

# ***Palladium Catalyzed Synthesis of Aromatic Carboxylic Acids with Silacarboxylic Acids***

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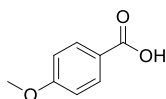
**Supporting Information**

## **Table of Contents**

<b>1. General experimental information</b>	<b>S3</b>
<b>2. Experimental data for compounds 1–32</b>	<b>S3</b>
<b>3. Pressure measurement studies</b>	<b>S19</b>
<b>4. Spectral data</b>	<b>S20</b>

## General methods

Dry solvents were prepared according to standard literature procedures.<sup>1</sup> All other chemicals were used as received from the suppliers unless mentioned otherwise. Starting materials were made according to literature procedures. Flash column chromatography was performed on silica gel 60 (230–400 mesh). <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. Chemical shifts are reported in ppm downfield to TMS ( $\delta = 0$ ) and referenced to the solvent residual peak,<sup>2</sup> using the following peak pattern abbreviations: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; pent, pentet; sext, sextet; sept, septet; m, multiplet; dd, doublet of doublets; dt, doublet of triplets; ddd, doublet of doublet of doublets; ddt, doublet of doublet of triplets, and td, triplet of doublets. HRMS was recorded on a LC TOF (ES).

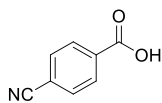


**4-Methoxybenzoic acid (1):** In an 8 mL vial equipped with a magnetic stir bar, 1-iodo-4-methoxybenzene (117 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (73 mg, 96%).

Alternatively, in a glove box under argon, 1-bromo-4-methoxybenzene (63  $\mu$ L, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed in an 8 mL vial and dissolved in dry dioxane (3.0 mL). The vial was closed and heated to 80°C for 16 hours at which point a solid precipitate had formed. The crude mixture was poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction, and concentrated *in vacuo* to leave the product as a colorless solid (66 mg, 87%). <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  (ppm) 12.61 (br s, 1H), 7.89 (d,  $J = 8.8$  Hz, 2H), 7.00 (d,  $J = 8.8$  Hz, 2H), 3.82 (s, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>)  $\delta$  (ppm) 167.0, 162.8, 131.3 (2C), 123.0, 113.8 (2C), 55.4. HRMS C<sub>8</sub>H<sub>8</sub>O<sub>3</sub> [M<sup>-</sup>]; calculated: 151.0395 found: 151.0401.

<sup>1</sup> Perrin, D.; Armarego, W. *Purification of Laboratory Chemicals 3rd Ed*, Pergamon Press, **1988**

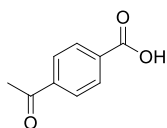
<sup>2</sup> Gottlieb, H. E., Kotlyar V., Nudelman A. *J. Org. Chem.* **1997**, 62, 7512–7515.



**4-Cyanobenzoic acid (2):** In an 8 mL vial equipped with a magnetic stir bar, 4-iodobenzonitrile (115 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (60 mg, 81%).

Alternatively, In a glove box under argon, 1-bromobenzonitrile (91 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed in an 8 ml vial and dissolved in dry dioxane (3.0 mL). The vial was closed and heated to 80°C for 16 hours at which point a solid precipitate had formed. The crude mixture was poured into water (40mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction, and concentrated *in vacuo* to leave the product as a colorless solid (70 mg, 95%).

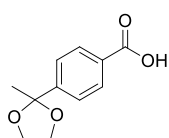
Alternatively, under an ambient atmosphere, 4-bromobenzonitrile (91 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were weighed in an 8 ml vial. The vial was flushed with argon for 2 min before dry dioxane (3.0 mL) was added; the vial was closed and heated to 80°C. After 16 hours, the crude mixture was poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction, and concentrated *in vacuo* to leave the product as a colorless solid (71 mg, 97%). <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ (ppm) 13.55 (br s, 1H), 8.07 (d, *J* = 8.6 Hz, 2H), 7.96 (d, *J* = 8.6Hz, 2H). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>) δ (ppm) 166.0, 134.8, 132.7 (2C), 129.9 (2C), 118.2, 115.1. HRMS C<sub>8</sub>H<sub>5</sub>NO<sub>2</sub> [M<sup>-</sup>]; calculated: 146.0242 found: 146.0248.



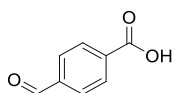
**4-Acetylbenzoic acid (3):** In an 8 mL vial equipped with a magnetic stir bar, 1-(4-iodophenyl)ethanone (123 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol),



$\text{Pd}(\text{dba})_2$  (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with  $\text{CH}_2\text{Cl}_2$  before the pH was adjusted to approx. 10. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (73 mg, 88%).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-d}_6$ )  $\delta$  (ppm) 13.29 (br s, 1H), 8.04 (m, 4H), 2.62 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-d}_6$ )  $\delta$  (ppm) 197.7, 166.7, 139.8, 134.5, 129.6 (2C), 128.3 (2C), 27.0. HRMS  $\text{C}_9\text{H}_8\text{O}_3[\text{M}^-]$ ; calculated: 163.0395 found: 163.0402.

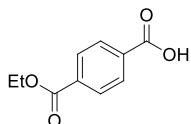


**4-(2-Methyl-1,3-dioxolan-2-yl)benzoic acid (4):** In an 8 mL vial equipped with a magnetic stir bar, (4-iodophenyl)-2-methyl-1,3-dioxolane (145 mg, 0.50 mmol),  $\text{MePh}_2\text{SiCOOH}$  (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol),  $\text{Pd}(\text{dba})_2$  (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with  $\text{CH}_2\text{Cl}_2$  before the pH was adjusted to approx. 10. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (91 mg, 88%).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-d}_6$ )  $\delta$  (ppm) 12.95 (br s, 1H), 7.93 (d,  $J = 8.5$  Hz, 2H), 7.53 (d,  $J = 8.4$  Hz, 2H), 4.00 (m, 2H), 3.69 (m, 2H), 1.56 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-d}_6$ )  $\delta$  (ppm) 167.1, 148.0, 130.4, 129.4 (2C), 125.3 (2C), 107.9, 64.2 (2C), 27.1. HRMS  $\text{C}_{11}\text{H}_{12}\text{O}_4[\text{M}^-]$ ; calculated: 207.0657 found: 207.0663.

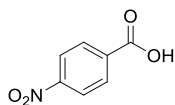


**4-Formylbenzoic acid (5):** In an 8 mL vial equipped with a magnetic stir bar, 4-iodobenzaldehyde (116 mg, 0.50 mmol),  $\text{MePh}_2\text{SiCOOH}$  (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol),  $\text{Pd}(\text{dba})_2$  (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with  $\text{CH}_2\text{Cl}_2$  before the pH was adjusted to approx. 10. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered

by suction and concentrated *in vacuo* to leave the product as a colorless solid (73 mg, 97%).  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  (ppm) 13.35 (br s, 1H), 10.09 (s, 1H), 8.12 (d,  $J$  = 8.4 Hz, 2H), 8.00 (d,  $J$  = 8.4 Hz, 2H).  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta$  (ppm) 192.9, 166.6, 138.9, 135.7, 129.9 (2C), 139.5 (2C). HRMS  $\text{C}_8\text{H}_6\text{O}_3$  [ $\text{M}^-$ ]; calculated: 149.0239 found: 149.0244.



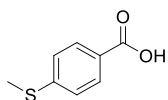
**4-(Ethoxycarbonyl)benzoic acid (6):** In an 8 mL vial equipped with a magnetic stir bar, ethyl 4-iodobenzoate (84  $\mu\text{L}$ , 0.50 mmol),  $\text{MePh}_2\text{SiCOOH}$  (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol),  $\text{Pd}(\text{dba})_2$  (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with  $\text{CH}_2\text{Cl}_2$  before the pH was adjusted to approx. 10. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (92 mg, 95%).  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  (ppm) 13.34 (br s, 1H), 8.07–8.05 (m, 4H), 4.34 (q,  $J$  = 7.2 Hz, 2H), 1.33 (t,  $J$  = 7.2 Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta$  (ppm) 166.6, 165.1, 134.8, 133.4, 129.6 (2C), 129.3 (2C), 61.1, 14.1. HRMS  $\text{C}_{10}\text{H}_{10}\text{O}_4$  [ $\text{M}^-$ ]; calculated: 193.0501 found: 193.0508.



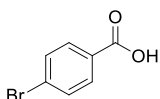
**4-Nitrobenzoic acid (7):** In an 8 mL vial equipped with a magnetic stir bar, 1-iodo-4-nitrobenzene (125 mg, 0.50 mmol),  $\text{MePh}_2\text{SiCOOH}$  (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol),  $\text{Pd}(\text{dba})_2$  (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with  $\text{CH}_2\text{Cl}_2$  before the pH was adjusted to approx. 10. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (81 mg, 96%).

Alternatively, In a glove box under argon, 1-bromo-4-nitrobenzene (101 mg, 0.50 mmol),  $\text{MePh}_2\text{SiCOOH}$  (182 mg, 0.75 mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol),  $\text{Pd}(\text{dba})_2$  (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed in an 8 mL vial and dissolved in dry dioxane (3.0 mL). The vial was closed and heated to 80°C for 16 hours at which point a solid precipitate had formed. The crude mixture was poured into water (40 mL) and diluted with  $\text{CH}_2\text{Cl}_2$  before the pH was adjusted to approx. 10.

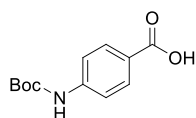
The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered by suction, and concentrated *in vacuo* to leave the product as a colorless solid (82 mg, 97%).  $^1\text{H}$ NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$ (ppm) 13.61 (br s, 1H), 8.29 (d,  $J$  = 8.9 Hz, 2H), 8.14 (d,  $J$  = 8.8 Hz, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ )  $\delta$  (ppm) 165.8, 150.0, 136.4, 130.7 (2C), 123.7 (2C). HRMS  $\text{C}_7\text{H}_5\text{NO}_4$  [ $\text{M}^-$ ]; calculated: 166.0140 found: 166.0146.



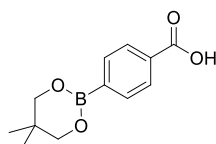
**4-(Methylthio)benzoic acid (8):** In an 8mL vial equipped with a magnetic stir bar, (4-iodophenyl)(methyl)sulfane (125 mg, 0.50 mmol),  $\text{MePh}_2\text{SiCOOH}$  (182mg, 0.75mmol), potassium trimethylsilanolate (128mg, 1.0mmol),  $\text{Pd}(\text{dba})_2$  (14.4mg, 0.025 mmol) and Xantphos (14.5mg, 0.025 mmol) were mixed together. Toluene (3.0mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at  $40^\circ\text{C}$  for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40mL) and diluted with  $\text{CH}_2\text{Cl}_2$  before the pH was adjusted to approx. 10. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40mL). The pH was then adjusted to 2-3 with hydrochloric acid (4M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (80 mg, 95%).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  (ppm) 12.81 (br s, 1H), 7.84 (d,  $J$  = 8.4 Hz, 2H), 7.32 (d,  $J$  = 8.4 Hz, 2H), 2.51 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ )  $\delta$  (ppm) 167.1, 144.8, 129.7 (2C), 126.7, 124.9 (2C), 14.0. HRMS  $\text{C}_8\text{H}_8\text{O}_2\text{S}$  [ $\text{M}^-$ ]; calculated: 167.0167 found: 167.0173



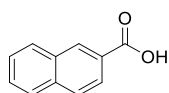
**4-Bromobenzoic acid (9):** In an 8 mL vial equipped with a magnetic stir bar, 1-bromo-4-iodobenzene (141 mg, 0.50 mmol),  $\text{MePh}_2\text{SiCOOH}$  (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol),  $\text{Pd}(\text{dba})_2$  (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at  $40^\circ\text{C}$  for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with  $\text{CH}_2\text{Cl}_2$  before the pH was adjusted to approx. 10. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (93 mg, 93%).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  (ppm) 13.16 (br s, 1H), 7.86 (d,  $J$  = 8.4 Hz, 2H), 7.69 (d,  $J$  = 8.4 Hz, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ )  $\delta$  (ppm) 166.6, 131.7 (2C), 131.3 (2C), 130.0, 126.9. HRMS  $\text{C}_7\text{H}_5\text{BrO}_2$  [ $\text{M}^-$ ]; calculated: 198.9395 found: 198.9400.



**4-((Tert-butoxycarbonyl)amino)benzoic acid (10):** In an 8 mL vial equipped with a magnetic stir bar, *tert*-butyl 4-iodophenylcarbamate (80 mg, 0.25 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (4.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (47 mg, 79%). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 12.60 (br s, 1H), 9.72 (s, 1H), 7.83 (d, *J* = 8.7 Hz, 2H), 7.55 (d, *J* = 8.7 Hz, 2H) 1.48 (s, 9H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 167.4, 153.0, 144.2, 130.8 (2C), 124.4, 117.6 (2C), 80.1, 28.5 (3C). HRMS C<sub>12</sub>H<sub>15</sub>NO<sub>4</sub> [M<sup>-</sup>]; calculated: 236.0923 found: 236.0928.

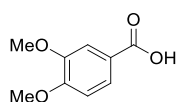


**4-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)benzoic acid (11):** In an 8 mL vial equipped with a magnetic stir bar, 2-(4-iodophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (158 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (83 mg, 71%). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 12.97 (br s, 1H), 7.92 (d, *J* = 7.6 Hz, 2H), 7.80 (d, *J* = 7.6 Hz, 2H), 3.76 (s, 4H), 0.95 (s, 6H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 167.3, 133.6 (2C), 132.5, 128.3 (2C), 71.5 (2C), 31.4, 21.3 (2C) (The aromatic signal from the boron substituted carbon was not observed due to coupling to boron). HRMS could not be obtained.

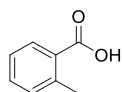


**2-Naphthoic acid (12):** In an 8 mL vial equipped with a magnetic stir bar, 2-iodonaphthalene (127 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub>

(14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (81 mg, 94%). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 13.09 (br s, 1H), 8.63 (s, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.00 (s, 2H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.65–7.56 (m, 2H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 167.5, 135.0, 132.2, 130.6, 129.3, 128.3, 128.2, 128.1, 127.7, 126.8, 125.2. HRMS C<sub>11</sub>H<sub>8</sub>O<sub>2</sub> [M<sup>−</sup>]; calculated: 171.0446 found: 171.0551.

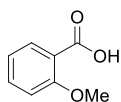


**3,4-Dimethoxybenzoic acid (13):** In an 8 mL vial equipped with a magnetic stir bar, 4-iodo-1,2-dimethoxybenzene (132 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (75mg, 83%). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 12.20 (br s, 1H), 7.12 (dd, *J* = 2 Hz, *J* = 8.4 Hz, 1H), 6.99 (d, *J* = 1.6 Hz, 1H), 6.58 (d, *J* = 8.4 Hz, 1H), 3.37 (s, 3H), 3.35 (s, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 147.6, 133.1, 128.8, 103.7, 103.4, 92.4, 91.5, 36.1, 35.9. HRMS C<sub>9</sub>H<sub>10</sub>O<sub>4</sub> [M<sup>−</sup>]; calculated: 181.0501 found: 181.0507.

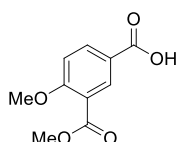


**2-Methylbenzoic acid (14):** In an 8 mL vial equipped with a magnetic stir bar, 1-iodo-2-methylbenzene (64μL, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (44 mg, 64%). <sup>1</sup>H NMR (400

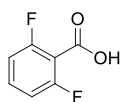
MHz, DMSO-*d*<sub>6</sub>)  $\delta$  12.78 (br s, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.43 (m, 1H), 7.29-7.25 (m, 2H), 2.52 (s, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) 168.7, 139.0, 131.7, 131.5, 130.5, 130.2, 125.8, 21.2. HRMS C<sub>8</sub>H<sub>8</sub>O<sub>2</sub> [M<sup>-</sup>]; calculated: 135.0446 found: 135.0451.



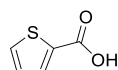
**2-Methoxybenzoic acid (15):** In an 8 mL vial equipped with a magnetic stir bar, 1-iodo-2-methoxybenzene (65  $\mu$ L, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (46 mg, 61%). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) 12.60 (br s, 1H), 7.63 (dd, *J* = 7.6 Hz, 1.6 Hz, 1H), 7.50 (ddd, *J* = 8.4 Hz, 7.2 Hz, 1.6 Hz, 1H), 7.11 (d, *J* = 8.4 Hz, 1H), 6.99 (dt, *J* = 0.8 Hz, 7.2 Hz, 1H), 3.81 (s, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) 167.4, 158.1, 133.1, 130.7, 121.3, 120.0, 112.4, 55.7. HRMS C<sub>8</sub>H<sub>8</sub>O<sub>3</sub> [M<sup>-</sup>]; calculated: 151.0395 found: 151.0399.



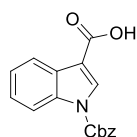
**4-Methoxy-3-(methoxycarbonyl)benzoic acid (16):** In an 8 mL vial equipped with a magnetic stir bar, methyl 5-iodo-2-methoxybenzoate (146 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (107 mg, 99%). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  12.92 (br s, 1H), 8.22 (d, *J* = 2.3 Hz, 1H), 8.09 (dd, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H), 7.25 (d, *J* = 8.8 Hz, 1H), 3.90 (s, 3H), 3.81 (s, 3H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) 165.3, 165.3, 161.6, 134.8, 132.4, 122.5, 119.7, 112.6, 56.3, 52.1. HRMS C<sub>10</sub>H<sub>10</sub>O<sub>5</sub> [M<sup>-</sup>]; calculated: 209.0450 found: 209.0454.



**2,6-Difluorobenzoic acid (17):** In an 8 mL vial equipped with a magnetic stir bar, 1,3-difluoro-2-iodobenzene (120 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (4.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (47 mg, 59%). <sup>1</sup>H-NMR (400 MHz, DMSO-d<sub>6</sub>) δ (ppm) 13.89 (br s, 1H), 7.59 (m, 1H), 7.21 (m, 2H). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>) δ (ppm) 162.3, 159.3 (dd, *J* = 249.9 Hz, *J* = 6.97 Hz, 2C), 133.0 (t, *J* = 10.3 Hz), 112.4, 112.2. (The aromatic resonance signal for the –COOH substituted carbon was not observed, probably due to prolonged relaxation time and Carbon-Fluorine coupling). <sup>19</sup>F NMR (377 MHz, DMSO-d<sub>6</sub>) -112.4 (s). HRMS C<sub>7</sub>H<sub>4</sub>F<sub>2</sub>O<sub>2</sub> [M<sup>-</sup>]; calculated: 157.0101 found: 157.0105.

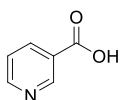


**Thiophene-2-carboxylic acid (18):** In an 8 mL vial equipped with a magnetic stir bar, 2-iodothiophene (55 μL, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (59 mg, 92%). <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ 13.04 (br s, 1H), 7.87 (dd, *J* = 5.0 Hz, *J* = 1.3 Hz, 1H), 7.73 (dd, *J* = 3.7 Hz, *J* = 1.3 Hz, 1H), 7.18 (dd, *J* = 5.0 Hz, *J* = 3.7 Hz, 1H). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>) δ (ppm) 162.9, 134.7, 133.2, 133.2, 128.2. HRMS C<sub>5</sub>H<sub>4</sub>SO<sub>2</sub> [M<sup>-</sup>]; calculated: 126.9854 found: 126.9858.

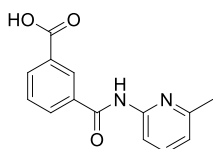


**1-((benzyloxy)carbonyl)-1H-indole-3-carboxylic acid (19):** In an 8 mL vial equipped with a magnetic stir bar, benzyl 3-iodo-1H-indole-1-carboxylate (189 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol),

potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo*. The pure compound was obtained by flash column chromatography (pentane:diethyl ether:formic acid - 100:10:1) as a colorless solid (138 mg, 93%). <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ 12.85 (br s, 1H), 8.21 (s, 1H), 8.13 (dd, *J* = 13.2 Hz, *J* = 7.9 Hz, 2H), 7.57 (d, *J* = 6.8 Hz, 2H), 7.48–7.36 (m, 5H), 5.51 (s, 2H). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>) δ (ppm) 164.7, 149.8, 135.1, 135.0, 131.4, 128.7 (2C), 128.5 (2C), 127.4, 125.4, 124.1, 121.4, 114.8, 113.2, 69.1 (The aromatic resonance signal for the –COOH substituted carbon was not observed, probably due to prolonged relaxation time). HRMS C<sub>17</sub>H<sub>13</sub>NO<sub>4</sub> [M<sup>–</sup>]; calculated: 294.0772 found: 294.0777.



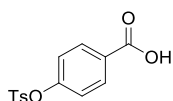
**Nicotinic acid (20):** In an 8 mL vial equipped with a magnetic stir bar, 3-iodopyridine (103 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (59 mg, 95%). <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ (ppm) 13.37 (br s, 1H), 9.08 (s, 1H), 8.80 (dd, *J* = 4.8 Hz, 1.2 Hz, 1H), 8.30 (dt, *J* = 8.0 Hz, 2.0 Hz, 1H), 7.57 (dd, *J* = 8.0 Hz, 4.8 Hz, 1H). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>) δ (ppm) 166.2, 152.9, 149.8, 137.5, 126.8, 124.0. HRMS C<sub>6</sub>H<sub>5</sub>NO<sub>2</sub> [M<sup>–</sup>]; calculated: 122.0248, found: 122.0250.



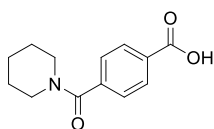
**3-(6-Methylpyridin-2-ylcarbamoyl)benzoic acid (21):** In an 8 mL vial equipped with a magnetic stir bar, 3-iodo-*N*-(6-methylpyridin-2-yl)benzamide (169 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182mg, 0.75mmol), potassium trimethylsilanolate (128mg, 1.0mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5mg, 0.025 mmol) were mixed together. Toluene (4.0 mL) was added and the vial was tightly sealed with a screw cap. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to



approx. 10. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (81 mg, 63%).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  (ppm) 13.21 (br s, 1H), 10.93 (s, 1H), 8.54 (s, 1H), 8.25 (d,  $J$  = 7.6 Hz, 1H), 8.12 (d,  $J$  = 7.6 Hz, 1H), 8.01 (d,  $J$  = 8.4 Hz, 1H), 7.73 (t,  $J$  = 8.0 Hz, 1H), 7.62 (t,  $J$  = 8.0 Hz, 1H), 7.04 (d,  $J$  = 7.6 Hz, 1H), 2.45 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ )  $\delta$  (ppm) 166.8, 165.3, 156.6, 151.4, 138.4, 134.6, 132.3, 132.1, 131.0, 129.1, 128.7, 119.2, 111.7, 23.6. HRMS  $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_3$  [ $\text{M}^-$ ]; calculated: 255.0770 found: 255.0775.

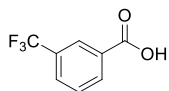


**4-(Tosyloxy)benzoic acid (22):** In a glove box under argon, 1-bromophenyl 4-methylbenzenesulfonate (164 mg, 0.50 mmol),  $\text{MePh}_2\text{SiCOOH}$  (182mg, 0.75mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol),  $\text{Pd}(\text{dba})_2$  (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed in an 8 ml vial and dissolved in dry dioxane (3.0 mL). The vial was closed and heated to  $80^\circ\text{C}$  for 16 hours at which point a solid precipitate had formed. The crude mixture was poured into water (40 mL) and diluted with  $\text{CH}_2\text{Cl}_2$  before the pH was adjusted to approx. 10. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered by suction, and concentrated *in vacuo* to leave the product as a colorless solid (145 mg, 99%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.05 (d,  $J$  = 8.8 Hz, 2H), 7.72 (d,  $J$  = 8.4 Hz, 2H), 7.33 (d,  $J$  = 8.4 Hz, 2H), 7.11 (d,  $J$  = 8.8 Hz, 2H), 2.46 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 170.9, 153.8, 146.0, 132.1 (3C), 130.1 (2C), 128.6 (2C), 128.0, 122.7 (2C), 21.9. HRMS  $\text{C}_{14}\text{H}_{12}\text{O}_5\text{S}$  [ $\text{M}^-$ ]; calculated: 291.0327 found: 291.0334.

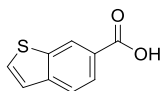


**4-(Piperidine-1-carbonyl)benzoic acid (23):** In a glove box under argon, (4-bromophenyl)(piperidin-1-yl)methanone (134 mg, 0.50 mmol),  $\text{MePh}_2\text{SiCOOH}$  (182mg, 0.75mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol),  $\text{Pd}(\text{dba})_2$  (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed in an 8 ml vial and dissolved in dry dioxane (3.0 mL). The vial was closed and heated to  $80^\circ\text{C}$  for 16 hours at which point a solid precipitate had formed. The crude mixture was poured into water (40 mL) and diluted with  $\text{CH}_2\text{Cl}_2$  before the pH was adjusted to approx. 10. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered by suction, and concentrated *in vacuo* to leave the product as a colorless solid (90 mg, 77%).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  (ppm) 13.15 (br s, 1H), 7.99 (d,  $J$  = 8.0 Hz, 2H), 7.47 (d,  $J$  = 8.0 Hz, 2H), 3.59 (br s, 2H), 3.22 (br s, 2H),

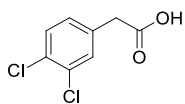
1.64-1.38 (m, 6H).  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta$  (ppm) 168.0, 166.8, 140.7, 131.3, 129.5 (2C), 126.8 (2C), 48.0, 42.3, 26.0, 25.3, 24.0. HRMS  $\text{C}_{13}\text{H}_{15}\text{NO}_3[\text{M}^-]$ ; calculated: 232.0974 found: 232.0979.



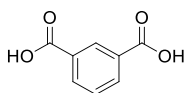
**3-(Trifluoromethyl)benzoic acid (24):** In a glove box under argon, 1-bromo-3-(trifluoromethyl)benzene (70  $\mu\text{L}$ , 0.50 mmol),  $\text{MePh}_2\text{SiCOOH}$  (182mg, 0.75mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol),  $\text{Pd}(\text{dba})_2$  (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed in an 8 ml vial and dissolved in dry dioxane (3.0 mL). The vial was closed and heated to  $80^\circ\text{C}$  for 16 hours at which point a solid precipitate had formed. The crude mixture was poured into water (40 mL) and diluted with  $\text{CH}_2\text{Cl}_2$  before the pH was adjusted to approx. 10. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered by suction, and concentrated *in vacuo* to leave the product as a colorless solid (94 mg, 98%).  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  (ppm) 13.52 (br s, 1H), 8.22 (d,  $J = 8.0$  Hz, 1H), 8.17 (s, 1H), 8.00 (d,  $J = 8.0$  Hz, 1H), 7.76 (t,  $J = 8.0$  Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta$  (ppm) 166.1, 133.3, 131.9, 130.2, 129.5 (q,  $J_{\text{C-F}} = 32$  Hz), 129.4 (q,  $J_{\text{C-F}} = 4$  Hz), 125.5 (q,  $J_{\text{C-F}} = 4$  Hz), 123.8 (q,  $J_{\text{C-F}} = 271$  Hz).  $^{19}\text{F}$  NMR (377 MHz, DMSO- $d_6$ ) 61.5 (s). HRMS  $\text{C}_8\text{H}_5\text{F}_3\text{O}_2[\text{M}^-]$ ; calculated: 189.0163 found: 189.0170.



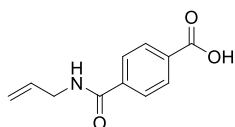
**Benzo[b]thiophene-6-carboxylic acid (25):** In a glove box under argon, 6-bromobenzo[b]thiophene (107 mg, 0.50 mmol),  $\text{MePh}_2\text{SiCOOH}$  (182mg, 0.75mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol),  $\text{Pd}(\text{dba})_2$  (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed in an 8 ml vial and dissolved in dry dioxane (3.0 mL). The vial was closed and heated to  $80^\circ\text{C}$  for 16 hours at which point a solid precipitate had formed. The crude mixture was poured into water (40 mL) and diluted with  $\text{CH}_2\text{Cl}_2$  before the pH was adjusted to approx. 10. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered by suction, and concentrated *in vacuo* to leave the product as a colorless solid (89 mg, 99%).  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  (ppm) 13.01 (br s, 1H), 8.64 (s, 1H), 8.01 (d,  $J = 5.6$  Hz, 1H), 7.98-7.92 (m, 2H), 7.55 (d,  $J = 5.6$  Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta$  (ppm) 167.5, 142.7, 139.1, 131.8, 126.7, 125.0, 124.6, 124.0, 123.6. HRMS  $\text{C}_9\text{H}_6\text{O}_2\text{S}[\text{M}^-]$ ; calculated: 177.0010 found: 177.0017.



**2-(3,4-Dichlorophenyl)acetic acid (26):** In a glove box under argon, 4-(bromomethyl)-1,2-dichlorobenzene (73  $\mu$ L, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182mg, 0.75mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed in an 8 ml vial and dissolved in dry dioxane (3.0 mL). The vial was closed and heated to 80°C for 16 hours at which point a solid precipitate had formed. The crude mixture was poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction, and concentrated *in vacuo* to leave the product as a colorless solid (101 mg, 98%). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) 12.53 (br s, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 1.6 Hz, 1H), 7.26 (dd, *J* = 2.0 Hz, 8.0 Hz, 1H) 3.63 (s, 2H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) 172.1, 136.3, 131.6, 130.7, 130.3, 130.1, 129.3, 39.3. HRMS C<sub>8</sub>H<sub>6</sub>Cl<sub>2</sub>O<sub>2</sub>[M<sup>-</sup>]; calculated: 202.9667 found: 202.9671.



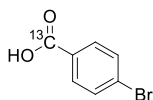
**Isophthalic acid (27):** In a glove box under argon 1,3-dibromobenzene (59 mg, 0.25 mmol), MePh<sub>2</sub>SiCOOH (182 mg, 0.75 mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (7.2 mg, 0.013 mmol) and Xantphos (7.2 mg, 0.013 mmol) were mixed in an 8 ml vial and dissolved in dry dioxane (3.0 mL). The vial was closed and heated to 80°C for 16 hours at which point a solid precipitate had formed. The crude mixture was poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction, and concentrated *in vacuo* to leave a colorless solid. The colorless solid obtained (40 mg) was an inseparable mixture of title compound (88%) and 3-bromobenzoic acid (7%). **Isophthalic acid:** <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) *inter alia* 13.06 (br s, 1H) 8.48 (br s, 1H), 8.16 (dd, *J* = 7.6 Hz, 1.6 Hz, 2H), 7.64 (t, *J* = 7.6 Hz, 1H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) 166.7 (2C), 133.5 (2C), 131.2 (2C), 130.0, 129.2. HRMS C<sub>8</sub>H<sub>6</sub>O<sub>4</sub> [M<sup>-</sup>]; calculated: 165.0188 found: 165.0194. **3-bromobenzoic acid:** <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) *inter alia* 8.03 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 8.0 Hz, 1H). HRMS C<sub>7</sub>H<sub>5</sub>BrO<sub>2</sub> [M<sup>-</sup>]; calculated: 198.9395 found: 198.9399.



**4-(Allylcarbamoyl)benzoic acid (28):** In a glove box under argon, *N*-allyl-4-bromobenzamide (120 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182mg, 0.75mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed in an 8 ml vial and dissolved in dry dioxane (3.0 mL). The vial was closed and heated to 80°C for 16 hours at which point a solid precipitate had formed. The crude mixture was poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction, and concentrated *in vacuo* to leave the product as a colorless solid (102 mg, 99%). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 13.21 (br s, 1H), 8.84 (t, *J* = 5.6 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 2H), 7.96 (d, *J* = 8.0 Hz, 2H), 5.89 (ddt, *J* = 17.2 Hz, 10.4 Hz, 5.2 Hz, 1H), 5.17 (dd, *J* = 17.2 Hz, 1.6 Hz, 1H), 5.09 (dd, *J* = 10.4 Hz, 1.6 Hz, 1H), 3.91 (t, *J* = 5.6 Hz, 2H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 166.9, 165.4, 138.2, 135.2, 133.0, 129.3 (2C), 127.5 (2C), 115.3, 41.7. HRMS C<sub>11</sub>H<sub>11</sub>NO<sub>3</sub>[M<sup>-</sup>]; calculated: 204.0661 found: 204.0663.

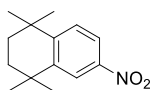


**(Z)-2-Methylbut-2-enoic acid (29):** In a glove box under argon, (Z)-2-bromobut-2-ene (68 mg, 0.50 mmol), MePh<sub>2</sub>SiCOOH (182mg, 0.75mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed in an 8 ml vial and dissolved in dry dioxane (3.0 mL). The vial was closed and heated to 80°C for 16 hours at which point a solid precipitate had formed. The crude mixture was poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction, and concentrated *in vacuo* to leave the product as a colorless solid (49mg, 97%). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 12.09 (br s, 1H), 6.77-6.70 (m, 1H), 1.75-1.71 (m, 6H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 168.8, 136.5, 128.7, 14.2, 12.0. HRMS C<sub>5</sub>H<sub>8</sub>O<sub>2</sub>[M<sup>-</sup>]; calculated: 99.0446 found: 99.0451.

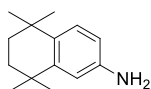


**[<sup>13</sup>C]-4-Bromobenzoic acid (30):** In an 8 mL vial equipped with a magnetic stir bar, 1-bromo-4-iodobenzene (141 mg, 0.50 mmol), MePh<sub>2</sub>Si<sup>13</sup>COOH (183 mg, 0.75 mmol), potassium trimethylsilanolate (108 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed together. Toluene (3.0 mL) was added and the vial was sealed. The reaction was allowed to stir at 40°C for 20 min at which point a solid precipitate had formed. The crude mixture was then poured into water (20 mL) and

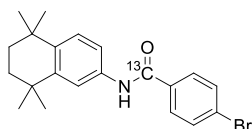
diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (3 x 40 mL). The pH was then adjusted to 2–3 with hydrochloric acid (1 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 40 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction and concentrated *in vacuo* to leave the product as a colorless solid (84 mg, 83%). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 13.21 (br s, 1H), 7.88–7.84 (m, 2H), 7.73–7.69 (m, 2H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 166.6 (<sup>13</sup>C-enriched), 131.7 (d, *J*<sub>C-C</sub> = 5 Hz, 2C), 131.3 (d, *J*<sub>C-C</sub> = 3 Hz, 2C), 130.0 (d, *J*<sub>C-C</sub> = 72 Hz), 126.9 (d, *J*<sub>C-C</sub> = 1 Hz). HRMS C<sub>6</sub><sup>13</sup>CH<sub>5</sub>BrO<sub>2</sub>[M<sup>+</sup>]; calculated: 199.9434 found: 199.9445.



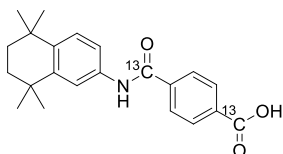
**1,1,4,4-Tetramethyl-6-nitro-1,2,3,4-tetrahydronaphthalene:** The starting material 1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene (2.00 g, 10.6 mmol) was dissolved in Ac<sub>2</sub>O (10 mL) and the mixture was cooled to 0°C. A solution of concentrated nitric acid (3.62 mL, 53.1 mmol) in Ac<sub>2</sub>O (1.5 mL) was then added dropwise from an addition funnel. The reaction mixture was stirred at room temperature for 1 hour and 30 min, at which point TLC analysis indicated full conversion of the starting material. The mixture was poured onto ice, and the aqueous phase was extracted with diethyl ether (3 x 50 mL) and the combined organic phases were washed with sat. NaHCO<sub>3</sub> (50 mL) until neutral pH, dried over MgSO<sub>4</sub>, filtered and concentrated *in vacuo*. The pure product (1.08 g, 44%) was obtained by flash column chromatography (pentane:dichloromethane - 10:2). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.17 (d, *J* = 2.5 Hz, 1H), 7.93 (dd, *J* = 2.5 Hz, 8.7 Hz, 1H), 7.46 (d, *J* = 8.7 Hz, 1H), 1.71 (s, 4H) 1.32 (s, 6H), 1.30 (s, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 152.9, 146.8, 146.1, 127.8, 121.9, 120.5, 35.0, 34.8, 34.6, 34.5, 31.7 (2C), 31.6 (2C).



**5,5,8,8-Tetramethyl-5,6,7,8-tetrahydronaphthalen-2-amine:** 1,1,4,4-tetramethyl-6-nitro-1,2,3,4-tetrahydronaphthalene (1.08 g, 4.63 mmol) was dissolved methanol (20 mL) and Pd/C 10 wt% (54 mg) and NH<sub>4</sub>HCO<sub>2</sub> (1.17 g, 18.52 mmol) was added. The mixture was stirred at reflux temperature for 2 hours, upon which time TLC analysis indicated full consumption of the starting material. The solution was filtered through a pad of Celite and concentrated *in vacuo*. The pure product was obtained by flash column chromatography (pentane:ethyl acetate – 10:1) as a colorless solid (898 mg, 96%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 7.21 (d, *J* = 8.4 Hz, 1H), 6.73 (d, *J* = 2.5 Hz, 1H), 6.61 (dd, *J* = 2.5 Hz, 8.4 Hz, 1H), 3.57 (s, 2H), 1.76 (s, 4H), 1.36 (s, 6H), 1.35 (s, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 145.8, 143.8, 135.2, 127.4, 113.6, 112.8, 35.3 (2C), 34.2, 33.5, 32.1 (2C), 31.9 (2C). HRMS C<sub>14</sub>H<sub>21</sub>N [M+H<sup>+</sup>]; calculated: 204.1752 found: 204.1750.



**[<sup>13</sup>C]-4-Bromo-*N*-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)benzamide (31):** Under an atmosphere of argon, 5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-amine (386 mg, 1.9 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (20 mL) before *N*-methyl morpholine (837 μL, 7.6 mmol), HOBT · H<sub>2</sub>O (582 mg, 3.8 mmol), EDC (728 mg, 3.8 mmol) and lastly [<sup>13</sup>C]-4-bromobenzoic acid (382 mg, 1.9 mmol) were added. The mixture was stirred at room temperature for 20 hours, at which point TLC analysis indicated full conversion of the amine. Diethyl ether (50mL) and hydrochloric acid (0.5 M, 50 mL) was added and the phases were separated. The aqueous phase was extracted with diethyl ether (3 x 50 mL) before the combined organic phases were dried over MgSO<sub>4</sub>, filtered and concentrated *in vacuo* to leave a solid crude. The pure product was obtained as a colorless solid (385 mg, 52%) by flash column chromatography (pentane:ethyl acetate:methanol – 10:0.4:0.2). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 7.75 (dd, *J* = 8.4 Hz, 3.7 Hz, 2H), 7.68 (br s, 1H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 1.8 Hz, 1H), 7.41 (dd, *J* = 8.4 Hz, 1.9 Hz, 1H), 7.31 (d, *J* = 8.5 Hz, 1H), 1.67 (s, 4H), 1.30 (s, 6H), 1.28 (s, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 164.7 (<sup>13</sup>C-enriched), 146.0, 141.9, 135.1, 134.1 (d, *J* = 66 Hz), 132.1 (d, *J* = 4 Hz, 2C), 128.7 (d, *J* = 2 Hz, 2C) 127.5, 126.5, 118.3, 118.2, 35.2, 35.1, 34.6, 34.2, 32.0 (2C), 32.0 (2C). HRMS C<sub>20</sub><sup>13</sup>CH<sub>24</sub>BrNO [M<sup>+</sup>]; calculated: 385.1002 found: 385.1007.



**[<sup>13</sup>C<sub>2</sub>]-4-(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydronaphthalen-2-ylcarbonyl)benzoic acid (32):** In a glove box under argon, **33** (193 mg, 0.50 mmol), MePh<sub>2</sub>Si<sup>13</sup>COOH (183 mg, 0.75 mmol), lithium trimethylsilanolate (96 mg, 1.0 mmol), Pd(dba)<sub>2</sub> (14.4 mg, 0.025 mmol) and Xantphos (14.5 mg, 0.025 mmol) were mixed in an 8 mL vial and dissolved in dry dioxane (3.0 mL). The vial was closed and heated to 80°C for 16 hours at which point a solid precipitate had formed. The crude mixture was poured into water (40 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> before the pH was adjusted to approx. 10. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (3 x 30 mL). The pH-value was then adjusted to 2–3 with hydrochloric acid (4 M) and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 30 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered by suction, and concentrated *in vacuo*. The crude residual was purified by flash column chromatography (CH<sub>2</sub>Cl<sub>2</sub>:diethyl ether:HCO<sub>2</sub>H – 10:0.1:0.03) to leave the product as a colorless solid (170 mg, 96%). <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ (ppm) 13.28 (br s, 1H), 10.26 (d, *J* = 3.2 Hz, 1H), 8.05 (m, 4H), 7.68 (d, *J* = 2.2 Hz, 1H), 7.58 (dd, *J* = 8.6 Hz, 2.2 Hz, 1H), 7.29 (d, *J* = 8.6 Hz, 1H), 1.64 (s, 4H), 1.25 (s, 6H), 1.23 (s, 6H). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>) δ (ppm) 166.8 (<sup>13</sup>C-enriched), 164.5 (<sup>13</sup>C-enriched), 144.6, 140.1, 138.8 (d, *J* = 64 Hz), 136.5, 133.2 (d, *J* = 71 Hz), 129.3 (dd, *J* = 4 Hz, 3 Hz, 2C), 127.9 (dd, *J* = 4 Hz, 3 Hz, 2C), 126.5, 118.4, 118.1, 34.6, 34.6, 34.0, 33.6, 31.7 (2C), 31.6 (2C). HRMS C<sub>20</sub><sup>13</sup>C<sub>2</sub>H<sub>25</sub>BrNO<sub>3</sub> [M<sup>+</sup>]; calculated: 352.1823 found: 352.1830.

## Pressure measurement studies

In order to monitor the reaction progress and completion time, the pressure development over the course of the carbonylation of 4-iodoanisole was measured as a function of time (Figure 1). Only a slight pressure decrease is observed after maximum pressure is attained after 200 seconds, while the reaction is judged finished after 600 seconds as displayed by the constant pressure.

In a 15 mL vial equipped with a magnetic stir bar, 4-iodoanisole (117 mg, 0.50 mmol),  $\text{MePh}_2\text{SiCOOH}$  (182 mg, 0.75 mmol), potassium trimethylsilanolate (128 mg, 1.0 mmol),  $\text{Pd}(\text{dba})_2$  (14.4 mg, 0.025 mmol), and XantPhos (14.5 mg, 0.025 mmol) were weighed off. Toluene (3.0 mL) was added, the vial was fitted with a manometer and the reaction was heated to 40 °C.

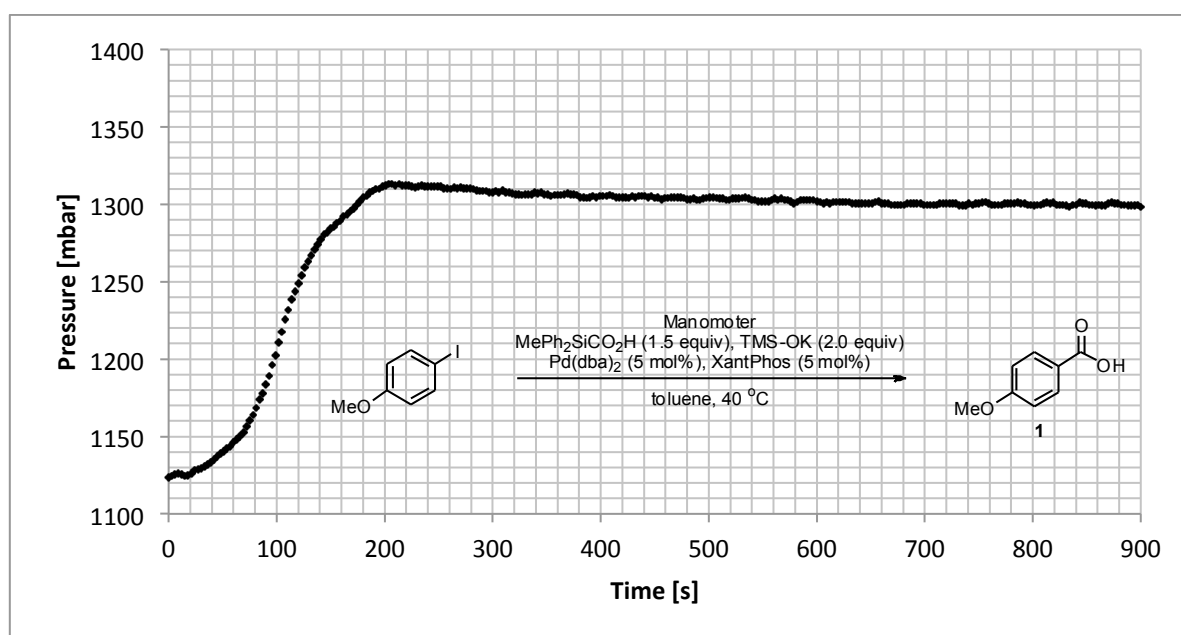
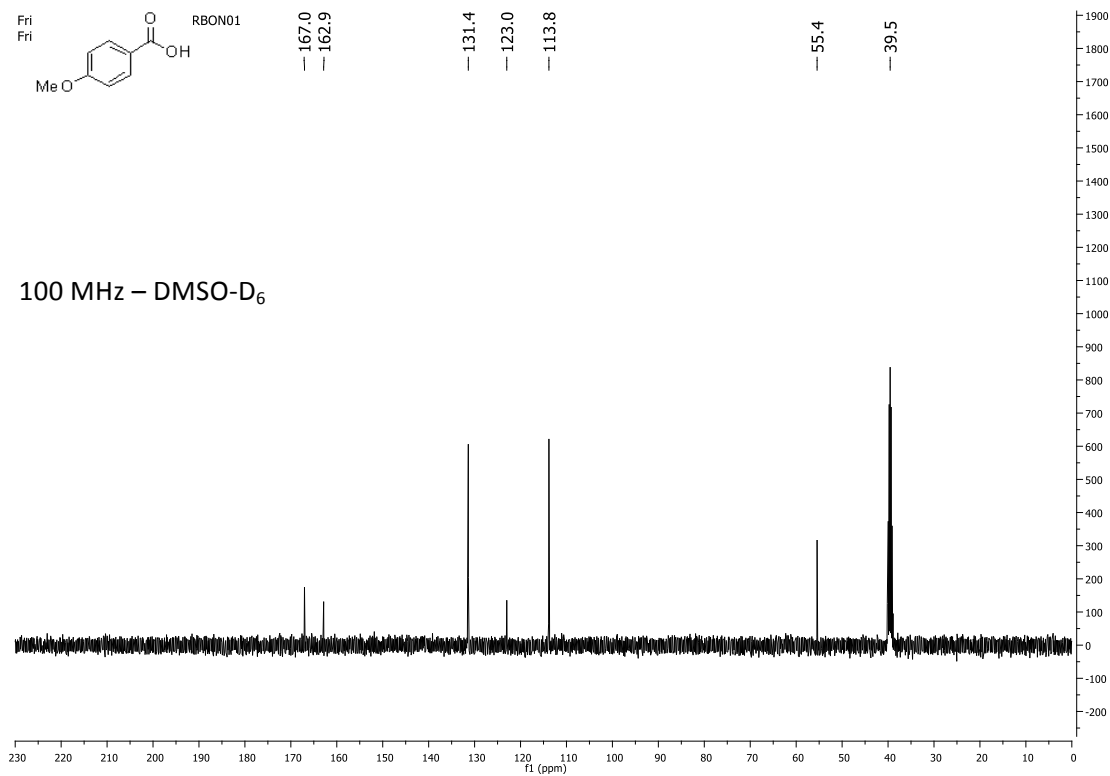
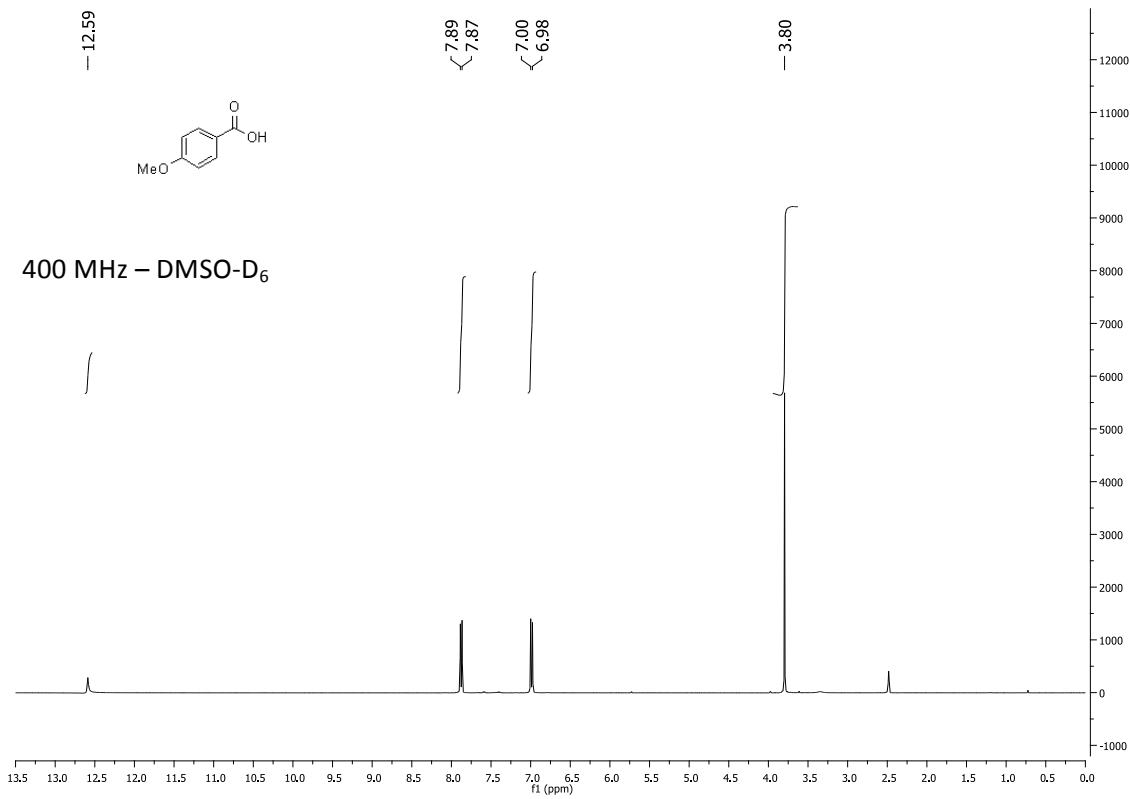


Figure 1: Pressure as a function of time during the formation of 4-methoxybenzoic acid from 4-iodoanisole.

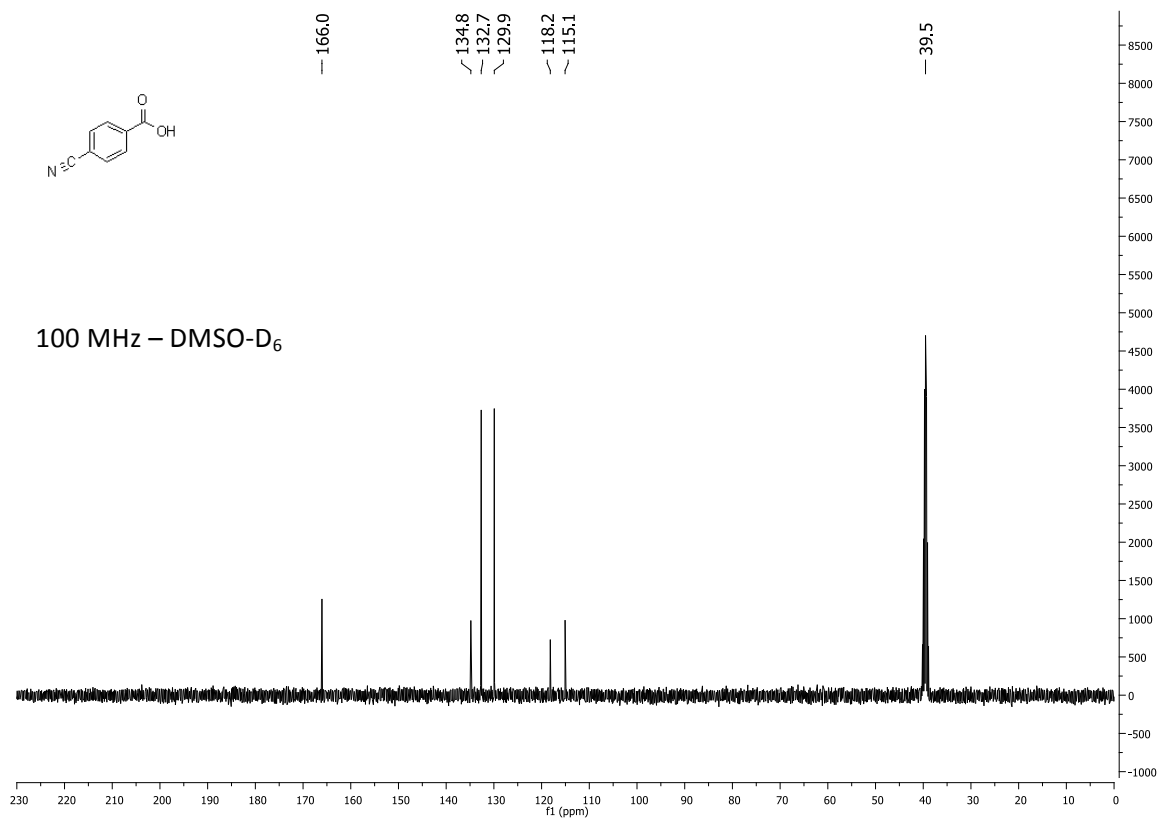
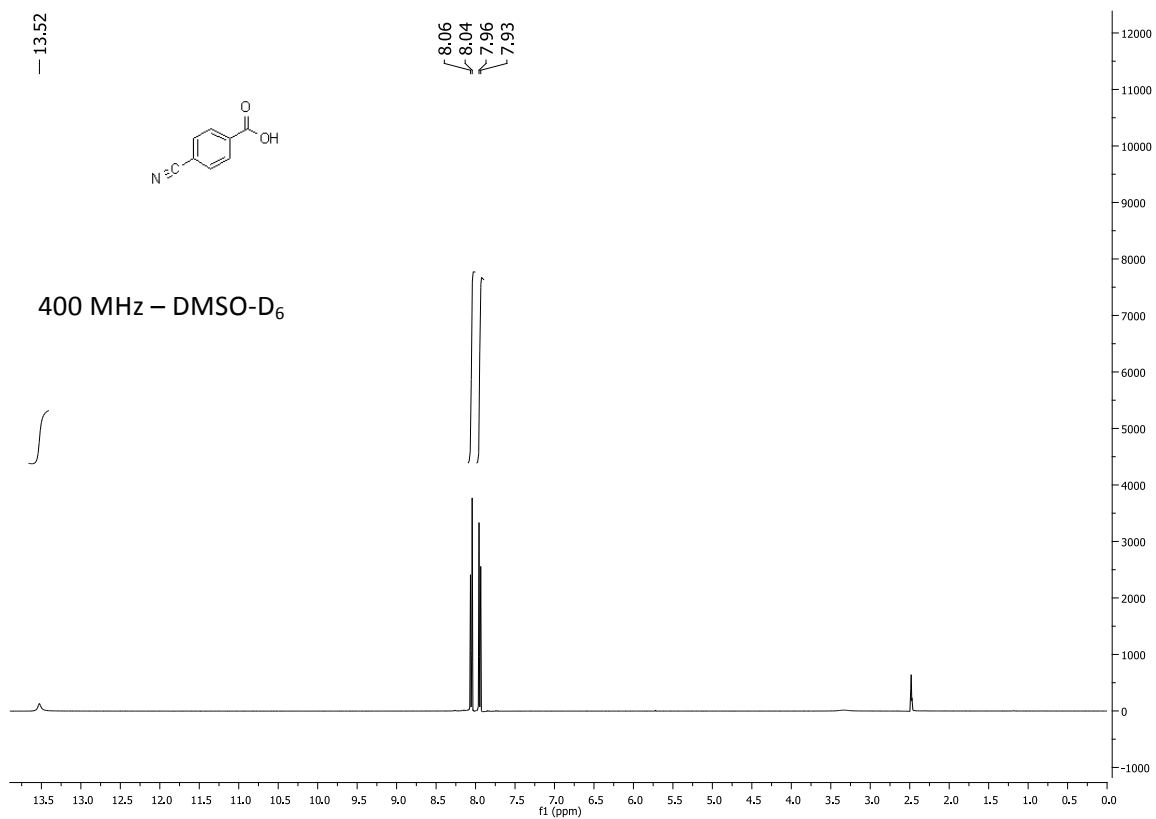
NMR Spectra

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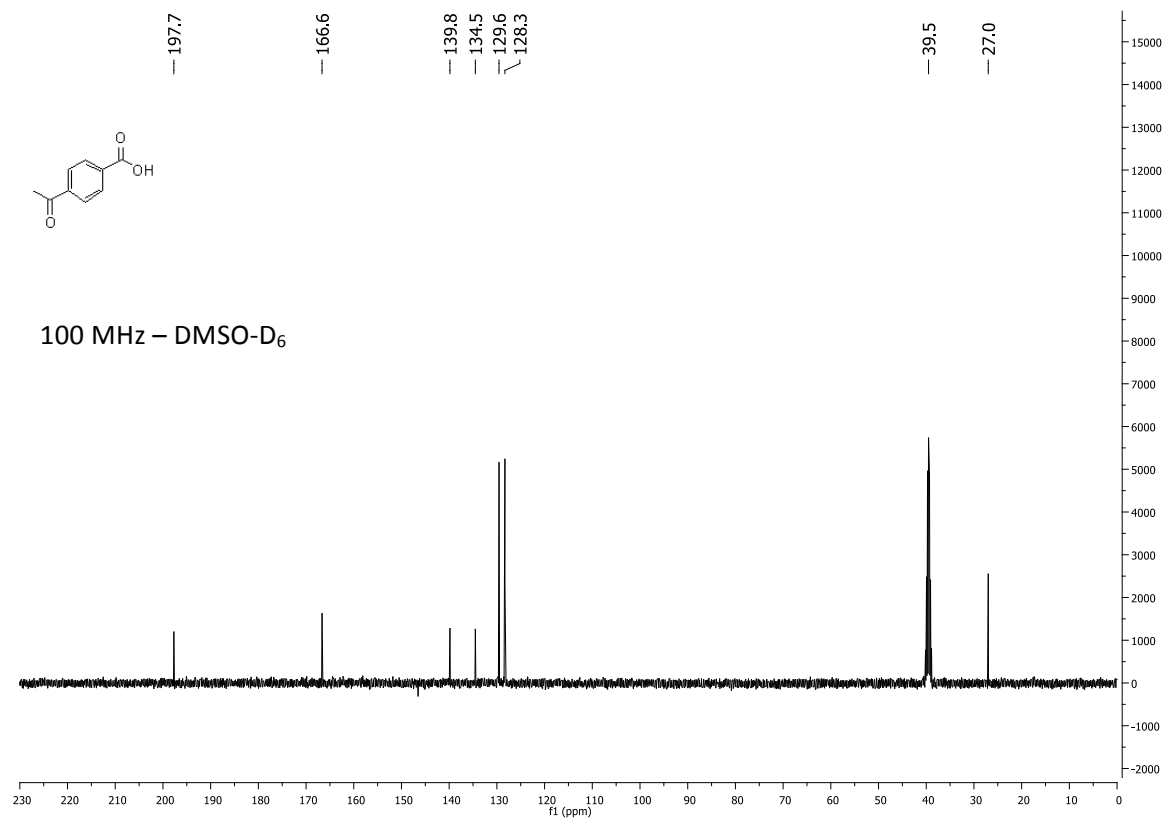
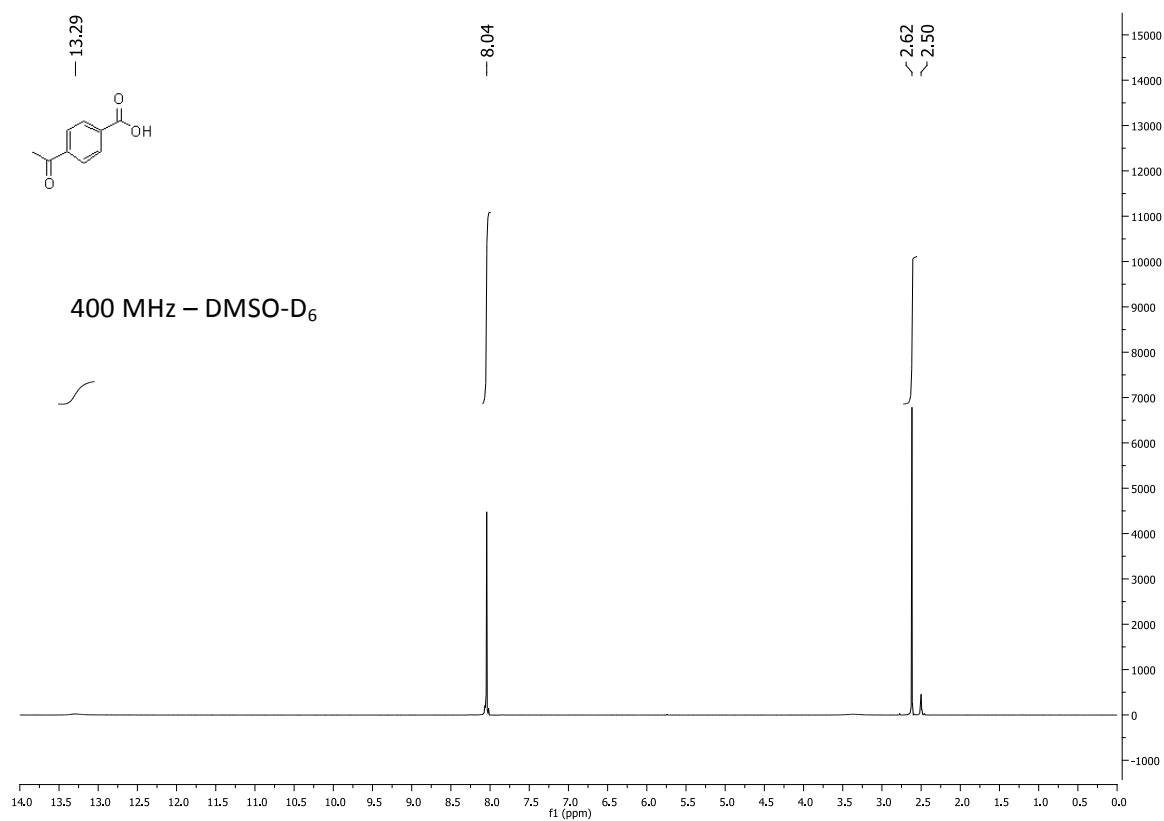




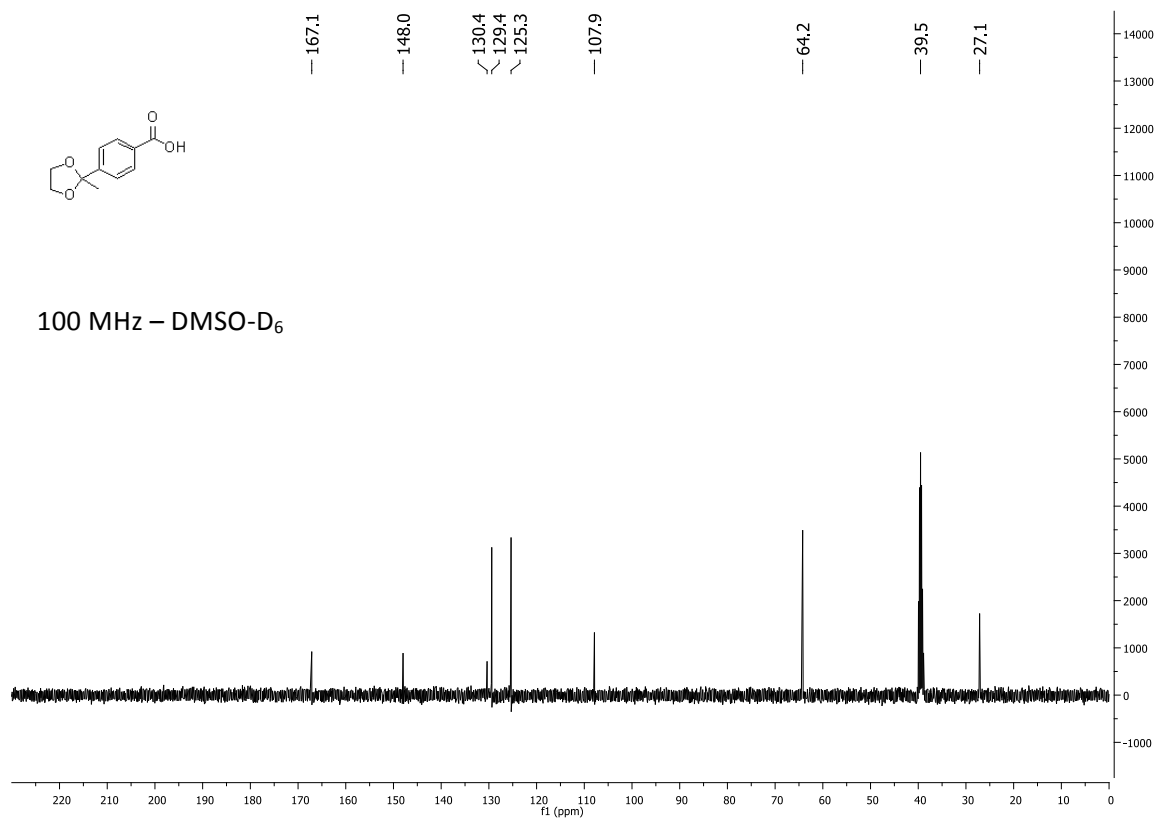
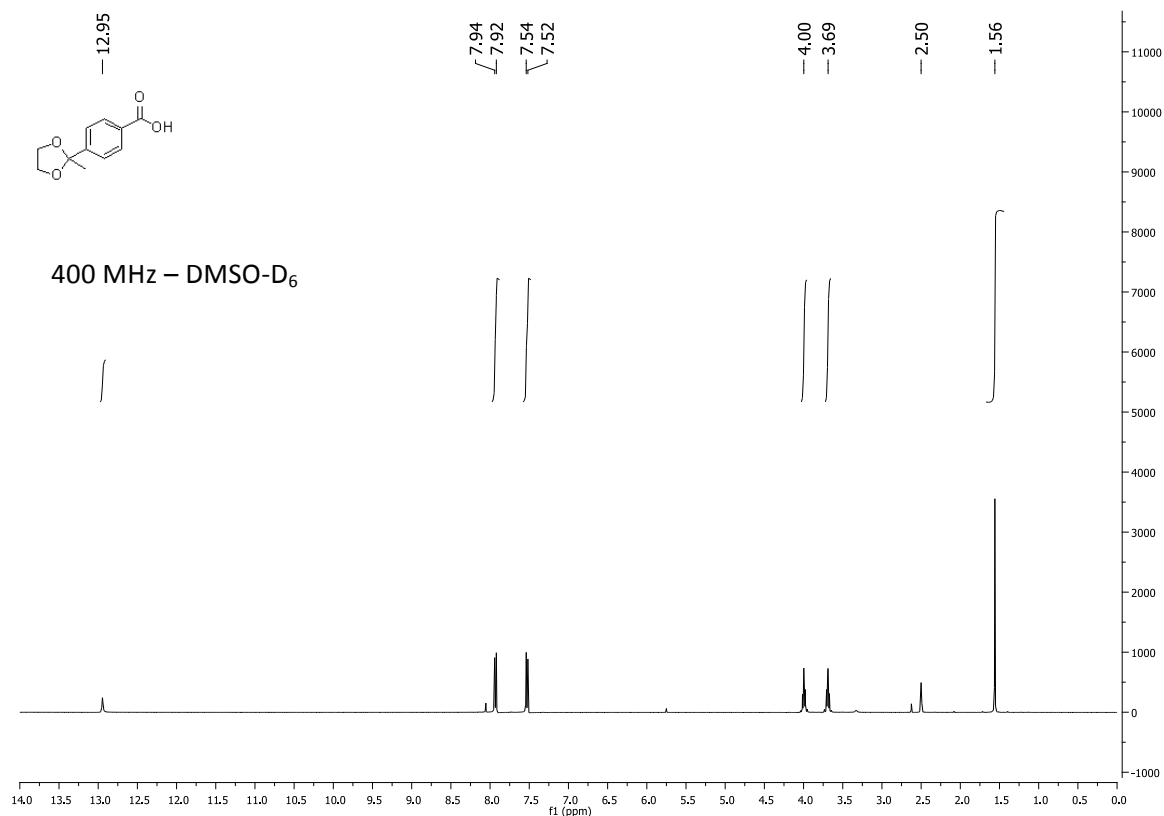
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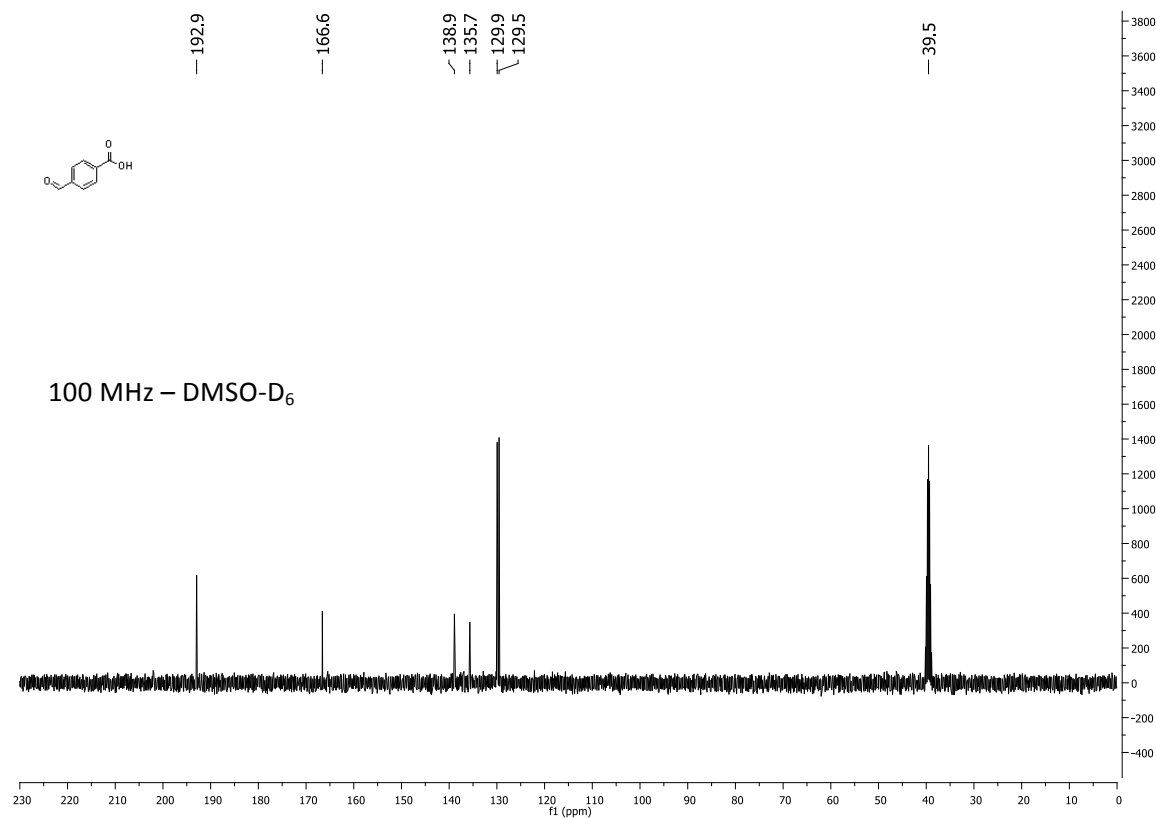
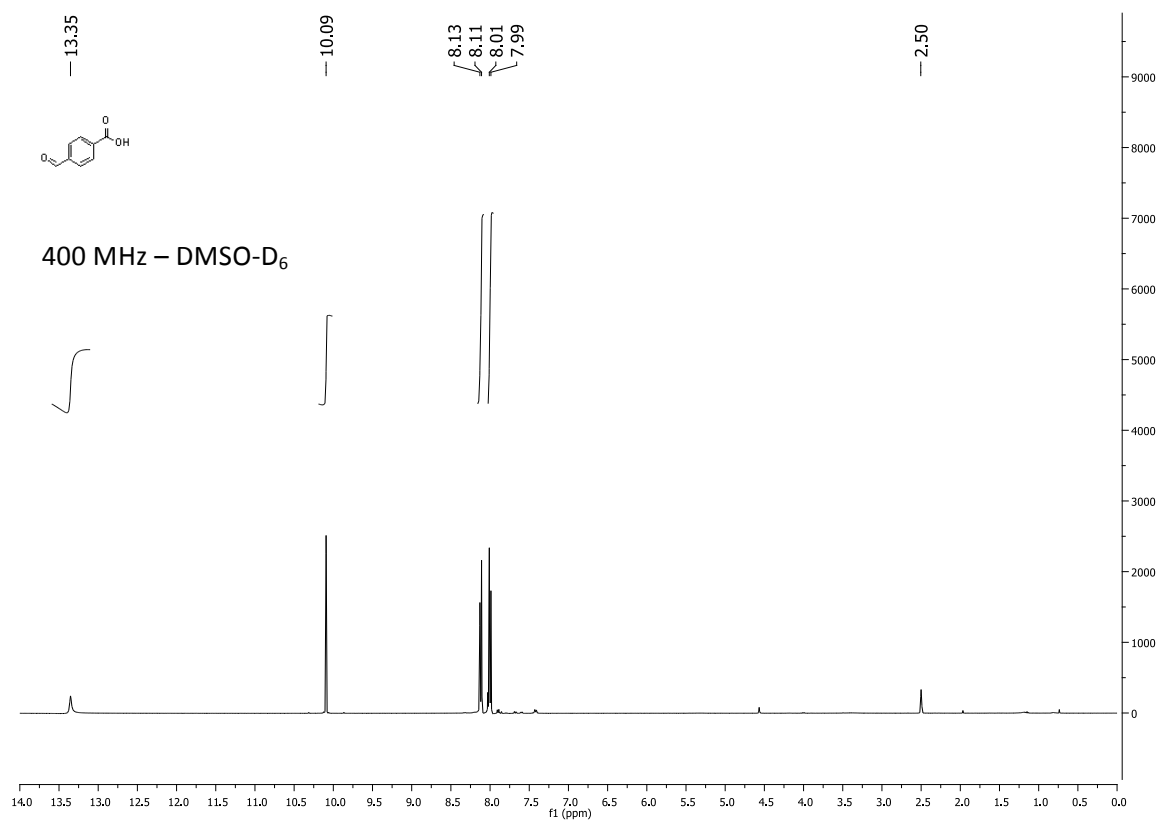
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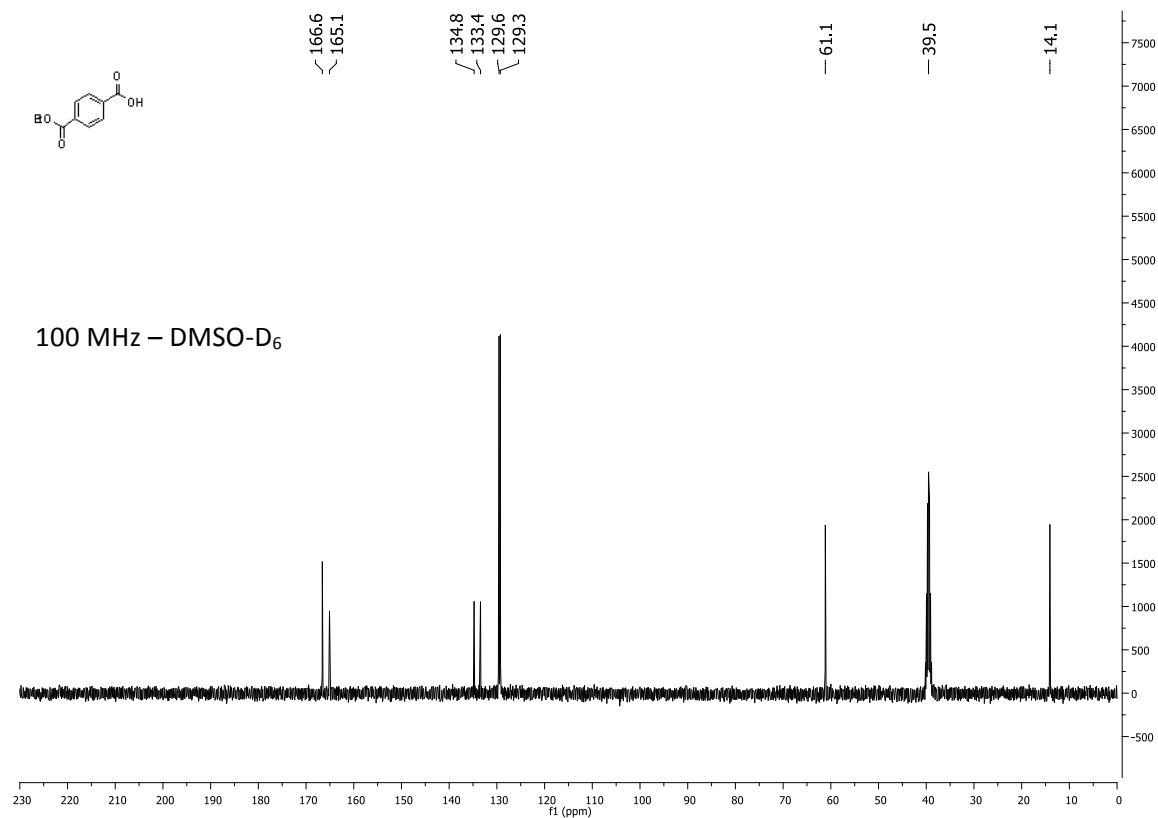
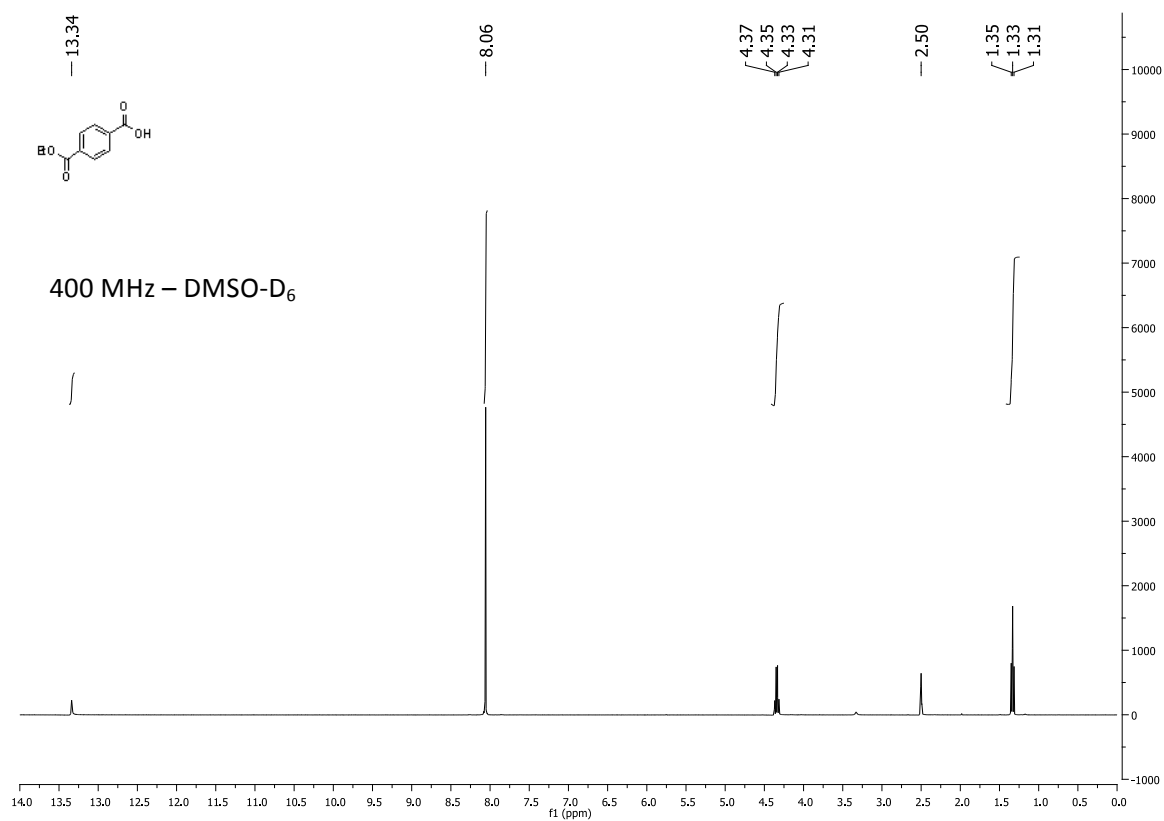
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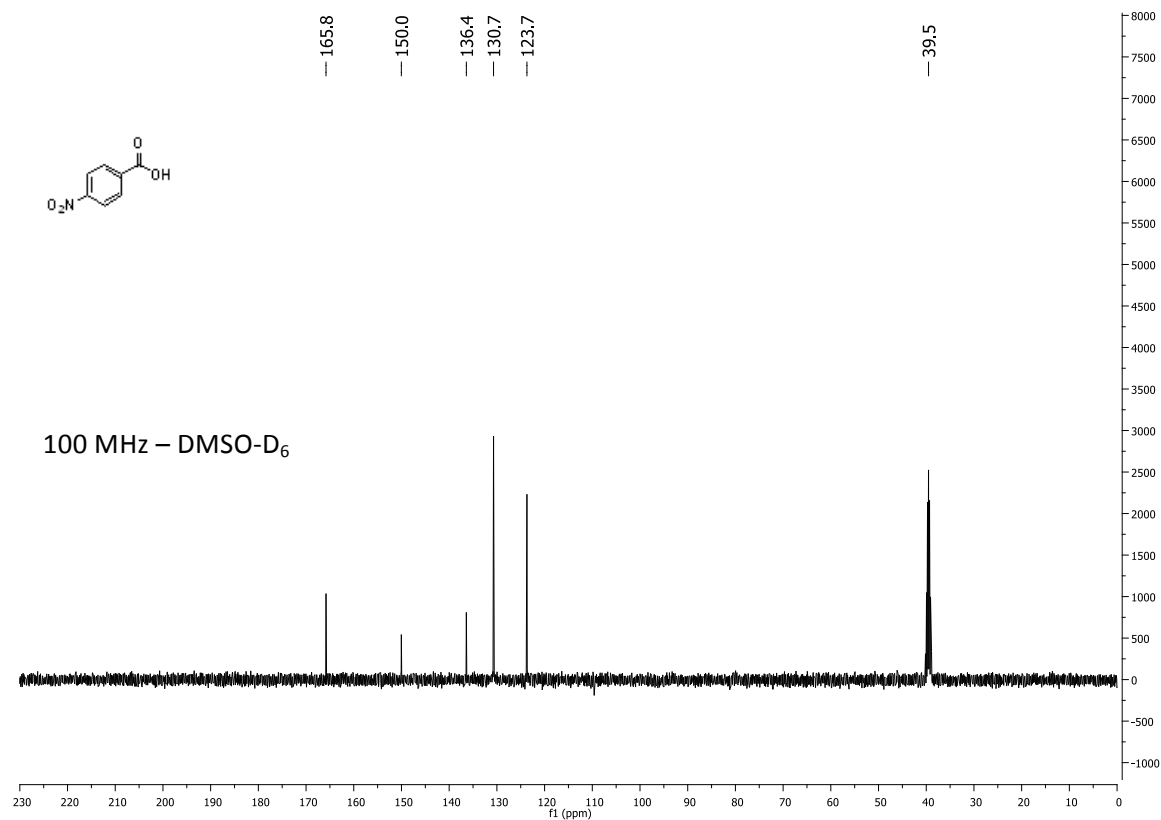
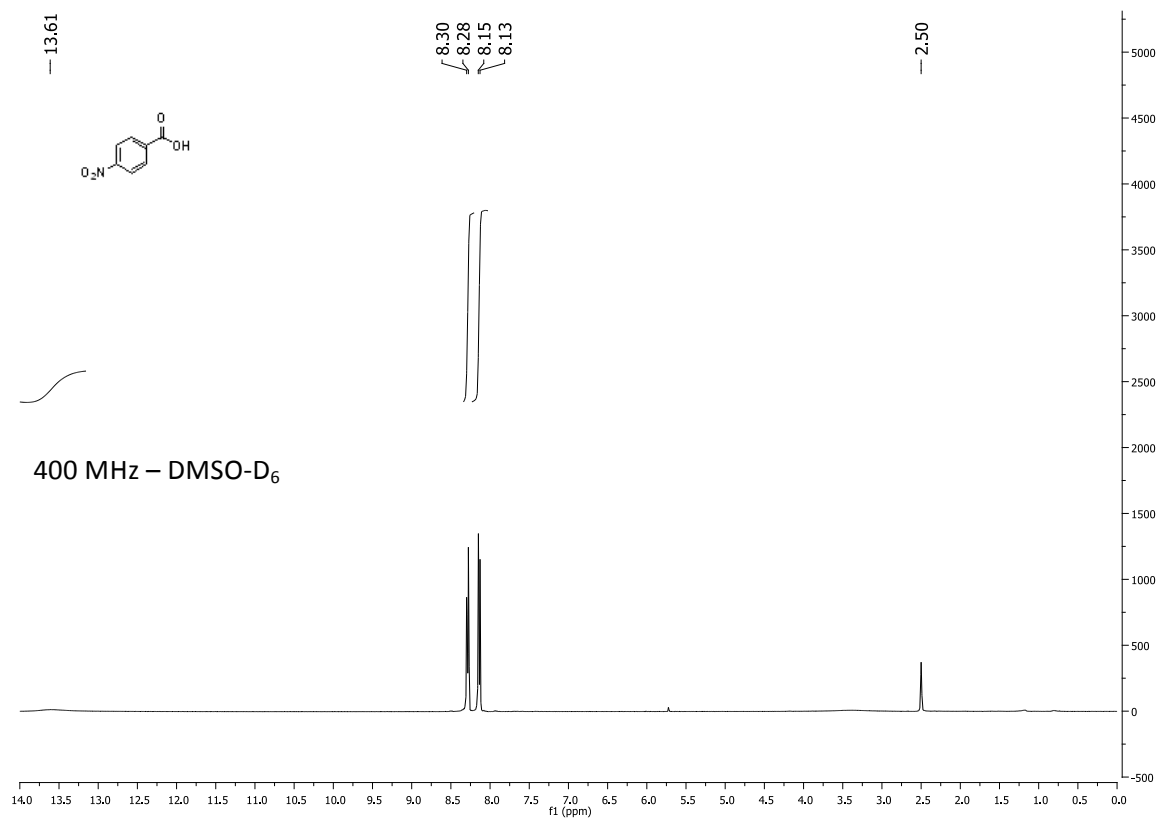
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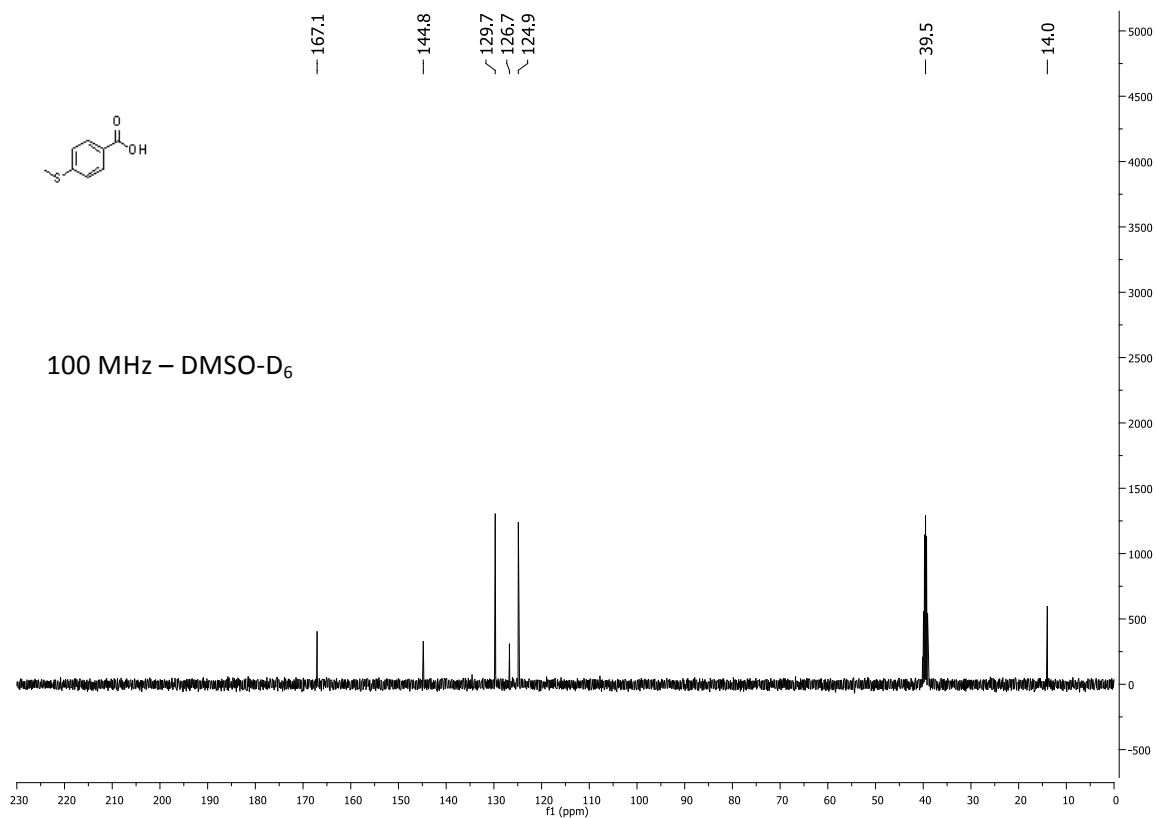
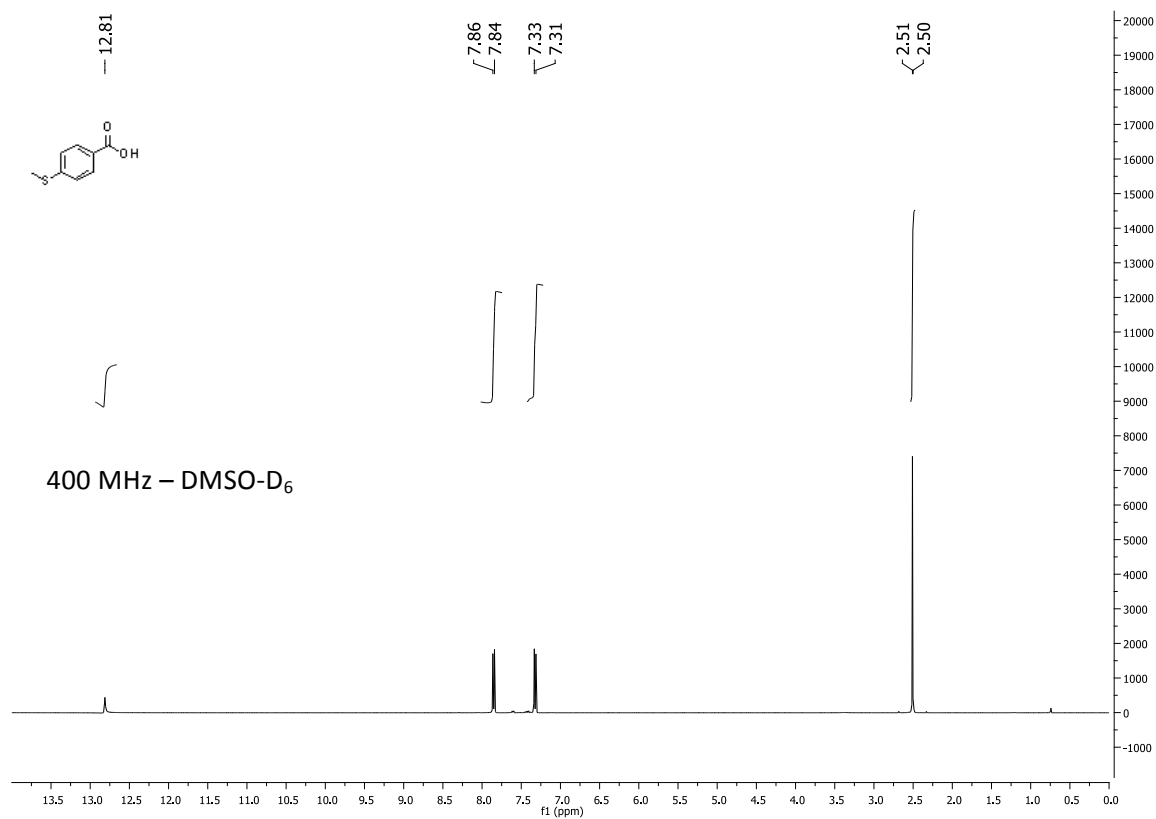
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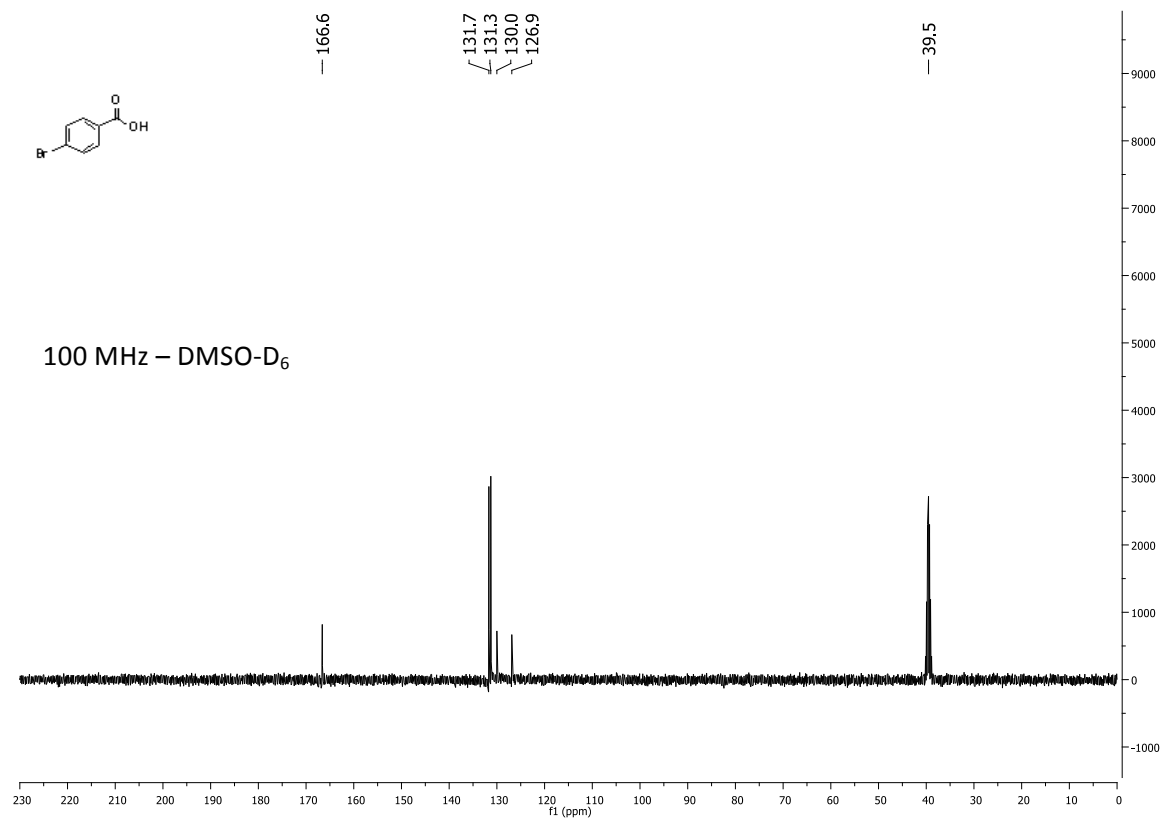
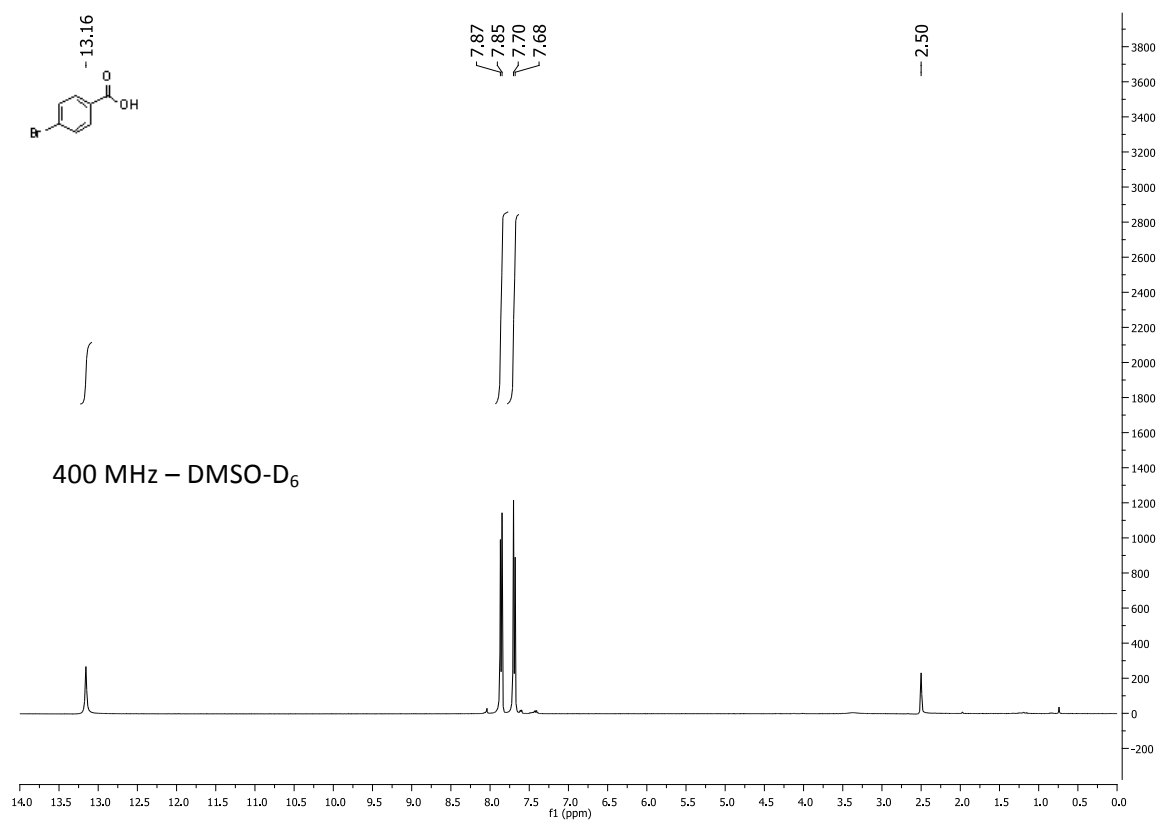
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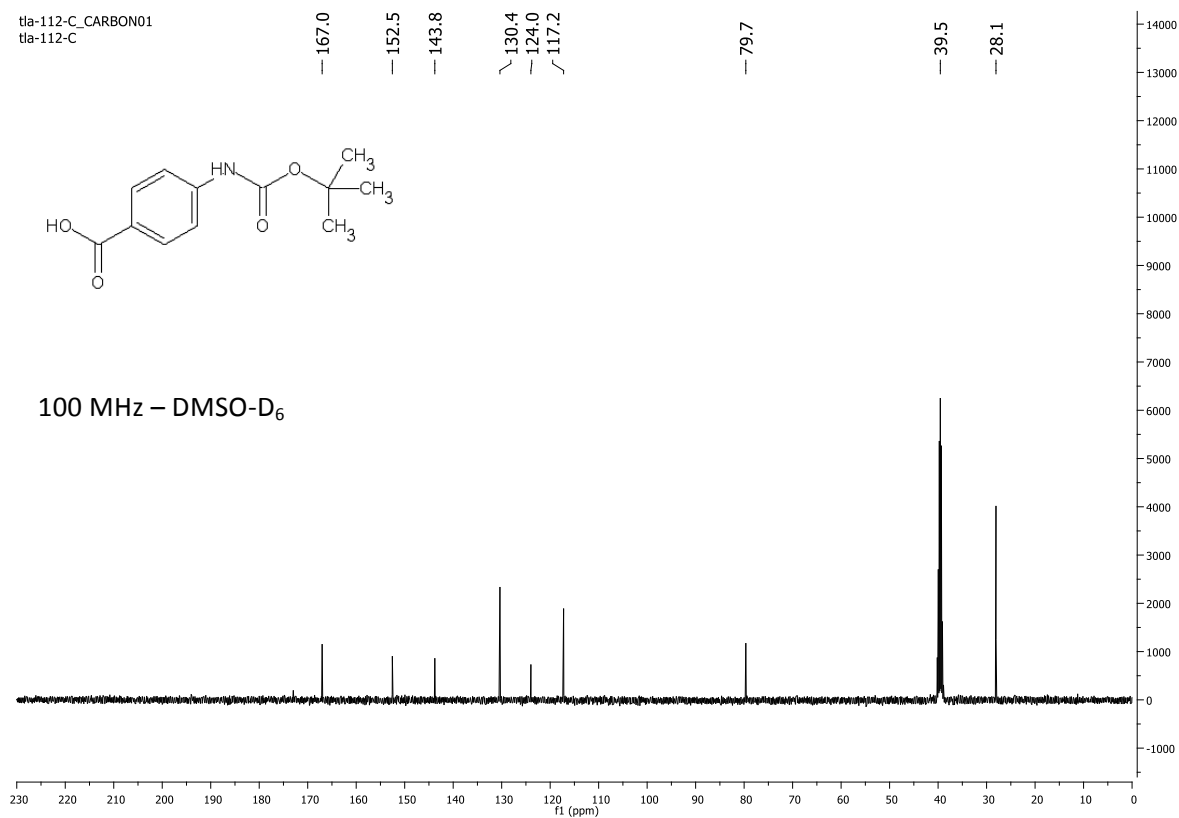
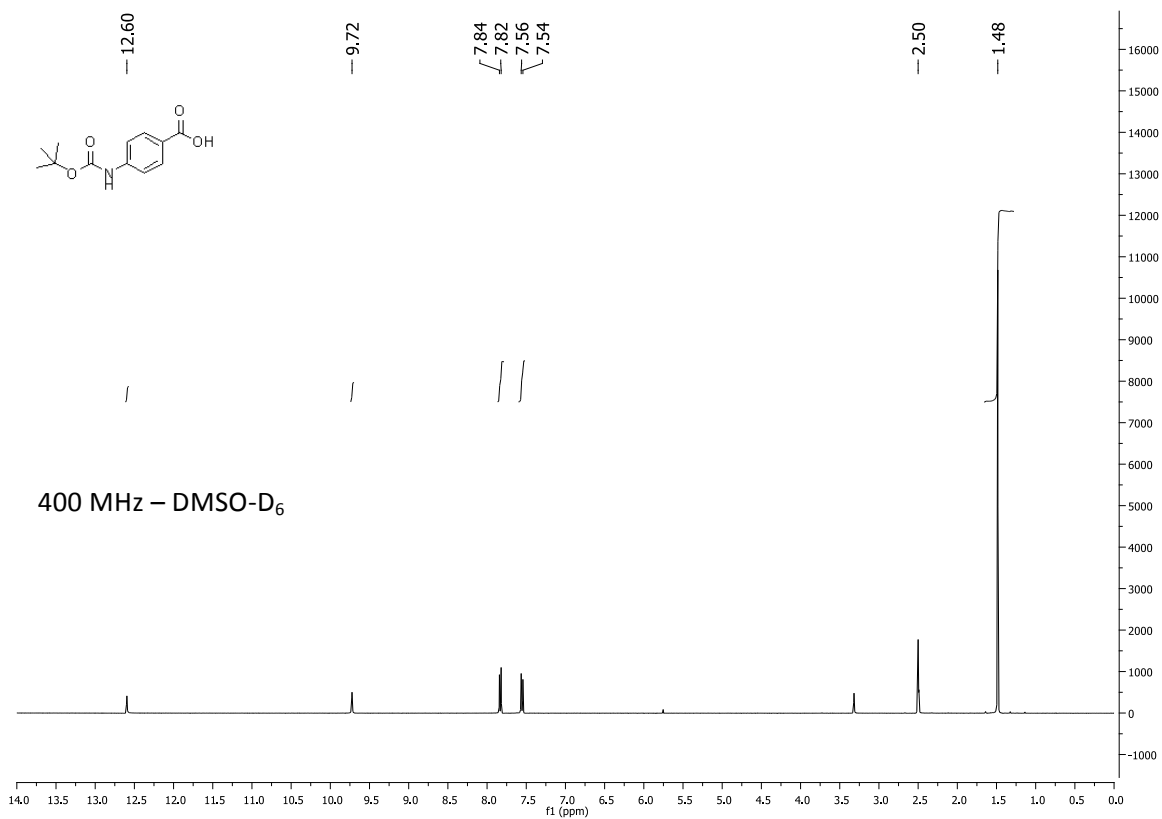


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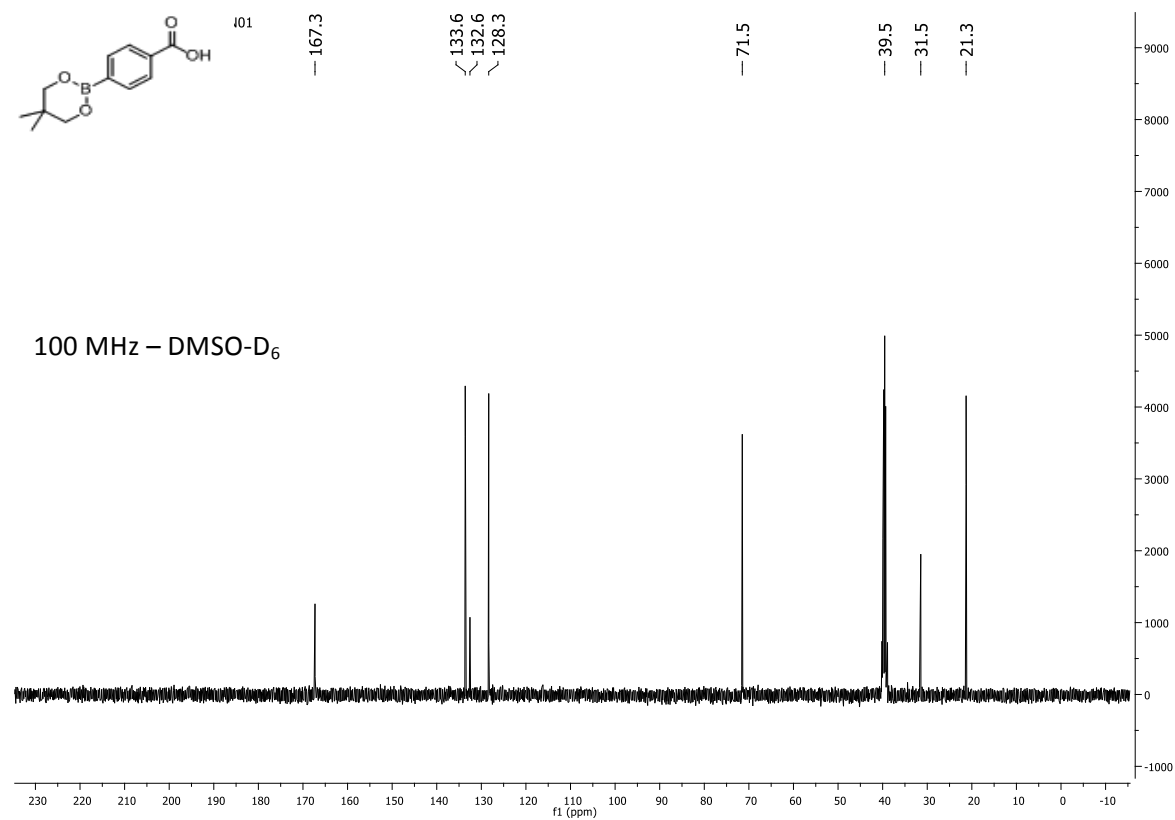
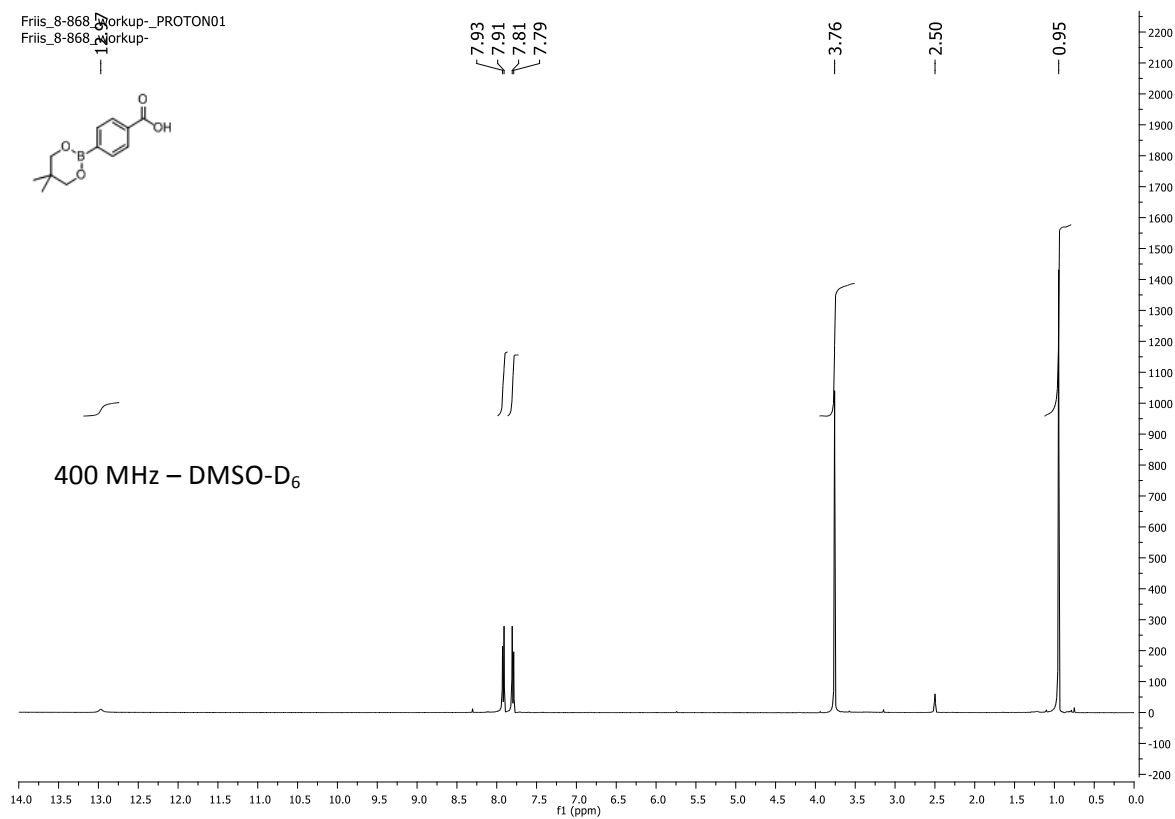




(10)



(11)



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Frils\_8-873-2 workup-

400 MHz – DMSO-D<sub>6</sub>

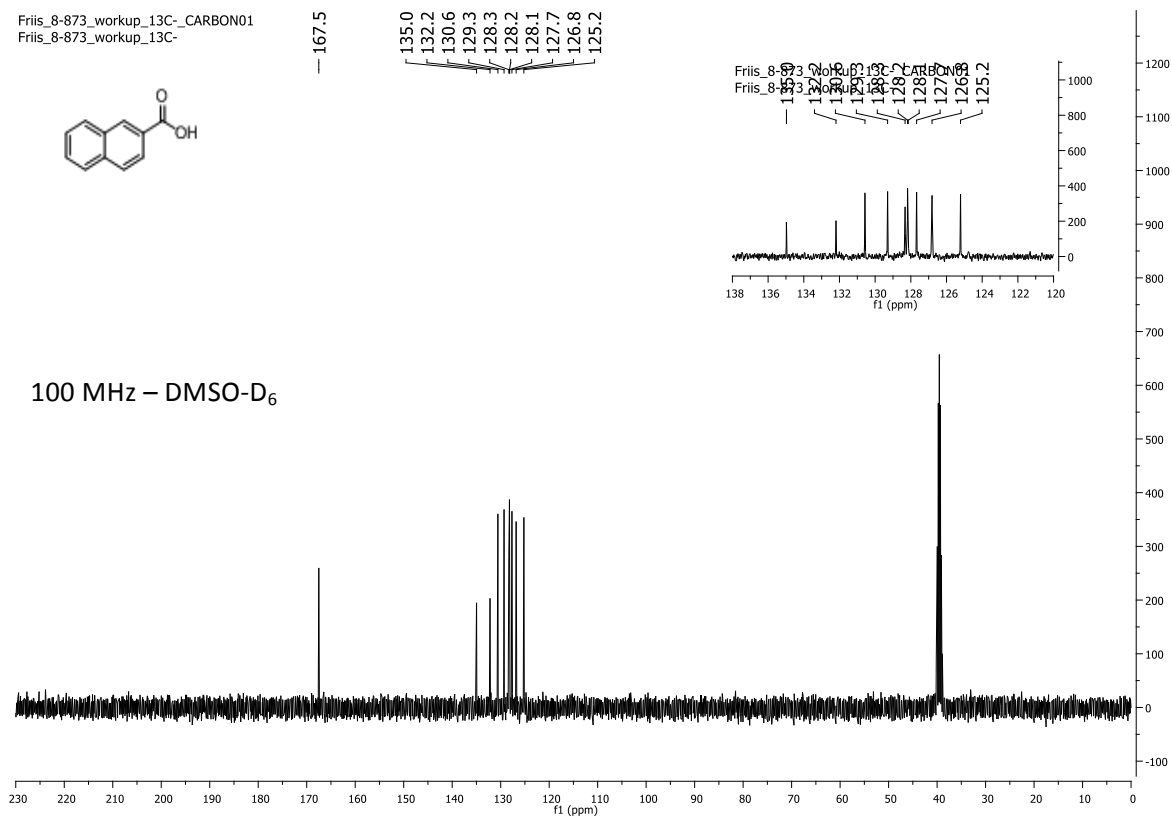
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8.00  
7.98  
7.96  
7.65  
7.56

— 2.50

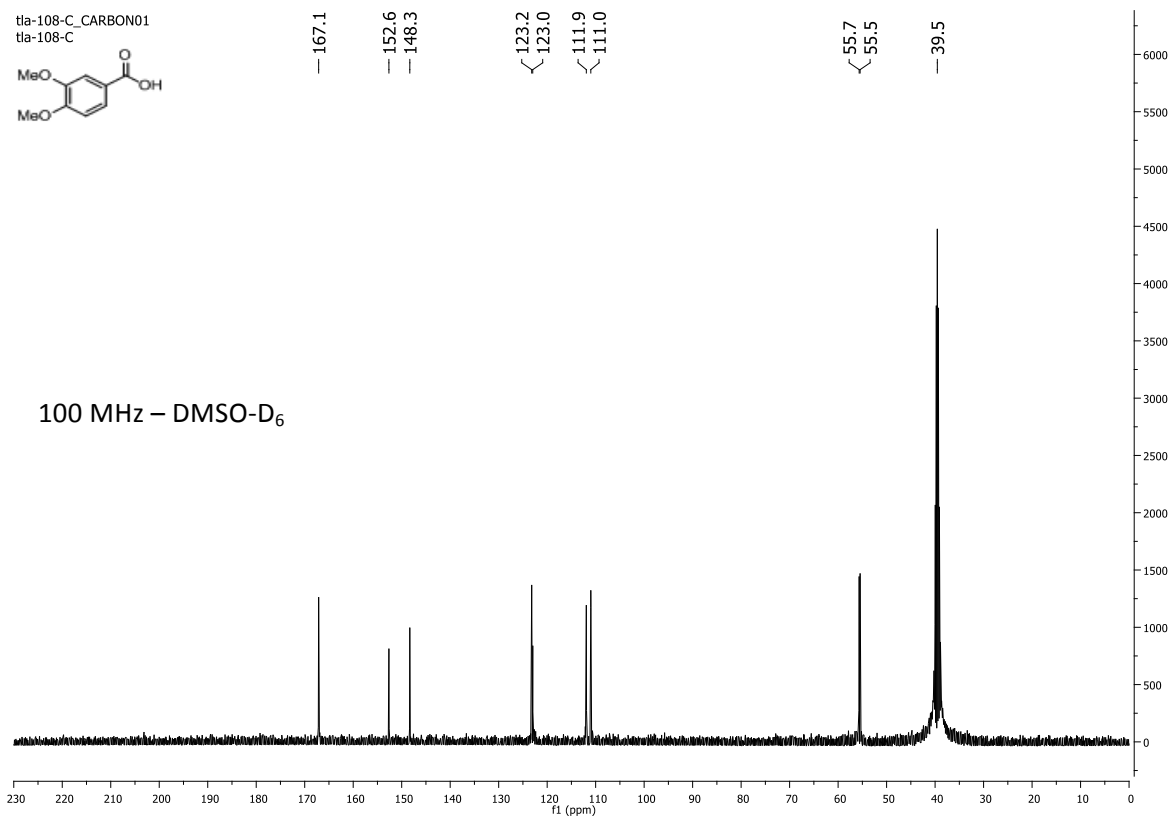
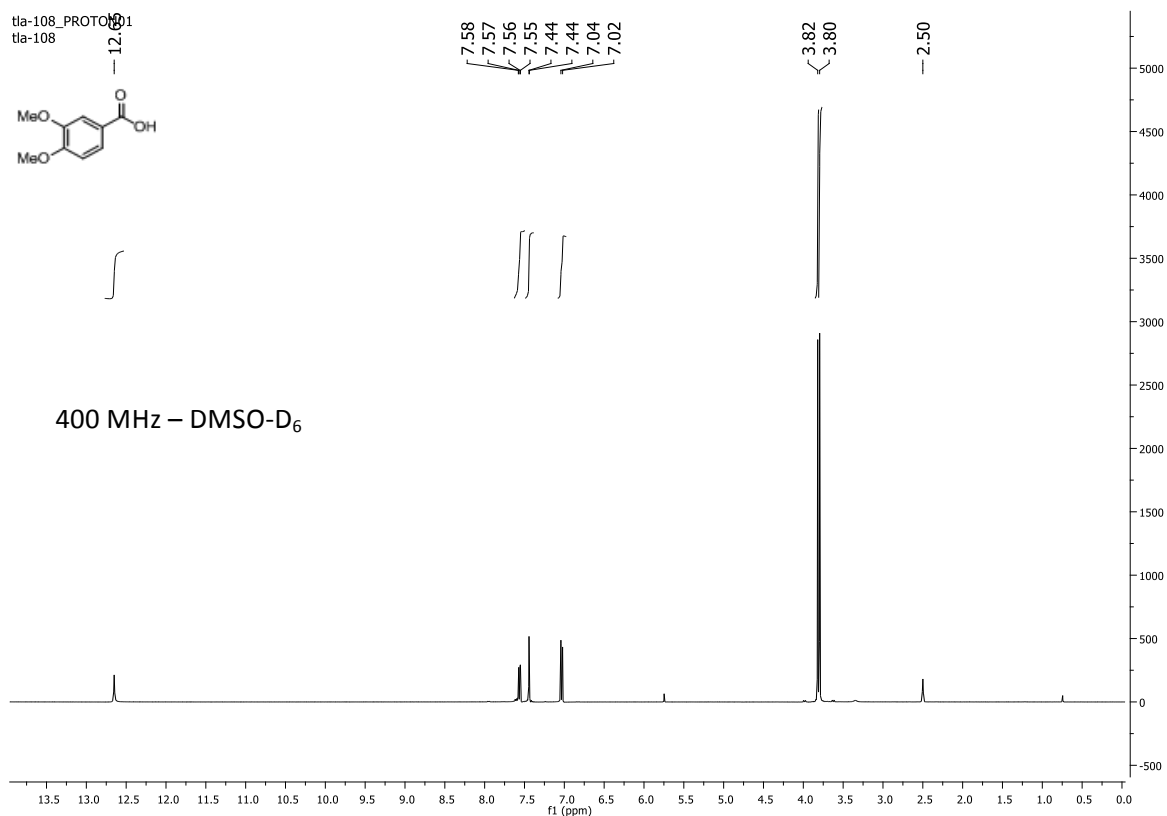
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8.63  
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7.56  
2.50  
1.0

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

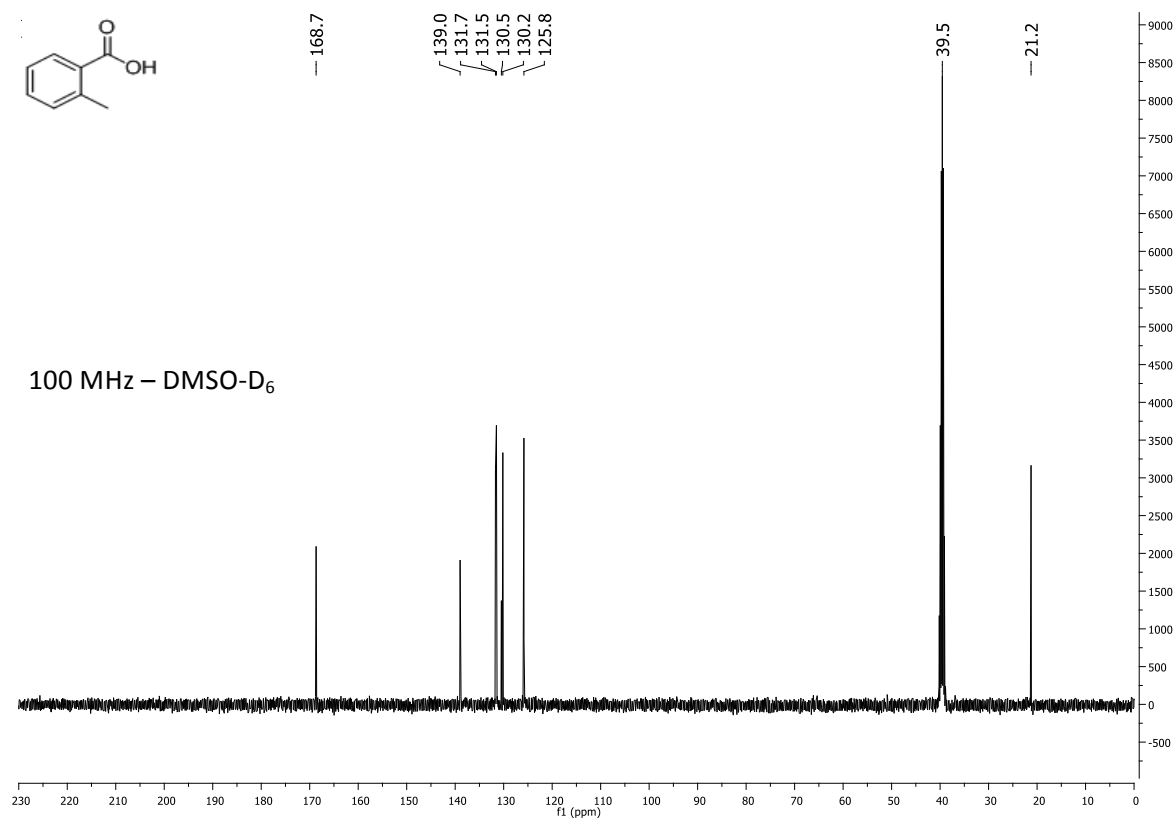
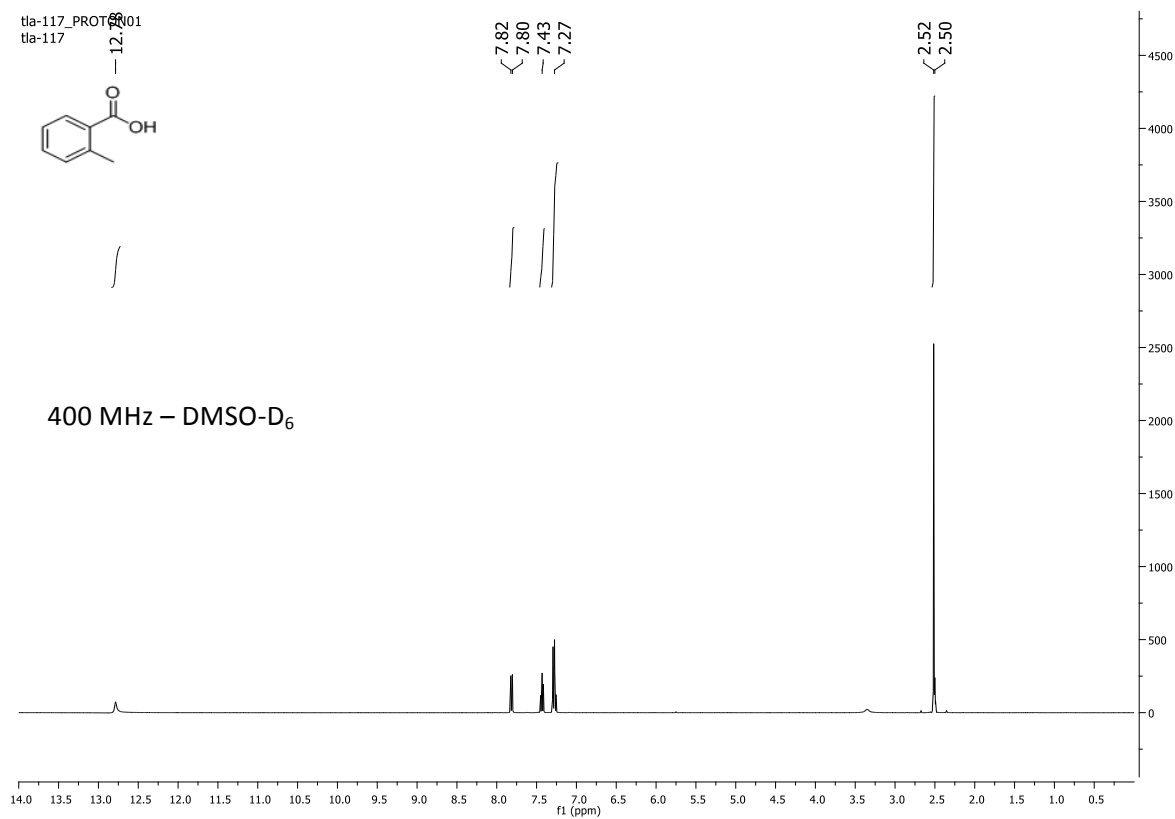
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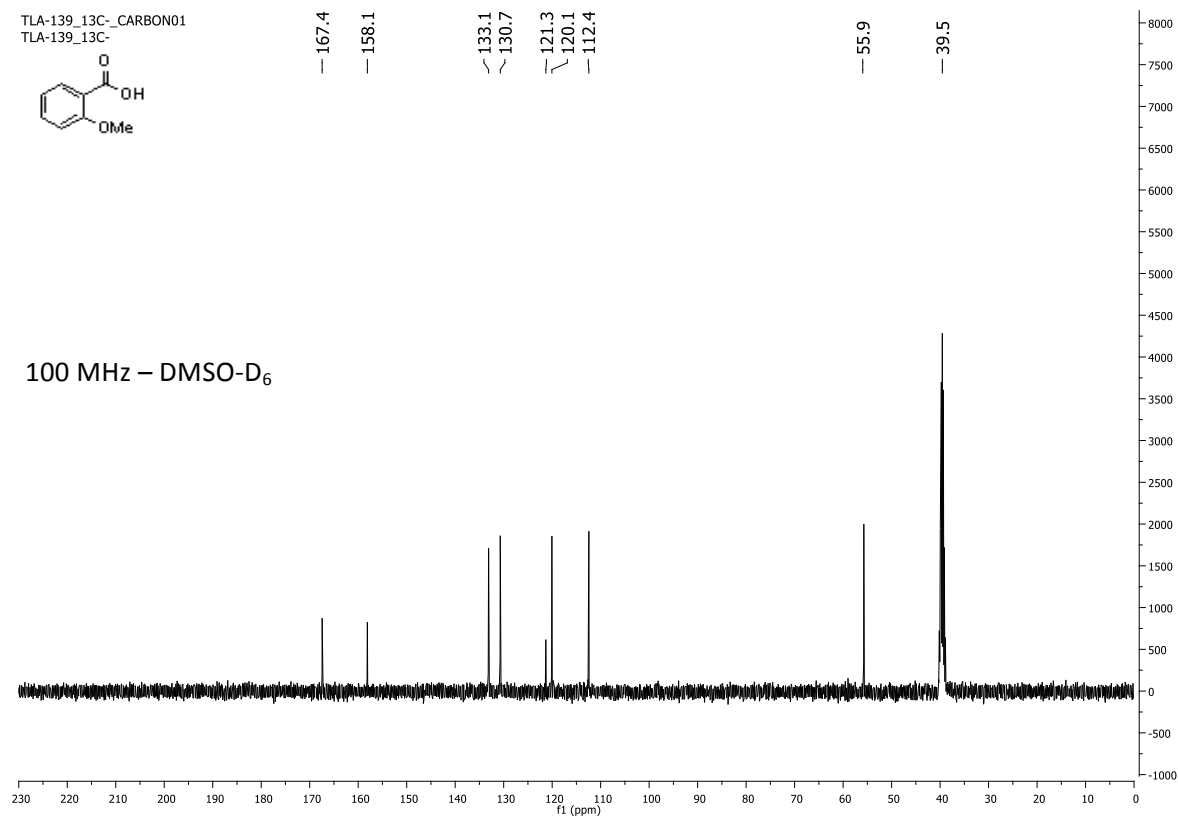
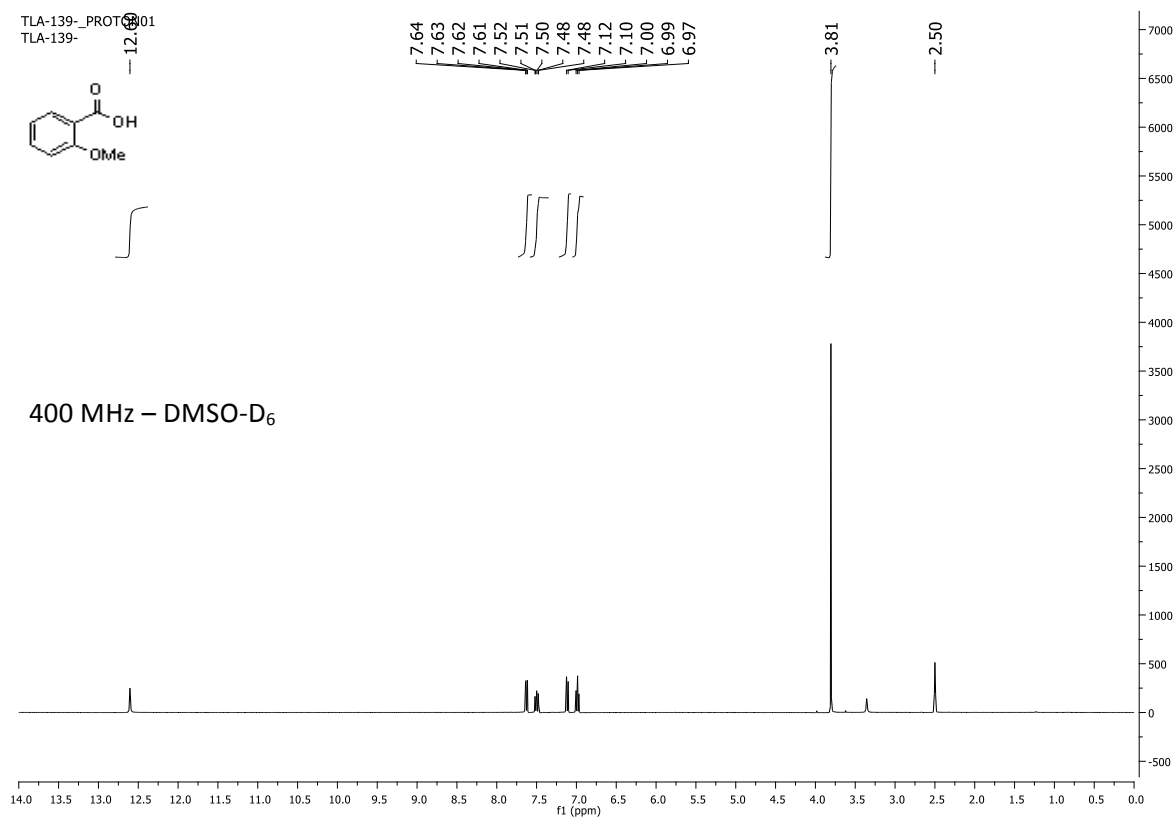
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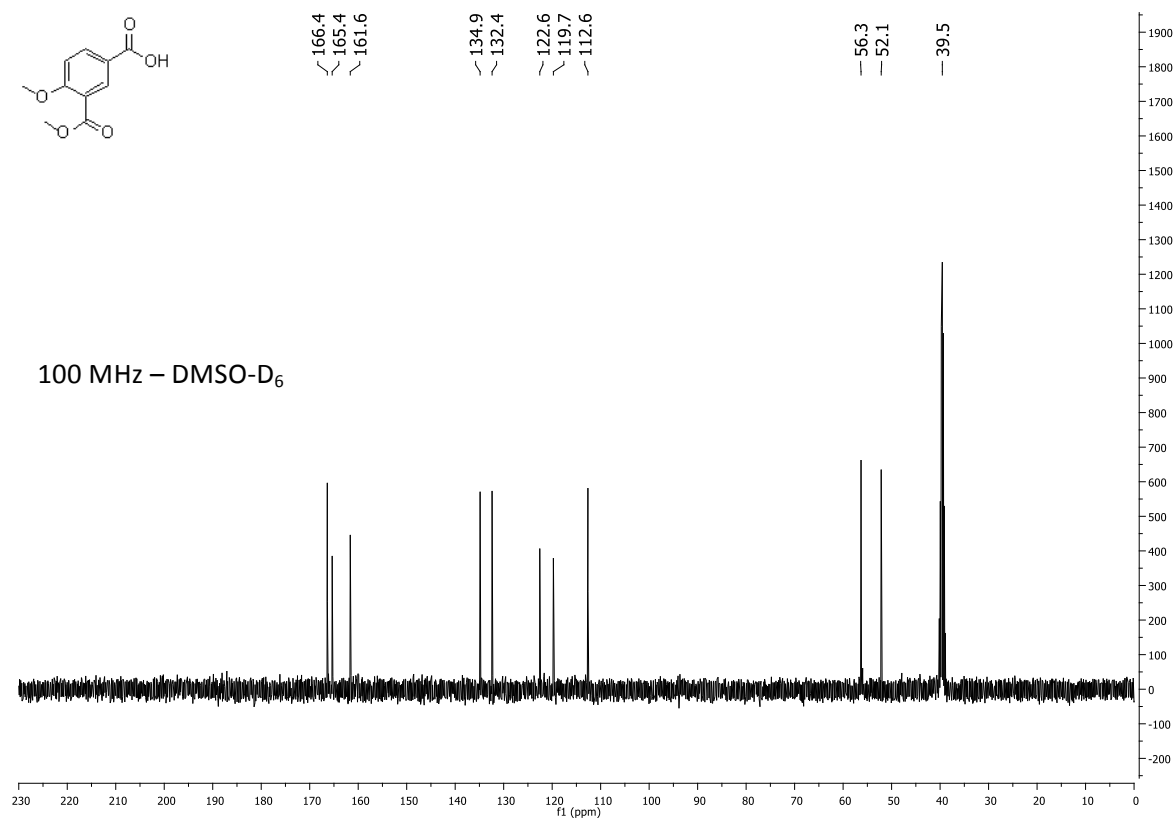
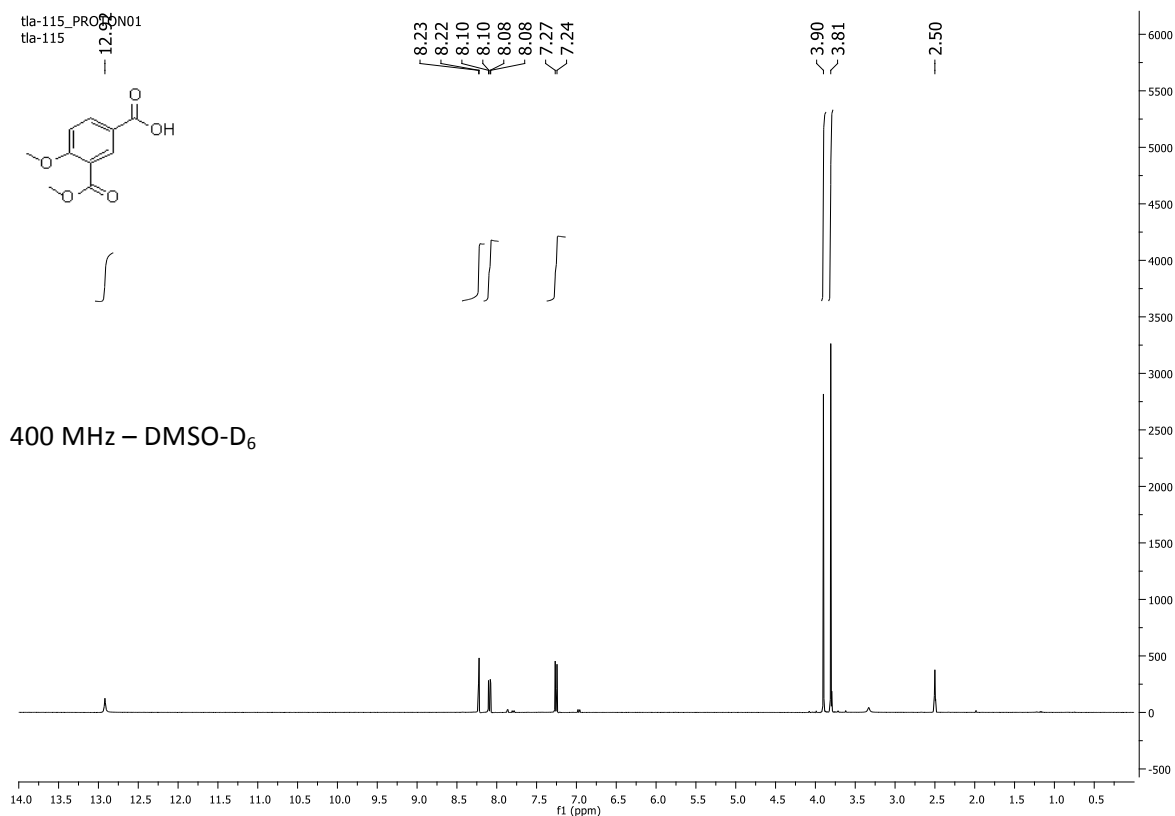
(14)



(15)



(16)



85-121\_PROTON1  
89-121

400 MHz – DMSO-D<sub>6</sub>

Chemical structure: 2,6-difluorobenzoic acid

Peak labels: 7.59, 7.20, 2.50

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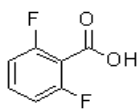
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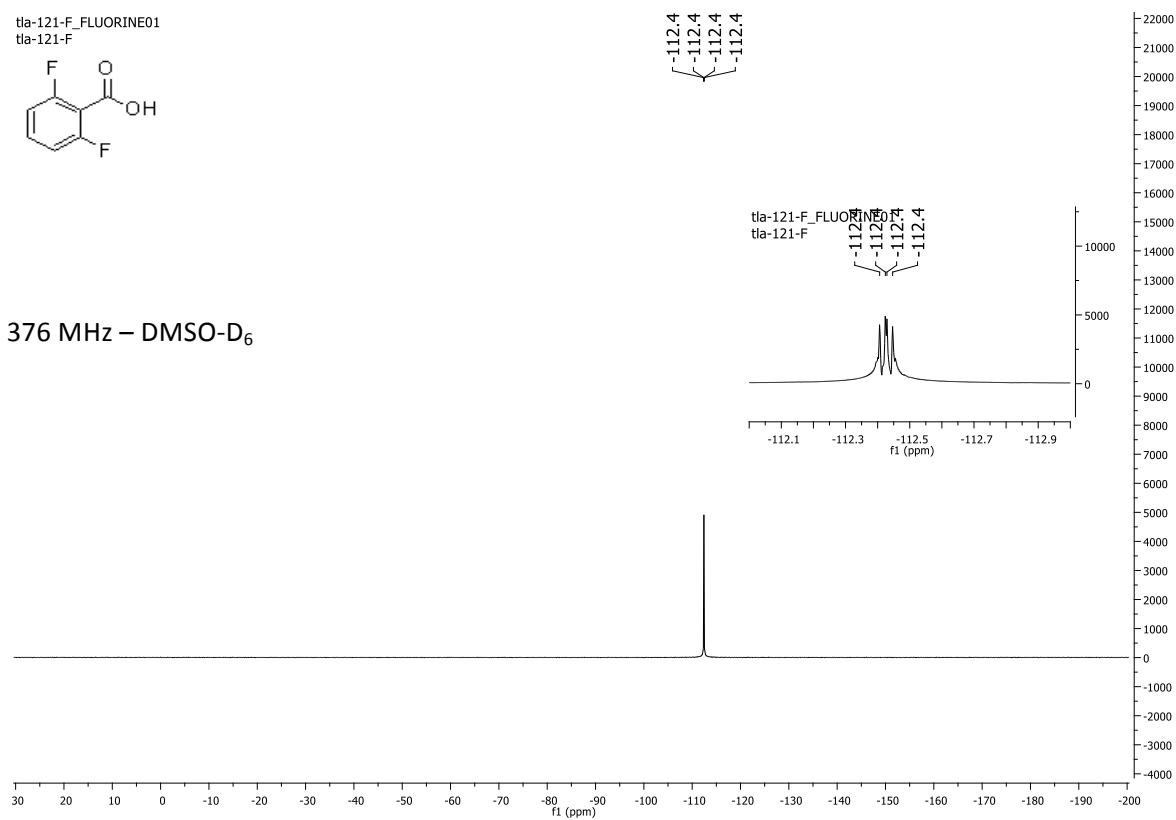




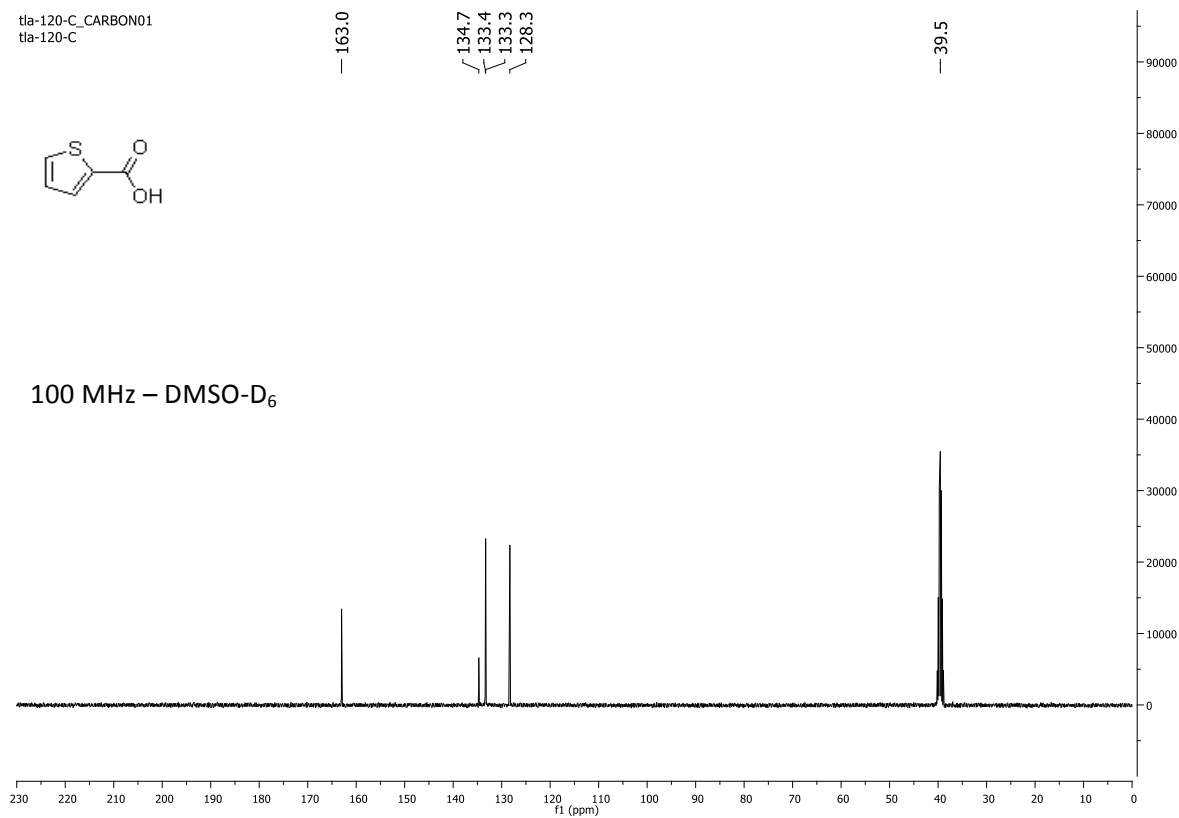
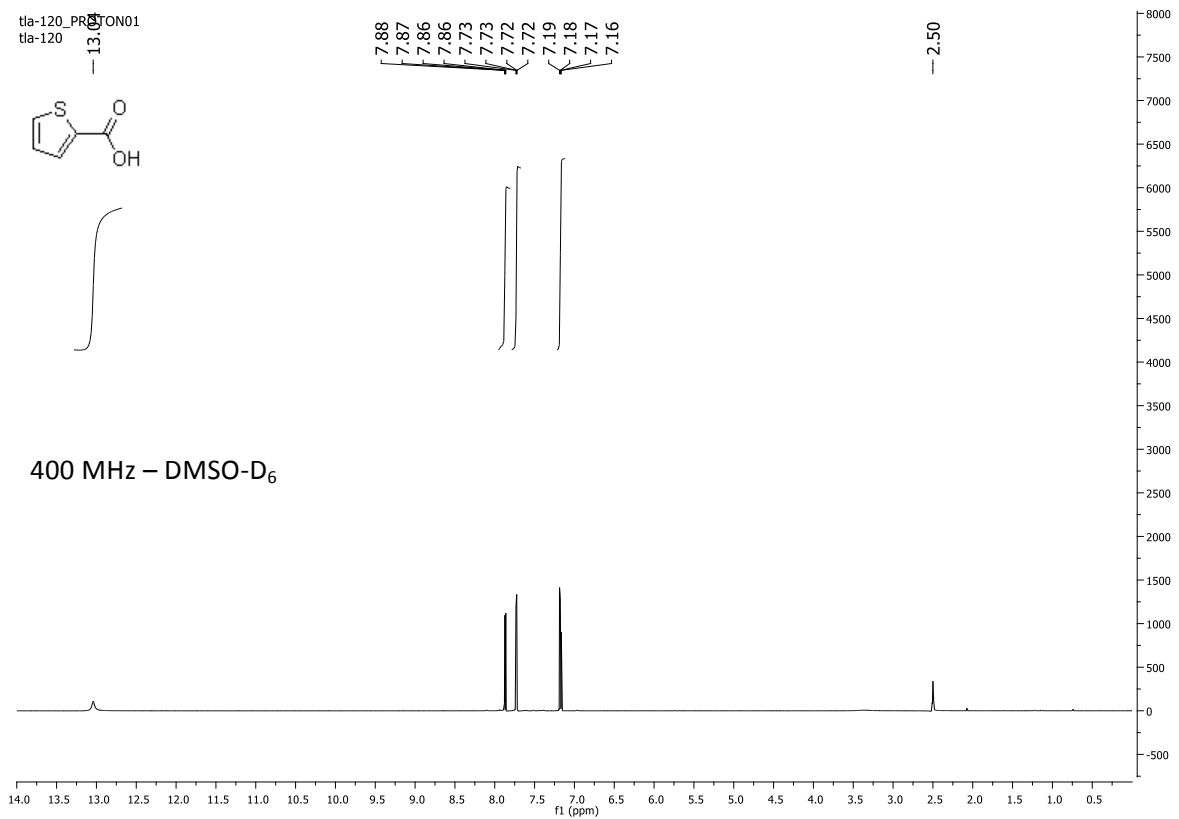
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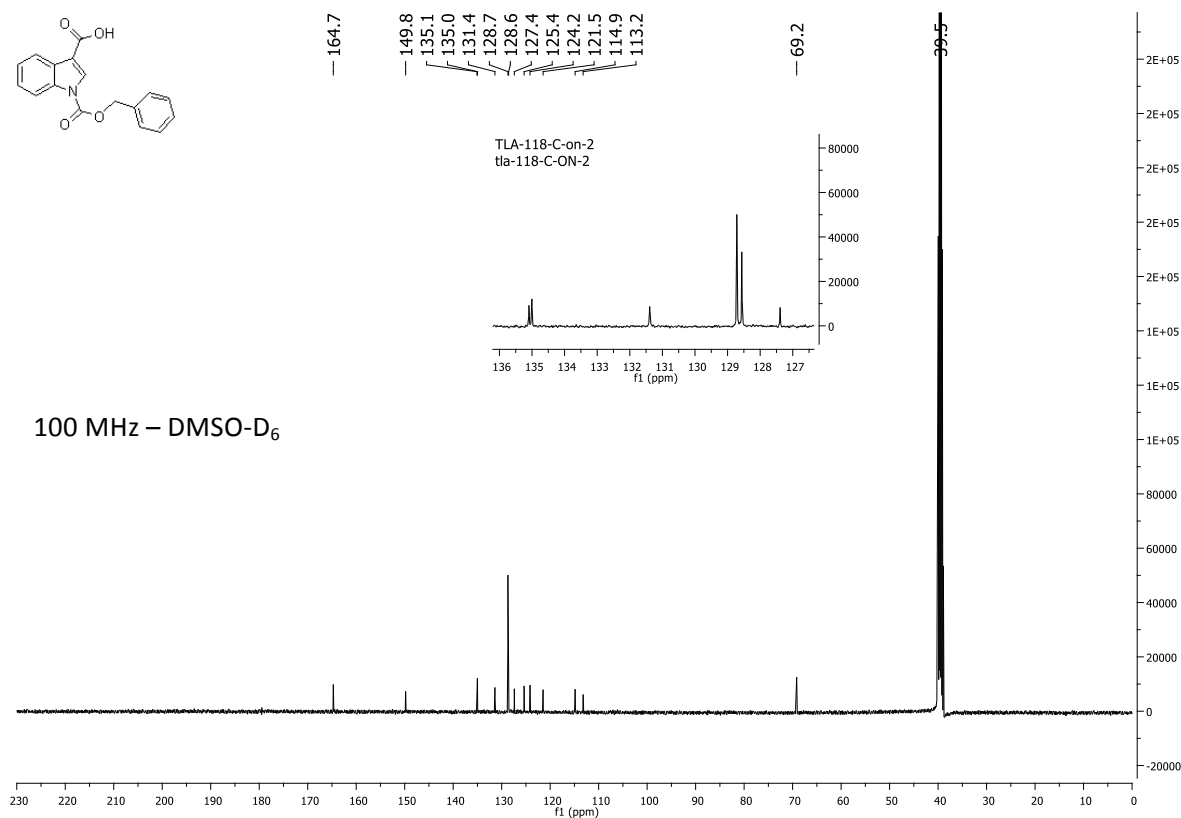
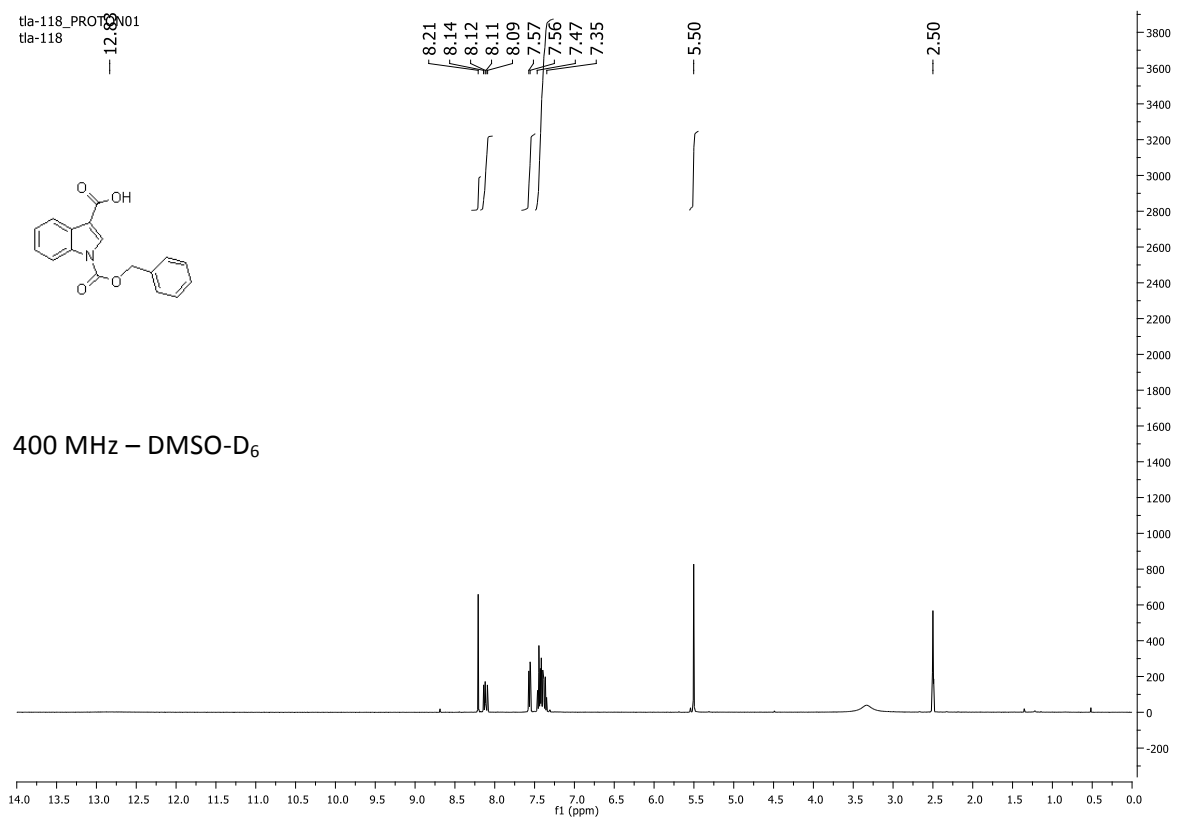
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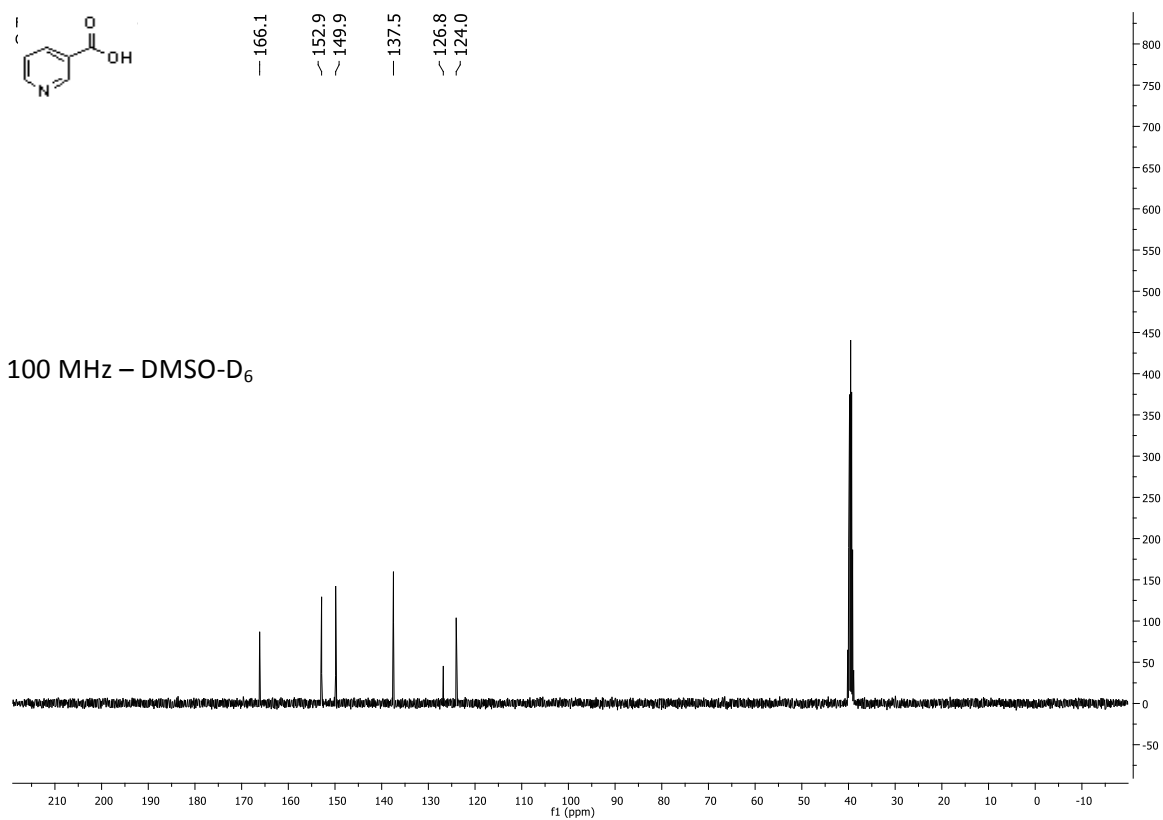
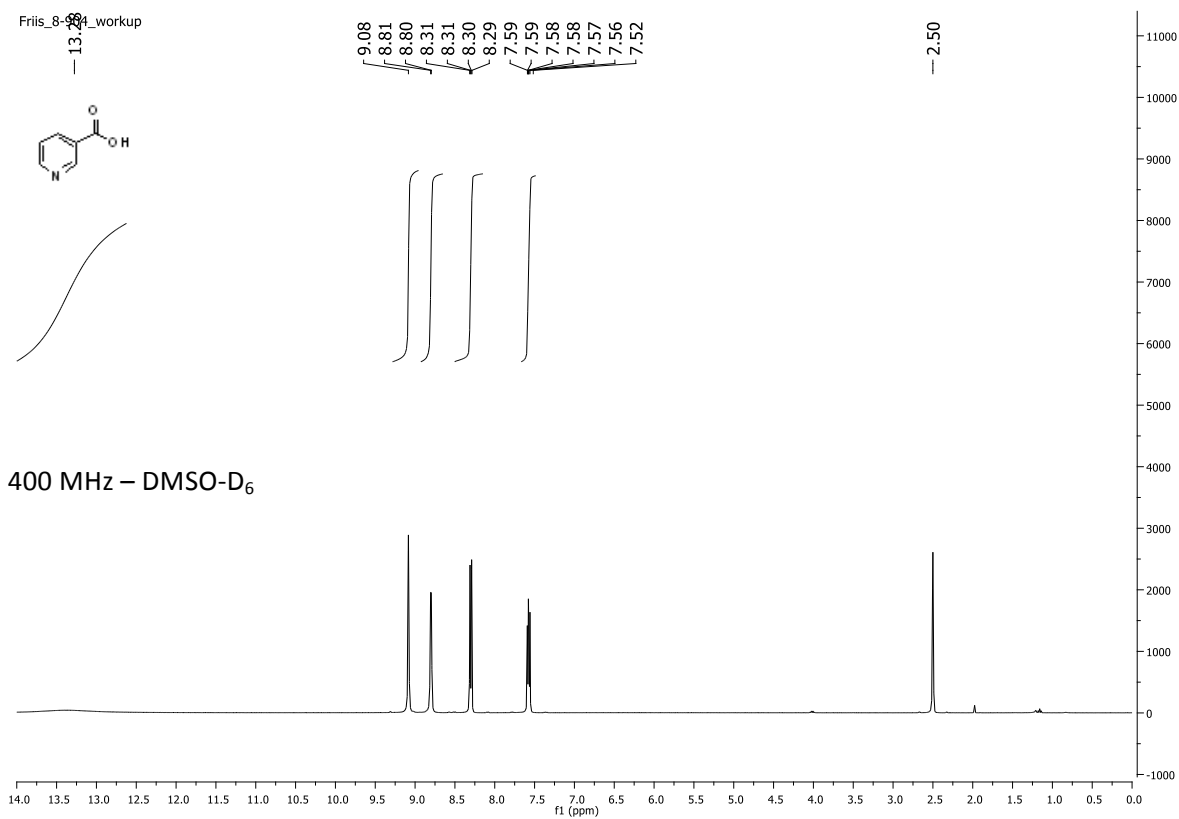
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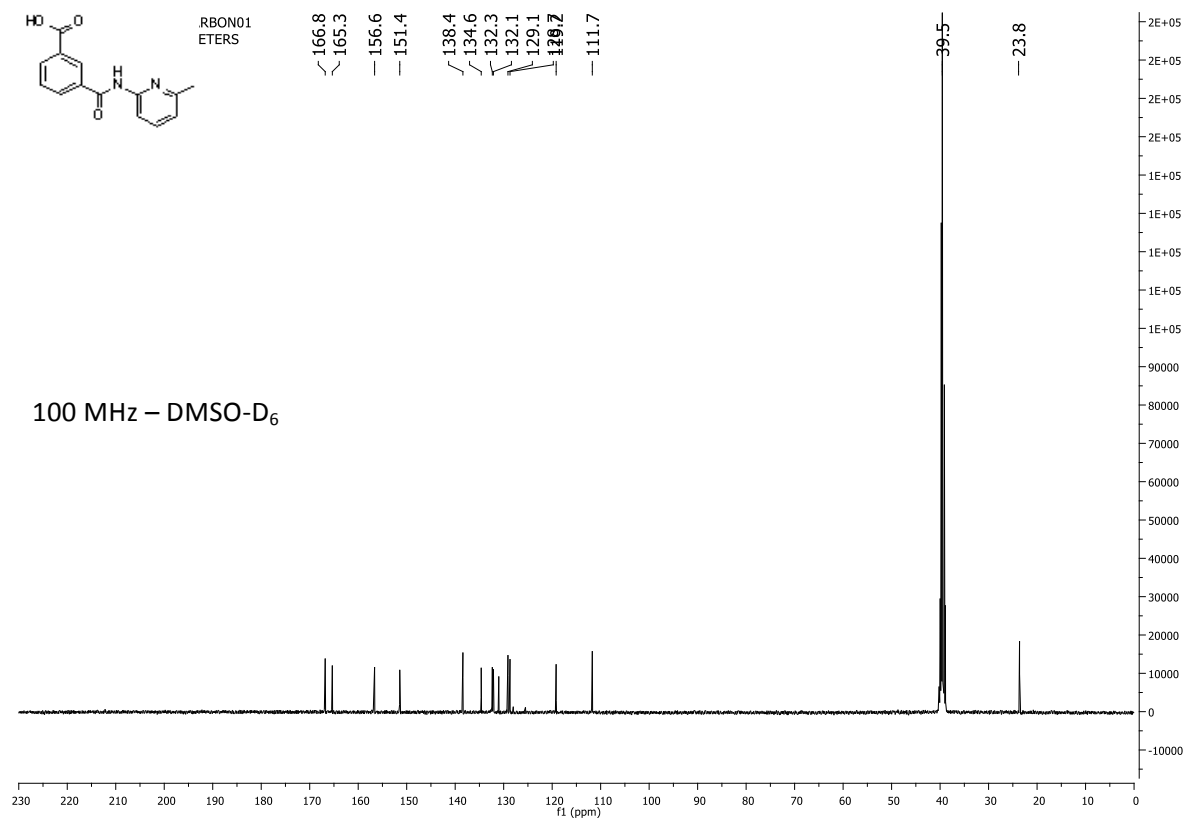
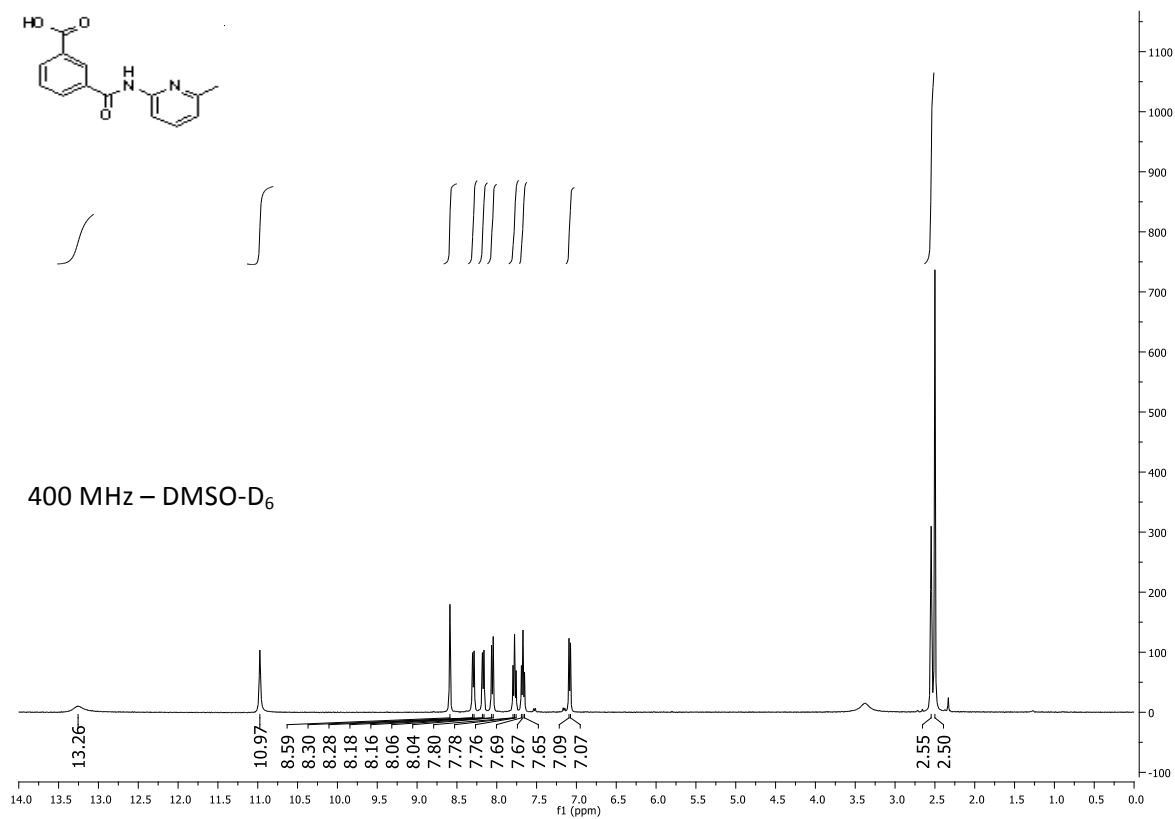
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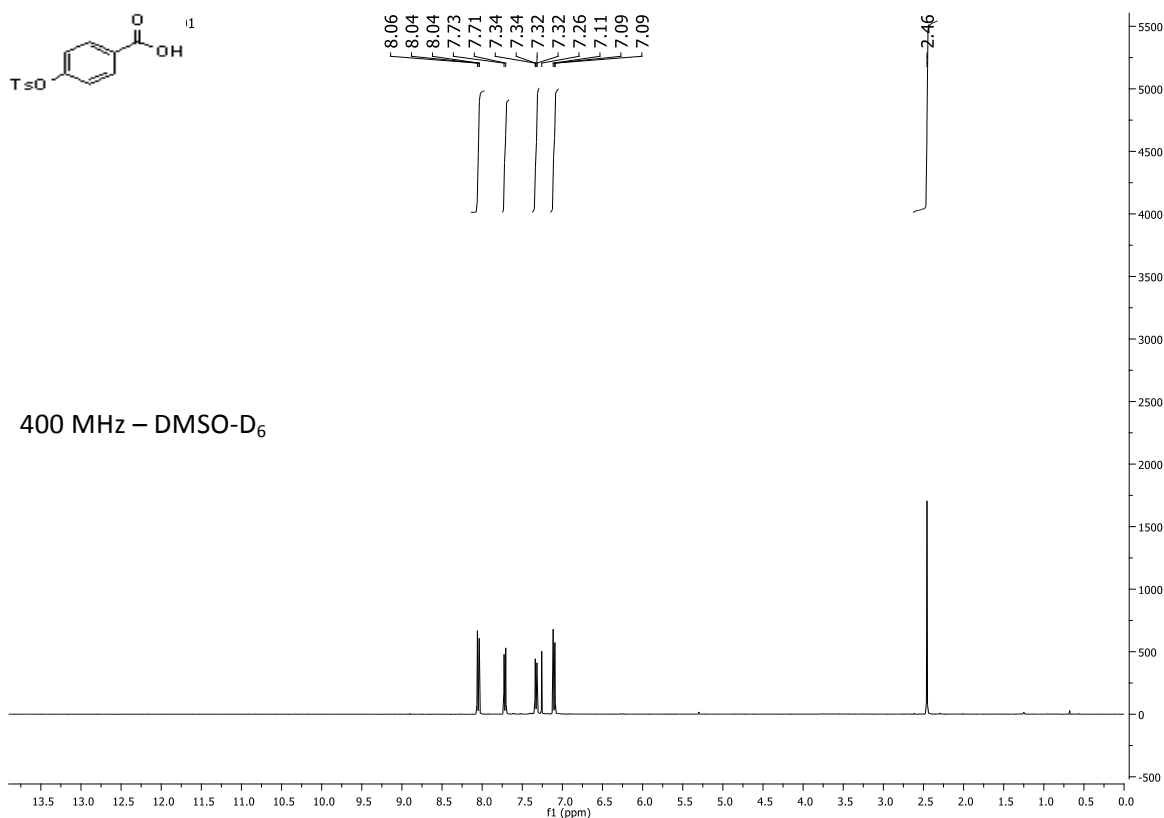
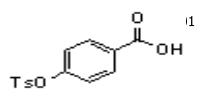
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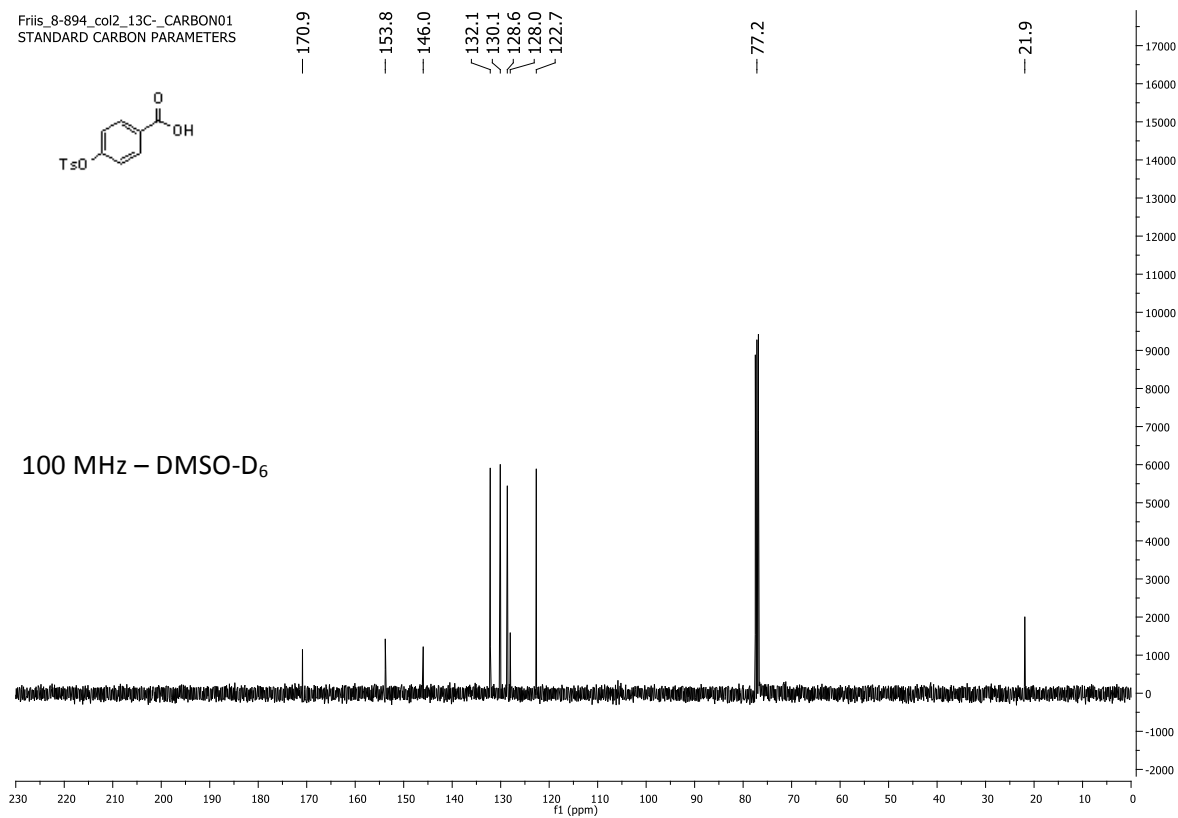
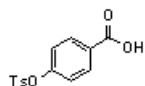
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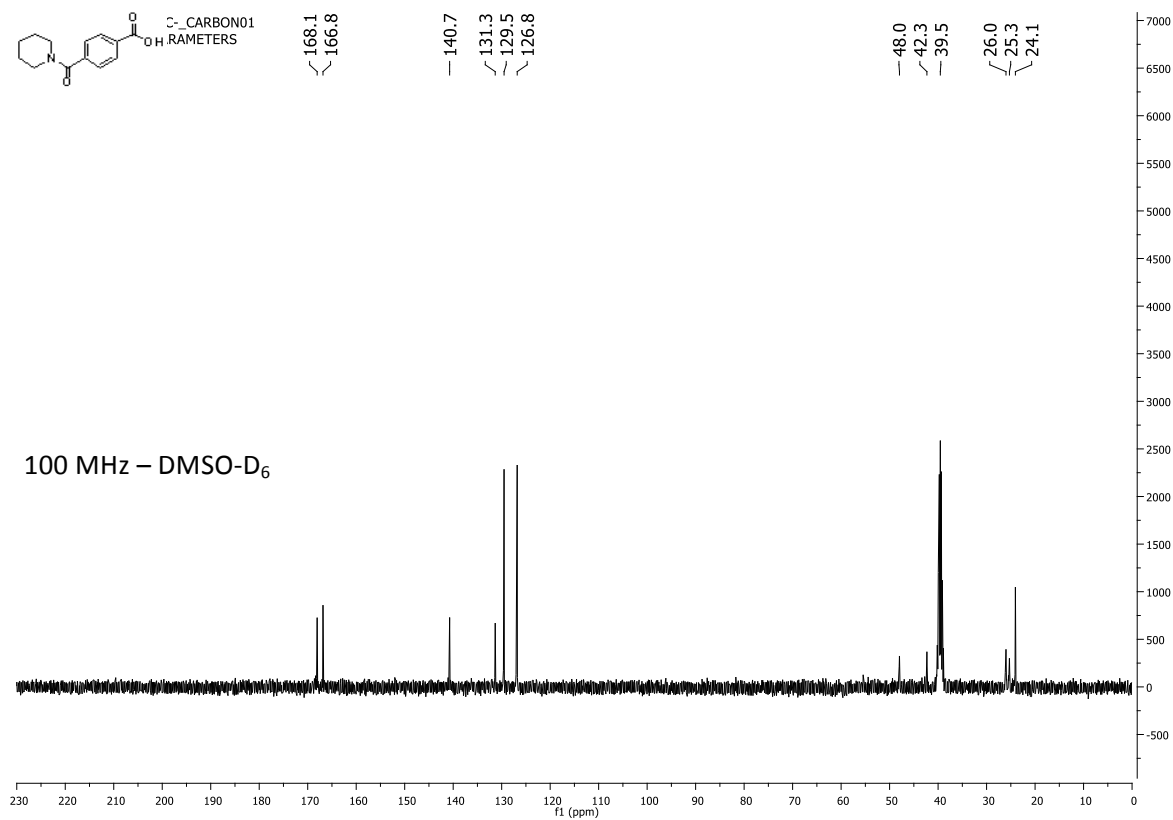
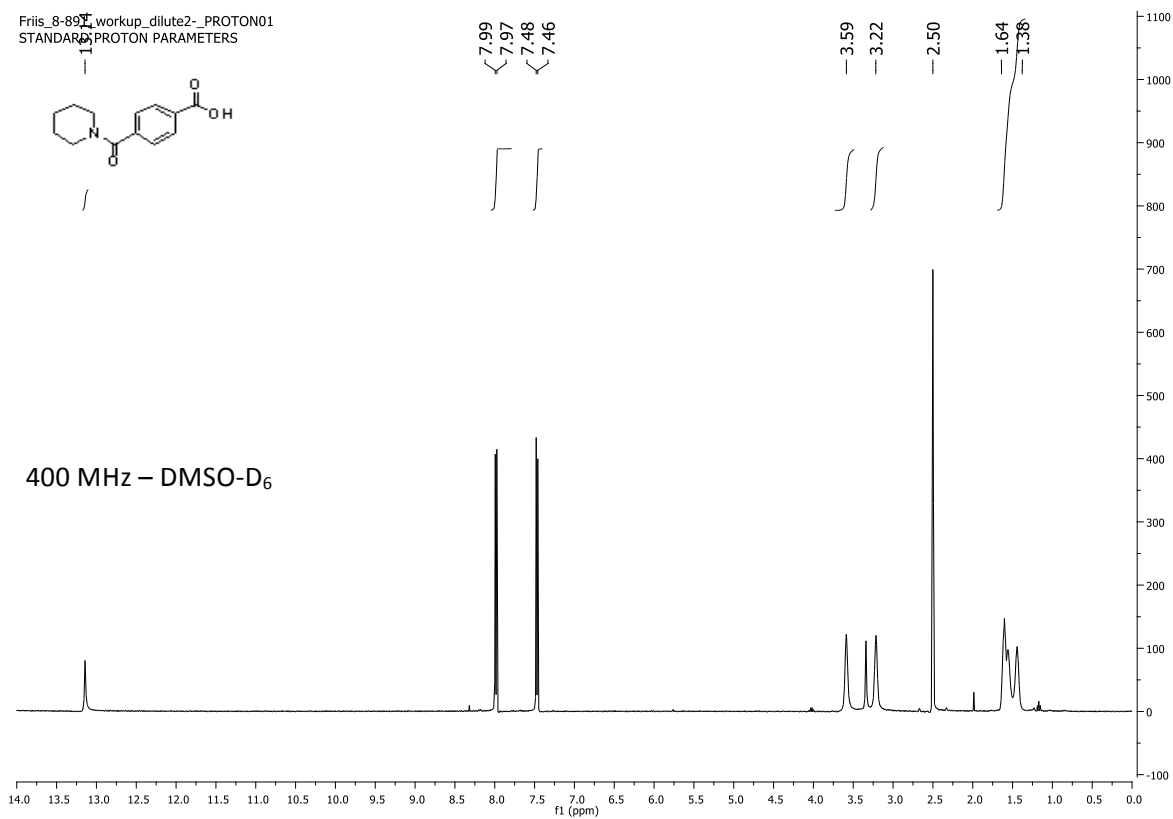
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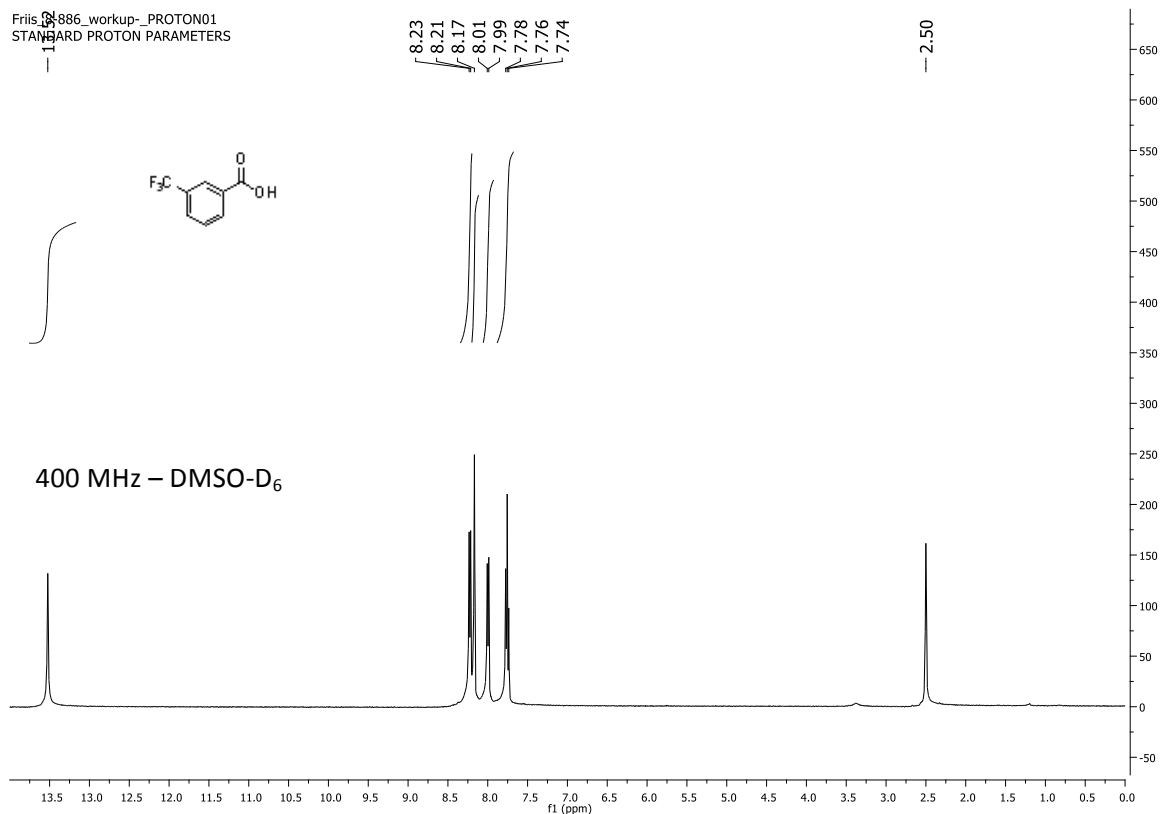


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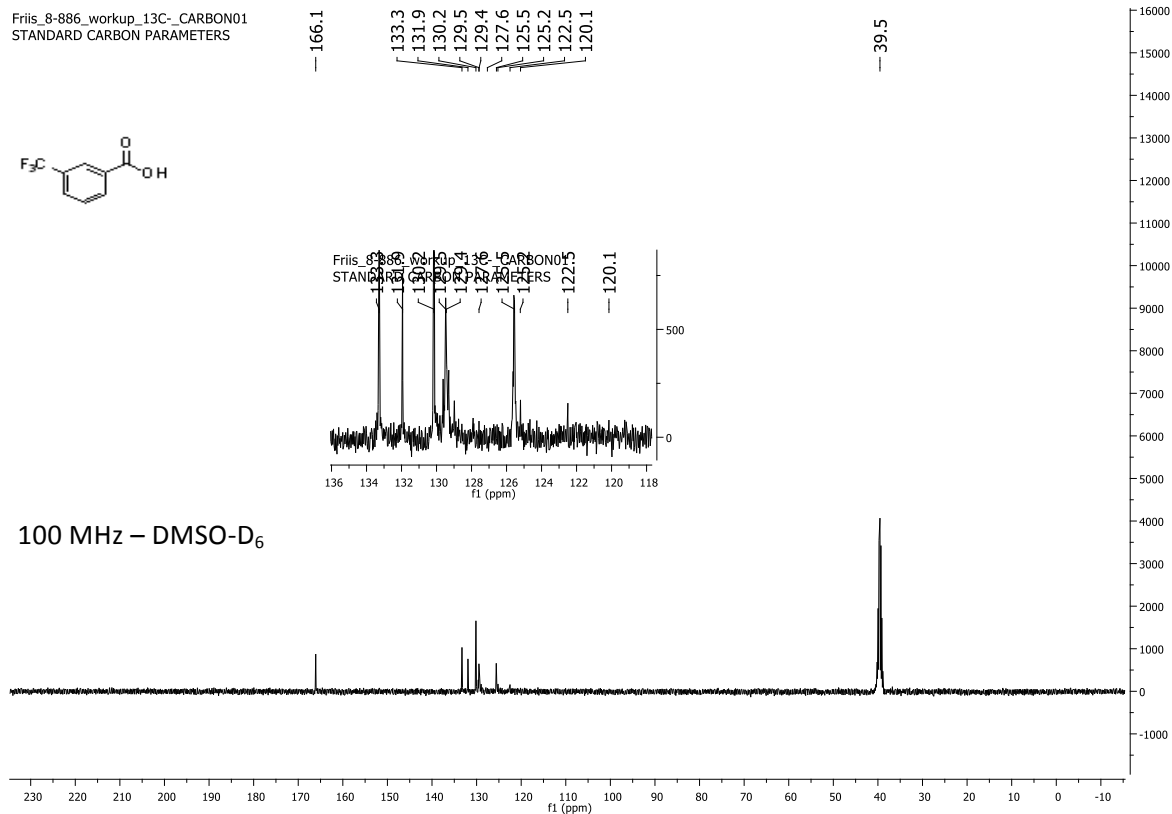


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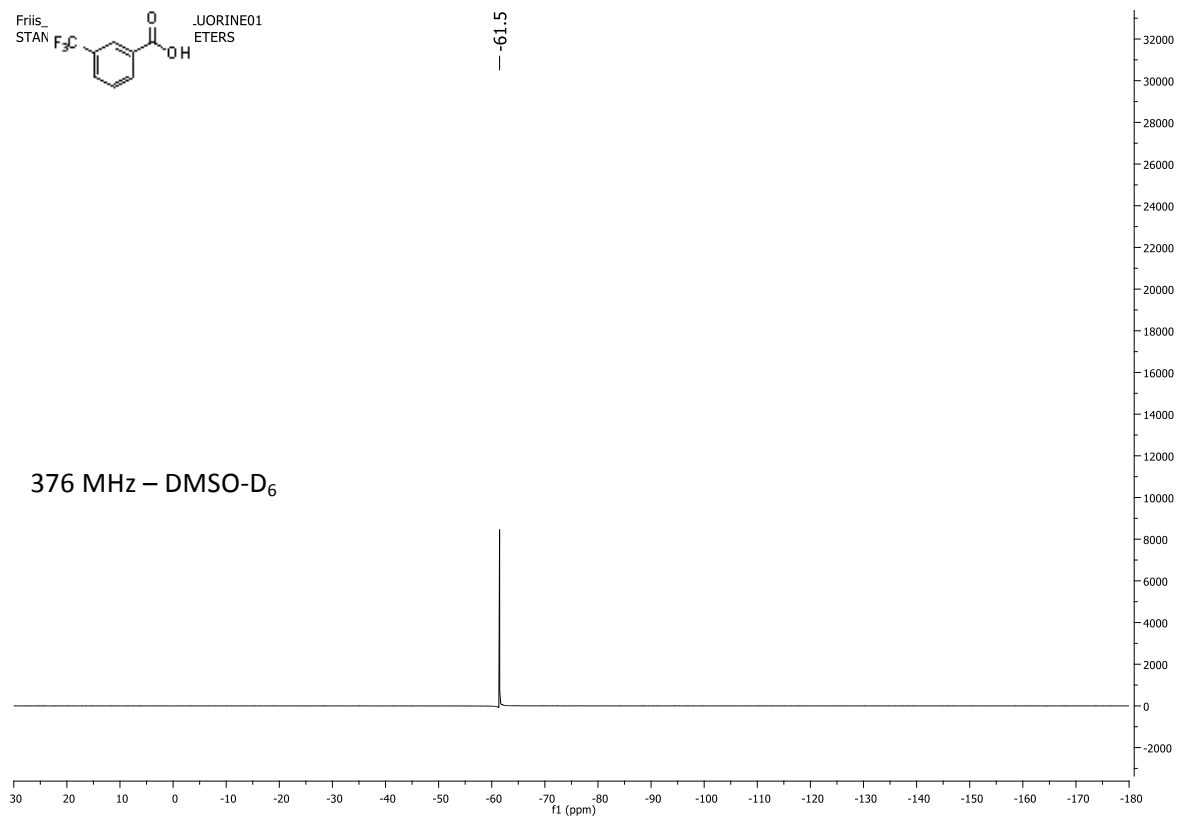
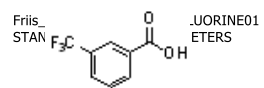
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STANDARD PROTON PARAMETERS



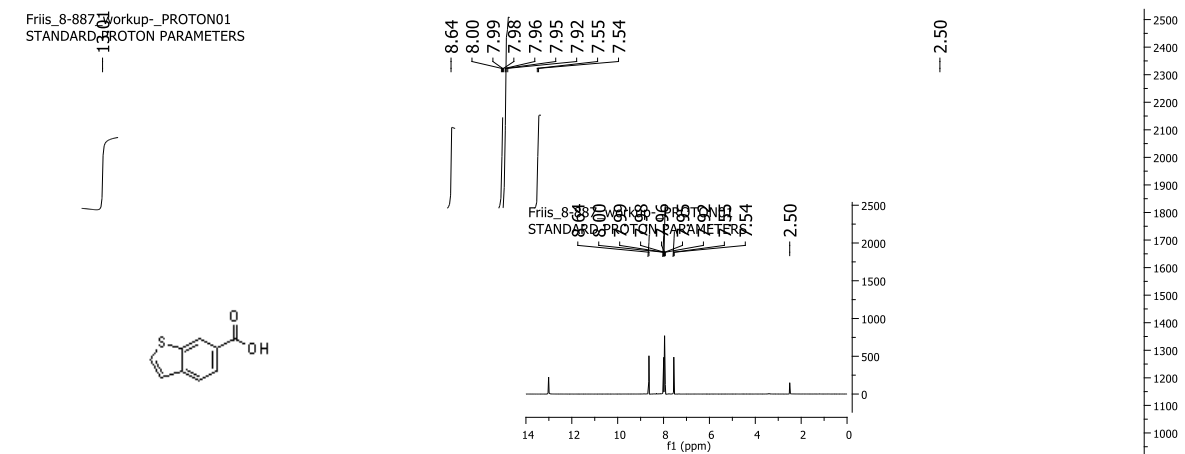
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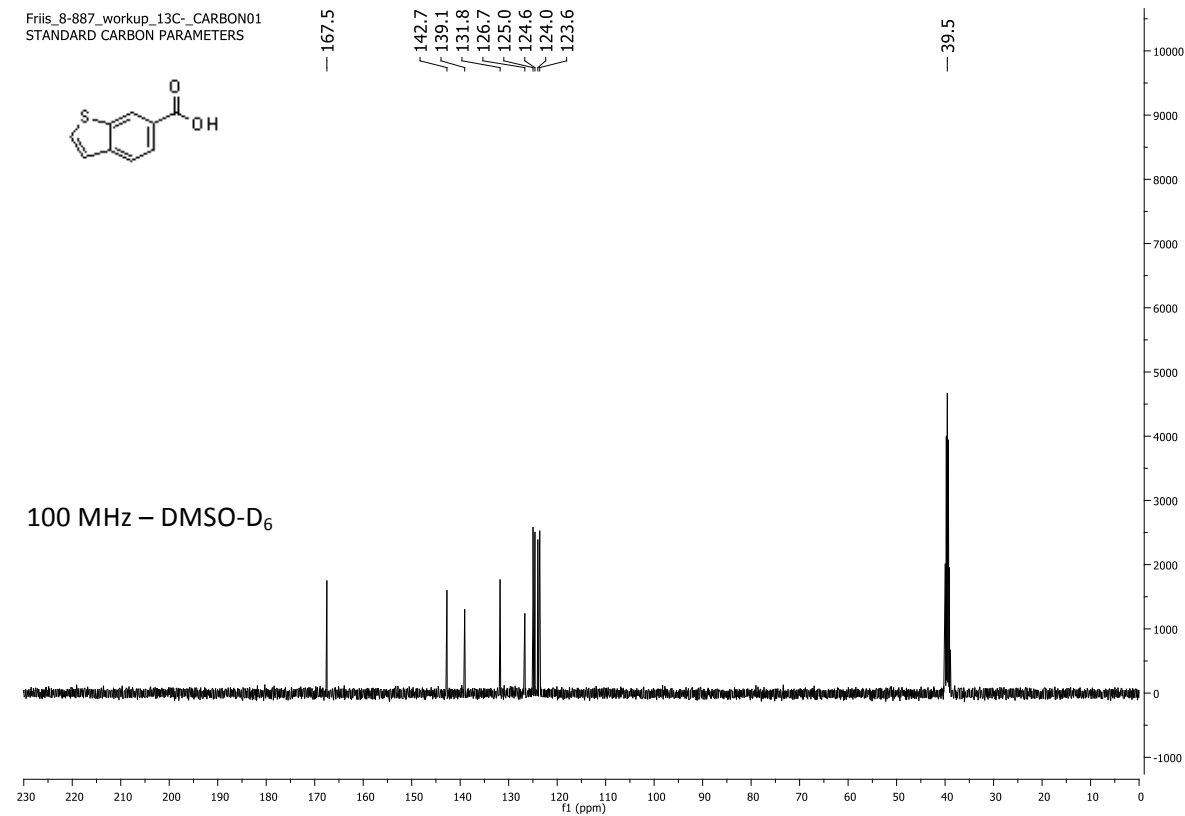
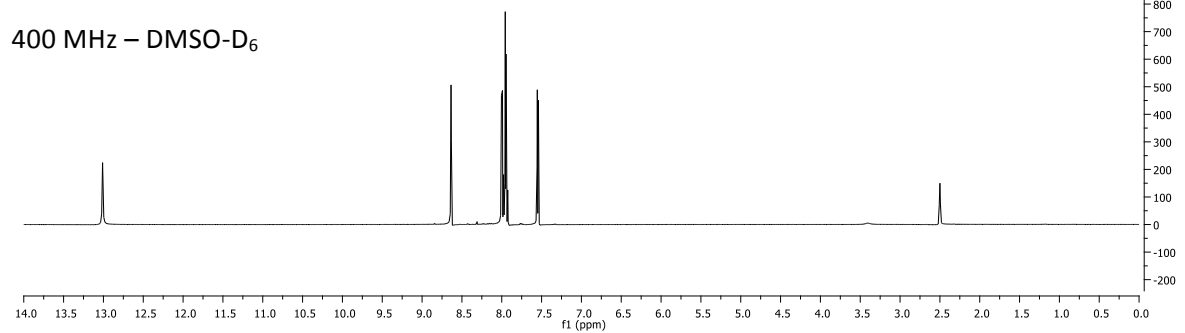




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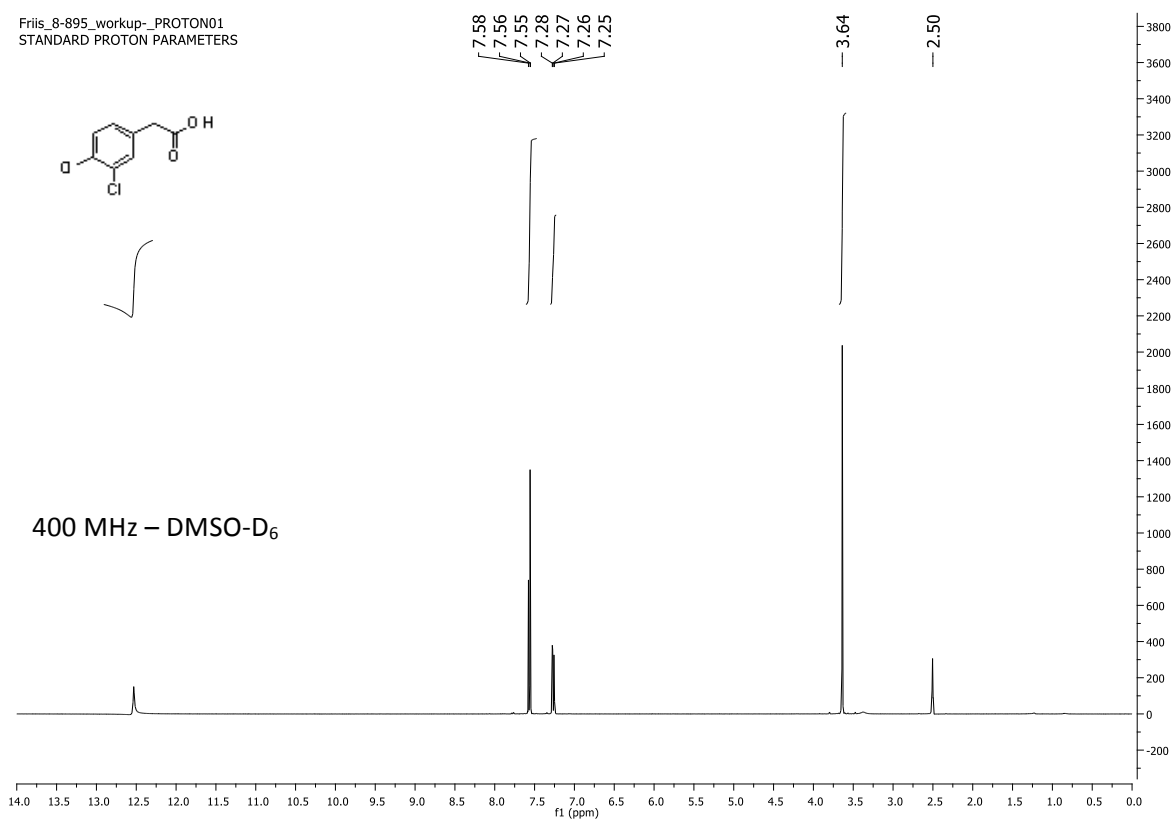
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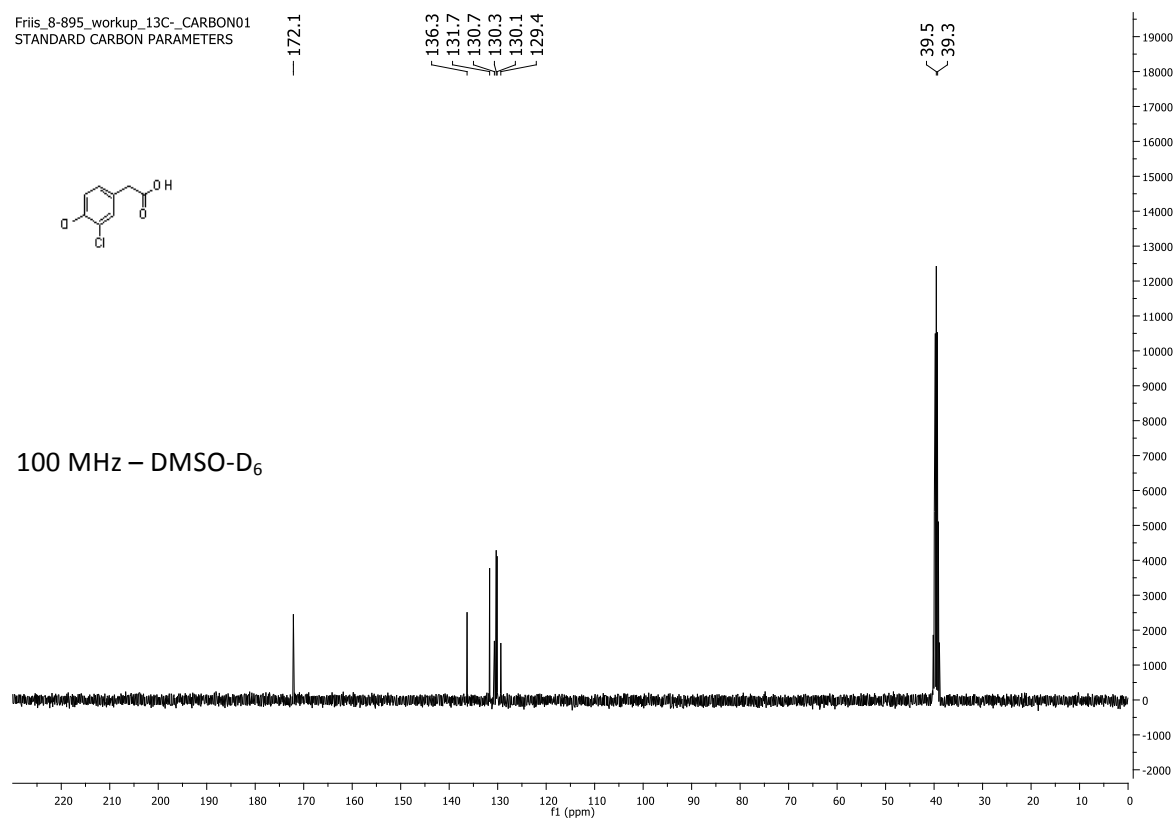
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STANDARD CARBON PARAMETERS



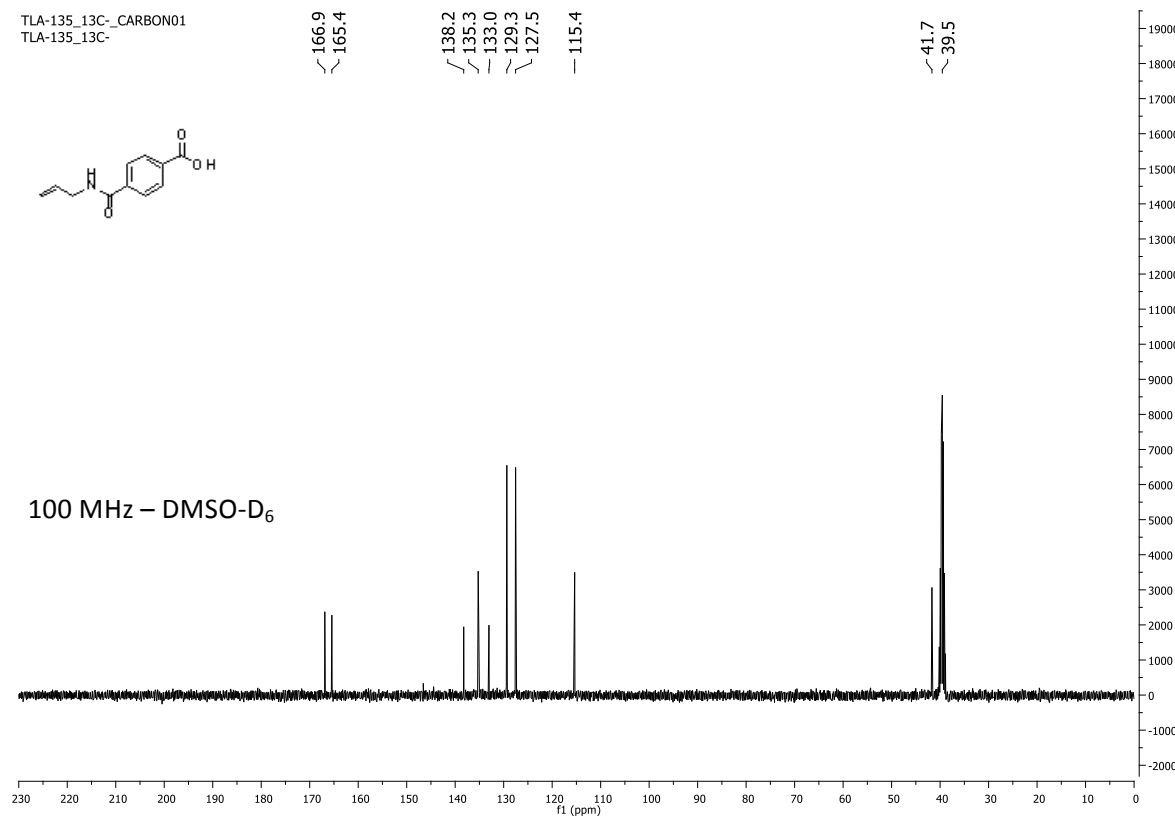
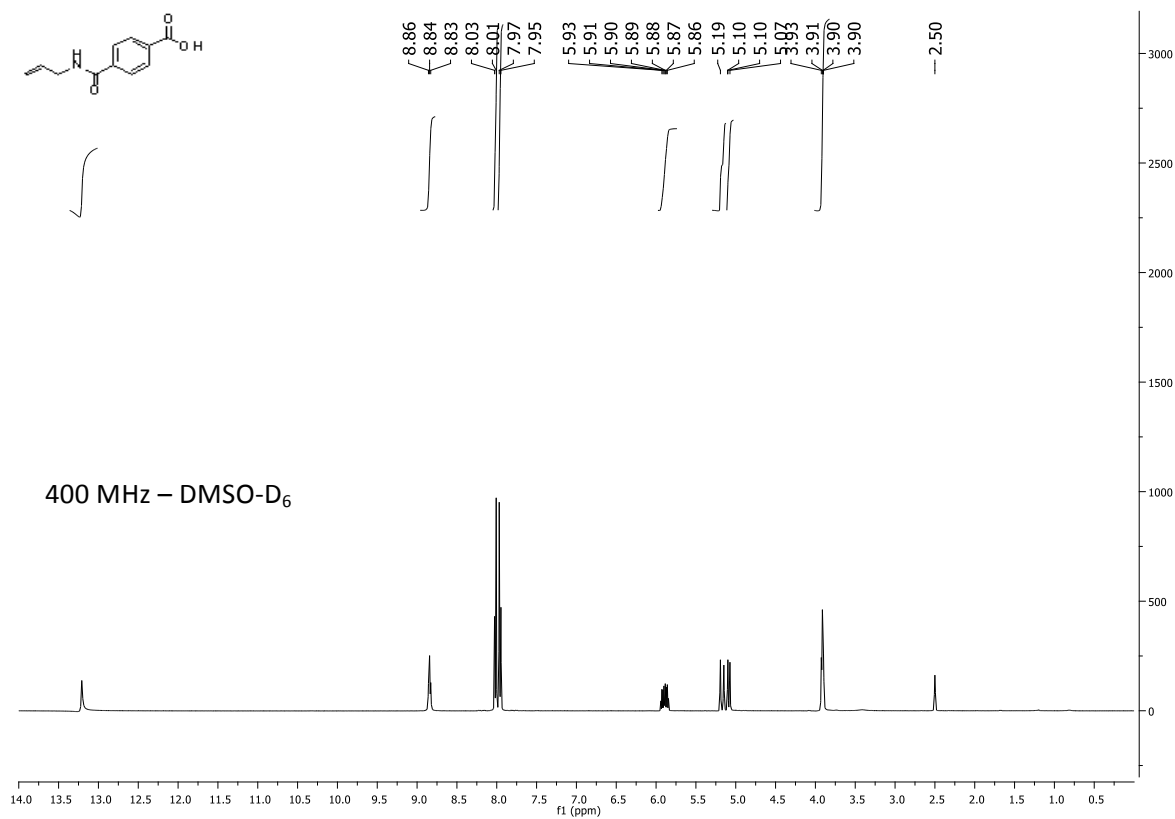
400 MHz – DMSO-D<sub>6</sub>

Chemical structure of terephthalic acid (1,4-benzenedicarboxylic acid) is shown in the top left corner. The spectrum displays the following chemical shifts (ppm) and integration values:

Chemical Shift (ppm)	Integration
8.48	8.17
8.17	8.15
8.15	8.03
8.03	7.94
7.94	7.92
7.92	7.84
7.84	7.82
7.82	7.66
7.66	7.64
7.64	7.62
7.62	7.49
7.49	7.47
7.47	7.45
2.50	— 2.50

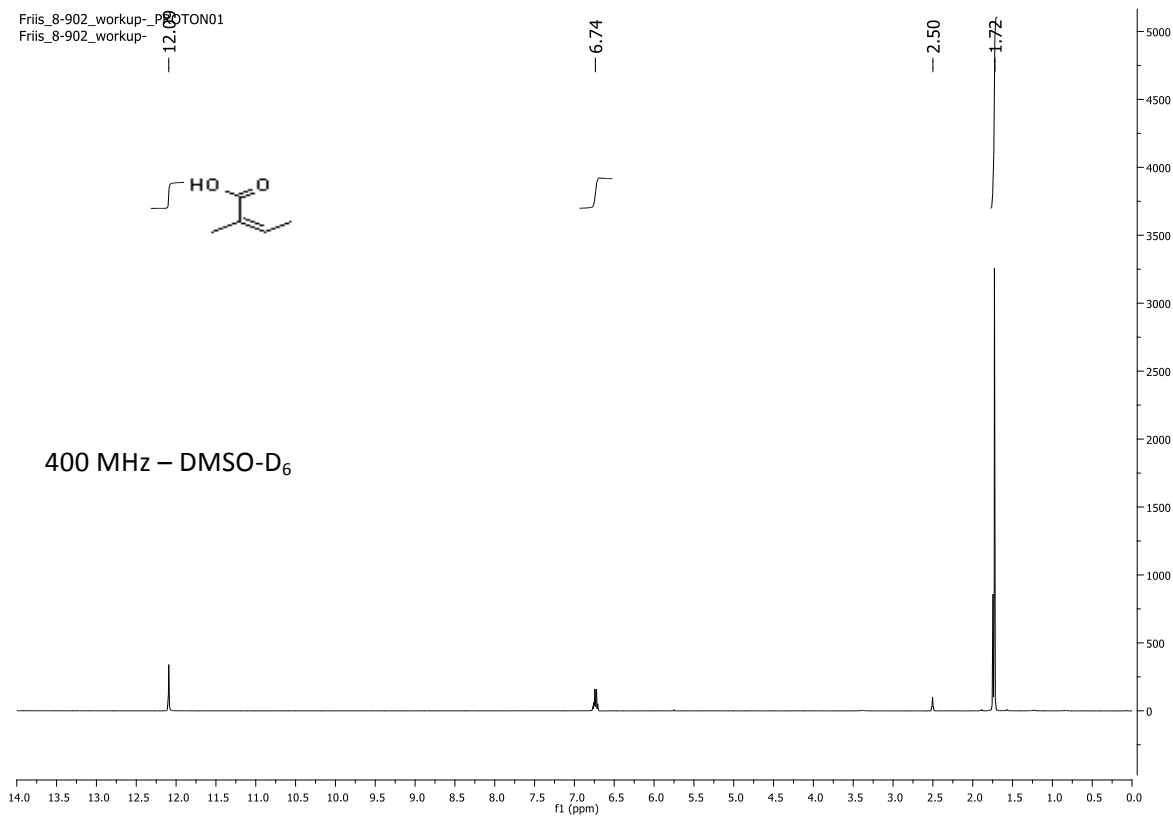
S48

(28)

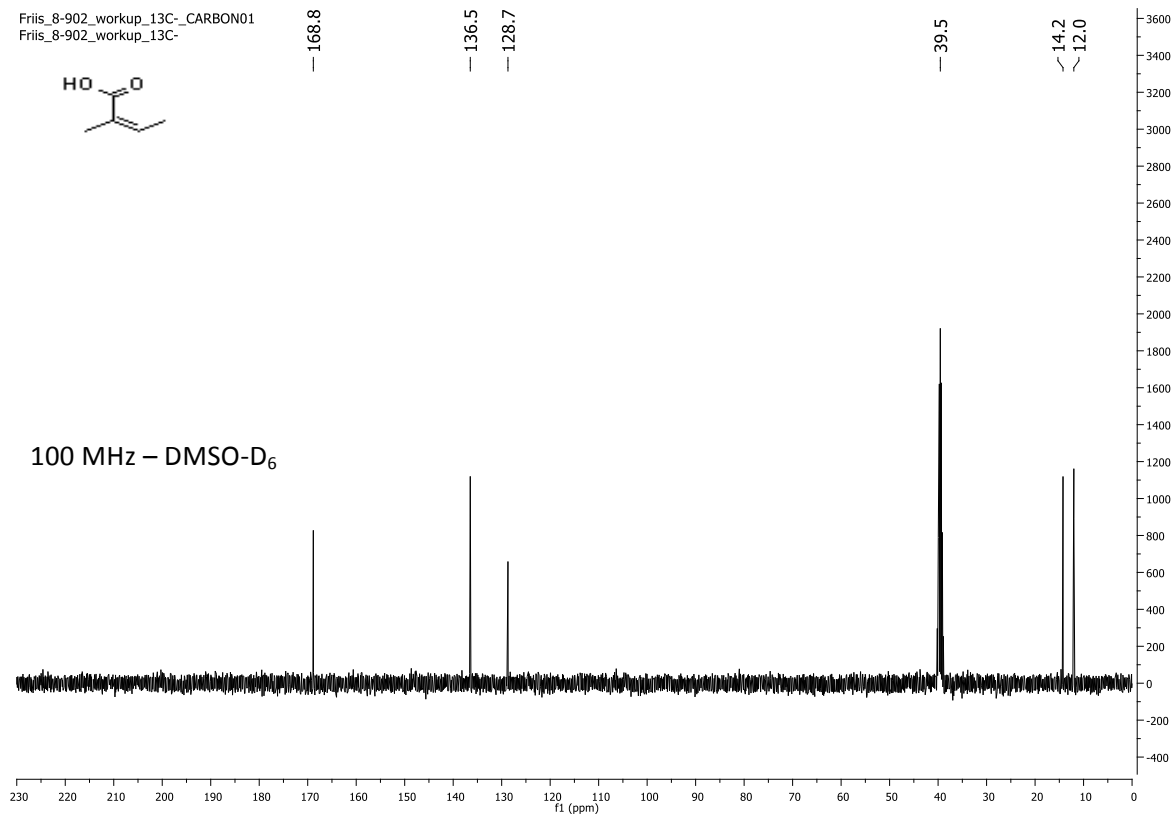


(29)

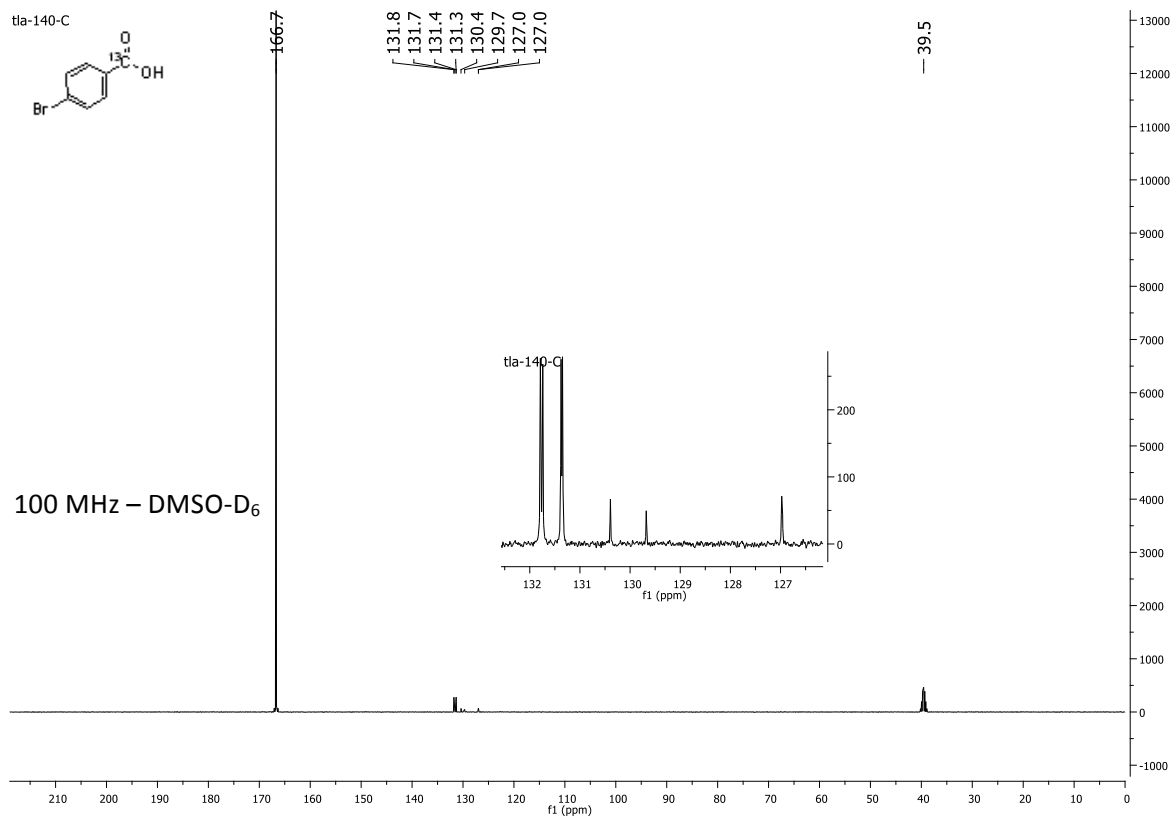
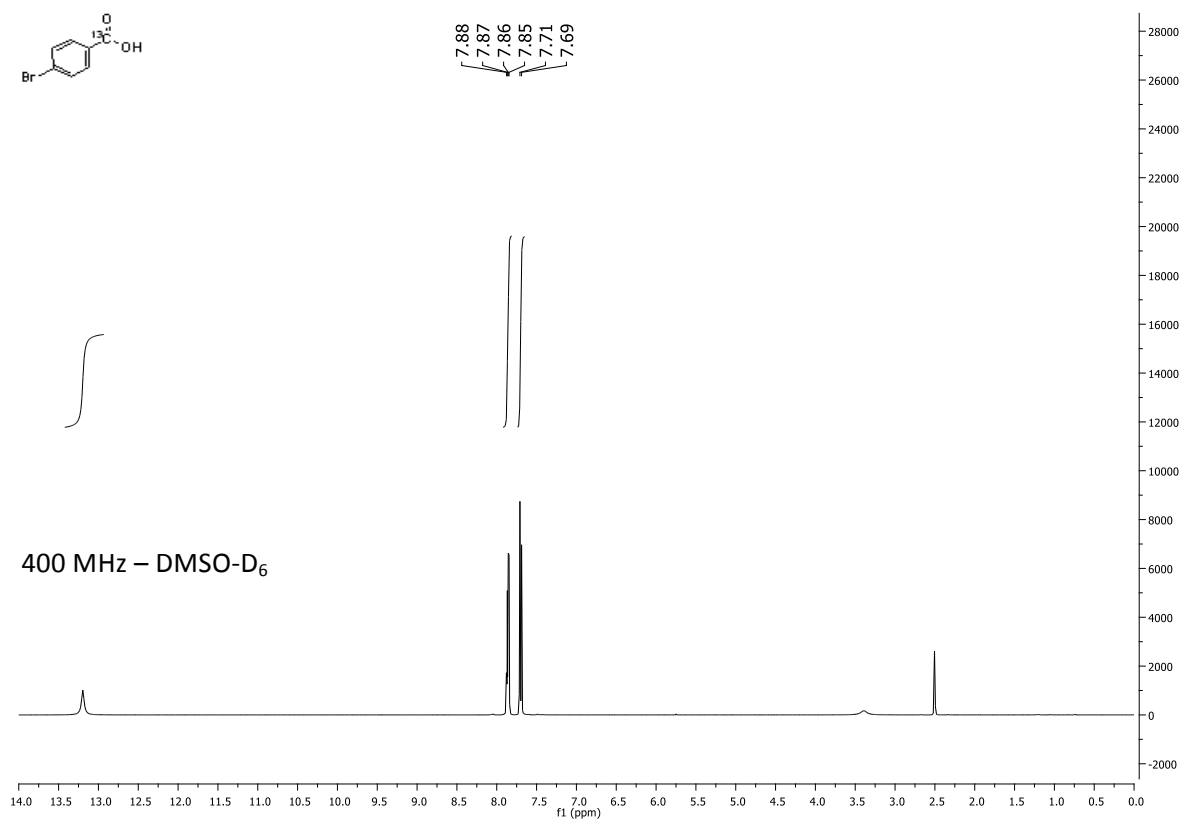
Friis\_8-902\_workup-<sup>1</sup>H-TON01  
Friis\_8-902\_workup-



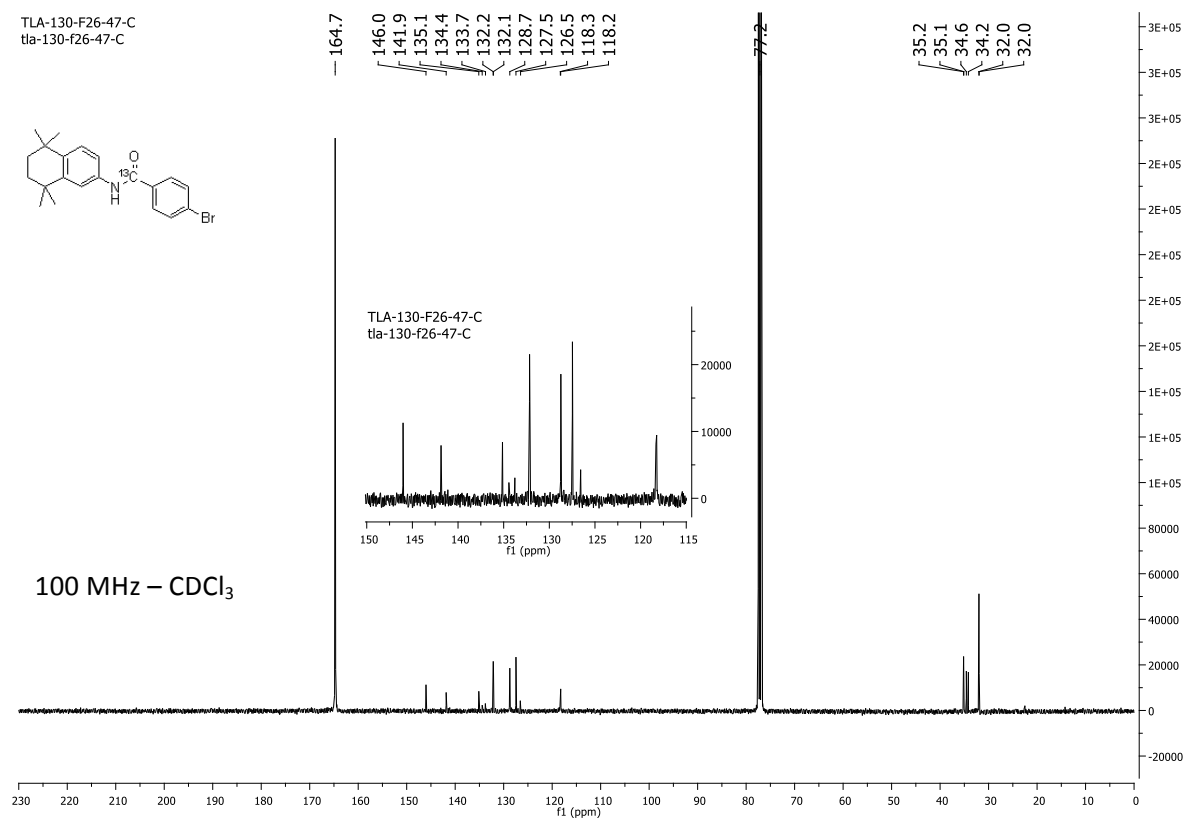
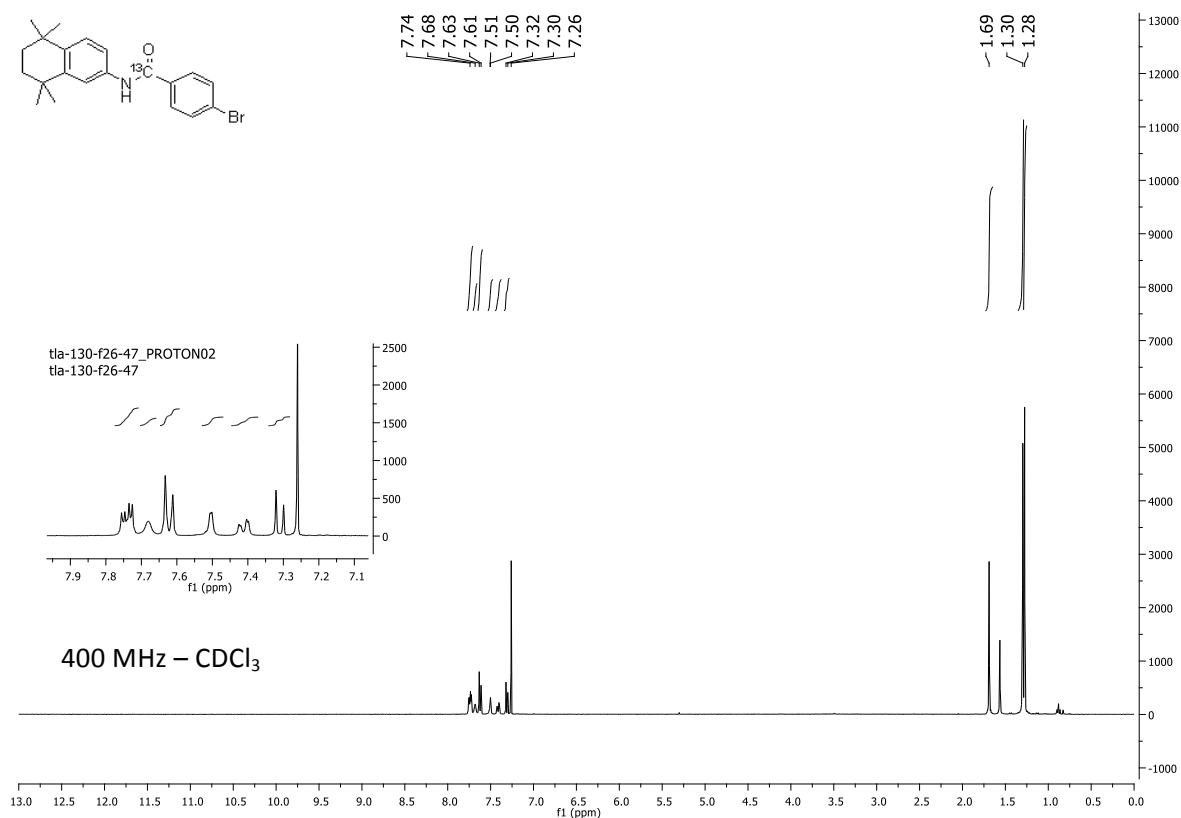
Friis\_8-902\_workup\_13C-CARBON01  
Friis\_8-902\_workup\_13C-



(30)

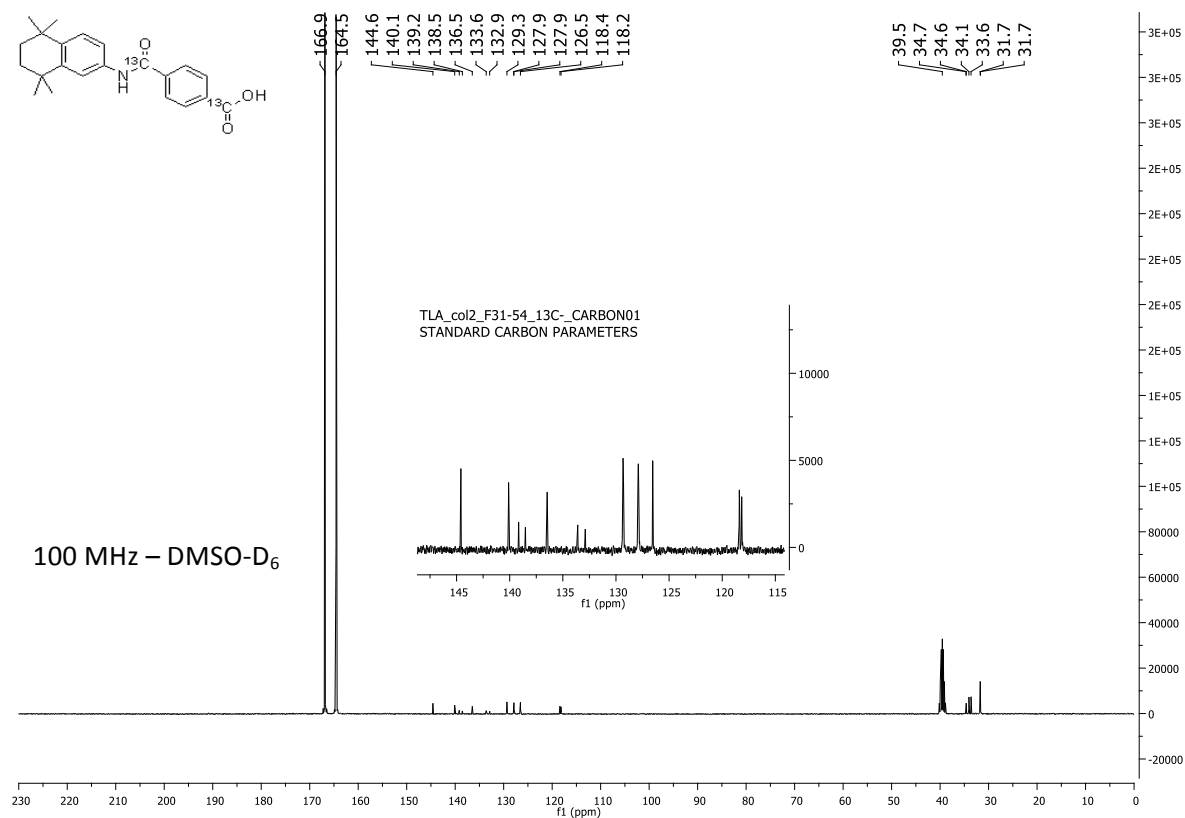
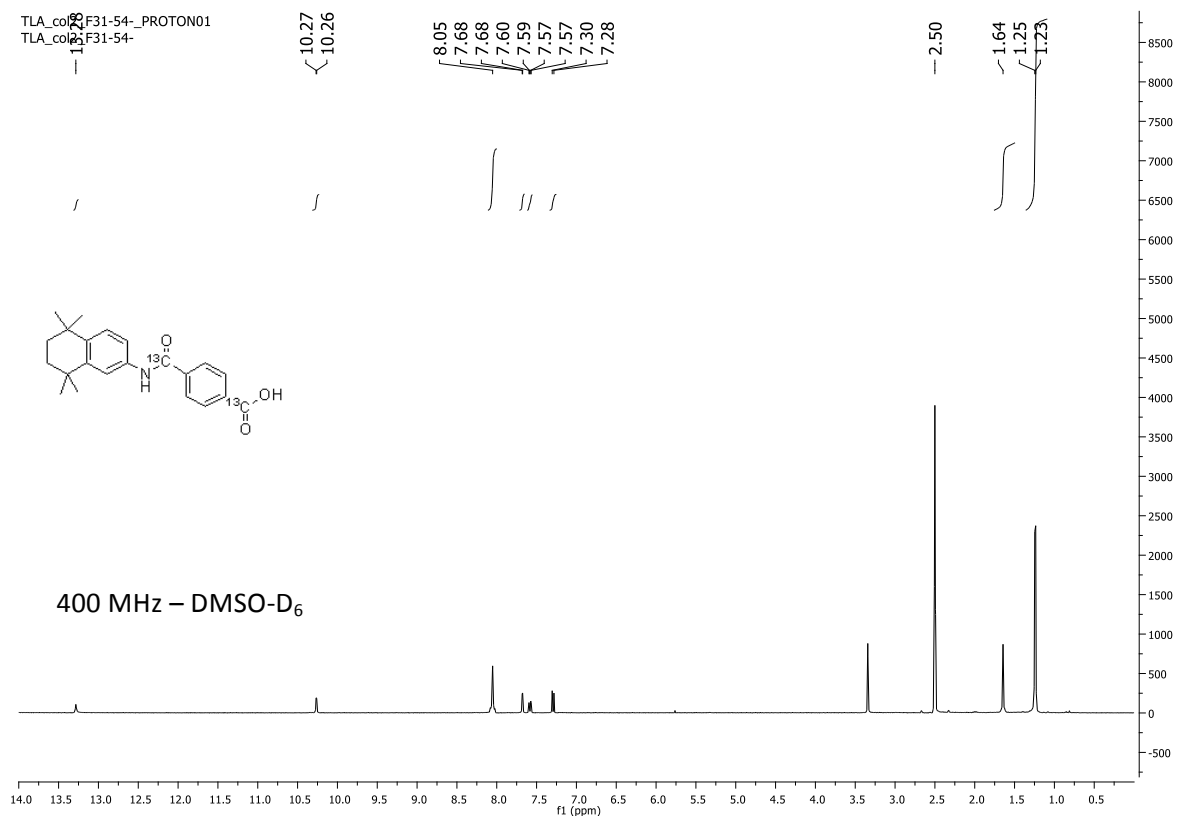


(31)

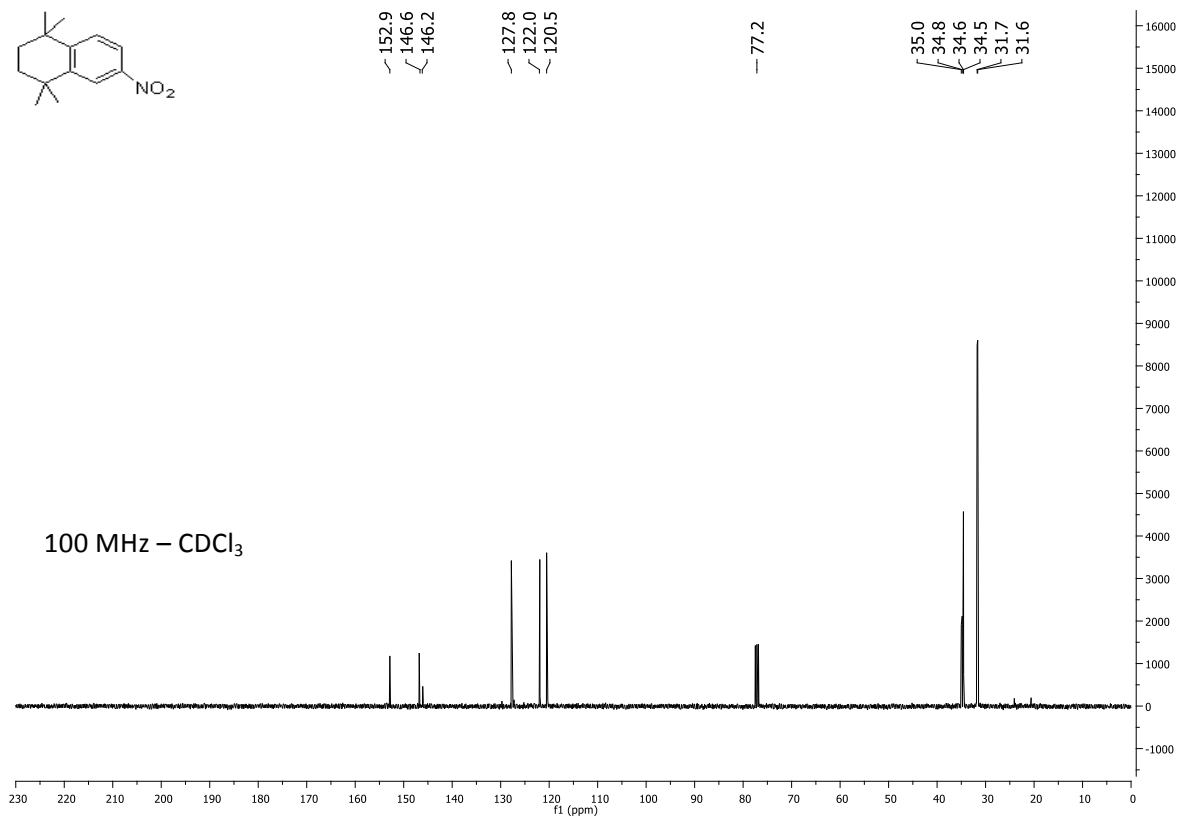
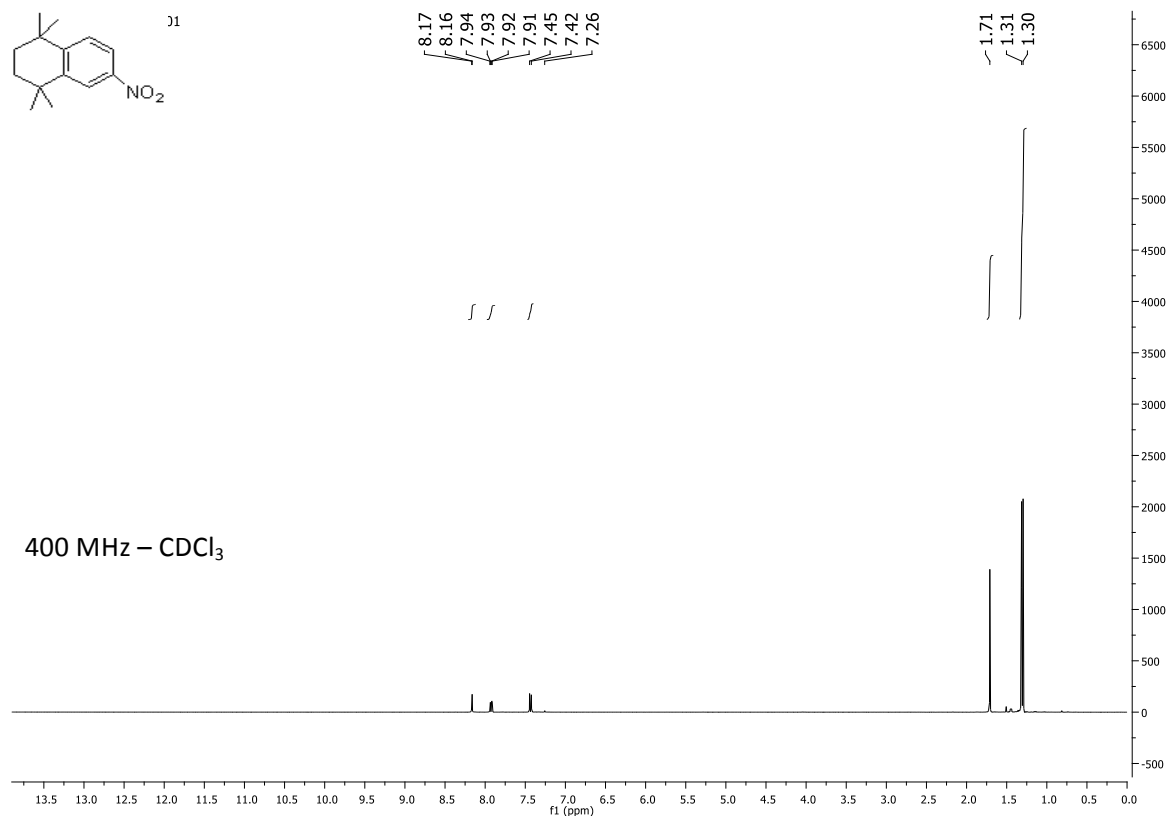




(32)



1,1,4,4-tetramethyl-6-nitro-1,2,3,4-tetrahydronaphthalene



5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-amine

