Supporting Information

Lewis Basic Salt-Promoted Organosilane Coupling Reactions with Aromatic Electrophiles

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I. General Information

General Reagent Information: Cesium fluoride (TCI catalog #C2204) and 18-crown-6 (Chem-Impex catalog #03901) were purchased from Fisher Scientific and stored in a nitrogen-filled glovebox prior to use. Benzyltrimethylsilane (catalog #QA-9873) was purchased from Combi-Blocks. 2,2,6,6-Tetramethyl-1-piperidinyloxy (TEMPO) was purchased from Millipore Sigma (catalog #426369, purified by sublimation, 99%). Anhydrous solvents: dimethyl sulfoxide (catalog #276855), tetrahydrofuran (catalog #186562), 1,2-dimethoxyethane (catalog #259527) and *N,N*-dimethylformamide (catalog #227056) were used as received from Millipore Sigma. Tetrahydrofuran and dichloromethane solvents were deoxygenated and dried by passage over packed columns of neutral alumina and copper (II) oxide under positive pressure of nitrogen. All other commercially available reagents and solvents were purchased from Alfa Aesar, Combi-Blocks, Acros Organics or Millipore Sigma and used as received. Column chromatography was performed using 40-63 µm silica gel (SiliaFlash® F60 from Silicycle) or Basic Alumina 60-325 Mesh (Fisher Chemical Cat. # A941-500). Preparative thin-layer chromatography (PTLC) was performed on silica gel 60Å F254 plates (20 x 20 cm, 1000 µm, SiliaPlate from Silicycle, #TLG-R10011B-341) and visualized with UV light (254 nm).

General Analytical Information: All new compounds were characterized by ^{1}H, ^{13}C and ^{19}F NMR spectroscopy, IR spectroscopy, mass spectrometry, melting point analysis (if solids) and specific rotation analysis (if chiral). NMR spectra were recorded on Bruker Avance NEO or Varian Inova 400 spectrometers. Chemical shifts for ^{1}H NMR are reported as follows: chemical shift in reference to residual $CHCl_3$ at 7.26 ppm (δ ppm), multiplicity (s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets, dq = doublet of quartets, qd = quartet of doublets, m = multiplet), coupling constant (Hz), and integration. Chemical shifts for ^{13}C NMR are reported in terms of chemical shift in reference to the $CDCl_3$ solvent signal (77.16 ppm). Chemical shifts for ^{19}F NMR are reported in terms of chemical shift in reference to an internal standard (fluorobenzene set to δ -112.96 ppm); reported ^{19}F NMR data are for proton-decoupled spectra and are provided in Section XIV. IR spectra were recorded on a Thermo Scientific Nicolet iS-50 FT-IR spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Melting points were measured on a Mel-Temp capillary melting point apparatus. Mass spectra were obtained via ESI-MS (Agilent 6210) or GC-MS (Agilent 7890B with Agilent 5977A MSD) provided by Colorado State University Analytical Resource Core – Molecular and Materials Analysis Center. Thin-layer chromatography (TLC) was performed on silica gel 60Å F254 plates (250 µm, SiliaPlate from Silicycle, #TLG-R10014B-323) and visualized with UV light (254 nm) and/or potassium permanganate stain.

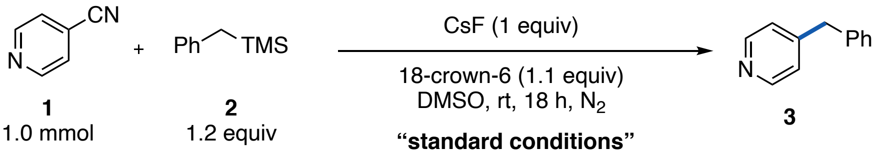
Nomenclature Note: The names provided for the structures below were obtained from ChemDraw Professional 20.0.

Note regarding safety of generated waste: Cyanide salt-containing waste that is produced as a byproduct in the reactions described below should be handled with great care. Cyanide is highly toxic and could lead to the release of poisonous HCN gas. Reaction setup and workup should be conducted in well-ventilated enclosures (e.g. fume hood). Aqueous cyanide-containing waste generated during workup should be stored at a basic pH in a designated “Cyanide Waste” container and disposed of safely in accordance with local guidelines.

II. Analysis and Optimization of Reaction Conditions

Optimization of arylation reaction. 4-Cyanopyridine (**1**) was used as a model arene substrate for the optimization of the arylation reaction using benzyltrimethylsilane (**2**). In a nitrogen-filled glovebox, to an oven-dried 2-dram glass vial (8 mL, Thermo Scientific, B7999-3) equipped with a magnetic stir bar was added 4-cyanopyridine (0.104 g, 1.0 mmol, 1.0 equiv), the Lewis base (1.0 mmol, 1 equiv), a solution of 18-crown-6 (1M in THF, 1.1 mL, 1.1 equiv) if noted, and anhydrous solvent (2.9 mL, 0.25 M of cyanoarene relative to total solvent volume). Benzyltrimethylsilane (229 µL, 1.2 mmol, 1.2 equiv) was added in one portion and the vial was sealed with a screw cap (Thermo Scientific, B7807-15) equipped with a 2.6 mm PTFE/Silicone Septa (Thermo Scientific, B7995-15). The sealed reaction vial was removed from the glovebox and the reaction mixture was vigorously stirred at room temperature for 18 h. The reaction vial was then opened and CH_2Br_2 (0.1 mmol, 7 µL) was added as an internal standard. The reaction mixture was analyzed by ^1H NMR spectroscopy and the product yield was determined by integration of the product methylene signal relative to CH_2Br_2 comparing to an authentic sample of 4-benzylpyridine (TCI Cat. # B0437) and whose characterization was further confirmed in the preparative scale arylation reaction in Section V of the Supporting Information. The optimized conditions and influences of changes in reaction parameters are shown in Table S1 below.

Table S1. Optimization of 4-cyanopyridine benzylation.



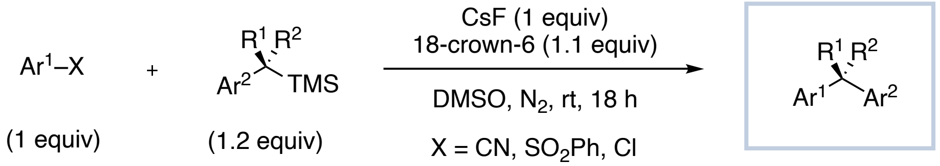
Entry	Deviation from standard conditions	^{1}H NMR yield
1	3 h	95%
2	strict absence of light	96%
3	set up in glovebox, stirred 18 h open to air	91%
4	60 ºC, 30 min	65%
5	no CsF, rt	0
6	no 18-crown-6, rt	80%
7	no CsF or 18-crown-6, rt	0
8	no CsF or 18-crown-6, 60 ºC	0
9	KF instead of CsF	83%
10	Cs_2CO_3 instead of CsF	35%
11	CsOH•H_2O instead of CsF	37%
12	KHF_2 instead of CsF	58%
13	K_3PO_4 instead of CsF	20%
14	NaOPh instead of CsF	43%
15	KF without 18-crown-6, rt	13%
17	KF without 18-crown-6, 100 ºC	84%
19	KOMe without 18-crown-6, rt	50%
21	KOMe without 18-crown-6, rt, NMP	83%
23	NaOPh without 18-crown-6, 60 ºC	72%
26	NaOPh without 18-crown-6, 100 ºC, NMP	89%
29	Cs_2CO_3 without 18-crown-6, 100 ºC	57%
30	anhydrous EtOAc instead of DMSO	21%
31	anhydrous DME instead of DMSO	53%
32	anhydrous NMP instead of DMSO	95%
33	anhydrous DMF instead of DMSO	95%

34	anhydrous MeCN instead of DMSO	52%
35	anhydrous acetone instead of DMSO	25%
36	CsF (99.9%) from Alfa Aesar (Cat.# 10019)	89%
37	CsF (99.9%) from Sigma Aldrich (Cat.# 289345)	83%
38	CsF (99.9%) from Strem (Cat.# 93-5518)	92%

Note on trace metals present in reaction components. To investigate the role of trace metals in this benzylation reaction, the Certificates of Analyses of various CsF were consulted. The data is provided below. Although we cannot rule out the role of trace metals in these reagents in the coupling reaction, we obtained consistent coupling results regardless of the supplier. Furthermore, the fact that 4-halopyridines do not couple under similar conditions also suggests that a transition metal-catalyzed process is not operative (see Section X).

Reagent	Trace Metals Detected (ppm)
CsF (99.9%) from Sigma Aldrich (cat. 289345) Lot#: 0000066330	Al (1.0ppm), B (0.3ppm), Ca (0.2ppm), Cr (1.0ppm), Fe (2.7ppm), K (4.4ppm), Li (0.5ppm), Na (2.4ppm), Ni (0.5ppm), Pb (0.3ppm), Rb (6.4ppm)
CsF (99.9%) from Alfa Aesar (cat. 10019) Lot#: U19F086	Al (0.9ppm), Ca (0.1ppm), Mg (<0.1ppm), K (17ppm), Li (<0.2ppm), Na (27ppm), Rb (58ppm), Ba (<0.5ppm)
CsF (99.9%) from Strem (cat. 93-5518) Lot#: 34902200	Al (0.9ppm), Ca (0.1ppm), Mg (<0.1ppm), K (17ppm), Li (<0.2ppm), Na (27ppm), Rb (58ppm), Ba (<0.5ppm)

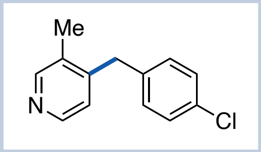
III. General Procedure for Arylation Reaction and Purification



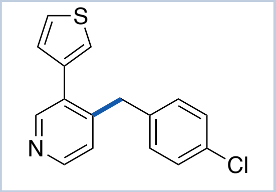
General benzyltrimethylsilane coupling procedure (GP1): In a nitrogen-filled glovebox, to an oven-dried 2-dram glass vial (8 mL, Thermo Scientific, B7999-3) equipped with a magnetic stir bar was added aryl electrophile (1.0 mmol, 1.0 equiv), benzyltrimethylsilane (1.2 mmol, 1.2 equiv), a solution of 18-crown-6 (1M in THF, 1.1 mL, 1.1 equiv) and anhydrous DMSO (2.9 mL, 0.25 M of aryl electrophile relative to total volume). Solid CsF (0.152 g, 1.0 mmol, 1.0 equiv) was added in one portion and the vial was sealed with a screw cap (Thermo Scientific, B7807-15) equipped with a 2.6 mm PTFE/Silicone Septa (Thermo Scientific, B7995-15). The reaction vial was removed from the glovebox and the reaction mixture was vigorously stirred at room temperature for 12 to 18 h as judged by TLC. The reaction mixture was poured into a separatory funnel containing EtOAc (50 mL) and diluted with brine (50 mL), taking care to not allow the pH to fall below pH = 7 by monitoring with pH indicator paper and adding sat. $NaHCO_{3(aq)}$ if necessary. The reaction mixture was extracted with EtOAc (3 x 15 mL), washed with H_2O (3 x 15 mL) and brine (2 x 25 mL) and dried over $MgSO_4$. After concentration under reduced pressure, the crude reaction mixture was purified *via* silica gel or basic Al_2O_3 flash chromatography using EtOAc/hexanes or Et_2O/hexanes to afford the product.

Note on reagent storage: Both cesium fluoride and 18-crown-6 are moderately hygroscopic and were thus stored an in inert atmosphere glovebox for long-term storage. For substrate scope studies, 1 mmol scale reactions were therefore setup inside of the glovebox according to General Procedure 1 (**GP1**). If the model reaction (1 mmol scale) is setup inside a glovebox but stirred open to air, a 91% yield is obtained (Table S1, entry 3). For comparison, using a standard Schlenk technique for reaction setup with CsF and 18-crown-6 that were stored outside of the glovebox (in a desiccator) led to a decreased yield of 66% for a 1 mmol scale reaction. For larger scale reactions (5-30 mmol, see Sections **V** and **VI** for procedures) we note that the use of a glovebox is not required provided that all reagents are properly stored (or dried) prior to their use.

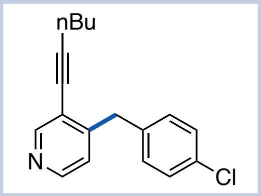
IV. Characterization of Diarylmethane Products



4-(4-Chlorobenzyl)-3-methylpyridine (4). GP1 was followed using 3-methylisonicotinonitrile (0.118 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (4-chlorobenzyl)trimethylsilane[1] (0.239 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 18 h. The product was purified *via* silica gel chromatography using 30% EtOAc in hexanes to afford **4** as a yellow oil (0.200 g, 0.92 mmol, 92% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 – 8.32 (m, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 5.0 Hz, 1H), 3.86 (s, 2H), 2.17 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.9, 147.8, 147.2, 136.7, 132.3, 131.9, 130.2, 128.7, 124.1, 38.0, 16.3. The spectroscopic data matches a previous literature report.[2]

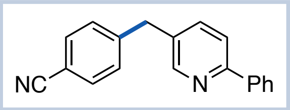


4-(4-Chlorobenzyl)-3-(thiophen-3-yl)pyridine (5). GP1 was followed using 3-(thiophen-3-yl)isonicotinonitrile[3] (0.186 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (4-chlorobenzyl)trimethylsilane[1] (0.239 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 12 h. The product was purified *via* silica gel chromatography using 30% Et_2O in hexanes to afford **5** as a white solid (0.269 g, 0.94 mmol, 94% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.47 (d, *J* = 5.0 Hz, 1H), 7.41 – 7.39 (m, 1H), 7.22 (d, *J* = 8.2 Hz, 2H), 7.18 – 7.17 (m, 1H), 7.08 – 7.05 (m, 2H), 6.92 (d, *J* = 8.2 Hz, 2H), 3.97 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.5, 148.8, 146.8, 137.7, 137.6, 132.8, 132.3, 130.1, 128.7, 128.6, 126.1, 124.7, 124.0, 38.1; **IR** (neat): 3102, 2923, 2360, 2159, 1953, 1903, 1653, 1584, 1487, 1094 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{16}H_{13}ClNS$ $(M+H)^+$ 286.0452; found 286.0447; **Melting point:** 49 – 52 °C.

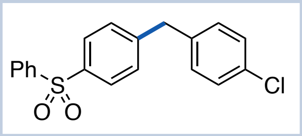


4-(4-Chlorobenzyl)-3-(hex-1-yn-1-yl)pyridine (6). GP1 was followed using 3-(hex-1-yn-1-yl)isonicotinonitrile (**SI-5**, 0.184 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (4-chlorobenzyl)trimethylsilane[1] (0.239 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 12 h. The product was purified *via* silica gel chromatography using 20% Et_2O in hexanes to afford **6** as a yellow oil (0.204 g, 0.72 mmol, 72% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.35 (d, *J* = 5.1 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 5.1 Hz, 1H), 4.06 (s, 2H), 2.45 (t, *J* = 7.0 Hz, 2H), 1.63 – 1.54 (m, 2H), 1.49

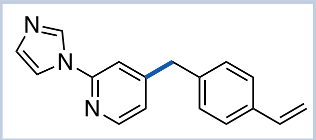
– 1.40 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (101 MHz, CDCl$_3$) δ 152.7, 150.5, 147.9, 137.1, 132.4, 130.3, 128.7, 123.5, 121.1, 98.2, 76.1, 38.9, 30.6, 22.0, 19.3, 13.6; **IR** (neat): 2957, 2930, 2871, 2360, 2228, 1899, 1584, 1490, 1428, 1066 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{18}H_{19}ClN$ (M+H)$^+$ 284.1201; found 284.1198.



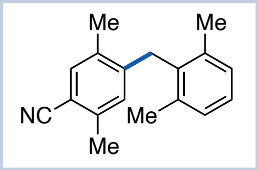
4-((6-Phenylpyridin-3-yl)methyl)benzonitrile (7). GP1 was followed using terephthalonitrile (0.128 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 2-phenyl-5-((trimethylsilyl)methyl)pyridine (**SI-13**, 0.290 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 12 h. The product was purified *via* silica gel chromatography using 15% EtOAc in hexanes to afford **7** as a white solid (0.149 g, 0.55 mmol, 55% yield). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.58 (d, *J* = 2.3 Hz, 1H), 8.02 (d, *J* = 8.6 Hz, 2H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.54 – 7.47 (m, 3H), 7.46 – 7.41 (m, 1H), 7.32 (d, *J* = 9.7 Hz, 2H), 4.07 (s, 2H); **^{13}C NMR** (101 MHz, CDCl$_3$) δ 156.0, 149.9, 145.5, 138.9, 137.2, 133.3, 132.5, 129.6, 129.0, 128.8, 126.8, 120.4, 118.8, 110.5, 38.7; **IR** (neat): 3053, 2926, 2854, 2359, 2342, 2229, 1605, 1560, 1501, 1047 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{19}H_{15}N_2$ (M+H)$^+$ 271.1230; found 271.1222; **Melting point:** 103 – 106 ºC.



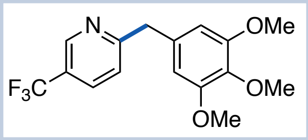
1-Chloro-4-(4-(phenylsulfonyl)benzyl)benzene (8). GP1 was followed using 4-(phenylsulfonyl)benzonitrile[4] (0.243 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (4-chlorobenzyl)trimethylsilane[1] (0.239 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified *via* silica gel chromatography using 10% EtOAc in hexanes to afford **8** as a white solid (0.309 g, 0.90 mmol, 90% yield). We note that a small amount (less than 10%) of sulfonyl substitution product was observed in the ^{1}H NMR spectrum of the crude reaction material that was separated during purification. **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.93 (d, *J* = 7.0 Hz, 2H), 7.86 (d, *J* = 8.4 Hz, 2H), 7.57 – 7.52 (m, 1H), 7.51 – 7.47 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 3.97 (s, 2H); **^{13}C NMR** (101 MHz, CDCl$_3$) δ 146.5, 141.7, 139.6, 137.9, 133.2, 132.5, 130.3, 129.7, 129.3, 128.8, 128.0, 127.6, 41.0; **IR** (neat): 3085, 2925, 2224, 1943, 1590, 1491, 1447, 1308, 1105 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{19}H_{16}ClO_2S$ (M+H)$^+$ 343.0554; found 343.0551; **Melting point:** 175 – 178 ºC.



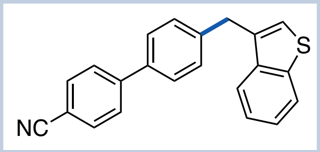
2-(1*H*-Imidazol-1-yl)-4-(4-vinylbenzyl)pyridine (9). GP1 was followed using 2-(1*H*-imidazol-1-yl)isonicotinonitrile[5] (0.170 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and trimethyl(4-vinylbenzyl)silane[6] (0.228 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified *via* silica gel chromatography using 60% EtOAc in hexanes to afford **9** as a yellow oil (0.235 g, 0.90 mmol, 90% yield). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.34 – 8.32 (m, 1H), 8.30 (s, 1H), 7.57 (s, 1H), 7.36 (d, *J* = 6.3 Hz, 2H), 7.15 – 7.14 (m, 2H), 7.12 – 7.11 (m, 2H), 7.03 – 7.02 (m, 1H), 6.68 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.72 (dd, *J* = 17.6, 0.6 Hz, 1H), 5.23 (dd, *J* = 10.9, 0.6 Hz, 1H), 4.00 (s, 2H); **^{13}C NMR** (101 MHz, CDCl$_3$) δ 153.6, 149.4, 149.1, 137.6, 136.4, 136.2, 135.0, 130.6, 129.2, 126.7, 122.6, 116.2, 114.0, 112.5, 41.0; **IR** (neat): 3116, 3051, 2923, 2360, 1696, 1604, 1562, 1499, 1307, 1267 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{17}H_{16}N_3$ (M+H)$^+$ 262.1339; found 262.1338.



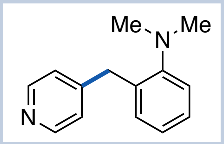
4-(2,6-Dimethylbenzyl)-2,5-dimethylbenzonitrile (10). GP1 was followed using 2,5-dimethylterephthalonitrile[7] (0.156 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (2,6-dimethylbenzyl)trimethylsilane **50** (0.231 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified *via* silica gel chromatography using 10% EtOAc in hexanes to afford **10** as a white solid (0.237 g, 0.95 mmol, 95% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.20 – 7.12 (m, 3H), 6.46 (s, 1H), 3.94 (s, 2H), 2.45 (s, 3H), 2.34 (s, 3H), 2.20 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.6, 139.7, 137.1, 135.3, 134.7, 133.2, 128.4, 128.0, 126.8, 118.6, 110.0, 32.7, 20.1, 20.0, 19.1; **IR** (neat): 2968, 2945, 2920, 2343, 2223, 1612, 1499, 1470, 1390 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{18}H_{20}N$ $(M+H)^+$ 250.1590; found 250.1588; **Melting point:** 66 – 69 ºC.



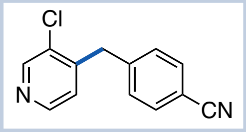
5-(Trifluoromethyl)-2-(3,4,5-trimethoxybenzyl)pyridine (11). GP1 was followed using 5-(trifluoromethyl)picolinonitrile (0.172 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and trimethyl(3,4,5-trimethoxybenzyl)silane[8] (0.305 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 12 h. The product was purified *via* silica gel chromatography using 17% EtOAc in hexanes to afford **11** as a yellow oil (0.262 g, 0.80 mmol, 80% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 7.83 (d, J = 9.5 Hz, 1H), 7.26 (d, J = 8.0 Hz, 1H), 6.47 (s, 2H), 4.15 (s, 2H), 3.83 (s, 6H), 3.82 (s, 3H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.3 (s, 3F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.9, 153.5, 146.3 (q, J = 4.1 Hz), 136.9, 134.0, 133.8 (q, J = 3.4 Hz), 124.5 (q, J = 33.0 Hz), 123.7 (q, J = 273.3 Hz), 122.8, 106.2, 60.9, 56.2, 45.0; **IR** (neat): 2940, 2839, 2360, 2342, 1733, 1636, 1590, 1325 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{16}H_{17}F_3NO_3$ $(M+H)^+$ 328.1155; found 328.1160.



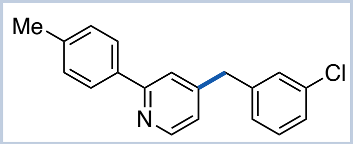
4'-(Benzo[*b*]thiophen-3-ylmethyl)-[1,1'-biphenyl]-4-carbonitrile (12). GP1 was followed using [1,1'-biphenyl]-4,4'-dicarbonitrile[9] (0.204 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (benzo[*b*]thiophen-3-ylmethyl)trimethylsilane[10] (0.264 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified *via* silica gel chromatography using 10% EtOAc in hexanes to afford **12** as a white solid (0.238 g, 0.73 mmol, 73% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 – 7.86 (m, 1H), 7.74 – 7.70 (m, 3H), 7.66 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 8.2 Hz, 2H), 7.39 – 7.34 (m, 4H), 7.08 (s, 1H), 4.26 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.3, 140.7, 140.2, 138.7, 137.2, 135.0, 132.6, 129.6, 127.5, 127.4, 124.4, 124.1, 123.4, 123.0, 121.9, 119.0, 110.8, 34.7; **IR** (neat): 3029, 2919, 2360, 2227, 2042, 1961, 1718, 1521 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{22}H_{16}NS$ $(M+H)^+$ 343.1263; found 343.1272; **Melting point:** 120 – 122 ºC.



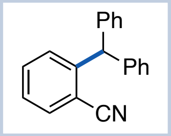
***N*,*N*-Dimethyl-2-(pyridin-4-ylmethyl)aniline (13).** GP1 was followed using 4-cyanopyridine (0.104 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and *N*,*N*-dimethyl-2-((trimethylsilyl)methyl)aniline[8] (0.249 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 14 h. The product was purified *via* silica gel chromatography using 30% EtOAc in hexanes to afford **13** as a yellow oil (0.106 g, 0.50 mmol, 50% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.50 (m, 2H), 7.29 – 7.24 (m, 1H), 7.22 – 7.17 (m, 1H), 7.13 (m, 2H), 7.08 – 7.02 (m, 2H), 4.11 (s, 2H), 2.66 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.1, 151.0, 149.7, 134.1, 130.9, 127.7, 124.4, 123.7, 120.2, 45.2, 36.3; **IR** (neat): 3067, 3023, 2979, 2826, 2783, 2215, 1596, 1492 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{14}H_{17}N_2$ $(M+H)^+$ 213.1386; found 213.1387.



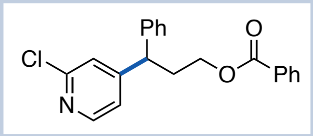
4-((3-Chloropyridin-4-yl)methyl)benzonitrile (14). GP1 was followed using 3-chloroisonicotinonitrile (0.139 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 4-((trimethylsilyl)methyl)benzonitrile[11] (0.227 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 14 h. The product was purified *via* silica gel chromatography using 20% EtOAc in hexanes to afford **14** as a white solid (0.206 g, 0.90 mmol, 90% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.32 (d, J = 5.0 Hz, 1H), 7.52 (d, J = 8.3 Hz, 2H), 7.22 (d, J = 8.3 Hz, 2H), 6.98 (d, J = 4.9 Hz, 1H), 4.07 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.6, 148.0, 145.8, 142.9, 132.5, 132.2, 129.8, 125.3, 118.6, 110.9, 38.6; **IR** (neat): 2963, 2924, 2854, 2228, 1608, 1415, 1400, 1290 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{13}H_{10}ClN_2$ $(M+H)^+$ 229.0527; found 229.0532.; **Melting point:** 75 – 78 ºC.



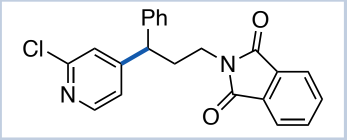
4-(3-Chlorobenzyl)-2-(*p*-tolyl)pyridine (15). GP1 was followed using 2-(*p*-tolyl)isonicotinonitrile[12] (0.194 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (3-chlorobenzyl)trimethylsilane[13] (0.239 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 18 h. The product was purified *via* silica gel chromatography using 5% EtOAc in hexanes to afford **15** as a colorless oil (0.261 g, 0.89 mmol, 89% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (d, J = 5.0 Hz, 1H), 7.91 (d, J = 8.1 Hz, 2H), 7.54 (s, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.27 – 7.23 (m, 3H), 7.13 – 7.10 (m, 1H), 7.02 (d, J = 4.4 Hz, 1H), 3.99 (s, 2H), 2.43 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.8, 149.8, 149.7, 141.1, 139.1, 136.5, 134.6, 130.0, 129.5, 129.2, 127.3, 127.0, 126.9, 122.4, 120.7, 41.1, 21.3; **IR** (neat): 3029, 2918, 2859, 2208, 1934, 1594, 1554, 1473 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{19}H_{17}ClN$ $(M+H)^+$ 294.1044; found 294.1047.



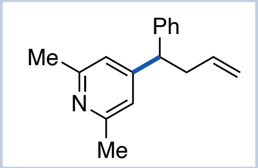
2-Benzhydrylbenzonitrile (16). GP1 was followed using phthalonitrile (0.128 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and benzhydryltrimethylsilane[14] (0.289 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 12 h. The product was purified *via* silica gel chromatography using 5% Et_2O in hexanes to afford **16** as a yellow solid (0.256 g, 0.95 mmol, 95% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.4 Hz, 2H), 7.43 – 7.38 (m, 4H), 7.36 – 7.31 (m, 4H), 7.21 – 7.19 (m, 4H), 5.70 (s, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.6, 142.5, 132.2, 130.3, 129.5, 129.4, 128.8, 128.7, 127.0, 119.0, 110.4, 56.9; **IR** (neat): 3052, 3033, 2360, 2226, 1956, 1596, 1491, 1448, 1272 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{20}H_{15}N$ $(M+NH_4)^+$ 287.1543; found 287.1557; **Melting point:** 98 – 102 ºC.



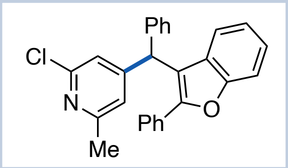
3-(2-Chloropyridin-4-yl)-3-phenylpropyl benzoate (17). GP1 was followed using 2-chloroisonicotinonitrile (0.139 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 3-phenyl-3-(trimethylsilyl)propyl benzoate (**SI-8**, 0.375 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 14 h. The product was purified *via* silica gel chromatography using 15% EtOAc in hexanes to afford **17** as a yellow oil (0.274 g, 0.68 mmol, 68% yield). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.16 (d, *J* = 5.2 Hz, 1H), 7.88 – 7.86 (m, 2H), 7.47 – 7.44 (m, 1H), 7.35 – 7.31 (m, 2H), 7.24 – 7.21 (m, 2H), 7.16 – 7.12 (m, 4H), 7.01 (dd, *J* = 5.2, 1.3 Hz, 1H), 4.26 – 4.12 (m, 2H), 4.03 (t, *J* = 7.8 Hz, 1H), 2.48 – 2.35 (m, 2H); **^{13}C NMR** (101 MHz, CDCl$_3$) δ 166.3, 156.5, 151.9, 149.8, 141.3, 133.1, 130.0, 129.5, 129.1, 128.4, 127.8, 127.4, 123.5, 122.0, 62.8, 47.3, 33.6; **IR** (neat): 3061, 2958, 1714, 1600, 1588, 1269, 1112 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for C$_{21}$H$_{19}$ClNO$_2$ (M+H)$^+$ 352.1099; found 352.1101.



2-(3-(2-Chloropyridin-4-yl)-3-phenylpropyl)isoindoline-1,3-dione (18). GP1 was followed using 2-chloroisonicotinonitrile (0.139 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 2-(3-(2-chloropyridin-4-yl)-3-phenylpropyl)isoindoline-1,3-dione (**SI-10**, 0.338 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified *via* silica gel chromatography using 15% EtOAc in hexanes to afford **18** as a yellow oil (0.189 g, 0.50 mmol, 50% yield). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.20 (d, *J* = 5.2 Hz, 1H), 7.78 – 7.76 (m, 2H), 7.68 – 7.66 (m, 2H), 7.29 – 7.21 (m, 5H), 7.18 – 7.16 (m, 1H), 7.10 (dd, *J* = 5.2, 1.1 Hz, 1H), 3.97 (t, *J* = 7.6 Hz, 1H), 3.70 (t, *J* = 7.1 Hz, 2H), 2.52 – 2.41 (m, 2H); **^{13}C NMR** (101 MHz, CDCl$_3$) δ 168.2, 156.3, 151.8, 149.7, 141.2, 134.0, 131.8, 129.0, 127.6, 127.2, 123.3, 123.1, 121.7, 48.5, 36.5, 33.0; **IR** (neat): 3060, 3029, 2955, 2928, 2342, 1772, 1707, 1615, 1394 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for C$_{22}$H$_{18}$ClN$_2$O$_2$ (M+H)$^+$ 377.1051; found 377.1055.

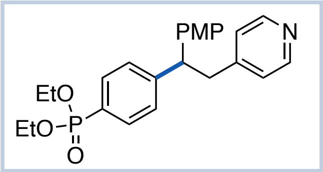


2,6-Dimethyl-4-(1-phenylbut-3-en-1-yl)pyridine (19). GP1 was followed using 2,6-dimethylisonicotinonitrile[15] (0.132 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and trimethyl(1-phenylbut-3-en-1-yl)silane[10] (0.245 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 14 h. The product was purified *via* silica gel chromatography using 0.5% MeOH in CH$_2$Cl$_2$ to afford **19** as a yellow oil (0.178 g, 0.75 mmol, 75% yield). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.22 – 7.18 (m, 2H), 7.13 – 7.09 (m, 3H), 6.74 (s, 2H), 5.64 – 5.54 (m, 1H), 4.94 (d, *J* = 17.1 Hz, 1H), 4.87 (d, *J* = 10.1 Hz, 1H), 3.80 (t, *J* = 7.8 Hz, 1H), 2.71 – 2.67 (m, 2H), 2.38 (s, 6H); **^{13}C NMR** (101 MHz, CDCl$_3$) δ 157.7, 153.8, 143.0, 136.1, 128.6, 127.9, 126.6, 119.8, 116.8, 50.6, 39.2, 24.5; **IR** (neat): 3062, 3026, 2977, 2921, 2851, 2341, 1641, 1599 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for C$_{17}$H$_{20}$N (M+H)$^+$ 238.1590; found 238.1588.

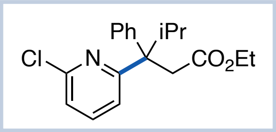


2-Chloro-6-methyl-4-(phenyl(2-phenylbenzofuran-3-yl)methyl)pyridine (20). GP1 was followed using 2-chloro-6-methylisonicotinonitrile[16] (0.153 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and trimethyl(phenyl(2-phenylbenzofuran-3-yl)methyl)silane[17]

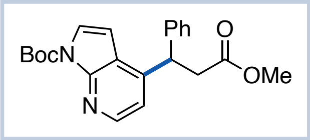
(0.428 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified *via* silica gel chromatography using 10% Et_2O in hexanes to afford **20** as a colorless crystalline solid (0.312 g, 0.76 mmol, 76% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 – 7.64 (m, 2H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.51 – 7.41 (m, 3H), 7.39 – 7.24 (m, 6H), 7.10 – 7.07 (m, 1H), 6.99 – 6.97 (m, 2H), 6.91 (s, 1H), 5.83 (s, 1H), 2.46 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.5, 155.3, 154.5, 153.0, 151.0, 140.1, 130.2, 129.1, 129.02, 128.98, 128.8, 128.7, 127.8, 127.4, 124.5, 122.9, 122.6, 121.6, 121.4, 115.5, 111.5, 46.6, 24.3; **IR** (neat): 3026, 2989, 2190, 2026, 2178, 1982, 1901, 1820, 1739, 1591 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{27}H_{21}ClNO$ $(M+H)^+$ 410.1306; found 410.1309; **Melting point:** 154 – 158 ºC.



Diethyl (4-(1-(4-methoxyphenyl)-2-(pyridin-4-yl)ethyl)phenyl)phosphonate (21). GP1 was followed using diethyl (4-cyanophenyl)phosphonate[18] (0.239 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 4-(2-(4-methoxyphenyl)-2-(trimethylsilyl)ethyl)pyridine[19] (0.343 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 14 h. The product was purified *via* silica gel chromatography using 2% MeOH in CH_2Cl_2 to afford **21** as a yellow oil (0.332 g, 0.78 mmol, 78% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 5.5 Hz, 2H), 7.70 (dd, *J* = 13.0, 8.2 Hz, 2H), 7.26 (dd, *J* = 8.1, 3.8 Hz, 2H), 7.07 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 5.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.21 (t, *J* = 7.9 Hz, 1H), 4.16 – 3.99 (m, 4H), 3.75 (s, 3H), 3.31 (dd, *J* = 8.0, 2.5 Hz, 2H), 1.29 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.4, 149.4, 149.0, 148.6 (d, *J* = 3.2 Hz), 134.6, 132.0 (d, *J* = 10.3 Hz), 128.9, 127.9 (d, *J* = 15.4 Hz), 126.5 (d, *J* = 190.6 Hz) 124.4, 114.0, 62.0 (d, *J* = 5.4 Hz), 55.2, 51.3, 41.3, 16.4 (d, *J* = 6.5 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 18.7; **IR** (neat): 3027, 2982, 2931, 2905, 2836, 2360, 1683, 1601 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{14}H_{29}NO_4P$ $(M+H)^+$ 426.1829; found 426.1823.

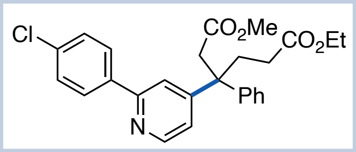


Ethyl 3-(6-chloropyridin-2-yl)-4-methyl-3-phenylpentanoate (22). GP1 was followed using 6-chloropicolinonitrile (0.139 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and ethyl 4-methyl-3-phenyl-3-(trimethylsilyl)pentanoate[20] (0.351 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 14 h. The product was purified *via* silica gel chromatography using 5% EtOAc in hexanes to afford **22** as a yellow oil (0.216 g, 0.65 mmol, 65% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (t, *J* = 7.8 Hz, 1H), 7.33 – 7.22 (m, 5H), 7.19 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.03 (dd, *J* = 7.8, 0.6 Hz, 1H), 3.85 (dq, *J* = 7.2, 2.2 Hz, 2H), 3.42 (d, *J* = 14.6 Hz, 1H), 3.20 – 3.11 (m, 2H), 1.00 (t, *J* = 7.1 Hz, 3H), 0.85 (dd, *J* = 6.7, 4.4 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.6, 164.7, 149.4, 142.6, 137.4, 129.2, 127.5, 126.4, 123.8, 121.6, 59.9, 55.8, 43.9, 31.9, 18.6, 18.5, 13.9; **IR** (neat): 3090, 2977, 2878, 2360, 1726, 1580, 1556, 1431, 1398 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{19}H_{23}ClNO_2$ $(M+H)^+$ 332.1412; found 332.1413.

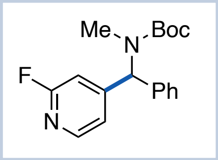


***tert*-Butyl 4-(3-methoxy-3-oxo-1-phenylpropyl)-1-methyl-1H-1λ4-pyrrolo[2,3-b]pyridine-1-carboxylate (23).** GP1 was followed using *tert*-butyl 4-cyano-1*H*-pyrrolo[2,3-*b*]pyridine-1-carboxylate[12] (0.243 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (0.291 g, 1.1 mmol, 1.1 equiv) and methyl 3-phenyl-3-

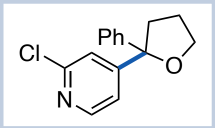
(trimethylsilyl)propanoate[21] (0.355 g, 1.5 mmol, 1.5 equiv). The product was purified *via* silica gel chromatography using 15% EtOAc in hexanes to afford **23** as a tan solid (0.266 g, 0.70 mmol, 70% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 5.0 Hz, 1H), 7.55 (d, *J* = 4.2 Hz, 1H), 7.26 – 7.14 (m, 5H), 7.07 (d, *J* = 5.0 Hz, 1H), 6.49 (d, *J* = 4.2 Hz, 1H), 4.91 (t, *J* = 7.9 Hz, 1H), 3.55 (s, 3H), 3.18 – 3.08 (m, 2H), 1.62 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.7, 148.5, 147.8, 145.4, 144.9, 141.7, 128.7, 127.6, 127.0, 126.2, 122.2, 116.2, 102.9, 84.0, 51.8, 43.8, 39.6, 28.0; **IR** (neat): 3160, 2978, 2953, 2360, 2192, 1741, 1713, 1590, 1430 cm^{-1}; **EA** Calcd. for $C_{23}H_{27}N_2O_4$: C, 69.85; H, 6.88; N, 7.08. Found: C, 68.90; H, 6.44; N, 7.16; **Melting point:** 160 – 163 ºC.



6-Ethyl 1-methyl 3-(2-(4-chlorophenyl)pyridin-4-yl)-3-phenylhexanedioate (24). GP1 was followed using 2-(4-chlorophenyl)isonicotinonitrile[22] (0.215 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 6-ethyl 1-methyl 3-phenyl-3-(trimethylsilyl)hexanedioate[23] (0.404 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 14 h. The product was purified *via* silica gel chromatography using 20% EtOAc in hexanes to afford **24** as a yellow oil (0.267 g, 0.59 mmol, 59% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 5.1 Hz, 1H), 7.78 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 1.2 Hz, 1H), 7.33 (d, *J* = 8.6 Hz, 2H), 7.26 – 7.20 (m, 2H), 7.19 – 7.17 (m, 1H), 7.13 – 7.06 (m, 2H), 7.01 (dd, *J* = 5.2, 1.8 Hz, 1H), 3.78 (q, *J* = 7.1 Hz, 2H), 3.51 (s, 3H), 3.10 – 3.02 (m, 2H), 2.77 – 2.61 (m, 2H), 2.17 – 1.99 (m, 2H), 0.85 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.4, 170.2, 157.1, 156.0, 149.2, 144.3, 137.4, 135.4, 129.0, 128.6, 128.4, 127.5, 127.1, 121.9, 119.8, 60.5, 51.7, 48.4, 42.3, 32.4, 29.4, 13.8; **IR** (neat): 3058, 2981, 2951, 2256, 1728, 1598, 1445, 1195 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{26}H_{27}ClNO_4$ $(M+H)^+$ 452.1623; found 452.1626.

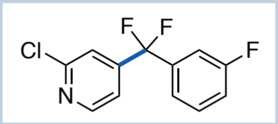


***tert*-Butyl ((2-fluoropyridin-4-yl)(phenyl)methyl)(methyl)carbamate (25).** GP1 was followed using 2-fluoroisonicotinonitrile (0.122 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and *tert*-butyl methyl(phenyl(trimethylsilyl)methyl)carbamate[24] (0.179 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified *via* silica gel chromatography using 5% EtOAc in hexanes to afford **25** as a clear colorless oil (0.285 g, 0.90 mmol, 90% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 5.2 Hz, 1H), 7.39 – 7.28 (m, 3H), 7.15 – 7.13 (m, 2H), 7.00 (d, *J* = 5.2 Hz, 1H), 6.74 (s, 1H), 6.57 (brs, 1H), 2.66 (s, 3H), 1.45 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -67.7; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.3 (d, *J* = 238.8 Hz), 155.8, 155.5 (d, *J* = 7.2 Hz), 147.7 (d, *J* = 15.2 Hz), 137.4, 129.1, 128.8, 128.2, 120.8 (d, *J* = 3.7 Hz), 108.6 (d, *J* = 38.2 Hz), 80.7, 61.8, 31.1, 28.3; **IR** (neat): 3064, 2976, 2931, 1687, 1609, 1439, 1405, 1314 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{18}H_{22}FN_2O_2$ $(M+H)^+$ 317.1660; found 317.1685.

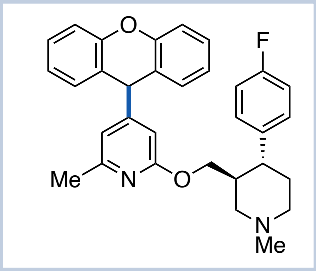


2-Chloro-4-(2-phenyltetrahydrofuran-2-yl)pyridine (26). GP1 was followed using 2-chloroisonicotinonitrile (0.139 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and trimethyl(2-phenyltetrahydrofuran-2-yl)silane[25] (0.265 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 12 h. The product was purified *via* silica gel chromatography using 10% EtOAc in hexanes to afford **26** as a yellow oil

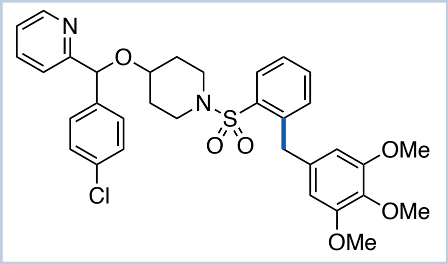
(0.135 g, 0.52 mmol, 52% yield). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.11 (d, *J* = 8.0 Hz, 1H), 7.30 – 7.25 (m, 3H), 7.19 – 7.14 (m, 2H), 7.11 – 7.08 (m, 2H), 3.94 – 3.85 (m, 2H), 2.50 – 2.44 (m, 1H), 2.32 – 2.26 (m, 1H), 1.88 – 1.71 (m, 2H); **^{13}C NMR** (101 MHz, CDCl$_3$) δ 159.1, 151.8, 149.6, 144.1, 128.6, 127.6, 125.7, 121.3, 119.8, 87.0, 67.9, 38.4, 25.4; **IR** (neat): 3058, 2978, 2878, 1587, 1542, 1459, 1370, 1313 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{15}H_{15}ClNO$ (M+H)$^+$ 260.0837; found 260.0838.



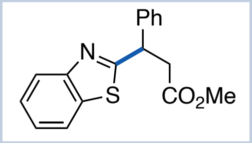
2-Chloro-4-(difluoro(3-fluorophenyl)methyl)pyridine (27). GP1 was followed using 2-chloroisonicotinonitrile (0.139 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (difluoro(3-fluorophenyl)methyl)trimethylsilane[26] (0.262 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 14 h. The product was purified *via* silica gel chromatography using 20% EtOAc in hexanes to afford **27** as a yellow oil (0.080 g, 0.31 mmol, 31% yield). We note that protodesilylation (1-(difluoromethyl)-3-fluorobenzene) is observed in the ^{1}H NMR spectrum of the crude reaction material as a significant side product. **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.41 (d, *J* = 5.1 Hz, 1H), 7.39 – 7.33 (m, 2H), 7.26 (d, *J* = 5.1 Hz, 1H), 7.20 – 7.07 (m, 3H); **^{19}F NMR** (376 MHz, CDCl$_3$) δ -92.8 (s, 2F), -110.6 (td, *J* = 8.8, 6.0 Hz, 1F); **^{13}C NMR** (101 MHz, CDCl$_3$) δ 162.7 (d, *J* = 249.5 Hz), 152.4, 150.4, 148.2 (t, *J* = 30.3 Hz), 137.8 (td, *J* = 25.0, 8.0 Hz), 130.8 (d, *J* = 8.1 Hz), 121.3 (td, *J* = 5.8, 3.5 Hz), 121.0 (t, *J* = 5.8 Hz), 118.8 (t, *J* = 5.1 Hz), 117.9 (t, *J* = 242.4 Hz), 117.8 (dt, *J* = 22.5, 2.4 Hz), 113.0 (dt, *J* = 24.0, 6.1 Hz); **IR** (neat): 3071, 2925, 1945, 1615, 1596, 1556, 1466, 1373 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{12}H_8ClF_3N$ (M+H)$^+$ 258.0292; found 258.0297.



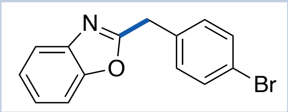
2-(((3*S*,4*R*)-4-(4-Fluorophenyl)-1-methylpiperidin-3-yl)methoxy)-6-methyl-4-(9*H*-xanthen-9-yl)pyridine (28). GP1 was followed using 2-(((3*S*,4*R*)-4-(4-fluorophenyl)-1-methylpiperidin-3-yl)methoxy)-6-methylisonicotinonitrile (**SI-11**, 0.339 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and trimethyl(9*H*-xanthen-9-yl)silane[27] (0.509 g, 2.0 mmol, 2.0 equiv) in 2.9 mL anhydrous DMSO for 18 h. The product was purified *via* silica gel chromatography using 10% MeOH in CH_2Cl_2 to afford **28** as a yellow oil (0.430 g, 0.87 mmol, 87% yield). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.26 – 7.11 (m, 6H), 7.06 – 6.89 (m, 6H), 6.47 (s, 1H), 6.31 (s, 1H), 5.10 (s, 1H), 4.03 (dd, *J* = 11.0, 2.7 Hz, 1H), 3.77 (dd, *J* = 10.8, 7.0 Hz, 1H), 3.24 – 3.21 (m, 1H), 3.01 – 2.98 (m, 1H), 2.48 – 2.39 (m, 2H), 2.37 (s, 3H), 2.25 (s, 3H), 2.13 – 2.01 (m, 2H), 1.96 – 1.72 (m, 2H); **^{19}F NMR** (376 MHz, CDCl$_3$) δ -116.7; **^{13}C NMR** (101 MHz, CDCl$_3$) δ 163.7, 161.6 (d, *J* = 245.0 Hz), 157.6, 156.7, 151.0, 139.6 (d, *J* = 3.0 Hz), 129.5, 129.0 (d, *J*= 7.7 Hz), 128.4, 123.4, 122.9 (d, *J*= 2.0 Hz), 116.8, 115.9, 115.3 (d, *J* = 21.1 Hz), 106.6, 66.5, 59.5, 56.1, 46.3, 43.9, 43.6, 41.2, 34.6, 24.2; **IR** (neat): 3068, 2936, 2850, 2784, 2689, 1604, 1510, 1454 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{32}H_{32}FN_2O_2$ (M+H)$^+$ 495.2442; found 495.2442.



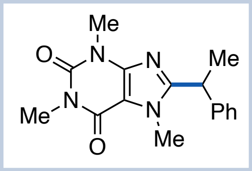
2-((4-Chlorophenyl)((1-((2-(3,4,5-trimethoxybenzyl)phenyl)sulfonyl) piperidin-4-yl)oxy)methyl)pyridine (29). GP1 was followed using 2-((4-((4 chlorophenyl)(pyridin-2-yl)methoxy)piperidin-1-yl)sulfonyl)benzonitrile (**SI-12**, 0.468 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and trimethyl(3,4,5-trimethoxybenzyl)silane[8] (0.305 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 12 h. The product was purified *via* silica gel chromatography using 40% EtOAc in hexanes to afford **29** as a white foam (0.312 g, 0.50 mmol, 50% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 4.3 Hz, 1H), 7.80 (d, *J* = 9.4 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.33 – 7.27 (m, 2H), 7.21 – 7.16 (m, 3H), 7.12 – 7.08 (m, 2H), 7.06 – 7.03 (m, 1H), 7.02 – 6.97 (m, 1H), 6.25 (s, 2H), 5.41 (s, 1H), 4.18 (s, 2H), 3.66 (s, 3H), 3.62 (s, 6H), 3.48 – 3.40 (m, 1H), 3.33 – 3.22 (m, 2H), 2.98 – 2.86 (m, 2H), 1.75 – 1.64 (m, 2H), 1.63 – 1.50 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.5, 153.4, 149.0, 140.8, 139.9, 137.2, 136.6, 136.2, 135.5, 133.6, 133.0, 132.3, 130.2, 128.7, 128.1, 126.5, 122.8, 120.7, 106.5, 81.2, 71.6, 61.0, 56.2, 42.45, 42.38, 38.3, 30.80, 30.76; **IR** (neat): 2953, 2860, 2824, 2342, 1589, 1469, 1336, 1266 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{33}H_{36}ClN_2O_6S$ $(M+H)^+$ 623.1977; found 623.1963; **Melting point:** 190 – 192 ºC.



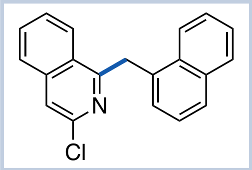
Methyl 3-(benzo[*d*]thiazol-2-yl)-3-phenylpropanoate (30). GP1 was followed using 2-chlorobenzothiazole (0.169 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and methyl 3-phenyl-3-(trimethylsilyl)propanoate[21] (0.289 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 12 h. The product was purified *via* silica gel chromatography using 5% EtOAc in hexanes to afford **30** as a yellow solid (0.223 g, 0.75 mmol, 75% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.1 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.32 – 7.24 (m, 3H), 7.22 – 7.10 (m, 4H), 4.84 (t, *J* = 7.6 Hz, 1H), 3.54 – 3.48 (m, 4H), 2.99 (dd, *J* = 16.4 ,7.3 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.1, 171.8, 153.0, 140.8, 135.6, 129.0, 128.1, 127.8, 126.0, 125.0, 123.1, 121.6, 51.9, 46.5, 39.9; **IR** (neat): 3105, 3055, 2959, 2919, 1740, 1514, 1368, 1119 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{17}H_{16}NO_2S$ $(M+H)^+$ 298.0896; found 298.0900; **Melting point:** 65 – 69 ºC.



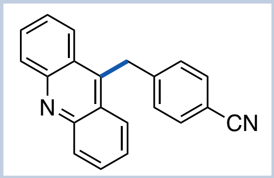
2-(4-Bromobenzyl)benzo[*d*]oxazole (31). GP1 was followed using 2-chlorobenzoxazole (0.154 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (4-bromobenzyl)trimethylsilane[28] (0.292 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 12 h. The product was purified *via* silica gel chromatography using 5% EtOAc in hexanes to afford **31** as a colorless oil (0.150 g, 0.52 mmol, 52% yield). We note approximately 3% of the corresponding triarylmethane product was observed in the ^{1}H NMR spectrum of the crude reaction material that was separated during purification. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 – 7.72 (m, 1H), 7.52 – 7.49 (m, 3H), 7.35 – 7.32 (m, 2H), 7.29 – 7.27 (m, 2H), 4.24 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.5, 151.0, 141.3, 133.8, 132.0, 130.8, 124.9, 124.4, 121.4, 119.9, 110.5, 34.7; The spectroscopic data matches a previous literature report.[29]



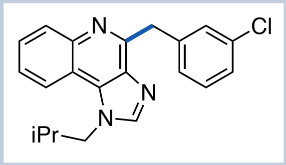
2-(1-Phenylethyl)caffeine (32). GP1 was followed using 2-chlorocaffeine[30] (0.229 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and trimethyl(1-phenylethyl)silane[31] (0.214 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 14 h. The product was purified *via* silica gel chromatography using 20% EtOAc in hexanes to afford **32** as a white solid (0.197 g, 0.66 mmol, 66% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 2H), 7.25 – 7.21 (m, 1H), 7.19 – 7.17 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 1H), 3.71 (s, 3H), 3.64 (s, 3H), 3.38 (s, 3H), 1.74 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.8, 155.5, 151.7, 147.8, 141.8, 129.0, 127.2, 127.1, 107.6, 38.2, 31.6, 29.8, 27.8, 21.3; **IR** (neat): 3054, 2979, 2919, 2846, 1740, 1964, 1694, 1602 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{16}H_{19}N_4O_2$ $(M+H)^+$ 299.1503; found 299.1505; **Melting point:** 158 – 161 ºC.



3-Chloro-1-(naphthalen-1-ylmethyl)isoquinoline (33). GP1 was followed using 1,3-dichloroisoquinoline (0.198 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and trimethyl(naphthalen-1-ylmethyl)silane[8] (0.257 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 14 h. The product was purified *via* silica gel chromatography using 20% EtOAc in hexanes to afford **33** as a yellow oil (0.185 g, 0.61 mmol, 61% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.64 – 7.61 (m, 2H), 7.57 (s 1H), 7.54 – 7.48 (m, 2H), 7.47 – 7.42 (m, 1H), 7.32 – 7.25 (m 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 7.1 Hz, 1H), 5.00 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.4, 144.6, 138.5, 135.1, 133.8, 131.9, 130.9, 128.9, 127.5, 127.2, 126.7, 126.5, 126.4, 126.1, 125.9, 125.5, 123.6, 119.0, 38.8; **IR** (neat): 3049, 2953, 2854, 1934, 1832, 1620, 1554, 1463 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{20}H_{15}ClN$ $(M+H)^+$ 304.0888; found 304.0883.



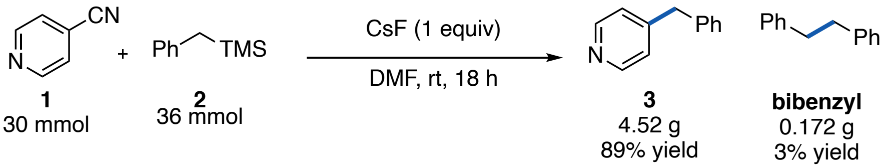
4-(Acridin-9-ylmethyl)benzonitrile (34). GP1 was followed using 9-chloroacridine[32] (0.214 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 4-((trimethylsilyl)methyl)benzonitrile[11] (0.227 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 14 h. The product was purified *via* silica gel chromatography using 20% EtOAc in hexanes to afford **34** as an orange solid (0.194 g, 0.66 mmol, 66% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.7 Hz, 2H), 8.08 (d, *J* = 8.8 Hz, 2H), 7.79 – 7.75 (m, 2H), 7.55 – 7.47 (m, 4H), 7.17 (d, *J* = 8.2 Hz, 2H), 5.02 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.9, 144.9, 141.5, 132.6, 130.6, 130.1, 129.0, 126.6, 125.5, 124.2, 118.7, 110.6, 33.2; **IR** (neat): 3020, 2989, 2935, 2360, 2229, 1977, 1627, 1613, 1468 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{21}H_{14}N_2$ $(M+H)^+$ 295.1230; found 295.1236; **Melting point:** 183 – 185 ºC.



4-(3-Chlorobenzyl)-1-isobutyl-1*H*-imidazo[4,5-*c*]quinoline (35). GP1 was followed using 4-chloro-1-(2-methylpropyl)-1H-imidazo[4,5-c]quinoline[33] (0.260 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (3-chlorobenzyl)trimethylsilane[13] (0.239 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 14 h. The product was purified by basic Al_2O_3

column chromatography using 20% EtOAc in hexanes to afford **35** as a colorless oil (0.140 g, 0.40 mmol, 40% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.0 Hz, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.88 (s, 1H), 7.69 – 7.64 (m, 1H), 7.60 – 7.56 (m, 1H), 7.52 (s, 1H), 7.44 (d, *J* = 7.4 Hz, 1H), 7.19 – 7.15 (m, 1H), 7.13 – 7.10 (m, 1H), 4.70 (s, 2H), 4.30 (d, *J* = 7.4 Hz, 2H), 2.39 – 2.29 (m, 1H), 1.02 (d, *J* = 6.6 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.0, 143.8, 141.1, 137.3, 134.1, 133.3, 130.5, 129.6, 129.4, 128.1, 127.7, 127.4, 126.5, 126.2, 120.1, 117.7, 55.2, 40.0, 28.9, 20.0; **IR** (neat): 3062, 2960, 2928, 2872, 1945, 1710, 1596, 1520 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{21}H_{21}ClN_3$ $(M+H)^+$ 350.1419; found 350.1421.

V. Preparative Scale Arylation Reaction

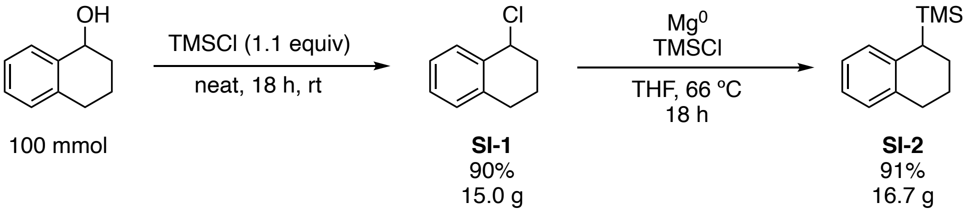


An oven-dried 250 mL round-bottom flask equipped with a magnetic stir-bar was charged with 4-cyanopyridine (3.12 g, 30.0 mmol, 1.0 equiv), CsF (4.56 g, 30.0 mmol, 1.0 equiv), diluted with anhydrous DMF (120 mL, 0.25 M) and sealed with a rubber septum. The septum was pierced with a nitrogen-inlet and a vent needle, and the reaction vessel headspace was flushed with nitrogen gas for 30 min while rapidly stirring. Benzyltrimethylsilane (6.85 mL, 36.0 mmol, 1.2 equiv) was added dropwise over 15 min *via* syringe. The vent needle was removed, and the reaction solution was stirred under a constant flow of nitrogen *via* a nitrogen inlet for 18 h and then poured into a separatory funnel containing H_2O (200 mL). The aqueous layer was extracted with EtOAc (3 x 100 mL) and the organic extracts were combined, washed with water (5 x 50 mL), brine (5 x 100 mL), dried over anhydrous $MgSO_4$, concentrated, and purified *via* silica gel chromatography using 15% EtOAc in hexanes to afford 4-benzylpyridine (4.52 g, 26.7 mmol, 89%) as a pale-yellow oil and bibenzyl (0.172 g, 0.94 mmol, 3%) as a white solid. The spectroscopic data match authentic samples.

4-Benzylpyridine (3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 5.9 Hz, 2H), 7.35 (td, *J* = 6.4, 1.2 Hz, 2H), 7.28 (td, *J* = 7.0, 1.4 Hz, 1H), 7.21 (d, *J* = 7.0 Hz, 2H), 7.13 (d, *J* = 5.9 Hz, 2H), 4.00 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.9, 138.9, 129.1, 128.8, 126.8, 124.3, 41.3.[40]

Bibenzyl. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 4H), 7.21 – 7.18 (m, 6H), 2.92 (s, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.2, 128.9, 128.8, 126.3, 38.4.[41]

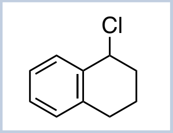
VI. Multigram Scale Sulfonylation/Benzylation Reaction



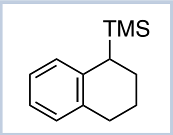
100 mmol

SI-1
90%
15.0 g

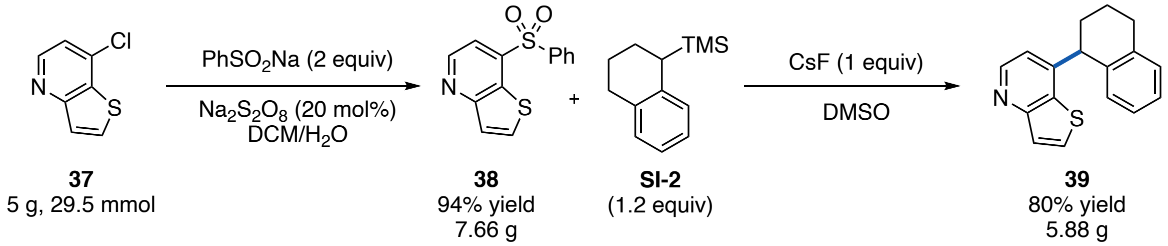
SI-2
91%
16.7 g



1-Chloro-1,2,3,4-tetrahydronaphthalene (SI-1). The title compound was prepared on 100 mmol scale starting from 1,2,3,4-tetrahydronaphthalen-1-ol using a previously reported procedure; the spectroscopic data match the literature.[34]



Trimethyl(1,2,3,4-tetrahydronaphthalen-1-yl)silane (SI-2). A flame-dried 250-mL round-bottom flask equipped with a magnetic stir bar and a reflux condenser was charged with magnesium turnings (2.41 g, 99 mmol, 1.1 equiv), anhydrous THF (130 mL), and chlorotrimethylsilane (17.1 mL, 135 mmol, 1.5 equiv). A solution of 1-chloro-1,2,3,4-tetrahydronaphthalene (**SI-1**, 15.0 g, 90 mmol, 1 equiv) in THF (50 mL) was added dropwise at 0 ºC over 30 min under nitrogen. After the addition was complete, the reaction mixture was refluxed at 70 ºC overnight and then allowed to cool to room temperature, quenched with saturated aqueous NH_4Cl solution (50 mL), and poured into a separatory funnel containing Et_2O (300 mL). The aqueous layer was separated and extracted with Et_2O (3 x 75 mL). The combined organic extracts were washed with water (100 mL), brine (100 mL), and dried over anhydrous $MgSO_4$. Purification *via* silica gel chromatography using hexanes as the eluent afforded **SI-2** as a yellow oil (16.7 g, 81.9 mmol, 91% yield). The spectroscopic data match a previous literature report.[35]

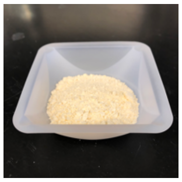


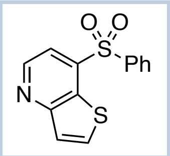
37
5 g, 29.5 mmol

38
94% yield
7.66 g

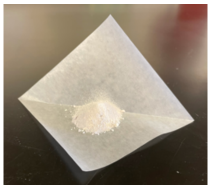
SI-2
(1.2 equiv)

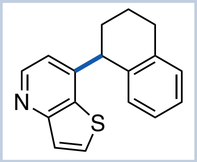
39
80% yield
5.88 g





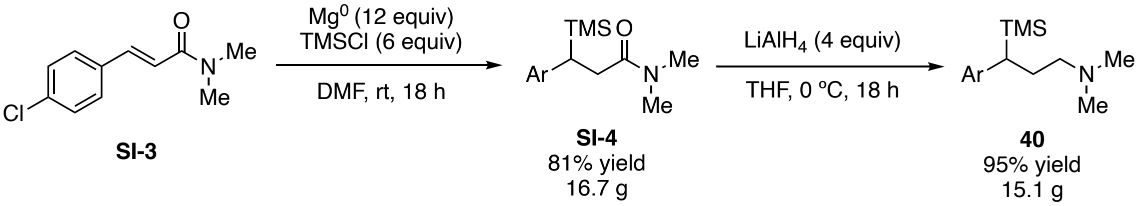
7-(Phenylsulfonyl)thieno[3,2-*b*]pyridine (38). A 250-mL round-bottom flask equipped with a magnetic stir bar was charged with benzenesulfinic acid sodium salt (9.68 g, 59.0 mmol, 2 equiv), sodium persulfate (1.4 g, 5.9 mmol, 20 mol%) and 7-chlorothieno[3,2-b]pyridine (**38**, 5.0 g, 29.5 mmol, 1 equiv). The solids were diluted with CH_2Cl_2 (118 mL) and H_2O (47 mL) and stirred overnight under a constant flow of nitrogen *via* a nitrogen inlet needle. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (100 mL) and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL) and the organic extracts were combined, dried over anhydrous $MgSO_4$ and concentrated. The residual solid was suspended in Et_2O and hexanes (1:1, approx. 200 mL) and the solid was collected *via* a fritted funnel to afford the title compound as a white solid (7.66 g, 27.7 mmol, 94% yield). ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 8.88 (d, *J* = 4.8 Hz, 1H), 8.09 – 8.07 (m, 2H), 7.91 (d, $J = 5.6$ Hz, 1H), 7.81 (d, $J = 4.8$ Hz, 1H), 7.64 – 7.59 (m, 2H), 7.53 – 7.50 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.0, 148.1, 143.4, 139.6, 134.5, 133.9, 129.6, 128.7, 128.2, 125.1, 117.0; **IR** (neat): 3124, 3061, 2926, 2219, 2041, 1979, 1582, 1531 cm-1; **HRMS (ESI)** *m/z* calcd. for $C_{13}H_{10}NO_2S_2$ $(M+H)^+$ 276.0147; found 276.0152; **Melting point:** 145 – 149 ºC.

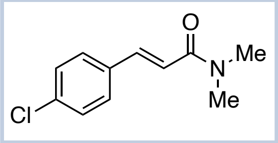




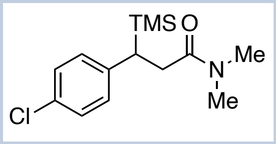
7-(1,2,3,4-Tetrahydronaphthalen-1-yl)thieno[3,2-*b*]pyridine (39). A flame-dried 250-mL round-bottom flask equipped with a magnetic stir bar was charged with 4-benzenesulfonyl pyridine (**38**, 7.66 g, 27.7 mmol, 1 equiv) and CsF (4.21 g, 27.7 mmol, 1 equiv). The reaction vessel was flushed with nitrogen for 30 min with a vent needle. The solid reagents were diluted with anhydrous DMSO (111 mL, 0.25 M) and trimethyl(1,2,3,4-tetrahydronaphthalen-1-yl)silane (**SI-2**, 6.82 g, 33.3 mmol, 1.2 equiv) was added dropwise under vigorous stirring and the reaction mixture was then stirred under nitrogen overnight at room temperature. The reaction mixture was quenched by adding brine (100 mL) and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 75 mL) and the organic extracts were combined, dried over anhydrous $MgSO_4$ and concentrated. The crude residue was purified *via* silica gel chromatography using 15% EtOAc in hexanes to afford **39** as a grey solid (5.88 g, 22.2 mmol, 80% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.60 (d, $J = 1.6$ Hz, 1H), 7.80 (d, $J = 2.0$ Hz, 1H), 7.68 – 7.66 (m, 1H), 7.57 (dd, $J = 5.6, 0.7$ Hz, 1H), 7.23 – 7.17 (m, 2H), 7.10 – 7.06 (m, 1H), 6.86 (d, $J = 7.7$ Hz, 1H), 4.34 (t, $J = 6.5$ Hz, 1H), 3.02 – 2.87 (m, 2H), 2.30 – 2.22 (m, 1H), 1.99 – 1.77 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.5, 148.7, 138.3, 138.1, 137.7, 133.2, 130.2, 130.1, 129.9, 129.3, 126.4, 126.0, 124.9, 43.0, 33.4, 29.6, 20.6; **IR** (neat): 3080, 2929, 2883, 2867, 2852, 2828, 1536, 1451, 1346 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{17}H_{16}NS$ $(M+H)^+$ 266.0998; found 266.0995; **Melting point:** 121 – 123 ºC.

VII. Chlorpheniramine Library Synthesis and Product Characterization

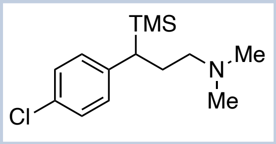




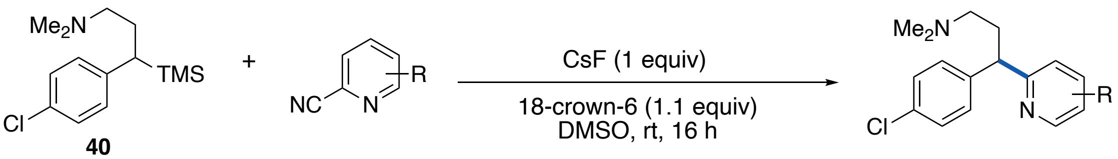
(*E*)-3-(4-Chlorophenyl)-*N*,*N*-dimethylacrylamide (SI-3). The title compound was prepared according to a previously reported procedure[34] using 4-chlorocinnamic acid (13.7 g, 75.0 mmol, 1 equiv), oxalyl chloride (9.5 mL, 112.5 mmol, 1.5 equiv), and two drops of DMF in CH_2Cl_2 (50 mL) to generate the corresponding acid chloride to which was added dimethylamine hydrochloride (7.3 g, 90 mmol, 1.2 equiv) in the presence of triethylamine (26.3 mL, 187.5 mmol, 2.5 equiv) in CH_2Cl_2 (50 mL) to afford **SI-3** as a white solid (15.3 g, 72.3 mmol, 97% yield). The NMR spectra indicates a >20:1 *E/Z* mixture and match previously reported data.[36]



3-(4-Chlorophenyl)-*N*,*N*-dimethyl-3-(trimethylsilyl)propenamide (SI-4). A flame-dried 500-mL round bottom flask equipped with a stir bar and addition funnel was cooled to room temperature under a stream of nitrogen and charged with magnesium turnings (21.2 g, 868 mmol, 12.0 equiv) and anhydrous DMF (362 mL, 0.2 M) and placed under a stream of nitrogen atmosphere *via* a nitrogen inlet needle. The flask was placed in an ice bath and chlorotrimethylsilane (55.0 mL, 434 mmol, 6.0 equiv) was added *via* syringe. A solution of (*E*)-3-(4-chlorophenyl)-*N*,*N*-dimethylacrylamide (**SI-3**, 15.3 g, 72.3 mmol, 1 equiv) in DMF (50 mL) was added dropwise over 1 h *via* an addition funnel at 0 ºC. The reaction mixture was stirred overnight at room temperature and then carefully quenched with saturated $NaHCO_3$ (100 mL) and transferred to a 1 L separatory funnel containing Et_2O (200 mL) and H_2O (300 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 x 100 mL), washed with brine (4 x 100 mL), dried over anhydrous $MgSO_4$, concentrated, and purified *via* silica gel chromatography using 20% EtOAc in hexanes to afford **SI-4** as a tan solid (16.7 g, 58.9 mmol, 81% yield). ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.5 Hz, 2H), 3.01 (s, 3H), 2.88 – 2.77 (m, 5H), 2.63 (dd, *J* = 14.5, 3.2 Hz, 1H), 0.00 (s, 9H); ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 171.7, 142.3, 130.0, 128.7, 128.1, 37.1, 35.5, 33.3, 31.7, -2.9; **IR** (neat): 3063, 2952, 2906, 1641, 1586, 1489, 1413, 1394 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{14}H_{23}ClNOSi$ $(M+H)^+$ 284.1232; found 284.1225; **Melting point:** 119 – 122 ºC.

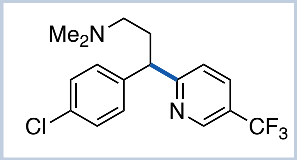


3-(4-Chlorophenyl)-*N*,*N*-dimethyl-3-(trimethylsilyl)propan-1-amine (40). A flame-dried 500-mL round bottom flask equipped with a stir bar and addition funnel was cooled to room temperature under a stream of nitrogen and charged with $LiAlH_4$ (8.9 g, 235.6 mmol, 4.0 equiv), anhydrous THF (295 mL, 0.2 M) and cooled to 0 ºC in an ice bath. A solution of 3-(4-chlorophenyl)-*N*,*N*-dimethyl-3-(trimethylsilyl)propenamide (**SI-4**, 16.7 g, 58.9 mmol, 1.0 equiv) in THF (50 mL) was added dropwise under nitrogen over 1 h and stirred overnight at room temperature. Fieser's workup[37] was performed and the reaction was transferred to a 1 L separatory funnel containing Et_2O (200 mL) and H_2O (300 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 x 100 mL), washed with brine (4 x 100 mL), dried over anhydrous $MgSO_4$, concentrated, and purified *via* silica gel chromatography using 30% EtOAc in hexanes to afford **40** as a yellow oil containing approximately 5% of protodesilylated byproduct (15.1 g, 56.0 mmol, 95% yield). ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.2 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 2.17 (s, 6H), 2.14 – 2.10 (m, 2H), 2.05 – 2.00 (m, 1H), 1.92 – 1.85 (m, 2H), -0.07 (s, 9H); ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 142.0, 129.9, 128.8, 128.2, 59.4, 45.5, 34.2, 27.4, -3.1; **IR** (neat): 3025, 2949, 2856, 2765, 1891, 1489, 1407, 1278 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{14}H_{25}ClNSi$ $(M+H)^+$ 270.1439; found 270.1425.

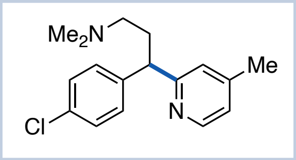


General procedure for chlorpheniramine library synthesis (GP2). In a nitrogen-filled glovebox, to an oven-dried 2-dram glass vial (8 mL, Thermo Scientific, B7999-3) equipped with a magnetic stir bar was added cyano- or haloarene (1.0 mmol, 1.0 equiv) and 3-(4-chlorophenyl)-

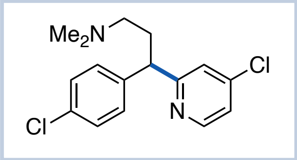
N,*N*-dimethyl-3-(trimethylsilyl)propan-1-amine (**40**) (0.324 g, 1.2 mmol, 1.2 equiv) which was diluted with 18-crown-6 (1M in THF, 1.1 mL, 1.1 equiv) and anhydrous DMSO (2.9 mL, 0.25 M relative to total volume). Solid CsF (0.152 g, 1.0 mmol, 1.0 equiv) was added in one portion and the vial was sealed with a screw cap (Thermo Scientific, B7807-15) equipped with a 2.6 mm PTFE/Silicone Septa (Thermo Scientific, B7995-15). Generally, a color change immediately occurred from clear to bright yellow, purple, or red. The reaction vial was removed from the glovebox and vigorously stirred at room temperature for 16 h. The reaction mixture was then poured into a separatory funnel and diluted with brine (50 mL), extracted with EtOAc (3 x 15 mL), washed with H_2O (3 x 15 mL) and brine (2 x 25 mL) and dried over anhydrous $MgSO_4$. After concentration under reduced pressure, the crude reaction mixture was purified on basic Al_2O_3 using EtOAc/CH_2Cl_2/Et_3N or MeOH/CH_2Cl_2 to afford the chlorpheniramine analogue product.



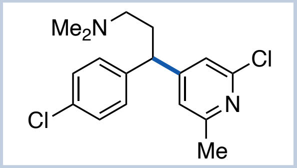
3-(4-Chlorophenyl)-*N*,*N*-dimethyl-3-(5-(trifluoromethyl)pyridin-2-yl)propan-1-amine (41). GP2 was followed using 5-(trifluoromethyl)picolinonitrile (0.172 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 3-(4-chlorophenyl)-*N*,*N*-dimethyl-3-(trimethylsilyl)propan-1-amine (**40**, 0.324 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified by column chromatography on basic Al_2O_3 using 3% EtOAc in CH_2Cl_2 with 0.1% Et_3N to afford **41** as a yellow oil (0.154 g, 0.45 mmol, 45% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 7.55 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.07 – 7.02 (m, 5H), 4.00 (t, *J* = 4.8 Hz, 1H), 2.25 – 2.17 (m, 1H), 2.00 – 1.92 (m, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.1, 146.3 (q, *J* = 4.1 Hz), 141.2, 133.5 (q, *J* = 3.5 Hz), 132.6, 129.5, 128.8, 124.6 (q, *J* = 33.2 Hz), 123.6 (q, *J* = 272.9 Hz), 122.7, 57.4, 50.4, 45.4, 32.8; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.3; **IR** (neat): 2945, 2860, 2818, 2769, 1606, 1573, 1490, 1326 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{17}H_{19}ClF_3N_2$ $(M+H)^+$ 343.1183; found 343.1188.



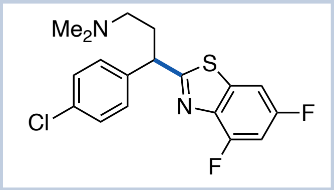
3-(4-Chlorophenyl)-*N*,*N*-dimethyl-3-(4-methylpyridin-2-yl)propan-1-amine (42). GP2 was followed using 4-methylpicolinonitrile (0.118 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 3-(4-chlorophenyl)-*N*,*N*-dimethyl-3-(trimethylsilyl)propan-1-amine (**40**, 0.324 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified by column chromatography on basic Al_2O_3 using 3% EtOAc in CH_2Cl_2 with 0.1% Et_3N to afford **42** as a yellow oil (0.231 g, 0.80 mmol, 80% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 5.0 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.95 (s, 1H), 6.89 (d, *J* = 5.1 Hz, 1H), 4.06 (t, *J* = 7.7 Hz, 1H), 2.44 – 2.32 (m, 1H), 2.26 (s, 3H), 2.20 – 2.13 (m, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.8, 149.1, 147.5, 142.4, 132.1, 129.4, 128.5, 123.6, 122.5, 57.7, 50.4, 45.5, 32.9, 21.0; **IR** (neat): 3012, 2942, 2815, 2766, 2202, 1603, 1489, 1460 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{17}H_{22}ClN_2$ $(M+H)^+$ 289.1466; found 289.1456.



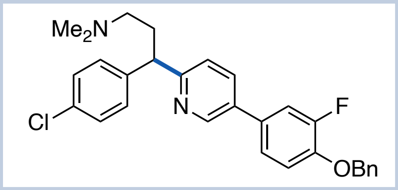
3-(4-Chlorophenyl)-3-(4-chloropyridin-2-yl)-*N*,*N*-dimethylpropan-1-amine (43). GP2 was followed using 4-chloropicolinonitrile (0.139 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 3-(4-chlorophenyl)-*N*,*N*-dimethyl-3-(trimethylsilyl)propan-1-amine (**40**, 0.324 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified by column chromatography on basic Al_2O_3 using 5% EtOAc in CH_2Cl_2 with 1% Et_3N to afford **43** as a yellow oil (0.155 g, 0.50 mmol, 50% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 5.3 Hz, 1H), 7.23 – 7.15 (m, 4H), 7.08 (d, *J* = 1.8 Hz, 1H), 7.03 (dd, *J* = 5.4, 2.0 Hz, 1H), 4.03 (t, *J* = 7.3 Hz, 1H), 2.37 – 2.28 (m, 1H), 2.15 – 2.05 (m, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.9, 150.3, 144.3, 141.4, 132.5, 129.4, 128.7, 123.2, 121.9, 57.4, 50.3, 45.4, 32.8; **IR** (neat): 3046, 2942, 2857, 2816, 2766, 1572, 1554, 1490 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{16}H_{19}Cl_2N_2$ $(M+H)^+$ 309.0920; found 309.0910.



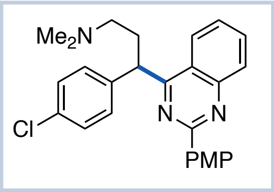
3-(2-Chloro-6-methylpyridin-4-yl)-3-(4-chlorophenyl)-*N*,*N*-dimethylpropan-1-amine (44). GP2 was followed using 2-chloro-6-methylisonicotinonitrile[16] (0.153 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 3-(4-chlorophenyl)-*N*,*N*-dimethyl-3-(trimethylsilyl)propan-1-amine (**40**, 0.324 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified by column chromatography on basic Al_2O_3 using 5% MeOH in CH_2Cl_2 to afford **44** as a yellow oil (0.291 g, 0.90 mmol, 90% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.03 (d, *J* = 8.5 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 6.76 (s, 1H), 6.67 (s, 1H), 3.74 (t, *J* = 7.6 Hz, 1H), 2.22 (s, 3H), 1.99 – 1.86 (m, 11H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.4, 156.8, 150.8, 140.8, 132.8, 129.2, 129.0, 121.4, 120.3, 57.0, 47.0, 45.4, 32.5, 24.2; **IR** (neat): 2944, 2859, 2768, 2230, 1595, 1549, 1491, 1460 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{17}H_{21}Cl_2N_2$ $(M+H)^+$ 323.1076; found 323.1064.



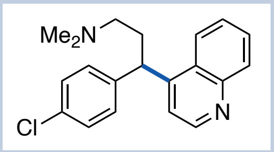
3-(4-Chlorophenyl)-3-(4,6-difluorobenzo[*d*]thiazol-2-yl)-*N*,*N*-dimethylpropan-1-amine (45). GP2 was followed using 2-chloro-4,6-difluorobenzo[*d*]thiazole[38] (0.206 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 3-(4-chlorophenyl)-*N*,*N*-dimethyl-3-(trimethylsilyl)propan-1-amine (**40**, 0.324 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified by column chromatography on basic Al_2O_3 using 5% MeOH in CH_2Cl_2 to afford **45** as a yellow oil (0.213 g, 0.58 mmol, 58% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28 – 7.21 (m, 4H), 7.20 – 7.18 (m, 1H), 6.87 (dt, *J* = 10.2, 2.3 Hz, 1H), 4.46 (t, *J* = 7.8 Hz, 1H), 2.56 – 2.49 (m, 1H), 2.26 – 2.10 (m, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -112.8, -117.5; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.5 (d, *J* = 3.0 Hz), 160.1 (dd, *J* = 248.3, 10.4 Hz), 155.2 (dd, *J* = 260.1, 13.4 Hz), 139.6, 138.8 (dd, *J* = 13.3, 2.5 Hz), 138.2 (dd, *J* = 12.7, 5.1 Hz), 133.5, 129.6, 129.2, 103.7 (dd, *J* = 26.5, 4.6 Hz), 102.1 (dd, *J* = 28.4, 22.0 Hz), 56.9, 47.6, 45.4, 33.4; **IR** (neat): 3088, 2943, 2859, 2769, 2193, 1620, 1576, 1490 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{18}H_{18}ClF_2N_2S$ $(M+H)^+$ 367.0842; found 367.0834.



3-(5-(4-(Benzyloxy)-3-fluorophenyl)pyridin-2-yl)-3-(4-chlorophenyl)-*N*,*N*-dimethylpropan-1-amine (46). GP2 was followed using 5-(4-(benzyloxy)-3-fluorophenyl)picolinonitrile (**SI-6**, 0.304 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 3-(4-chlorophenyl)-*N*,*N*-dimethyl-3-(trimethylsilyl)propan-1-amine (**40**, 0.324 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified by column chromatography on basic Al_2O_3 using 5% MeOH in CH_2Cl_2 to afford **46** as a yellow oil (0.451 g, 0.95 mmol, 95% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 2.4 Hz, 1H), 7.58 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.38 – 7.33 (m, 2H), 7.32 – 7.26 (m, 2H), 7.26 – 7.15 (m, 6H), 7.14 – 7.09 (m, 2H), 6.97 (t, *J* = 8.5 Hz, 1H), 5.09 (s, 2H), 4.08 (t, *J* = 7.4 Hz, 1H), 2.42 – 2.33 (m, 1H), 2.21 – 2.08 (m, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -132.7; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.9, 154.3, 151.9, 147.4, 146.6 (d, *J* = 10.9 Hz), 142.1, 136.3, 134.4, 133.0 (d, *J* = 1.8 Hz), 132.3, 131.3 (d, *J* = 6.7 Hz), 129.4, 128.7, 128.2, 127.4, 122.7, 122.6 (d, *J* = 3.5 Hz), 116.1 (d, *J* = 2.3 Hz), 114.8 (d, *J* = 19.3 Hz), 71.4, 57.6, 50.2, 45.5, 32.9; **IR** (neat): 3032, 2941, 2858, 2767, 1620, 1556, 1480, 1466 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{29}H_{29}ClFN_2O$ $(M+H)^+$ 475.1947; found 475.1936.

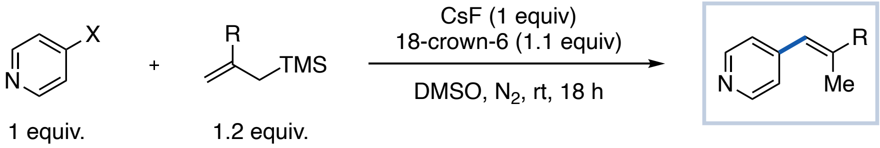


3-(4-Chlorophenyl)-3-(2-(4-methoxyphenyl)quinazolin-4-yl)-*N*,*N*-dimethylpropan-1-amine (47). GP2 was followed using 2-(4-methoxyphenyl)quinazoline-4-carbonitrile[39] (0.261 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 3-(4-chlorophenyl)-*N*,*N*-dimethyl-3-(trimethylsilyl)propan-1-amine (**40**, 0.324 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified by column chromatography on basic Al_2O_3 using 3% EtOAc in CH_2Cl_2 with 0.1% Et_3N to afford **47** as a yellow oil (0.389 g, 0.90 mmol, 90% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 8.9 Hz, 2H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.80 (d, *J* = 8.6 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.26 – 7.23 (m, 1H), 7.21 (d, *J* = 8.5 Hz, 2H), 7.02 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.9 Hz, 2H), 4.84 (t, *J* = 7.0 Hz, 1H), 3.69 (s, 3H), 2.60 – 2.51 (m, 1H), 2.22 – 2.14 (m, 1H), 2.12 – 2.04 (m, 2H), 2.01 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.7, 161.9, 159.7, 151.4, 141.2, 133.3, 132.6, 131.2, 130.3, 129.8, 129.4, 128.8, 126.6, 124.5, 122.2, 114.0, 57.5, 55.5, 45.6, 45.3, 33.4; **IR** (neat): 3068, 2937, 2836, 2767, 1605, 1583, 1545, 1285 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{26}H_{27}ClN_3O$ $(M+H)^+$ 432.1837; found 432.1822.

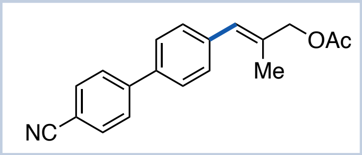


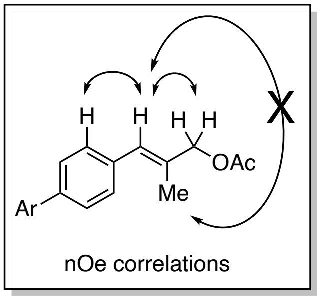
3-(4-Chlorophenyl)-*N*,*N*-dimethyl-3-(quinolin-4-yl)propan-1-amine (48). GP2 was followed using 4-chloroquinoline (0.164 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 3-(4-chlorophenyl)-*N*,*N*-dimethyl-3-(trimethylsilyl)propan-1-amine (**40**, 0.324 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified by column chromatography on basic Al_2O_3 using 2% MeOH in CH_2Cl_2 with 1% Et_3N to afford **48** as a yellow oil (0.214 g, 0.66 mmol, 66% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 4.6 Hz, 1H), 7.88 (dd, *J* = 8.5, 2.8 Hz, 2H), 7.46 – 7.42 (m, 1H), 7.30 – 7.26 (m, 1H), 7.14 (d, *J* = 4.6 Hz, 1H), 7.08 – 6.98 (m, 4H), 4.66 (t, *J* = 7.8 Hz, 1H), 2.13 – 2.05 (m, 2H), 2.03 – 1.95 (m, 8H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.2, 149.8, 148.7, 141.6, 132.4, 130.4, 129.4, 129.1, 128.8, 127.2, 126.6, 123.6, 119.0, 57.3, 45.6, 42.6, 33.6; **IR** (neat): 3032, 2970, 2816, 2766, 1614, 1507, 1490, 1461 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{20}H_{22}ClN_2$ $(M+H)^+$ 325.1466; found 325.1457.

VIII. Additional Organosilane Coupling Reactions



General coupling procedure using allyltrimethylsilanes (GP3): In a nitrogen-filled glovebox, to an oven-dried 2-dram glass vial (8 mL, Thermo Scientific, B7999-3) equipped with a magnetic stir bar was added aryl electrophile (1.0 mmol, 1.0 equiv), allyltrimethylsilane (1.2 mmol, 1.2 equiv), a solution of 18-crown-6 (1M in THF, 1.1 mL, 1.1 equiv) and anhydrous DMSO (2.9 mL, 0.25 M relative to total volume). Solid CsF (0.152 g, 1.0 mmol, 1.0 equiv) was added in one portion and the vial was sealed with a screw cap (Thermo Scientific, B7807-15) equipped with a 2.6 mm PTFE/Silicone Septa (Thermo Scientific, B7995-15). The reaction vial was removed from the glovebox and the reaction mixture was vigorously stirred at room temperature for 18 h. The reaction mixture was poured into a separatory funnel and diluted with brine (50 mL), extracted with EtOAc (3 x 15 mL), washed with H_2O (3 x 15 mL) and brine (2 x 25 mL) and dried over $MgSO_4$. After concentration under reduced pressure, the crude reaction mixture was purified *via* silica gel chromatography using EtOAc/hexanes or Et_2O/hexanes to afford the diarylmethane product.





(*E*)-3-(4'-Cyano-[1,1'-biphenyl]-4-yl)-2-methylallyl acetate (54). GP3 was followed using [1,1'-biphenyl]-4,4'-dicarbonitrile[9] (0.204 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and 2-[(acetoxymethyl)allyl]trimethylsilane (0.224 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO at 60 ºC for 18 h. The product was purified *via* silica gel chromatography using 60% CH_2Cl_2 in hexanes to afford **54** as a purple solid as a 10:1 alkene isomeric mixture (5% yield of 2-((4'-isocyano-[1,1'-biphenyl]-4-yl)methyl)allyl acetate and 51% yield of a >20:1 *E*/*Z* styrene mixture confirmed *via* nOe ^{1}H NMR analysis; 0.163 g, 0.56 mmol, 56% total yield). Major (*E*)-alkene peaks: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 – 7.67 (m, 4H), 7.57 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 6.55 (s, 1H), 4.66 (s, 2H), 2.13 (s, 3H), 1.94 (d, *J* = 0.9 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.9, 145.2, 137.6, 137.4, 134.0, 132.7, 129.7, 127.6, 127.3, 127.0, 119.0, 110.9, 70.0, 21.1, 15.8; Minor (*Z*)-alkene diagnostic peaks: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.3 Hz, 2H), 6.16 (d, *J* = 1.6 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 134.7, 129.6, 127.7, 127.1, 110.8, 70.0, 20.9; Allylated arene isomer diagnostic peaks: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 5.17 (s, 1H), 5.01 (s, 1H), 4.50 (s, 2H), 3.45 (s, 2H), 2.06 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.8, 145.4, 142.9, 139.4, 129.8, 127.6, 127.3, 126.7, 118.7, 114.8, 66.3, 39.8, 29.8; **IR** (neat): 3030, 2920, 2852, 2226, 1732, 1606, 1493 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{19}H_{18}NO_2$ $(M+Na)^+$ 314.1151; found 314.1187; **Melting point:** 151 – 154 ºC.

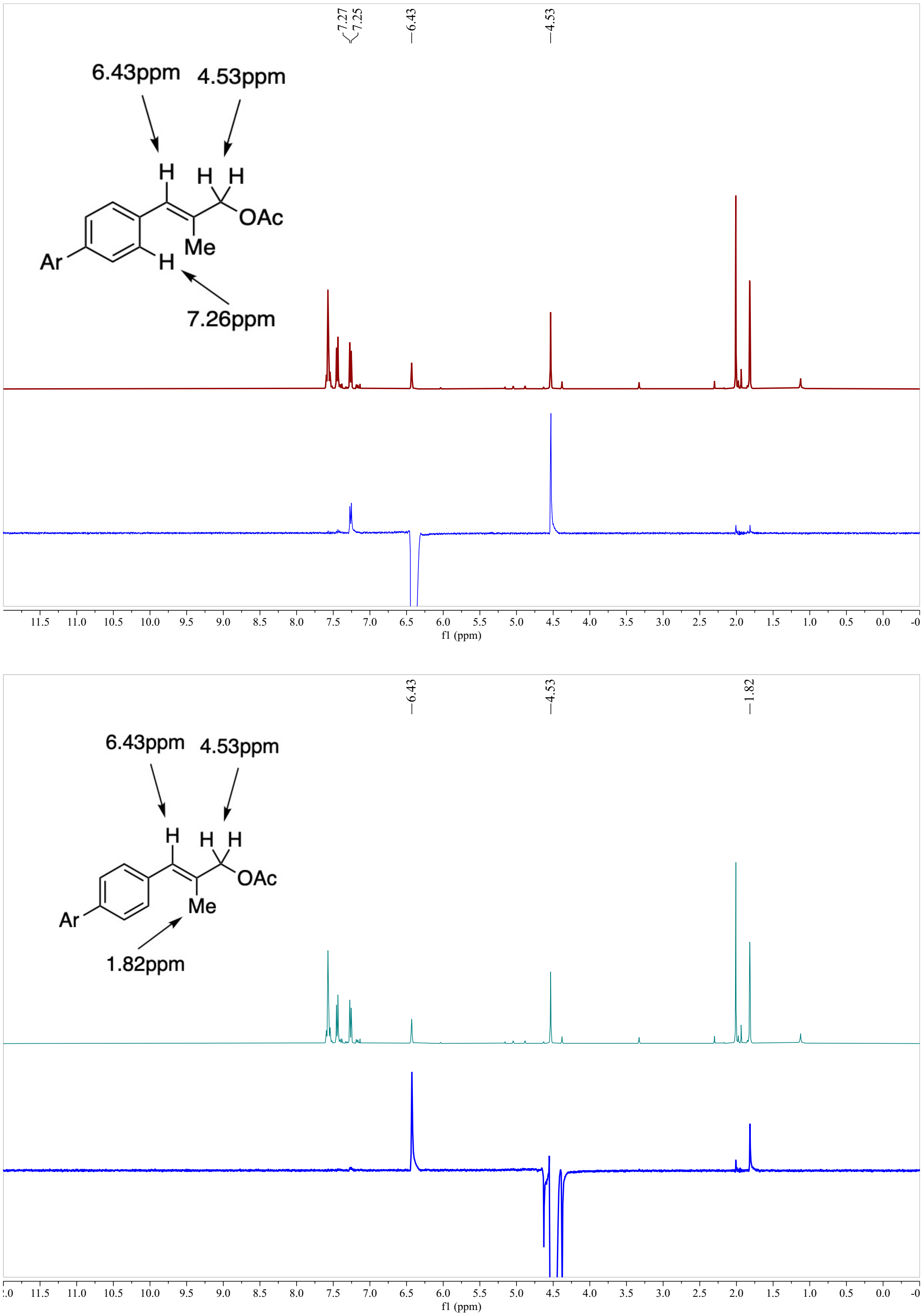
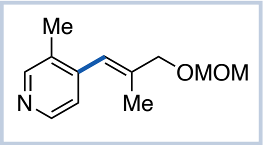
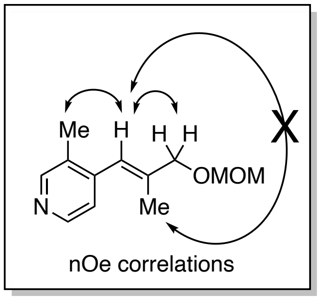


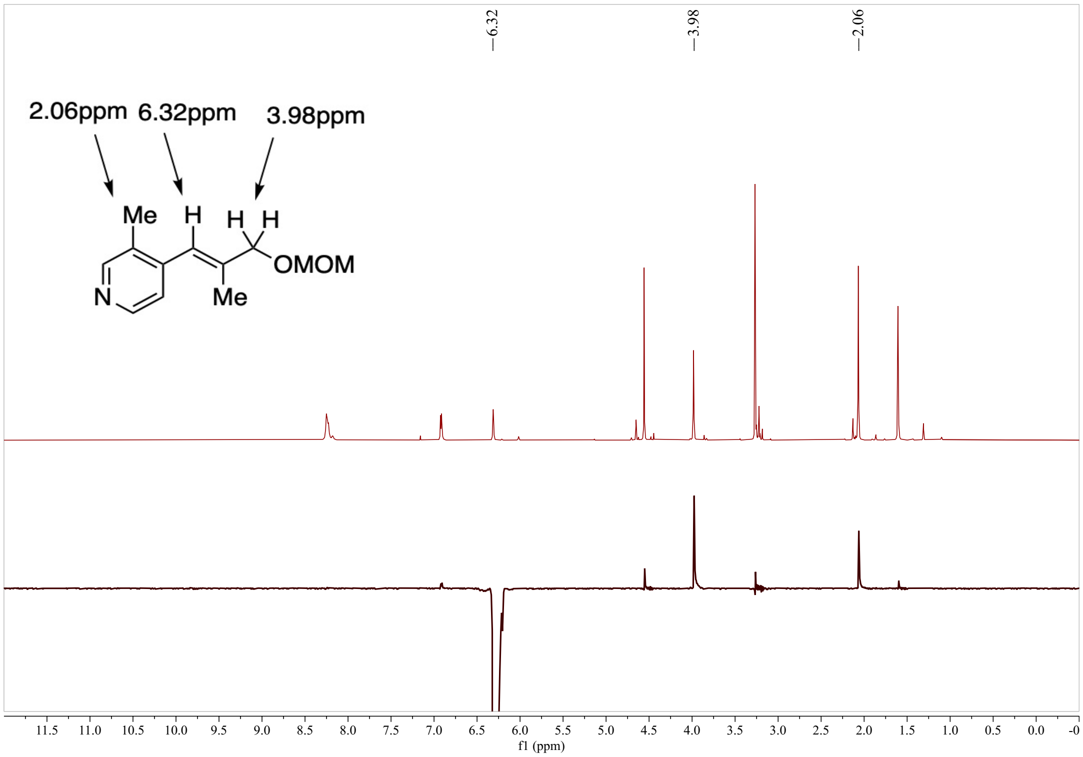
Fig. S1: ^{1}H NMR 1D Selective nOe Correlation Spectra for **54**.





nOe correlations

(*E*)-4-(3-(Methoxymethoxy)-2-methylprop-1-en-1-yl)-3-methylpyridine (55). GP3 was followed using 3-methylisonicotinonitrile (0.118 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (2-((methoxymethoxy)methyl)allyl)trimethylsilane[40] (0.226 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 16 h. The product was purified *via* silica gel chromatography using 10% EtOAc in hexanes to afford **55** as a colorless oil (0.197 g, 0.95 mmol, 95% yield, *E*:*Z* = 10:1 confirmed *via* nOe ^{1}H NMR analysis) along with <5% of signals characteristic of a vinyl ether alkene isomer. **^{1}H NMR** (400 MHz, $CDCl_3$) δ Major isomer: 8.35 – 8.33 (m, 2H), 7.02 (d, *J* = 4.9 Hz, 1H), 6.41 (s, 1H), 4.66 (s, 2H), 4.08 (s, 2H), 3.37 (s, 3H), 2.17 (s, 3H), 1.71 (d, *J* = 1.0 Hz, 3H); Minor isomer diagnostic peaks: 6.12 (brs, 1H), 4.75 (s, 2H), 3.32 (s, 3H), 2.23 (s, 3H), 1.41 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ Major peaks: 150.7, 147.0, 144.5, 138.0, 131.6, 123.5, 122.8, 95.8, 72.2, 55.4, 16.6, 15.5; Minor diagnostic peaks: 150.4, 147.4, 139.5, 96.3, 55.8, 32.2, 17.3, 16.2; **IR** (neat): 2930, 2885, 2823, 2360, 1722, 1591, 1442, 1405 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{12}H_{18}NO_2$ $(M+H)^+$ 208.1332; found 208.1321.



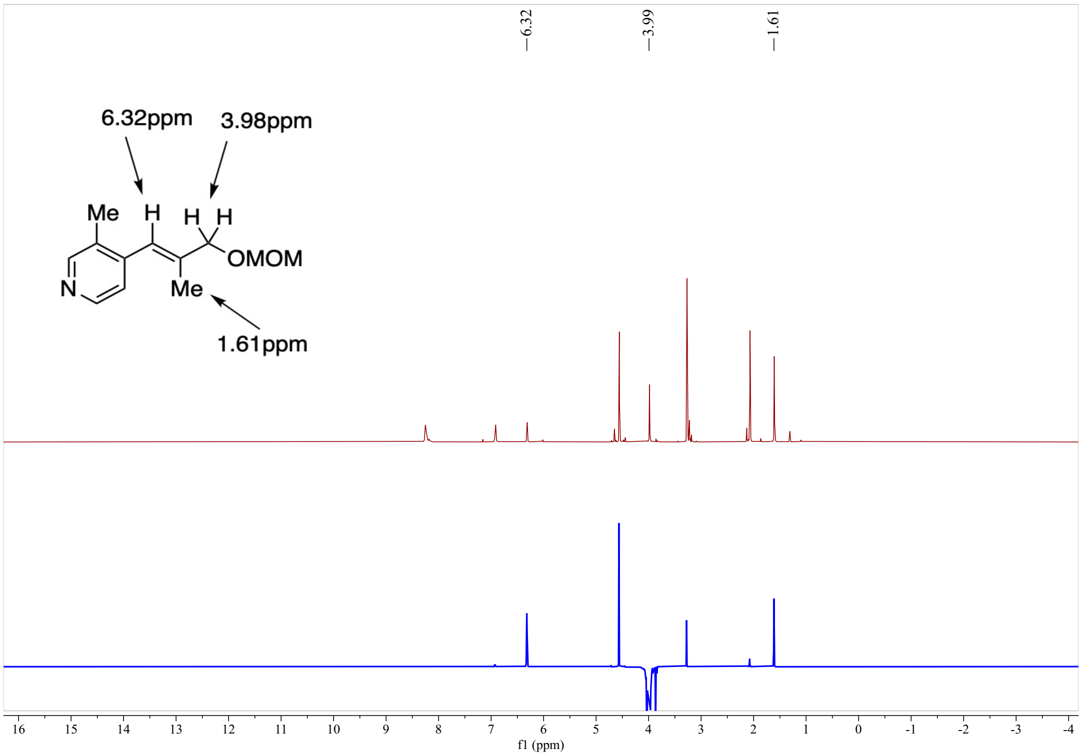
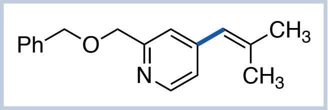
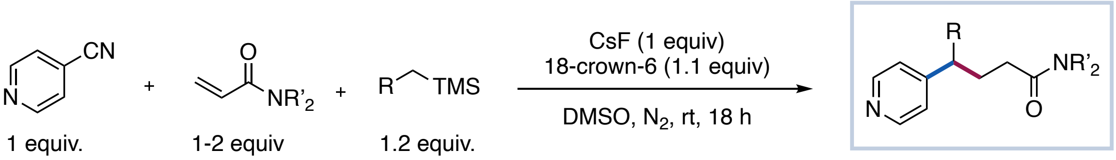


Fig. S2: ^{1}H NMR 1D Selective nOe Correlation Spectrum of **55**.

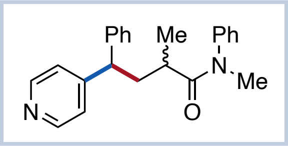


2-((Benzyloxy)methyl)-4-(2-methylprop-1-en-1-yl)pyridine (56). GP3 was followed using 2-((benzyloxy)methyl)-4-(phenylsulfonyl)pyridine (**SI-15**, 0.339 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and methallyltrimethylsilane (0.154 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO at 60 ºC for 16 h. The product was purified by column chromatography on basic Al_2O_3 using 10% EtOAc in hexanes to afford **56** as a colorless oil (0.144 g, 0.57 mmol, 57% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.45 (d, J = 5.0 Hz, 1H), 7.39 – 7.25 (m, 6H), 7.04 (d, J = 4.6 Hz, 1H), 6.19 (s, 1H), 4.69 (s, 2H), 4.64 (s, 2H), 1.92 (s, 3H), 1.89 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.2, 148.8, 147.1, 140.5, 138.1, 128.5, 127.9, 127.8, 123.3, 122.3, 121.3, 73.2, 73.0, 27.3, 19.8; **IR** (neat): 3063, 2924, 2854, 2215, 1656, 1599, 1546, 1453 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{17}H_{20}NO$ $(M+H)^+$ 254.1539; found 254.1536. **Note:** the title product was isolated with a minor alkene isomer in a >20:1 ratio; diagnostic ^{1}H NMR shifts of minor isomer: δ 4.87 (s, 1H), 4.85 (s, 1H), 3.30 (s, 2H), 1.66 (s, 3H).

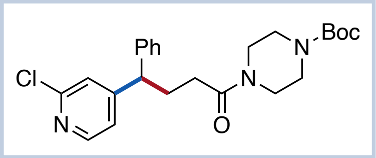
IX. Tandem Arylation/Michael Addition to Acrylamides



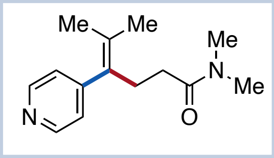
General coupling procedure for three-component reaction (GP4): In a nitrogen-filled glovebox, to an oven-dried 2-dram glass vial (8 mL, Thermo Scientific, B7999-3) equipped with a magnetic stir bar was added cyanoarene (1.0 mmol, 1.0 equiv), acrylamide (1 – 2 equiv), allyl- or benzyltrimethylsilane (1.2 mmol, 1.2 equiv), a solution of 18-crown-6 (1M in THF, 1.1 mL, 1.1 equiv) and anhydrous DMSO (2.9 mL, 0.25 M of cyanoarene relative to total volume). Solid CsF (0.152 g, 1.0 mmol, 1.0 equiv) was added in one portion and the vial was sealed with a screw cap (Thermo Scientific, B7807-15) equipped with a 2.6 mm PTFE/Silicone Septa (Thermo Scientific, B7995-15). The reaction vial was removed from the glovebox and the mixture was vigorously stirred at room temperature for 18 h. The reaction mixture was poured into a separatory funnel and diluted with brine (50 mL), extracted with EtOAc (3 x 15 mL), washed with H_2O (3 x 15 mL) and brine (2 x 25 mL) and dried over $MgSO_4$. After concentration under reduced pressure, the crude reaction mixture was purified *via* silica gel chromatography using EtOAc/hexanes or Et_2O/hexanes.



***N*,2-Dimethyl-*N*,4-diphenyl-4-(pyridin-4-yl)butanamide (57).** GP4 was followed using 4-cyanopyridine (0.104 g, 1.0 mmol, 1.0 equiv), *N*-methyl-*N*-phenylmethacrylamide[41] (0.351 g, 2.0 mmol, 2.0 equiv), CsF (0.182 g, 1.2 mmol, 1.2 equiv), 18-crown-6 (1 M in THF, 1.2 mL, 1.2 mmol, 1.2 equiv) and benzyltrimethylsilane (0.197 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 18 h. The product was purified *via* silica gel chromatography using 50% EtOAc in hexanes to afford **57** as a yellow oil (0.327 g, 0.95 mmol, 95% yield, d.r. = 1:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 3.4 Hz, 2H), 8.42 (d, *J* = 3.4 Hz, 2H), 7.37 – 7.16 (m, 15H), 7.11 (d, *J* = 5.1 Hz, 2H), 7.06 – 7.01 (m, 3H), 6.81 (d, *J* = 5.6 Hz, 2H), 6.73 (d, *J* = 5.6 Hz, 2H), 4.04 – 4.00 (m, 1H), 3.97 – 3.93 (m, 1H), 3.24 (s, 6H), 2.53 – 2.33 (m, 4H), 2.14 – 1.96 (m, 2H), 1.09 (d, *J* = 6.5 Hz, 3H), 1.06 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.8, 175.6, 153.8, 153.0, 149.8, 149.5, 143.32, 143.28, 142.6, 141.8, 129.5, 129.4, 128.8, 128.5, 128.0, 127.6, 127.55, 127.49, 127.0, 126.85, 126.83, 126.5, 123.3, 122.9, 48.0, 47.9, 39.0, 38.9, 37.3, 34.4, 34.3, 18.3, 18.0; **IR** (neat): 3060, 2971, 2874, 2238, 1946, 1648, 1594, 1495 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{23}H_{25}N_2O$ $(M+H)^+$ 345.1961; found 345.1955.

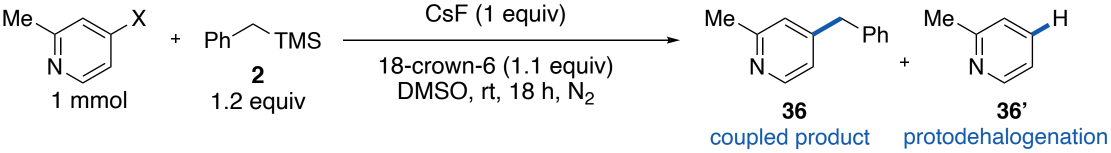


***tert*-Butyl 4-(4-(2-chloropyridin-4-yl)-4-phenylbutanoyl)piperazine-1-carboxylate (58).** GP4 was followed using 2-chloroisonicotinonitrile (0.139 g, 1.0 mmol, 1.0 equiv), *tert*-butyl 4-acryloylpiperazine-1-carboxylate[42] (0.240 g, 1.0 mmol, 1.0 equiv), CsF (0.182 g, 1.2 mmol, 1.2 equiv), 18-crown-6 (1 M in THF, 1.2 mL, 1.2 mmol, 1.2 equiv) and benzyltrimethylsilane (0.197 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 18 h. The product was purified *via* silica gel chromatography using 45% EtOAc in hexanes to afford **58** as a yellow oil (0.226 g, 0.51 mmol, 51% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 5.2 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.27 – 7.26 (m, 1H), 7.22 – 7.20 (m, 3H), 7.11 (dd, *J* = 5.2, 1.1 Hz, 1H), 4.01 (dd, *J* = 8.6, 7.1 Hz, 1H), 3.59 – 3.58 (m, 2H), 3.41 – 3.35 (m, 4H), 3.28 – 3.27 (m, 2H), 2.49 – 2.33 (m, 2H), 2.28 – 2.24 (m, 2H), 1.47 (s, 9H); **^{13}C NMR** (101 MHz, CDCl$_3$) δ 170.5, 157.0, 154.5, 151.8, 149.7, 141.5, 129.0, 128.0, 127.3, 123.5, 122.0, 80.3, 49.5, 45.1, 43.8, 41.4, 30.7, 29.8, 28.4; **IR** (neat): 3058, 2976, 2861, 2243, 1691, 1642, 1588, 1494 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{24}H_{31}ClN_3O_3$ $(M+H)^+$ 444.2048; found 444.2033.



***N*,*N*,5-Trimethyl-4-(pyridin-4-yl)hex-4-enamide (59).** GP4 was followed using 4-cyanopyridine (0.104 g, 1.0 mmol, 1.0 equiv), *N*,*N*-dimethylacrylamide (0.198 g, 2.0 mmol, 2.0 equiv), CsF (0.182 g, 1.2 mmol, 1.2 equiv), 18-crown-6 (1 M in THF, 1.2 mL, 1.2 mmol, 1.2 equiv) and methallyltrimethylsilane (0.154 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 18 h. The product was purified *via* silica gel chromatography using 5% MeOH in CH$_2$Cl$_2$ to afford **59** as a yellow oil (0.146 g, 0.63 mmol, 63% yield; isolated material contains <5% of signals characteristic of an alkene isomer). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.47 (d, *J* = 5.4 Hz, 2H), 7.00 (d, *J* = 6.0 Hz, 2H), 2.82 (s, 3H), 2.80 (s, 3H), 2.66 – 2.62 (m, 2H), 2.16 – 2.12 (m, 2H), 1.80 (s, 3H), 1.51 (s, 3H); **^{13}C NMR** (101 MHz, CDCl$_3$) δ 172.1, 151.5, 149.6, 131.6, 130.7, 124.4, 37.1, 35.3, 31.7, 29.1, 22.2, 20.3; **IR** (neat): 3018, 2926, 2859, 2342, 1737, 1640, 1594, 1492 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{14}H_{21}N_2O$ $(M+H)^+$ 233.1648; found 233.1636.

X. Analysis of Arene Coupling Partner Leaving Group



Coupling of alternative arene electrophiles: In a nitrogen-filled glovebox, to an oven-dried 2-dram glass vial (8 mL, Thermo Scientific, B7999-3) equipped with a magnetic stir bar was added the arene coupling partner (1.0 mmol, 1.0 equiv), benzyltrimethylsilane (1.2 mmol, 1.2 equiv), a solution of 18-crown-6 (1M in THF, 1.1 mL, 1.1 equiv) and anhydrous DMSO (2.9 mL, 0.25 M relative to total volume). Solid CsF (0.152 g, 1.0 mmol, 1.0 equiv) was added in one portion and the vial was sealed with a screw cap (Thermo Scientific, B7807-15) equipped with a 2.6 mm PTFE/Silicone Septa (Thermo Scientific, B7995-15). The reaction vial was removed from the glovebox and the reaction solution was vigorously stirred at room temperature for 18 h. The reaction vial was then opened and CH$_2$Br$_2$ (0.1 mmol, 7 μL) was added as an internal standard. The reaction mixture was analyzed by ^{1}H NMR spectroscopy and the yield of **36** and **36’** (2-methylpyridine) were determined by integration of the product benzylic methylene or aryl C–H signal relative to CH$_2$Br$_2$. The spectral data of **36** match a previous report.[43] The influences of changes in the leaving group are shown in Table S2 below.

Table S2. Effect of leaving group "X" on reaction outcome.

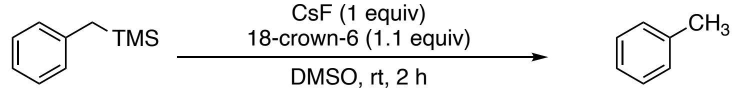
X	% 36	% 36'	% Ar-X Remaining
F	0	0	100
Cl	0	0	88
Br	0	1	50
I	0	67	12
NO_2	0	0	0
CN	95%	0	0
$PhSO_2$	70%	0	0

XI. Studies on Reaction Trends, Selectivity and Observed Byproducts

(a) Experiments concerning the selectivity for benzylic arylation over protonation

Introduction. Lewis base-promoted addition reactions using benzyltrimethylsilane are proposed to proceed through hypercoordinate silicates or potentially discrete benzyl carbanions.[44] These intermediates are likely very basic and thus protodesilylation could be a competing pathway with arylation. We performed studies described below to examine the potential for this competition and its implications for reaction selectivity. While these experiments cannot rule out formation of a discrete benzylic carbanion as the active coupling intermediate, they clearly demonstrate the selectivity for arylation over competing proton transfer from acidic C–H bonds (from the solvent, substrate and products).

Protodesilylation. To initially test for the potential of competing proton transfer, we removed 4-cyanopyridine from the standard reaction conditions in DMSO and observed near quantitative protodesilylation in 2 h at rt. **Procedure:** benzyltrimethylsilane (**2**, 0.082 g, 0.5 mmol, 1 equiv) was added to CsF (0.076 g, 0.5 mmol, 1 equiv) and 18-crown-6 (0.146 g, 0.55 mmol, 1.1 equiv) in anhydrous DMSO and stirred for 2 h, at which time the reaction was quenched with a drop of H_2O to homogenize any salts and CH_2Br_2 (0.1 mmol, 7 μL) was added as an internal standard. An aliquot was taken, diluted with d_6-DMSO, and ^1H NMR spectroscopy was used to determine conversion to $PhCH_3$ relative to CH_2Br_2 (80% conversion to $PhCH_3$). Spectra obtained for this experiment are shown below. **Note:** the same results were obtained without the addition of H_2O prior to ^1H NMR analysis.



2 (1 equiv)

49, 80% yield

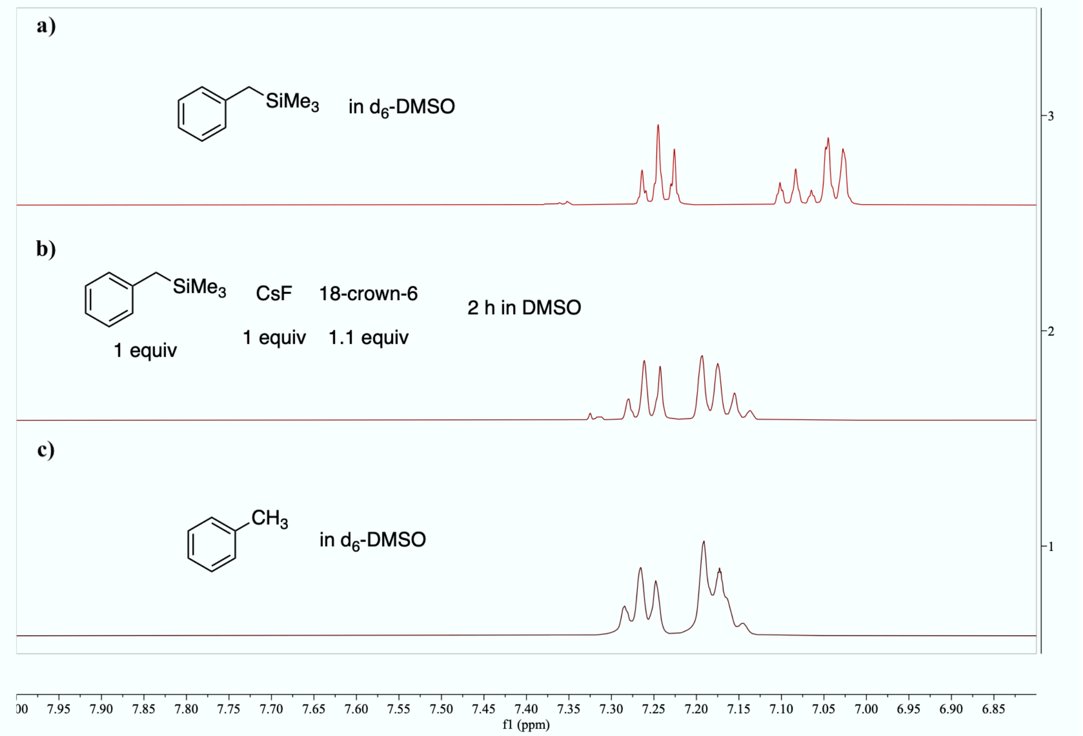


Fig. S3. Aromatic ^{1}H NMR region of a) BnTMS, b) BnTMS + CsF/18-crown-6 in DMSO for 2 h, c) PhMe in d_6-DMSO.

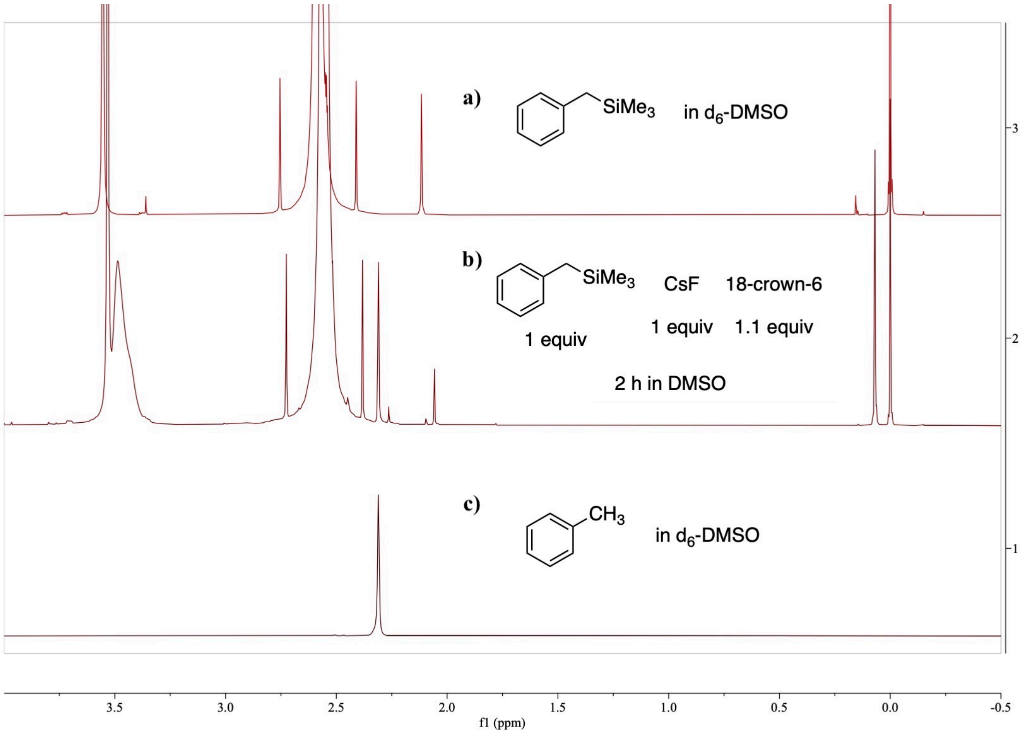
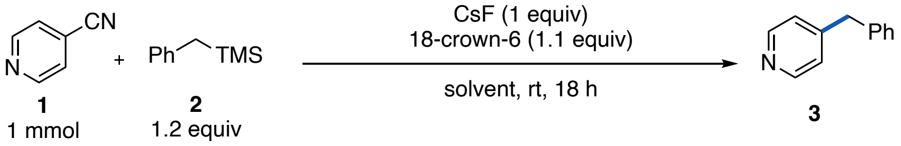


Fig. S4. Aliphatic ^{1}H NMR spectral region of a) BnTMS, b) BnTMS + CsF/18-crown-6, c) PhMe in d_6-DMSO.

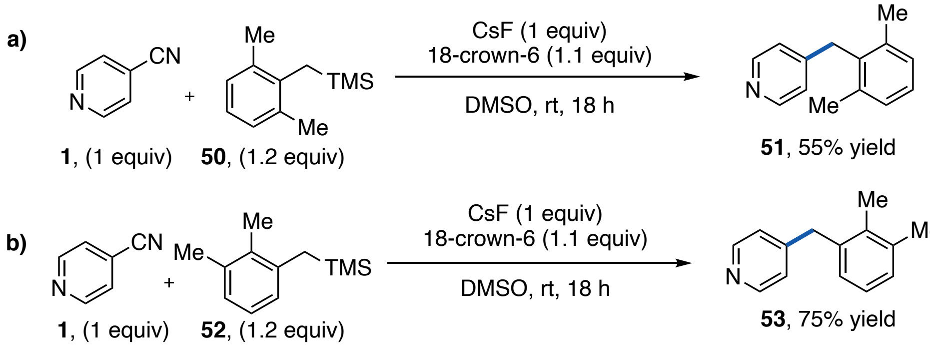
Benzylic arylation experiments in other solvents. Our experiments above suggest a competition between arylation and protonation could occur in solvents more acidic than toluene or in the presence of substrates that have C–H bonds more acidic than toluene. The reported substrate scope and selectivity for monoarylation indicates that proton transfer from acidic C–H bonds in the substrates and products is not a significant competing pathway. We also examined the standard arylation reaction in solvents significantly more acidic than toluene (pK_a = 43 in DMSO).[45] Under the standard reaction conditions (see GP1), coupling of benzyltrimethylsilane to 4-cyanopyridine occurs using five solvents more acidic than toluene as shown in Table S3. These experiments show a greater k_{rel} for arylation over competing proton transfer from solvent C–H bonds.

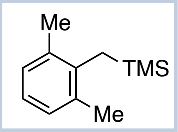
Table S3. Coupling in solvents more acidic than toluene.



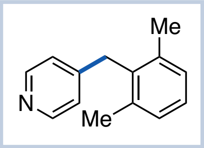
Solvent	pK_a (DMSO)	Coupling Yield
DMSO	36	95%
NMP	<35	95%
MeCN	31	52%
EtOAc	30	21%
acetone	27	25%

Arylation selectivity for isomeric benzyltrimethylsilanes. We next examined the potential for regiospecific arylation of benzyltrimethylsilane isomers. As described below, we synthesized two benzyltrimethylsilane isomers *via* Mg-mediated silylation of benzyl halides and subjected each to the standard reaction conditions (GP1). Each reaction gave the corresponding site-specific arylation product, indicating that a reversible proton transfer event from a different acidic C–H bond or the solvent does not occur prior to arylation.





(2,6-Dimethylbenzyl)trimethylsilane (50). A 100-mL flame-dried 3-neck round bottom flask equipped with a stir bar and a reflux condenser was cooled to room temperature under a stream of nitrogen and charged with magnesium turnings (0.865 g, 11.0 mmol, 1.1 equiv), a crystal of iodine, diluted with THF (50 mL) and chlorotrimethylsilane (6.16 mL, 48.5 mmol, 1.5 equiv), and placed in an ice-bath under a stream of nitrogen. A solution of 2,6-dimethylbenzyl chloride (5.0 g, 10.0 mmol, 1.0 equiv) in THF (20 mL) was added dropwise at 0 ºC. The reaction was then refluxed for 2 h, cooled, and quenched by the addition of saturated aqueous NH_4Cl (20 mL). The resulting mixture was poured into a separatory funnel and the layers separated. The aqueous layer was extracted with Et_2O (3×50 mL) and the combined organic extracts were washed with water (2 x 50 mL), brine (50 mL), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified *via* silica gel chromatography using hexanes to afford **50** as a colorless oil (1.92 g, 10.0 mmol, 100% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.05 – 7.00 (m, 2H), 6.95 – 6.91 (m, 1H), 2.27 (s, 6H), 2.19 (s, 2H), 0.06 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.2, 134.7, 128.0, 123.8, 21.3, 20.2, 0.1; **IR** (neat): 3069, 2953, 2916, 2359, 1583, 1473, 1443, 1260 cm^{-1}; **HRMS (ESI)** $[M+Na]^+$ calcd. For $[C_{12}H_{17}F_5NO]^+$ 215.1226, 215.1243 found.



4-(2,6-Dimethylbenzyl)pyridine (51). GP1 was followed using 4-cyanopyridine (0.104 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (2,6-dimethylbenzyl)trimethylsilane (**50**, 0.231 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 18 h. The product was purified *via* silica gel chromatography using 20% EtOAc in hexanes to afford **51** as a yellow oil (0.109 g, 0.55 mmol, 55% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.46 (brs, 2H), 7.15 – 7.07 (m, 3H), 6.94 (d, J = 4.6 Hz, 2H), 4.04 (s, 2H), 2.22 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.8, 149.4, 137.2, 135.0, 128.4, 127.0, 123.5, 34.6, 20.3; **IR** (neat): 3067, 3022, 2943, 2856, 1698, 1599, 1512, 1413 cm^{-1}; **HRMS (ESI)** *m/z* calcd. For $C_{14}H_{16}N$ $(M+H)^+$ 198.1277; found 198.1277. **Note:** the crude reaction material was analyzed by ^{1}H NMR to verify that only one diarylmethane isomer was formed; this spectrum is provided below in Figure S5.

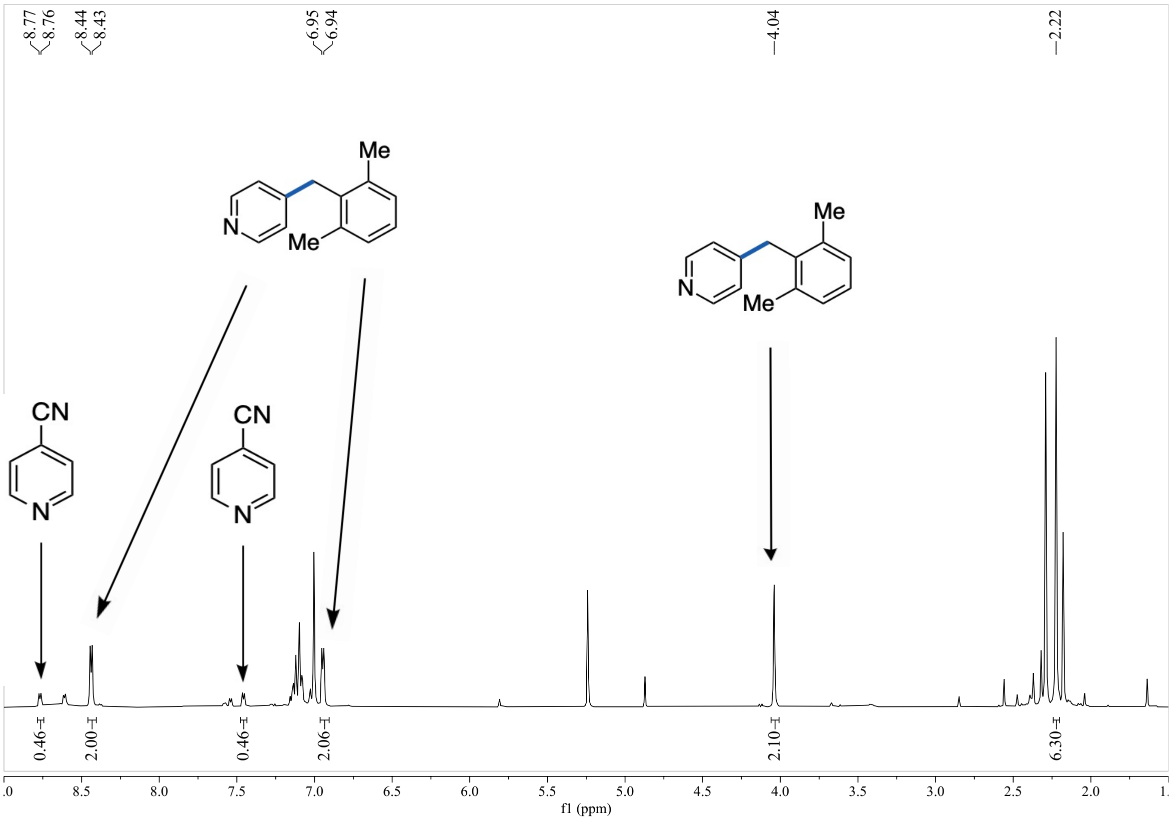
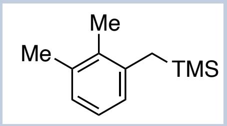
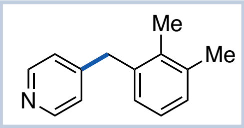


Fig. S5. ^{1}H NMR spectrum of crude reaction mixture showing formation of compound **51** with no **53** formed.



(2,3-Dimethylbenzyl)trimethylsilane (52). A 100-mL flame-dried 3-neck round bottom flask equipped with a stir bar and a reflux condenser was cooled to room temperature under a stream of nitrogen and charged with magnesium turnings (0.267 g, 11.0 mmol, 1.1 equiv), a crystal of iodine, diluted with THF (50 mL) and chlorotrimethylsilane (1.90 mL, 15.0 mmol, 1.5 equiv), and placed in an ice-bath under a stream of nitrogen. A solution of 1-(bromomethyl)-2,3-dimethylbenzene (1.99 g, 10.0 mmol, 1.0 equiv) in THF (20 mL) was added dropwise at 0 ºC. The reaction mixture was refluxed for 2 h, cooled, and quenched by the addition of saturated aqueous NH_4Cl (20 mL). The resulting mixture was poured into a separatory funnel and the layers separated. The aqueous layer was extracted with Et_2O (3×50 mL) and the combined organic extracts were washed with water (2 x 50 mL), brine (50 mL), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by silica gel chromatography using hexanes to afford **52** as a colorless oil (1.92 g, 10.0 mmol, 100% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.00 – 6.83 (m, 3H), 2.27 (s, 3H), 2.14 (s, 5H), 0.01 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.8, 136.8, 133.2, 127.0, 126.0, 125.1, 24.5, 21.1, 16.2, -1.2; **IR** (neat): 3064, 3014, 2953, 2897, 2360, 1585, 1471, 1416 cm^{-1}; **HRMS (ESI)** *m/z* calcd. For $C_{12}H_{20}Si$ $(M+Na)^+$ 215.1226; found 215.1242.



4-(2,3-Dimethylbenzyl)pyridine (53). GP1 was followed using 4-cyanopyridine (0.104 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and (2,3-dimethylbenzyl)trimethylsilane (**52**, 0.231 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 18 h. The product was purified *via* silica gel chromatography using 20% EtOAc in hexanes to afford **53** as a yellow oil (0.148 g, 0.75 mmol, 75% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 3.4 Hz, 2H), 7.12 – 6.98 (m, 5H), 4.01 (s, 2H), 2.29 (s, 3H), 2.09 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.1, 149.8, 137.5, 136.6, 135.3, 128.9, 128.3, 125.8, 124.0, 39.6, 20.8, 15.6; **IR** (neat): 3067, 3021, 2918, 2860, 1936, 1597, 1494, 1440 cm^{-1}; **HRMS (ESI)** *m/z* calcd. For $C_{14}H_{16}N$ $(M+H)^+$ 198.1277; found 198.1276. **Note:** the crude reaction material was analyzed by ^{1}H NMR to verify that only one diarylmethane isomer was formed; this spectrum is provided below in Figure S6.

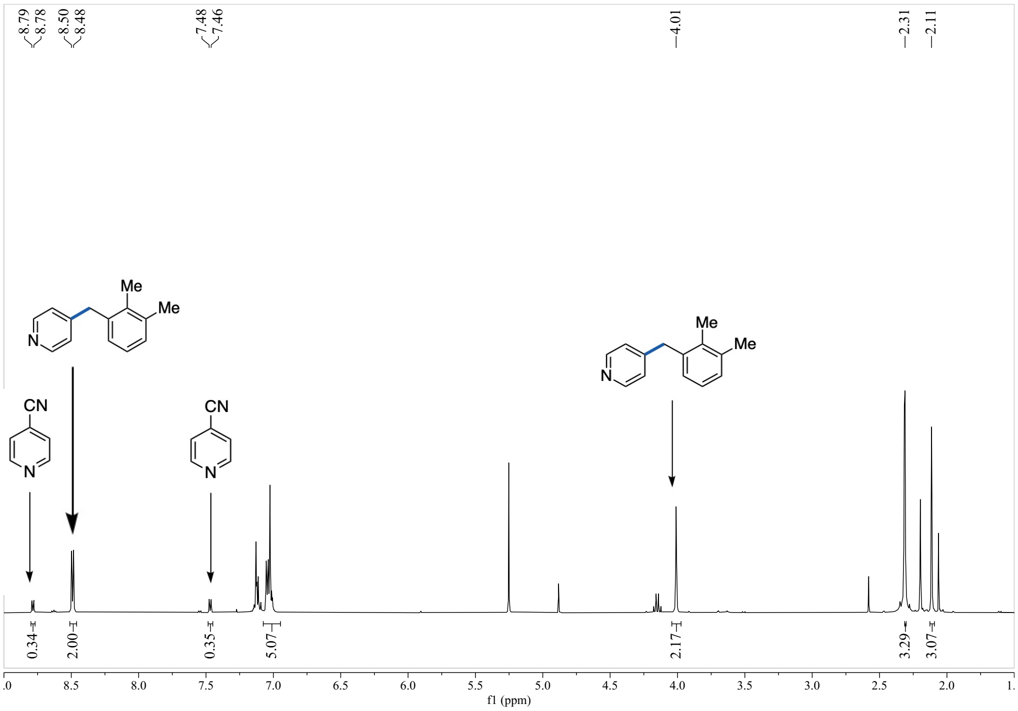


Fig. S6: ^{1}H NMR spectrum of crude reaction mixture showing formation of compound **53** with no **51** formed.

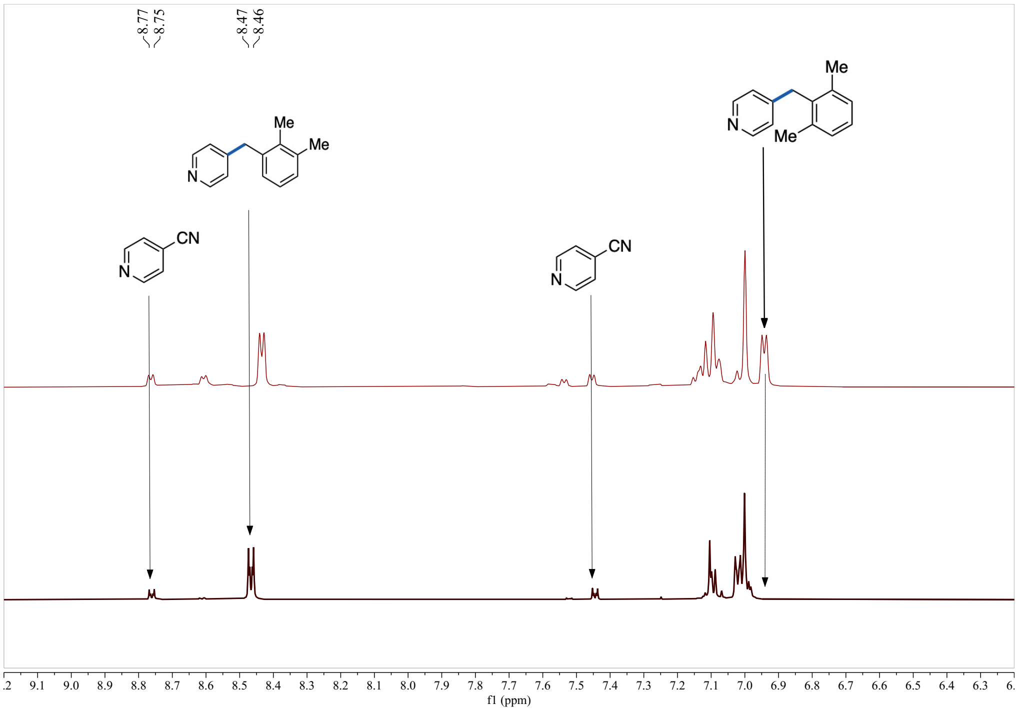


Fig. S7: Aromatic region of crude ^{1}H NMR spectra of the two previous experiments for the synthesis of **51** and **53**, showing only **51** formed (top) and only **53** formed (bottom).

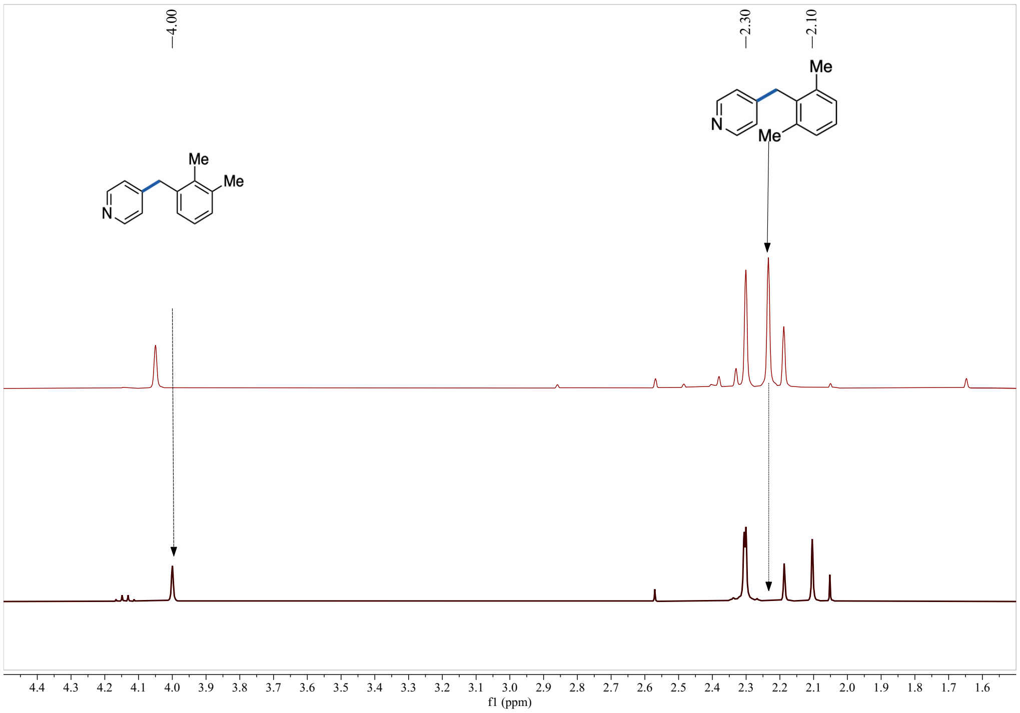
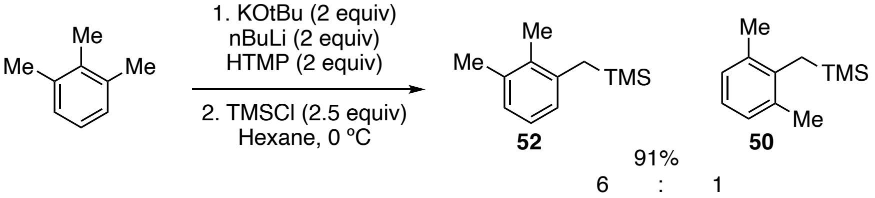


Fig. S8: Benzylic region of crude ^{1}H NMR spectra of the two previous experiments for the synthesis of **51** and **53**, showing only **51** formed (top) and only **53** formed (bottom).

Direct comparison to deprotonative benzylic silylation/arylation. Our findings suggested that a Lewis base-promoted coupling protocol offers unique site-selectivity compared to a deprotonative approach. To examine this issue, 1,2,3-trimethylbenzene was subjected to O'Shea's LiNK[8] deprotonative silylation conditions resulting in a 6:1 mixture of benzyltrimethylsilanes **52** and **50**. This mixture was subjected to the standard arylation conditions (GP1) with 4-cyanopyridine and analyzed by ^{1}H NMR spectroscopy. The purified material yielded an identical 6:1 mixture of **53** and **51**. These comparisons demonstrate that a deprotonation approach cannot be easily used to selectively couple products with multiple similarly acidic benzylic C–H bonds; meanwhile, benzyltrimethylsilanes can be regioselectively prepared *via* numerous known methods and they undergo regiospecific arylation using this Lewis base-promoted coupling method.



Procedure for deprotonative silylation of 1,2,3-trimethylbenzene: This method was adapted from a previously reported procedure.[8] A 100-mL flame-dried round bottom flask equipped with a stir bar was cooled to room temperature under a stream of nitrogen and charged with KO-*t*-Bu (2.24 g, 20.0 mmol, 2.0 equiv), diluted with anhydrous hexanes (25 mL), and placed in an ice-bath under a stream of nitrogen. 2,2,6,6-Tetramethylpiperidine (2.83 g, 20.0 mmol, 2.0 equiv) was added dropwise, followed by the dropwise addition of nBuLi (1.6 M, 12.5 mL, 20.0 mmol, 2.0 equiv). The reaction was stirred for 5 min at 0 ºC at which time 1,2,3-trimethylbenzene (1.20 g, 10.0 mmol, 1.0 equiv) was added dropwise. The reaction was stirred for 15 min before the dropwise addition of chlorotrimethylsilane (2.72 g, 25.0 mmol, 2.5 equiv) at 0 ºC. After stirring for an additional 1 h at 0 ºC, aqueous 2 M HCl (20 mL) was added slowly and the reaction was poured into a separatory funnel and the layers separated. The aqueous layer was extracted with Et_2O (3×50 mL) and the combined organic extracts were washed with water (2 x 50 mL), brine (50 mL), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by silica gel chromatography using hexanes to afford a 6:1 mixture of **52**:**50** as a colorless oil (1.75 g, 9.1 mmol, 91% yield).

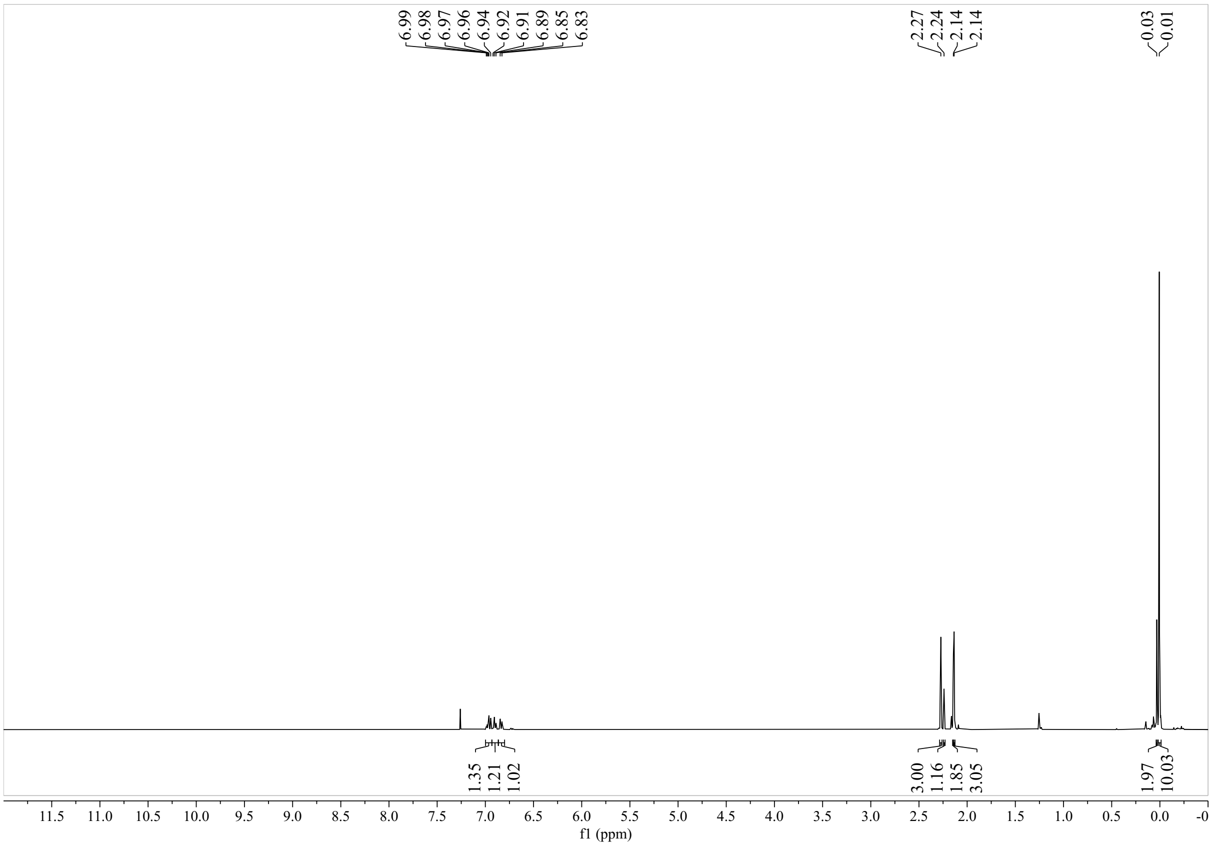
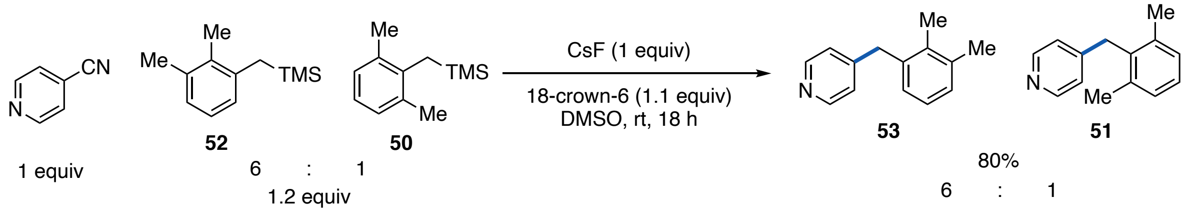


Fig. S9: ^{1}H NMR spectrum showing a 6:1 mixture of **52** and **50** formed *via* deprotonative silylation.



Coupling to 4-cyanopyridine: GP1 was followed using 4-cyanopyridine (0.104 g, 1.0 mmol, 1.0 equiv), CsF (0.152 g, 1.0 mmol, 1.0 equiv), 18-crown-6 (1 M in THF, 1.1 mL, 1.1 mmol, 1.1 equiv) and the 6:1 mixture of benzyltrimethylsilanes from above (**52** and **50**, 0.231 g, 1.2 mmol, 1.2 equiv) in 2.9 mL anhydrous DMSO for 18 h. The product was purified *via* silica gel chromatography using 20% EtOAc in hexanes to afford a 6:1 mixture of **53** and **51** as a yellow oil (0.158 g, 0.80 mmol, 80% yield).

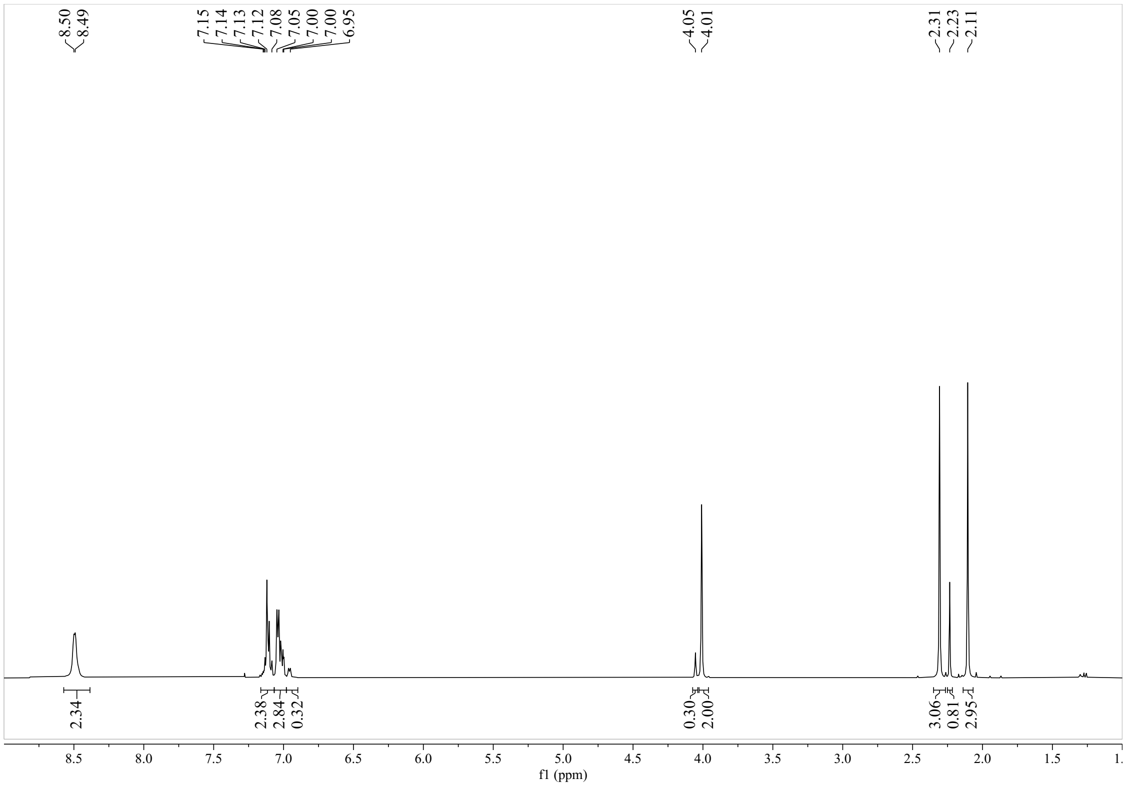


Fig. S10: ^{1}H NMR spectrum showing a 6:1 mixture of **53** and **51** formed from the above reaction.

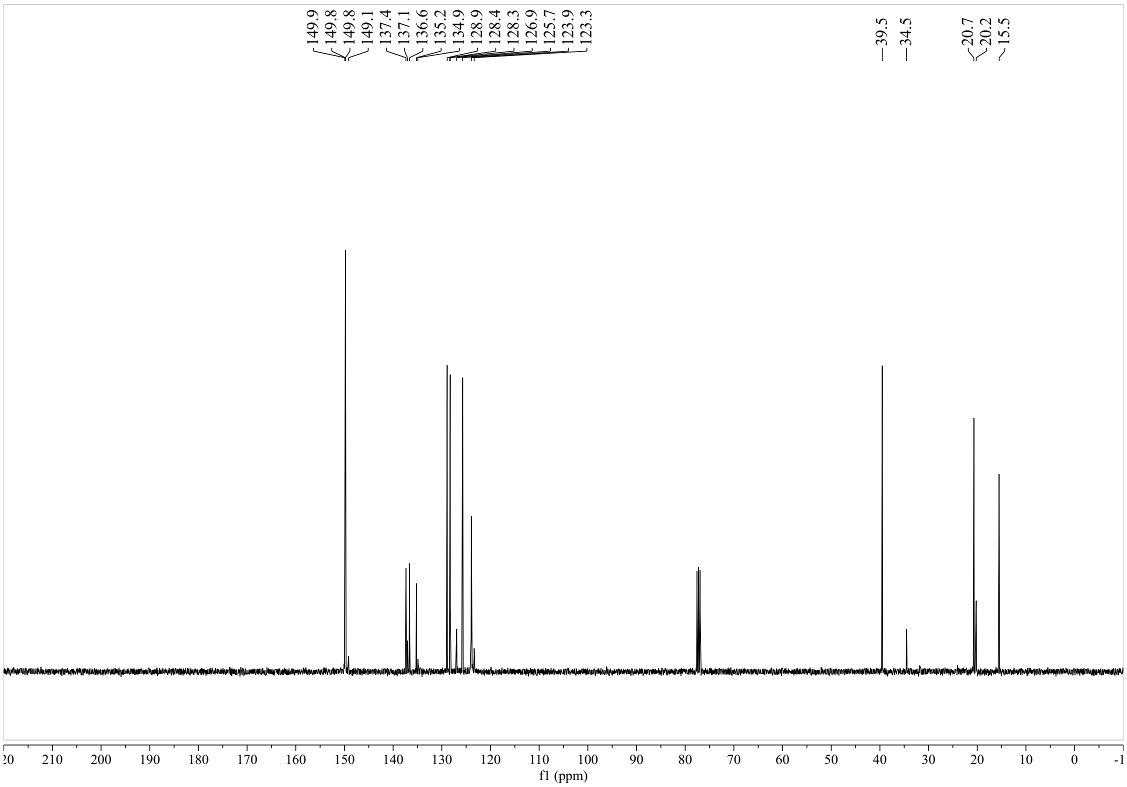


Fig. S11: ^{13}C NMR spectrum showing a 6:1 mixture of **53** and **51** formed from the above reaction.

(b) Experiments concerning aromatic electrophile coupling partner

Reactivity trends of 4-substituted pyridines under variable conditions. Under the standard reaction conditions, no coupling to 4-halopyridines is observed using the 4-halo-2-methylpyridine substrates shown in Table S2 in Section X "Analysis of Arene Coupling Partner Leaving Group". These experiments suggest either (a) a unique reaction pathway is possible for 4-cyanopyridines and 4-sulfonylpyridines; or (b) the 4-cyano and 4-sulfonylpyridines are more active electrophiles for polar S_NAr pathways for this reaction. To further evaluate this issue, 4-activated 2-phenylpyridine derivatives were examined in the standard benzyltrimethylsilane coupling reaction at room temperature in a variety of solvents. For 4-fluoro-2-phenylpyridine, low benzylation yield (**SI-17**) in DMF and dioxane was observed, and no benzylation product was formed in DMSO. Competing multiarylation leads to the formation of triarylmethane derivatives (**SI-19**) and tetraarylmethanes (**SI-20**) in low amounts. No diarylmethane product was observed in the case of 4-chloro-2-phenylpyridine in any solvent with trace amounts of triarylmethane derivatives and tetraarylmethane. The diarylmethane yield did not increase at elevated temperatures for these halogenated substrates, although greater quantities of tri- and tetraarylmethane products were observed. For these substrates, reactions conducted in DMF led to significant side product formation resulting from olefination of DMF by benzyltrimethylsilane. In contrast, for 2-phenylisonicotinonitrile (**SI-16**) high yields are obtained under the standard coupling protocol, with trace amounts of triarylmethanol and no tetraarylmethane. In DMSO (standard coupling solvent) low amounts of the 5-C–H benzylation product also forms (**SI-18**). Ultimately, these studies clearly show the superiority of 4-cyanopyridines for high yields and high monoarylation selectivity. These studies also suggest a polar S_NAr pathway is available for 4-halopyridines although it is not favored over competing proton transfer side reactions and thus low selectivity and yields are obtained.[46] The results are shown in Table S4 below.

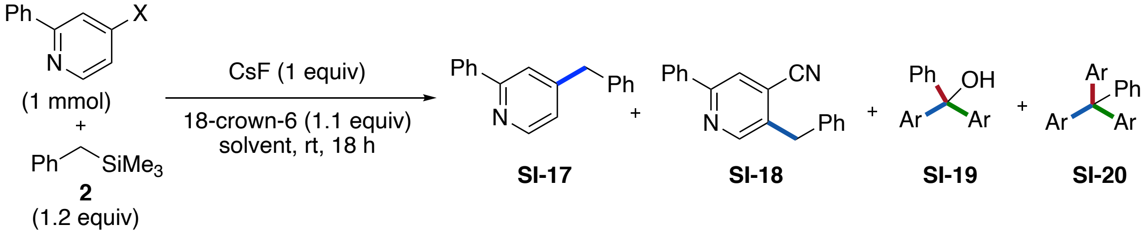


Table S4. Evaluation of direct substitution of 4-substituted pyridines

X = F

Solvent	% yield SI-17	% yield SI-18	% yield SI-19	% yield SI-20
DMSO	0	0	0	0
DMF	10[a]	0	12	0
1,4-Dioxane	2	0	1	0

X = Cl

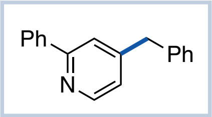
Solvent	% yield SI-17	% yield SI-18	% yield SI-19	% yield SI-20
DMSO	0	0	0	0
DMF	0[a]	0	3	1
1,4-Dioxane	0	0	0	0

X = CN

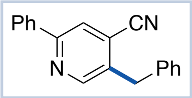
Solvent	% yield SI-17	% yield SI-18	% yield SI-19	% yield SI-20
DMSO	77	4	0	0
DMF	71[b]	3	0	0
1,4-Dioxane	10	4	0	0

Yields based on ^{1}H NMR yield relative to CH_2Br_2. [a]In the reactions of X = F and Cl in DMF, the major product was β-*N*,*N*-dimethylaminostyrene formed via Peterson olefination of DMF with benzyltrimethylsilane. [b]The reaction of X = CN in DMF showed no formation of β-*N*,*N*-dimethylaminostyrene.

Benzylation of 2-phenylisonicotinonitrile under standard conditions on 1 mmol scale: In a nitrogen-filled glovebox, to an oven-dried 2-dram glass vial (8 mL, Thermo Scientific, B7999-3) equipped with a magnetic stir bar was added 2-phenylisonicotinonitrile **SI-16** (0.180 g, 1.0 mmol, 1.0 equiv), a solution of 18-crown-6 (1M in THF, 1.1 mL, 1.1 equiv), benzyltrimethylsilane (0.197 g, 1.2 mmol, 1.2 equiv), and anhydrous solvent (2.9 mL, 0.25 M aryl electrophile relative to total volume). Solid CsF (0.152 g, 1.0 mmol, 1.0 equiv) was added in one portion and the vial was sealed with a screw cap (Thermo Scientific, B7807-15) equipped with a 2.6 mm PTFE/Silicone Septa (Thermo Scientific, B7995-15). The reaction vial was removed from the glovebox and the solution was vigorously stirred at room temperature for 18 h. The reaction mixture was poured into a separatory funnel and diluted with brine (50 mL), extracted with EtOAc (3 x 15 mL), washed with H_2O (3 x 15 mL) and brine (2 x 25 mL) and dried over $MgSO_4$. After concentration under reduced pressure, CH_2Br_2 (7 µL, 0.1 mmol) was added to the crude reaction mixture and analyzed by ^{1}H NMR spectroscopy by comparison to the diarylmethane methylene signal. The crude reaction mixture was purified *via* silica gel chromatography using 10% EtOAc in hexanes to afford 4-benzyl-2-phenylpyridine **SI-17** as a colorless oil (0.189 g, 0.77 mmol, 77% yield) and 5-benzyl-2-phenylisonicotinonitrile **SI-18** as a yellow oil (0.011 g, 0.04 mmol, 4% yield).



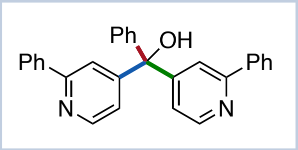
4-Benzyl-2-phenylpyridine (SI-17). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.63 (d, *J* = 5.0 Hz, 1H), 8.01 (d, *J* = 7.7 Hz, 2H), 7.60 (s, 1H), 7.52 – 7.48 (m, 2H), 7.46 – 7.42 (m, 1H), 7.39 – 7.36 (m, 2H), 7.31 – 7.25 (m, 3H), 7.09 (d, *J* = 5.0 Hz, 1H), 4.06 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.7, 150.9, 149.8, 139.5, 139.0, 129.1, 129.0, 128.84, 128.78, 127.1, 126.8, 122.8, 121.2, 41.5; **IR** (neat): 3030, 2920, 2859, 2120, 1930, 1601, 1515, 1112, 1010 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{18}H_{16}N$ (M+H)$^+$ 246.1277; found 246.1281.



5-Benzyl-2-phenylisonicotinonitrile (SI-18). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.77 – 7.75 (m, 2H), 7.70 (s, 1H), 7.31 – 7.23 (m, 3H), 7.15 – 7.05 (m, 5H), 4.02 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.5, 151.6, 137.9, 137.4, 136.4, 130.1, 129.2, 129.1, 129.0, 127.3, 126.9, 122.3, 121.4, 116.3, 37.5; **IR** (neat): 3100, 2931, 2235, 2106, 1866, 1699, 1644, 1597, 1450, 1389 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{19}H_{15}N_2$ $(M+H)^+$ 271.1230; found 271.1229.

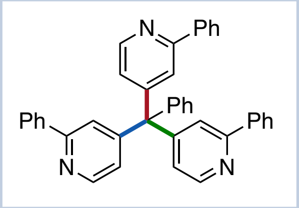
Benzylation of 4-substitued-2-phenylpyridines under standard conditions: In a nitrogen-filled glovebox, to an oven-dried 2-dram glass vial (8 mL, Thermo Scientific, B7999-3) equipped with a magnetic stir bar was added 4-substituted-2-phenylpyridine (1.0 mmol, 1.0 equiv), solid 18-crown-6 (0.291 g, 1.1 mmol, 1.1 equiv), benzyltrimethylsilane (0.197 g, 1.2 mmol, 1.2 equiv), and anhydrous solvent (4.0 mL, 0.25 M relative to total volume). Solid CsF (0.152 g, 1.0 mmol, 1.0 equiv) was added in one portion and the vial was sealed with a screw cap (Thermo Scientific, B7807-15) equipped with a 2.6 mm PTFE/Silicone Septa (Thermo Scientific, B7995-15). The reaction vial was removed from the glovebox and the solution was vigorously stirred overnight at room temperature. The reaction mixture was poured into a separatory funnel containing brine (50 mL), extracted with EtOAc (3 x 15 mL), washed with H_2O (3 x 15 mL) and brine (2 x 25 mL) and dried over $MgSO_4$. After concentration under reduced pressure, CH_2Br_2 (7 µL, 0.1 mmol) was added to the reaction mixture and the mixture was analyzed by ^{1}H NMR spectroscopy. The results are shown in Table S4.

Benzylation of 4-fluoro-2-phenylpyridine at 100 ºC: In a nitrogen-filled glovebox, to an oven-dried 2-dram glass vial (8 mL, Thermo Scientific, B7999-3) equipped with a magnetic stir bar was added 4-fluoro-2-phenylpyridine (0.173 g, 1.0 mmol, 1.0 equiv), solid 18-crown-6 (0.291 g, 1.1 mmol, 1.1 equiv), benzyltrimethylsilane (0.197 g, 1.2 mmol, 1.2 equiv), and anhydrous 1,4-dioxane (4.0 mL, 0.25 M relative to total volume). Solid CsF (0.152 g, 1.0 mmol, 1.0 equiv) was added in one portion and the vial was sealed with a screw cap (Thermo Scientific, B7807-15) equipped with a 2.6 mm PTFE/Silicone Septa (Thermo Scientific, B7995-15). The reaction vial was removed from the glovebox and the solution was vigorously stirred at 100 ºC for 18 h. The reaction mixture was cooled and poured into a separatory funnel containing brine (50 mL), extracted with EtOAc (3 x 15 mL), washed with H_2O (3 x 15 mL) and brine (2 x 25 mL) and dried over $MgSO_4$. After concentration under reduced pressure, the crude reaction mixture was purified *via* silica gel chromatography using 10 to 80% EtOAc in hexanes to afford phenylbis(2-phenylpyridin-4-yl)methanol **SI-19** as a white solid (0.158 g, 0.38 mmol, 38% yield) and 4,4',4"-(phenylmethanetriyl)tris(2-phenylpyridine) **SI-20** as a yellow oil (0.055 g, 0.10 mmol, 10% yield).



Phenylbis(2-phenylpyridin-4-yl)methanol (SI-19). ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 5.3 Hz, 2H), 7.99 – 7.88 (m, 4H), 7.80 (s, 2H), 7.44 – 7.33 (m, 9H),7.30 – 7.27 (m, 2H), 7.14 (d, *J* = 4.2 Hz, 2H), 4.03 (brs, 1H); ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 157.7, 155.0, 149.5, 144.4, 139.0, 129.2, 128.8, 128.7, 128.4, 127.9, 127.1, 121.1, 119.4, 80.9; **IR** (neat): 3160, 3031, 2960, 1585, 1491, 1420, 1290, 1100, 1100 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{29}H_{23}N_2O$ $(M+H)^+$ 415.1805; found 415.1819.

4,4',4''-(Phenylmethanetriyl)tris(2-phenylpyridine) (SI-20). ^{1}**H NMR** (400 MHz, CDCl$_3$) δ 8.70 (d, *J* = 7.6 Hz, 3H), 7.89 – 7.87 (m, 6H), 7.69 (d, *J* = 1.2 Hz, 3H), 7.47 – 7.32 (m, 15H), 7.19 (dd, *J* = 5.3, 1.7 Hz, 3H); ^{13}**C NMR** (101 MHz, CDCl$_3$) δ 157.9, 153.9, 149.9, 142.7, 139.0, 130.7, 129.5, 129.0, 128.8, 127.8, 127.1, 124.1, 122.4, 64.9; **IR** (neat): 3030, 2931, 2200, 1901, 1644, 1590, 1481, 1404, 1263 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{40}H_{30}N_3$ $(M+H)^+$ 552.2434; found 552.2463.

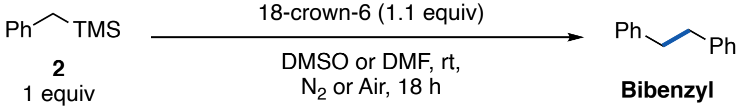


(c) Experiments regarding byproduct formation in arylation reactions

Discussion on the observation of bibenzyl formation during standard coupling reactions. As reported in Section V of the Supporting Information, during the preparative scale-up of the model substrate using DMF as solvent without 18-crown-6 present, we observed formation of bibenzyl in 3% yield. Bibenzyl side products are often observed in low quantities (1-5%) for reactions with various benzyltrimethylsilanes and aryl electrophiles reported in Table 1. These observations are consistent with the formation of benzylic radicals during the course of the reaction. Control studies conducted in the absence of 4-cyanopyridine showed that oxygen can affect the formation of bibenzyl as a background reaction. This observation illustrates that caution should be taken when assigning a source of benzylic radical formation (i.e. cyanoarene or trace oxygen). We note that observation of such a reaction with oxygen is consistent with fluoride activation of benzyltrimethysilanes promoting the formation of benzylic radicals in the presence of oxidants (no bibenzyl is formed if fluoride is left out).

Effect of oxygen on bibenzyl formation. To evaluate the effect that oxygen has on the standard coupling conditions (GP1) without 4-cyanopyridine, control reactions were set up and run under an inert atmosphere and air. For reactions performed under air, all reagents were added in a nitrogen-filled glovebox except for benzyltrimethylsilane. The reaction vials were removed from the glovebox, opened to air, and stirred for 10 minutes with an air hose blowing directly on the vials. Benzyltrimethylsilane was then added in one portion. The results are summarized in Table S5 and show that a background reaction between oxygen and benzyltrimethylsilane can lead to bibenzyl formation. Bibenzyl can also be observed in low amounts in reactions and conditions that were attempted to be kept oxygen-free. This finding led to difficulty in assigning significance to the observation of side products that likely originate from benzylic radical species.

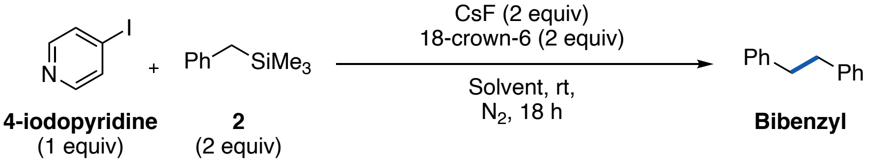
Table S5. Effect of oxygen on standard coupling conditions without 4-cyanopyridine.



Solvent, atmosphere	GC Bibenzyl Yield
DMSO, N_2	<0.2%
DMSO, Air	3.12%
DMF, N_2	0.27%
DMF, Air	3.9%

Bibenzyl formation while attempting reaction of 4-iodopyridine. In contrast to the above experiments, we note that when benzyltrimethylsilane coupling was attempted with 4-iodo-2-methylpyridine (Table S2) a significant quantity of dehalogenated pyridine and bibenzyl product was observed. The quantity of bibenzyl formed is significantly greater than can be explained by reaction with trace oxygen. Instead, bibenzyl and 2-methylpyridine may be formed *via* SET and C–I bond cleavage and benzylic radical dimerization. Alternatively, a halogenophilic attack on 4-iodo-2-methypyridine is a potential alternative pathway that could generate benzyl iodide that reacts with another equivalent of benzyltrimethylsilane.[47] Regardless, this observation sheds more light into the unique reactivity of cyano and sulfonylarenes compared to aryl halides. To further investigate this observation, 4-iodopyridine was subjected to the standard coupling conditions (GP1) using 2 equivalents each of benzyltrimethylsilane, cesium fluoride, and 18-crown-6 ether. The crude reaction mixtures were analyzed by ^{1}H NMR spectroscopy to determine the amount of bibenzyl formation. The results are shown in Table S6 below.

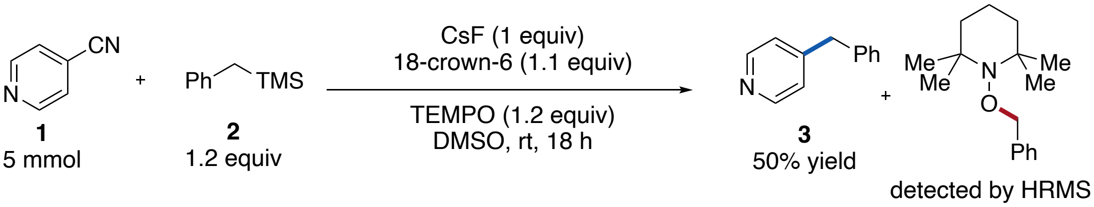
Table S6. Dehalogenation of 4-iodopyridine in reactions with benzyltrimethylsilane.[a]



Solvent	Bibenzyl Yield[a]
DMSO	21%
DMF	16%
1,4-Dioxane	20%
MeCN	6%
NMP	11%
DME	14%

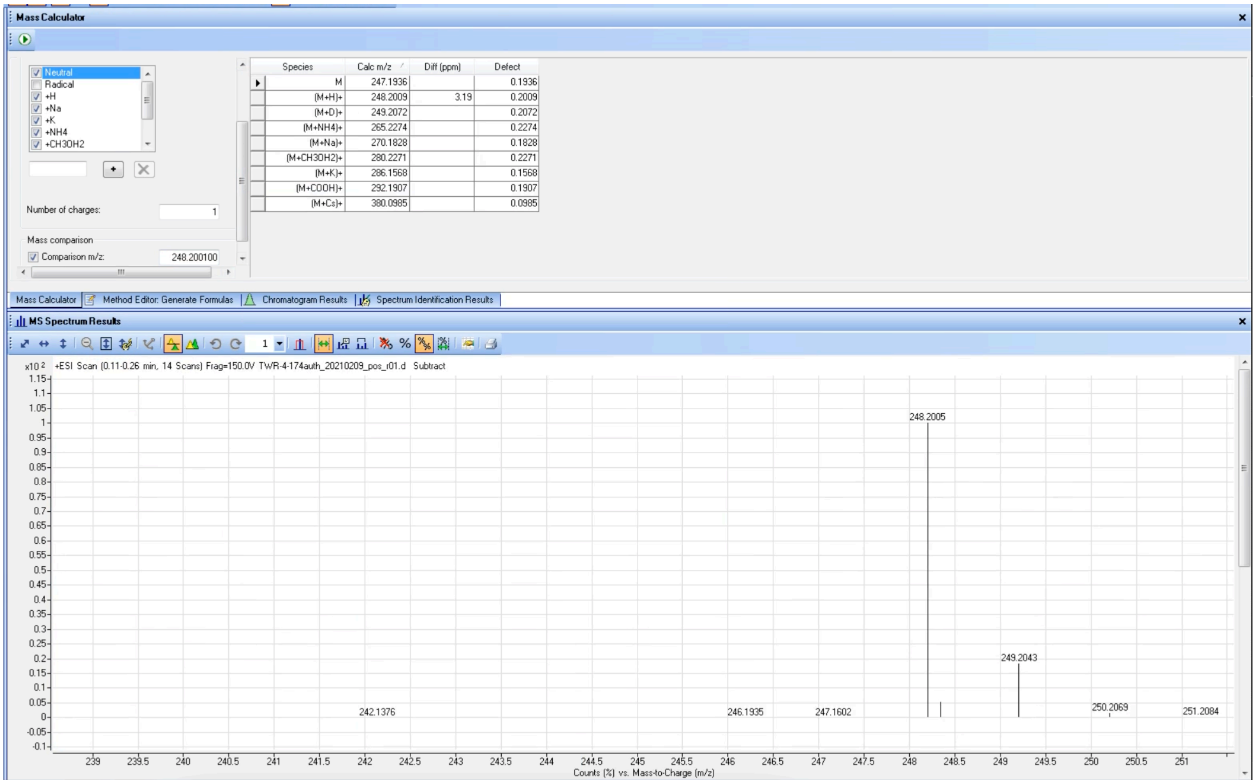
[a] Yields based on ^{1}H NMR yield relative to CH_2Br_2.

Discussion on the inclusion of TEMPO additive. Under the standard coupling conditions (GP1) with the addition of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), we observe diminished yield of the coupling product and the TEMPO-benzyl adduct was observed *via* HRMS (ESI).



General Procedure for TEMPO additive experiment: In a nitrogen-filled glovebox, to an oven-dried 100 mL round-bottom flask equipped with a magnetic stir bar was added 4-cyanopyridine (0.521 g, 5.0 mmol, 1.0 equiv), TEMPO (Millipore Sigma cat. #426369, purified by sublimation, 99%, 0.938 g, 6.0 mmol, 1.2 equiv), benzyltrimethylsilane (0.986 g, 6.0 mmol, 1.2 equiv), a solution of 18-crown-6 (1M in THF, 5.5 mL, 5.5 mmol, 1.1 equiv) and anhydrous DMSO (14.5

mL, 0.25 M relative to total volume). Solid CsF (0.760 g, 5.0 mmol, 1.0 equiv) was added in one portion and the vial was sealed with a rubber septum. The reaction flask was removed from the glovebox and vigorously stirred at room temperature for 18 h under a constant stream of nitrogen. The reaction mixture was poured into a separatory funnel and diluted with brine (50 mL), extracted with EtOAc (3 x 15 mL), washed with H_2O (3 x 15 mL) and brine (2 x 25 mL) and dried over $MgSO_4$. After concentration under reduced pressure, the crude reaction mixture was purified *via* silica gel chromatography using 5% EtOAc in hexanes to remove the excess TEMPO before analysis by ^{1}H NMR and HRMS (ESI). It was determined by ^{1}H NMR spectroscopy that the reaction produced 4-benzylpyridine in 50% yield and the TEMPO-benzyl adduct was detected by HRMS (but not by ^{1}H NMR). **HRMS (ESI)** *m/z* calcd. for $C_{16}H_{26}NO$ $(M+H)^+$ 248.2009; found 248.2008. The HRMS spectrum matched that of an authentic sample prepared by a reported procedure.[48] **Authentic HRMS (ESI)** *m/z* calcd. for $C_{16}H_{26}NO$ $(M+H)^+$ 248.2009; found 248.2005.



☑ Neutral
☐ Radical
☑ +H
☑ +Na
☑ +K
☑ +NH4
☑ +CH3OH2

Number of charges: 1

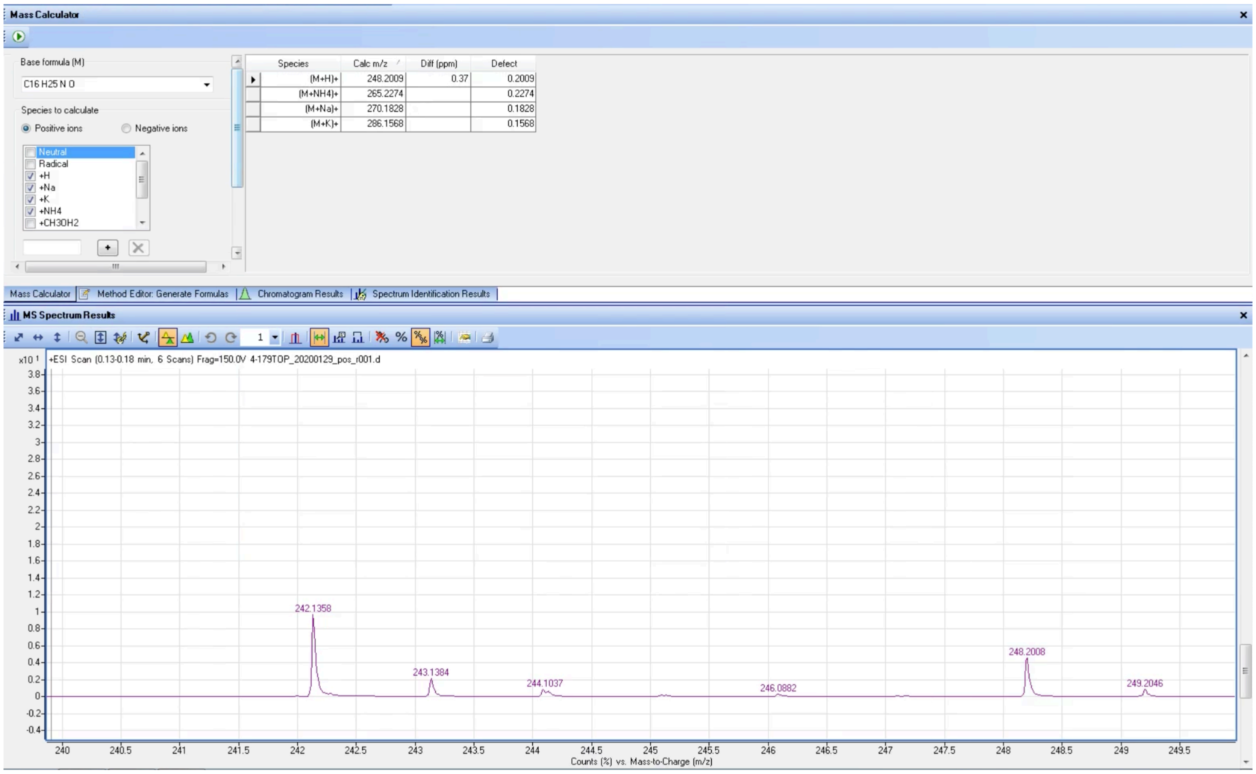
Mass comparison

☑ Comparison m/z: 248.200100

Species	Calc m/z	Diff (ppm)	Defect
M	247.1936		0.1936
(M+H)+	248.2009	3.19	0.2009
(M+D)+	249.2072		0.2072
(M+NH4)+	265.2274		0.2274
(M+Na)+	270.1828		0.1828
(M+CH3OH2)+	280.2271		0.2271
(M+K)+	286.1568		0.1568
(M+COOH)+	292.1907		0.1907
(M+Cs)+	380.0985		0.0985

+ESI Scan (0.11-0.26 min, 14 Scans) Frag=150.0V TWR-4-174auth_20210209_pos_r01.d Subtract

Fig. S12: HRMS (ESI) Spectrum of Authentic TEMPO–benzyl adduct.


Mass Calculator

Base formula (M)

C16 H25 N O

Species to calculate

● Positive ions ○ Negative ions

☐ Neutral
☐ Radical
☑ +H
☑ +Na
☑ +K
☑ +NH4
☐ +CH3OH2

Species	Calc m/z	Diff (ppm)	Defect
(M+H)+	248.2009	0.37	0.2009
(M+NH4)+	265.2274		0.2274
(M+Na)+	270.1828		0.1828
(M+K)+	286.1568		0.1568

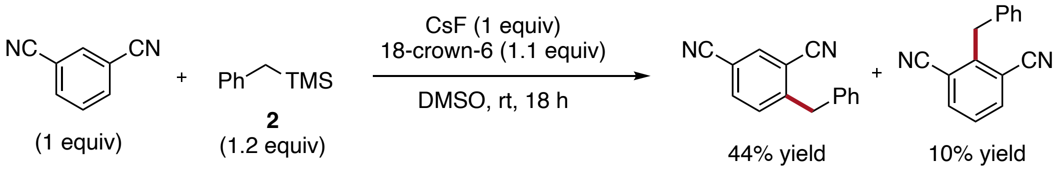
MS Spectrum Results

+ESI Scan (0.13-0.18 min, 6 Scans) Frag=150.0V 4-179TOP_20200129_pos_r001.d

Fig. S13: HRMS (ESI) Spectrum of TEMPO–benzyl adduct from the additive experiment.

Observations of C–H Benzylation of Cyanoarenes. In the case of 2-phenyl-4-cyanopyridine (**SI-16**) above, a C–H benzylation side product was observed and characterized. To further probe this reactivity, we examined the reaction of benzyltrimethylsilane with two dicyanoarenes that are known to give C–H benzylation isomers in photoinduced electron transfer reactions. Interestingly, the observed isomeric mixtures are similar with those reported in PET reactions. However, we also note that C–H benzylation of 1,3-dicyanobenzene has been reported using benzylzinc chloride in conjunction with an oxidative workup (see references noted below). In the reactions conducted below no oxidizing reagent is used, although oxidation could occur *via* alternative pathways or during workup. Overall, these experiments are potentially explainable by either pathway.

Observation of C–H benzylation of isophthalonitrile. Under the standard coupling conditions (GP1) using isophthalonitrile, C–H benzylation of the 2- and 4-positions were observed. The observation of C–H benzylation products is analogous to observations made *via* PET-enabled reactions as reported in "Photoalkylation of Dicyanoarenes with Alkyltriphenylborate salts" Lan, J. Y.; Schuster, G. B. *J. Am. Chem. Soc.* **1985**, *107*, 6710 – 6711 and also in "Transition-Metal-Free Cross-Coupling of Aryl and N-Heteroaryl Cyanides with Benzylic Zinc Reagents" Quinio, P.; Roman, D. S.; Leoń, T.; William, S.; Karaghiosoff, K.; Knochel, P. *Org. Lett.* **2015**, *17*, 4396 – 4399, although the 2-benzyl regioisomer was not reported in the latter report.



General Procedure for benzylation of isophthalonitrile: In a nitrogen-filled glovebox, to an oven-dried 2-dram glass vial (8 mL, Thermo Scientific, B7999-3) equipped with a magnetic stir bar was added isophthalonitrile (0.128 g, 1.0 mmol, 1.0 equiv), a solution of 18-crown-6 (1M in THF, 1.1 mL, 1.1 equiv), benzyltrimethylsilane (0.197 g, 1.2 mmol, 1.2 equiv), and anhydrous DMSO (2.9 mL, 0.25 M relative to total volume). Solid CsF (0.152 g, 1.0 mmol, 1.0 equiv) was added in one portion and the vial was sealed with a screw cap (Thermo Scientific, B7807-15) equipped with a 2.6 mm PTFE/Silicone Septa (Thermo Scientific, B7995-15). The reaction vial was removed from the glovebox and the solution was vigorously stirred at room temperature for 18 h. The reaction mixture was poured into a separatory funnel and diluted with brine (50 mL), extracted with EtOAc (3 x 15 mL), washed with H_2O (3 x 15 mL) and brine (2 x 25 mL) and dried over $MgSO_4$. After concentration under reduced pressure, the crude reaction mixture was purified *via* silica gel chromatography using 10% Et_2O in hexanes to afford an inseparable 4:1 mixture of benzylated products (0.118 g, 0.54 mmol, 54% yield) as a white solid. **Major product** (44%, 4-benzylisophthalonitrile) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.62 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 1H), 7.23 – 7.18 (m, 2H), 7.16 – 7.13 (m, 1H), 7.10 – 7.08 (m, 2H), 4.13 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.0, 137.0, 136.1, 135.8, 131.1, 129.04, 129.01, 127.32, 116.7, 116.0, 114.1, 111.5, 40.4; **Minor product diagnostic peaks** (10%, 2-benzylisophthalonitrile) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.8, 2H), 7.35 (t, *J* = 7.8 Hz, 1H), 4.31 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.3, 137.1, 136.8, 128.9, 128.8, 127.8, 127.28, 116.6, 114.8, 39.0. The spectral data matched the data previously reported.[49] **EA** Calcd. for $C_{15}H_{10}N_2$: C, 82.55; H, 4.62; N, 12.84. Found: C, 82.57; H, 4.72, N, 12.94; **Melting point:** 126 – 129 °C.

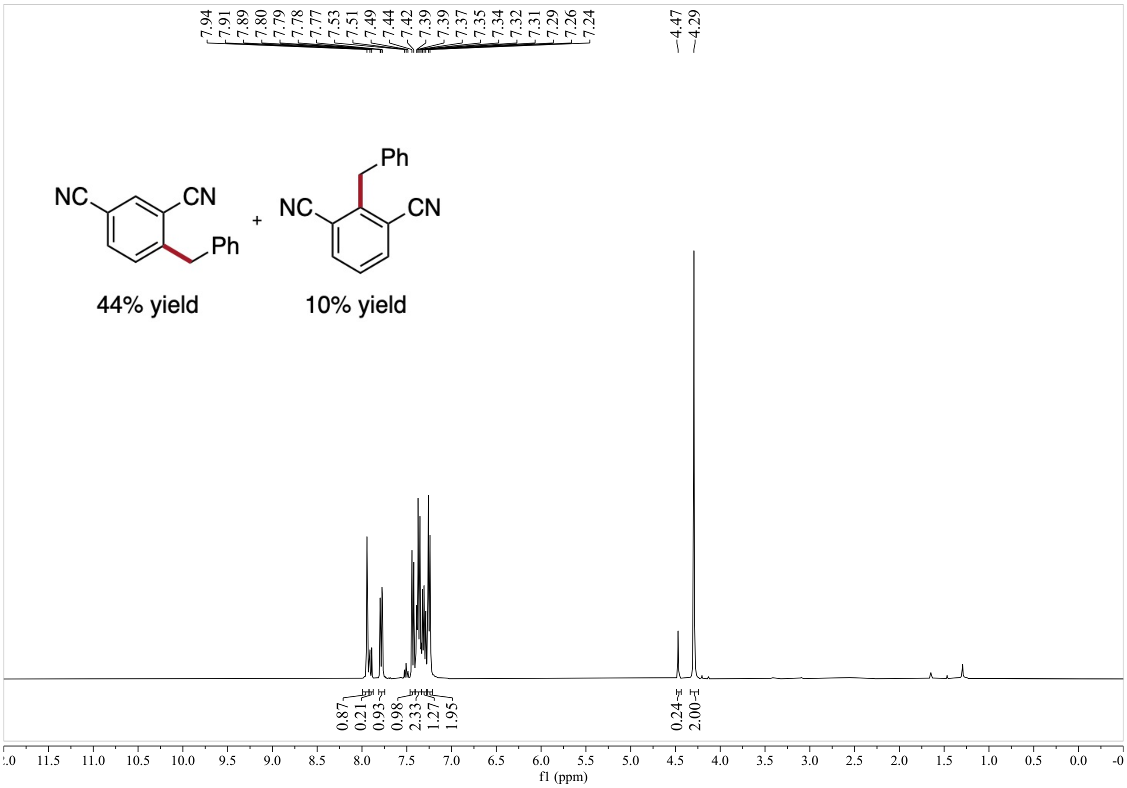


Fig. S14: Isolated ^{1}H NMR Spectrum of benzylation of isophthalonitrile.

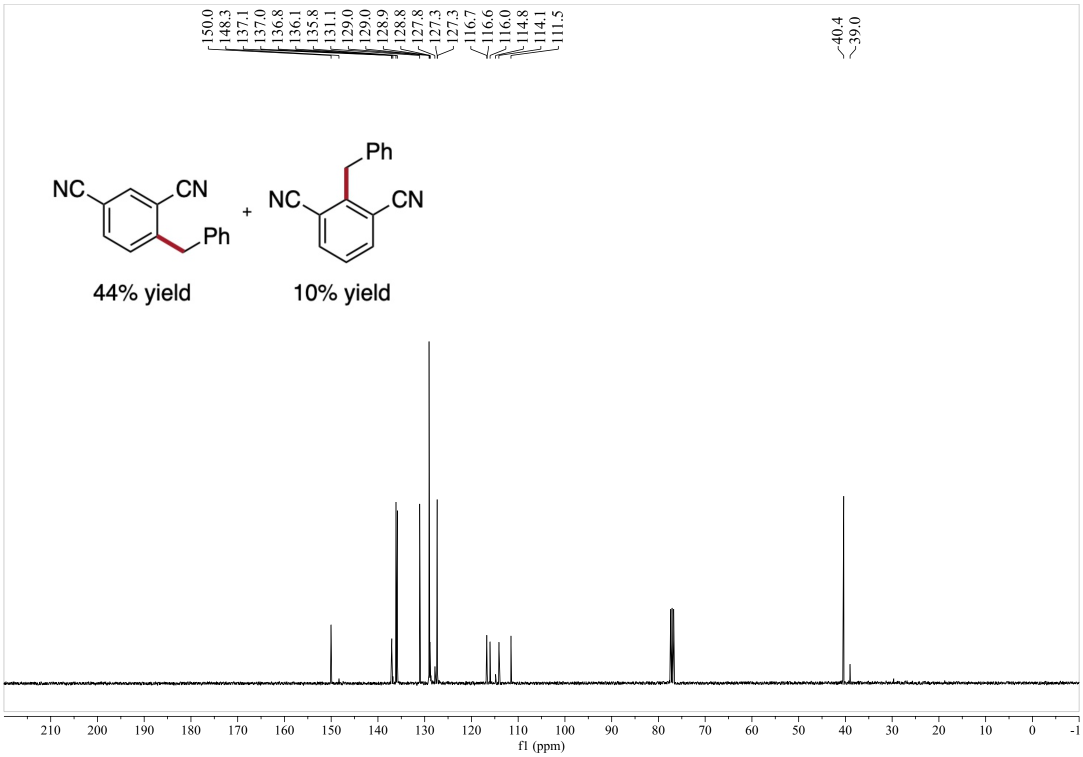
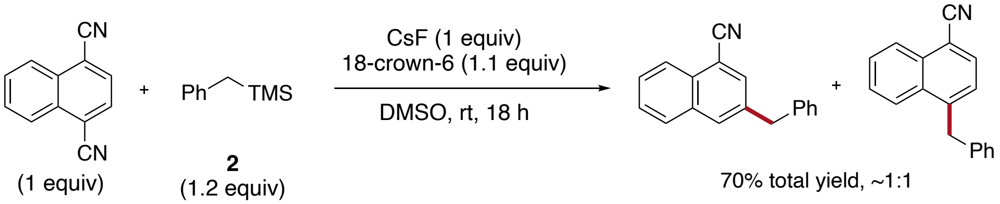


Fig. 15: Isolated ^{13}C NMR Spectrum of benzylation of isophthalonitrile.

Observation of C–H benzylation of naphthalene-1,4-dicarbonitrile. Under the standard coupling conditions (GP1) using naphthalene-1,4-dicarbonitrile, benzylation of the 3- and 4-positions was observed. The observation of these products is similar to observations reported in "Photoalkylation of Dicyanoarenes with Alkyltriphenylborate salts" Lan, J. Y.; Schuster, G. B. *J. Am. Chem. Soc.* **1985**, *107*, 6710 – 6711 and in "Photoinduced Electron-Transfer Reactions of Arylmethyl-Substituted 14 Group Compounds: Photoarylmethylation and Photooxygenation" Tamai, T.; Mizuno, K.; Hashida, I.; Otsuji, Y. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3747 – 3754. The products were isolated as an inseparable mixture containing unidentified side products. Characterization of the ^{1}H NMR spectrum and elemental analysis data matched those reported in the aforementioned references.



General Procedure for benzylation of naphthalene-1,4-dicarbonitrile: In a nitrogen-filled glovebox, to an oven-dried 2-dram glass vial (8 mL, Thermo Scientific, B7999-3) equipped with a magnetic stir bar was added naphthalene-1,4-dicarbonitrile (0.178 g, 1.0 mmol, 1.0 equiv), a solution of 18-crown-6 (1M in THF, 1.1 mL, 1.1 equiv), benzyltrimethylsilane (0.197 g, 1.2 mmol, 1.2 equiv), and anhydrous DMSO (2.9 mL, 0.25 M relative to total volume). Solid CsF (0.152 g, 1.0 mmol, 1.0 equiv) was added in one portion and the vial was sealed with a screw cap (Thermo Scientific, B7807-15) equipped with a 2.6 mm PTFE/Silicone Septa (Thermo Scientific, B7995-15). The reaction vial was removed from the glovebox and the solution was vigorously stirred at room temperature for 18 h. The reaction mixture was poured into a separatory funnel and diluted with brine (50 mL), extracted with EtOAc (3 x 15 mL), washed with H_2O (3 x 15 mL) and brine (2 x 25 mL) and dried over $MgSO_4$. After concentration under reduced pressure, the crude reaction mixture was purified *via* silica gel chromatography using 10% EtOAc in hexanes to afford an inseparable approximate 1:1 mixture of benzylated products (0.170 g, 0.70 mmol, 70% yield) contaminated with unidentifiable side products. Characteristic peaks for the diarylmethane products are observed at 4.49 and 4.15 ppm in the ^{1}H NMR (Fig. 16), and 41.4 and 39.1 ppm in the ^{13}C NMR (Fig. 17) respectively. **Benzylated Product 1** (4-benzyl-1-naphthonitrile) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 – 7.15 (m, 11H), 4.49 (s, 2H); **Benzylated Product 2** (3-benzyl-1-naphthonitrile) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 – 7.15 (m, 11H), 4.15 (s, 2H); this sample was also submitted for elemental analysis; **EA** Calcd. for $C_{18}H_{13}N$: C, 88.86; H, 5.39; N, 5.76. Found: C, 87.14; H, 5.41, N, 5.53; The ^{1}H NMR spectral data and melting point range are in agreement with those previously reported.[50]

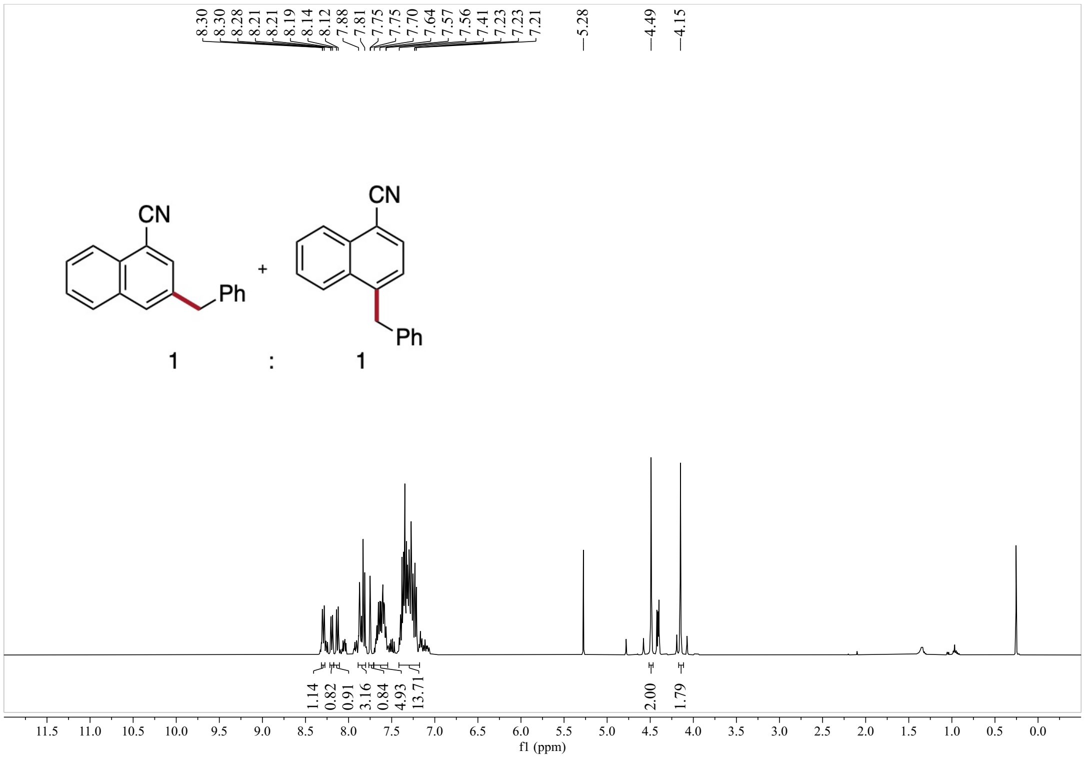


Fig. S16: Crude ^{1}H NMR Spectrum of benzylation of naphthalene-1,4-dicarbonitrile.

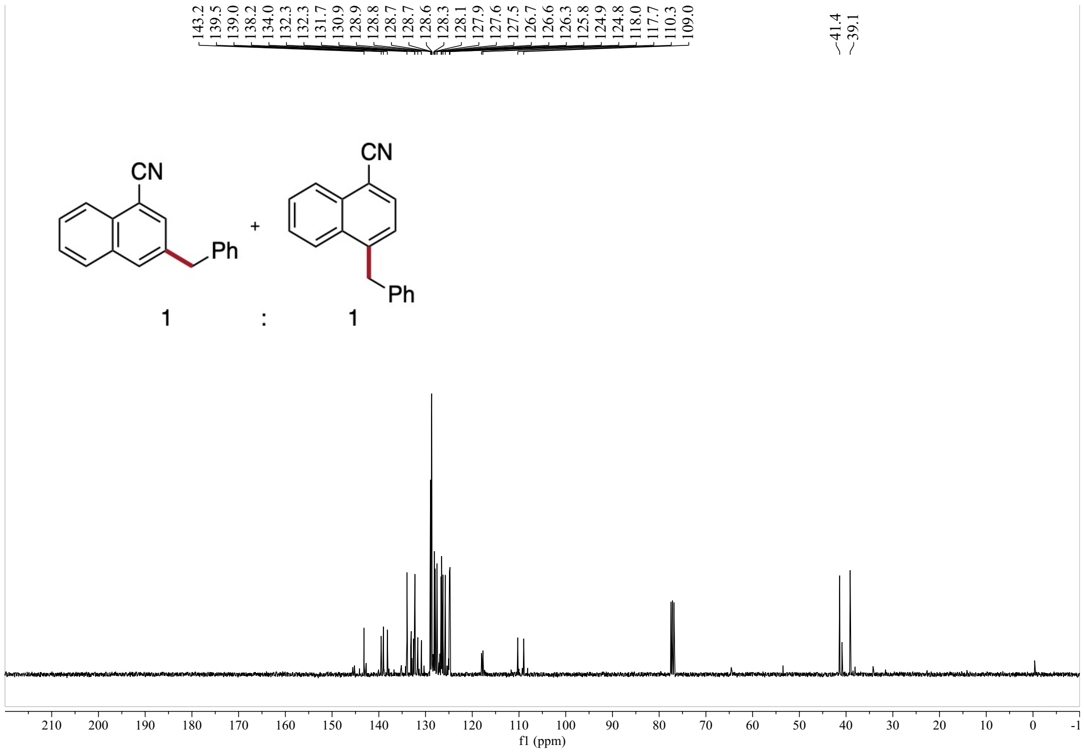
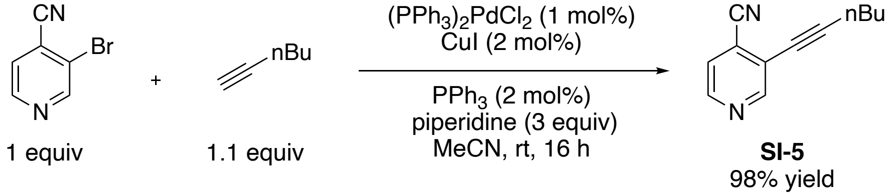
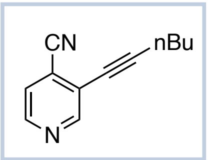


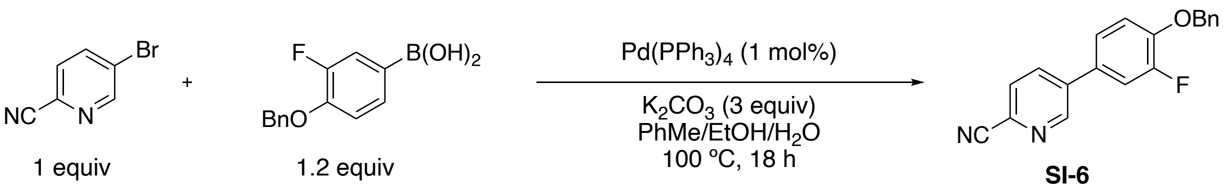
Fig. S17: Crude ^{13}C NMR Spectrum of benzylation of naphthalene-1,4-dicarbonitrile.

XII. Starting Material Syntheses and Characterization

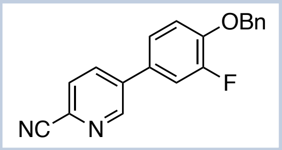




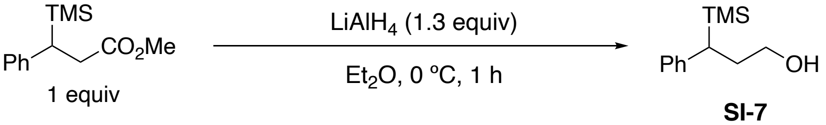
3-(Hex-1-yn-1-yl)isonicotinonitrile (SI-5). A 50-mL flame-dried round bottom flask was cooled to room temperature under a stream of nitrogen and charged with 3-bromo-4-cyanopyridine (0.550 g, 3.0 mmol, 1.0 equiv), 1-hexyne (0.271 g, 3.3 mmol, 1.1 equiv), $(PPh_3)_2PdCl_2$ (21.0 mg, 0.03 mmol, 0.01 equiv), CuI (11.4 mg, 0.06 mmol, 0.02 equiv), PPh_3 (15.7 mg, 0.06 mmol, 0.02 equiv), piperidine (0.766 g, 9.0 mmol, 3.0 equiv), and diluted with MeCN (6.0 mL). The reaction mixture was stirred for 16 h and then concentrated under vacuum. The crude reaction mixture was purified directly *via* silica gel chromatography using 2% Et_2O in hexanes to afford **SI-5** as a yellow oil (0.542 g, 2.9 mmol, 98% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.56 (d, J = 5.0 Hz, 1H), 7.43 (d, J = 5.0 Hz, 1H), 2.48 (t, J = 7.0 Hz, 2H), 1.64 – 1.57 (m, 2H), 1.52 – 1.43 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.0, 147.9, 124.8, 123.1, 122.4, 115.4, 101.7, 74.4, 30.2, 21.9, 19.3, 13.5; **IR** (neat): 2958, 2933, 2872, 2227, 1578, 1480, 1400, 1343 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{12}H_{13}N_2$ $(M+H)^+$ 185.1073; found 185.1072.



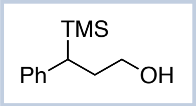
SI-6
quant.



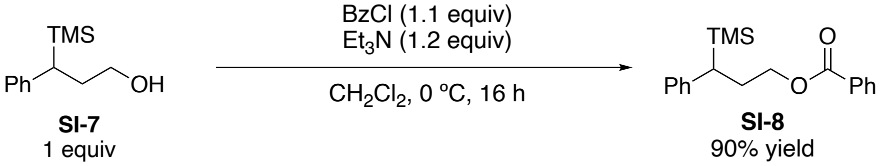
5-(4-(Benzyloxy)-3-fluorophenyl)picolinonitrile (SI-6). A 50-mL flame-dried round bottom flask was cooled to room temperature under a stream of nitrogen and charged with 5-bromo-2-cyanopyridine (1.83 g, 10.0 mmol, 1.0 equiv), (4-(benzyloxy)-3-fluorophenyl)boronic acid (2.96 g, 12.0 mmol, 1.2 equiv), $Pd(PPh_3)_4$ (116 mg, 0.1 mmol, 0.01 equiv), and K_2CO_3 (4.15 g, 30.0 mmol, 3.0 equiv). The flask was sealed with a rubber septum equipped with a nitrogen inlet and a vent needle and the contents of the flask were flushed with nitrogen for 5 minutes. Degassed toluene (30.0 mL, 0.33 M), EtOH (15.0 mL, 0.66 M) and H_2O (15.0 mL, 0.66 M) were added *via* syringe. The reaction mixture was stirred vigorously at 100 ºC for 18 h under a stream of nitrogen and then allowed to cool to room temperature. The crude reaction mixture was poured into a separatory funnel containing brine (100 mL) and extracted with EtOAc (3 x 50 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude residue was purified directly *via* silica gel chromatography using 10% EtOAc in hexanes to afford **SI-6** as a light yellow solid (3.04 g, 10.0 mmol, 100% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.87 (d, *J* = 2.3 Hz, 1H), 7.92 (dd, *J* = 8.0, 2.3 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.49 – 7.44 (m, 2H), 7.43 – 7.29 (m, 5H), 7.14 (t, *J* = 8.5 Hz, 1H), 5.21 (s, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -131.8; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.2 (d, *J* = 249.2 Hz), 149.1, 147.9 (d, *J* = 10.8 Hz), 138.3 (d, *J* = 1.9 Hz), 135.9, 134.3, 132.0, 129.0 (d, *J* = 6.7 Hz), 128.7, 128.5, 128.4, 127.4, 123.3 (d, *J* = 3.4 Hz), 117.3, 116.1 (d, *J* = 2.3 Hz), 115.1 (d, *J* = 19.8 Hz); **IR** (neat): 3052, 2938, 2877, 2360, 2229, 1614, 1519, 1270 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{19}H_{14}FN_2O$ $(M+H)^+$ 305.1085; found 305.1080; **Melting point:** 119 – 123 ºC.

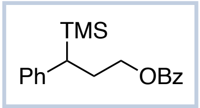


SI-7
95% yield

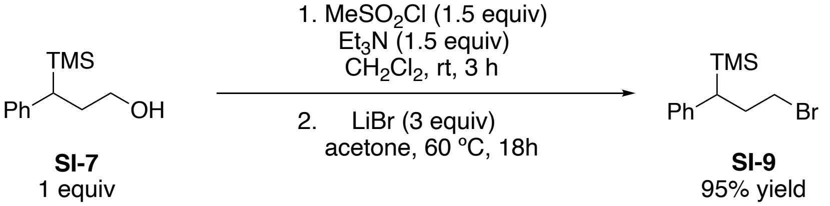


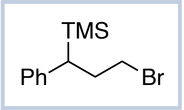
3-Phenyl-3-(trimethylsilyl)propan-1-ol (SI-7). A 250-mL flame-dried round bottom flask was cooled to room temperature under a stream of nitrogen and charged with $LiAlH_4$ (0.987 g, 26.0 mmol, 1.3 equiv) and diluted with anhydrous Et_2O (70.0 mL). A solution of methyl 3-phenyl-3-(trimethylsilyl)propanoate[21] (4.73 g, 20.0 mmol, 1.0 equiv) in anhydrous Et_2O (10.0 mL, 0.25 M total volume) was added dropwise at 0 ºC and the reaction was then allowed to warm to room temperature and stirred for 1 h. The reaction mixture was cooled to 0 ºC and slowly quenched with saturated aqueous NH_4Cl, (25 mL) extracted with Et_2O (3 x 50 mL), washed with brine (50 mL), and dried over anhydrous $MgSO_4$. After concentration, the crude material was purified directly by silica gel chromatography (15% EtOAc in hexanes) to afford **SI-7** as a white solid (3.96 g, 19.0 mmol, 95% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.22 (m, 2H), 7.12 – 7.08 (m, 1H), 7.06 – 7.03 (m, 2H), 3.59 – 3.54 (m, 1H), 3.48 – 3.42 (m, 1H), 2.16 (dd, *J* = 11.9, 3.8 Hz, 1H), 2.09 – 1.93 (m, 2H), 1.79 (brs, 1H), -0.03 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.9, 128.2, 127.6, 124.6, 62.2, 32.8, 32.1, -3.0.; **IR** (neat): 3238, 3025, 2932, 2853, 1493, 1385, 1286, 1244 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{12}H_{21}OSi$ $(M+Na)^+$ 231.1176; found 231.1161; **Melting point:** 69 – 74 ºC.



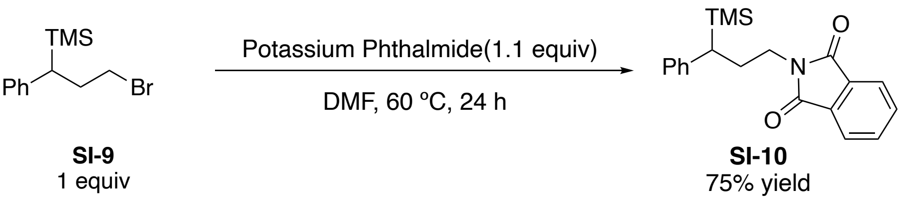


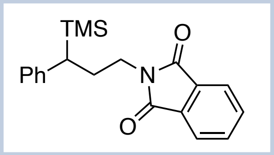
3-Phenyl-3-(trimethylsilyl)propyl benzoate (SI-8). A 50-mL flame-dried round bottom flask was cooled to room temperature under a stream of nitrogen and charged with 3-phenyl-3-(trimethylsilyl)propan-1-ol (**SI-7**, 1.04 g, 5.0 mmol, 1.0 equiv), triethylamine (0.607 g, 6.0 mmol, 1.2 equiv), and diluted with CH_2Cl_2 (10 mL) and the flask was placed in an ice bath. Benzoyl chloride (0.773 g, 5.5 mmol, 1.1 equiv) was added dropwise at 0 ºC. The reaction mixture was allowed to warm to room temperature and stirred for 16 h and then concentrated under vacuum. The crude reaction mixture was purified directly *via* silica gel chromatography using 5% Et_2O in hexanes to afford **SI-8** as a yellow oil (0.844 g, 4.5 mmol, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 – 7.97 (m, 2H), 7.59 – 7.55 (m, 1H), 7.46 – 7.42 (m, 2H), 7.29 – 7.25 (m, 2H), 7.14 – 7.08 (m 3H), 4.32 – 4.26 (m, 1H), 4.23 – 4.16 (m, 1H), 2.34 – 2.18 (m, 3H), 0.00 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.5, 142.4, 132.8, 130.5, 129.5, 128.31, 128.28, 127.6, 124.7, 64.9, 33.5, 28.5, -3.0; **IR** (neat): 3061, 2954, 2339, 1716, 1601, 1450, 1269, 1157 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{19}H_{25}O_2Si$ $(M+Na)^+$ 335.1438; found 335.1428.



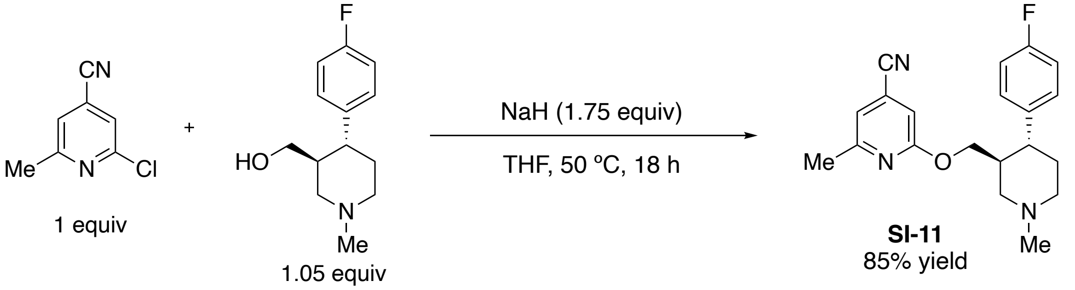


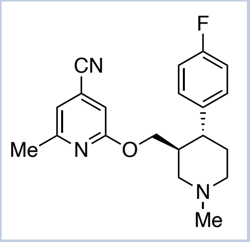
(3-Bromo-1-phenylpropyl)trimethylsilane (SI-9). A 50-mL flame-dried round bottom flask was cooled to room temperature under a stream of nitrogen and charged with 3-phenyl-3-(trimethylsilyl)propan-1-ol (**SI-7**, 3.77 g, 18.1 mmol, 1.0 equiv) and diluted with anhydrous CH_2Cl_2 (36.2 mL, 0.5 M). The reaction vessel was cooled in an ice bath to 0 ºC and triethylamine (3.78 mL, 27.1 mmol, 1.5 equiv) was added, followed by the dropwise addition of methanesulfonyl chloride (2.10 mL, 27.1 mmol, 1.5 equiv). The reaction mixture was allowed to warm to room temperature over 3 h and was quenched with water (20 mL), extracted with CH_2Cl_2 (3 x 50 mL), washed with brine (2 x 50 mL), and dried over anhydrous Na_2SO_4. After concentration under vacuum, the crude residue was dissolved in acetone (50 mL) and LiBr (4.72 g, 54.3 mmol, 3.0 equiv) was added in one portion. The reaction flask was equipped with a reflux condenser and heated to 60 ºC for 18 h and then allowed to cool to room temperature. The acetone was removed under vacuum and the crude residue was dissolved in Et_2O (100 mL). Water (20 mL) was added, and the aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic extracts were washed with brine (2 x 50 mL) and dried over anhydrous Na_2SO_4. After concentration under vacuum, the crude residue was purified directly *via* silica gel chromatography using hexanes to afford **SI-9** as a colorless oil (4.66 g, 17.2 mmol, 95% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.25 (m, 2H), 7.15 – 7.11 (m, 1H), 7.07 – 7.05 (m, 2H), 3.44 – 3.36 (m, 1H), 3.25 – 3.15 (m, 1H), 2.45 – 2.36 (m, 1H), 2.30 – 2.17 (m, 2H), 0.00 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.6, 128.5, 127.7, 125.0, 35.8, 33.9, 33.0, -2.9; **IR** (neat): 3081, 2954, 2360, 1600, 1489, 1450, 1248, 1220 cm^{-1}.



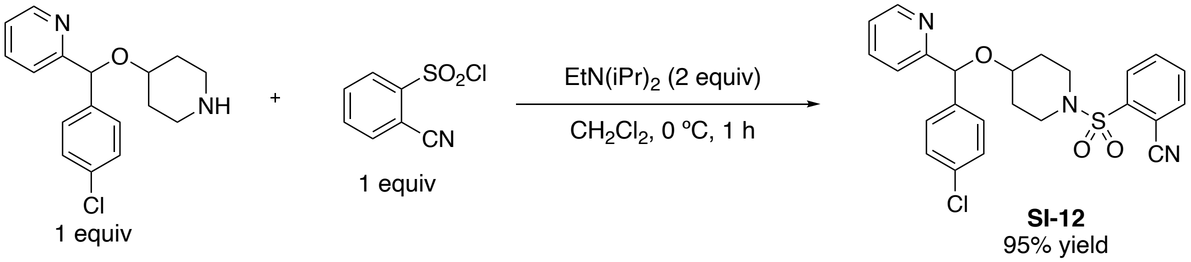


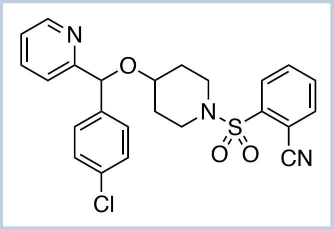
2-(3-Phenyl-3-(trimethylsilyl)propyl)isoindoline-1,3-dione (SI-10). A 50-mL flame-dried round bottom flask was cooled to room temperature under N_2 and charged with (3-bromo-1-phenylpropyl)trimethylsilane (**SI-9**, 0.814 g, 3.0 mmol, 1.0 equiv) and diluted with anhydrous DMF (15.0 mL). Potassium phthalimide (0.611 g, 3.3 mmol, 1.1 equiv) was added in one portion at room temperature. The reaction mixture was heated at 60 ºC for 24 h, cooled to room temperature, diluted with H_2O (20 mL), and extracted with EtOAc (3 x 25 mL). The combined organic extracts were washed with H_2O (2 x 50 mL), brine (2 x 50 mL), and dried over anhydrous Na_2SO_4. After concentration under reduced pressure, the crude residue was purified directly *via* silica gel chromatography using 10% EtOAc in hexanes to afford **SI-10** as a white solid (0.759 g, 75% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 2H), 7.61 – 7.56 (m, 2H), 7.12 – 7.07 (m, 2H), 7.04 – 6.98 (m, 2H), 6.91 – 6.86 (m, 1H), 3.73 – 3.61 (m, 1H), 3.59 – 3.50 (m, 1H), 2.32 – 2.20 (m, 1H), 2.10 – 2.06 (m, 1H), 2.03 – 1.90 (m, 1H), -0.11 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.2, 142.1, 133.5, 132.1, 128.1, 127.3, 124.3, 122.9, 38.5, 34.9, 27.5, -3.2; **IR** (neat): 3022, 2950, 2924, 1771, 1708, 1614, 1466, 1396, 1256 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{20}H_{24}NO_2Si$ $(M+H)^+$ 338.1571; found 338.1560; **Melting point:** 59 – 61 ºC.



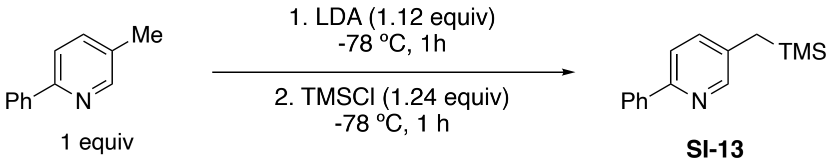


2-(((3*S*,4*R*)-4-(4-Fluorophenyl)-1-methylpiperidin-3-yl)methoxy)-6-methylisonicotinonitrile (SI-11). A 100 mL flame-dried round bottom flask was charged with (3*S*,4*R*)-4-(4-fluorophenyl)-3-hydroxymethyl-1-methylpiperidine (1.29 g, 5.78 mmol, 1.05 equiv) and diluted with anhydrous THF (22.0 mL, 0.25 M). In one portion, NaH (0.385 g, 60% in mineral oil, 9.63 mmol, 1.75 equiv) was added at room temperature. The reaction mixture was heated to 50 ºC for 30 minutes and then allowed to cool to room temperature. In one portion, 2-chloro-6-methylisonicotinonitrile[16] (0.839 g, 5.5 mmol, 1.0 equiv) was added. The reaction mixture was heated to 50 ºC overnight and then allowed to cool to room temperature. Water (10 mL) was slowly added and the THF was removed *in vacuo*. The crude residue was diluted with more water (50 mL) and extracted with EtOAc (3 x 25 mL). The combined organic extracts were then washed with brine (2 x 50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The product was purified *via* silica gel chromatography using 5% MeOH in CH_2Cl_2 to afford **SI-11** as a viscous yellow oil (1.59 g, 4.68 mmol, 85% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.11 – 7.07 (m, 2H), 6.88 – 6.84 (m, 2H), 6.73 (s, 1H), 6.59 (s, 1H), 4.03 (dd, *J* = 11.1, 2.6 Hz, 1H), 3.73 (dd, *J* = 10.9, 7.1 Hz, 1H), 3.09 – 3.06 (m, 1H), 2.88 – 2.86 (m, 1H), 2.35 – 2.25 (m, 8H), 2.00 – 1.87 (m, 2H), 1.79 – 1.69 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -116.4; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.1, 161.5 (d, *J* = 245.0 Hz), 158.2, 139.4 (d, *J* = 3.1 Hz), 128.8 (d, *J* = 7.7 Hz), 122.3, 116.7, 116.5, 115.3 (d, *J*= 21.1 Hz), 110.3, 67.1, 59.3, 56.0, 46.3, 43.7, 41.1, 34.7, 23.9; **IR** (neat): 2939, 2846, 2783, 2690, 1603, 1556, 1510, 1333 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{20}H_{23}FN_3O$ $(M+H)^+$ 340.1820; found 340.1808.

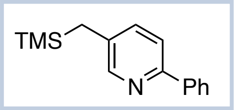




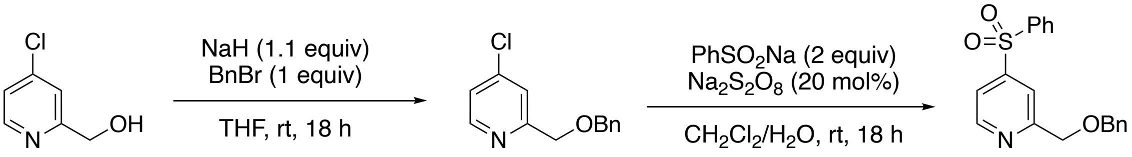
2-((4-((4-chlorophenyl)(pyridin-2-yl)methoxy)piperidin-1-yl)sulfonyl)benzonitrile (SI-12). A flame-dried 100-mL round-bottom flask equipped with a magnetic stir bar was charged with 2-[(4-chlorophenyl)(4-piperidinyloxy)methyl]pyridine (1.0 g, 3.30 mmol, 1.0 equiv), *N*,*N*-diisopropylethylamine (1.15 mL, 6.6 mmol, 2.0 equiv), diluted with CH_2Cl_2 (15 mL), and placed in an ice-water bath. Solid 2-cyanobenzenesulfonyl chloride (0.665 g, 3.30 mmol, 1.0 equiv) was added in one portion and the reaction mixture was vigorously stirred under nitrogen at room temperature for 1 h. The reaction mixture was quenched by adding water (50 mL) and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL) and the organic extracts were combined, washed with saturated aqueous NH_4Cl (2 x 50 mL), dried over anhydrous $MgSO_4$ and concentrated. The crude residue was purified *via* silica gel chromatography using 30% EtOAc in hexanes to afford **SI-12** as a beige solid (1.47 g, 3.14 mmol, 95% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.48 (dd, *J* = 5.8, 1.8 Hz, 1H), 8.02 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.85 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.75 – 7.63 (m, 3H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.24 (d, *J* = 8.5 Hz, 2H), 7.15 (dd, *J* = 7.5, 6.0 Hz, 1H), 5.54 (s, 1H), 3.62 – 3.57 (m, 1H), 3.52 – 3.45 (m, 2H), 3.19 – 3.13 (m, 2H), 1.95 – 1.75 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.5, 149.0, 140.8, 139.8, 137.2, 135.7, 133.6, 133.0, 132.7, 130.4, 128.7, 128.2, 122.8, 120.7, 116.3, 110.9, 81.2, 71.1, 43.1 (x2), 30.6 (x2); **IR** (neat): 3067, 2930, 2863, 2230, 1732, 1588, 1489, 1352 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{24}H_{23}ClN_3O_3S$ $(M+H)^+$ 468.1143; found 468.1136; **Melting point:** 188 – 191 ºC.



SI-13
70% yield

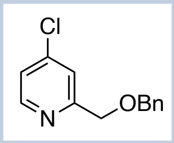


2-Phenyl-5-((trimethylsilyl)methyl)pyridine (SI-13). A 100-mL flame-dried round bottom flask was cooled to room temperature under N_2 and charged with diisopropylamine (1.74 mL, 12.4 mmol, 1.24 equiv), anhydrous THF (50 mL), and cooled to 0 ºC in an ice bath. A solution of nBuLi (7.0 mL, 1.6 M in hexanes, 11.2 mmol, 1.12 equiv) was added dropwise and then the reaction flask was placed in a -78 ºC dry ice/acetone bath. A solution of 5-methyl-2-phenylpyiridine (1.69 g, 10.0 mmol, 1.0 equiv) in THF (15 mL) was added dropwise and the reaction mixture was stirred at -78 ºC for 1 h followed by the dropwise addition of chlorotrimethylsilane (1.57 mL, 12.4 mmol, 1.24 equiv). After stirring for an additional 1 h at -78 ºC, the reaction mixture was quenched by the addition of 10 mL saturated aqueous NH_4Cl at -78 °C and warmed to room temperature, poured into a separatory funnel containing Et_2O (100 mL) and saturated aqueous $NaHCO_3$ (50 mL), extracted with Et_2O (3 x 50 mL), and dried over anhydrous $MgSO_4$. After concentration *in vacuo*, the crude residue was purified directly *via* silica gel chromatography using 10% Et_2O in hexanes to afford **SI-13** as a colorless amorphous solid (1.69 g, 7.0 mmol, 70% yield). ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 8.35 (d, J = 1.8 Hz, 1H), 7.95 (d, J = 7.3 Hz, 2H), 7.55 (d, J = 8.1 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.34 – 7.30 (m, 2H), 2.04 (s, 2H), 0.00 (s, 9H); ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 153.3, 149.0, 139.4, 135.9, 134.7, 128.7, 128.4, 126.5, 119.9, 23.7, -2.0; **IR** (neat): 3066, 2929, 2230, 1733, 1588, 1489, 1352, 1295 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{15}H_{20}NSi$ $(M+H)^+$ 242.1360; found 242.1354.

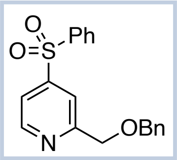


SI-14
90% yield

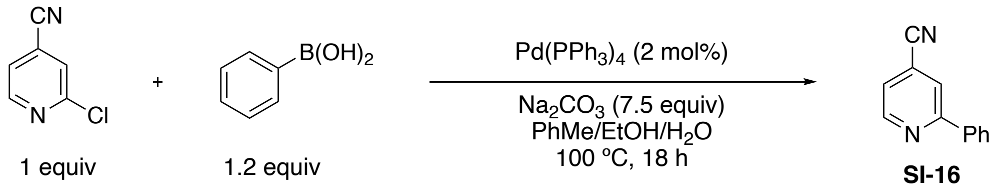
SI-15
91% yield



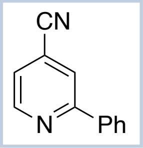
2-((Benzyloxy)methyl)-4-chloropyridine (SI-14). A flame-dried 100-mL round-bottom flask equipped with a magnetic stir bar was charged with (4-chloropyridin-2-yl)methanol (1.44 g, 10.0 mmol, 1.0 equiv) and dissolved in anhydrous THF (34 mL, 0.3 M). Sodium hydride (0.440 g, 11.0 mmol, 1.1 equiv) was added in one portion under nitrogen at room temperature. The reaction mixture was stirred for 30 min and then cooled to 0 ºC in an ice bath. Benzyl bromide (1.2 mL, 10.0 mmol, 1.0 equiv) was added *via* syringe and the reaction mixture was stirred overnight at room temperature. The reaction mixture was quenched by the slow addition of brine (20 mL), diluted with Et_2O (50 mL), and the organic layer was separated. The aqueous layer was extracted with Et_2O (3 x 20 mL) and the organic extracts were combined, dried over anhydrous $MgSO_4$ and concentrated. The crude residue was purified *via* silica gel chromatography using 15% EtOAc in hexanes to afford **SI-14** as a yellow oil (2.10 g, 9 mmol, 90% yield). ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 8.41 (d, J = 5.3 Hz, 1H), 7.53 – 7.52 (m, 1H), 7.41 – 7.34 (m, 4H), 7.32 – 7.28 (m, 1H), 7.18 – 7.15 (m, 1H), 4.66 (s, 2H), 4.65 (s, 2H); ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 160.4, 149.9, 144.8, 137.6, 128.5, 127.85, 127.79, 122.6, 121.5, 73.1, 72.3; **IR** (neat): 3062, 3030, 2859, 2231, 1576, 1557, 1467, 1353 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{13}H_{13}ClNO$ $(M+H)^+$ 234.0680; found 234.0677.



2-((Benzyloxy)methyl)-4-(phenylsulfonyl)pyridine (SI-15). A 100-mL round-bottom flask equipped with a magnetic stir bar was charged with benzenesulfinic acid sodium salt (2.81 g, 17.1 mmol, 2 equiv), sodium persulfate (0.410 g, 1.72 mmol, 20 mol%) and 2-((benzyloxy)methyl)-4-chloropyridine (**SI-14**, 2.0 g, 8.6 mmol, 1 equiv). The solids were diluted with CH_2Cl_2 (35 mL) and H_2O (14 mL) and vigorously stirred under nitrogen overnight. The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ (50 mL) and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL) and the organic extracts were combined, dried over anhydrous $MgSO_4$ and concentrated. The crude residue was purified *via* silica gel chromatography using 30% EtOAc in hexanes to afford **SI-15** as a white solid (2.66 g, 7.83 mmol, 91% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 5.0 Hz, 1H), 8.02 – 7.95 (m, 3H), 7.67 (dd, *J* = 5.1, 1.5 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.56 – 7.50 (m, 2H), 7.40 – 7.28 (m, 5H), 4.72 (s, 2H), 4.66 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.2, 150.5, 150.4, 139.7, 137.4, 134.1, 129.6, 128.5, 128.1, 127.93, 127.86, 119.1, 118.1, 73.2, 72.2; **IR** (neat): 3059, 2917, 2881, 2161, 1929, 1776, 1581, 1475, 1365 cm^{-1}; **HRMS (ESI)** *m/z* calcd. for $C_{19}H_{18}NO_3S$ $(M+H)^+$ 340.1002; found 340.1002; **Melting point:** 135 – 138 ºC.



SI-16
79% yield



2-Phenylisonicotinonitrile (SI-16). A 50-mL flame-dried round bottom flask was cooled to room temperature under a stream of nitrogen and charged with 2-chloroisonicotinonitrile (1.39 g, 10.0 mmol, 1.0 equiv), phenylboronic acid (1.46 g, 12.0 mmol, 1.2 equiv), $Pd(PPh_3)_4$ (232 mg, 0.2 mmol, 0.02 equiv), and Na_2CO_3 (7.95 g, 75.0 mmol, 7.5 equiv). The flask was sealed with a rubber septum equipped with a nitrogen inlet and a vent needle and the contents of the flask were flushed with nitrogen for 15 minutes. Degassed toluene (30.0 mL, 0.33 M), EtOH (7.7 mL, 1.33 M) and H_2O (30.0 mL, 0.33 M) were added *via* syringe. The reaction mixture was stirred vigorously at 100 ºC for 18 h under a stream of nitrogen and then allowed to cool to room temperature. The crude reaction mixture was poured into a separatory funnel containing brine (100 mL) and extracted with Et_2O (3 x 50 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude residue was purified directly *via* silica gel chromatography using 10% Et_2O in hexanes to afford **SI-16** as a white solid (1.42 g, 7.9 mmol, 79% yield). The spectroscopic data matched a previous literature report.[51]

XIII. References

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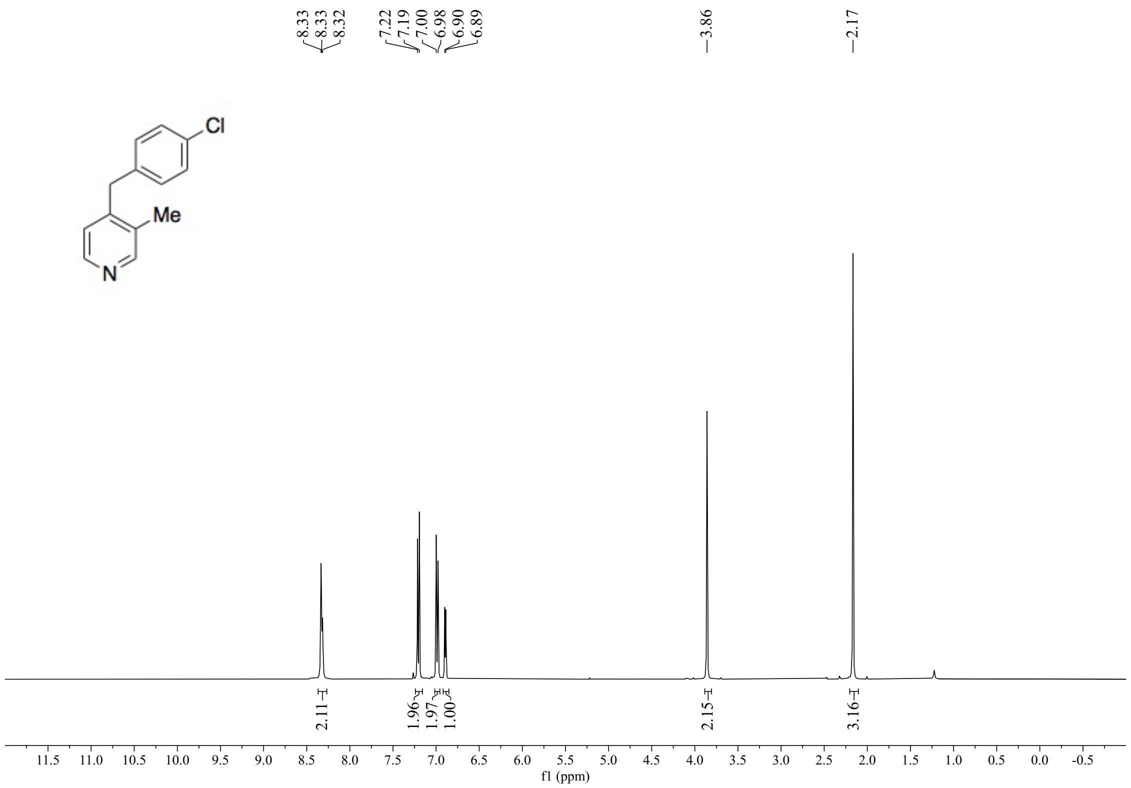
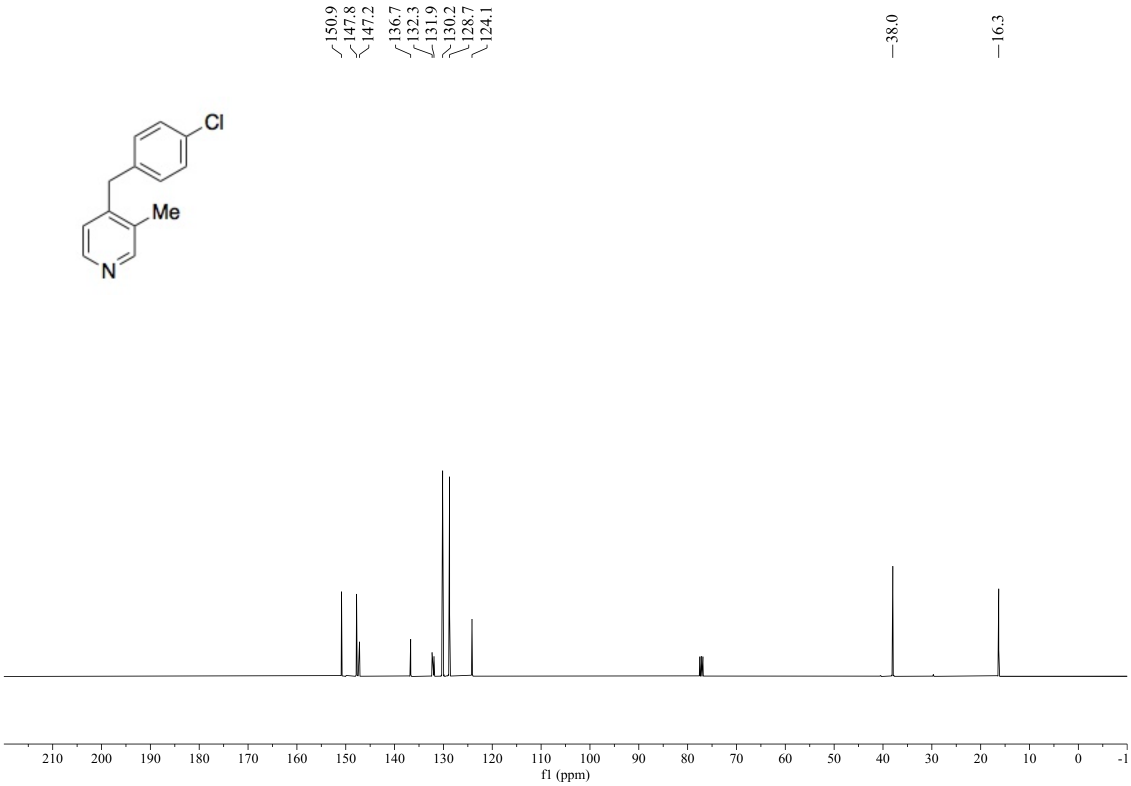
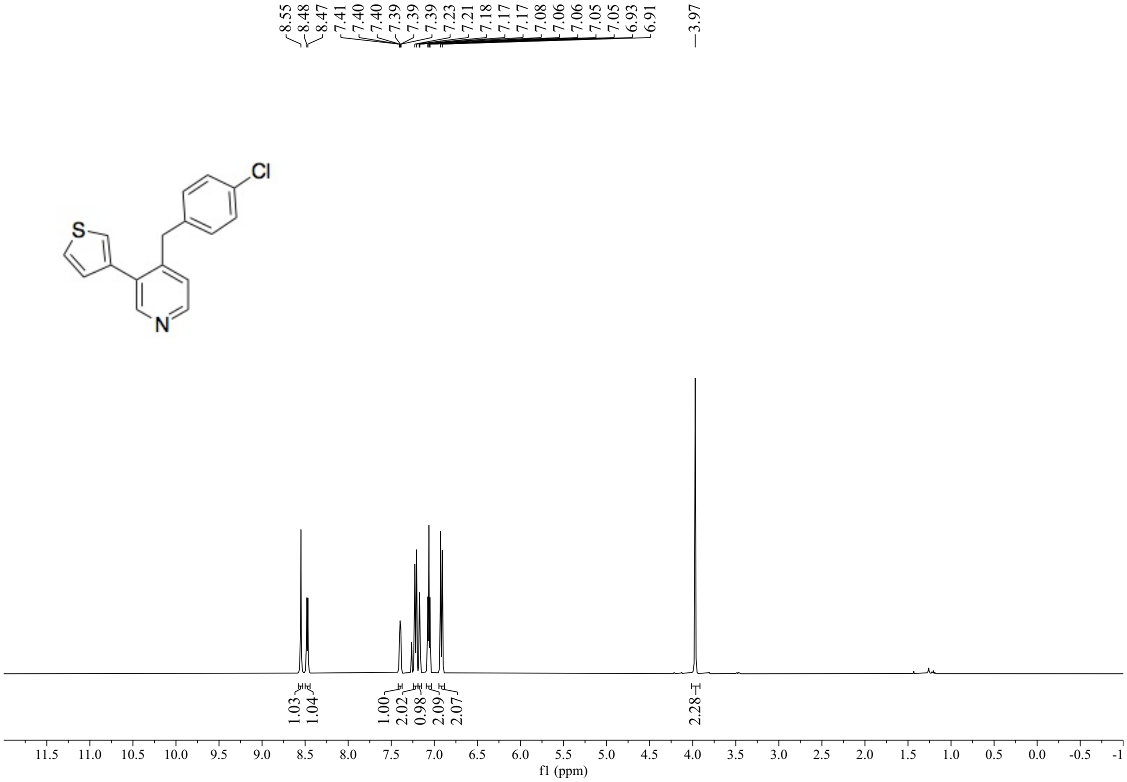
XIV. NMR Spectra



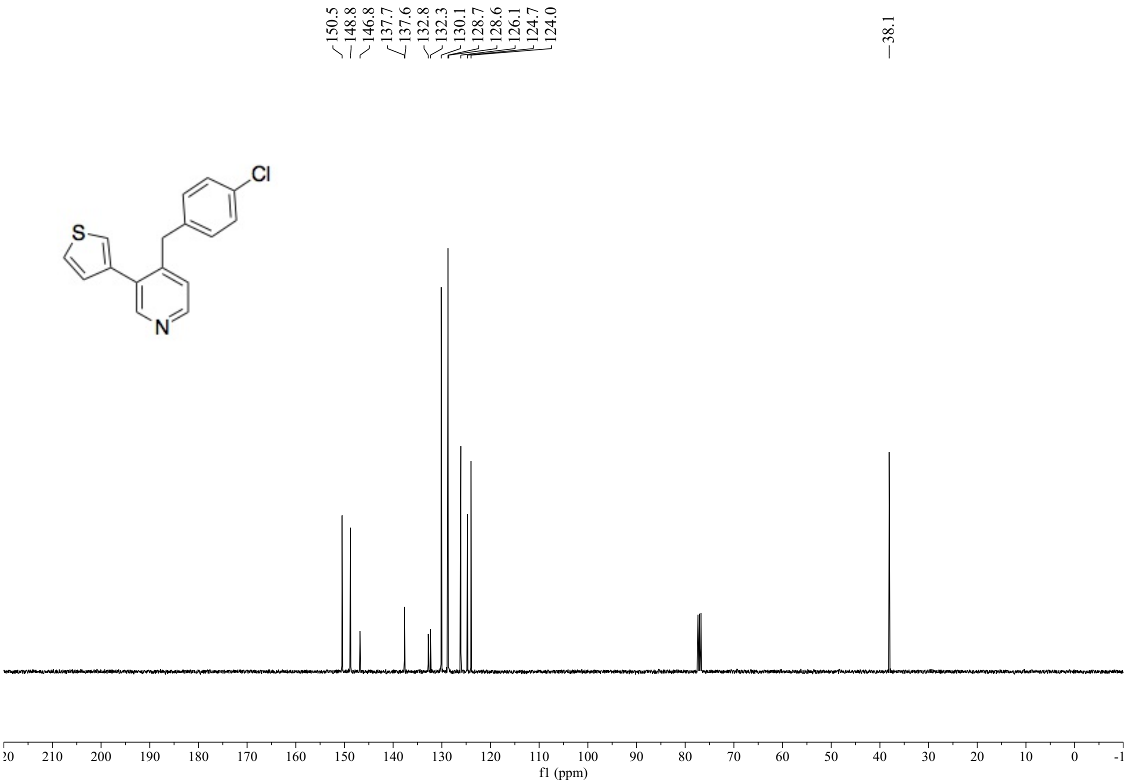
^{1}H NMR of compound **4** (400 MHz, $CDCl_3$)



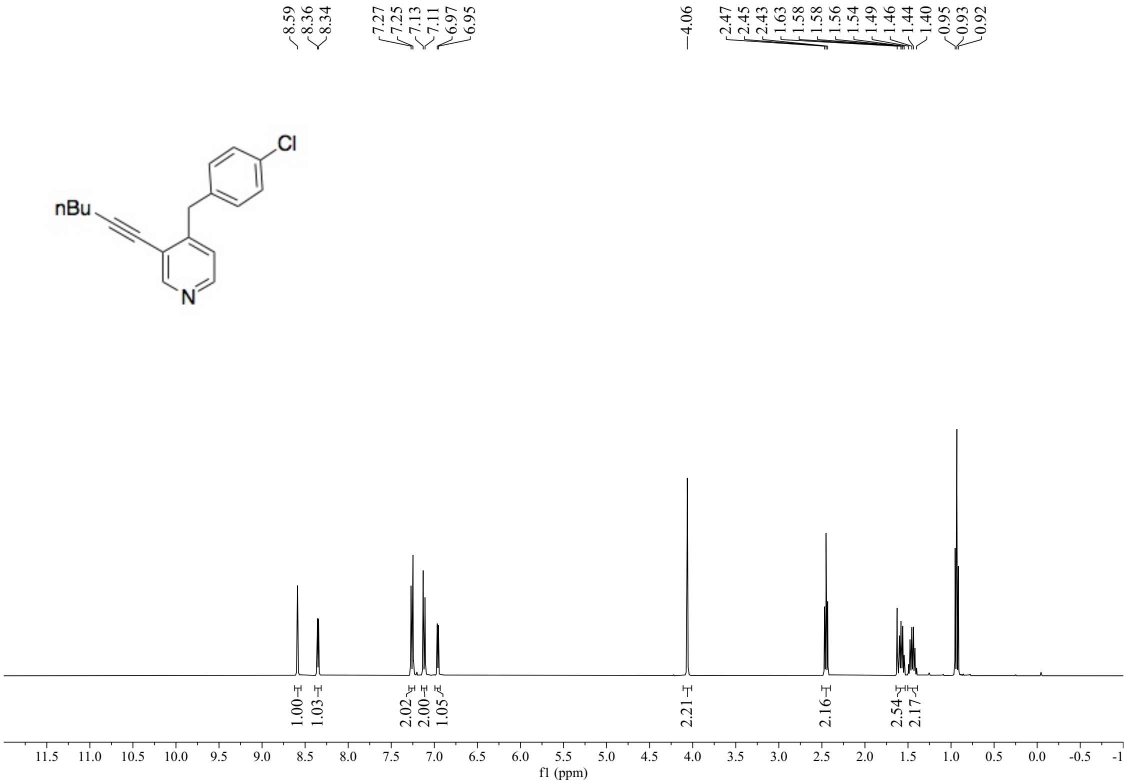
^{13}C NMR of compound **4** (101 MHz, $CDCl_3$)



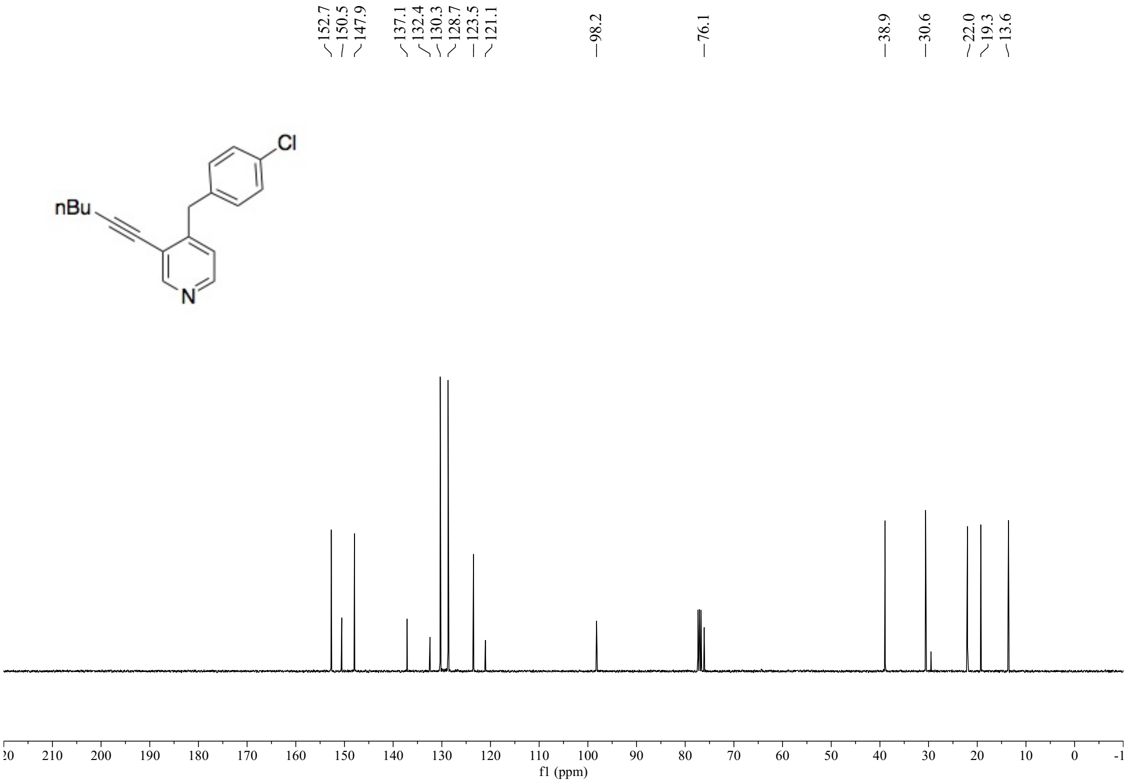
¹H NMR of compound **5** (400 MHz, $CDCl_3$)



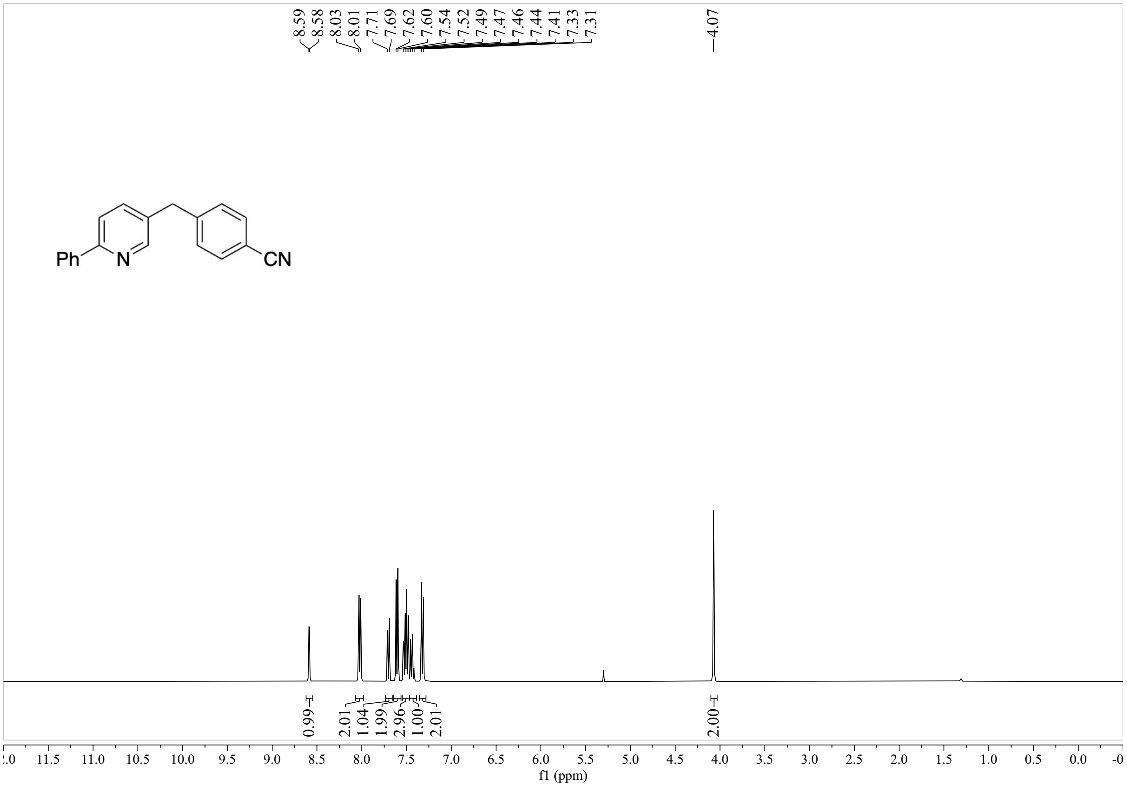
¹³C NMR of compound **5** (101 MHz, $CDCl_3$)



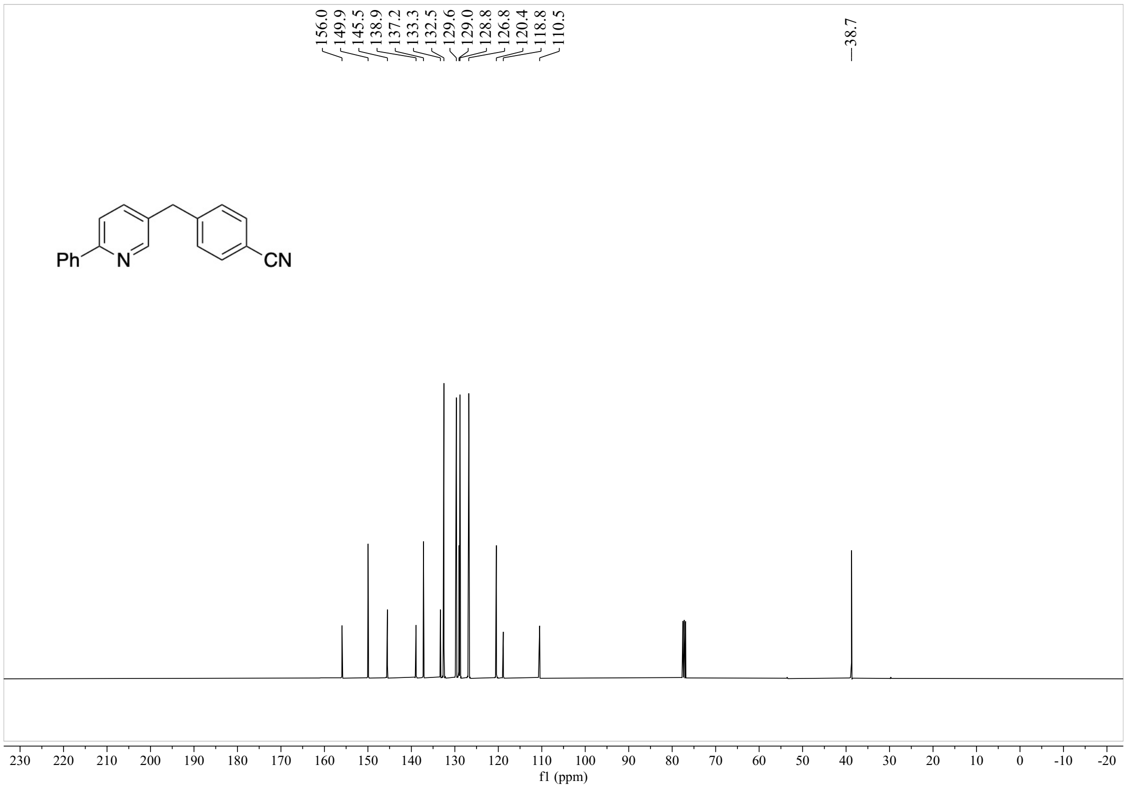
^{1}H NMR of compound **6** (400 MHz, CDCl$_3$)



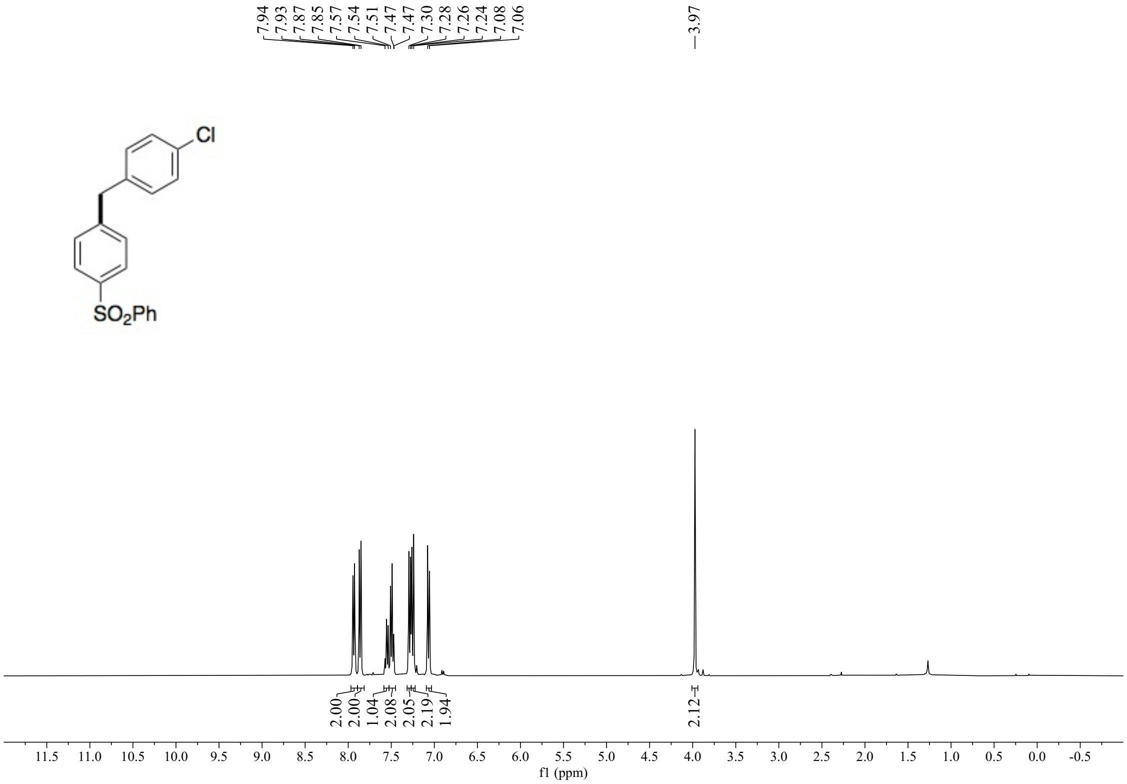
^{13}C NMR of compound **6** (101 MHz, CDCl$_3$)



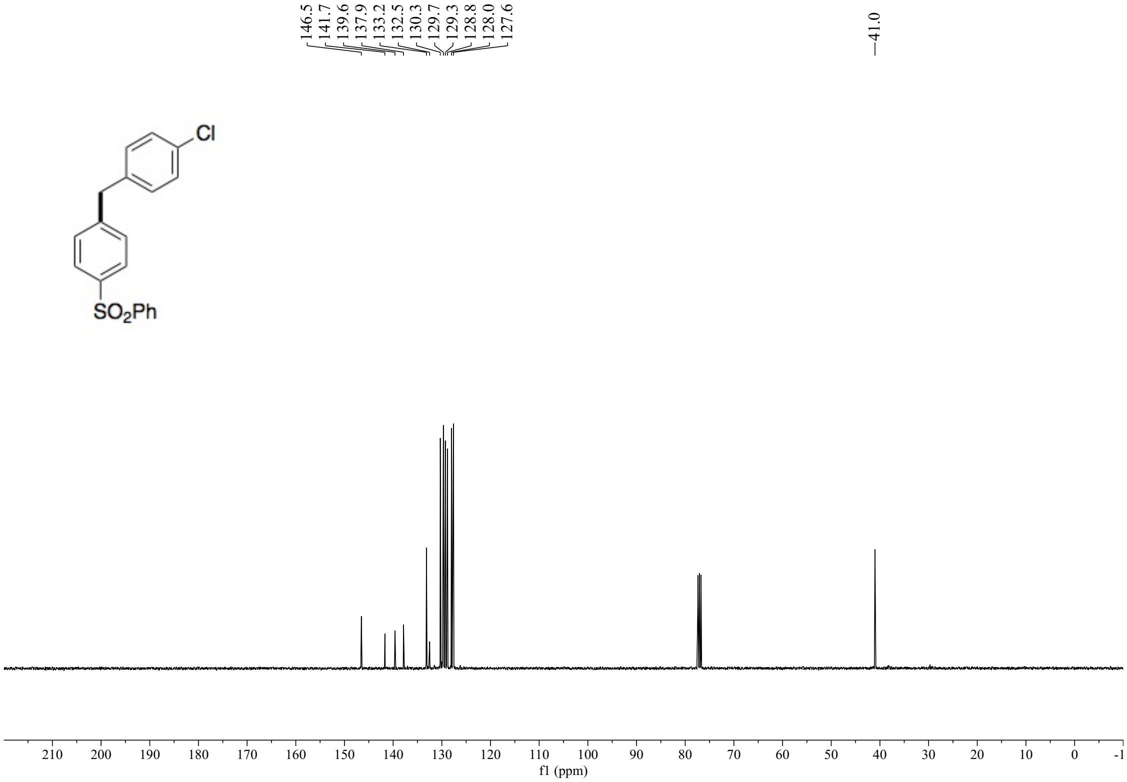
^{1}H NMR of compound **7** (400 MHz, CDCl$_3$)



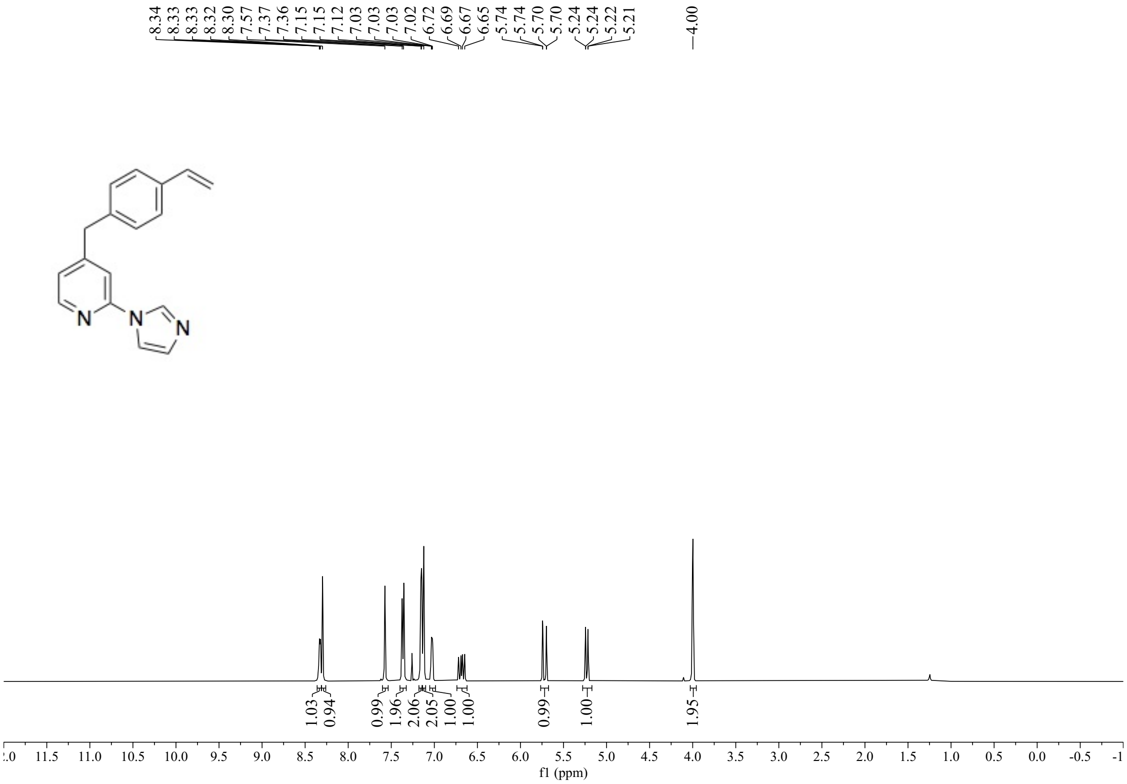
^{13}C NMR of compound **7** (101 MHz, CDCl$_3$)



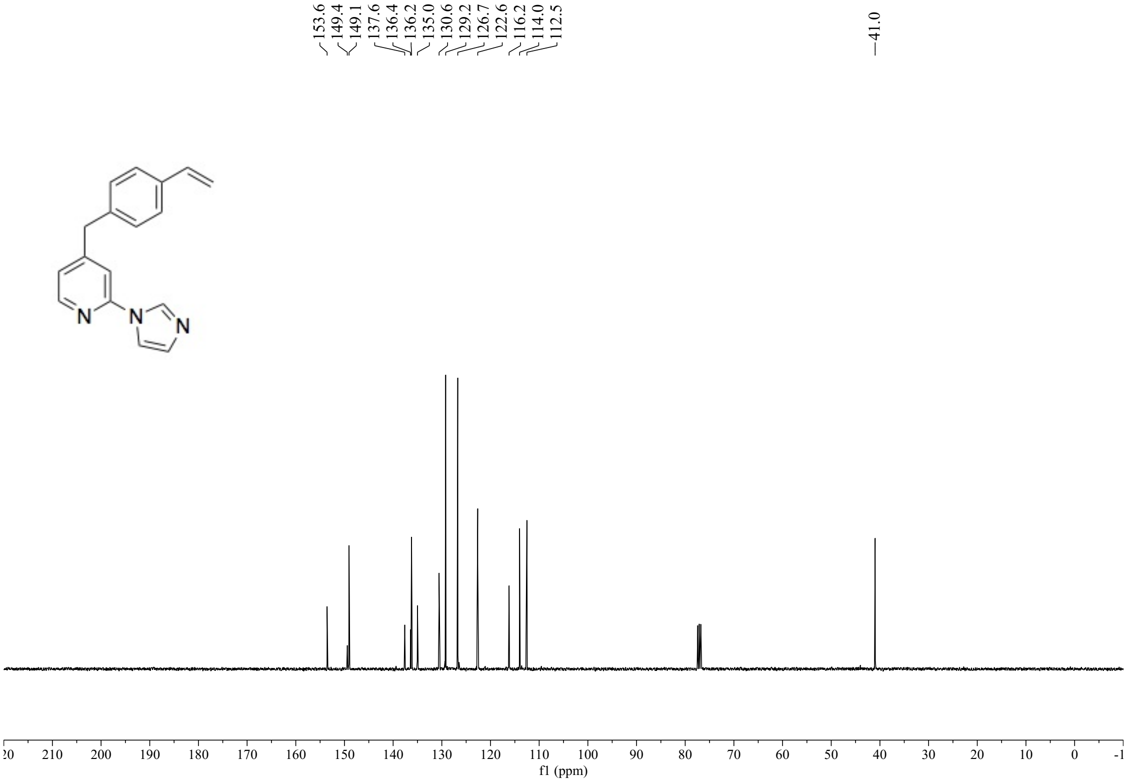
^{1}H NMR of compound **8** (400 MHz, CDCl$_3$)



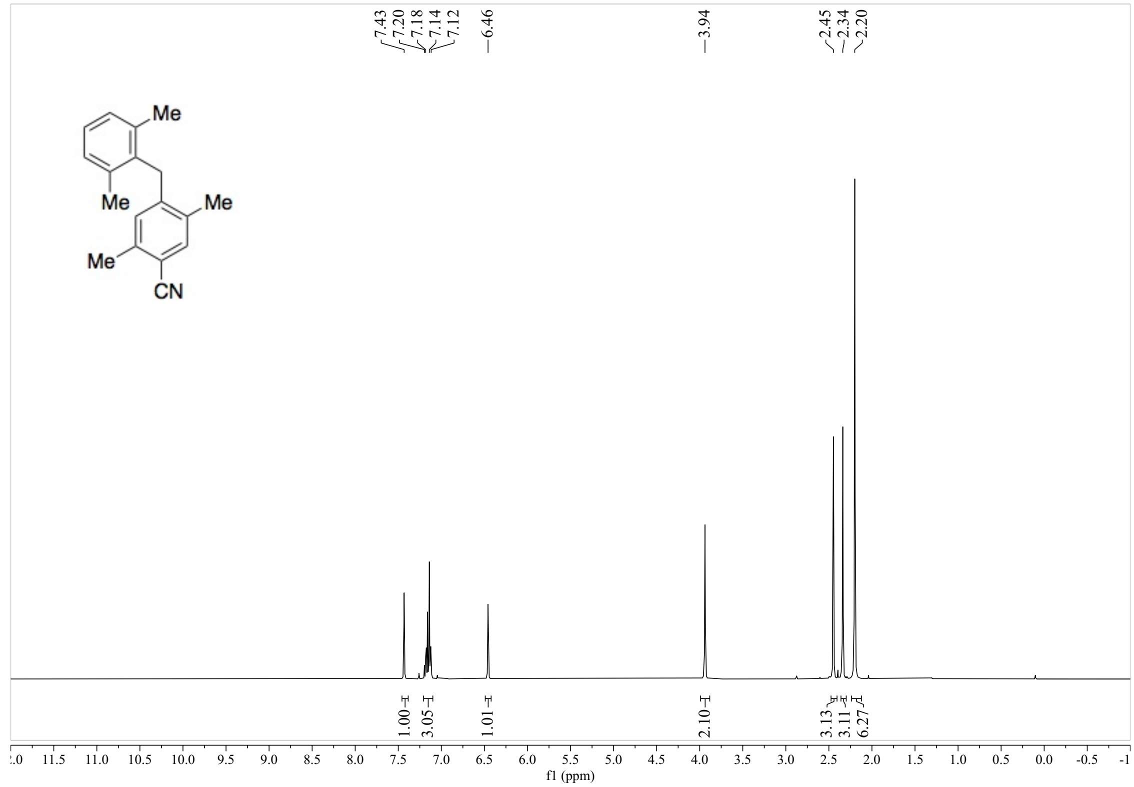
^{13}C NMR of compound **8** (101 MHz, CDCl$_3$)



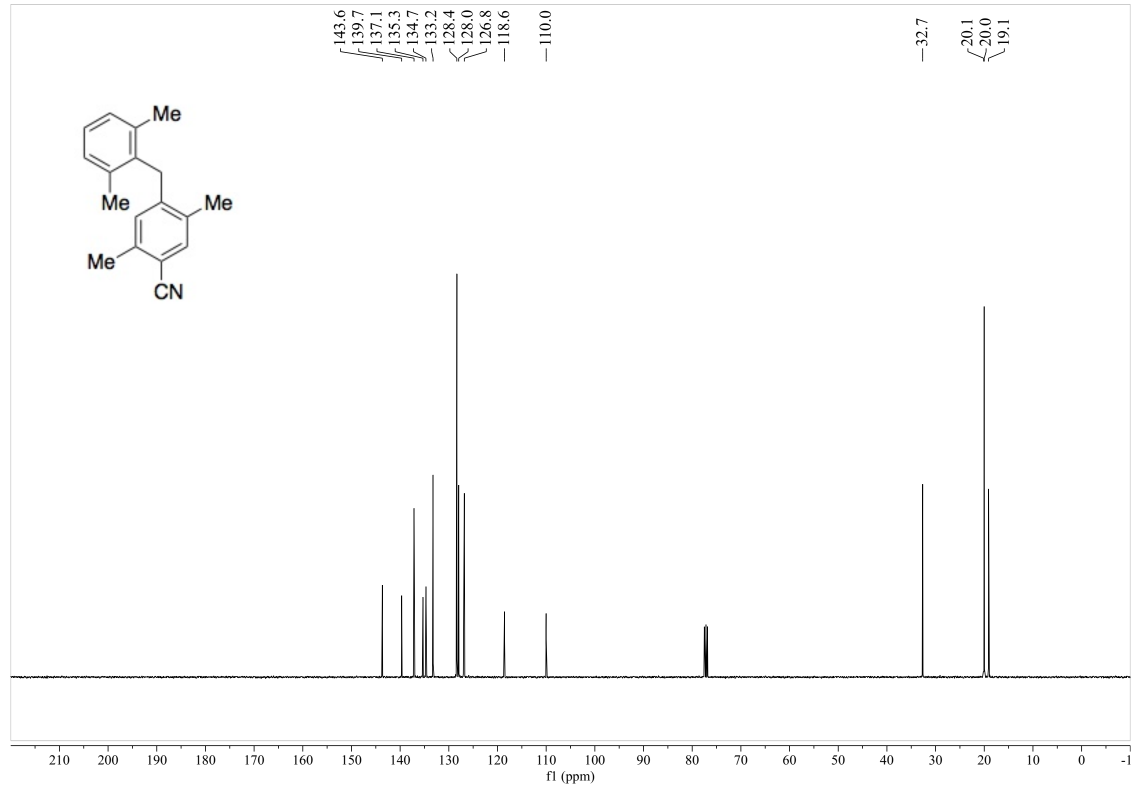
^{1}H NMR of compound **9** (400 MHz, CDCl$_3$)



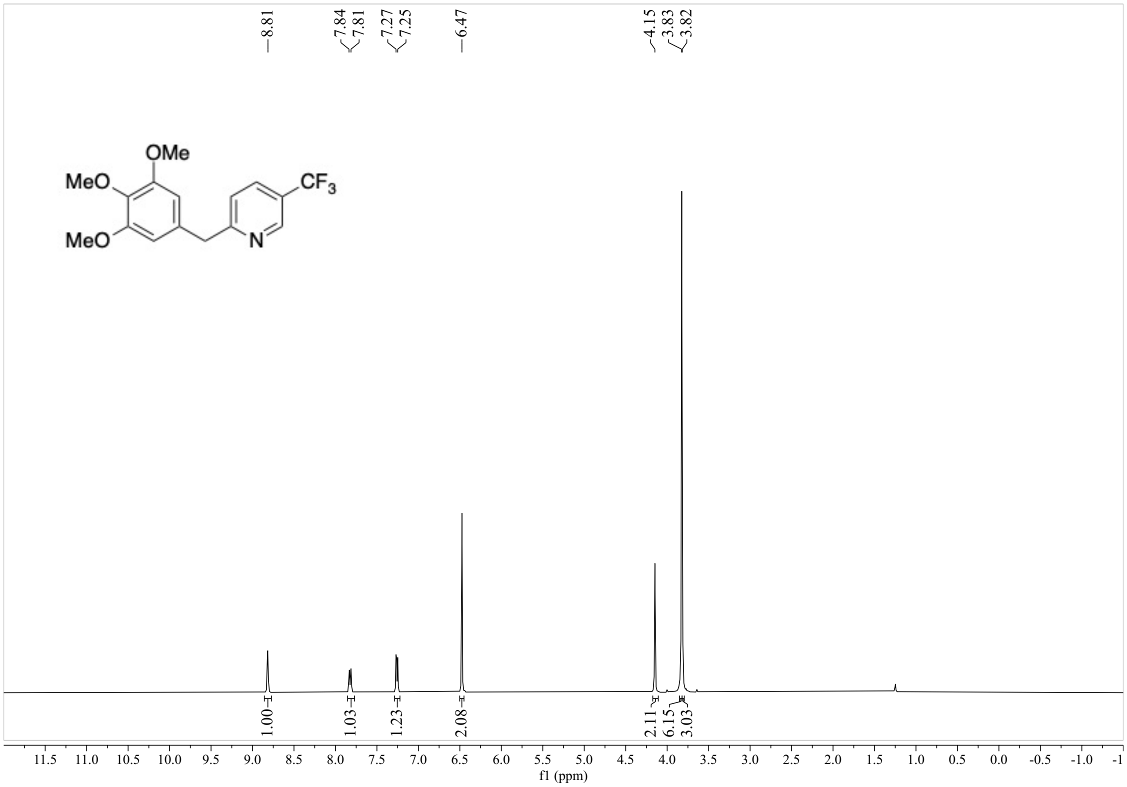
^{13}C NMR of compound **9** (101 MHz, CDCl$_3$)



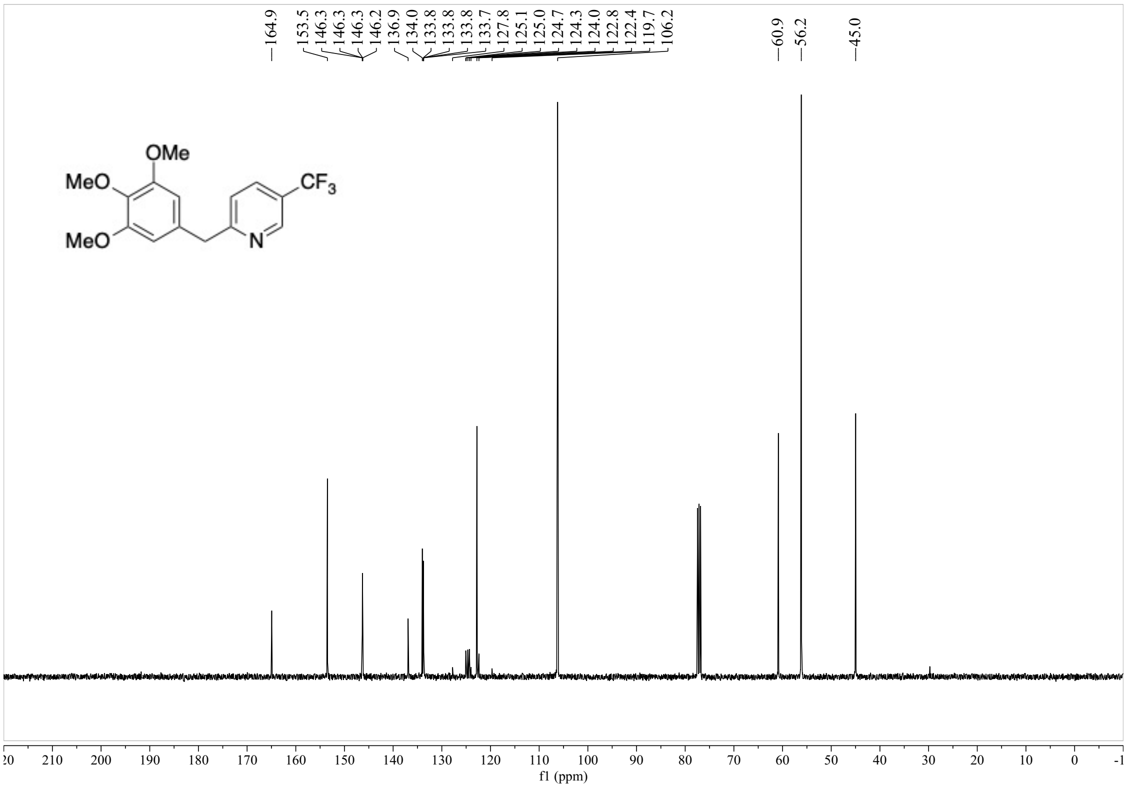
^{1}**H NMR** of compound **10** (400 MHz, CDCl$_3$)



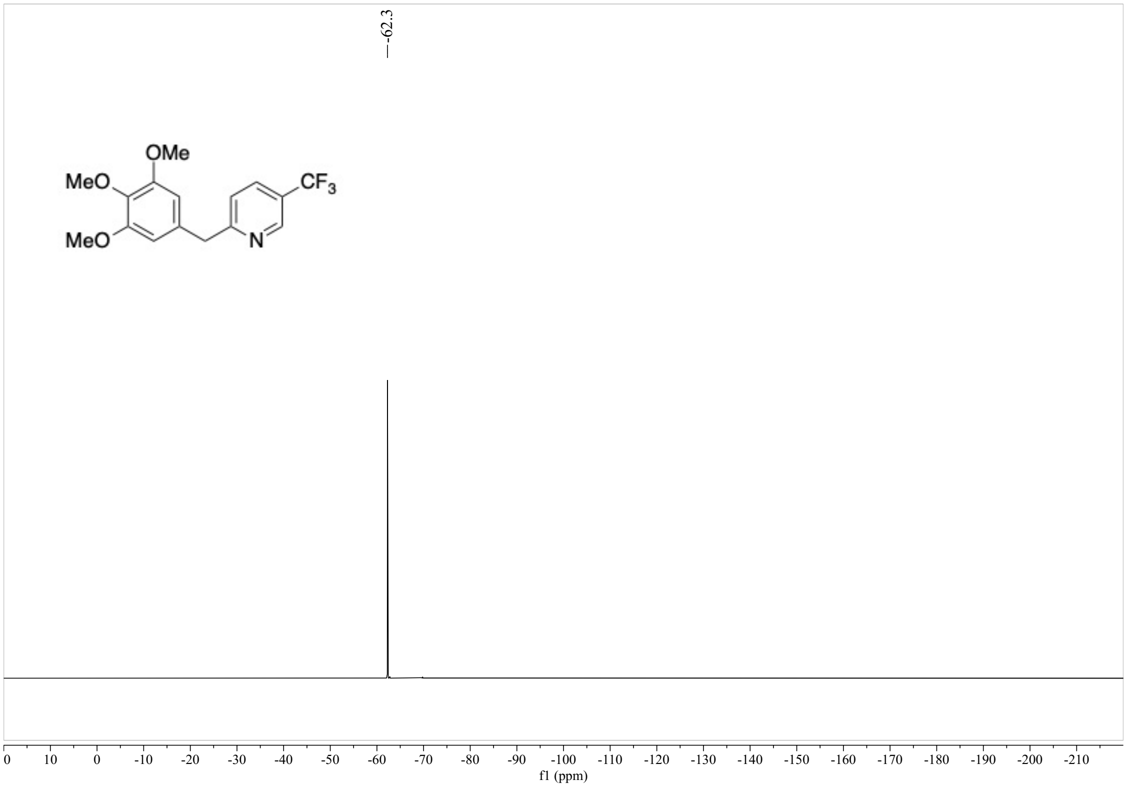
^{13}**C NMR** of compound **10** (101 MHz, CDCl$_3$)



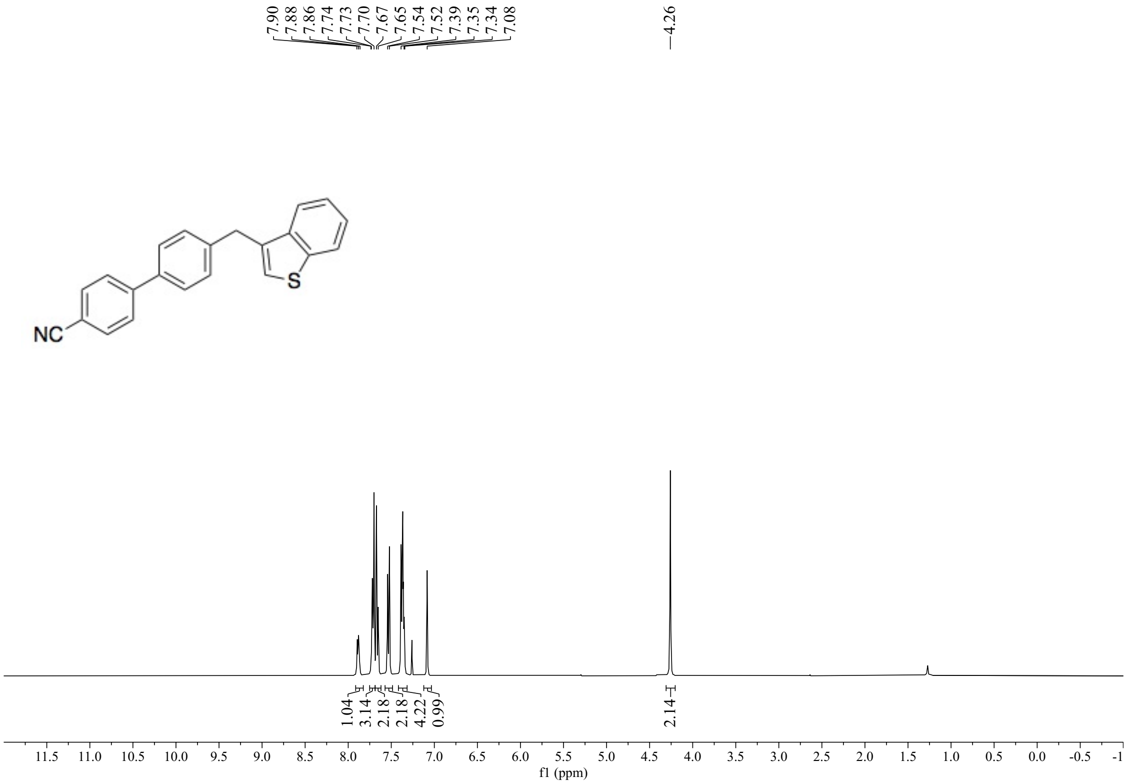
^{1}**H NMR** of compound **11** (400 MHz, CDCl$_3$)



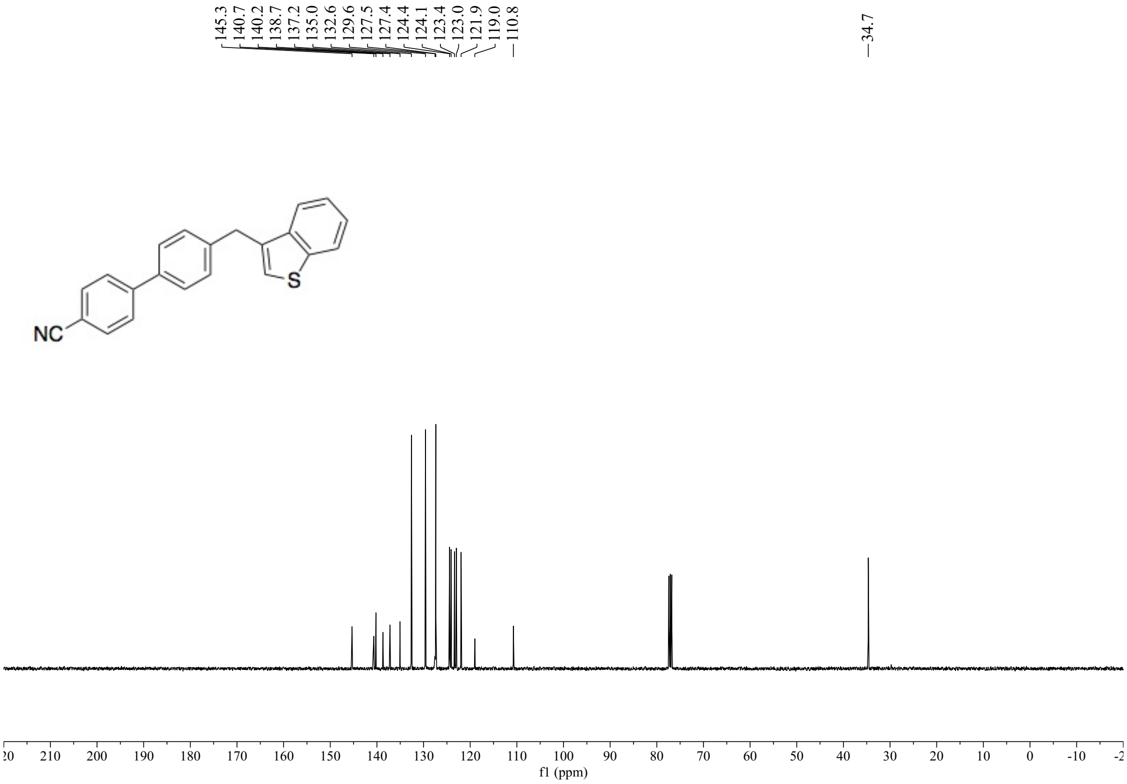
^{13}**C NMR** of compound **11** (101 MHz, CDCl$_3$)



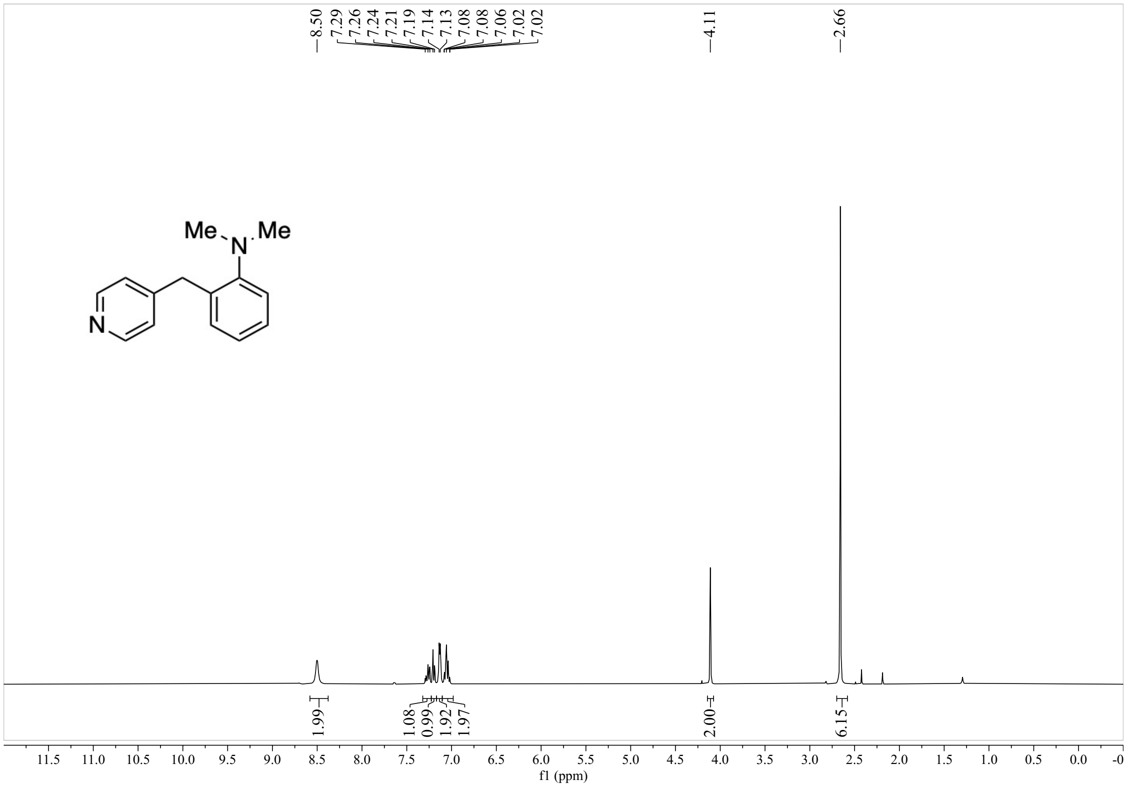
^{19}**F NMR** (proton decoupled) of compound **11** (376 MHz, CDCl$_3$)



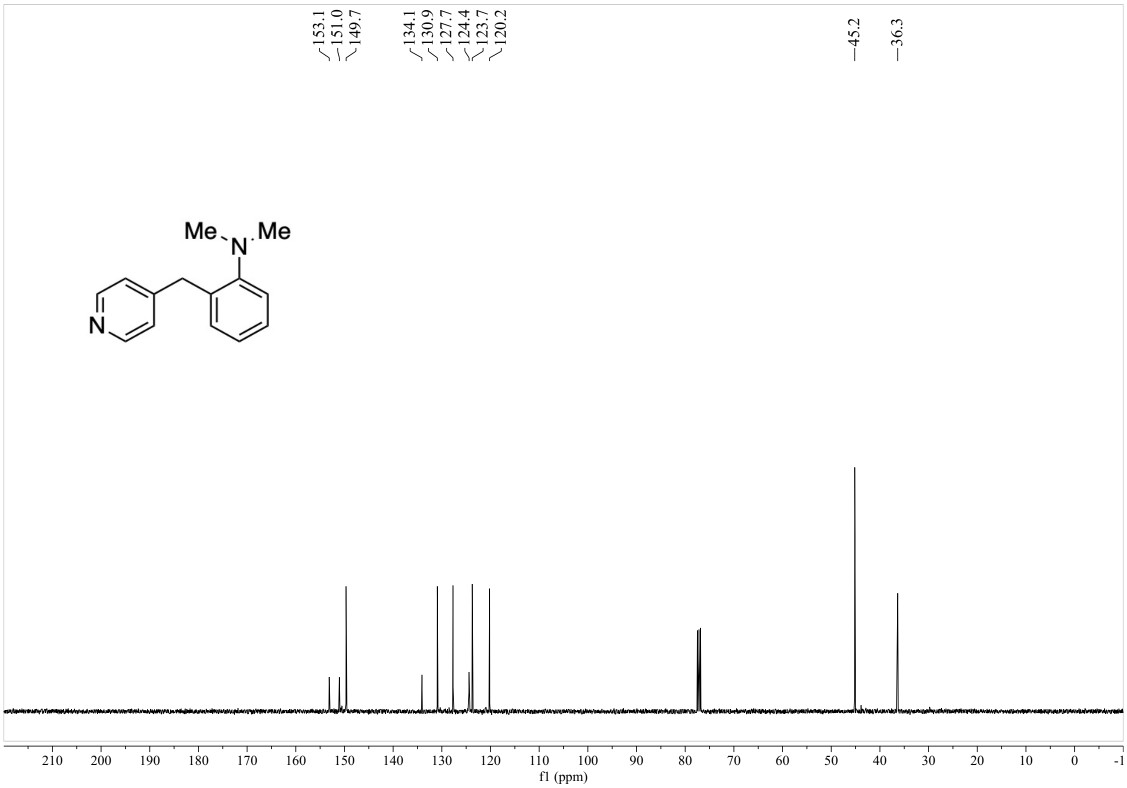
^{1}H NMR of compound **12** (400 MHz, CDCl$_3$)



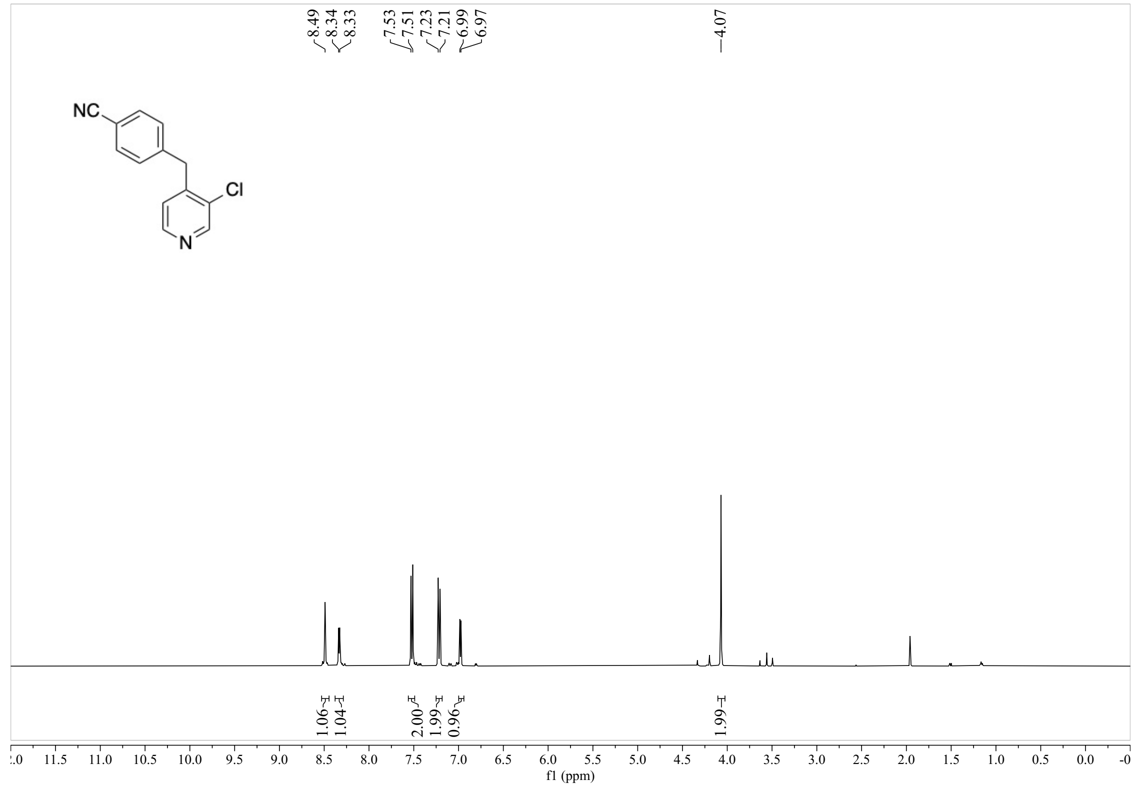
^{13}C NMR of compound **12** (101 MHz, CDCl$_3$)



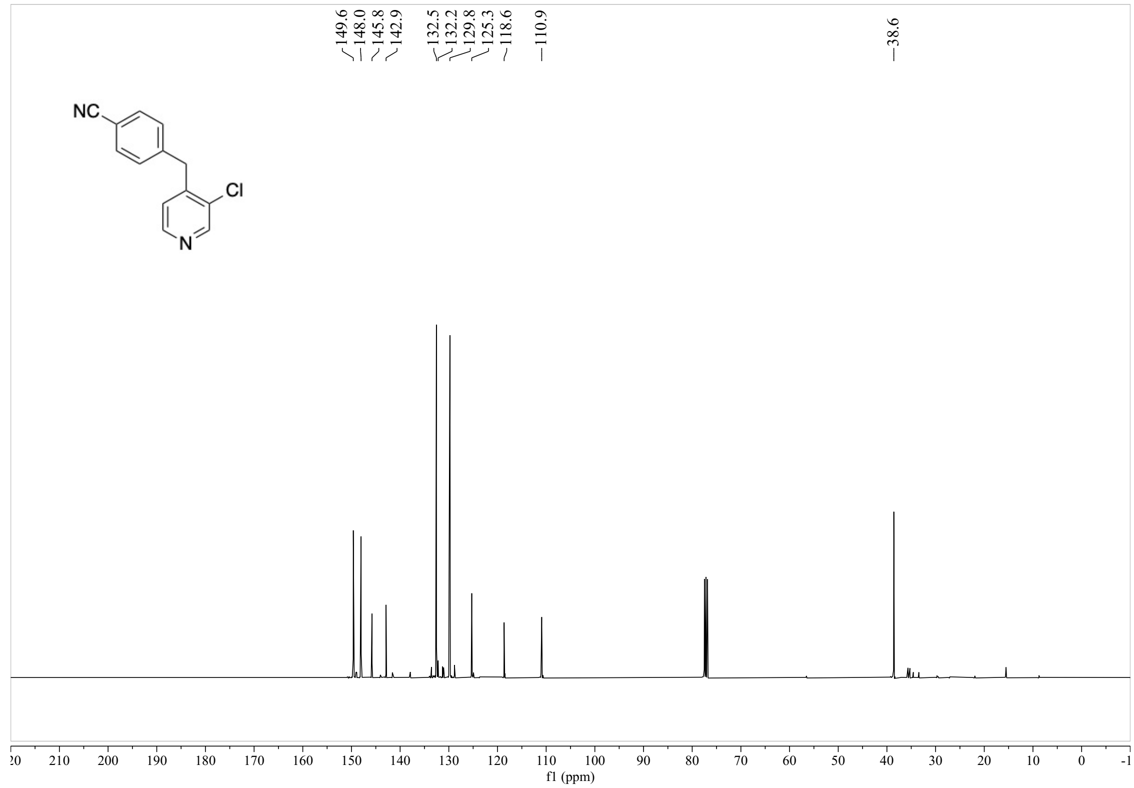
^{1}H NMR of compound **13** (400 MHz, $CDCl_3$)



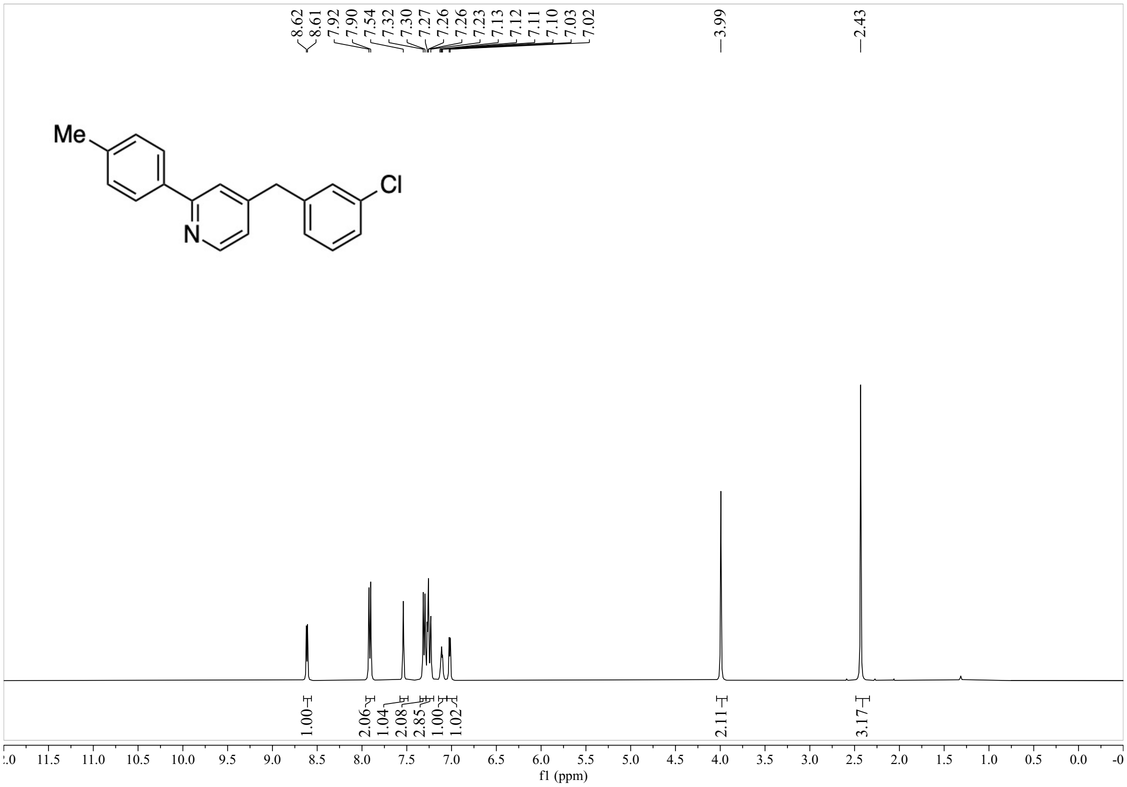
^{13}C NMR of compound **13** (101 MHz, $CDCl_3$)



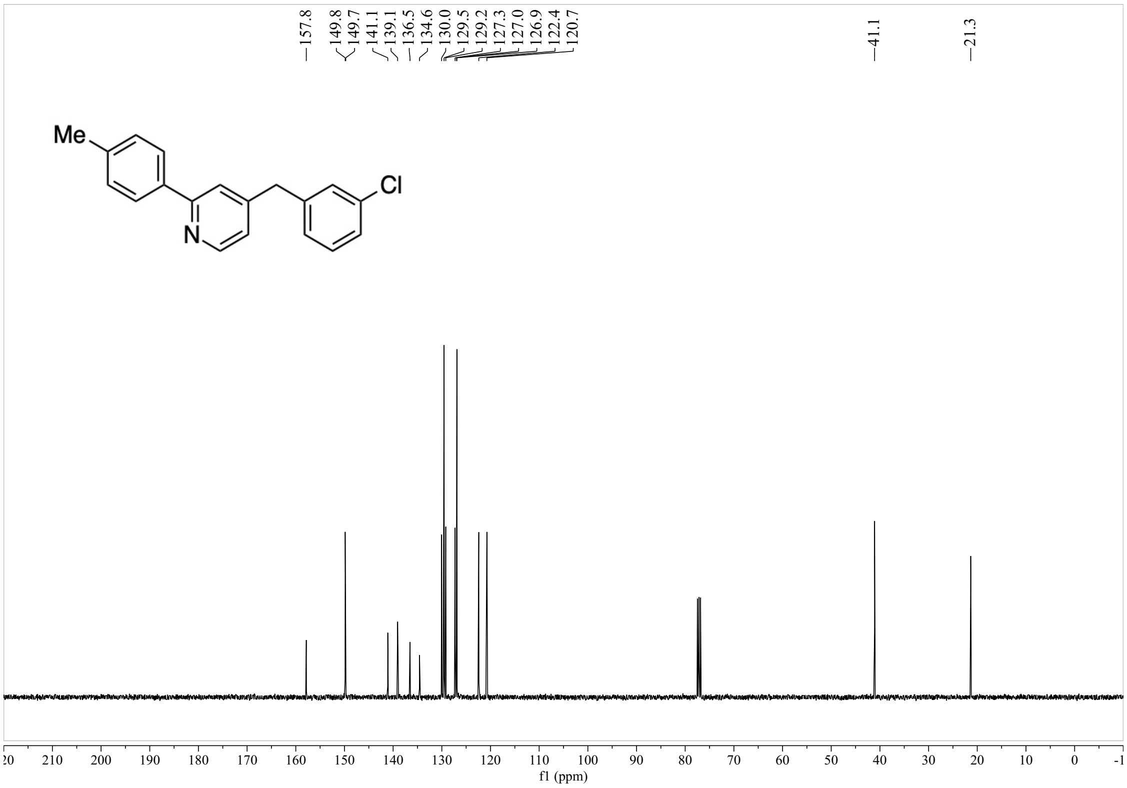
^{1}**H NMR** of compound **14** (400 MHz, CDCl$_3$)



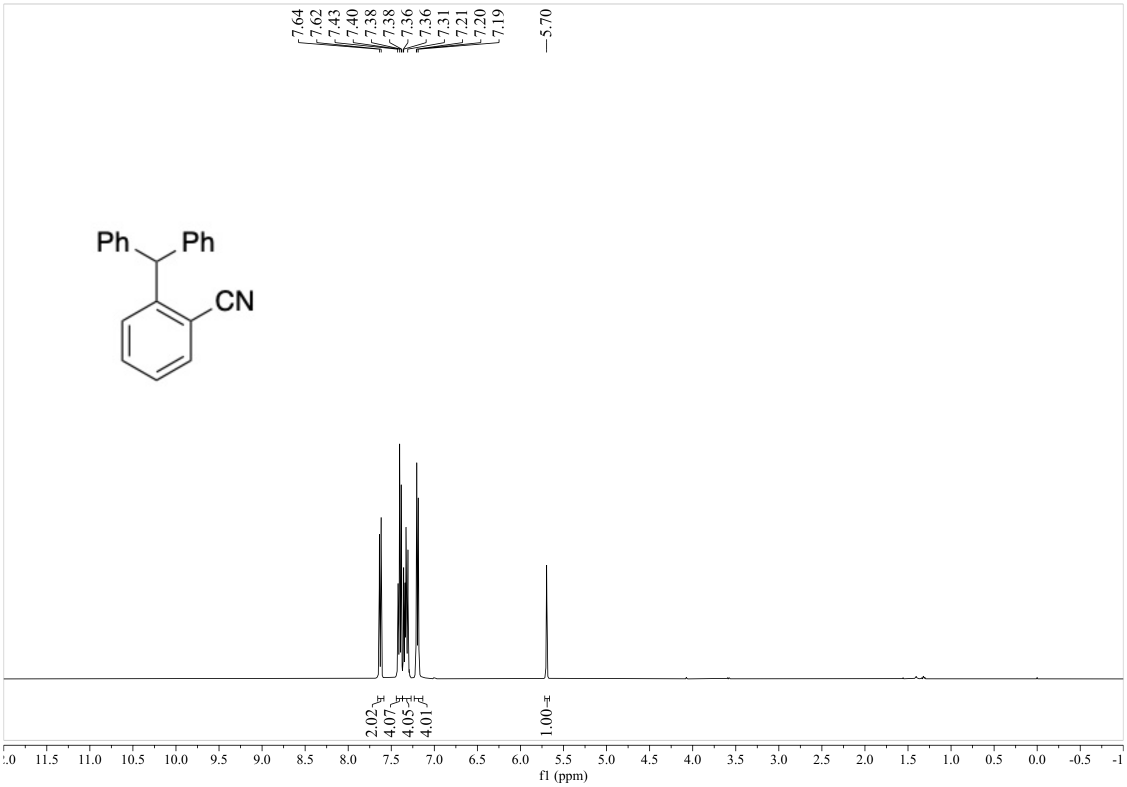
^{13}**C NMR** of compound **14** (101 MHz, CDCl$_3$)



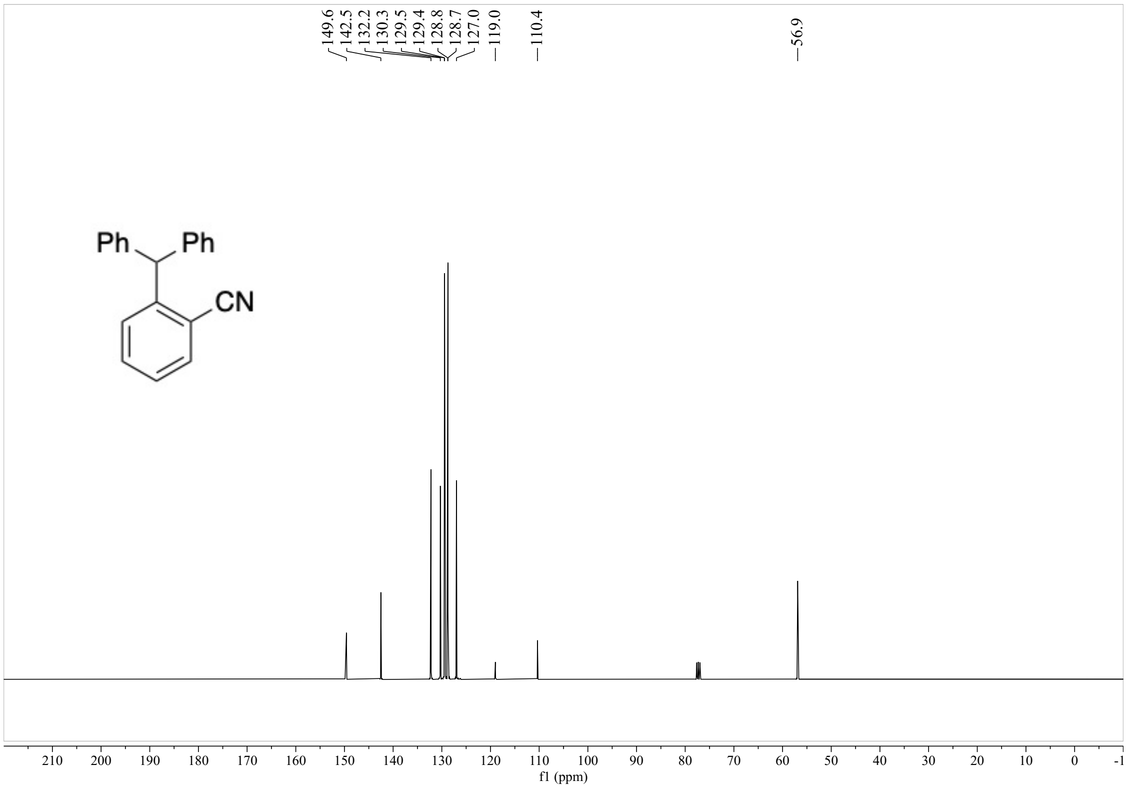
^{1}**H NMR** of compound **15** (400 MHz, CDCl$_3$)



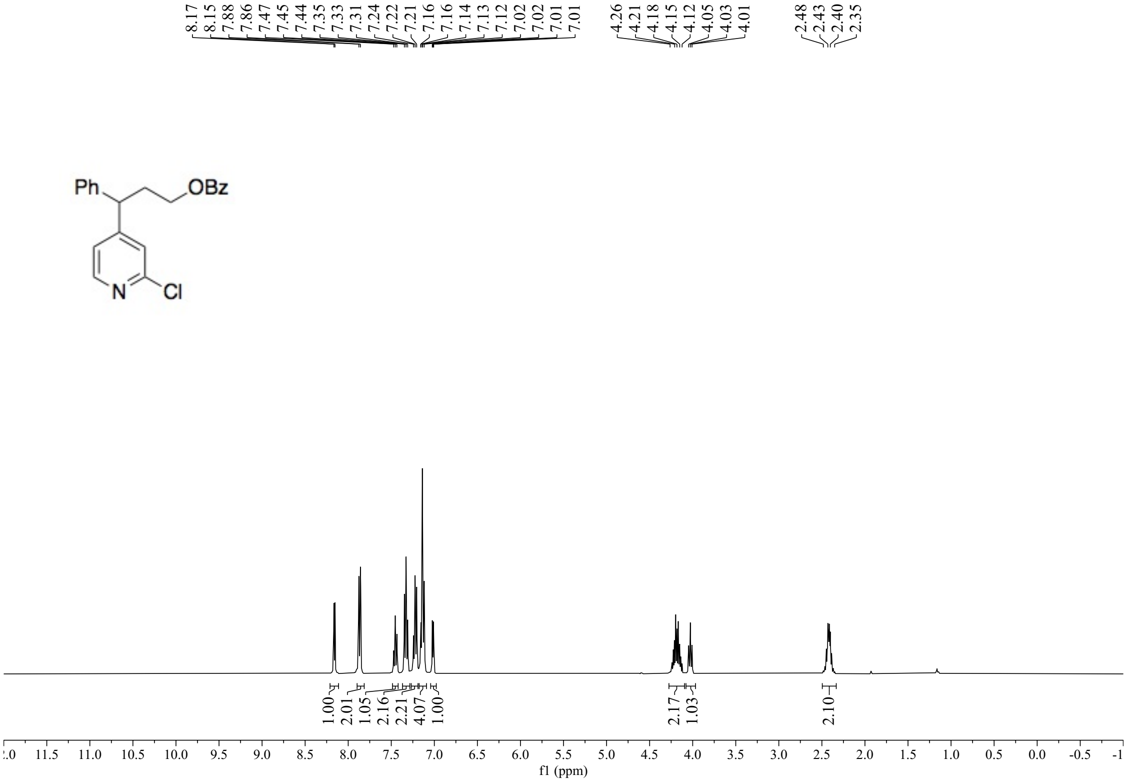
^{13}**C NMR** of compound **15** (101 MHz, CDCl$_3$)



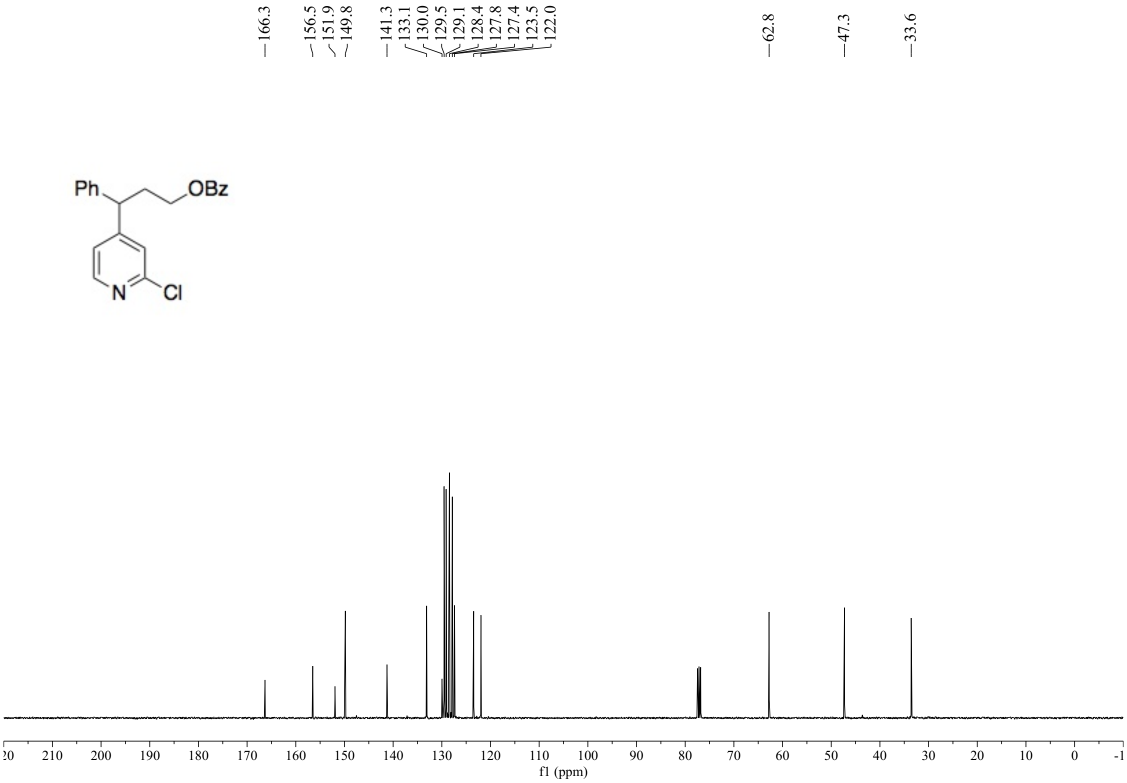
^{1}H NMR of compound **16** (400 MHz, CDCl$_3$)



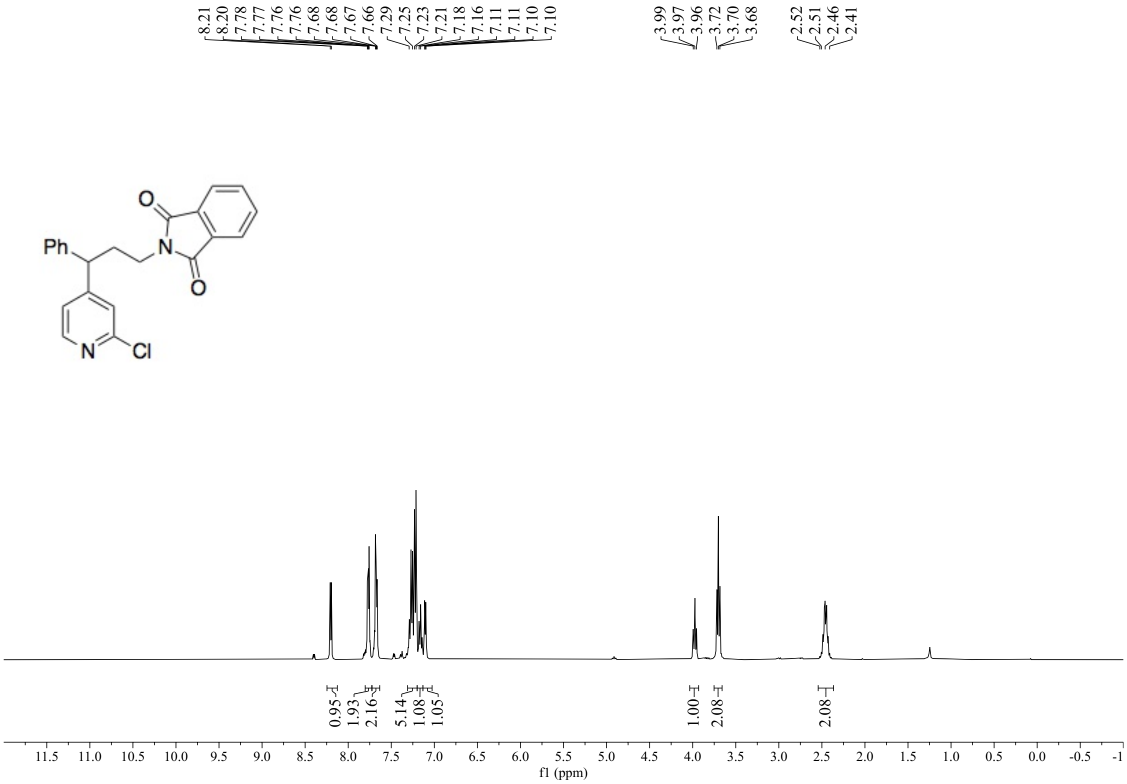
^{13}C NMR of compound **16** (101 MHz, CDCl$_3$)



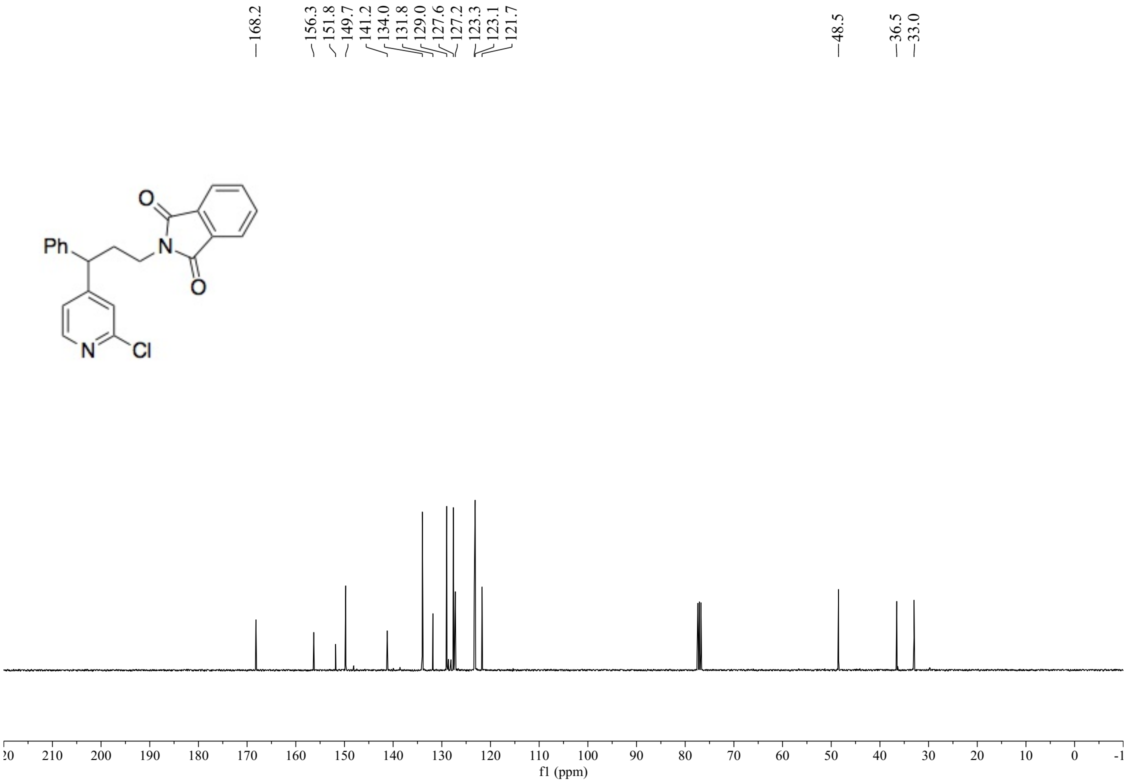
^{1}**H NMR** of compound **17** (400 MHz, CDCl$_3$)



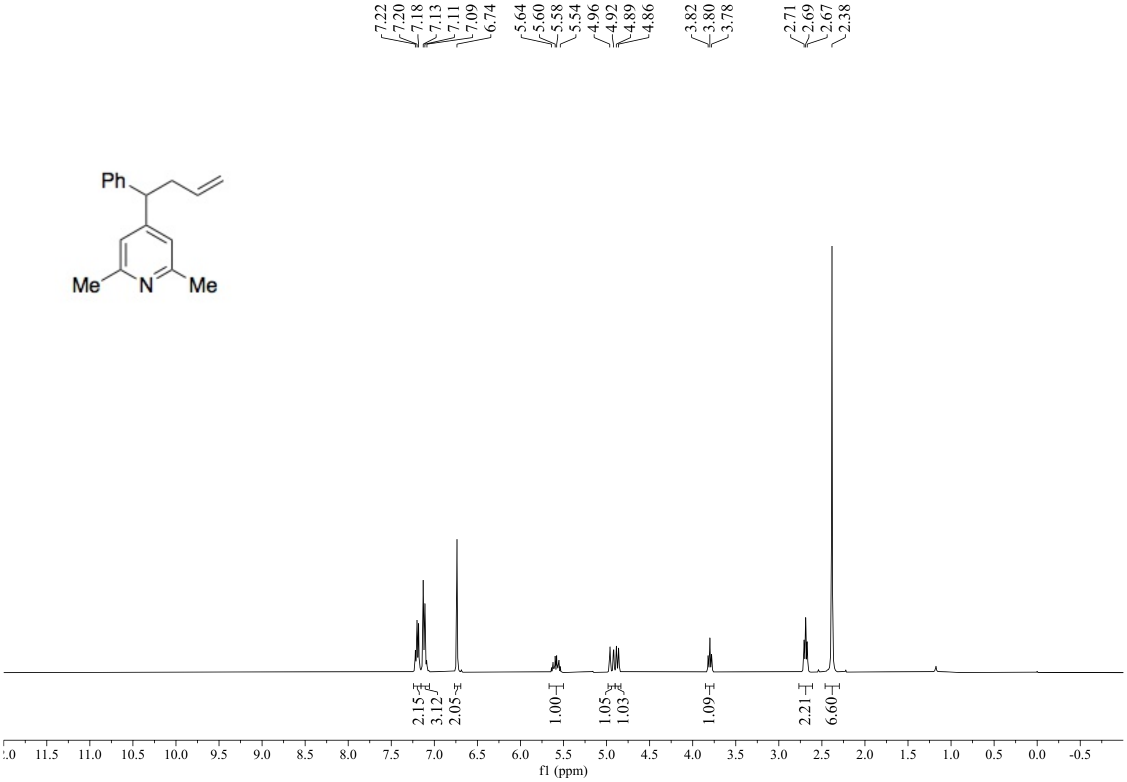
^{13}**C NMR** of compound **17** (101 MHz, CDCl$_3$)



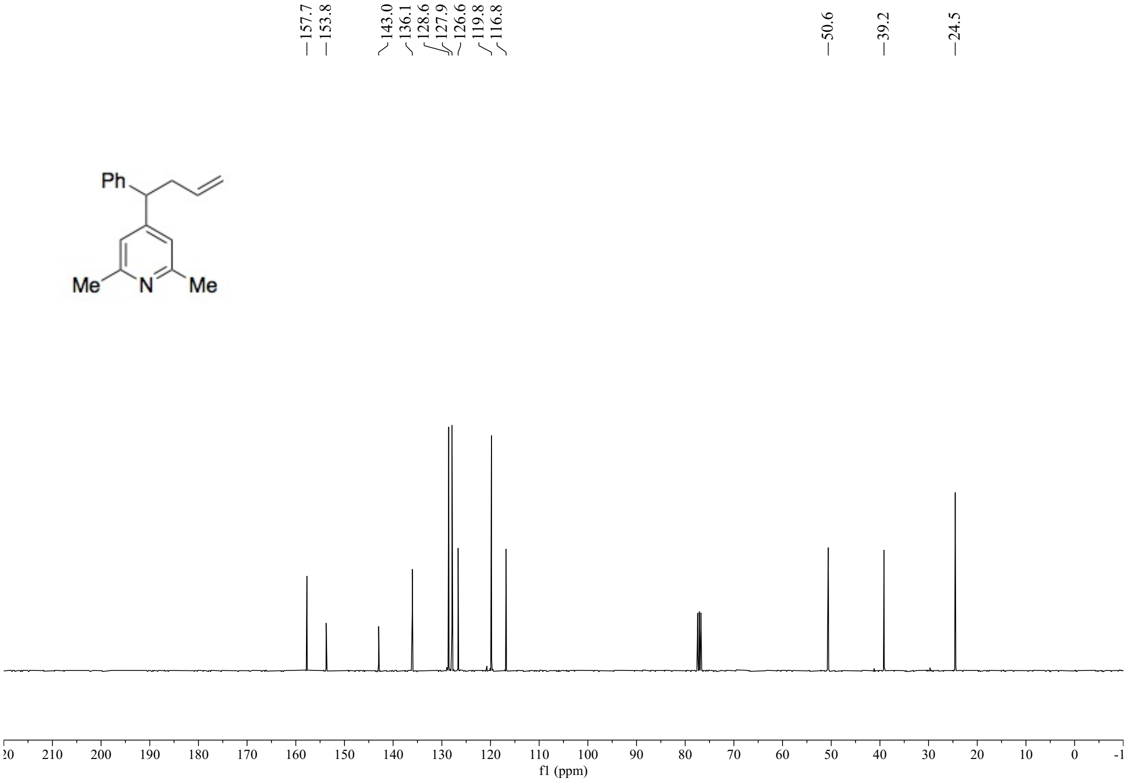
^{1}H NMR of compound **18** (400 MHz, CDCl$_3$)



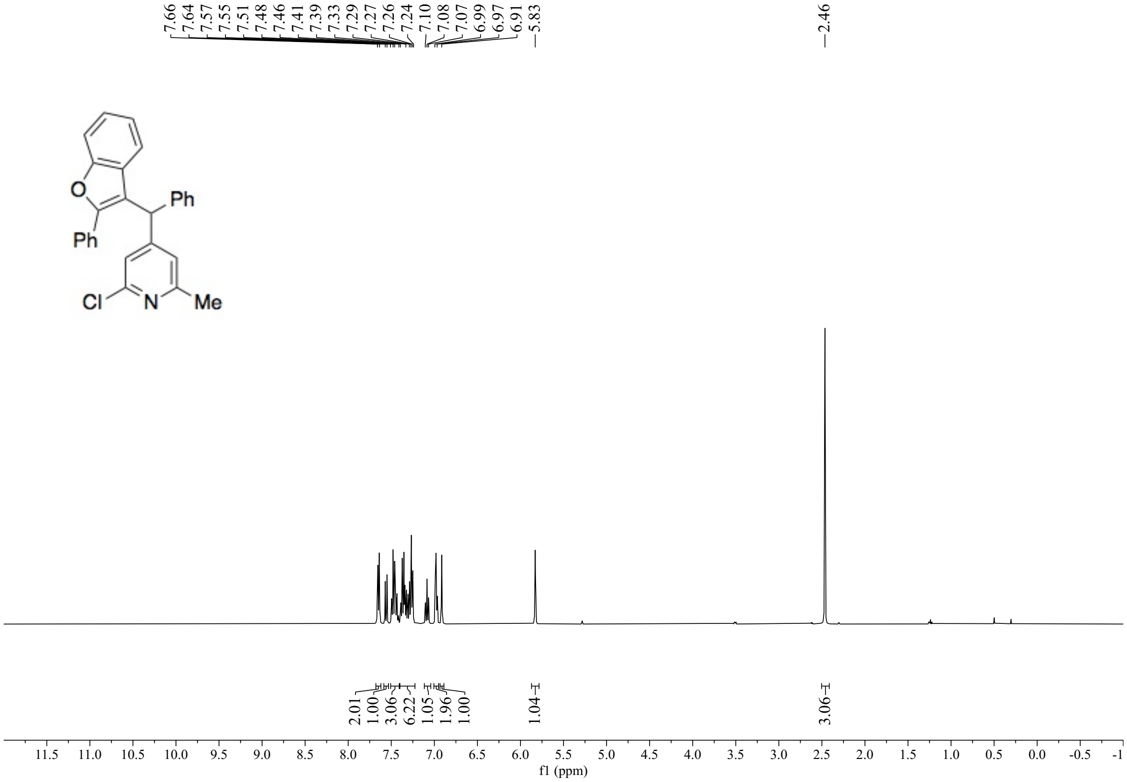
^{13}C NMR of compound **18** (101 MHz, CDCl$_3$)



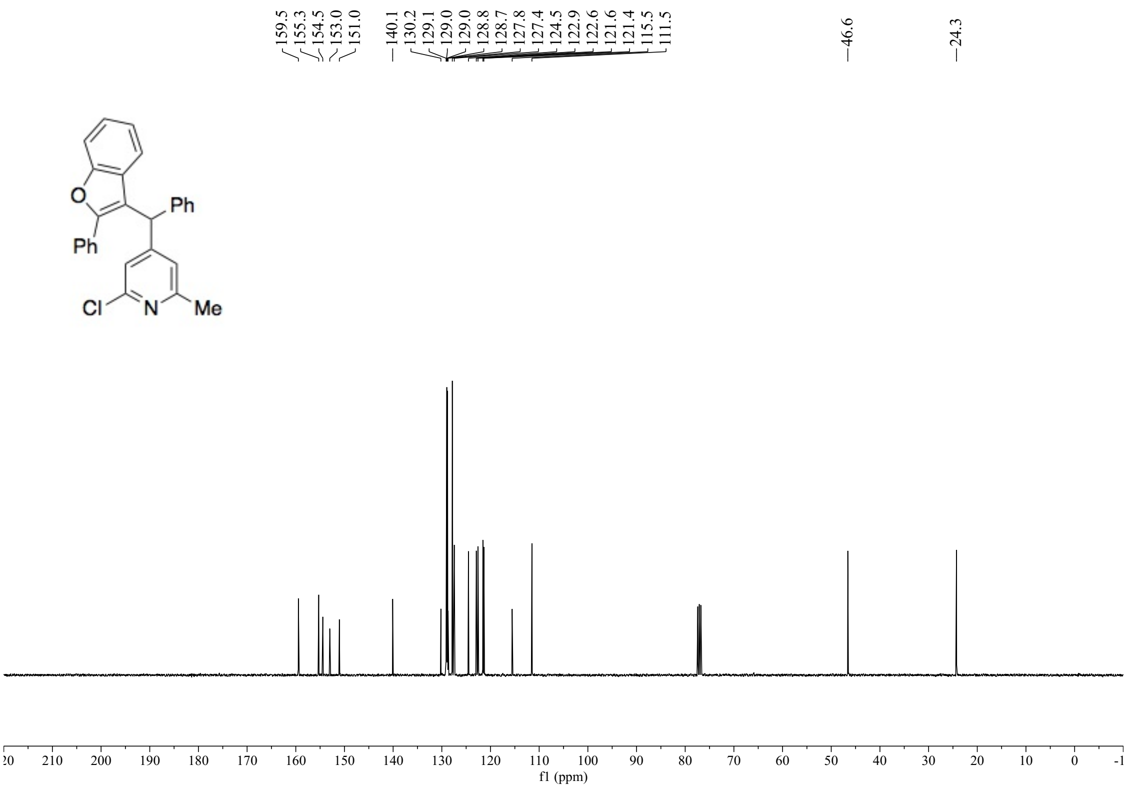
^{1}H NMR of compound **19** (400 MHz, CDCl$_3$)



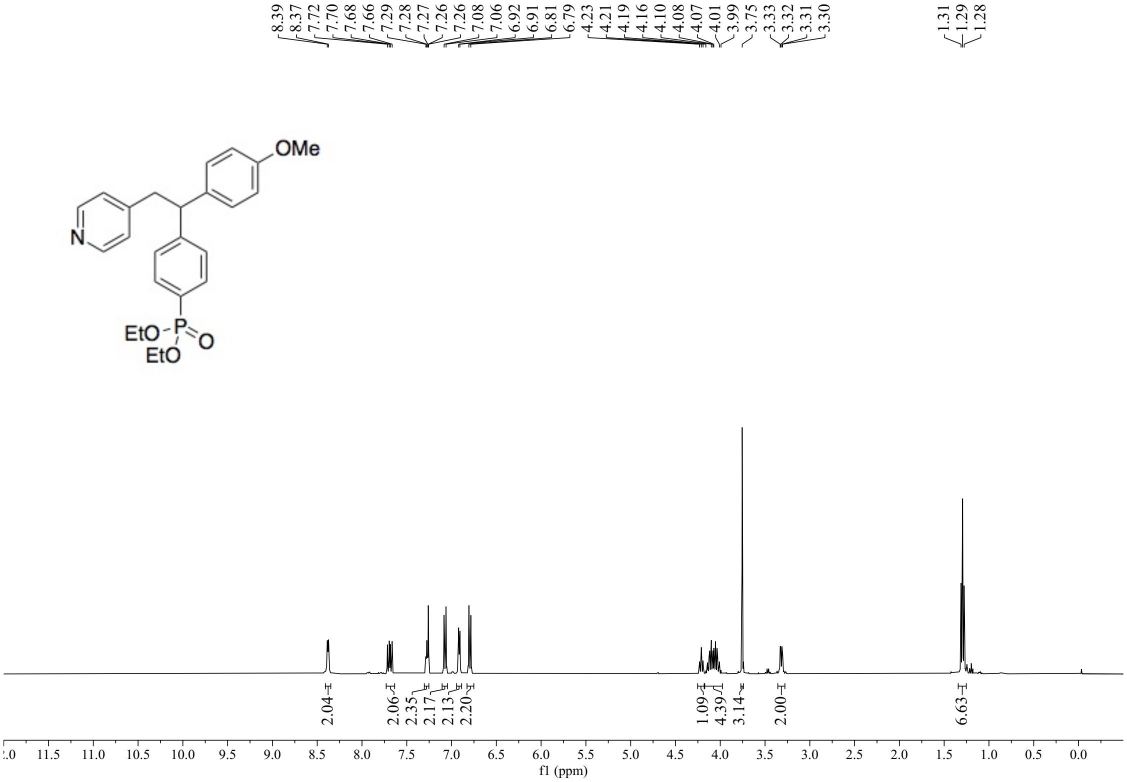
^{13}C NMR of compound **19** (101 MHz, CDCl$_3$)



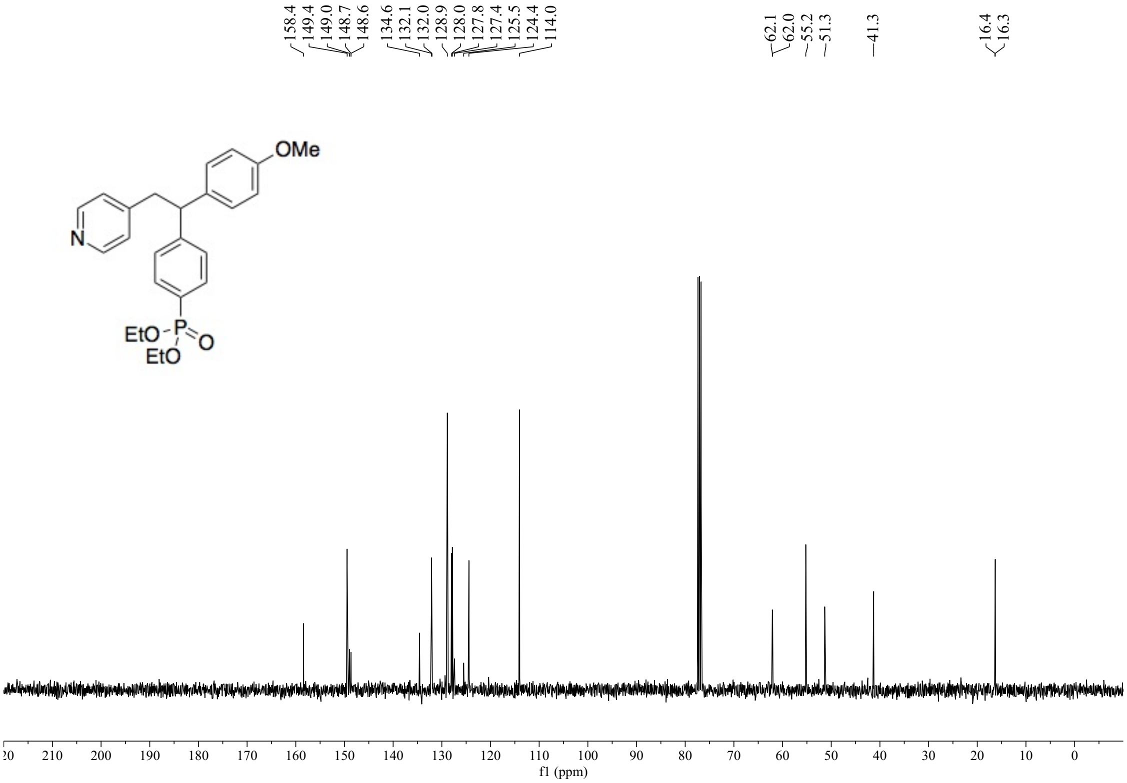
^{1}H NMR of compound **20** (400 MHz, CDCl$_3$)



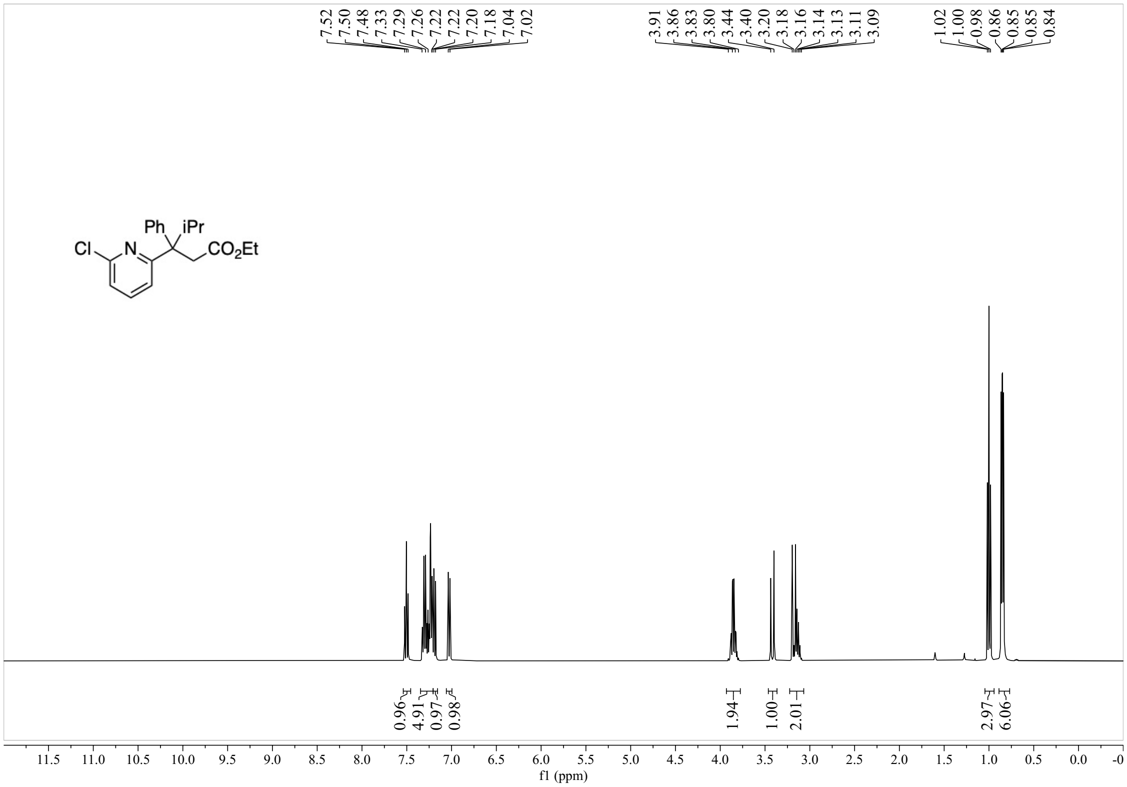
^{13}C NMR of compound **20** (101 MHz, CDCl$_3$)



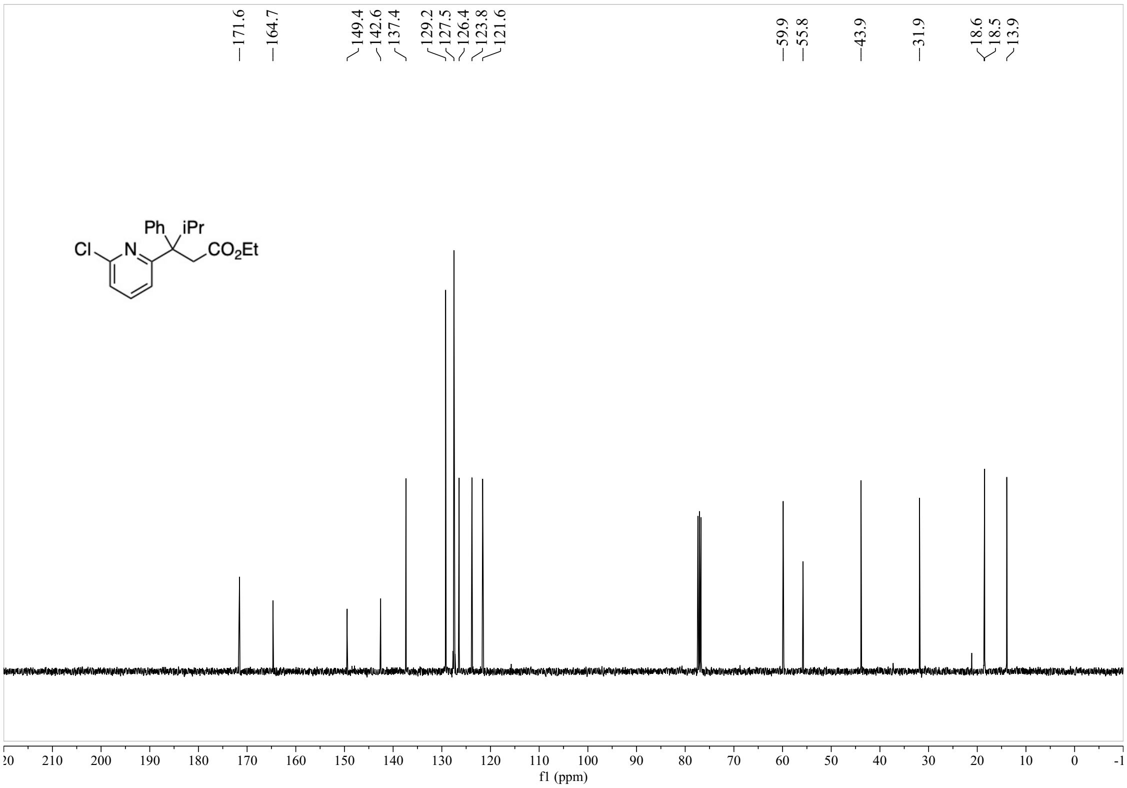
¹H NMR of compound **21** (400 MHz, $CDCl_3$)



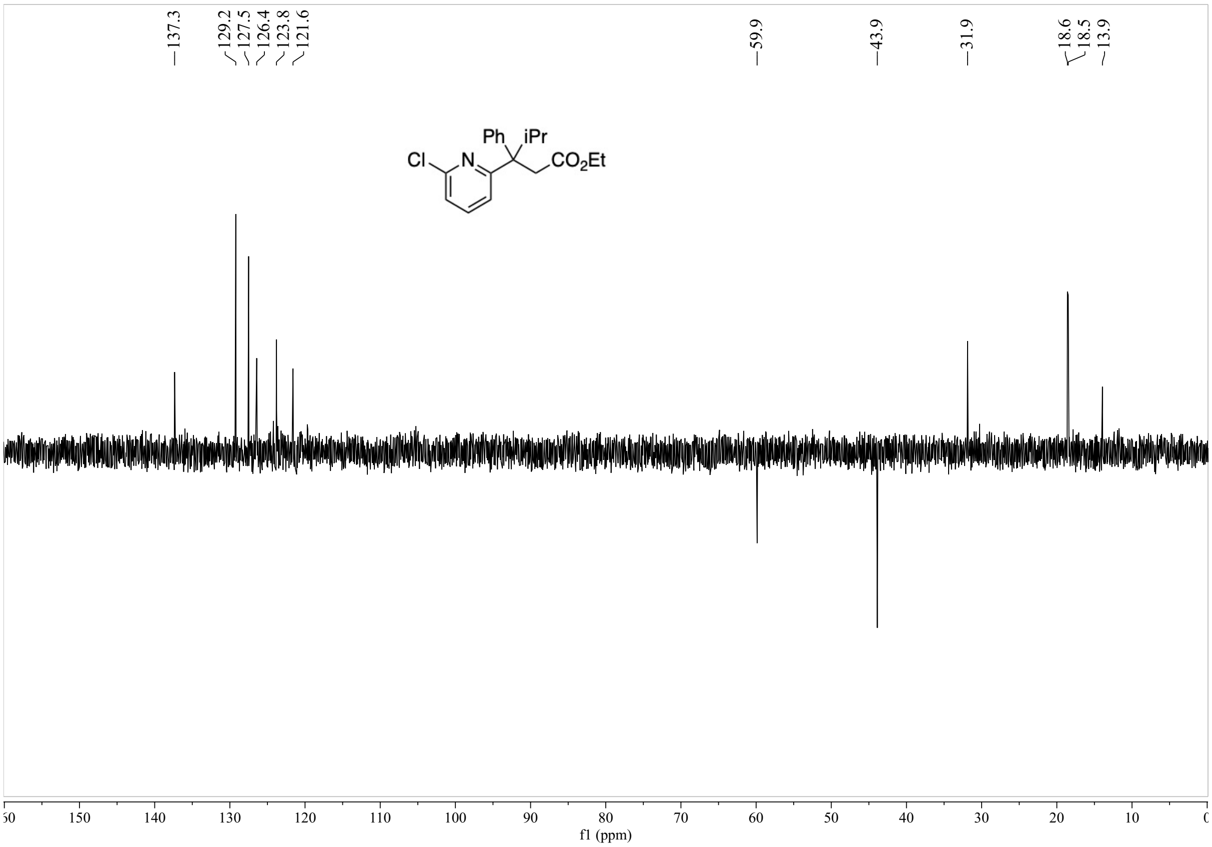
¹³C NMR of compound **21** (101 MHz, $CDCl_3$)



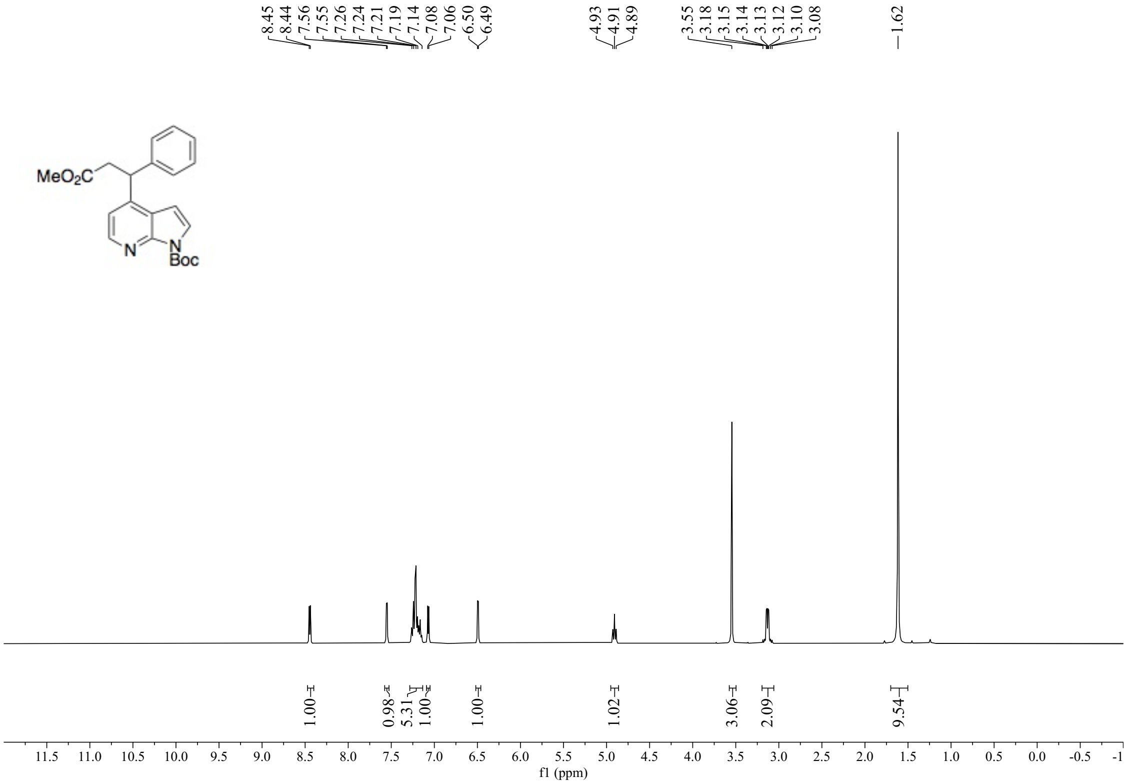
^{1}H NMR of compound **22** (400 MHz, CDCl$_3$)



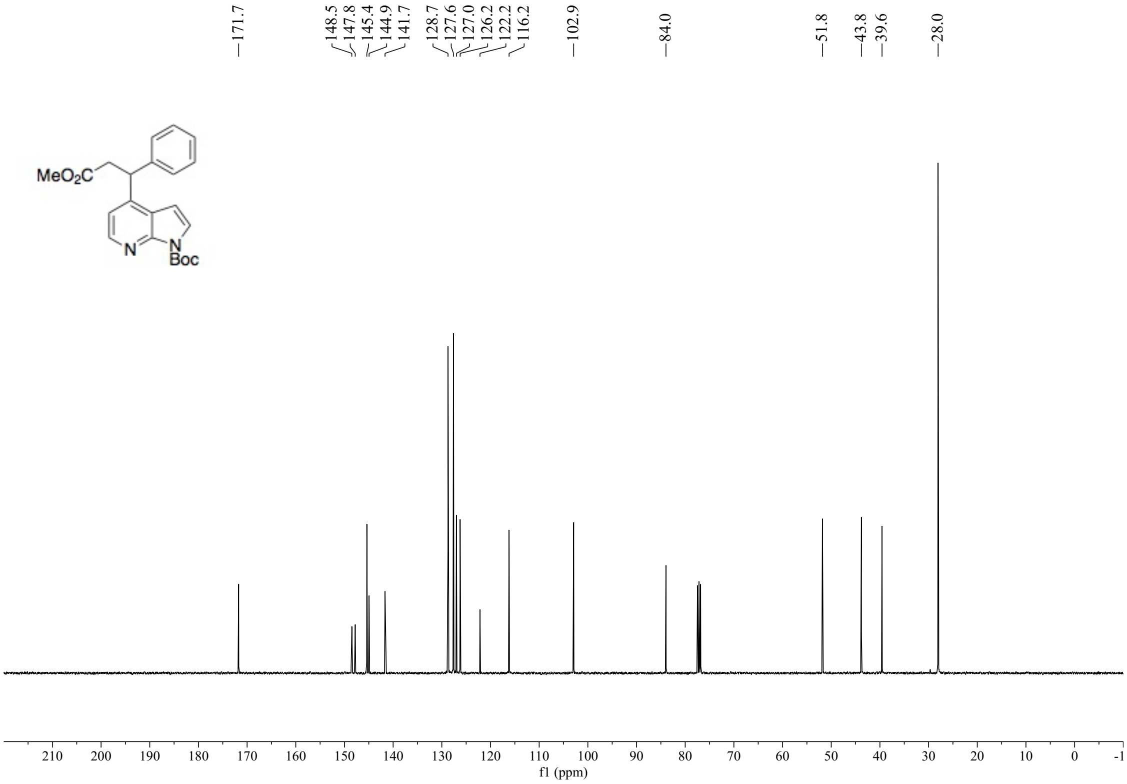
^{13}C NMR of compound **22** (101 MHz, CDCl$_3$)



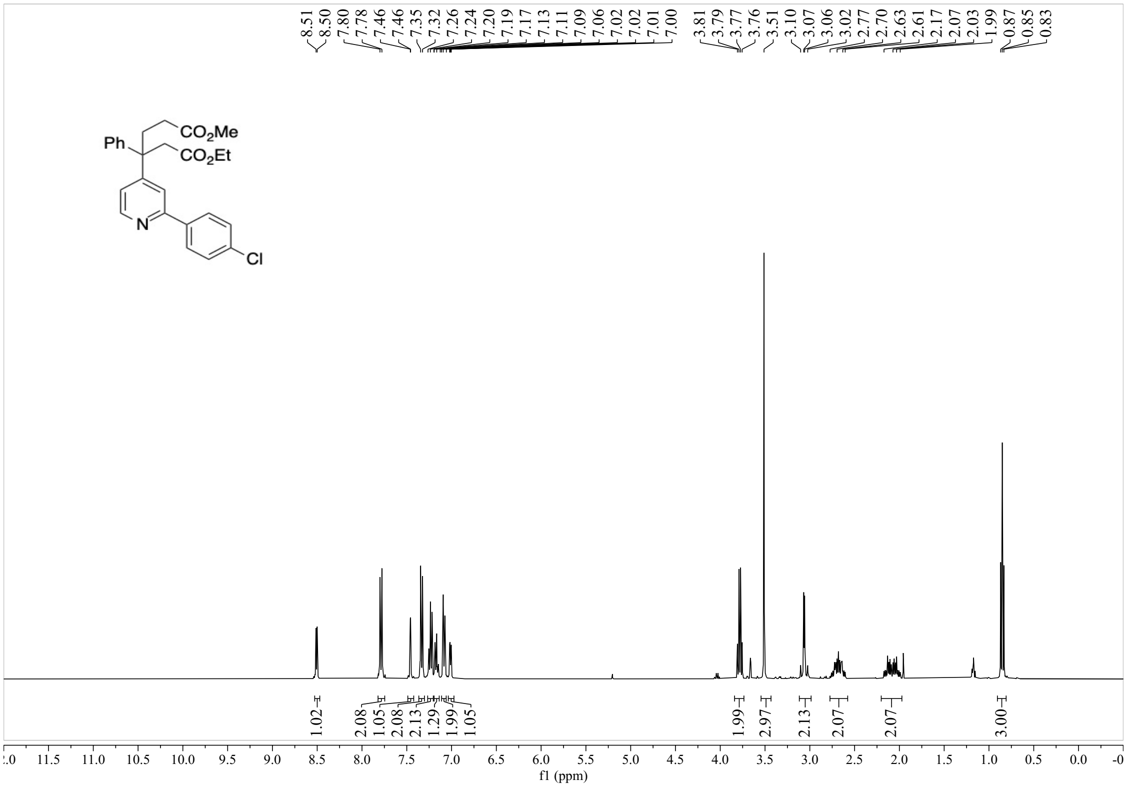
DEPT-135 NMR of compound **22** (400 MHz, $CDCl_3$)



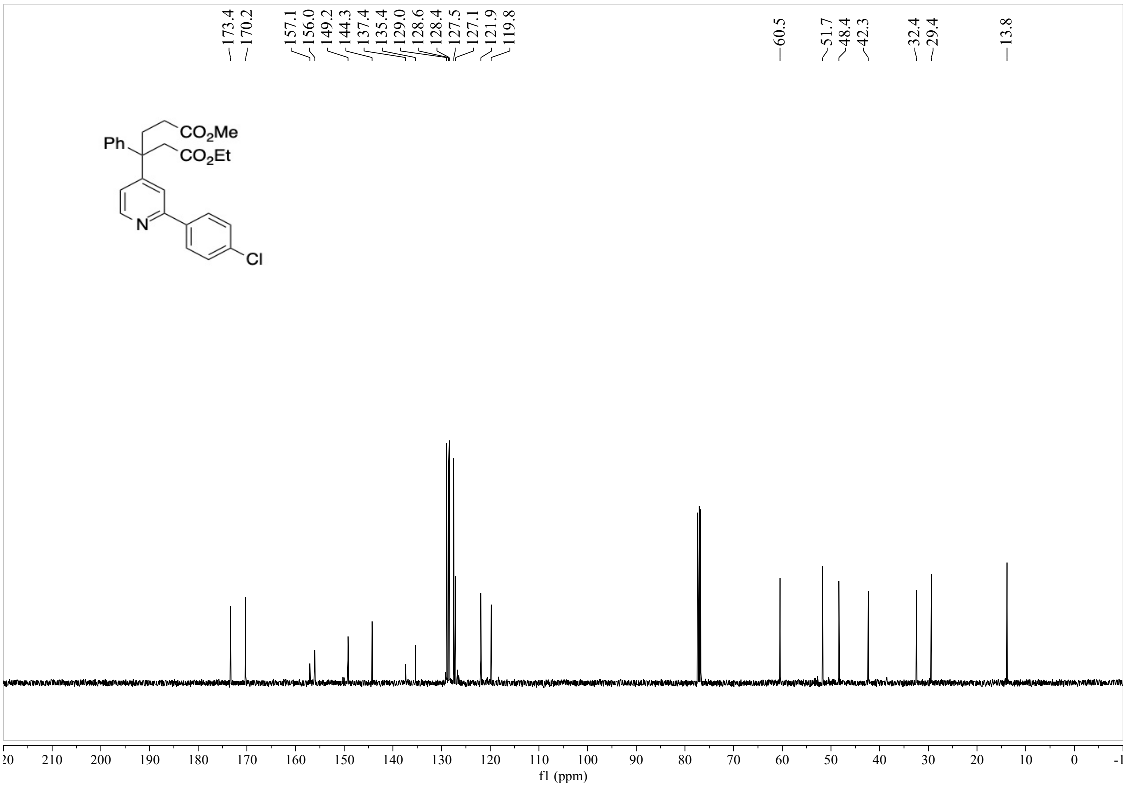
^{1}H NMR of compound **23** (400 MHz, CDCl$_3$)



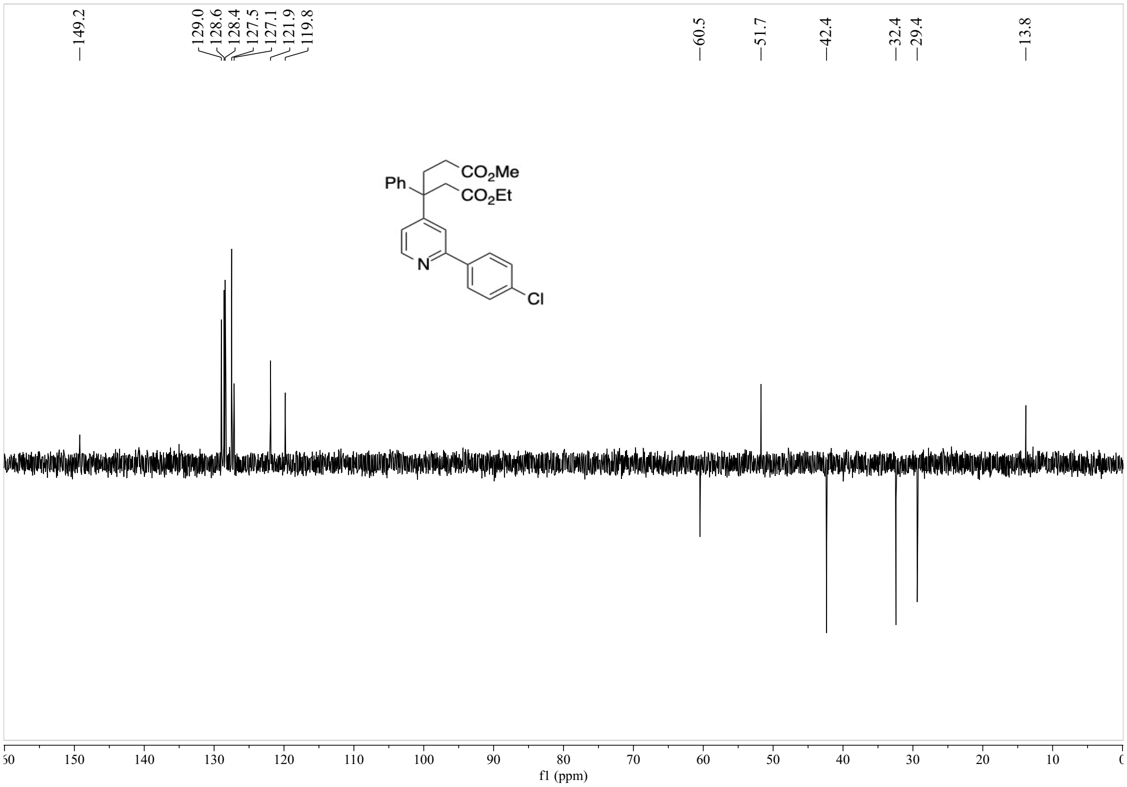
^{13}C NMR of compound **23** (101 MHz, CDCl$_3$)



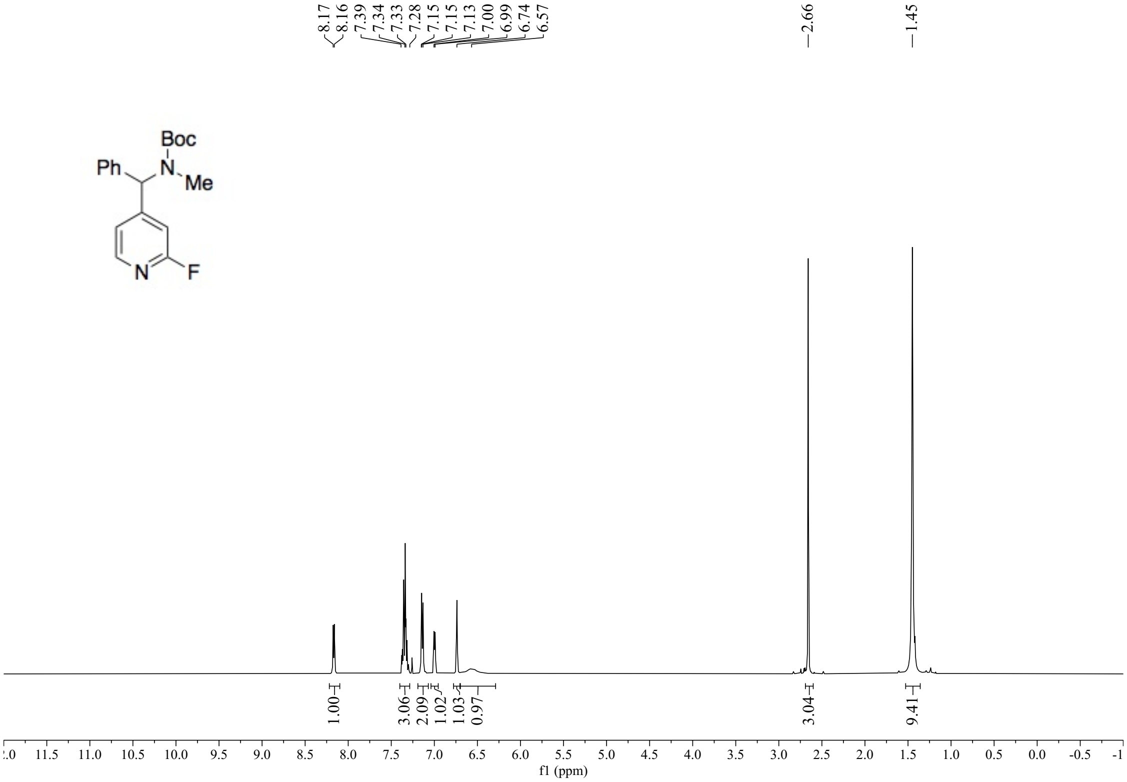
^{1}**H NMR** of compound **24** (400 MHz, CDCl$_3$)



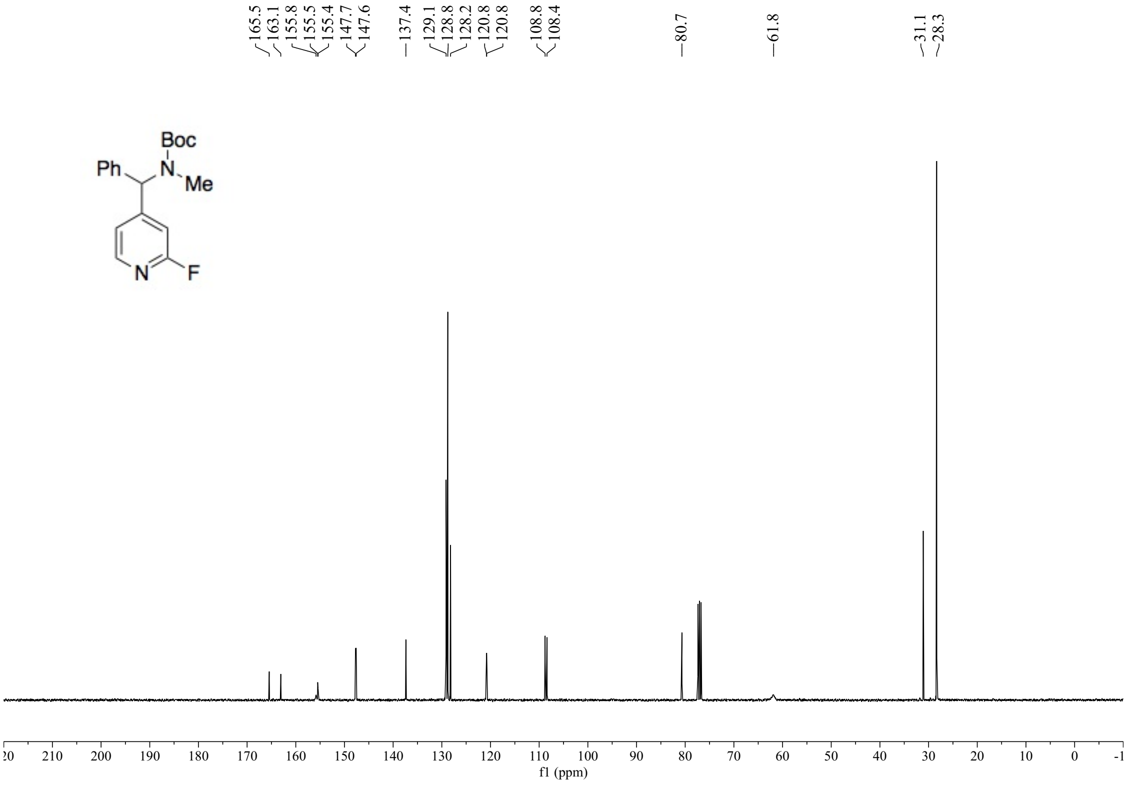
^{13}**C NMR** of compound **24** (101 MHz, CDCl$_3$)



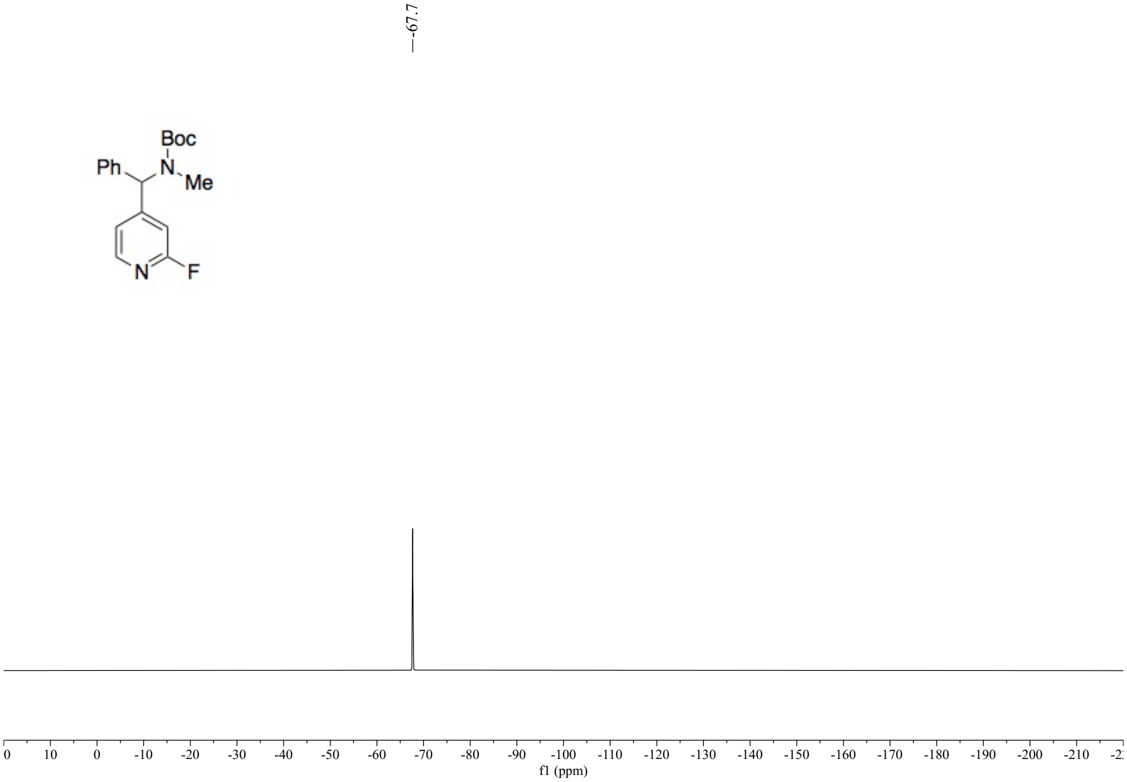
DEPT-135 NMR of compound **24** (400 MHz, $CDCl_3$)



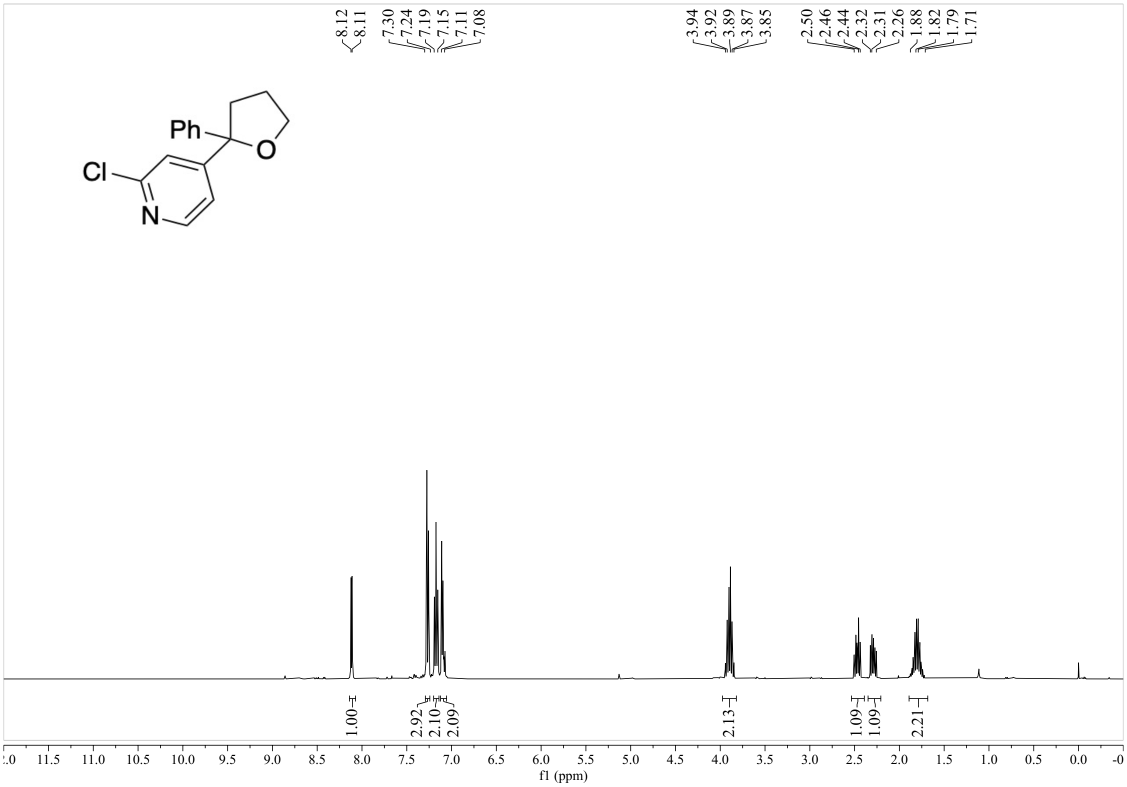
^{1}**H NMR** of compound **25** (400 MHz, CDCl$_3$)



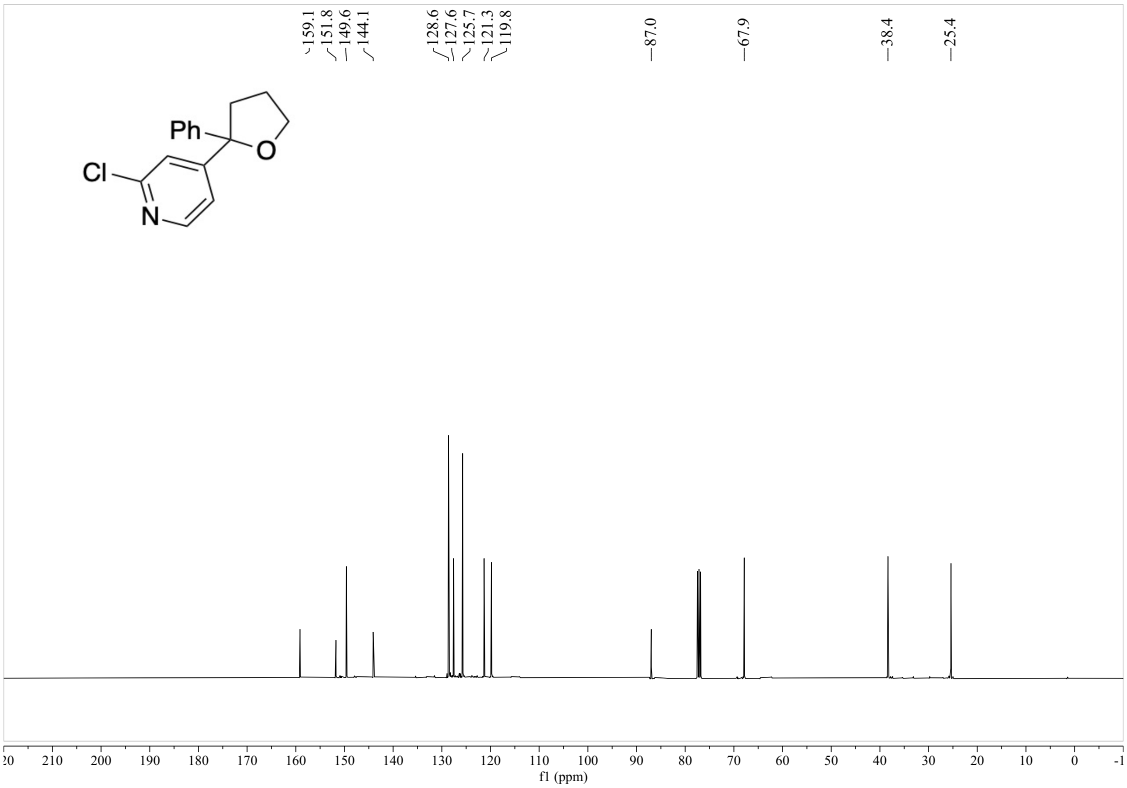
^{13}**C NMR** of compound **25** (101 MHz, CDCl$_3$)



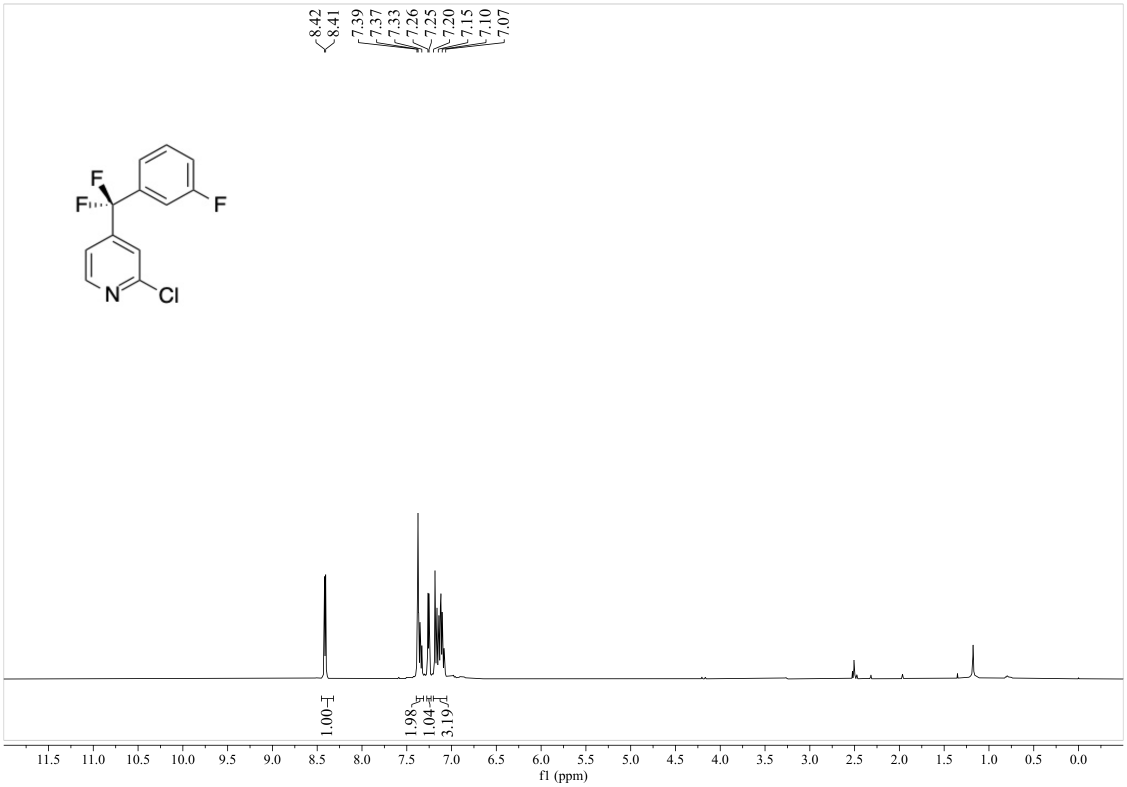
^{19}**F NMR** (proton decoupled) of compound **25** (376 MHz, $CDCl_3$)



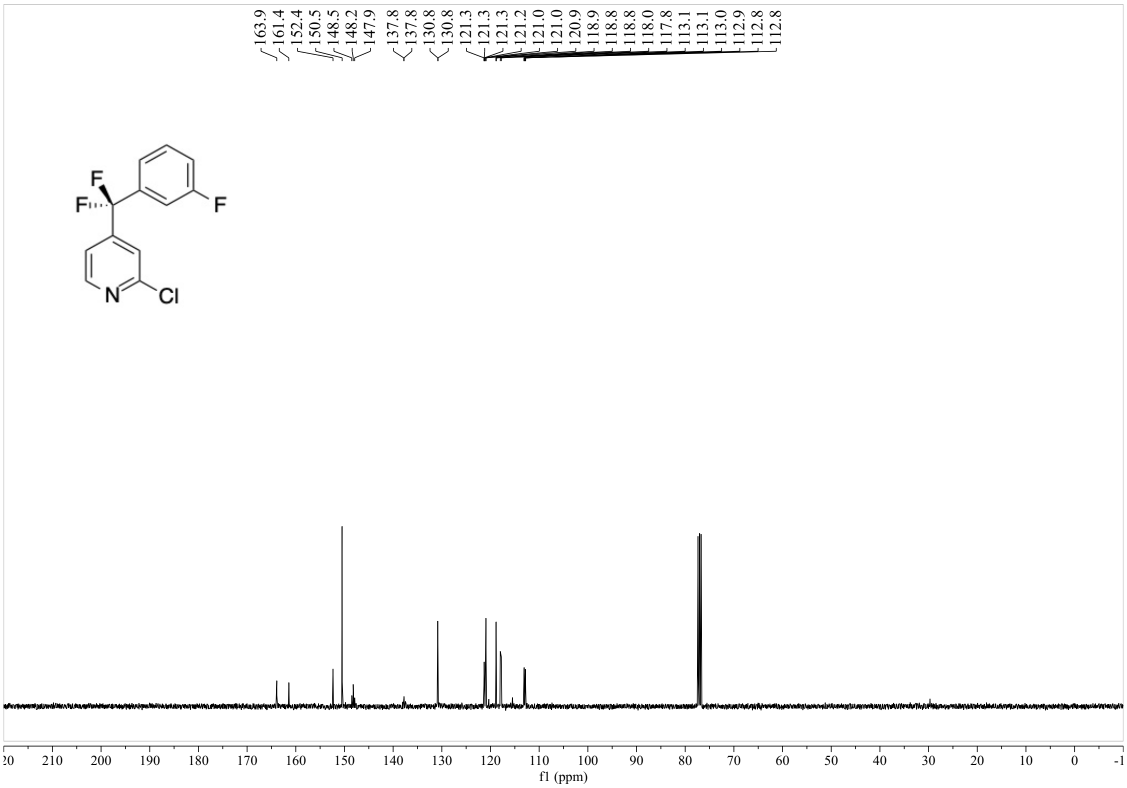
^{1}H NMR of compound **26** (400 MHz, $CDCl_3$)



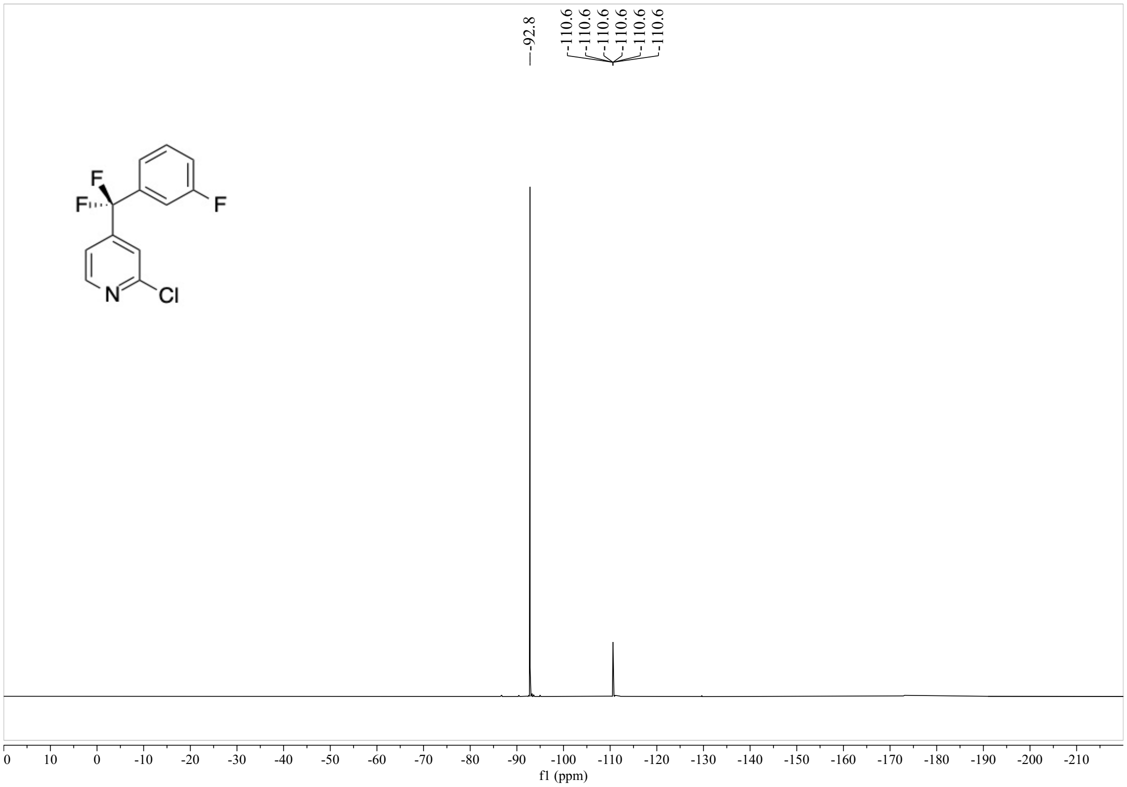
^{13}C NMR of compound **26** (101 MHz, $CDCl_3$)



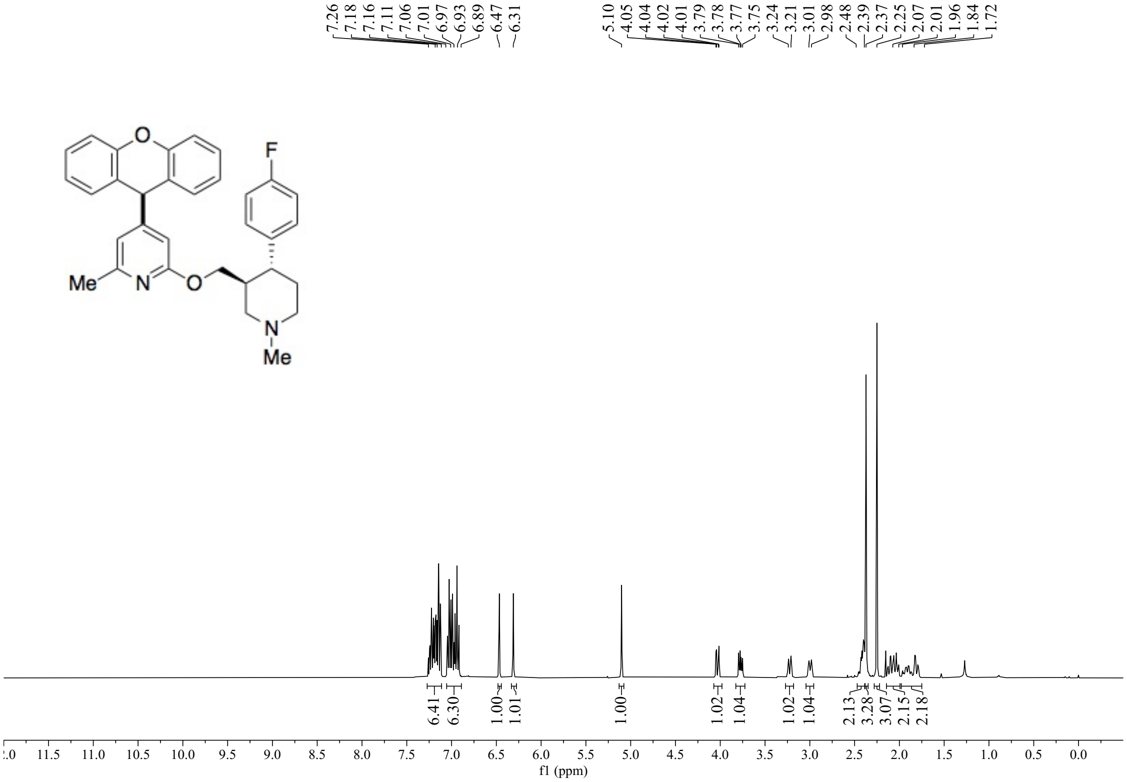
^{1}**H NMR** of compound **27** (400 MHz, CDCl$_3$)



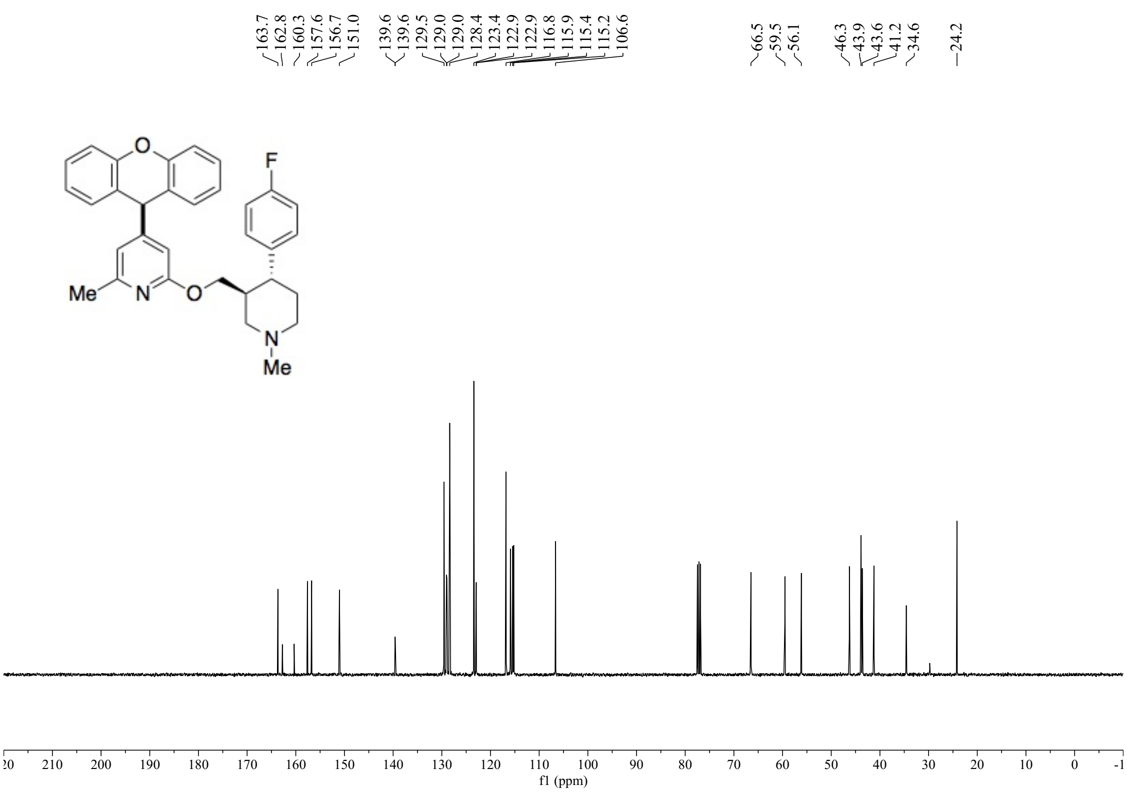
^{13}**C NMR** of compound **27** (101 MHz, CDCl$_3$)



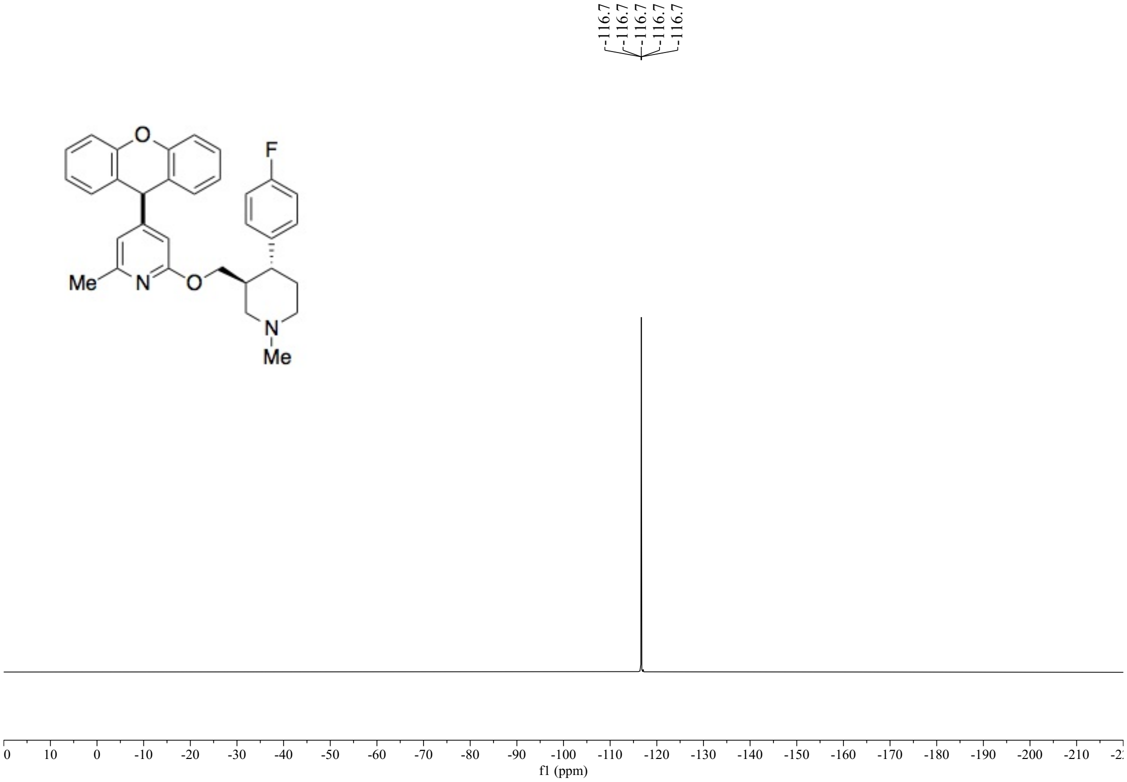
^{19}F NMR (proton coupled) of compound **27** (376 MHz, $CDCl_3$)



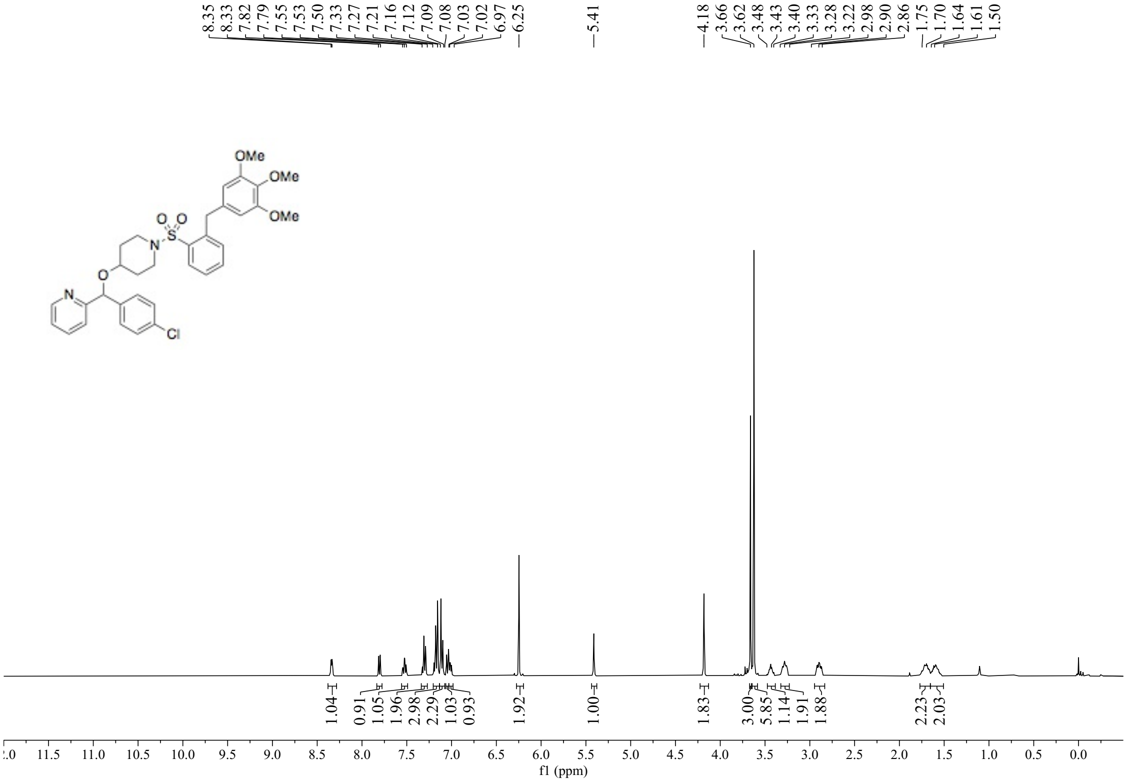
^{1}H NMR of compound **28** (400 MHz, $CDCl_3$)



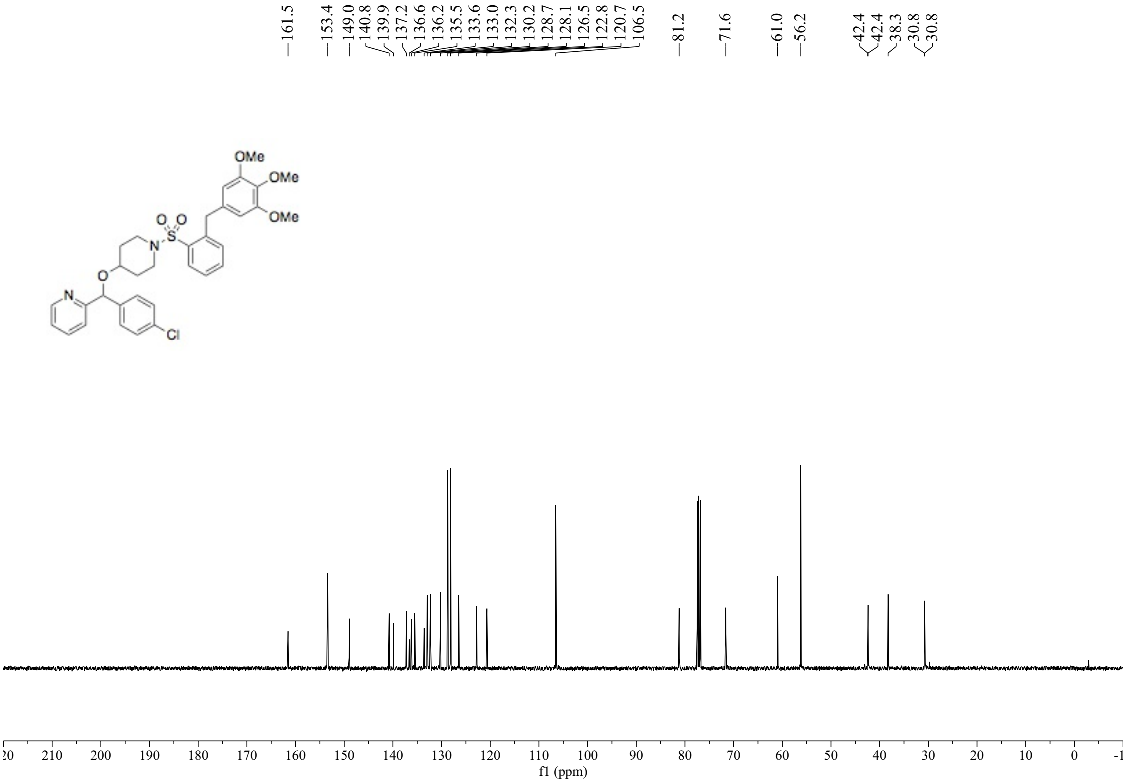
^{13}C NMR of compound **28** (101 MHz, $CDCl_3$)



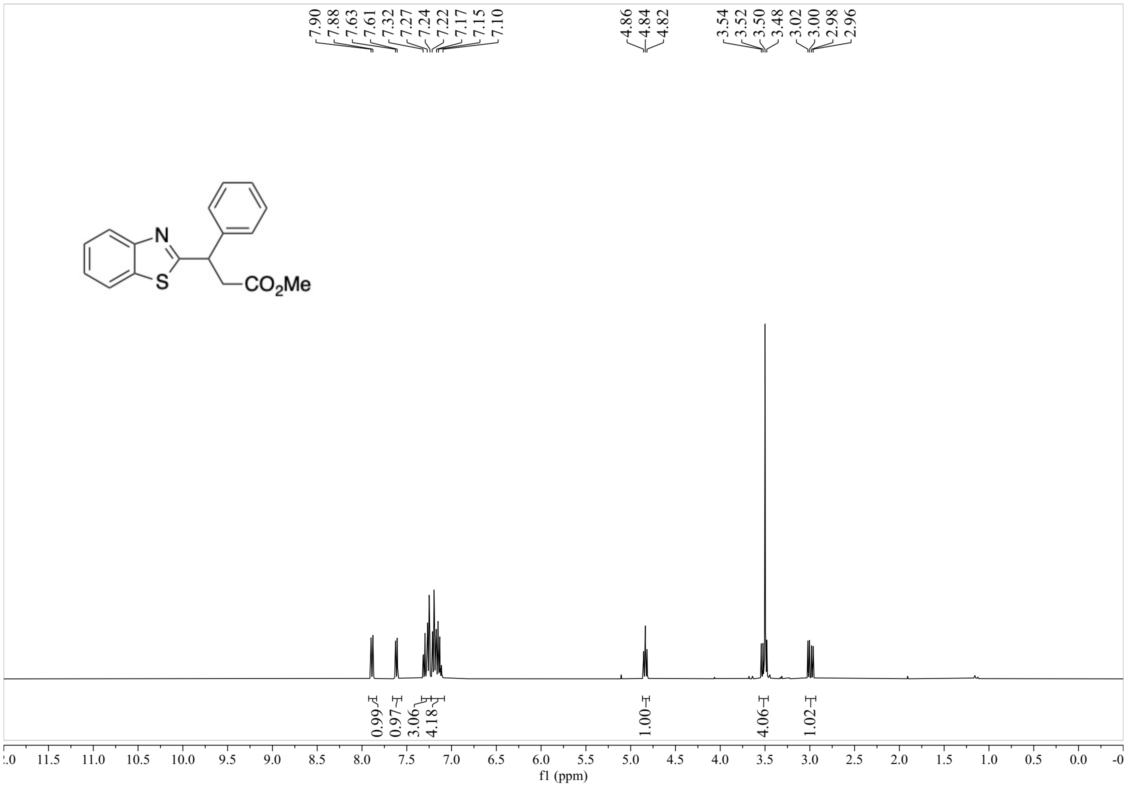
^{19}F NMR (proton coupled) of compound **28** (376 MHz, CDCl$_3$)



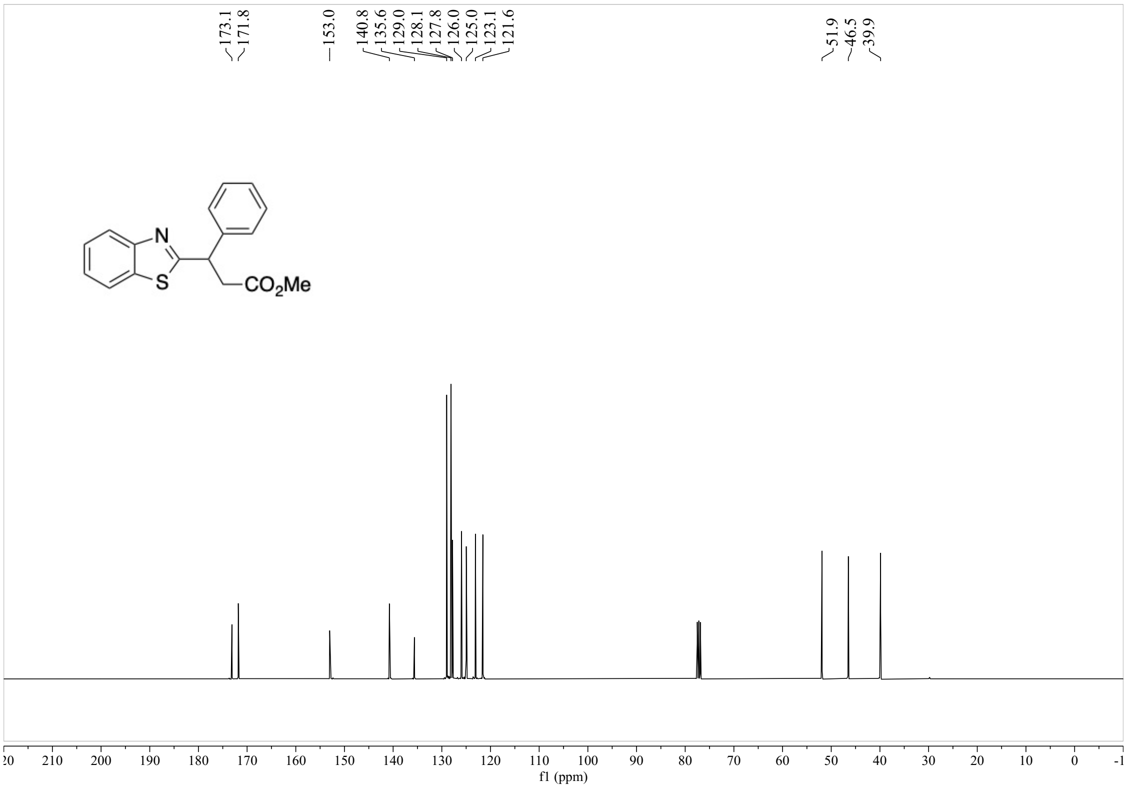
^{1}H NMR of compound **29** (400 MHz, $CDCl_3$)



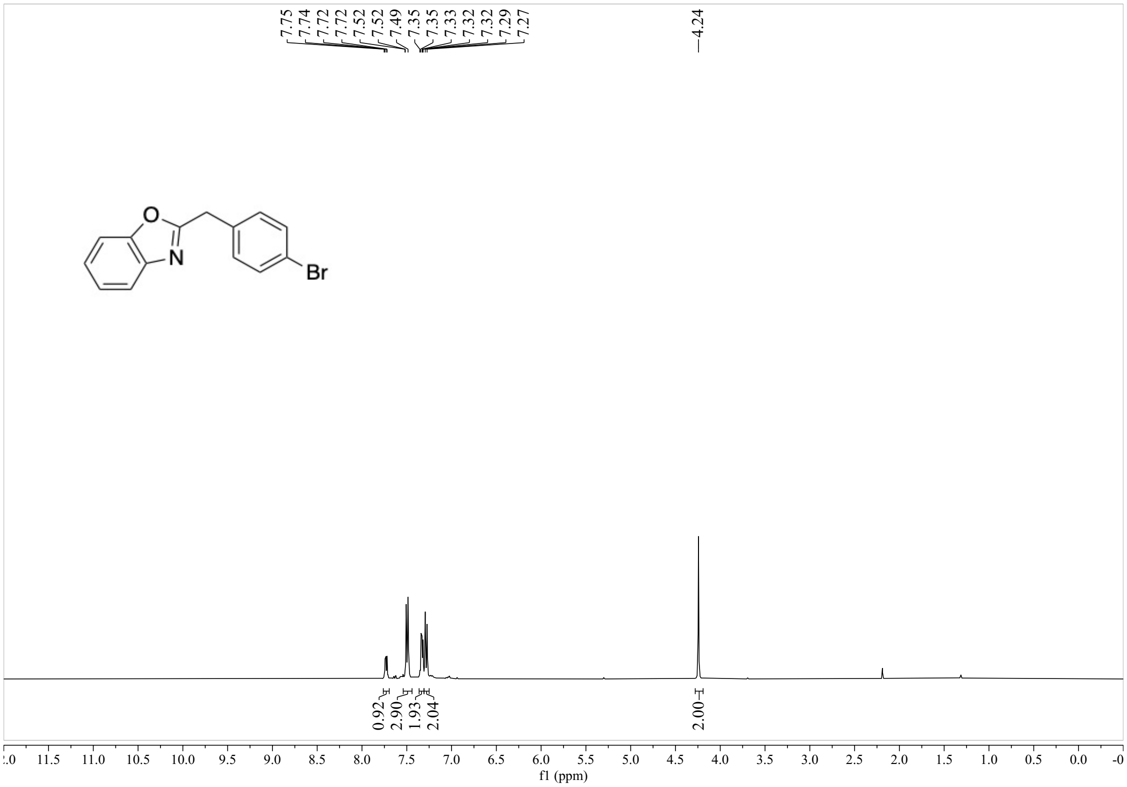
^{13}C NMR of compound **29** (101 MHz, $CDCl_3$)



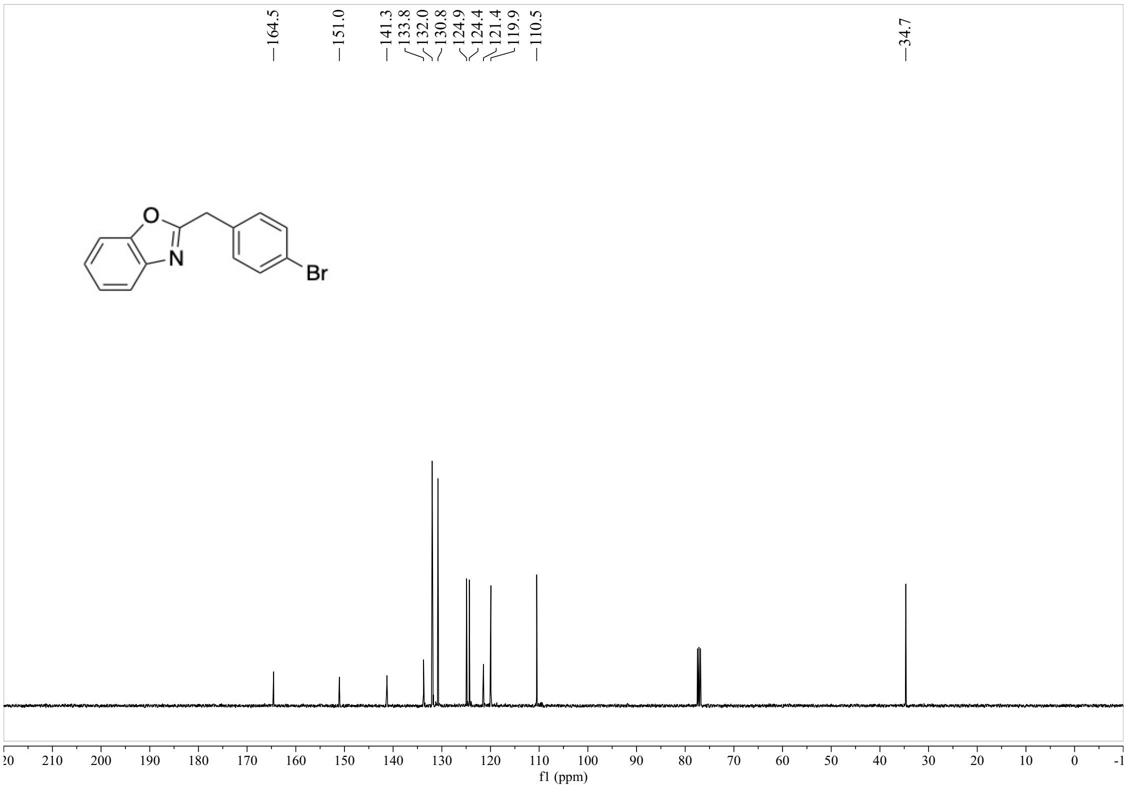
^{1}**H NMR** of compound **30** (400 MHz, $CDCl_3$)



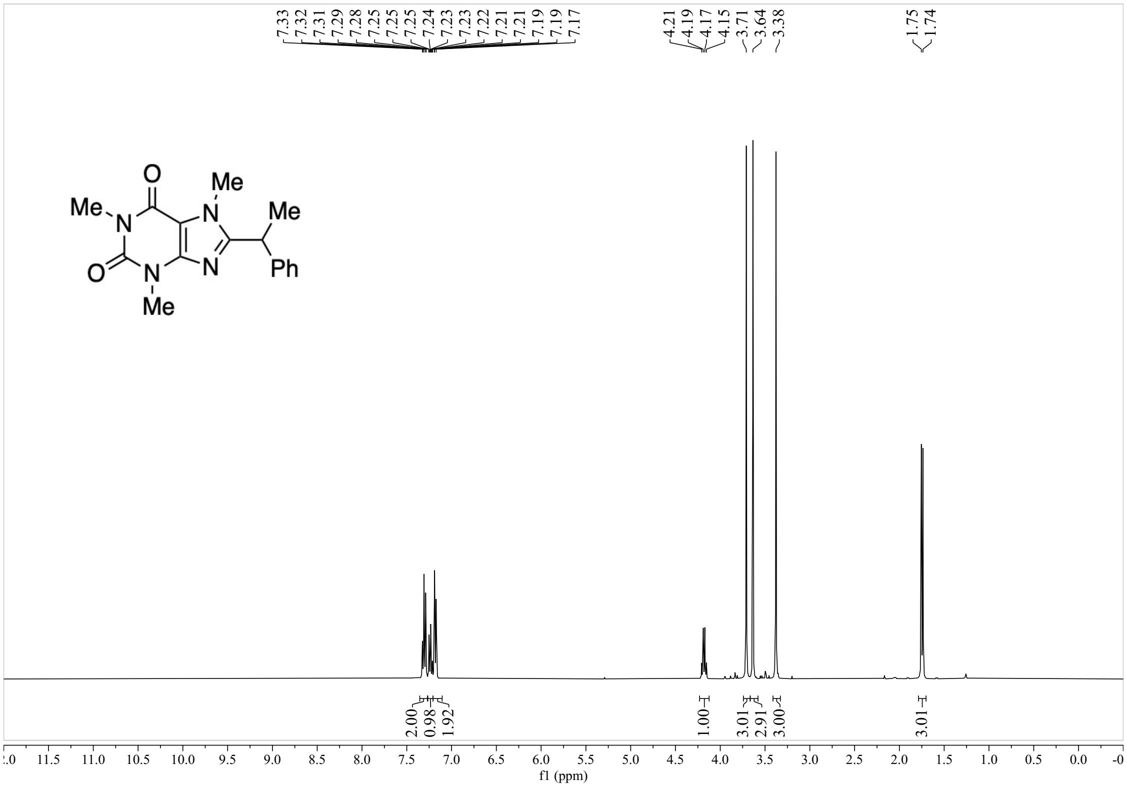
^{13}**C NMR** of compound **30** (101 MHz, $CDCl_3$)



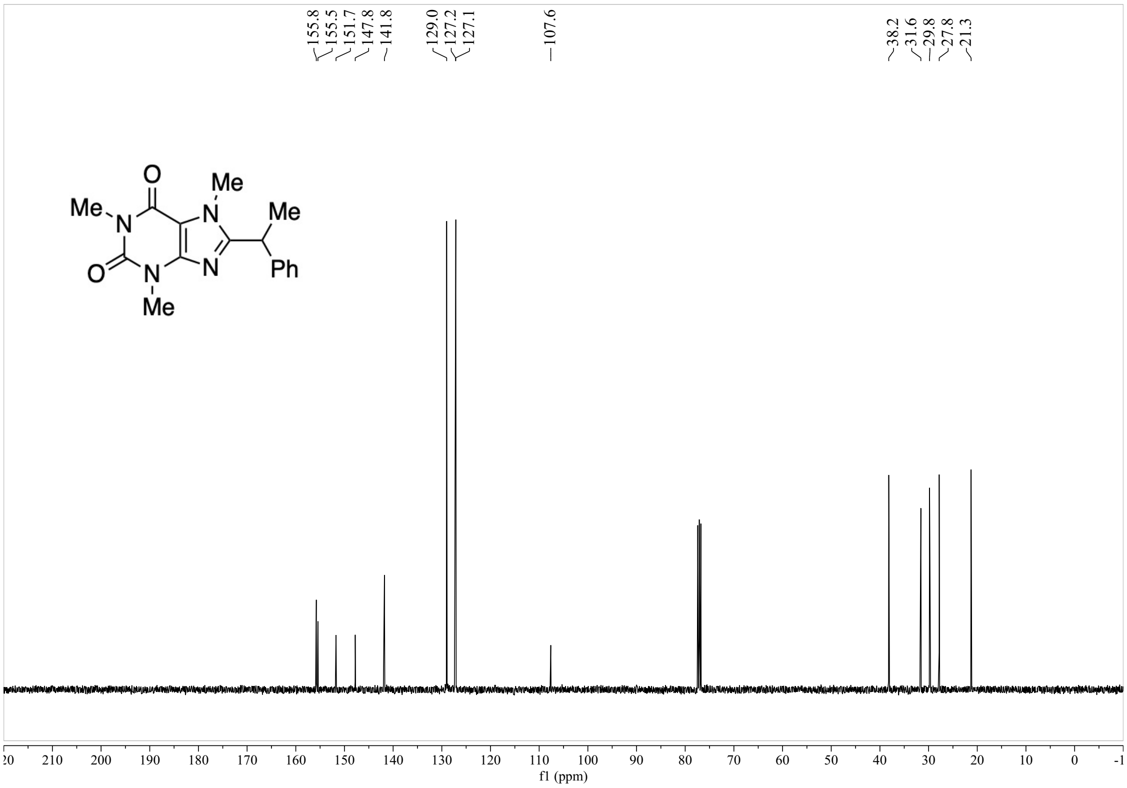
¹H NMR of compound **31** (400 MHz, $CDCl_3$)



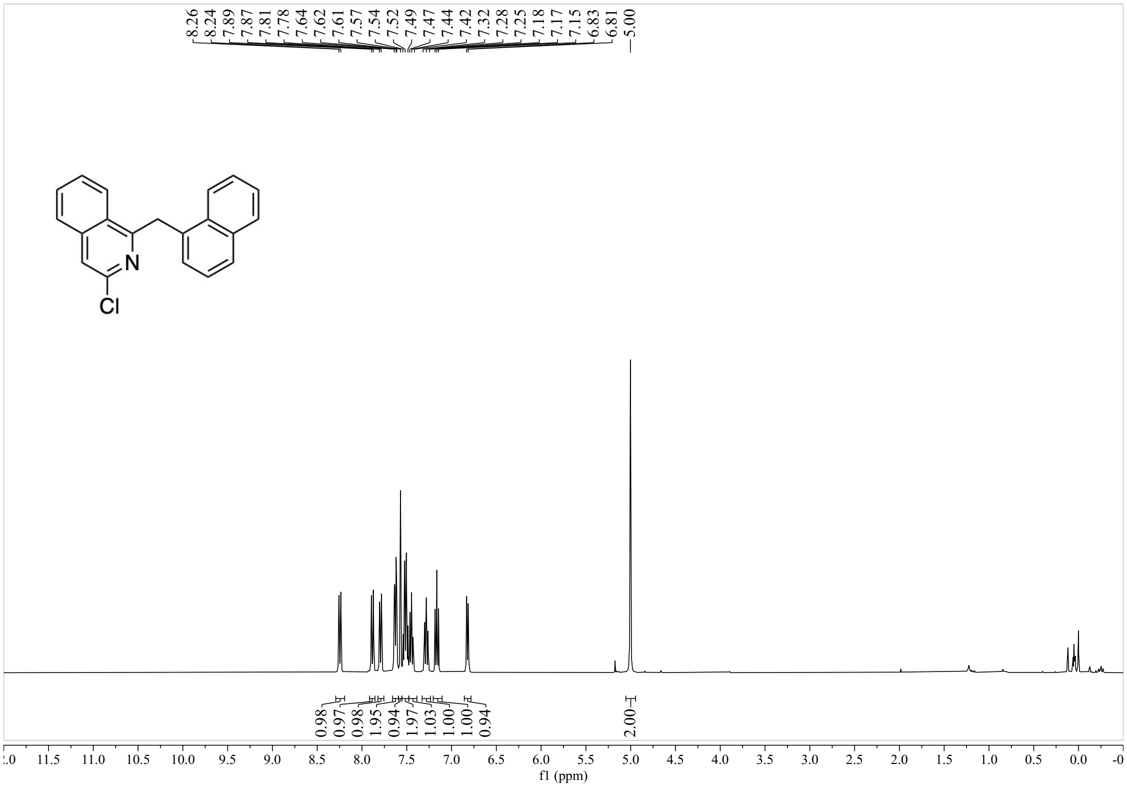
¹³C NMR of compound **31** (101 MHz, $CDCl_3$)



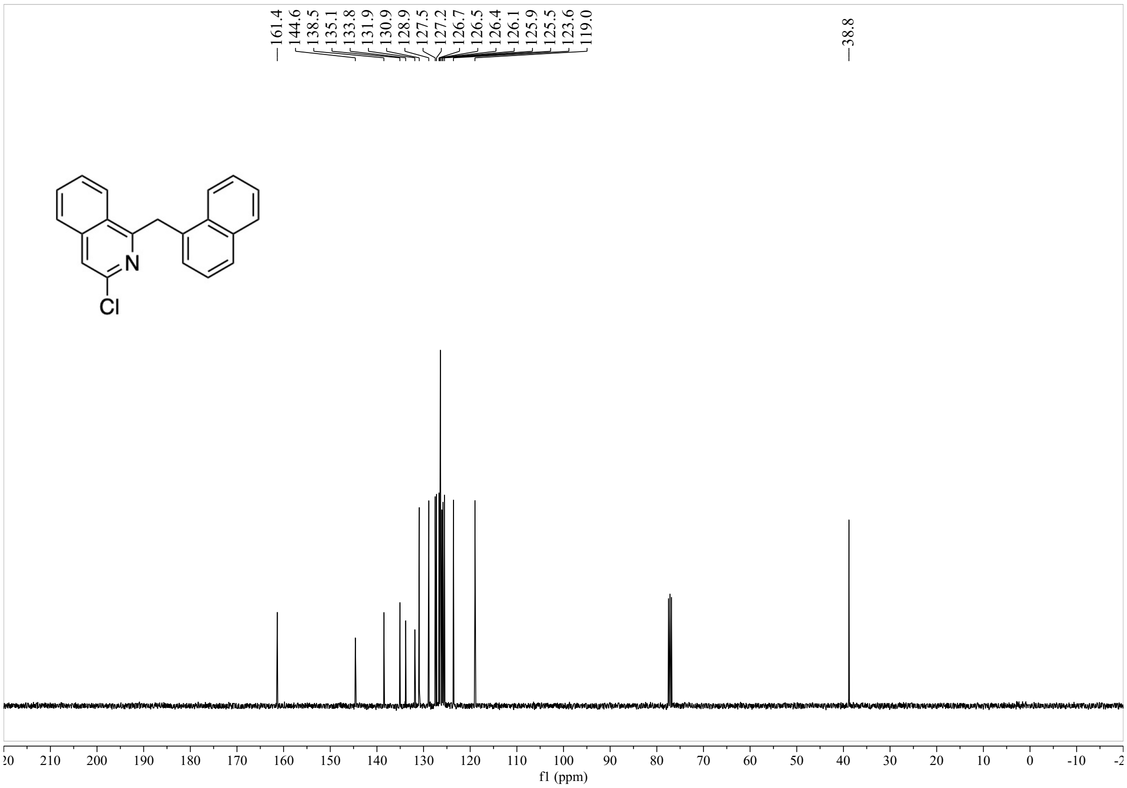
^{1}H NMR of compound **32** (400 MHz, $CDCl_3$)



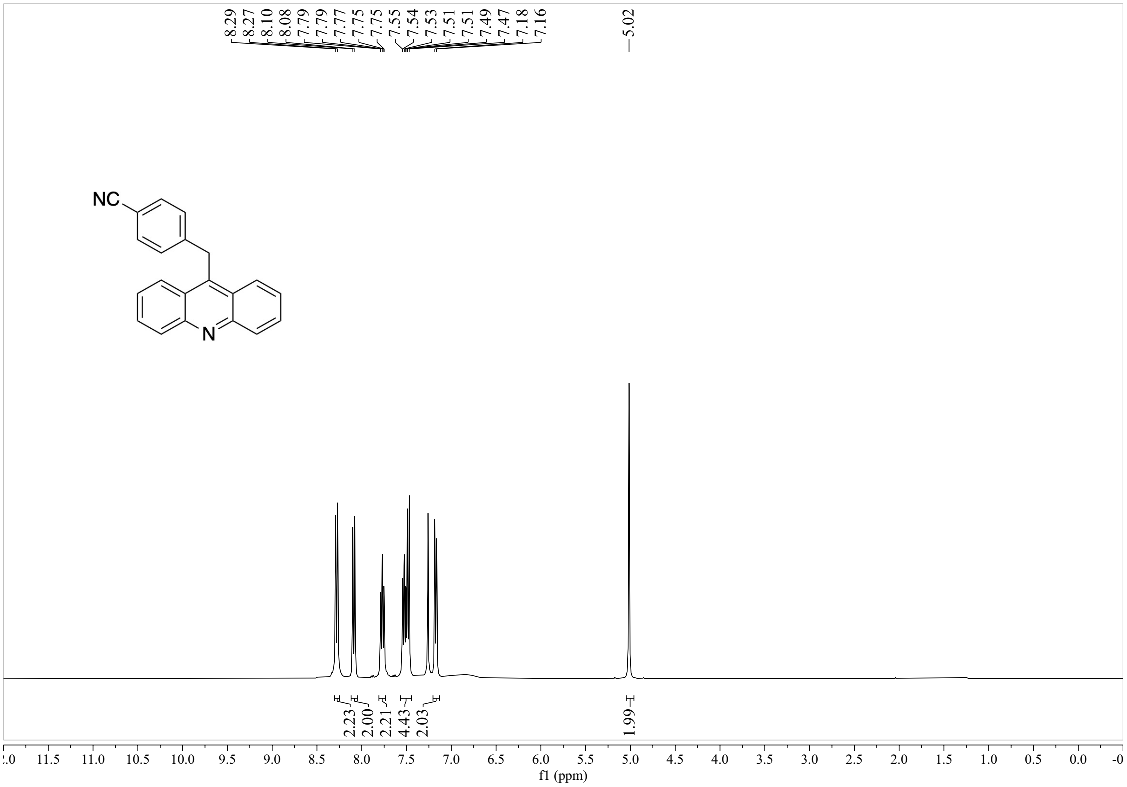
^{13}C NMR of compound **32** (101 MHz, $CDCl_3$)



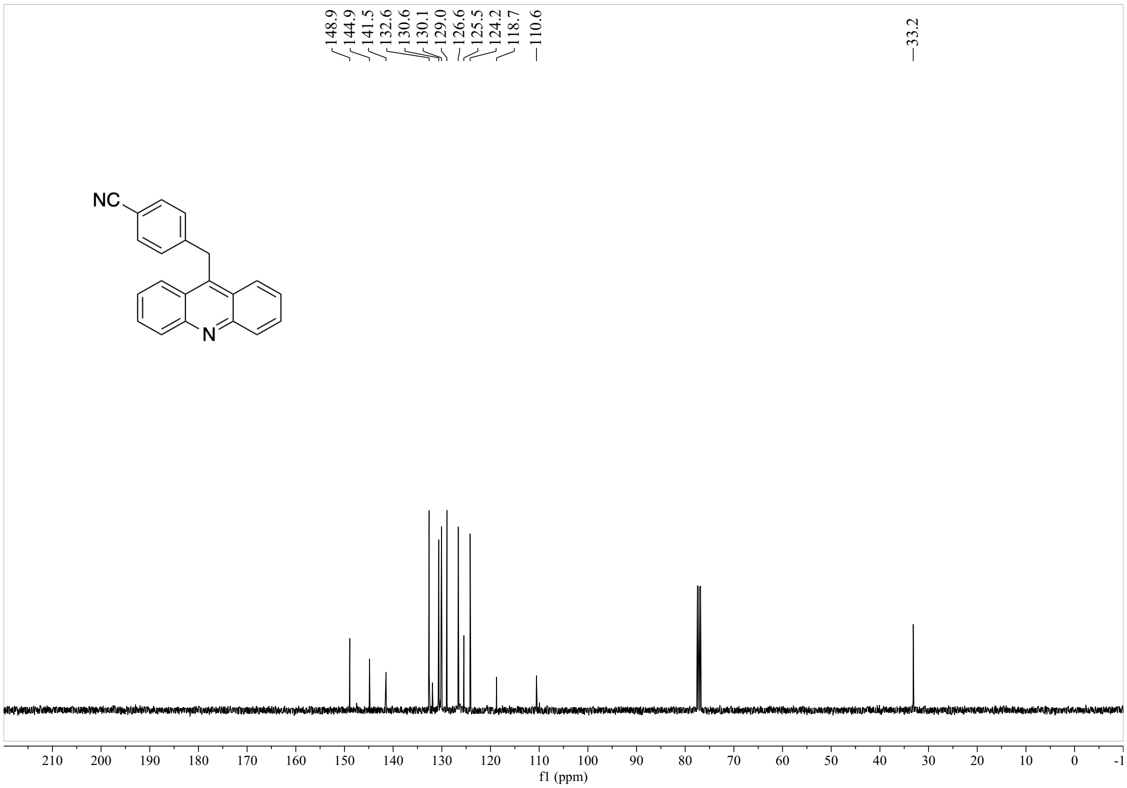
^{1}H NMR of compound **33** (400 MHz, CDCl$_3$)



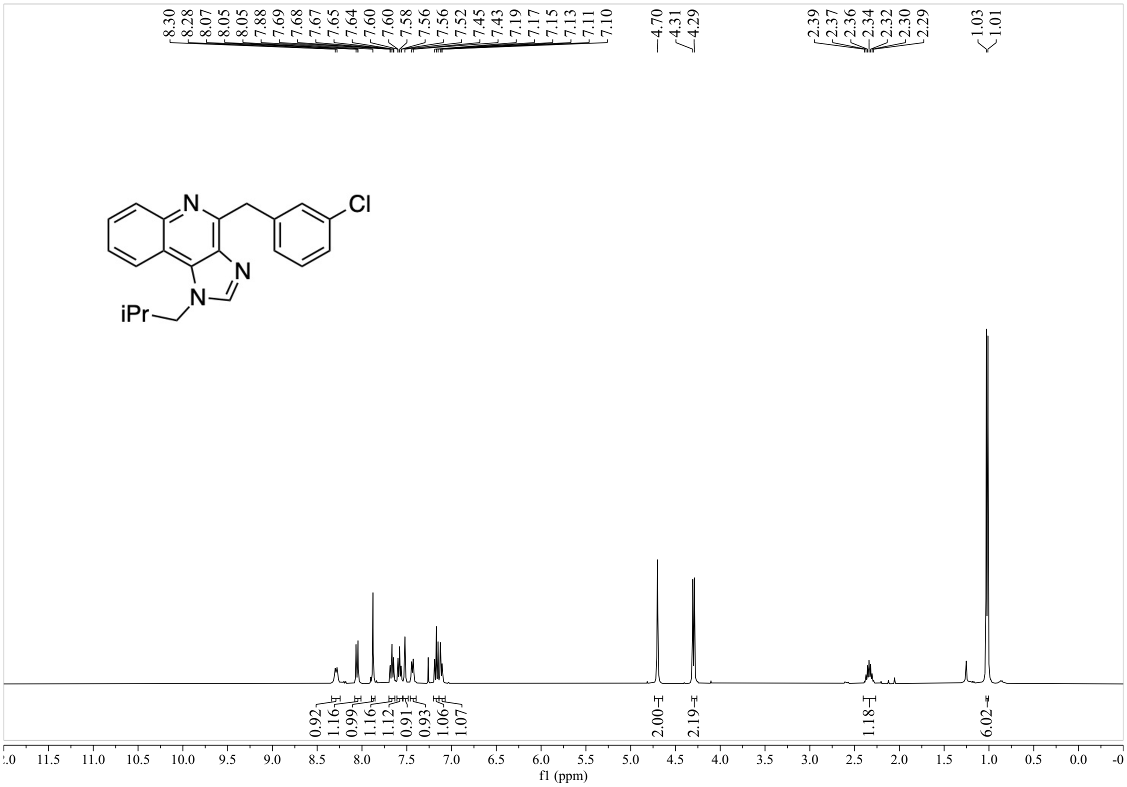
^{13}C NMR of compound **33** (101 MHz, CDCl$_3$)



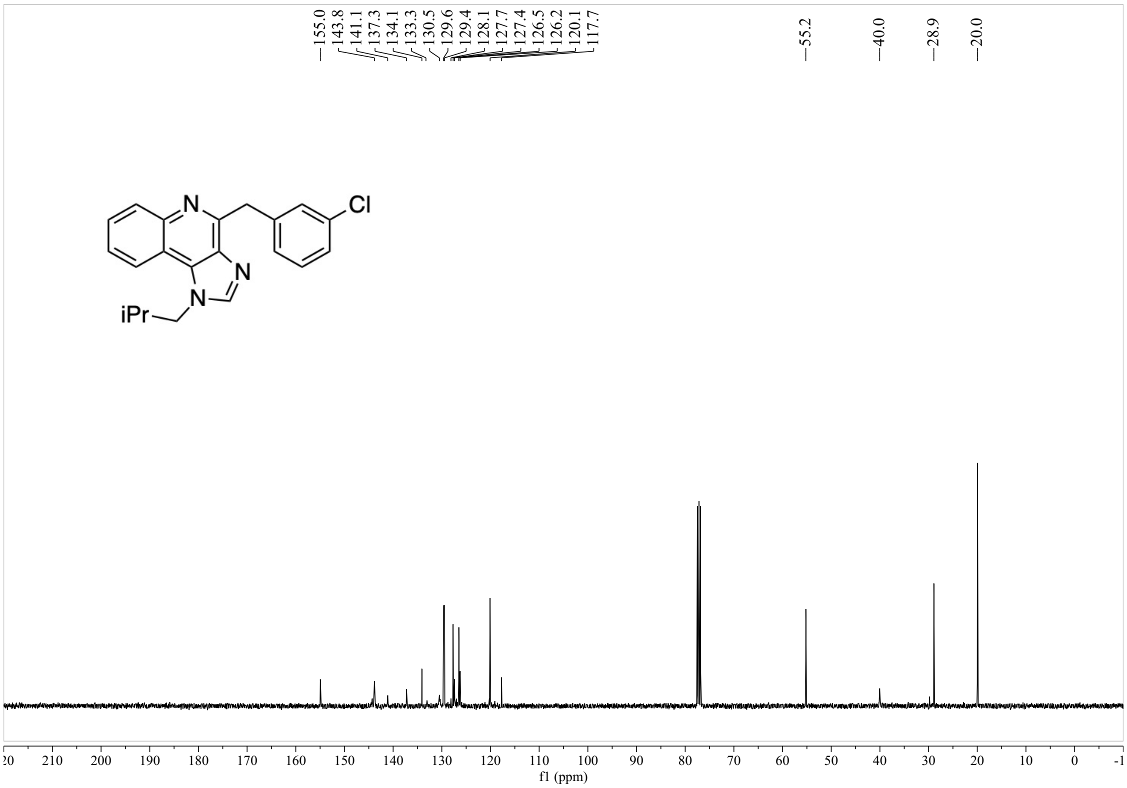
^{1}H NMR of compound **34** (400 MHz, $CDCl_3$)



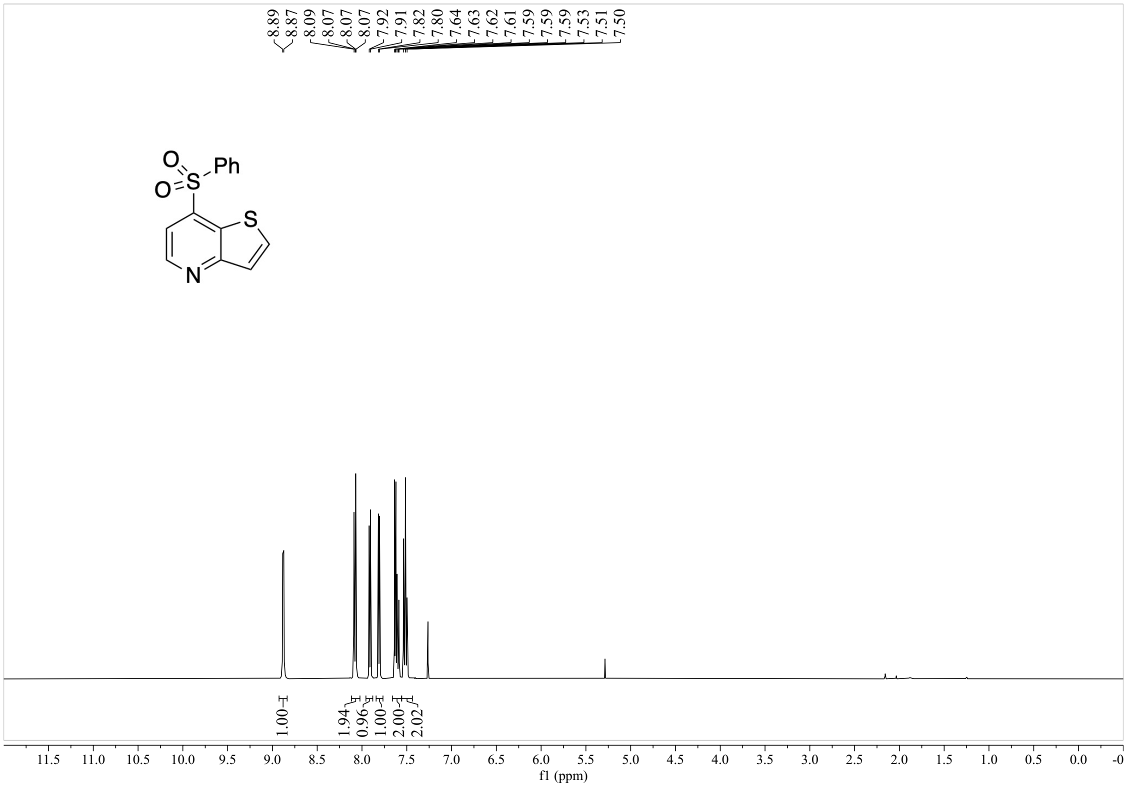
^{13}C NMR of compound **34** (101 MHz, $CDCl_3$)



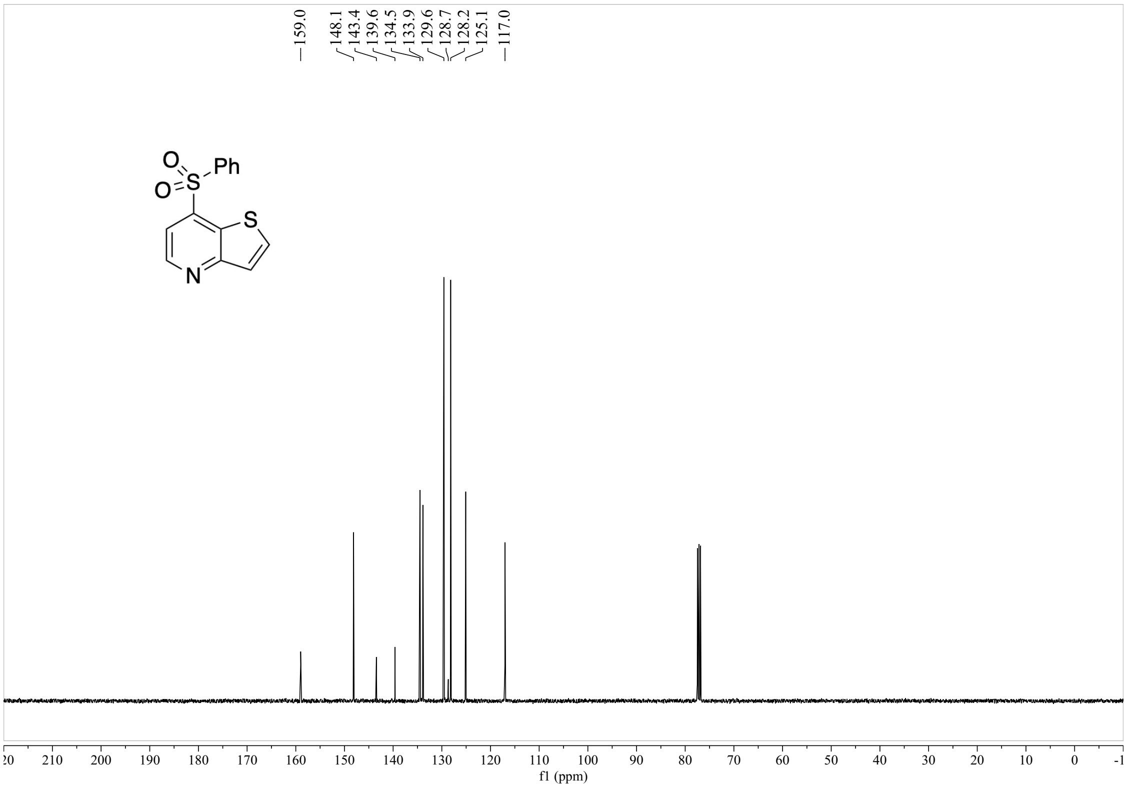
^{1}**H NMR** of compound **35** (400 MHz, CDCl$_3$)



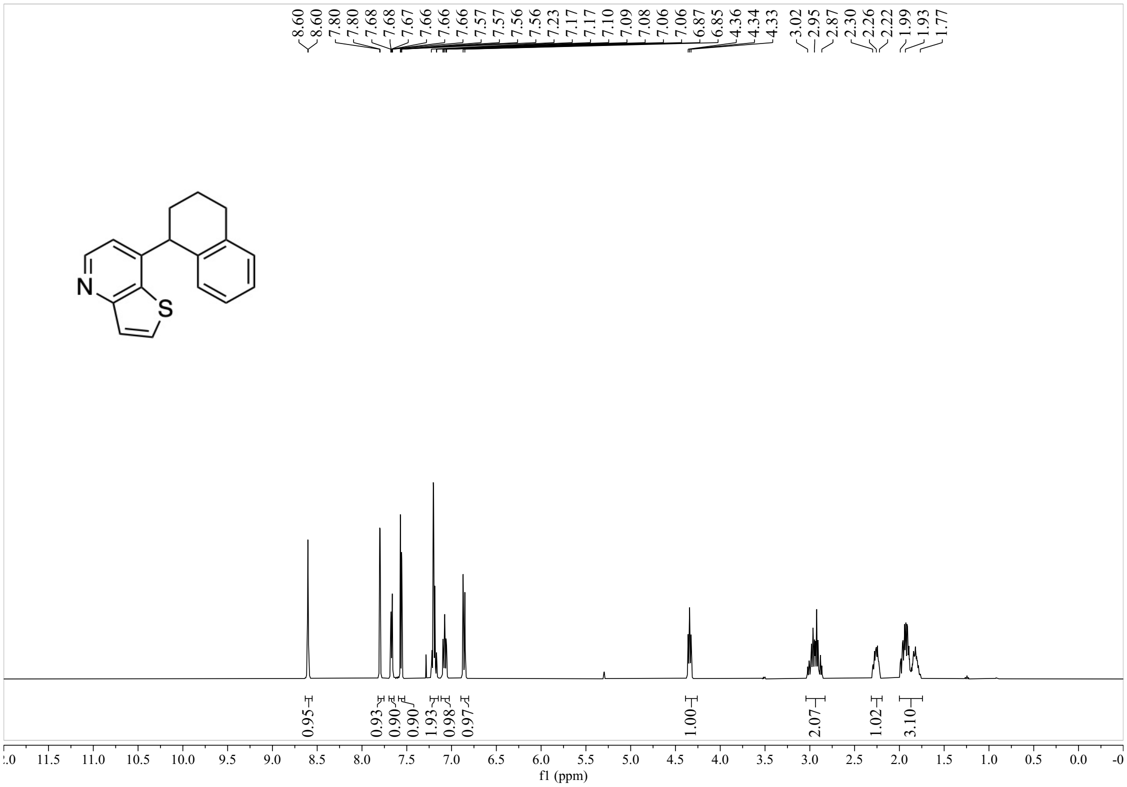
^{13}**C NMR** of compound **35** (101 MHz, CDCl$_3$)



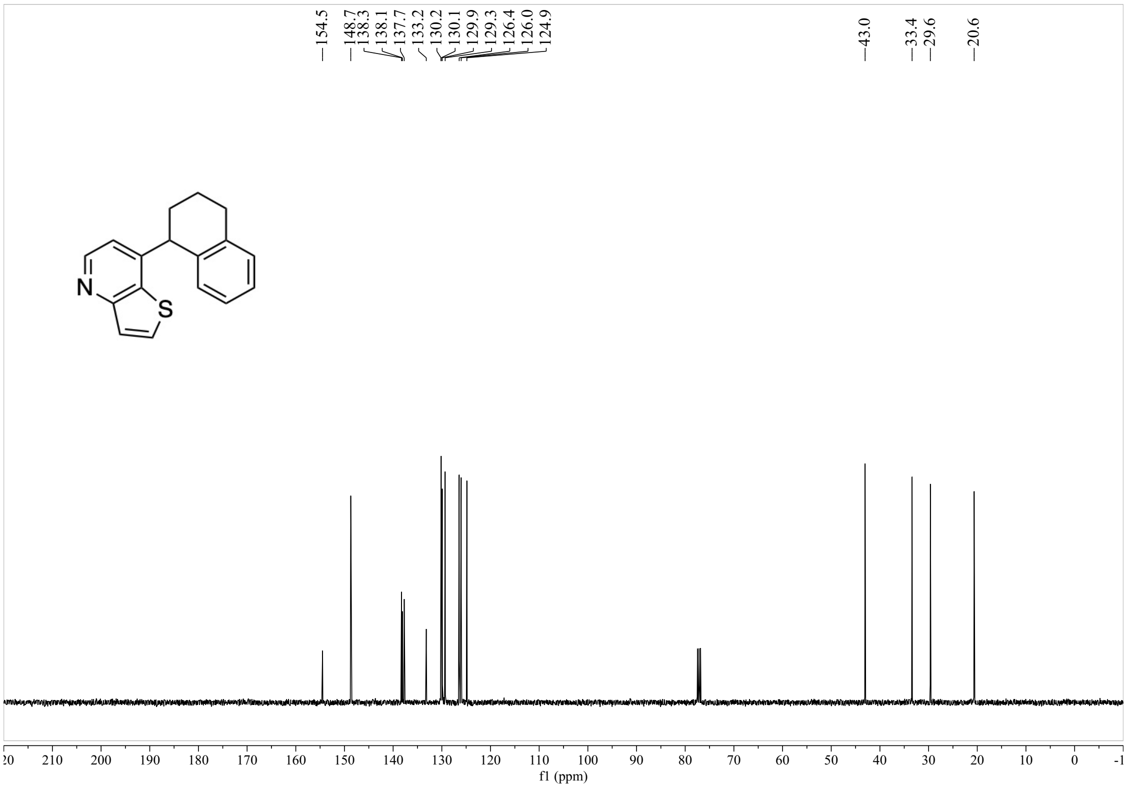
^{1}**H NMR** of compound **38** (400 MHz, CDCl$_3$)



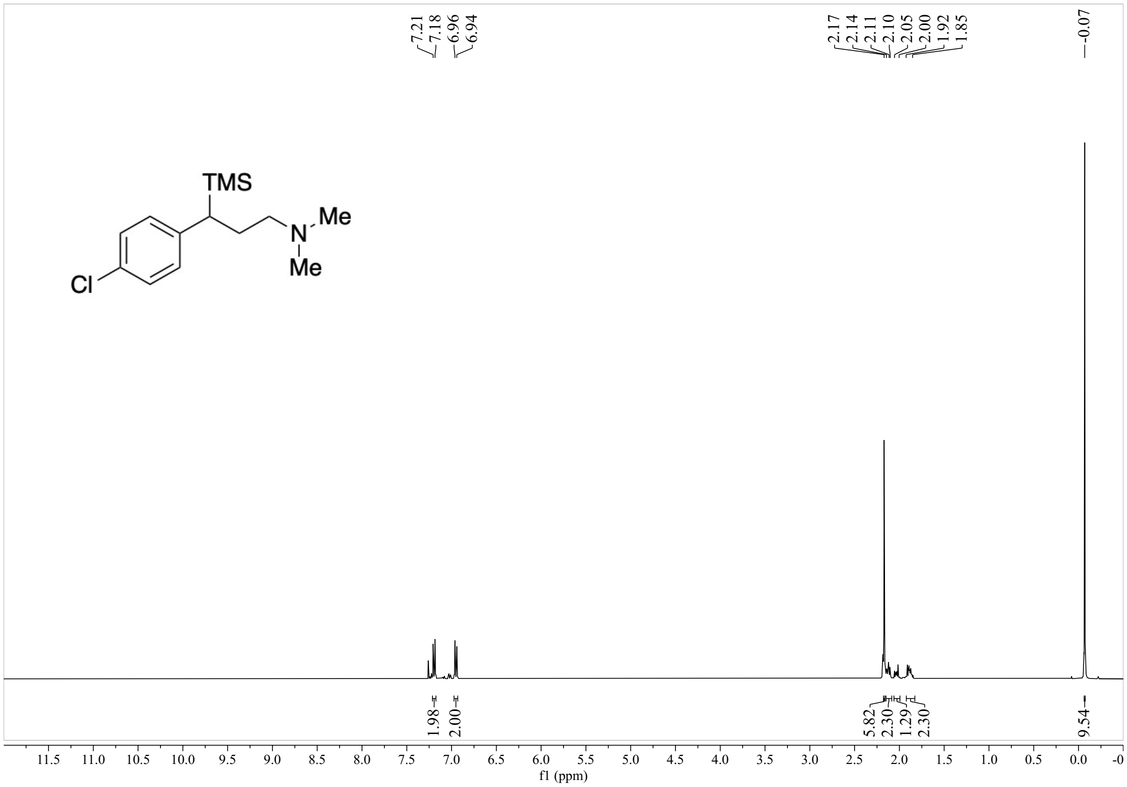
^{13}**C NMR** of compound **38** (101 MHz, CDCl$_3$)



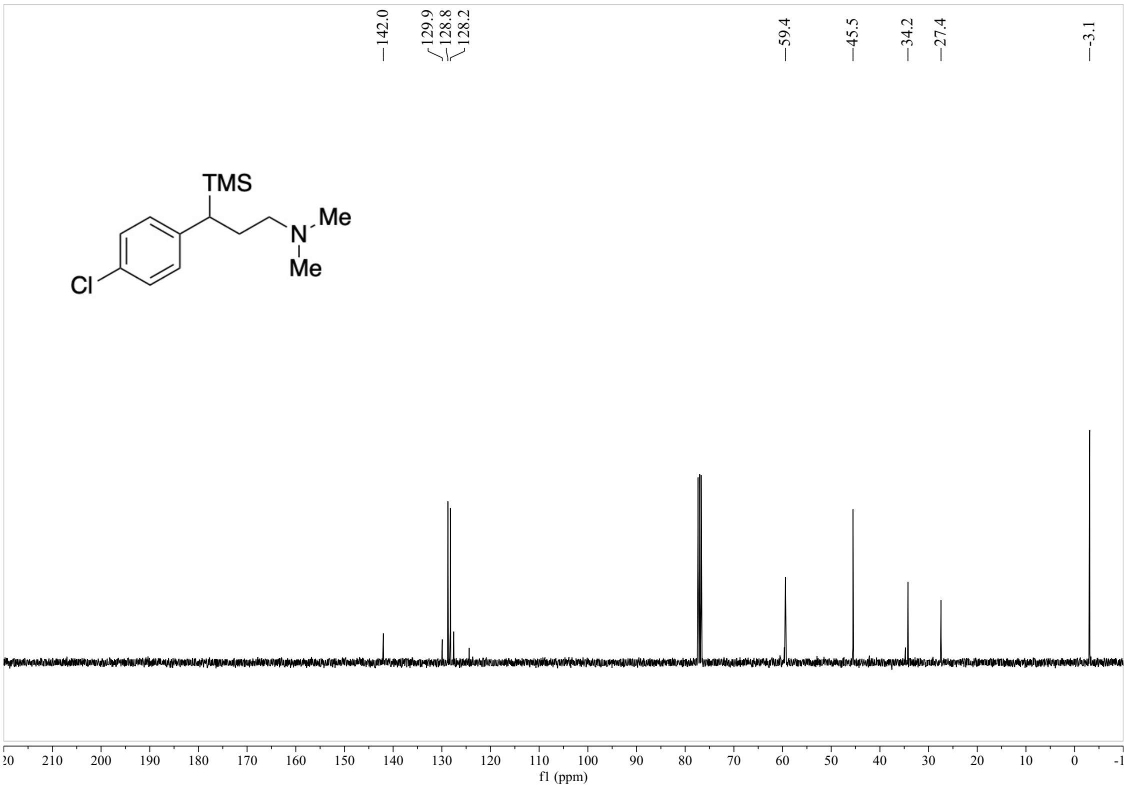
^{1}H NMR of compound **39** (400 MHz, CDCl$_3$)



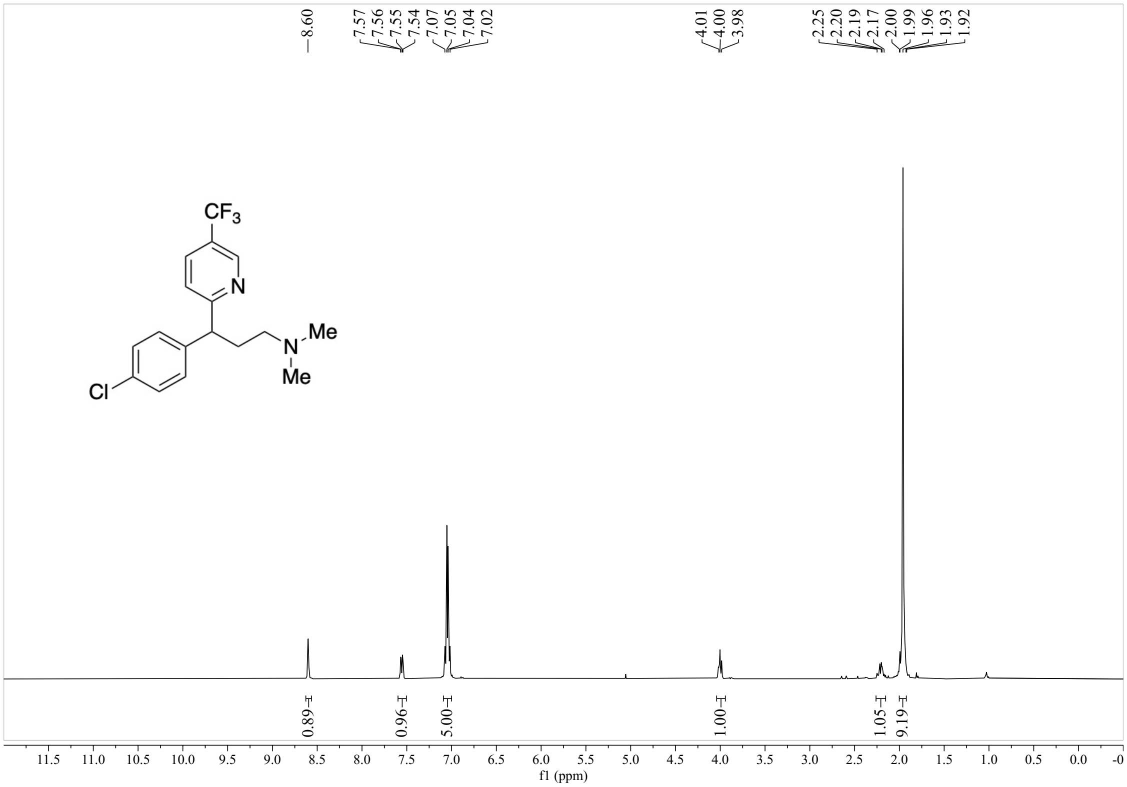
^{13}C NMR of compound **39** (101 MHz, CDCl$_3$)



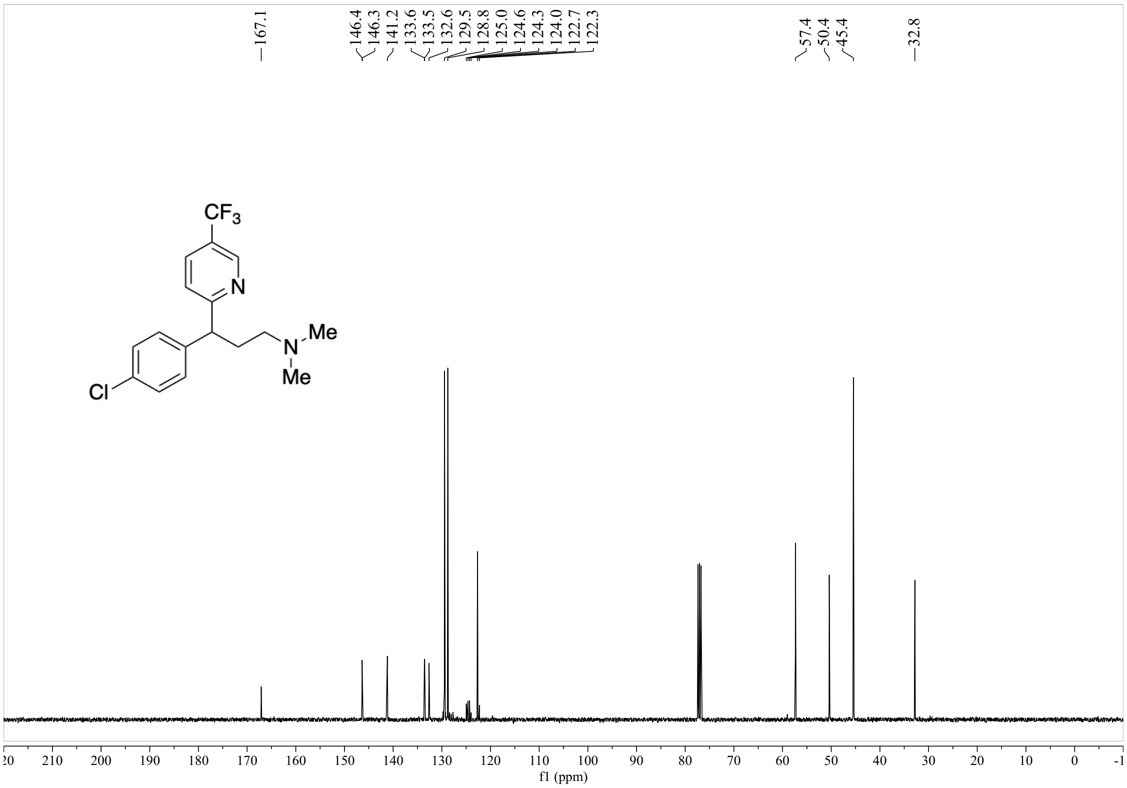
^{1}**H NMR** of compound **40** (400 MHz, $CDCl_3$)



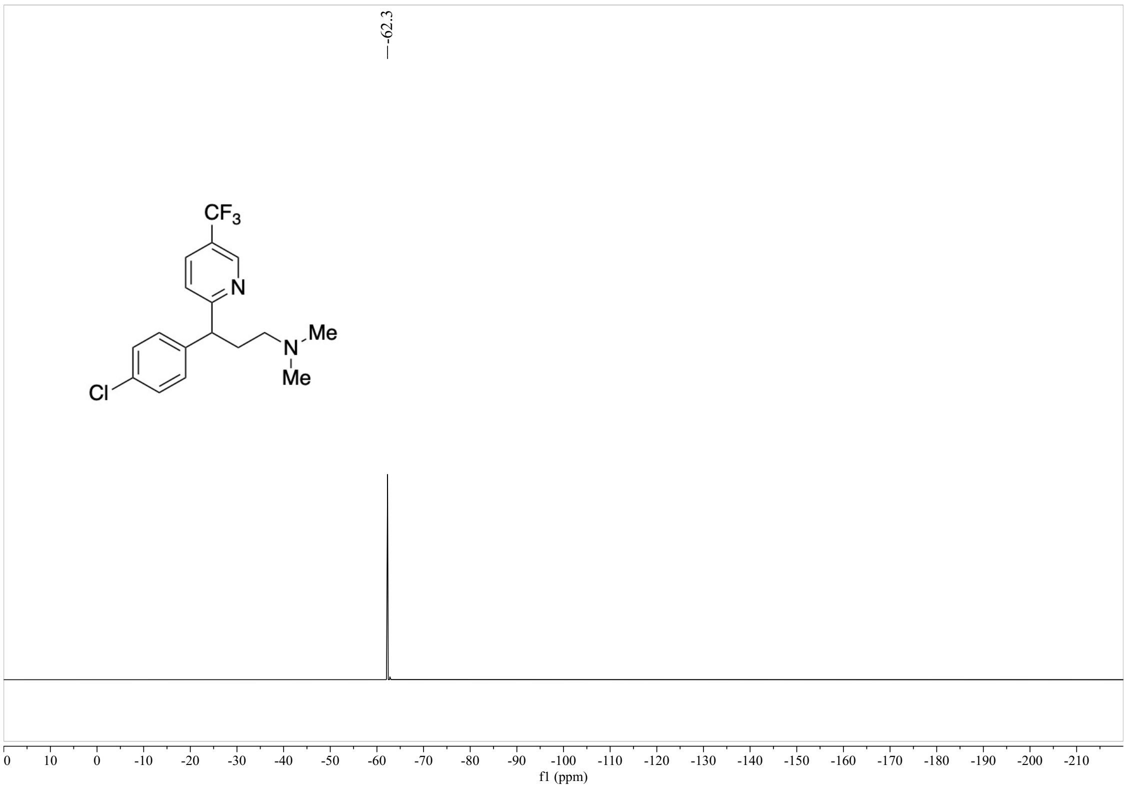
^{13}**C NMR** of compound **40** (101 MHz, $CDCl_3$)



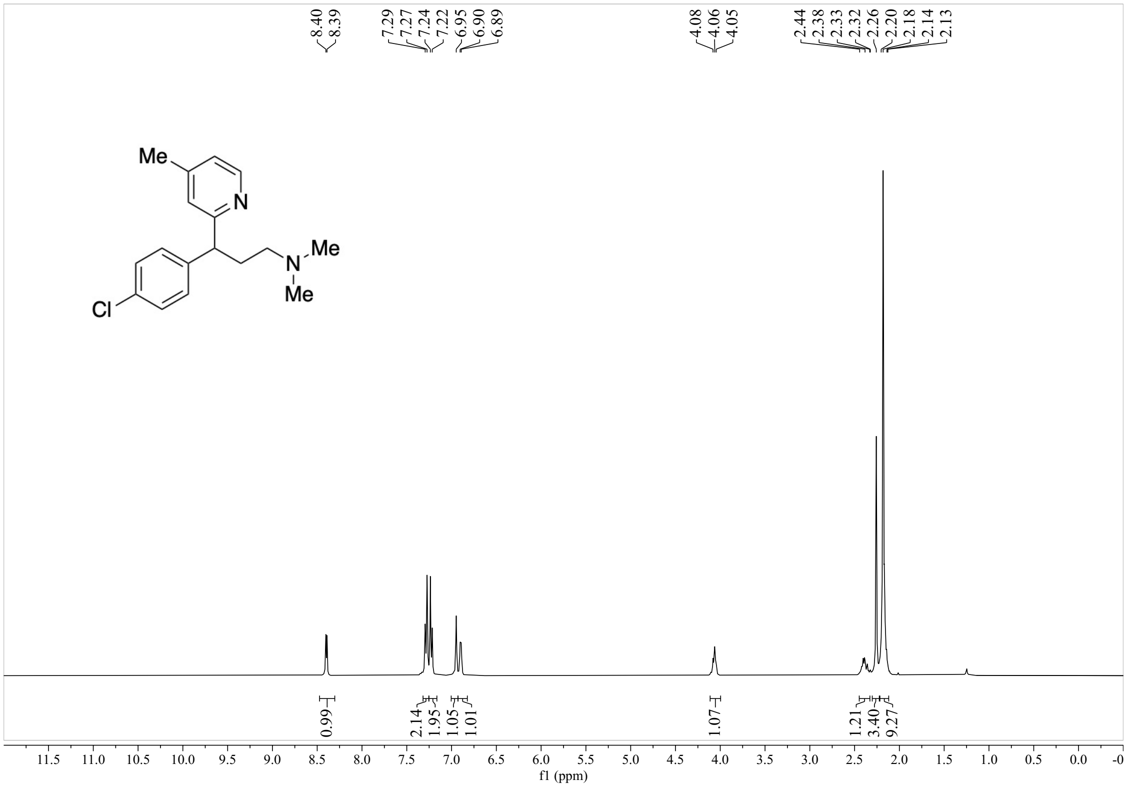
^{1}H NMR of compound **41** (400 MHz, CDCl$_3$)



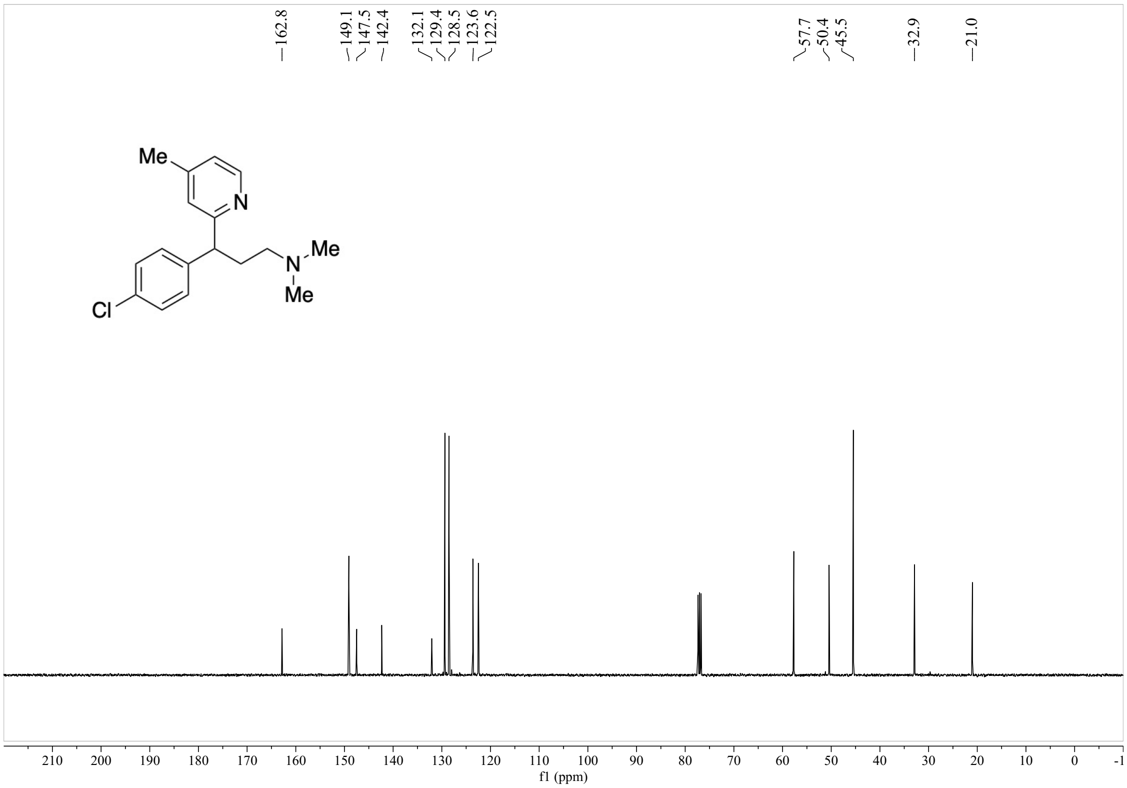
^{13}C NMR of compound **41** (101 MHz, CDCl$_3$)



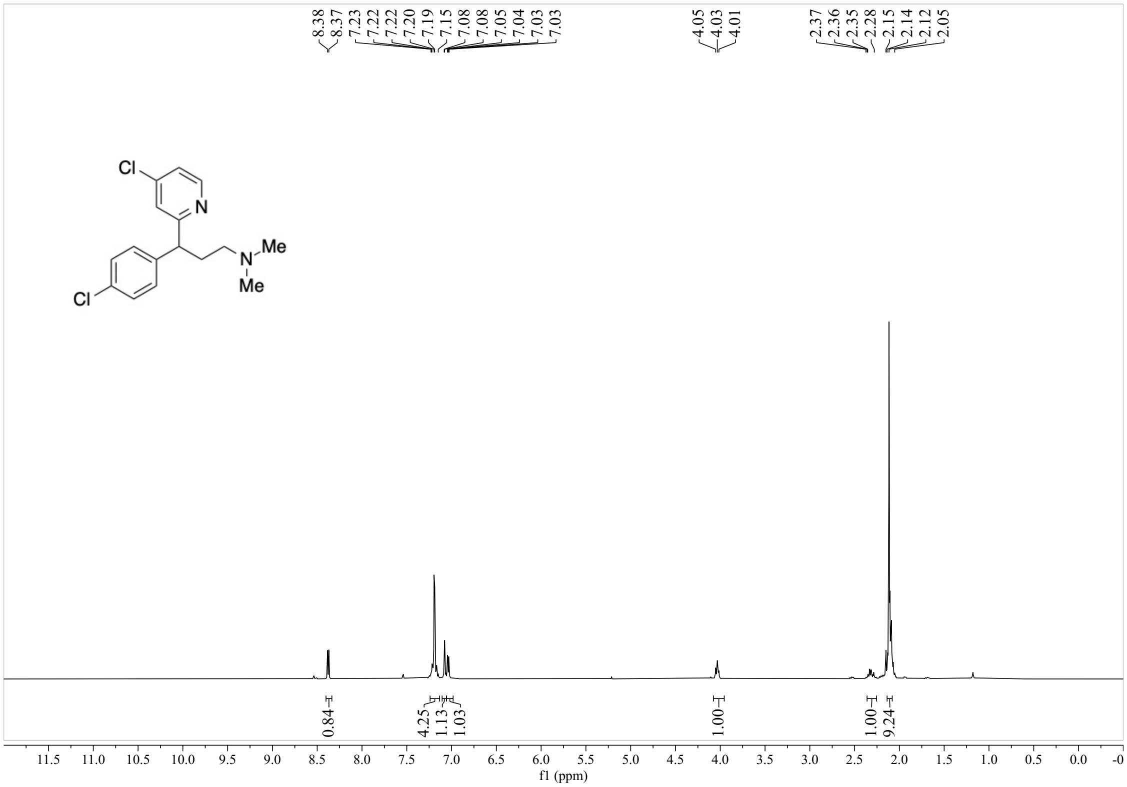
^{19}F NMR (proton decoupled) of compound **41** (376 MHz, $CDCl_3$)



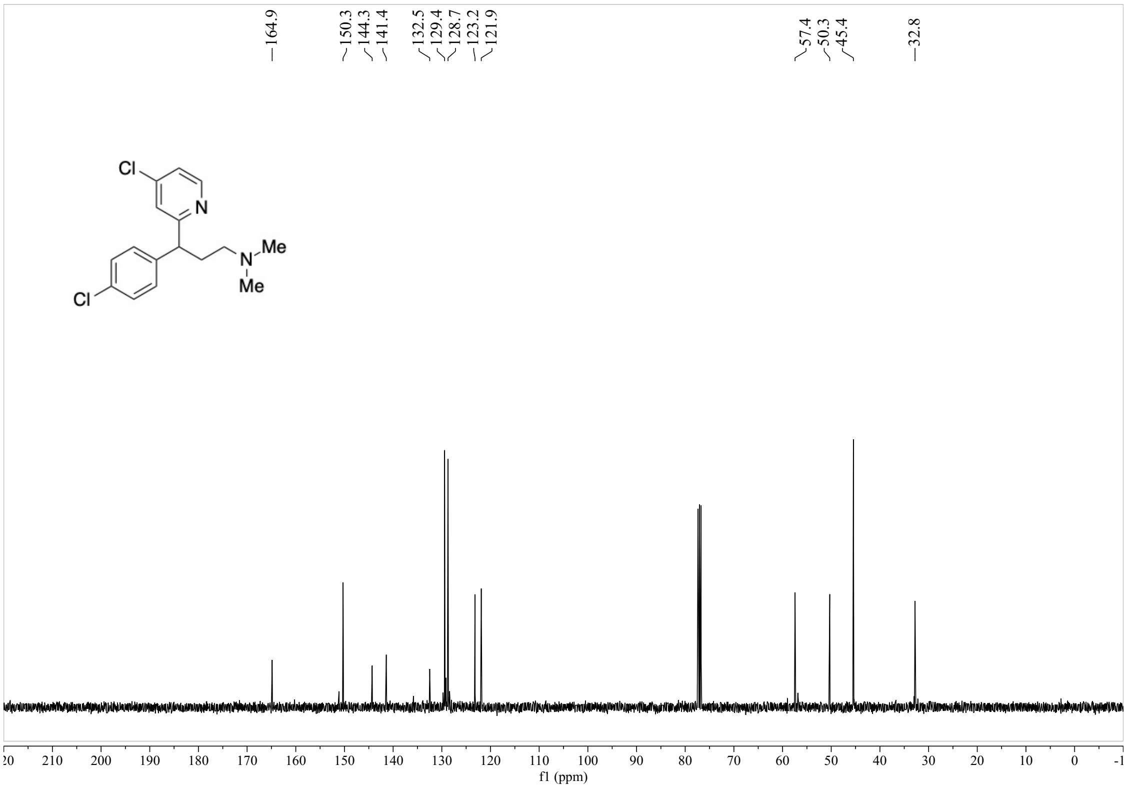
^{1}**H NMR** of compound **42** (400 MHz, CDCl$_3$)



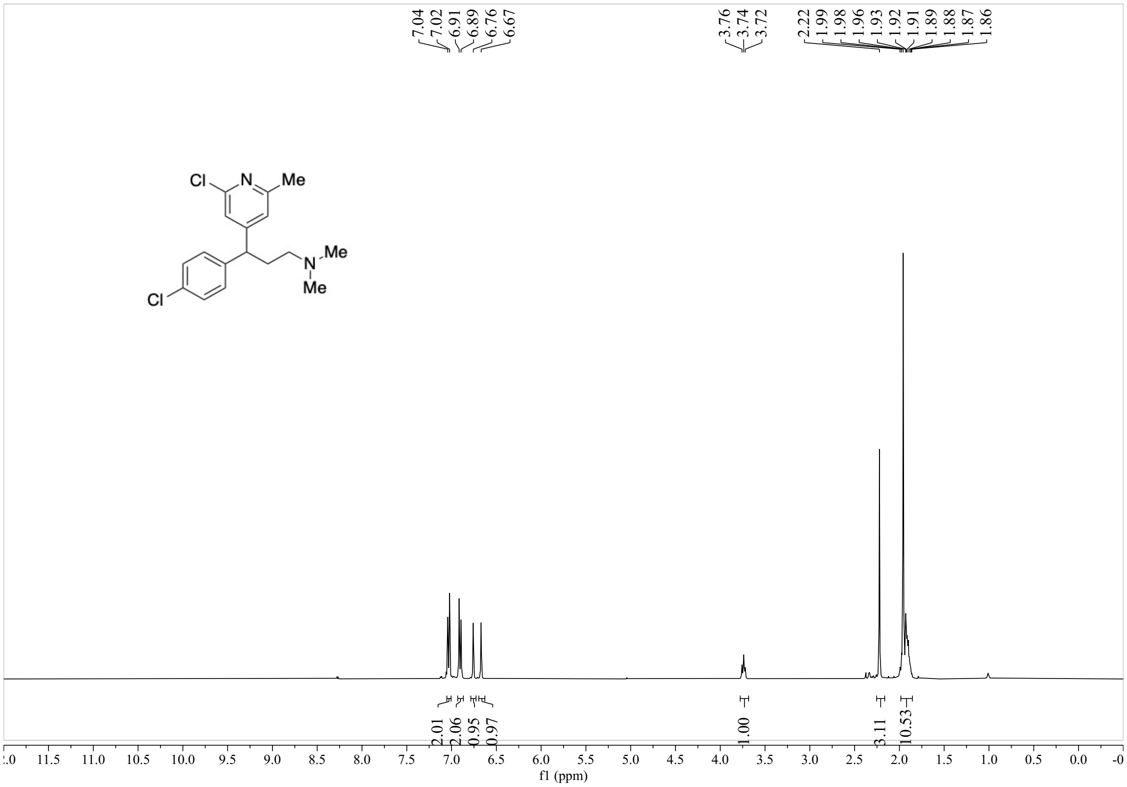
^{13}**C NMR** of compound **42** (101 MHz, CDCl$_3$)



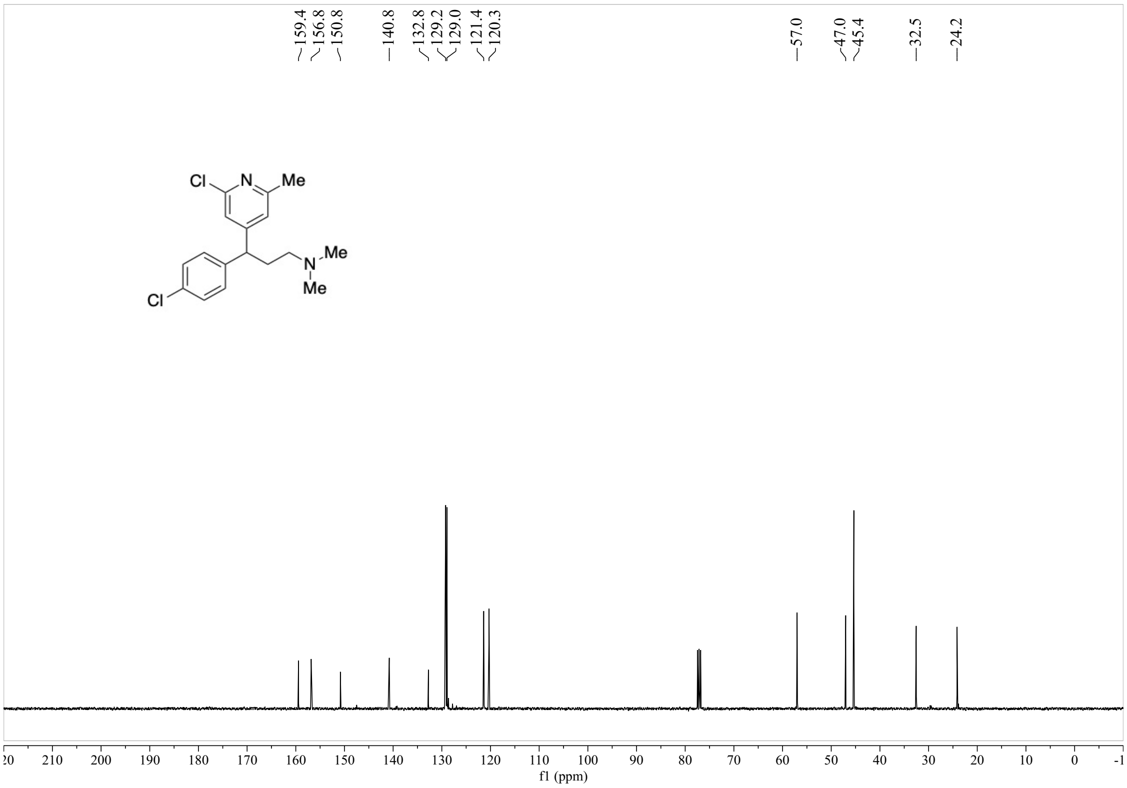
¹H NMR of compound **43** (400 MHz, $CDCl_3$)



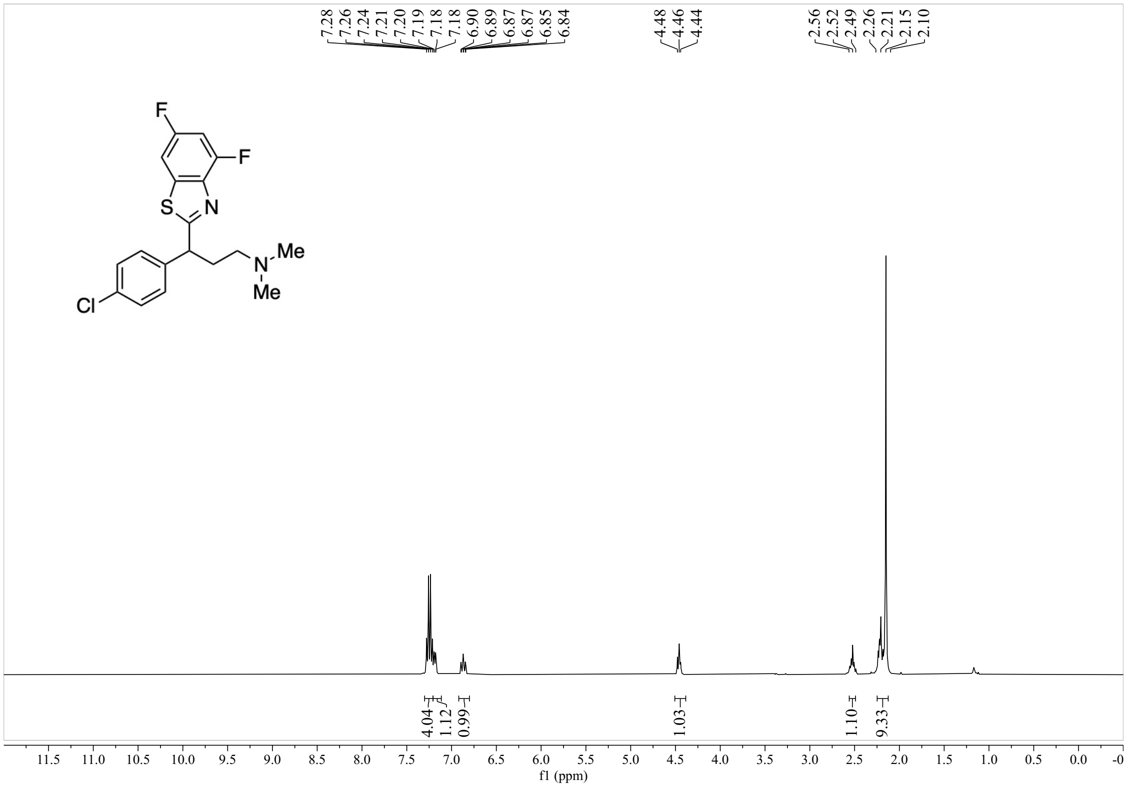
¹³C NMR of compound **43** (101 MHz, $CDCl_3$)



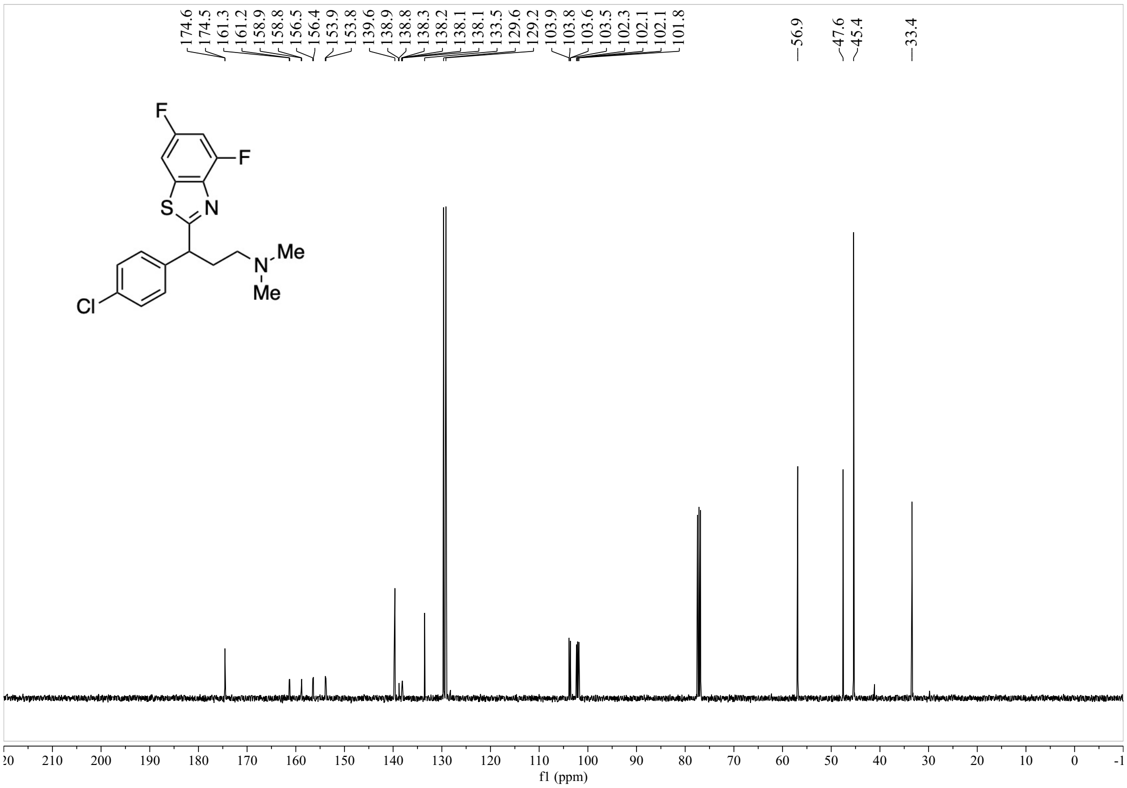
¹H NMR of compound **44** (400 MHz, CDCl₃)



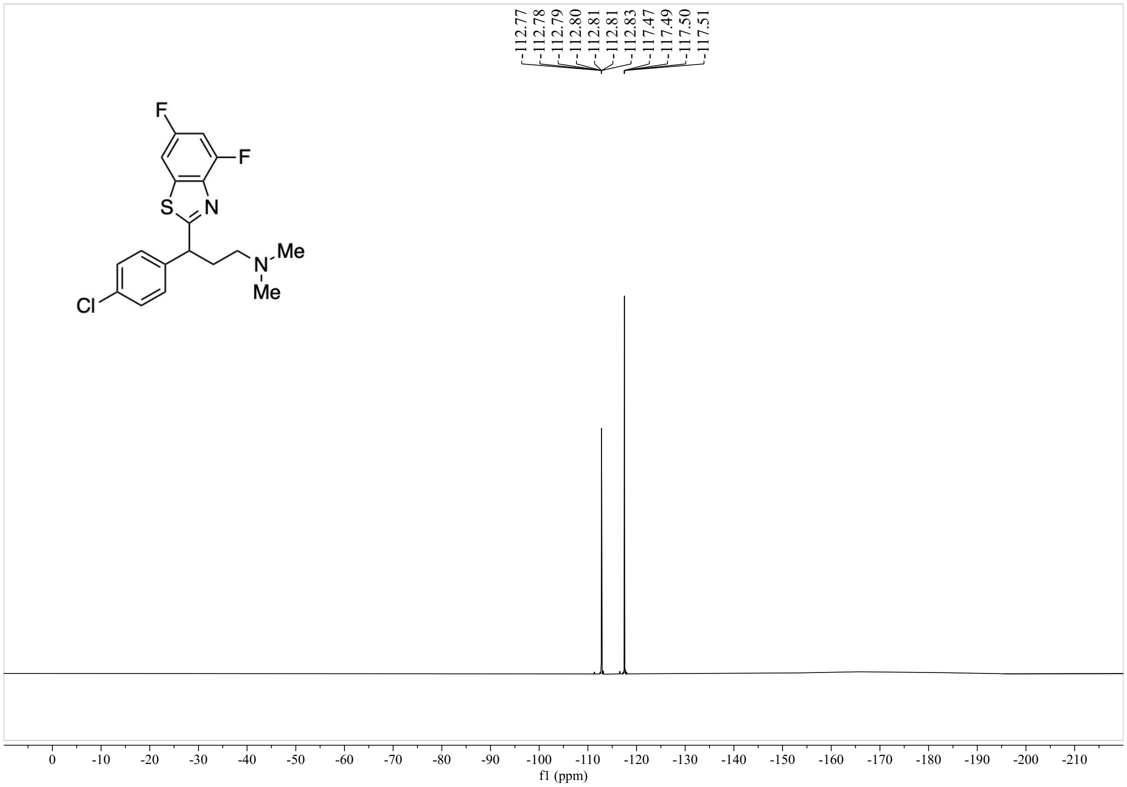
¹³C NMR of compound **44** (101 MHz, CDCl₃)



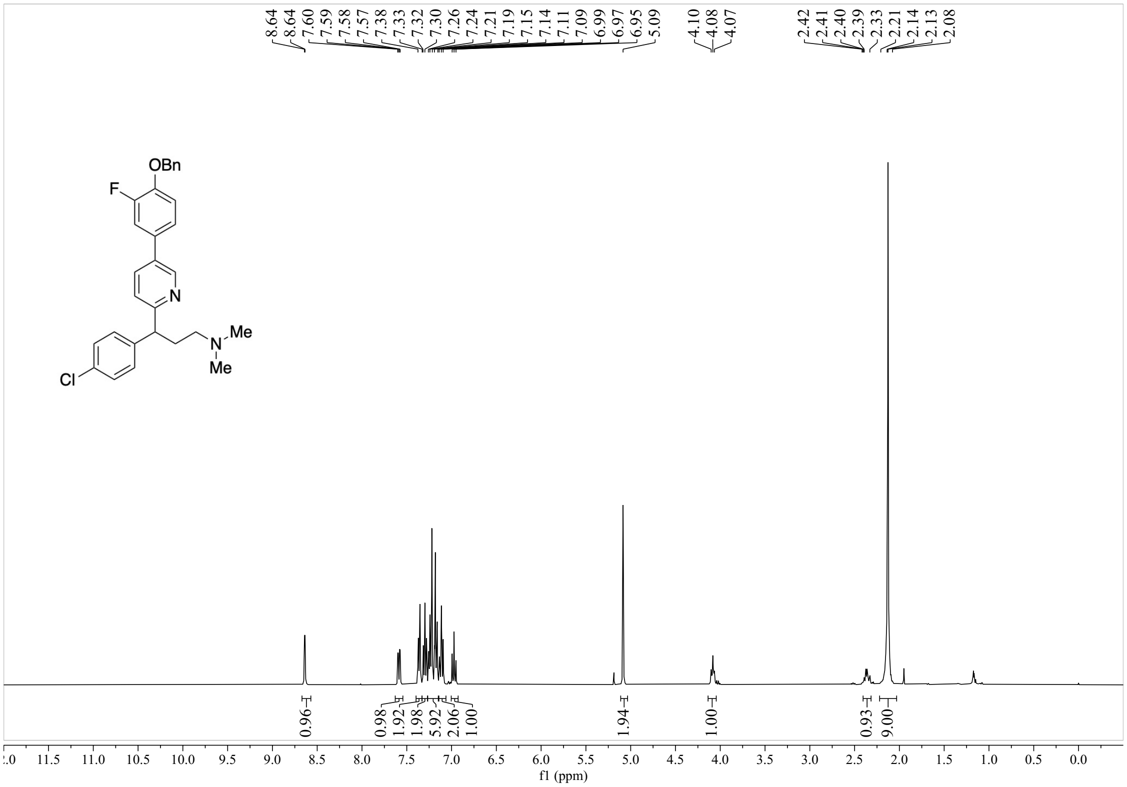
^{1}**H NMR** of compound **45** (400 MHz, CDCl$_3$)



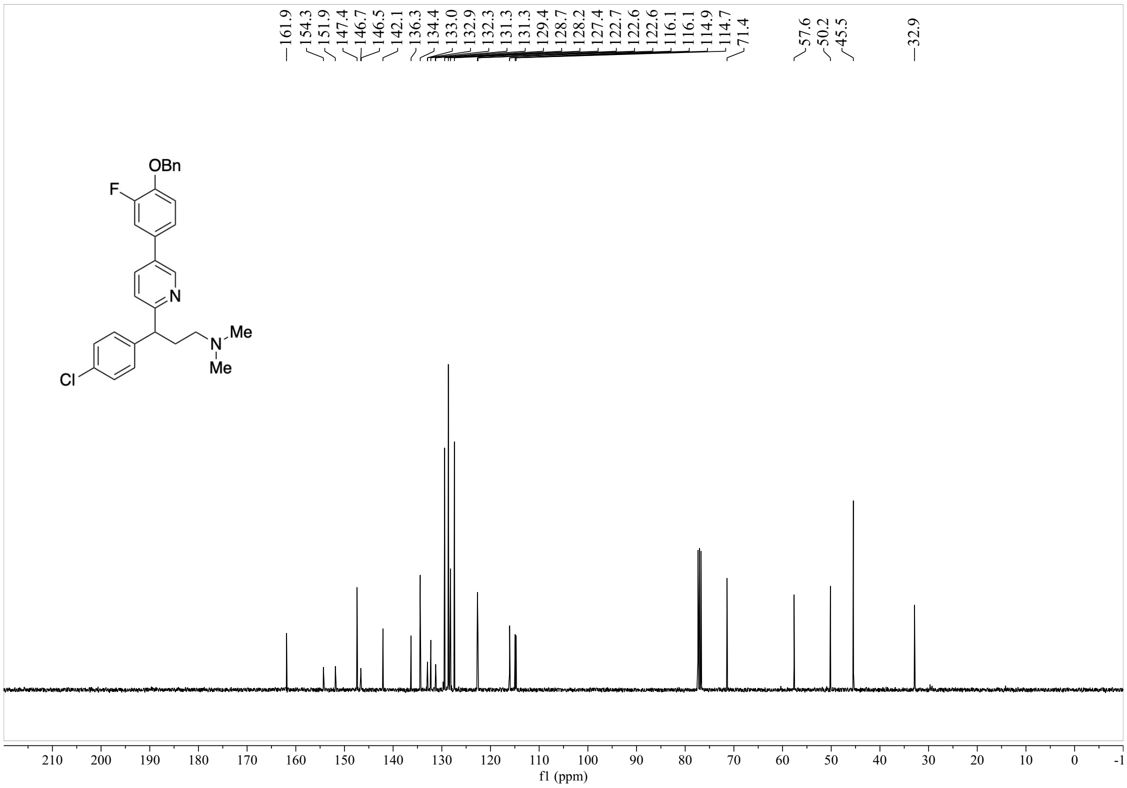
^{13}**C NMR** of compound **45** (101 MHz, CDCl$_3$)



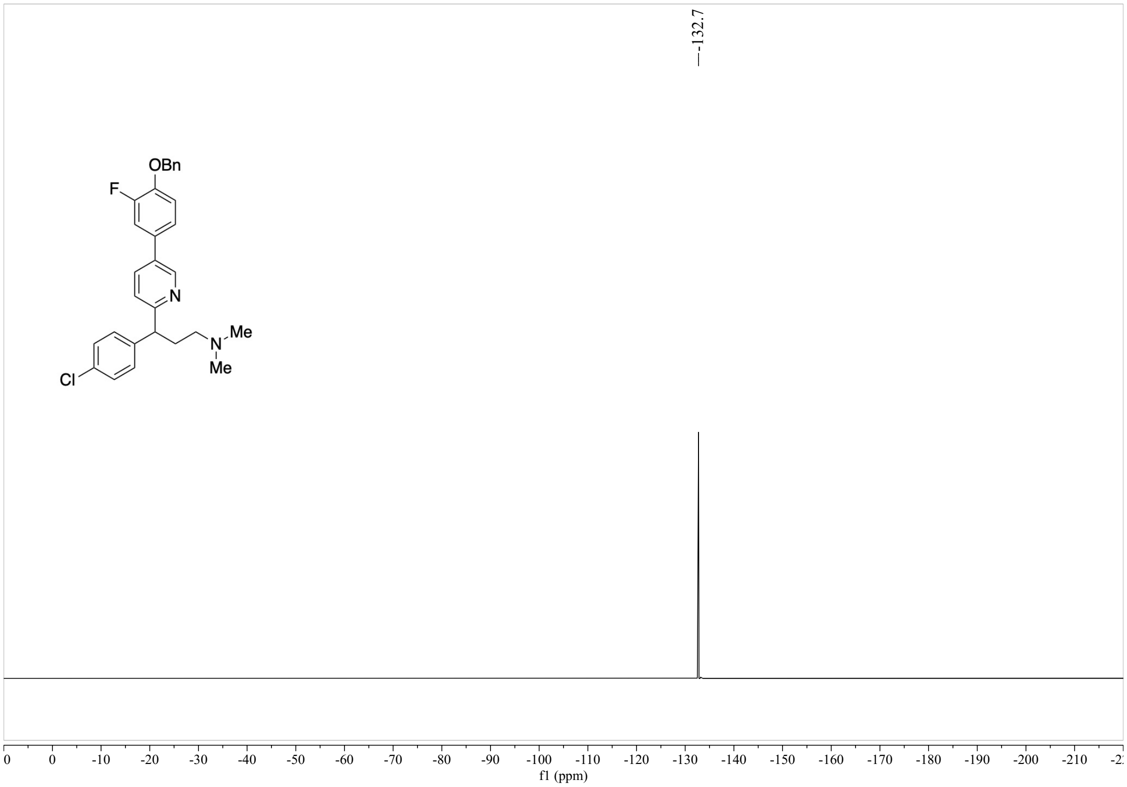
^{19}F NMR (proton coupled) of compound **45** (376 MHz, CDCl$_3$)



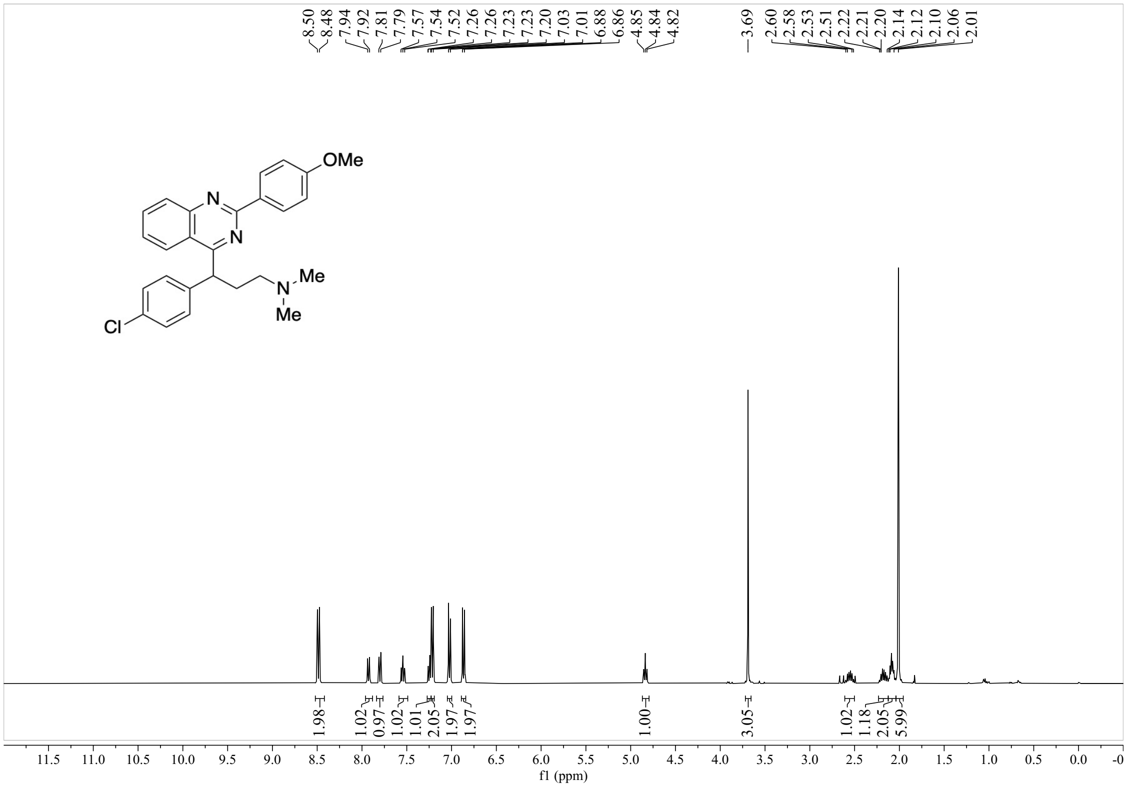
^{1}H NMR of compound **46** (400 MHz, $CDCl_3$)



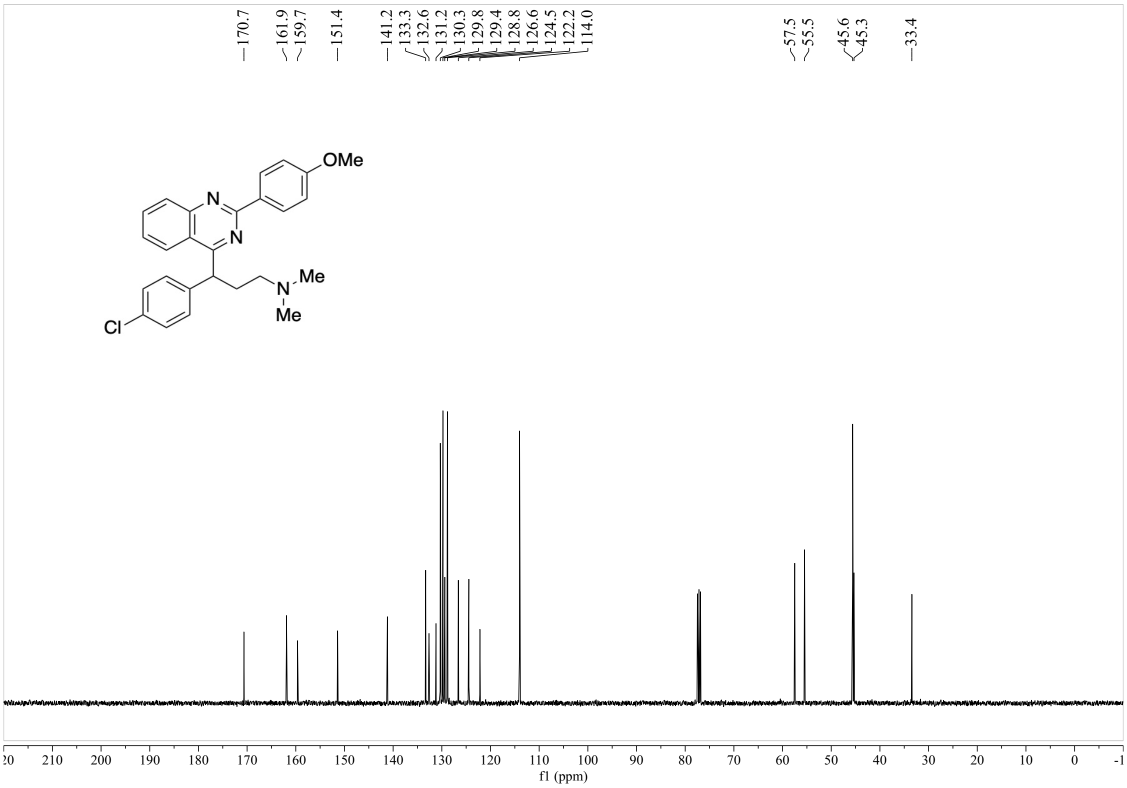
^{13}C NMR of compound **46** (101 MHz, $CDCl_3$)



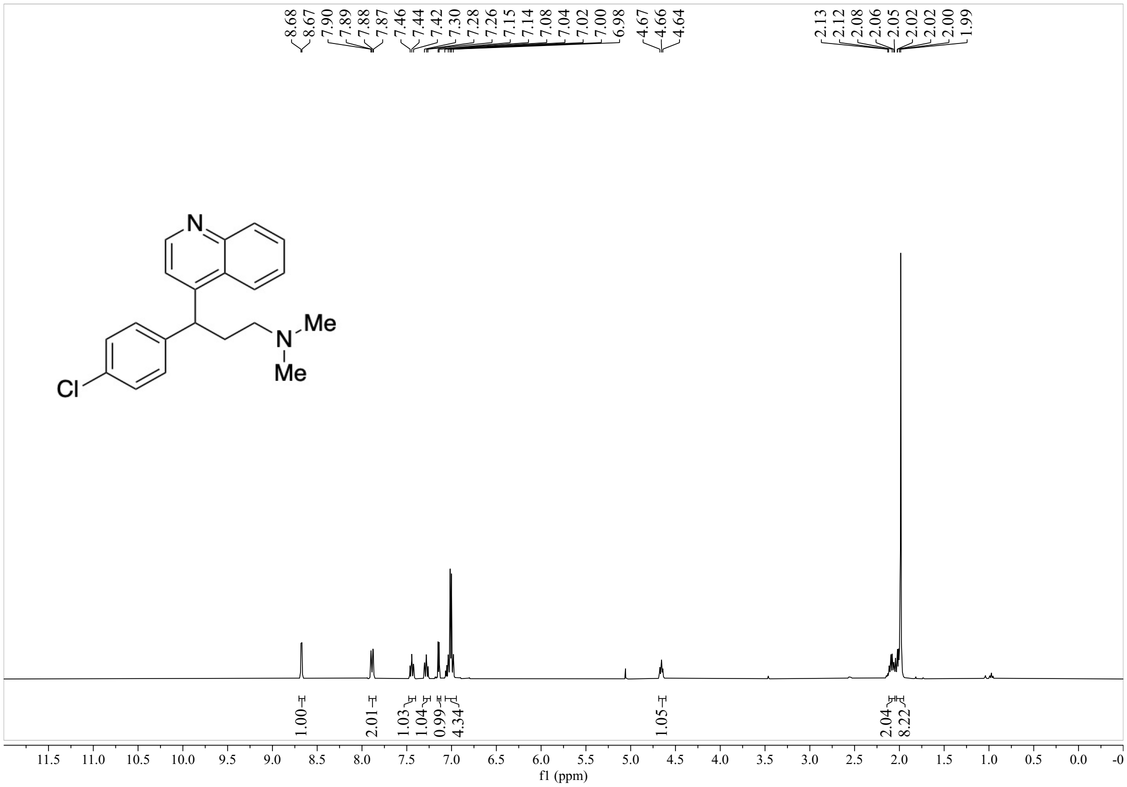
^{19}F NMR (proton decoupled) of compound 4**6** (376 MHz, $CDCl_3$)



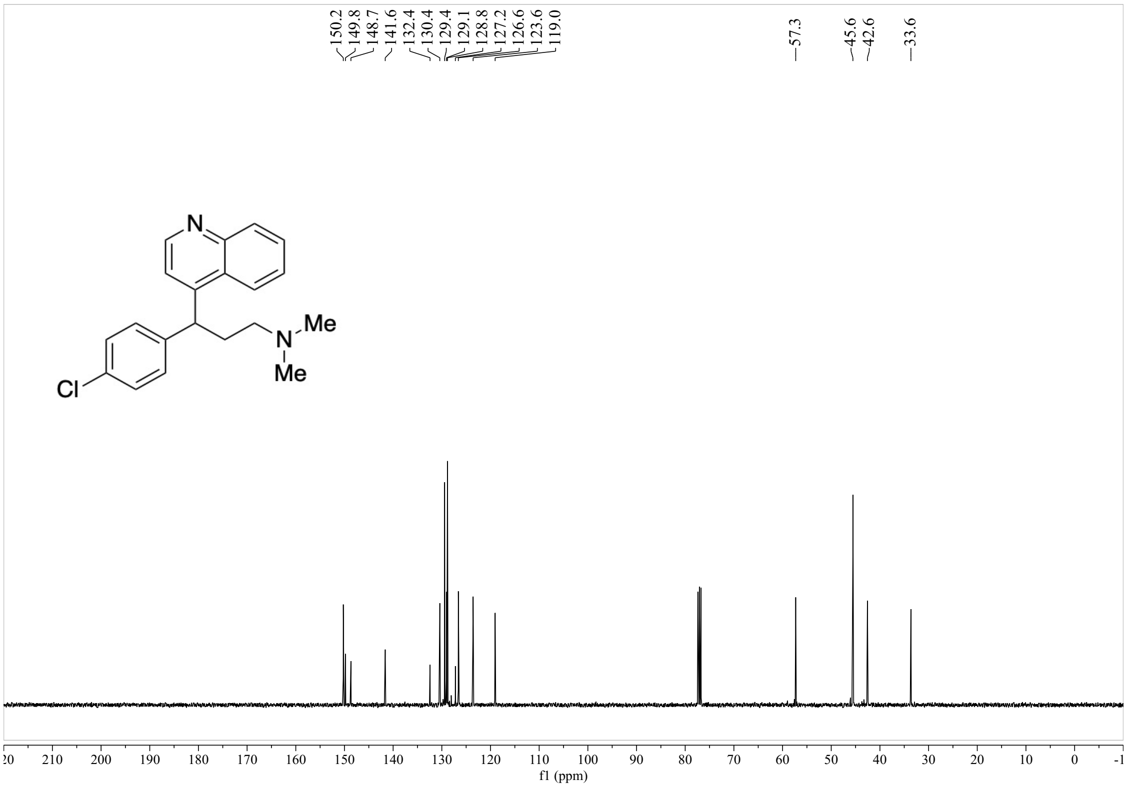
^{1}H NMR of compound **47** (400 MHz, CDCl$_3$)



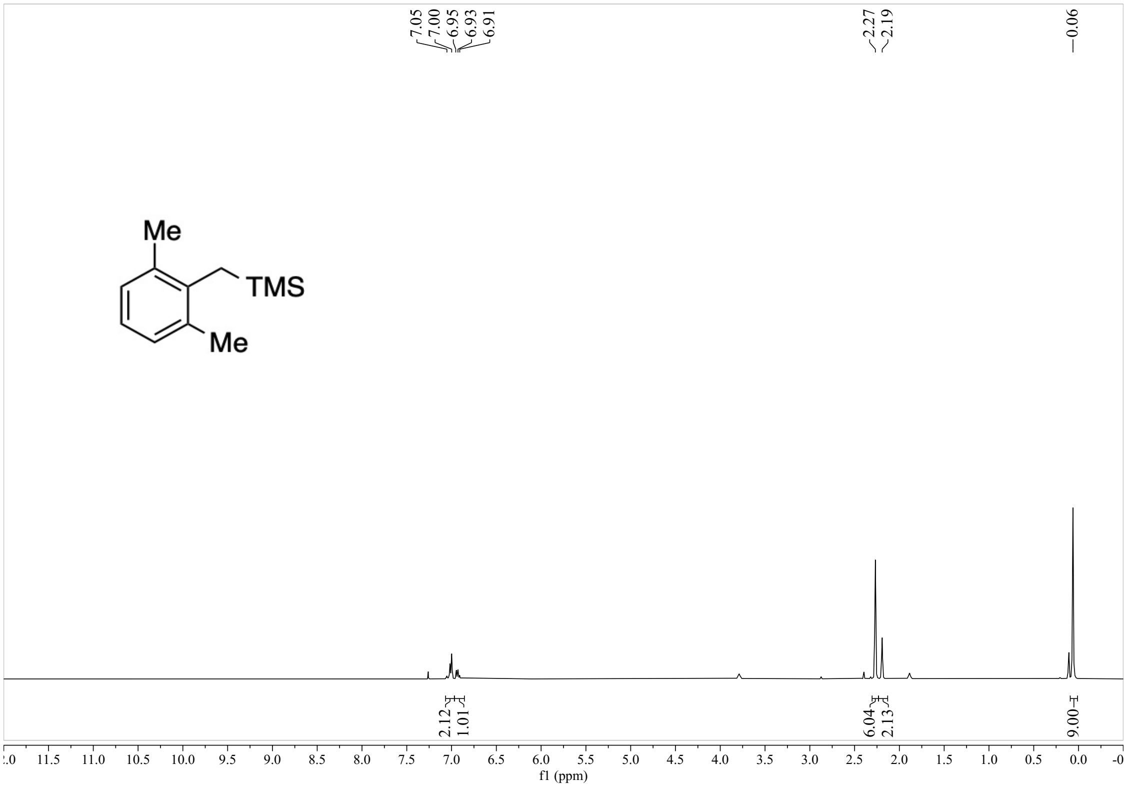
^{13}C NMR of compound **47** (101 MHz, CDCl$_3$)



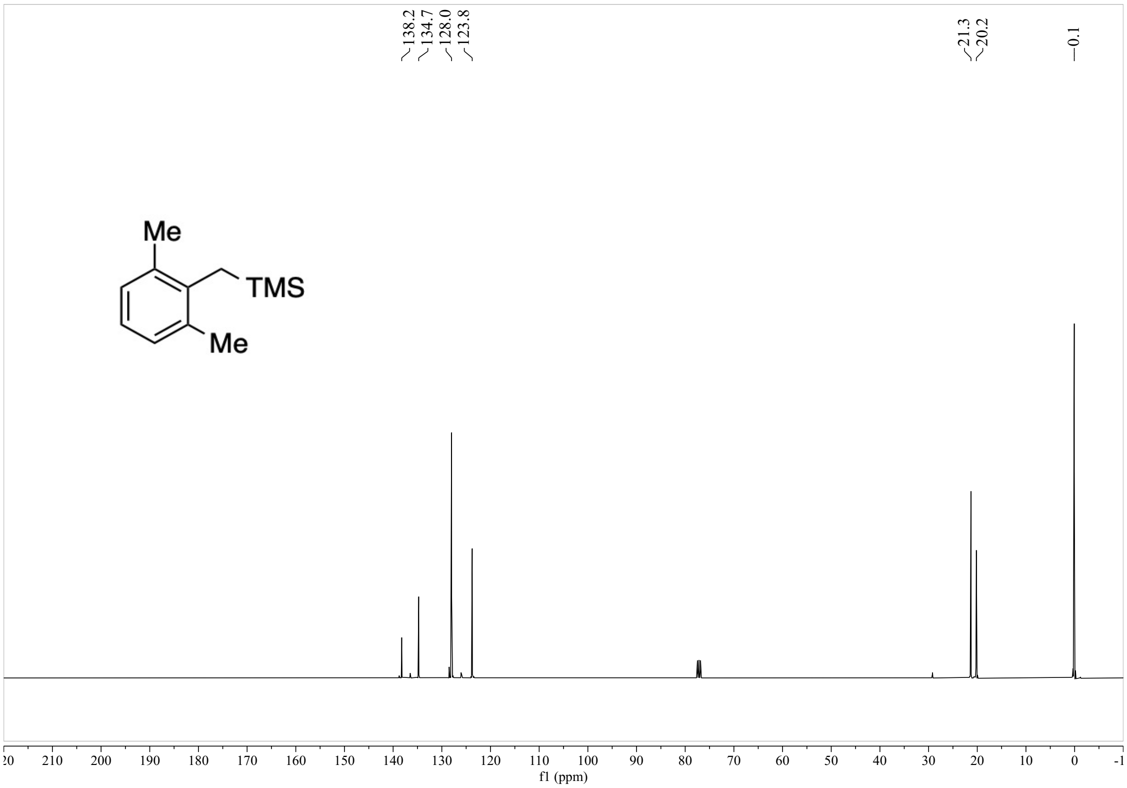
^{1}**H NMR** of compound **48** (400 MHz, CDCl$_3$)



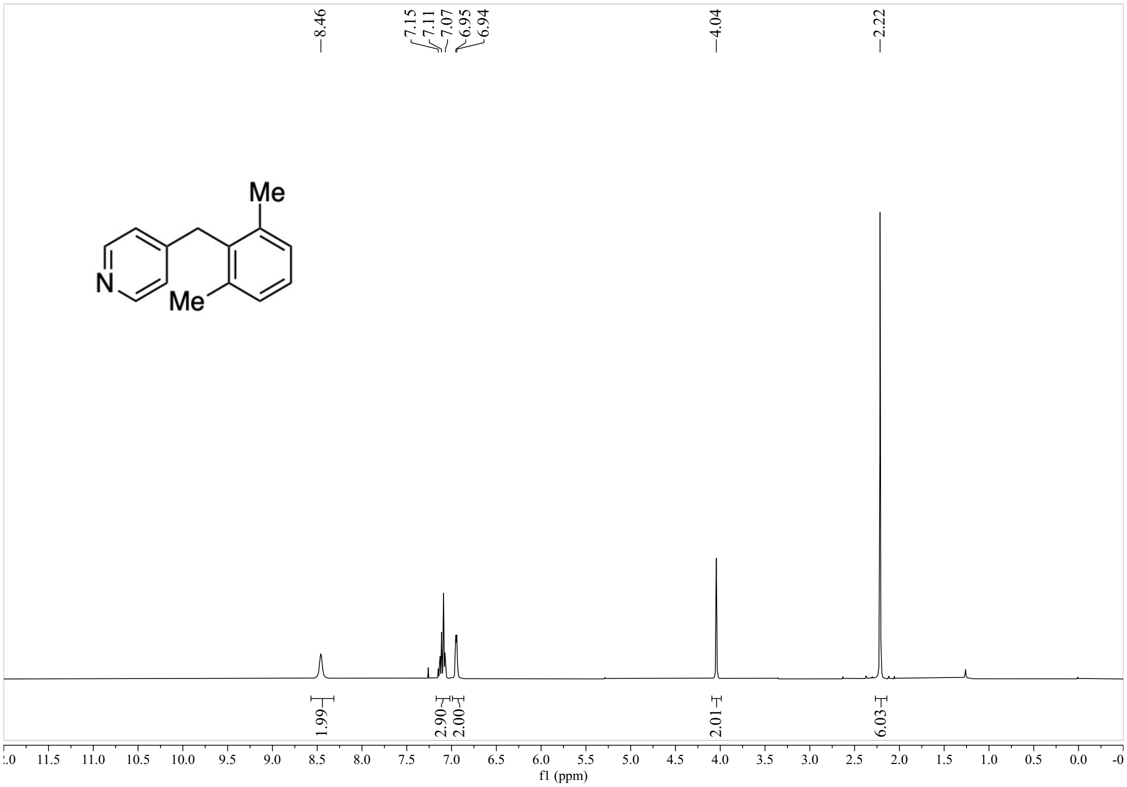
^{13}**C NMR** of compound **48** (101 MHz, CDCl$_3$)



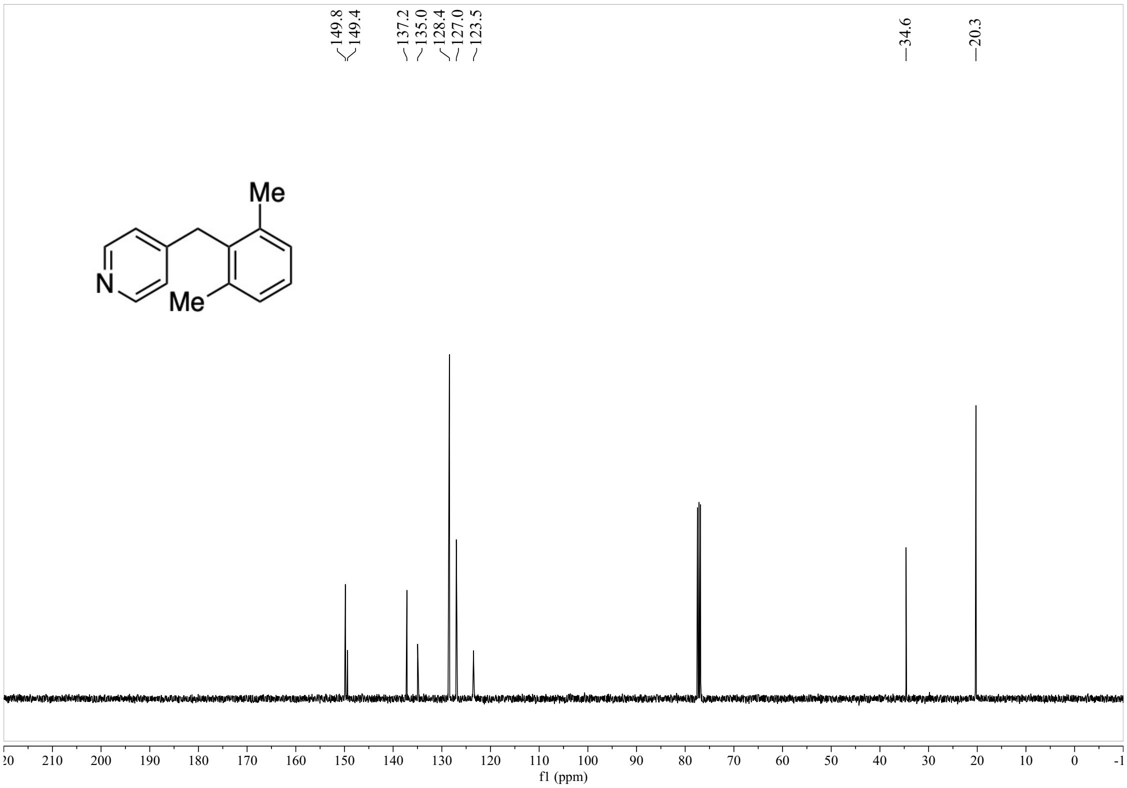
^{1}H NMR of compound **50** (400 MHz, $CDCl_3$)



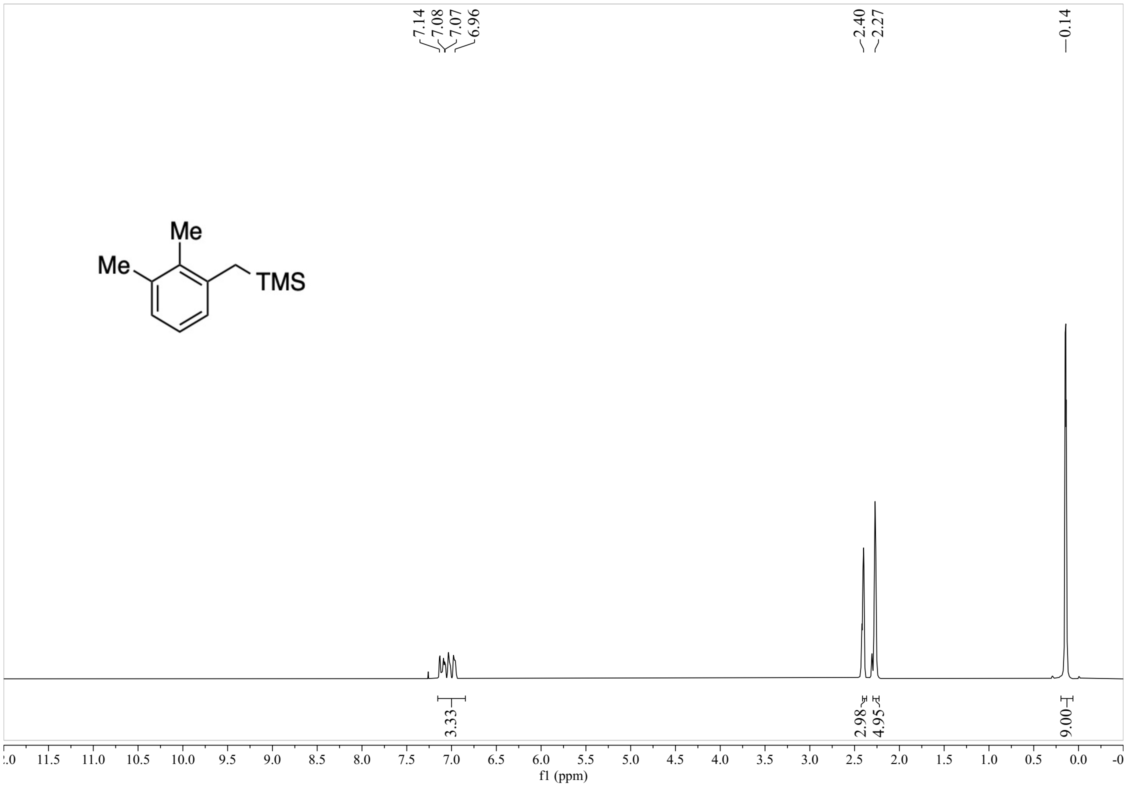
^{13}C NMR of compound **50** (101 MHz, $CDCl_3$)



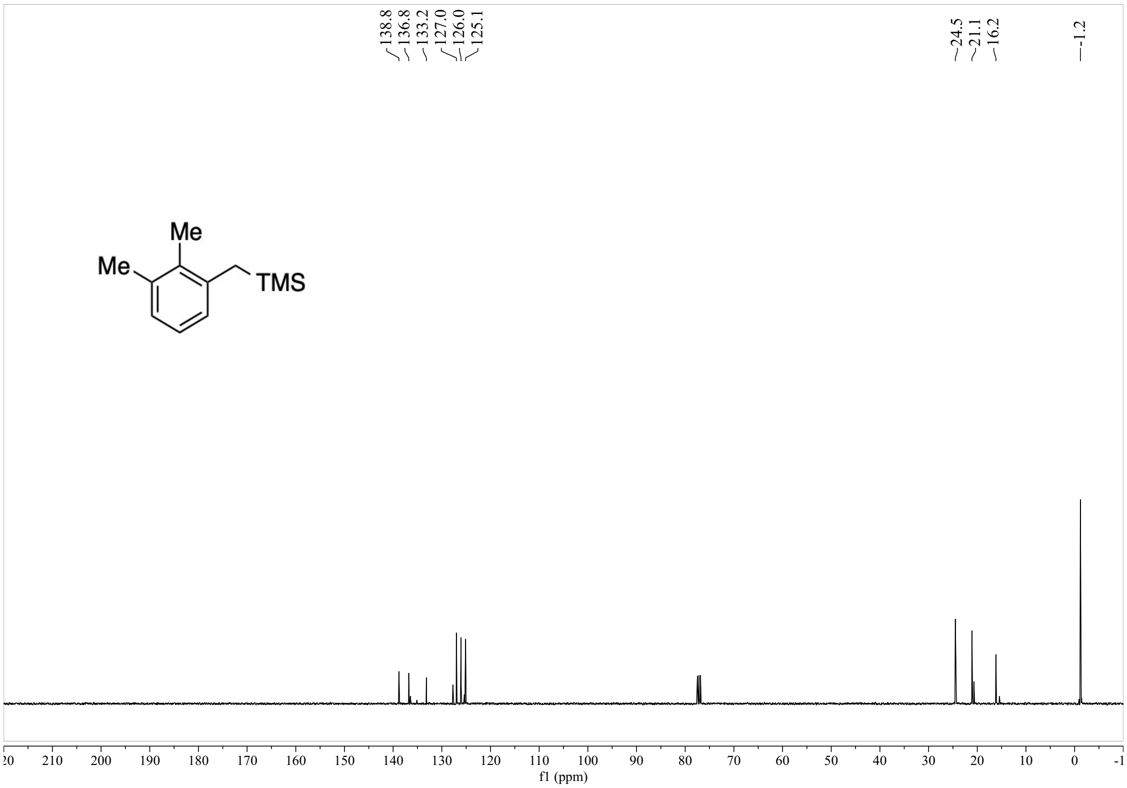
^{1}H NMR of compound **51** (400 MHz, CDCl$_3$)



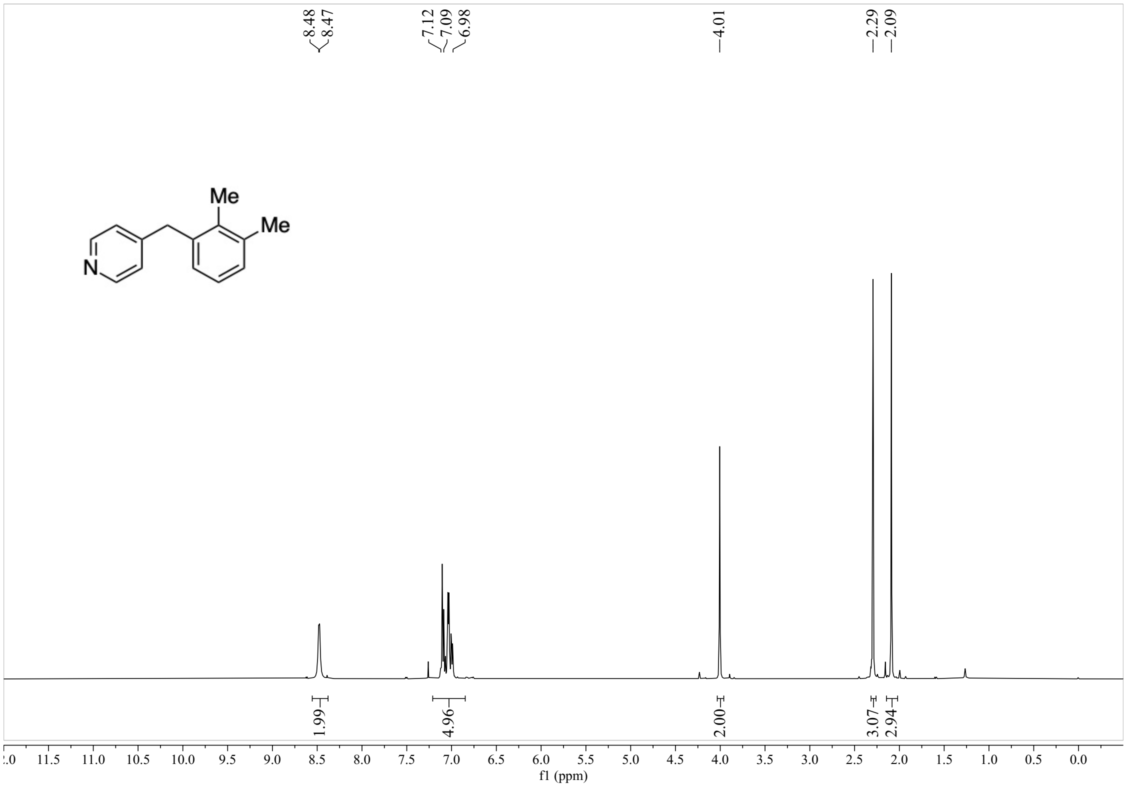
^{13}C NMR of compound **51** (101 MHz, CDCl$_3$)



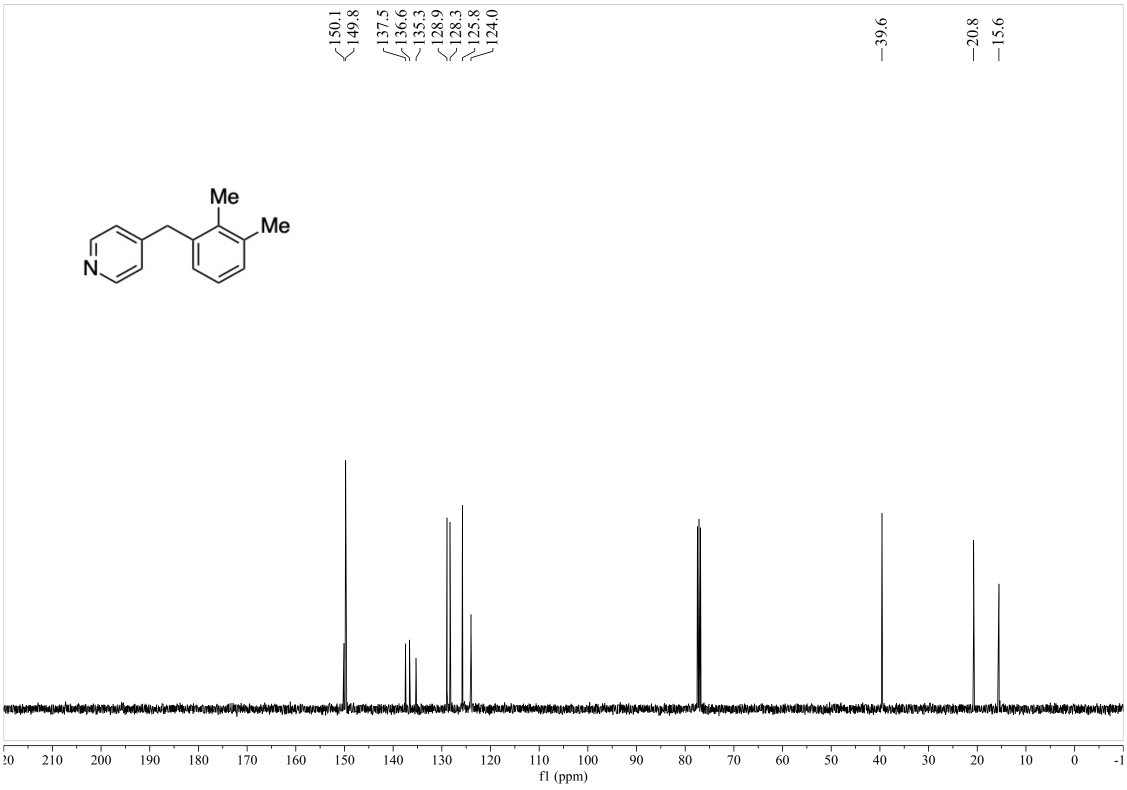
^{1}H NMR of compound **52** (400 MHz, CDCl$_3$)



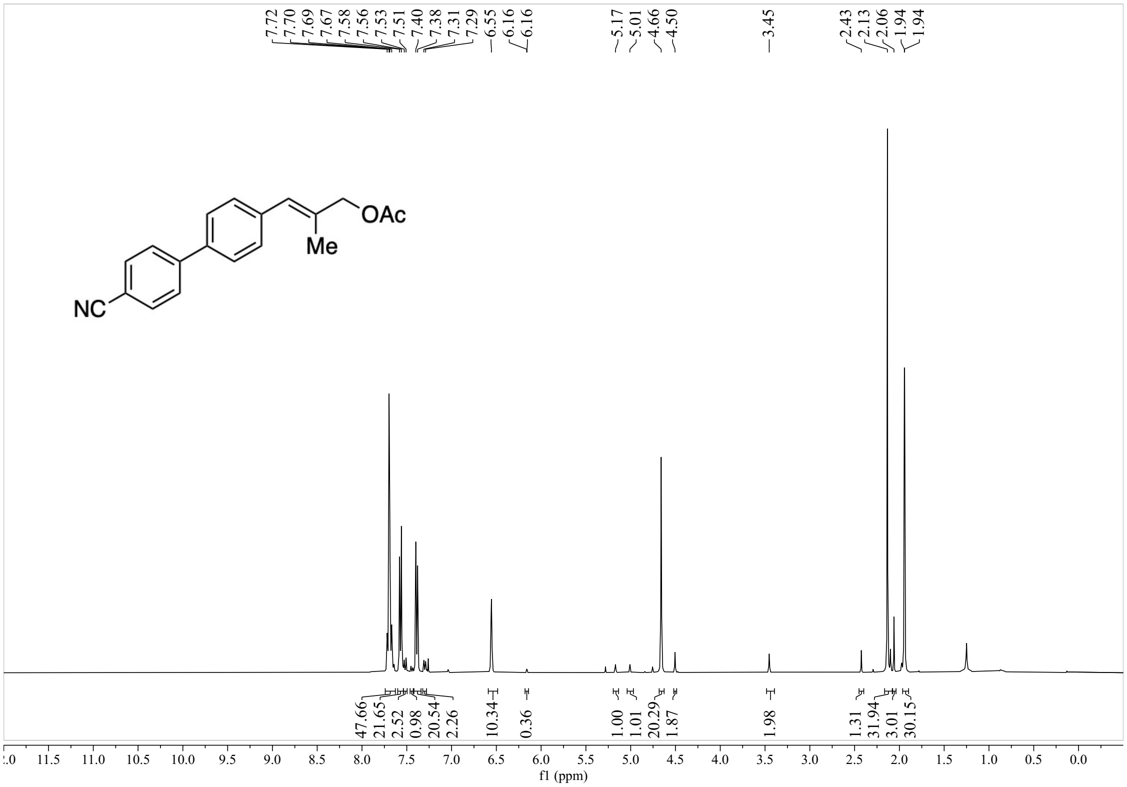
^{13}C NMR of compound **52** (101 MHz, CDCl$_3$)



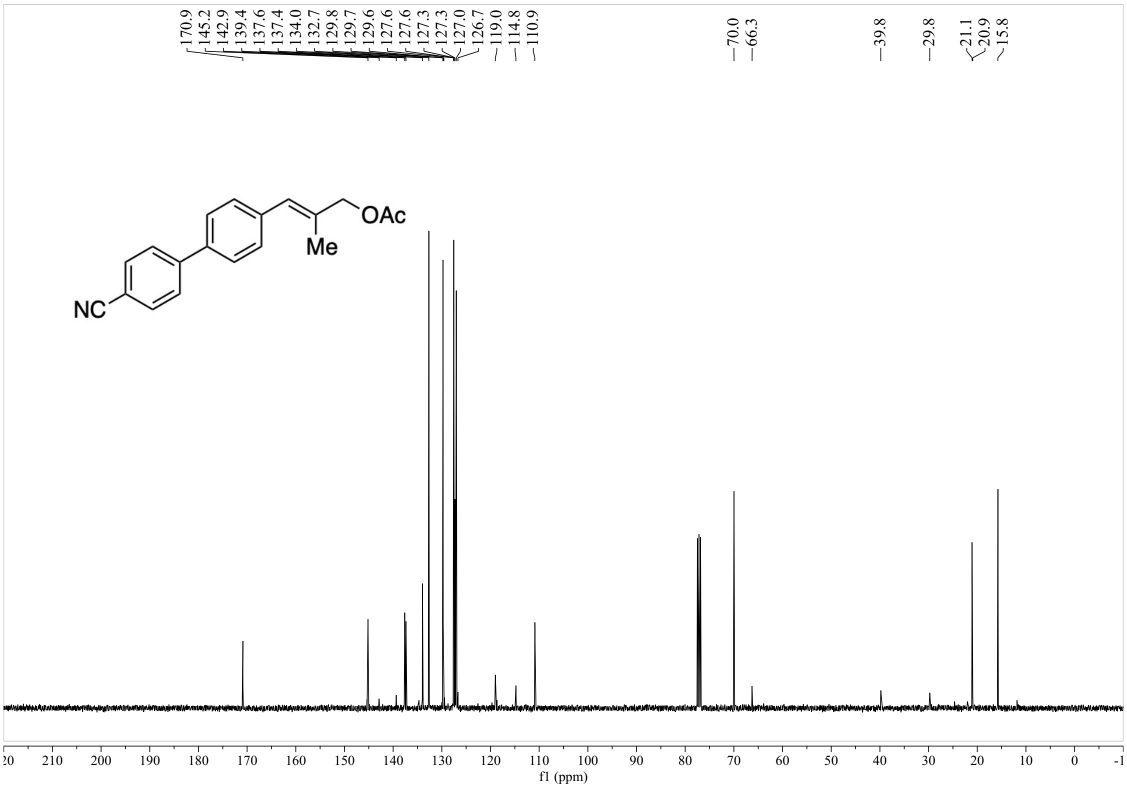
^{1}**H NMR** of compound **53** (400 MHz, CDCl$_3$)



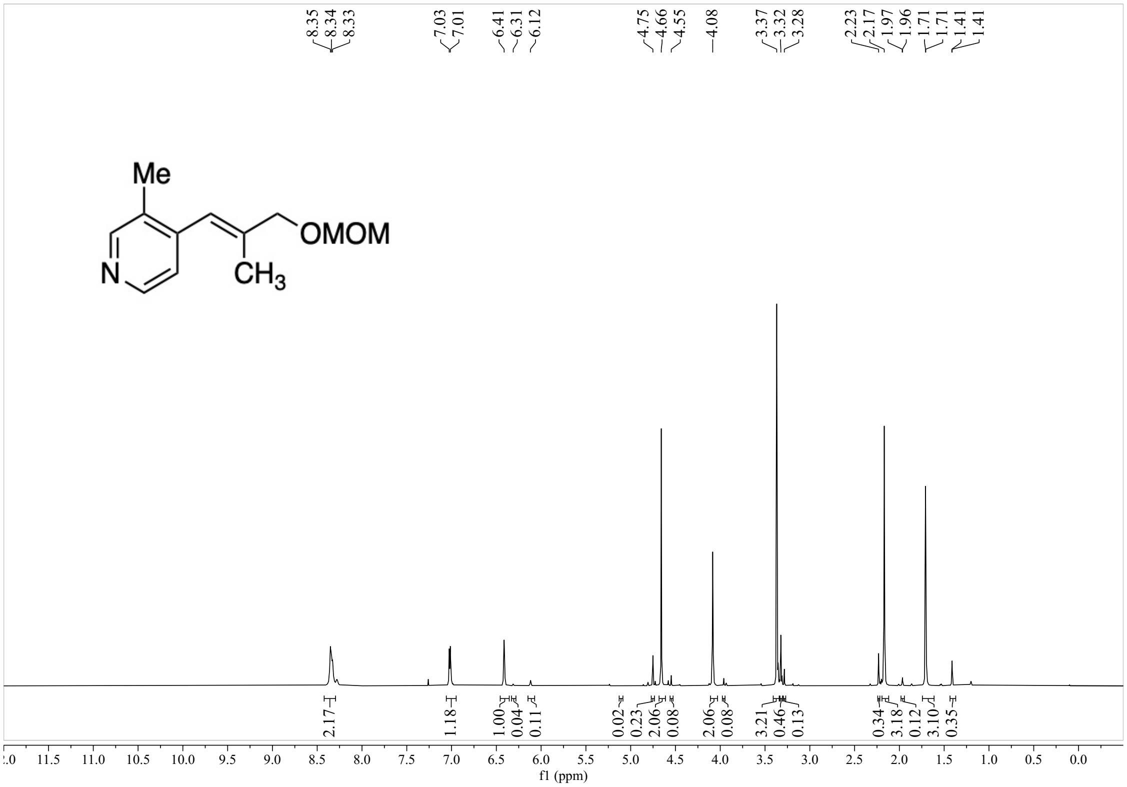
^{13}**C NMR** of compound **53** (101 MHz, CDCl$_3$)



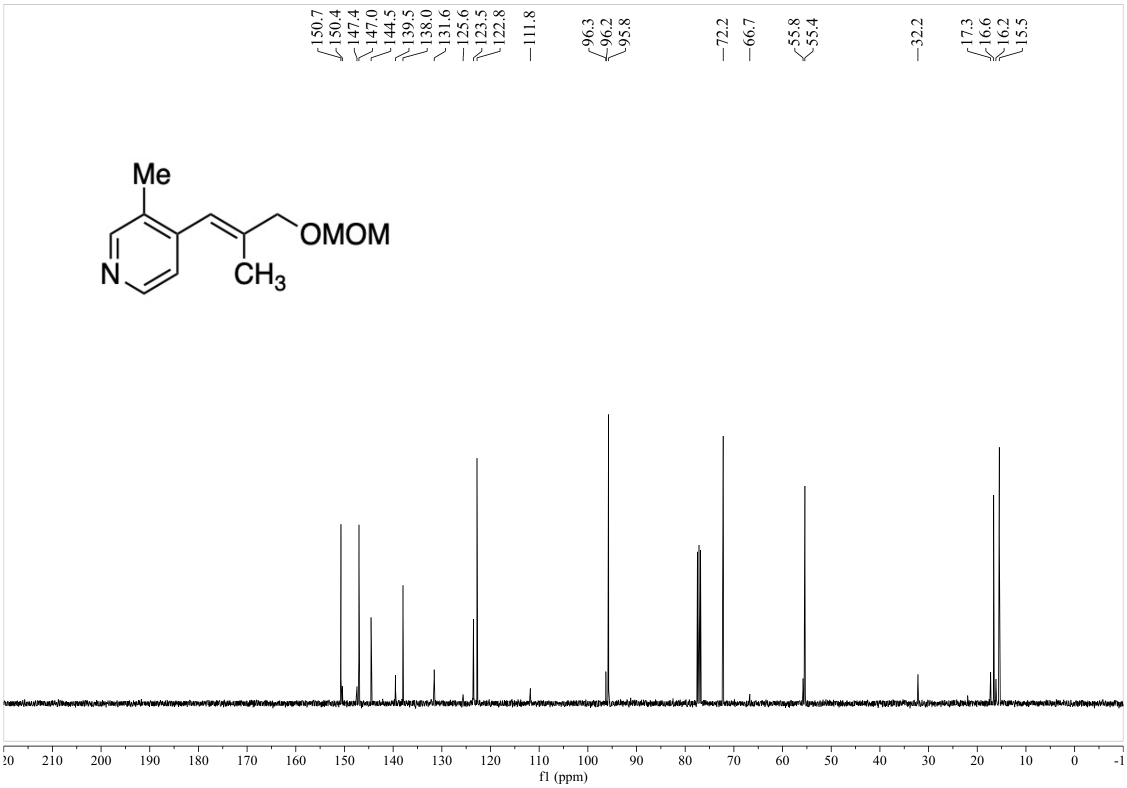
^{1}**H NMR** of compound **54** with minor isomers (400 MHz, CDCl$_3$)



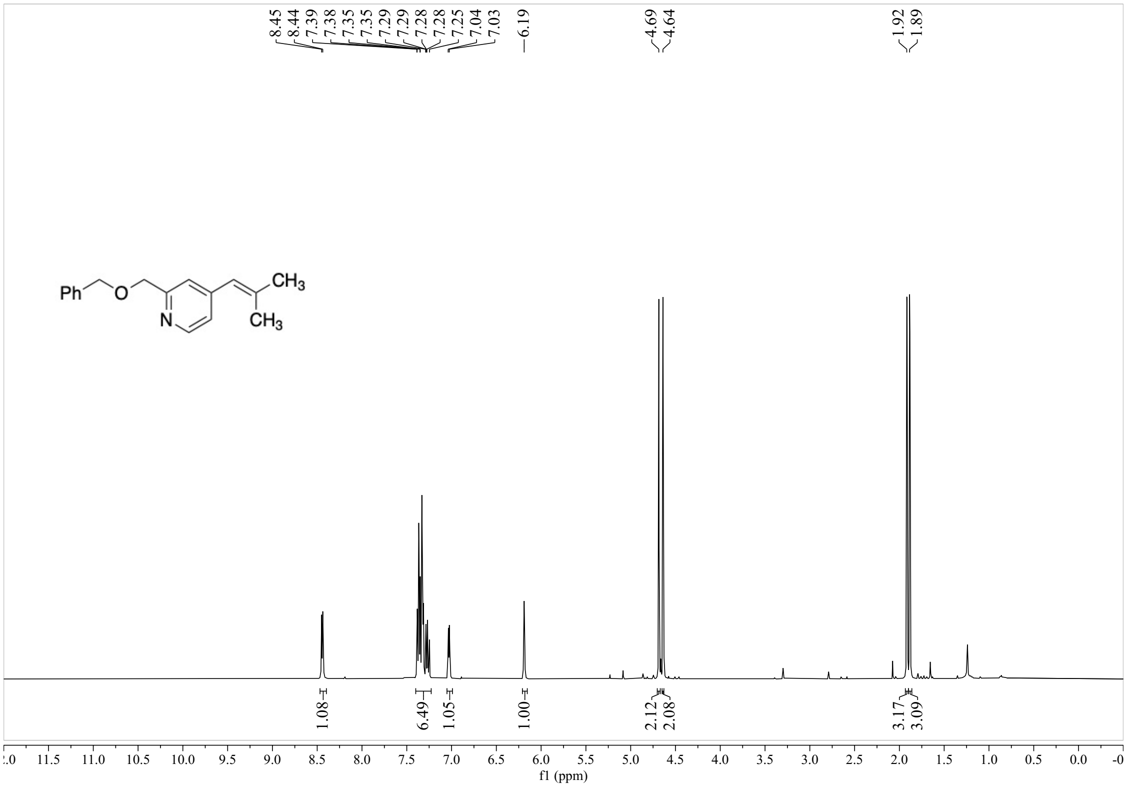
^{13}**C NMR** of compound **54** with minor isomers (101 MHz, CDCl$_3$)



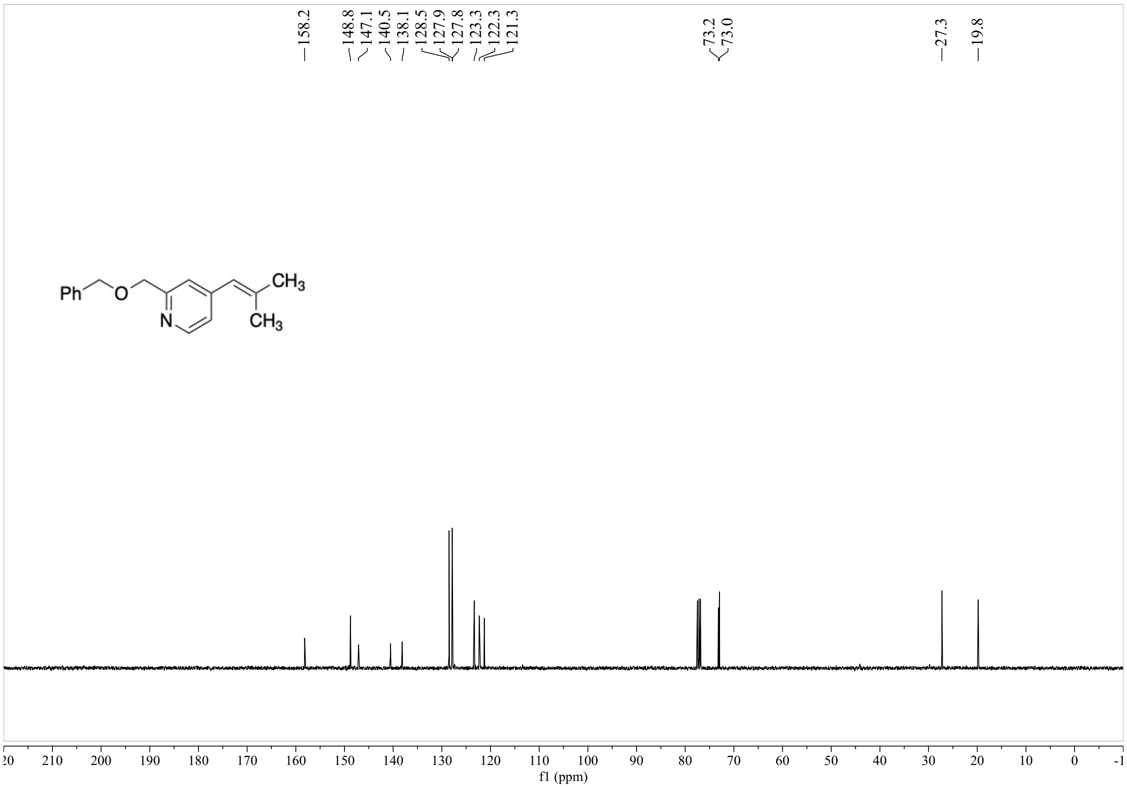
^{1}H NMR of compound **55** with minor isomers (400 MHz, CDCl$_3$)



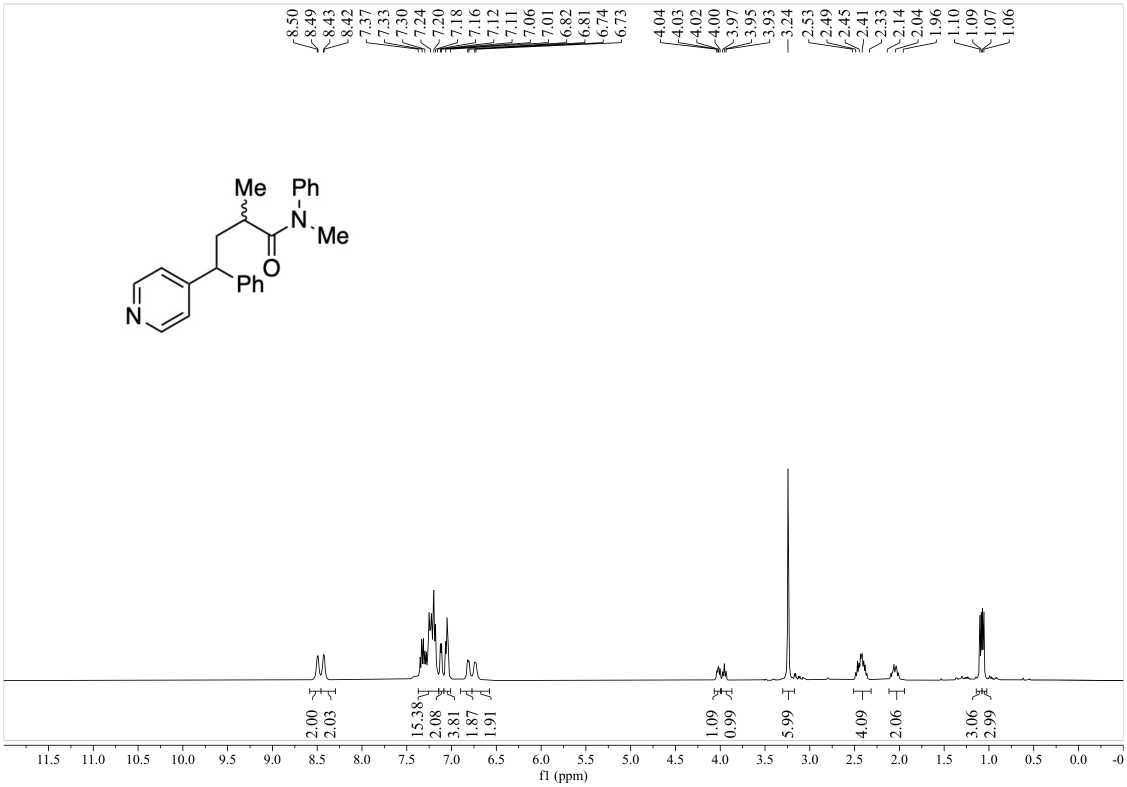
^{13}C NMR of compound **55** with minor isomers (101 MHz, CDCl$_3$)



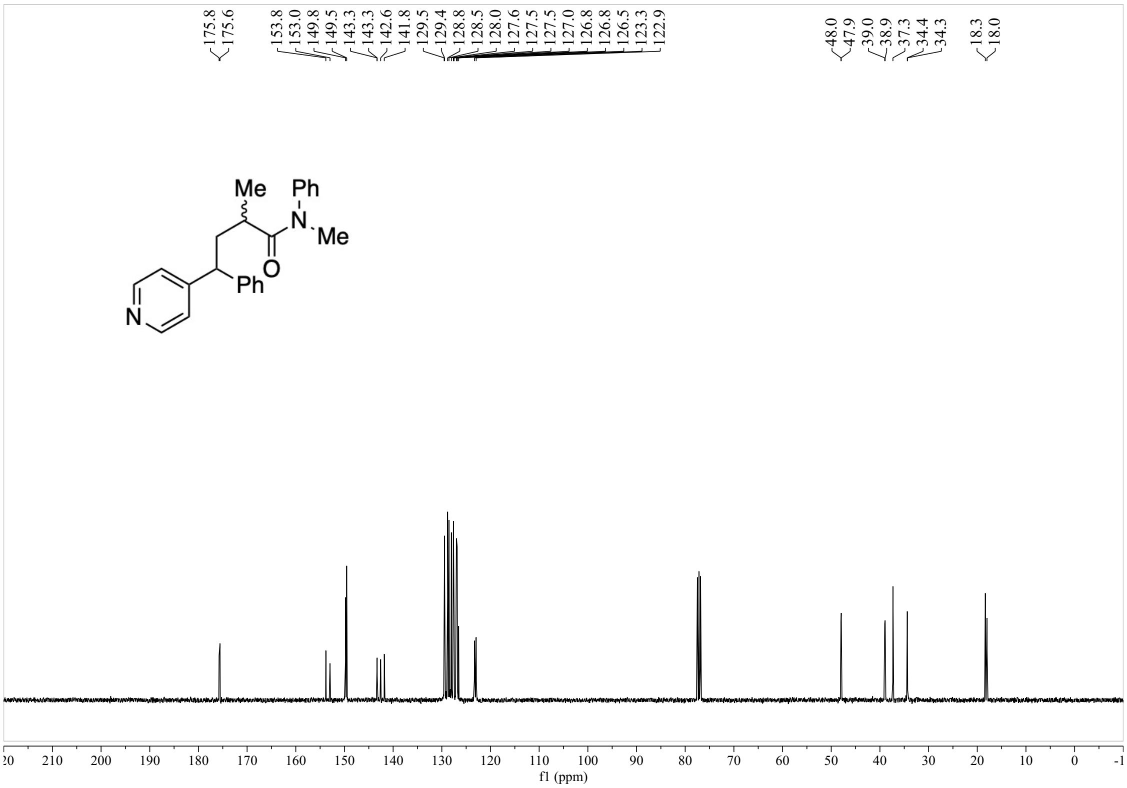
^{1}H NMR of compound **56** (400 MHz, CDCl$_3$)



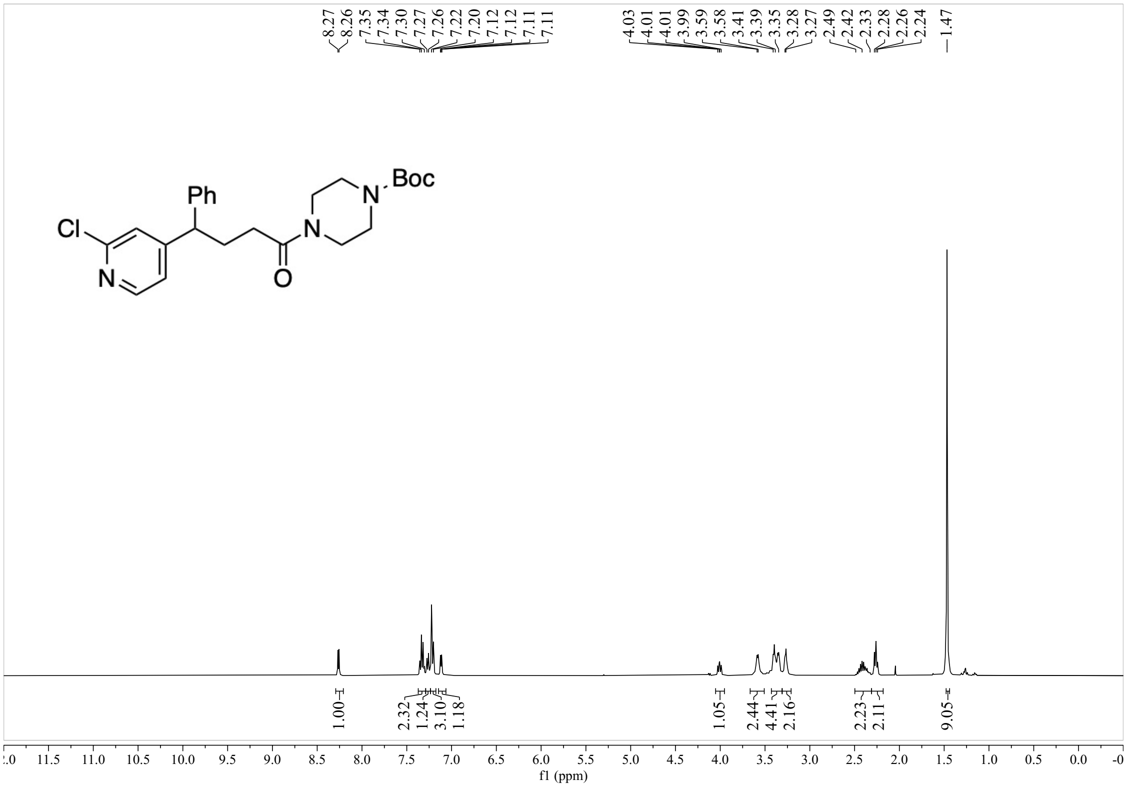
^{13}C NMR of compound **56** (101 MHz, CDCl$_3$)



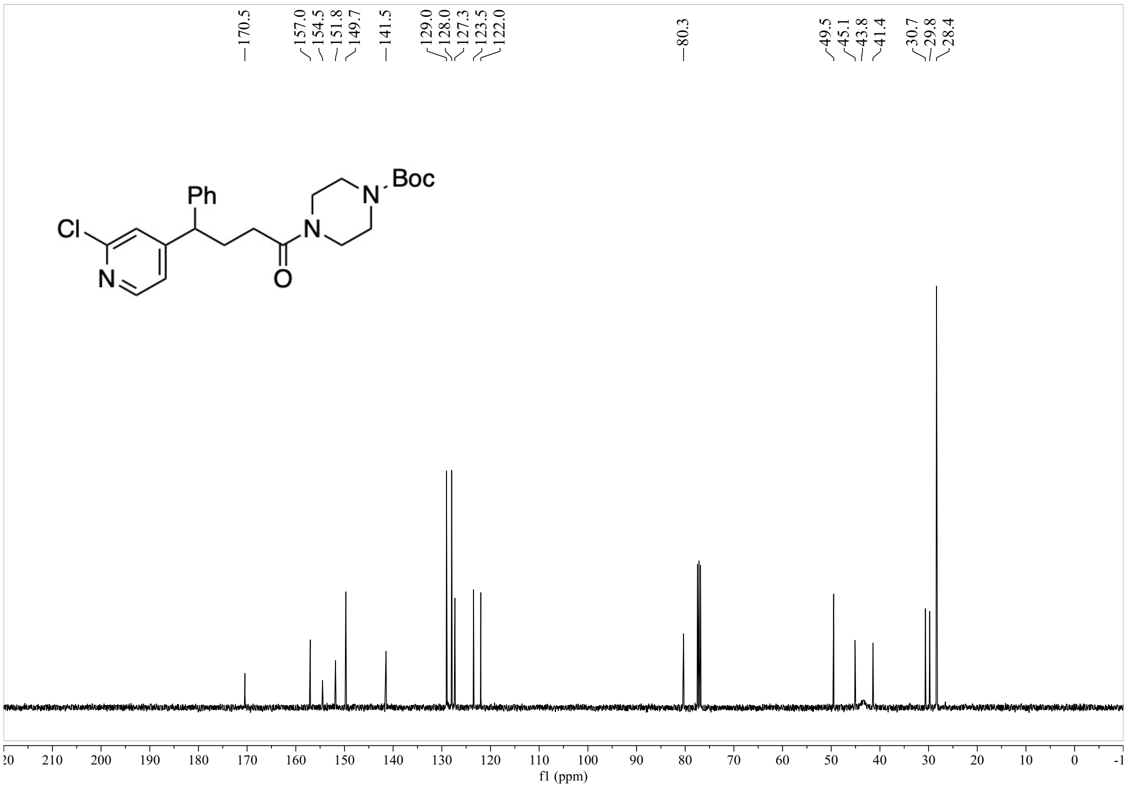
^{1}**H NMR** of compound **57** as a 1:1 diastereomeric ratio (400 MHz, CDCl$_3$)



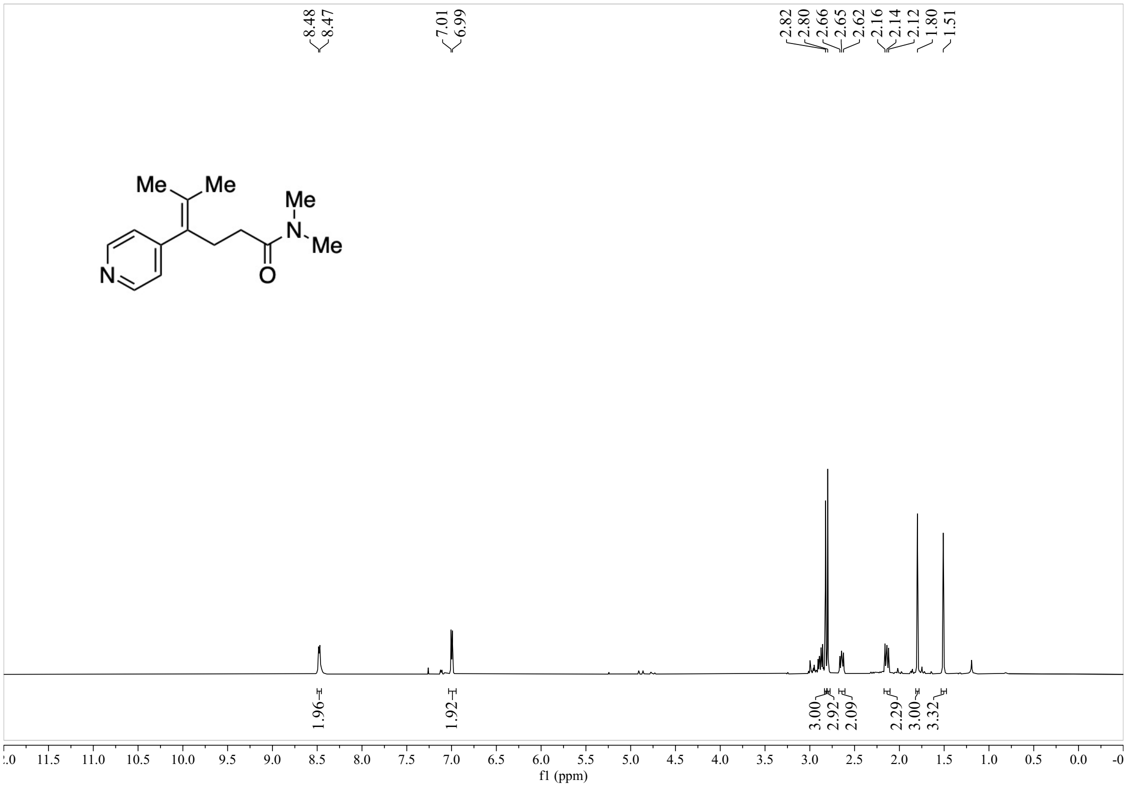
^{13}**C NMR** of compound **57** as a 1:1 diastereomeric ratio (101 MHz, CDCl$_3$)



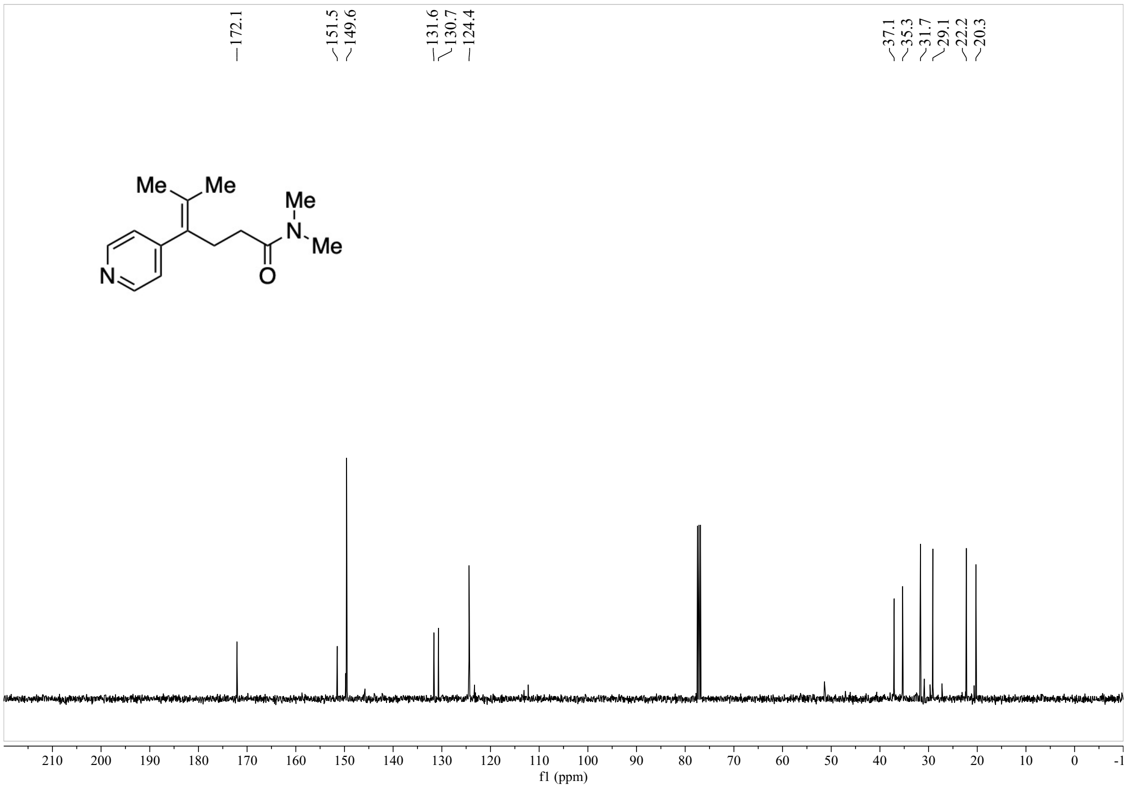
^{1}**H NMR** of compound **58** (400 MHz, CDCl$_3$)



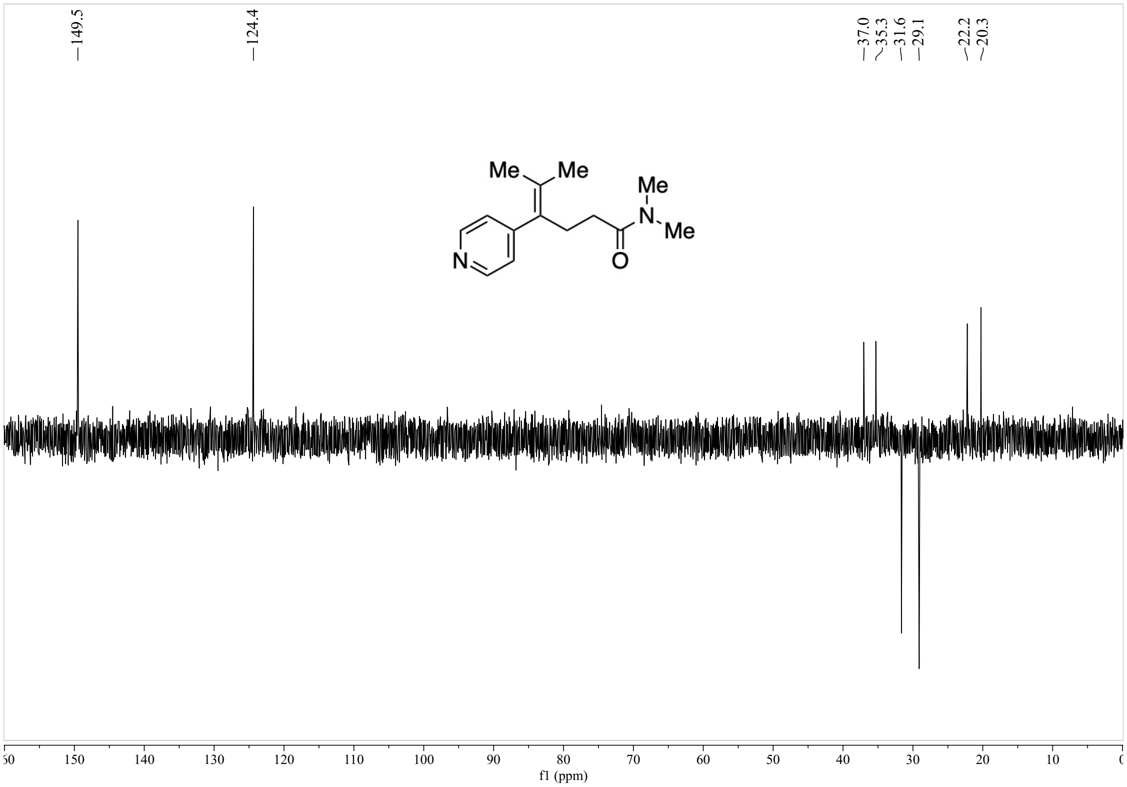
^{13}**C NMR** of compound **58** (101 MHz, CDCl$_3$)



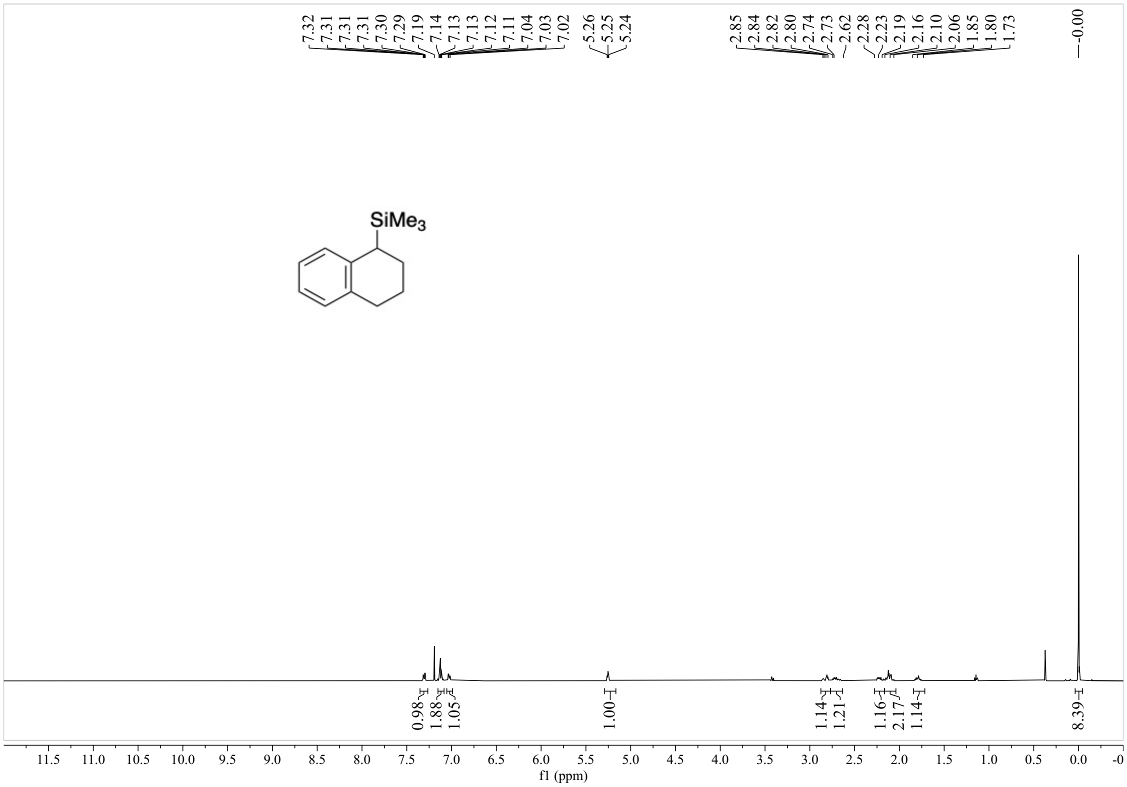
^{1}H NMR of compound **59** (400 MHz, CDCl$_3$)



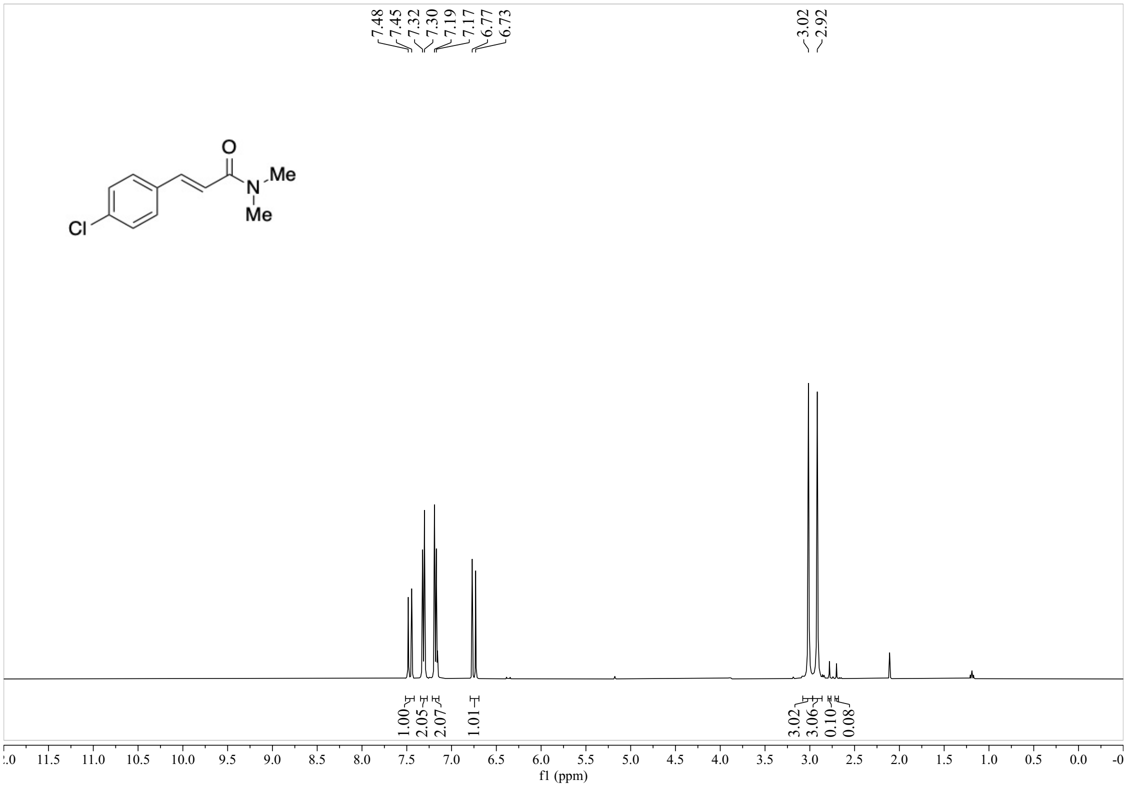
^{13}C NMR of compound **59** (101 MHz, CDCl$_3$)



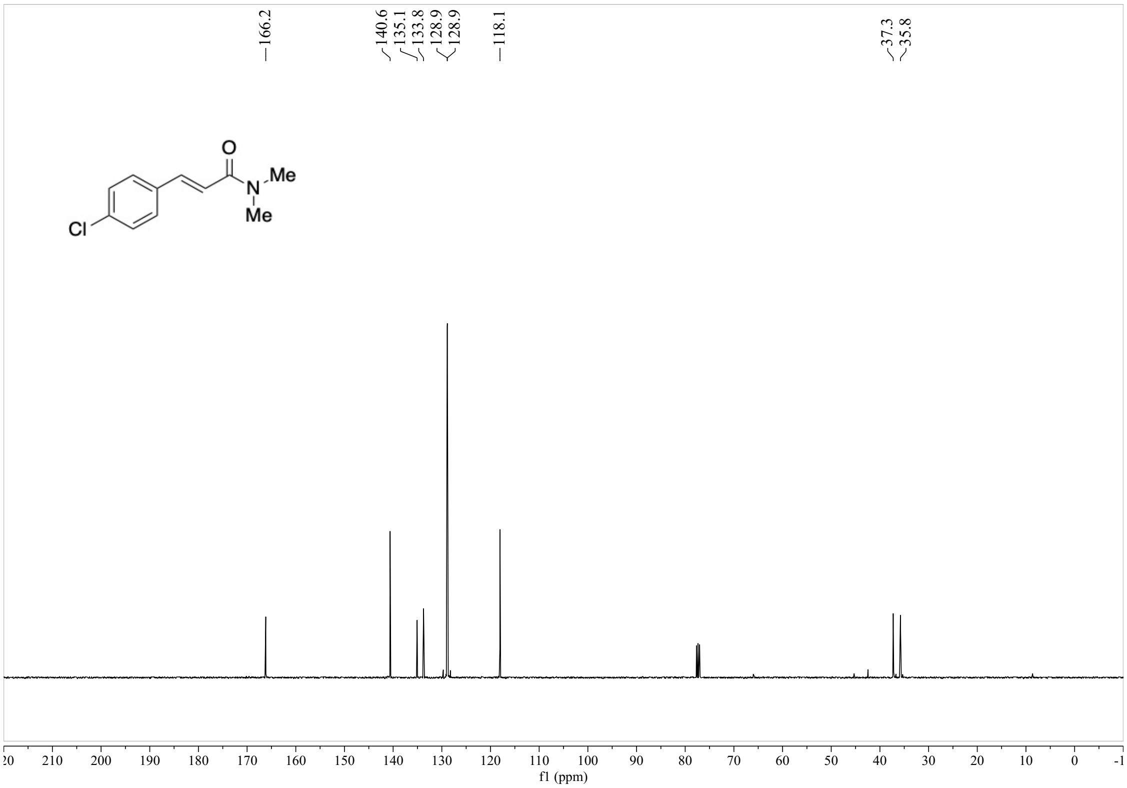
DEPT-135 NMR of compound **59** (400 MHz, $CDCl_3$)



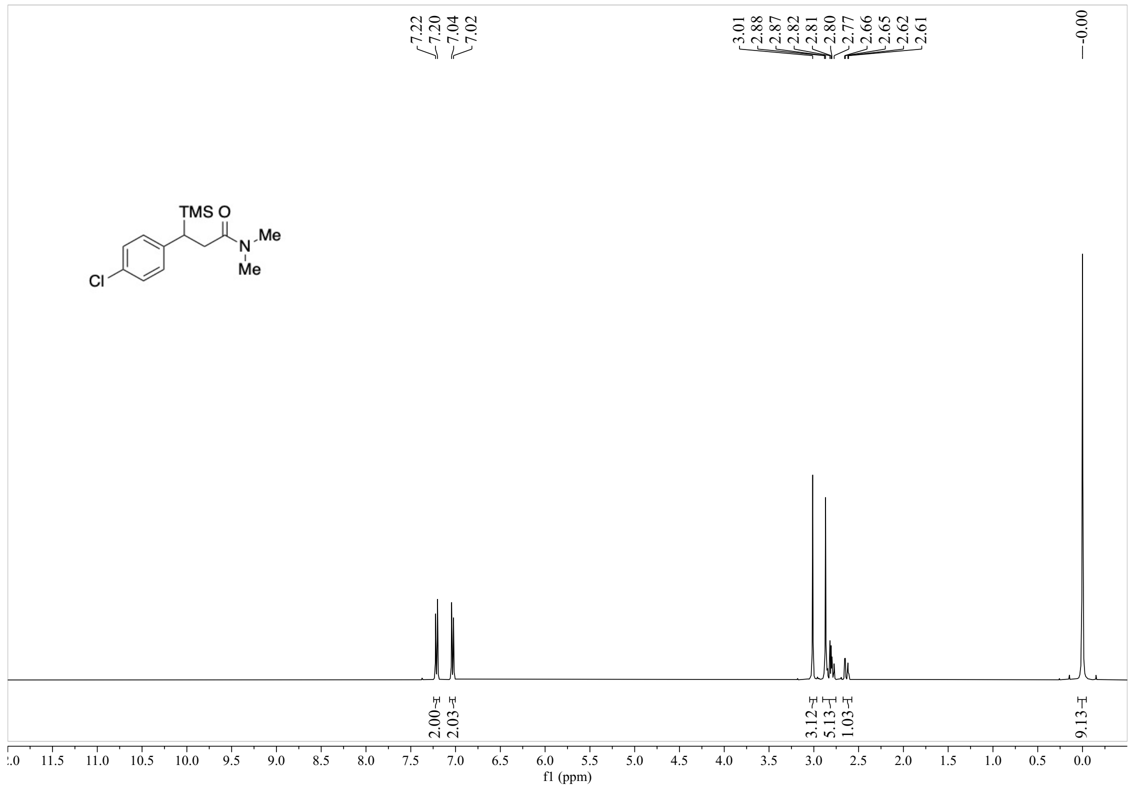
^{1}H NMR of compound **SI-2** (400 MHz, $CDCl_3$)



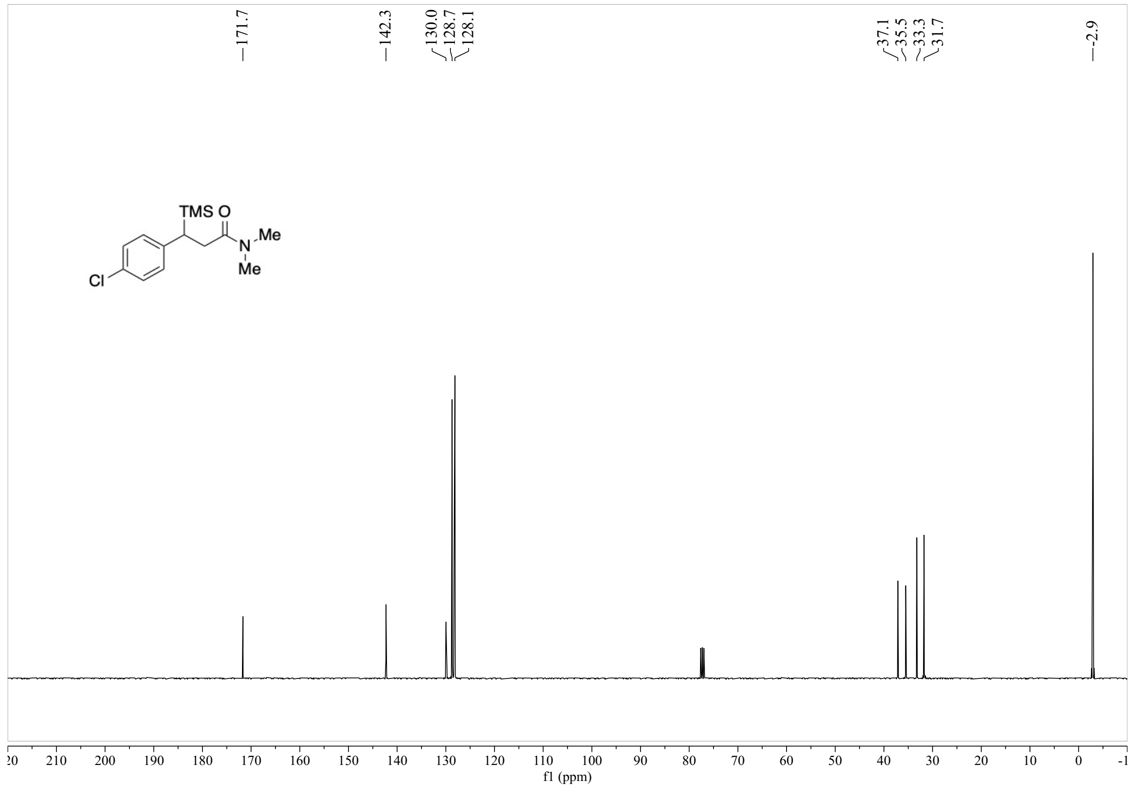
^{1}H NMR of compound **SI-3** (400 MHz, CDCl$_3$)



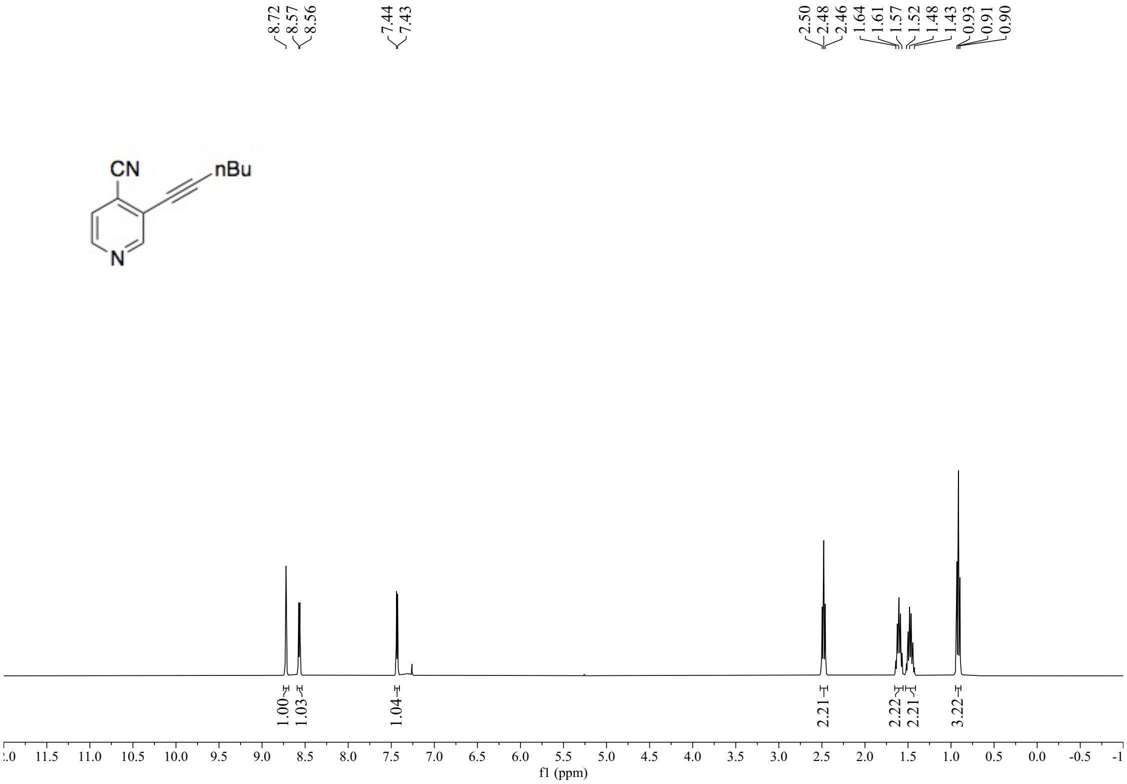
^{13}C NMR of compound **SI-3** (101 MHz, CDCl$_3$)



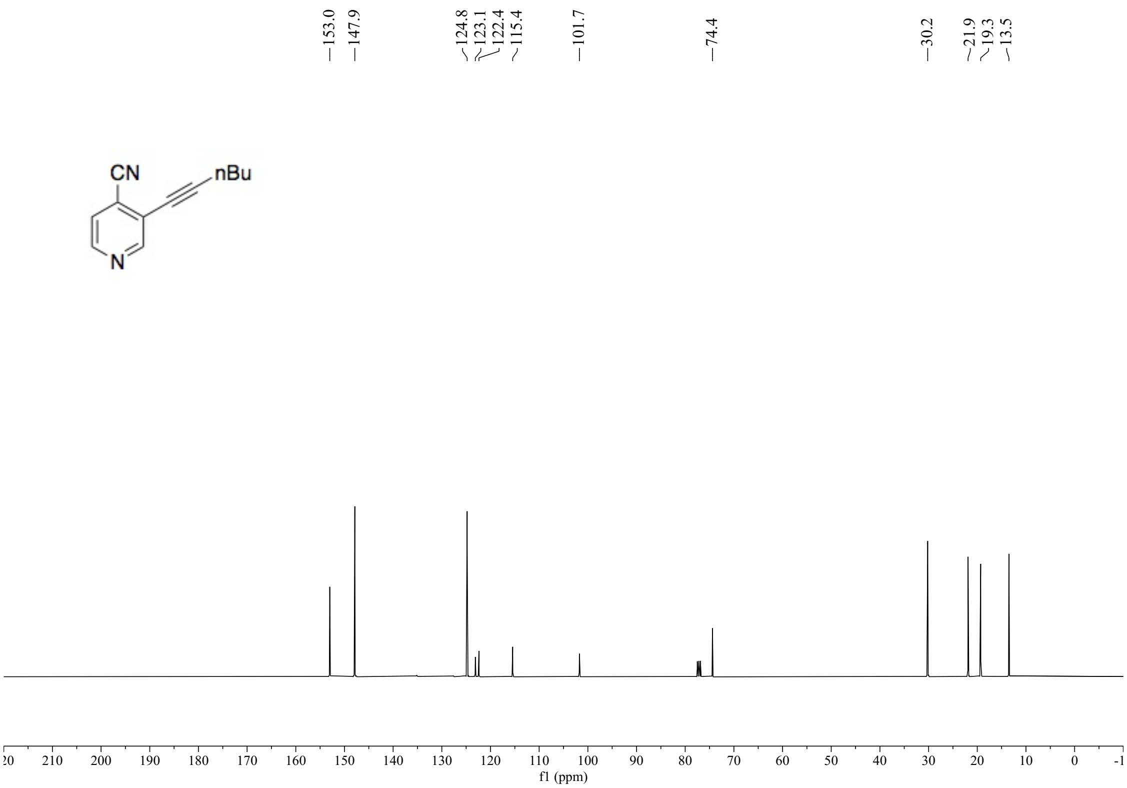
^{1}**H NMR** of compound **SI-4** (400 MHz, CDCl$_3$)



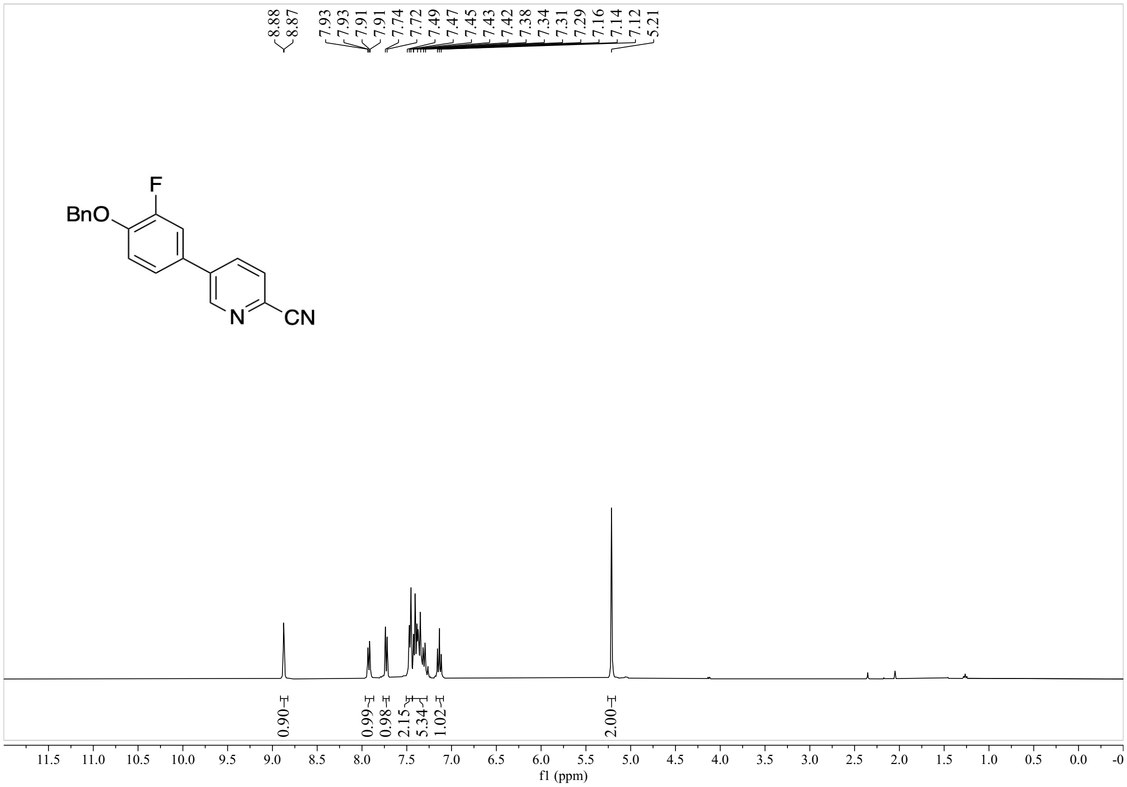
^{13}**C NMR** of compound **SI-4** (101 MHz, CDCl$_3$)



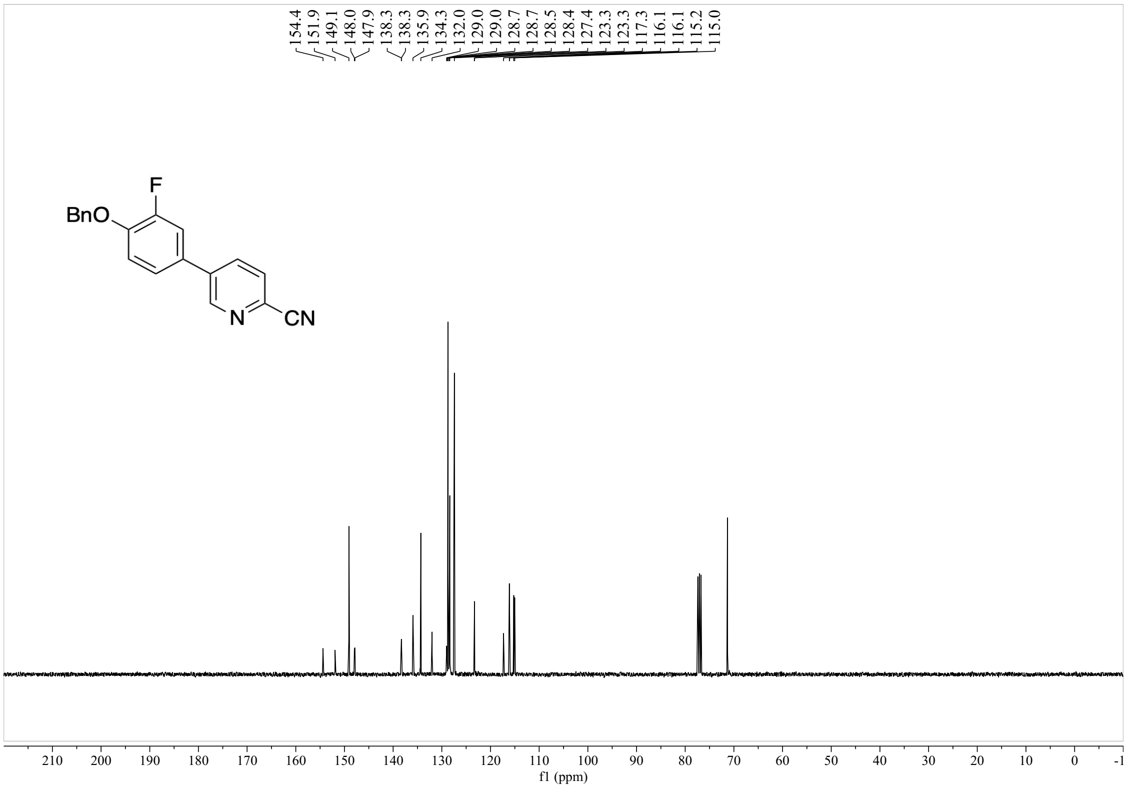
^{1}H NMR of compound **SI-5** (400 MHz, CDCl$_3$)



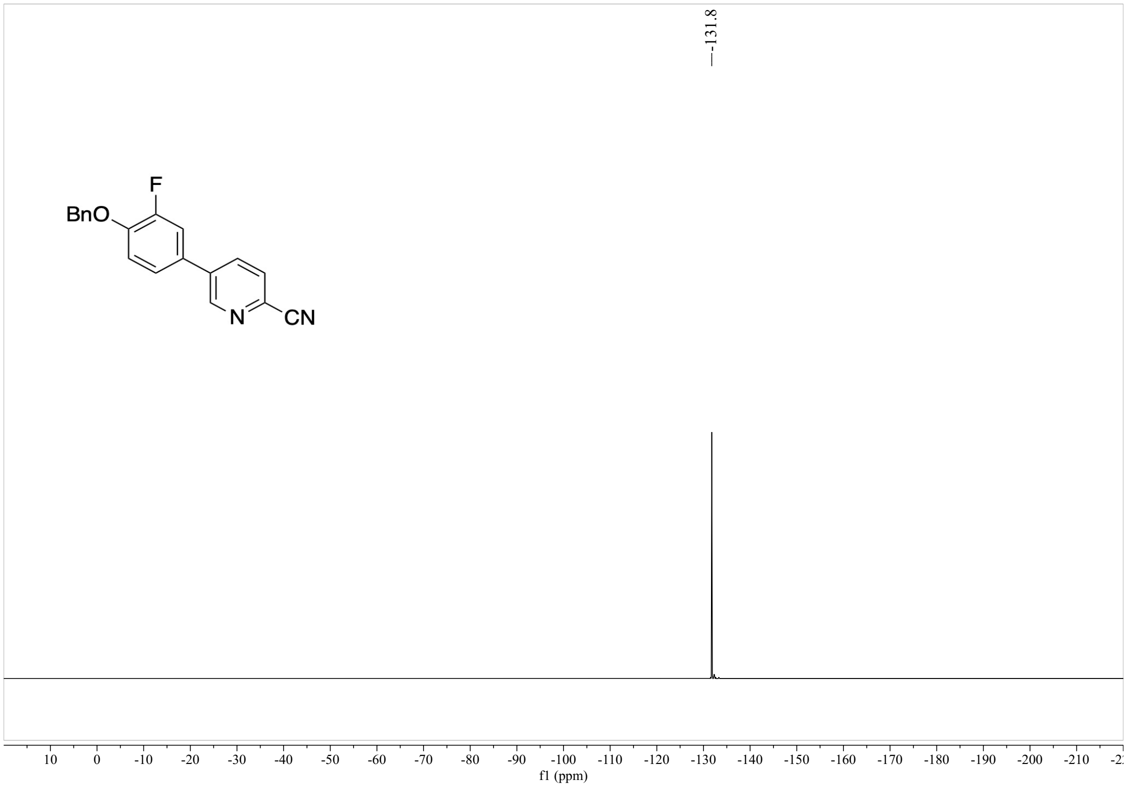
^{13}C NMR of compound **SI-5** (101 MHz, CDCl$_3$)



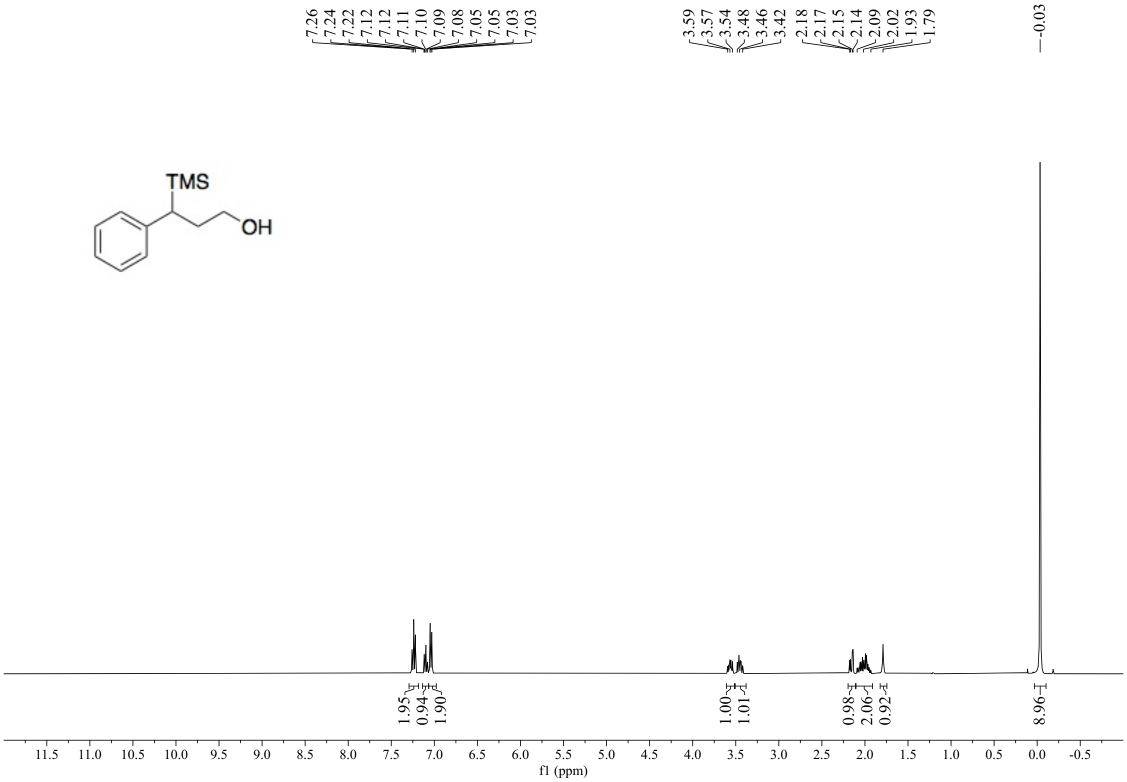
^{1}H NMR of compound **SI-6** (400 MHz, $CDCl_3$)



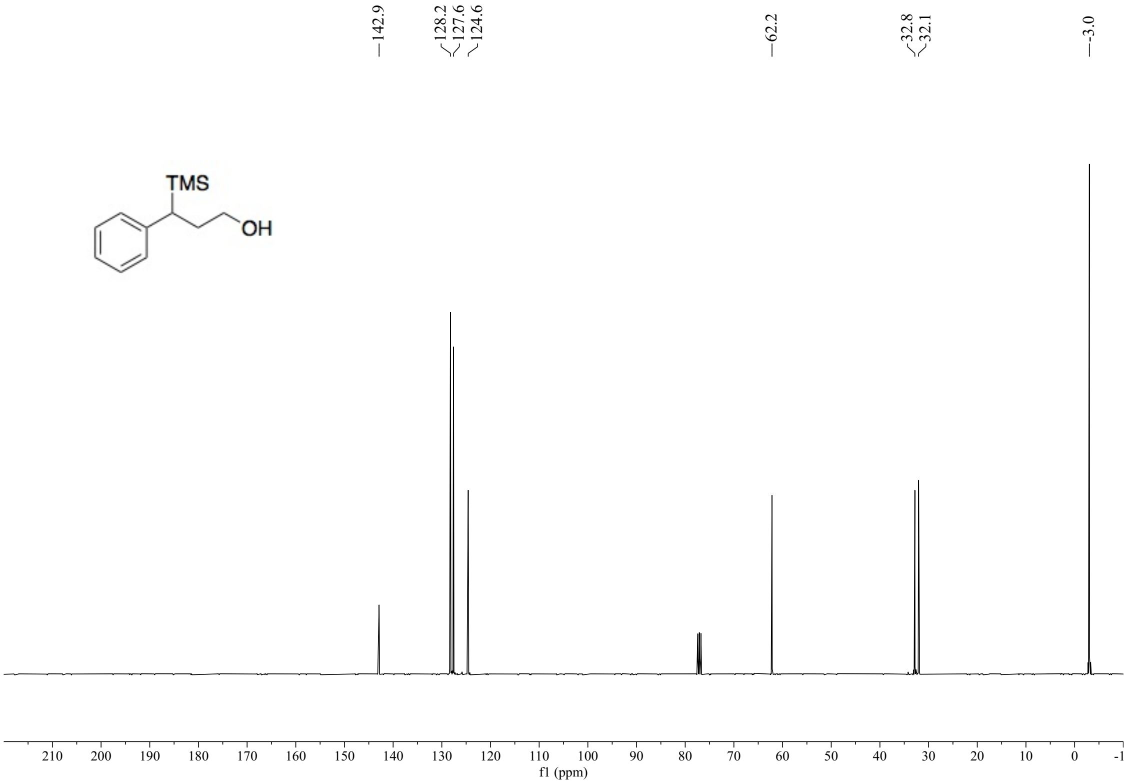
^{13}C NMR of compound **SI-6** (101 MHz, $CDCl_3$)



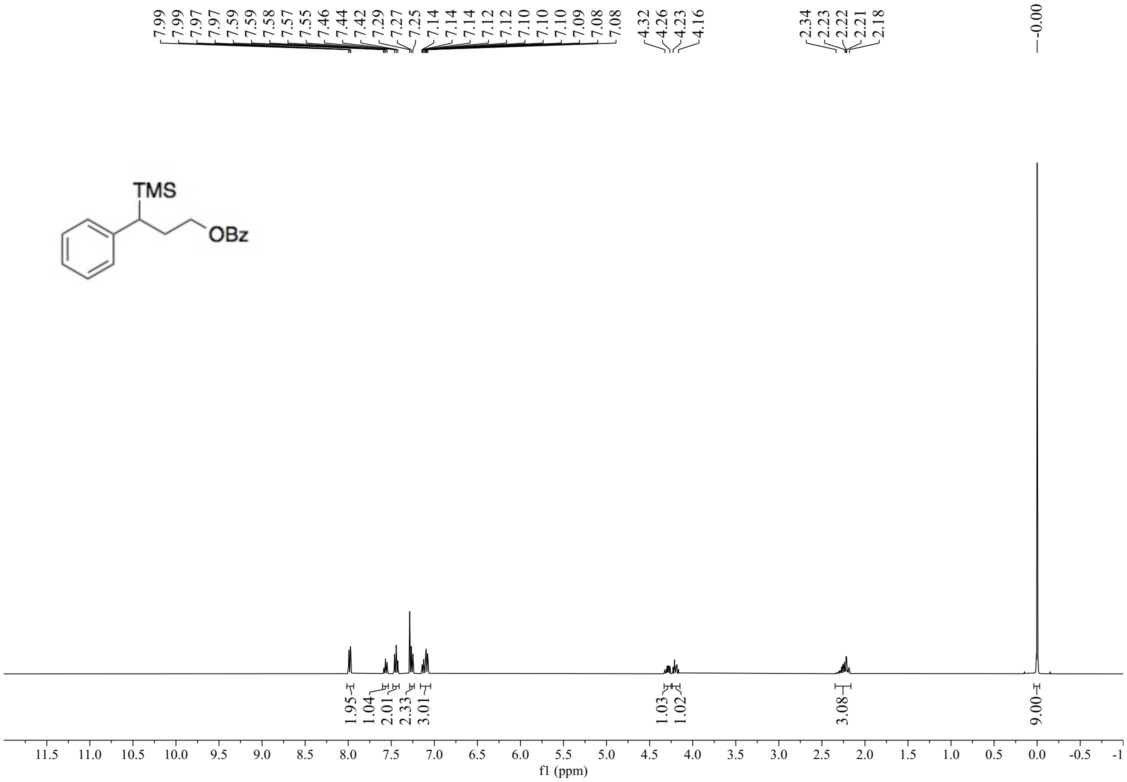
^{19}F NMR (proton decoupled) of compound **SI-6** (376 MHz, $CDCl_3$)



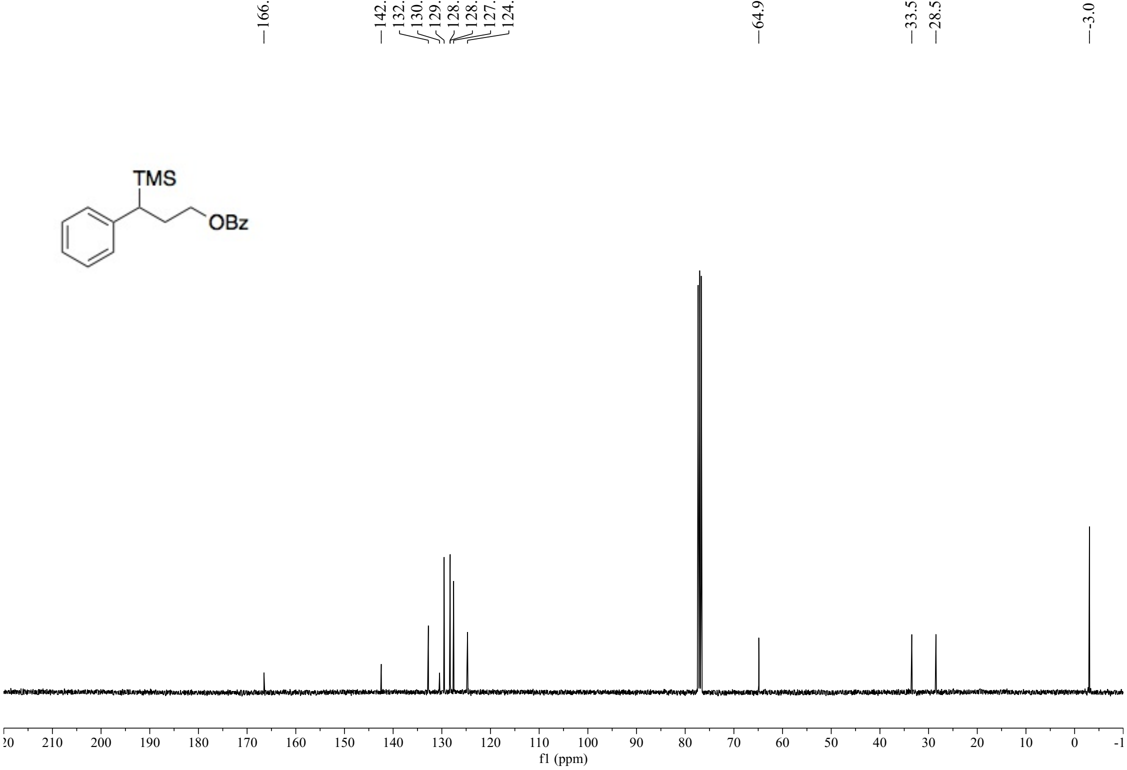
^{1}**H NMR** of compound **SI-7** (400 MHz, CDCl$_3$)



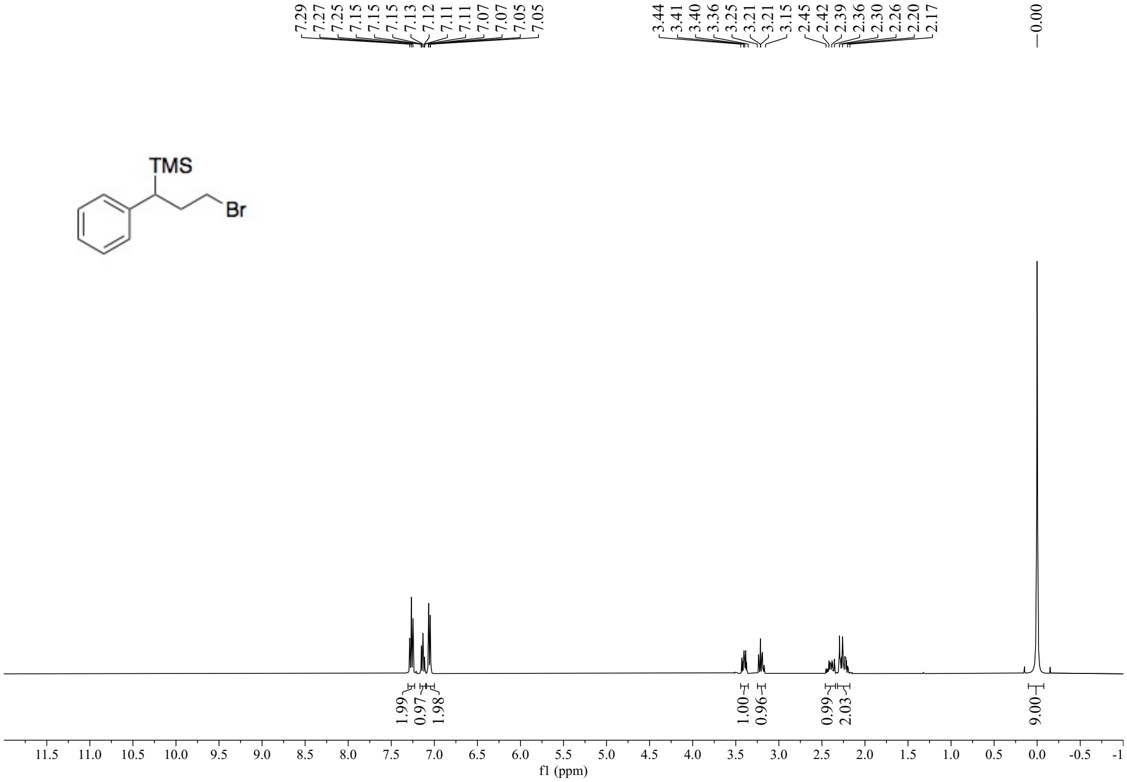
^{13}**C NMR** of compound **SI-7** (101 MHz, CDCl$_3$)



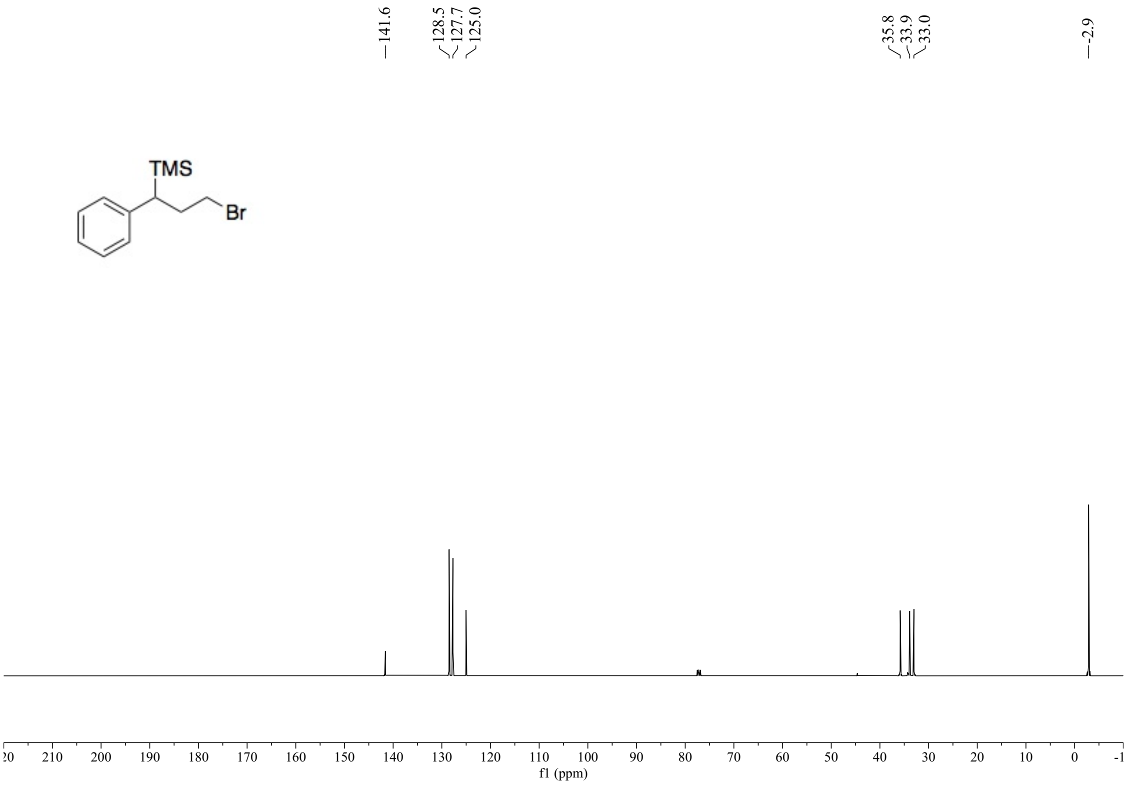
^{1}**H NMR** of compound **SI-8** (400 MHz, $CDCl_3$)



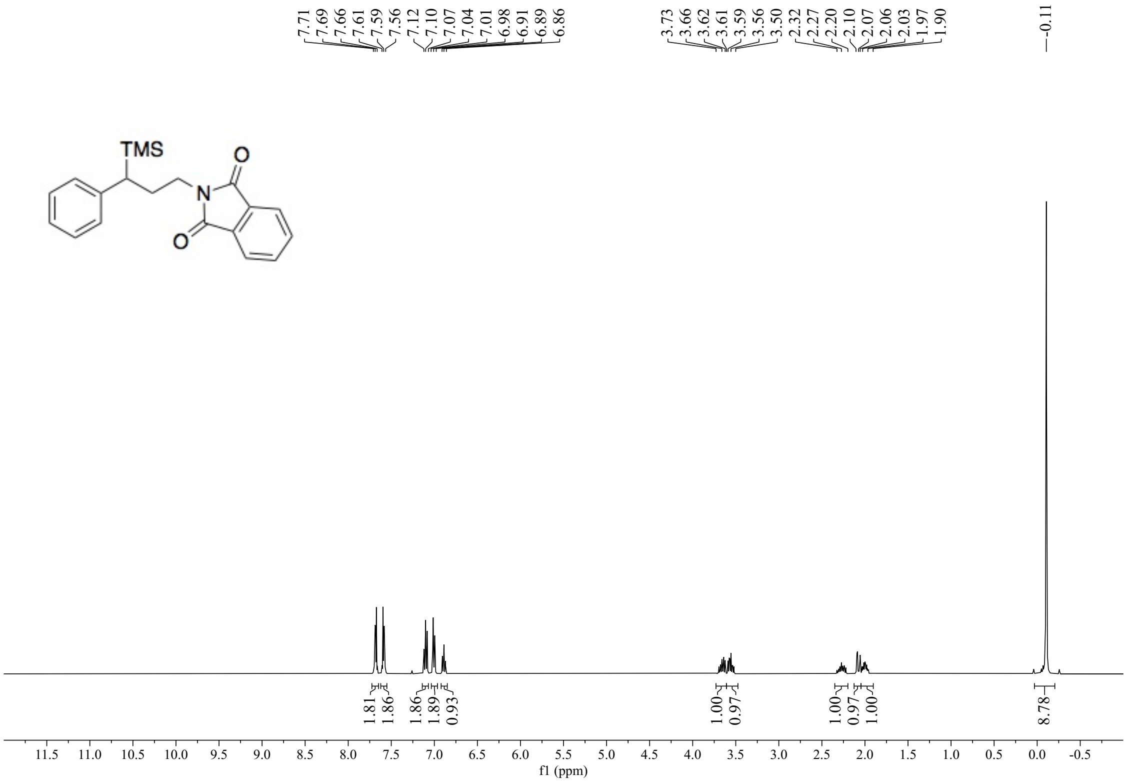
^{13}**C NMR** of compound **SI-8** (101 MHz, $CDCl_3$)



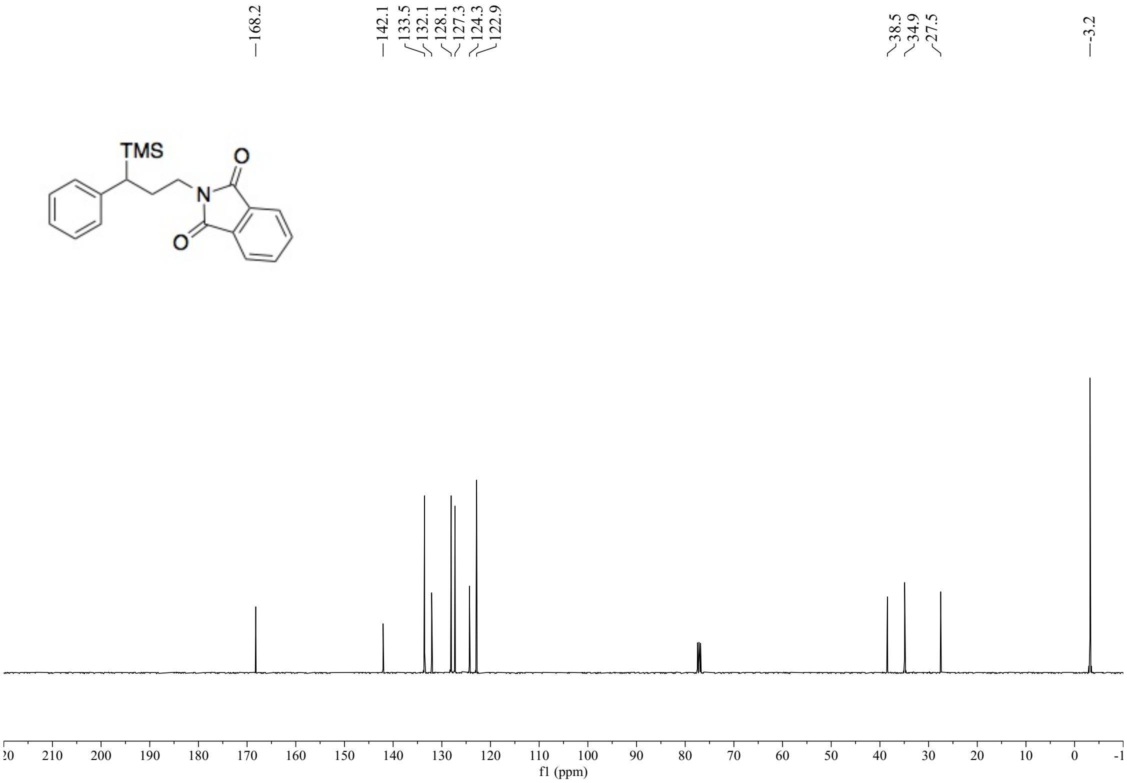
^{1}**H NMR** of compound **SI-9** (400 MHz, $CDCl_3$)



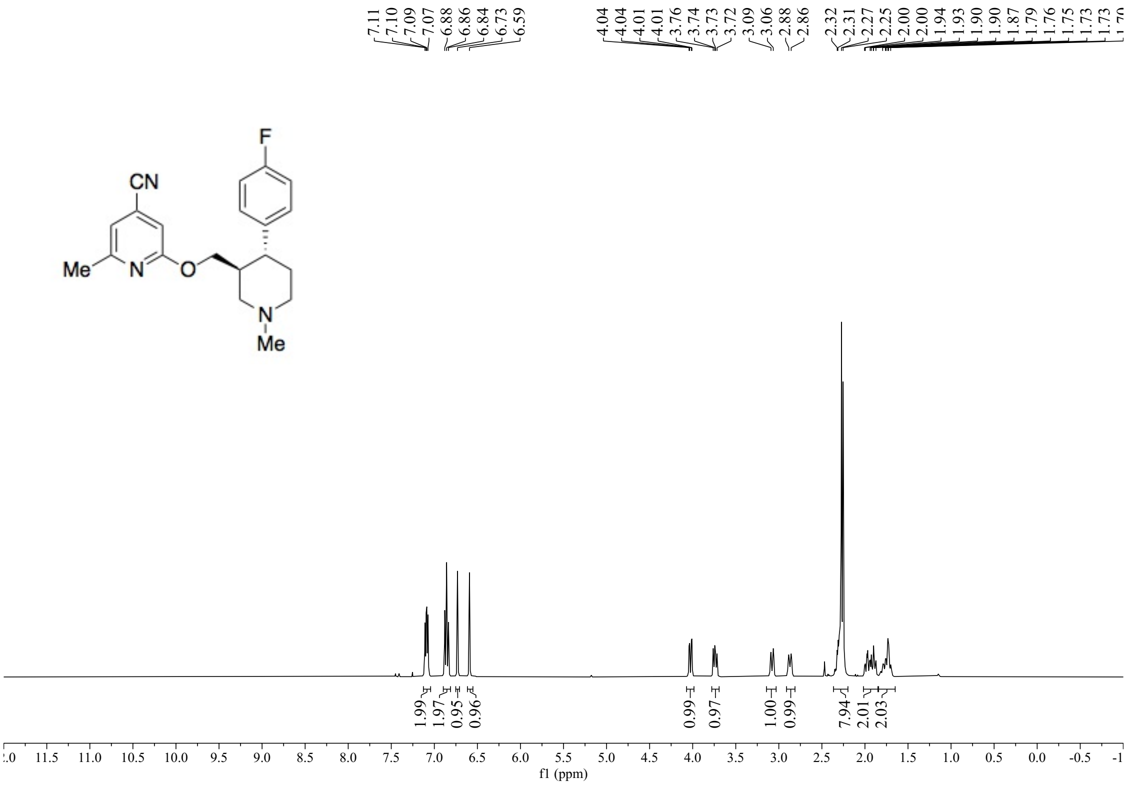
^{13}**C NMR** of compound **SI-9** (101 MHz, $CDCl_3$)



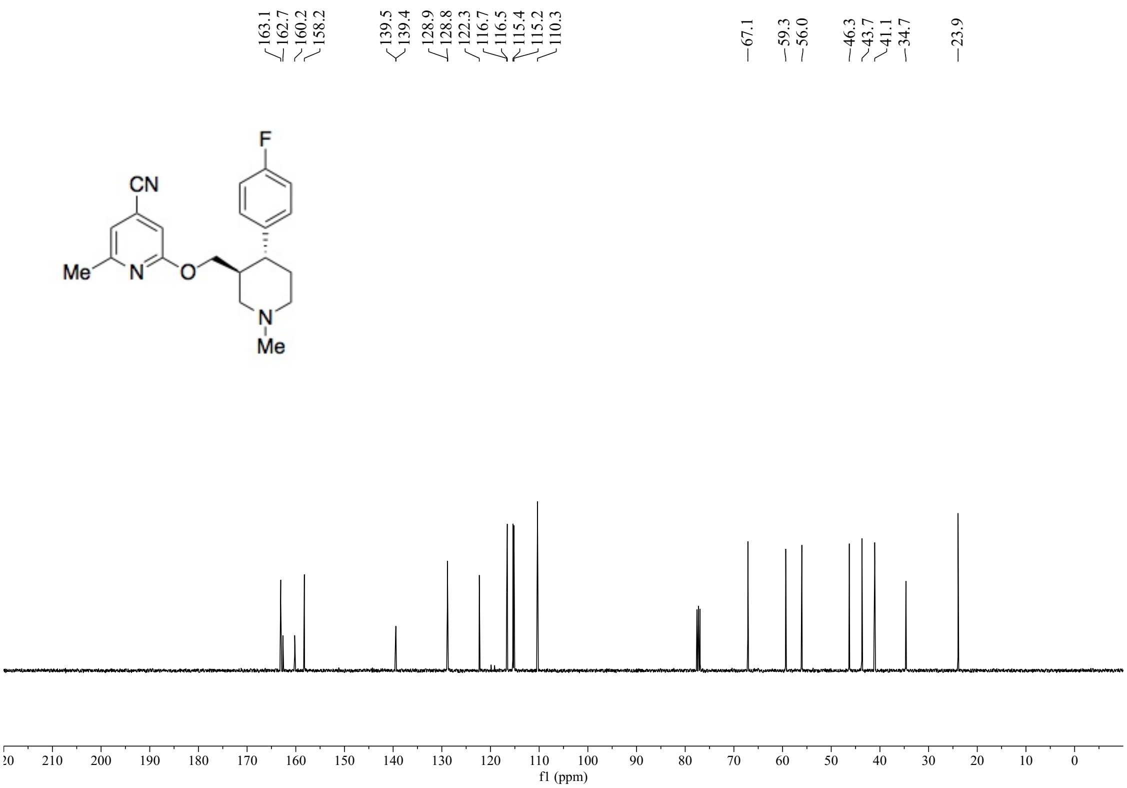
¹H NMR of compound **SI-10** (400 MHz, CDCl₃)



¹³C NMR of compound **SI-10** (101 MHz, CDCl₃)

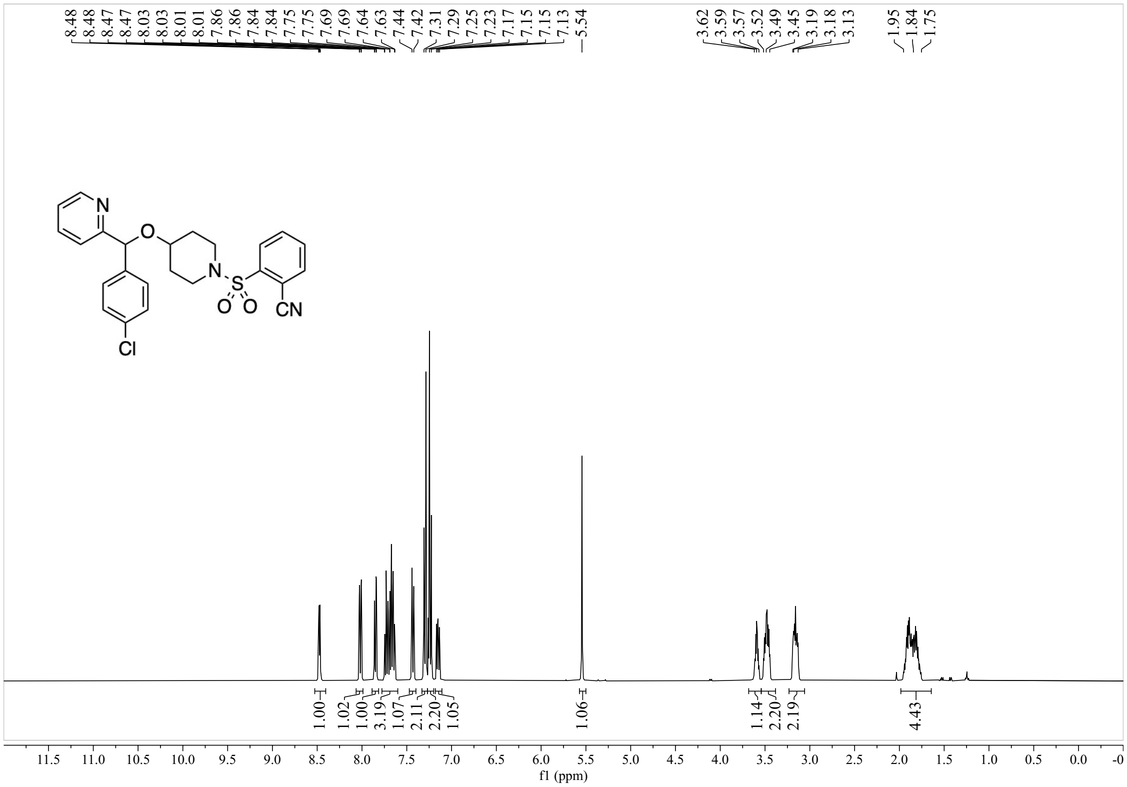


¹H NMR of compound **SI-11** (400 MHz, CDCl₃)

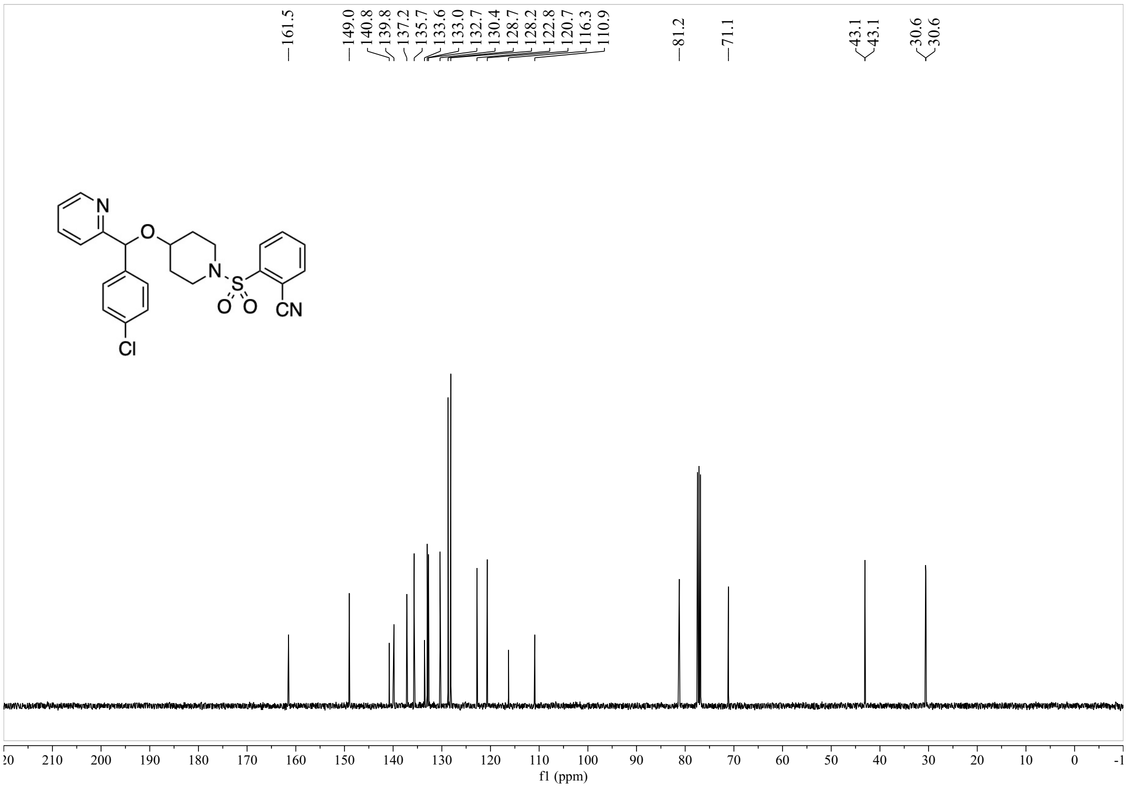


¹³C NMR of compound **SI-11** (101 MHz, CDCl₃)

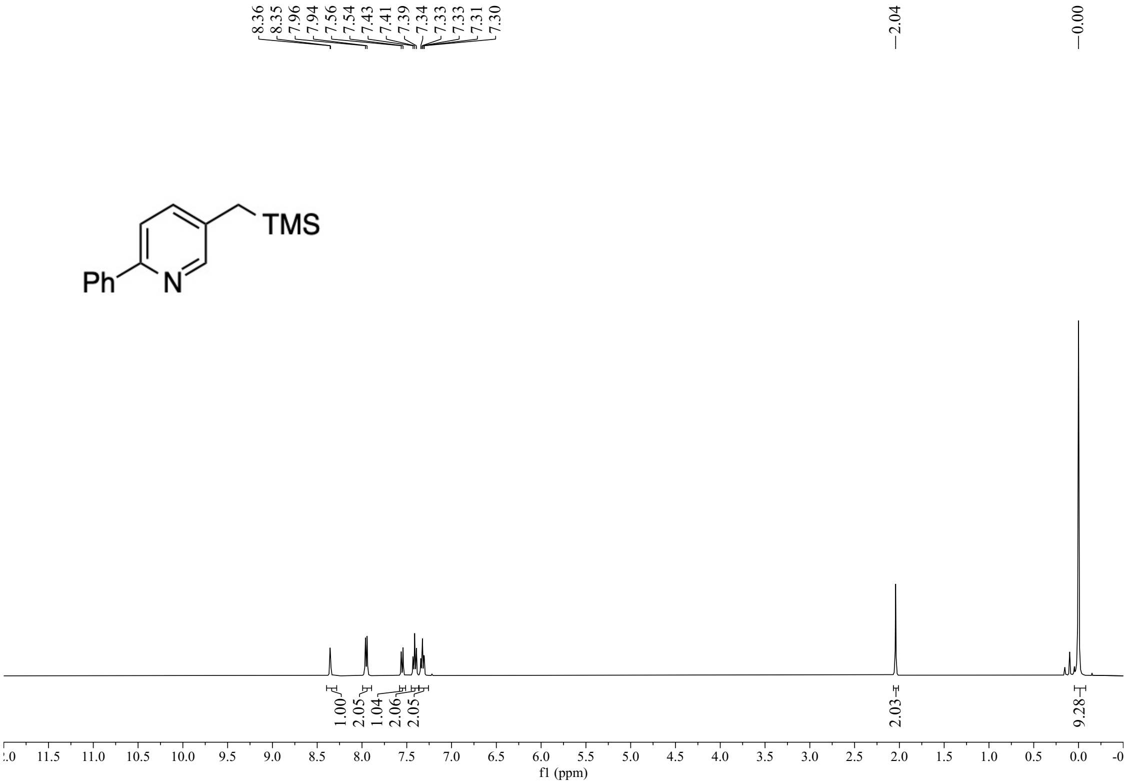
^{19}F NMR (proton decoupled) of compound **SI-11** (376 MHz, CDCl$_3$)



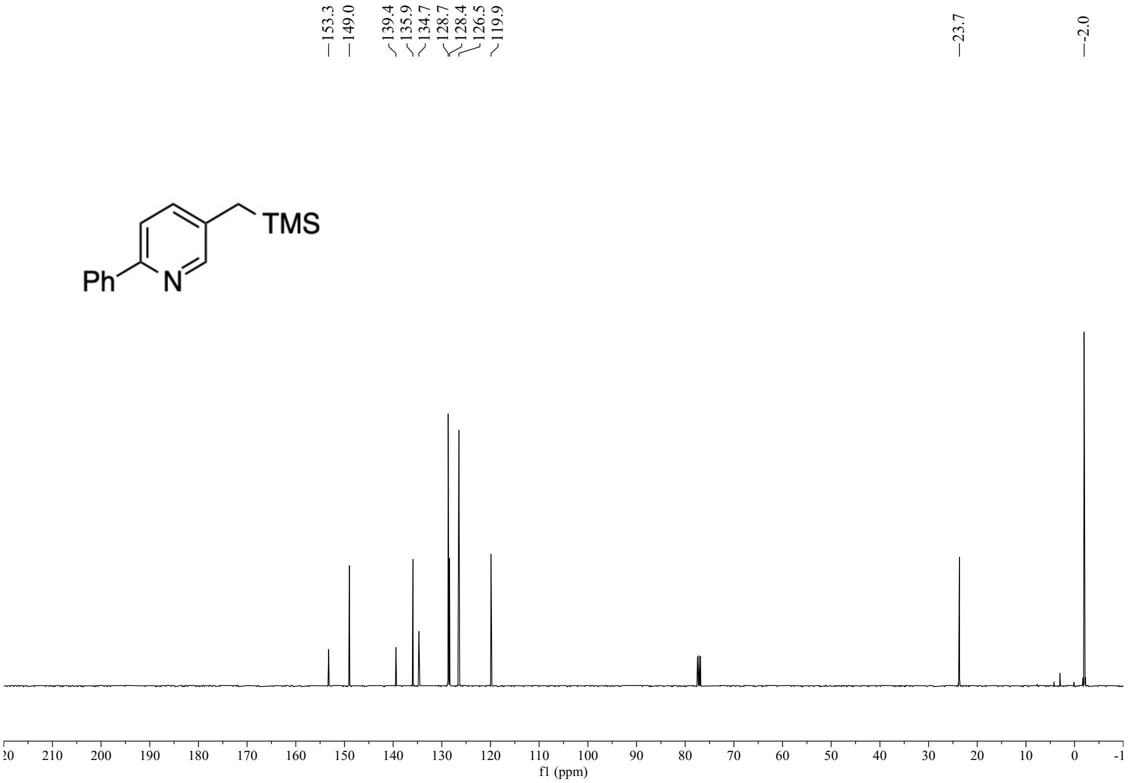
^{1}H NMR of compound **SI-12** (400 MHz, $CDCl_3$)



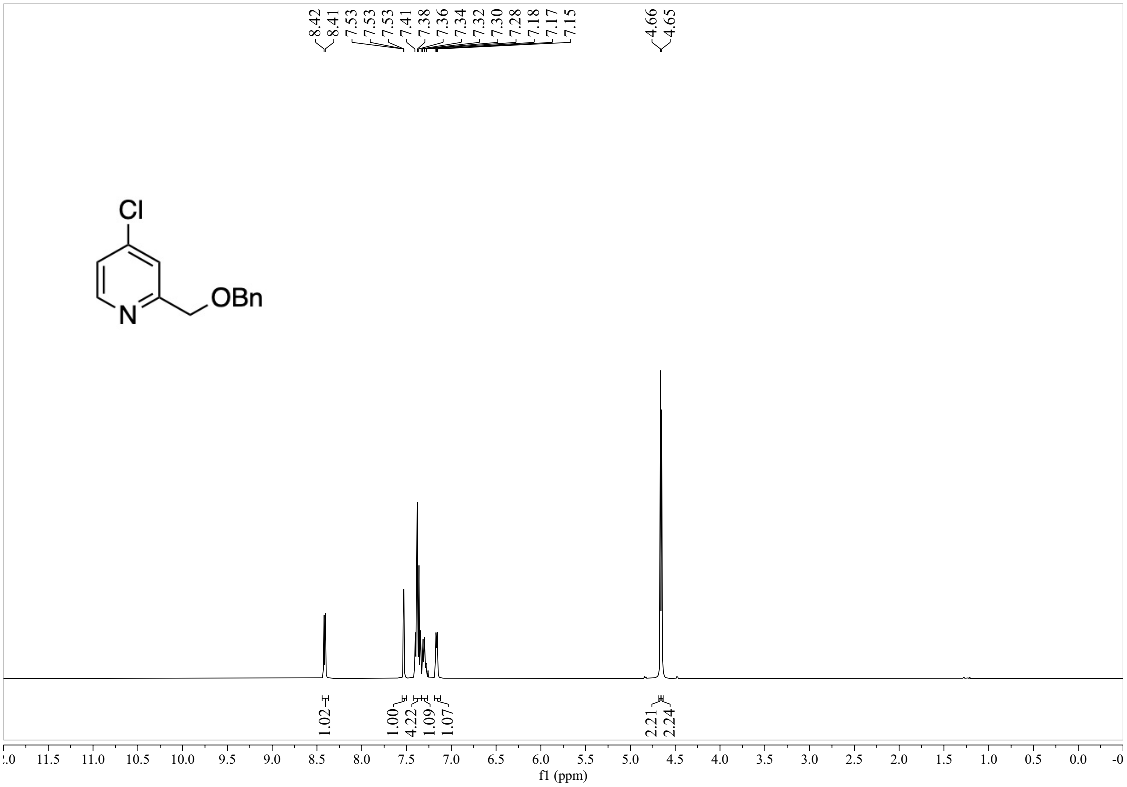
^{13}C NMR of compound **SI-12** (101 MHz, $CDCl_3$)



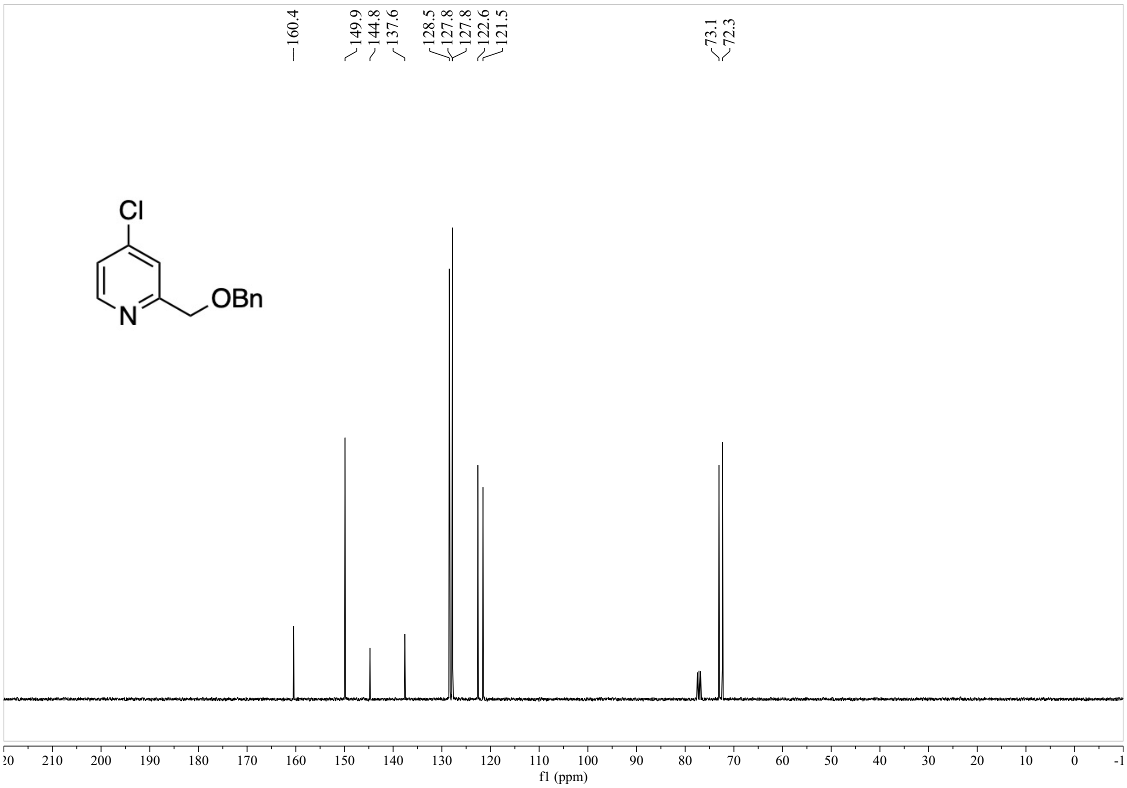
^{1}H NMR of compound **SI-13** (400 MHz, $CDCl_3$)



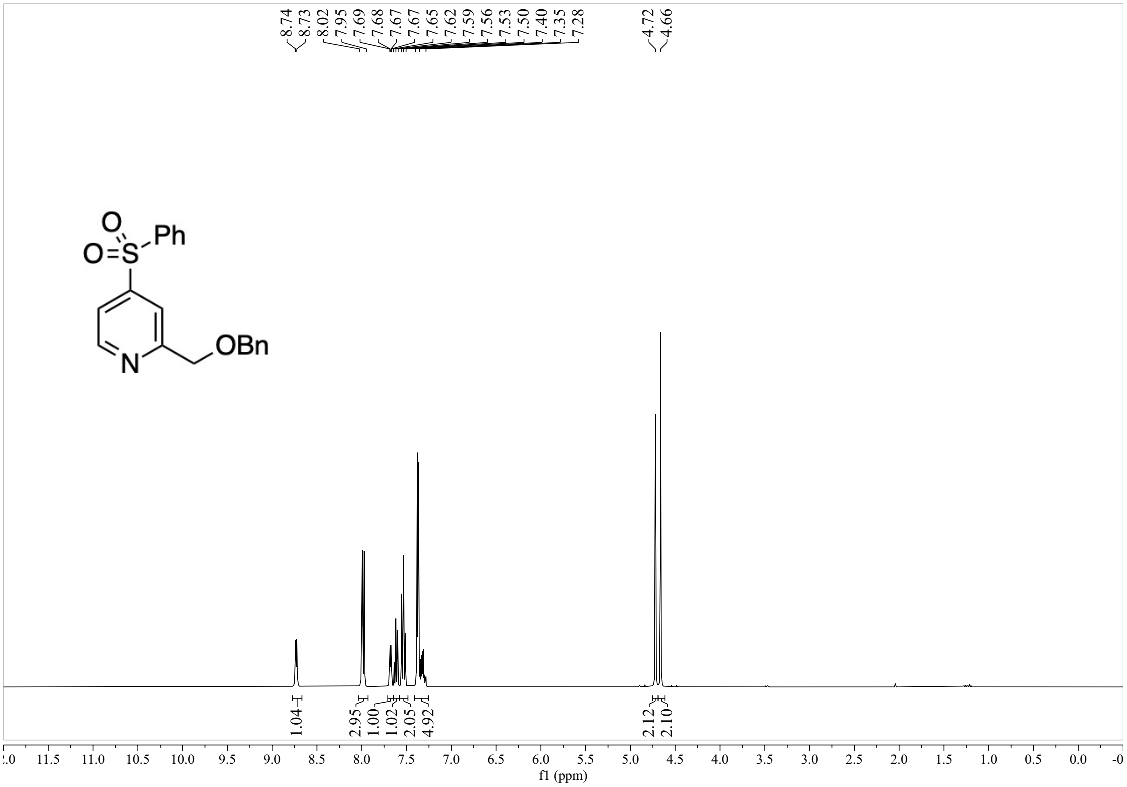
^{13}C NMR of compound **SI-13** (101 MHz, $CDCl_3$)



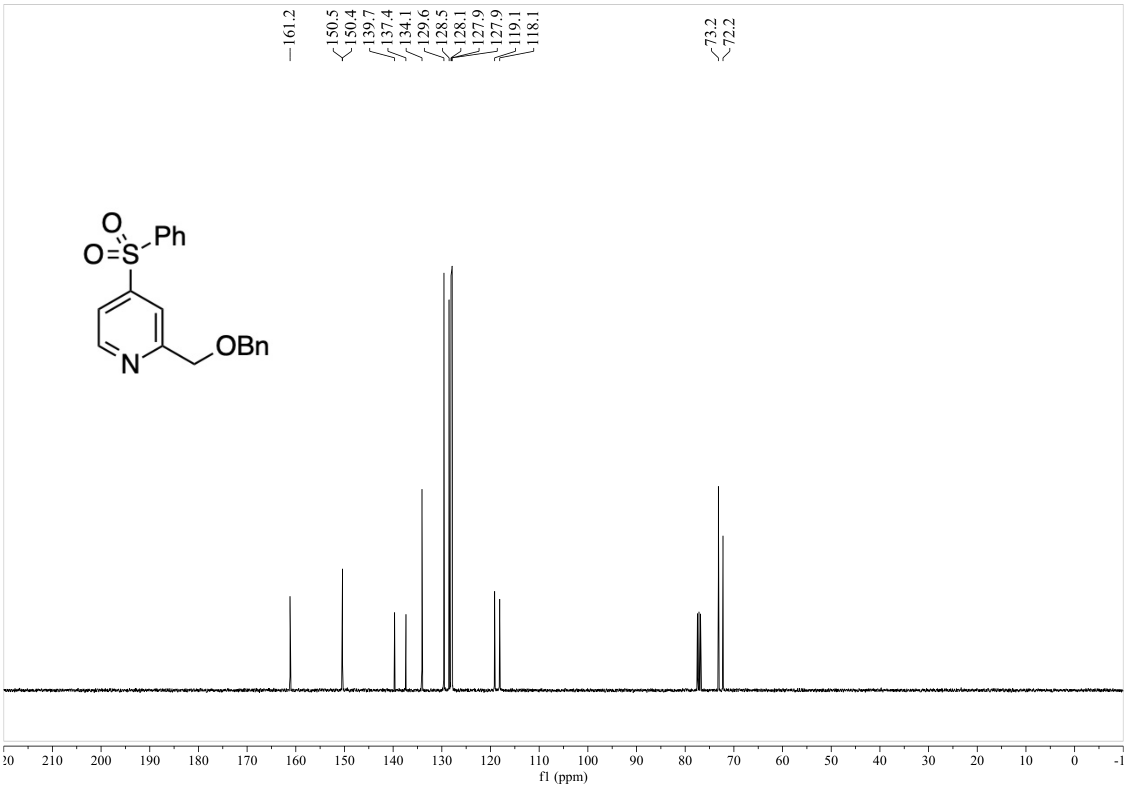
^{1}H NMR of compound **SI-14** (400 MHz, $CDCl_3$)



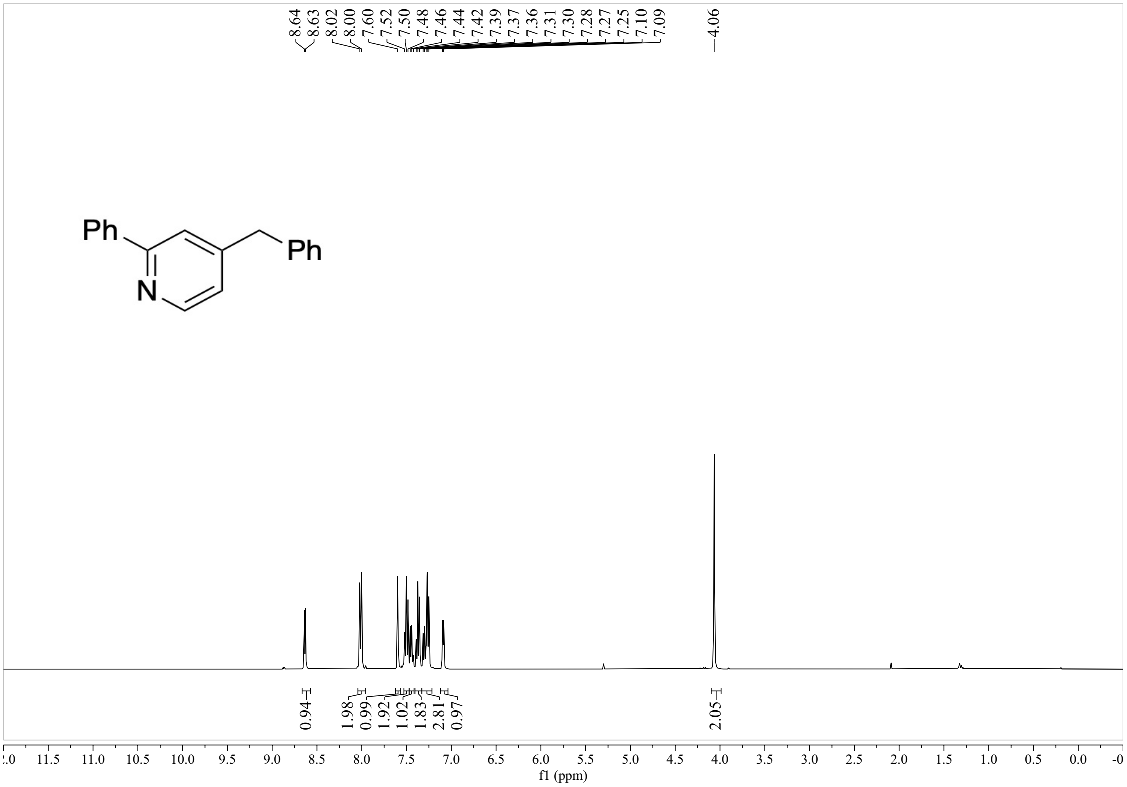
^{13}C NMR of compound **SI-14** (101 MHz, $CDCl_3$)



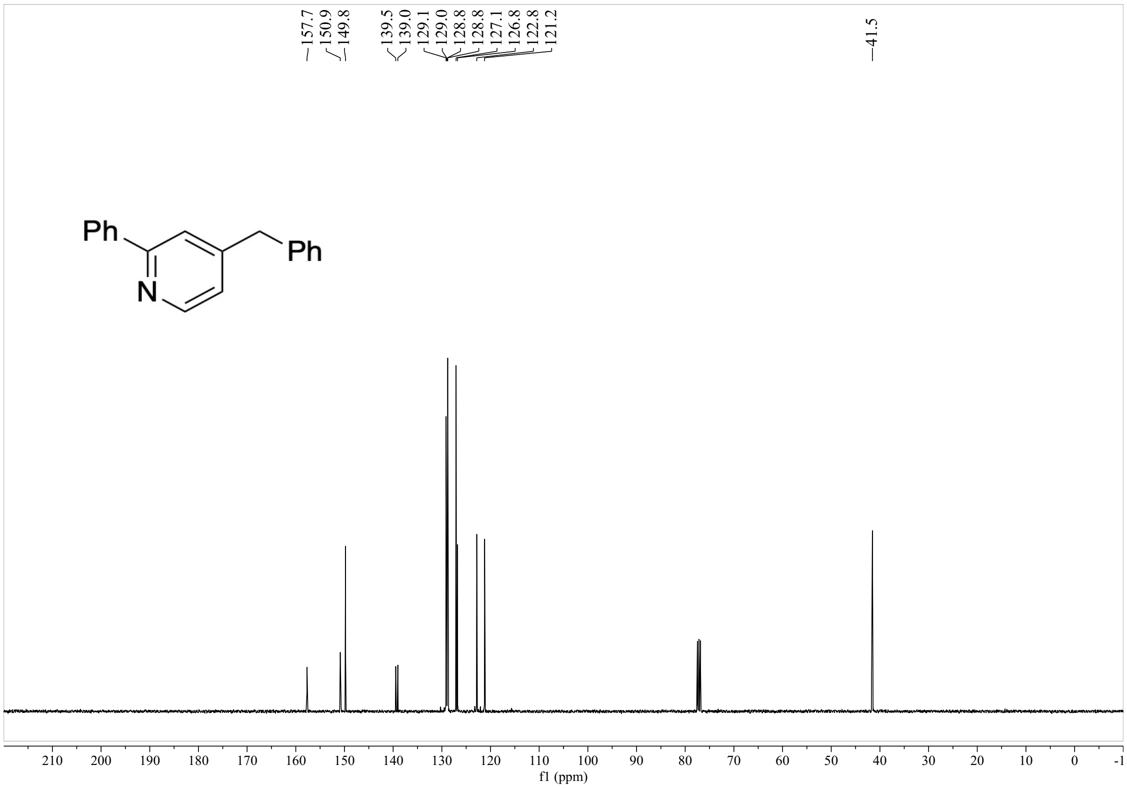
^{1}H NMR of compound **SI-15** (400 MHz, CDCl$_3$)



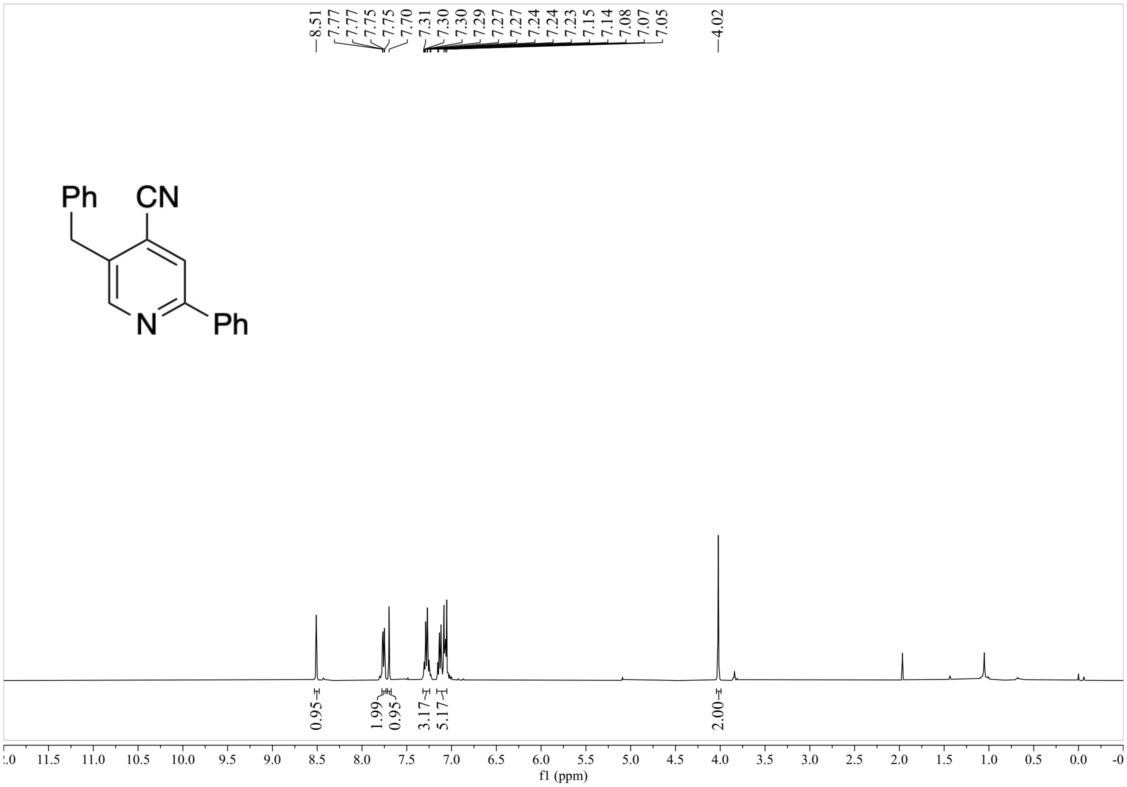
^{13}C NMR of compound **SI-15** (101 MHz, CDCl$_3$)



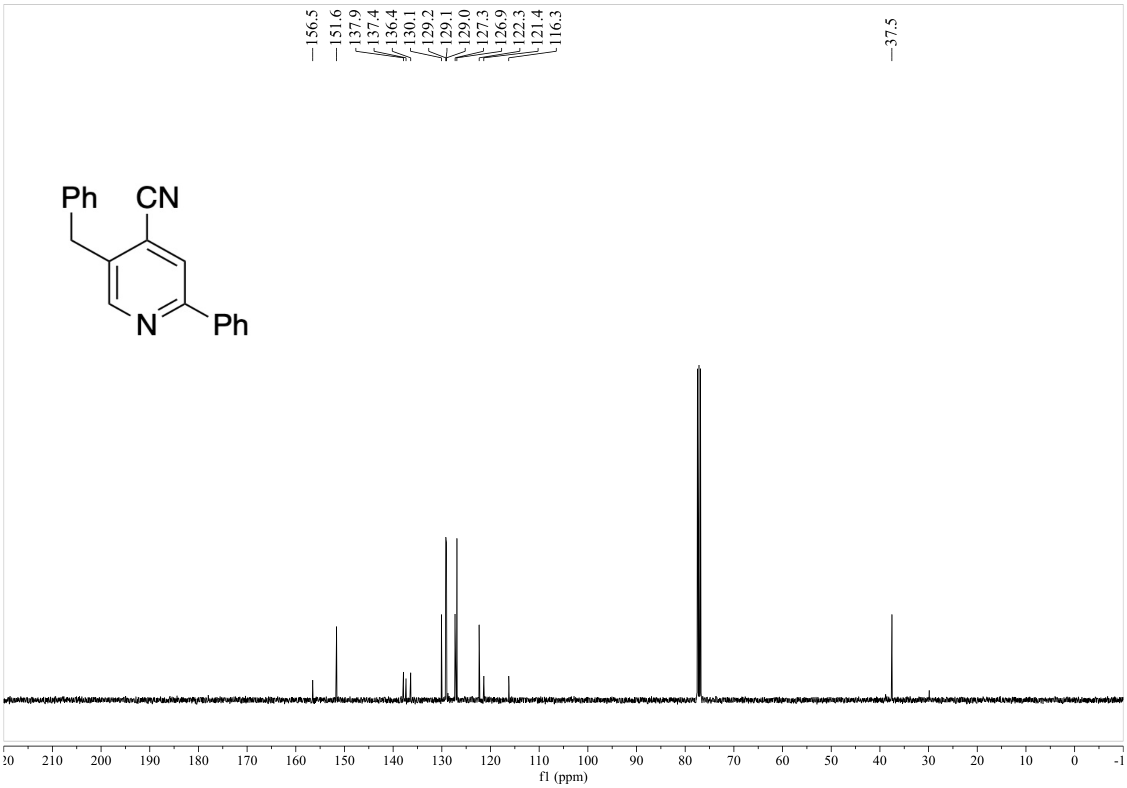
^{1}H NMR of compound **SI-17** (400 MHz, CDCl₃)



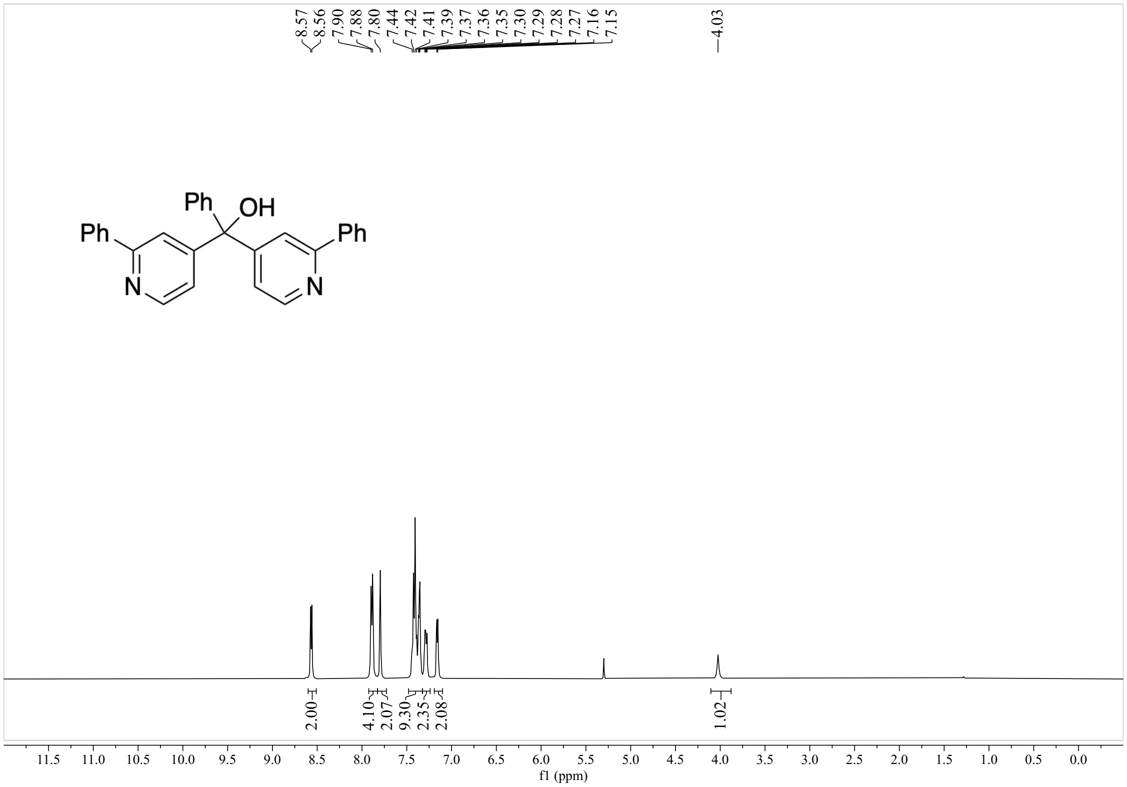
^{13}C NMR of compound **SI-17** (101 MHz, CDCl₃)



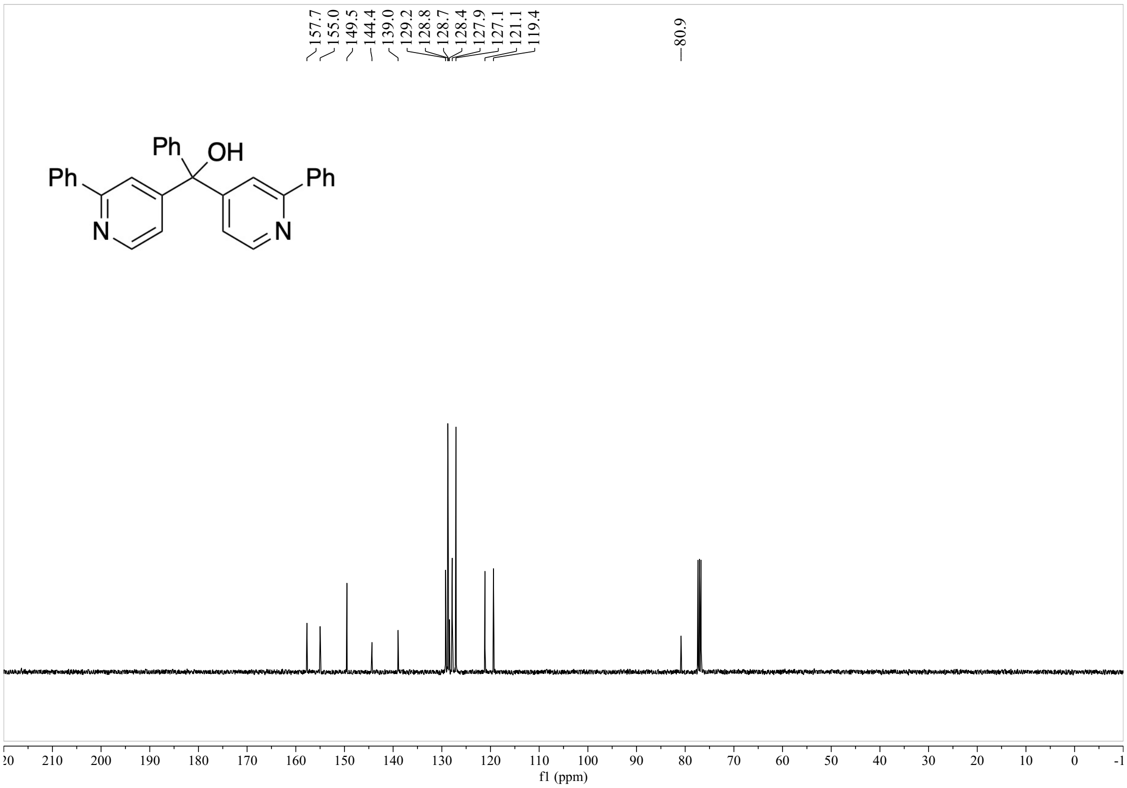
^{1}**H NMR** of compound **SI-18** (400 MHz, CDCl$_3$)



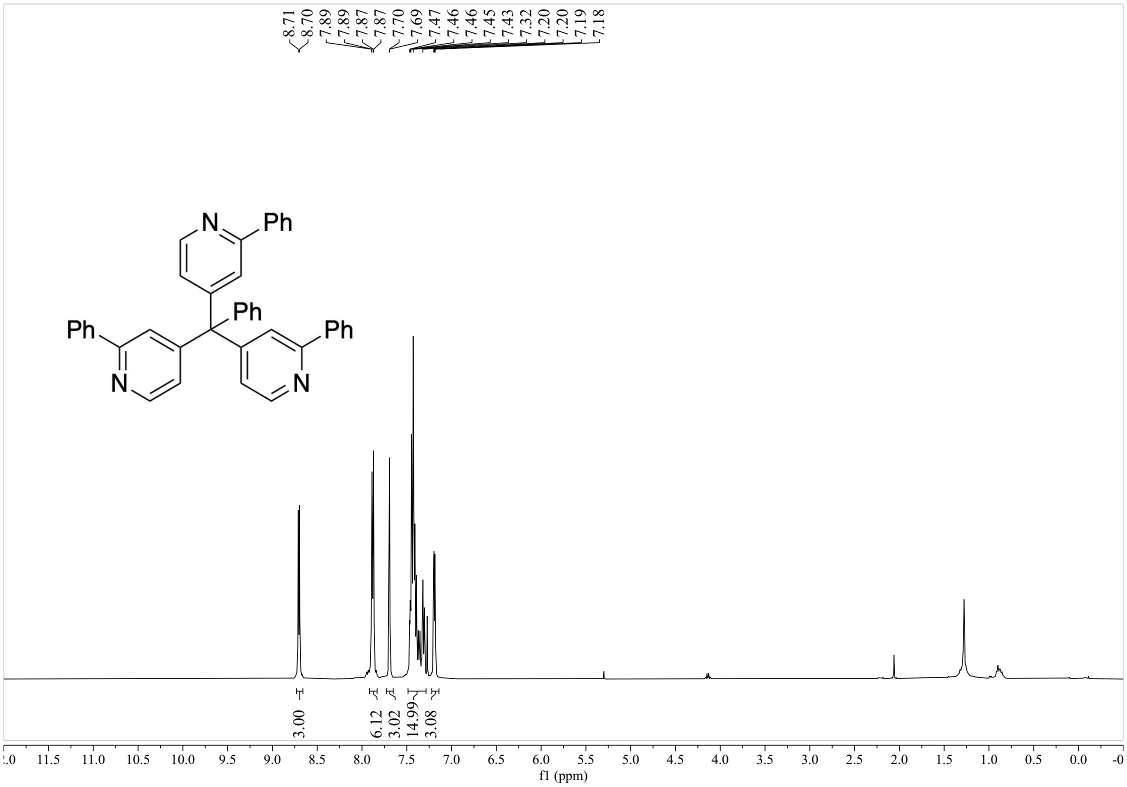
^{13}**C NMR** of compound **SI-18** (101 MHz, CDCl$_3$)



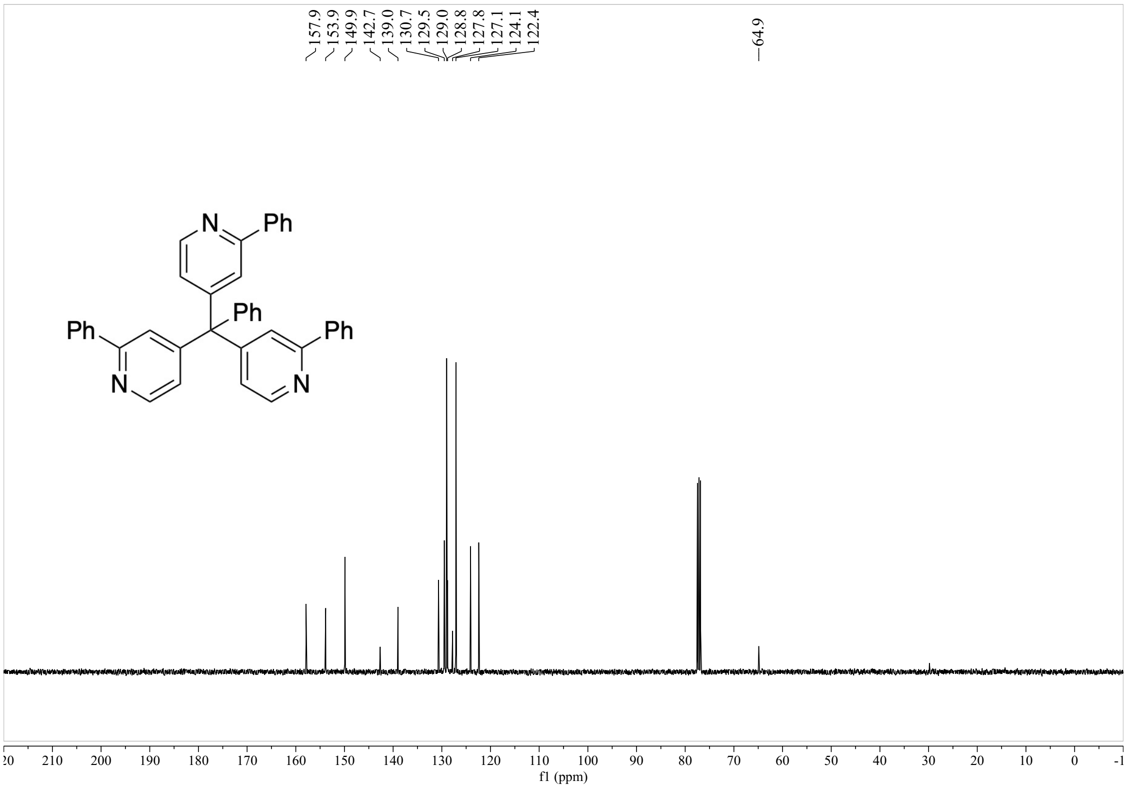
^{1}H NMR of compound **SI-19** (400 MHz, CDCl$_3$)



^{13}C NMR of compound **SI-19** (101 MHz, CDCl$_3$)



^{1}**H NMR** of compound **SI-20** (400 MHz, $CDCl_3$)



^{13}**C NMR** of compound **SI-20** (101 MHz, $CDCl_3$)