Palladium-Catalyzed Norbornene-Mediated *ortho*-Amination *ipso*-Amidation: Sequential C-N Bond Formation

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Supporting Information

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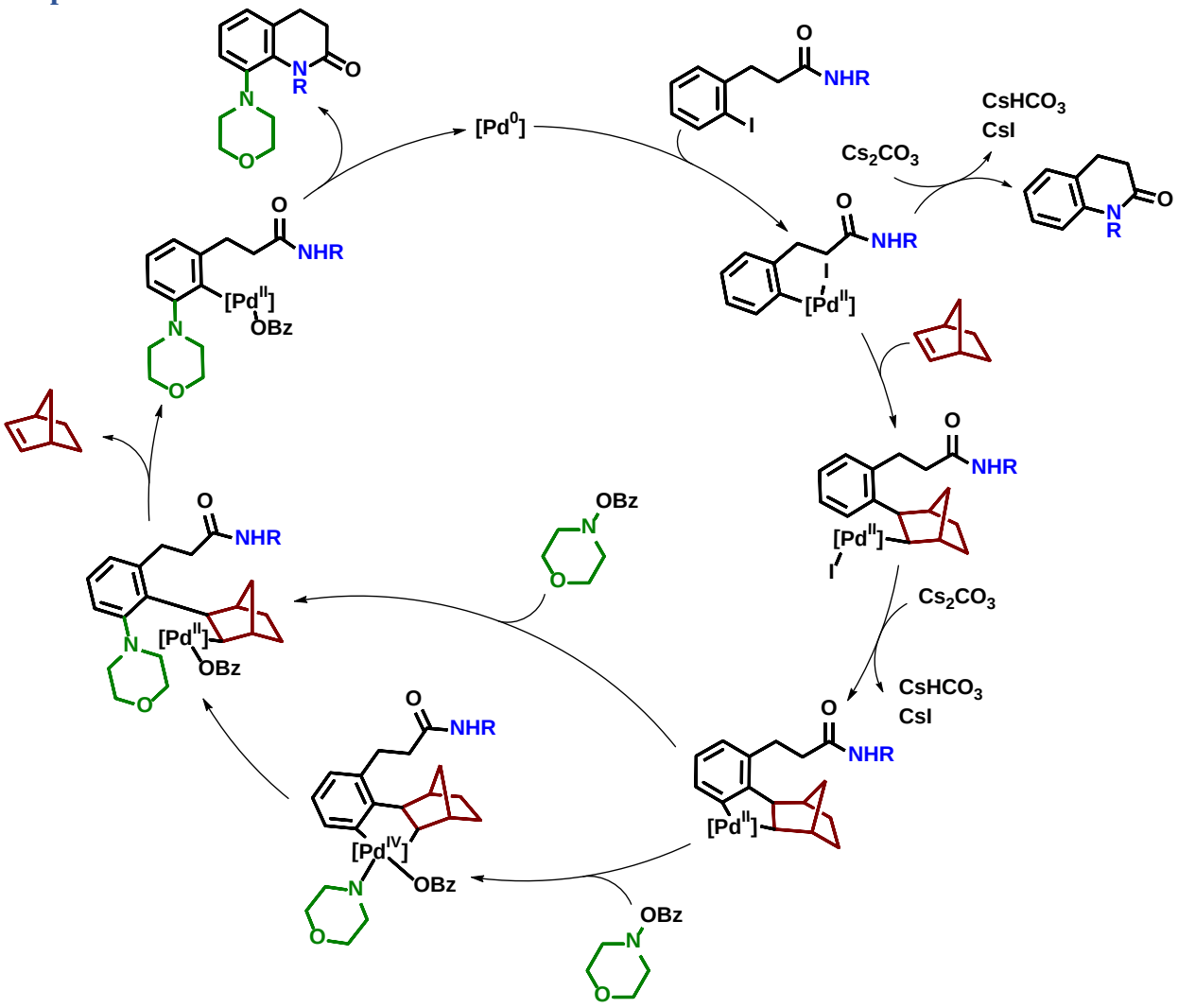
General Considerations

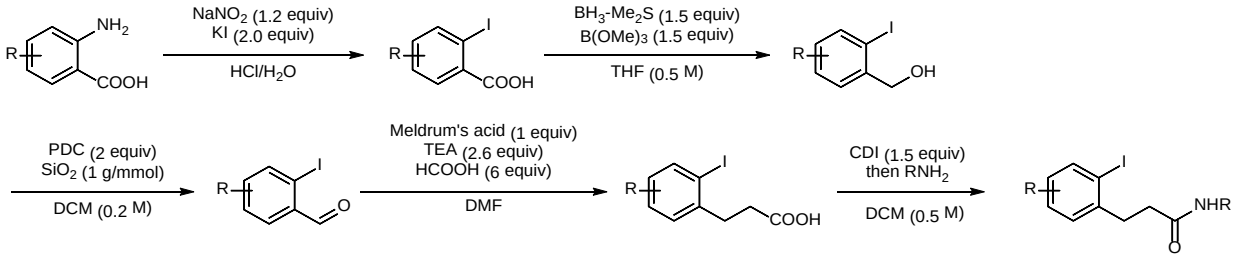
All reactions were performed in a dry environment under an inert atmosphere of argon unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) and visualized under UV light or by $KMNO_4$ staining. Flash column chromatography was performed with Silicycle 46-60 µm silica gel. Catalytic reactions were performed in 2 dram vials equipped with a Teflon sealed cap. Toluene was distilled over calcium hydride before each catalytic reaction. THF was distilled over sodium/benzophenone. DMF was purchased from Fisher Chemical and used as received. Dichloromethane was distilled over calcium hydride. 1,3,5-Trimethoxybenzene was dried over night under vacuum and stored in a dessicator. Cesium carbonate was crushed in a mortar and pestle and dried overnight under vacuum (0.5 mbar) at 130 ^oC in a Schlenk flask prior to use. $Pd(PPh_3)_4$ was purchased from Sigma Aldrich and kept in the freezer. All starting materials were purchased from Combi-Blocks or Sigma Aldrich and used as received. *O*-benzoylhydroxylamines were synthesized following previous methods[1].

^1H and ^{13}C NMR were obtained on a Varian Mercury 300 or 400, Bruker Avance III 400 or an Agilent DD2 500 equipped with a 5mm Xses Cold Probe. Measurements were referenced to the solvent. NMR data is referenced as chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad), coupling constant (Hz), integration. HRMS were obtained on a JEOL AccuTOF-DART. Melting points were done on a Fisher-Johns Melting Point Apparatus and uncorrected. IR Spectra were obtained dissolved in $CHCl_3$ on a NaCl disk on a Shimadzu FTIR-8400S FT-IR spectrometer or by ATR.

Proposed Mechanism



General Procedures



General Procedure A: The 2-aminocarboxylic acid (10 mmol) was added to a 250 mL rb flask with 14 mL of conc. HCl and 14 mL of water. The suspension was cooled to 0 ºC followed by the addition of sodium nitrite (830 mg, 12 mmol, 1.2 equiv) in 5 mL of water. The reaction was stirred for 30 min at 0 ºC. Then KI (3.32 g, 20 mmol, 2 equiv) was added in 5 mL of water to the solution. The reaction was heated to 90 ºC for 90 minutes. The reaction was cooled and quenched with a saturated solution of sodium sulfite. It was then transferred to a 500 mL separatory funnel with ethyl acetate and acidifed with conc. HCl. The product was extracted with EtOAc (3 x 200 mL) then dried over magnesium sulfate and filtered. The filtrate was concentrated and used with no further purification.

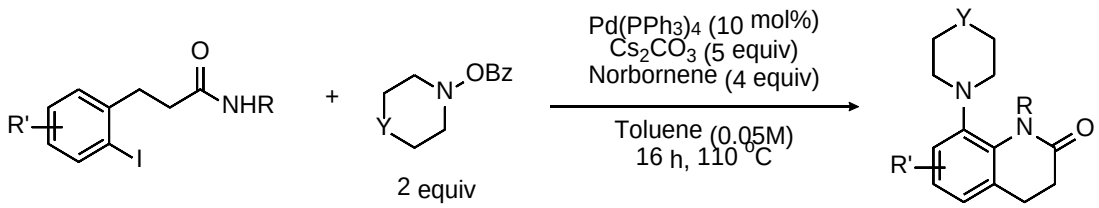
General Procedure B: The iodoacid (typically 10 mmol) was dissolved in THF (0.5M) at r.t. Trimethylborate (1.5 equiv) was added followed by a dropwise addition of borane-dimethylsufide complex (1.5 equiv). The reaction was stirred overnight at r.t. typically for 16 h. An extra equivalence of borane was added if starting material was observed by TLC. The reaction was quenched with methanol when the starting material was consumed by TLC. The crude was dried under reduced pressure. The crude was redissolved in methanol and dried again, repeating twice more. The crude solid was dissolved in EtOAc (100 mL) and washed with water (3 x 100 mL). The crude solid was purified by flash column chromatography if necessary. Followed literature procedure[2]

General Procedure C: The 2-iodobenzyl alcohol was dissolved in dichloromethane (0.2M) with silica gel (1 g/mmol). The slurry was stirred at r.t. followed by the addition of PDC (2 equiv). The reaction was stirred until the starting material was consumed by TLC typically 6 h. The crude was filtered through a silica gel pad with ethyl acetate and hexane. The crude aldehyde was purified if required by flash column chromatography in ethyl acetate and hexane.

General Procedure D: The 2-iodobenzaldehyde (typically 7-8 mmol) and Meldrum's acid (1 equiv) were added to a 9.5 dr vial. A premade solution of triethylamine (2.6 equiv) and formic acid (6 equiv) prepared at 0 ºC was added and the reaction was stirred at 65 ºC. DMF was added as needed to dissolve the starting material, no more than 3 mL. The reaction was stirred for 12 h. Then water (2 mL) was added and the reaction was stirred at 90 ºC until the Meldrum's acid was hydrolyzed by TLC, typically 6 h. The product was extracted with ethyl acetate (3 x 100 mL) from 1M HCl (100 mL) then partially concentrated and washed with water (4 x 100 mL). The organic layer was dried over magnesium sulfate and filtered. The filtrate was concentrated, and

the product was purified by flash column chromatography in a methanol/dichloromethane mixture.

General Procedure E: The acid (typically 1 mmol) was dissolved in DCM (0.5 M). CDI (1.5 equiv) was added and stirred at room temperature for 2 h. Then methylamine (33% wt. in EtOH, 8 equiv) was added and stirred at room temperature for 1 h. Then the reaction was diluted in ethyl acetate and washed with 1 M HCl (2 x 50 mL) followed by sat. $NaHCO_3$ (50 mL). The organic layer was dried over sodium sulfate, filtered, and concentrated. The crude was purified by flash column chromatography with mixtures of ethyl acetate and hexane.



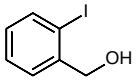
General Procedure F

Cesium carbonate was dried under vacuum (0.5 mbar) at 130 °C overnight in a Schlenk flask. The base was cooled to room temperature and kept under argon prior to use. The base was removed from the from the flask under inert gas flow and transferred to a scintillation vial which was kept in a 120 °C oven and cooled under argon. 2 Dram vials were kept in 120 °C oven and cooled under argon prior to use and during the weighing process. Cesium carbonate (326 mg, 1 mmol, 5 equiv) was weighed directly in to the vial. Then $Pd(PPh_3)_4$ (23 mg, 0.02 mmol, 10 mol%) was added. Then the amide substrate (0.2 mmol) followed by the *O*-benzoylhydroxyamine (0.4 mmol, 2 equiv) were added. In the case of liquid substrates or benozylhydroxyamines they were added first to the vial by directly weighing the liquid in to the reaction vial. The reaction vial was dried under vacuum (0.5 mbar) for 10 minutes then put back under argon. Then a dry solution of norbornene (75 mg, 4 equiv) in freshly distilled toluene (4 mL, 0.05 M) was added under argon. The Teflon cap was quickly placed on the vial under argon flow and sealed with Teflon tape. The reaction was stirred at room temperature for 10 minutes before being placed in a pre-heated oil bath at 110 °C stirring at 900 rpm. The stir rate was important for the reaction as at lower stir rates the cesium carbonate would occasionally aggregate on the bottom of the vial. After 16 h the reaction was cooled to room temperature then filtered through a celite pad. The reaction was dried under reduced pressure. The product was purified via flash column chromatography in the indicated solvent system then dried under vacuum to obtain the final product.

For reactions done on a 1 mmol scale the procedure was repeated using a 9.5 dr vial with cesium carbonate (1.63 g, 5 mmol, 5 equiv), $Pd(PPh_3)_4$ (115 mg, 0.1 mmol, 10 mol%), amide substrate (1 mmol), *O*-benzoylhydroxyamine (2 mmol, 2 equiv), norbornene (375 mg, 4 mmol, 4 equiv), and toluene (20 mL).

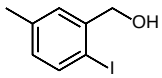
Characterization of benzyl alcohol and aldehyde precursors

(2-iodophenyl)methanol



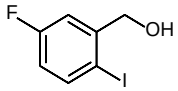
Synthesized by General Procedure B using 40 mmol of 2-iodobenzoic acid. Obtained white solid, (9.00 g, 96%). The alcohol was used with no further purification.

(2-iodo-5-methylphenyl)methanol



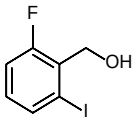
Synthesized by General Procedure B using 10 mmol of 2-iodo-5-methylbenzoic acid. Obtained oil, (2.06 g, 83%). The alcohol was used with no further purification.

(5-fluoro-2-iodophenyl)methanol



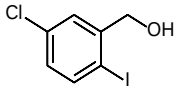
Synthesized by General Procedure B using 8 mmol of 4-fluoro-2-iodobenzoic acid, borane-dimethylsulfide complex (2.3 mL, 24 mmol, 3 equiv), and trimethylborate (2.68 mL, 24 mmol, 3 equiv). Obtained off-white solid, 1.95 g (96%). The alcohol was used with no further purification.

(2-fluoro-6-iodophenyl)methanol



Synthesized by General Procedure B using 8 mmol of 6-fluoro-2-iodobenzoic acid, borane-dimethylsulfide complex (2.3 mL, 24 mmol, 3 equiv), and trimethylborate (2.68 mL, 24 mmol, 3 equiv). Obtained yellow oil, 1.8 g (89%). The alcohol was used with no further purification.

(5-chloro-2-iodophenyl)methanol



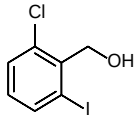
Synthesized by General Procedure A starting with 20 mmol of 6-chloro-2-aminobenzoic acid and continued to the next step with no further purification. Following General Procedure B using crude iodoacid with 40 mL of THF, borane-dimethylsulfide complex (2.85 mL, 30 mmol, 1.5 equiv), and trimethylborate (3.3 mL, 30 mmol, 1.5 equiv). After 6 h another 1 equiv of borane

was added. Crude alcohol was purified by flash column chromatography, 20% EtOAc/Hex. Obtained off-white solid, 4.35 g (81%). Spectroscopic data is consistent with literature.[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 2.5 Hz, 1H), 7.00 (dd, *J* = 8.4, 2.6 Hz, 1H), 4.64 (s, 2H), 2.03 (s, 1H).

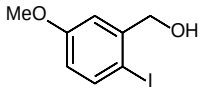
^{13}C NMR (100 MHz, $CDCl_3$) δ 144.3, 140.0, 135.0, 129.2, 128.3, 93.6, 68.8.

(2-chloro-6-iodophenyl)methanol



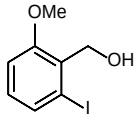
Synthesized by General Procedure A starting with 10 mmol of 6-chloro-2-aminobenzoic acid and continued to the next step with no further purification. Followed General Procedure B with borane-dimethylsulfide complex (2.3 mL, 20 mmol, 2 equiv), and trimethylborate (2.8 mL, 20 mmol, 2 equiv) and refluxed for 6 h. Obtained white solid, 1.9 g (71%). The alcohol was used with no further purification.

(2-iodo-5-methoxyphenyl)methanol



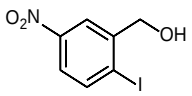
Synthesized by General Procedure B using 10 mmol of 2-iodo-5-methoxybenzoic acid. Obtained oil, (2.30 g, 87%). The alcohol was used with no further purification.

(2-iodo-6-methoxyphenyl)methanol



Synthesized by General Procedure A starting with 10 mmol of 6-methoxy-2-aminobenzoic acid and continued to the next step with no further purification. Followed General Procedure B with borane-dimethylsulfide complex (2.3 mL, 20 mmol, 2 equiv), and trimethylborate (2.8 mL, 20 mmol, 2 equiv) and refluxed for 6 h. Obtained clear oil, 1.94 g (73%). The alcohol was used with no further purification.

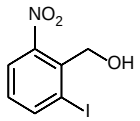
(2-iodo-5-nitrophenyl)methanol



Synthesized by General Procedure A starting with 10 mmol of 5-nitro-2-aminobenzoic acid and continued to the next step with no further purification. Followed General Procedure B with

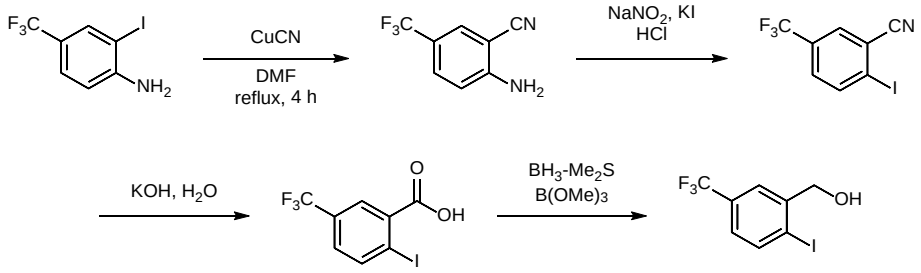
borane-dimethylsulfide complex (2.3 mL, 20 mmol, 2 equiv), and trimethylborate (2.8 mL, 20 mmol, 2 equiv) and refluxed for 6 h. Obtained yellow solid, 2.25 g (81%). The alcohol was used with no further purification.

(2-iodo-6-nitrophenyl)methanol



Synthesized by General Procedure A starting with 10 mmol of 6-nitro-2-aminobenzoic acid and continued to the next step with no further purification. Followed General Procedure B with borane-dimethylsulfide complex (2.3 mL, 20 mmol, 2 equiv), and trimethylborate (2.8 mL, 20 mmol, 2 equiv) and refluxed for 6 h. Obtained yellow solid, 1.20 g (43%). The alcohol was used with no further purification.

(2-iodo-5-(trifluoromethyl)phenyl)methanol



2-iodo-4-(trifluoromethyl)aniline (2.87 g, 10 mmol) was dissolved in DMF (20 mL). CuCN (1.15 g, 12.8 mmol, 1.28 eq) was added and the reaction was heated to reflux for 4 h. Cooled to r.t. then added water and extracted with ethyl acetate (3 x 100 mL). The organic extracts washed with H_2O (5 x 200 mL) then they were dried with sodium sulfate, filtered and dried under reduced pressure.

H_2O (14 mL) and HCl (14 mL, 12M) was added to the crude benzonitrile and cooled to 0 ^oC then and sodium nitrite (1.73 g, 25 mmol, 2.5 equiv) was added in 7 mL of water. The reaction was stirred for 30 min then KI (4.02 g, 24.2 mmol, 2.42 equiv) dissolved in water (7 mL) and added dropwise. The reaction was heated to 95 ^oC and stirred 4 h. The reaction was cooled to r.t. and quenched with aqueous sodium sulfite and extracted with ethyl acetate (3 x 100 mL). Dried organic extracts with sodium sulfate, filtered, and dried under reduced pressure.

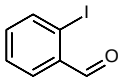
The crude iodobenzonitrile was suspended in H_2O (50 mL) and KOH (4 g, 71 mmol, 7.1 equiv) was added. The suspension was heated to reflux for 16 h. The solution was cooled to r.t., acidifed with 12 M HCl, and extracted with EtOAc (3 x 100 mL). The organic extracts were dried over sodium sulfate, filtered, and rotovapped.

The crude was redissolved in THF (20 mL) then trimethylborate (2.23 mL, 20 mmol, 2 equiv) and borane-dimethylsulfide (1.9 mL, 20 mmol, 2 equiv) was added. The reaction was stirred at r.t. for 8 h. The reaction was quenched with methanol then dried to a white solid. The crude

solid was purified with flash column chromatography with 30% EtOAc/Hex. Obtained white solid, 300 mg (10%). Spectroscopic data is consistent with literature.[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.1 Hz, 1H), 7.80 – 7.73 (m, 1H), 7.26 – 7.21 (m, 1H), 4.72 (d, *J* = 5.4 Hz, 2H), 2.11 (t, *J* = 5.9 Hz, 1H).

2-iodobenzaldehyde

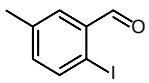


Synthesized by General Procedure C using 38.5 mmol of alcohol and PDC (28.2 g, 76.9 mmol, 2 equiv) with 38 g of silica gel. The product was purified by a short column, 20% EtOAc/Hex obtaining a yellow oil which solidified upon standing (8.3 g, 93%). Experimental spectra matched literature.[4]

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.91 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.32 (td, *J* = 7.6, 1.8 Hz, 1H).

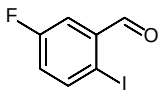
^{13}C NMR (100 MHz, $CDCl_3$) δ 195.8, 140.7, 135.5, 135.2, 130.3, 128.7, 100.7.

2-iodo-5-methylbenzaldehyde



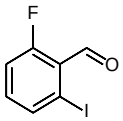
Synthesized by General Procedure C using 8.3 mmol of alcohol and PDC (6.24 g, 16.6 mmol, 2 equiv). The crude product was carried forward with no further purification after filtration assuming quantitative conversion.

5-fluoro-2-iodobenzaldehyde



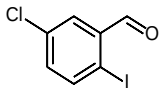
Synthesized by General Procedure C using 7.7 mmol of alcohol and PDC (7.46 g, 19.8 mmol, 2.57 equiv) with 20 g of silica gel. Obtained 1.97 g of oil (80%). The crude aldehyde was used with no further purification.

2-fluoro-6-iodobenzaldehyde



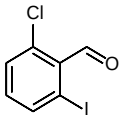
Synthesized by General Procedure C using 8.3 mmol of alcohol and PDC (6.21 g, 16.5 mmol, 2.32 equiv) with 17 g of silica gel. The crude aldehyde was used with no further purification. 1.96 g (95%) of a slightly yellow oil.

5-chloro-2-iodobenzaldehyde



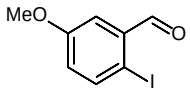
Synthesized by General Procedure C using 16.2 mmol of alcohol and PDC (11.9 g, 32.4 mmol, 2 equiv) with 16 g of silica gel. The crude aldehyde was used with no further purification. Obtained a yellow solid, 4.11 g (95%).

2-chloro-6-iodobenzaldehyde



Synthesized by General Procedure C using 7.1 mmol of alcohol and PDC (5.2 g, 14.2 mmol, 2 equiv) with 7 g of silica gel. The crude aldehyde was used with no further purification, obtained a yellow solid, 1.41 g (75%).

2-iodo-5-methoxybenzaldehyde

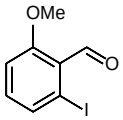


Synthesized by General Procedure C using 8.7 mmol of crude alcohol and PDC (6.57 g, 17.5 mmol, 2 equiv) with 9 g of silica gel. The aldehyde was purified with flash column chromatography with 20% EtOAc/Hex. Obtained a yellow solid, 1.90 g (83%). Spectroscopic data is consistent with literature.[5]

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.00 (s, 1H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.40 (d, *J* = 3.2 Hz, 1H), 6.90 (dd, *J* = 8.7, 3.2 Hz, 1H), 3.83 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 195.6, 160.2, 141.0, 135.6, 123.4, 113.5, 89.8, 55.6.

2-iodo-6-methoxybenzaldehyde



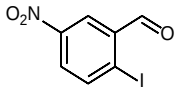
Synthesized by General Procedure C using 7.35 mmol of alcohol and PDC (5.4 g, 14.7 mmol, 2 equiv) with 7 g of silica gel. The aldehyde was purified with flash column chromatography with

20% EtOAc/Hex. 1.55 g of off white solid (84%). Spectroscopic data is consistent with literature[6].

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.17 (s, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.09 – 7.02 (m, 1H), 6.92 (d, *J* = 8.3 Hz, 1H), 3.84 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 161.9, 135.1, 133.8, 124.9, 112.0, 96.4, 56.1.

2-iodo-5-nitrobenzaldehyde

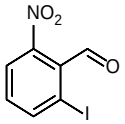


Synthesized by General Procedure C using 8.0 mmol of crude alcohol and PDC (6.07 g, 16.1 mmol, 2 equiv) with 8 g of silica gel. The aldehyde was purified with flash column chromatography with 20% EtOAc/Hex. Obtained a yellow solid, 2.05 (92%). Spectroscopic data is consistent with literature.[7]

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.10 (s, 1H), 8.64 (d, *J* = 2.7 Hz, 1H), 8.19 (d, *J* = 8.5 Hz, 1H), 8.11 (dd, *J* = 8.6, 2.7 Hz, 1H).

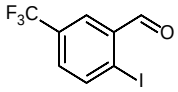
^{13}C NMR (126 MHz, $CDCl_3$) δ 193.3, 148.6, 142.0, 136.2, 128.6, 124.6, 107.2.

2-iodo-6-nitrobenzaldehyde



Synthesized by General Procedure C using 4.3 mmol of crude alcohol and PDC (3.16 g, 8.6 mmol, 2 equiv) with 4 g of silica gel. The crude aldehyde was used with no further purification assuming quantitative conversion.

2-iodo-5-(trifluoromethyl)benzaldehyde

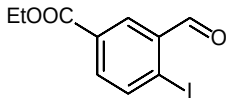


Synthesized by General Procedure C using 1 mmol of alcohol and PDC (0.73 g, 2 mmol, 2 equiv). with 1 g of silica gel. The crude aldehyde was purified with flash column chromatography with 10% EtOAc/Hex. Obtained oily residue, 260 mg (70%). Spectroscopic data is consistent with literature[8]

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 8.12 (s, 1H), 8.11 (d, *J* = 6.4 Hz, 1H), 7.57 – 7.49 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 194.2, 141.4, 135.7, 131.3, 126.9, 124.6, 121.9, 104.2.

ethyl 3-formyl-4-iodobenzoate



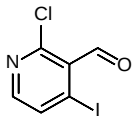
Following previous literature procedures [9] 4-iodo-3-methylbenzoic acid (2.65 g, 10.1 mmol) was dissolved in ethanol (20 mL) and H_2SO_4 (1 mL) was added. The solution was refluxed for 12 h. TLC indicated no remaining starting material. The reaction was diluted in EtOAc and washed with saturated $NaHCO_3$ (100 mL) and water (3 x 100 mL). The organic layer was dried over sodium sulfate, filtered, and concentrated. The crude ester was used without further purification.

The crude ester was dissolved in acetic acid (16 mL), acetic anhydride (17 mL) and sulfuric acid (2.5 mL). The reaction was cooled to 0 ºC and CrO_3 (3.0 g, 30 mmol, 3 equiv) was added slowly portionwise. The reaction was stirred at 0 ºC for 1 h and warmed to room temperature stirring for an additional 2 h. Water was added and the reaction was extracted with EtOAc (3 x 100 mL). The organic extracts were dried over sodium sulfate, and filtered through a silica gel plug. The filtrate was concentrated. The crude was dissolved in THF (20 mL) and 1 M HCl (10 mL) and refluxed for 12 h. The crude was diluted in ethyl acetate and water then washed with water (3 x 100 mL). The organic layer was dried over sodium sulfate, filtered, and concentrated. The product was purified with column chromatography 10% EtOAc/Hex. Obtained 320 mg (10% over two steps) of off-white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.40 (d, *J* = 2.2 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.85 (dd, *J* = 8.2, 2.2 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 194.7, 165.1, 141.1, 135.5, 135.4, 131.5, 131.1, 105.6, 61.7, 14.3.

2-chloro-4-iodonicotinaldehyde



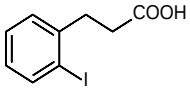
Diisopropylamine (2.24 mL, 16 mmol, 1.52 equiv) and THF (25 mL) was cooled to -78 ºC. nBuLi (6 mL, 15 mmol, 1.43 equiv) was added dropwise. Stirred for 10 min then added chloro-3-iodopyridine (2.51 g, 10.5 mmol) in THF (15 mL) slowly. Stirred for 3 h. Then added ethyl formate (2.17 mL, 27 mmol, 2.57 equiv) and stirred for 1.5 h at -78 ºC. Added 10 mL H_2O to quench reaction and warmed to r.t. Added ethyl acetate and washed with water (3 x 100 mL). Organic layer was dried over sodium sulfate, filtered, and concentrated. The crude was purified with flash column chromatography, 10% EtOAc/Hex. Obtained a yellow solid, 1.18 g (42%). Spectroscopic data consistent with literature [10]

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.20 (s, 1H), 8.07 (d, *J* = 5.2 Hz, 1H), 7.94 (d, *J* = 5.1 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 189.8, 152.9, 151.7, 136.1, 129.7, 108.1.

Characterization of 3-(2-iodophenyl)-propanoic acids

3-(2-iodophenyl)propanoic acid

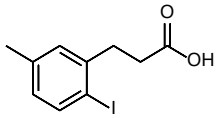


Synthesized by General Procedure D with 2-iodobenzaldehyde (7.44 g, 32.1 mmol), Meldrum's acid (4.62 g, 32.1 mmol, 1.0 equiv), formic acid (8.25 mL, 192 mmol, 6 equiv), and TEA (11.6 mL, 83 mmol, 2.6 equiv) with 10 mL of DMF. Isolated by flash column chromatography with 2% MeOH/DCM. Obtained white solid, 6.97 g (79%). Spectroscopic data is consistent with literature.[11]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.33 – 7.23 (m, 2H), 6.91 (ddd, *J* = 7.9, 6.7, 2.4 Hz, 1H), 3.06 (dd, *J* = 8.6, 7.1 Hz, 2H), 2.69 (dd, *J* = 8.5, 7.2 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 178.8, 142.6, 139.7, 129.5, 128.6, 128.4, 100.3, 35.6, 34.2.

3-(2-iodo-5-methylphenyl)propanoic acid



Synthesized by General Procedure D with 3-methyl-6-iodobenzaldehyde (2.04 g, 8.3 mmol), Meldrum's acid (1.2 g, 8.3 mmol, 1 equiv), formic acid (1.1 mL, 25 mmol, 3 equiv), and TEA (1.5 mL, 10.8 mmol, 1.3 equiv) with 2 mL of DMF. Isolated by flash column chromatography 2% MeOH/DCM. Obtained white solid, 1.21 g (50%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 1H), 7.11 (d, *J* = 1.9 Hz, 1H), 6.78 (dd, *J* = 8.0, 1.8 Hz, 1H), 3.10 – 3.02 (m, 2H), 2.77 – 2.64 (m, 2H), 2.32 (s, 3H).

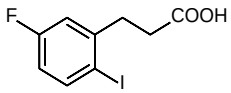
^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 142.4, 139.4, 138.6, 130.5, 129.4, 96.1, 35.5, 34.3, 20.9.

IR (ATR) 2970, 2937, 2918, 2878, 1774, 1735, 1692, 1435, 1360, 1336, 1309, 1221, 1209, 1194, 1073, 1007, 940, 806

HRMS (DART, M-1) Calculated for $C_{10}H_{10}IO_4$ 288.9726, found 288.9726

MP 106-108 °C

3-(5-fluoro-2-iodophenyl)propanoic acid



Synthesized by General Procedure D with 3-fluoro-6-iodobenzaldehyde (1.97 g, 6.7 mmol), Meldrum's acid (1.14 g, 6.7 mmol, 1 equiv), formic acid (2.03 mL, 40.2 mmol, 6 equiv), and TEA (2.86 mL, 17.4 mmol, 2.6 equiv) with 2 mL of DMF. Isolated by flash column chromatography 2% MeOH/DCM. Obtained white solid, 1.11 g (48%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 8.7, 5.7 Hz, 1H), 7.01 (dd, *J* = 9.5, 3.0 Hz, 1H), 6.70 (ddd, *J* = 8.7, 8.1, 3.0 Hz, 1H), 3.07 – 3.01 (m, 2H), 2.72 – 2.67 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.1, 163.1 (d, *J* = 247.8 Hz), 144.7 (d, *J* = 7.2 Hz), 140.6 (d, *J* = 7.9 Hz), 116.7 (d, *J* = 22.3 Hz), 115.7 (d, *J* = 21.6 Hz), 92.9 (d, *J* = 3.1 Hz), 35.5, 33.7.

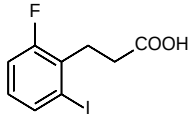
^{19}F NMR (377 MHz, $CDCl_3$) δ -113.81

IR (ATR) 3025, 2966, 2945, 2917, 2895, 2635, 2562, 1698, 1573, 1462, 1400, 1294, 1226, 1150, 1015, 876, 804

HRMS (DART, M-1) Calculated for $C_9H_7FIO_2$ 292.9475, found 292.9478

MP 137-138 °C

3-(2-fluoro-6-iodophenyl)propanoic acid



Synthesized by General Procedure D with 2-fluoro-6-iodobenzaldehyde (1.96 g, 7.85 mmol), Meldrum's acid (1.13 g, 7.85 mmol, 1 equiv), formic acid (2.02 mL, 47.1 mmol, 6 equiv), and TEA (2.84 mL, 20.4 mmo, 2.6 equiv) with 2 mL of DMF. Isolated by flash column chromatography 2% MeOH/DCM. Obtained white powder, 1.14 g (50%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.03 (ddd, *J* = 9.5, 8.3, 1.2 Hz, 1H), 6.92 (td, *J* = 8.1, 5.8 Hz, 1H), 3.15 (ddd, *J* = 10.4, 6.3, 2.3 Hz, 2H), 2.67 – 2.59 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.8, 160.1 (d, *J* = 250.1 Hz), 135.2 (d, *J* = 3.6 Hz), 130.5 (d, *J* = 17.2 Hz), 129.5 (d, *J* = 8.9 Hz), 115.6 (d, *J* = 23.1 Hz), 100.8 (d, *J* = 3.5 Hz), 32.9 (d, *J* = 1.1 Hz), 29.0 (d, *J* = 2.8 Hz).

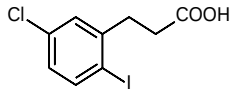
^{19}F NMR (377 MHz, $CDCl_3$) δ -111.10.

IR (ATR) 3032, 2973, 2947, 2781, 2706, 2629, 2563, 2513, 1695, 1598, 1567, 1442, 1406, 1311, 1239, 1224, 1176, 1154, 846, 774

HRMS (DART, M-1) Calculated for $C_9H_7FIO_2$ 292.9475, 292.9478

MP 168-170 °C

3-(5-chloro-2-iodophenyl)propanoic acid



Synthesized by General Procedure D with 3-chloro-6-iodobenzaldehyde (2.0 g, 7.5 mmol), Meldrum's acid (1.08 g, 7.5 mmol, 1 equiv), formic acid (4.12 mL, 96 mmol, 12.8 equiv), and TEA (6.7 mL, 4.8 mmol, 6.4 equiv) with no DMF. Isolated by flash column chromatography 2% MeOH/DCM, required two columns. Obtained white solid, 0.90 g (39%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 1H), 7.25 (d, *J* = 2.5 Hz, 1H), 6.92 (dd, *J* = 8.4, 2.5 Hz, 1H), 3.07 – 3.00 (m, 2H), 2.75 – 2.63 (m, 2H).

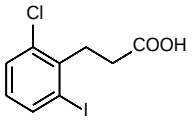
^{13}C NMR (126 MHz, $CDCl_3$) δ 178.1, 144.4, 140.6, 134.7, 129.5, 128.5, 97.2, 35.4, 33.8.

IR (ATR) 3074, 3049, 2960, 2940, 2628, 2554, 2509, 1689, 1576, 1427, 1407, 1289, 1198, 1097, 1012, 875, 813

HRMS (DART, M-1) Calculated for $C_9H_7ClIO_2$ 308.9179, found 308.9187

MP 140-142 °C

3-(2-chloro-6-iodophenyl)propanoic acid



Synthesized by General Procedure D with 2-chloro-6-iodobenzaldehyde (1.416 g, 5.4 mmol), Meldrum's acid (776 mg, 5.4 mmol, 1 equiv), formic acid (1.4 mL, 32.3 mmol, 6 equiv), and TEA (1.95 mL, 14.0 mmol, 2.6 equiv) with 2 mL of DMF. Isolated by flash column chromatography 2% MeOH/DCM. Obtained white solid, 1.30 g (78%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.64 (s, 1H), 7.75 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.36 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.85 (t, *J* = 7.9 Hz, 1H), 3.36 – 3.30 (m, 2H), 2.68 – 2.59 (m, 2H).

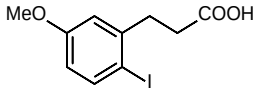
^{13}C NMR (126 MHz, $CDCl_3$) δ 178.6, 140.0, 138.4, 133.7, 123.0, 129.3, 101.0, 34.2, 32.0.

IR (ATR) 3052, 2971, 2950, 2937, 2912, 2703, 2627, 2560, 1694, 1553, 1426, 1407, 1297, 1217, 1134, 773, 716

HRMS (DART, M-1) Calculated for $C_9H_7ClIO_2$ 308.9179, found 308.9185

MP 187-188 °C

3-(2-iodo-5-methoxyphenyl)propanoic acid



Synthesized by General Procedure D with 3-methoxy-6-iodobenzaldehyde (1.9 g, 7.24 mmol), Meldrum's acid (1.04 g, 7.24 mmol, 1 equiv), formic acid (1.86 mL, 43.4 mmol, 6 equiv), and TEA (2.62 mL, 18.8 mmol, 2.6 equiv) with 2 mL of DMF. Isolated by flash column chromatography 2% MeOH/DCM. Obtained white solid, 1.45 g (65%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.44 (s, 1H), 7.68 (d, *J* = 8.7 Hz, 1H), 6.84 (d, *J* = 3.0 Hz, 1H), 6.53 (dd, *J* = 8.7, 3.0 Hz, 1H), 3.77 (s, 3H), 3.06 – 2.96 (m, 2H), 2.72 – 2.65 (m, 2H).

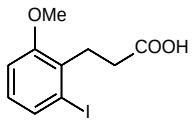
^{13}C NMR (126 MHz, $CDCl_3$) δ 178.6, 160.1, 143.6, 140.0, 115.6, 114.3, 88.6, 55.3, 35.7, 34.1.

IR (ATR) 3011, 2994, 2963, 2936, 2923, 2836, 1697, 1562, 1463, 1429, 1400, 1291, 1255, 1236, 1163, 1058, 949, 870, 807, 790

HRMS (DART, M-1) Calculated for $C_{10}H_{10}IO_3$ 304.9675, found 304.9680

MP 158-160 °C

3-(2-iodo-6-methoxyphenyl)propanoic acid



Synthesized by General Procedure D with 2-methoxy-6-iodobenzaldehyde (1.55 g, 6.2 mmol), Meldrum's acid (894 mg, 6.2 mmol, 1 equiv), formic acid (1.59 mL, 37.2 mmol, 6 equiv), and TEA (2.25 mL, 16.1 mmol, 2.6 equiv) with 2 mL of DMF. Isolated by flash column chromatography 2% MeOH/DCM. Obtained white solid, 1.12 g (59%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.70 (s, 1H), 7.42 (dd, *J* = 7.9, 1.1 Hz, 1H), 6.90 (t, *J* = 8.1 Hz, 1H), 6.82 (dd, *J* = 8.2, 1.1 Hz, 1H), 3.81 (s, 3H), 3.21 – 3.13 (m, 2H), 2.60 – 2.53 (m, 2H).

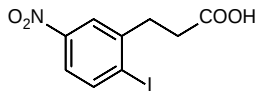
^{13}C NMR (126 MHz, $CDCl_3$) δ 179.5, 157.4, 131.4, 131.4, 129.0, 110.3, 101.6, 55.6, 32.7, 30.4.

IR (ATR) 3014, 2973, 2946, 2919, 2840, 2699, 2611, 2551, 2500, 1694, 1585, 1565, 1460, 1429, 1409, 1301, 1256, 1215, 1204, 1180, 1027, 919, 761

HRMS (DART, M-1) Calculated for $C_{10}H_{10}IO_3$ 304.9675, found 304.9677

MP 178-180 °C

3-(2-iodo-5-nitrophenyl)propanoic acid



Synthesized by General Procedure D with 3-nitro-6-iodobenzaldehyde (2.05 g, 7.4 mmol), Meldrum's acid (1.07 g, 7.4 mmol, 1 equiv), formic acid (1.9 mL, 44.4 mmol, 6 equiv), and TEA (2.68 mL, 19.2 mmol, 2.6 equiv) with 2 mL of DMF. Isolated by flash column chromatography 2% MeOH/DCM. Obtained yellow solid, 1.42 g (60%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.83 (s, 1H), 8.10 (d, *J* = 2.7 Hz, 1H), 8.03 (d, *J* = 8.6 Hz, 1H), 7.77 (dd, *J* = 8.6, 2.7 Hz, 1H), 3.16 (t, *J* = 7.7 Hz, 2H), 2.76 (t, *J* = 7.7 Hz, 2H).

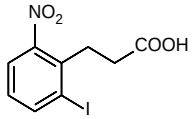
^{13}C NMR (126 MHz, $CDCl_3$) δ 177.8, 148.3, 144.6, 140.7, 123.7, 122.7, 108.5, 35.5, 33.4.

IR (ATR) 3098, 3039, 2942, 2918, 2855, 2706, 2629, 1699, 1515, 1431, 1338, 1303, 1276, 1216, 1015, 892, 813, 736

HRMS (DART, M-1) Calculated for $C_9H_7INO_4$ 319.9420, found 319.9420

MP 190-194 °C

3-(2-iodo-6-nitrophenyl)propanoic acid



Synthesized by General Procedure D with 2-nitro-6-iodobenzaldehyde (1.08 g, 4.3 mmol), Meldrum's acid (623 mg, 4.3 mmol, 1 equiv), formic acid (1.11 mL, 26.0 mmol, 6 equiv), and TEA (1.56 mL, 11.25 mmol, 2.6 equiv) with 2 mL of DMF. Isolated by flash column chromatography 2% MeOH/DCM. Obtained yellow solid, 416 mg (30%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.9 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 3.28 – 3.17 (m, 2H), 2.92 – 2.76 (m, 2H).

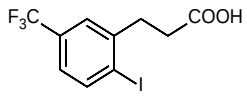
^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 150.6, 144.0, 136.3, 129.0, 124.6, 102.8, 32.7, 32.6.

IR (ATR) 3079, 2918, 2704, 2628, 2559, 2511, 1694, 1522, 1432, 1406, 1349, 1293, 1219, 1080, 901, 861, 678, 799, 743, 697

HRMS (DART, M+1) Calculated for $C_9H_9INO_4$ 321.9576, found 321.9579

MP 185-186 °C

3-(2-iodo-5-(trifluoromethyl)phenyl)propanoic acid, AW-11-49



Synthesized by General Procedure D with 3-trifluoromethyl-6-iodobenzaldehyde (261 mg, 0.7 mmol), Meldrum's acid (105 mg, 0.7 mmol, 1 equiv), formic acid (0.18 mL, 4.4 mmol, 6 equiv), and TEA (0.26 mL, 1.9 mmol, 2.6 equiv) with 1 mL of DMF. Isolated by flash column chromatography 2% MeOH/DCM. Obtained white solid, 180 mg (75%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.2 Hz, 1H), 7.50 (s, 1H), 7.17 (d, *J* = 8.2 Hz, 1H), 3.12 (t, *J* = 7.8 Hz, 2H), 2.74 – 2.70 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.1, 143.7, 140.2, 131.1 (q, *J* = 32.8 Hz), 126.0 (q, *J* = 3.8 Hz), 124.8 (q, *J* = 3.7 Hz), 123.8 (q, *J* = 272.3 Hz), 104.4 (q, *J* = 1.7 Hz), 35.5, 33.7.

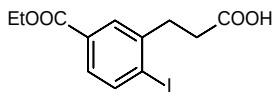
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.92.

IR (ATR) 3032, 2926, 2627, 2575, 1698, 1600, 1406, 1329, 1222, 1161, 1120, 1082, 1013, 892, 824, 751

HRMS (DART, M-1) Calculated for $C_{10}H_7F_3IO_2$ 342.9443, found 342.9450

MP 112-114 °C

3-(5-(ethoxycarbonyl)-2-iodophenyl)propanoic acid, AW-11-50



Synthesized by General Procedure D with ethyl 3-formyl-4-iodobenzoate (284 mg, 0.8 mmol), Meldrum's acid (113 mg, 0.7 mmol, 1 equiv), formic acid (0.20 mL, 4.7 mmol, 6 equiv), and TEA (0.28 mL, 1.9 mmol, 2.6 equiv) with 1 mL of DMF. Isolated by flash column chromatography 2% MeOH/DCM. Obtained white solid, 200 mg (72%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 10.9 Hz, 2H), 7.90 (s, 1H), 7.55 (dd, *J* = 8.2, 2.1 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.16 – 3.08 (m, 2H), 2.75 – 2.69 (m, 2H), 1.39 (t, *J* = 7.1 Hz, 3H).

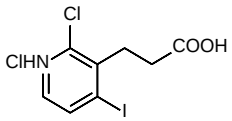
^{13}C NMR (126 MHz, $CDCl_3$) δ 178.1, 166.1, 143.1, 139.9, 130.9, 123.0, 128.9, 106.3, 61.3, 35.5, 33.9, 14.3.

IR (ATR) 2988, 2943, 2913, 2698, 2626, 2553, 2688, 1591, 1401, 1286, 1247, 1193, 1105, 1102, 942, 756

HRMS (DART, M-1) Calculated for $C_{12}H_{12}IO_4$ 346.9780, found 346.9787

MP 158-160 °C

3-(2-chloro-4-iodopyridin-3-yl)propanoic acid HCl salt`



Synthesized by General Procedure D with 2-chloro-4-iodonicotinaldehyde (1.0 g, 3.8 mmol), Meldrum's acid (545 mg, 3.8 mmol, 1 equiv), formic acid (0.97 mL, 22.7 mmol, 6 equiv), and TEA (1.37 mL, 9.8 mmol, 2.6 equiv) with 2 mL of DMF. Isolated by flash column chromatography 5% MeOH/DCM. Obtained slightly yellow solid as the HCl salt of the product, 293 mg (22%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.89 (d, *J* = 5.1 Hz, 1H), 7.87 (d, *J* = 5.1 Hz, 1H), 3.33 (s, 1H), 3.13 – 3.07 (m, 2H), 2.44 – 2.38 (m, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 173.21, 149.41, 148.36, 137.64, 134.84, 115.03, 33.82, 32.02.

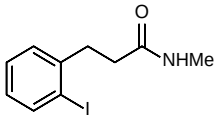
IR (ATR) 3072, 2951, 2918, 2500, 1718, 1556, 1531, 1428, 1367, 1267, 1210, 1170, 1127, 1007, 839, 786, 736

MP 210-212 °C

HRMS (M+1) Calculated for $C_8H_8ClINO_2$ 311.9288, found 311.9287

Characterization of substrates

3-(2-iodophenyl)-N-methylpropanamide (1a)

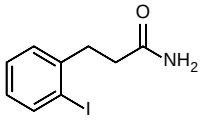


Synthesized by General Procedure E with 3-(2-iodophenyl)propanoic acid (2.07 g, 7.5 mmol), CDI (1.82 g, 11.3 mmol, 1.5 equiv), methylamine (7.5 mL, 60 mmol, 8 equiv), and DCM (15 mL). The product was purified by flash column chromatography with 60% EtOAc/Hex. The product appeared as a white solid, 1.86 g (86%). Spectroscopic data is consistent with literature[12]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.27 – 7.22 (m, 2H), 6.87 (ddd, *J* = 7.9, 5.6, 3.4 Hz, 1H), 5.64 (s, 1H), 3.09 – 3.00 (m, 2H), 2.77 (d, *J* = 4.8 Hz, 3H), 2.47 – 2.41 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.2, 143.4, 139.5, 129.7, 128.5, 128.6, 100.2, 36.7, 26.3.

3-(2-iodophenyl)propenamide (1b)

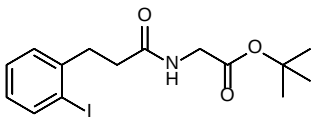


3-(2-iodophenyl)propanoic acid (1.1 g, 4 mmol) was dissolved in DCM (16 mL). Oxalyl chloride was added (0.48 mL, 5.6 mmol, 1.4 equiv) was added followed by DMF (0.1 mL). The reaction was stirred at r.t. for 12 h the dried under reduced pressure. The acid chloride was dissolved in THF (20 mL) then 10 equiv of NH_4OH (18 M) was added and the reaction was stirred for 6 h. The reaction was diluted in EtOAc and washed with 1 M HCl (2 x 100 mL) then sat. $NaHCO_3$ (100 mL). The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude was purified by flash column chromatography (EtOAc/Hex/MeOH 80:18:2). Obtained white solid (775 mg, 71%). Spectroscopic data is consistent with literature[12]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dt, *J* = 7.9, 0.8 Hz, 1H), 7.30 – 7.25 (m, 2H), 6.94 – 6.83 (m, 1H), 5.76 (s, 1H), 5.50 (s, 1H), 3.11 – 3.03 (m, 2H), 2.56 – 2.47 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 143.1, 139.6, 129.7, 128.9, 128.3, 100.2, 36.4, 36,0.

tert-butyl (3-(2-iodophenyl)propanoyl)glycinate (1c)



Synthesized by General Procedure E with 3-(2-iodophenyl)propanoic acid (552 mg, 2.0 mmol) and CDI (486 mg, 3 mmol, 1.5 equiv) were stirred in DCM (7 mL) for 1 h. Then tert-butyl glycinate hydrochloride (369 mg, 2.2 mmol, 1.1 equiv) and TEA (0.31 mL, 2.2 mmol, 1.1 equiv)

were added and the reaction was stirred for 2 h. The product was purified by flash column chromatography with 20% EtOAc/Hex. The product appeared as an oil, 453 mg (58%).

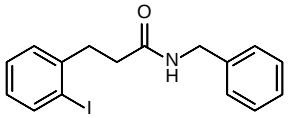
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.7 Hz, 1H), 7.28 (m, 2H), 6.96 – 6.86 (m, 1H), 6.03 (s, 1H), 3.95 (d, *J* = 4.8 Hz, 2H), 3.16 – 3.01 (m, 2H), 2.61 – 2.51 (m, 2H), 1.49 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 169.1, 143.3, 139.6, 129.7, 128.6, 128.2, 100.3, 82.4, 42.1, 36.6, 36.5, 28.1.

IR (ATR) 3314, 2975, 2936, 1732, 1640, 1530, 1390, 1367, 1237, 1154, 1013, 1004, 844, 737

HRMS (DART, M+1) Calculated for $C_{15}H_{21}INO_3$ 390.0566, found 390.0564

N-benzyl-3-(2-iodophenyl)propenamide (1d)



Synthesized by General Procedure E with 3-(2-iodophenyl)propanoic acid (552 mg, 2.0 mmol) and CDI (486 mg, 3 mmol, 1.5 equiv) were stirred in DCM (7 mL) for 1 h. Then benzylamine (0.33 mL, 3 mmol, 1.5 equiv) and the reaction was stirred for 2 h. The product was purified by flash column chromatography with 50% EtOAc/Hex. The product appeared as white solid, 675 mg (92%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.79 (m, 1H), 7.33 – 7.22 (m, 5H), 7.18 (ddt, *J* = 7.3, 1.3, 0.6 Hz, 2H), 6.93 – 6.85 (m, 1H), 5.73 (s, 1H), 4.41 (d, *J* = 5.7 Hz, 2H), 3.14 – 3.07 (m, 2H), 2.57 – 2.47 (m, 2H).

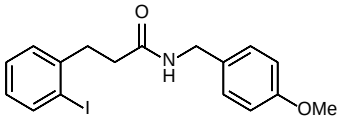
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 143.2, 139.5, 138.1, 129.9, 128.7, 128.6, 128.2, 127.7, 127.5, 100.2, 43.6, 36.8, 36.7.

IR (ATR) 3292, 1635, 1544, 1452, 1409, 1293, 1216, 1013, 751, 696

HRMS (DART, M+1) Calculated for $C_{16}H_{17}INO$ 366.0355, found 366.0353

MP 186-187 °C

3-(2-iodophenyl)-N-(4-methoxybenzyl)propenamide (1e)



3-(2-iodophenyl)propanoic acid (276 mg, 1 mmol) was dissolved in DCM (7.5 mL). EDC (288 mg, 1.5 mmol, 1.5 equiv) was added followed by 4-methoxybenzylamine (0.2 mL, 1.5 mmol, 1.5 equiv) and TEA (0.21 mL, 1.5 mmol, 1.5 equiv). The reaction was stirred at r.t. for 12 h. The reaction was diluted in EtOAc and washed with 1 M HCl (2 x 100 mL) then sat. $NaHCO_3$ (100 mL). The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude was purified by flash column chromatography, 30% EtOAc/Hex. Obtained white solid (219 mg, 55%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.7 Hz, 1H), 7.29 – 7.22 (m, 2H), 7.15 – 7.08 (m, 3H), 6.89 (ddd, *J* = 7.9, 5.1, 3.9 Hz, 1H), 6.85 – 6.78 (m, 2H), 5.69 (s, 1H), 4.33 (d, *J* = 5.6 Hz, 2H), 3.78 (s, 3H), 3.11 – 3.03 (m, 2H), 2.52 – 2.46 (m, 2H).

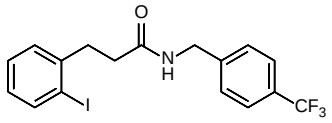
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 159.0, 143.3, 139.5, 130.2, 129.9, 129.1, 128.5, 128.2, 114.0, 100.2, 55.3, 43.1, 36.8, 36.7.

IR (ATR) 3289, 3046, 2933, 2834, 1642, 1613, 1555, 1514, 1464, 1451, 1434, 1298, 1254, 1226, 1174, 1032, 1014, 812, 742

HRMS (DART, M+1) Calculated for $C_{17}H_{19}INO_2$ 396.0461 found 396.0463

MP 160-162 °C

3-(2-iodophenyl)-N-(4-(trifluoromethyl)benzyl)propenamide (1f)



3-(2-iodophenyl)propanoic acid (458 mg, 1.66 mmol) was dissolved in DCM (15 mL). EDC (651 mg, 3.4 mmol, 2 equiv) was added followed by 4-trifluoromethylbenzylamine (0.48 mL, 3.4 mmol, 2 equiv) and TEA (0.84 mL, 6 mmol, 3.6 equiv). The reaction was stirred at r.t. for 12 h. The reaction was diluted in EtOAc and washed with 1 M HCl (2 x 100 mL) then sat. $NaHCO_3$ (100 mL). The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude was purified by flash column chromatography, 20 -> 40% EtOAc/Hex. Obtained white solid (327 mg, 38%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.28 – 7.22 (m, 4H), 6.95 – 6.87 (m, 1H), 5.88 (s, 1H), 4.45 (d, *J* = 6.0 Hz, 2H), 3.14 – 3.07 (m, 2H), 2.59 – 2.51 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.6, 143.0, 142.3, 139.6, 130.0, 129.7 (q, *J* = 32.4 Hz), 128.6, 128.3, 127.8, 125.5 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 272.0 Hz), 100.2, 43.0, 36.7, 36.6.

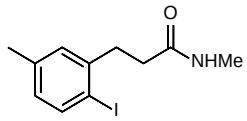
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.51.

IR (ATR) 3277, 3074, 1639, 1544, 1418, 1326, 1158, 1121, 1107, 1066, 1013, 832, 752, 721

HRMS (DART, M+1) Calculated for $C_{17}H_{16}F_3INO$ 434.0229 found 434.0237

MP 165-167 °C

3-(2-iodo-5-methylphenyl)-N-methylpropanamide (1g)



Synthesized by General Procedure E with 3-(5-methyl-2-iodophenyl)propanoic acid (290 mg, 1.0 mmol), CDI (243 mg, 1.5 mmol, 1.5 equiv), methylamine (1 mL, 8 mmol, 8 equiv), and DCM (3

mL). The product was purified by flash column chromatography with 50% EtOAc/Hex. The product appeared as a white solid, 163 mg (54%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 1.9 Hz, 1H), 6.72 (dd, *J* = 8.0, 2.2 Hz, 1H), 5.38 (s, 1H), 3.05 – 2.99 (m, 2H), 2.79 (d, *J* = 4.8 Hz, 3H), 2.46 – 2.41 (m, 2H), 2.26 (s, 3H).

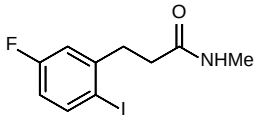
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.3, 143.0, 139.1, 138.5, 130.6, 129.1, 96.0, 36.9, 36.6, 26.3, 20.8.

IR (ATR) 3297, 2933, 1662, 1638, 1561, 1414, 1379, 1234, 1228, 1010, 805

HRMS (DART, M+1) Calculated for $C_{10}H_{15}INO$ 304.0198, found 304.0196

MP 155-158 °C

3-(5-fluoro-2-iodophenyl)-N-methylpropanamide (1h)



Synthesized by General Procedure E with 3-(5-fluoro-2-iodophenyl)propanoic acid (294 mg, 1.0 mmol), CDI (243 mg, 1.5 mmol, 1.5 equiv), methylamine (1 mL, 8 mmol, 8 equiv), and DCM (3 mL). The product was purified by flash column chromatography with 50% EtOAc/Hex. The product appeared as a white solid, 250 mg (81%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 8.7, 5.7 Hz, 1H), 7.01 (dd, *J* = 9.5, 3.0 Hz, 1H), 6.67 (td, *J* = 8.4, 3.0 Hz, 1H), 5.41 (s, 1H), 3.09 – 3.01 (m, 2H), 2.80 (d, *J* = 4.8 Hz, 3H), 2.51 – 2.40 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.9, 163.0 (d, *J* = 247.8 Hz), 145.6 (d, *J* = 7.2 Hz), 140.4 (d, *J* = 7.8 Hz), 116.7 (d, *J* = 22.1 Hz), 115.5 (d, *J* = 21.7 Hz), 92.9 (d, *J* = 3.1 Hz), 36.6, 36.2, 26.4.

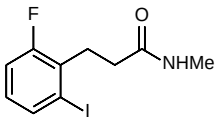
^{19}F NMR (377 MHz, $CDCl_3$) δ -113.90.

IR (ATR) 3298, 3057, 2966, 2936, 1634, 1566, 1461, 1403, 1224, 1158, 1018, 797

HRMS (DART, M+1) Calculated for $C_{10}H_{12}FINO$ 307.9948, found 307.9940

MP 162-165 °C

3-(2-fluoro-6-iodophenyl)-N-methylpropanamide (1i)



Synthesized by General Procedure E with 3-(2-fluoro-6-iodophenyl)propanoic acid (294 mg, 1.0 mmol), CDI (243 mg, 1.5 mmol, 1.5 equiv), methylamine (1 mL, 8 mmol, 8 equiv), and DCM (3 mL). The product was purified by flash column chromatography with 50% EtOAc/Hex. The product appeared as a white solid, 258 mg (84%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.02 (ddd, *J* = 9.5, 8.3, 1.2 Hz, 1H), 6.90 (td, *J* = 8.1, 5.7 Hz, 1H), 5.44 (s, 1H), 3.14 (ddd, *J* = 10.7, 5.9, 2.3 Hz, 2H), 2.83 (d, *J* = 4.8 Hz, 3H), 2.45 – 2.36 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.9, 160.0 (d, *J* = 250.1 Hz), 135.1 (d, *J* = 3.6 Hz), 131.3 (d, *J* = 17.3 Hz), 129.3 (d, *J* = 8.8 Hz), 115.6 (d, *J* = 23.2 Hz), 100.9 (d, *J* = 3.6 Hz), 35.3, 30.1 (d, *J* = 2.7 Hz), 26.3

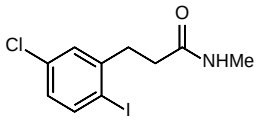
^{19}F NMR (377 MHz, $CDCl_3$) δ -111.08.

IR (ATR) 3296, 3106, 2973, 2942, 2878, 1638, 1567, 1440, 1410, 1237, 1174, 1153, 1001, 849, 777, 770

HRMS (DART, M+1) Calculated for $C_{10}H_{12}FINO$ 307.9948, found 307.9943

MP 182-184 °C

3-(5-chloro-2-iodophenyl)-N-methylpropanamide (1j)



Synthesized by General Procedure E with 3-(5-chloro-2-iodophenyl)propanoic acid (311 mg, 1.0 mmol), CDI (243 mg, 1.5 mmol, 1.5 equiv), methylamine (1 mL, 8 mmol, 8 equiv), and DCM (3 mL). The product was purified by flash column chromatography with 50% EtOAc/Hex. The product appeared as a white solid, 288 mg (89%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.4 Hz, 1H), 7.24 (d, *J* = 2.5 Hz, 1H), 6.89 (dd, *J* = 8.4, 2.6 Hz, 1H), 5.53 (s, 1H), 3.06 – 2.99 (m, 2H), 2.79 (d, *J* = 4.7 Hz, 3H), 2.47 – 2.40 (m, 2H).

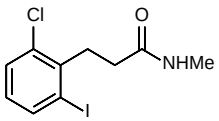
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.7, 145.2, 140.4, 134.79, 129.6, 128.3, 128.3, 97.2, 36.5, 36.3, 26.4.

IR (ATR) 3304, 2923, 1645, 1552, 1459, 1383, 1310, 1244, 1095, 1011, 868, 806

HRMS (DART, M+1) Calculated for $C_{10}H_{12}ClINO$ 323.9652 found 323.9652

MP 184-186 °C

3-(2-chloro-6-iodophenyl)-N-methylpropanamide (1k)



Synthesized by General Procedure E with 3-(2-chloro-6-iodophenyl)propanoic acid (310 mg, 1.0 mmol), CDI (243 mg, 1.5 mmol, 1.5 equiv), methylamine (1 mL, 8 mmol, 8 equiv), and DCM (3 mL). The product was purified by flash column chromatography with 60% EtOAc/Hex. The product appeared as a white solid, 265 mg (82%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.33 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.81 (t, *J* = 8.0 Hz, 1H), 5.61 (s, 1H), 3.34 – 3.27 (m, 2H), 2.84 (d, *J* = 4.8 Hz, 3H), 2.42 – 2.36 (m, 2H).

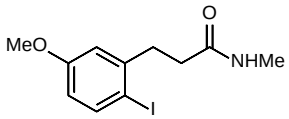
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.9, 140.8, 138.4, 133.6, 129.9, 129.0, 101.1, 35.4, 34.4, 26.4.

IR (ATR) 3300, 2974, 2950, 2936, 1639, 1571, 1552, 1424, 1406, 1233, 1130, 1052, 767, 717

HRMS (DART, M+1) Calculated for $C_{10}H_{12}ClINO$ 323.9652, found 323.9645

MP 216-219 °C

3-(2-iodo-5-methoxyphenyl)-N-methylpropanamide (1l)



Synthesized by General Procedure E with 3-(5-methoxy-2-iodophenyl)propanoic acid (306 mg, 1.0 mmol), CDI (243 mg, 1.5 mmol, 1.5 equiv), methylamine (1 mL, 8 mmol, 8 equiv), and DCM (3 mL). The product was purified by flash column chromatography with 70% EtOAc/Hex. The product appeared as a white solid, 272 mg (85%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.7 Hz, 1H), 6.83 (d, *J* = 3.0 Hz, 1H), 6.50 (dd, *J* = 8.7, 3.0 Hz, 1H), 5.50 (s, 1H), 3.75 (s, 3H), 3.04 – 2.99 (m, 2H), 2.79 (d, *J* = 4.8 Hz, 3H), 2.46 – 2.41 (m, 2H).

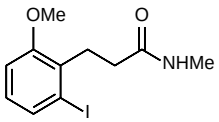
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.2, 160.1, 144.4, 139.9, 115.4, 114.4, 88.6, 55.4, 36.9, 36.8, 26.4.

IR (ATR) 3307, 3261, 3078, 2965, 2940, 1632, 1565, 1465, 1409, 1264, 1246, 1156, 1049, 1107, 874, 810

HRMS (DART, M+1) Calculated for $C_{11}H_{15}INO_2$ 320.0148 found 320.0159

MP 171-173 °C

3-(2-iodo-6-methoxyphenyl)-N-methylpropanamide (1m)



Synthesized by General Procedure E with 3-(2-iodo-6-methoxyphenyl)propanoic acid (306 mg, 1.0 mmol), CDI (243 mg, 1.5 mmol, 1.5 equiv), methylamine (1 mL, 8 mmol, 8 equiv), and DCM (3 mL). The product was purified by flash column chromatography with 70 -> 80% EtOAc/Hex. The product appeared as a white solid, 260 mg (82%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 7.8, 1.1 Hz, 1H), 6.87 (t, *J* = 8.0 Hz, 1H), 6.80 (dd, *J* = 8.3, 1.1 Hz, 1H), 5.65 (s, 1H), 3.79 (s, 3H), 3.15 – 3.09 (m, 2H), 2.81 (d, *J* = 4.8 Hz, 3H), 2.38 – 2.33 (m, 2H).

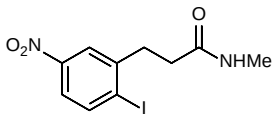
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 157.3, 132.1, 131.4, 128.8, 110.3, 101.7, 55.7, 35.2, 31.3, 26.4.

IR (ATR) 3269, 3093, 2936, 2833, 1638, 1563, 1456, 1445, 1256, 1029, 765

HRMS (DART, M+1) Calculated for $C_{11}H_{15}INO_2$ 320.0148, found 320.0146

MP 168-171 °C

3-(2-iodo-5-nitrophenyl)-N-methylpropanamide (1n)



Synthesized by General Procedure E with 3-(5-nitro-2-iodophenyl)propanoic acid (321 mg, 1.0 mmol), CDI (243 mg, 1.5 mmol, 1.5 equiv), methylamine (1 mL, 8 mmol, 8 equiv), and DCM (3 mL). The product was purified by flash column chromatography with 70% EtOAc/Hex. The product appeared as a white solid, 260 mg (78%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 2.8, 0.4 Hz, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 7.74 (dd, *J* = 8.7, 2.7 Hz, 1H), 5.46 (s, 1H), 3.22 – 3.14 (m, 2H), 2.82 (d, *J* = 4.9 Hz, 3H), 2.55 – 2.48 (m, 2H).

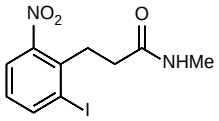
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 148.3, 145.6, 140.5, 123.6, 122.4, 108.5, 36.4, 35.8, 26.4.

IR (ATR), 3272, 3092, 1948, 2906, 1640, 1564, 1519, 1334, 1277, 1015, 819, 738

HRMS (DART, M+1) Calculated for $C_{10}H_{12}IN_2O_3$ 334.9893, found 334.9907

MP 215-217 °C

3-(2-iodo-6-nitrophenyl)-N-methylpropanamide (1o)



Synthesized by General Procedure E with 3-(2-iodo-6-nitrophenyl)propanoic acid (321 mg, 1.0 mmol), CDI (243 mg, 1.5 mmol, 1.5 equiv), methylamine (1 mL, 8 mmol, 8 equiv), and DCM (3 mL). The product was purified by flash column chromatography with 70% EtOAc/Hex. The product appeared as a white solid, 304 mg (91%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.75 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.07 (t, *J* = 8.0 Hz, 1H), 5.55 (s, 1H), 3.27 – 3.17 (m, 2H), 2.85 (d, *J* = 4.0 Hz, 3H), 2.65 – 2.53 (m, 2H).

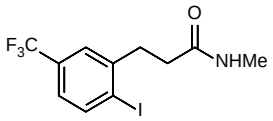
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 150.5, 144.0, 137.1, 128.7, 128.7, 124.4, 102.7, 35.1, 33.9, 26.4.

IR (ATR) 3297, 3110, 2937, 1636, 1572, 1520, 1365, 1346, 1291, 1233, 698

HRMS (DART, M+1) Calculated for $C_{10}H_{12}IN_2O_3$ 334.9893, found 334.9898

MP 227-229 °C

3-(2-iodo-5-(trifluoromethyl)phenyl)-N-methylpropanamide (1p)



Synthesized by General Procedure E with 3-(5-trifluoromethyl-2-iodophenyl)propanoic acid (160 mg, 0.48 mmol), CDI (116 mg, 0.72 mmol, 1.5 equiv), methylamine (0.72 mL, 5.75 mmol, 8 equiv), and DCM (2 mL). The product was purified by flash column chromatography with 50% EtOAc/Hex. The product appeared as a white solid, 141 mg (83%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.2 Hz, 1H), 7.48 (d, *J* = 2.2 Hz, 1H), 7.14 (dd, *J* = 8.3, 2.2 Hz, 1H), 5.46 (s, 1H), 3.16 – 3.11 (m, 2H), 2.80 (d, *J* = 4.8 Hz, 3H), 2.49 – 2.44 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.7, 144.6, 140.1, 131.0 (q, *J* = 32.7 Hz), 130.0, 126.0 (q, *J* = 3.8 Hz), 124.6 (q, *J* = 3.7 Hz), 123.8 (q, *J* = 272.4 Hz), 104.4 (q, *J* = 1.7 Hz), 36.6, 36.3, 26.3.

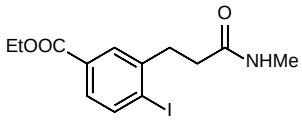
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.88.

IR (ATR) 3305, 3090, 2966, 2943, 1640, 1568, 1405, 1328, 1178, 1157, 1122, 1078, 1014, 889, 821

HRMS (DART, M+1) Calculated for $C_{11}H_{12}F_3INO$ 357.9916, found 357.9912

MP 182-184 °C

ethyl 4-iodo-3-(3-(methylamino)-3-oxopropyl)benzoate (1q)



Synthesized by General Procedure E with 3-(5-(ethoxycarbonyl)-2-iodophenyl)propanoic acid (170 mg, 0.49 mmol), CDI (119 mg, 0.73 mmol, 1.5 equiv), methylamine (0.73 mL, 5.86 mmol, 8 equiv), and DCM (2 mL). The product was purified by flash column chromatography with 70% EtOAc/Hex. The product appeared as a white solid, 116 mg (66%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 – 7.83 (m, 2H), 7.49 (dd, *J* = 8.2, 2.2 Hz, 1H), 5.79 (s, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.14 – 3.06 (m, 2H), 2.78 (d, *J* = 4.8 Hz, 3H), 2.48 – 2.38 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H).

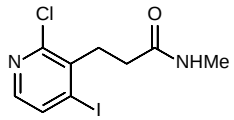
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.9, 166.1, 143.9, 139.7, 130.9, 129.9, 128.7, 106.4, 61.2, 36.6, 36.4, 26.4, 14.3.

IR (ATR) 3298, 2940, 1715, 1639, 1564, 1404, 1383, 1302, 1279, 1251, 1232, 1188, 1107, 1015, 757

HRMS (DART, M+1) Calculated for $C_{13}H_{17}INO_3$ 362.0253, found 362.0248

MP 170-171 °C

3-(2-chloro-4-iodopyridin-3-yl)-N-methylpropanamide (1r)



Synthesized by General Procedure E with 3-(2-chloro-4-iodopyridin-3-yl)propanoic acid hydrochloride (348 mg, 1.0 mmol), CDI (243 mg, 1.5 mmol, 1.5 equiv), methylamine (1 mL, 8 mmol, 8 equiv), and DCM (3 mL). The reaction was diluted in EtOAc and washed with water (2 x 100 mL). Then the organic layer was dried over sodium sulfate, filtered, and rotovapped. The product was purified by flash column chromatography with 70 -> 90% EtOAc/Hex. The product appeared as a white solid, 195 mg (60%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 5.1 Hz, 1H), 7.69 (d, *J* = 5.1 Hz, 1H), 5.56 (s, 1H), 3.34 – 3.28 (m, 2H), 2.85 (d, *J* = 4.8 Hz, 3H), 2.45 – 2.40 (m, 2H).

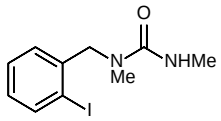
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 150.1, 147.5, 138.2, 134.2, 112.9, 34.6, 33.7, 26.5.

IR (ATR) 3294, 3099, 2948, 1643, 1548, 1529, 1445, 1367, 1235, 1141, 1082, 1002, 819, 738

HRMS (DART, M+1) Calculated for $C_9H_{11}ClIN_2O$ 324.9605, found 324.9616

MP 216-217 °C

1-(2-iodobenzyl)-1,3-dimethylurea (1s)



2-Iodobenzaldehyde (494 mg, 2 mmol) was dissolved in MeOH (4 mL) and methylamine (0.35 mL, 4 mmol, 2 equiv, 40% wt. soln in H_2O). The yellow solution was stirred for 1 h at rt then $NaBH_4$ (76 mg, 2 mmol, 1 equiv) was added. The reaction was stirred for 1 h at rt. Then 50 mL of H_2O was added and extracted in EtOAc (3 x 50 mL) then dried over $MgSO_4$, filtered, and concentrated. The crude amine was used for the next step with no further purification.

The amine was dissolved in 4 mL of dry CH_2Cl_2 (4 mL). Then CDI (486 mg, 3 mmol, 2 equiv) was added and the reaction was stirred for 2 h. Then methylamine (3 mL, 24 mmol, 8 equiv, 33% wt in EtOH) was added and stirred for 2 h. Then the reaction was quenched with H_2O and extracted with EtOAc (50 mL). The organic layer was washed with HCl (1M, 2 x 50 mL) then sat. $NaHCO_3$ (50 mL) and dried over magnesium sulfate. The product solution was filtered and rotovapped to dryness. The crude was purified with flash column chromatography with 70% -> 80% EtOAc with 1% MeOH. The product appeared as a white solid, 304 mg (50%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.27 (td, *J* = 7.5, 1.3 Hz, 1H), 7.12 – 7.06 (m, 1H), 6.95 – 6.84 (m, 1H), 4.39 (s, 2H), 4.27 (s, 1H), 2.86 (s, 3H), 2.76 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 139.6, 139.3, 129.0, 128.7, 127.5, 98.1, 57.5, 34.8, 27.8.

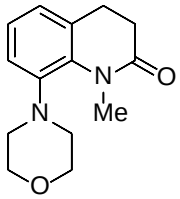
IR 3317, 2950, 2916, 2850, 1627, 1529, 1435, 1376, 1298, 1243, 1008, 744

HRMS (DART, M+1) Calculated for $C_{10}H_{14}IN_2O$ 305.0151, found 305.015

MP 166-168 °C

Characterization of products of the catalytic reaction

1-methyl-8-morpholino-3,4-dihydroquinolin-2(1H)-one (2a)



Synthesized by General Procedure F. The product was purified by flash column chromatography 50 -> 70% EtOAc/Hex. Product appeared as a white solid (38 mg, 77%) (1 mmol scale, 160 mg, 65%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (dd, *J* = 8.2, 7.3 Hz, 1H), 6.95 (dd, *J* = 8.2, 1.5 Hz, 1H), 6.90 (ddt, *J* = 7.3, 1.6, 0.9 Hz, 1H), 3.85 (b, 4H), 3.45 (s, 3H), 2.90 (b, 4H), 2.86 – 2.80 (m, 2H), 2.59 – 2.51 (m, 2H).

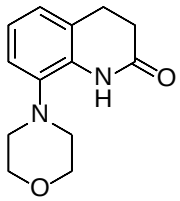
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 142.8, 134.2, 132.4, 124.7, 122.0, 118.0, 67.0, 50.9, 33.5, 32.7, 26.4.

IR (NaCl) 2957, 2911, 2853, 2822, 1678, 1589, 1481, 1464, 1452, 1360, 1240, 1117, 787, 772

HRMS (DART, M+1) Calculated for $C_{14}H_{19}N_2O_2$ 247.1447, found, 247.1452

MP 133-135 °C

8-morpholino-3,4-dihydroquinolin-2(1H)-one (2b)



Synthesized by General Procedure F. The product was purified by flash column chromatography 49:49:2 EtOAc/DCM/MeOH. Product appeared as an off white solid (16 mg, 35%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.07 (dd, *J* = 6.0, 3.3 Hz, 1H), 7.00 – 6.96 (m, 2H), 3.85 (b, 4H), 3.03 – 2.95 (m, 2H), 2.85 (b, 4H), 2.69 – 2.61 (m, 2H).

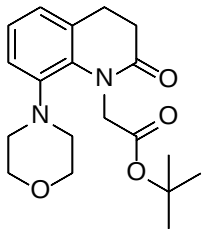
^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6, 138.7, 132.2, 124.4, 124.1, 123.0, 119.5, 67.3, 52.5, 30.7, 25.5.

IR (NaCl) 3252, 2949, 2918, 2859, 1684, 1487, 1472, 1452, 1404, 1371, 1298, 1260, 1238, 1196, 1111, 1009, 909, 853, 810, 748

HRMS (DART, M+1) Calculated for $C_{13}H_{17}N_2O_2$ 233.1290, found 233.1290

MP 161-164 °C

tert-butyl 2-(8-morpholino-2-oxo-3,4-dihydroquinolin-1(2H)-yl)acetate (2c)



Synthesized by General Procedure F. The product was purified by flash column chromatography 20 -> 30% EtOAc/Hex. Product appeared as oil which solidified upon standing (43 mg, 62%) (1mmol scale, 190 mg, 55%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (t, *J* = 7.7 Hz, 1H), 6.93 (m, 2H), 5.02 (s, 2H), 3.85 (b, 4H), 2.9 (b, 4H), 2.98 – 2.91 (m, 2H), 2.63 – 2.53 (m, 2H), 1.35 (s, 9H).

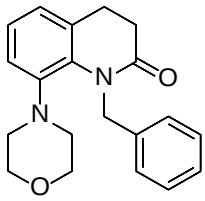
^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 168.3, 142.3, 133.4, 132.9, 125.0, 122.5, 117.9, 81.4, 66.9, 51.0, 45.7, 32.7, 28.0, 26.4.

IR (NaCl) 2976, 2853, 1740, 1682, 1589, 1478, 1462, 1452, 1425, 1368, 1298, 1285, 1179, 1157, 1117, 1001, 966, 791, 750

HRMS (DART, M+1) Calculated for $C_{19}H_{27}N_2O_4$ 347.1971, found 347.1971

MP 134-136 °C

1-benzyl-8-morpholino-3,4-dihydroquinolin-2(1H)-one (2d)



Synthesized by General Procedure F. The product was purified by flash column chromatography 40% EtOAc/Hex. Product appeared as oil which solidified upon drying, slightly brown solid (41 mg, 64%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 – 7.09 (m, 3H), 7.09 – 7.04 (m, 2H), 6.99 (dd, *J* = 8.2, 7.3 Hz, 1H), 6.89 – 6.82 (m, 2H), 5.61 (s, 2H), 3.91 (b, 4H), 2.94 (b, 4H), 2.78 – 2.69 (m, 2H), 2.63 – 2.54 (m, 2H).

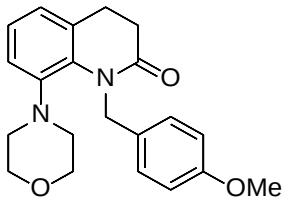
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 142.7, 138.5, 133.6, 131.8, 128.1, 127.7, 126.9, 124.9, 122.0, 117.5, 67.0, 50.7, 44.1, 33.1, 26.3.

IR (NaCl) 2957, 2853, 1674, 1589, 1478, 1452, 1360, 1238, 1179, 1119, 962, 789, 758, 741, 700

HRMS (DART, M+1) Calculated for $C_{20}H_{23}N_2O_2$ 323.1760, found 323.1759

MP 115-118 °C

1-(4-methoxybenzyl)-8-morpholino-3,4-dihydroquinolin-2(1H)-one (2e)



Synthesized by General Procedure F. The product was purified by flash column chromatography 40% EtOAc/Hex. Product appeared as oil (31 mg, 44%)

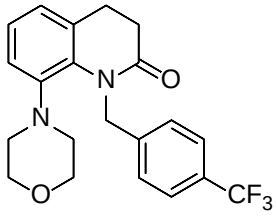
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 – 6.96 (m, 3H), 6.87 (dd, *J* = 8.3, 1.5 Hz, 1H), 6.85 – 6.80 (m, 1H), 6.67 (d, *J* = 8.7 Hz, 2H), 5.54 (s, 2H), 3.92 (b, 4H), 3.71 (s, 3H), 3.04 (b, 4H), 2.71 – 2.65 (m, 2H), 2.59 – 2.51 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 158.5, 142.7, 133.8, 131.7, 130.7, 129.1, 124.9, 121.9, 117.3, 113.5, 67.0, 55.1, 50.6, 43.3, 33.2, 26.3.

IR (NaCl) 2959, 2957, 2853, 1678, 1663, 1649, 1589, 1512, 1479, 1460, 1377, 1362, 1300, 1288, 1240, 1175, 1119, 1032, 995, 963, 789, 750

HRMS (DART, M+1) Calculated for $C_{21}H_{25}N_2O_3$ 353.1865, found 353.1867

8-morpholino-1-(4-(trifluoromethyl)benzyl)-3,4-dihydroquinolin-2(1H)-one (2f)



Synthesized by General Procedure F. The product was purified by flash column chromatography 15% EtOAc/DCM. Product appeared as oil (33 mg, 42%).

^{1}H NMR (500 MHz, $CDCl_3$)) δ 7.42 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.03 (dd, *J* = 8.2, 7.3 Hz, 1H), 6.89 (m, 2H), 5.66 (s, 2H), 3.90 (b, 4H), 2.95 (b, 4H), 2.78 – 2.72 (m, 2H), 2.64 – 2.55 (m, 2H).

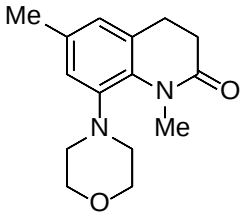
^{13}C NMR (126 MHz, $CDCl_3$)) δ 172.7, 142.6 (q, *J* = 1.4 Hz), 142.5, 133.4, 131.6, 129.1 (q, *J* = 32.4 Hz), 127.9, 125.2, 125.1 (q, *J* = 3.8 Hz), 122.3, 124.1 (q, *J* = 272.0 Hz), 117.7, 67.0, 50.8, 43.8, 32.9, 26.3.

^{19}F NMR (377 MHz, $CDCl_3$) δ -62.48.

IR (NaCl) 2961, 2853, 1674, 1618, 1589, 1479, 1452, 1360, 1325, 1163, 1121, 1067

HRMS (DART, M+1) Calculated for $C_{21}H_{22}F_3N_2O_2$ 391.1633, found 391.1633

1,6-dimethyl-8-morpholino-3,4-dihydroquinolin-2(1H)-one (2g)



Synthesized by General Procedure F. The product was purified by flash column chromatography 50% EtOAc/Hex. Product appeared as oil which solidified after standing overnight (38 mg, 73%), product coeluted with 3% impurity, spectroscopically pure sample obtained after second column in 1% MeOH/DCM.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74 (s, 1H), 6.72 (s, 1H), 3.84 (b, 4H), 3.44 (s, 3H), 2.89 (b, 4H), 2.81 – 2.76 (m, 2H), 2.58 – 2.49 (m, 2H), 2.30 (s, 3H).

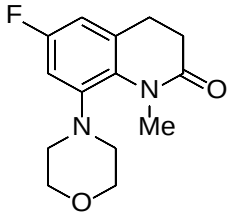
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 142.5, 134.4, 132.2, 131.8, 122.8, 118.5, 67.0, 50.9, 33.4, 32.8, 26.5, 21.0.

IR (NaCl) 2955, 2853, 1674, 1589, 1481, 1452, 1360, 1294, 1236, 1192, 1117, 995, 877, 752

HRMS (DART, M+1) Calculated for $C_{15}H_{21}N_2O_2$ 261.1603, found 261.1603

MP 101-103 °C

6-fluoro-1-methyl-8-morpholino-3,4-dihydroquinolin-2(1H)-one (2h)



Synthesized by General Procedure F reaction run at 120 °C, after 16 h at 110 °C starting material remaining. The product was purified by flash column chromatography 40% EtOAc/Hex, coeluted with cyclobutane byproduct (20% impurity). Second column 0.5% MeOH/DCM. Product appeared as a white solid, 21 mg (40%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.65 (dd, *J* = 10.6, 2.8 Hz, 1H), 6.63 – 6.60 (m, 1H), 3.85 (b, 4H), 3.40 (b, 4H), 2.88 (s, 3H), 2.83 – 2.77 (m, 2H), 2.58 – 2.50 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 159.5 (d, *J* = 244.7 Hz), 144.1 (d, *J* = 8.6 Hz), 134.0 (d, *J* = 9.1 Hz), 130.1 (d, *J* = 3.3 Hz), 108.5 (d, *J* = 22.8 Hz), 104.9 (d, *J* = 24.1 Hz), 66.8, 50.6, 33.26, 32.6, 26.7.

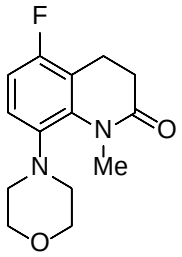
^{19}F NMR (377 MHz, $CDCl_3$) δ -116.96.

IR (NaCl) 2959, 2853, 1674, 1603, 1479, 1454, 1364, 1269, 1516, 1140, 1117, 1005

HRMS (DART, M+1) Calculated for $C_{14}H_{18}F_2O_2$ 265.1352, found 265.1357

MP 95-100 °C

5-fluoro-1-methyl-8-morpholino-3,4-dihydroquinolin-2(1H)-one (2i)



Synthesized by General Procedure F. The product was purified by flash column chromatography 50 -> 60% EtOAc/Hex. Product appeared as oil which solidified upon standing, 24 mg (45%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92 (dd, *J* = 9.0, 5.6 Hz, 1H), 6.82 (dd, *J* = 9.0, 8.0 Hz, 1H), 4.00 – 3.66 (b, 4H), 3.47 (s, 3H), 2.94 – 2.73 (m, 6H, overlap), 2.61 – 2.51 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.3, 155.4 (d, *J* = 240.7 Hz), 138.9 (d, *J* = 2.8 Hz), 135.9 (d, *J* = 5.9 Hz), 119.2 (d, *J* = 21.2 Hz), 118.8 (d, *J* = 9.1 Hz), 111.4 (d, *J* = 22.8 Hz), 67.0, 51.3, 33.7, 31.9, 18.7 (d, *J* = 3.1 Hz).

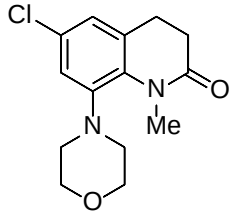
^{19}F NMR (377 MHz, $CDCl_3$) δ -124.49.

IR (NaCl) 2959, 2853, 1678, 1605, 1603, 1491, 1452, 1356, 1236, 1115, 1011, 995, 943, 878

HRMS (DART, M+1) Calculated for $C_{14}H_{18}FN_2O_2$ 265.1352, found 265.1355

MP 115-118 °C

6-chloro-1-methyl-8-morpholino-3,4-dihydroquinolin-2(1H)-one (2j)



Synthesized by General Procedure F. The product was purified by flash column chromatography 50 -> 60% EtOAc/Hex. Product appeared as white solid, 28 mg (50%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (d, *J* = 2.3 Hz, 1H), 6.89 (d, *J* = 2.3 Hz, 1H), 3.84 (b, 4H), 3.40 (s, 3H), 2.88 (b, 4H), 2.82 – 2.77 (m, 2H), 2.58 – 2.49 (m, 2H).

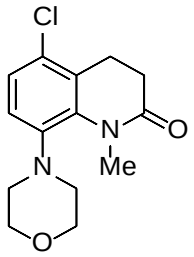
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 143.6, 133.8, 132.8, 129.7, 121.8, 118.2, 66.8, 50.7, 33.2, 32.4, 26.3.

IR (NaCl) 2959, 2853, 1680, 1584, 1471, 1452, 1356, 1117

HRMS (DART, M+1) Calculated for $C_{14}H_{18}ClN_2O_2$ 281.1057, found 281.1060

MP 152-154 °C

5-chloro-1-methyl-8-morpholino-3,4-dihydroquinolin-2(1H)-one (2k)



Synthesized by General Procedure F. The product was purified by flash column chromatography 60% EtOAc/Hex. Product appeared as white solid, 32 mg (57%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.8 Hz, 1H), 6.89 (d, *J* = 8.8 Hz, 1H), 3.84 (b, 4H), 3.41 (s, 3H), 2.99 – 2.93 (m, 2H), 2.87 (b, 4H), 2.59 – 2.51 (m, 2H).

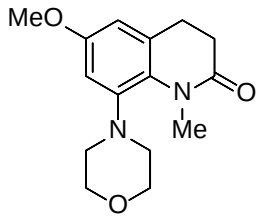
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 141.4, 135.6, 130.5, 126.7, 125.4, 118.6, 66.9, 50.8, 33.7, 32.0, 23.7.

IR (NaCl) 2959, 2853, 1684, 1582, 1474, 1449, 1424, 1354, 1240, 1121

HRMS (DART, M+1) Calculated for $C_{14}H_{18}ClN_2O_2$ 281.1057, 281.1061

MP 133-135 °C

6-methoxy-1-methyl-8-morpholino-3,4-dihydroquinolin-2(1H)-one (2l)



Synthesized by General Procedure F. The product was purified by flash column chromatography 80% Et_2O/Hex -> 100% Et_2O. Product appeared as oil which solidified upon standing overnight , 20 mg (36%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.49 (d, *J* = 2.8 Hz, 1H), 6.46 (d, *J* = 2.8 Hz, 1H), 3.84 (b, 4H), 3.79 (s, 3H), 3.41 (s, 3H), 2.90 (b, 4H), 2.83 – 2.76 (m, 2H), 2.57 – 2.50 (m, 2H).

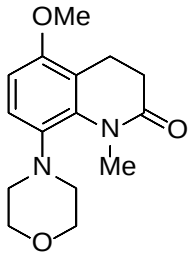
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 156.6, 143.9, 133.4, 127.7, 106.6, 104.2, 67.0, 55.5, 50.8, 33.4, 32.8, 27.0.

IR (NaCl) 2957, 2853, 1670, 1582, 1603, 1485, 1364, 1194, 1117

HRMS (DART, M+1) Calculated for $C_{15}H_{21}N_2O_3$ 277.1552, found 277.1547

MP 121-123 °C

5-methoxy-1-methyl-8-morpholino-3,4-dihydroquinolin-2(1H)-one (2m)



Synthesized by General Procedure F. The product was purified by flash column chromatography 80 -> 90% Et_2O/Hex. Product appeared as oil residue which solidified upon standing overnight, 33 mg (60%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.93 (d, *J* = 8.9 Hz, 1H), 6.66 (d, *J* = 8.9 Hz, 1H), 3.84 (b, 4H), 3.80 (s, 3H), 3.46 (s, 3H), 2.93 – 2.76 (m, 6H, overlap), 2.54 – 2.45 (m, 2H).

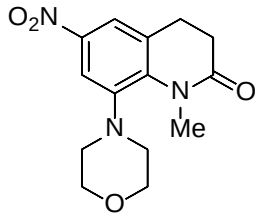
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 152.1, 136.6, 136.0, 120.6, 118.2, 107.1, 67.1, 55.8, 51.6, 34.1, 32.2, 19.1.

IR (NaCl) 2959, 2853, 1674, 1586, 1493, 1452, 1358, 1238, 1117, 1053

HRMS (DART, M+1) Calculated for $C_{15}H_{21}N_2O_3$ 277.1552, found 277.1558

MP 138-140 °C

1-methyl-8-morpholino-6-nitro-3,4-dihydroquinolin-2(1H)-one (2n)



Synthesized by General Procedure F. The product was purified by flash column chromatography 80% Et_2O/Hex -> 100% Et_2O. Product appeared as yellow solid, 30 mg (52%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 2.6 Hz, 1H), 7.79 (d, *J* = 2.5 Hz, 1H), 3.87 (b, 4H), 3.44 (s, 3H), 3.06 – 2.81 (m, 6H, overlap), 2.64 – 2.56 (m, 2H).

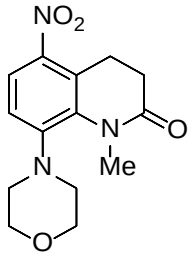
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.1, 144.0, 142.9, 139.7, 132.9, 117.1, 113.8, 66.6, 50.6, 33.1, 32.0, 26.2.

IR (NaCl) 2957, 2853, 1682, 1582, 1514, 1358, 1323, 1302, 1250, 1113, 988

HRMS (DART, M+1) Calculated for $C_{14}H_{18}N_3O_4$ 292.1297, found 292.1297

MP 193-194 °C

1-methyl-8-morpholino-5-nitro-3,4-dihydroquinolin-2(1H)-one (2o)



Synthesized by General Procedure F. The product was purified by flash column chromatography 80% Et_2O/Hex -> 100% Et_2O. Product appeared as yellow solid, 15 mg (26%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 9.1 Hz, 1H), 6.99 (d, *J* = 9.2 Hz, 1H), 3.87 (b, 4H), 3.35 (s, 3H), 3.27 – 3.17 (m, 2H), 3.01 (b, 4H), 2.58 – 2.49 (m, 2H).

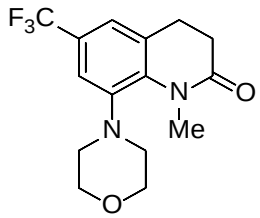
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.8, 146.8, 142.8, 134.8, 130.0, 121.9, 117.0, 66.6, 49.9, 33.1, 31.7, 23.2.

IR (NaCl) 2957, 2853, 1678, 1582, 1514, 1450, 1360, 1337, 1242, 1121

HRMS (DART, M+1) Calculated for $C_{14}H_{18}N_3O_4$ 292.1297, found 292.1305

MP 181-183 °C

1-methyl-8-morpholino-6-(trifluoromethyl)-3,4-dihydroquinolin-2(1H)-one (2p)



Synthesized by General Procedure F. The product was purified by flash column chromatography 30 -> 50% EtOAc/Hex. Product appeared as white solid, 34 mg (54%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (s, 1H), 7.15 (s, 1H), 3.85 (b, 4H), 3.43 (s, 3H), 2.92 (b, 4H), 2.90 – 2.85 (m, 2H), 2.62 – 2.54 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 142.8, 136.9 (q, *J* = 1.3 Hz), 132.9, 126.6 (q, *J* = 32.6 Hz), 123.9 (q, *J* = 272.0 Hz), 118.7 (q, *J* = 3.7 Hz), 115.1 (q, *J* = 3.9 Hz), 66.7, 50.6, 33.1, 32.3, 26.3.

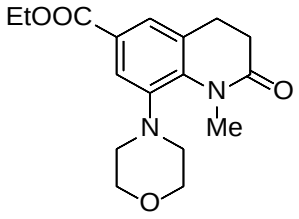
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.21.

IR (NaCl) 2966, 2859, 1674, 1377, 1354, 1310, 1298, 1233, 1159, 1115, 1007, 876

HRMS (DART, M+1) Calculated for $C_{15}H_{18}F_3N_2O_2$ 315.1320, found 315.1317

MP 165-167 °C

ethyl 1-methyl-8-morpholino-2-oxo-1,2,3,4-tetrahydroquinoline-6-carboxylate (2q)



Synthesized by General Procedure F. The product was purified by flash column chromatography 40 -> 60% EtOAc/Hex. Product appeared as white solid, 49 mg (78%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.61 (m, 1H), 7.58 (d, *J* = 1.7 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.85 (b, 4H), 3.45 (s, 3H), 2.93 (b, 4H), 2.89 – 2.85 (m, 2H), 2.59 – 2.55 (m, 2H), 1.38 (t, *J* = 7.1 Hz, 3H).

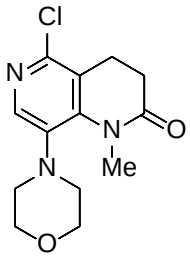
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.57, 166.03, 142.47, 138.10, 132.09, 126.52, 123.18, 119.65, 66.84, 61.03, 50.85, 33.30, 32.40, 26.18, 14.39, 14.37, 14.36.

IR (NaCl) 2957, 2853, 1713, 1682, 1582, 1514, 1451, 1370, 1346, 1300, 1279, 1261, 1221, 1117

HRMS (DART, M+1) Calculated for $C_{17}H_{23}N_2O_4$ 319.1658, found 319.1657

MP 132-133 °C

5-chloro-1-methyl-8-morpholino-3,4-dihydro-1,6-naphthyridin-2(1H)-one (2r)



Synthesized by General Procedure F. The product was purified by flash column chromatography 50 -> 60% EtOAc/Hex with 1% MeOH. Product appeared as white solid, 14 mg (25%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1H), 3.85 (b, 4H), 3.44 (s, 3H), 3.02 – 2.88 (m, 6H, overlap), 2.68 – 2.56 (m, 2H).

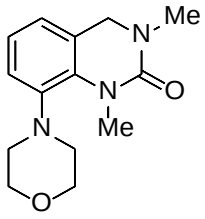
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.6, 144.2, 143.1, 139.8, 137.1, 124.3, 66.6, 50.8, 32.5, 31.3, 22.8.

IR (NaCl) 2969, 2834, 1674, 1557, 1462, 1427, 1344, 1317, 1256, 1119, 982

HRMS (DART, M+1) Calculated for $C_{13}H_{17}ClN_3O_2$ 282.1009, found 282.1016

MP 210-212 °C

1,3-dimethyl-8-morpholino-3,4-dihydroquinazolin-2(1H)-one (2s)



Synthesized by General Procedure F. The product was purified by flash column chromatography 50 -> 60% EtOAc/Hex. Product appeared as oily residue, 16 mg (30%)

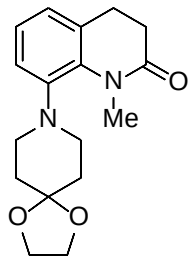
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 – 6.95 (m, 2H), 6.79 (ddt, *J* = 7.1, 1.7, 0.9 Hz, 1H), 4.18 (s, 2H), 3.84 (b, 4H), 3.46 (s, 3H), 2.95 (s, 3H), 2.89 (b, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 141.5, 133.0, 127.2, 123.6, 119.9, 118.8, 67.0, 51.1, 50.7, 35.3, 34.4.

IR (NaCl) 2957, 2853, 1667, 1485, 1452, 1441, 1398, 1323, 1300, 1281, 1234, 1117, 1007, 783, 739

HRMS (DART, M+1) Calculated for $C_{14}H_{20}N_3O_2$ 262.1569, found 262.1565

1-methyl-8-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3,4-dihydroquinolin-2(1H)-one (2t)



Synthesized by General Procedure F. The product was purified by flash column chromatography 30 -> 40% EtOAc/Hex. Product appeared as oil,42 mg (70%) (on 1mmol scale, 180 mg, 60%)

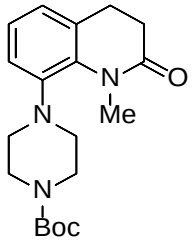
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.98 – 6.95 (m, 2H), 6.84 (t, *J* = 4.4 Hz, 1H), 3.95 (s, 4H), 3.42 (s, 3H), 3.08 (s, 2H), 2.91 – 2.74 (m, 4H, overlap), 2.55 – 2.45 (m, 2H), 1.99 – 1.83 (m, 2H), 1.83 – 1.65 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 143.2, 134.2, 132.1, 124.5, 121.8, 118.9, 106.6, 64.3, 49.0, 35.1, 33.1, 32.7, 26.5.

IR (NaCl) 2957, 2853, 1674, 1582, 1553, 1514, 1464, 1451, 1362, 1344, 1317, 1256, 1125, 1121, 1103

HRMS (DART, M+1) Calculated for $C_{17}H_{23}N_2O_3$ 303.1709, found 303.1705

tert-butyl 4-(1-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-8-yl)piperazine-1-carboxylate (2u)



Synthesized by General Procedure F. The product was purified by flash column chromatography 30 -> 50% EtOAc/Hex. Product appeared as oily residue, 49 mg (71%) (on 1mmol scale, 240 mg, 70%)

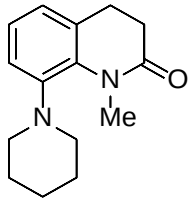
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 – 6.99 (m, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.90 (d, *J* = 8.5 Hz, 1H), 4.06 (s, 2H), 3.44 (s, 3H), 3.05 (b, 4H), 2.86 – 2.79 (m, 2H), 2.65 (b, 2H), 2.58 – 2.54 (m, 2H), 1.47 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 154.7, 142.8, 134.5, 132.4, 124.7, 122.3, 118.5, 79.9, 50.7, 33.6, 32.7, 28.4, 26.5.

IR (NaCl) 2957, 2853, 1690, 1674, 1582, 1553, 1514, 1479, 1451, 1366, 1344, 1317, 1256, 1238, 1171, 1121, 999

HRMS (DART, M+1) Calculated for $C_{19}H_{28}N_3O_3$ 346.2131, found 346.2132

1-methyl-8-(piperidin-1-yl)-3,4-dihydroquinolin-2(1H)-one (2v)



Synthesized by General Procedure F. The product was purified by flash column chromatography 20 -> 30% EtOAc/DCM. Product appeared as oil which solidified upon standing overnight, white solid 16 mg (33%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 – 6.95 (m, 2H), 6.87 – 6.84 (m, 1H), 3.46 (s, 3H), 3.13 (b, 2H), 2.86 – 2.77 (m, 2H), 2.65 – 2.42 (m, 4H, overlap), 1.80 (b, 1H), 1.71 (m,4H), 1.28 (b, 1H).

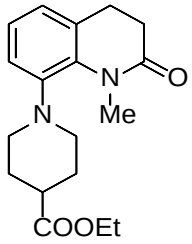
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 144.4, 134.2, 132.1, 124.5, 121.4, 118.6, 52.1, 33.1, 32.8, 26.5, 26.2, 24.2.

IR (NaCl) 2934, 2851, 1676, 1589, 1464, 1362, 1240, 1117, 968

HRMS (M+1) Calculated for $C_{15}H_{21}N_2O$ 245.1654, found 245.1664

MP 103-105 °C

ethyl 1-(1-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-8-yl)piperidine-4-carboxylate (2w)



Synthesized by General Procedure F. The product was purified by flash column chromatography 30 -> 50% EtOAc/pentanes. Product appeared as a white solid, 38 mg (60%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 – 6.91 (m, 2H), 6.91 – 6.81 (m, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.42 (s, 3H), 3.20 (b, 2H), 2.83 – 2.77 (m, 2H), 2.63 – 2.38 (m, 4H, overlap), 2.32 (b, 1H), 1.93 (b, 4H), 1.25 (t, *J* = 7.1 Hz, 3H).

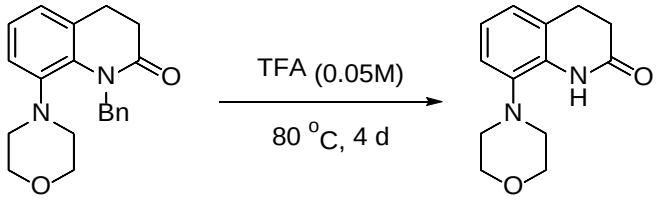
^{13}C NMR (126 MHz, $CDCl_3$) δ 174.8, 172.7, 143.4, 134.3, 132.2, 124.5, 118.6, 60.5, 50.8, 41.4, 33.2, 32.7, 28.7, 26.5, 14.2.

IR (NaCl) 2952, 2808, 1732, 1676, 1589, 1464, 1362, 1310, 1190, 1170, 1045

HRMS (DART, M+1) Calculated for $C_{18}H_{25}N_2O_3$ 317.1865, found 317.1861

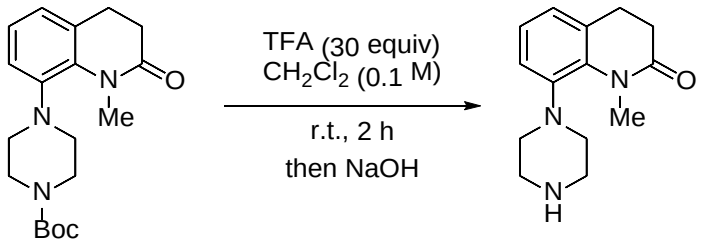
Product Derivatization

8-morpholino-3,4-dihydroquinolin-2(1H)-one (2b via deprotection)



Product 2d (32 mg, 0.1 mmol) was dissolved in TFA (2 mL, 0.05 M). The reaction was stirred at 80 °C in a sealed vial for 4 days. The reaction was rotovapped to dryness and purified by flash column chromatography with CH_2Cl_2:EtOAc:MeOH (49:49:2). Obtained product as a slightly off white solid 19 mg (82%). Characterization matched the spectroscopic data for product 2b.

1-methyl-8-(piperazin-1-yl)-3,4-dihydroquinolin-2(1H)-one (3a)



Product 2u (35 mg, 0.1 mmol) was dissolved in dry CH_2Cl_2 (1 mL) then TFA (0.23 mL, 30 equiv). The reaction was stirred for 2 h at room temperature. Then the reaction was quenched with 6 M NaOH and rapidly stirred for 30 min at room temperature. The crude was extracted with dichloromethane (3 x 5 mL), then dried over magnesium sulfate and filtered. The product was dried under reduced pressure to obtain the amine product as a yellow oil (25 mg, >99%).

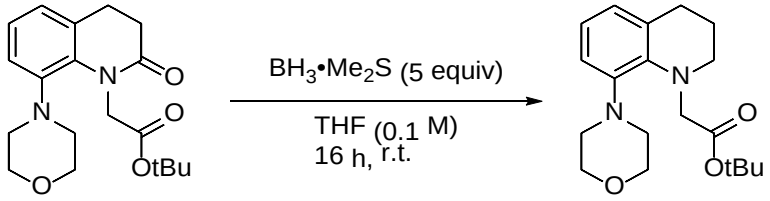
^{1}H NMR (400 MHz, MeOD) δ 7.11 – 6.99 (m, 2H), 6.98 – 6.89 (m, 1H), 3.44 (s, 3H), 3.00 (t, *J* = 4.8 Hz, 4H), 2.86 – 2.77 (m, 2H), 3.15 – 2.57 (b, 4H, overlap), 2.56 – 2.47 (m, 2H).

^{13}C NMR (100 MHz, MeOD) δ 175.4, 144.8, 135.2, 133.8, 126.4, 123.2, 119.7, 52.4, 46.6, 34.4, 33.6, 27.1.

IR (NaCl) 2945, 2822, 1672, 1589, 1479, 1462, 1364, 1321, 1240, 1194, 1126

HRMS (DART, M+1) Calculated for $C_{14}H_{20}N_3O$ 246.1620, found 246.1616

tert-butyl 2-(8-morpholino-3,4-dihydroquinolin-1(2H)-yl)acetate (3b)



Product 2c (69 mg, 0.2 mmol) was dissolved in dry THF (2 mL). Then borane-dimethylsulfide complex (95 µL, 1.0 mmol, 5 equiv) was added slowly. The reaction was stirred for 16 h at room temperature. The reaction was slowly quenched with methanol added dropwise. The reaction was purified via flash column chromatography 5% ->10% EtOAc/pentane. The product appeared as a white solid, 56 mg (84%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (dd, *J* = 7.9, 7.2 Hz, 1H), 6.81 – 6.72 (m, 2H), 4.12 (s, 2H), 3.80 (t, *J* = 4.6 Hz, 4H), 3.20 – 3.13 (m, 2H), 3.05 (b, 4H), 2.78 (t, *J* = 6.5 Hz, 2H), 1.84 – 1.75 (m, 2H), 1.47 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.32, 143.44, 139.93, 129.71, 124.52, 120.95, 116.44, 80.66, 67.62, 54.36, 50.33, 49.57, 28.44, 28.24, 18.54.

IR (NaCl) 2934, 2853, 1742, 1471, 1368, 1236, 1217, 1153, 1136, 1119, 959

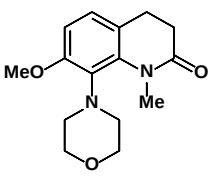
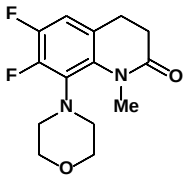
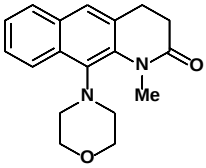
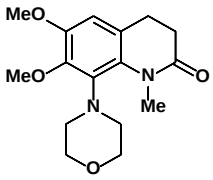
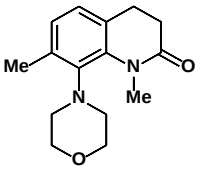
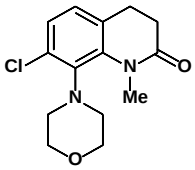
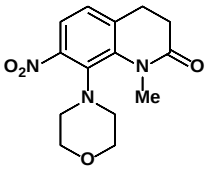
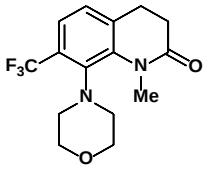
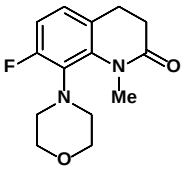
HRMS (DART, M+1) Calculated for $C_{19}H_{29}N_2O_3$ 333.2178, found 333.2183

MP 115-117 °C

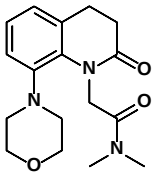
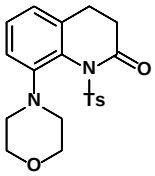
Unsuccessful Substrates

The following products could not be generated or were generated in very low yields

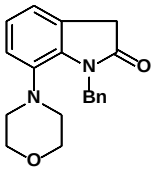
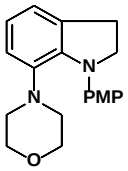
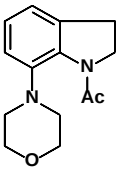
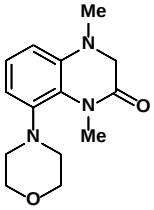
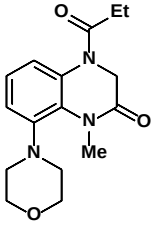
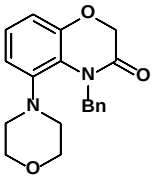
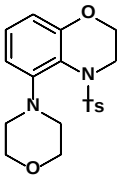
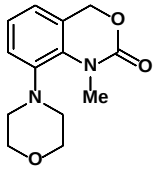
Substitution *para* to the tether

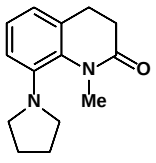
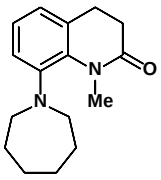
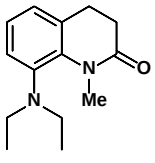
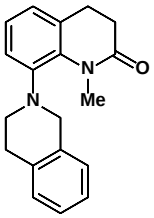
Other Amides

Other Heterocycles

Other *O*-benozylhydroxylamine

X-Ray Structure of 2n

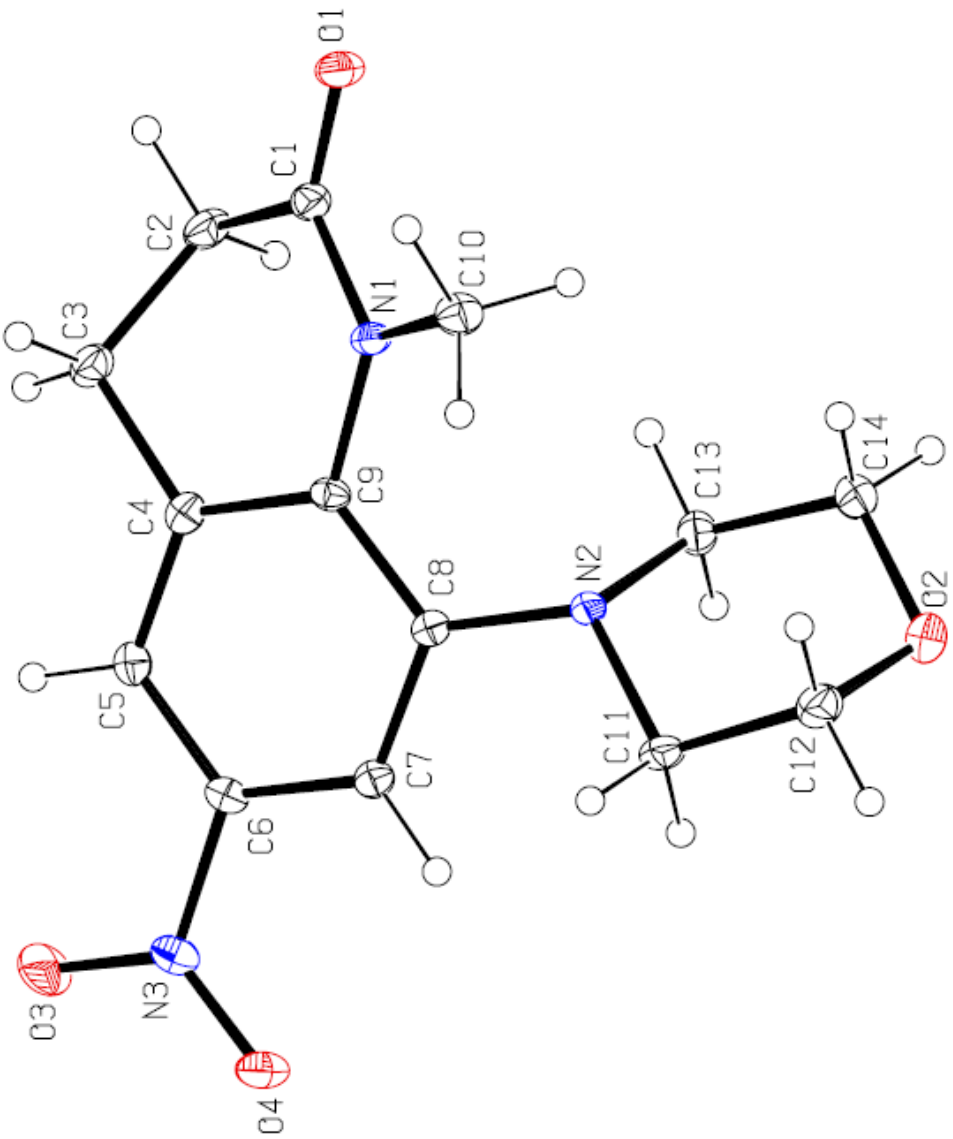


Table 1. Crystal data and structure refinement for d17122a_a.

Identification code	d17122a_a	
Empirical formula	C14 H17 N3 O4	
Formula weight	291.30	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 9.800(2) Å	□= 90°.
	b = 17.619(4) Å	□= 104.339(10)°.
	c = 8.006(2) Å	□ = 90°.
Volume	1339.3(6) $Å^3$	
Z	4	
Density (calculated)	1.445 Mg/m^3	
Absorption coefficient	0.108 mm^{-1}	
F(000)	616	
Crystal size	0.270 x 0.070 x 0.060 mm^3	
Theta range for data collection	2.145 to 27.560°.	
Index ranges	-11<=h<=12, -18<=k<=22, -10<=l<=10	
Reflections collected	8954	
Independent reflections	3076 [R(int) = 0.0719]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.6427	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3076 / 0 / 191	
Goodness-of-fit on F^2	1.000	
Final R indices [I>2sigma(I)]	R1 = 0.0546, wR2 = 0.1033	
R indices (all data)	R1 = 0.1199, wR2 = 0.1251	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.245 and -0.283 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)

for d17122a_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	6191(2)	5253(1)	-791(2)	27(1)
O(2)	5938(2)	2751(1)	5678(2)	30(1)
O(3)	9559(2)	6943(1)	8843(2)	37(1)
O(4)	9464(2)	5832(1)	9953(2)	28(1)
N(1)	7156(2)	5054(1)	2054(2)	18(1)
N(2)	7311(2)	4108(1)	5067(2)	17(1)
N(3)	9279(2)	6259(1)	8702(3)	23(1)
C(1)	6497(2)	5505(1)	675(3)	22(1)
C(2)	6217(3)	6308(1)	1120(3)	26(1)
C(3)	7506(3)	6628(1)	2382(3)	24(1)
C(4)	7876(2)	6129(1)	3956(3)	19(1)
C(5)	8446(2)	6429(1)	5567(3)	20(1)
C(6)	8707(2)	5952(1)	6985(3)	19(1)
C(7)	8371(2)	5189(1)	6835(3)	18(1)
C(8)	7777(2)	4875(1)	5226(3)	16(1)
C(9)	7605(2)	5345(1)	3754(3)	16(1)
C(10)	7559(3)	4292(1)	1612(3)	24(1)
C(11)	7914(3)	3614(1)	6542(3)	24(1)
C(12)	7433(3)	2809(1)	6073(3)	29(1)
C(13)	5767(2)	4046(1)	4598(3)	22(1)
C(14)	5336(3)	3227(1)	4237(3)	26(1)

Table 3. Bond lengths [Å] and angles [°] for d17122a_a.

O(1)-C(1)	1.221(3)
O(2)-C(12)	1.424(3)
O(2)-C(14)	1.430(3)
O(3)-N(3)	1.236(2)
O(4)-N(3)	1.229(2)
N(1)-C(1)	1.383(3)
N(1)-C(9)	1.419(3)
N(1)-C(10)	1.468(3)
N(2)-C(8)	1.423(3)
N(2)-C(11)	1.468(3)
N(2)-C(13)	1.470(3)
N(3)-C(6)	1.454(3)
C(1)-C(2)	1.500(3)
C(2)-C(3)	1.517(3)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(4)	1.506(3)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(5)	1.378(3)
C(4)-C(9)	1.407(3)
C(5)-C(6)	1.385(3)
C(5)-H(5A)	0.9500
C(6)-C(7)	1.381(3)
C(7)-C(8)	1.390(3)
C(7)-H(7A)	0.9500
C(8)-C(9)	1.416(3)
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-C(12)	1.512(3)

C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.512(3)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-H(14A)	0.9900
C(14)-H(14B)	0.9900

C(12)-O(2)-C(14)	109.44(17)
C(1)-N(1)-C(9)	122.02(18)
C(1)-N(1)-C(10)	115.70(18)
C(9)-N(1)-C(10)	121.62(18)
C(8)-N(2)-C(11)	115.78(17)
C(8)-N(2)-C(13)	112.31(16)
C(11)-N(2)-C(13)	110.22(17)
O(4)-N(3)-O(3)	122.56(19)
O(4)-N(3)-C(6)	119.13(18)
O(3)-N(3)-C(6)	118.32(19)
O(1)-C(1)-N(1)	120.9(2)
O(1)-C(1)-C(2)	123.7(2)
N(1)-C(1)-C(2)	115.4(2)
C(1)-C(2)-C(3)	109.7(2)
C(1)-C(2)-H(2A)	109.7
C(3)-C(2)-H(2A)	109.7
C(1)-C(2)-H(2B)	109.7
C(3)-C(2)-H(2B)	109.7
H(2A)-C(2)-H(2B)	108.2
C(4)-C(3)-C(2)	109.20(18)
C(4)-C(3)-H(3A)	109.8
C(2)-C(3)-H(3A)	109.8
C(4)-C(3)-H(3B)	109.8

C(2)-C(3)-H(3B)	109.8
H(3A)-C(3)-H(3B)	108.3
C(5)-C(4)-C(9)	120.4(2)
C(5)-C(4)-C(3)	121.13(19)
C(9)-C(4)-C(3)	118.5(2)
C(4)-C(5)-C(6)	118.9(2)
C(4)-C(5)-H(5A)	120.5
C(6)-C(5)-H(5A)	120.5
C(7)-C(6)-C(5)	121.8(2)
C(7)-C(6)-N(3)	118.2(2)
C(5)-C(6)-N(3)	119.91(19)
C(6)-C(7)-C(8)	120.2(2)
C(6)-C(7)-H(7A)	119.9
C(8)-C(7)-H(7A)	119.9
C(7)-C(8)-C(9)	118.34(18)
C(7)-C(8)-N(2)	120.83(19)
C(9)-C(8)-N(2)	120.79(19)
C(4)-C(9)-C(8)	119.83(19)
C(4)-C(9)-N(1)	118.04(19)
C(8)-C(9)-N(1)	122.12(18)
N(1)-C(10)-H(10A)	109.5
N(1)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
N(1)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
N(2)-C(11)-C(12)	108.48(19)
N(2)-C(11)-H(11A)	110.0
C(12)-C(11)-H(11A)	110.0
N(2)-C(11)-H(11B)	110.0
C(12)-C(11)-H(11B)	110.0
H(11A)-C(11)-H(11B)	108.4
O(2)-C(12)-C(11)	111.32(18)

O(2)-C(12)-H(12A)	109.4
C(11)-C(12)-H(12A)	109.4
O(2)-C(12)-H(12B)	109.4
C(11)-C(12)-H(12B)	109.4
H(12A)-C(12)-H(12B)	108.0
N(2)-C(13)-C(14)	109.92(18)
N(2)-C(13)-H(13A)	109.7
C(14)-C(13)-H(13A)	109.7
N(2)-C(13)-H(13B)	109.7
C(14)-C(13)-H(13B)	109.7
H(13A)-C(13)-H(13B)	108.2
O(2)-C(14)-C(13)	111.5(2)
O(2)-C(14)-H(14A)	109.3
C(13)-C(14)-H(14A)	109.3
O(2)-C(14)-H(14B)	109.3
C(13)-C(14)-H(14B)	109.3
H(14A)-C(14)-H(14B)	108.0

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for d17122a_a. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	28(1)	37(1)	16(1)	3(1)	2(1)	-3(1)
O(2)	36(1)	24(1)	30(1)	4(1)	7(1)	-7(1)
O(3)	54(1)	20(1)	34(1)	-9(1)	2(1)	-4(1)
O(4)	32(1)	32(1)	16(1)	-1(1)	1(1)	2(1)
N(1)	20(1)	20(1)	13(1)	1(1)	2(1)	0(1)
N(2)	19(1)	16(1)	15(1)	3(1)	0(1)	-2(1)
N(3)	22(1)	25(1)	20(1)	-5(1)	2(1)	2(1)
C(1)	17(1)	29(1)	18(1)	4(1)	3(1)	-3(1)
C(2)	29(2)	26(1)	21(1)	9(1)	3(1)	2(1)
C(3)	29(2)	21(1)	22(1)	5(1)	6(1)	1(1)
C(4)	19(1)	19(1)	21(1)	2(1)	7(1)	2(1)
C(5)	21(1)	18(1)	23(1)	-1(1)	6(1)	-1(1)
C(6)	16(1)	22(1)	17(1)	-4(1)	2(1)	1(1)
C(7)	18(1)	19(1)	18(1)	1(1)	4(1)	1(1)
C(8)	15(1)	18(1)	16(1)	1(1)	5(1)	2(1)
C(9)	13(1)	21(1)	14(1)	-1(1)	2(1)	2(1)
C(10)	28(2)	24(1)	20(1)	-4(1)	8(1)	2(1)
C(11)	28(2)	23(1)	16(1)	5(1)	-1(1)	1(1)
C(12)	41(2)	22(1)	23(1)	3(1)	5(1)	-1(1)
C(13)	24(1)	21(1)	23(1)	-2(1)	8(1)	-3(1)
C(14)	24(1)	25(1)	26(2)	1(1)	3(1)	-4(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for d17122a_a.

	x	y	z	U(eq)
H(2A)	5400	6321	1639	31
H(2B)	5989	6620	60	31
H(3A)	8306	6648	1834	29
H(3B)	7309	7150	2715	29
H(5A)	8657	6955	5702	24
H(7A)	8546	4878	7835	22
H(10A)	7884	4316	550	35
H(10B)	6744	3953	1439	35
H(10C)	8319	4097	2552	35
H(11A)	7595	3782	7564	28
H(11B)	8955	3641	6825	28
H(12A)	7771	2644	5064	35
H(12B)	7849	2468	7048	35
H(13A)	5373	4358	3562	27
H(13B)	5388	4240	5553	27
H(14A)	4296	3188	3970	31
H(14B)	5645	3049	3216	31

Table 6. Torsion angles [°] for d17122a_a.

C(9)-N(1)-C(1)-O(1)	175.8(2)
C(10)-N(1)-C(1)-O(1)	5.0(3)
C(9)-N(1)-C(1)-C(2)	-3.4(3)
C(10)-N(1)-C(1)-C(2)	-174.22(19)
O(1)-C(1)-C(2)-C(3)	-135.0(2)
N(1)-C(1)-C(2)-C(3)	44.2(3)
C(1)-C(2)-C(3)-C(4)	-57.1(2)
C(2)-C(3)-C(4)-C(5)	-146.5(2)
C(2)-C(3)-C(4)-C(9)	32.5(3)
C(9)-C(4)-C(5)-C(6)	-1.9(3)
C(3)-C(4)-C(5)-C(6)	177.0(2)
C(4)-C(5)-C(6)-C(7)	-2.1(3)
C(4)-C(5)-C(6)-N(3)	-178.6(2)
O(4)-N(3)-C(6)-C(7)	1.1(3)
O(3)-N(3)-C(6)-C(7)	-178.8(2)
O(4)-N(3)-C(6)-C(5)	177.8(2)
O(3)-N(3)-C(6)-C(5)	-2.2(3)
C(5)-C(6)-C(7)-C(8)	1.2(3)
N(3)-C(6)-C(7)-C(8)	177.8(2)
C(6)-C(7)-C(8)-C(9)	3.6(3)
C(6)-C(7)-C(8)-N(2)	-174.5(2)
C(11)-N(2)-C(8)-C(7)	-20.2(3)
C(13)-N(2)-C(8)-C(7)	107.6(2)
C(11)-N(2)-C(8)-C(9)	161.79(19)
C(13)-N(2)-C(8)-C(9)	-70.4(2)
C(5)-C(4)-C(9)-C(8)	6.8(3)
C(3)-C(4)-C(9)-C(8)	-172.2(2)
C(5)-C(4)-C(9)-N(1)	-173.5(2)
C(3)-C(4)-C(9)-N(1)	7.5(3)
C(7)-C(8)-C(9)-C(4)	-7.5(3)
N(2)-C(8)-C(9)-C(4)	170.52(19)

C(7)-C(8)-C(9)-N(1)	172.82(19)
N(2)-C(8)-C(9)-N(1)	-9.1(3)
C(1)-N(1)-C(9)-C(4)	-24.1(3)
C(10)-N(1)-C(9)-C(4)	146.2(2)
C(1)-N(1)-C(9)-C(8)	155.6(2)
C(10)-N(1)-C(9)-C(8)	-34.1(3)
C(8)-N(2)-C(11)-C(12)	-173.79(18)
C(13)-N(2)-C(11)-C(12)	57.4(2)
C(14)-O(2)-C(12)-C(11)	60.7(2)
N(2)-C(11)-C(12)-O(2)	-60.3(2)
C(8)-N(2)-C(13)-C(14)	173.19(18)
C(11)-N(2)-C(13)-C(14)	-56.1(2)
C(12)-O(2)-C(14)-C(13)	-58.6(2)
N(2)-C(13)-C(14)-O(2)	56.7(2)

Symmetry transformations used to generate equivalent atoms:

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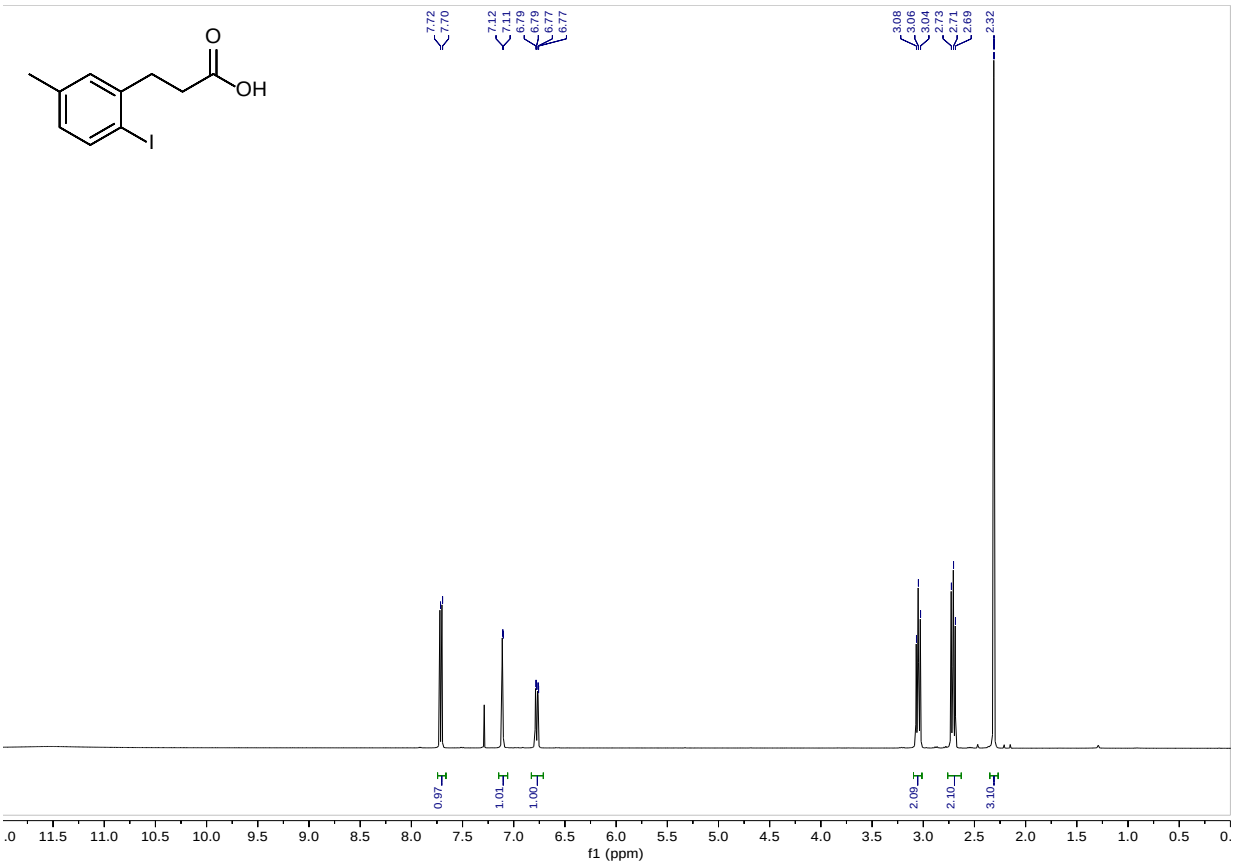
NMR Spectras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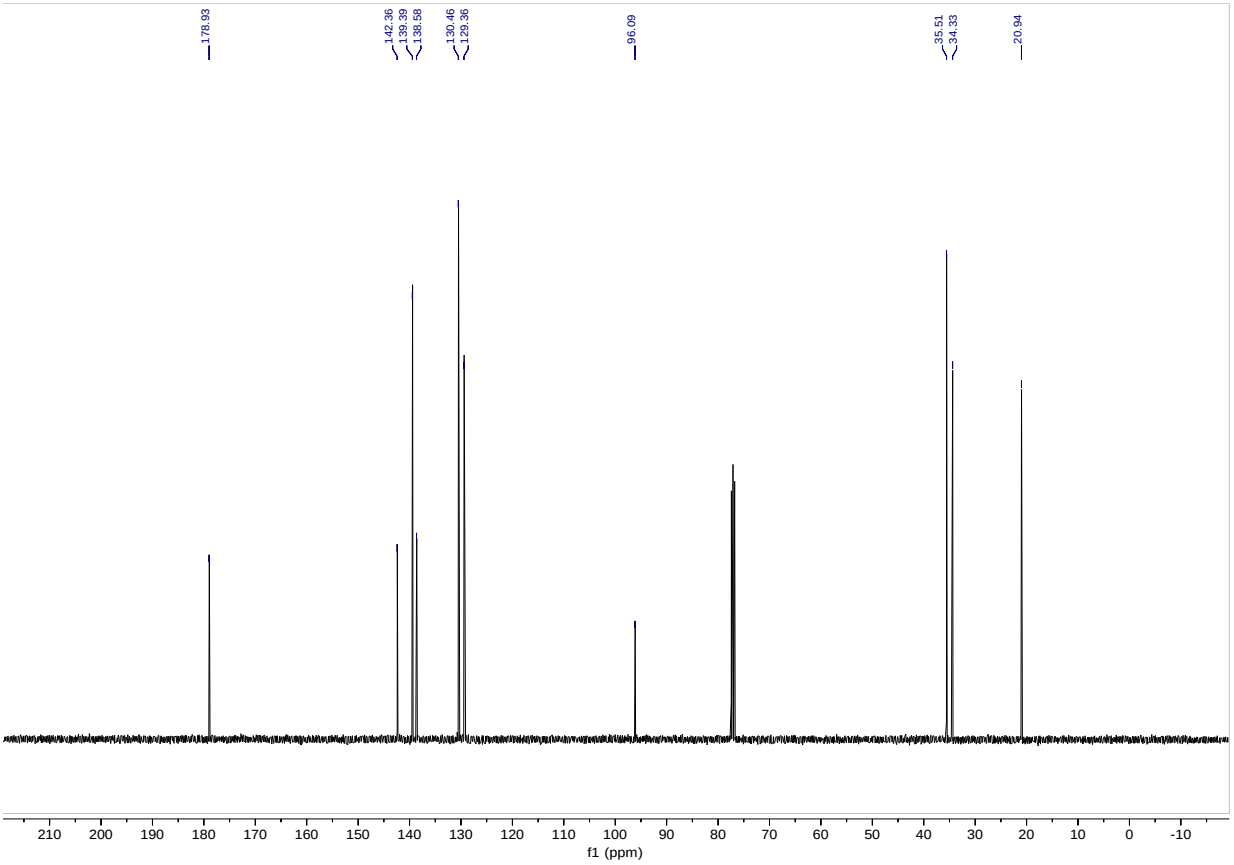
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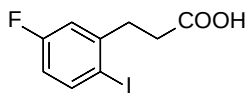
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I

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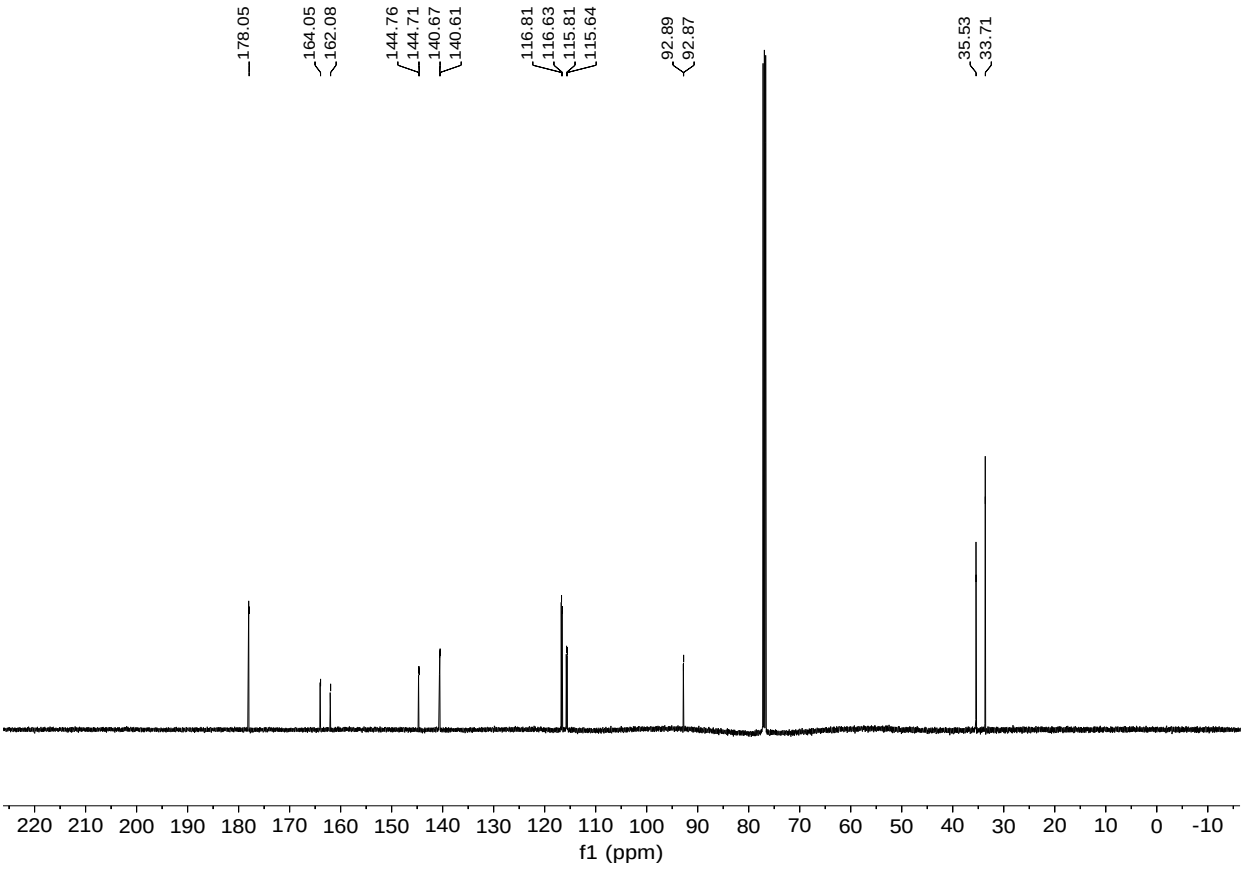
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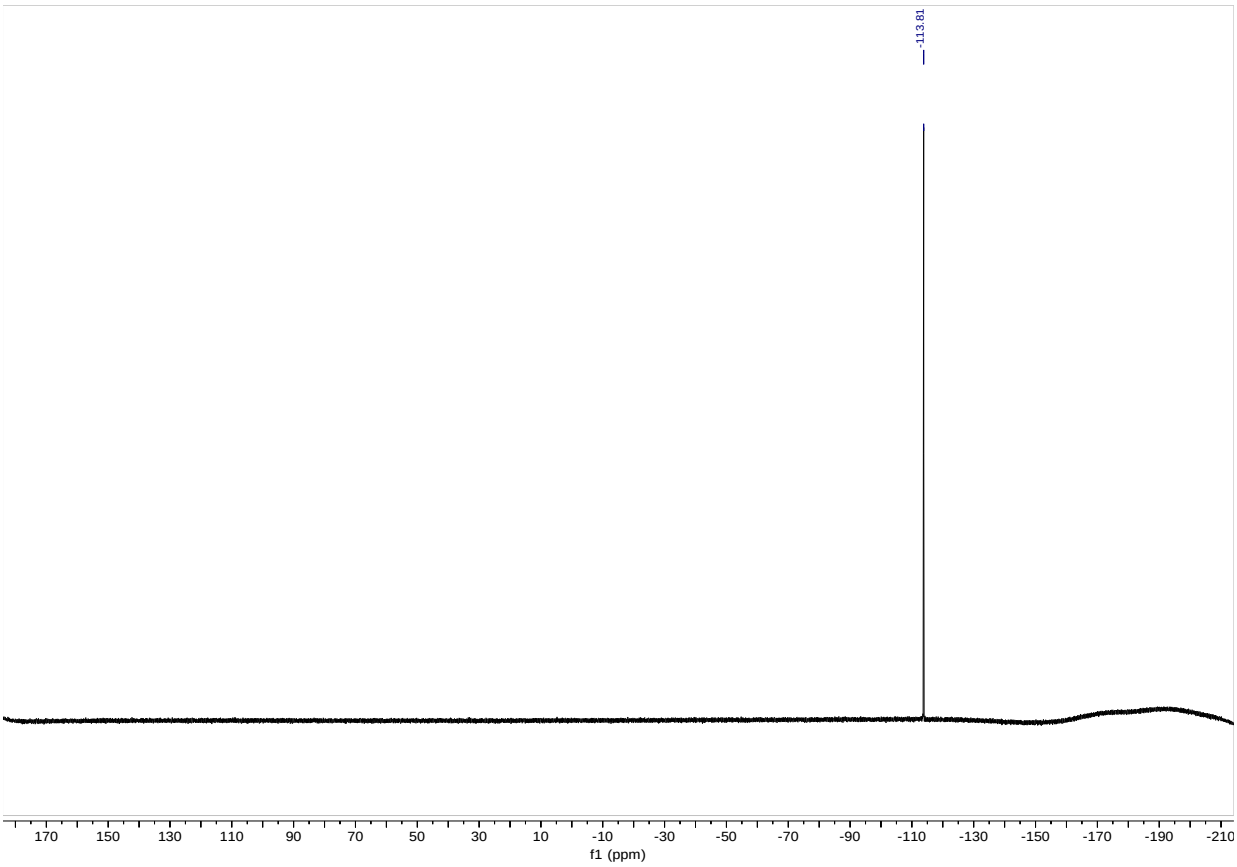
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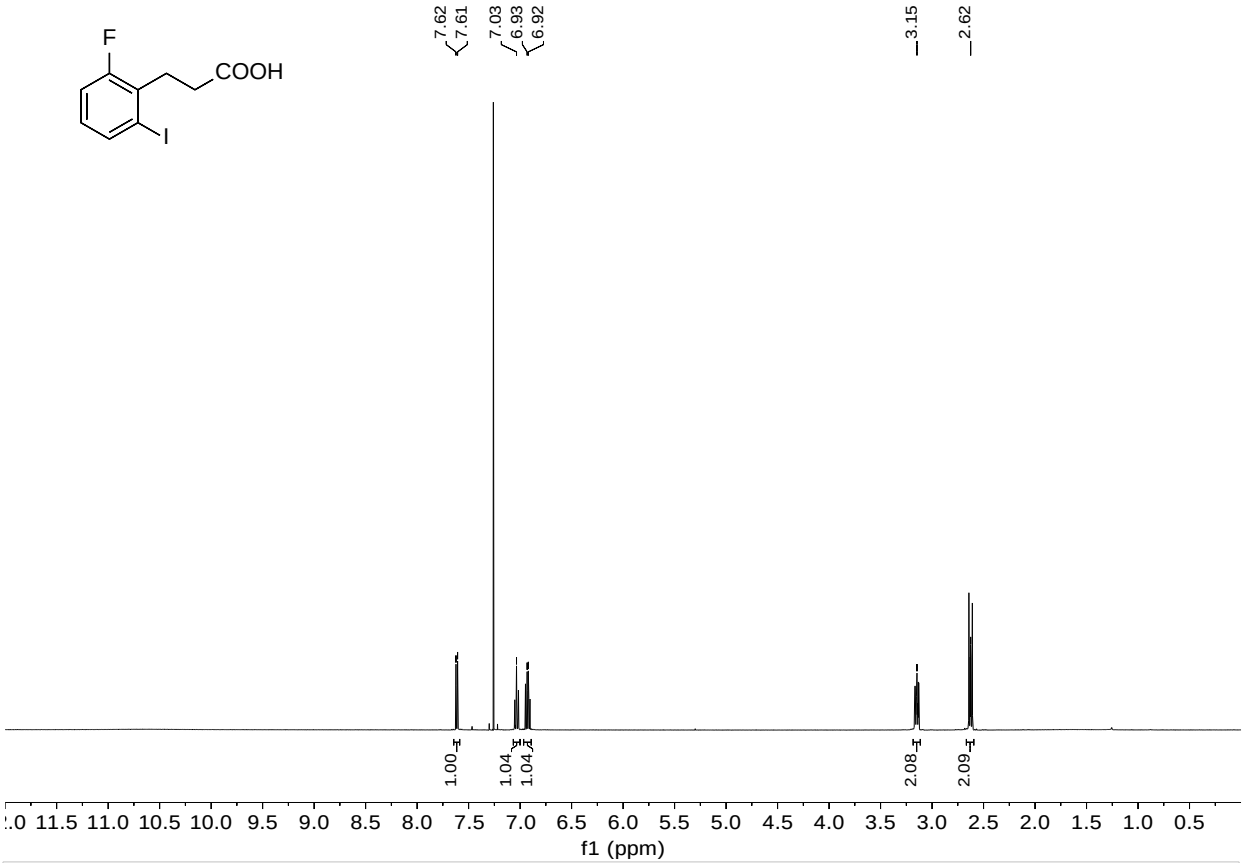
f1 (ppm)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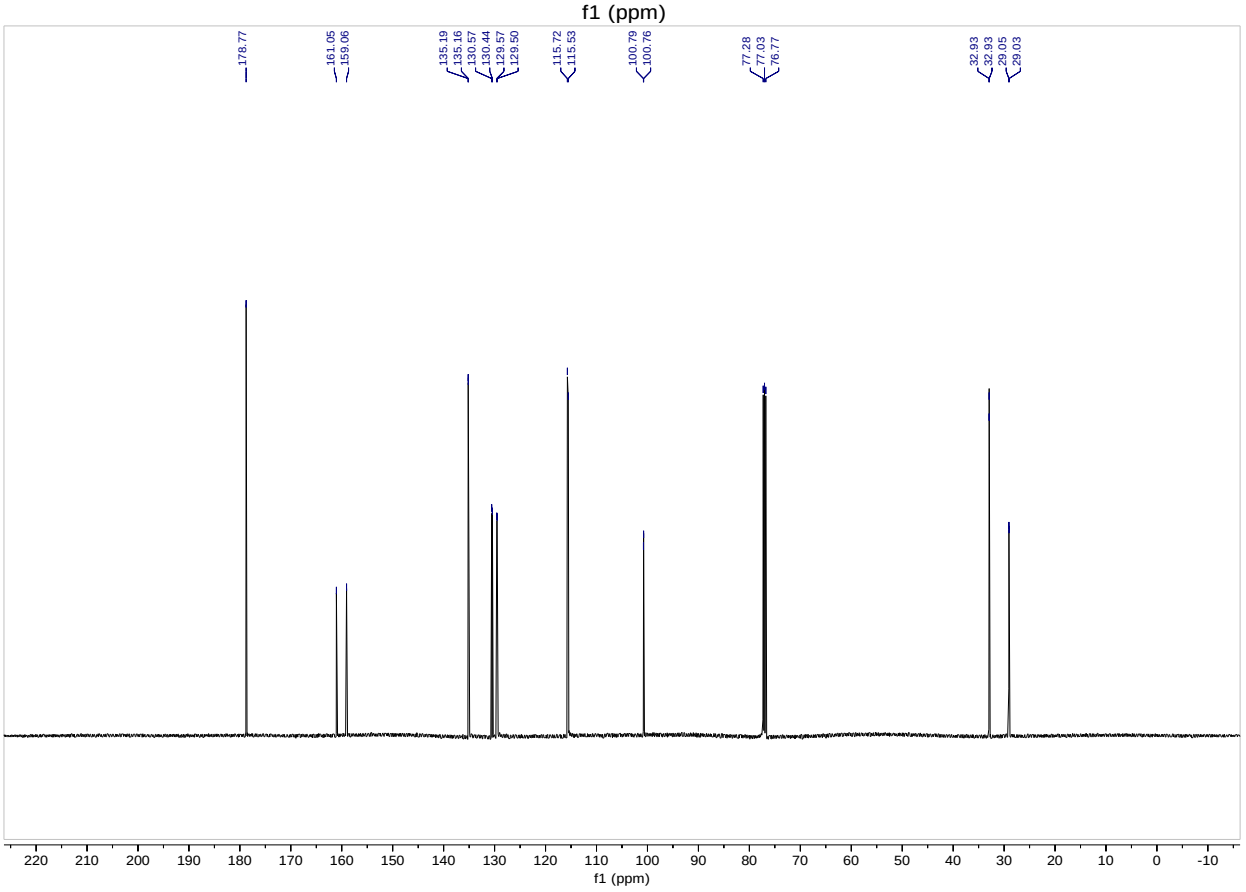
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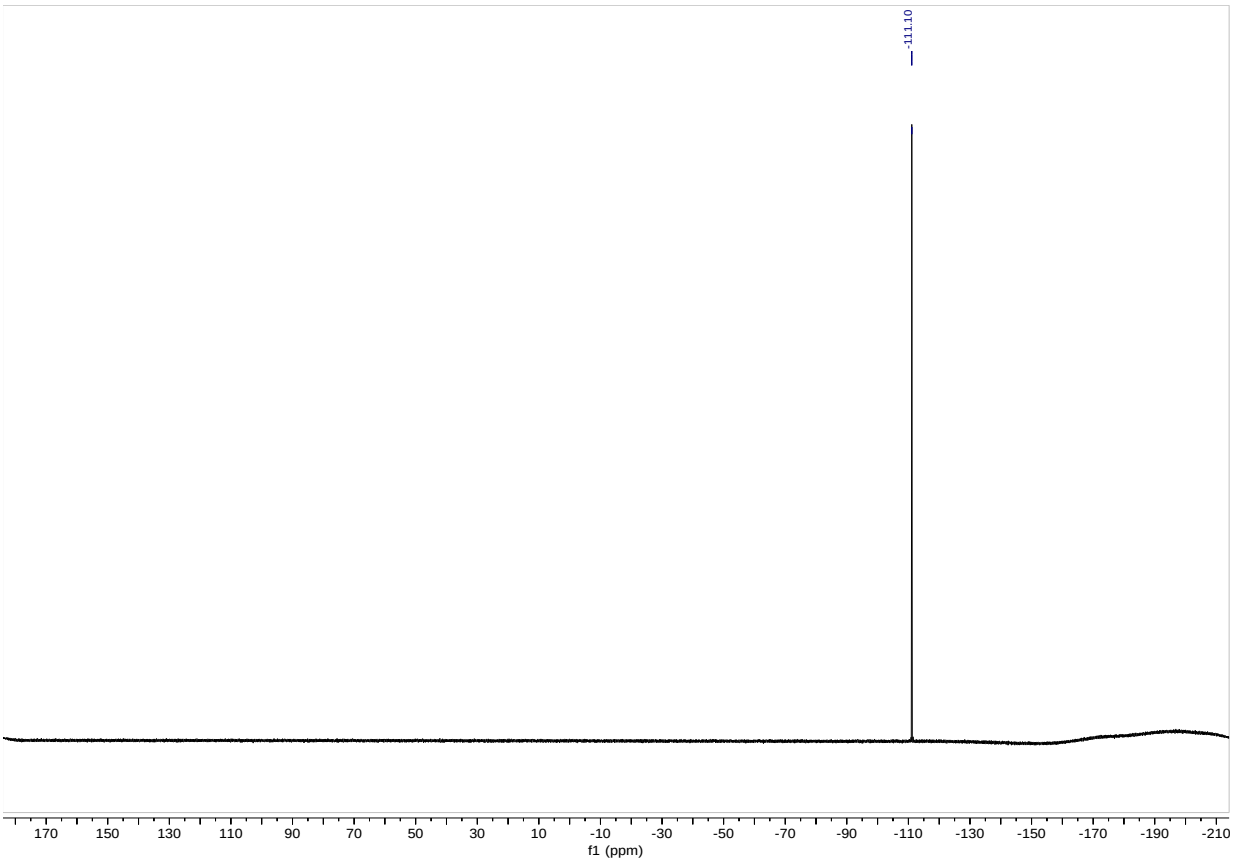
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-170
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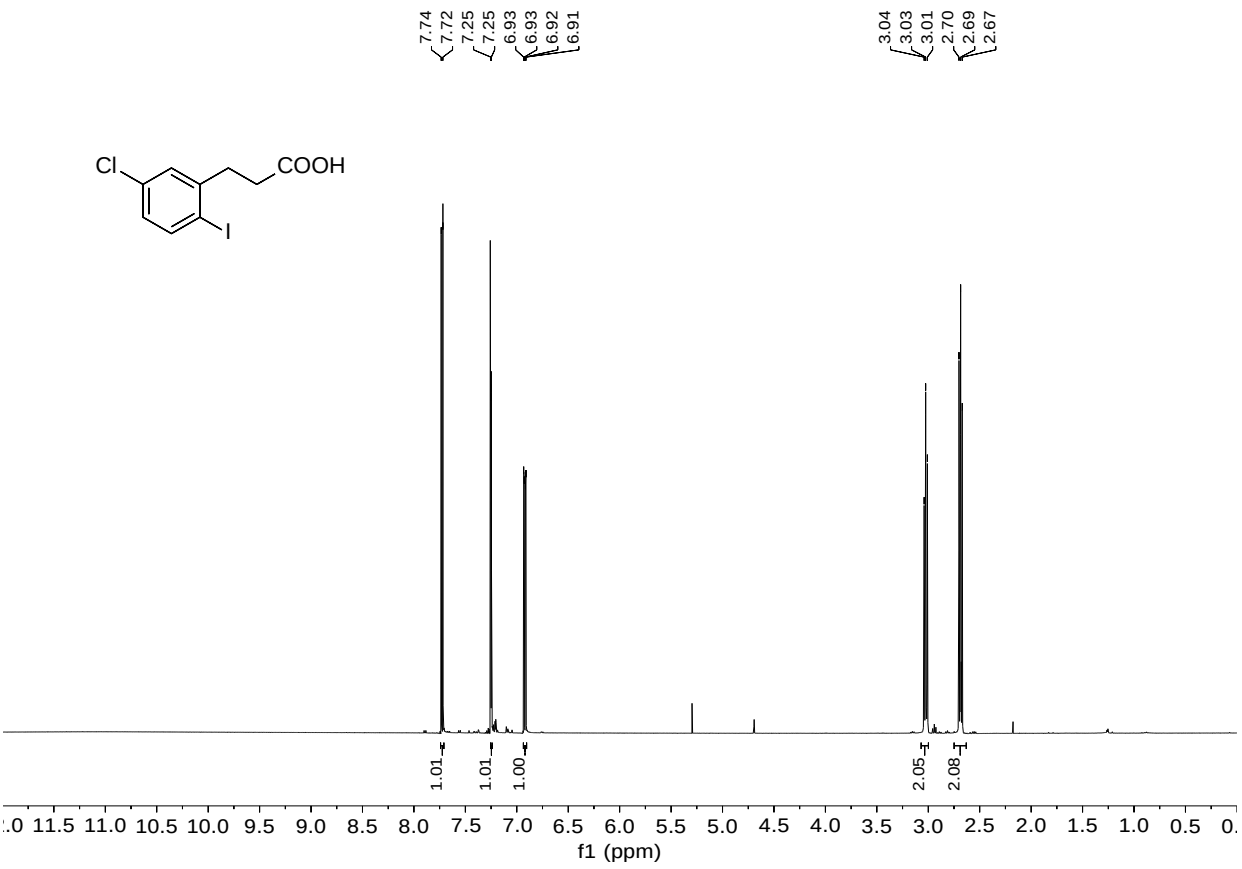
f1 (ppm)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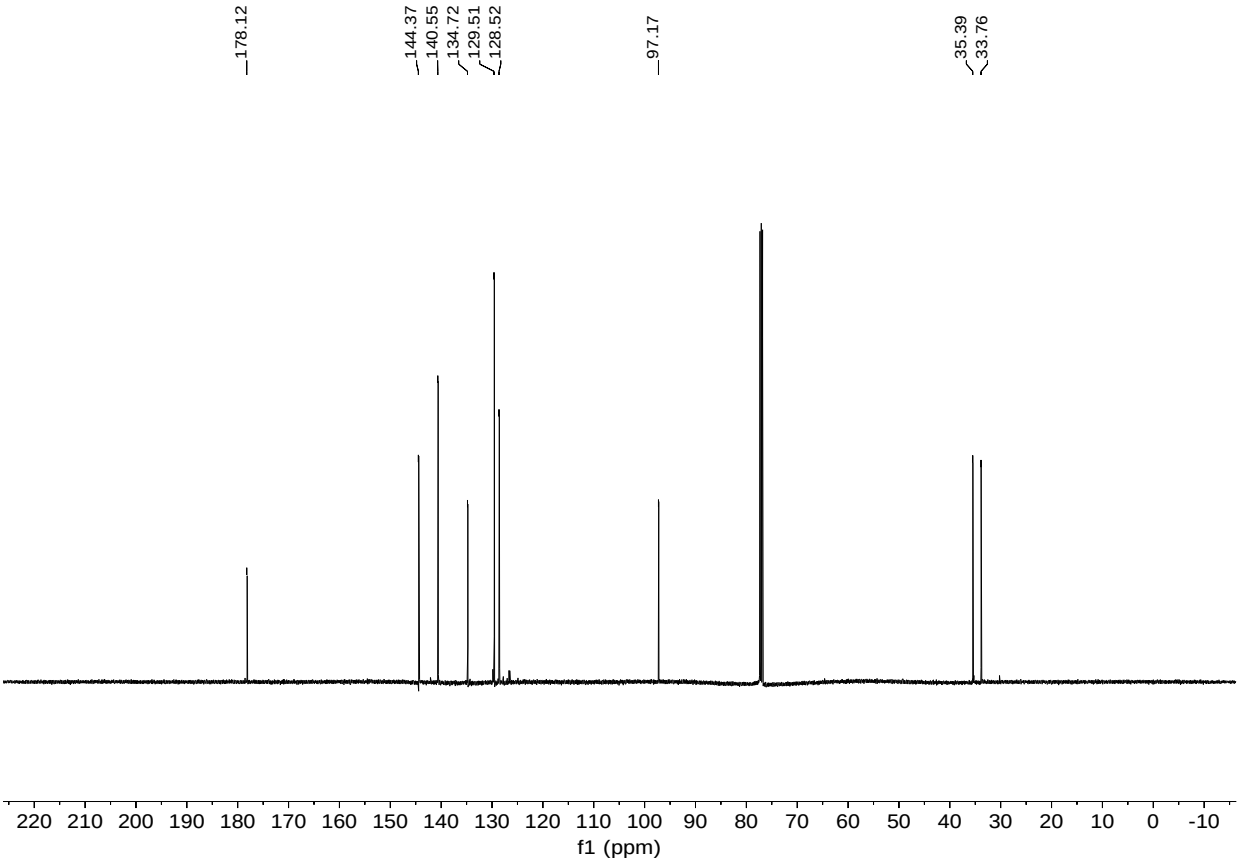
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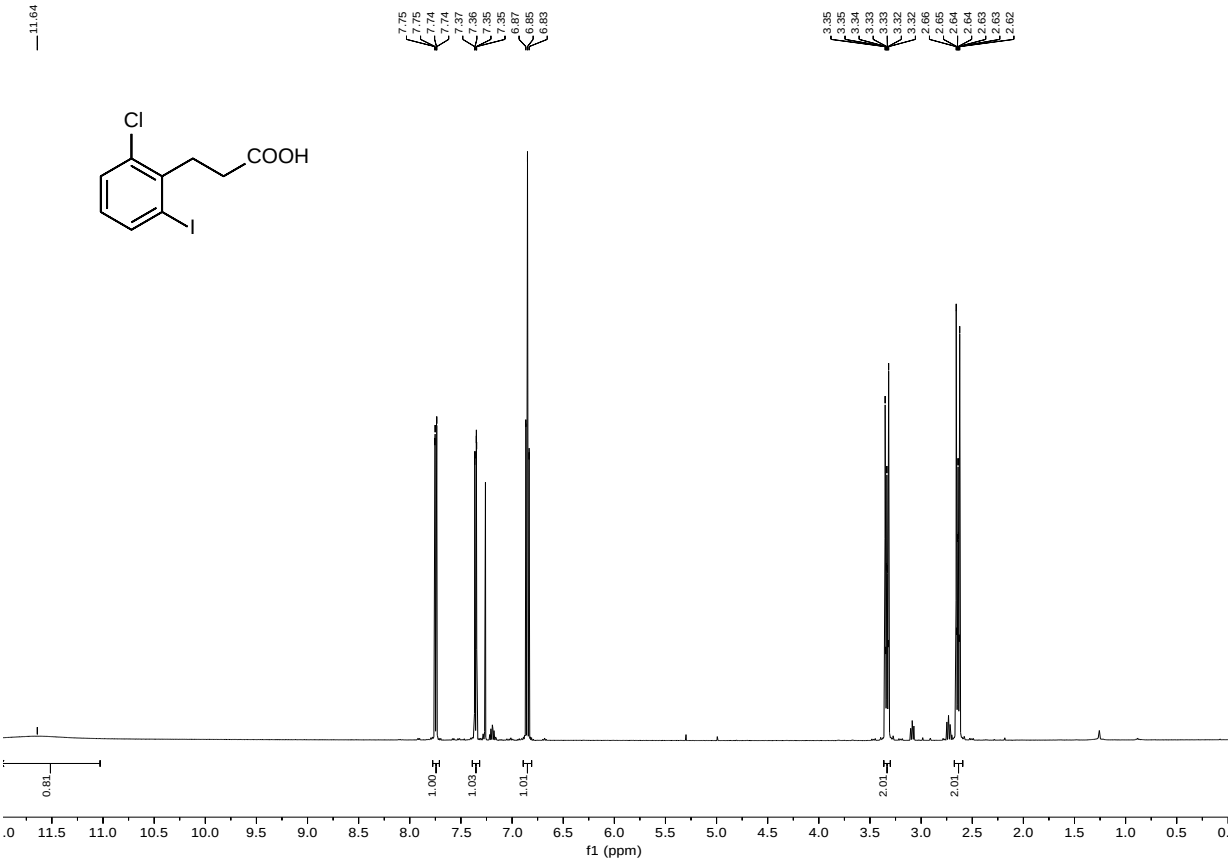
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3.33
3.33
3.32
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2.64
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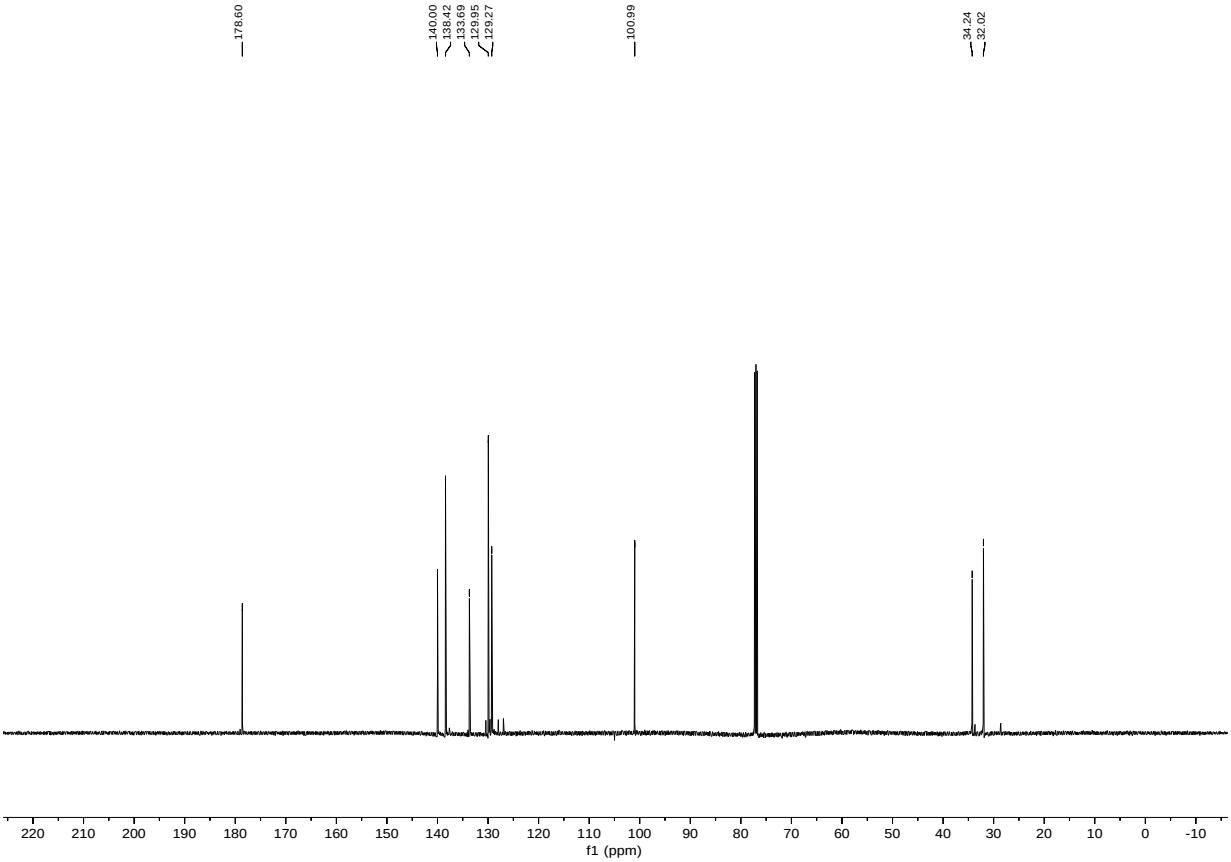
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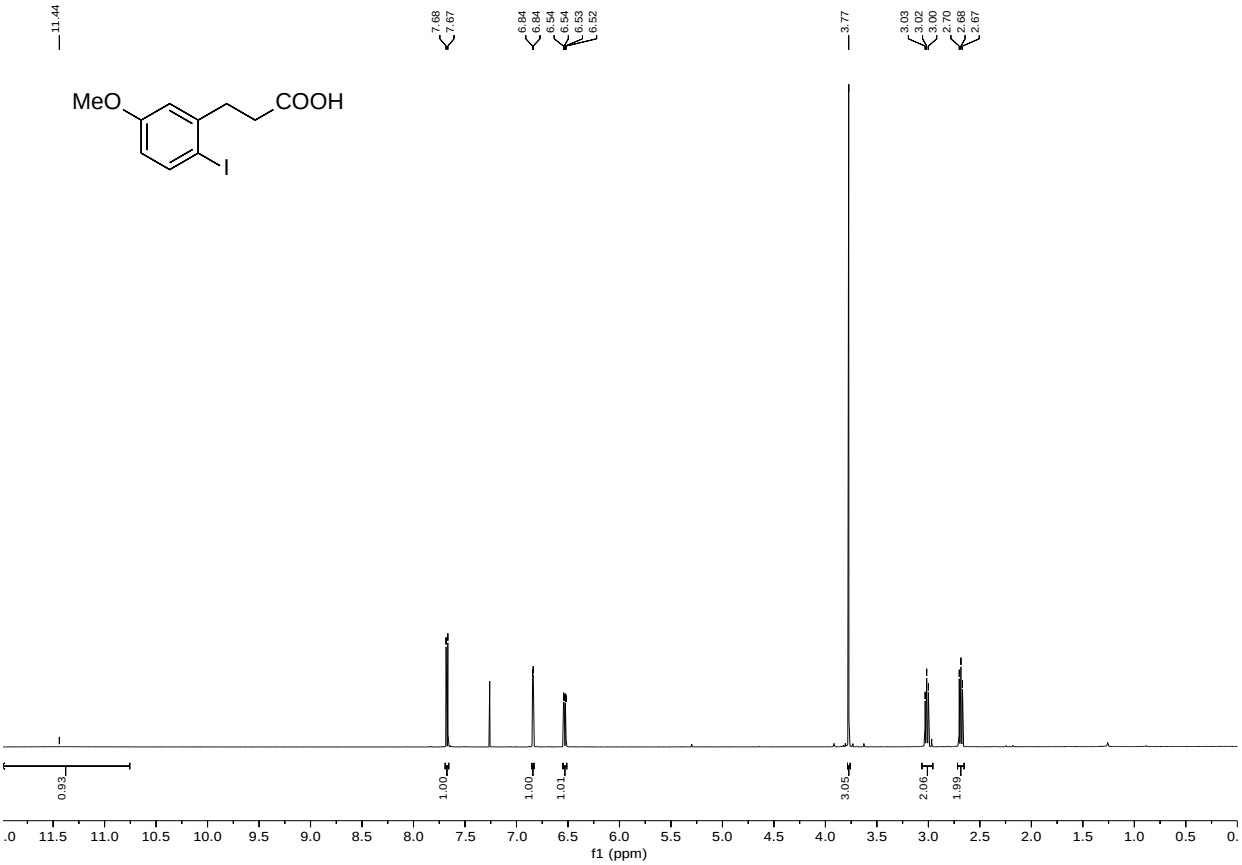
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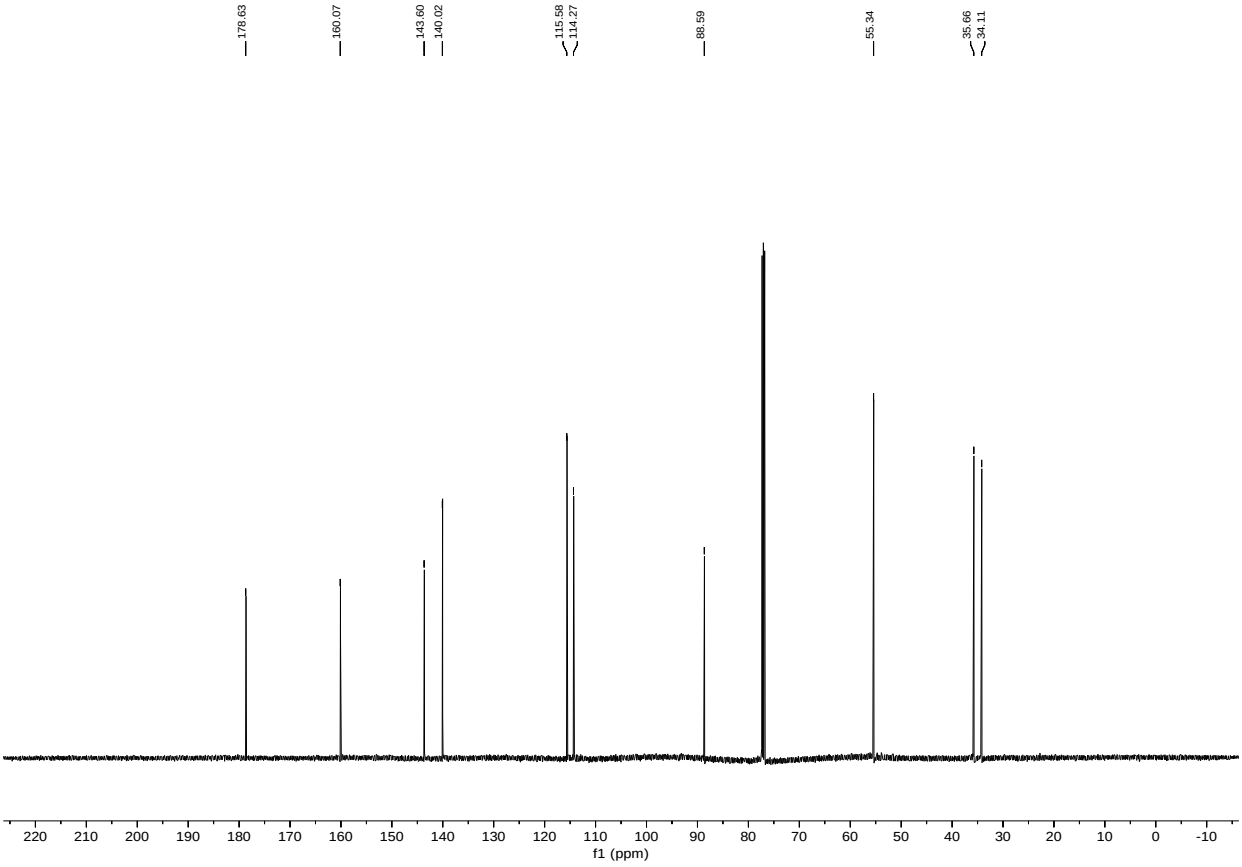
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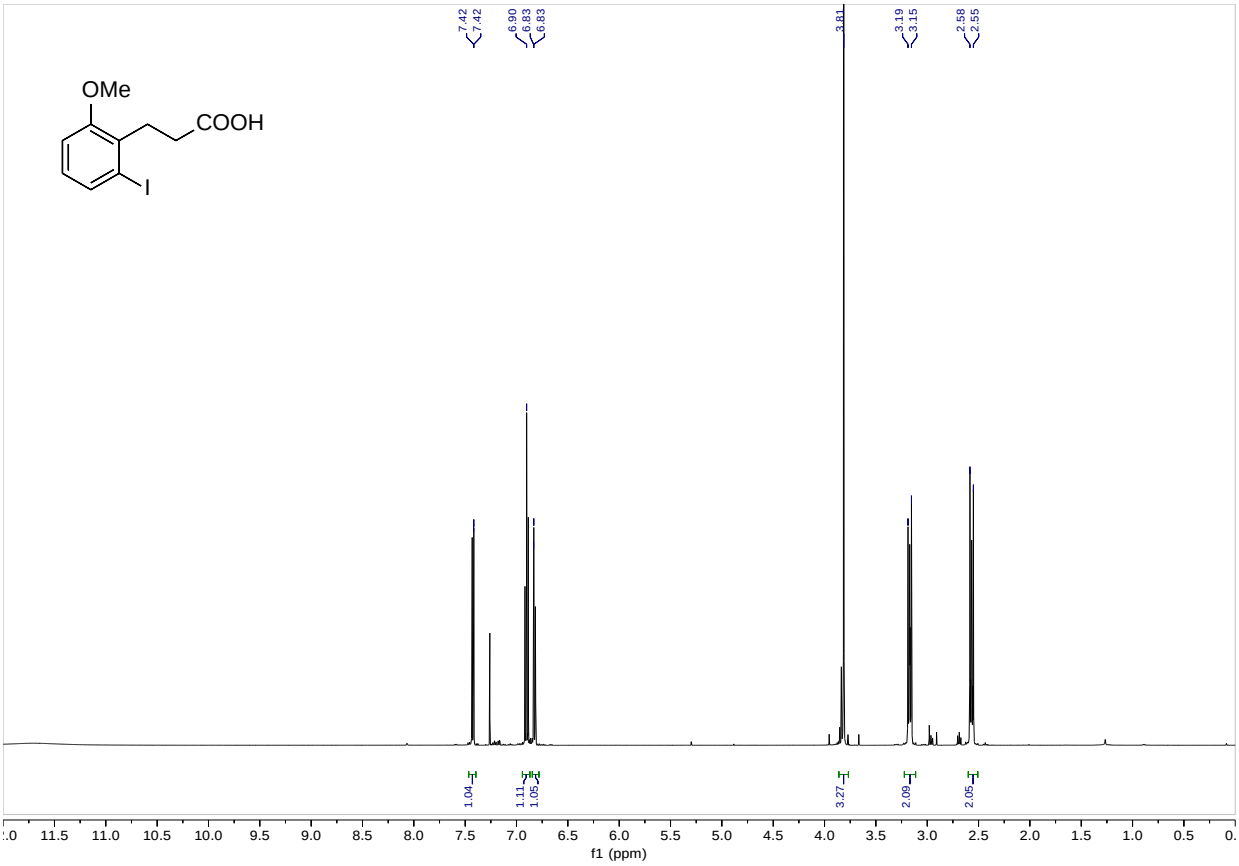
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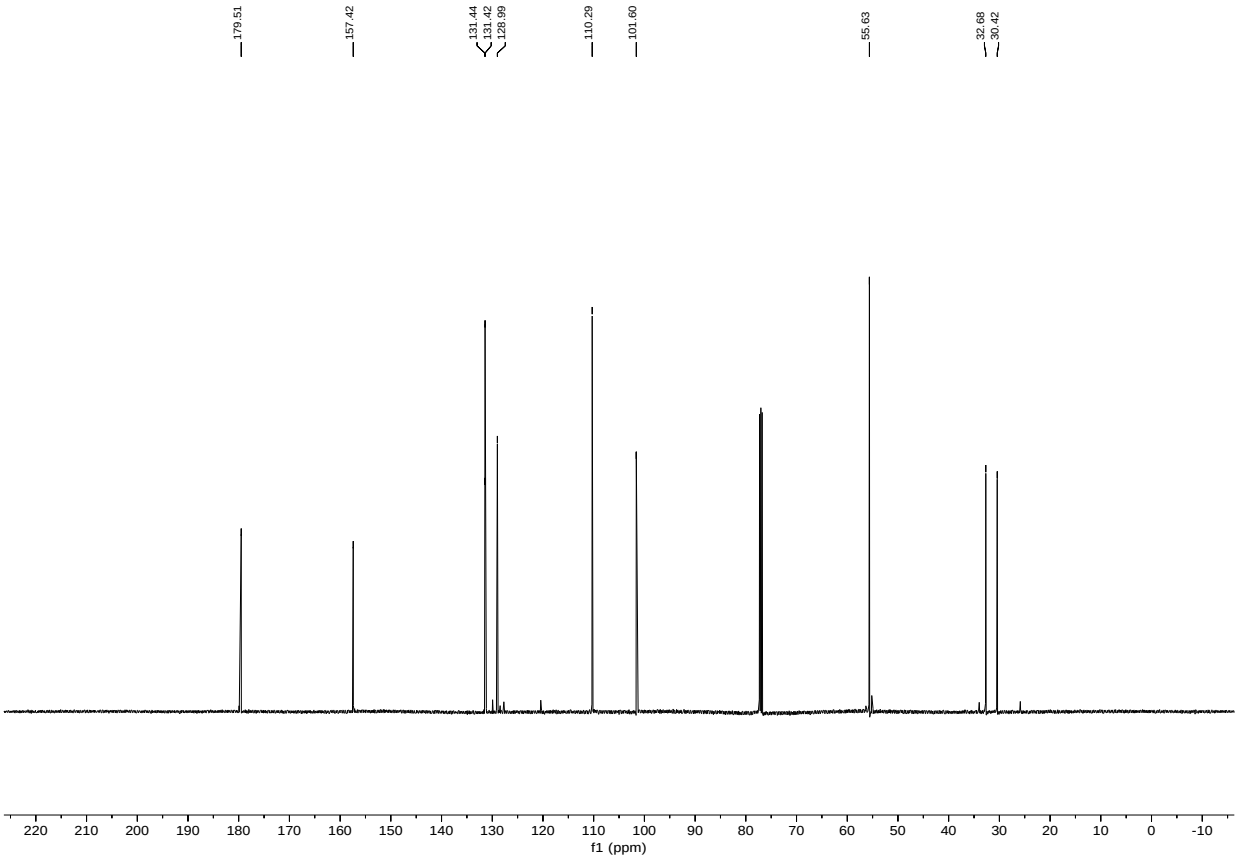
f1 (ppm)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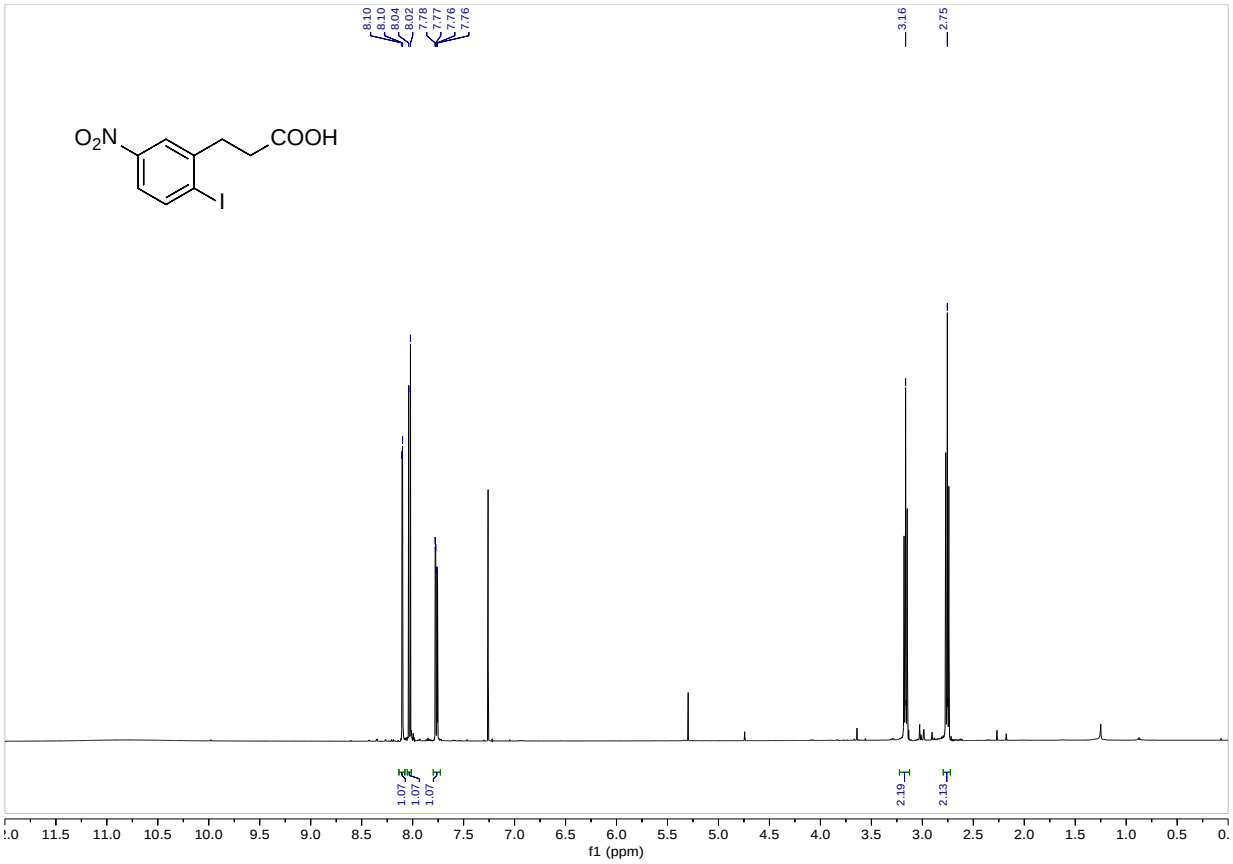
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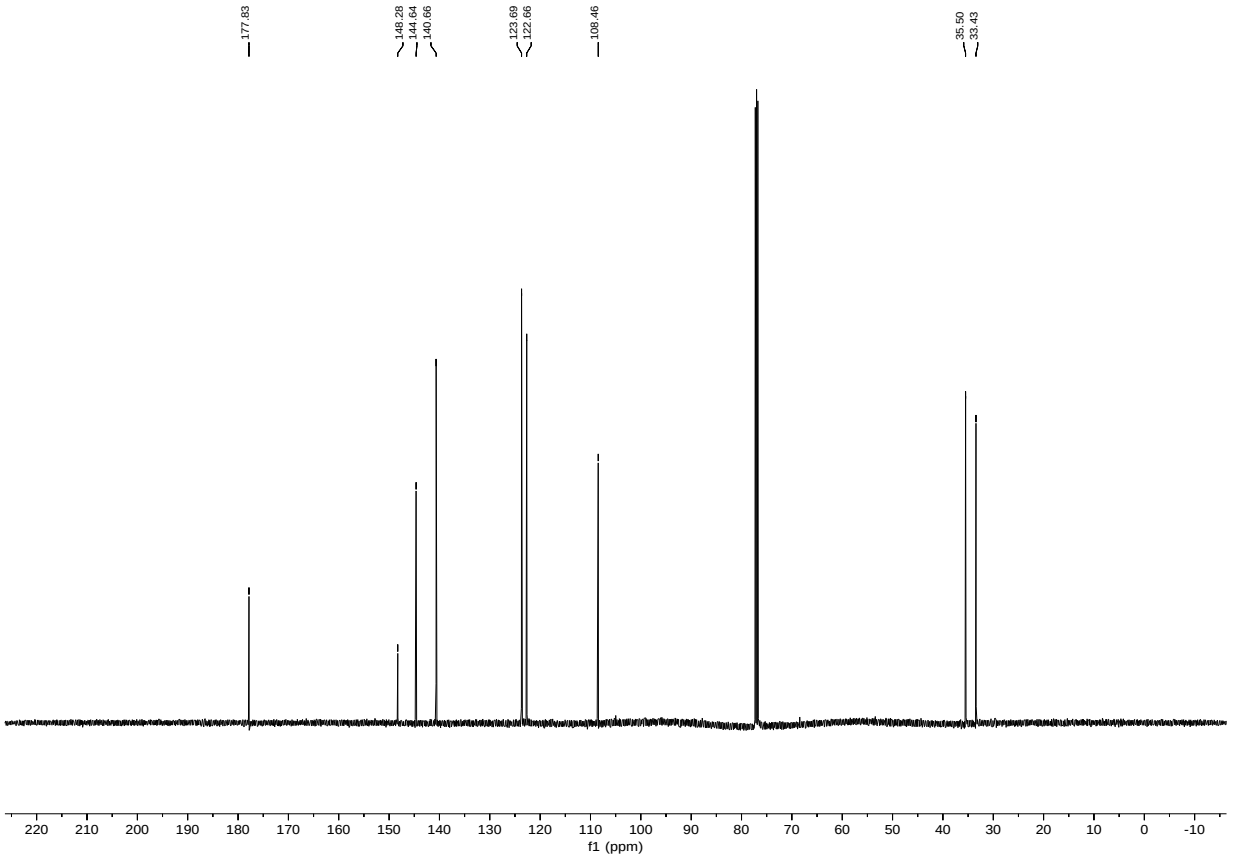
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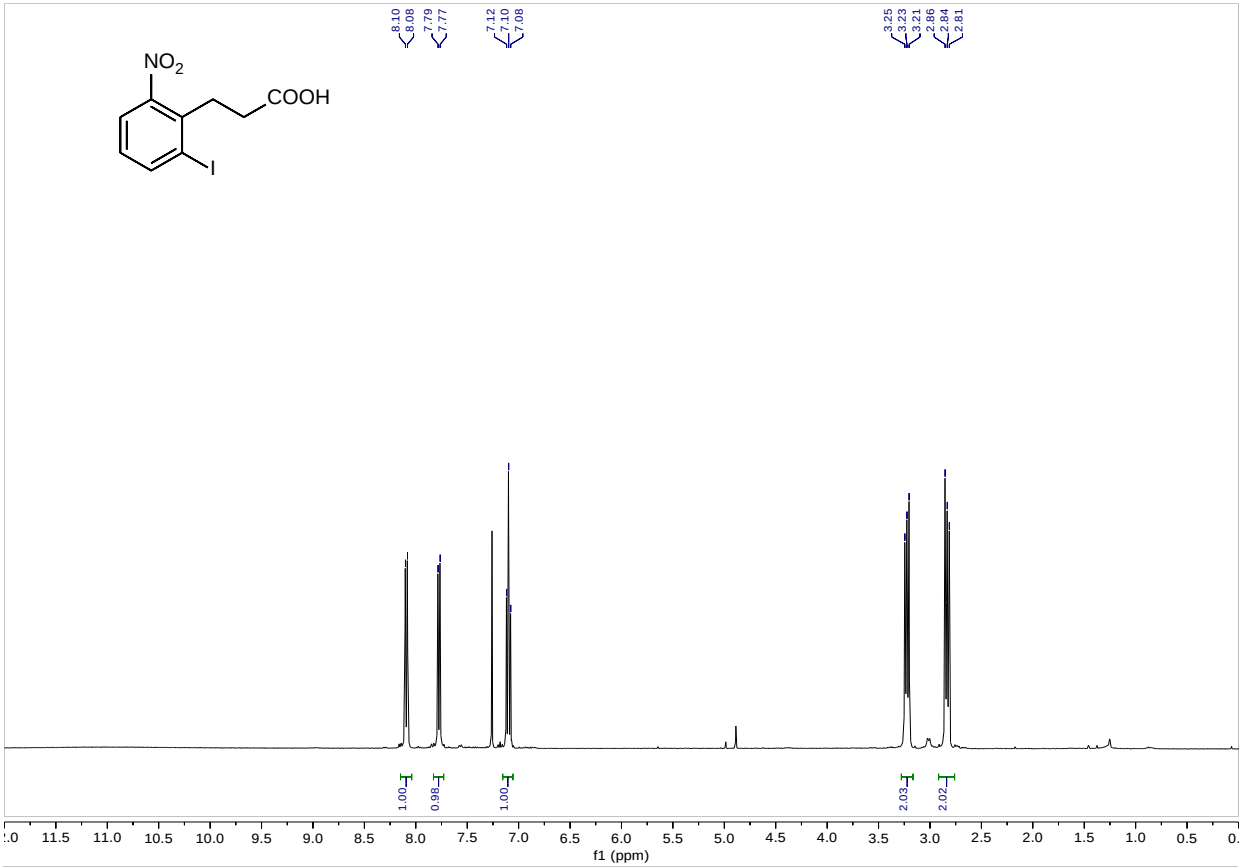
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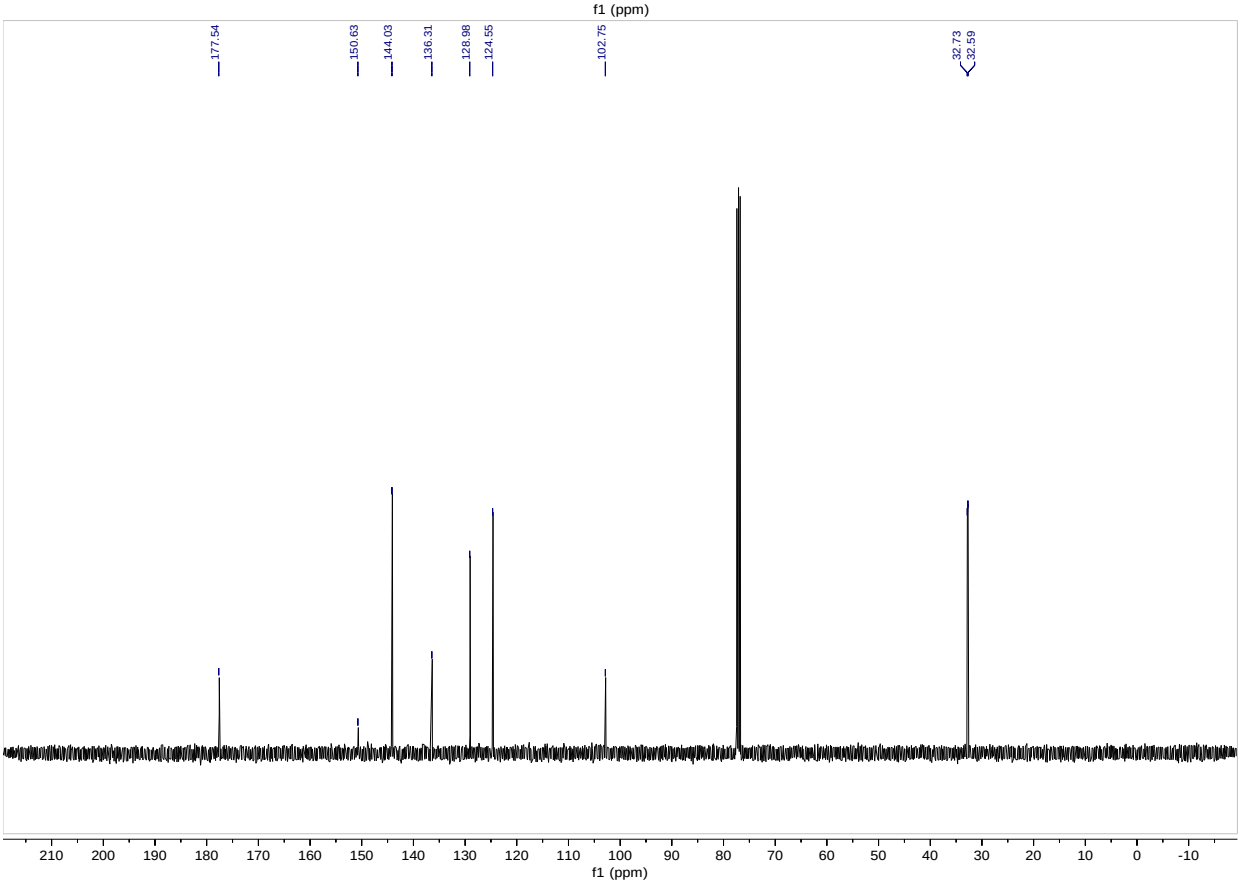
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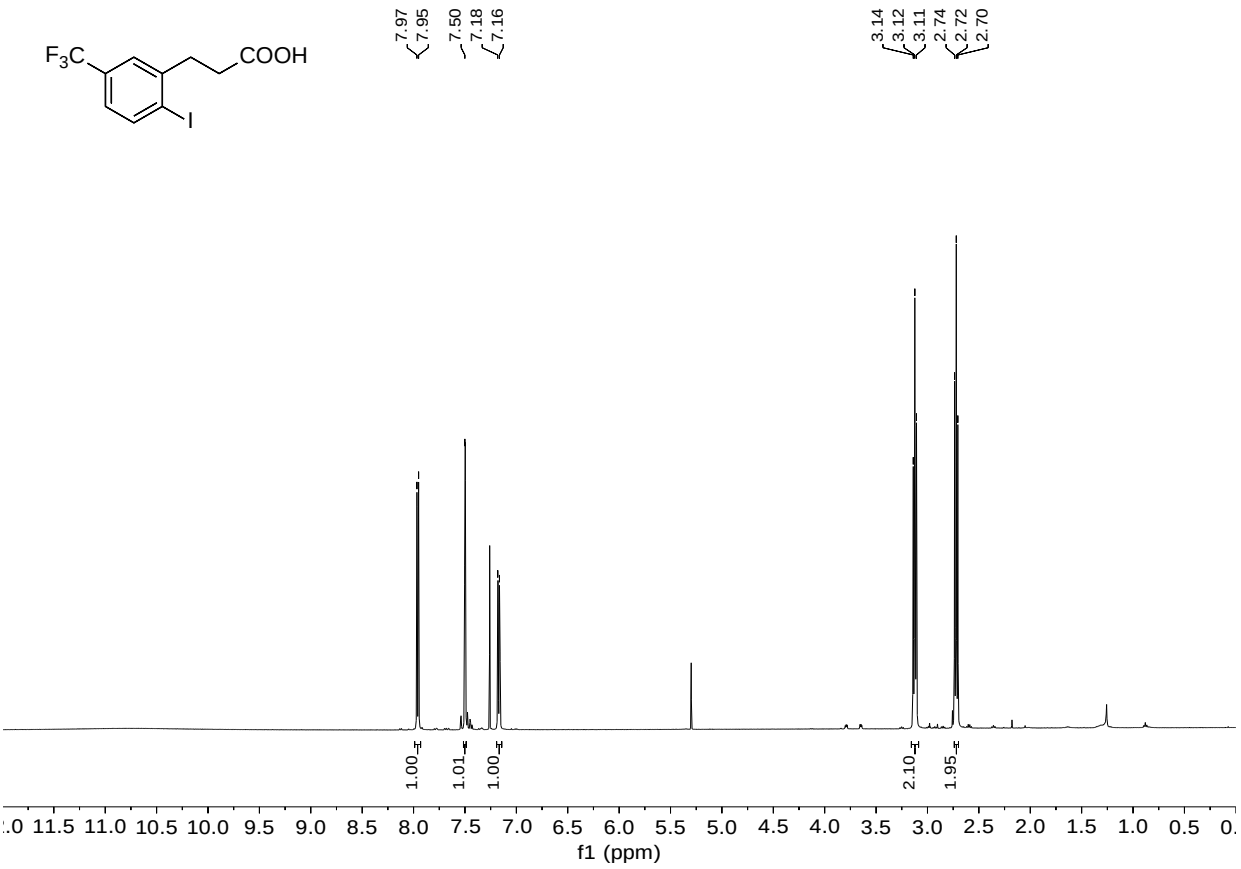
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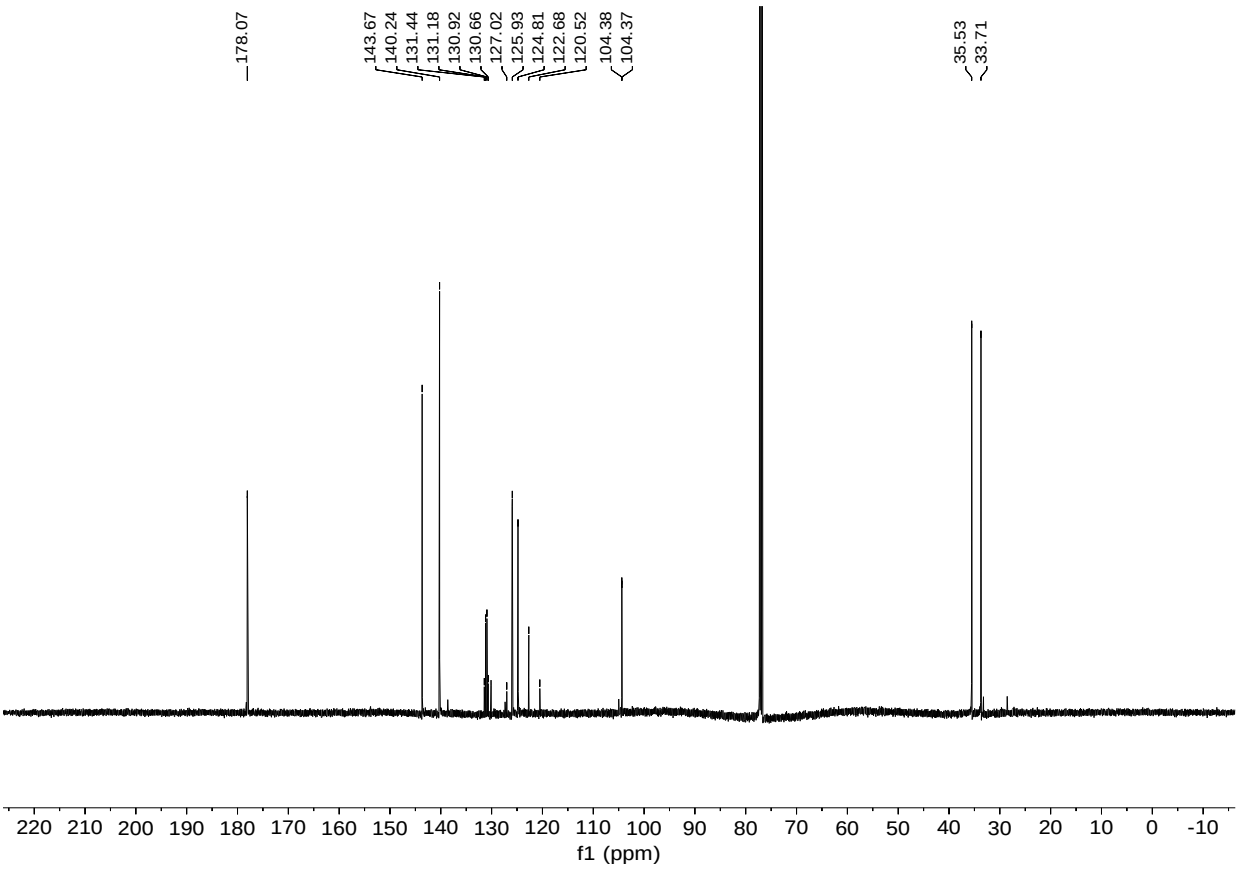
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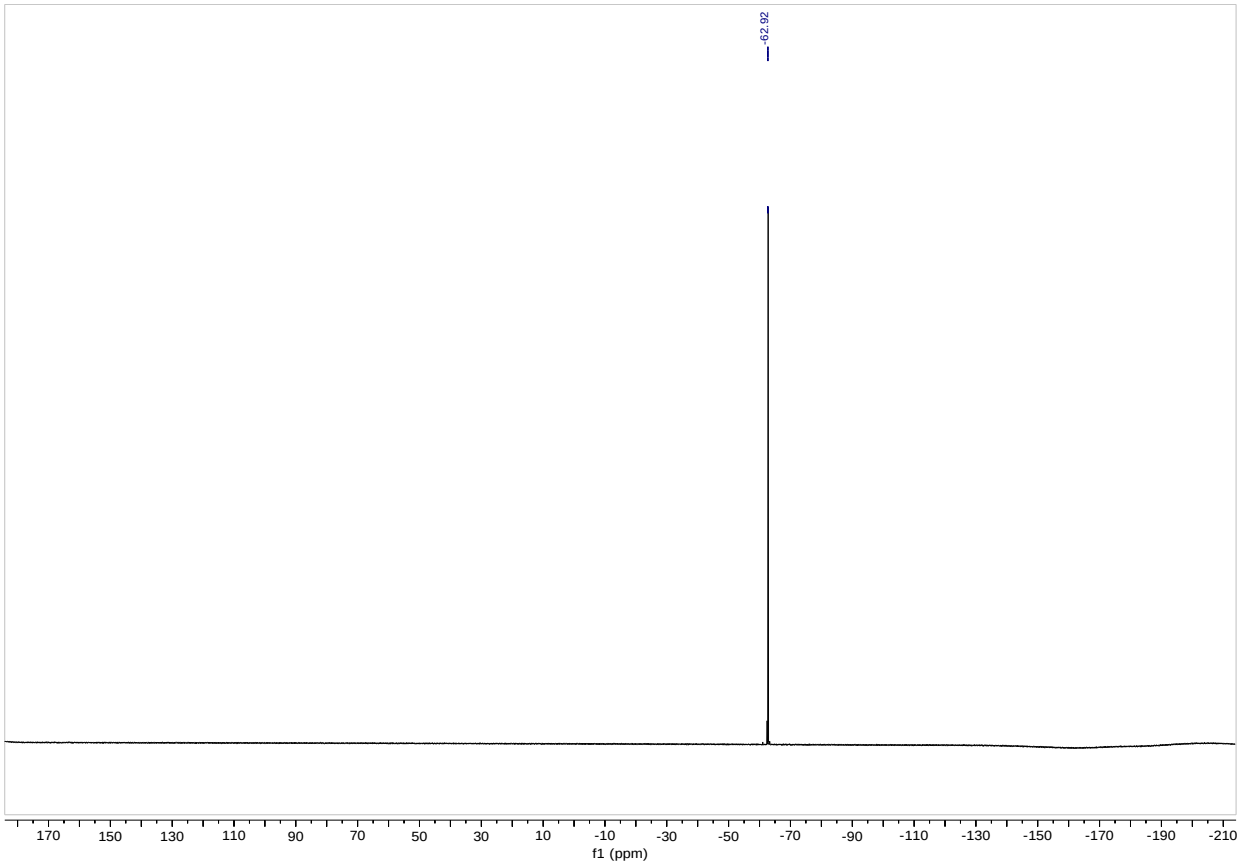
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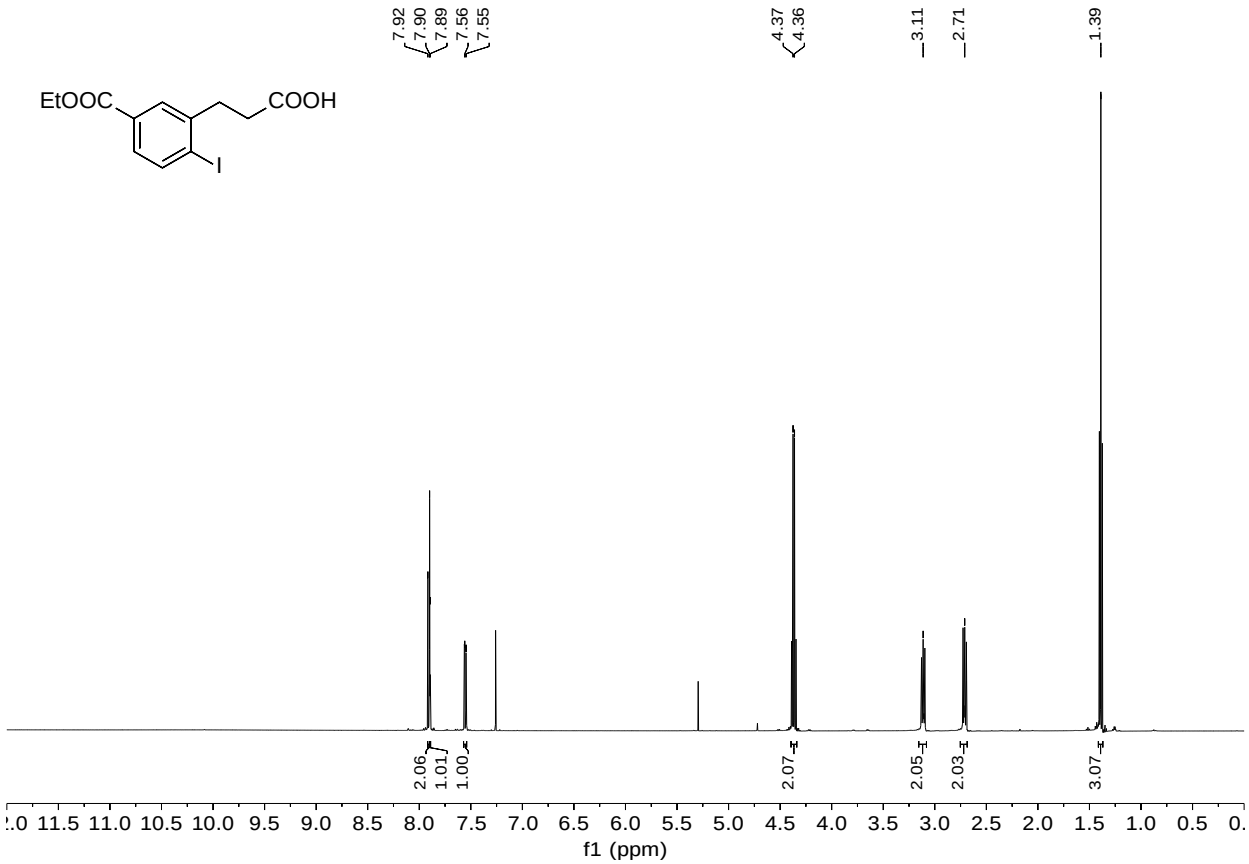
-210
f1 (ppm)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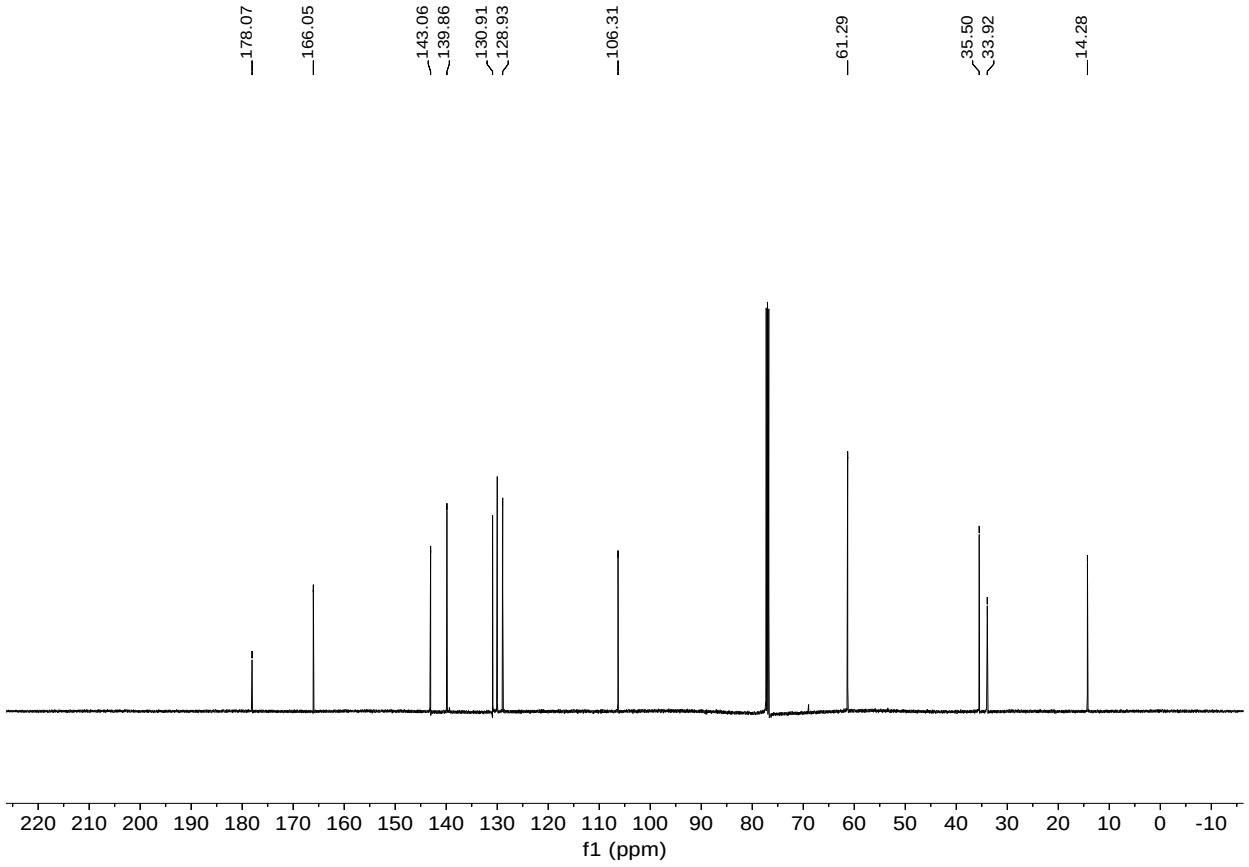
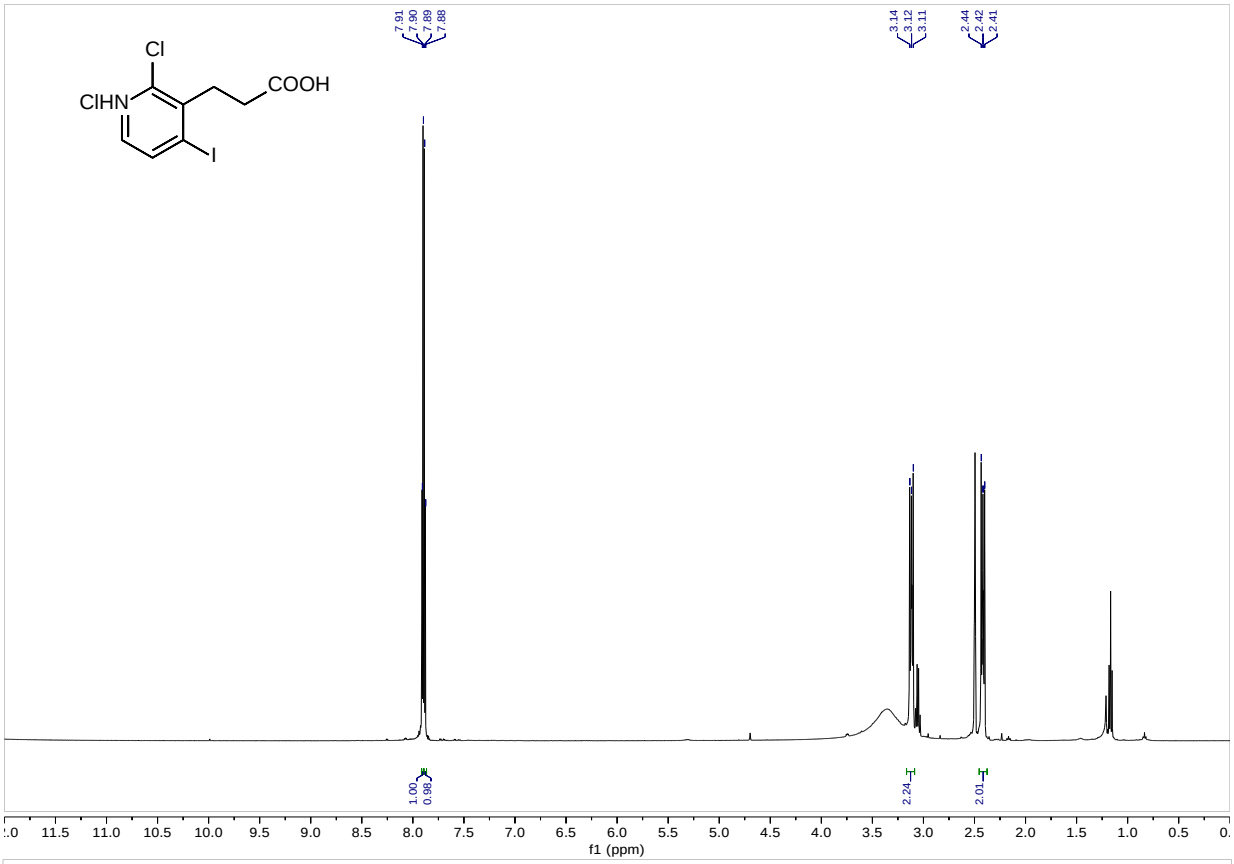
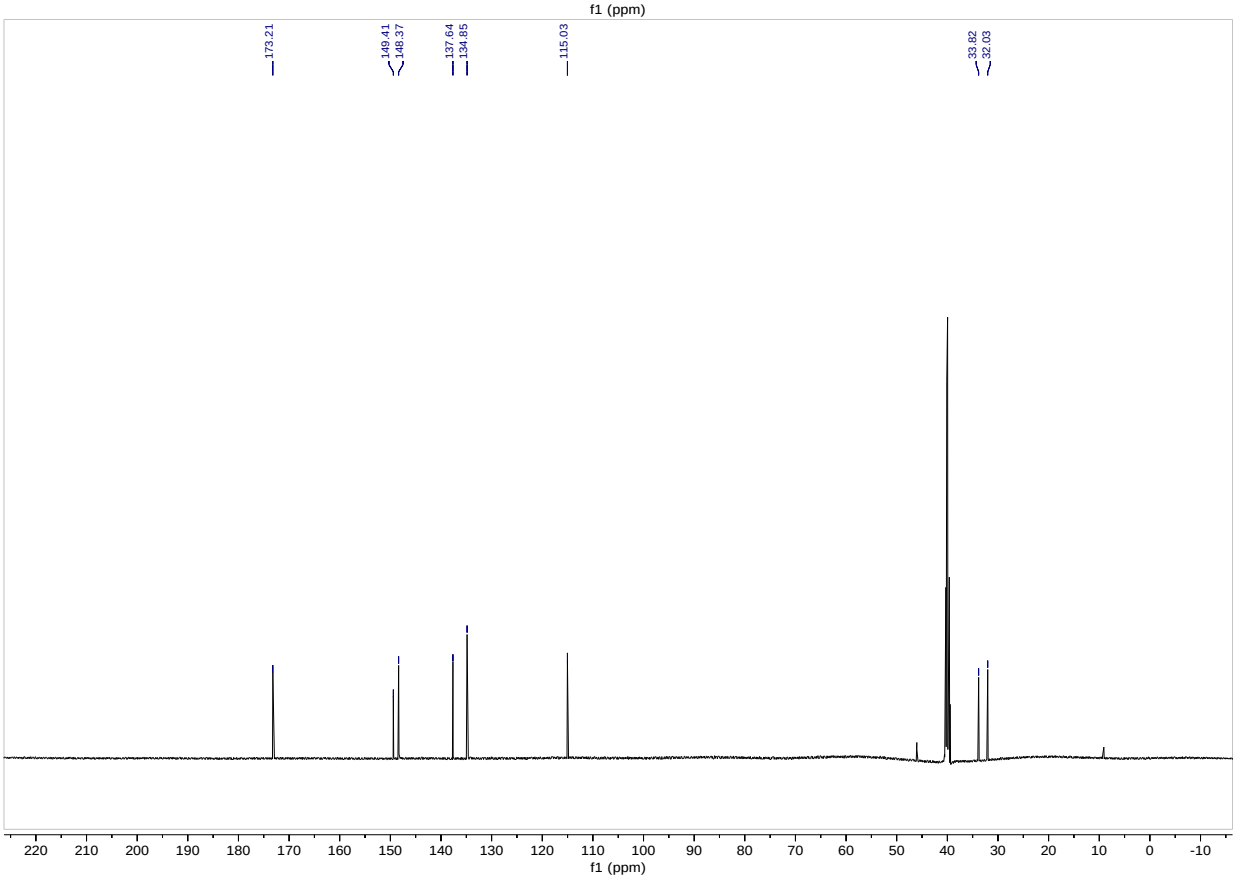
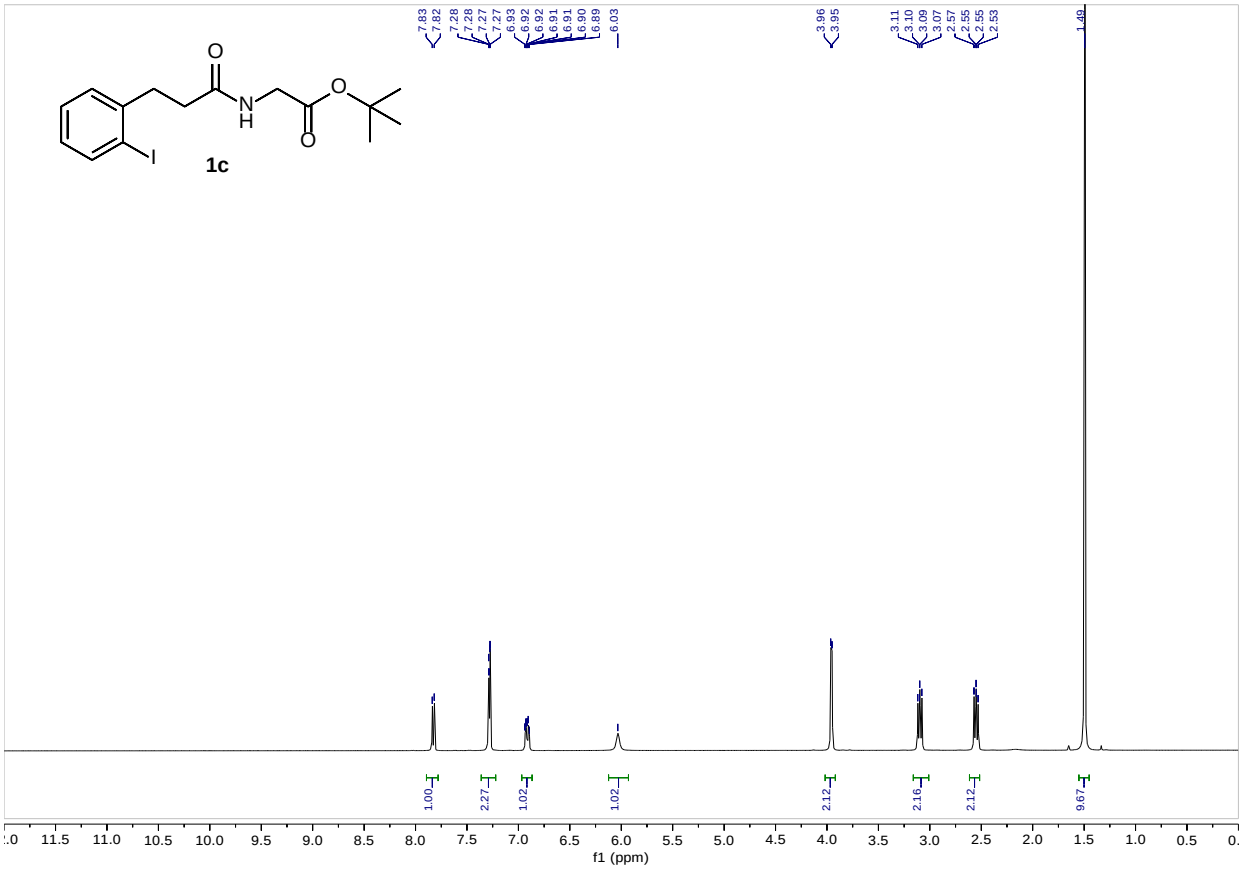
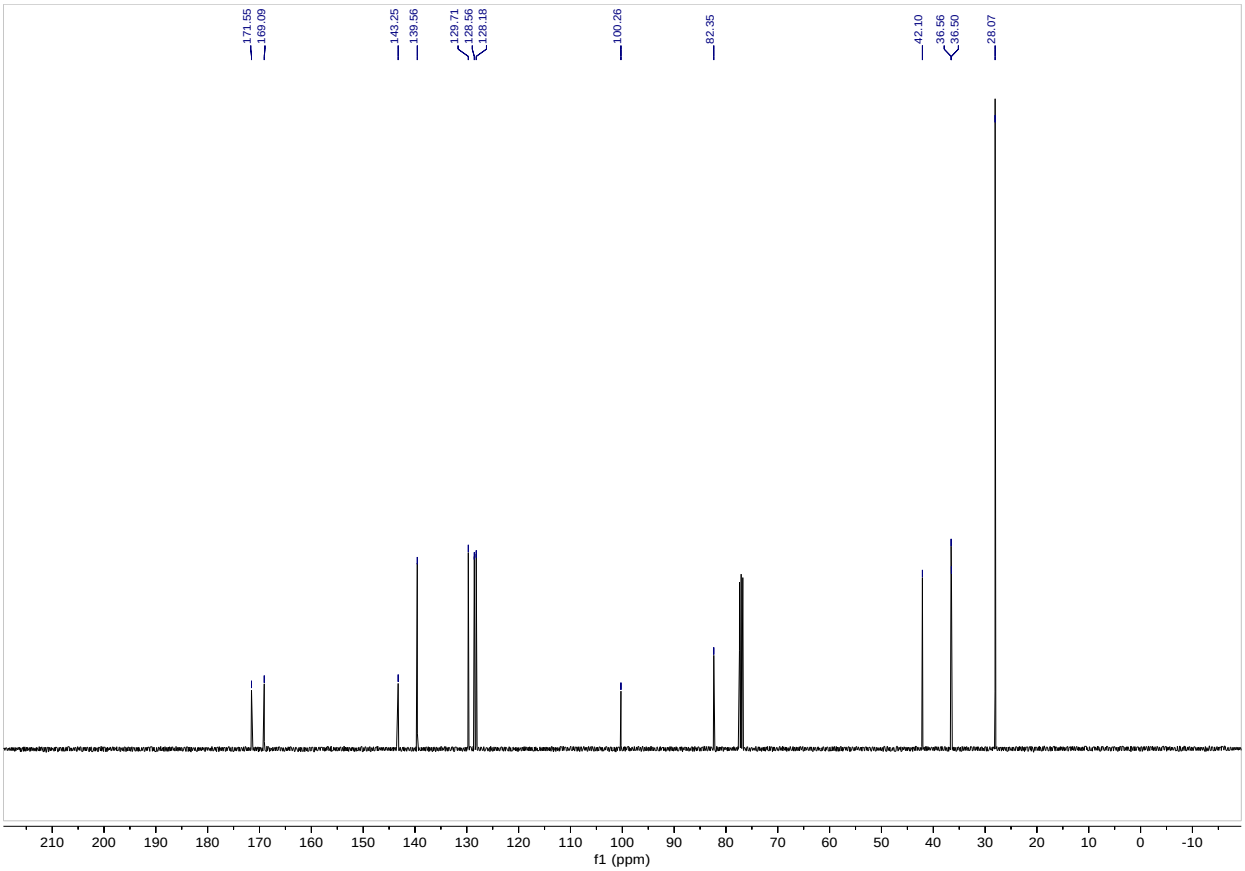
4.36
3.11
2.71
1.39
EtOOC
COOH
I
2.06
1.01
1.00
2.07
2.05
2.03
3.07
f1 (ppm)


178.07
166.05
143.06
139.86
130.91
128.93
106.31
61.29
35.50
33.92
14.28
f1 (ppm)


Cl
ClHN
COOH
I
7.91
7.90
7.89
7.88
3.14
3.12
3.11
2.44
2.42
2.41
1.00
0.98
2.24
2.01
f1 (ppm)


173.21
149.41
148.37
137.64
134.85
115.03
33.82
32.03
f1 (ppm)


1c
7.83
7.82
7.28
7.28
7.27
7.27
6.93
6.92
6.92
6.91
6.91
6.90
6.89
6.03
3.96
3.95
3.11
3.10
3.09
3.07
2.57
2.55
2.55
2.53
1.49
1.00
2.27
1.02
1.02
2.12
2.16
2.12
9.67
f1 (ppm)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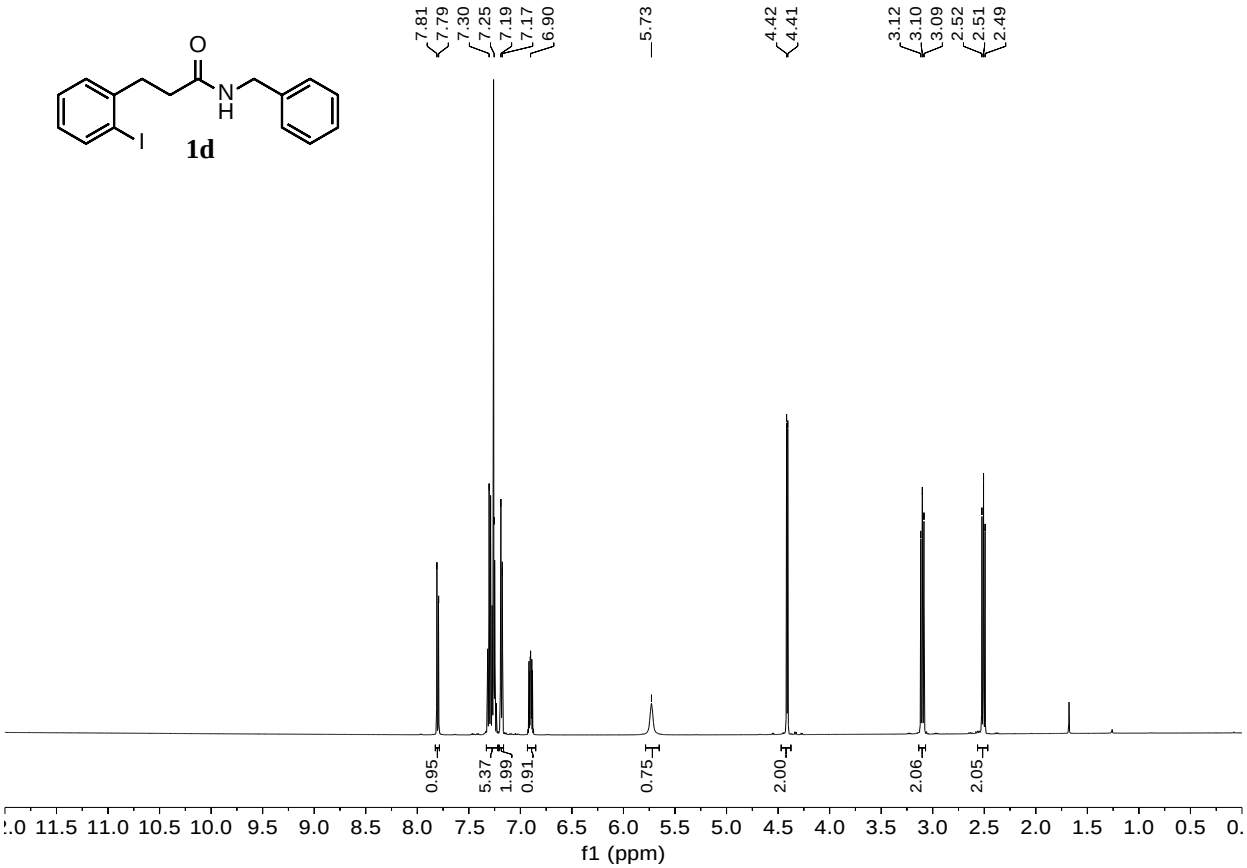
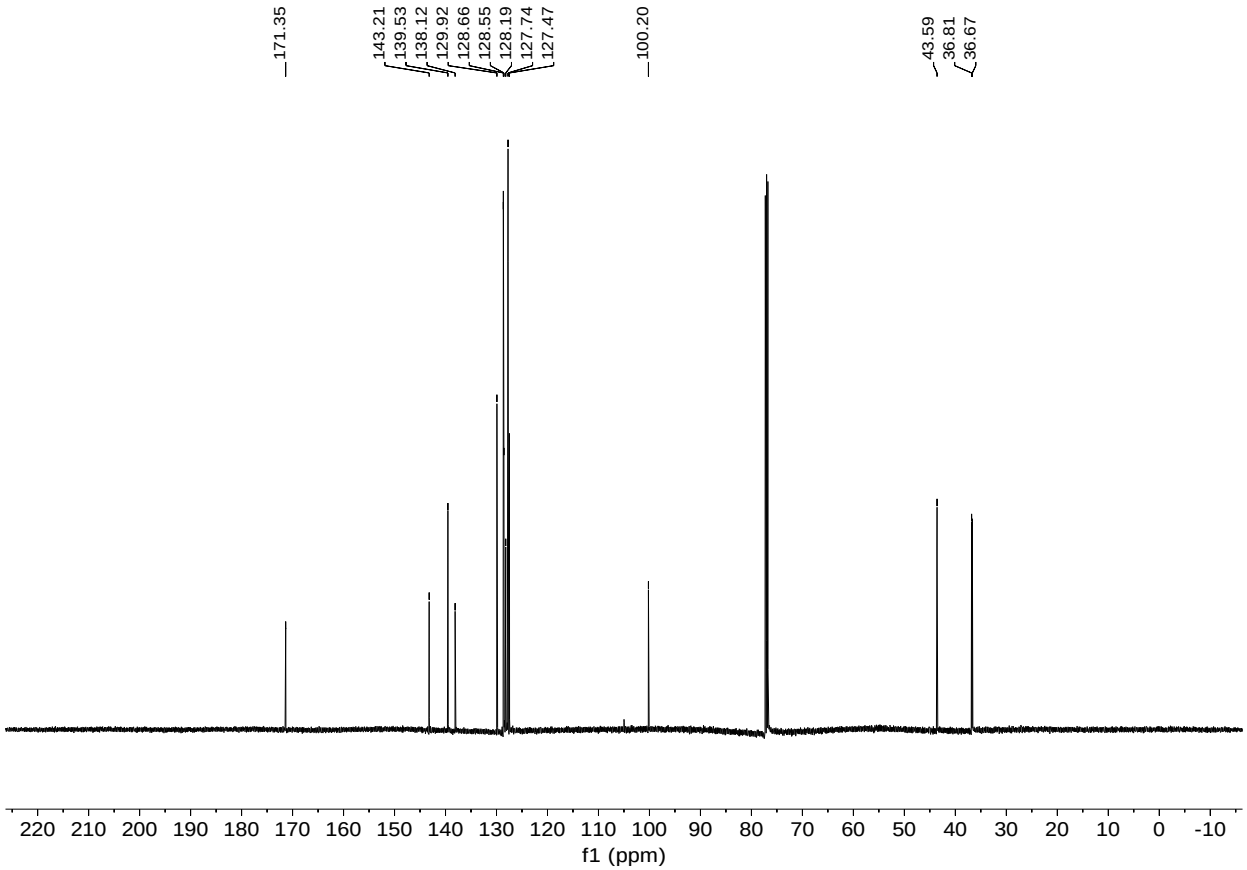
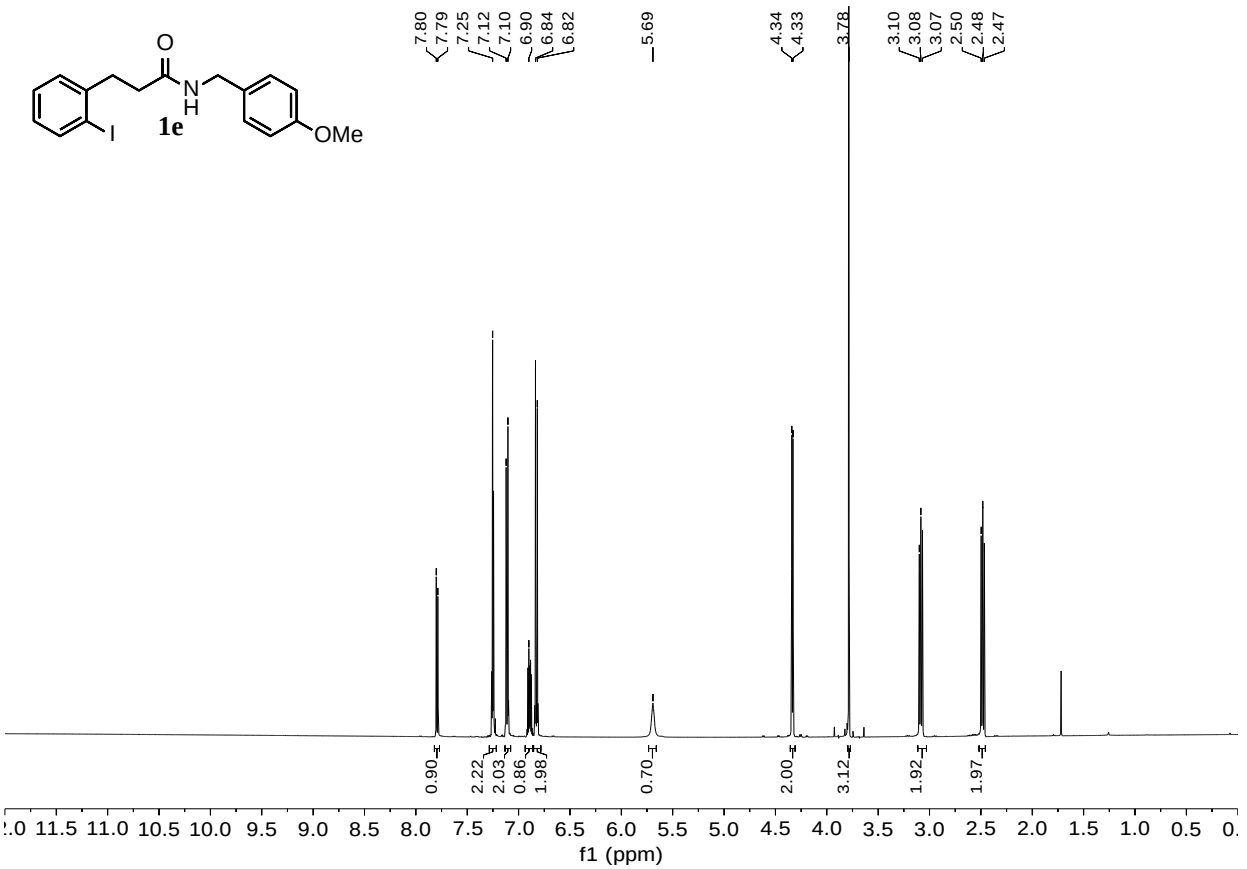
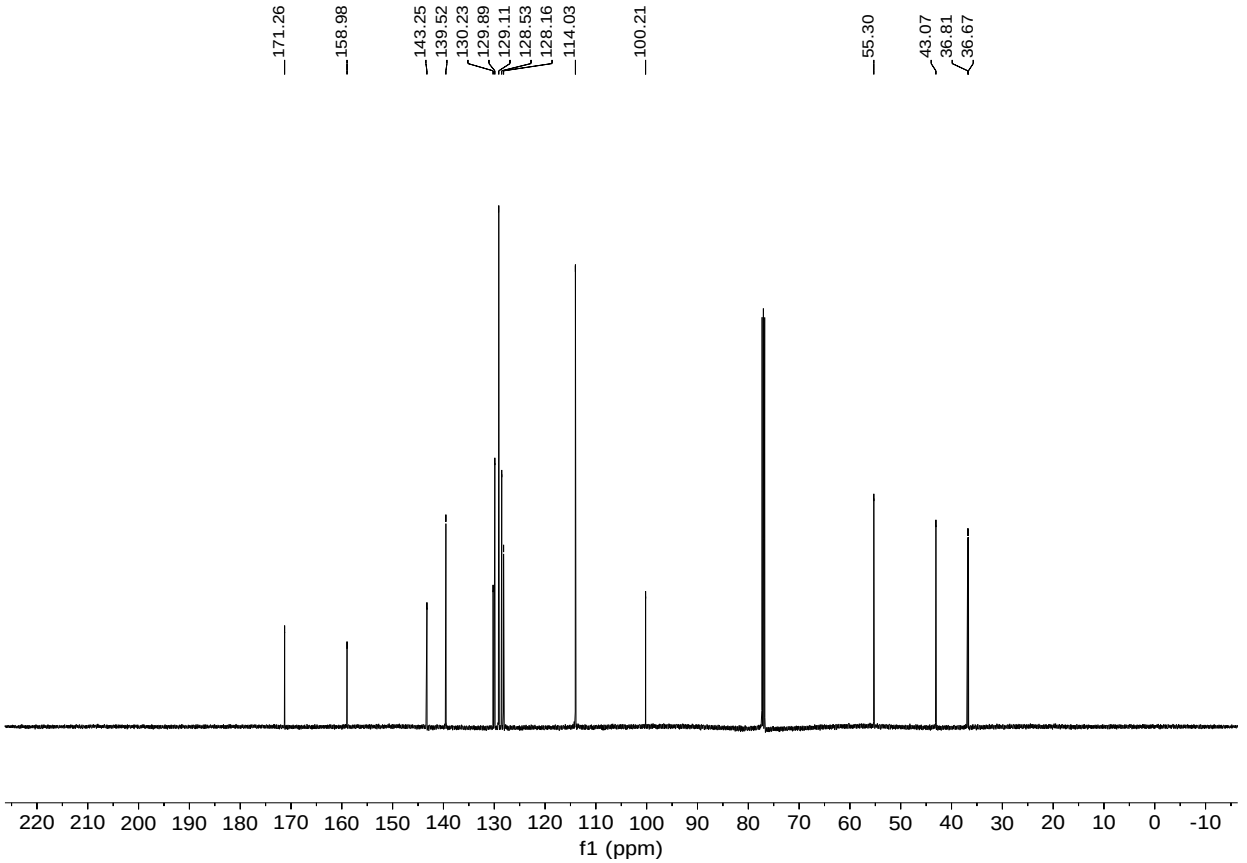
128.56
128.18
100.26
82.35
42.10
36.56
36.50
28.07
f1 (ppm)


O
N
H
I
1d
7.81
7.79
7.30
7.25
7.19
7.17
6.90
5.73
4.42
4.41
3.12
3.10
3.09
2.52
2.51
2.49
0.95
5.37
1.99
0.91
0.75
2.00
2.06
2.05
f1 (ppm)


171.35
143.21
139.53
138.12
129.92
128.66
128.55
128.19
127.74
127.47
100.20
43.59
36.81
36.67
f1 (ppm)


O
N
H
I
OMe
1e
7.80
7.79
7.25
7.12
7.10
6.90
6.84
6.82
5.69
4.34
4.33
3.78
3.10
3.08
3.07
2.50
2.48
2.47
0.90
2.22
2.03
0.86
1.98
0.70
2.00
3.12
1.92
1.97
f1 (ppm)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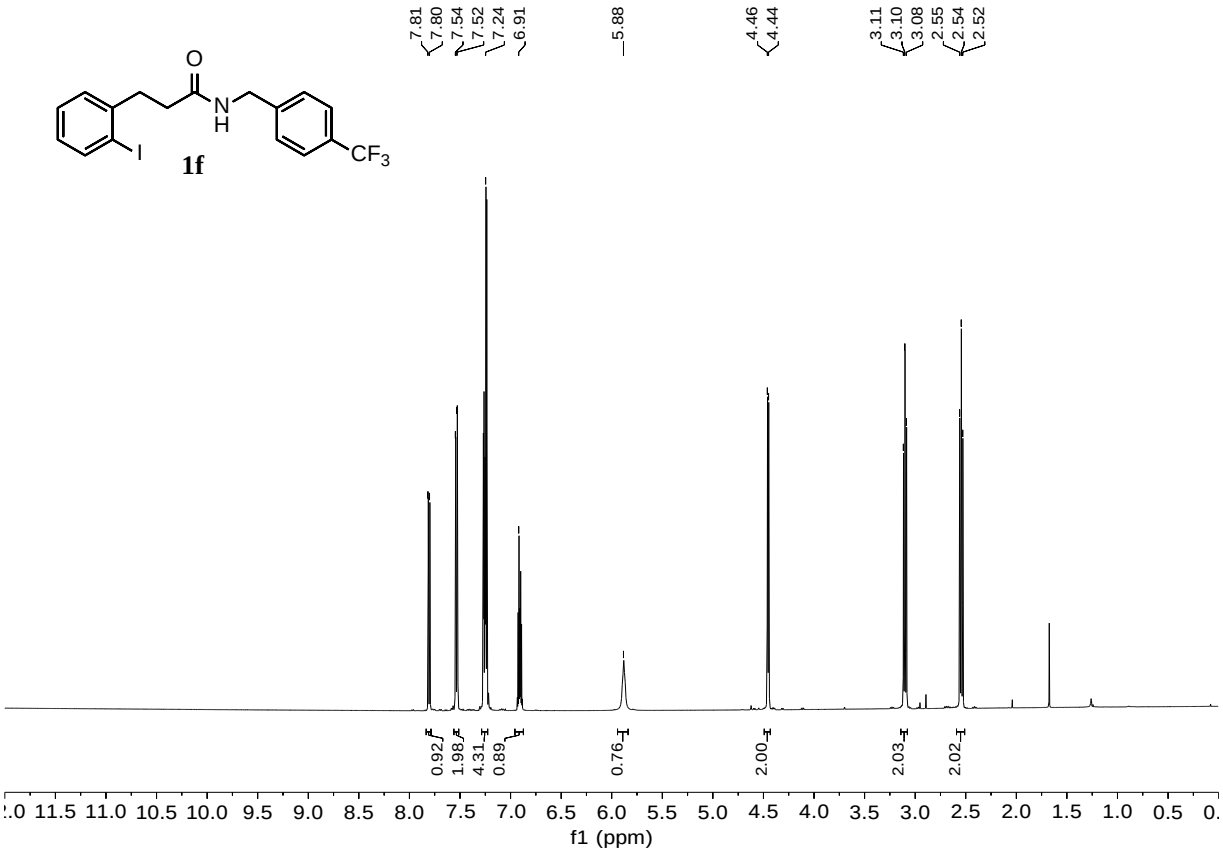
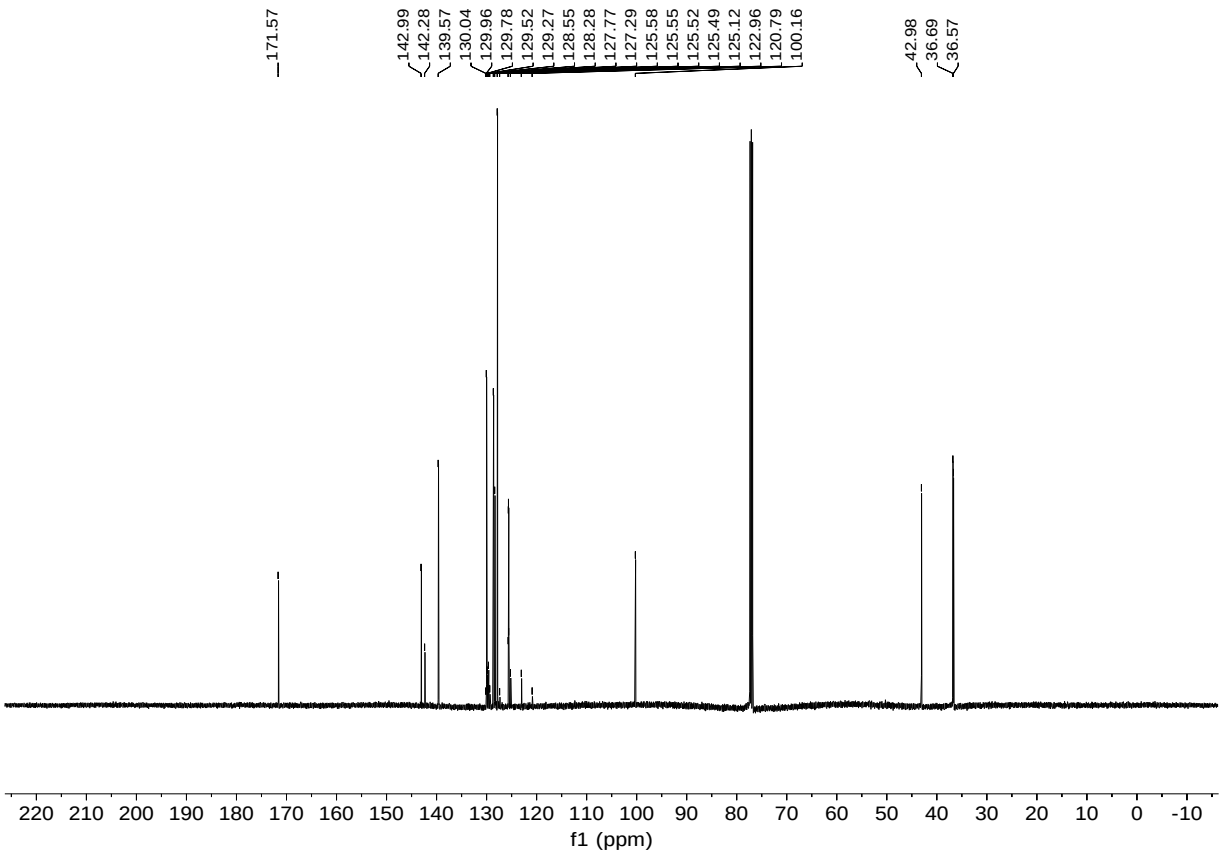
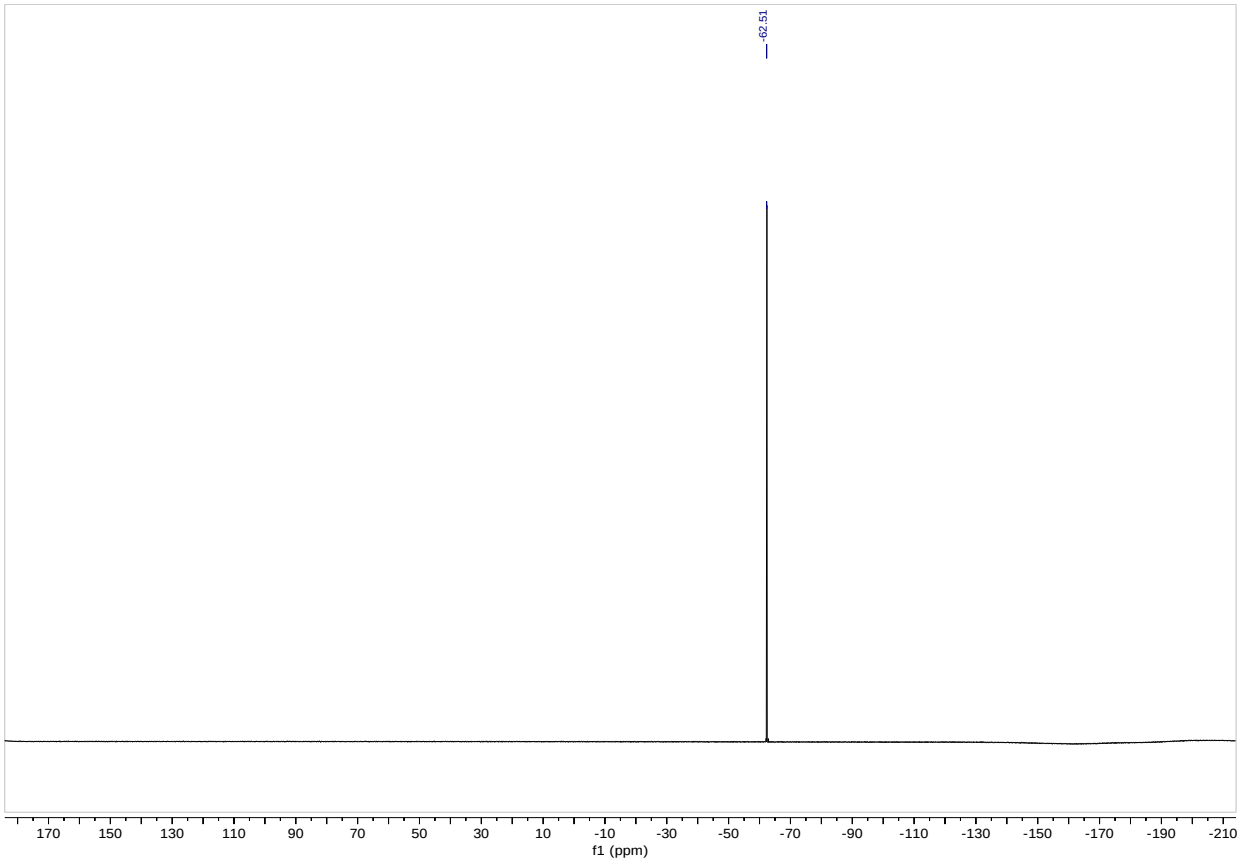
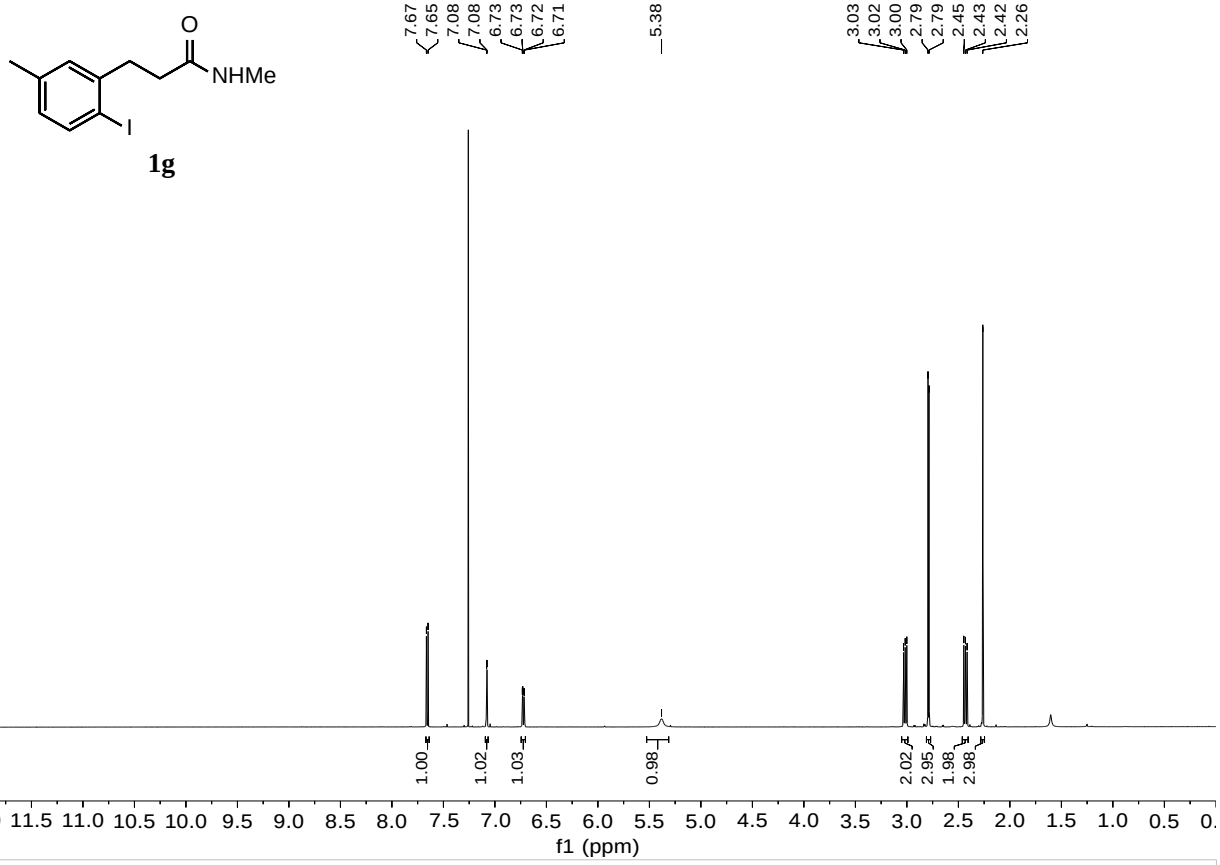
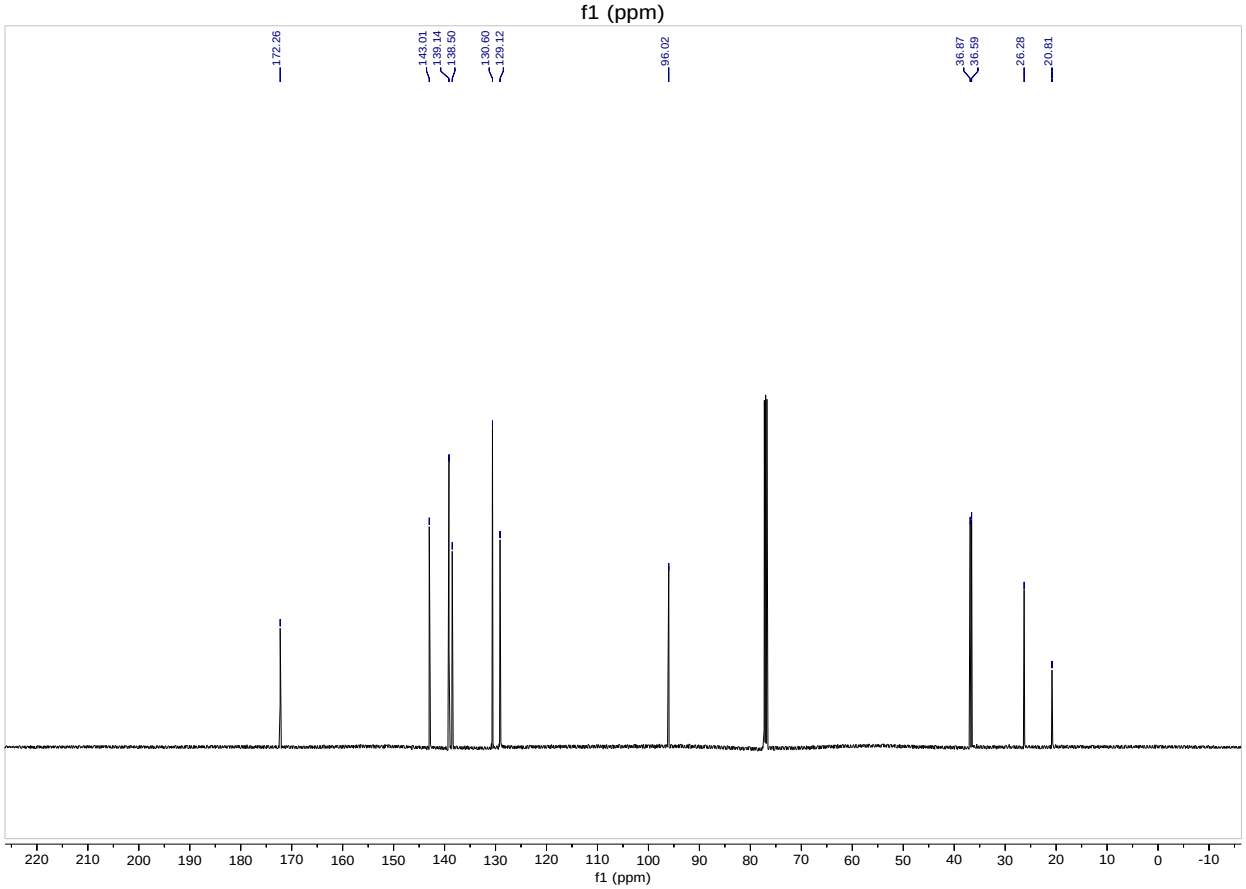
158.98
143.25
139.52
130.23
129.89
129.11
128.53
128.16
114.03
100.21
55.30
43.07
36.81
36.67
f1 (ppm)

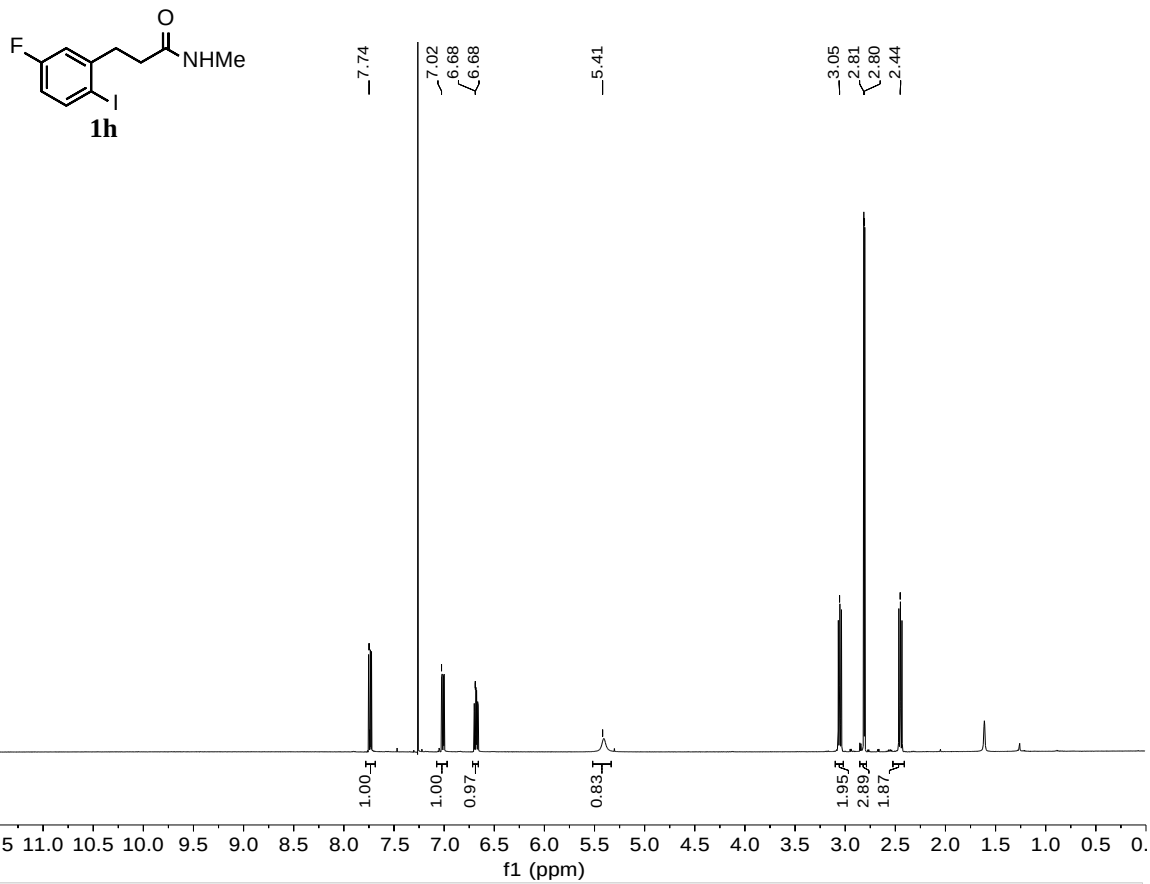

7.81
7.80
7.54
7.52
7.24
6.91
5.88
4.46
4.44
3.11
3.10
3.08
2.55
2.54
2.52
O
N
H
I
CF3
1f
0.92
1.98
4.31
0.89
0.76
2.00
2.03
2.02
f1 (ppm)

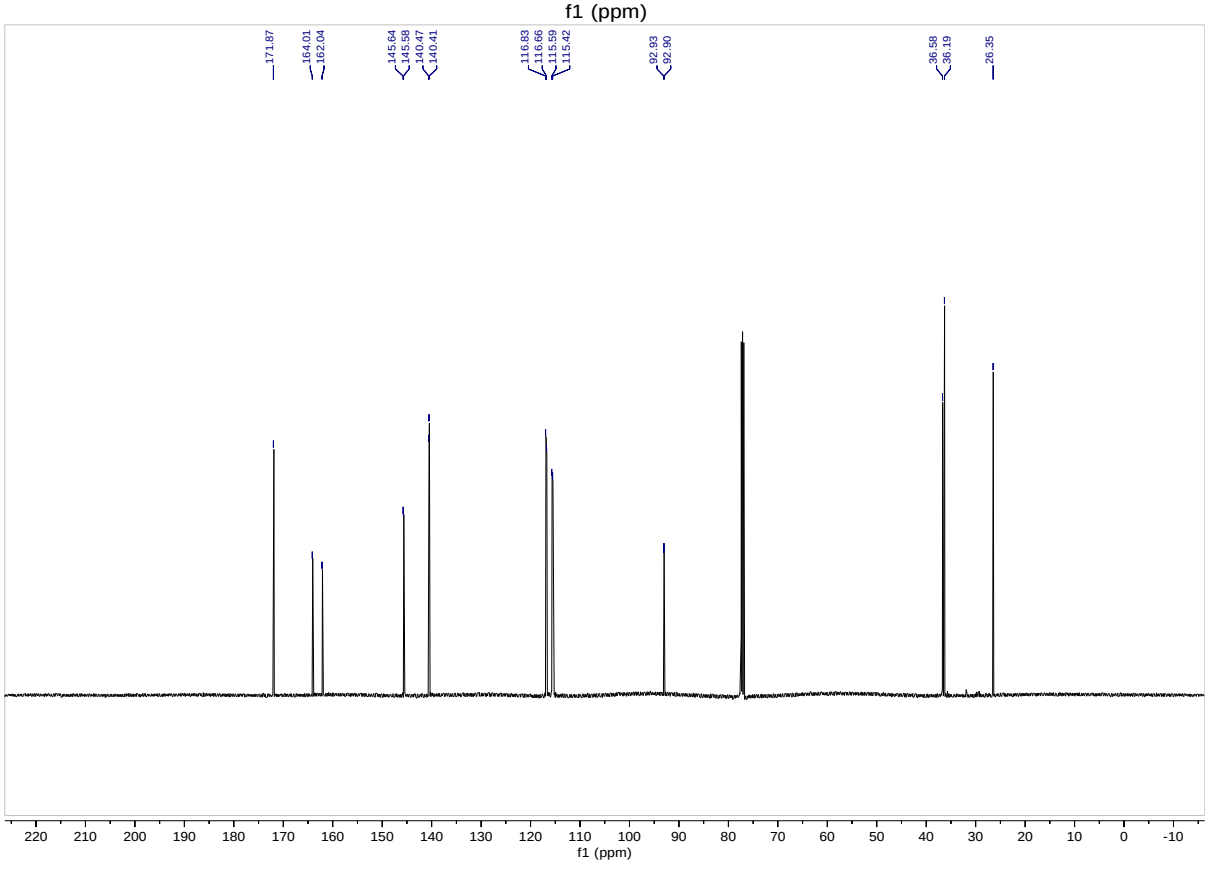

171.57
142.99
142.28
139.57
130.04
129.96
129.78
129.52
129.27
128.55
128.28
127.77
127.29
125.58
125.55
125.52
125.49
125.12
122.96
120.79
100.16
42.98
36.69
36.57
f1 (ppm)

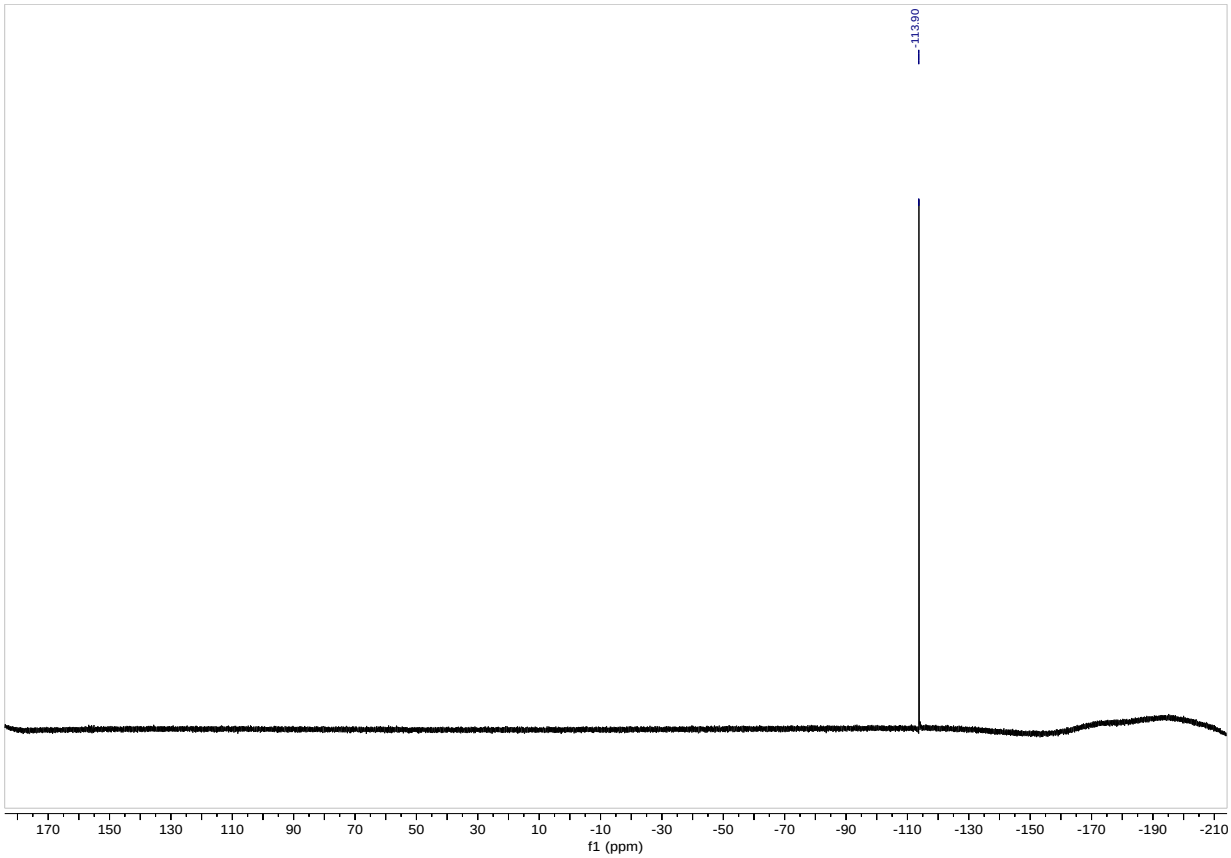

-62.51
170
150
130
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

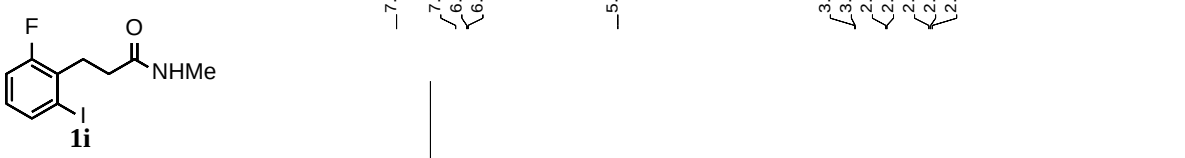

O
NHMe
I
1g
7.67
7.65
7.08
7.08
6.73
6.73
6.72
6.71
5.38
3.03
3.02
3.00
2.79
2.79
2.45
2.43
2.42
2.26
1.00
1.02
1.03
0.98
2.02
2.95
1.98
2.98
f1 (ppm)


172.26
143.01
139.14
138.50
130.60
129.12
96.02
36.87
36.59
26.28
20.81
f1 (ppm)


F
O
NHMe
I
1h
7.74
7.02
6.68
6.68
5.41
3.05
2.81
2.80
2.44
1.00
1.00
0.97
0.83
1.95
2.89
1.87
f1 (ppm)

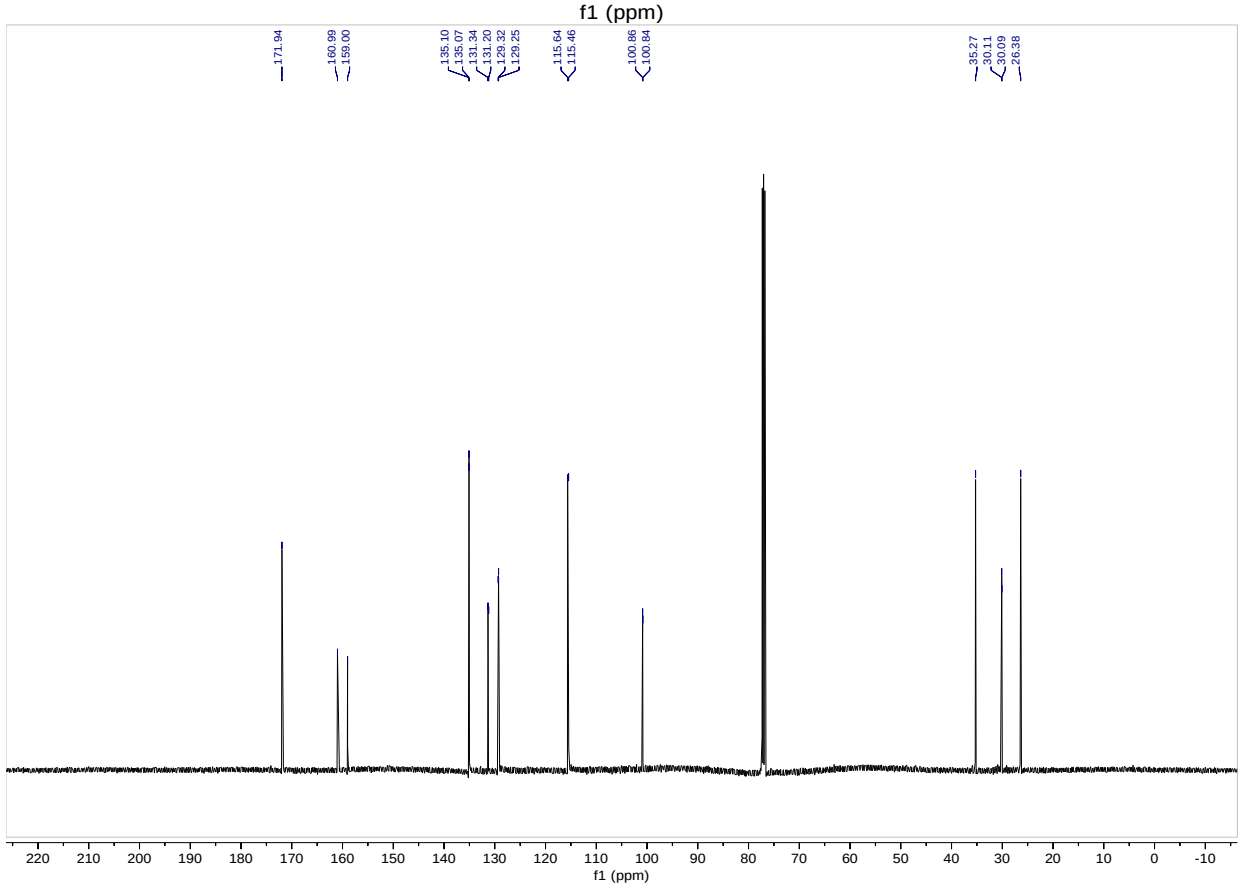

171.87
164.01
162.04
145.64
145.58
140.47
140.41
116.83
116.66
115.59
115.42
92.93
92.90
36.58
36.19
26.35
f1 (ppm)


-113.90
170
150
130
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)


F
O
NHMe
I

1i

7.59
7.02
6.91
6.90
5.44
3.14
3.13
2.84
2.83
2.42
2.40
2.38
1.00
1.01
1.03
0.83
2.00
2.95
1.93
f1 (ppm)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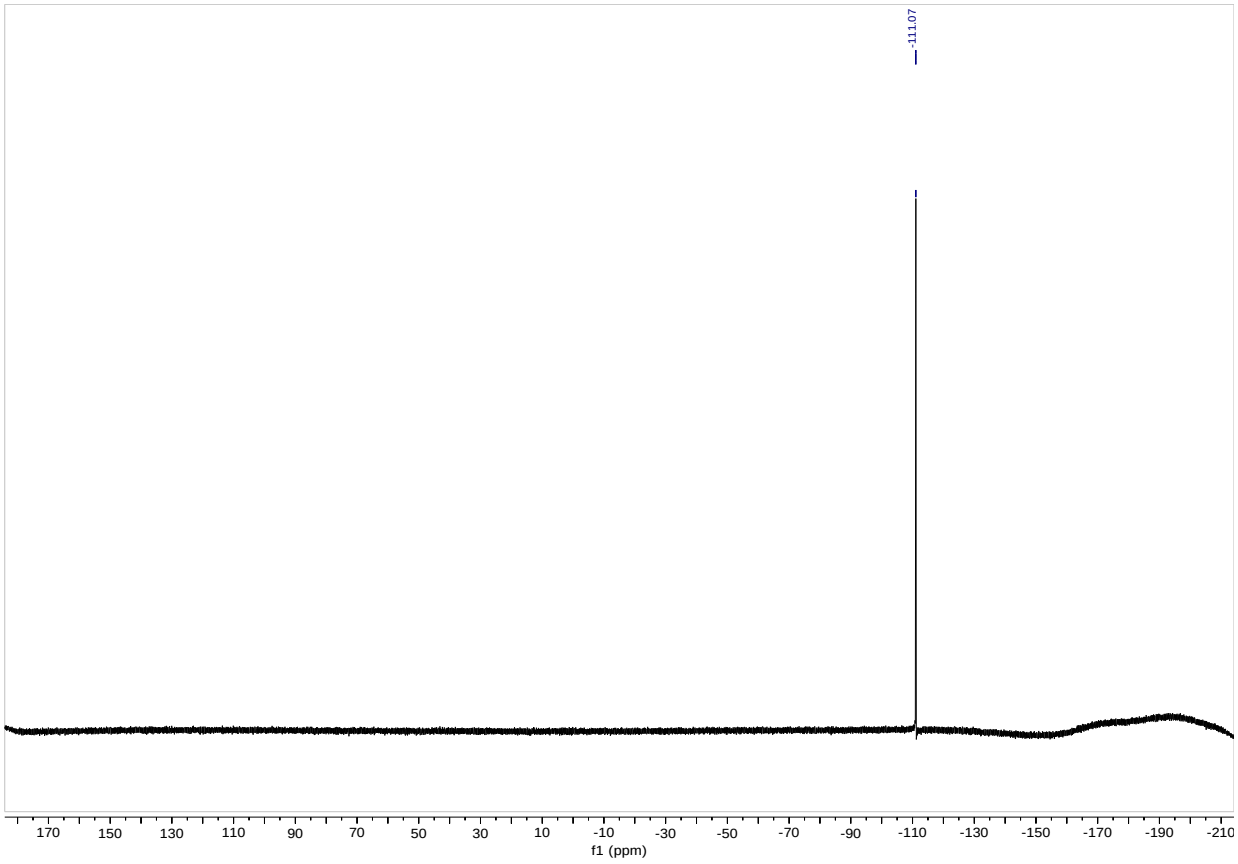
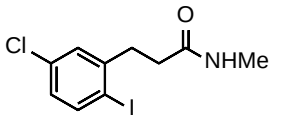
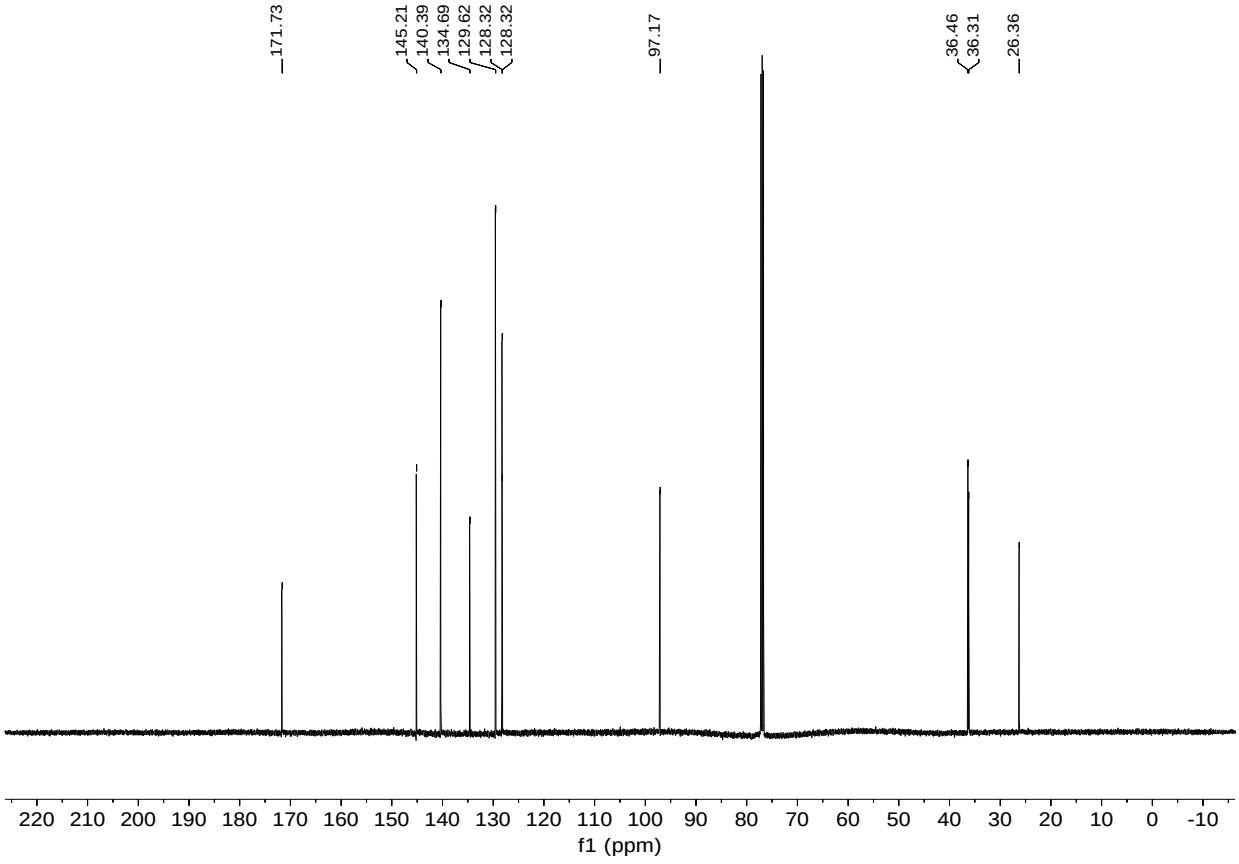
159.00
135.10
135.07
131.34
131.20
129.32
129.25
115.64
115.46
100.86
100.84
35.27
30.11
30.09
26.38
f1 (ppm)

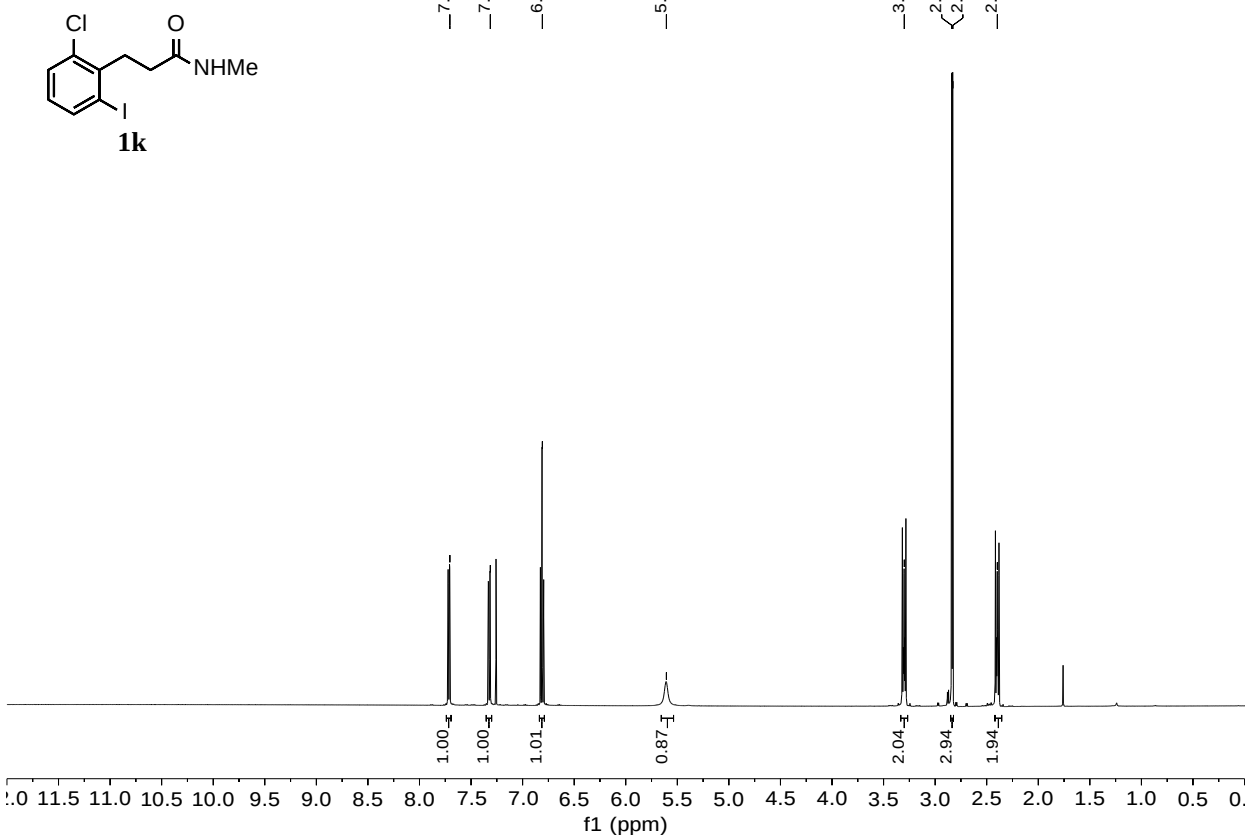

-111.07
170
150
130
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

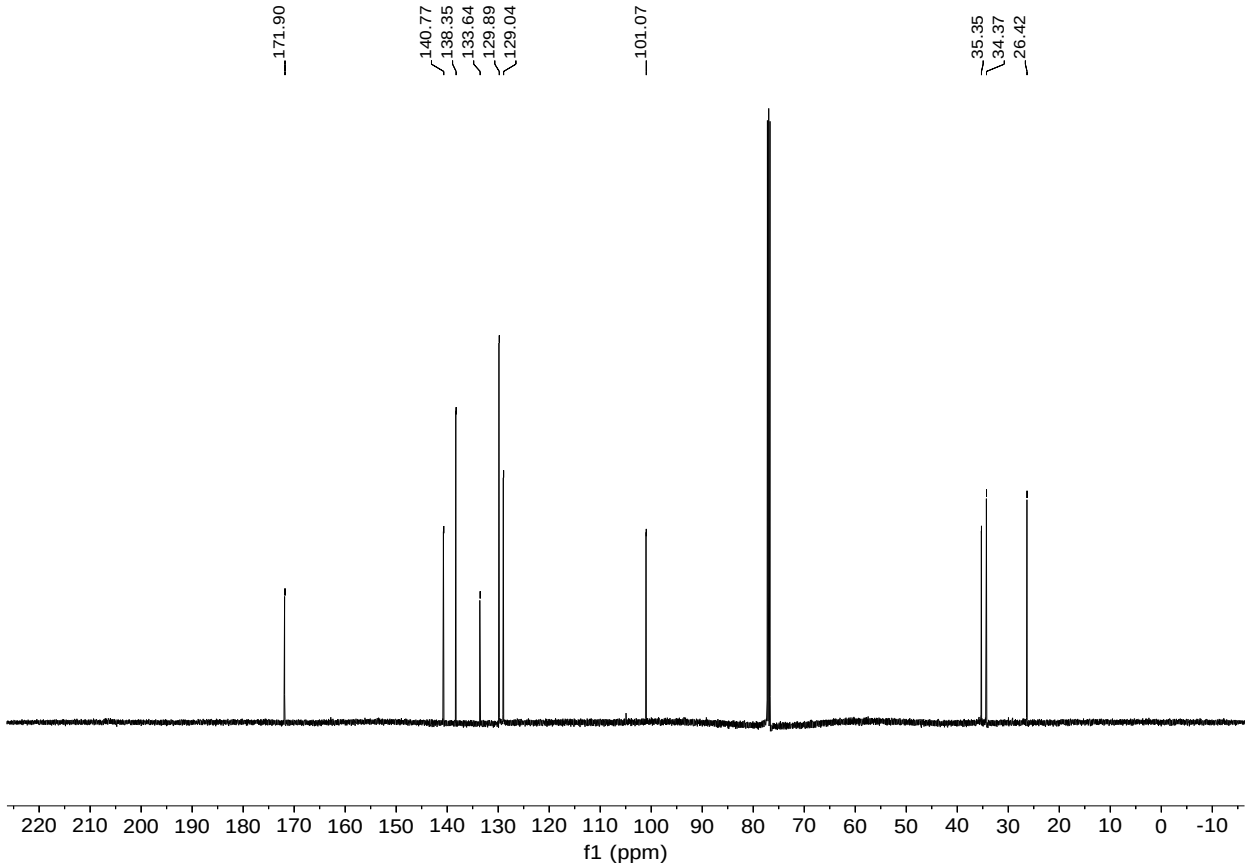

O
Cl
NHMe
I

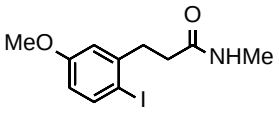
1j

7.70
7.69
7.26
7.24
7.23
6.90
6.89
6.88
6.88
5.53
3.04
3.02
3.01
2.80
2.79
2.45
2.43
2.41
1.00
0.98
0.99
0.86
2.02
2.97
1.97
f1 (ppm)


171.73
145.21
140.39
134.69
129.62
128.32
128.32
97.17
36.46
36.31
26.36
f1 (ppm)

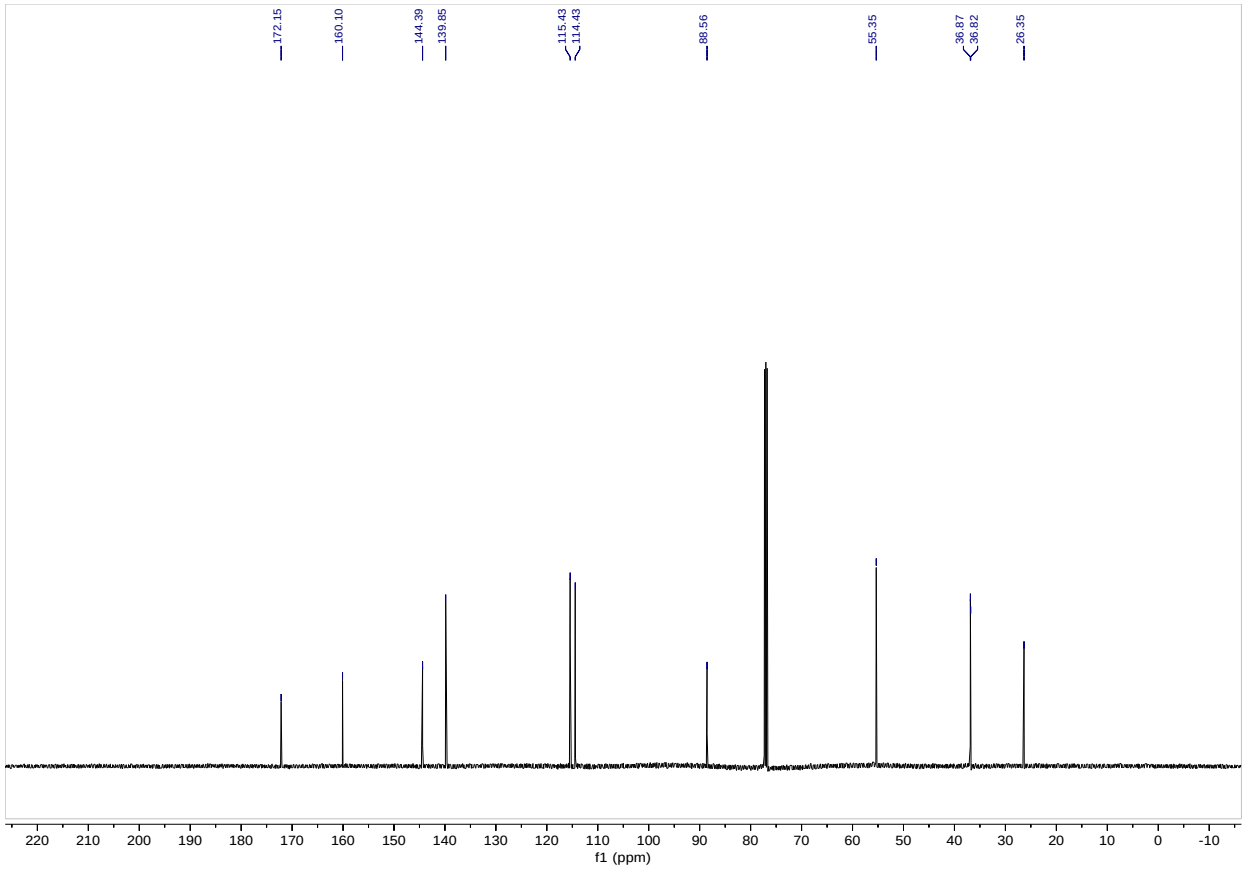

Cl
O
NHMe
I
1k
7.71
7.32
6.81
5.61
3.30
2.84
2.83
2.40
1.00
1.00
1.01
0.87
2.04
2.94
1.94
f1 (ppm)

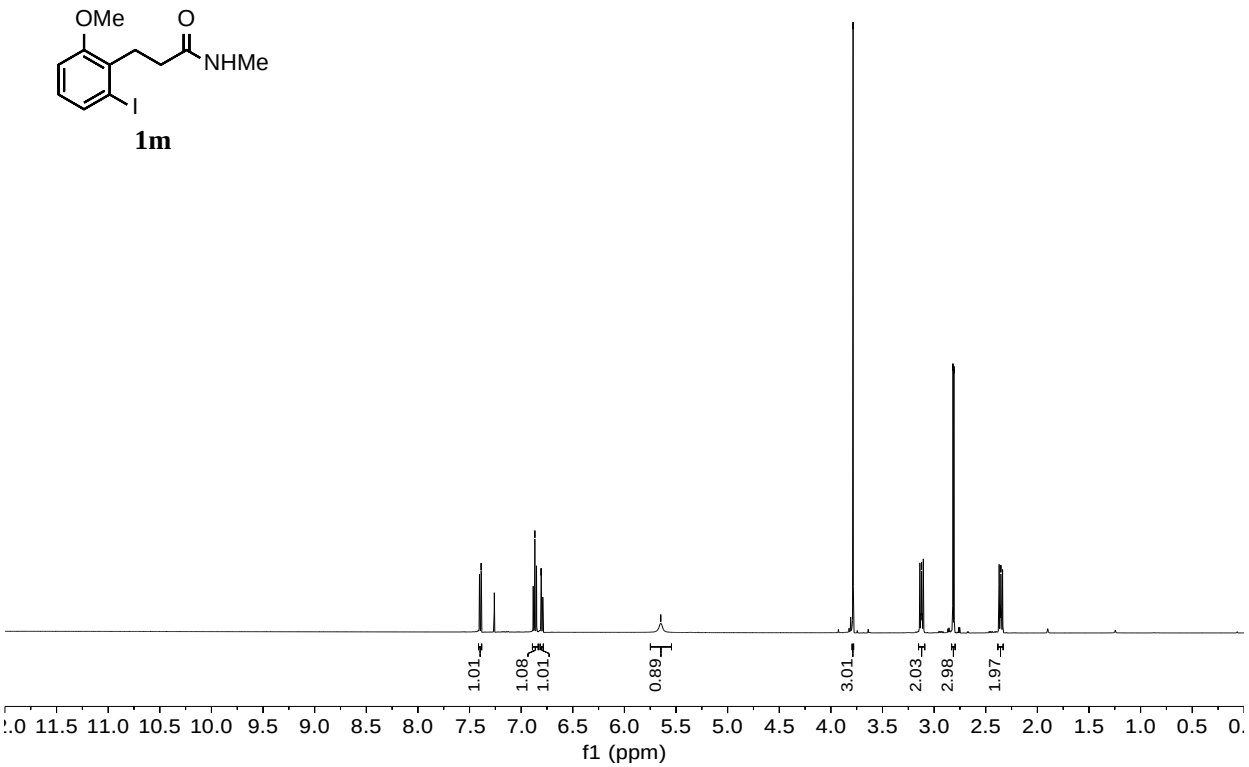

171.90
140.77
138.35
133.64
129.89
129.04
101.07
35.35
34.37
26.42
f1 (ppm)


O
MeO
NHMe
I

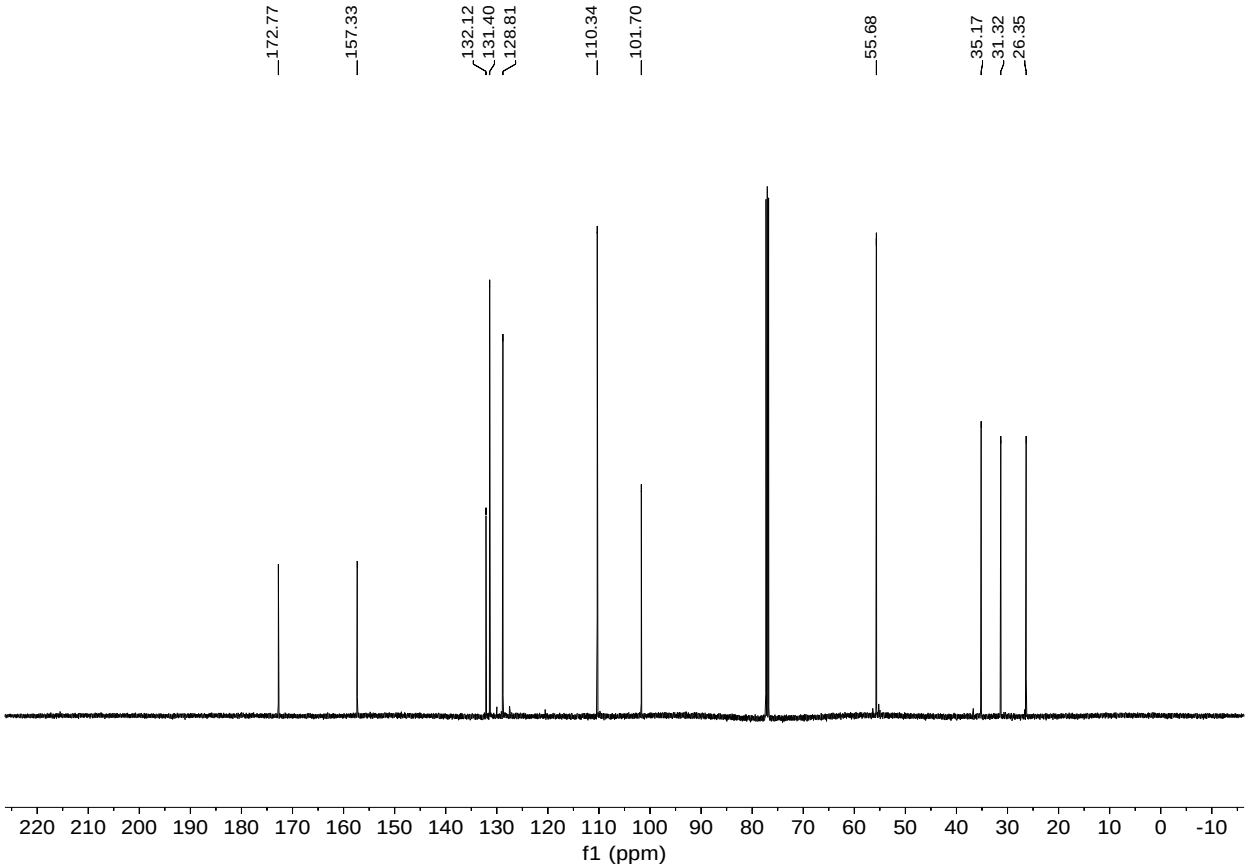
1l

7.65
7.63
6.83
6.83
6.52
6.51
6.50
6.49
5.50
3.75
3.03
3.01
3.00
2.79
2.78
2.45
2.43
2.42
1.00
0.99
1.00
0.87
3.01
2.00
2.93
1.95
f1 (ppm)


172.15
160.10
144.39
139.85
115.43
114.43
88.56
55.35
36.87
36.82
26.35
f1 (ppm)


OMe
O
NHMe
I
7.39
6.87
6.81
5.65
3.79
3.12
2.82
2.81
2.35
1.01
1.08
1.01
0.89
3.01
2.03
2.98
1.97
f1 (ppm)

1m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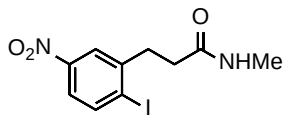
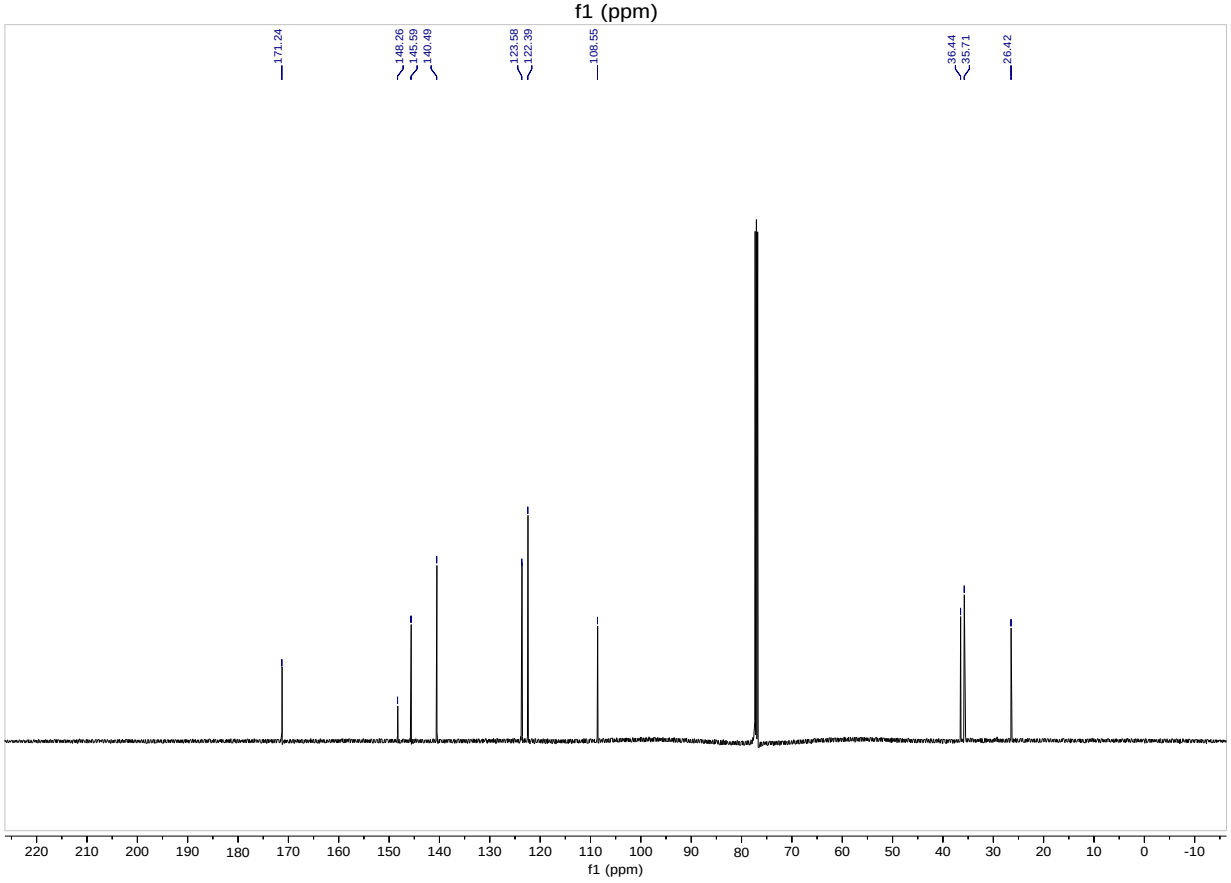
131.40
128.81
110.34
101.70
55.68
35.17
31.32
26.35
f1 (ppm)


O
O_2N
NHMe
I

1n

8.08
8.00
7.75
5.46
3.18
2.83
2.82
2.51
1.00
1.05
1.02
0.82
2.08
2.95
2.03
f1 (ppm)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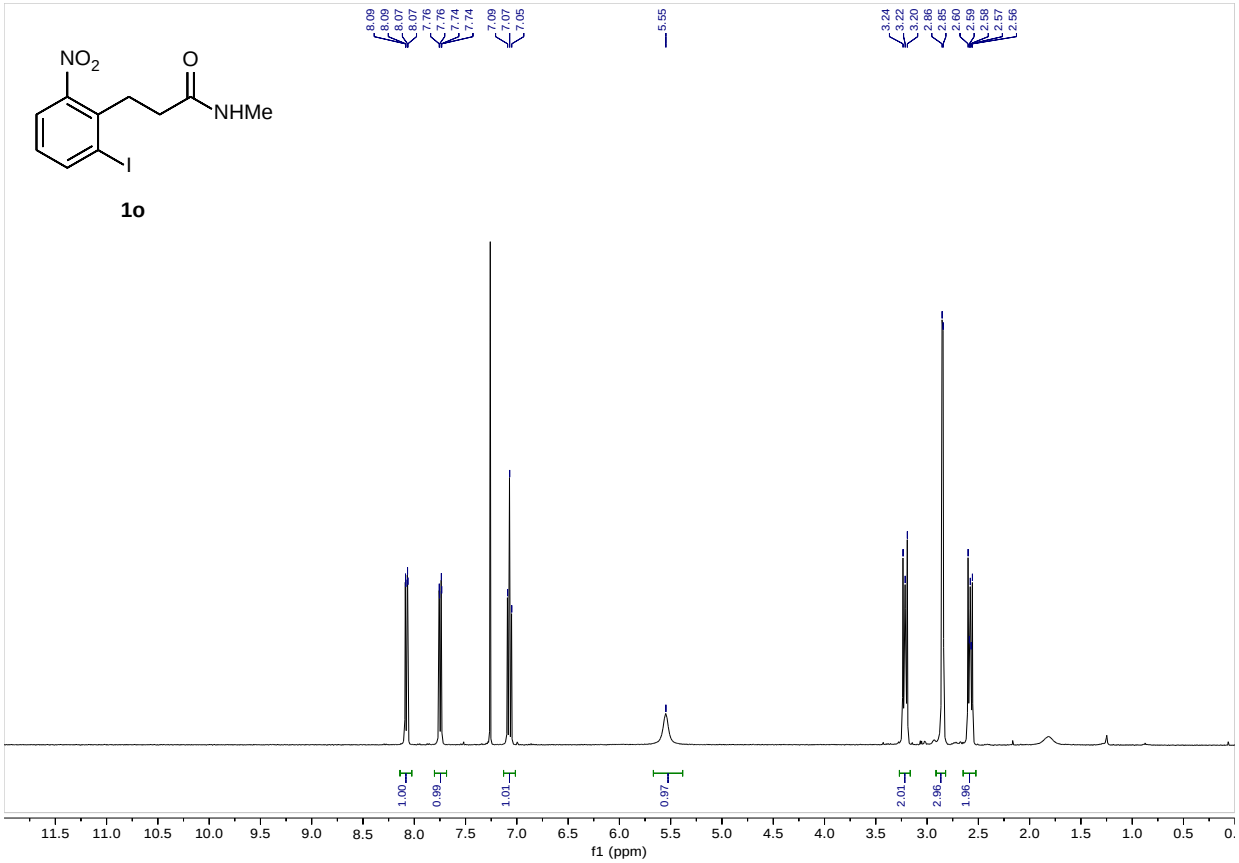
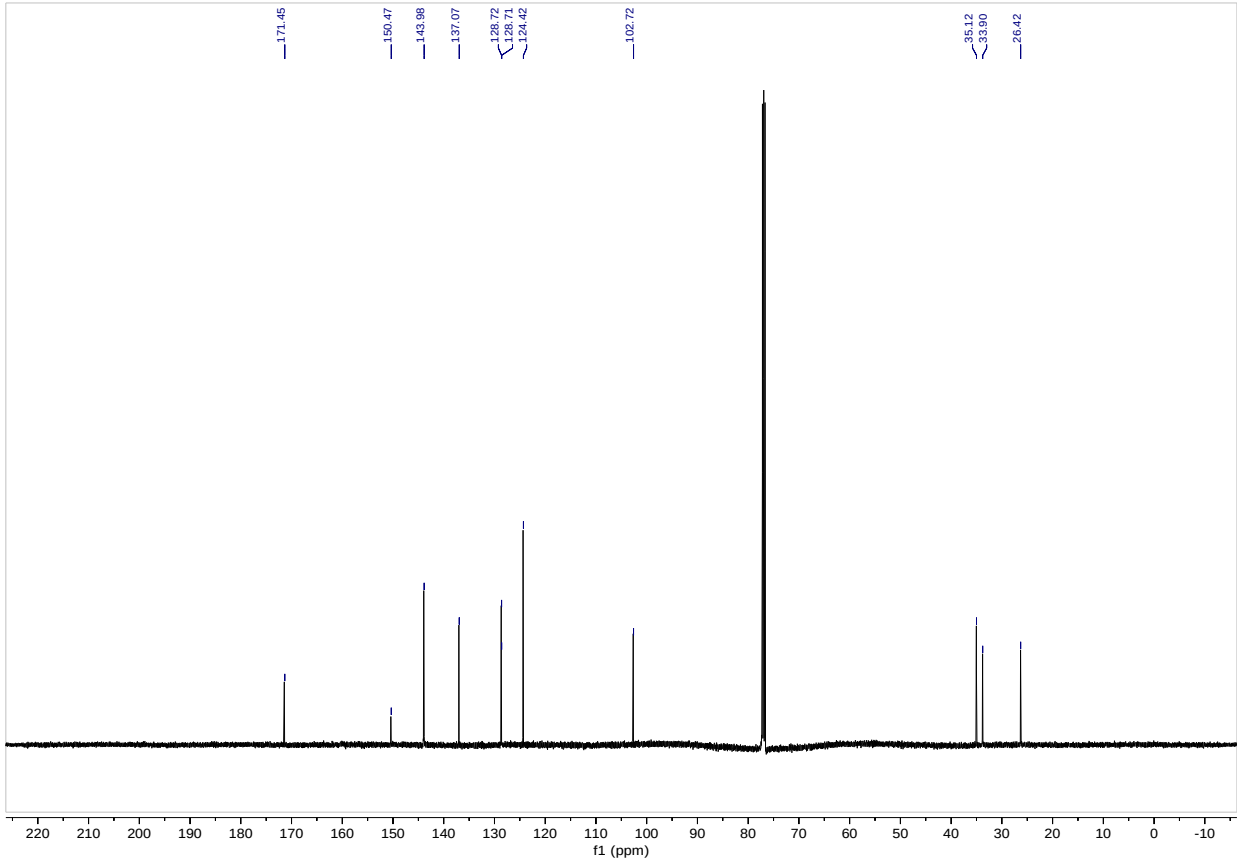
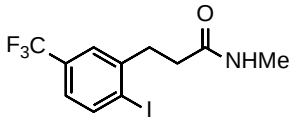
148.26
145.59
140.49
123.58
122.39
108.55
36.44
35.71
26.42
f1 (ppm)


NO2
O
NHMe
I
8.09
8.09
8.07
8.07
7.76
7.76
7.74
7.74
7.09
7.07
7.05
5.55
3.24
3.22
3.20
2.86
2.85
2.60
2.59
2.58
2.57
2.56
1.00
0.99
1.01
0.97
2.01
2.96
1.96
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

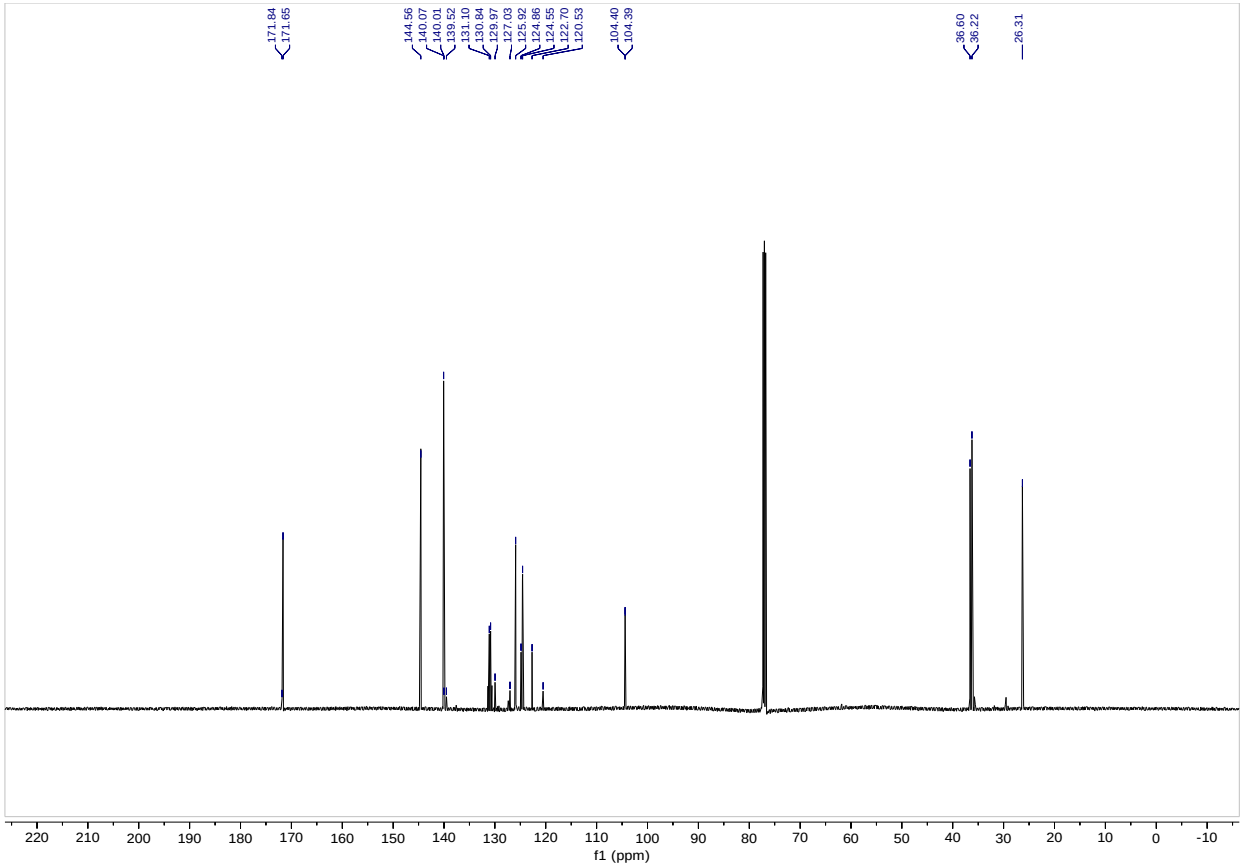
1o

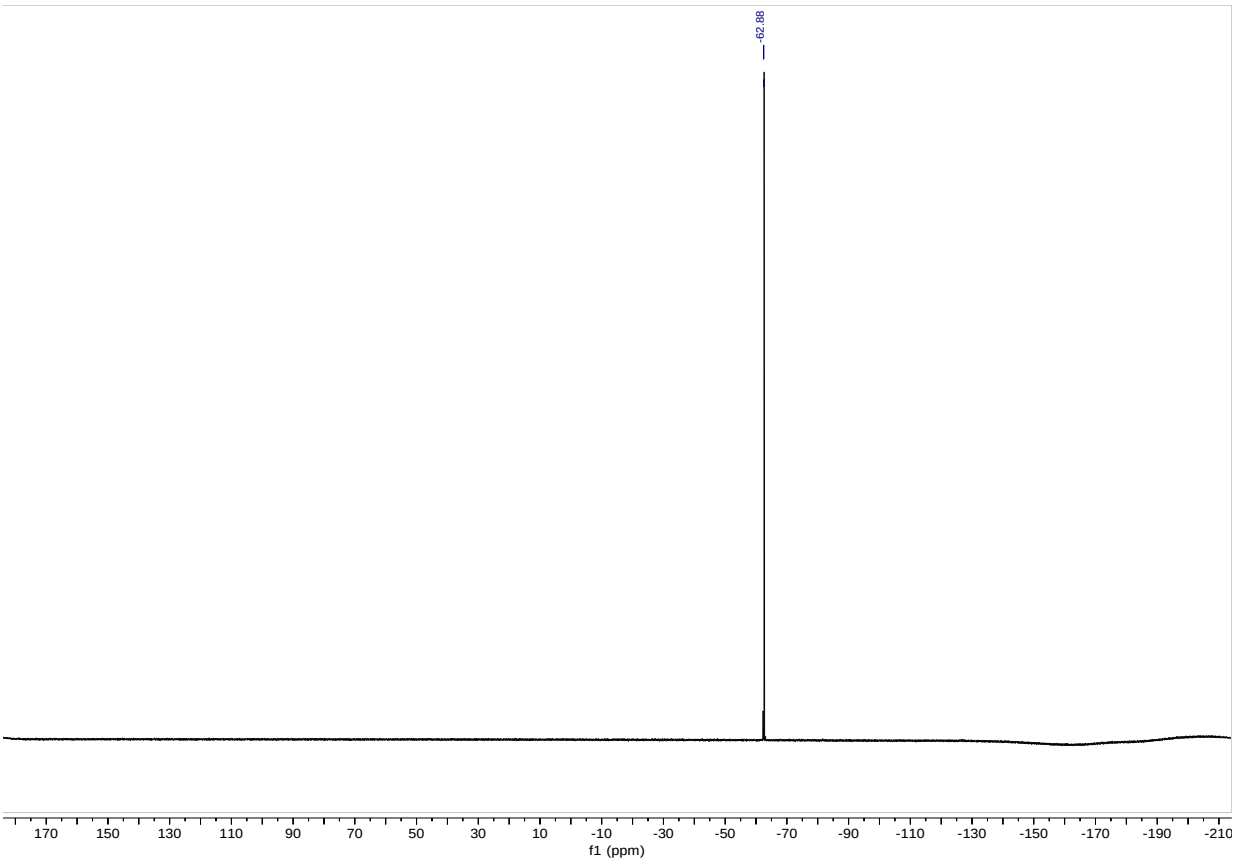

171.45
150.47
143.98
137.07
128.72
128.71
124.42
102.72
35.12
33.90
26.42
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

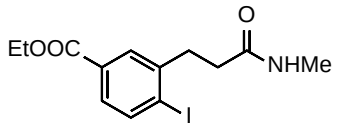

O
F3C
NHMe
I

1p

7.94
7.92
7.48
7.48
7.15
7.15
7.14
7.13
5.46
3.15
3.13
3.12
2.80
2.79
2.48
2.46
2.44
1.00
1.00
1.00
0.98
2.08
3.00
1.99
f1 (ppm)

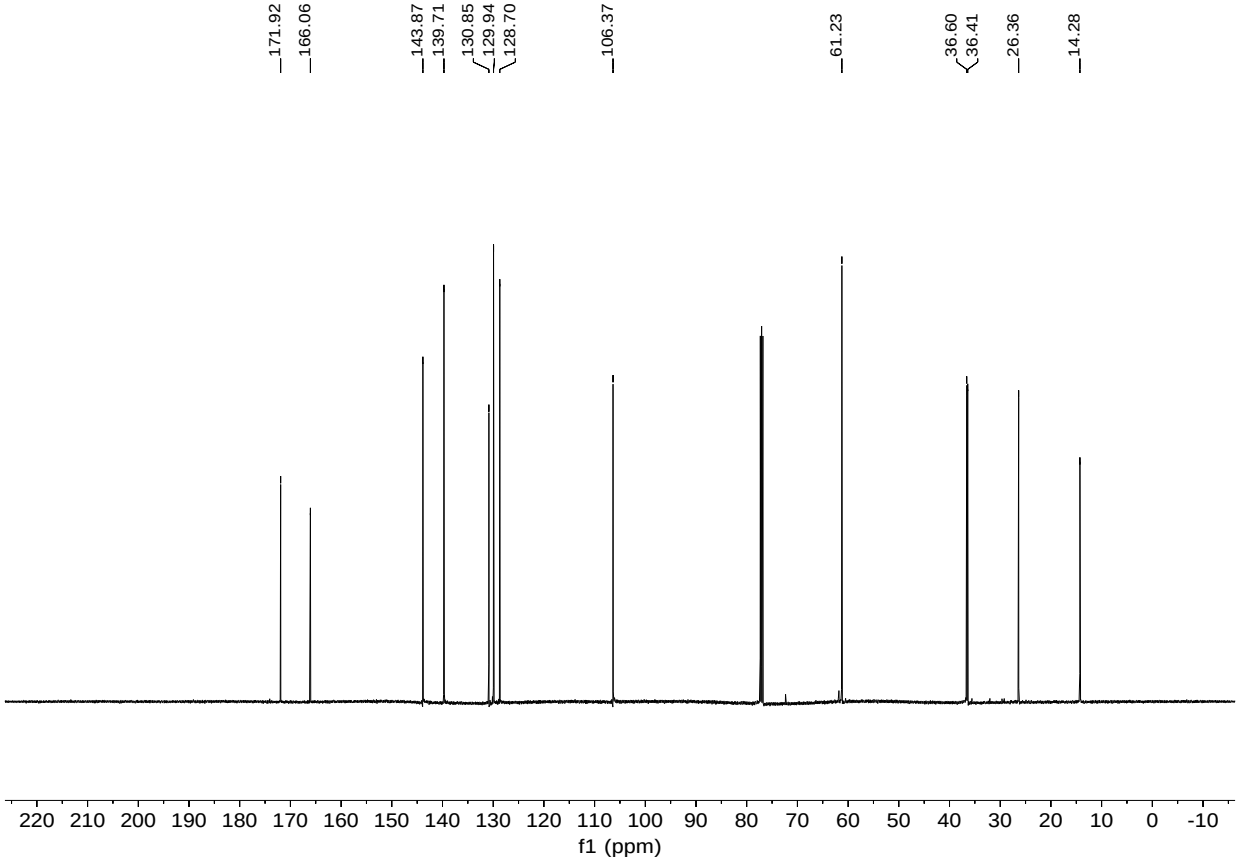

171.84
171.65
144.56
140.07
140.01
139.52
131.10
130.84
129.97
127.03
125.92
124.86
124.55
122.70
120.53
104.40
104.39
36.60
36.22
26.31
f1 (ppm)

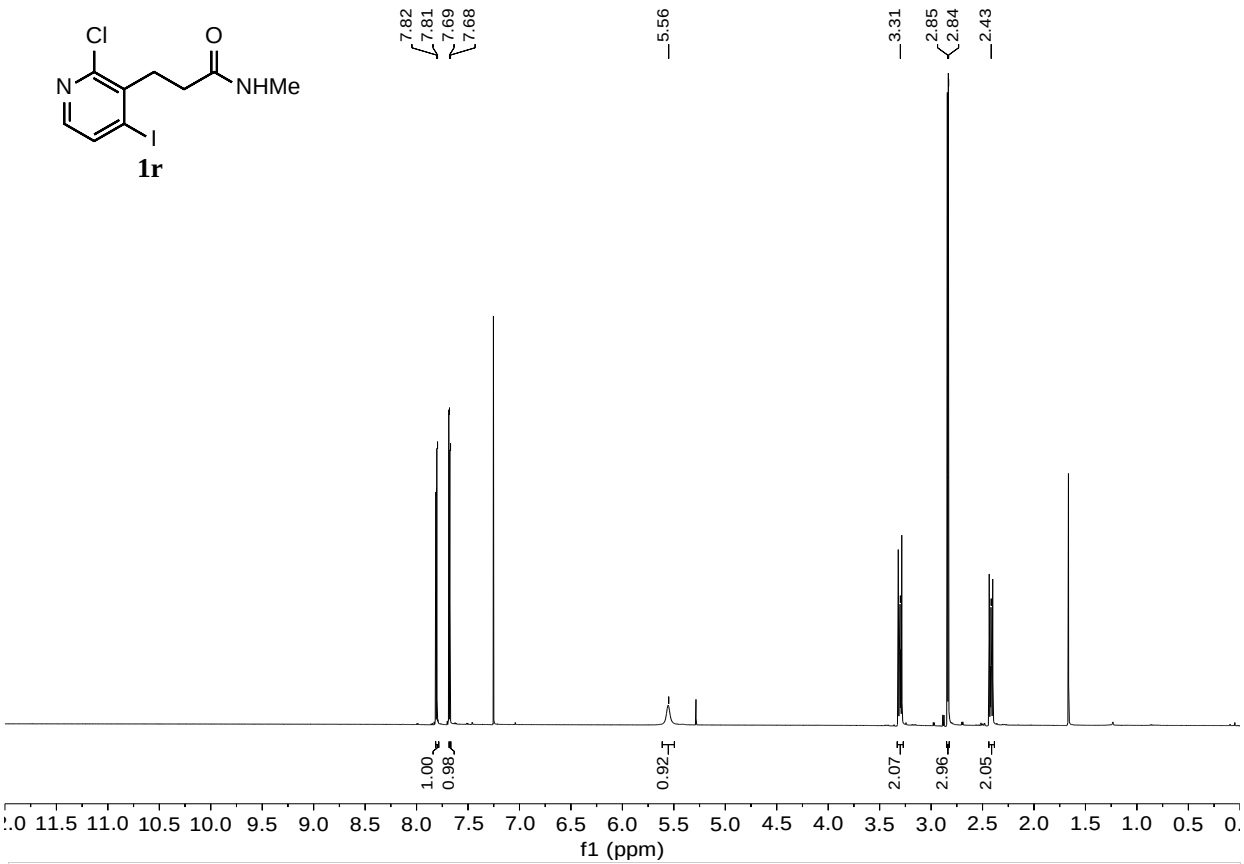

-62.88
170
150
130
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

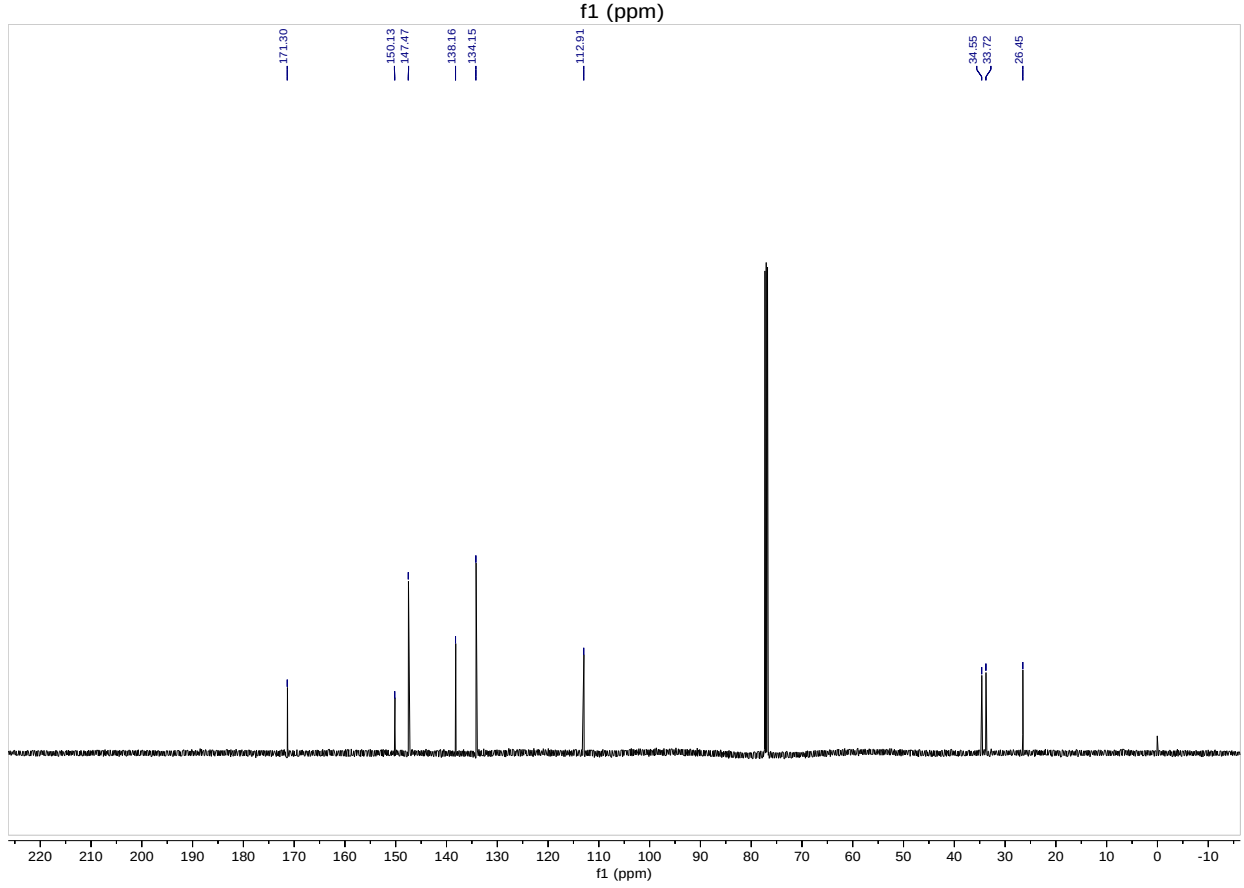

O
EtOOC
NHMe
I

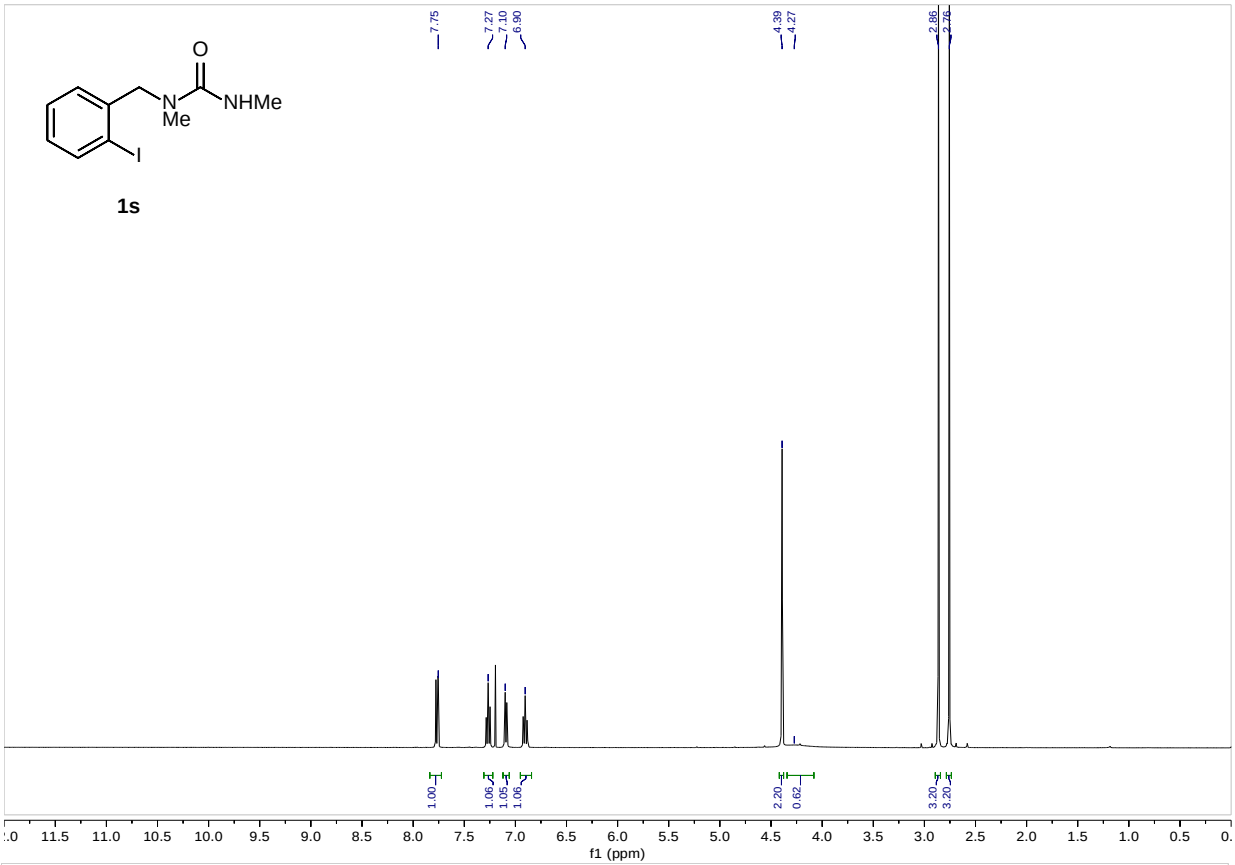
1q

7.86
7.84
7.84
7.50
7.50
7.49
7.48
5.79
4.35
4.33
4.32
4.30
3.10
3.08
3.06
2.79
2.78
2.47
2.45
2.43
1.37
1.35
1.34
1.91
1.00
0.96
2.00
1.96
2.90
1.91
2.92
f1 (ppm)

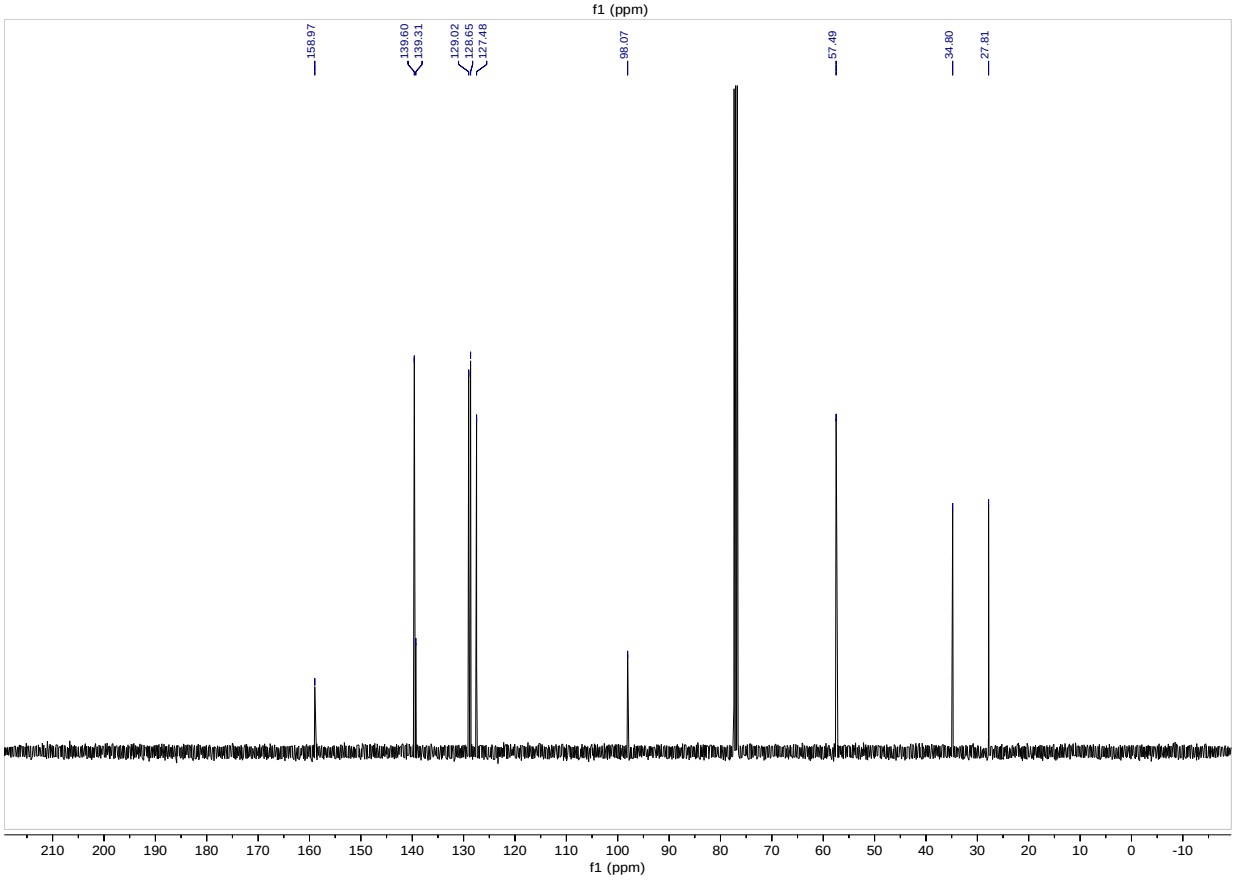

171.92
166.06
143.87
139.71
130.85
129.94
128.70
106.37
61.23
36.60
36.41
26.36
14.28
f1 (ppm)

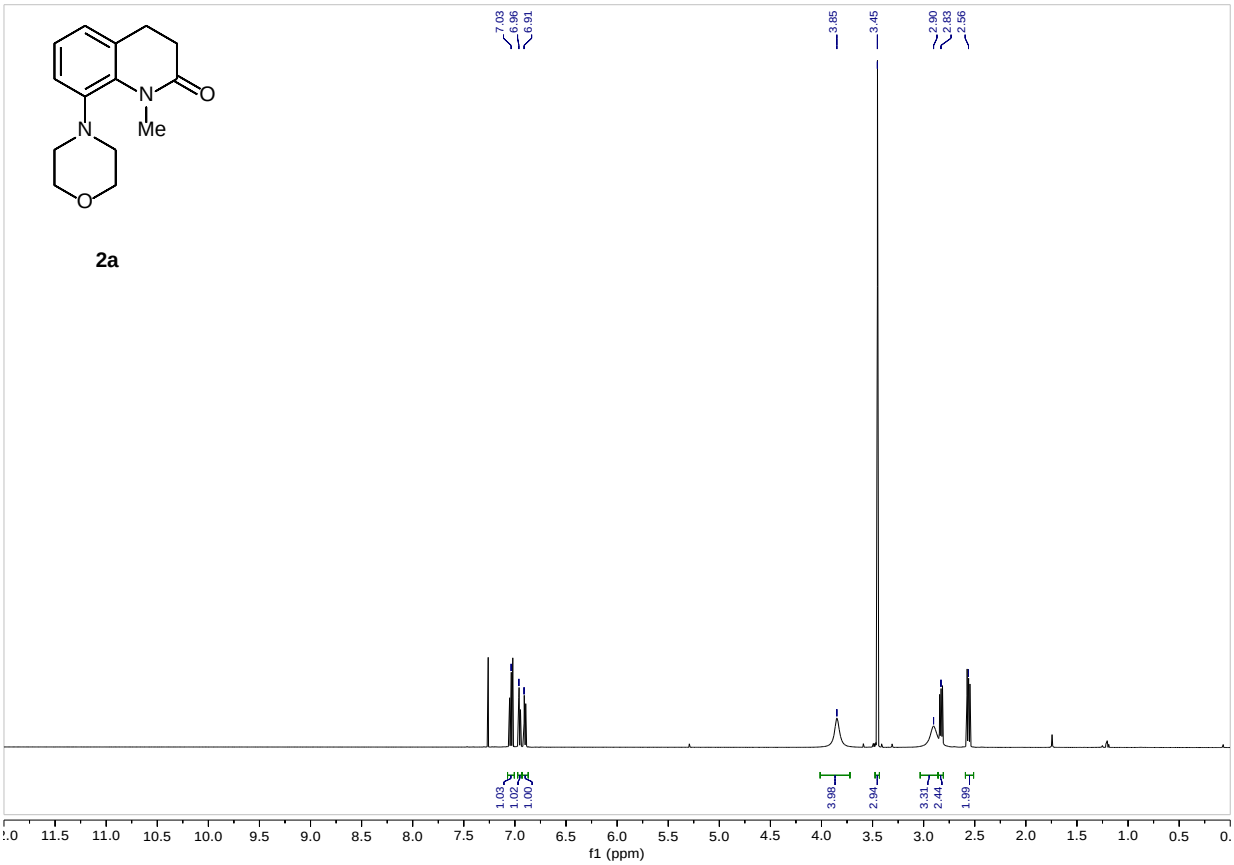

Cl
O
N
NHMe
I
1r
7.82
7.81
7.69
7.68
5.56
3.31
2.85
2.84
2.43
1.00
0.98
0.92
2.07
2.96
2.05
f1 (ppm)


171.30
150.13
147.47
138.16
134.15
112.91
34.55
33.72
26.45
f1 (ppm)

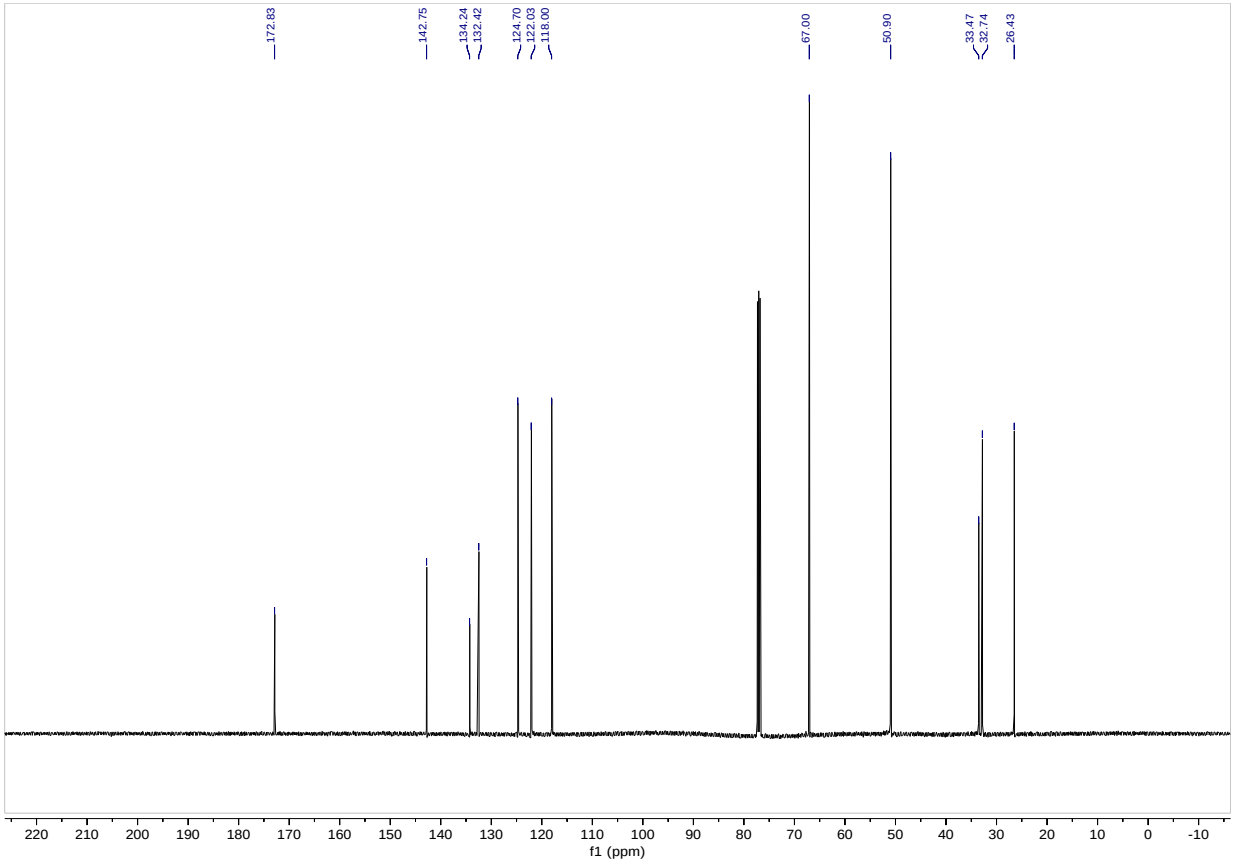

O
N
Me
NHMe
I
7.75
7.27
7.10
6.90
4.39
4.27
2.86
2.78
1.00
1.06
1.05
1.06
2.20
0.62
3.20
3.20
f1 (ppm)

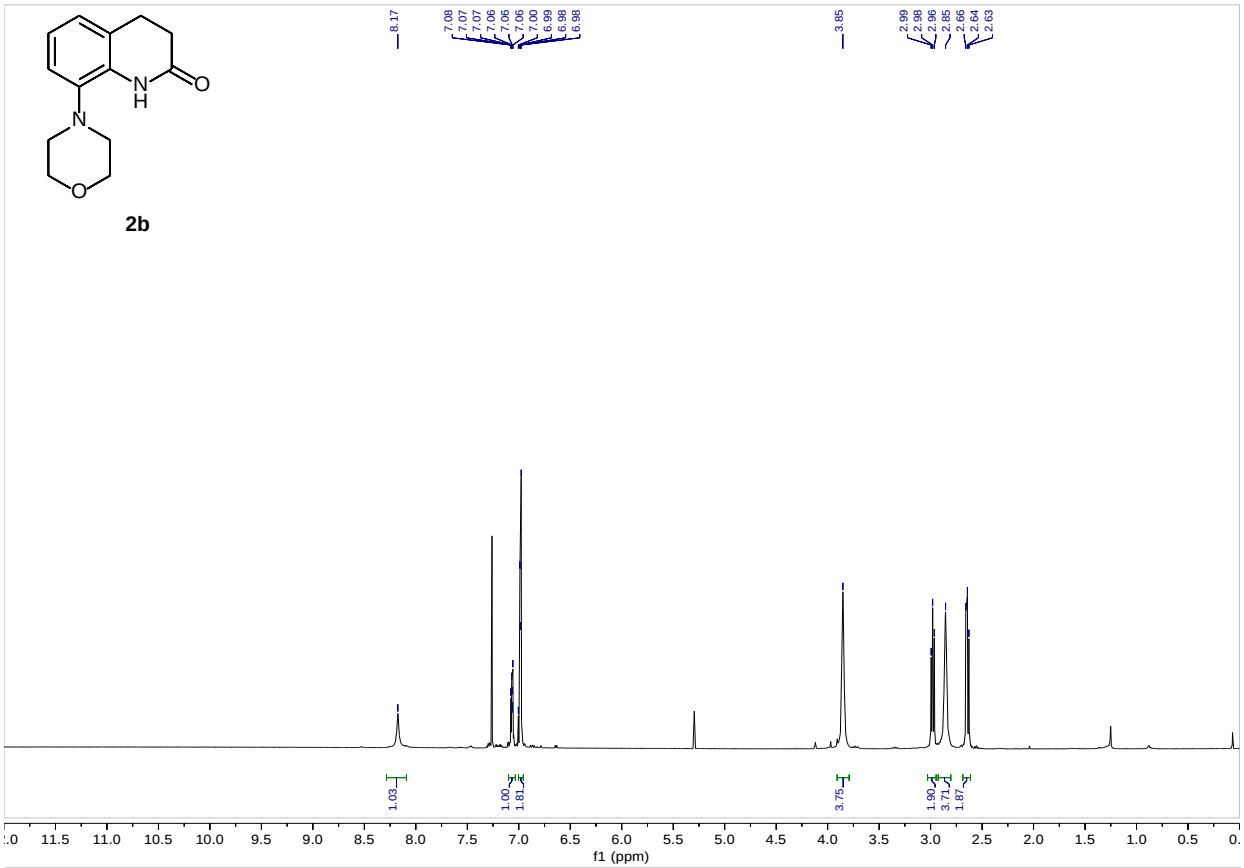
1s


158.97
139.60
139.31
129.02
128.65
127.48
98.07
57.49
34.80
27.81
f1 (ppm)

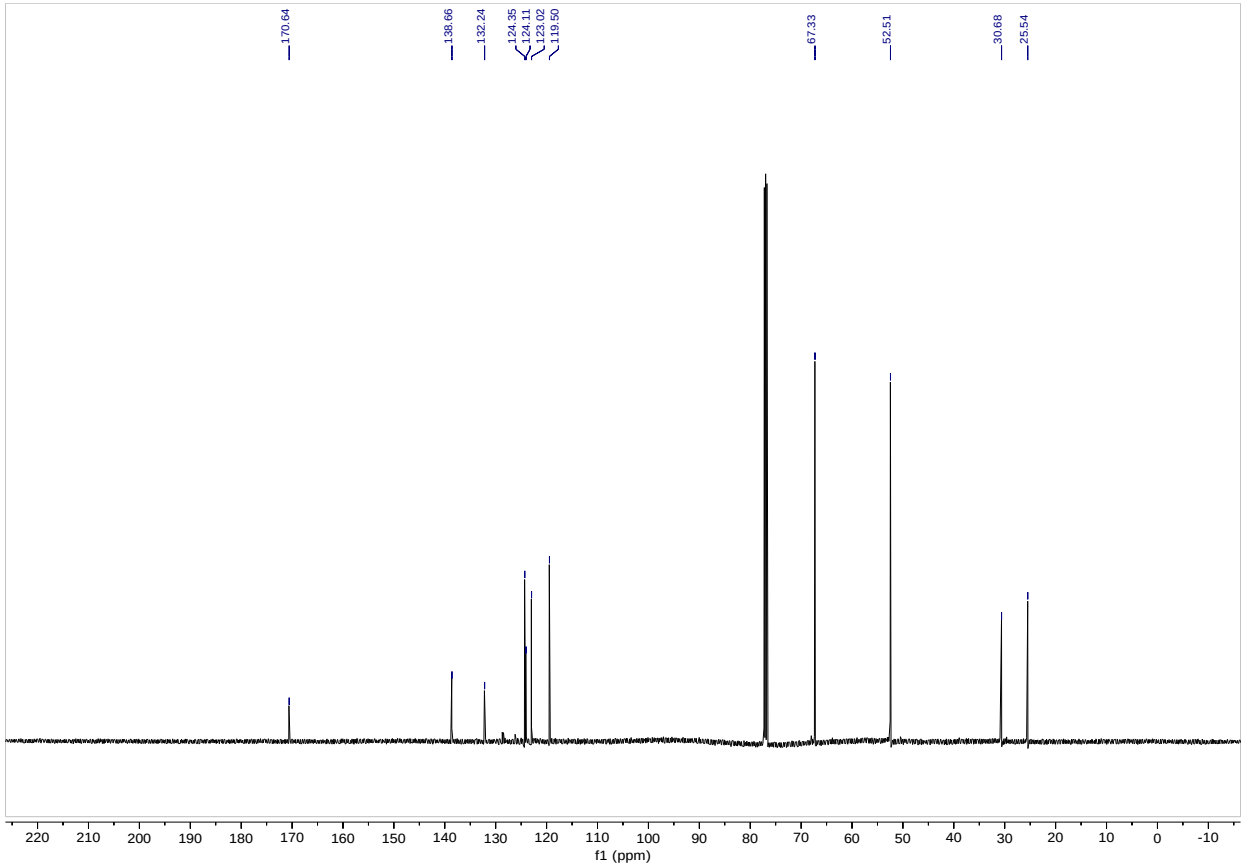

7.03
6.96
6.91
3.85
3.45
2.90
2.83
2.56
N
O
N
Me
O
1.03
1.02
1.00
3.98
2.94
3.31
2.44
1.99
f1 (ppm)

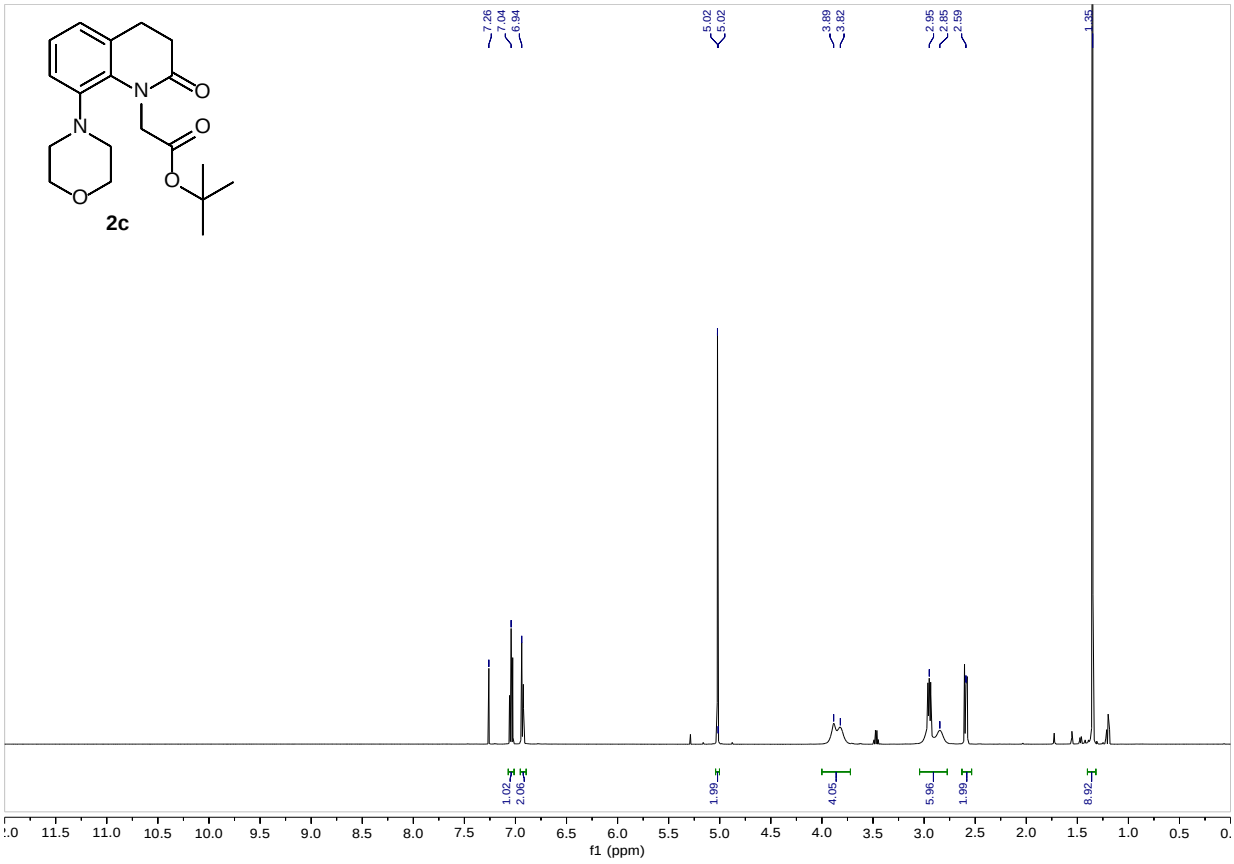
2a


172.83
142.75
134.24
132.42
124.70
122.03
118.00
67.00
50.90
33.47
32.74
26.43
f1 (ppm)

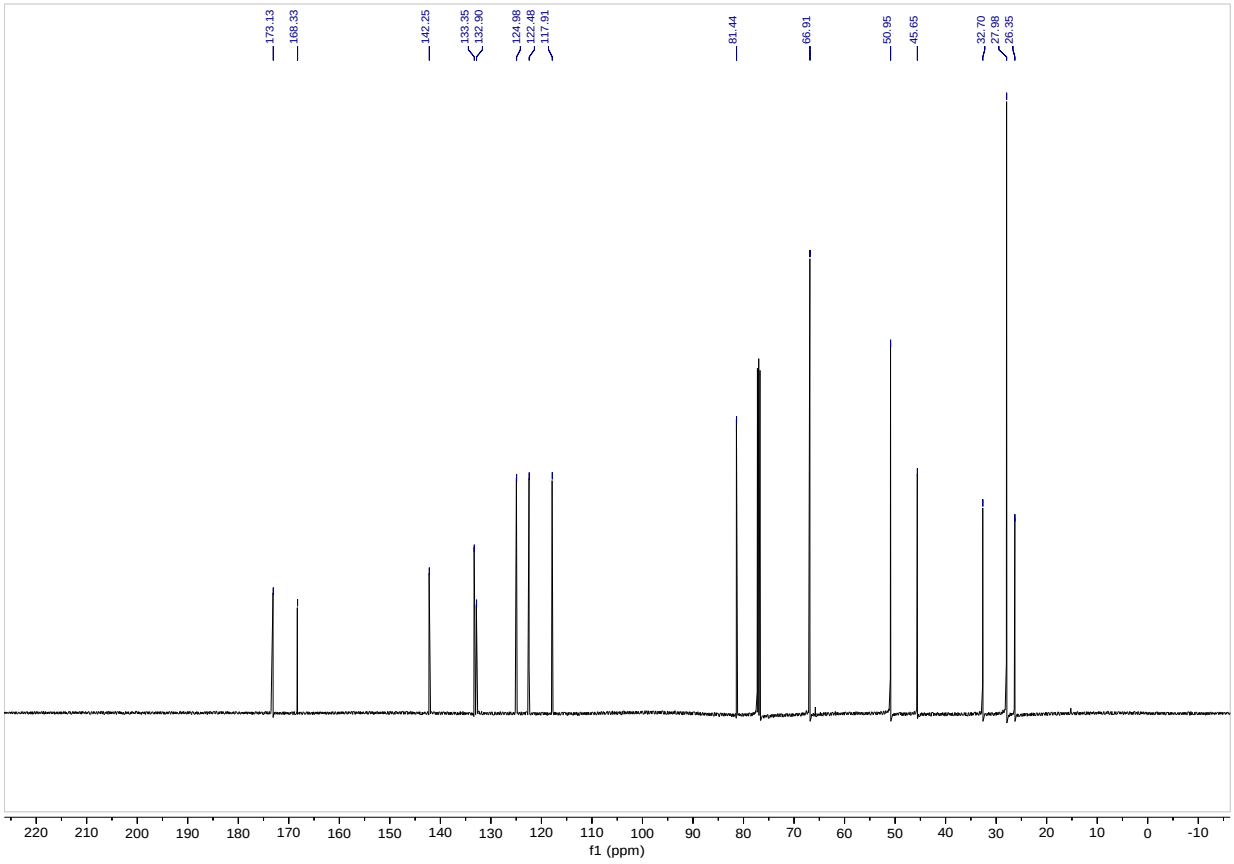

8.17
7.08
7.07
7.07
7.06
7.06
7.06
7.00
6.99
6.98
6.98
3.85
2.99
2.98
2.96
2.85
2.66
2.64
2.63
1.03
1.00
1.81
3.75
1.90
3.71
1.87
f1 (ppm)

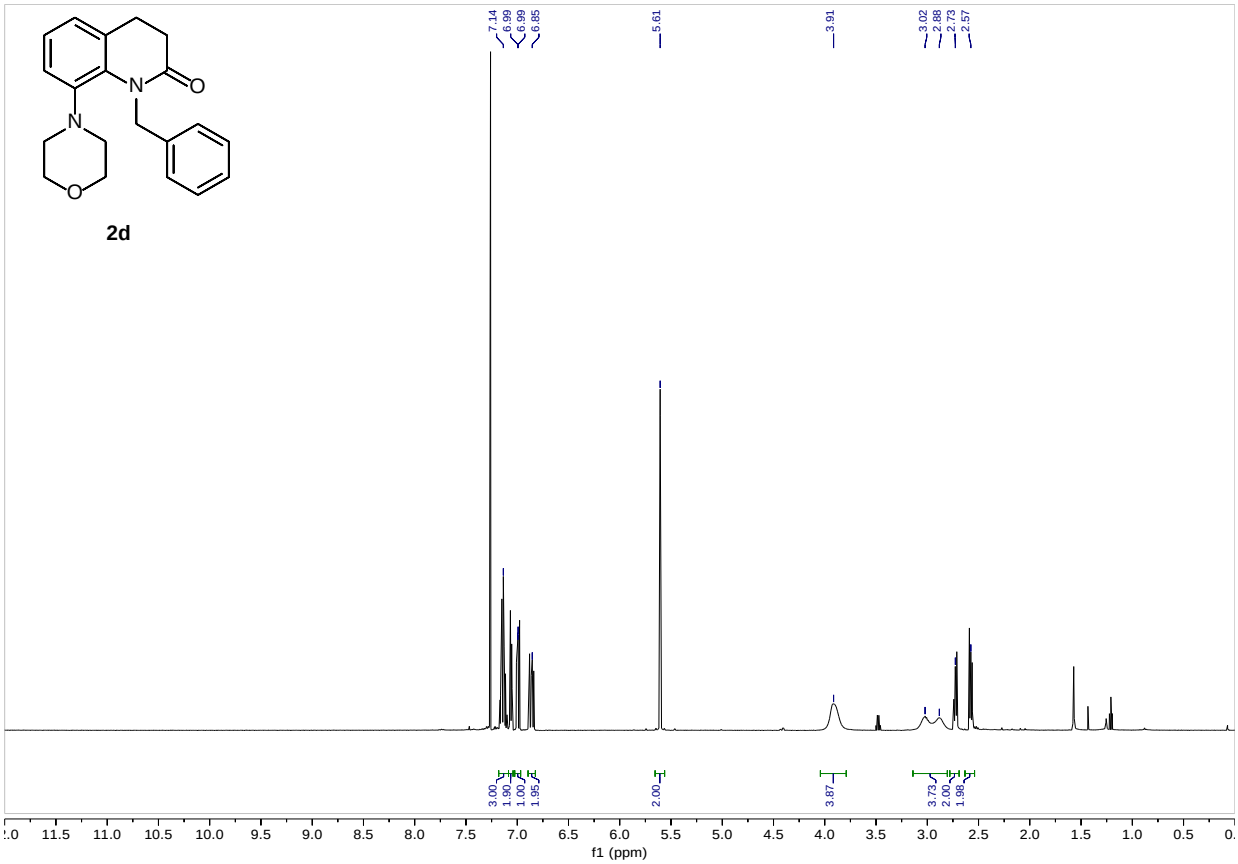
2b


170.64
138.66
132.24
124.35
124.11
123.02
119.50
67.33
52.51
30.68
25.54
f1 (ppm)

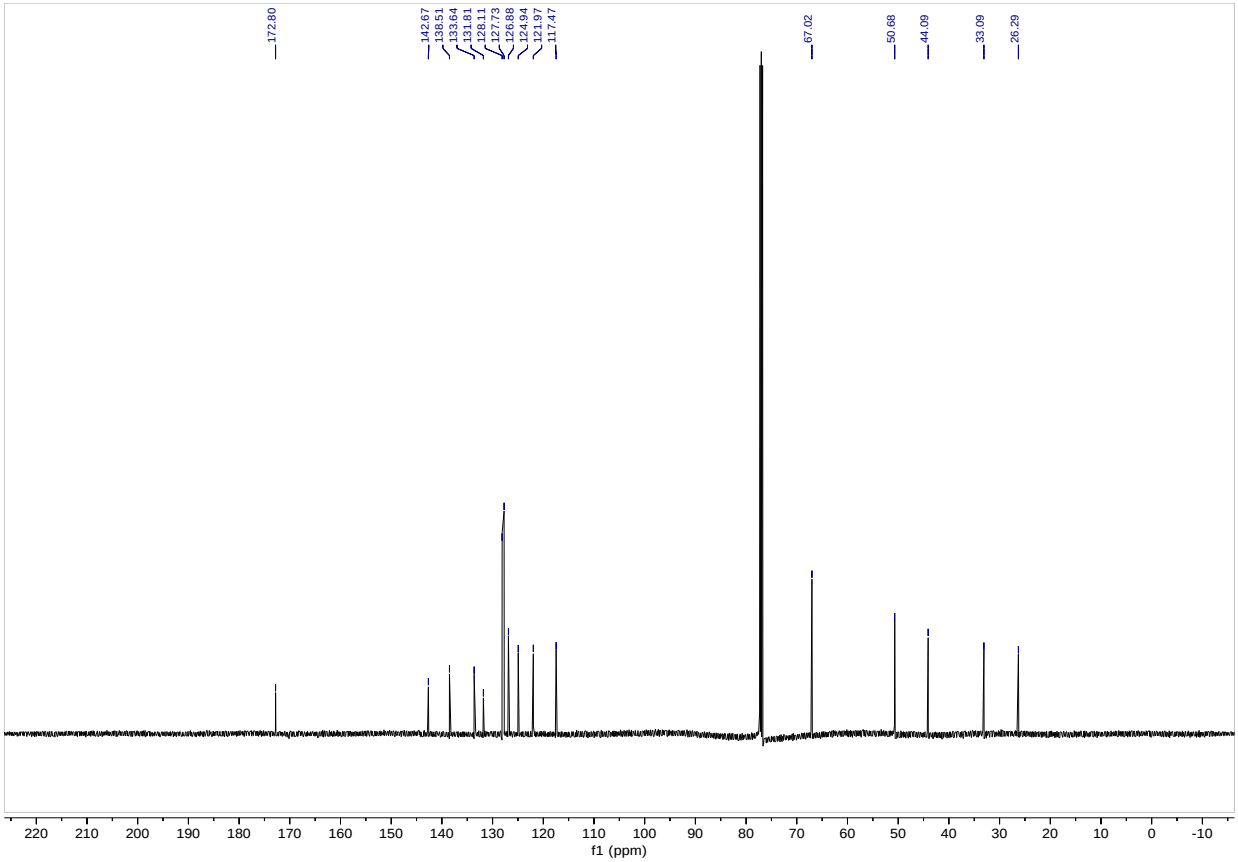

7.26
7.04
6.94
5.02
5.02
3.89
3.82
2.95
2.85
2.59
1.35
1.02
2.06
1.99
4.05
5.96
1.99
8.92
f1 (ppm)

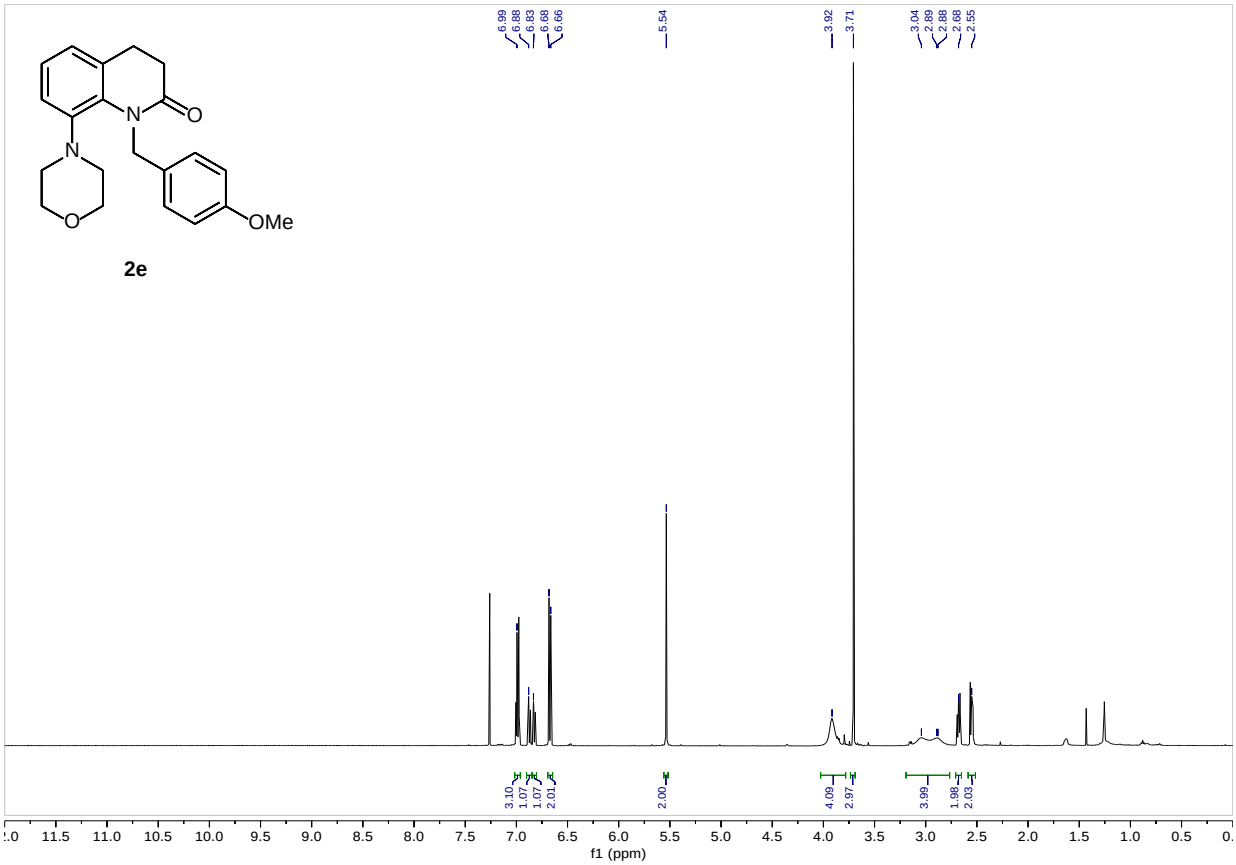
2c


173.13
168.33
142.25
133.35
132.90
124.98
122.48
117.91
81.44
66.91
50.95
45.65
32.70
27.98
26.35
f1 (ppm)

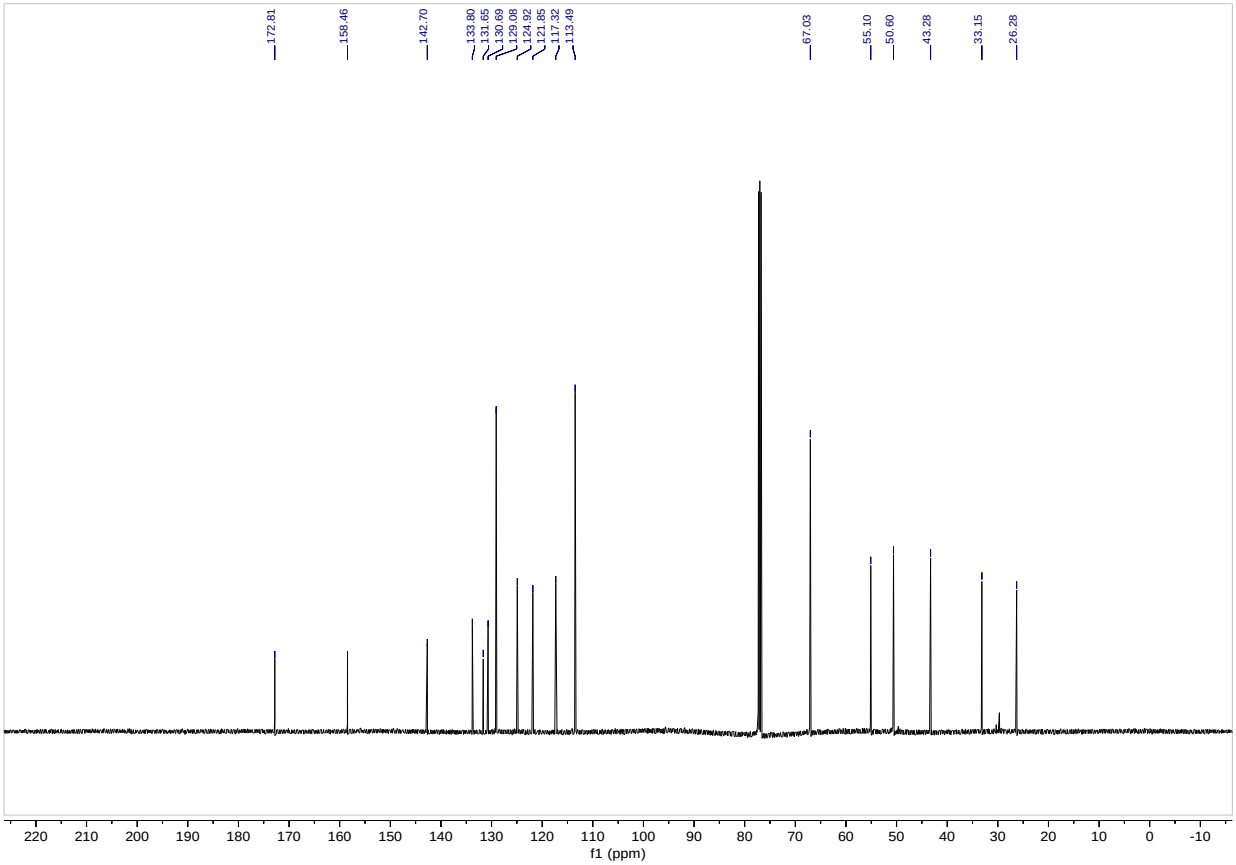

7.14
6.99
6.99
6.85
5.61
3.91
3.02
2.88
2.73
2.57
3.00
1.90
1.00
1.95
2.00
3.87
3.73
2.00
1.98
f1 (ppm)

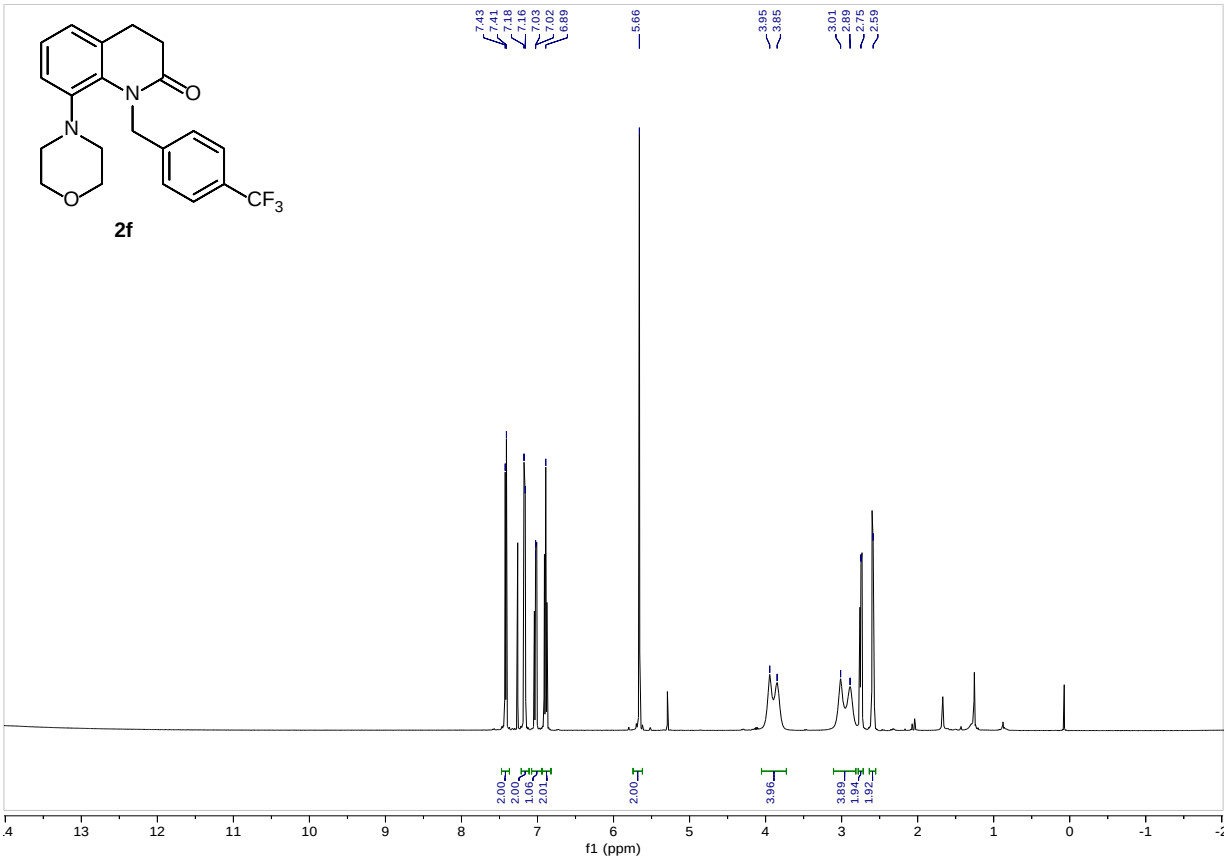
2d

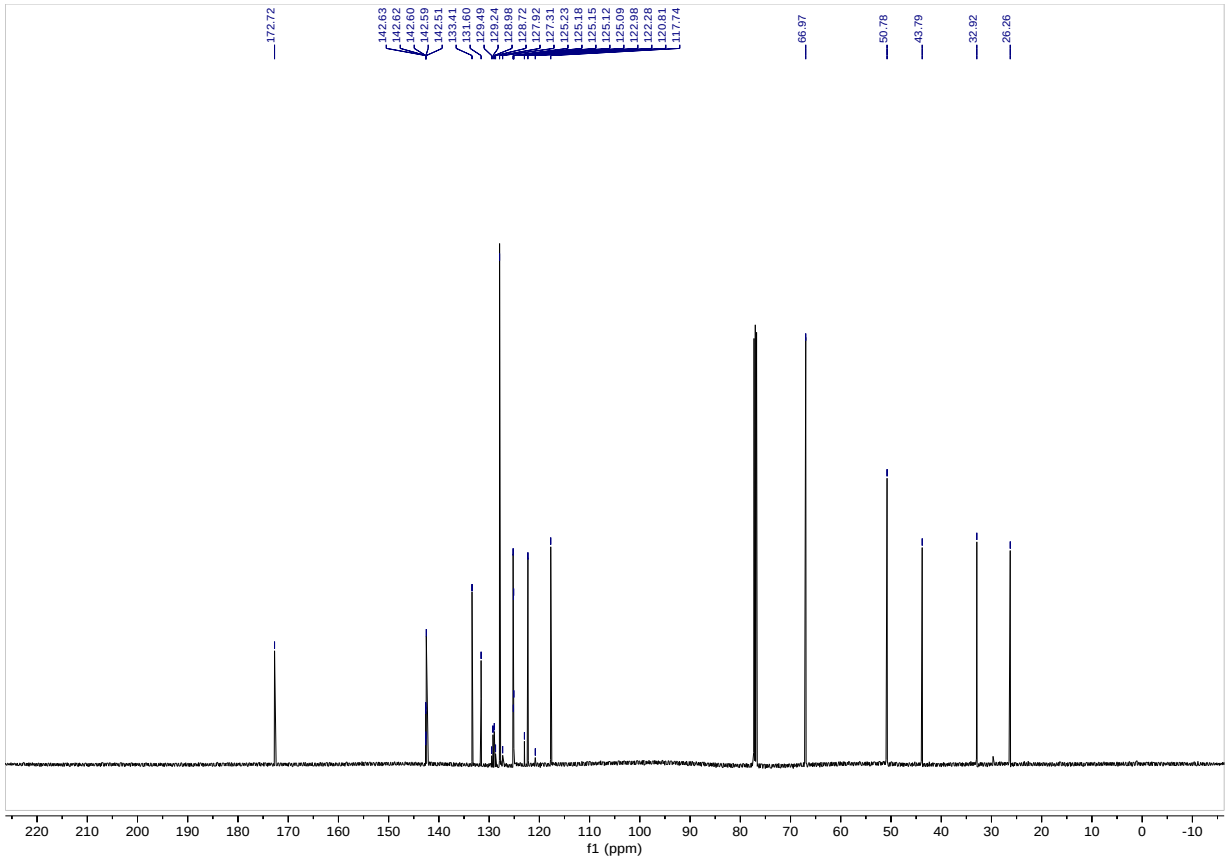

172.80
142.67
138.51
133.64
131.81
128.11
127.73
126.88
124.94
121.97
117.47
67.02
50.68
44.09
33.09
26.29
f1 (ppm)

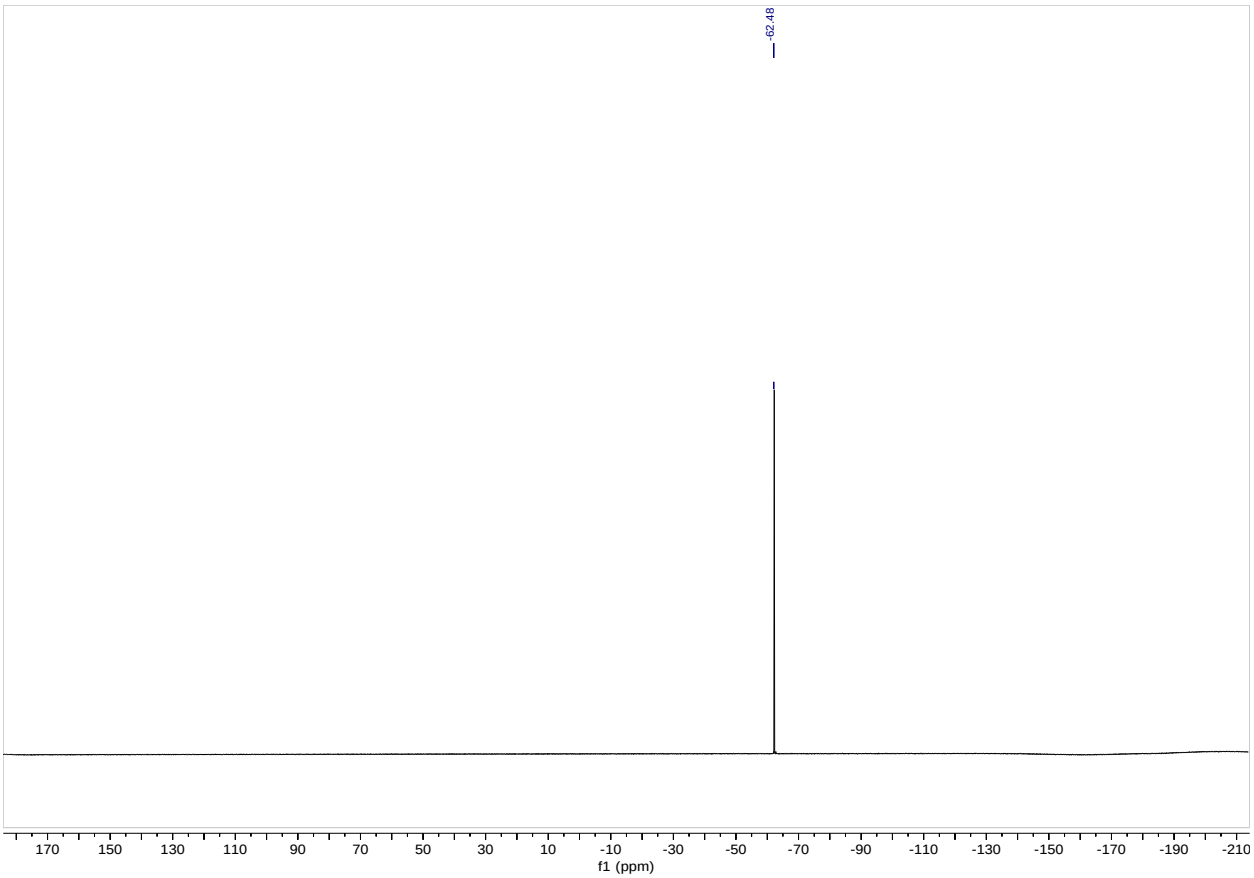

6.99
6.88
6.83
6.68
6.66
5.54
3.92
3.71
3.04
2.89
2.88
2.68
2.55
3.10
1.07
1.07
2.01
2.00
4.09
2.97
3.99
1.98
2.03
f1 (ppm)

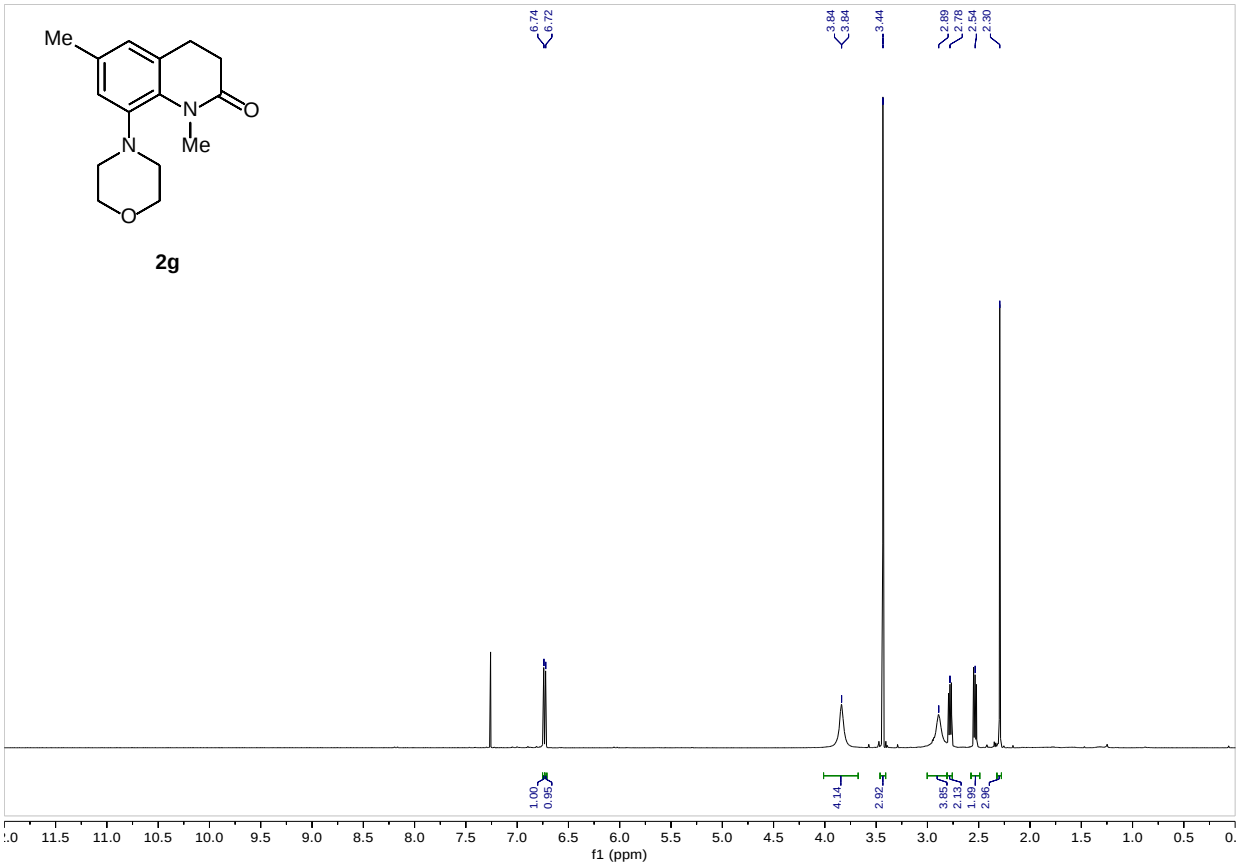
2e


172.81
158.46
142.70
133.80
131.65
130.69
129.08
124.92
121.85
117.32
113.49
67.03
55.10
50.60
43.28
33.15
26.28
f1 (ppm)

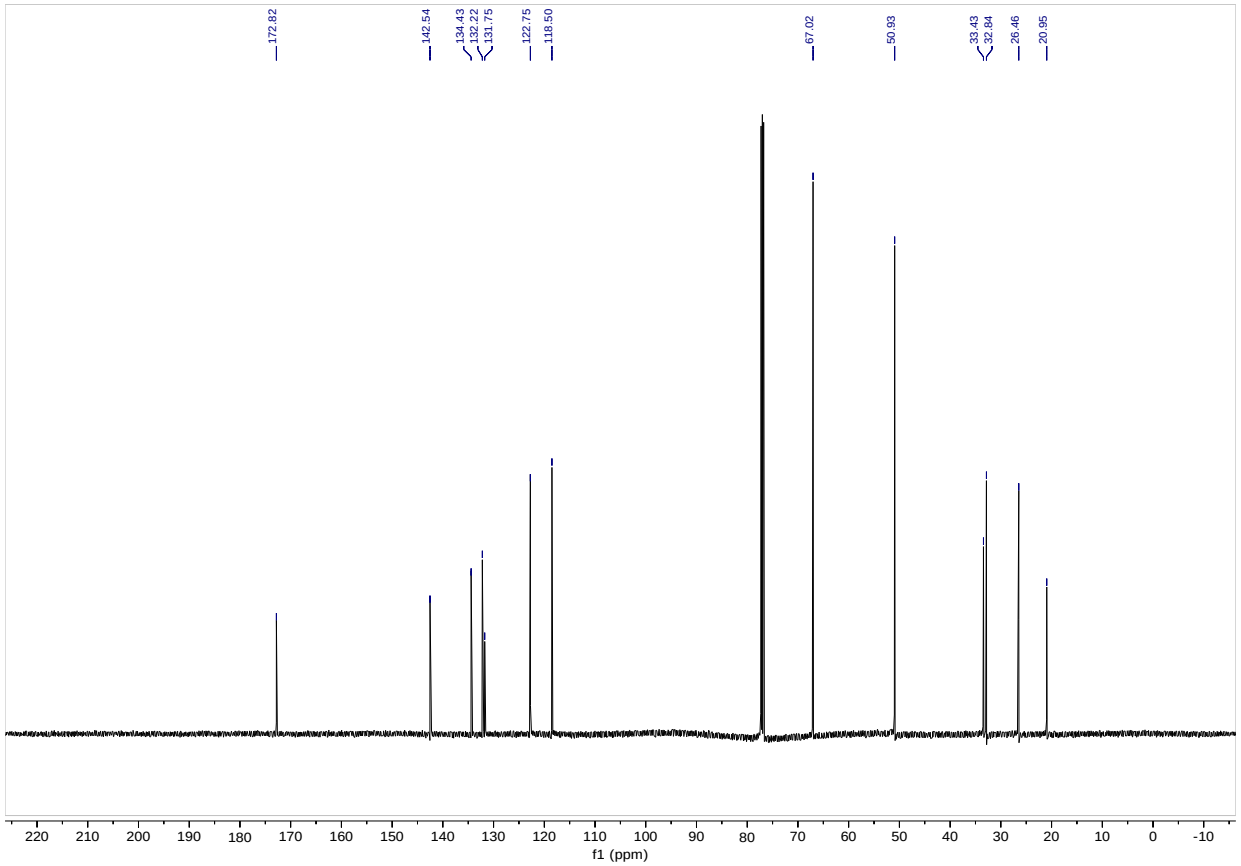

7.43
7.41
7.18
7.16
7.03
7.02
6.89
5.66
3.95
3.85
3.01
2.89
2.75
2.59
O
N
N
O
CF3
2f
2.00
2.00
1.06
2.01
2.00
3.96
3.89
1.94
1.92
f1 (ppm)

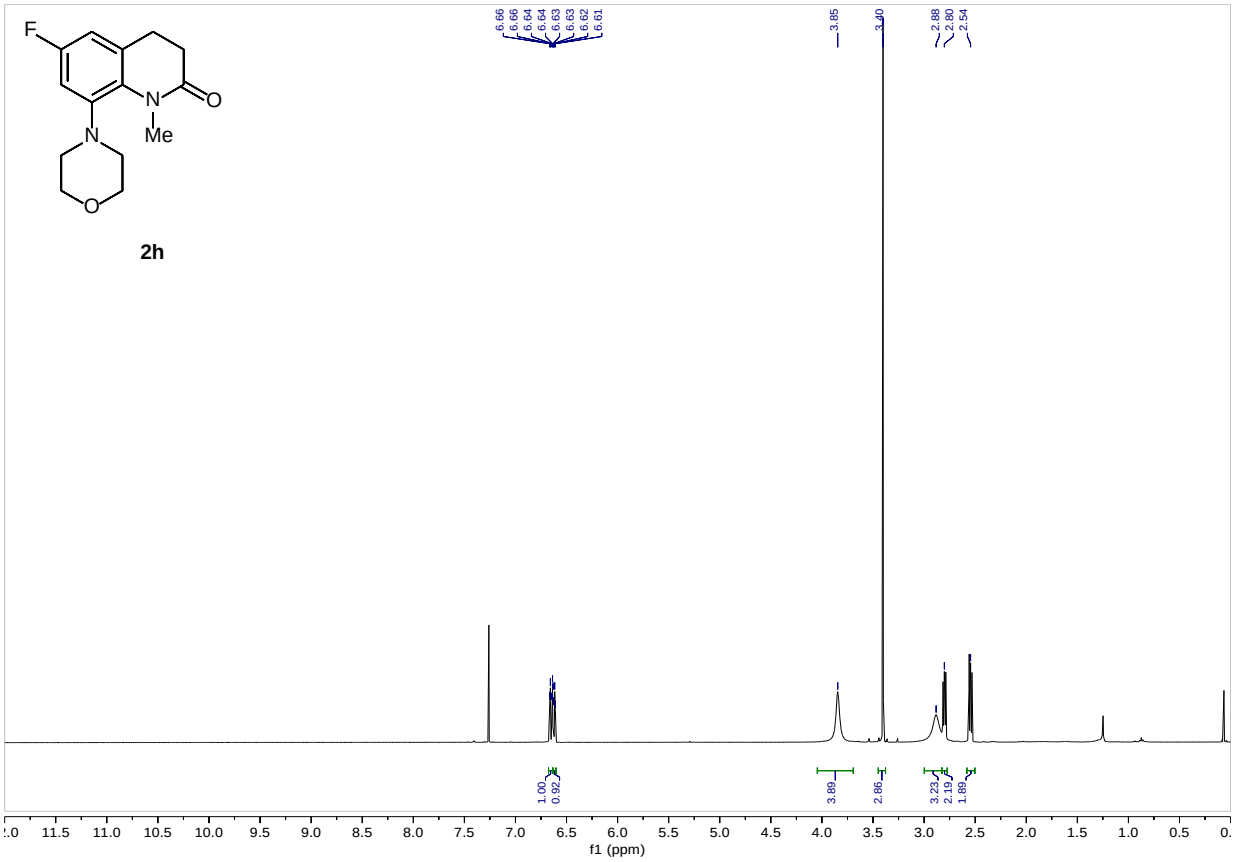

172.72
142.63
142.62
142.60
142.59
142.51
133.41
131.60
129.49
129.24
128.98
128.72
127.92
127.31
125.23
125.18
125.15
125.12
125.09
122.98
122.28
120.81
117.74
66.97
50.78
43.79
32.92
26.26
f1 (ppm)


-62.48
170
150
130
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

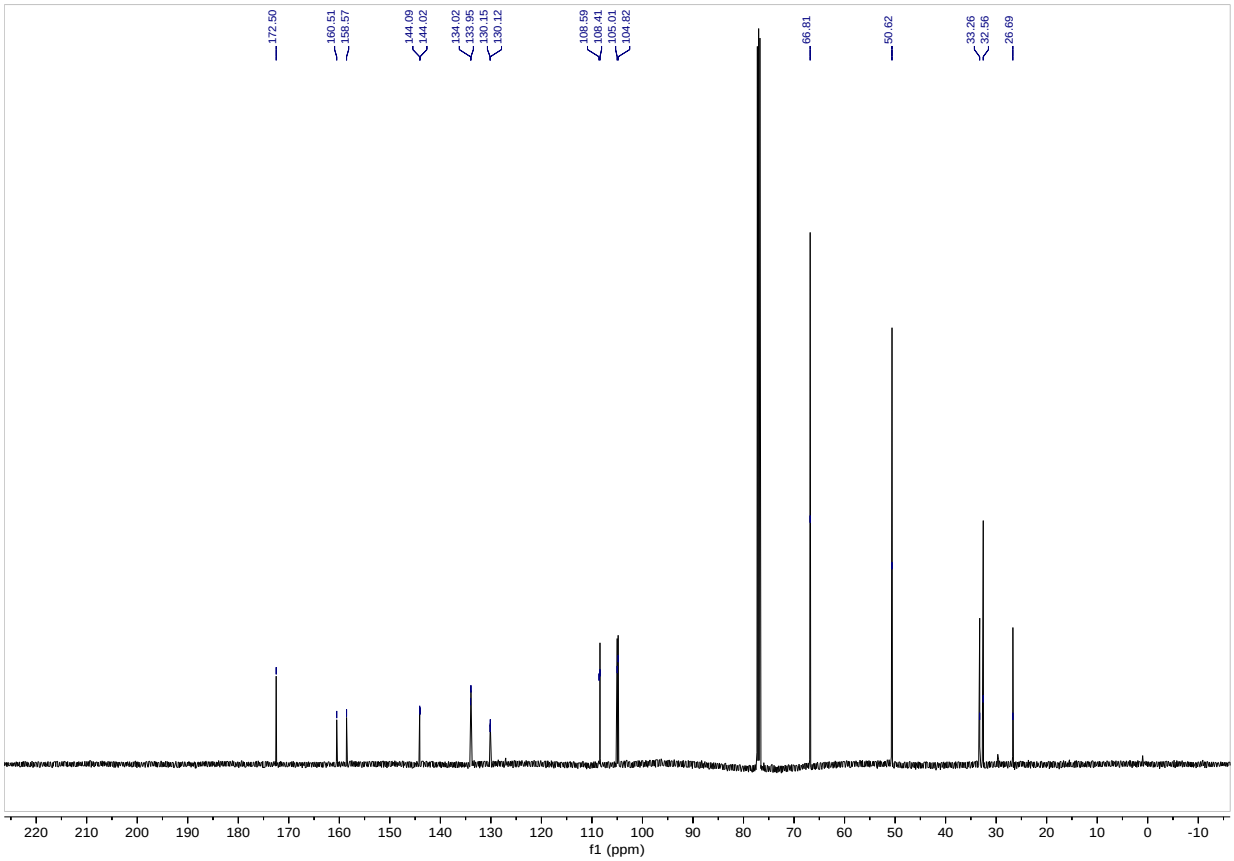

Me
N
O
N
Me
O
6.74
6.72
3.84
3.84
3.44
2.89
2.78
2.54
2.30
1.00
0.95
4.14
2.92
3.85
2.13
1.99
2.96
f1 (ppm)

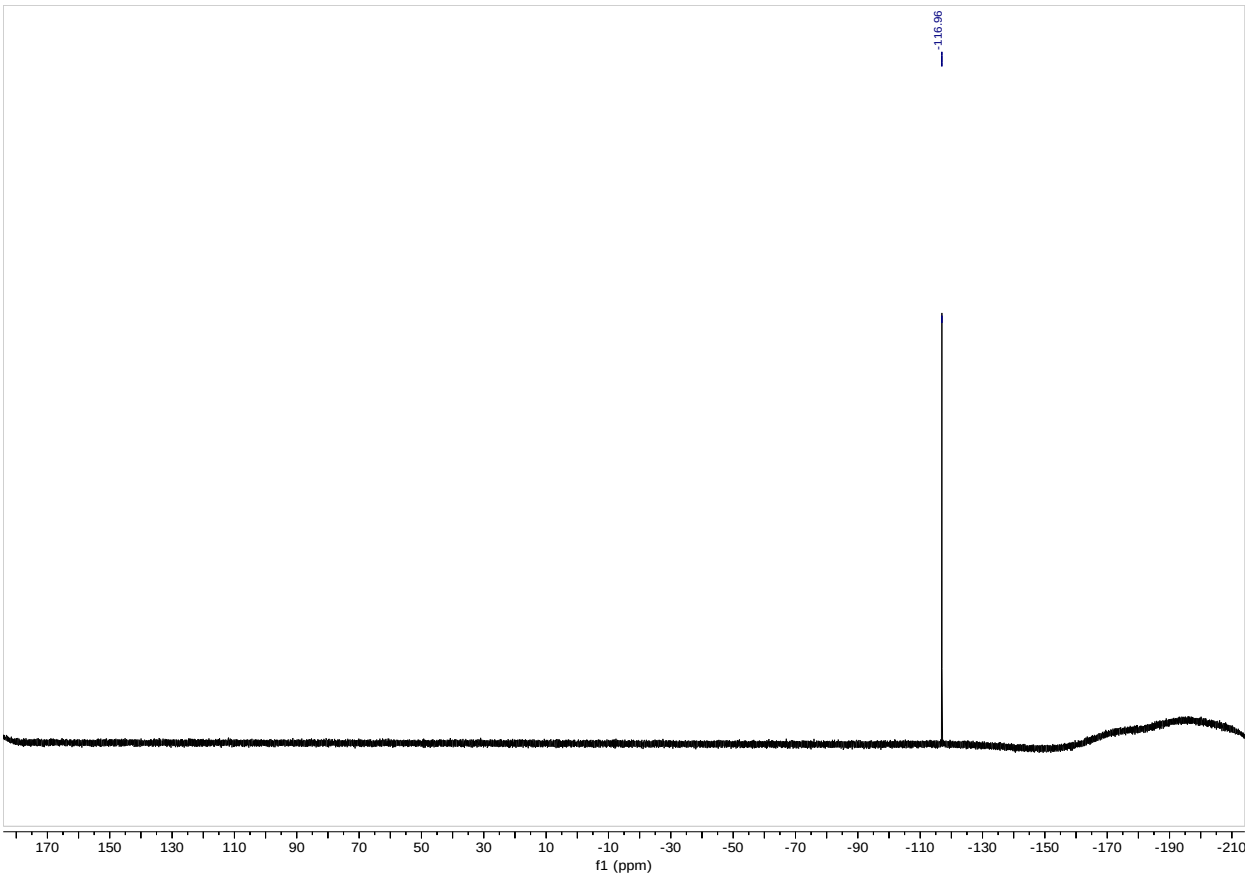
2g

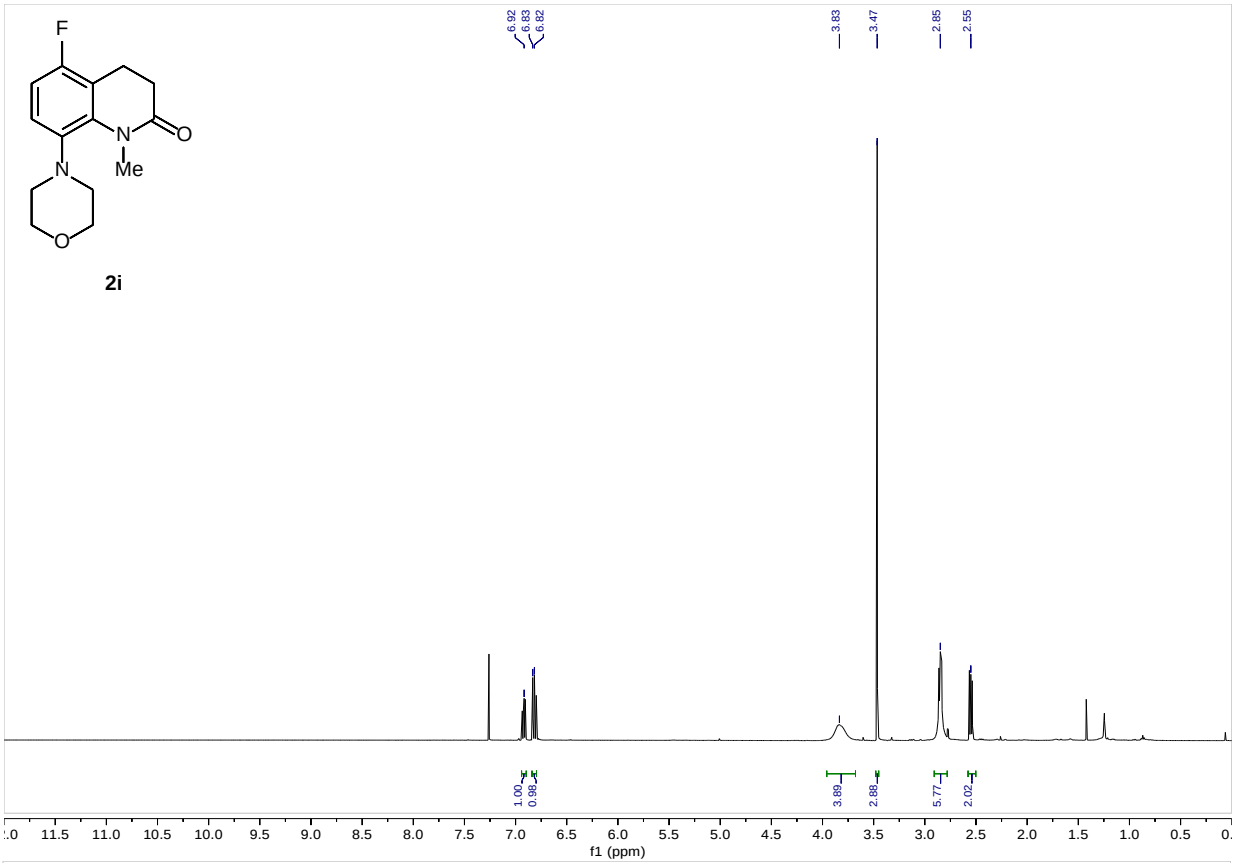

172.82
142.54
134.43
132.22
131.75
122.75
118.50
67.02
50.93
33.43
32.84
26.46
20.95
f1 (ppm)


F
N
O
N
Me
O
6.66
6.66
6.64
6.64
6.63
6.63
6.62
6.61
3.85
3.40
2.88
2.80
2.54
1.00
0.92
3.89
2.86
3.23
2.19
1.89
f1 (ppm)

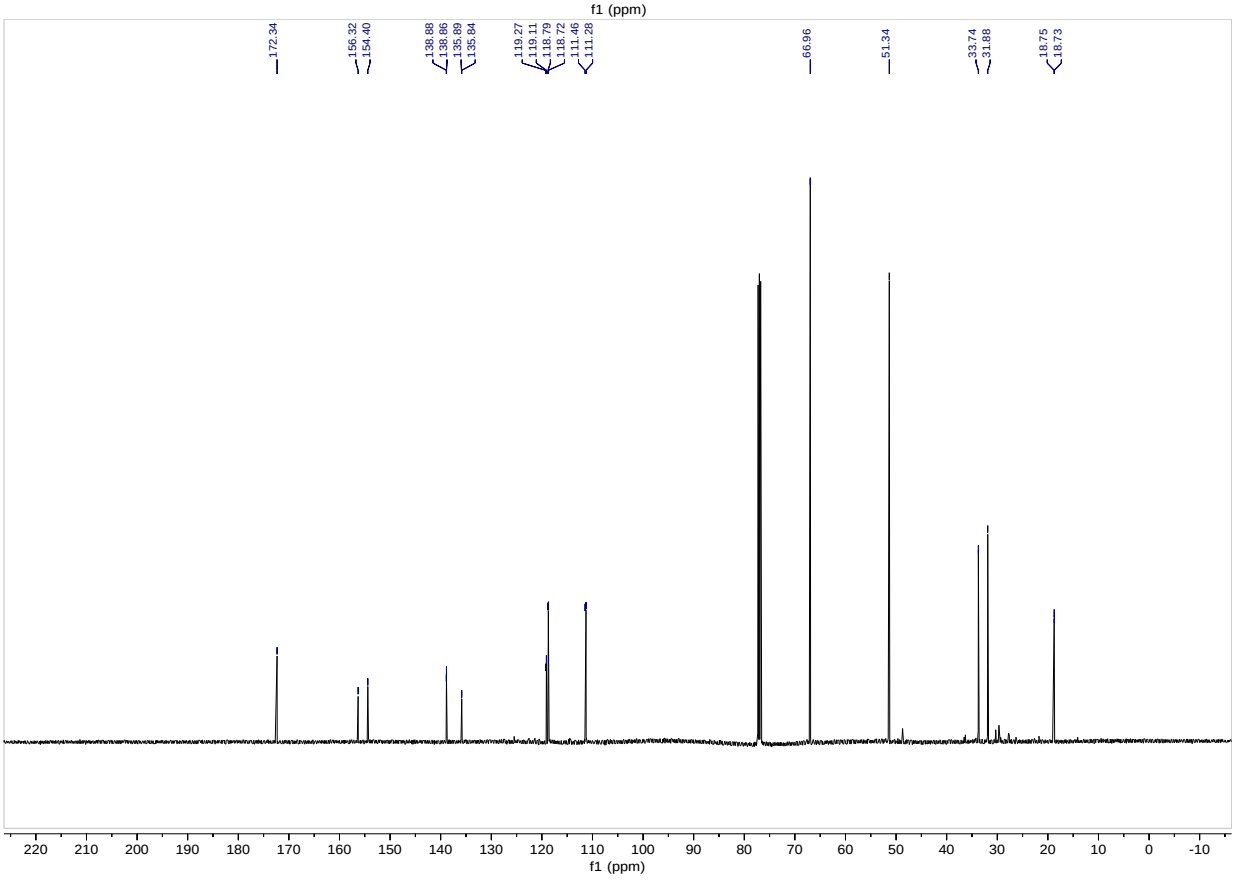
2h

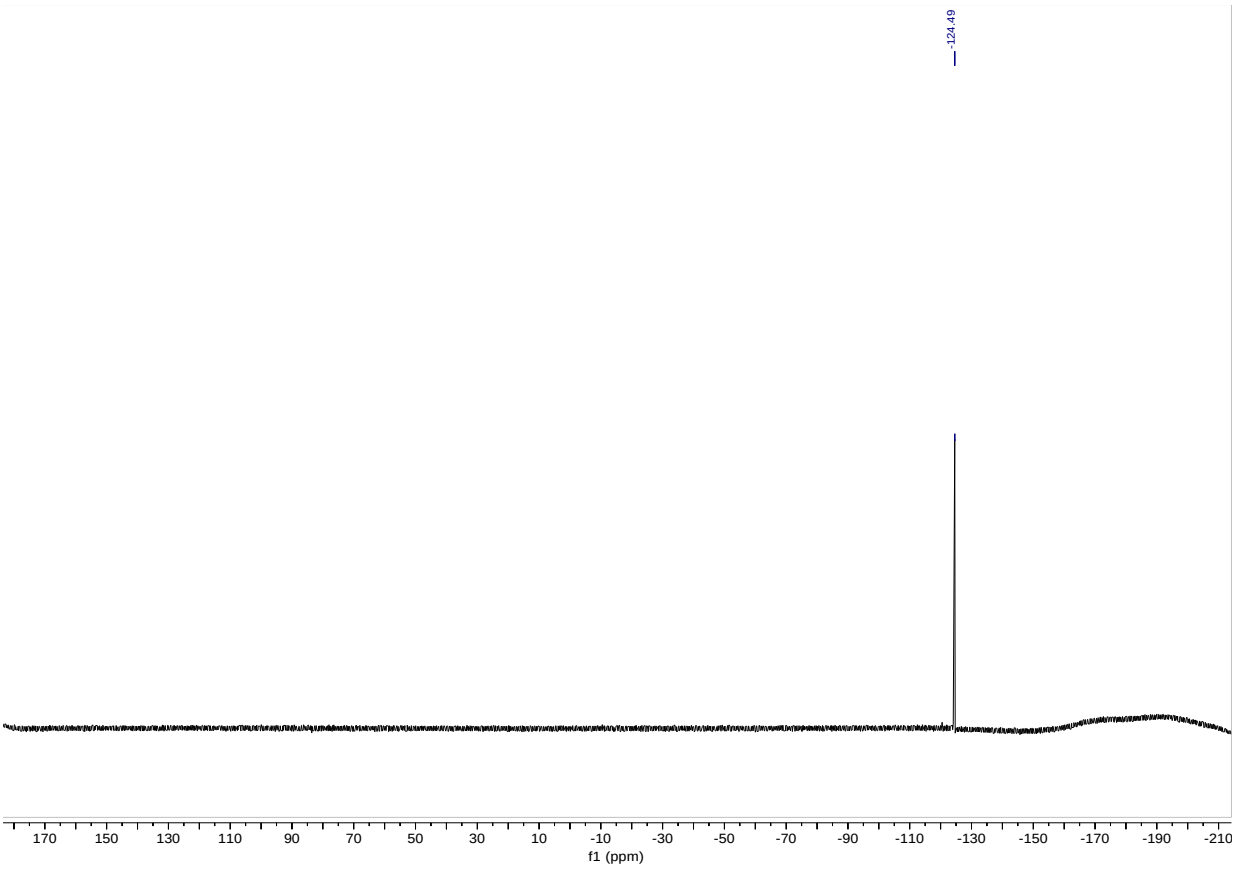

172.50
160.51
158.57
144.09
144.02
134.02
133.95
130.15
130.12
108.59
108.41
105.01
104.82
66.81
50.62
33.26
32.56
26.69
f1 (ppm)

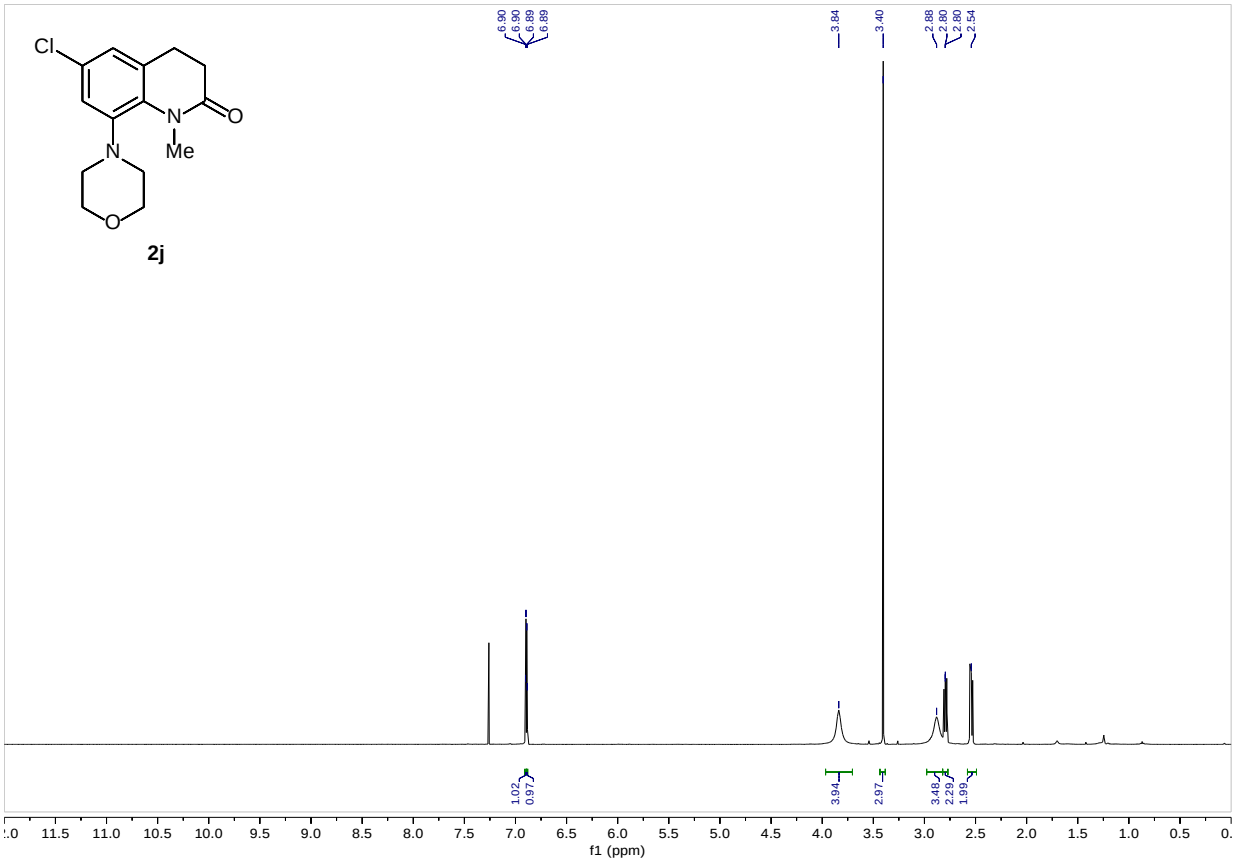

-116.96
170
150
130
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)


F
N
O
N
Me
O
6.92
6.83
6.82
3.83
3.47
2.85
2.55
1.00
0.98
3.89
2.88
5.77
2.02
f1 (ppm)

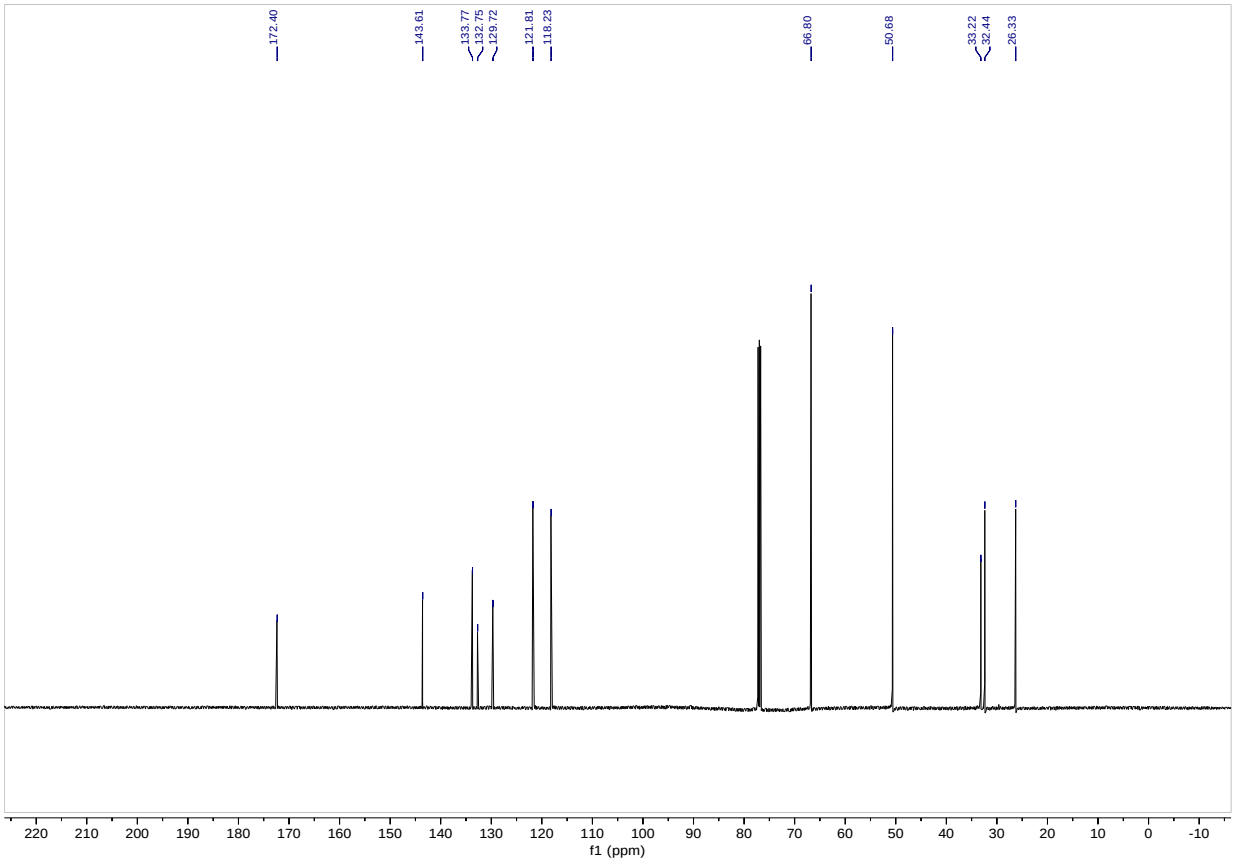
2i

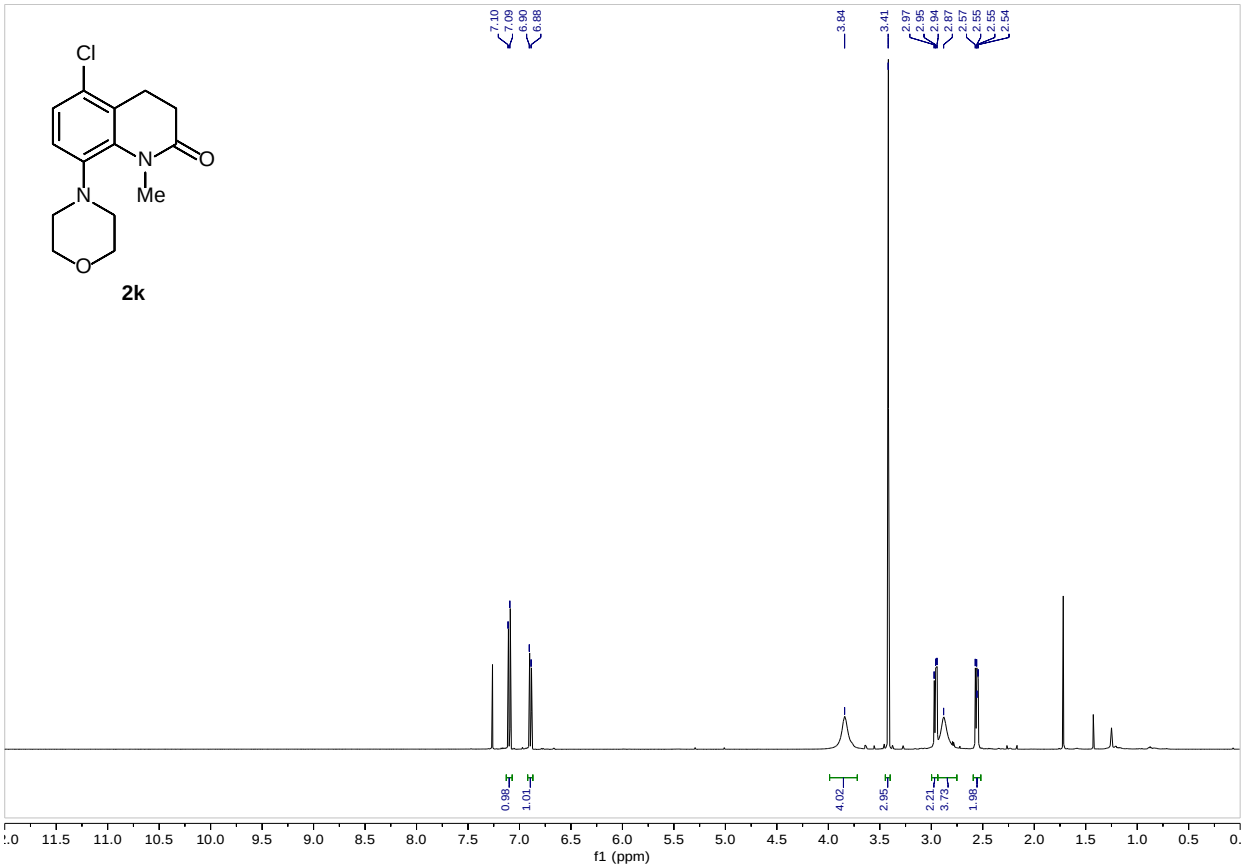

172.34
156.32
154.40
138.88
138.86
135.89
135.84
119.27
119.11
118.79
118.72
111.46
111.28
66.96
51.34
33.74
31.88
18.75
18.73
f1 (ppm)

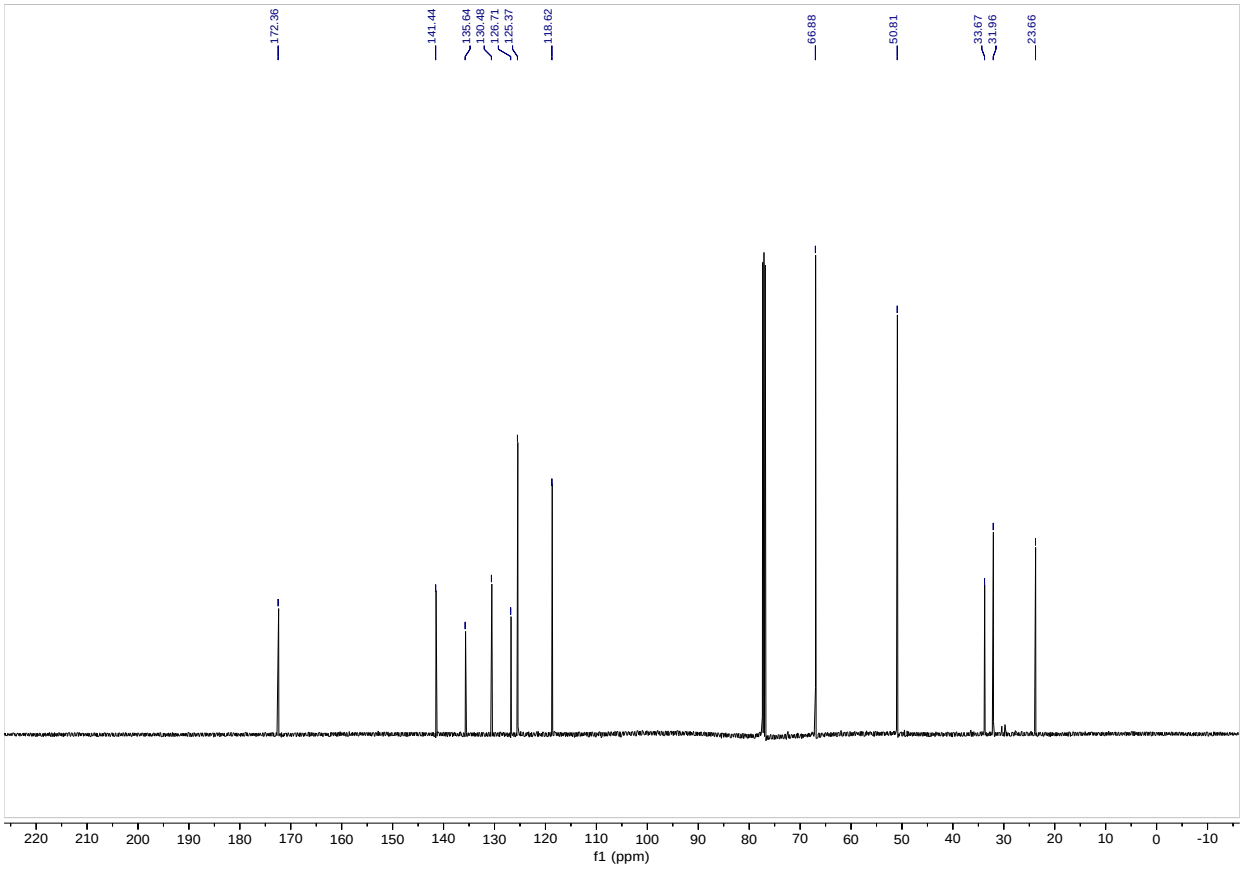

-124.49
170
150
130
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

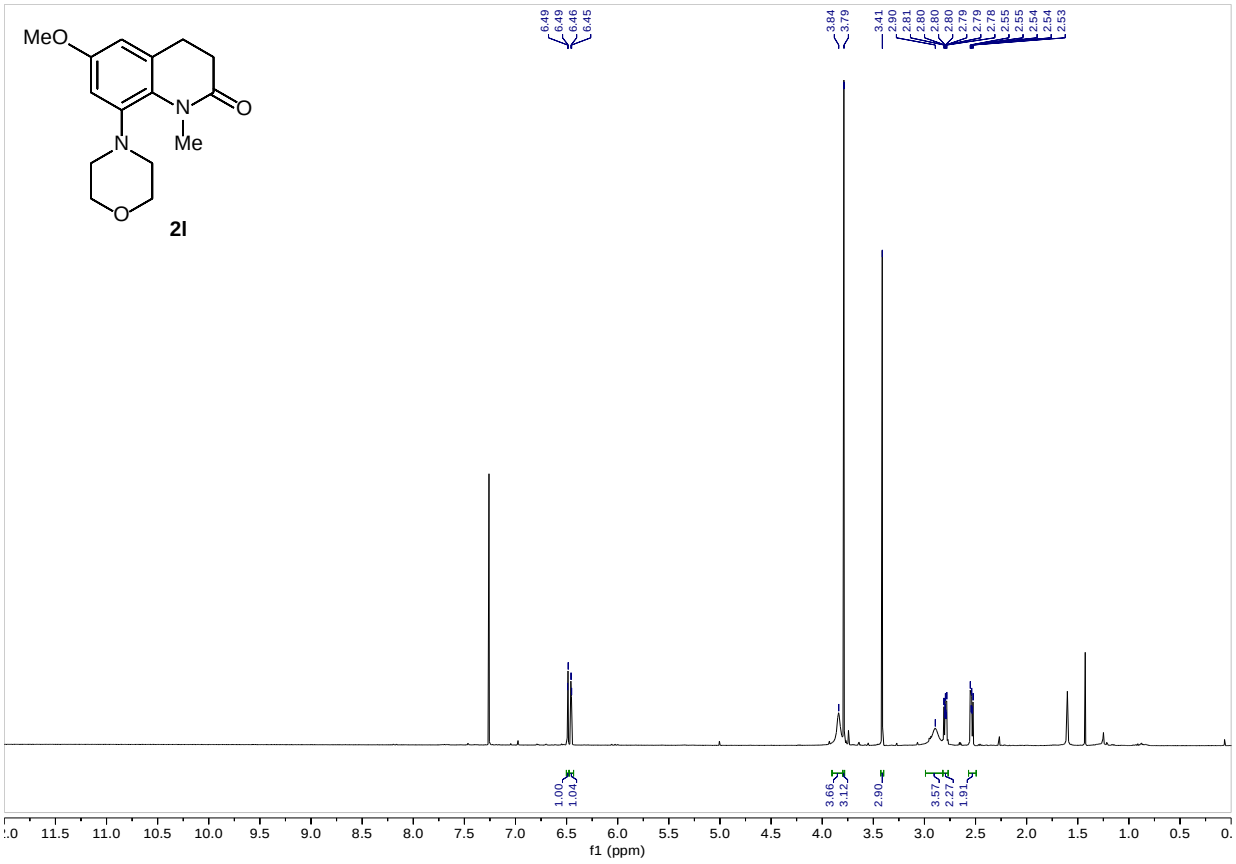

Cl
N
O
N
Me
O
6.90
6.90
6.89
6.89
3.84
3.40
2.88
2.80
2.80
2.54
1.02
0.97
3.94
2.97
3.48
2.29
1.99
f1 (ppm)

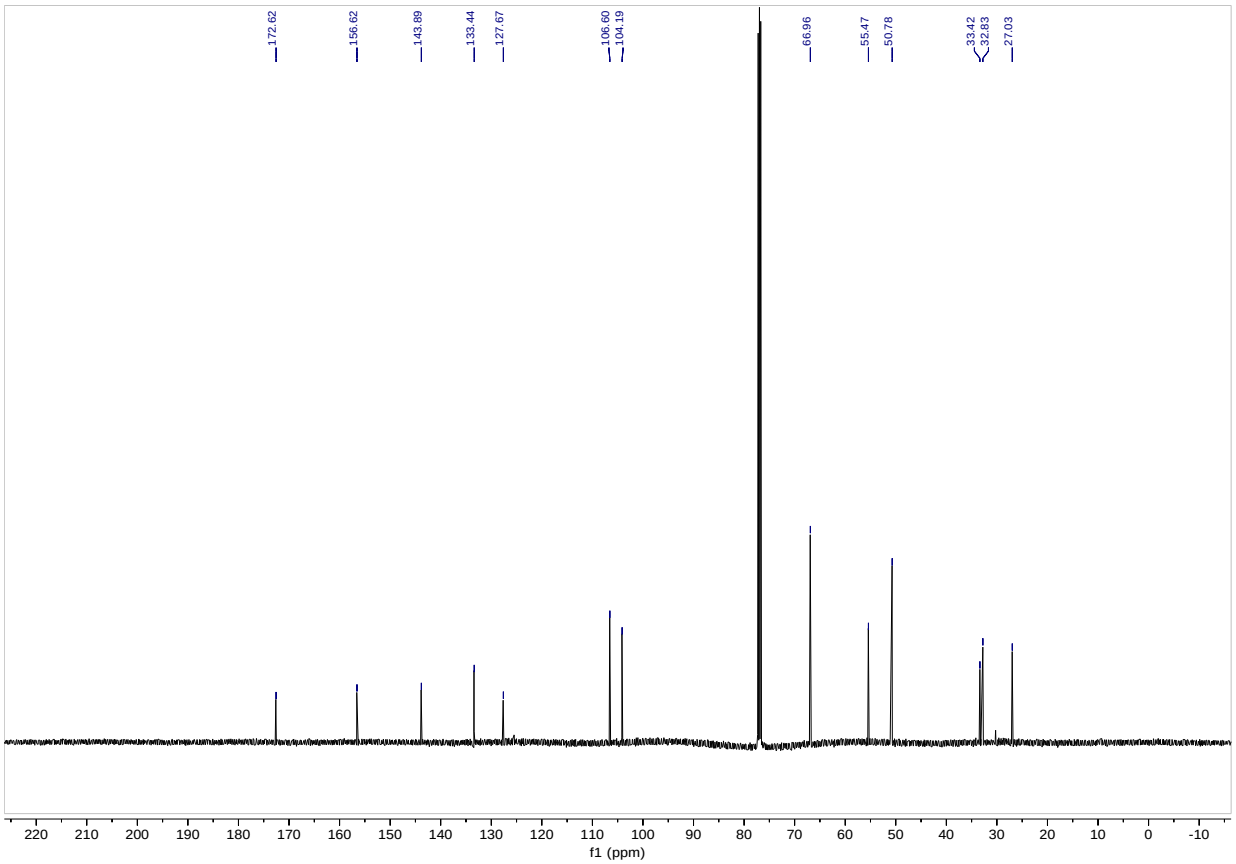
2j

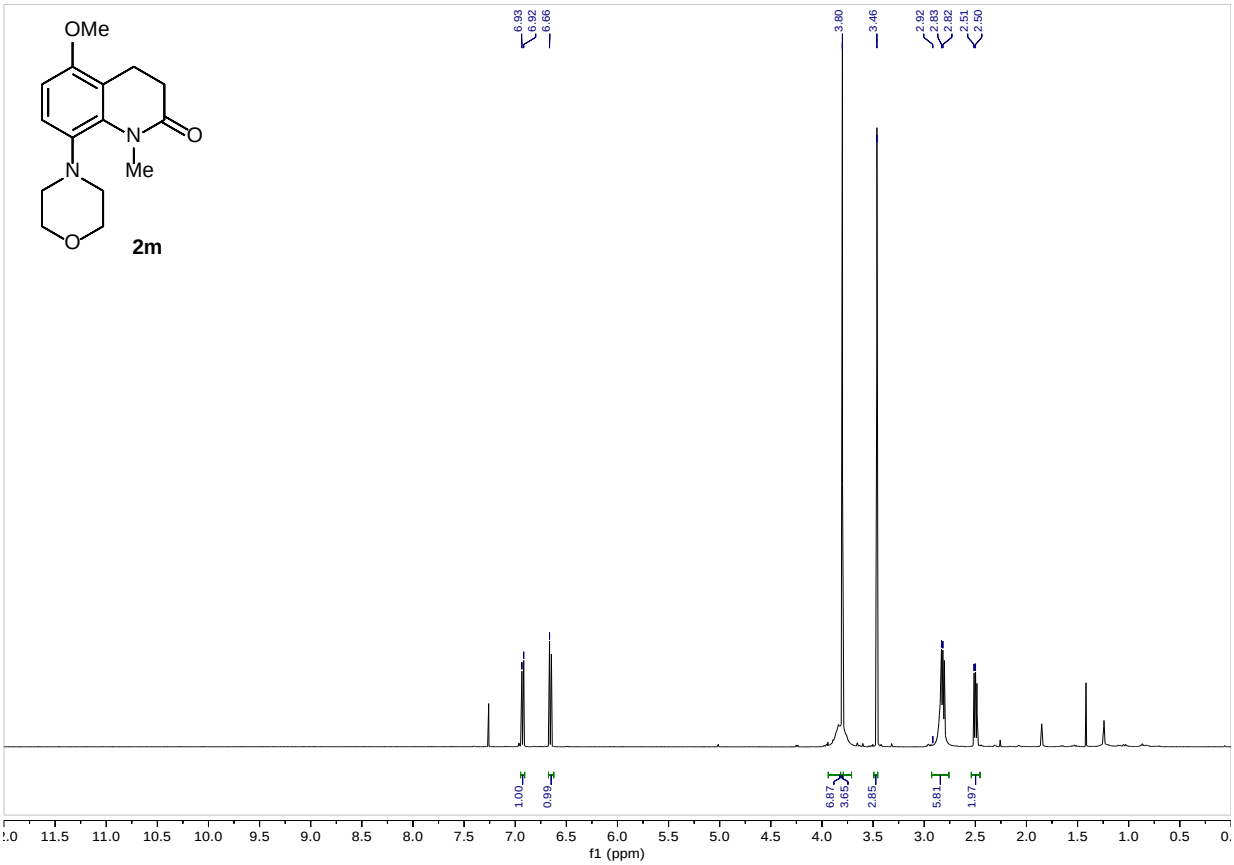

172.40
143.61
133.77
132.75
129.72
121.81
118.23
66.80
50.68
33.22
32.44
26.33
f1 (ppm)

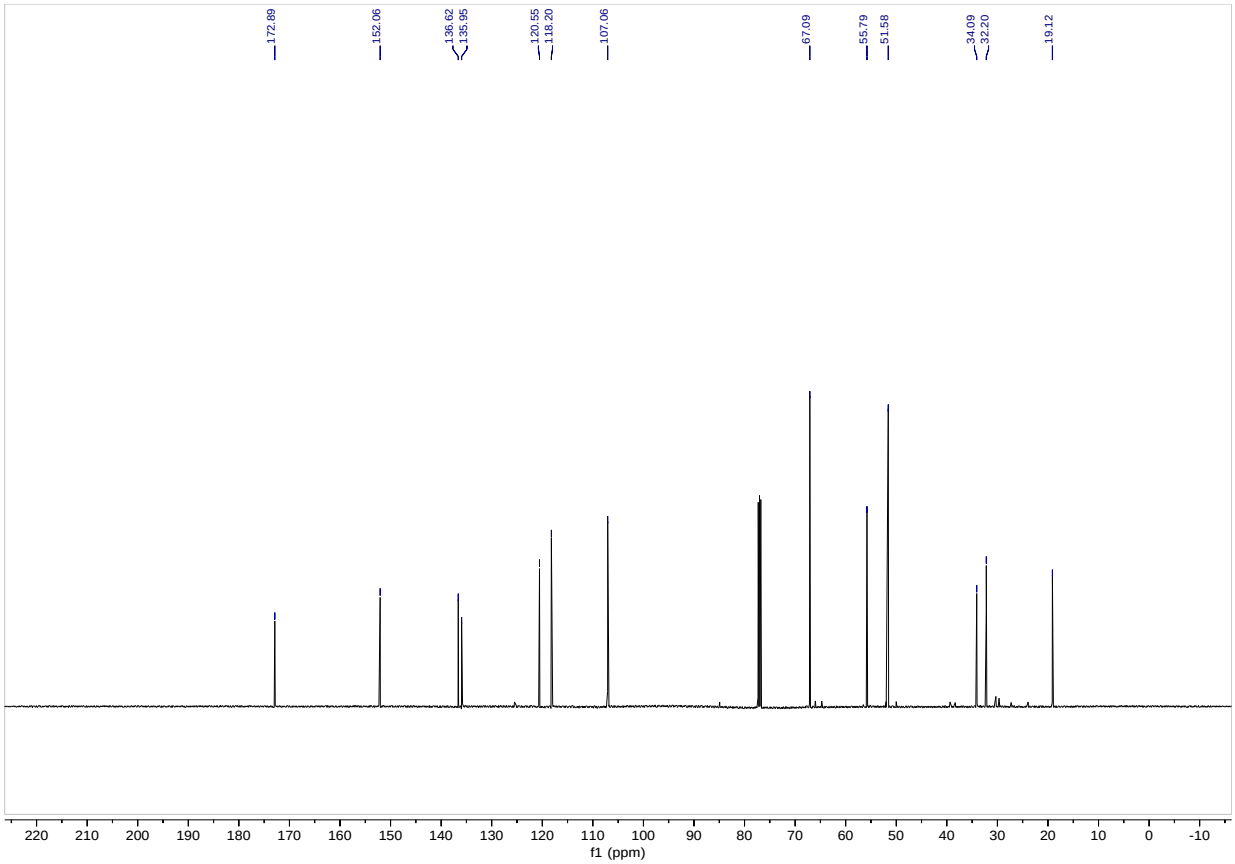

Cl
N
O
N
Me
O
2k
7.10
7.09
6.90
6.88
3.84
3.41
2.97
2.95
2.94
2.87
2.57
2.55
2.55
2.54
0.98
1.01
4.02
2.95
2.21
3.73
1.98
f1 (ppm)

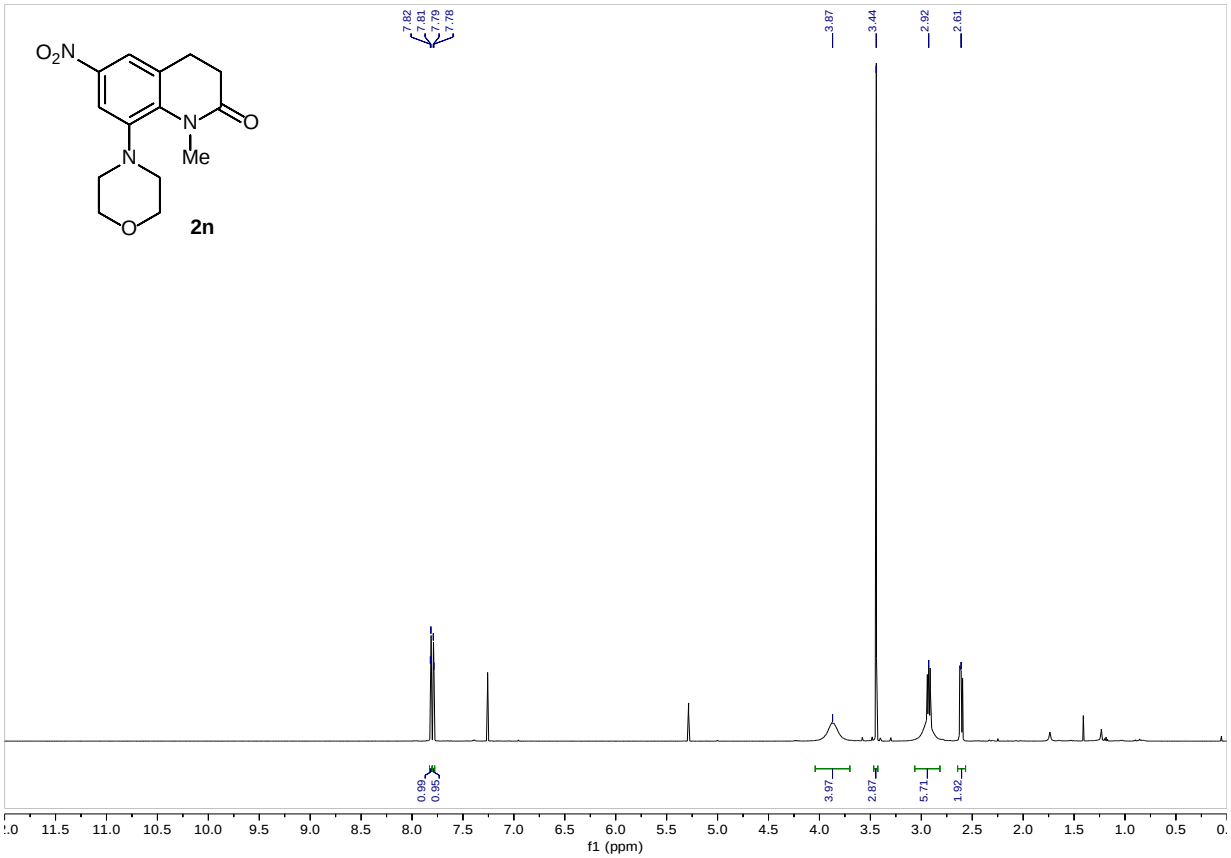

172.36
141.44
135.64
130.48
126.71
125.37
118.62
66.88
50.81
33.67
31.96
23.66
f1 (ppm)

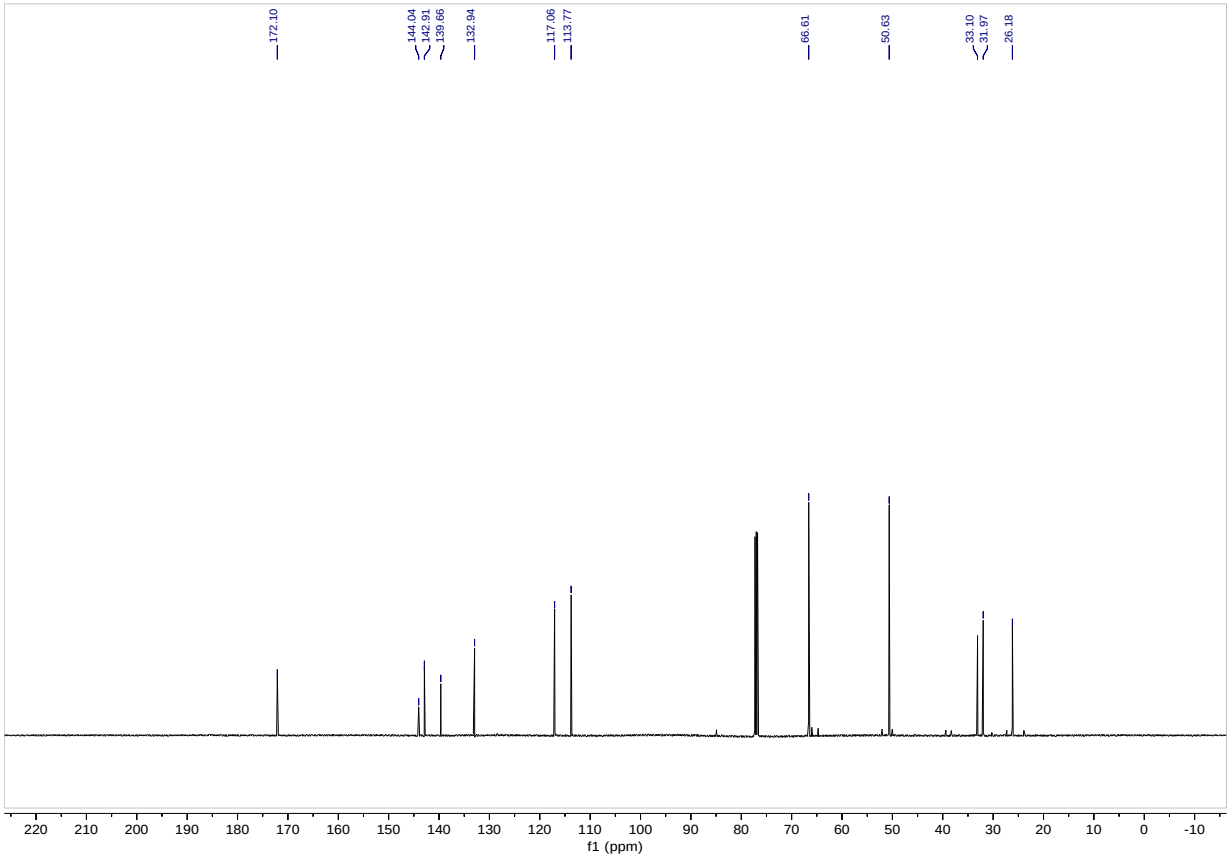

MeO
N
O
Me
N
O
2l
6.49
6.49
6.46
6.45
3.84
3.79
3.41
2.90
2.81
2.80
2.80
2.80
2.79
2.79
2.78
2.55
2.54
2.54
2.53
1.00
1.04
3.66
3.12
2.90
3.57
2.27
1.91
f1 (ppm)

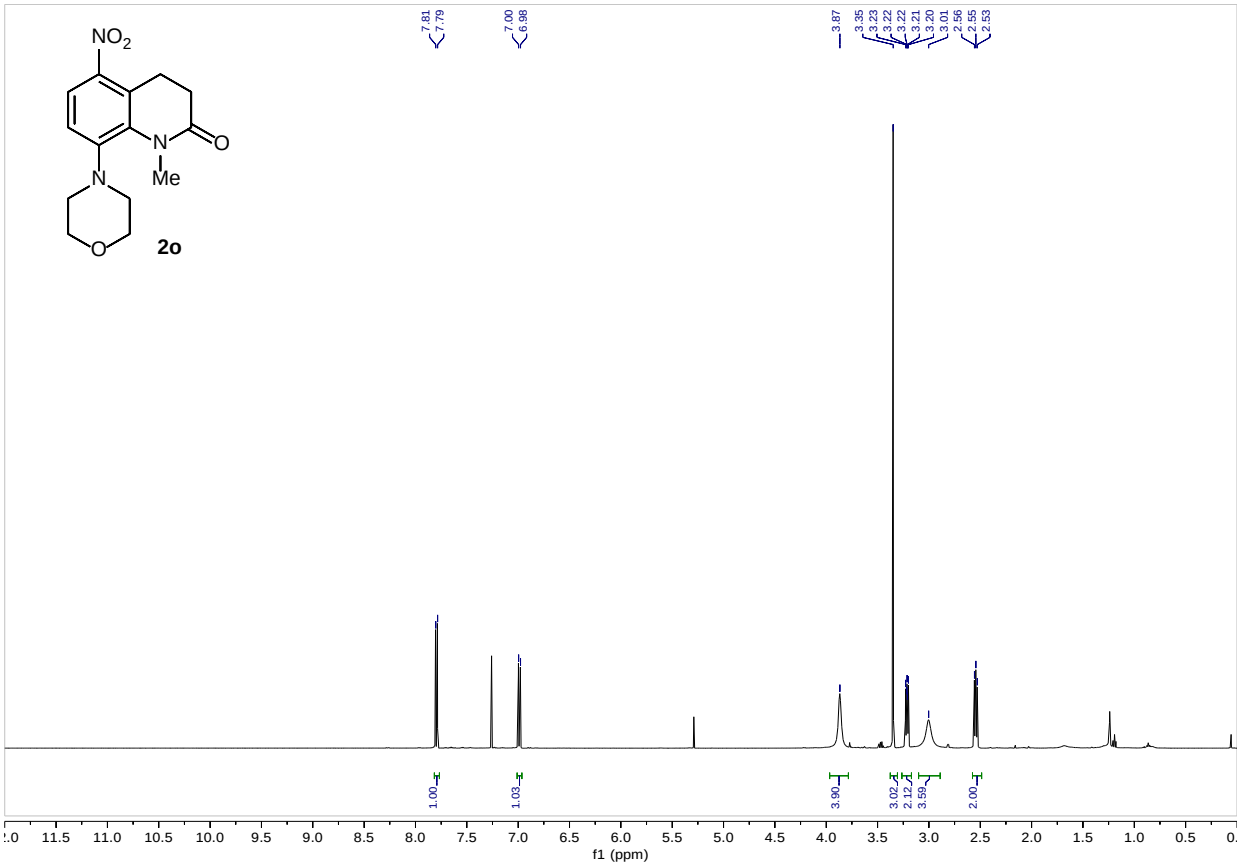

172.62
156.62
143.89
133.44
127.67
106.60
104.19
66.96
55.47
50.78
33.42
32.83
27.03
f1 (ppm)

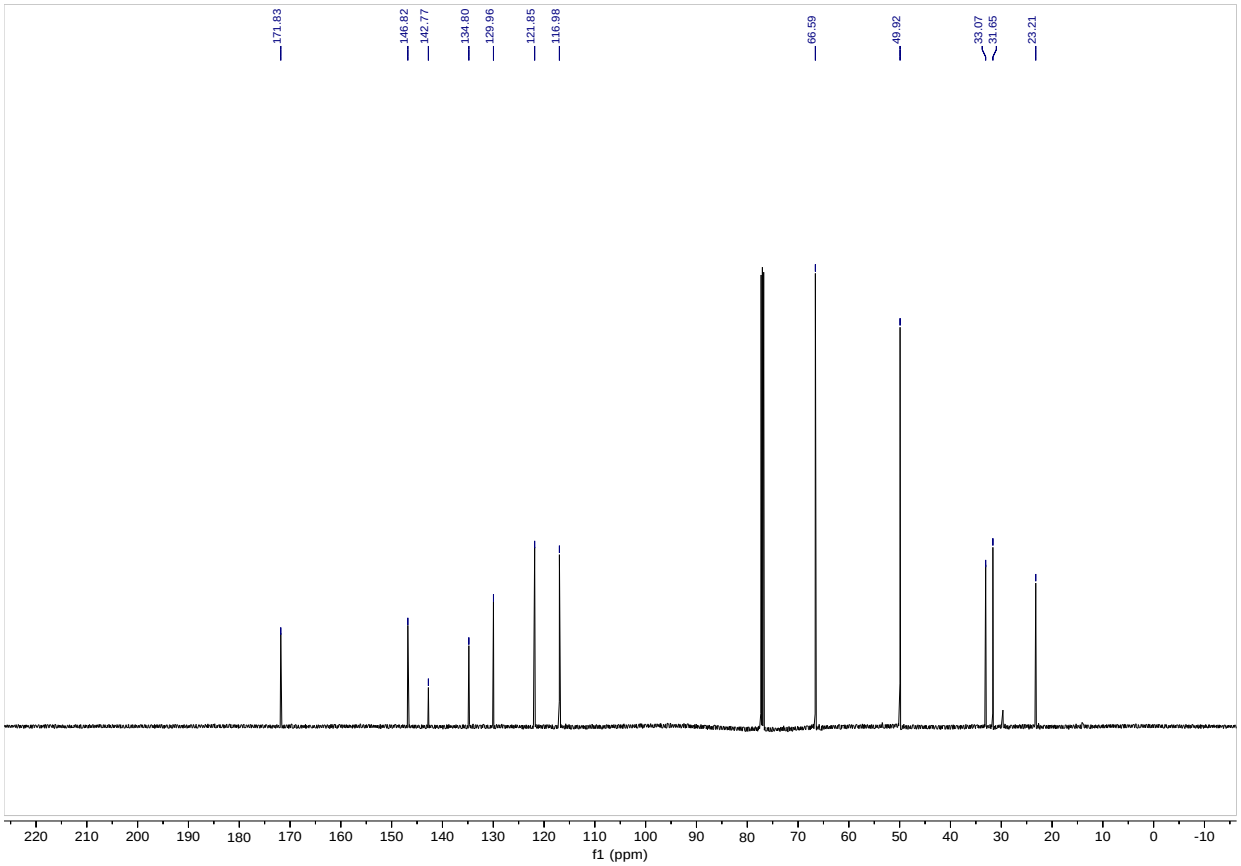

OMe
N
O
N
Me
O
2m
6.93
6.92
6.66
3.80
3.46
2.92
2.83
2.82
2.51
2.50
1.00
0.99
6.87
3.65
2.85
5.81
1.97
f1 (ppm)

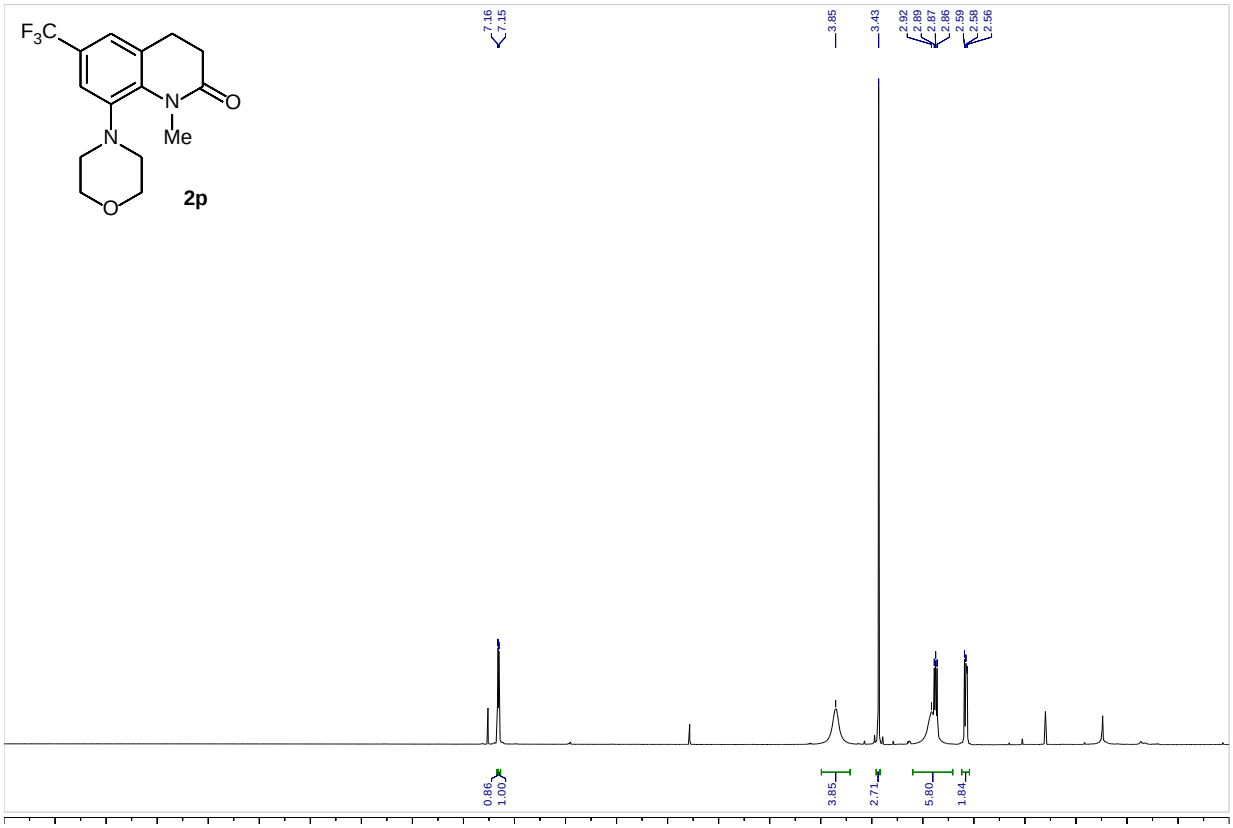

172.89
152.06
136.62
135.95
120.55
118.20
107.06
67.09
55.79
51.58
34.09
32.20
19.12
f1 (ppm)

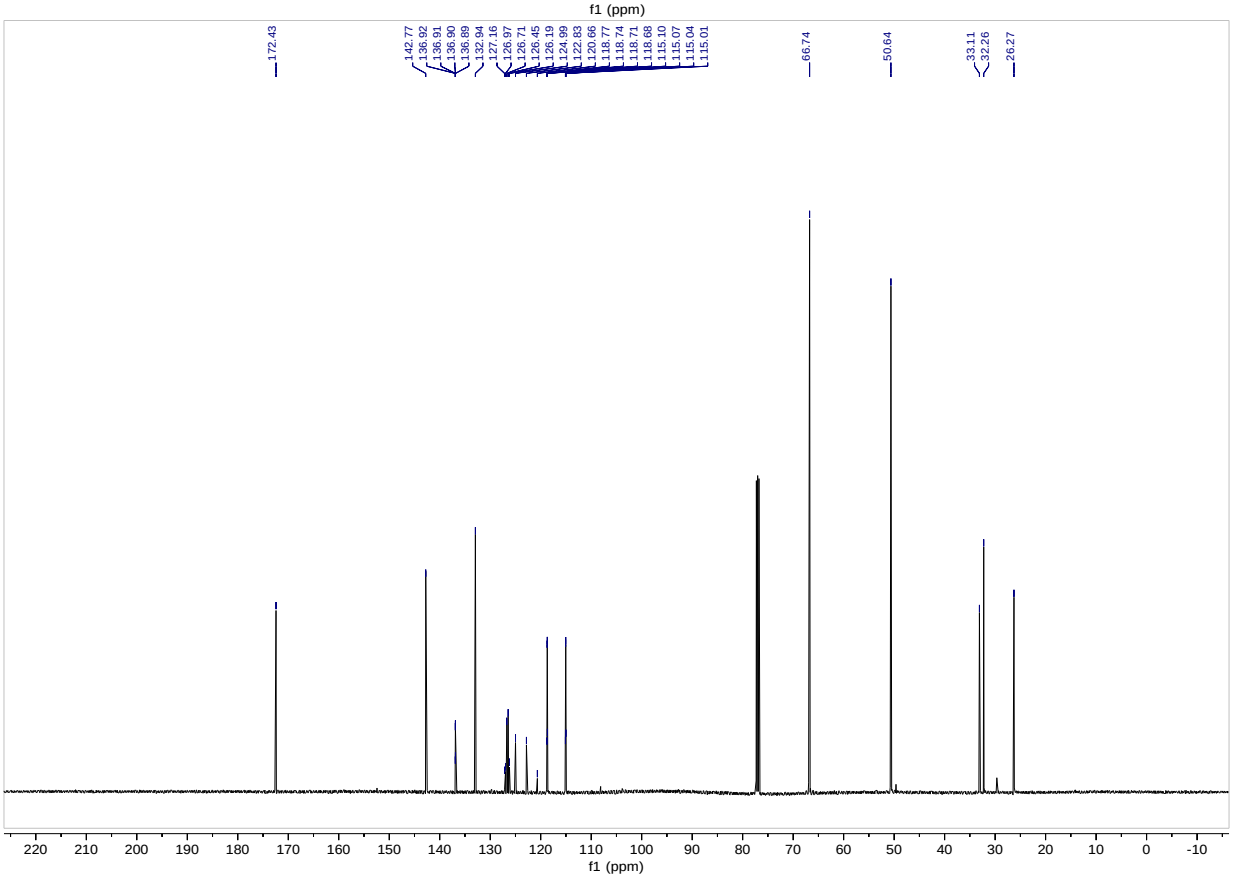

O2N
N
O
N
Me
O
2n
7.82
7.81
7.79
7.78
3.87
3.44
2.92
2.61
0.99
0.95
3.97
2.87
5.71
1.92
f1 (ppm)

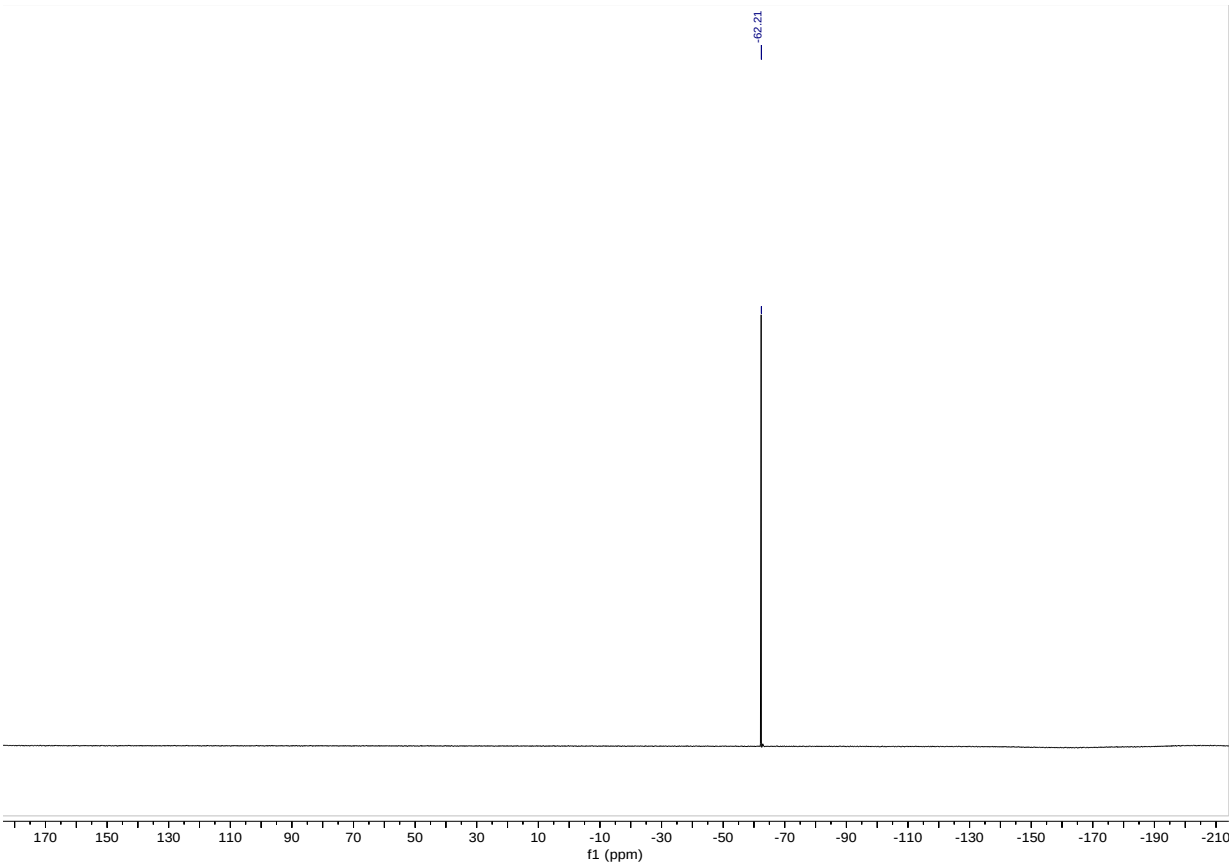

172.10
144.04
142.91
139.66
132.94
117.06
113.77
66.61
50.63
33.10
31.97
26.18
f1 (ppm)

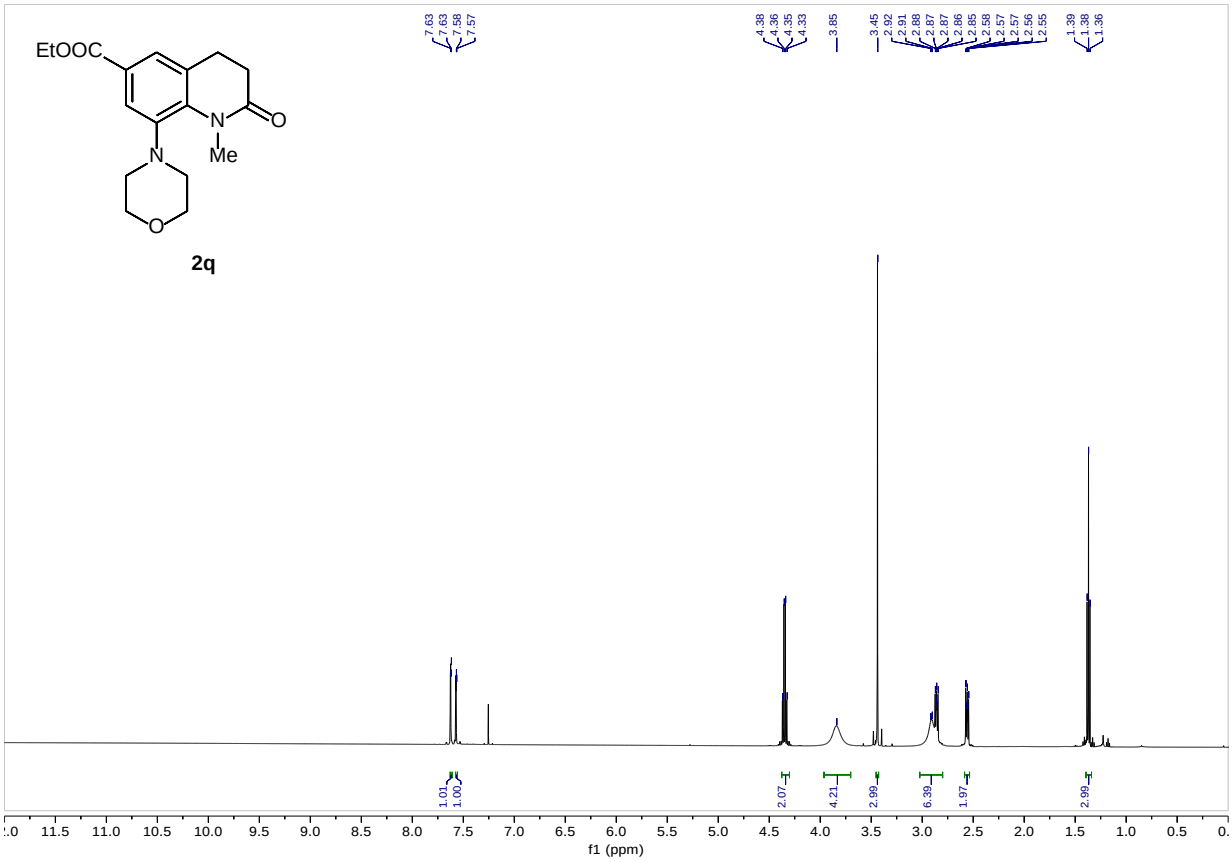

NO2
N
O
N
Me
O
2o
7.81
7.79
7.00
6.98
3.87
3.35
3.23
3.22
3.22
3.21
3.20
3.01
2.56
2.55
2.53
1.00
1.03
3.90
3.02
2.12
3.59
2.00
f1 (ppm)


171.83
146.82
142.77
134.80
129.96
121.85
116.98
66.59
49.92
33.07
31.65
23.21
f1 (ppm)

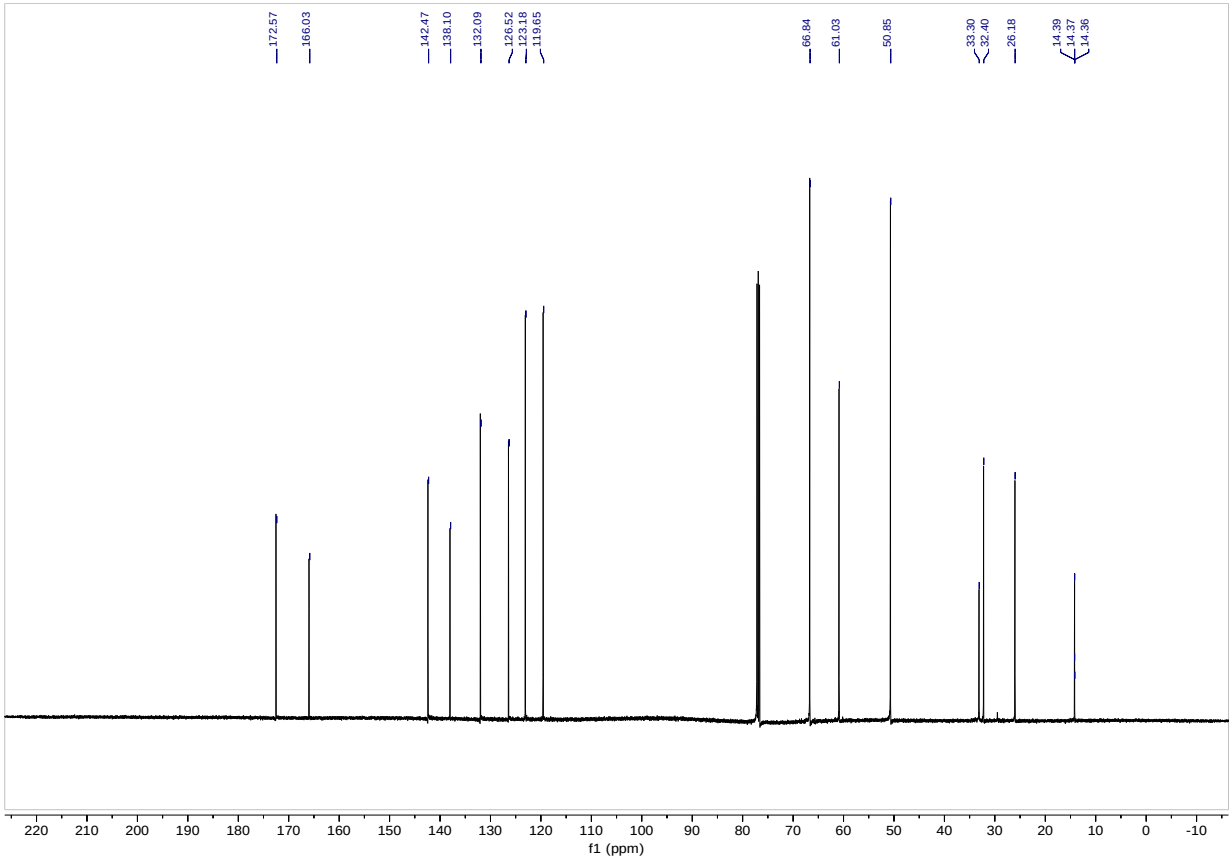

F3C
N
O
N
Me
O
2p
7.16
7.15
3.85
3.43
2.92
2.89
2.87
2.86
2.59
2.58
2.56
0.86
1.00
3.85
2.71
5.80
1.84
f1 (ppm)

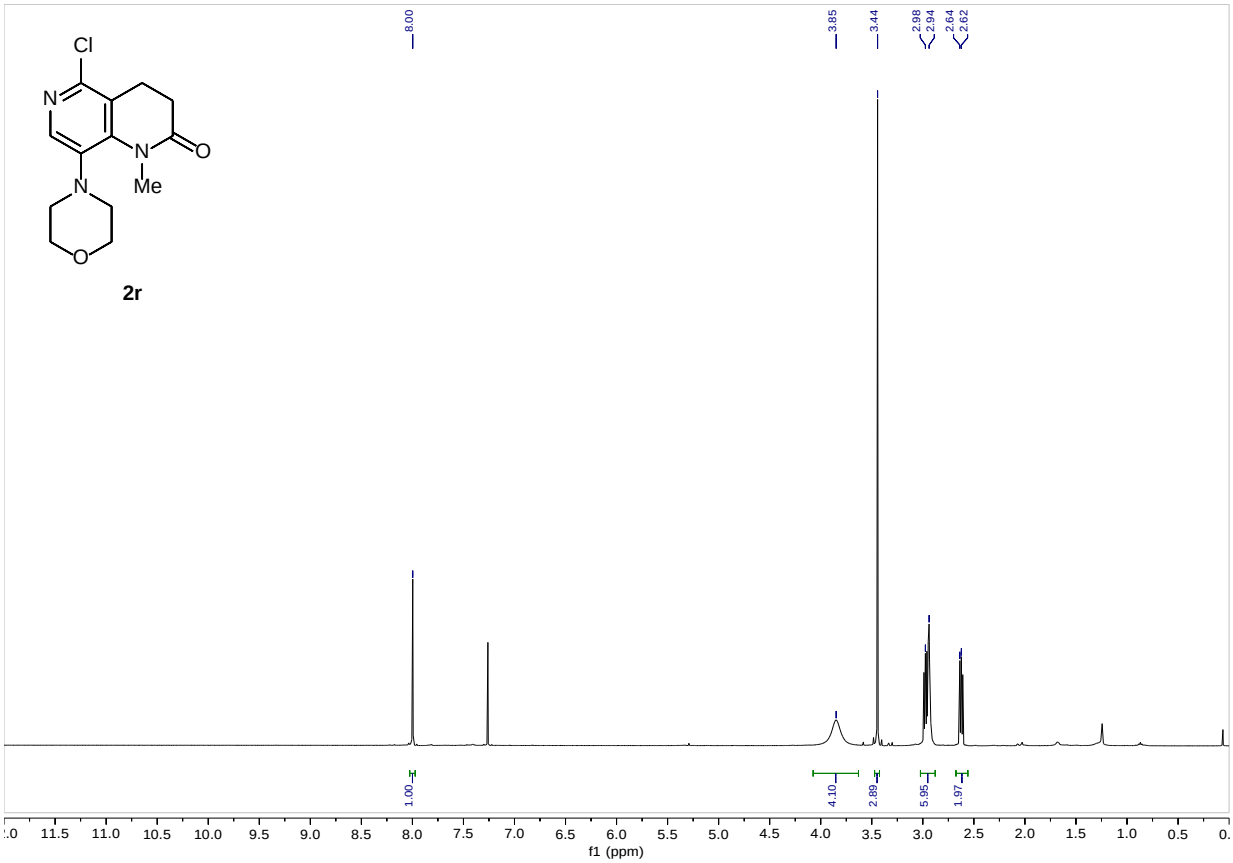

172.43
142.77
136.92
136.91
136.90
136.89
132.94
127.16
126.97
126.71
126.45
126.19
124.99
122.83
120.66
118.77
118.74
118.71
118.68
115.10
115.07
115.04
115.01
66.74
50.64
33.11
32.26
26.27
f1 (ppm)

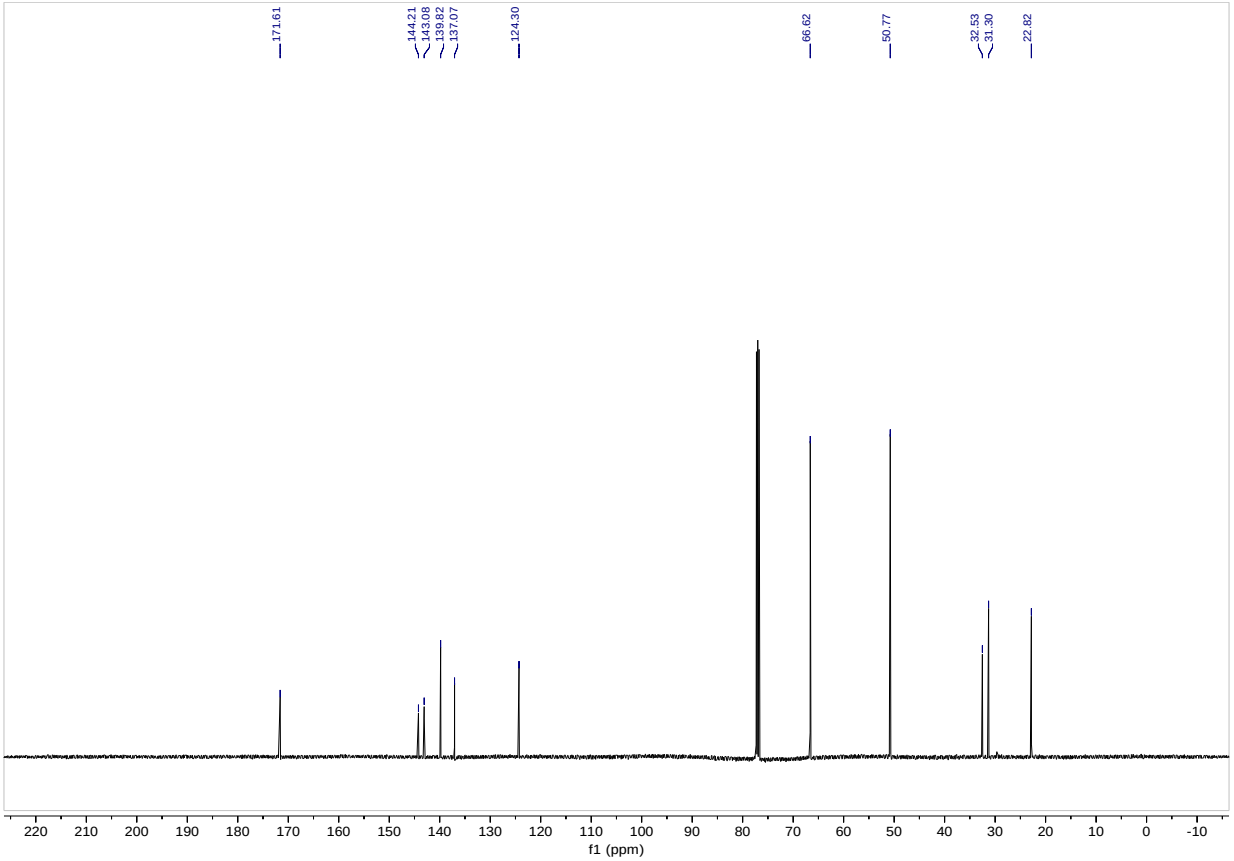

-62.21
170
150
130
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

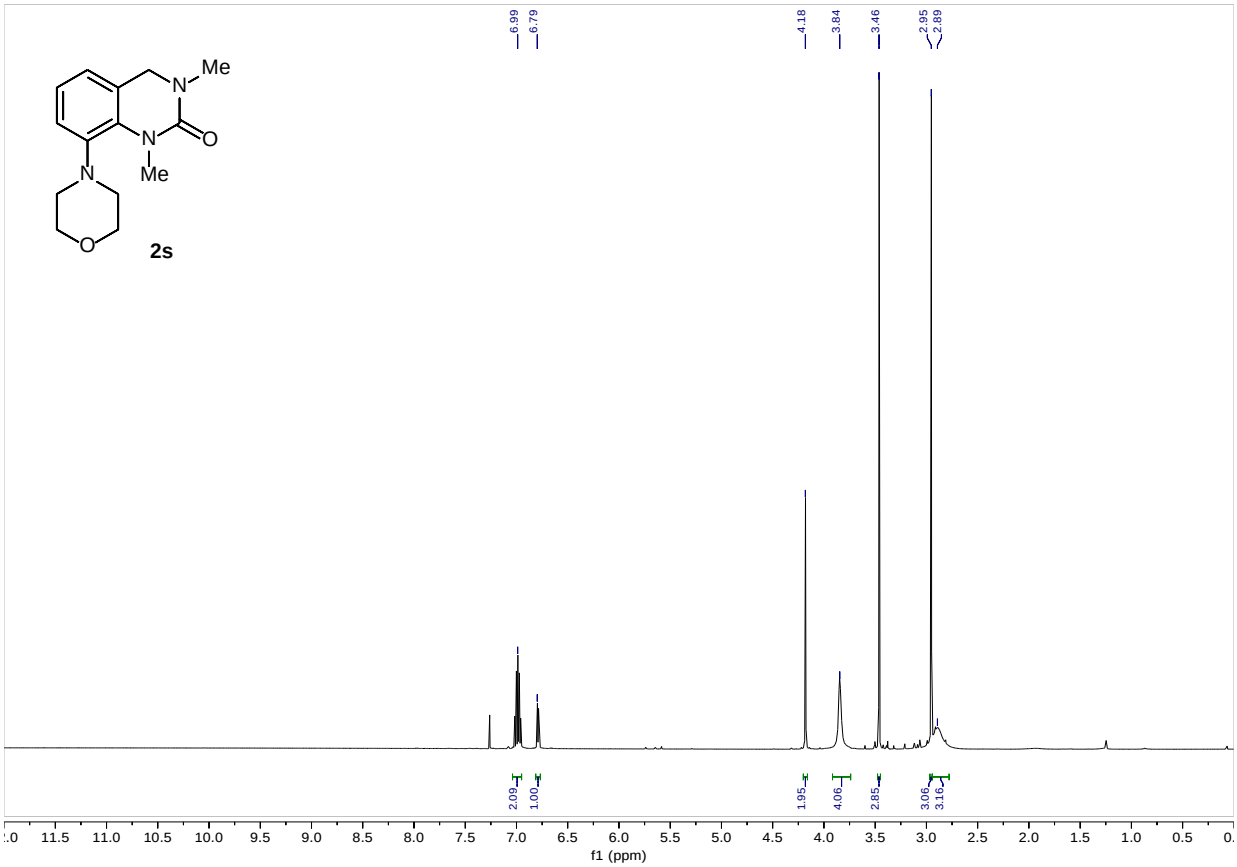

EtOOC
N
O
Me
N
O
7.63
7.63
7.58
7.57
4.38
4.36
4.35
4.33
3.85
3.45
2.92
2.91
2.88
2.87
2.87
2.86
2.85
2.58
2.57
2.57
2.56
2.55
1.39
1.38
1.36
1.01
1.00
2.07
4.21
2.99
6.39
1.97
2.99
f1 (ppm)

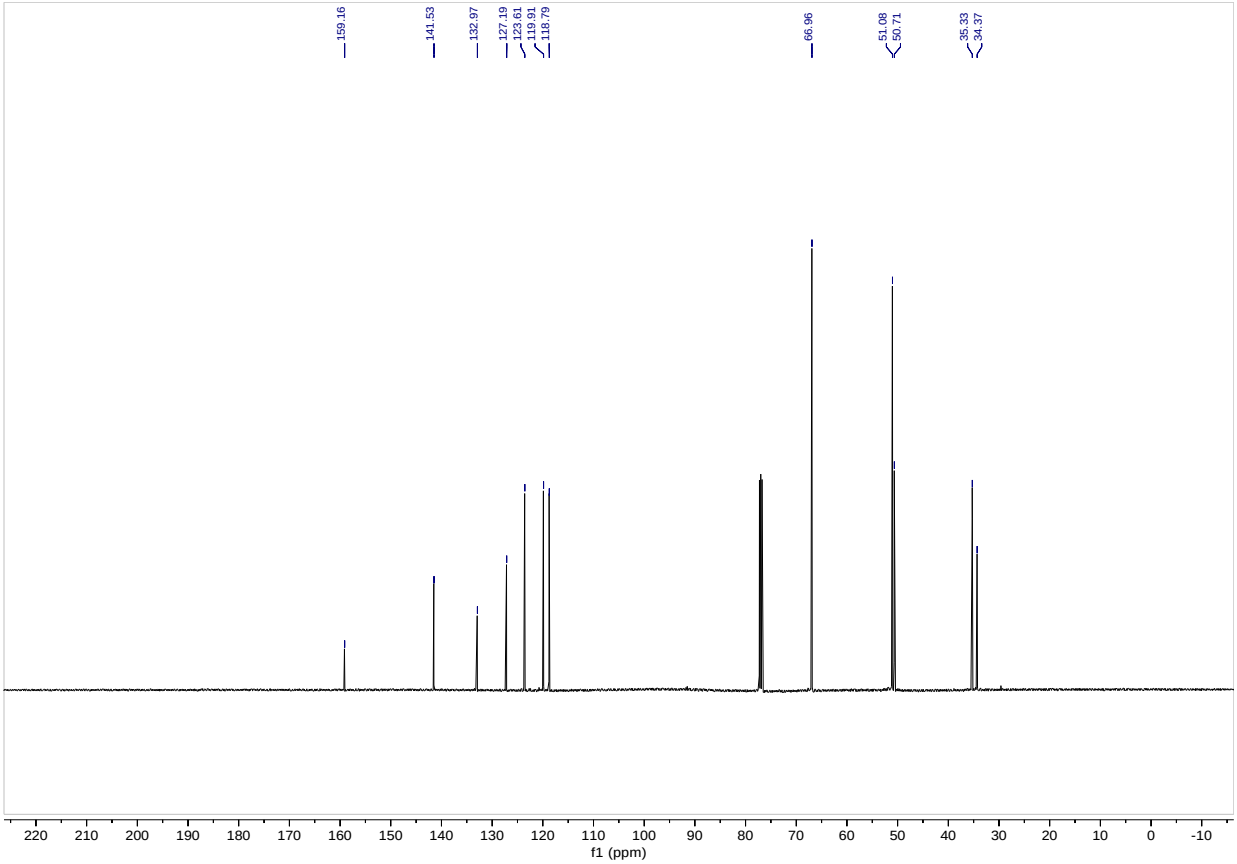
2q

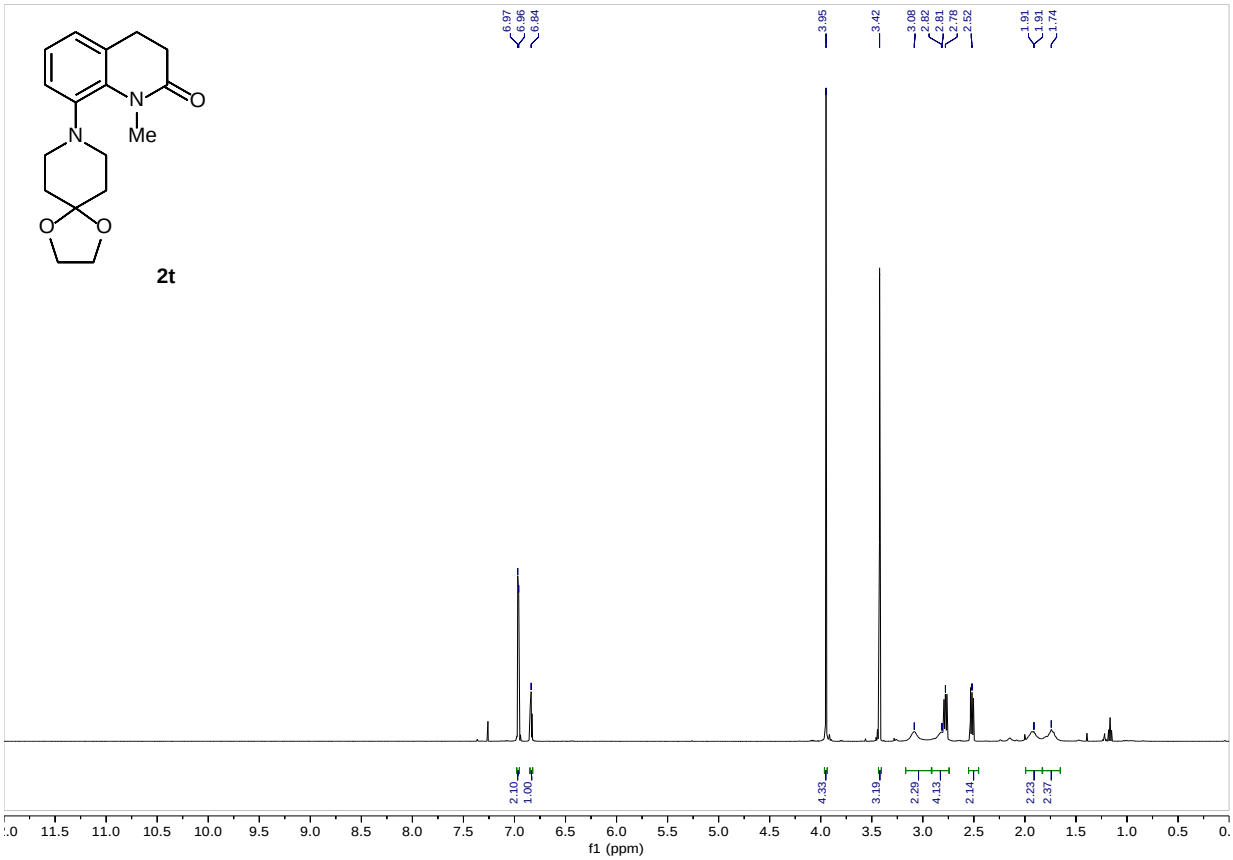

172.57
166.03
142.47
138.10
132.09
126.52
123.18
119.65
66.84
61.03
50.85
33.30
32.40
26.18
14.39
14.37
14.36
f1 (ppm)


Cl
N
N
Me
O
N
O
2r
8.00
3.85
3.44
2.98
2.94
2.64
2.62
1.00
4.10
2.89
5.95
1.97
f1 (ppm)


171.61
144.21
143.08
139.82
137.07
124.30
66.62
50.77
32.53
31.30
22.82
f1 (ppm)


6.99
6.79
4.18
3.84
3.46
2.95
2.89
Me
N
N
O
Me
N
O
2s
2.09
1.00
1.95
4.06
2.85
3.06
3.16
f1 (ppm)


159.16
141.53
132.97
127.19
123.61
119.91
118.79
66.96
51.08
50.71
35.33
34.37
f1 (ppm)


6.97
6.96
6.84
3.95
3.42
3.08
2.82
2.81
2.78
2.52
1.91
1.91
1.74
2.10
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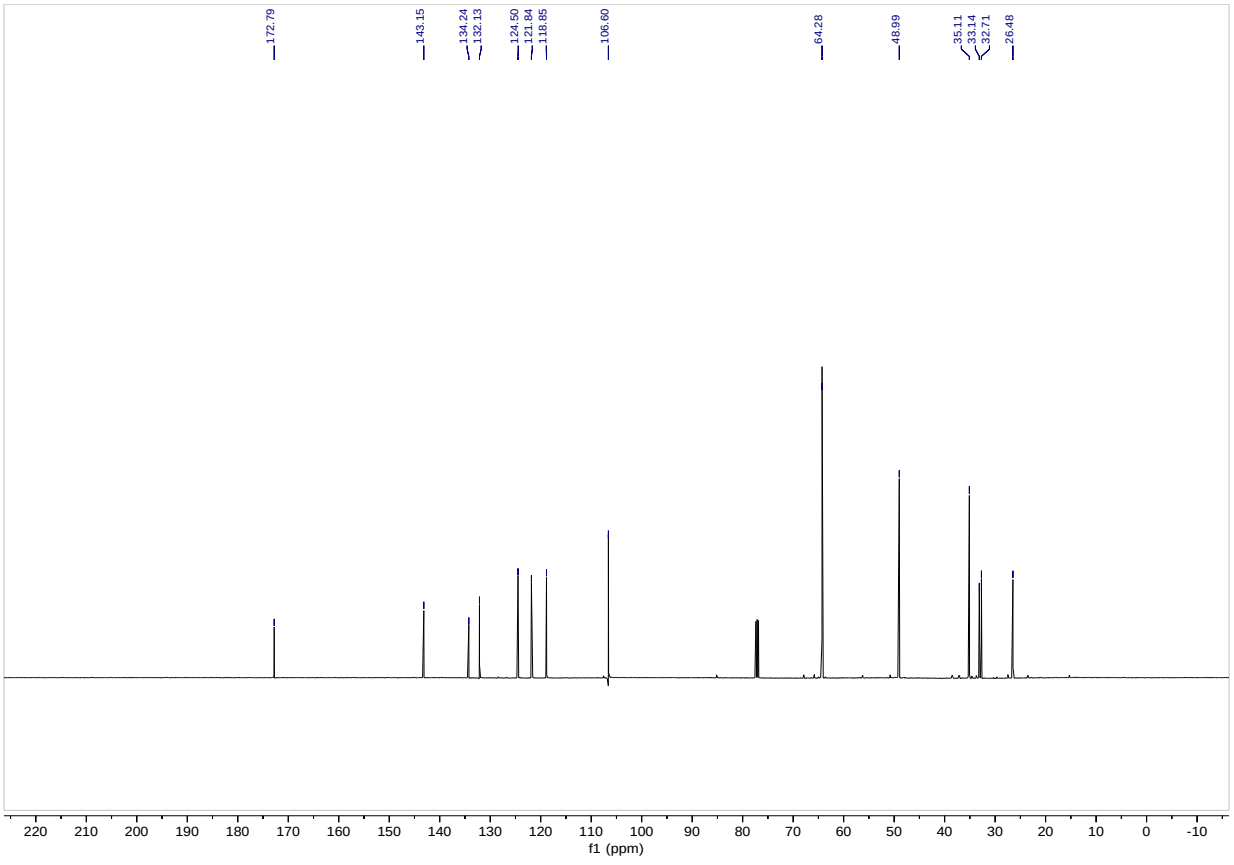
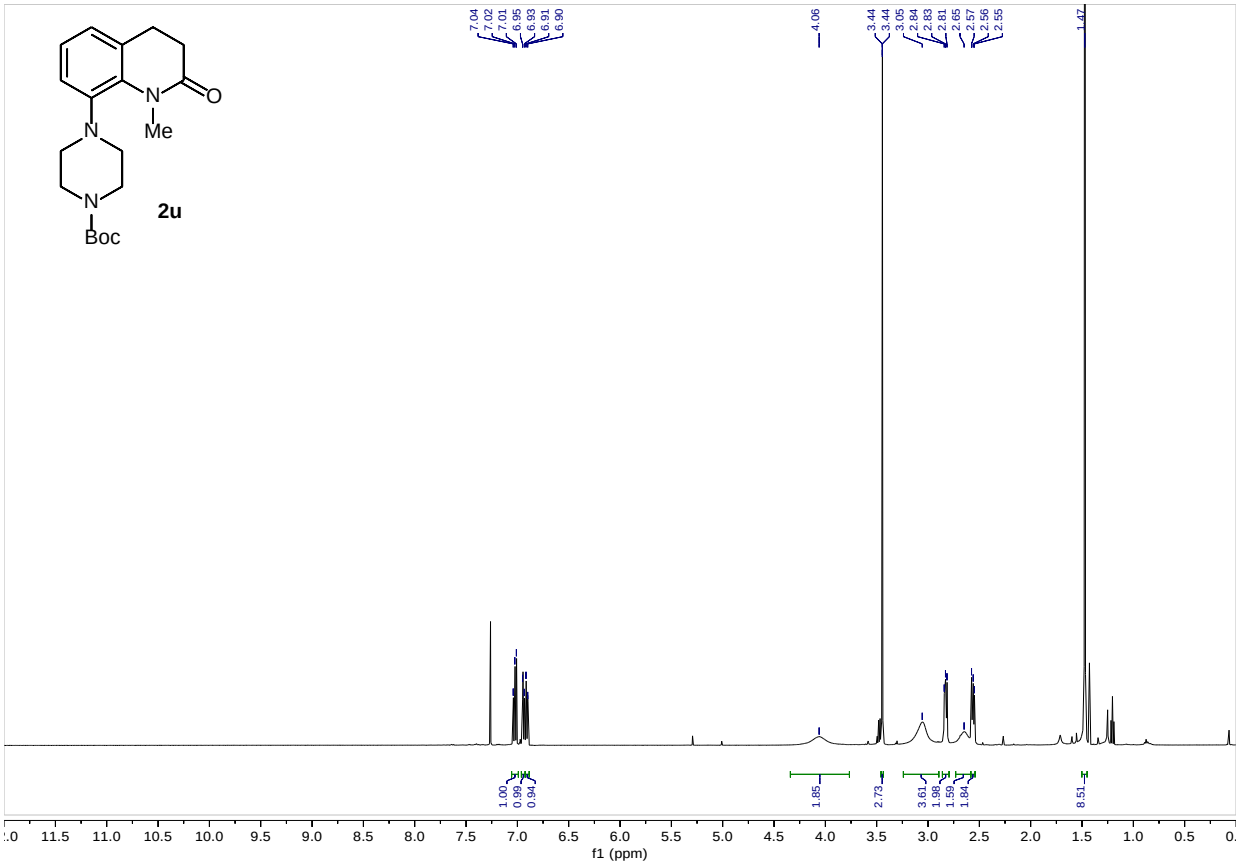
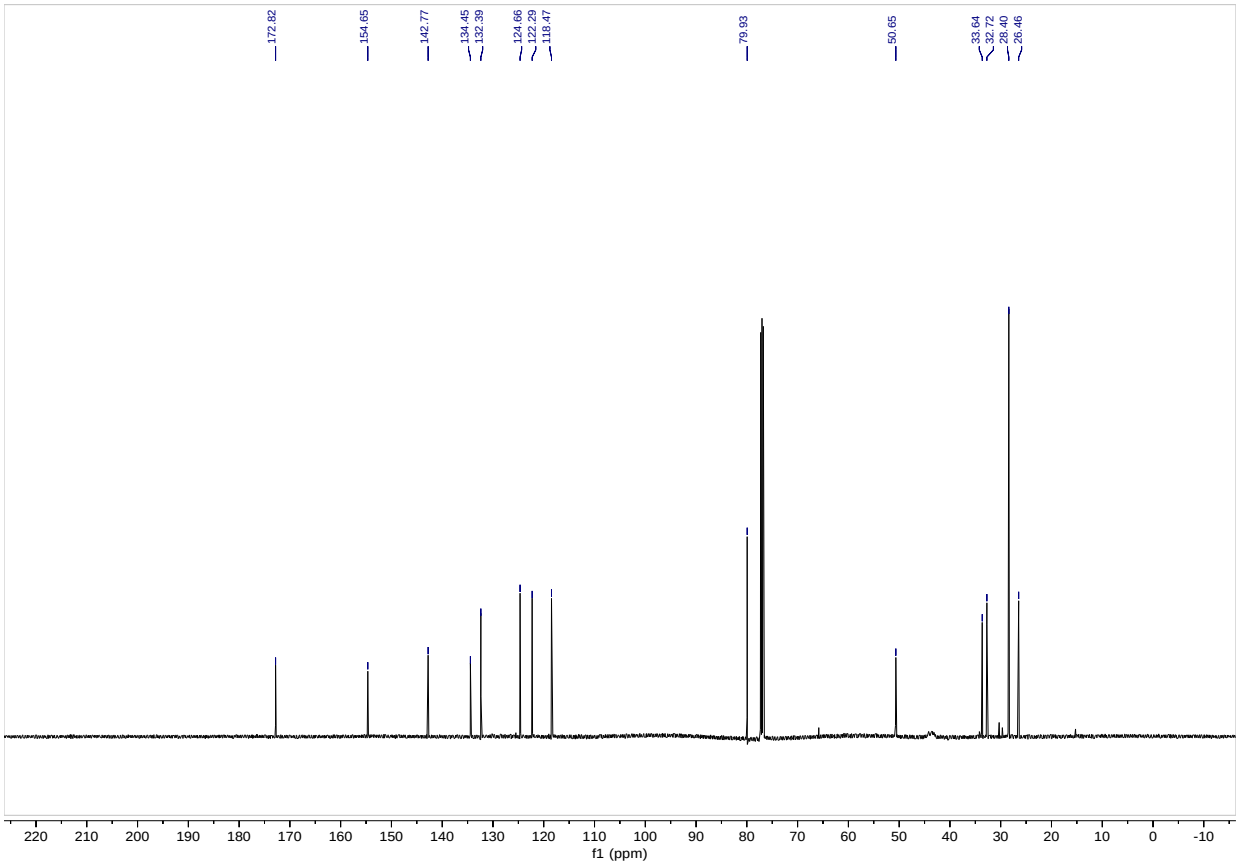
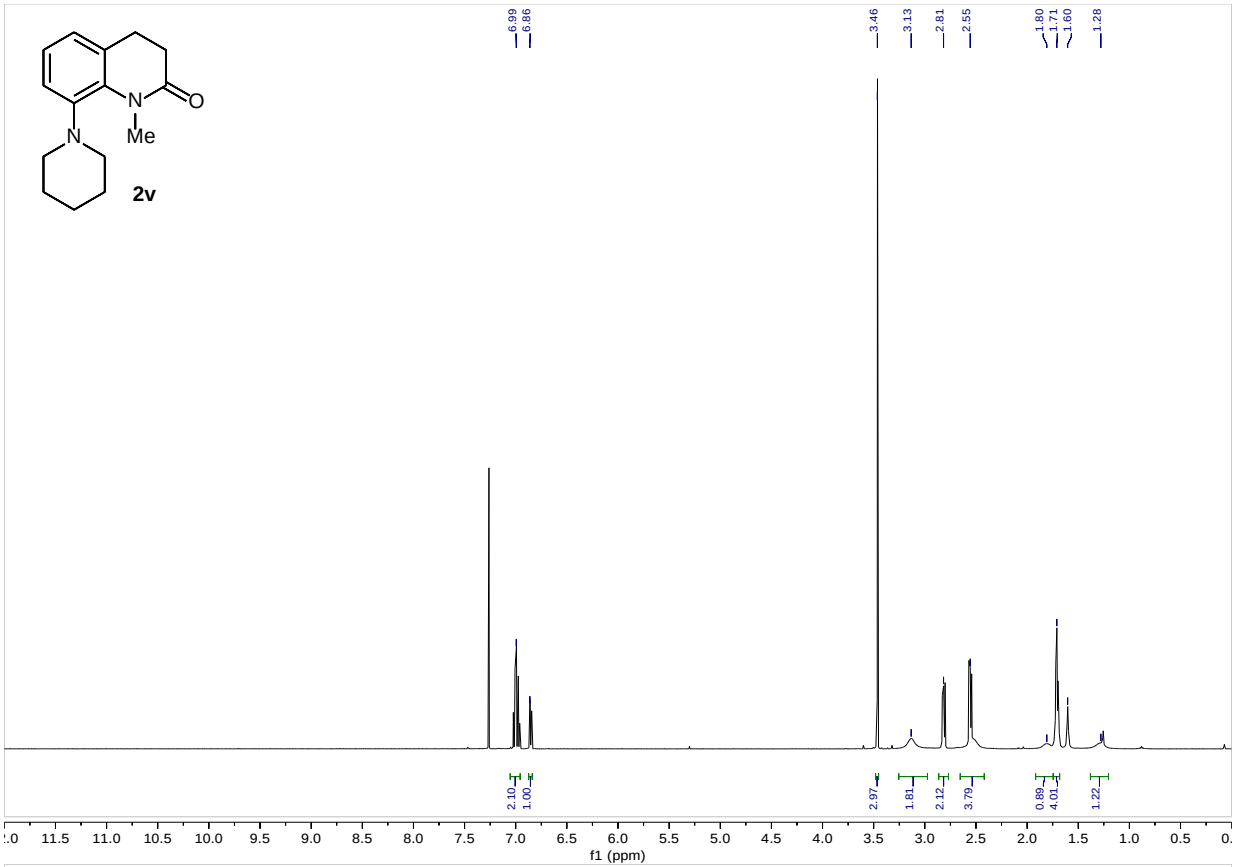
4.33
3.19
2.29
4.13
2.14
2.23
2.37
f1 (ppm)

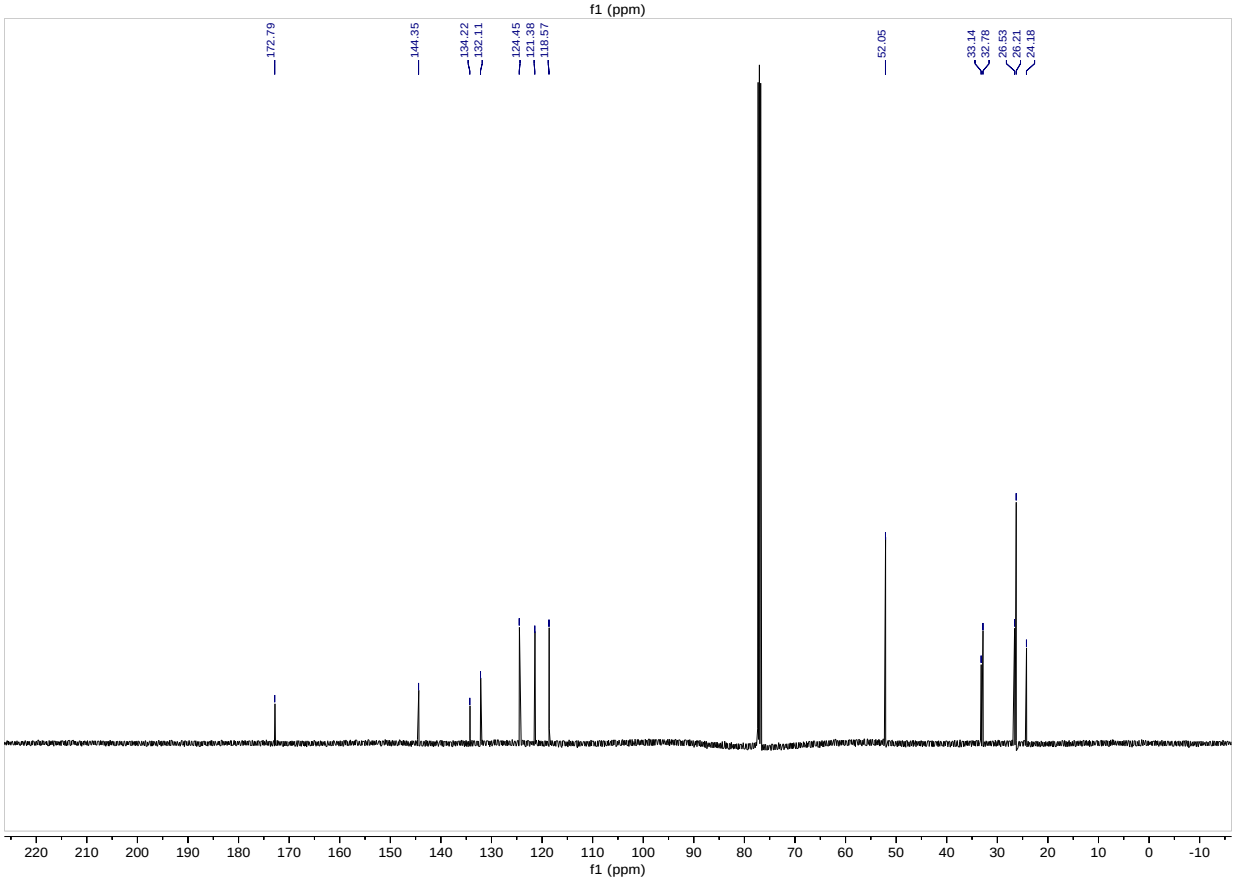
2t

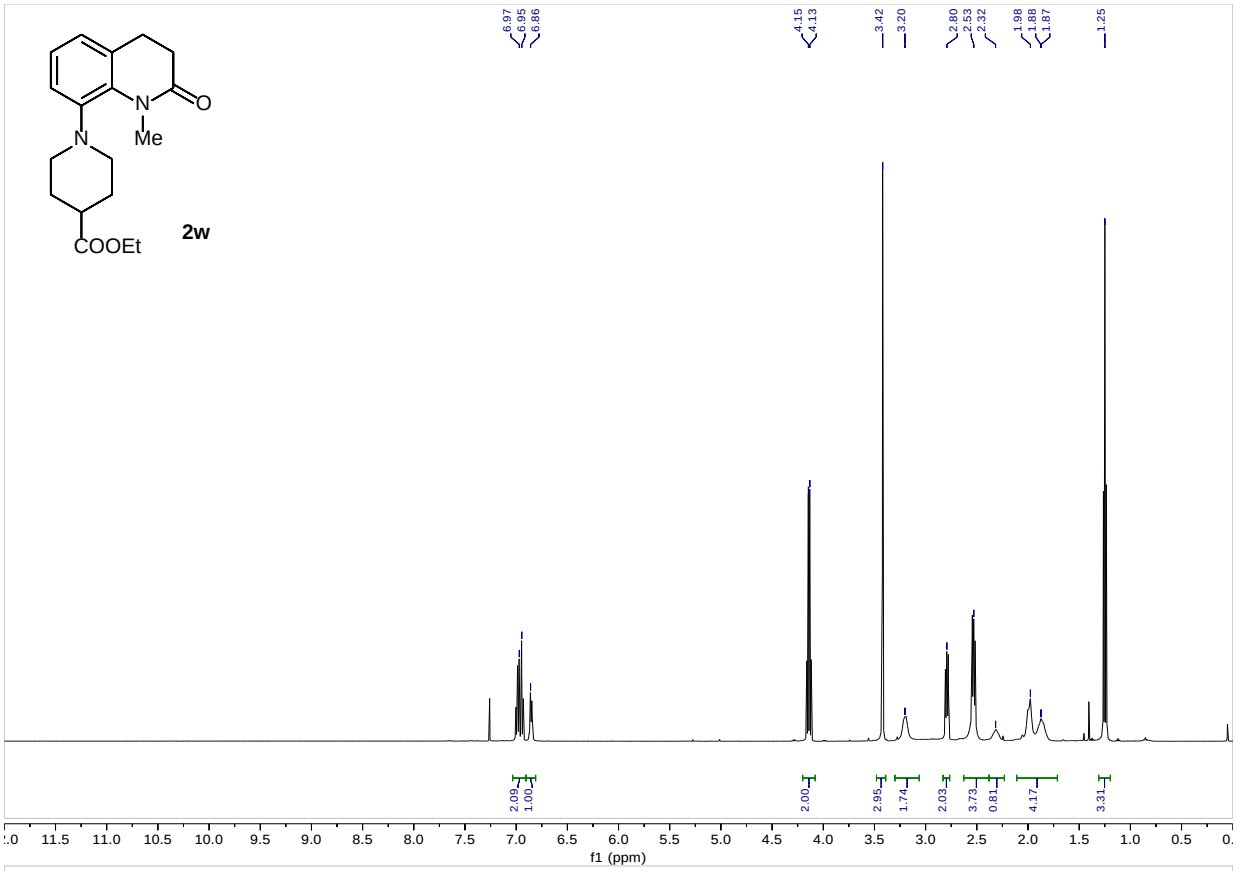

172.79
143.15
134.24
132.13
124.50
121.84
118.85
106.60
64.28
48.99
35.11
33.14
32.71
26.48
f1 (ppm)

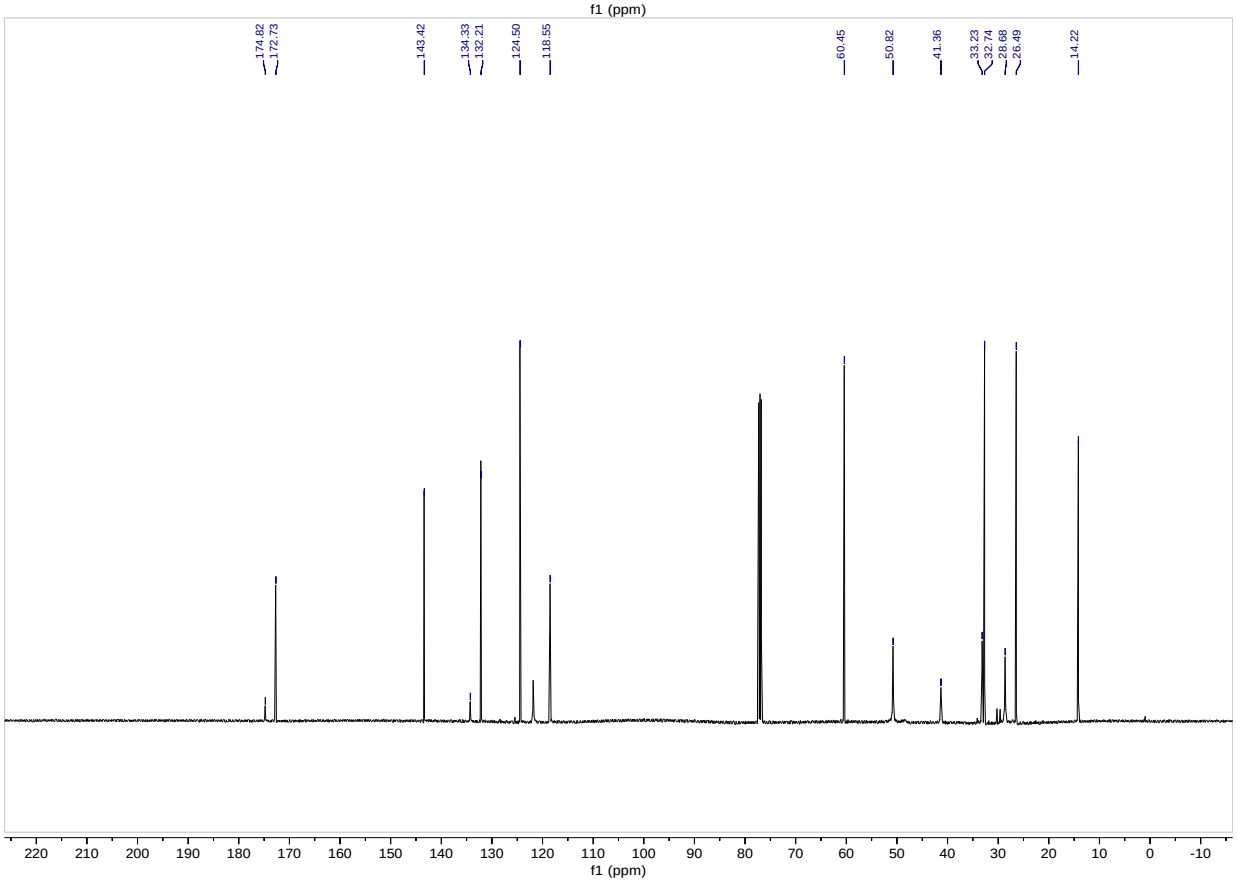

7.04
7.02
7.01
6.95
6.93
6.91
6.90
4.06
3.44
3.44
3.05
2.84
2.83
2.81
2.65
2.57
2.56
2.55
1.47
N
O
Me
N
N
Boc
2u
1.00
0.99
0.94
1.85
2.73
3.61
1.98
1.59
1.84
8.51
f1 (ppm)

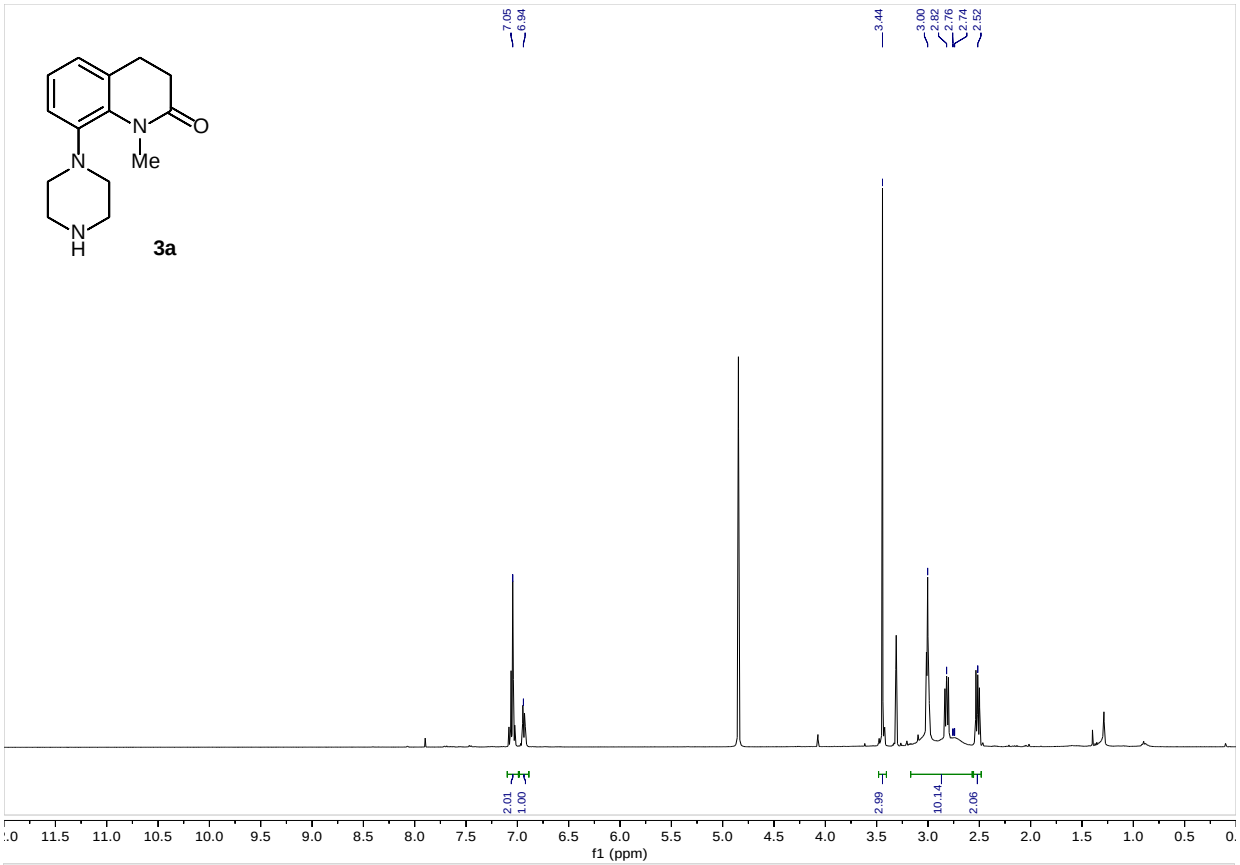

172.82
154.65
142.77
134.45
132.39
124.66
122.29
118.47
79.93
50.65
33.64
32.72
28.40
26.46
f1 (ppm)

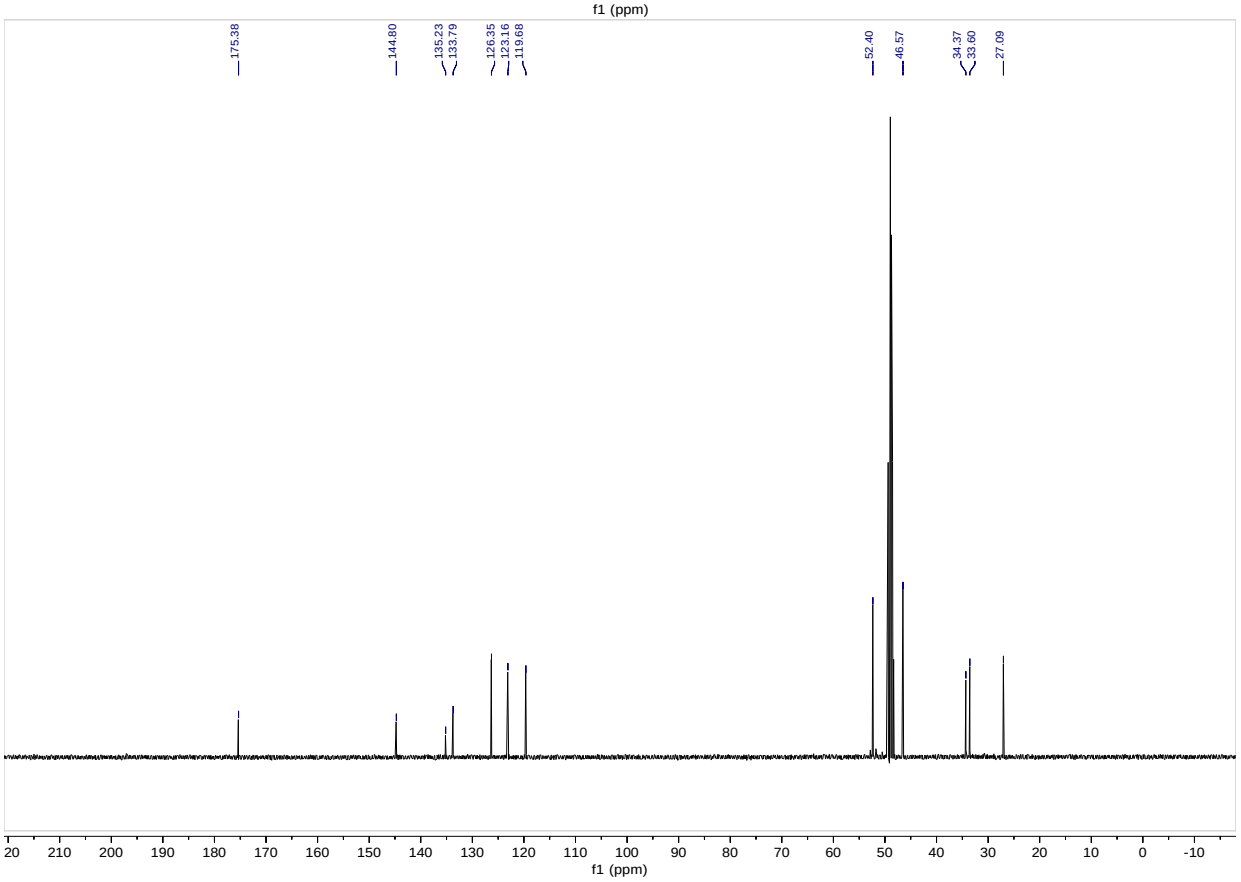

6.99
6.86
3.46
3.13
2.81
2.55
1.80
1.71
1.60
1.28
N
O
N
Me
2v
2.10
1.00
2.97
1.81
2.12
3.79
0.89
4.01
1.22
f1 (ppm)

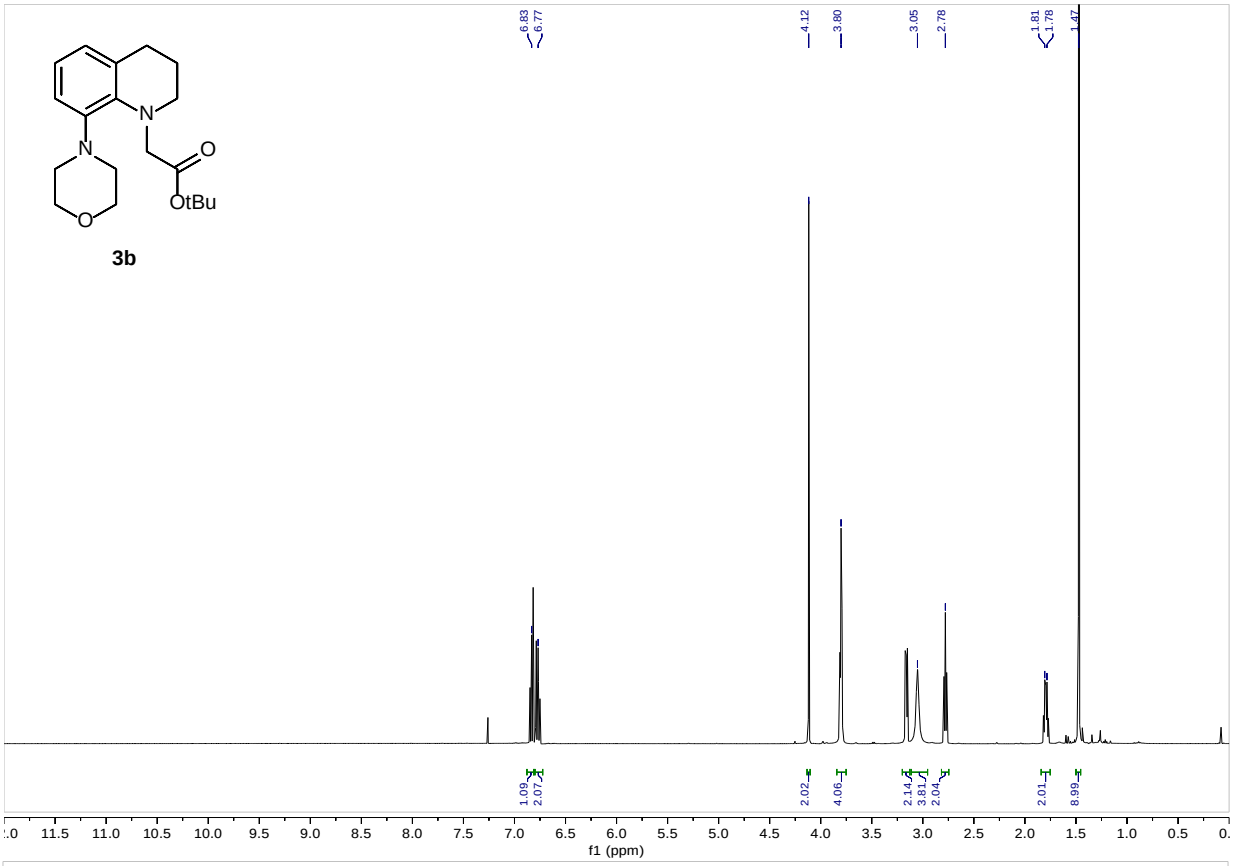

172.79
144.35
134.22
132.11
124.45
121.38
118.57
52.05
33.14
32.78
26.53
26.21
24.18
f1 (ppm)


6.97
6.95
6.86
4.15
4.13
3.42
3.20
2.80
2.53
2.32
1.98
1.88
1.87
1.25
N
O
N
Me
COOEt
2w
2.09
1.00
2.00
2.95
1.74
2.03
3.73
0.81
4.17
3.31
f1 (ppm)

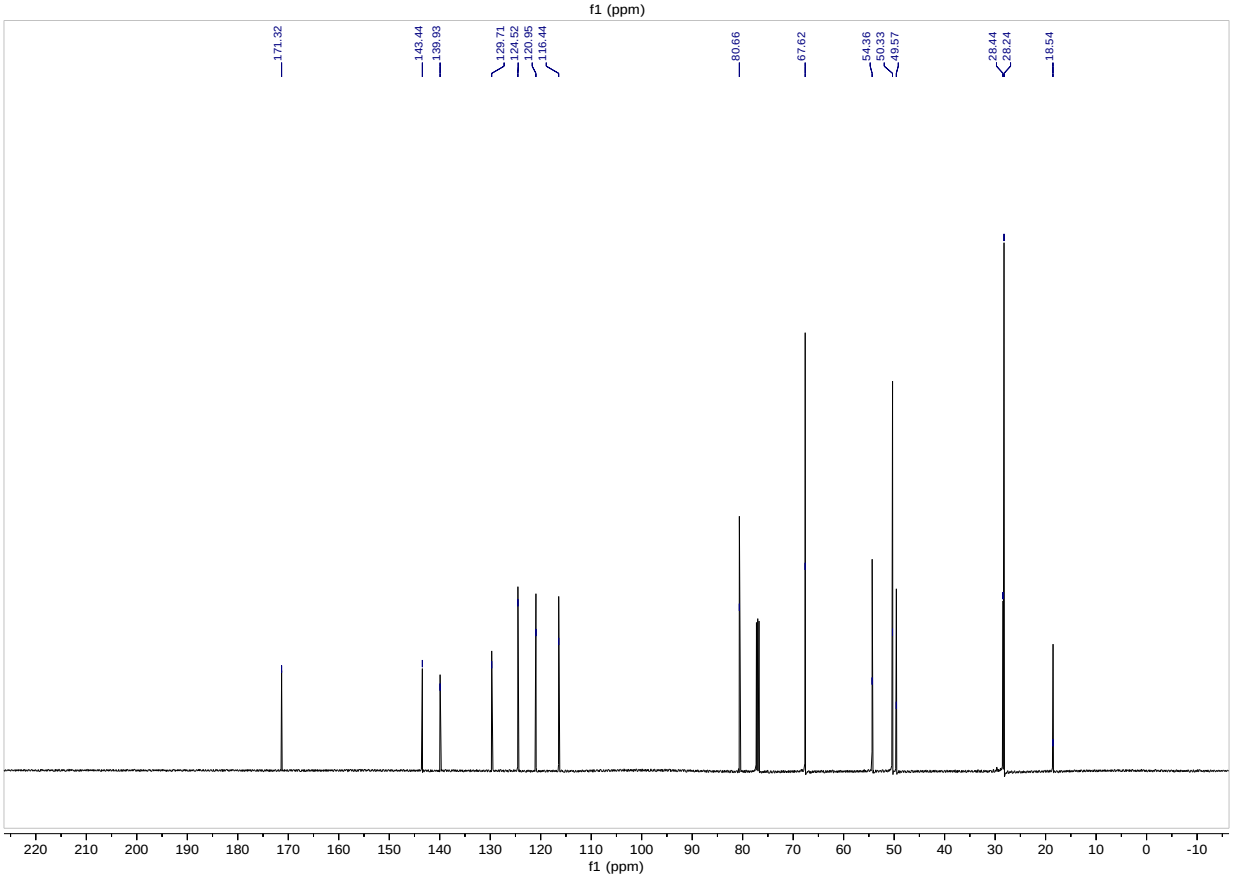

174.82
172.73
143.42
134.33
132.21
124.50
118.55
60.45
50.82
41.36
33.23
32.74
28.68
26.49
14.22
f1 (ppm)


7.05
6.94
3.44
3.00
2.82
2.76
2.74
2.52
N
O
Me
N
N
H
3a
2.01
1.00
2.99
10.14
2.06
f1 (ppm)


175.38
144.80
135.23
133.79
126.35
123.16
119.68
52.40
46.57
34.37
33.60
27.09
f1 (ppm)


6.83
6.77
4.12
3.80
3.05
2.78
1.81
1.78
1.47
1.09
2.07
2.02
4.06
2.14
3.81
2.04
2.01
8.99
f1 (ppm)

3b


171.32
143.44
139.93
129.71
124.52
120.95
116.44
80.66
67.62
54.36
50.33
49.57
28.44
28.24
18.54
f1 (ppm)