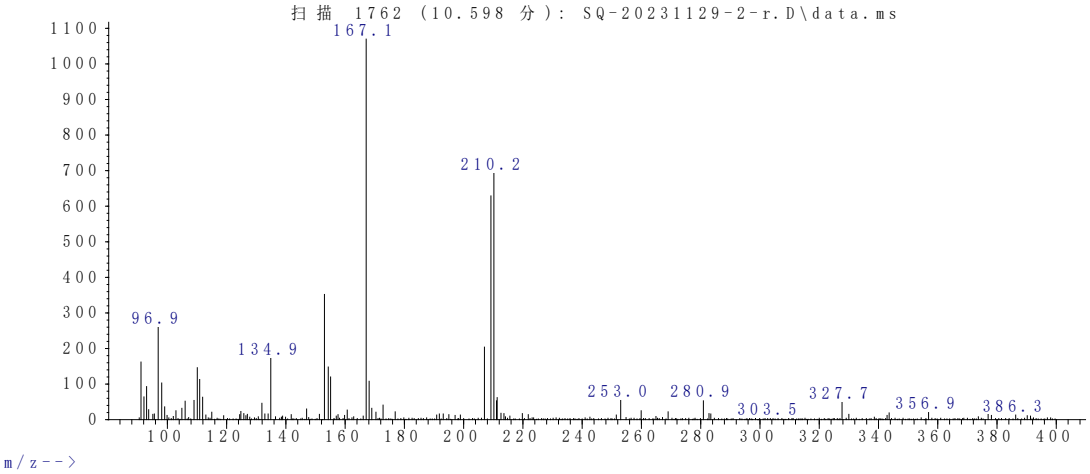


Figure S11. GC-MS detail (Time: 10.598 minutes)

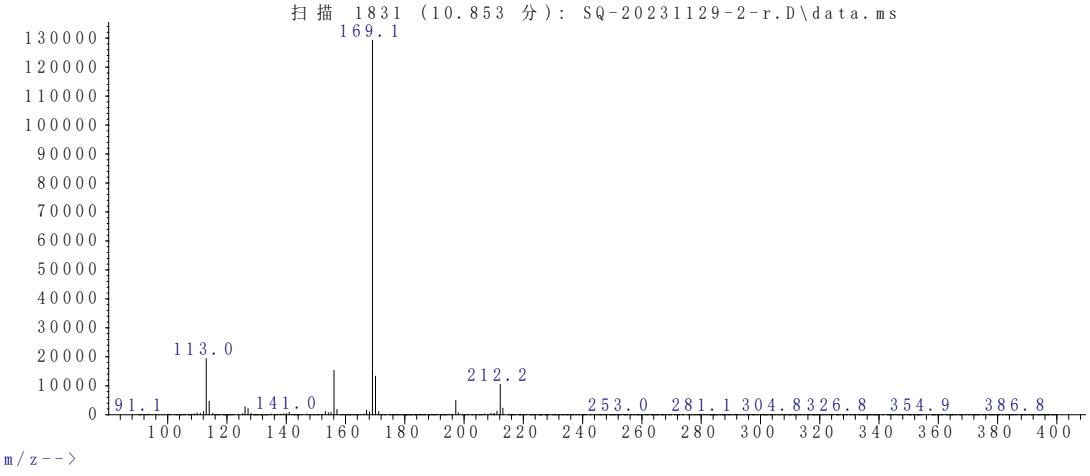


Figure S12. GC-MS detail (Time: 10.853 minutes)

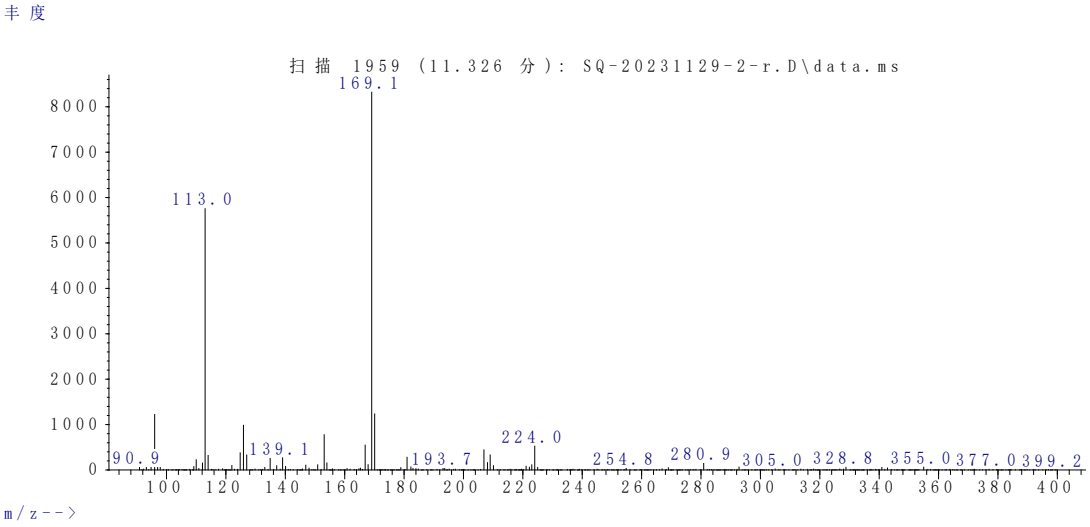


Figure S13. GC-MS detail (Time: 11.326 minutes)

22. GC-MS data for the reaction of (4-ethylphenyl)boronic acid and 4h

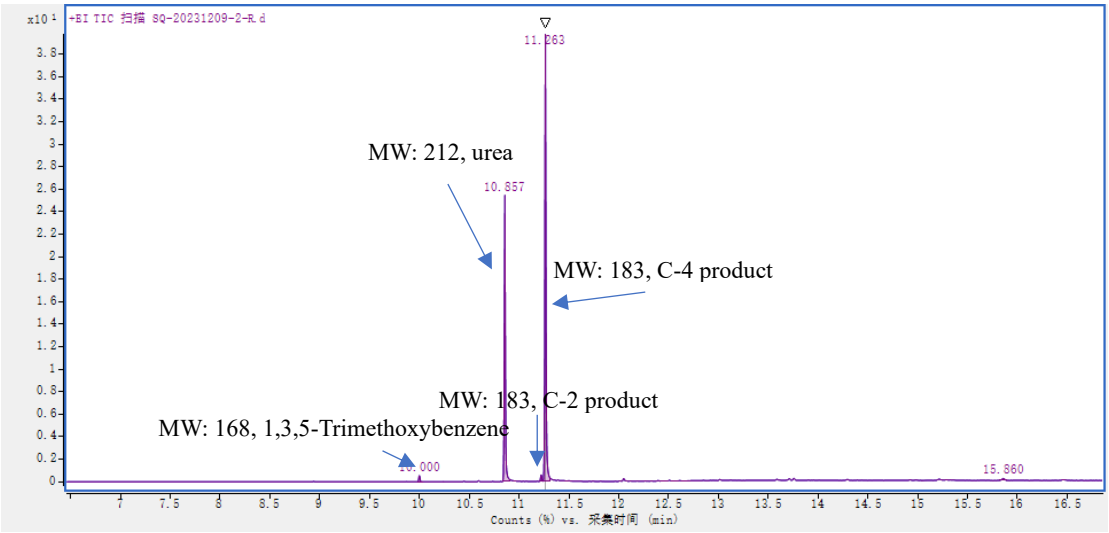


Figure S14. Crude GC-MS of **4h** and (4-ethylphenyl)boronic acid

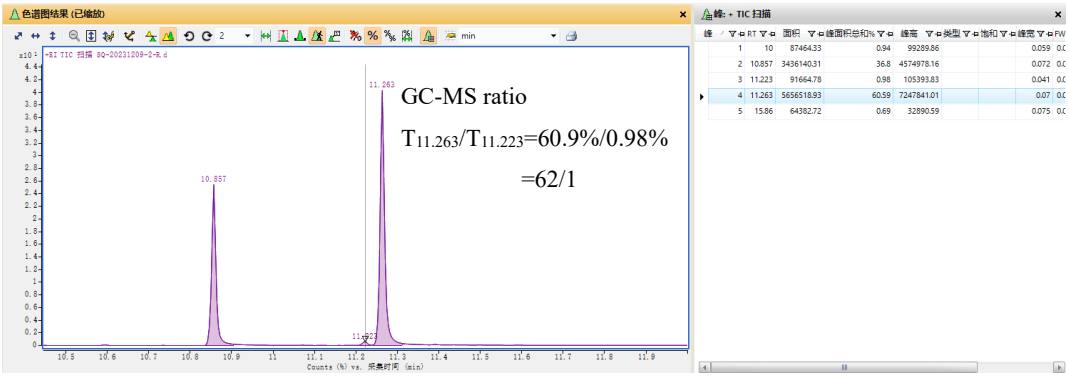


Figure S15. Crude GC-MS ratio of **4h** and (4-ethylphenyl)boronic acid

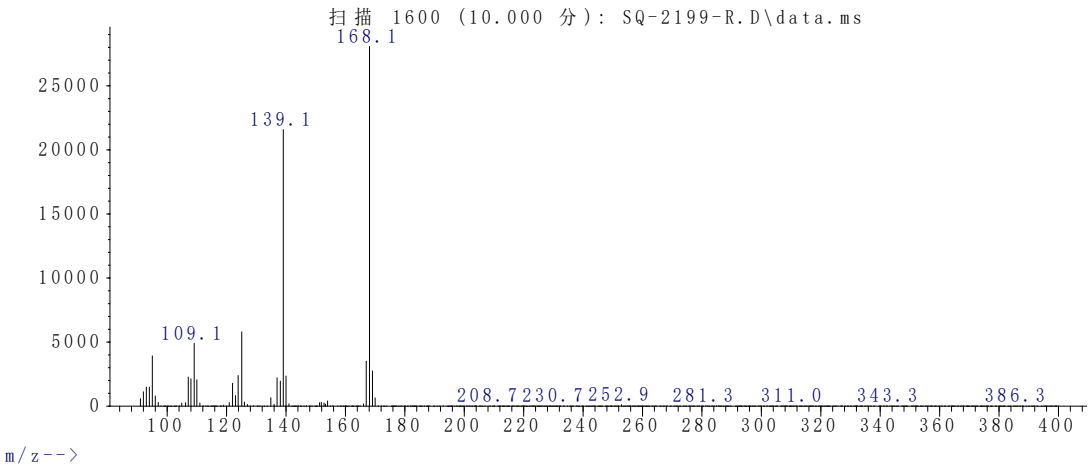


Figure S16. GC-MS detail (Time: 10.000 minutes)

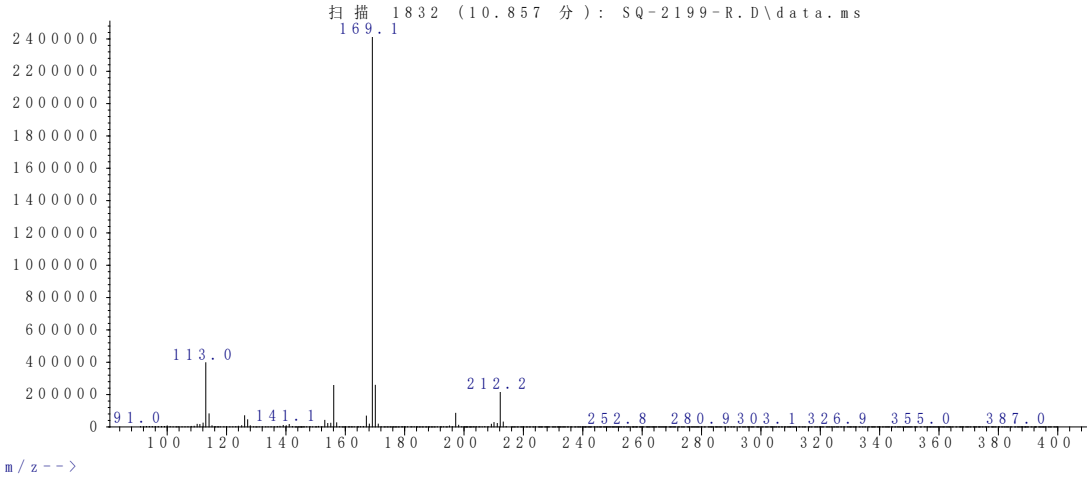


Figure S17. GC-MS detail (Time: 10.857 minutes)

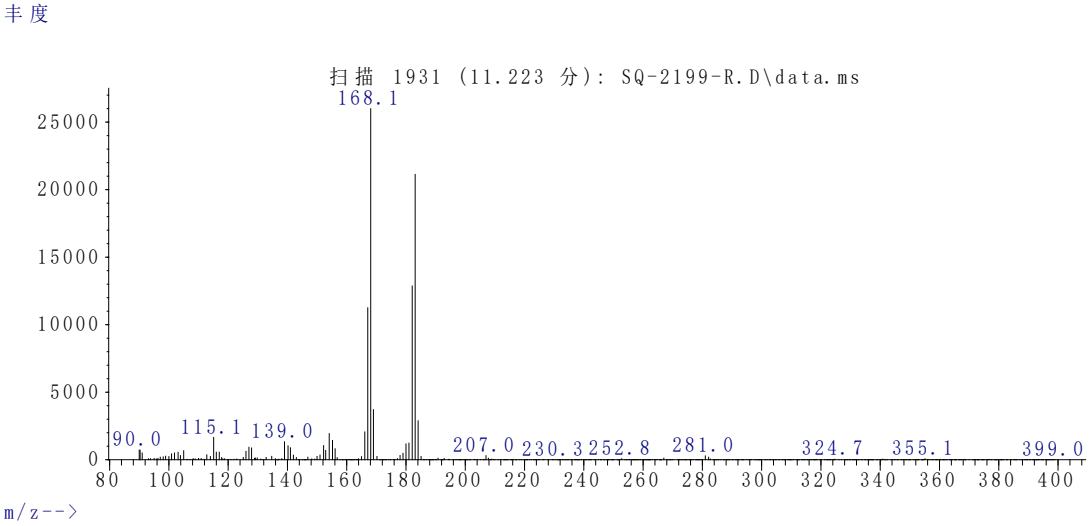


Figure S18. GC-MS detail (Time: 11.223 minutes)

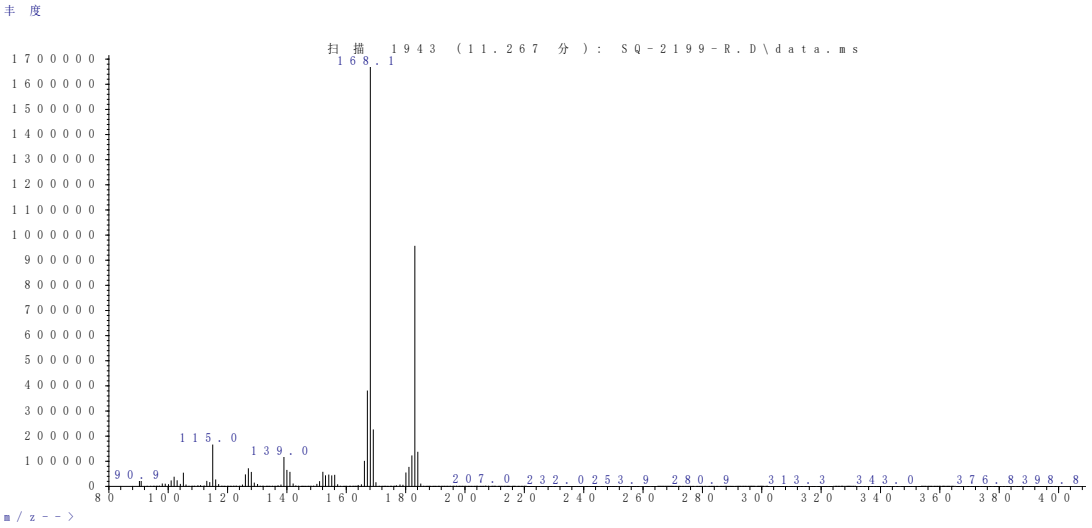


Figure S19. GC-MS detail (Time: 11.267 minutes)

23. GC-MS data after oxidation of S-4s and *n*-pentylMgBr

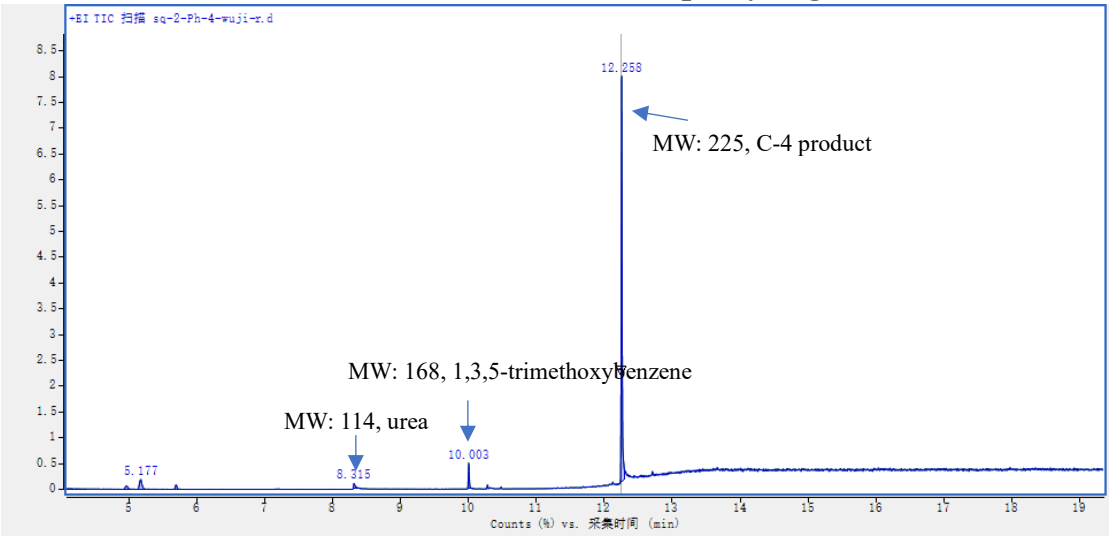


Figure S20. Crude GC-MS after oxidation of **S-4s** and *n*-pentylMgBr

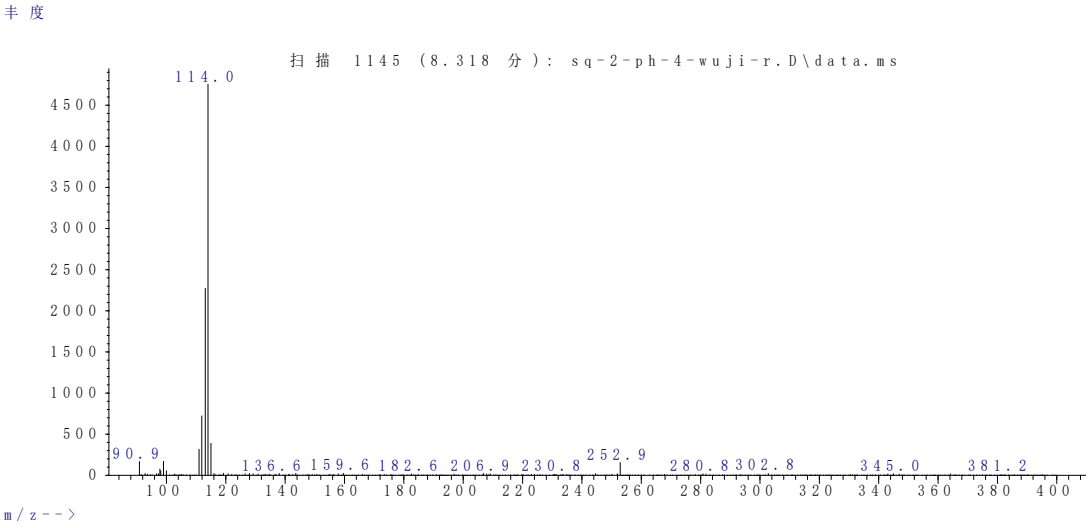


Figure S21. GC-MS detail (Time: 8.318 minutes)

Figure S22. GC-MS detail (Time: 10.007 minutes)

Figure S23. GC-MS detail (Time: 12.258 minutes)

24. X-ray data of 4a and 4h

X-ray Structure of Pyridinium 4a

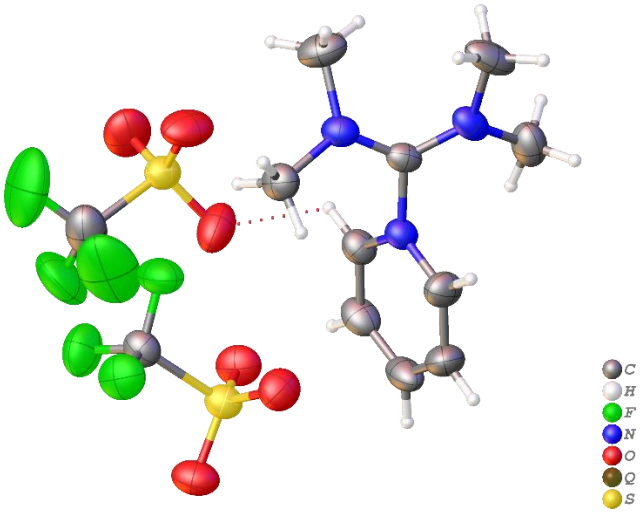


Figure S24. X-ray Structure of Pyridinium **4a**

Table 1 Crystal data and structure refinement for 4a.

Identification code	**4a**
CCDC number	2328544
Empirical formula	$C_{12}H_{17}F_6N_3O_6S_2$
Formula weight	477.40
Temperature/K	222.99(10)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	9.8561(4)
b/Å	14.1484(5)
c/Å	14.0248(6)
α/°	90
β/°	95.009(4)
γ/°	90
Volume/Å^3	1948.25(13)
Z	4
ρ_{calc}g/cm^3	1.628
μ/mm^{-1}	3.359
F(000)	976.0
Crystal size/mm^3	0.15 × 0.09 × 0.028
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.896 to 145.72
Index ranges	$-11 \le h \le 12$, $-17 \le k \le 10$, $-17 \le l \le 17$
Reflections collected	7440

Independent reflections	3771 [R_{int} = 0.0650, R_{sigma} = 0.0745]
Data/restraints/parameters	3771/0/266
Goodness-of-fit on F^2	1.027
Final R indexes [I>=2σ (I)]	R_1 = 0.0697, wR_2 = 0.1840
Final R indexes [all data]	R_1 = 0.0828, wR_2 = 0.2074
Largest diff. peak/hole / e $Å^{-3}$	0.58/-0.52

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters ($Å^2$×10^3) for 4a. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	x	y	z	U(eq)
C1	3279(4)	1623(2)	3220(2)	33.7(6)
C2	3804(4)	2925(2)	4287(3)	39.9(7)
C3	3752(4)	3364(3)	5147(3)	48.7(9)
C4	3228(4)	2874(3)	5894(3)	52.6(9)
C5	2797(4)	1950(3)	5764(3)	54.7(10)
C6	2845(4)	1537(3)	4887(3)	48.0(8)
C7	4636(5)	1452(3)	1863(3)	60.3(11)
C8	5706(4)	1303(3)	3525(3)	45.9(8)
C9	1811(6)	779(3)	2004(3)	62.0(12)
C10	835(4)	1958(3)	3055(3)	56.5(10)
N1	3326(3)	2033.3(18)	4165.0(19)	34.4(6)
N2	4451(3)	1472.0(19)	2886(2)	38.4(6)
N3	2053(3)	1454(2)	2807(2)	41.3(7)
C11	8353(5)	4124(4)	3994(4)	68.5(13)
F1	9387(4)	4041(3)	3453(4)	123.8(18)
F2	8633(4)	4874(3)	4568(3)	106.2(13)
F3	8289(5)	3365(3)	4515(4)	137(2)
O1	7048(4)	5143(2)	2733(3)	73.3(10)
O2	5832(4)	4481(2)	3967(3)	68.8(9)
O3	6544(4)	3470(2)	2751(2)	72.1(10)
S1	6769.2(9)	4323.0(6)	3272.1(6)	41.2(3)
C12	8671(4)	1020(3)	5616(3)	43.7(8)
F4	8276(3)	791(2)	4715.9(18)	66.8(7)
F5	9508(3)	1742.3(19)	5600(2)	71.4(8)
F6	9356(3)	288.4(18)	5999(2)	64.4(7)
O4	6557(3)	2063.3(19)	5799(2)	54.4(7)
O5	7778(3)	1462(2)	7230(2)	56.5(7)
O6	6448(3)	405(2)	6173(2)	56.7(7)
S2	7185.2(9)	1269.2(5)	6284.3(6)	39.4(3)

Table 3 Anisotropic Displacement Parameters ($Å^2$×10^3) for 4a. The Anisotropic

displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U11	U22	U33	U23	U13	U12
C1	45.3(17)	25.1(13)	29.9(15)	-0.1(11)	-1.3(12)	-2.9(12)
C2	41.9(17)	34.0(15)	42.9(18)	-3.1(13)	-1.4(14)	-2.3(14)
C3	49.4(19)	41.3(19)	54(2)	-16.5(15)	-3.9(17)	3.7(16)
C4	41.6(18)	72(2)	43(2)	-22.0(18)	-2.6(14)	8.0(18)
C5	55(2)	74(3)	35.1(19)	-2.7(17)	7.2(16)	-6(2)
C6	56(2)	45.8(18)	43(2)	1.7(15)	7.0(16)	-11.6(17)
C7	78(3)	63(2)	41(2)	0.6(17)	16(2)	16(2)
C8	43.2(19)	47.0(19)	47(2)	0.9(15)	3.1(15)	9.9(15)
C9	91(3)	46(2)	43(2)	0.4(16)	-22(2)	-22(2)
C10	42.2(19)	60(2)	65(3)	12.8(19)	-3.0(17)	-1.3(18)
N1	37.3(13)	32.6(12)	32.6(14)	-2.3(10)	-0.4(10)	-2.2(11)
N2	47.5(16)	34.1(13)	33.0(14)	-2.9(10)	0.9(11)	3.6(12)
N3	47.7(16)	34.8(13)	39.3(15)	4.0(11)	-8.0(12)	-9.1(12)
C11	57(2)	63(3)	84(4)	23(2)	-3(2)	0(2)
F1	61(2)	106(3)	210(5)	25(3)	41(3)	27(2)
F2	93(2)	123(3)	95(3)	-11(2)	-36(2)	-35(2)
F3	136(4)	118(3)	149(4)	85(3)	-41(3)	-6(3)
O1	80(2)	64.3(19)	76(2)	31.1(16)	4.6(18)	-6.8(17)
O2	61.0(18)	65.1(18)	84(2)	-19.0(16)	28.9(17)	-14.6(15)
O3	107(3)	61.4(18)	48.7(17)	-18.6(14)	11.7(17)	-23.0(18)
S1	47.7(5)	36.9(5)	39.0(5)	-0.7(3)	3.7(3)	-4.7(3)
C12	45.0(18)	38.8(17)	46(2)	-0.7(14)	-2.8(14)	3.8(15)
F4	65.2(15)	89.9(19)	44.8(13)	-10.8(12)	1.4(11)	12.4(14)
F5	64.1(16)	56.9(14)	95(2)	-2.4(13)	19.3(15)	-14.9(12)
F6	63.8(15)	58.7(14)	70.4(17)	5.4(12)	3.4(12)	22.2(12)
O4	63.5(17)	43.7(14)	55.5(17)	4.8(12)	2.6(13)	14.6(13)
O5	72.6(19)	52.4(15)	43.0(15)	-8.7(12)	-2.8(13)	7.0(14)
O6	63.6(17)	45.7(14)	61.5(18)	-8.3(12)	9.9(14)	-8.5(13)
S2	47.1(5)	30.0(4)	40.4(5)	-1.5(3)	0.6(3)	3.0(3)

Table 4 Bond Lengths for 4a.

Atom	Atom	Length/Å		Atom	Atom	Length/Å
C1	N1	1.444(4)		C11	F2	1.346(7)
C1	N2	1.302(5)		C11	F3	1.305(6)
C1	N3	1.315(5)		C11	S1	1.807(5)
C2	C3	1.362(5)		O1	S1	1.425(3)
C2	N1	1.352(4)		O2	S1	1.418(3)
C3	C4	1.393(7)		O3	S1	1.418(3)
C4	C5	1.382(6)		C12	F4	1.328(5)
C5	C6	1.366(6)		C12	F5	1.314(5)
C6	N1	1.352(5)		C12	F6	1.324(4)

C7	N2	1.462(5)		C12	S2	1.841(4)
C8	N2	1.481(5)		O4	S2	1.427(3)
C9	N3	1.479(5)		O5	S2	1.428(3)
C10	N3	1.465(6)		O6	S2	1.425(3)
C11	F1	1.327(7)				

Table 5 Bond Angles for 4a.

Atom	Atom	Atom	Angle/°		Atom	Atom	Atom	Angle/°
N2	C1	N1	115.9(3)		F3	C11	F2	109.3(5)
N2	C1	N3	128.4(3)		F3	C11	S1	111.1(4)
N3	C1	N1	115.6(3)		O1	S1	C11	103.1(2)
N1	C2	C3	119.9(3)		O2	S1	C11	102.8(3)
C2	C3	C4	119.0(4)		O2	S1	O1	113.8(2)
C5	C4	C3	120.1(3)		O2	S1	O3	114.0(2)
C6	C5	C4	119.3(4)		O3	S1	C11	104.2(3)
N1	C6	C5	119.6(4)		O3	S1	O1	116.6(2)
C2	N1	C1	118.3(3)		F4	C12	S2	110.5(3)
C6	N1	C1	119.6(3)		F5	C12	F4	107.8(3)
C6	N1	C2	122.1(3)		F5	C12	F6	108.4(3)
C1	N2	C7	123.1(3)		F5	C12	S2	112.8(3)
C1	N2	C8	122.0(3)		F6	C12	F4	106.9(3)
C7	N2	C8	114.9(3)		F6	C12	S2	110.1(3)
C1	N3	C9	122.3(4)		O4	S2	C12	103.83(18)
C1	N3	C10	123.2(3)		O4	S2	O5	114.72(18)
C10	N3	C9	114.4(3)		O5	S2	C12	103.34(19)
F1	C11	F2	106.5(5)		O6	S2	C12	101.59(17)
F1	C11	S1	111.3(4)		O6	S2	O4	115.3(2)
F2	C11	S1	109.6(4)		O6	S2	O5	115.41(19)
F3	C11	F1	108.9(5)					

Table 6 Hydrogen Bonds for 4a.

D	H	A	d(D-H)/Å	d(H-A)/Å	d(D-A)/Å	D-H-A/°
C2	H2	O2	0.94	2.40	3.034(5)	124.7
C2	H2	O51	0.94	2.50	3.096(5)	121.3

Table 7 Torsion Angles for 4a.

A	B	C	D	Angle/°		A	B	C	D	Angle/°
C2	C3	C4	C5	1.4(6)		N3	C1	N2	C8	-153.3(3)
C3	C2	N1	C1	174.3(3)		F1	C11	S1	O1	-56.1(4)
C3	C2	N1	C6	-3.0(5)		F1	C11	S1	O2	-174.7(4)
C3	C4	C5	C6	-2.4(6)		F1	C11	S1	O3	66.1(4)
C4	C5	C6	N1	0.7(6)		F2	C11	S1	O1	61.5(4)
C5	C6	N1	C1	-175.3(4)		F2	C11	S1	O2	-57.1(4)

C5	C6	N1	C2	2.0(6)		F2	C11	S1	O3	-176.3(4)
N1	C1	N2	C7	-153.3(3)		F3	C11	S1	O1	-177.6(5)
N1	C1	N2	C8	27.0(4)		F3	C11	S1	O2	63.8(5)
N1	C1	N3	C9	-160.1(3)		F3	C11	S1	O3	-55.4(5)
N1	C1	N3	C10	24.0(5)		F4	C12	S2	O4	-62.2(3)
N1	C2	C3	C4	1.3(5)		F4	C12	S2	O5	177.7(3)
N2	C1	N1	C2	66.2(4)		F4	C12	S2	O6	57.8(3)
N2	C1	N1	C6	-116.4(4)		F5	C12	S2	O4	58.6(3)
N2	C1	N3	C9	20.2(5)		F5	C12	S2	O5	-61.4(3)
N2	C1	N3	C10	-155.7(4)		F5	C12	S2	O6	178.6(3)
N3	C1	N1	C2	-113.5(3)		F6	C12	S2	O4	179.9(3)
N3	C1	N1	C6	63.8(4)		F6	C12	S2	O5	59.8(3)
N3	C1	N2	C7	26.4(5)		F6	C12	S2	O6	-60.1(3)

Table 8 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 4a.

Atom	x	y	z	U(eq)
H2	4171	3241	3779	48
H3	4065	3988	5235	58
H4	3168	3172	6488	63
H5	2474	1609	6273	66
H6	2545	911	4786	58
H7A	4780	806	1665	90
H7B	5420	1833	1740	90
H7C	3829	1705	1506	90
H8A	6292	1853	3522	69
H8B	6181	757	3299	69
H8C	5466	1186	4171	69
H9A	1767	1120	1402	93
H9B	958	451	2058	93
H9C	2550	325	2026	93
H10A	191	1510	3282	85
H10B	419	2281	2493	85
H10C	1086	2416	3553	85

X-ray Structure of Pyridinium 4h

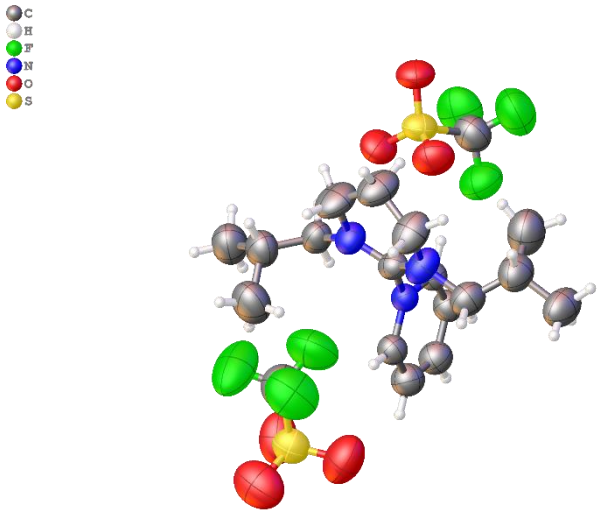


Figure S25. X-ray Structure of Pyridinium **4h**

Table 9. Crystal data and structure refinement for 4h.

Identification code	**4h**
CCDC number	2328545
Empirical formula	$C_{19}H_{29}F_6N_3O_6S_2$
Formula weight	573.57
Temperature/K	273.00
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	10.7560(6)
b/Å	14.3931(8)
c/Å	17.2752(8)
α/°	90
β/°	99.796(3)
γ/°	90
Volume/Å^3	2635.4(2)
Z	4
ρ_{calc}g/cm^3	1.446
μ/mm^{-1}	1.683
F(000)	1192.0
Crystal size/mm^3	0.12 × 0.09 × 0.07
Radiation	GaKα (λ = 1.34138)
2Θ range for data collection/°	6.996 to 119.156
Index ranges	-13 ≤ h ≤ 13, -18 ≤ k ≤ 18, -22 ≤ l ≤ 22
Reflections collected	30685
Independent reflections	5713 [R_{int} = 0.0593, R_{sigma} = 0.0511]
Data/restraints/parameters	5713/1319/631

Goodness-of-fit on F^2	1.008
Final R indexes [I>=2σ (I)]	R_1 = 0.1185, wR_2 = 0.2230
Final R indexes [all data]	R_1 = 0.1782, wR_2 = 0.2486
Largest diff. peak/hole / e $Å^{-3}$	0.51/-0.45

Table 10. Fractional Atomic Coordinates (×10⁴) and Equivalent Isotropic Displacement Parameters (Å²×10³) for 4h. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
S1	-2500(5)	3384(4)	3972(3)	78.2(11)
F1	-4871(7)	3273(7)	3944(6)	143(3)
F2	-4138(11)	4401(8)	4602(5)	157(3)
F3	-4410(10)	4423(7)	3347(5)	125(3)
O1	-2756(8)	2823(6)	3293(3)	97(2)
O2	-1665(6)	4125(6)	3909(5)	110(3)
O3	-2192(11)	2884(8)	4681(4)	98(3)
C18	-4019(5)	3925(6)	3974(5)	106(2)
S2	-3051(4)	4185(3)	-1358(2)	88.1(12)
S2A	-2985(7)	4301(5)	-1203(5)	113(2)
O4A	-3797(9)	4921(7)	-876(8)	108(4)
O5A	-1768(6)	4719(8)	-1149(7)	141(4)
O5	-4119(5)	3614(5)	-1640(5)	126(3)
O6A	-3403(12)	3991(10)	-1990(5)	158(4)
O4	-2252(6)	4235(6)	-1936(4)	159(3)
O6	-3373(11)	5104(4)	-1146(7)	156(4)
N1	-987(4)	5179(4)	2044(3)	58(3)
C2	-891(4)	5501(4)	1297(3)	68.9(18)
C3	-1969(5)	5765(4)	782(2)	83(2)
C4	-3144(4)	5708(4)	1012(3)	84(3)
C5	-3240(4)	5386(4)	1758(3)	72(2)
C6	-2162(5)	5122(4)	2274(2)	63(2)
N2	331(6)	4048(4)	2652(4)	74.2(19)
N3	694(6)	5607(4)	3024(5)	81(2)
C1	64(7)	4948(5)	2611(4)	63.6(12)
C7	1360(10)	3709(6)	3261(6)	112(3)
C8	1721(11)	4386(6)	3877(6)	111(3)
C9	1784(9)	5379(6)	3617(7)	107(3)
C10	-366(7)	3296(5)	2193(4)	78.8(18)
C11	426(9)	2703(7)	1763(6)	96(2)
C12	-394(10)	1911(6)	1337(6)	118(3)

C13	1021(10)	3205(7)	1136(6)	131(3)
C14	371(8)	6591(5)	2920(5)	90(2)
C15	144(11)	7078(5)	3624(6)	103(2)
C16	-907(11)	6584(7)	3966(7)	138(3)
C17	-192(11)	8090(5)	3502(6)	114(3)
N2A	833(15)	4285(12)	2502(9)	66(5)
N3A	234(17)	5449(11)	3298(8)	74(6)
C1A	30(17)	4938(9)	2635(11)	63.6(12)
C4A	-2928(11)	5859(11)	918(7)	75(7)
C3A	-3211(9)	5274(10)	1504(8)	56(5)
C2A	-2258(12)	4978(10)	2099(7)	50(5)
N1A	-1022(10)	5266(11)	2109(7)	53(8)
C6A	-739(9)	5852(9)	1522(8)	54(4)
C5A	-1692(12)	6148(10)	927(7)	71(5)
C7A	1963(18)	4042(16)	3067(11)	81(6)
C8A	2240(30)	4800(20)	3620(20)	127(12)
C9A	1200(20)	5208(18)	3972(11)	86(7)
C10A	580(20)	3782(15)	1762(12)	92(3)
C11A	400(20)	2774(19)	1736(14)	97(3)
C12A	80(30)	2230(20)	968(11)	121(5)
C13A	-720(20)	2660(20)	2180(15)	115(5)
C14A	-560(18)	6230(11)	3448(17)	96(3)
C15A	130(30)	7097(11)	3616(16)	103(3)
C16A	770(20)	7502(17)	2965(12)	104(5)
C17A	-560(30)	7910(16)	3935(18)	117(6)
S1A	-2506(13)	3659(10)	4098(8)	90(2)
O1A	-2480(20)	3287(16)	3346(9)	100(4)
O2A	-1890(20)	4523(13)	4231(14)	120(5)
O3A	-2520(30)	3099(17)	4767(11)	81(5)
F1A	-4890(20)	3691(17)	4252(14)	135(5)
F2A	-4090(20)	4778(16)	3429(14)	118(5)
F3A	-3650(20)	4767(16)	4621(14)	135(5)
C18A	-4029(13)	4217(13)	4026(11)	117(3)
F6	-2862(8)	3658(8)	105(6)	166(4)
F4	-1825(9)	2828(5)	-557(6)	185(4)
F5	-1206(7)	4178(6)	-228(5)	171(3)
C19	-2206(6)	3674(5)	-465(3)	129(3)
F7	-4044(8)	2961(8)	-729(8)	163(4)
F9	-2153(9)	2813(10)	-872(8)	183(5)

F8	-2283(14)	3624(13)	122(7)	168(4)
C19A	-2919(8)	3320(5)	-541(5)	127(3)

Table 11. Anisotropic Displacement Parameters ($Å^2×10^3$) for 4h. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U11	U22	U33	U23	U13	U12
S1	86.9(15)	84(2)	62.8(18)	9.9(15)	9.0(12)	-6.3(15)
F1	97(4)	169(7)	171(6)	-6(5)	45(4)	-20(4)
F2	174(7)	161(7)	146(5)	-26(5)	59(5)	4(5)
F3	121(6)	123(6)	127(5)	28(4)	8(4)	18(5)
O1	112(5)	105(5)	69(3)	-6(3)	2(3)	1(4)
O2	107(4)	108(5)	119(5)	21(4)	28(4)	-13(4)
O3	117(7)	102(6)	72(4)	24(4)	9(4)	11(4)
C18	107(4)	115(5)	102(4)	0(4)	33(4)	0(4)
S2	70.3(18)	101(2)	94(2)	1.3(18)	17.1(16)	-13.2(16)
S2A	95(3)	119(4)	126(4)	3(3)	23(3)	4(3)
O4A	93(6)	93(6)	143(8)	-9(6)	38(6)	31(5)
O5A	103(6)	143(7)	182(8)	-6(6)	33(6)	-28(6)
O5	73(4)	126(6)	171(6)	-44(5)	0(4)	-4(4)
O6A	152(8)	181(8)	146(8)	5(7)	41(7)	-31(7)
O4	109(6)	226(8)	143(6)	-3(6)	18(5)	1(6)
O6	145(7)	118(6)	207(8)	10(6)	33(6)	24(6)
N1	55(3)	58(3)	61(3)	1.7(16)	14.2(17)	3.4(16)
C2	69(2)	70(2)	69(2)	-0.4(18)	14.3(18)	0.6(18)
C3	85(3)	82(3)	82(3)	2.5(19)	13.3(19)	0.4(19)
C4	81(3)	83(3)	86(3)	4.0(19)	12.0(19)	2.1(19)
C5	68(3)	75(3)	72(3)	-2.6(19)	12.8(18)	2.4(18)
C6	59(3)	64(3)	64(3)	-0.4(18)	11.7(17)	-1.6(17)
N2	70(4)	70(4)	79(4)	2(3)	5(3)	12(3)
N3	59(3)	66(4)	112(5)	6(3)	-3(3)	2(3)
C1	58(2)	67(3)	66(3)	9(2)	11(2)	8(2)
C7	114(6)	98(6)	109(6)	24(5)	-22(5)	21(5)
C8	114(6)	98(6)	106(6)	19(5)	-23(5)	7(5)
C9	82(5)	96(6)	132(7)	-1(5)	-18(5)	10(5)
C10	83(4)	67(3)	91(4)	3(3)	28(3)	1(3)
C11	95(4)	93(4)	105(4)	-3(3)	33(3)	7(3)
C12	132(6)	104(6)	124(6)	-11(5)	42(5)	-3(5)
C13	135(6)	136(7)	135(6)	-9(6)	57(5)	-2(6)
C14	91(4)	79(4)	97(4)	3(3)	10(3)	-4(3)

C15	111(4)	94(4)	101(4)	-7(3)	4(4)	7(4)
C16	145(7)	112(6)	159(7)	-17(6)	35(6)	5(6)
C17	138(7)	83(5)	112(6)	-6(5)	-5(5)	0(5)
N2A	64(8)	76(9)	55(8)	-1(7)	2(6)	17(7)
N3A	77(9)	65(8)	81(9)	5(7)	10(7)	-5(7)
C1A	58(2)	67(3)	66(3)	9(2)	11(2)	8(2)
C4A	74(7)	75(7)	76(7)	1(2)	12(2)	0(2)
C3A	54(5)	57(5)	56(5)	-2(2)	11(2)	1(2)
C2A	49(5)	50(5)	50(5)	-1(2)	10(2)	0(2)
N1A	51(9)	52(9)	55(9)	1(2)	11(2)	3(2)
C6A	55(5)	55(5)	53(5)	0(2)	9(2)	0(2)
C5A	71(6)	71(6)	72(6)	1(2)	11(2)	-1(2)
C7A	69(9)	86(10)	89(10)	21(8)	12(8)	29(8)
C8A	119(14)	134(14)	125(14)	15(10)	12(9)	-14(10)
C9A	85(10)	94(11)	79(10)	6(8)	15(8)	-3(8)
C10A	93(5)	91(5)	98(5)	0(5)	31(5)	8(5)
C11A	98(5)	93(5)	104(5)	-2(5)	32(5)	4(5)
C12A	130(9)	113(9)	126(9)	-8(9)	40(8)	9(9)
C13A	114(9)	110(9)	123(9)	2(9)	25(8)	5(9)
C14A	99(6)	93(5)	98(6)	-7(5)	19(5)	0(5)
C15A	108(5)	93(5)	103(5)	-6(5)	10(5)	4(5)
C16A	108(9)	92(9)	110(9)	-7(8)	11(8)	-5(8)
C17A	124(9)	99(9)	125(10)	-15(9)	14(9)	4(8)
S1A	90(3)	107(5)	77(4)	19(4)	26(3)	-3(4)
O1A	105(8)	110(9)	90(7)	7(7)	29(6)	4(8)
O2A	123(9)	119(9)	119(9)	7(8)	19(8)	-20(8)
O3A	87(9)	96(9)	59(7)	15(7)	15(6)	12(7)
F1A	116(8)	155(9)	141(9)	-6(8)	41(7)	-18(8)
F2A	111(9)	116(10)	131(8)	25(8)	35(7)	14(8)
F3A	135(10)	130(10)	140(8)	-37(8)	19(8)	-15(8)
C18A	113(5)	128(6)	113(5)	1(5)	31(5)	-1(5)
F6	164(7)	210(7)	134(6)	25(6)	53(6)	-9(7)
F4	194(7)	144(6)	181(7)	-21(6)	-71(6)	49(6)
F5	132(6)	214(7)	156(6)	-25(6)	-3(5)	-43(5)
C19	119(5)	131(5)	134(5)	-4(4)	14(4)	-1(4)
F7	153(8)	137(7)	203(9)	-14(7)	45(7)	-33(6)
F9	178(8)	138(7)	193(9)	-42(7)	-84(8)	37(7)
F8	164(8)	186(7)	139(7)	17(7)	-15(7)	18(7)
C19A	116(5)	133(5)	129(5)	-19(5)	8(5)	1(5)

Table 12. Bond Lengths for 4h.

Atom	Atom	Length/Å		Atom	Atom	Length/Å
S1	O1	1.411(2)		C15	C17	1.507(10)
S1	O2	1.410(2)		N2A	C1A	1.323(14)
S1	O3	1.410(2)		N2A	C7A	1.466(15)
S1	C18	1.811(2)		N2A	C10A	1.454(15)
F1	C18	1.306(2)		N3A	C1A	1.347(13)
F2	C18	1.307(2)		N3A	C9A	1.467(15)
F3	C18	1.307(2)		N3A	C14A	1.463(16)
S2	O5	1.4294(12)		C1A	N1A	1.407(13)
S2	O4	1.4267(12)		C4A	C3A	1.3900
S2	O6	1.4298(12)		C4A	C5A	1.3900
S2	C19	1.807(2)		C3A	C2A	1.3900
S2A	O4A	1.4311(12)		C2A	N1A	1.3900
S2A	O5A	1.4295(12)		N1A	C6A	1.3900
S2A	O6A	1.4290(12)		C6A	C5A	1.3900
S2A	C19A	1.811(2)		C7A	C8A	1.440(16)
N1	C2	1.3900		C8A	C9A	1.483(16)
N1	C6	1.3900		C10A	C11A	1.462(17)
N1	C1	1.404(6)		C11A	C12A	1.531(16)
C2	C3	1.3900		C11A	C13A	1.546(16)
C3	C4	1.3900		C14A	C15A	1.453(17)
C4	C5	1.3900		C15A	C16A	1.534(16)
C5	C6	1.3900		C15A	C17A	1.533(15)
N2	C1	1.326(8)		S1A	O1A	1.410(2)
N2	C7	1.474(9)		S1A	O2A	1.409(2)
N2	C10	1.470(8)		S1A	O3A	1.410(2)
N3	C1	1.306(8)		S1A	C18A	1.810(2)
N3	C9	1.457(9)		F1A	C18A	1.305(2)
N3	C14	1.462(8)		F2A	C18A	1.305(2)
C7	C8	1.446(10)		F3A	C18A	1.305(2)
C8	C9	1.504(10)		F6	C19	1.306(2)
C10	C11	1.490(9)		F4	C19	1.303(2)
C11	C12	1.549(10)		F5	C19	1.304(2)
C11	C13	1.531(10)		F7	C19A	1.305(2)
C14	C15	1.460(10)		F9	C19A	1.304(2)
C15	C16	1.536(10)		F8	C19A	1.305(2)

Table 13. Bond Angles for 4h.

Atom	Atom	Atom	Angle/°		Atom	Atom	Atom	Angle/°
1	S1	C18	101.5(5)		C1A	N2A	C7A	123.1(12)
O2	S1	O1	113.8(5)		C1A	N2A	C10A	118.5(15)

O2	S1	C18	105.2(5)		C10A	N2A	C7A	118.5(14)
O3	S1	O1	114.4(6)		C1A	N3A	C9A	122.5(12)
O3	S1	O2	113.3(7)		C1A	N3A	C14A	123.7(15)
O3	S1	C18	107.3(5)		C14A	N3A	C9A	113.5(15)
F1	C18	S1	108.5(5)		N2A	C1A	N3A	121.2(12)
F1	C18	F2	104.0(7)		N2A	C1A	N1A	127.1(14)
F1	C18	F3	103.7(8)		N3A	C1A	N1A	111.3(12)
F2	C18	S1	116.2(7)		C3A	C4A	C5A	120.0
F3	C18	S1	113.4(7)		C4A	C3A	C2A	120.0
F3	C18	F2	109.7(8)		C3A	C2A	N1A	120.0
O5	S2	O6	113.8(7)		C2A	N1A	C1A	124.7(14)
O5	S2	C19	108.3(4)		C6A	N1A	C1A	115.0(14)
O4	S2	O5	109.59(17)		C6A	N1A	C2A	120.0
O4	S2	O6	109.47(17)		C5A	C6A	N1A	120.0
O4	S2	C19	110.0(5)		C6A	C5A	C4A	120.0
O6	S2	C19	105.5(5)		C8A	C7A	N2A	108(2)
O4A	S2A	C19A	101.4(6)		C7A	C8A	C9A	119.2(19)
O5A	S2A	O4A	108.98(17)		N3A	C9A	C8A	105(2)
O5A	S2A	C19A	110.5(6)		N2A	C10A	C11A	121.6(17)
O6A	S2A	O4A	117.2(9)		C10A	C11A	C12A	123(2)
O6A	S2A	O5A	109.30(17)		C10A	C11A	C13A	102(2)
O6A	S2A	C19A	109.2(6)		C12A	C11A	C13A	107.1(14)
C2	N1	C6	120.0		C15A	C14A	N3A	113.8(17)
C2	N1	C1	123.2(5)		C14A	C15A	C16A	117(2)
C6	N1	C1	116.7(5)		C14A	C15A	C17A	118(2)
N1	C2	C3	120.0		C17A	C15A	C16A	106.2(14)
C4	C3	C2	120.0		O1A	S1A	C18A	105.2(13)
C3	C4	C5	120.0		O2A	S1A	O1A	113.8(13)
C4	C5	C6	120.0		O2A	S1A	O3A	116.1(17)
C5	C6	N1	120.0		O2A	S1A	C18A	91.0(12)
C1	N2	C7	119.4(6)		O3A	S1A	O1A	122.8(15)
C1	N2	C10	127.2(6)		O3A	S1A	C18A	100.1(13)
C10	N2	C7	113.1(6)		F1A	C18A	S1A	113.8(15)
C1	N3	C9	120.1(6)		F2A	C18A	S1A	104.4(15)
C1	N3	C14	123.1(6)		F2A	C18A	F1A	131.0(19)
C9	N3	C14	116.8(6)		F2A	C18A	F3A	102(2)
N2	C1	N1	114.3(6)		F3A	C18A	S1A	93.4(15)
N3	C1	N1	119.3(6)		F3A	C18A	F1A	104.9(17)
N3	C1	N2	126.4(6)		F6	C19	S2	113.1(6)
C8	C7	N2	112.1(7)		F4	C19	S2	113.6(6)
C7	C8	C9	116.2(8)		F4	C19	F6	107.3(2)
N3	C9	C8	110.6(7)		F4	C19	F5	107.3(2)
N2	C10	C11	114.1(6)		F5	C19	S2	108.0(5)

C10	C11	C12	109.3(7)		F5	C19	F6	107.1(2)
C10	C11	C13	115.2(9)		F7	C19A	S2A	102.5(8)
C13	C11	C12	106.5(7)		F7	C19A	F8	132.6(11)
C15	C14	N3	115.6(7)		F9	C19A	S2A	96.8(9)
C14	C15	C16	109.7(8)		F9	C19A	F7	107.3(2)
C14	C15	C17	114.7(8)		F9	C19A	F8	107.3(2)
C17	C15	C16	109.1(8)		F8	C19A	S2A	104.6(10)

Table 14. Torsion Angles for 4h.

A	B	C	D	Angle/°		A	B	C	D	Angle/°
O1	S1	C18	F1	54.2(8)		C9	N3	C1	N1	179.8(9)
O1	S1	C18	F2	171.0(8)		C9	N3	C1	N2	-2.2(16)
O1	S1	C18	F3	-60.4(7)		C9	N3	C14	C15	-56.5(12)
O2	S1	C18	F1	173.1(7)		C10	N2	C1	N1	-2.0(13)
O2	S1	C18	F2	-70.2(8)		C10	N2	C1	N3	179.9(9)
O2	S1	C18	F3	58.4(7)		C10	N2	C7	C8	-158.6(9)
O3	S1	C18	F1	-66.1(9)		C14	N3	C1	N1	-0.9(14)
O3	S1	C18	F2	50.7(9)		C14	N3	C1	N2	177.1(9)
O3	S1	C18	F3	179.3(8)		C14	N3	C9	C8	158.5(9)
O4A	S2A	C19A	F7	71.8(7)		N2A	C1A	N1A	C2A	98(3)
O4A	S2A	C19A	F9	-178.8(7)		N2A	C1A	N1A	C6A	-75(3)
O4A	S2A	C19A	F8	-68.9(8)		N2A	C7A	C8A	C9A	46(4)
O5A	S2A	C19A	F7	-172.8(7)		N2A	C10A	C11A	C12A	177(2)
O5A	S2A	C19A	F9	-63.4(6)		N2A	C10A	C11A	C13A	58(3)
O5A	S2A	C19A	F8	46.5(7)		N3A	C1A	N1A	C2A	-89(2)
O5	S2	C19	F6	-64.1(6)		N3A	C1A	N1A	C6A	98(2)
O5	S2	C19	F4	58.6(6)		N3A	C14A	C15A	C16A	62(3)
O5	S2	C19	F5	177.5(5)		N3A	C14A	C15A	C17A	-169(2)
O6A	S2A	C19A	F7	-52.5(9)		C1A	N2A	C7A	C8A	-19(3)
O6A	S2A	C19A	F9	56.9(8)		C1A	N2A	C10A	C11A	-120(3)
O6A	S2A	C19A	F8	166.8(8)		C1A	N3A	C9A	C8A	34(3)
O4	S2	C19	F6	176.2(5)		C1A	N3A	C14A	C15A	-123(3)
O4	S2	C19	F4	-61.2(6)		C1A	N1A	C6A	C5A	174.0(14)
O4	S2	C19	F5	57.8(5)		C4A	C3A	C2A	N1A	0.0
O6	S2	C19	F6	58.2(6)		C3A	C4A	C5A	C6A	0.0
O6	S2	C19	F4	-179.2(6)		C3A	C2A	N1A	C1A	-173.3(16)
O6	S2	C19	F5	-60.2(6)		C3A	C2A	N1A	C6A	0.0
N1	C2	C3	C4	0.0		C2A	N1A	C6A	C5A	0.0
C2	N1	C6	C5	0.0		N1A	C6A	C5A	C4A	0.0
C2	N1	C1	N2	-97.5(9)		C5A	C4A	C3A	C2A	0.0
C2	N1	C1	N3	80.7(9)		C7A	N2A	C1A	N3A	3(4)
C2	C3	C4	C5	0.0		C7A	N2A	C1A	N1A	175(2)
C3	C4	C5	C6	0.0		C7A	N2A	C10A	C11A	60(3)

C4	C5	C6	N1	0.0		C7A	C8A	C9A	N3A	-53(4)
C6	N1	C2	C3	0.0		C9A	N3A	C1A	N2A	-12(4)
C6	N1	C1	N2	85.9(8)		C9A	N3A	C1A	N1A	175(2)
C6	N1	C1	N3	-95.8(9)		C9A	N3A	C14A	C15A	63(3)
N2	C7	C8	C9	-41.0(15)		C10A	N2A	C1A	N3A	-178(2)
N2	C10	C11	C12	177.3(8)		C10A	N2A	C1A	N1A	-5(4)
N2	C10	C11	C13	-62.8(11)		C10A	N2A	C7A	C8A	162(2)
N3	C14	C15	C16	-56.7(11)		C14A	N3A	C1A	N2A	175(2)
N3	C14	C15	C17	-179.8(8)		C14A	N3A	C1A	N1A	1(3)
C1	N1	C2	C3	-176.5(6)		C14A	N3A	C9A	C8A	-152(2)
C1	N1	C6	C5	176.7(5)		O1A	S1A	C18A	F1A	95(2)
C1	N2	C7	C8	16.1(14)		O1A	S1A	C18A	F2A	-53.7(18)
C1	N2	C10	C11	125.6(10)		O1A	S1A	C18A	F3A	-157.4(17)
C1	N3	C9	C8	-22.1(15)		O2A	S1A	C18A	F1A	-150(2)
C1	N3	C14	C15	124.1(10)		O2A	S1A	C18A	F2A	61.3(18)
C7	N2	C1	N1	-175.9(8)		O2A	S1A	C18A	F3A	-42.3(17)
C7	N2	C1	N3	6.0(15)		O3A	S1A	C18A	F1A	-33(2)
C7	N2	C10	C11	-60.2(11)		O3A	S1A	C18A	F2A	178.1(18)
C7	C8	C9	N3	44.0(16)		O3A	S1A	C18A	F3A	74(2)

Table 15. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 4h.

Atom	x	y	z	U(eq)
H2	-105	5540	1143	83
H3	-1905	5981	282	100
H4	-3865	5885	667	100
H5	-4026	5348	1912	86
H6	-2226	4907	2773	75
H7A	1092	3142	3488	134
H7B	2087	3561	3020	134
H8A	2542	4213	4165	133
H8B	1125	4348	4239	133
H9A	1807	5788	4066	129
H9B	2551	5476	3403	129
H10A	-1041	3566	1817	95
H10B	-749	2905	2545	95
H11	1102	2426	2145	115
H12A	-713	1533	1717	177
H12B	109	1536	1050	177
H12C	-1087	2172	980	177
H13A	419	3244	658	197
H13B	1749	2866	1040	197
H13C	1270	3820	1315	197

H14A	1051	6904	2721	108
H14B	-380	6644	2522	108
H15	918	7041	4014	124
H16A	-1615	6478	3556	206
H16B	-1164	6966	4366	206
H16C	-598	6000	4189	206
H17A	393	8382	3215	171
H17B	-150	8389	4002	171
H17C	-1031	8144	3209	171
H4A	-3565	6058	519	90
H3A	-4037	5081	1497	67
H2A	-2447	4586	2491	60
H6A	88	6045	1529	65
H5A	-1503	6540	535	86
H7AA	1817	3475	3342	98
H7AB	2669	3939	2795	98
H8AA	2617	5291	3355	153
H8AB	2880	4579	4044	153
H9AA	882	4764	4311	103
H9AB	1493	5757	4275	103
H10C	1270	3917	1483	111
H10D	-172	4053	1456	111
H11A	1149	2488	2053	116
H12D	-733	2415	696	181
H12E	72	1575	1082	181
H12F	706	2350	644	181
H13D	-668	2063	2433	172
H13E	-1496	2702	1815	172
H13F	-689	3139	2568	172
H14C	-1215	6319	2994	115
H14D	-970	6077	3891	115
H15A	820	6944	4042	123
H16D	266	7380	2463	157
H16E	1587	7218	2988	157
H16F	875	8160	3039	157
H17D	-1060	7681	4303	176
H17E	-1094	8214	3508	176
H17F	52	8345	4193	176

Table 16. Atomic Occupancy for 4h.

Atom	Occupancy		Atom	Occupancy		Atom	Occupancy
S1	0.713(13)		F1	0.713(13)		F2	0.713(13)
F3	0.713(13)		O1	0.713(13)		O2	0.713(13)

O3	0.713(13)		C18	0.713(13)		S2	0.587(5)
S2A	0.413(5)		O4A	0.413(5)		O5A	0.413(5)
O5	0.587(5)		O6A	0.413(5)		O4	0.587(5)
O6	0.587(5)		N1	0.749(5)		C2	0.749(5)
H2	0.749(5)		C3	0.749(5)		H3	0.749(5)
C4	0.749(5)		H4	0.749(5)		C5	0.749(5)
H5	0.749(5)		C6	0.749(5)		H6	0.749(5)
N2	0.749(5)		N3	0.749(5)		C1	0.749(5)
C7	0.749(5)		H7A	0.749(5)		H7B	0.749(5)
C8	0.749(5)		H8A	0.749(5)		H8B	0.749(5)
C9	0.749(5)		H9A	0.749(5)		H9B	0.749(5)
C10	0.749(5)		H10A	0.749(5)		H10B	0.749(5)
C11	0.749(5)		H11	0.749(5)		C12	0.749(5)
H12A	0.749(5)		H12B	0.749(5)		H12C	0.749(5)
C13	0.749(5)		H13A	0.749(5)		H13B	0.749(5)
H13C	0.749(5)		C14	0.749(5)		H14A	0.749(5)
H14B	0.749(5)		C15	0.749(5)		H15	0.749(5)
C16	0.749(5)		H16A	0.749(5)		H16B	0.749(5)
H16C	0.749(5)		C17	0.749(5)		H17A	0.749(5)
H17B	0.749(5)		H17C	0.749(5)		N2A	0.251(5)
N3A	0.251(5)		C1A	0.251(5)		C4A	0.251(5)
H4A	0.251(5)		C3A	0.251(5)		H3A	0.251(5)
C2A	0.251(5)		H2A	0.251(5)		N1A	0.251(5)
C6A	0.251(5)		H6A	0.251(5)		C5A	0.251(5)
H5A	0.251(5)		C7A	0.251(5)		H7AA	0.251(5)
H7AB	0.251(5)		C8A	0.251(5)		H8AA	0.251(5)
H8AB	0.251(5)		C9A	0.251(5)		H9AA	0.251(5)
H9AB	0.251(5)		C10A	0.251(5)		H10C	0.251(5)
H10D	0.251(5)		C11A	0.251(5)		H11A	0.251(5)
C12A	0.251(5)		H12D	0.251(5)		H12E	0.251(5)
H12F	0.251(5)		C13A	0.251(5)		H13D	0.251(5)
H13E	0.251(5)		H13F	0.251(5)		C14A	0.251(5)
H14C	0.251(5)		H14D	0.251(5)		C15A	0.251(5)
H15A	0.251(5)		C16A	0.251(5)		H16D	0.251(5)
H16E	0.251(5)		H16F	0.251(5)		C17A	0.251(5)
H17D	0.251(5)		H17E	0.251(5)		H17F	0.251(5)
S1A	0.287(13)		O1A	0.287(13)		O2A	0.287(13)
O3A	0.287(13)		F1A	0.287(13)		F2A	0.287(13)
F3A	0.287(13)		C18A	0.287(13)		F6	0.587(5)
F4	0.587(5)		F5	0.587(5)		C19	0.587(5)
F7	0.413(5)		F9	0.413(5)		F8	0.413(5)

25. Different pyridine C-4 selective functionalizations via C-C bond formation

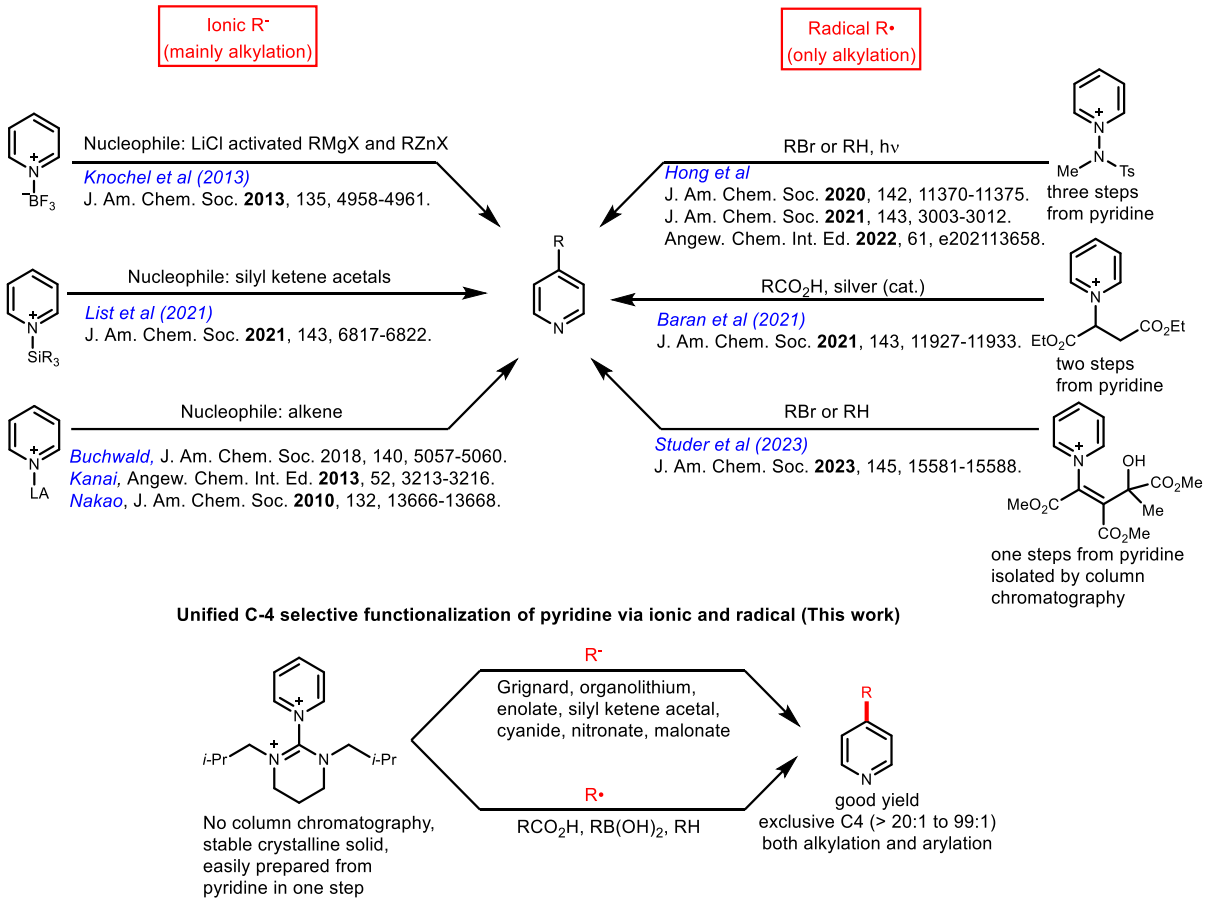


Figure S26. different pyridine C-4 selective functionalization strategies

26. References

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27. Copies of NMR spectroscopy

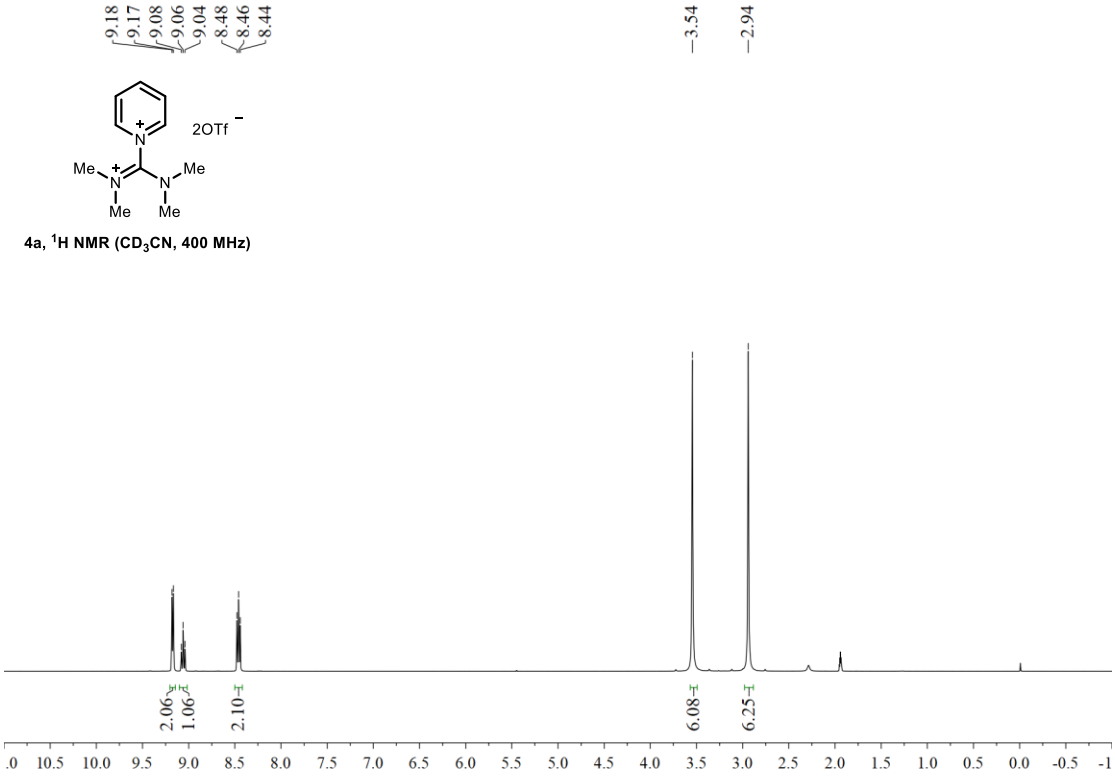


Figure S27. ^{1}H NMR of **4a** (CD_3CN, 400 MHz)

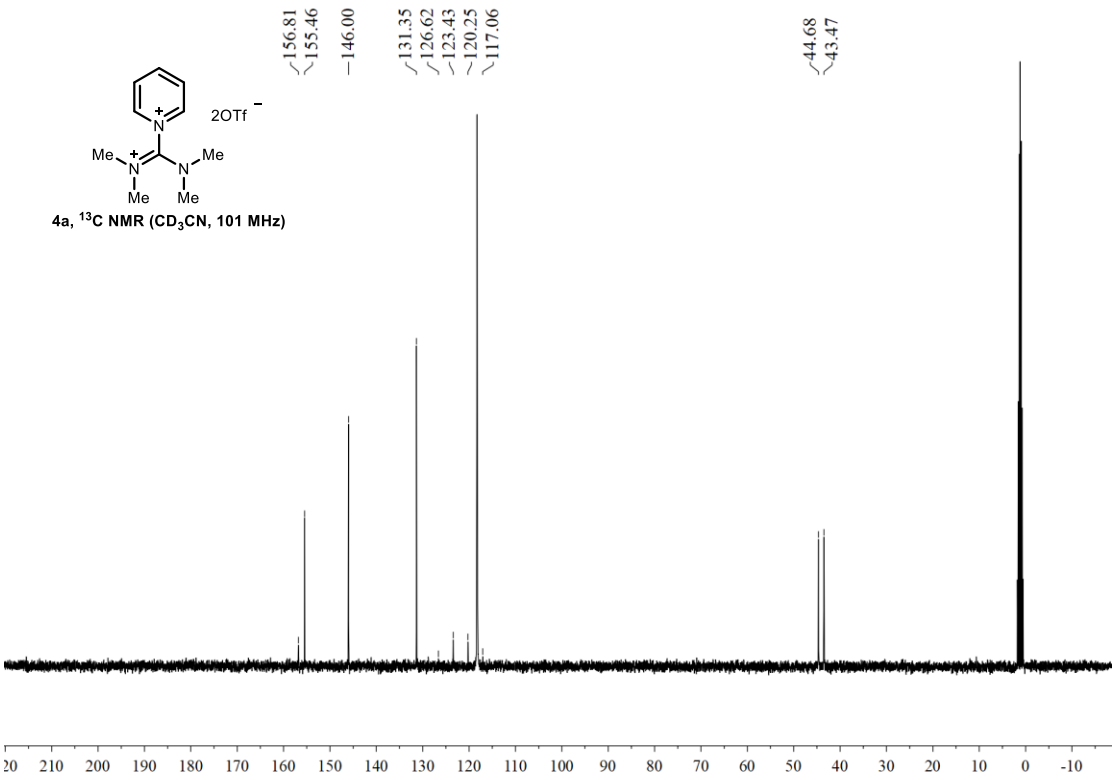


Figure S28. ^{13}C NMR of **4a** (CD_3CN, 101 MHz)

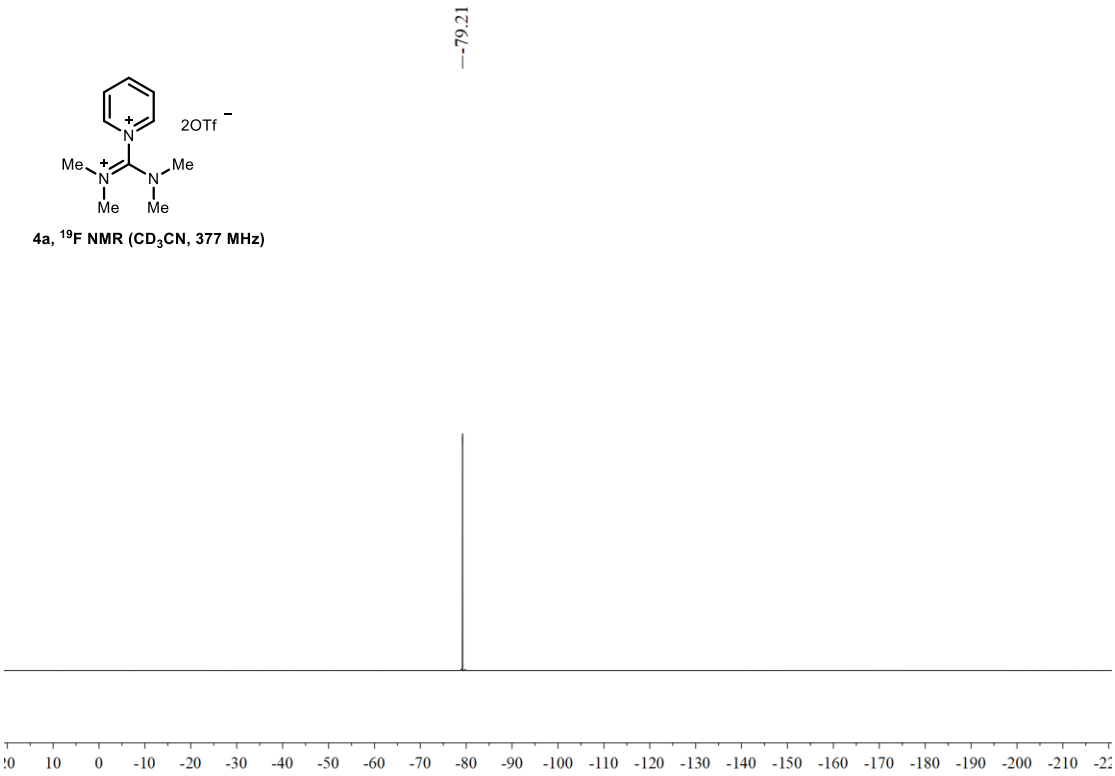


Figure S29. ^{19}F NMR of **4a** (CD_3CN, 377 MHz)

Figure S30. ^{1}H NMR of **4b** (D_2O, 600 MHz)

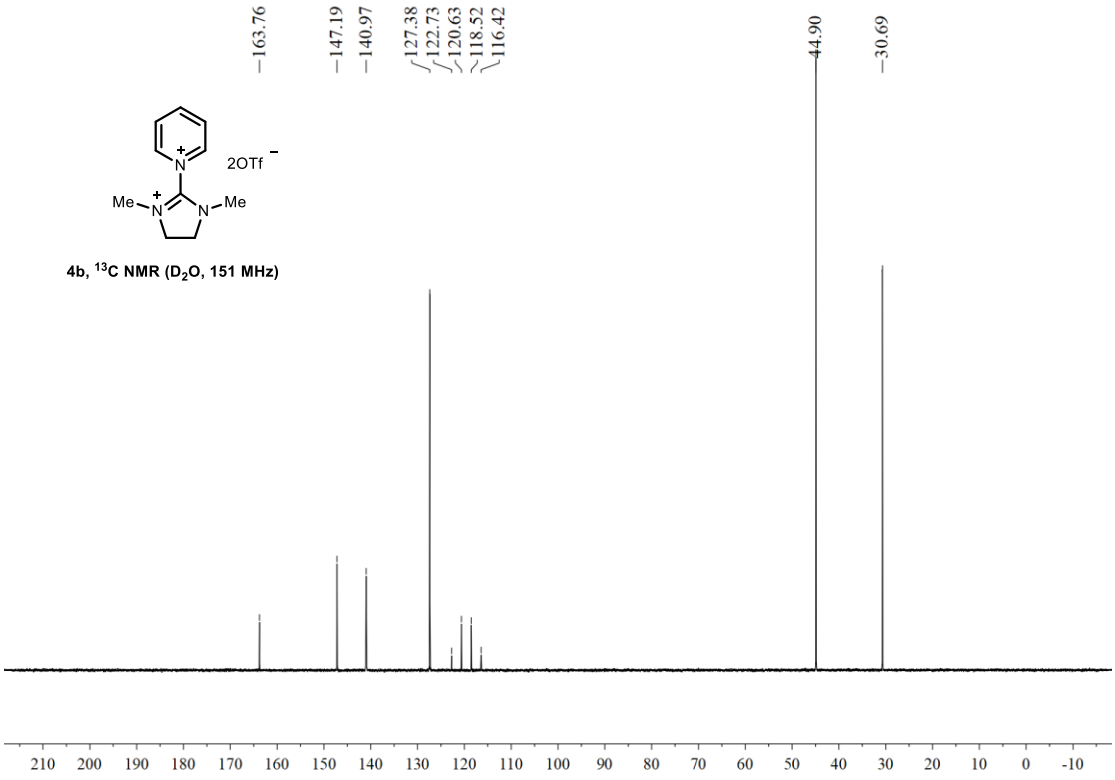


Figure S31. ^{13}C NMR of **4b** (D_2O, 151 MHz)

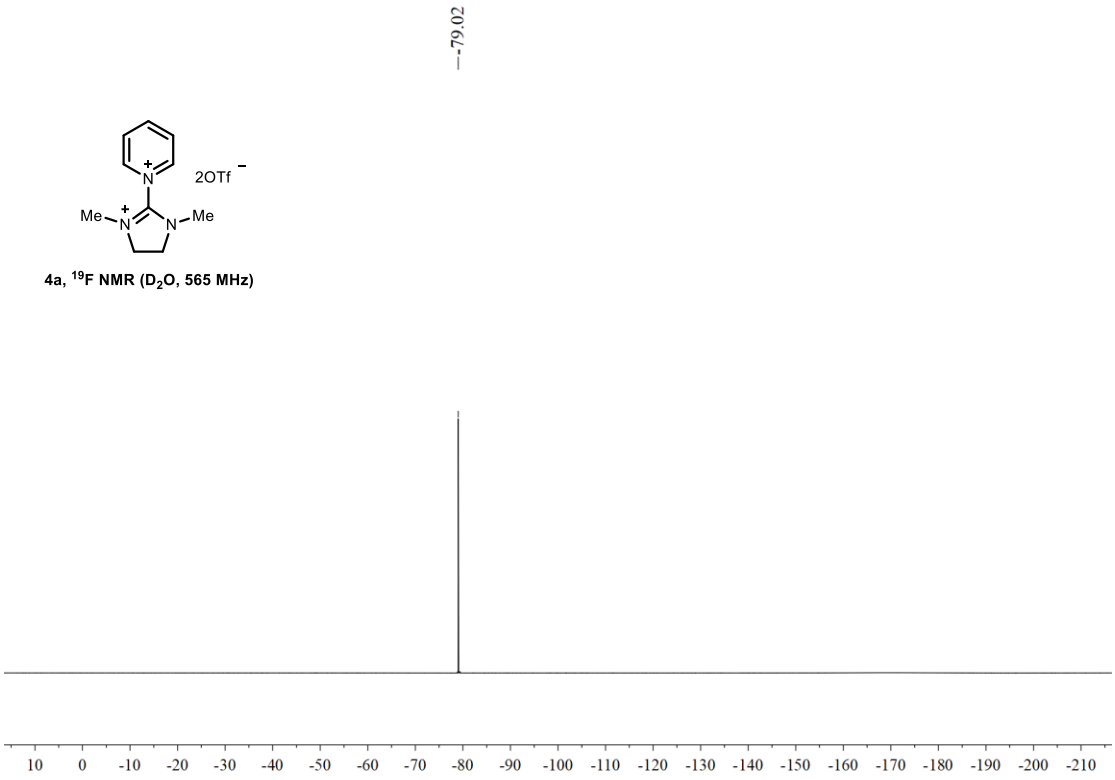


Figure S32. ^{19}F NMR of **4b** (D_2O, 565 MHz)

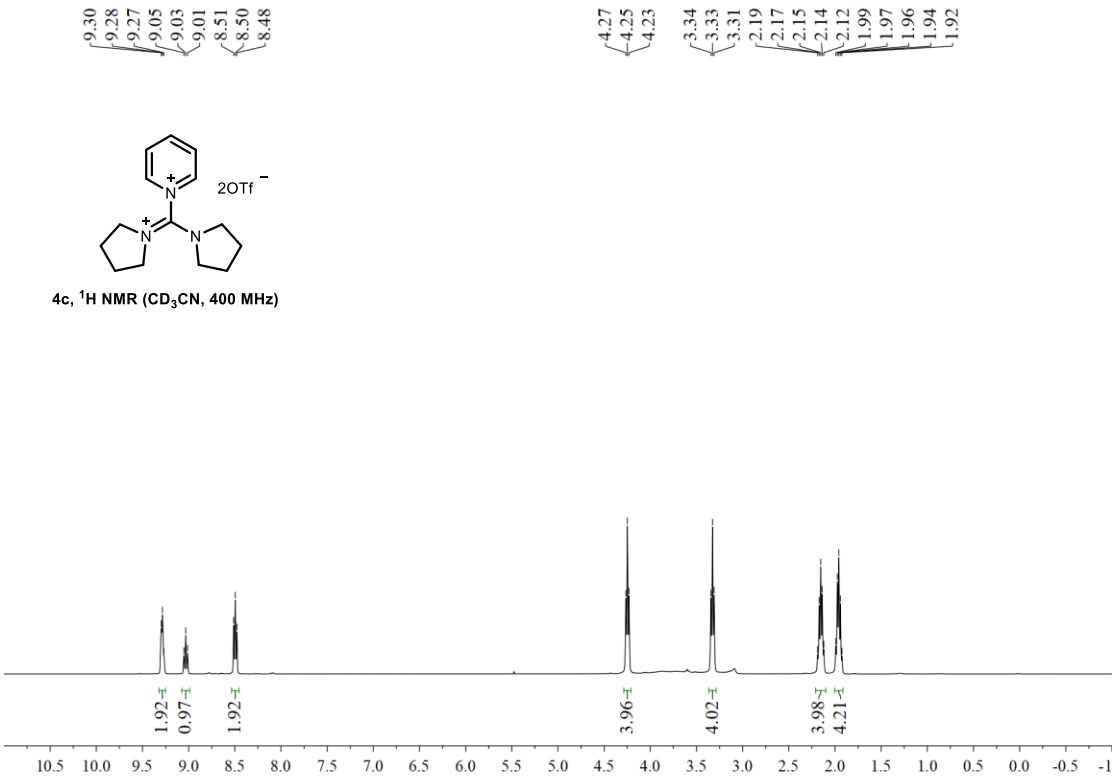


Figure S33. ^{1}H NMR of **4c** (CD_3CN, 400 MHz)

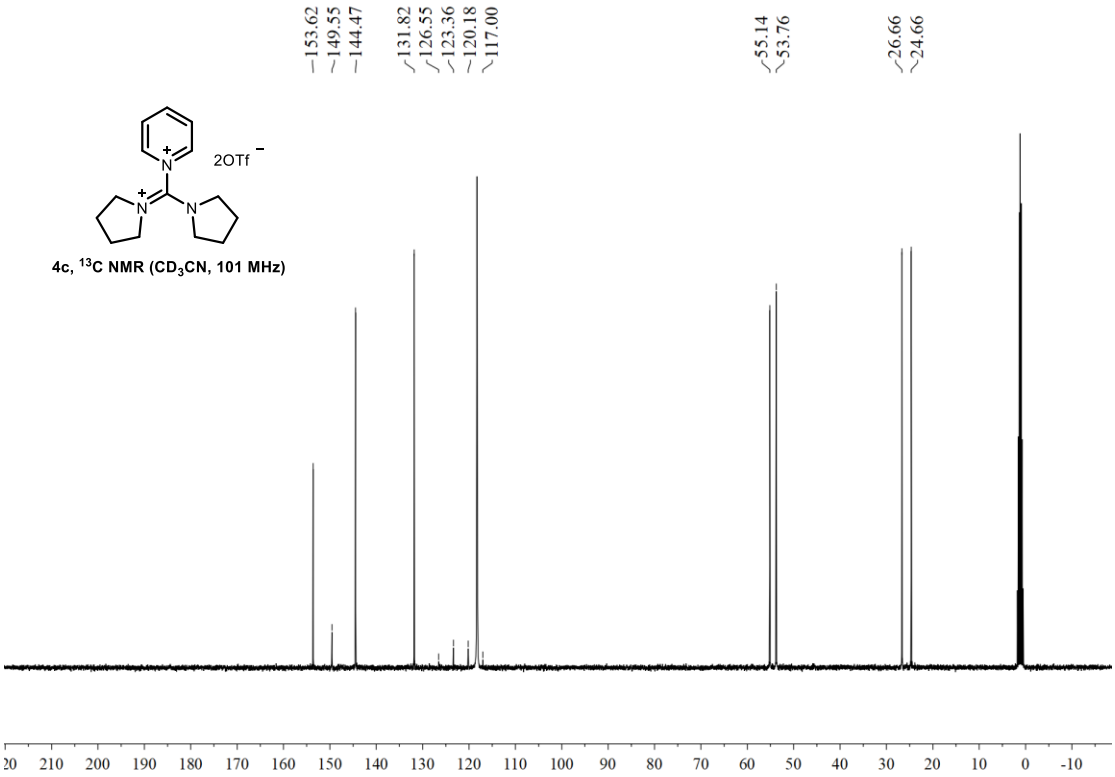


Figure S34. ^{13}C NMR of **4c** (CD_3CN, 101 MHz)

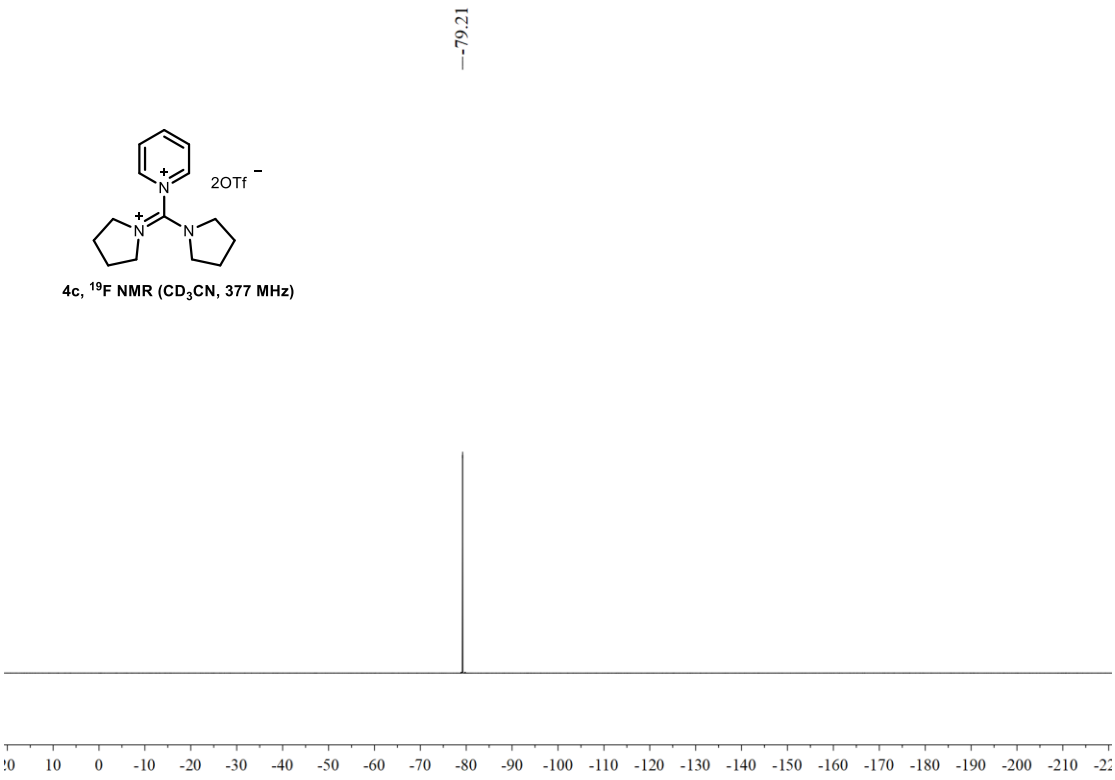


Figure S35. ^{19}F NMR of **4c** (CD_3CN, 377 MHz)

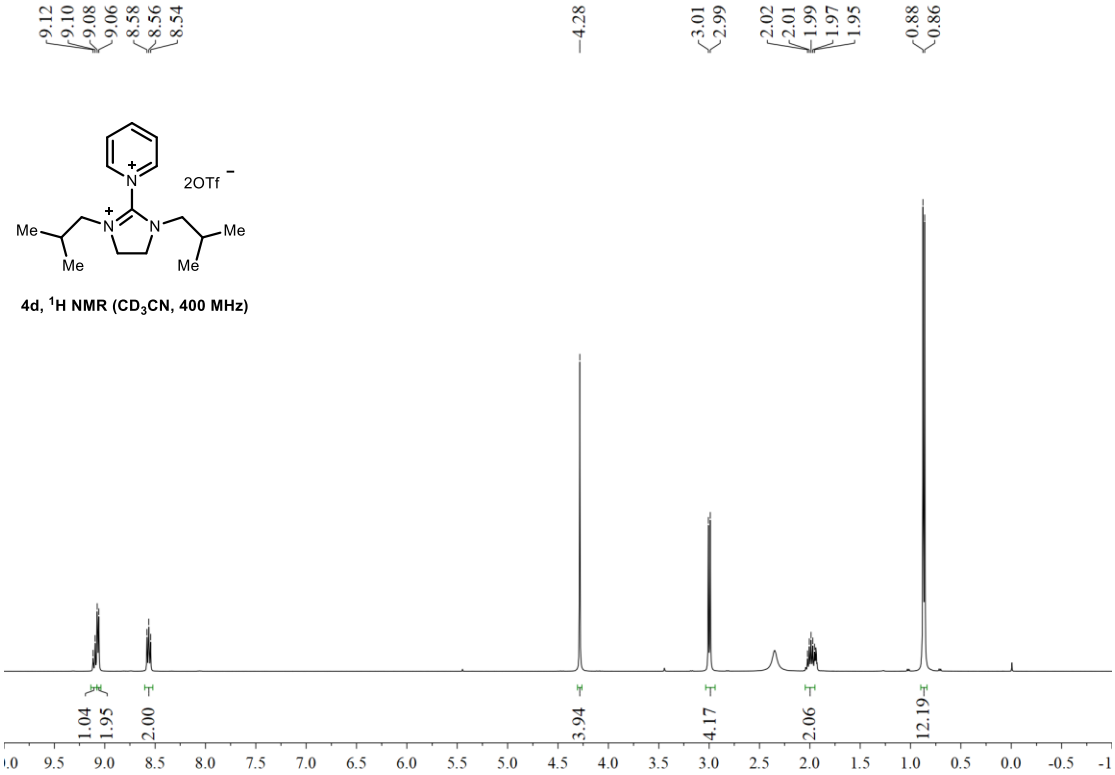


Figure S36. ^{1}H NMR of **4d** (CD_3CN, 400 MHz)

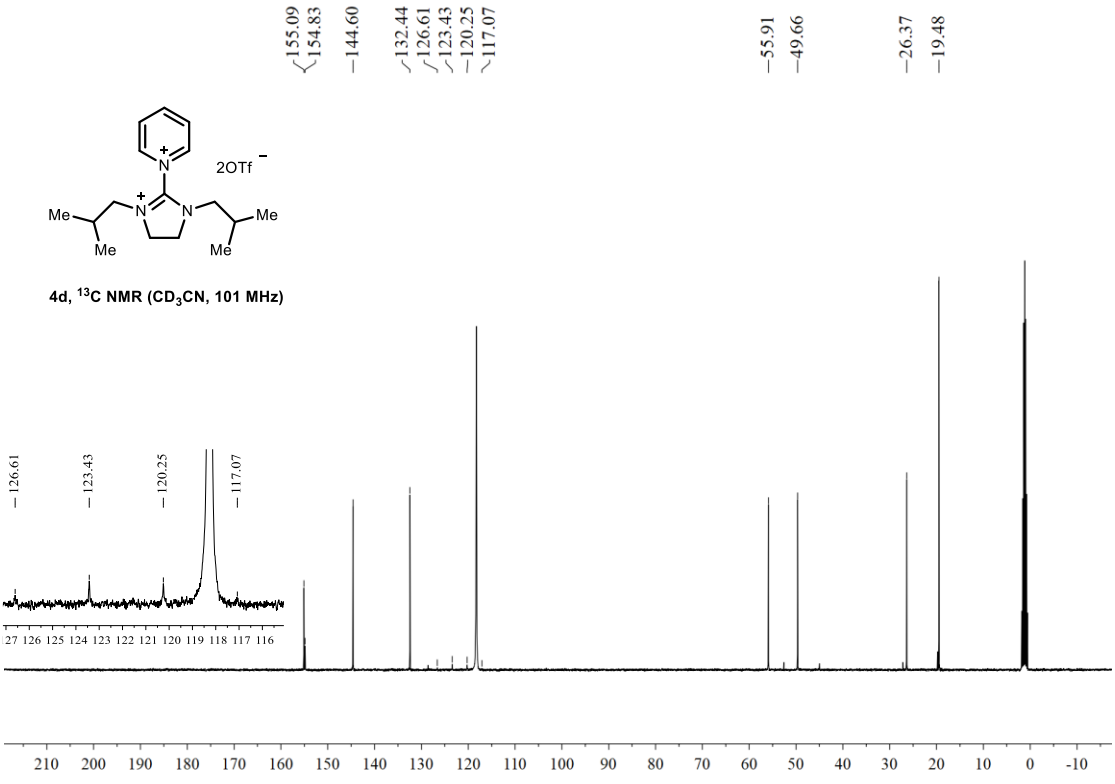


Figure S37. ^{13}C NMR of **4d** (CD_3CN, 101 MHz)

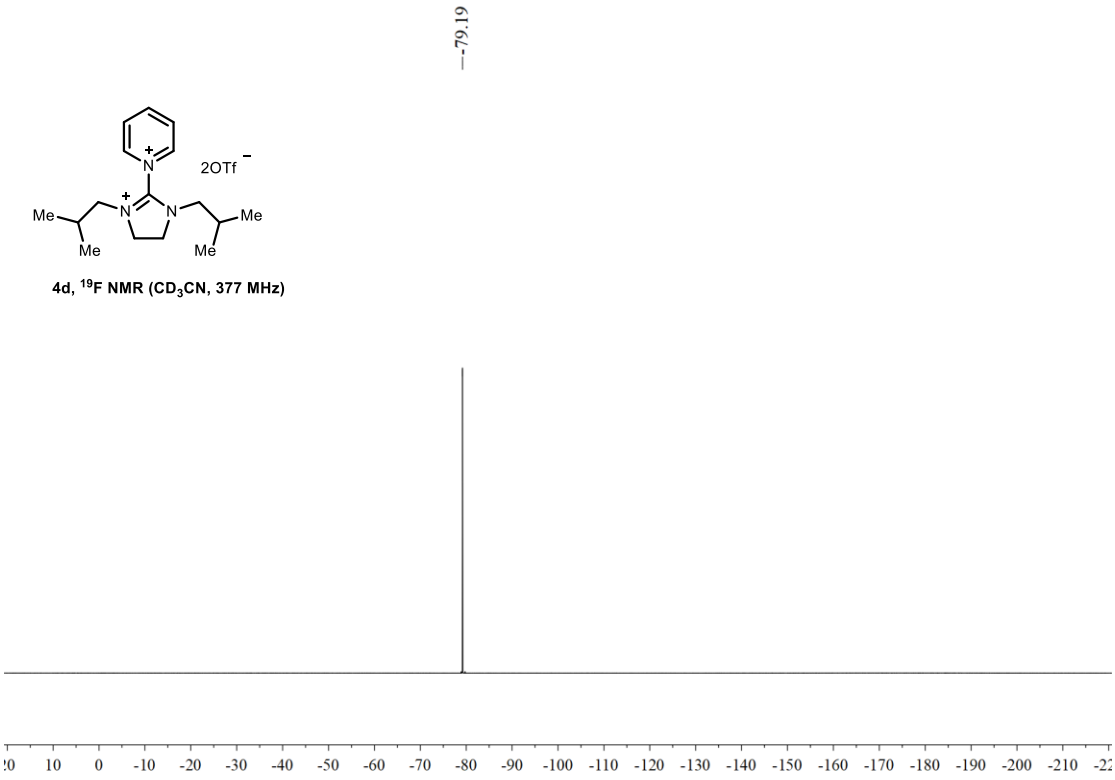


Figure S38. ^{19}F NMR of **4d** (CD_3CN, 377 MHz)

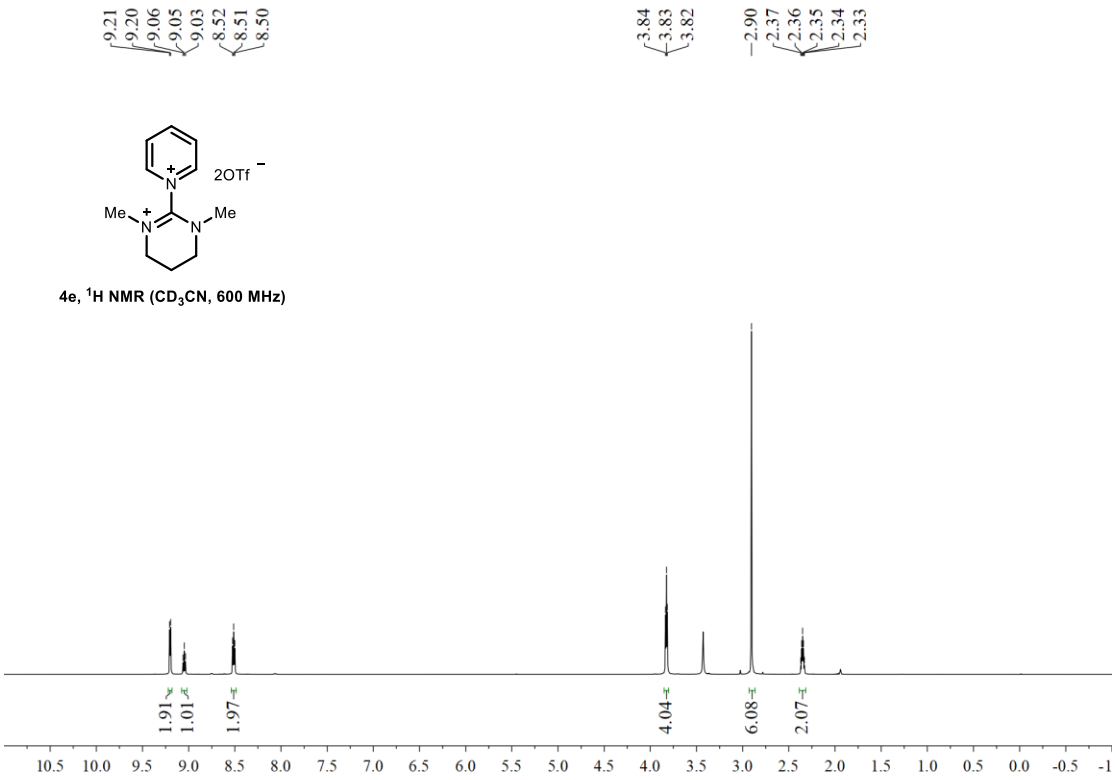


Figure S39. ^{1}H NMR of **4e** (CD_3CN, 600 MHz)

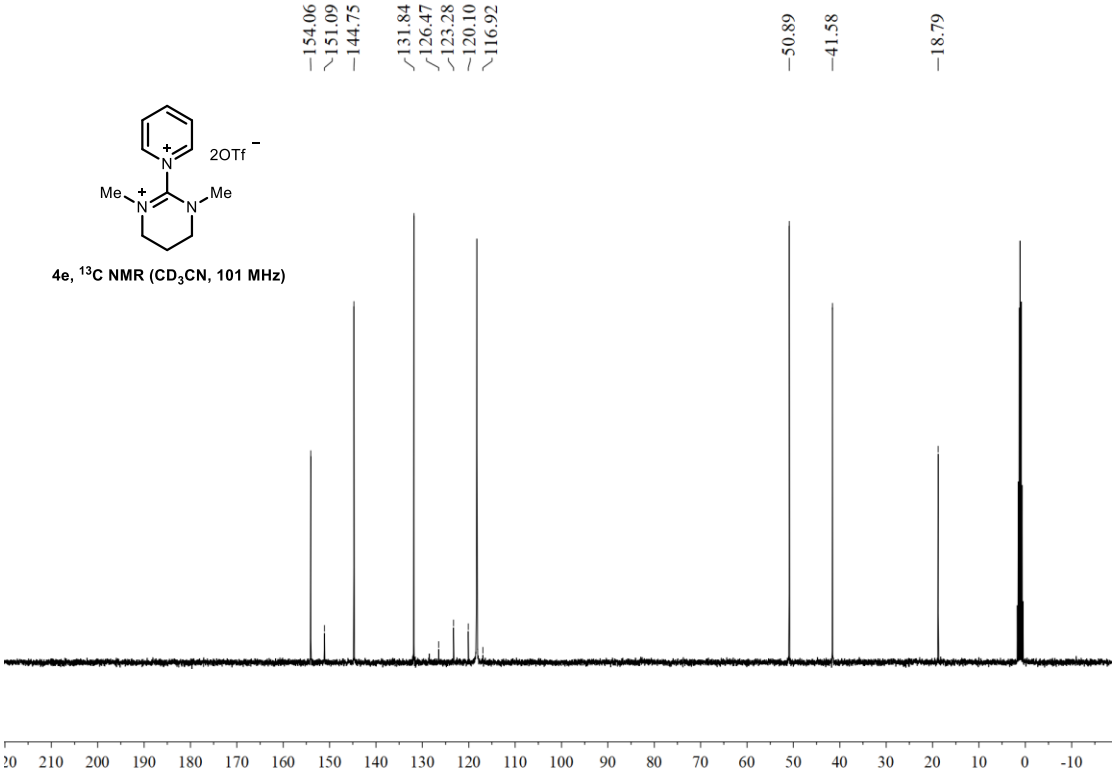


Figure S40. ^{13}C NMR of **4e** (CD_3CN, 101 MHz)

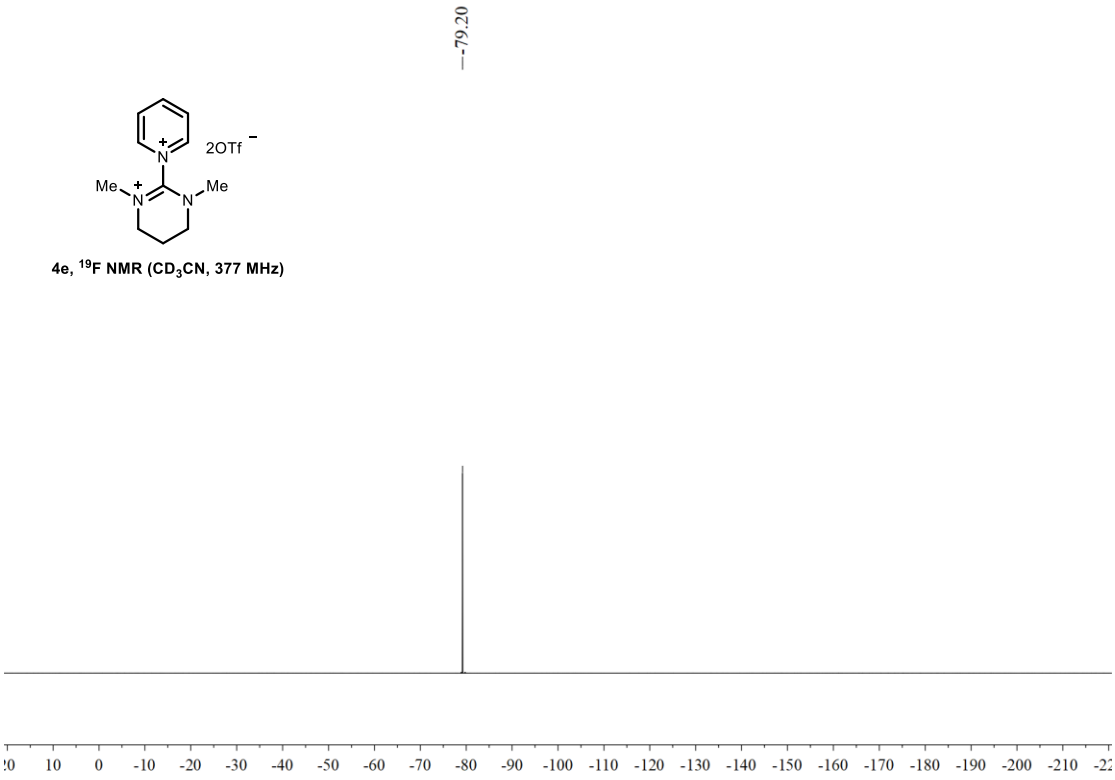


Figure S41. ^{19}F NMR of **4e** (CD_3CN, 377 MHz)

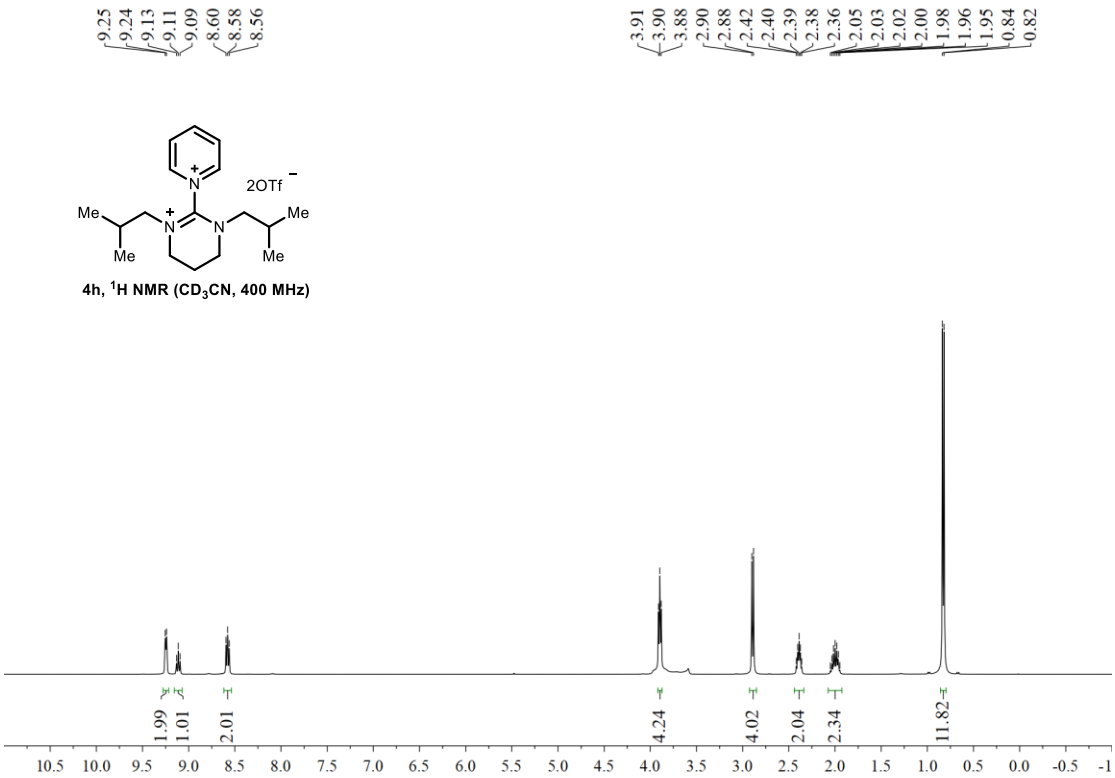


Figure S42. ^{1}H NMR of **4h** (CD_3CN, 400 MHz)

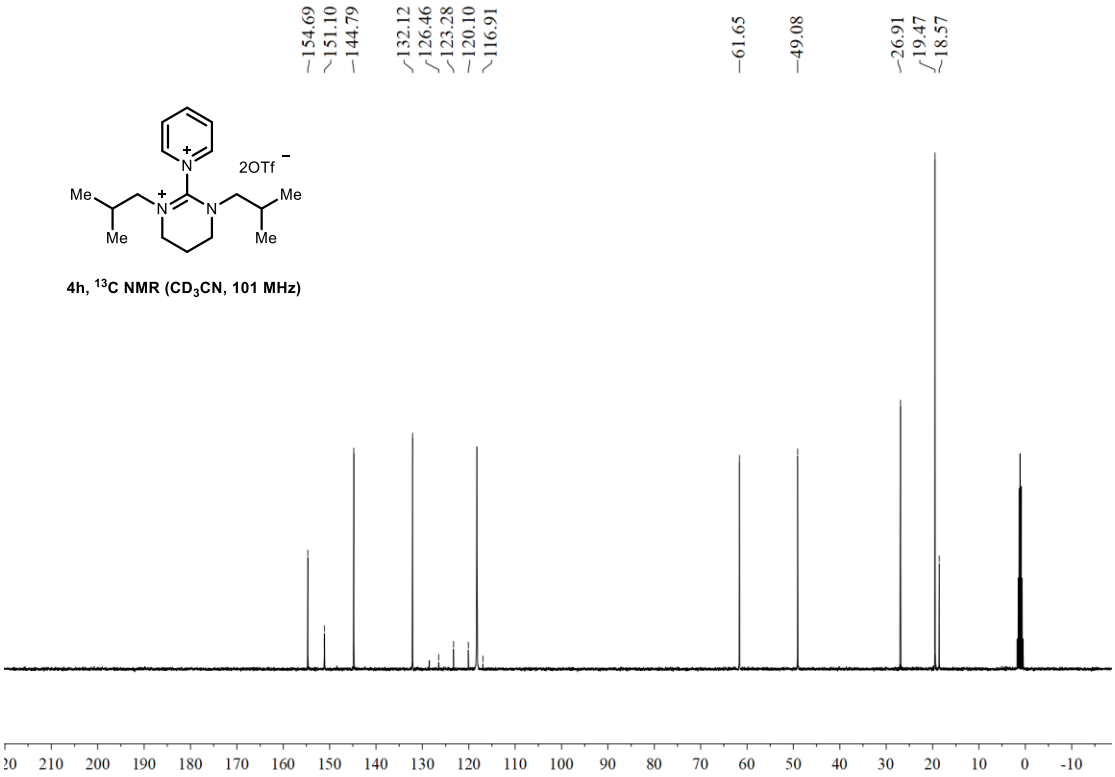


Figure S43. ^{13}C NMR of **4h** (CD_3CN, 101 MHz)

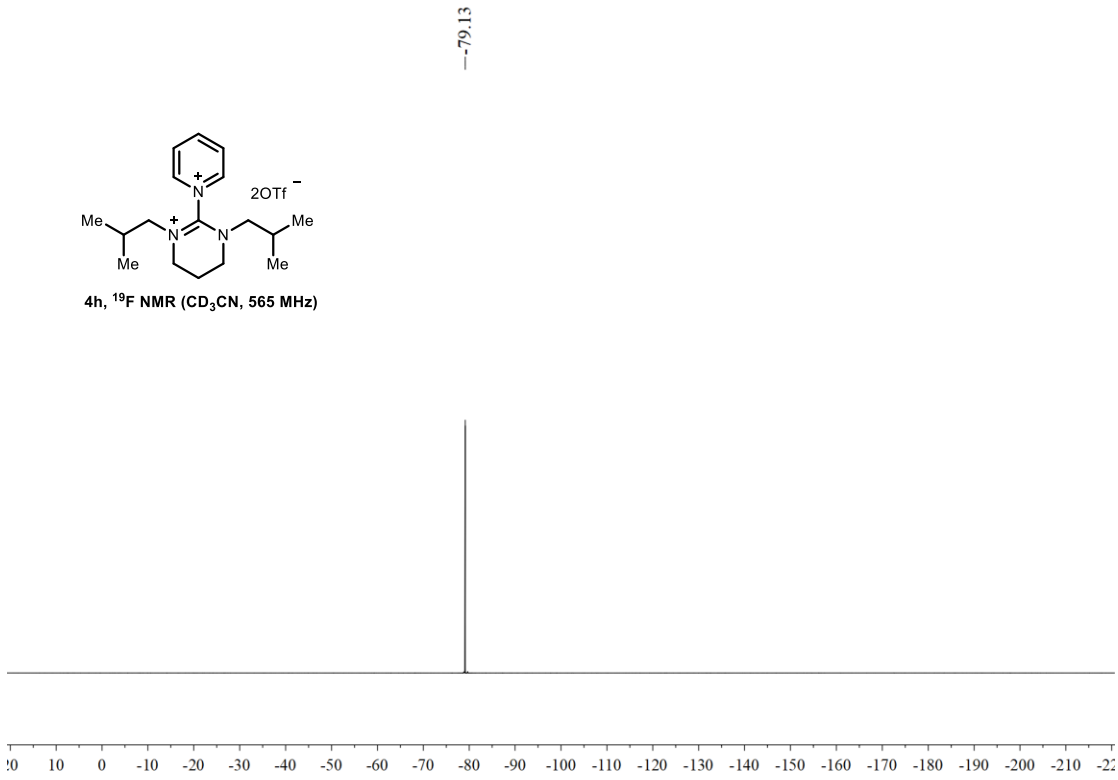


Figure S44. ^{19}F NMR of **4h** (CD_3CN, 565 MHz)

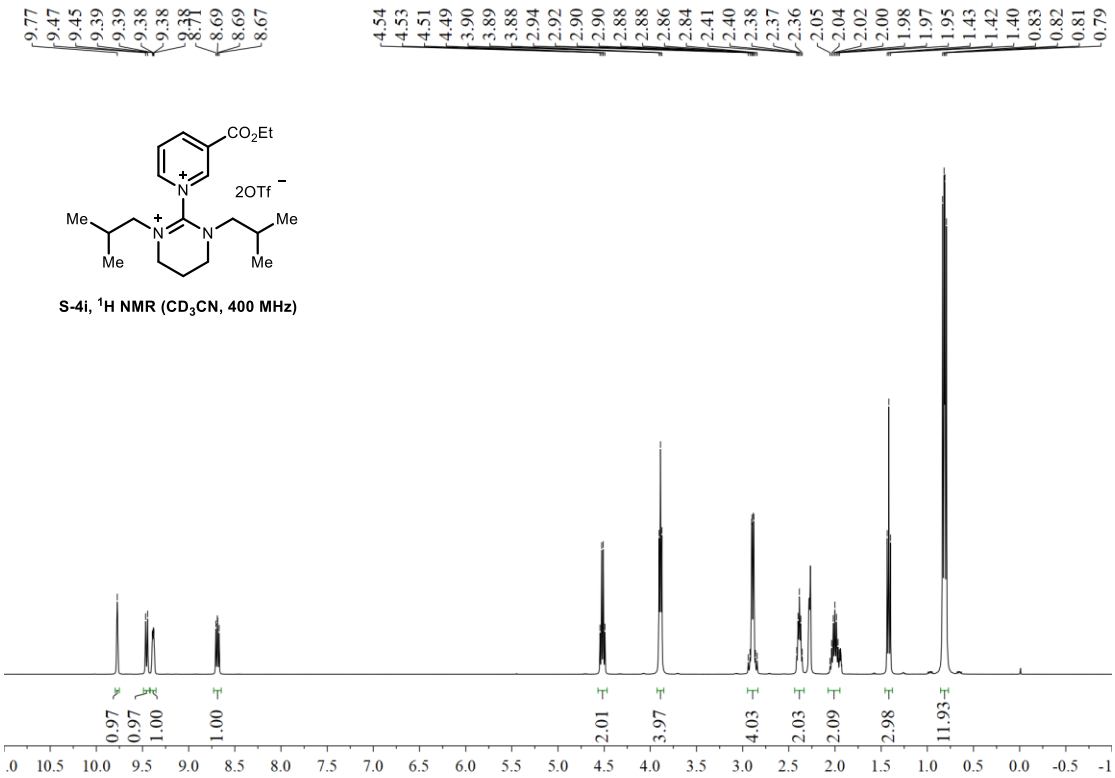


Figure S45. ^{1}H NMR of **S-4i** (CD_3CN, 400 MHz)

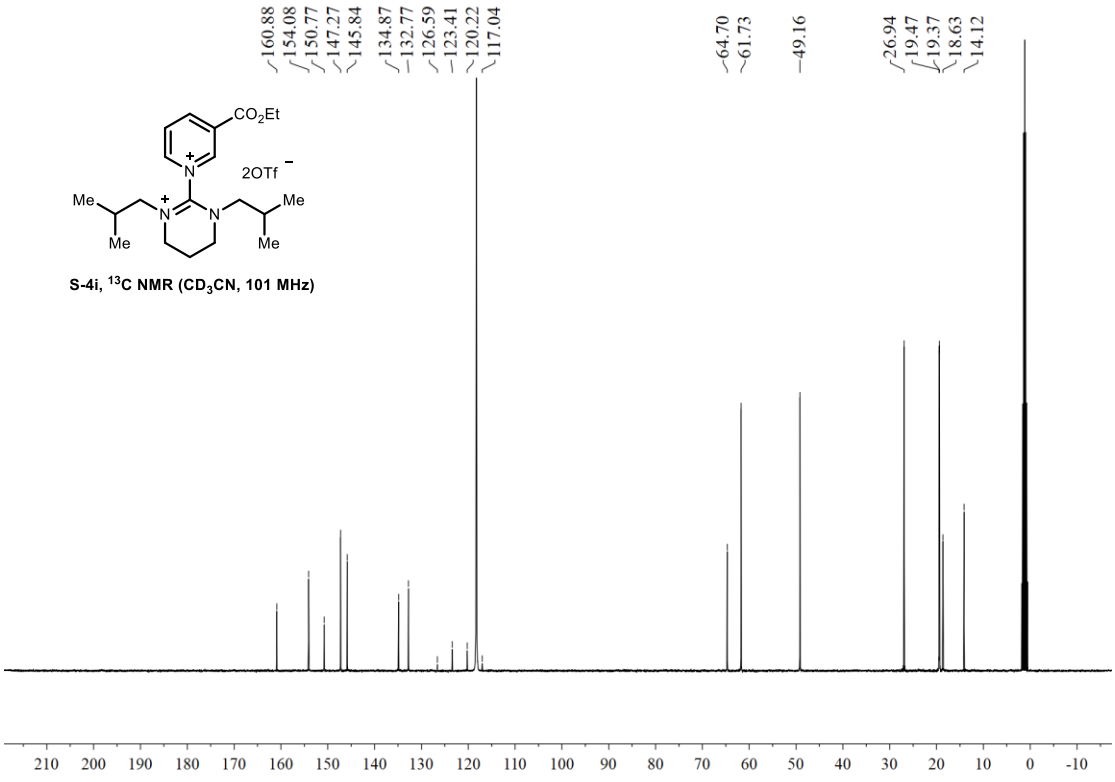


Figure S46. ^{13}C NMR of **S-4i** (CD_3CN, 101 MHz)

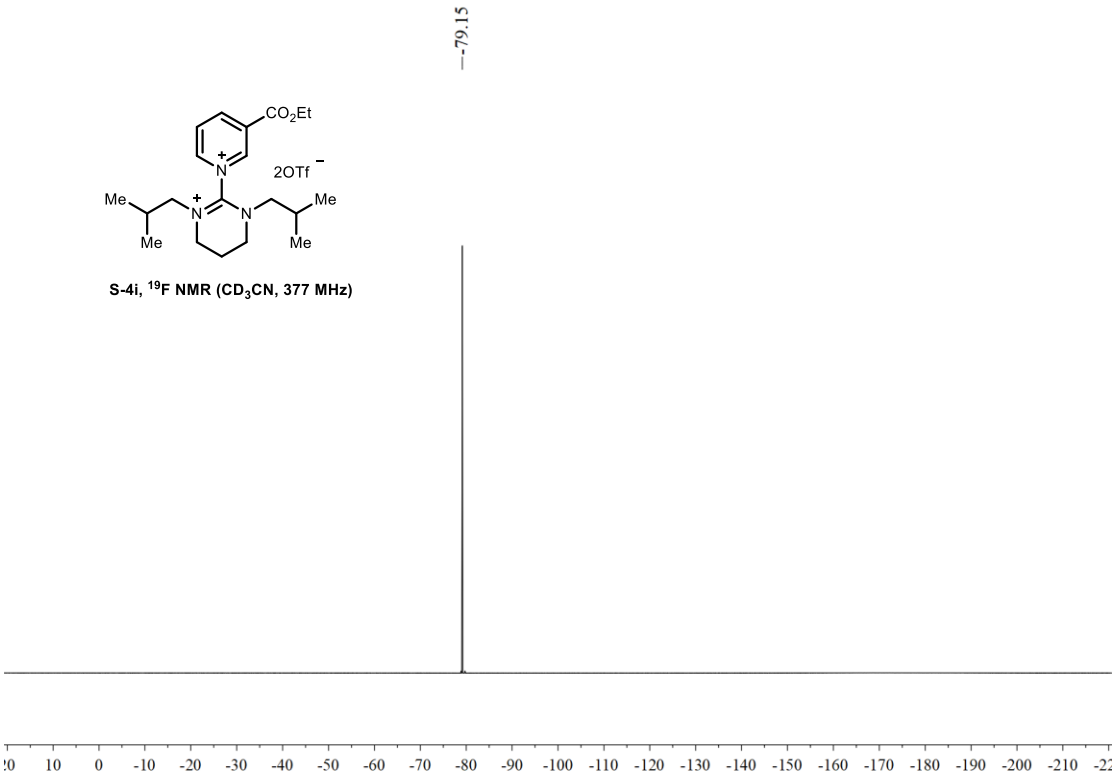
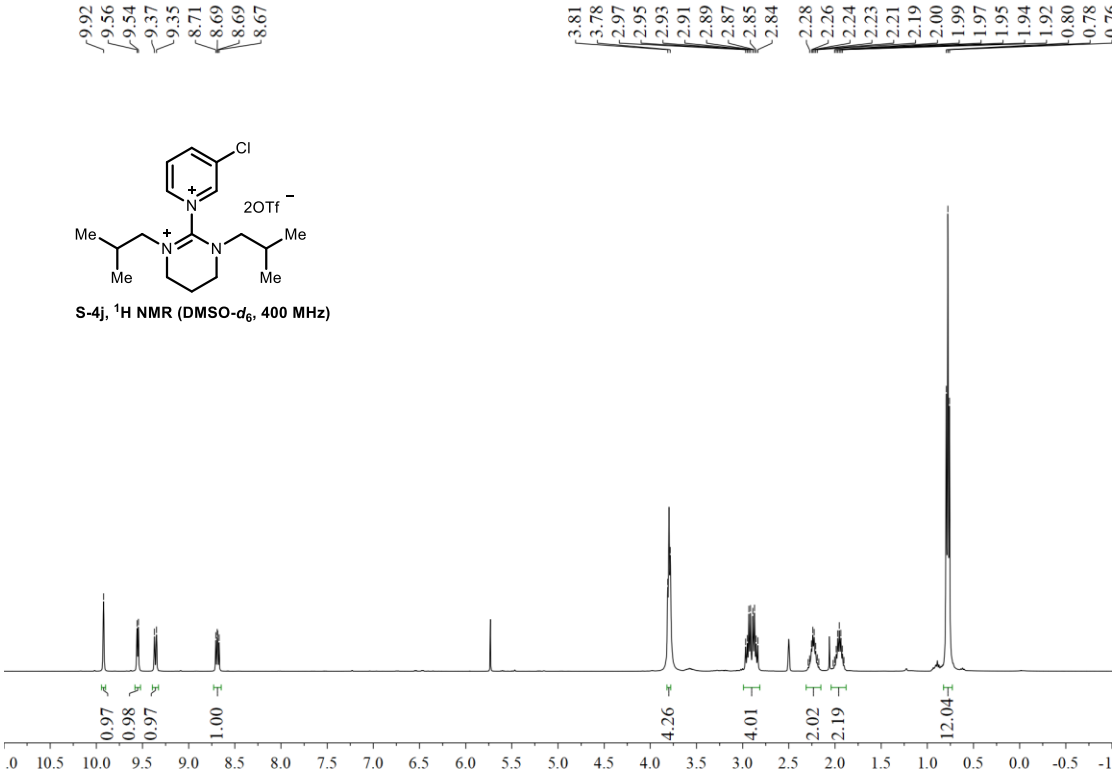
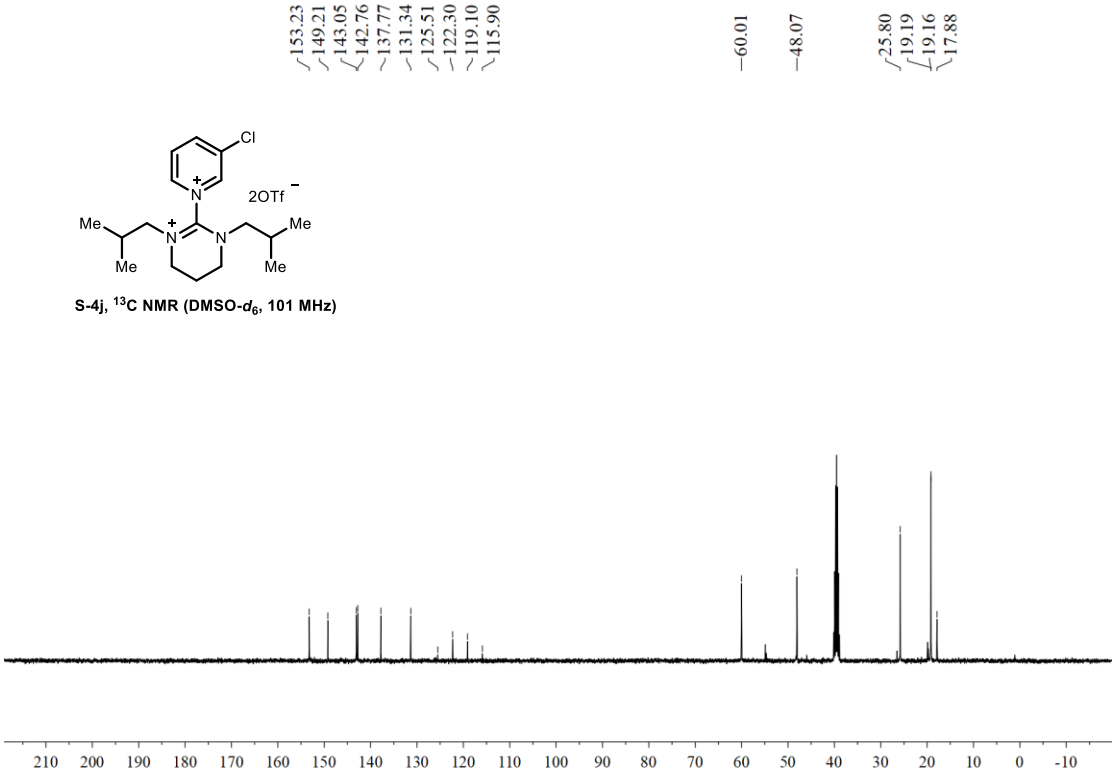


Figure S47. ^{19}F NMR of **S-4i** (CD_3CN, 377 MHz)



S-4j, ^{1}H NMR (DMSO-d_6, 400 MHz)

Figure S48. ^{1}H NMR of **S-4j** (DMSO-d_6, 400 MHz)



S-4j, ^{13}C NMR (DMSO-d_6, 101 MHz)

Figure S49. ^{13}C NMR of **S-4j** (DMSO-d_6, 101 MHz)

Figure S50. ^{19}F NMR of **S-4j** (DMSO-d_6, 377 MHz)

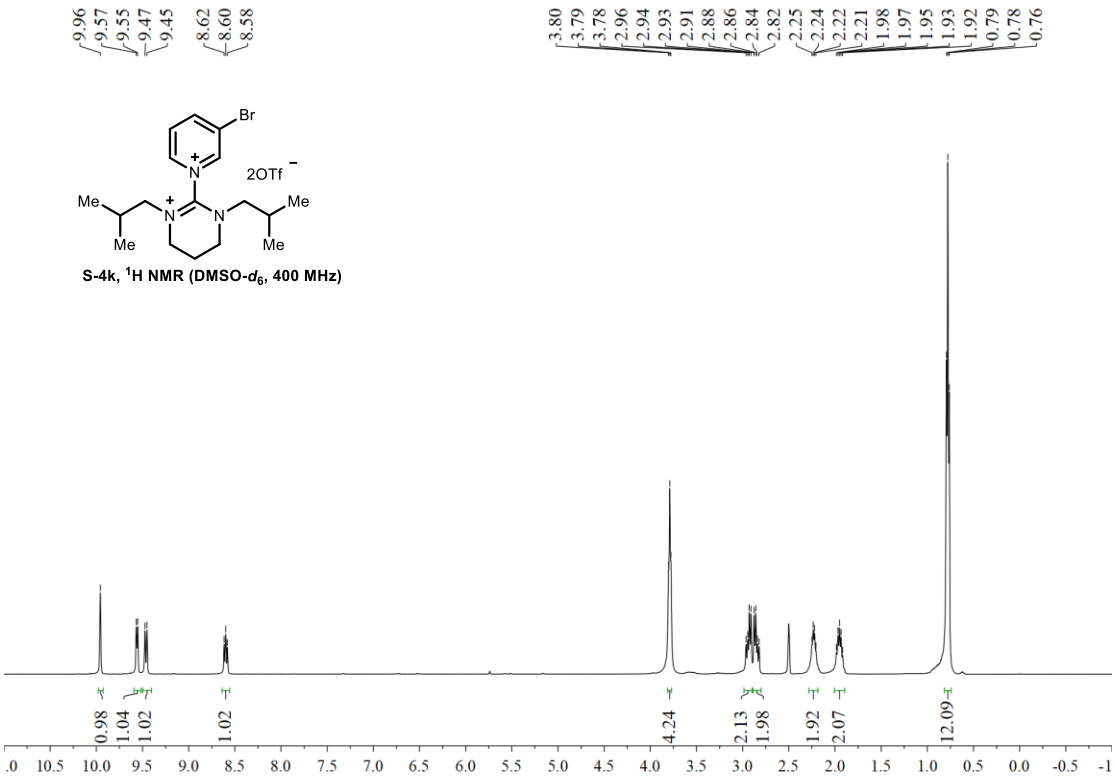


Figure S51. ^{1}H NMR of **S-4k** (DMSO-d_6, 400 MHz)

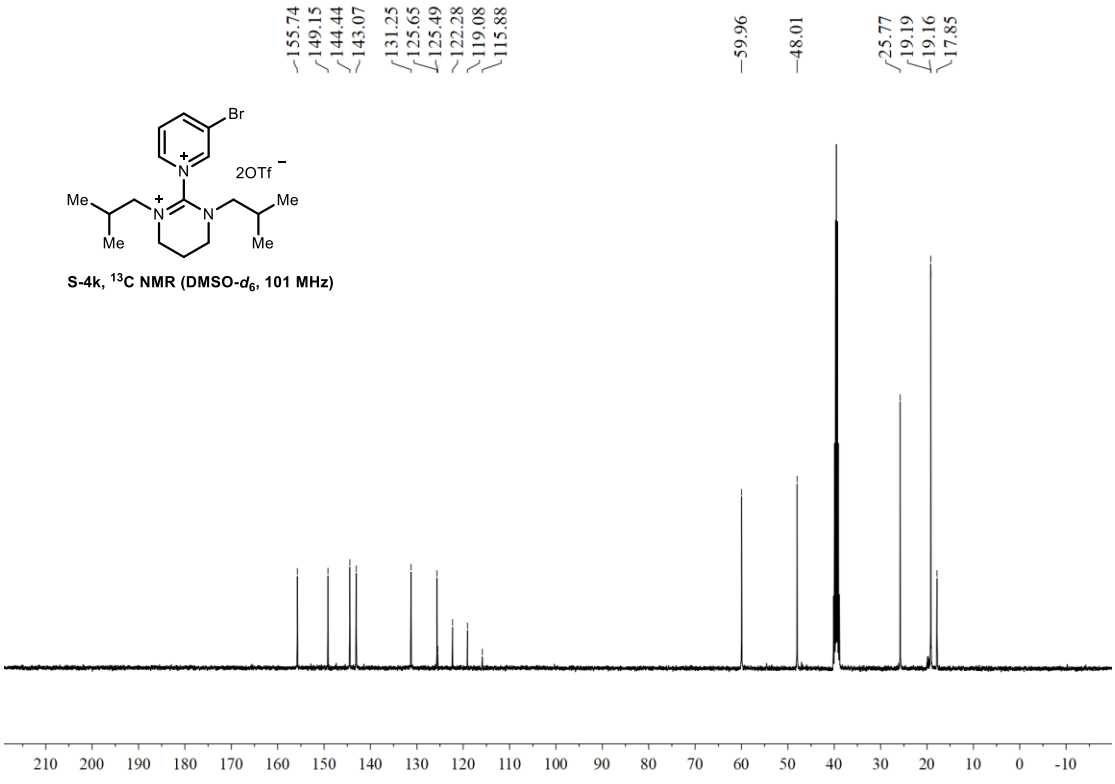


Figure S52. ^{13}C NMR of **S-4k** (DMSO-d_6, 101 MHz)

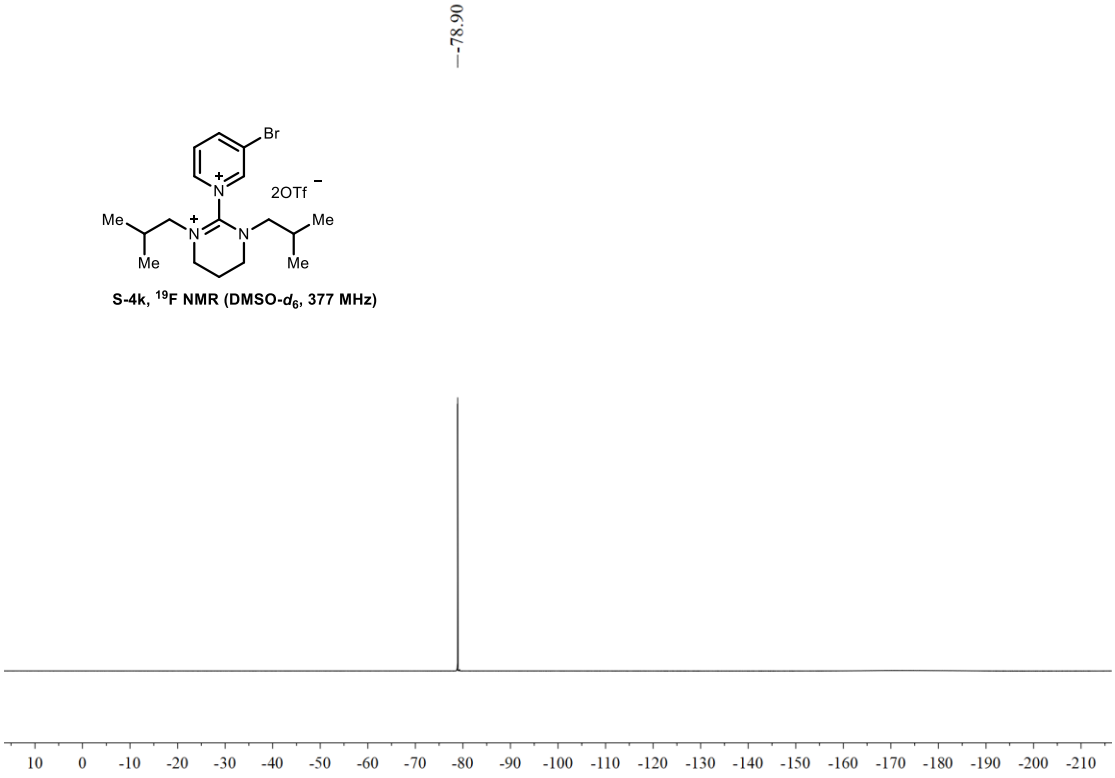


Figure S53. ^{19}F NMR of **S-4k** (DMSO-d_6, 377 MHz)

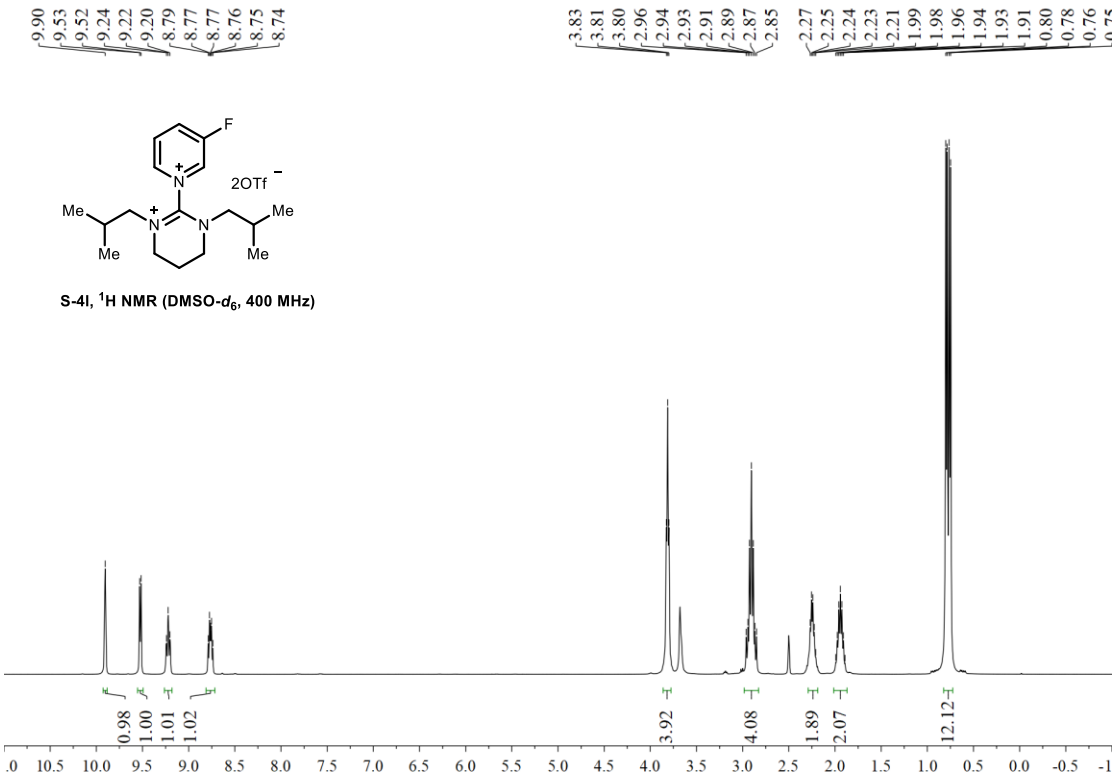


Figure S54. ^{1}H NMR of **S-4l** (DMSO-d_6, 400 MHz)

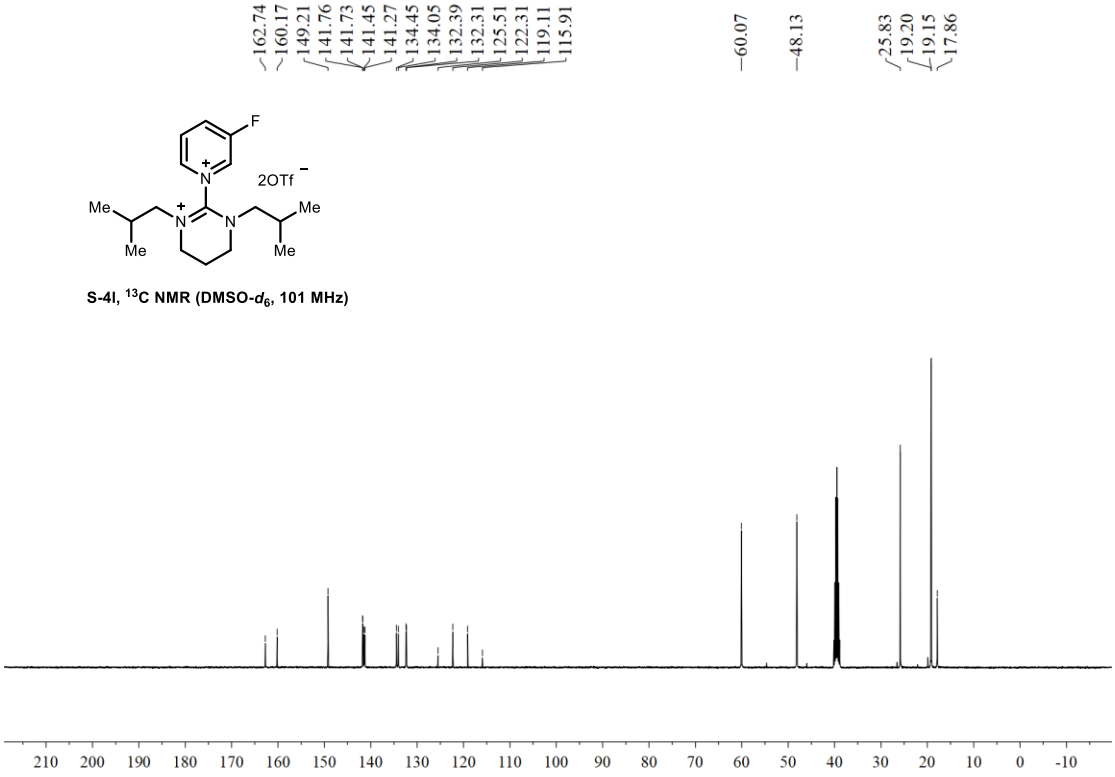


Figure S55. ^{13}C NMR of **S-4l** (DMSO-d_6, 101 MHz)

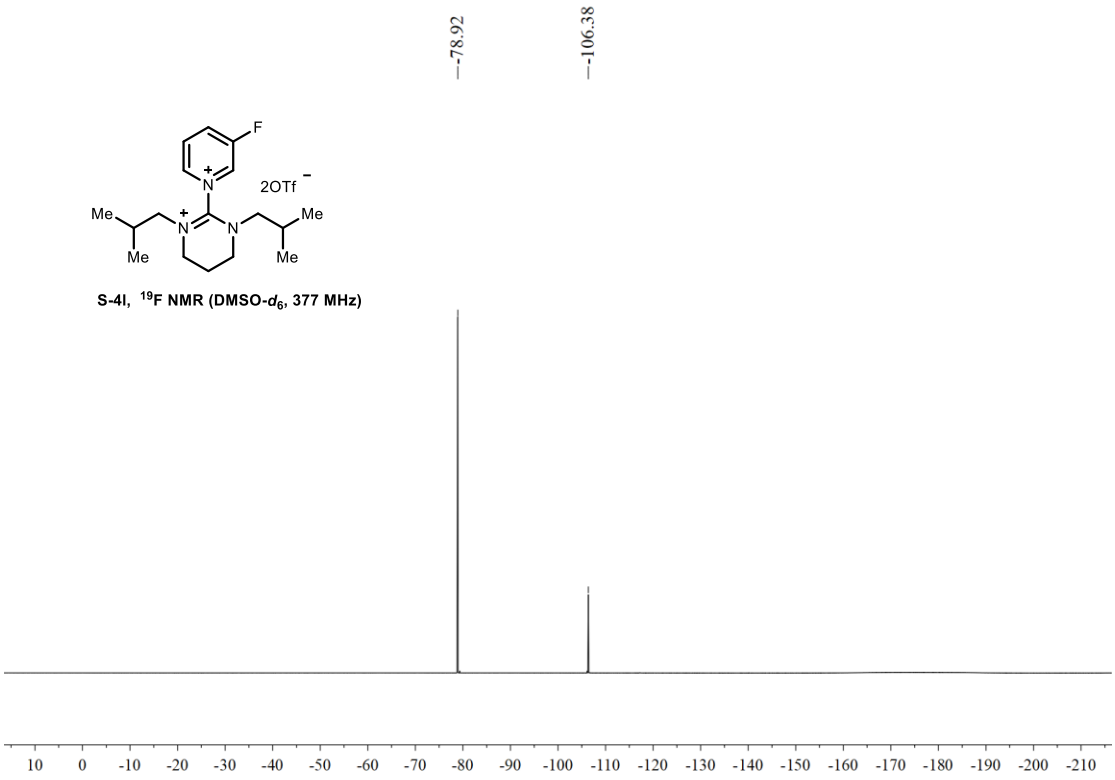


Figure S56. ^{19}F NMR of **S-4l** (DMSO-d_6, 377 MHz)

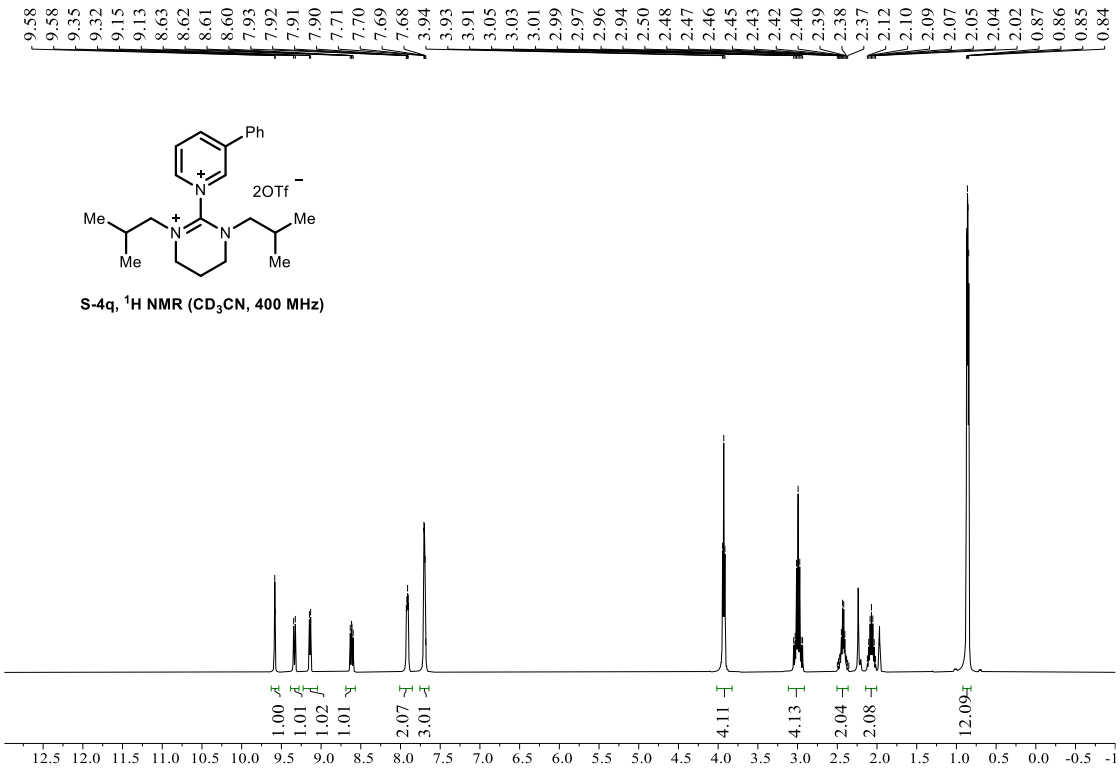


Figure S57. ^{1}H NMR of **S-4q** (CD_3CN, 400 MHz)

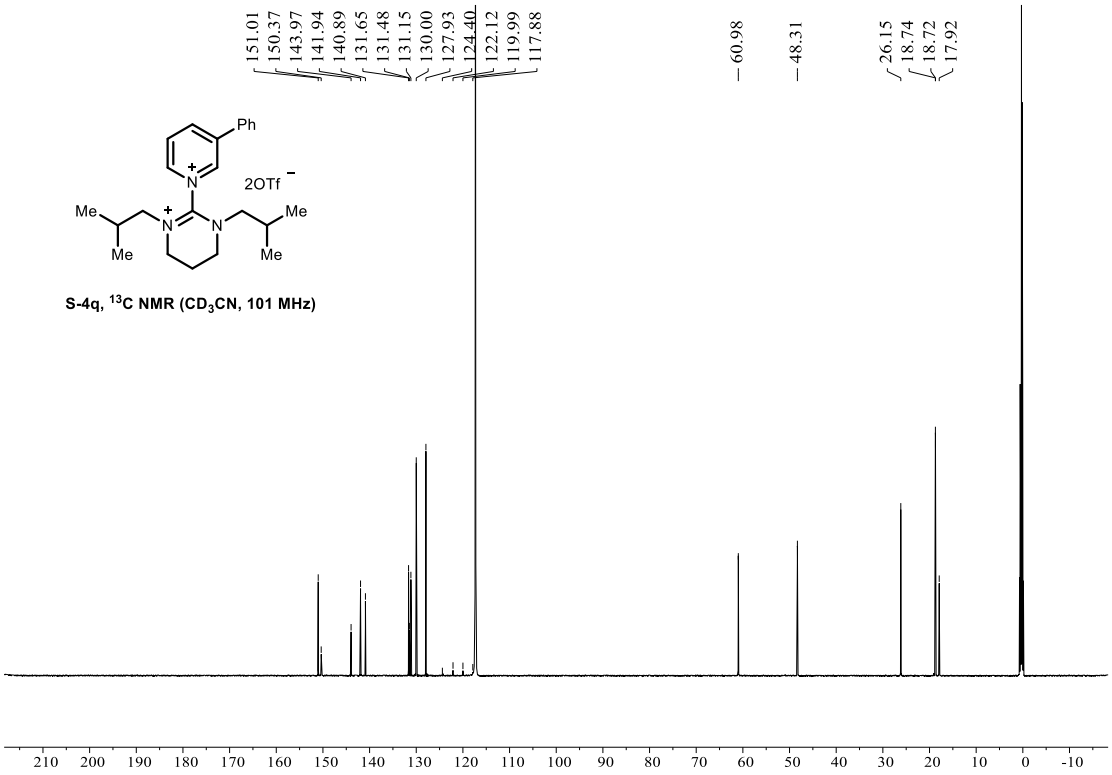


Figure S58. ^{13}C NMR of **S-4q** (CD_3CN, 101 MHz)

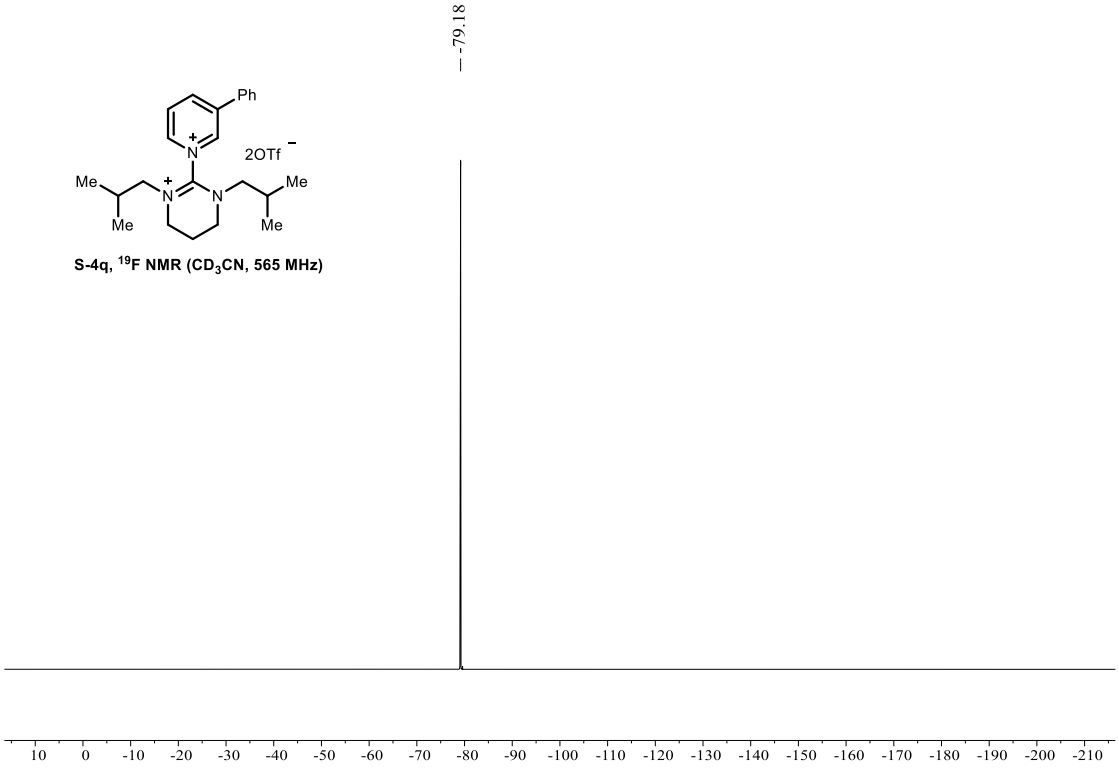


Figure S59. ^{19}F NMR of **S-4q** (CD_3CN, 565 MHz)

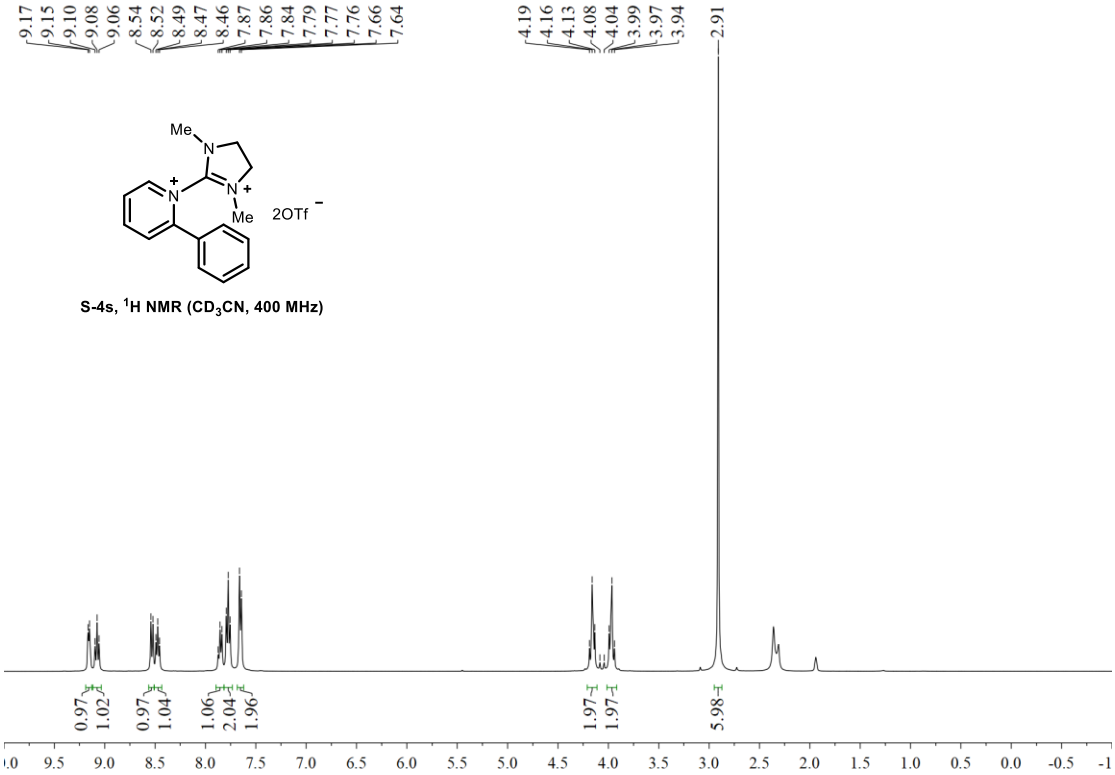


Figure S60. ^{1}H NMR of **S-4s** (CD_3CN, 400 MHz)

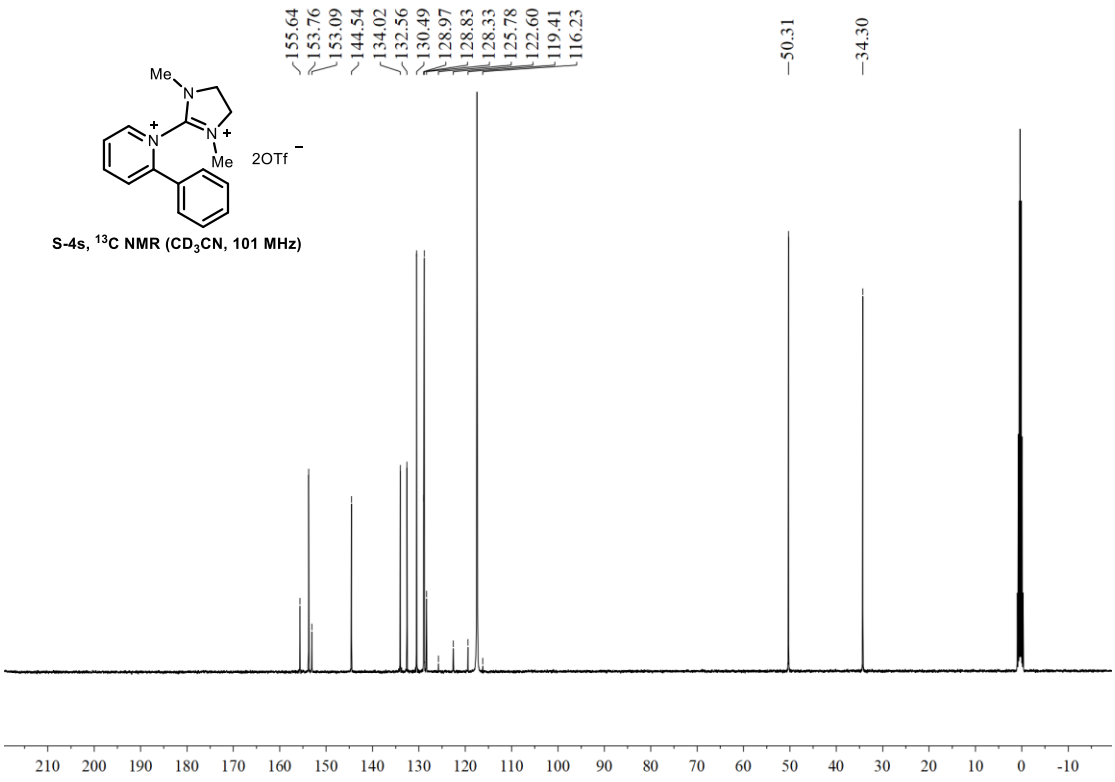


Figure S61. ^{13}C NMR of **S-4s** (CD_3CN, 101 MHz)

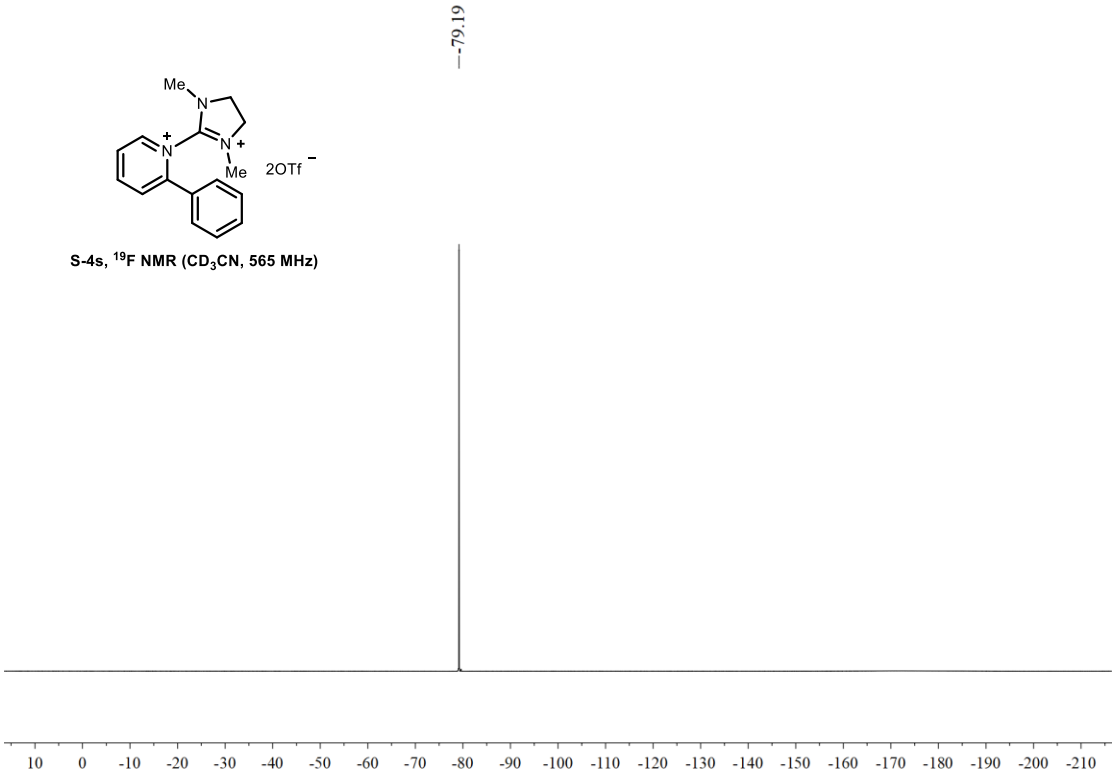


Figure S62. ^{19}F NMR of **S-4s** (CD_3CN, 565 MHz)

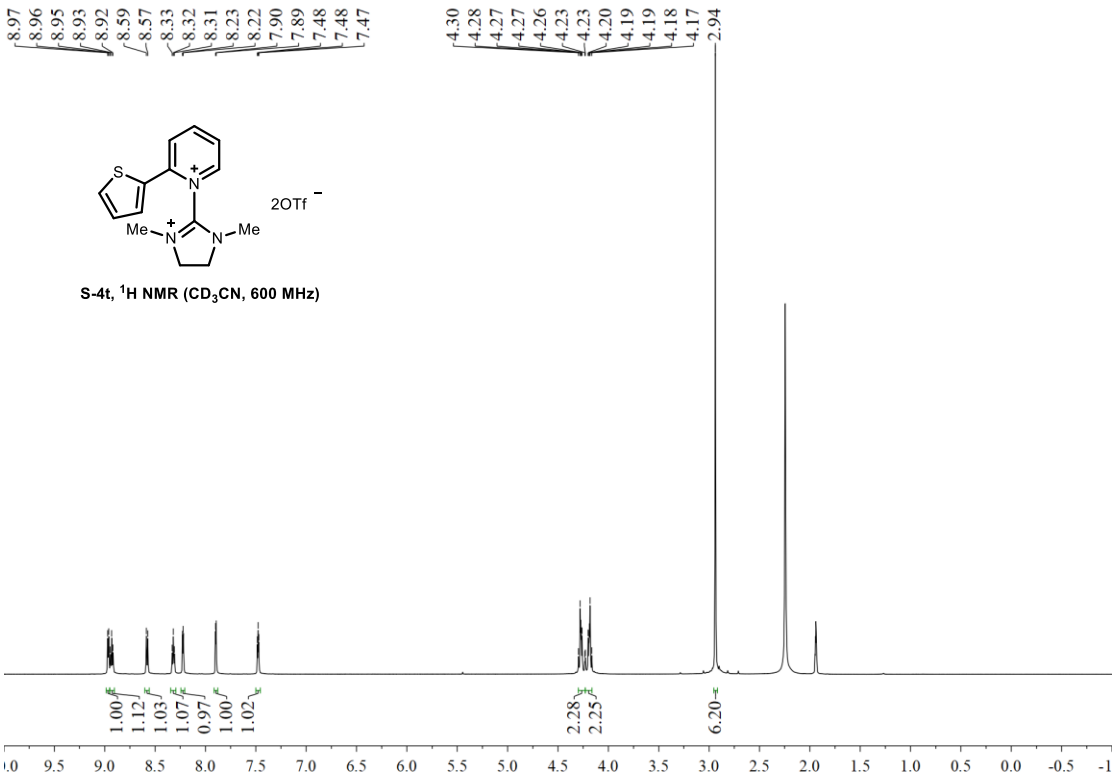


Figure S63. ^{1}H NMR of **S-4t** (CD_3CN, 600 MHz)

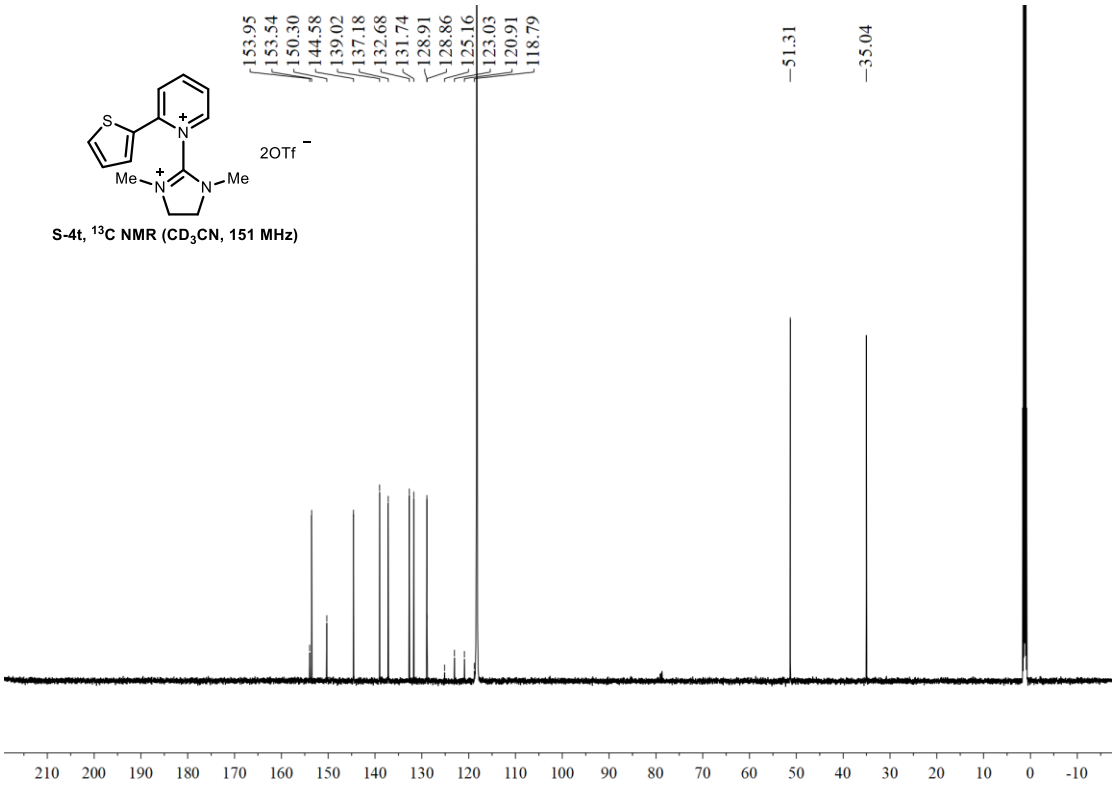


Figure S64. ^{13}C NMR of **S-4t** (CD_3CN, 151 MHz)

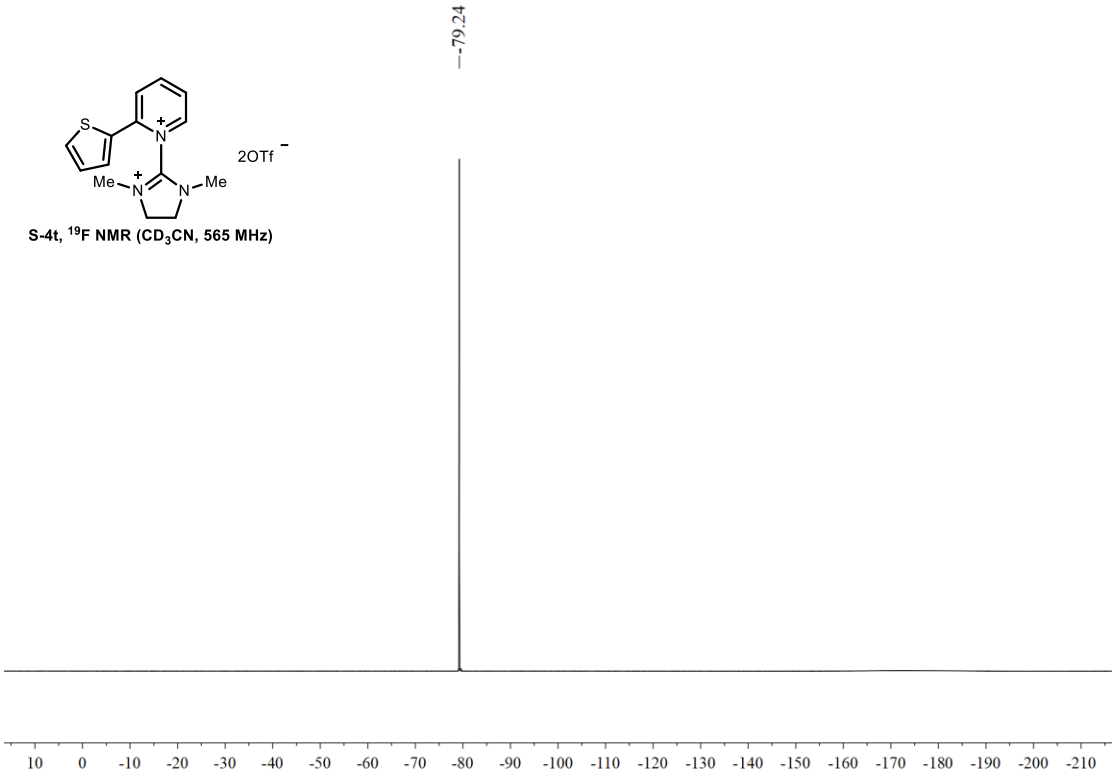


Figure S65. ^{19}F NMR of **S-4t** (CD_3CN, 565 MHz)

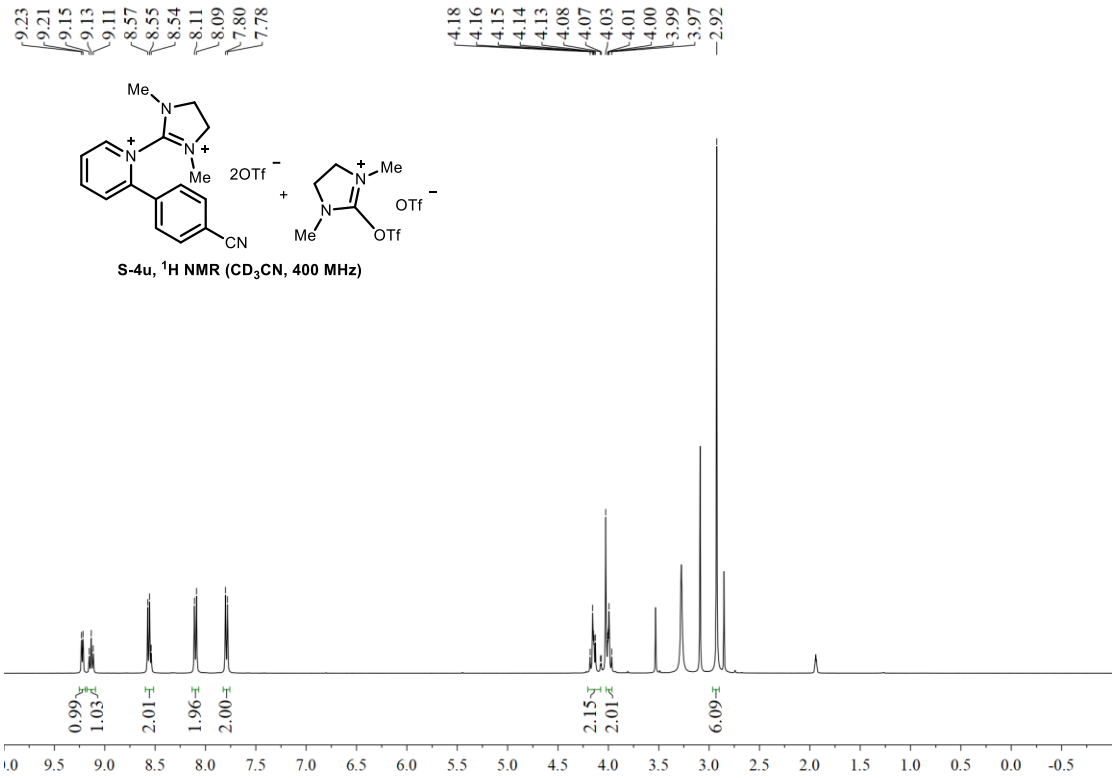


Figure S66. ^{1}H NMR of **S-4u** (CD_3CN, 400 MHz)

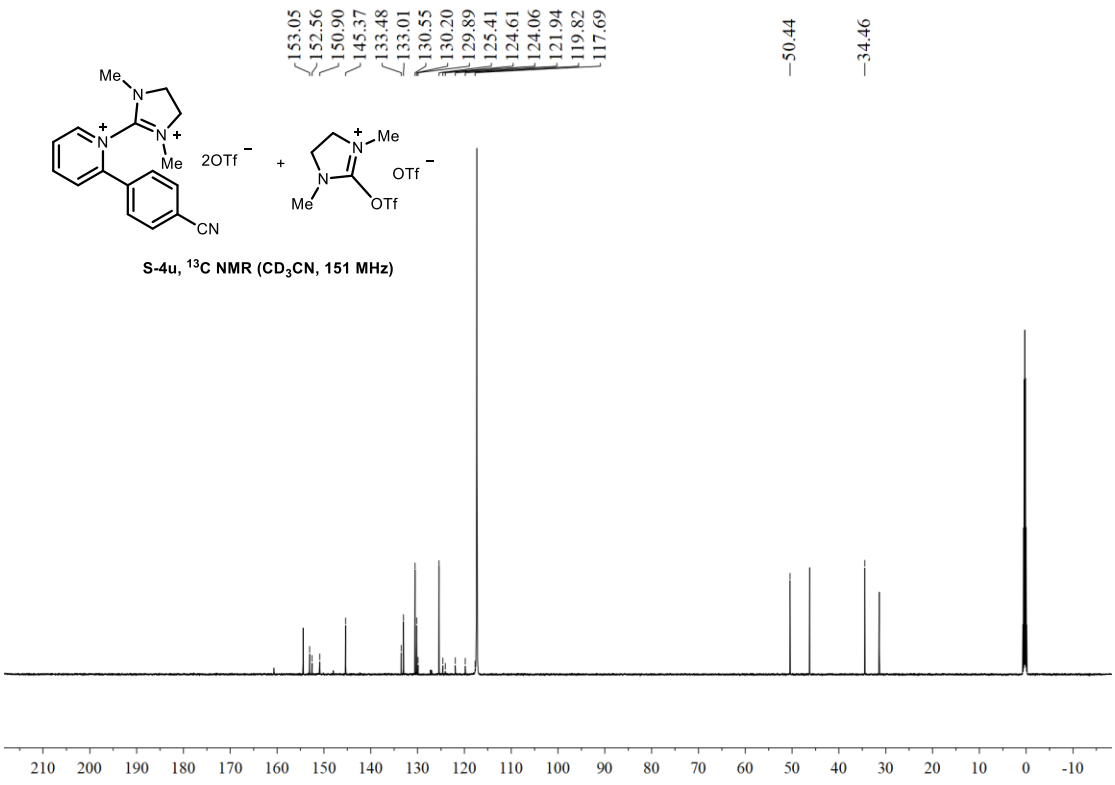


Figure S67. ^{13}C NMR of **S-4u** (CD_3CN, 151 MHz)

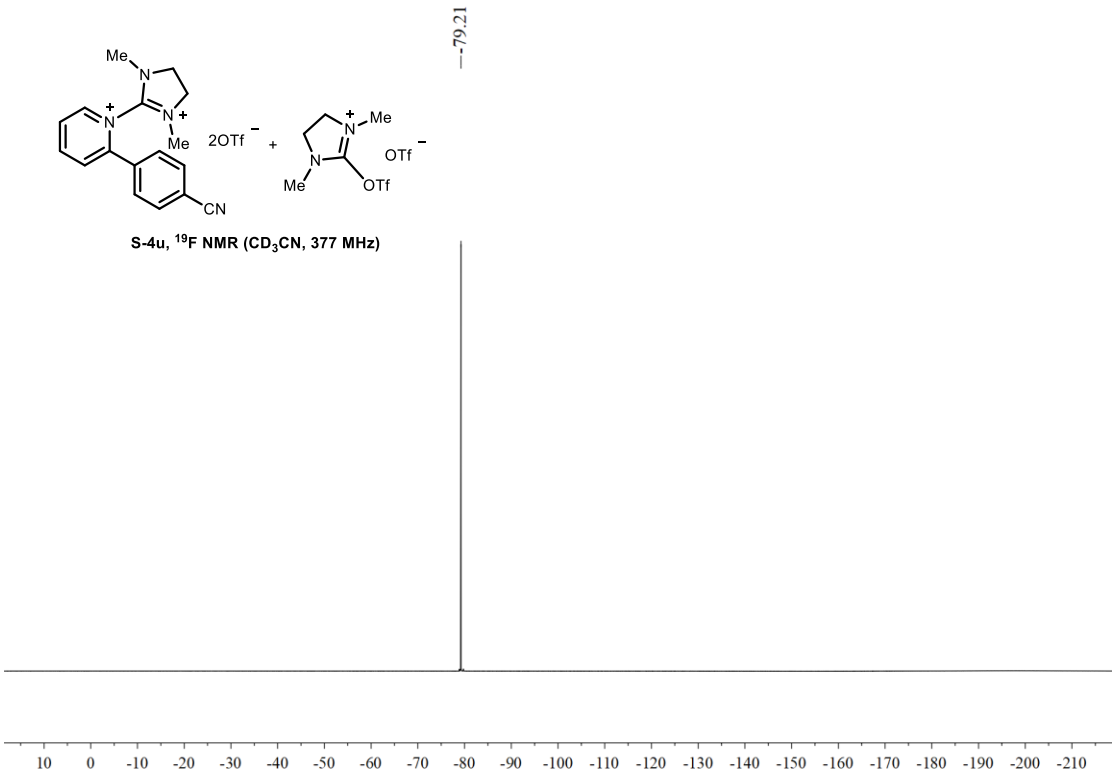


Figure S68. ^{19}F NMR of **S-4u** (CD_3CN, 377 MHz)

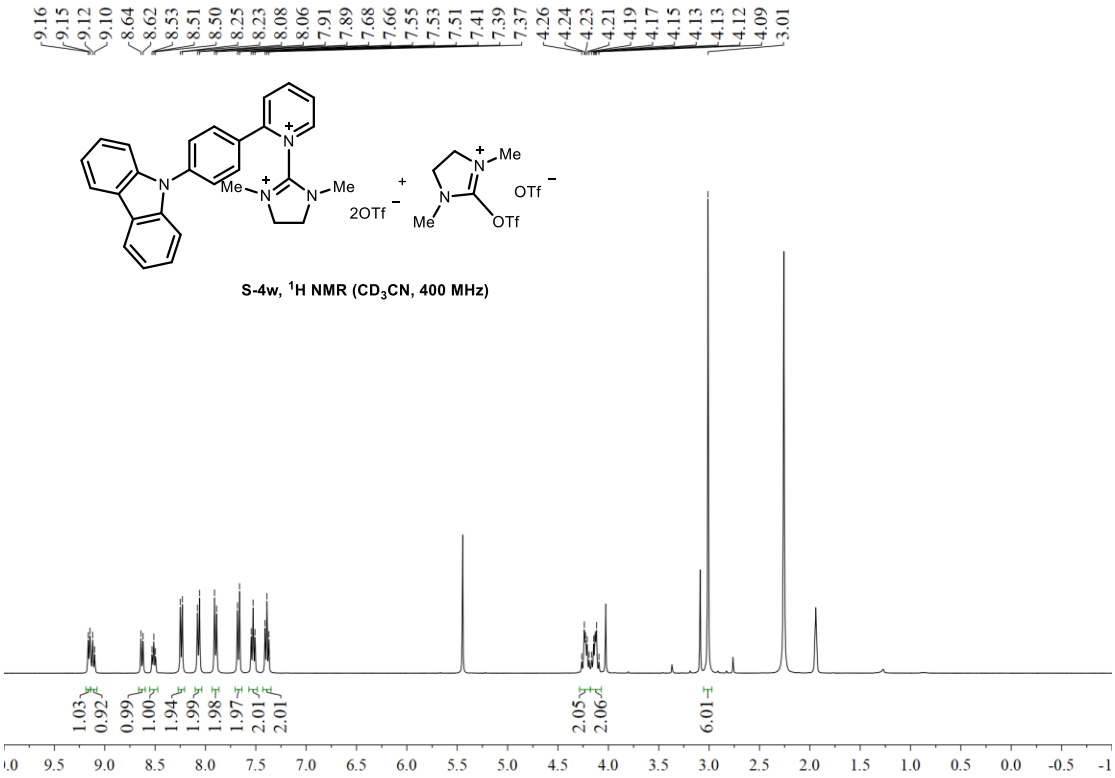


Figure S69. ^{1}H NMR of **S-4w** (CD_3CN, 400 MHz)

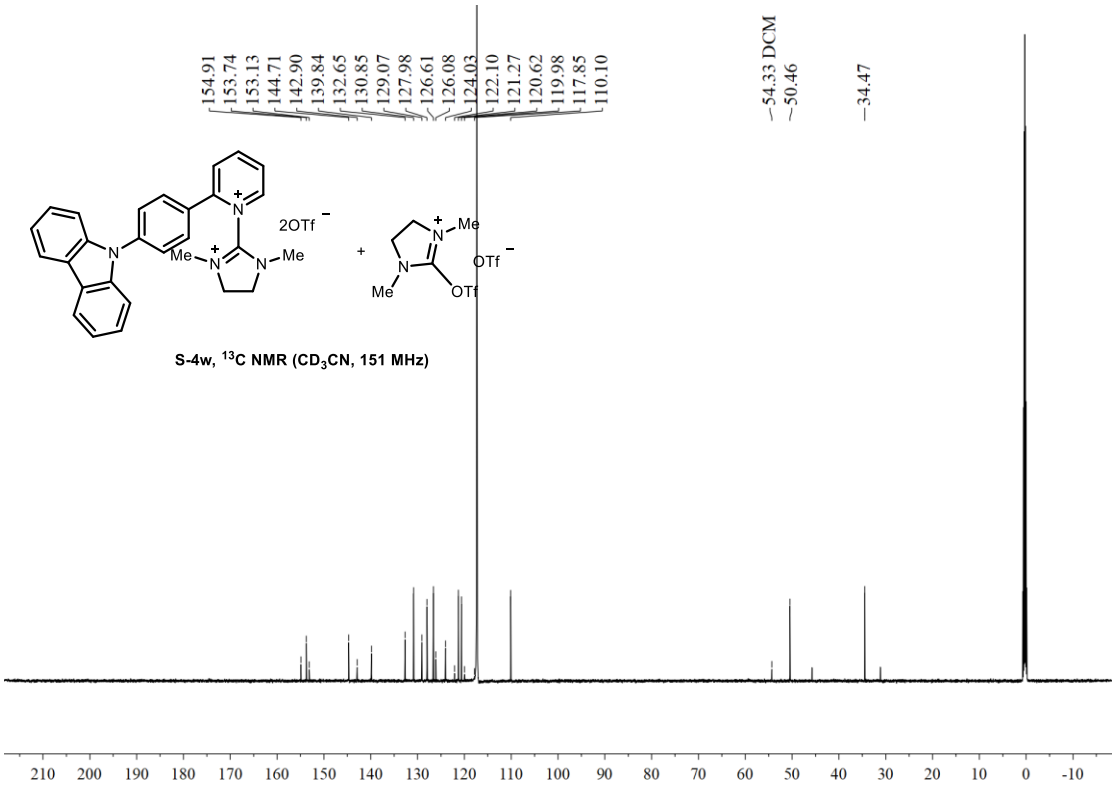


Figure S70. ^{13}C NMR of **S-4w** (CD_3CN, 151 MHz)

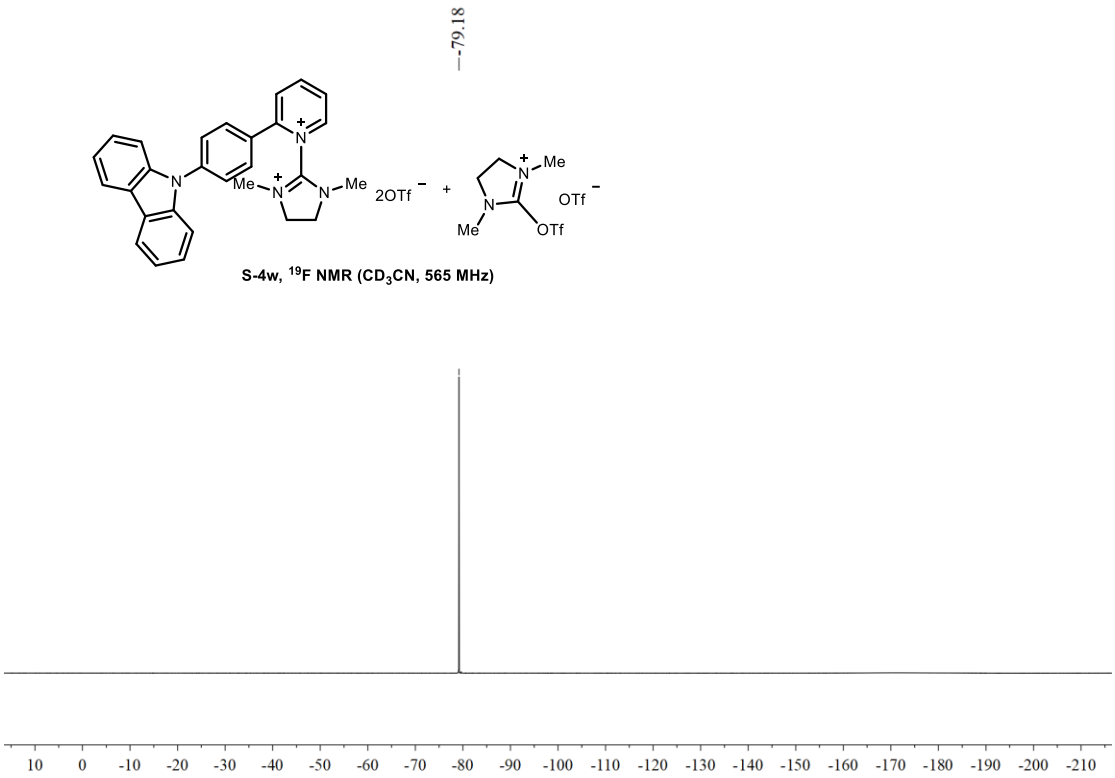


Figure S71. ^{19}F NMR of **S-4w** (CD_3CN, 565 MHz)

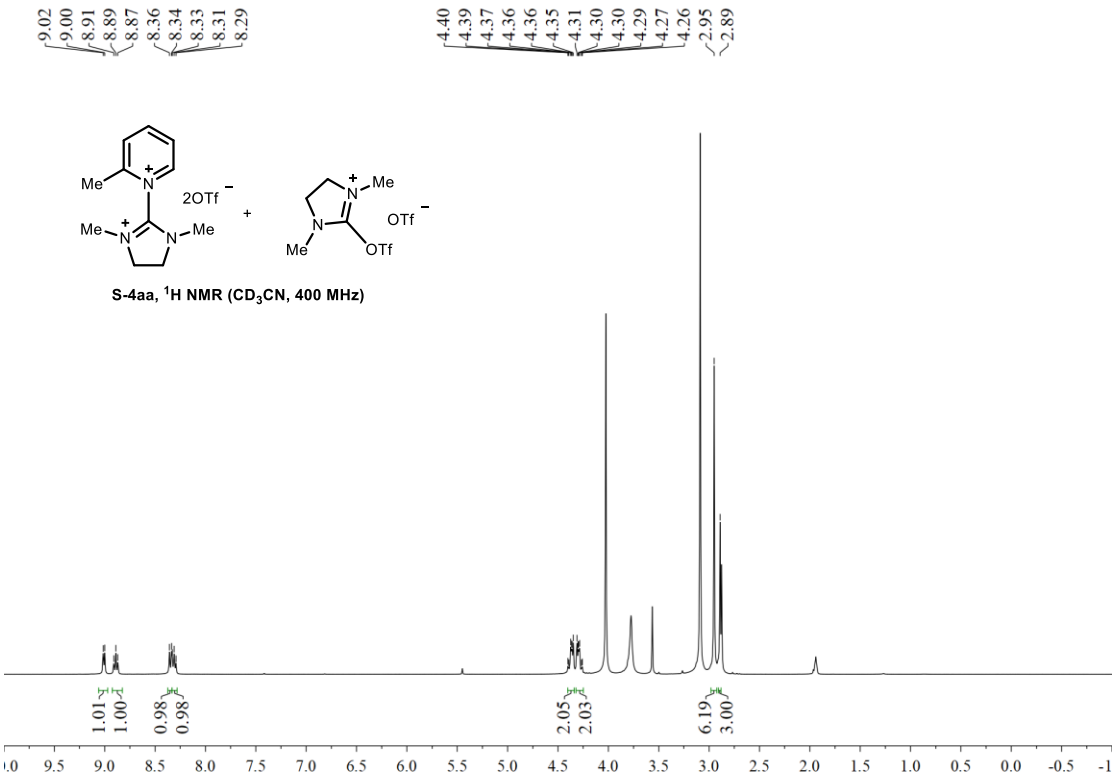


Figure S72. ^{1}H NMR of **S-4aa** (CD_3CN, 400 MHz)

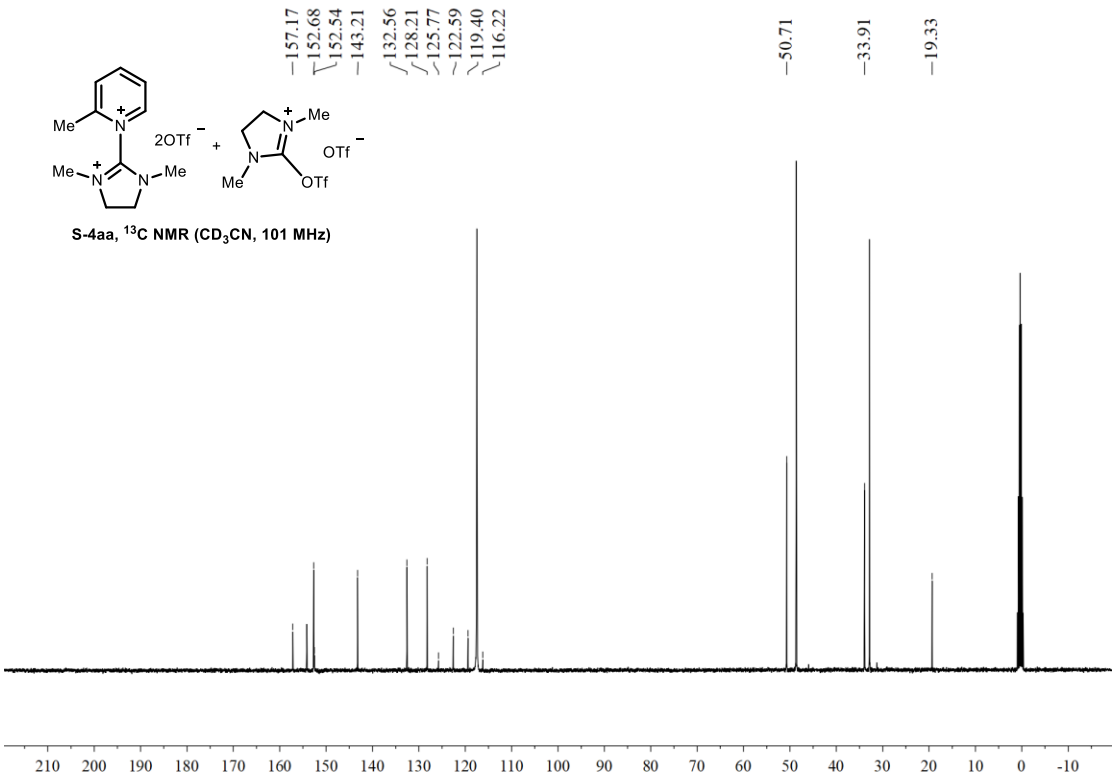


Figure S73. ^{13}C NMR of **S-4aa** (CD_3CN, 101 MHz)

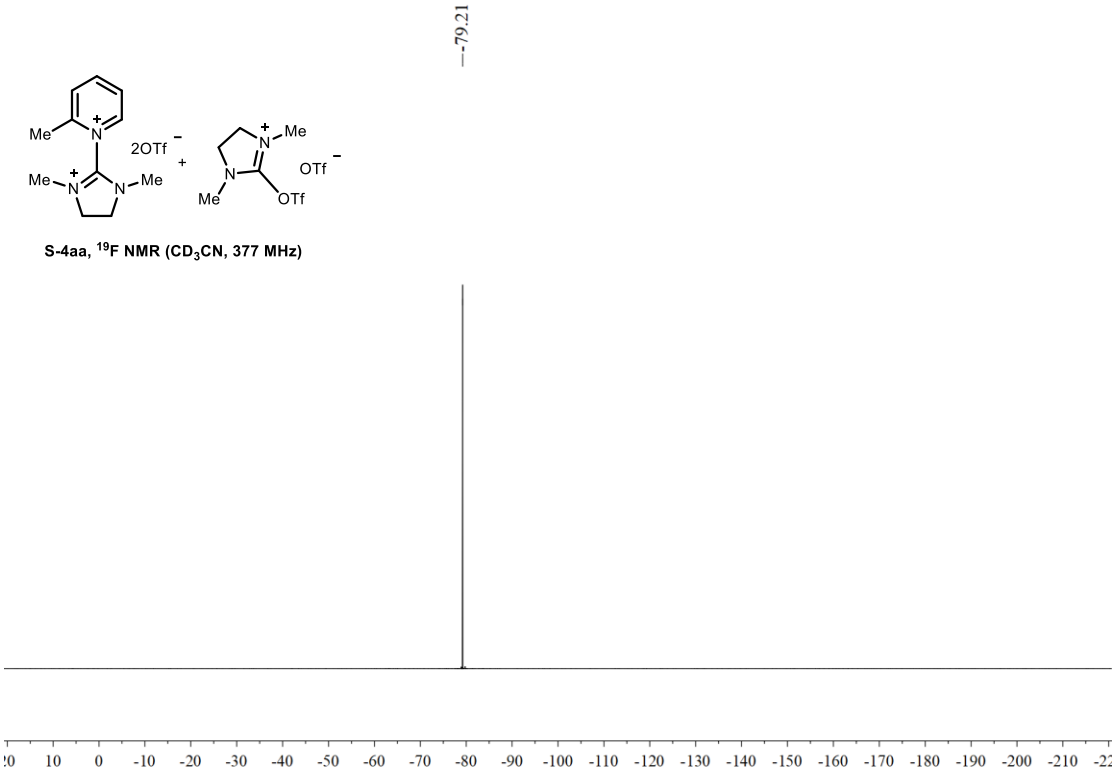


Figure S74. ^{19}F NMR of **S-4aa** (CD_3CN, 377 MHz)

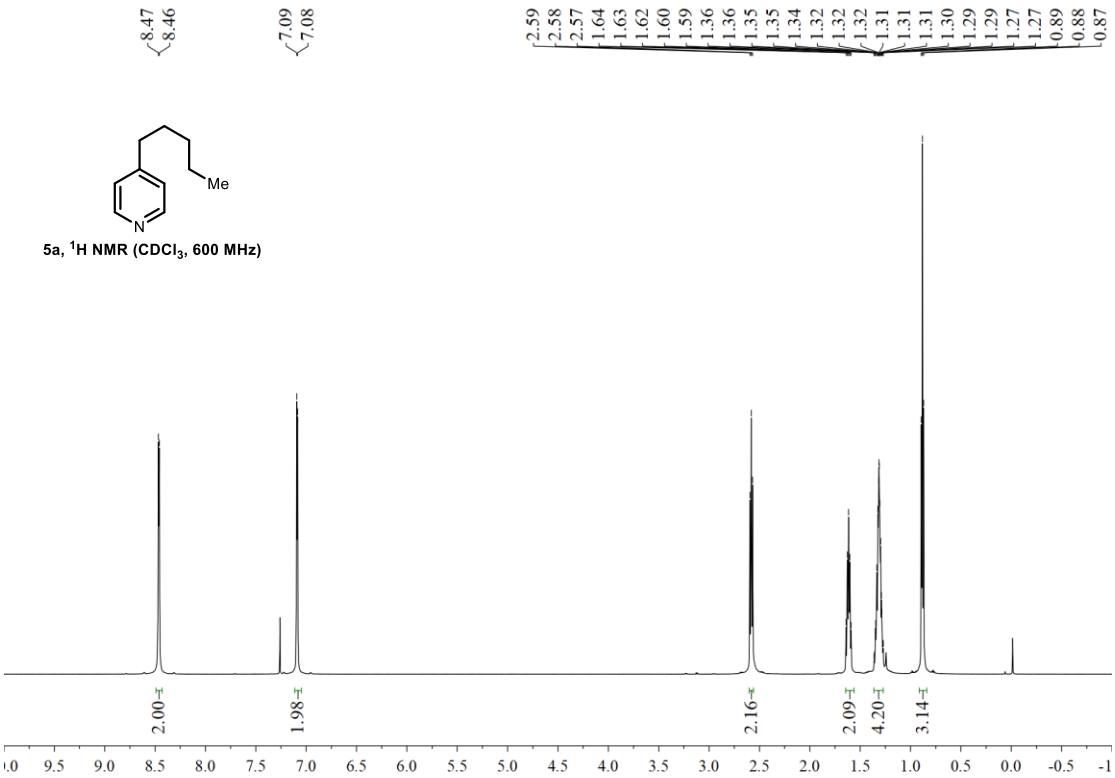


Figure S75. ^{1}H NMR of **5a** ($CDCl_3$, 600 MHz)

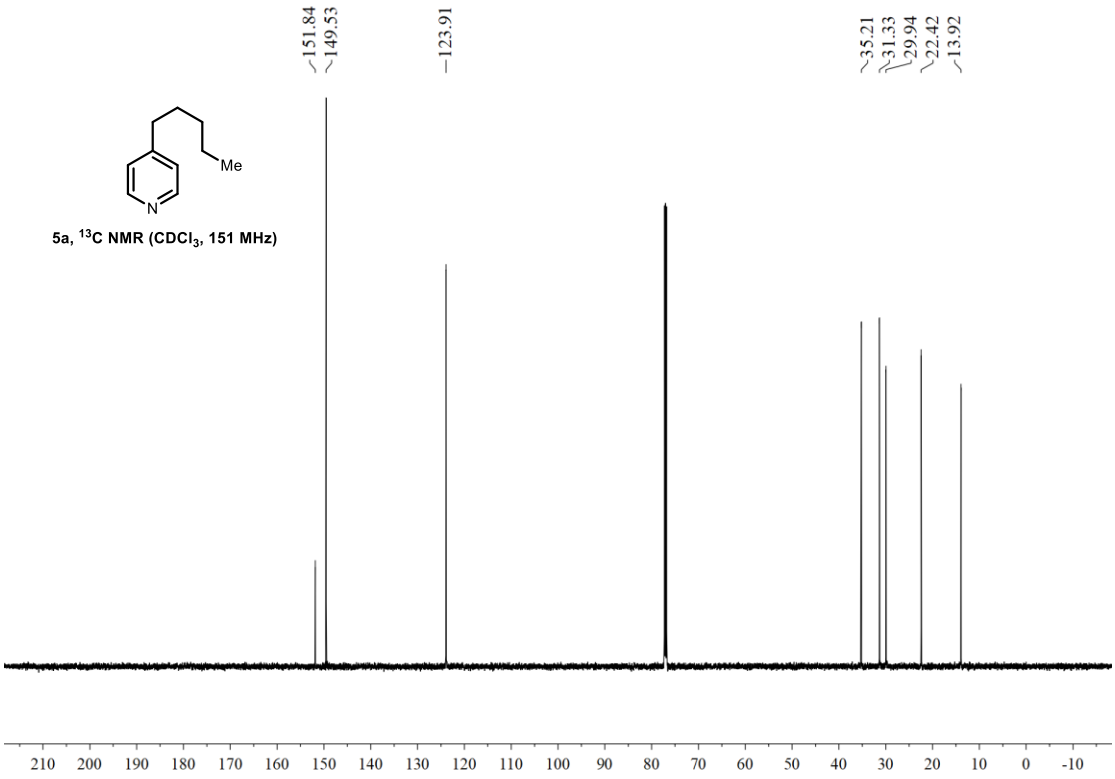


Figure S76. ^{13}C NMR of **5a** ($CDCl_3$, 151 MHz)

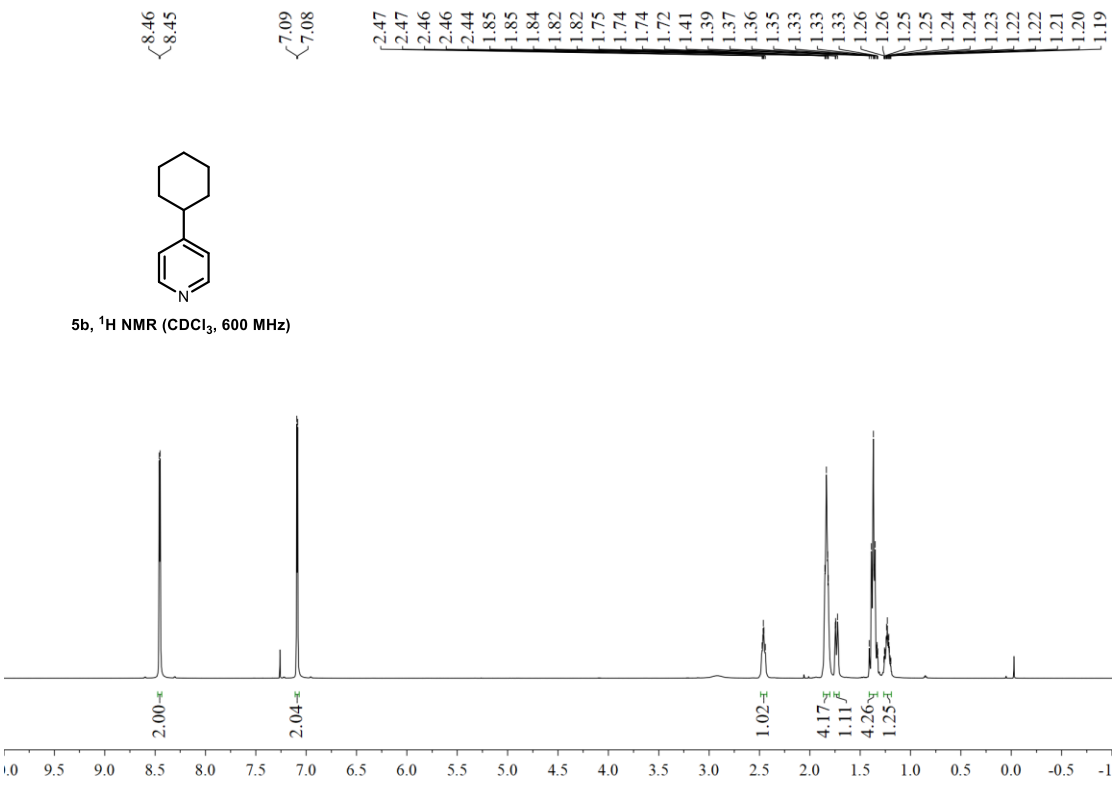


Figure S77. ^{1}H NMR of **5b** (CDCl$_3$, 600 MHz)

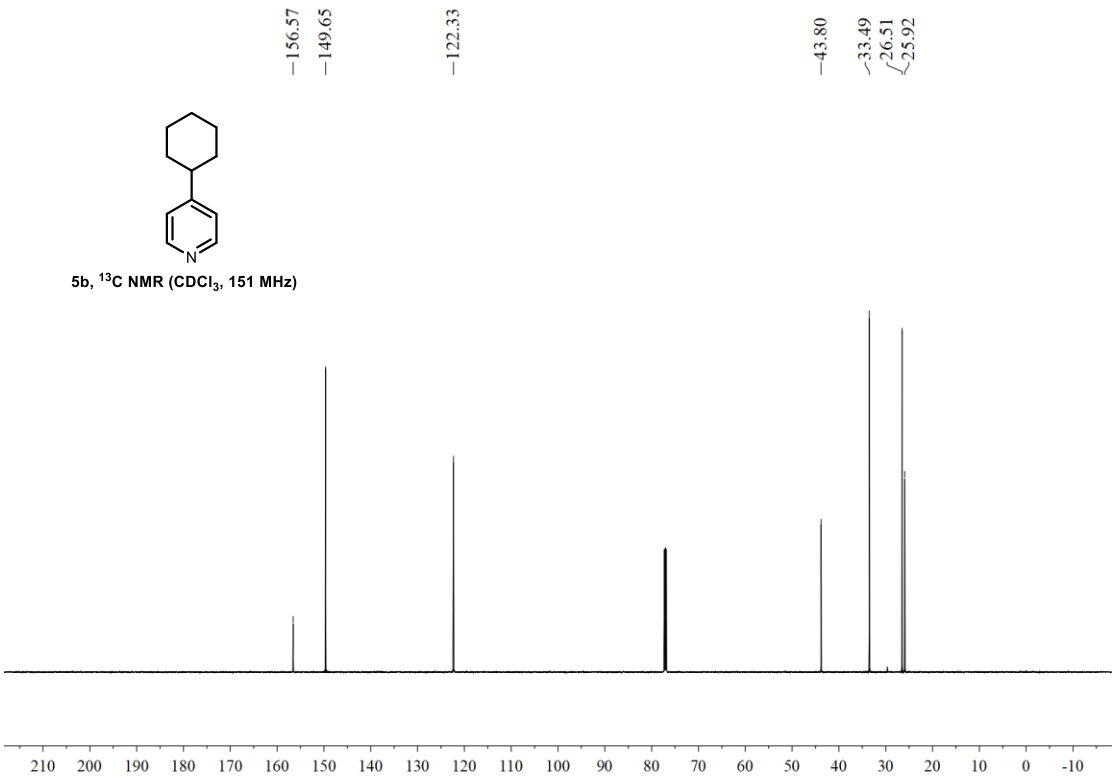


Figure S78. ^{13}C NMR of **5b** (CDCl$_3$, 151 MHz)

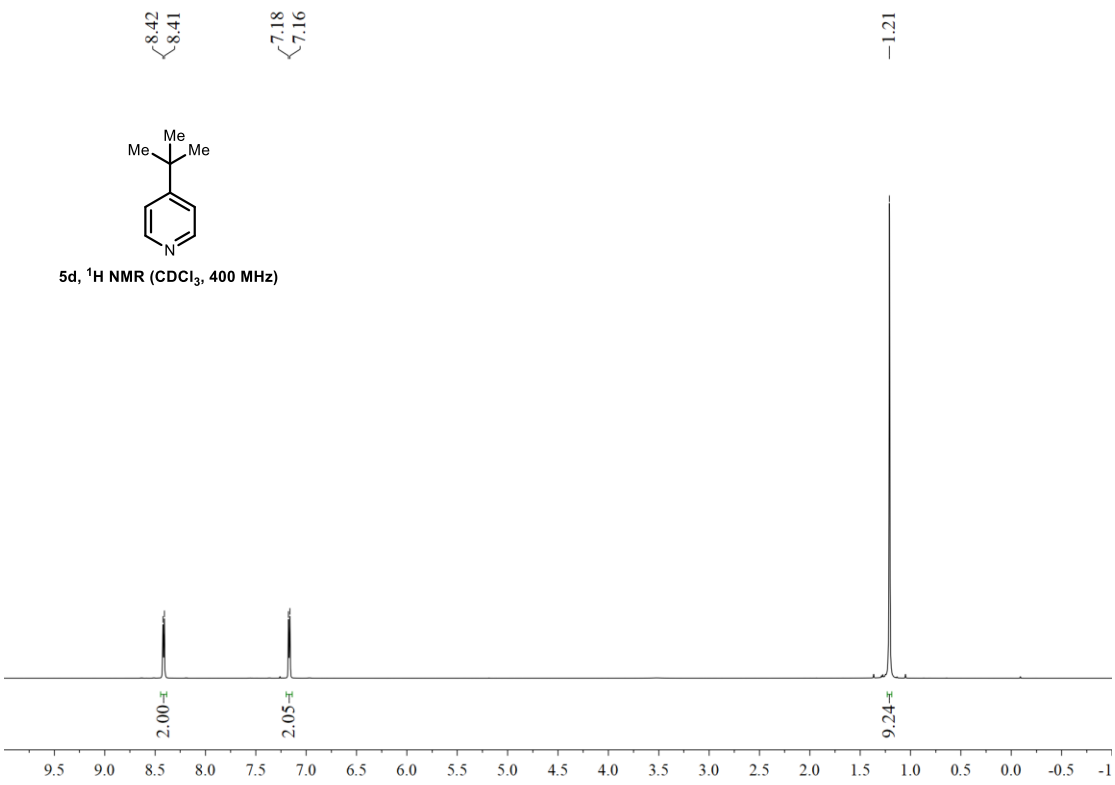


Figure S79. ^{1}H NMR of **5d** (CDCl$_3$, 400 MHz)

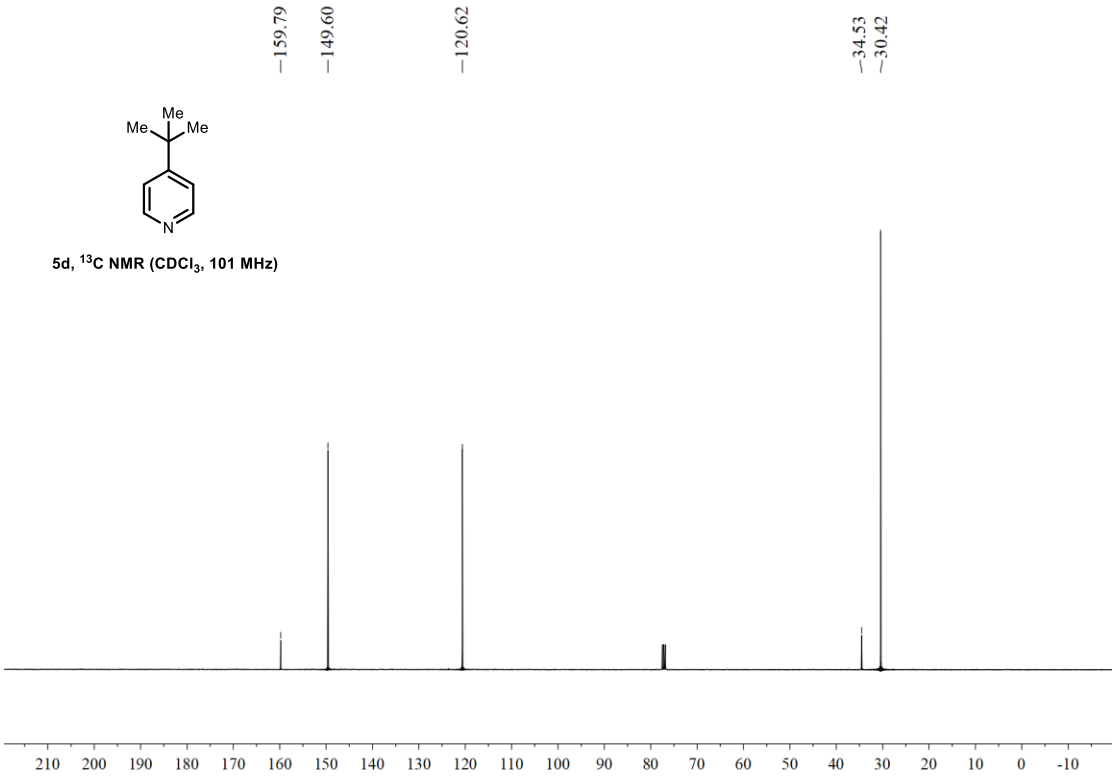


Figure S80. ^{13}C NMR of **5d** (CDCl$_3$, 101 MHz)

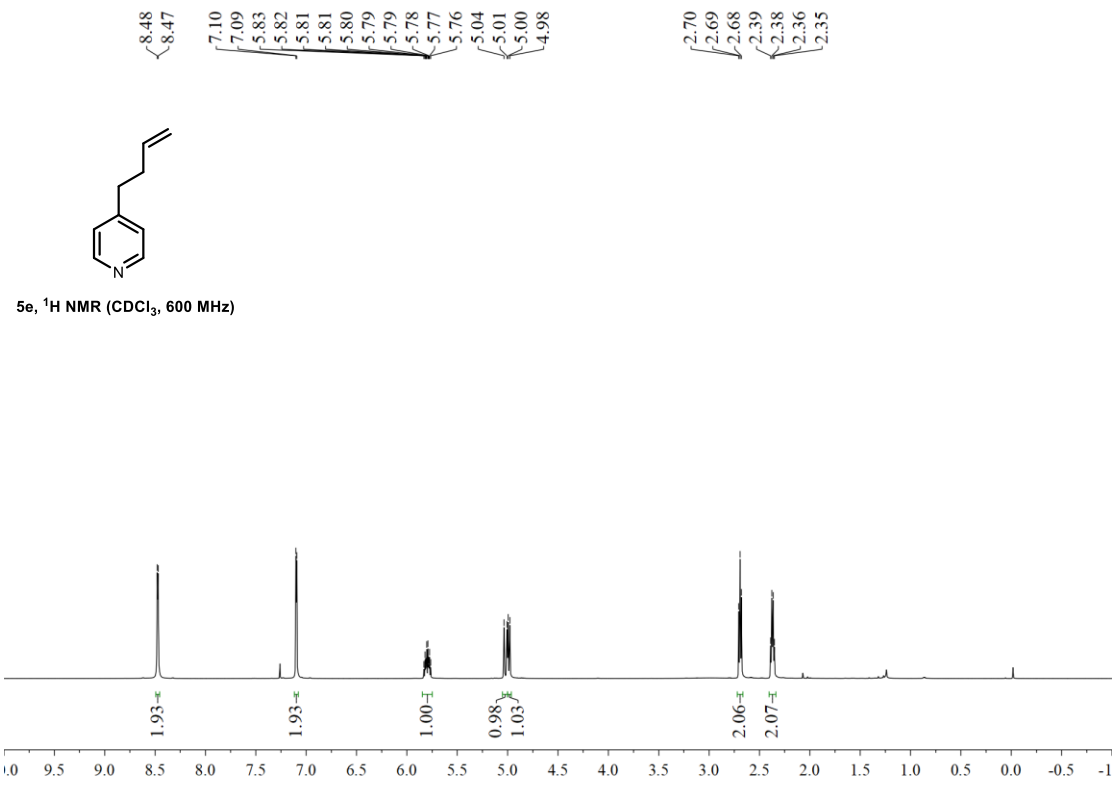


Figure S81. ^{1}H NMR of **5e** ($CDCl_3$, 600 MHz)

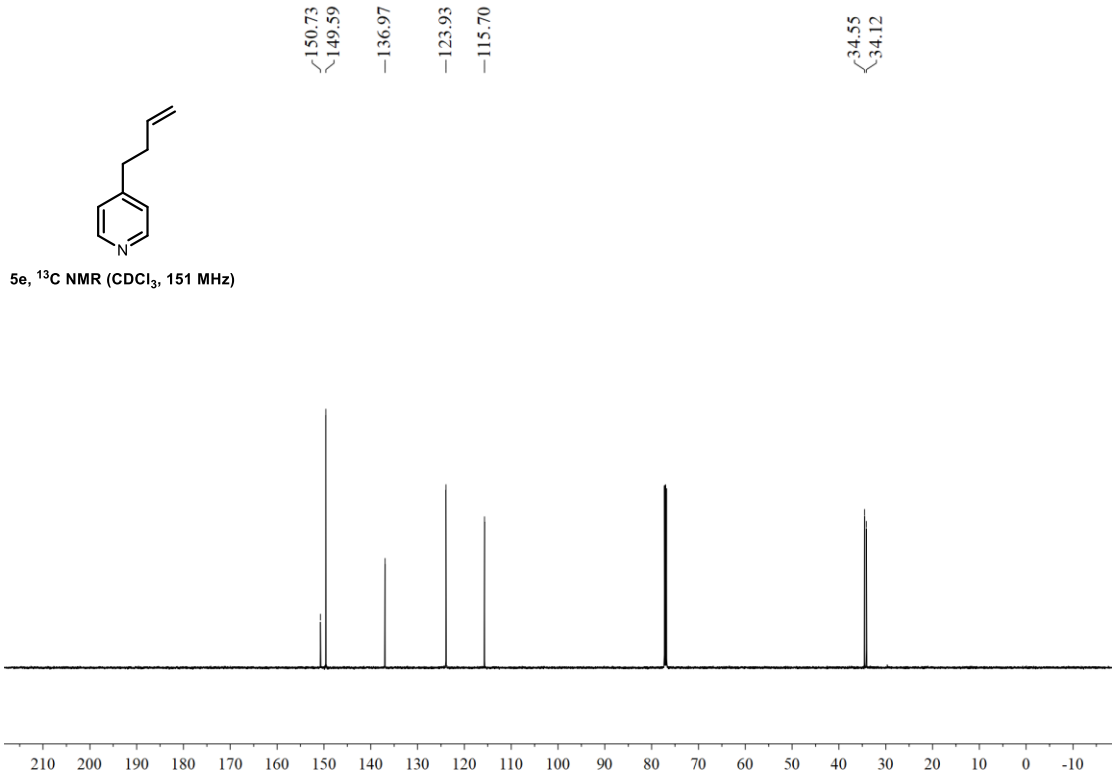


Figure S82. ^{13}C NMR of **5e** ($CDCl_3$, 151 MHz)

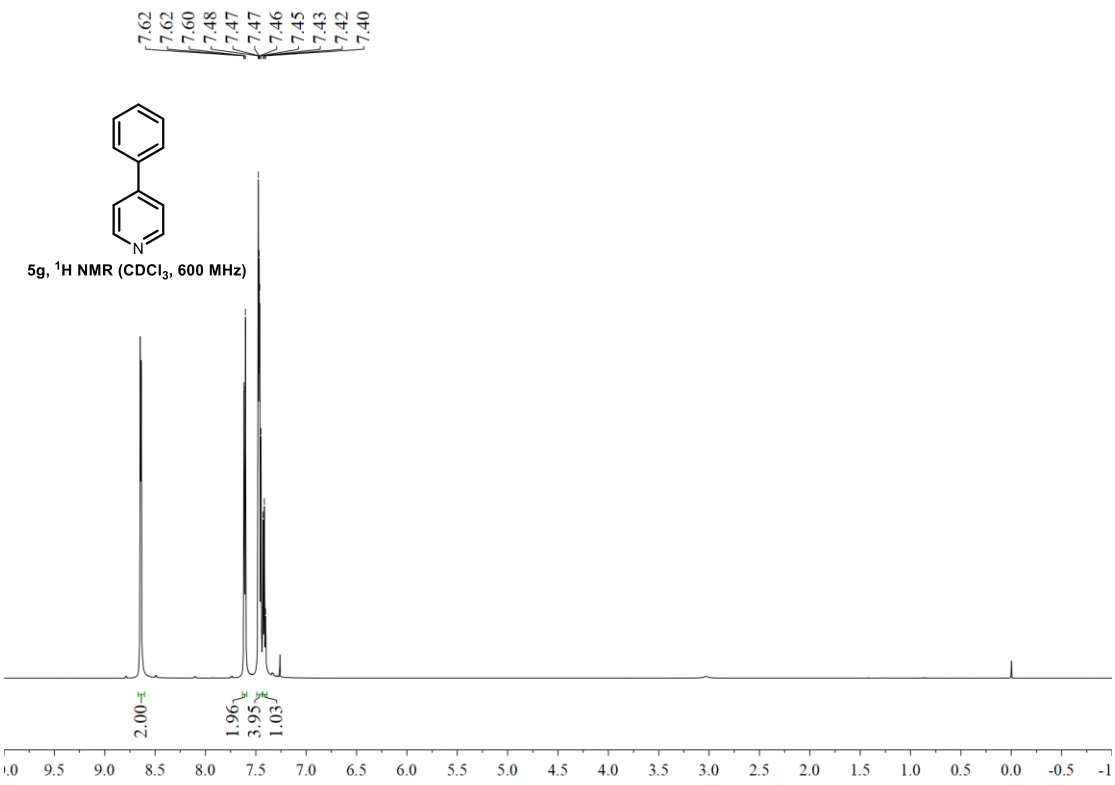


Figure S83. ^{1}H NMR of **5g** ($CDCl_3$, 600 MHz)

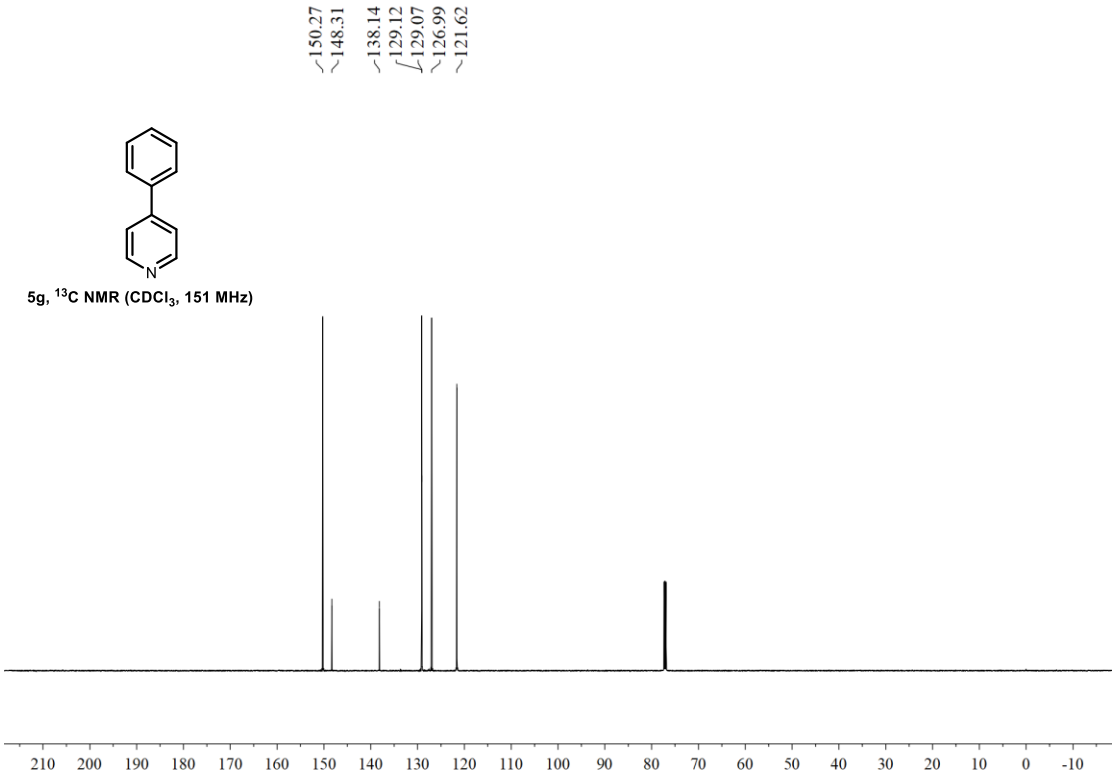


Figure S84. ^{13}C NMR of **5g** ($CDCl_3$, 151 MHz)

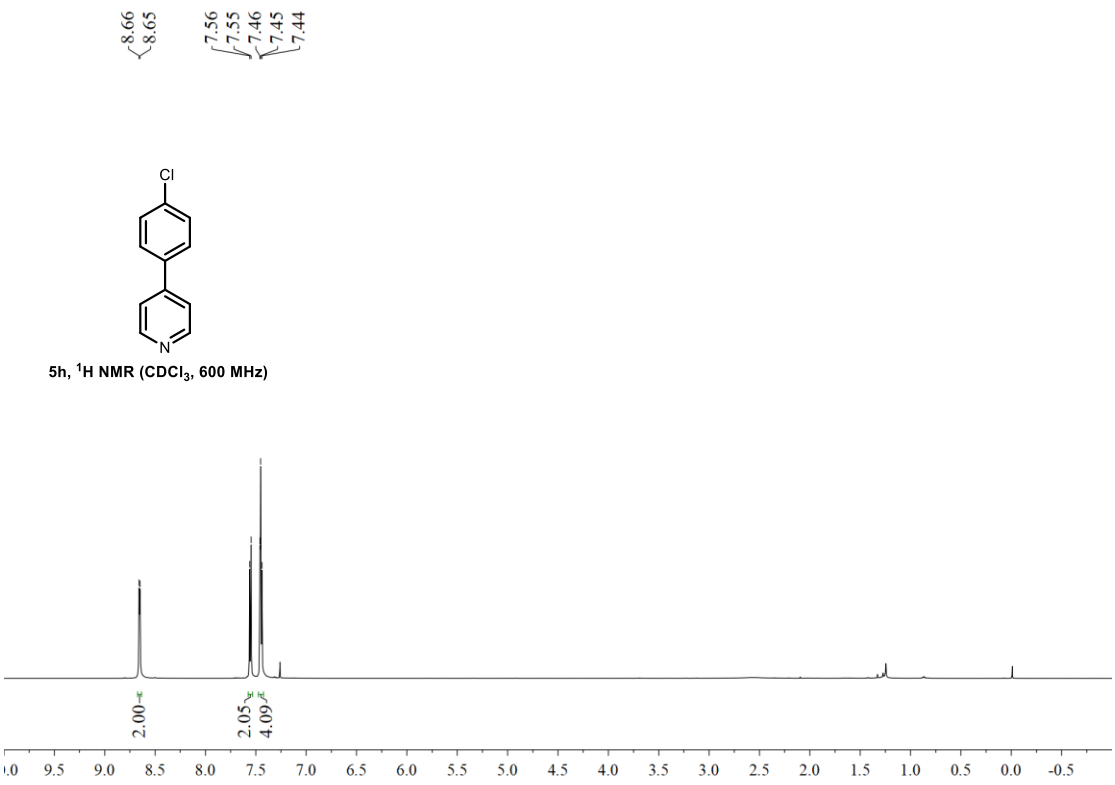


Figure S85. ^{1}H NMR of **5h** ($CDCl_3$, 600 MHz)

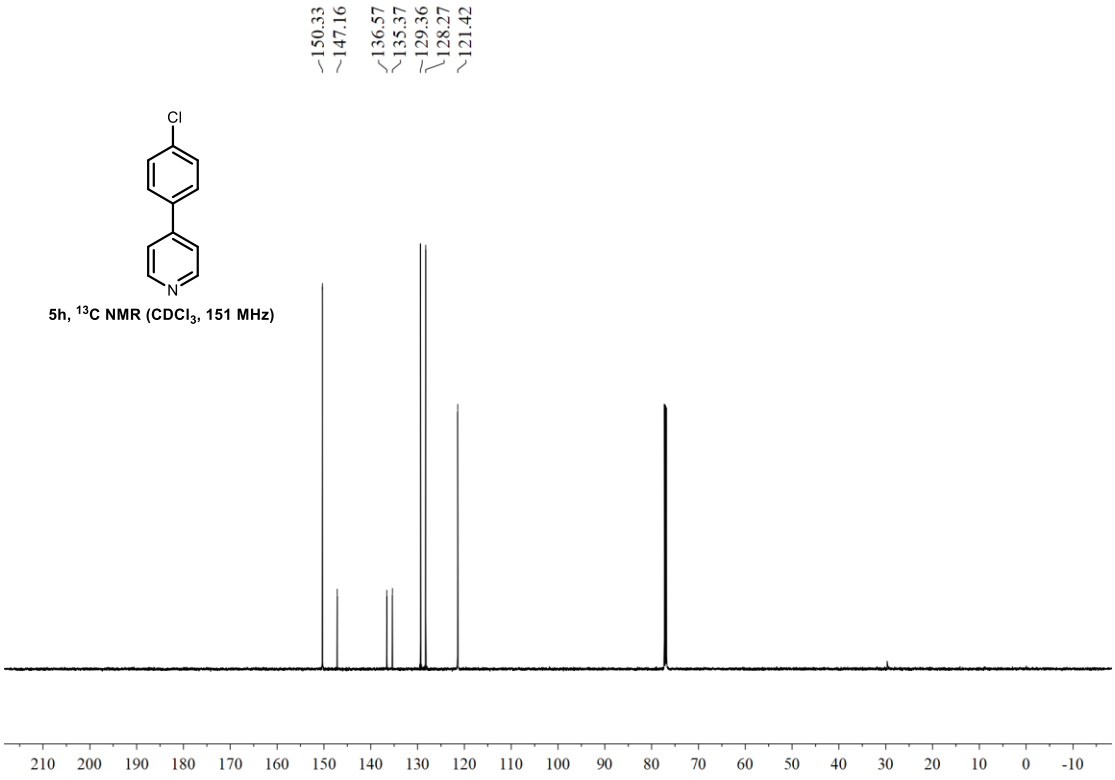


Figure S86. ^{13}C NMR of **5h** ($CDCl_3$, 151 MHz)

Figure S87. ^{1}H NMR of **5i** ($CDCl_3$, 600 MHz)

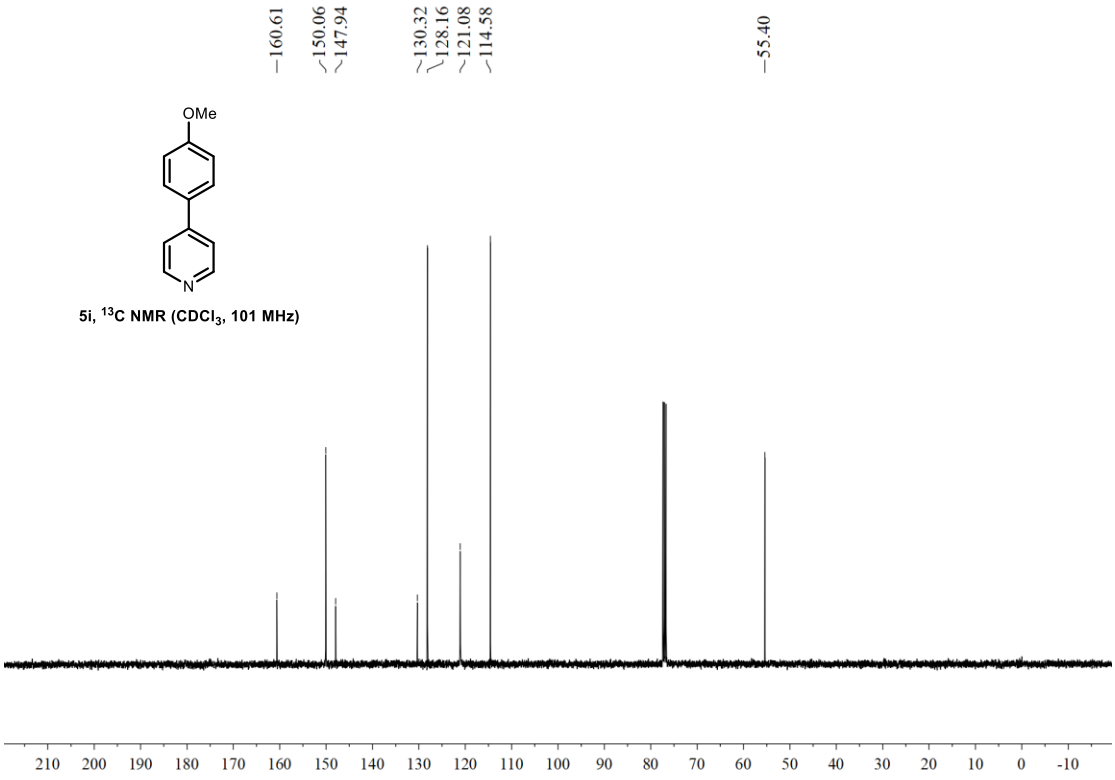


Figure S88. ^{13}C NMR of **5i** ($CDCl_3$, 101 MHz)

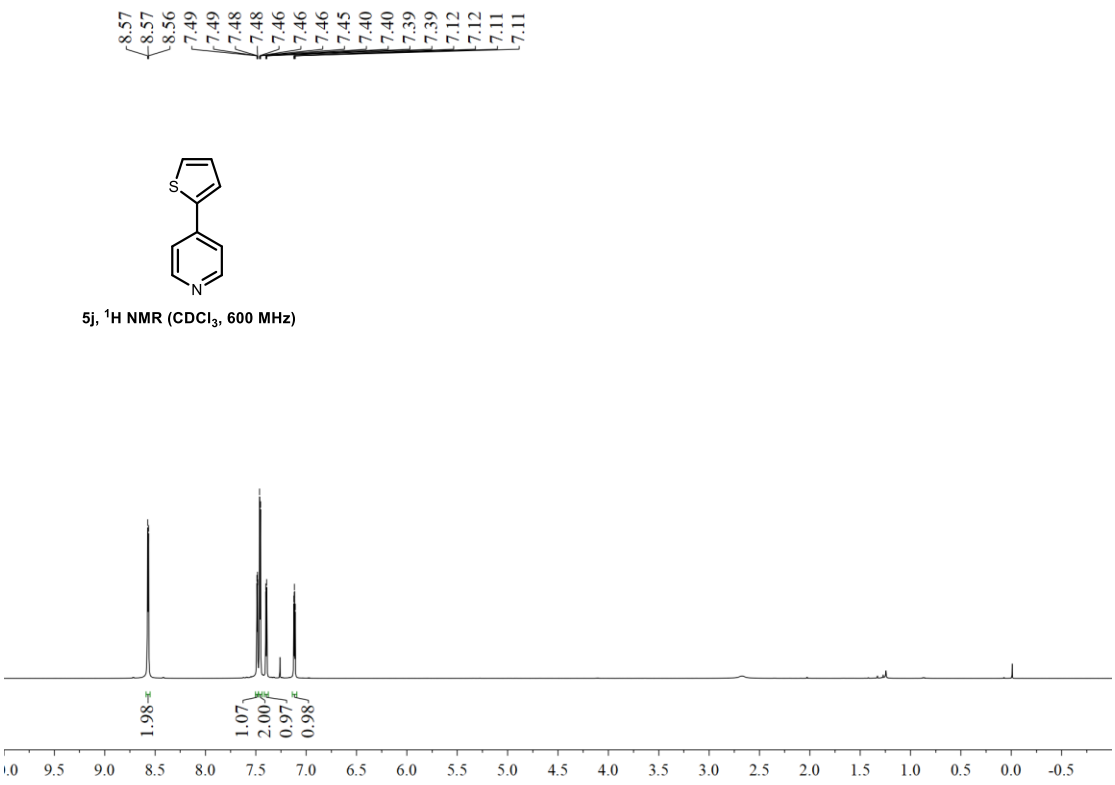


Figure S89. ^{1}H NMR of **5j** ($CDCl_3$, 600 MHz)

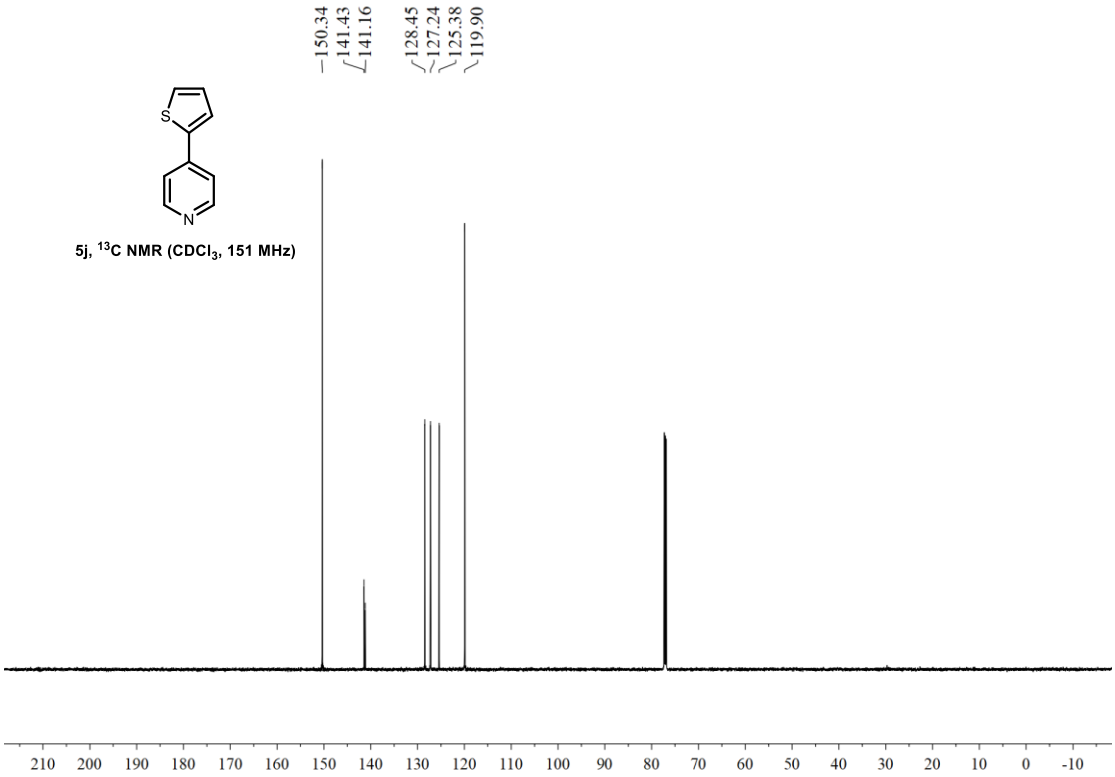


Figure S90. ^{13}C NMR of **5j** ($CDCl_3$, 151 MHz)

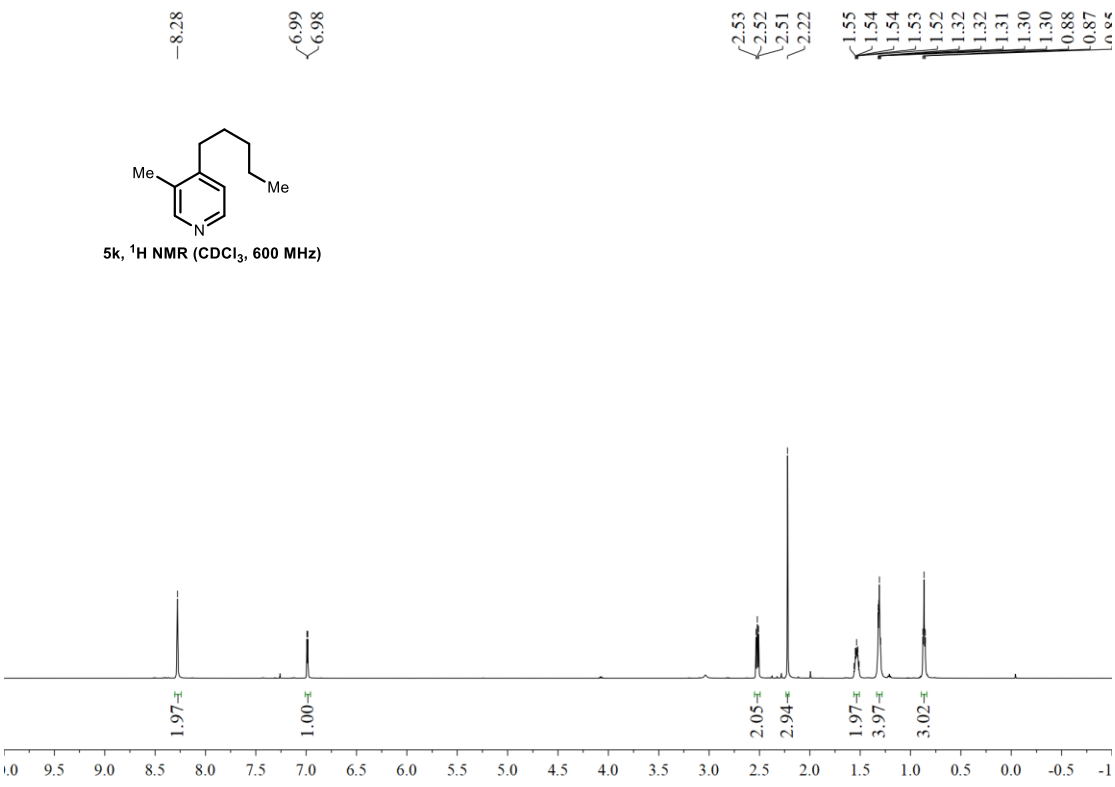


Figure S91. ^{1}H NMR of **5k** ($CDCl_3$, 600 MHz)

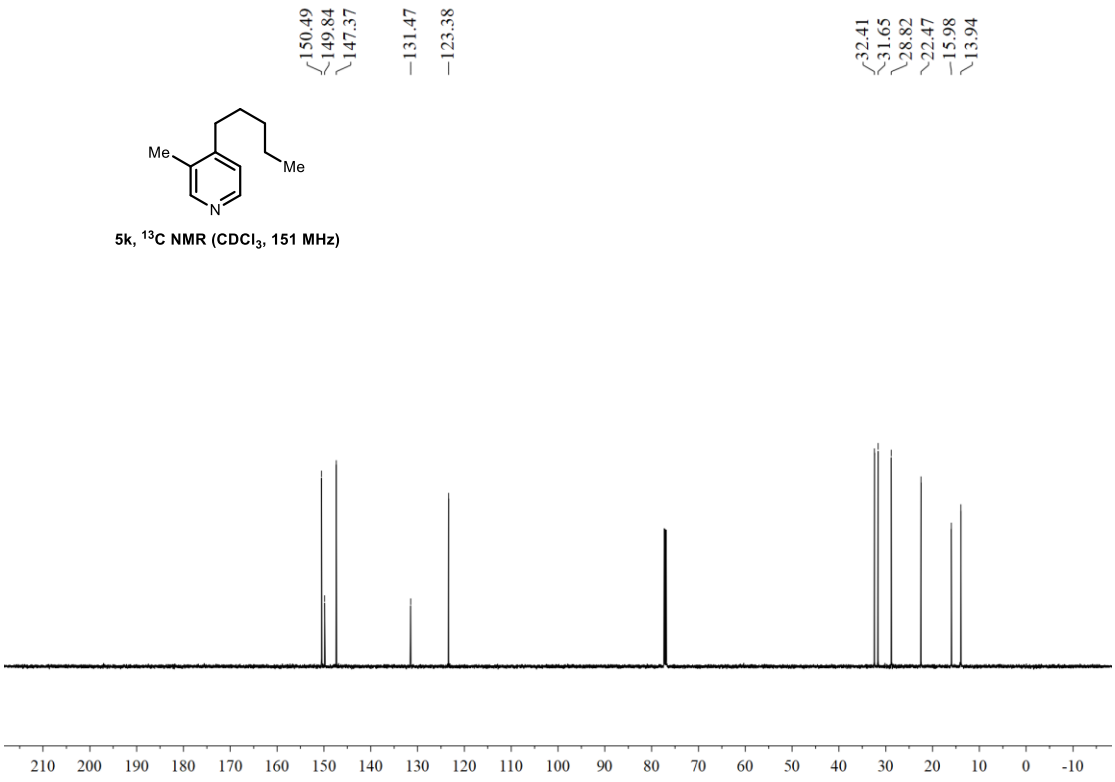


Figure S92. ^{13}C NMR of **5k** ($CDCl_3$, 151 MHz)

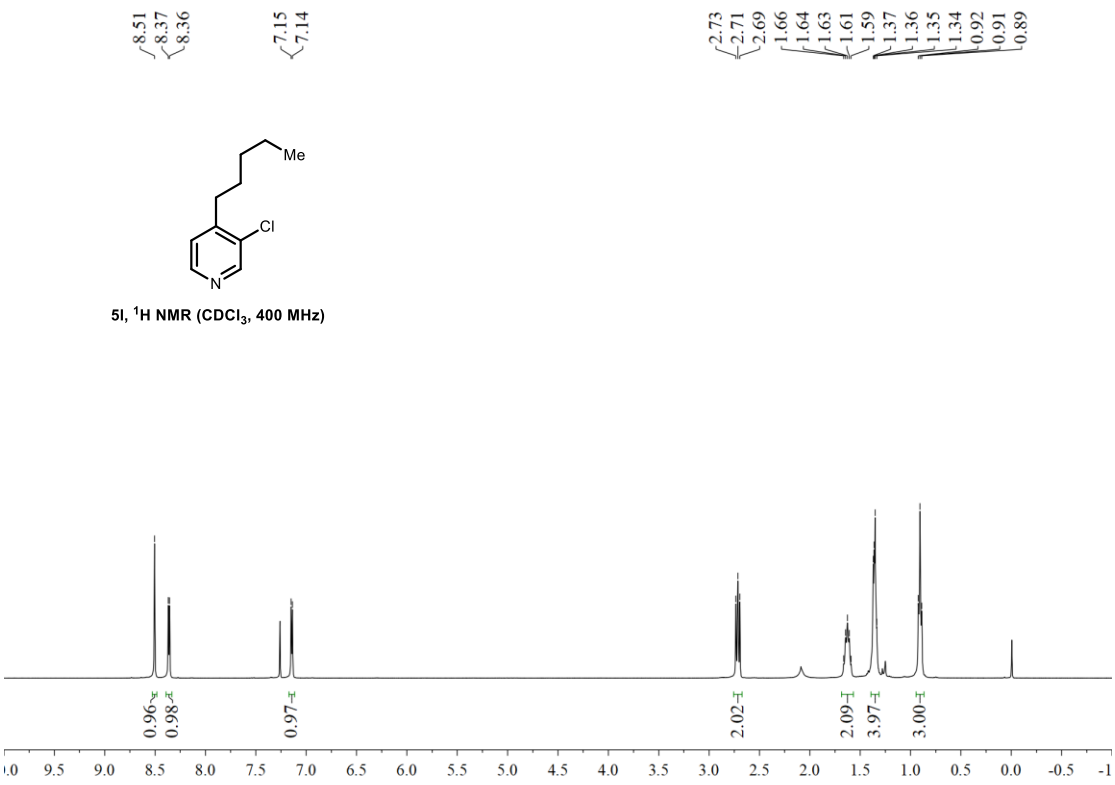


Figure S93. ^{1}H NMR of **5l** ($CDCl_3$, 400 MHz)

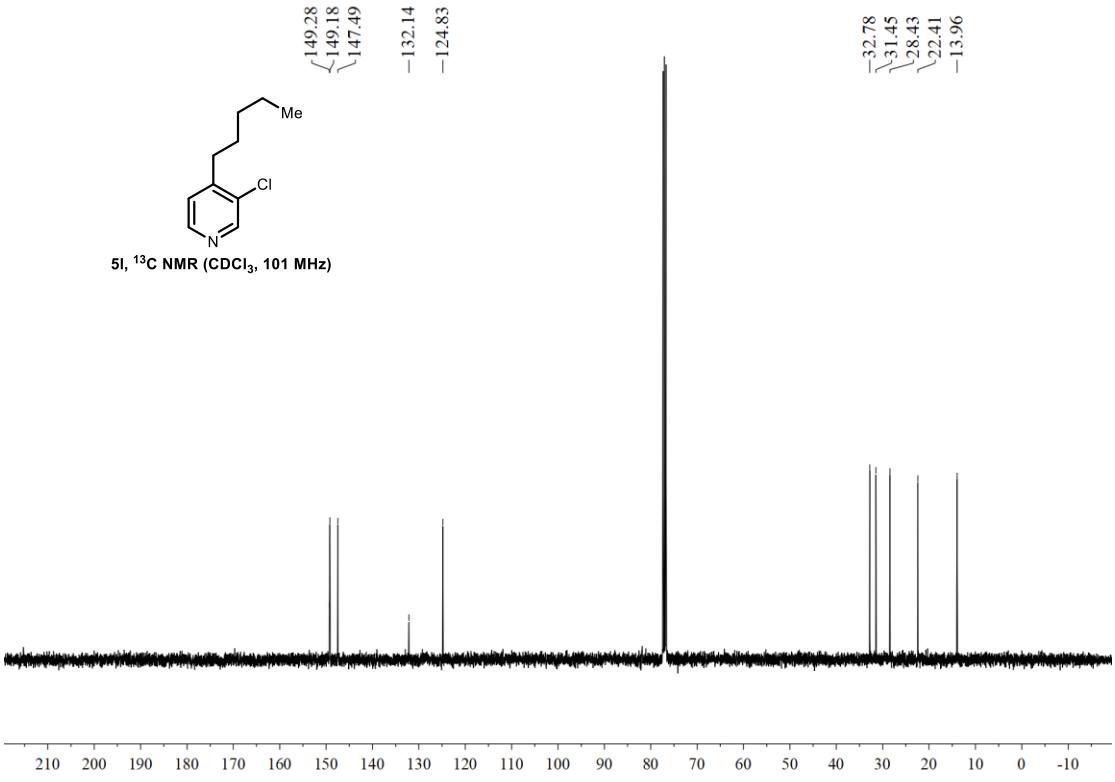


Figure S94. ^{13}C NMR of **5l** ($CDCl_3$, 101 MHz)

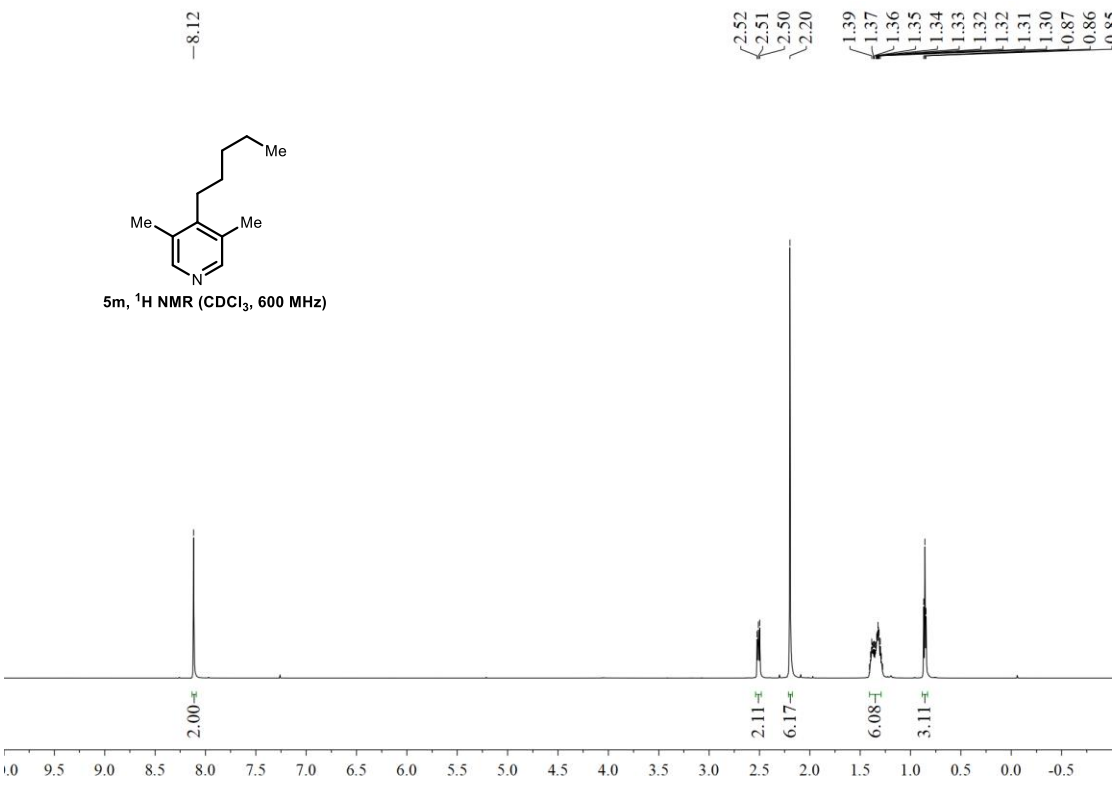


Figure S95. ^{1}H NMR of **5m** ($CDCl_3$, 600 MHz)

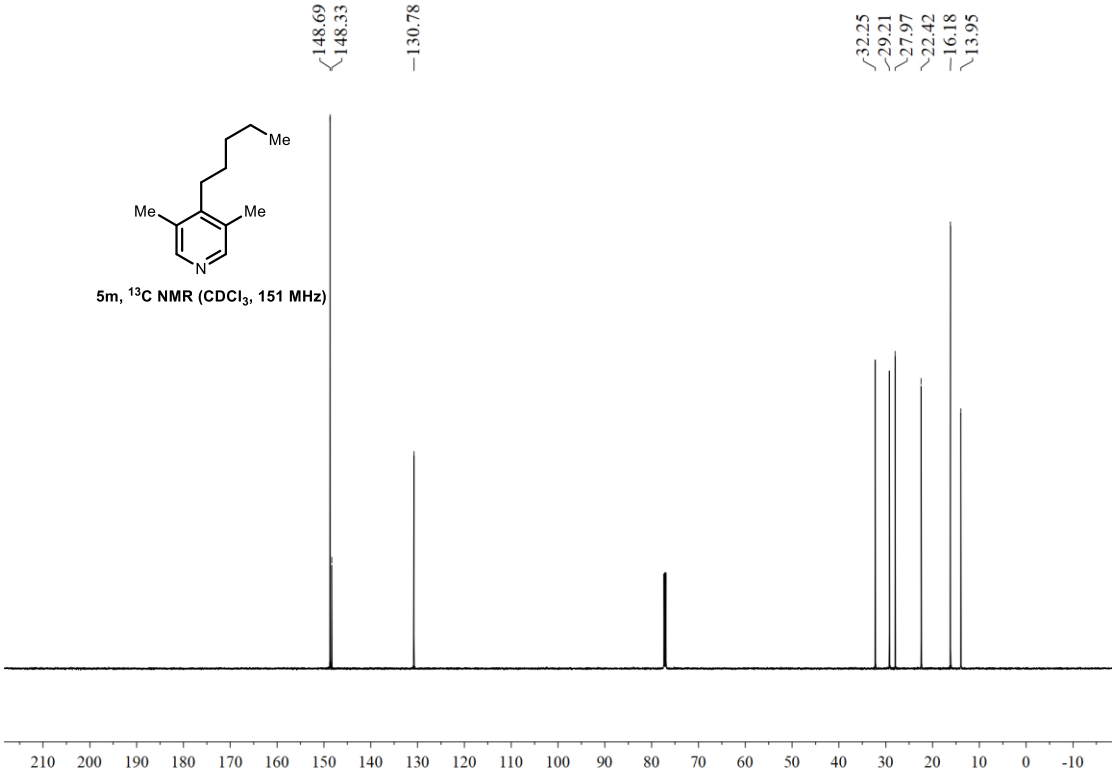


Figure S96. ^{13}C NMR of **5m** ($CDCl_3$, 151 MHz)

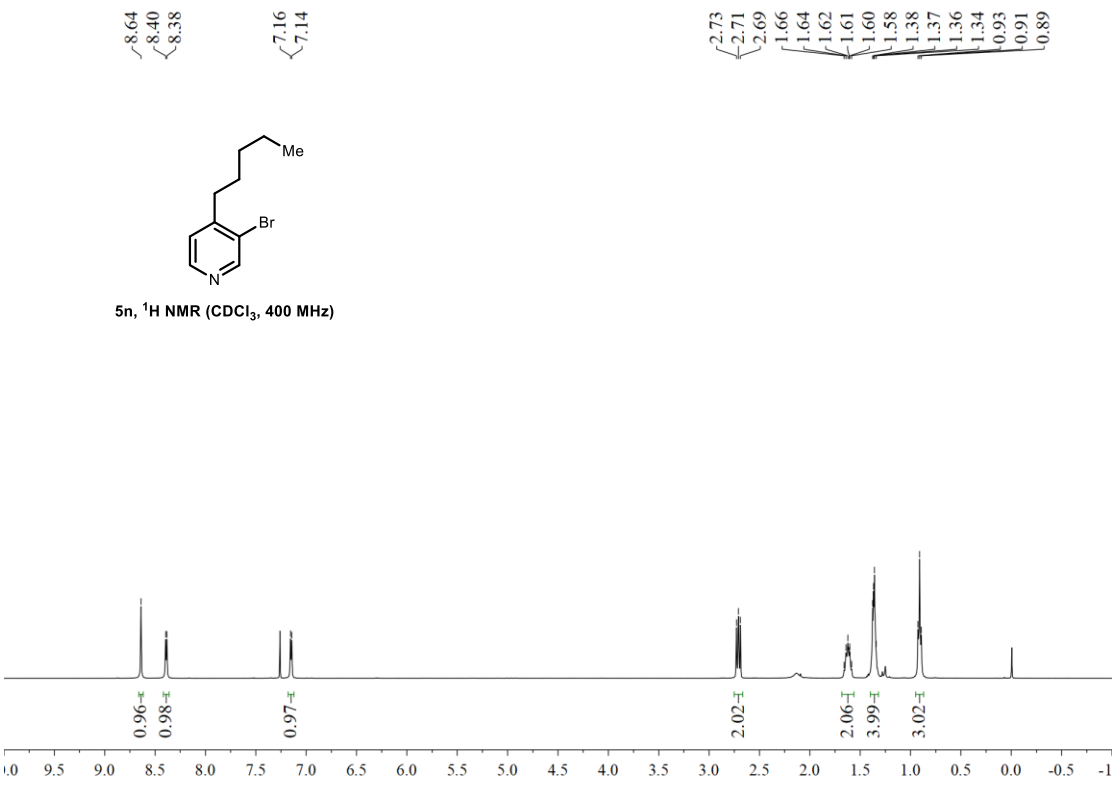


Figure S97. ^{1}H NMR of **5n** ($CDCl_3$, 400 MHz)

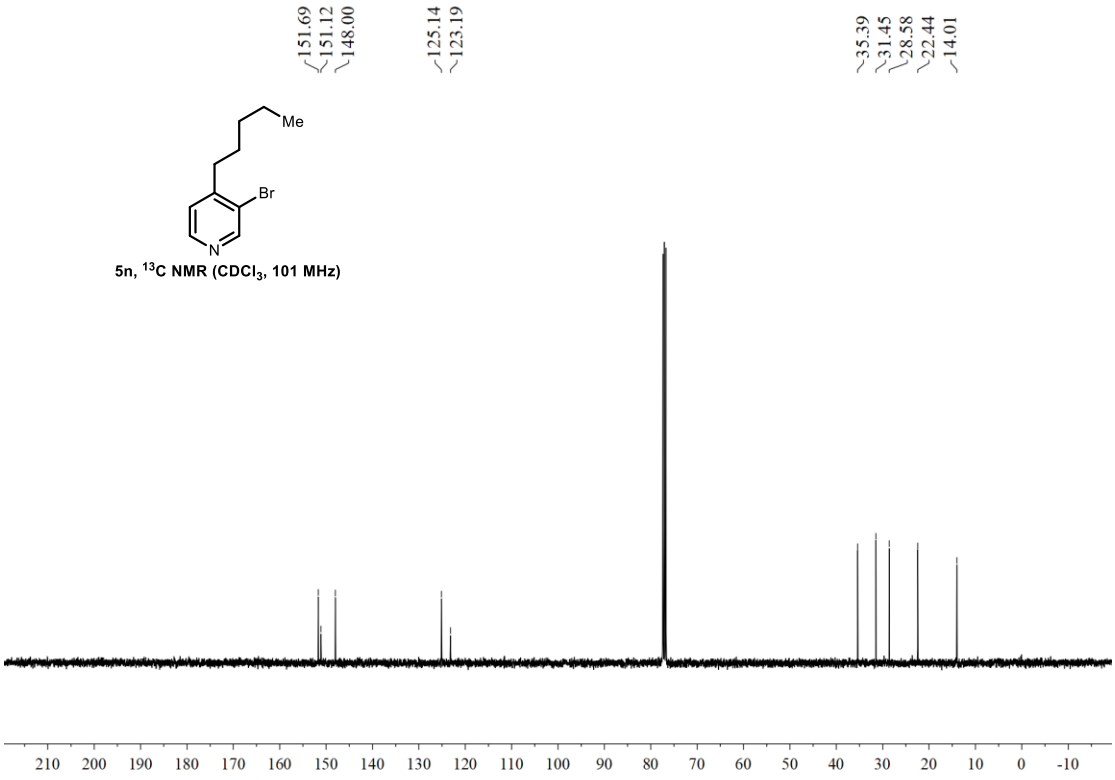


Figure S98. ^{13}C NMR of **5n** ($CDCl_3$, 101 MHz)

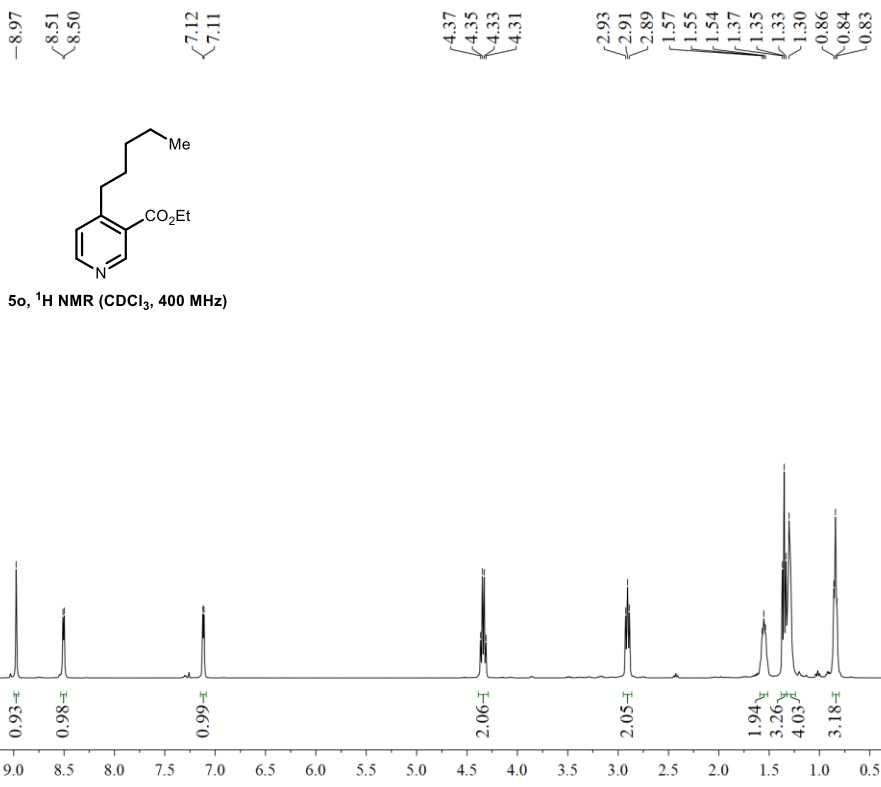


Figure S99. ^{1}H NMR of **5o** ($CDCl_3$, 400 MHz)

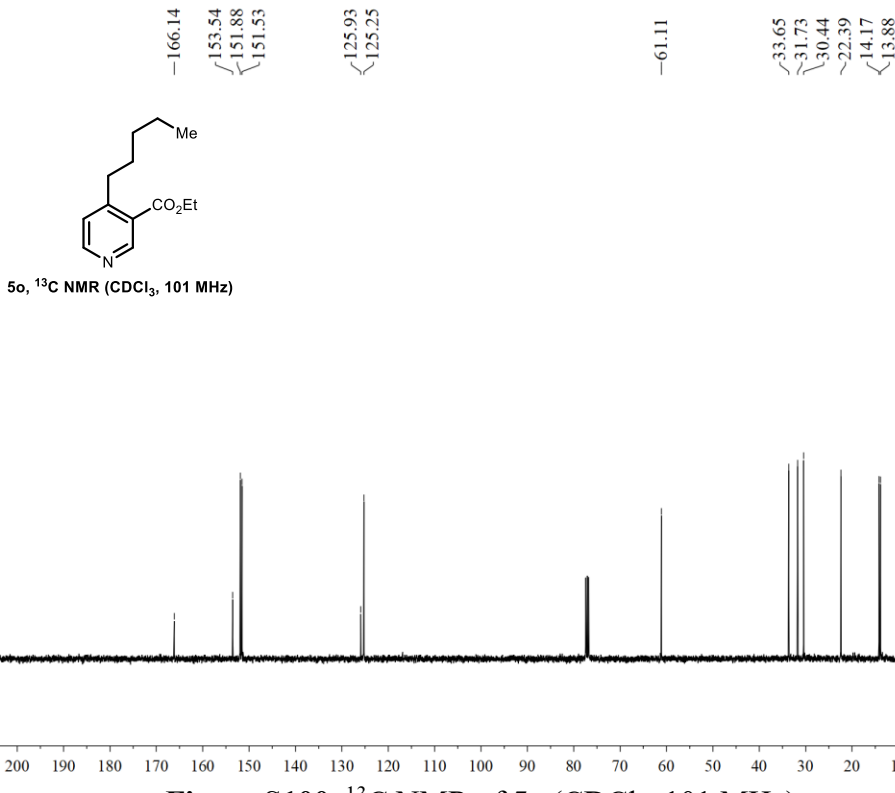


Figure S100. ^{13}C NMR of **5o** ($CDCl_3$, 101 MHz)

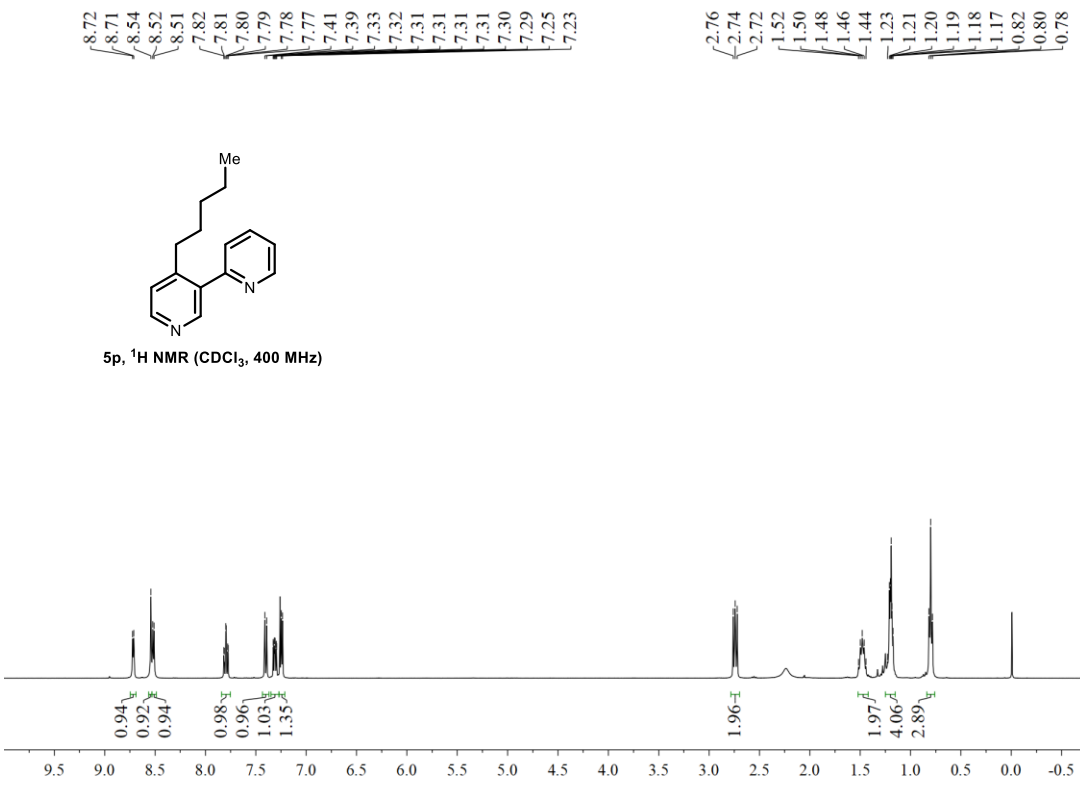


Figure S101. ^{1}H NMR of **5p** ($CDCl_3$, 400 MHz)

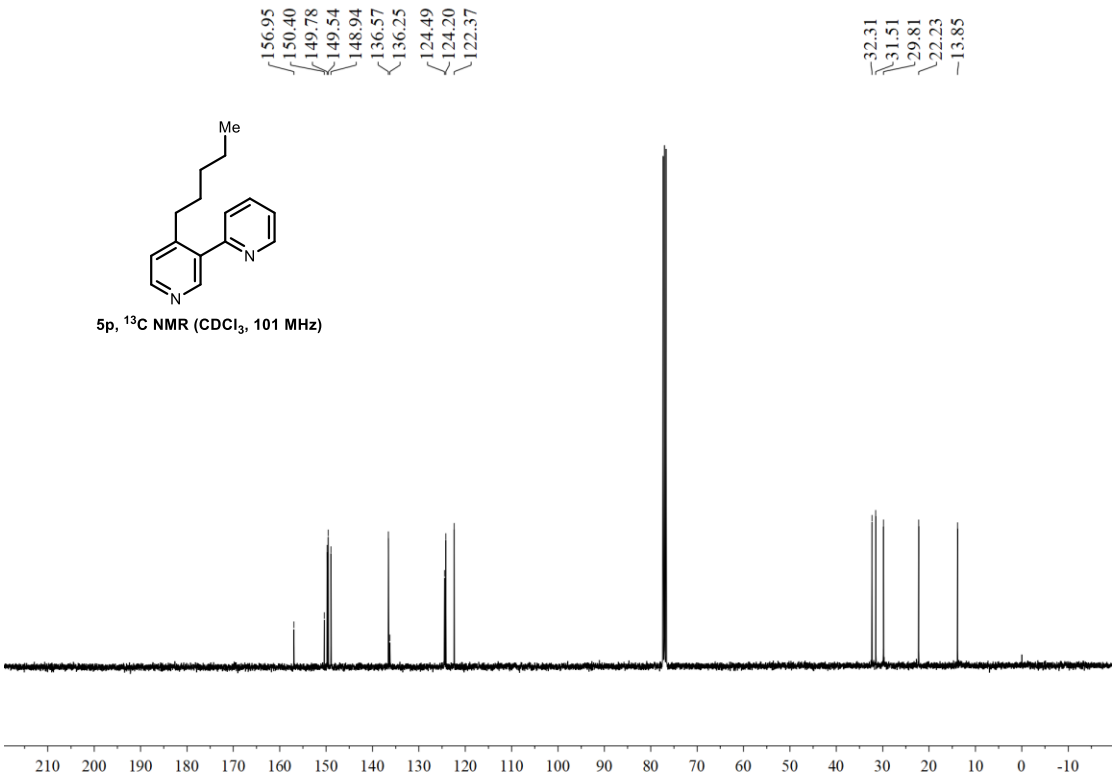


Figure S102. ^{13}C NMR of **5p** ($CDCl_3$, 101 MHz)

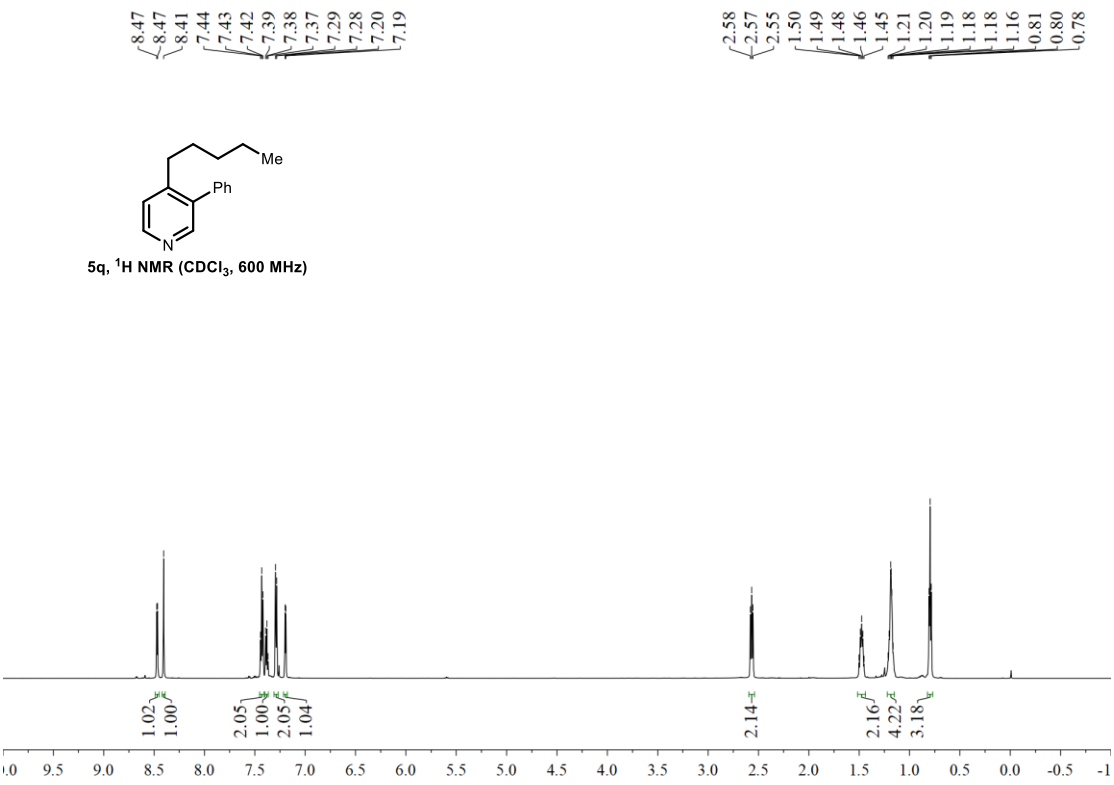


Figure S103. ^{1}H NMR of **5q** ($CDCl_3$, 600 MHz)

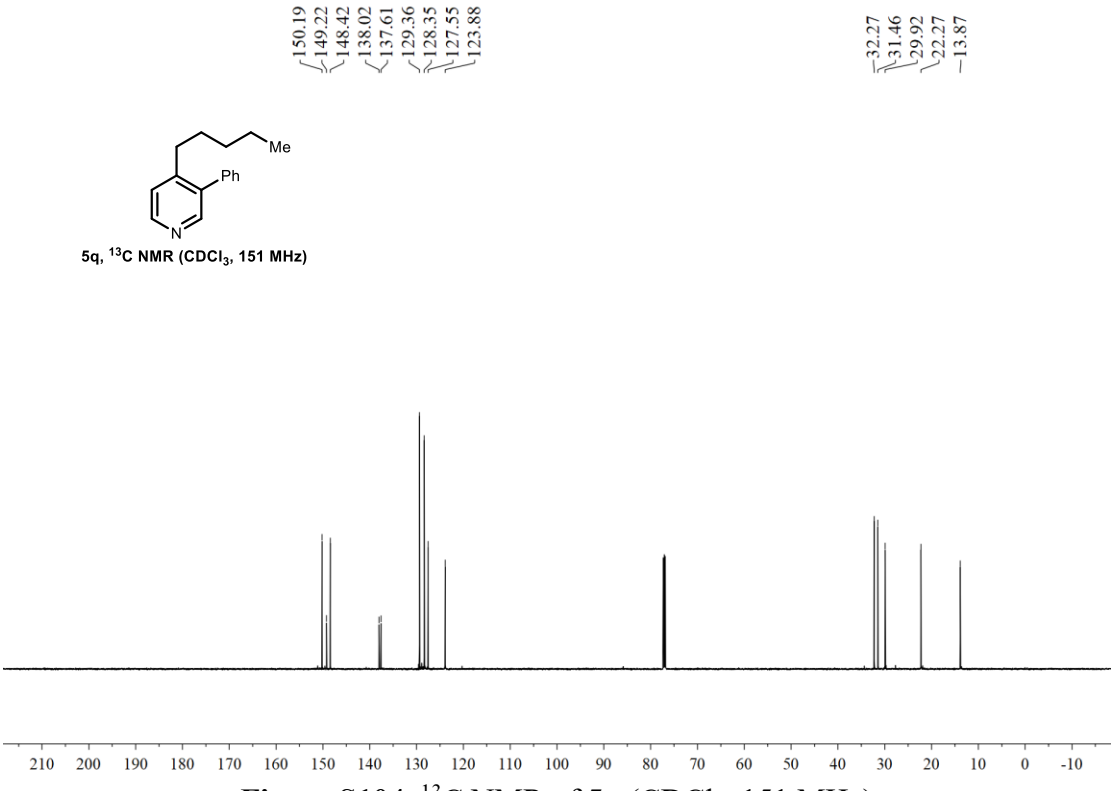


Figure S104. ^{13}C NMR of **5q** ($CDCl_3$, 151 MHz)

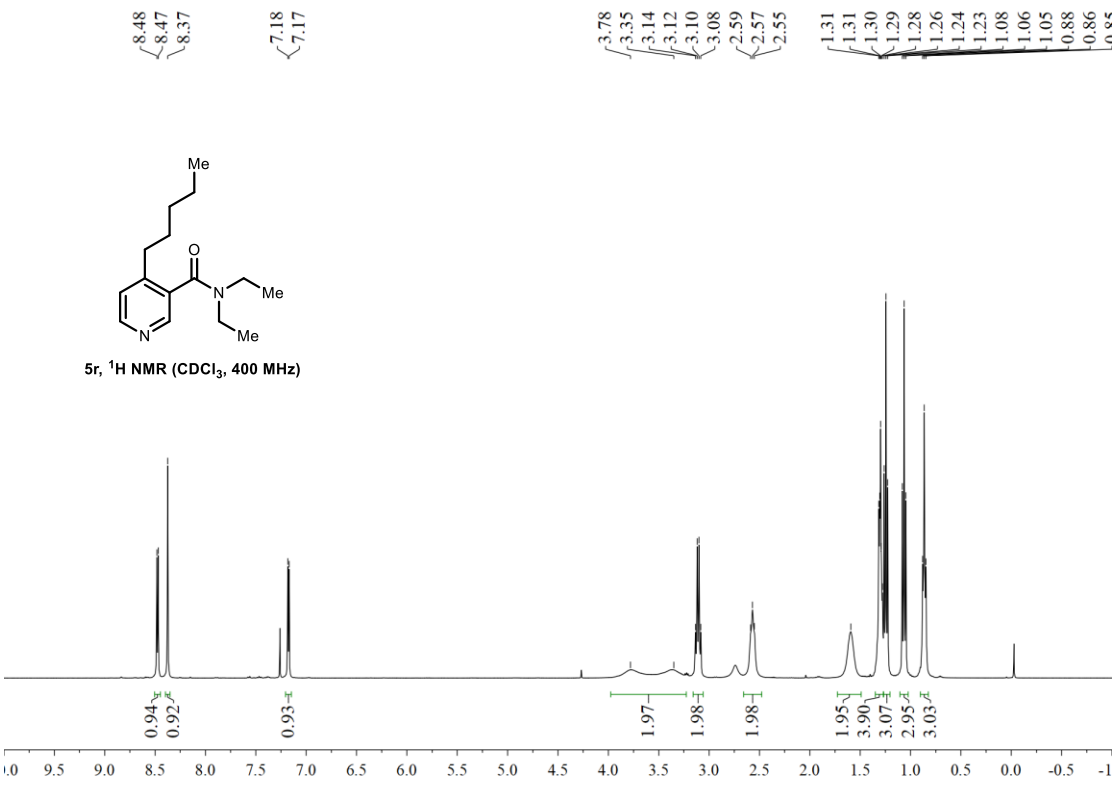


Figure S105. ^{1}H NMR of **5r** ($CDCl_3$, 400 MHz)

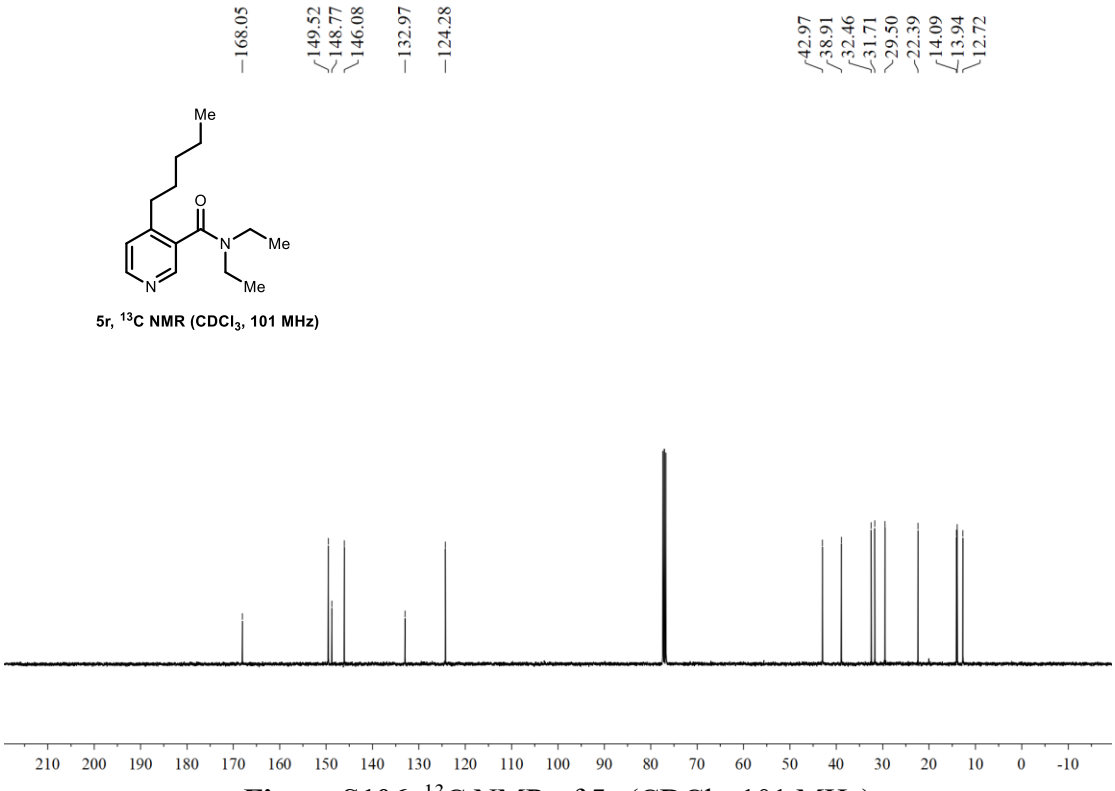


Figure S106. ^{13}C NMR of **5r** ($CDCl_3$, 101 MHz)

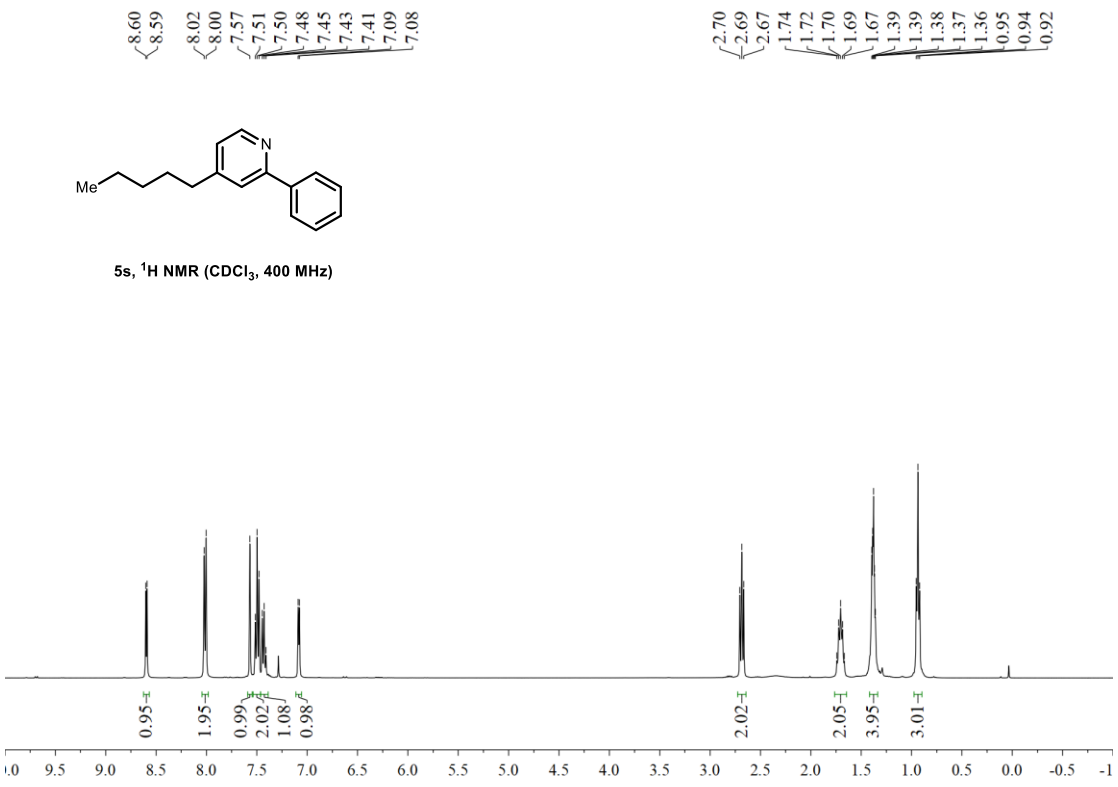


Figure S107. ^{1}H NMR of **5s** ($CDCl_3$, 400 MHz)

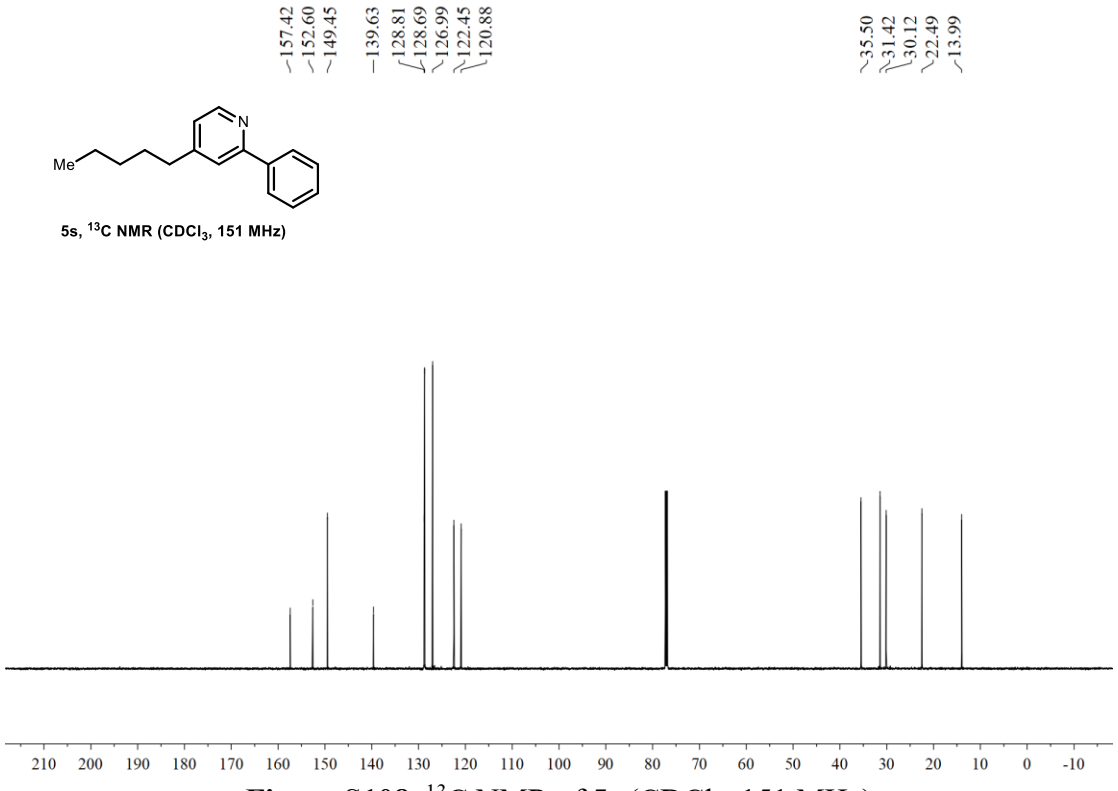


Figure S108. ^{13}C NMR of **5s** ($CDCl_3$, 151 MHz)

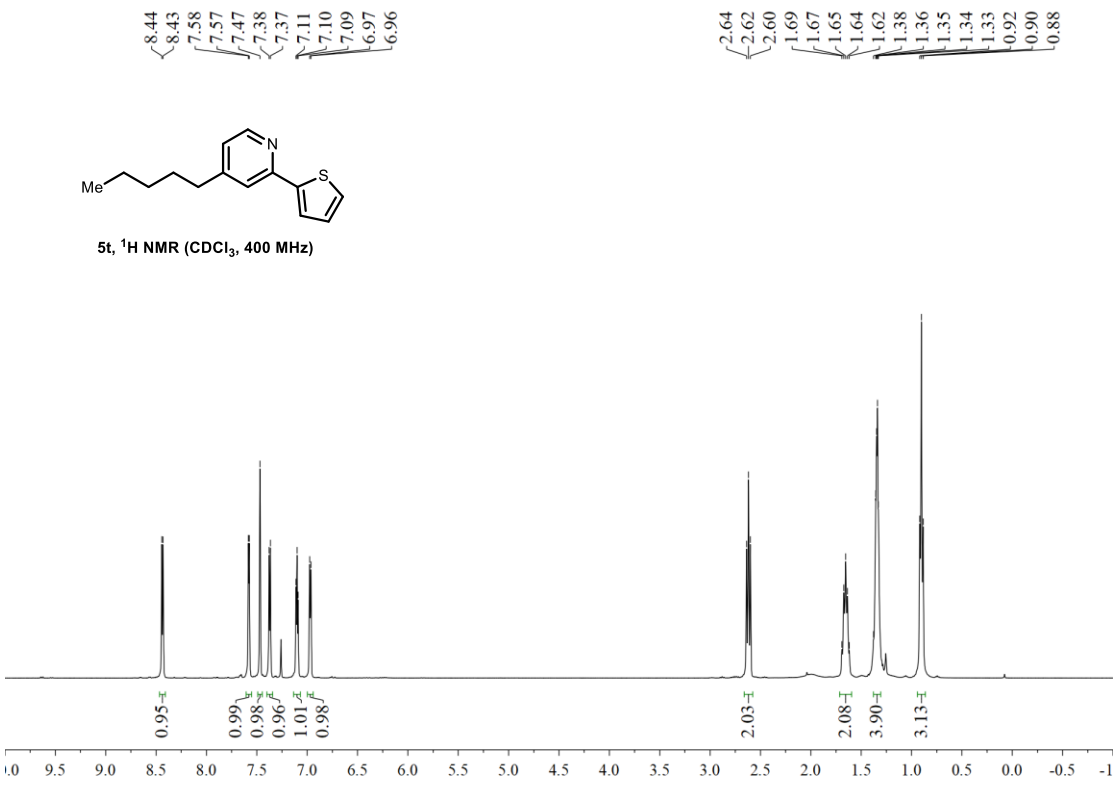


Figure S109. ^{1}H NMR of **5t** ($CDCl_3$, 400 MHz)

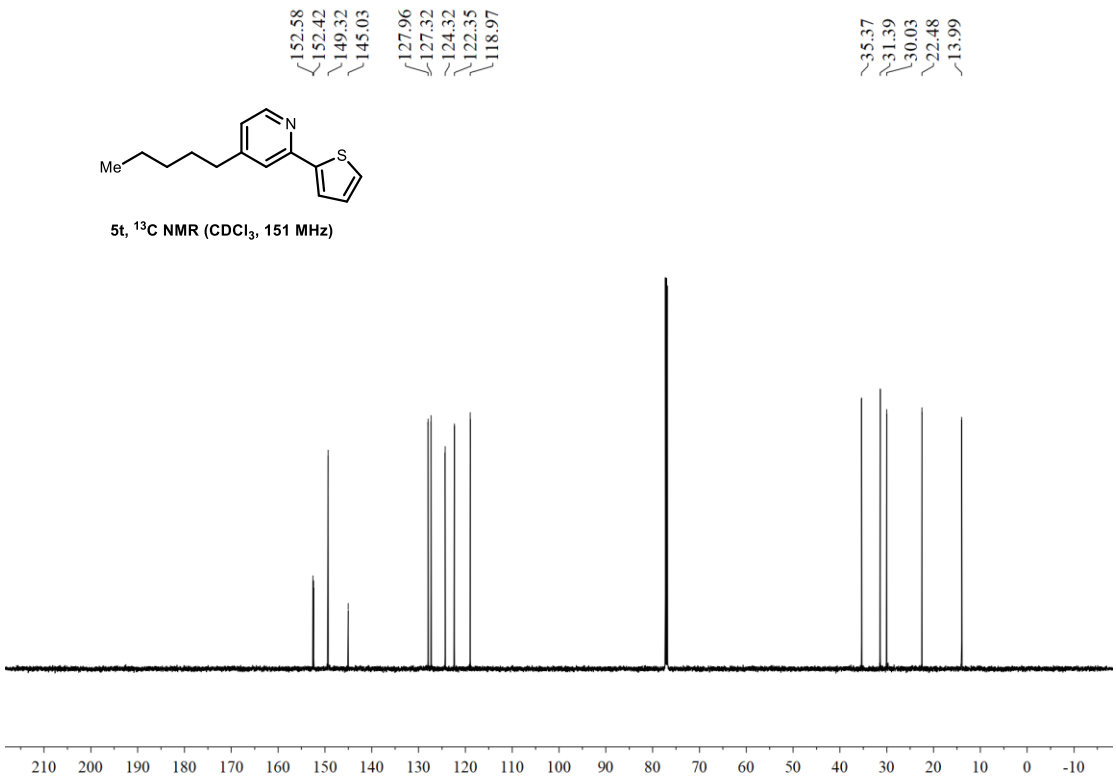


Figure S110. ^{13}C NMR of **5t** ($CDCl_3$, 151 MHz)

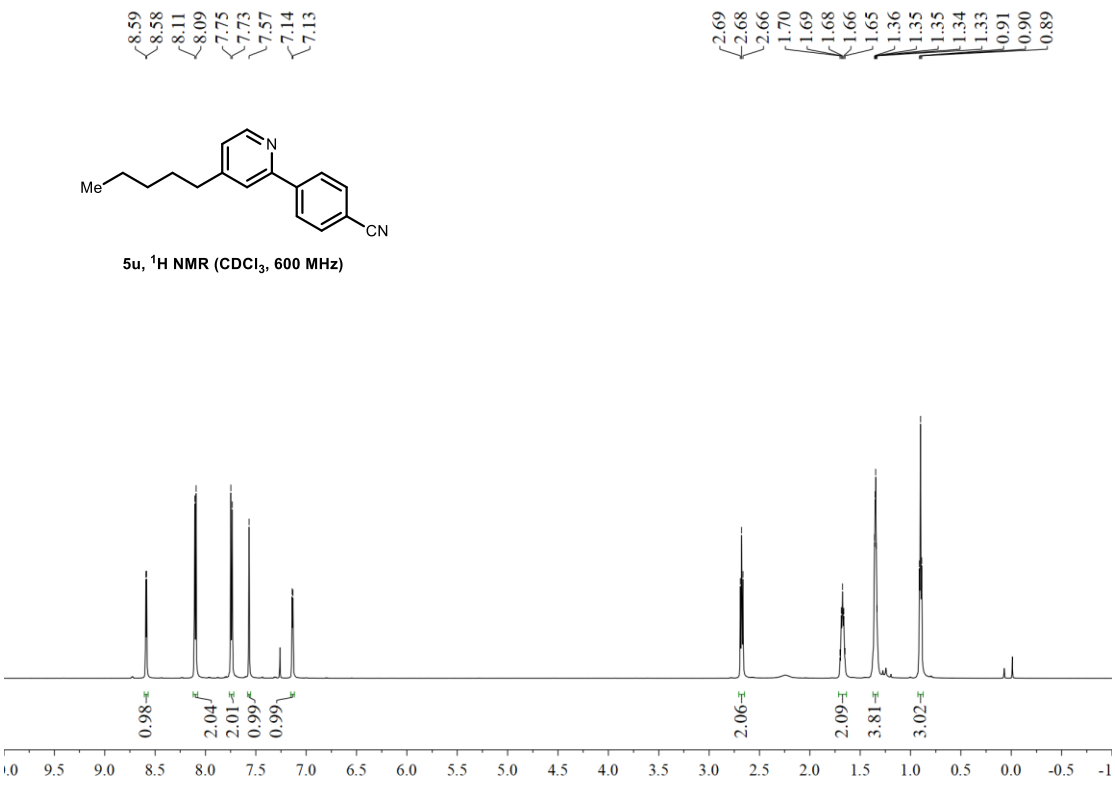


Figure S111. ^{1}H NMR of **5u** ($CDCl_3$, 600 MHz)

Figure S112. ^{13}C NMR of **5u** ($CDCl_3$, 151 MHz)

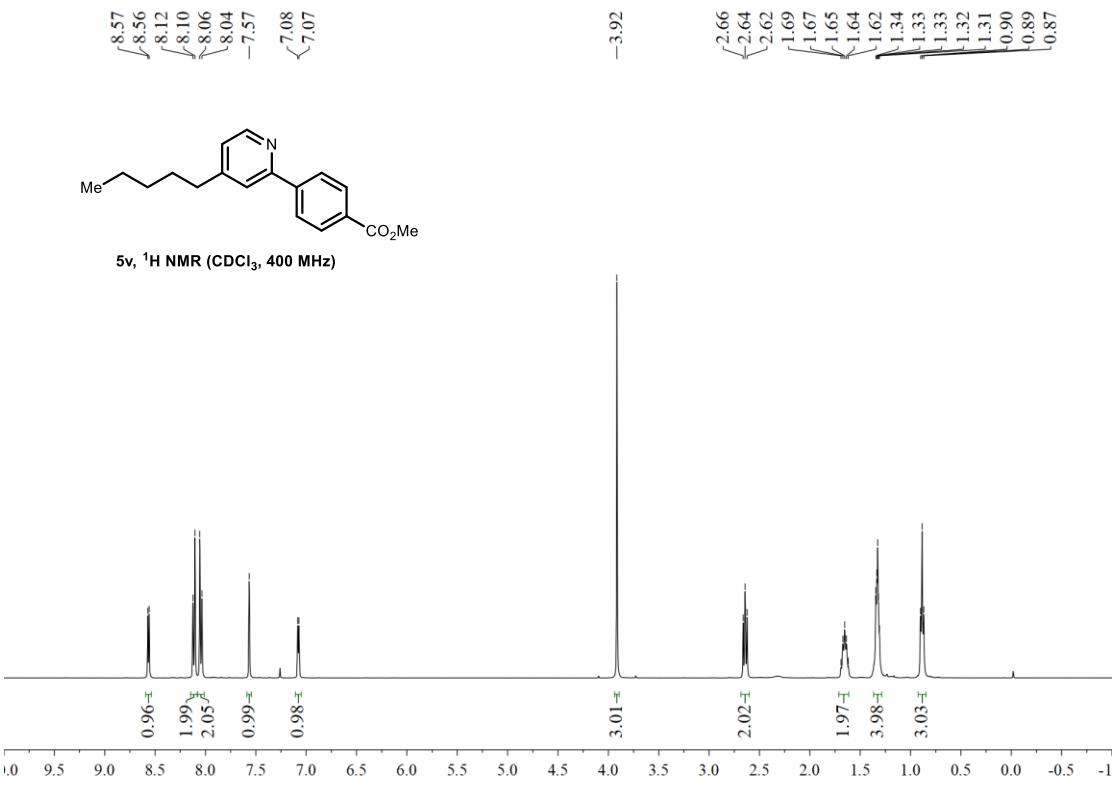


Figure S113. ^{1}H NMR of **5v** ($CDCl_3$, 400 MHz)

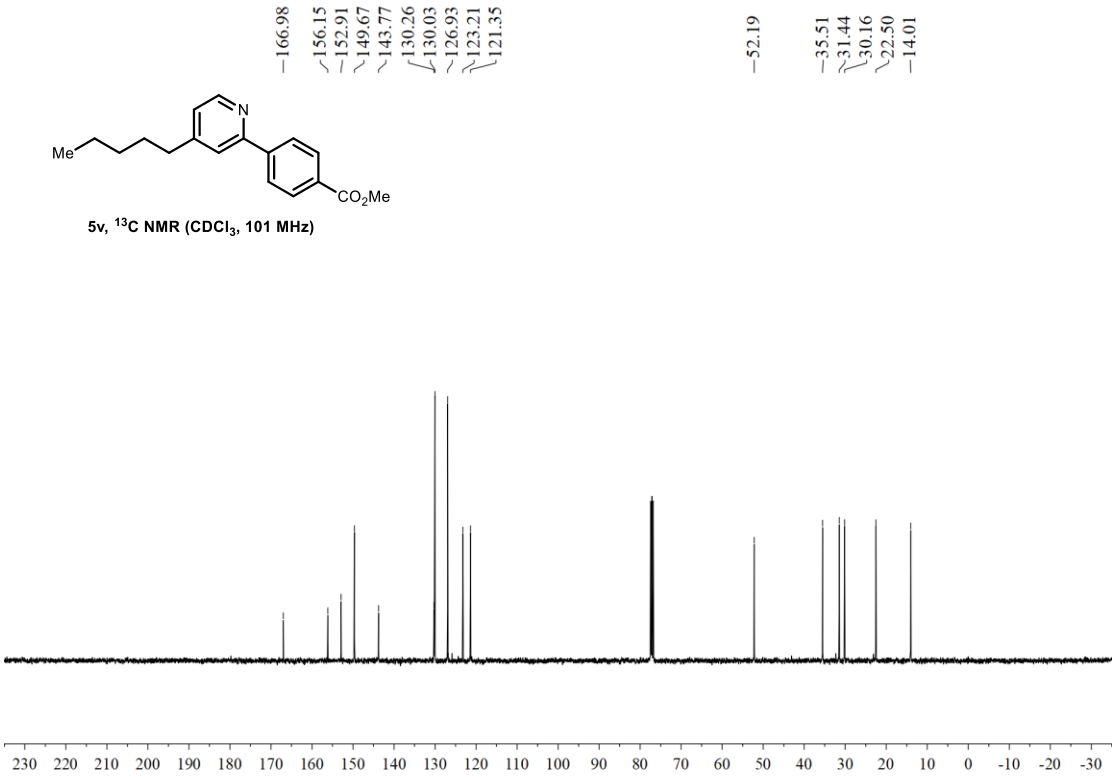


Figure S114. ^{13}C NMR of **5v** ($CDCl_3$, 101 MHz)

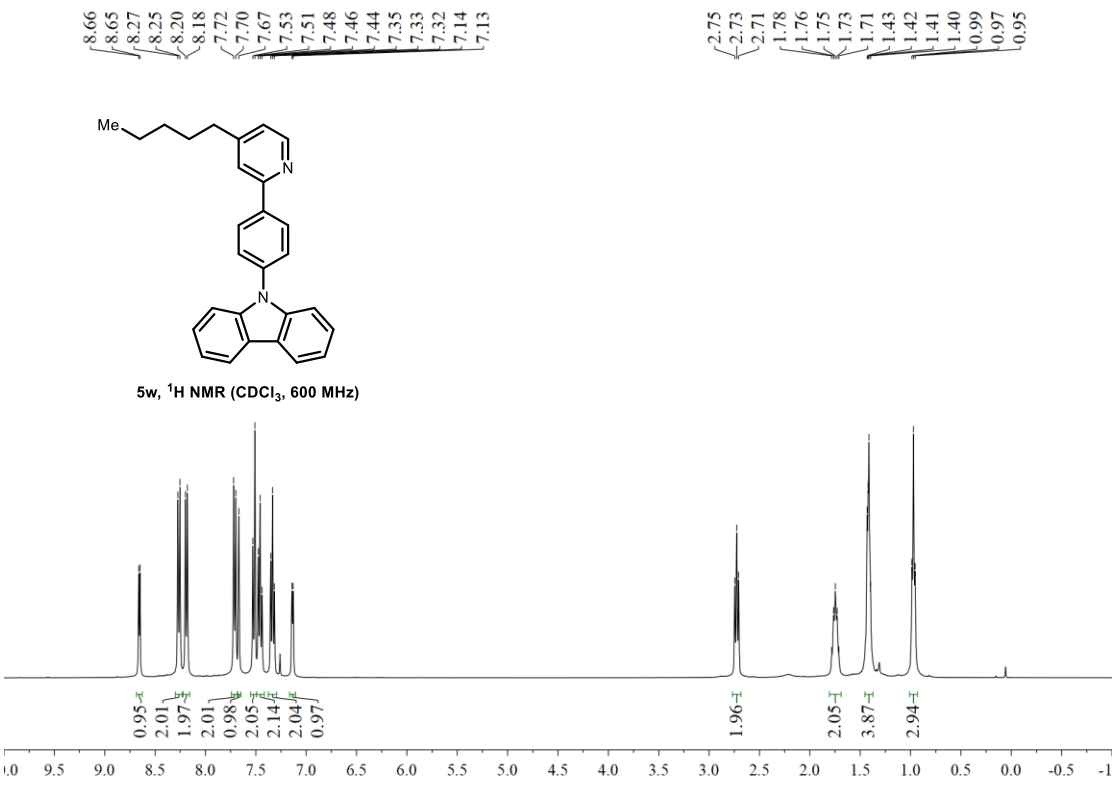


Figure S115. ^{1}H NMR of **5w** ($CDCl_3$, 600 MHz)

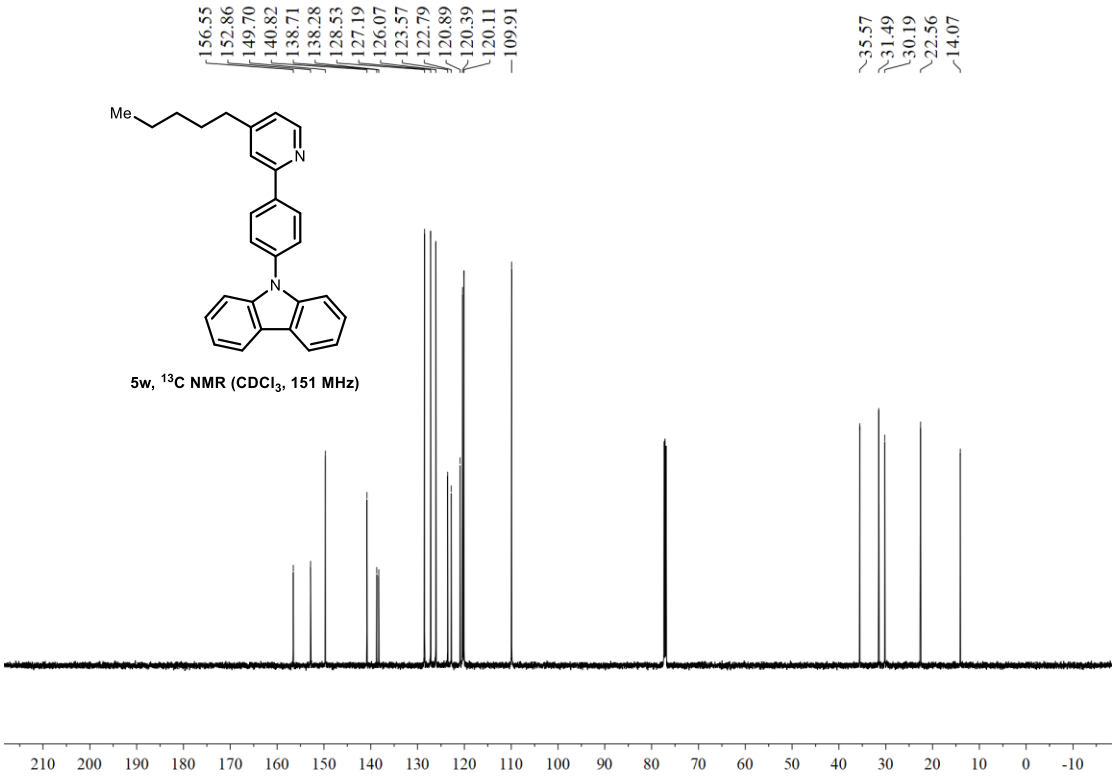


Figure S116. ^{13}C NMR of **5w** ($CDCl_3$, 151 MHz)

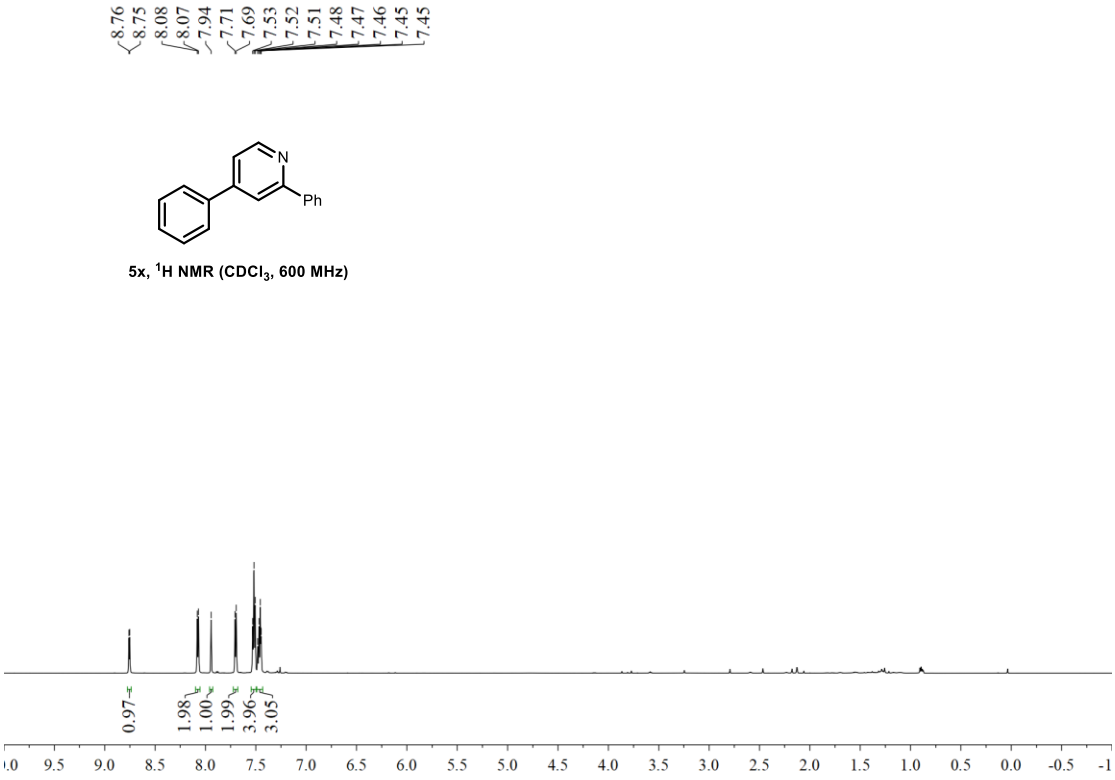


Figure S117. ^{1}H NMR of **5x** ($CDCl_3$, 600 MHz)

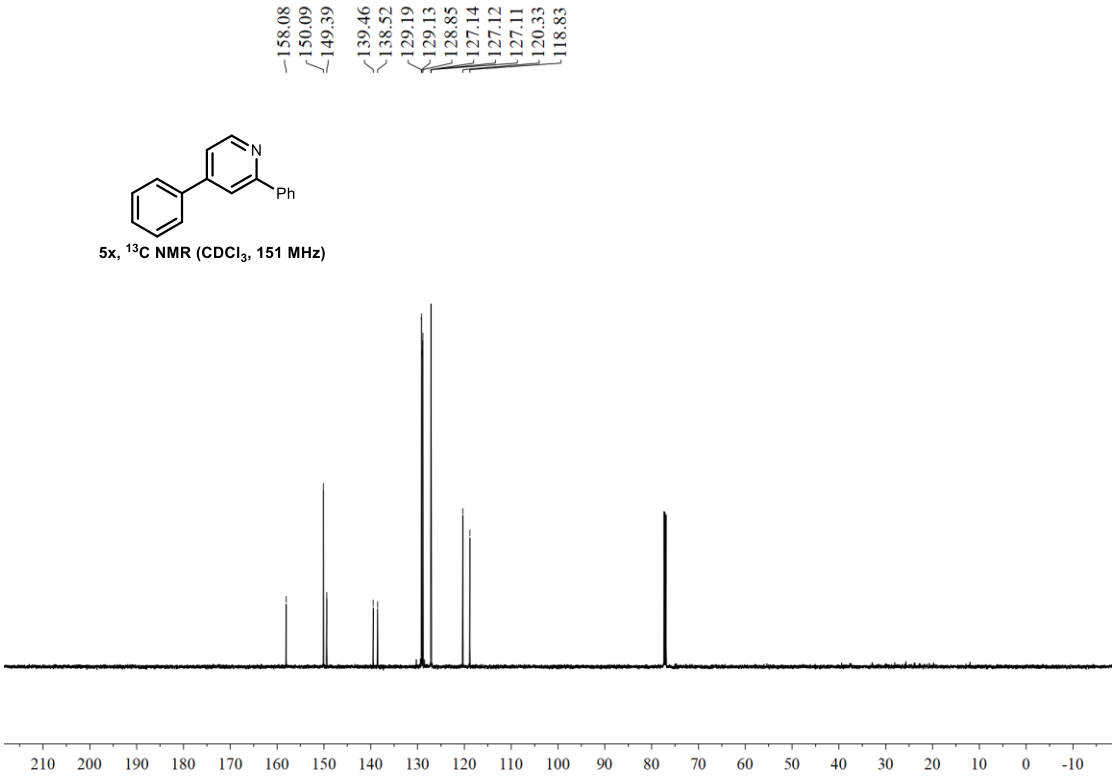


Figure S118. ^{13}C NMR of **5x** ($CDCl_3$, 151 MHz)

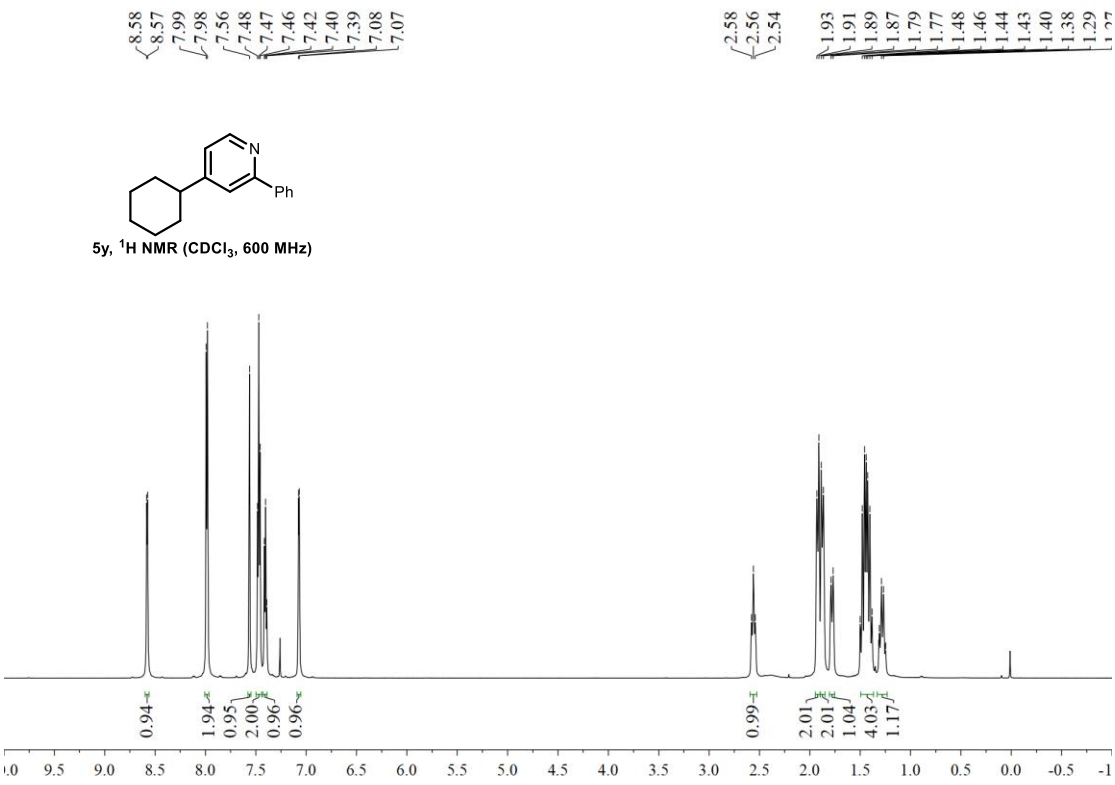


Figure S119. ^{1}H NMR of **5y** ($CDCl_3$, 600 MHz)

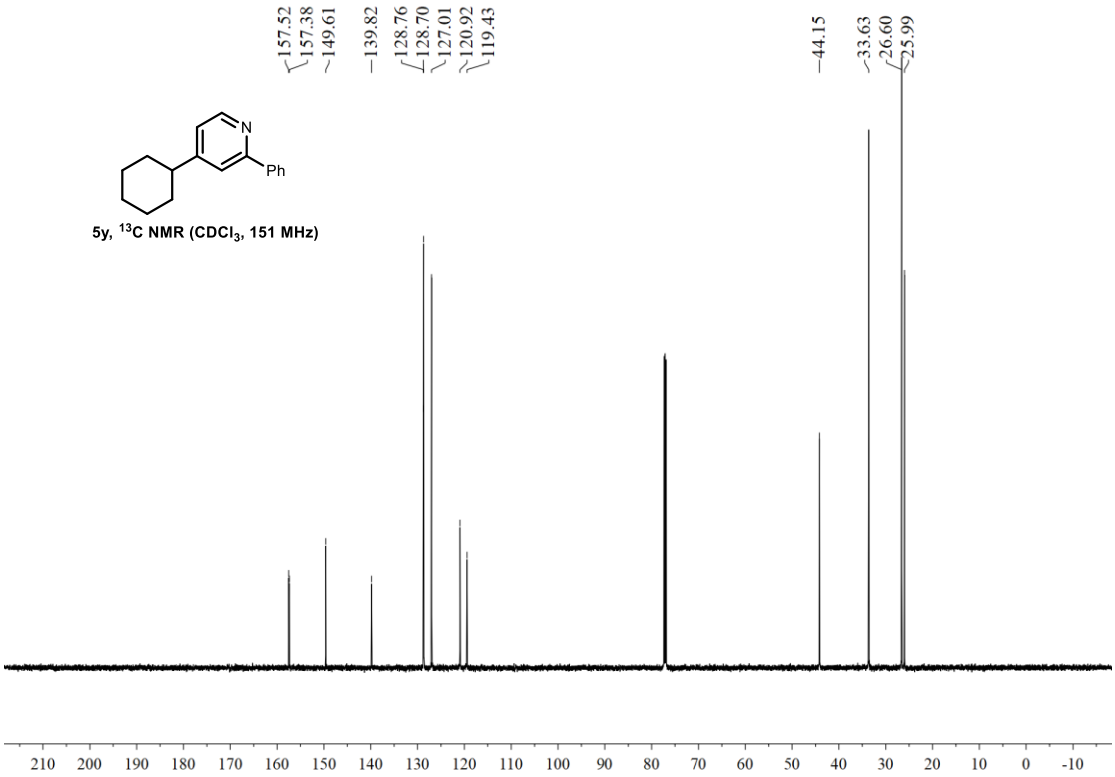
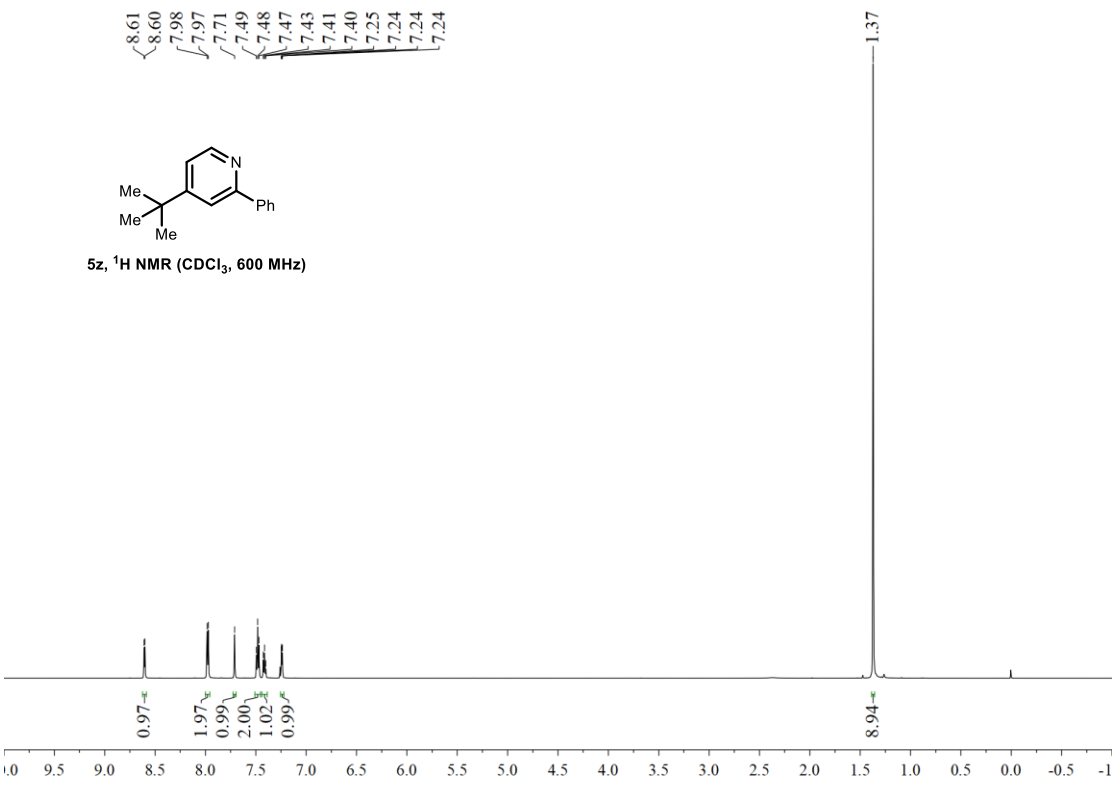
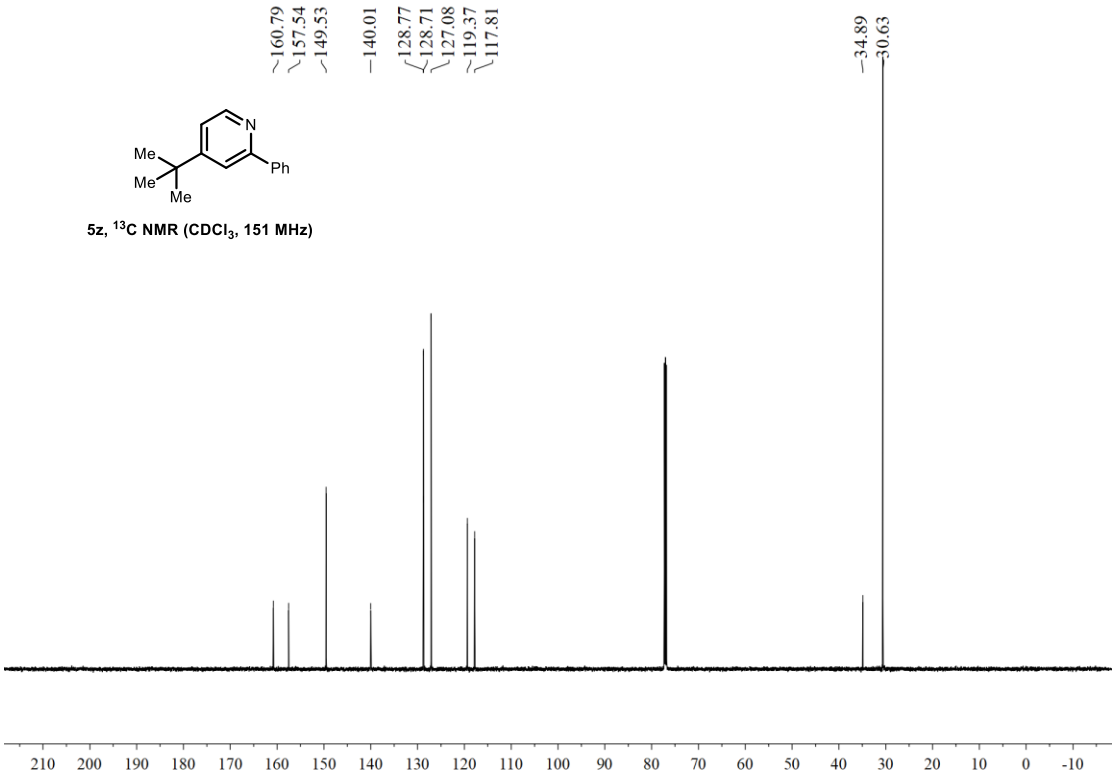


Figure S120. ^{13}C NMR of **5y** ($CDCl_3$, 151 MHz)



5z, ^{1}H NMR ($CDCl_3$, 600 MHz)

Figure S121. ^{1}H NMR of **5z** ($CDCl_3$, 600 MHz)



5z, ^{13}C NMR ($CDCl_3$, 151 MHz)

Figure S122. ^{13}C NMR of **5z** ($CDCl_3$, 151 MHz)

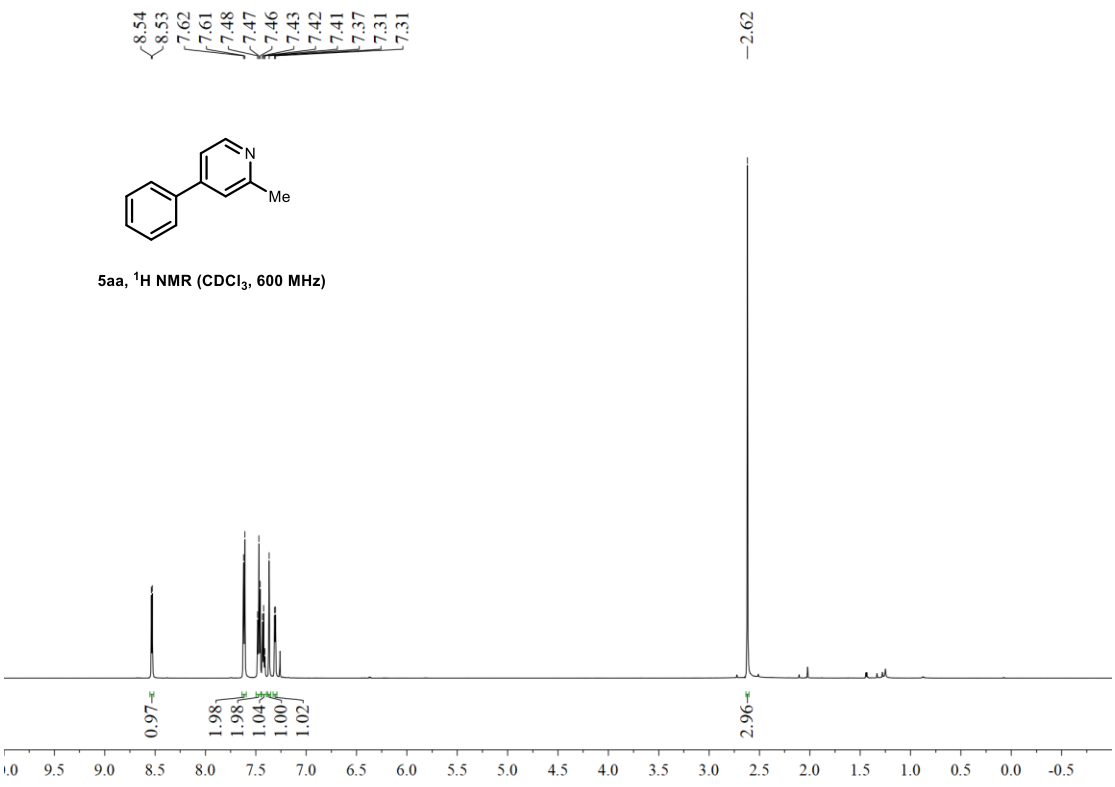


Figure S123. ^{1}H NMR of **5aa** ($CDCl_3$, 600 MHz)

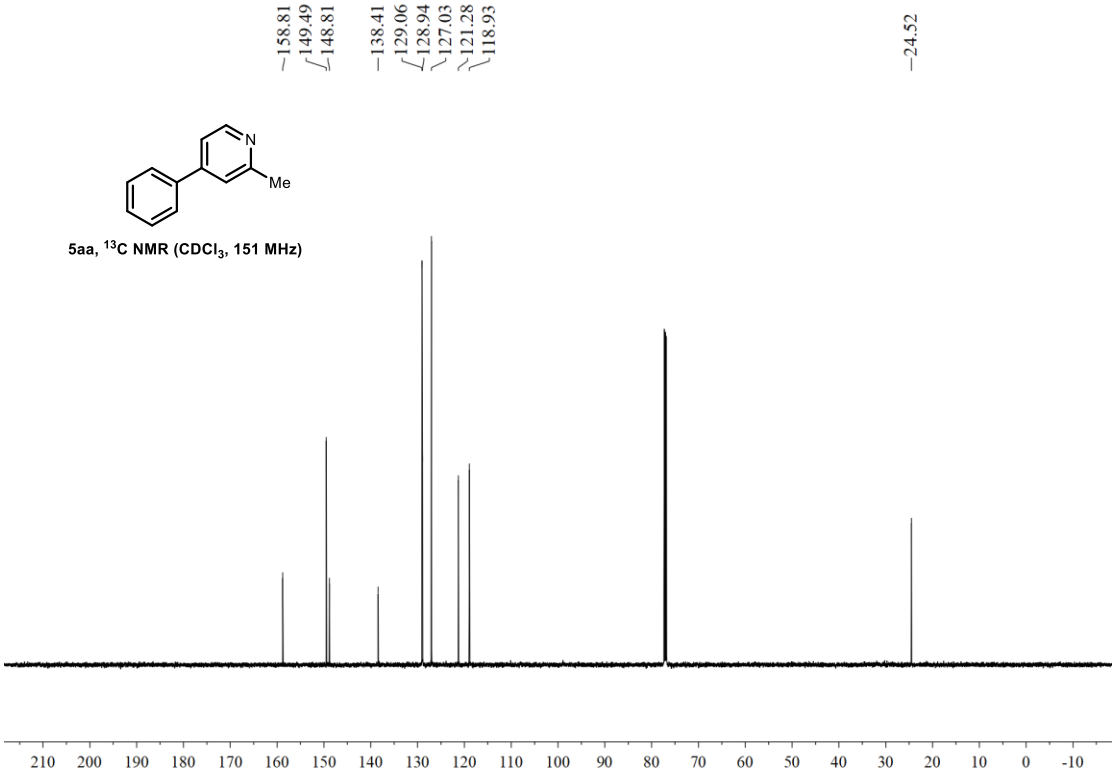


Figure S124. ^{13}C NMR of **5aa** ($CDCl_3$, 151 MHz)

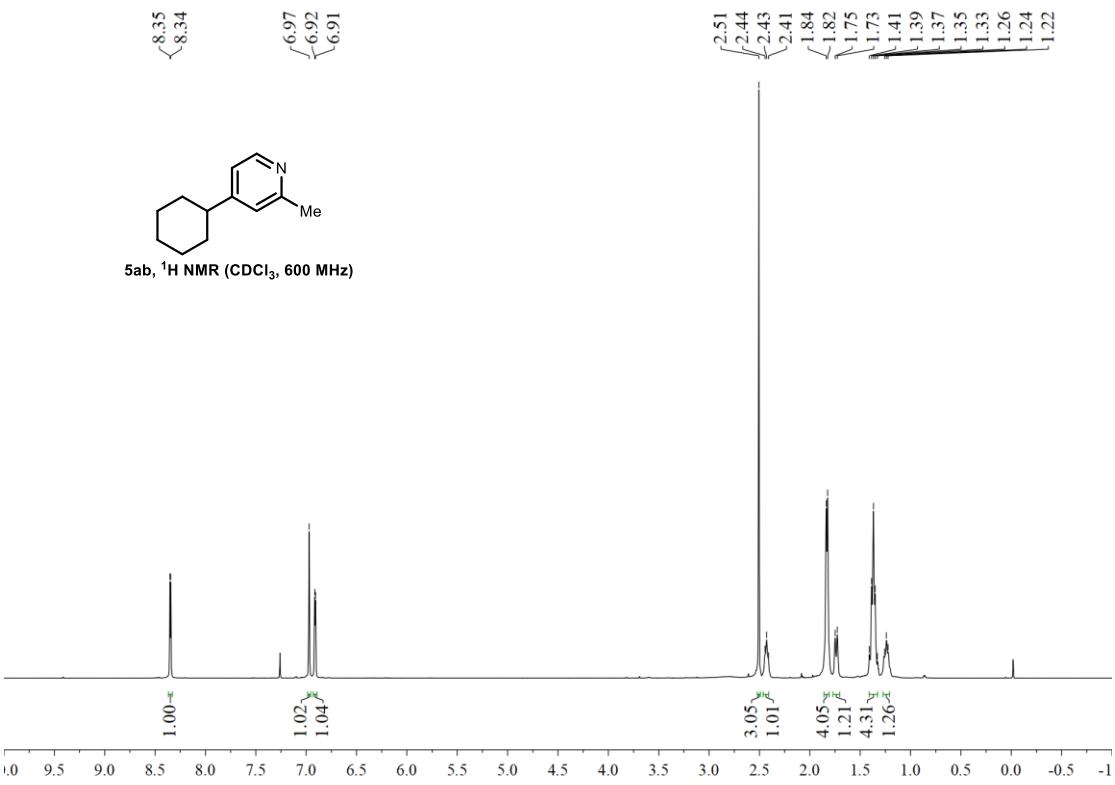


Figure S125. ^{1}H NMR of **5ab** (CDCl$_3$, 600 MHz)

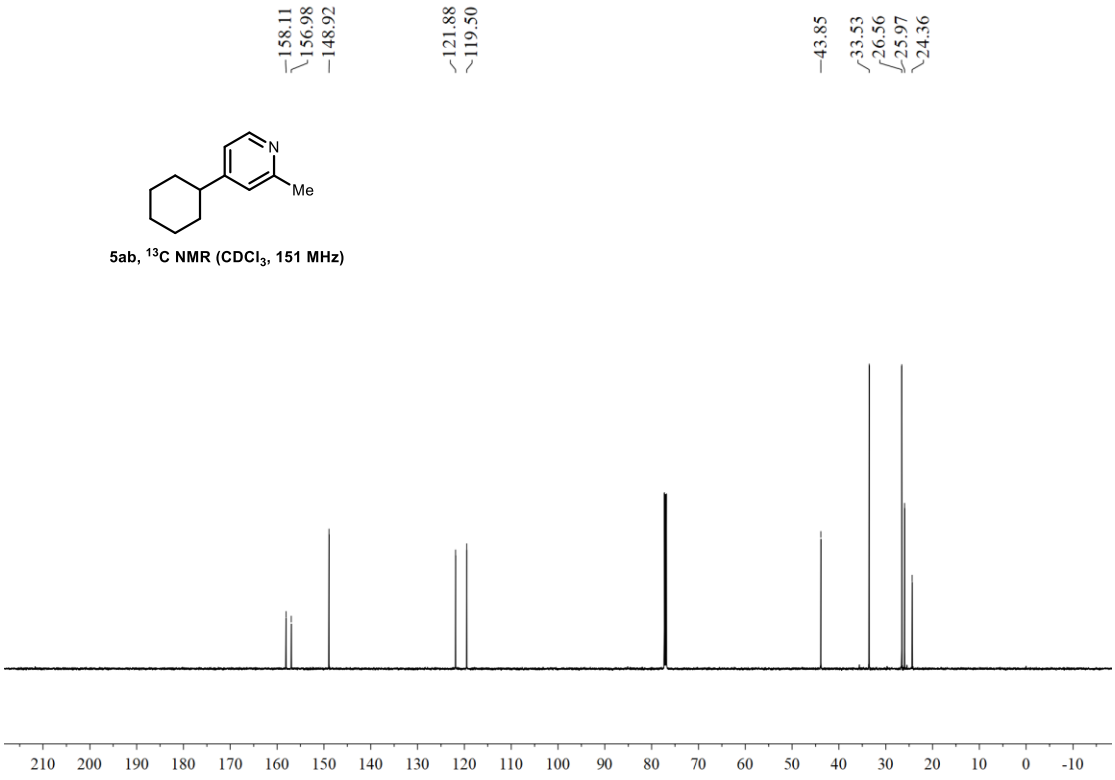


Figure S126. ^{13}C NMR of **5ab** (CDCl$_3$, 151 MHz)

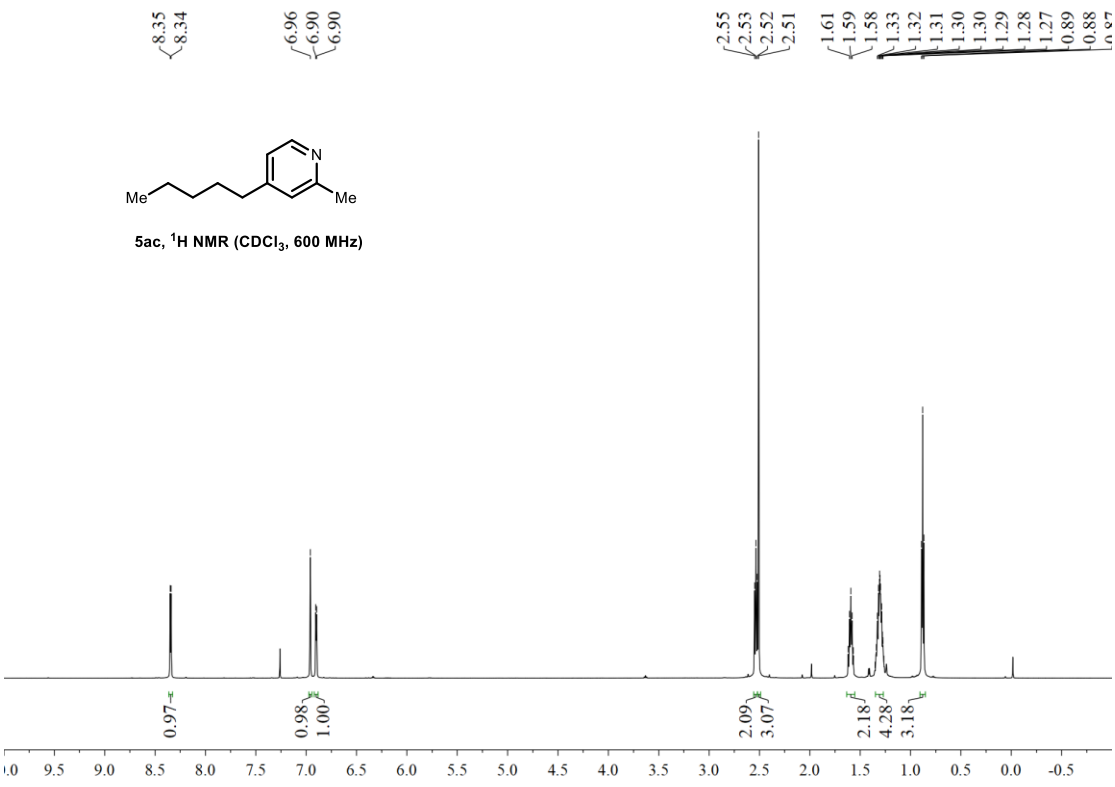


Figure S127. ^{1}H NMR of **5ac** ($CDCl_3$, 600 MHz)

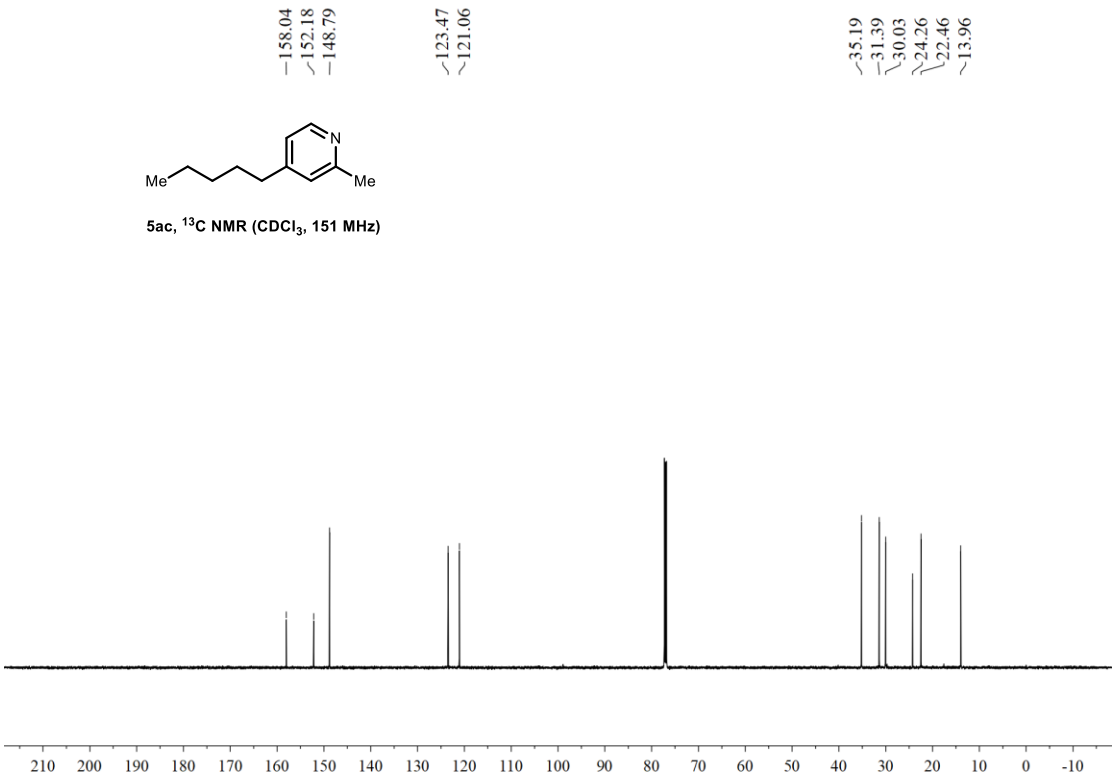


Figure S128. ^{13}C NMR of **5ac** ($CDCl_3$, 151 MHz)

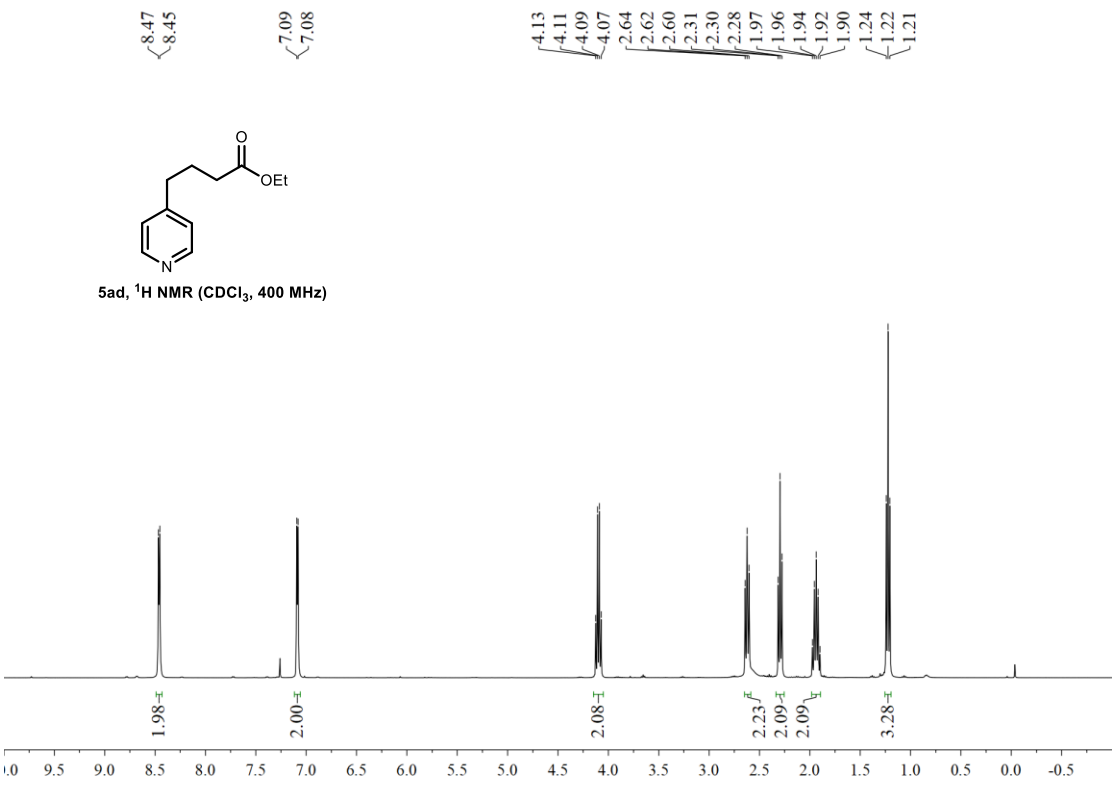


Figure S129. ^{1}H NMR of **5ad** ($CDCl_3$, 400 MHz)

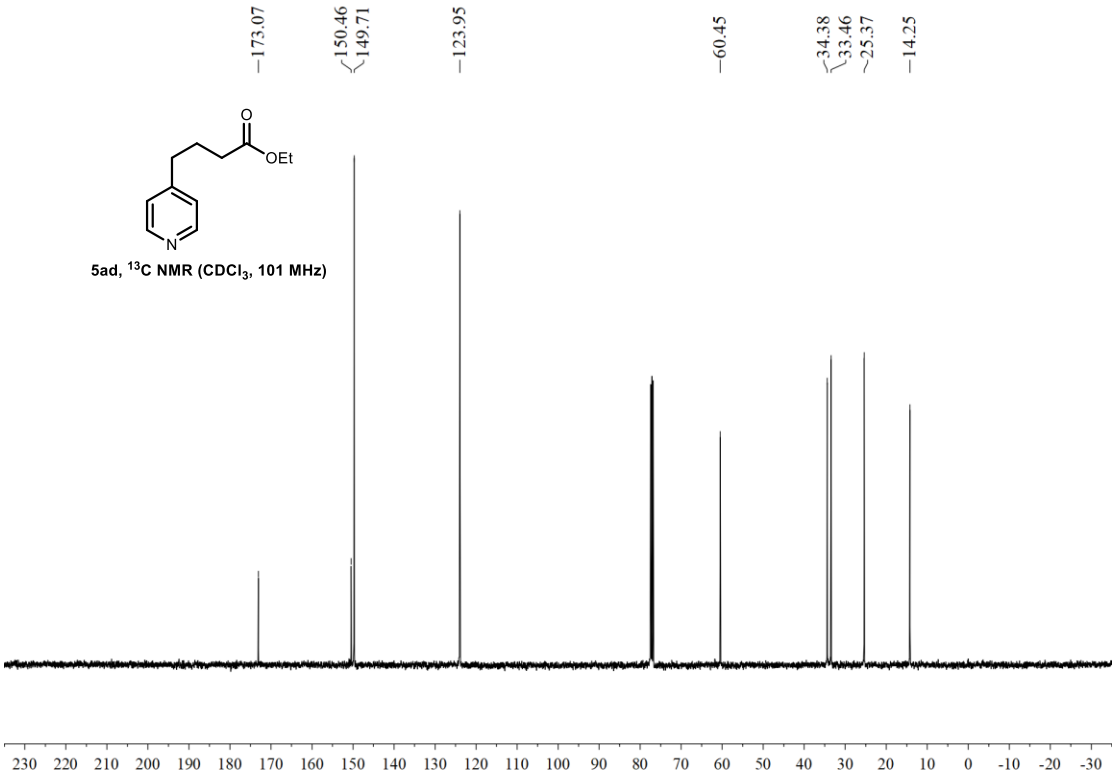


Figure S130. ^{13}C NMR of **5ad** ($CDCl_3$, 101 MHz)

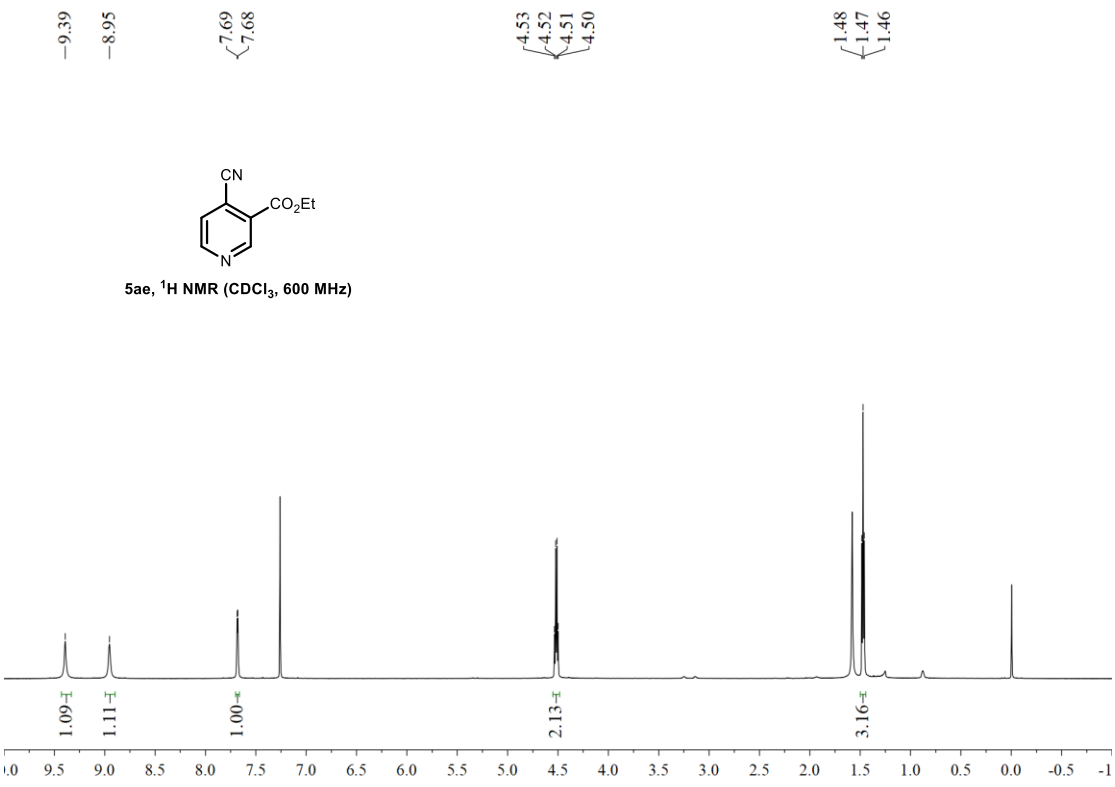


Figure S131. ^{1}H NMR of **5ae** ($CDCl_3$, 600 MHz)

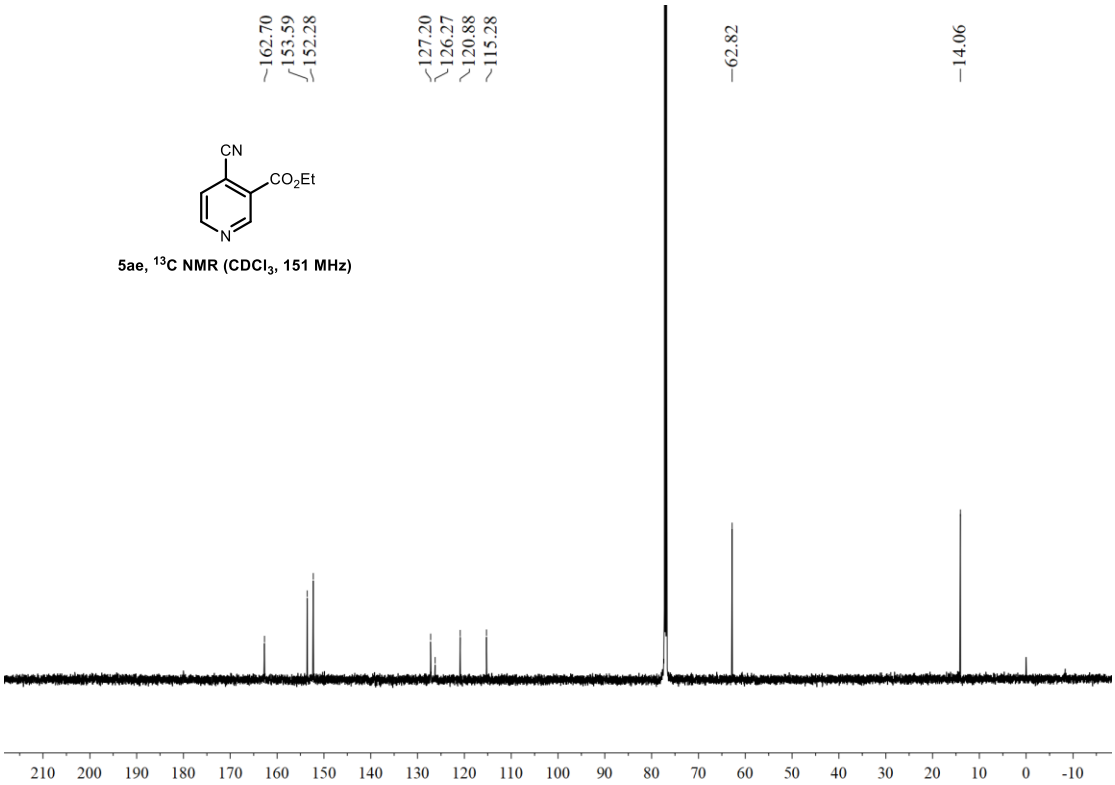


Figure S132. ^{13}C NMR of **5ae** ($CDCl_3$, 151 MHz)

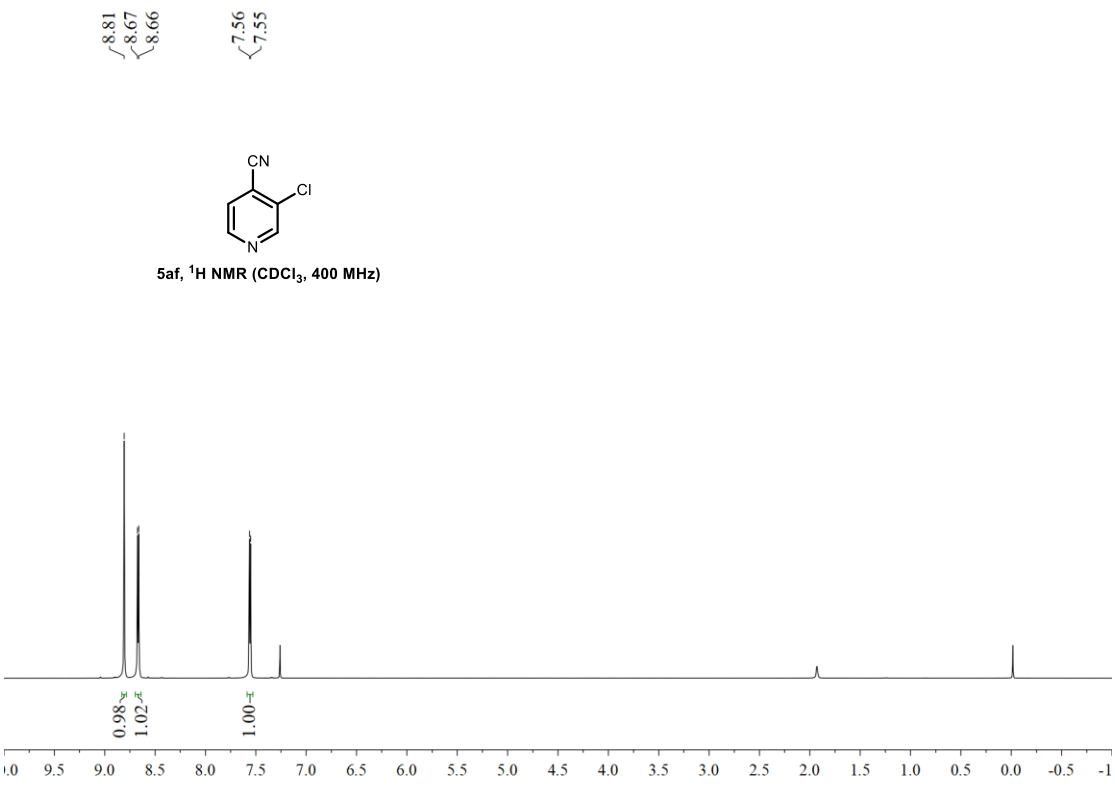


Figure S133. ^{1}H NMR of **5af** ($CDCl_3$, 400 MHz)

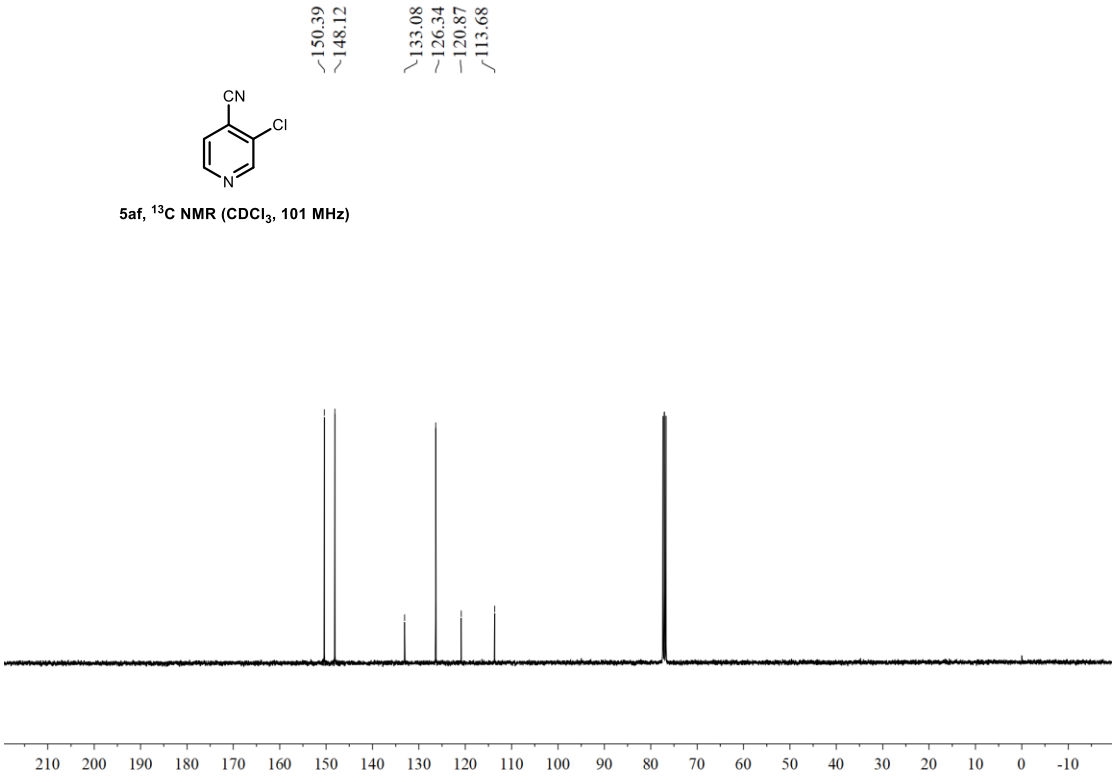


Figure S134. ^{13}C NMR of **5af** ($CDCl_3$, 101 MHz)

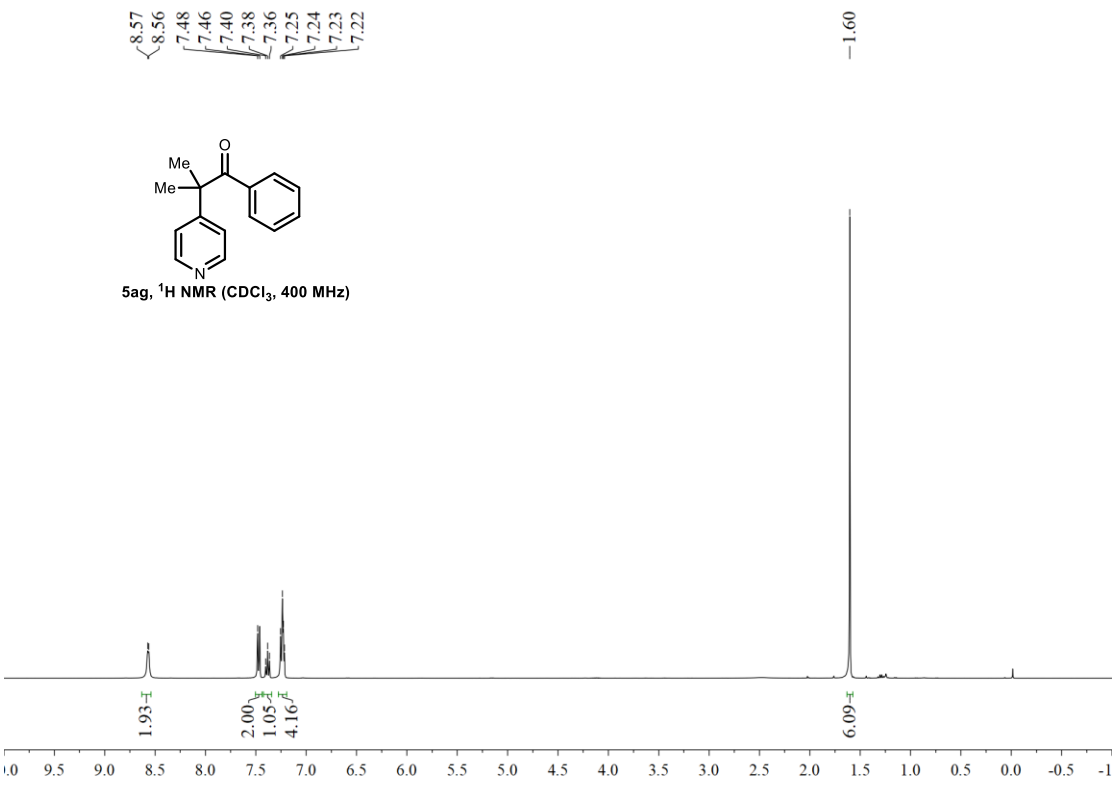


Figure S135. ^{1}H NMR of **5ag** ($CDCl_3$, 400 MHz)

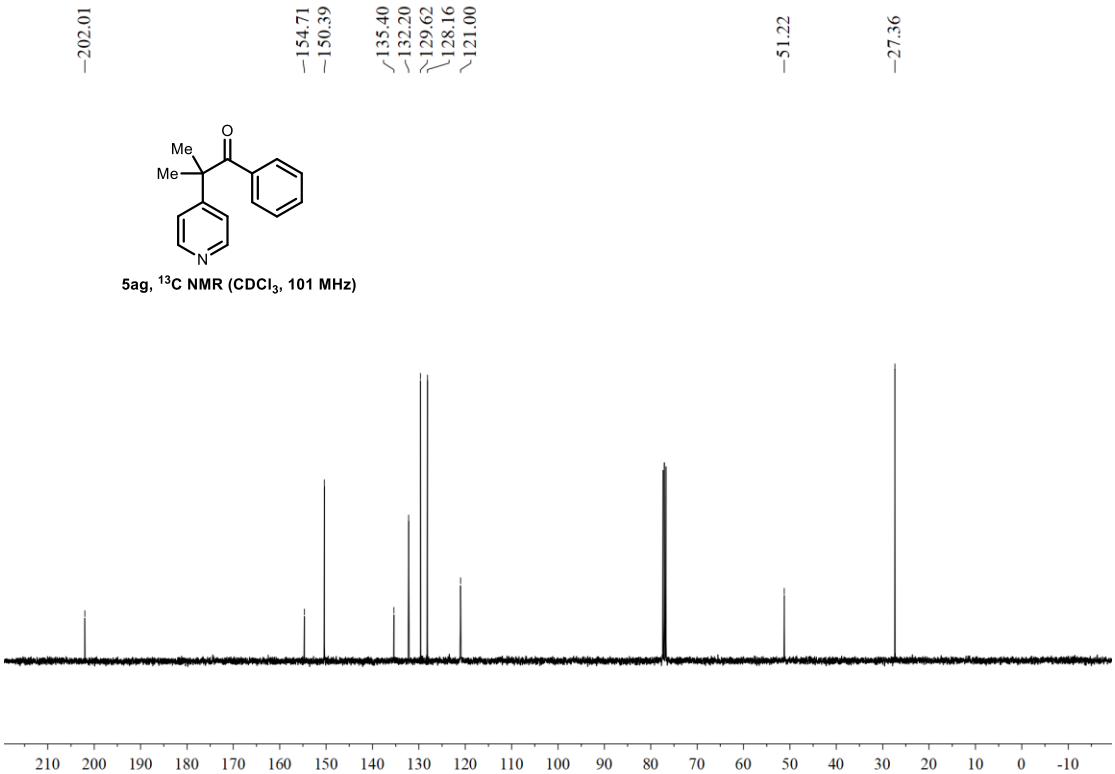


Figure S136. ^{13}C NMR of **5ag** ($CDCl_3$, 101 MHz)

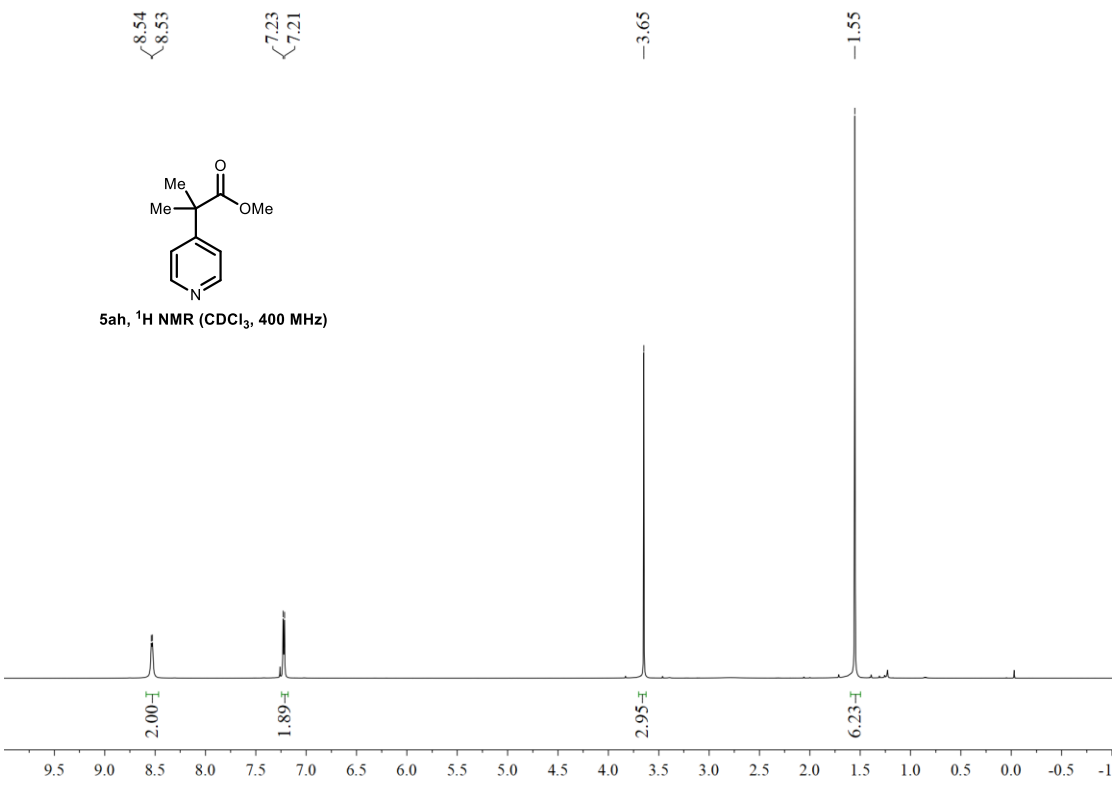


Figure S137. ^{1}H NMR of **5ah** ($CDCl_3$, 400 MHz)

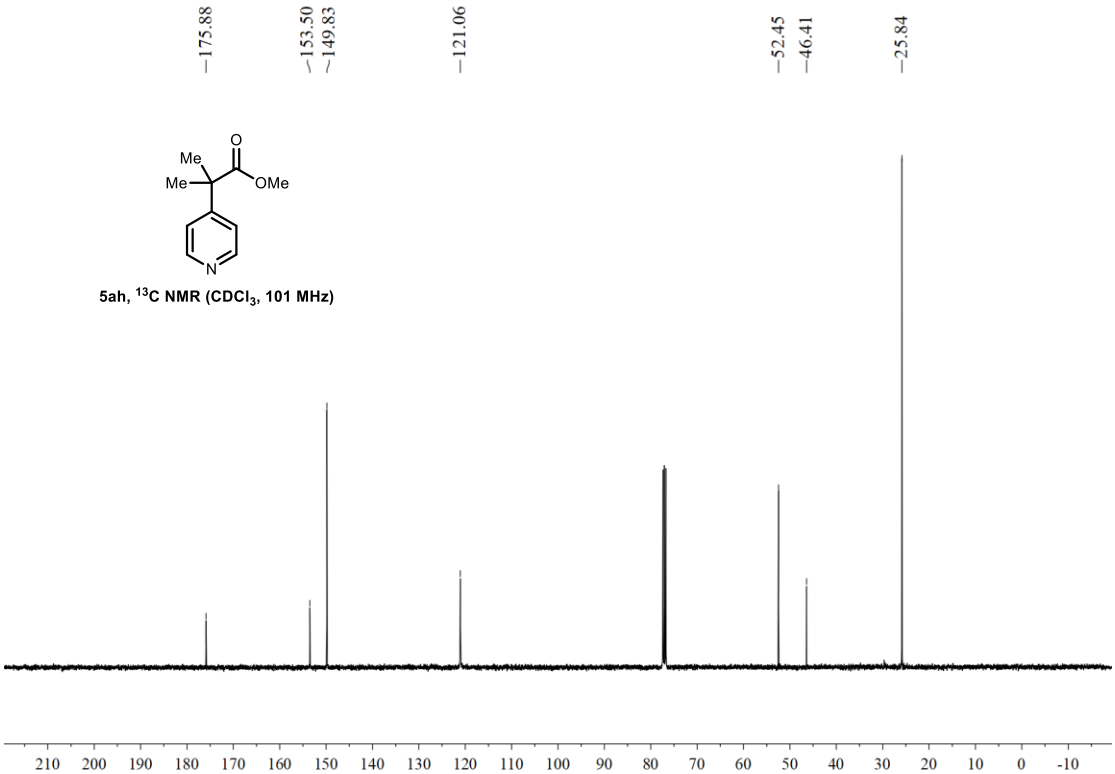


Figure S138. ^{13}C NMR of **5ah** ($CDCl_3$, 101 MHz)

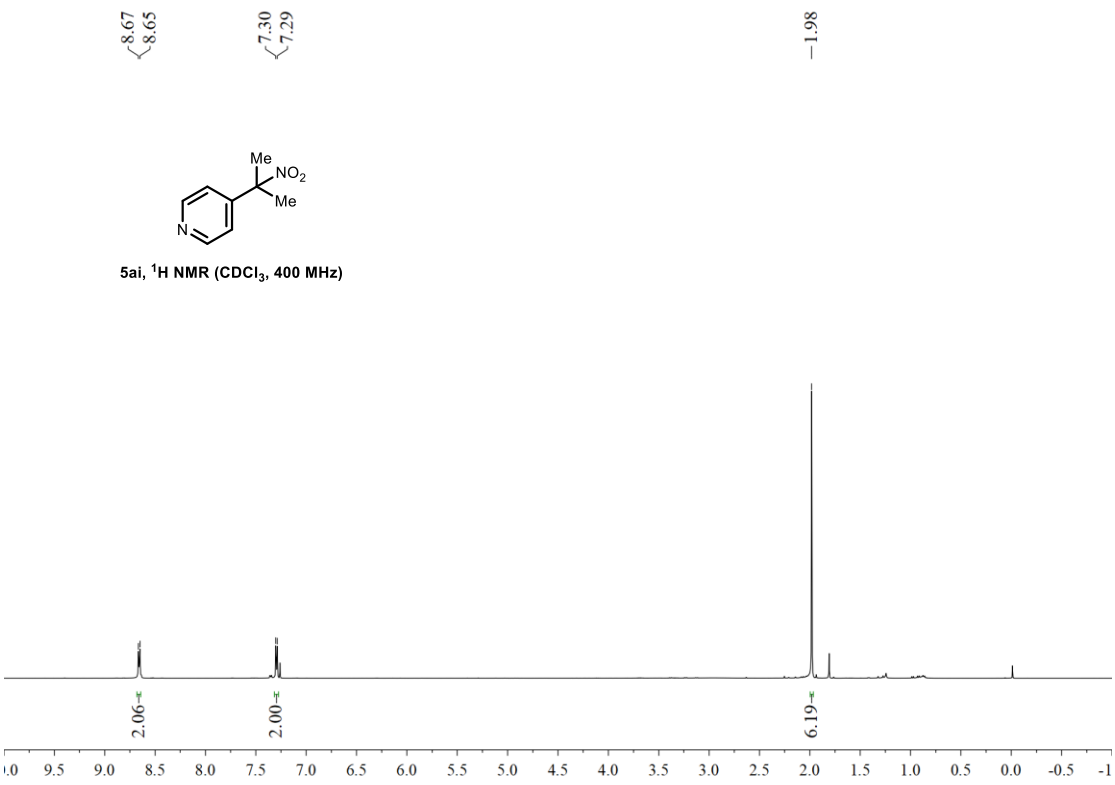


Figure S139. ^{1}H NMR of **5ai** ($CDCl_3$, 400 MHz)

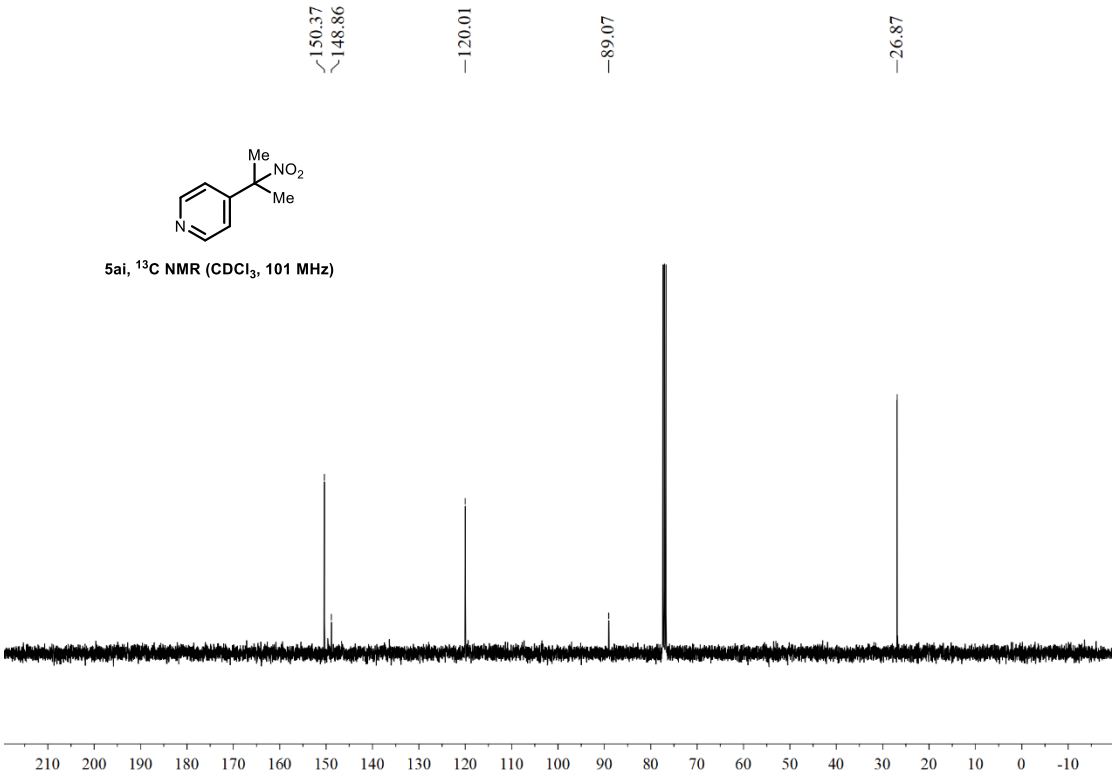


Figure S140. ^{13}C NMR of **5ai** ($CDCl_3$, 101 MHz)

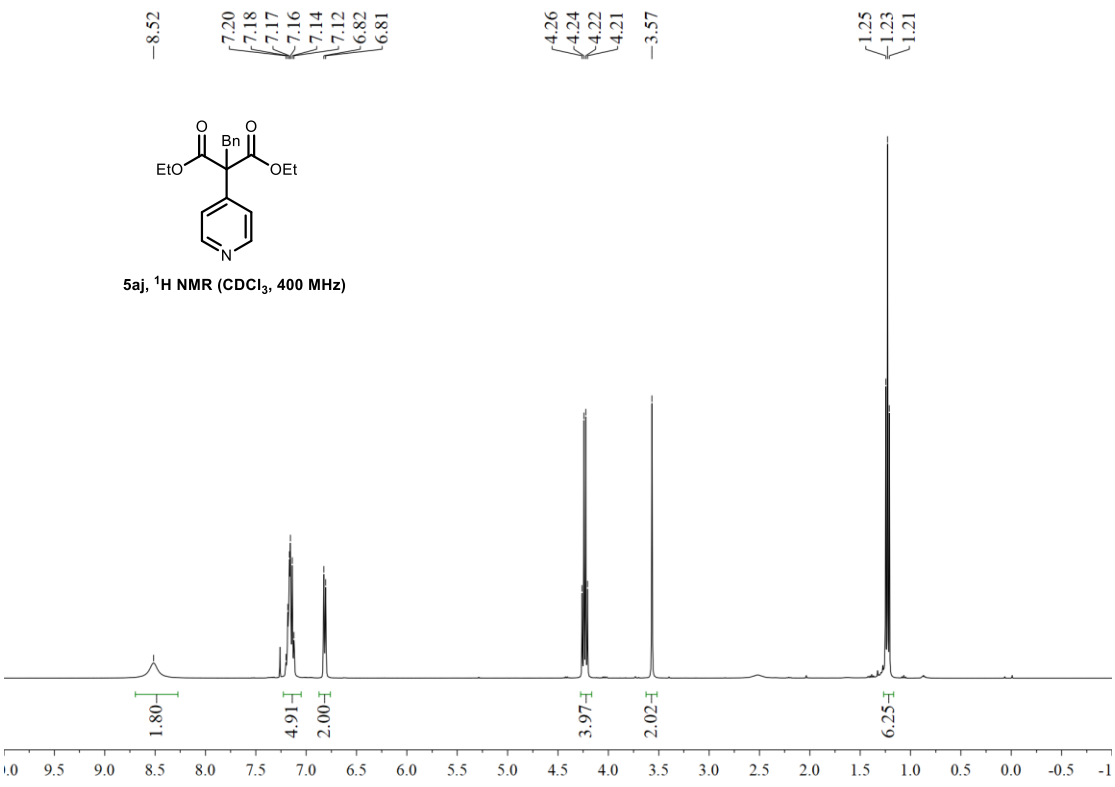


Figure S141. ^{1}H NMR of **5aj** ($CDCl_3$, 400 MHz)

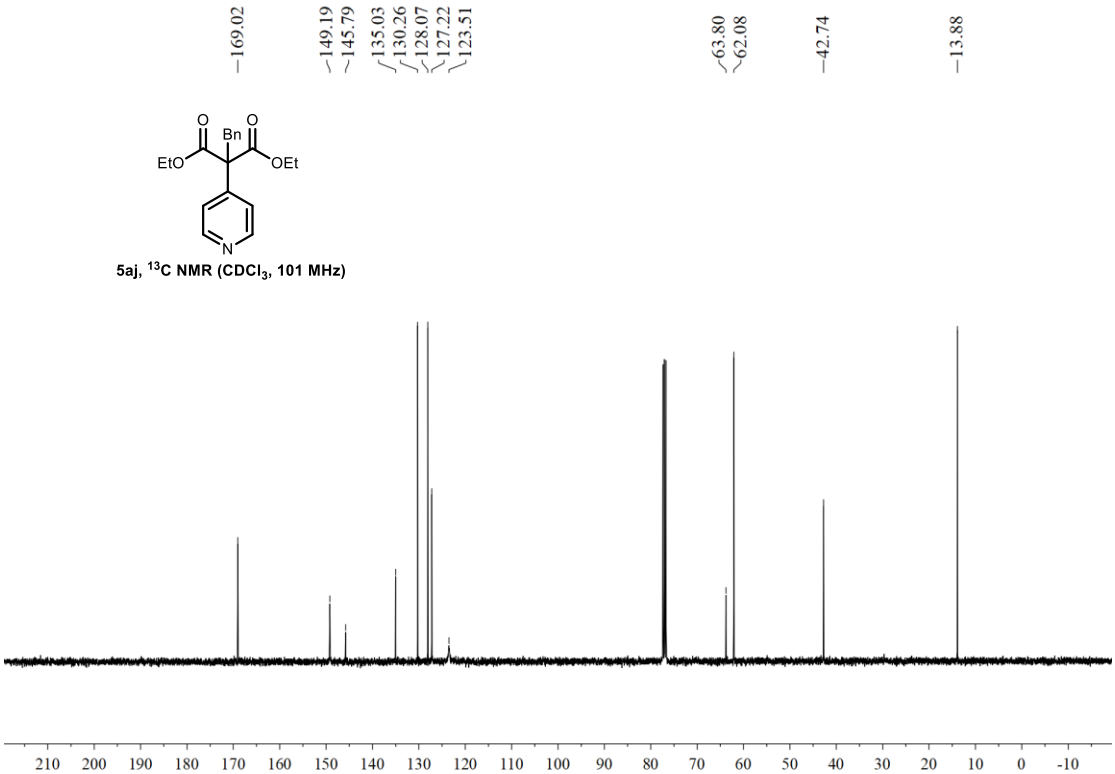


Figure S142. ^{13}C NMR of **5aj** ($CDCl_3$, 101 MHz)

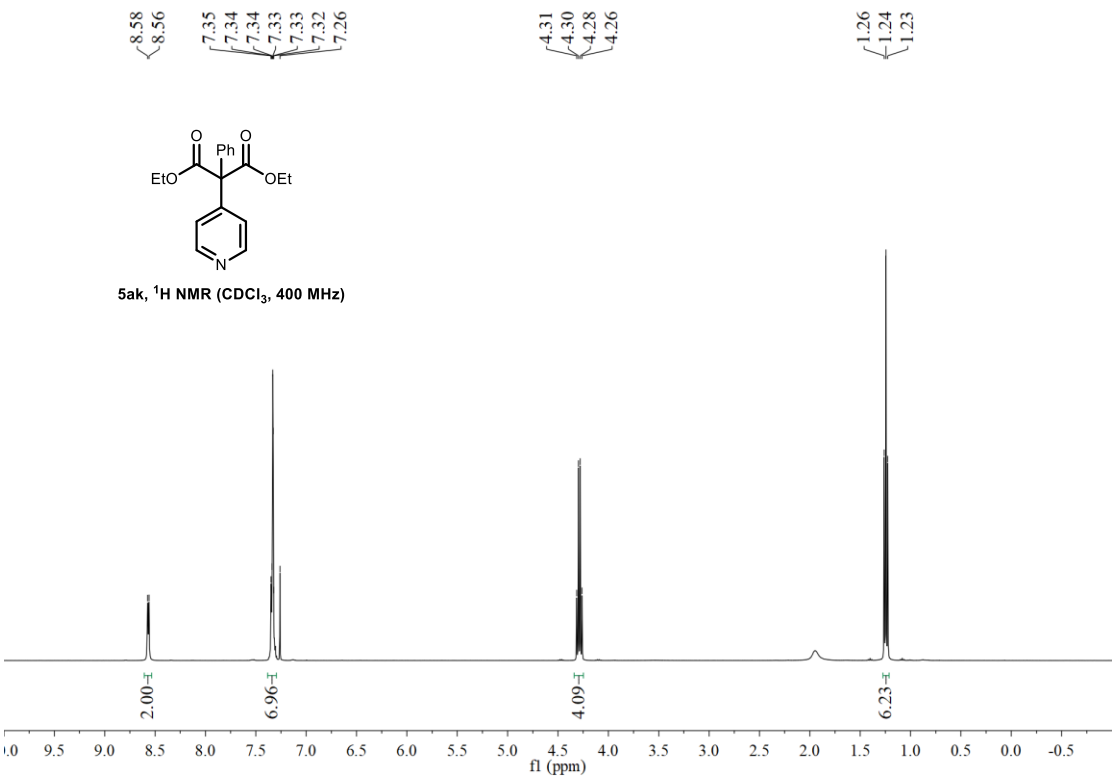


Figure S143. ^{1}H NMR of **5ak** ($CDCl_3$, 400 MHz)

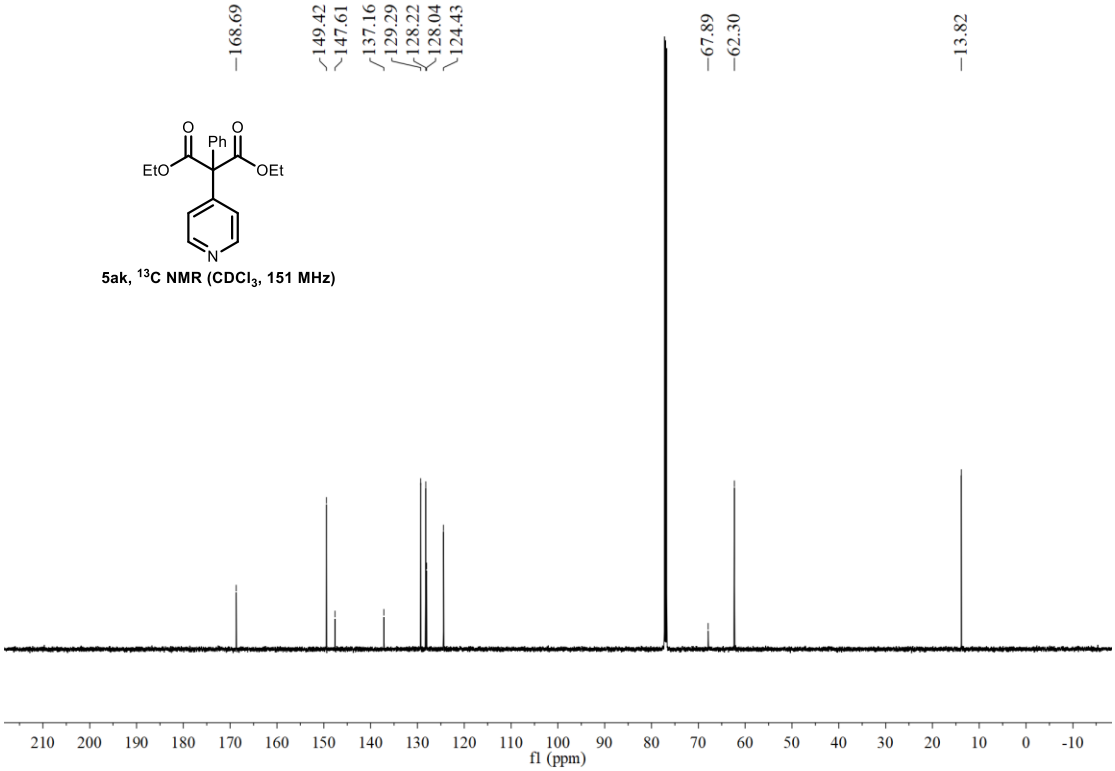


Figure S144. ^{13}C NMR of **5ak** ($CDCl_3$, 151 MHz)

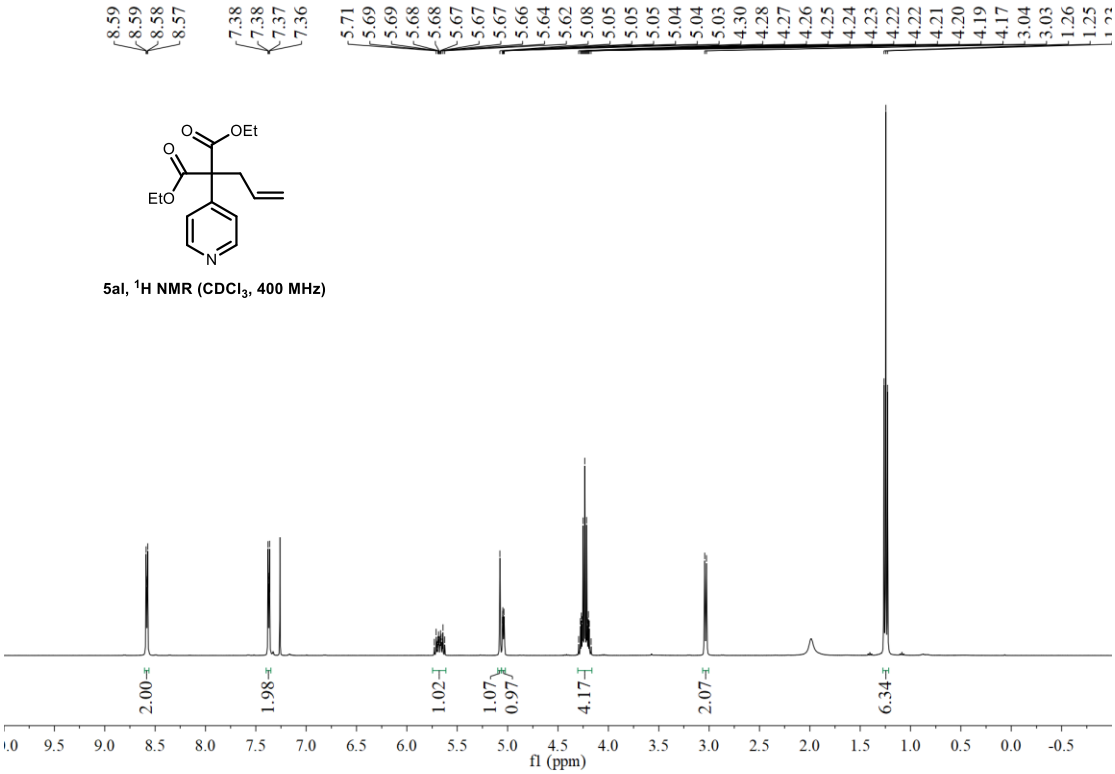


Figure S145. ^{1}H NMR of **5al** ($CDCl_3$, 400 MHz)

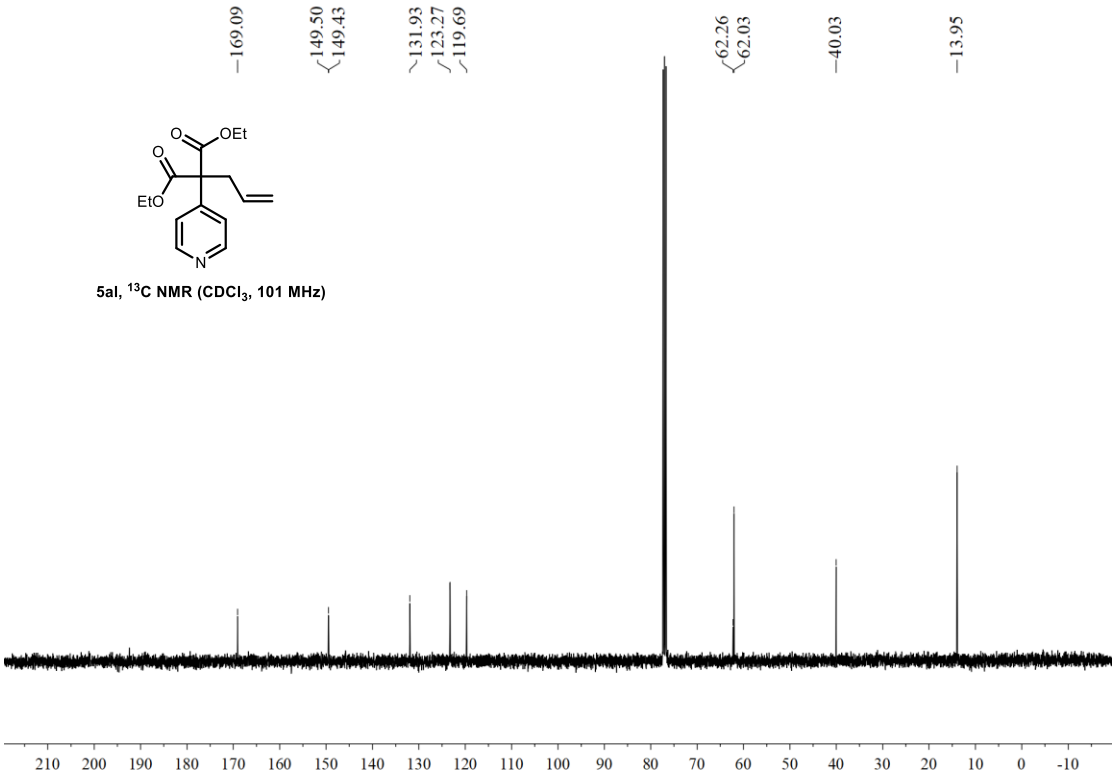


Figure S146. ^{13}C NMR of **5al** ($CDCl_3$, 101 MHz)

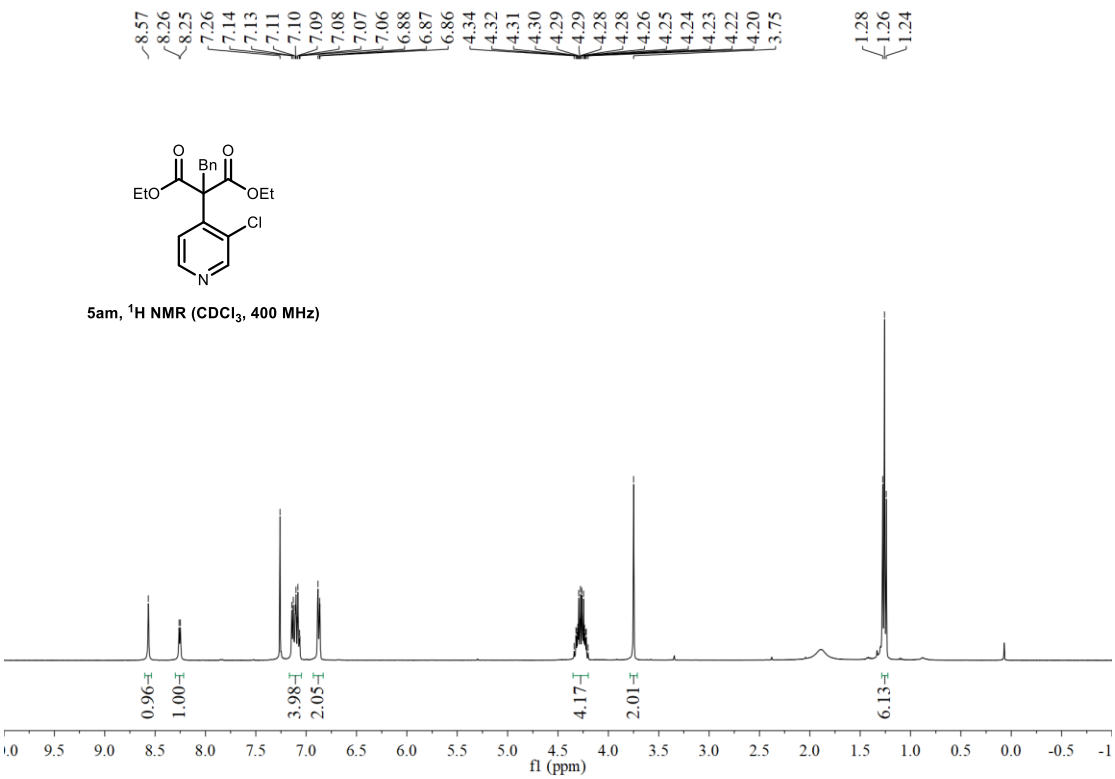


Figure S147. ^{1}H NMR of **5am** ($CDCl_3$, 400 MHz)

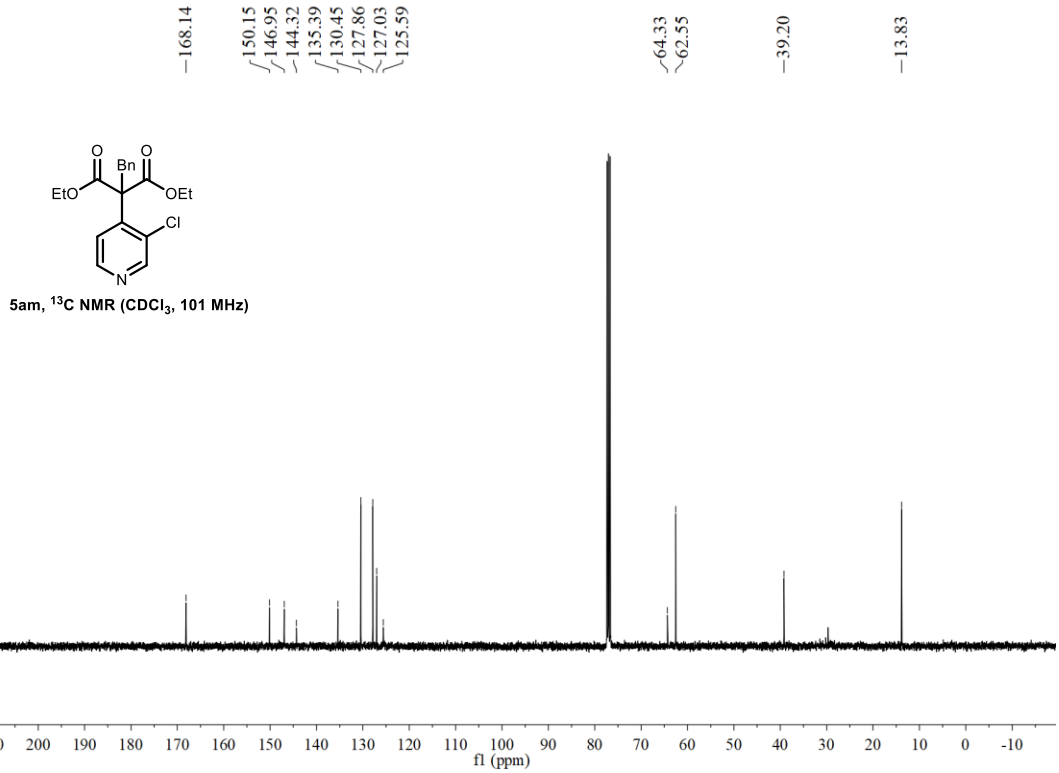


Figure S148. ^{13}C NMR of **5am** ($CDCl_3$, 101 MHz)

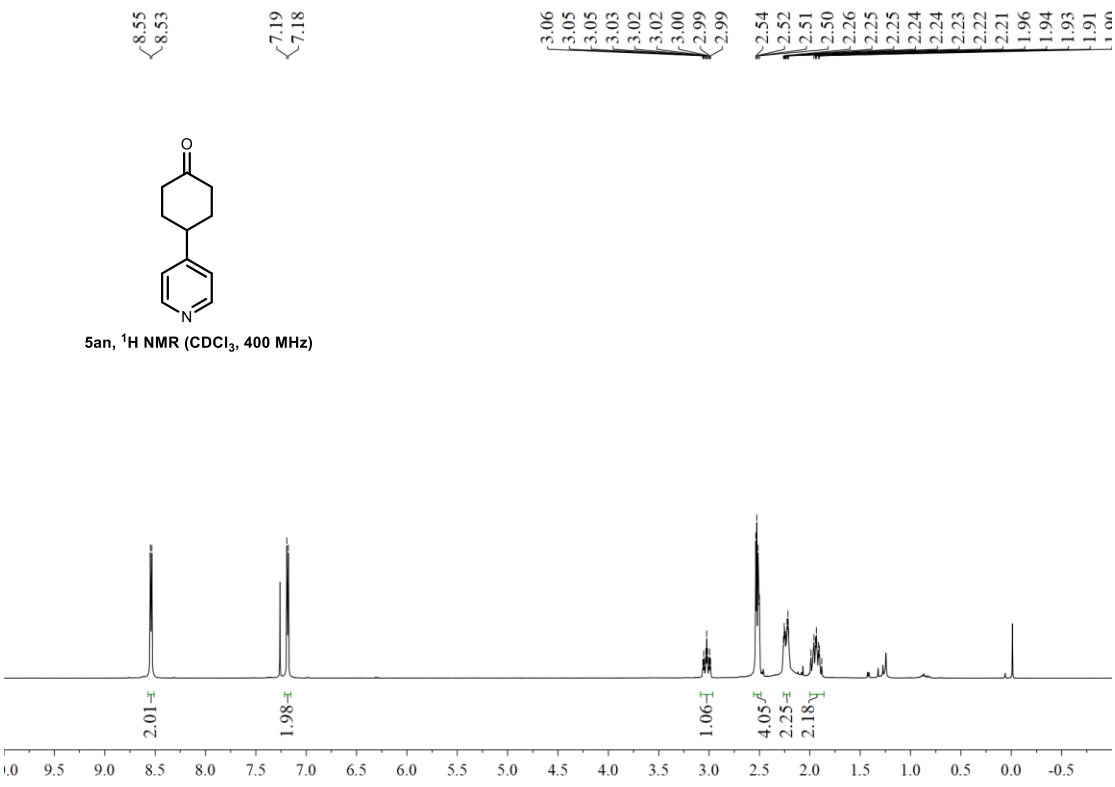


Figure S149. ^{1}H NMR of **5an** ($CDCl_3$, 400 MHz)

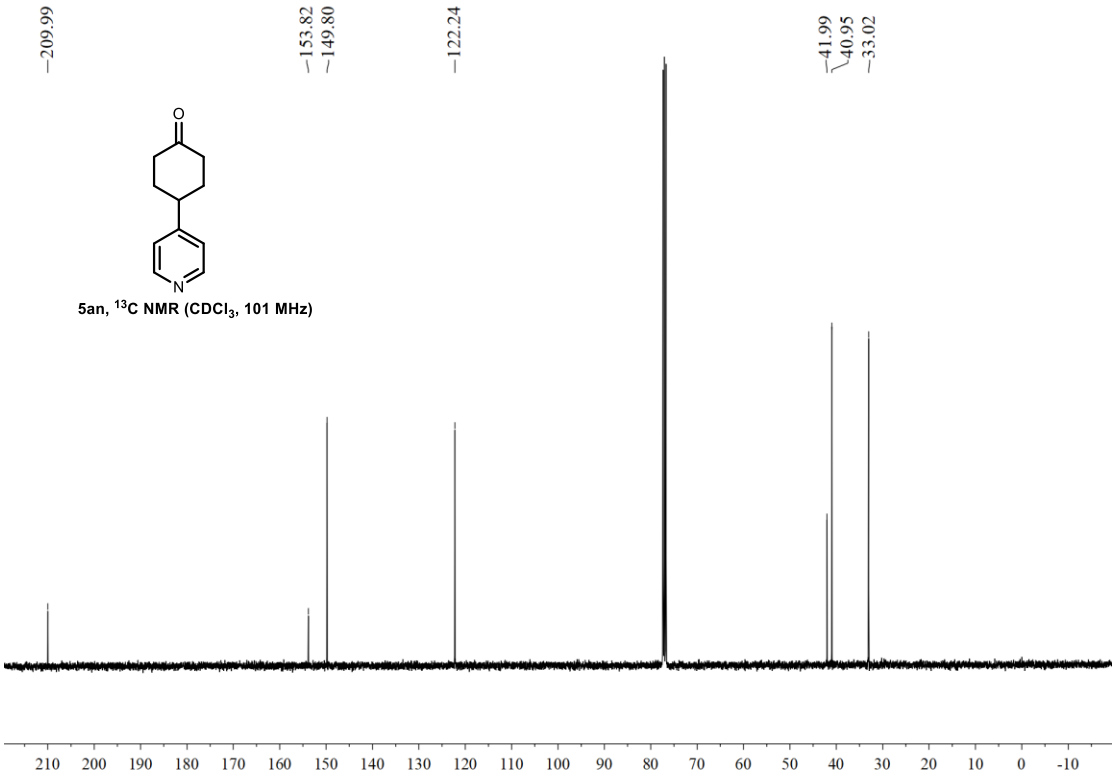


Figure S150. ^{13}C NMR of **5an** ($CDCl_3$, 101 MHz)

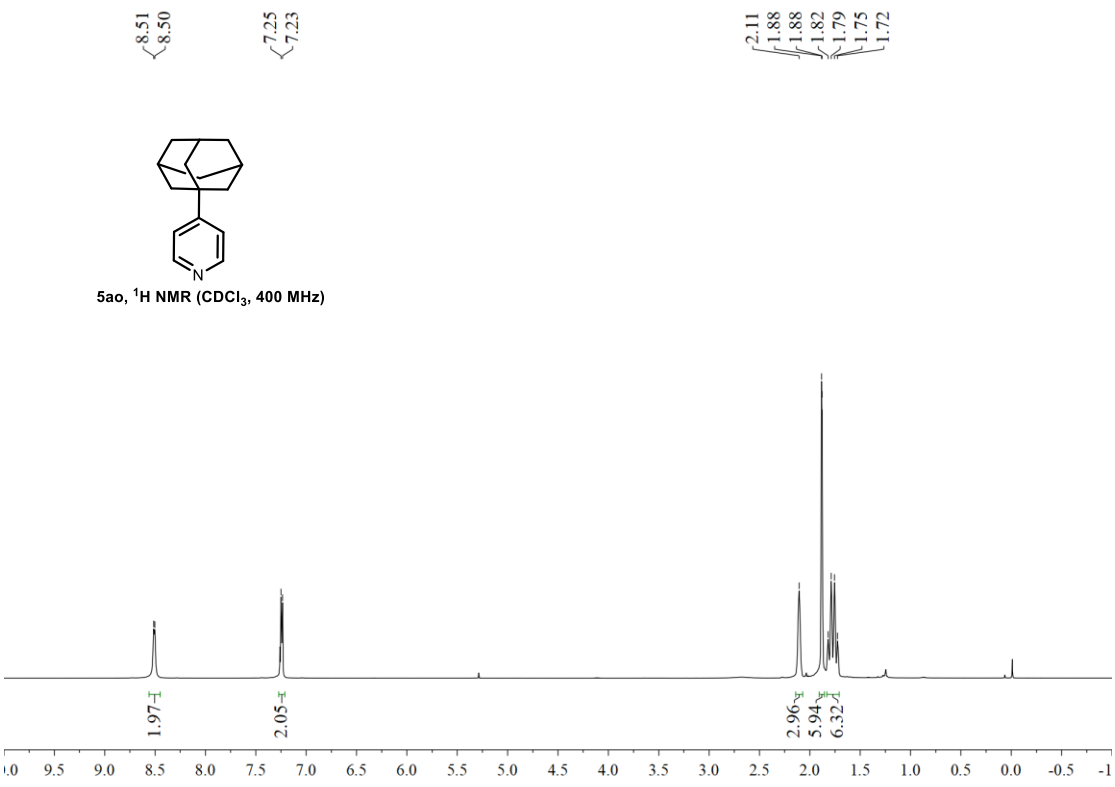


Figure S151. ^{1}H NMR of **5ao** ($CDCl_3$, 400 MHz)

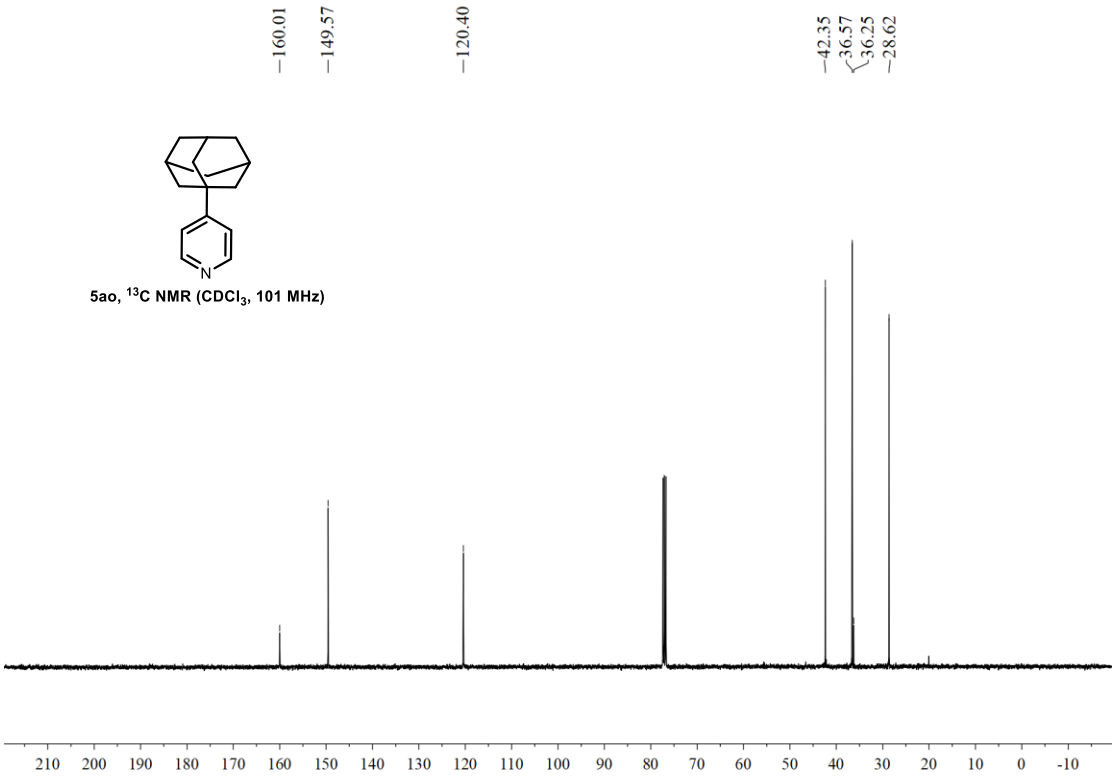


Figure S152. ^{13}C NMR of **5ao** ($CDCl_3$, 101 MHz)

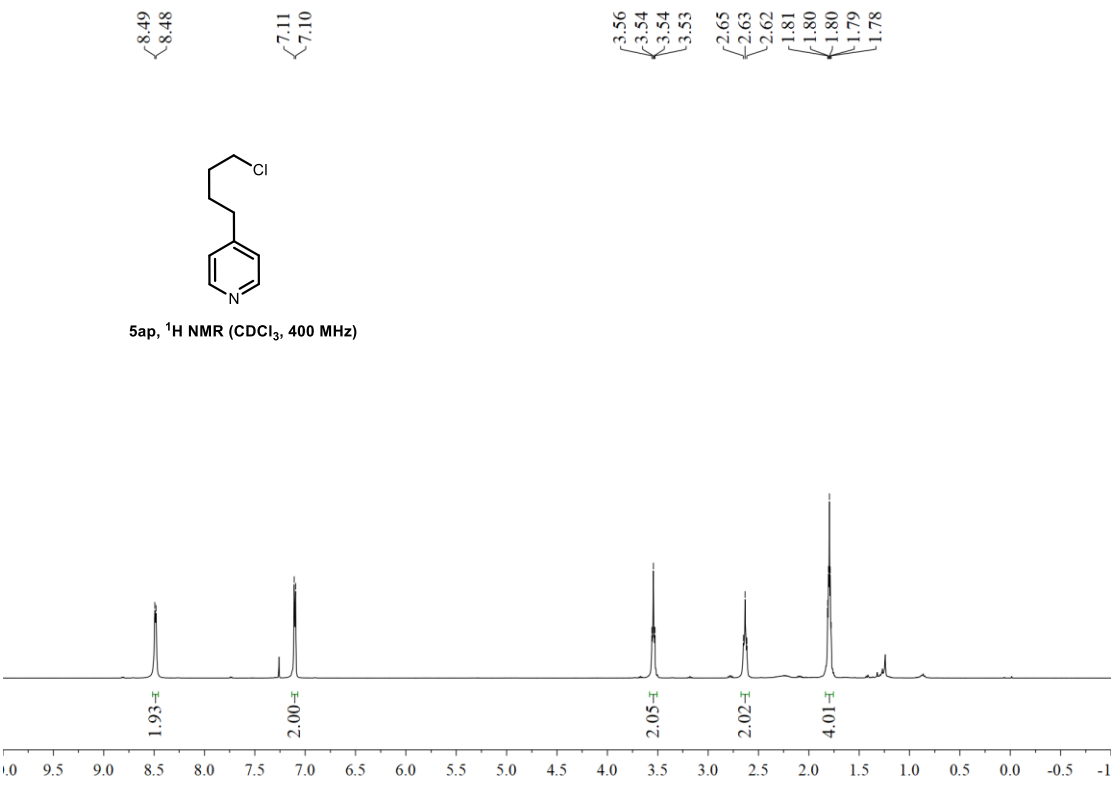


Figure S153. ^{1}H NMR of **5ap** ($CDCl_3$, 400 MHz)

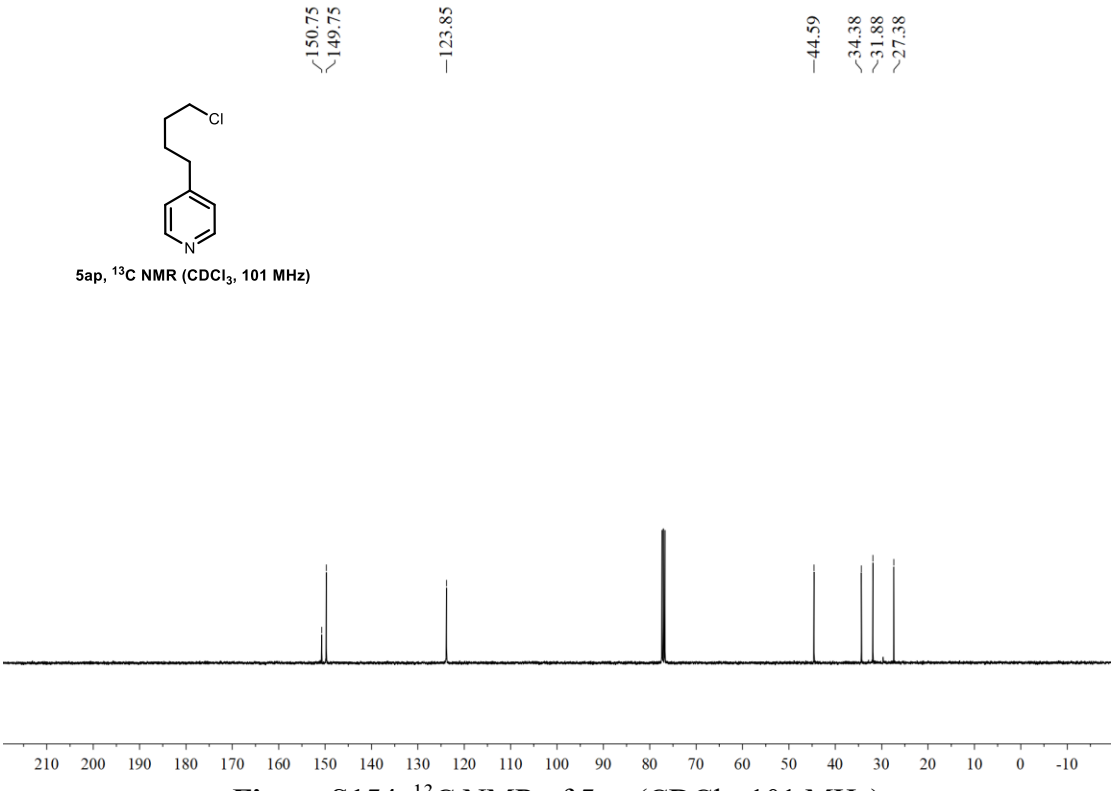


Figure S154. ^{13}C NMR of **5ap** ($CDCl_3$, 101 MHz)

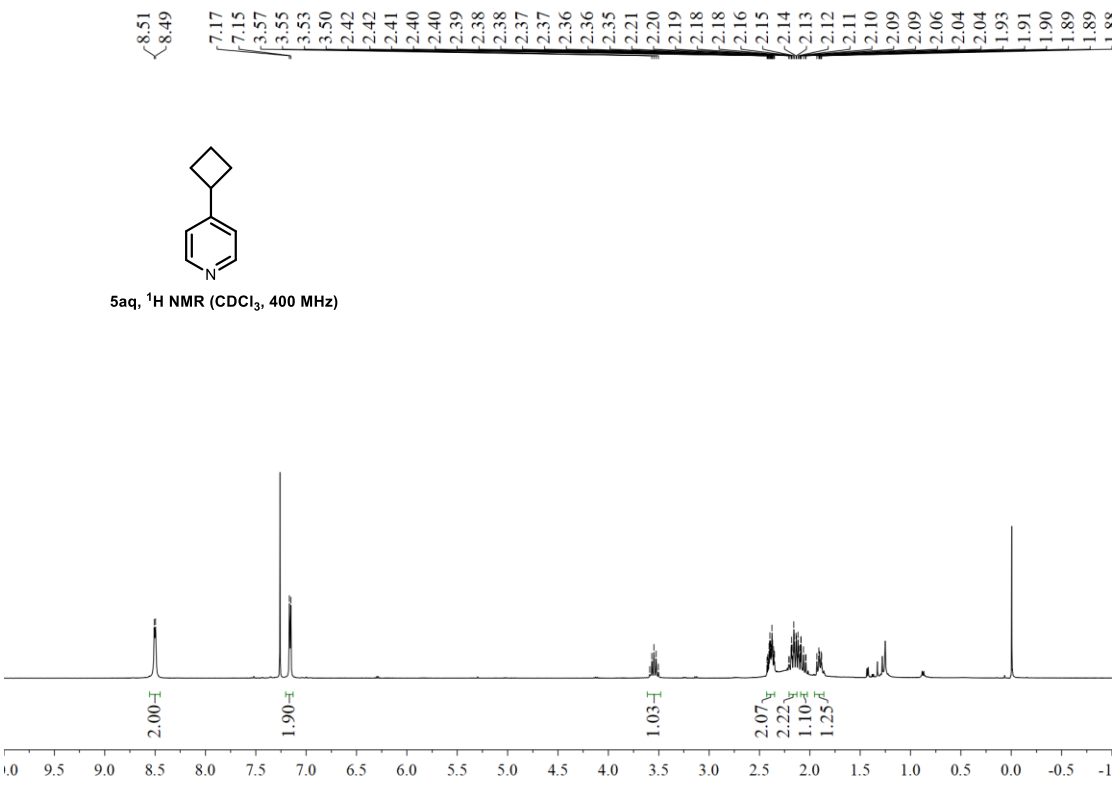


Figure S155. ^{1}H NMR of **5aq** ($CDCl_3$, 400 MHz)

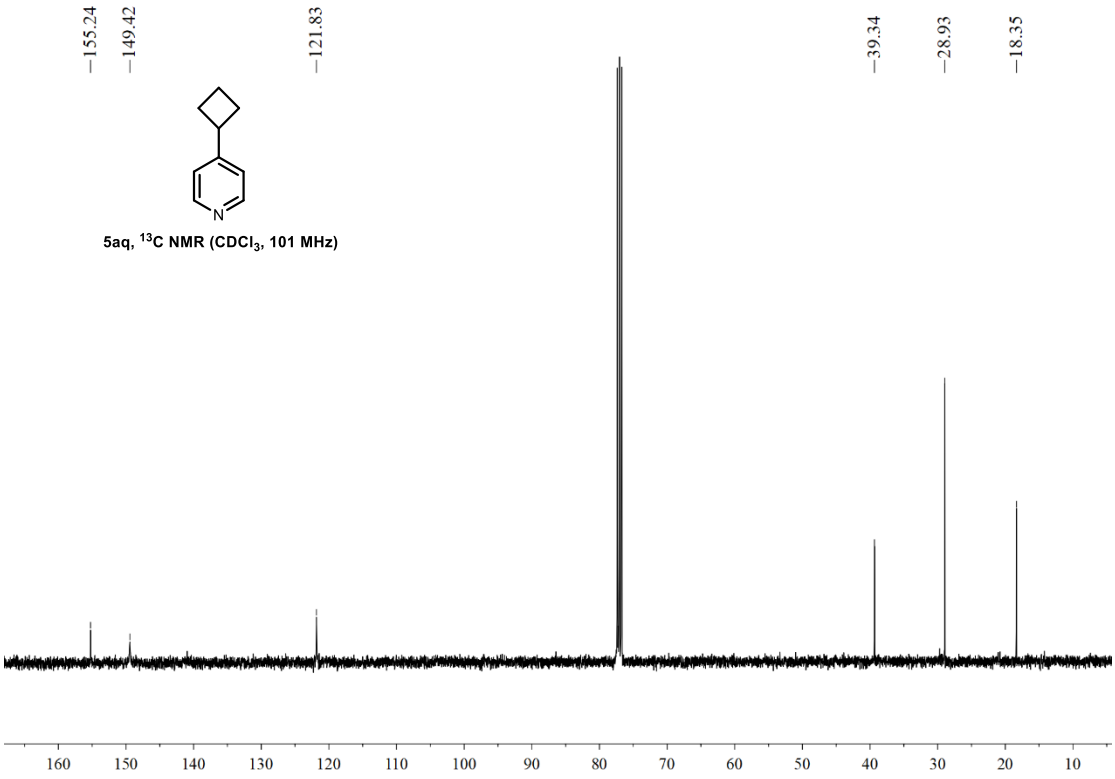


Figure S156. ^{13}C NMR of **5aq** ($CDCl_3$, 101 MHz)

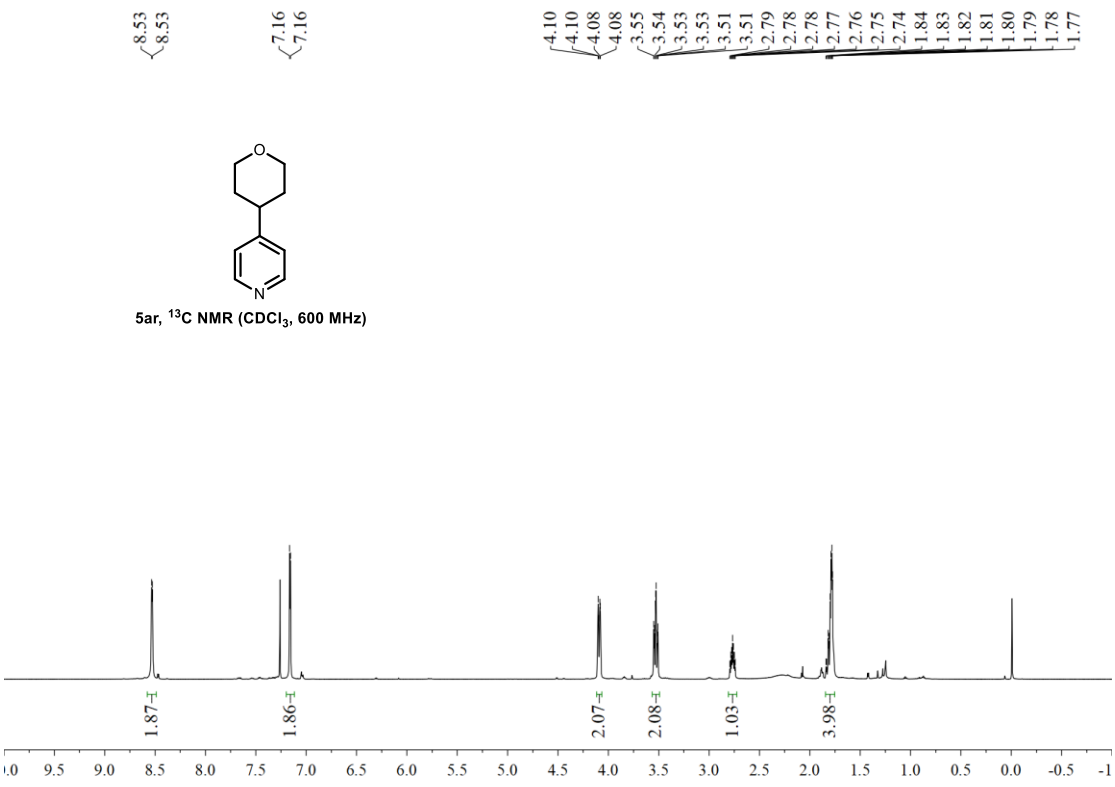


Figure S157. ^{1}H NMR of **5ar** ($CDCl_3$, 600 MHz)

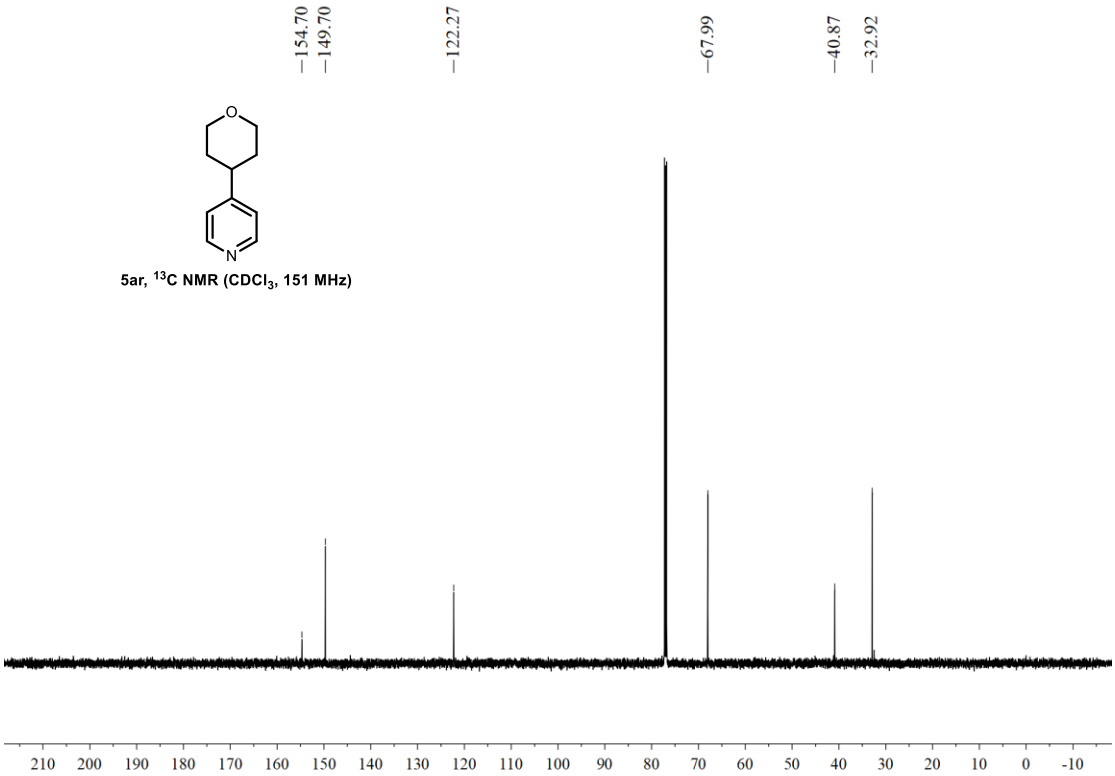


Figure S158. ^{13}C NMR of **5ar** ($CDCl_3$, 151 MHz)

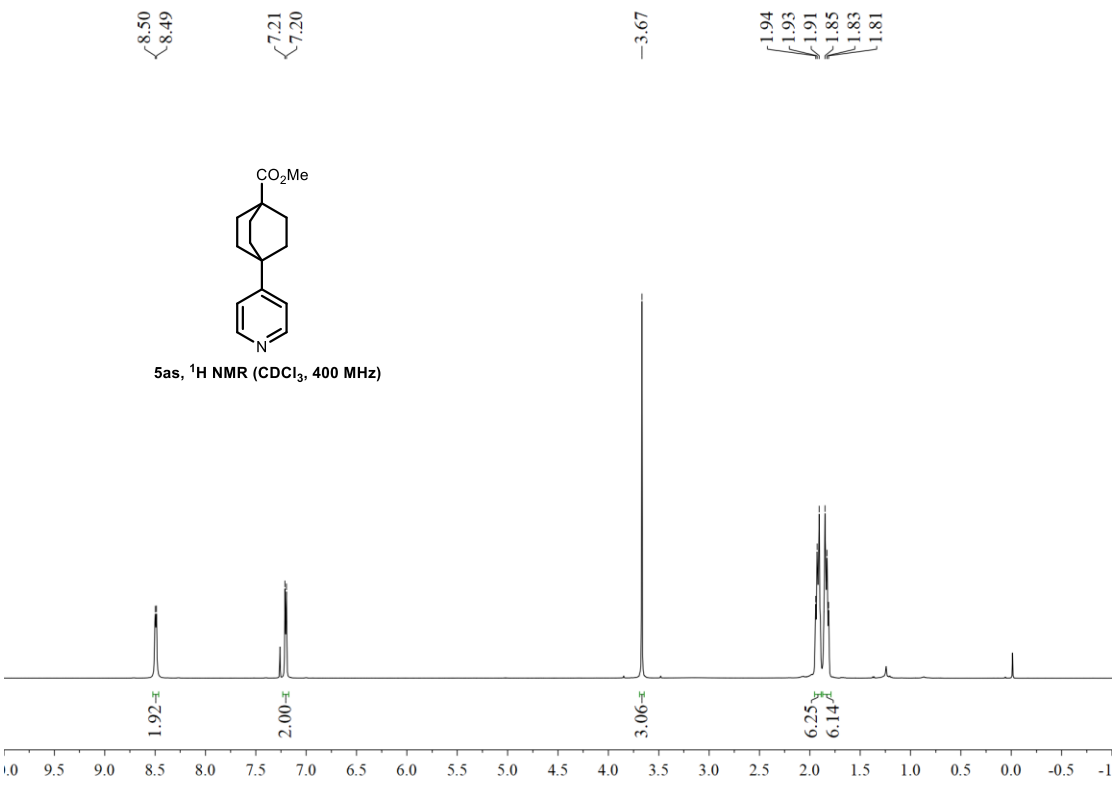


Figure S159. ^{1}H NMR of **5as** ($CDCl_3$, 400 MHz)

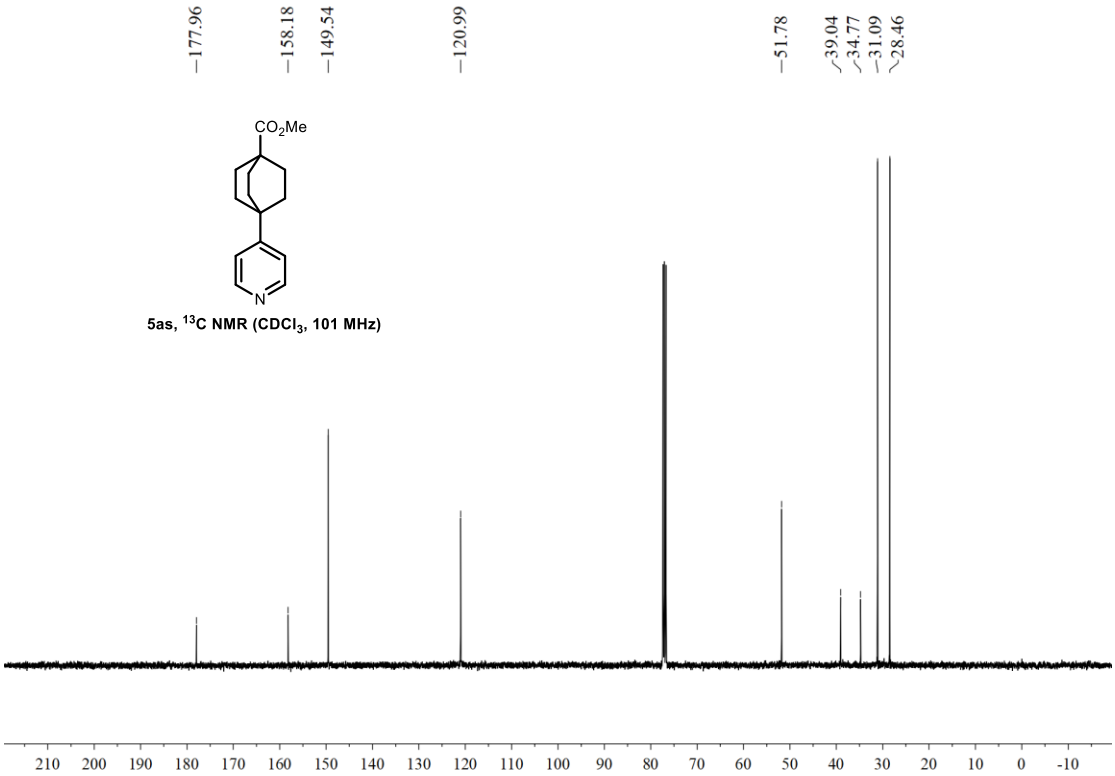


Figure S160. ^{13}C NMR of **5as** ($CDCl_3$, 101 MHz)

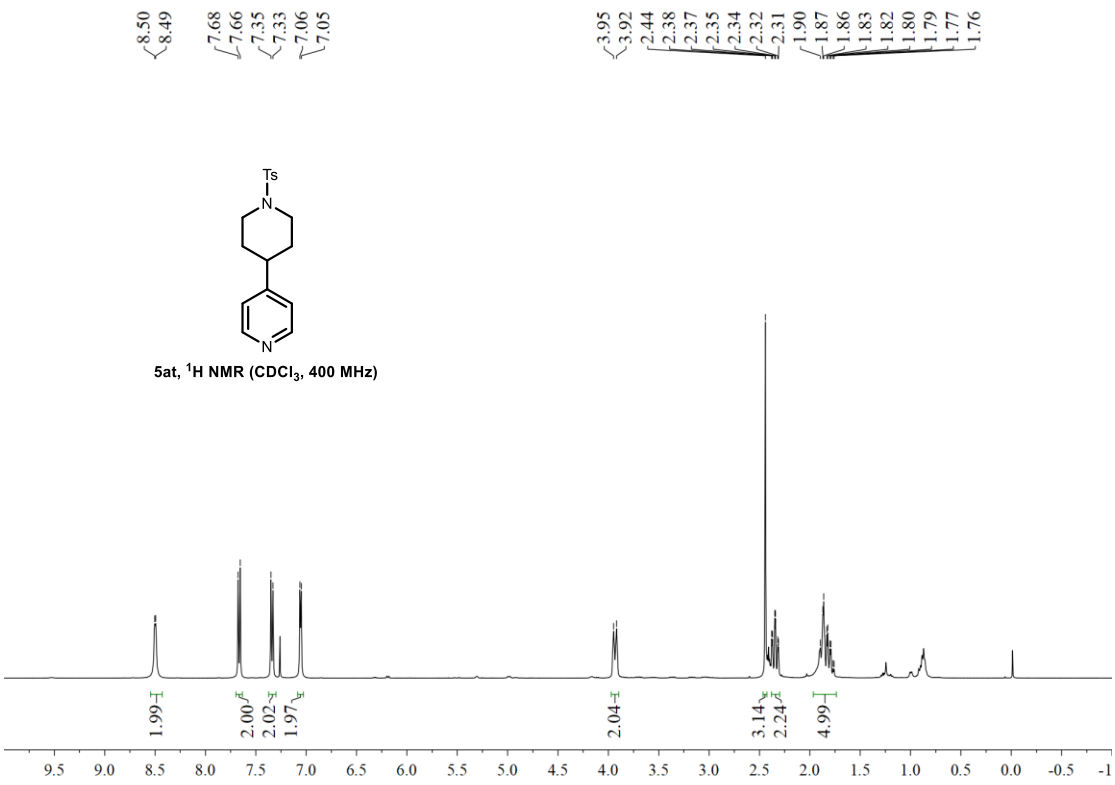


Figure S161. ^{1}H NMR of **5at** ($CDCl_3$, 400 MHz)

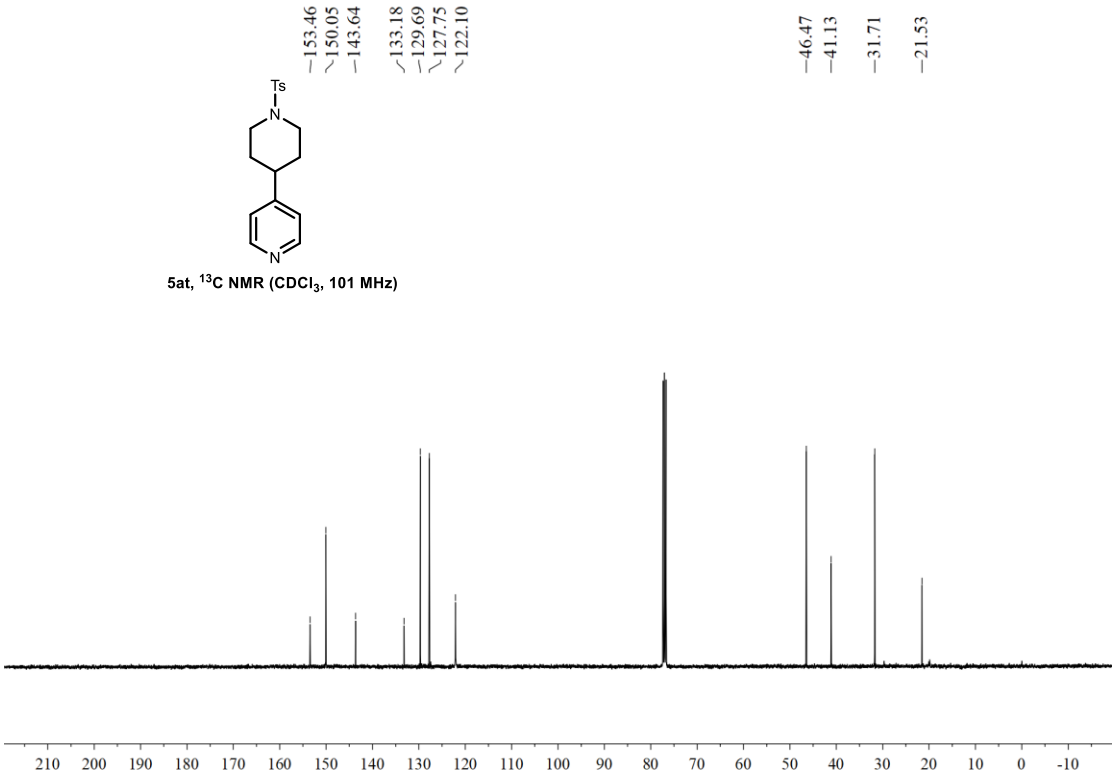


Figure S162. ^{13}C NMR of **5at** ($CDCl_3$, 101 MHz)

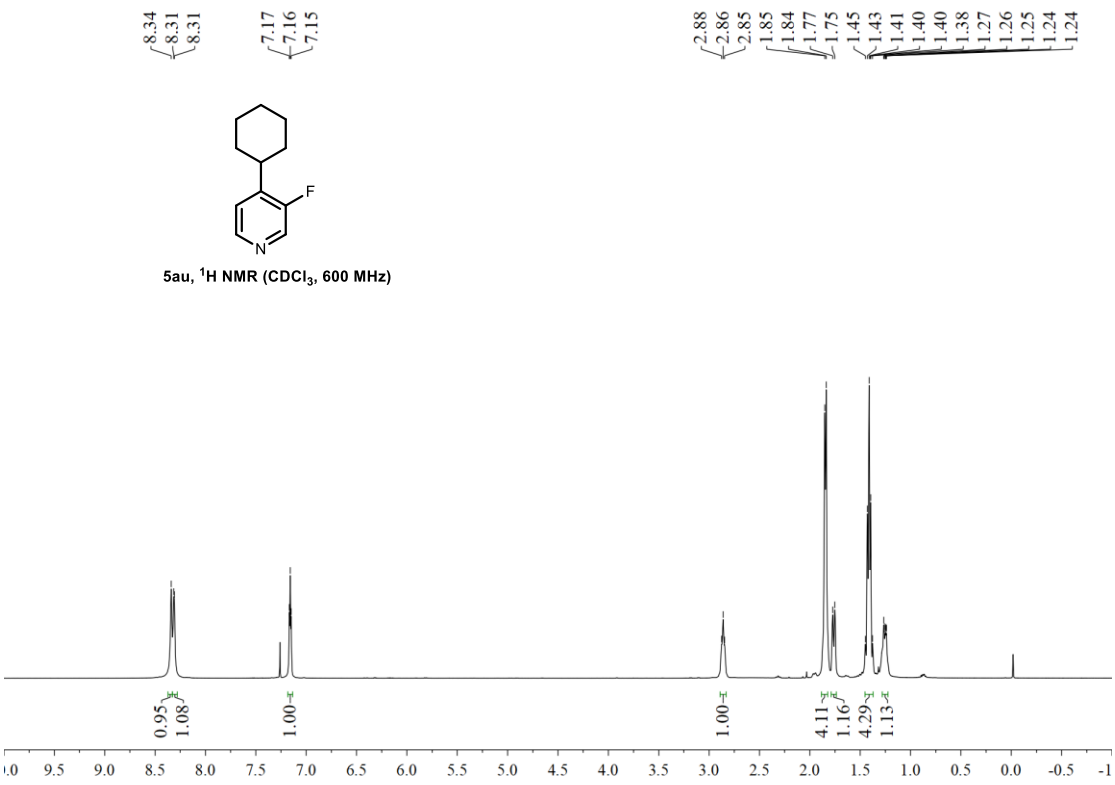


Figure S163. ^{1}H NMR of **5au** ($CDCl_3$, 600 MHz)

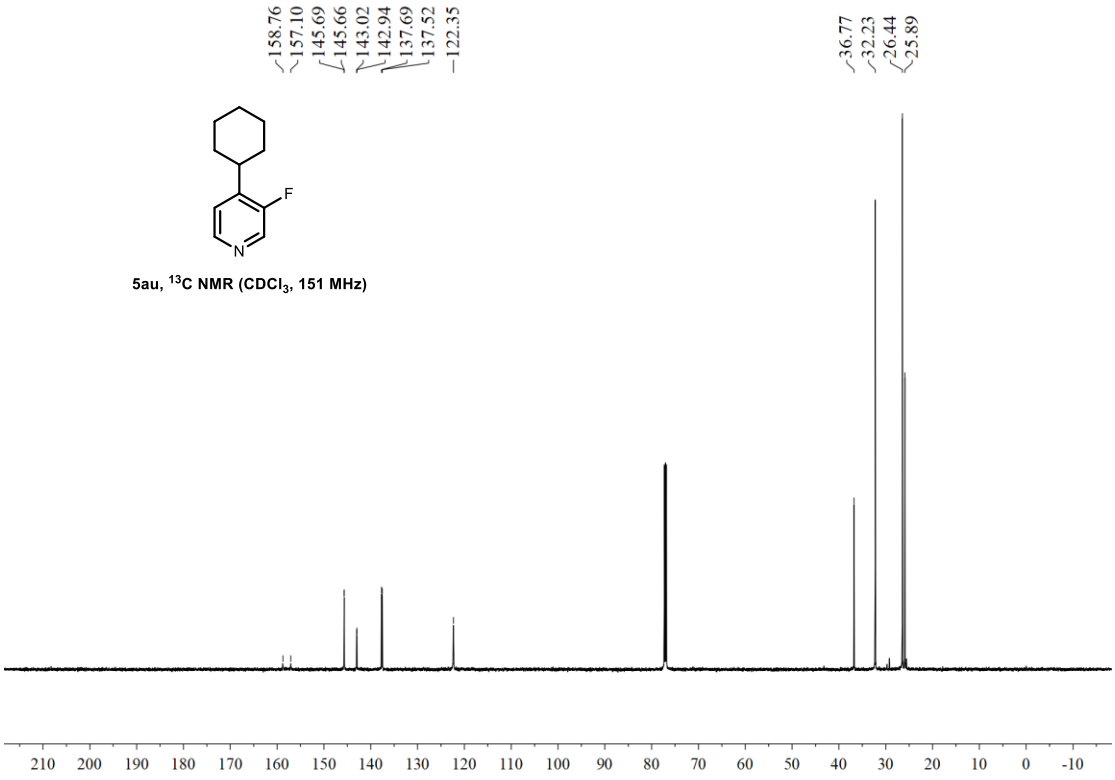


Figure S164. ^{13}C NMR of **5au** ($CDCl_3$, 151 MHz)

Figure S165. ^{19}F NMR of **5au** ($CDCl_3$, 565 MHz)

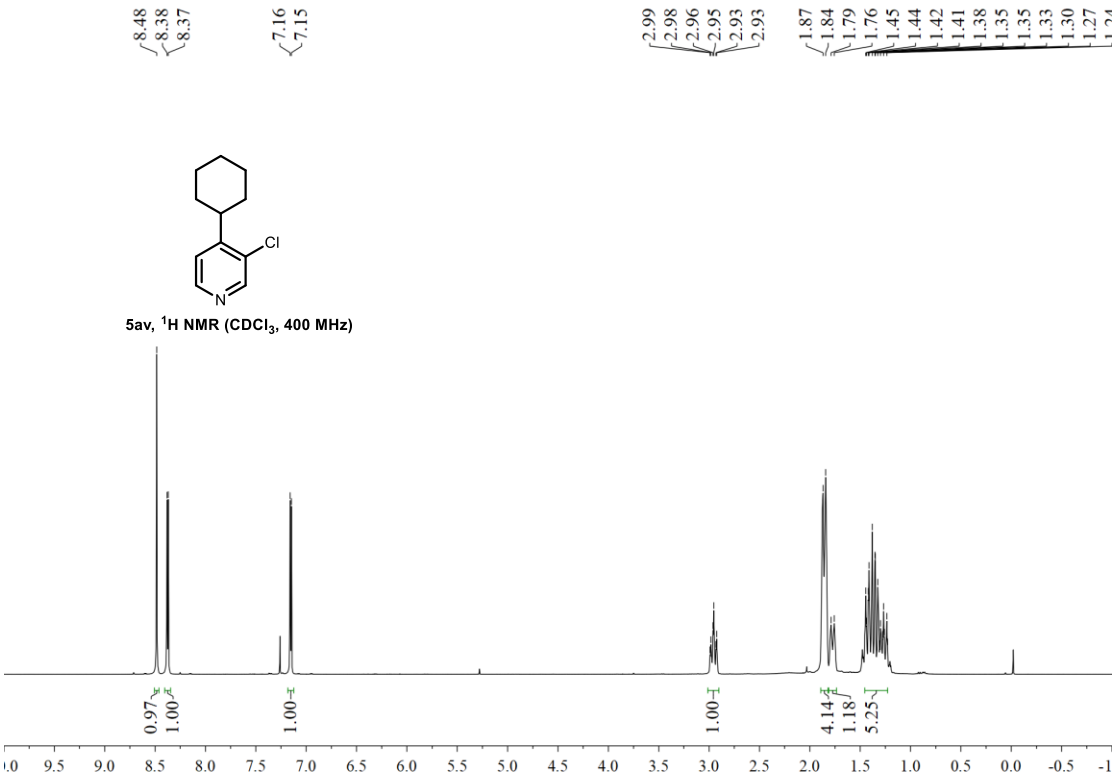


Figure S166. ^{1}H NMR of **5av** ($CDCl_3$, 400 MHz)

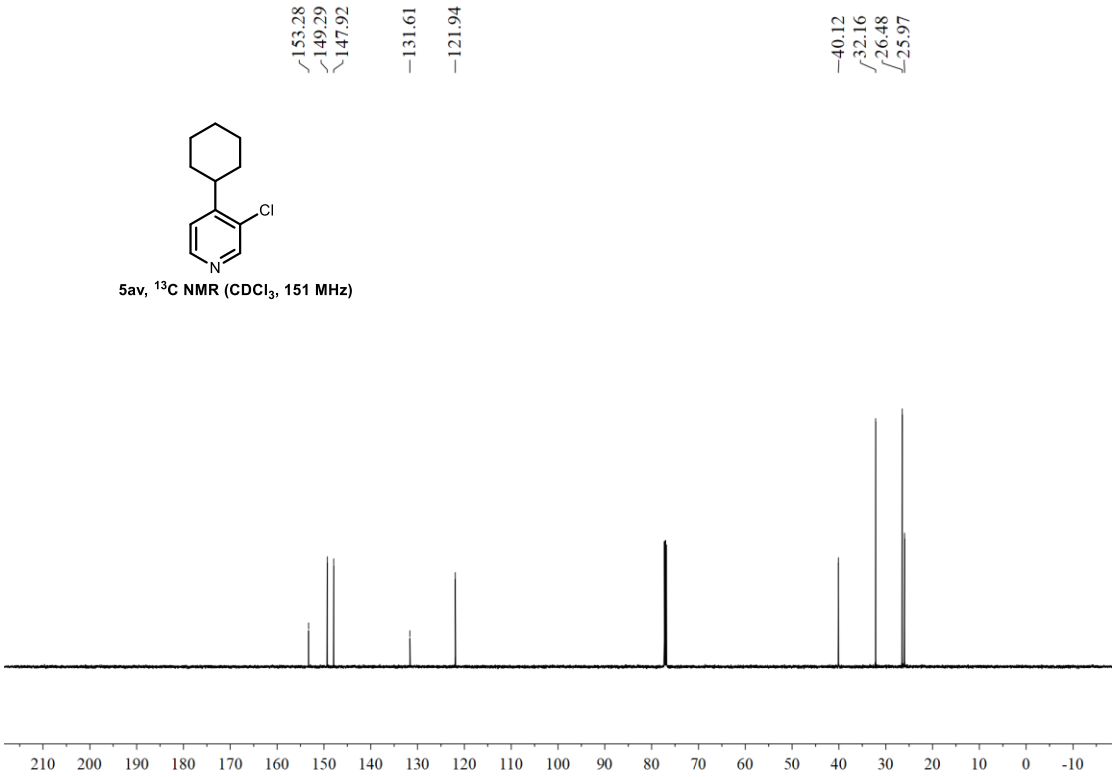


Figure S167. ^{13}C NMR of **5av** ($CDCl_3$, 151 MHz)

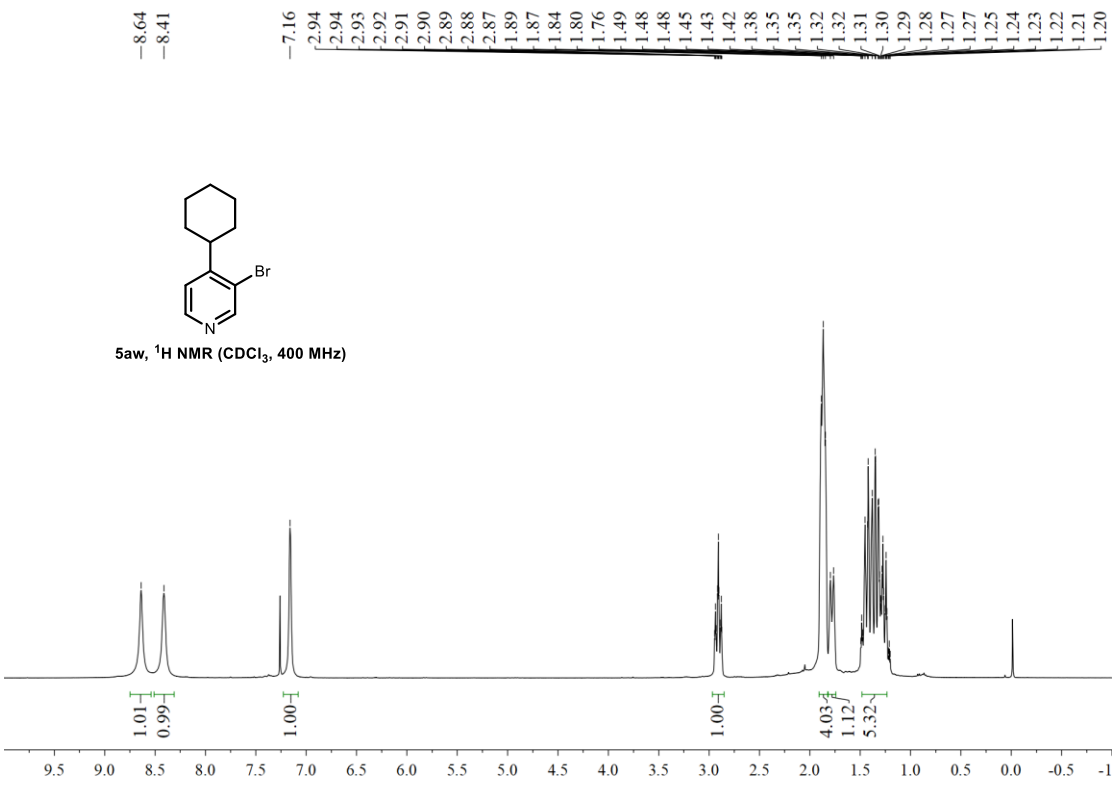


Figure S168. ^{1}H NMR of **5aw** ($CDCl_3$, 400 MHz)

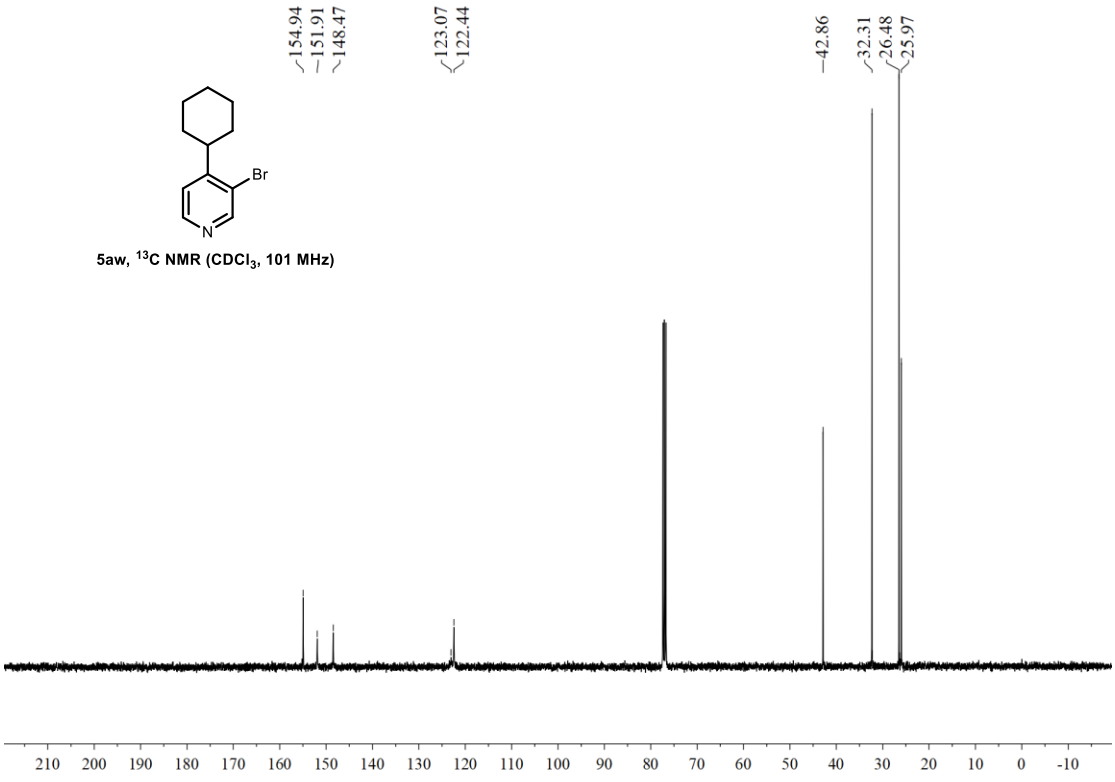


Figure S169. ^{13}C NMR of **5aw** ($CDCl_3$, 101 MHz)

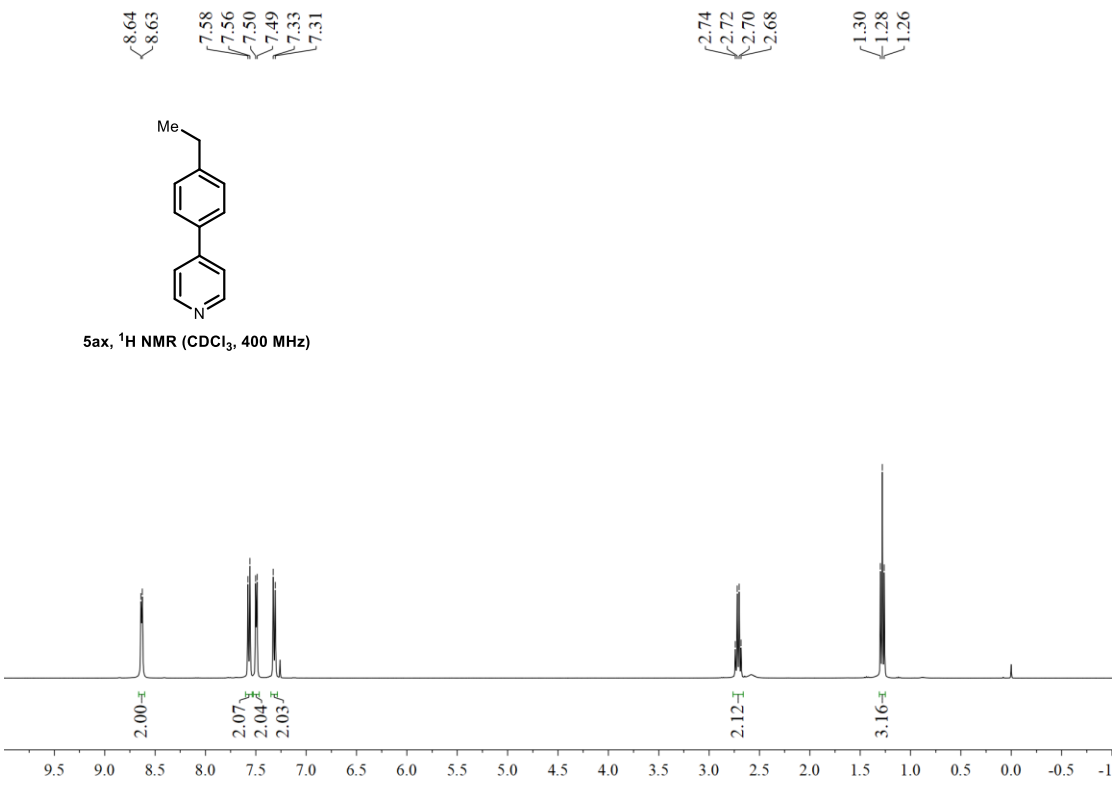


Figure S170. ^{1}H NMR of **5ax** (CDCl$_3$, 400 MHz)

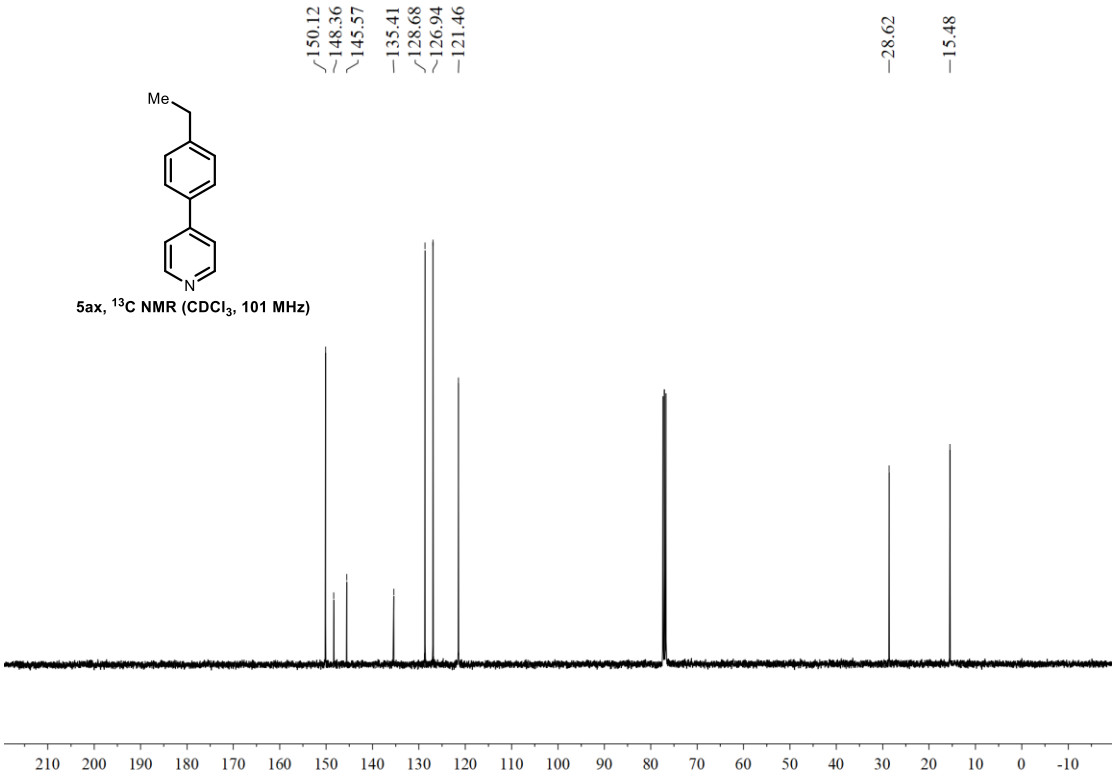


Figure S171. ^{13}C NMR of **5ax** (CDCl$_3$, 101 MHz)

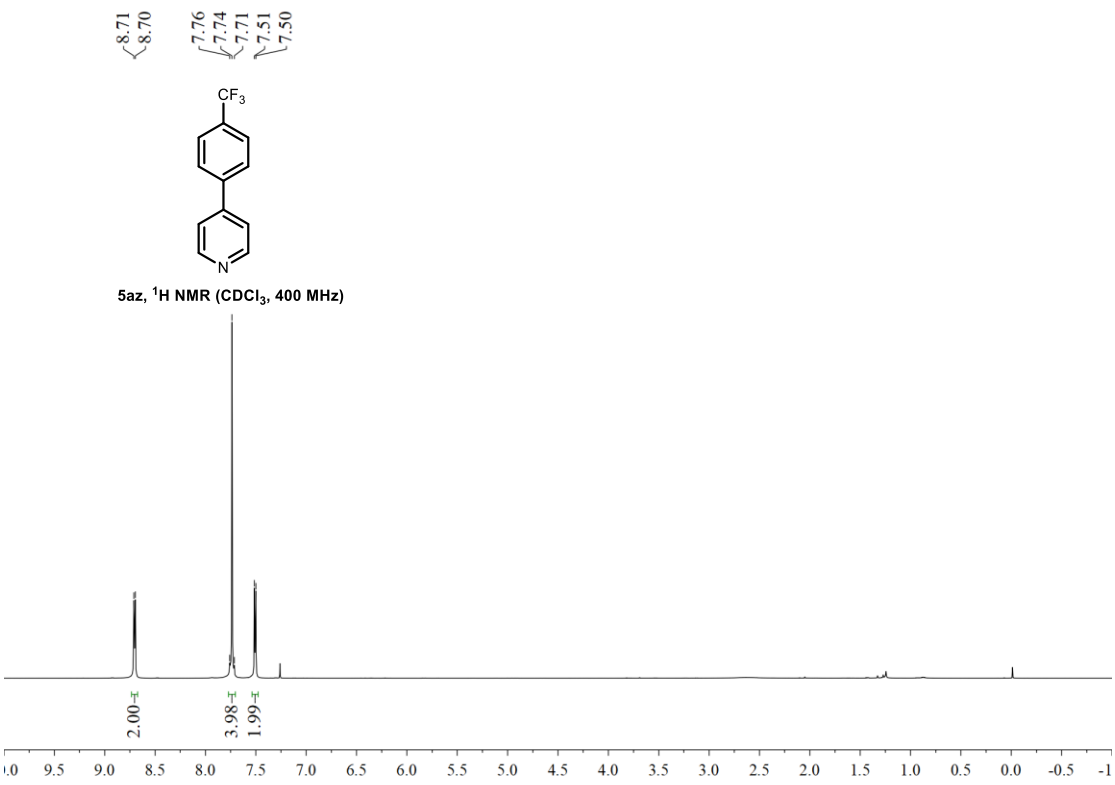


Figure S172. ^{1}H NMR of **5az** ($CDCl_3$, 400 MHz)

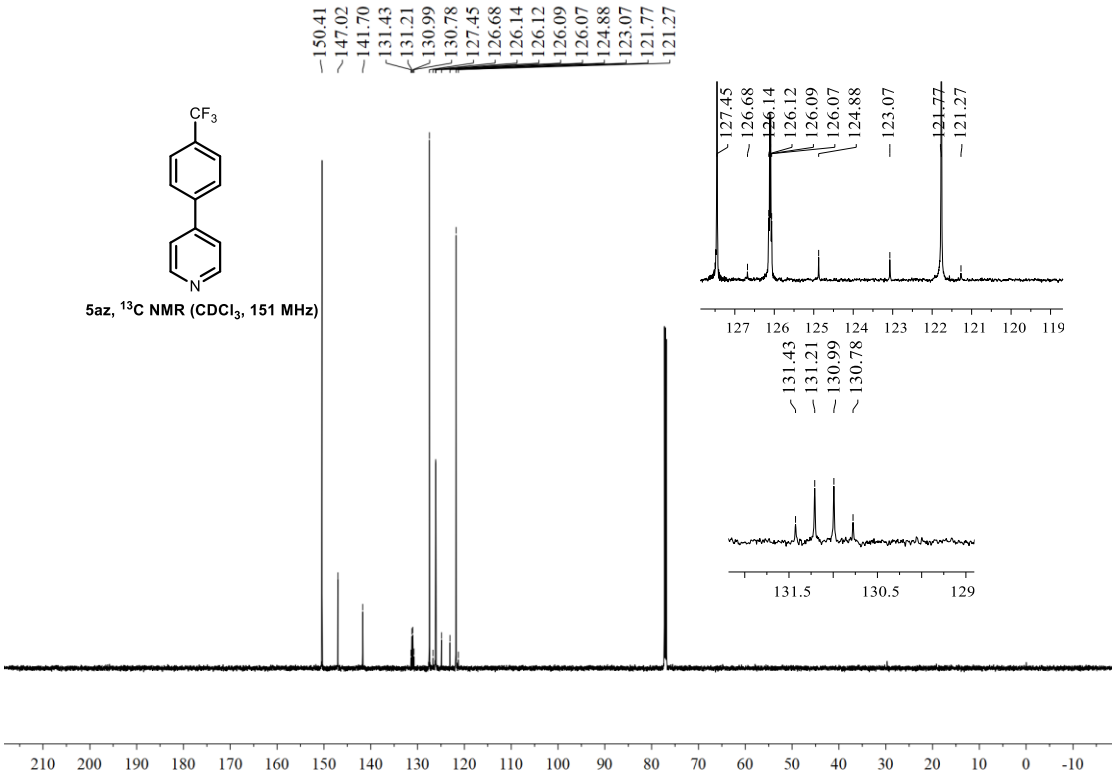


Figure S173. ^{13}C NMR of **5az** ($CDCl_3$, 151 MHz)

Figure S174. ^{19}F NMR of **5az** ($CDCl_3$, 377 MHz)

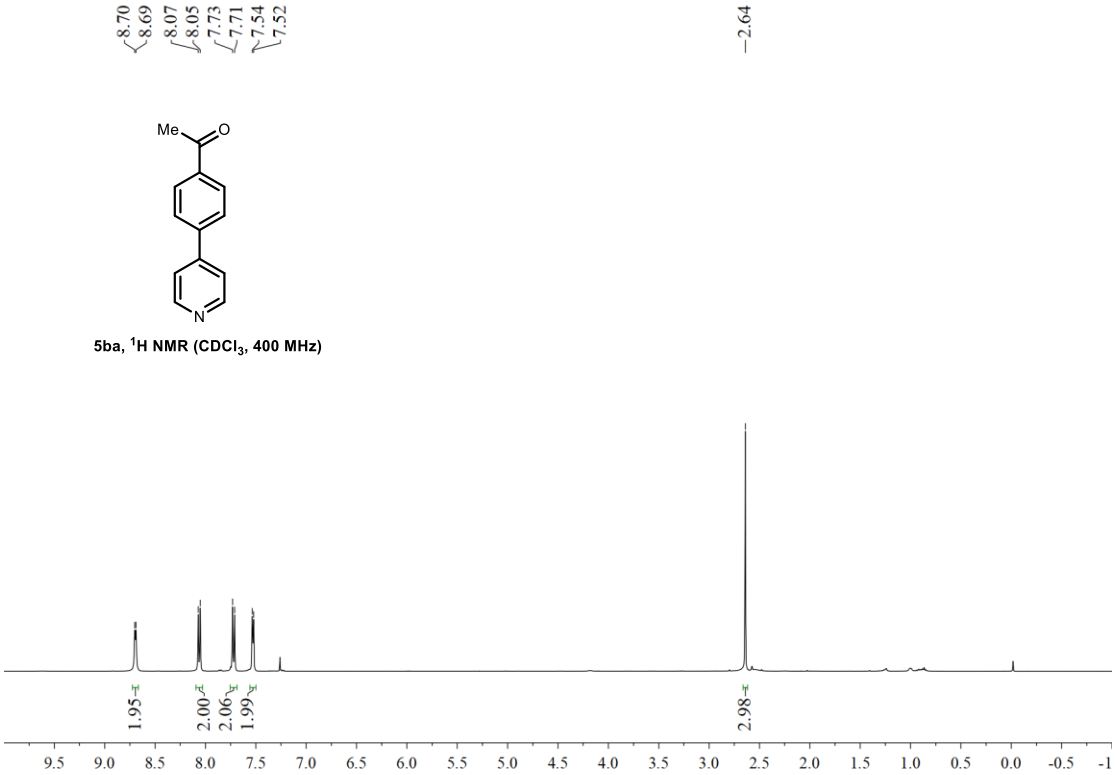


Figure S175. ^{1}H NMR of **5ba** ($CDCl_3$, 400 MHz)

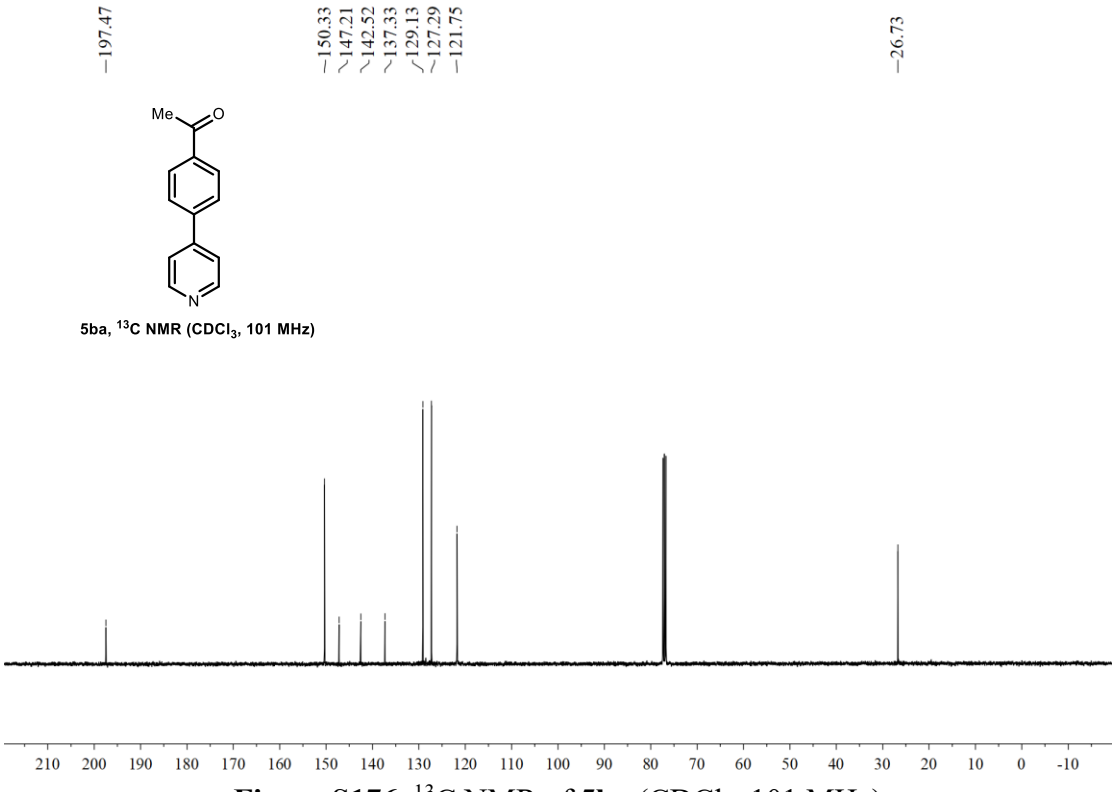


Figure S176. ^{13}C NMR of **5ba** ($CDCl_3$, 101 MHz)

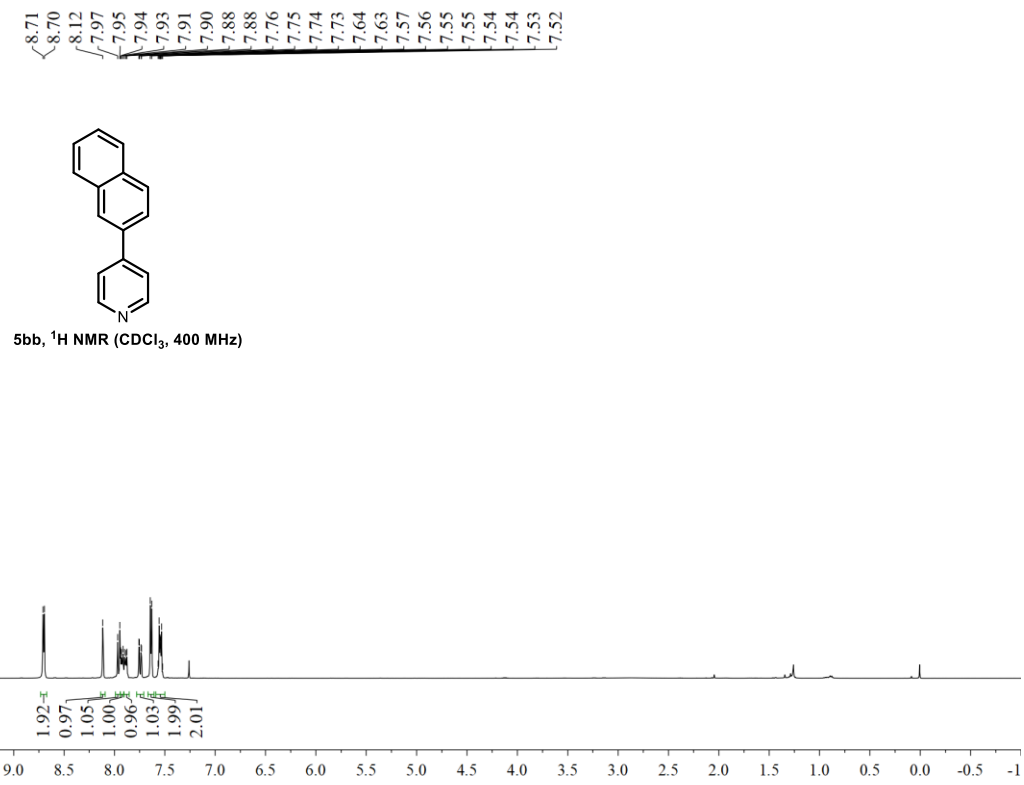


Figure S177. ^{1}H NMR of **5bb** ($CDCl_3$, 400 MHz)

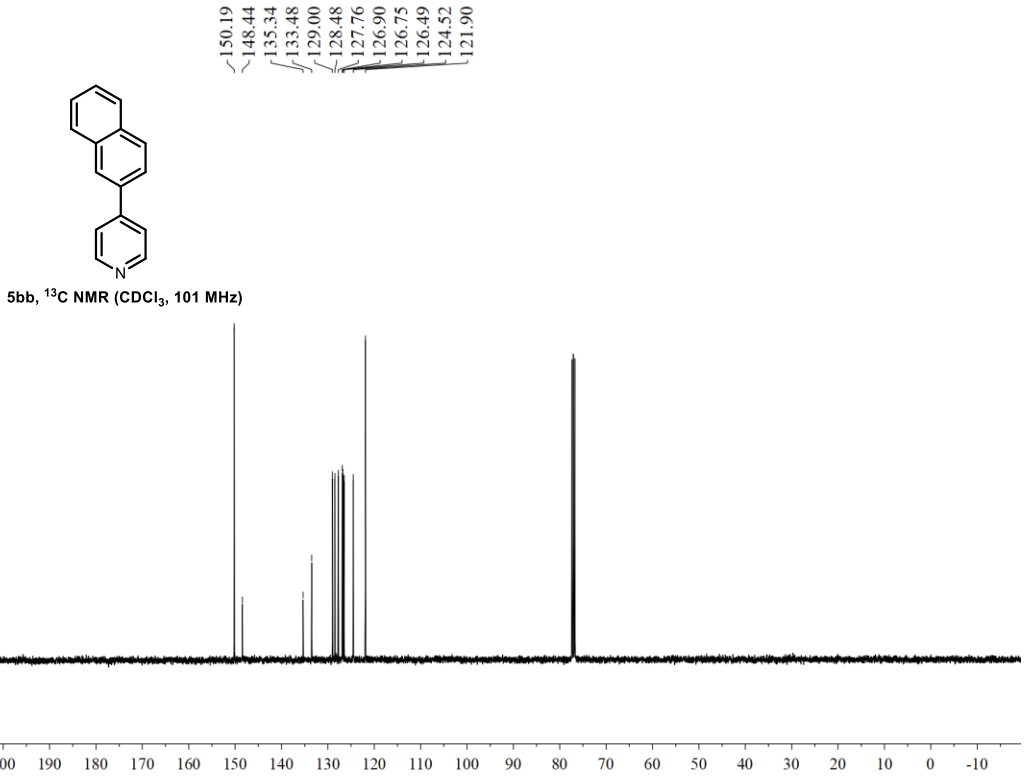


Figure S178. ^{13}C NMR of **5bb** ($CDCl_3$, 101 MHz)

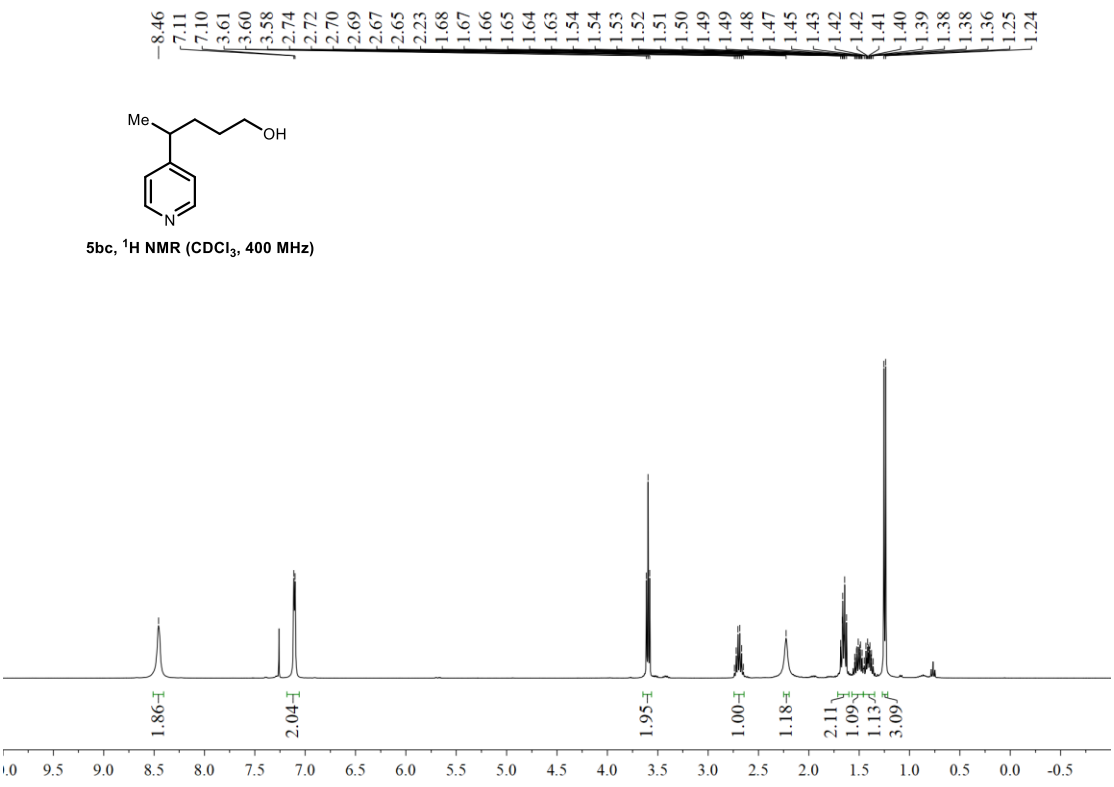


Figure S179. ^{1}H NMR of **5bc** (CDCl$_3$, 400 MHz)

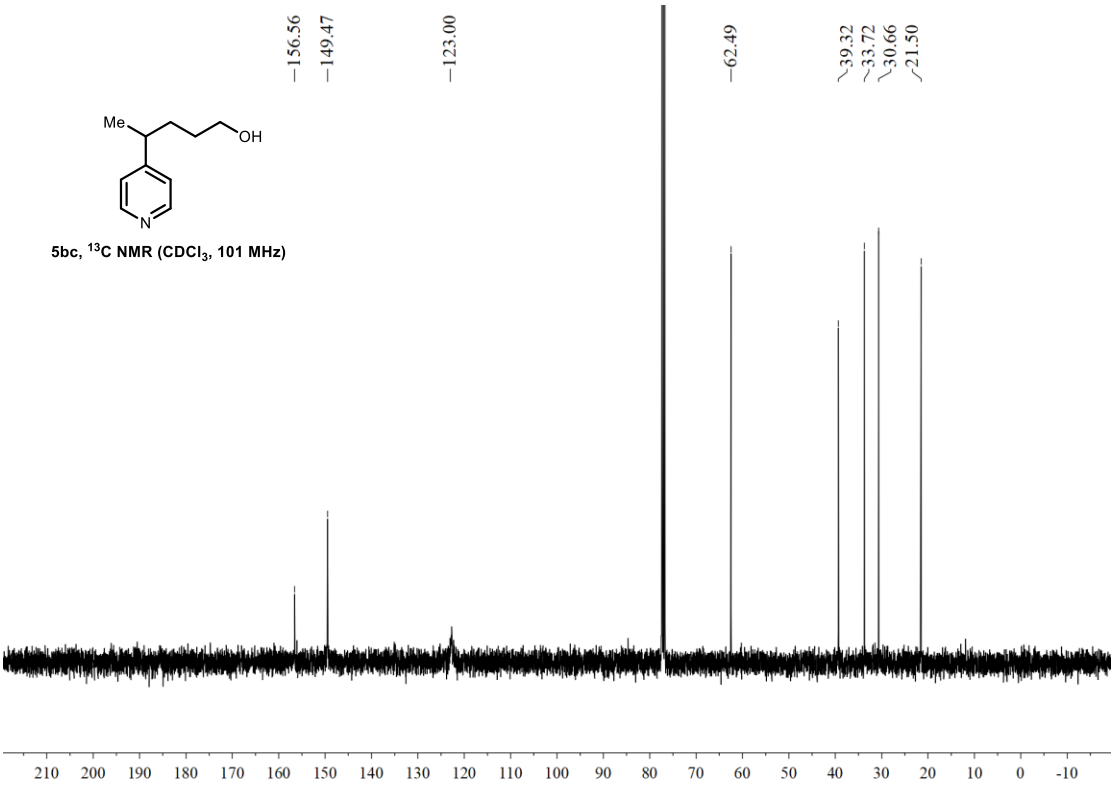


Figure S180. ^{13}C NMR of **5bc** (CDCl$_3$, 101 MHz)

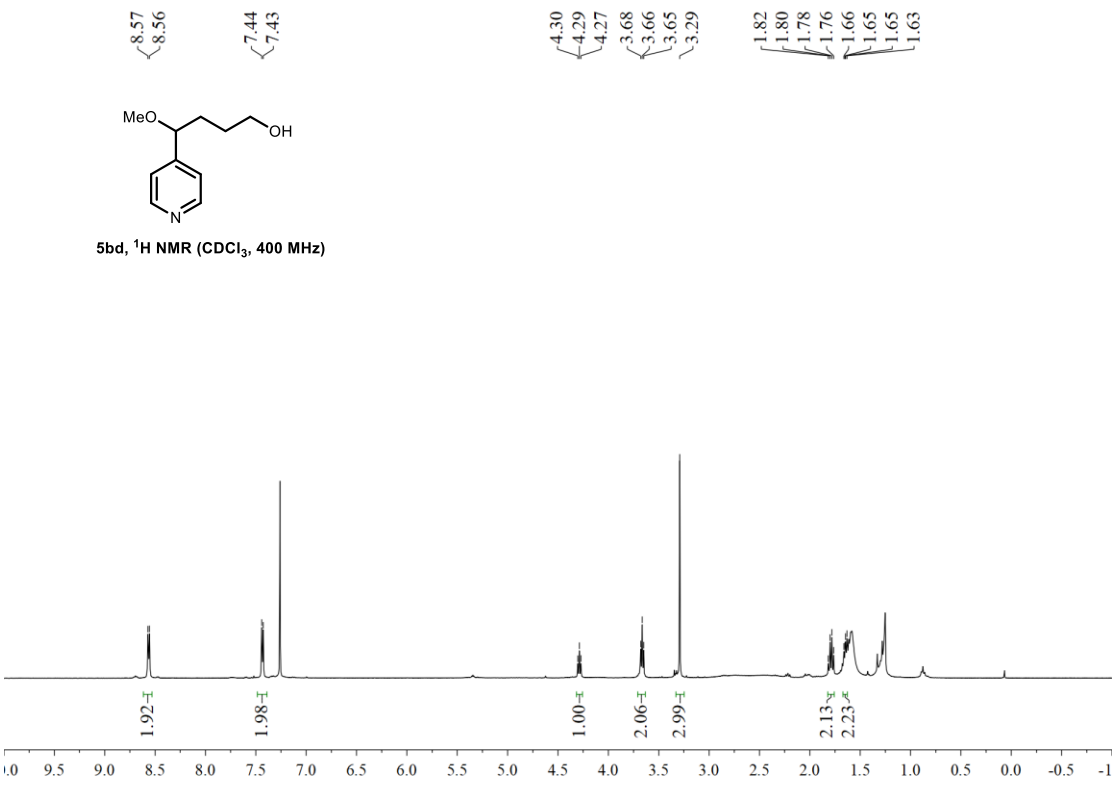


Figure S181. ^{1}H NMR of **5bd** ($CDCl_3$, 400 MHz)

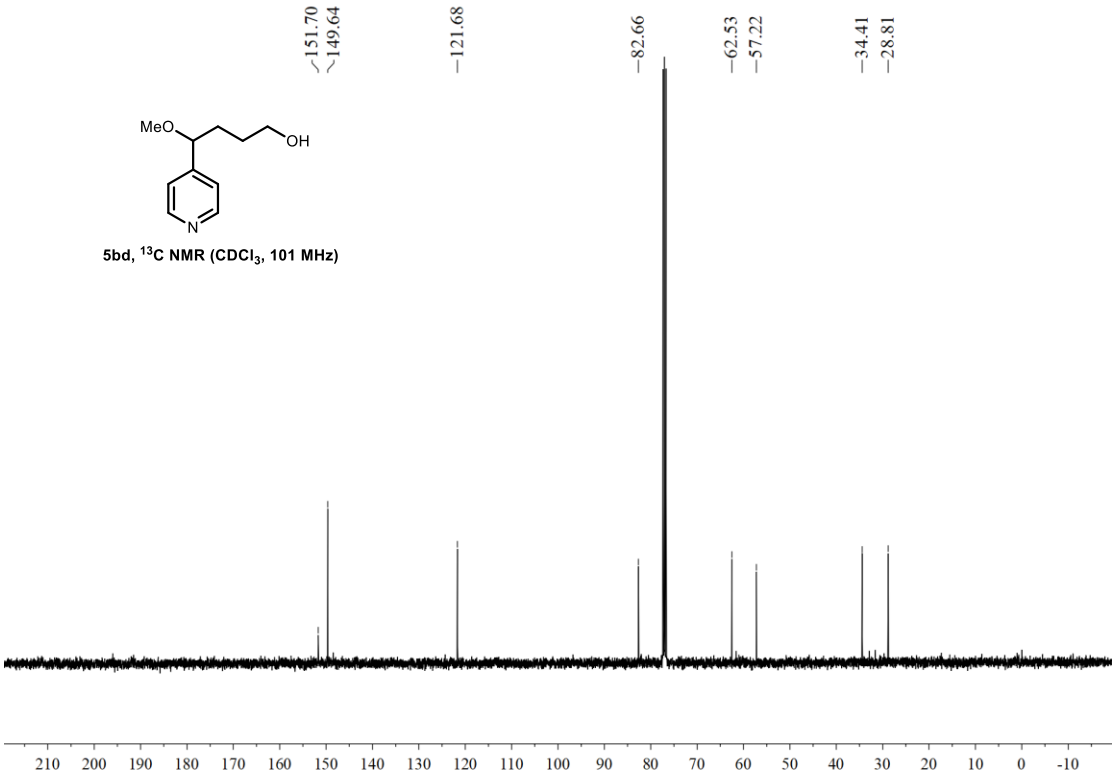


Figure S182. ^{13}C NMR of **5bd** ($CDCl_3$, 101 MHz)

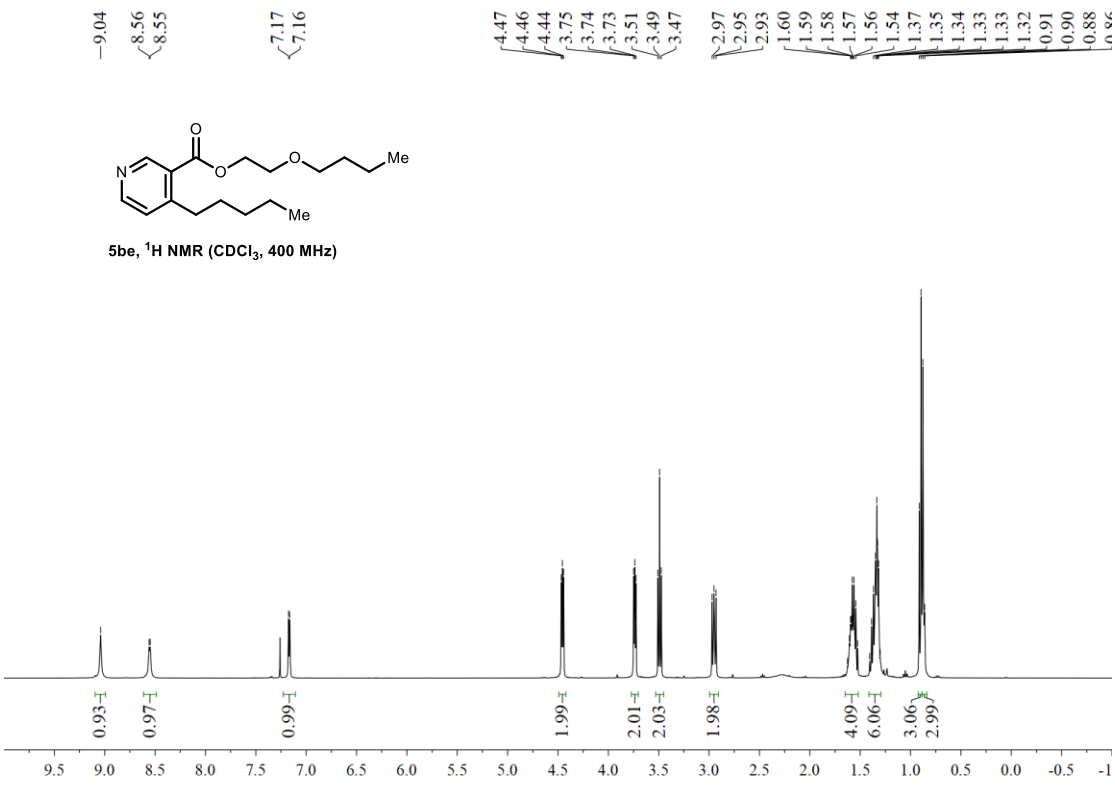


Figure S183. ^{1}H NMR of **5be** ($CDCl_3$, 400 MHz)

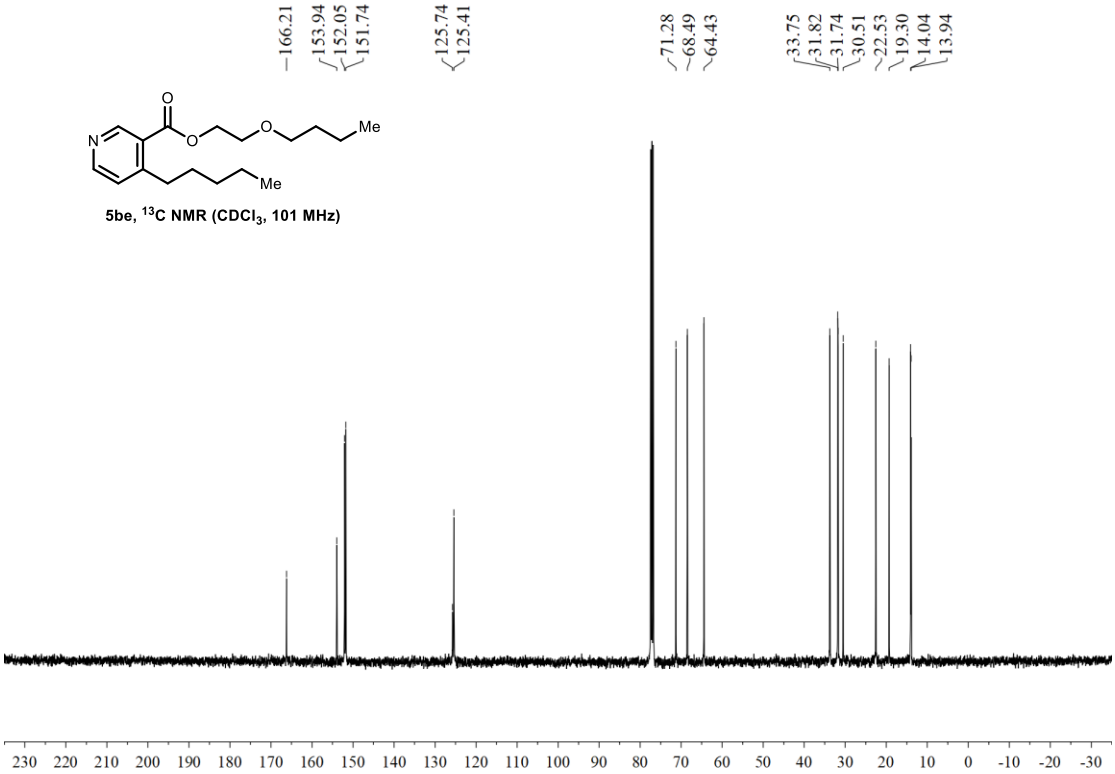


Figure S184. ^{13}C NMR of **5be** ($CDCl_3$, 101 MHz)

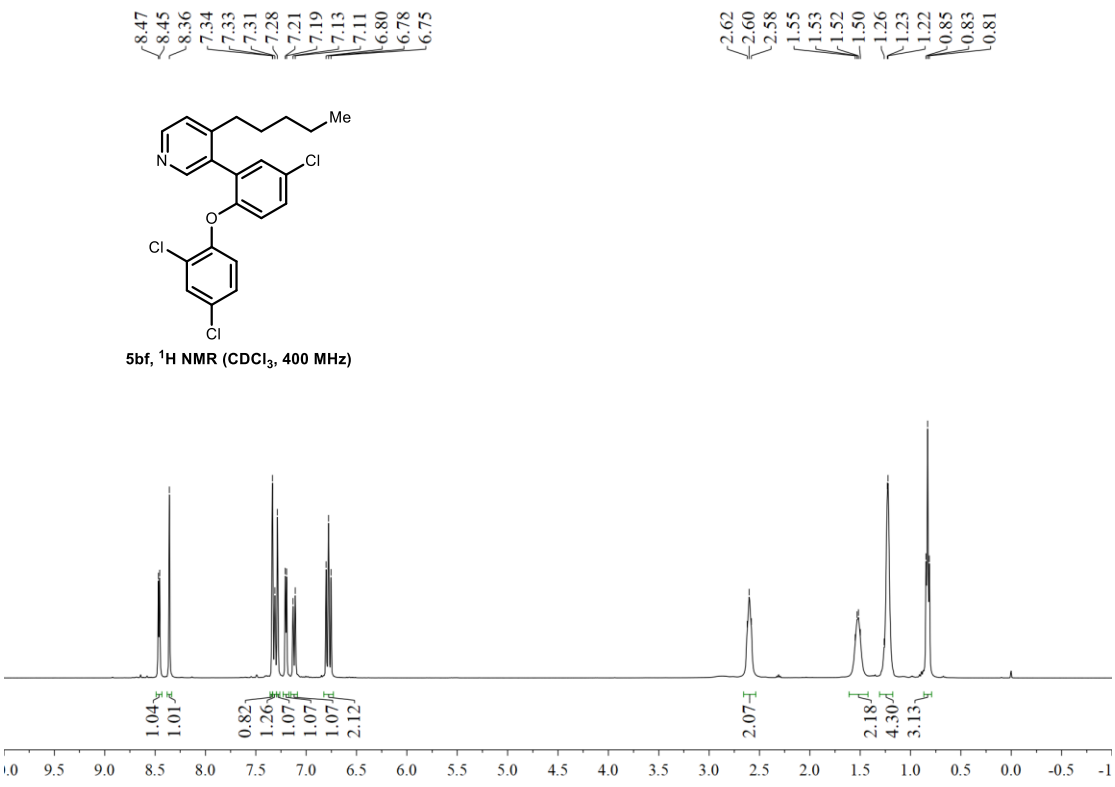


Figure S185. ^{1}H NMR of **5bf** ($CDCl_3$, 400 MHz)

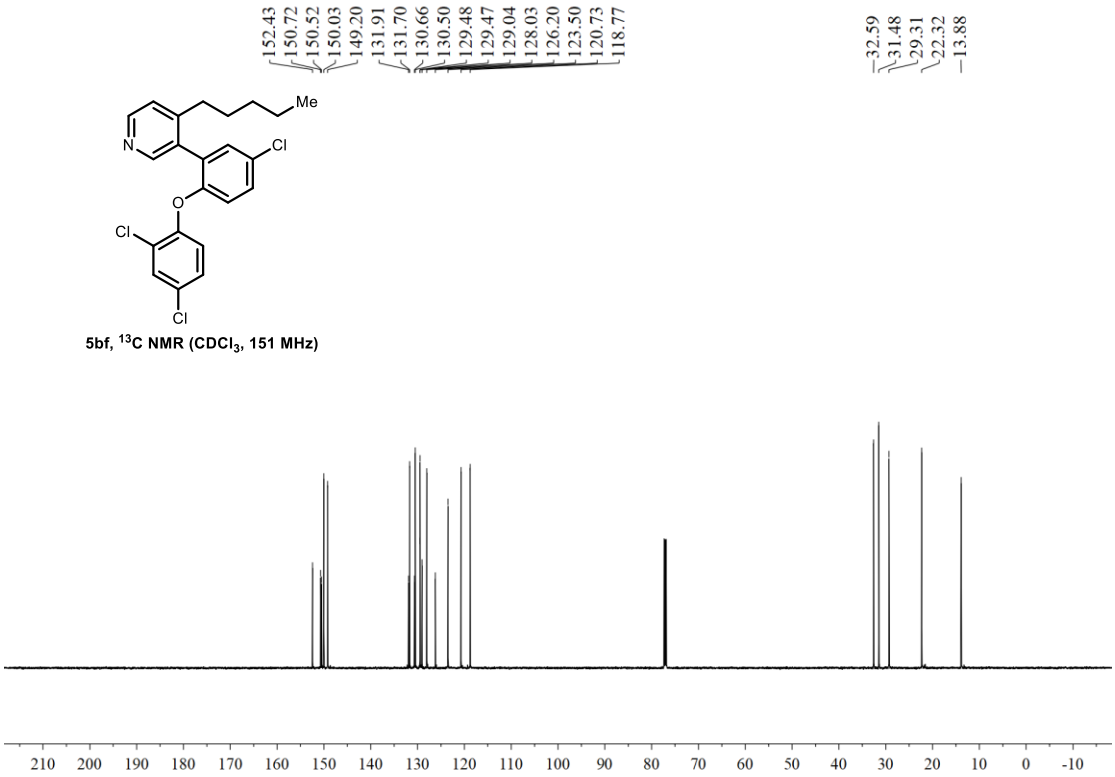


Figure S186. ^{13}C NMR of **5bf** ($CDCl_3$, 151 MHz)

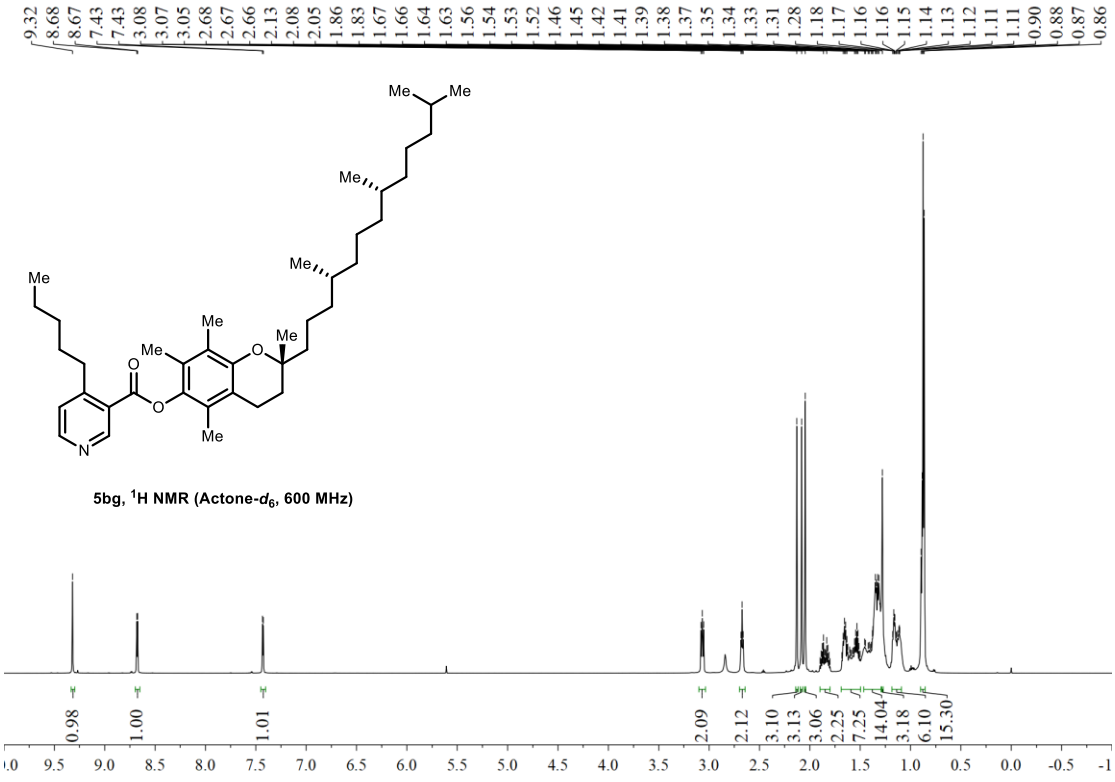


Figure S187. ^{1}H NMR of **5bg** (Actone-d_6, 600 MHz)

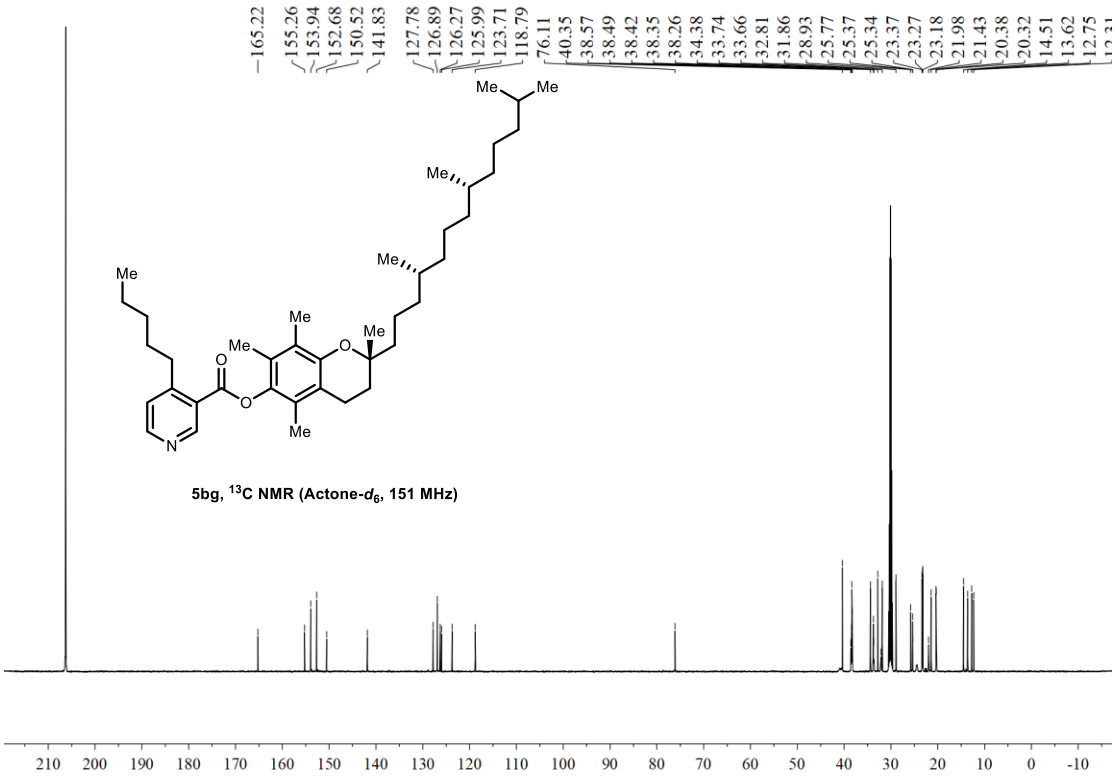


Figure S188. ^{13}C NMR of **5bg** (Actone-d_6, 151 MHz)

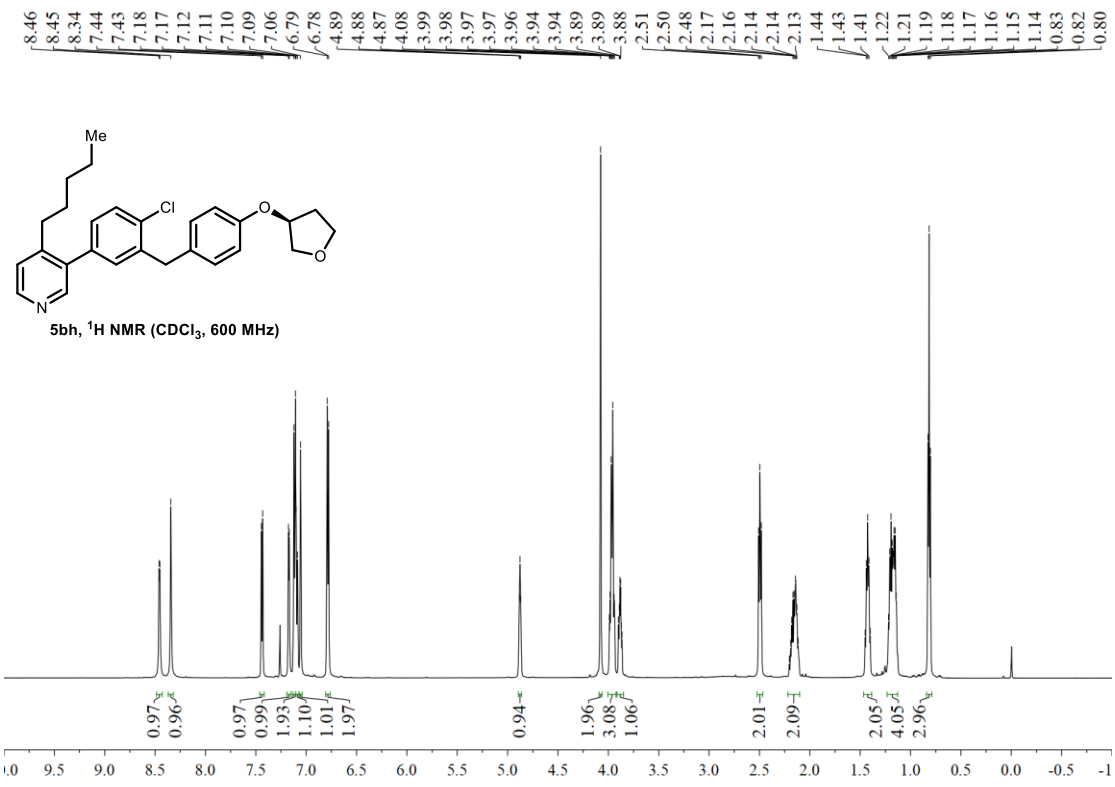


Figure S189. ^{1}H NMR of **5bh** ($CDCl_3$, 600 MHz)

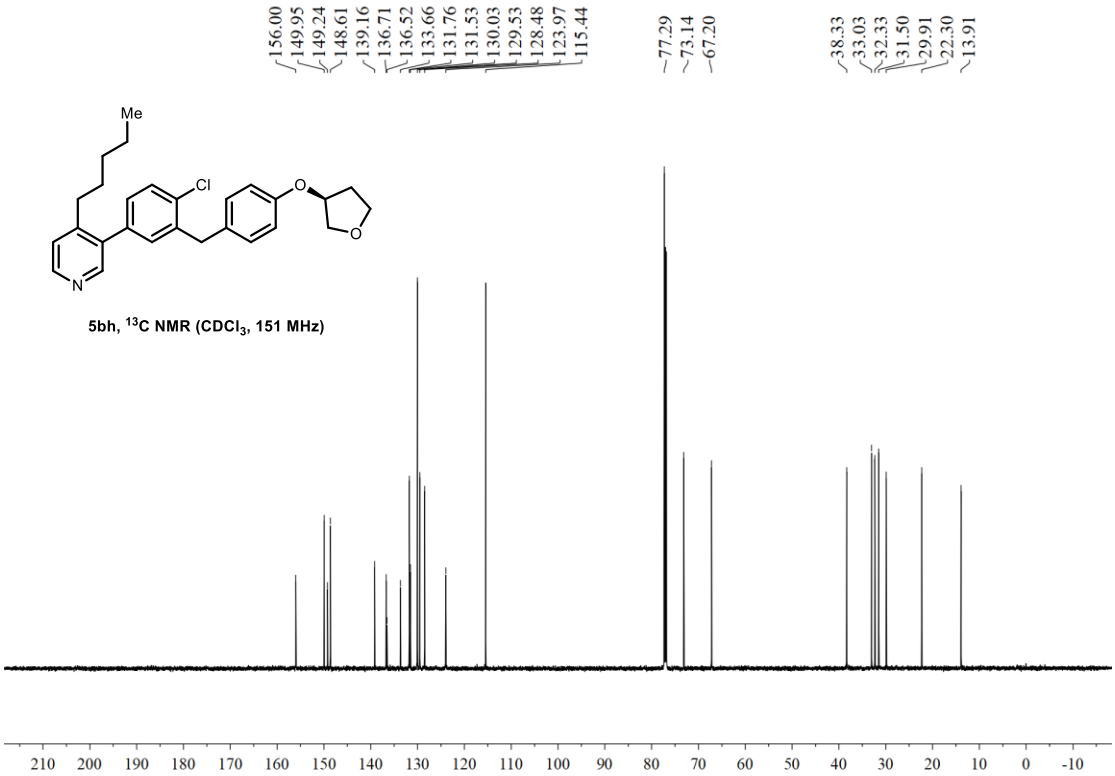


Figure S190. ^{13}C NMR of **5bh** ($CDCl_3$, 151 MHz)

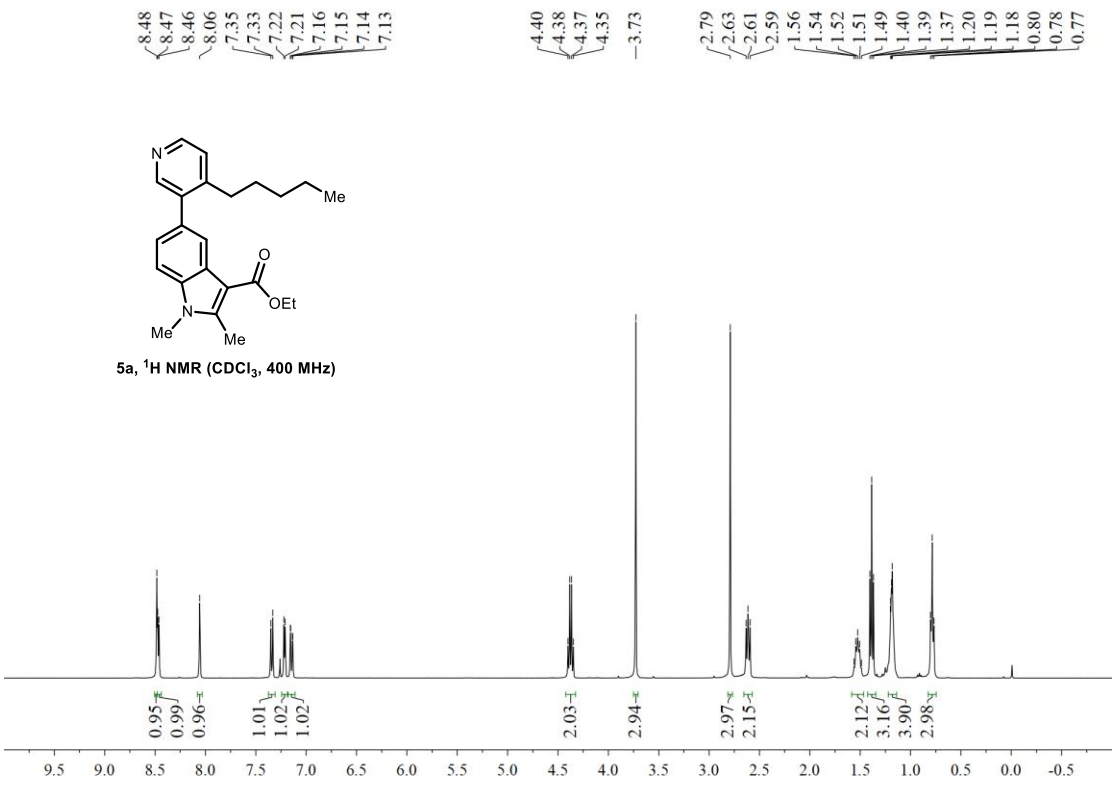


Figure S191. ^{1}H NMR of **5bi** ($CDCl_3$, 400 MHz)

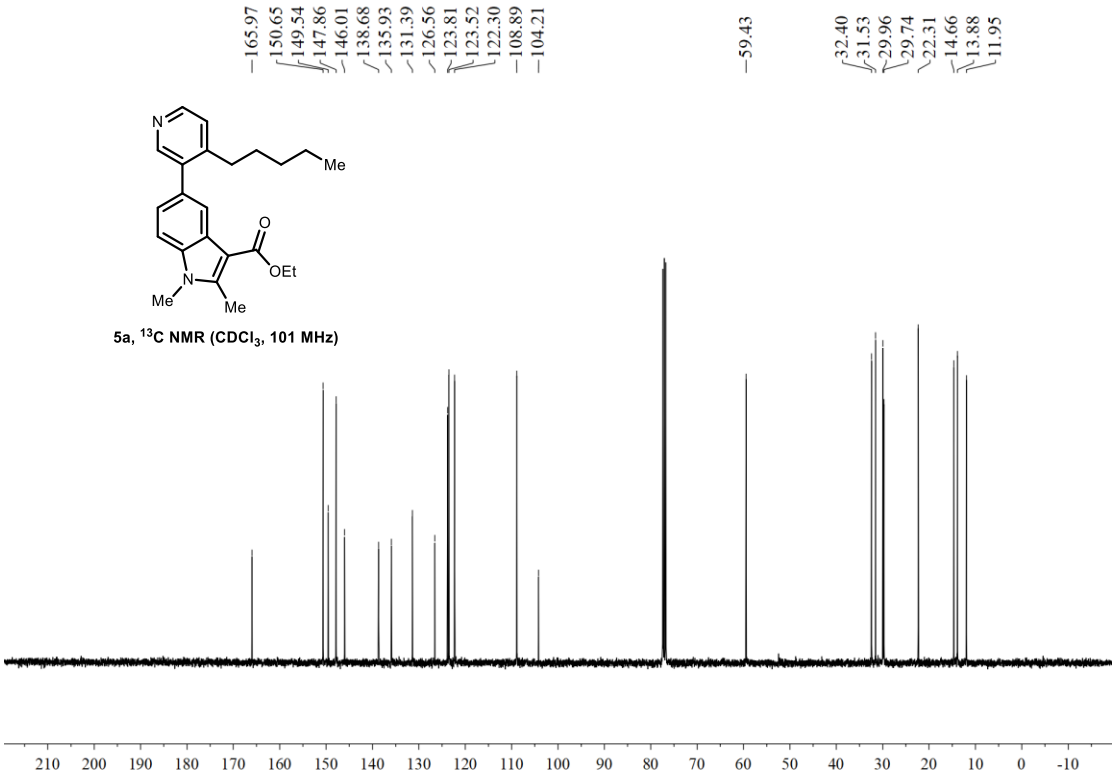


Figure S192. ^{13}C NMR of **5bi** ($CDCl_3$, 101 MHz)

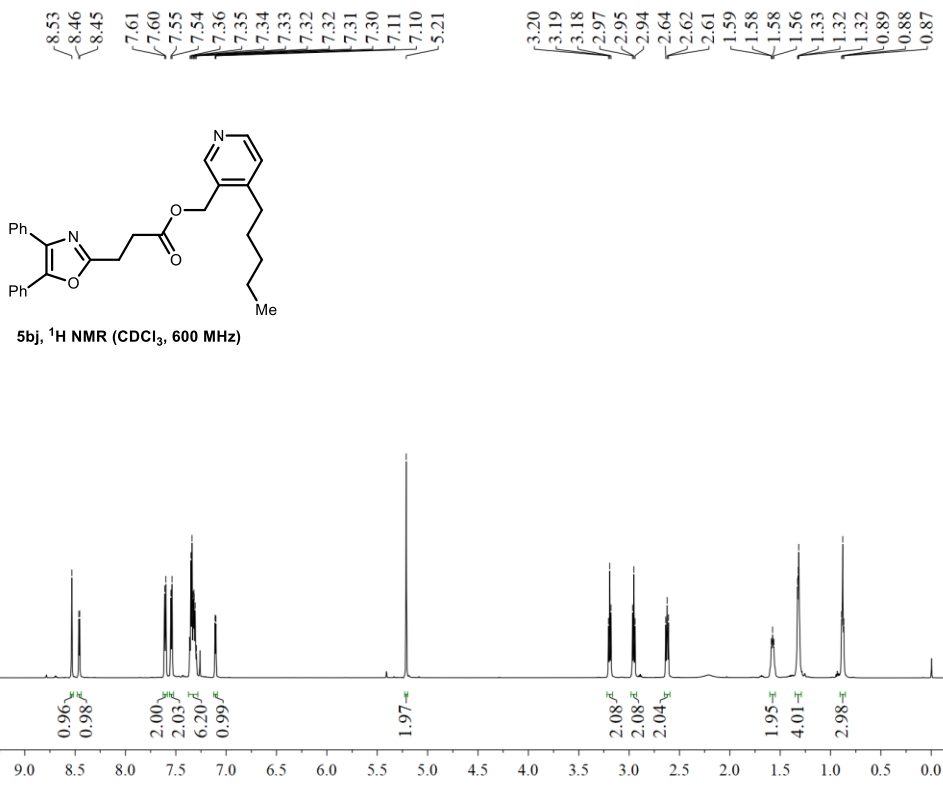


Figure S193. ^{1}H NMR of **5bj** ($CDCl_3$, 600 MHz)

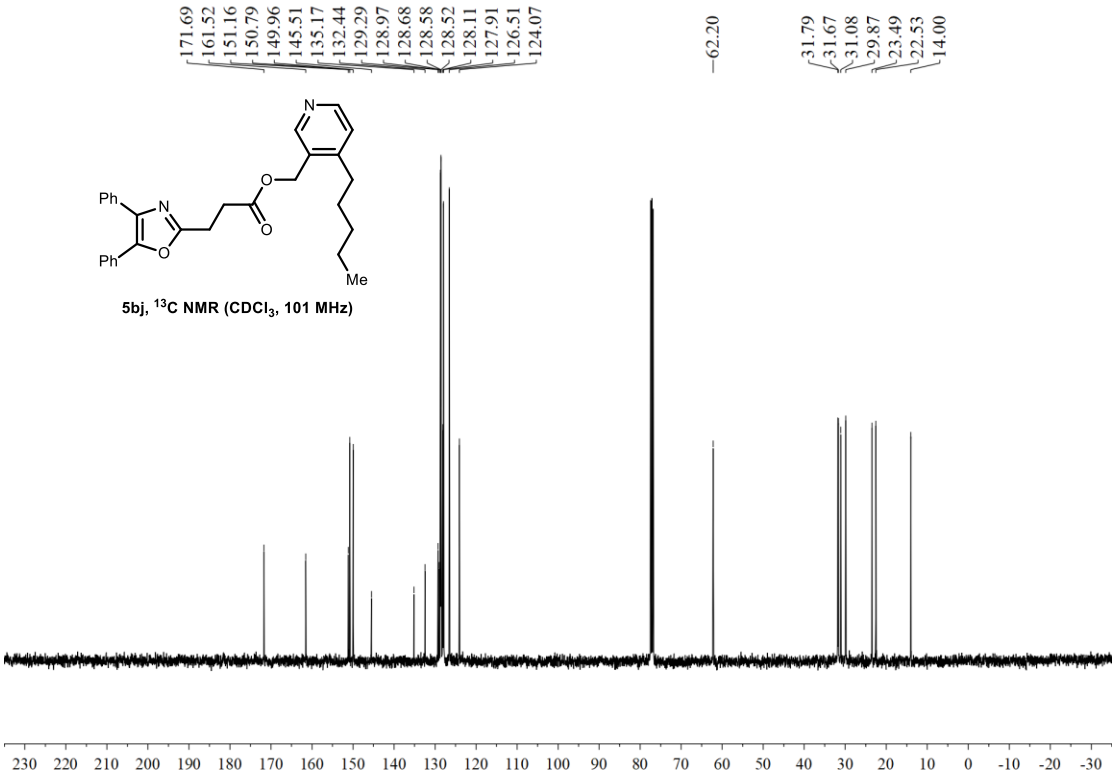


Figure S194. ^{13}C NMR of **5bj** ($CDCl_3$, 101 MHz)

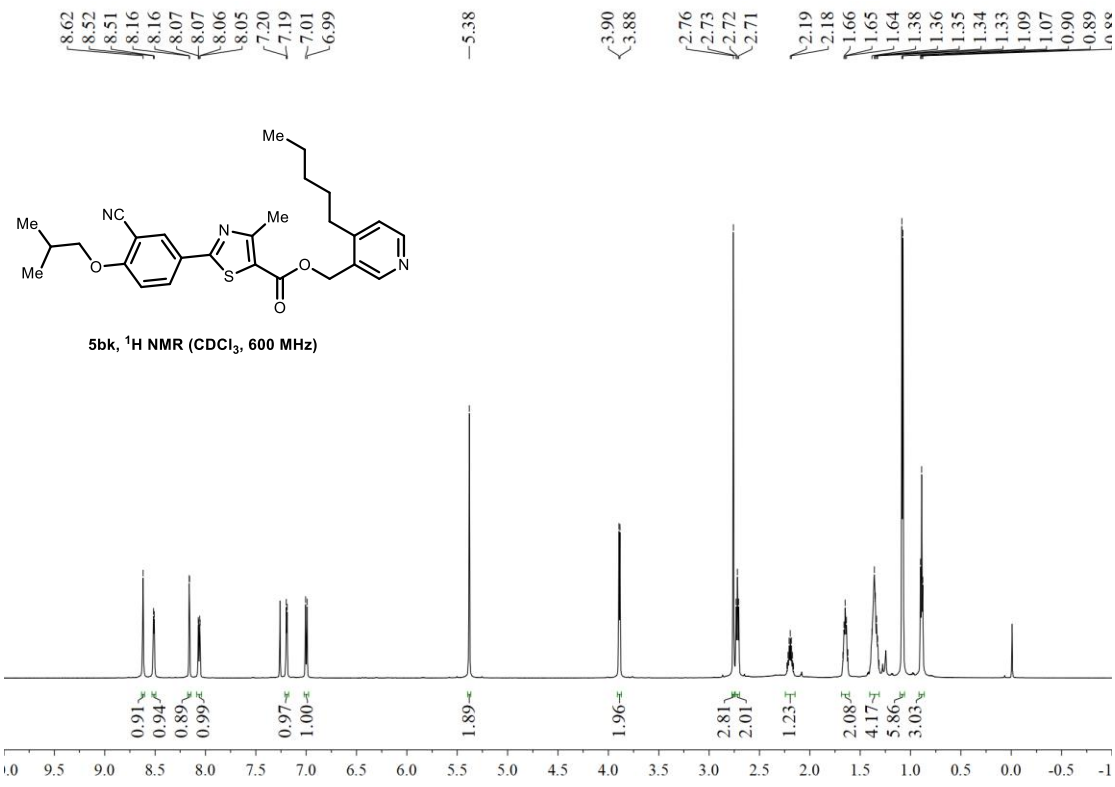


Figure S195. ^{1}H NMR of **5bk** ($CDCl_3$, 600 MHz)

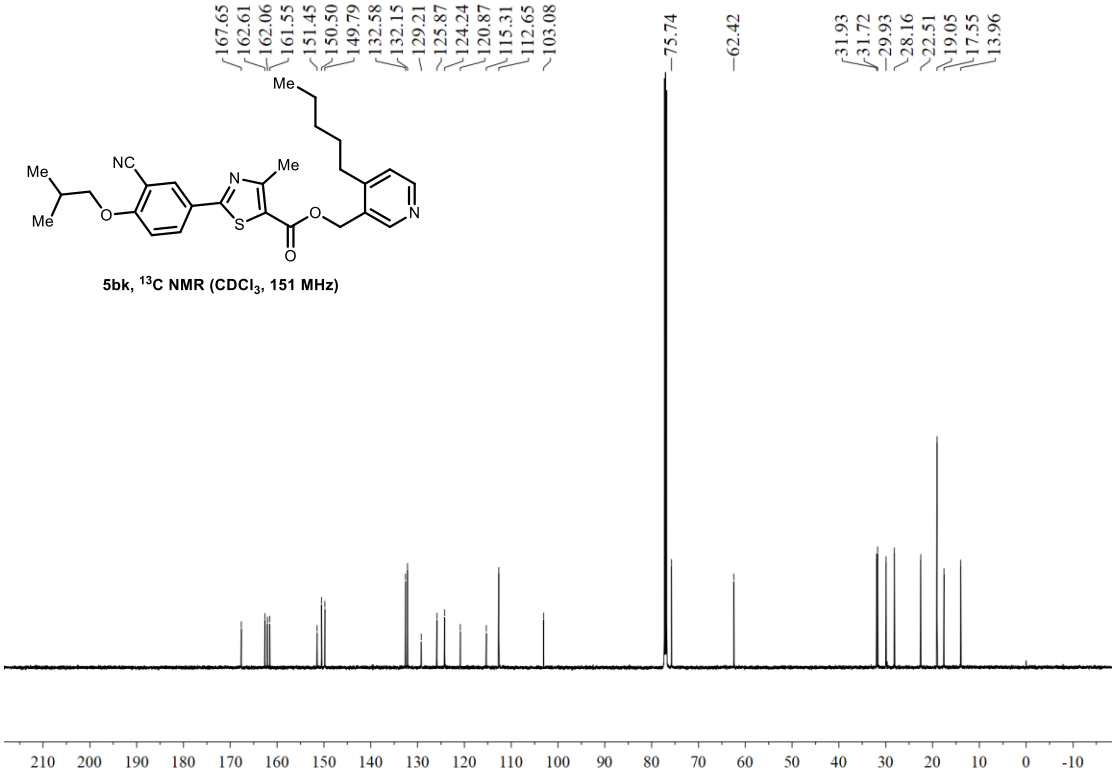


Figure S196. ^{13}C NMR of **5bk** ($CDCl_3$, 151 MHz)

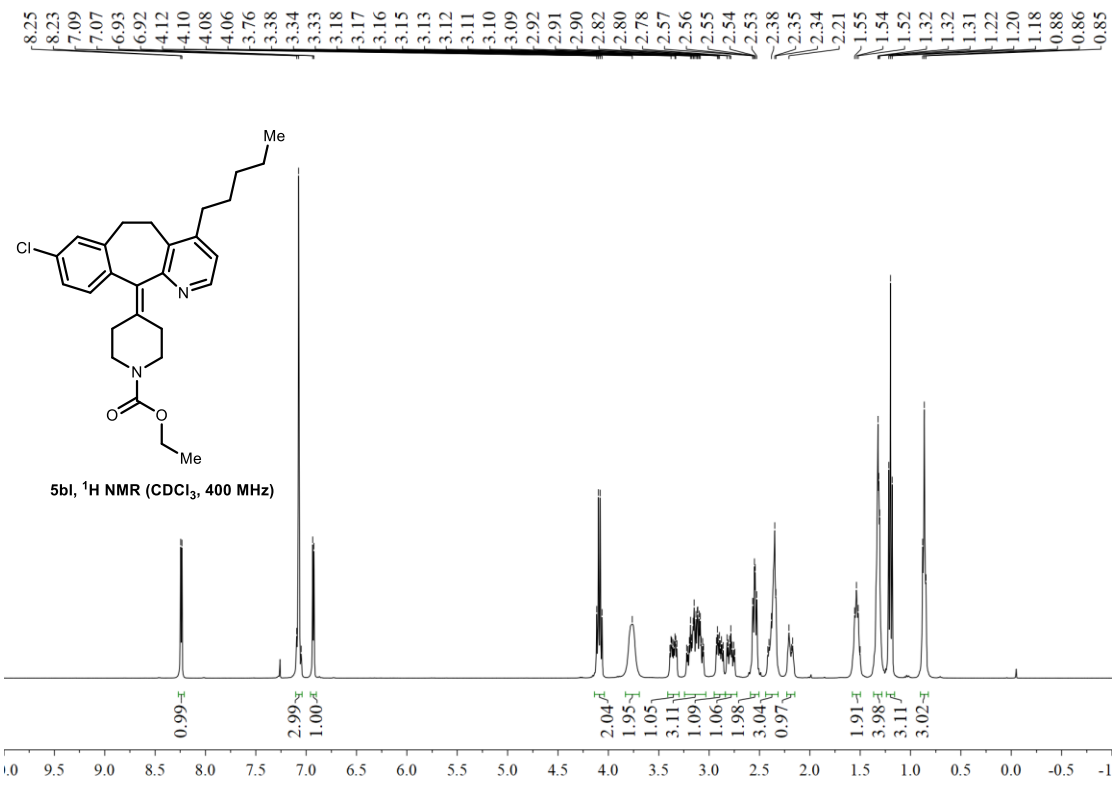


Figure S197. ^{1}H NMR of **5bl** (CDCl$_3$, 400 MHz)

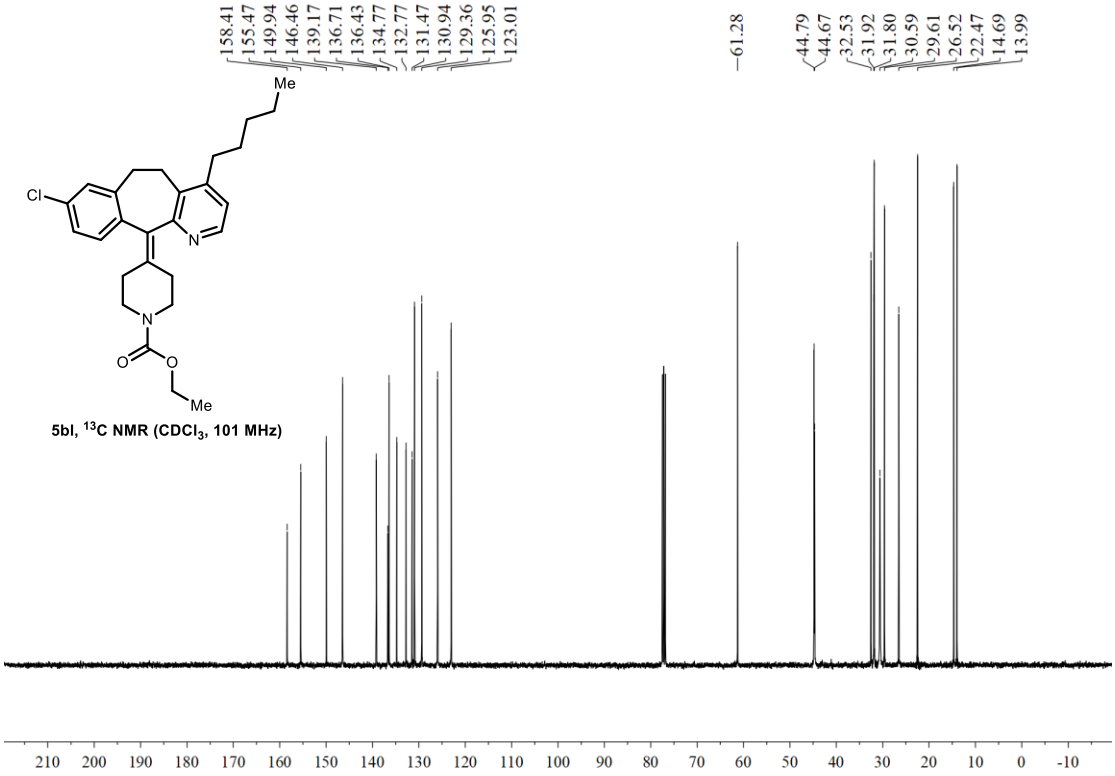


Figure S198. ^{13}C NMR of **5bl** (CDCl$_3$, 101 MHz)

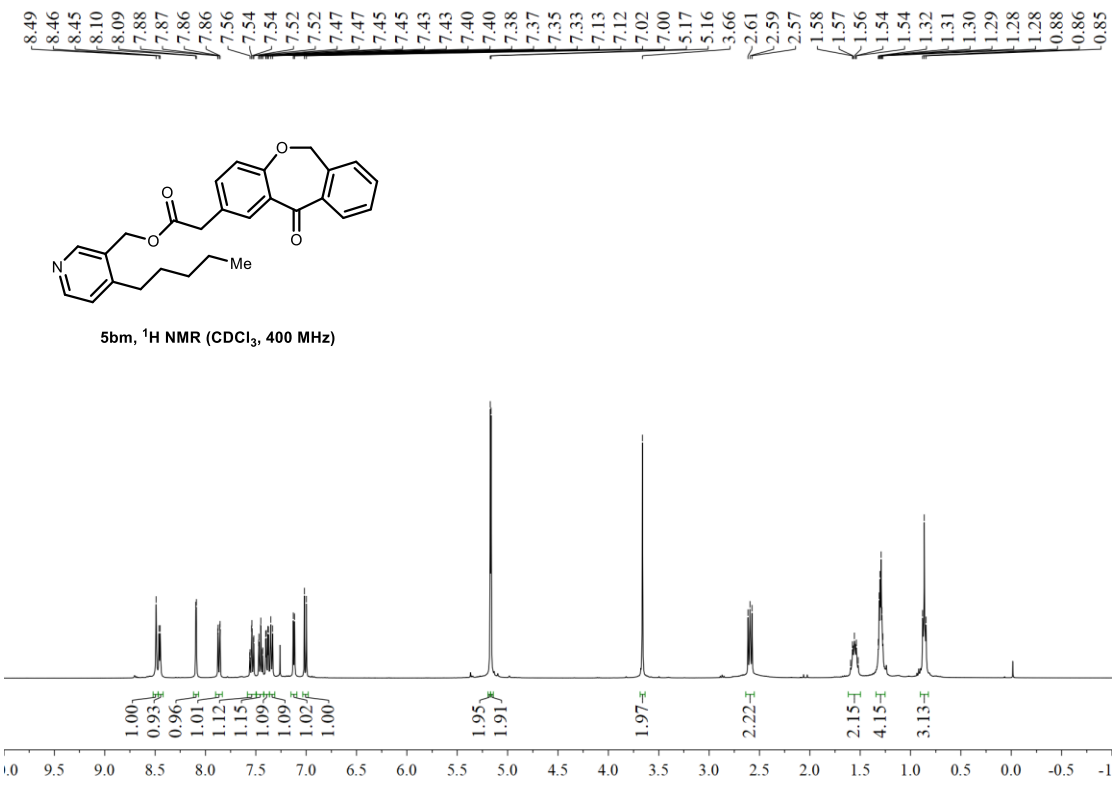


Figure S199. ^{1}H NMR of **5bm** (CDCl$_3$, 400 MHz)

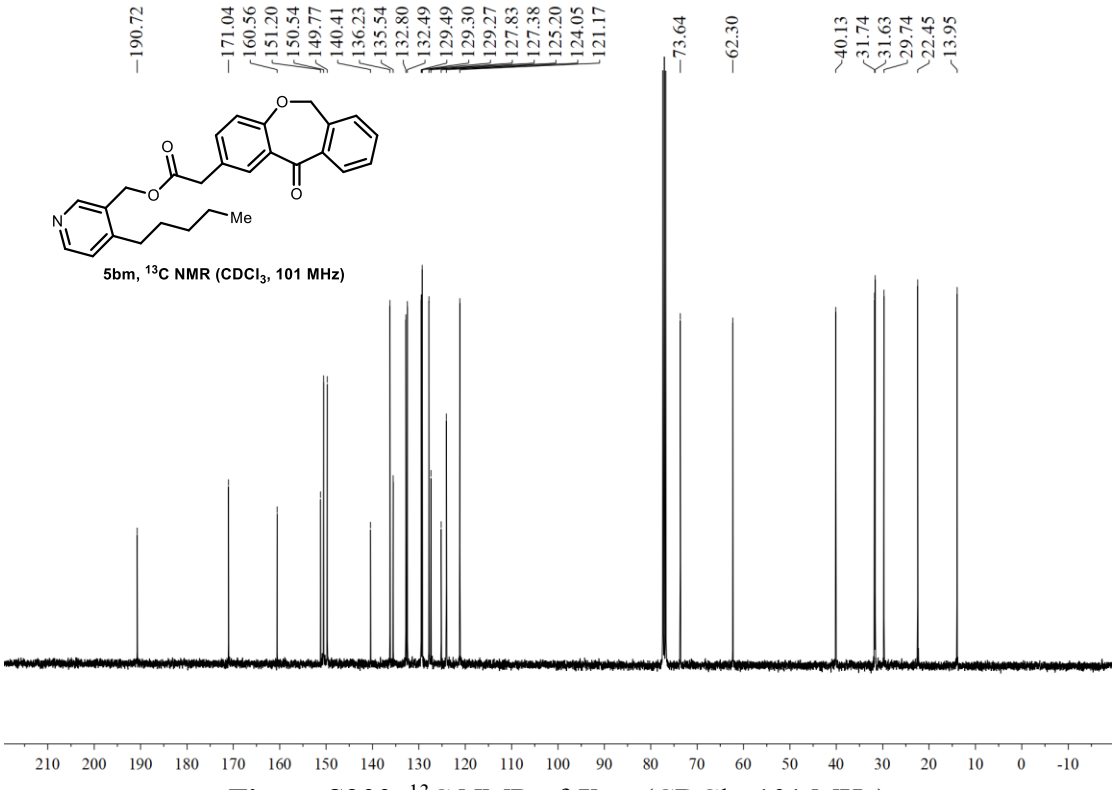


Figure S200. ^{13}C NMR of **5bm** (CDCl$_3$, 101 MHz)

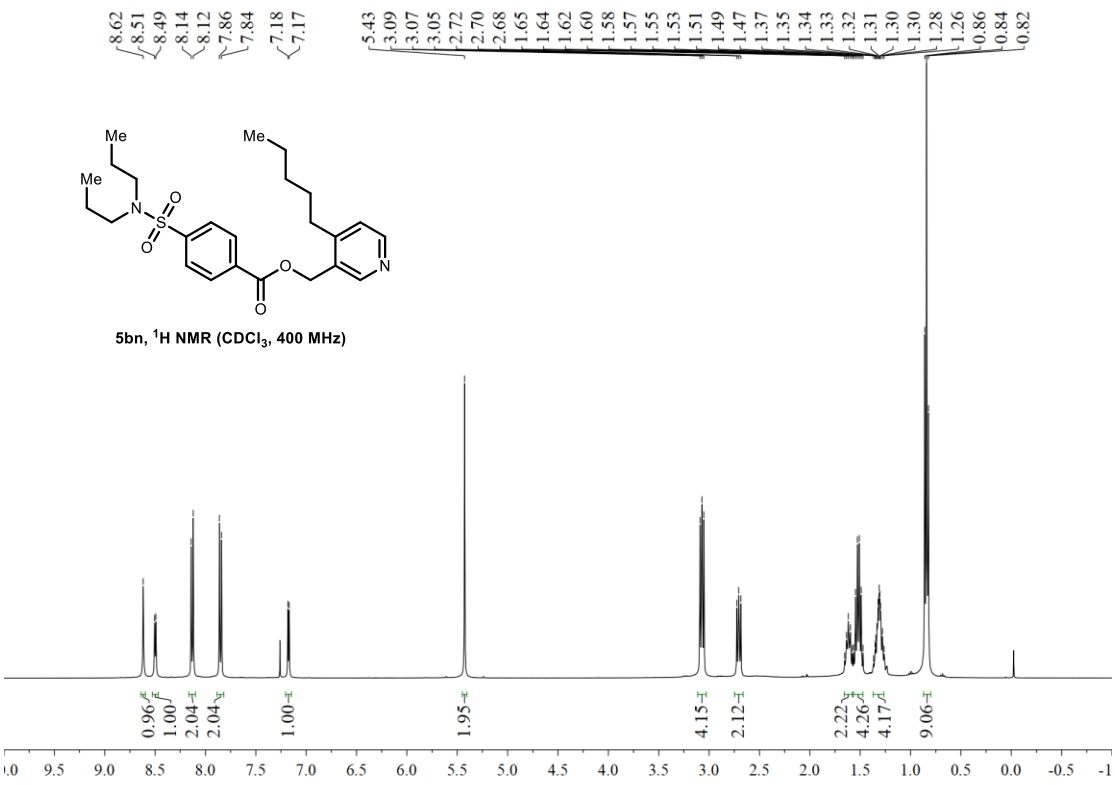


Figure S201. ^{1}H NMR of **5bn** ($CDCl_3$, 400 MHz)

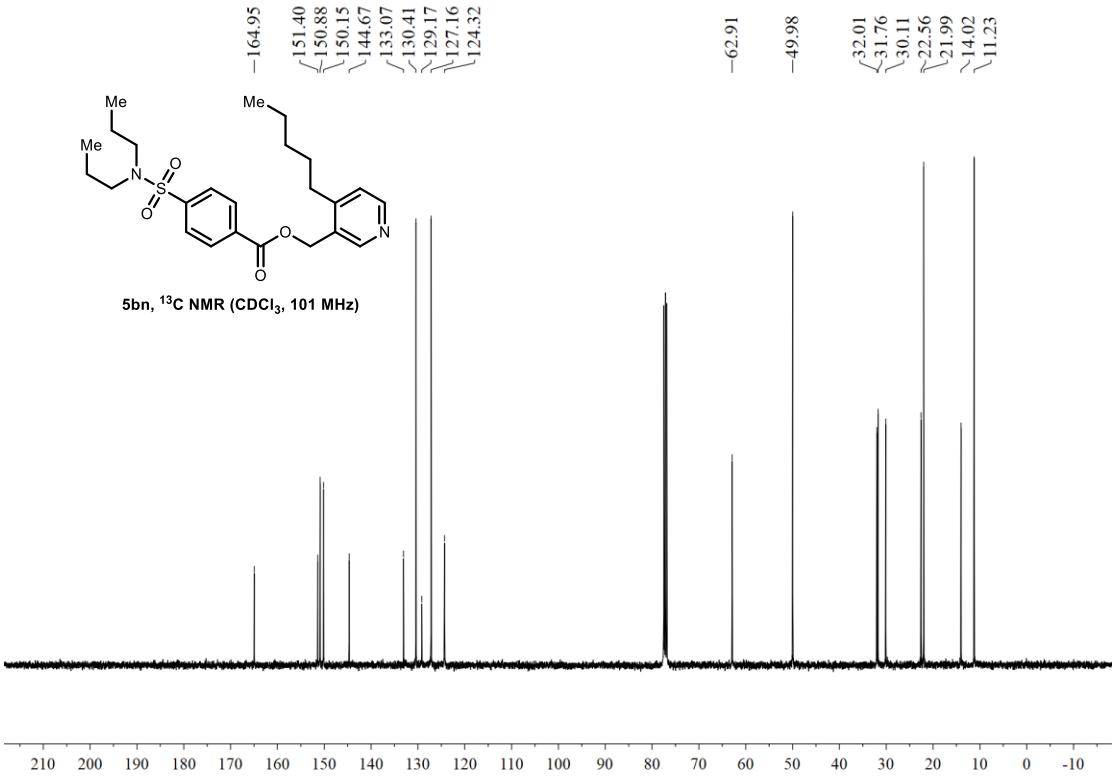


Figure S202. ^{13}C NMR of **5bn** ($CDCl_3$, 101 MHz)

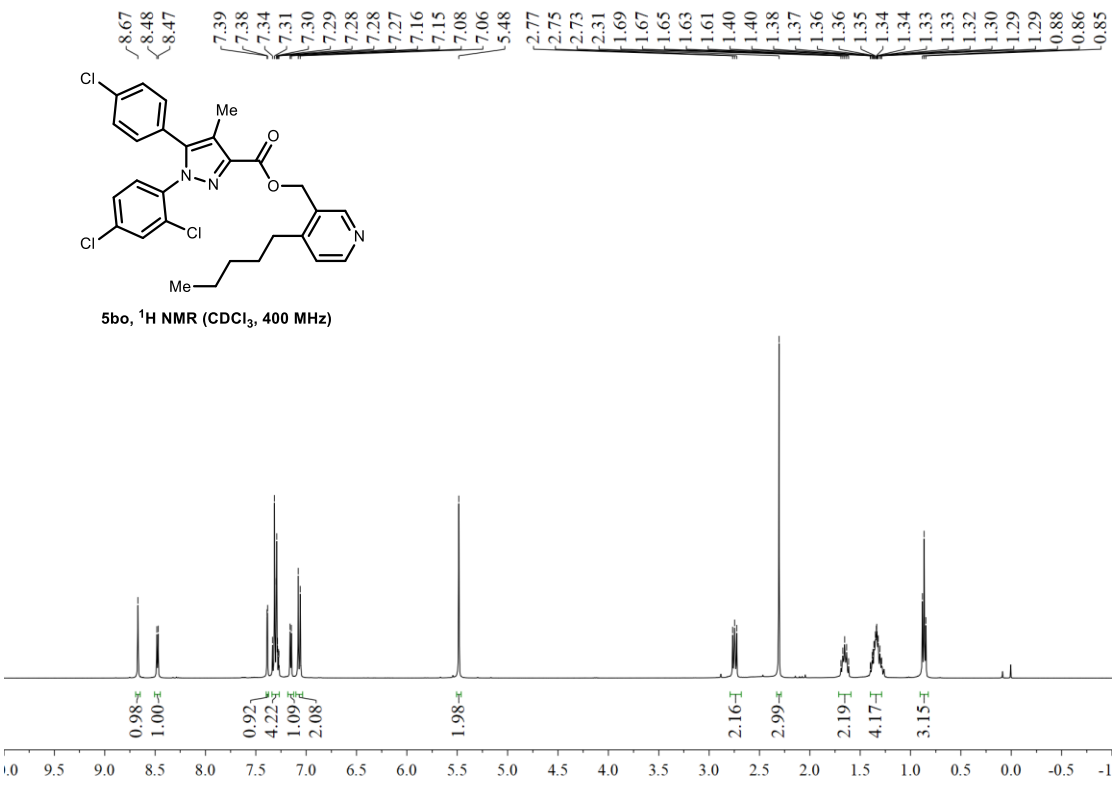


Figure S203. ^{1}H NMR of **5bo** ($CDCl_3$, 400 MHz)

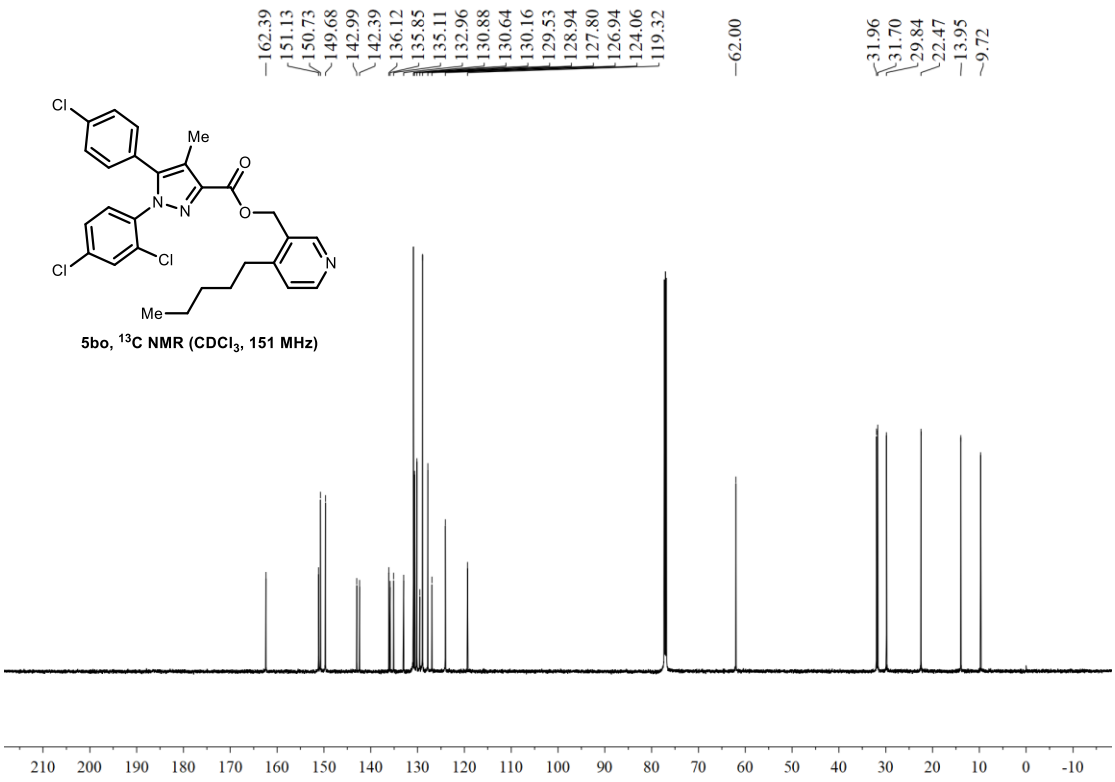


Figure S204. ^{13}C NMR of **5bo** ($CDCl_3$, 151 MHz)

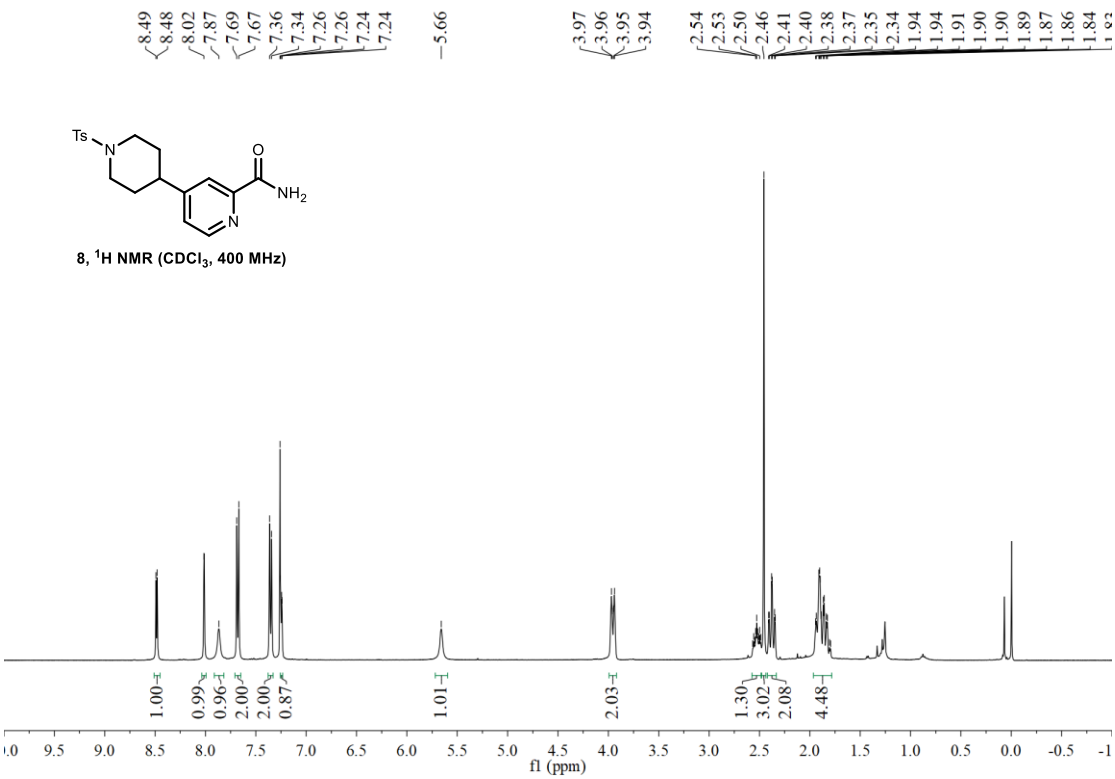


Figure 205. ^{1}H NMR of **8** ($CDCl_3$, 400 MHz)

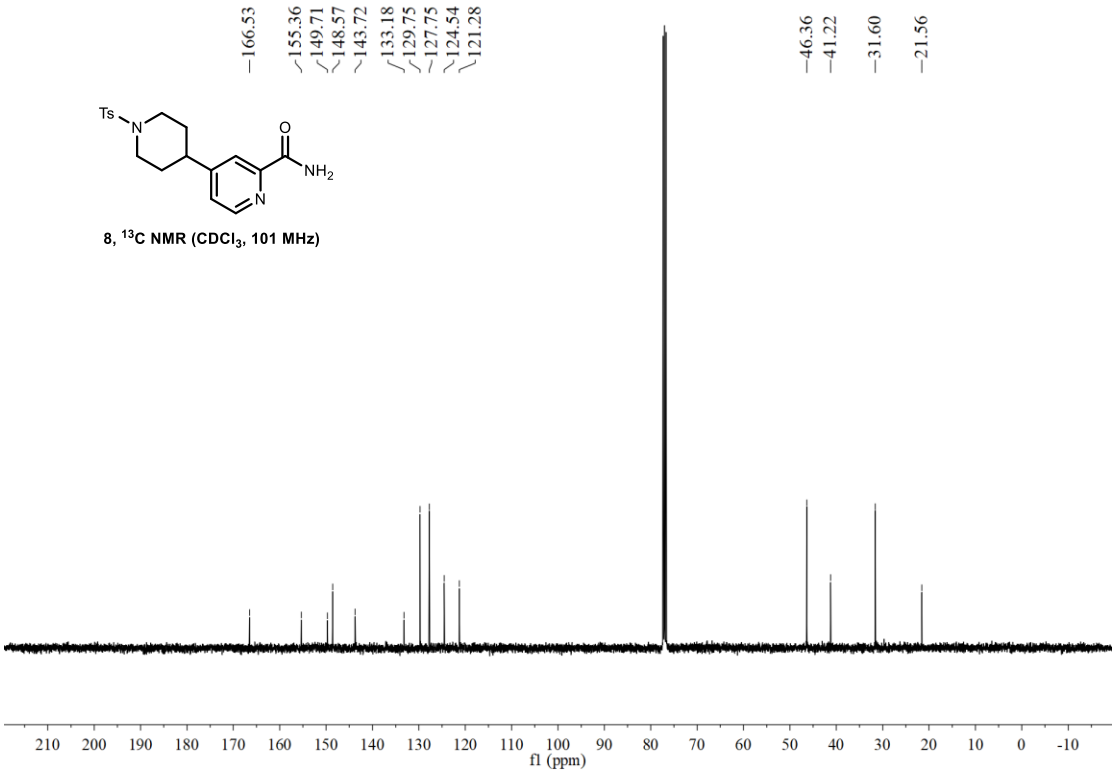


Figure S206. ^{13}C NMR of **8** ($CDCl_3$, 101 MHz)

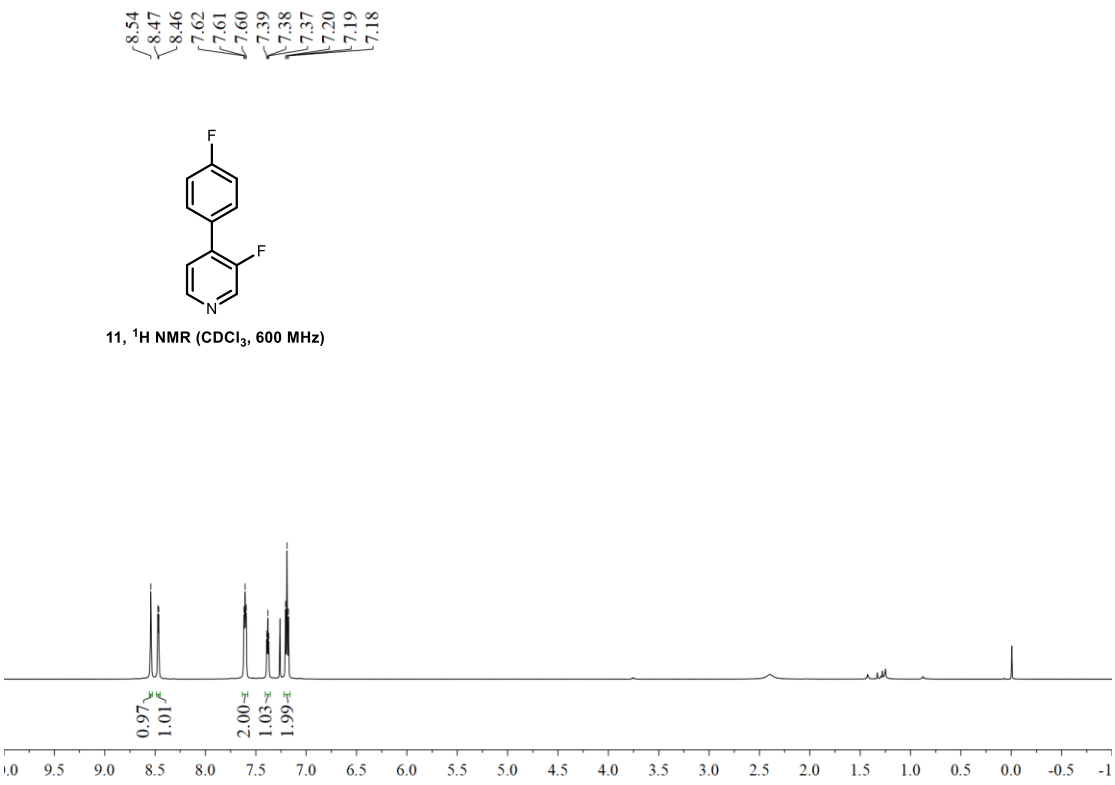


Figure S207. ^{1}H NMR of **11** ($CDCl_3$, 600 MHz)

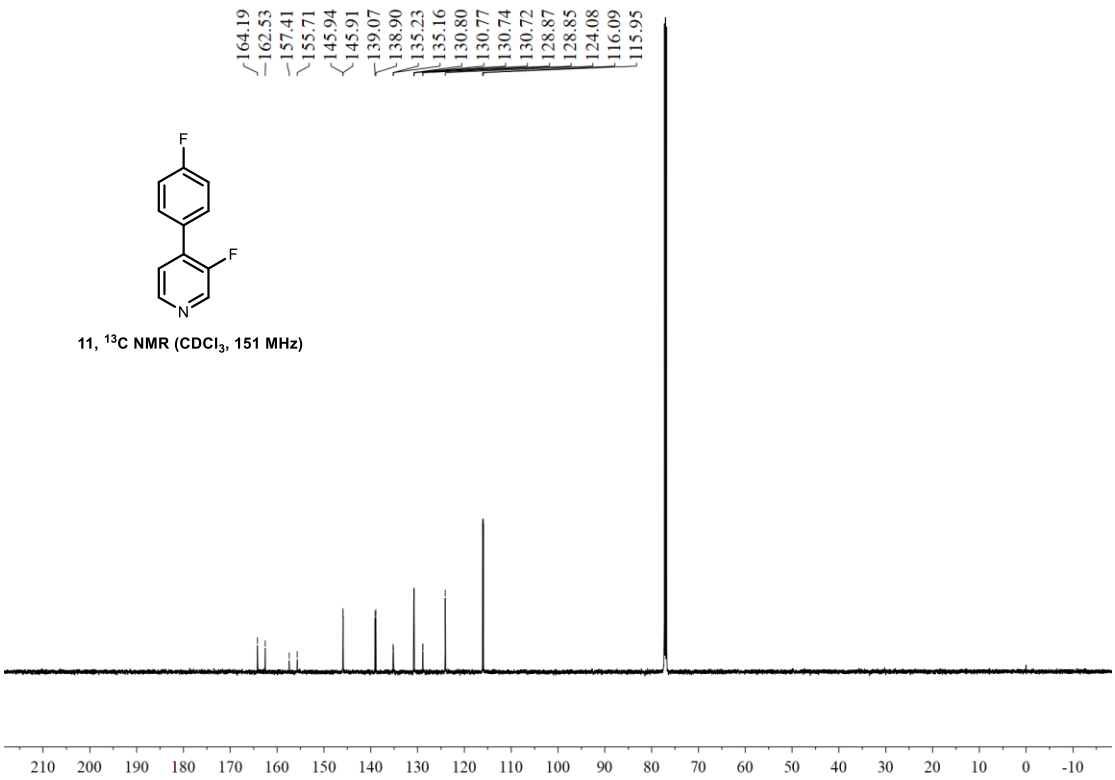


Figure S208. ^{13}C NMR of **11** ($CDCl_3$, 151 MHz)

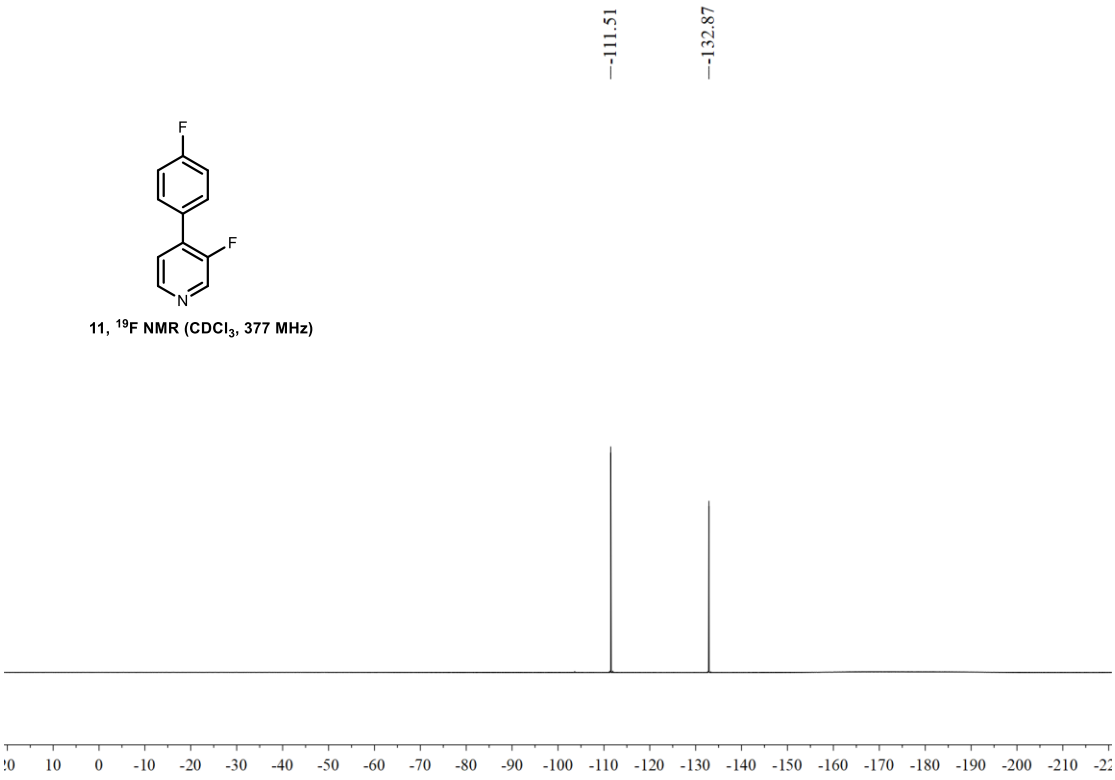


Figure S209. ^{19}F NMR of **11** ($CDCl_3$, 377 MHz)

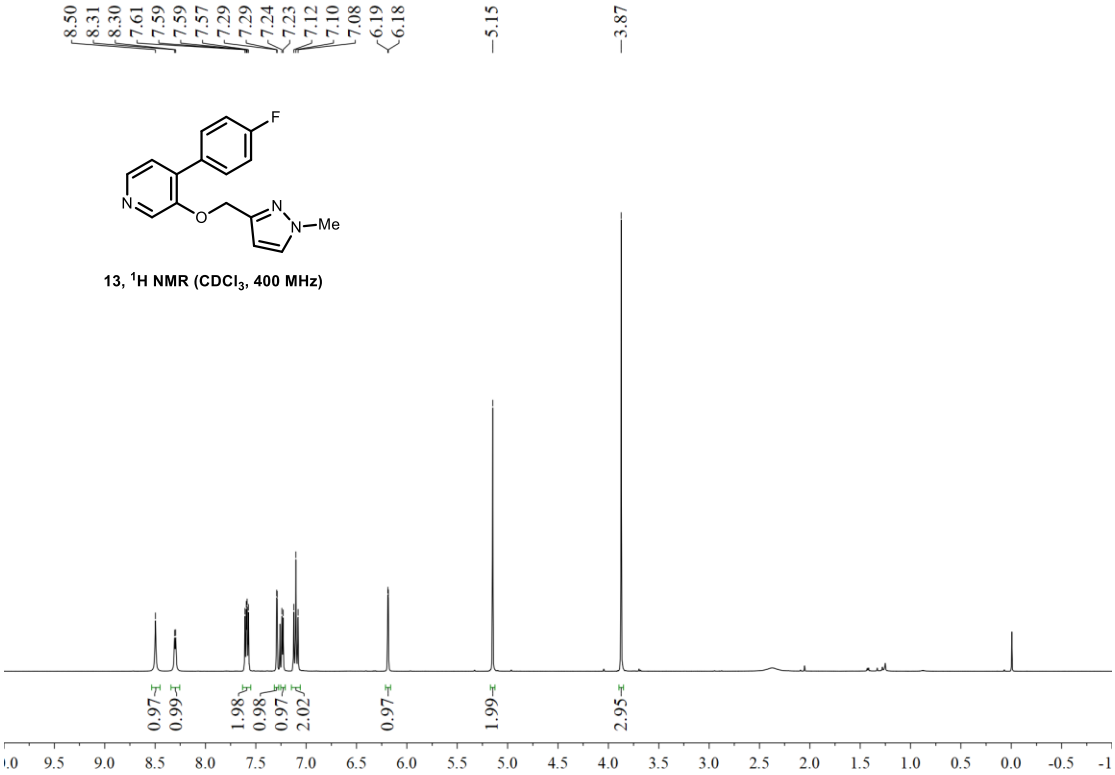


Figure S210. ^{1}H NMR of **13** ($CDCl_3$, 400 MHz)

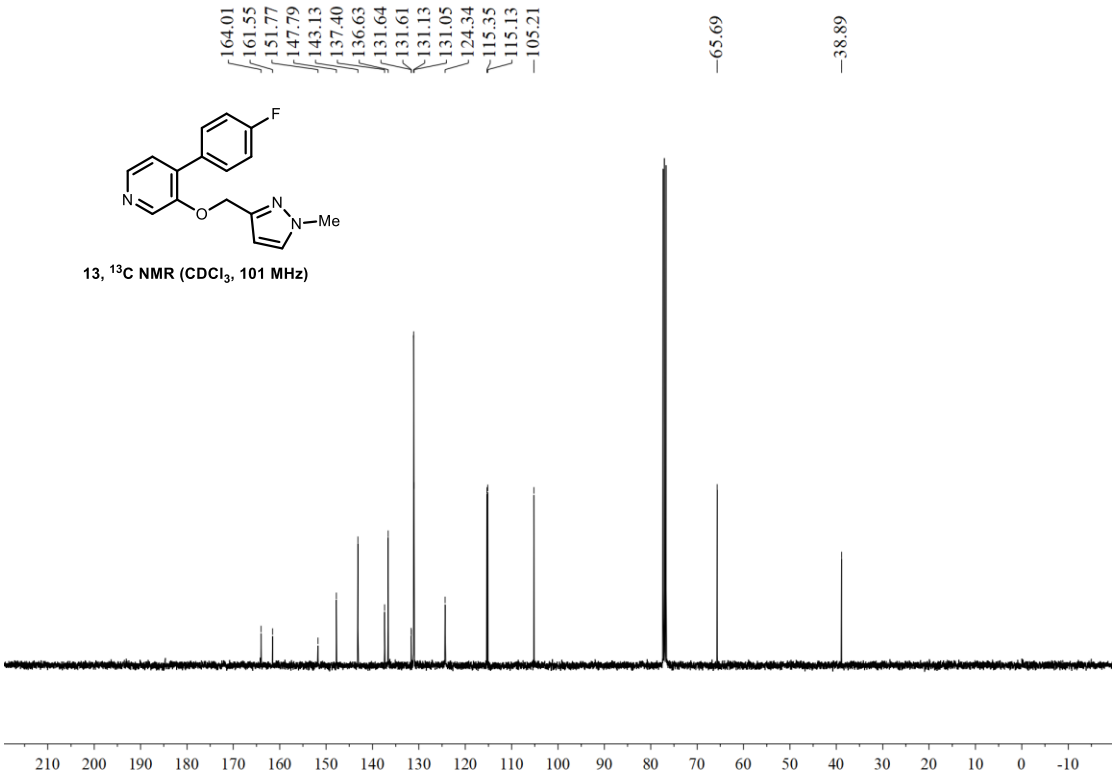


Figure S211. ^{13}C NMR of **13** ($CDCl_3$, 101 MHz)

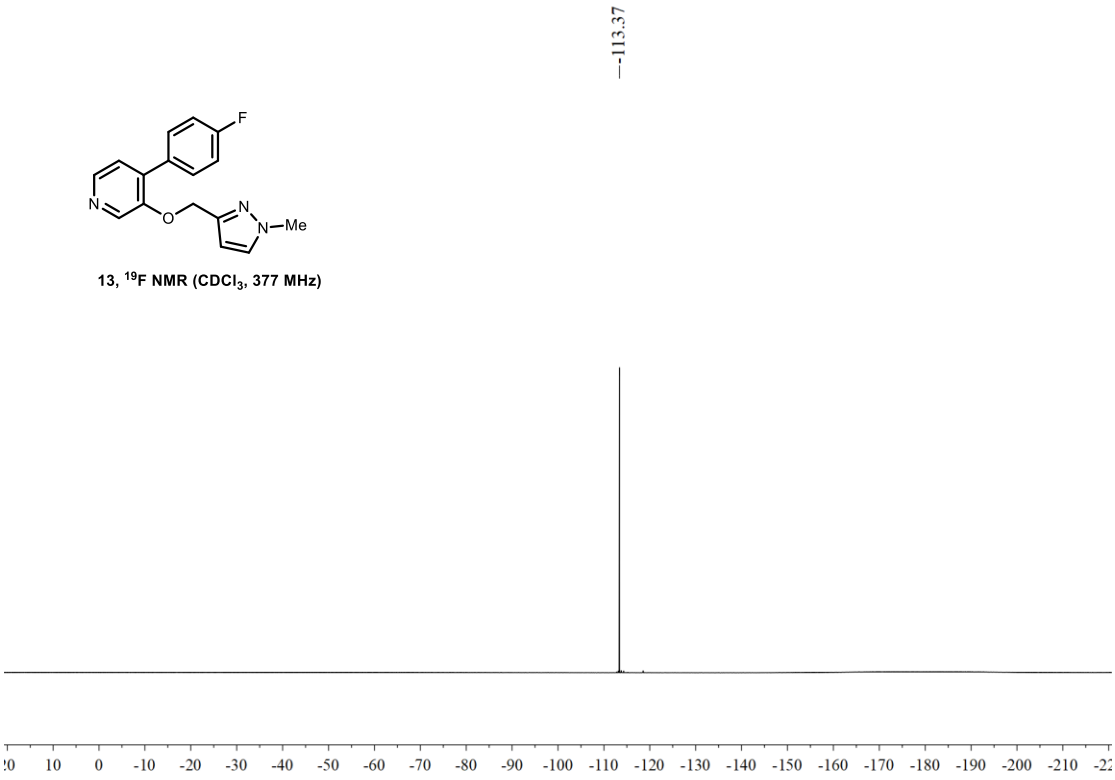


Figure S212. ^{19}F NMR of **13** ($CDCl_3$, 377 MHz)

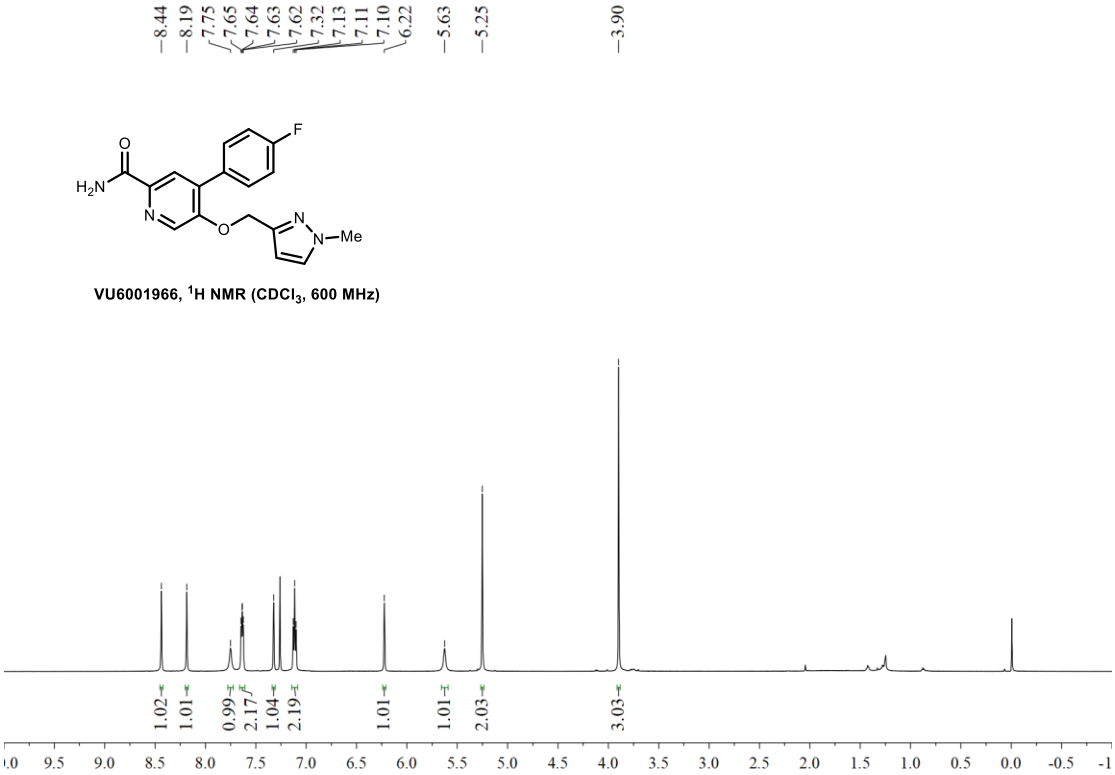


Figure S213. ^{1}H NMR of **VU6001966** ($CDCl_3$, 600 MHz)

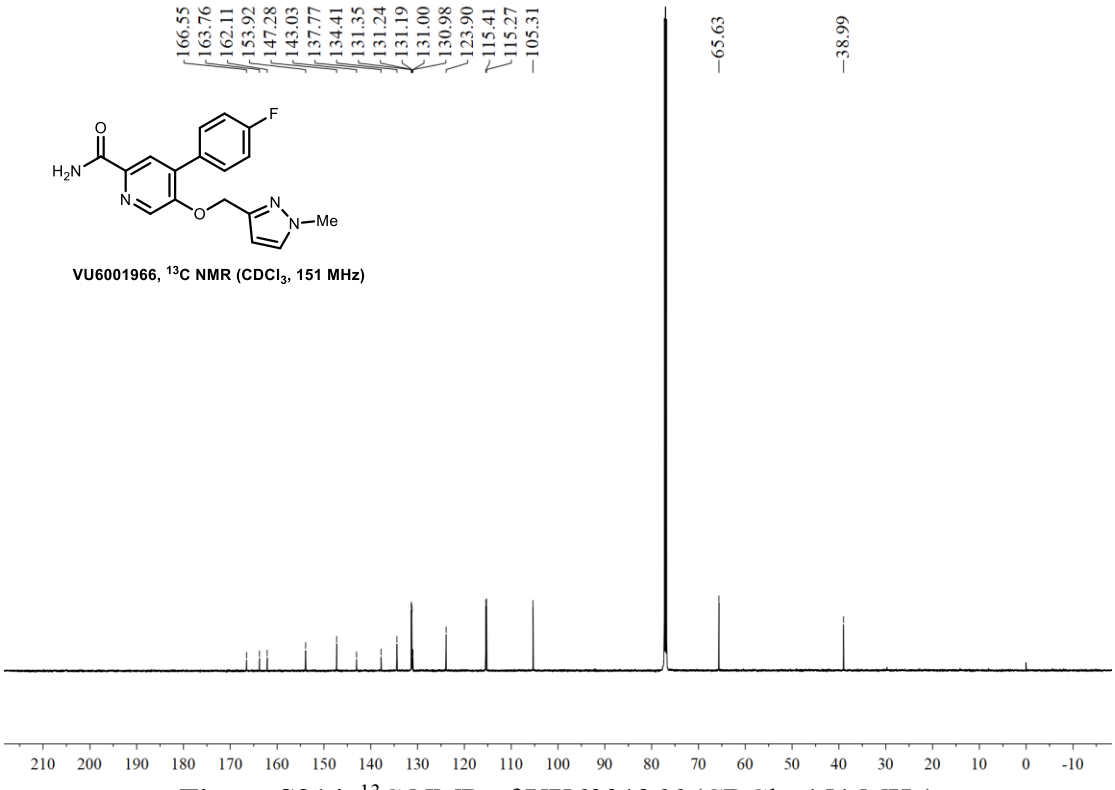


Figure S214. ^{13}C NMR of **VU6001966** ($CDCl_3$, 151 MHz)

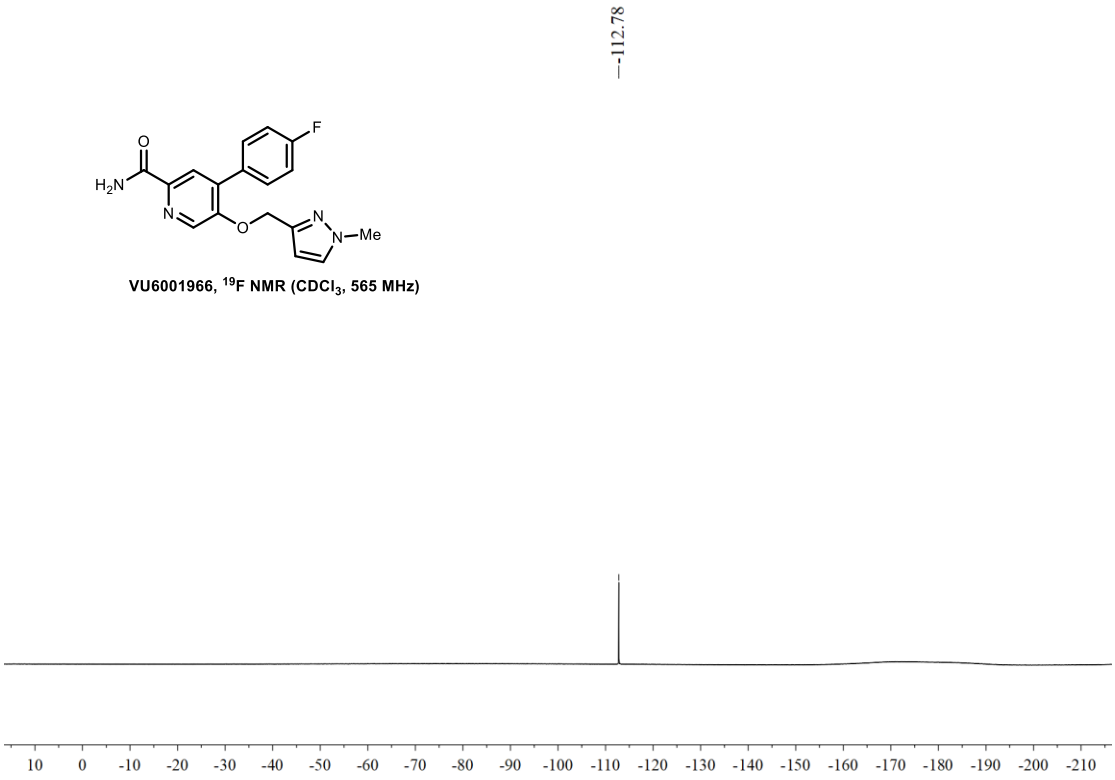


Figure S215. ^{19}F NMR of **VU6001966** ($CDCl_3$, 565 MHz)

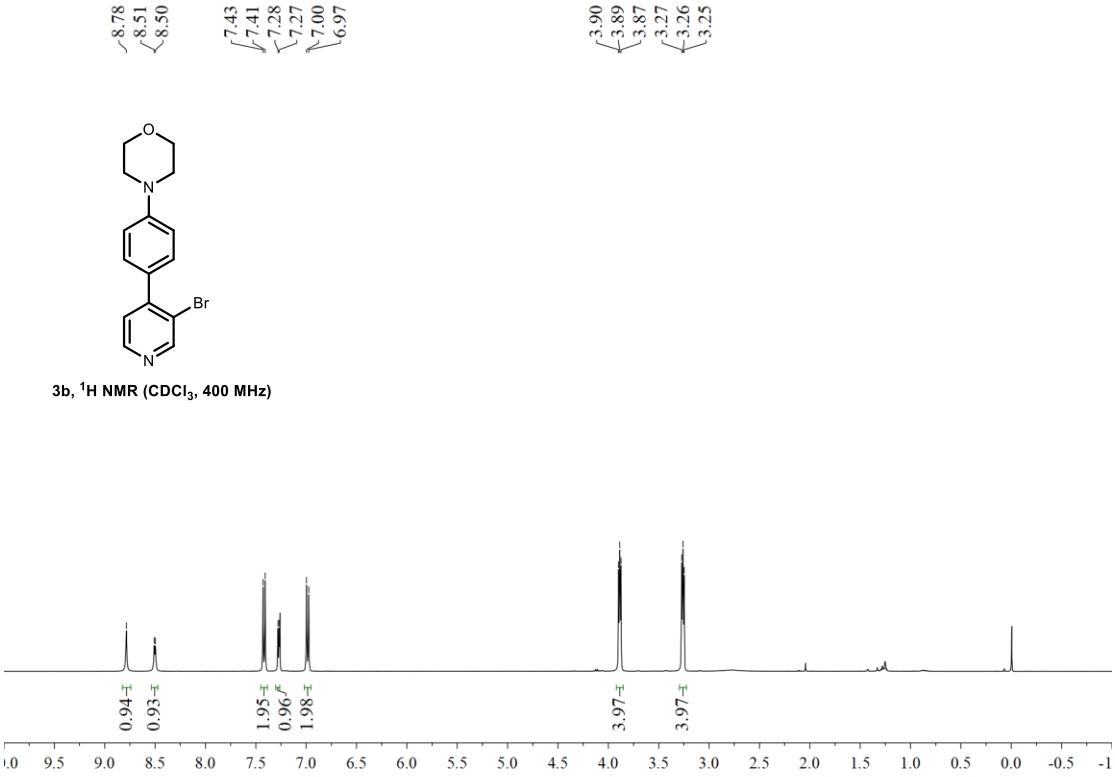


Figure S216. ^{1}H NMR of **17** ($CDCl_3$, 400 MHz)

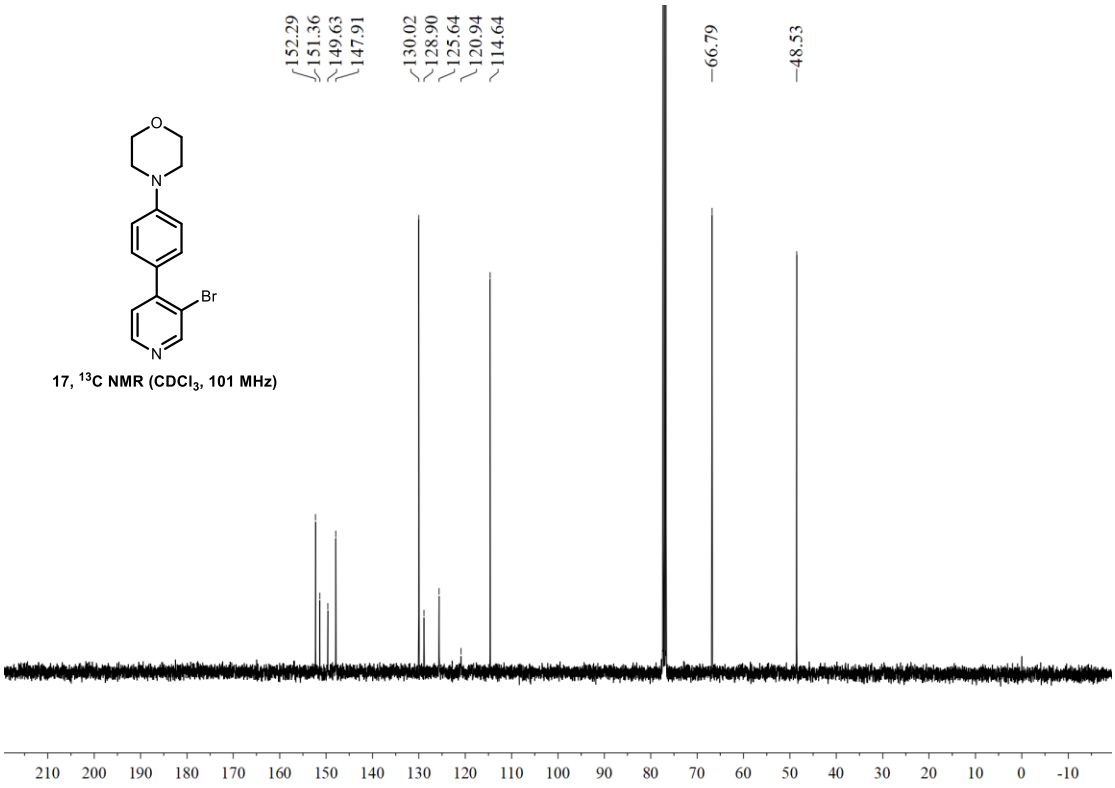


Figure S217. ^{13}C NMR of **17** ($CDCl_3$, 101 MHz)

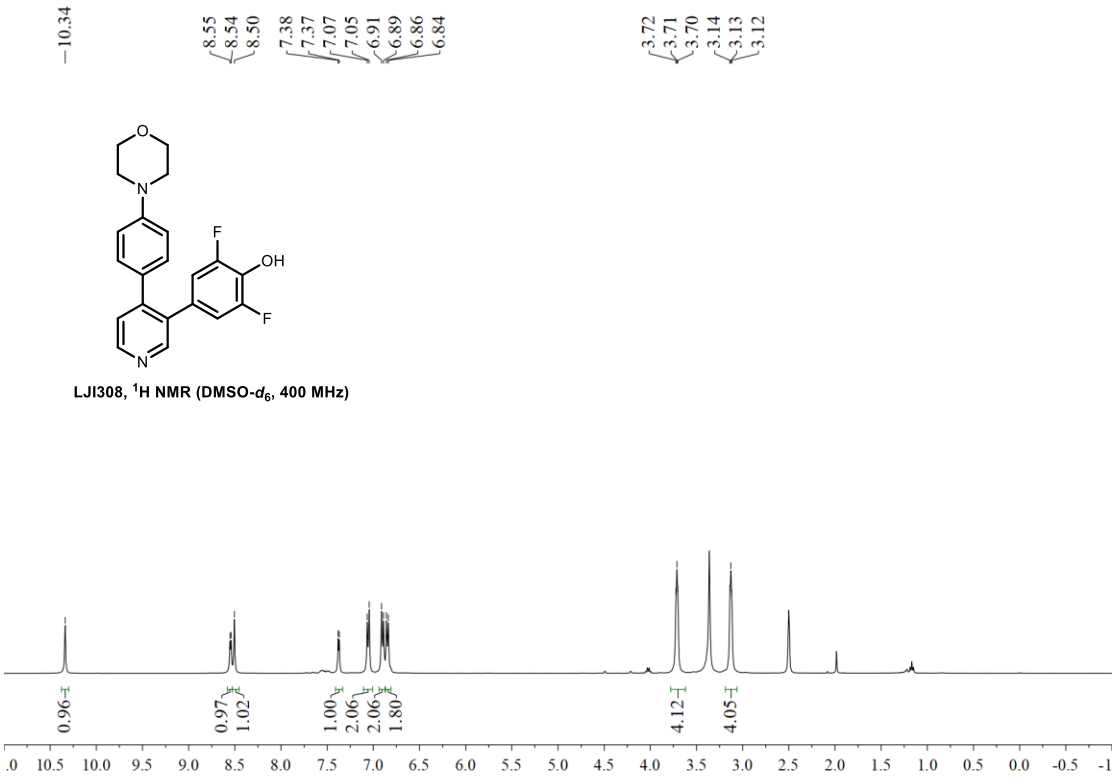


Figure S218. ^{1}H NMR of **LJI308** (DMSO-d_6, 400 MHz)

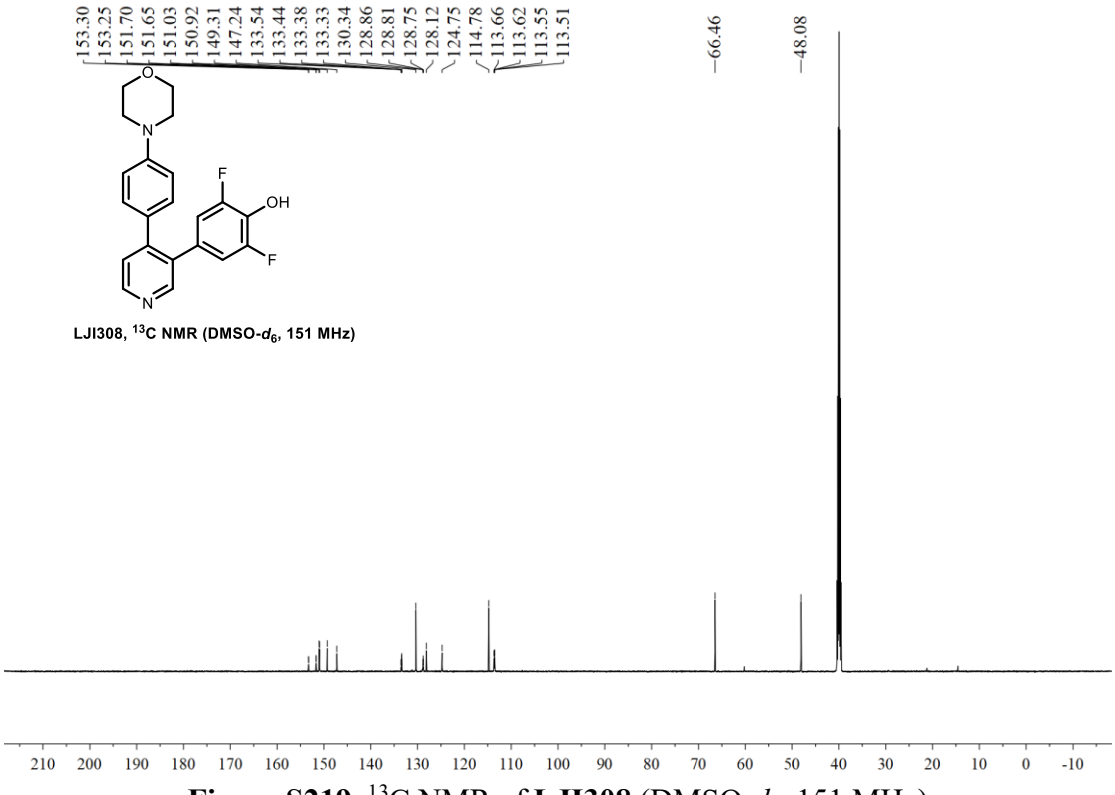


Figure S219. ^{13}C NMR of **LJI308** (DMSO-d_6, 151 MHz)

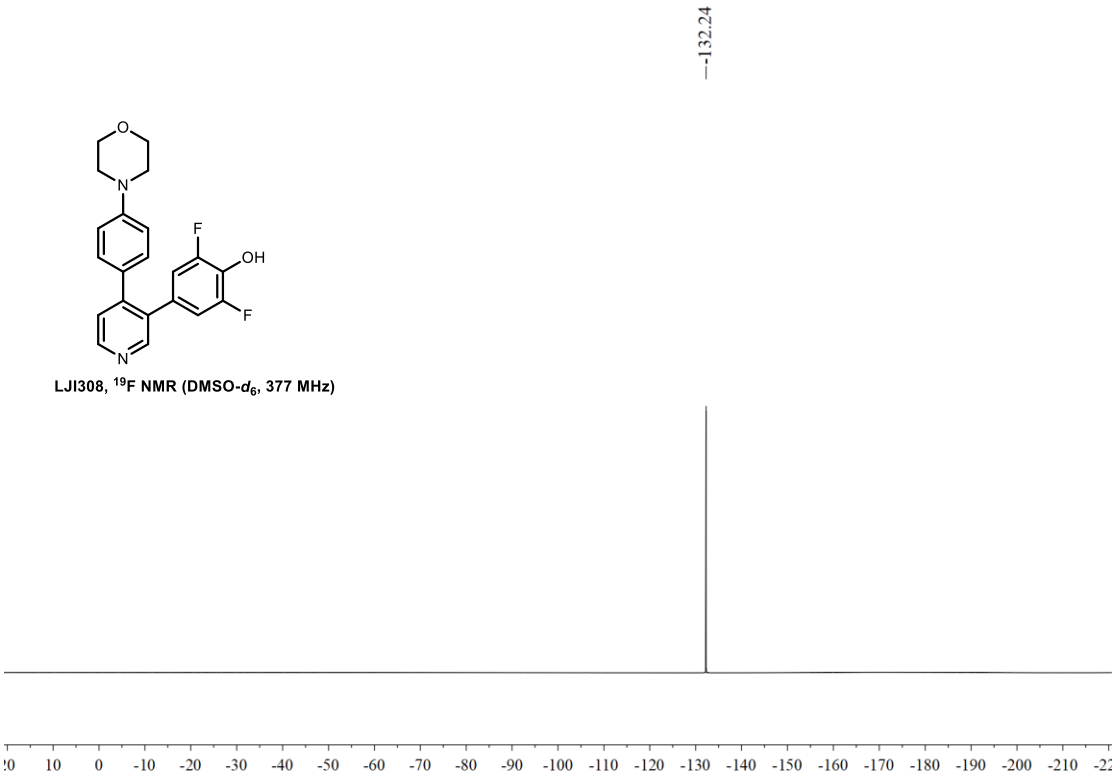


Figure S220. ^{19}F NMR of **LJI308** (DMSO-d_6, 377 MHz)