-Supporting Information-

C(sp^2)–H trifluoromethylation of enamides using $TMSCF_3$: access to trifluoromethylated isoindolinones, isoquinolinones, 2-pyridinones and other heterocycles.

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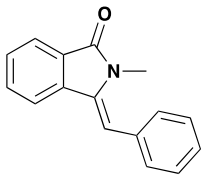
General

Unless otherwise mentioned, all the chemicals were purchased from commercial sources and used without further purification. Acetonitrile (MeCN) was distilled from P_2O_5 and stored over molecular sieves in a Strauss flask under N_2. Flash column chromatography was performed to isolate products with suitable eluent as determined by TLC. ^1H, ^{13}C, and ^{19}F spectra were recorded on 400 MHz or 500 MHz Varian NMR spectrometers. ^1H NMR chemical shifts were determined relative to $CDCl_3$ as the internal standard at δ 7.26 ppm. ^{13}C NMR shifts were determined relative to $CDCl_3$ at δ 77.16 ppm. ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ at δ 0.00 ppm. Mass spectra were recorded on a high-resolution mass spectrometer, EI or ESI mode. Starting materials isoindolinones **(1a-1d)**,[1-2] **1e**,[3] isoquinolinones **(1f-1h)**,[4-7] 2-pyridones **(1j-1k** and **1m-1q)**,[8] **1l**, enamides **1r**,[11-13] and **1s**[13] benzosultam **1t**[14-16] were synthesized according to reported procedures. *N*-Methyl-2-pyridone **1i**, 5-Methyl-1-phenyl-2-(1H)-pyridone (pirfenidone, **1q**) and anhydrous pyridine were purchased from Sigma-Aldrich and used as received. Copper complex, (phen)$CuCF_3$ was purchased from STREM Chemicals and used as received. 4-hydroxy-2-methyl-2*H*-benzo[*e*][1,2]thiazine 1,1-dioxide and caffeine were purchased from AK Scientific and used as received.

Synthesis and NMR spectroscopic data of starting materials:

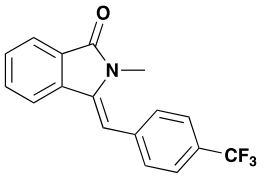
(*Z*)-3-benzylidene-2-methylisoindolin-1-one (1a)



Inside an argon glovebox, N-methyl-2-iodobenzamide (2 mmol, 522.0 mg), CuCl (0.2 mmol, 19.8 mg), PPh_3 (0.6 mmol, 157 mg), n-tetrabutylammonium bromide (3 mmol, 967 mg) and Cs_2CO_3 (6 mmol, 1955 mg) were placed in a crimp-top vial and sealed with a septum. Outside the glovebox, phenylacetylene (3.0 mmol, 330 μL) and degassed water (4 mL) were added sequentially by syringe under a stream of nitrogen. The vial was then placed in an oil bath preheated to 130˚C and stirred for 30 min. Subsequently, the reaction mixture was allowed to cool down to room temperature and diluted with EtOAc (10 mL). This mixture was then filtered through a short pad of Celite. The resulting filtrate was poured into 10 mL of a 0.1 M solution of NH_4OH and further extracted with EtOAc (3 times, 15 mL). The organic layers were combined, washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography using an EtOAc/hexanes system (gradient from 0% - 25%). The combined fractions were concentrated on a rotary evaporator to afford the product **1a** (82% yield, 385.9 mg). **^{1}H NMR (**500 MHz, $CDCl_3$) δ 7.86 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.60 (td, *J* = 7.5, 1.2 Hz, 1H), 7.49 (td, *J* = 7.5, 0.9 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.37 – 7.30 (m, 3H), 6.79 (s, 1H), 3.04 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.1, 138.1, 136.3, 134.9, 132.0, 129.8, 129.1, 128.6, 128.2, 127.6, 123.3, 119.4, 106.7, 30.7. This data corresponds to the previously reported structure.[1]

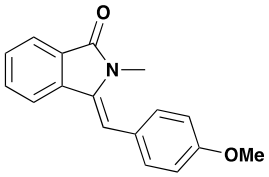
(*Z*)-2-methyl-3-(4-(trifluoromethyl)benzylidene)isoindolin-1-one (1b)

Inside an argon glovebox, N-methyl-2-iodobenzamide (2 mmol, 522.1 mg), CuCl (0.2 mmol, 19.8 mg), PPh_3 (0.6 mmol, 157 mg), n-tetrabutylammonium bromide (3 mmol, 967 mg) and Cs_2CO_3 (6 mmol, 1955 mg) were placed in a crimp-top vial and sealed with a septum. Outside the glovebox, 4-trifluoromethylphenylacetylene (3 mmol, 489



μL) and degassed water (4 mL) were added sequentially by syringe under a stream of nitrogen. The vial was then placed in an oil bath preheated to 130˚C and stirred for 30 min. Subsequently, the reaction mixture was allowed to cool down to room temperature and diluted with EtOAc (10 mL). This mixture was then filtered through a short pad of Celite. The resulting filtrate was poured into 10 mL of a 0.1 M solution of NH_4OH and further extracted with EtOAc (3 times, 15 mL). The organic layers were combined, washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography using an EtOAc/hexanes system (gradient from 0% to 15%). The combined fractions were concentrated on a rotary evaporator to afford the product. Obtained as a pale-yellow solid (73% yield, 443 mg). **^{1}H NMR** (399 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.75 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.68 – 7.59 (m, 3H), 7.52 (tt, *J* = 7.5, 7.5, 1.1 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 2H), 6.73 (s, 1H), 3.03 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.0, 138.8, 137.9, 137.6, 132.9 (d, *J* = 218.2 Hz), 130.1 , 129.6 (q, *J* = 32.7 Hz), 129.6 , 128.6, 125.2 (q, *J* = 3.8, 3.7, 3.7 Hz), 124.2 (q, *J* = 272.0 Hz), 123.5, 119.5, 30.8 . **^{19}F NMR** (282 MHz, $CDCl_3$) δ -63.1 (s, 3F). This data corresponds to the previously reported structure.[1]

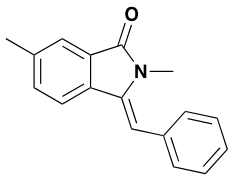
(*Z*)-3-(4-methoxybenzylidene)-2-methylisoindolin-1-one (1c)



Inside an argon glovebox, N-methyl-2-iodobenzamide (2 mmol, 522.1 mg), CuCl (0.2 mmol, 19.8 mg), PPh_3 (0.6 mmol, 157 mg), n-tetrabutylammonium bromide (3 mmol, 967 mg) and Cs_2CO_3 (6 mmol, 1955 mg) were placed in a crimp-top vial and sealed with a septum. Outside the glovebox, 4-methoxyphenylacetylene (3 mmol, 389μL) and degassed water (4 mL) were added sequentially by syringe under a stream of nitrogen. The vial was then placed in an oil bath preheated to 130˚C and stirred for 30 min. Subsequently, the reaction mixture was allowed to cool down to room temperature and diluted with EtOAc (10 mL). This mixture was then filtered through a short pad of Celite. The resulting filtrate was poured into 10 mL of a 0.1 M solution of NH_4OH and further extracted with EtOAc (3 times, 15 mL). The organic layers were combined, washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography using a EtOAc/hexanes system (gradient from 0% to 25%). The combined fractions were concentrated on a rotary evaporator to afford the product Obtained as a pale-yellow solid (91% yield, 483.0 mg). **^{1}H NMR** (399 MHz, $CDCl_3$) δ 7.85 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.73 (dt, *J* = 7.8, 0.9 Hz, 1H), 7.58 (td, *J* = 7.5, 1.2 Hz, 1H), 7.48 (td, *J* = 7.5, 0.9 Hz, 1H), 7.31 – 7.24 (m, 2H), 6.95 – 6.91 (m, 2H), 6.74 (s, 1H), 3.85 (s, 3H), 3.07 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.1, 159.2, 138.3, 135.8, 131.9, 131.1, 128.9, 128.6, 127.1, 123.3, 119.3, 113.8, 106.6, 55.5, 30.7. This data corresponds to the previously reported structure.[1]

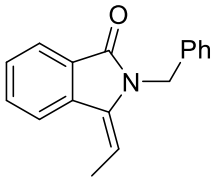
(*Z*)-3-benzylidene-2,6-dimethylisoindolin-1-one (1d)

Inside an argon glovebox, 2-iodo-*N*,5-dimethylbenzamide (2 mmol, 550.2 mg), CuCl (0.2 mmol, 19.8 mg), PPh_3 (0.6 mmol, 157 mg), n-tetrabutylammonium bromide (3 mmol, 967 mg) and Cs_2CO_3 (6 mmol, 1955 mg) were placed in a crimp-top vial and sealed with a septum. Outside the glovebox, phenylacetylene (3 mmol, 330 μL) and degassed water (4 mL) were added sequentially by syringe under a stream of nitrogen. The vial was then placed in



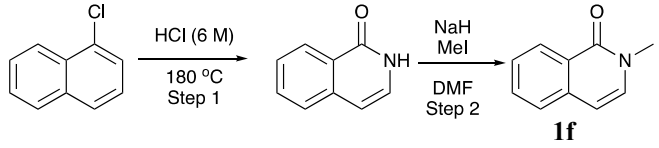
an oil bath preheated to 130˚C and stirred for 30 min. Subsequently, the reaction mixture was allowed to cool down to room temperature and diluted with EtOAc (10 mL). This mixture was then filtered through a short pad of Celite. The resulting filtrate was poured into 10 mL of a 0.1 M solution of NH_4OH and further extracted with EtOAc (3 times, 15 mL). The organic layers were combined, washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography using an EtOAc/hexanes system (gradient from 0% to 15%). The combined fractions were concentrated on a rotary evaporator to afford the product. Obtained as an off-white powder (m.p.134-135˚C) (71% yield, 354 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 (dq, *J* = 1.6, 0.8 Hz, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.42 – 7.28 (m, 6H), 6.72 (s, 1H), 3.02 (s, 3H), 2.48 (s, 3H). **^{13}C NMR** (126 MHz, $CDCL_3$) δ 169.2, 139.4, 136.4, 135.7, 135.1, 133.1, 129.9, 128.9, 128.2, 127.5, 123.5, 119.2, 105.9, 30.7, 21.7. **HRMS-ES+** (M) Calculated for $C_{17}H_{15}ON$ = 249.11537, found = 249.11519. **FT/IR** (ν_{max} (neat) cm-1): 3025, 2945, 1692, 1652, 1598, 1494, 1443, 1430, 1380, 1333, 1304, 1217, 1114, 1026, 956, 836, 777, 745, 697, 645, 616, 519, 420. The data matches reported values.[2]

(*E*)-2-benzyl-3-ethylideneisoindolin-1-one (1e)



This starting material was prepared following a previously reported procedure[3] and spectral data matches the reported values. **^{1}H NMR** (399 MHz, cdcl3) δ 7.95 (d, J = 7.7 Hz, 1H), 7.84 (d, J = 7.8 Hz, 1H), 7.60 (td, J = 7.6, 1.3 Hz, 1H), 7.54 – 7.47 (m, 1H), 7.33 – 7.21 (m, 5H), 5.47 (q, J = 7.6 Hz, 1H), 5.01 (s, 2H), 2.13 (d, J = 7.5 Hz, 3H).

SM10Me: 2-methylisoquinolin-1(2*H*)-one (1f)

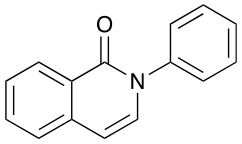


1f

Step 1: Adapted from a reported method.[4] To a crimp-top microwave vial charged with 1-chloroisoquinoline (6 mmol, 654 mg), 6M HCl (15.0 mL) was added under air. The vial was then heated in the microwave reactor to 180˚C for 40 minutes. The vial was allowed to cool down to room temperature, the solid removed by vacuum filtration and washed with cold water and diethyl ether, followed by drying under vacuum. Isoquinolin-1(2*H*)-one was obtained as a white solid (702 mg, 81% yield). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.25 (s, 1H), 8.17 (d, *J* = 8.3 Hz, 1H), 7.79 – 7.56 (m, 2H), 7.57 – 7.35 (m, 1H), 7.25 – 6.99 (m, 1H), 6.54 (d, *J* = 7.2 Hz, 1H). The data matched the reported compound.[5] **Step 2:** The synthesis was performed according to a reported procedure.[6] In an argon glovebox, the above obtained white solid (Isoquinolin-1(2*H*)-one, 3.91 mmol, 568 mg) and anhydrous K_2CO_3 (2 equiv, 1081 mg) were weighed into an oven-dried vial. Anhydrous methanol (5 mL), followed by MeI (2 equiv, 487 µL), was added via syringe under N_2. The mixture was stirred for 22 hours at reflux temperature. After concentrating the resultant mixture under reduced pressure, the residue was dissolved in water and extracted with $CHCl_3$ three times. The combined organic layers were dried over $MgSO_4$ and purified by silica gel chromatography (gradient of 0 – 50% EtOAc in hexanes). The required fractions were concentrated under

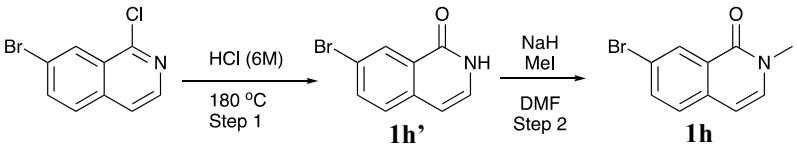
reduced pressure to afford 2-methylisoquinolin-1(2*H*)-one **(1f)** as a white solid (89% yield, 554 mg). **^{1}H NMR** (399 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.1 Hz, 1H), 7.63 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.54 – 7.42 (m, 2H), 7.07 (d, *J* = 7.3 Hz, 1H), 6.49 (d, *J* = 7.3 Hz, 1H), 3.61 (s, 3H). This data matches reported values.[6]

2-phenylisoquinolin-1(2*H*)-one (1g)



Prepared according to a reported procedure.[7] To a crimp-top vial charged with isoquinolin-1(2*H*)-one (6.89 mmol, 1.0 g), CuI (10 mol %, 127.6 mg) and K_2CO_3 (1 equiv, 0.925 g), DMF (8 mL) and PhI (2 equiv, 1.5 mL) were added by syringe under N_2. The mixture was stirred at 150 ˚C for 6 hours. The vial was then allowed to cool down to room temperature and the mixture diluted with EtOAc (13 mL). NH_4OH (0.1 M aqueous solution, 25 mL) was added, the layers separated, and the aqueous layer was extracted with EtOAc (10 mL) two more times. The combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography (gradient of 0 % to 20 % EtOAc in hexanes) afforded **1f** as a white solid (71 % yield, 1.08 g) **^{1}H NMR** (399 MHz, $CDCl_3$) δ 8.48 (d, *J* = 8.1 Hz, 1H), 7.68 (ddd, *J* = 8.2, 7.1, 1.4 Hz, 1H), 7.58 – 7.48 (m, 4H), 7.46 – 7.39 (m, 3H), 7.19 (d, *J* = 7.4 Hz, 1H), 6.57 (d, *J* = 7.5 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.1, 141.5, 137.2, 132.7, 132.3, 129.4, 128.4, 128.2, 127.3, 127.0, 126.7, 126.1, 106.3. This data matches reported values. [8]

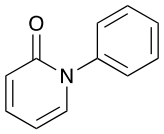
7-bromo-2-methylisoquinolin-1(2*H*)-one (1h)



Step 1: Adapted from a reported method.[4] To a crimp-top microwave vial charged with 7-bromo-1-chloroisoquinoline (6 mmol, 1455 mg), 6M HCl (15.0 mL) was added under air. The vial was then heated in the microwave reactor to 180˚C for 40 minutes. The vial was allowed to cool down to room temperature, the solid removed by vacuum filtration and washed with cold water and diethyl ether, followed by drying under vacuum. 7-bromoisoquinolin-1(2*H*)-one **(1h')** was obtained as a yellow solid (1155 mg, 86% yield). **^{1}H NMR** (399 MHz, DMSO-d_6) δ 11.43 (s, 1H), 8.26 (d, *J* = 2.2 Hz, 1H), 7.85 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.22 (dd, *J* = 6.8, 5.8 Hz, 1H), 6.57 (d, *J* = 6.9 Hz, 1H). These data matched the reported values.[9] **Step 2:** Adapted from a reported procedure.[6] In an argon glovebox, the above obtained yellow solid (7-bromoisoquinolin-1(2*H*)-one, 3.91 mmol, 568 mg) and anhydrous K_2CO_3 (2 equiv, 1081 mg) were weighed into an oven-dried vial. Anhydrous methanol (5 mL), followed by MeI (2 equiv, 487 µL), was added via syringe under N_2. The mixture was stirred for 22 hours at reflux temperature. After concentrating the resultant mixture under reduced pressure, the residue was dissolved in water and extracted with $CHCl_3$ three times. The combined organic layers were dried over $MgSO_4$ and purified by silica gel chromatography (gradient of 0 – 50% EtOAc in hexanes). The appropriate fractions were concentrated under reduced pressure to afford 7-bromo-2-methylisoquinolin-1(2*H*)-one **(1h)** as a white solid (89% yield, 554 mg). **^{1}H NMR** (399 MHz, $CDCl_3$) δ 8.57 (dt, *J* = 2.1, 0.6 Hz, 1H), 7.71 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.09 (d, *J* = 7.3 Hz, 1H), 6.45 (dd, *J* = 7.3, 0.7 Hz, 1H), 3.60 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$)

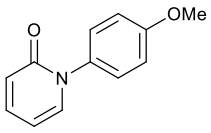
δ 161.6, 135.9, 135.4, 133.0, 130.5, 127.7, 127.6, 120.8, 105.5, 37.3. **HRMS ESI$^+$ (M+H$^+$)** calculated for $C_{10}H_9NOBr$ = 237.9868, found = 237.9868. **FT/IR (ν^{-1}_{max} cm^{-1})** 3417, 1086, 2919, 2849, 1646, 1612, 1590, 1543, 1489, 1438, 1409, 1394, 1380, 1348, 1315, 1290, 1245, 1209, 1184, 1158, 1128, 1066, 967, 957, 889, 828, 787, 757, 722, 705, 692, 596, 567, 519, 493, 466.

1-phenylpyridin-2(1*H*)-one (1j)



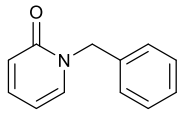
Prepared according to a reported procedure.[7] To a crimp-top vial charged with pyridin-2(1*H*)-one (13.4 mmol, 1.27 g), CuI (10 mol %, 255.2 mg) and K_2CO_3 (1 equiv, 1.85 g), DMF (16 mL) and PhI (2 equiv, 3 mL) were added by syringe under N_2. The mixture was stirred at 150 ˚C for 6 hours. The vial was then allowed to cool down to room temperature and the mixture diluted with EtOAc (25 mL). NH_4OH (0.1 M aqueous solution, 50 mL) was added, the layers separated, and the aqueous layer was extracted with EtOAc (15 mL) two more times. The combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue thus obtained was washed withhexanes, passed through a pad of silica using EtOAc followed by washing the silica pad with additional EtOAc (15 mL) to collect residual product. Upon removal of EtOAc, the solid obtained was recrystallized by dissolving the residue in a *minimal amount* of hot EtOAc, cooling it to room temperature and then addinghexanes (slowly, excess), followed by vacuum filtration to afford the product as a pale-yellow solid (70 % yield, 1.60 g). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 – 7.46 (m, 2H), 7.44 – 7.36 (m, 4H), 7.33 (ddt, *J* = 6.9, 2.1, 0.6 Hz, 1H), 6.66 (dt, *J* = 9.3, 0.7 Hz, 1H), 6.24 (td, *J* = 6.7, 1.3 Hz, 1H). This data matches that of previous reports.[7]

1-(4-methoxyphenyl)pyridin-2(1H)-one (1k)



Following a known procedure.[7] To an oven-dried crimp-top vial charged with 2-hydroxypyridine (1.34 mmol, 127.4 mg), K_2CO_3 (1.34 mmol, 185.2 mg), 4-iodoanisole (2.68 mmol, 646 mg) and CuI (10 mol %, 25.5 mg), DMF (2 mL) was added by syringe. The mixture was stirred at 150 ˚C in an oil bath overnight (16 hours), following which the vial was allowed to cool down to room temperature. The contents were diluted with NH_4OH (0.1 M, 50 mL) and the product was extracted using EtOAc (3 times, 15 mL each). The organic layers were combined, washed with brine and dried over $MgSO_4$. The extract was purified by column chromatography (gradient of 0% to 50% EtOAc in hexanes) to afford the product as a white solid (60 % yield, 161 mg) **^{1}H NMR** (399 MHz, $CDCl_3$) δ 7.38 (dddd, J = 9.3, 6.6, 2.1, 0.5 Hz, 1H), 7.34 – 7.28 (m, 3H), 7.02 – 6.96 (m, 2H), 6.65 (ddd, J = 9.3, 1.4, 0.7 Hz, 1H), 6.24 – 6.18 (m, 1H), 3.85 (s, 3H). The NMR data matches reported values.[8]

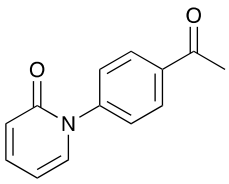
1-benzylpyridin-2(1H)-one (1l)



Prepared according to a reported procedure.[10] To a mixture of 2-hydroxypyridine (761 mg, 8 mmol, 1 equiv), and potassium carbonate (2.76 g, 20 mmol, 2.5 equiv) in acetone was added benzyl bromide (1.19 mL, 10 mmol, 1.25 equiv) and the mixture was heated at reflux for 20h. It was then cooled to room temperature and the solids were filtered off and washed with acetone. The filtrate was

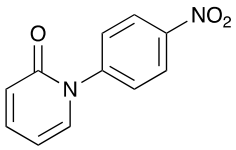
concentrated in vacuo, and the residue was partitioned between water and chloroform. The aqueous layer was further extracted with chloroform, and the organic layers were gathered, dried over magnesium sulfate and evaporated to dryness. The resulting yellow oil was purified by flash chromatography using ethyl acetate/petroleum ether (1:2 to 1:1) as eluent. The product was obtained as a white solid (1.30 g, 88%). **^{1}H NMR** (399 MHz, $CDCl_3$) δ 7.37 – 7.23 (m, 7H), 6.62 (ddd, J = 9.2, 1.4, 0.7 Hz, 1H), 6.13 (td, J = 6.7, 1.4 Hz, 1H), 5.15 (s, 2H). The spectral data matches the previously reported.[10]

1-(4-acetylphenyl)pyridin-2(1*H*)-one (1m)



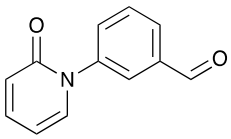
Adapted from a known procedure.[7] To an oven-dried crimp-top vial charged with 2-hydroxypyridine (1.34 mmol, 127.4 mg), K_2CO_3 (1.34 mmol, 185.2 mg), 4-iodoacetophenone (2.68 mmol, 659.4 mg) and CuI (10 mol %, 25.5 mg), DMF (2 mL) was added by syringe. The mixture was stirred at 150 ˚C in an oil bath overnight (16 hours), following which the vial was allowed to cool down to room temperature. The contents were diluted with NH_4OH (0.1 M, 50 mL) and the product was extracted using EtOAc (3 times, 15 mL each). The organic layers were combined, washed with brine and dried over $MgSO_4$. The extract was purified by column chromatography (gradient of 0% to 40% EtOAc in hexanes) to afford the product as a yellow solid (40 % yield, 114.0 mg). **m.p.:** 159-160 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (dt, *J* = 8.8, 2.3 Hz, 2H), 7.52 (dt, *J* = 8.9, 2.2 Hz, 2H), 7.41 (ddd, *J* = 9.3, 6.6, 2.1 Hz, 1H), 7.33 (ddd, *J* = 6.9, 2.1, 0.8 Hz, 1H), 6.67 (ddd, *J* = 9.3, 1.3, 0.8 Hz, 1H), 6.28 (td, *J* = 6.7, 1.3 Hz, 1H), 2.64 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.0, 162.1, 144.7, 140.2, 137.3, 136.8, 129.5, 126.9, 122.2, 106.4, 26.8. **HRMS EI$^+$ (M+H$^+$)** Calculated for $C_{13}H_{10}NO_2$ = 214.0868, found = 214.0866.

1-(4-nitrophenyl)pyridin-2(1*H*)-one (1n)



Prepared according to a reported procedure.[7] To an oven-dried crimp-top vial charged with 2-hydroxypyridine (1.34 mmol, 127.4 mg), K_2CO_3 (1.34 mmol, 185.2 mg), 4-Iodonitrobenzene (2.68 mmol, 667.3 mg) and CuI (10 mol %, 25.5 mg), DMF (2 mL) was added by syringe. The mixture was stirred at 150 ˚C in an oil bath overnight (16 hours), following which the vial was allowed to cool down to room temperature. The contents were diluted with NH_4OH (0.1 M, 50 mL) and the product was extracted using EtOAc (3 times, 15 mL each). The organic layers were combined, washed with brine and dried over $MgSO_4$. The extract was purified by column chromatography (gradient of 0% to 50% EtOAc in hexanes) to afford the product as a yellow solid (90 % yield, 268 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.37 (dt, *J* = 9.1, 2.8, 2.2 Hz, 2H), 7.63 (dt, *J* = 9.0, 2.8 Hz, 2H), 7.44 (ddd, *J* = 9.4, 6.6, 2.1 Hz, 1H), 7.33 (ddd, *J* = 6.9, 2.1, 0.8 Hz, 1H), 6.68 (ddd, *J* = 9.4, 1.3, 0.8 Hz, 1H), 6.32 (td, *J* = 6.8, 1.2 Hz, 1H). The NMR data matches reported values.[7]

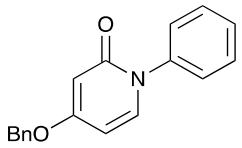
3-(2-oxopyridin-1(2*H*)-yl)benzaldehyde (1o)



Adapted from a reported procedure.[7] To an oven-dried crimp-top vial charged with 2-hydroxypyridine (1.34 mmol, 127.4 mg), K_2CO_3 (1.34 mmol, 185.2 mg), 3-

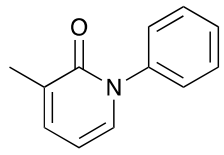
Iodobenzaldehyde (2.68 mmol, 621.8 mg) and CuI (10 mol %, 25.5 mg), DMF (2 mL) was added by syringe. The mixture was stirred at 150 ˚C in an oil bath overnight (16 hours), following which the vial was allowed to cool down to room temperature. The contents were diluted with NH_4OH (0.1 M, 50 mL) and the product was extracted using EtOAc (3 times, 15 mL each). The organic layers were combined, washed with brine and dried over $MgSO_4$. The extract was purified by column chromatography (gradient of 0% to 50% EtOAc in hexanes) to afford the product as an off-white solid (46 % yield, 123 mg) **m.p.:** 121-122 ˚C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.04 (s, 1H), 7.93 (dq, J = 7.3, 1.4 Hz, 1H), 7.90 (s, 1H), 7.72 – 7.69 (m, 1H), 7.66 (t, J = 7.7 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.36 – 7.32 (m, 1H), 6.66 (d, J = 8.3 Hz, 1H), 6.28 (tt, J = 6.8, 1.2 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 191.0, 162.2, 141.8, 140.3, 137.6, 137.5, 132.7, 130.2, 129.8, 127.4, 122.2, 106.5. **HRMS ESI$^+$ (M+H$^+$):** calculated for $C_{12}H_{10}NO_2$ = 200.0712, found = 200.0719.

4-(benzyloxy)-1-phenylpyridin-2(1*H*)-one (1p)



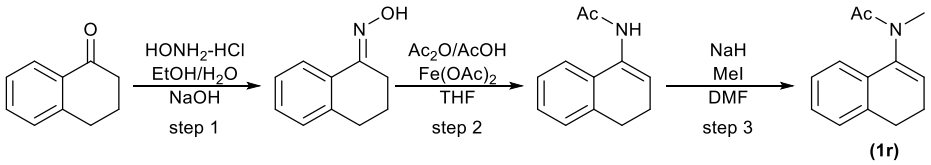
Adapted from a reported procedure.[7] To a crimp-top vial charged with 4-(benzyloxy)pyridin-2(1*H*)-one (5.26 mmol, 1.08 g), CuI (10 mol %, 102 mg) and K_2CO_3 (1 equiv, 741 mg), DMF (8 mL) and PhI (2 equiv, 1.2 mL) were added by syringe under N_2. The mixture was stirred at 150 ˚C for 6 hours. The vial was then allowed to cool down to room temperature and the mixture diluted with EtOAc (40 mL). NH_4OH (0.1 M aqueous solution, 100 mL) was added, the layers separated, and the aqueous layer was extracted with EtOAc (25 mL) two more times. The combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The extract was purified by column chromatography (gradient of EtOAc in hexanes 0% - 60%) and the appropriate fractions were concentrated to afford the product as a white solid (61 % yield, 907 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.50 – 7.45 (m, 2H), 7.44 – 7.34 (m, 8H), 7.23 (d, *J* = 7.3 Hz, 1H), 6.15 – 5.99 (m, 2H), 5.05 (s, 2H). The NMR data matches reported values.[8]

3-methyl-1-phenylpyridin-2(1*H*)-one



This substrate was used to probe the selectivity towards the 3-position in this class of substrates. Prepared by adapting a reported procedure. [7] To a crimp-top vial charged with **3-methylpyridin-2-ol** (5.36 mmol, 660 mg), CuI (10 mol %, 102 mg) and K_2CO_3 (1 equiv, 741 mg), DMF (8 mL) and PhI (2 equiv, 1.2 mL) were added by syringe under N_2. The mixture was stirred at 150 ˚C overnight (16 hours). The vial was then allowed to cool down to room temperature and the mixture diluted with EtOAc (40 mL). NH_4OH (0.1 M aqueous solution, 100 mL) was added, the layers separated, and the aqueous layer was extracted with EtOAc (25 mL) two more times. The combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The extract was purified by column chromatography (gradient of EtOAc in hexanes 0% - 30%) and the required fractions were concentrated to afford the product as a white solid (81 % yield, 804 mg). **^{1}H NMR** (399 MHz, $CDCl_3$) δ 7.50 – 7.43 (m, 2H), 7.42 – 7.35 (m, 3H), 7.28 – 7.24 (m, 1H), 7.24 – 7.20 (m, 1H), 6.15 (t, *J* = 6.8 Hz, 1H), 2.19 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.8, 141.4, 137.0, 135.4, 130.9, 129.2, 128.3, 126.7, 105.6, 17.4. NMR data matched reported values.[11]

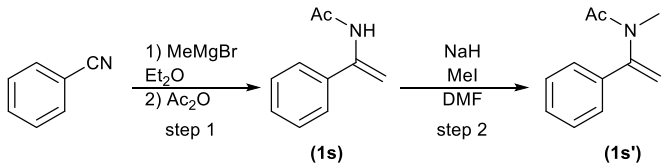
***N*-(3,4-dihydronaphthalen-1-yl)-*N*-methylacetamide (1r)**



Step 1 (oxime synthesis): Adapted from a reported procedure.[12] A mixture of 1-tetralone (2.924 g, 20.001 mmol), hydroxylamine hydrochloride (2.168 g, 31.202 mmol), and 83% EtOH soln in water (8.7 mL) was placed in a crimp-top vial with a magnetic stir bar. Freshly ground sodium hydroxide (4 g, 100.008 mmol) was added in portions under air. The vial was capped and heated to reflux for 15 minutes with occasional shaking to facilitate mixing. After this, the vial was allowed to cool to room temperature. The contents were poured into a soln of HCl in water (~1.5 M), enough to quench residual NaOH. The precipitate was suction filtered, washed thoroughly with water, and dried under vacuum to give the crude oxime as a light brown solid (2.80 g, 87% yield), which was used without further purification for the next step. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.07 – 7.73 (m, 1H), 7.32 – 7.13 (m, 3H), 2.83 (t, *J* = 6.7 Hz, 2H), 2.77 (t, *J* = 6.4, 5.6 Hz, 2H), 1.89 (p, *J* = 6.4 Hz, 2H). **Step 2:** Performed according to a reported procedure.[13] To an oven-dried crimp-top vial equipped with a magnetic stir bar charged with (*E*)-3,4-dihydronaphthalen-1(2H)-one oxime (1.128 g, 7 mmol), THF (0.504 g, 9.4 mL, 7 mmol) was added by syringe. To this stirring solution, acetic anhydride (1.320 mL, 14 mmol) and acetic acid (1.201 mL, 21 mmol) were added by syringe, followed by purging the vial with N_2 for 20 minutes. Subsequently, iron (II) acetate (2.435 g, 14 mmol) was added, and the reaction vial was recapped. The mixture was heated at 65℃ and stirred for 16 hours. The mixture was then poured into a 250 mL separatory funnel with 20 mL water and neutralized with 1 g sodium bicarbonate (solid). The aqueous solution was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ (20 mL) and brine (20 mL), dried with MgSO, filtered, and concentrated *in vacuo*. The extract was purified by flash chromatography (gradient of 0% -30%% EtOAc in hexanes) and *N*-(3,4-dihydronaphthalen-1-yl)acetamide was obtained (554 mg) as an orange solid. The solid was dissolved in EtOAc (~30 mL) and stirred with activated charcoal for ~1 hour. Charcoal was removed by vacuum filtration through celite washing with EtOAc. Concentration of the filtrate yielded *N*-(3,4-dihydronaphthalen-1-yl)acetamide in 31% yield (400 mg). **^{1}H NMR** (500 MHz, $CDCl_3$)(mixture of rotamers) δ 7.24 – 7.06 (m, 4H), 6.81 (s, 1H), 6.68 (s, 0.37H), 6.44 (t, *J* = 4.9 Hz, 0.75H), 5.97 (s, 0.25H), 2.84 (t, *J* = 8.2 Hz, 1H), 2.76 (t, *J* = 7.9 Hz, 3H), 2.46 – 2.33 (m, 3H), 2.17 (s, 3H), 1.96 (s, 1H). The NMR data matches reported values.[13] **Step 3:** Performed according to a reported procedure.[14] To an oven-dried, sealed crimp-top vial charged with *N*-(3,4-dihydronaphthalen-1-yl)-*N*-methylacetamide (1 mmol, 187.2 mg), and NaH (1.5 equiv, 36 mg) cooled to 0 ˚C, 3 mL of dry DMF was added slowly by syringe under N_2. The resulting suspension was stirred at 0 ˚C for 10 min, followed by addition of MeI (2 equiv) dropwise. The solution was warmed to room temperature and stirred for 16 hours. Excess sodium hydride was quenched by adding 1 mL of water at 0 ˚C. The solution as diluted with 50 mL of water, the organic layer extracted with ethyl acetate three times (15 mL each). The combined organic layer was concentrated under reduced pressure and *N*-(3,4-dihydronaphthalen-1-yl)-*N*-methylacetamide **(1r)** was isolated by flash column chromatography (gradient of 30 % EtOAc in hexanes)

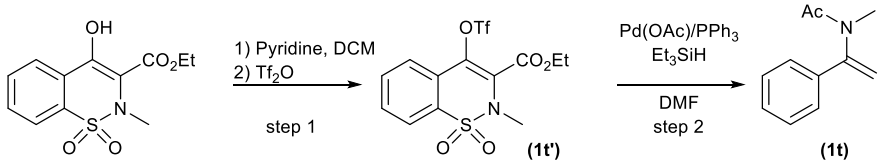
as a white solid (95 % yield, 190 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 – 7.17 (m, 3H), 7.04 – 7.01 (m, 1H), 5.99 (t, *J* = 4.6 Hz, 1H), 3.13 (s, 3H), 2.85 (td, *J* = 8.3, 7.6, 4.3 Hz, 2H), 2.49 – 2.38 (m, 2H), 1.97 (s, 3H). The NMR data matches the reported values.[14]

***N*-methyl-*N*-(1-phenylvinyl)acetamide (1s')**



Step 1: To a 250 mL 2-neck flask (fitted with a condenser) charged with MeMgBr (18 mmol, 3M soln in Et_2O, 6 mL) in Et_2O (50 mL), a solution of PhCN (17 mmol, 1.75 mL) in Et_2O (20 mL) was added dropwise at 0 ˚C. The solution was refluxed overnight (16 h) at 45 ˚C. A solution of Ac_2O (17 mmol, 1.607 mL) in Et_2O (20 mL) was added dropwise to the resulting solution at 0 ˚C. This solution was refluxed for 8 hours. At room temperature, MeOH was added till all the precipitate dissolved. 85 mL of a 1:1 mixture of EtOAc:H_2O was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 times, 20 mL each time). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and **1s** was obtained as a white solid (62 % yield, 1.67 g) following column chromatography (gradient of 0% to 25% EtOAc in hexanes). The spectral data matches reported values.[14] **Step 2:** Prepared according to a reported procedure. To a crimp-top vial charged with **1s** (2 mmol, 322.4 mg) and NaH (1.1 eq, 52.8 mg), DMF (5 mL) was quickly added via syringe. The mixture was stirred at room temperature for 5 mins, followed by addition of MeI (4 eq, 498 µL). The solution was refluxed overnight (16 hours), cooled to room temperature and diluted with EtOAc (20 mL). Cold water (~0 ˚C) was added slowly (caution; effervescence) and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 times, 15 mL each time). The combined organic layers were washed with water (2 times, 50 mL) and brine (once, 50 mL), and subsequently dried over $MgSO_4$. Column chromatography (gradient of 0% to 20 % EtOAc in hexanes) afforded **1s'** in 84 % yield (294 mg). The spectral data matches reported values.[14]

Ethyl 2-methyl-2*H*-benzo[*e*][1,2]thiazine-3-carboxylate 1,1-dioxide (1t)



Step 1: Adapted from a reported procedure.[15] To an oven dried crimp-top vial charged with 4-hydroxy-2-methyl-2*H*-benzo[*e*][1,2]thiazine 1,1-dioxide (2 mmol, 566 mg), DCM (20 mL), pyridine (2 equiv, 330 µL) were added sequentially at room temperature, followed by Tf_2O (1.2 equiv, 400 µL) at 0 ˚C). The mixture was stirred at 0 ˚C for 10 mins, the ice bath was removed, and then the mixture was stirred for an additional 24 hours. Next, the contents of

the vial were poured into water (60 mL) and an extraction with DCM was performed (10 mL, three times). The organic layers were combined, dried over $MgSO_4$ and the product was purified by silica gel chromatography (gradient of 0 % - 25 % EtOAc in hexanes). The appropriate fractions were combined, and the product **1t'** was obtained as an off-white solid (**m.p.:**105-106 ˚C), (92 % yield, 764 mg). **^{1}H NMR** (399 MHz, $CDCl_3$) δ 7.93 – 7.90 (m, 1H), 7.85 – 7.82 (m, 1H), 7.83 – 7.70 (m, 2H), 4.45 (q, *J* = 7.2 Hz, 2H), 3.22 (s, 3H), 1.44 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.0, 138.0, 133.8, 132.7, 132.0, 129.2, 127.4, 124.7, 122.9, 118.4 (q, *J* = 321.3 Hz), 63.6, 36.2, 14.00. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -73.3 (s, 3F). **HRMS EI+ (M + Na^+)** Calculated for $NaC_{13}H_{12}F_3NO_7S_2$ = 437.9905, found = 437.9897. **FT/IR (ν^{-1}_{max} cm^{-1}):** 1648, 1603, 1558, 1452, 1441, 1403, 1381, 1339, 1308, 1271, 1229, 1170, 1144, 1118, 1065, 1043, 1021, 929, 883, 867, 832, 806, 784, 769, 726, 648, 611, 572, 561, 524, 508, 506, 487, 468, 452, 437, 417, 405. **Step 2 product:** Adapted from reported procedures.[16,17] To an oven-dried crimp-top vial charged with triflate **1t'** (1.84 mmol, 764 mg), $Pd(OAc)_2$ (2 mol %, 8.3 mg) and PPh_3 (2 mol %, 9.7 mg), DMF (10 mL) and Et_3SiH (2.5 equiv, 705 µL) were added sequentially by syringe. The mixture was stirred at 60 ˚C for 24 hours. The mixture was then diluted with EtOAc (75 mL) and washed with $NaHCO_3$, water and brine (75 mL each). The organic layer was dried over $MgSO_4$, filtered and concentrated to afford a brown solid. The solid was washed with hexanes (2 mL, 2 times), re-dissolved in $CHCl_3$ and then concentrated under reduced pressure to afford the product **1t** as a light-brown solid (65 % yield, 320 mg). **m.p.:** 103 – 105 ˚C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 – 7.86 (m, 1H), 7.68 – 7.62 (m, 2H), 7.57 (s, 1H), 7.57 – 7.53 (m, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 3.26 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.5, 133.9, 133.6, 132.4, 130.9, 130.7, 129.3, 122.7, 122.5, 62.3, 36.5, 14.4. **FT/IR (ν^{-1}_{max} cm^{-1}):** 1720, 1613, 1475, 1443, 1426, 1375, 1363, 1331, 1310, 1302, 1286, 1226, 1170, 1144, 1133, 1073, 1058, 1013, 965, 919, 902, 880, 867, 776, 770, 737, 730, 686, 587, 559, 513, 482, 472, 460, 435, 407. **HRMS EI+ (M)** Calculated for $C_{12}H_{13}NO_4S$ = 267.05653, found = 267.05567.

Table S1. Optimization of the reaction conditions.

The following table is the full reaction optimization experiments. The manuscript shows only a summary of the screening studies.

Entry	Solvent	Oxidant (equiv)	$TMSCF_3$ (equiv)	KF (equiv)	Additive	Yield (%)[b]
1	CH_3CN	PIDA (2)	4	4	-	22
2	CH_3CN	PIFA (2)	4	4	-	42
3	MeOH	PIFA (2)	4	4	-	0
4	$PhCH_3$	PIFA (2)	4	4	-	0
5	THF	PIFA (2)	4	4	-	15
6	EtCN	PIFA (2)	4	4	-	17
7	CH_3CN	PIFA (2)	2	2	-	52
8	CH_3CN	PIFA	1.5	1.5	-	52
9[c]	CH_3CN	PIFA	1.5	1.5	-	29
10[d]	CH_3CN	PIFA	1.5	1.5	-	26
11	CH_3CN	PIFA	1.5	1.5	CuCl	59
12	CH_3CN	PIFA	1.5	1.5	$Cu(OTf)_2$	56
13	CH_3CN	PIFA	1.5	1.5	$Fe(OAc)_2$	7
14	CH_3CN	PIFA	1.5	1.5	$ZnCl_2$	30
15	CH_3CN	PIFA	1.5	1.5	$Cu(OAc)_2$	62
16[e]	**CH_3CN**	PIFA	**2.0**	**1.5**	**$Cu(OAc)_2$**	**73**
17[f]	CH_3CN	PIFA	1.5	1.5	$Cu(OAc)_2$	39

18	CH_3CN	PIFA	1.5	1.5	$Cu(MeCN)_4PF_6$	29
19	CH_3CN	PIFA	1.5	1.5	$Cu(MeCN)_4BF_4$	36

[a] Conditions: **1a** (0.25 mmol), solvent (2.5 mL), 0.1 equiv of additive unless otherwise specified, room temperature for 1h. [b] Yield determined by ^{19}F NMR spectroscopy using $PhCF_3$ as internal standard. [c] Reaction performed at 0 °C. [d] Reaction performed at 80 °C. [e] 0.3 equiv of additive. [f] 1 equiv of additive. PIFA = bis(trifluoroacetoxy)iodobenzene; PIDA = diacetoxyiodobenzene. **2a** was obtained as a (3:1) mixture of *E*:*Z* isomers in all cases.

General procedures for C(sp^2)–H trifluoromethylation

Method A

In an argon glovebox, starting material **1** (0.25 mmol), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg) and $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial equipped with a stir bar. The vial was sealed with a septum and brought outside the glovebox. Subsequently, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe under a stream of N_2. The mixture was then stirred at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography using appropriate solvent system (*vide infra*).

Method B

In an argon glovebox, starting material **1** (0.25 mmol), PIFA (3 equiv, 322.6 mg), KF (3 equiv, 43.6 mg) and $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial equipped with a stir bar. The vial was sealed with a septum and brought outside the glovebox. Subsequently, CH_3CN (2.5 mL) and $TMSCF_3$ (4.5 equiv, 165 µL) were added in quick succession to the vial by syringe under a stream of N_2. The mixture was then stirred at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography using appropriate solvent system (*vide infra*).

Method C

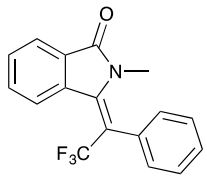
In an argon glovebox, starting material **1** (0.25 mmol), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg) and $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial (*vial 1*) equipped with a stir bar. Into a second vial, also equipped with a stir bar (*vial 2*), PIFA (1.5 equiv, 161.3 mg) and KF (1.5 equiv, 21.8 mg) were charged. Both vials were then sealed with a septum and brought outside the glovebox. Subsequently, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession by syringe to *vial 1* under a stream of N_2. The mixture was then stirred at room temperature for 1 hour. After this time, this solution was transferred into *vial 2*, followed by addition of $TMSCF_3$ (2 equiv, 75 µL) by syringe. **Note*: *To ensure full transfer of the contents, a small amount of CH_3CN (0.5 mL) was used to wash vial 1, and then transferred to vial 2.* This mixture was further stirred at room temperature for an additional 1 hour, then diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography using appropriate solvent system (*vide infra*).

Synthesis and NMR spectroscopic data of products

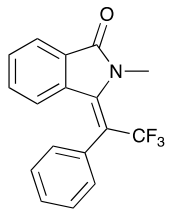
Note: in the case of products **2a-2d, geometrical isomers where assigned based on the observed C–F coupling (quartet) between the N–Me and CF_3 groups present in the Z-isomer. Such coupling was not seen in the E-isomer.*

2-methyl-3-(2,2,2-trifluoro-1-phenylethylidene)isoindolin-1-one (2a)

Prepared following general *method A*. In an argon glovebox, (*Z*)-3-benzylidene-2-methylisoindolin-1-one **(1a)** (0.25 mmol, 58.8 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 8% EtOAc in hexanes). The two isomers (*E*:*Z* = 3:1, determined by ^{19}F NMR) were obtained in a combined yield of 66% (50 mg) as a white solid.

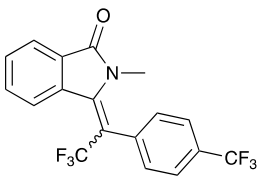


Shifts of major **(*E*-2a): ^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.19 (d, J = 7.2 Hz, 1H), 7.90 – 7.88 (m, 1H), 7.67 (t, J = 7.1 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.46 – 7.40 (m, 3H), 7.36 – 7.33 (m, 2H), 2.59 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.6, 143.2 (q, J = 3.2 Hz), 134.2, 133.1 (q, J = 2.2 Hz), 132.9, 131.9, 130.7, 129.9, 129.3, 128.4, 125.5 (q, J = 7.7 Hz), 124.3 (q, J = 272.7 Hz), 123.5, 111.4 (q, J = 33.7 Hz), 31.0. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -54.3 (s, 3F). **HRMS EI$^+$ (M)** Calculated for $C_{17}H_{12}ONF_3$ = 303.08710, found = 303.08762. **m.p.:** 119-122 ˚C



Shifts of minor isomer **(*Z*-2a): ^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (d, J = 7.5 Hz, 1H), 7.59 – 7.51 (m, 1H), 7.54 – 7.47 (m, 2H), 7.40 – 7.34 (m, 3H), 7.12 (t, J = 7.8 Hz, 1H), 5.73 (d, J = 8.1, 0.8 Hz, 1H), 3.58 (q, J = 2.9 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.0, 141.8 (q, J = 3.7, 3.2 Hz), 137.2, 133.8 (q, J = 2.6 Hz), 132.4, 131.6, 130.2, 129.6, 129.4, 129.2, 125.2, 123.5, 123.2 (q, J = 272.1 Hz), 110.7 (q, J = 33.8 Hz), 30.2 (q, J = 7.3 Hz). **^{19}F NMR** (470 MHz, $CDCl_3$) δ -50.8 (q, *J* = 2.6 Hz, 3F). **HRMS EI$^+$ (M)** Calculated for $C_{17}H_{12}ONF_3$ = 303.08710, found = 303.08762. **m.p.:** 111-112 ˚C

2-methyl-3-(2,2,2-trifluoro-1-(4-(trifluoromethyl)phenyl)ethylidene)isoindolin-1-one (2b)

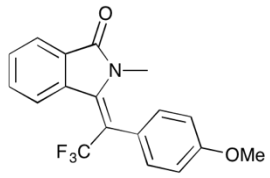


Prepared following general *method A*. In an argon glovebox, (*Z*)-2-methyl-3-(4-(trifluoromethyl)benzylidene)isoindolin-1-one **(1b)** (0.25 mmol, 75.8 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 8% EtOAc in hexanes). The two inseparable isomers (*E*:*Z* = 4:1, determined by

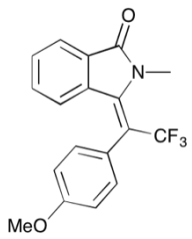
^{19}F NMR) were obtained in a combined yield of 60% (56 mg) as a yellow solid. Only shifts of the major isomer reported for clarity. **(*E*-2b) ^{1}H NMR** (399 MHz, $CDCl_3$) δ 8.19 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 7.4 Hz, 1H), 7.72 – 7.68 (m, 3H), 7.61 (td, J = 7.4, 0.9 Hz, 1H), 7.50 (d, J = 7.7 Hz, 2H), 2.59 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.4, 144.1 (q, *J* = 3.3 Hz), 137.1, 134.0, 134.0, 133.1, 132.5, 132.4 (q, *J* = 7.9 Hz), 131.5 (q, *J* = 32.9 Hz), 131.1, 129.7, 125.6 (q, *J* = 7.6 Hz), 125.4 (q, *J* = 3.7 Hz), 123.9 (q, *J* = 272.4 Hz), 123.8 (q, *J* = 272.4 Hz), 31.3. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -54.0 (s, 3F), -63.3 (s, 3F). **^{19}F NMR** of minor isomer (**Z-2b)** (470 MHz) δ -50.2 (q, *J* = 2.3 Hz, 3F), -63.2 (s, 3F). **HRMS EI+ (M)** Calculated for $C_{18}H_{11}NOF_6$ = 371.07447, found = 371.07434. **FT/IR (ν^{-1}_{max} cm^{-1}):** 1718, 1617, 1589, 1473, 1449, 1430, 1409, 1370, 1322, 1293, 1272, 1198, 1160, 1103, 1065, 1029, 1020, 979, 938, 927, 868, 839, 815, 802, 771, 750, 701, 679, 664, 631, 601, 556, 521, 480, 457, 453, 406.

2-methyl-3-(2,2,2-trifluoro-1-(4-methoxyphenyl)ethylidene)isoindolin-1-one (2c)

Prepared following general *method A*. In an argon glovebox, (*Z*)-2-methyl-3-(4-(trifluoromethyl)benzylidene)isoindolin-1-one **(1c)** (0.25 mmol, 66.3 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 8% EtOAc in hexanes). The two isomers (*E*:*Z* = 4:1) were obtained in a combined yield of 69% (57 mg) as a white solid.



Shifts of the major isomer **(*E*-2c): ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.17 (dt, J = 8.1, 0.7 Hz, 4H), 7.88 (ddd, J = 7.4, 1.4, 0.7 Hz, 1H), 7.66 (td, J = 7.7, 1.4 Hz, 1H), 7.57 (td, J = 7.4, 0.9 Hz, 1H), 7.27 – 7.23 (m, 2H), 6.96 – 6.91 (m, 2H), 3.86 (s, 3H), 2.63 (s, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.6, 160.3, 143.3 (q, J = 3.1 Hz), 134.3, 133.2, 132.8, 130.6, 129.9, 125.5 (q, J = 7.7 Hz), 125.1 (q, J = 2.3 Hz), 124.4 (q, J = 272.6 Hz), 123.4 (q, J = 2.6 Hz), 113.9, 111.1 (q, J = 33.6 Hz), 55.5, 31.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -54.9 (s, 3F). **HRMS EI^{+} (M)** Calculated for $C_{18}H_{14}NO_2F_3$ = 333.09766, found = 333.09806. **FT/IR (ν^{-1}_{max} cm^{-1}):** 1696, 1652, 1605, 1574, 1510, 1471, 1456, 1424, 1395, 1342, 1326, 1292, 1240, 1173, 1087, 1029, 972, 953, 941, 887, 829, 814, 770, 741, 720, 692, 634, 612, 588, 560, 539, 515, 505, 474, 456, 418, 408. **m.p:** 131-133 ˚C.

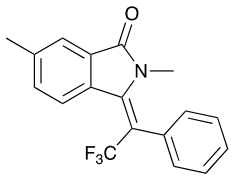


Shifts of the minor isomer **(Z-2c): ^{1}H NMR** (399 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 8.7 Hz, 2H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.02 (d, *J* = 8.6 Hz, 2H), 5.87 (d, *J* = 8.1 Hz, 1H), 3.91 (s, 3H), 3.56 (q, *J* = 2.9 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.1, 160.6, 141.9 (q, J = 2.9 Hz), 137.4, 133.0, 132.4, 130.1, 129.2, 125.8 (q, J = 2.3 Hz), 125.2, 123.5, 123.3 (q, J = 272.0 Hz), 114.8, 110.4 (q, J = 33.6 Hz), 55.6, 30.3 (q, J = 7.2 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -51.5 (q, *J* = 2.9 Hz, 3F). **HRMS EI^{+} (M)** Calculated for $C_{18}H_{14}NO_2F_3$ = 333.09766, found = 333.09806. **FT/IR (ν^{-1}_{max} cm^{-1}):** 1696, 1652, 1605, 1574, 1510, 1471, 1456,

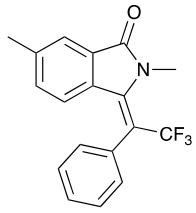
1424, 1395, 1342, 1326, 1292, 1240, 1173, 1087, 1029, 972, 953, 941, 887, 829, 814, 770, 741, 720, 692, 634, 612, 588, 560, 539, 515, 505, 474, 456, 418, 408. **m.p:** 119-122 ˚C.

2,6-dimethyl-3-(2,2,2-trifluoro-1-phenylethylidene)isoindolin-1-one (2d)

Prepared following general *method A*. In an argon glovebox, (*Z*)-3-benzylidene-2,6-dimethylisoindolin-1-one (**1d**) (0.25 mmol, 62.3 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 8% EtOAc in hexanes). The two isomers (*E*:*Z* = 5:1) were obtained in a combined yield of 64% (51 mg) as a white solid.

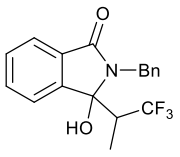


Shifts of major isomer **(*E*-2d): ^{1}H NMR** (399 MHz, $CDCl_3$) 8.05 (d, J = 8.2 Hz, 1H), 7.68 (s, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.44 – 7.39 (m, 3H), 7.36 – 7.32 (m, 2H), 2.57 (s, 3H), 2.49 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.7, 143.3 (q, J = 3.2 Hz), 141.4, 133.8, 133.2 (q, J = 2.3 Hz), 132.0, 131.6, 130.1, 129.2, 128.4, 125.3 (q, J = 7.6 Hz), 124.4 (q, J = 272.6 Hz), 123.7, 110.6 (q, J = 33.6 Hz), 30.9, 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -54.4 (s, 3F). **HRMS EI+ (M):** calculated for $C_{18}H_{14}ONF_3$ = 317.10275, found = 317.10220. **FT/IR (ν^{-1}_{max} cm^{-1}):** 1722, 1705, 1610, 1490, 1468, 1443, 1428, 1366, 1327, 1288, 1275, 1202, 1176, 1150, 1101, 1038, 1030, 997, 983, 961, 944, 899, 879, 826, 791, 771, 755, 714, 700, 671, 650, 620, 599, 556, 526, 504, 471, 456, 447, 432, 416. **m.p:** 110-112 ˚C.



Shifts of minor isomer **(*Z*-2d): ^{1}H NMR** (399 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.57 – 7.43 (m, 3H), 7.36 (d, J = 8.4 Hz, 2H), 6.93 (d, J = 7.6 Hz, 1H), 5.58 (d, J = 8.2 Hz, 1H), 3.56 (q, J = 2.8 Hz, 3H), 2.34 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.1, 142.0 (q, J = 2.9 Hz), 140.8, 134.6, 134.0 (q, J = 2.3 Hz), 133.3, 131.7, 129.5, 129.4, 129.3, 125.0, 123.7, 123.3 (q, J = 271.9 Hz), 109.9 (q, J = 33.9 Hz), 30.2 (q, J = 7.3 Hz), 21.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -50.5 (q, *J* = 2.89 Hz, 3F). **FT/IR (ν^{-1}_{max} cm^{-1}):** 1721, 1617, 1580, 1488, 1464, 1443, 1377, 1275, 1200, 1174, 1149, 1102, 1036, 995, 944, 924, 896, 880, 819, 789, 754, 713, 699, 683, 642, 620, 600, 557, 521, 511, 481, 453, 442, 420, 409. **HRMS EI+ (M):** calculated for $C_{18}H_{14}ONF_3$ = 317.10275, found = 317.10220. **m.p:** 124-125 ˚C.

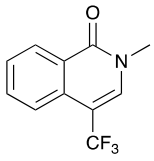
2-benzyl-3-hydroxy-3-(1,1,1-trifluoropropan-2-yl)isoindolin-1-one (2e)



Prepared using general *method A*. Implementing a modification in the work-up procedure (see below). In an argon glovebox, (*E*)-2-benzyl-3-ethylideneisoindolin-1-one (**1e**) (0.25 mmol, 63 mg mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room

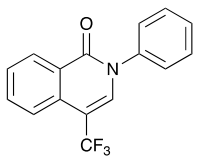
temperature for 1 hour. After this time, the mixture was diluted with EtOAC (5 mL) and HCl (1M, 5ml) was added to the reaction mixture. The layers were separated and the aqueous layer was further extracted with EtOAc (3 mL x 3). The combined organic layers were washed with water (10 mL), brine (10 mL) and dried over MgSO4 and evaporated to dryness under reduced pressure. The residue was further purified by column chromatography using a gradient of 0% - 10% EtOAc in hexanes. Obtained as an inseparable mixture of diastereomers in a 4:1 ratio. White solid, 40% yield, 33 mg. ***Note:* If basic work-up (NH_4OH) is implemented, large amounts of *N*-benzylphthalimide and lower yields of **2e** are obtained. Shifts of major isomer reported for clarity. **^{1}H NMR** (399 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 7.2, 1.5 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.60 (td, *J* = 7.5, 1.4 Hz, 1H), 7.57 – 7.54 (m, 1H), 7.48 (d, *J* = 7.7 Hz, 2H), 7.35 – 7.27 (m, 3H), 4.75 (d, *J* = 15.3 Hz, 1H), 4.62 (d, *J* = 15.2 Hz, 1H), 3.08 – 2.94 (m, 1H), 2.65 (s, 1H), 0.62 (d, *J* = 7.1 Hz, 3H). In order to observe signal corresponding to CF_3 group due to concentration, ^{13}C Shifts of the diastereomeric mixture is reported: **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.8, 167.2, 144.6, 143.6, 138.1, 137.7, 132.7, 132.2, 131.7, 131.4, 130.3, 129.7, 129.1, 128.9, 128.8, 128.8, 128.7, 127.8, 127.6, 126.7 (q, *J* = 280.1 Hz), 125.7 (q, J = 280.4 Hz), 123.9, 123.6, 123.3, 92.0 (q, *J* = 1.4 Hz), 89.6 (q, *J* = 1.9 Hz), 43.9 (q, *J* = 26.2 Hz), 43.8 (q, *J* = 25.4 Hz), 42.9, 42.4, 10.1 (q, *J* = 2.3 Hz), 9.7 (q, *J* = 2.5 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -64.7 (d, *J* = 9.6 Hz, 3F). ^{19}F Shift of minor isomer: δ -68.5 (d, *J* = 8.3 Hz). **HRMS ES+** calculated for $C_{18}H_{15}F_3NO$ ($M\text{-}OH^+$) = 318.1106; found = 318.1155. **FT/IR (ν^{-1}_{max} cm^{-1}):** 3260.56, 2359.96, 2338.27, 1680.18, 1613.64, 1352.82, 1264.59, 1181.67, 1139.24, 1065.00, 1010.52, 957.002, 911.683, 832.113, 745.835, 710.158

2-methyl-4-(trifluoromethyl)isoquinolin-1(2*H*)-one (2f)



Prepared following general *method B*. In an argon glovebox, 2-methylisoquinolin-1(2*H*)-one **(1f)** (0.25 mmol, 39.8 mg), PIFA (3 equiv, 322.6 mg), KF (3 equiv, 43.6 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (4.5 equiv, 165 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 7% EtOAc in hexanes). The product was obtained in 54% yield (31 mg) as a white solid **m.p:** 91-93 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.49 (d, J = 8.2 Hz, 1H), 7.80 (d, J = 8.8 Hz, 1H), 7.74 (t, J = 7.3 Hz, 1H), 7.62 – 7.55 (m, 2H), 3.66 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.4, 133.5 (q, J = 7.3 Hz), 133.1, 132.1, 128.5, 128.0, 125.8, 124.0 (q, J = 271.5 Hz), 123.5 (q, J = 2.3 Hz), 106.8 (q, J = 32.0 Hz), 37.7. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.4 (s, 3F). **FT/IR (ν^{-1}_{max} cm^{-1}):** 3018, 3047, 2956, 2925, 1660, 1637, 1609, 1559, 1494, 1457, 1403, 1350, 1319, 1297, 1262, 1195, 1145, 1104, 1075, 990, 934, 898, 870, 835, 793, 764, 754, 707, 691, 662, 623, 545, 537, 498, 460, 439, 432, 421, 408. **HRMS EI+ (M):** calculated for $C_{11}H_8ONF_3$ = 227.05580, found = 227.05635.

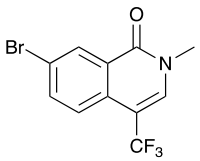
2-phenyl-4-(trifluoromethyl)isoquinolin-1(2*H*)-one (2g)



Prepared following general *method B*. In an argon glovebox, 2-phenylisoquinolin-1(2*H*)-one (**1g**) (0.25 mmol, 55.3 mg), PIFA (3 equiv, 322.6 mg), KF (3 equiv, 43.6 mg), $Cu(OAc)_2$ (30

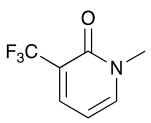
mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (4.5 equiv, 165 μL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 7% EtOAc in hexanes). The product was obtained in 44% yield (32 mg) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 8.1 Hz, 1H), 7.85 (d, *J* = 7.9 Hz, 1H), 7.80 (t, *J* = 7.7 Hz, 1H), 7.69 (s, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.43 (d, *J* = 7.6 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.7, 140.6, 133.6, 133.4 (q, *J* = 7.3 Hz), 132.0, 129.7, 129.1, 129.0, 128.4, 126.9, 126.3, 124.1 (q, *J* = 271.0 Hz), 123.6 (q, *J* = 2.3 Hz), 107.2 (q, *J* = 32.1 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.5 (s, 3F). **FT/IR (ν^{-1}_{max} cm^{-1}):** 1673, 1645, 1605, 1596, 1558, 1490, 1456, 1404, 1359, 1326, 1282, 1256, 1219, 1182, 1143, 1110, 1070, 1037, 976, 896, 799, 770, 757, 743, 706, 694, 667, 626, 585, 455, 408. **HRMS ES$^+$ (M+H$^+$):** calculated for $C_{16}H_{10}F_3NO$ = 290.0793, found = 290.0798.

7-bromo-2-methyl-4-(trifluoromethyl)isoquinolin-1(2*H*)-one (2h)



Prepared following general *method B*. In an argon glovebox, 7-bromo-2-methylisoquinolin-1(2*H*)-one (**1h**) (0.25 mmol, 59.5 mg), PIFA (3 equiv, 322.6 mg), KF (3 equiv, 43.6 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (4.5 equiv, 165 μL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 8% EtOAc in hexanes). The product was obtained in 55% yield (42 mg) as a white solid. **m.p:** 180-183 ˚C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.63 (d, J = 2.2 Hz, 1H), 7.83 (dd, J = 8.7, 2.2 Hz, 1H), 7.66 (dd, J = 8.8, 1.8 Hz, 1H), 7.58 (s, 1H), 3.65 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.0, 136.2, 133.7 (q, *J* = 7.2 Hz), 131.1, 130.6, 127.1, 125.1 (q, *J* = 2.2 Hz), 124.8 (q, *J* = 270.9 Hz), 122.1, 106.3 (q, *J* = 32.4 Hz), 37.6. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -61.5 (s, 3F). **FT/IR (ν^{-1}_{max} cm^{-1}):** 1663, 1643, 1598, 1574, 1542, 1488, 1441, 1415, 1363, 1347, 1315, 1264, 1248, 1191, 1160, 1102, 1074, 1004, 941, 928, 904, 820, 810, 788, 754, 714, 703, 673, 640, 605, 549, 544, 535, 497, 465, 446, 419, 410. **HRMS EI+ (M):** calculated for $C_{11}H_7ONF_3Br$ = 304.96631, found = 304.96716.

1-methyl-3-(trifluoromethyl)pyridin-2(1*H*)-one (2i)



Prepared following general *method A*. In an argon glovebox, PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL), pyridin-2(1*H*)-one (**1i**) (0.25 mmol, 24.5 μL) and $TMSCF_3$ (2 equiv, 75 μL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$. Subsequently the organic layer was concentrated, and hexanes were added to precipitate a solid. The supernatant was discarded, and to the solid residue further dried

under vacuum to yield **2i** as a brown solid in 73% yield (32 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.1 Hz, 1H), 7.52 (d, *J* = 6.9 Hz, 1H), 6.25 (t, *J* = 7.0 Hz, 1H), 3.60 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.5 (s, 3F). The NMR data matches reported values.[18]

1-gram scale reaction: In an argon glovebox, PIFA (1.5 equiv, 3.96 g), KF (1.5 equiv, 534.5 mg), $Cu(OAc)_2$ (30 mol %, 501.3 mg) were weighed into an oven-dried 250 ml round bottom flask equipped with a magnetic stir bar. To the sealed flask, under N_2, CH_3CN (92 mL), pyridin-2(1*H*)-one (**1i**) (9.2 mmol, 895 µL), and $TMSCF_3$ (2 equiv, 1.36 mL) were added in quick succession by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (200 mL) and extracted with EtOAc three times (60 mL each time). The combined organic layers were dried over $MgSO_4$. Subsequently the organic layer was concentrated, and to the residue haxanes was added (150 mL) and a solid precipitated. This flask was kept in a freezer (-20 ˚C) overnight (16 h). The supernatant was discarded, and the solid residue washed with hexanes (two times, 20 mL each time) and dried under vacuum to yield **2i** as a brown solid in 60% yield (982 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.1 Hz, 1H), 7.52 (d, *J* = 6.9 Hz, 1H), 6.25 (t, *J* = 7.0 Hz, 1H), 3.60 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.5 (s, 3F). The NMR data matches reported values.[18]

1-phenyl-3-(trifluoromethyl)pyridin-2(1*H*)-one (2j)

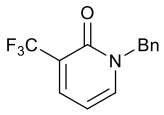
Prepared following general *method A*. In an argon glovebox, 1-phenylpyridin-2(1*H*)-one (**1j**) (0.25 mmol, 42.8 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 30% EtOAc in hexanes). The product was obtained in 78% yield (47 mg) as a white solid. **m.p:** 63-64 ˚C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.1 Hz, 1H), 7.57 (d, *J* = 7.0 Hz, 1H), 7.53 – 7.48 (m, 2H), 7.47 – 7.42 (m, 1H), 7.41 – 7.36 (m, 2H), 6.32 (t, *J* = 7.0 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.3, 142.0, 139.9, 139.4 (q, *J* = 5.1 Hz), 129.5, 129.2, 126.6, 122.7 (q, *J* = 271.9 Hz), 121.7 (q, *J* = 30.9 Hz), 104.1.**^{19}F NMR** (470 MHz, $CDCl_3$) δ -66.5 (s, 3F). **HRMS ES$^+$ (M+H$^+$)** Calculated for $C_{12}H_9NOF_3$ = 240.0636, found = 240.0628. **FT/IR (ν^{-1}_{max} cm^{-1}):** 1667, 1611, 1592, 1552, 1491, 1457, 1374, 1315, 1293, 1270, 1253, 1154, 1122, 1078, 1054, 1038, 1021, 1001, 972, 966, 947, 942, 918, 865, 837, 798, 774, 758, 722, 691, 642, 607, 582, 539, 530, 518, 480, 455, 431, 413, 405.

1-(4-methoxyphenyl)-3-(trifluoromethyl)pyridin-2(1H)-one (2k)

Prepared following general *method C*. In an argon glovebox, 1-(4-methoxyphenyl)pyridin-2(1H)-one (**1k**) (0.25 mmol, 50.3 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL)

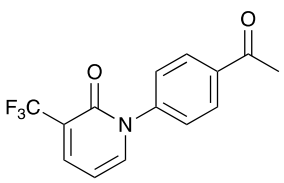
were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour. The solution was then transferred to another crimp-top vial charged with PIFA (1.5 equiv, 161.3 mg) and KF (1.5 equiv, 21.8 mg), followed by addition of $TMSCF_3$ (2 equiv, 75 µL) [vial was washed with 0.5 mL CH_3CN to ensure complete transfer of material]. The solution was stirred for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 30% EtOAc in hexanes). The product was obtained in 79% yield (53 mg) as a brown solid. **^{1}H NMR** (399 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 7.4, 1.1 Hz, 0H), 7.55 (dd, *J* = 6.8, 2.2 Hz, 1H), 7.32 – 7.30 (m, 1H), 7.29 (dd, *J* = 2.3, 0.5 Hz, 1H), 7.01 – 6.99 (m, 1H), 6.98 (dd, *J* = 2.3, 0.5 Hz, 1H), 6.29 (t, *J* = 7.0 Hz, 1H), 3.85 (d, *J* = 0.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.9, 158.5 (d, *J* = 1.5 Hz), 142.3, 139.3 (q, *J* = 5.0 Hz), 132.7, 127.7, 122.8 (q, *J* = 271.9 Hz), 121.8 (q, *J* = 30.9 Hz), 114.7, 104.0, 55.7. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.5 (s, 3F). **HRMS ES$^+$** Calculated for $C_{13}H_{11}F_3NO_2$ ($M+H^+$) = 270.0736; found = 270.0816. **FT/IR** (V-1 max, cm-1): 3109.65, 3057.1, 3012.75, 2940.43, 2848.83, 1663.3, 1596.77, 1248.2, 1121.89, 1074.64, 1026.43, 815.742

1-benzyl-3-(trifluoromethyl)pyridin-2(1H)-one (2l)



Prepared following general *method A*. In an argon glovebox, 1-benzylpyridin-2(1H)-one (**1l**) (0.25 mmol, 46.3 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 30% EtOAc in hexanes). The product was obtained in 50% yield (31 mg) as a brown solid. **^{1}H NMR** (399 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.1, 2.2 Hz, 1H), 7.48 (dd, *J* = 6.9, 2.1 Hz, 1H), 7.40 – 7.30 (m, 5H), 6.21 (t, *J* = 7.0 Hz, 1H), 5.17 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.6, 141.2, 138.8 (q, *J* = 5.0 Hz), 135.5, 129.2, 128.7, 128.6, 122.8 (q, *J* = 271.7 Hz), 121.0 (q, *J* = 30.9 Hz), 104.3, 52.3. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.5 (s, 3F). **HRMS ES$^+$** Calculated for $C_{13}H_{11}F_3NO$ ($M+H^+$) = 254.0787; found = 254.0826. **FT/IR** (V-1 max, cm-1): 3085.55, 3063.37, 1661.86, 1602.07, 1560.61, 1453.58, 1391.39, 1314.73, 1186.01, 1124.30, 1077.53, 1058.25, 961.823, 865.400

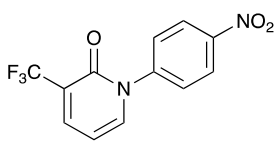
1-(4-acetylphenyl)-3-(trifluoromethyl)pyridin-2(1*H*)-one (2m)



Prepared following general *method C*. In an argon glovebox, 1-(4-acetylphenyl)pyridin-2(1*H*)-one (**1k**) (0.25 mmol, 53.3 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour. The solution was then transferred to another crimp-top vial charged with PIFA (1.5 equiv, 161.3 mg) and KF (1.5 equiv, 21.8 mg), followed by addition of TMSCF3 (2 equiv, 75 µL) [vial

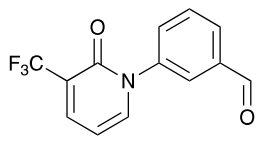
was washed with 0.5 mL CH_3CN to ensure complete transfer of material]. The solution was stirred for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 30% EtOAc in hexanes). The product was obtained in 61% yield (43 mg) as a white solid (**m.p:** 121-123 ˚C). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.08 (d, J = 8.1 Hz, 2H), 7.84 (d, J = 7.0 Hz, 1H), 7.55 (dd, J = 6.8, 2.1 Hz, 1H), 7.52 (d, J = 8.0 Hz, 2H), 6.36 (t, J = 7.0 Hz, 1H), 2.64 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 196.9, 158.0, 143.5, 141.2, 139.7 (q, *J* = 4.9 Hz), 137.4, 129.6, 127.0, 122.6 (q, *J* = 271.9 Hz), 122.1 (q, *J* = 31.0 Hz), 104.6, 26.9. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -66.6 (s, 3F). **HRMS ES$^+$ (M+H$^+$)** Calculated for $C_{14}H_{11}NO_2F_3$ = 282.0742, found = 282.0743. **FT/IR (ν^{-1}_{max} cm^{-1}):** 1671, 1615, 1598, 1582, 1558, 1507, 1449, 1411, 1378, 1361, 1315, 1266, 1152, 1115, 1073, 1055, 1031, 962, 864, 845, 758, 732, 686, 624, 592, 582, 533, 480, 467, 429, 418, 404.

1-(4-nitrophenyl)-3-(trifluoromethyl)pyridin-2(1*H*)-one (2n)



Prepared following general *method C*. In an argon glovebox, 1-(4-nitrophenyl)pyridin-2(1*H*)-one (**1k**) (0.25 mmol, 54.1 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour. The solution was then transferred to another crimp-top vial charged with PIFA (1.5 equiv, 161.3 mg) and KF (1.5 equiv, 21.8 mg), followed by addition of TMSCF3 (2 equiv, 75 µL) [vial was washed with 0.5 mL CH_3CN to ensure complete transfer of material]. The solution was stirred for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 40% EtOAc in hexanes). The product was obtained in 55% yield (39 mg) as a pale-yellow solid. **m.p:** 157-159 ˚C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.37 (d, J = 8.2 Hz, 2H), 7.87 (d, J = 7.0 Hz, 1H), 7.64 (d, J = 8.2 Hz, 2H), 7.55 (dd, J = 7.0, 2.0 Hz, 1H), 6.41 (t, J = 7.0 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 157.7, 147.8, 144.8, 140.7, 140.0 (q, *J* = 5.1 Hz), 127.9, 124.9, 122.4 (q, *J* = 272.1 Hz), 122.4 (q, *J* = 31.4 Hz), 105.0. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -66.6 (s, 3F). **HRMS ES$^+$ (M+H$^+$)** Calculated for $C_{12}H_8N_2O_3F_3$ = 285.0487, found = 285.0485. **FT/IR (ν^{-1}_{max} cm^{-1}):** 3122, 3090, 1667, 1615, 1553, 1516, 1495, 1450, 1419, 1376, 1348, 1311, 1275, 1256, 1157, 1124, 1111, 1075, 1056, 1032, 1015, 953, 867, 853, 811, 801, 778, 753, 733, 694, 663, 604, 534, 515, 497, 445, 420.

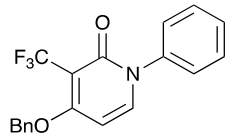
3-(2-oxo-3-(trifluoromethyl)pyridin-1(2*H*)-yl)benzaldehyde (2o)



Prepared following general *method A*. In an argon glovebox, 3-(2-oxopyridin-1(2*H*)-yl)benzaldehyde (**1l**) (0.25 mmol, 49.8 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were

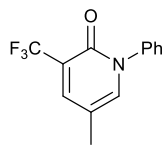
dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 30% EtOAc in hexanes). The product was obtained in 48% yield (32 mg) as a colorless liquid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.06 (s, 1H), 7.98 (d, *J* = 7.0 Hz, 1H), 7.92 (s, 1H), 7.86 (d, *J* = 7.0 Hz, 1H), 7.75 – 7.66 (m, 2H), 7.59 (dd, *J* = 6.9, 2.0 Hz, 1H), 6.38 (t, *J* = 7.0 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 190.8, 158.1 (q, *J* = 1.2 Hz), 141.3, 140.6, 139.8 (q, *J* = 5.1 Hz), 137.7, 132.6, 130.5, 130.3, 127.3, 122.5 (q, *J* = 272.0 Hz), 122.1 (q, *J* = 31.2 Hz), 104.7. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -66.6 (s, 3F). **HRMS ES$^+$ (M+H$^+$)** Calculated for $C_{13}H_9NO_2F_3$ = 268.0585, found = 268.0581. **FT/IR (ν^{-1}_{max} cm^{-1}):** 1668, 1612, 1601, 1554, 1482, 1454, 1374, 1318, 1278, 1122, 1043, 966, 921, 897, 863, 762, 731, 708, 691, 645, 598, 534, 475, 448, 438, 416, 409.

4-(benzyloxy)-1-phenyl-3-(trifluoromethyl)pyridin-2(1*H*)-one (2p)



Prepared following general *method C*. In an argon glovebox, 4-(benzyloxy)-1-phenylpyridin-2(1*H*)-one (**1m**) (0.25 mmol, 69.3 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 μL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour. The solution was then transferred to another crimp-top vial charged with PIFA (1.5 equiv, 161.3 mg) and KF (1.5 equiv, 21.8 mg), followed by addition of $TMSCF_3$ (2 equiv, 75 μL) [vial was washed with 0.5 mL CH_3CN to ensure complete transfer of material]. The solution was stirred for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 30% EtOAc in hexanes). The product was obtained in 68% (59 mg) yield as a white solid **(m.p:** 166-168 ˚C). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.48 – 7.44 (m, 3H), 7.43 – 7.41 (m, 5H), 7.39 – 7.35 (m, 1H), 7.35 – 7.30 (m, 2H), 6.17 (d, *J* = 7.9 Hz, 1H), 5.28 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.1, 159.5, 141.7, 139.9, 135.1, 129.4, 129.0, 129.0, 128.7, 126.9, 126.8, 123.7 (q, *J* = 273.7 Hz), 104.1 (q, *J* = 30.0 Hz), 95.2, 71.4. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -57.9 (s, 3F). **HRMS ES$^+$ (M+H$^+$)** Calculated for $C_{19}H_{15}NO_2F_3$ = 346.1055, found = 346.1057. **FT/IR (ν^{-1}_{max} cm^{-1}):** 1660, 1605, 1593, 1535, 1475, 1455, 1444, 1360, 1325, 1273, 1249, 1220, 1172, 1160, 1134, 1099, 1079, 1053, 1038, 1029, 1001, 970, 910, 829, 790, 781, 768, 756, 736, 728, 694, 667, 645, 617, 583, 555, 536, 517, 495, 478, 448, 432, 425, 414, 404.

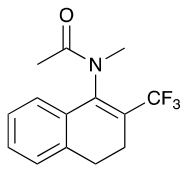
5-methyl-1-phenyl-3-(trifluoromethyl)pyridin-2(1H)-one (2q, Pirfenidone analog)



Prepared following general *method C*. In an argon glovebox, 5-methyl-1-phenylpyridin-2(1H)-one (Pirfenidone, **1q**) (0.25 mmol, 46.3 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 μL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour. The solution was then transferred to another crimp-top vial charged with PIFA (1.5 equiv, 161.3 mg) and KF (1.5 equiv, 21.8 mg), followed by addition of $TMSCF_3$ (2 equiv, 75 μL) [vial was washed with 0.5 mL CH_3CN to ensure complete transfer of material]. The solution was stirred for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL

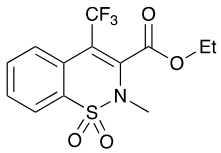
each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 30% EtOAc in hexanes). The product was obtained in 44% (28 mg) yield as a white solid. **^{1}H NMR** (399 MHz, $CDCl_3$) δ 7.69 (d, *J* = 2.2 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.46 – 7.40 (m, 1H), 7.40 – 7.36 (m, 2H), 7.35 (s, 1H), 2.17 (d, *J* = 1.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.7, 141.9 (q, *J* = 5.0 Hz), 140.1, 139.5, 129.5, 129.0, 126.7, 122.8 (q, *J* = 271.9 Hz), 121.1 (q, *J* = 30.7 Hz), 113.2, 17.1. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.4 (s, 3F). **HRMS ES$^+$** Calculated for $C_{13}H_{11}F_3NO$ ($M+H^+$) = 254.0787; found = 254.0826. **FT/IR** (V-1 max, cm-1): 3061.92, 2926.93, 2855.58, 2361.89, 2338.27, 1678.73, 1618.95, 1550.97, 1492.15, 1373.07, 1334.02, 1255.43, 1129.12, 914.093

_N_-methyl-_N_-(2-(trifluoromethyl)-3,4-dihydronaphthalen-1-yl)acetamide (2r)



Prepared following general *method B*. In an argon glovebox, *N*-(3,4-dihydronaphthalen-1-yl)-*N*-methylacetamide (**1o**) (0.25 mmol, 59.5 mg), PIFA (3 equiv, 322.6 mg), KF (3 equiv, 43.6 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (4.5 equiv, 165 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 8% EtOAc in hexanes). The product was obtained in 77% yield (52 mg) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.4 Hz, 1H), 7.31 – 7.21 (m, 2H), 7.14 (d, *J* = 7.7 Hz, 1H), 3.11 (s, 3H), 2.94 (t, *J* = 8.4 Hz, 2H), 2.63 (t, *J* = 8.2 Hz, 2H), 1.92 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.4, 141.9 (q, *J* = 3.9 Hz), 137.3, 130.5, 130.4, 128.3, 127.7, 124.4 (q, *J* = 29.3 Hz), 124.2, 123.5 (q, *J* = 273.1 Hz), 35.8 (q, *J* = 1.8 Hz), 26.9, 22.5 (q, *J* = 2.7 Hz), 21.3. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -64.2. **HRMS EI$^+$ (M):** calculated for $C_{14}H_{14}ONF_3$ = 269.10275, found = 269.10252. **FT/IR (ν^{-1}_{max} cm^{-1}):** 1743, 1652, 1634, 1576, 1559, 1472, 1455, 1430, 1372, 1345, 1318, 1287, 1273, 1235, 1121, 1158, 1115, 1082, 1037, 1026, 977, 949, 864, 828, 778, 755, 737, 720, 667, 625, 541, 489, 468, 465, 435, 420, 405.

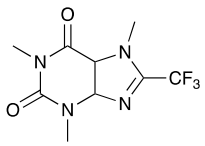
ethyl 2-methyl-4-(trifluoromethyl)-2*H*-benzo[*e*][1,2]thiazine-3-carboxylate 1,1-dioxide (2t)



Prepared following general *method C*. In an argon glovebox, ethyl 2-methyl-2*H*-benzo[*e*][1,2]thiazine-3-carboxylate 1,1-dioxide **(1q)** (0.25 mmol, 66.8 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour. The solution was then transferred to another crimp-top vial charged with PIFA (1.5 equiv, 161.3 mg) and KF (1.5 equiv, 21.8 mg), followed by addition of $TMSCF_3$ (2 equiv, 75 µL) [vial was washed with 0.5 mL CH_3CN to ensure complete transfer of material]. The solution was stirred for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0 % - 20 % EtOAc in hexanes). The product was obtained as a viscous, colorless oil (32 % yield, 27 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.1 Hz, 1H),

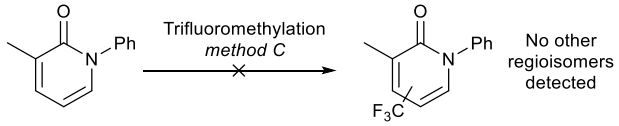
7.76 (d, J = 8.3 Hz, 1H), 7.71 (t, J = 7.7 Hz, 1H), 7.63 (t, J = 7.5 Hz, 1H), 4.46 (q, J = 7.2 Hz, 2H), 3.32 (s, 3H), 1.42 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.4, 132.5, 131.7, 130.3, 129.4, 126.2 (q, J = 2.9 Hz), 125.3 (q, J = 272.4 Hz), 122.1, 117.1 (q, J = 2.8 Hz), 110.4 (q, J = 32.6 Hz), 63.7, 33.0, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -55.8 (s, 3F). **FT/IR (ν^{-1}_{max} cm^{-1}):** 2985, 2923, 2850, 1739, 1604, 1593, 1480, 1467, 1443, 1350, 1327, 1287, 1235, 1209, 1119, 1084, 1060, 1009, 944, 909, 856, 838, 802, 764, 747, 724, 694, 681, 644, 626, 583, 555, 502, 462,455. **HRMS ESI$^+$ (M+H$^+$):** calculated for $C_{13}H_{13}F_3NO_4S$ = 336.0517, found = 336.0510.

1,3,7-trimethyl-8-(trifluoromethyl)-3,4,5,7-tetrahydro-1*H*-purine-2,6-dione (2u)



Prepared following general *method C*. In an argon glovebox, 1,3,7-trimethyl-3,4,5,7-tetrahydro-1*H*-purine-2,6-dione **(1m)** (0.25 mmol, 48.5 mg), PIFA (1.5 equiv, 161.3 mg), KF (1.5 equiv, 21.8 mg), $Cu(OAc)_2$ (30 mol %, 13.6 mg) were weighed into an oven-dried crimp-top vial. Under N_2, CH_3CN (2.5 mL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe. The mixture was then allowed to stir at room temperature for 1 hour. The solution was then transferred to another crimp-top vial charged with PIFA (1.5 equiv, 161.3 mg) and KF (1.5 equiv, 21.8 mg), followed by addition of $TMSCF_3$ (2 equiv, 75 µL) [vial was washed with 0.5 mL CH_3CN to ensure complete transfer of material]. The solution was stirred for 1 hour, diluted with 0.1M NH_4OH (10 mL) and extracted with EtOAc three times (3 mL each time). The combined organic layers were dried over $MgSO_4$, and the compound was isolated by column chromatography (gradient of 0% - 50% EtOAc in hexanes). The product was obtained in 56% yield (37 mg) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.15 (q, J = 1.2 Hz, 3H), 3.59 (s, 3H), 3.42 (s, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.9 (q, J = 1.3 Hz, 3F). This data matches previous reports.[19]

Attempted trifluoromethylation of 3-methyl-1-phenylpyridin-2(1H)-one

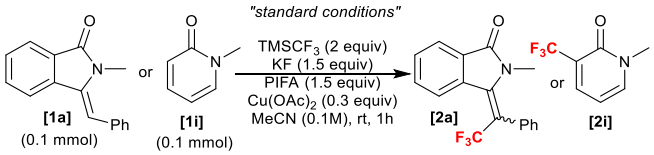


In the case of 2-pyridinones, selectivity toward the 3-position was always observed. Following general *method C*, the trifluoromethylation of a substrate in which this position was blocked such as in 3-methyl-1-phenylpyridin-2(1H)-one afforded only traces of CF_3-containing products, as detected by GC-MS. No efforts to isolate these products were undertaken.

Control experiments

In order to gain information regarding the reaction pathway, several control experiments were conducted using starting material **1a** or **1i** as model substrate. The results are summarized in Scheme S1.

Table S2. Control Experiments [a]



Entry	Substrate	variation from the "standard" conditions	Yield (%)
1	**[1a]**	with BHT (1 equiv)	**[2a]** <1%[b]
2	**[1a]**	with TEMPO (1 equiv)	**[2a]** <1%[b] + TEMPO-CF_3 54%[c]
3	no substrate	with TEMPO (1 equiv)	TEMPO-CF_3 70%[c]
4	**[1i]**	$Cu(OAc)_2$ (1 equiv) and No PIFA	**[2i]**, n.d.
5	**[1i]**	PIFA (1.5 equiv) added to entry 4 after 1 h and stirred further for 1 h	**[2i]**, 2%[b](6%)[b,d]
6	**[1i]**	(phen)$CuCF_3$ (1.5 equiv) instead of $TMSCF_3$, KF, $Cu(OAc)_2$	**[2i]**,9%[b]

[a] Standard conditions: Unless otherwise indicated, substrate **1a** or **1i** (0.25 mmol) PIFA (1.5 equiv), KF (1.5 equiv), $TMSCF_3$ (2 equiv), $Cu(OAc)_2$ (0.3 equiv), MeCN (0.1 M), rt, 1h. [b] Based on substrate. [c] Based on TEMPO. [d] After 24 h of reaction.

Table S2, entry 1.

Performed using general *method A*. In an argon glovebox, starting material **1a** (0.1 mmol, 23.5 mg, 1 equiv), PIFA (1.5 equiv, 64.5 mg), KF (1.5 equiv, 8.7 mg), $Cu(OAc)_2$ (30 mol %, 5.5 mg) and 2,6-di-*tert*-butyl-4-methylphenol (BHT) (0.1 mmol, 22 mg) were weighed into an oven-dried crimp-top vial equipped with a stir bar. The vial was sealed with a septum and brought outside the glovebox. Subsequently, CH_3CN (1 mL) and $TMSCF_3$ (2 equiv, 30 µL) were added in quick succession to the vial by syringe under a stream of N_2. The mixture was then stirred at room temperature for 1 hour. After this time, benzotrifluoride ($PhCF_3$) (10 uL, 0.081 mmol) was added as internal standard (δ -63.7 ppm), and the mixture was then analyzed directly by ^{19}F NMR (unlocked). The product ***E*-2a** was formed in less only 0.3% (δ -54.7) and the corresponding *Z*-isomer (δ -51.5 ppm) was not observed. The main fluorine-containing compounds observed were residual Me_3SiCF_3 (δ -67.8 ppm), CF_3H (δ -80.4 ppm) and Me_3SiF (δ -158 ppm) (Figure S1).

Figure S1. ^{19}F NMR of Table S2, entry 1

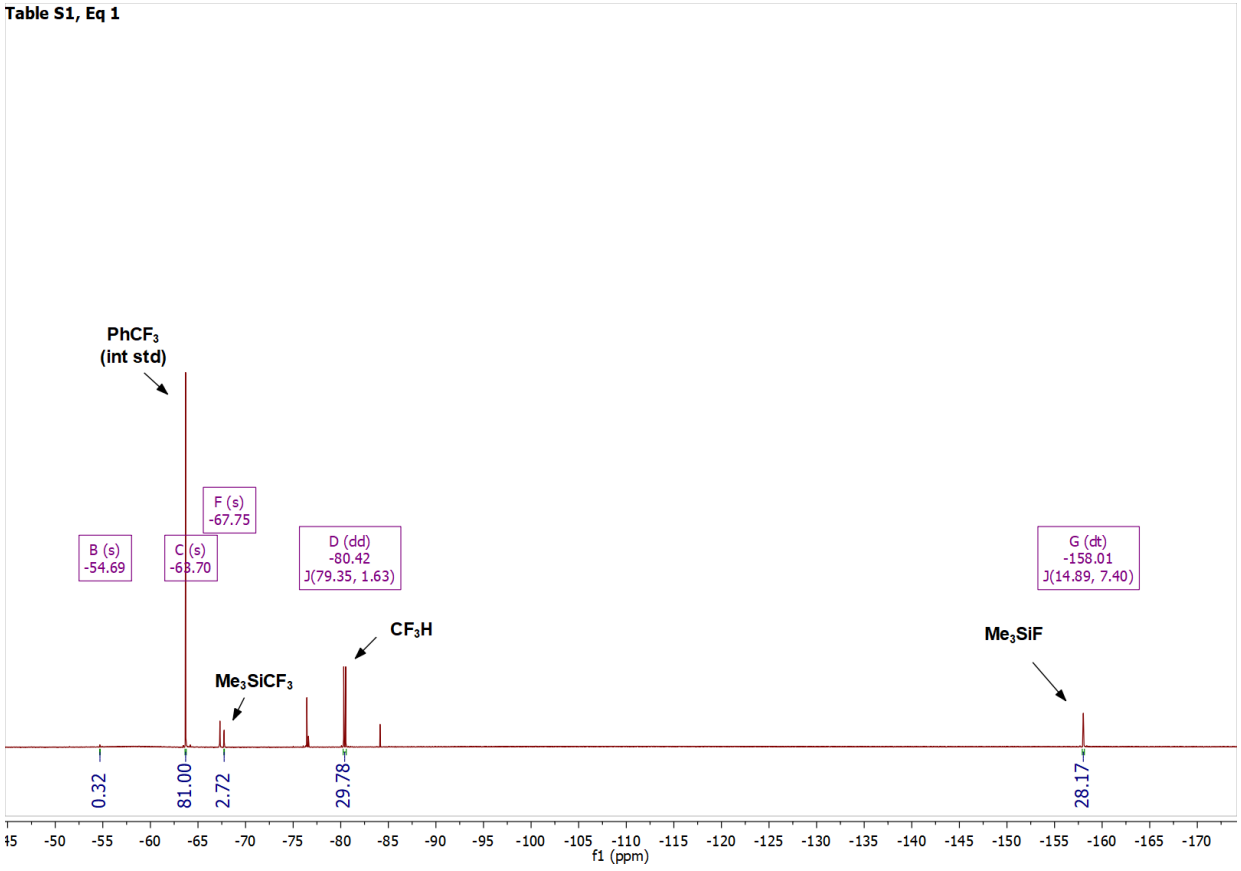


Table S2, entry 2.

Performed using general *method A*. In an argon glovebox, starting material **1a** (0.1 mmol, 23.5 mg, 1 equiv), PIFA (1.5 equiv, 64.5 mg), KF (1.5 equiv, 8.7 mg), $Cu(OAc)_2$ (30 mol %, 5.5 mg) and 2,2,6,6-Tetramethyl-1-piperidinyloxyl (TEMPO) (0.1 mmol, 15.6 mg) were weighed into an oven-dried crimp-top vial equipped with a stir bar. The vial was sealed with a septum and brought outside the glovebox. Subsequently, CH_3CN (1 mL) and $TMSCF_3$ (2 equiv, 30 µL) were added in quick succession to the vial by syringe under a stream of N_2. The mixture was then stirred at room temperature for 1 hour. After this time, benzotrifluoride ($PhCF_3$) (10 uL, 0.081 mmol) was added as internal standard (δ -63.7 ppm), and the mixture was then analyzed directly by ^{19}F NMR (unlocked). The product ***E*-2a** was formed in only 0.1% (δ -54.7) and the corresponding *Z*-isomer (δ -51.5 ppm) was not observed. The main fluorine-containing compounds observed were TEMPO-CF_3 adduct formed in 54% yield, (δ -56.5 ppm), CF_3H (δ -80.4 ppm) and Me_3SiF (δ -158 ppm) (Figure S2).

Figure S2. ^{19}F NMR of Table S2, entry 2

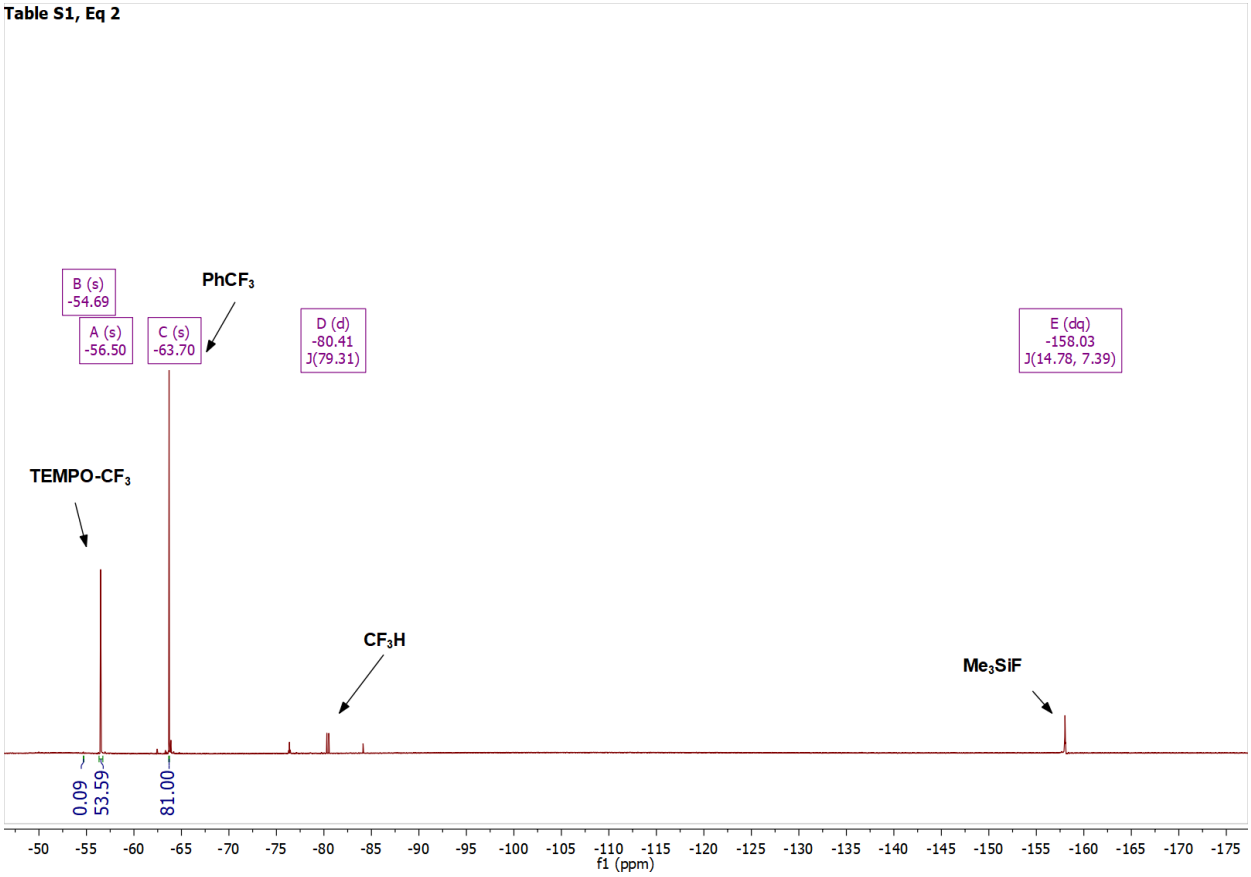


Table S2, entry 3.

It's possible that formation of TEMPO-CF_3 adduct could proceed via nucleophilic attack of CF_3^- anion on s TEMPO-derived oxoammonium intermediate. Because TEMPO-derived oxoammonium ion could form under acidic conditions[20] during the progress of the reaction, a control experiment was thus conducted in the absence of substrate **1a**. In this manner the generation of 1 equiv of TFA is precluded, enabling us to rule out such possibility. In an argon glovebox, PIFA (1.5 equiv, 64.5 mg), KF (1.5 equiv, 8.7 mg), $Cu(OAc)_2$ (30 mol %, 5.5 mg) and 2,2,6,6-Tetramethyl-1-piperidinyloxyl (TEMPO) (0.1 mmol, 15.6 mg) were weighed into an oven-dried crimp-top vial equipped with a stir bar. The vial was sealed with a septum and brought outside the glovebox. Subsequently, CH_3CN (1 mL) and $TMSCF_3$ (2 equiv, 30 µL) were added in quick succession to the vial by syringe under a stream of N_2. The mixture was then stirred at room temperature for 1 hour. After this time, benzotrifluoride $PhCF_3$ (10 uL, 0.081 mmol) was added as internal standard (δ -63.7 ppm), and the mixture was then analyzed directly by ^{19}F NMR (unlocked). In this case the TEMPO-CF_3 adduct (δ -56.5 ppm) formed in a higher yield of 64%, along with small amounts of CF_3H (δ -80.4 ppm) and Me_3SiF (δ -158 ppm) (Figure S3).

Figure S3. 19F NMR of Table S2, entry 3

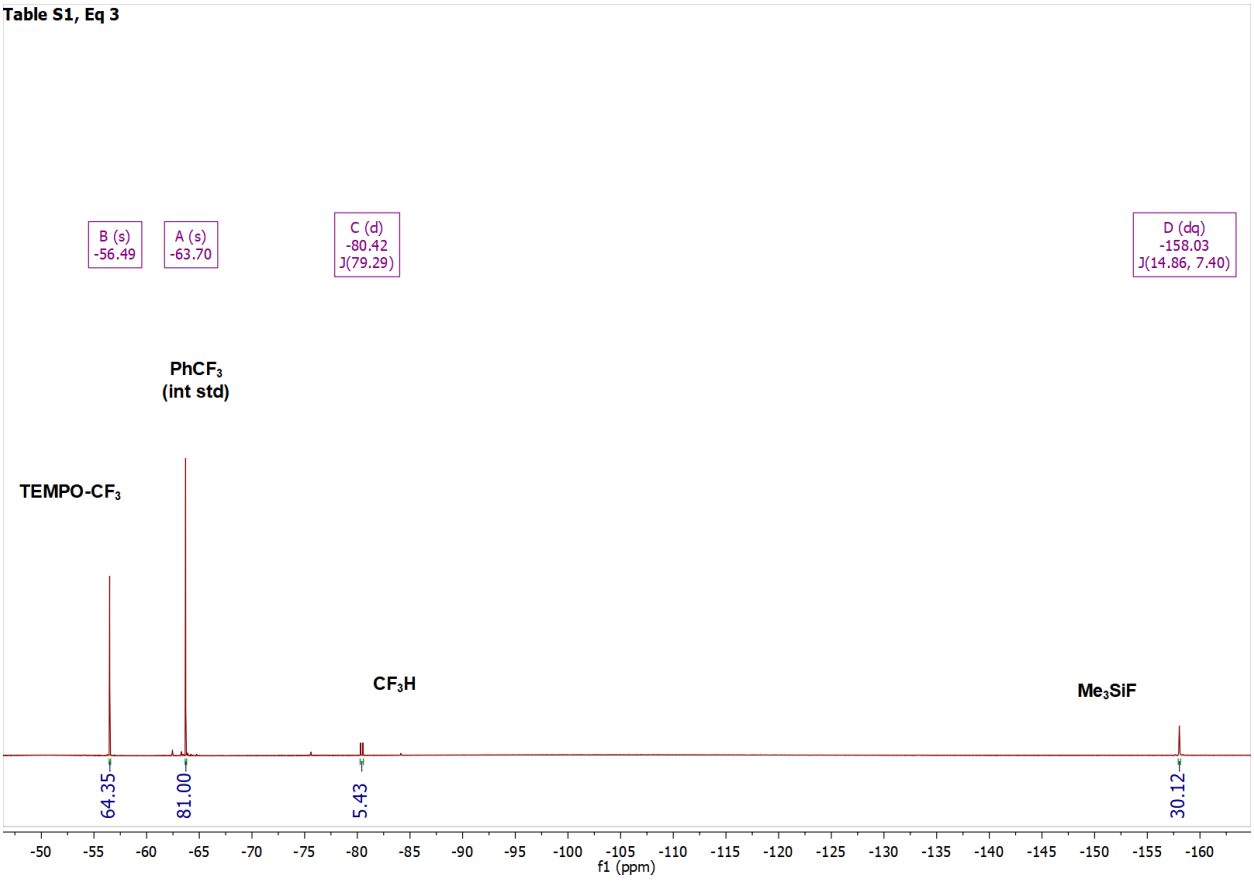


Table S2, entry 4.

To rule out the possibility of $Cu(OAc)_2$ serving as the oxidant for CF_3- anion, a control experiment was performed using stoichiometric amounts of this salt, in the absence of PIFA. In an argon glovebox, Cu(OAc) (1 equiv, 0.25 mmol, 45.4 mg), KF (1.5 equiv, 22 mg) were weighed into an oven-dried crimp-top vial equipped with a stir bar. The vial was sealed with a septum and brought outside the glovebox. Subsequently, CH_3CN (2.5 mL), **1i** (0.25 mmol, 24.5 uL) and $TMSCF_3$ (2 equiv, 75 µL) were added in quick succession to the vial by syringe under a stream of N_2. A deep-blue solution formed, and this mixture was then stirred at room temperature for 1 hour. After this time, trifluoromethoxybenzene, $PhOCF_3$ (20 uL, 0.16 mmol) was added as internal standard (δ -58.0 ppm), and the mixture was then analyzed directly by ^{19}F NMR (unlocked). In this case, no product **2i** could be detected. The only fluorine-containing species observed were $PhOCF_3$ (-58.0 ppm), unreacted $TMSCF_3$ (-66.7 ppm) TMSF (-154 ppm), CF_3H (-79.2 ppm), and several signals which were assigned to $[CuCF_3]$ species (-26.1 ppm, -31.1 ppm and -40.1 ppm). (Figure S4)

Figure S4. 19F NMR of Table S2, entry 4

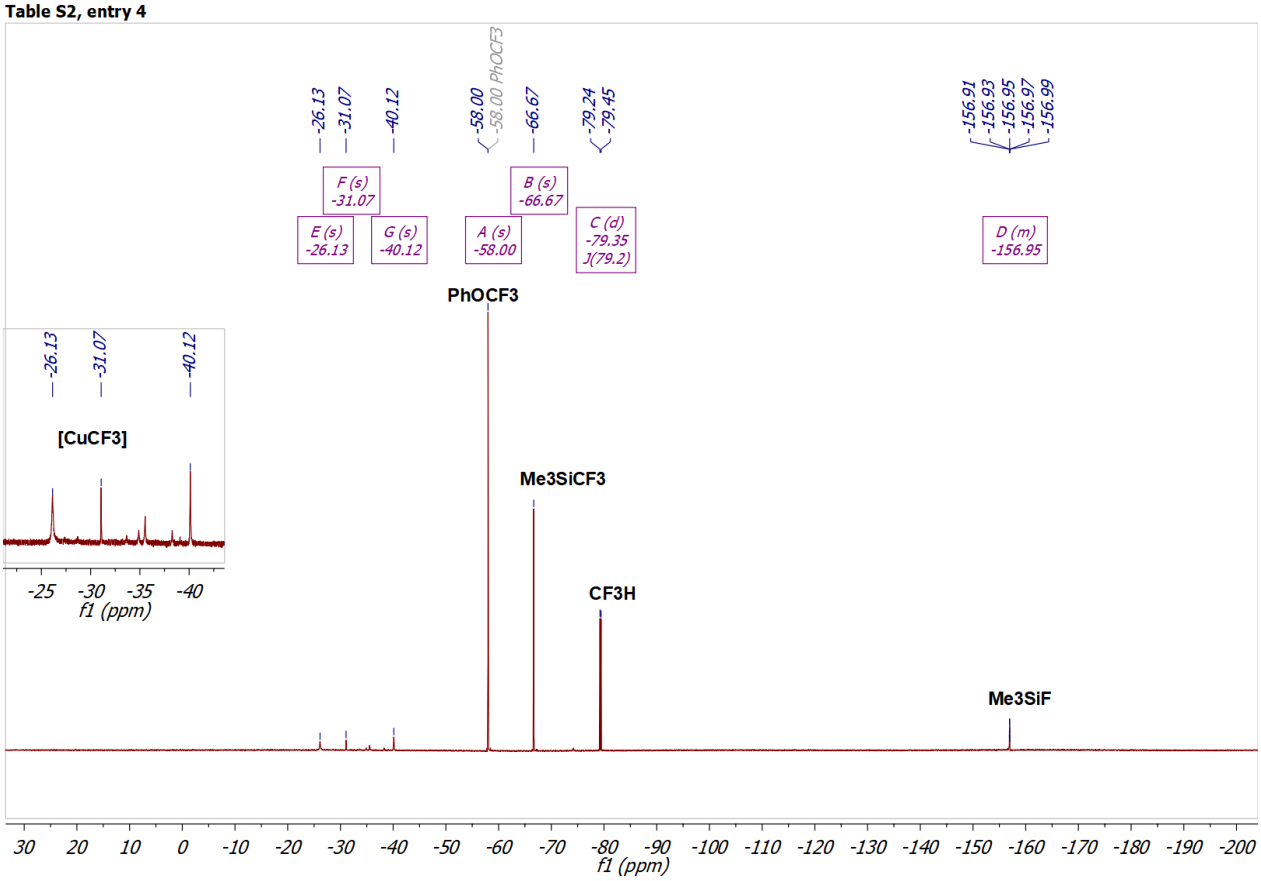


Table S2, entry 5.

The deep-blue solution obtained from entry 4, was transferred via syringe under a stream of N_2, to a crimp-top vial containing PIFA (1.5 equiv, 161 mg) and this mixture was further stirred at room temperature for 1h. After this time, the contents were then analyzed by ^{19}F NMR. Product **2i** was formed in only 2% (-65.6 ppm), and several [$CuCF_3$] species remained unreacted (-28.8 ppm, -40.4 ppm). The yield of **2i** increased to 6% after 24h (Figure S5a and S5b).

Figure S5a. 19F NMR of Table S2, entry 5 after 1h of reaction time

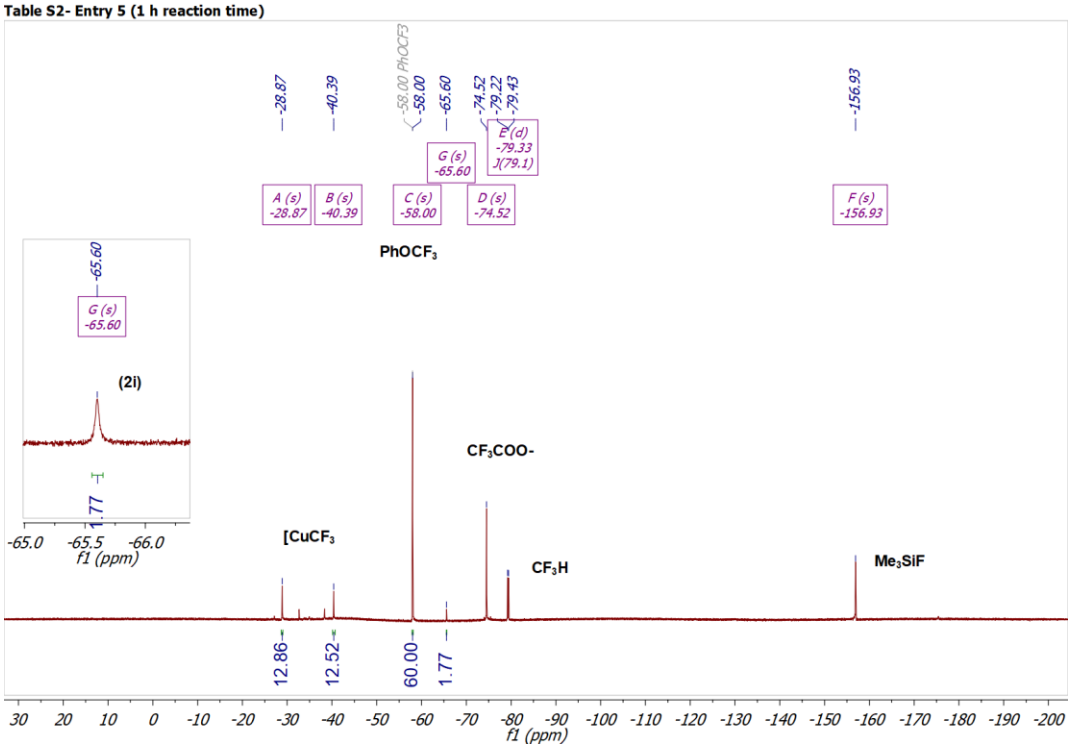


Figure S5b. 19F NMR of Table S1, entry 5 after 24h of reaction time

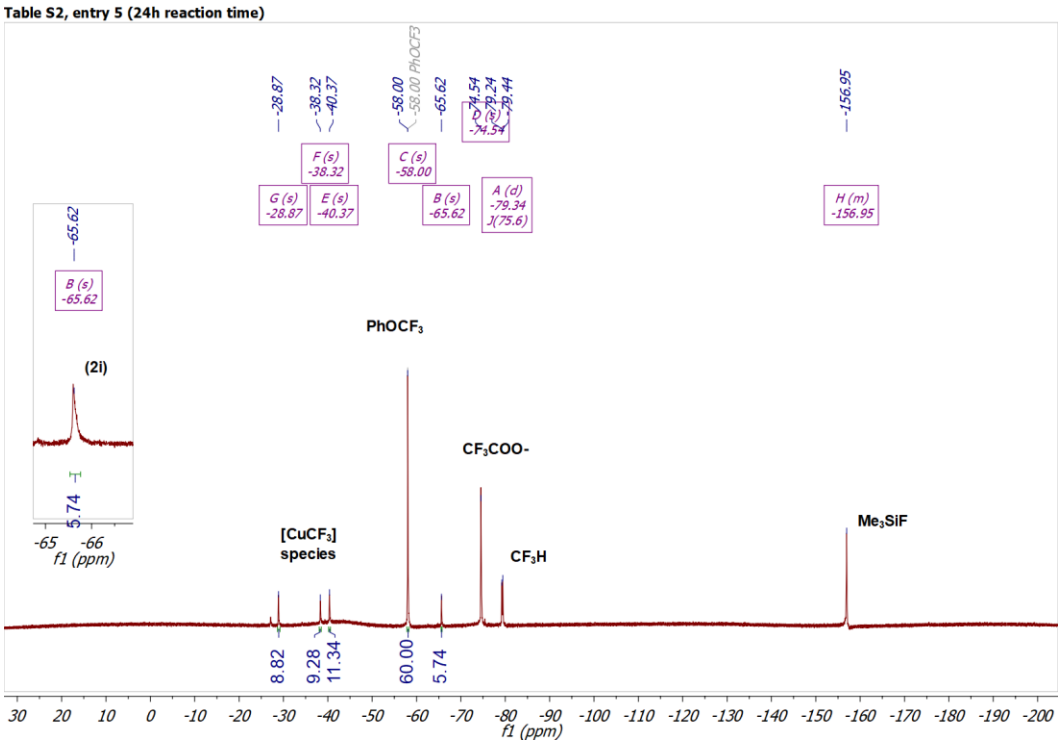
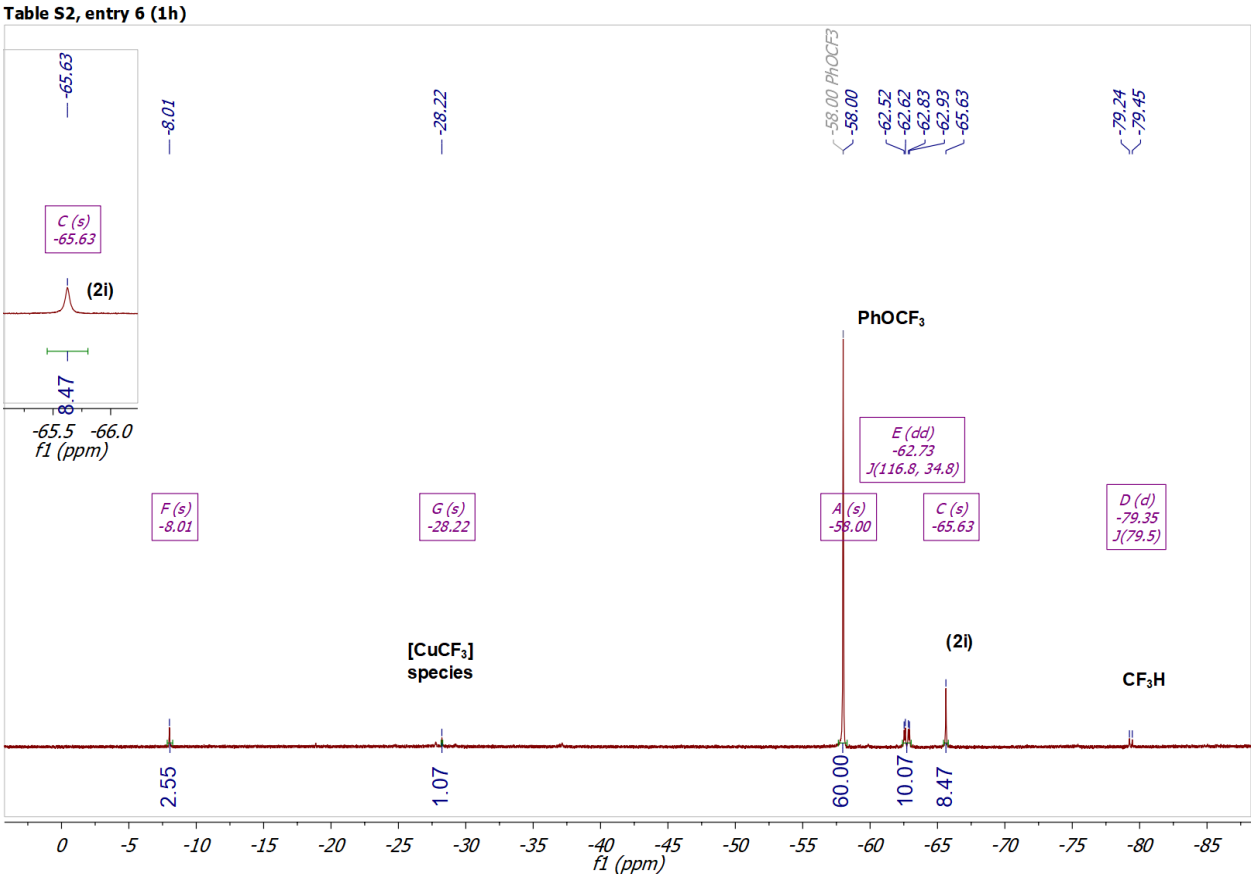


Table S2, entry 6.

In order to test the role of [$CuCF_3$] species in our oxidative trifluoromethylation protocol, a well-defined, commercially available trifluoromethylcopper complex, (phen)$CuCF_3$, was utilized instead of $TMSCF_3$, KF, and $Cu(OAc)_2$ combination. In an argon glovebox, (phen)$CuCF_3$ (1.5 equiv, 0.375 mmol, 117.3 mg) and PIFA (1.5 equiv, 161 mg) were weighed into an oven-dried crimp-top vial equipped with a stir bar. The vial was sealed with a septum and brought outside the glovebox. Subsequently, CH_3CN (2.5 mL) and **1i** (0.25 mmol, 24.5 uL) were added in quick succession to the vial by syringe under a stream of N_2. A vigorous reaction ensued and a light-green precipitate formed (likely an oxidation of Cu(I) reagent by PIFA). Upon stirring this mixture for 1h at room temperature, trifluoromethoxybenzene, $PhOCF_3$ (20 uL, 0.16 mmol) was added as internal standard (δ -58.0 ppm), and the mixture was then analyzed directly by ^{19}F NMR (unlocked). In this case, **2i** (-65.6 ppm) was formed in only 9% yield. Small amounts of [$CuCF_3$] (-28.2 ppm), CF_3H (-79.5 (d, 79 Hz), TMSF and two unidentified fluorine-containing species (-62.7 ppm (dd, J = 116.8, 34.8 Hz) and -8.0 ppm (s)) were detected. No increased in yield of **2i** was observed after 24h.

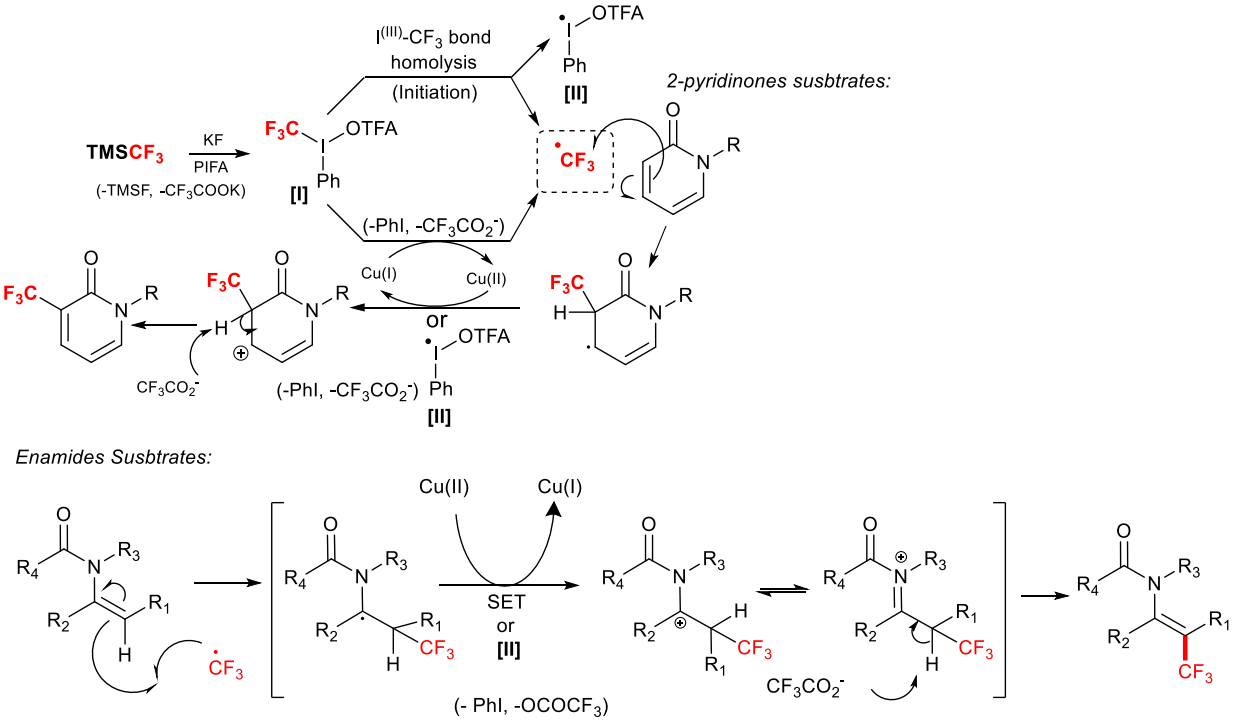
Figure S5b. 19F NMR of Table S1, entry 6 after 1h of reaction time



Mechanistic Hypothesis

Based on the results obtained from the control experiments and previous literature reports, it is likely that the active trifluoromethylating species is a CF_3 radical derived from $TMSCF_3$. At this point it is not known whether this is a free radical species or a Cu-associated radical. Though several [$CuCF_3$] species have been detected during the course of our investigations, it is likely that they do not play a dominant role for the oxidative C–H trifluoromethylation to occur. In addition, we have established that PIFA is an essential component for the reaction, as Cu(II) in stoichiometric amounts was ineffective for the desired transformation (Table S2, entry 4). Furthermore, our initial investigations showed that [Cu] salts are not strictly necessary as the reaction also proceeds in a metal-free manner, albeit with diminished yields (Table S1, entries 1-10). Based on these observations, we proposed the following as a possible reaction pathway (Scheme S2).

Scheme S2. Proposed Mechanism



Upon activation by fluoride, CF_3-release from $TMSCF_3$ and ligand exchange with PIFA, furnishes intermediate **[I]** which could give rise to CF_3 radical and iodosyl radical **[II]** via $I^{(III)}$–CF_3 homolytic cleavage (initiation). Reaction of CF_3 radical with substrates leads to a carbon centered radical which is then oxidized to a carbocation (or iminium ion in the case of enamides) by either Cu(II) (with concomitant generation of Cu(I) ions) or species **[II]** (with concomitant generation of Ph–I and CF_3COO^-). Subsequent deprotonation of this carbocation species furnishes the desired trifluoromethylated product. In addition, intermediate **[I]** can also give rise to CF_3 radical, Ph–I and CF_3COO^- upon single electron transfer (SET) process from Cu(I); this in turn, regenerates Cu(II), thus closing the catalytic cycle. Though the reaction also proceeds in a metal-free fashion, we surmised that the enhanced yields of

trifluoromethylated products observed in the presence of catalytic amounts of Cu(II), could be due to the inhibition of side polymerization reactions by reversible binding of Cu(II) to the carbon-centered radical. In fact, such scenario has been described for other copper catalyzed oxidations.[21] This, in addition to the SET processes mentioned above facilitated by [Cu].

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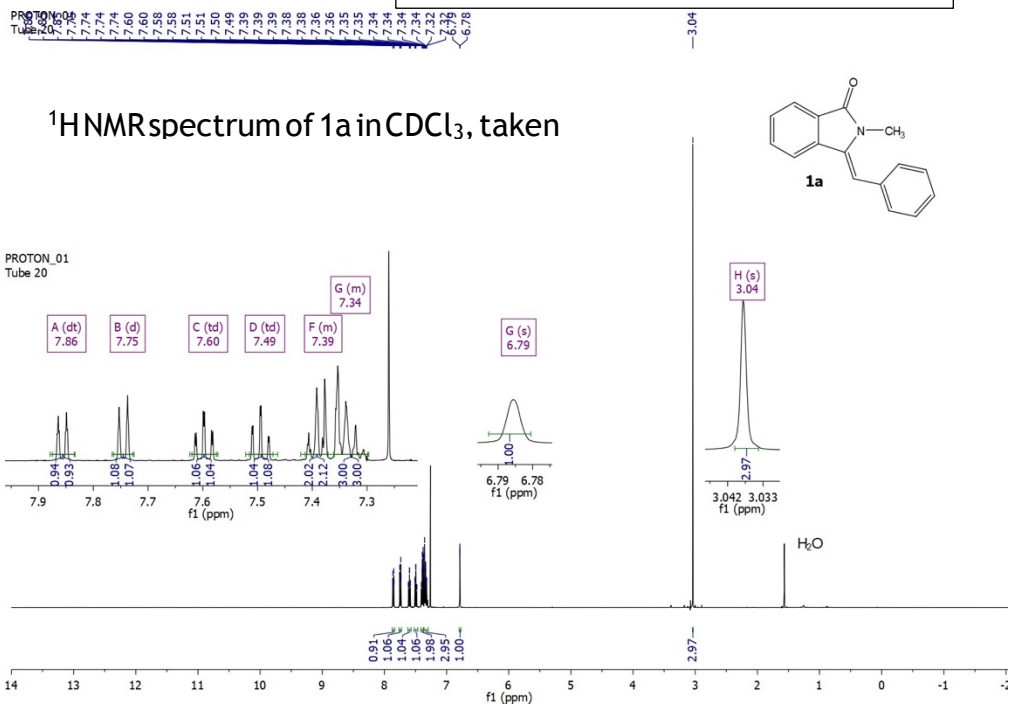
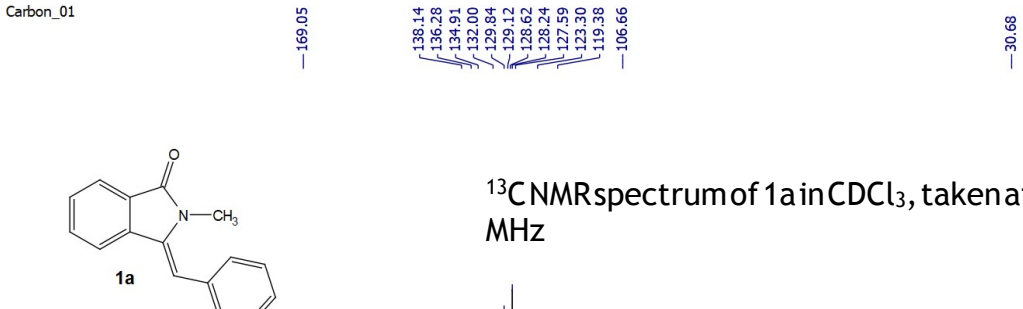
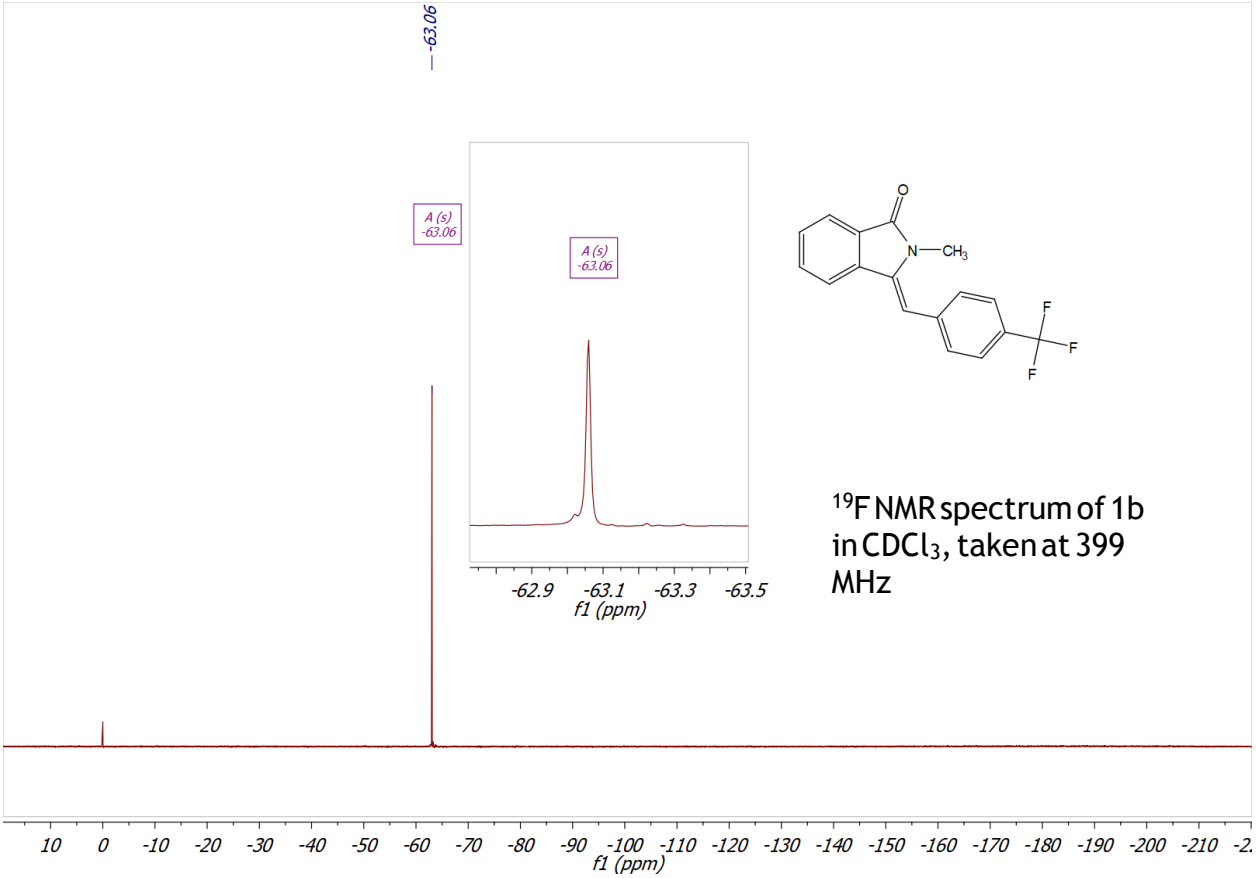
NMR spectroscopic data of starting materials



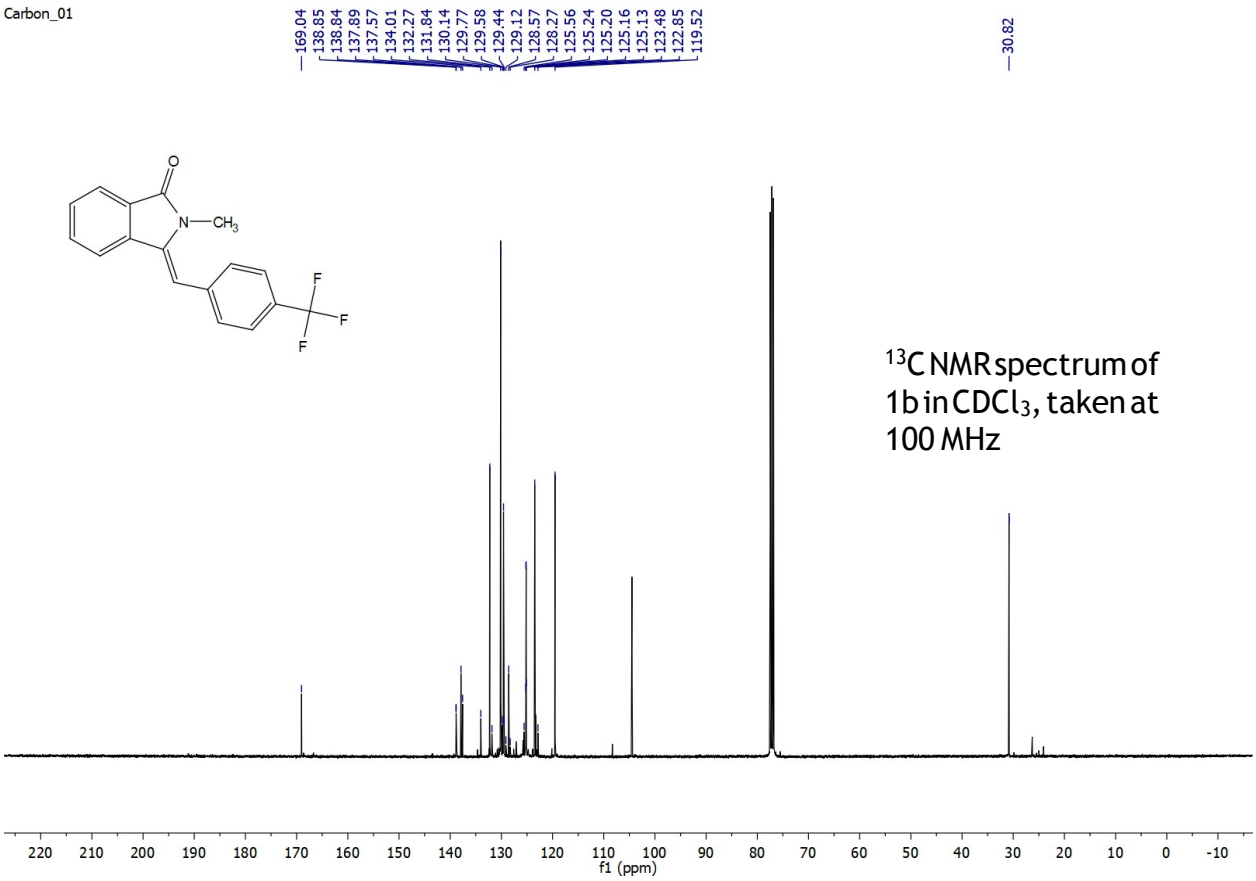
^{1}H NMR spectrum of 1a in $CDCl_3$, taken



^{13}C NMR spectrum of 1a in $CDCl_3$, taken at 100 MHz



^{19}F NMR spectrum of 1b in $CDCl_3$, taken at 399 MHz



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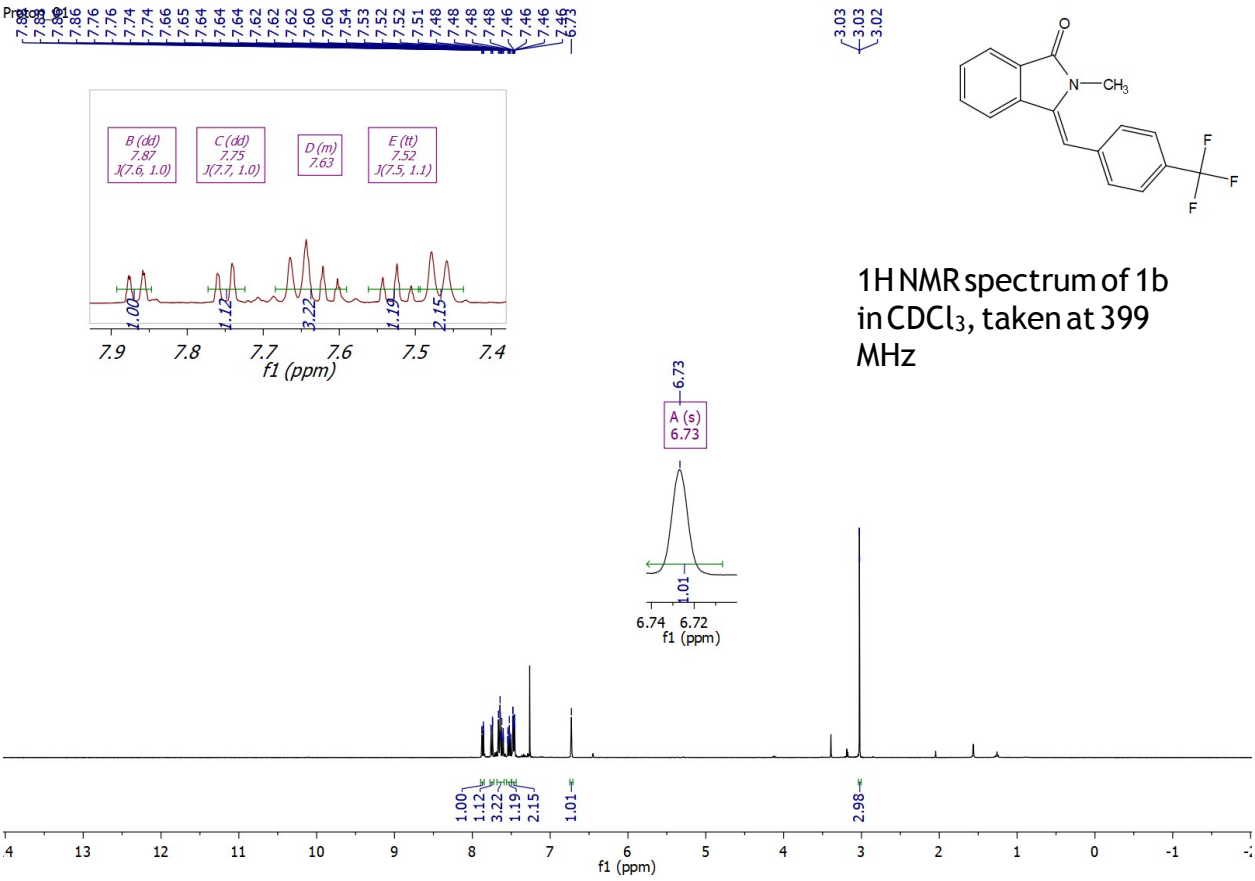

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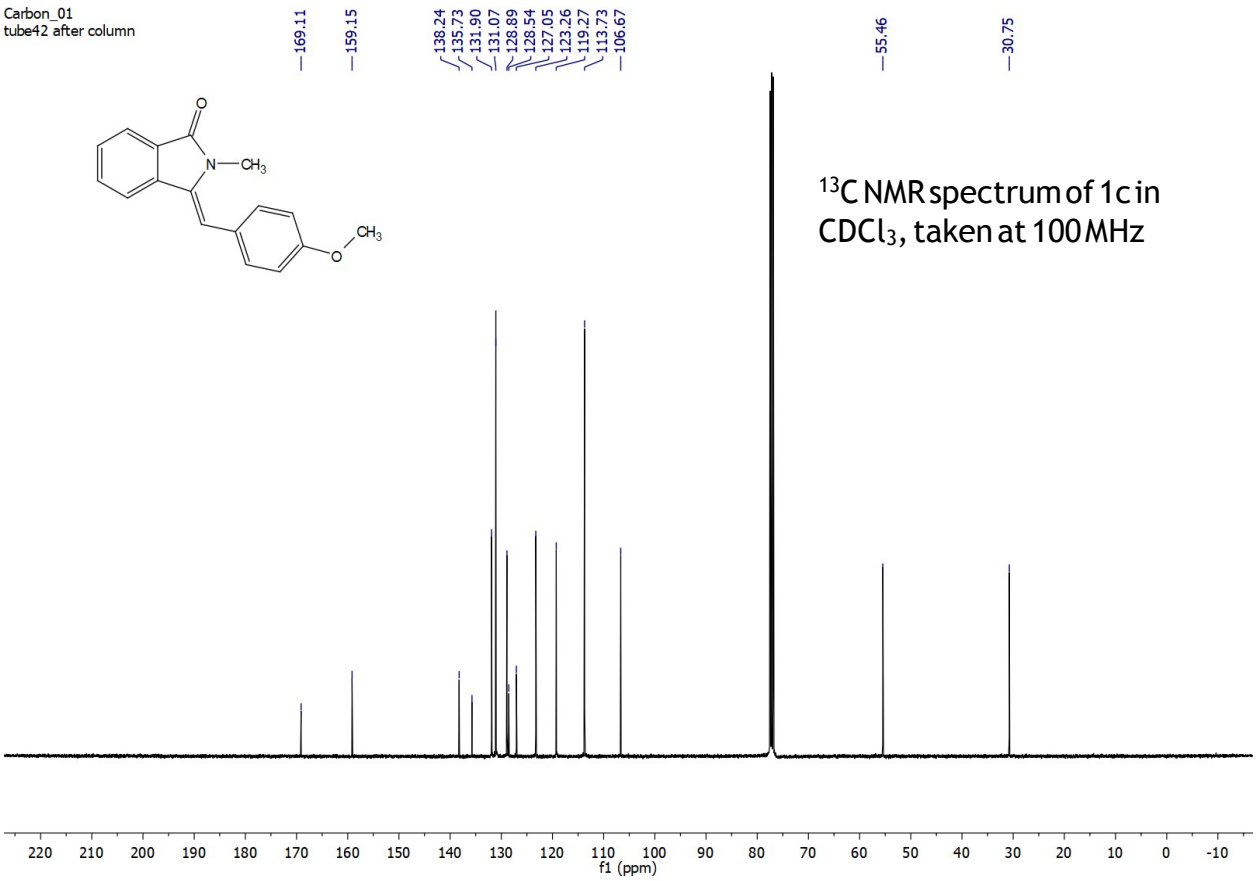

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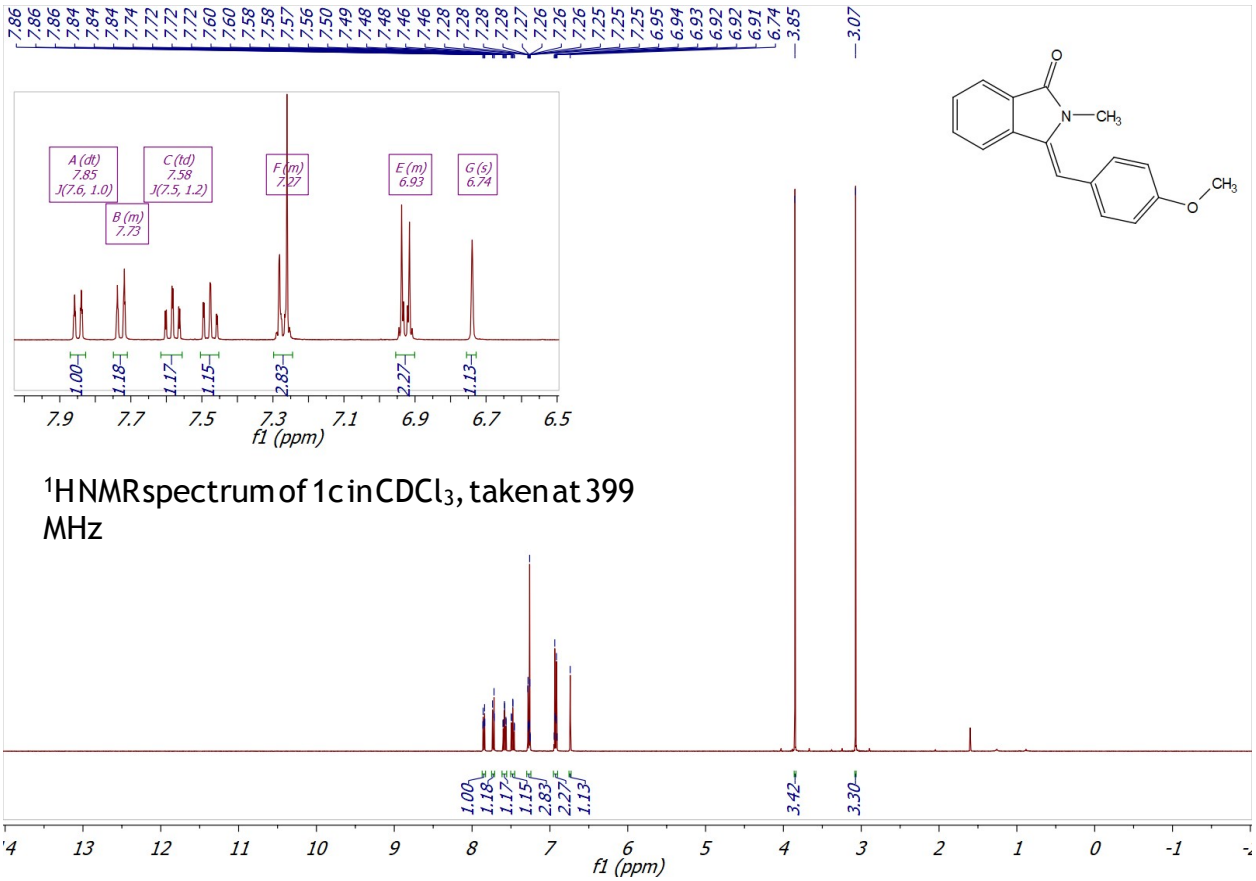

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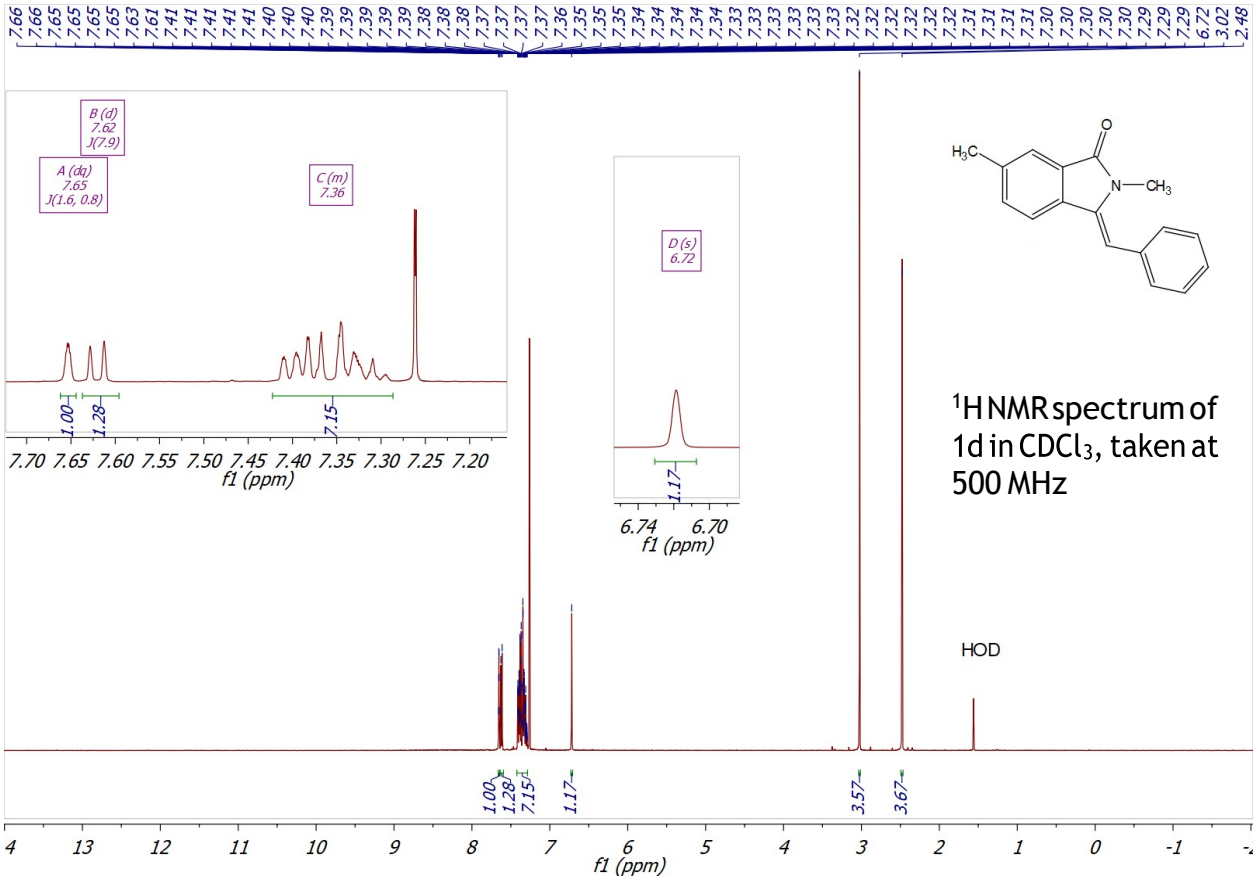

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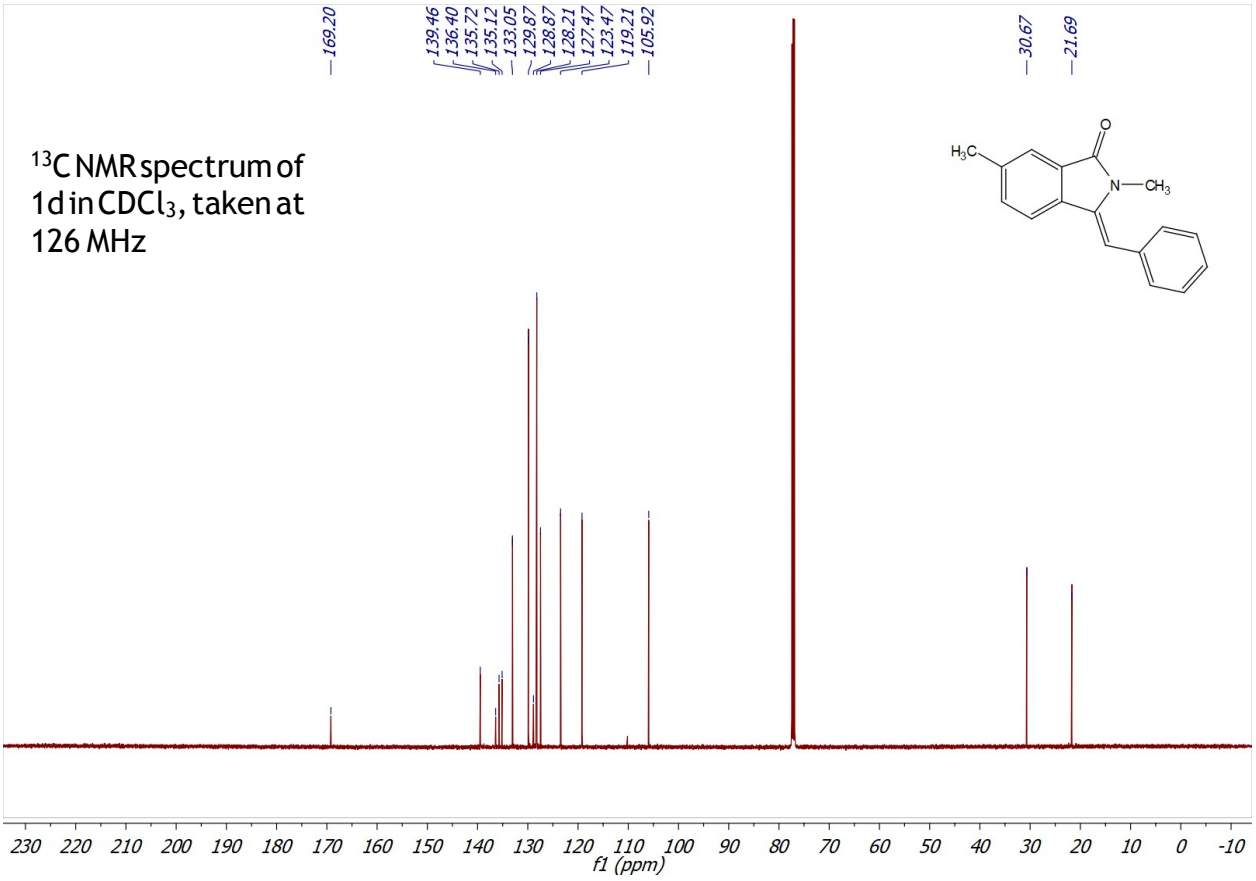
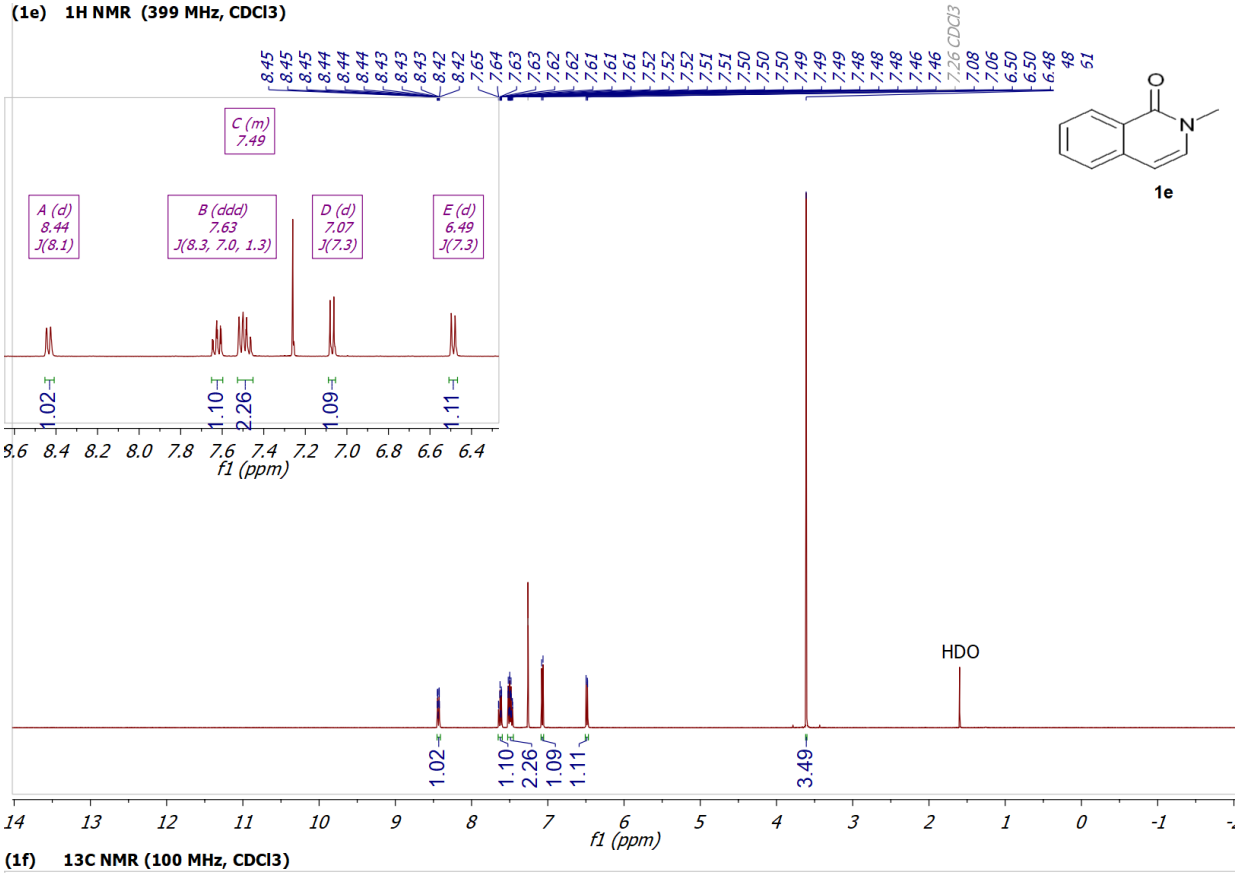


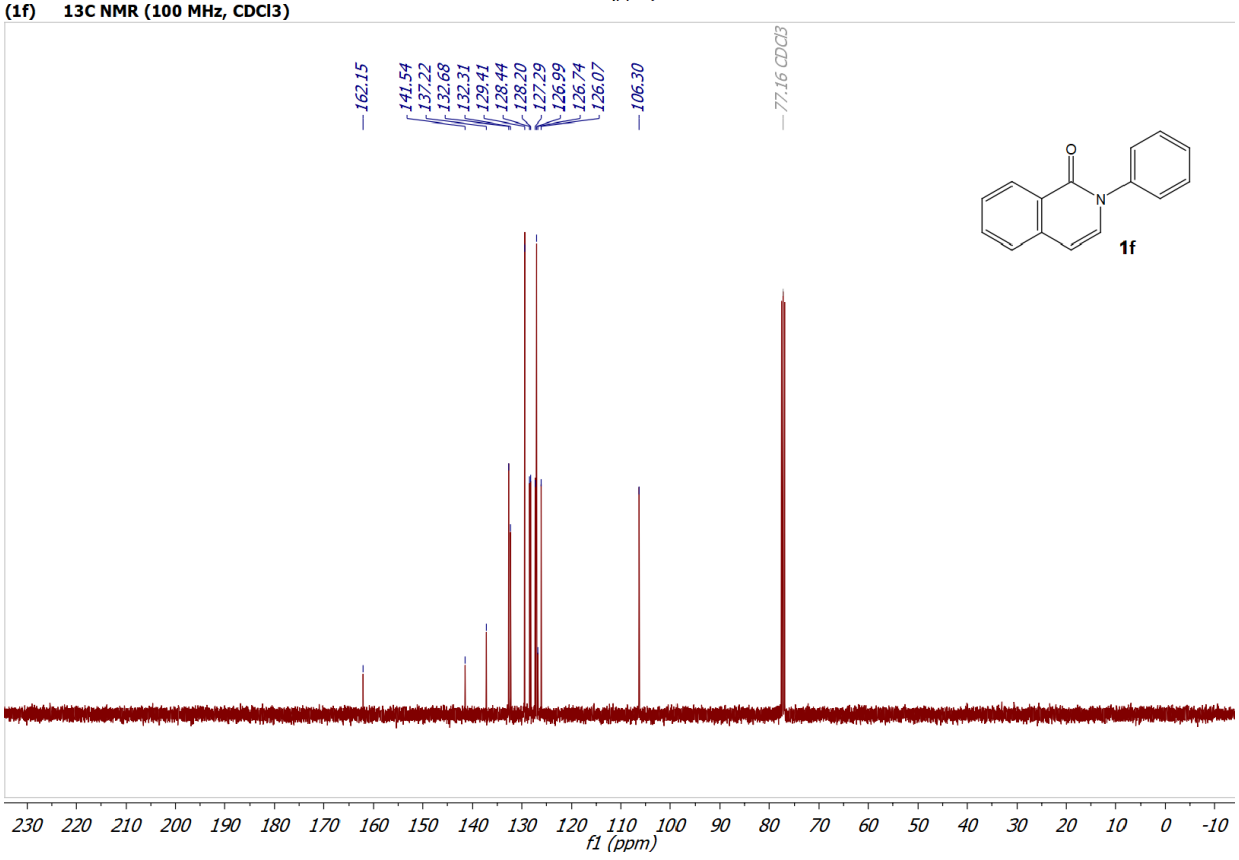
^{13}C NMR spectrum of 1d in $CDCl_3$, taken at 126 MHz

(1e) 1H NMR (399 MHz, CDCl3)



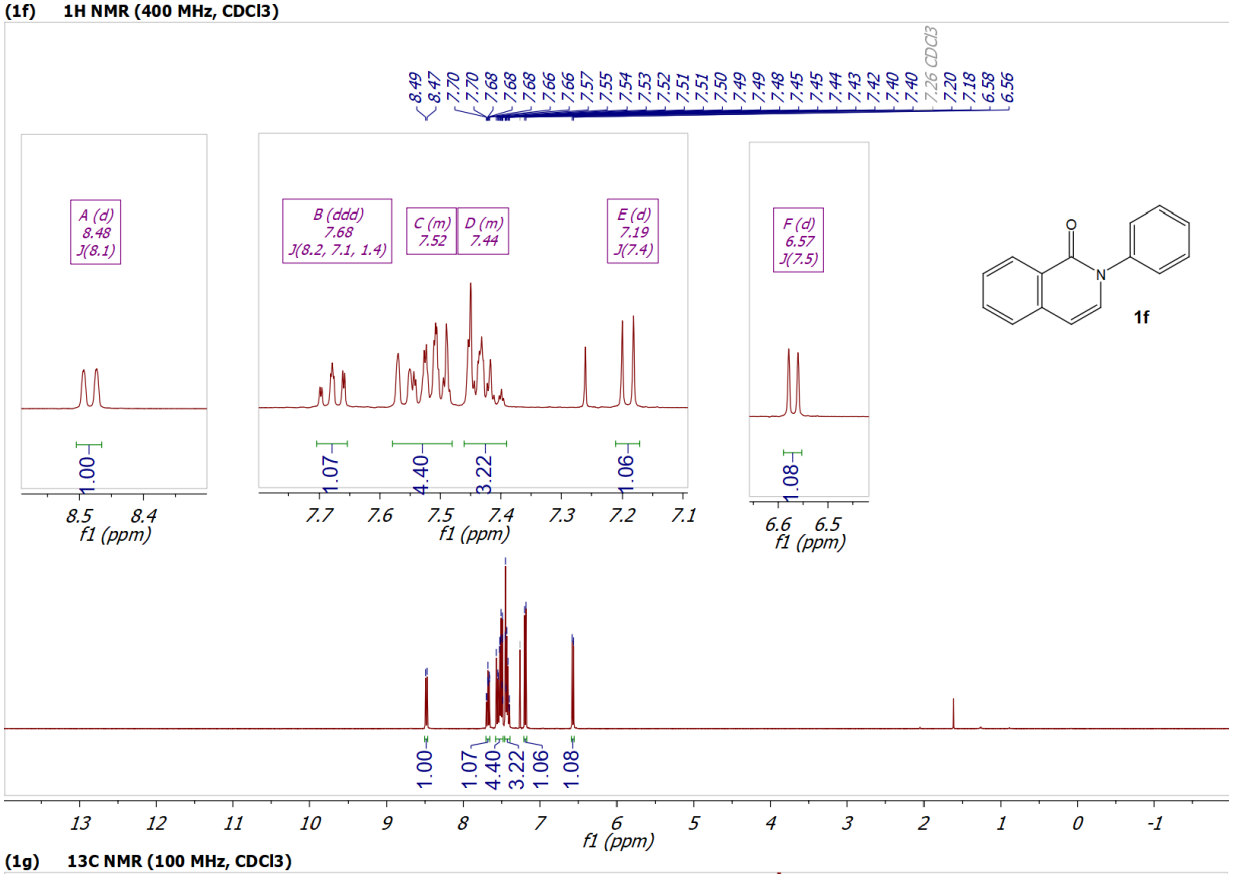
1e

(1f) 13C NMR (100 MHz, CDCl3)

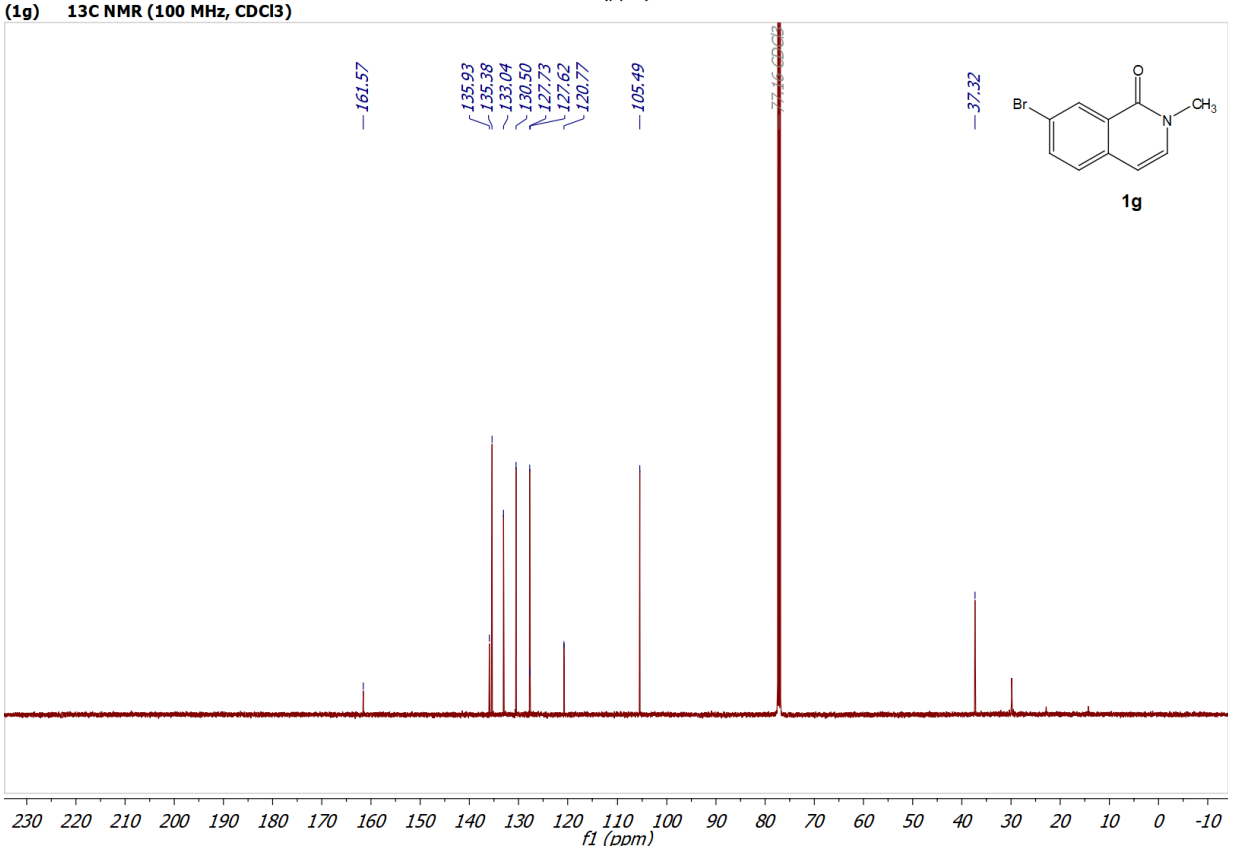


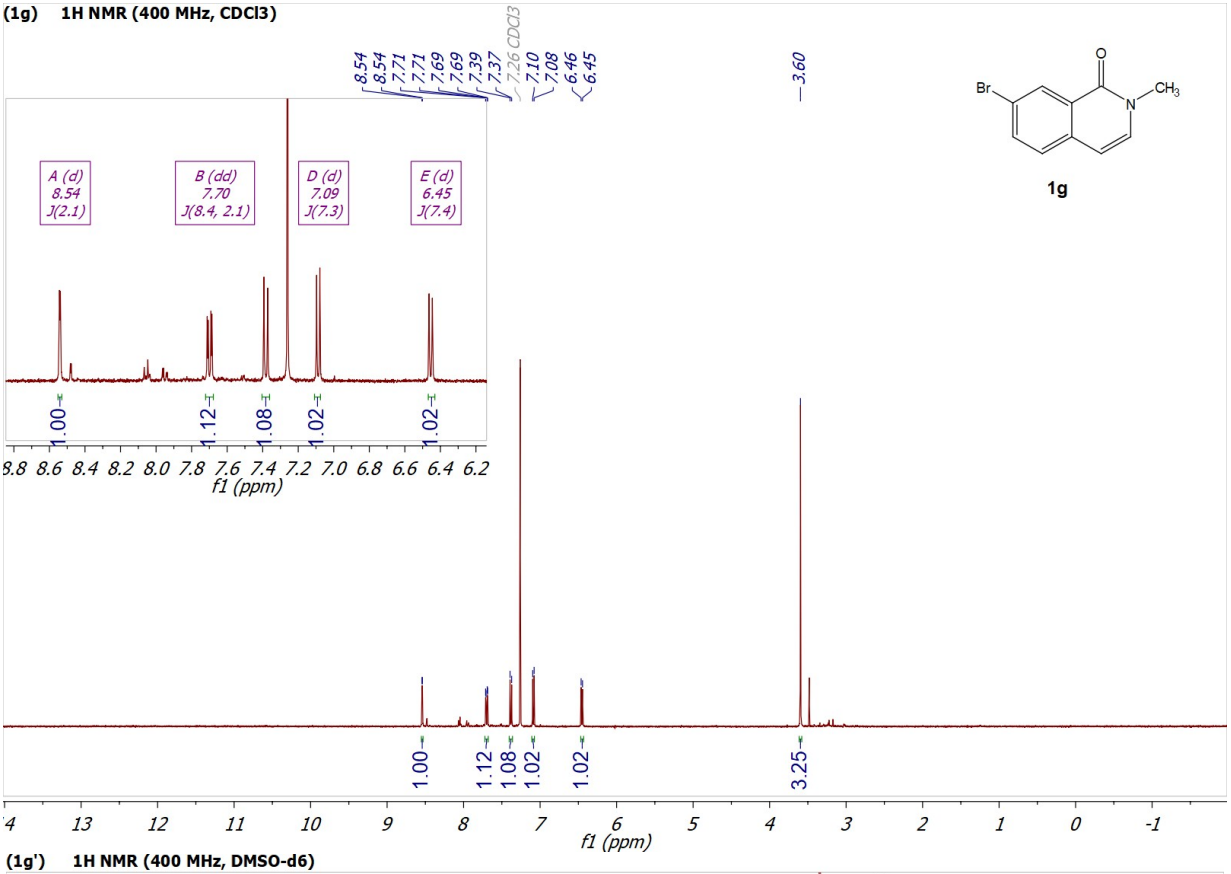
1f

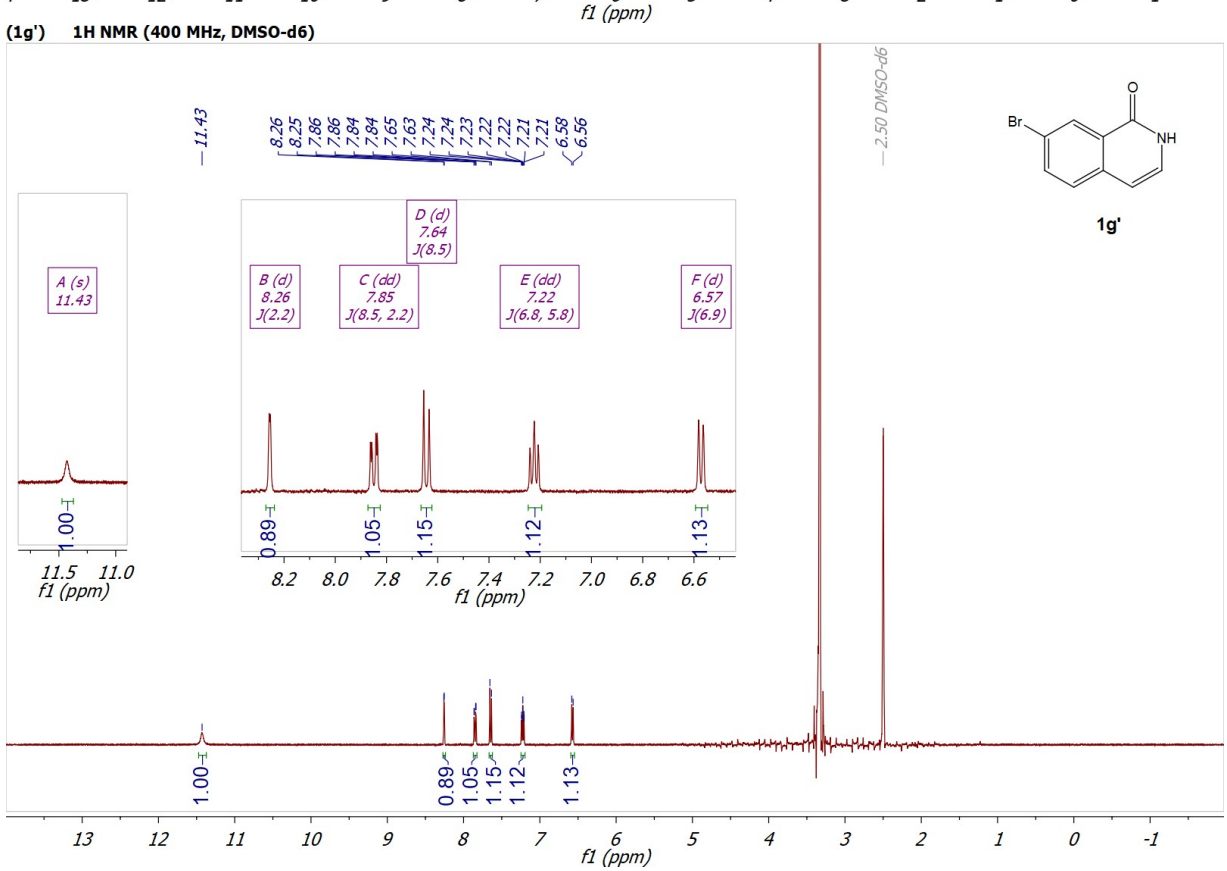
(1f) 1H NMR (400 MHz, CDCl3)

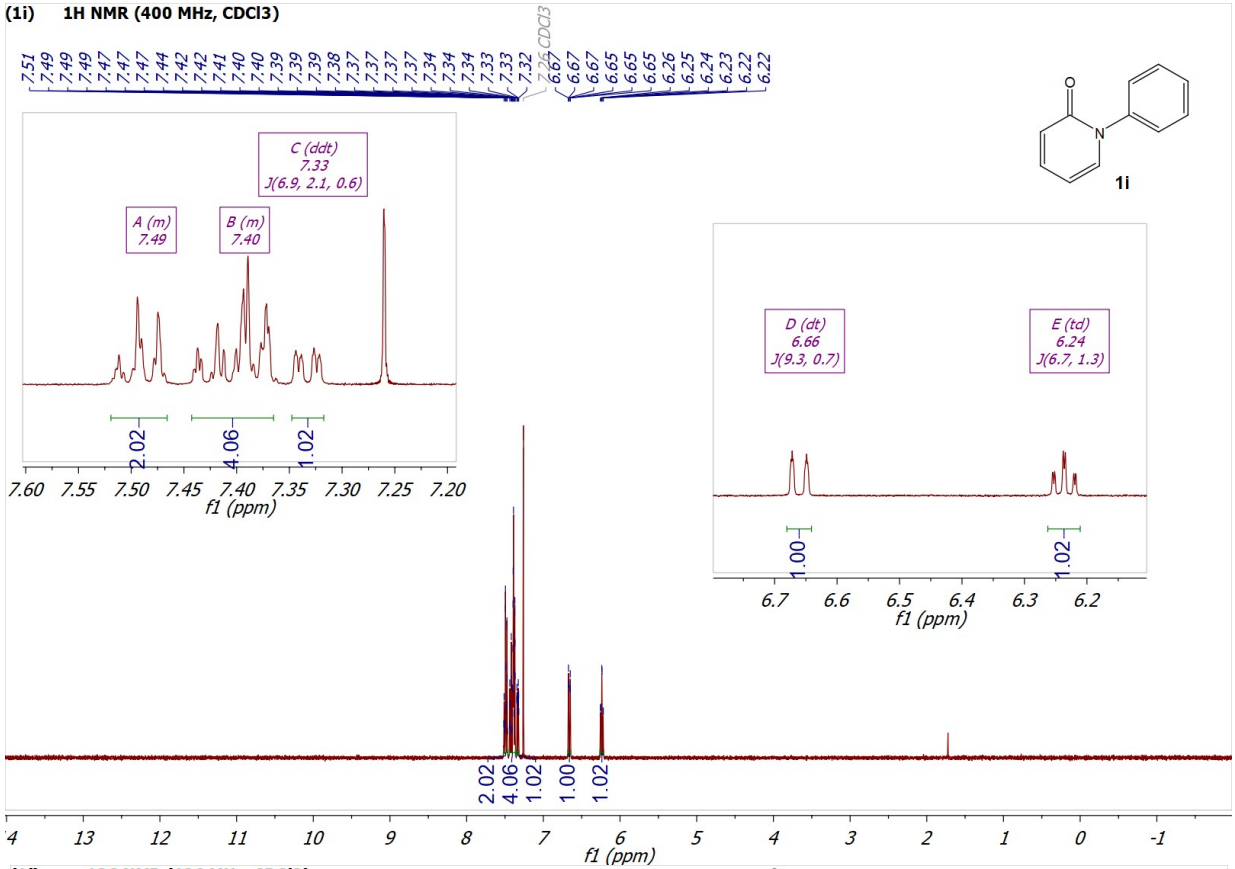


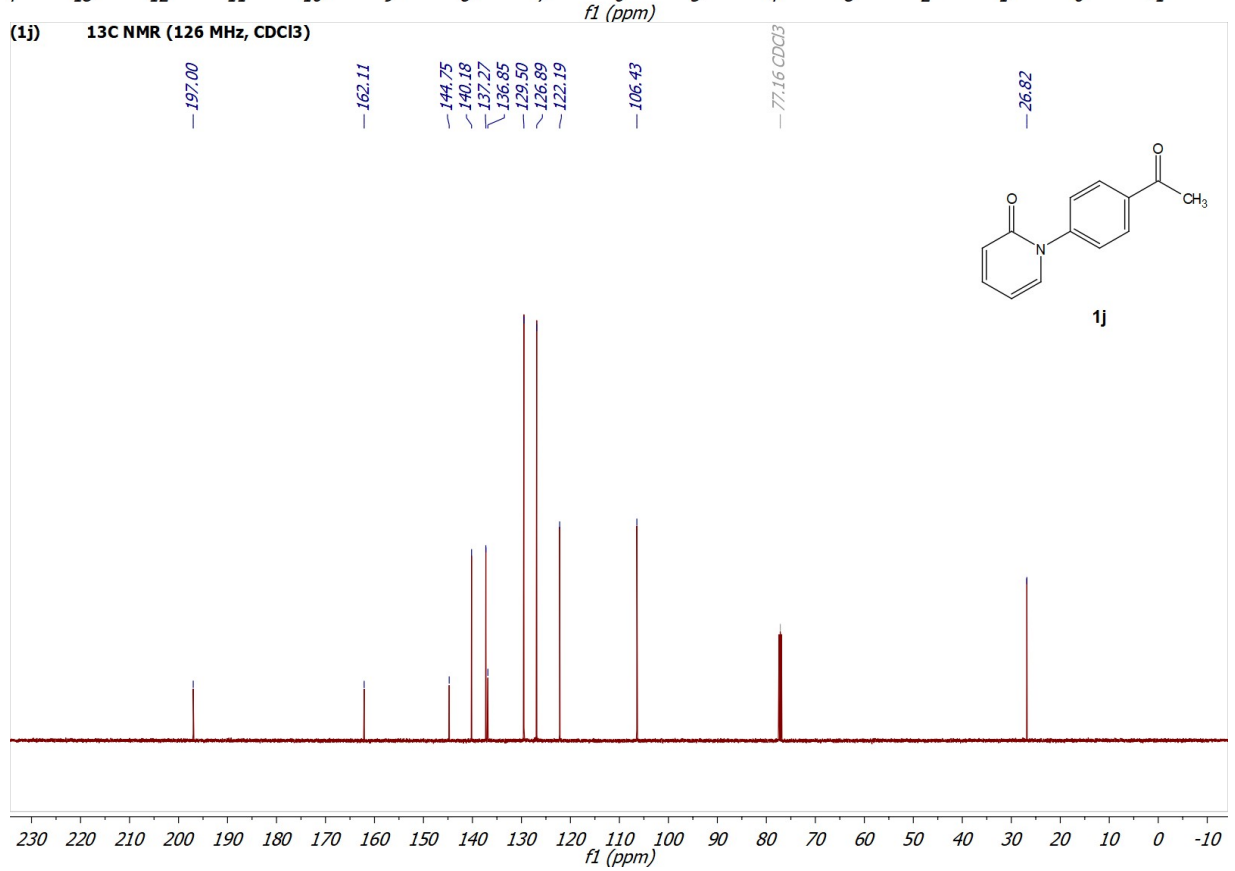
(1g) 13C NMR (100 MHz, CDCl3)

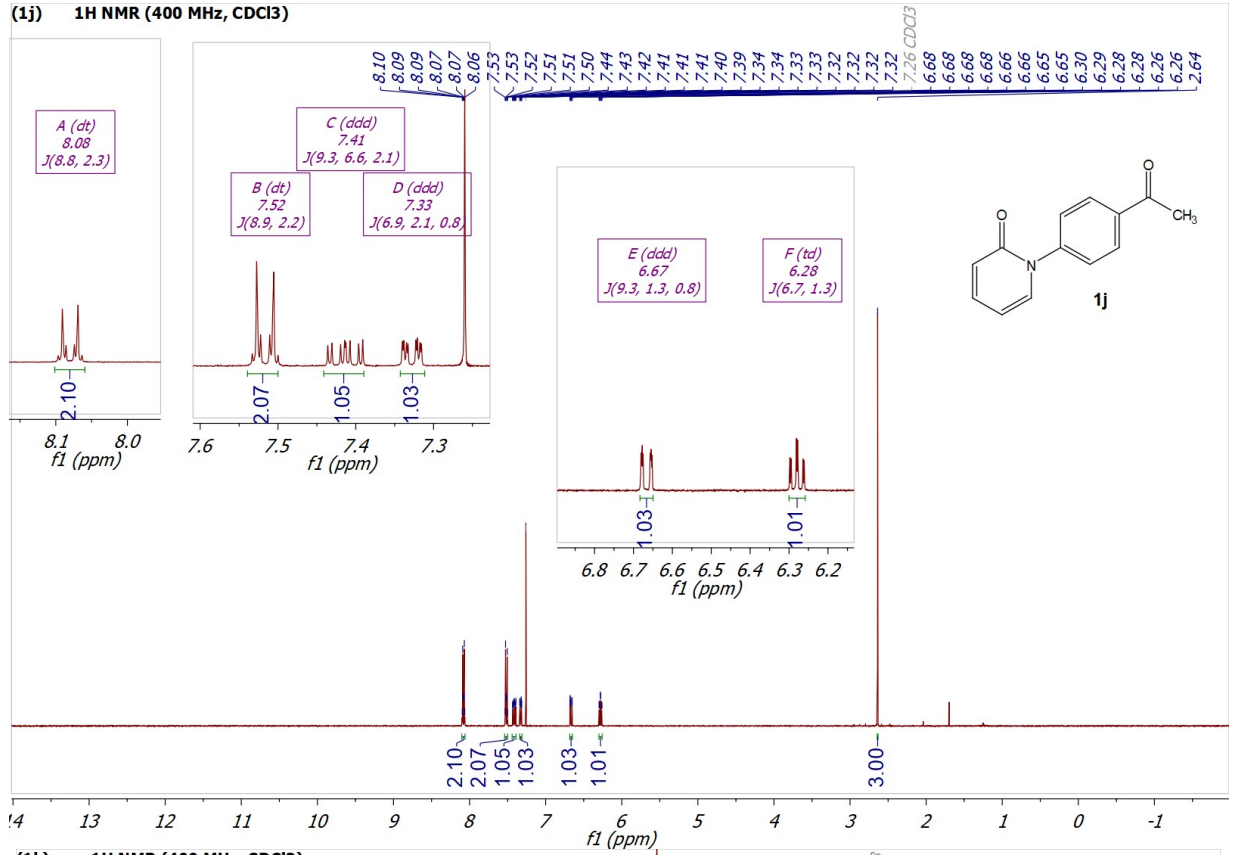


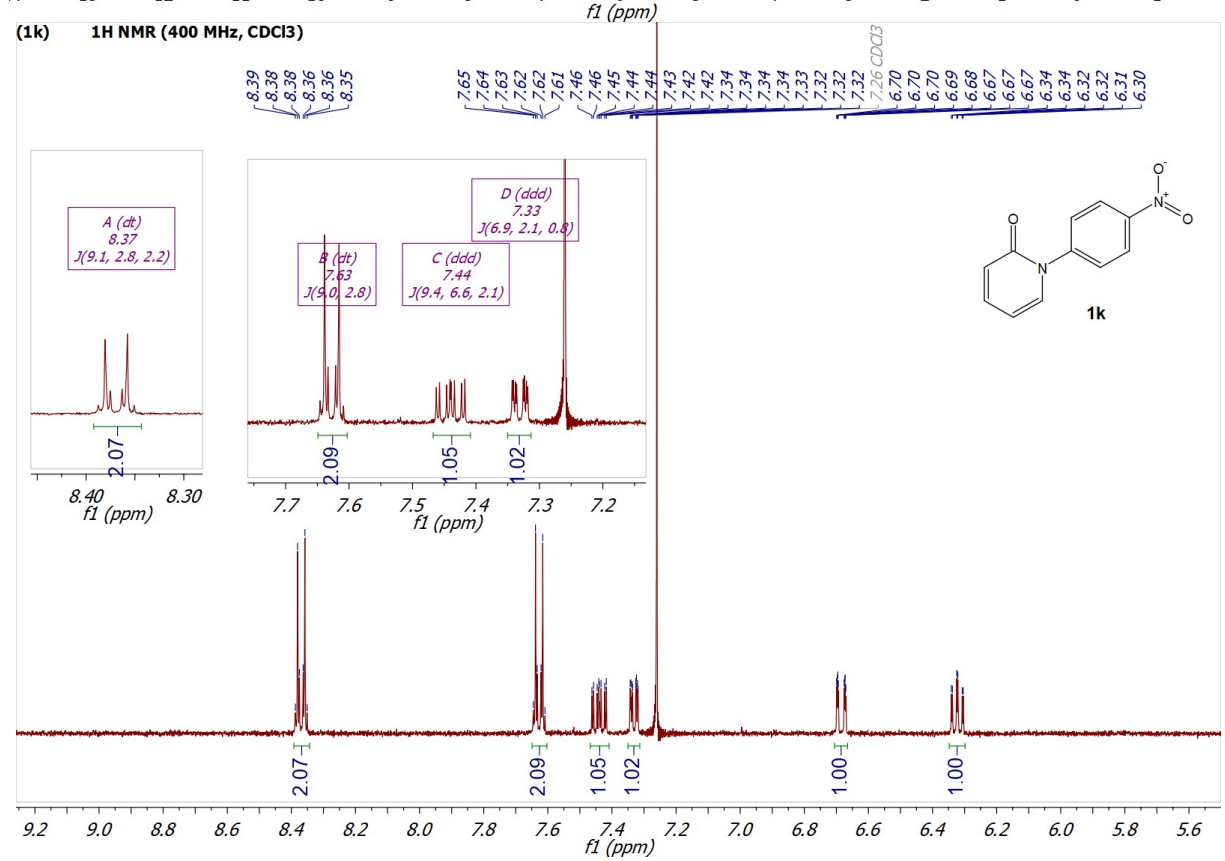

(1g) 1H NMR (400 MHz, CDCl3)
8.54
8.54
7.71
7.71
7.69
7.69
7.39
7.37
7.26 CDCl3
7.10
7.08
6.46
6.45
3.60
A (d)
8.54
J(2.1)
B (dd)
7.70
J(8.4, 2.1)
D (d)
7.09
J(7.3)
E (d)
6.45
J(7.4)
1.00
1.12
1.08
1.02
1.02
1.00
1.12
1.08
1.02
1.02
3.25
f1 (ppm)
Br
O
N
CH3
1g

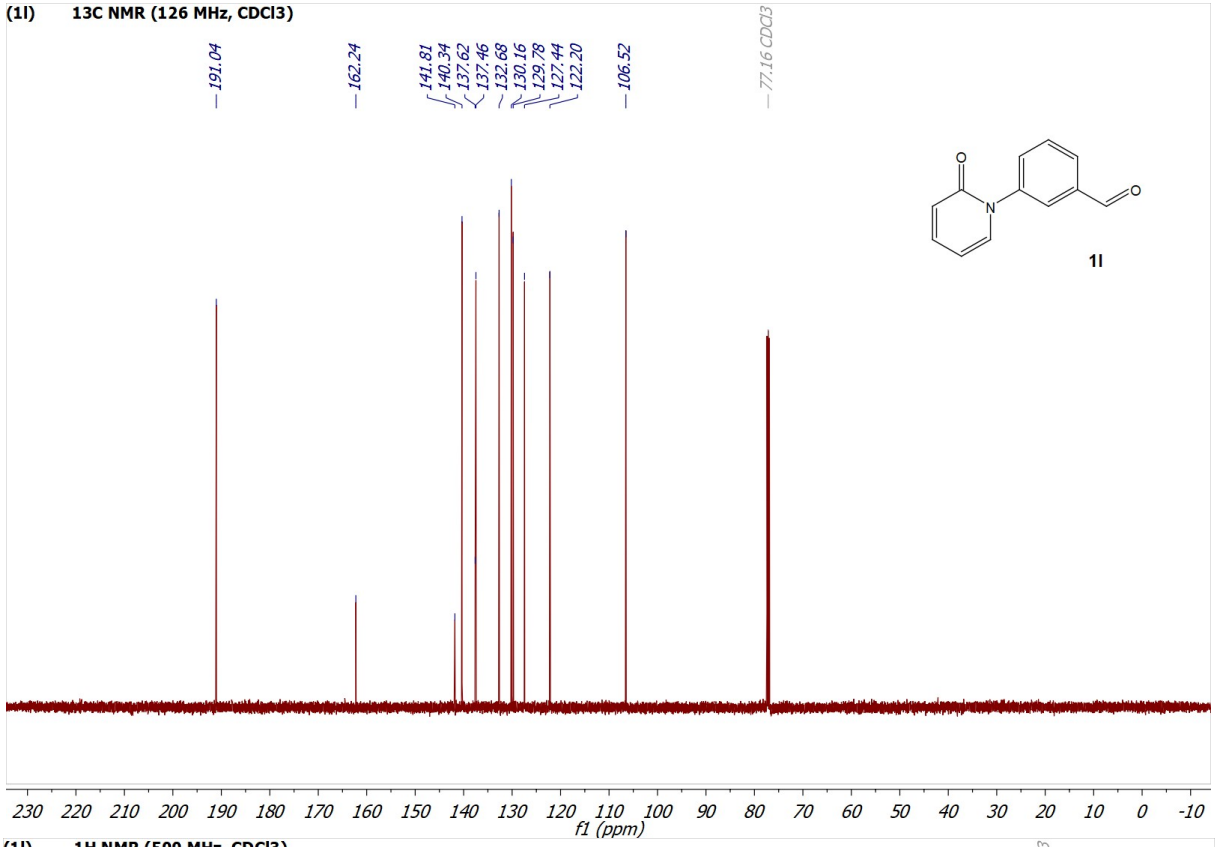

(1g') 1H NMR (400 MHz, DMSO-d6)
11.43
8.26
8.25
7.86
7.86
7.84
7.84
7.65
7.63
7.24
7.24
7.23
7.22
7.22
7.21
7.21
6.58
6.56
2.50 DMSO-d6
A (s)
11.43
D (d)
7.64
J(8.5)
B (d)
8.26
J(2.2)
C (dd)
7.85
J(8.5, 2.2)
E (dd)
7.22
J(6.8, 5.8)
F (d)
6.57
J(6.9)
1.00
0.89
1.05
1.15
1.12
1.13
1.00
0.89
1.05
1.15
1.12
1.13
f1 (ppm)
Br
O
NH
1g'

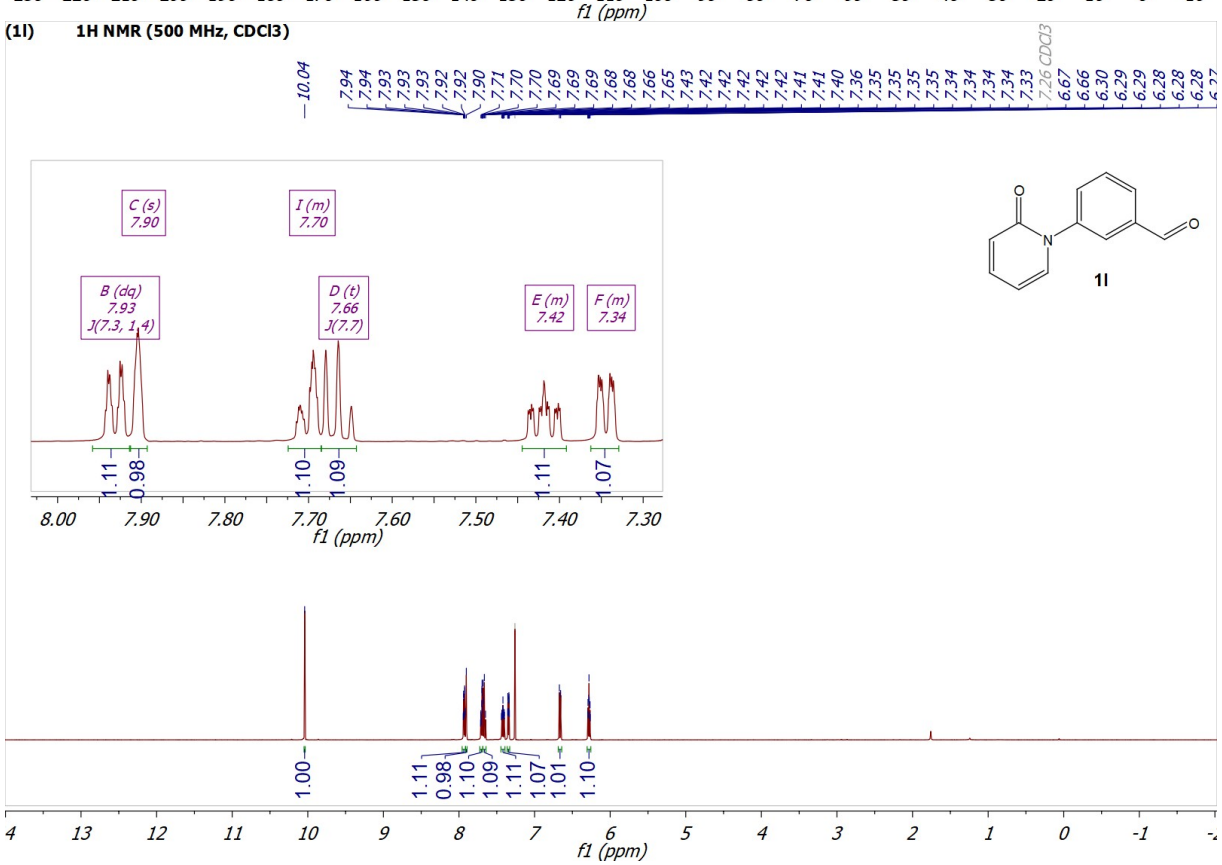

(1i) 1H NMR (400 MHz, CDCl3)
7.51 7.49 7.49 7.47 7.47 7.44 7.42 7.41 7.40 7.40 7.39 7.39 7.38 7.37 7.37 7.37 7.34 7.34 7.33 7.32 7.26 CDCl3 6.67 6.67 6.65 6.65 6.26 6.25 6.24 6.23 6.22 6.22
C (ddt)
7.33
J(6.9, 2.1, 0.6)
A (m)
7.49
B (m)
7.40
2.02
4.06
1.02
7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20
f1 (ppm)
D (dt)
6.66
J(9.3, 0.7)
E (td)
6.24
J(6.7, 1.3)
1.00
1.02
6.7 6.6 6.5 6.4 6.3 6.2
f1 (ppm)
2.02 4.06 1.02 1.00 1.02
4 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)
1i


(1j) 13C NMR (126 MHz, CDCl3)
197.00 162.11 144.75 140.18 137.27 136.85 129.50 126.89 122.19 106.43 77.16 CDCl3 26.82
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
1j

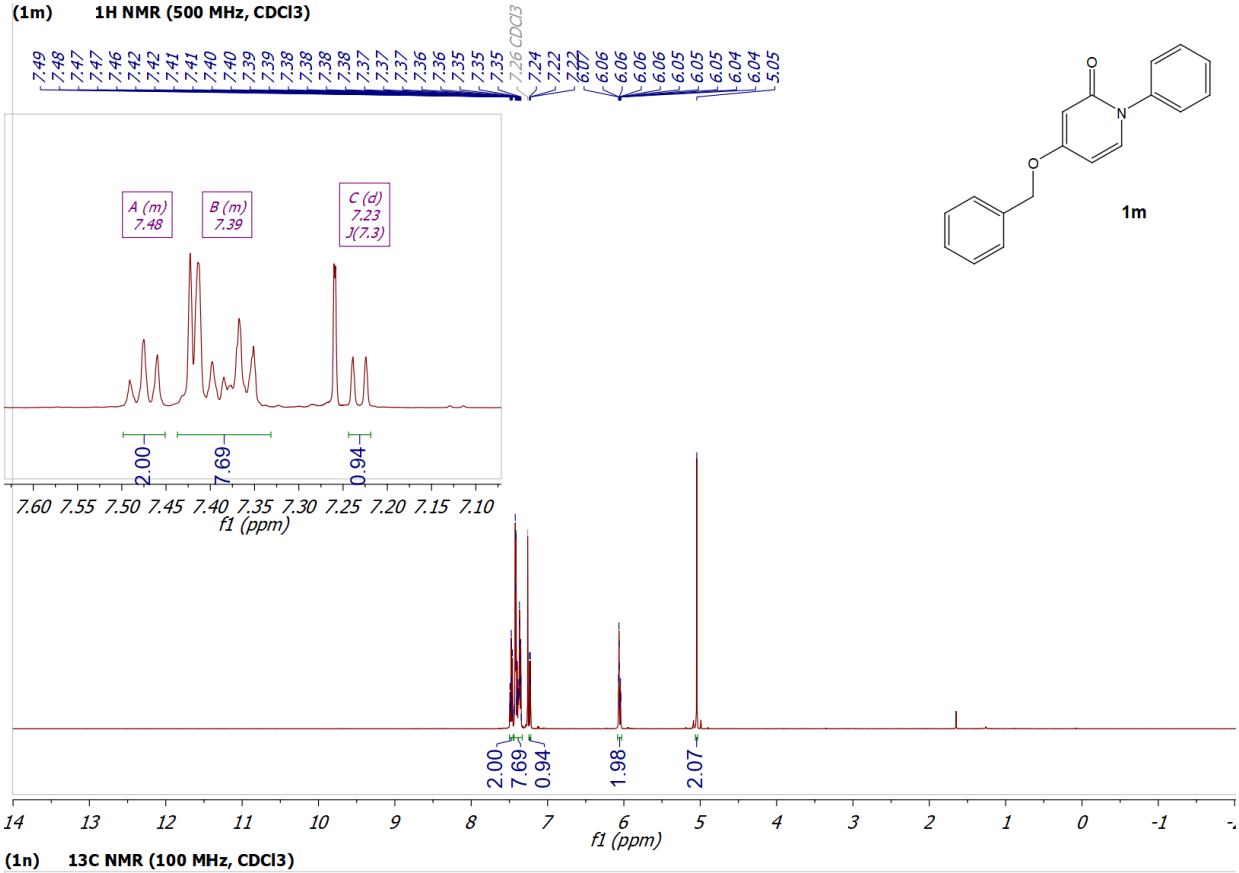

(1j) 1H NMR (400 MHz, CDCl3)
A (dt)
8.08
J(8.8, 2.3)
B (dt)
7.52
J(8.9, 2.2)
C (ddd)
7.41
J(9.3, 6.6, 2.1)
D (ddd)
7.33
J(6.9, 2.1, 0.8)
E (ddd)
6.67
J(9.3, 1.3, 0.8)
F (td)
6.28
J(6.7, 1.3)
1j
f1 (ppm)


(1k) 1H NMR (400 MHz, CDCl3)
A (dt)
8.37
J(9.1, 2.8, 2.2)
B (dt)
7.63
J(9.0, 2.8)
C (ddd)
7.44
J(9.4, 6.6, 2.1)
D (ddd)
7.33
J(6.9, 2.1, 0.8)
1k
f1 (ppm)


(1l) 13C NMR (126 MHz, CDCl3)
191.04
162.24
141.81
140.34
137.62
137.46
132.68
130.16
129.78
127.44
122.20
106.52
77.16 CDCl3
1l
f1 (ppm)

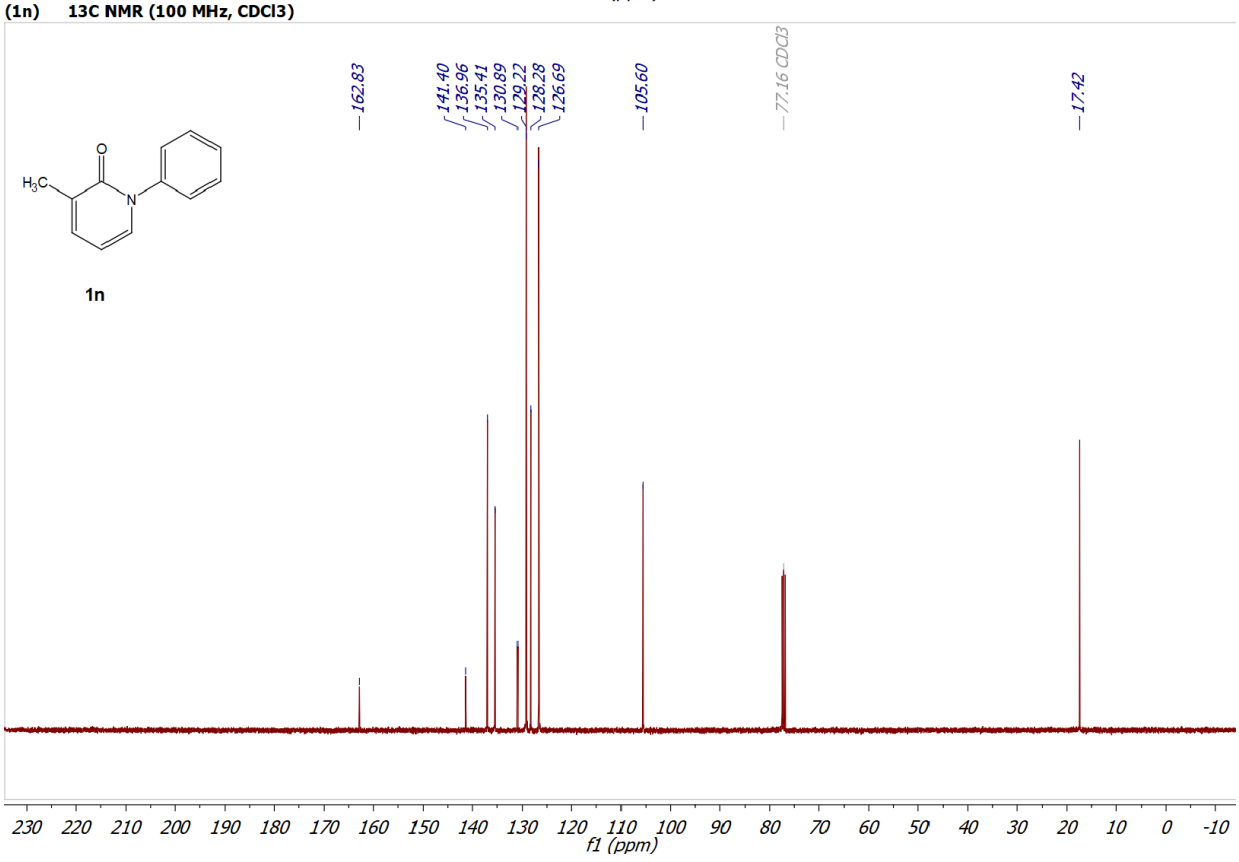

(1l) 1H NMR (500 MHz, CDCl3)
10.04
7.26 CDCl3
C (s) 7.90
I (m) 7.70
B (dq) 7.93 J(7.3, 1.4)
D (t) 7.66 J(7.7)
E (m) 7.42
F (m) 7.34
1l
f1 (ppm)

(1m) 1H NMR (500 MHz, CDCl3)



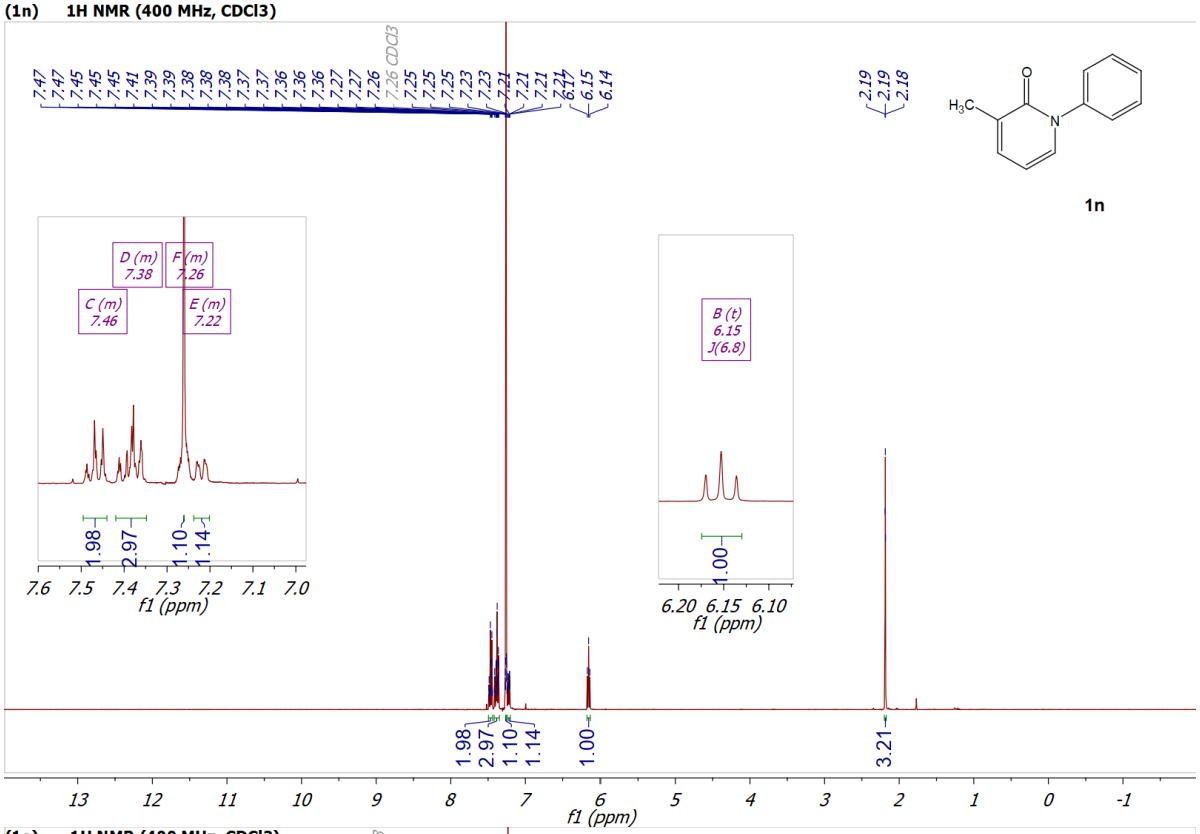
1m

(1n) 13C NMR (100 MHz, CDCl3)

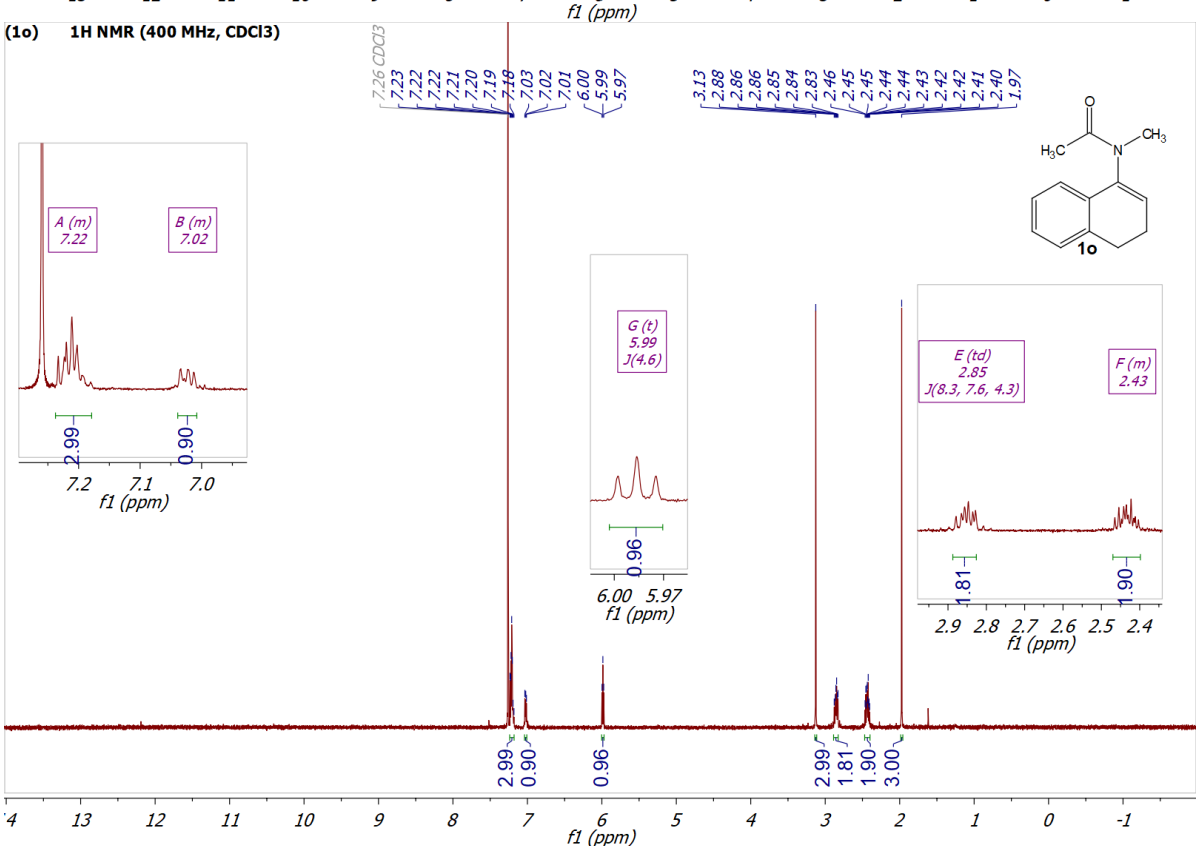


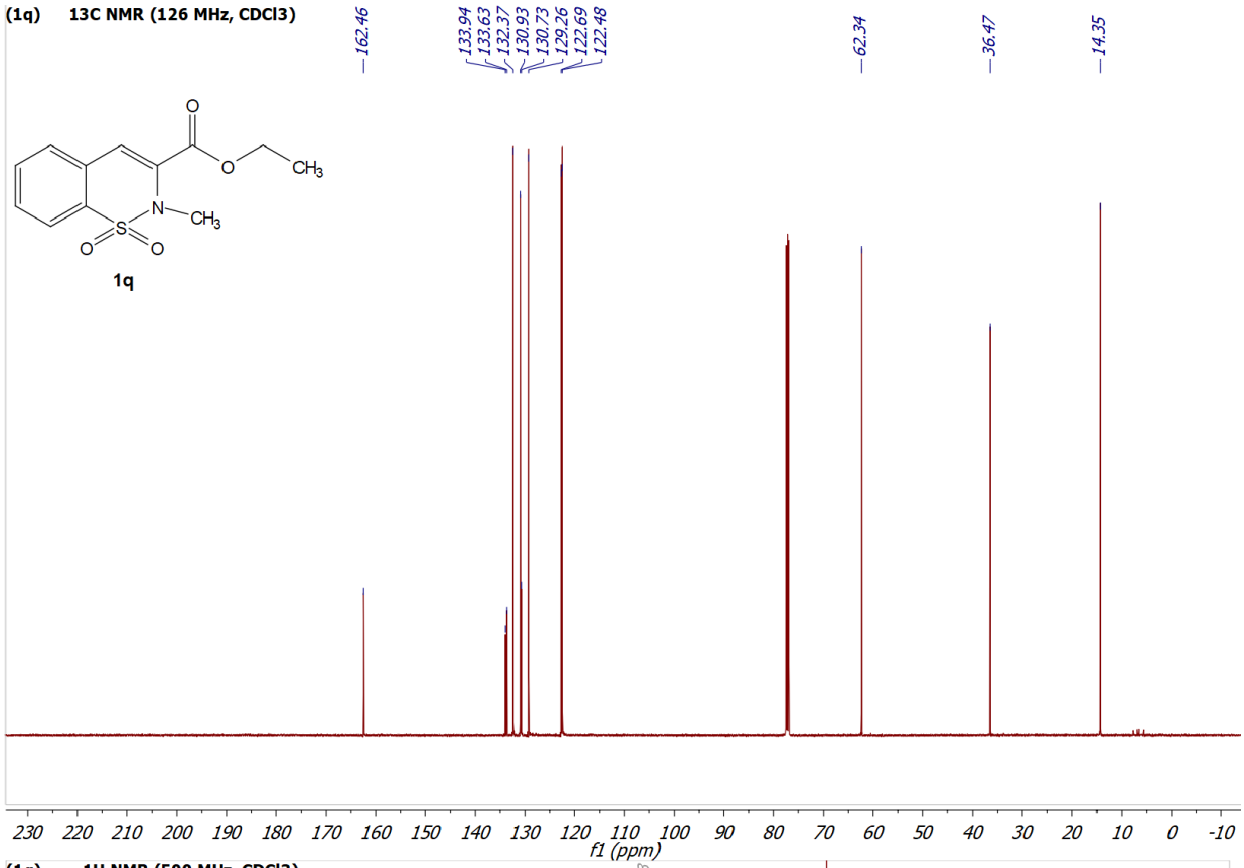
1n

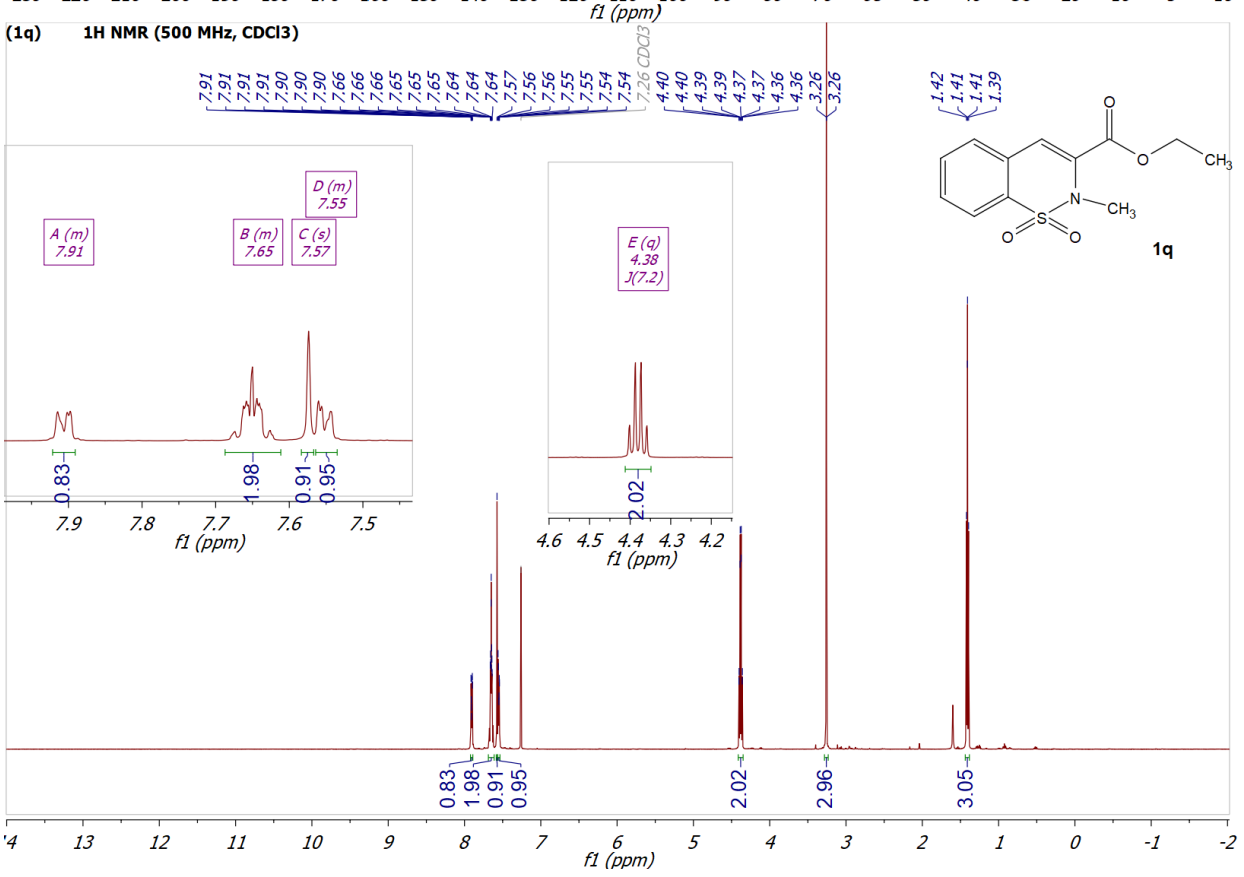
(1n) 1H NMR (400 MHz, CDCl3)



(1o) 1H NMR (400 MHz, CDCl3)

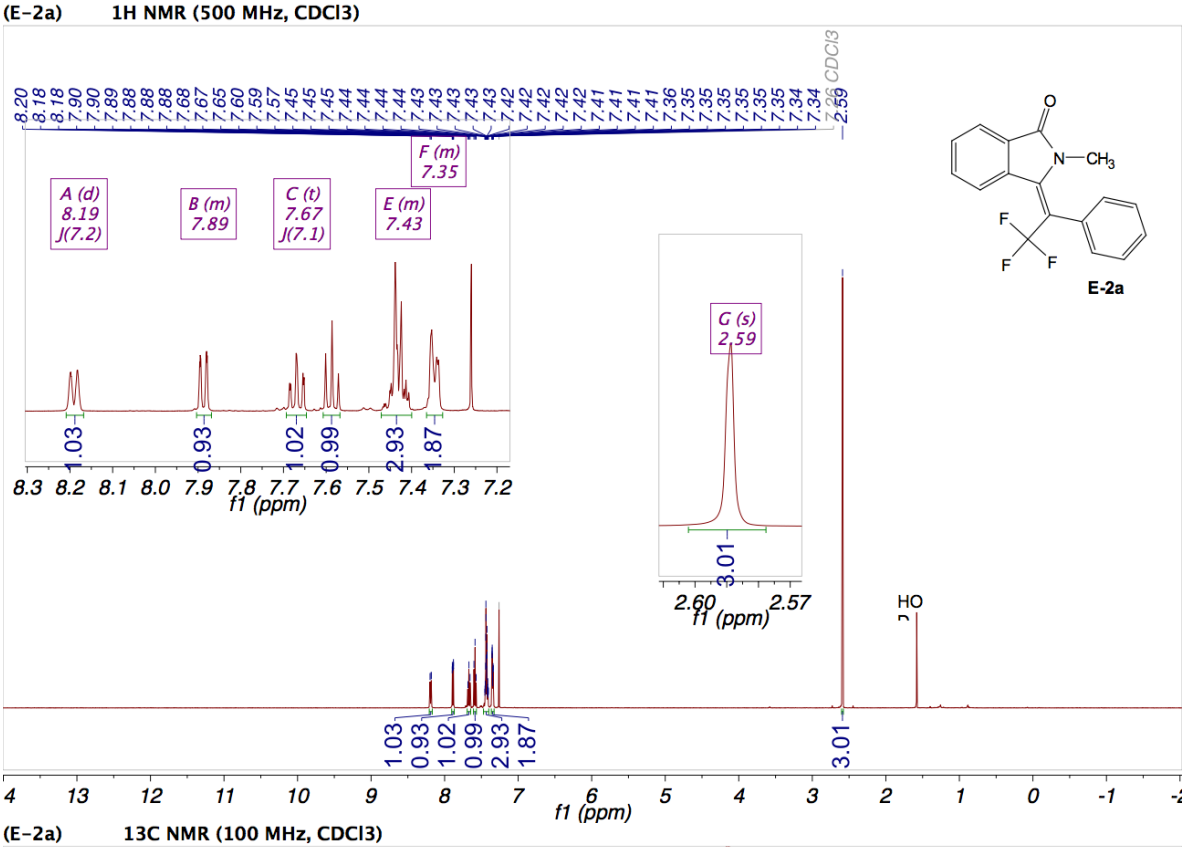



(1q) 13C NMR (126 MHz, CDCl3)
162.46
133.94
133.63
132.37
130.93
130.73
129.26
122.69
122.48
62.34
36.47
14.35
1q
f1 (ppm)


(1q) 1H NMR (500 MHz, CDCl3)
7.26 CDCl3
A (m) 7.91
B (m) 7.65
C (s) 7.57
D (m) 7.55
E (q) 4.38 J(7.2)
1.42
1.41
1.39
0.83
1.98
0.91
0.95
2.02
2.96
3.05
1q
f1 (ppm)

NMR spectroscopic data of products

(E-2a) 1H NMR (500 MHz, CDCl3)



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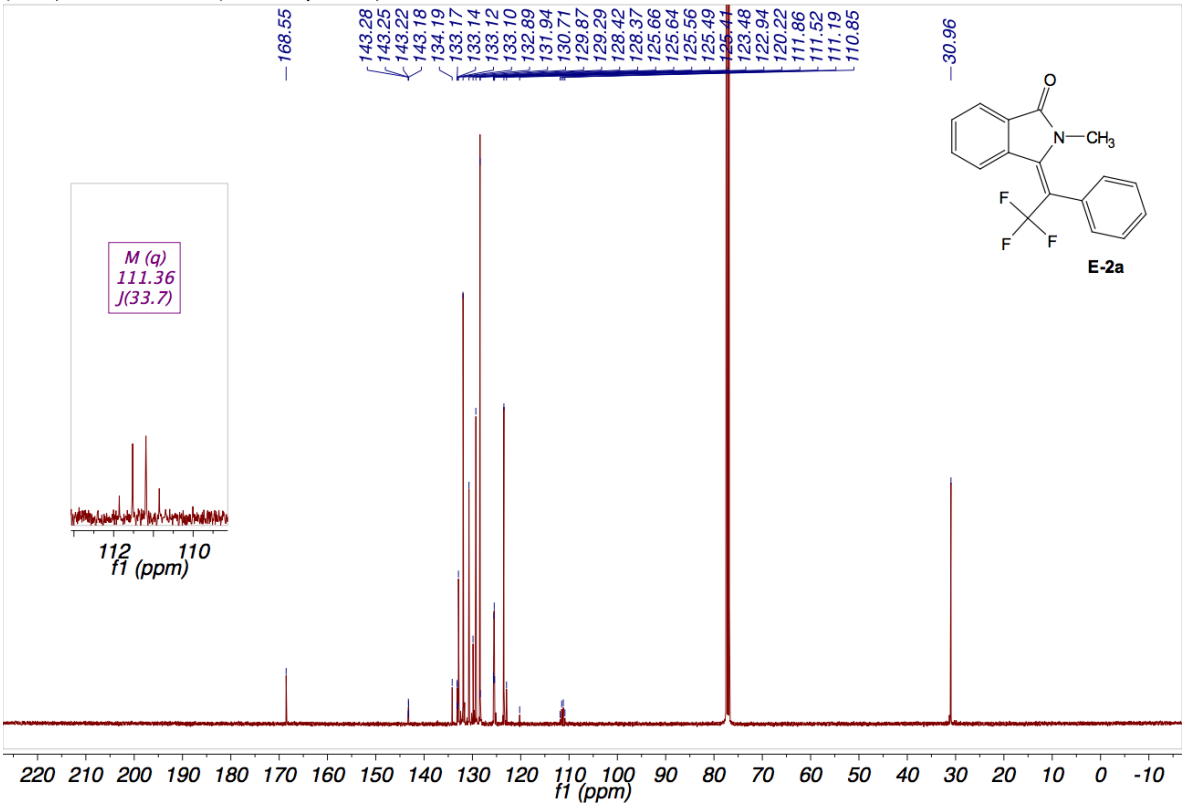

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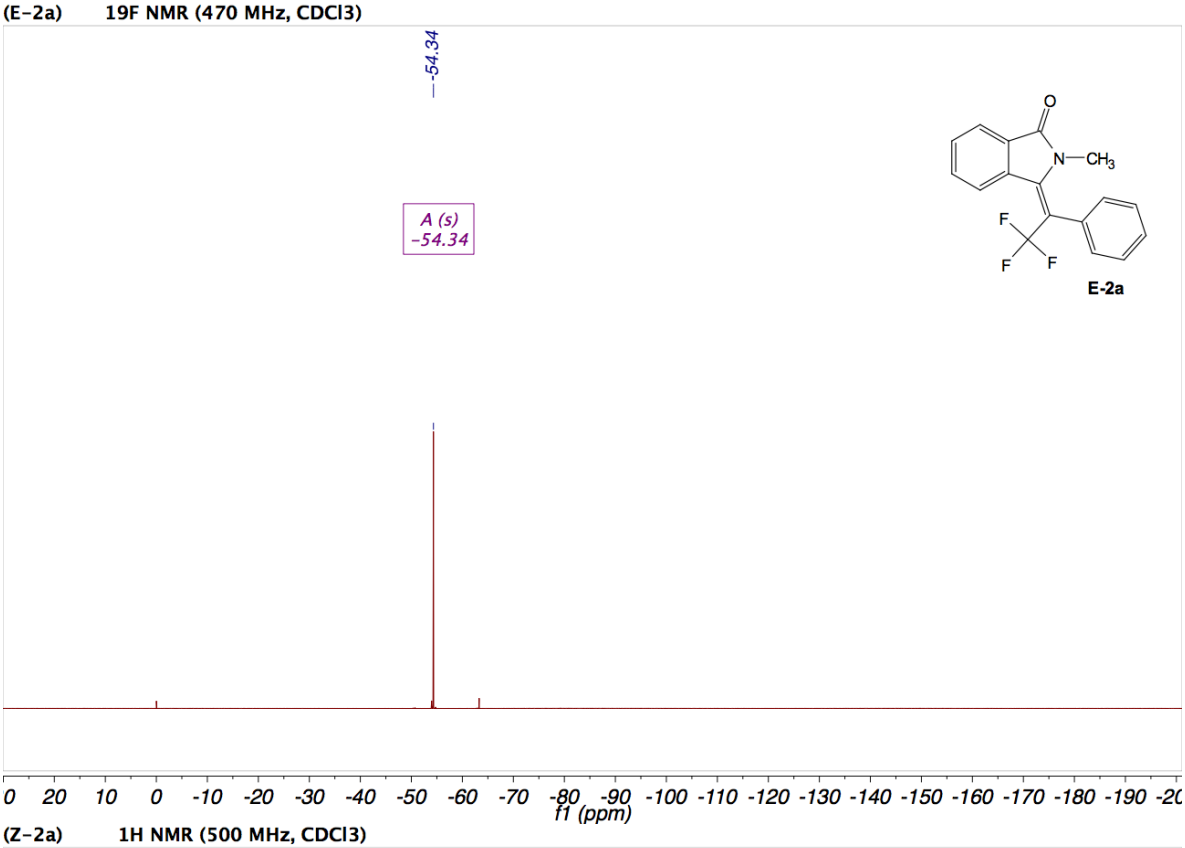

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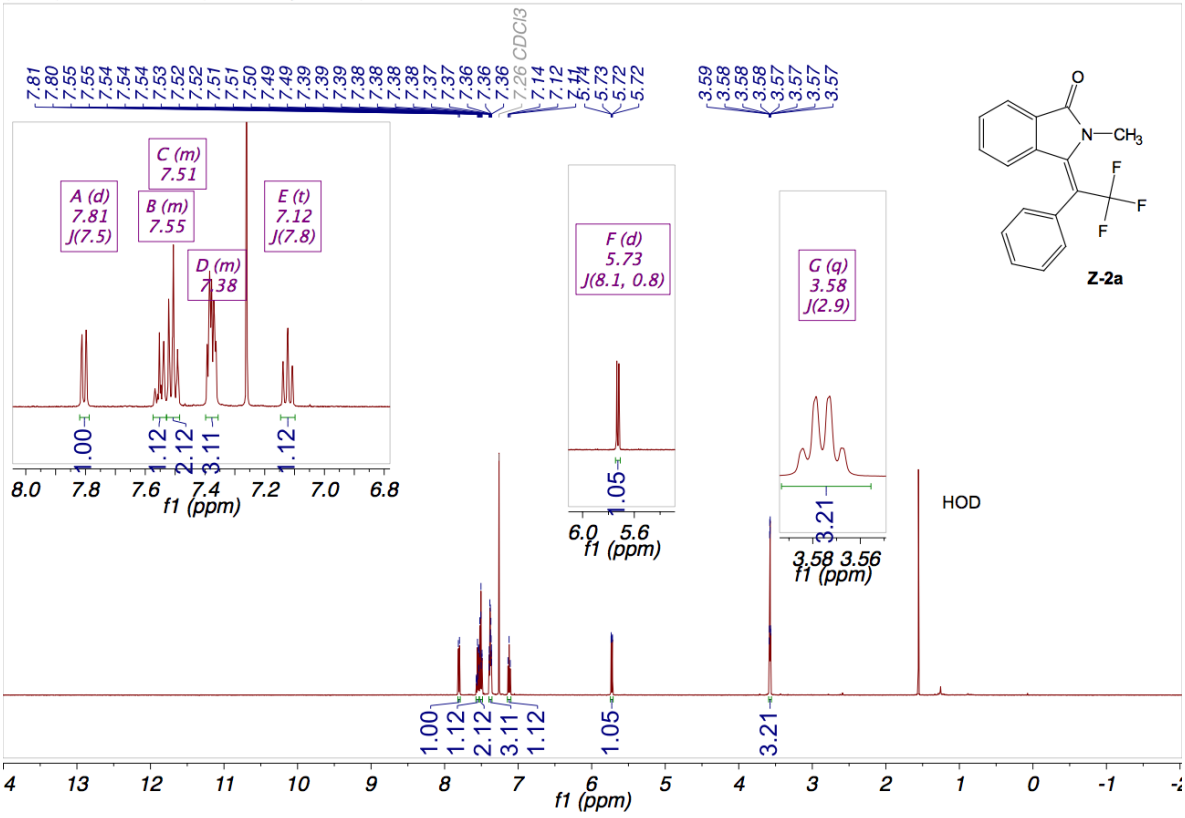
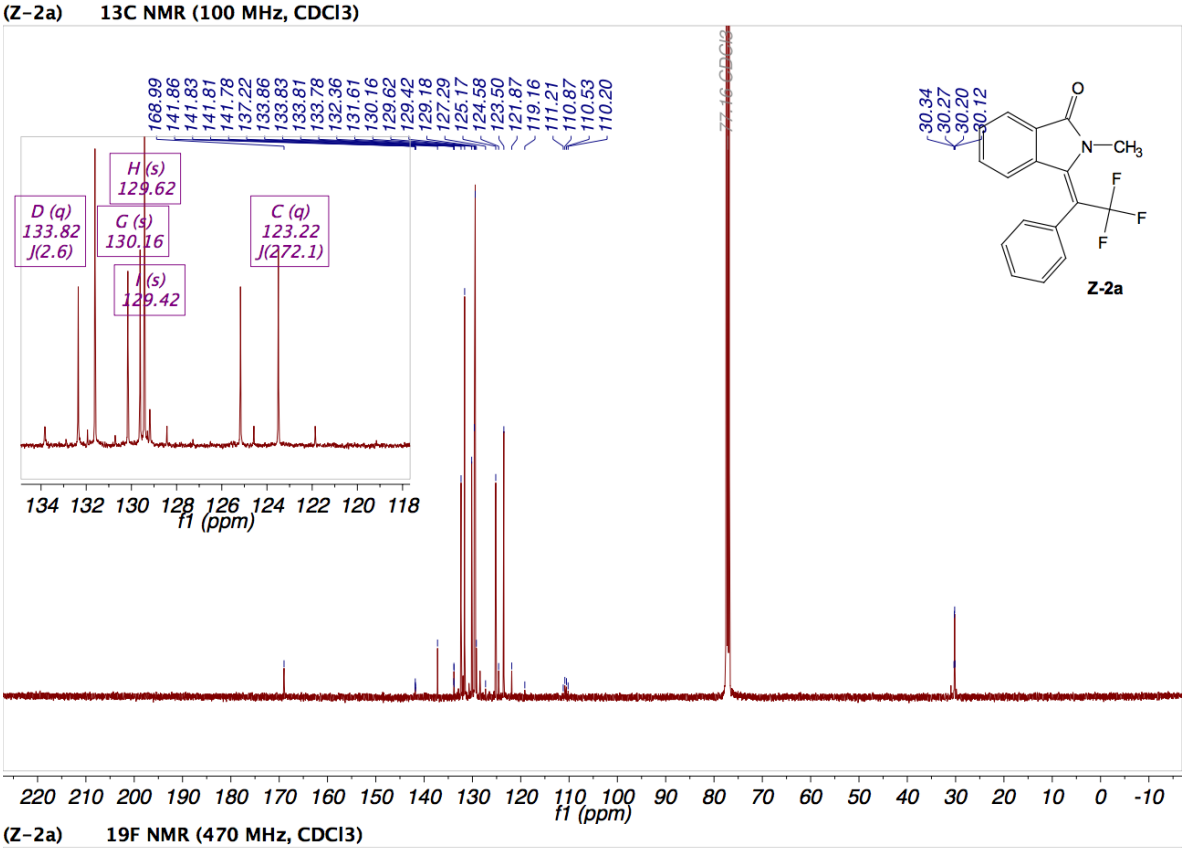
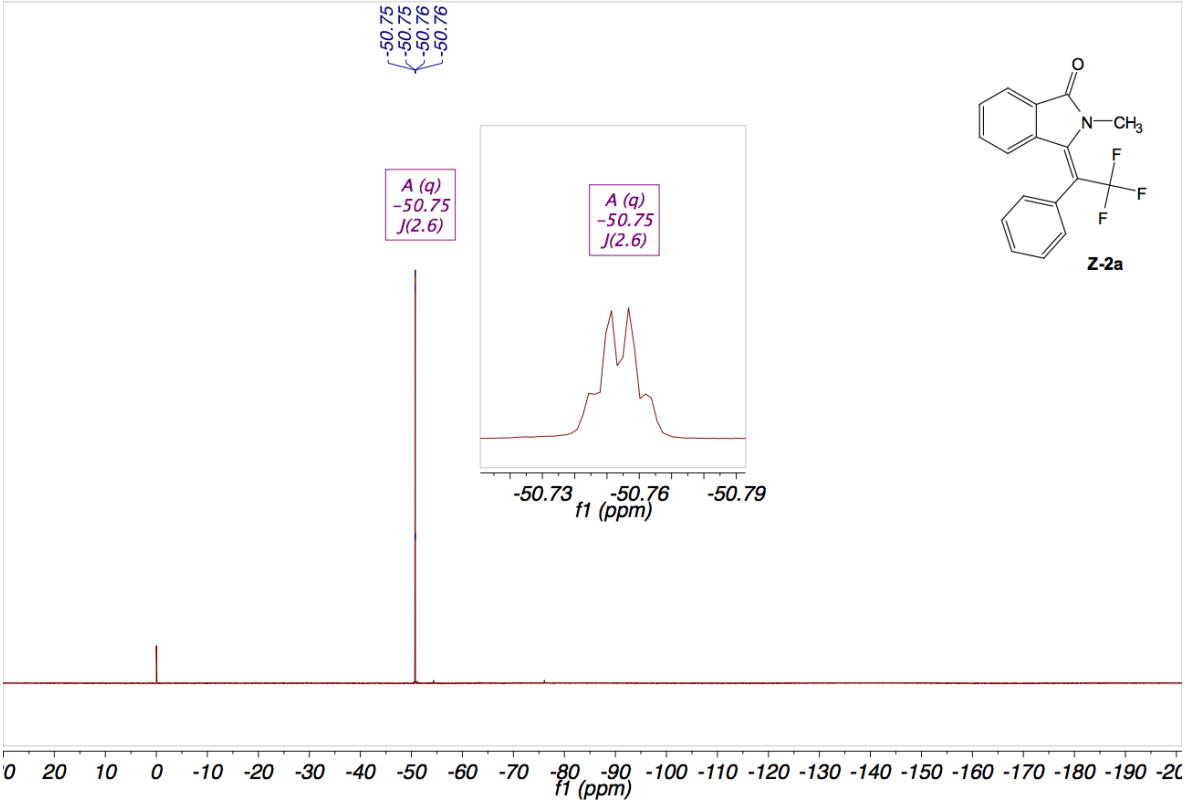


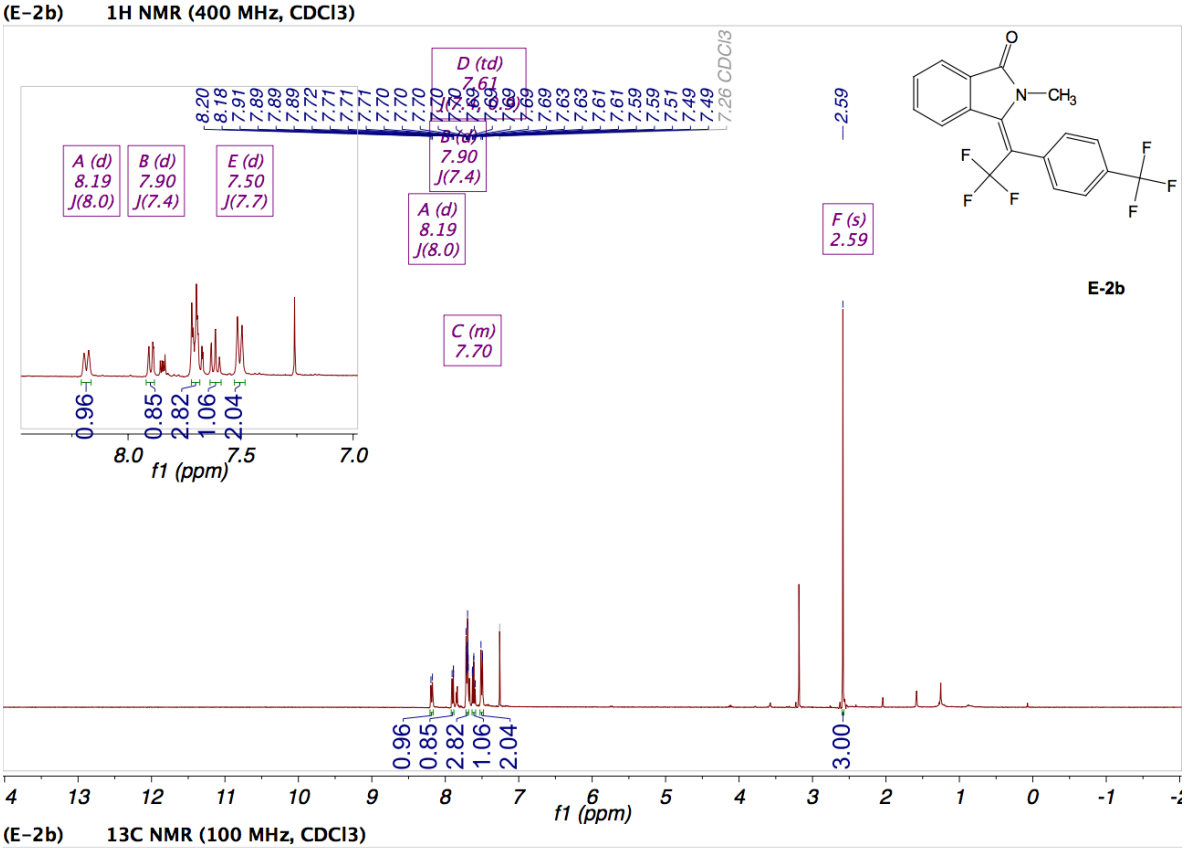
(Z-2a) 13C NMR (100 MHz, CDCl3)



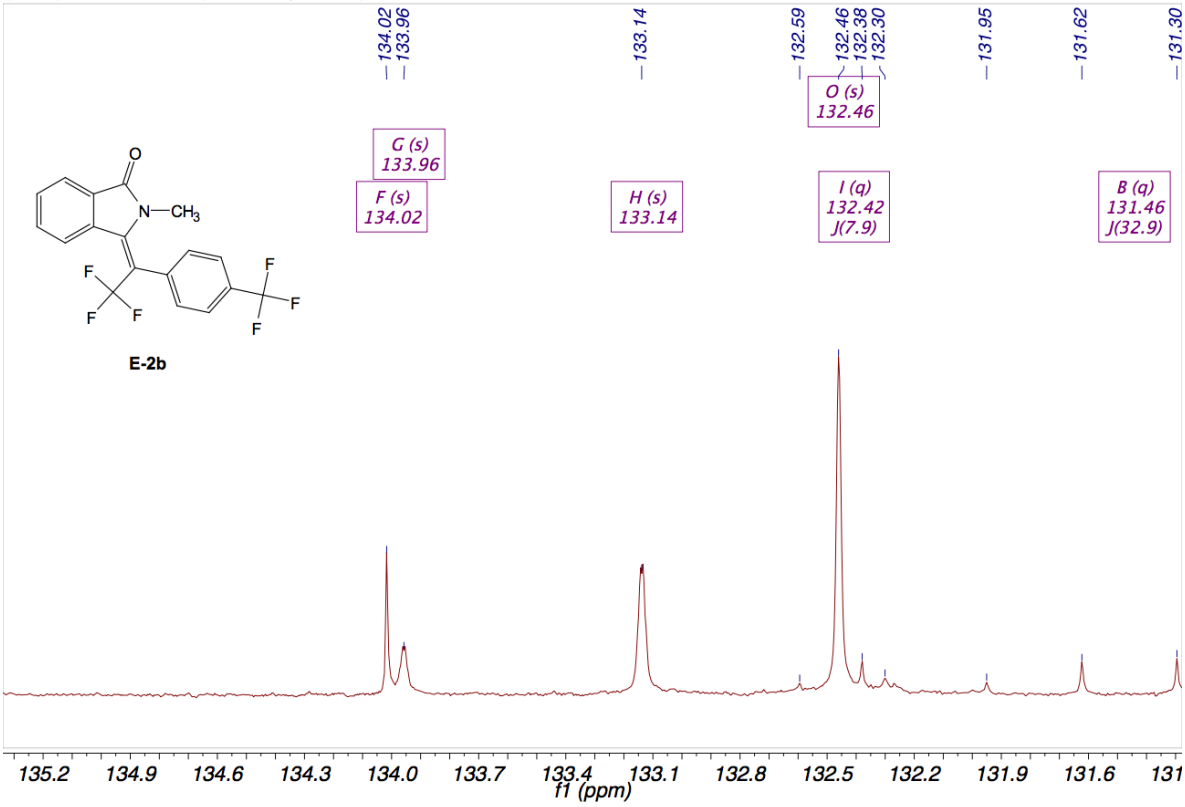
(Z-2a) 19F NMR (470 MHz, CDCl3)



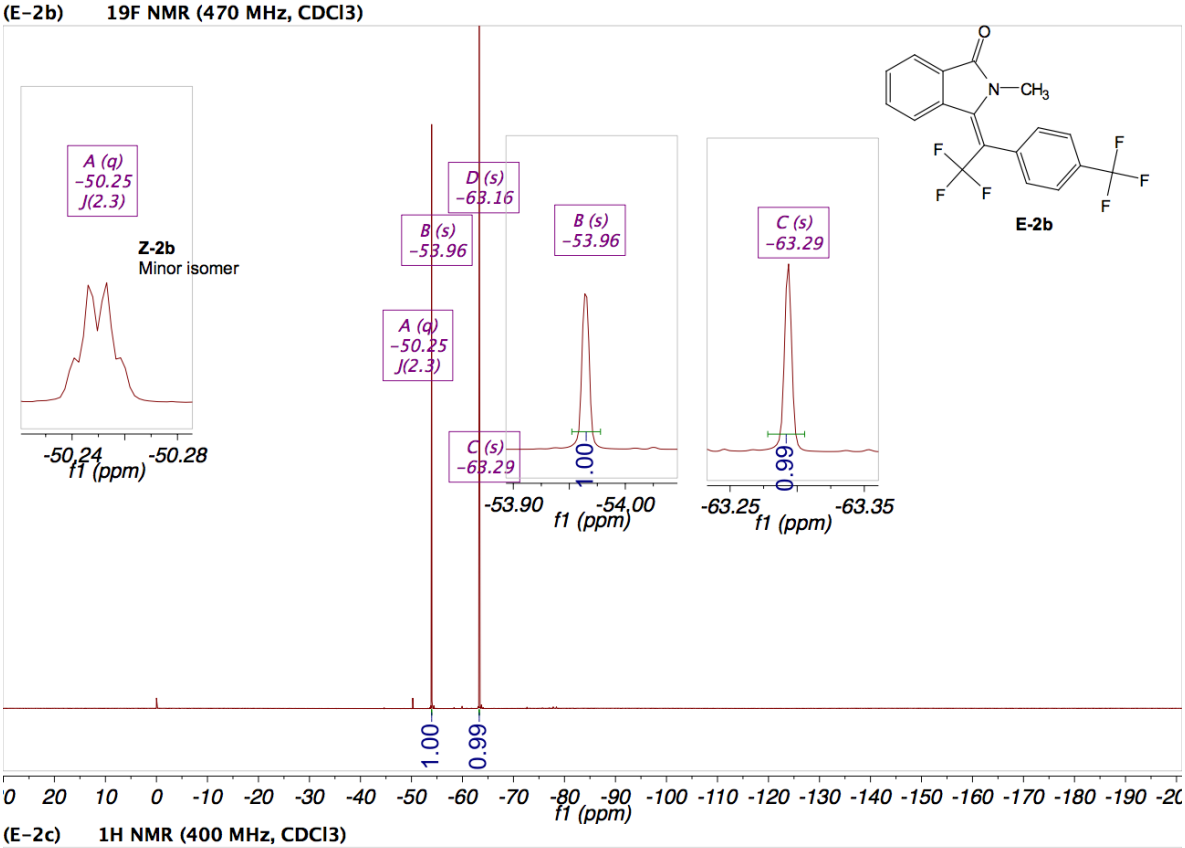
(E-2b) 1H NMR (400 MHz, CDCl3)



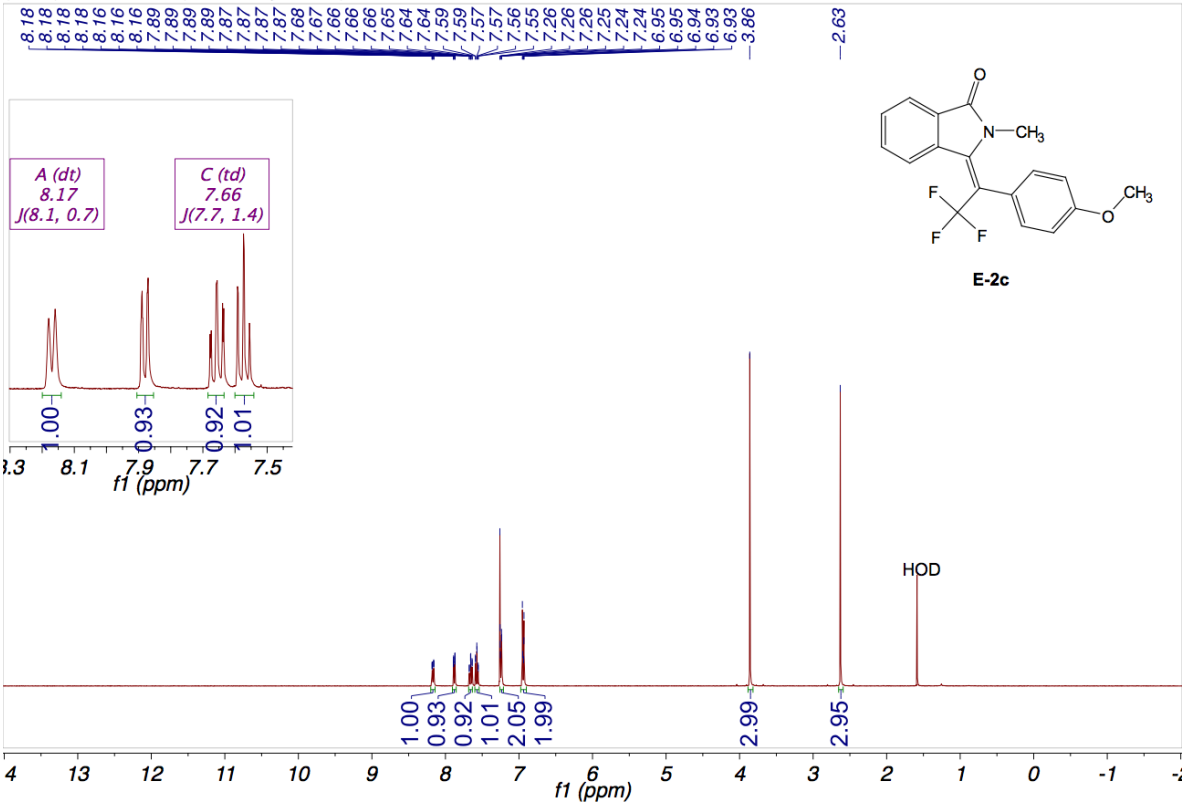
(E-2b) 13C NMR (100 MHz, CDCl3)



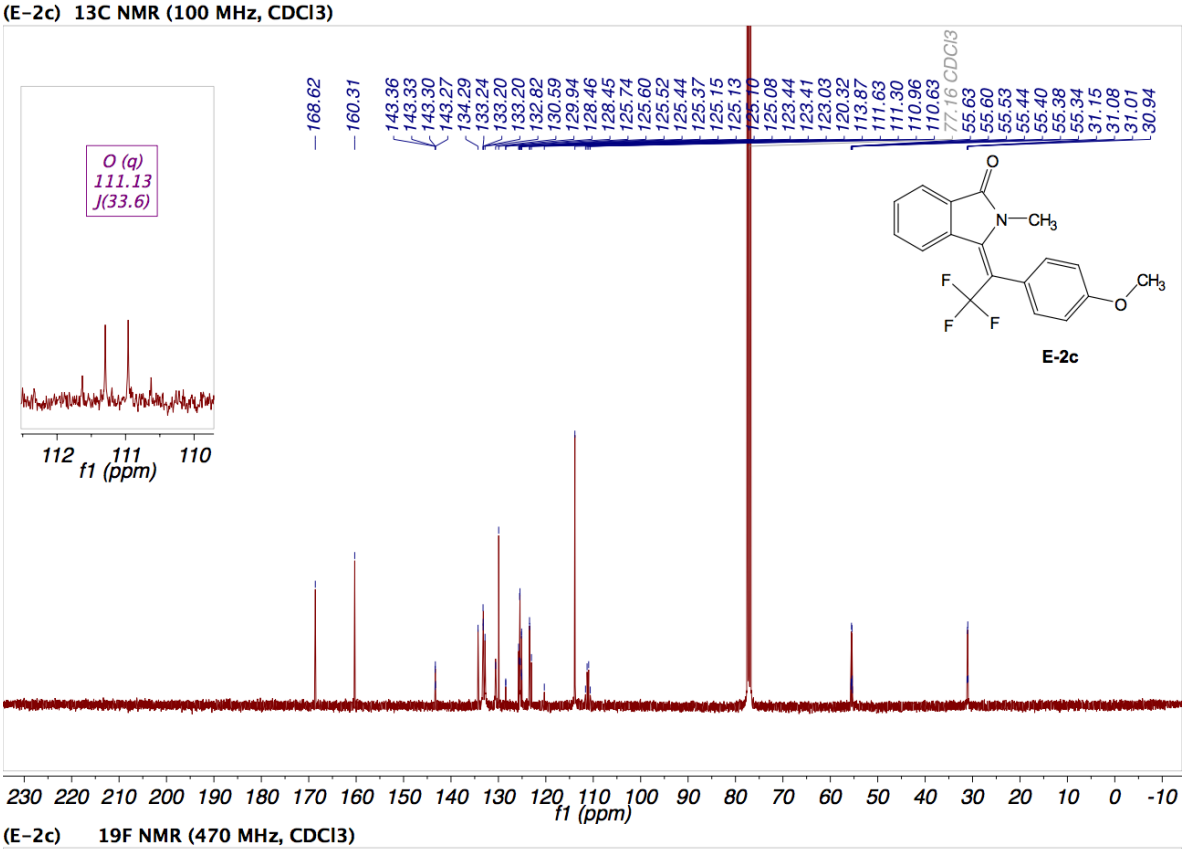
(E-2b) 19F NMR (470 MHz, CDCl3)



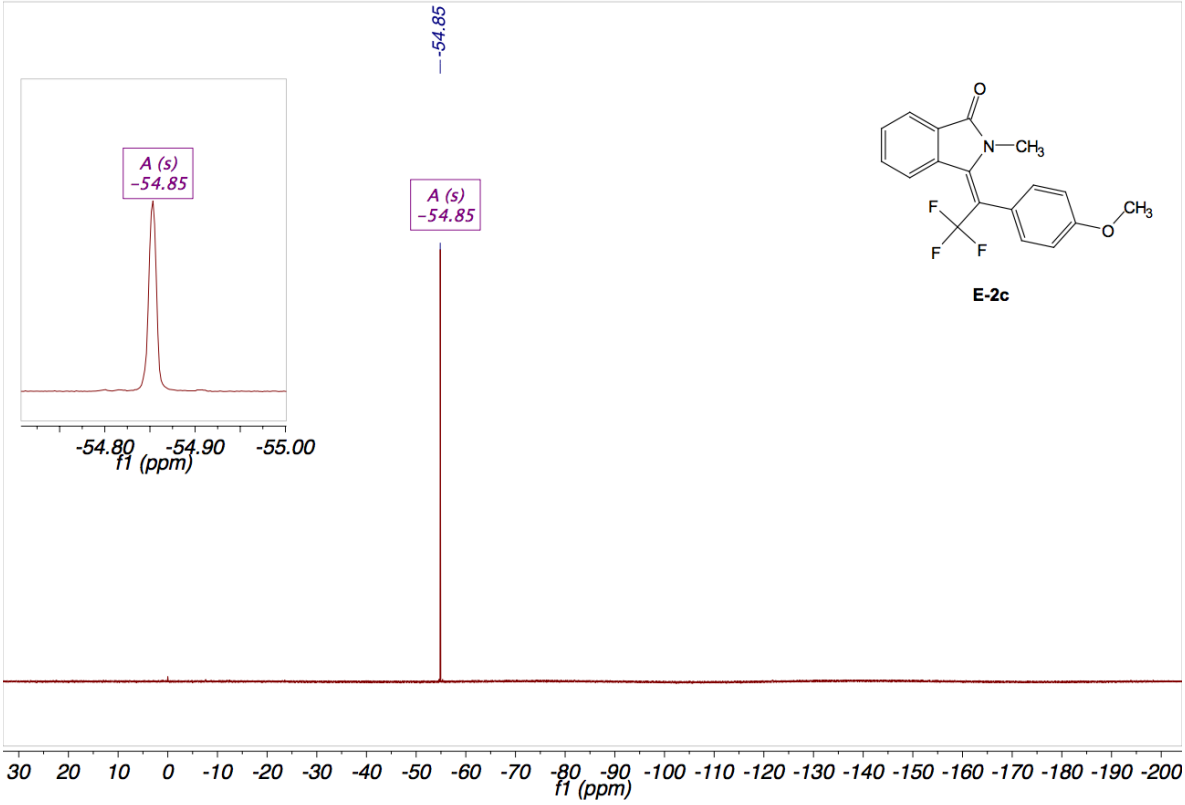
(E-2c) 1H NMR (400 MHz, CDCl3)



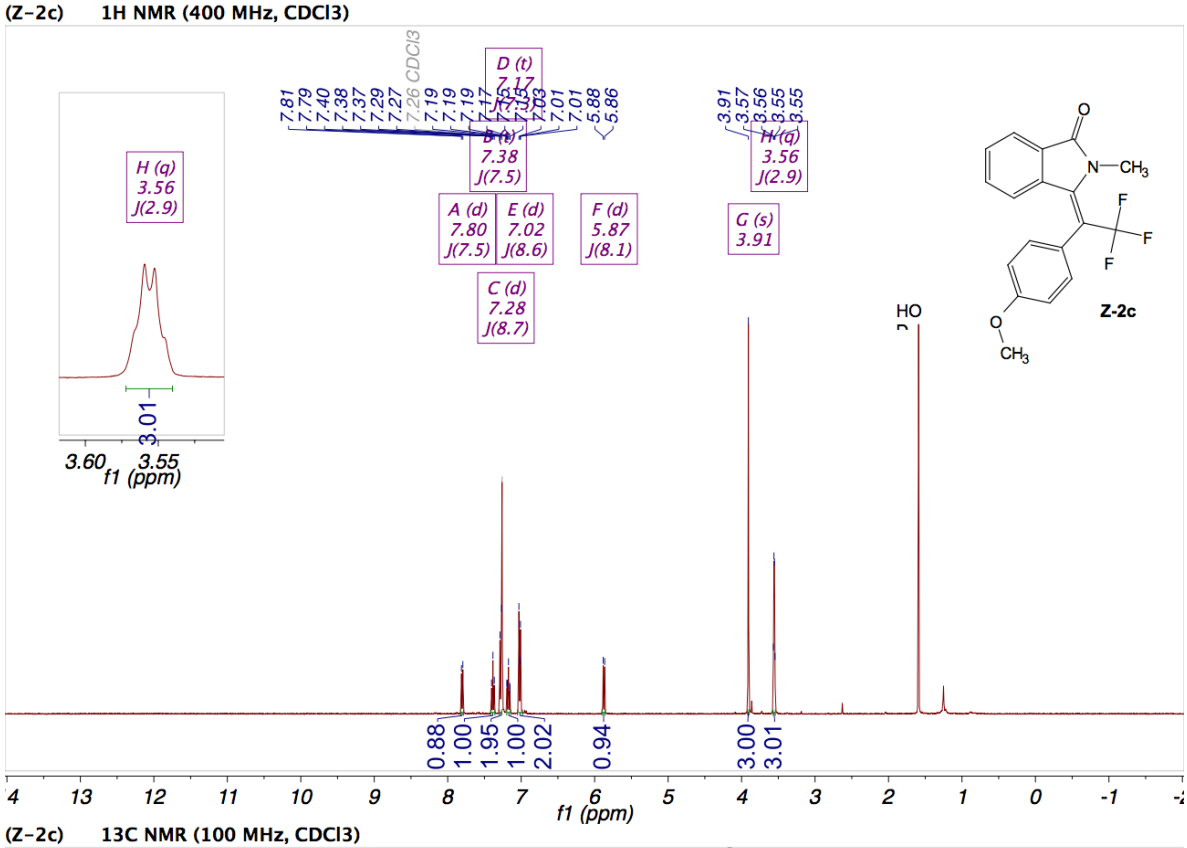
(E-2c) 13C NMR (100 MHz, CDCl3)



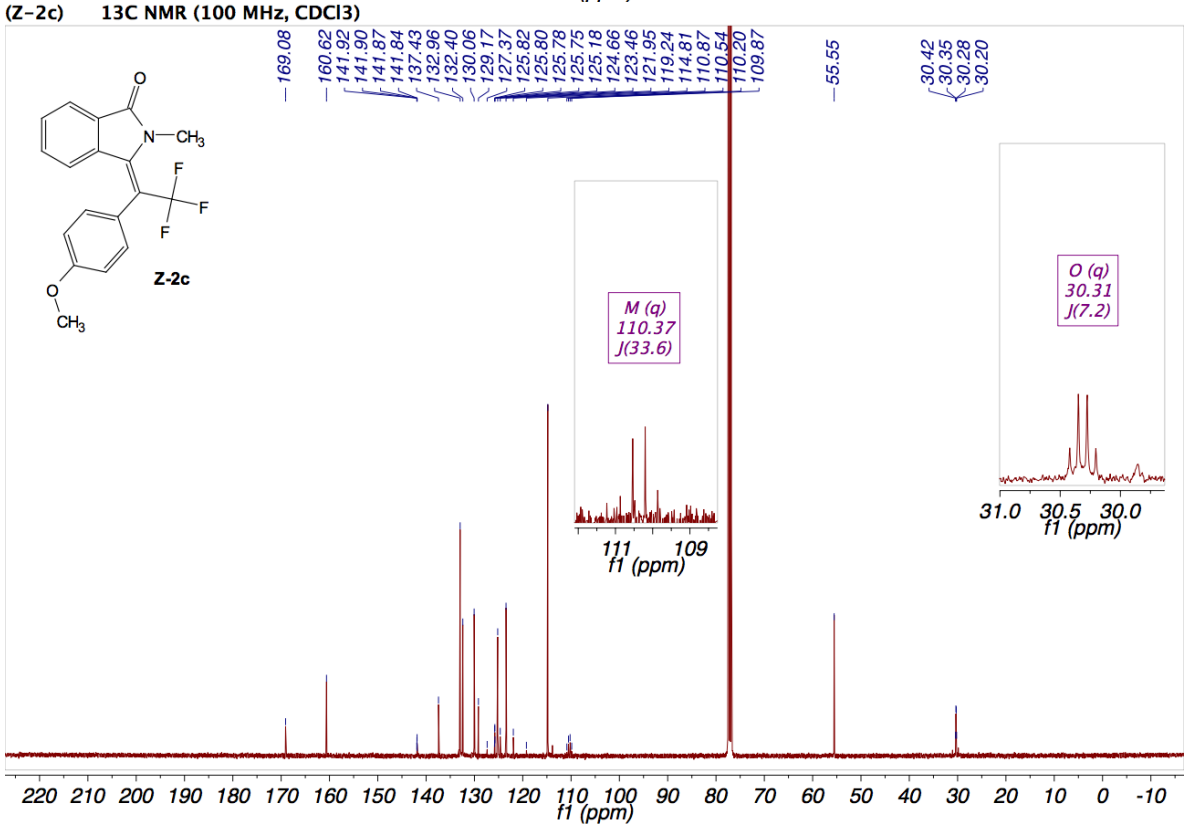
(E-2c) 19F NMR (470 MHz, CDCl3)



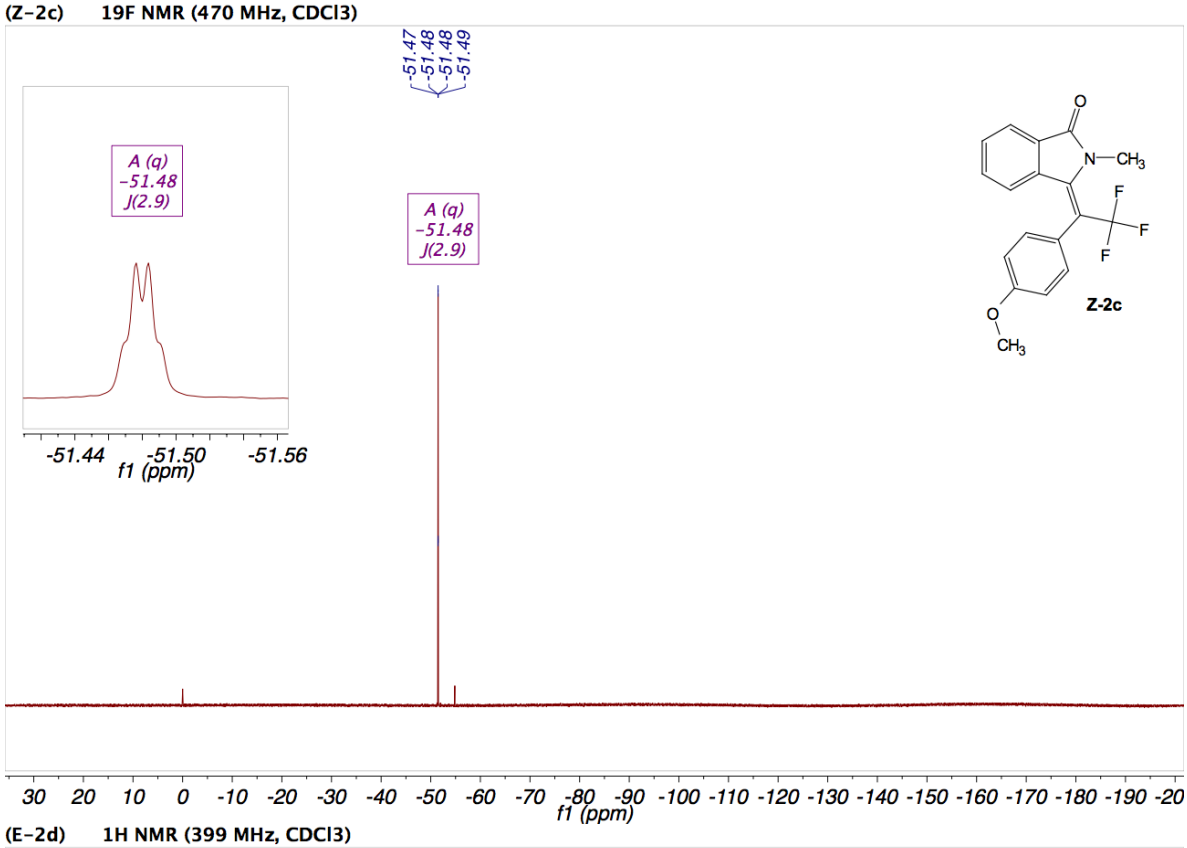
(Z-2c) 1H NMR (400 MHz, CDCl3)



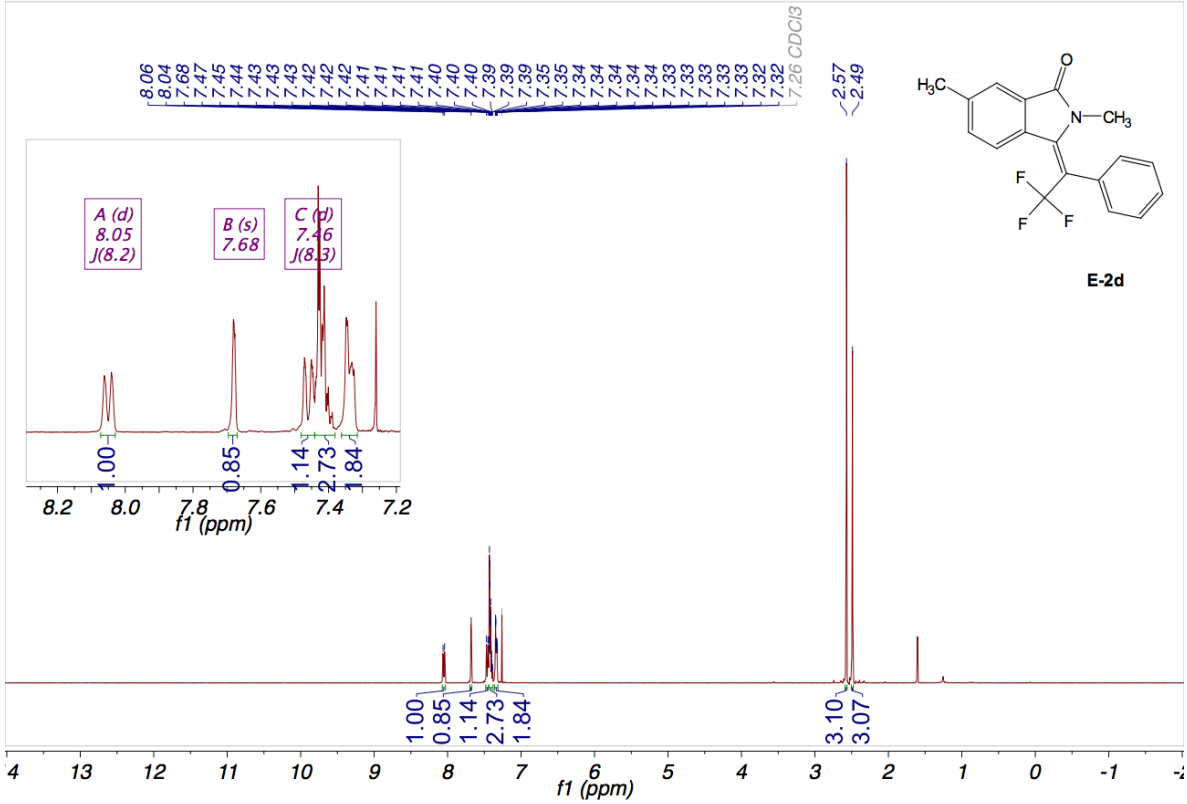
(Z-2c) 13C NMR (100 MHz, CDCl3)



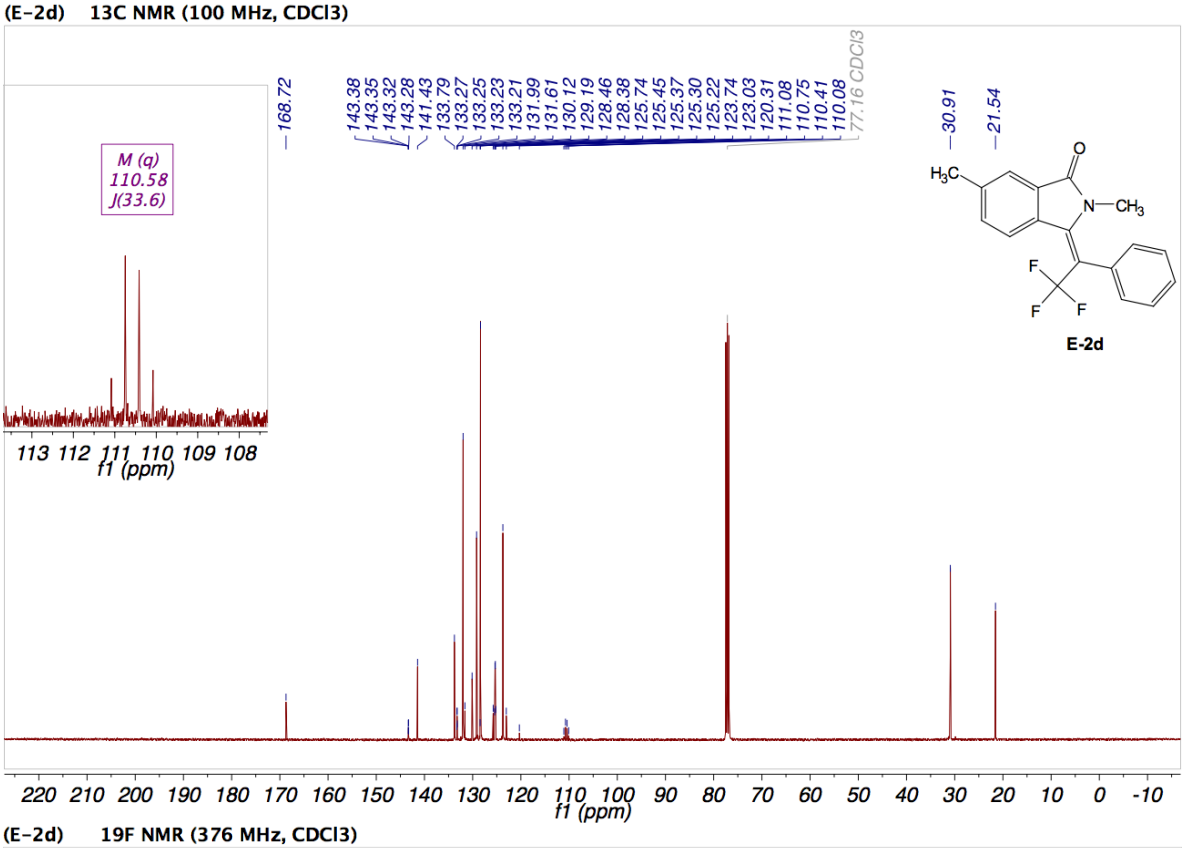
(Z-2c) 19F NMR (470 MHz, CDCl3)



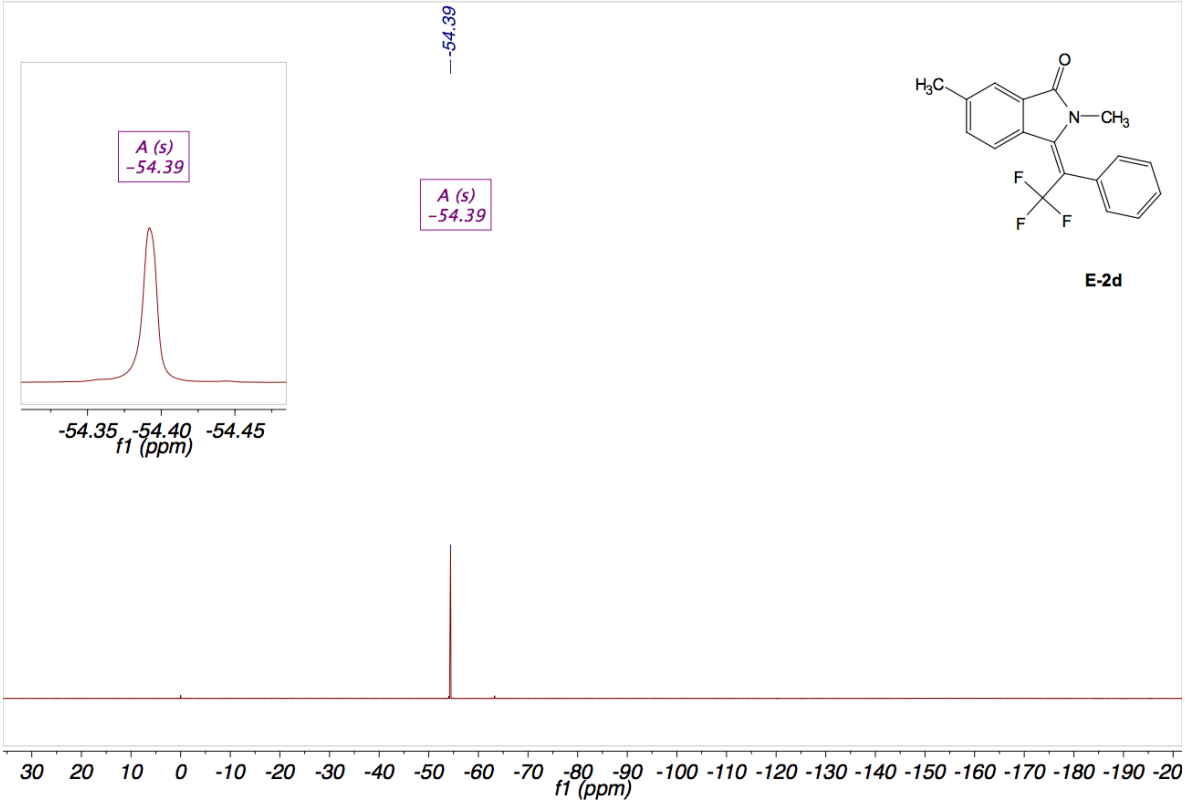
(E-2d) 1H NMR (399 MHz, CDCl3)



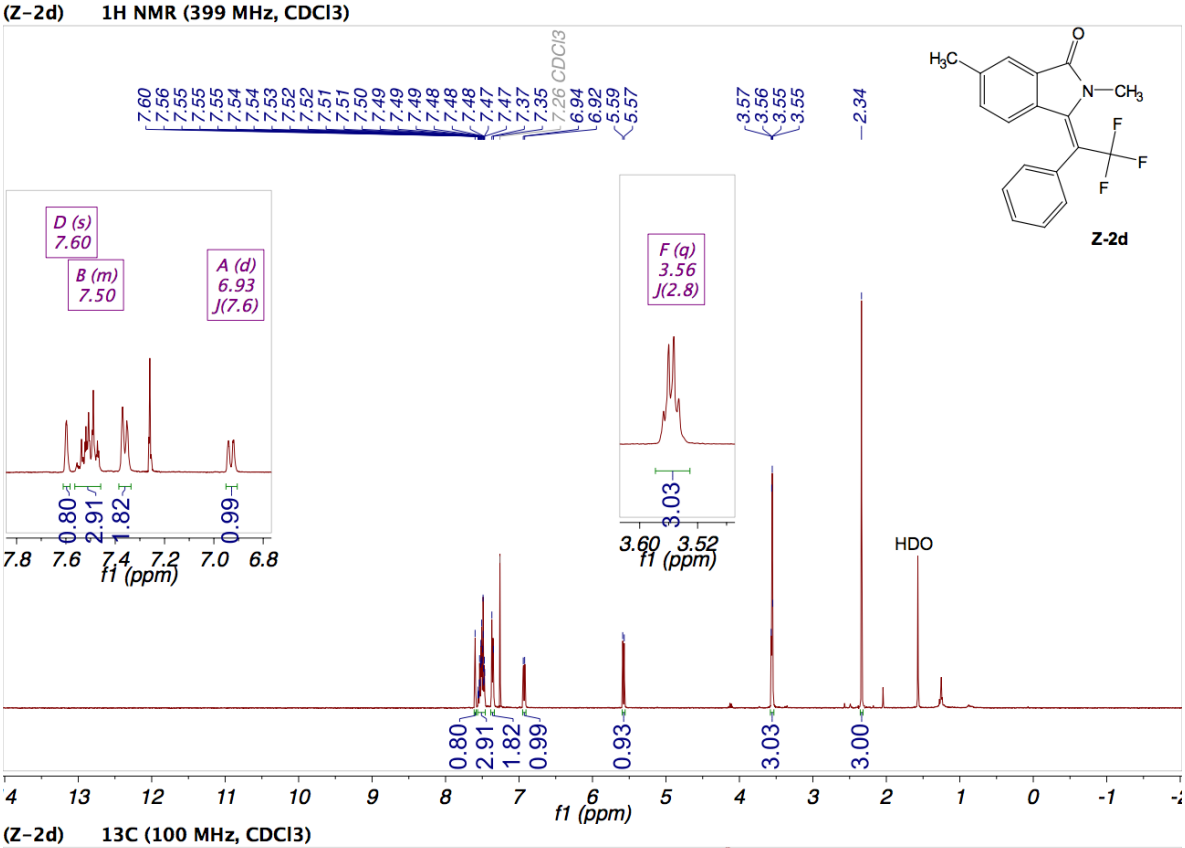
(E-2d) 13C NMR (100 MHz, CDCl3)



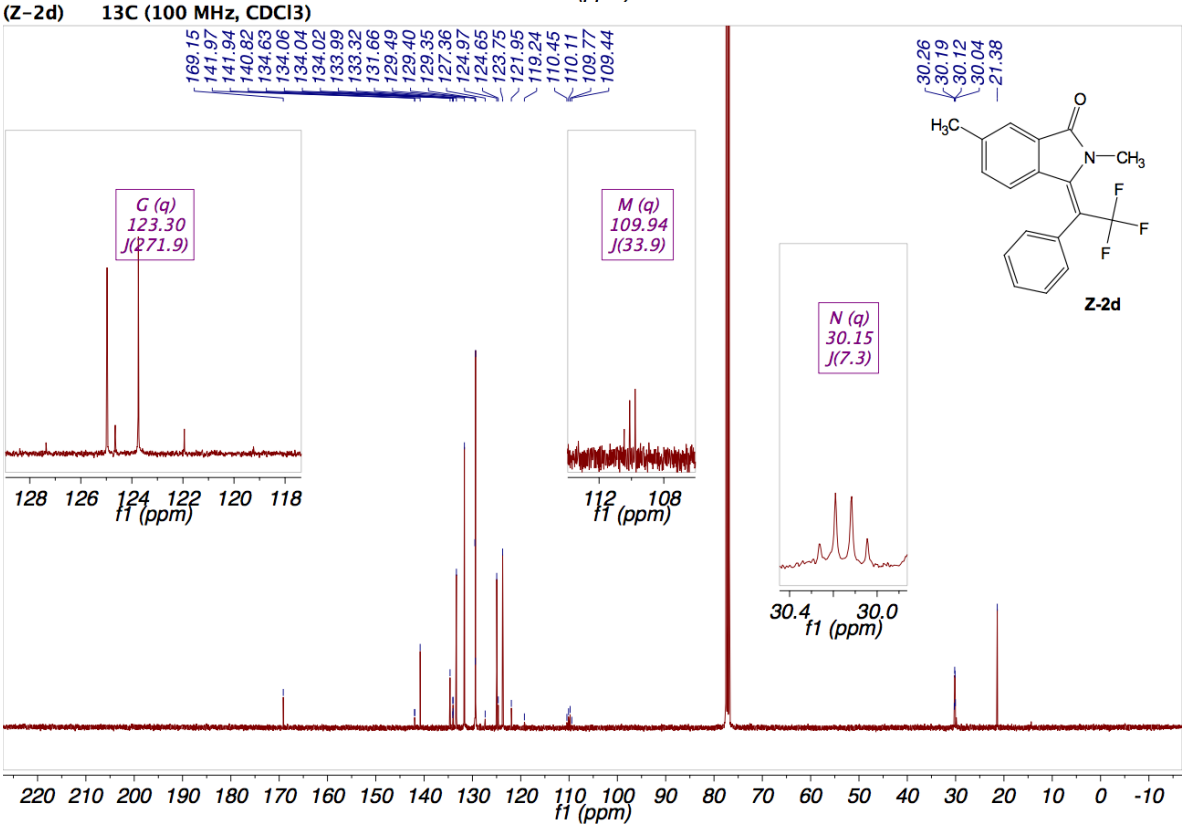
(E-2d) 19F NMR (376 MHz, CDCl3)



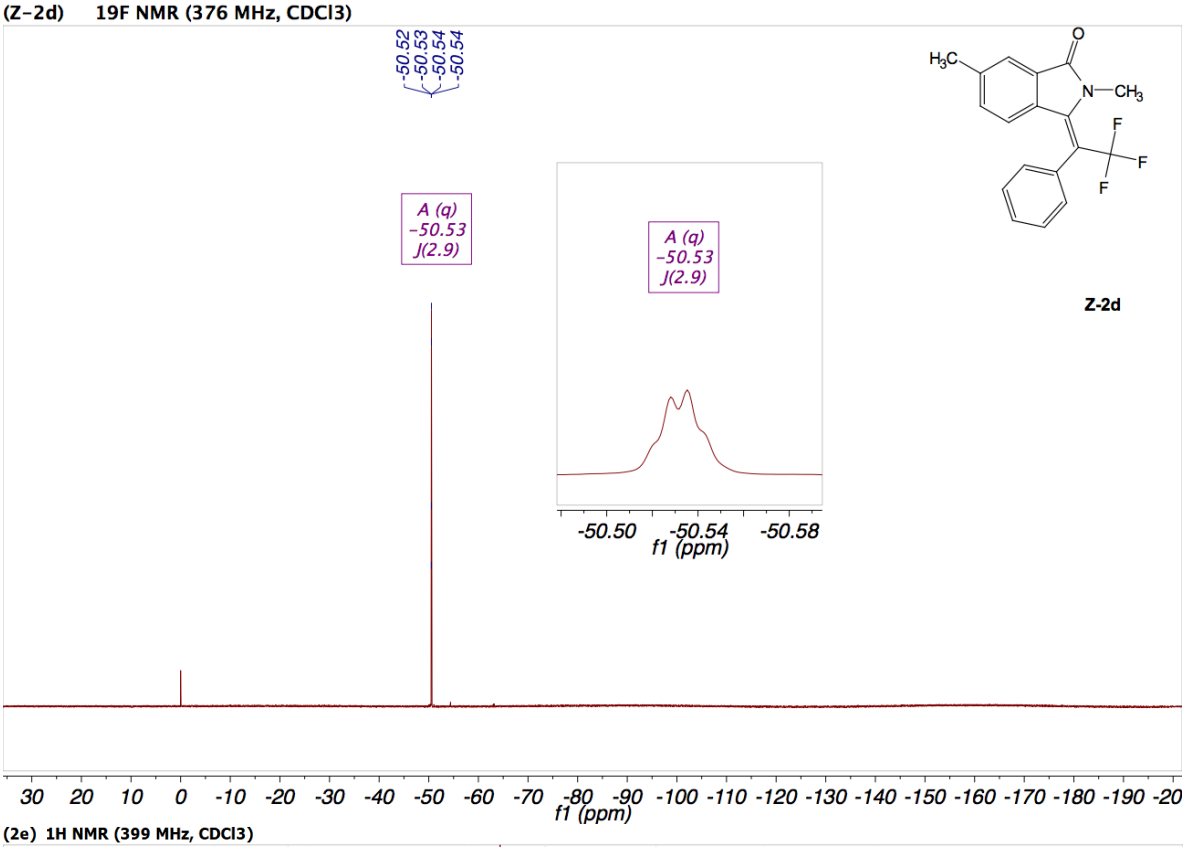
(Z-2d) 1H NMR (399 MHz, CDCl3)



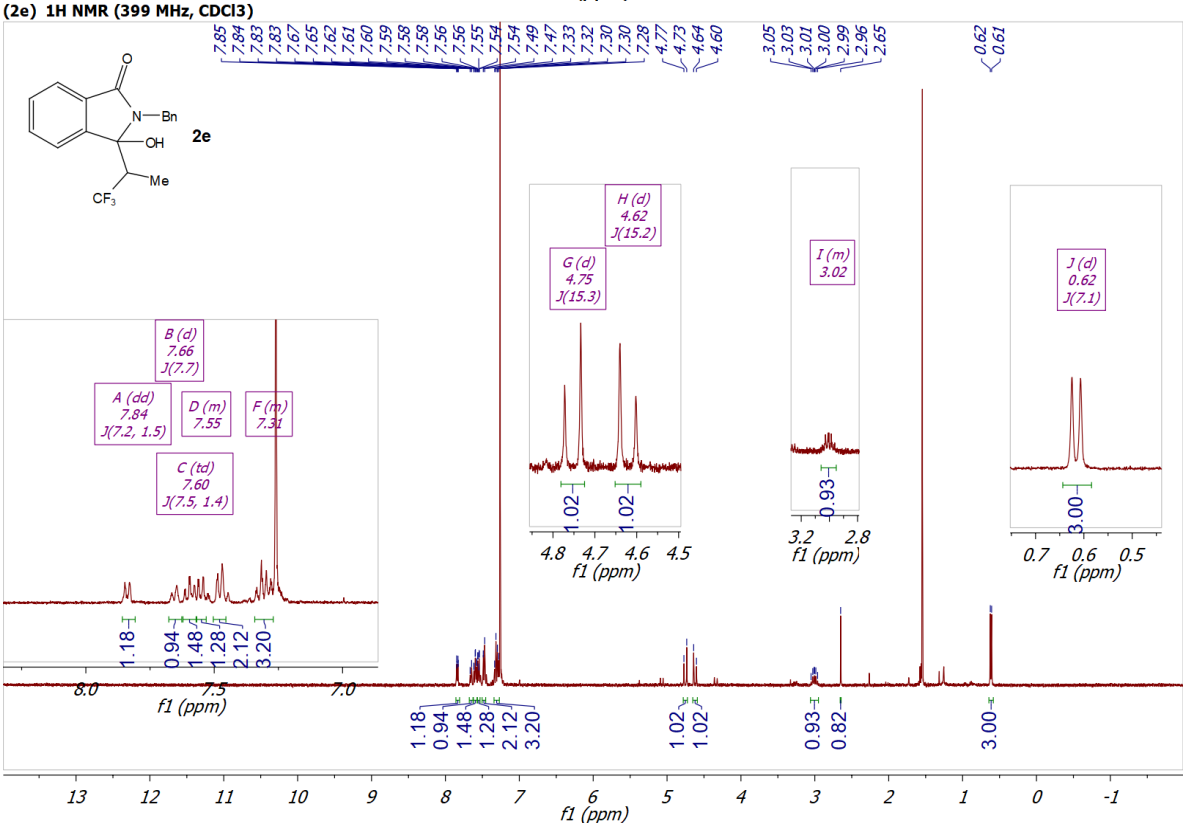
(Z-2d) 13C (100 MHz, CDCl3)



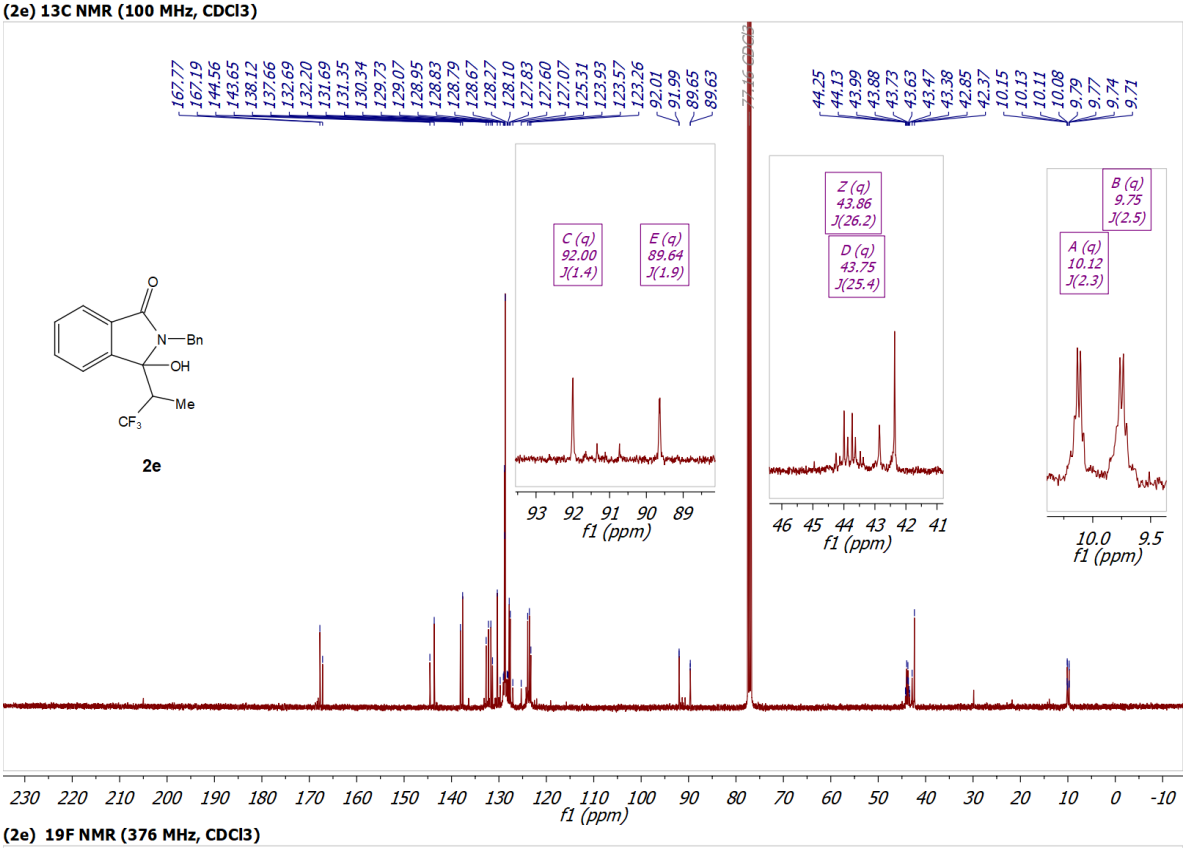
(Z–2d) 19F NMR (376 MHz, CDCl3)



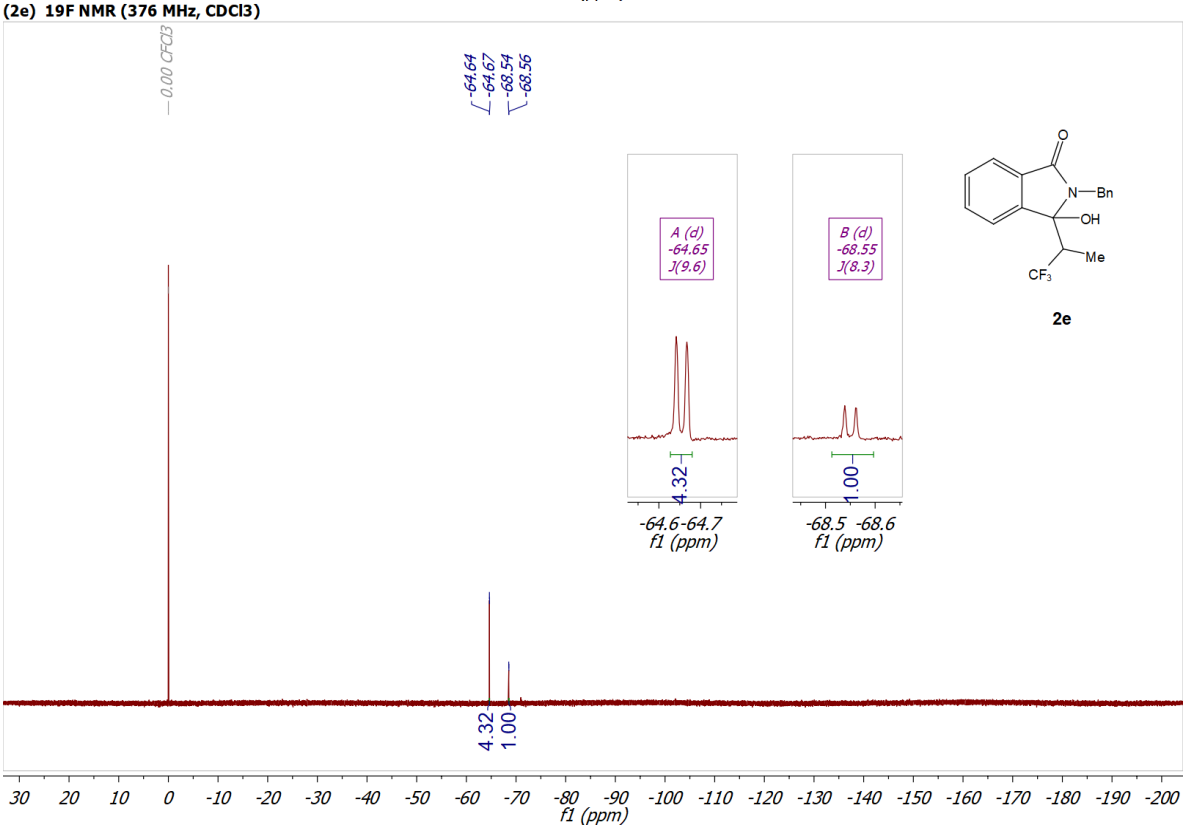
(2e) 1H NMR (399 MHz, CDCl3)



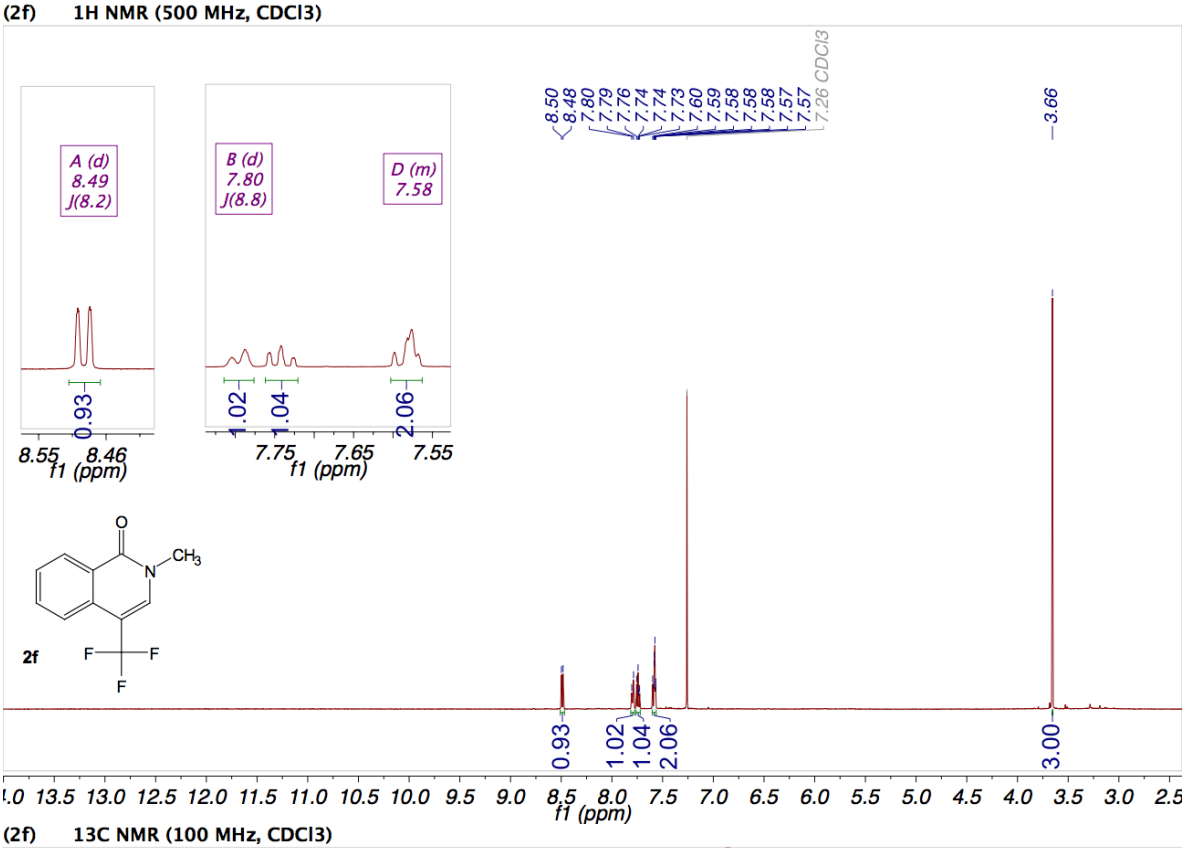
(2e) 13C NMR (100 MHz, CDCl3)



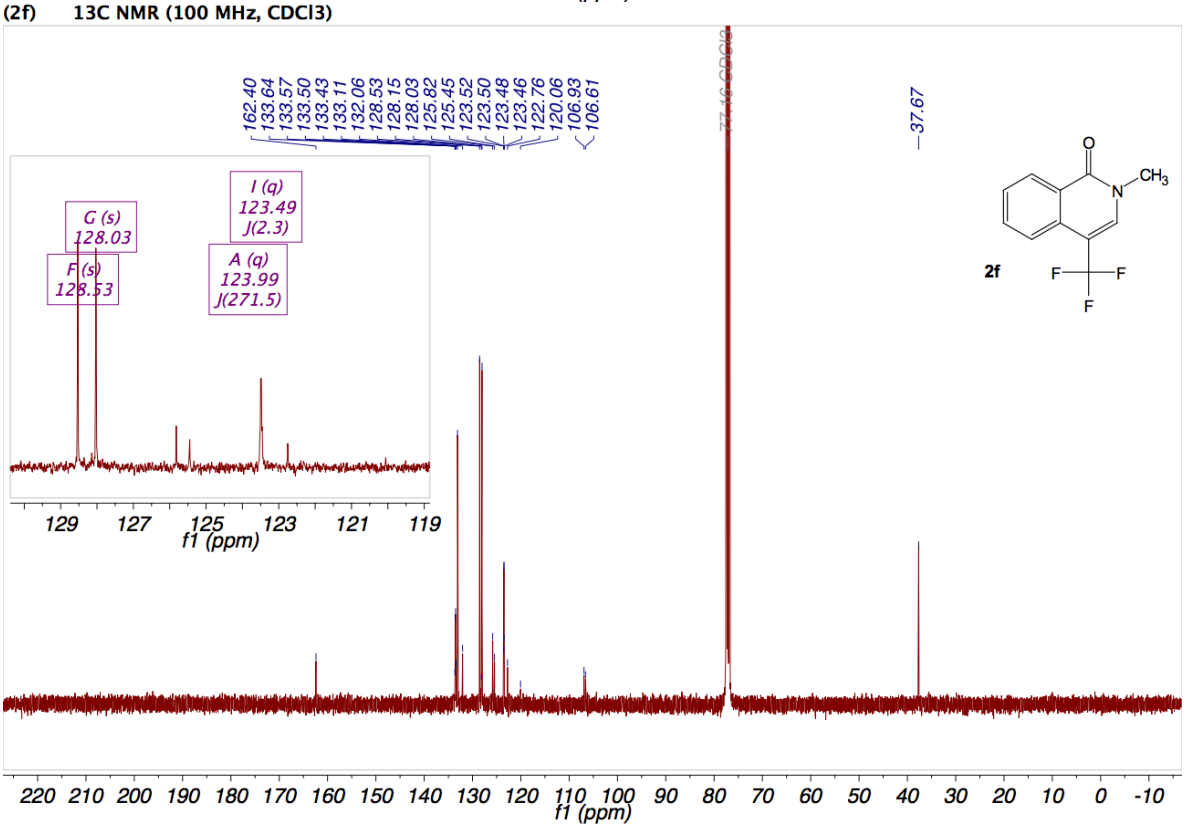
(2e) 19F NMR (376 MHz, CDCl3)



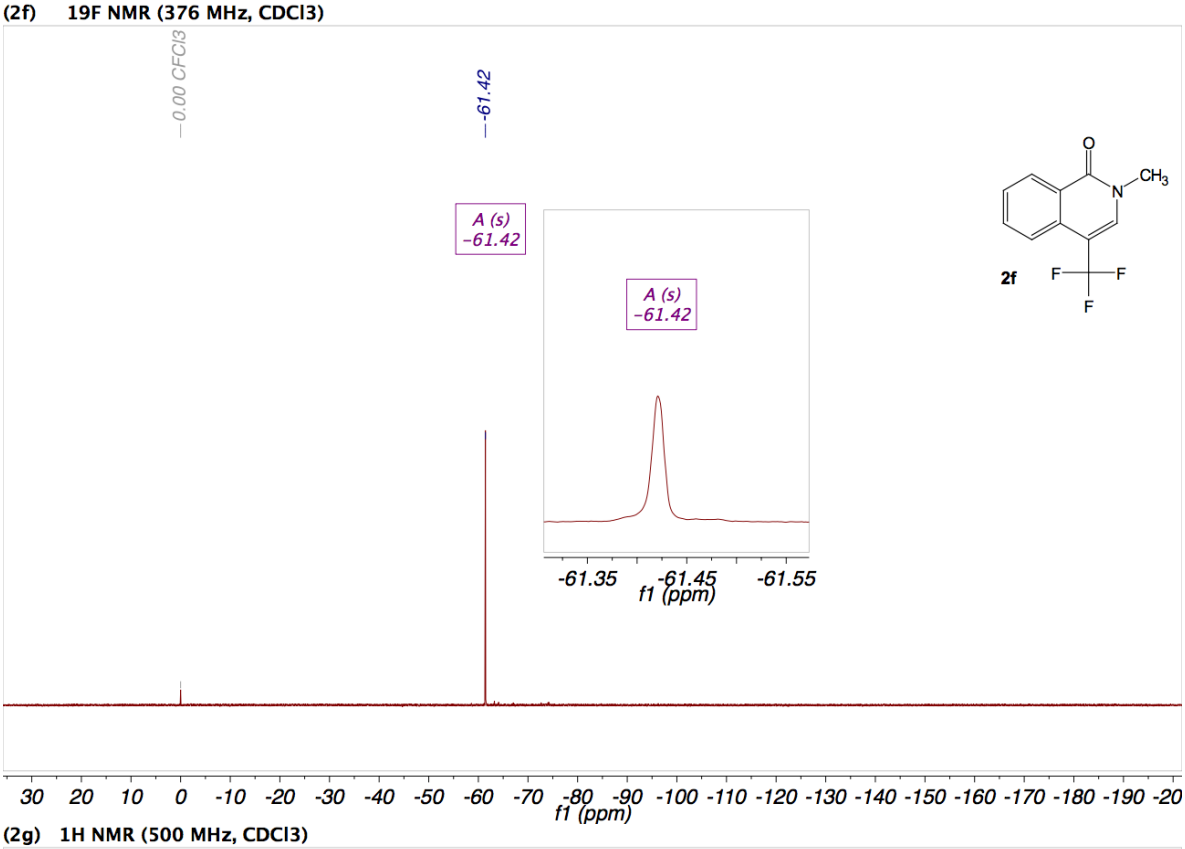
(2f) 1H NMR (500 MHz, CDCl3)



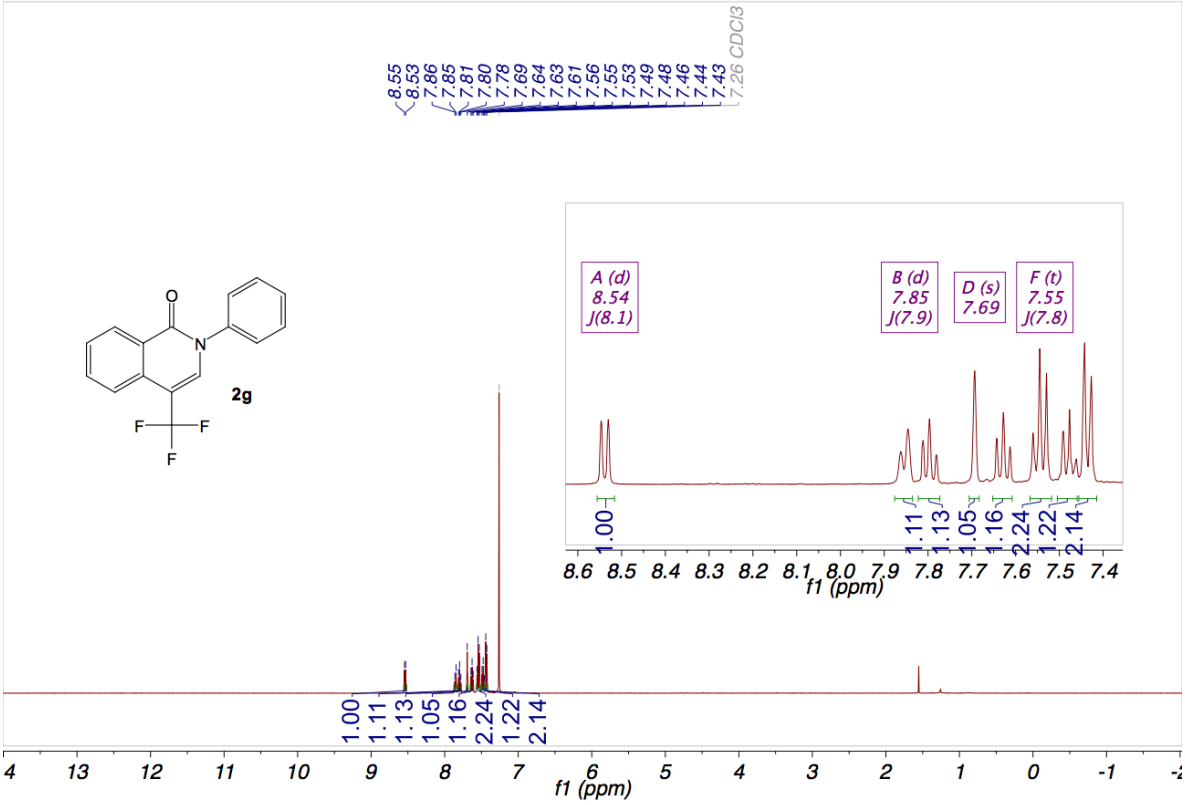
(2f) 13C NMR (100 MHz, CDCl3)



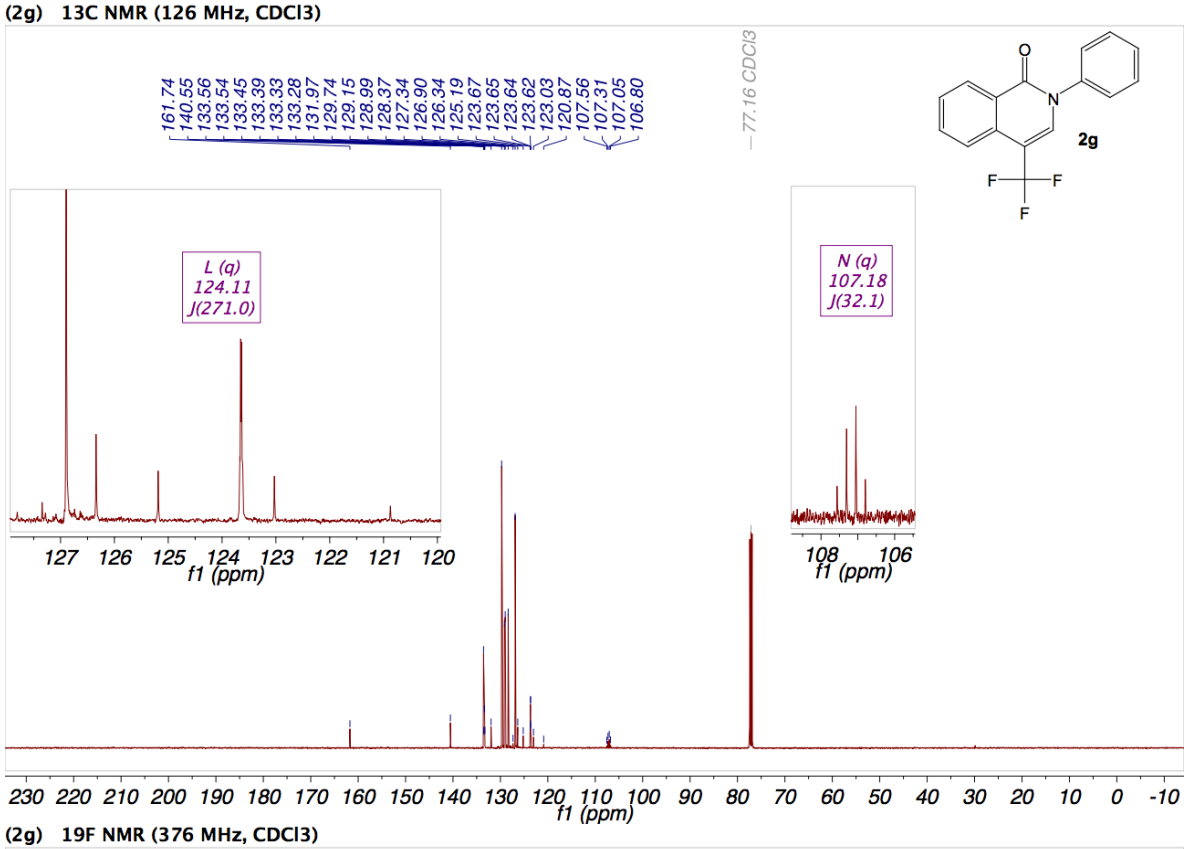
(2f) 19F NMR (376 MHz, CDCl3)



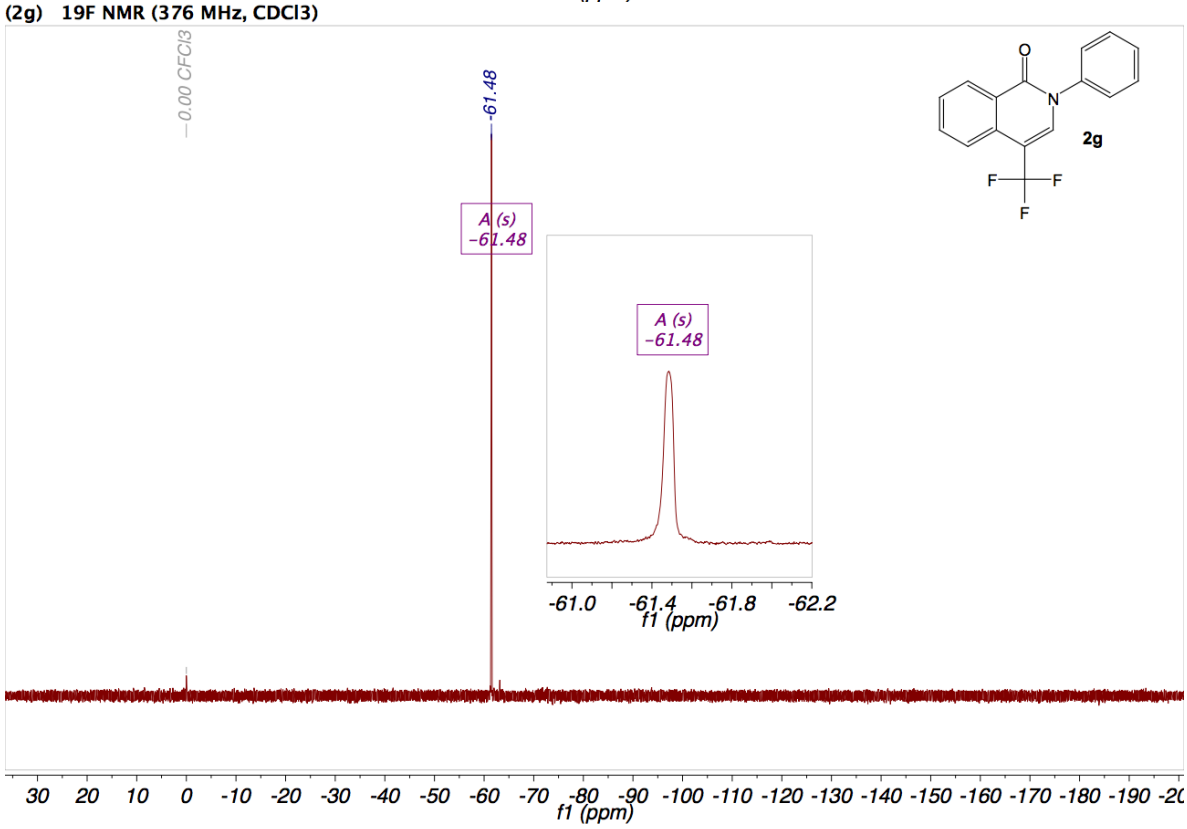
(2g) 1H NMR (500 MHz, CDCl3)



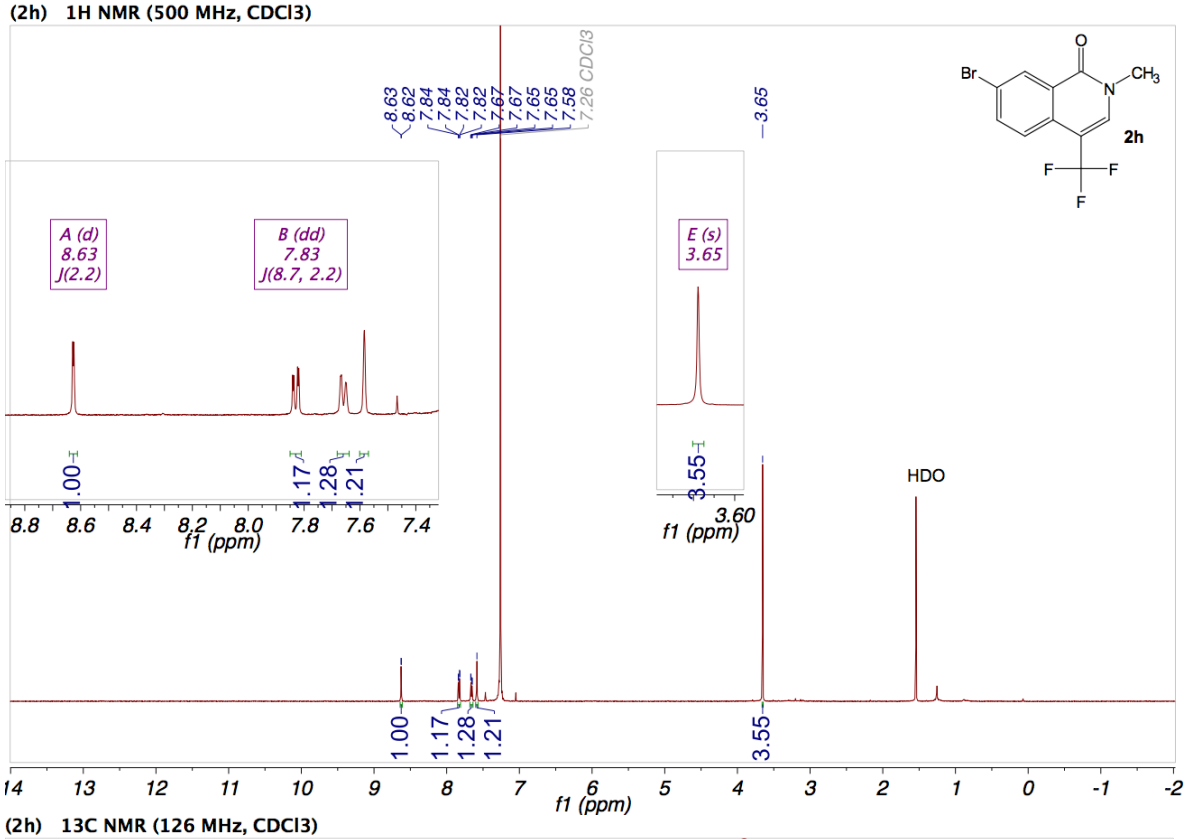
(2g) 13C NMR (126 MHz, CDCl3)



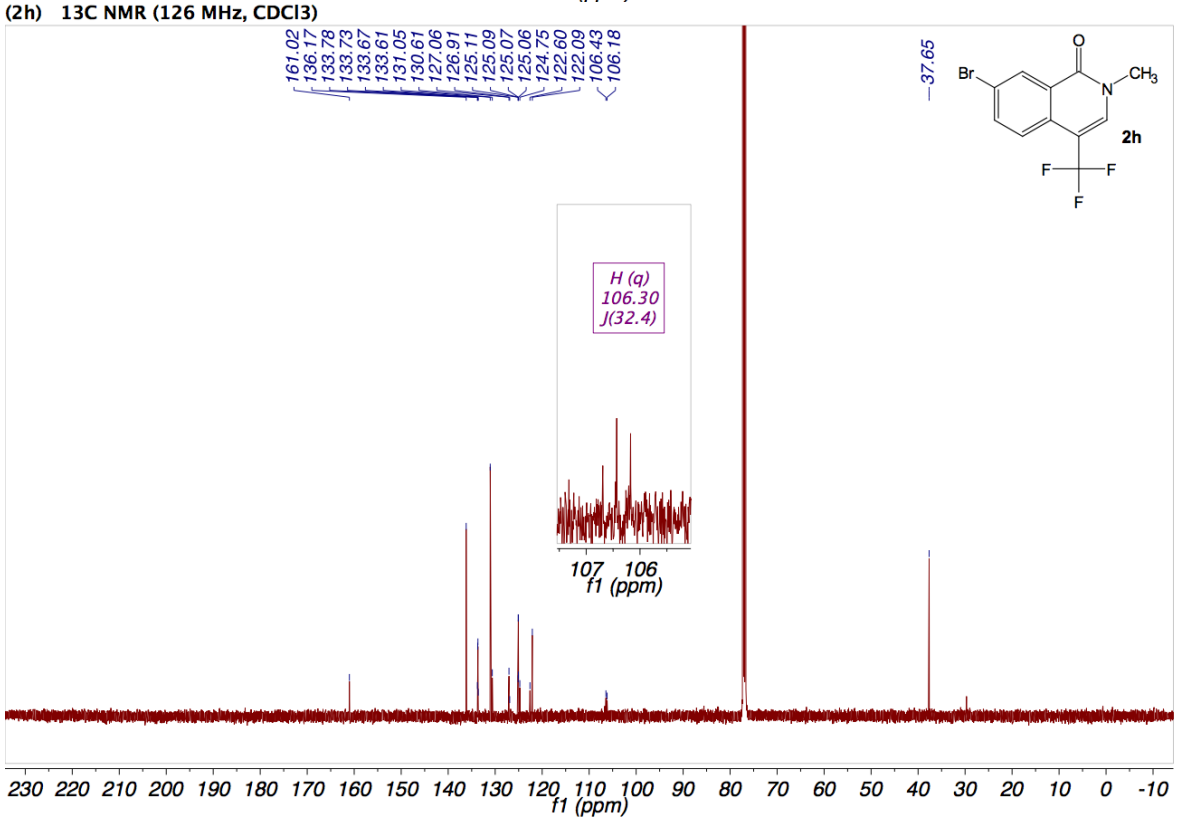
(2g) 19F NMR (376 MHz, CDCl3)



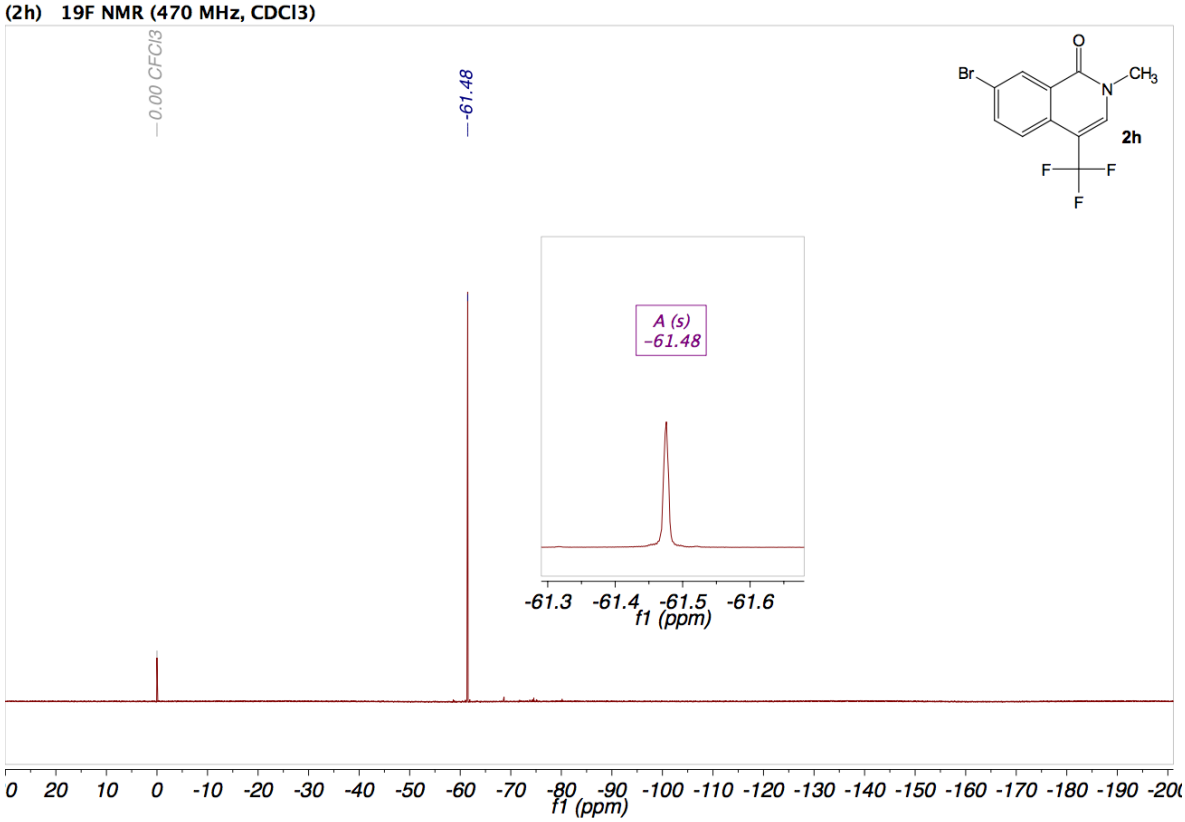
(2h) 1H NMR (500 MHz, CDCl3)



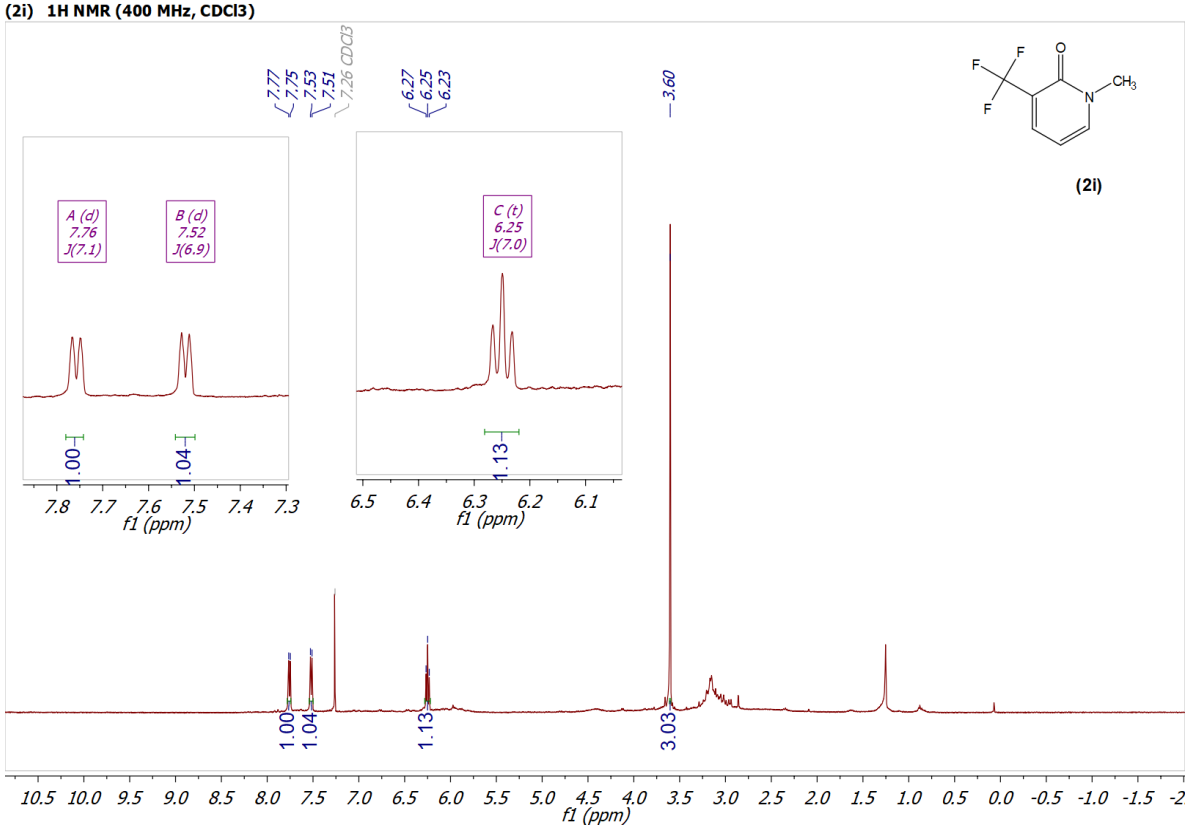
(2h) 13C NMR (126 MHz, CDCl3)



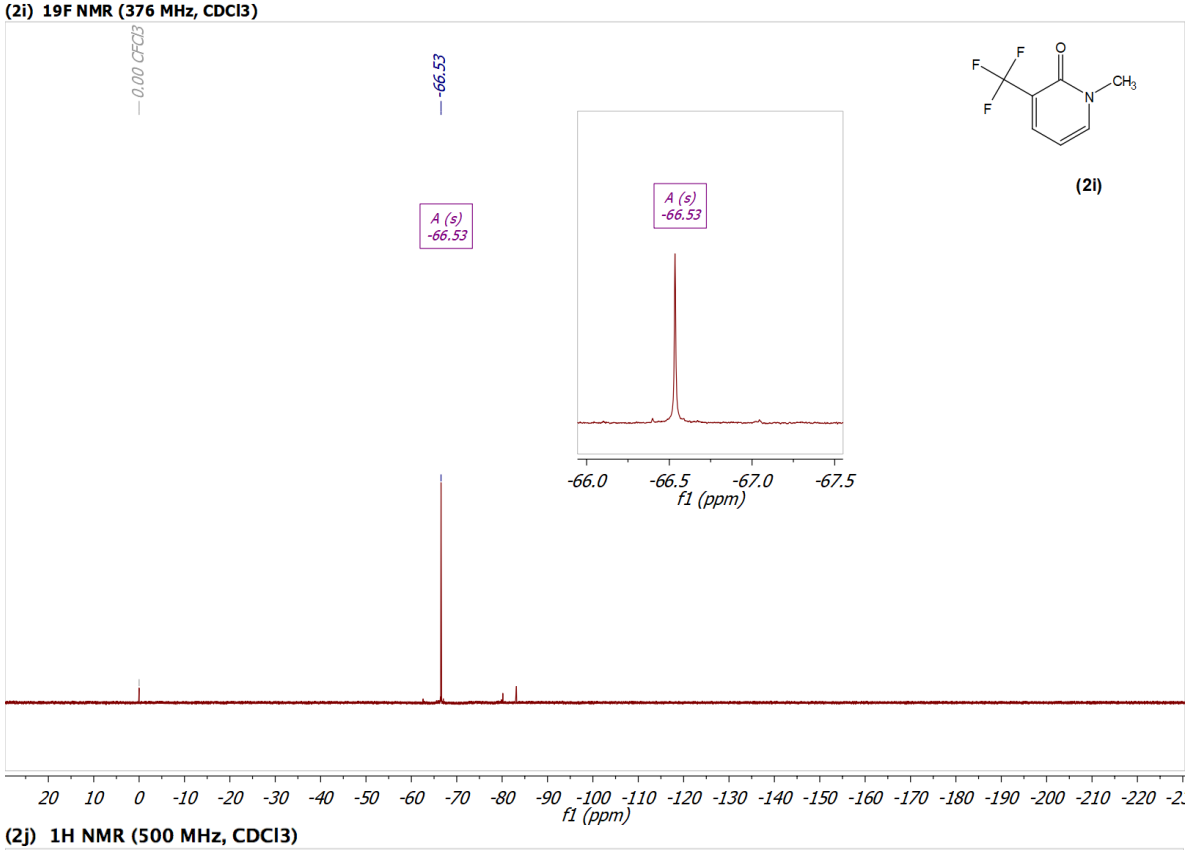
(2h) 19F NMR (470 MHz, CDCl3)



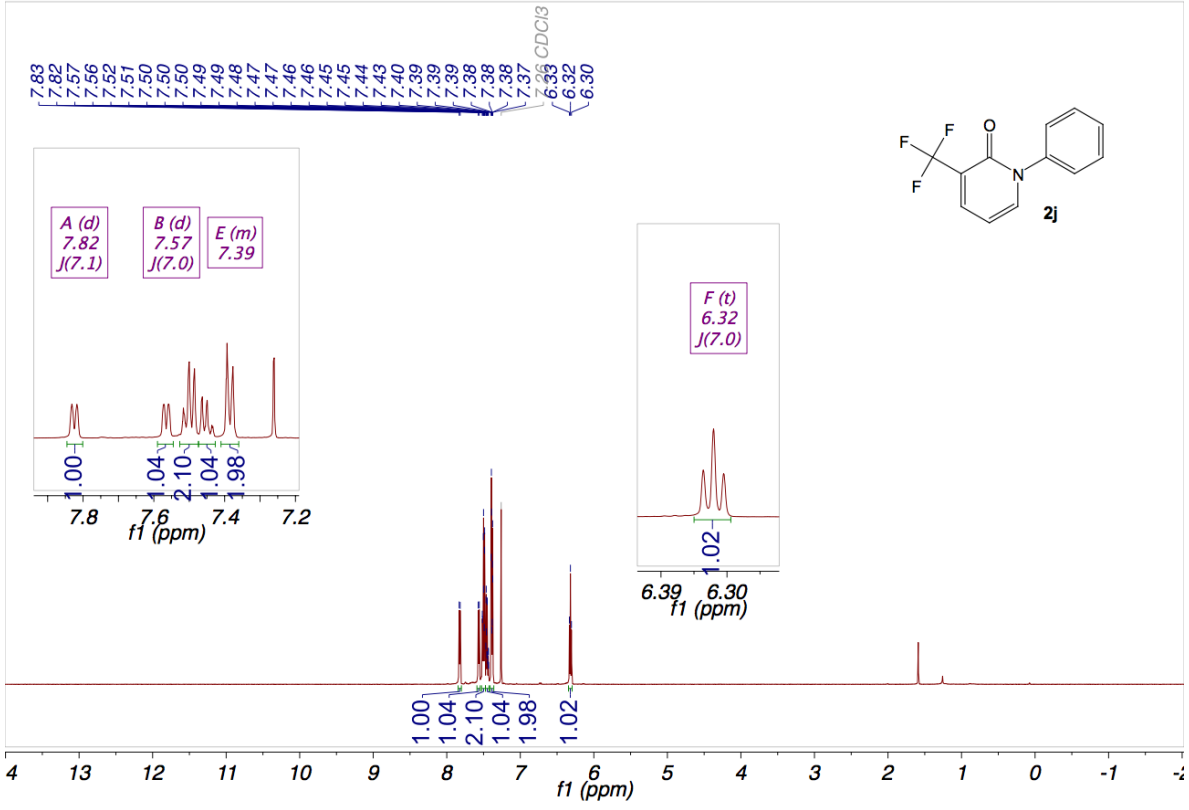
(2i) 1H NMR (400 MHz, CDCl3)



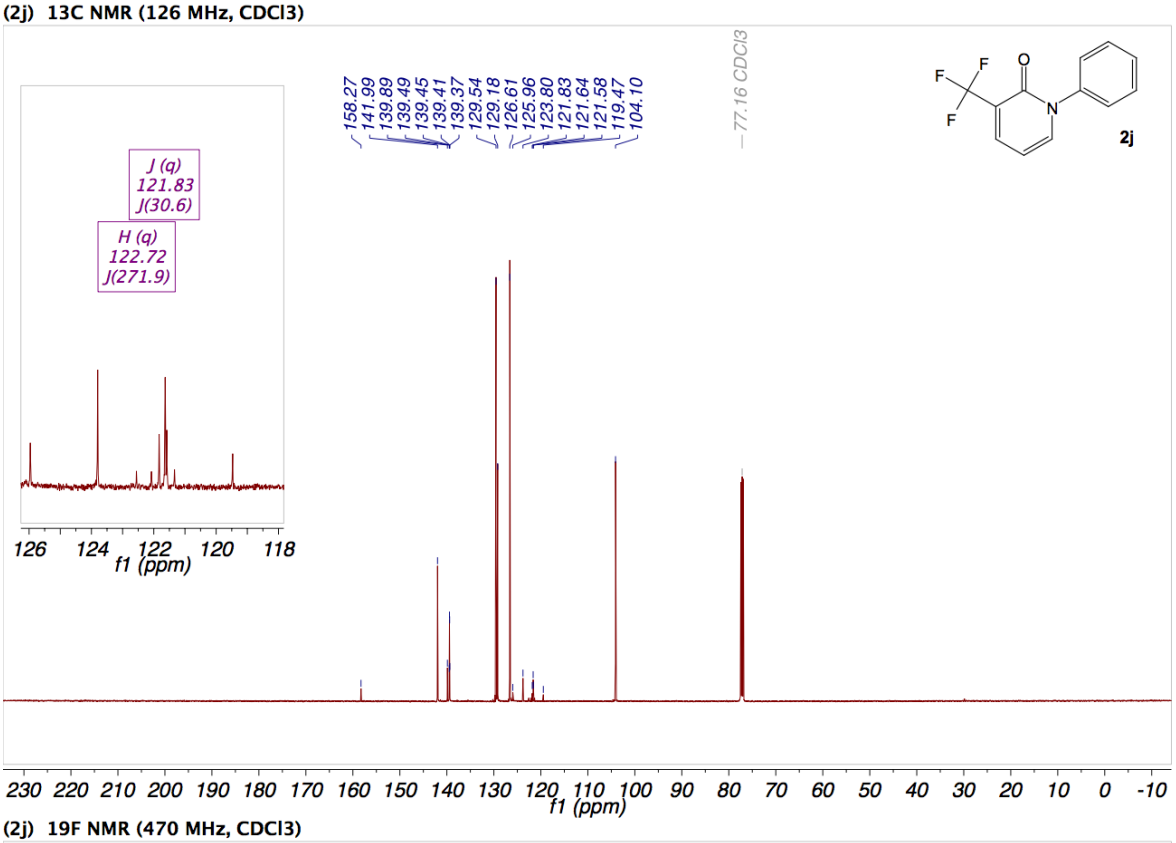
(2i) 19F NMR (376 MHz, CDCl3)



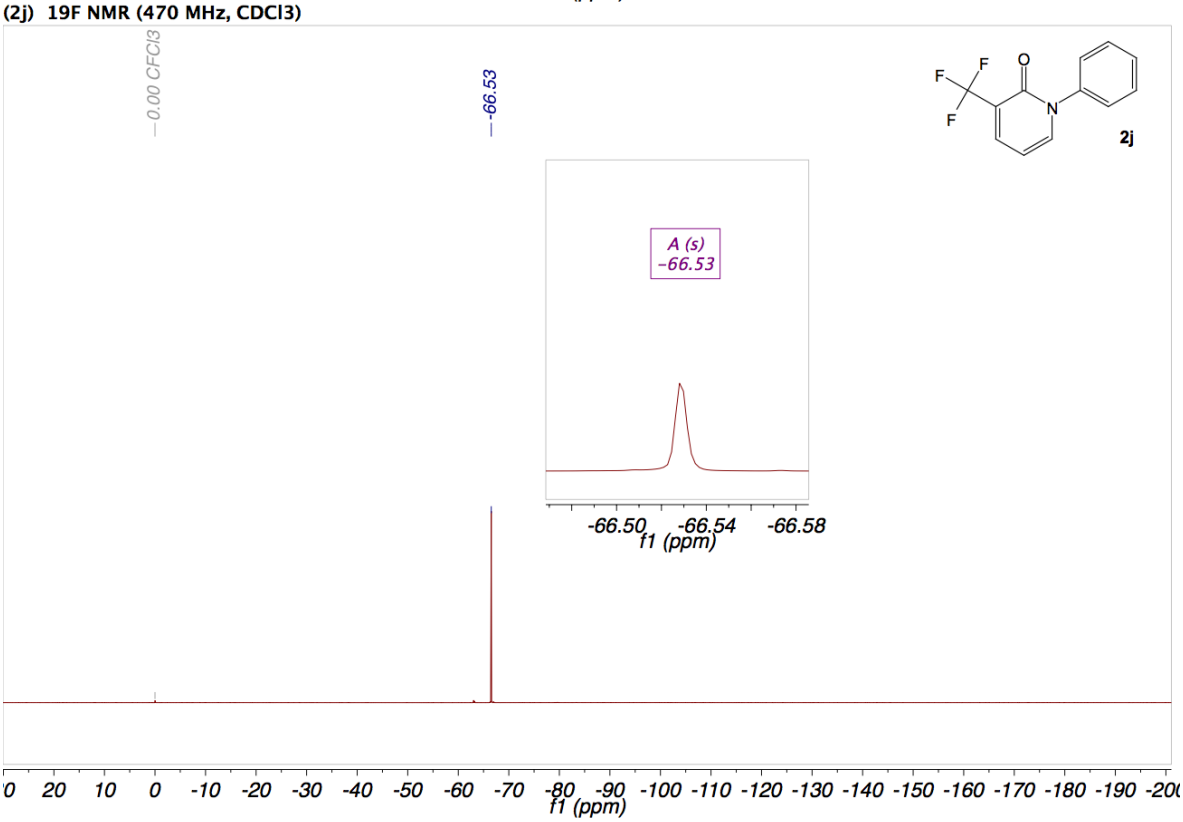
(2j) 1H NMR (500 MHz, CDCl3)

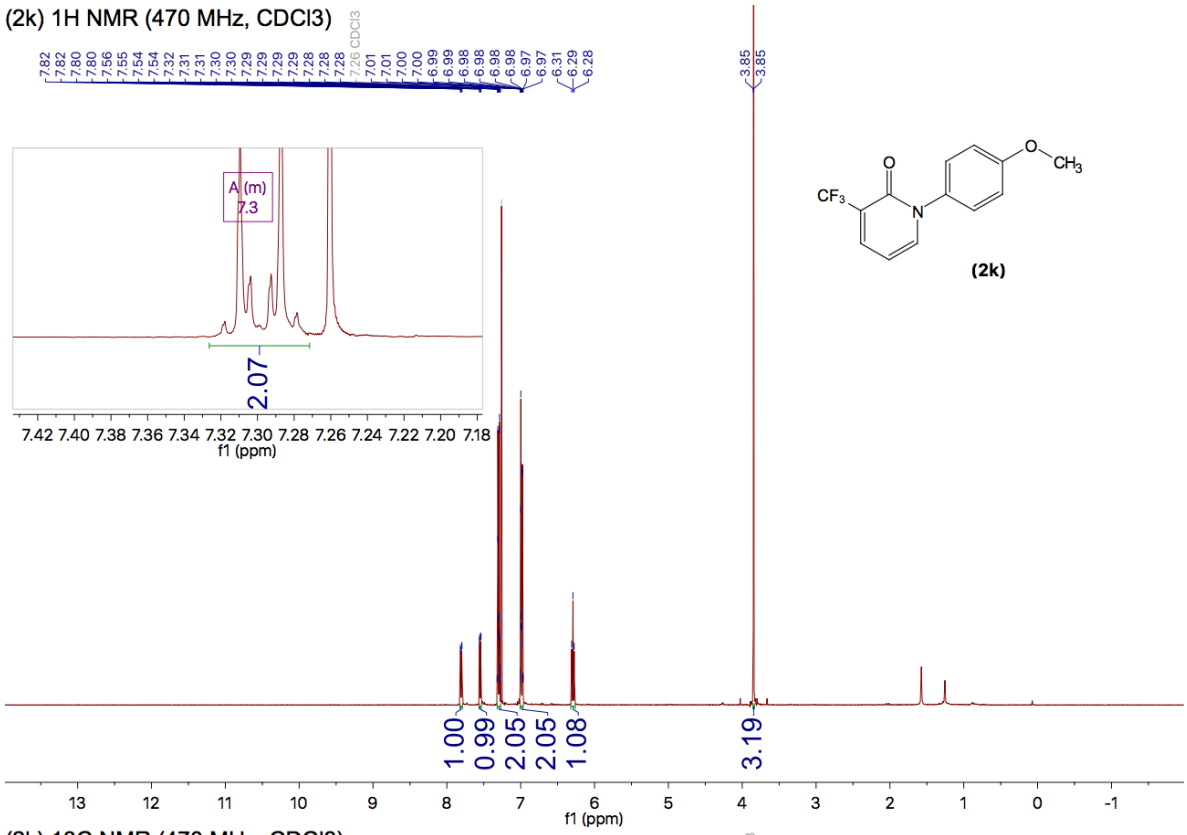


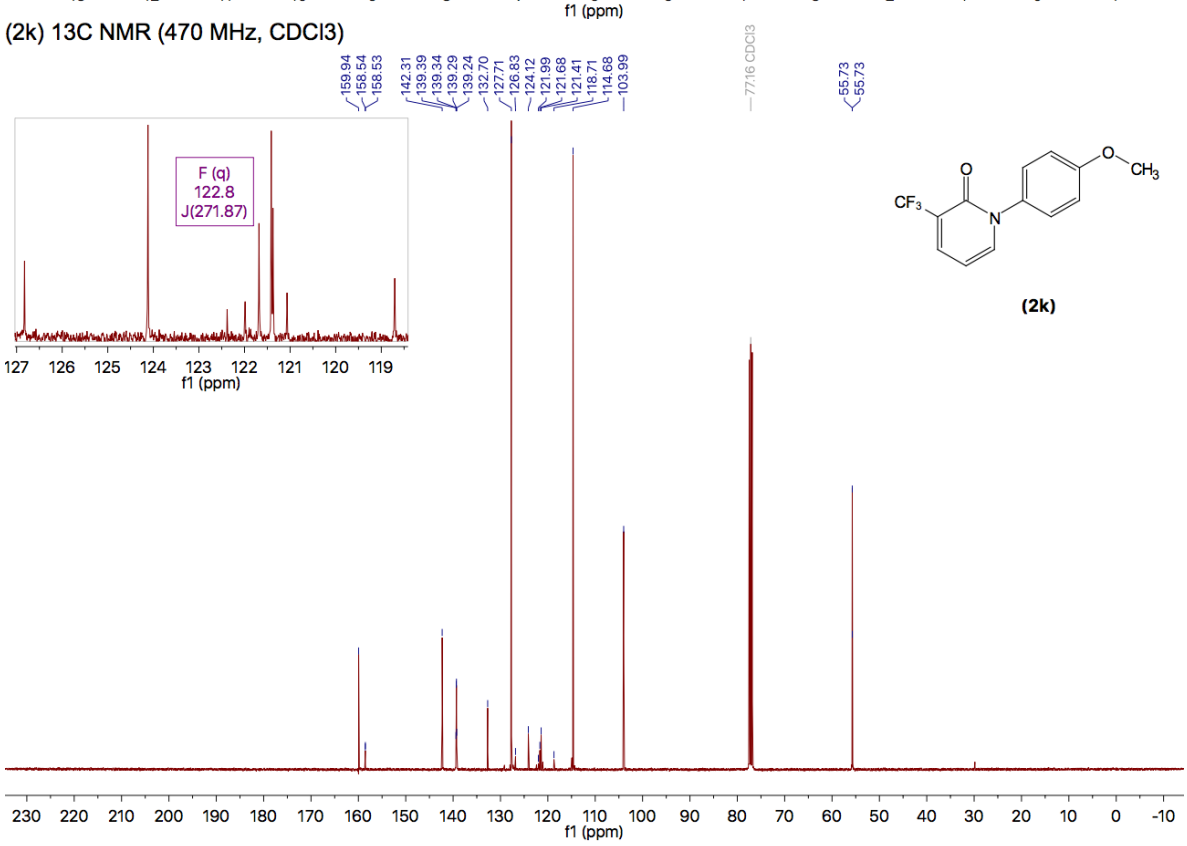
(2j) 13C NMR (126 MHz, CDCl3)



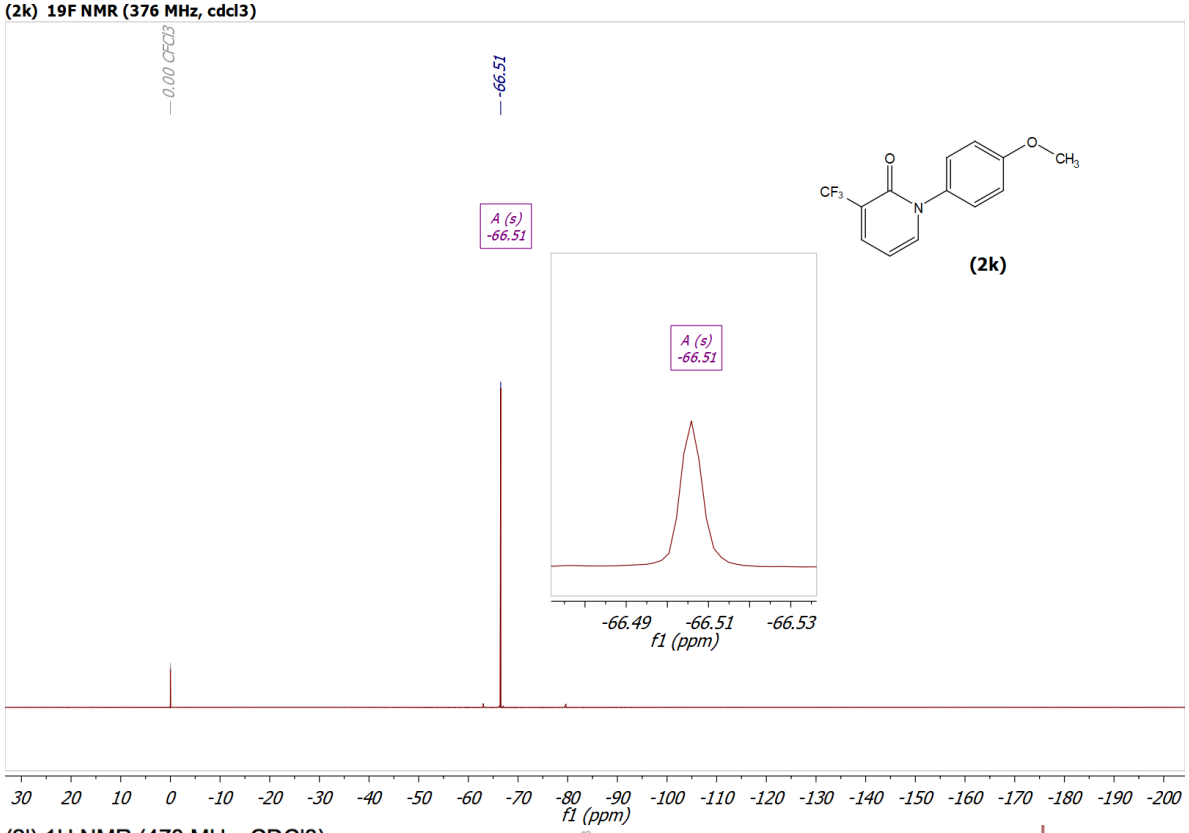
(2j) 19F NMR (470 MHz, CDCl3)



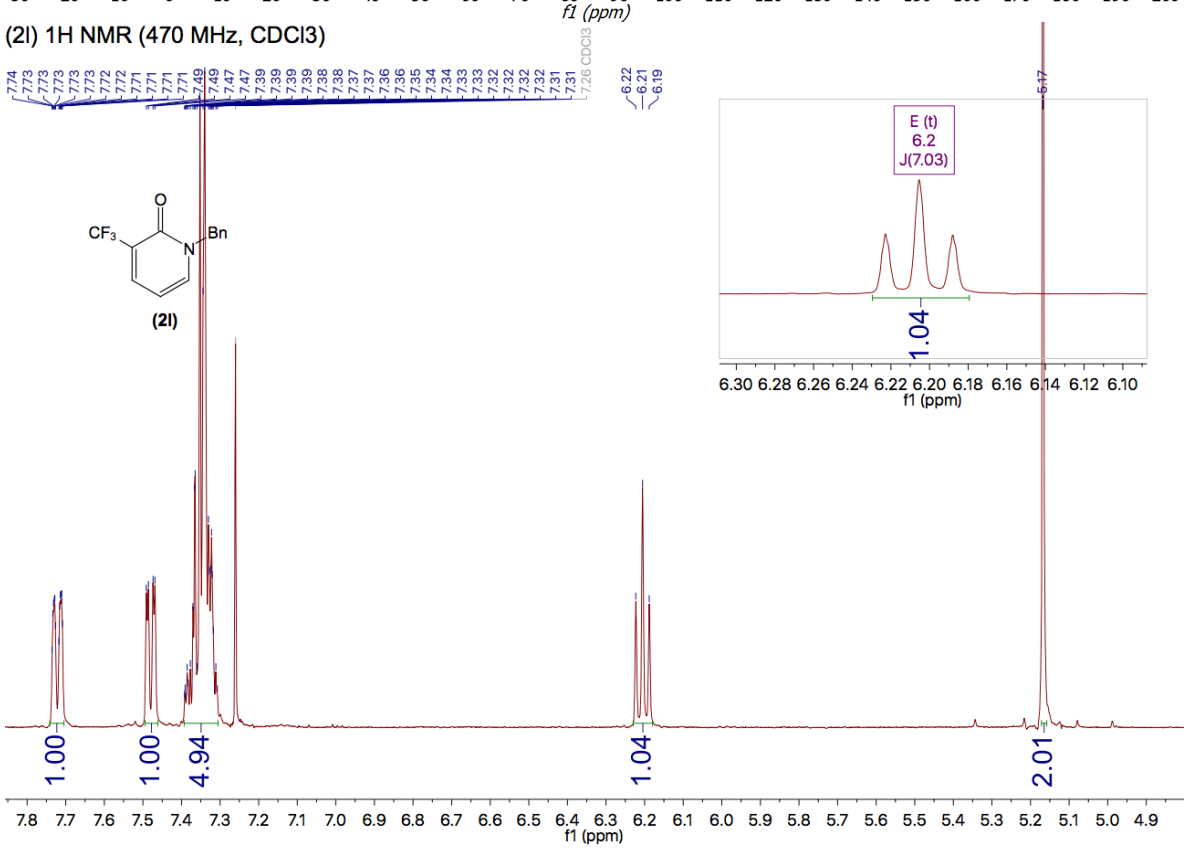

(2k) 1H NMR (470 MHz, CDCl3)
A (m)
7.3
2.07
1.00
0.99
2.05
2.05
1.08
3.19
(2k)


(2k) 13C NMR (470 MHz, CDCl3)
F (q)
122.8
J(271.87)
(2k)

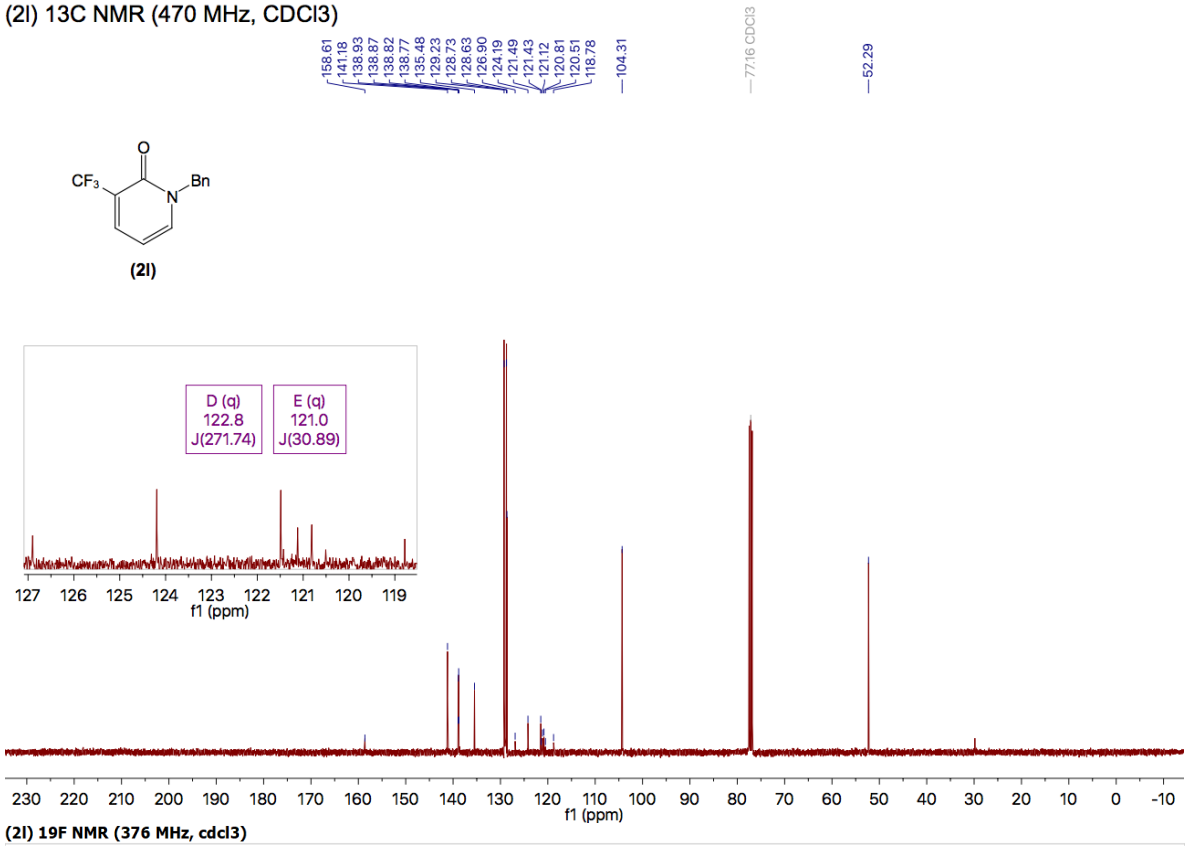
(2k) 19F NMR (376 MHz, cdcl3)



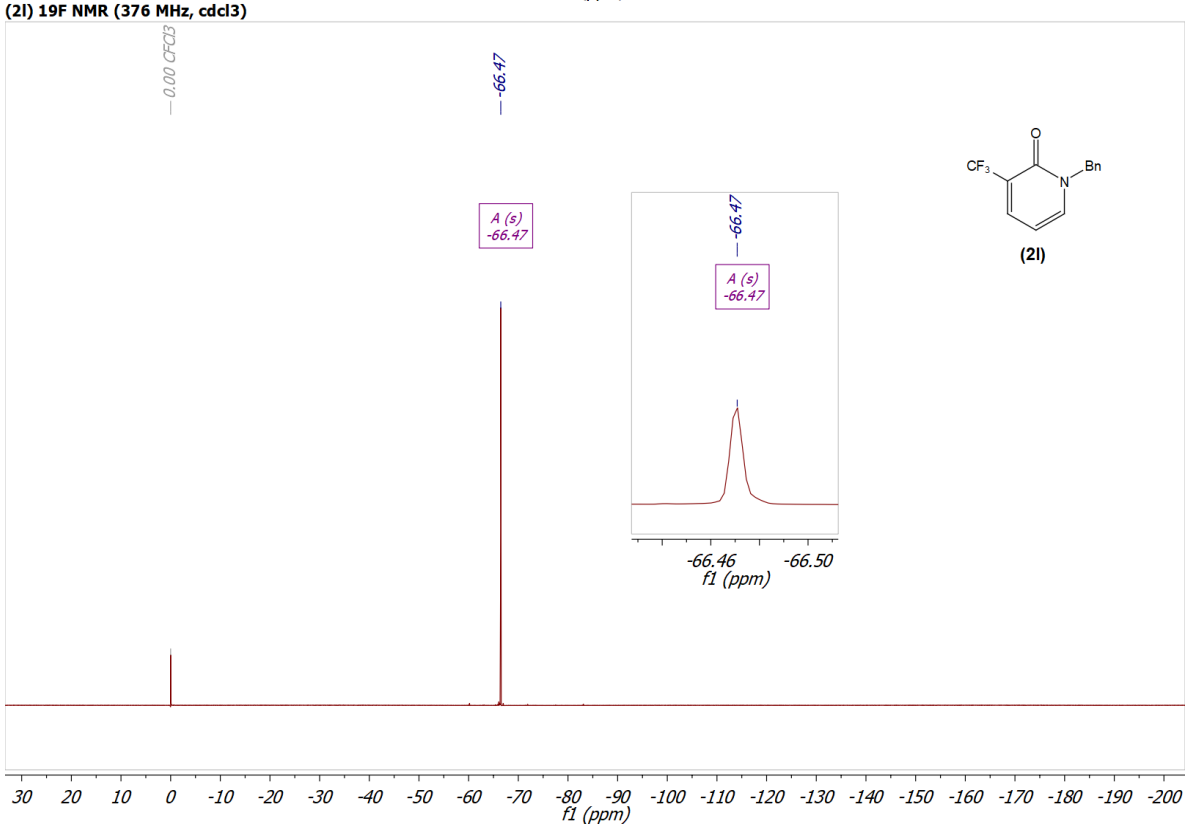
(2l) 1H NMR (470 MHz, CDCl3)



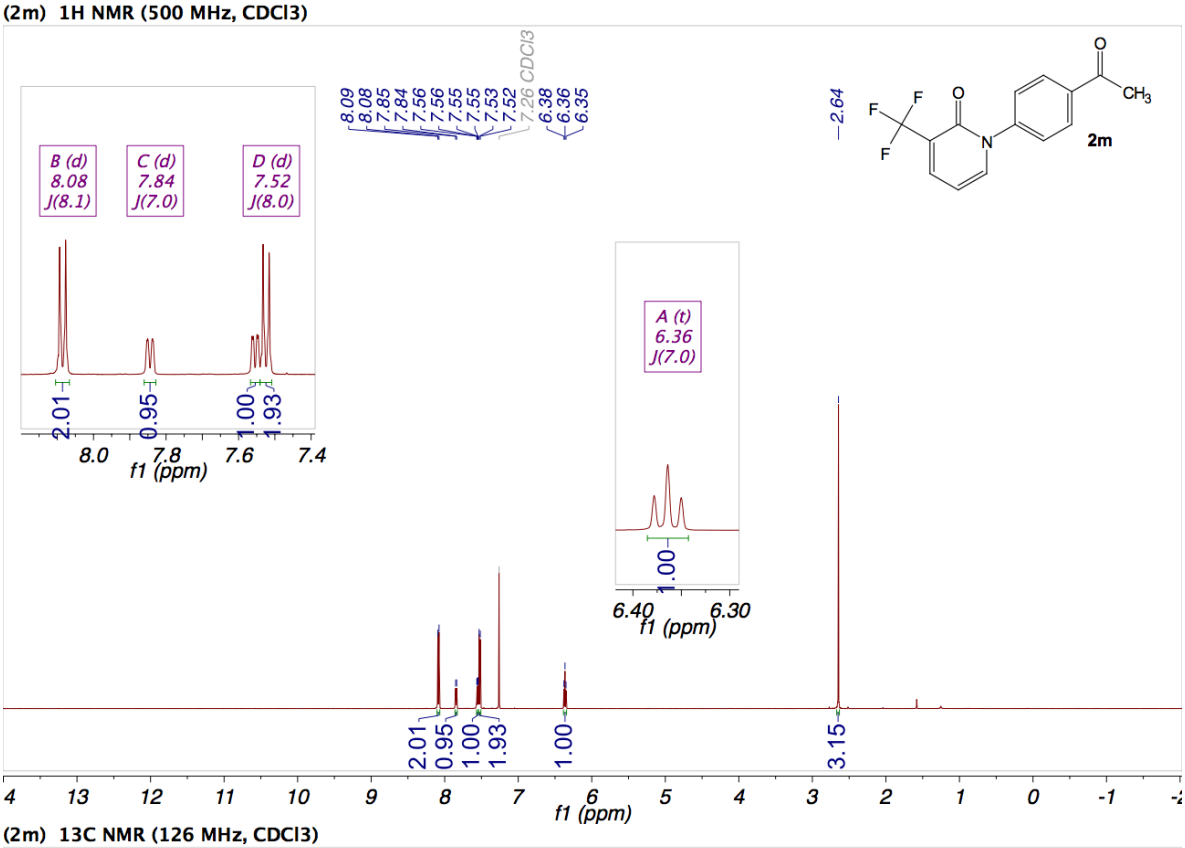
(2l) 13C NMR (470 MHz, CDCl3)



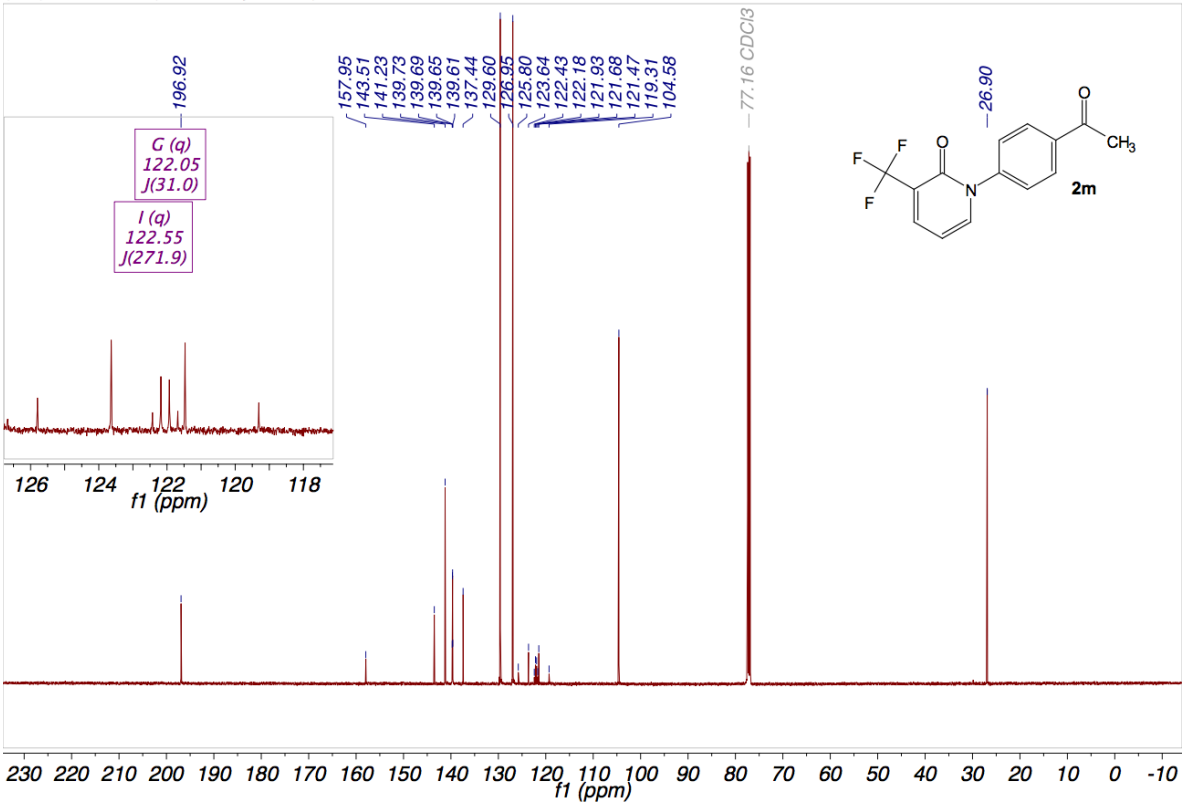
(2l) 19F NMR (376 MHz, cdcl3)



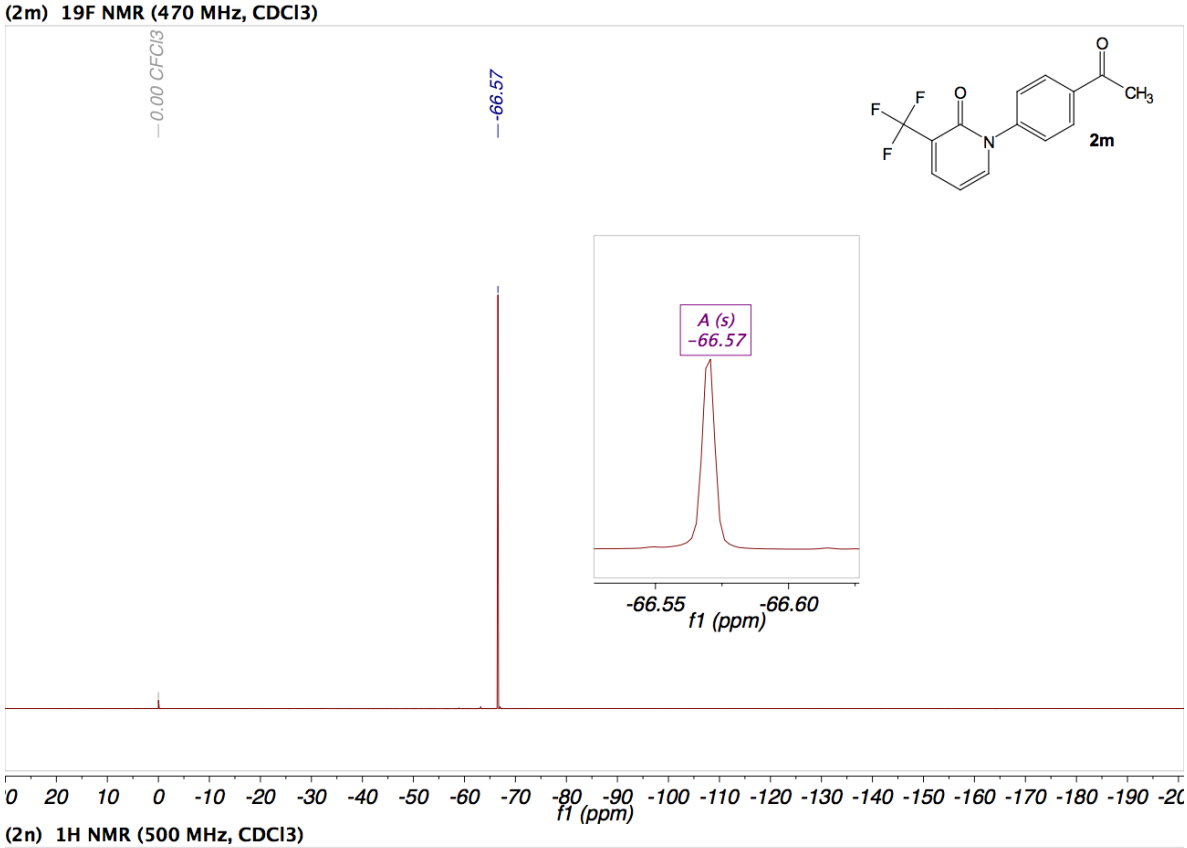
(2m) 1H NMR (500 MHz, CDCl3)



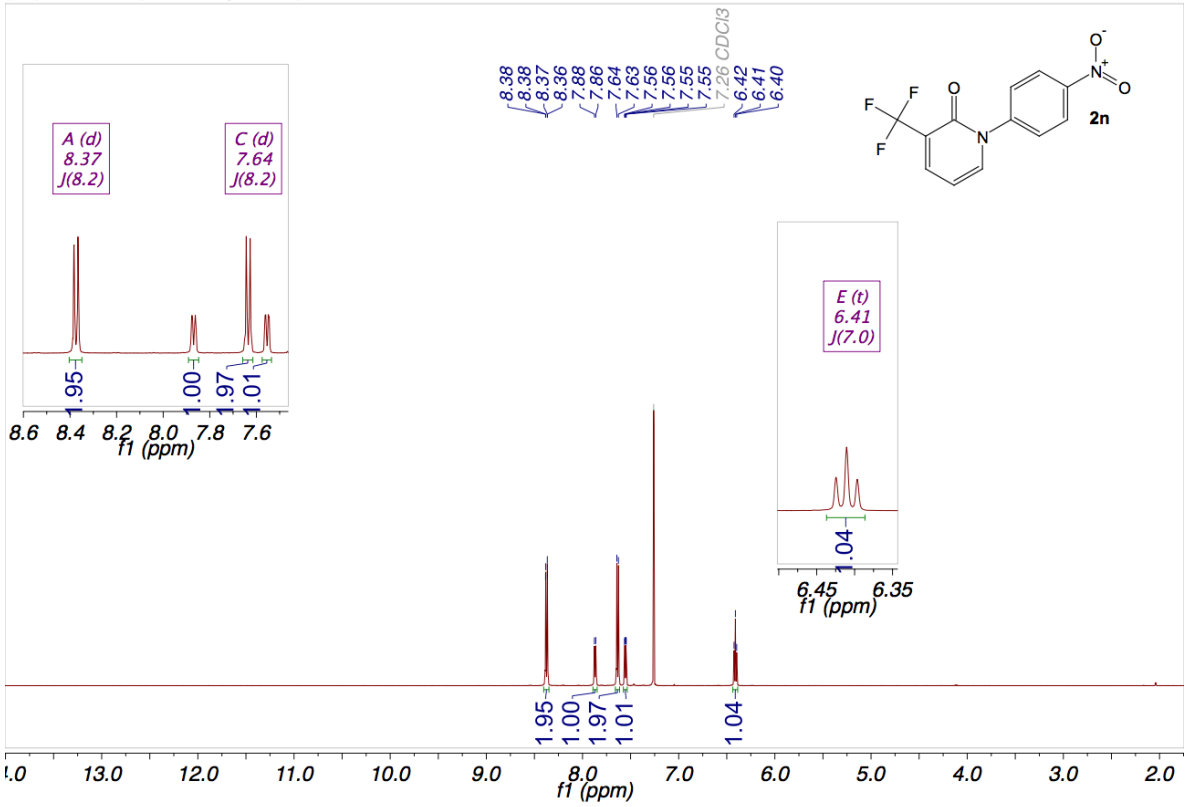
(2m) 13C NMR (126 MHz, CDCl3)



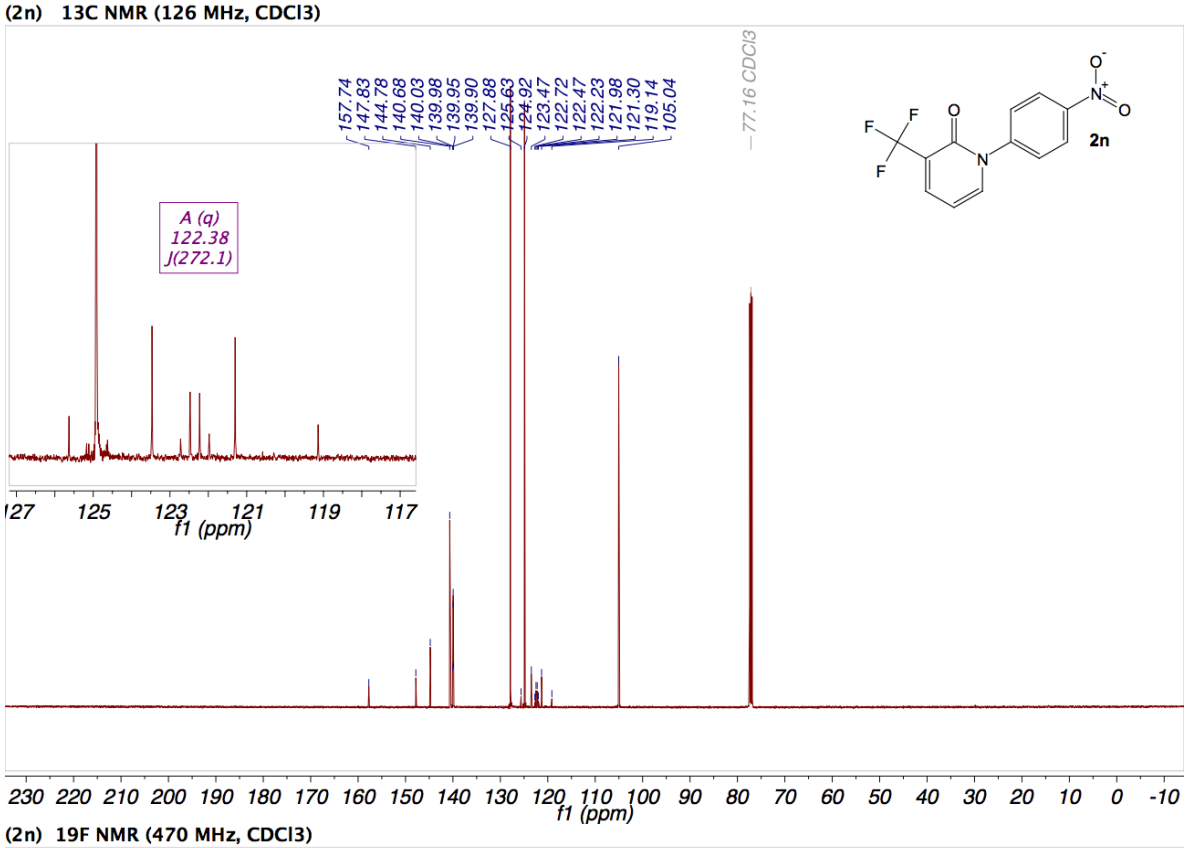
(2m) 19F NMR (470 MHz, CDCl3)



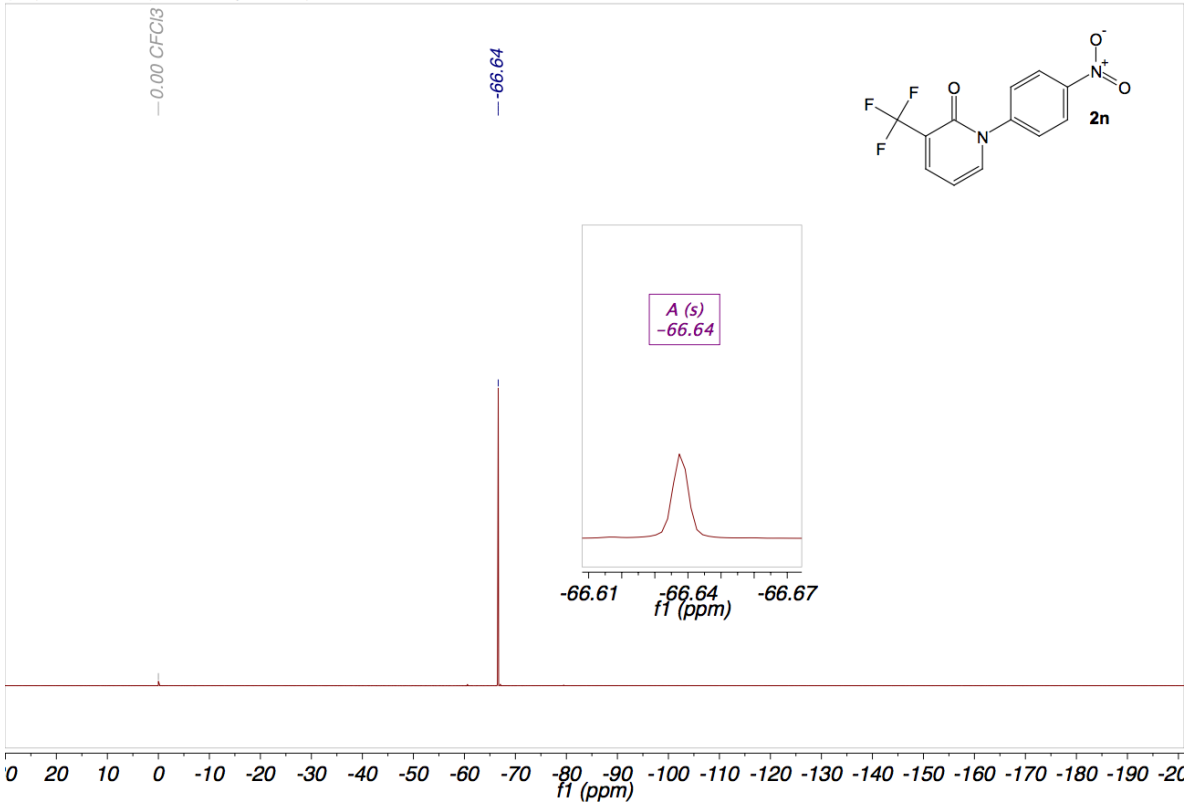
(2n) 1H NMR (500 MHz, CDCl3)



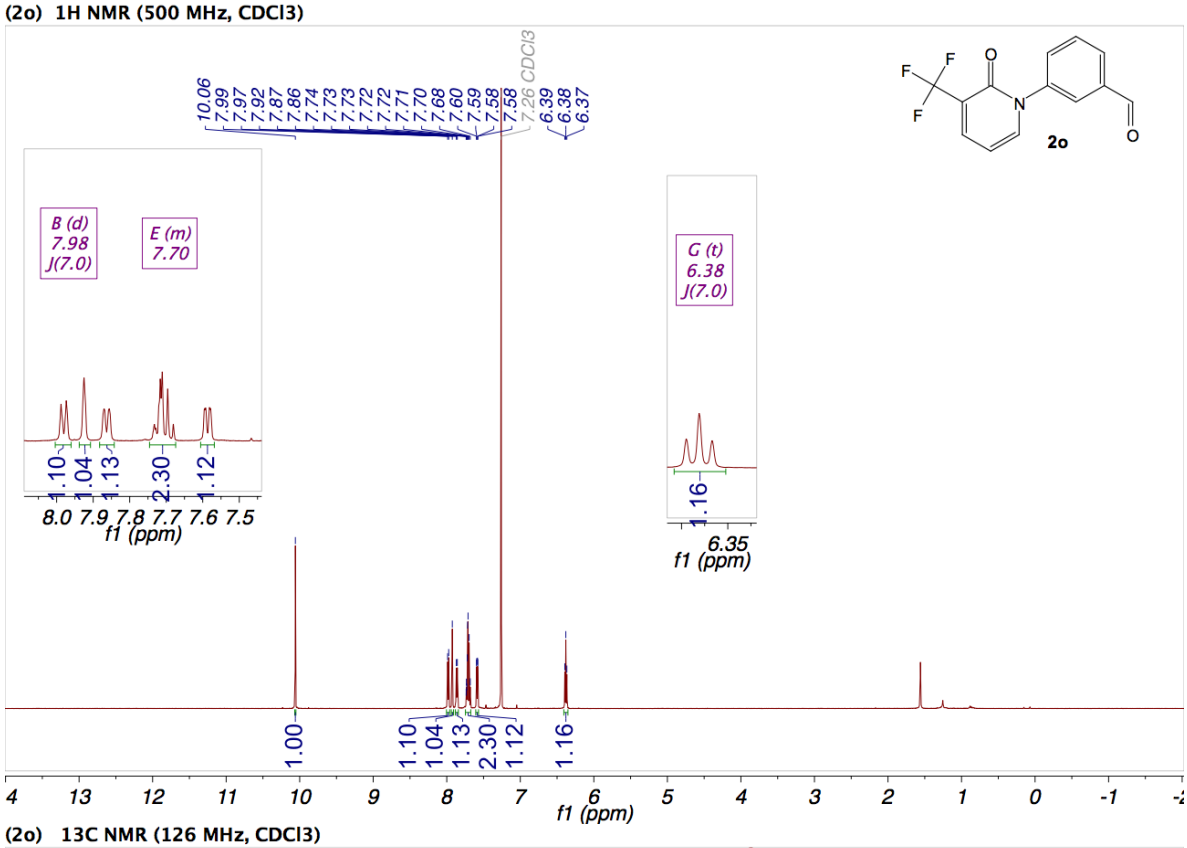
(2n) 13C NMR (126 MHz, CDCl3)



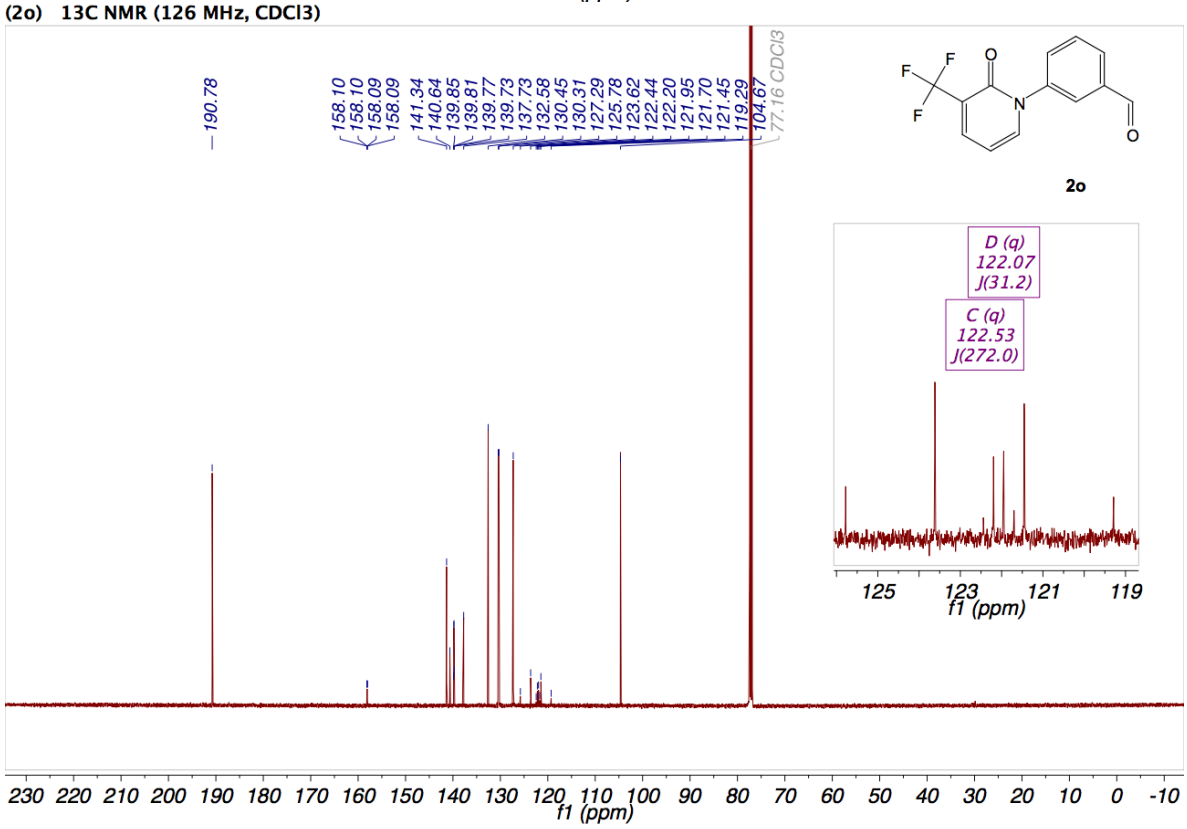
(2n) 19F NMR (470 MHz, CDCl3)



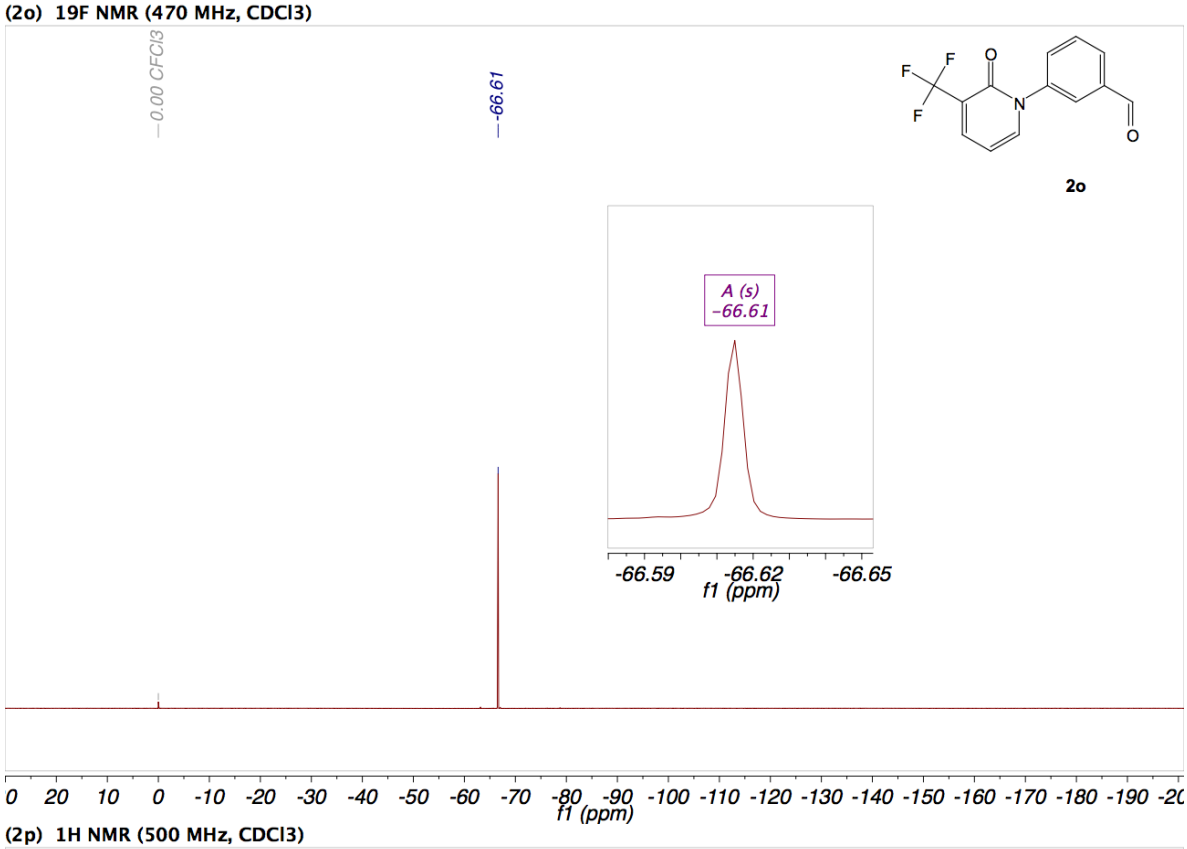
(2o) 1H NMR (500 MHz, CDCl3)



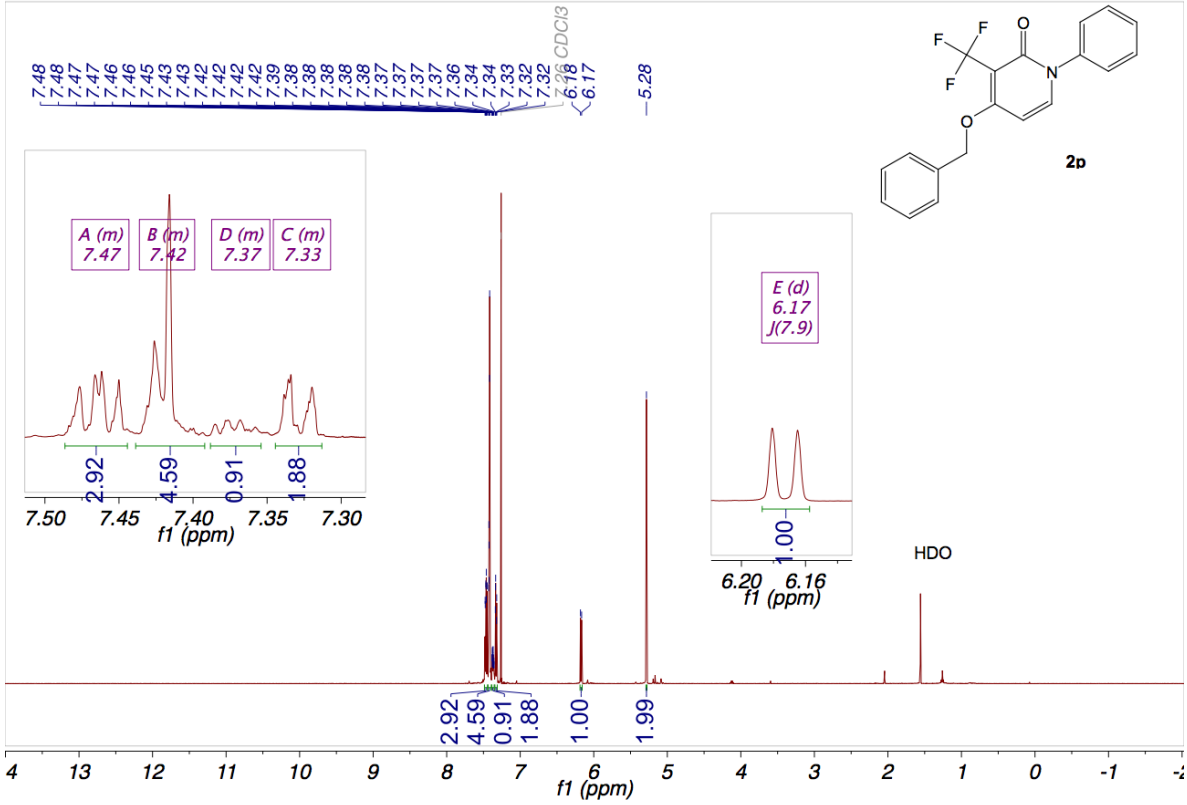
(2o) 13C NMR (126 MHz, CDCl3)



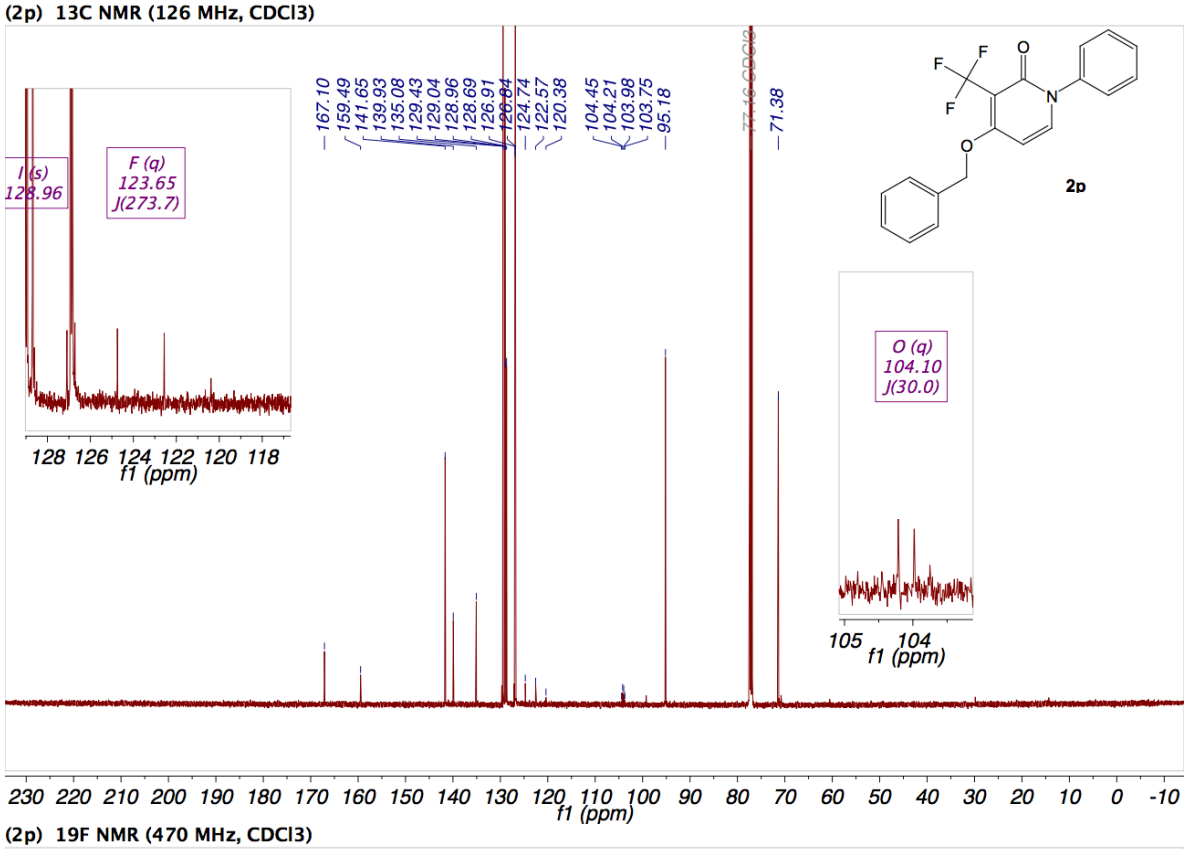
(2o) 19F NMR (470 MHz, CDCl3)



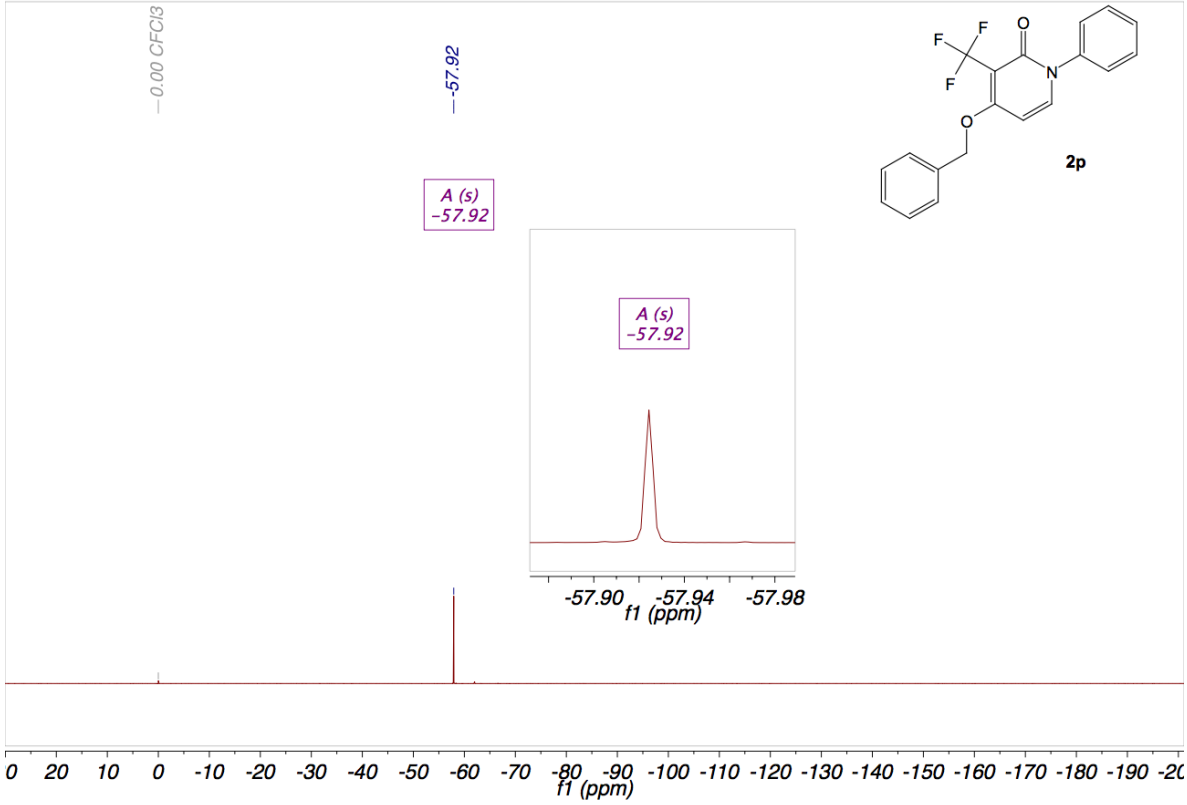
(2p) 1H NMR (500 MHz, CDCl3)



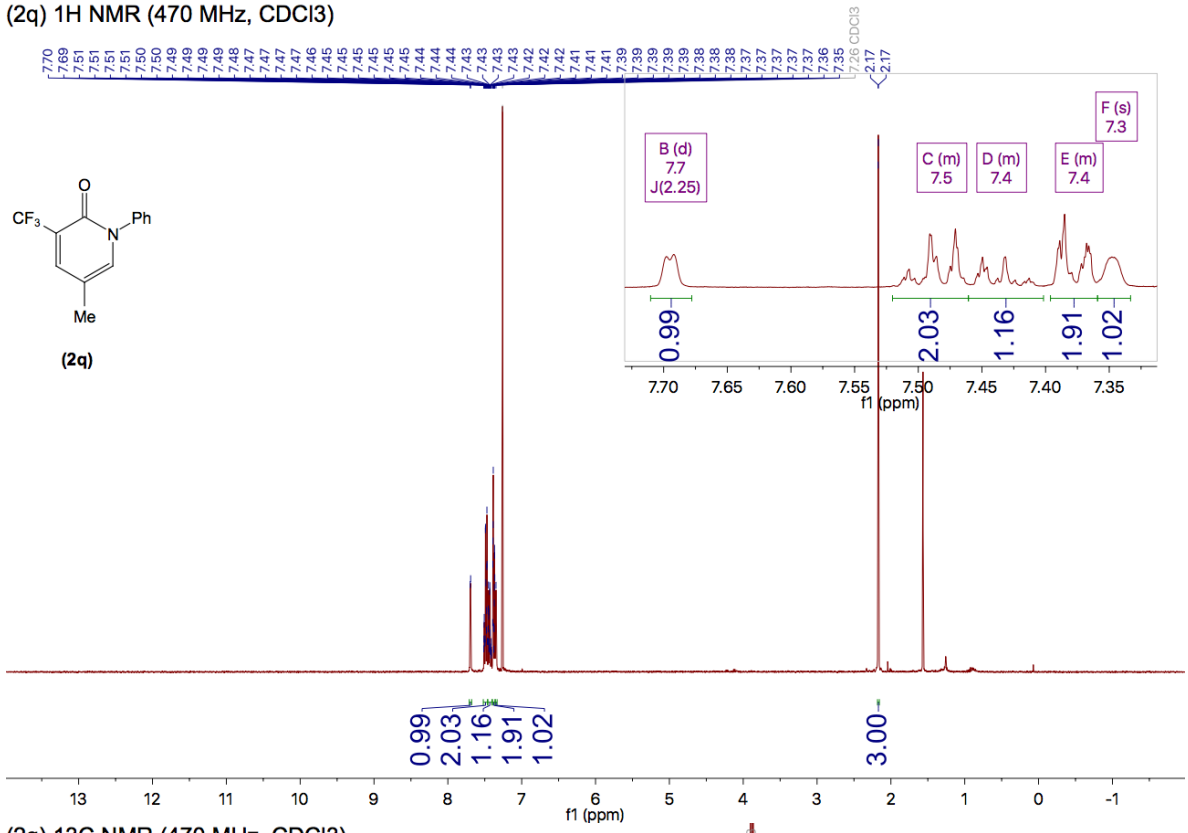
(2p) 13C NMR (126 MHz, CDCl3)



(2p) 19F NMR (470 MHz, CDCl3)

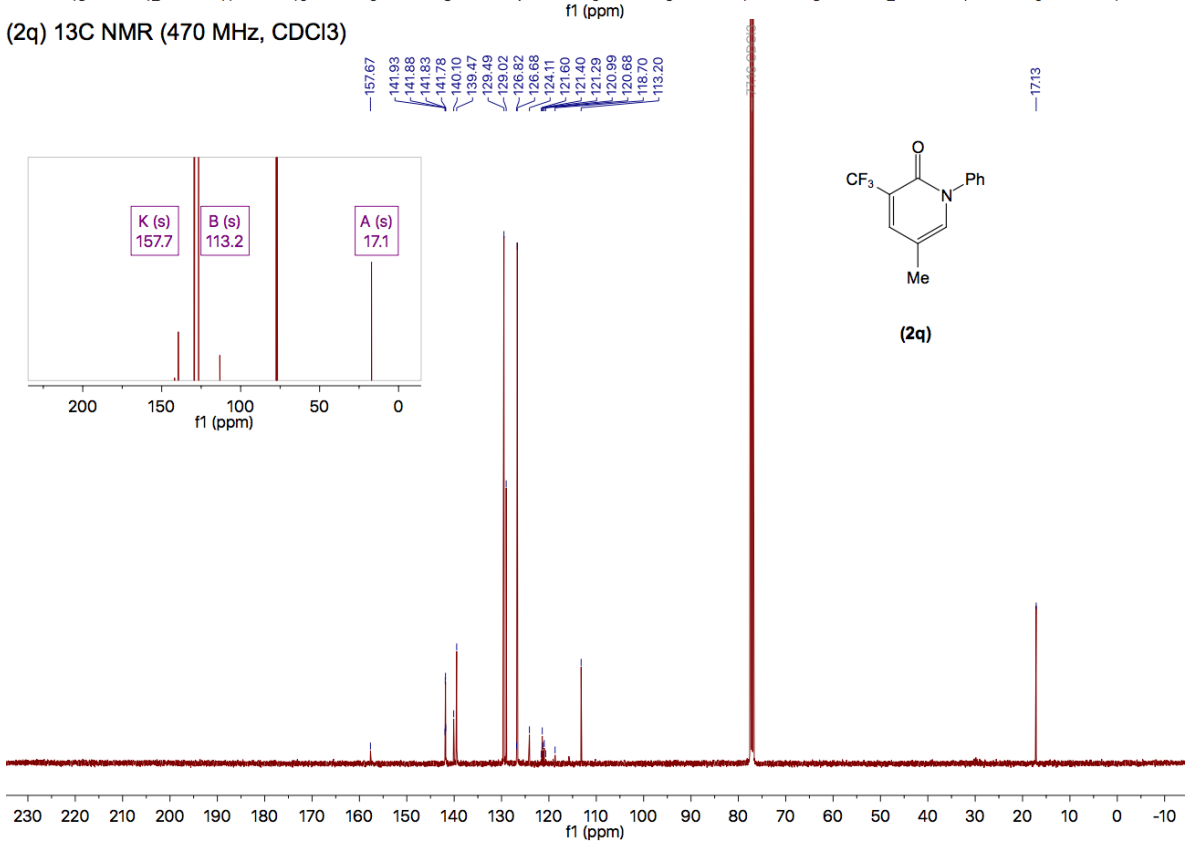


(2q) 1H NMR (470 MHz, CDCl3)



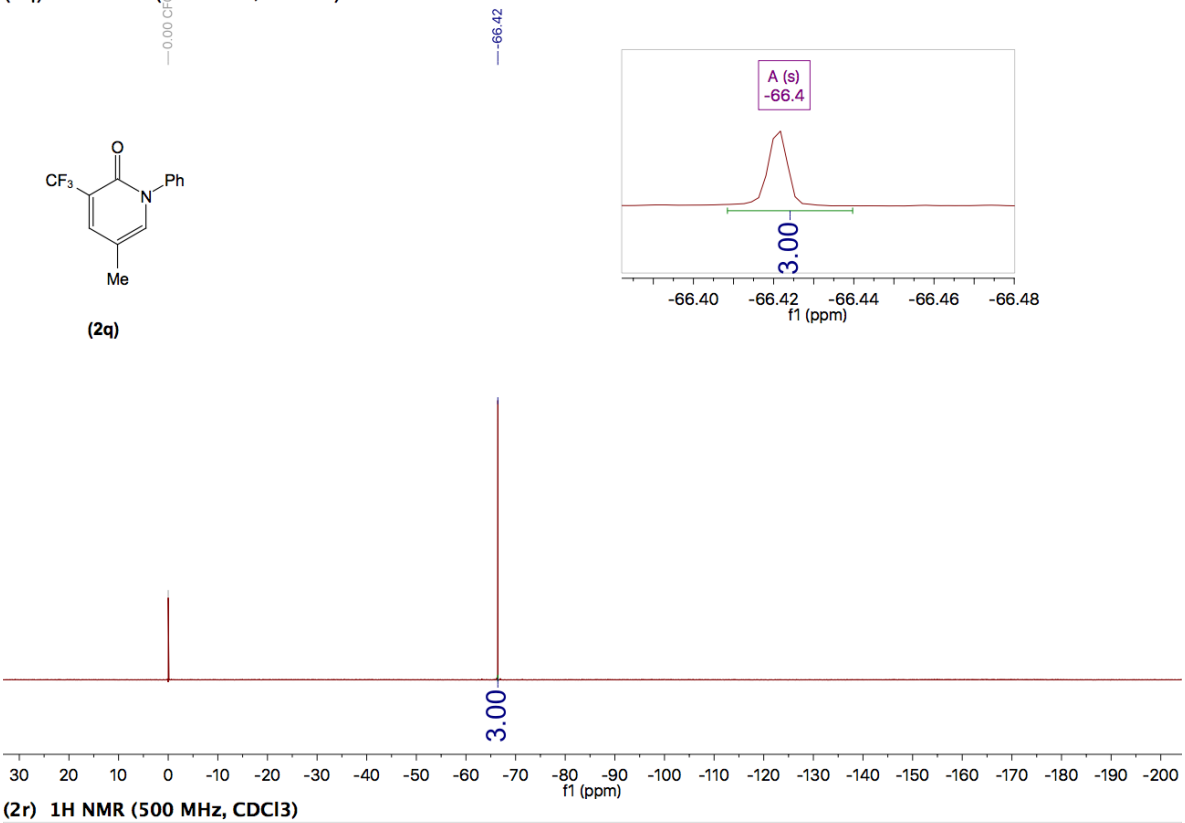
(2q)

(2q) 13C NMR (470 MHz, CDCl3)



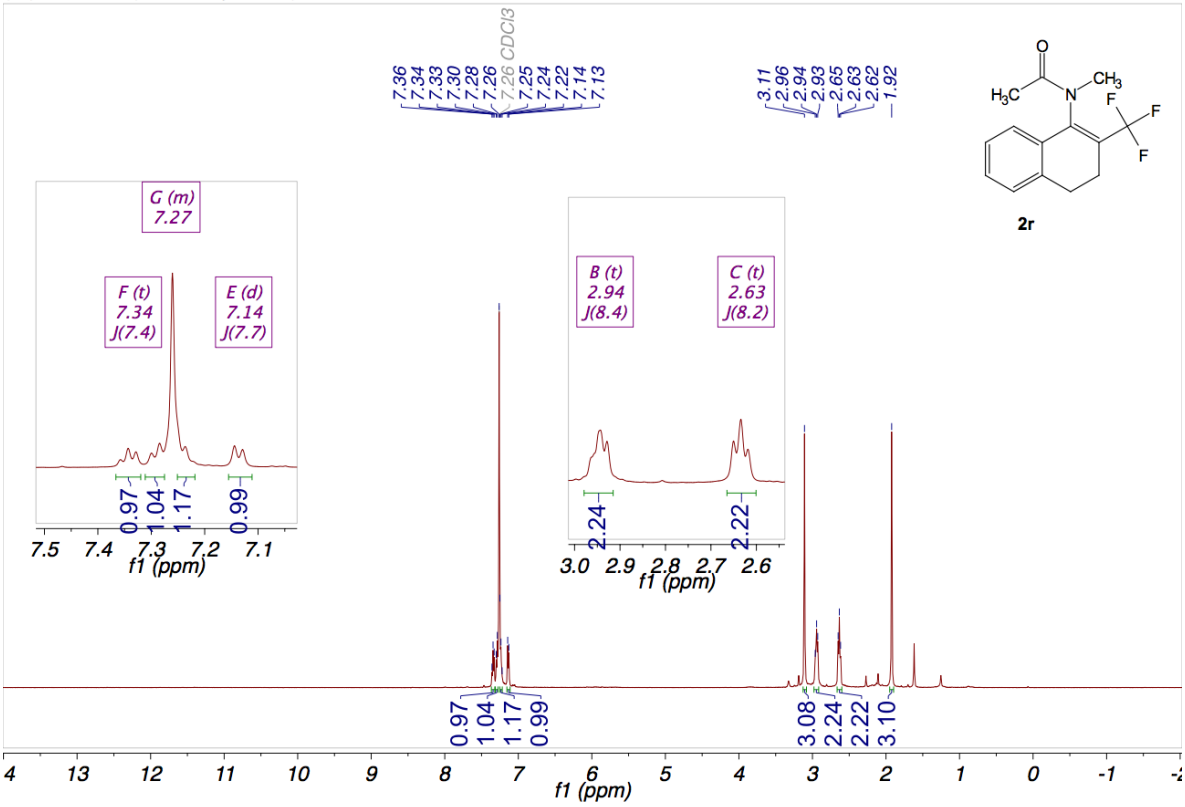
(2q)

(2q) 19F NMR (470 MHz, CDCl3)



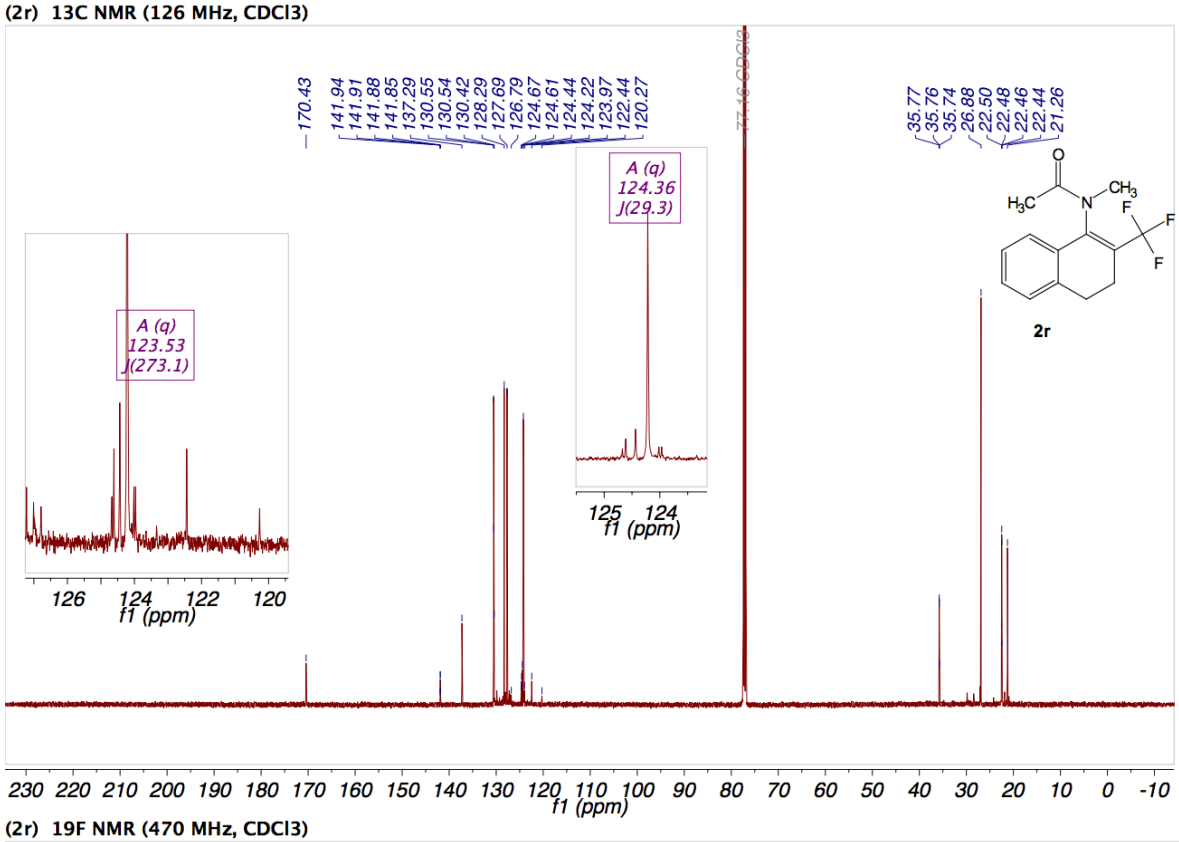
(2q)

(2r) 1H NMR (500 MHz, CDCl3)

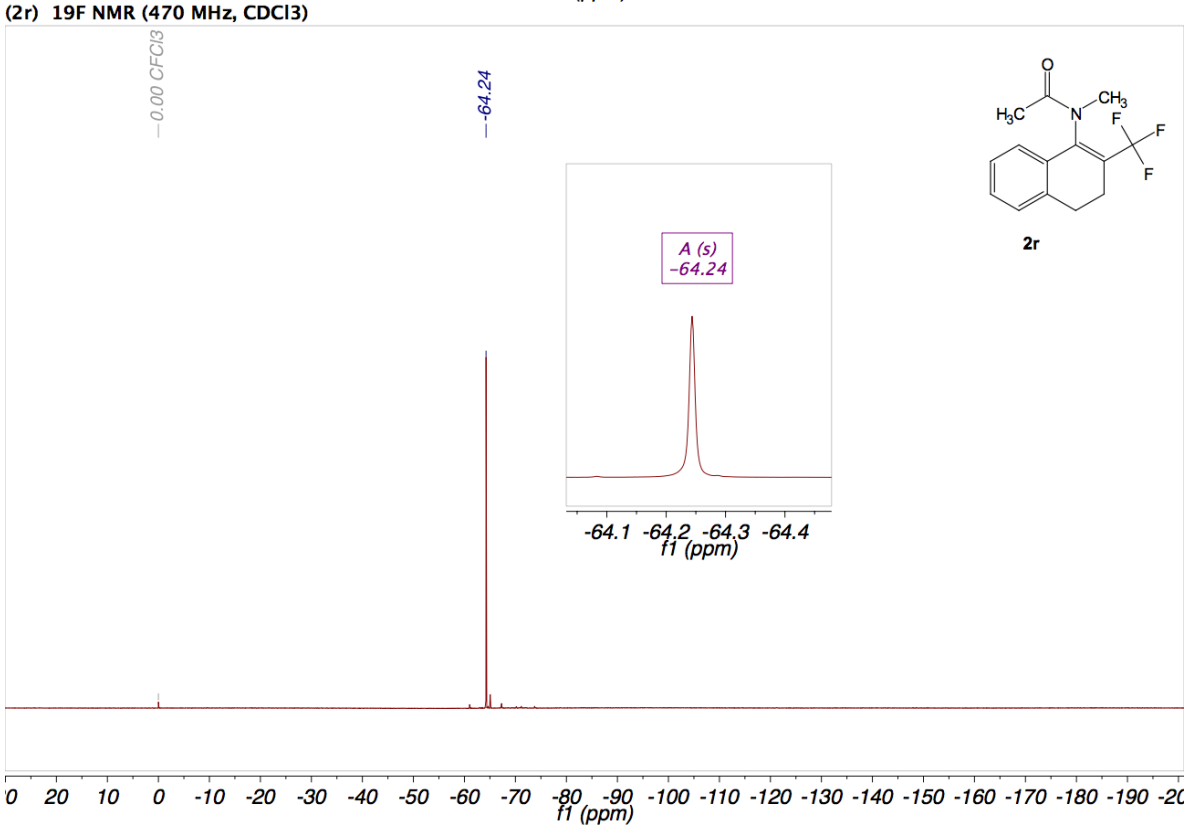


2r

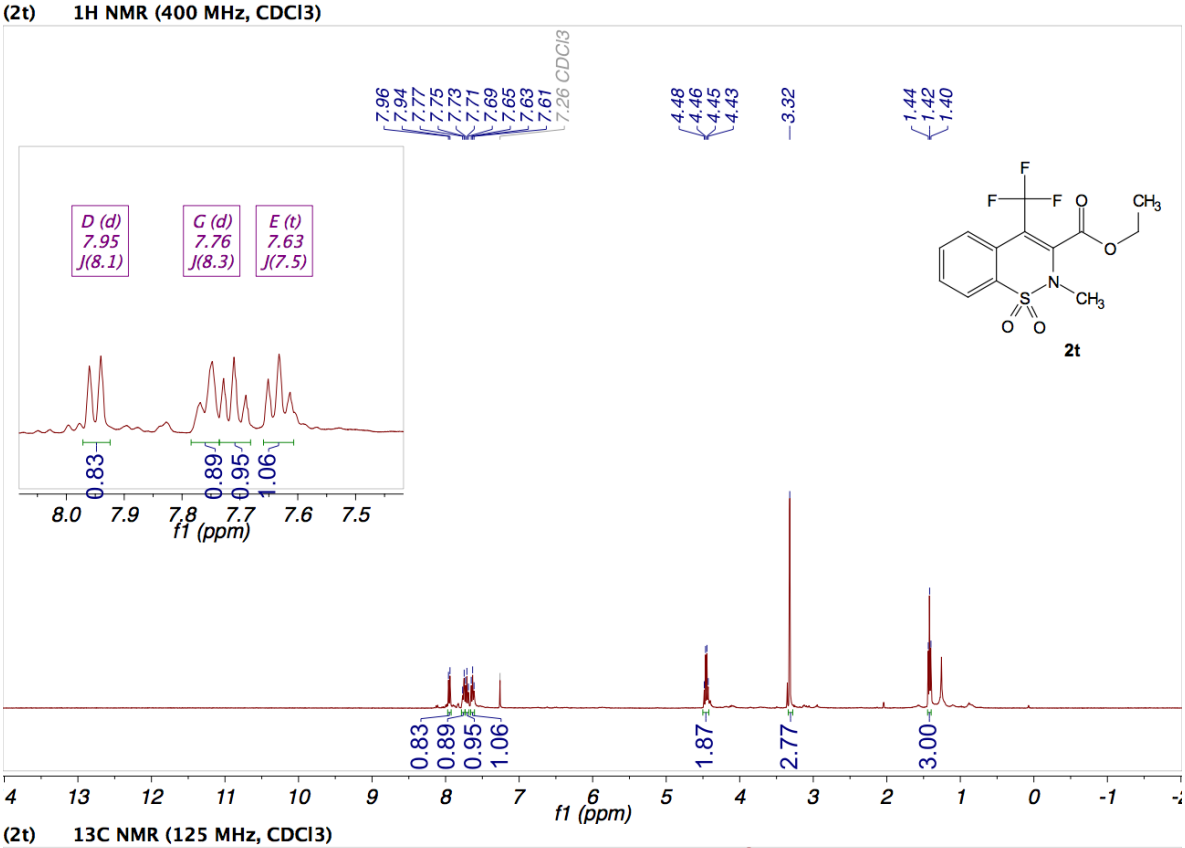
(2r) 13C NMR (126 MHz, CDCl3)



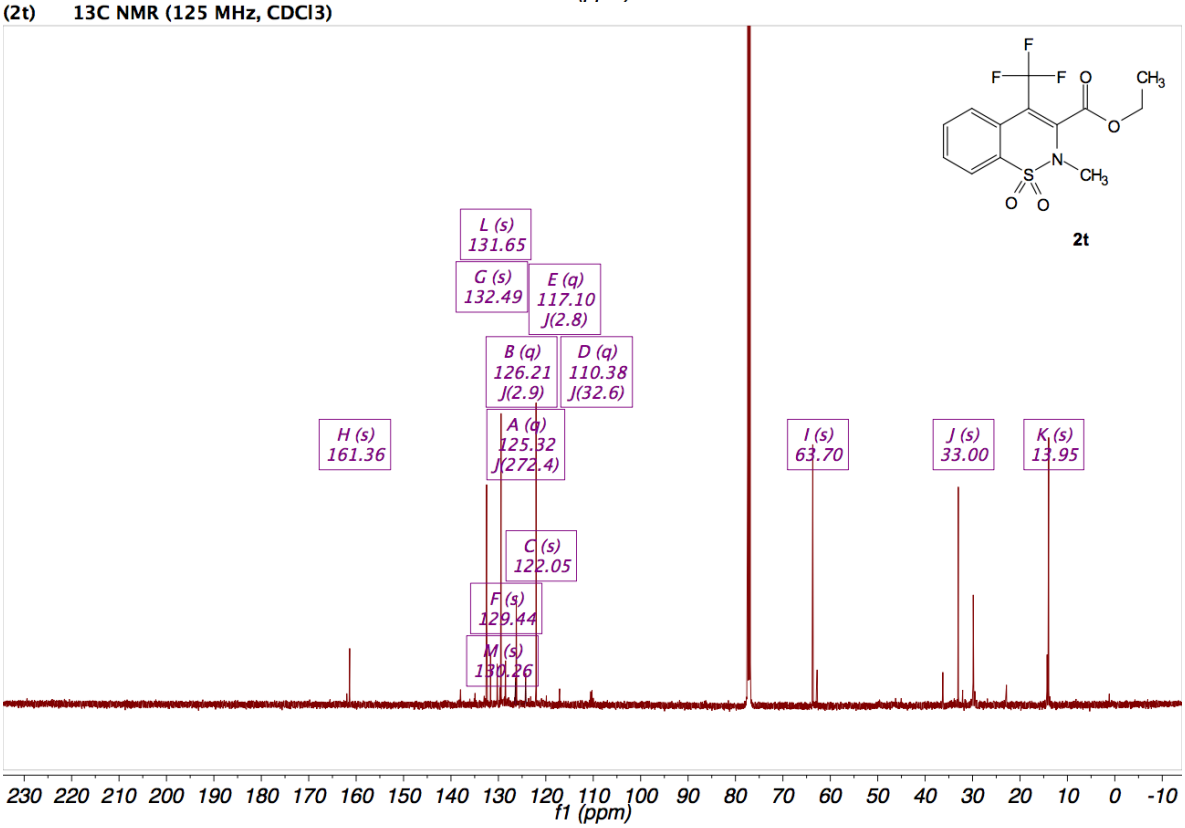
(2r) 19F NMR (470 MHz, CDCl3)



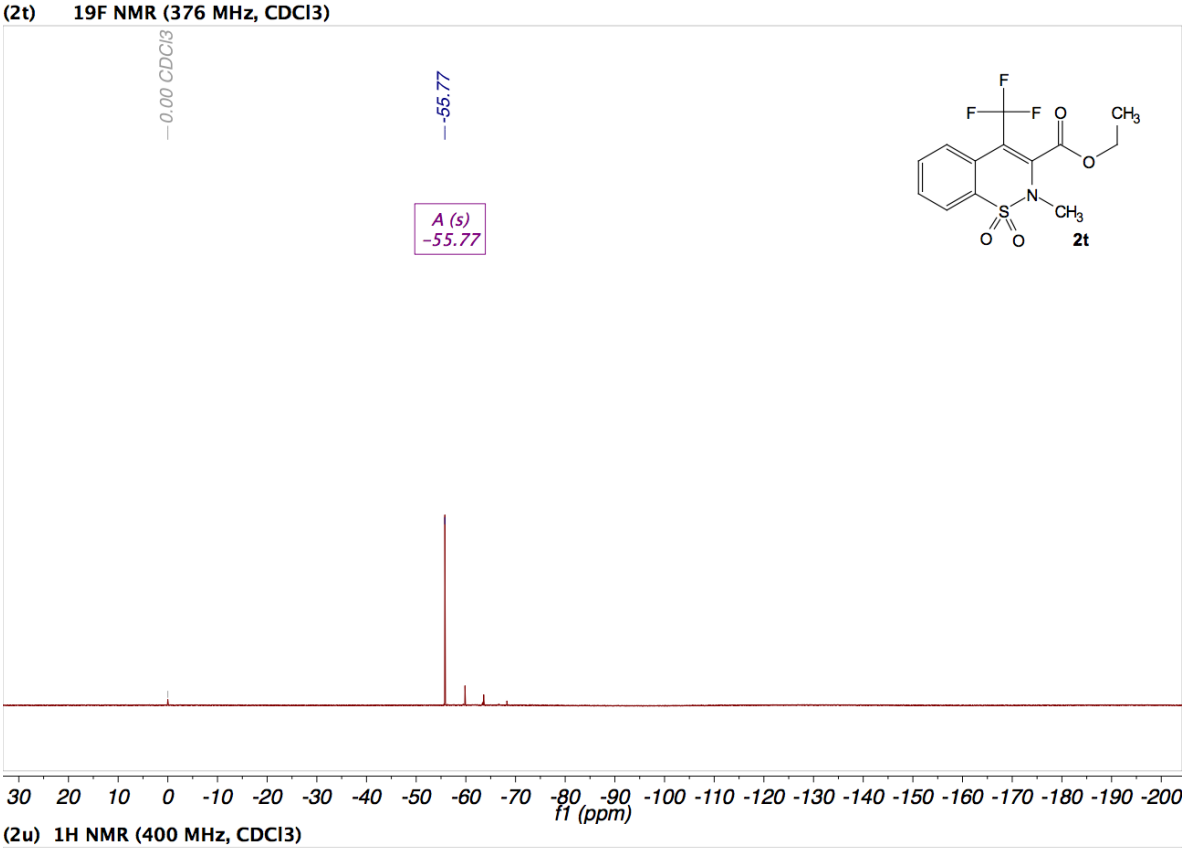
(2t) 1H NMR (400 MHz, CDCl3)



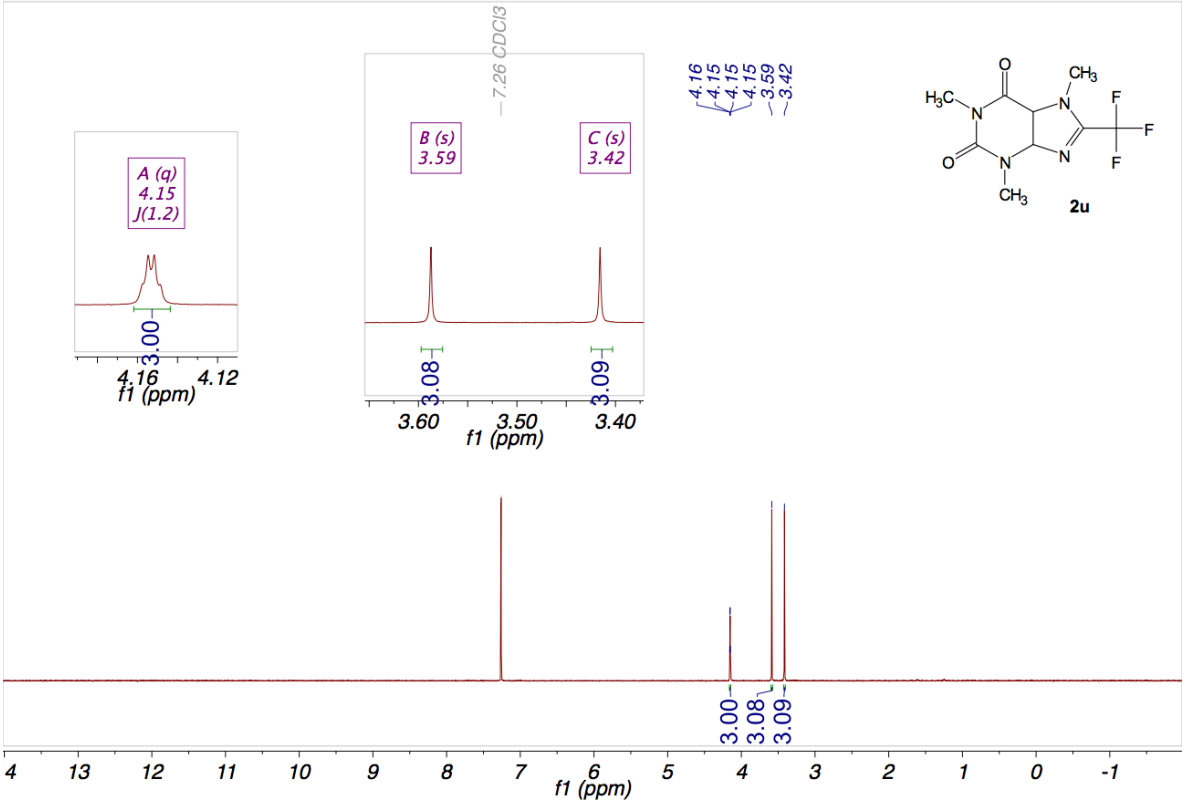
(2t) 13C NMR (125 MHz, CDCl3)



(2t) 19F NMR (376 MHz, CDCl3)



(2u) 1H NMR (400 MHz, CDCl3)



(2u) 19F NMR (376 MHz, CDCl3)