Electronic Supplementary Information

A chemoselective hydroxycarbonylation and ^{13}C-labeling of aryl diazonium salts using formic acid as C-1 source

Shuvam Mondal,[‡a] Shantanu Nandi,[‡a] Subhodeep Das,[a] and Ranjan Jana*[a]

[a]Organic and Medicinal Chemistry Division, CSIR-Indian Institute of Chemical Biology.

4 Raja S. C. Mullick Road, Jadavpur, Kolkata-700032, West Bengal, India.
E-mail: rjana@iicb.res.in

[‡]S.M and S.N contributed equally.

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General Information:

All manipulations with air-sensitive reagents were carried out under a dry nitrogen atmosphere. Unless otherwise stated, all commercial reagents were used without additional purification. Solvents were dried using standard methods and distilled before use. TLC was performed on silica gel plates (Merck silica gel 60, f254), and the spots were visualized with UV light (254 and 365 nm). Formic acid puriss AR (98-100%), DCC were purchased from Spectrochem India. $Pd(OAc)_2$, ^{13}C-labelled formic acid (95 wt% in H_2O, 99 atom% ^{13}C) were purchased from Sigma. Commercially available Emplura grade DMF from Merck was used as a solvent for this reaction. ^1H NMR was recorded at 400 MHz (JEOL-JNM-ECZ400S/L1) and 600 MHz (Bruker-Avance 600) frequency and ^{13}C NMR spectra were recorded at 100 MHz (JEOL-JNM-ECZ400S/L1) and 150 MHz (Bruker-Avance) frequency in $CDCl_3$ solvent using TMS as the internal standard. ^{19}F NMR was recorded at 376 MHz frequency (JEOL-JNM-ECZ400S/L1). Chemical shifts were measured in parts per million (ppm) referenced to 0.0 ppm for tetramethylsilane. The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. = broad. Coupling constants, *J* were reported in Hertz unit (Hz). HRMS (m/z) were measured using ESI techniques Q-Tof Micro mass spectrometer respectively. In mass spectrometric studies, ^{13}C atom is denoted by "Ci".

Synthesis of the starting materials:

General procedure (Method A) for the synthesis of the Aryl Diazonium Salt:[1]

Aniline (5 mmol) was taken in a 50 mL round-bottom flask and cooled in an ice bath, and tetrafluoroboric acid solution (48 wt % in H_2O, 1.7 mL) was added at 0 °C. A precipitate was formed which was dissolved in a minimum amount of distilled water. Sodium nitrite (345 mg, 5 mmol) in distilled water (2 mL) was added dropwise to the reaction mixture and allowed to stir for 1 h at 0 °C. A thick precipitate was formed and collected by filtration. Then, it was washed with diethyl ether (10 mL) two times. The residue was recrystallized with acetonitrile/diethyl ether to give the desired aryldiazonium tetrafluoroborate as a crystalline solid.

Preparation of *N,N*-dipropyl-4-benzenesulfonamide diazonium salt:

(Step I): (B) was synthesized from 4-Nitro sulphonyl chloride **(A)** according to the literature report.[2]

(Step II): In a 100 mL R.B, **(B)** (1 equiv,5 mmol), K_2CO_3 (3 equiv,15 mmol), MeCN (15 mL) and *n*-propyl iodide were taken and the mixture was refluxed for 12 h. Thereafter, the reaction mixture was allowed to cool at room temperature and filtered on a celite pad and washed with EtOAc. The filtrate was concentrated on vacuum and the desired product **(C)** was purified by column chromatography on silica gel (eluting with Ethyl Acetate/Hexane). (Yield 90%)

(Step III): In a 100 mL R.B, **(C)** (1 equiv, 4 equiv), iron powder (3 equiv), NH_4Cl (5 equiv) were taken. After adding 40 mL of MeOH/H_2O (1:1), it was refluxed for 3 h. Then, the reaction mixture was allowed to cool at room temperature and filtered on a celite pad, and washed with EtOAc. The filtrate was concentrated in vacuum and work up with EtOAc-Water. Then, the desired product **(D)** was isolateds by column chromatography on silica gel (eluting with Ethyl Acetate/Hexane). (Yield 75%)

(Step IV): Aniline **(D)** (2 mmol) was taken in a 50 mL round bottom flask and cooled in an ice bath, and tetrafluoroboric acid solution (48 wt % in H_2O, 0.7 mL) was added at 0 °C. To the precipitate, 1 mL of distilled water was added. Then, Sodium nitrite (138 mg, 2 mmol) in distilled water (2 mL) was added dropwise to the reaction mixture and allowed to stir for 1 h at 0 °C. A thick precipitate was formed

and collected by filtration. The precipitate was washed with diethyl ether (6 mL) two times. The resulting precipitate was recrystallized with acetonitrile/diethyl ether to give the desired aryldiazonium tetrafluoroborate as a yellowish solid.(Yield 60%)

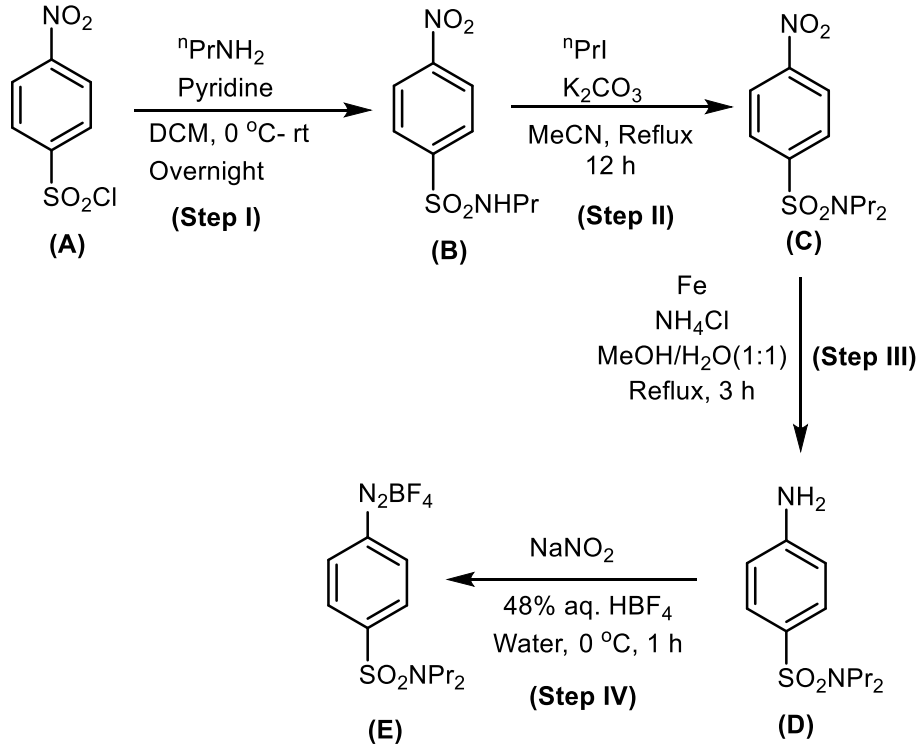


Figure 1: *N,N*-dipropyl-4-benzenesulfonamide diazonium salt Preparation.

General procedure (Method B) for hydroxycarbonylation reaction of aryl diazonium salt (0.5 mmol scale):

To an oven-dried 15 mL pressure tube equipped with a Teflon cap and magnetic stir bar, freshly prepared aryldiazonium salt (0.5 mmol, 1 equiv), $Pd(OAc)_2$ (3 mol%, 3.4 mg), DCC (237 mg, 1.15 mmol, 2.3 equiv), and DMF (1.5 mL) were added. After, purging with a little N_2 gas, HCOOH acid (57 µL, 1.5 mmol, 3 equiv) was added to it via a micro syringe and sealed the cap immediately. After 2 h of stirring, the reaction mixture was filtered and concentrated under a reduced pressure. Next, a work-up with ethyl acetate-water (or DCM-water) was carried out and the crude product was purified by column chromatography on silica gel (eluting with Ethyl Acetate/Hexane) to isolate the desired product.

General procedure for ^{13}C-labelled hydroxycarbonylation reaction of aryl diazonium salt:

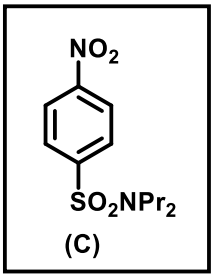
Method B was followed to perform the synthesis.

General procedure for hydroxycarbonylation (Method C) reaction of aryl diazonium salt (5 mmol scale):

To an oven-dried 250 mL two-neck equipped with a magnetic stir bar and balloon (empty, no gas) set-up with an adapter, freshly prepared aryldiazonium salt (5 mmol, 1 equiv), $Pd(OAc)_2$ (3 mol%, 34 mg), and DMF (8 mL) were added. After purging the reaction vessel with nitrogen gas, the system was sealed with a septum immediately. Formic acid (HCOOH, 570 µL, 15 mmol, 3 equiv.) was added via syringe. Subsequently, a solution of DCC (2.37 g, 11.5 mmol, 2.3 equiv.) in 7 mL of DMF was slowly

added dropwise via a syringe. The reaction mixture was stirred for 2 hours at room temperature. It is to be noted that in situ CO gas generation using DCC and HCOOH is an exothermic process. So, a water bath (room temperature or lower) was used to maintain the ambient temperature.

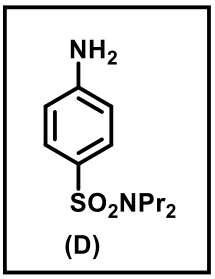
Spectral data



4-nitro-*N,N*-dipropylbenzenesulfonamide (C).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 – 8.32 (m, 2H), 7.99 – 7.97 (m, 2H), 3.14 – 3.10 (m, 4H), 1.60 – 1.51 (m, 4H), 0.87 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 146.4, 128.3, 124.4, 50.1, 22.0, 11.2.

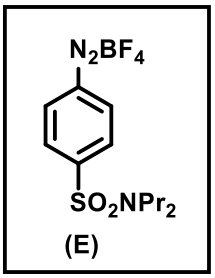


4-amino-*N,N*-dipropylbenzenesulfonamide (D):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.58 (m, 2H), 6.77 – 6.73 (m, 2H), 3.05 – 3.01 (m, 4H), 1.59 – 1.50 (m, 4H), 0.86 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 130.2, 129.3, 128.4, 118.6, 115.4, 50.2, 22.2, 11.4.

HRMS (ESI, m/z) calcd. for $C_{12}H_{21}N_2O_2S$ $[M+H]^+$: 257.1324; found: 257.1329.

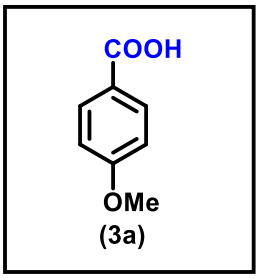


***N,N*-dipropyl-4-benzenesulfonamide diazonium salt (E):**

^{1}H NMR (400 MHz, Acetone-d_6) δ 9.07 – 9.03 (m, 2H), 8.49 – 8.46 (m, 2H), 3.27 – 3.23 (m, 4H), 1.63 –1.54 (m, 4H), 0.85 (t, *J* = 7.4 Hz, 6H).

^{19}F NMR (376 MHz, Acetone-d_6) δ -150.72, -150.77.

^{13}C NMR (100 MHz, Acetone-d_6) δ 152.2, 135.1, 130.3, 120.2, 50.8, 22.7, 11.3.

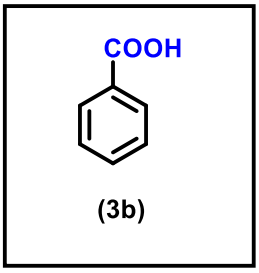


(3a)

4-methoxybenzoic acid (3a): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (62 mg, 81%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.60 (s, 1H), 7.91 – 7.87 (m, 2H), 7.03 – 6.99 (m, 2H), 3.82 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.0, 162.8, 131.3, 123.0, 113.8, 55.4.

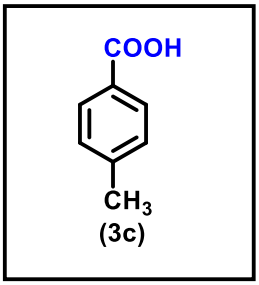


(3b)

Benzoic acid (3b): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (40 mg, 66%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.94 (s, 1H), 7.97 – 7.94 (m, 2H), 7.63 – 7.59 (m, 1H), 7.51 – 7.47 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.4, 132.9, 130.8, 129.3, 128.6.

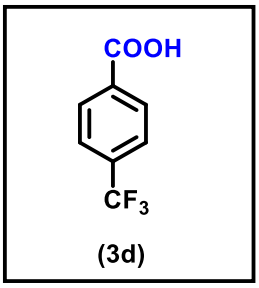


(3c)

4-methylbenzoic acid (3c): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (48 mg, 70%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.77 (s, 1H), 7.84 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 2.34 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.4, 143.1, 129.4, 129.2, 128.1, 21.2.



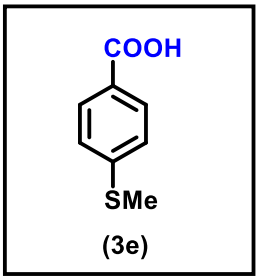
(3d)

4-(trifluoromethyl)benzoic acid (3d): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (63 mg, 66%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.46 (s, 1H), 8.12 (d, J = 8.1 Hz, 2H), 7.83 (d, J = 7.8 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.3, 134.7, 132.6 (q, J = 32.0 Hz), 130.1, 125.6, 123.9 (q, J = 271.2 Hz).

^{19}F NMR (376 MHz, DMSO-d_6) δ -61.46.

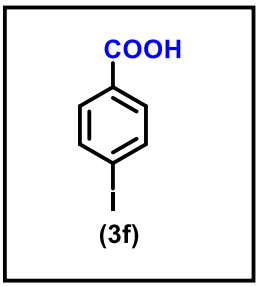


(3e)

4-(methylthio)benzoic acid (3e): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (67 mg, 80%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.82 (s, 1H), 7.86 – 7.83 (m, 2H), 7.35 – 7.32 (m, 2H), 2.52 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.0, 144.8, 129.7, 126.7, 124.9, 13.9.

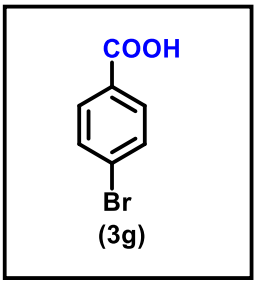


(3f)

4-iodobenzoic acid (3f): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (66 mg, 50%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.12 (s, 1H), 7.86 (d, J = 6.8 Hz, 2H), 7.69 (d, J = 8.0 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.9, 137.6, 131.1, 130.3, 101.2.

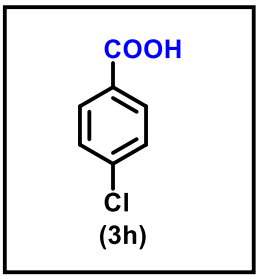


(3g)

4-bromobenzoic acid (3g): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (66 mg, 66%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 – 7.84 (m, 2H), 7.72– 7.69 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.7, 131.8, 131.4, 130.1, 127.0.

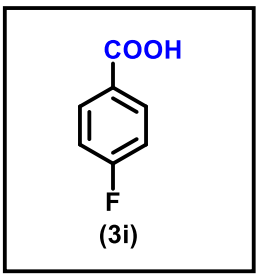


(3h)

4-chlorobenzoic acid (3h): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (55 mg, 70%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.15 (s, 1H), 7.93 (d, J = 8.5 Hz, 2H), 7.52 (d, J = 8.4 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.5, 137.9, 131.2, 129.7, 128.7.



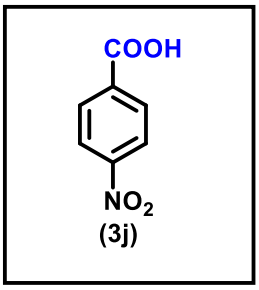
(3i)

4-fluorobenzoic acid (3i): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (51 mg, 72%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.03 – 7.98 (m, 2H), 7.35 – 7.30 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.4, 164.9 (d, J = 250.5 Hz), 132.1 (d, J = 9.5 Hz), 127.4 (d, J = 2.6 Hz), 115.7 (d, J = 22.0 Hz).

^{19}F NMR (376 MHz, DMSO-d_6) δ -106.82.

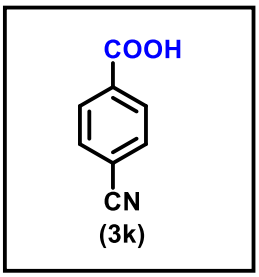


(3j)

4-nitrobenzoic acid (3j): Column chromatography (SiO_2, eluting with 1:1 hexane/ethyl acetate) afforded the desired product as a white solid (57 mg, 68%).

^{1}H NMR (400 MHz, Acetone-d_6) δ 8.38 – 8.34 (m, 2H), 8.29 – 8.26 (m, 2H).

^{13}C NMR (100 MHz, Acetone-d_6) δ 166.0, 151.6, 136.9, 131.8, 124.5.

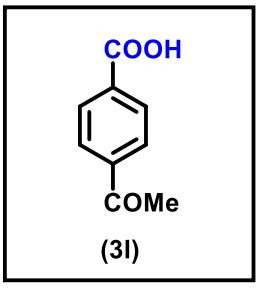


(3k)

4-cyanobenzoic acid (3k): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (39.7 mg, 54%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.56 (s, 1H), 8.09 – 8.07 (m, 2H), 7.99 – 7.97 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.0, 134.8, 132.7, 129.9, 118.2, 115.1.

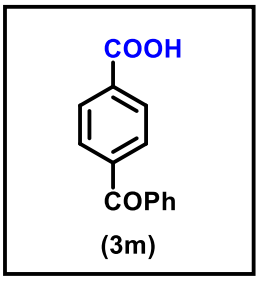


(3l)

4-acetylbenzoic acid (3l): Column chromatography (SiO_2, eluting with 3:2 hexane/ethyl acetate) afforded the desired product as a white solid (60 mg, 73%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.31 (s, 1H), 8.04 (s, 4H), 2.62 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 197.8, 166.7, 139.9, 134.5, 129.6, 128.3, 27.0.

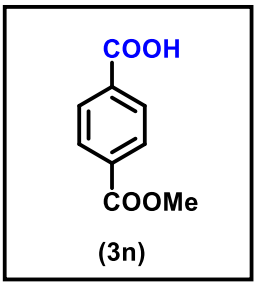


(3m)

4-benzoylbenzoic acid (3m): Column chromatography (SiO_2, eluting with 3:2 hexane/ethyl acetate) afforded the desired product as a white solid (80 mg, 71%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.33 (s, 1H), 8.11 – 8.08 (m, 2H), 7.83 – 7.80 (m, 2H), 7.77 – 7.74 (m, 2H), 7.72 – 7.67 (m, 1H), 7.57 (t, *J* = 7.6 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 195.4, 166.7, 140.6, 136.5, 134.0, 133.1, 129.8, 129.7, 129.4, 128.7.

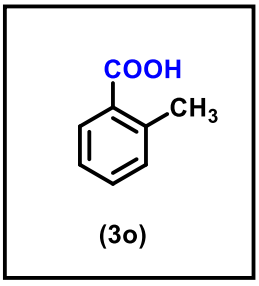


(3n)

4-(methoxycarbonyl)benzoic acid (3n): Column chromatography (SiO_2, eluting with 3:2 hexane/ethyl acetate) afforded the desired product as a white solid (55 mg, 61%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.34 (s, 1H), 8.06 (s, 4H), 3.88 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.6, 165.6, 134.8, 133.2, 129.6, 129.3, 52.5.

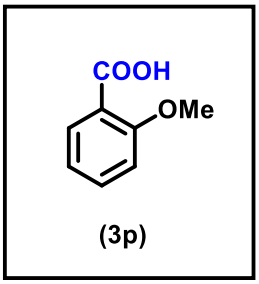


(3o)

2-methylbenzoic acid (3o): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (42 mg, 61%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.46 (td, *J* = 7.5, 1.5 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 2H), 2.68 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 141.5, 133.1, 132.1, 131.7, 128.5, 126.0, 22.3.

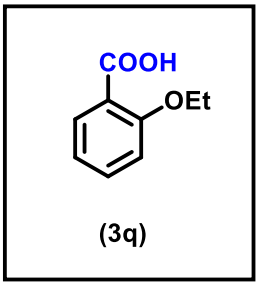


(3p)

2-methoxylbenzoic acid (3p): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (49 mg, 65%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.56 (s, 1H), 7.63 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.11 (d, *J* = 8.3 Hz, 1H), 6.99 (td, *J* = 7.5, 1.0 Hz, 1H), 3.81 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.3, 158.1, 133.0, 130.6, 121.3, 120.0, 112.4, 55.7.

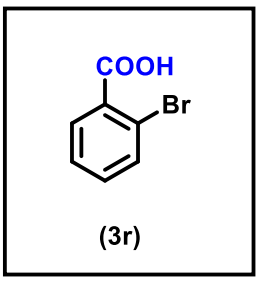


(3q)

2-ethoxylbenzoic acid (3q): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a colourless liquid (52 mg, 63%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.49 (s, 1H), 7.61 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.46 (ddd, *J* = 8.4, 7.4, 1.8 Hz, 1H), 7.09 (d, *J* = 8.1 Hz, 1H), 6.97 (td, *J* = 7.5, 0.9 Hz, 1H), 4.08 (q, *J* = 7.0 Hz, 2H), 1.32 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.5, 157.2, 132.8, 130.5, 121.8, 120.0, 113.5, 64.0, 14.6.

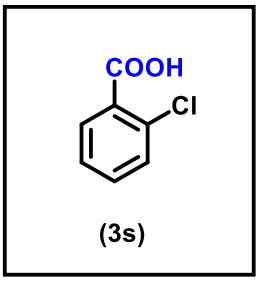


(3r)

2-bromobenzoic acid (3r): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (30 mg, 30%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.38 (s, 1H), 7.75 – 7.70 (m, 2H), 7.49 – 7.41 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.4, 133.8, 132.5, 130.6, 127.7, 119.9.

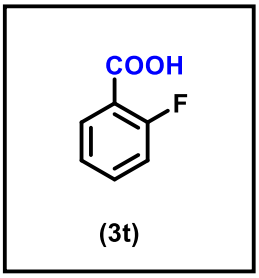


(3s)

2-chlorobenzoic acid (3s): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (33 mg, 42%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.02 (m, 1H), 7.52 – 7.46 (m, 2H), 7.38 – 7.34 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 134.9, 133.7, 132.6, 131.7, 128.6, 126.9.



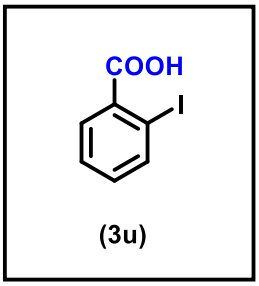
(3t)

2-fluorobenzoic acid (3t): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (35 mg, 50%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.23 (s, 1H), 7.86 (td, J = 7.7, 2.0 Hz, 1H), 7.65 – 7.60 (m, 1H), 7.32 – 7.27 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 165.1 (d, J = 2.6 Hz), 161.1 (d, J = 256.7 Hz), 134.7 (d, J = 9.0 Hz), 131.9, 124.5 (d, J = 3.6 Hz), 119.3 (d, J = 10.3 Hz), 116.9 (d, J = 22.1 Hz).

^{19}F NMR (376 MHz, DMSO-d_6) δ 110.53.

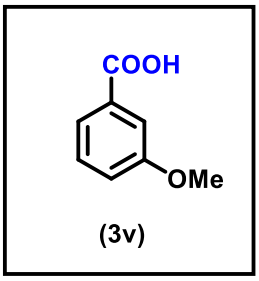


(3u)

2-iodobenzoic acid (3u): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (11 mg, 9%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.98 (d, J = 7.9 Hz, 1H), 7.70 (d, J = 7.7 Hz, 1H), 7.47 (t, J = 7.0 Hz, 1H), 7.25 – 7.21 (m, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 168.2, 140.6, 137.0, 132.5, 130.1, 128.2, 94.1.

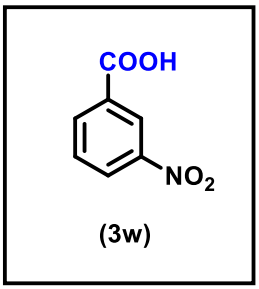


(3v)

3-methoxybenzoic acid (3v): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (49 mg, 64%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.98 (s, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.18 (dd, *J* = 8.1, 2.7 Hz, 1H), 3.80 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.1, 159.2, 132.2, 129.7, 121.6, 118.9, 113.9, 55.2.

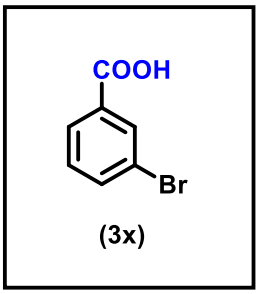


(3w)

3-nitrobenzoic acid (3w): Column chromatography (SiO_2, eluting with 1:1 hexane/ethyl acetate) afforded the desired product as a white solid (50 mg, 60%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.69 (s, 1H), 8.61 – 8.60 (m, 1H), 8.46 (dd, *J* = 8.2, 2.4 Hz, 1H), 8.34 (d, *J* = 7.7 Hz, 1H), 7.81 (t, *J* = 8.0 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 165.5, 147.9, 135.4, 132.5, 130.6, 127.3, 123.7.

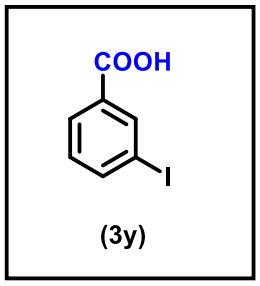


(3x)

3-bromobenzoic acid (3x): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (63 mg, 63%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.32 (s, 1H), 8.04 (t, *J* = 1.8 Hz, 1H), 7.93 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.84 – 7.82 (m, 1H), 7.48 (t, *J* = 7.9 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.0, 135.6, 133.1, 131.7, 130.9, 128.3, 121.7.

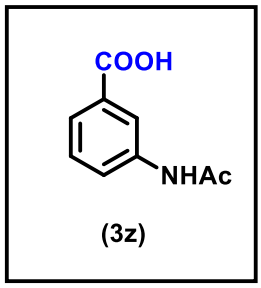


(3y)

3-iodobenzoic acid (3y): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (71 mg, 57%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.24 (s, 1H), 8.23 (t, *J* = 2.0 Hz, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.94 (d, *J* = 7.7 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 165.9, 141.3, 137.6, 132.9, 130.8, 128.6, 94.7.

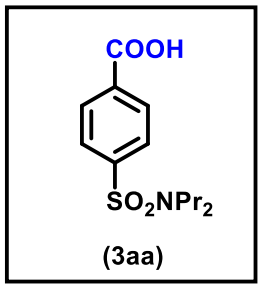


(3z)

3-acetamidobenzoic acid (3z): Column chromatography (SiO_2, eluting with 5:1 hexane/ethyl acetate) afforded the desired product as a white solid (54 mg, 60%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.89 (s, 1H), 10.10 (s, 1H), 8.20 (t, *J* = 1.9 Hz, 1H), 7.81 – 7.79 (m, 1H), 7.60 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.40 (t, *J* = 7.9 Hz, 1H), 2.05 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 168.5, 167.2, 139.5, 131.2, 128.9, 123.8, 123.0, 119.7, 24.0.

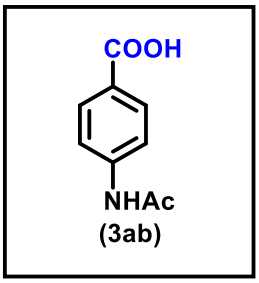


(3aa)

4-(*N,N*-dipropylsulfamoyl)benzoic acid (3aa): Column chromatography (SiO_2, eluting with 3:2 hexane/ethyl acetate) afforded the desired product as a white solid (87 mg, 61%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.49 (s, 1H), 8.13 – 8.11 (m, 2H), 7.92 – 7.89 (m, 2H), 3.07 – 3.03 (m, 4H), 1.51 – 1.42 (m, 4H), 0.80 (t, *J* = 7.4 Hz, 6H).

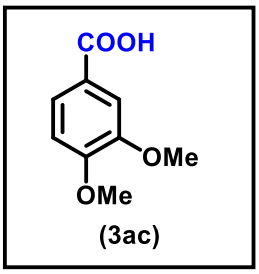
^{13}C NMR (100 MHz, DMSO-d_6) δ 166.2, 143.2, 134.3, 130.2, 127.0, 49.6, 21.6, 10.9.



4-acetamidobenzoic acid (3ab): Column chromatography (SiO_2, eluting with 2% MeOH in DCM) afforded the desired product as a white solid (77 mg, 86%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.66 (s, 1H), 10.23 (s, 1H), 7.88 – 7.85 (m, 2H), 7.70 – 7.66 (m, 2H), 2.08 (s, 3H).

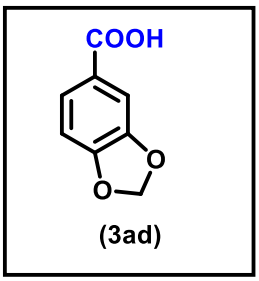
^{13}C NMR (100 MHz, DMSO-d_6) δ 168.9, 166.9, 143.3, 130.4, 124.9, 118.2, 24.2.



3,4-dimethoxybenzoic acid (3ac): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (71 mg, 78%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.65 (s, 1H), 7.56 (dd, J = 8.5, 2.0 Hz, 1H), 7.44 (d, J = 2.0 Hz, 1H), 7.04 (d, J = 8.4 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H).

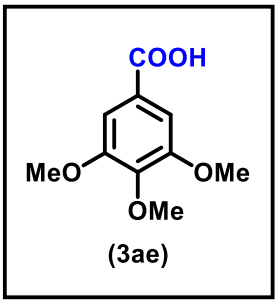
^{13}C NMR (100 MHz, DMSO-d_6) δ 167.1, 152.6, 148.3, 123.2, 123.0, 111.9, 111.0, 55.6, 55.4.



benzo[d][1,3]dioxole-5-carboxylic acid (3ad): Column chromatography (SiO_2, eluting with 3:2 hexane/ethyl acetate) afforded the desired product as a white solid (66 mg, 79%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.74 (s, 1H), 7.54 (dd, J = 8.1, 1.6 Hz, 1H), 7.36 (d, J = 1.6 Hz, 1H), 6.99 (d, J = 8.1 Hz, 1H), 6.11 (s, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.6, 151.1, 147.5, 125.0, 124.7, 108.8, 108.1, 101.9.

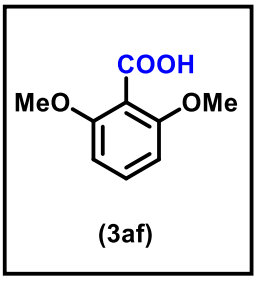


(3ae)

3,4,5-trimethoxybenzoic acid (3ae): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (79 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 3.93 (s, 3H), 3.92 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 153.1, 143.1, 124.3, 107.6, 61.1, 56.4.

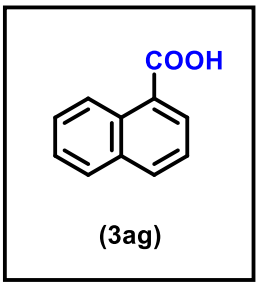


(3af)

2,6-dimethoxybenzoic acid (3af): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (28 mg, 31%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.69 (s, 1H), 7.31 (t, J = 8.4 Hz, 1H), 6.68 (d, J = 8.4 Hz, 2H), 3.75 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.7, 156.1, 130.4, 114.4, 104.1, 55.8.

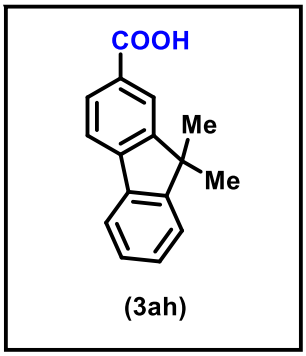


(3ag)

1-naphthoic acid (3ag): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (58 mg, 67%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.16 (s, 1H), 8.87 (dd, J = 8.6, 1.2 Hz, 1H), 8.17 – 8.13 (m, 2H), 8.01 (dd, J = 8.1, 1.8 Hz, 1H), 7.66 – 7.62 (m, 1H), 7.60 – 7.56 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 168.7, 133.5, 133.0, 130.7, 129.9, 128.6, 127.8, 127.6, 126.2, 125.5, 124.9.



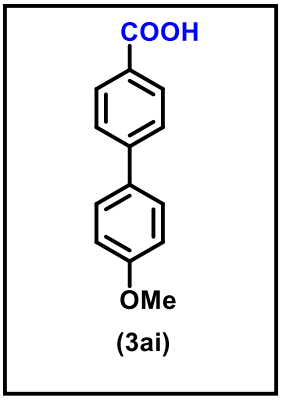
(3ah)

9,9-dimethyl-9H-fluorene-2-carboxylic acid (3ah): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (73 mg, 61%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.89 (s, 1H), 8.10 (d, *J* = 1.5 Hz, 1H), 7.98 – 7.90 (m, 3H), 7.62 – 7.58 (m, 1H), 7.42 – 7.36 (m, 2H), 1.46 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.5, 154.3, 153.3, 143.1, 137.4, 129.5, 128.8, 128.5, 127.3, 123.7, 123.0, 121.1, 120.1, 46.6, 26.6.

HRMS (ESI, m/z) calcd. for $C_{16}H_{13}O_2$ $[M-H]^-$: 237.0916; found: 237.0919.

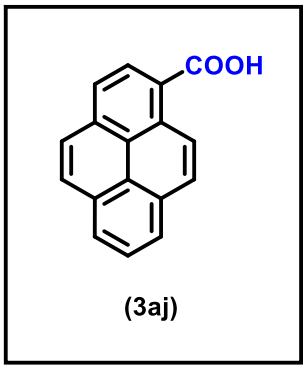


(3ai)

4'-methoxy-[1,1'-biphenyl]-4-carboxylic acid (3ai): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (88 mg, 77%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.88 (s, 1H), 7.98 (d, *J* = 8.3 Hz, 2H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.7 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.2, 159.6, 144.0, 131.2, 129.9, 128.9, 128.1, 126.1, 114.5, 55.2.

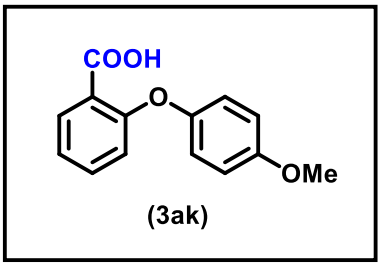


(3aj)

pyrene-1-carboxylic acid (3aj): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a yellowish solid (75 mg, 61%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.34 (s, 1H), 9.23 (d, *J* = 9.4 Hz, 1H), 8.62 (d, *J* = 8.1 Hz, 1H), 8.41 – 8.39 (m, 2H), 8.37 – 8.32 (m, 3H), 8.25 (d, *J* = 9.0 Hz, 1H), 8.15 (t, *J* = 7.6 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 169.1, 133.6, 130.6, 130.1, 129.8, 129.5, 129.1, 128.4, 127.2, 126.7, 126.5, 126.2, 124.7, 124.5, 124.0, 123.4.



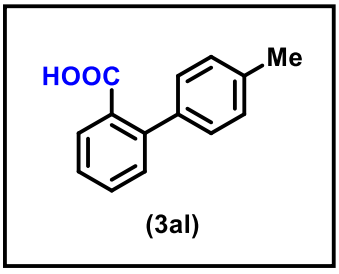
(3ak)

2-(4-methoxyphenoxy)benzoic acid (3ak): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (77 mg, 63%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.85 (s, 1H), 7.78 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.51 – 7.46 (m, 1H), 7.17 (td, *J* = 7.5, 1.1 Hz, 1H), 6.93 (d, *J* = 1.5 Hz, 4H), 6.85 (dd, *J* = 8.3, 1.1 Hz, 1H), 3.73 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.8, 156.3, 155.4, 150.2, 133.2, 131.2, 123.6, 122.9, 119.9, 119.0, 115.0, 55.4.

HRMS (ESI, m/z) calcd. for $C_{14}H_{11}O_4$ $[M-H]^-$: 243.0657; found: 243.0668.

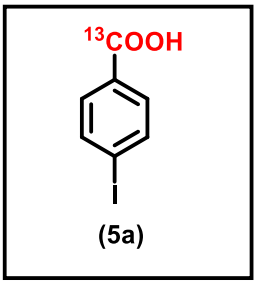


(3al)

4'-methyl-[1,1'-biphenyl]-2-carboxylic acid (3al): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (28 mg, 26%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.8 Hz, 1H), 7.55 (td, *J* = 7.6, 1.4 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 7.7 Hz, 1H), 7.25 (d, *J* = 7.9 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 2.40 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 173.5, 143.4, 138.2, 137.2, 132.2, 131.3, 130.8, 129.5, 129.0, 128.5, 127.1, 21.4.



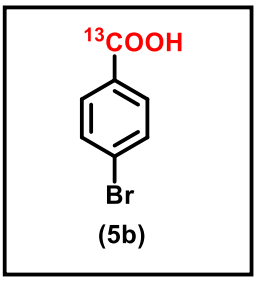
(5a)

(^{13}C)-labeled 4-iodobenzoic acid (5a): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (31 mg, 50%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.11 (s, 1H), 7.89 (d, J = 7.9 Hz, 2H), 7.69 (dd, J = 8.1, 3.9 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.9, 137.6 (d, J = 4.3 Hz), 131.1 (d, J = 2.0 Hz), 130.3 (d, J = 72.1 Hz), 101.2.

HRMS (ESI, m/z) calcd. for $C_6{}^{13}CH_4IO_2$ $[M-H]^-$: 247.9290; found: 247.9293.



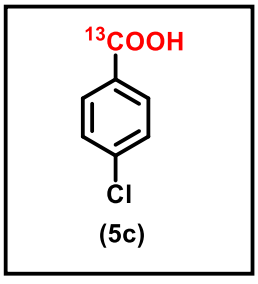
(5b)

(^{13}C)-labeled 4-bromobenzoic acid (5b): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (33 mg, 65%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.17 (s, 1H), 7.86 (dd, J = 8.4, 3.8 Hz, 2H), 7.71 (d, J = 8.2 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.6, 131.7 (d, J = 4.4 Hz), 131.3 (d, J = 2.4 Hz), 130.0 (d, J = 72.1 Hz), 126.9.

HRMS (ESI, m/z) calcd. for $C_6{}^{13}CH_4BrO_2$ $[M-H]^-$: 199.9429; found: 199.9434.



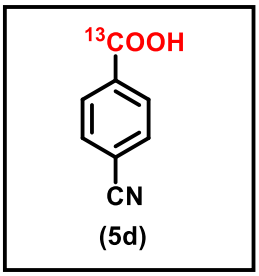
(5c)

(^{13}C)-labeled 4-chlorobenzoic acid (5c): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (26 mg, 66%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.17 (s, 1H), 7.96 – 7.92 (m, 2H), 7.58 – 7.56 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 166.5, 137.8, 131.1 (d, J = 2.4 Hz), 129.6 (d, J = 72.3 Hz), 128.8 (d, J = 4.6 Hz).

HRMS (ESI, m/z) calcd. for $C_6{}^{13}CH_4ClO_2$ $[M-H]^-$: 155.9934; found: 155.9939.



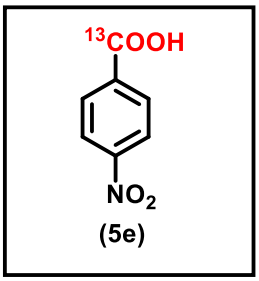
(5d)

(^{13}C)-labeled 4-cyanobenzoic acid (5d): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (19 mg, 50%).

^{1}H NMR (400 MHz, Acetone-d_6) δ 8.22 – 8.18 (m, 2H), 7.96 – 7.93 (m, 2H).

^{13}C NMR (100 MHz, Acetone-d_6) δ 166.3, 135.4 (d, J = 72.2 Hz), 133.4 (d, J = 4.3 Hz), 131.1 (d, J = 1.9 Hz), 118.7, 117.0.

HRMS (ESI, m/z) calcd. for $C_7{}^{13}CH_4NO_2$ $[M\text{-}H]^-$: 147.0276; found: 147.0279.



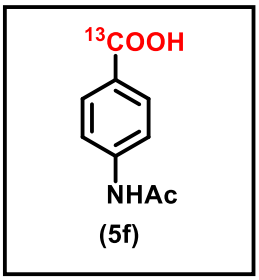
(5e)

(^{13}C)-labeled 4-nitrobenzoic acid (5e): Column chromatography (SiO_2, eluting with 1:1 hexane/ethyl acetate) afforded the desired product as a white solid (29 mg, 68%).

^{1}H NMR (400 MHz, Acetone-d_6) δ 8.39 – 8.36 (m, 2H), 8.30 – 8.27 (m, 2H).

^{13}C NMR (100 MHz, Acetone-d_6) δ 166.1, 151.6, 137.0 (d, J = 72.1 Hz), 131.8 (d, J = 3.0 Hz), 124.5 (d, J = 4.6 Hz).

HRMS (ESI, m/z) calcd. for $C_6{}^{13}CH_4NO_4$ $[M\text{-}H]^-$: 167.0174; found: 167.0177.



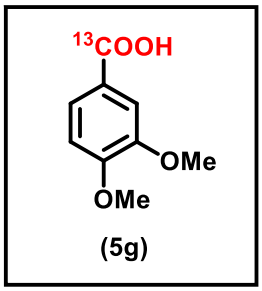
(5f)

(^{13}C)-labeled 4-acetamidobenzoic acid (5f): Column chromatography (SiO_2, eluting with 2% MeOH in DCM) afforded the desired product as a white solid (38 mg, 85%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.65 (s, 1H), 10.23 (s, 1H), 7.89 – 7.85 (m, 2H), 7.70 – 7.67 (m, 2H), 2.08 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 168.9, 166.9, 143.3, 130.4 (d, J = 2.0 Hz), 124.9 (d, J = 73.0 Hz), 118.2 (d, J = 4.0 Hz), 24.2.

HRMS (ESI, m/z) calcd. for $C_8{}^{13}CH_8NO_3$ $[M\text{-}H]^-$: 179.0538; found: 179.0546.



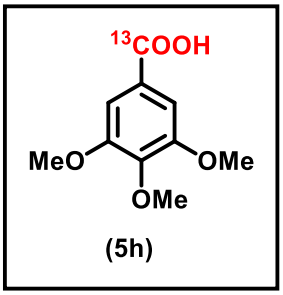
(5g)

(^{13}C)-labeled 3,4-dimethoxybenzoic acid (5g): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (34 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) δ δ 7.78 (ddd, *J* = 8.4, 4.1, 1.9 Hz, 1H), 7.60 (dd, *J* = 4.3, 2.0 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 3.96 (s, 3H), 3.95 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 153.9, 148.8 (d, *J* = 5.5 Hz), 124.7 (d, *J* = 2.4 Hz), 121.8 (d, *J* = 74.9 Hz), 112.5 (d, *J* = 2.9 Hz), 110.5 (d, *J* = 5.3 Hz), 56.2, 56.2.

HRMS (ESI, m/z) calcd. for $C_8{}^{13}CH_{11}O_4$ $[M+H]^+$: 184.0691; found: 184.0699.



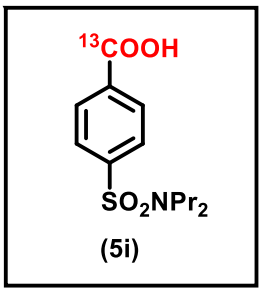
(5h)

(^{13}C)-labeled 3,4,5-trimethoxybenzoic acid (5h): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (39 mg, 74%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 4.6 Hz, 2H), 3.93 (s, 2H), 3.93 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 153.1 (d, *J* = 6.6 Hz), 143.1, 124.2 (d, *J* = 74.0 Hz), 107.6 (d, *J* = 2.6 Hz), 61.1, 56.4.

HRMS (ESI, m/z) calcd. for $C_9{}^{13}CH_{11}O_5$ $[M-H]^-$: 212.0640; found: 212.0637.



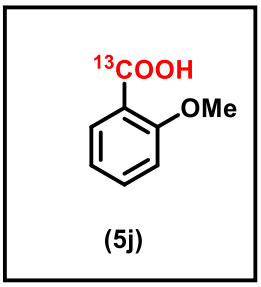
(5i)

(^{13}C)-labeled 4-(*N,N*-dipropylsulfamoyl)benzoic acid (5i): Column chromatography (SiO_2, eluting with 3:2 hexane/ethyl acetate) afforded the desired product as a white solid (44 mg, 61%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 – 8.21 (m, 2H), 7.93 – 7.91 (m, 2H), 3.14 – 3.10 (m, 4H), 1.61 – 1.51 (m, 4H), 0.88 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 145.3, 132.6 (d, *J* = 72.8 Hz), 131.0 (d, *J* = 2.0 Hz), 127.3 (d, *J* = 4.6 Hz), 50.1, 22.1, 11.3.

HRMS (ESI, m/z) calcd. for $C_{12}{}^{13}CH_{18}NO_4S$ $[M-H]^-$: 285.0991; found: 285.0992.



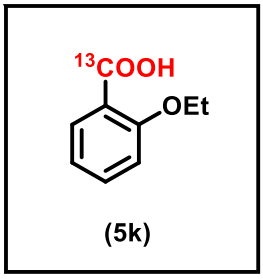
(5j)

(^{13}C)-labeled 2-methoxybenzoic acid (5j): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (25 mg, 65%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.77 (s, 1H), 8.21 – 8.17 (m, 1H), 7.60 – 7.56 (m, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 8.3 Hz, 1H), 4.08 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 158.2, 135.2, 134.0, 122.4 (d, *J* = 4.3 Hz), 117.8 (d, *J* = 68.3 Hz), 111.8 (d, *J* = 2.7 Hz), 56.8.

HRMS (ESI, m/z) calcd. for $C_7{}^{13}CH_9O_3$ $[M+H]^+$: 154.0586; found: 154.0579.



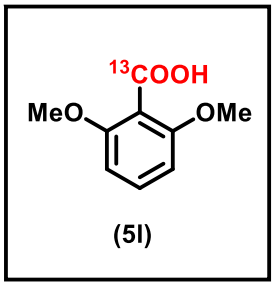
(5k)

(^{13}C)-labeled 2-ethoxybenzoic acid (5k): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a colourless liquid (26 mg, 62%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.03 (s, 1H), 8.16 (ddd, *J* = 7.8, 4.6, 1.8 Hz, 1H), 7.54 (ddd, *J* = 8.5, 7.4, 1.8 Hz, 1H), 7.13 – 7.09 (m, 1H), 7.03 (dt, *J* = 8.5, 1.3 Hz, 1H), 4.32 (q, *J* = 7.0 Hz, 2H), 1.55 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 157.6, 135.1, 133.8, 122.3 (d, *J* = 4.1 Hz), 117.8 (d, *J* = 68.4 Hz), 112.7 (d, *J* = 3.0 Hz), 66.1, 14.7.

HRMS (ESI, m/z) calcd. for $C_8{}^{13}CH_{11}O_4$ $[M+H]^+$: 184.0691; found: 184.0698.



(5l)

(^{13}C)-labeled 2,6-dimethoxybenzoic acid (5l): Column chromatography (SiO_2, eluting with 2:1 hexane/ethyl acetate) afforded the desired product as a white solid (14 mg, 30%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, *J* = 8.4 Hz, 1H), 6.60 (dd, *J* = 8.5, 1.6 Hz, 2H), 3.88 (s, 3H).

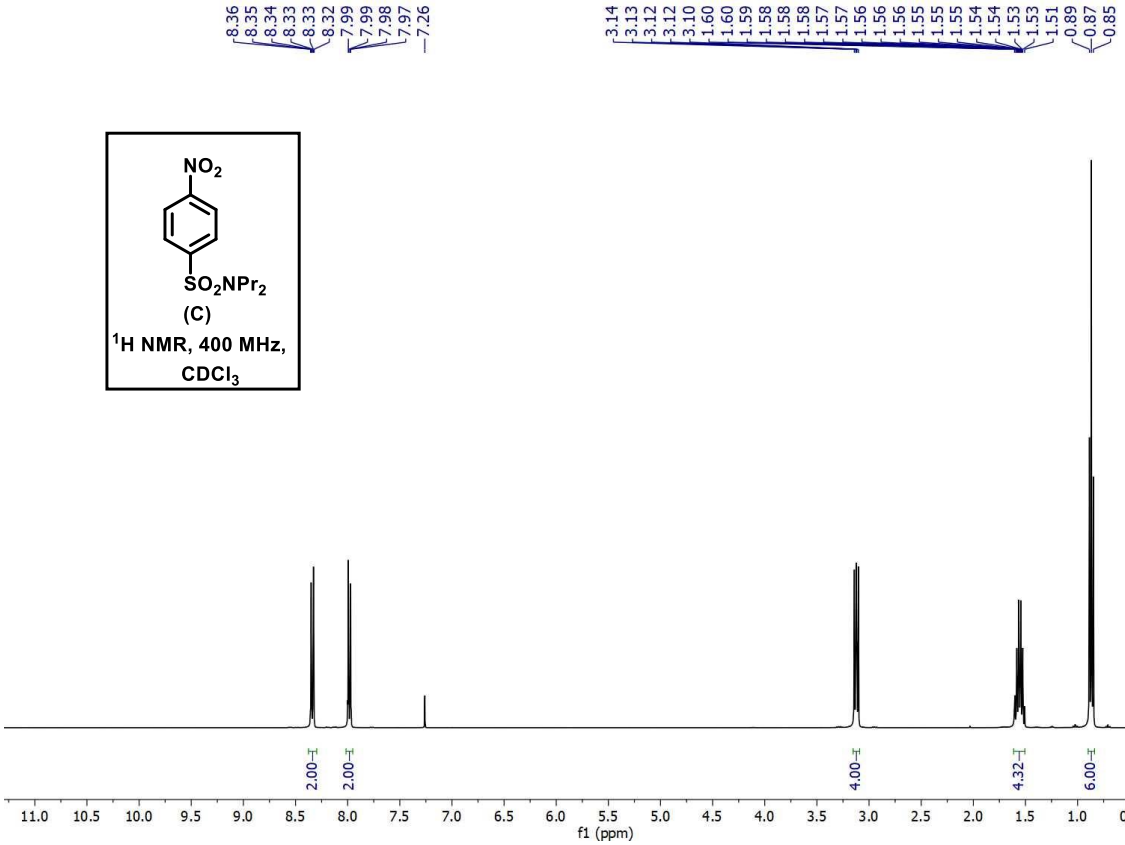
^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 158.0, 132.0, 111.8 (d, *J* = 73.5 Hz), 104.3 (d, *J* = 2.4 Hz), 56.3.

HRMS (ESI, m/z) calcd. for $C_8{}^{13}CH_{11}O_4$ $[M+H]^+$: 184.0691; found: 184.0698.

References:

1. A. Polley, K. Varalaxmi and R. Jana, *ACS Omega*, 2018, **3**, 14503–14516.
2. S. Yrjölä, T. Parkkari, D. Navia-Paldanius, T. Laitinen, A. A. Kaczor, T. Kokkola, F. Adusei-Mensah, J. R. Savinainen, J. T. Laitinen, A. Poso, A. Alexander, J. Penman, L. Stott, M. Anskat, A. J. Irving and T. J. Nevalainen, *Eur. J. Med. Chem.*, 2016, **107**, 119-132.

NMR spectra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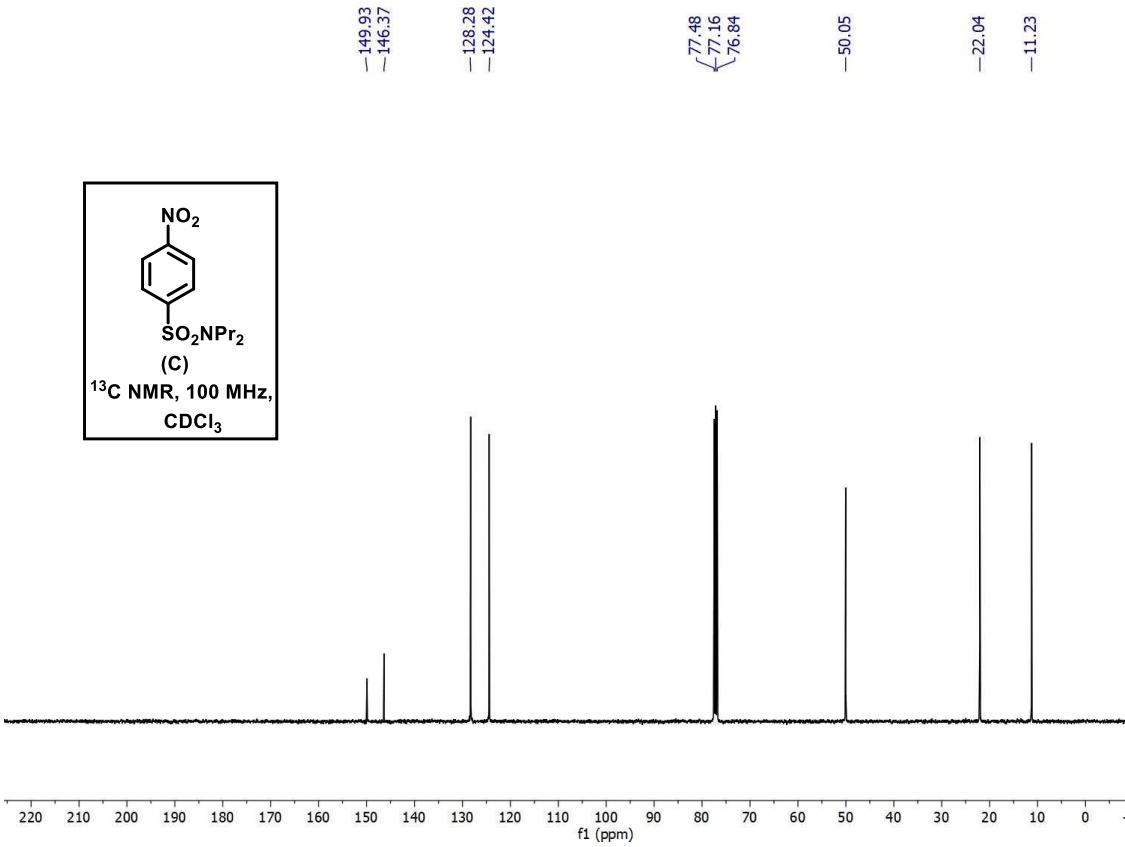
8.35
8.34
8.33
8.33
8.32
7.99
7.99
7.98
7.97
7.26
3.14
3.13
3.12
3.12
3.10
1.60
1.60
1.59
1.58
1.58
1.58
1.57
1.57
1.56
1.56
1.56
1.55
1.55
1.55
1.54
1.54
1.53
1.53
1.51
0.89
0.87
0.85
NO2
SO2NPr2
(C)
1H NMR, 400 MHz,
CDCl3
2.00
2.00
4.00
4.32
6.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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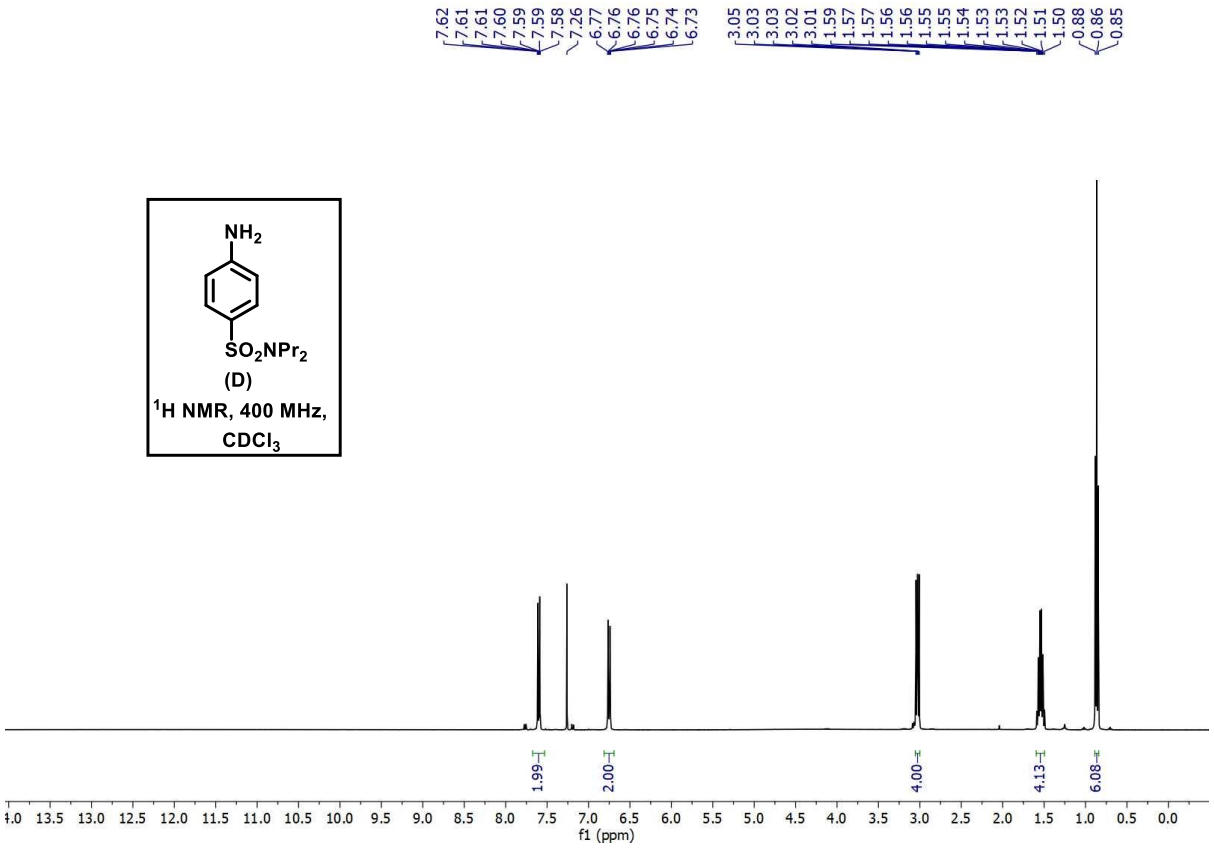
146.37
128.28
124.42
77.48
77.16
76.84
50.05
22.04
11.23
NO2
SO2NPr2
(C)
13C NMR, 100 MHz,
CDCl3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)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7.61
7.61
7.60
7.59
7.59
7.58
7.26
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6.76
6.76
6.75
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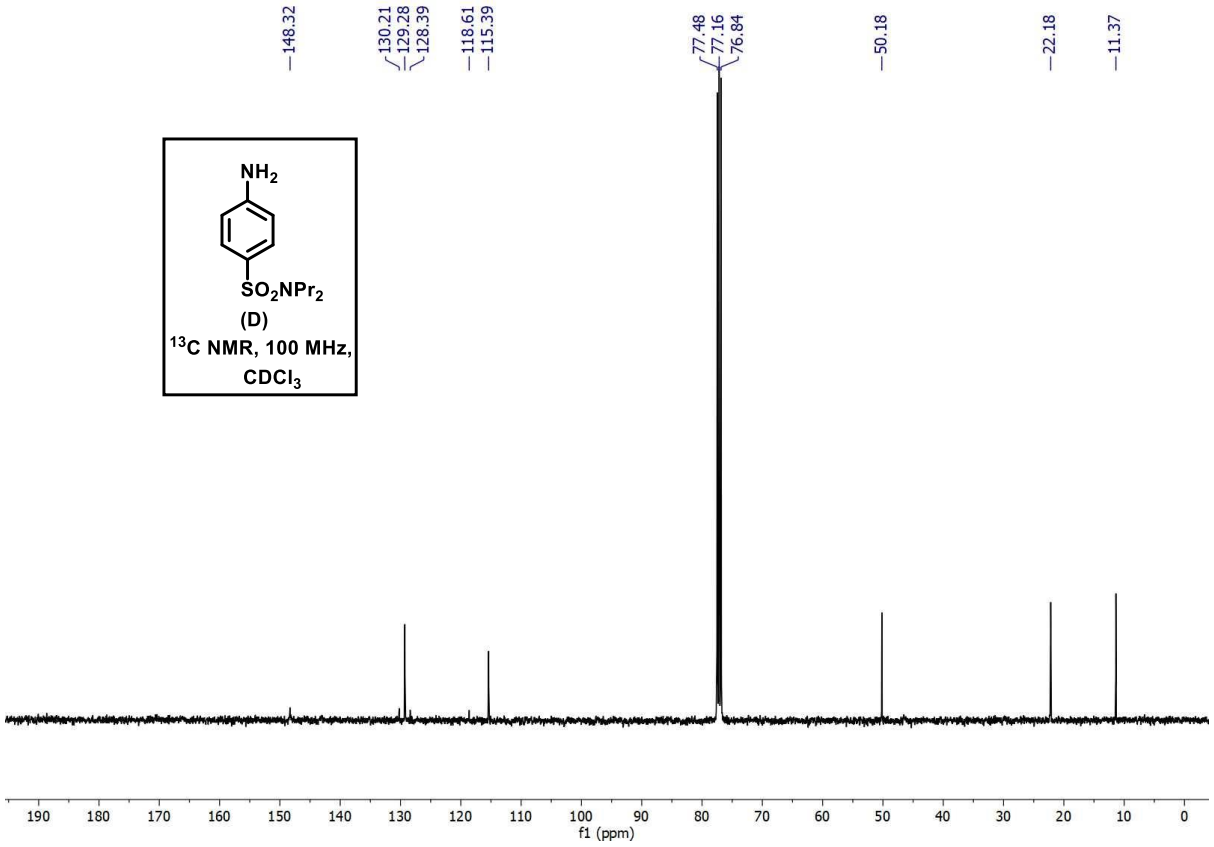
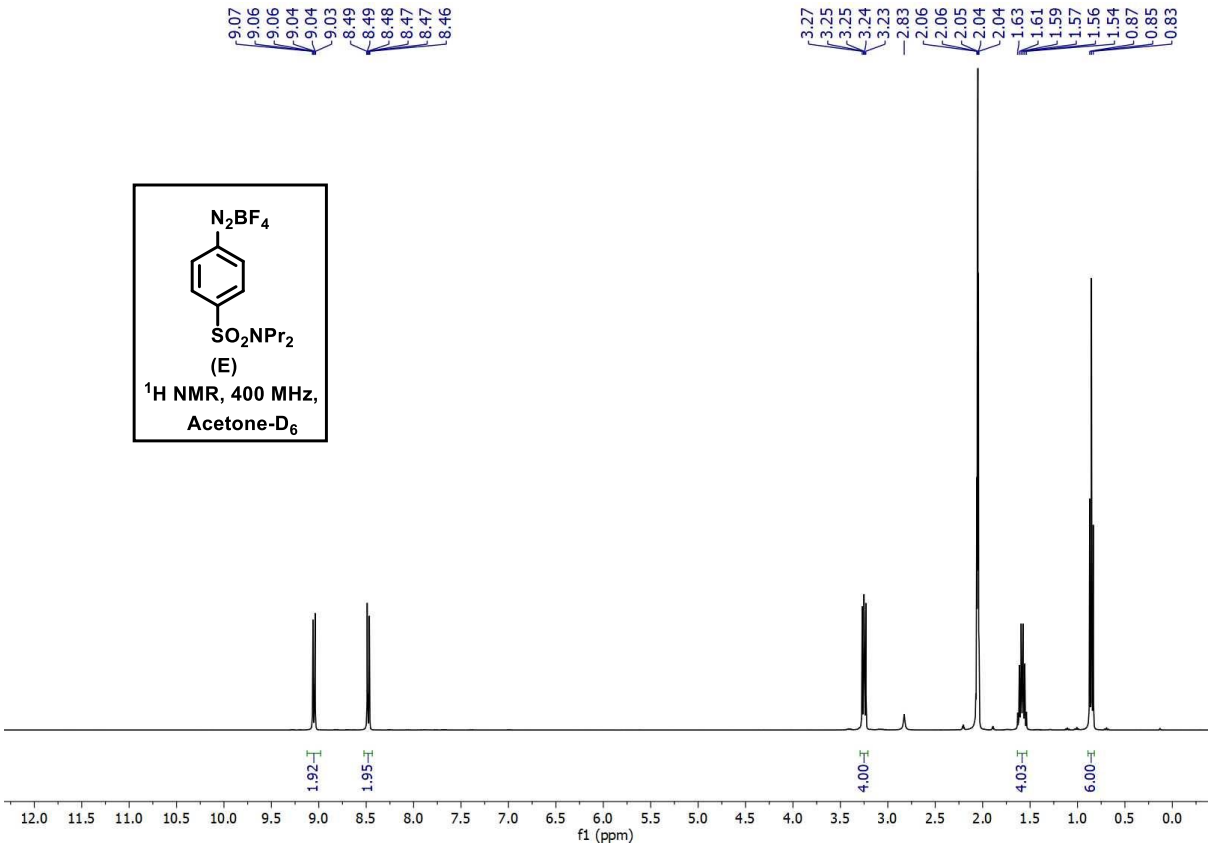
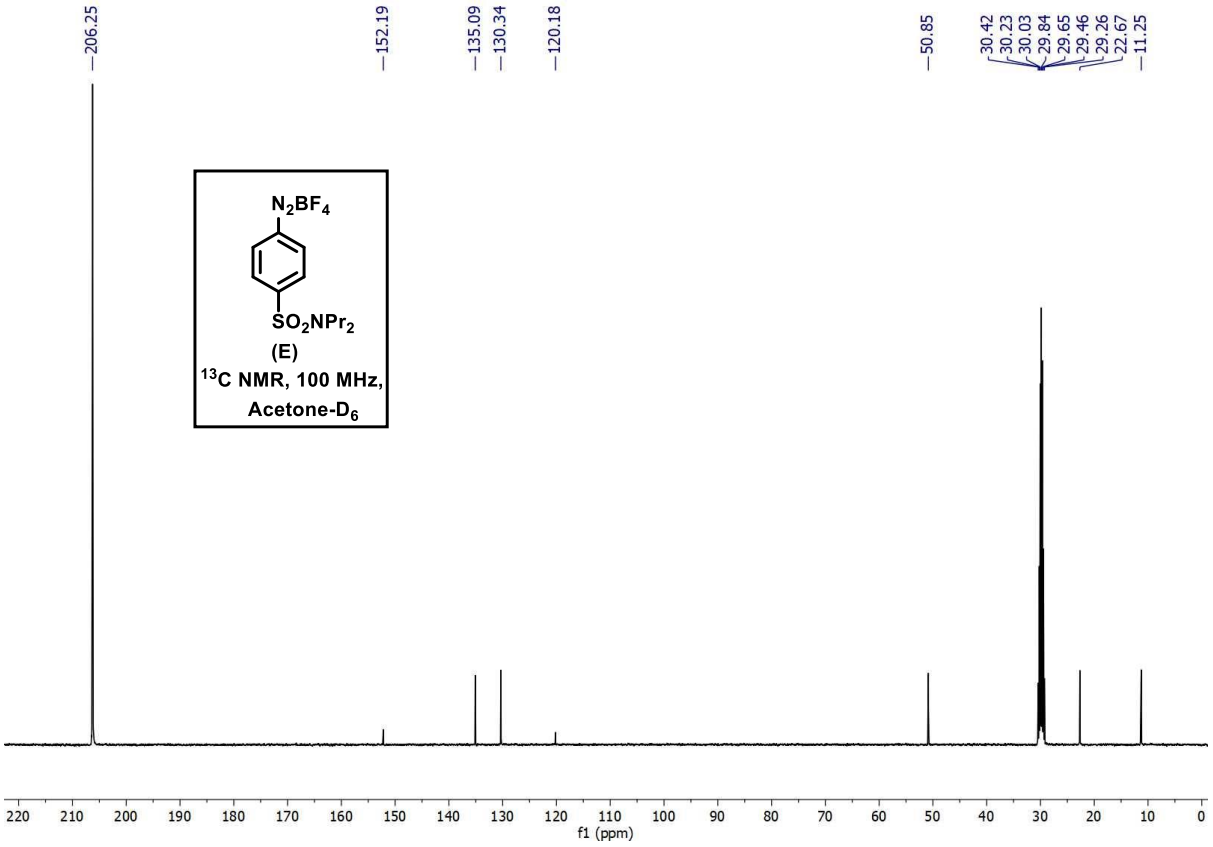
6.73
3.05
3.03
3.03
3.02
3.01
1.59
1.57
1.57
1.56
1.56
1.55
1.55
1.54
1.53
1.53
1.52
1.51
1.50
0.88
0.86
0.85
NH2
SO2NPr2
(D)
1H NMR, 400 MHz,
CDCl3
1.99
2.00
4.00
4.13
6.08
f1 (ppm)


148.32
130.21
129.28
128.39
118.61
115.39
77.48
77.16
76.84
50.18
22.18
11.37
NH2
SO2NPr2
(D)
13C NMR, 100 MHz,
CDCl3
f1 (ppm)


9.07
9.06
9.06
9.04
9.04
9.03
8.49
8.49
8.48
8.47
8.47
8.46
3.27
3.25
3.25
3.24
3.23
2.83
2.06
2.06
2.05
2.04
2.04
1.63
1.61
1.59
1.57
1.56
1.54
0.87
0.85
0.83
N2BF4
SO2NPr2
(E)
1H NMR, 400 MHz,
Acetone-D6
1.92
1.95
4.00
4.03
6.00
f1 (ppm)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130.34
120.18
50.85
30.42
30.23
30.03
29.84
29.65
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29.26
22.67
11.25
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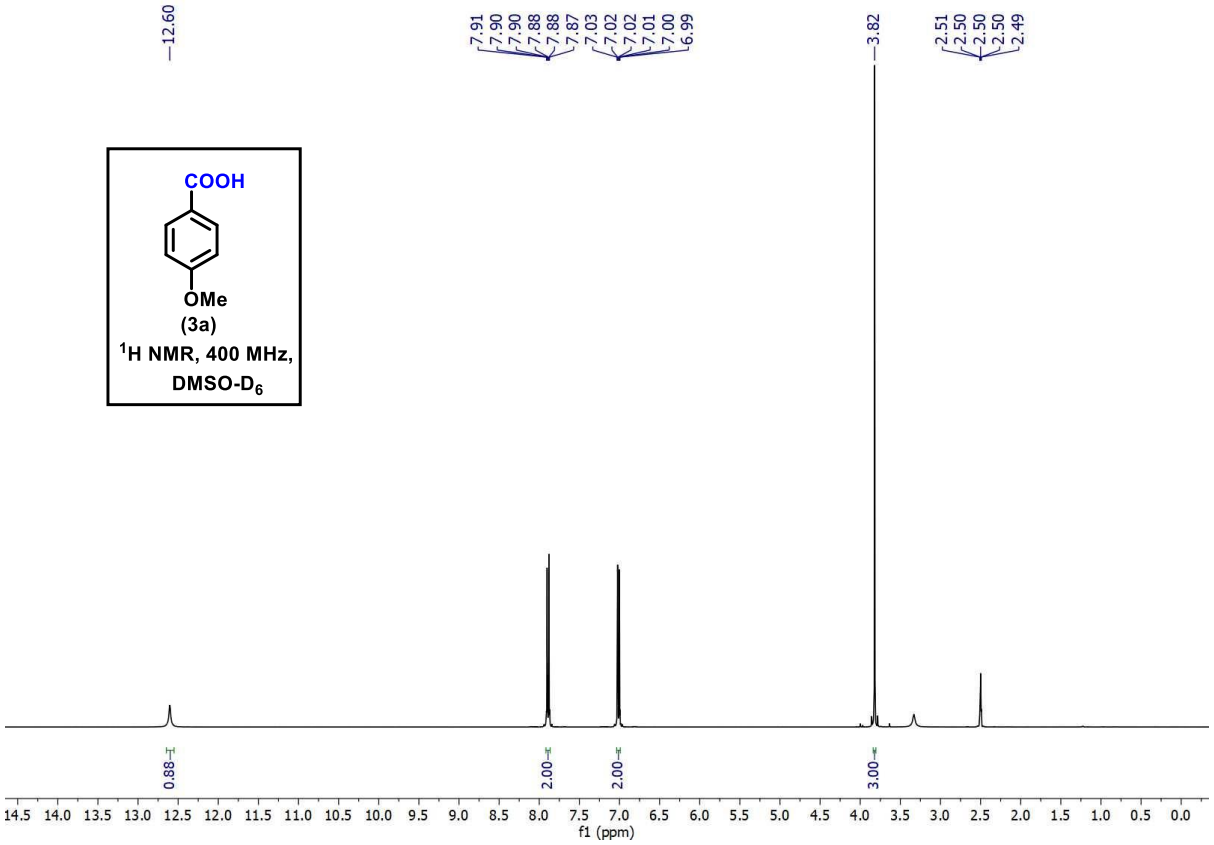
SO2NPr2
(E)
13C NMR, 100 MHz,
Acetone-D6
f1 (ppm)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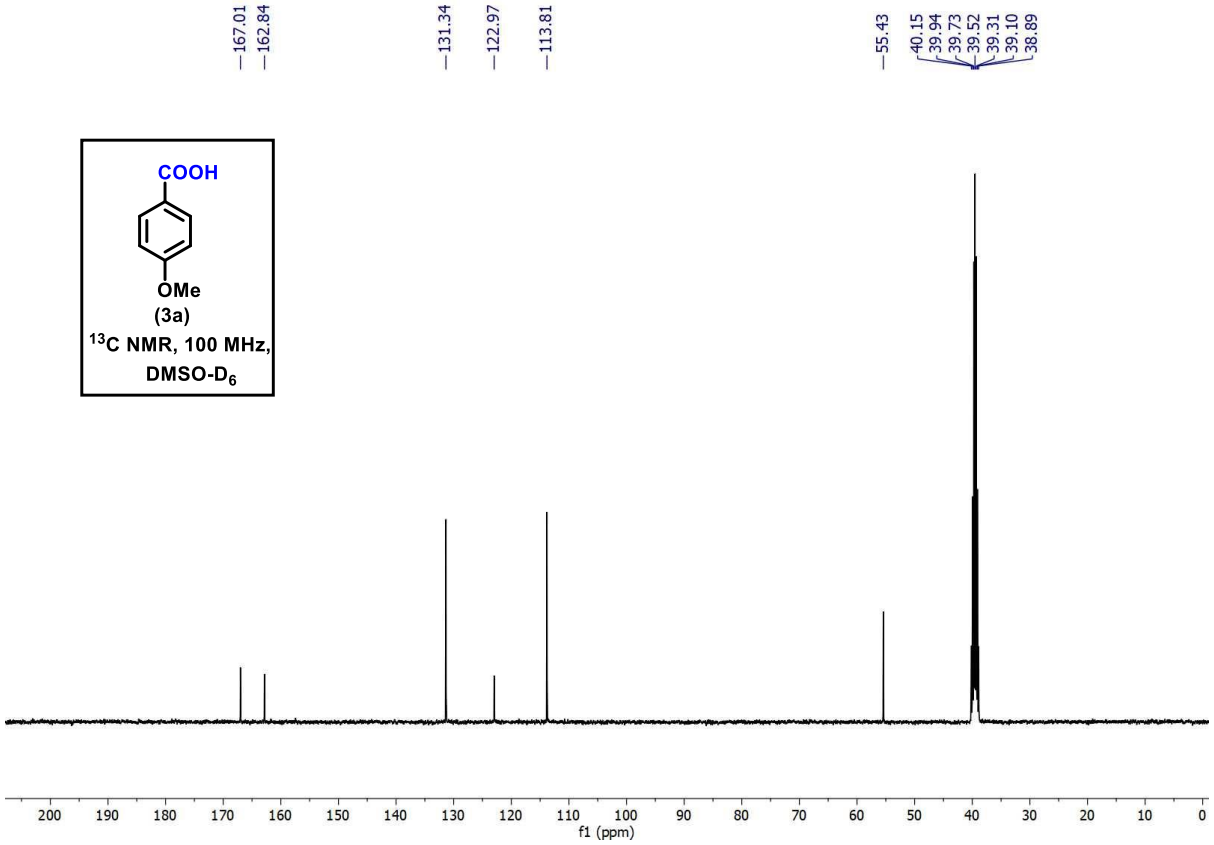
7.90
7.90
7.88
7.88
7.87
7.03
7.02
7.02
7.01
7.00
6.99
3.82
2.51
2.50
2.50
2.50
2.49
COOH
OMe
(3a)
1H NMR, 400 MHz,
DMSO-D6
0.88
2.00
2.00
3.00
f1 (ppm)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131.34
122.97
113.81
55.43
40.15
39.94
39.73
39.52
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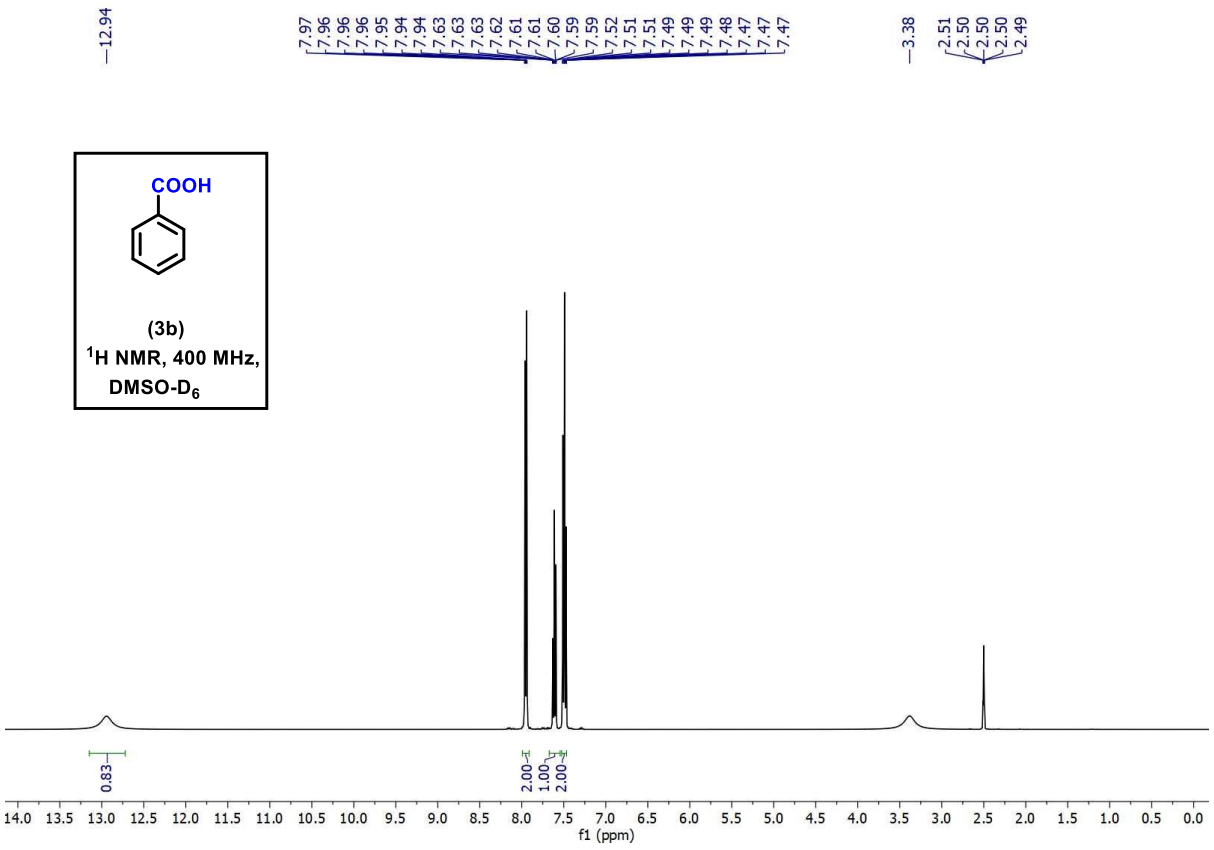
39.10
38.89
COOH
OMe
(3a)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)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7.96
7.95
7.94
7.94
7.63
7.63
7.62
7.61
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7.60
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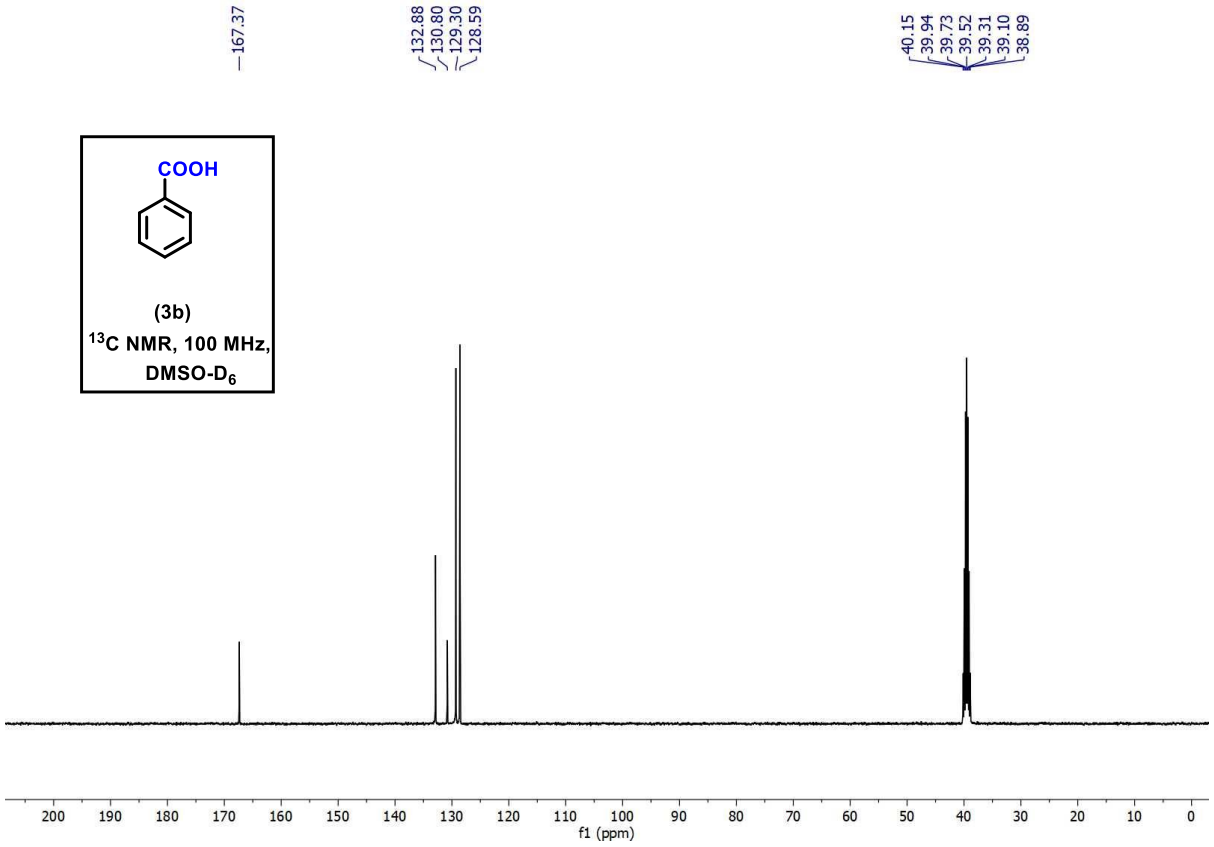
7.49
7.49
7.48
7.47
7.47
7.47
3.38
2.51
2.50
2.50
2.50
2.49
COOH
(3b)
1H NMR, 400 MHz,
DMSO-D6
0.83
2.00
1.00
2.00
f1 (ppm)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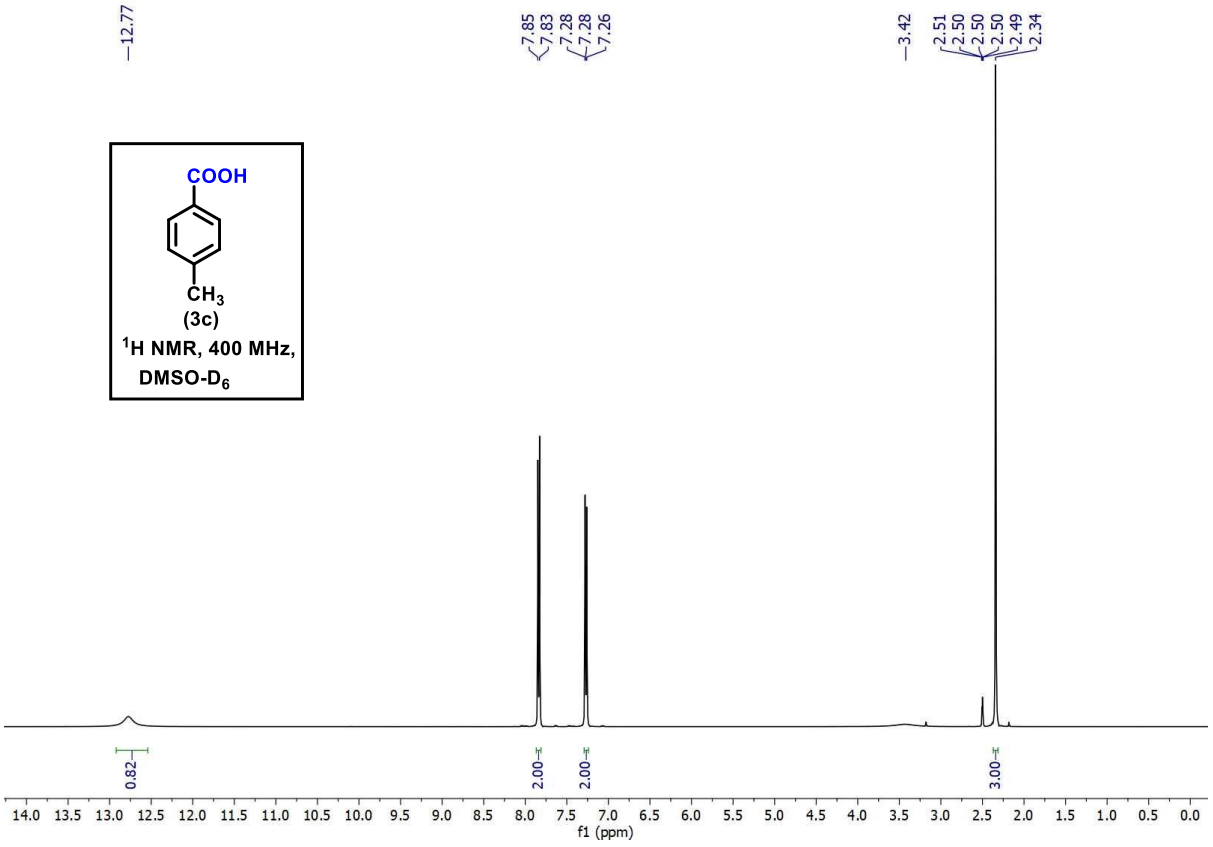
130.80
129.30
128.59
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
(3b)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)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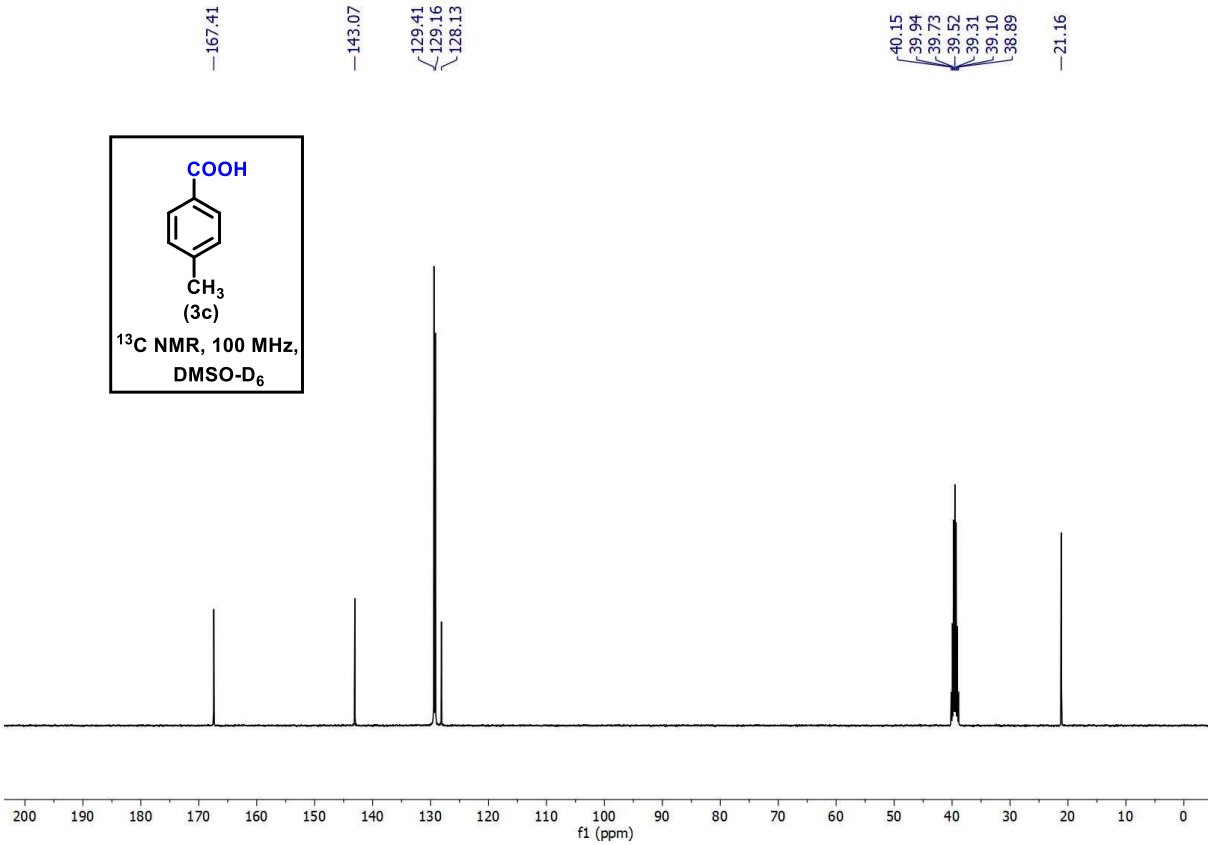
7.83
7.28
7.28
7.26
3.42
2.51
2.50
2.50
2.50
2.49
2.34
COOH
CH3
(3c)
1H NMR, 400 MHz,
DMSO-D6
0.82
2.00
2.00
3.00
f1 (ppm)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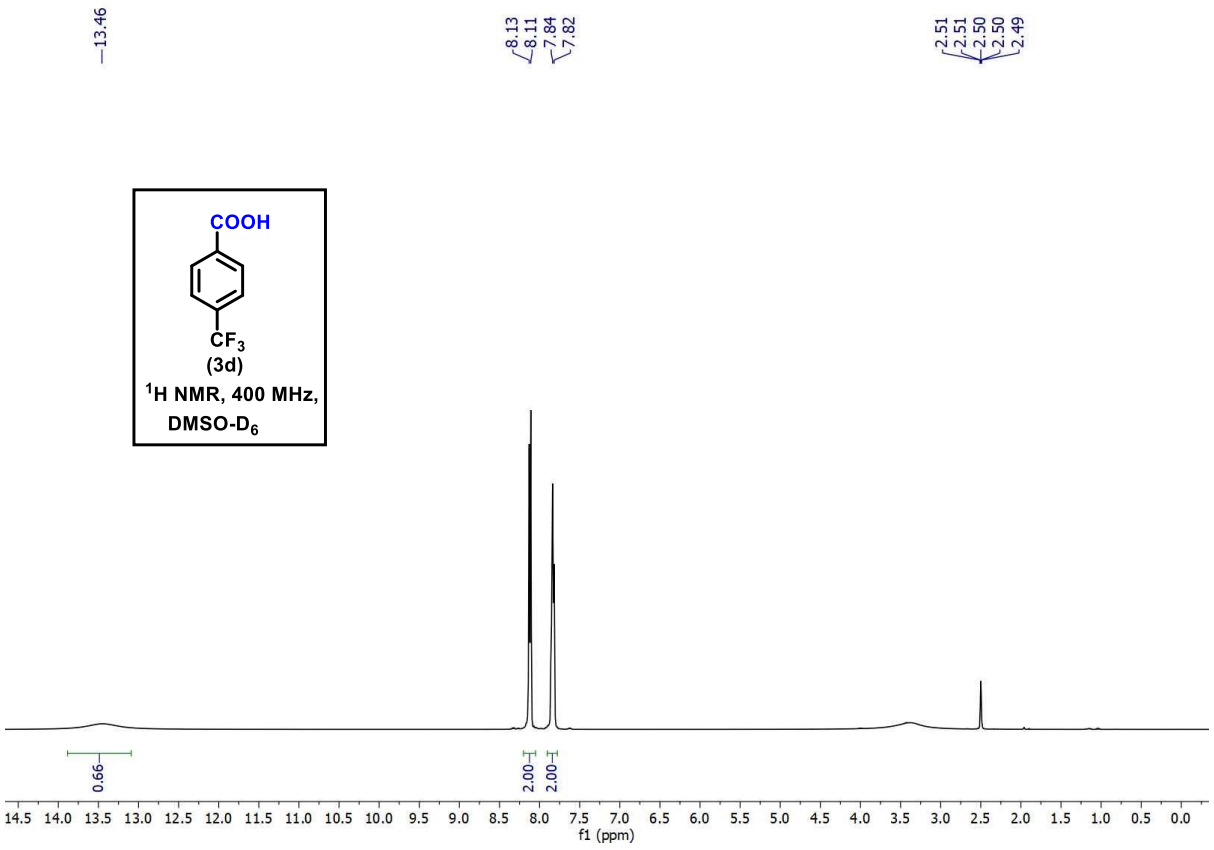
129.16
128.13
40.15
39.94
39.73
39.52
39.31
39.10
38.89
21.16
COOH
CH3
(3c)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)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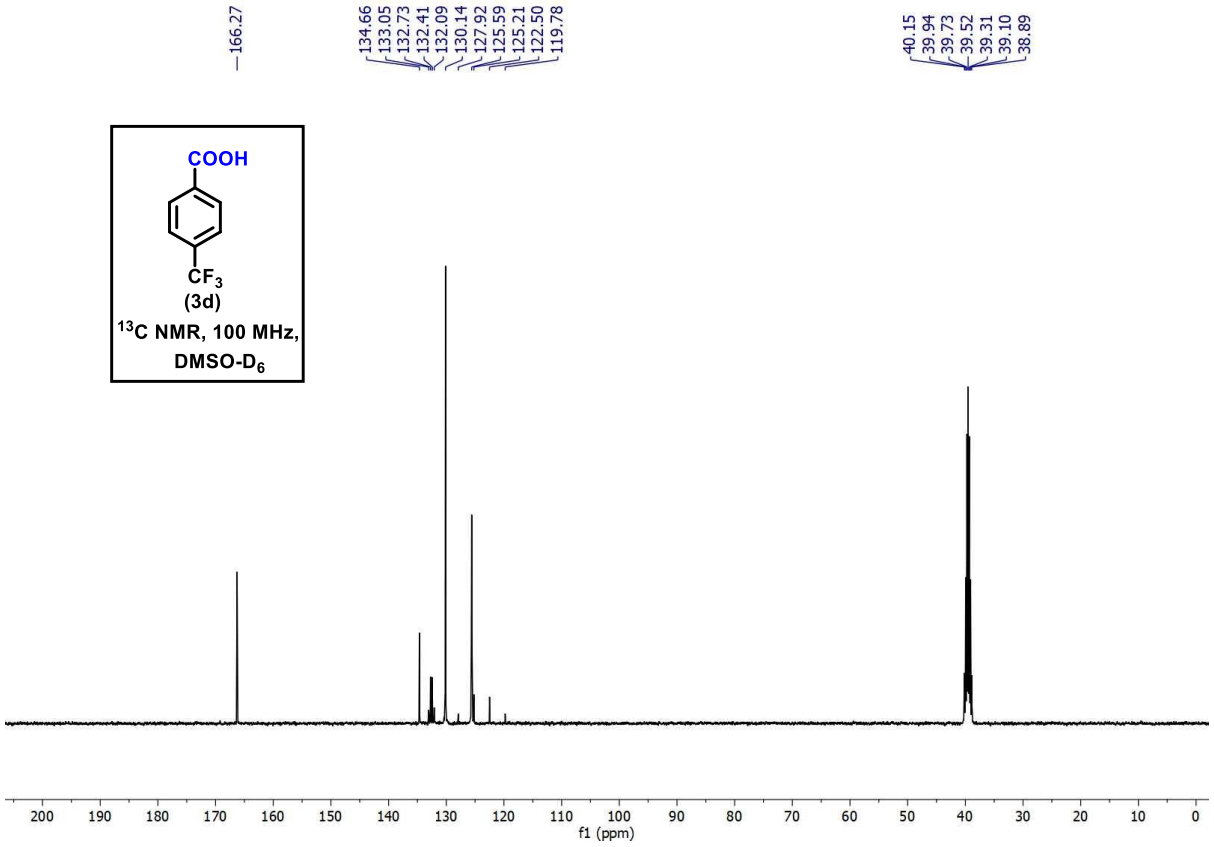
7.84
7.82
2.51
2.51
2.50
2.50
2.49
COOH
CF3
(3d)
1H NMR, 400 MHz,
DMSO-D6
0.66
2.00
2.00
f1 (ppm)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134.66
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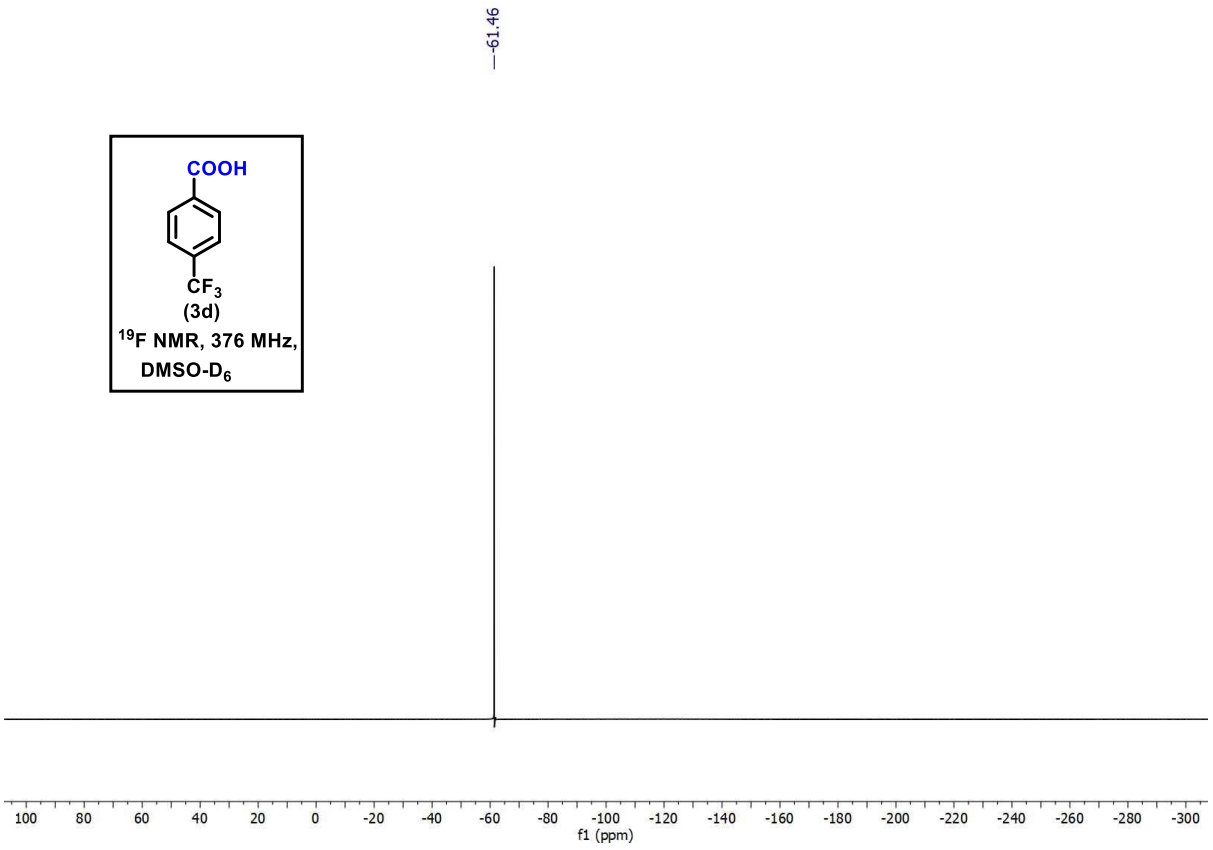
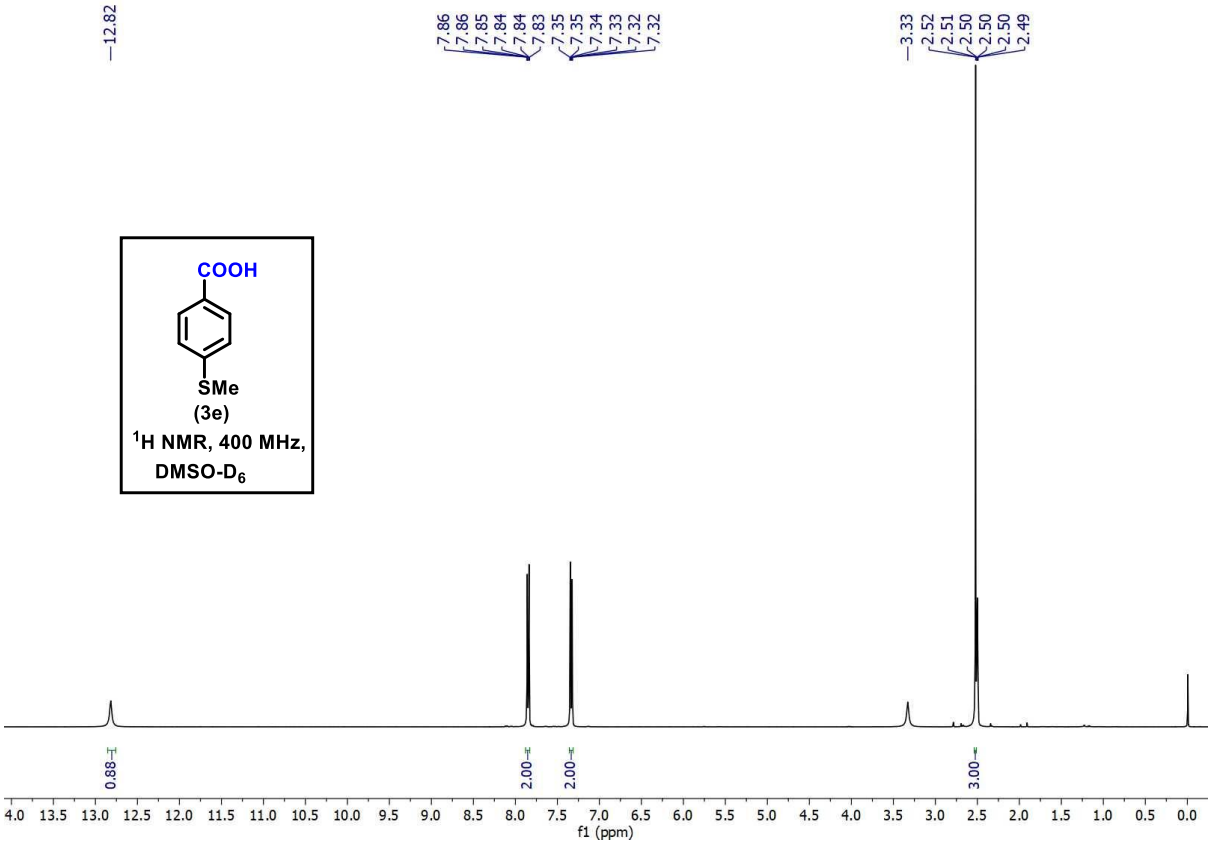
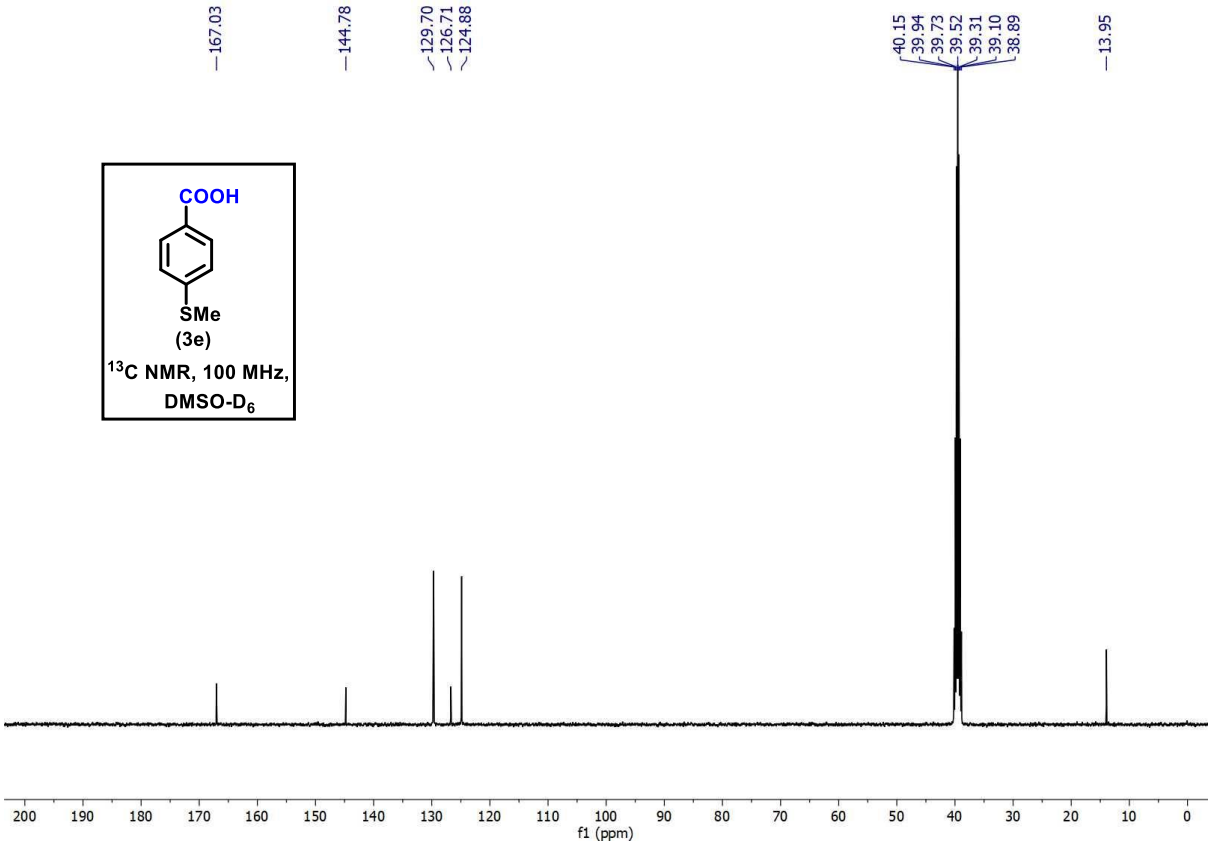
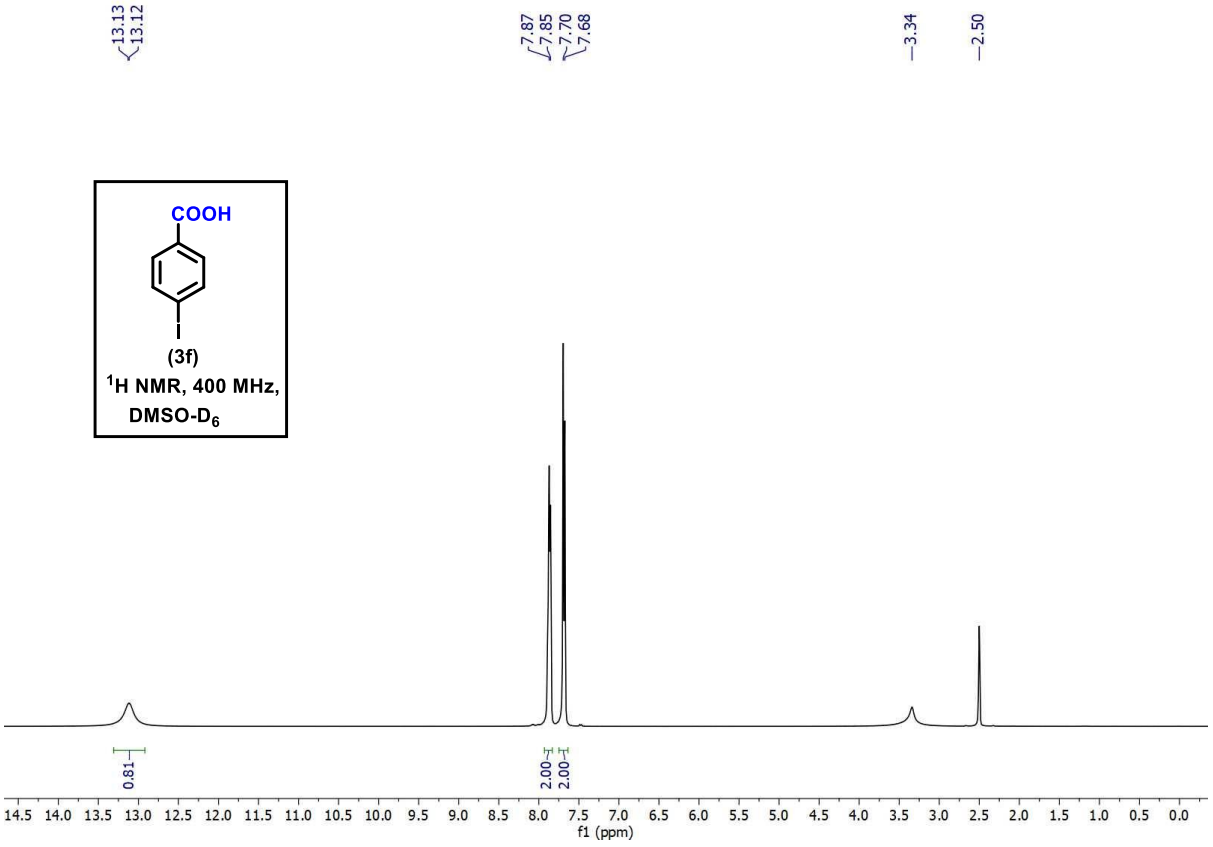
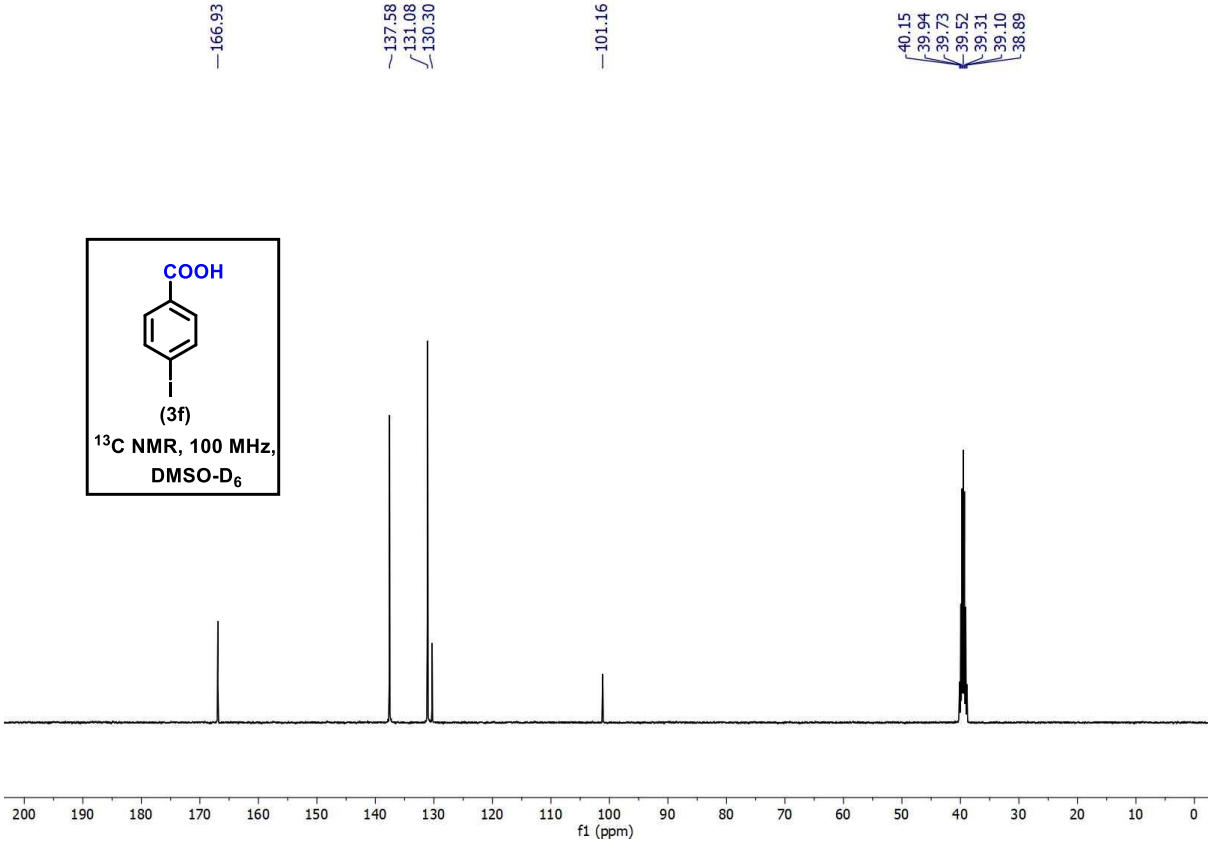
132.41
132.09
130.14
127.92
125.59
125.21
122.50
119.78
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
CF3
(3d)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


-61.46
COOH
CF3
(3d)
19F NMR, 376 MHz,
DMSO-D6
100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240 -260 -280 -300
f1 (ppm)


12.82
7.86
7.86
7.85
7.84
7.84
7.83
7.35
7.35
7.34
7.33
7.32
7.32
3.33
2.52
2.51
2.50
2.50
2.50
2.49
COOH
SMe
(3e)
1H NMR, 400 MHz,
DMSO-D6
0.88
2.00
2.00
3.00
f1 (ppm)


167.03
144.78
129.70
126.71
124.88
40.15
39.94
39.73
39.52
39.31
39.10
38.89
13.95
COOH
SMe
(3e)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


13.13
13.12
7.87
7.85
7.70
7.68
3.34
2.50
COOH
(3f)
1H NMR, 400 MHz,
DMSO-D6
0.81
2.00
2.00
14.5 14.0 13.5 13.0 12.5 12.0 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 0.0
f1 (ppm)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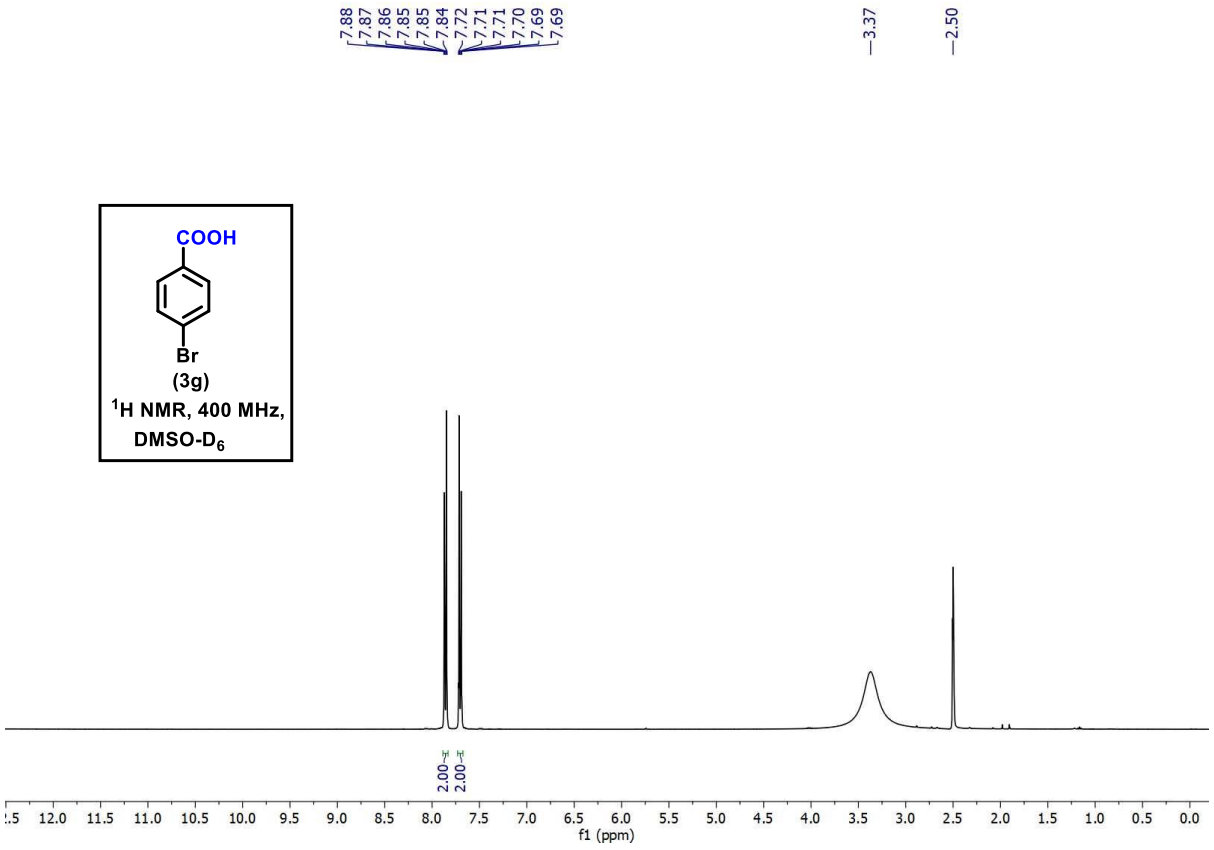
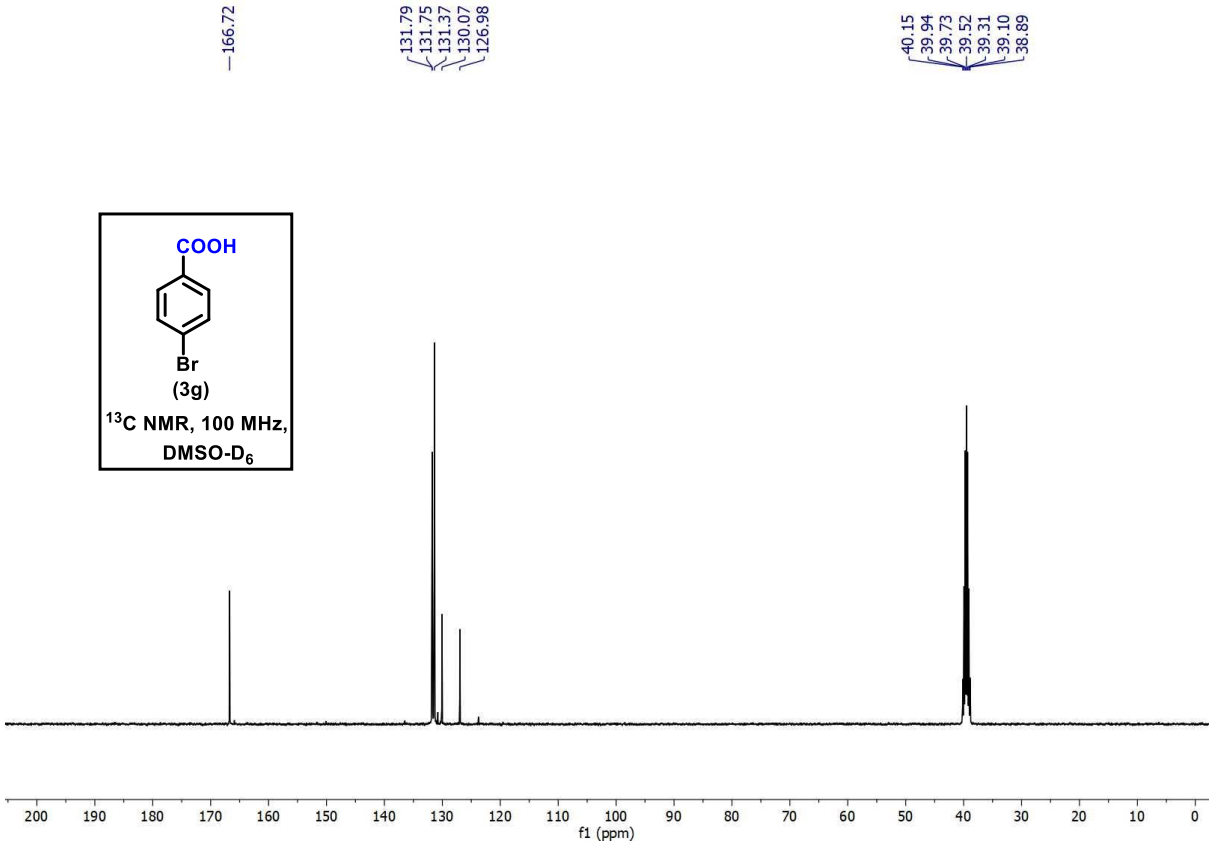
137.58
131.08
130.30
101.16
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
(3f)
13C NMR, 100 MHz,
DMSO-D6
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.88
7.87
7.86
7.85
7.85
7.84
7.72
7.71
7.71
7.70
7.69
7.69
3.37
2.50
COOH
Br
(3g)
1H NMR, 400 MHz,
DMSO-D6
2.00
2.00
f1 (ppm)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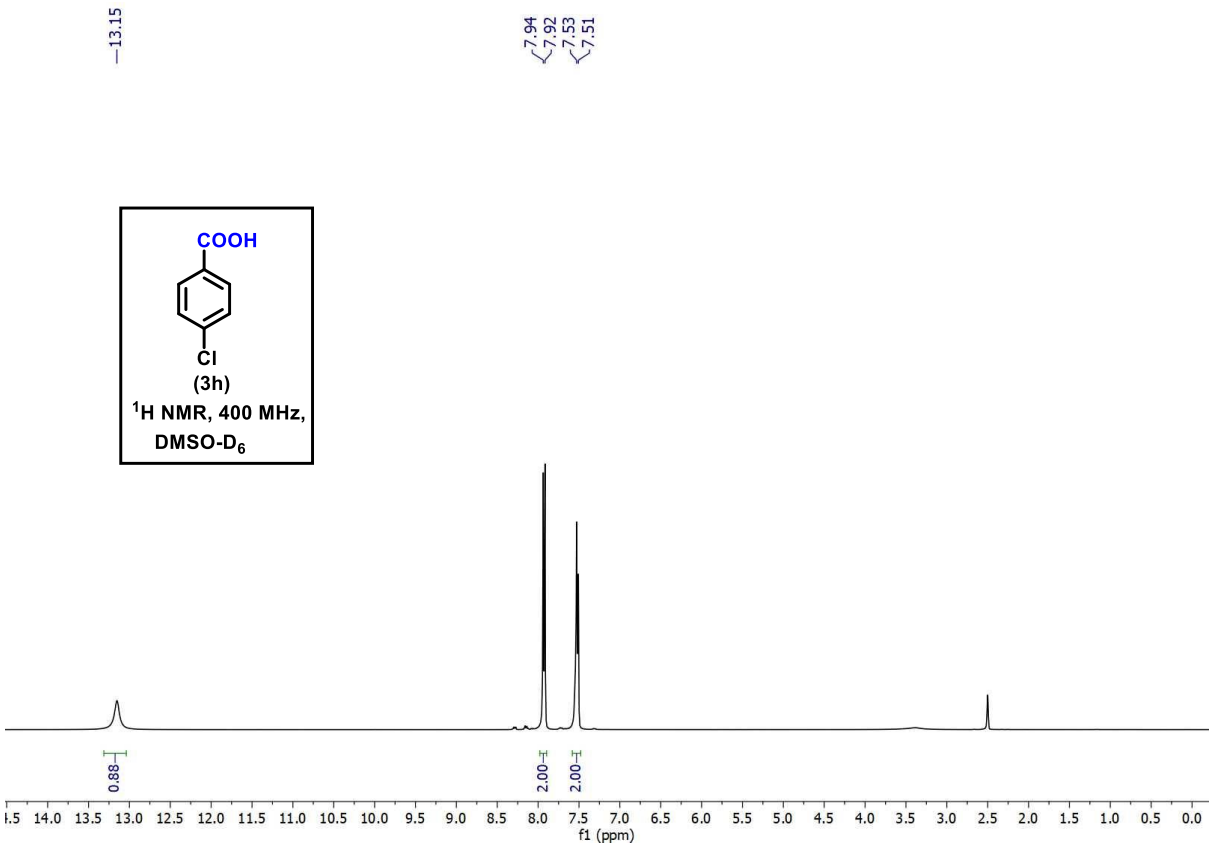
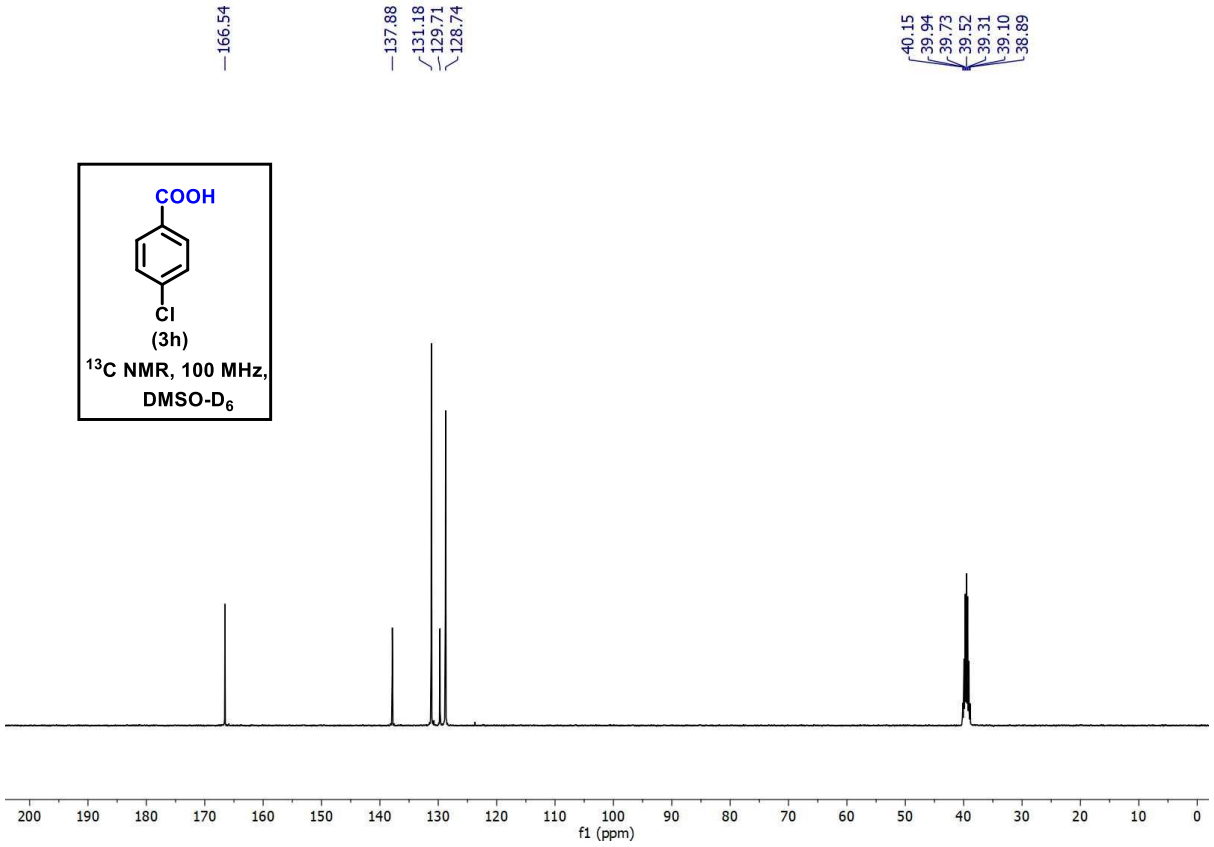
131.79
131.75
131.37
130.07
126.98
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
Br
(3g)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


13.15
7.94
7.92
7.53
7.51
COOH
Cl
(3h)
1H NMR, 400 MHz,
DMSO-D6
0.88
2.00
2.00
f1 (ppm)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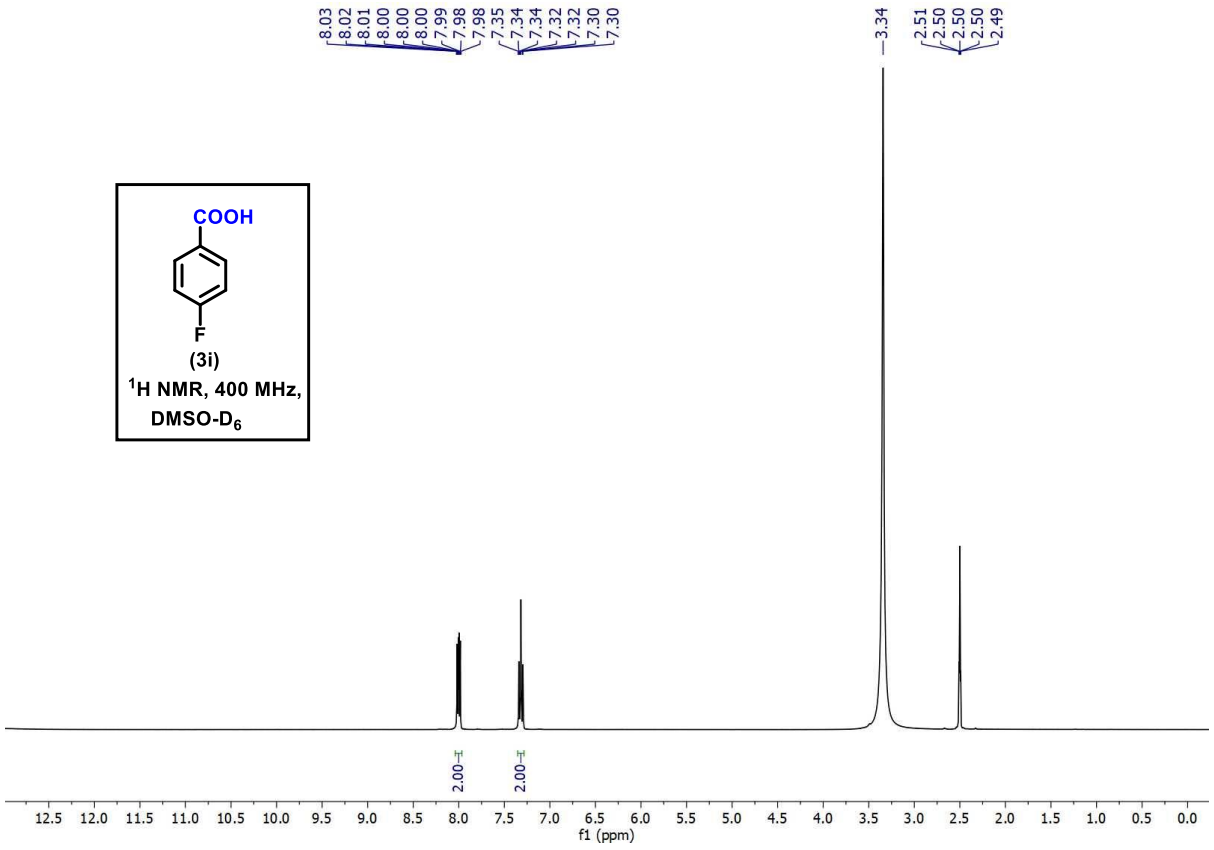
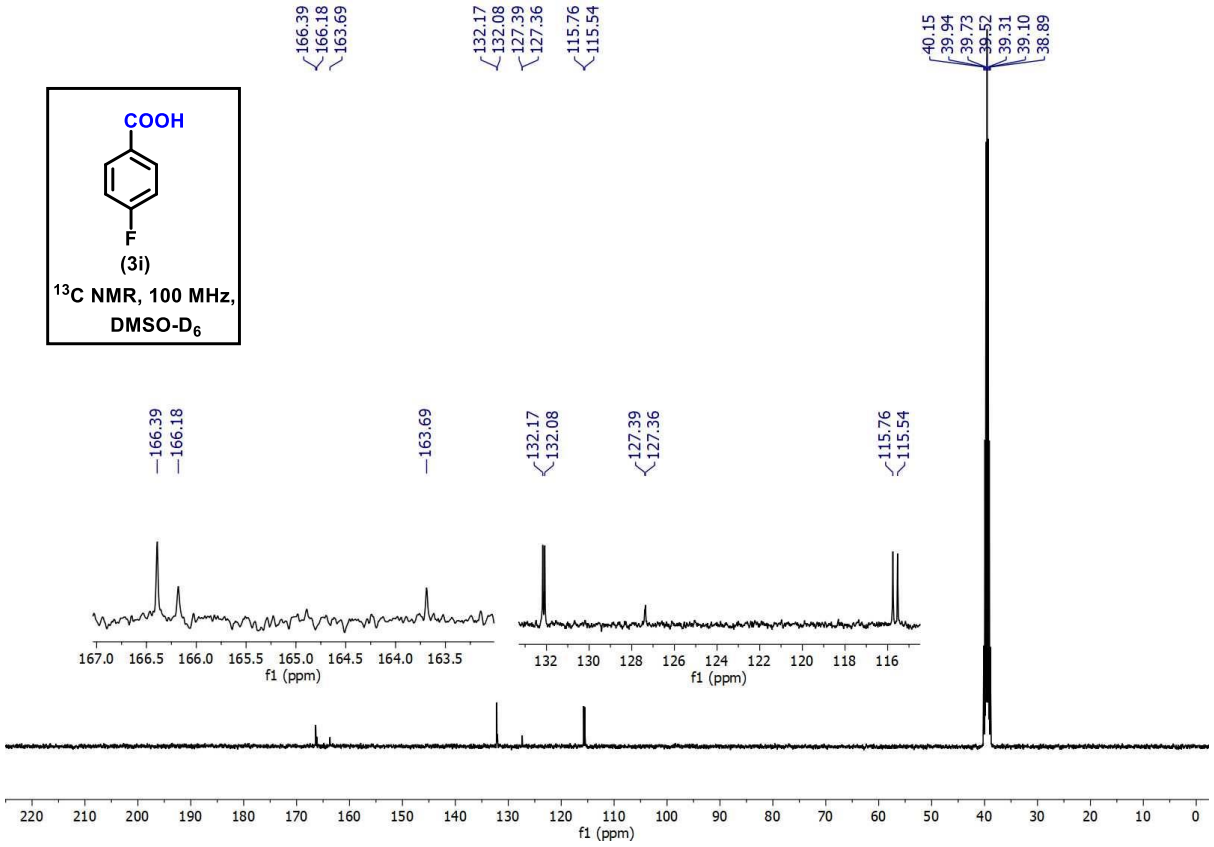
137.88
131.18
129.71
128.74
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
Cl
(3h)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


8.03
8.02
8.01
8.00
8.00
8.00
7.99
7.98
7.98
7.35
7.34
7.34
7.32
7.32
7.30
7.30
3.34
2.51
2.50
2.50
2.50
2.49
COOH
F
(3i)
1H NMR, 400 MHz,
DMSO-D6
2.00
2.00
f1 (ppm)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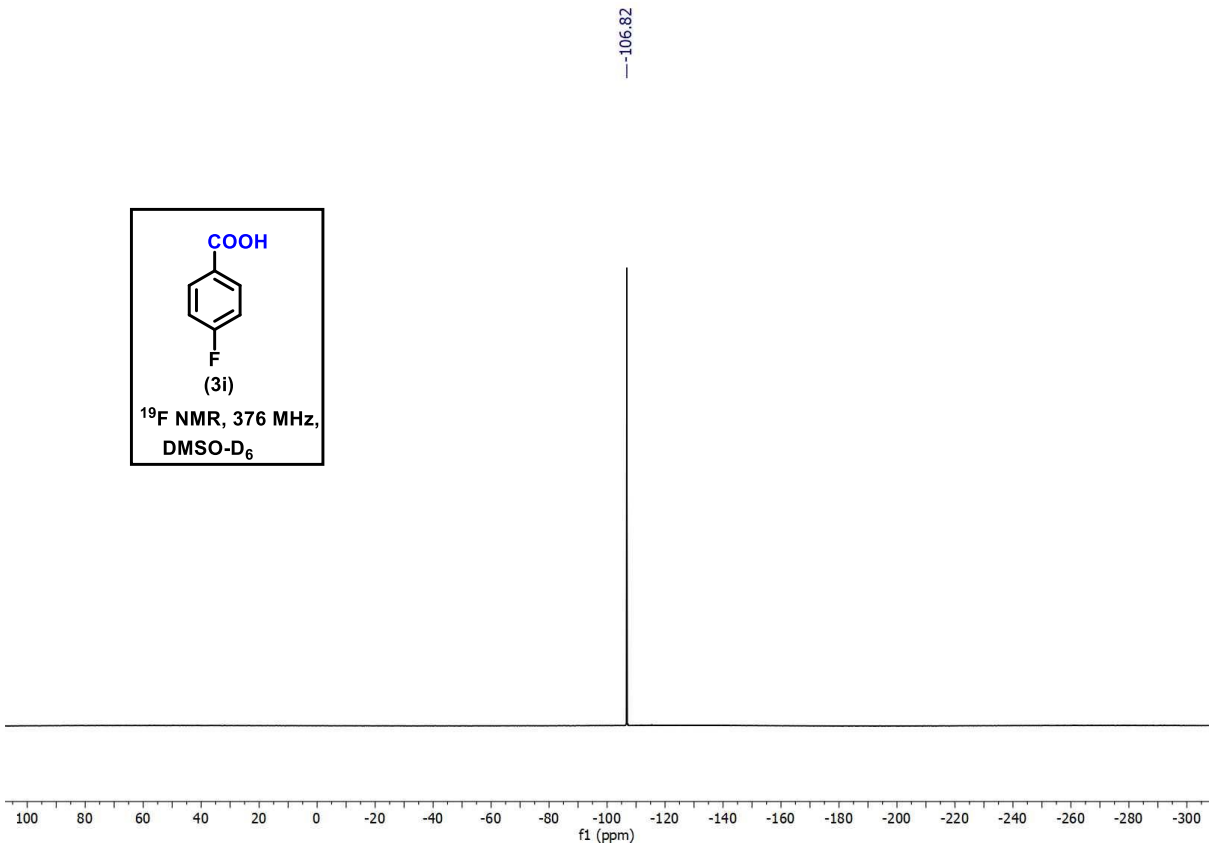
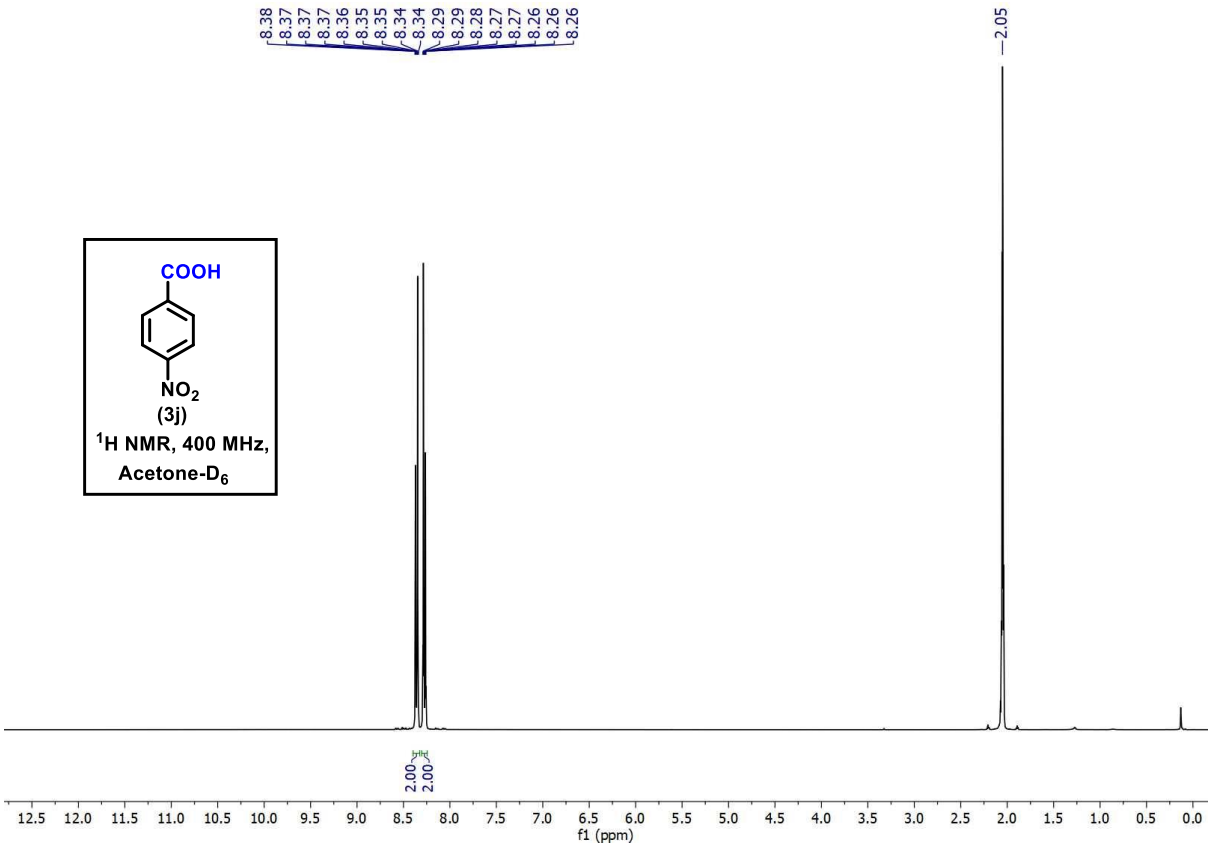
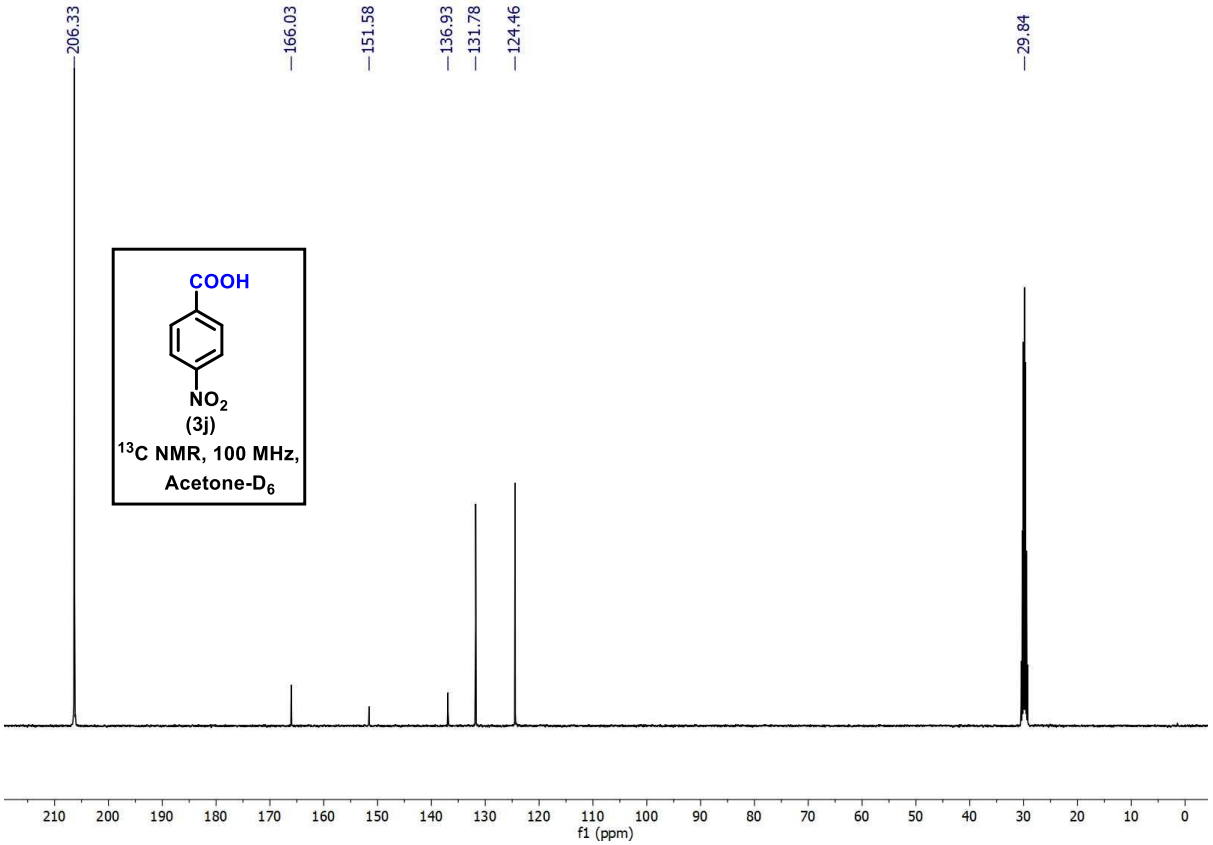
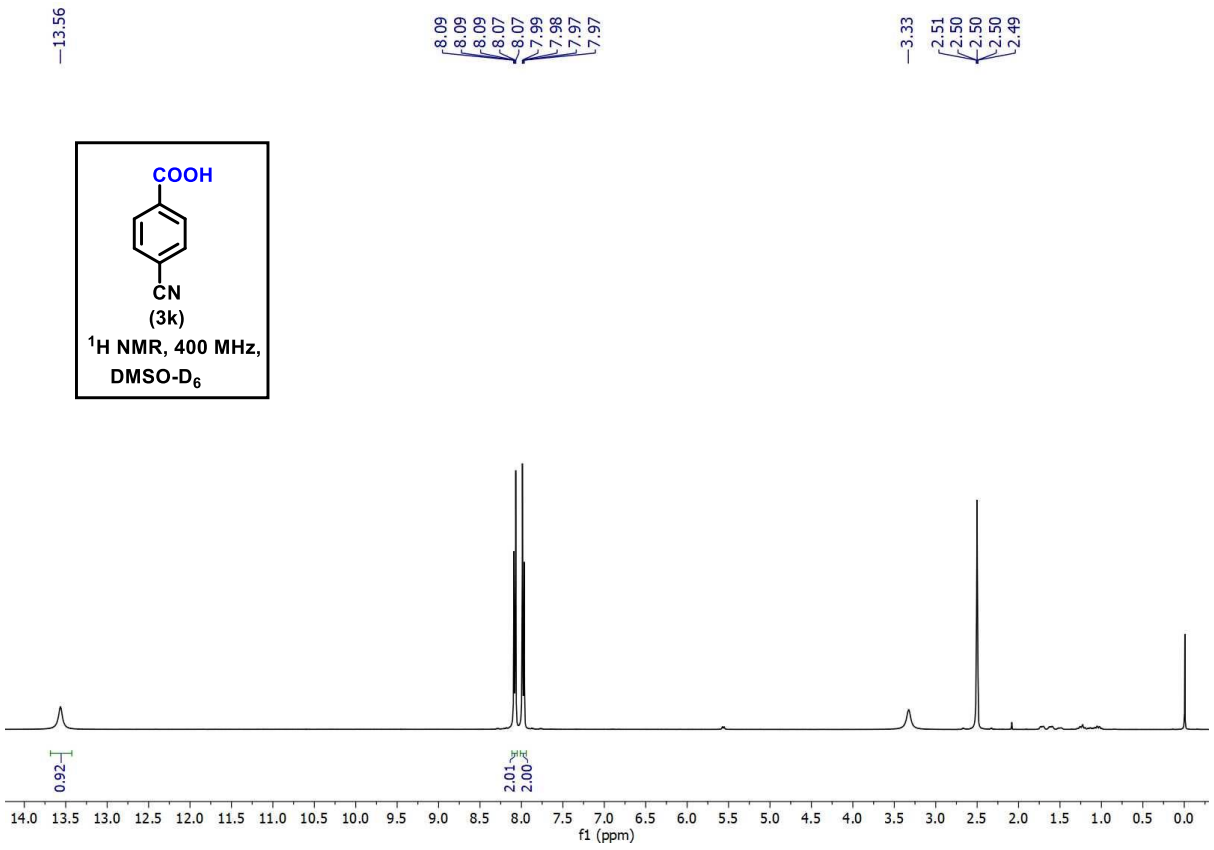
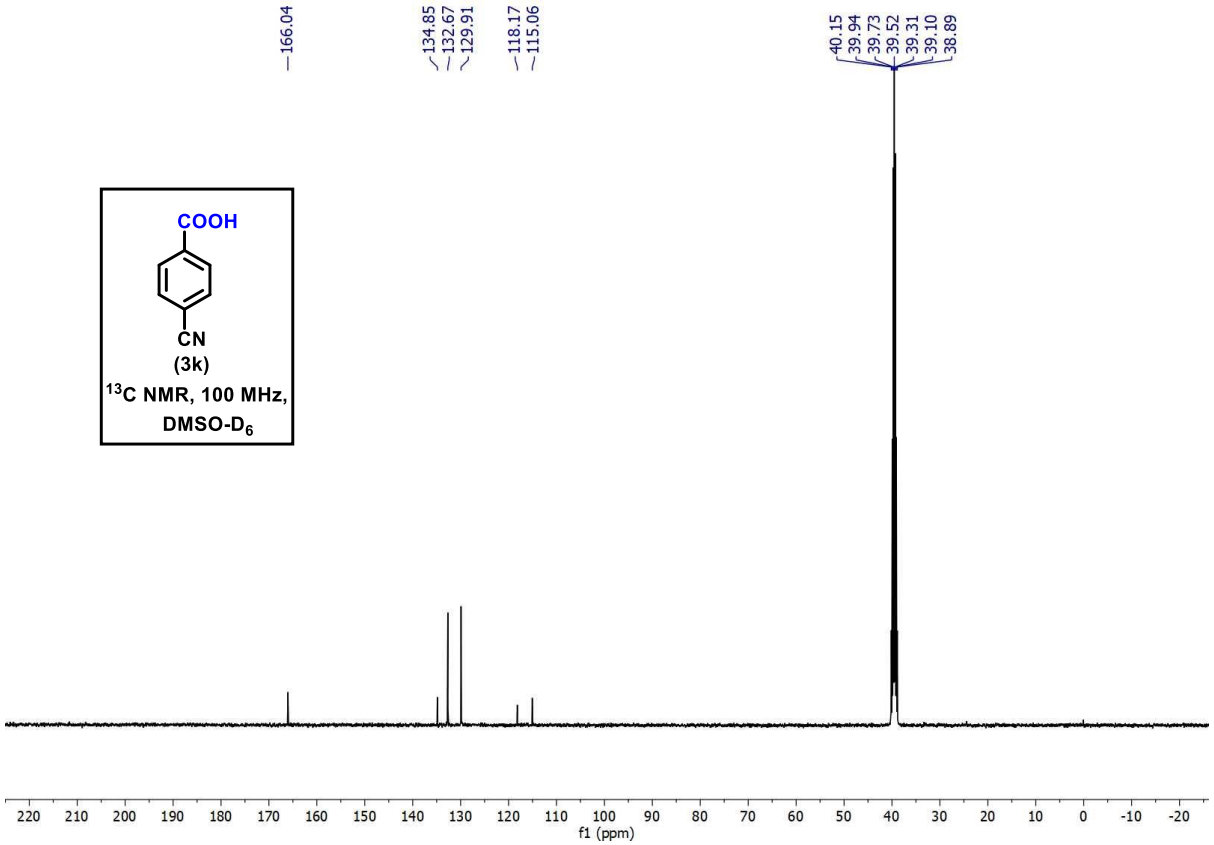
166.18
163.69
132.17
132.08
127.39
127.36
115.76
115.54
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
F
(3i)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)
f1 (ppm)
f1 (ppm)

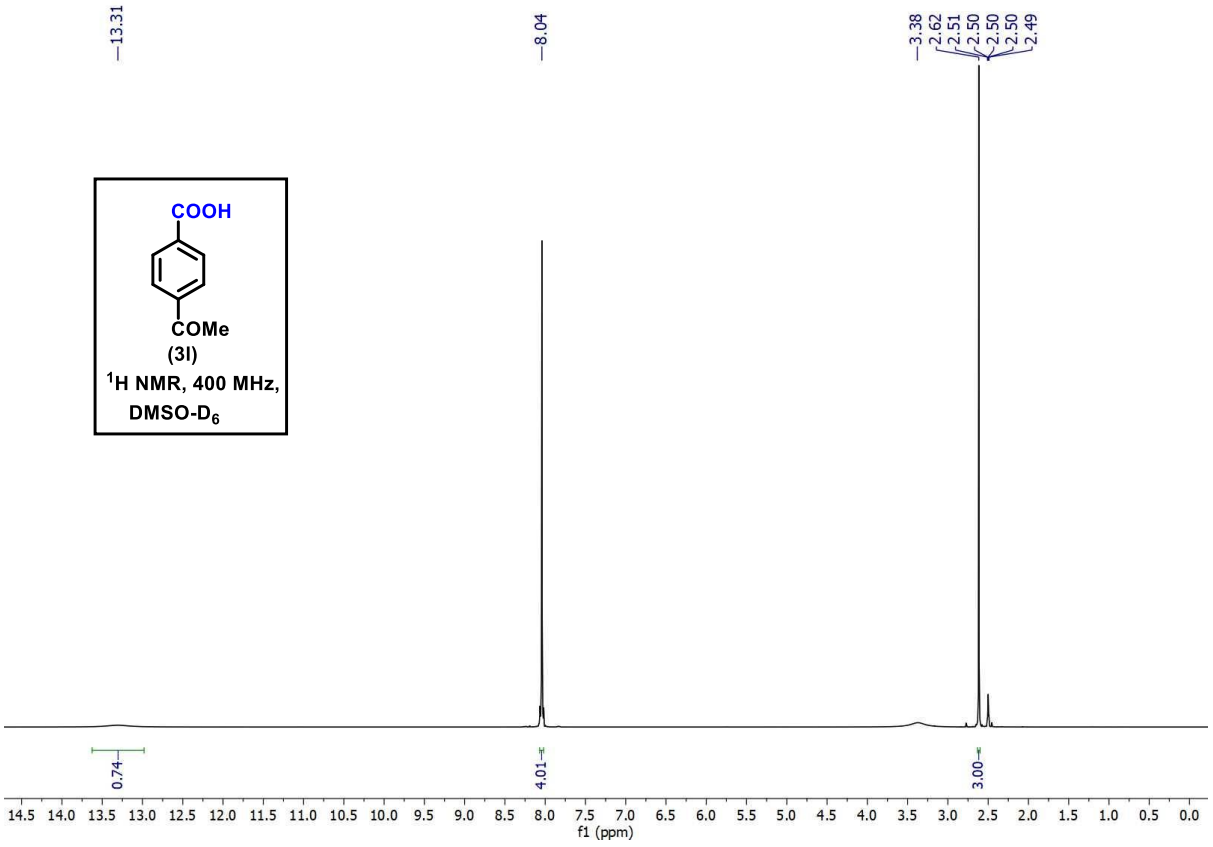

-106.82
COOH
F
(3i)
19F NMR, 376 MHz,
DMSO-D6
100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240 -260 -280 -300
f1 (ppm)

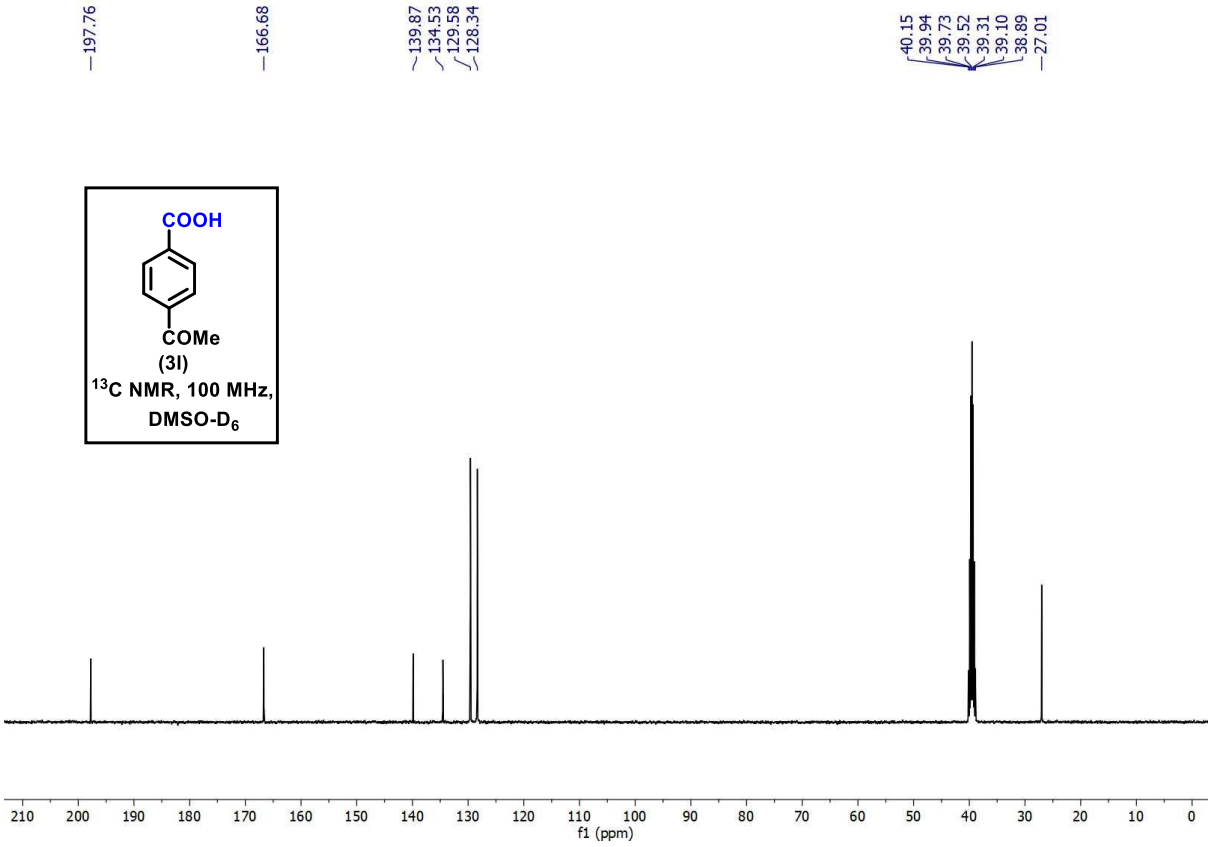

8.38
8.37
8.37
8.37
8.36
8.35
8.35
8.34
8.34
8.29
8.29
8.28
8.27
8.27
8.26
8.26
8.26
2.05
COOH
NO2
(3j)
1H NMR, 400 MHz,
Acetone-D6
2.00
2.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


206.33
166.03
151.58
136.93
131.78
124.46
29.84
COOH
NO2
(3j)
13C NMR, 100 MHz,
Acetone-D6
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


13.56
8.09
8.09
8.09
8.07
8.07
7.99
7.98
7.97
7.97
3.33
2.51
2.50
2.50
2.50
2.49
COOH
CN
(3k)
1H NMR, 400 MHz,
DMSO-D6
0.92
2.01
2.00
14.0 13.5 13.0 12.5 12.0 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 0.0
f1 (ppm)


166.04
134.85
132.67
129.91
118.17
115.06
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
CN
(3k)
13C NMR, 100 MHz,
DMSO-D6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


13.31
8.04
3.38
2.62
2.51
2.50
2.50
2.50
2.49
COOH
COMe
(3l)
^{1}H NMR, 400 MHz,
DMSO-D$_6$
0.74
4.01
3.00
14.5 14.0 13.5 13.0 12.5 12.0 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 0.0
f1 (ppm)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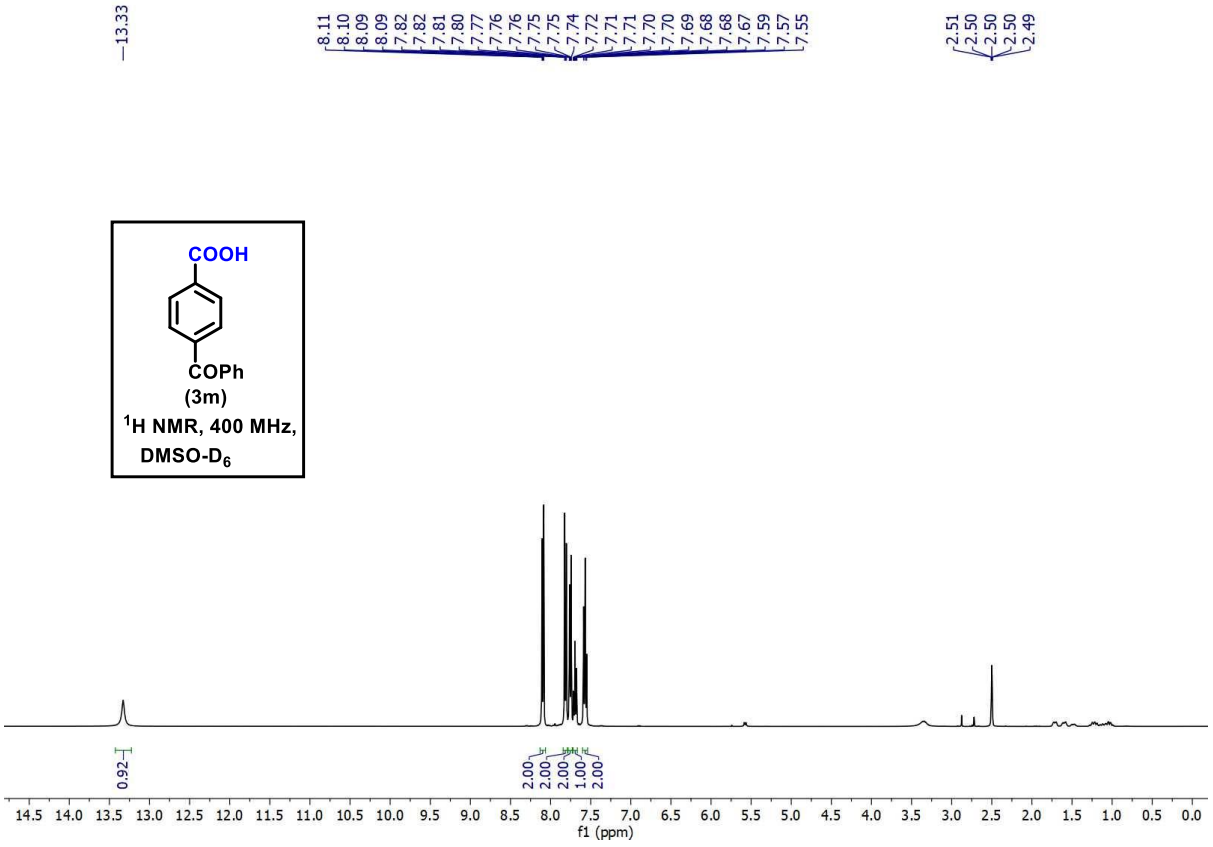
139.87
134.53
129.58
128.34
40.15
39.94
39.73
39.52
39.31
39.10
38.89
27.01
COOH
COMe
(3l)
^{13}C NMR, 100 MHz,
DMSO-D$_6$
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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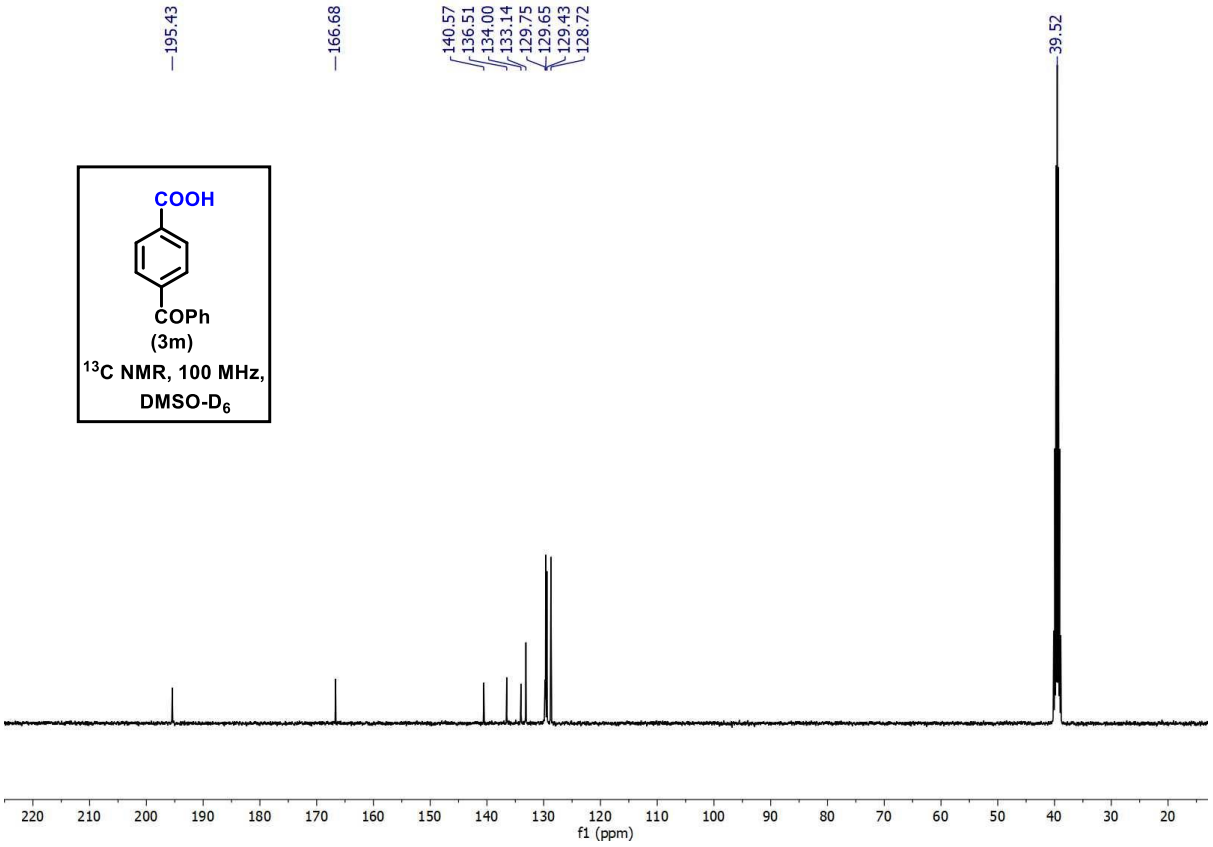
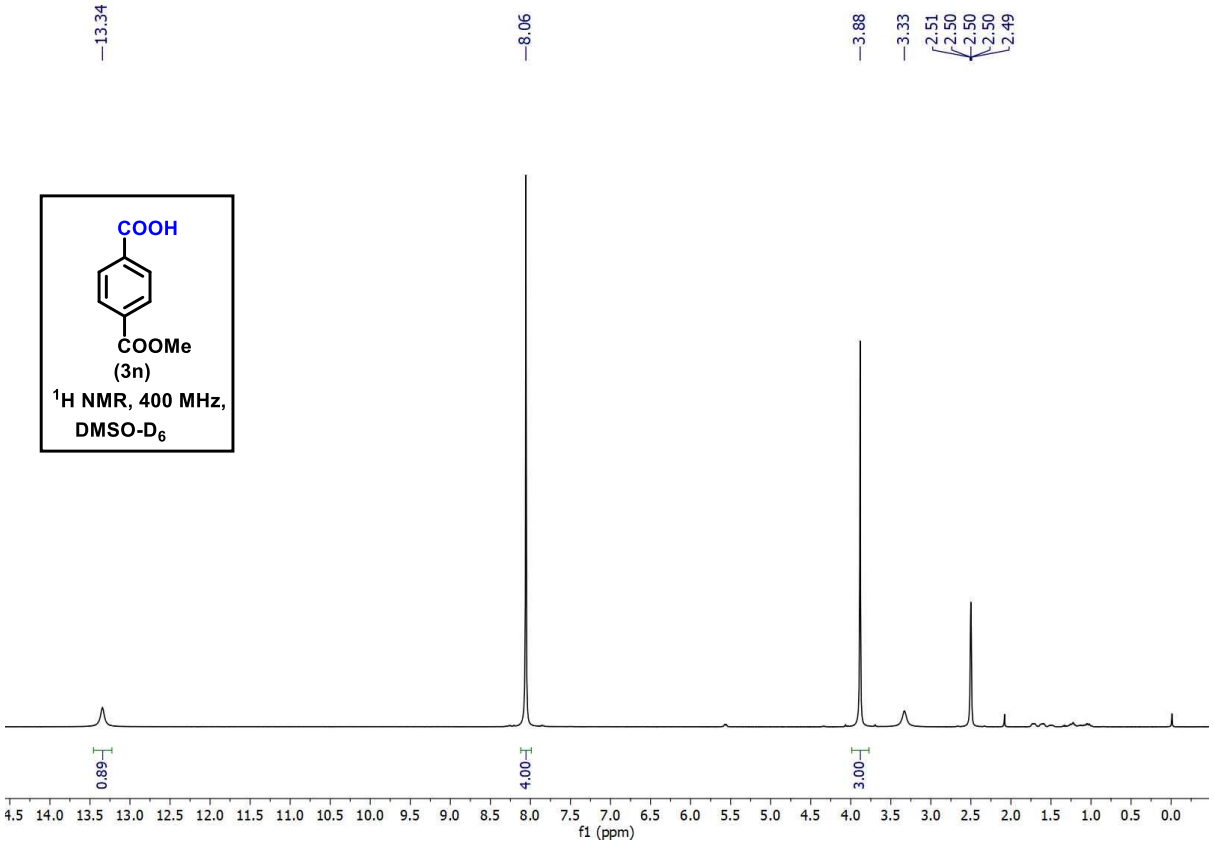
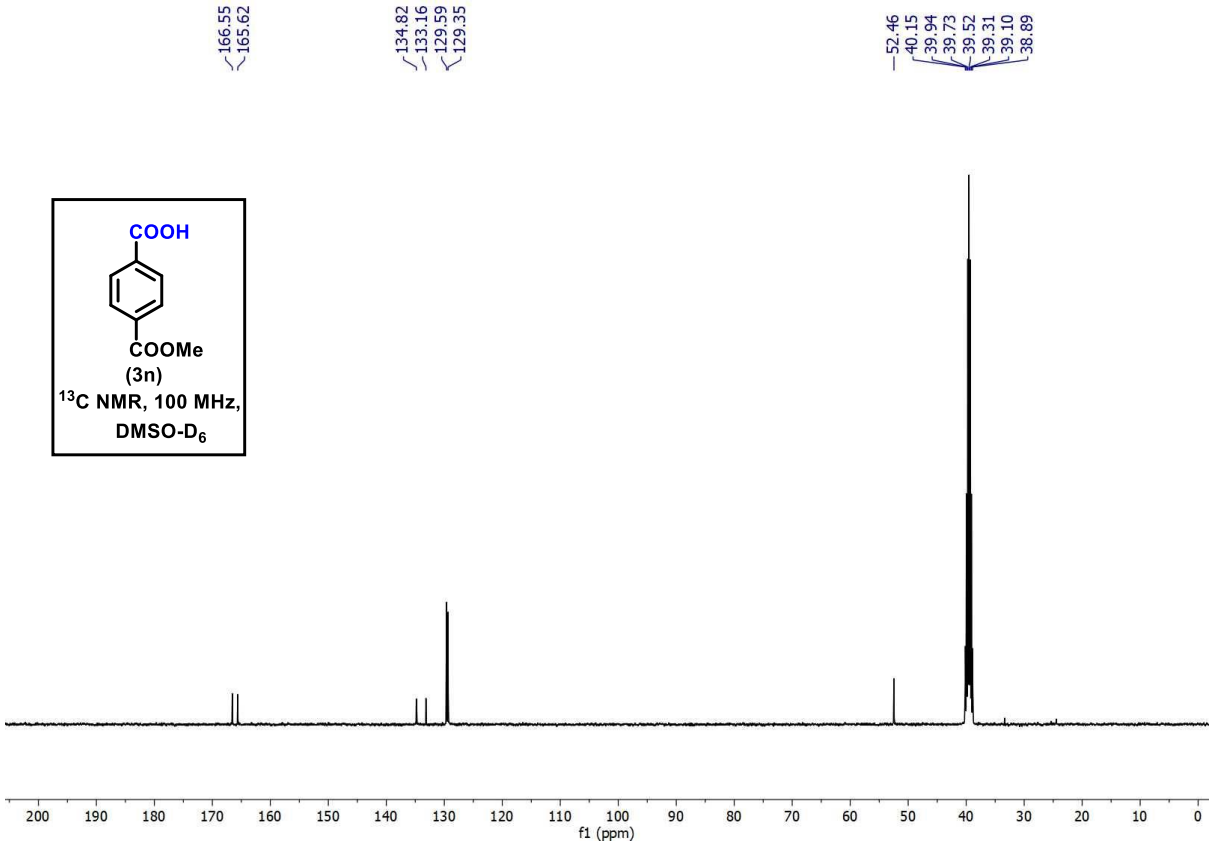
8.11
8.10
8.09
8.09
7.82
7.82
7.81
7.80
7.77
7.76
7.76
7.75
7.75
7.74
7.72
7.71
7.71
7.70
7.70
7.69
7.68
7.68
7.67
7.59
7.57
7.55
2.51
2.50
2.50
2.50
2.49
COOH
COPh
(3m)
1H NMR, 400 MHz,
DMSO-D6
0.92
2.00
2.00
2.00
1.00
2.00
f1 (ppm)


195.43
166.68
140.57
136.51
134.00
133.14
129.75
129.65
129.43
128.72
39.52
COOH
COPh
(3m)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


13.34
8.06
3.88
3.33
2.51
2.50
2.50
2.50
2.49
COOH
COOMe
(3n)
1H NMR, 400 MHz,
DMSO-D6
0.89
4.00
3.00
f1 (ppm)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165.62
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133.16
129.59
129.35
52.46
40.15
39.94
39.73
39.52
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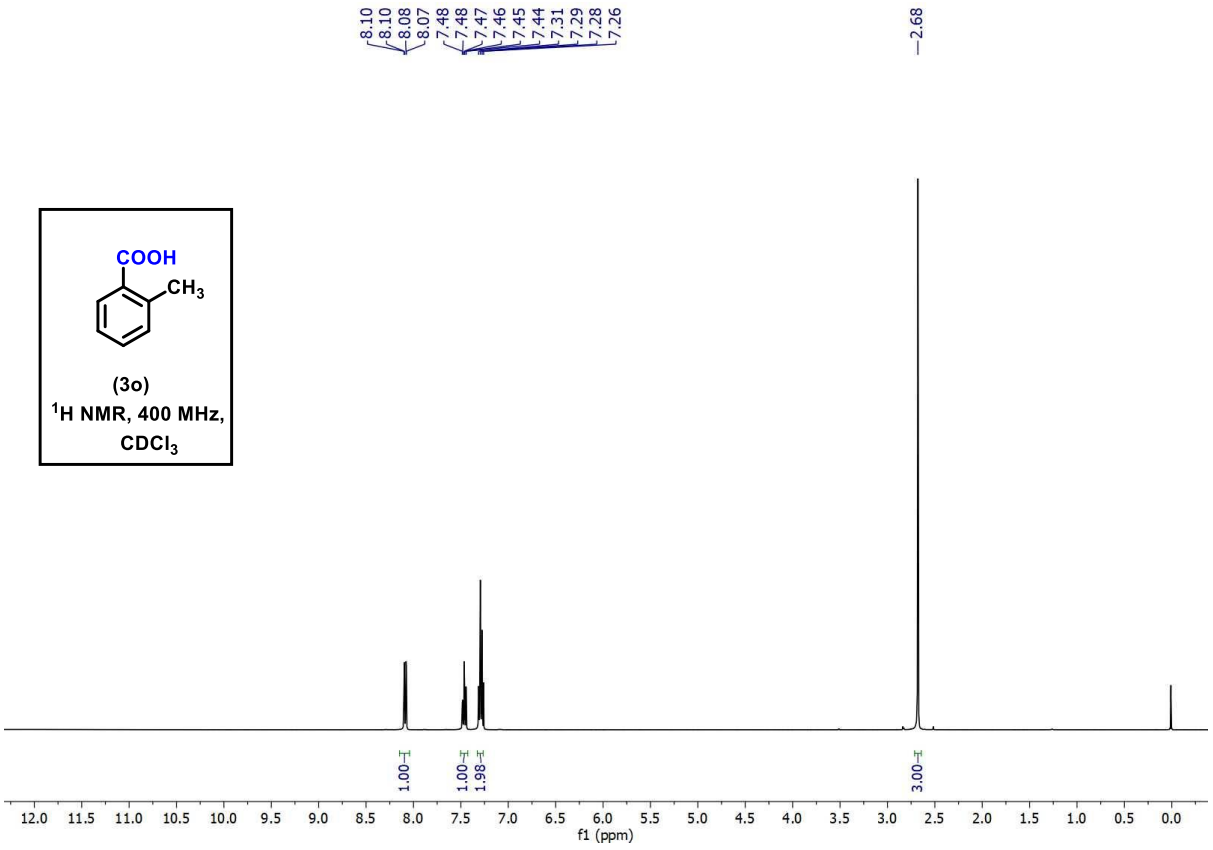
39.10
38.89
COOH
COOMe
(3n)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)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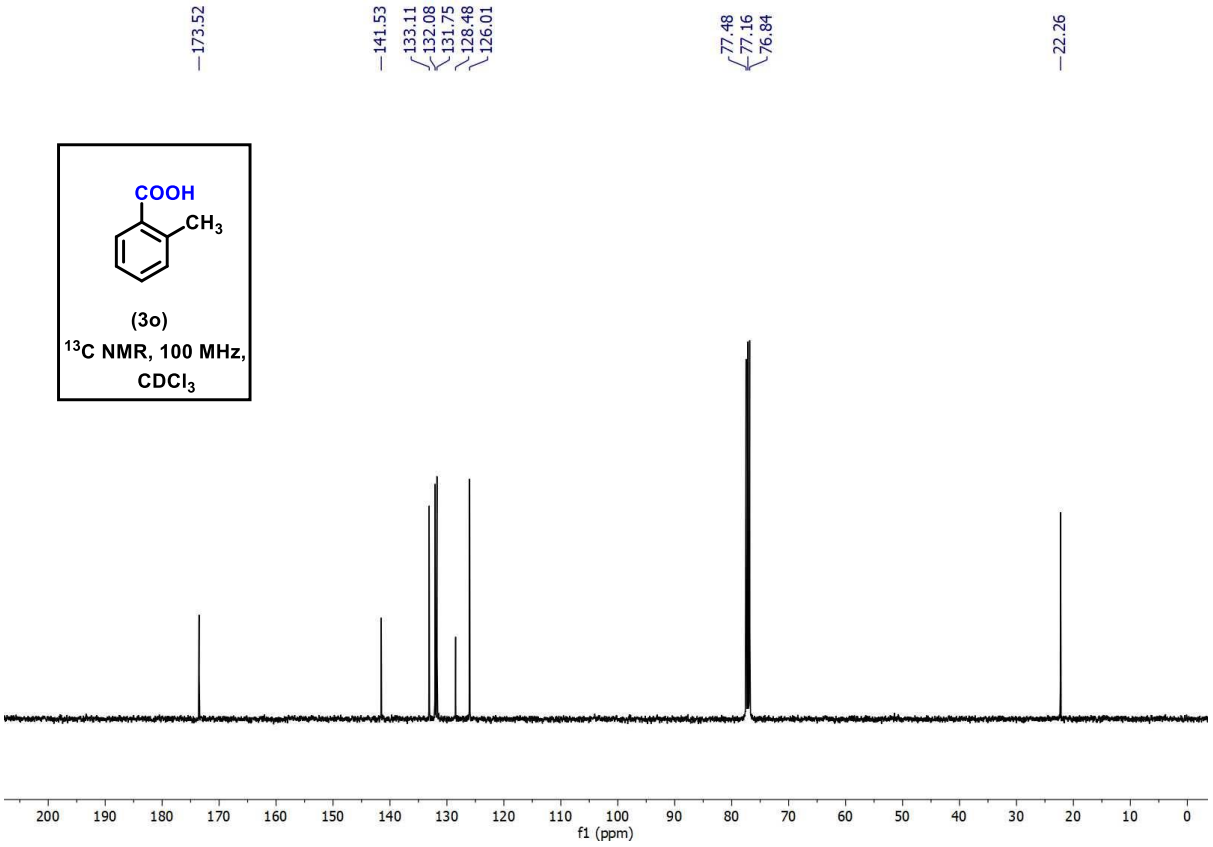
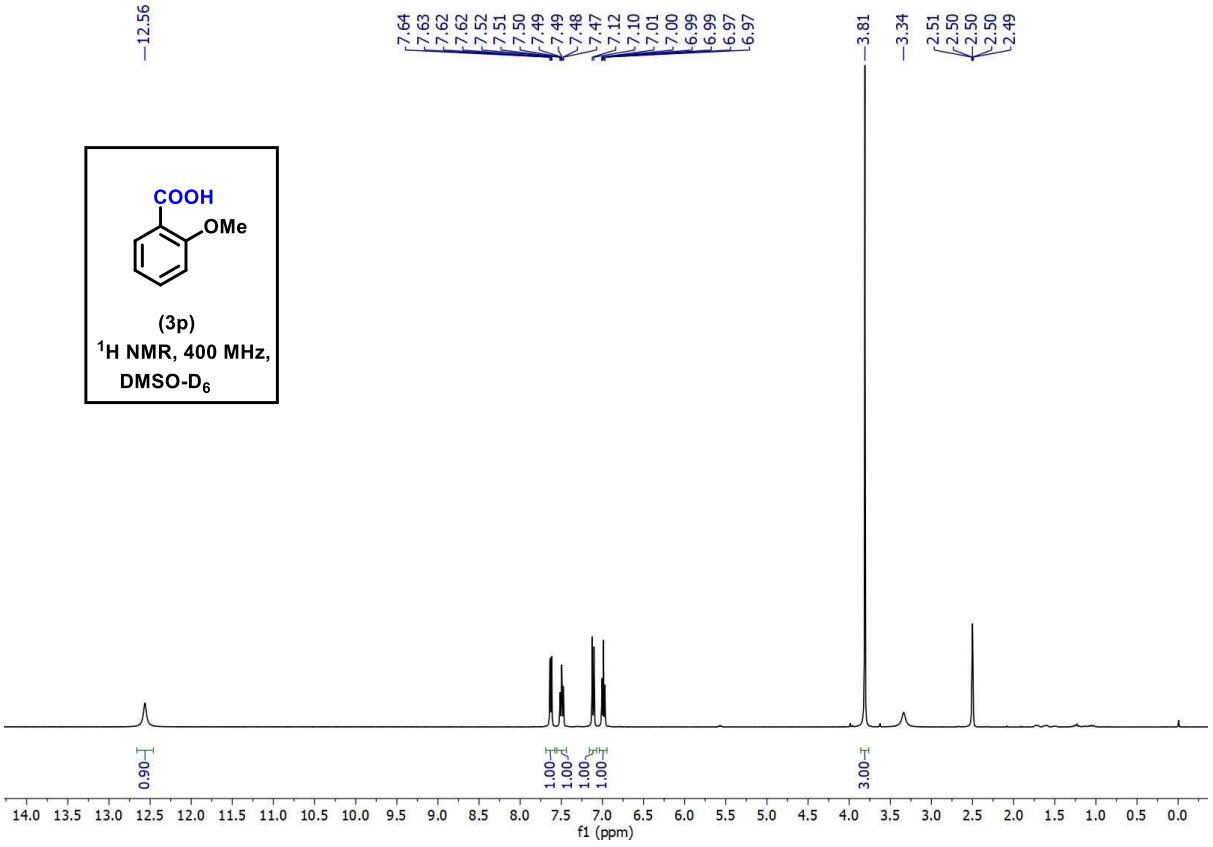
8.10
8.08
8.07
7.48
7.48
7.47
7.46
7.45
7.44
7.31
7.29
7.28
7.26
2.68
COOH
CH3
(3o)
1H NMR, 400 MHz,
CDCl3
1.00
1.00
1.98
3.00
f1 (ppm)


173.52
141.53
133.11
132.08
131.75
128.48
126.01
77.48
77.16
76.84
22.26
COOH
CH3
(3o)
13C NMR, 100 MHz,
CDCl3
f1 (ppm)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7.63
7.62
7.62
7.52
7.51
7.50
7.49
7.49
7.48
7.47
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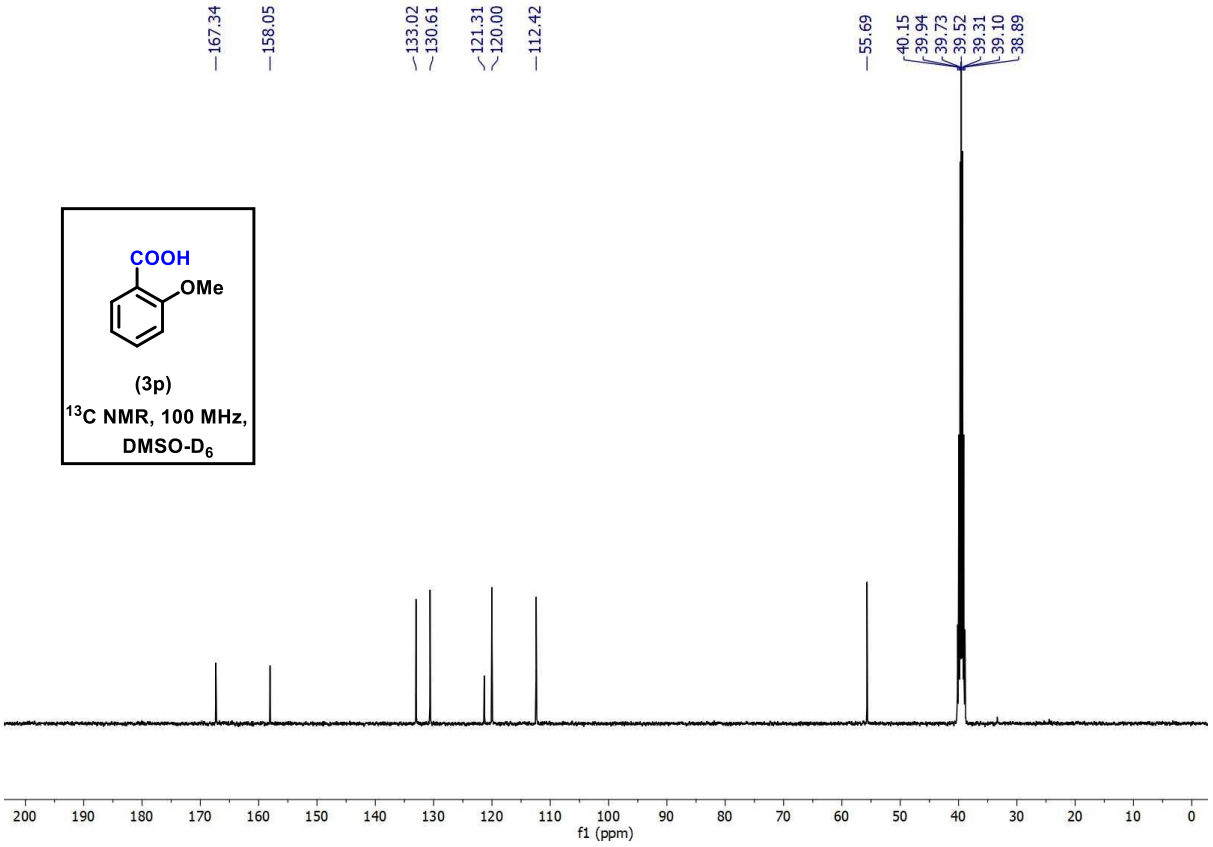
7.10
7.01
7.00
6.99
6.99
6.97
6.97
3.81
3.34
2.51
2.50
2.50
2.50
2.49
COOH
OMe
(3p)
1H NMR, 400 MHz,
DMSO-D6
0.90
1.00
1.00
1.00
1.00
3.00
f1 (ppm)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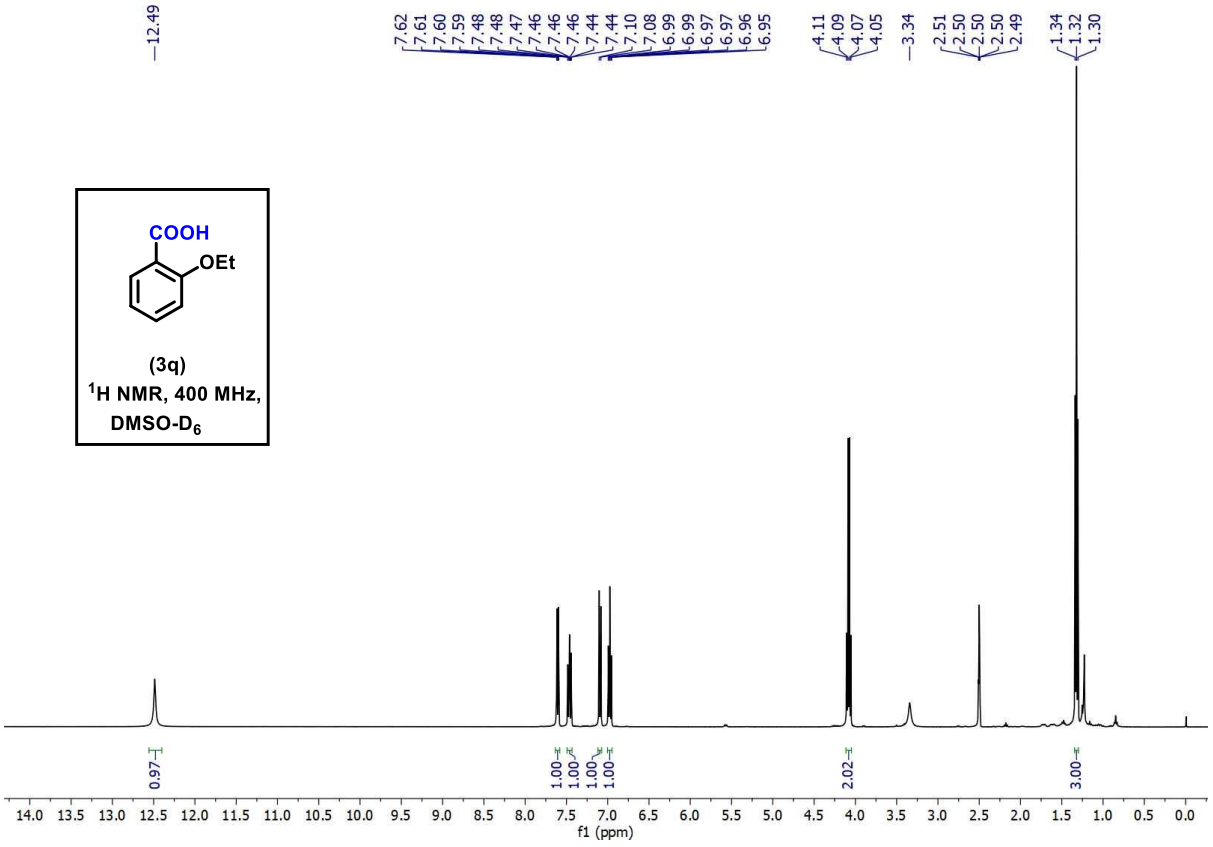
120.00
112.42
55.69
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
OMe
(3p)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)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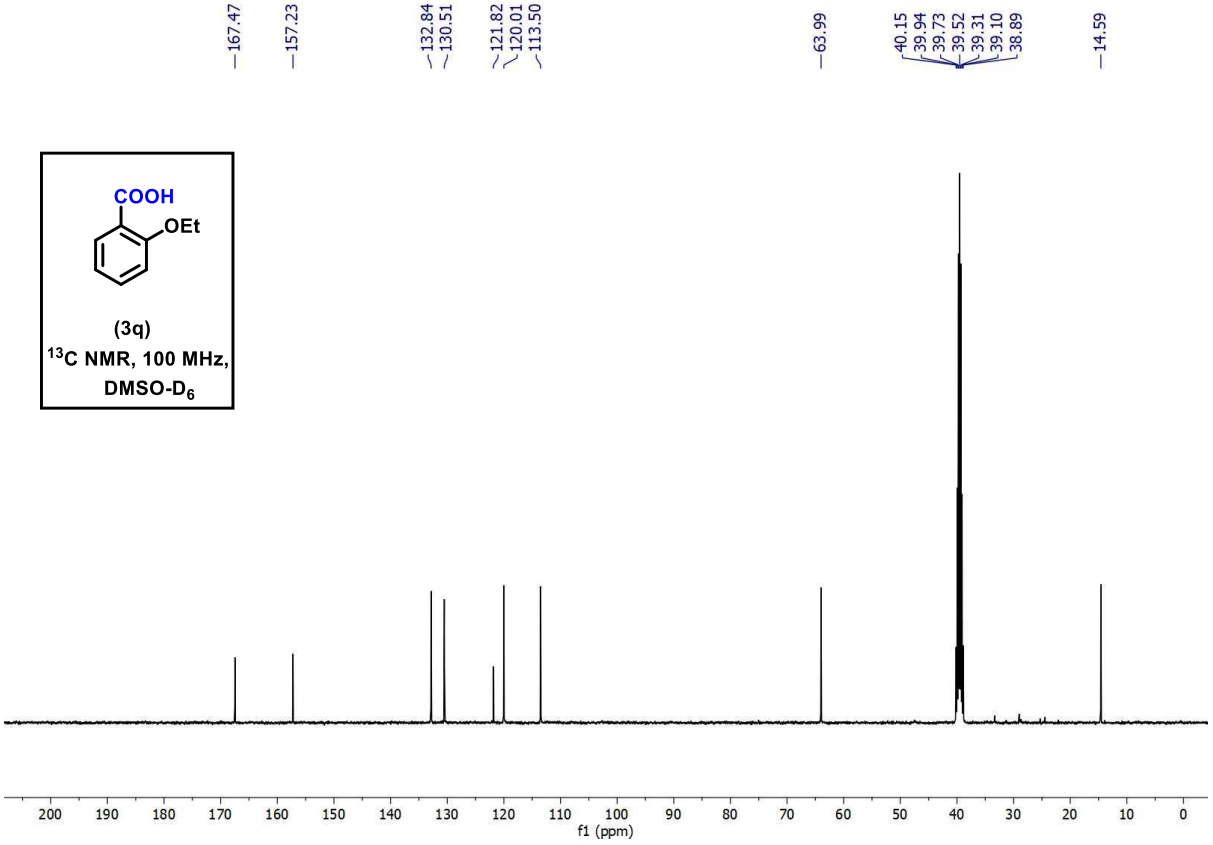
7.59
7.48
7.48
7.47
7.46
7.46
7.46
7.44
7.44
7.10
7.08
6.99
6.99
6.97
6.97
6.96
6.95
4.11
4.09
4.07
4.05
3.34
2.51
2.50
2.50
2.50
2.49
1.34
1.32
1.30
COOH
OEt
(3q)
1H NMR, 400 MHz,
DMSO-D6
0.97
1.00
1.00
1.00
1.00
2.02
3.00
f1 (ppm)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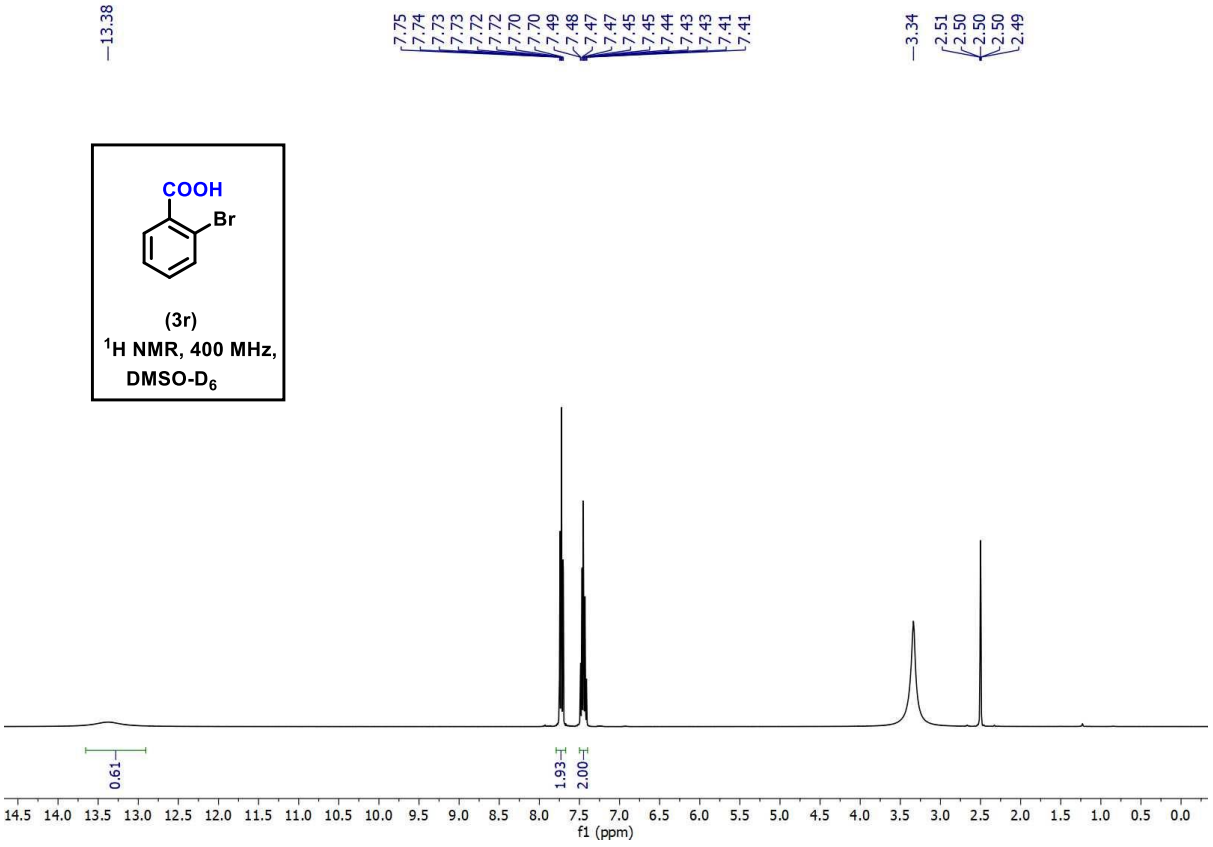
130.51
121.82
120.01
113.50
63.99
40.15
39.94
39.73
39.52
39.31
39.10
38.89
14.59
COOH
OEt
(3q)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)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7.73
7.73
7.72
7.72
7.70
7.70
7.49
7.48
7.47
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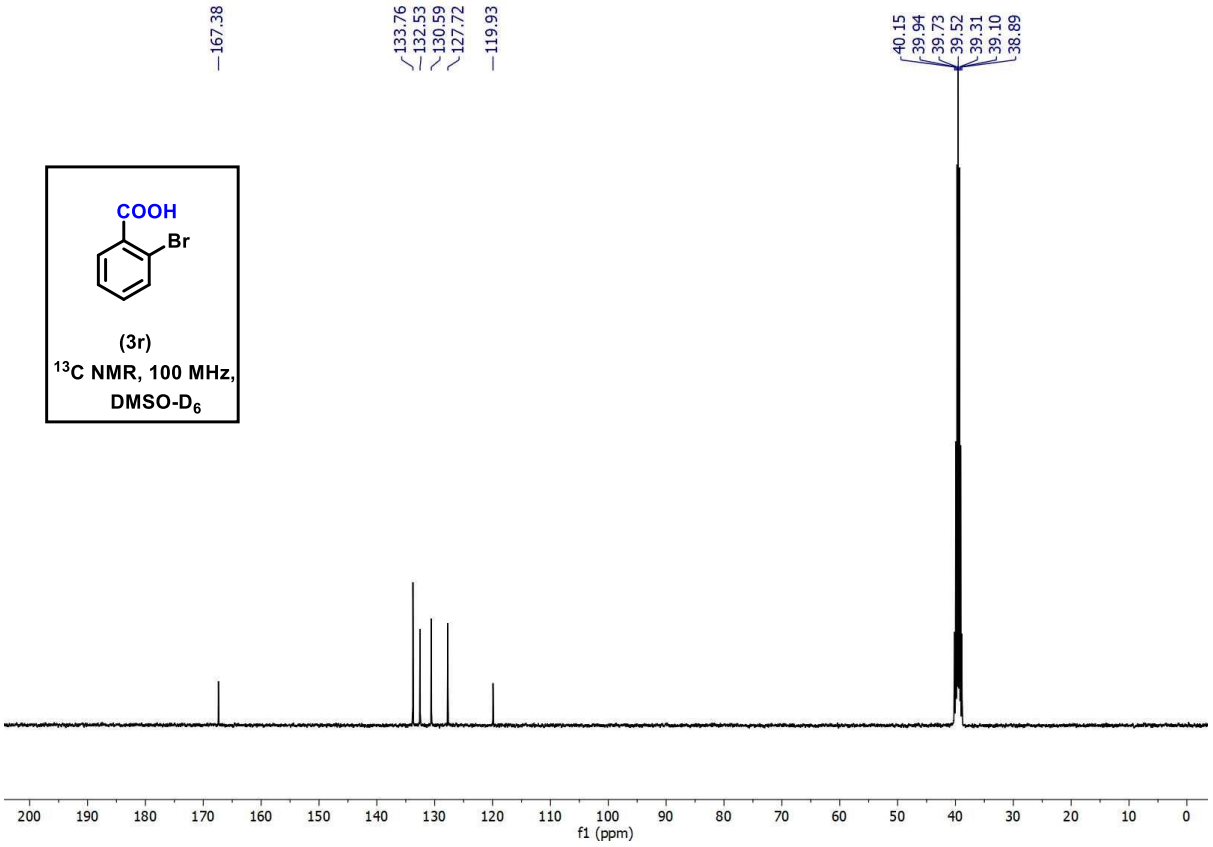
7.45
7.45
7.44
7.43
7.43
7.41
7.41
3.34
2.51
2.50
2.50
2.50
2.49
COOH
Br
(3r)
1H NMR, 400 MHz,
DMSO-D6
0.61
1.93
2.00
f1 (ppm)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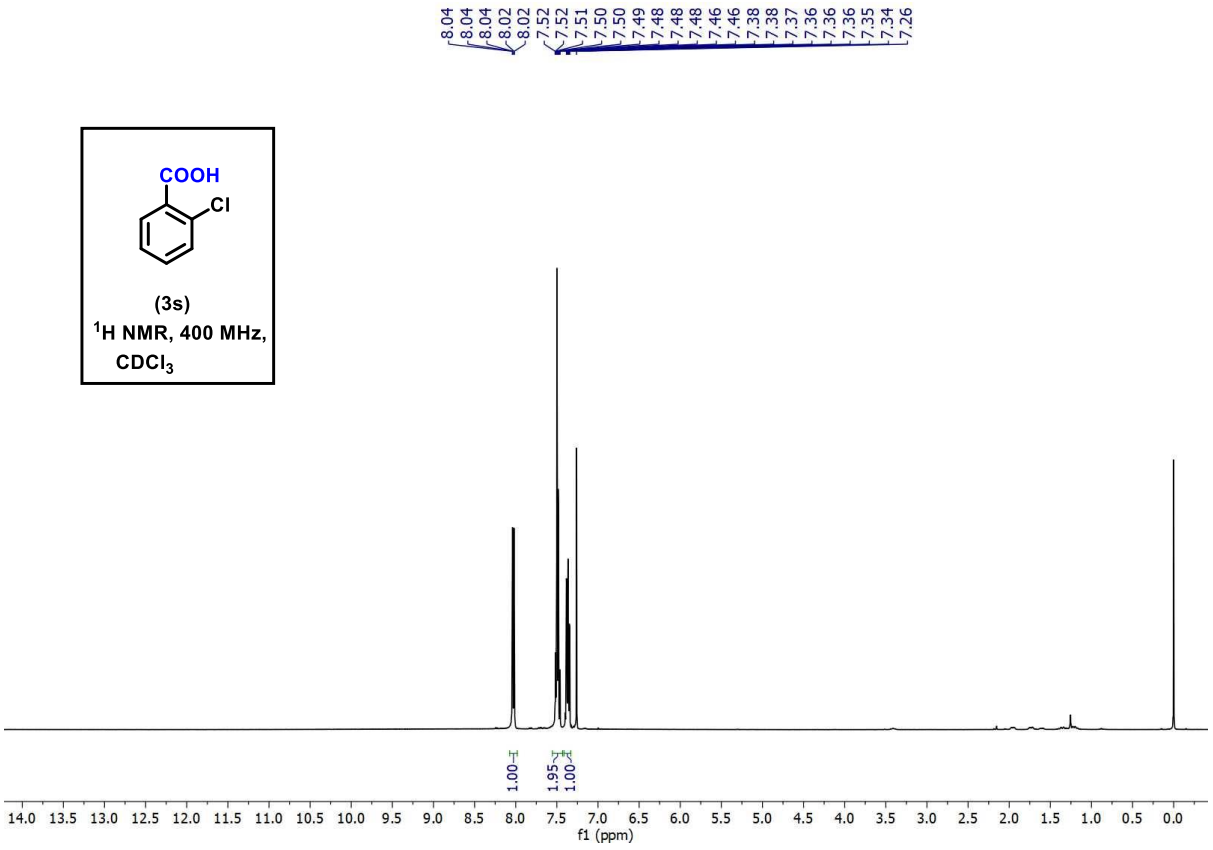
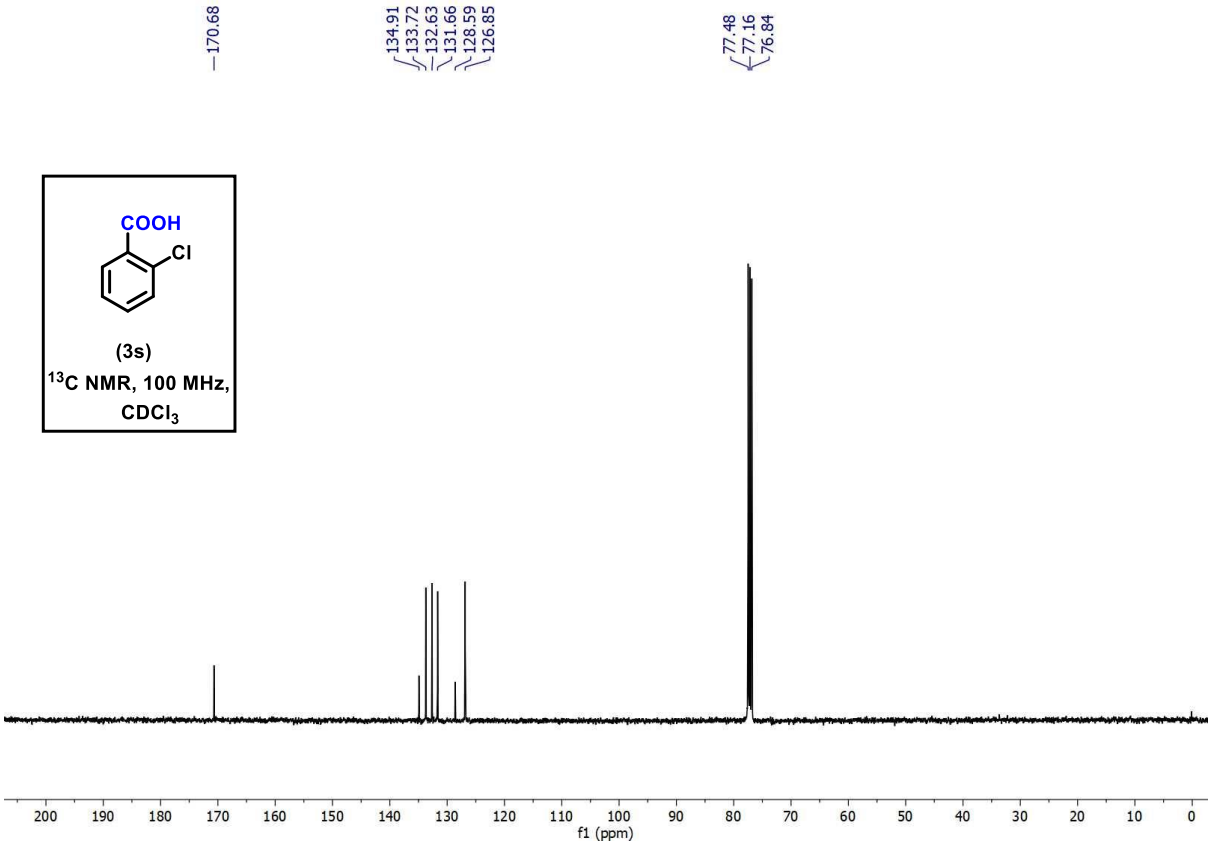
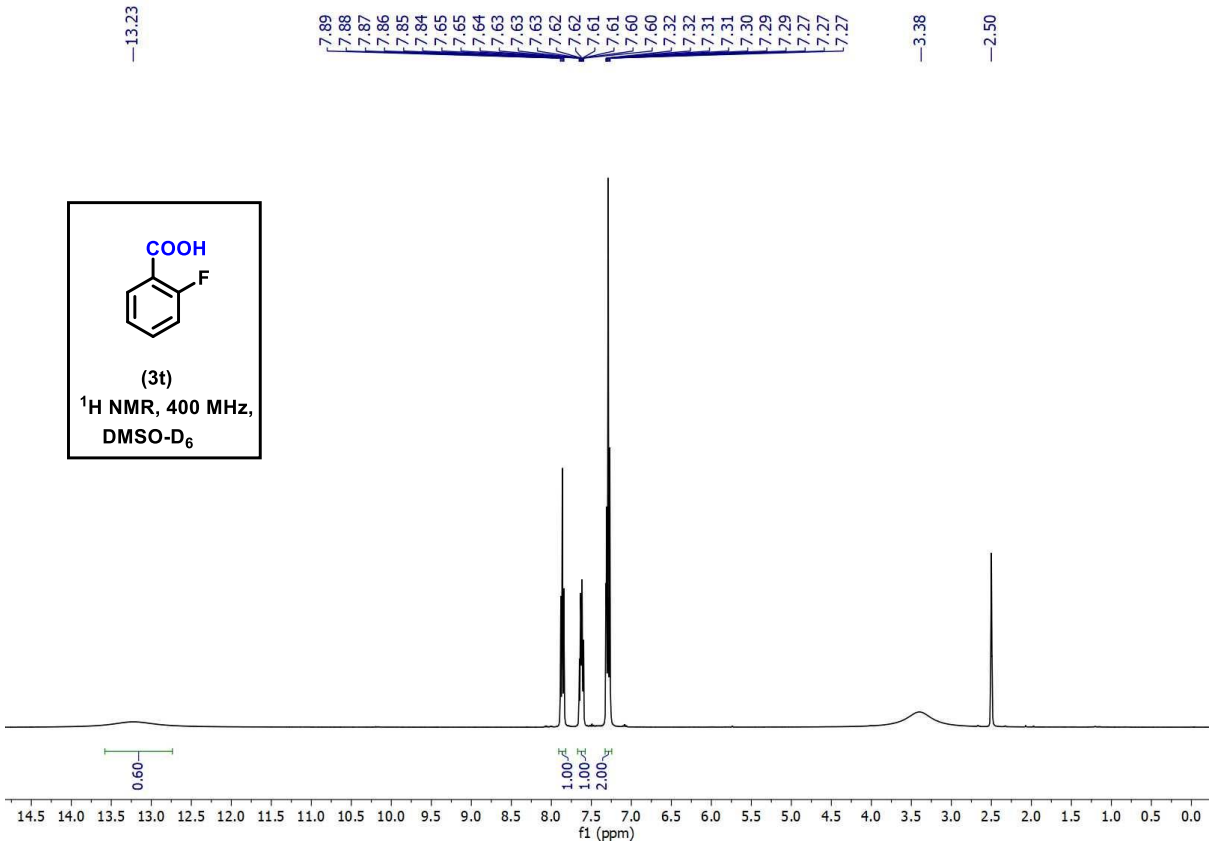
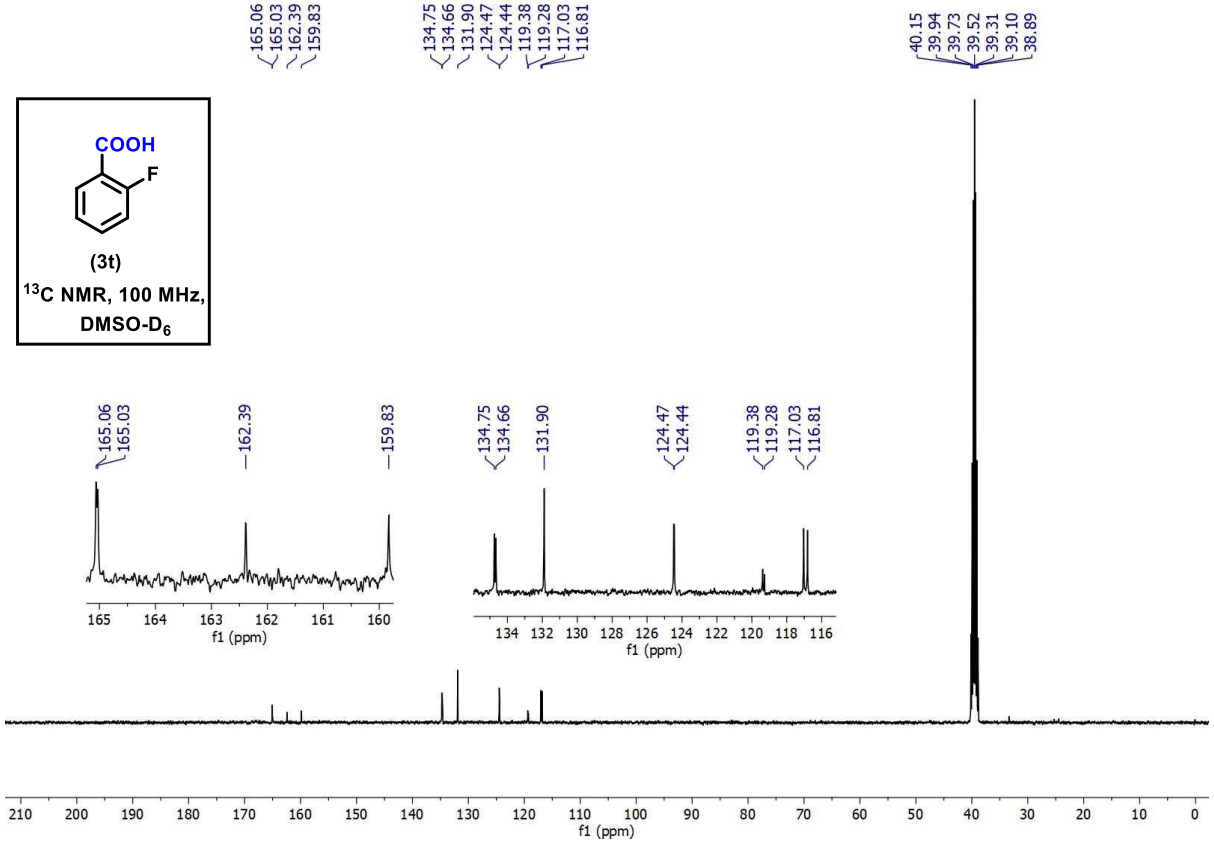
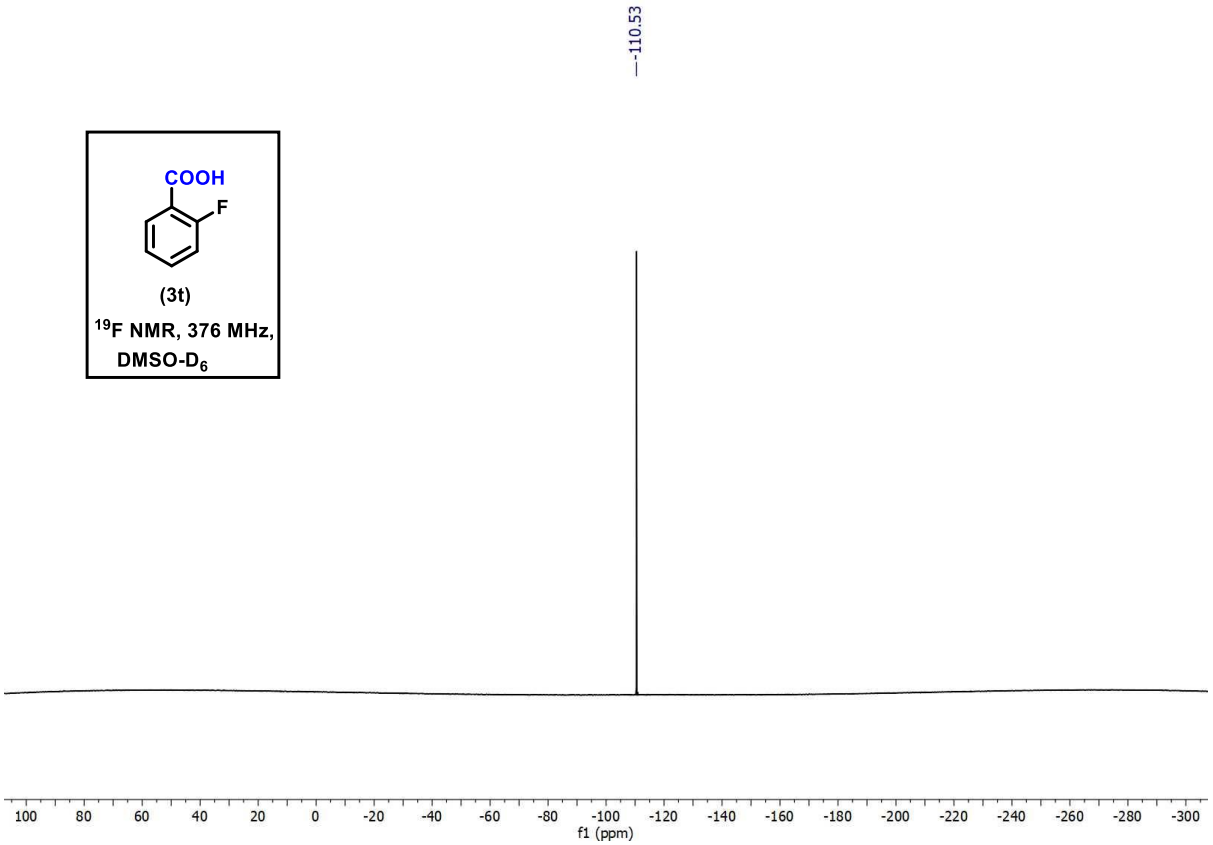
130.59
127.72
119.93
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
Br
(3r)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)

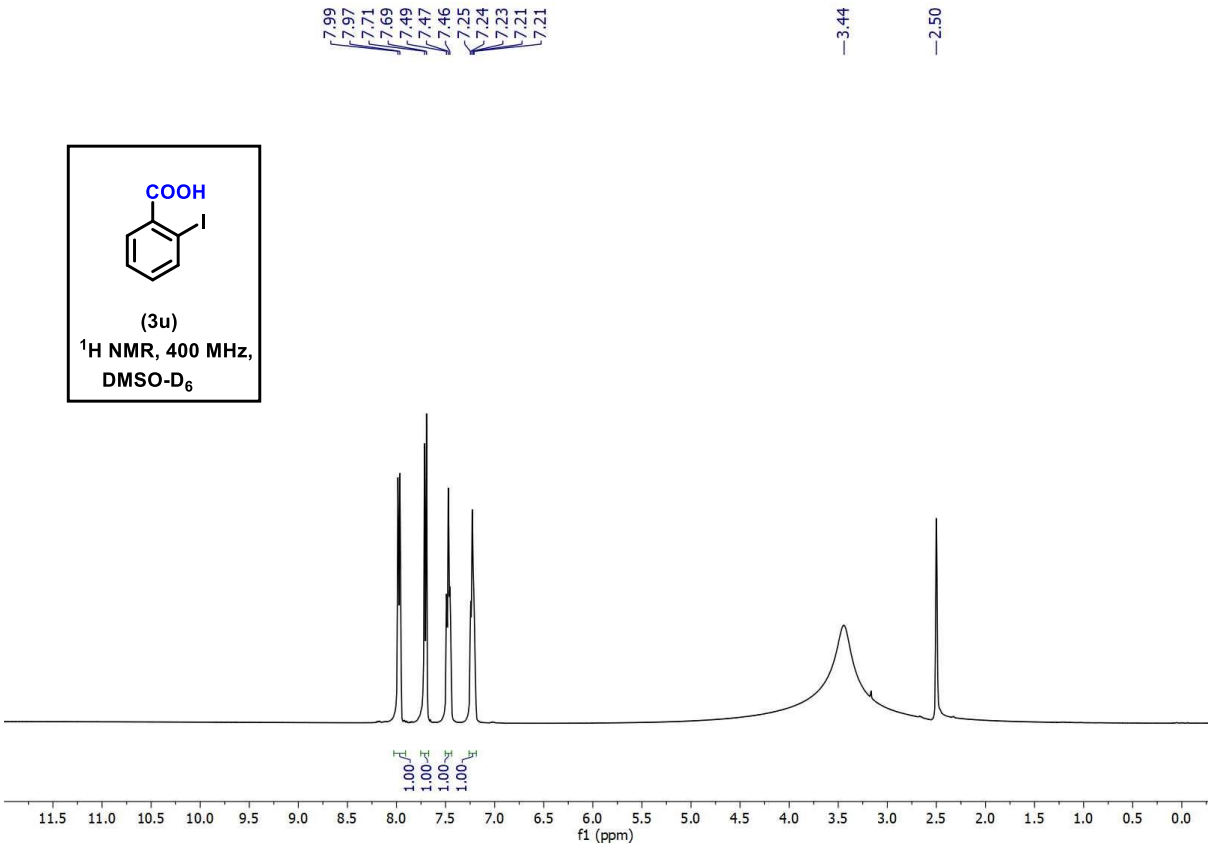

8.04
8.04
8.04
8.02
8.02
7.52
7.52
7.51
7.50
7.50
7.49
7.48
7.48
7.48
7.46
7.46
7.38
7.38
7.37
7.36
7.36
7.36
7.35
7.34
7.26
COOH
Cl
(3s)
1H NMR, 400 MHz,
CDCl3
1.00
1.95
1.00
14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

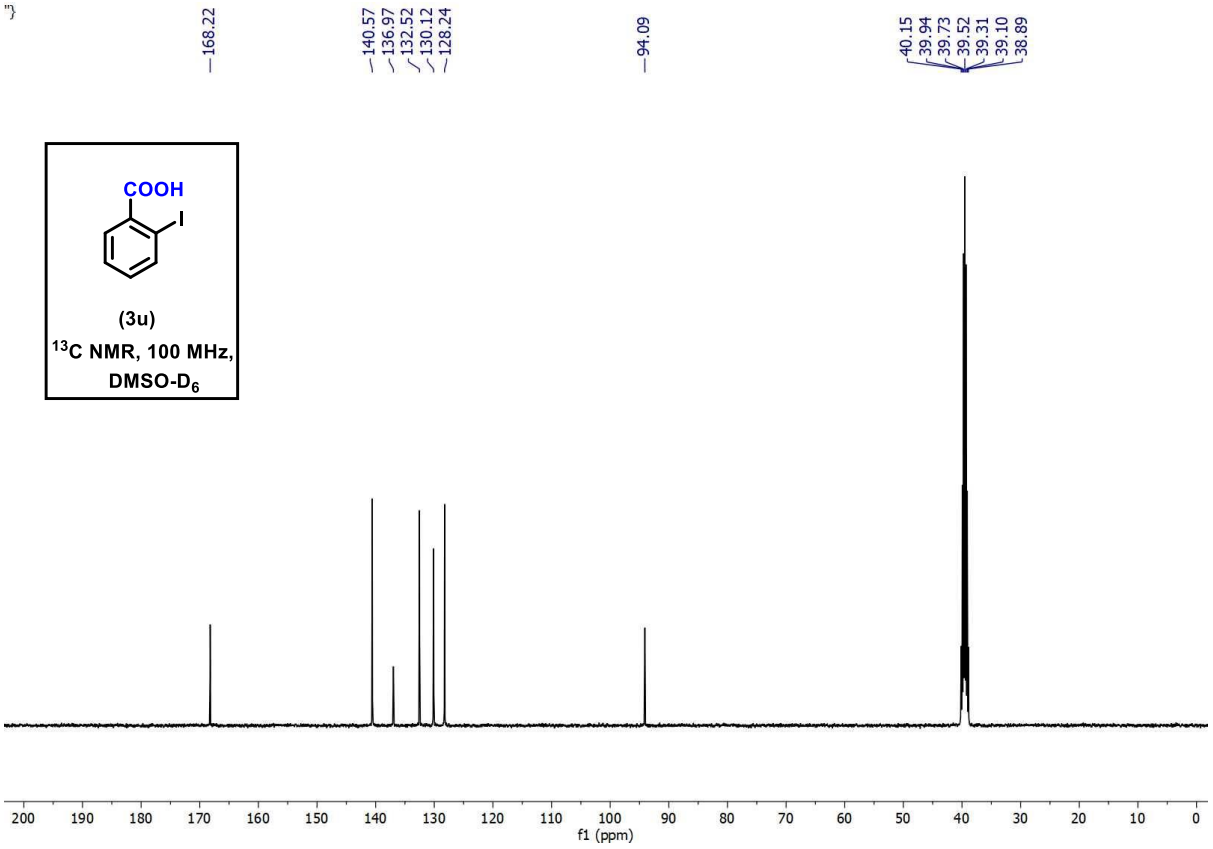

170.68
134.91
133.72
132.63
131.66
128.59
126.85
77.48
77.16
76.84
COOH
Cl
(3s)
13C NMR, 100 MHz,
CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

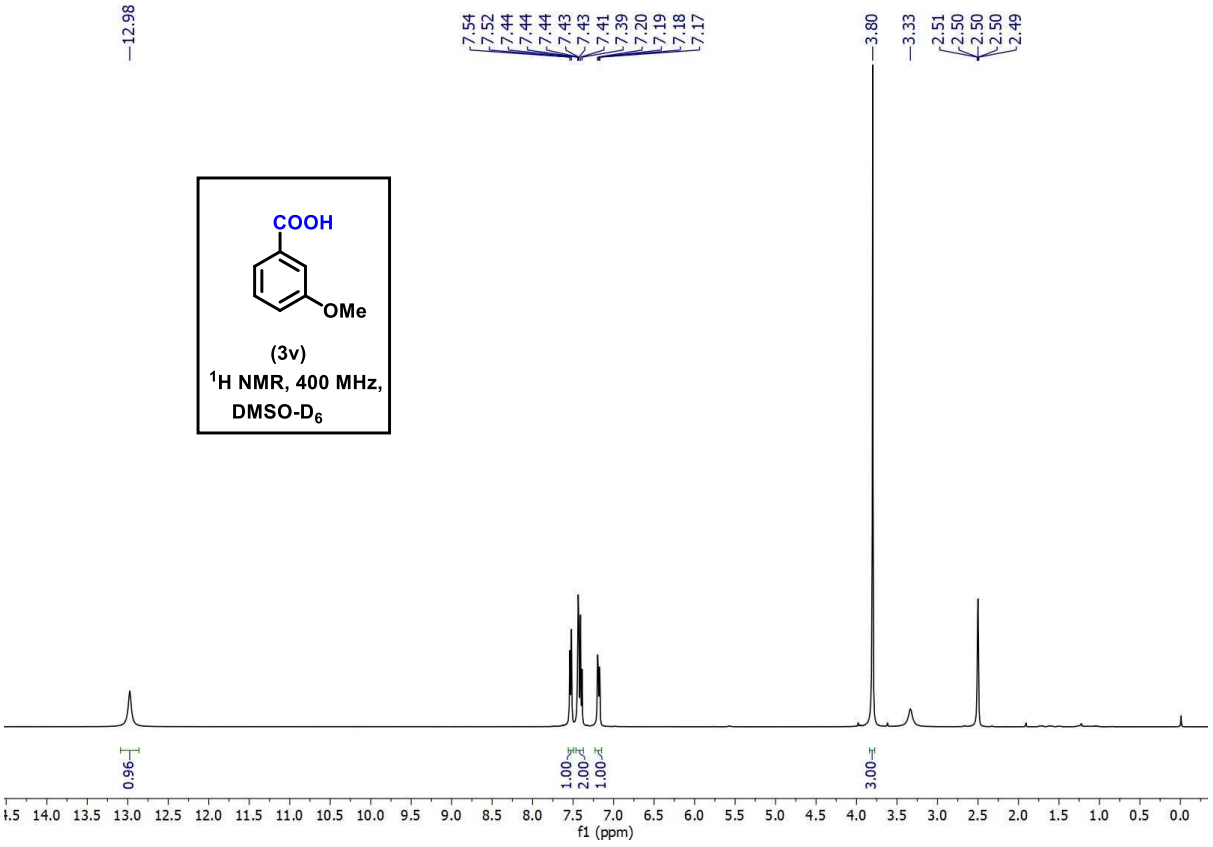

13.23
7.89
7.88
7.87
7.86
7.85
7.84
7.65
7.65
7.64
7.63
7.63
7.63
7.62
7.62
7.61
7.61
7.60
7.60
7.32
7.32
7.31
7.31
7.30
7.29
7.29
7.27
7.27
7.27
3.38
2.50
COOH
F
(3t)
1H NMR, 400 MHz,
DMSO-D6
0.60
1.00
1.00
2.00
f1 (ppm)


165.06
165.03
162.39
159.83
134.75
134.66
131.90
124.47
124.44
119.38
119.28
117.03
116.81
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
F
(3t)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


-110.53
COOH
F
(3t)
19F NMR, 376 MHz,
DMSO-D6
100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240 -260 -280 -300
f1 (ppm)


7.99
7.97
7.71
7.69
7.49
7.47
7.46
7.25
7.24
7.23
7.21
7.21
3.44
2.50
COOH
I
(3u)
1H NMR, 400 MHz,
DMSO-D6
1.00
1.00
1.00
1.00
f1 (ppm)


168.22
140.57
136.97
132.52
130.12
128.24
94.09
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
I
(3u)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)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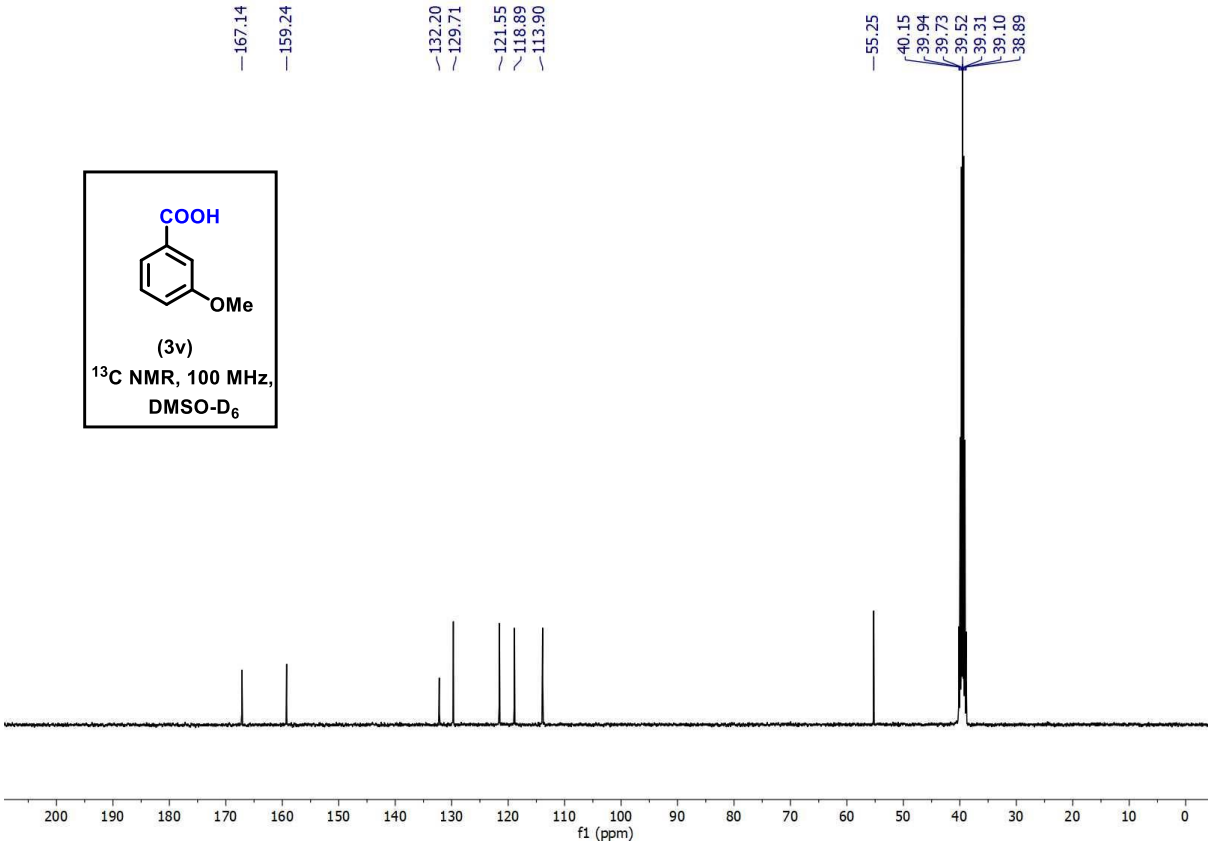
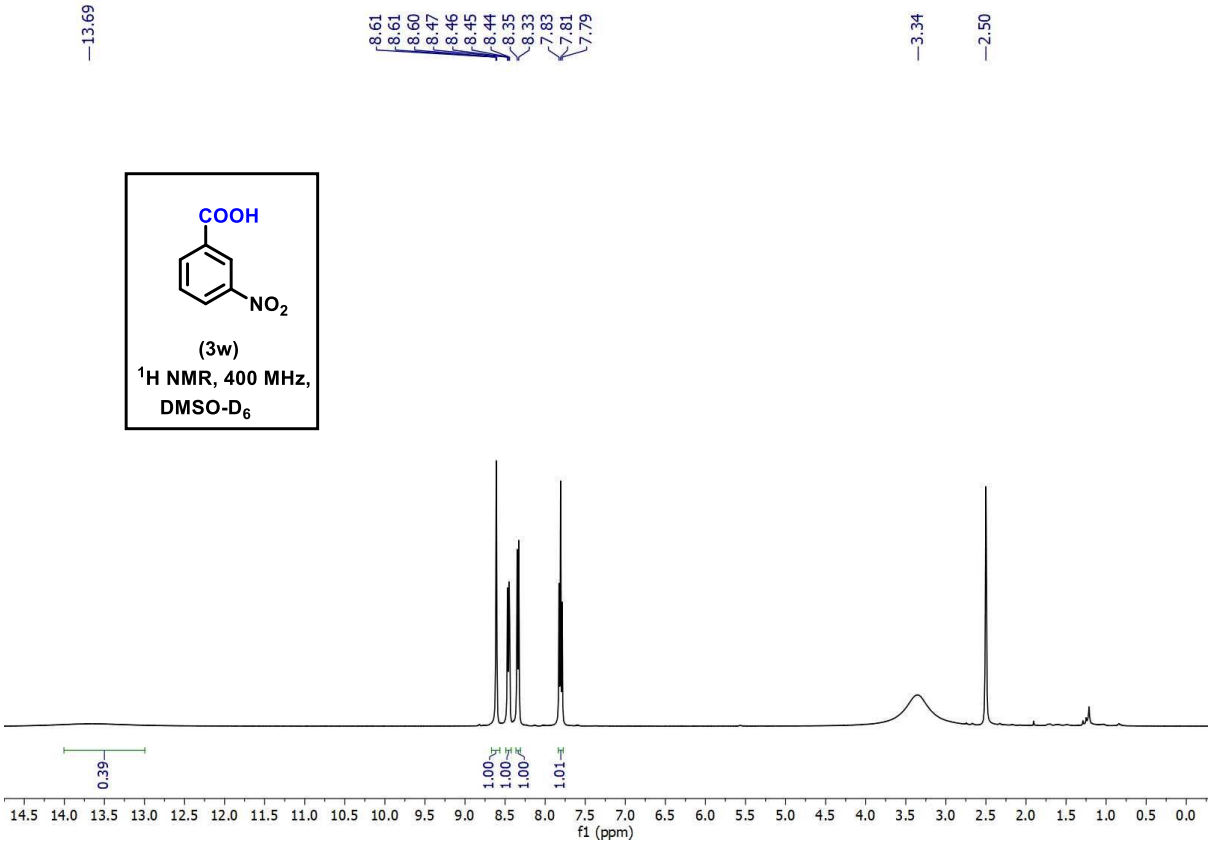
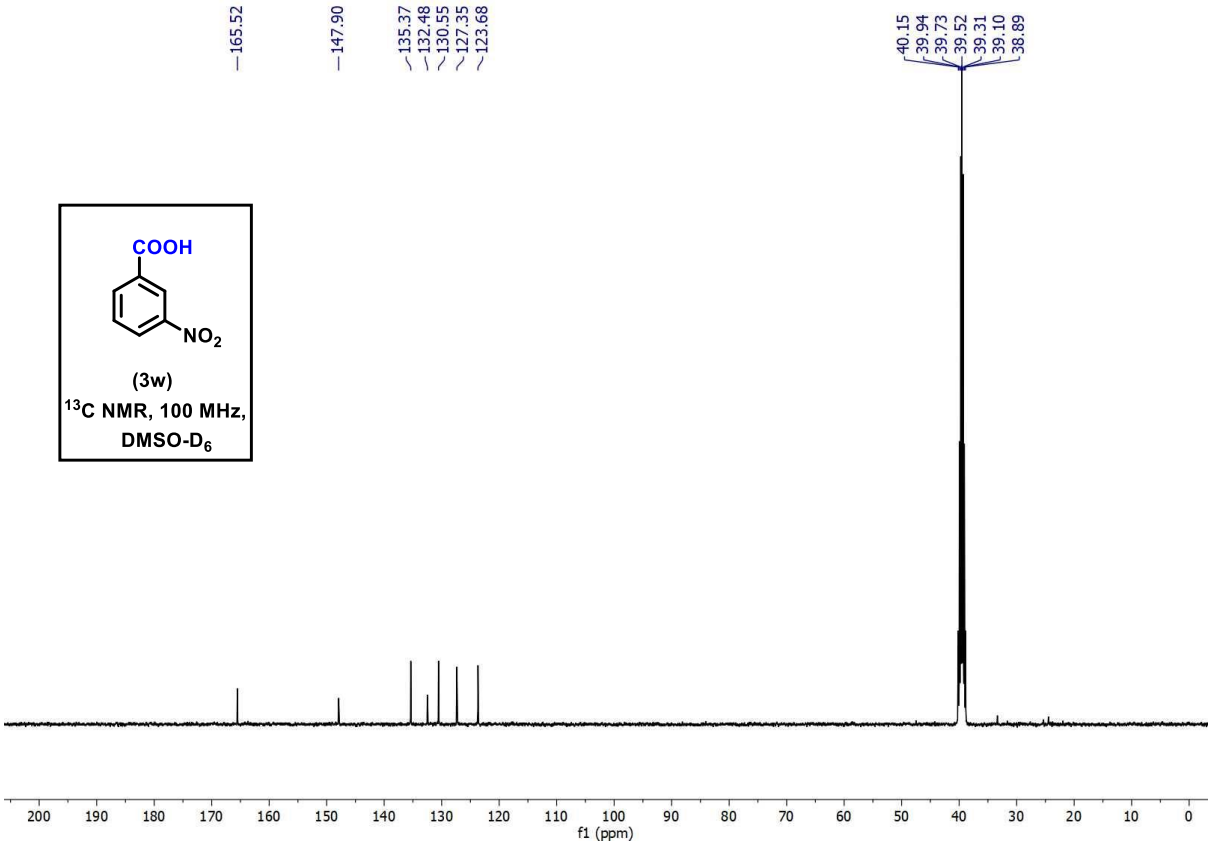
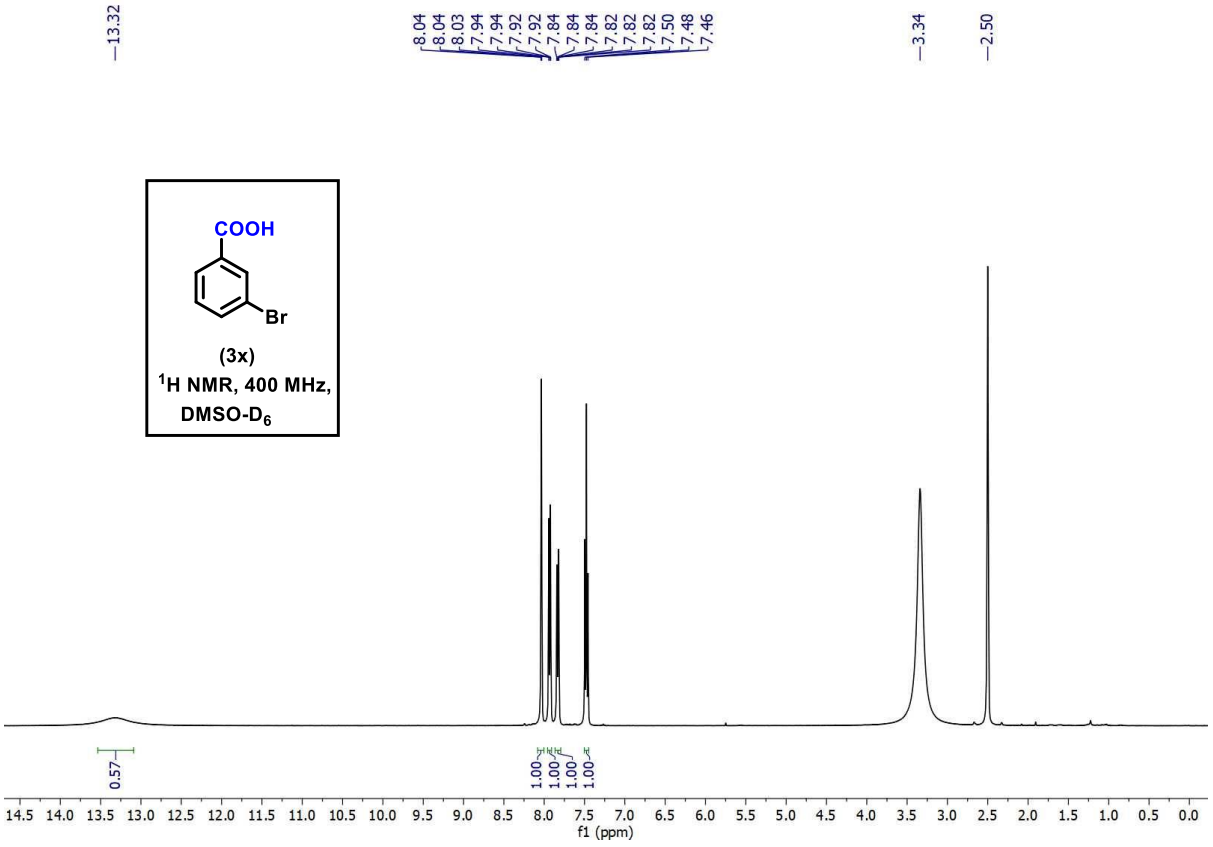
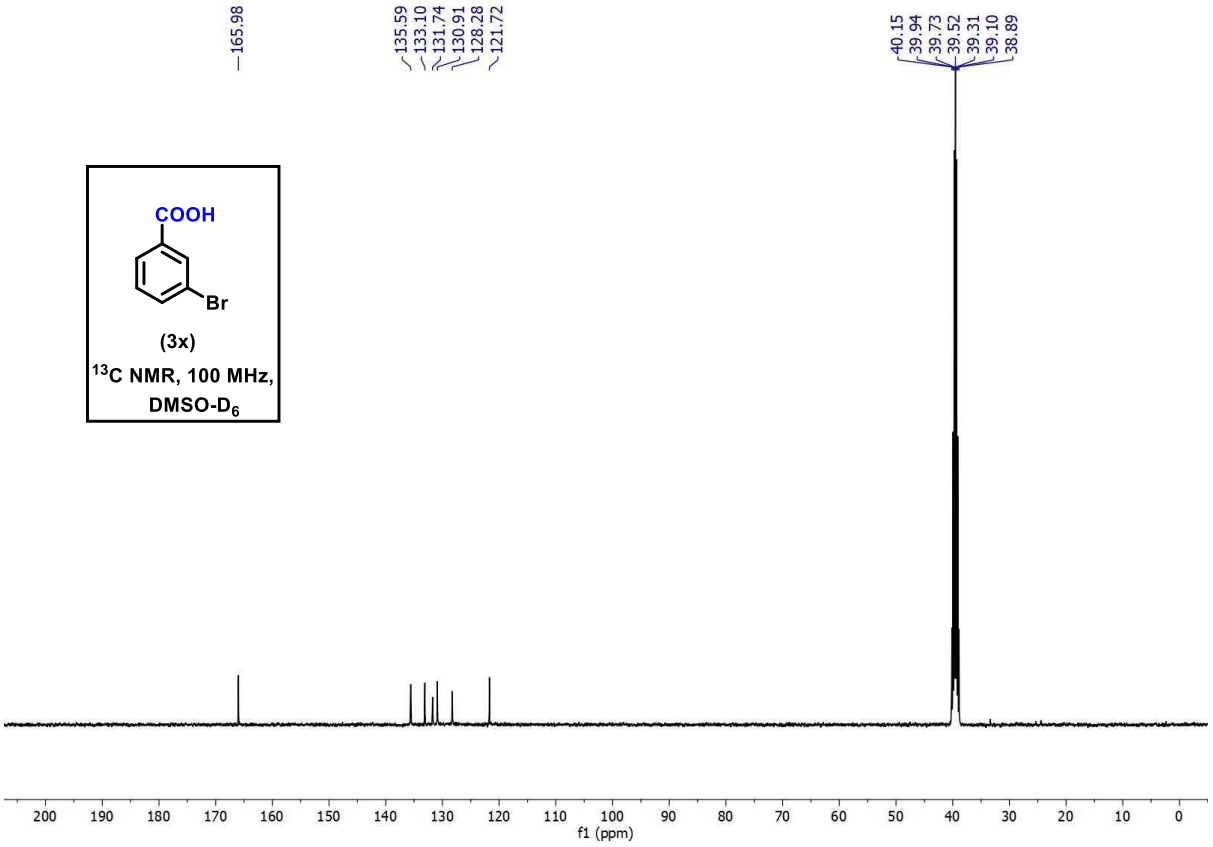
7.54
7.52
7.44
7.44
7.44
7.43
7.43
7.41
7.39
7.20
7.19
7.18
7.17
3.80
3.33
2.51
2.50
2.50
2.50
2.49
COOH
OMe
(3v)
1H NMR, 400 MHz,
DMSO-D6
0.96
1.00
2.00
1.00
3.00
f1 (ppm)


167.14
159.24
132.20
129.71
121.55
118.89
113.90
55.25
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
OMe
(3v)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


13.69
8.61
8.61
8.60
8.47
8.46
8.45
8.44
8.35
8.33
7.83
7.81
7.79
3.34
2.50
COOH
NO2
(3w)
1H NMR, 400 MHz,
DMSO-D6
0.39
1.00
1.00
1.00
1.01
14.5 14.0 13.5 13.0 12.5 12.0 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 0.0
f1 (ppm)


165.52
147.90
135.37
132.48
130.55
127.35
123.68
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
NO2
(3w)
13C NMR, 100 MHz,
DMSO-D6
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


13.32
8.04
8.04
8.03
7.94
7.94
7.92
7.92
7.84
7.84
7.84
7.82
7.82
7.82
7.50
7.48
7.46
3.34
2.50
COOH
Br
(3x)
1H NMR, 400 MHz,
DMSO-D6
0.57
1.00
1.00
1.00
1.00
f1 (ppm)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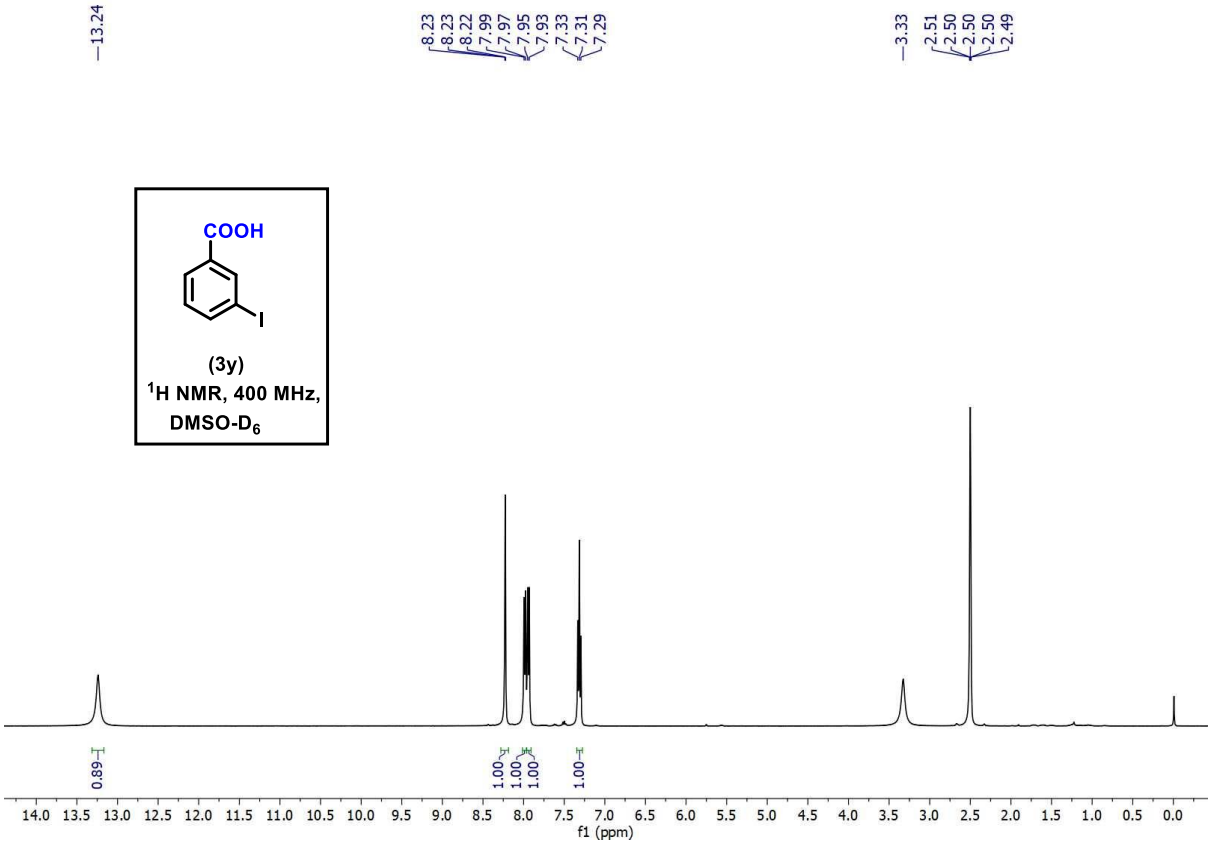
135.59
133.10
131.74
130.91
128.28
121.72
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
Br
(3x)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)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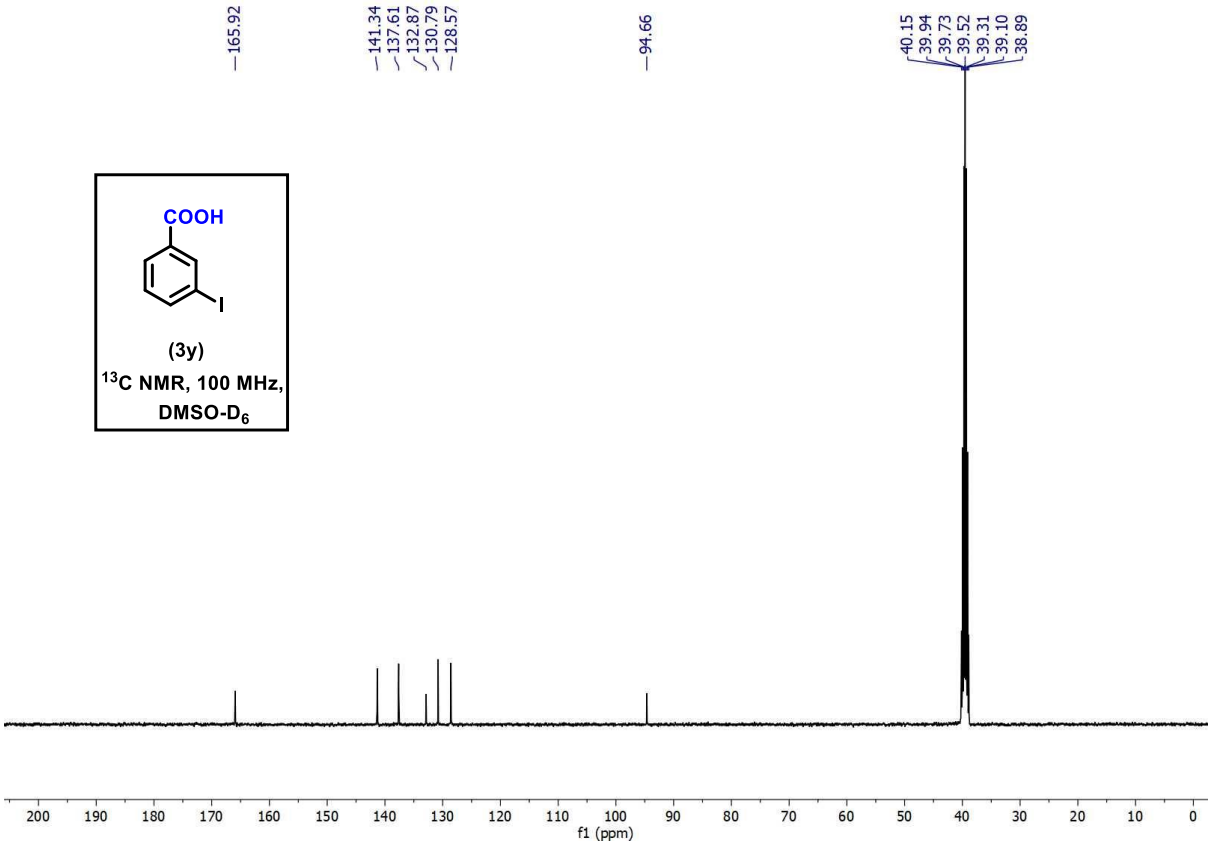
8.23
8.23
8.22
7.99
7.97
7.95
7.93
7.33
7.31
7.29
3.33
2.51
2.50
2.50
2.50
2.49
COOH
I
(3y)
1H NMR, 400 MHz,
DMSO-D6
0.89
1.00
1.00
1.00
1.00
f1 (ppm)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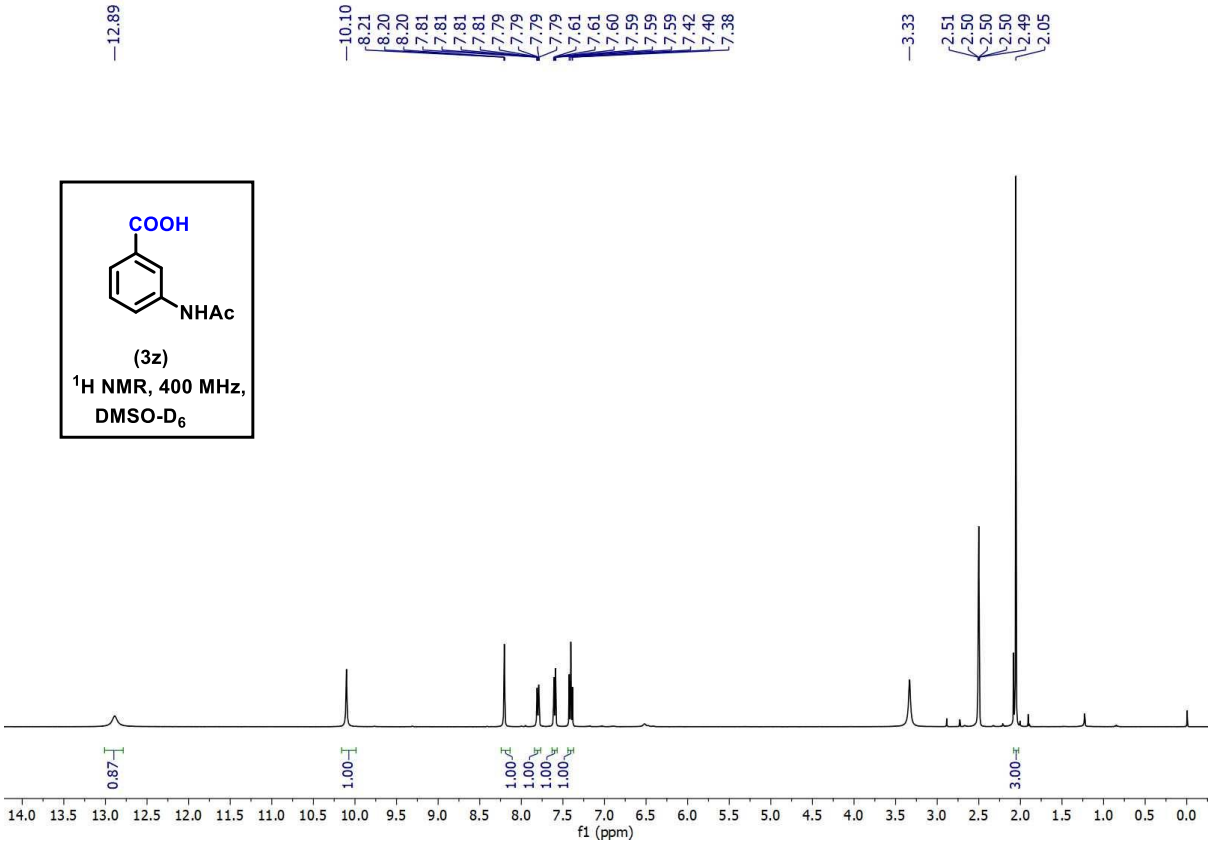
141.34
137.61
132.87
130.79
128.57
94.66
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
I
(3y)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)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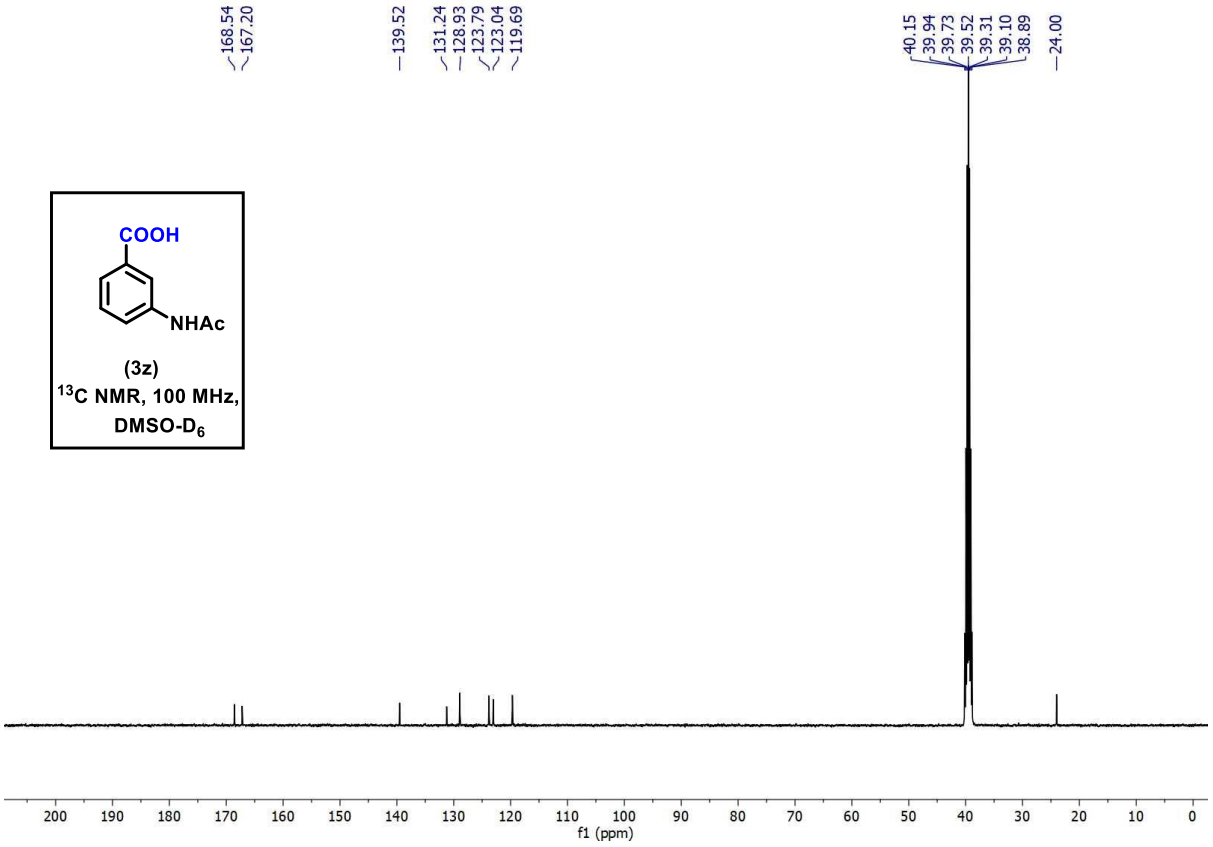
10.10
8.21
8.20
8.20
7.81
7.81
7.81
7.81
7.79
7.79
7.79
7.79
7.61
7.61
7.60
7.59
7.59
7.59
7.42
7.40
7.38
3.33
2.51
2.50
2.50
2.50
2.49
2.05
COOH
NHAc
(3z)
1H NMR, 400 MHz,
DMSO-D6
0.87
1.00
1.00
1.00
1.00
1.00
3.00
f1 (ppm)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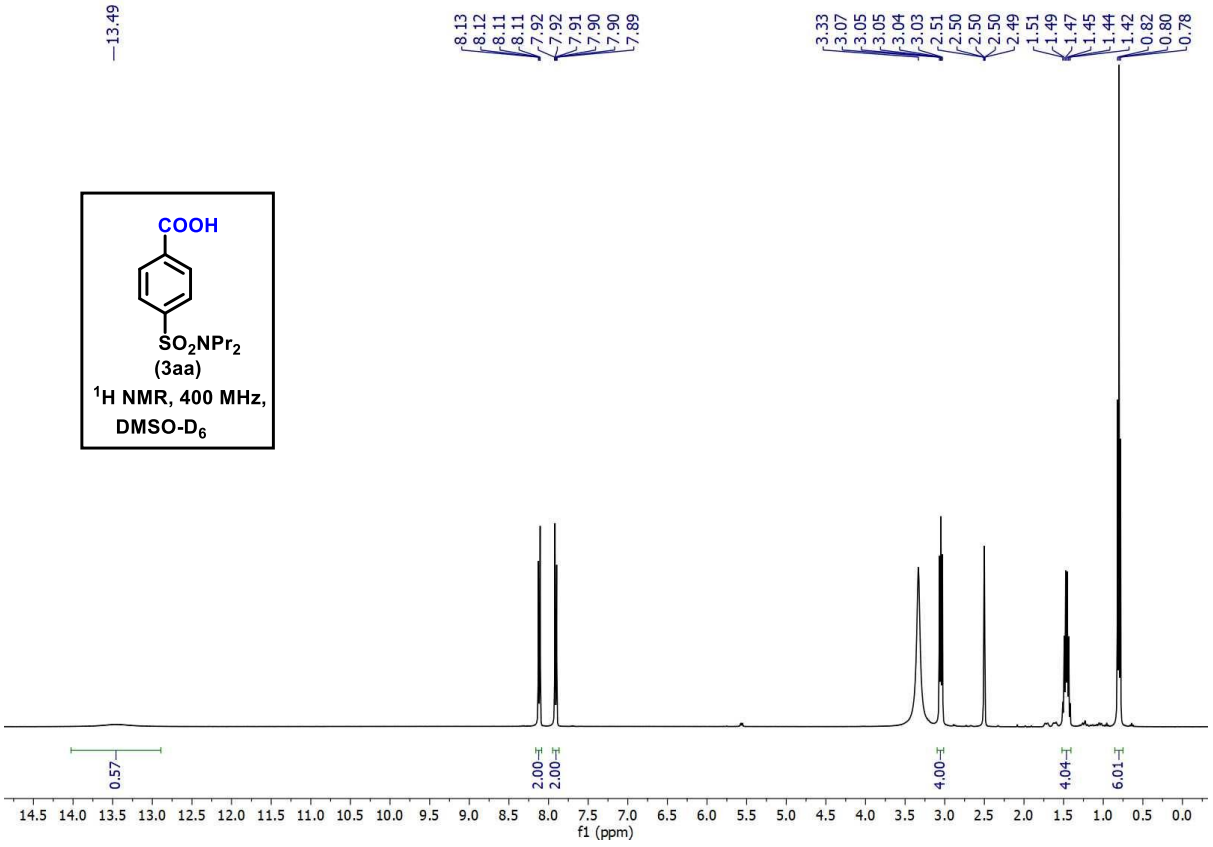
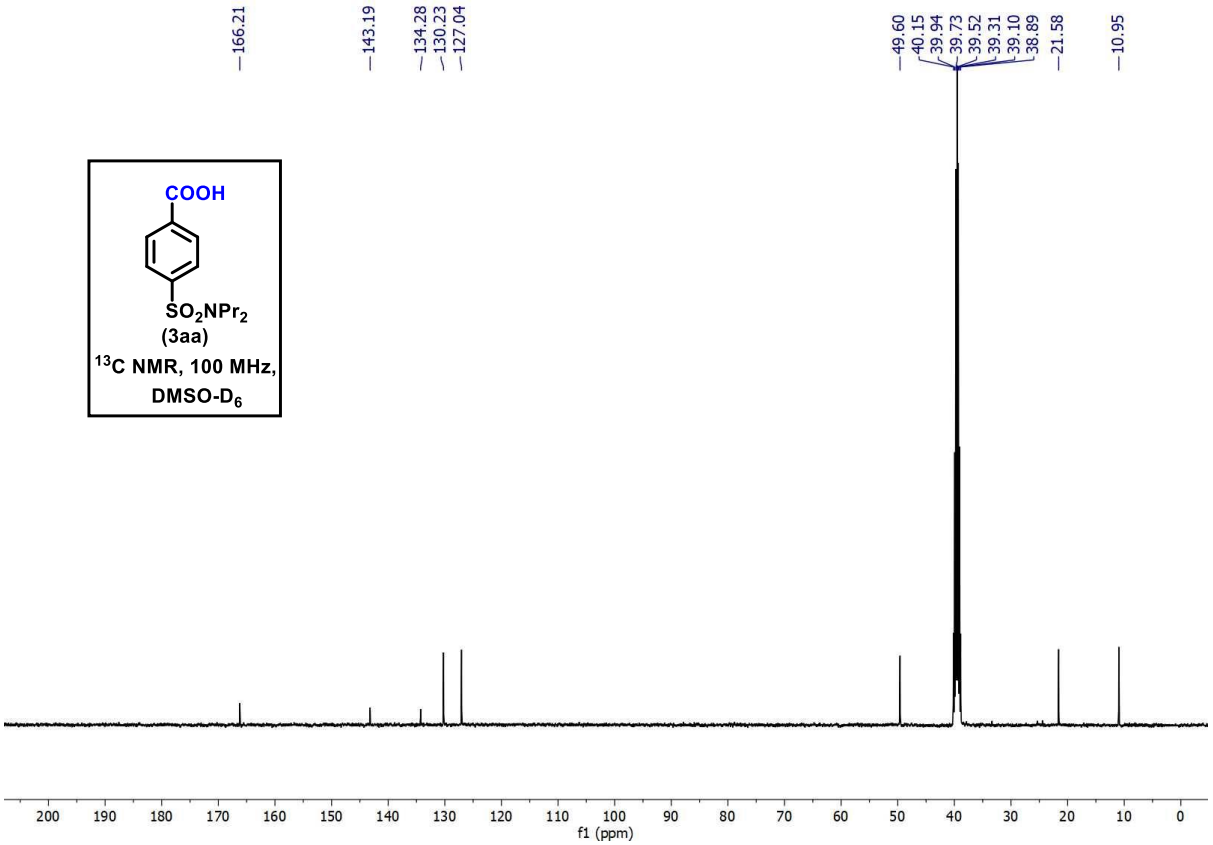
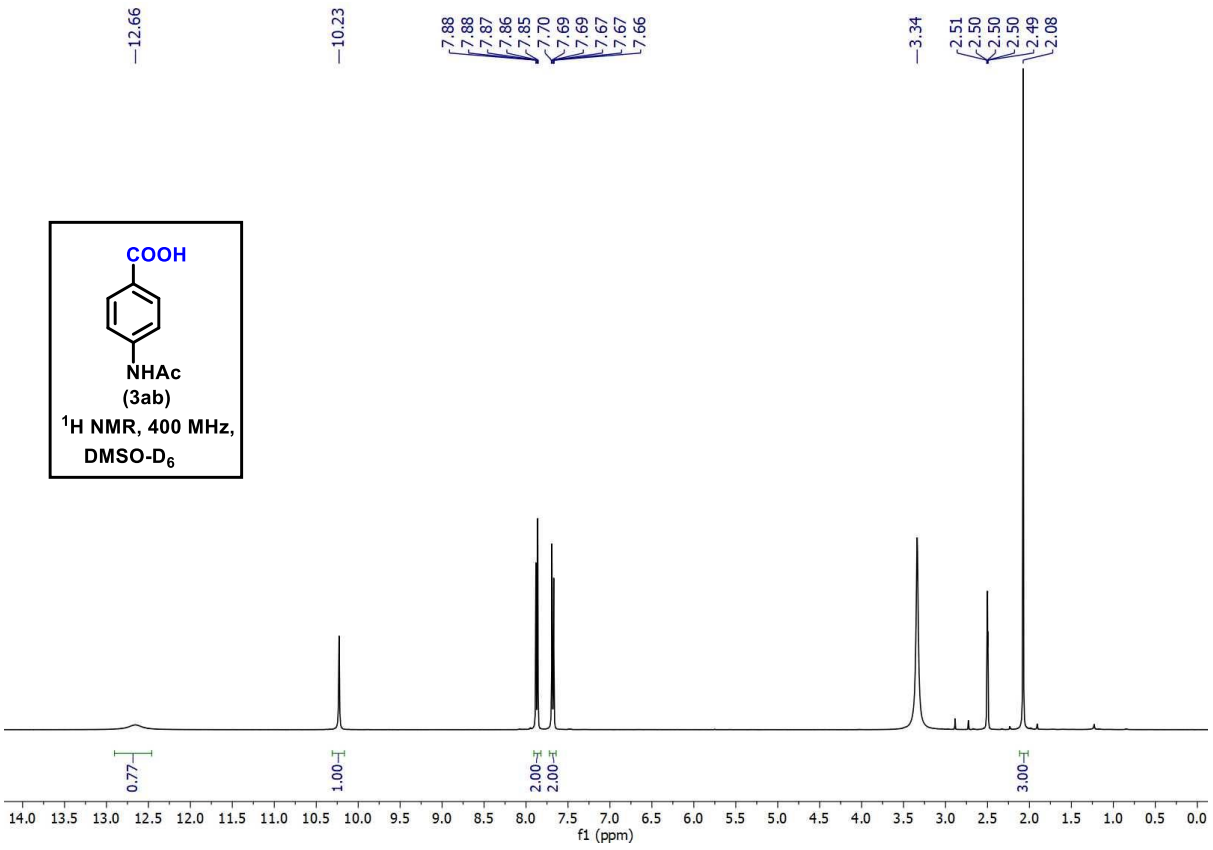
167.20
139.52
131.24
128.93
123.79
123.04
119.69
40.15
39.94
39.73
39.52
39.31
39.10
38.89
24.00
COOH
NHAc
(3z)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


13.49
8.13
8.12
8.11
8.11
7.92
7.92
7.91
7.90
7.90
7.89
3.33
3.07
3.05
3.05
3.04
3.03
2.51
2.50
2.50
2.50
2.49
1.51
1.49
1.47
1.45
1.44
1.42
0.82
0.80
0.78
COOH
SO2NPr2
(3aa)
1H NMR, 400 MHz,
DMSO-D6
0.57
2.00
2.00
4.00
4.04
6.01
f1 (ppm)


166.21
143.19
134.28
130.23
127.04
49.60
40.15
39.94
39.73
39.52
39.31
39.10
38.89
21.58
10.95
COOH
SO2NPr2
(3aa)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)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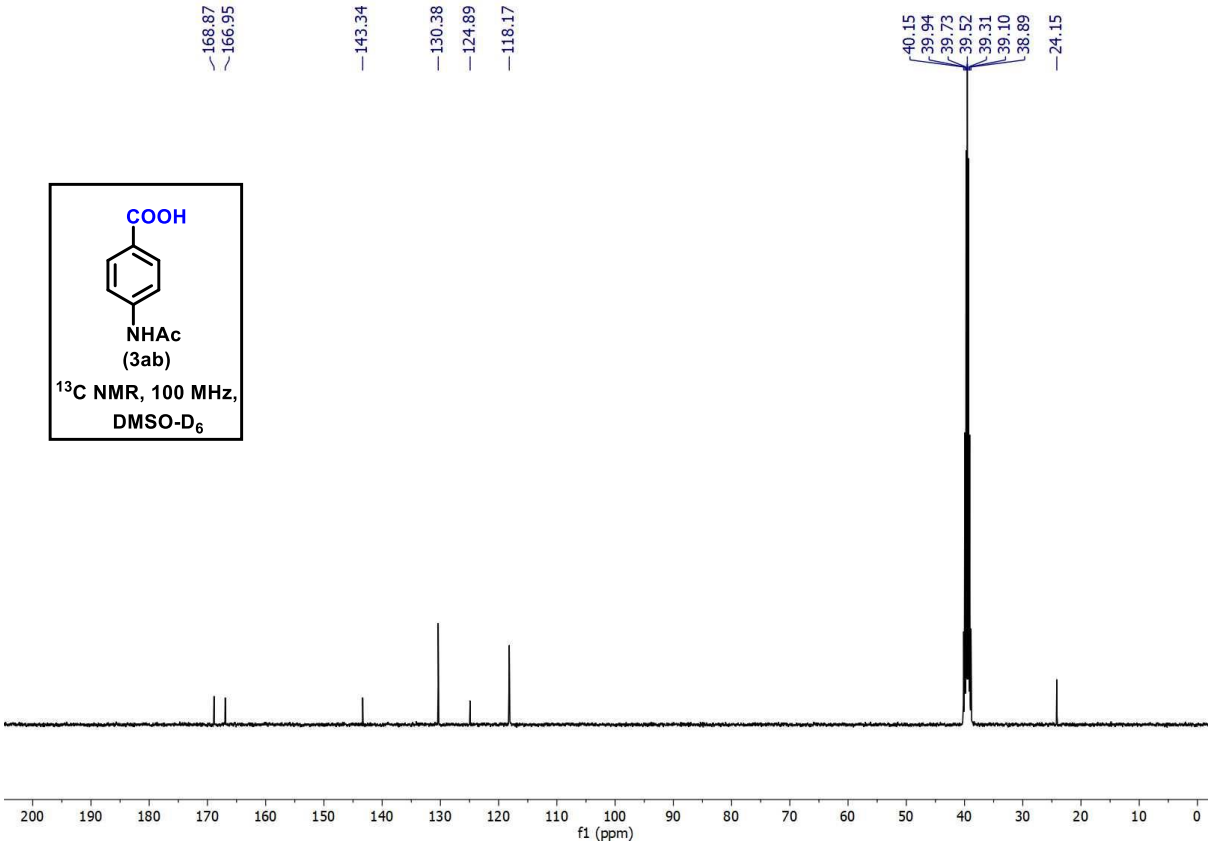
7.88
7.88
7.87
7.86
7.85
7.70
7.69
7.69
7.67
7.67
7.66
3.34
2.51
2.50
2.50
2.50
2.49
2.08
COOH
NHAc
(3ab)
1H NMR, 400 MHz,
DMSO-D6
0.77
1.00
2.00
2.00
3.00
f1 (ppm)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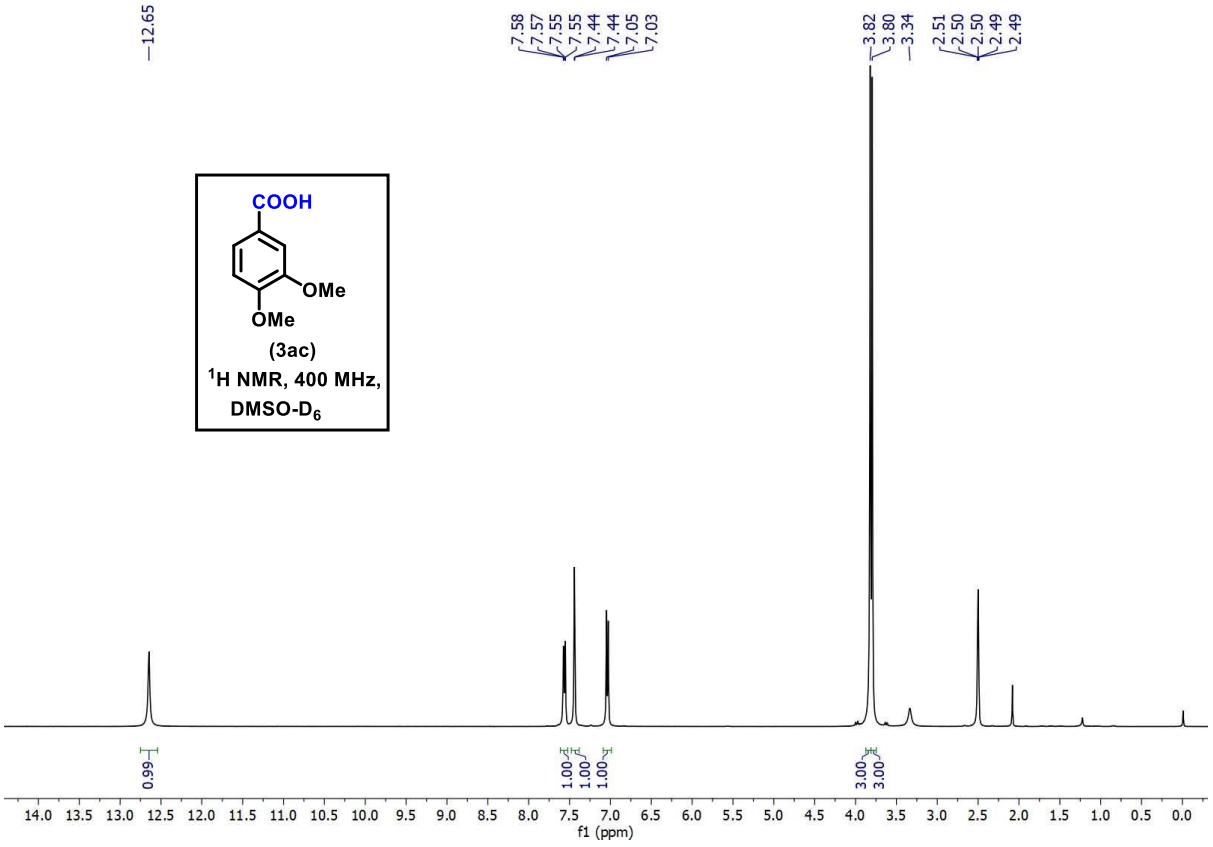
130.38
124.89
118.17
40.15
39.94
39.73
39.52
39.31
39.10
38.89
24.15
COOH
NHAc
(3ab)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)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7.58
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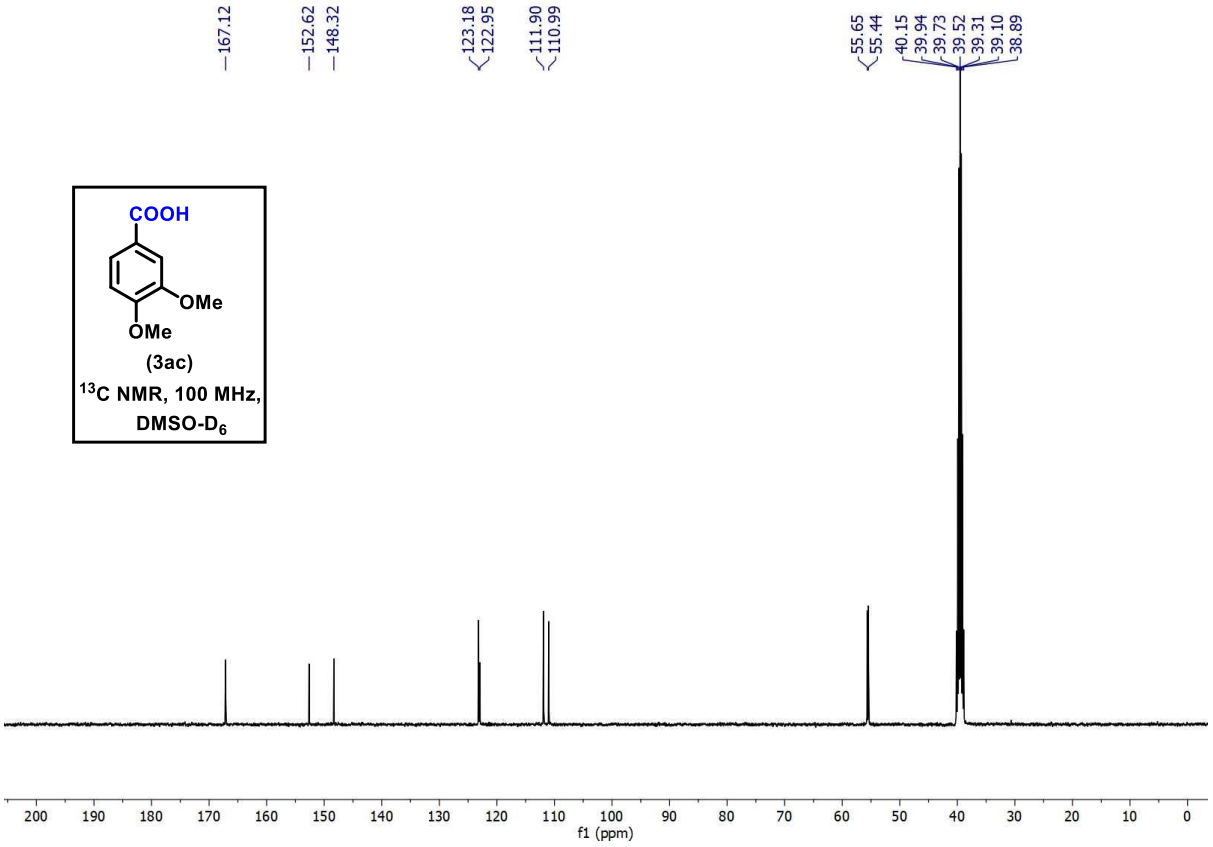
7.55
7.55
7.44
7.44
7.05
7.03
3.82
3.80
3.34
2.51
2.50
2.50
2.49
2.49
COOH
OMe
OMe
(3ac)
1H NMR, 400 MHz,
DMSO-D6
0.99
1.00
1.00
1.00
3.00
3.00
f1 (ppm)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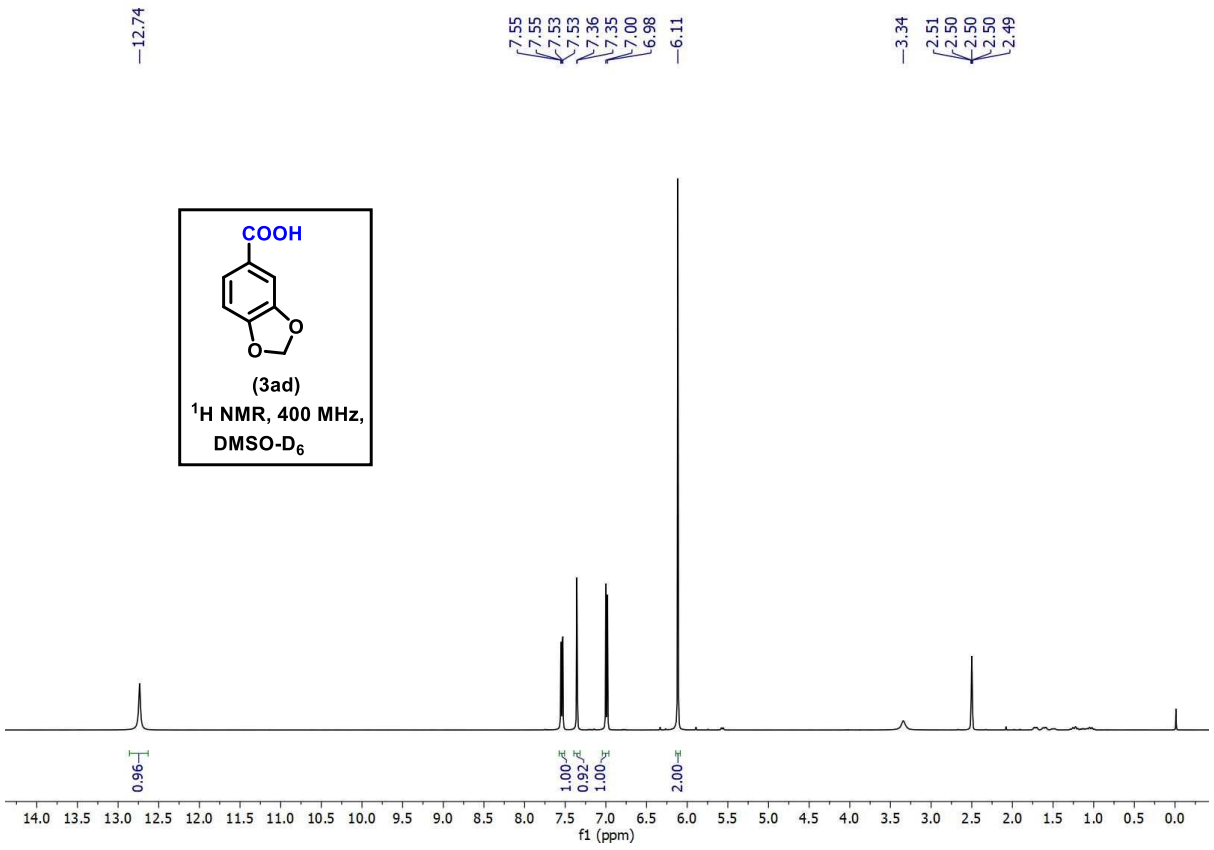
123.18
122.95
111.90
110.99
55.65
55.44
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
OMe
OMe
(3ac)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)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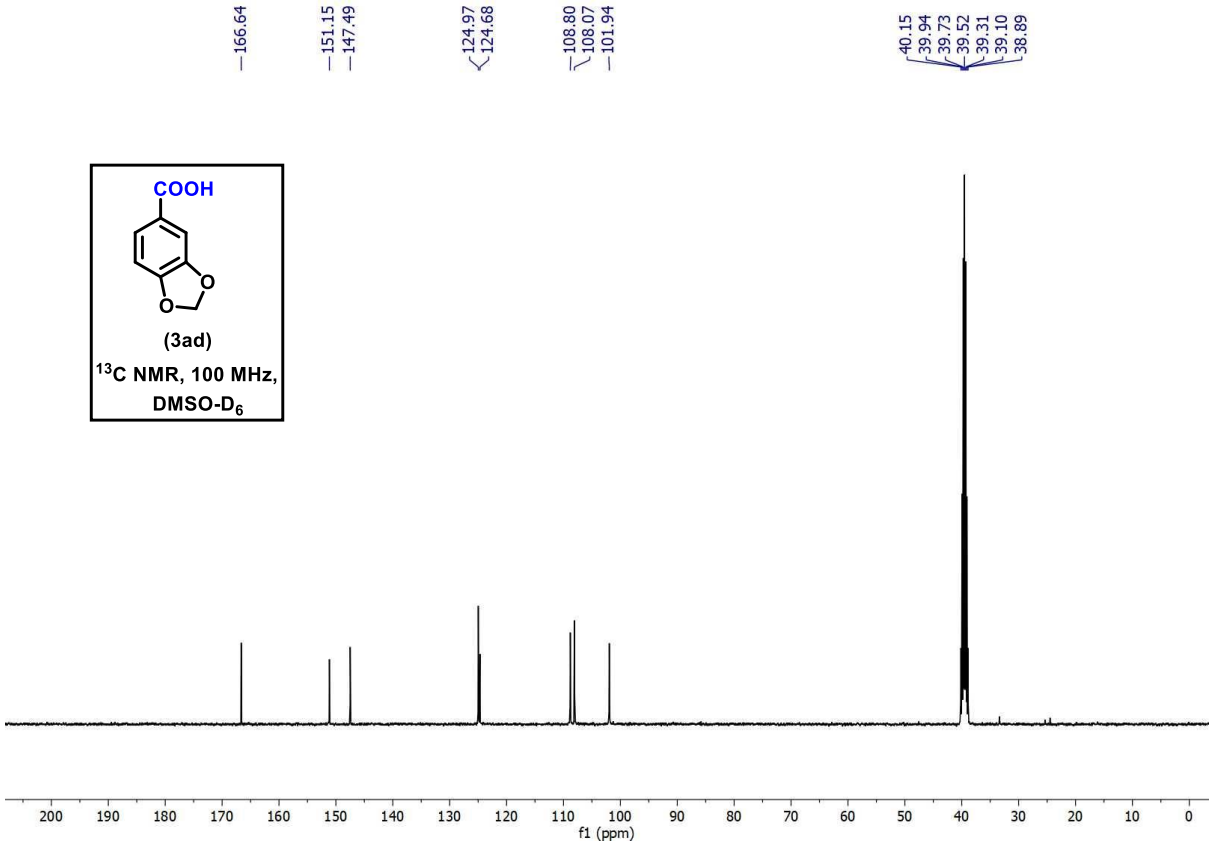
7.55
7.53
7.53
7.36
7.35
7.00
6.98
6.11
3.34
2.51
2.50
2.50
2.50
2.49
COOH
(3ad)
1H NMR, 400 MHz,
DMSO-D6
0.96
1.00
0.92
1.00
2.00
f1 (ppm)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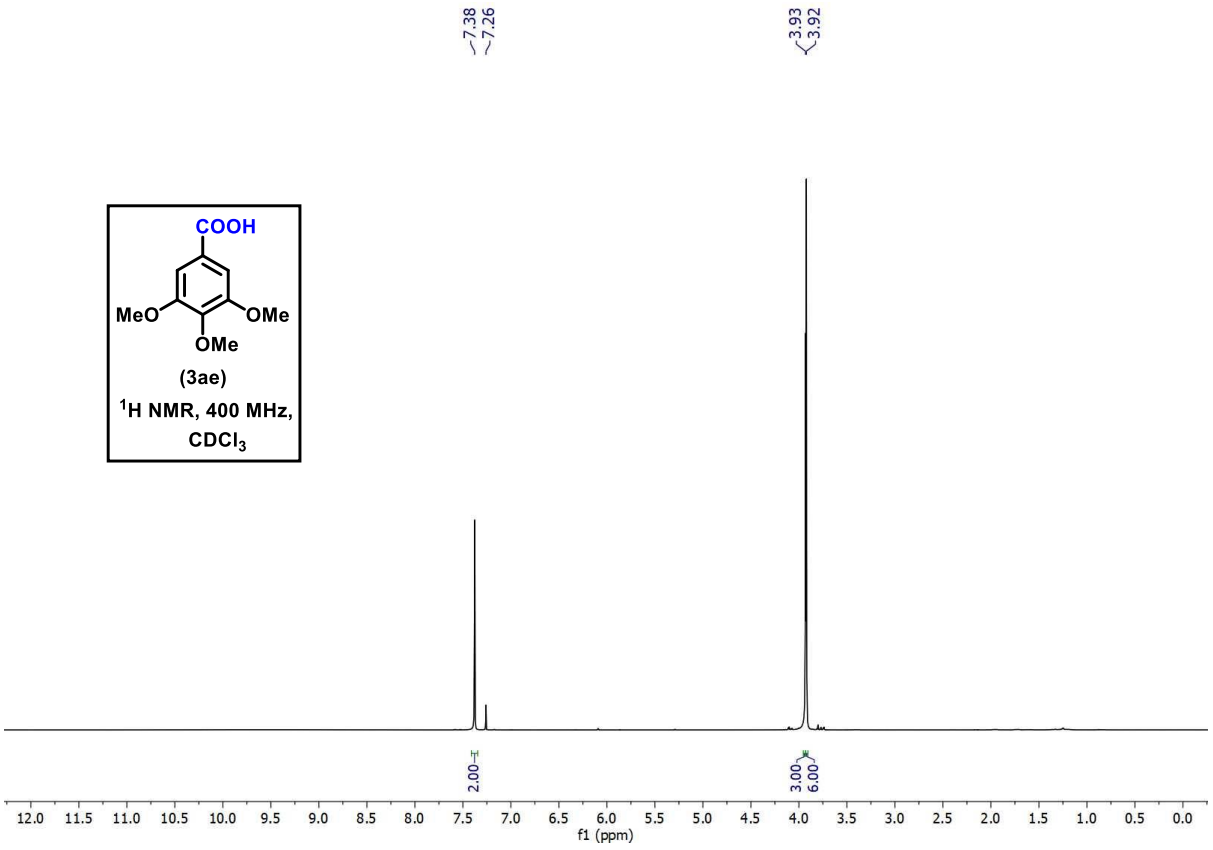
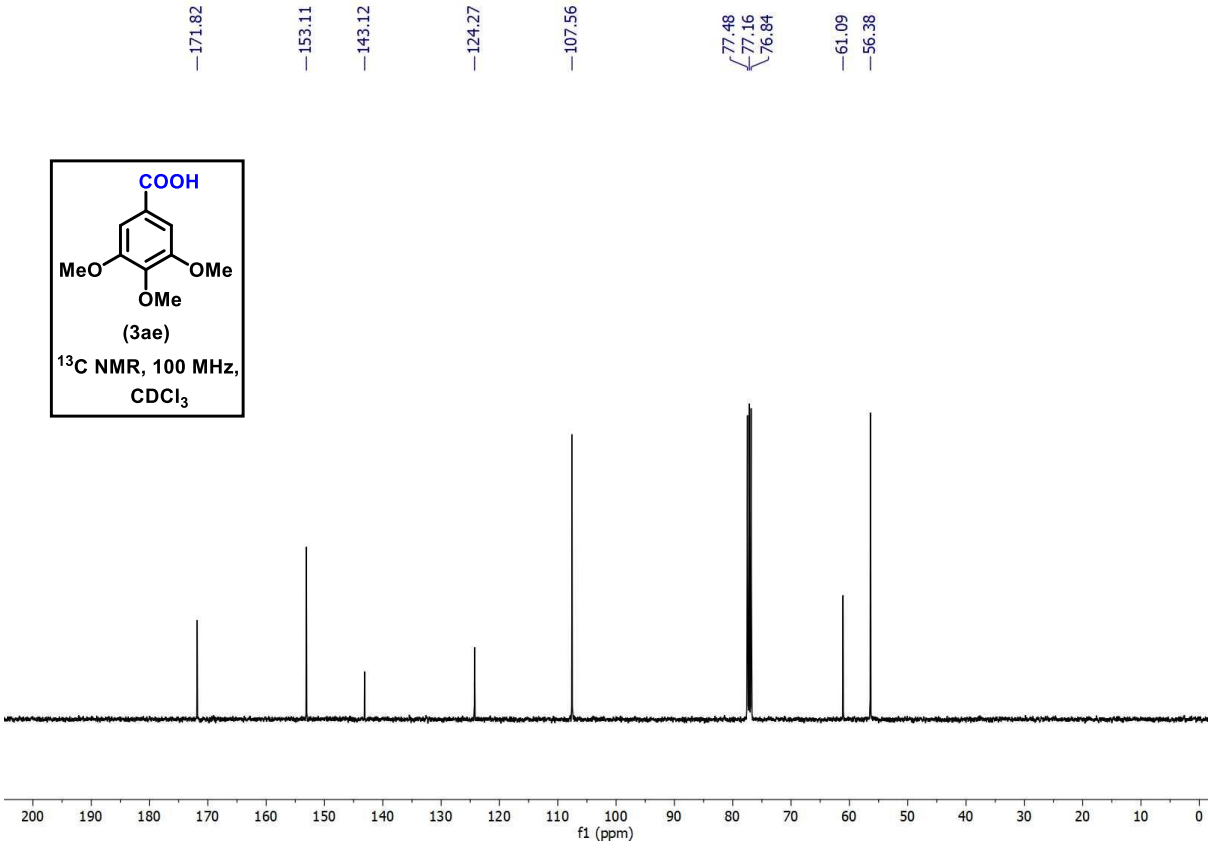
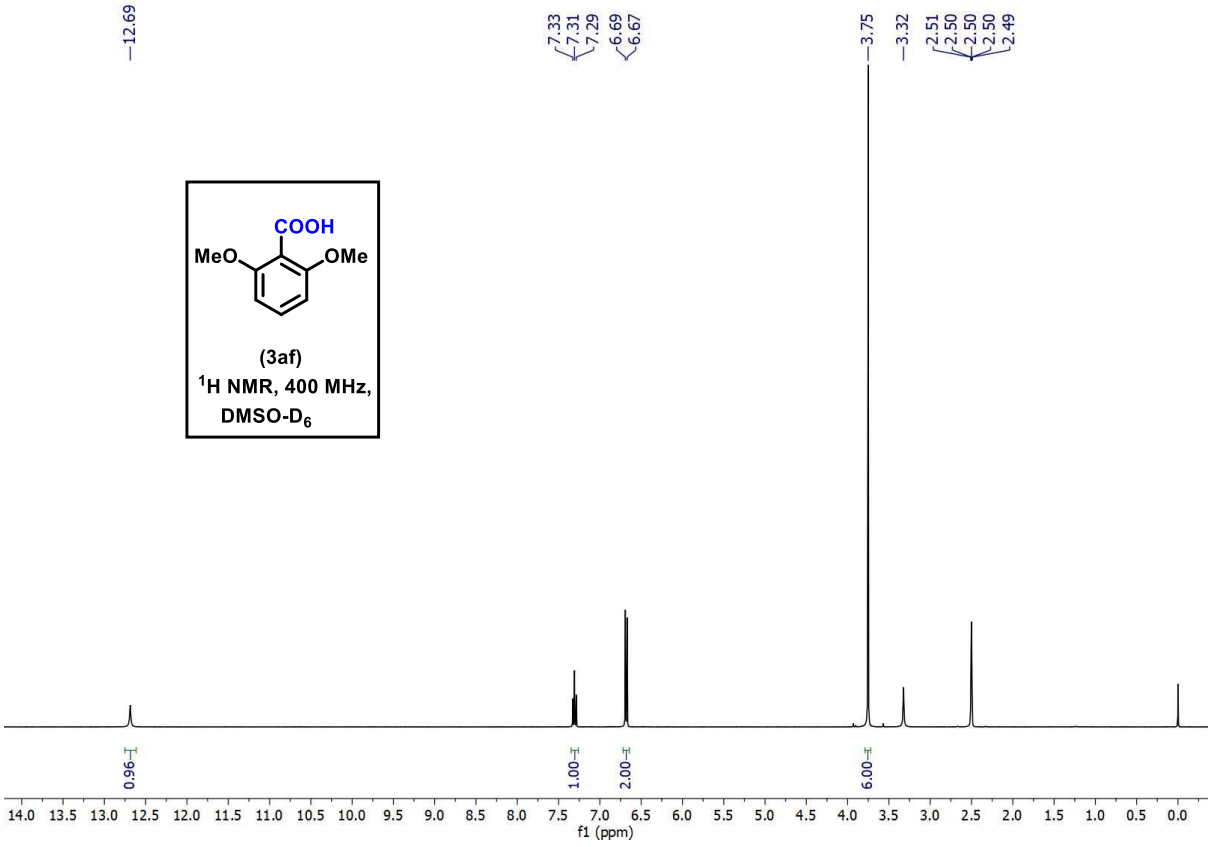
147.49
124.97
124.68
108.80
108.07
101.94
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
(3ad)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


7.38
7.26
3.93
3.92
COOH
MeO
OMe
OMe
(3ae)
^{1}H NMR, 400 MHz,
$CDCl_3$
2.00
3.00
6.00
f1 (ppm)


171.82
153.11
143.12
124.27
107.56
77.48
77.16
76.84
61.09
56.38
COOH
MeO
OMe
OMe
(3ae)
^{13}C NMR, 100 MHz,
$CDCl_3$
f1 (ppm)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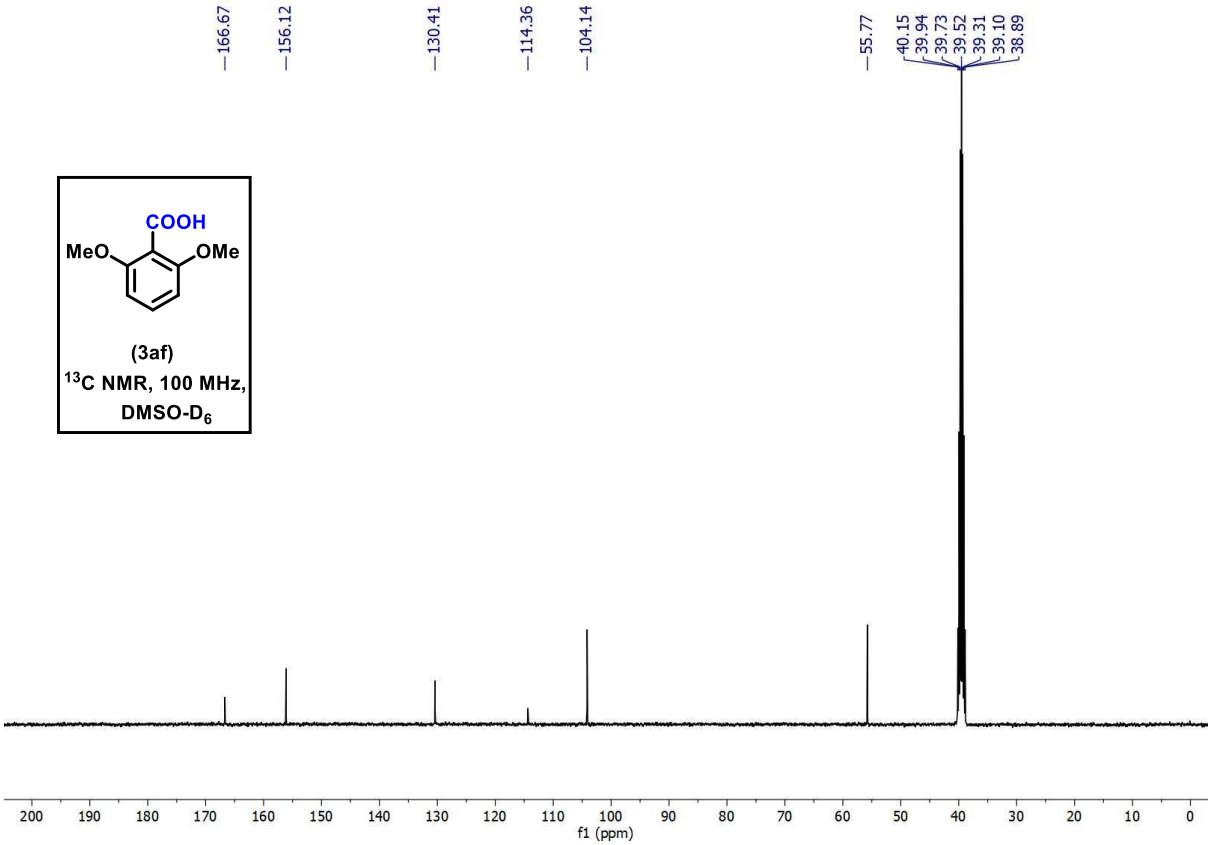
7.33
7.31
7.29
6.69
6.67
3.75
3.32
2.51
2.50
2.50
2.50
2.49
COOH
MeO
OMe
(3af)
1H NMR, 400 MHz,
DMSO-D6
0.96
1.00
2.00
6.00
f1 (ppm)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156.12
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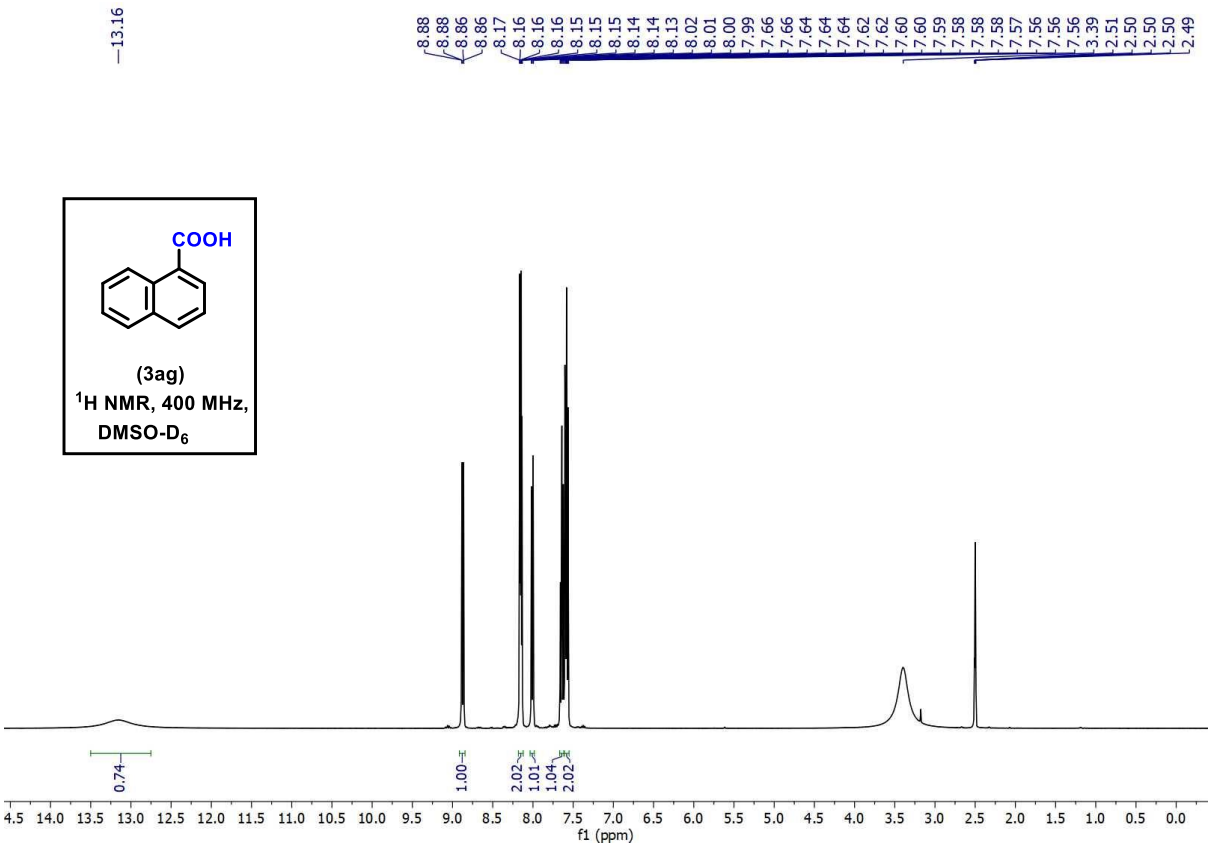
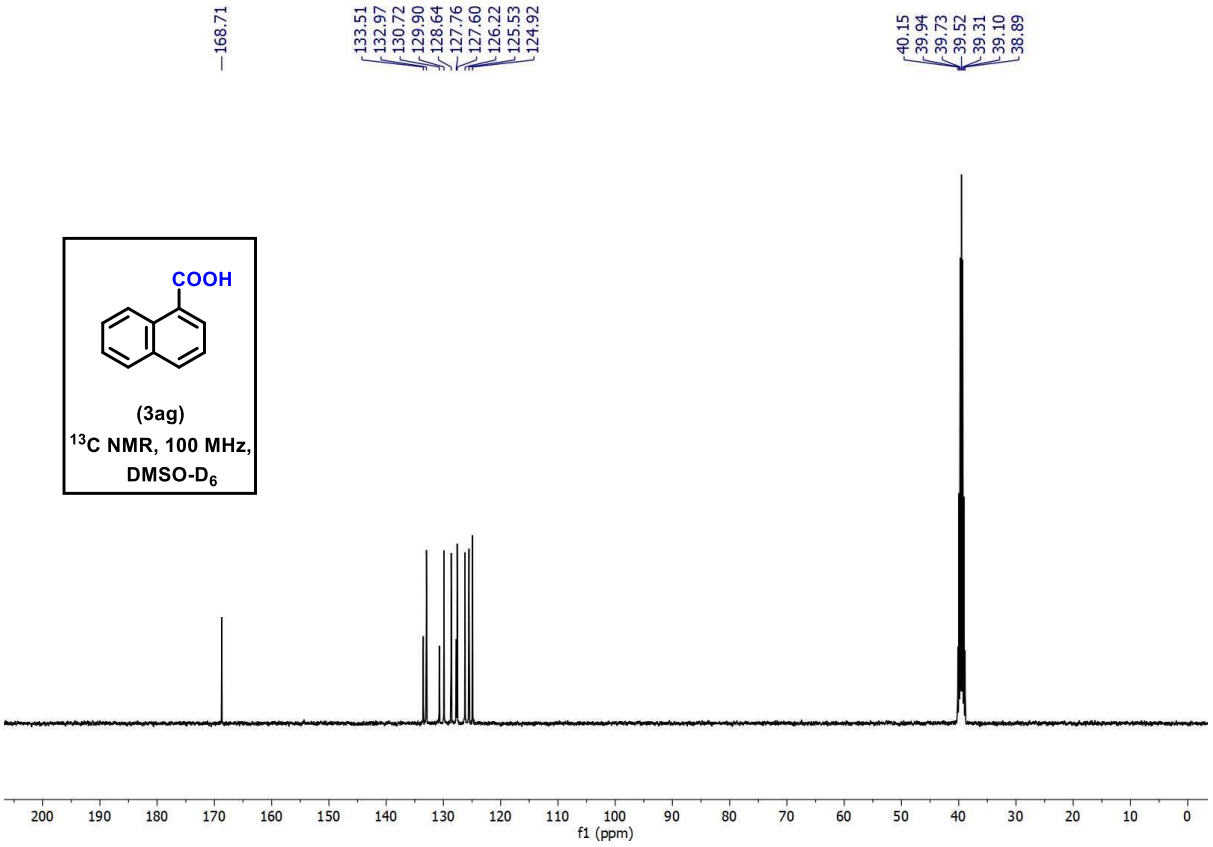
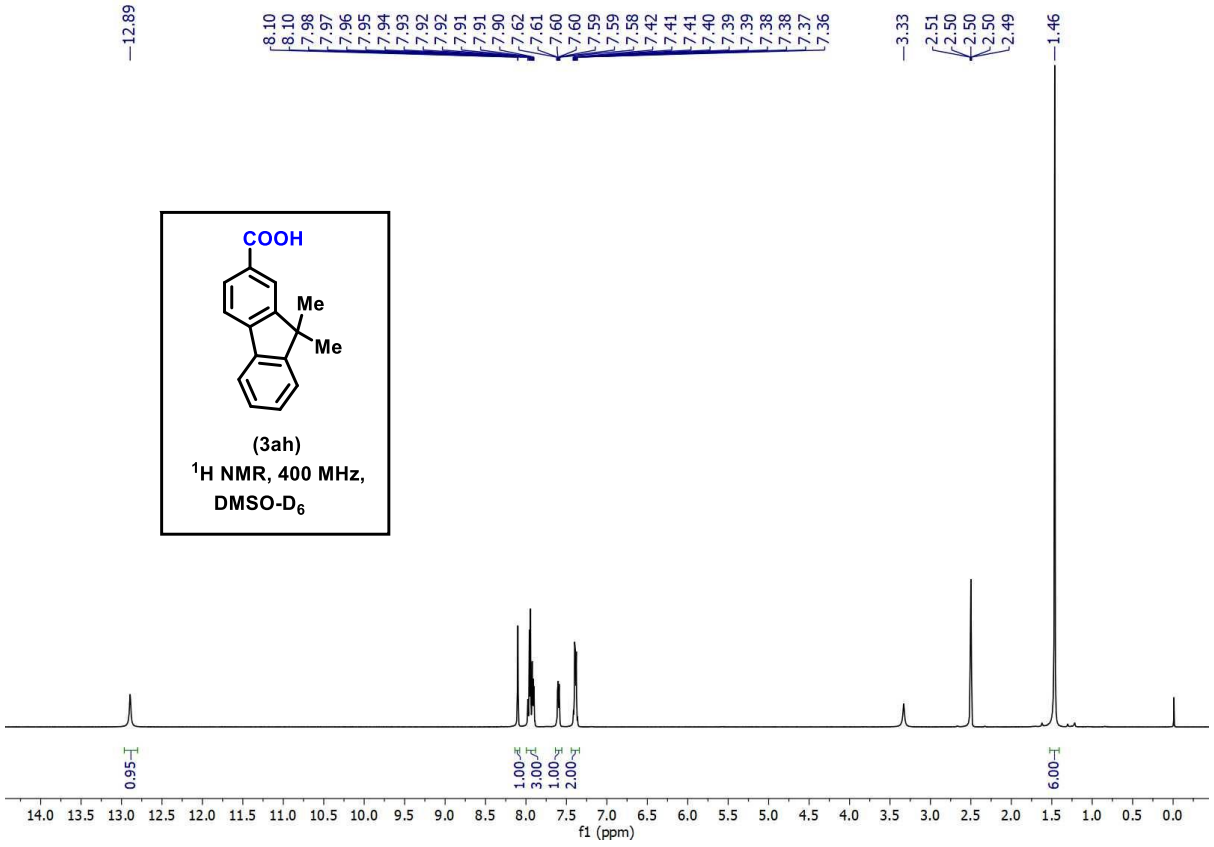
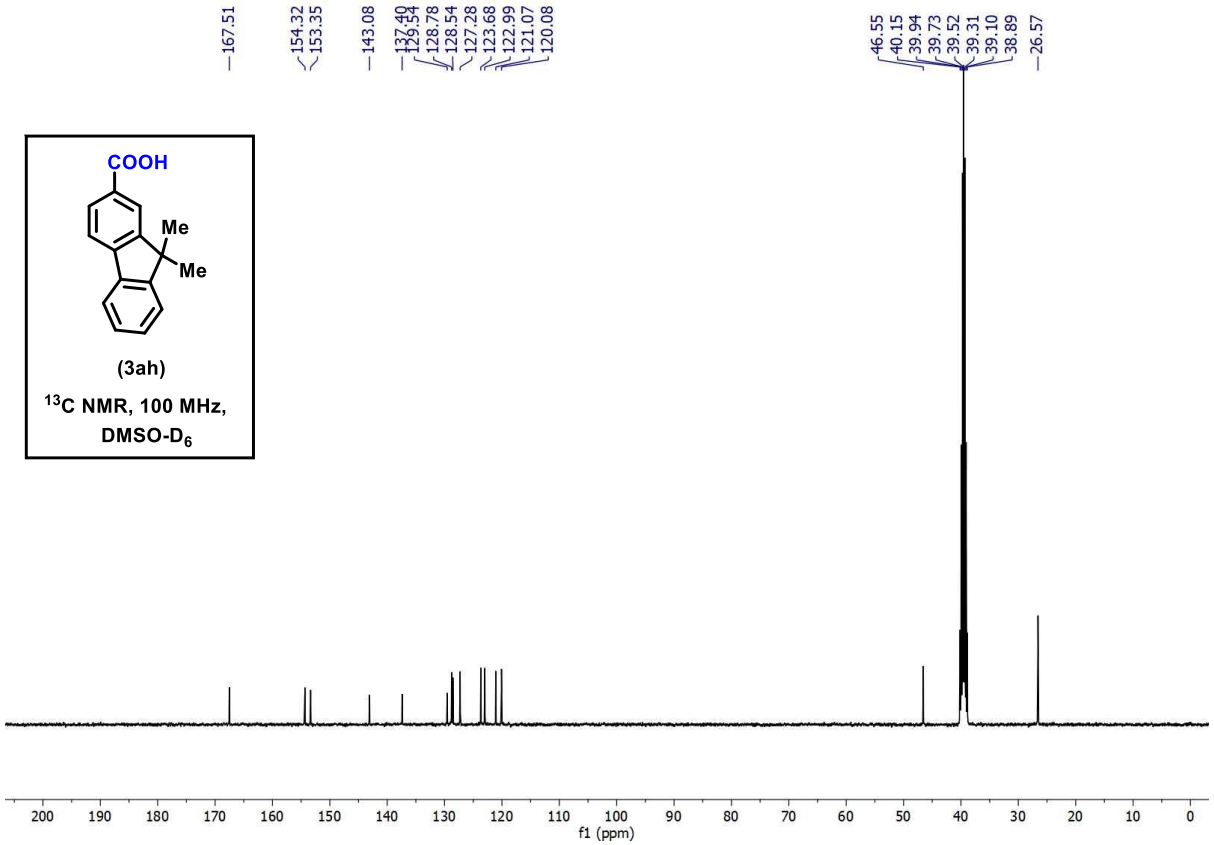
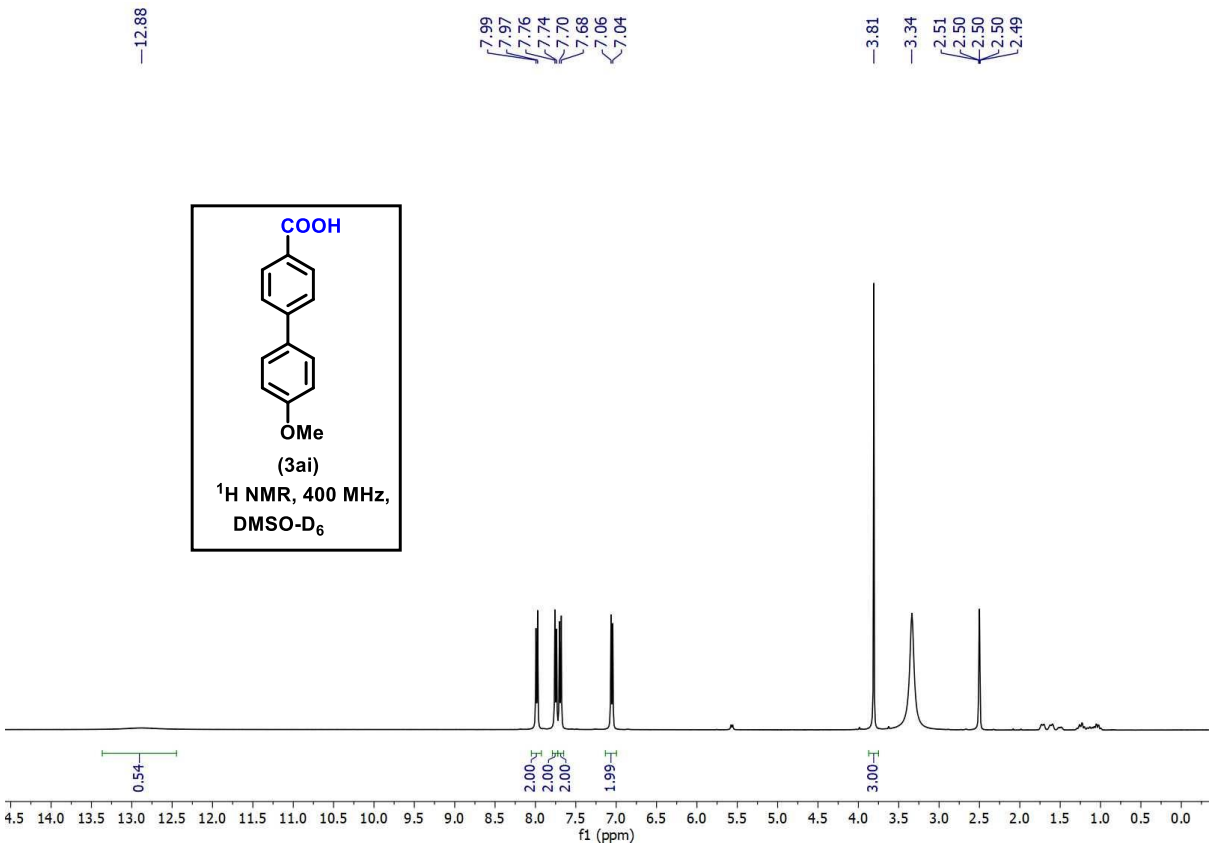
114.36
104.14
55.77
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
MeO
OMe
(3af)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)

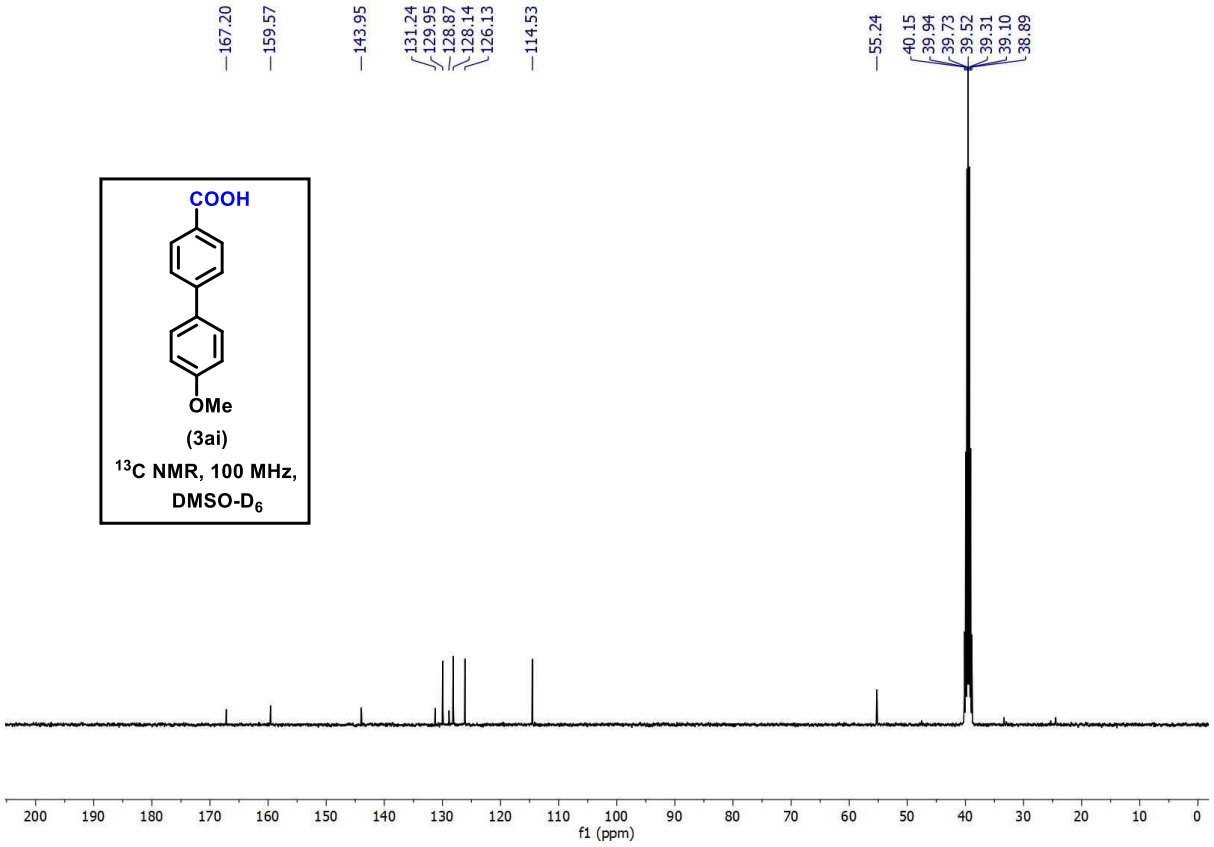

13.16
8.88 8.88 8.86 8.86 8.17 8.16 8.16 8.16 8.15 8.15 8.15 8.14 8.14 8.14 8.13 8.02 8.01 8.00 7.99 7.66 7.66 7.64 7.64 7.64 7.62 7.62 7.60 7.60 7.59 7.58 7.58 7.58 7.57 7.56 7.56 7.56 3.39 2.51 2.50 2.50 2.50 2.49
COOH
(3ag)
1H NMR, 400 MHz,
DMSO-D6
0.74
1.00
2.02
1.01
1.04
2.02
f1 (ppm)


168.71
133.51 132.97 130.72 129.90 128.64 127.76 127.60 126.22 125.53 124.92
40.15 39.94 39.73 39.52 39.31 39.10 38.89
COOH
(3ag)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


12.89
8.10
8.10
7.98
7.97
7.96
7.95
7.94
7.93
7.92
7.92
7.91
7.91
7.90
7.62
7.61
7.60
7.60
7.59
7.59
7.58
7.42
7.41
7.41
7.40
7.39
7.38
7.38
7.37
7.36
3.33
2.51
2.50
2.50
2.50
2.49
1.46
COOH
Me
Me
(3ah)
1H NMR, 400 MHz,
DMSO-D6
0.95
1.00
3.00
1.00
2.00
6.00
f1 (ppm)


167.51
154.32
153.35
143.08
137.40
125.54
128.78
128.54
127.28
123.68
122.99
121.07
120.08
46.55
40.15
39.94
39.73
39.52
39.31
39.10
38.89
26.57
COOH
Me
Me
(3ah)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


12.88
7.99
7.97
7.76
7.74
7.70
7.68
7.06
7.04
3.81
3.34
2.51
2.50
2.50
2.50
2.49
COOH
OMe
(3ai)
1H NMR, 400 MHz,
DMSO-D6
0.54
2.00
2.00
2.00
1.99
3.00
f1 (ppm)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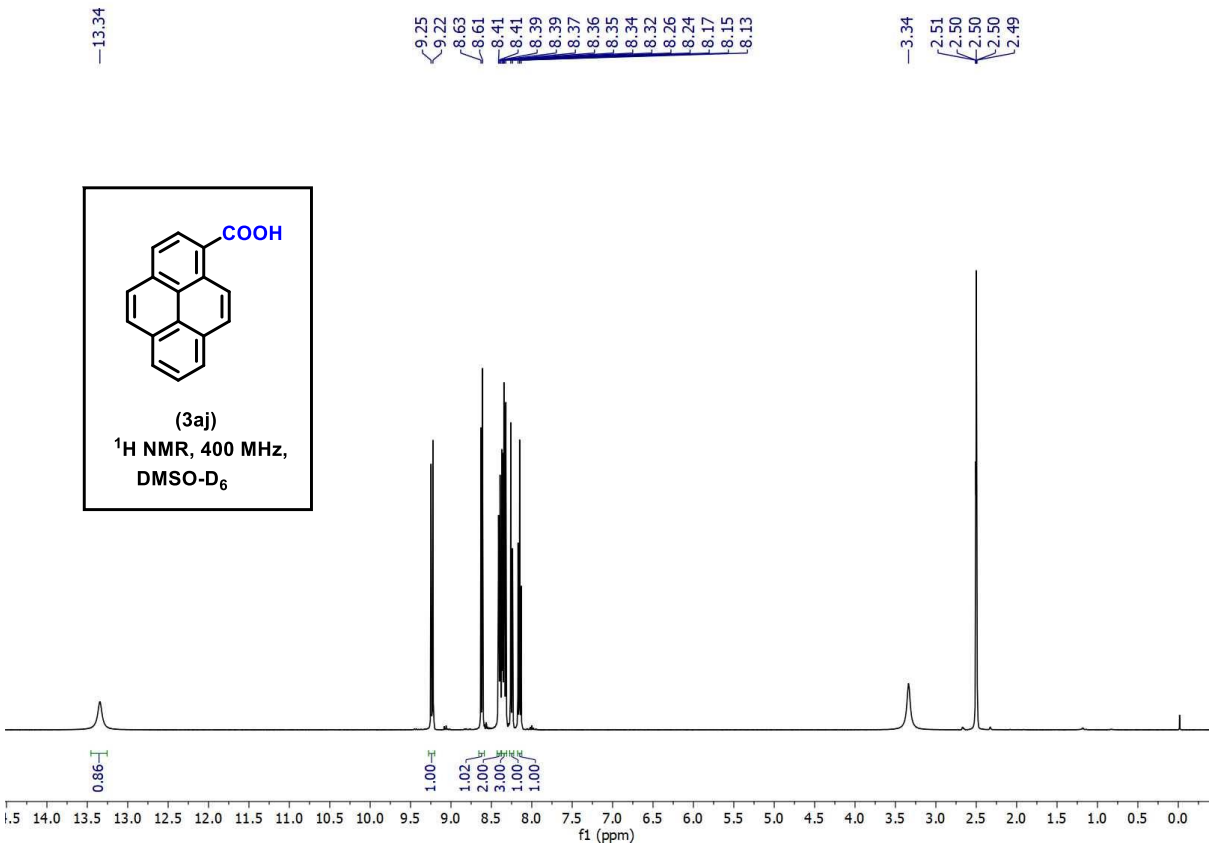
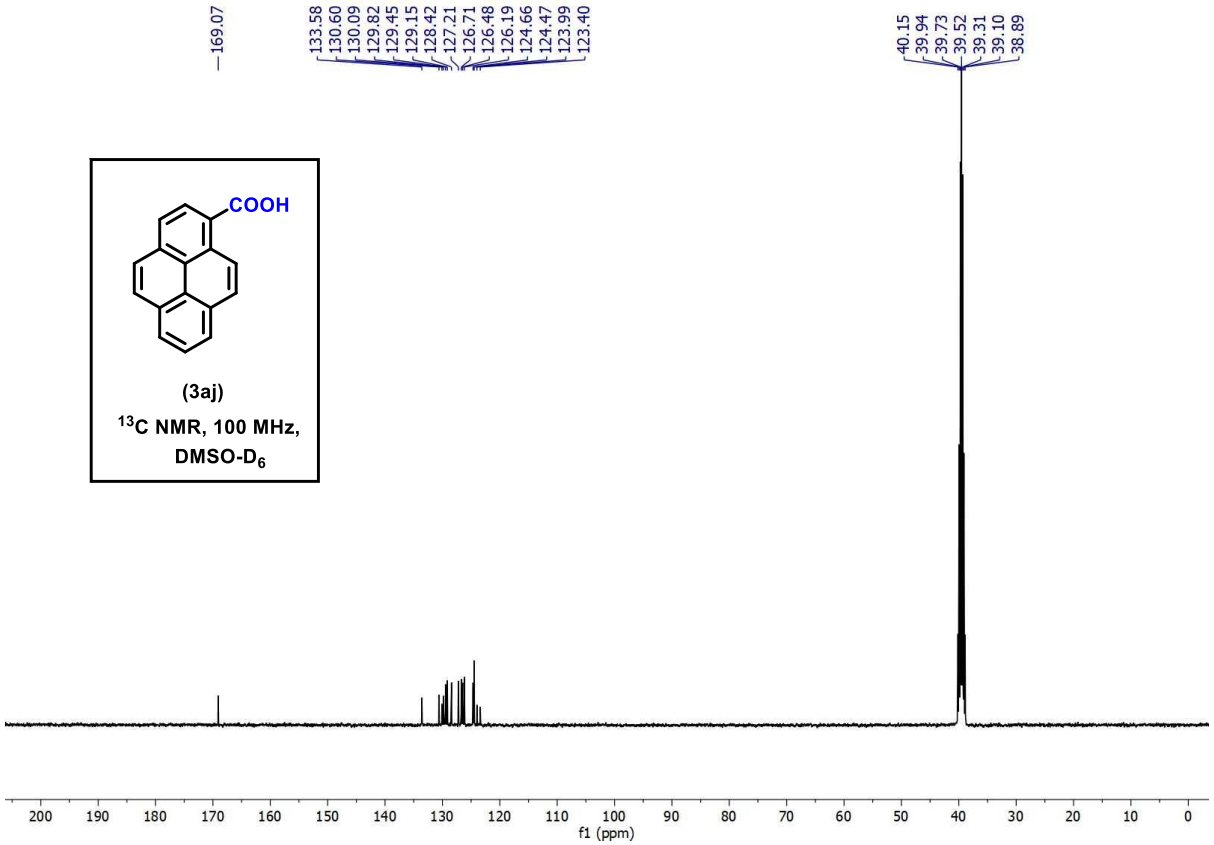
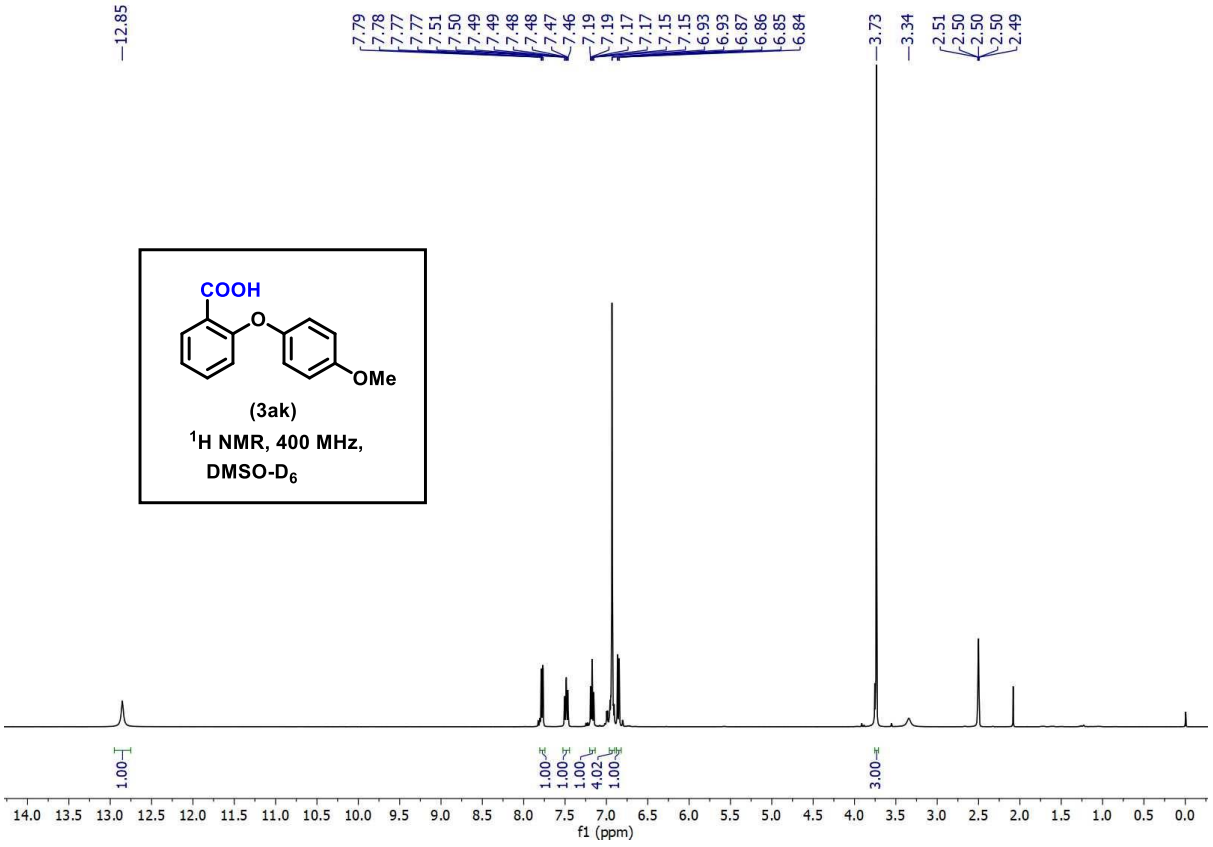
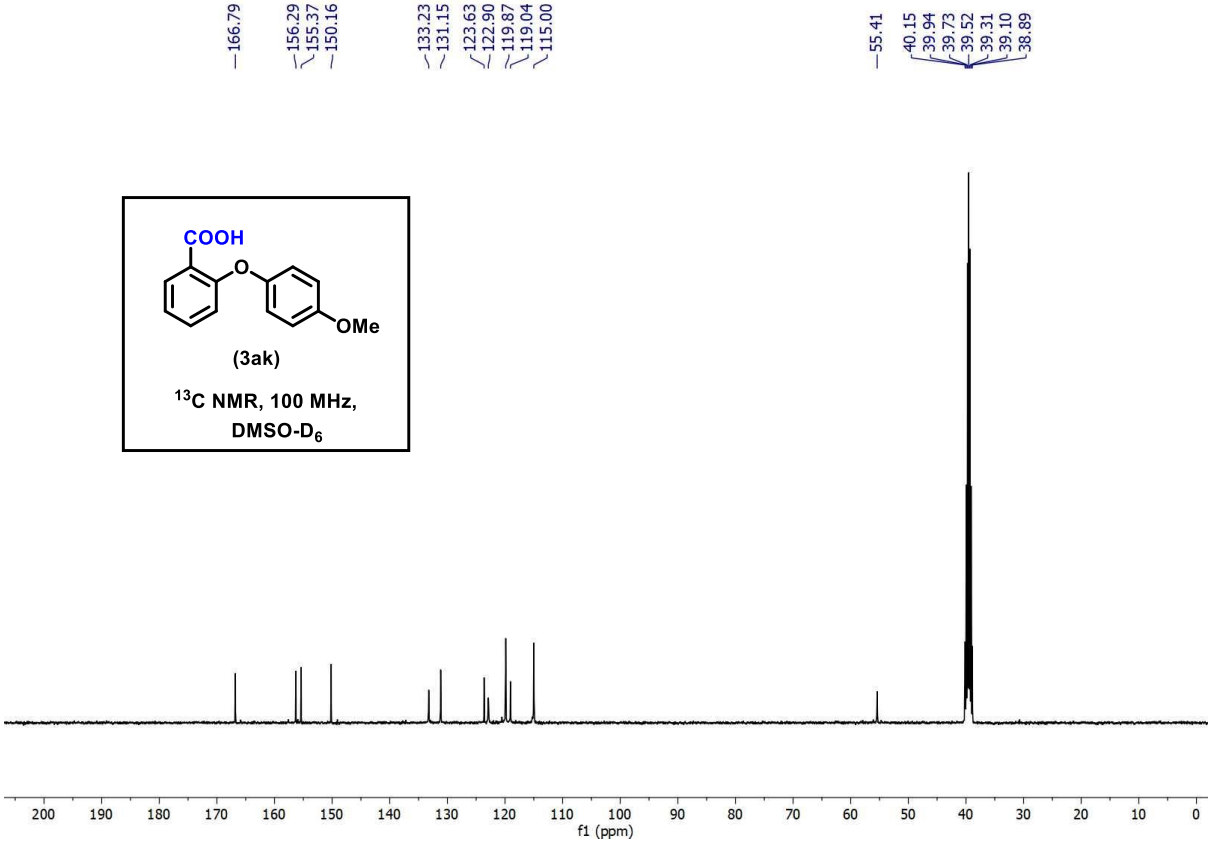
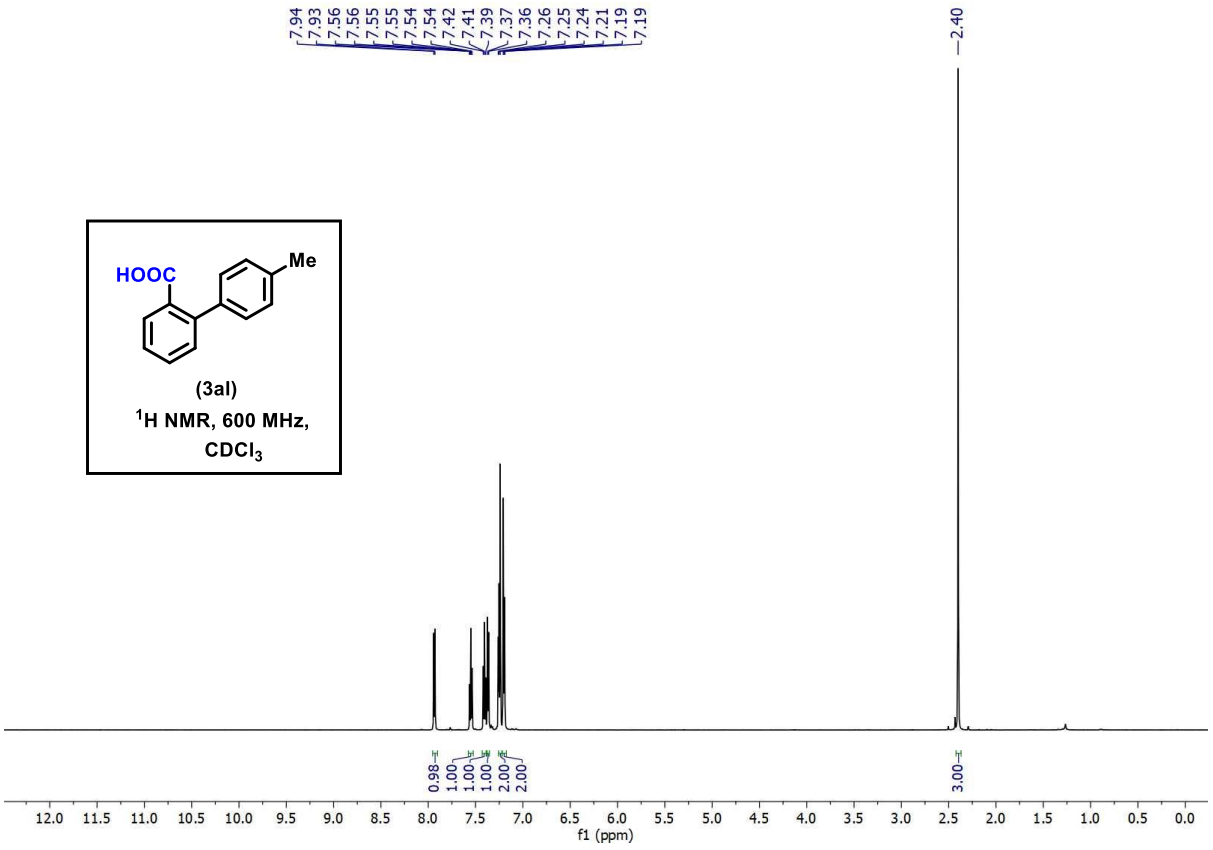
159.57
143.95
131.24
129.95
128.87
128.14
126.13
114.53
55.24
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
OMe
(3ai)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)

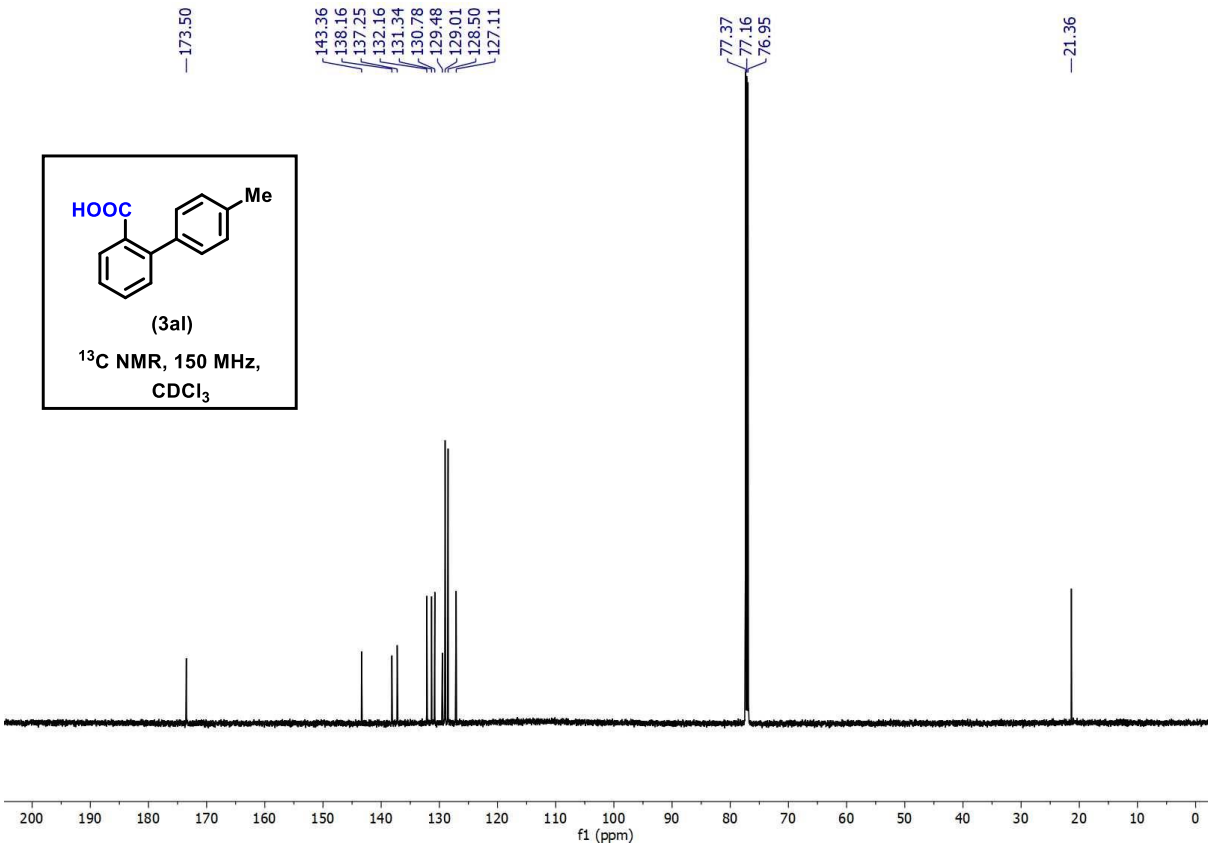

13.34
9.25
9.22
8.63
8.61
8.41
8.41
8.39
8.39
8.37
8.36
8.35
8.34
8.32
8.26
8.24
8.17
8.15
8.13
3.34
2.51
2.50
2.50
2.50
2.49
COOH
(3aj)
1H NMR, 400 MHz,
DMSO-D6
0.86
1.00
1.02
2.00
3.00
1.00
1.00
f1 (ppm)

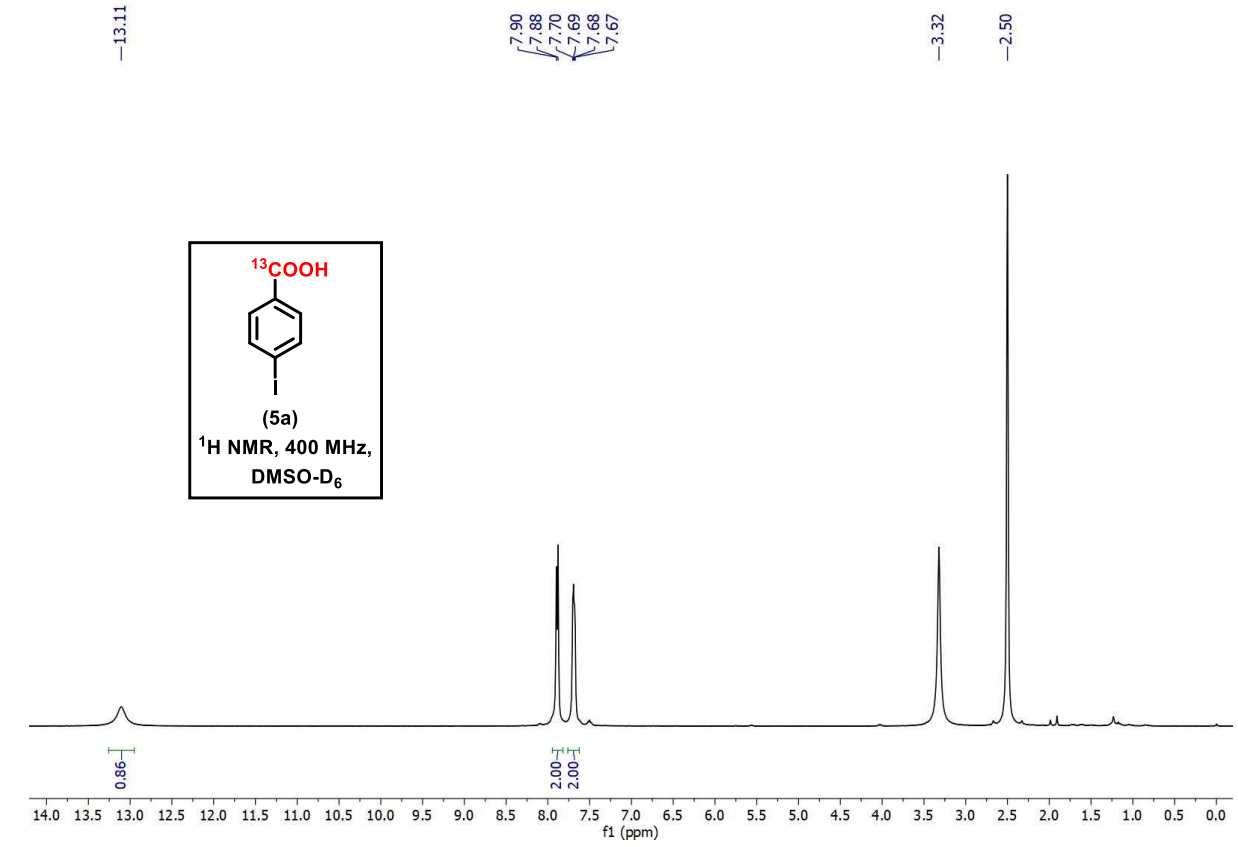

169.07
133.58
130.60
130.09
129.82
129.45
129.15
128.42
127.21
126.71
126.48
126.19
124.66
124.47
123.99
123.40
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
(3aj)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)

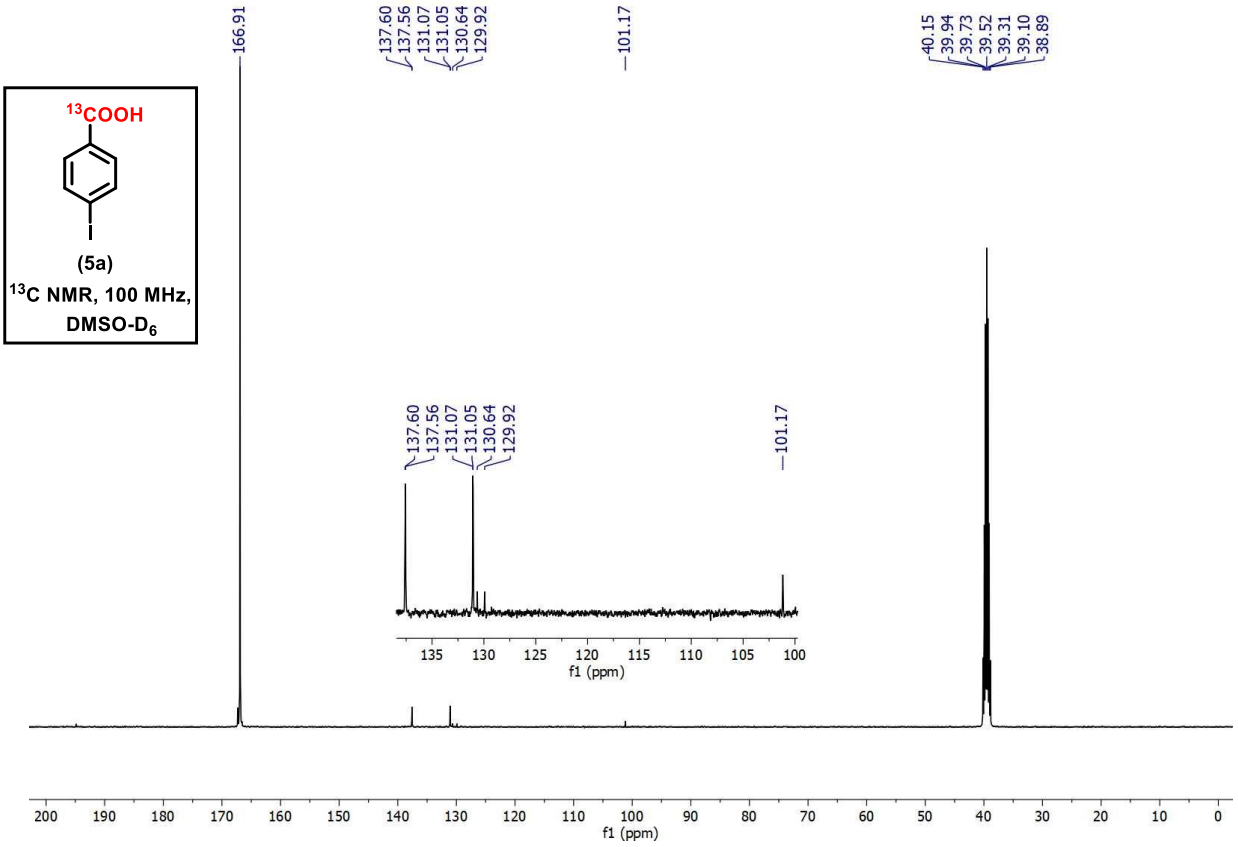

12.85
7.79
7.78
7.77
7.77
7.51
7.50
7.49
7.49
7.48
7.48
7.47
7.46
7.19
7.19
7.17
7.17
7.15
7.15
6.93
6.93
6.87
6.86
6.85
6.84
3.73
3.34
2.51
2.50
2.50
2.50
2.49
COOH
O
OMe
(3ak)
1H NMR, 400 MHz,
DMSO-D6
1.00
1.00
1.00
1.00
4.02
3.00
f1 (ppm)

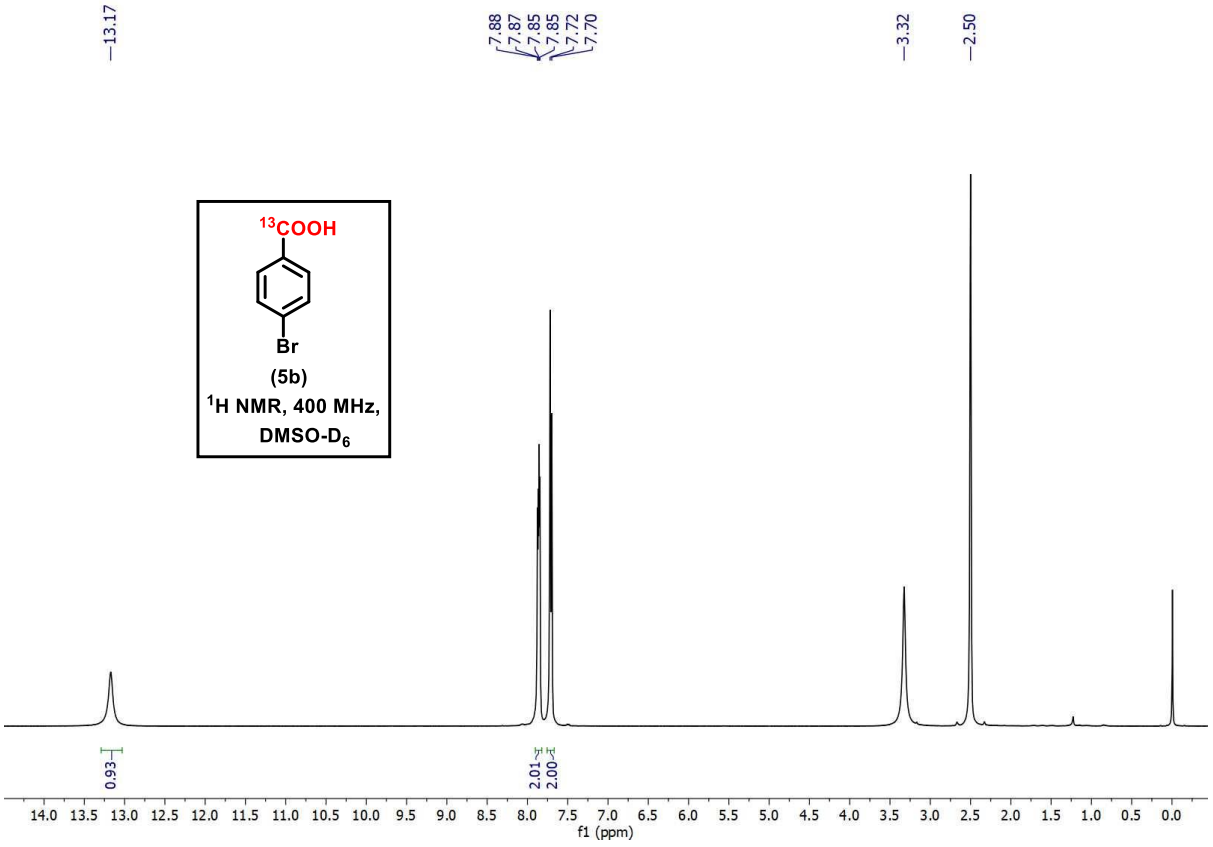

166.79
156.29
155.37
150.16
133.23
131.15
123.63
122.90
119.87
119.04
115.00
55.41
40.15
39.94
39.73
39.52
39.31
39.10
38.89
COOH
O
OMe
(3ak)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)

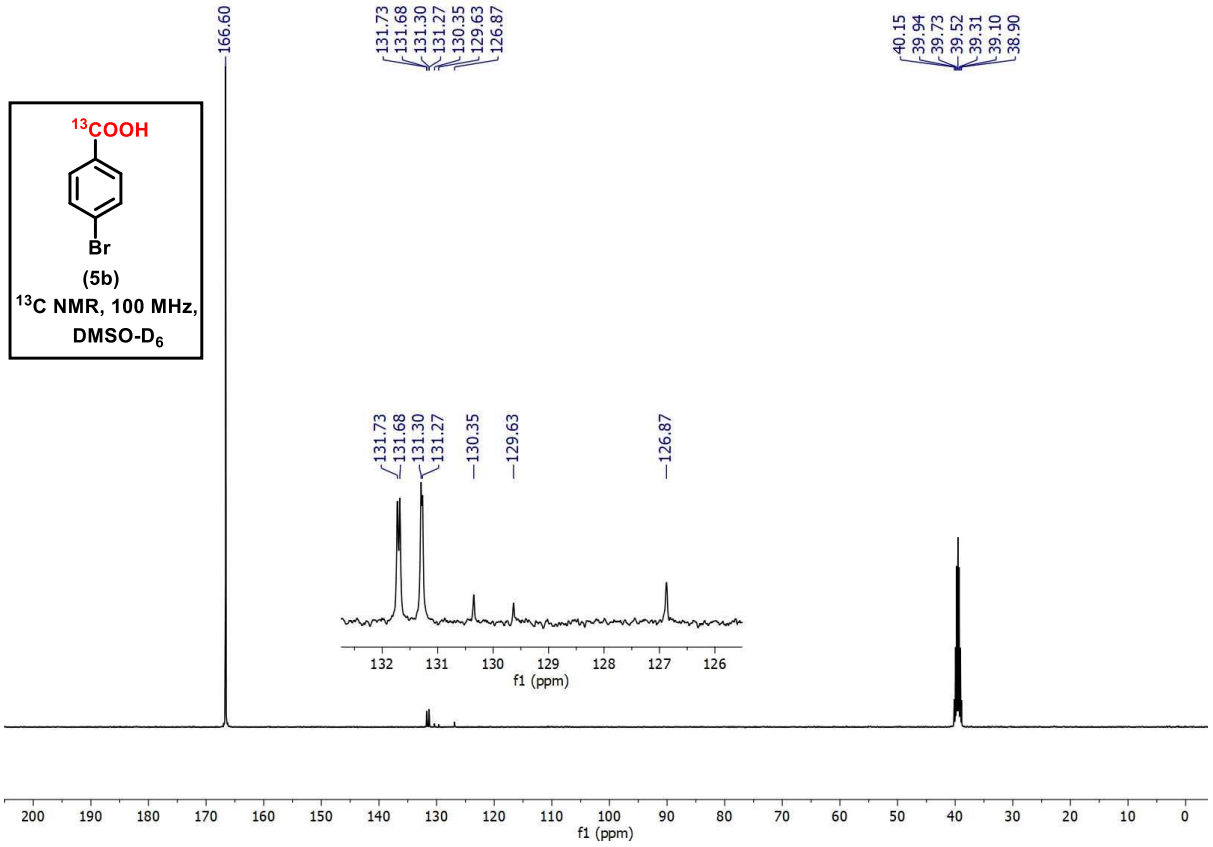

7.94
7.93
7.56
7.56
7.55
7.55
7.54
7.54
7.42
7.41
7.39
7.37
7.36
7.26
7.25
7.24
7.21
7.19
7.19
2.40
HOOC
Me
(3al)
1H NMR, 600 MHz,
CDCl3
0.98
1.00
1.00
1.00
2.00
2.00
3.00
f1 (ppm)

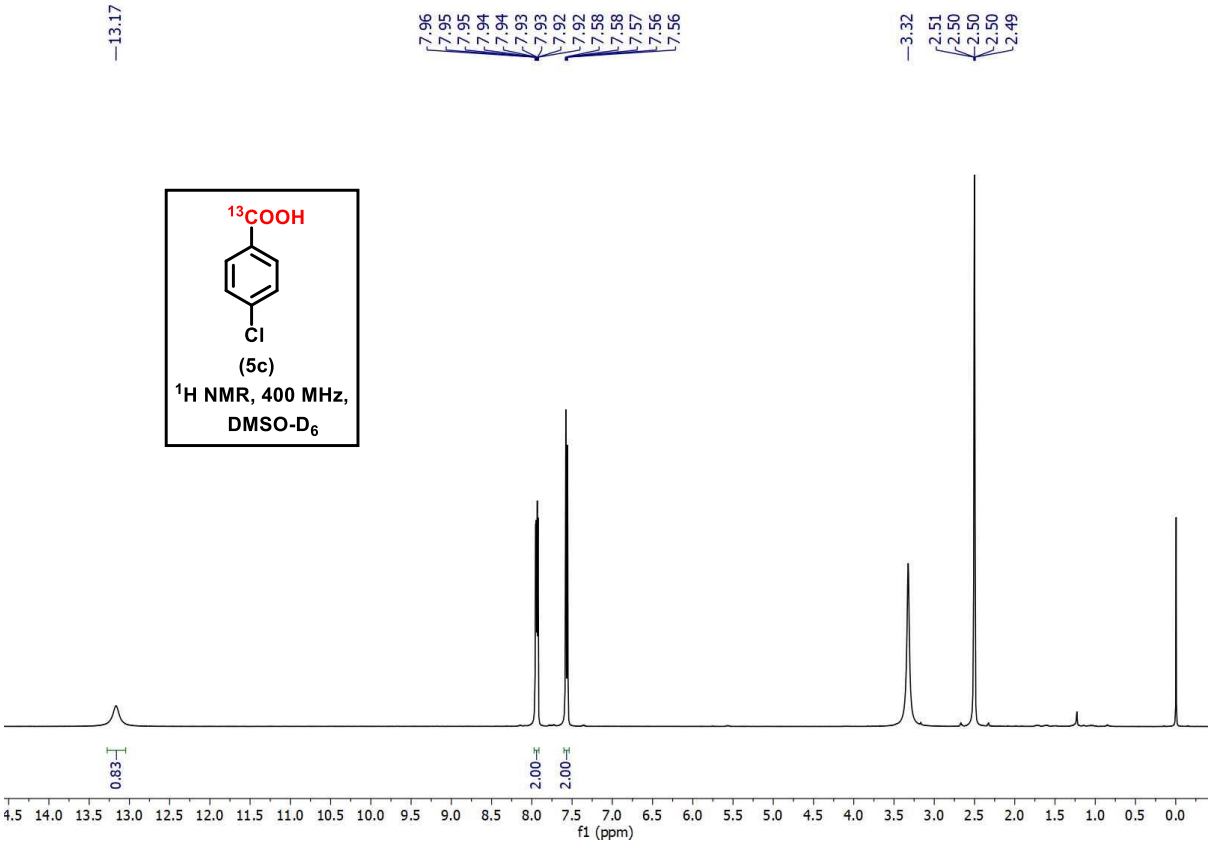

173.50
143.36
138.16
137.25
132.16
131.34
130.78
129.48
129.01
128.50
127.11
77.37
77.16
76.95
21.36
HOOC
Me
(3al)
13C NMR, 150 MHz,
CDCl3
f1 (ppm)

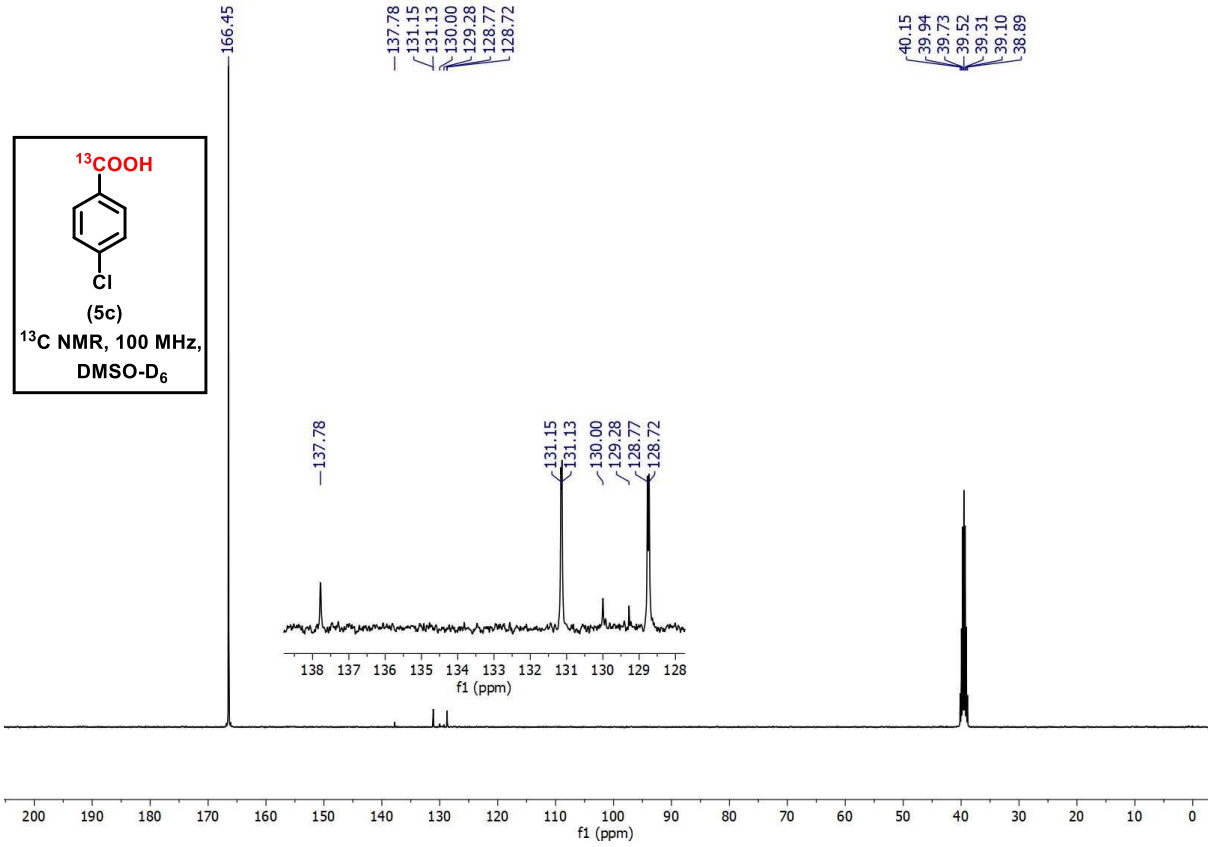

13.11
7.90
7.88
7.70
7.69
7.68
7.67
3.32
2.50
13COOH
(5a)
1H NMR, 400 MHz,
DMSO-D6
0.86
2.00
2.00
f1 (ppm)


166.91
137.60
137.56
131.07
131.05
130.64
129.92
101.17
40.15
39.94
39.73
39.52
39.31
39.10
38.89
13COOH
(5a)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


13.17
7.88
7.87
7.85
7.85
7.72
7.70
3.32
2.50
13COOH
Br
(5b)
1H NMR, 400 MHz,
DMSO-D6
0.93
2.01
2.00
f1 (ppm)


166.60
131.73
131.68
131.30
131.27
130.35
129.63
126.87
40.15
39.94
39.73
39.52
39.31
39.10
38.90
13COOH
Br
(5b)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)


13.17
7.96
7.95
7.95
7.94
7.94
7.93
7.93
7.92
7.92
7.58
7.58
7.57
7.56
7.56
3.32
2.51
2.50
2.50
2.50
2.49
13COOH
Cl
(5c)
1H NMR, 400 MHz,
DMSO-D6
0.83
2.00
2.00
f1 (ppm)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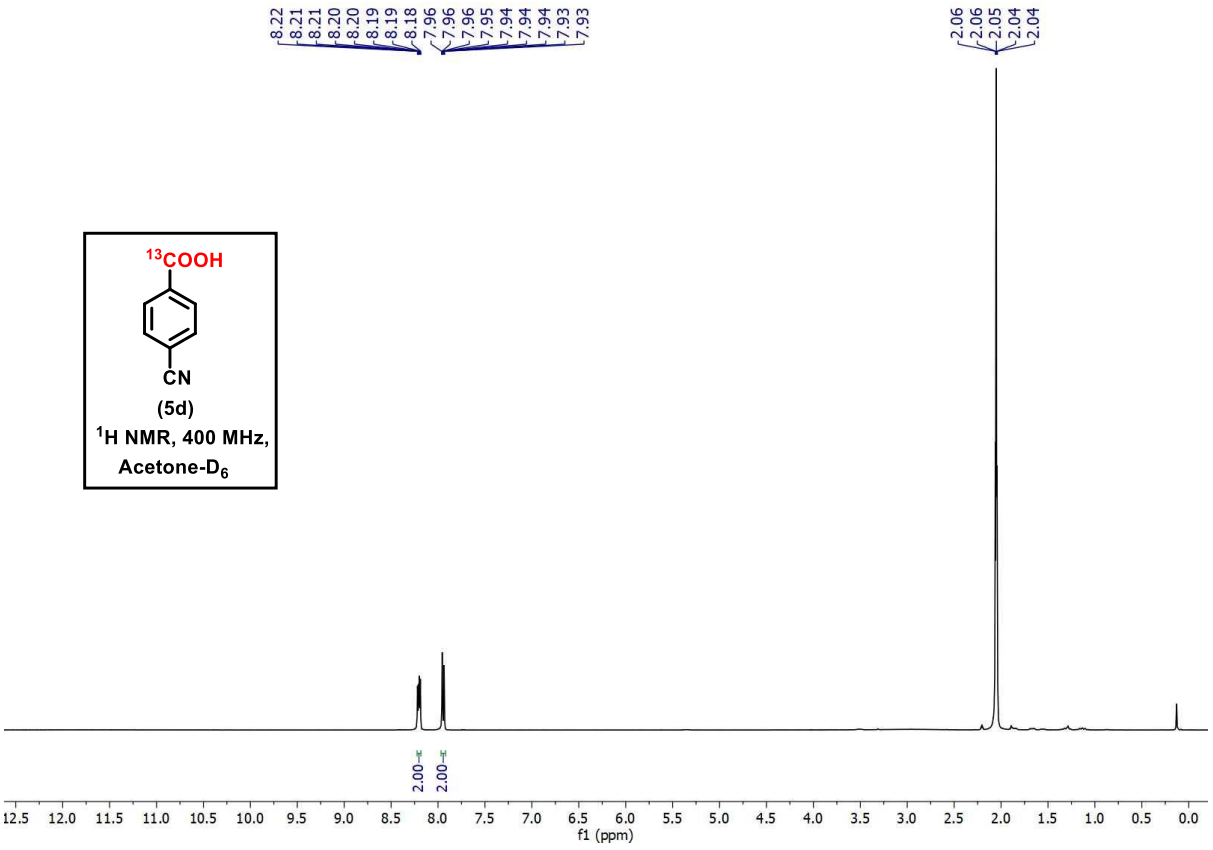
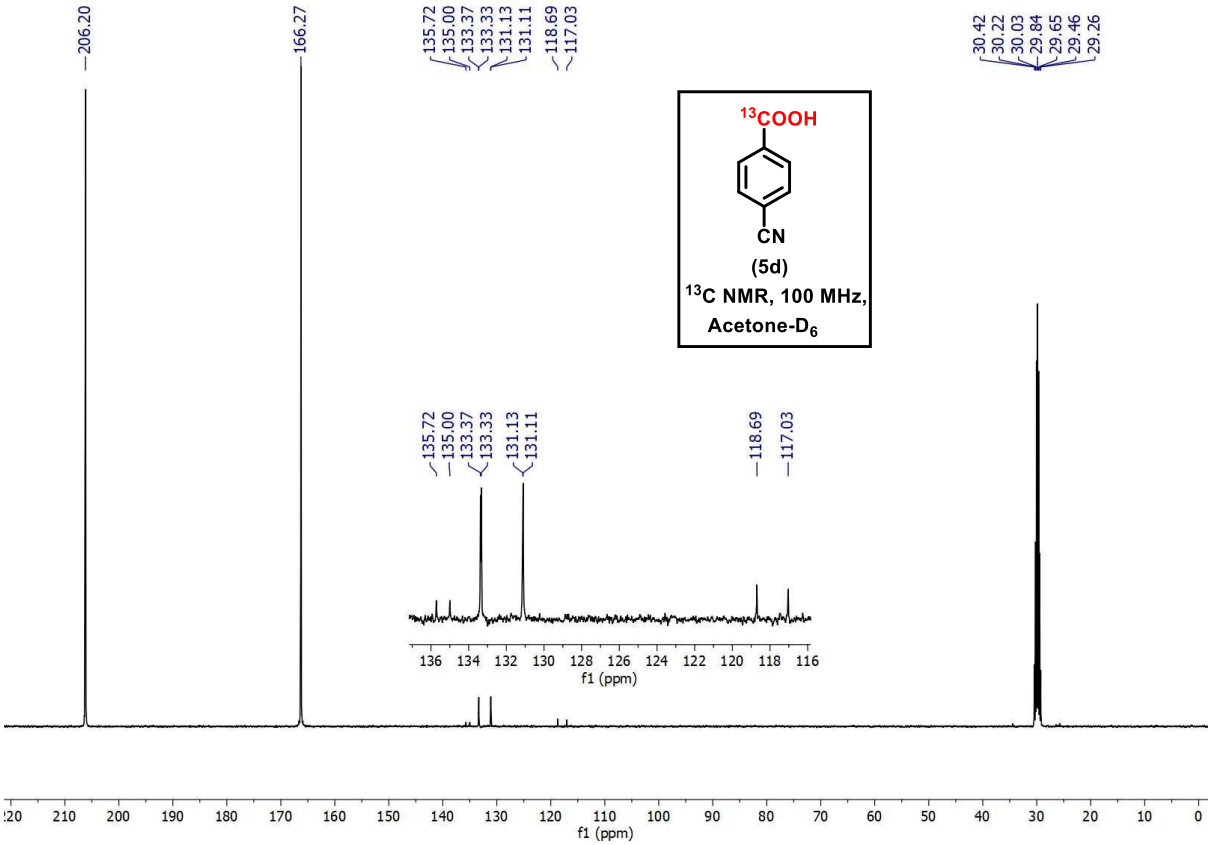
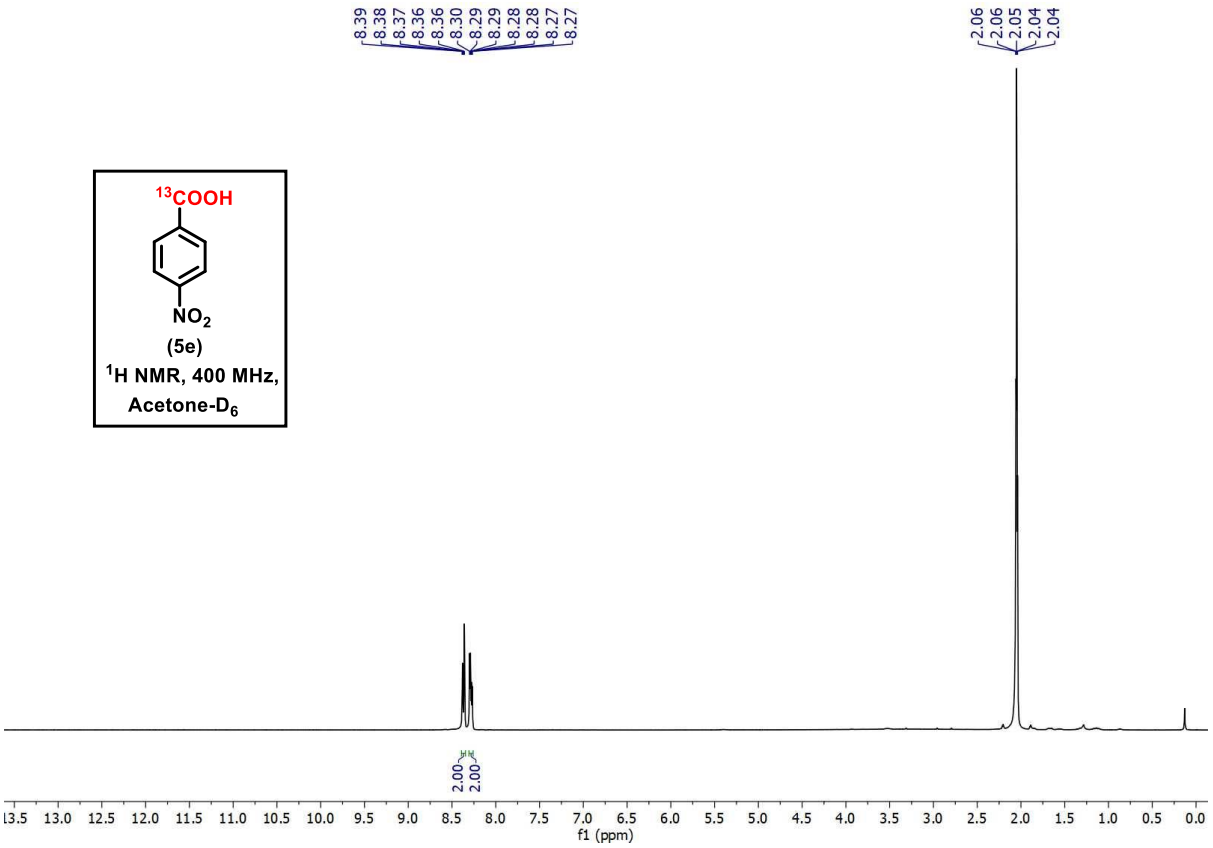
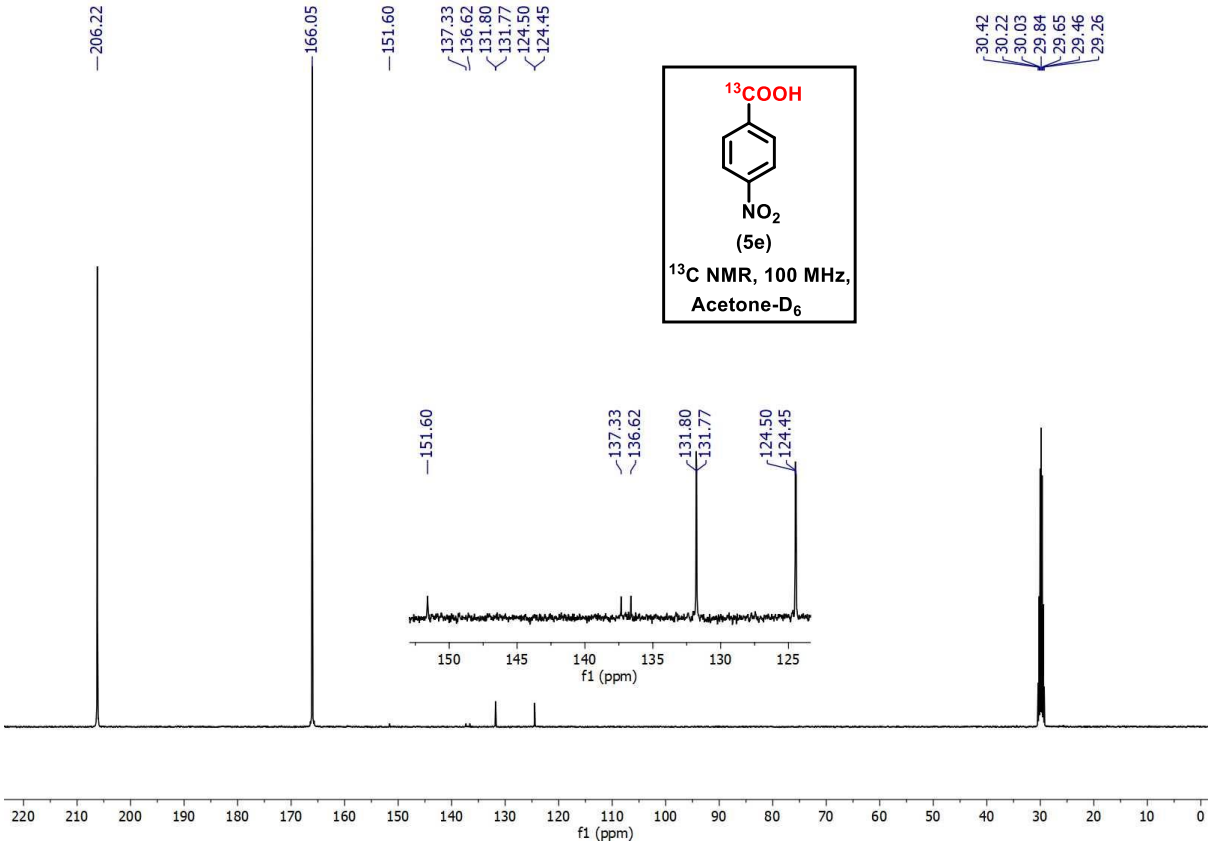
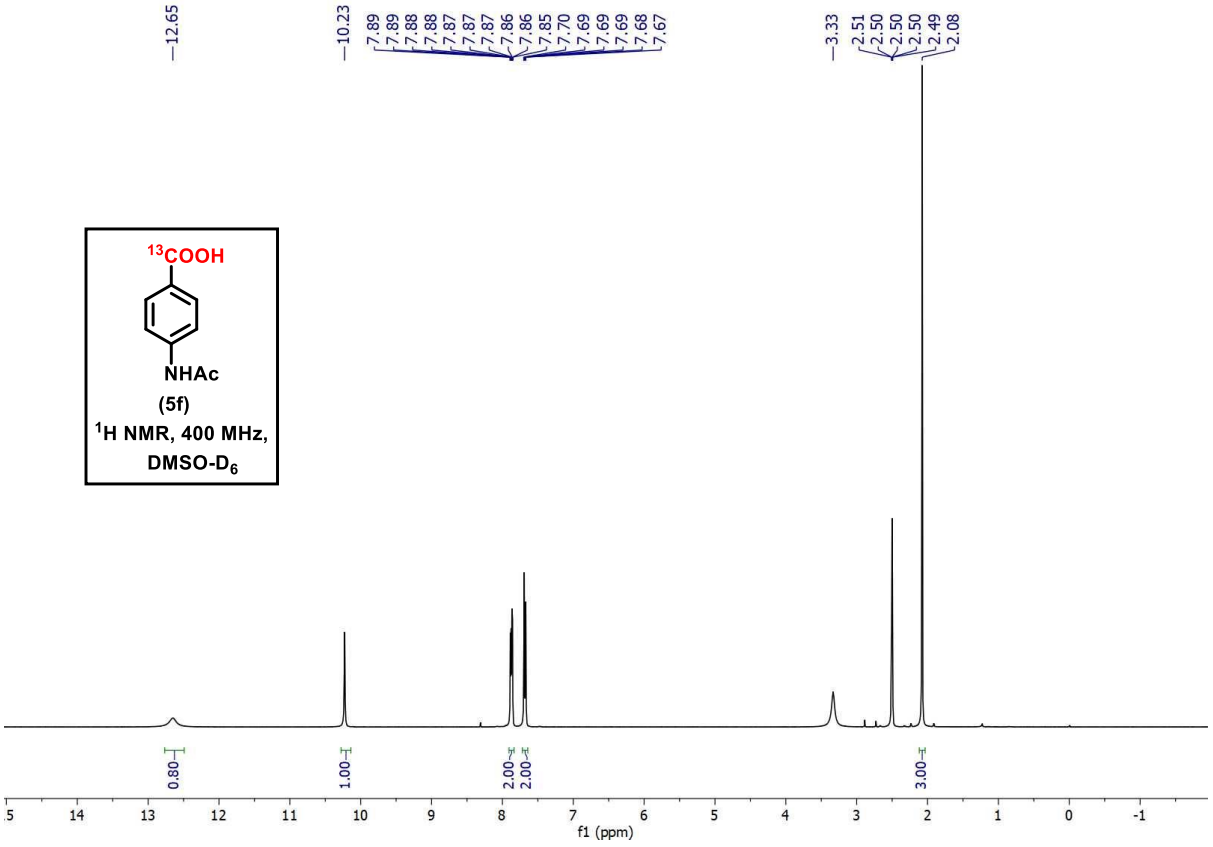
137.78
131.15
131.13
130.00
129.28
128.77
128.72
40.15
39.94
39.73
39.52
39.31
39.10
38.89
13COOH
Cl
(5c)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)

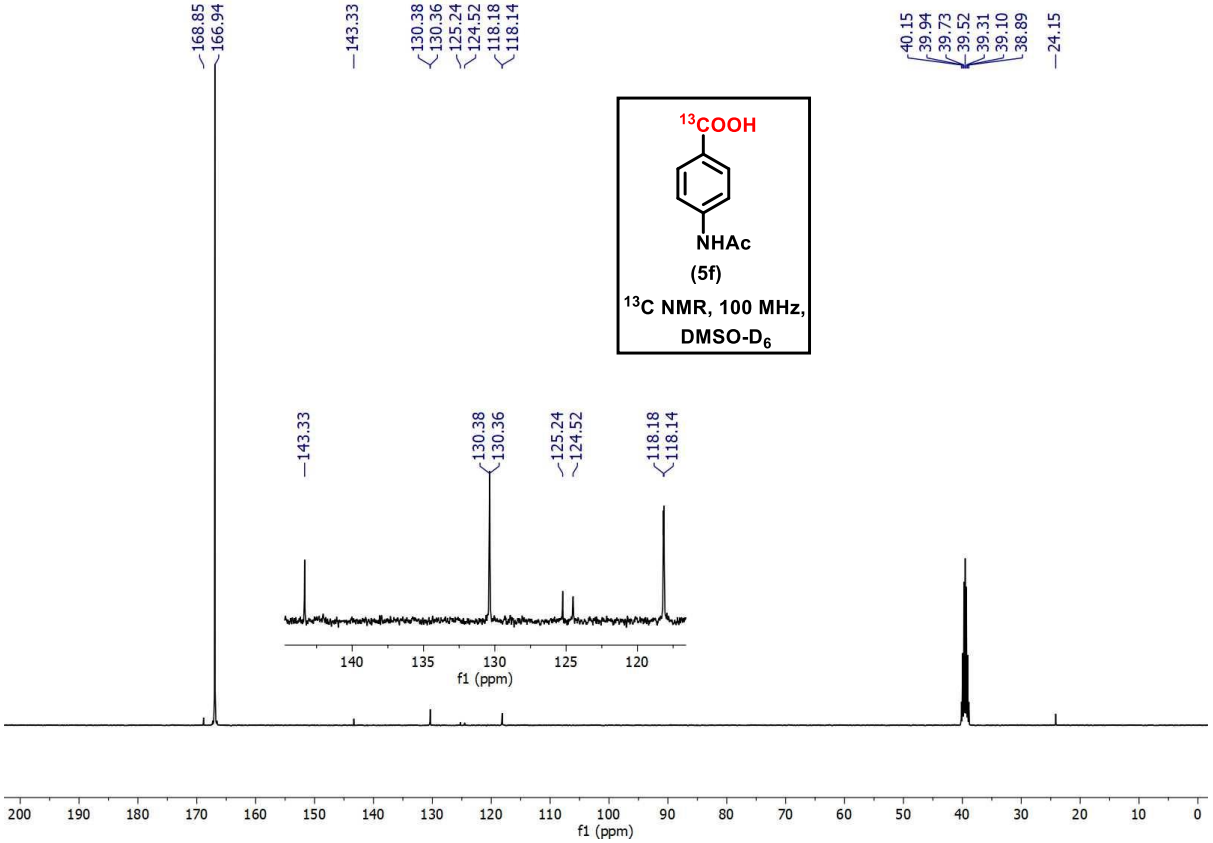

8.22
8.21
8.21
8.20
8.20
8.19
8.19
8.18
7.96
7.96
7.96
7.95
7.94
7.94
7.94
7.93
7.93
2.06
2.06
2.05
2.04
2.04
13COOH
CN
(5d)
1H NMR, 400 MHz,
Acetone-D6
2.00
2.00
f1 (ppm)

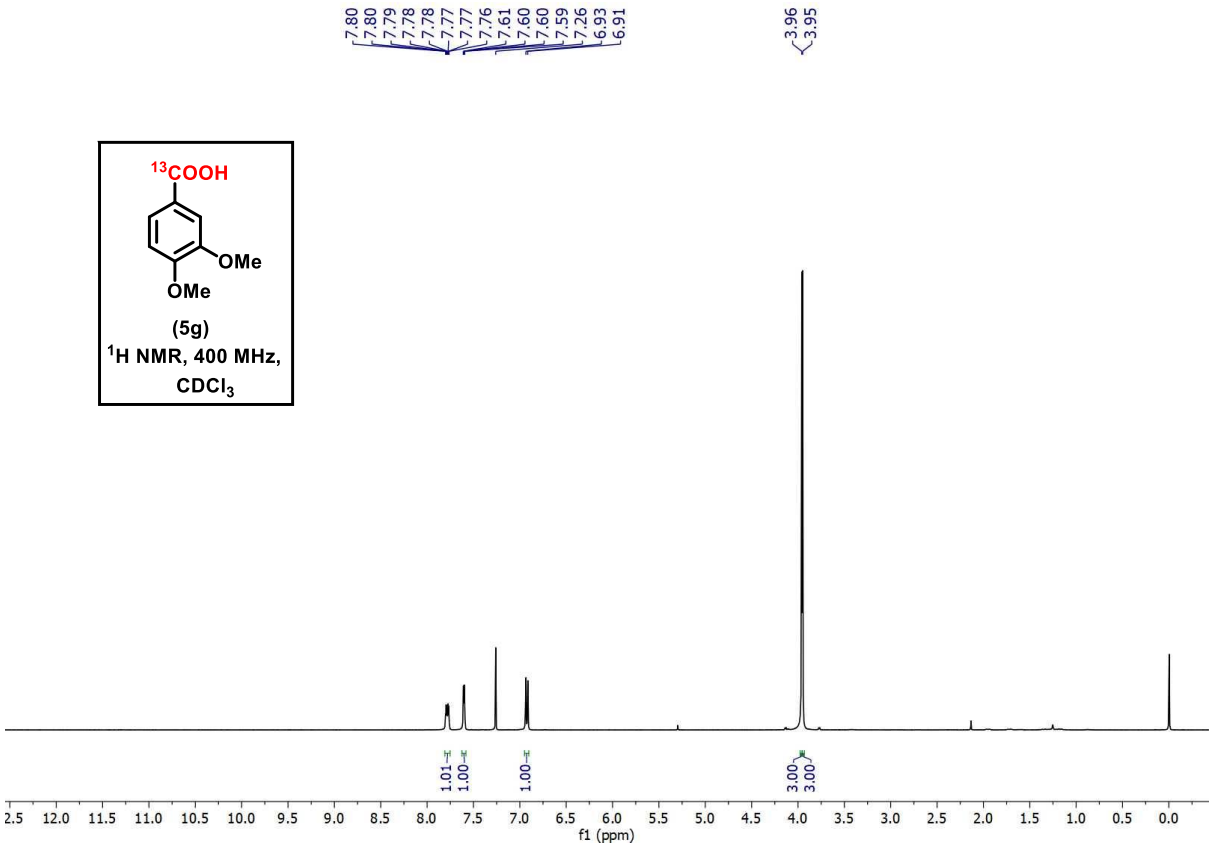

206.20
166.27
135.72
135.00
133.37
133.33
131.13
131.11
118.69
117.03
30.42
30.22
30.03
29.84
29.65
29.46
29.26
13COOH
CN
(5d)
13C NMR, 100 MHz,
Acetone-D6
f1 (ppm)

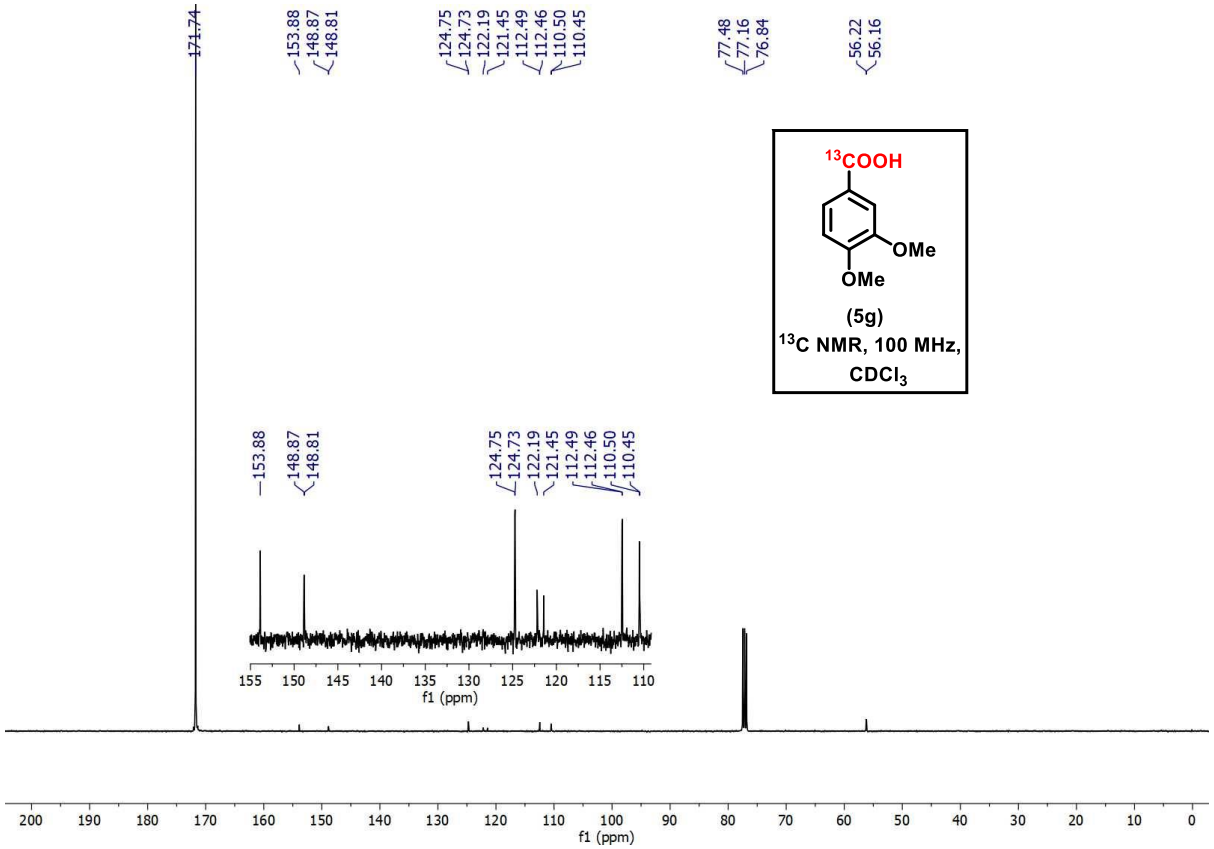

8.39
8.38
8.37
8.36
8.36
8.30
8.29
8.29
8.28
8.28
8.27
8.27
2.06
2.06
2.05
2.04
2.04
13COOH
NO2
(5e)
1H NMR, 400 MHz,
Acetone-D6
2.00
2.00
f1 (ppm)

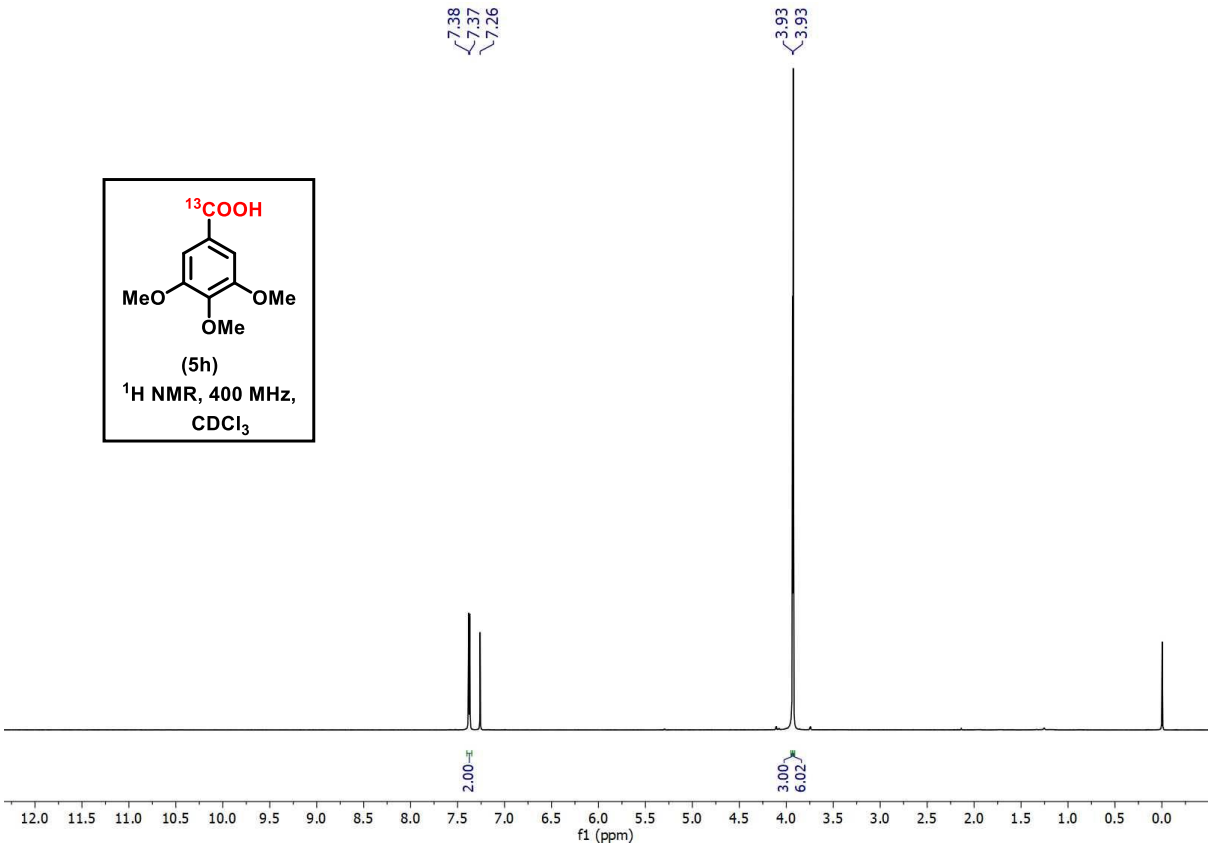

206.22
166.05
151.60
137.33
136.62
131.80
131.77
124.50
124.45
30.42
30.22
30.03
29.84
29.65
29.46
29.26
13COOH
NO2
(5e)
13C NMR, 100 MHz,
Acetone-D6
f1 (ppm)
f1 (ppm)

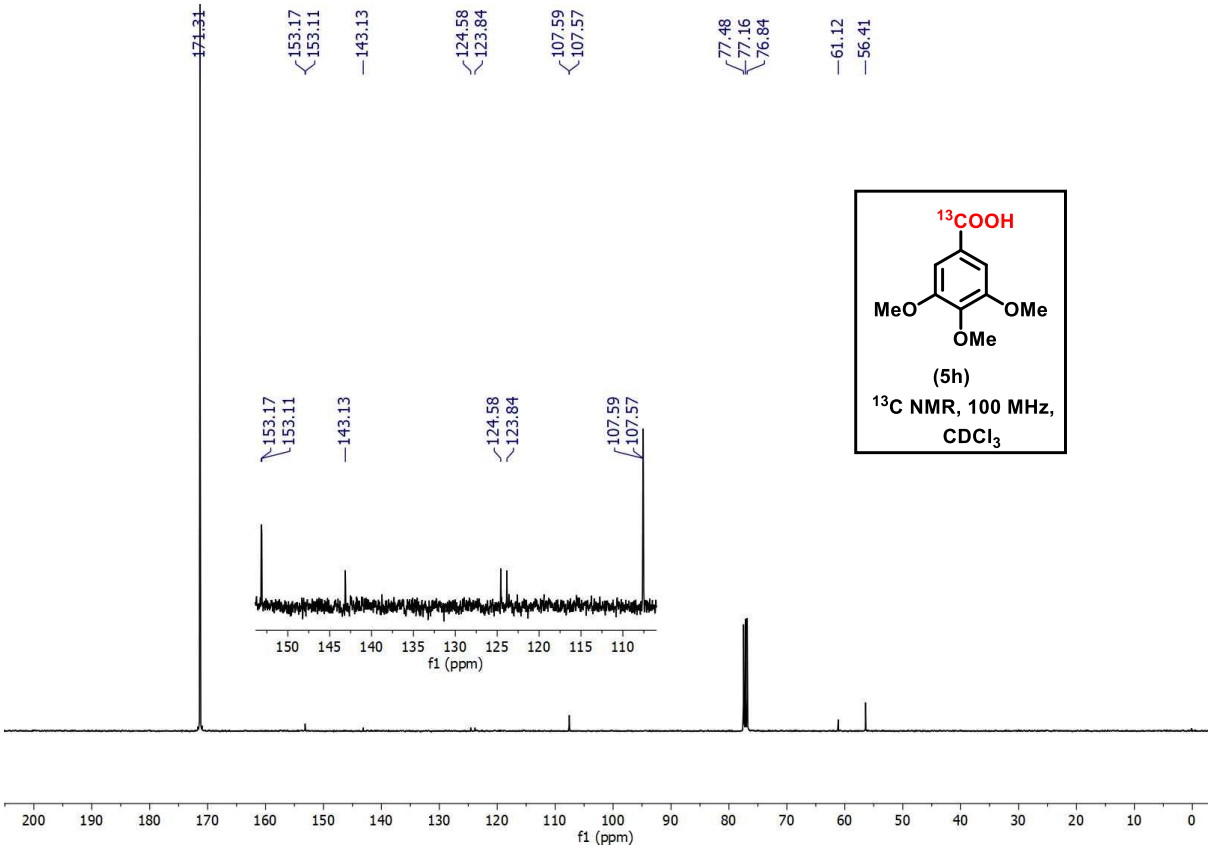

12.65
10.23
7.89
7.89
7.88
7.88
7.87
7.87
7.87
7.86
7.86
7.85
7.70
7.69
7.69
7.69
7.68
7.67
3.33
2.51
2.50
2.50
2.50
2.49
2.08
13COOH
NHAc
(5f)
1H NMR, 400 MHz,
DMSO-D6
0.80
1.00
2.00
2.00
3.00
f1 (ppm)

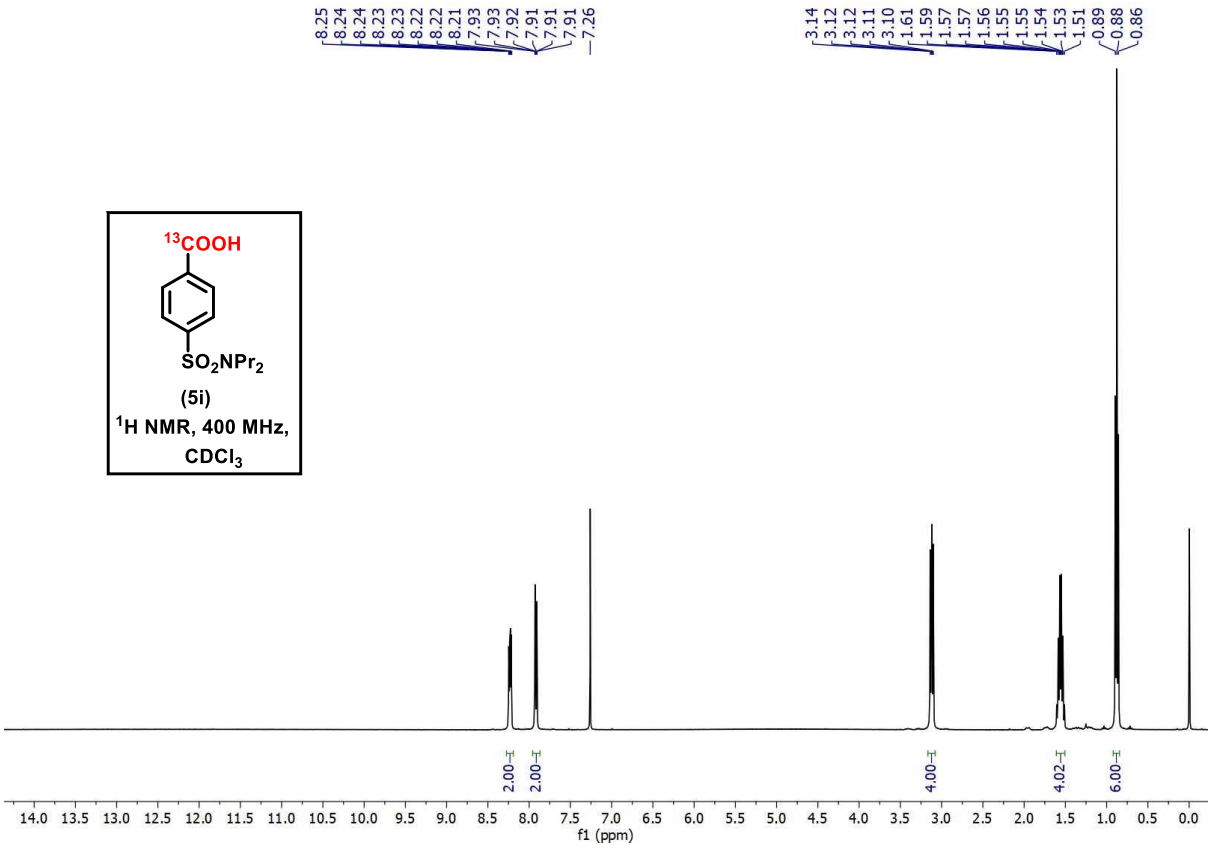

168.85
166.94
143.33
130.38
130.36
125.24
124.52
118.18
118.14
40.15
39.94
39.73
39.52
39.31
39.10
38.89
24.15
13COOH
NHAc
(5f)
13C NMR, 100 MHz,
DMSO-D6
f1 (ppm)

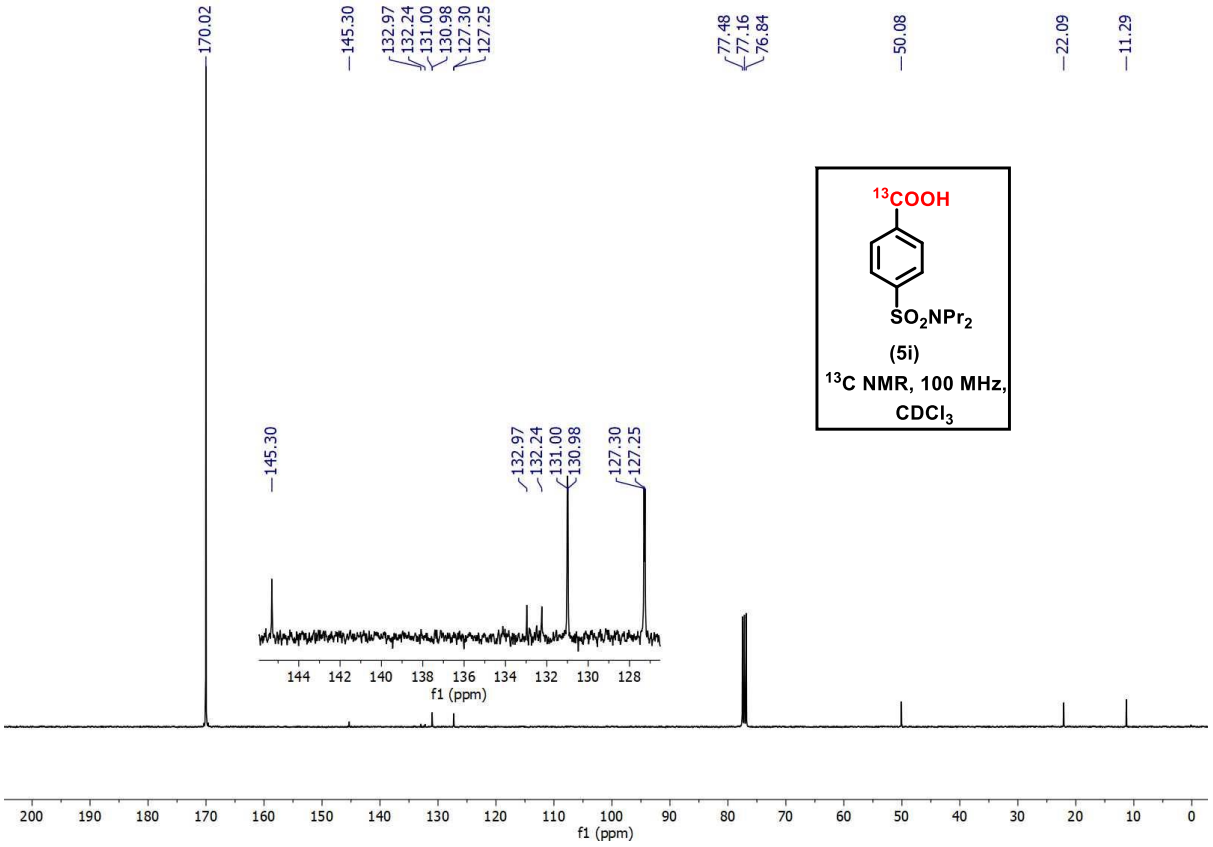

7.80
7.80
7.79
7.78
7.78
7.77
7.77
7.76
7.61
7.60
7.60
7.59
7.26
6.93
6.91
3.96
3.95
13COOH
OMe
OMe
(5g)
1H NMR, 400 MHz,
CDCl3
1.01
1.00
1.00
3.00
3.00
f1 (ppm)

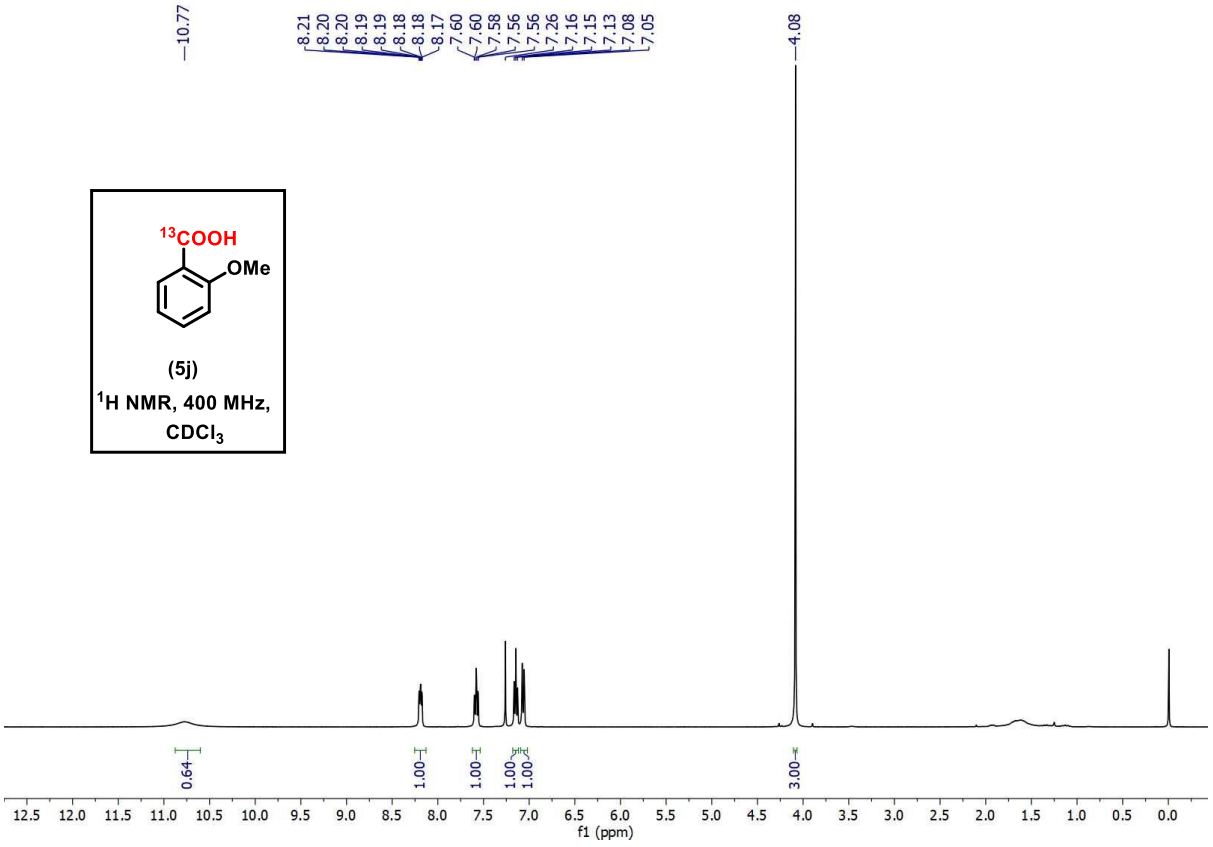

171.74
153.88
148.87
148.81
124.75
124.73
122.19
121.45
112.49
112.46
110.50
110.45
77.48
77.16
76.84
56.22
56.16
13COOH
OMe
OMe
(5g)
13C NMR, 100 MHz,
CDCl3
f1 (ppm)


7.38
7.37
7.26
3.93
3.93
13COOH
MeO
OMe
OMe
(5h)
1H NMR, 400 MHz,
CDCl3
2.00
3.00
6.02
f1 (ppm)


171.31
153.17
153.11
143.13
124.58
123.84
107.59
107.57
77.48
77.16
76.84
61.12
56.41
13COOH
MeO
OMe
OMe
(5h)
13C NMR, 100 MHz,
CDCl3
f1 (ppm)


8.25
8.24
8.24
8.23
8.23
8.22
8.22
8.21
7.93
7.93
7.92
7.91
7.91
7.91
7.26
3.14
3.12
3.12
3.11
3.10
1.61
1.59
1.57
1.57
1.56
1.55
1.55
1.54
1.53
1.51
0.89
0.88
0.86
13COOH
SO2NPr2
(5i)
1H NMR, 400 MHz,
CDCl3
2.00
2.00
4.00
4.02
6.00
f1 (ppm)


170.02
145.30
132.97
132.24
131.00
130.98
127.30
127.25
77.48
77.16
76.84
50.08
22.09
11.29
13COOH
SO2NPr2
(5i)
13C NMR, 100 MHz,
CDCl3
f1 (ppm)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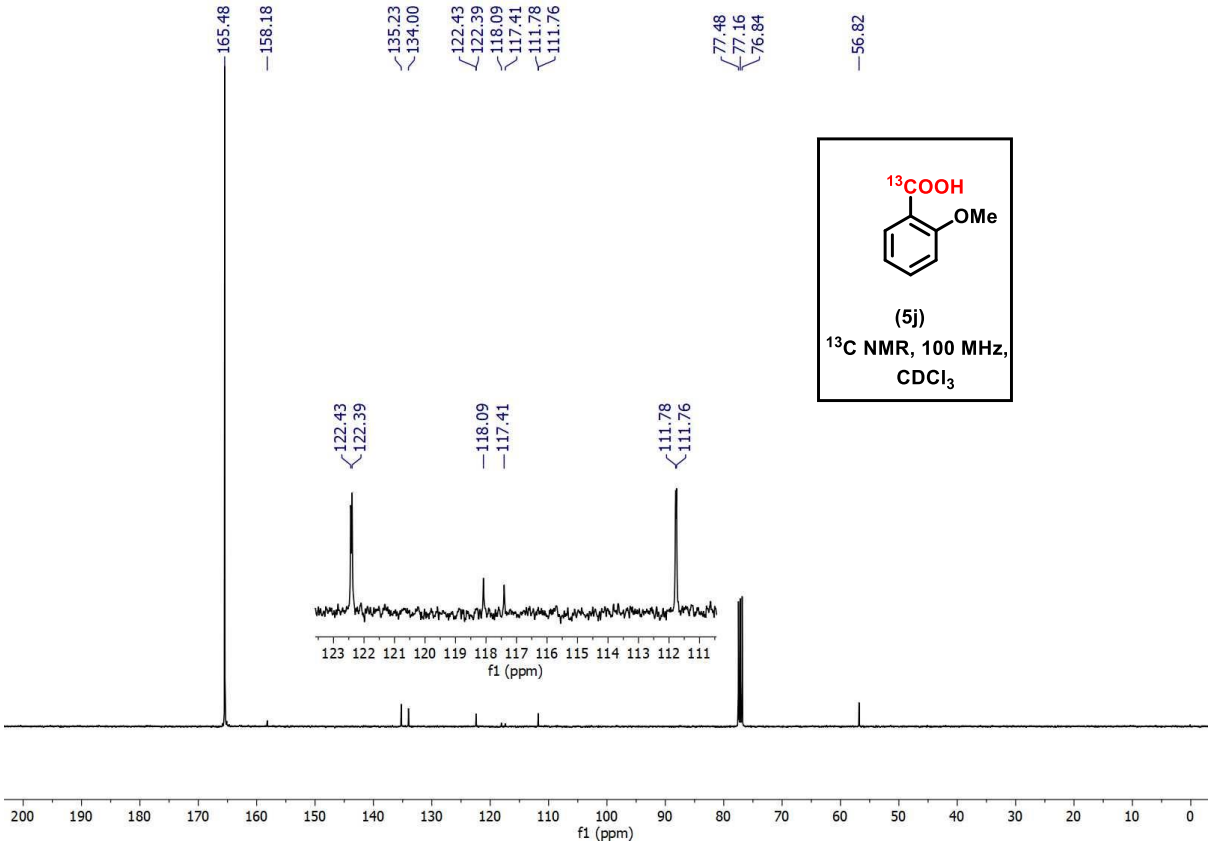
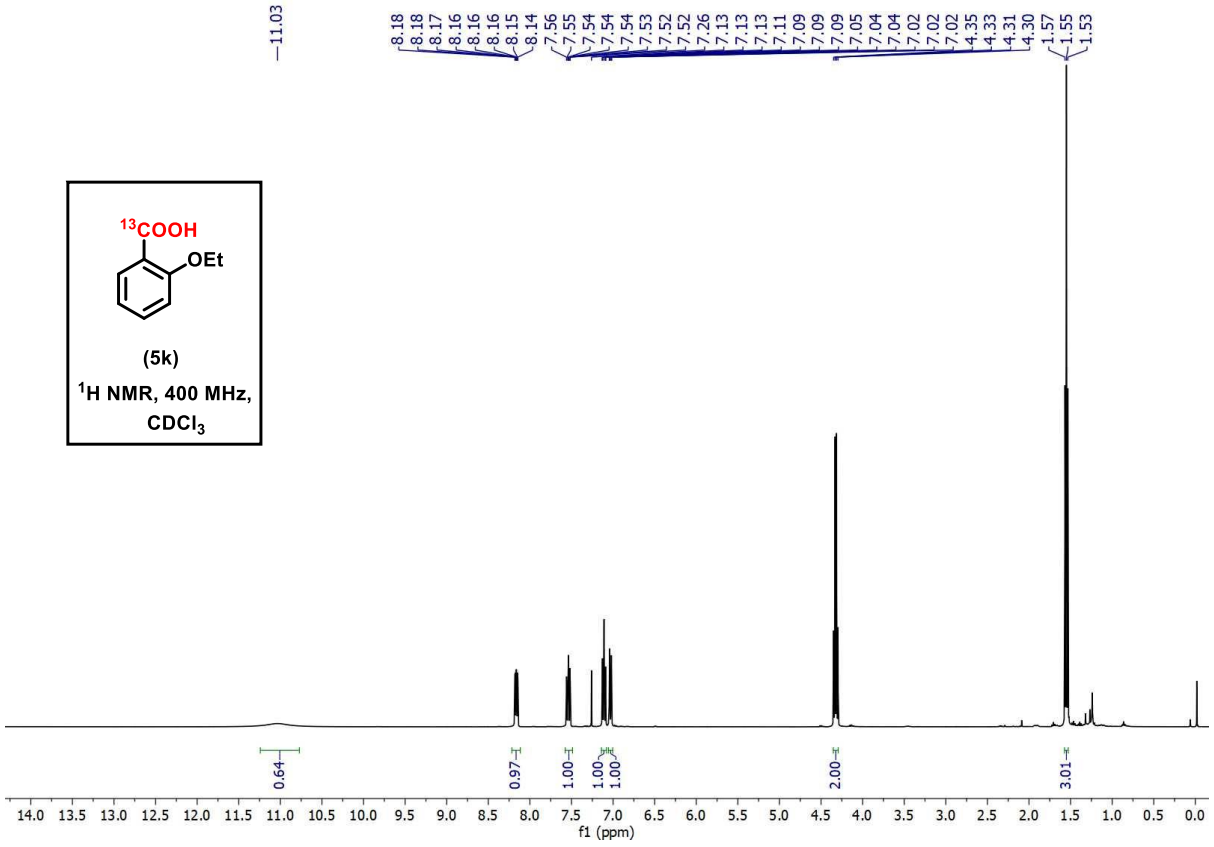
8.20
8.20
8.19
8.19
8.18
8.18
8.17
7.60
7.60
7.58
7.56
7.56
7.26
7.16
7.15
7.13
7.08
7.05
4.08
13COOH
OMe
(5j)
1H NMR, 400 MHz,
CDCl3
0.64
1.00
1.00
1.00
1.00
3.00
f1 (ppm)


165.48
158.18
135.23
134.00
122.43
122.39
118.09
117.41
111.78
111.76
77.48
77.16
76.84
56.82
13COOH
OMe
(5j)
13C NMR, 100 MHz,
CDCl3
f1 (ppm)
f1 (ppm)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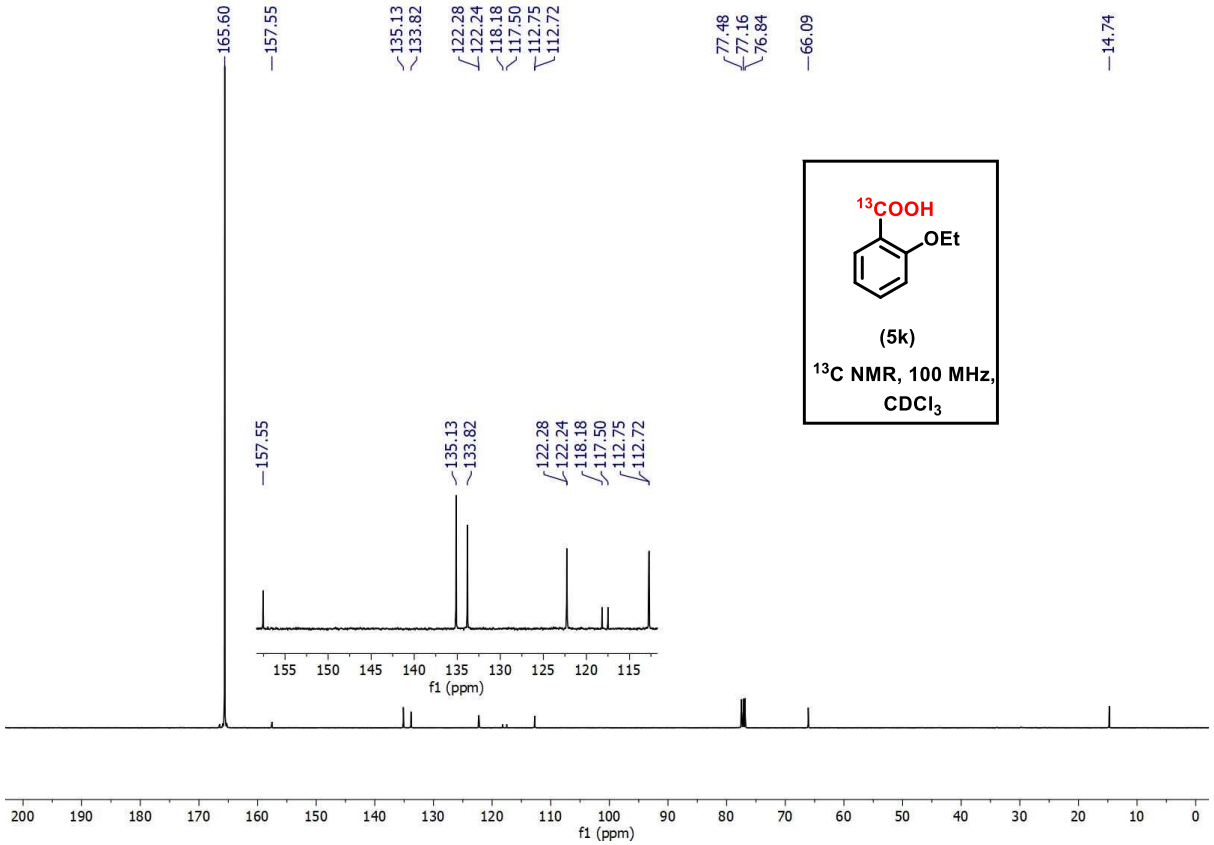
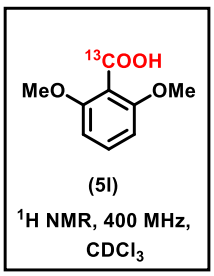
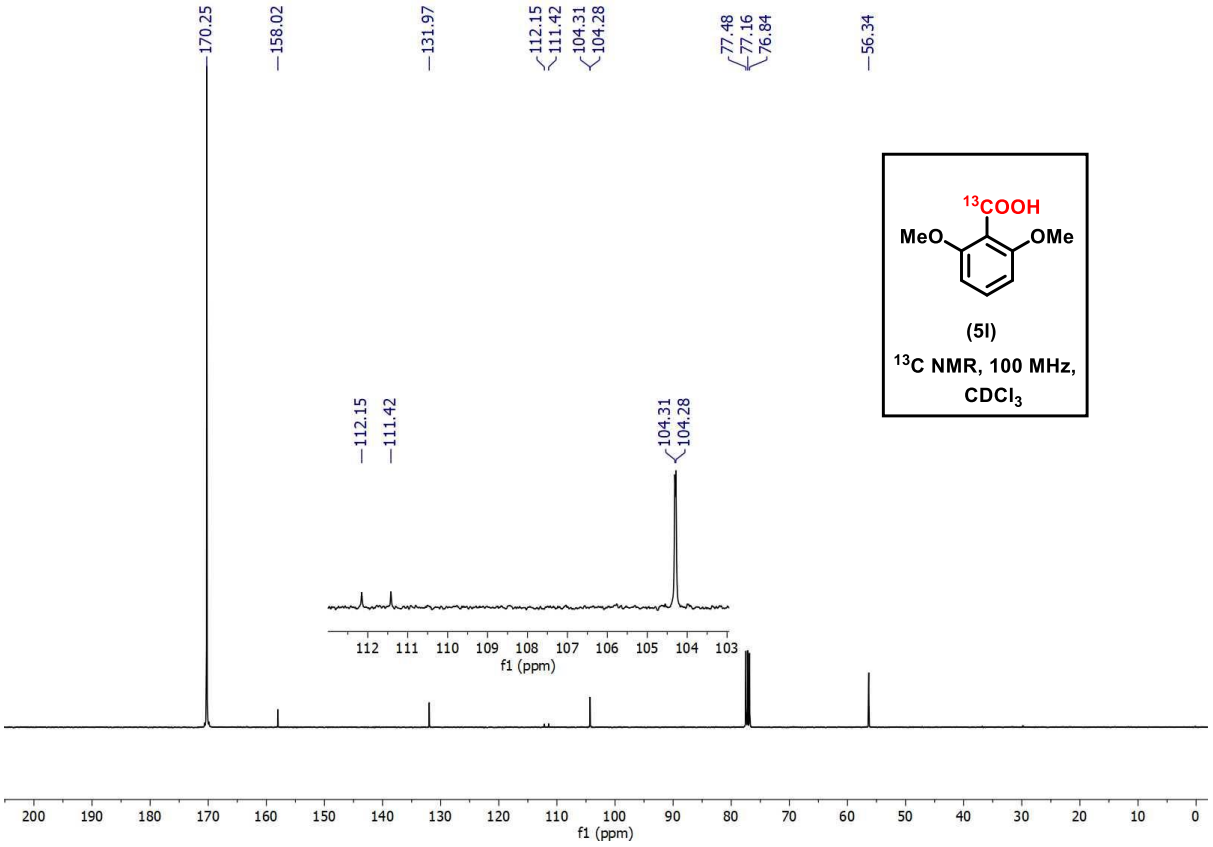
8.18
8.18
8.17
8.16
8.16
8.16
8.15
8.14
7.56
7.55
7.54
7.54
7.54
7.53
7.52
7.52
7.26
7.13
7.13
7.11
7.09
7.09
7.09
7.05
7.04
7.04
7.02
7.02
7.02
4.35
4.33
4.31
4.30
1.57
1.55
1.53
13COOH
OEt
(5k)
1H NMR, 400 MHz,
CDCl3
0.64
0.97
1.00
1.00
1.00
2.00
3.01
f1 (ppm)


165.60
157.55
135.13
133.82
122.28
122.24
118.18
117.50
112.75
112.72
77.48
77.16
76.84
66.09
14.74
13COOH
OEt
(5k)
13C NMR, 100 MHz,
CDCl3
f1 (ppm)



(5l)

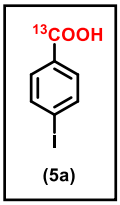
^{1}H NMR, 400 MHz, $CDCl_3$



(5l)

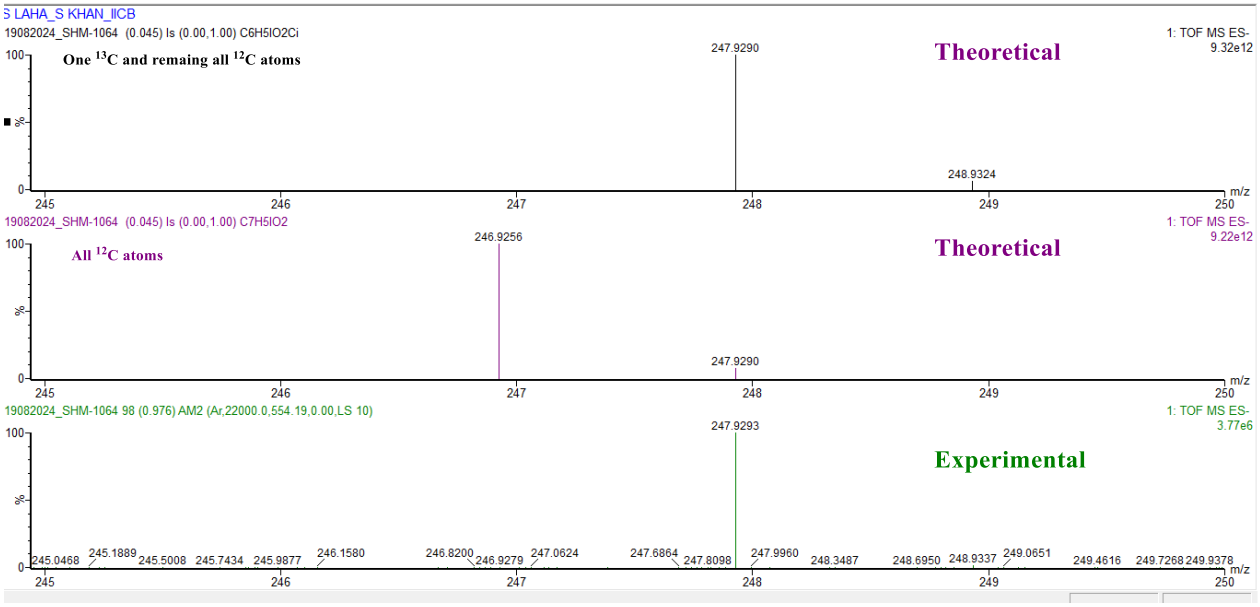
^{13}C NMR, 100 MHz, $CDCl_3$

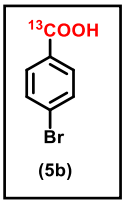
Isotopic enrichment studies by HRMS



(5a)

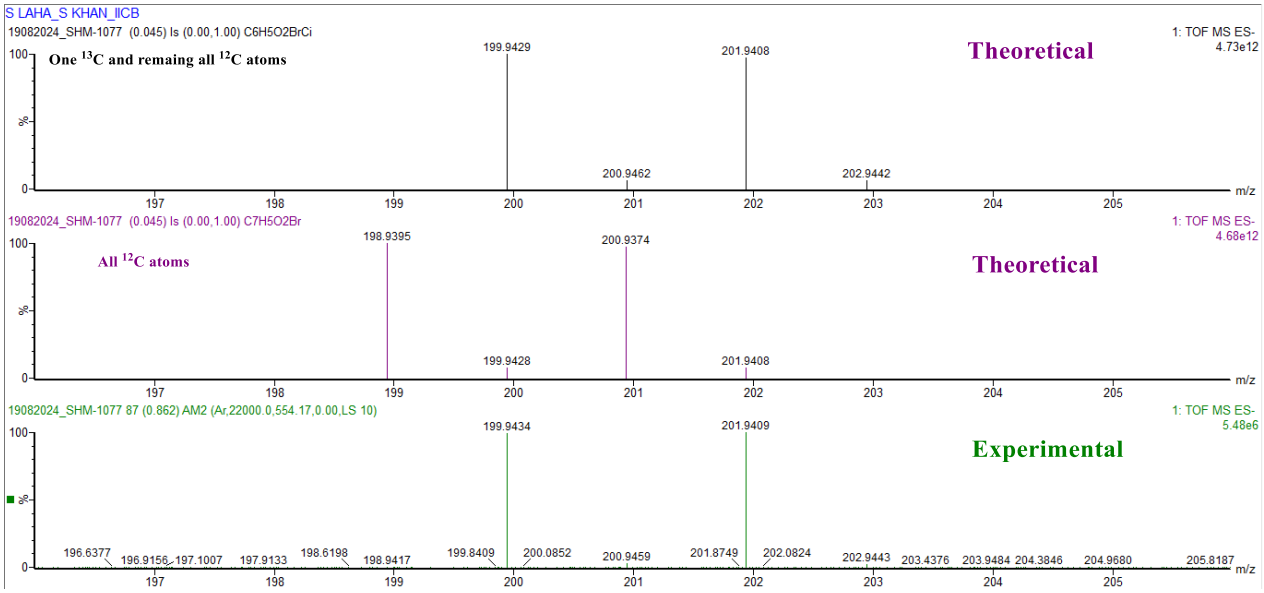
HRMS (ESI, m/z) calcd. for $C_6{}^{13}CH_4IO_2$ [M-H]$^-$: 247.9290; found: 247.9293.

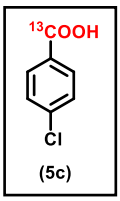




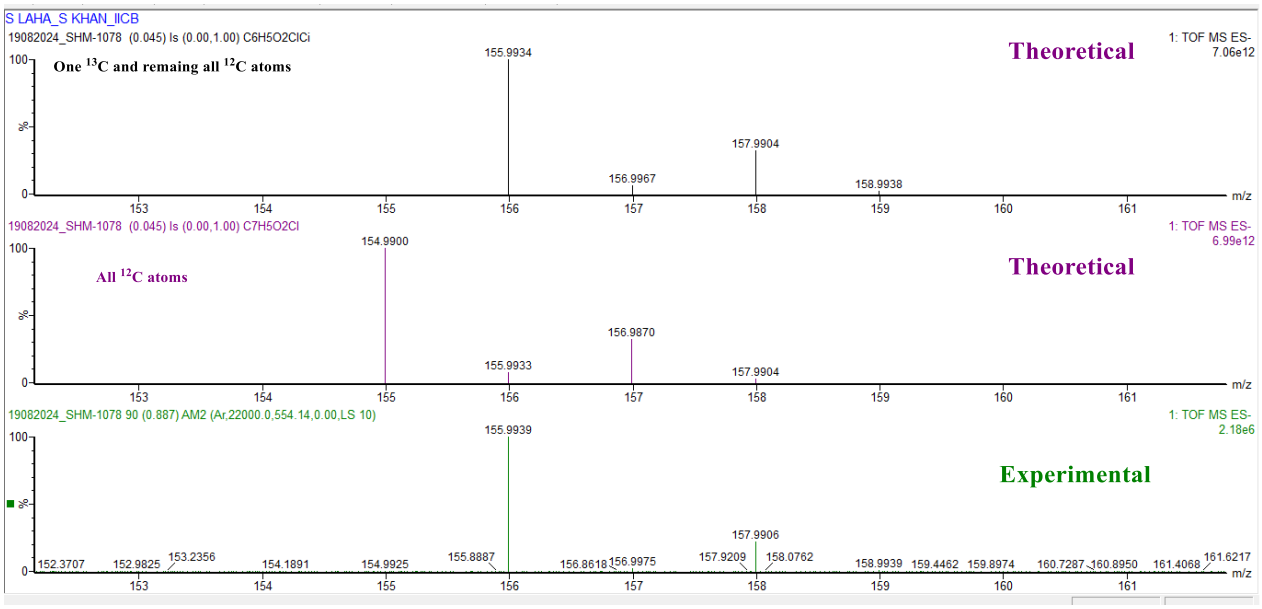
(5b)

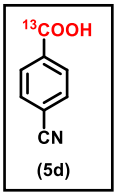
HRMS (ESI, m/z) calcd. for $C_6{}^{13}CH_4BrO_2$ [M-H]$^-$: 199.9429; found: 199.9434.



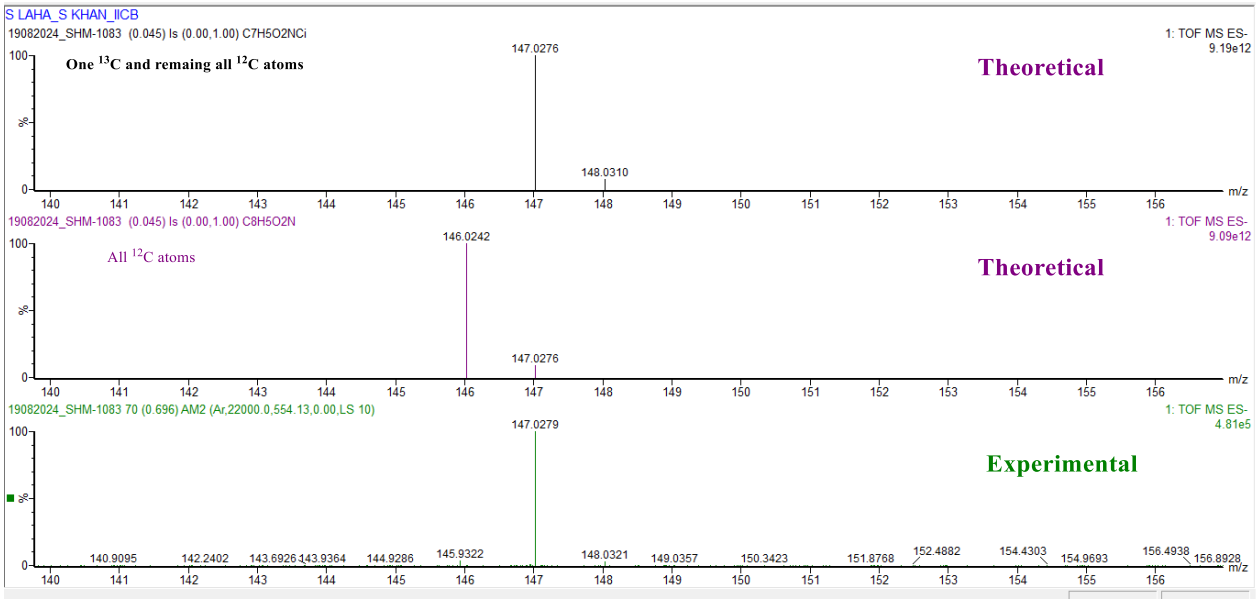


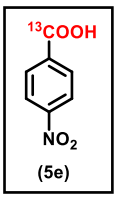
HRMS (ESI, m/z) calcd. for $C_6{}^{13}CH_4ClO_2$ $[M-H]^-$: 155.9934; found: 155.9939.



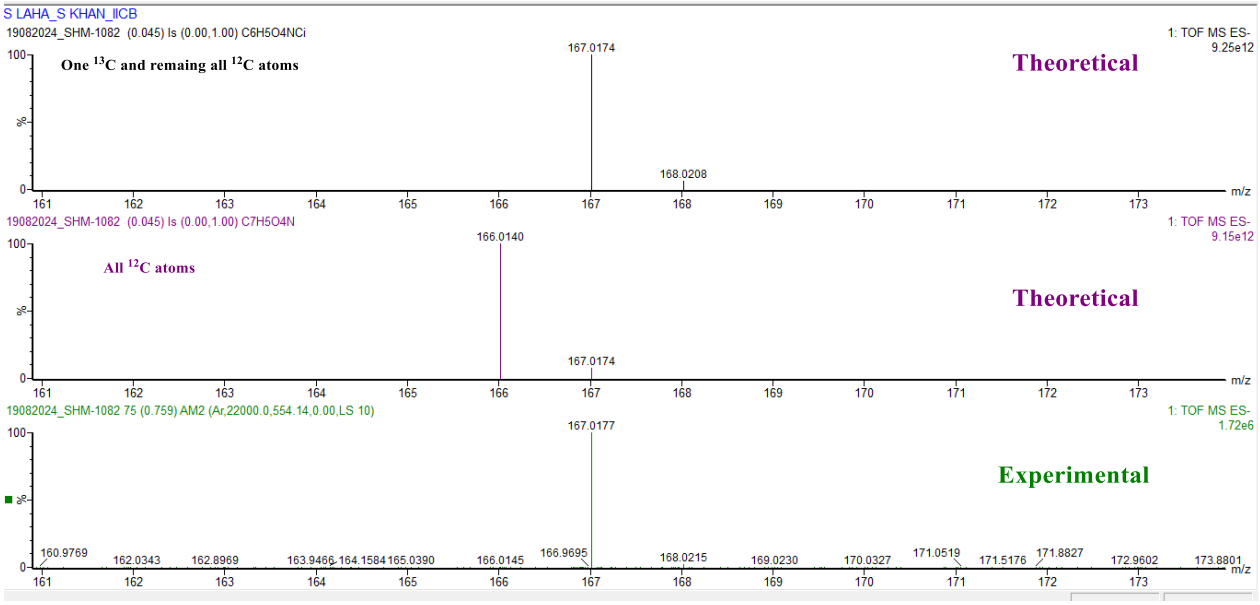


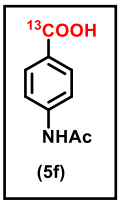
HRMS (ESI, m/z) calcd. for $C_7{}^{13}CH_4NO_2$ $[M-H]^-$: 147.0276; found: 147.0279.



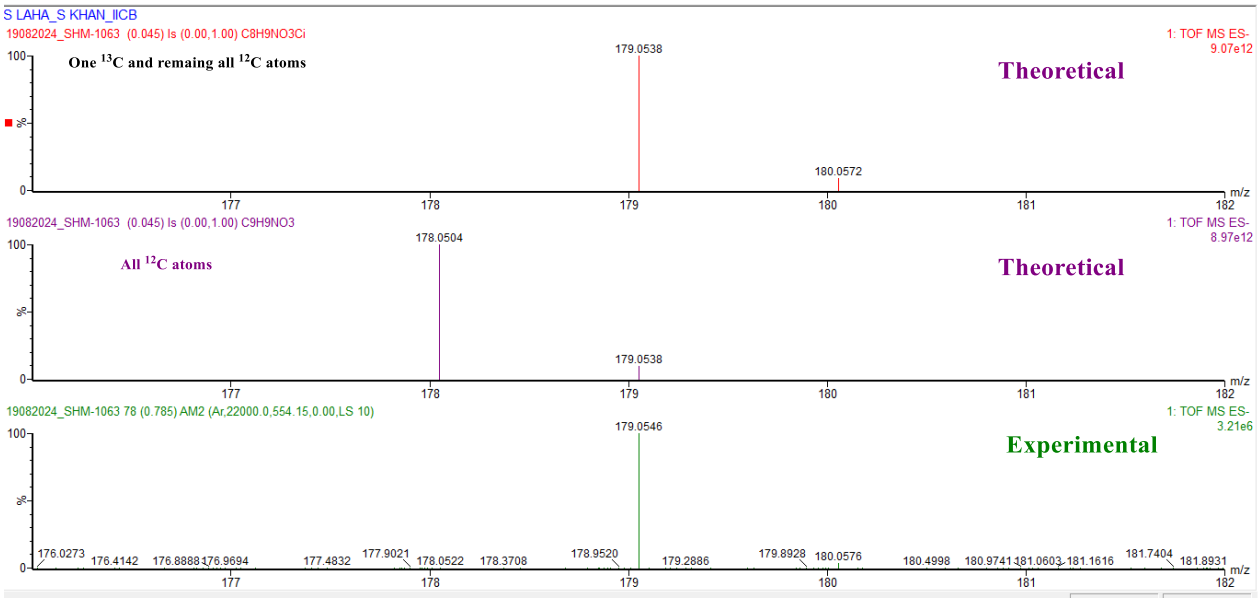


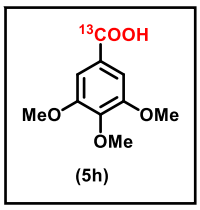
HRMS (ESI, m/z) calcd. for $C_6{}^{13}CH_4NO_4$ $[M-H]^-$: 167.0174; found: 167.0177.



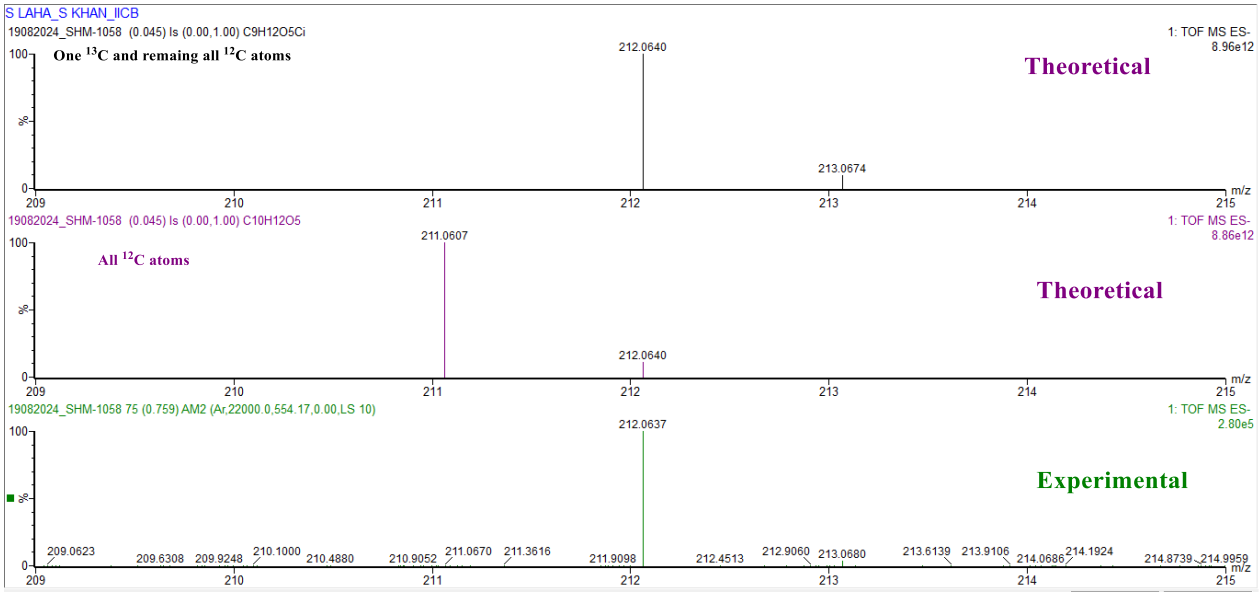


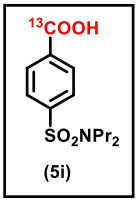
HRMS (ESI, m/z) calcd. for $C_8{}^{13}CH_8NO_3$ $[M-H]^-$: 179.0538; found: 179.0546.



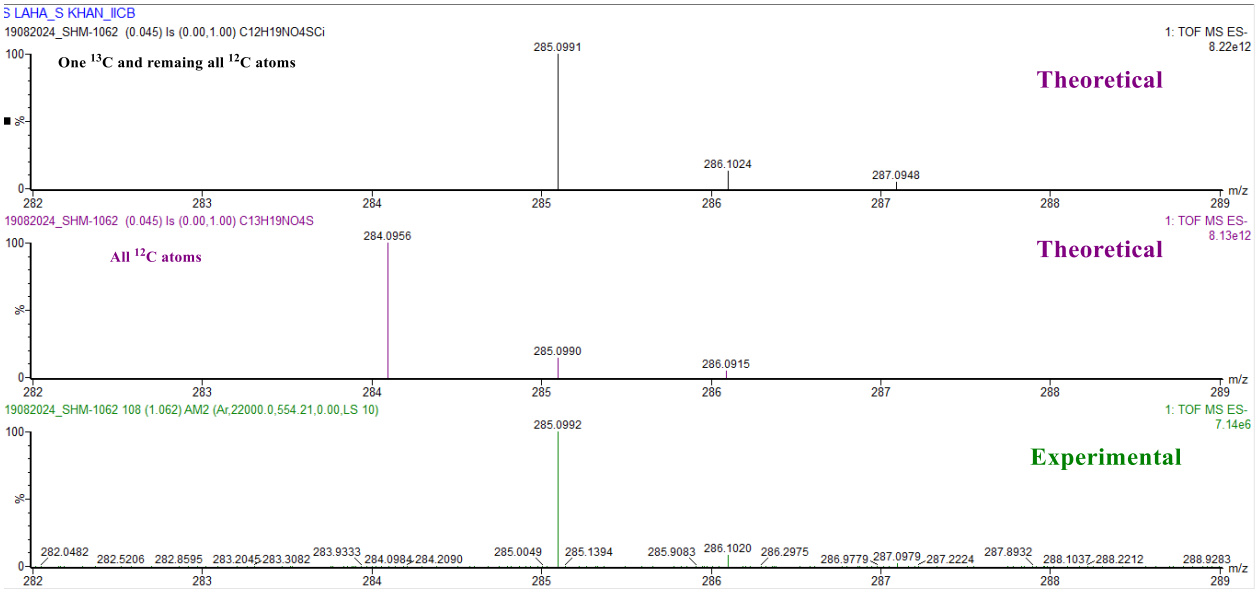


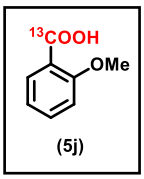
HRMS (ESI, m/z) calcd. for $C_9{}^{13}CH_{11}O_5$ $[M-H]^-$: 212.0640; found: 212.0637.



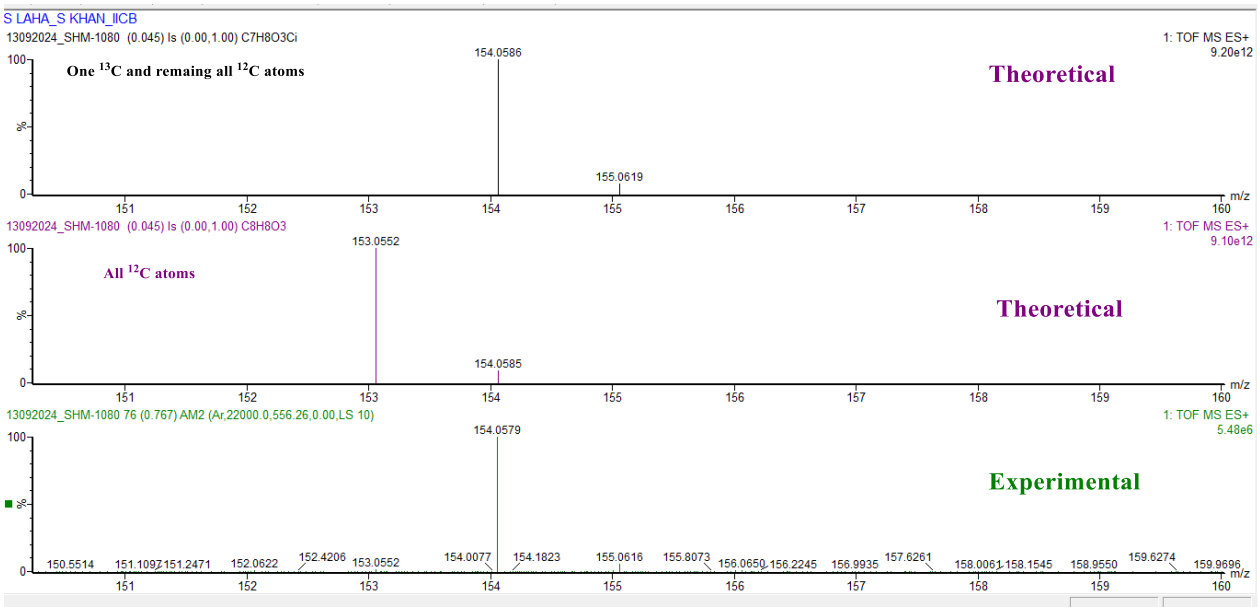


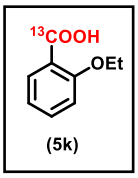
HRMS (ESI, m/z) calcd. for $C_{12}{}^{13}CH_{18}NO_4S$ $[M-H]^-$: 285.0991; found: 285.0992.



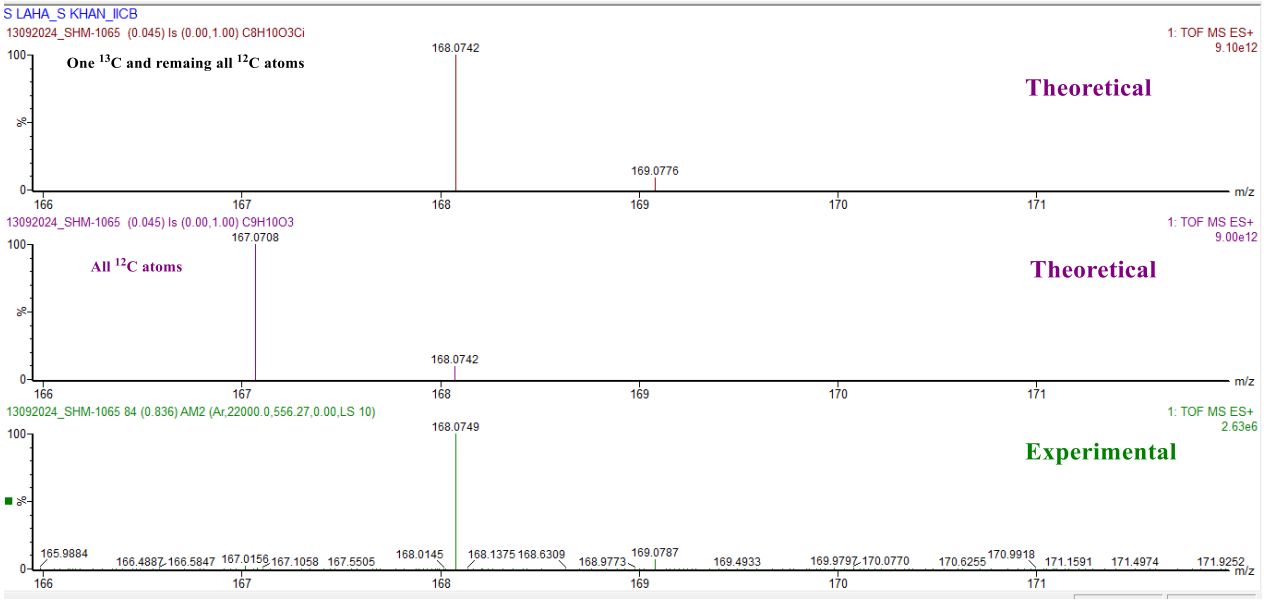


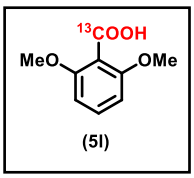
HRMS (ESI, m/z) calcd. for $C_7{}^{13}CH_9O_3$ $[M+H]^+$: 154.0586; found: 154.0579.





HRMS (ESI, m/z) calcd. for $C_8{}^{13}CH_{11}O_3$ $[M+H]^+$: 168.0742; found: 168.0749.





(5l)

HRMS (ESI, m/z) calcd. for $C_8{}^{13}CH_{11}O_4$ $[M+H]^+$: 184.0691; found: 184.0698.