Supporting Information for
Reductive Cyclizations of Nitroarenes to Hydroxamic Acids by Visible Light Photoredox Catalysis

Megan A. Cismesia, Michael A. Ischay, Tehshik P. Yoon*
Department of Chemistry, University of Wisconsin–Madison, 1101 University Ave, Madison, WI, 53706

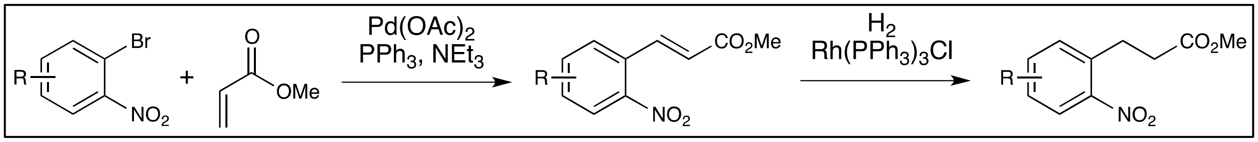
Table of Contents

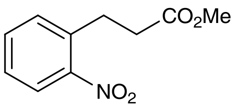
I. Synthesis of Starting Materials S1

II. ^{1}H NMR and ^{13}C NMR Spectra S8

I. Synthesis of Starting Materials

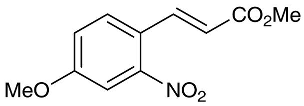
Methyl 2-(2-nitrophenyl)acetate[1] and **2-(2-nitrophenyl)-1-phenylethanone**[2] were prepared from known procedures.





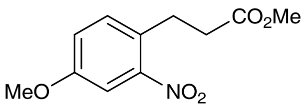
(S1)

Methyl 3-(2-nitrophenyl)propanoate (S1): Prepared using a modification of a procedure reported by Zhu.[3] To an oven-dried 150 mL glass pressure vessel containing a magnetic stirbar was added 945 mg (4.56 mmol) methyl 2-nitrocinnamate[4] and 30 mL degassed 1:1 mixture of THF and *t*-BuOH. H_2 gas was bubbled through the solution and the vessel was charged with 419 mg (0.453 mmol) Wilkinson's catalyst. The vessel was fitted with a regulator and pressurized to 30 psi with H_2 gas. The reaction was allowed to stir for 2 days before being passed through a silica plug. Purification by column chromatography (20:1 hexanes:ethyl acetate) yielded 758 mg (3.62 mmol, 79%) of a yellow oil. All spectra data were consistent with reported values.[3]



(S2)

(*E*)-Methyl 3-(4-methoxy-2-nitrophenyl)acrylate (S2): An oven-dried Schlenk flask with magnetic stirbar was charged with 252 mg (1.08 mmol) 4-bromo-3-nitroanisole, 0.20 mL (2.2 mmol) methyl acrylate, 5.3 mg (0.024 mmol) $Pd(OAc)_2$, 11.2 mg (0.0427 mmol) triphenylphosphine, and 0.40 mL (2.9 mmol) triethylamine. The reaction was sealed under N_2 and heated gradually to 125 °C for 5 h. An additional portion of $Pd(OAc)_2$ was added and the reaction was heated to 125 °C for an additional 1 h before being cooled to room temperature and passed through a silica plug. Purification by column chromatography (5:1 hexanes:ethyl acetate) yielded 189 mg (0.80 mmol, 73%) of a yellow solid. All spectra data were consistent with reported values.[5]



(S3)

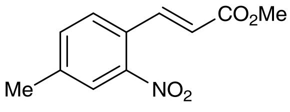
Methyl 3-(4-methoxy-2-nitrophenyl)propanoate (S3): An oven-dried 150 mL glass pressure vessel containing a magnetic stirbar was charged with 500 mg (2.11 mmol) **S2** and 15 mL degassed 1:1 mixture of THF and *t*-BuOH. H_2 gas was bubbled through the solution and the vessel was charged with 154 mg (0.166 mmol) Wilkinson's catalyst. The vessel was fitted with a regulator and pressurized to 30 psi with H_2 gas. The reaction was allowed to stir for 6 days before being passed through a silica plug. Purification by column chromatography (8:1 hexanes:ethyl acetate) yielded 490 mg (2.05 mmol, 97%) of a brown oil.

IR (thin film, NaCl): 2952, 2842, 1735, 1531 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, J = 2.8 Hz, 1H), 7.30 (d, J = 8.5 Hz, 1H), 7.09 (dd, J = 8.5, 2.8 Hz, 1H), 3.85 (s, 3H), 3.67 (s, 3H), 3.15 (t, J = 7.5 Hz, 2H), 2.69 (t, J = 7.5 Hz, 2H).

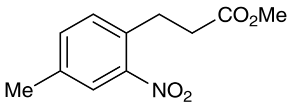
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 158.5, 149.5, 133.0, 127.5, 120.0, 109.4, 55.8, 51.7, 34.8, 27.8.

HRMS (ESI) calc'd for $[C_{11}H_{13}NO_5+NH_4]^+$ requires *m/z* 257.1132, found *m/z* 257.1125.



(S4)

(*E*)-Methyl 3-(4-methyl-2-nitrophenyl)acrylate (S4): An oven-dried Schlenk flask with magnetic stirbar was charged with 496 mg (2.06 mmol) 4-bromo-3-nitrotoluene (90%), 0.40 mL (4.4 mmol) methyl acrylate, 10.8 mg (0.0481 mmol) $Pd(OAc)_2$, 23.3 mg (0.0888 mmol) triphenylphosphine, and 1.0 mL (7.2 mmol) triethylamine. The reaction was sealed under N_2 and heated gradually to 125 °C for 6 h before cooled to room temperature and passed through a silica plug. Purification by column chromatography (9:1 hexanes:ethyl acetate) yielded 308 mg (1.4 mmol, 68%) of a yellow solid. All spectra data were consistent with reported values.[5]



(S5)

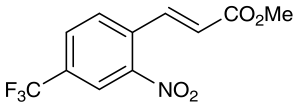
Methyl 3-(4-methyl-2-nitrophenyl)propanoate (S5): To an oven-dried 150 mL glass pressure vessel containing a magnetic stirbar was added 327 mg (1.48 mmol) **S4** and 10 mL degassed 1:1 mixture of THF and *t*-BuOH. H_2 gas was bubbled through the solution and the vessel was charged with 114 mg (0.123 mmol) Wilkinson's catalyst. The vessel was fitted with a regulator and pressurized to 30 psi with H_2 gas. The reaction was allowed to stir for 2 days before being passed through a silica plug. Purification by column chromatography (8:1 hexanes:ethyl acetate) yielded 251 mg (1.13 mmol, 76%) of a brown oil.

IR (thin film, NaCl): 2953, 1739, 1529 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 1.4 Hz, 1H), 7.34 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.28 (d, *J* = 7.5 Hz, 1H), 3.67 (s, 3H), 3.18 (t, *J* = 7.5 Hz, 2H), 2.71 (t, *J* = 7.5 Hz, 2H), 2.40 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 149.2, 138.2, 134.3, 132.8, 132.2, 125.4, 51.9, 35.0, 28.3, 21.0.

HRMS (ESI) calc'd for $[C_{11}H_{13}NO_4+Na]^+$ requires *m/z* 246.0737, found *m/z* 246.0741.



(S6)

(*E*)-Methyl 3-(2-nitro-4-(trifluoromethyl)phenyl)acrylate (S6): An oven-dried Schlenk flask with magnetic stirbar was charged with 0.33 mL (2.2 mmol) 4-bromo-3-nitrobenzotrifluoride, 0.40 mL (4.4 mmol) methyl acrylate, 10.1 mg (0.0450 mmol) $Pd(OAc)_2$, 23.8 mg (0.0907 mmol) triphenylphosphine, and 0.40 mL (2.9 mmol) triethylamine. The reaction was sealed under N_2 and heated gradually to 125 °C for 21 h before being cooled to room temperature and passed through a silica plug. Purification by column chromatography (20:1 hexanes:ethyl acetate) yielded 346 mg (1.3 mmol, >10:1 E:Z, 58%) of a yellow solid.

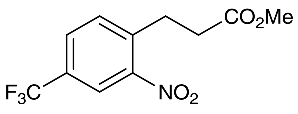
mp = 77.6–79.3 °C.

IR (thin film, NaCl): 3096, 2956, 1718, 1540, 1324 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 1.7 Hz, 1H), 8.13 (d, *J* = 15.9 Hz, 1H), 7.92 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 6.43 (d, *J* = 15.9 Hz, 1H), 3.86 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.6, 148.1, 138.7, 134.1, 132.6 (q, *J* = 35.3 Hz), 130.2, 130.0 (q, *J* = 3.8 Hz), 124.9, 122.5 (q, *J* = 273.4 Hz), 122.4 (q, *J* = 3.8 Hz), 52.2.

HRMS (ESI) calc'd for $[C_{11}H_8F_3NO_4+NH_4]^+$ requires *m/z* 293.0744, found *m/z* 293.0735.



(S7)

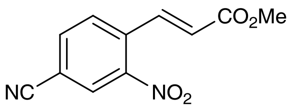
Methyl 3-(2-nitro-4-(trifluoromethyl)phenyl)propanoate (S7): To an oven-dried 150 mL glass pressure vessel containing a magnetic stirbar was added 307 mg (1.11 mmol) **S6** and 8 mL degassed 1:1 mixture of THF and *t*-BuOH. H_2 gas was bubbled through the solution and the vessel was charged with 86.6 mg (0.0936 mmol) Wilkinson's catalyst. The vessel was fitted with a regulator and pressurized to 30 psi with H_2 gas. The reaction was allowed to stir for 24 h before another portion of catalyst was added. The reaction was pressurized to 30 psi of H_2 and allowed to stir for another 24 h before being passed through a silica plug. Purification by column chromatography (20:1 hexanes:ethyl acetate) yielded 238 mg (0.859 mmol, 77%) of a yellow oil.

IR (thin film, NaCl): 2956, 1735, 1540, 1327 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 1.0 Hz 1H), 7.80 (dd, *J* = 8.1, 1.3 Hz 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 3.68 (s, 3H), 3.30 (t, *J* = 7.4 Hz, 2H), 2.76 (t, *J* = 7.4 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.3, 149.2, 139.6, 133.3, 130.4 (q, *J* = 34.0 Hz), 129.5 (q, *J* = 3.8 Hz), 122.8 (q, *J* = 273.4 Hz), 122.3 (q, *J* = 3.8 Hz), 51.9, 34.2, 28.2.

HRMS (ESI) calc'd for $[C_{11}H_{10}F_3NO_4+Na]^+$ requires *m/z* 300.0455, found *m/z* 300.0454.



(S8)

(*E*)-Methyl 3-(4-cyano-2-nitrophenyl)acrylate (S8): An oven-dried Schlenk flask with magnetic stirbar was charged with 502 mg (2.21 mmol) 4-bromo-3-nitrobenzonitrile, 0.40 mL (4.4 mmol) methyl acrylate, 9.2 mg (0.041 mmol) $Pd(OAc)_2$, 22.7 mg (0.0865 mmol) triphenylphosphine, and 0.40 mL (2.9 mmol) triethylamine. The reaction was sealed under N_2 and heated gradually to 125 °C for 21 h before being cooled to room temperature and passed through a silica plug. Purification by column chromatography (20:1 hexanes:ethyl acetate) yielded 289 mg (1.3 mmol, 8:1 E:Z, 56%) of a tan solid.

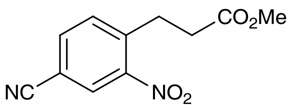
mp = 43.4–45.6 °C.

IR (thin film, NaCl): 3061, 2959, 2243, 1718, 1532 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, *J* = 1.7 Hz, 1H), 8.10 (d, *J* = 15.9 Hz, 1H), 7.93 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 6.45 (d, *J* = 15.9 Hz, 1H), 3.86 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.4, 148.1, 138.1, 136.2, 134.8, 130.3, 128.6, 125.6, 116.1, 114.3, 52.3.

HRMS (ESI) calc'd for $[C_{11}H_8N_2O_4+NH_4]^+$ requires *m/z* 250.0823, found *m/z* 250.0822.



(S9)

Methyl 3-(4-cyano-2-nitrophenyl)propanoate (S9): To an oven-dried 150 mL glass pressure vessel containing a magnetic stirbar was added 313 mg (1.35 mmol) **S8** and 10 mL degassed 1:1 mixture of THF and *t*-BuOH. H_2 gas was bubbled through the solution and the vessel was charged with 295 mg (0.319 mmol) Wilkinson's catalyst. The vessel was fitted with a regulator and pressurized to 40 psi with H_2 gas. The reaction was allowed to stir for 3 days before being passed through a silica plug. Purification by column chromatography (4:1 hexanes:ethyl acetate) yielded 167 mg (0.713 mmol, 53%) of a yellow solid.

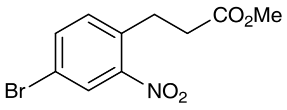
mp = 137.3–138.6 °C.

IR (thin film, NaCl): 2955, 2237, 1735, 1535 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 1.7 Hz, 1H), 7.82 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 3.68 (s, 3H), 3.30 (t, *J* = 7.3 Hz, 2H), 2.76 (t, *J* = 7.3 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.1, 149.3, 140.8, 135.8, 133.6, 128.5, 116.4, 112.1, 51.9, 33.9, 28.3.

HRMS (ESI) calc'd for $[C_{11}H_{10}N_2O_4+NH_4]^+$ requires *m/z* 252.0979, found *m/z* 252.0981.


(S10)

Methyl 3-(4-bromo-2-nitrophenyl)propanoate (S10): In a round-bottom flask with magnetic stirbar was dissolved 528 mg (2.52 mmol) methyl 3-(2-nitrophenyl)propanoate and 500 mg (2.81 mmol) *N*-bromosuccinimide in 1.3 mL sulfuric acid and 12.6 mL trifluoroacetic acid. The reaction was stirred for 2 days, and then diluted with ethyl acetate and washed with 50 mL water, 50 mL saturated $NaHCO_3$, and 50 mL brine. The organic layer was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by column chromatography (50:1 hexanes:ethyl acetate) yielded 176 mg (0.611 mmol, 24%) of a yellow solid.

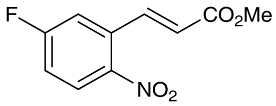
mp = 47.8–49.1 °C.

IR (thin film, NaCl): 2952, 2850, 1734, 1528 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 2.1 Hz, 1H), 7.66 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.31 (d, *J* = 8.3 Hz, 1H), 3.67 (s, 3H), 3.18 (t, *J* = 7.4 Hz, 2H), 2.71 (t, *J* = 7.4 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 149.6, 136.2, 134.5, 133.6, 127.8, 120.6, 51.8, 34.3, 27.9.

HRMS (ESI) calc'd for $[C_{10}H_{10}BrNO_4+NH_4]^+$ requires *m/z* 305.0132, found *m/z* 305.0136.


(S11)

(*E*)-Methyl 3-(5-fluoro-2-nitrophenyl)acrylate (S11): An oven-dried Schlenk flask with magnetic stirbar was charged with 155 mg (0.705 mmol) 2-bromo-4-fluoro-1-nitrobenzene,[6] 0.13 mL (1.4 mmol) methyl acrylate, 3.2 mg (0.014 mmol) $Pd(OAc)_2$, 7.8 mg (0.030 mmol) triphenylphosphine, and 0.12 mL (0.86 mmol) triethylamine. The reaction was sealed under N_2 and heated gradually to 125 °C for 2 days before being cooled to room temperature and passed through a silica plug. Purification by column chromatography (9:1 hexanes:ethyl acetate) yielded 89.5 mg (0.40 mmol, 10:1 E:Z, 56%) of a yellow solid.

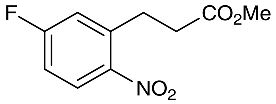
mp = 76.7–77.8 °C.

IR (thin film, NaCl): 3081, 2961, 1717, 1525 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 8.9, 5.0 Hz, 1H), 8.13 (d, *J* = 15.8Hz, 1H), 7.30 (dd, *J* = 8.8, 2.7 Hz, 1H), 7.23 (ddd, *J* = 9.6, 7.1, 2.8 Hz, 1H), 6.35 (d, *J* = 15.8 Hz, 1H), 3.84 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 164.8 (d, *J* = 258.3 Hz), 144.3, 139.3, 133.9 (d, *J* = 8.8 Hz), 127.9 (d, *J* = 8.8 Hz), 123.9, 117.2 (d, *J* = 22.7 Hz), 116.0 (d, *J* = 23.9 Hz), 52.1.

HRMS (ESI) calc'd for $[C_{10}H_8FNO_4+NH_4]^+$ requires *m/z* 243.0776, found *m/z* 243.0775.


(S12)

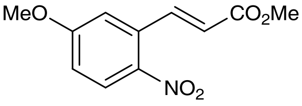
Methyl 3-(5-fluoro-2-nitrophenyl)propanoate (S12): To an oven-dried 150 mL glass pressure vessel containing a magnetic stirbar was added 146 mg (0.646 mmol) **S11** and 4.5 mL degassed 1:1 mixture of THF and *t*-BuOH. H_2 gas was bubbled through the solution and the vessel was charged with 123 mg (0.133 mmol) Wilkinson's catalyst. The vessel was fitted with a regulator and pressurized to 40 psi with H_2 gas. The reaction was allowed to stir for 2 days before being passed through a silica plug. Purification by column chromatography (9:1 hexanes:ethyl acetate) yielded 87.1 mg (0.383 mmol, 59%) of a yellow oil.

IR (thin film, NaCl): 2953, 2850, 1737, 1527 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 9.1, 5.2 Hz, 1H), 7.12 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.07 (ddd, *J* = 8.8, 7.1, 2.8 Hz, 1H), 3.69 (s, 3H), 3.25 (t, *J* = 7.4 Hz, 2H), 2.74 (t, *J* = 7.4 Hz, 2H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 172.5, 164.6 (d, *J* = 256.9 Hz), 145.2, 139.4 (d, *J* = 9.0 Hz), 127.9 (d, *J* = 10.0 Hz), 118.9 (d, *J* = 23.4 Hz), 114.7 (d, *J* = 23.1 Hz), 51.8, 34.2, 28.6.

HRMS (ESI) calc'd for $[C_{10}H_{10}FNO_4+Na]^+$ requires *m/z* 250.0487, found *m/z* 250.0487.



(S13)

(*E*)-Methyl 3-(5-methoxy-2-nitrophenyl)acrylate (S13): An oven-dried Schlenk flask with magnetic stirbar was charged with 780 mg (3.36 mmol) 3-bromo-4-nitroanisole,[7] 0.61 mL (6.8 mmol) methyl acrylate, 15.6 mg (0.0695 mmol) Pd(OAc)$_2$, 36.4 mg (0.139 mmol) triphenylphosphine, and 1.2 mL (8.6 mmol) triethylamine. The reaction was sealed under N$_2$ and heated gradually to 125 °C for 3 h. An additional 0.30 mL of methyl acrylate was added and the reaction was heated to 125 °C for an additional 3 h before being cooled to room temperature and passed through a silica plug. Purification by column chromatography (8:1 hexanes:ethyl acetate) yielded 659 mg (2.8 mmol, >10:1 E:Z, 83%) of a yellow solid.

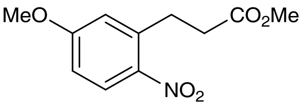
mp = 43.1–43.9 °C.

IR (thin film, NaCl): 3017, 2953, 1719, 1585 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.21 (d, *J* = 15.8 Hz, 1H), 8.14 (d, *J* = 8.8 Hz, 1H), 7.04 – 6.93 (m, 2H), 6.30 (d, *J* = 15.8 Hz, 1H), 3.93 (s, 3H), 3.83 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 194.7, 166.2, 163.4, 141.5, 133.7, 127.7, 122.7, 114.9, 114.2, 56.1, 52.0.

HRMS (ESI) calc'd for $[C_{11}H_{11}NO_5+NH_4]^+$ requires *m/z* 255.0976, found *m/z* 255.0988.



(S14)

Methyl 3-(5-methoxy-2-nitrophenyl)propanoate (S14): To an oven-dried 150 mL glass pressure vessel containing a magnetic stirbar was added 415 mg (1.75 mmol) **S13** and 11 mL degassed 1:1 mixture of THF and *t*-BuOH. H$_2$ gas was bubbled through the solution and the vessel was charged with 131 mg (0.142 mmol) Wilkinson's catalyst. The vessel was fitted with a regulator and pressurized to 30 psi with H$_2$ gas. The reaction was allowed to stir for 2 days before being passed through a silica plug. Purification by column chromatography (5:1 hexanes:ethyl acetate) yielded 365 mg (1.53 mmol, 87%) of a yellow solid.

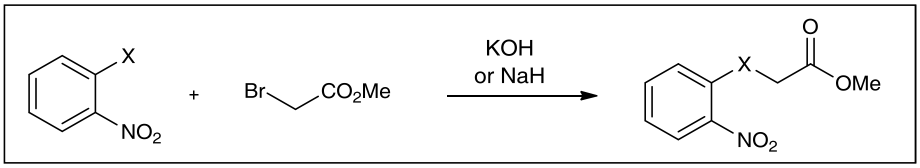
mp = 117.2–118.2 °C.

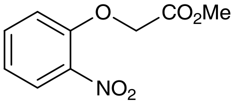
IR (thin film, NaCl): 2952, 2845, 1735, 1516 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.08 (d, J = 8.7 Hz, 1H), 6.89 – 6.78 (m, 2H), 3.88 (s, 3H), 3.68 (s, 3H), 3.27 (t, J = 7.5 Hz, 2H), 2.73 (t, J = 7.6 Hz, 2H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 172.9, 163.2, 142.0, 139.0, 127.9, 117.0, 112.5, 55.8, 51.7, 34.5, 29.4.

HRMS (ESI) calc'd for $[C_{11}H_{13}NO_5+NH_4]^+$ requires m/z 257.1132, found m/z 257.1137.





(S15)

Methyl 2-(2-nitrophenoxy)acetate (S15): To a suspension of 409 mg (7.28 mmol) KOH in 74 mL ethanol was added 1.00 g (7.20 mmol) 2-nitrophenol. The reaction was allowed to stir 30 min before the solvent was removed *in vacuo*. 50 mL of DMF and 0.82 mL (8.7 mmol) of bromomethyl acetate were added and the reaction was allowed to stir overnight before being diluted with ethyl acetate and washed with three 100 mL portions of water and one 100 mL portion of brine. The organic layer was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by column chromatography (5:1 hexanes:ethyl acetate) yielded 768 mg (3.6 mmol, 51%) of a yellow solid.

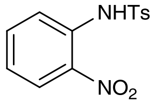
mp = 54.2–54.7 °C.

IR (thin film, NaCl): 2954, 2922, 1743, 1507 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.53 (ddd, *J* = 8.4, 7.4, 1.7 Hz, 1H), 7.11 (ddd, *J* = 8.3, 7.5, 1.1 Hz, 1H), 7.00 (dd, *J* = 8.4, 1.2 Hz, 1H), 4.80 (s, 2H), 3.80 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.2, 151.1, 140.3, 134.0, 125.8, 121.7, 115.1, 66.4, 52.4.

HRMS (ESI) calc'd for $[C_9H_9NO_5+NH_4]^+$ requires *m/z* 229.0819, found *m/z* 229.0809.



(S16)

4-Methyl-*N*-(2-nitrophenyl)benzenesulfonamide (S16): To a round-bottom flask with magnetic stirbar was added 500 mg (3.62 mmol) 2-nitroaniline, 1.03 g (5.41 mmol) *p*-toluenesulfonylchloride, 0.44 mL (5.4 mmol) pyridine, and 9 mL dichloromethane. The reaction was stirred overnight. The next day, the reaction was poured onto water, and the organic layer was washed with twice with 50 mL water and once with 50 mL brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by column chromatography (10:1 hexanes:ethyl acetate) and recrystallization (hexanes and ethyl acetate) yielded 605 mg (2.1 mmol, 57%) of a yellow solid.

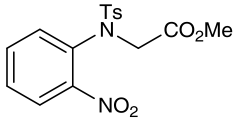
mp = 114.7–115.5 °C.

IR (thin film, NaCl): 3285, 3057, 1529, 1348, 1170 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.11 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.84 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.58 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.15 (ddd, *J* = 8.5, 7.3, 1.3 Hz, 1H), 2.39 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.8, 136.9, 135.8, 135.6, 133.9, 130.0, 127.2, 126.1, 123.7, 121.0, 21.6.

HRMS (ESI) calc'd for $[C_{13}H_{12}N_2O_4S+NH_4]^+$ requires *m/z* 310.0857, found *m/z* 310.0842.



(S17)

Methyl 2-(4-methyl-*N*-(2-nitrophenyl)phenylsulfonamido)acetate (S17): In a round-bottom flask with magnetic stirbar was placed 1.00 g (3.44 mmol) **S16** and 205 mg (5.13 mmol) NaH (60% dispersion) in 8 mL DMF. The reaction was stirred 15 min before 0.49 mL (5.2 mmol) of bromomethyl acetate was added and the flask was heated to 80 °C overnight. After cooling to room temperature, the reaction was diluted with ethyl acetate and the organic layer was washed with twice with 50 mL water and once with 50 mL brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by column chromatography (4:1 hexanes:ethyl acetate) yielded 1.06 g (2.9 mmol, 84%) of a yellow solid.

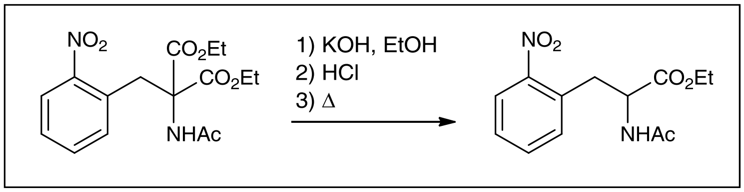
mp = 104.0–105.1 °C.

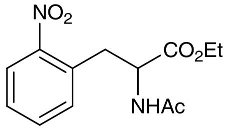
IR (thin film, NaCl): 2954, 1754, 1533, 1352, 1161 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.73 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.57 (td, *J* = 7.7, 1.7 Hz, 1H), 7.52 (td, *J* = 7.7, 1.7 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.23 (d, *J* = 7.9 Hz, 2H), 4.62 (apparent s, 1H), 3.74 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.9, 149.0, 144.2, 136.0, 135.1, 133.5, 132.1, 130.1, 129.5, 127.7, 125.3, 53.1, 52.3, 21.6.

HRMS (ESI) calc'd for $[C_{16}H_{16}N_2O_6S+Na]^+$ requires *m/z* 387.0622, found *m/z* 387.0634.





(S18)

Ethyl 2-acetamido-3-(2-nitrophenyl)propanoate (S18): In a round-bottom flask with magnetic stirbar was placed 161 mg (2.87 mmol) KOH in 3 mL of ethanol. 997 mg (2.83 mmol) diethyl 2-acetamido-2-(2-nitrobenzyl)malonate[8] was added and stirred for 1 h. The reaction was acidified with concentrated HCl and solvent was removed *in vacuo*. 6 mL of dioxane was added and the reaction was heated to reflux for 1 h before cooling to room temperature. The reaction was diluted with ethyl acetate and washed twice with saturated $NaHCO_3$ and once with brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by column chromatography (2:1 hexanes:ethyl acetate) yielded 488 mg (1.74 mmol, 61%) of a yellow solid.

mp = 74.6–75.1 °C.

IR (thin film, NaCl): 3276, 2985, 1740, 1654, 1577 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (dd, J = 8.5, 1.4 Hz, 1H), 7.56 (td, J = 7.7, 1.4 Hz, 1H), 7.46 – 7.38 (m, 2H), 6.27 (s, 1H), 4.91 (X of ABX, J = 8.1, 6.1 Hz, 1H), 4.19 4.14 (AB of ABX_3, J = 10.7, 7.2 Hz, 2H), 3.50 3.34 (AB of ABX, J = 13.8, 8.1, 6.1 Hz, 2H), 1.94 (s, 3H), 1.23 (X_3 of ABX_3, J = 7.2 Hz, 3H).

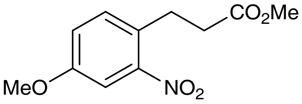
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 169.8, 149.8, 133.0, 132.7, 131.5, 128.2, 124.8, 61.9, 53.0, 34.7, 23.0, 14.0.

HRMS (ESI) calc'd for $[C_{13}H_{16}N_2O_5+H]^+$ requires *m/z* 281.1132, found *m/z* 281.1127.

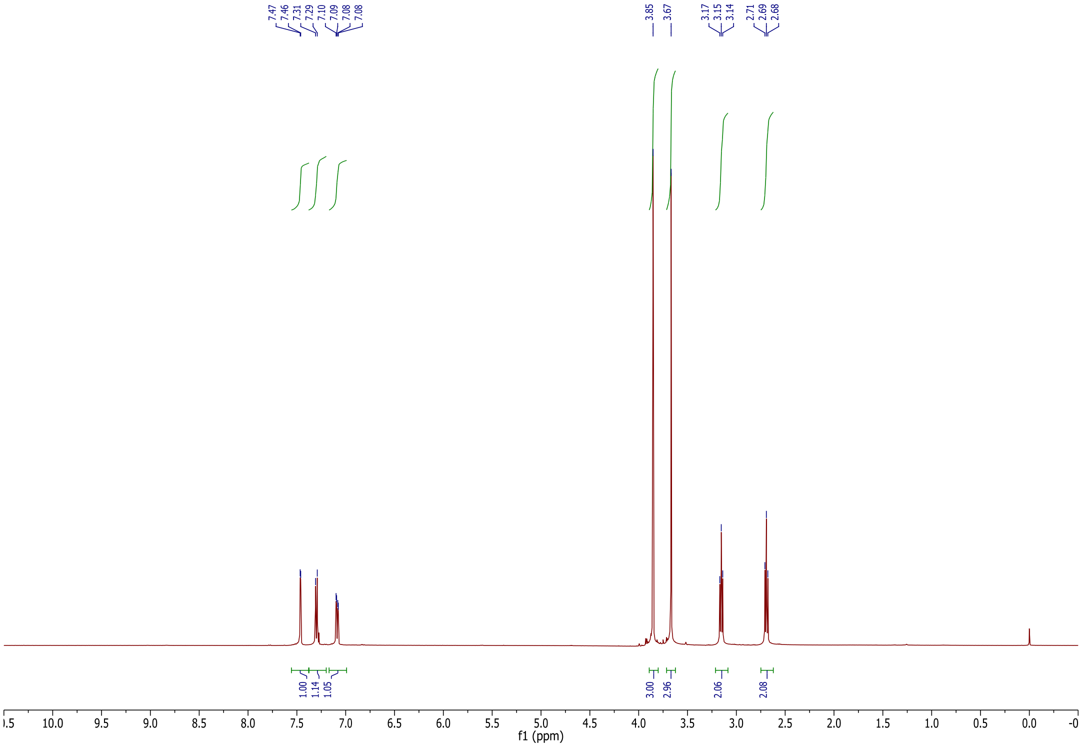
References

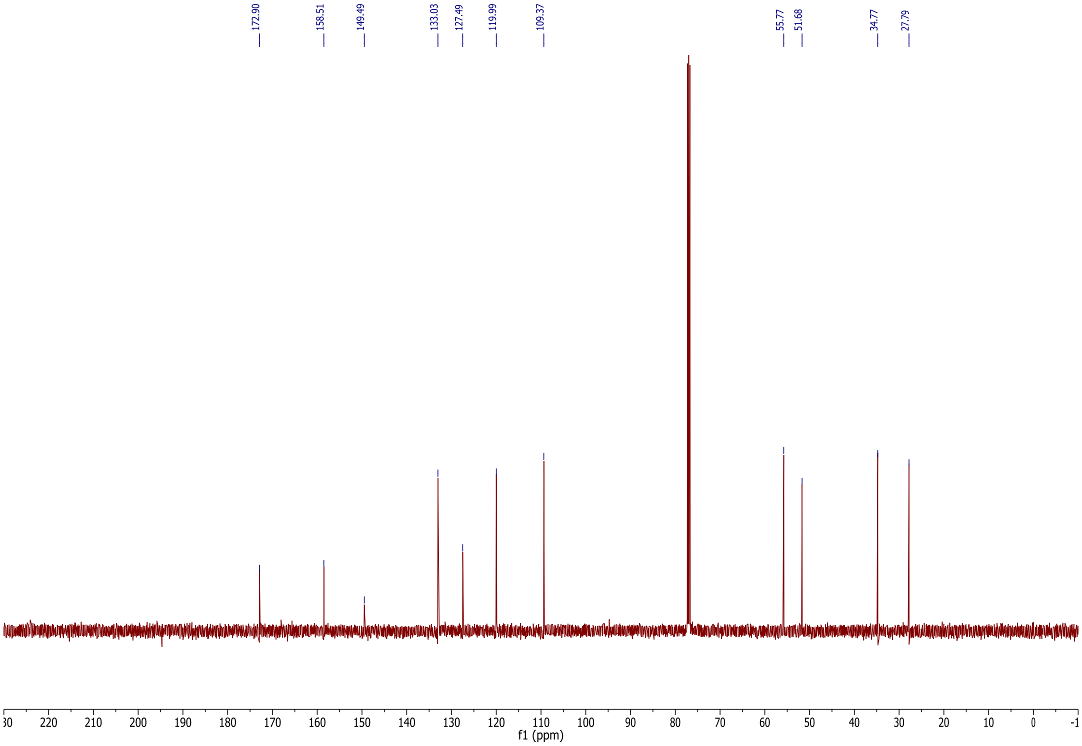
[1] Motoyama, Y.; Kamo, K.; Nagashima, H. *Org. Lett.* **2009**, *11*, 1345.
[2] Daniela, B.; Polaczkowa, W. *Rocz. Chem.* **1965**, *39*, 545.
[3] Jourdant, A.; González-Zamora, E.; Zhu, J. *J. Org. Chem.* **2002,** *67*, 3163.
[4] Park, S. J.; Park, S. J.; Lee, M. J.; Rhim, H.; Kim, Y.; Lee, J.-H.; Chung, B. Y.; Lee, J. Y. *Bioorg. Med. Chem.* **2006,** *14*, 3502.
[5] Le Callonnec, F.; Fouquet, E.; Felpin, F.-X. *Org Lett.* **2011**, *13*, 2646.
[6] Schlosser, M.; Ginanneschi, A.; Leroux, F. *Eur. J. Org. Chem.* **2006**, 2956.
[7] Zhang, Y. J.; Wei, H.; Zhang, W. *Tetrahedron* **2009**, *65*, 1281.
[8] Varnavas, A.; Lassiani, L.; Valenta, V.; Mennuni, L.; Makovec, F.; Hadjipavlou-Litina, D. *Eur. J. Med. Chem.* **2005**, *40*, 563.

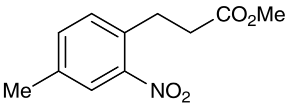
I. ^{1}H NMR and ^{13}C NMR Spectra



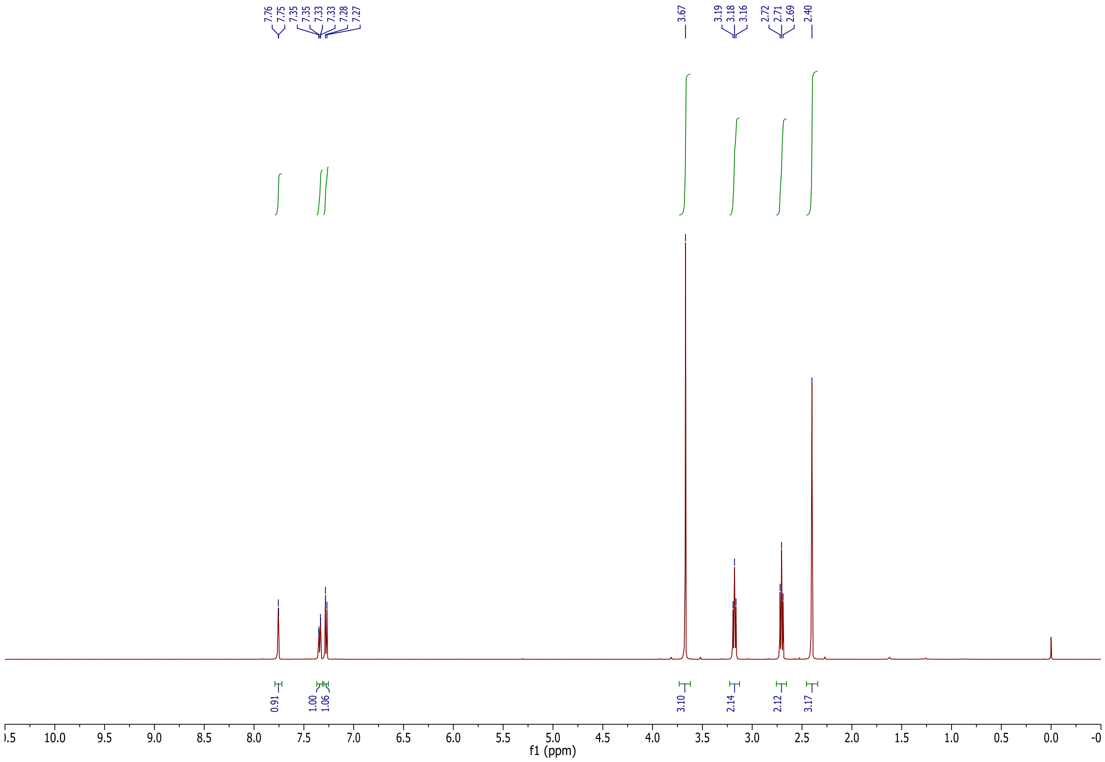
(S3)

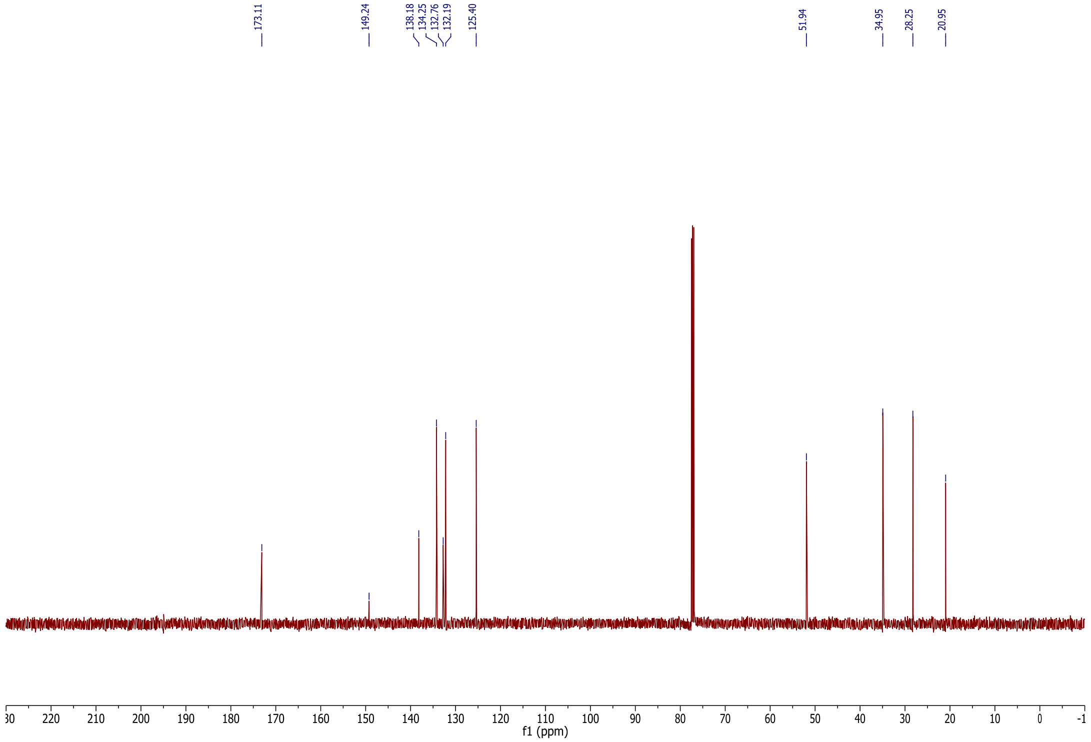


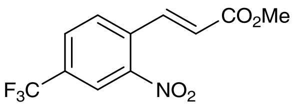



CO2Me
Me
NO2

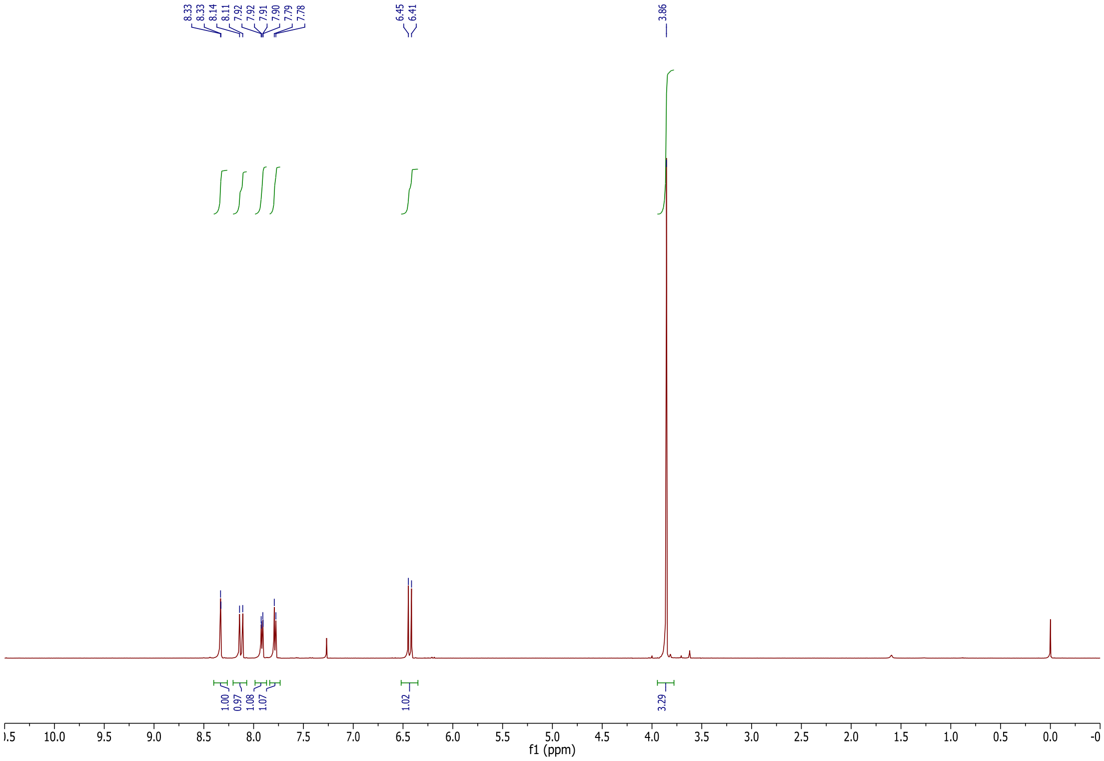
(S5)

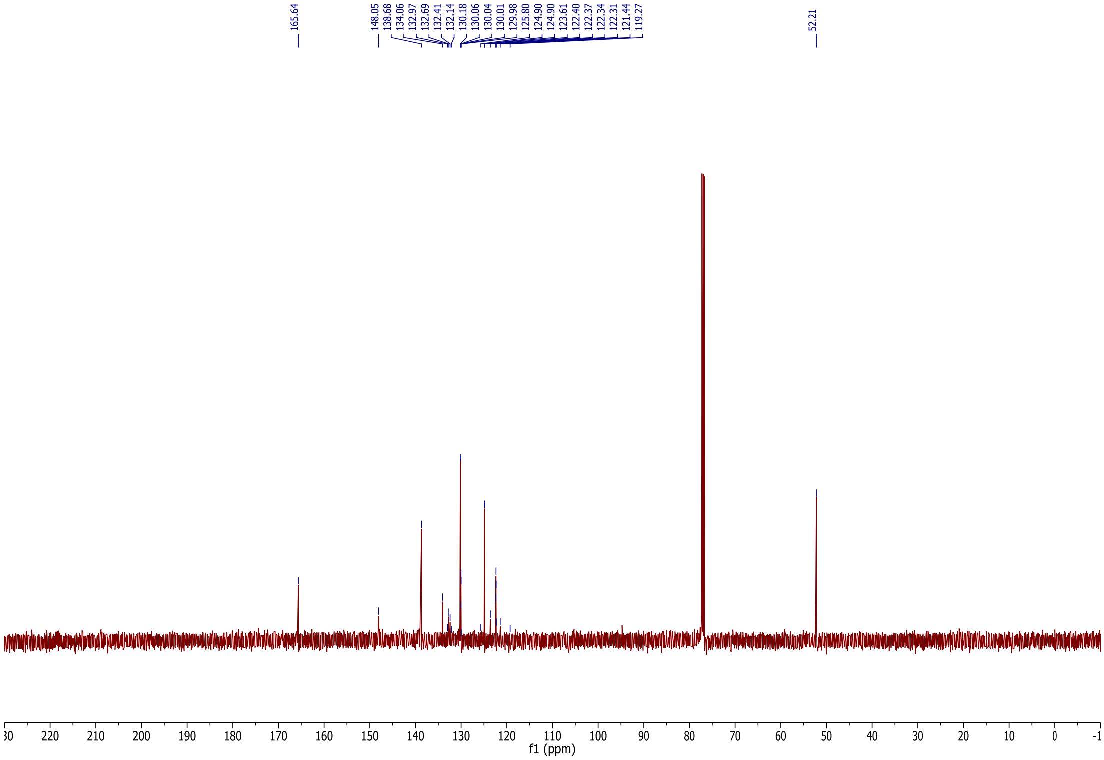

7.76
7.75
7.35
7.35
7.33
7.33
7.28
7.27
3.67
3.19
3.18
3.16
2.72
2.71
2.69
2.40
0.91
1.00
1.06
3.10
2.14
2.12
3.17
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

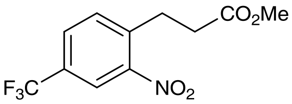

173.11
149.24
138.18
134.25
132.76
132.19
125.40
51.94
34.95
28.25
20.95
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


CO2Me
F3C
NO2

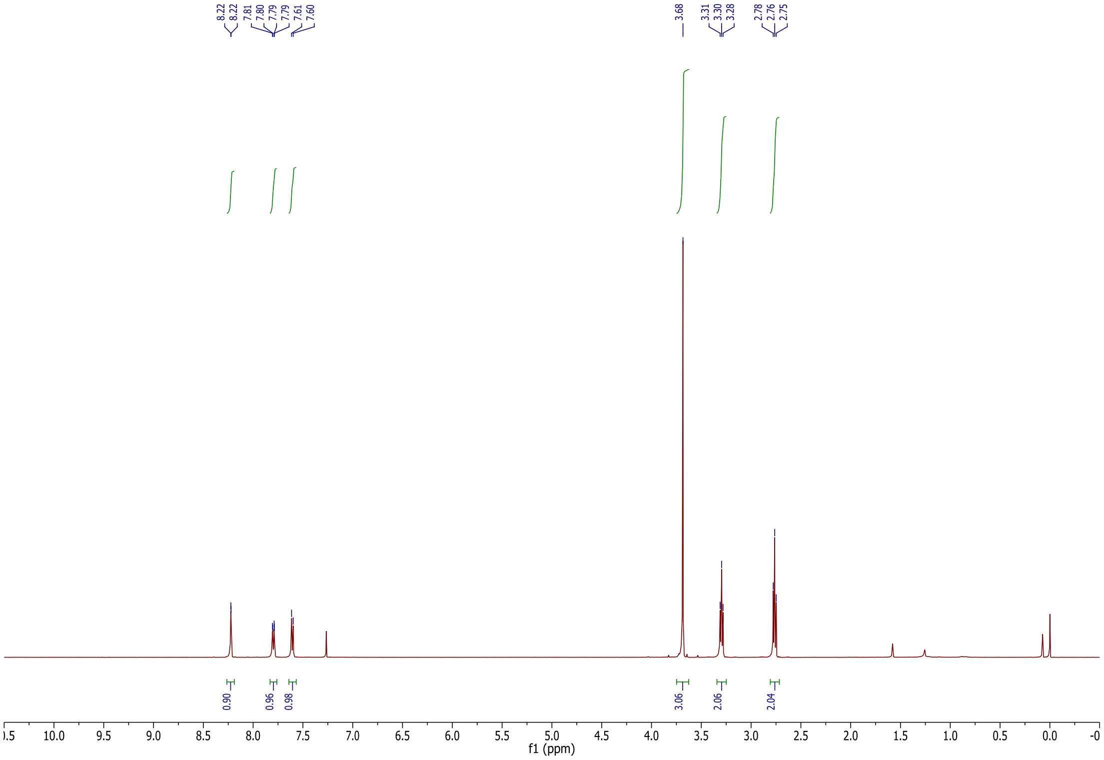
(S6)

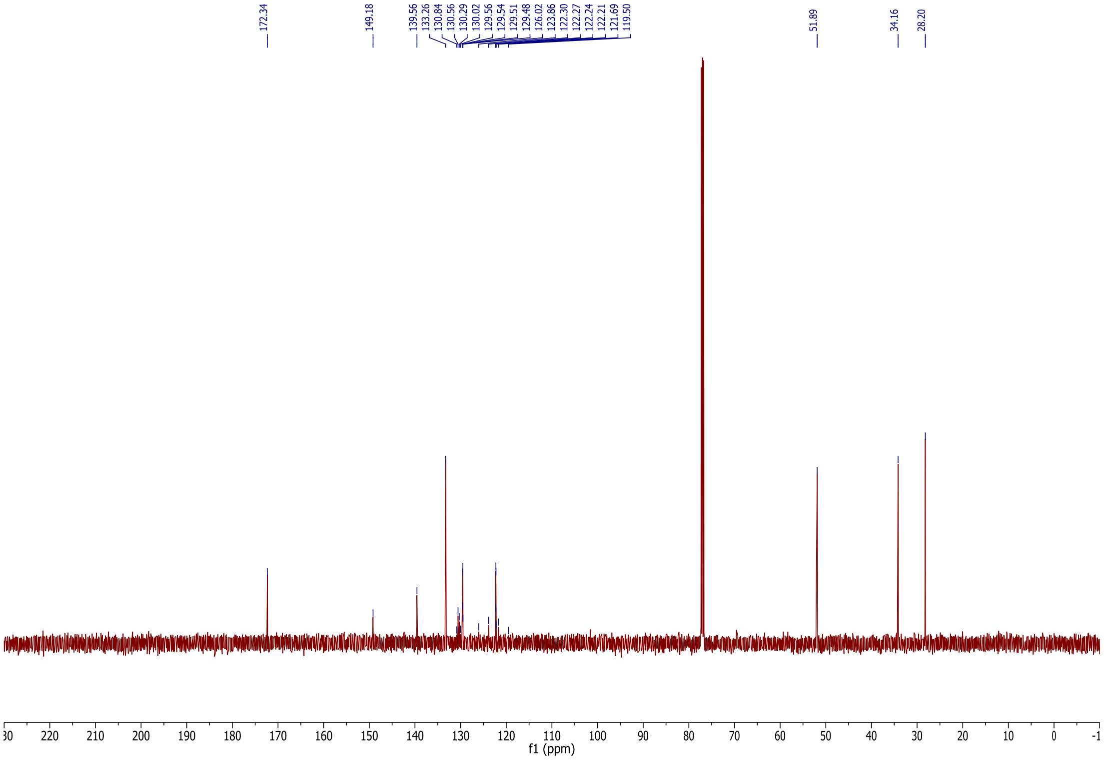

8.33
8.33
8.14
8.11
7.92
7.92
7.91
7.90
7.79
7.78
6.45
6.41
3.86
1.00
0.97
1.08
1.07
1.02
3.29
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

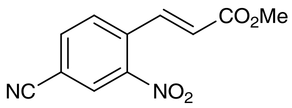

165.64
148.05
138.68
134.06
132.97
132.69
132.41
132.14
130.18
130.06
130.04
130.01
129.98
125.80
124.90
124.90
123.61
122.40
122.37
122.34
122.31
121.44
119.27
52.21
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


CO2Me
F3C
NO2

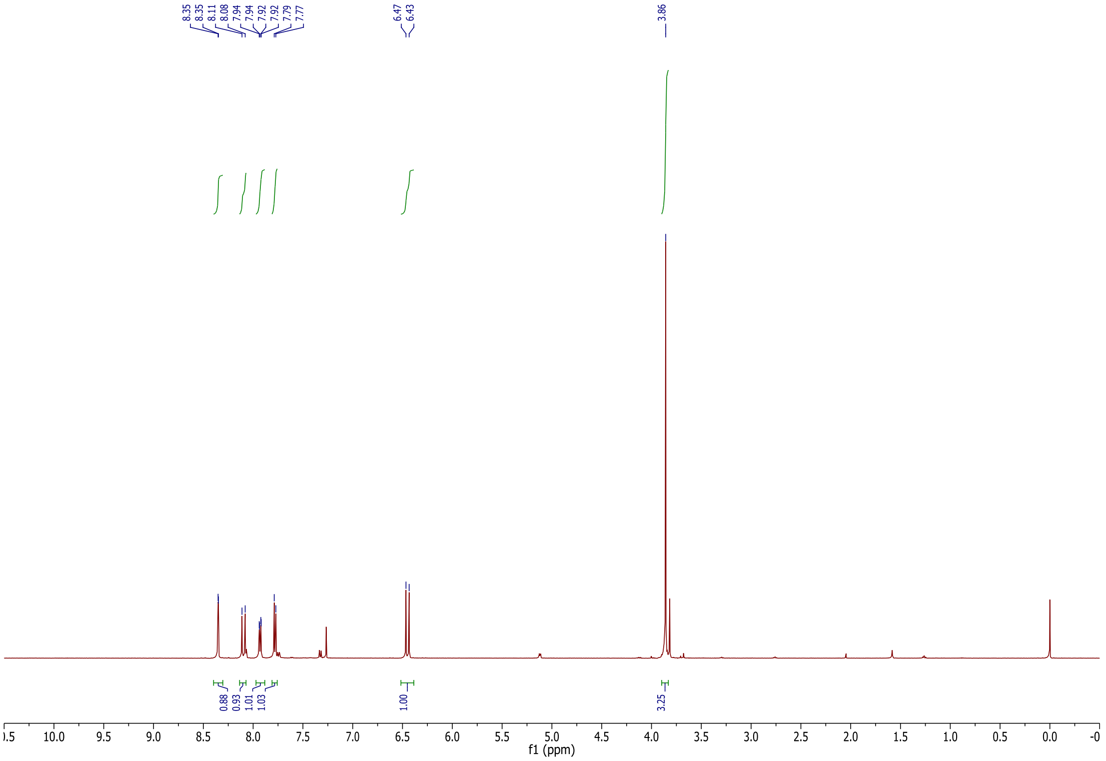
(S7)

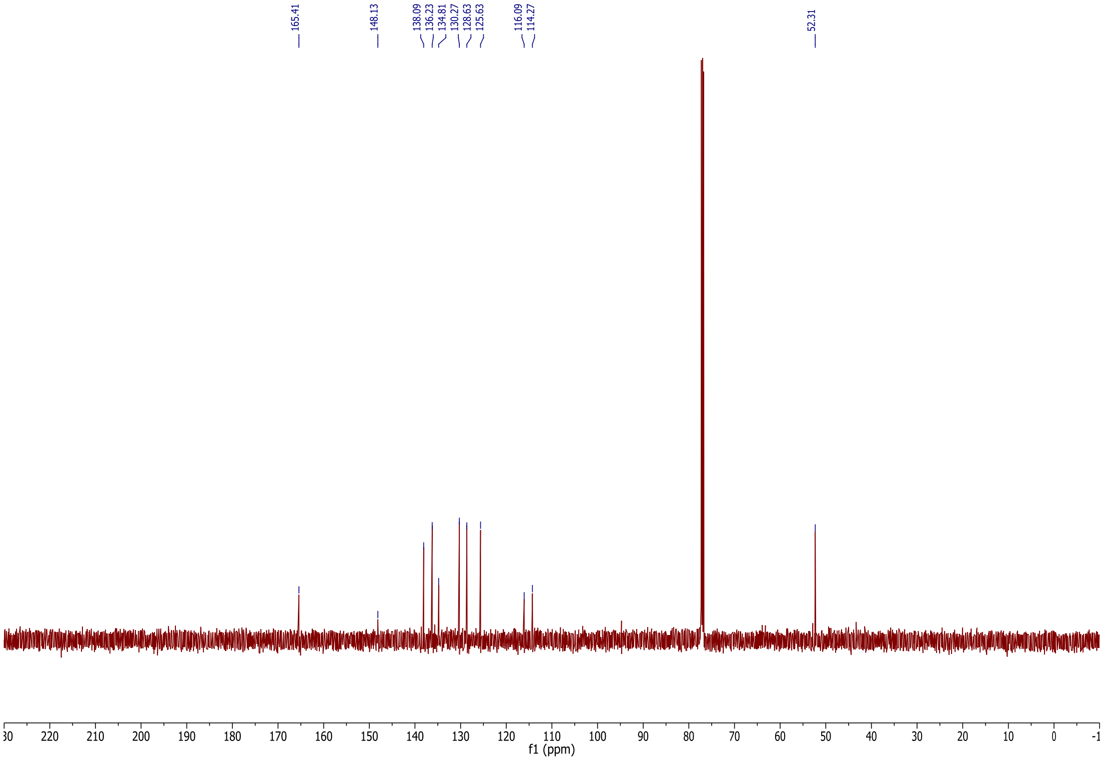

8.22
8.22
7.81
7.80
7.79
7.79
7.61
7.60
3.68
3.31
3.30
3.28
2.78
2.76
2.75
0.90
0.96
0.98
3.06
2.06
2.04
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

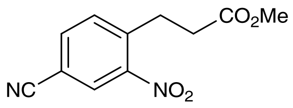

172.34
149.18
139.56
133.26
130.84
130.56
130.29
130.02
129.56
129.54
129.51
129.48
126.02
123.86
122.30
122.27
122.24
122.21
121.69
119.50
51.89
34.16
28.20
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


CO2Me
NC
NO2

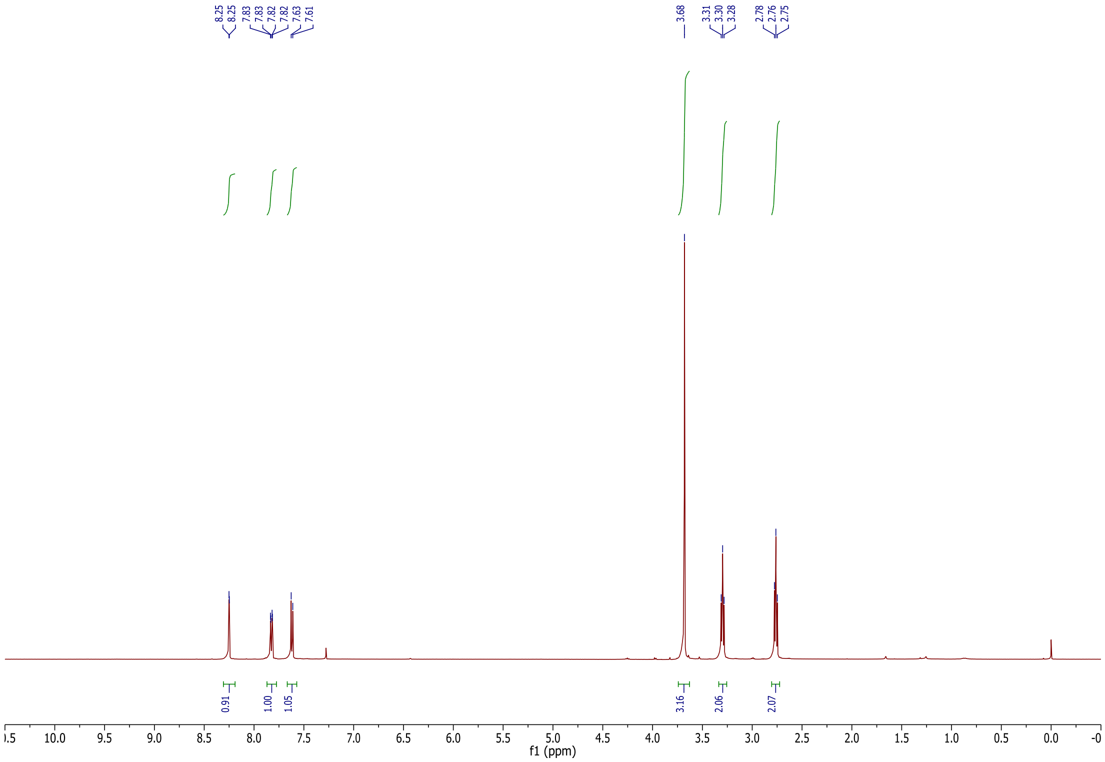
(S8)

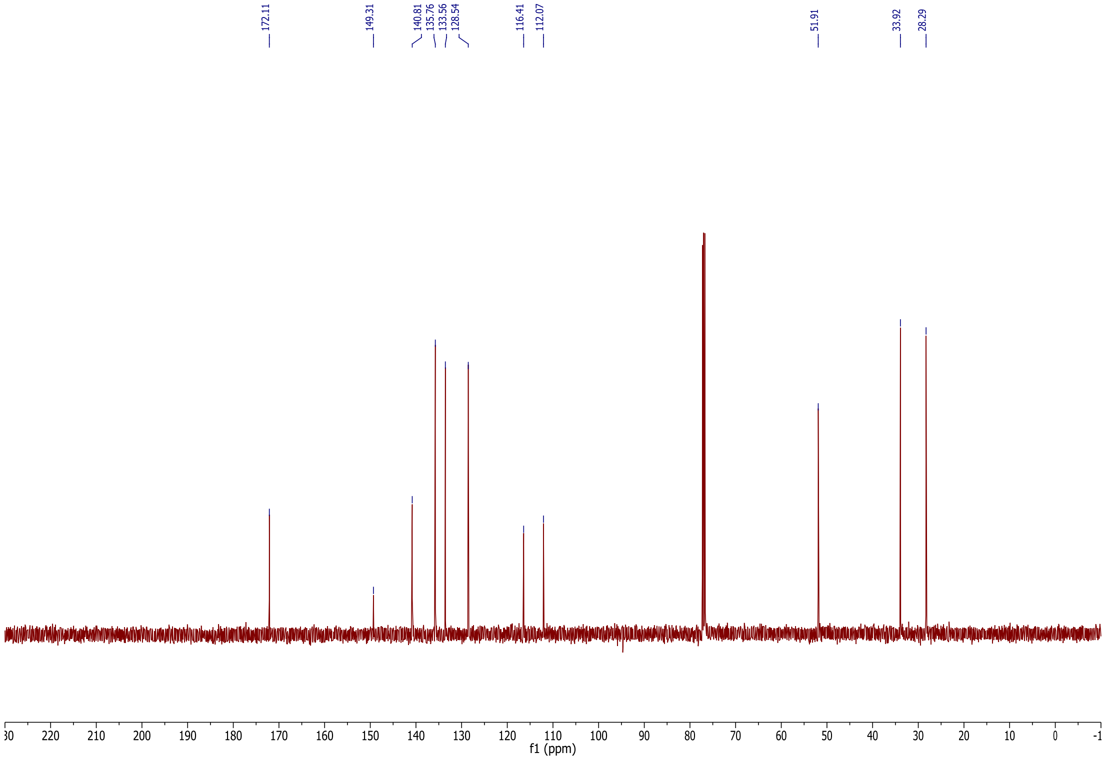

8.35
8.35
8.11
8.08
7.94
7.94
7.92
7.92
7.79
7.77
6.47
6.43
3.86
0.88
0.93
1.01
1.03
1.00
3.25
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

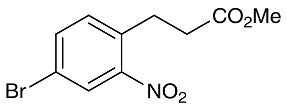

165.41
148.13
138.09
136.23
134.81
130.27
128.63
125.63
116.09
114.27
52.31
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


CO2Me
NC
NO2

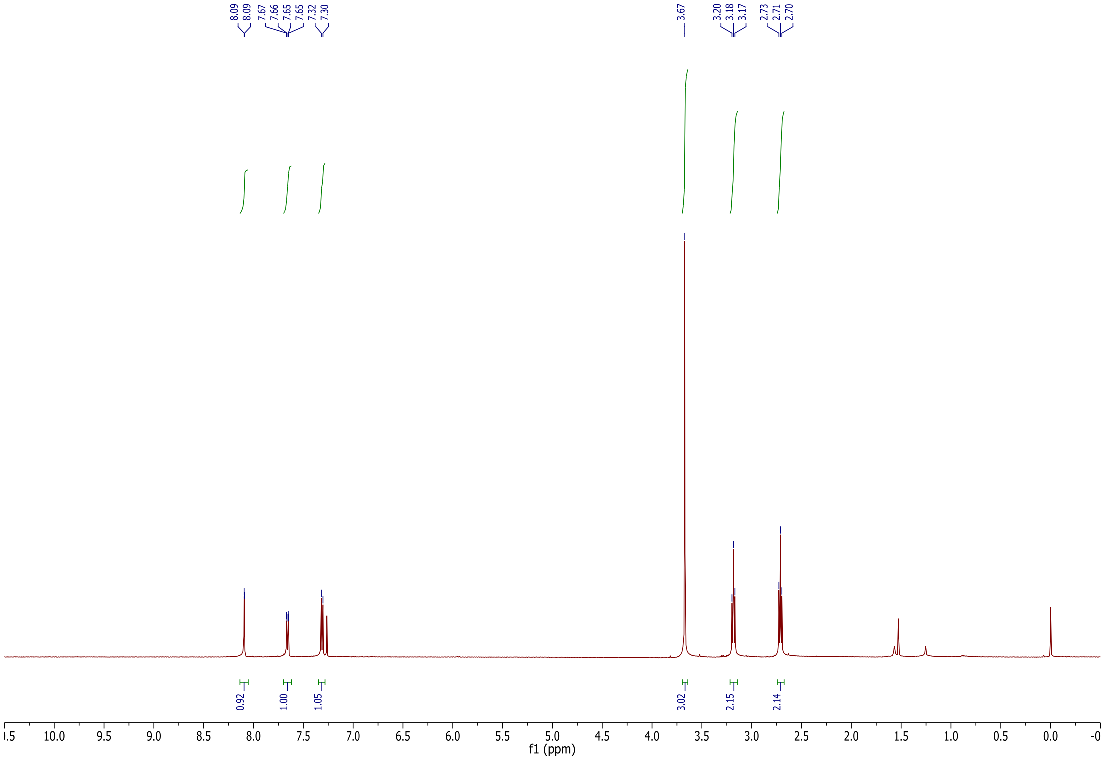
(S9)

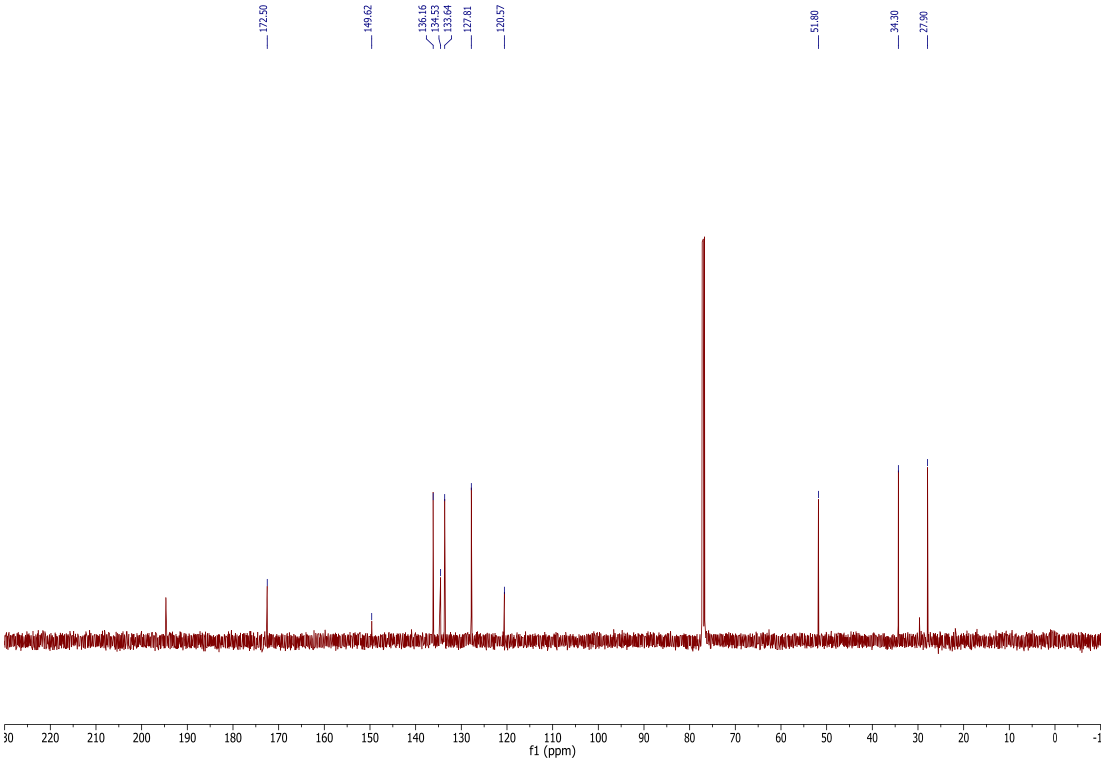

8.25
8.25
7.83
7.82
7.82
7.82
7.63
7.61
3.68
3.31
3.30
3.28
2.78
2.76
2.75
0.91
1.00
1.05
3.16
2.06
2.07
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

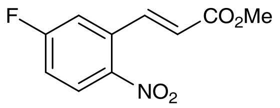

172.11
149.31
140.81
135.76
133.56
128.54
116.41
112.07
51.91
33.92
28.29
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


CO2Me
Br
NO2

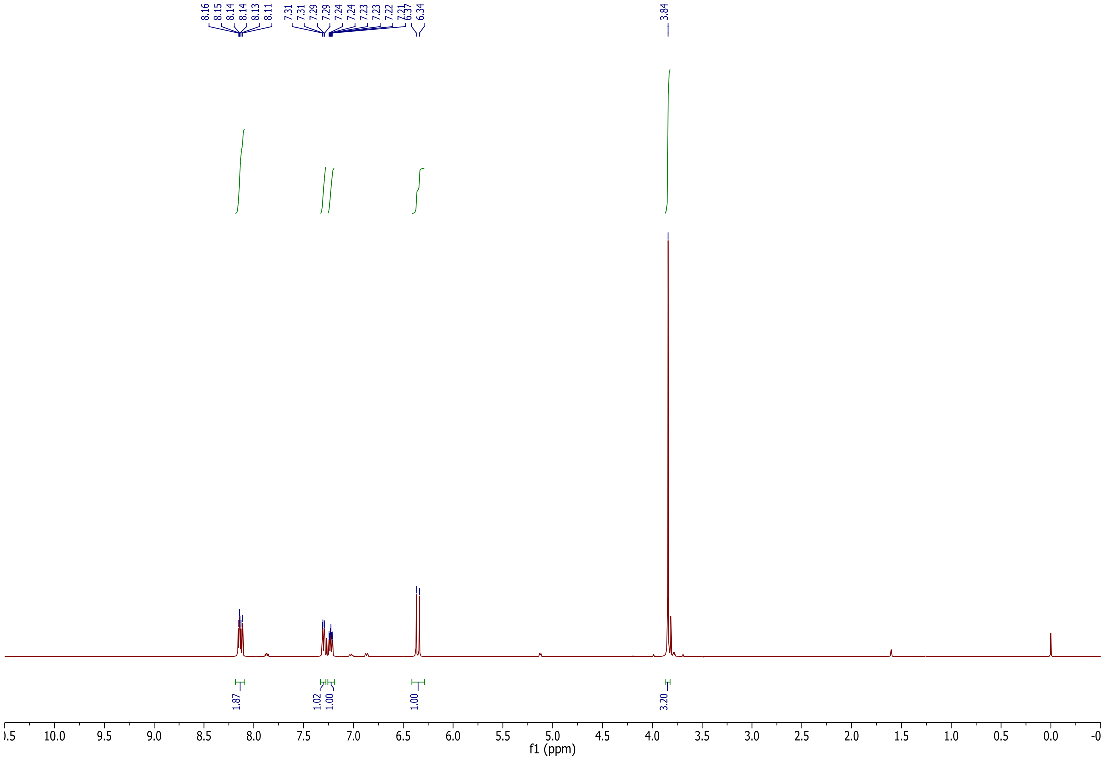
(S10)

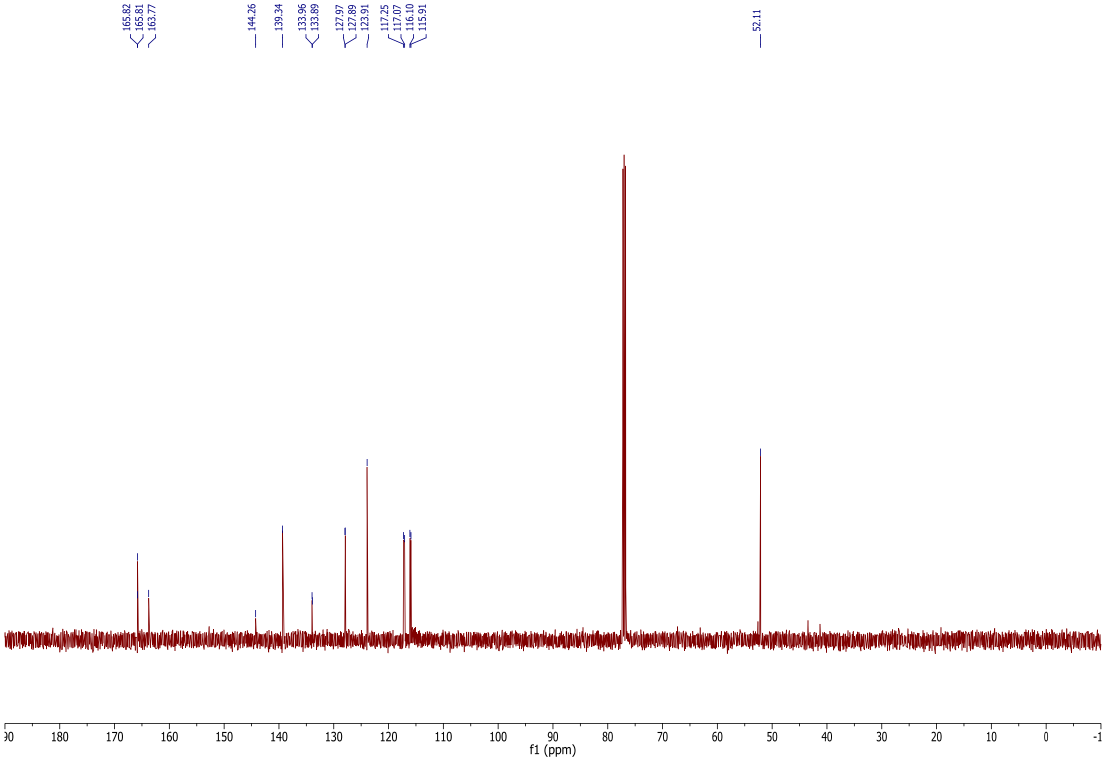

8.09
8.09
7.67
7.66
7.65
7.65
7.32
7.30
3.67
3.20
3.18
3.17
2.73
2.71
2.70
0.92
1.00
1.05
3.02
2.15
2.14
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

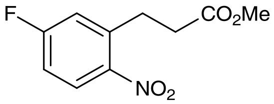

172.50
149.62
136.16
134.53
133.64
127.81
120.57
51.80
34.30
27.90
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


F
CO2Me
NO2

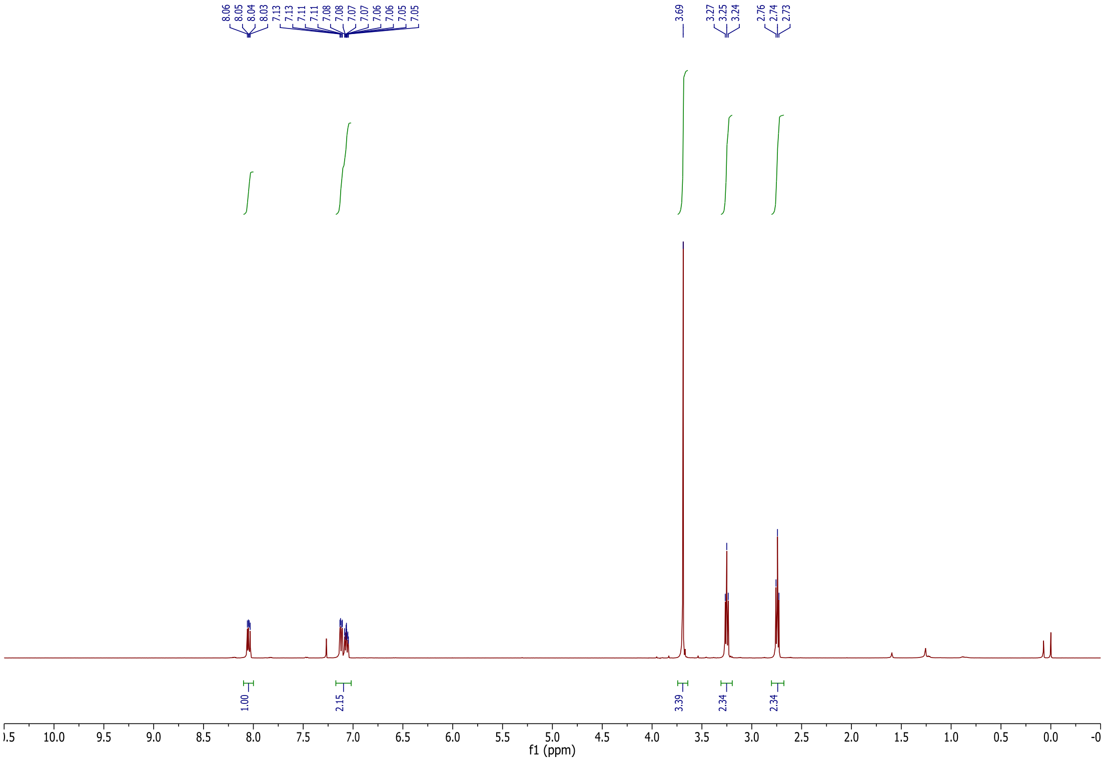
(S11)

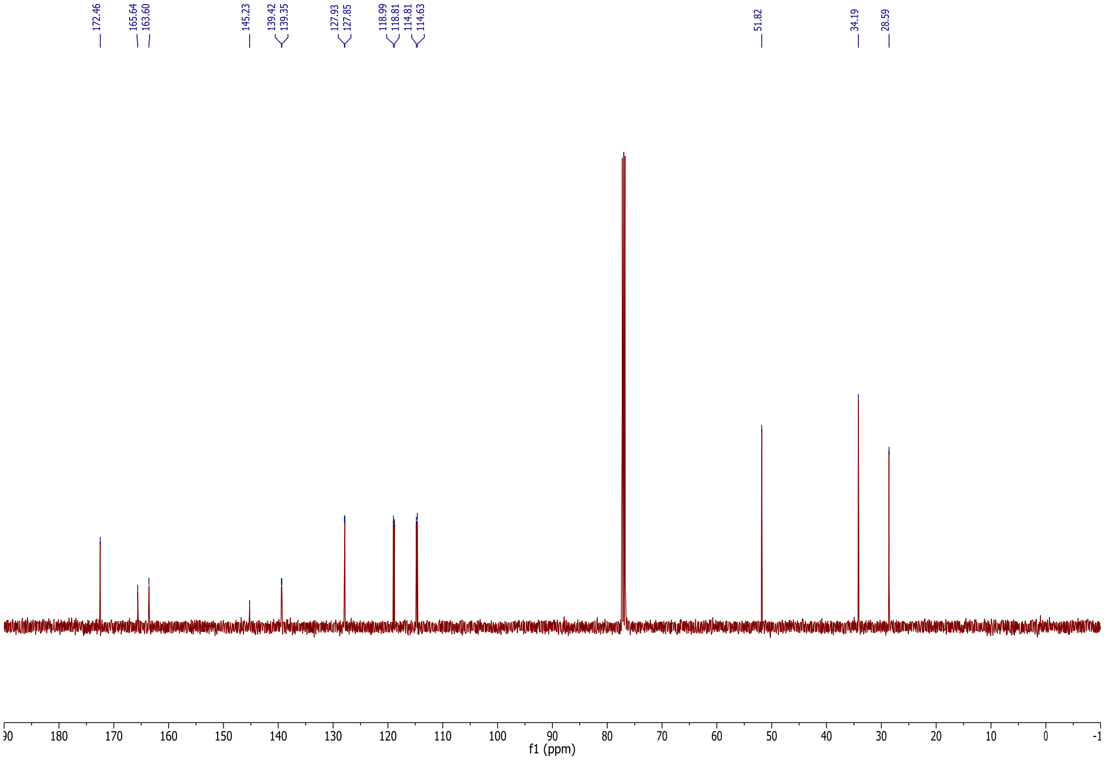

8.16
8.15
8.14
8.14
8.13
8.11
7.31
7.31
7.29
7.29
7.24
7.24
7.23
7.23
7.22
7.21
6.37
6.34
3.84
1.87
1.02
1.00
1.00
3.20
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

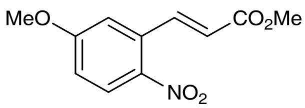

165.82
165.81
163.77
144.26
139.34
133.96
133.89
127.97
127.89
123.91
117.25
117.07
116.10
115.91
52.11
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F
CO2Me
NO2

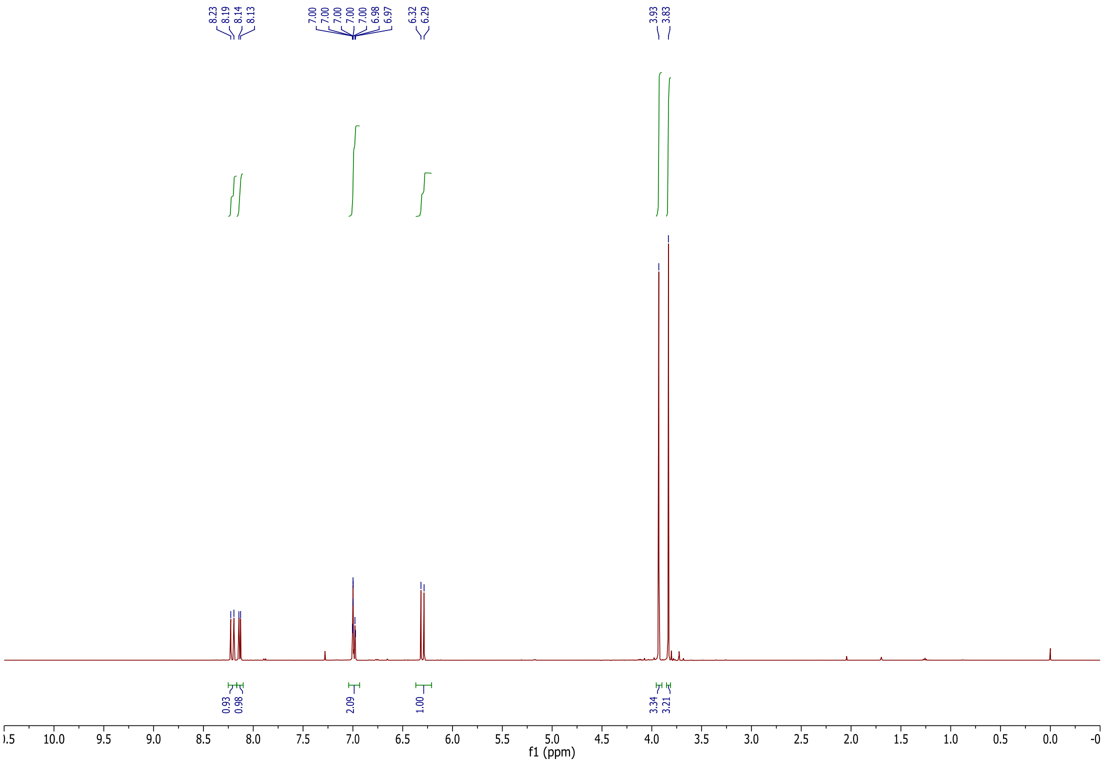
(S12)

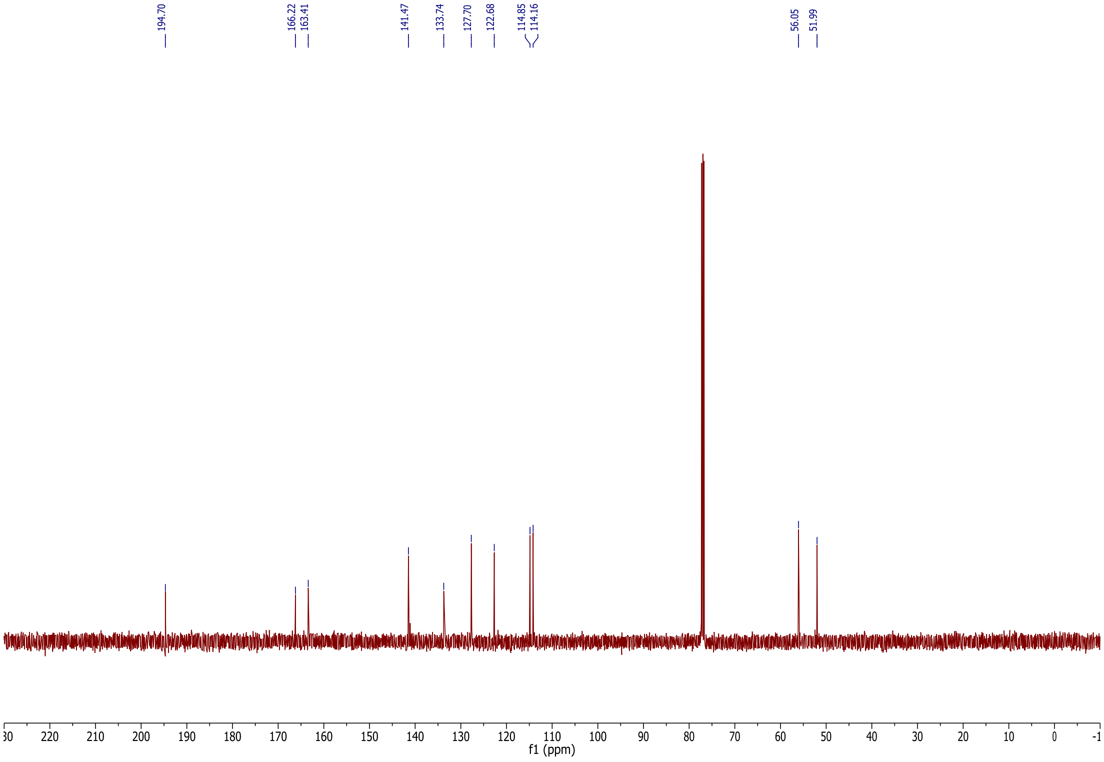

8.06
8.05
8.04
8.03
7.13
7.13
7.11
7.11
7.08
7.08
7.07
7.07
7.06
7.06
7.05
7.05
3.69
3.27
3.25
3.24
2.76
2.74
2.73
1.00
2.15
3.39
2.34
2.34
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

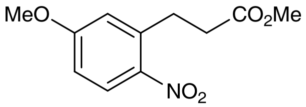

172.46
165.64
163.60
145.23
139.42
139.35
127.93
127.85
118.99
118.81
114.81
114.63
51.82
34.19
28.59
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


MeO
CO2Me
NO2

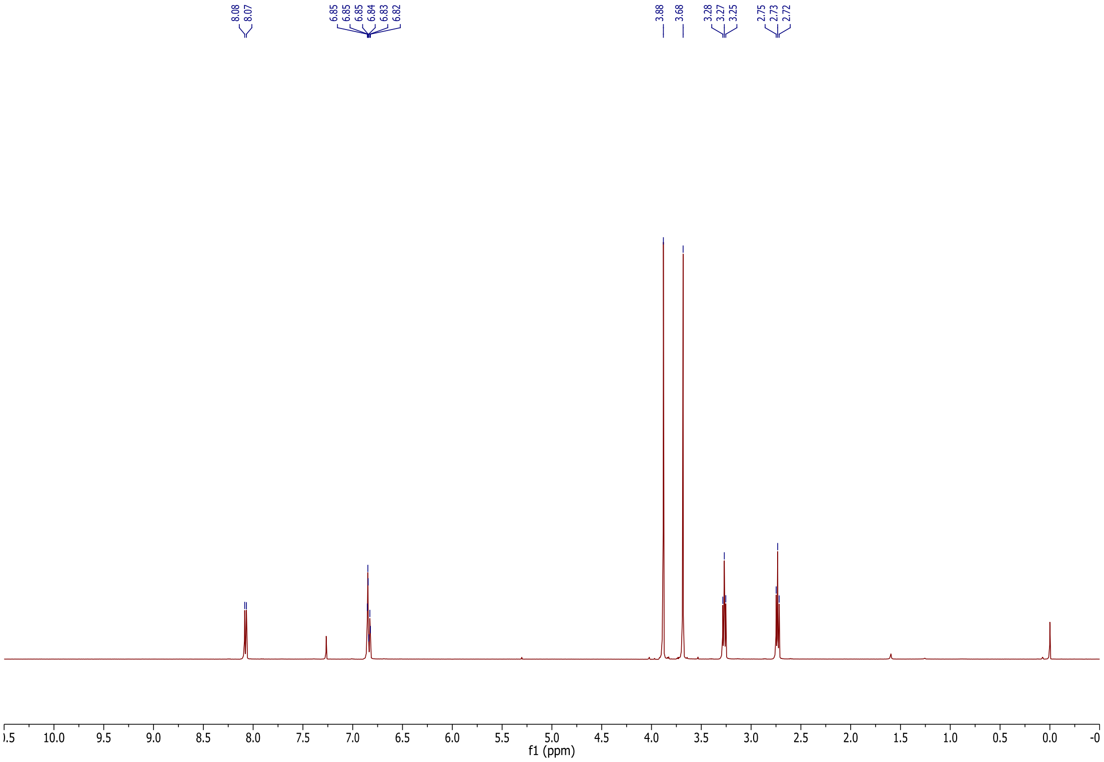
(S13)

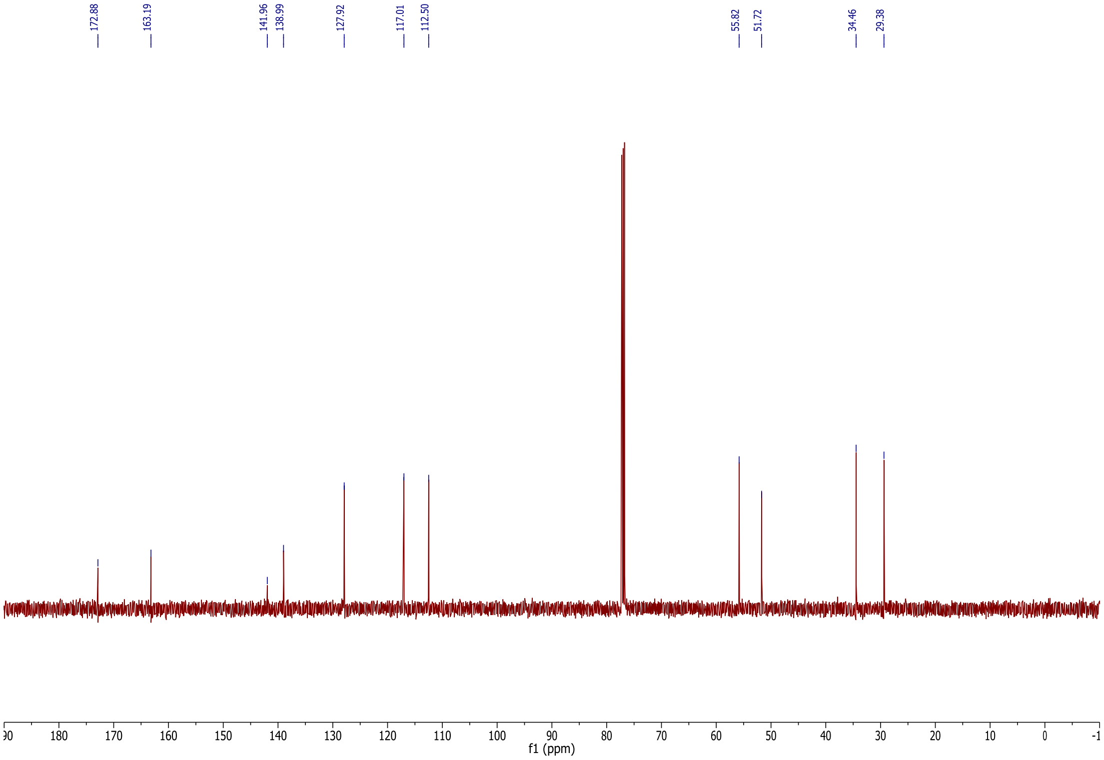

8.23
8.19
8.14
8.13
7.00
7.00
7.00
7.00
7.00
6.98
6.97
6.32
6.29
3.93
3.83
0.93
0.98
2.09
1.00
3.34
3.21
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

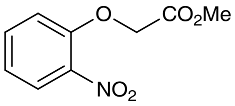

194.70
166.22
163.41
141.47
133.74
127.70
122.68
114.85
114.16
56.05
51.99
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


MeO
CO$_2$Me
NO$_2$

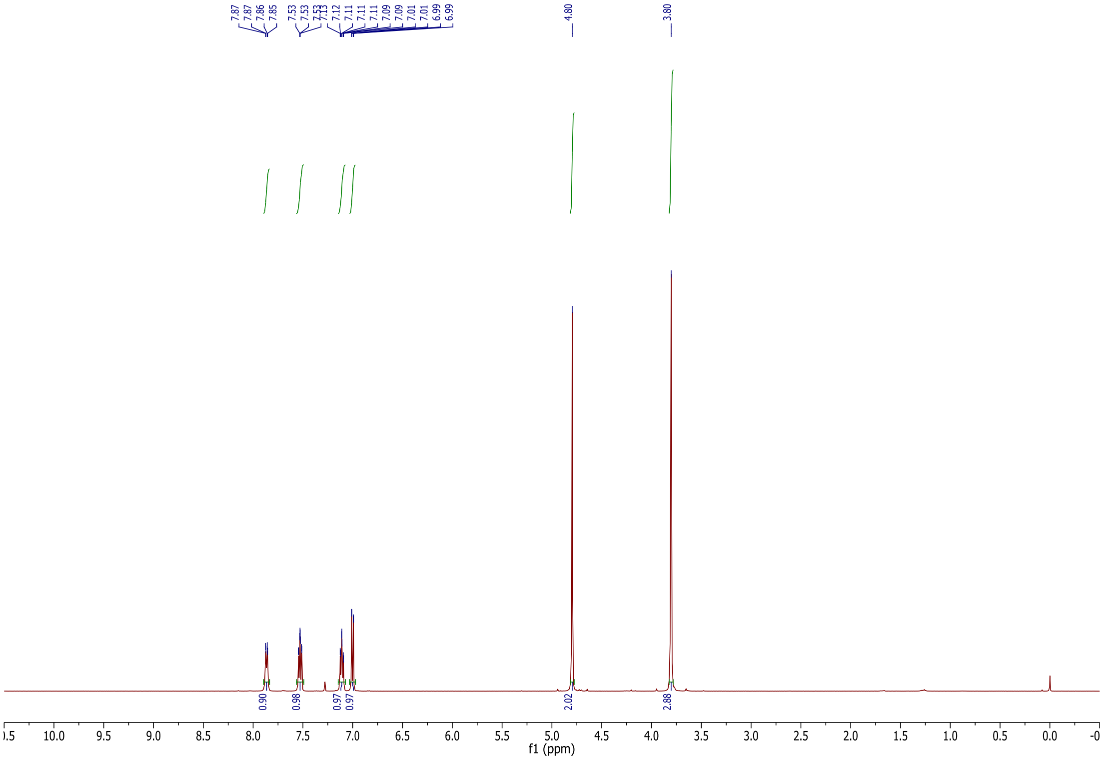
(S14)

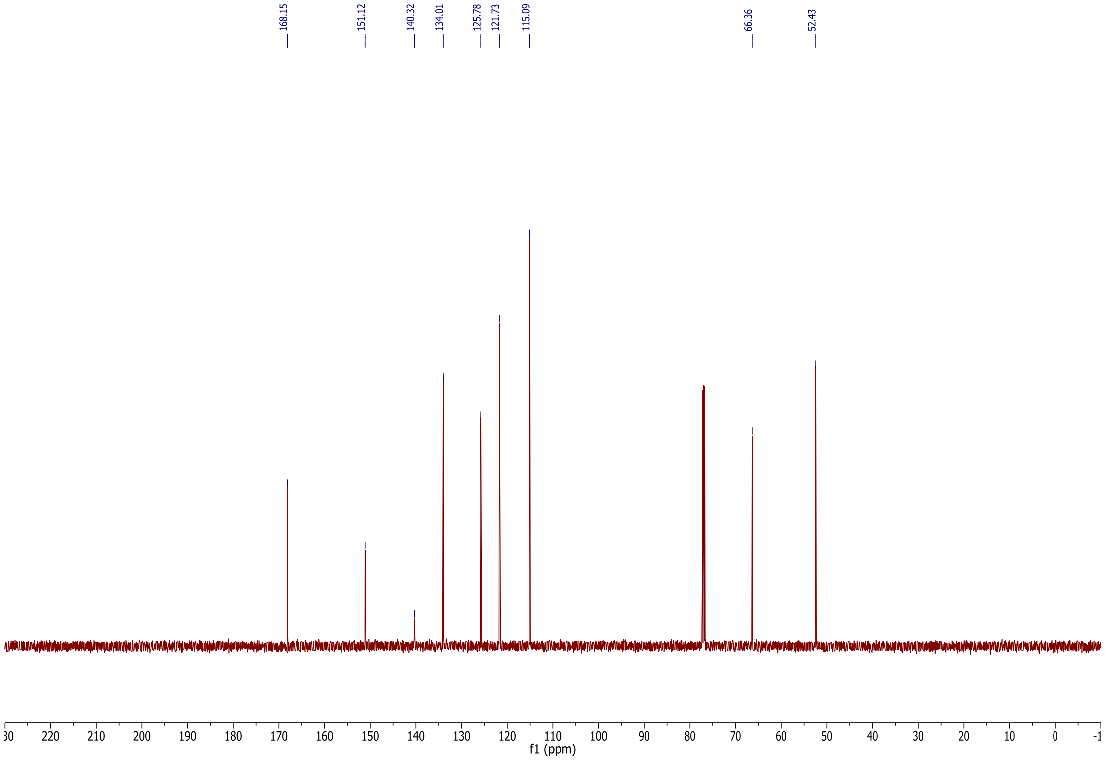

8.08
8.07
6.85
6.85
6.85
6.84
6.83
6.82
3.88
3.68
3.28
3.27
3.25
2.75
2.73
2.72
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

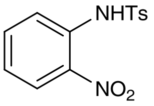

172.88
163.19
141.96
138.99
127.92
117.01
112.50
55.82
51.72
34.46
29.38
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
CO2Me
NO2

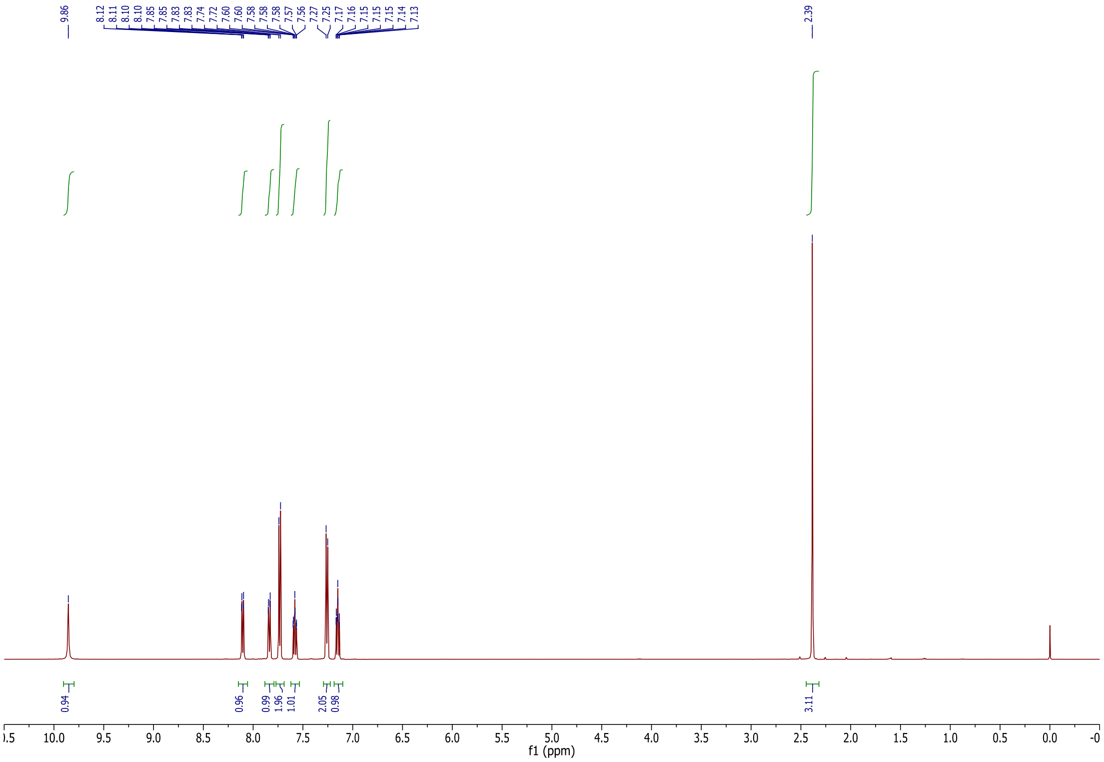
(S15)

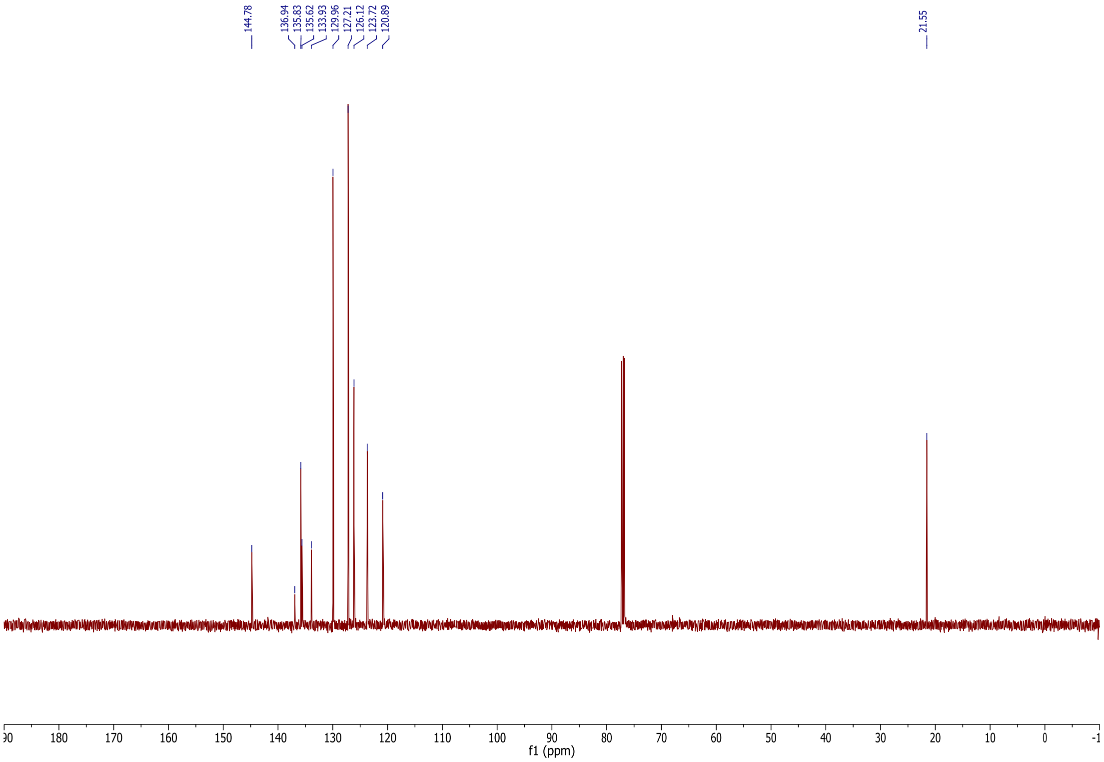

7.87
7.87
7.86
7.85
7.53
7.53
7.53
7.13
7.12
7.11
7.11
7.11
7.09
7.09
7.01
7.01
6.99
6.99
4.80
3.80
0.90
0.98
0.97
0.97
2.02
2.88
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

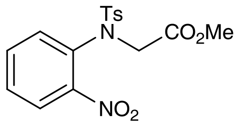

168.15
151.12
140.32
134.01
125.78
121.73
115.09
66.36
52.43
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


NHTs
NO2

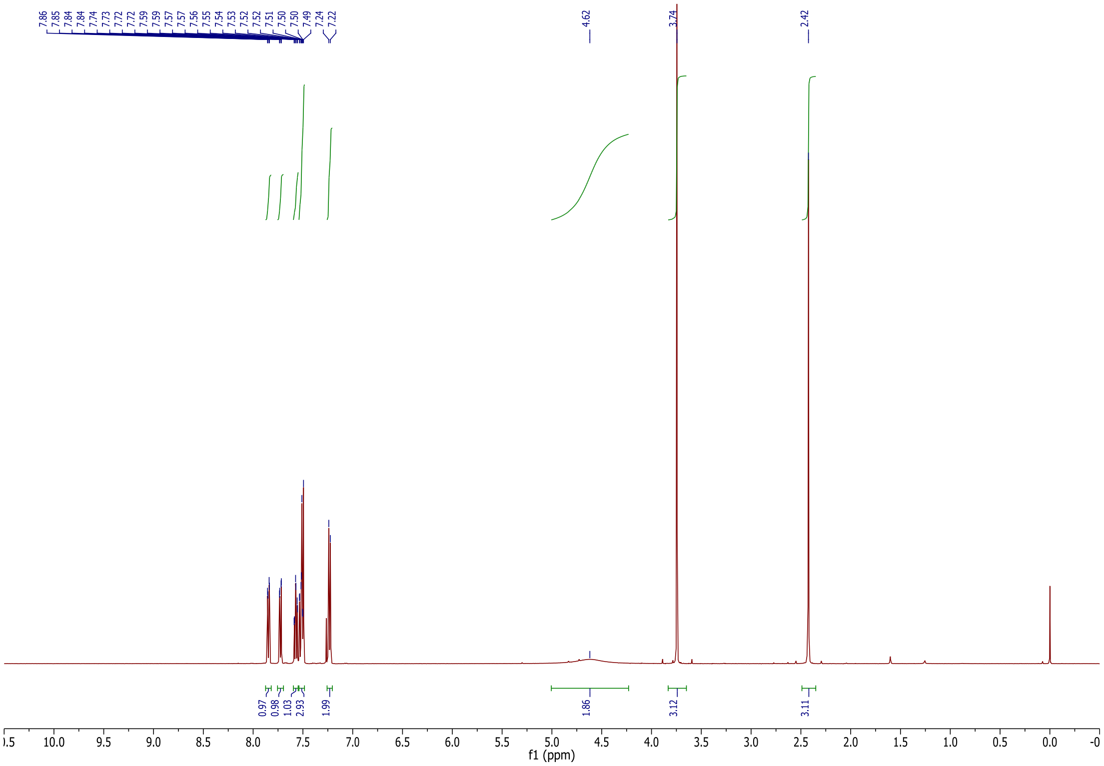
(S16)

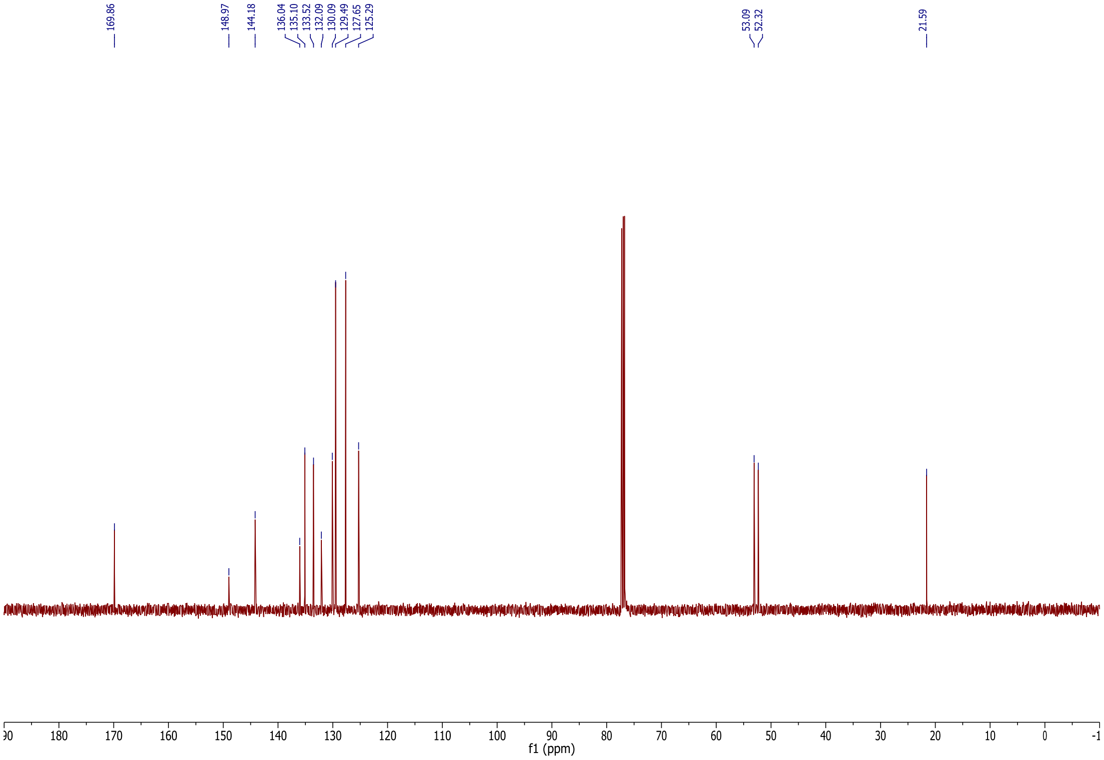

9.86
8.12
8.11
8.10
8.10
7.85
7.85
7.83
7.83
7.74
7.72
7.60
7.60
7.58
7.58
7.58
7.57
7.56
7.27
7.25
7.17
7.16
7.15
7.15
7.15
7.14
7.13
2.39
0.94
0.96
0.99
1.96
1.01
2.05
0.98
3.11
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

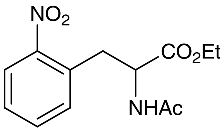

144.78
136.94
135.83
135.62
133.93
129.96
127.21
126.12
123.72
120.89
21.55
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Ts
N
CO2Me
NO2

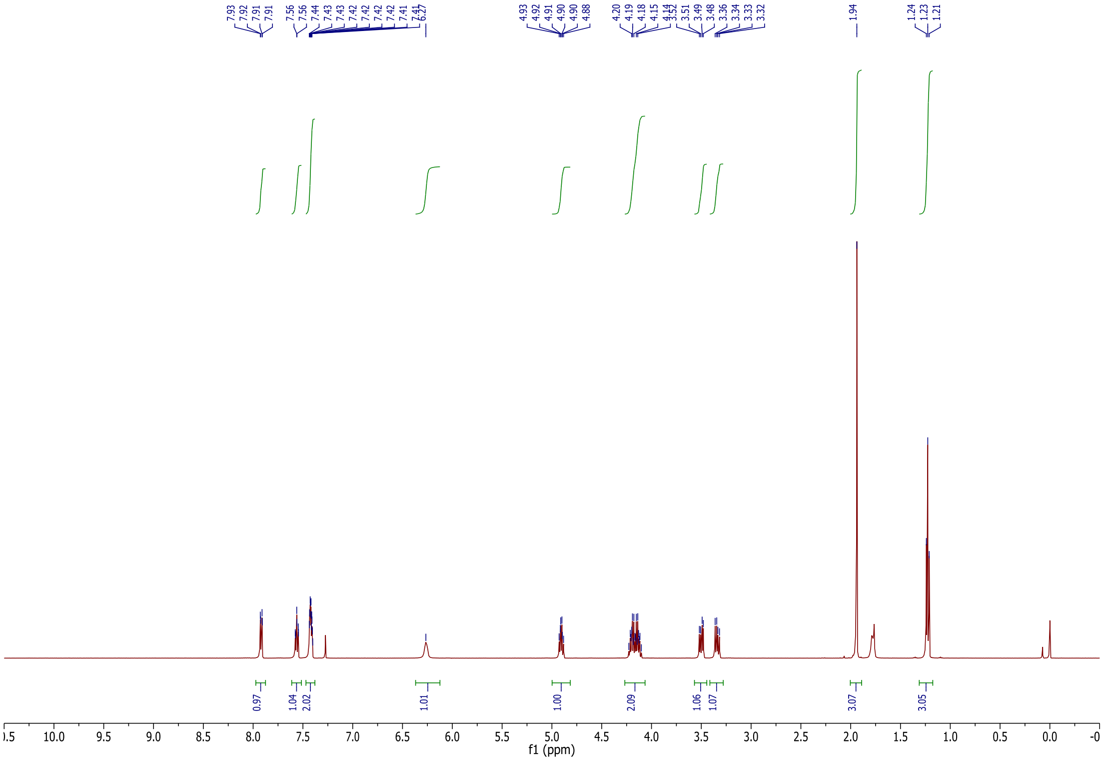
(S17)

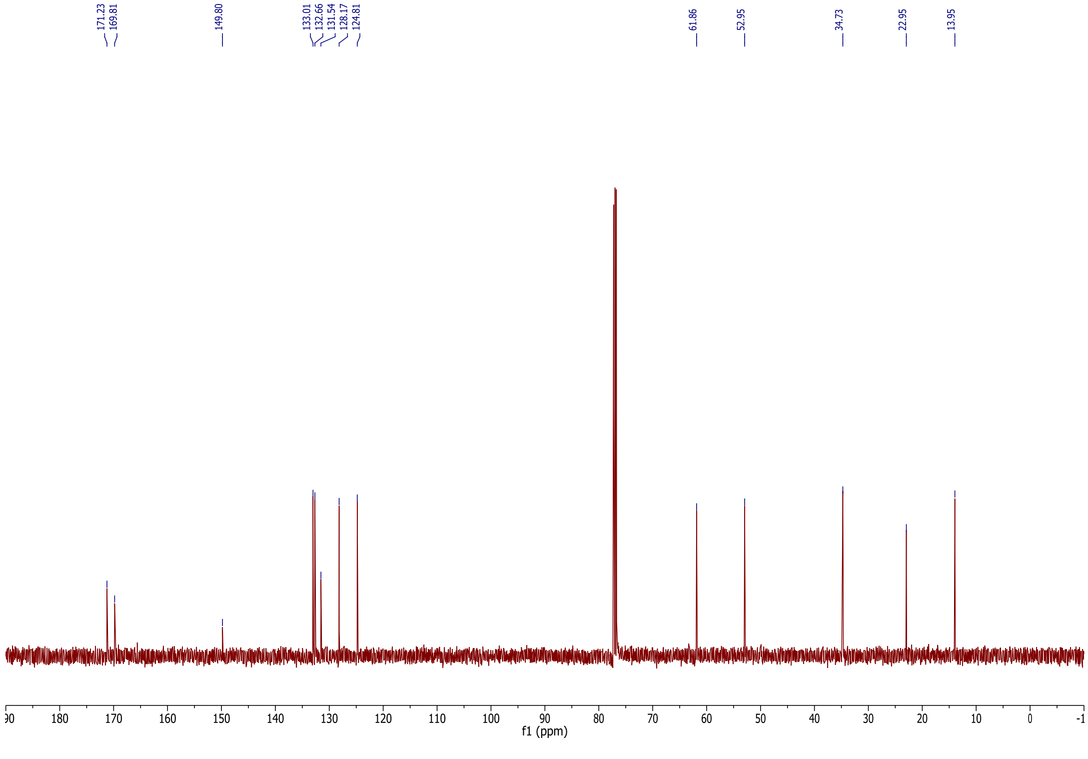

7.86
7.85
7.84
7.84
7.74
7.73
7.72
7.72
7.59
7.59
7.57
7.57
7.56
7.55
7.54
7.53
7.52
7.52
7.51
7.50
7.50
7.49
7.24
7.22
4.62
3.74
2.42
0.97
0.98
1.03
2.93
1.99
1.86
3.12
3.11
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

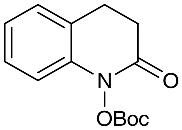

169.86
148.97
144.18
136.04
135.10
133.52
132.09
130.09
129.49
127.65
125.29
53.09
52.32
21.59
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


NO2
CO2Et
NHAc

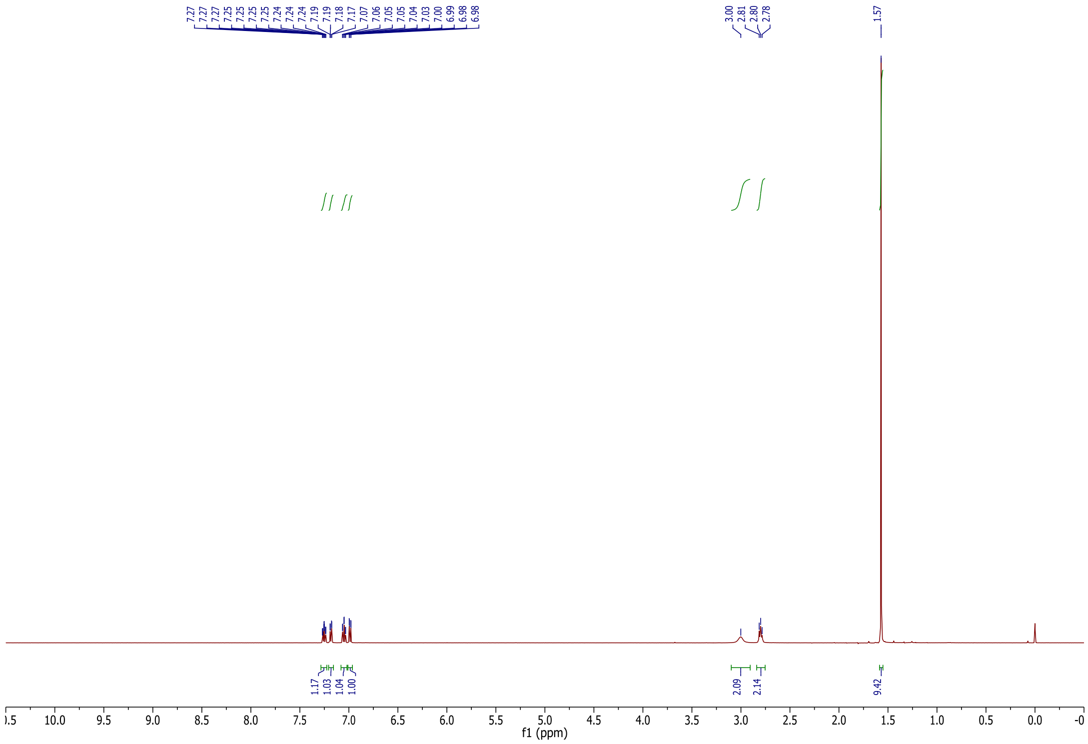
(S18)

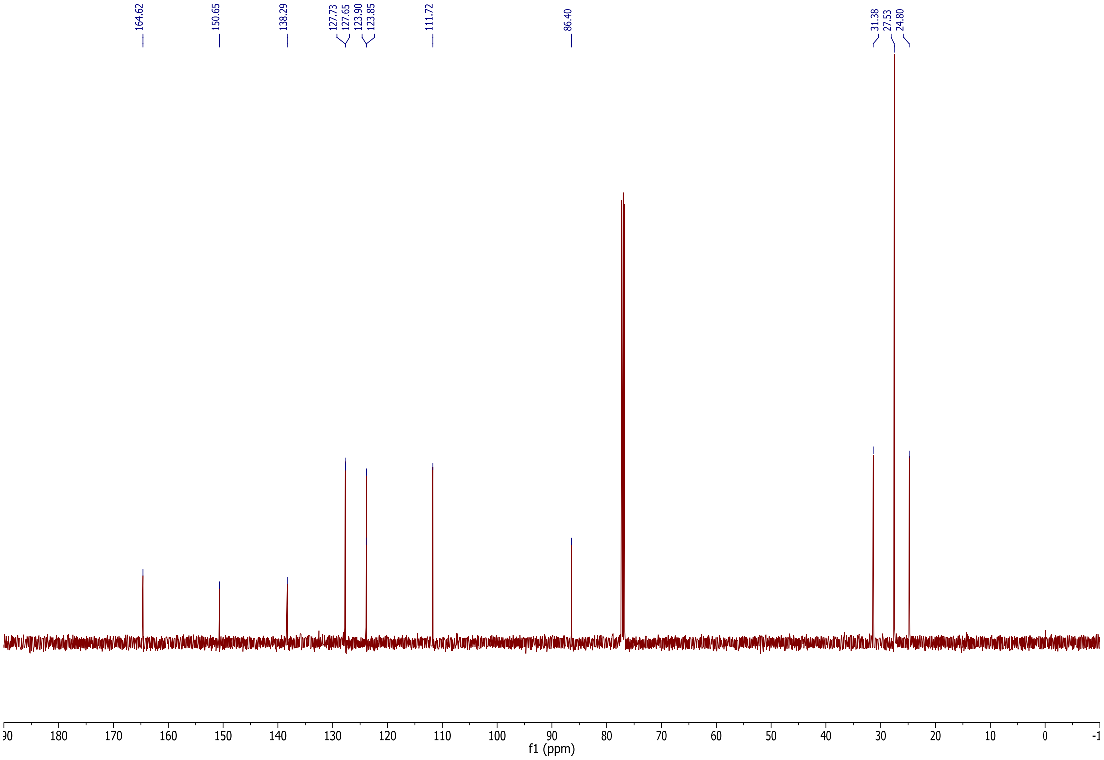

7.93
7.92
7.91
7.91
7.56
7.56
7.44
7.43
7.43
7.42
7.42
7.42
7.42
7.41
7.41
6.27
4.93
4.92
4.91
4.90
4.90
4.88
4.20
4.19
4.18
4.15
4.14
3.52
3.51
3.49
3.48
3.36
3.34
3.33
3.32
1.94
1.24
1.23
1.21
0.97
1.04
2.02
1.01
1.00
2.09
1.06
1.07
3.07
3.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

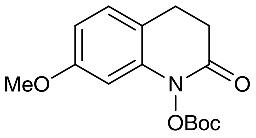

171.23
169.81
149.80
133.01
132.66
131.54
128.17
124.81
61.86
52.95
34.73
22.95
13.95
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



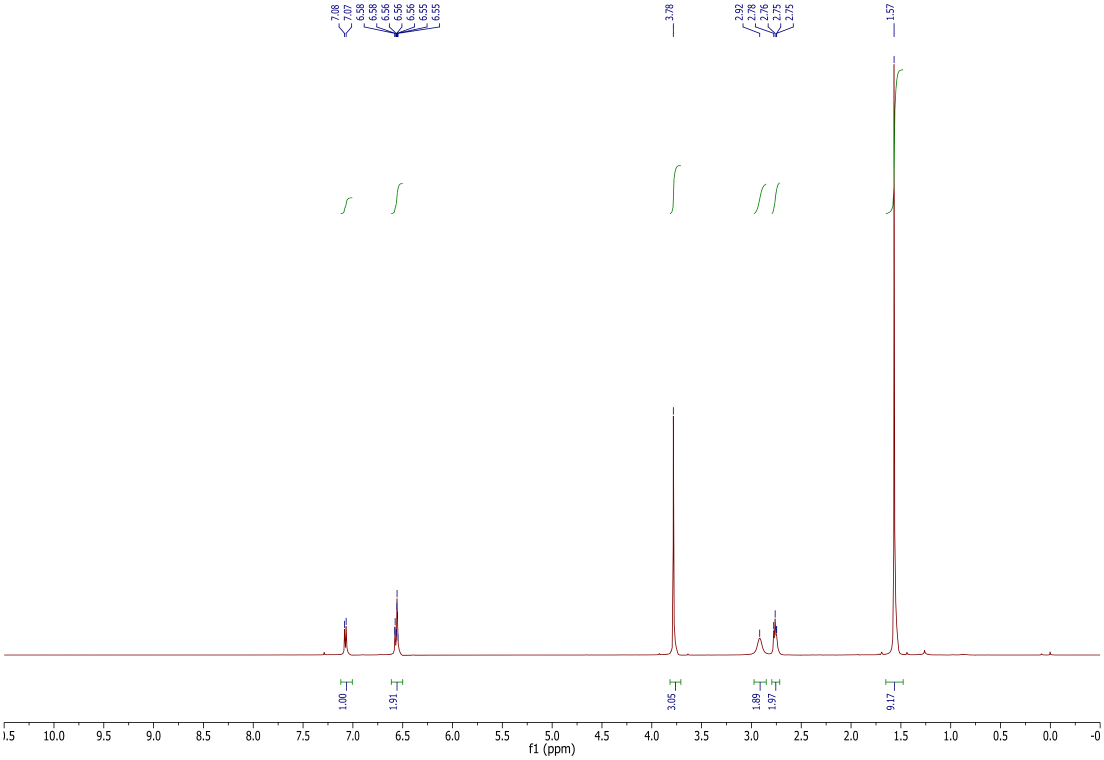
(Table 2, Entry 1)

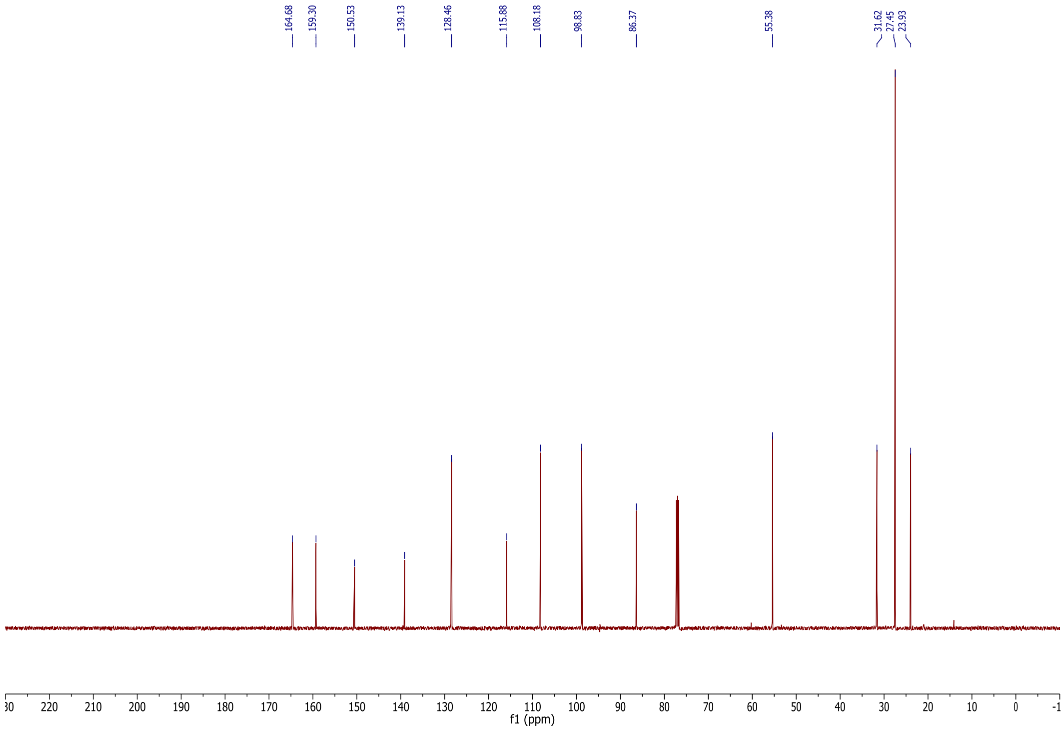


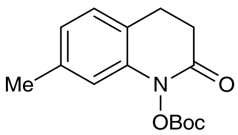




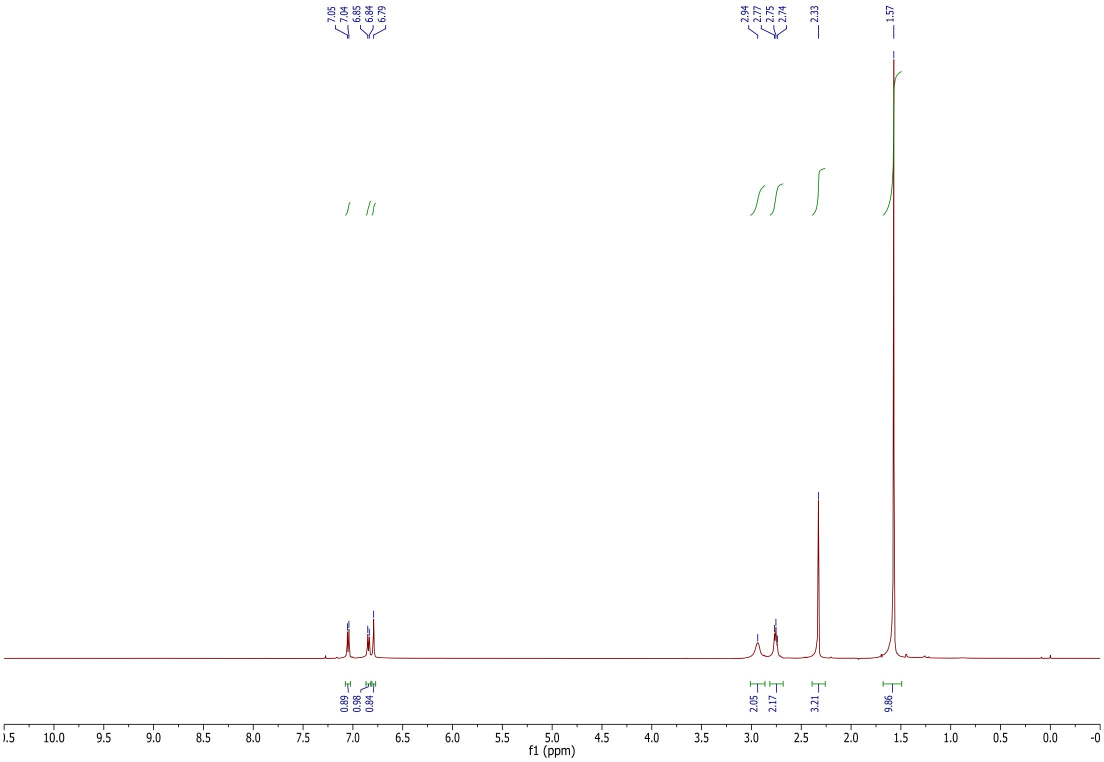
(Table 2, Entry 2)

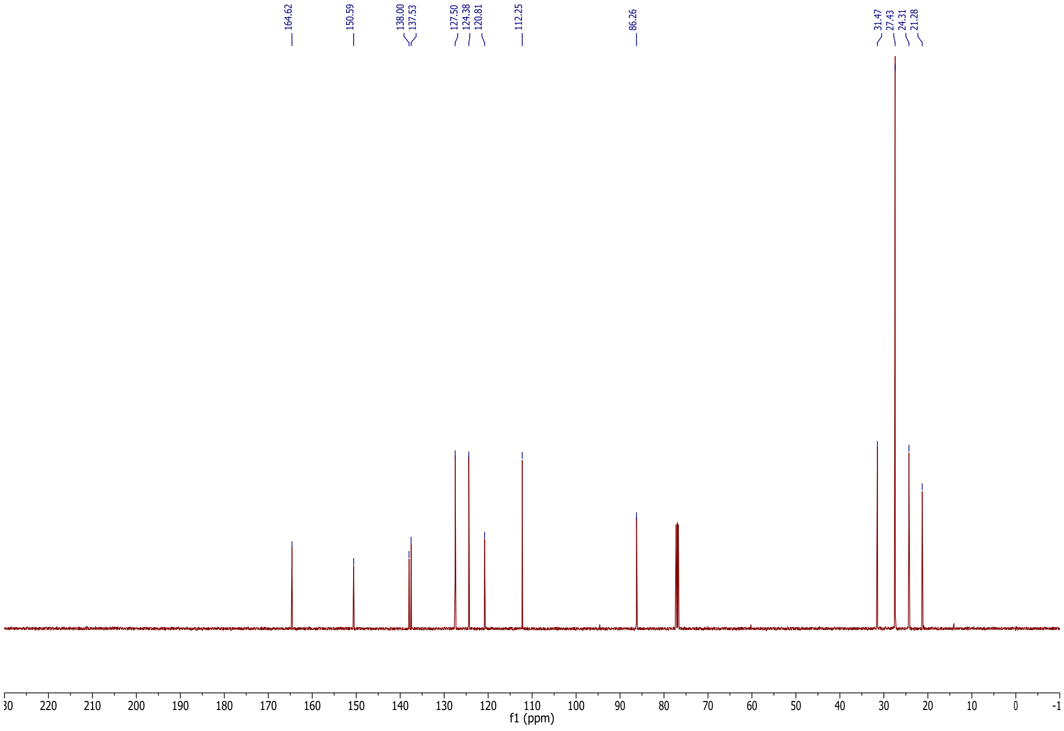


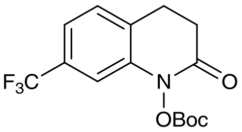




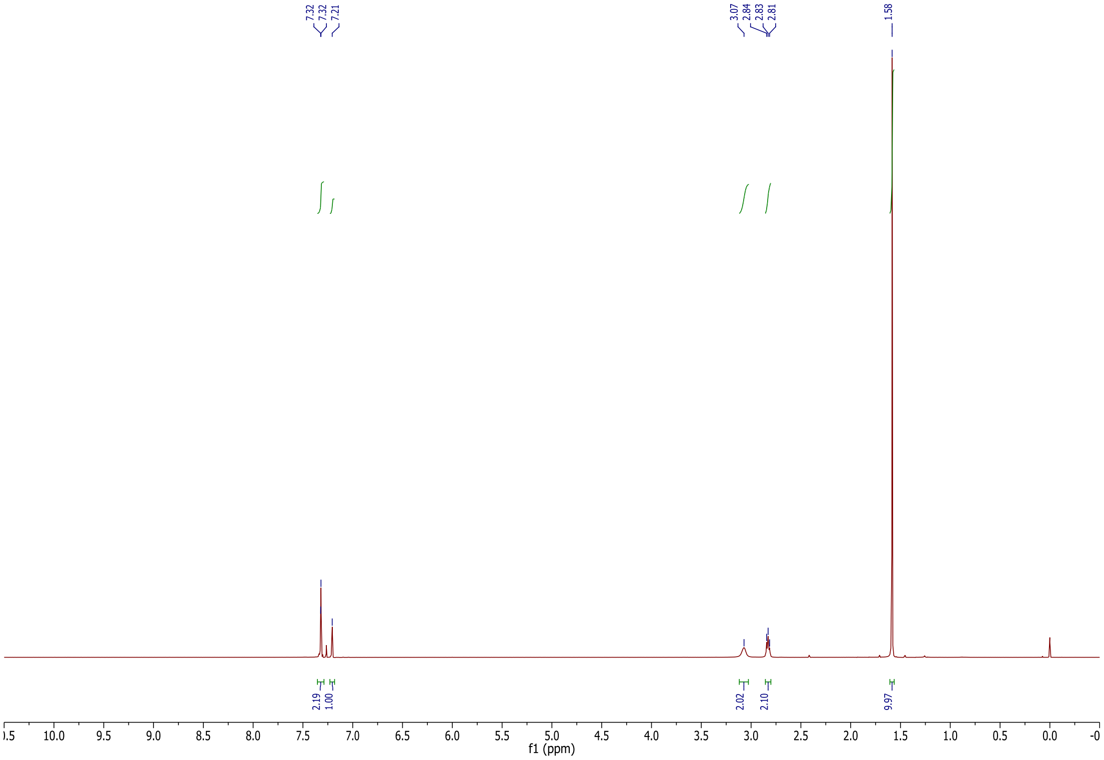
(Table 2, Entry 3)

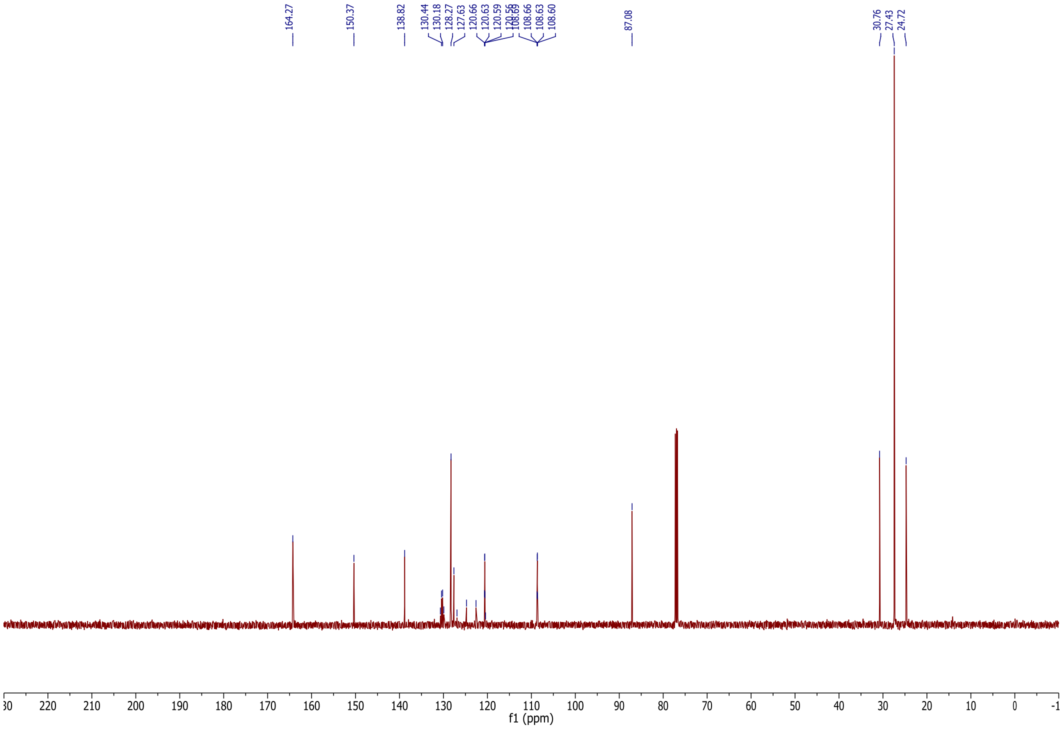


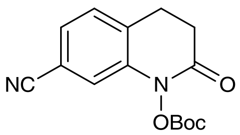




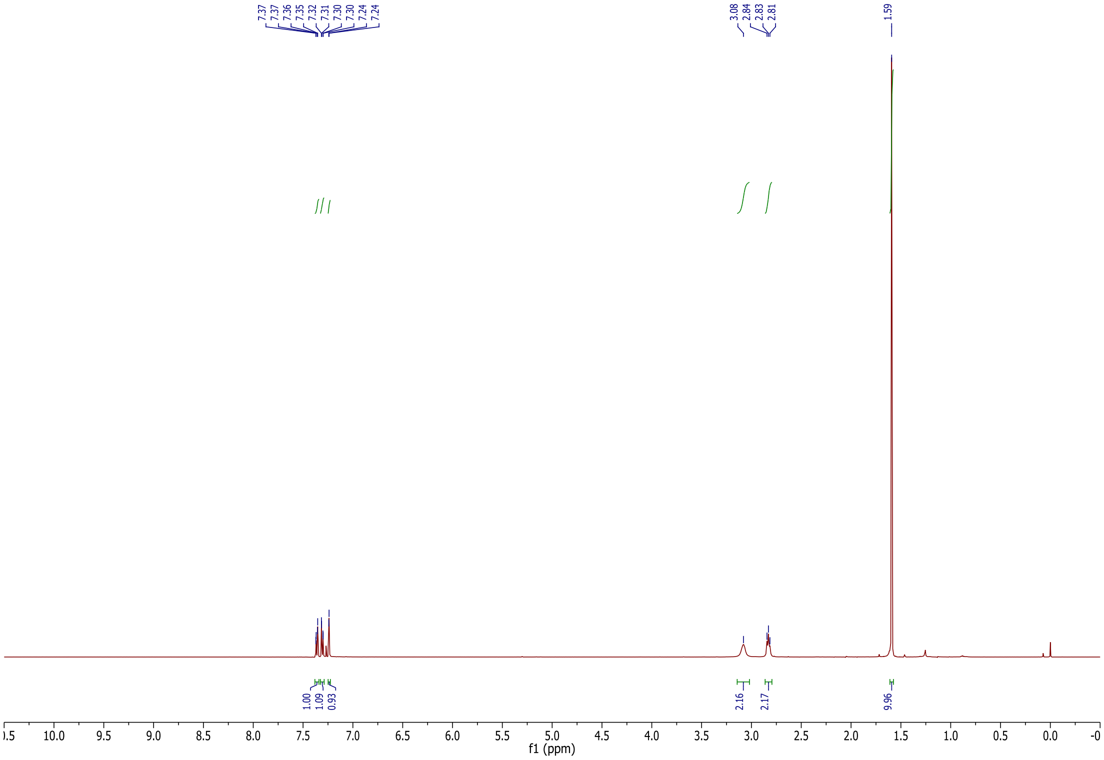
(Table 2, Entry 4)

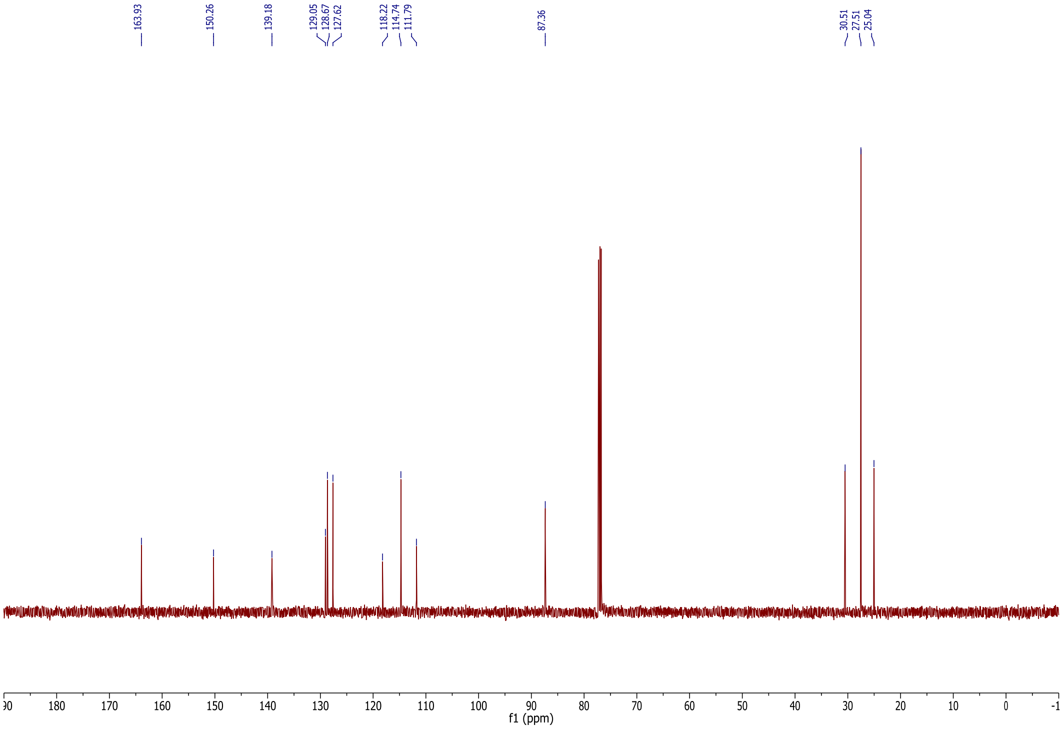


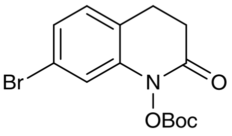




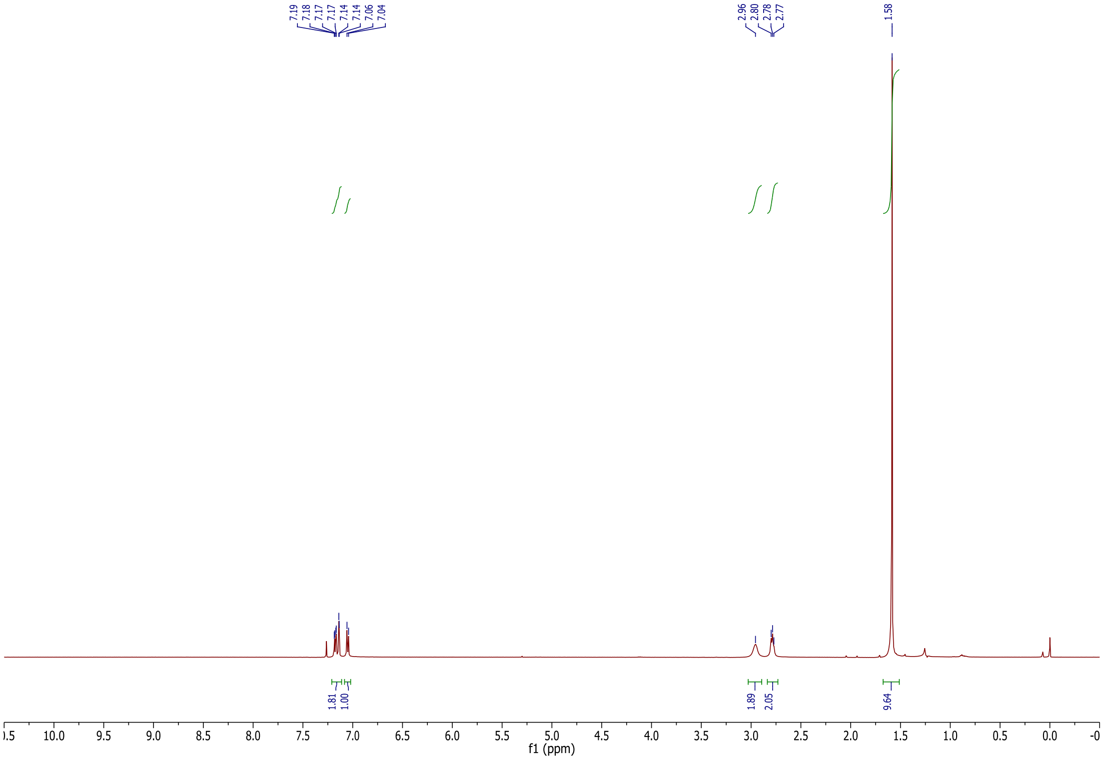
(Table 2, Entry 5)

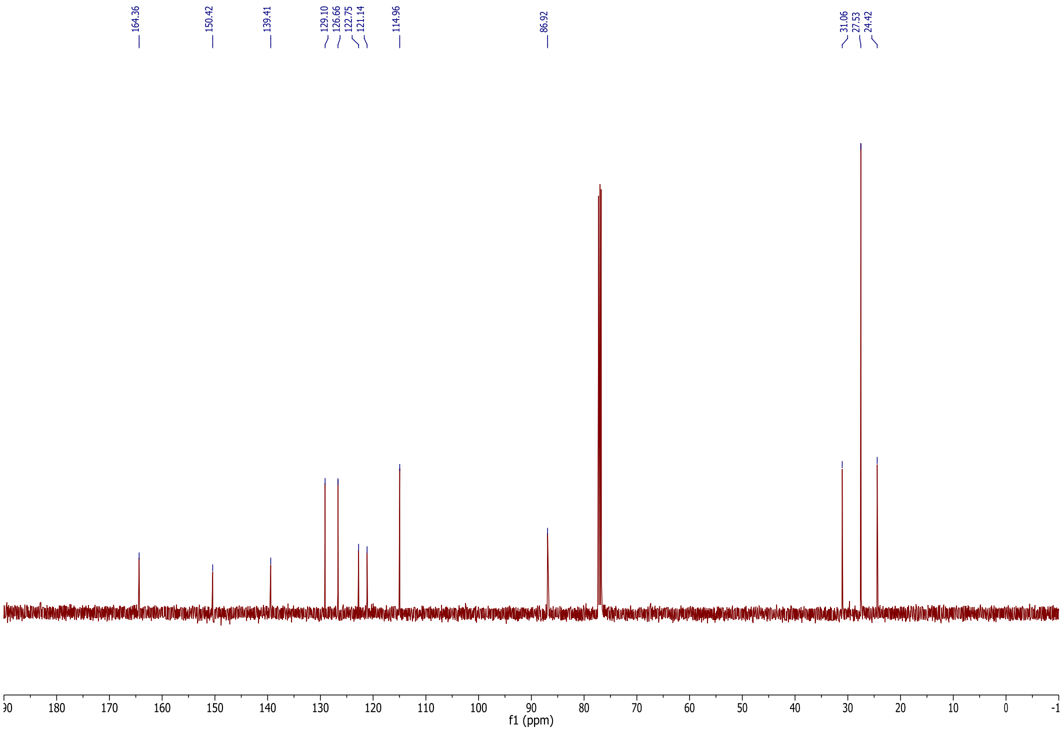


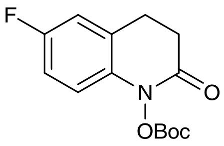




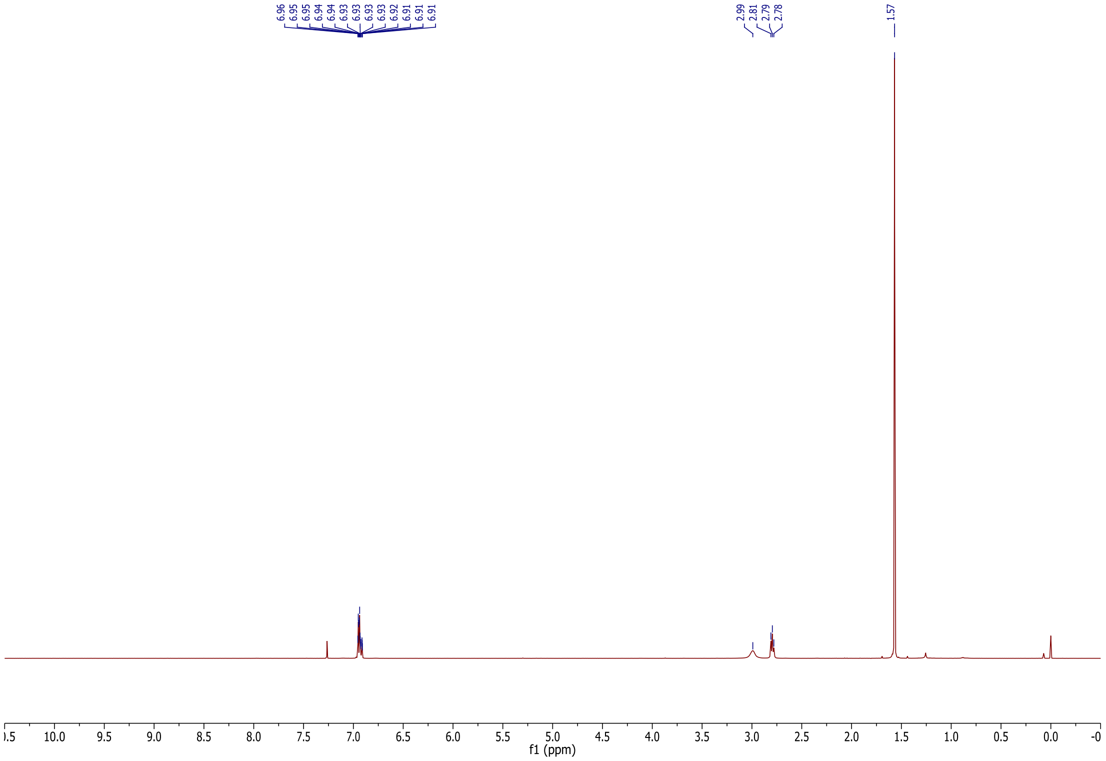
(Table 2, Entry 6)

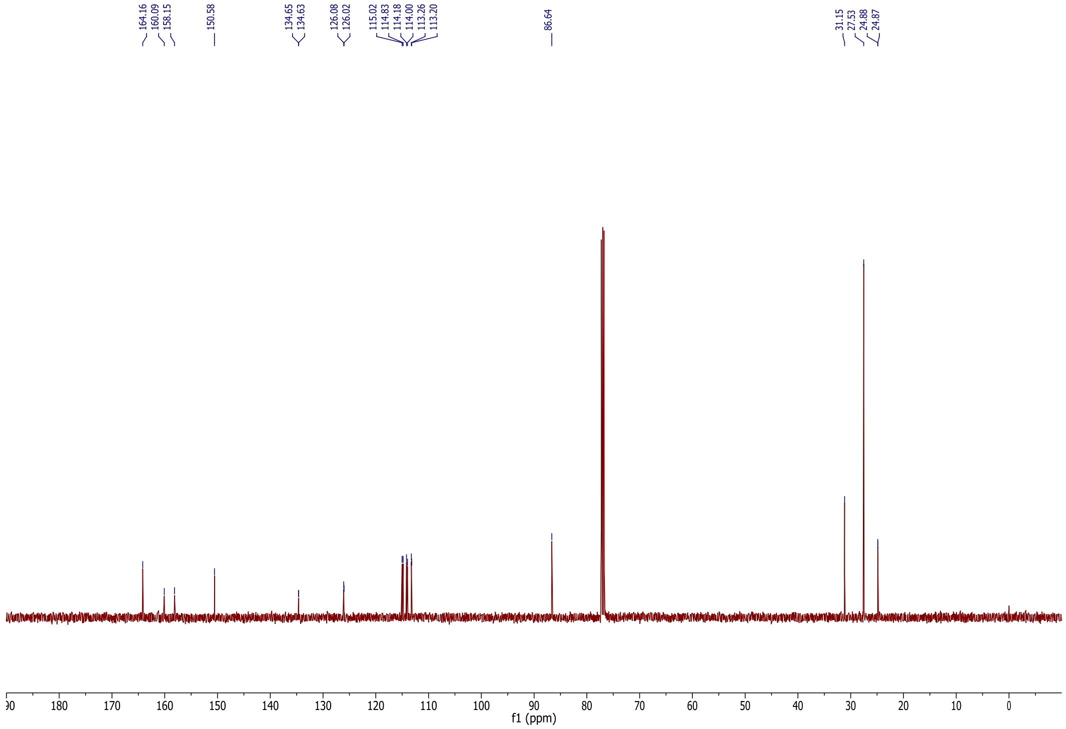


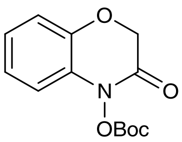




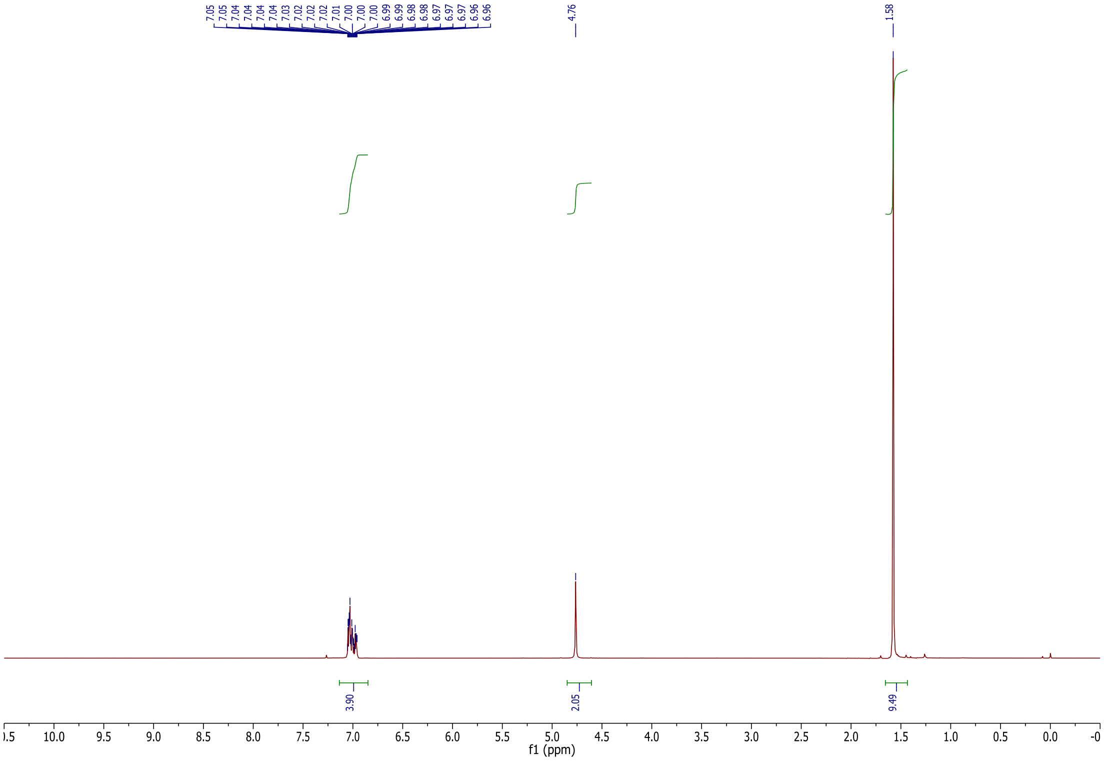
(Table 2, Entry 7)

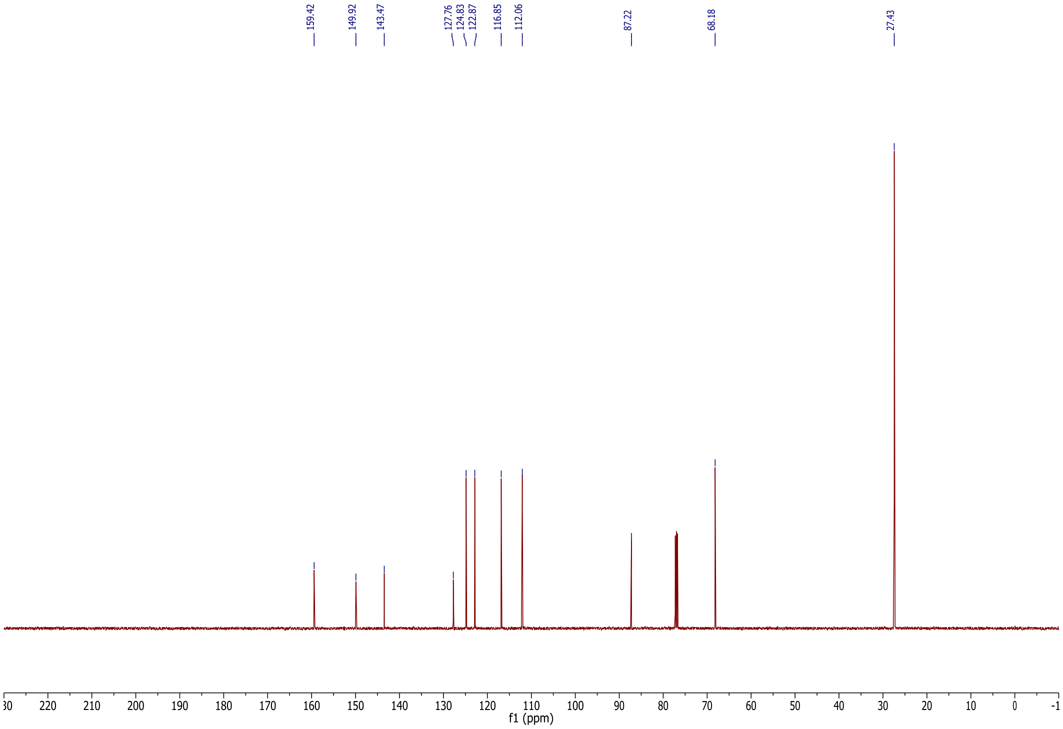


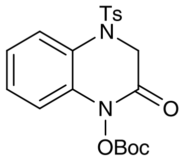




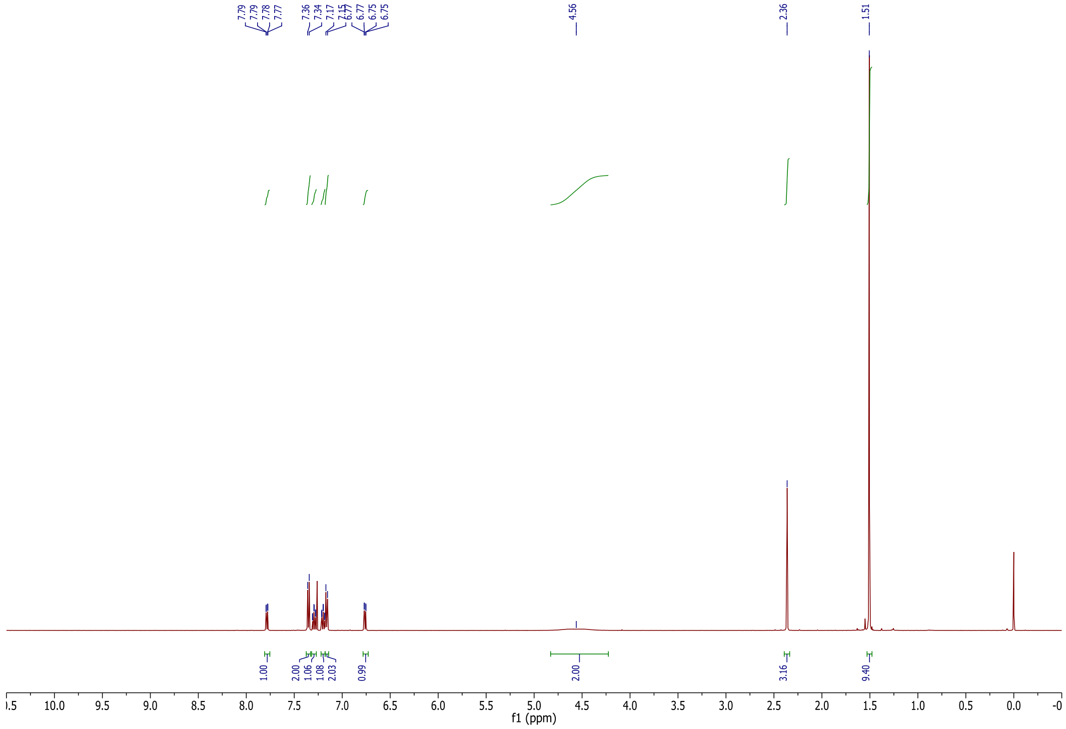
(Table 2, Entry 9)

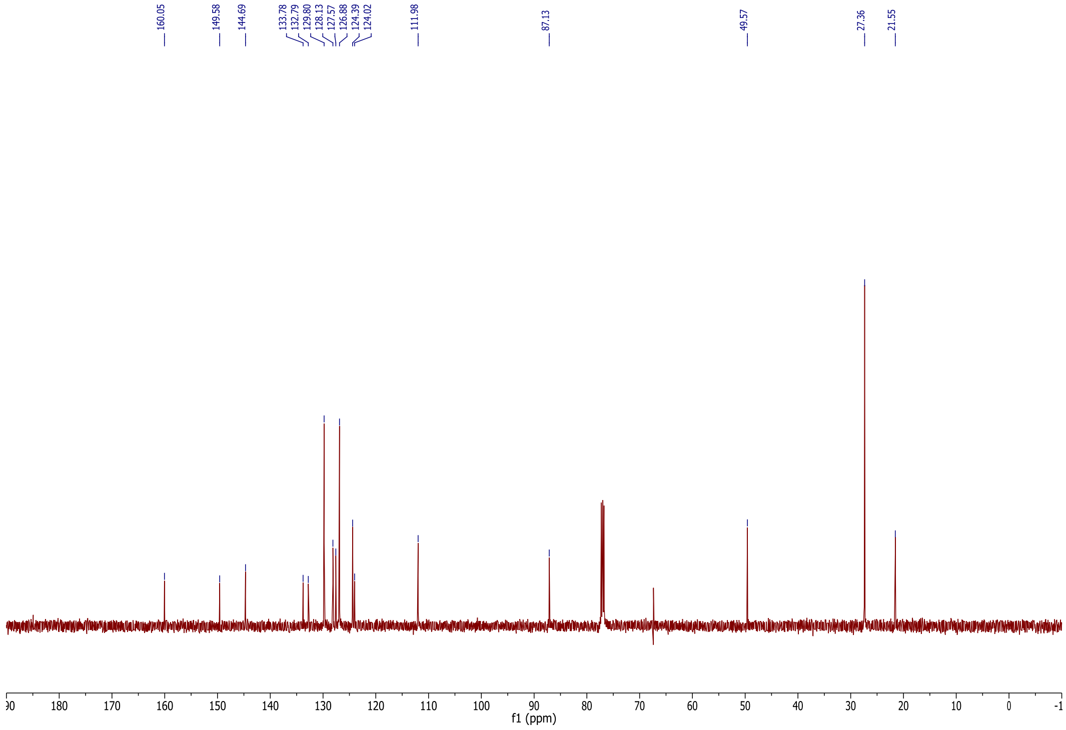


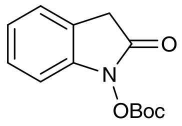




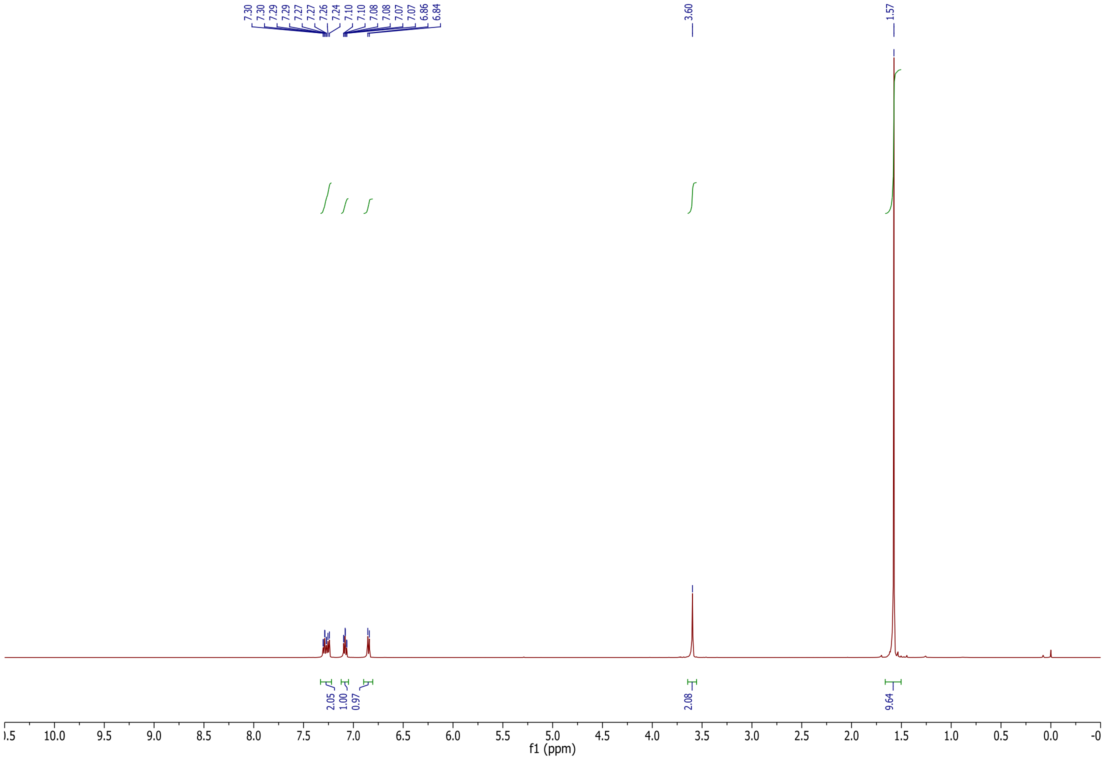
(Table 2, Entry 10)

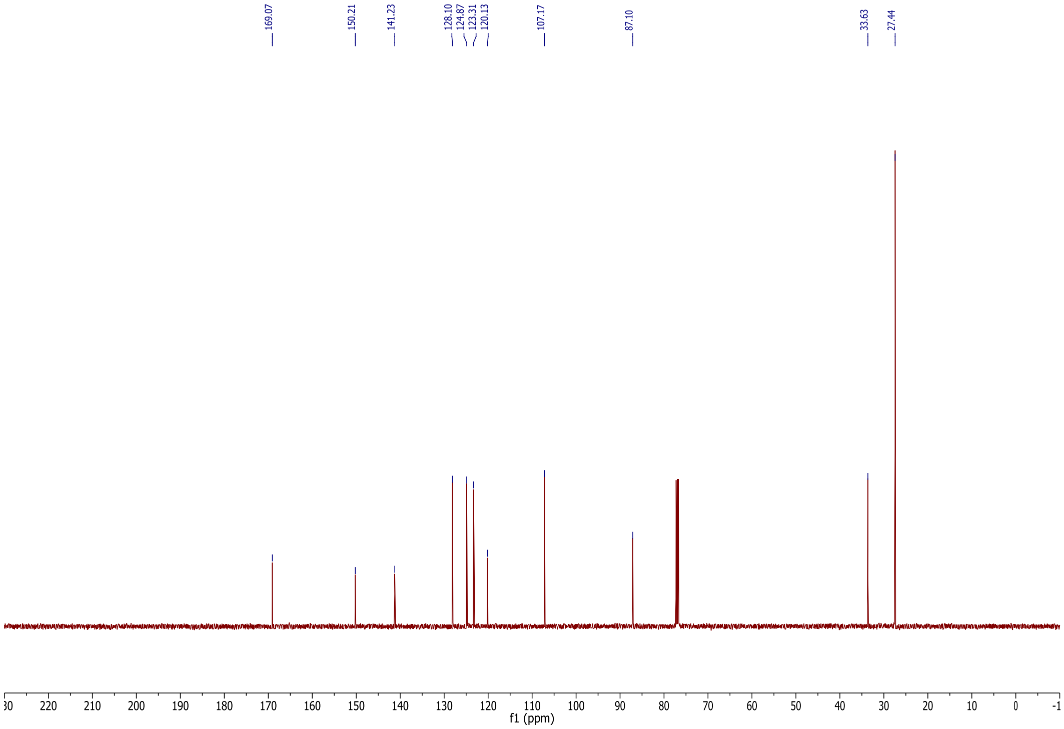


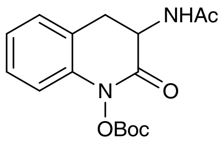




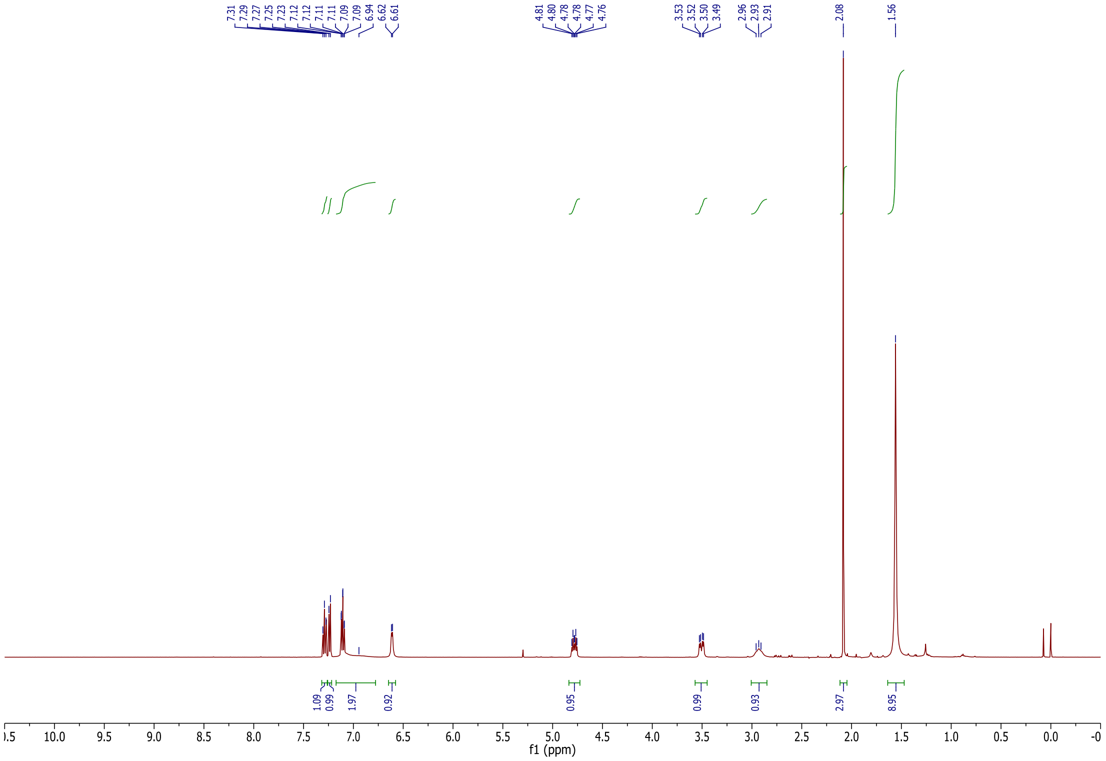
(Table 2, Entry 11)

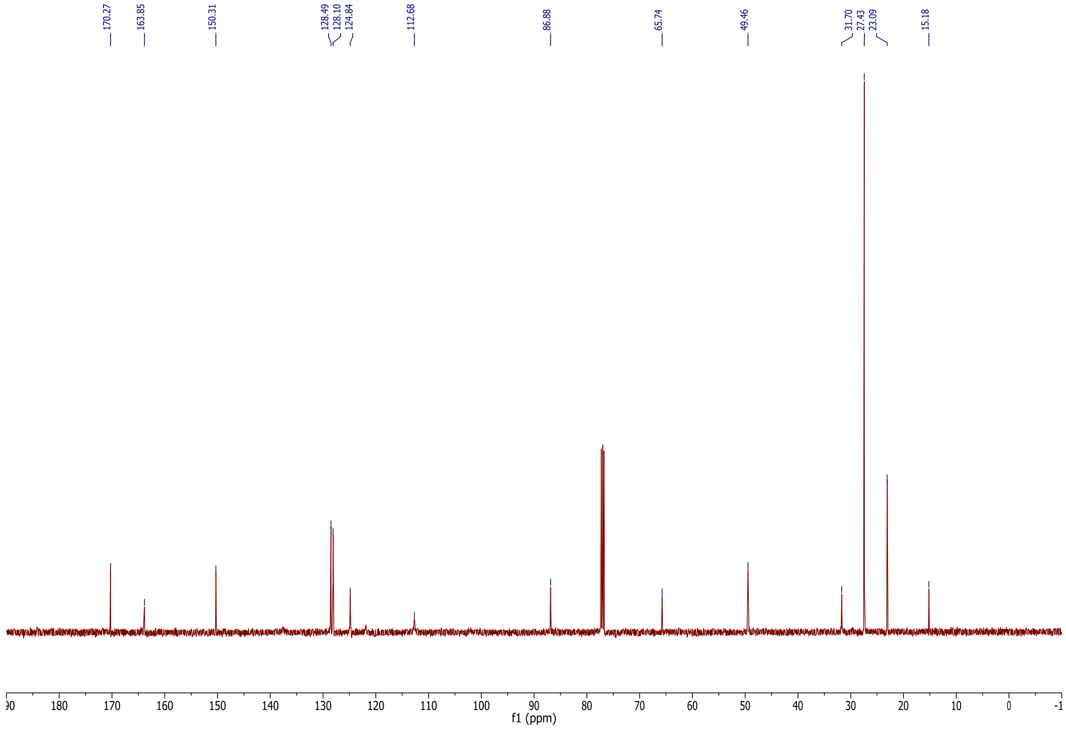


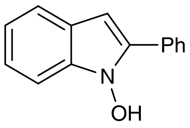




(Table 2, Entry 12)







(Equation 1, 12)