Copper-Catalyzed Olefinic C-H Trifluoromethylation of Enamides at Room Temperature

Chao Feng and Teck-Peng Loh*

Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371

teckpeng@ntu.edu.sg.

Supporting Information

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General information

$Cu(MeCN)_4PF_6$, CuCl, anhydrous MeOH were purchased from commercial suppliers and used as received unless otherwise noted. All reactions were carried out using standard Schlenk technic. THF was freshly distilled under sodium/benzophenone ketyl. Reactions were monitored through thin layer chromatography [Merck 60 F254 precoated silica gel plate (0.2 mm thickness)]. Subsequent to elution, spots were visualized using UV radiation (254 nm) on Spectroline Model ENF-24061/F 254 nm. Further visualization was possible using basic solution of potassium permanganate or acidic solution of ceric molybdate as stain, followed by heating on a hot plate. Flash chromatography was performed using Merck silica gel 60 with distilled solvents. HRMS spectra were recorded on a Waters Q–Tof Permier Spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded using Bruker Avance 400 MHz spectrometers. ^{19}F spectra were recorded (external standard α,α,α-trifluorotoluene (-63.73 ppm) ^{19}F) using Bruker Avance 300 MHz spectrometers. Chemical shifts for ^{1}H NMR spectra are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of $SiMe_4$ (δ 0.00, singlet). Multiplicities were given as: s (singlet); brs (broad singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet); ddd (doublets of doublets of doublet); td (triplet of doublet); m (multiplets); ddt (doublet of doublet of triplet) and etc. Coupling constants are reported as a *J* value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-*d* (δ 77.00, triplet).

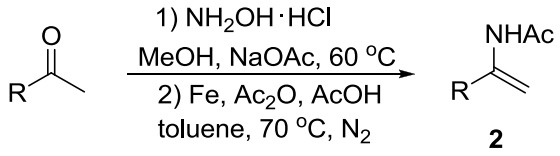
Experimental section

Substrate synthesis

2a-2d, 2g-2r were synthesized using reported method.[1]

Tognis' reagent 1 was synthesized following the reported method.[2]

General reaction scheme



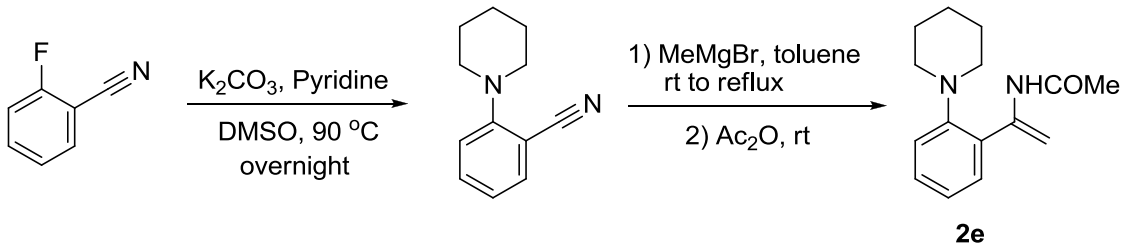
2

Synthetic procedure: a) A mixture of ketone (10 mmol), NaOAc (12 mmol) and hydroxylamine hydrochloride (12 mmol) in methanol (5mL) was stirred for 2 h at 60 ºC. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate (2×50 mL) dried over $MgSO_4$. The organic solvent was evaporated to afford the ketoxime pure enough for next step. b) To an oven-dried 50 mL two-neck RBF assembled with condenser was added ketoxime. The flask was vacuumed and backfilled with N_2 for three times. Anhydrous toluene (20 mL) was added followed by acetic anhydride (30 mmol), acetic acid (30 mmol) and iron powder (20 mmol). The reaction flask was put into a 70 °C preheated oil bath and allowed to stir for 5 hours under nitrogen atmosphere. After cooling to room temperature, ethyl acetate was added and the mixture was filtered through a short pad of celite. The solution thus obtained was evaporated to product crude enamide, which was directly purified by column chromatography.

[1] a) M. Berg, R. M. Haak, A. J. Minnaard, A. H. M. Vries, J. G. Vries, B. L. Feringa, *Adv. Synth. Catal*. 2002, **344**, 1003; b) M. J. Burk, G. Casy, N. B. Johnsonn, *J. Org. Chem.* 1998, **63**, 6084; c) H. Zhou, W. J. Chung, Y. H. Xu, T. P. Loh, *Chem. Commun*. 2009, 3472.

[2] K. Stanek, R. Koller, A. Togni, *J. Org. Chem.* 2008, **73**, 7678.

Reaction scheme for 2e synthesis

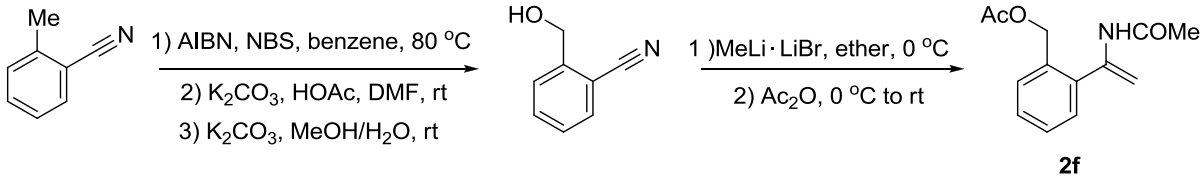


2e

Synthetic procedure: a) An 50 mL RBF was charged with 2-fluorobenzonitrile (10 mmol), K_2CO_3 (20 mmol), pyridine (12 mmol), and DMSO (5 mL) sequentially. The reaction flask was subjected to a 90 ^oC preheated oil bath and stirred overnight, at which time the resulting mixture was cooled down to room temperature, diluted with ethyl acetate, and washed thoroughly with water. Removal of the solvent in *vacuo* and purification of the residue by silica gel column chromatography afforded the desired product 2-(piperidin-1-yl)benzonitrile in 90% yield.

b) To an oven-dried 50 mL two-neck RBF assembled with condenser was added 2-(piperidin-1-yl)benzonitrile and dry toluene (15 mL). MeMgBr (12 mmol, 3M in ether) was added to the solution under N_2 at room temperature. After stirring 10 minutes, the mixture was subjected to a 110 ^oC preheated oil bath and stirred overnight. After cooling to room temperature, Ac_2O (15 mmol) was added into the solution dropwise and the resulting mixture was stirred at room temperature for 2 hours, at which time saturated $NaHCO_3$ solution was added followed by extraction with ethyl acetate (2×50 mL), and drying over $MgSO_4$. The organic solvent was evaporated and the residue was subjected to column chromatography on silica gel to deliver the product **2e** in 56% yield.

Reaction scheme for 2f synthesis



2f

Synthetic procedure: a) The mixture of *o*-tolunitrile (20 mmol), NBS (21 mmol), and AIBN (1 mmol) in benzene (20 ml) was stirred at 80 °C for 1 h. After cooling to room temperature, the reaction was quenched with water and the mixture was extracted with ether followed by drying over $MgSO_4$. The organic solvent was evaporated to give the residue which is used directly in next step without purification.

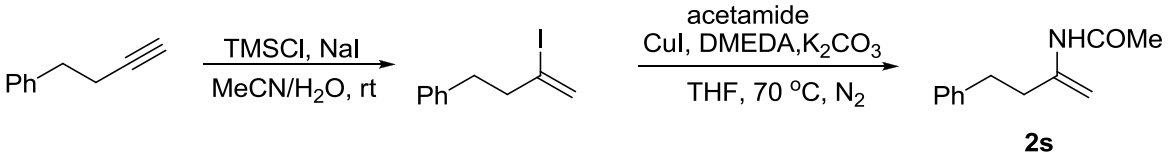
b) To a suspension of AcOH (80 mmol) and K_2CO_3 (80 mmol) in DMF (90 mL) was added the crude 2-(bromomethyl)benzonitrile in DMF (10 mL) at room temperature, and the mixture was stirred at the same temperature for 1 hour. After quenching with water the mixture was extracted with ether followed by drying over $MgSO_4$. The organic solvent was evaporated to give the residue which is used directly in next step without purification.

c) To a suspension of K_2CO_3 (100 mmol) in 30 mL MeOH/H_2O (2:1) was added the above obtained 2-cyanobenzyl acetate. The mixture was stirred at room temperature and the progress of reaction was monitored through TLC. Once the reaction finished, water was added and thus resulting solution was extracted with ethyl acetate. After drying over $MgSO_4$, the organic solvent was evaporated and the residue was subjected to silica gel column chromatography to afford the desired product 2-(hydroxymethyl)benzonitrile in 75% yield.

d) To an oven-dried 50 mL two-neck RBF assembled with condenser was added 2-(hydroxymethyl)benzonitrile (5 mmol) and dry ether (10 mL). MeLi·LiBr

(7.5 mmol, 1M in ether) was slowly added into the solution under N_2 at 0 ^oC. After stirring for 2 hours at the same temperature, Ac_2O (15 mmol) was added and the resulting mixture was stirred at room temperature overnight. Saturated $NaHCO_3$ solution was added followed by extraction with ethyl acetate (2×50 mL), and drying over $MgSO_4$. The organic solvent was evaporated and the residue was subjected to column chromatography on silica gel to deliver the product **2f** in 23% yield.

Reaction scheme for 2s synthesis



2s

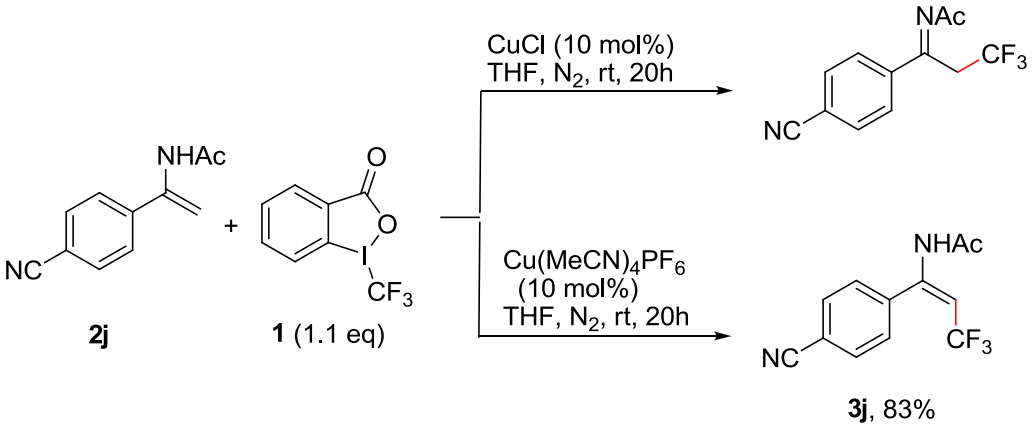
Synthetic procedure: a) At room temperature TMSCl (10 mmol) was added to a solution of NaI (10 mmol) in MeCN (10 mL) followed by H_2O (5 mmol). After stirring for 10 minutes, but-3-ynylbenzene (6 mmol) was added and the resulting solution was stirred for 1 hour at room temperature. The reaction was quenched with H_2O (20 mL) and extracted with ethyl acetate followed by drying over $MgSO_4$. The organic solvent was evaporated to give the crude (3-iodobut-3-enyl)benzene, which is used directly in next step without further purification.

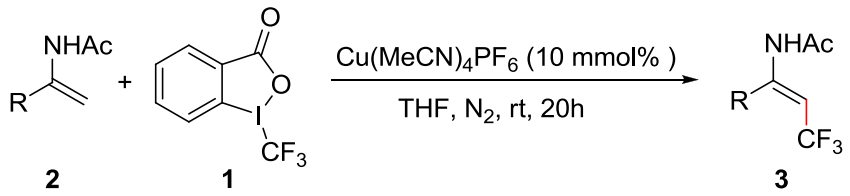
b) To an oven-dried 50 mL two-neck RBF assembled with condenser was added CuI (1.5 mmol), K_2CO_3 (9 mmol), acetamide (12 mmol). The flask was vacuumed and backfilled with N_2 for three times. Anhydrous THF (5 mL) was added followed by DMEDA (3 mmol) and crude (3-iodobut-3-enyl)benzene. The reaction flask was put into a 70 ^oC preheated oil bath and allowed to stir overnight. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate (2×50 mL) followed by drying over $MgSO_4$.

The organic solvent was evaporated and the residue was subjected to column chromatography on silica gel to deliver the product **2s** in 33% yield.

Copper-catalyzed olefinic C-H trifluoromethylation of enamides

General reaction scheme

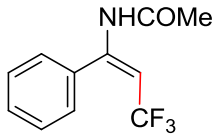




Synthetic procedure: An oven-dried 5mL Schlenk tube was charged with Tognis' regent **1** (0.11 mmol), **2** (0.1 mmol), $Cu(MeCN)_4PF_6$ (0.01 mmol) in sequence. The Schlenk tube was vacuumed and backfilled with nitrogen for three times followed by adding anhydrous THF (0.5 mL) through syringe and then closed tightly. After stirring at room temperature for 20 hours, saturated $NaHCO_3$ solution (20 mL) was added and the resulting mixture was extracted with dichloromethane (2x20 mL). Removal of the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the desired product **3**.

Characterization of products

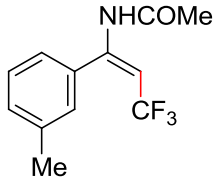
(*E*)-*N*-(3,3,3-trifluoro-1-phenylprop-1-enyl)acetamide:



3a

Yield: 90%; White solid. m.p. = 141-143 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.08 (s, 3H), 6.72 (s, 1H), 7.05 (q, $^{3}J_{HF}$ = 8.24 Hz, 1H), 7.34-7.38 (m, 2H), 7.40-7.47 (m, 3H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.9, 103.0 (q, *J* = 35.10 Hz), 122.9, 125.6, 128.1 (d, *J* = 1.35 Hz), 128.6, 129.8, 135.0, 143.7 (q, *J* = 5.70 Hz), 169.0 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.22 (d, $^{3}J_{HF}$ = 8.27 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{11}H_{11}NOF_3$ $[M+H]^+$ 230.0793, found: 230.0782.

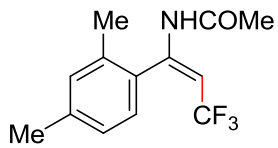
(*E*)-*N*-(3,3,3-trifluoro-1-m-tolylprop-1-enyl)acetamide:



3b

Yield: 86%; White solid. m.p. = 137-139 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.08 (s, 3H), 2.39 (s, 3H), 6.68 (s, 1H), 7.04 (q, $^{3}J_{HF}$ = 8.28 Hz, 1H), 7.16 (s, 2H), 7.24-7.32 (m, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 21.3, 24.9, 102.7 (q, *J* = 34.80 Hz), 122.9, 125.2 (d, *J* = 1.39 Hz), 125.6, 128.5, 128.6 (d, *J* = 1.28 Hz), 130.5, 134.9, 138.5, 143.9 (q, *J* = 6.04 Hz), 168.9 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.24 (d, $^{3}J_{HF}$ = 8.33 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{12}H_{13}NOF_3$ $[M+H]^+$ 244.0949, found: 244.0959.

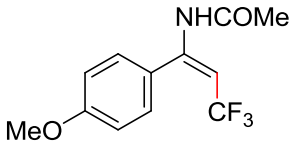
(*E*)-*N*-(1-(2,4-dimethylphenyl)-3,3,3-trifluoroprop-1-enyl)acetamide:



3c

Yield: 84%; White solid. m.p. = 144-146 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.06 (s, 3H), 2.27 (s, 3H), 2.34 (s, 3H), 6.56 (s, 1H), 7.02-7.13 (m, 4H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 18.8, 21.2, 24.8, 103.5 (q, *J* = 34.71 Hz), 122.9, 125.6, 126.5, 128.9 (d, *J* = 1.30 Hz), 131.1, 131.4, 135.6, 139.6, 143.3 (q, *J* = 5.91 Hz), 169.0 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -41.15 (d, $^{3}J_{HF}$ = 10.94 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{13}H_{14}NOF_3Na$ $[M+Na]^+$ 280.0925, found: 280.0924.

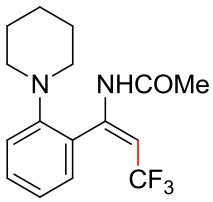
(*E*)-*N*-(3,3,3-trifluoro-1-(4-methoxyphenyl)prop-1-enyl)acetamide:



3d

Yield: 77%; White solid. m.p. = 142-144 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.09 (s, 3H), 3.83 (s, 3H), 6.69 (s, 1H), 6.89-7.00 (m, 3H), 7.27-7.30 (m, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.9, 55.3, 102.9 (q, *J* = 34.85 Hz), 114.0, 123.0, 125.7, 127.2, 129.5 (d, *J* = 1.49 Hz), 143.5 (q, *J* = 6.30 Hz), 160.6, 169.0 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.15 (d, $^{3}J_{HF}$ = 8.32 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{12}H_{13}NO_2F_3$ $[M+H]^+$ 260.0898, found: 260.0890.

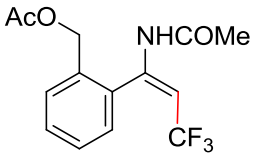
(*E*)-*N*-(3,3,3-trifluoro-1-(2-(piperidin-1-yl)phenyl)prop-1-enyl)acetamide:



3e

Yield: 90%; White solid. m.p. = 131-133 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.58-1.60 (m, 2H), 1.64-1.69 (m, 4H), 2.10 (s, 3H), 2.99-3.01 (m, 4H), 7.01-7.14 (m, 3H), 7.35-7.39 (m, 2H), 8.00 (s, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.0, 24.9, 26.8, 52.6, 102.9 (q, *J* = 34.97 Hz), 118.8, 119.2, 122.3, 123.1, 125.8, 127.5, 130.8, 132.1 (q, *J* = 3.09 Hz), 144.7 (q, *J* = 6.40 Hz), 150.2, 169.1 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.12 (d, $^{3}J_{HF}$ = 8.81 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{16}H_{20}N_2OF_3$ $[M+H]^+$ 313.1528, found: 313.1527.

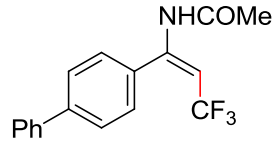
(*E*)-2-(1-acetamido-3,3,3-trifluoroprop-1-enyl)benzyl acetate:



3f

Yield: 76%; White solid. m.p. = 107-109 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.08 (s, 3H), 2.11 (s, 3H), 4.96 (d, *J* = 13.03 Hz, 1H), 5.17 (d, *J* = 13.03 Hz, 1H), 7.19 (q, $^{3}J_{HF}$ = 8.15 Hz, 1H), 7.27-7.29 (m, 1H), 7.34-7.38 (m, 1H)7.41-7.45 (m, 2H), 7.56 (s, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 21.0, 24.8, 63.9, 104.3 (q, *J* = 34.82 Hz), 122.8, 125.5, 128.3 (d, *J* = 4.38 Hz), 129.7 (d, *J* = 1.67 Hz), 130.0, 133.2, 134.1, 142.4 (q, *J* = 5.93 Hz), 169.4, 171.3 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -55.24 (d, $^{3}J_{HF}$ = 8.10 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{14}H_{15}NO_3F_3$ $[M+H]^+$ 302.1004, found: 302.1003.

(*E*)-*N*-(1-(biphenyl-4-yl)-3,3,3-trifluoroprop-1-enyl)acetamide:

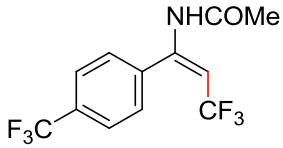


3g

Yield: 84%; White solid. m.p. = 164-166 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.10 (s, 3H), 6.75 (s, 1H), 7.08 (q, $^{3}J_{HF}$ = 8.27 Hz, 1H), 7.37-7.48 (m, 5H), 7.58-7.65 (m, 4H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.9, 103.1 (q, *J* =

34.96 Hz), 122.9, 125.6, 127.1, 127.3, 127.9, 128.6 (d, *J* = 1.70 Hz), 128.9, 133.8, 139.9, 142.7, 143.5 (q, *J* = 5.99 Hz), 169.0 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.11 (d, $^3J_{HF}$ = 8.33 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{17}H_{14}NOF_3Na$ $[M+Na]^+$ 328.0925, found: 328.0912.

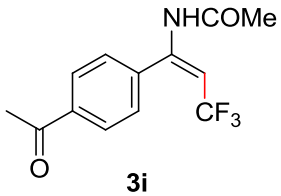
(*E*)-*N*-(3,3,3-trifluoro-1-(4-(trifluoromethyl)phenyl)prop-1-enyl)acetamide:



3h

Yield: 84%; White solid. m.p. = 98-100 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.08 (s, 3H), 6.77 (s, 1H), 7.08 (q, $^3J_{HF}$ = 8.28 Hz, 1H), 7.49 (d, *J* = 8.10 Hz, 2H), 7.70 (d, *J* = 8.15 Hz, 2H), ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.8, 103.9 (q, *J* = 35.18 Hz), 122.3, 122.6, 125.0, 125.3, 125.7 (q, *J* = 3.85 Hz), 127.7, 127.9, 128.8 (d, *J* = 1.45 Hz), 132.0 (q, *J* = 32.73 Hz), 138.3, 142.3 (q, *J* = 5.94 Hz), 169.0 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.34 (d, $^3J_{HF}$ = 8.25 Hz, 3F); -63.93 (s, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{12}H_{10}NOF_6$ $[M+H]^+$ 298.0667, found: 298.0658.

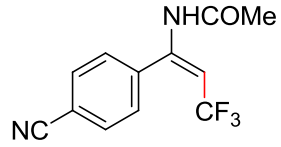
(*E*)-*N*-(1-(4-acetylphenyl)-3,3,3-trifluoroprop-1-enyl)acetamide:



3i

Yield: 92%; White solid. m.p. = 126-128 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.15 (s, 3H), 2.56 (s, 3H), 7.09 (q, $^3J_{HF}$ = 8.37 Hz, 1H), (s, 1H), 7.26 (s, 1H), 7.43 (d, *J* = 8.24 Hz, 2H), 7.87 (d, *J* = 8.24 Hz, 2H), ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.8, 26.6, 103.5 (q, *J* = 34.86 Hz), 122.7, 125.4, 128.4, 128.6, 137.5, 139.3, 142.8 (q, *J* = 6.06 Hz), 169.3, 197.7 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.18 (d, $^3J_{HF}$ = 8.28 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{13}H_{12}NO_2F_3Na$ $[M+Na]^+$ 294.0718, found: 294.0724.

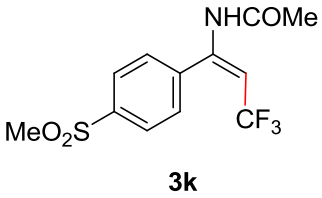
(*E*)-*N*-(1-(4-cyanophenyl)-3,3,3-trifluoroprop-1-enyl)acetamide:



3j

Yield: 83%; White solid. m.p. = 159-161 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.11 (s, 3H), 7.02 (s, 1H), 7.09 (q, $^3J_{HF}$ = 8.27 Hz, 1H), 7.50 (d, *J* = 8.24 Hz, 2H), 7.66 (d, *J* = 8.37 Hz, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.7, 104.0 (q, *J* = 35.13 Hz), 113.4, 118.0, 122.5, 125.2, 129.4 (d, *J* = 1.37 Hz), 132.3, 139.2, 141.9 (q, *J* = 6.21 Hz), 169.2 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.26 (d, $^3J_{HF}$ = 8.24 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{12}H_{10}N_2OF_3$ $[M+H]^+$ 255.0745, found: 255.0747.

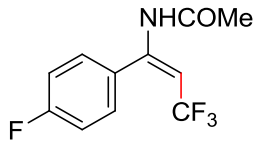
(*E*)-*N*-(3,3,3-trifluoro-1-(4-(methylsulfonyl)phenyl)prop-1-enyl)acetamide:



3k

Yield: 85%; Light yellow solid. m.p. = 163-165 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.15 (s, 3H), 3.01 (s, 3H), 7.14 (q, $^{3}J_{HF}$ = 8.42 Hz, 1H), 7.55 (d, *J* = 8.20 Hz, 2H), 7.62 (s, 1H), 7.75 (d, *J* = 8.29 Hz, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.7, 44.6, 103.7 (q, *J* = 34.93 Hz), 122.7, 125.4, 127.2, 129.8 (d, *J* = 1.25 Hz), 140.2, 140.6, 142.2 (q, *J* = 5.92 Hz), 169.6 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -53.92 (d, $^{3}J_{HF}$ = 8.34 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{12}H_{13}NO_3F_3S$ $[M+H]^+$ 308.0568, found: 308.0575.

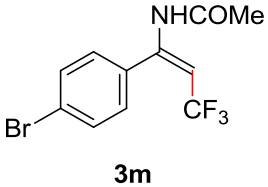
(*E*)-*N*-(3,3,3-trifluoro-1-(4-fluorophenyl)prop-1-enyl)acetamide:



3l

Yield: 80%; White solid. m.p. = 175-177 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.10 (s, 3H), 6.66 (s, 1H), 7.04 (q, $^{3}J_{HF}$ = 8.29 Hz, 1H), 7.08-7.14 (m, 2H), 7.33-7.36 (m, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.9, 103.5 (q, *J* = 34.82 Hz), 115.8 (d, *J* = 21.82 Hz), 122.8, 125.5, 130.3 (dd, J_1 = 8.64 Hz, *J2* = 1.42 Hz), 130.9 (d, *J* = 3.67 Hz), 142.7 (q, *J* = 6.07 Hz), 162.4 (d, *J* = 250.60 Hz), 168.9 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.29 (d, $^{3}J_{HF}$ = 8.22 Hz, 3F), -111.38 (s, 1F) ppm; **HRMS (ESI, m/z):** calcd for $C_{11}H_{10}NOF_4$ $[M+H]^+$ 248.0699, found: 248.0709.

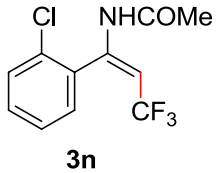
(*E*)-*N*-(1-(4-bromophenyl)-3,3,3-trifluoroprop-1-enyl)acetamide:



3m

Yield: 85%; White solid. m.p. = 143-145 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.09 (s, 3H), 6.69 (s, 1H), 7.04 (q, $^{3}J_{HF}$ = 8.30 Hz, 1H), 7.22-7.25 (m, 2H), 7.55-7.58 (m, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.8, 103.6 (q, *J* = 34.98 Hz), 122.7, 124.2, 125.4, 129.8 (d, *J* = 1.41 Hz), 131.9, 133.7, 142.6 (q, *J* = 6.30 Hz), 168.9 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.24 (d, $^{3}J_{HF}$ = 8.33 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{11}H_{10}NOF_3Br$ $[M+H]^+$ 307.9898, found: 307.9897.

(*E*)-*N*-(1-(2-chlorophenyl)-3,3,3-trifluoroprop-1-enyl)acetamide:

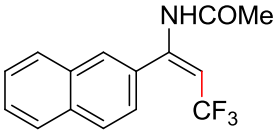


3n

Yield: 84%; White solid. m.p. = 155-157 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.10 (s, 3H), 6.67 (s, 1H), 7.13 (q, $^{3}J_{HF}$ = 8.10 Hz, 1H), 7.30-7.35 (m, 2H), 7.37-7.41 (m, 1H), 7.46 (d, *J* =

7.90 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.8, 104.5 (q, *J* = 34.86 Hz), 122.6, 125.2, 126.9, 129.9, 130.9 (d, *J* = 1.45 Hz), 131.1, 132.7, 133.3, 140.8 (q, *J* = 5.95 Hz), 169.1 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -56.17 (d, $^3J_{HF}$ = 8.19 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{11}H_{10}NOF_3Cl$ $[M+H]^+$ 264.0403, found: 264.0395.

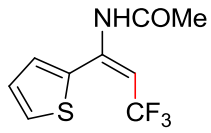
(*E*)-*N*-(3,3,3-trifluoro-1-(naphthalen-2-yl)prop-1-enyl)acetamide:



3o

Yield: 83%; White solid. m.p. = 153-155 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.07 (s, 3H), 6.79 (s, 1H), 7.12 (q, $^3J_{HF}$ = 8.25 Hz, 1H), 7.41 (dd, J_1 = 8.44 Hz, J_2 = 1.56 Hz, 1H), 7.53-7.59 (m, 2H), 7.84-7.90 (m, 4H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.9, 103.3 (q, *J* = 34.74 Hz), 122.9, 125.2 (d, *J* = 1.31 Hz), 125.6, 126.9, 127.3, 127.8, 127.9 (d, *J* = 1.51 Hz), 128.3, 128.5, 132.2, 132.7, 133.5, 143.7 (q, *J* = 5.85 Hz), 169.0 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.16 (d, $^3J_{HF}$ = 8.27 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{15}H_{13}NOF_3$ $[M+H]^+$ 280.0949, found: 280.0946.

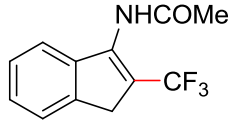
(*E*)-*N*-(3,3,3-trifluoro-1-(thiophen-2-yl)prop-1-enyl)acetamide:



3p

Yield: 40%; Light yellow solid. m.p. = 134-136 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.12 (s, 3H), 6.79 (s, 1H), 7.05-7.07 (m, 2H), 7.25 (d, *J* = 3.48 Hz, 1H), 7.45 (d, *J* = 4.95 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** 24.9, 105.3 (q, *J* = 35.34 Hz), 122.6, 125.3, 127.3, 127.9, 129.8 (d, *J* = 2.06 Hz), 134.4, 136.9 (q, *J* = 6.49 Hz), 168.7 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.69 (d, $^3J_{HF}$ = 8.15 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_9H_9NOF_3S$ $[M+H]^+$ 236.0357, found: 236.0357.

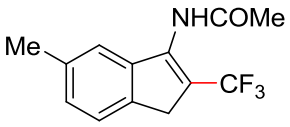
***N*-(2-(trifluoromethyl)-1H-inden-3-yl)acetamide:**



3q

Yield: 87%; White solid. m.p. = 173-175 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.20 (s, 3H), 3.54 (s, 2H), 7.30-7.34 (m, 2H), 7.40-7.45 (m, 2H), 7.50 (s, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 23.4, 35.4, 121.9, 122.8, 124.0, 124.6, 126.7, 127.7, 139.2, 140.3 (q, *J* = 4.35 Hz), 140.9, 168.9 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -59.69 (s, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{12}H_{11}NOF_3$ $[M+H]^+$ 242.0793, found: 242.0795.

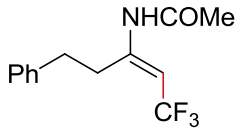
***N*-(5-methyl-2-(trifluoromethyl)-1H-inden-3-yl)acetamide:**



3r

Yield: 86%; White solid. m.p. = 191-193 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 2.22 (s, 3H), 2.38 (s, 3H), 3.51 (s, 2H), 7.14 (d, *J* = 7.57 Hz, 1H), 7.23 (s, 1H), 7.30 (d, *J* = 7.58 Hz, 1H), 7.40 (s,1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 21.5, 23.5, 35.0, 121.9, 123.2, 123.7, 124.6, 128.7, 136.5, 138.1, 139.4, 140.2 (q, *J* = 4.27 Hz), 168.8 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -59.64 (s, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{13}H_{13}NOF_3$ $[M+H]^+$ 256.0949, found: 256.0950.

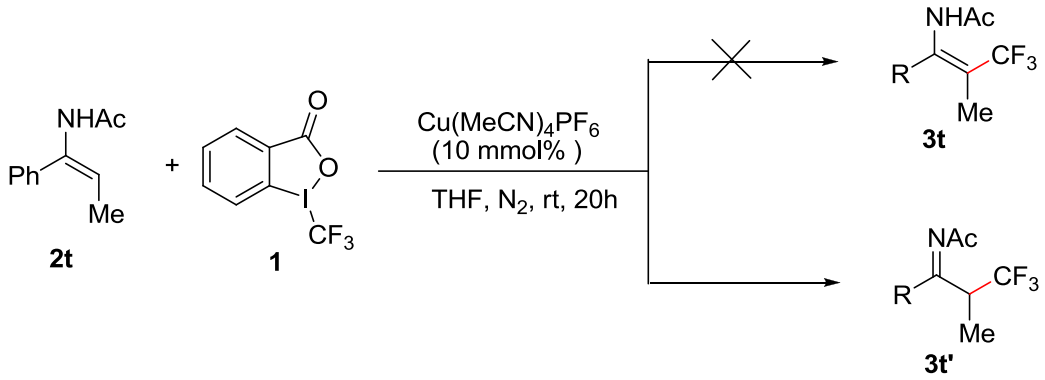
(*E*)-*N*-(1,1,1-trifluoro-5-phenylpent-2-en-3-yl)acetamide:



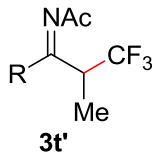
3s

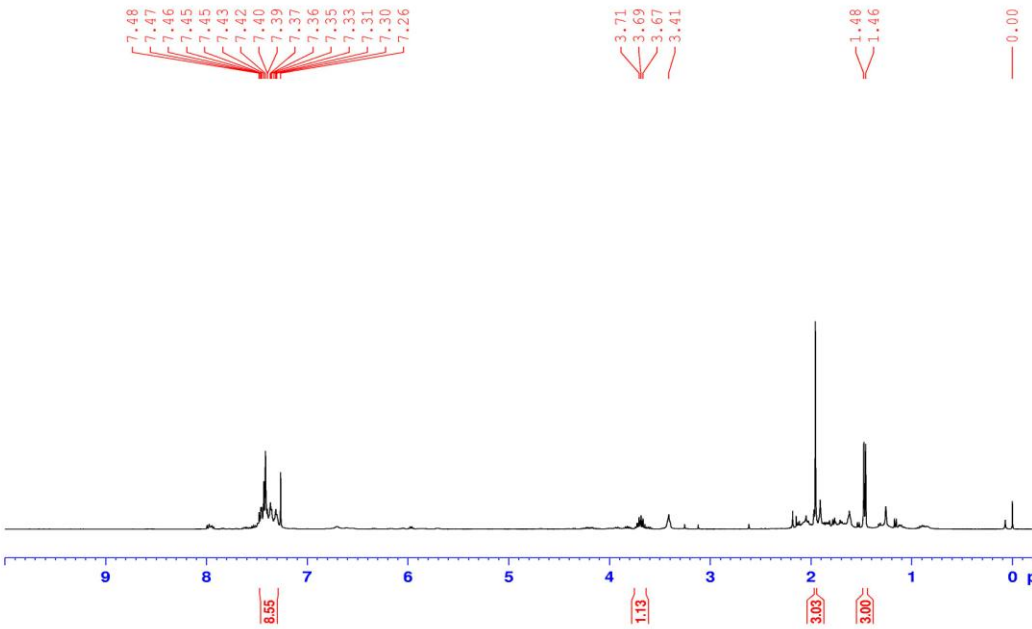
Yield: 60%; White solid. m.p. = 77-79 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 1.8 (s, 3H), 2.60(t, *J* = 7.38 Hz, 2H), 2.88 (t, *J* = 7.39 Hz, 2H), 6.21 (s, 1H), 6.76 (q, $^{3}J_{HF}$ = 8.75 Hz, 1H), 7.2-7.29 (m, 3H), 7.32-7.36 (m, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.6, 33.9, 34.9, 102.3 (q, *J* = 35.07 Hz), 123.7, 126.4, 126.8, 128.4, 128.9, 140.1, 144.7 (q, *J* = 5.90 Hz), 168.9 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -54.84 (d, $^{3}J_{HF}$ = 8.74 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{13}H_{15}NOF_3$ $[M+H]^+$ 258.1106, found: 258.1107.

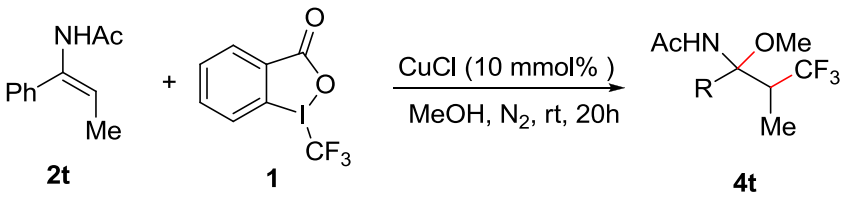
Reactivity profile of *β*-substituted acyclic enamides toward Tognis' reagent 1.



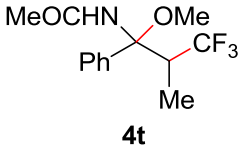
When **2t** was reacted with Tognis' reagent **1** with the optimized reaction condition for olefinic trifluoromethylation, the *α*-trifluoromethyl imine **3t'** was formed instead of the expected product **3t.** We surmise the reactivity difference between acylic enamide **2t** and cyclic enamides **2q** and **2r** could be attributed to the steric repulsion (which makes the **3t** unfavorable) and thermodynamic stability of endo alkene skeleton in the case of cyclic substrates or ring strain (which promotes the 1,3-hydrogen shift to afford **3q** and **3r**).

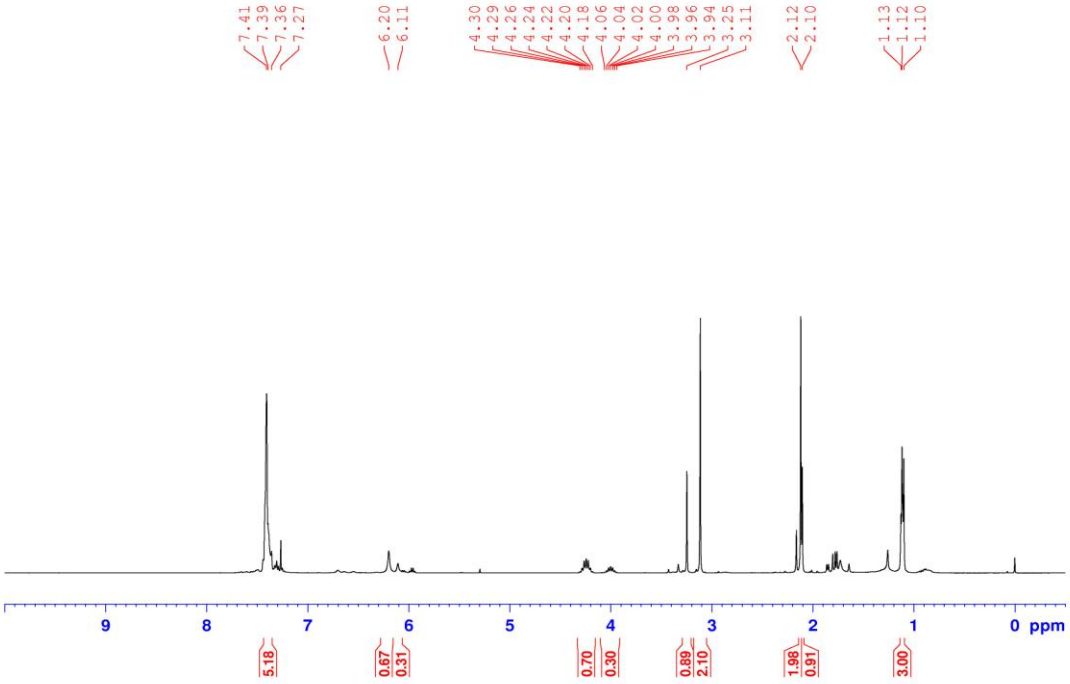






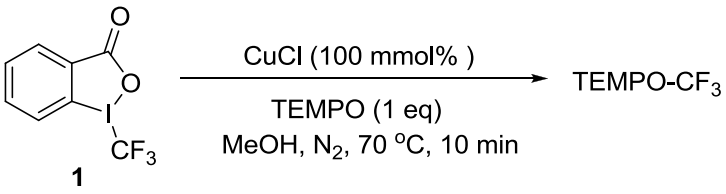
When **2t** was reacted with Tognis' reagent **1** with the optimized reaction condition for oxytrifluoromethylation the desired product **4t** was formed in almost quantitative yield.



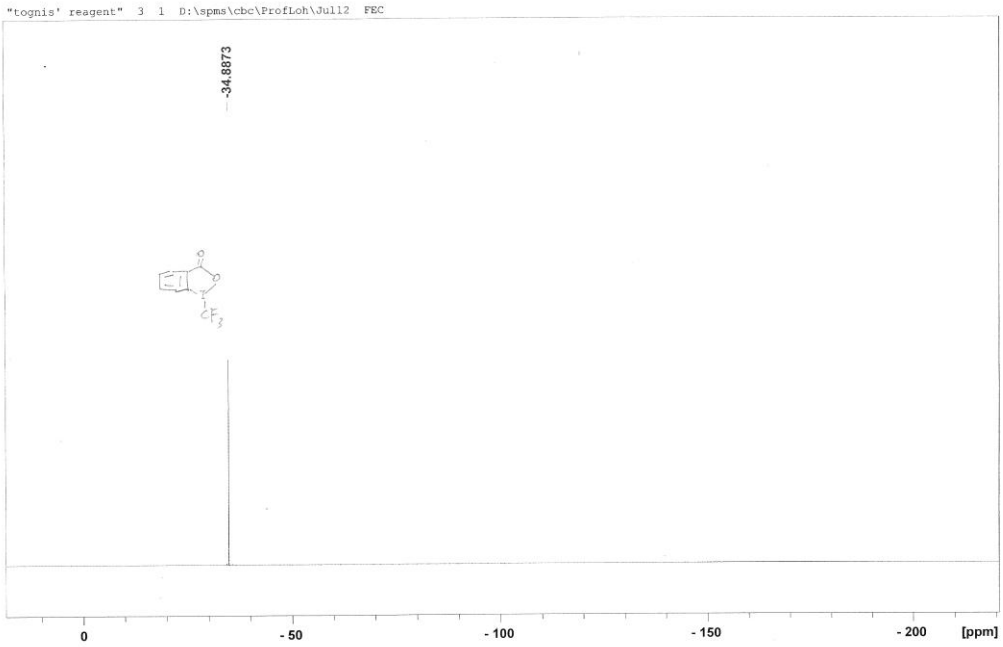


Control experiments

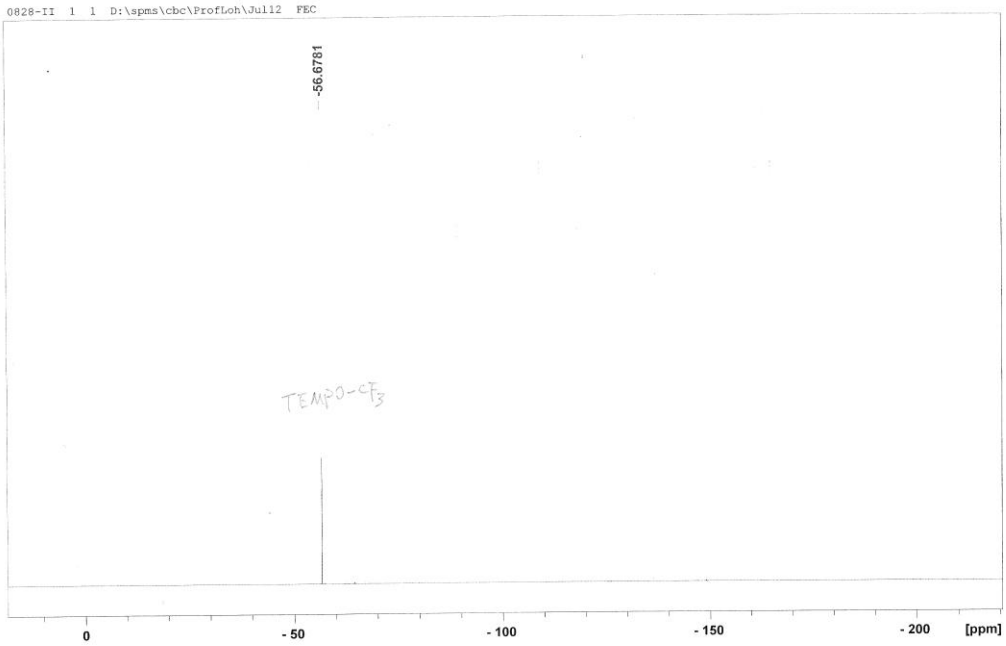
1) Follow Wang's method for the generation of TEMPO-CF_3. [3]



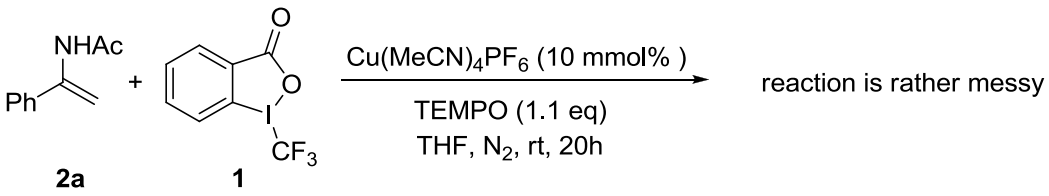
The ^{19}F NMR of Tognis' reagent **1** and TEMPO-CF_3



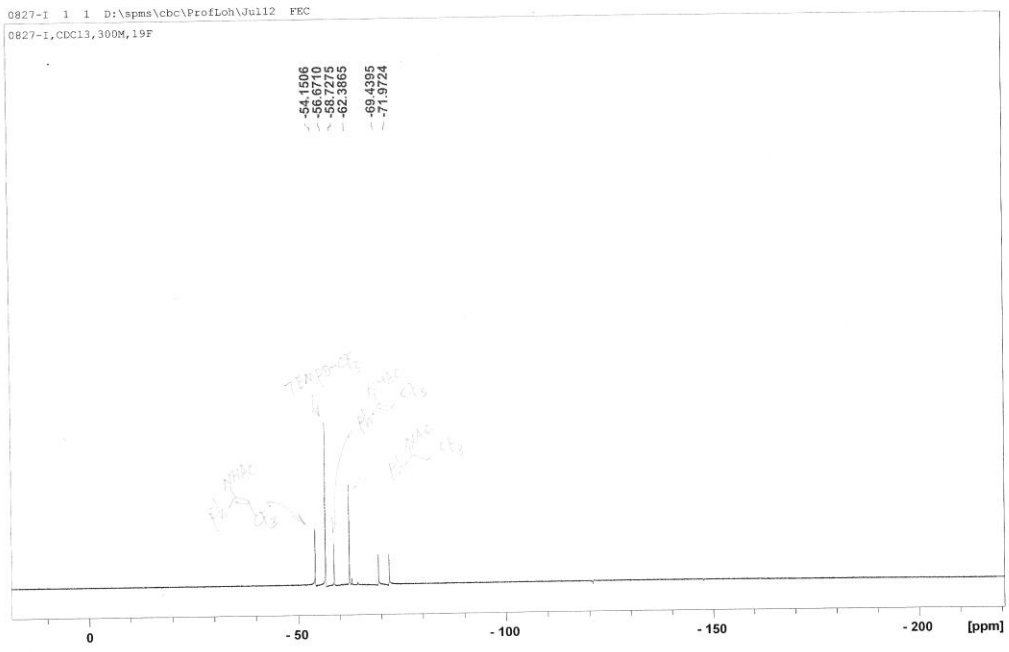
[3] X. Wang, Y. Ye, S. Zhang, J. Feng, Y. Xu, Y. Zhang and J. Wang, *J. Am. Chem. Soc.*, 2011, **133**, 16410.



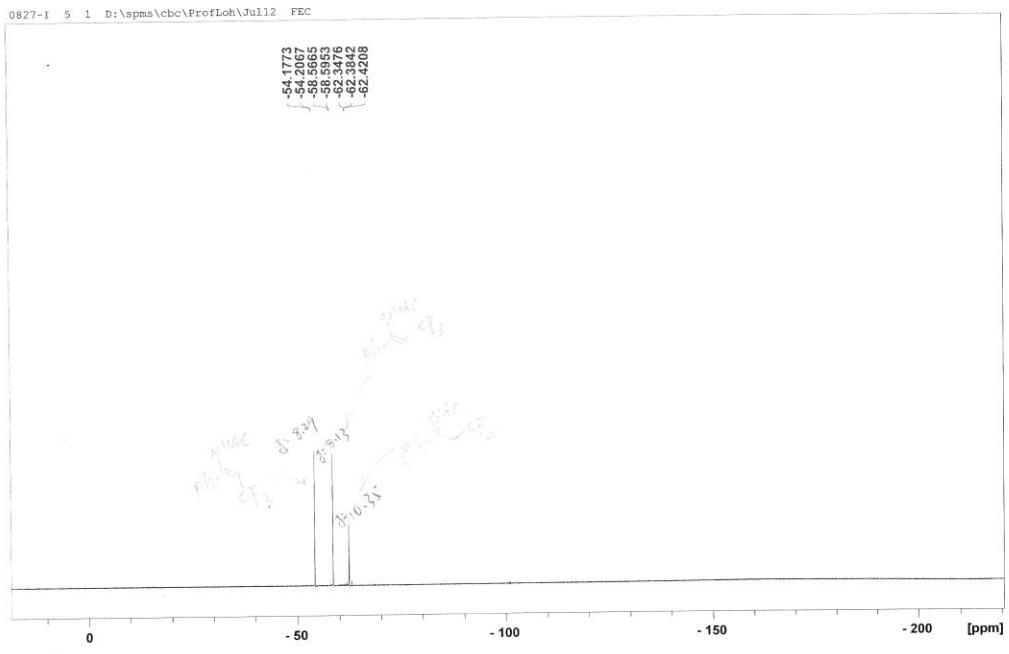
2) TEMPO as radical scavenger



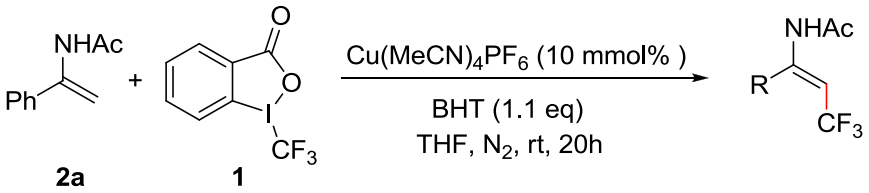
General procedure: An oven-dried 5mL Schlenk tube was charged with Tognis' regent **1** (0.11 mmol), **2a** (0.1 mmol), $Cu(MeCN)_4PF_6$ (0.01 mmol) in sequence. The Schlenk tube was vacuumed and backfilled with nitrogen for three times followed by adding TEMPO (0.11 mmol) and anhydrous THF (0.5 mL) through syringe and then closed tightly. After stirring at room temperature for 20 hours the solvent was evaporated and the crude mixture was dissolved in $CDCl_3$ for ^{19}F (decoupled) analysis.



The above crude mixture was washed with saturated $NaHCO_3$ solution (20 mL) and extracted with dichloromethane (2x20 mL). After evaporation of organic solvent, the crude product was subjected to vacuum and the resulting mixture was dissolved in $CDCl_3$ for ^{19}F (non-decoupled) analysis.



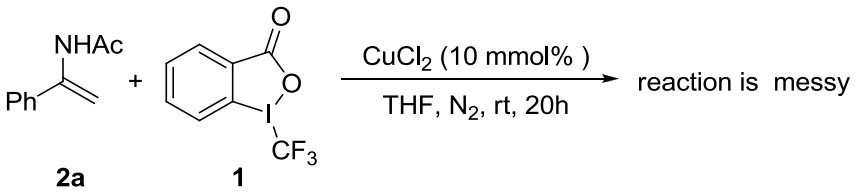
3) BHT as radical scavenger



isolated yield 88%

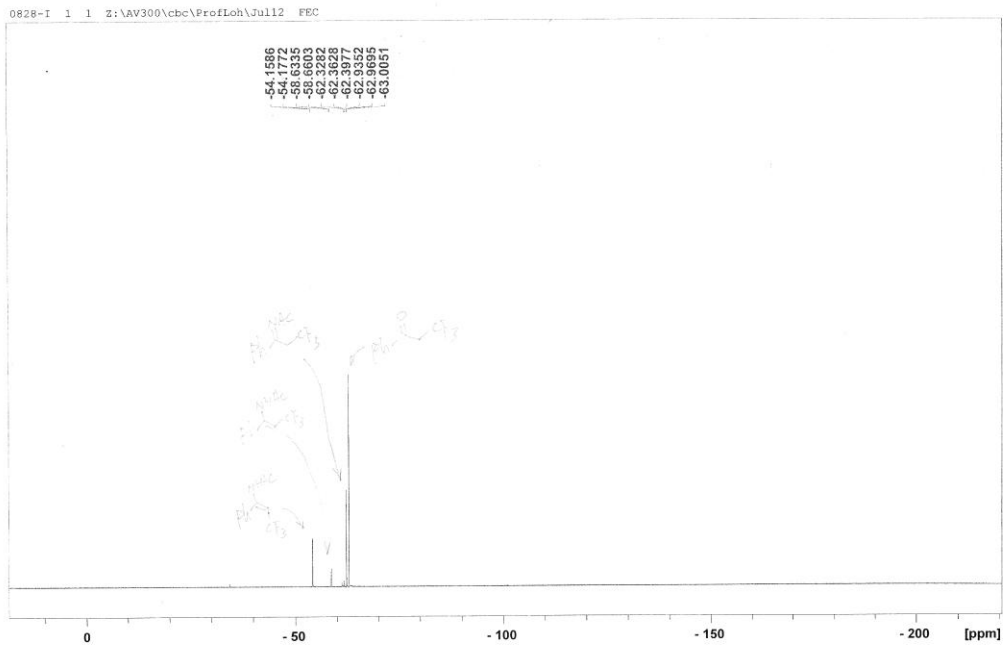
General procedure: An oven-dried 5mL Schlenk tube was charged with Tognis' regent **1** (0.11 mmol), **2a** (0.1 mmol), $Cu(MeCN)_4PF_6$ (0.01 mmol), BHT (0.11 mmol) in sequence. The Schlenk tube was vacuumed and backfilled with nitrogen for three times followed by adding anhydrous THF (0.5 mL) through syringe and then closed tightly. After stirring at room temperature for 20 hours, saturated $NaHCO_3$ solution (20 mL) was added and the resulting mixture was extracted with dichloromethane (2x20 mL). Removal of the solvent in vacuo and purification of the residue by silica gel column chromatography afforded the desired product **3a** (88% yield) .

4) $CuCl_2$ as catalyst



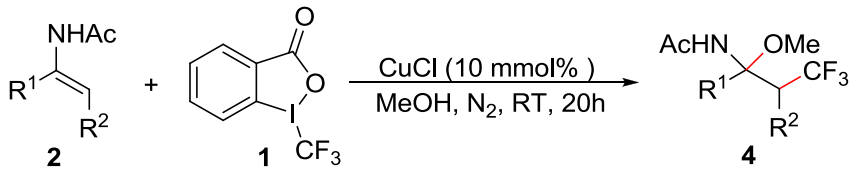
2a **1**

General procedure: An oven-dried 5mL Schlenk tube was charged with Tognis' regent **1** (0.11 mmol), **2a** (0.1 mmol), $CuCl_2$ (0.01 mmol) in sequence. The Schlenk tube was vacuumed and backfilled with nitrogen for three times followed by adding anhydrous THF (0.5 mL) through syringe and then closed tightly. After stirring at room temperature for 20 hours the solvent was evaporated and the crude mixture was dissolved in $CDCl_3$ for ^{19}F (non-decoupled) analysis.



Copper-catalyzed oxytrifluoromethylation of enamides

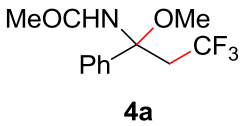
General reaction scheme



Synthetic procedure: An oven-dried 5mL Schlenk tube was charged with Tognis' regent **1** (0.11 mmol), **2** (0.1 mmol), CuCl (0.01 mmol) in sequence. The Schlenk tube was vacuumed and backfilled with nitrogen for three times followed by adding anhydrous MeOH (0.5 mL) through syringe and then closed tightly. After stirring at room temperature for 20 hours, saturated $NaHCO_3$ solution (20 mL) was added and the resulting mixture was extracted with dichloromethane (2x20 mL). Removal of the solvent in vacuo afforded the desired product **4**, which is pure enough for NMR characterization.

Characterization of products

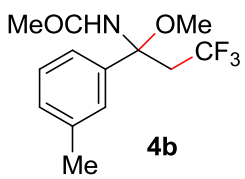
N-(3,3,3-trifluoro-1-methoxy-1-phenylpropyl)acetamide:



4a

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.50 (s, 3H), 3.10 (s, 3H), 3.28-3.37 (m, 1H), 3.42-3.51 (m, 1H), 6.32 (s, 1H), 7.35-7.44 (m, 5H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.0, 40.4 (q, J = 26.81 Hz), 49.9, 86.5 (d, J = 2.82 Hz), 123.5, 125.9, 126.3, 128.6, 128.8, 138.9, 170.2 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -62.98 (t, $^3J_{HF}$ = 10.19 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{12}H_{14}NO_2F_3Na$ $[M+Na]^+$ 284.0874, found: 284.0878.

N-(3,3,3-trifluoro-1-methoxy-1-m-tolylpropyl)acetamide:

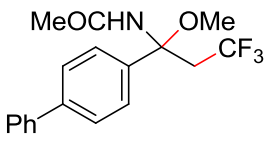


4b

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.09 (s, 3H), 2.39 (s, 3H), 3.10 (s, 3H), 3.29-3.37 (m, 1H), 3.43-3.56 (m, 1H), 6.15 (s, 1H), 7.17-7.32 (m, 4H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 21.6, 24.2, 40.4 (q, J = 26.75 Hz), 49.9, 86.5 (d, J = 3.26 Hz), 123.0, 123.5, 126.3, 126.4, 128.5, 129.6, 138.4, 138.9, 170.0 ppm; **^{19}F**

NMR (282 MHz, $CDCl_3$): δ -61.78 (t, $^3J_{HF}$ = 10.50 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{13}H_{16}NO_2F_3Na$ $[M+Na]^+$ 298.1031, found: 298.1035.

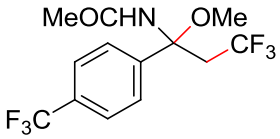
***N*-(1-(biphenyl-4-yl)-3,3,3-trifluoro-1-methoxypropyl)acetamide:**



4g

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.09 (s, 3H), 3.14 (s, 3H), 3.32-3.56 (m, 2H), 6.23 (s, 1H), 7.34-7.38 (m, 1H), 7.43-7.50 (m, 4H), 7.58-7.64 (m, 4H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.1, 40.2 (q, *J* = 26.68 Hz), 50.0, 86.5, 123.6, 126.3, 126.4, 127.1, 127.3, 127.7, 128.8, 137.9, 140.1, 141.6, 170.1 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -61.62 (t, $^3J_{HF}$ = 10.46 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{18}H_{18}NO_2F_3Na$ $[M+Na]^+$ 360.1187, found: 360.1185.

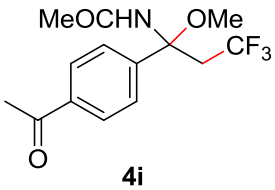
***N*-(3,3,3-trifluoro-1-methoxy-1-(4(trifluoromethyl)phenyl)propyl)acetamide:**



4h

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.06 (s, 3H), 3.14 (s, 3H), 3.32-3.43 (m, 2H), 6.23 (s, 1H), 7.58 (d, *J* = 8.36 Hz, 2H), 7.67 (d, *J* = 8.36 Hz, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.0, 39.8 (q, *J* = 26.86 Hz), 50.3, 86.3 (d, *J* = 2.83Hz), 122.4, 123.3, 125.1, 125.6 (q, *J* = 3.62 Hz), 126.1, 126.6, 131.0 (q, *J* = 32.62 Hz), 143.2, 170.0 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -61.61 (t, $^3J_{HF}$ = 10.35 Hz, 3F), -63.76 (s, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{13}H_{13}NO_2F_6Na$ $[M+Na]^+$ 352.0748, found: 352.0757.

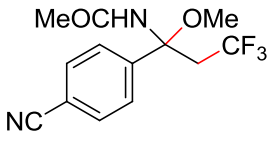
***N*-(1-(4-acetylphenyl)-3,3,3-trifluoro-1-methoxypropyl)acetamide:**



4i

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.09 (s, 3H), 2.61 (s, 3H), 3.15 (s, 3H), 3.38 (q, *J* = 10.38 Hz, 2H), 6.34 (s, 1H), 7.56 (d, *J* = 8.42 Hz, 2H), 7.97 (d, *J* = 8.44 Hz, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.0, 26.6, 39.9 (q, *J* = 27.02 Hz), 50.2, 86.3 (d, *J* = 2.83 Hz), 123.4, 126.1, 126.4, 128.6, 137.2, 144.2, 170.0, 197.5 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -61.60 (t, $^3J_{HF}$ = 10.35 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{14}H_{16}NO_3F_3Na$ $[M+Na]^+$ 326.0980, found: 326.0986.

***N*-(1-(4-cyanophenyl)-3,3,3-trifluoro-1-methoxypropyl)acetamide:**

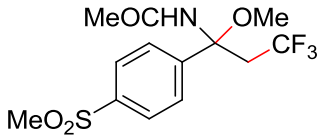


4j

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.08 (s, 3H), 3.18 (s, 3H), 3.23-3.39 (m, 2H), 6.21 (s, 1H), 7.59 (d, *J* = 8.39 Hz, 2H), 7.70 (d, *J* = 8.31 Hz, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.0, 39.7 (q, *J* = 27.09 Hz), 50.5, 86.1 (d, *J* =

3.05 Hz), 112.7, 118.2, 127.0, 132.4, 144.6, 169.9 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -61.51 (t, $^3J_{HF}$ = 10.28 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{13}H_{13}N_2O_2F_3Na$ $[M+Na]^+$ 309.0827, found: 309.0829.

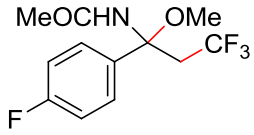
***N*-(3,3,3-trifluoro-1-methoxy-1-(4(methylsulfonyl)phenyl)propyl)acetamide:**



4k

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.09 (s, 3H), 3.06 (s, 3H), 3.17 (s, 3H), 3.27-3.43 (m, 2H), 6.51 (s, 1H), 7.68 (d, *J* = 8.50 Hz, 2H), 7.90 (d, *J* = 8.48 Hz, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.0, 40.1 (q, *J* = 27.12 Hz), 44.4, 50.4, 86.1 (d, *J* = 2.67 Hz), 123.2, 126.0, 127.4, 127.5, 140.5, 145.7, 170.3 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -61.45 (t, $^3J_{HF}$ = 10.32 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{13}H_{16}NO_4F_3SNa$ $[M+Na]^+$ 362.0650, found: 362.0655.

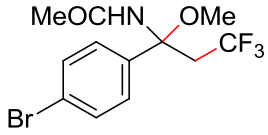
***N*-(3,3,3-trifluoro-1-(4-fluorophenyl)-1-methoxypropyl)acetamide:**



4l

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.07 (s, 3H), 3.11 (s, 3H), 3.31-3.44 (m, 2H), 6.15 (s, 1H), 7.07-7.11 (m, 2H), 7.40-7.44 (m, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.1, 40.1 (q, *J* = 26.98 Hz), 50.0, 86.3 (d, *J* = 2.88 Hz), 115.5, 115.7, 123.5, 126.2, 128.0, 128.0, 135.0, 162.8 (d, *J* = 248.08 Hz), 170.0 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -61.75 (t, $^3J_{HF}$ = 10.48 Hz, 3F), -113.89--113.94 (m, 1F) ppm; **HRMS (ESI, m/z):** calcd for $C_{12}H_{13}NO_2F_4Na$ $[M+Na]^+$ 302.0780, found: 302.0779.

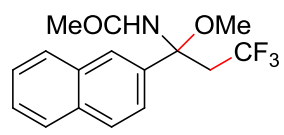
***N*-(1-(4-bromophenyl)-3,3,3-trifluoro-1-methoxypropyl)acetamide:**



4m

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.06 (s, 3H), 3.11 (s, 3H), 3.29-3.43 (m, 2H), 6.17 (s, 1H), 7.31 (d, *J* = 8.52 Hz, 2H), 7.53 (d, *J* = 8.64 Hz, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.1, 39.8 (q, *J* = 26.88 Hz), 50.1, 86.3 (d, *J* = 2.14 Hz), 123.1, 123.4, 126.2, 127.8, 131.8, 138.3, 170.0 ppm; **^{19}F NMR (282 MHz, $CDCl_3$):** δ -61.66 (t, $^3J_{HF}$ = 10.46 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{12}H_{13}NO_2F_3NaBr$ $[M+Na]^+$ 361.9979, found: 361.9986.

***N*-(3,3,3-trifluoro-1-methoxy-1-(naphthalen-2-yl)propyl)acetamide:**

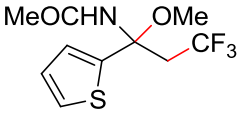


4o

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.10 (s, 3H), 3.13 (s, 3H), 3.40-3.64 (m, 2H), 6.31 (s, 1H), 7.50-7.54 (m, 3H), 7.84-7.89 (m, 4H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 24.2,

39.9 (q, *J* = 26.96 Hz), 50.1, 86.7 (d, *J* = 2.71 Hz), 123.2, 125.5, 126.6, 126.9, 127.6, 128.4, 128.8, 132.8, 133.2, 136.4, 170.0 ppm; **^{19}F NMR (282 MHz, CDCl$_3$):** δ -61.69 (t, $^3J_{HF}$ = 10.64 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{16}H_{16}NO_2F_3Na$ $[M+Na]^+$ 334.1031, found: 334.1045.

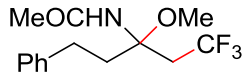
***N*-(3,3,3-trifluoro-1-methoxy-1-(thiophen-2-yl)propyl)acetamide:**



4p

^{1}H NMR (400 MHz, CDCl$_3$): δ 2.06 (s, 3H), 3.15 (s, 3H), 3.39-3.55 (m, 2H), 6.23 (s, 1H), 6.98-7.00 (m, 1H), 7.07 (d, *J* = 3.29 Hz, 1H), 7.35 (d, *J* = 5.05 Hz, 1H) ppm; **^{13}C NMR (100 MHz, CDCl$_3$):** δ 24.0, 39.7 (q, *J* = 26.89 Hz), 50.1, 85.1 (d, *J* = 3.08 Hz), 123.4, 126.0, 126.1, 126.6, 126.8, 128.9, 143.9, 169.8 ppm; **^{19}F NMR (282 MHz, CDCl$_3$):** δ -62.36 (t, $^3J_{HF}$ = 10.35 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{10}H_{12}NO_2F_3NaS$ $[M+Na]^+$ 290.0439, found: 290.0439.

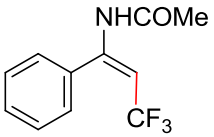
***N*-(1,1,1-trifluoro-3-methoxy-5-phenylpentan-3-yl)acetamide:**



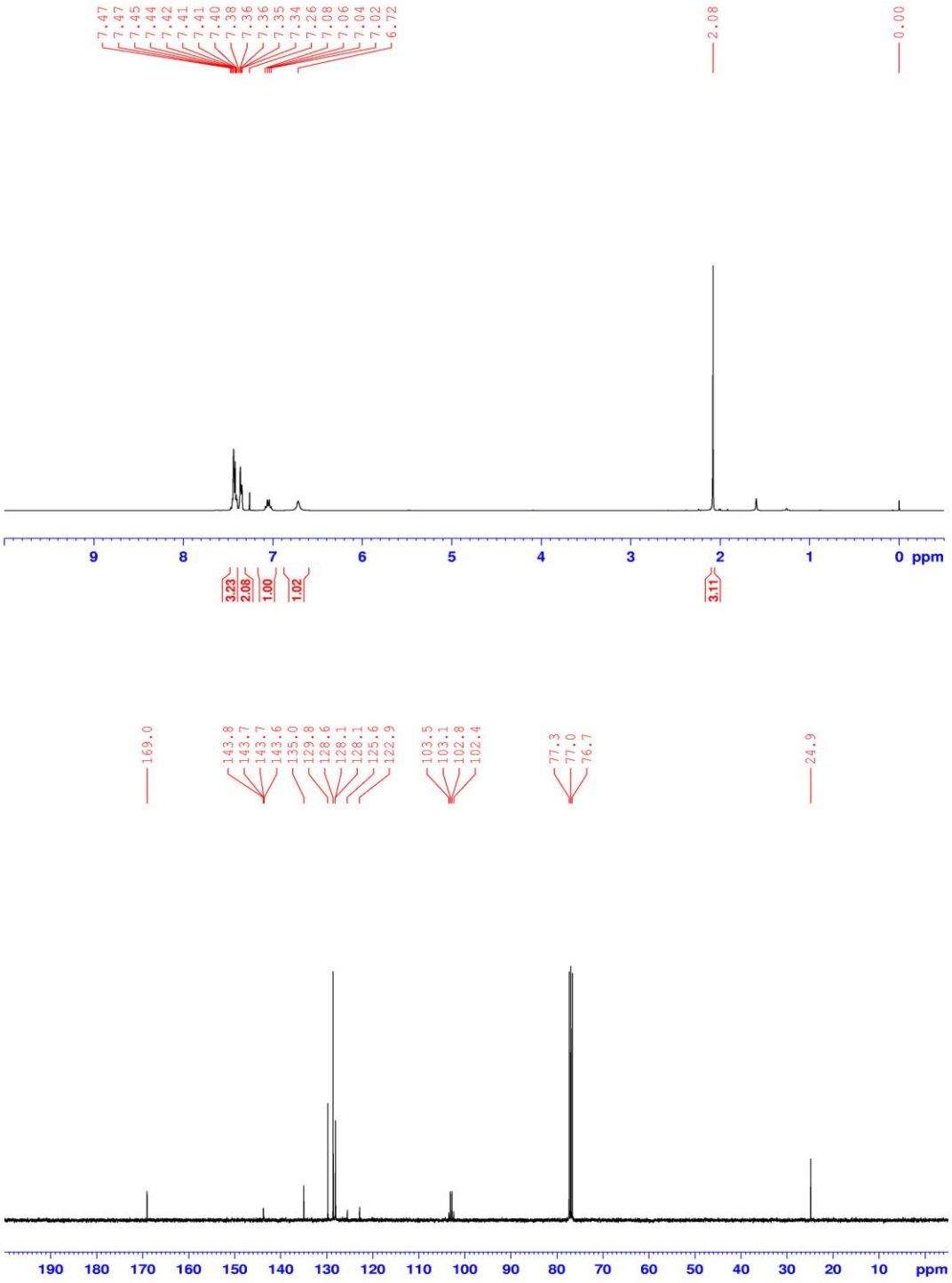
4s

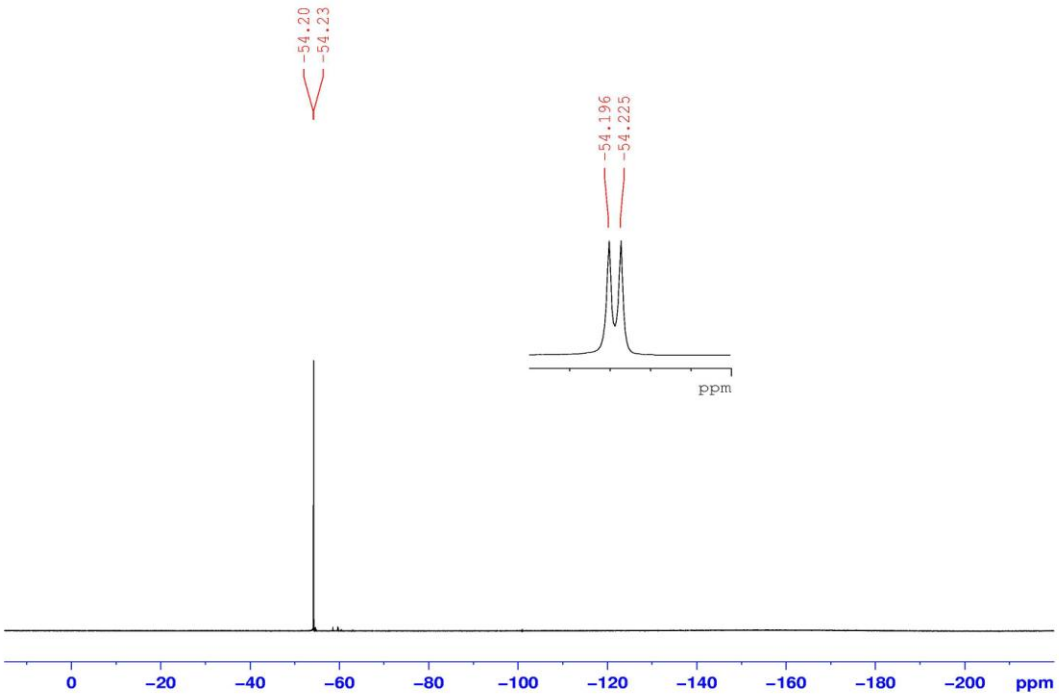
^{1}H NMR (400 MHz, CDCl$_3$): δ 1.95 (s, 3H), 2.02-2.11 (m, 1H), 2.28-2.36 (m, 1H), 2.63 (t, *J* = 8.40 Hz, 2H), 2.88-3.00 (m, 1H), 3.12-3.21 (m, 1H), 3.28 (s, 3H), 5.60 (s, 1H), 7.17-7.22 (m, 3H), 7.27-7.31 (m, 3H) ppm; **^{13}C NMR (100 MHz, CDCl$_3$):** δ 24.0, 28.7, 35.8, 35.9 (q, *J* = 26.65 Hz), 48.8, 85.9 (d, *J* = 2.35 Hz), 123.8, 126.2, 126.5, 128.3, 128.6, 140.8, 169.7 ppm; **^{19}F NMR (282 MHz, CDCl$_3$):** δ -62.38 (t, $^3J_{HF}$ = 11.00 Hz, 3F) ppm; **HRMS (ESI, m/z):** calcd for $C_{14}H_{18}NO_2F_3Na$ $[M+Na]^+$ 312.1187, found: 312.1187.

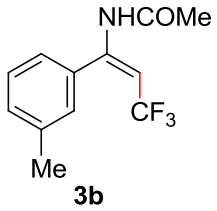
^{1}H and ^{13}C NMR spectra of products



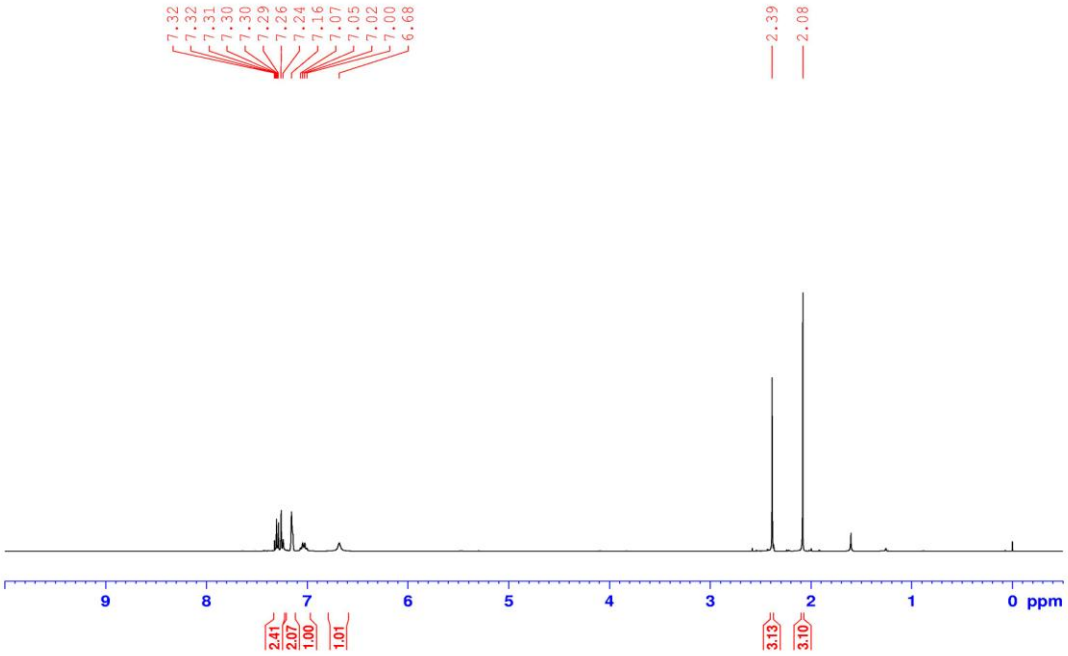
3a

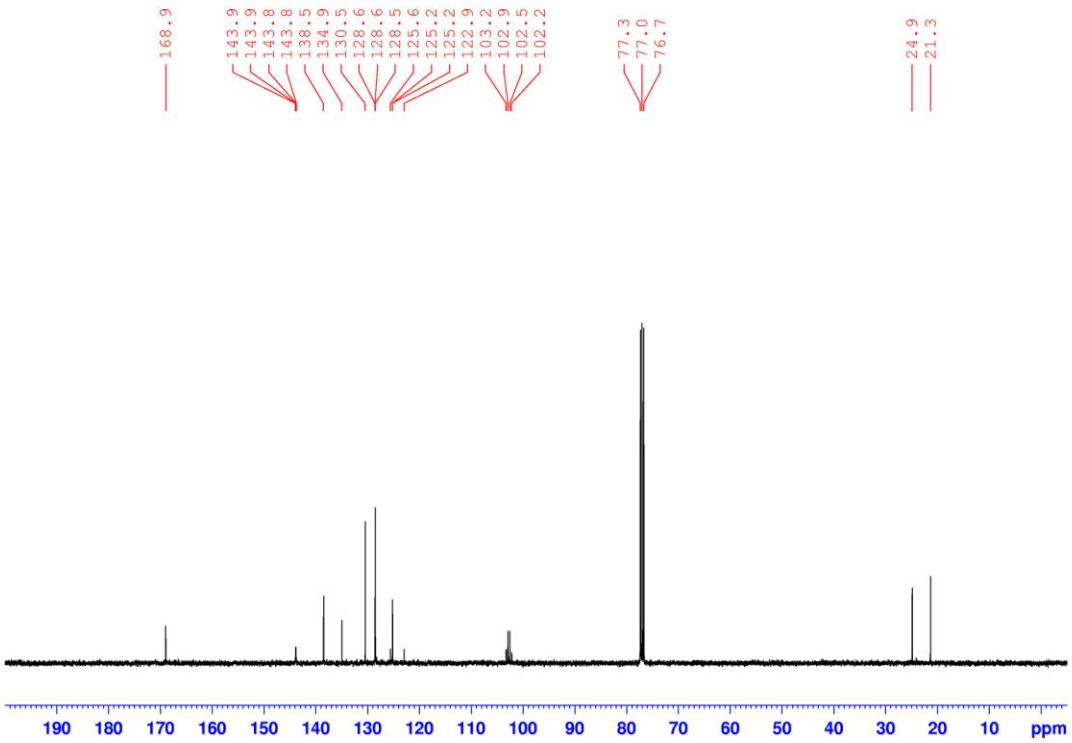


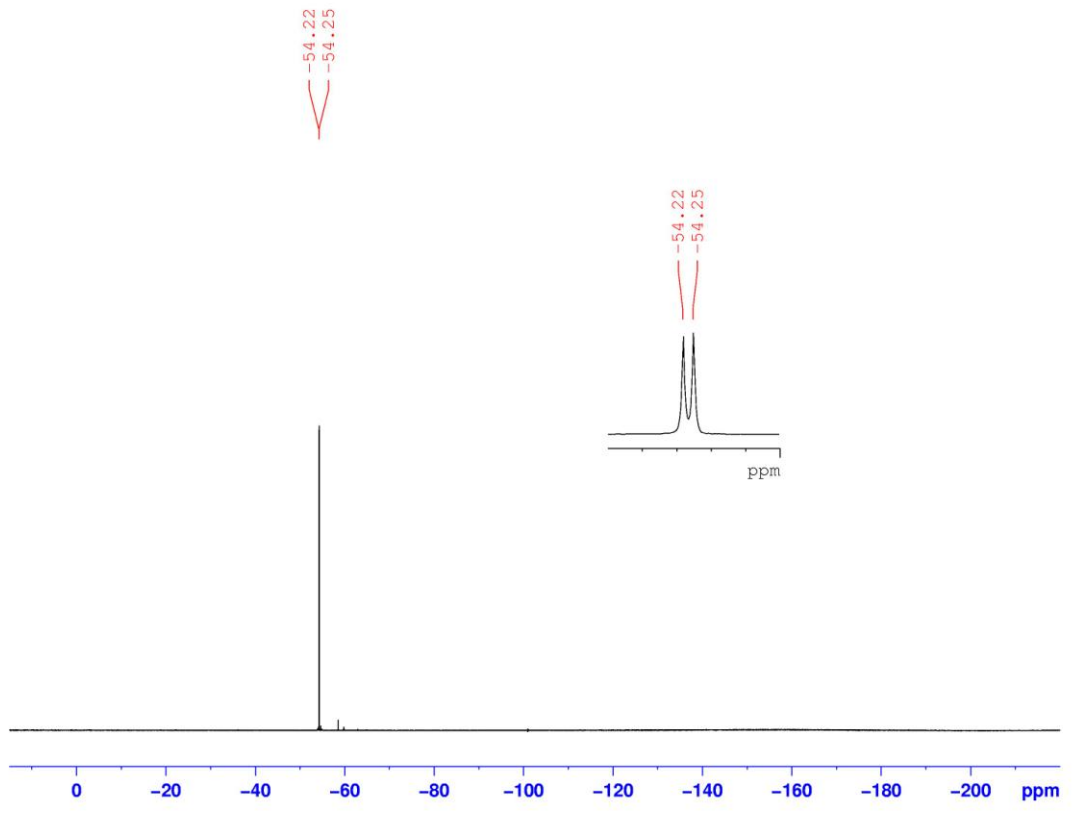


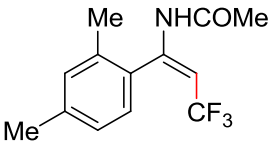


3b

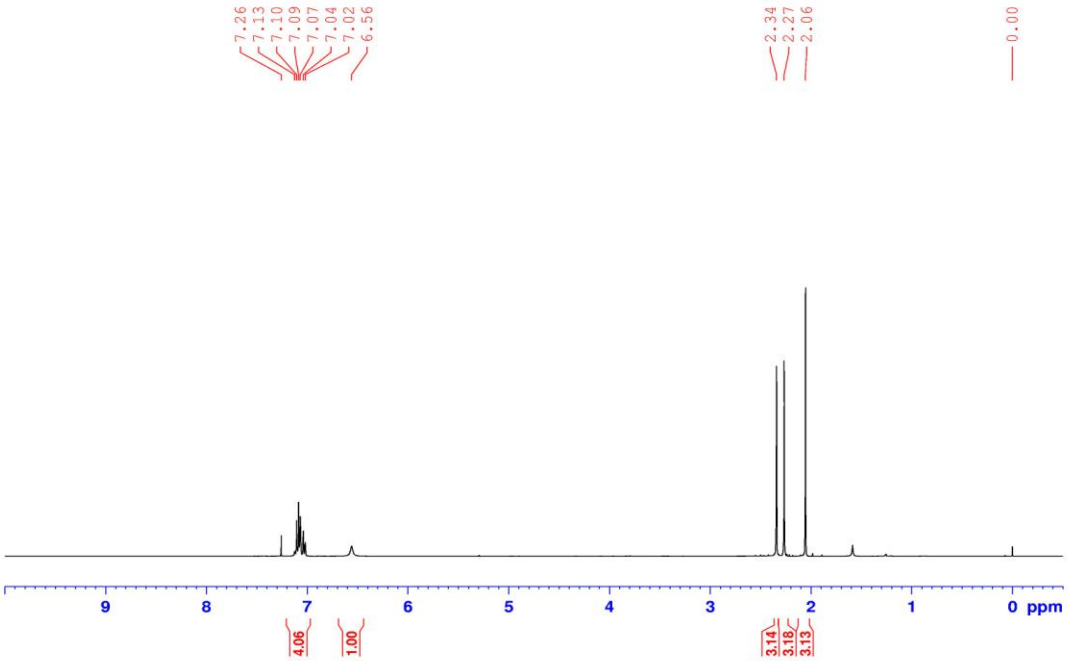


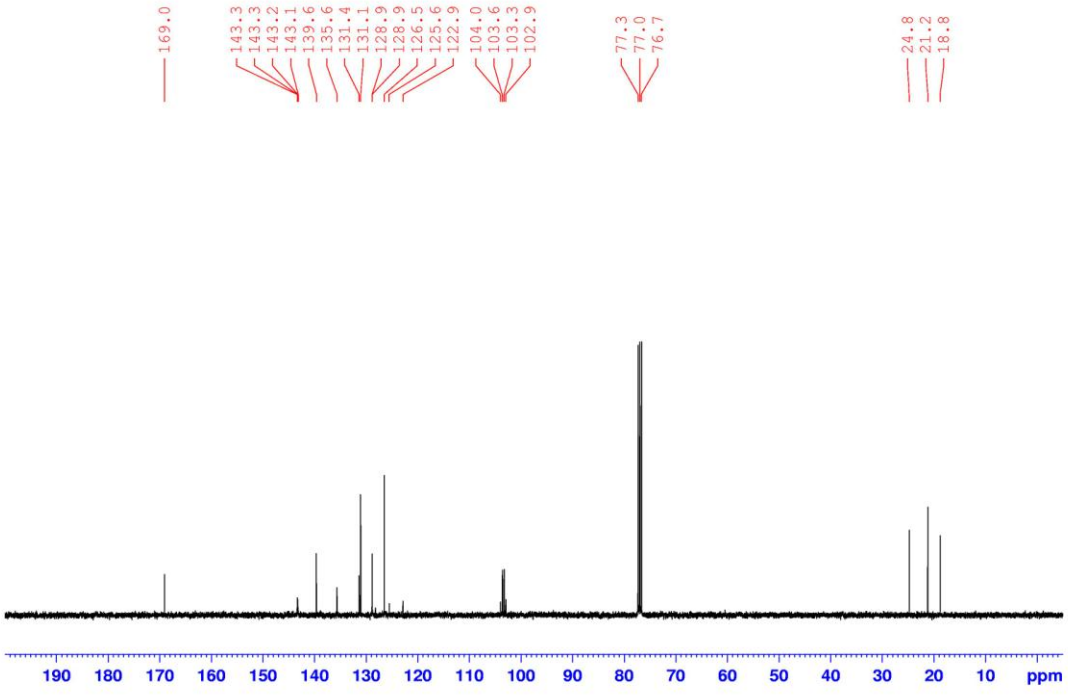

168.9
143.9
143.9
143.8
143.8
138.5
134.9
130.5
128.6
128.6
128.5
125.6
125.2
125.2
122.9
103.2
102.9
102.5
102.2
77.3
77.0
76.7
24.9
21.3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

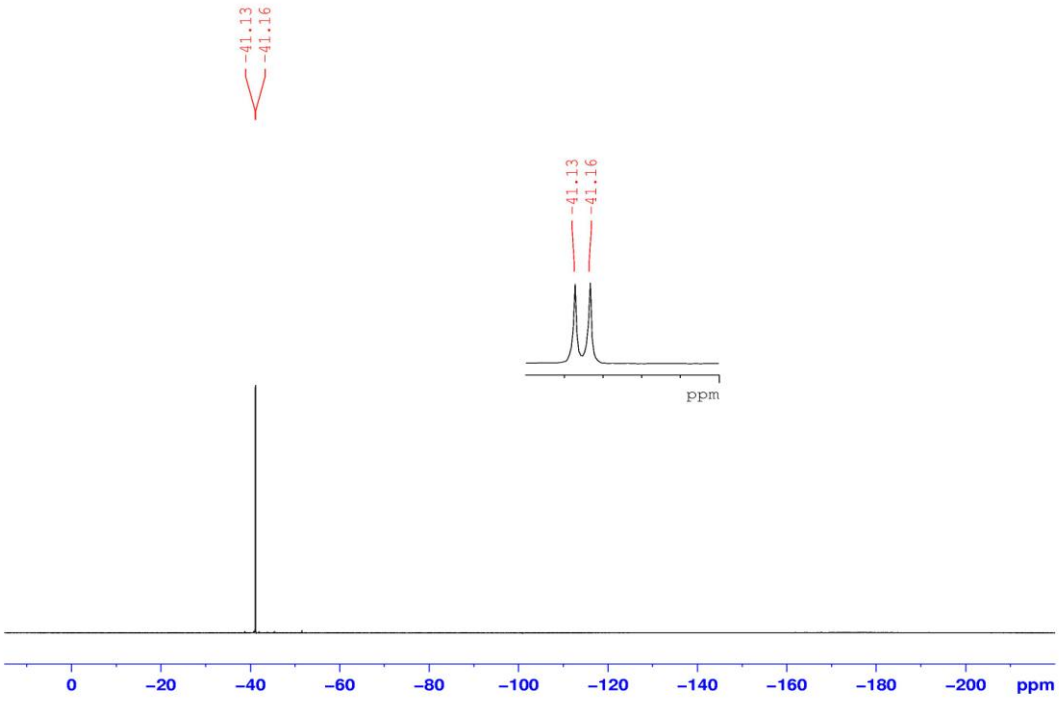

-54.22
-54.25
-54.22
-54.25
ppm
0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 ppm

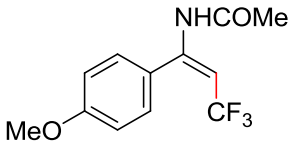


3c

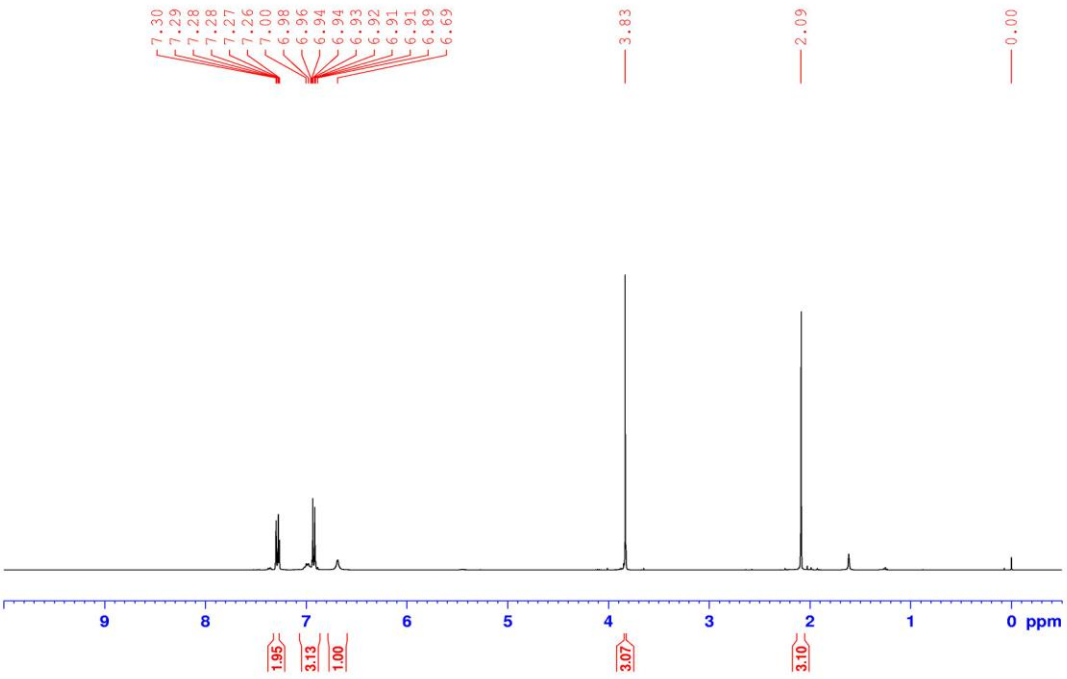


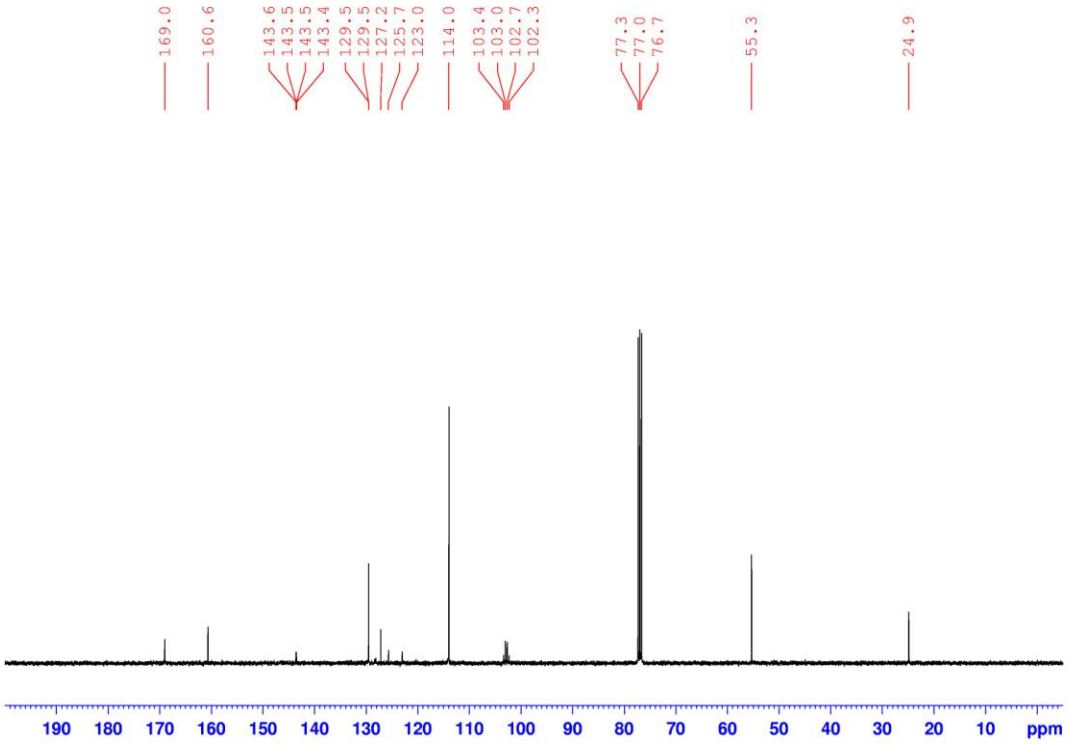


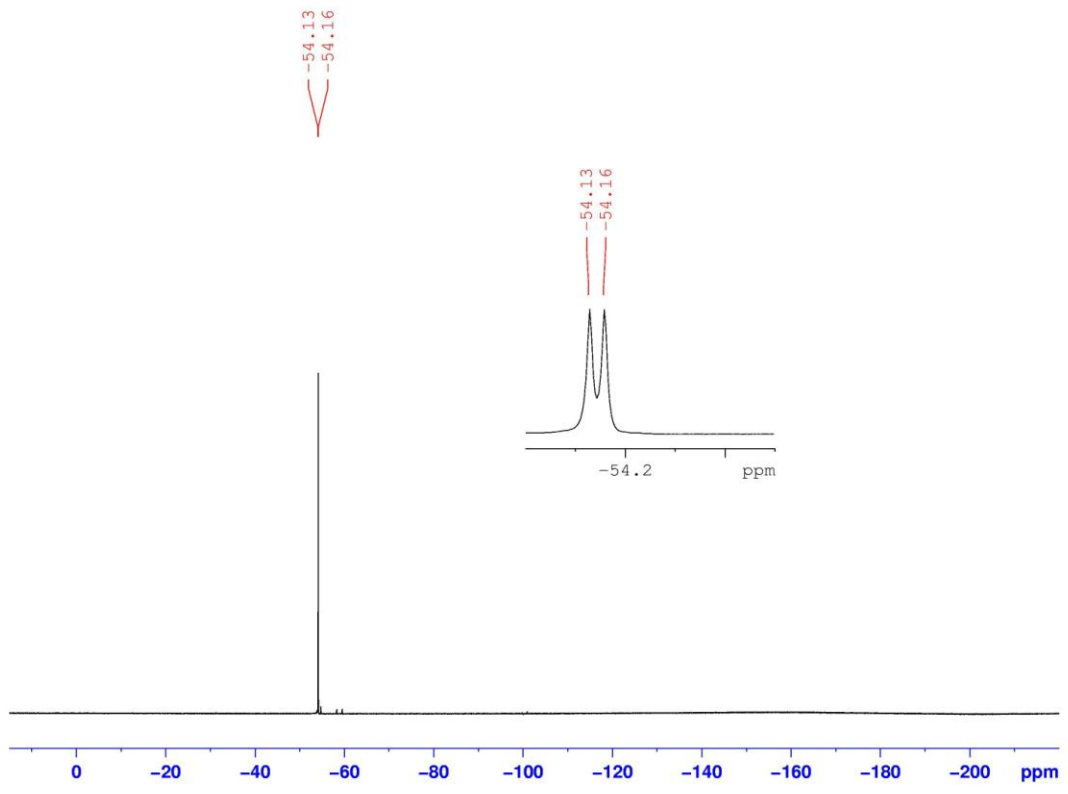


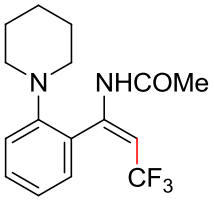


3d

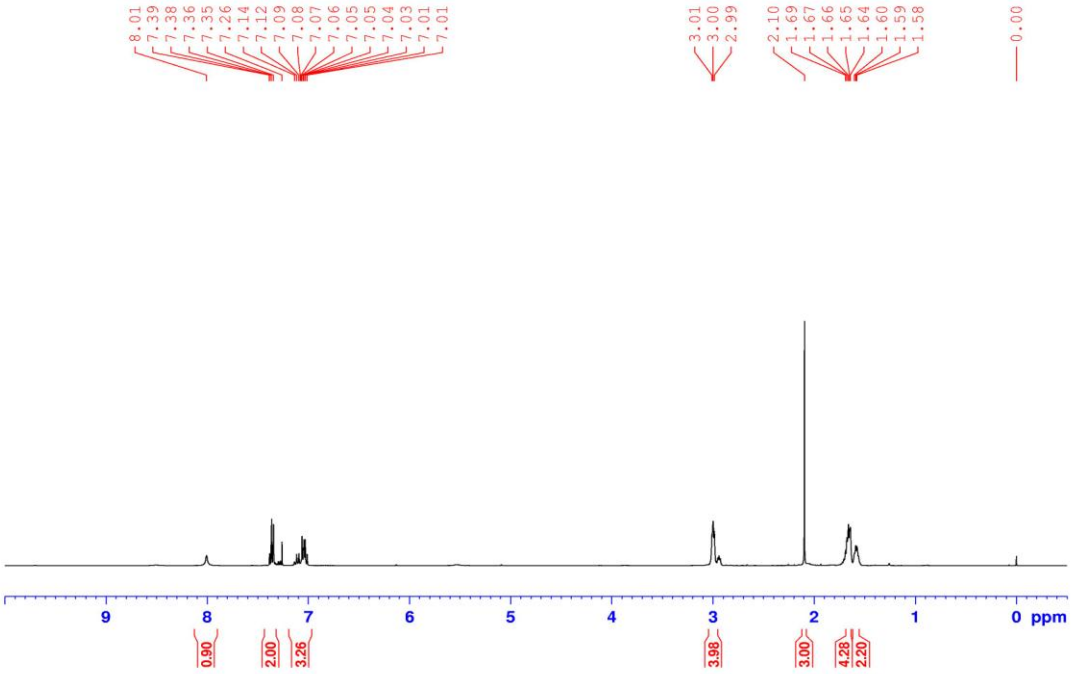


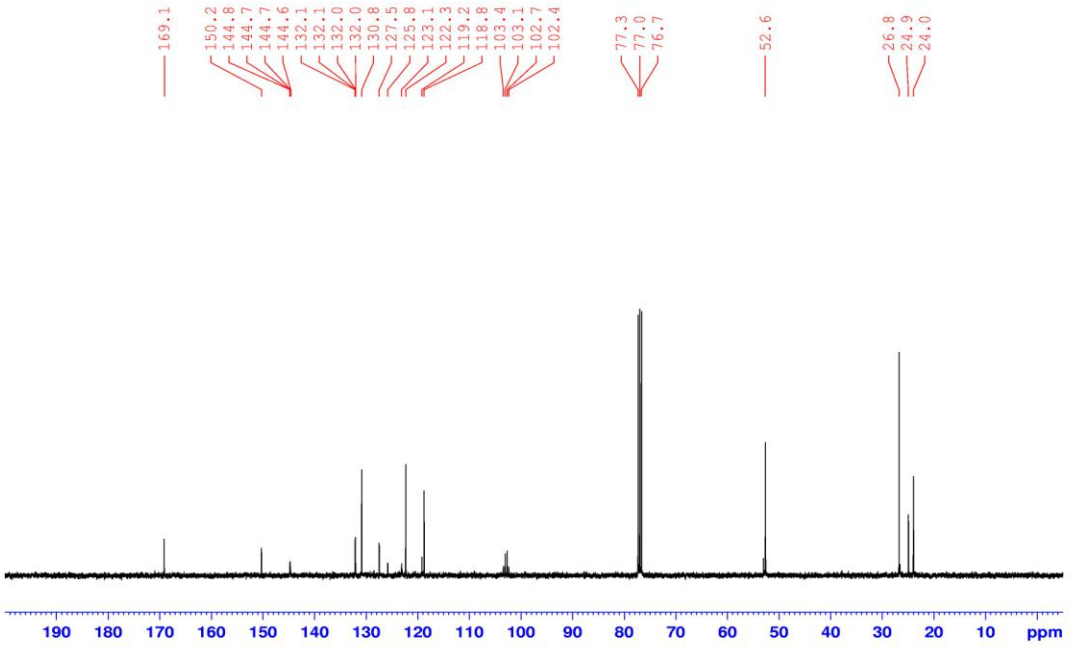


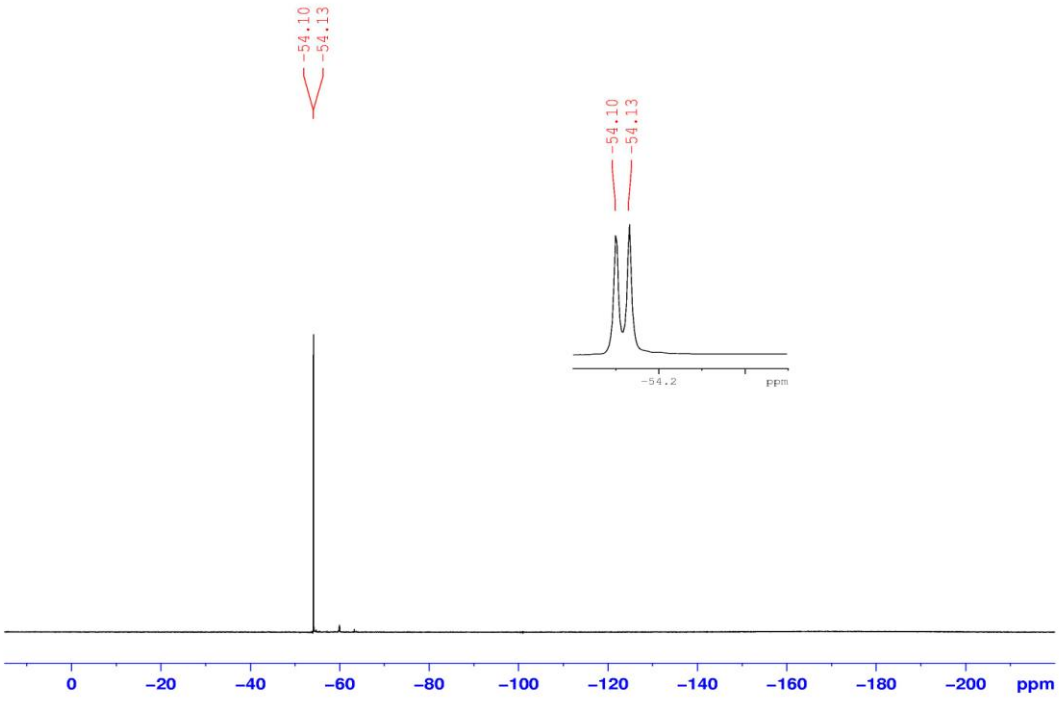




3e



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-54.13
-54.10
-54.13
-54.2
ppm
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-20
-40
-60
-80
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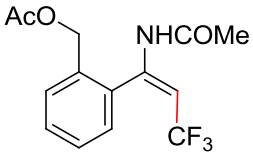
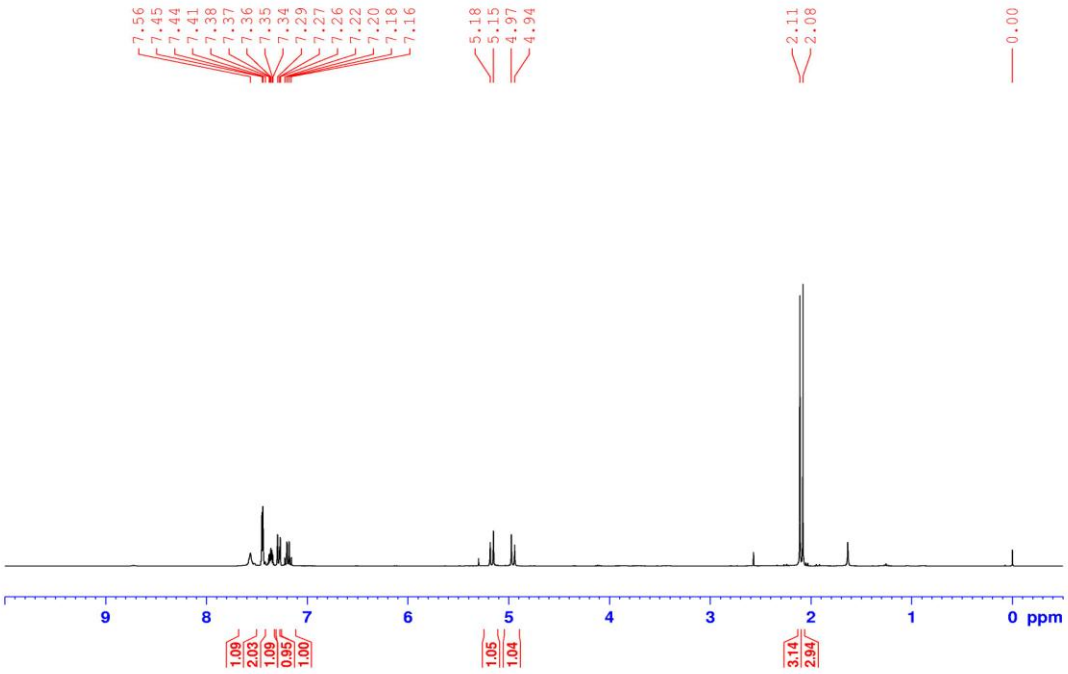
-180
-200
ppm


AcO
NHCOMe
CF3

3f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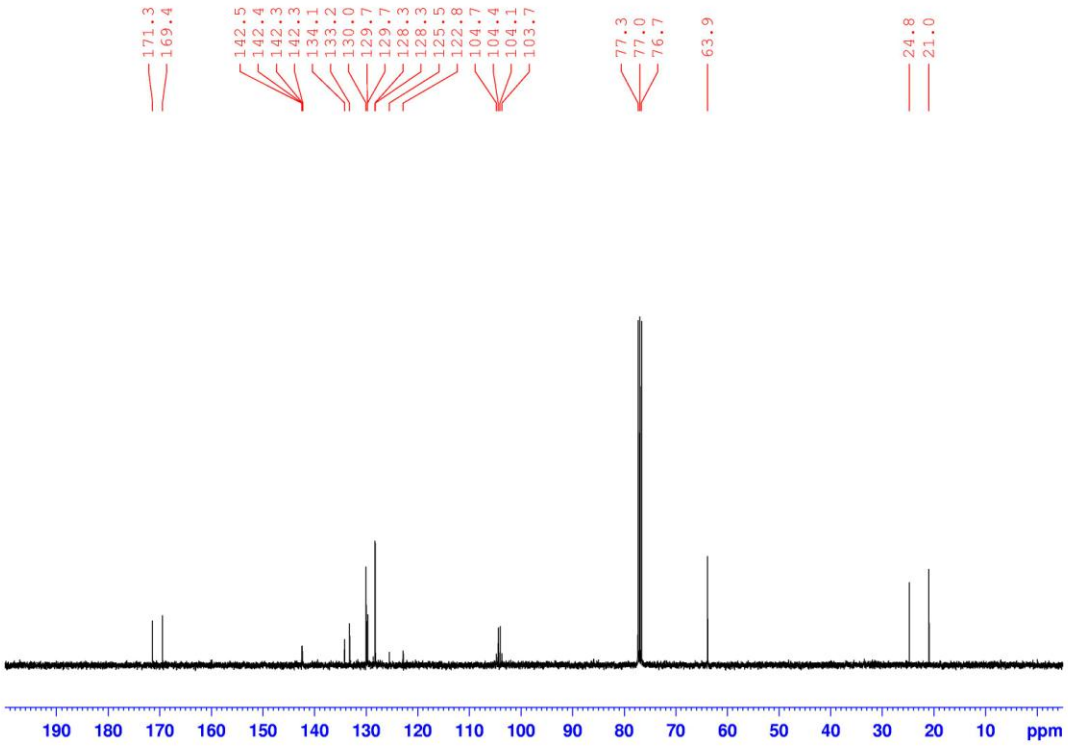
7.45
7.44
7.41
7.38
7.37
7.36
7.35
7.34
7.29
7.27
7.26
7.22
7.20
7.18
7.16
5.18
5.15
4.97
4.94
2.11
2.08
0.00
9
8
7
6
5
4
3
2
1
0 ppm
1.09
2.03
1.09
0.95
1.00
1.05
1.04
3.14
2.94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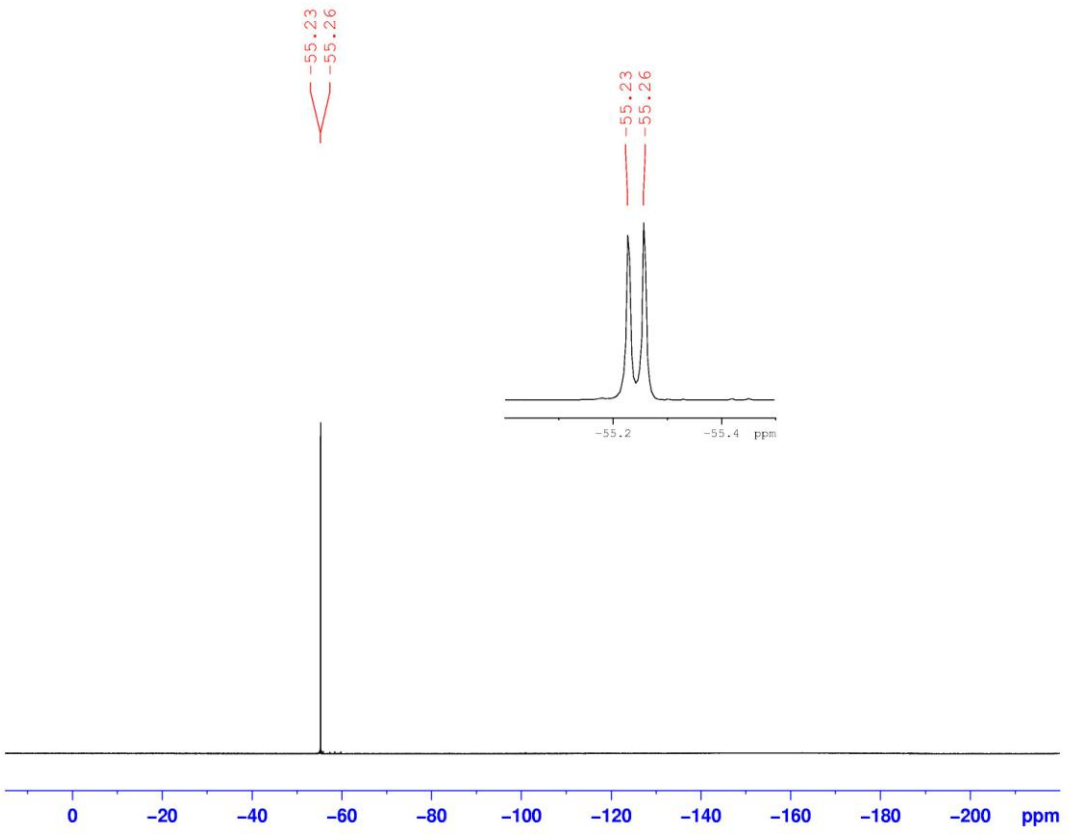
169.4
142.5
142.4
142.3
142.3
134.1
133.2
130.0
129.7
129.7
128.3
128.3
125.5
122.8
104.7
104.4
104.1
103.7
77.3
77.0
76.7
63.9
24.8
21.0
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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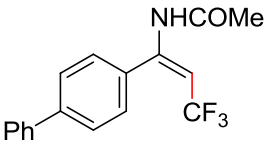
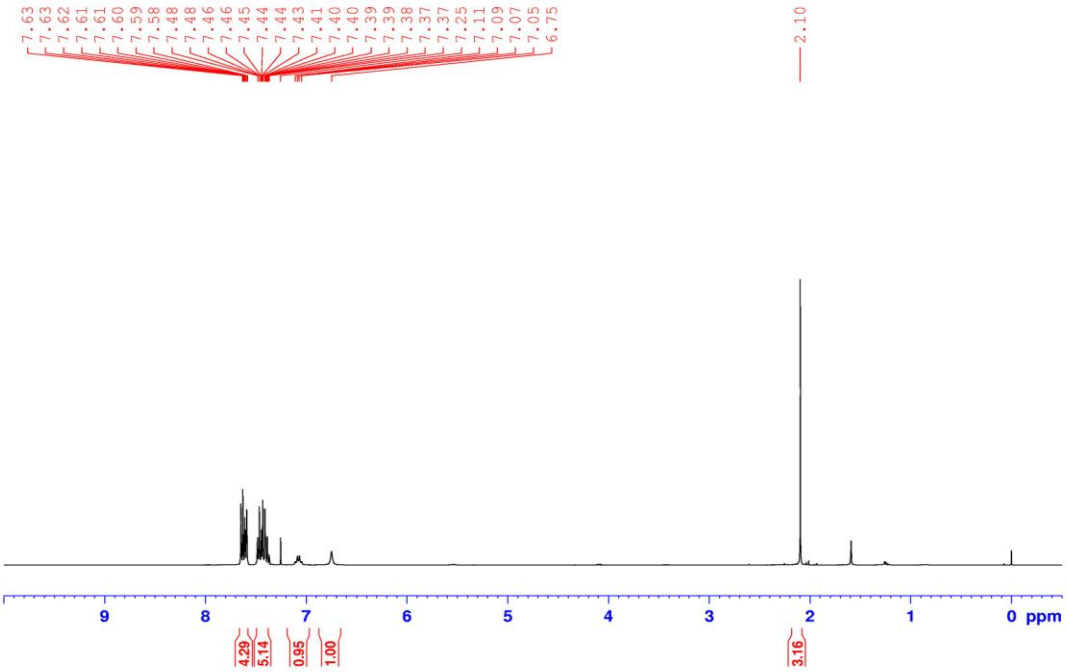
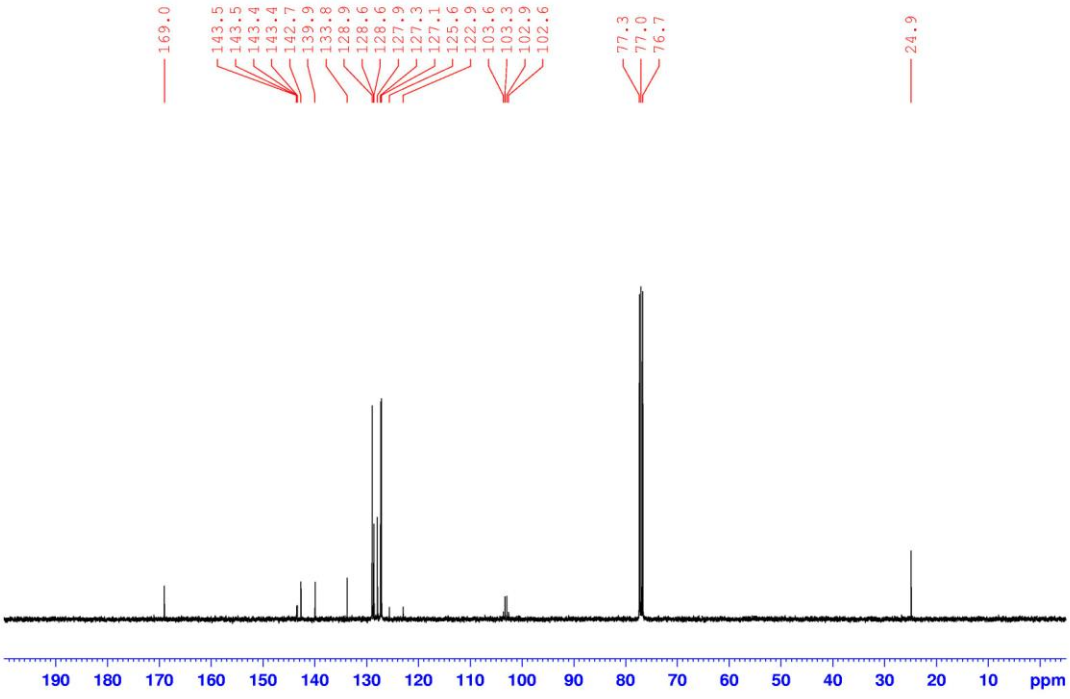
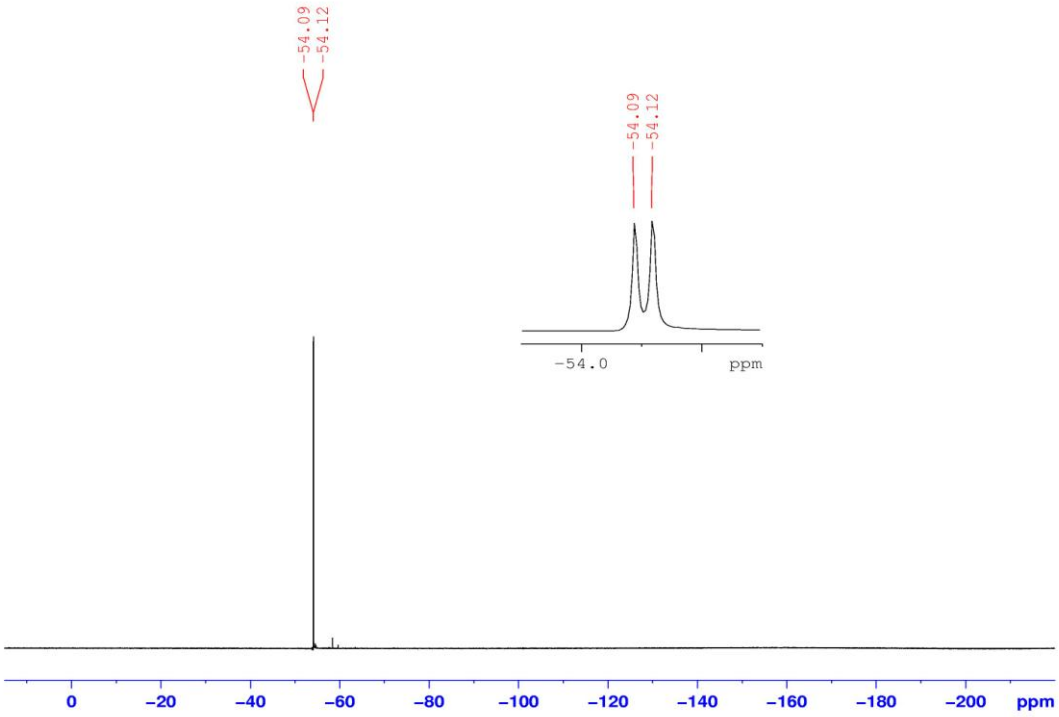
-55.26
-55.23
-55.26
-55.2
-55.4 ppm
0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 ppm



3g



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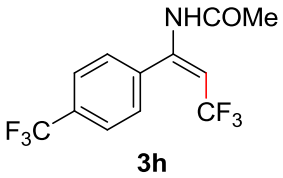
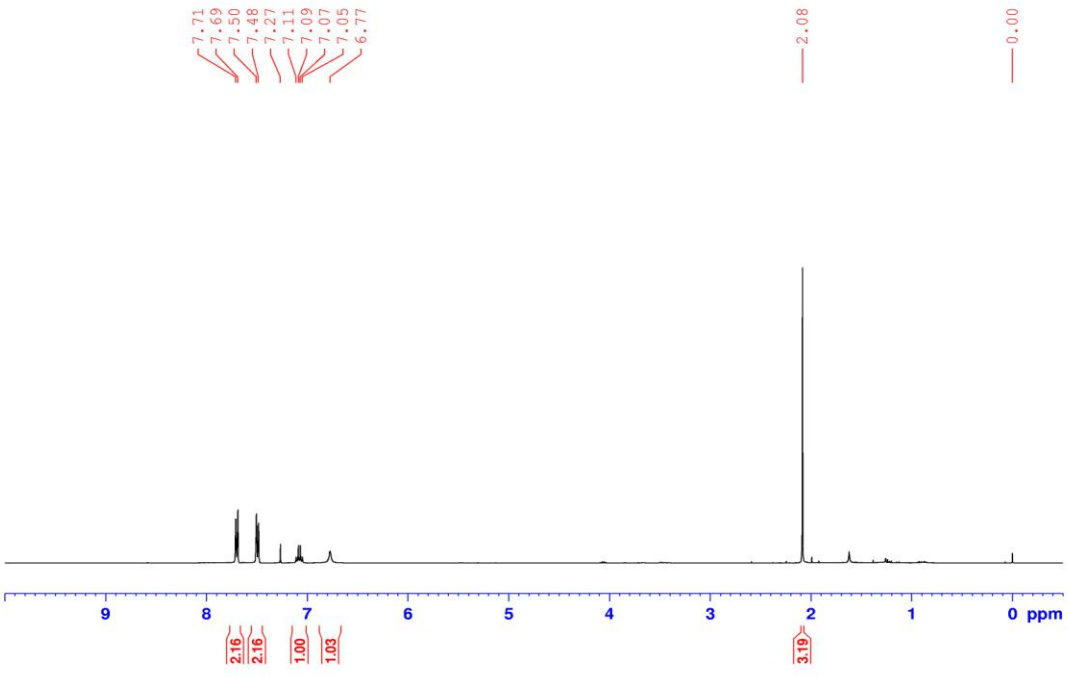
-54.12
-54.09
-54.12
-54.0
ppm
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm


NHCOMe
F3C
CF3

3h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7.69
7.50
7.48
7.27
7.11
7.09
7.07
7.05
6.77
2.08
0.00
9
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6
5
4
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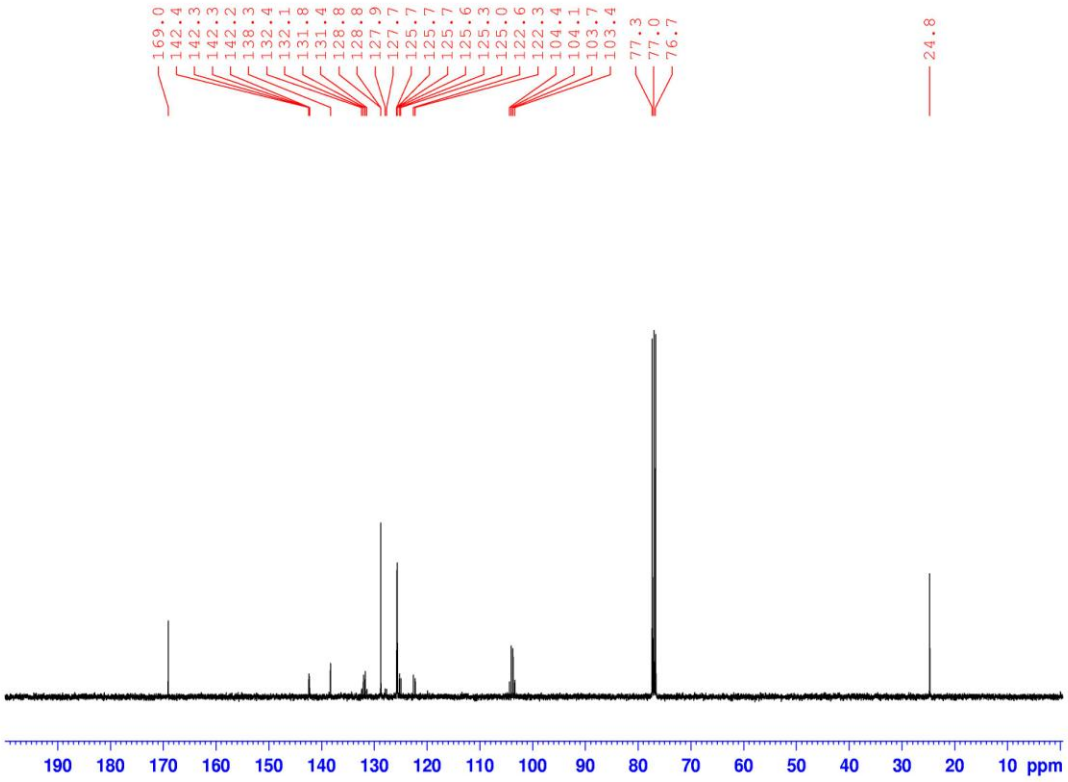
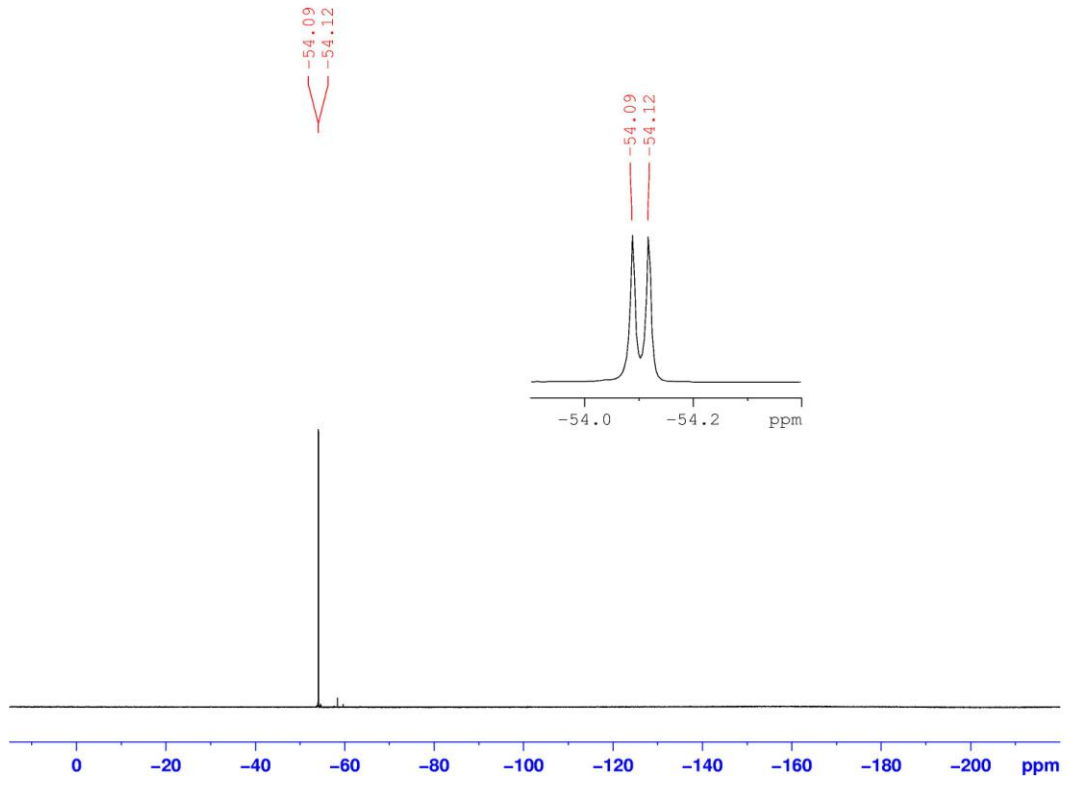
0 ppm
2.16
2.16
1.00
1.03
3.19


169.0
142.4
142.3
142.3
142.2
138.3
132.4
132.1
131.8
131.4
128.8
128.8
127.9
127.7
125.7
125.7
125.7
125.6
125.3
125.0
122.6
122.3
104.4
104.1
103.7
103.4
77.3
77.0
76.7
24.8
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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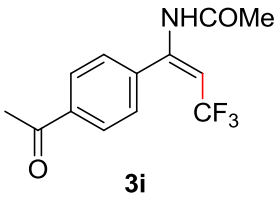
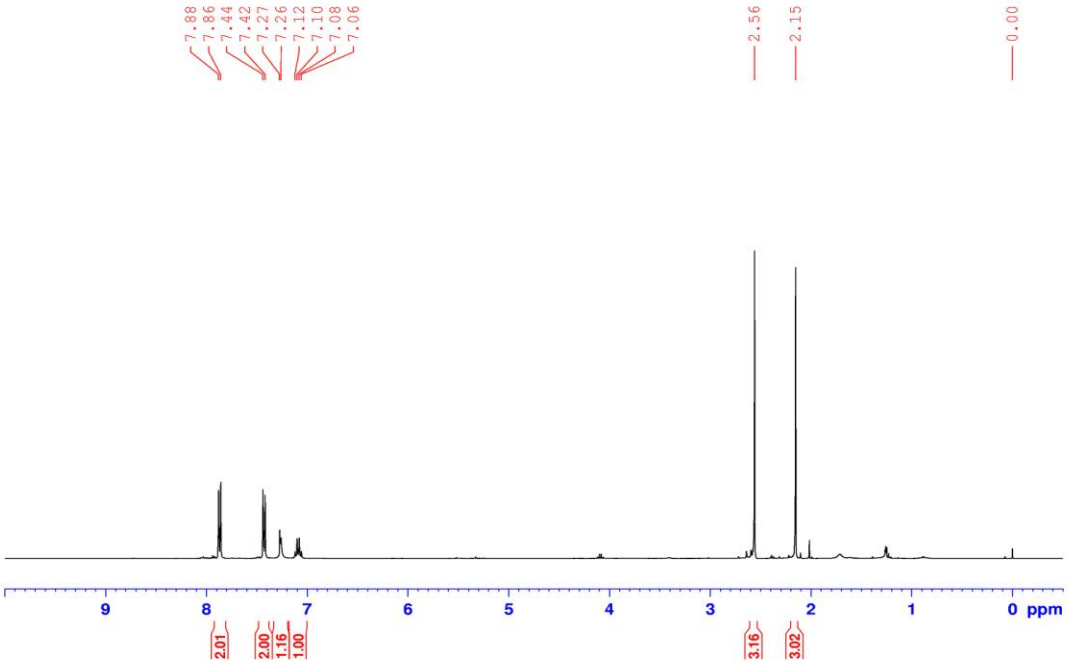
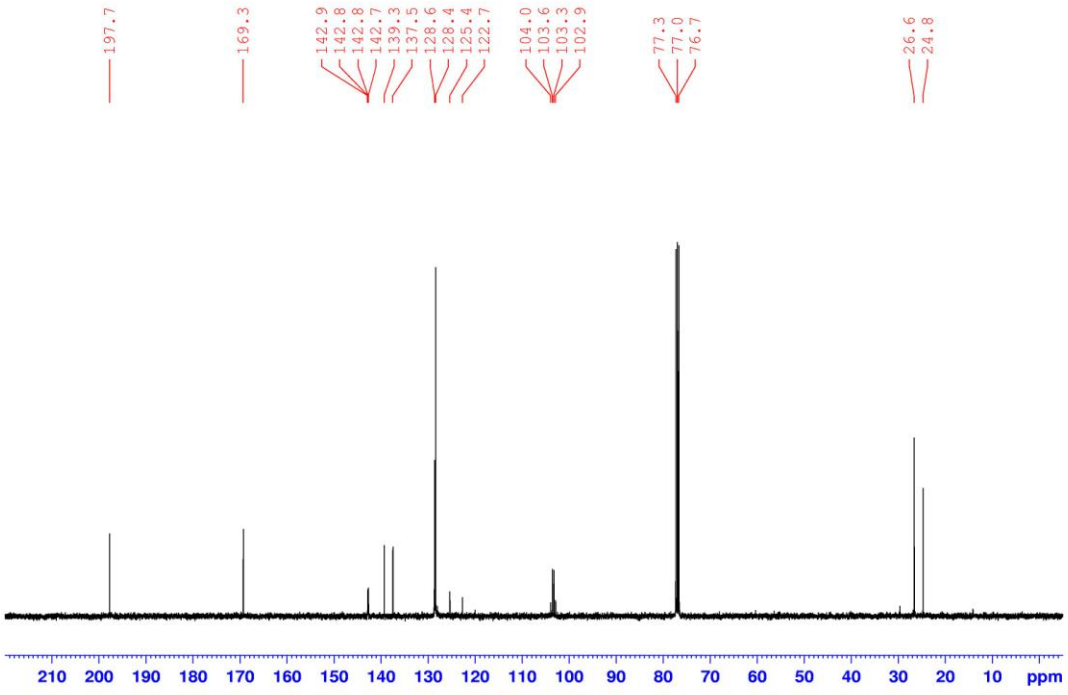
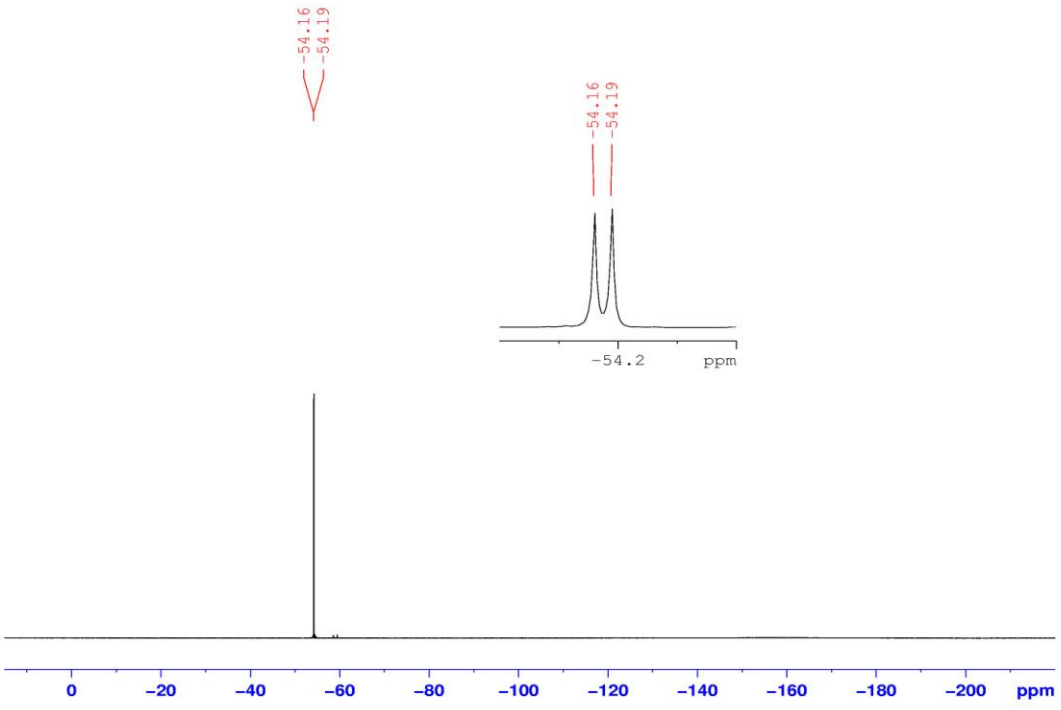
-54.12
-54.09
-54.12
-54.0
-54.2
ppm
0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 ppm

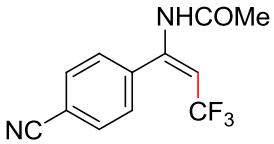


3i









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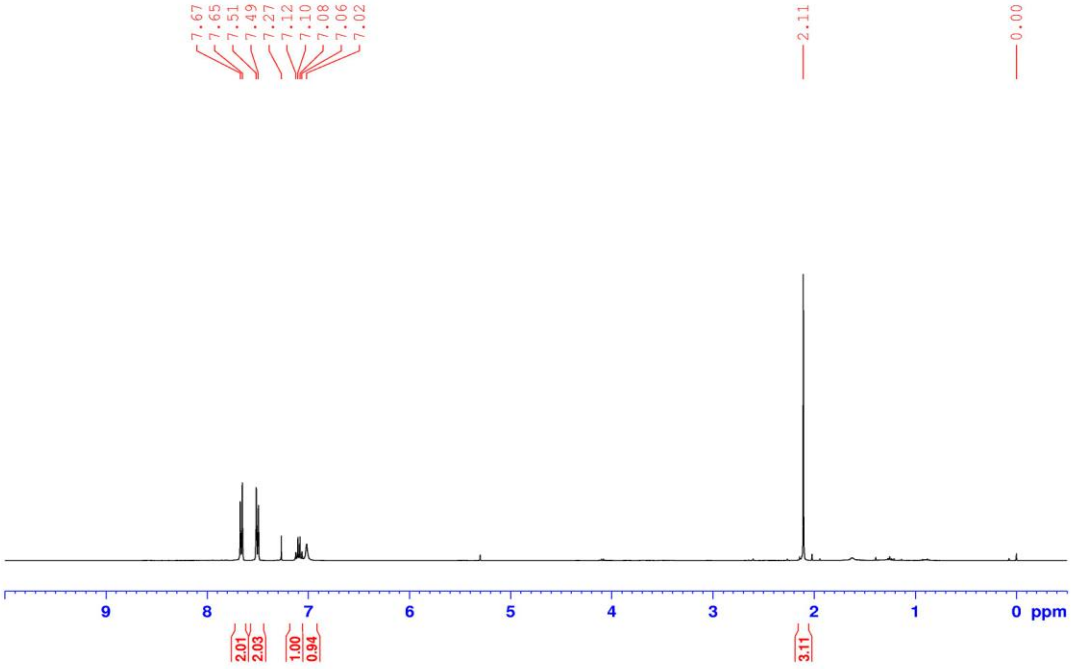

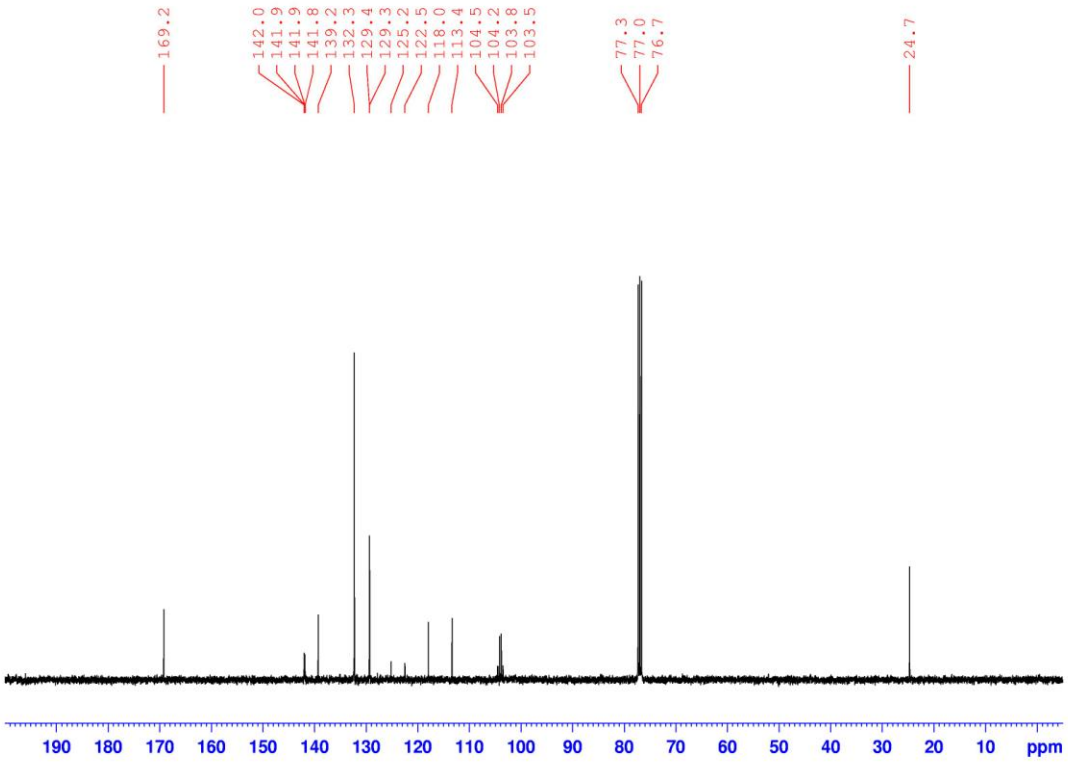
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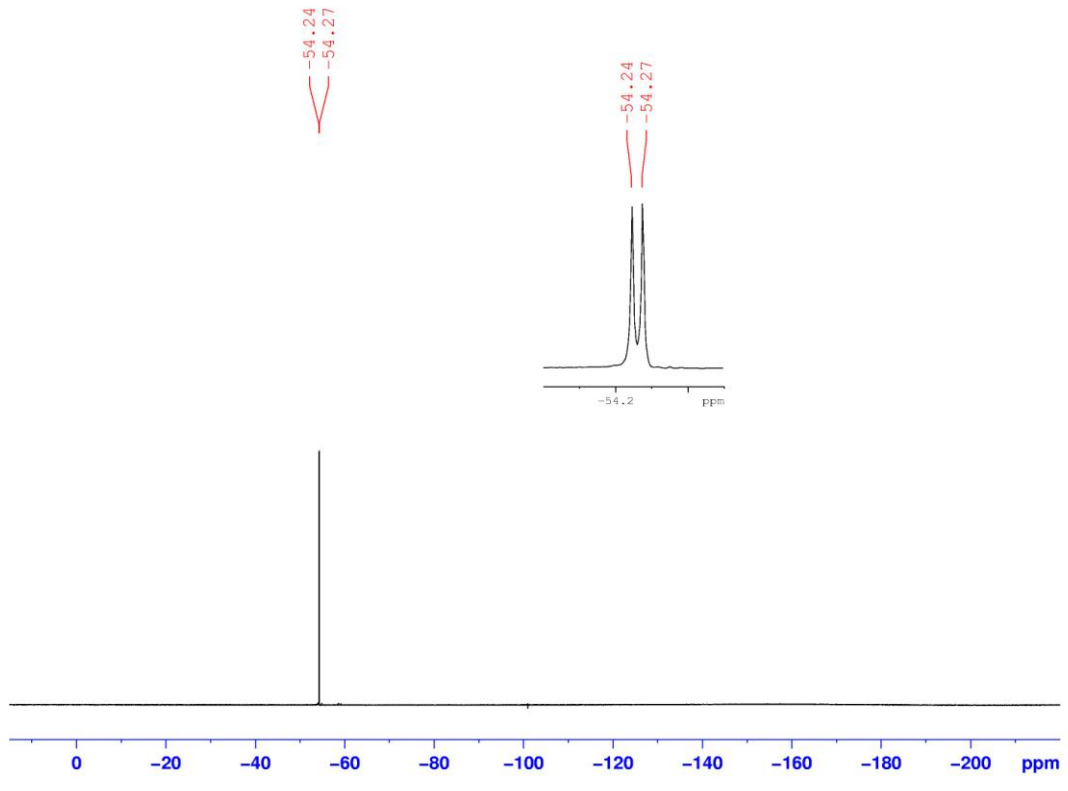
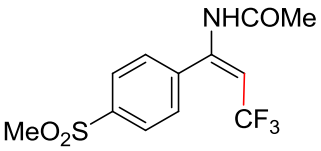
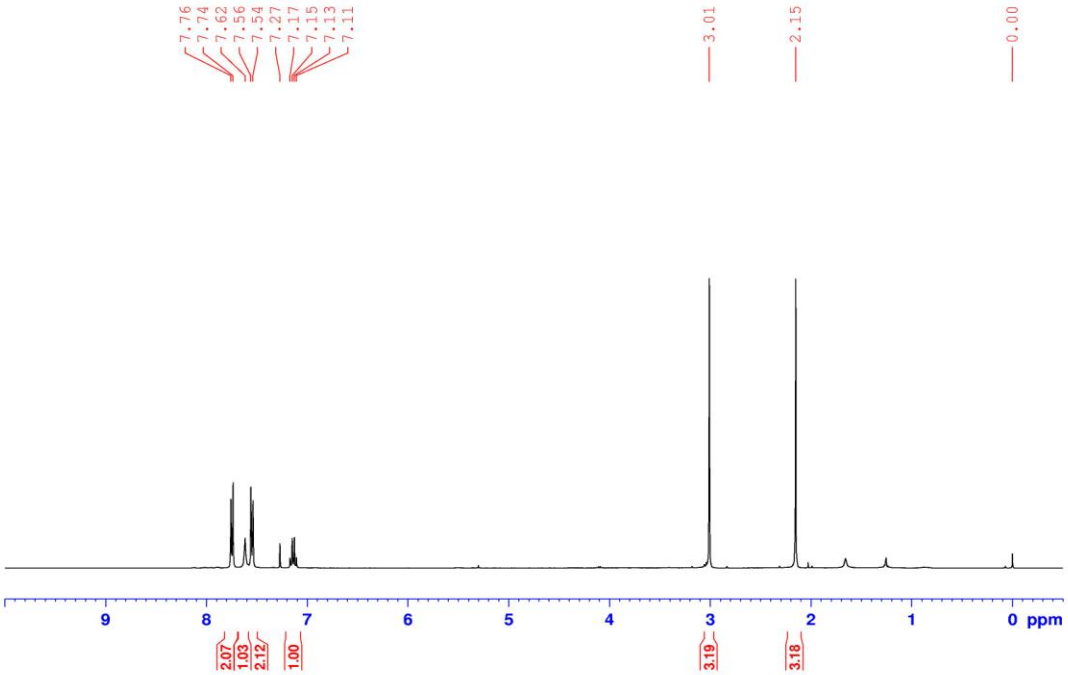
141.9
141.8
139.2
132.3
129.4
129.3
125.2
122.5
118.0
113.4
104.5
104.2
103.8
103.5
77.3
77.0
76.7
24.7
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


-54.24
-54.27
-54.24
-54.27
-54.2
ppm
0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 ppm


NHCOMe
MeO2S
CF3

3k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7.27
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7.13
7.11
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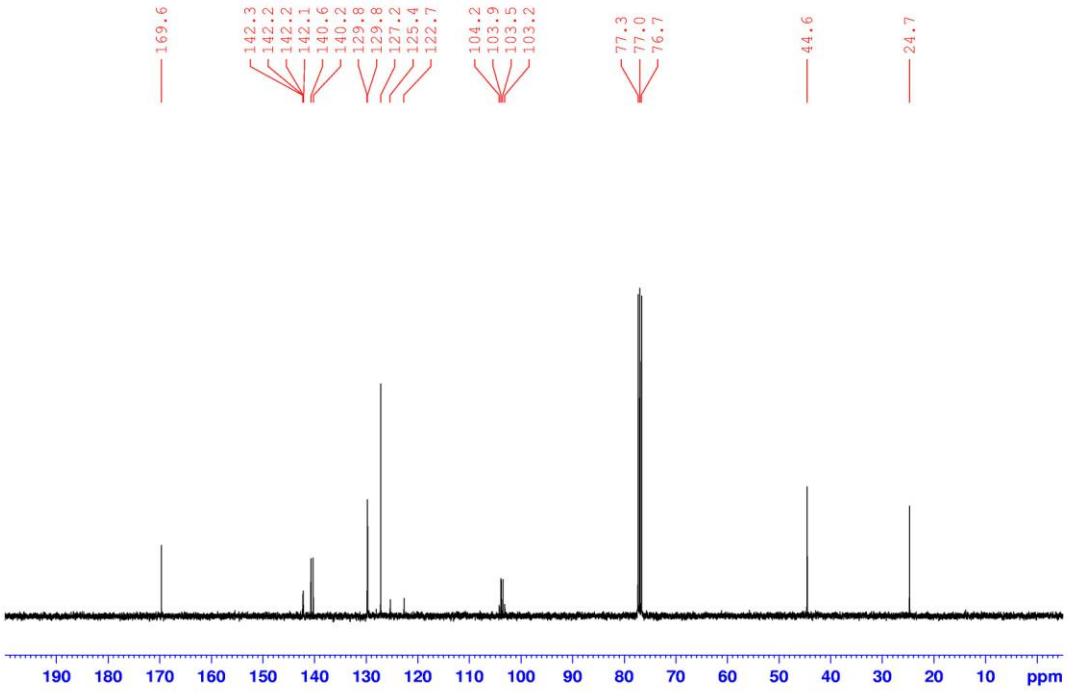
2.15
0.00
9
8
7
6
5
4
3
2
1
0 ppm
2.07
1.03
2.12
1.00
3.19
3.18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142.2
142.2
142.1
140.6
140.2
129.8
127.2
125.4
122.7
104.2
103.9
103.5
103.2
77.3
77.0
76.7
44.6
24.7
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150
140
130
120
110
100
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80
70
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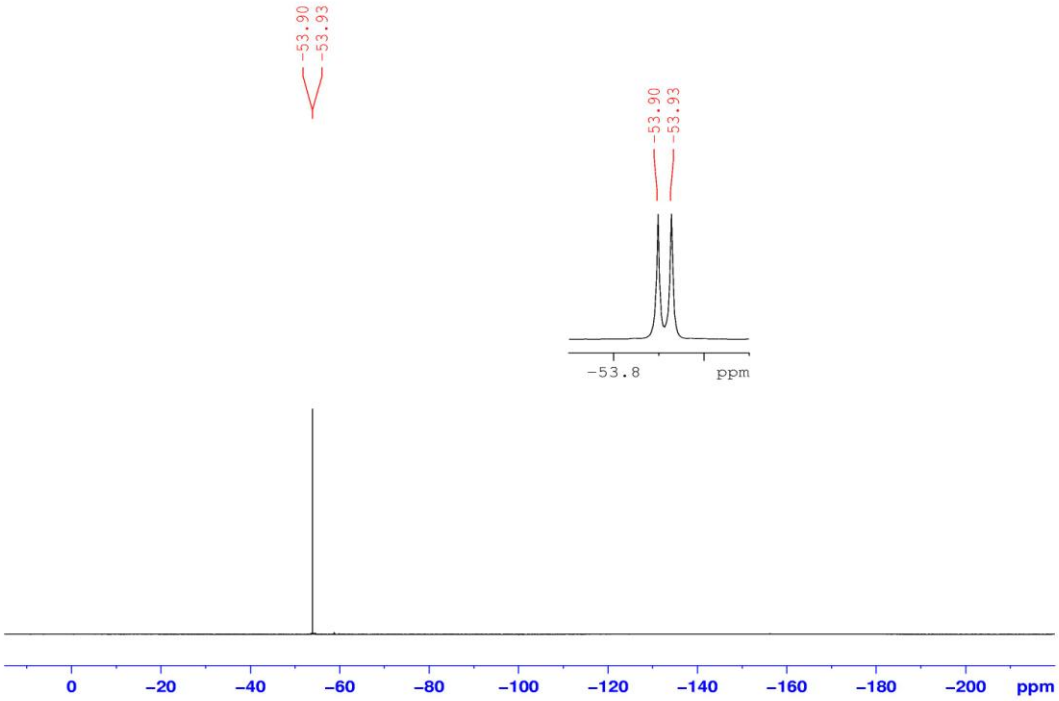
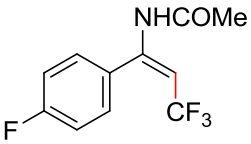
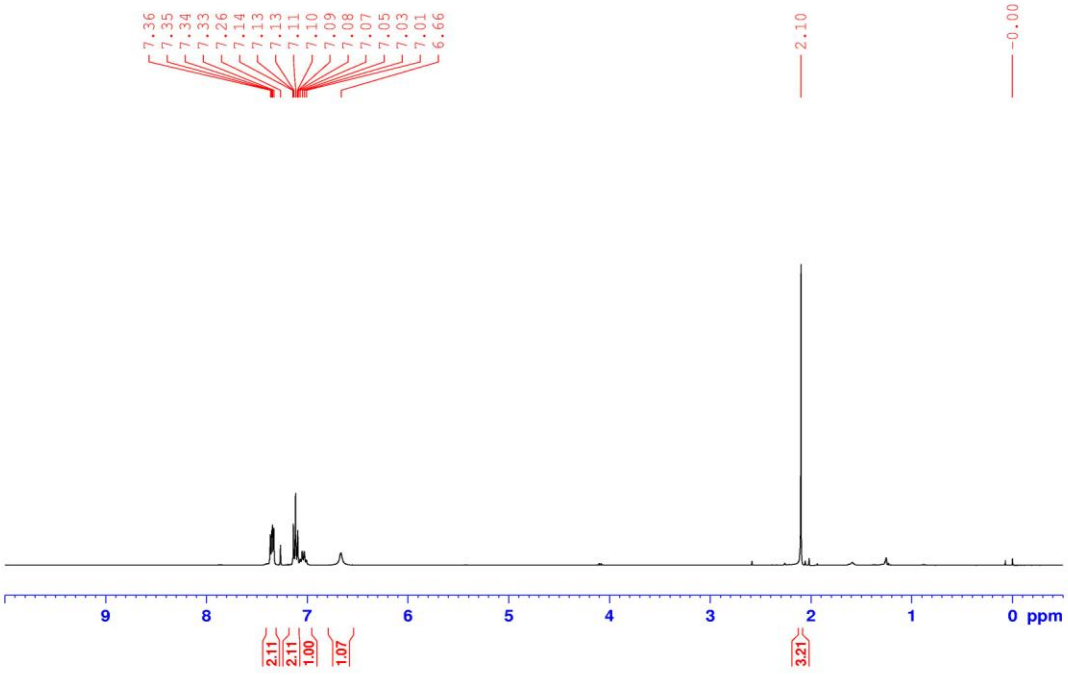
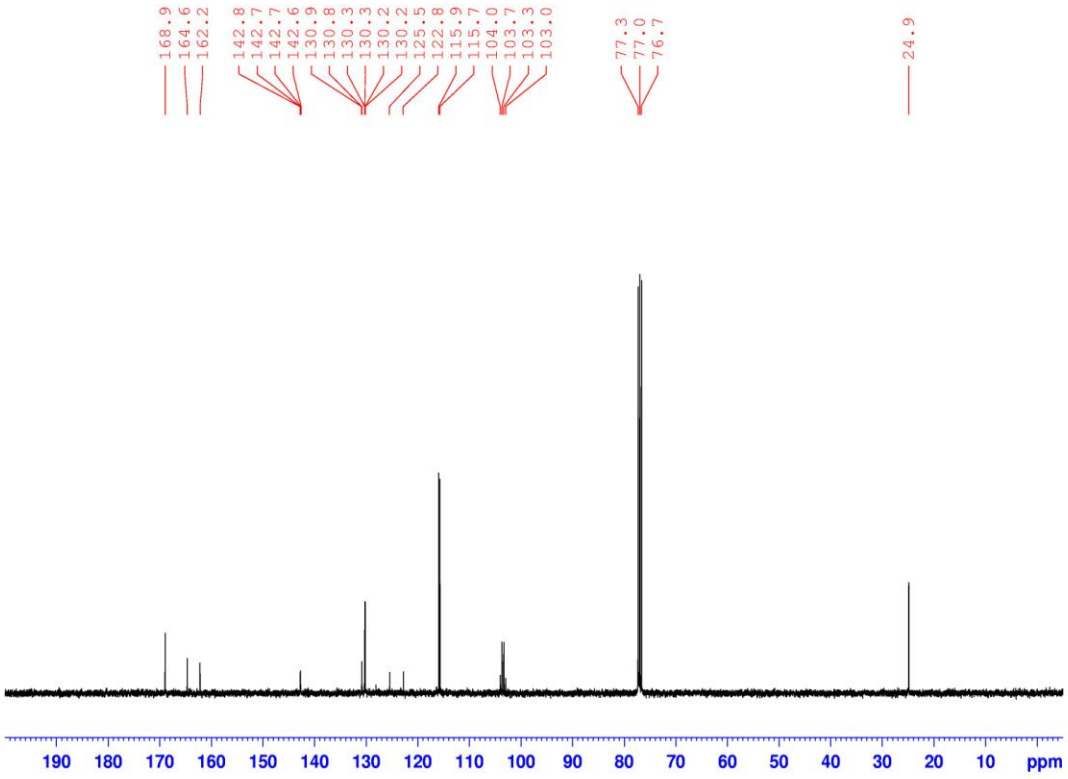
50
40
30
20
10
ppm

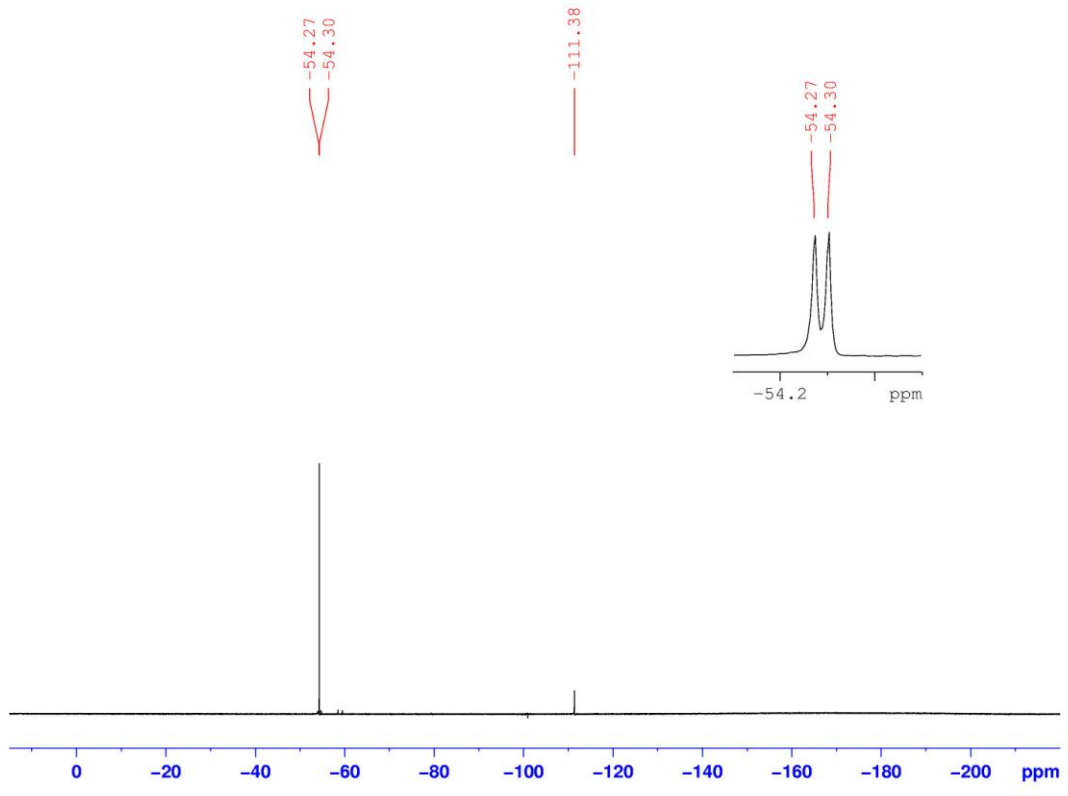


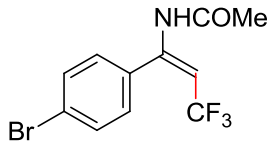


3l

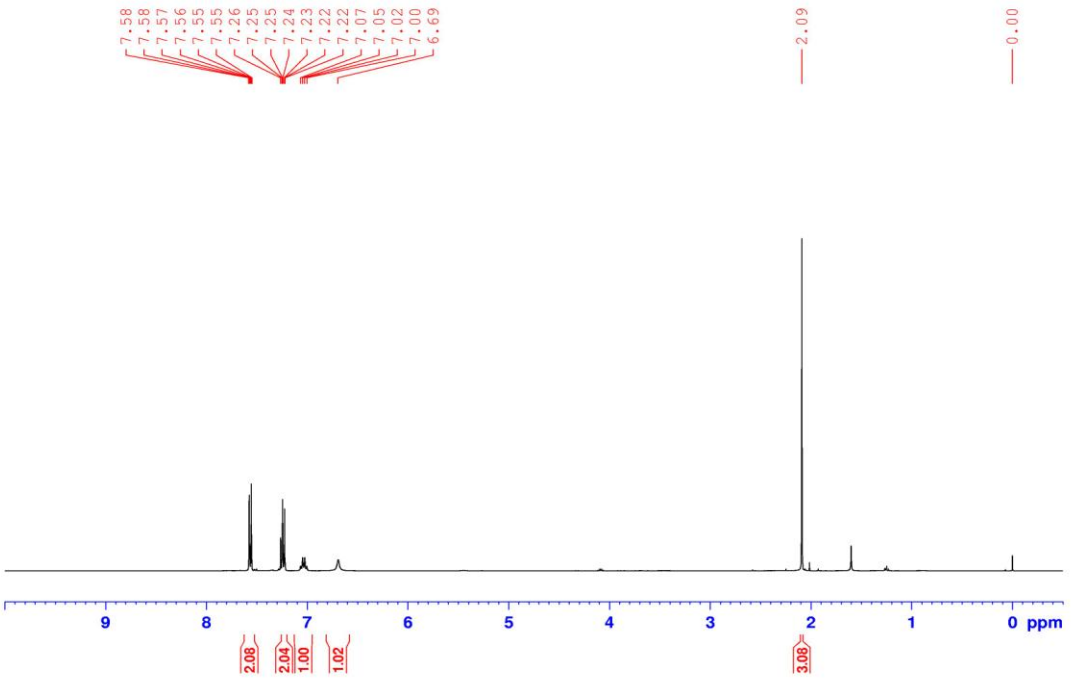


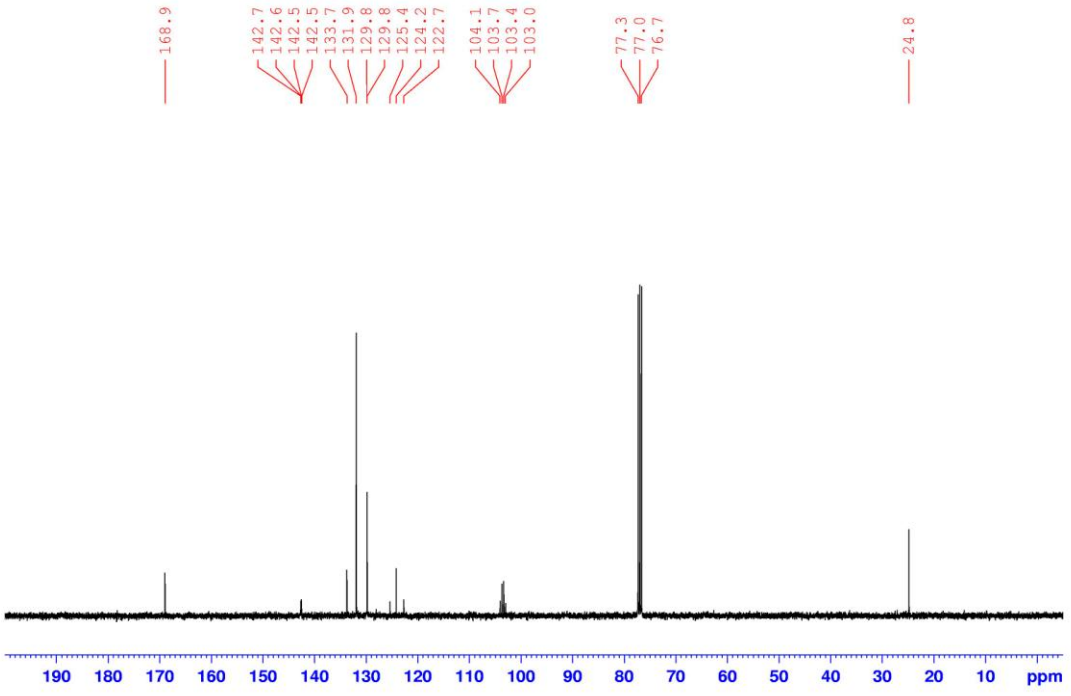


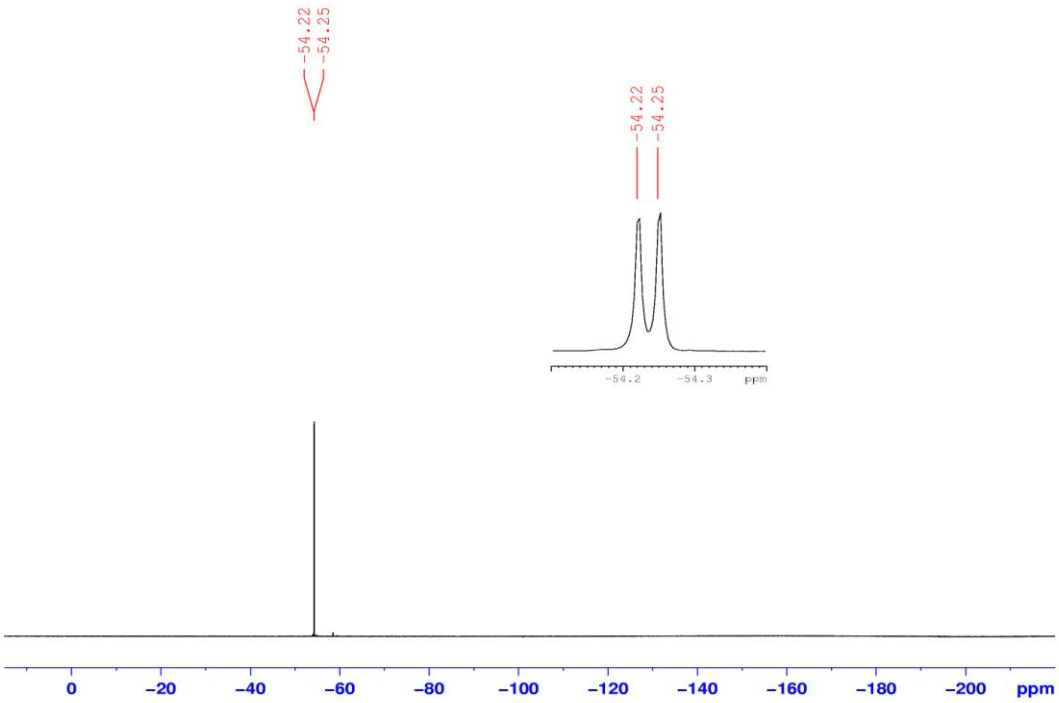


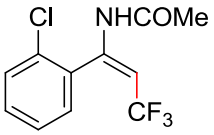


3m

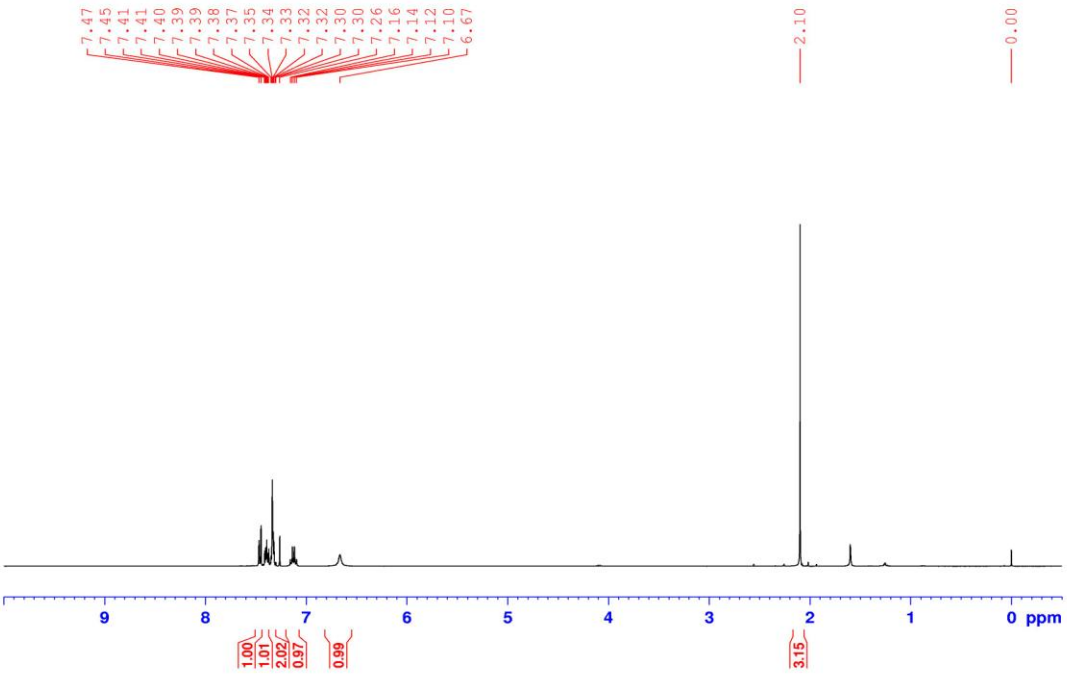


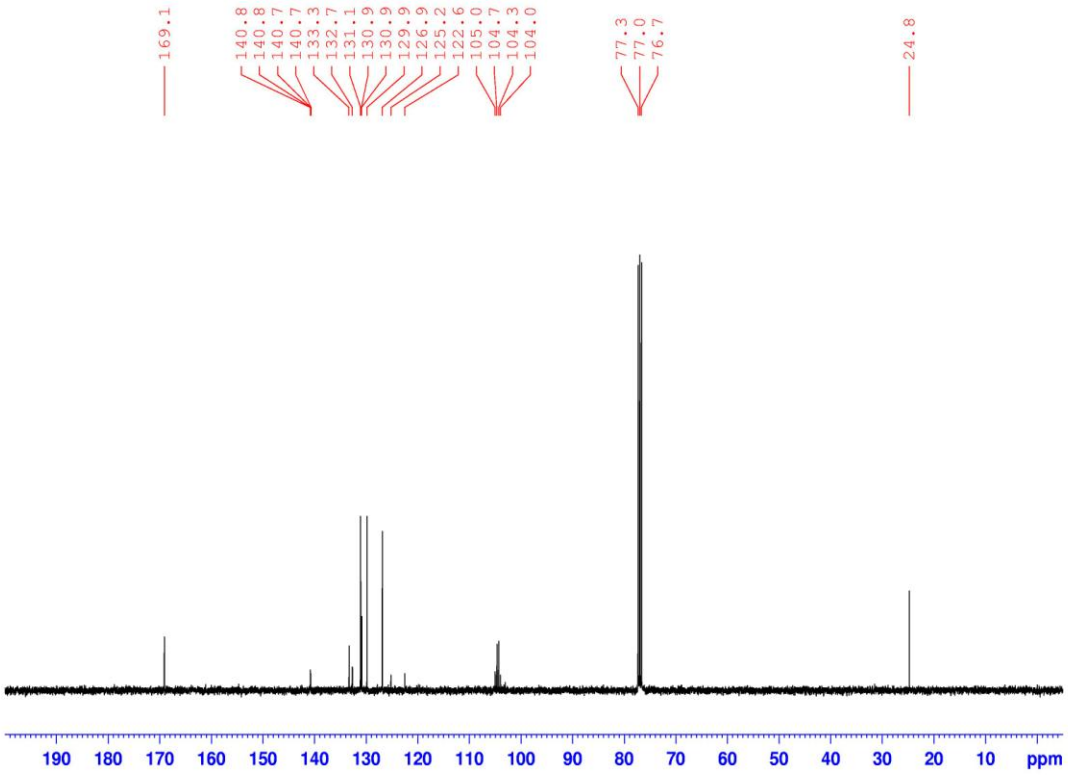


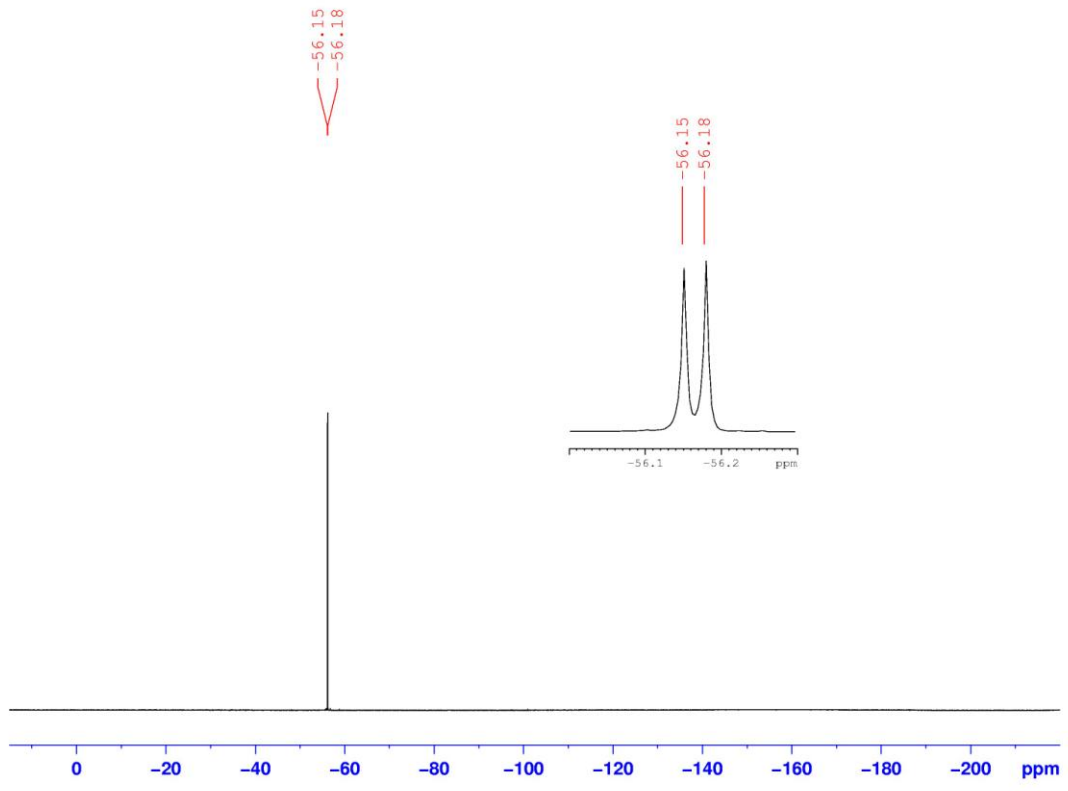


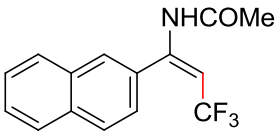


3n

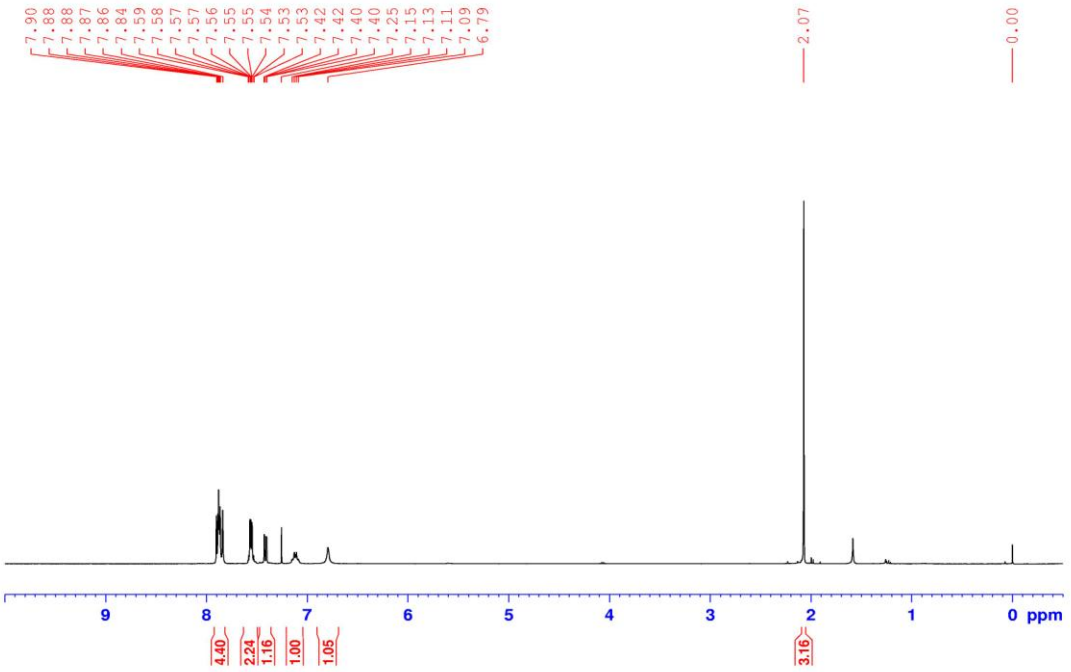







NHCOMe
CF3

3o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7.58
7.57
7.57
7.56
7.55
7.55
7.54
7.53
7.53
7.42
7.40
7.40
7.25
7.15
7.13
7.11
7.09
6.79
2.07
0.00
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2.24
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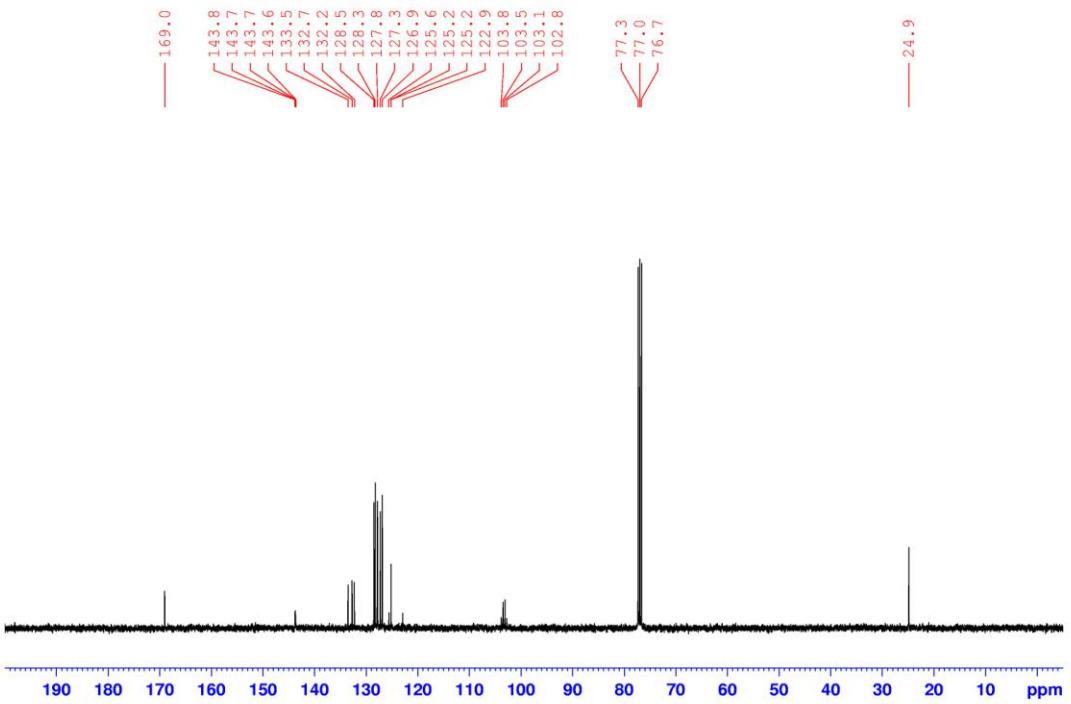
1.00
1.05
3.16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132.2
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128.3
127.8
127.3
126.9
125.6
125.2
125.2
122.9
103.8
103.5
103.1
102.8
77.3
77.0
76.7
24.9
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150
140
130
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30
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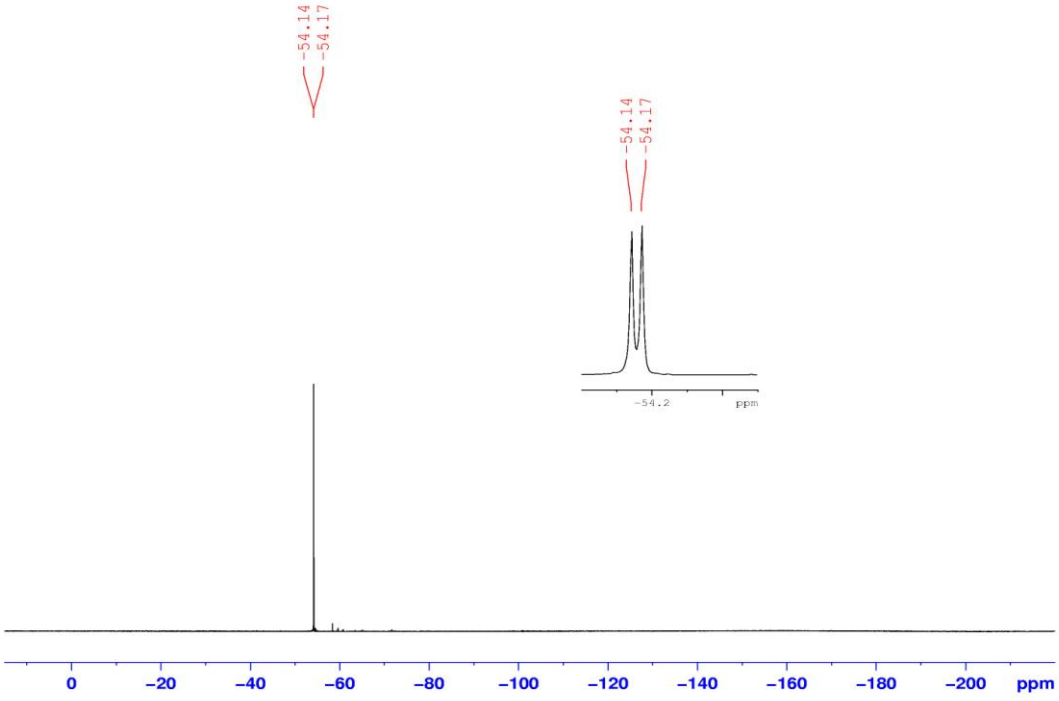
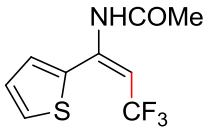
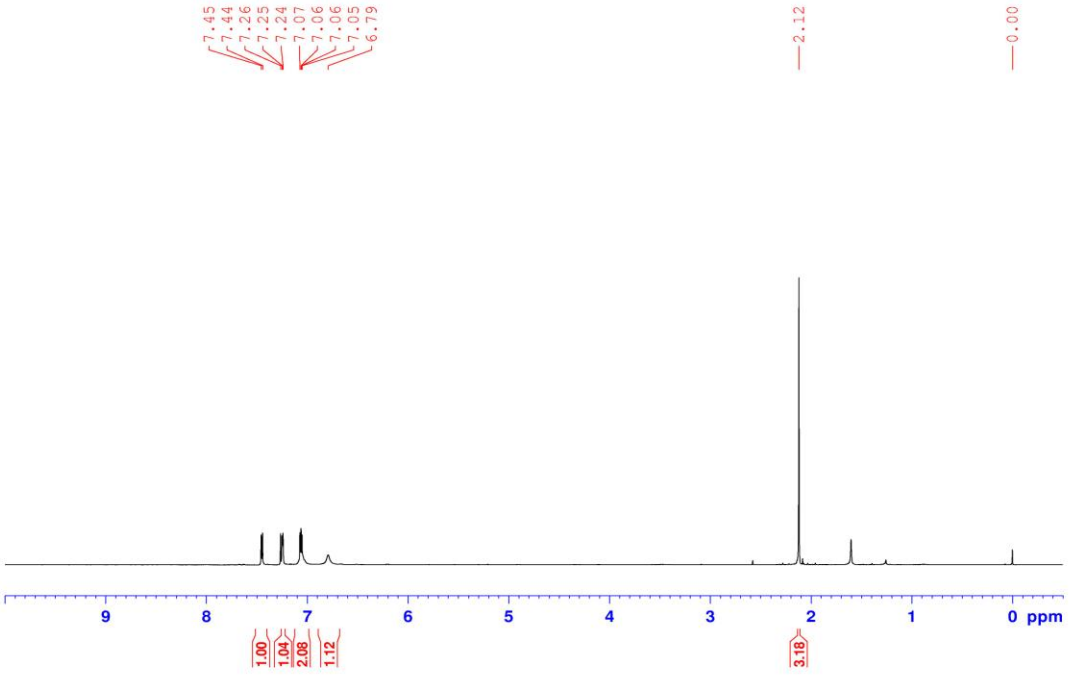
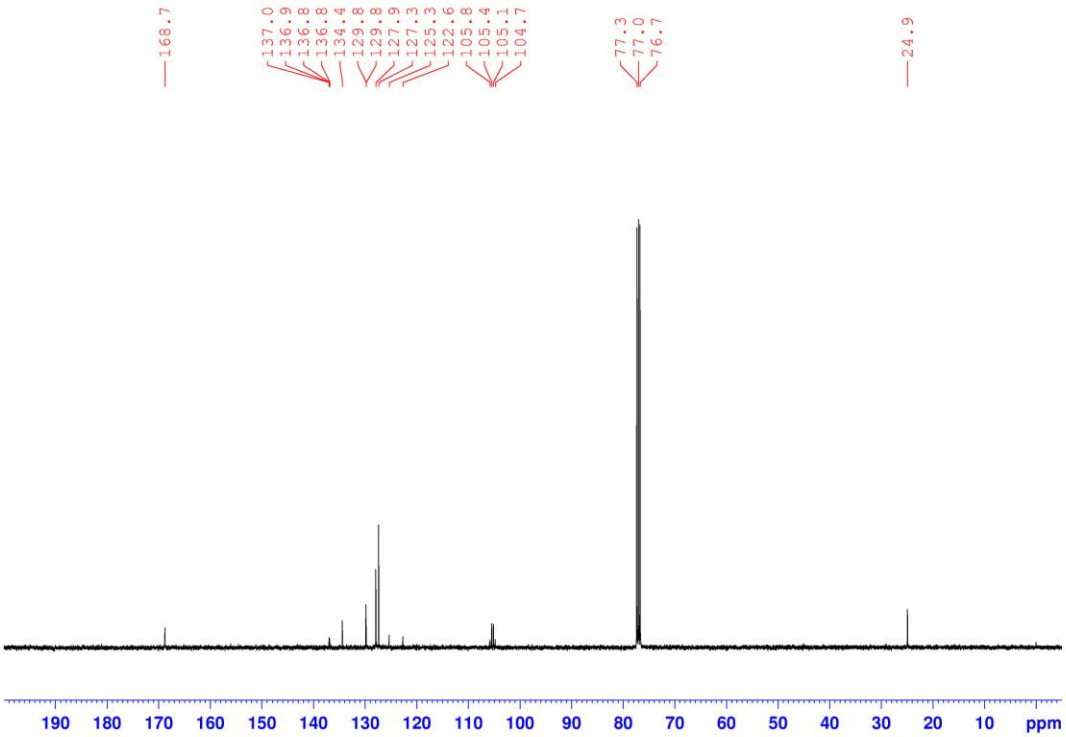
10
ppm

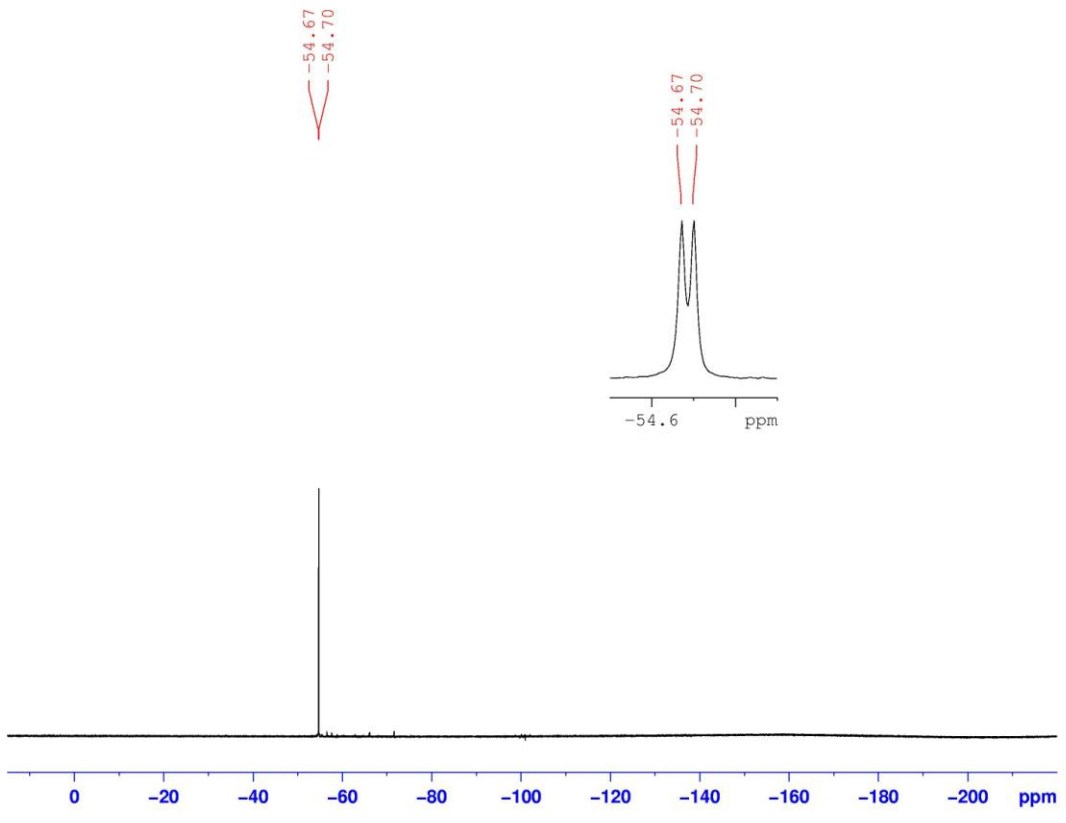


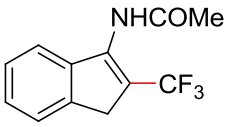


3p

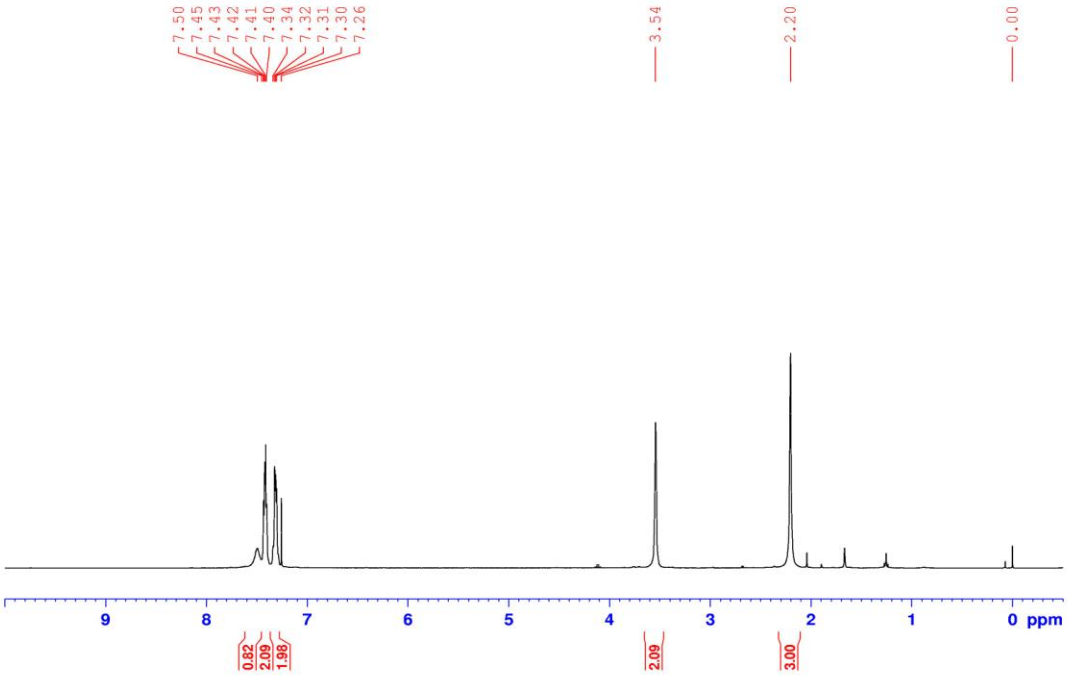


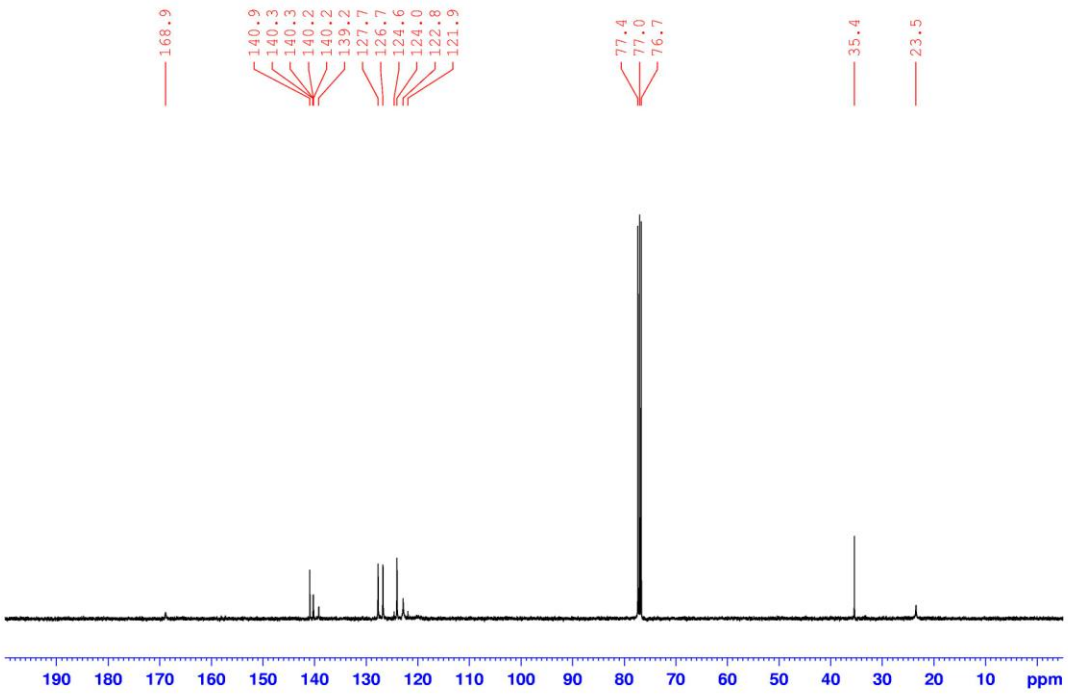


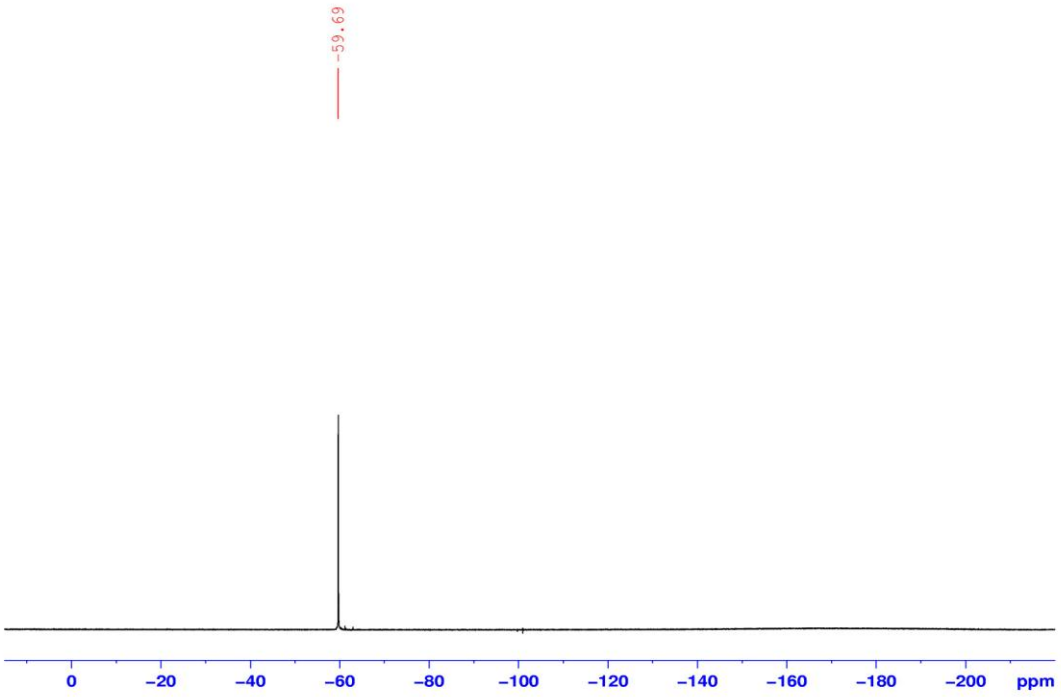


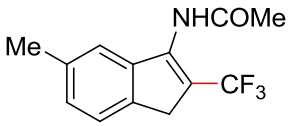


3q









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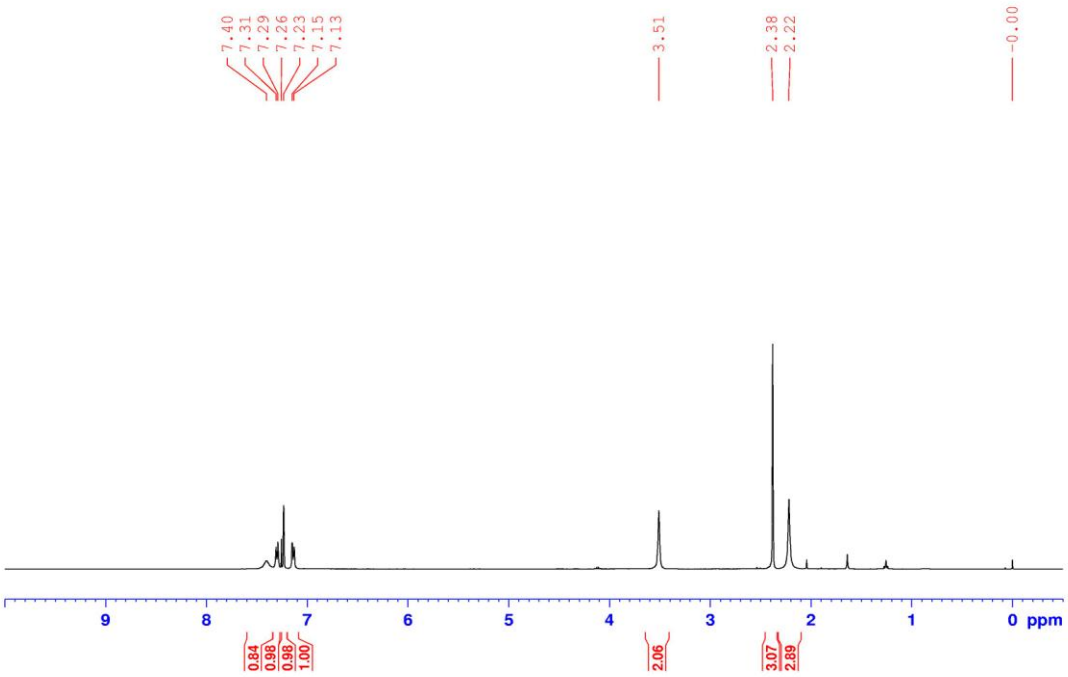

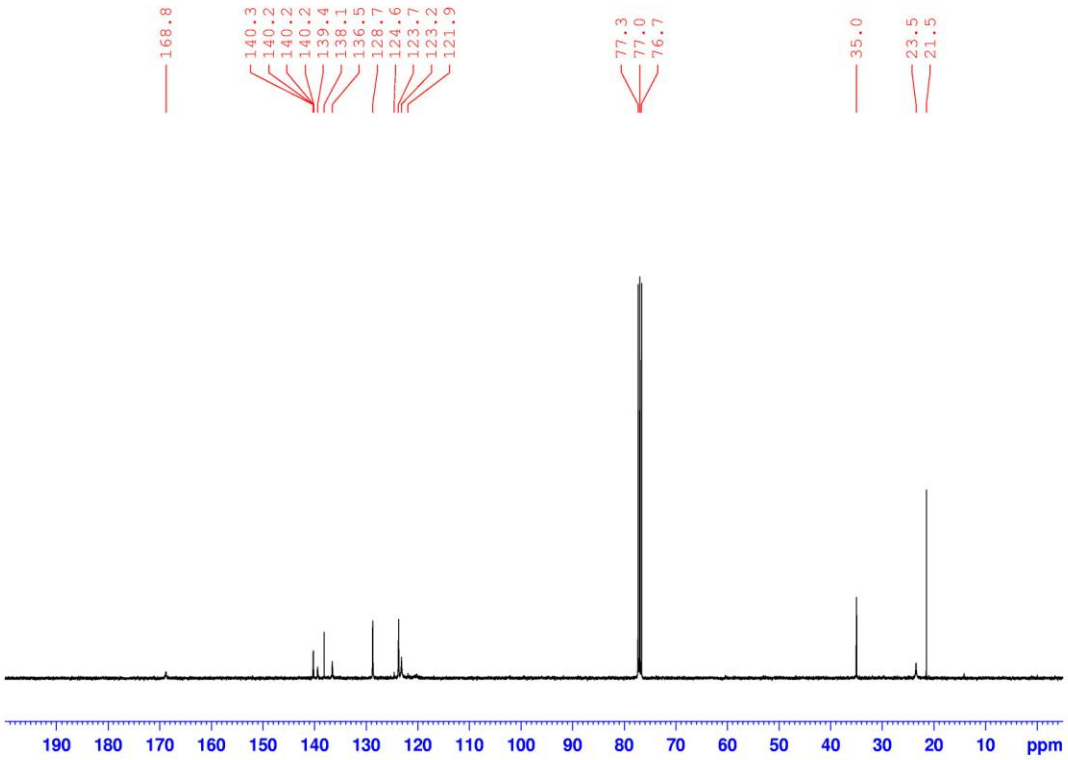

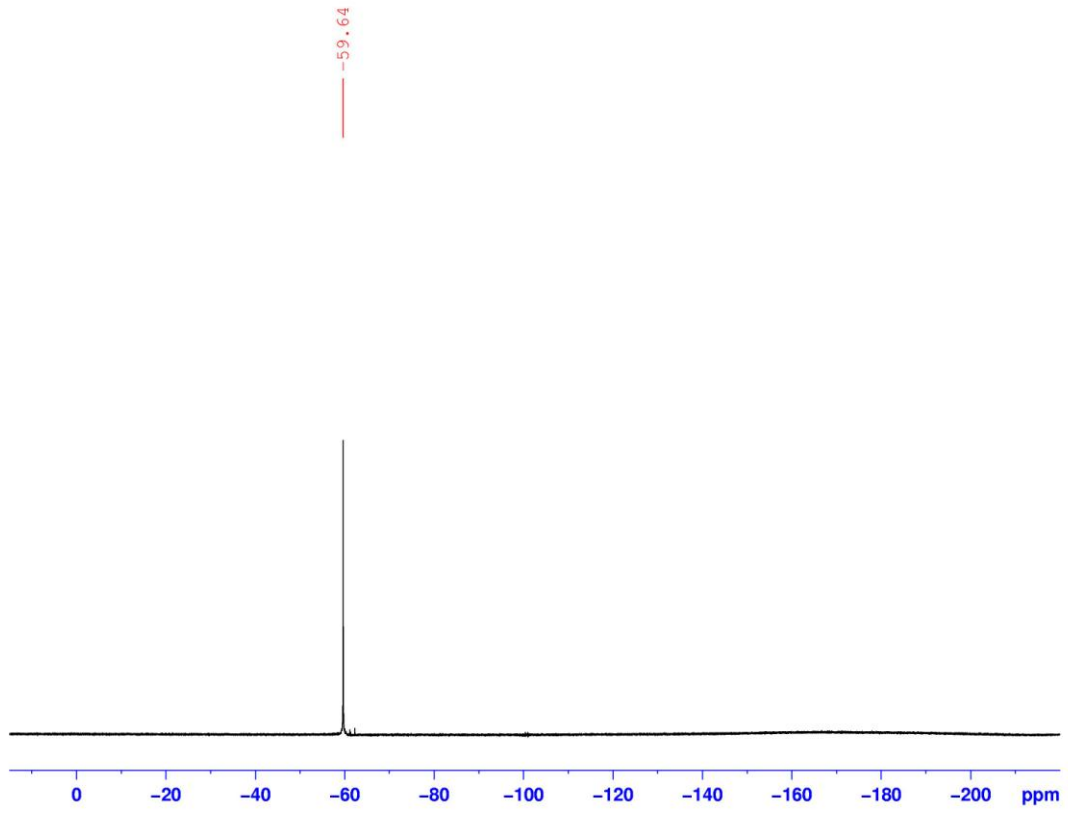

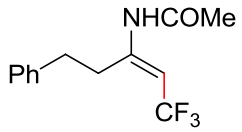
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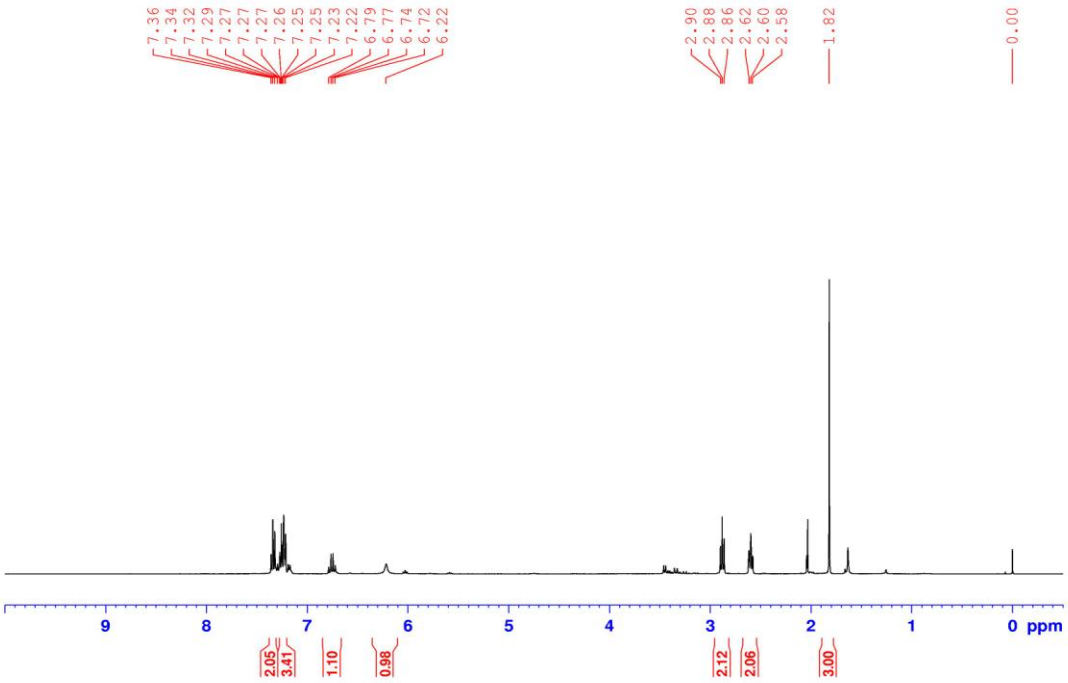
Ph
CF3

3s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7.26
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7.23
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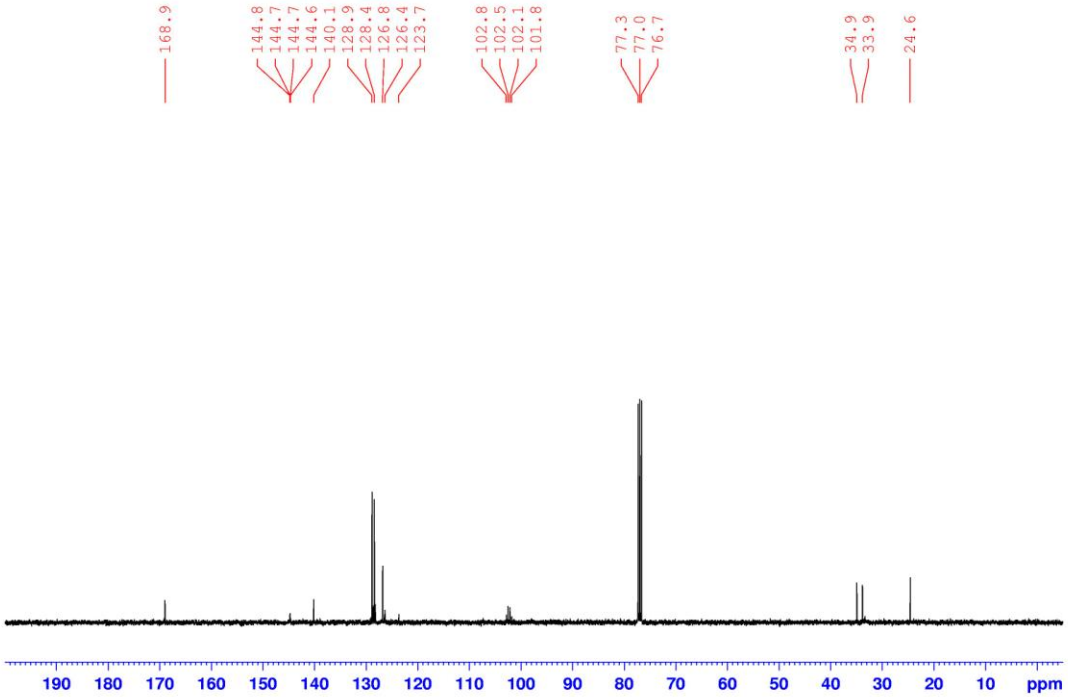
6.79
6.77
6.74
6.72
6.22
2.90
2.88
2.86
2.62
2.60
2.58
1.82
0.00
9
8
7
6
5
4
3
2
1
0 ppm
2.05
3.41
1.10
0.98
2.12
2.06
3.00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144.7
144.7
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140.1
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128.4
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126.4
123.7
102.8
102.5
102.1
101.8
77.3
77.0
76.7
34.9
33.9
24.6
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180
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150
140
130
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110
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70
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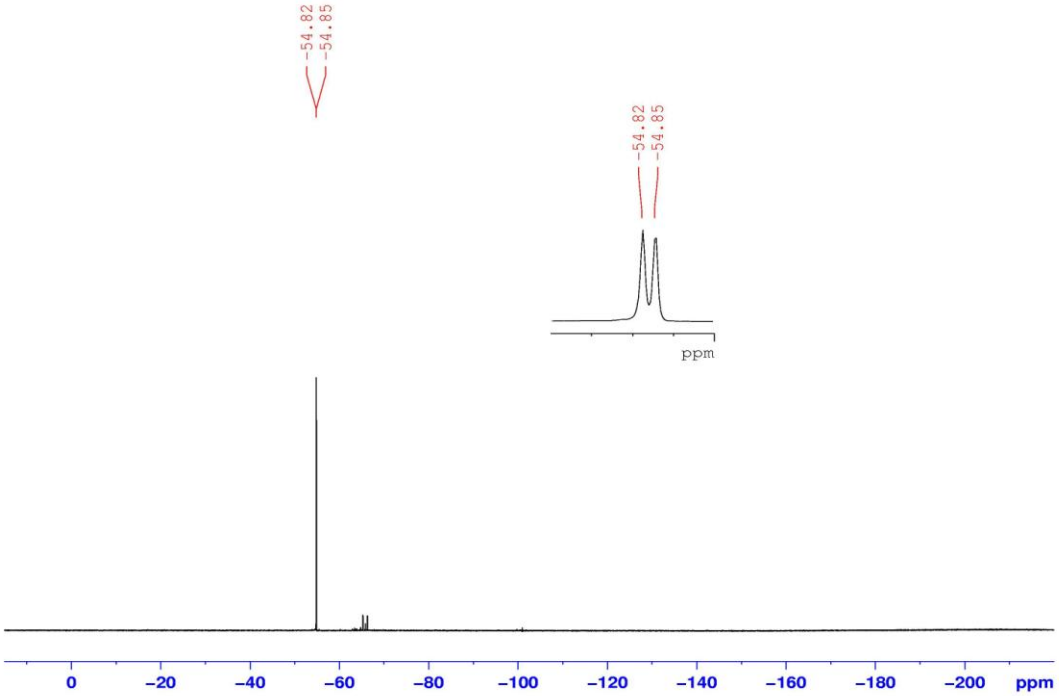
30
20
10
ppm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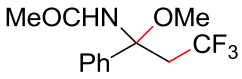
MeOCHN
OMe
CF3
Ph

4a


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7.39
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7.37
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7.27
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3.51
3.50
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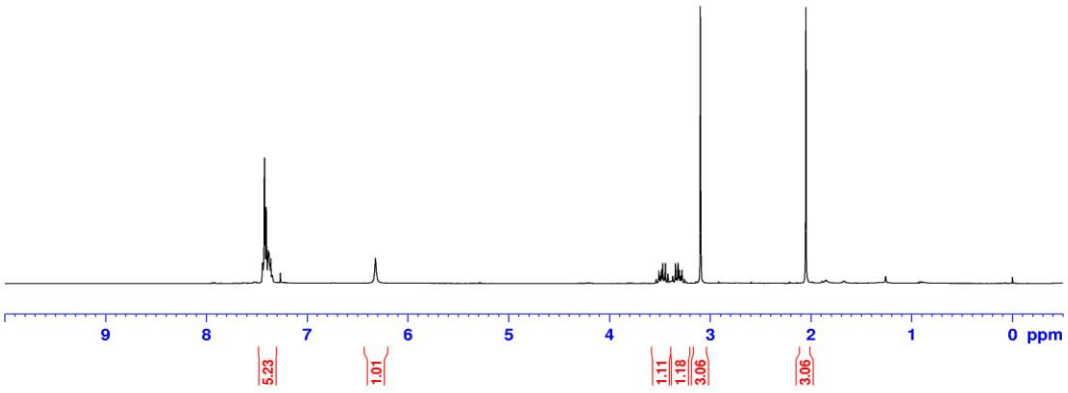
3.31
3.29
3.28
3.10
2.05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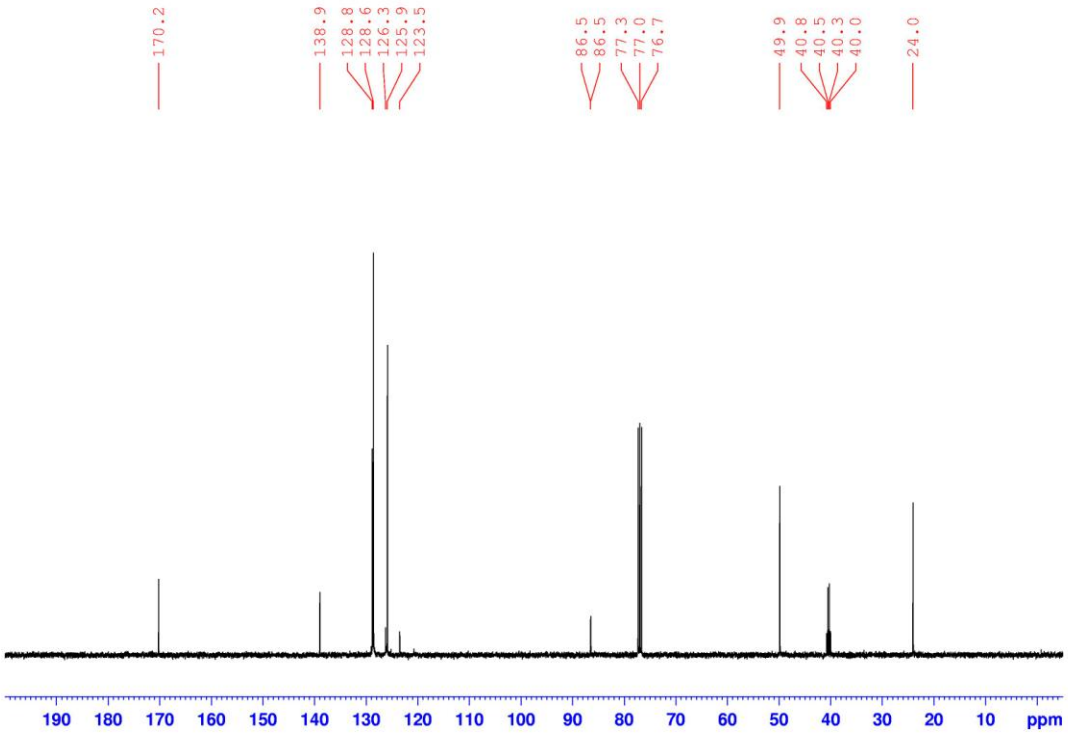
3.06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128.8
128.6
126.3
125.9
123.5
86.5
86.5
77.3
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76.7
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40.3
40.0
24.0
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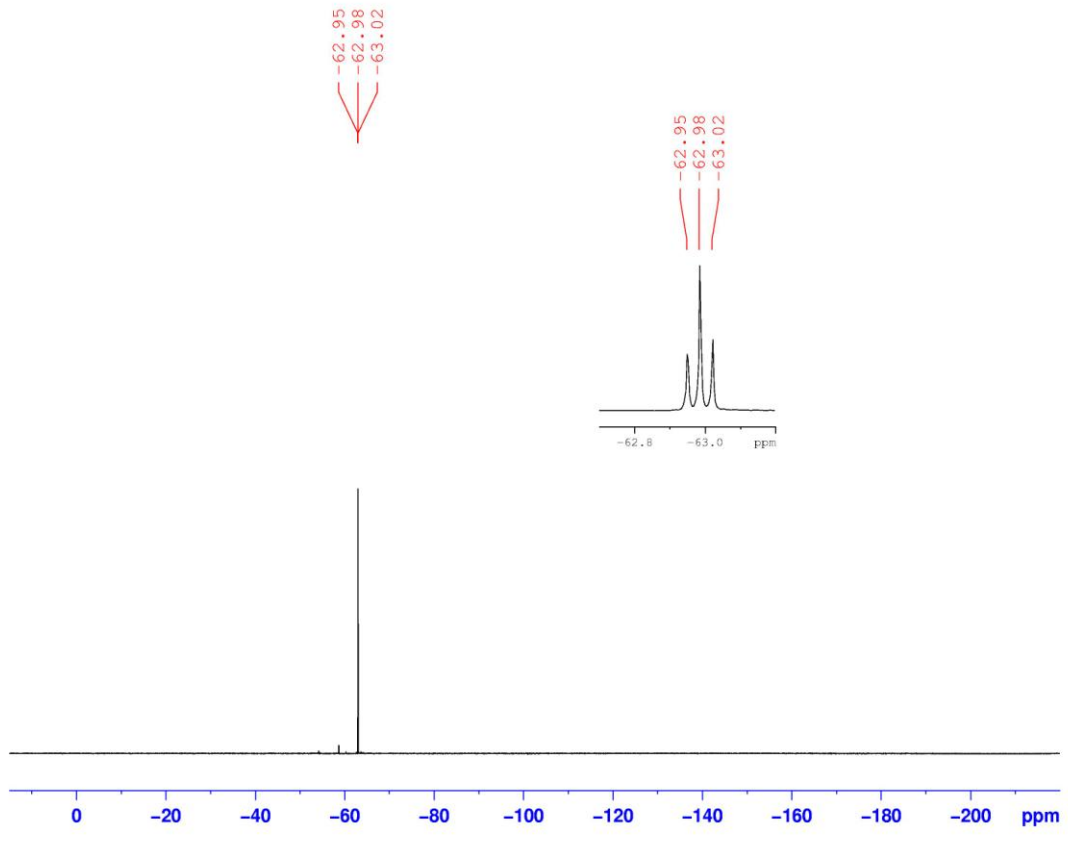
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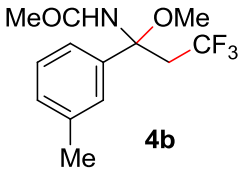
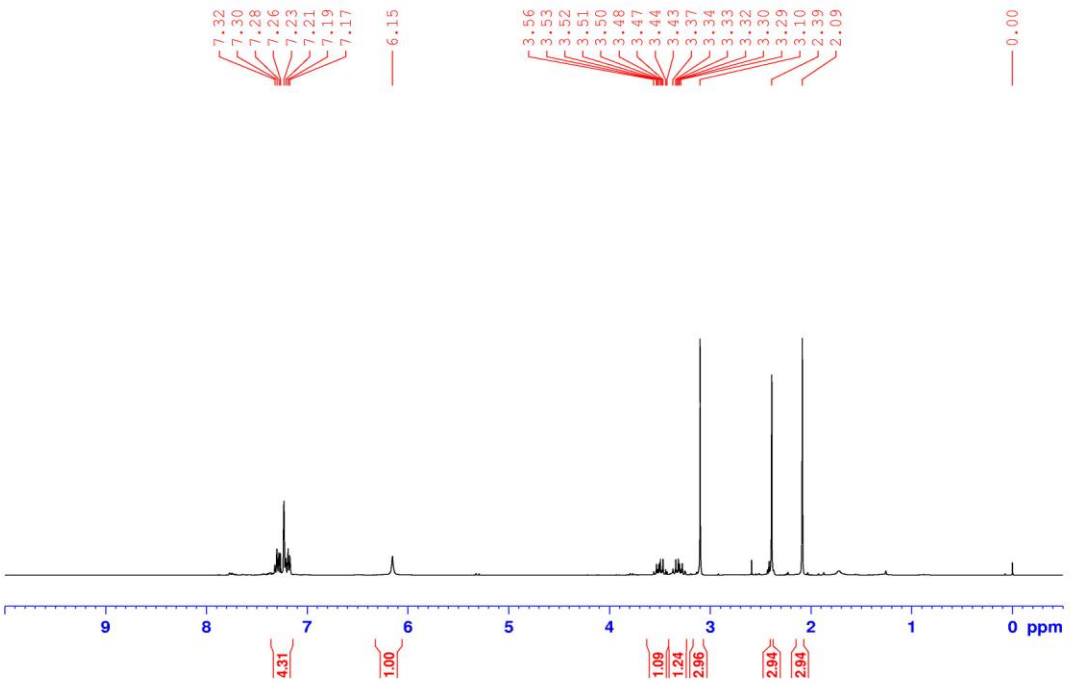
-62.8
-63.0
ppm
0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 ppm


MeOCHN
OMe
CF3
Me

4b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3.51
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3.48
3.47
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3.43
3.37
3.34
3.33
3.32
3.30
3.29
3.10
2.39
2.09
0.00
9
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2
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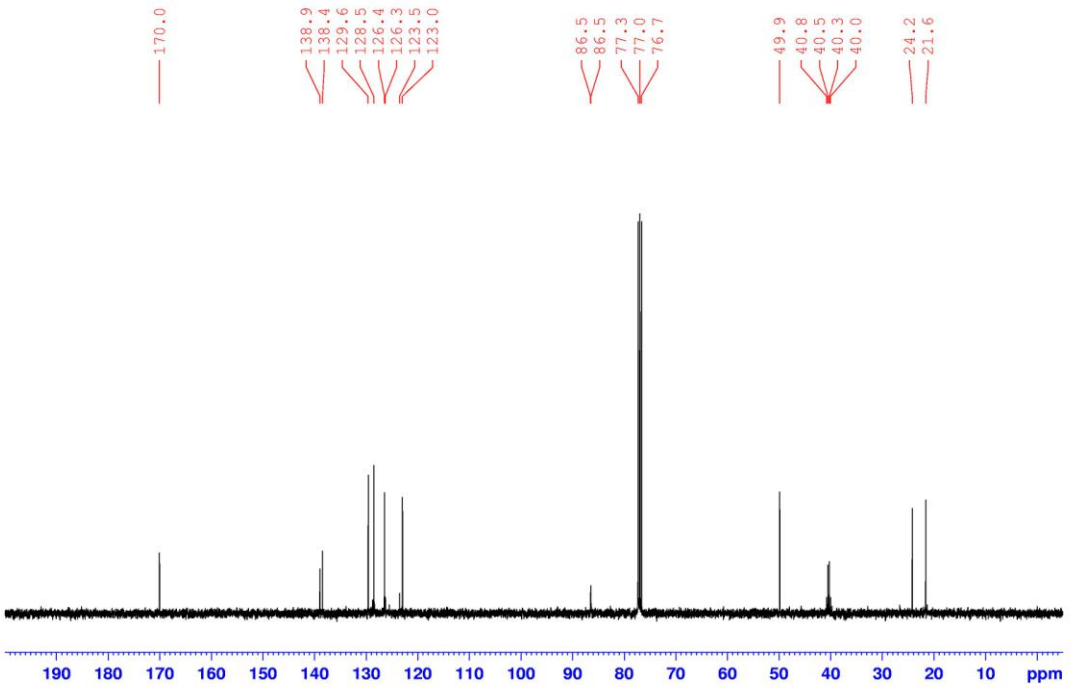
2.94
2.94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86.5
86.5
77.3
77.0
76.7
49.9
40.8
40.5
40.3
40.0
24.2
21.6
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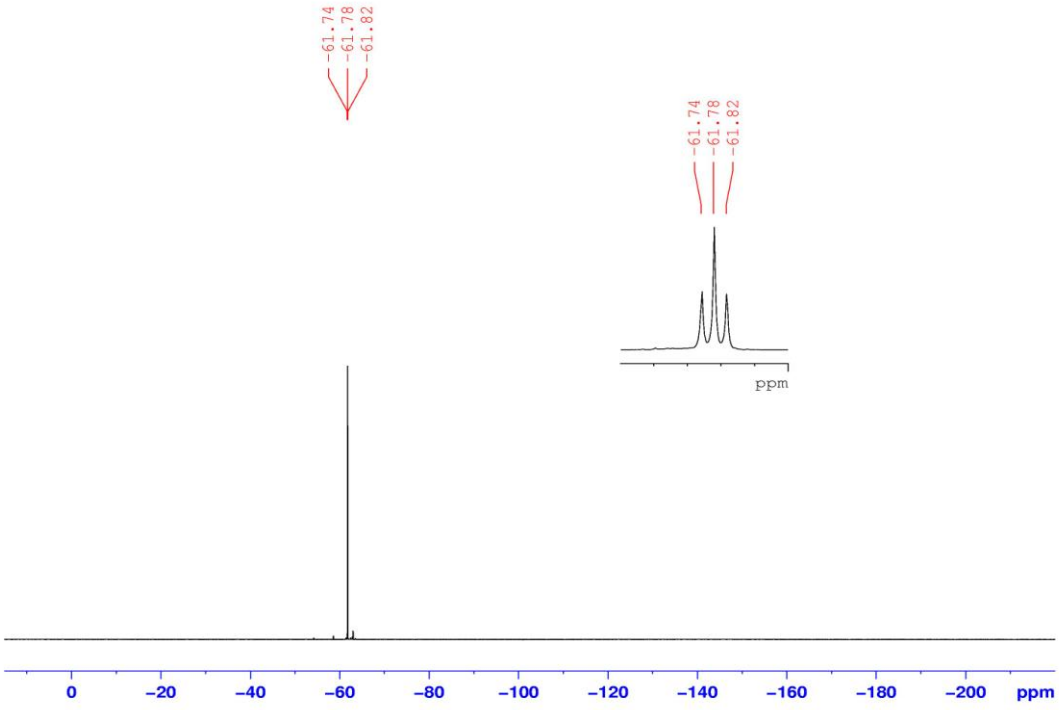

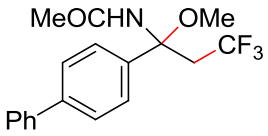

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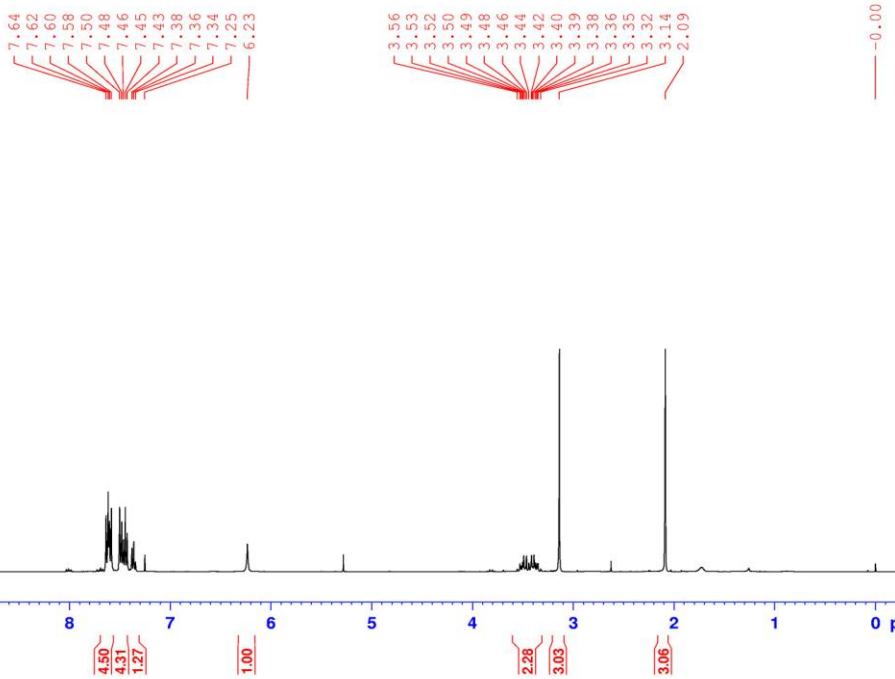

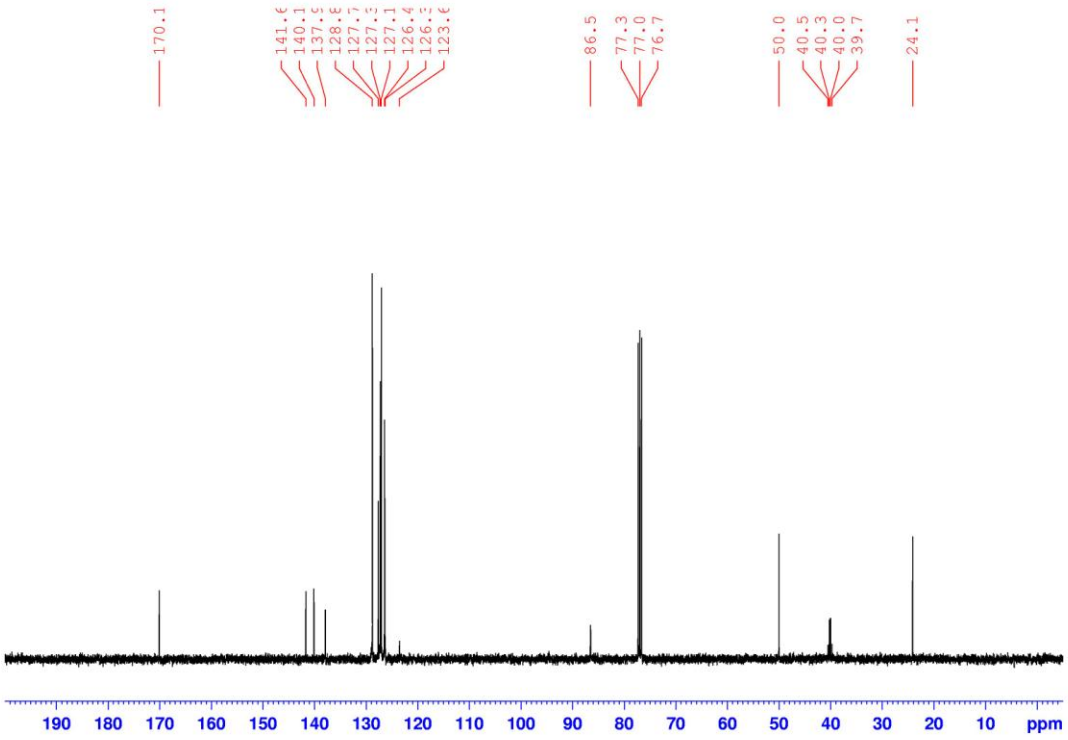

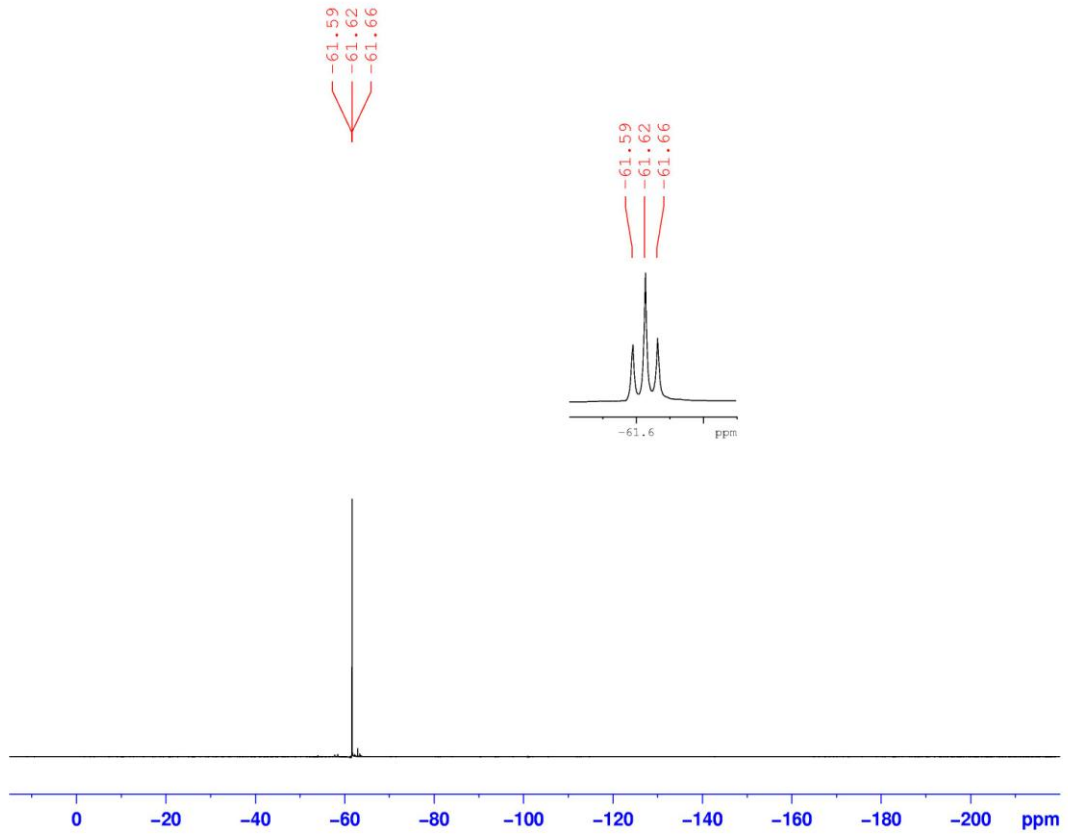

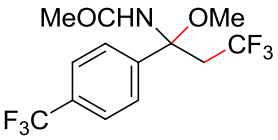

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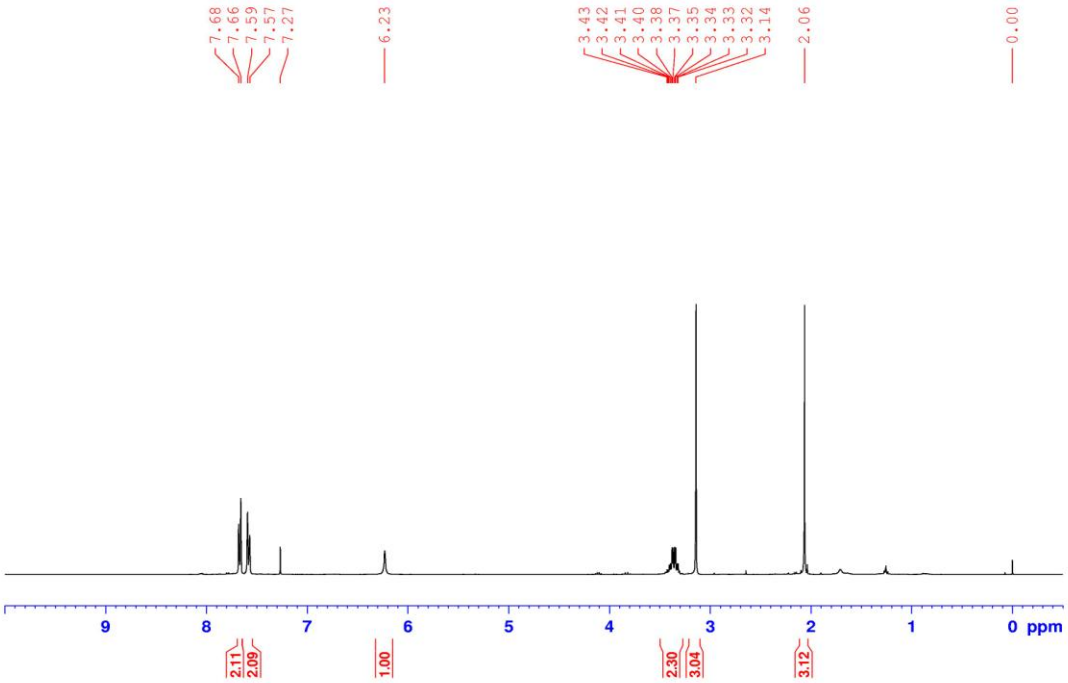
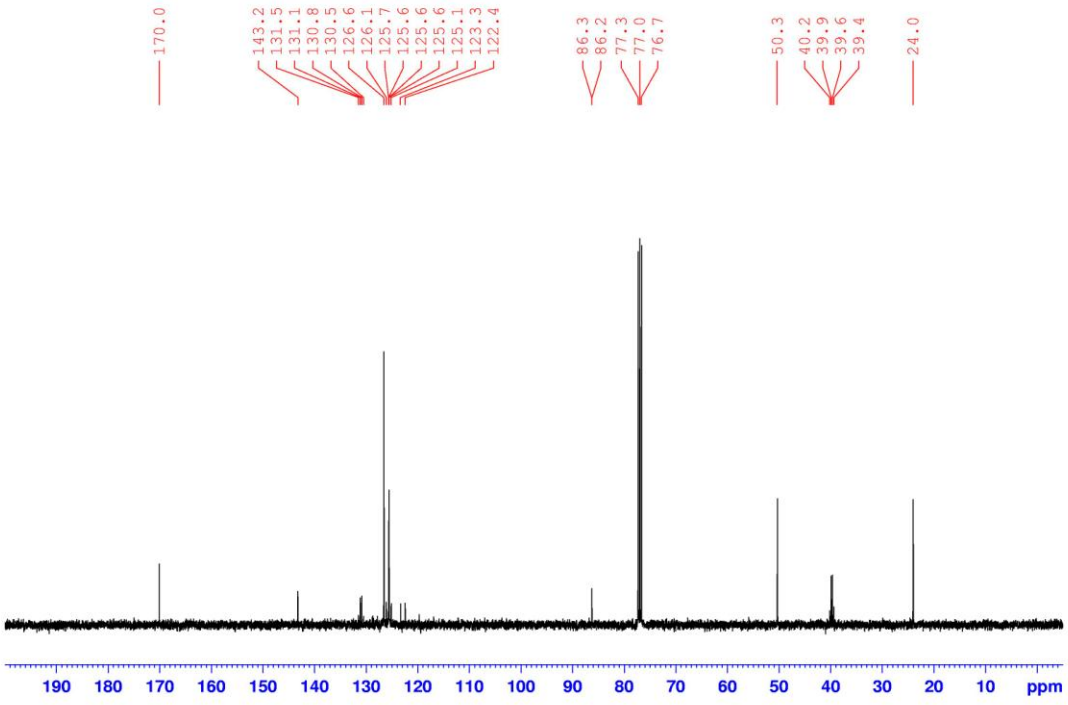
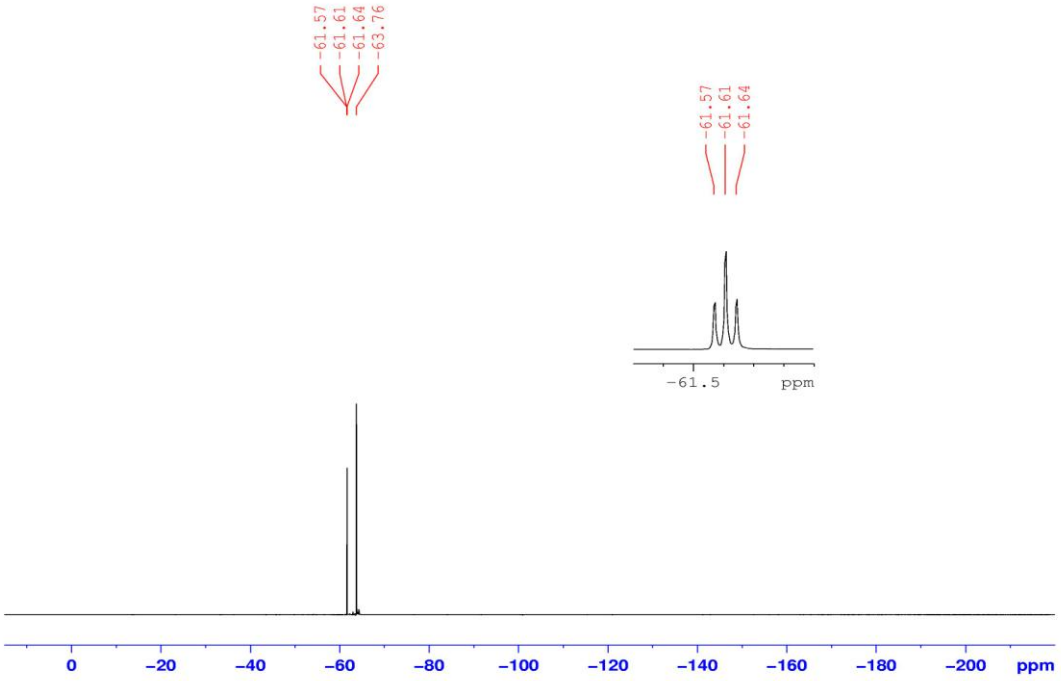
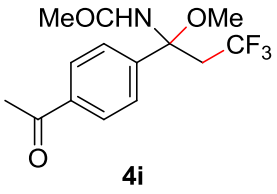
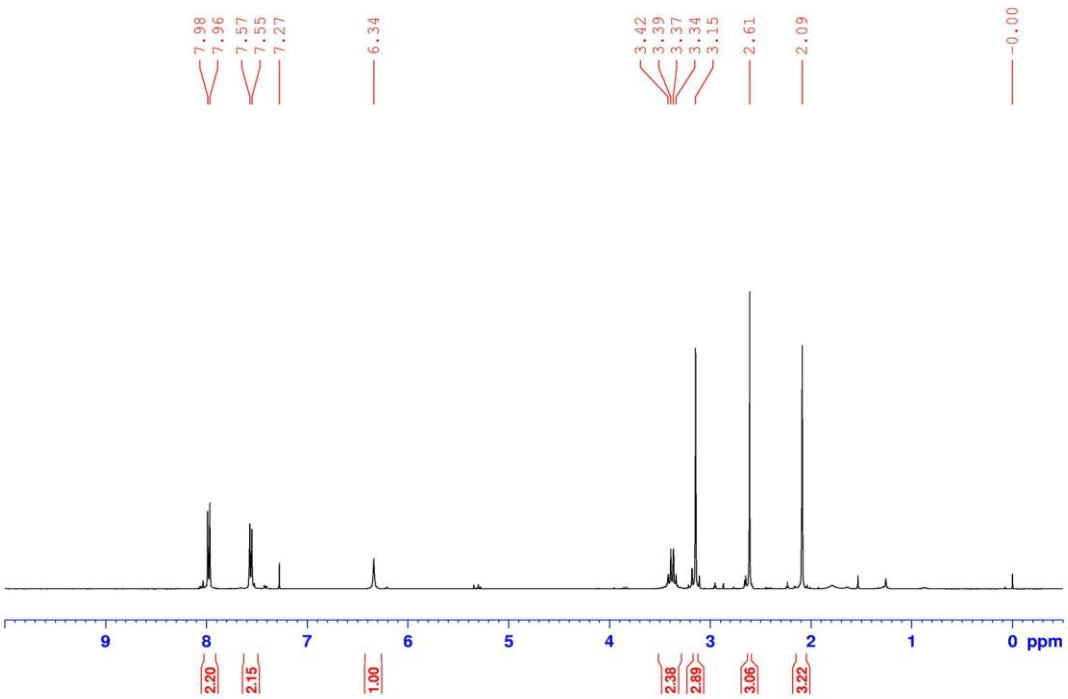


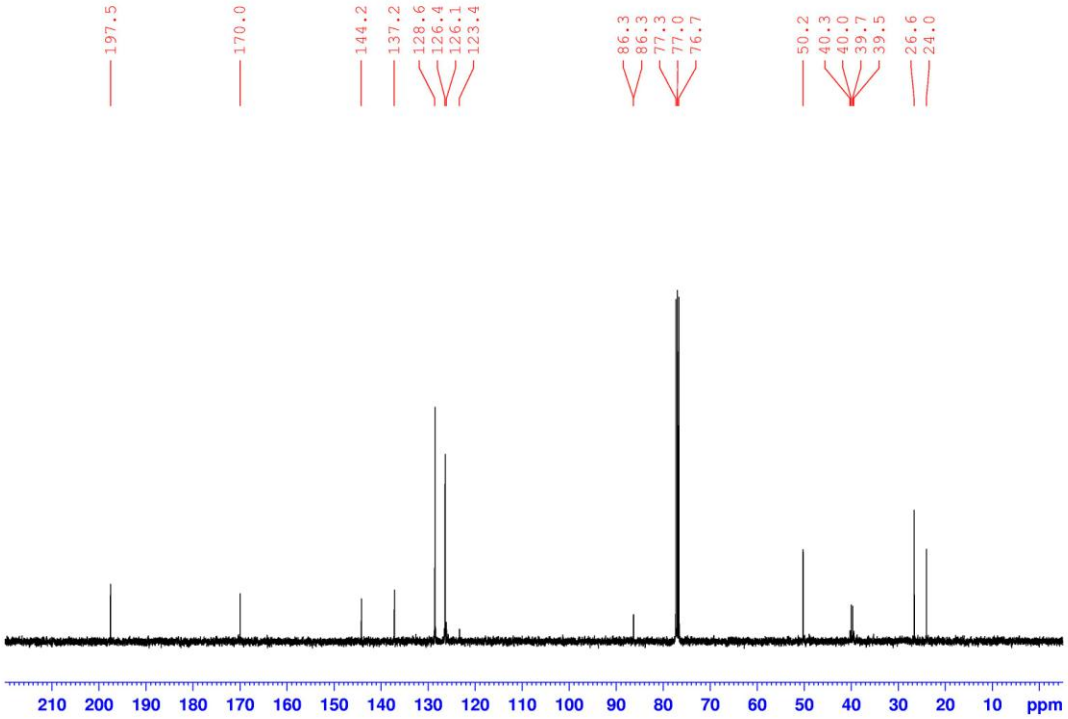


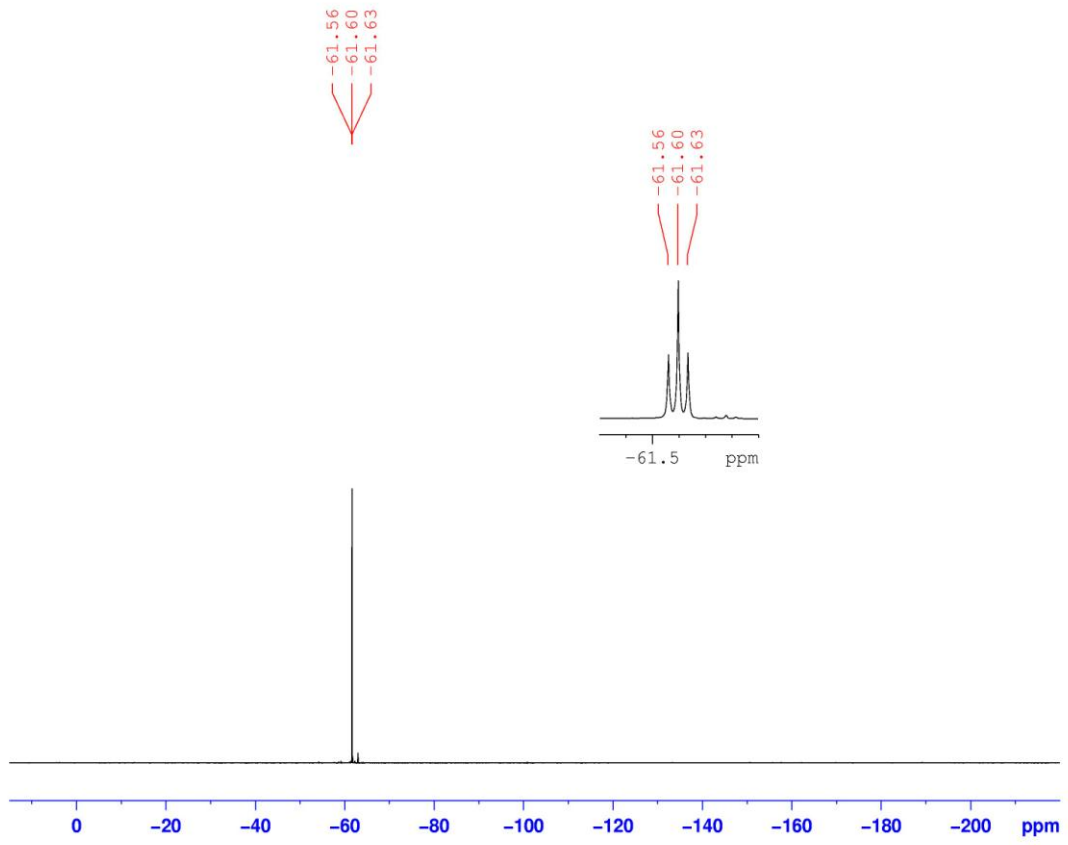


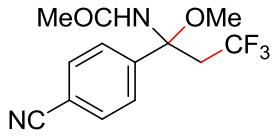


4i





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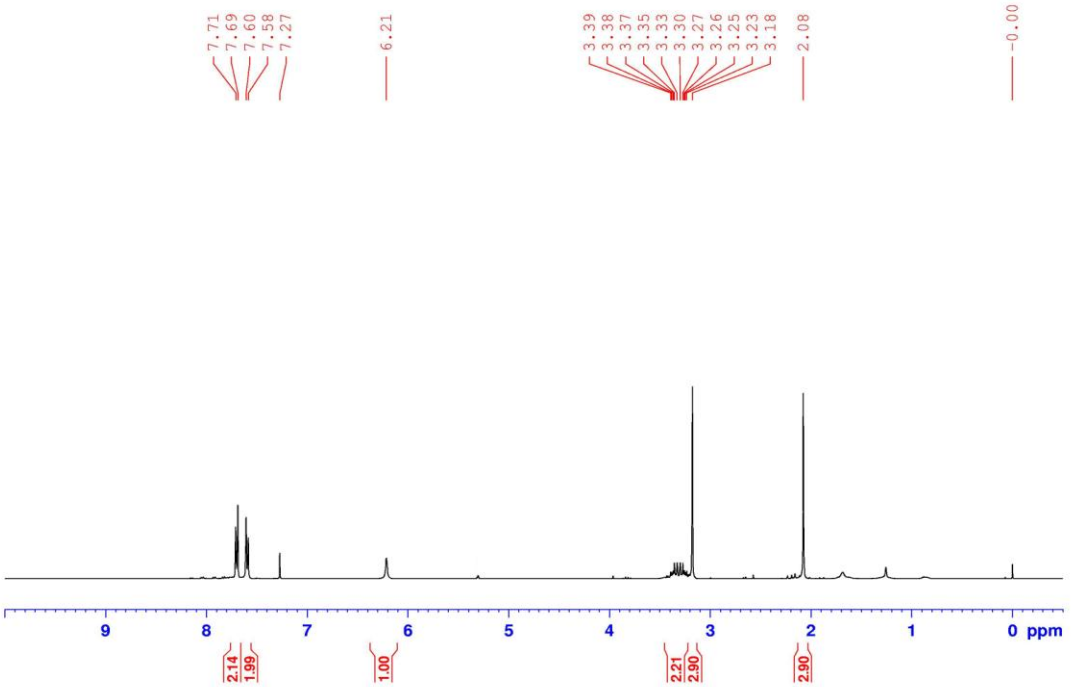
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3.23
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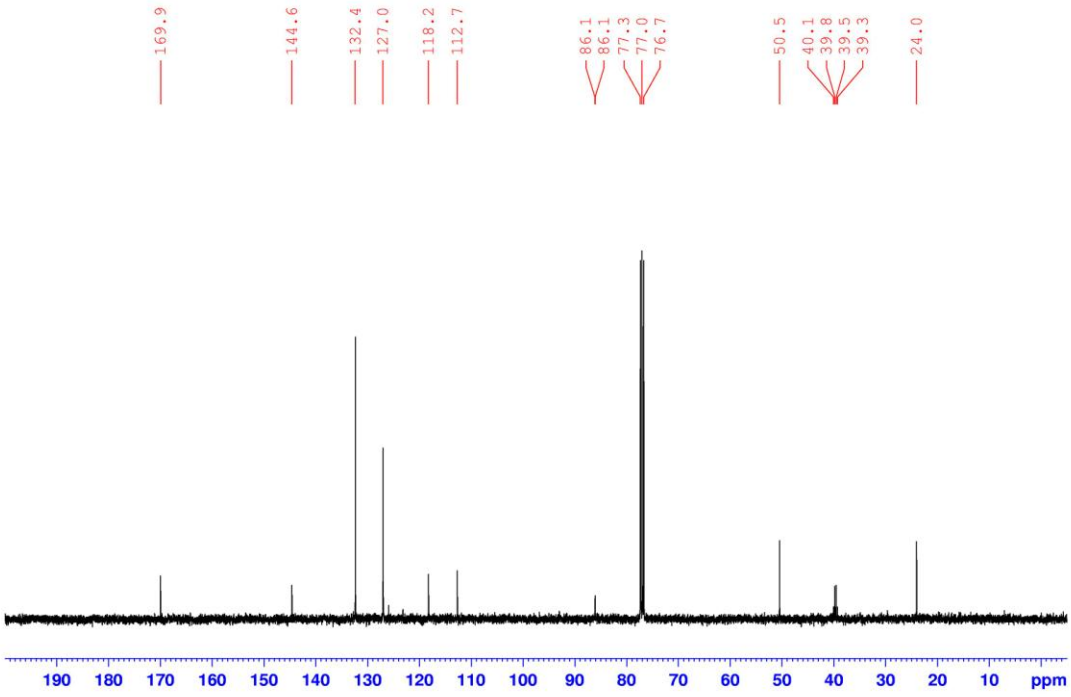
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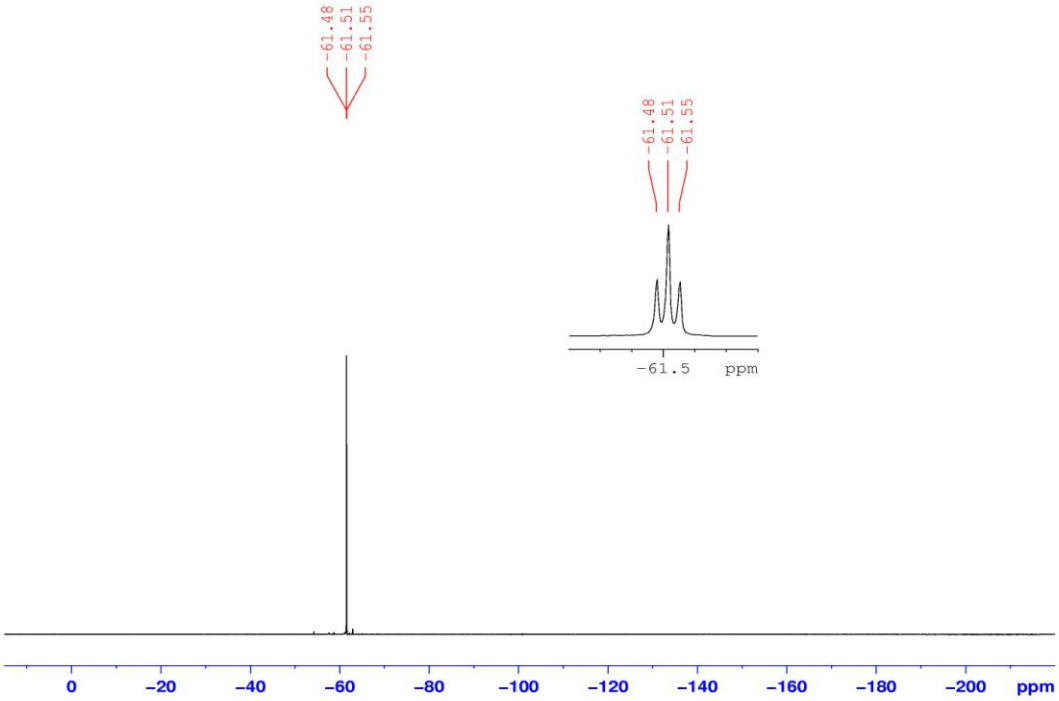
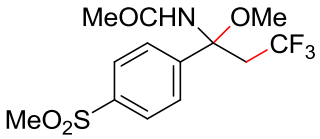
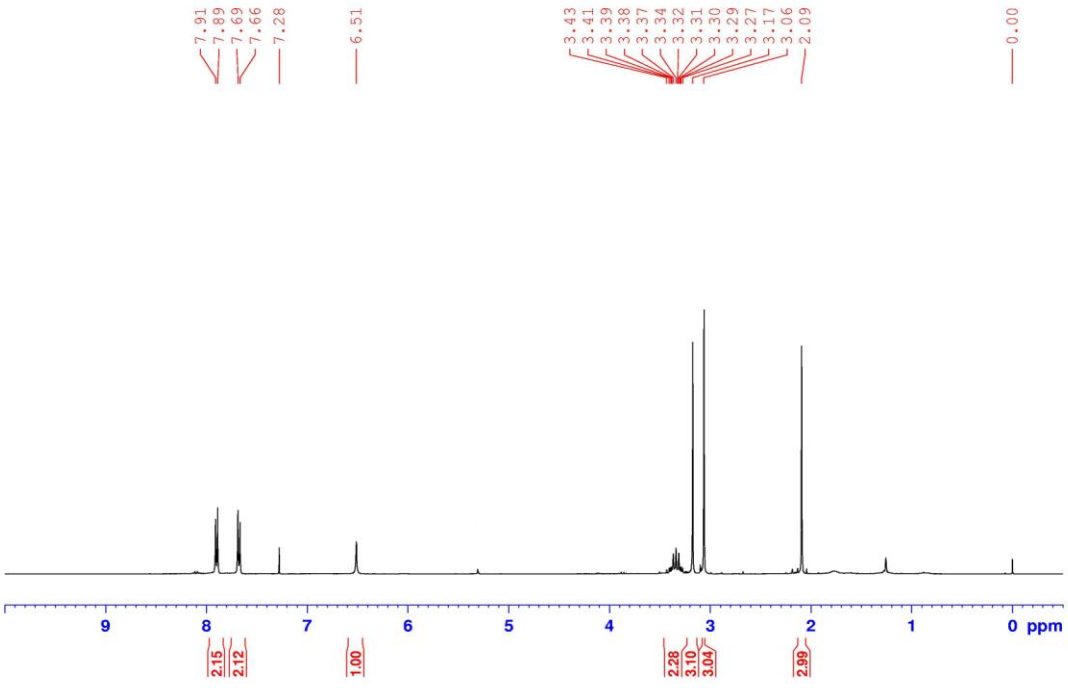
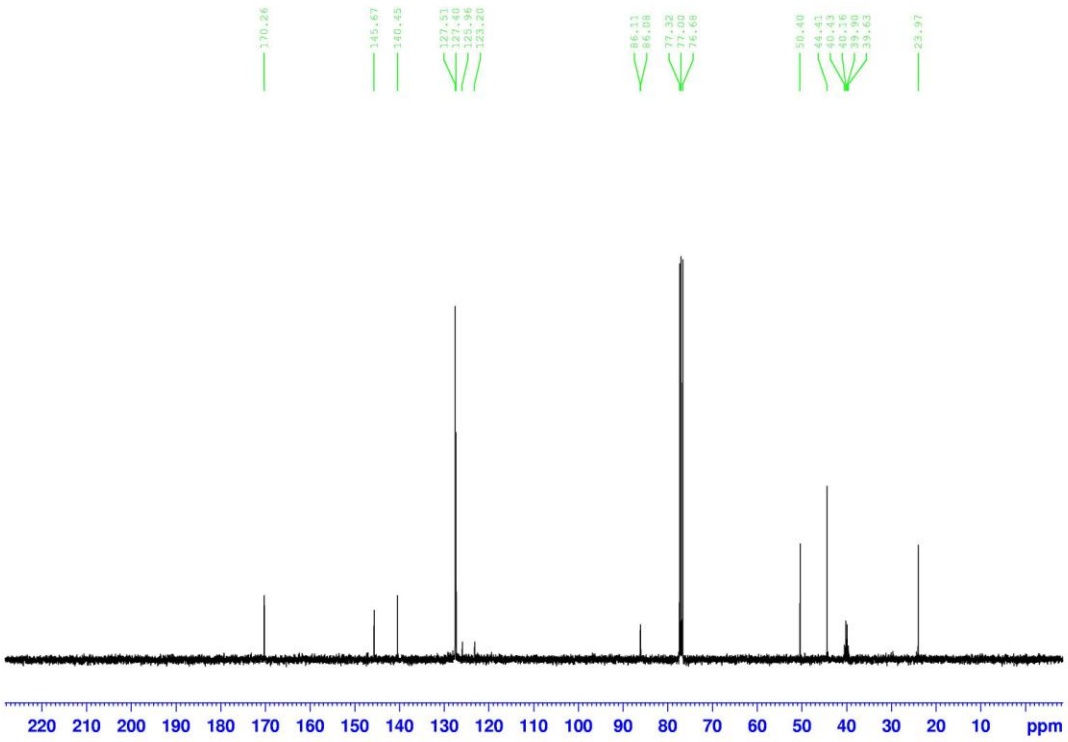
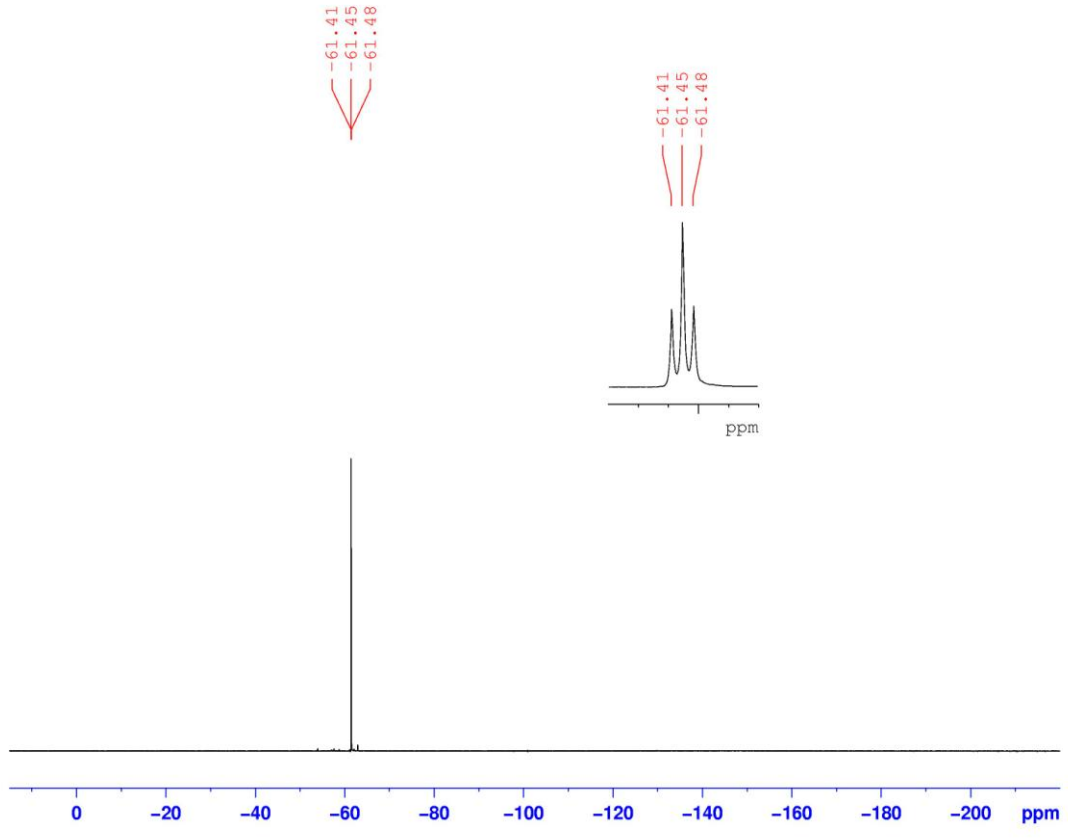


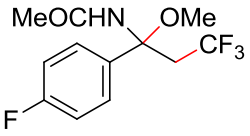


4k





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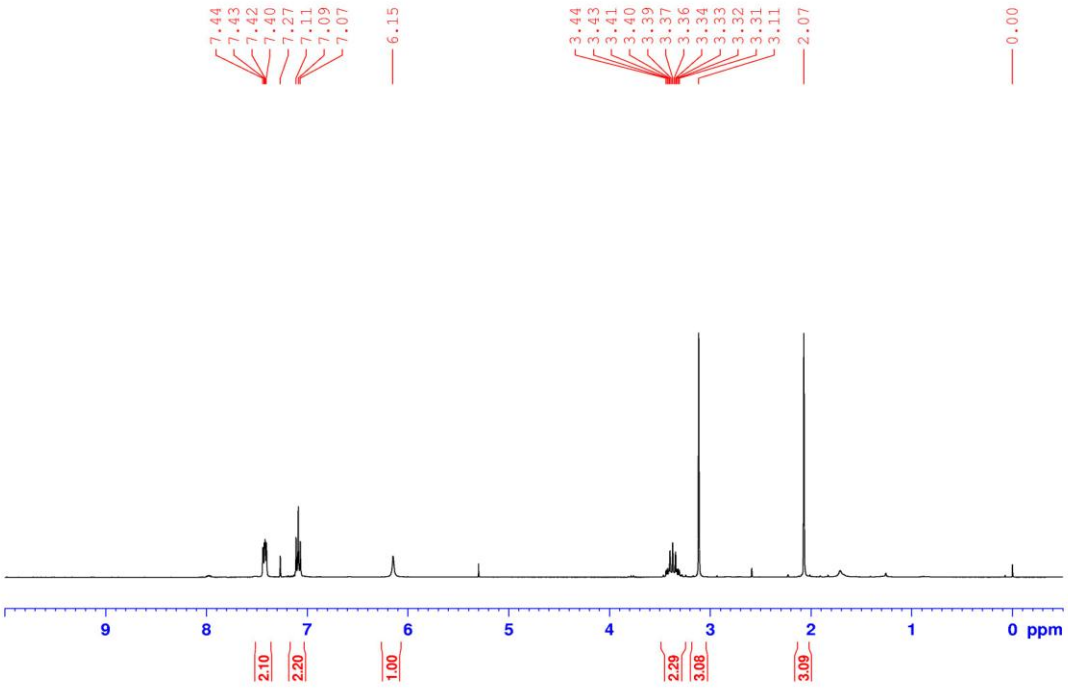
CF3
F

4l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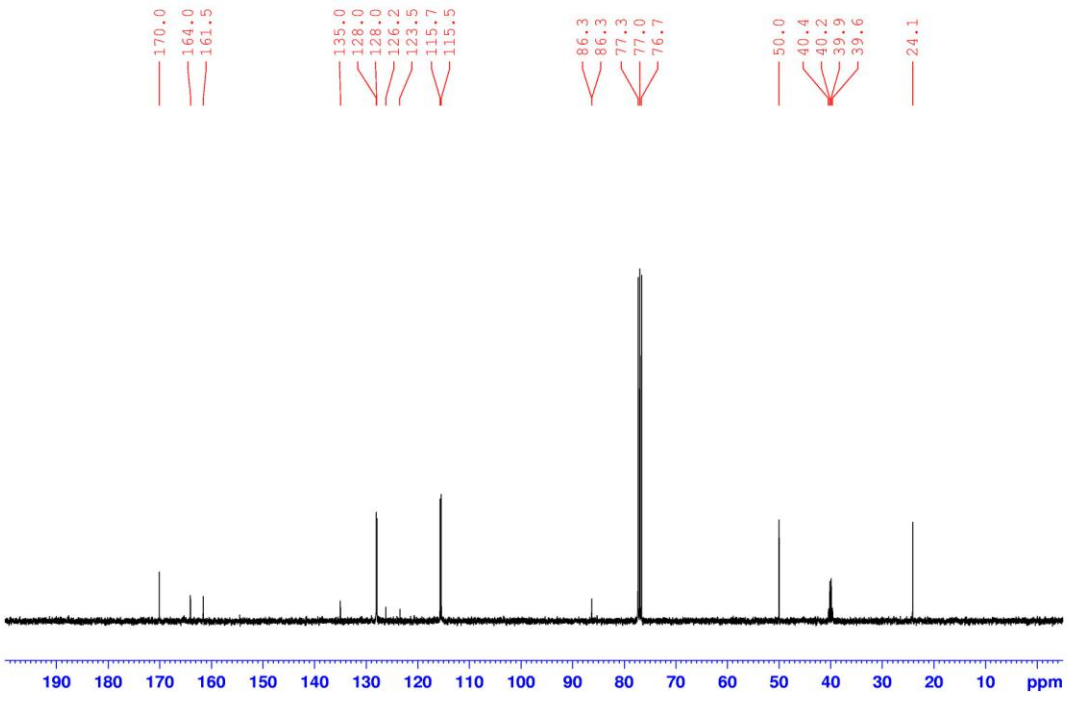
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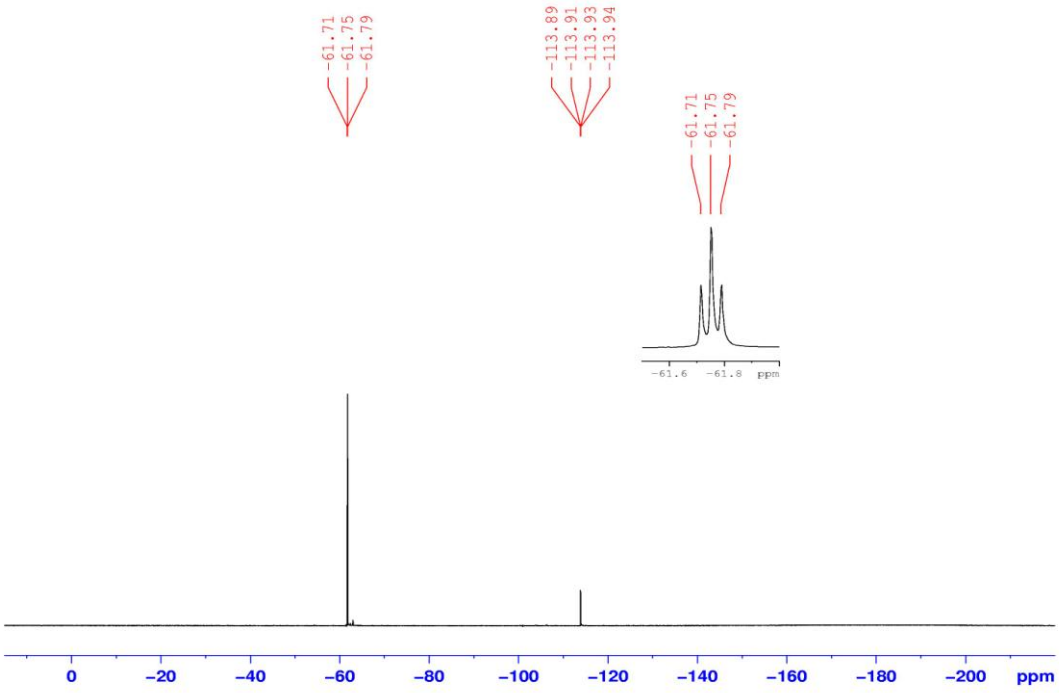
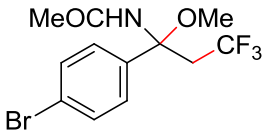
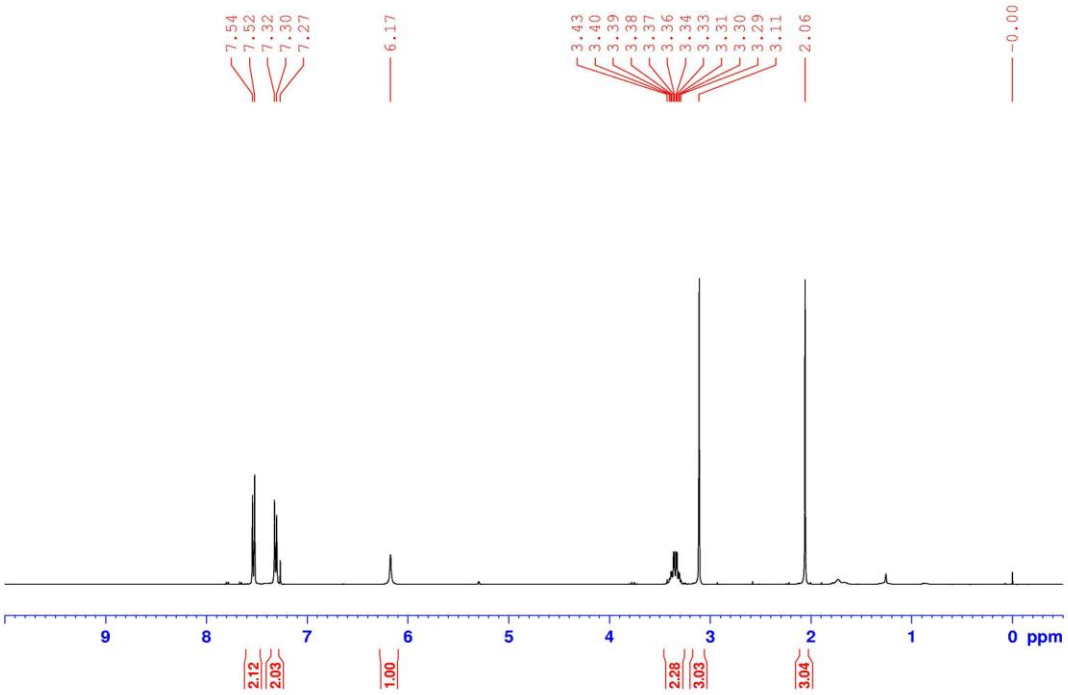
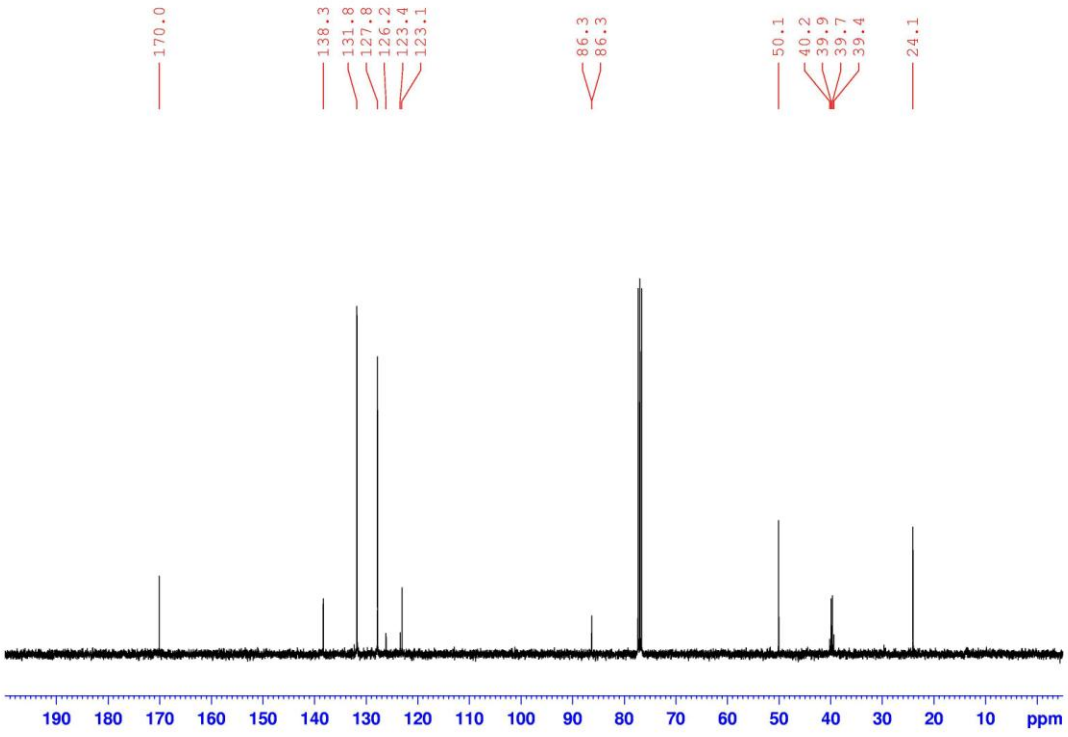




4m

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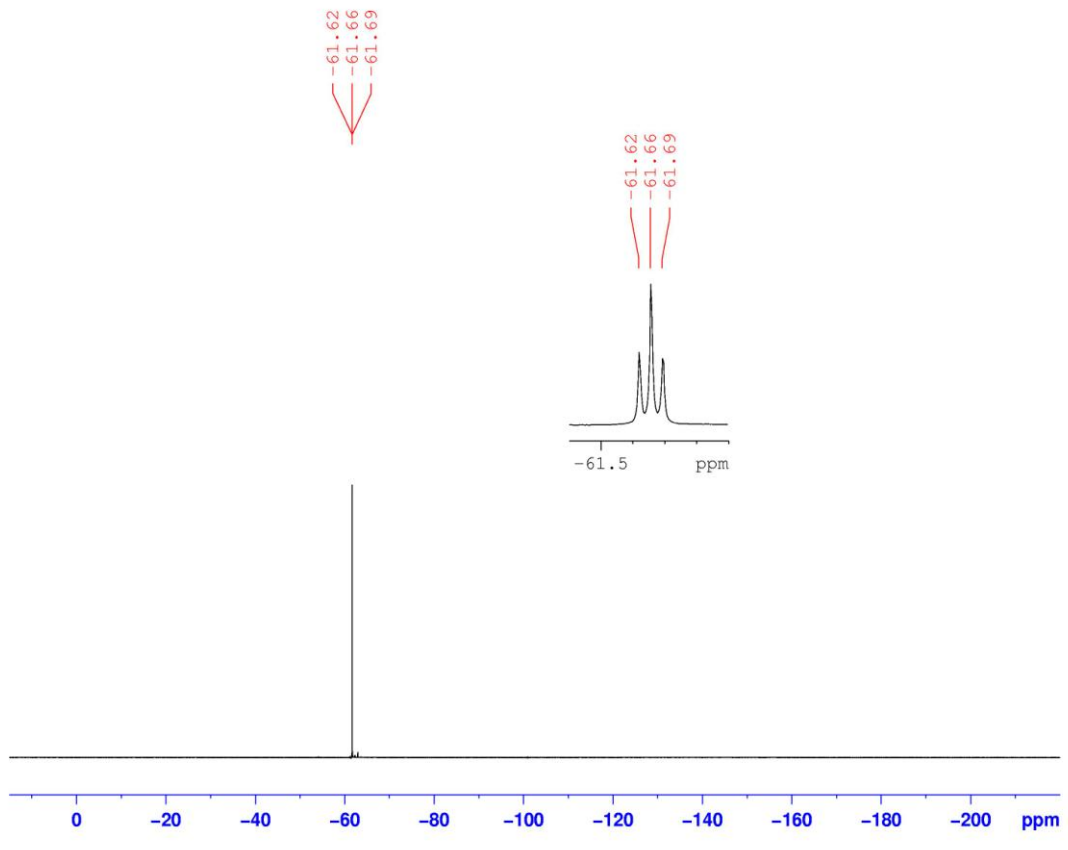
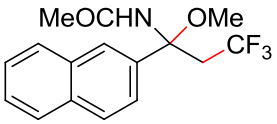
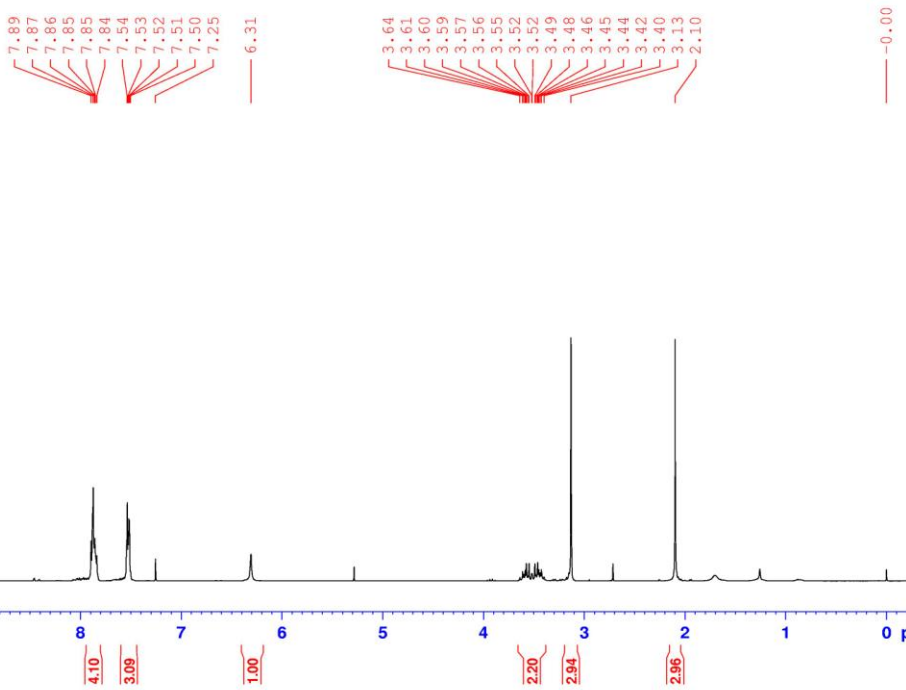
40.2
39.9
39.7
39.4
24.1
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


-61.62
-61.66
-61.69
-61.62
-61.66
-61.69
-61.5 ppm
0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 ppm


MeOCHN
OMe
CF3

4o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7.87
7.86
7.85
7.85
7.84
7.54
7.53
7.52
7.51
7.50
7.25
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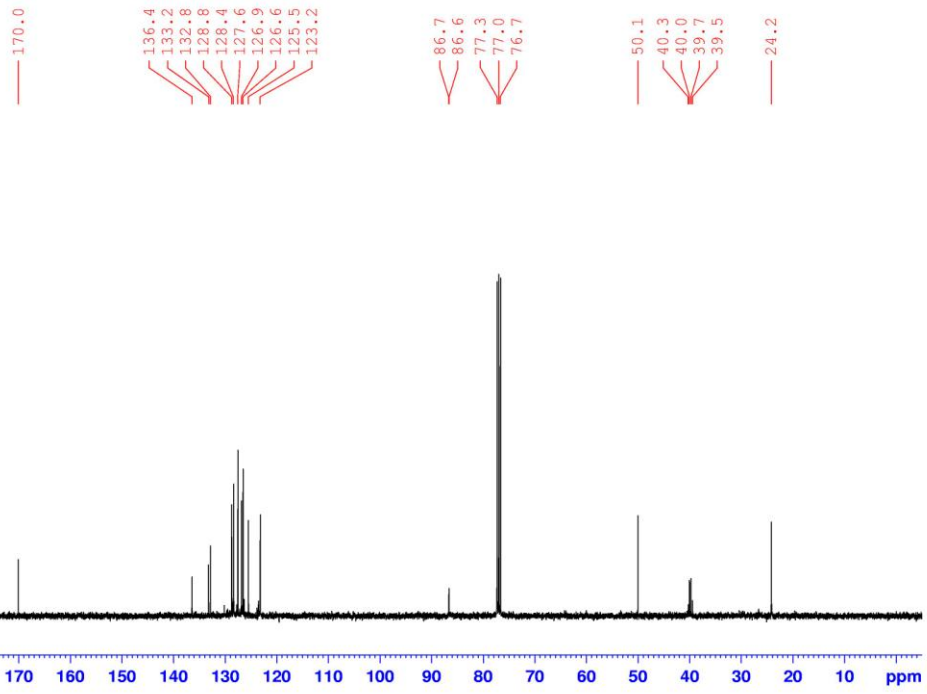
3.64
3.61
3.60
3.59
3.57
3.56
3.55
3.52
3.52
3.49
3.48
3.46
3.45
3.44
3.42
3.40
3.13
2.10
0.00
9
8
7
6
5
4
3
2
1
0 ppm
4.10
3.09
1.00
2.20
2.94
2.96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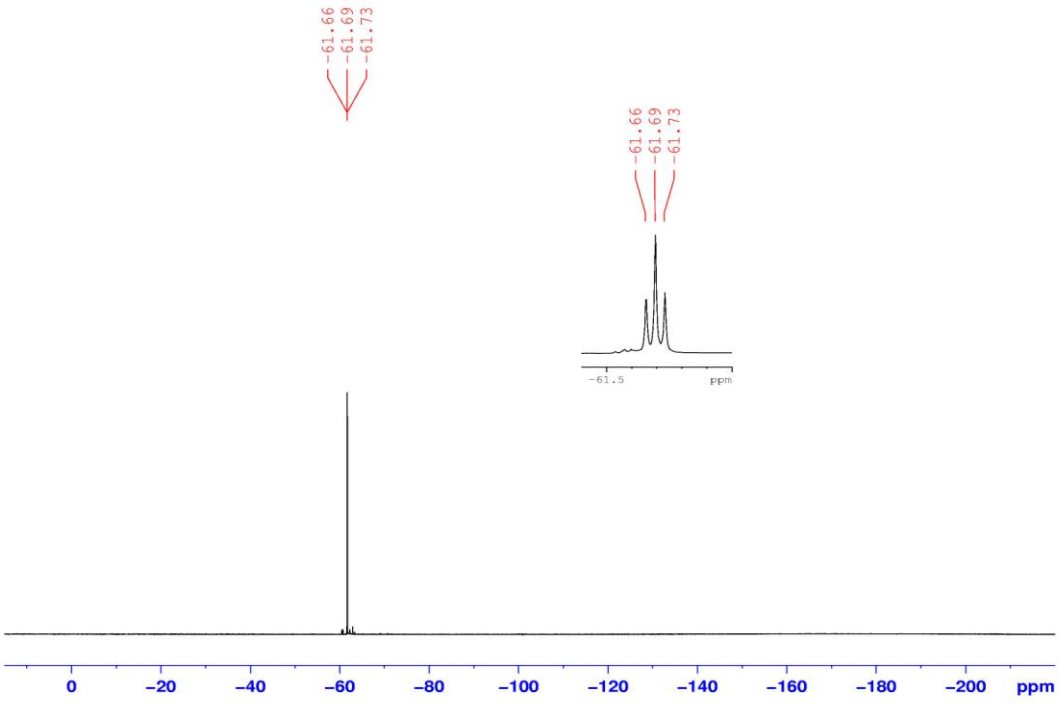
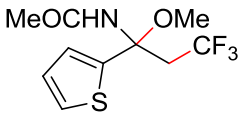
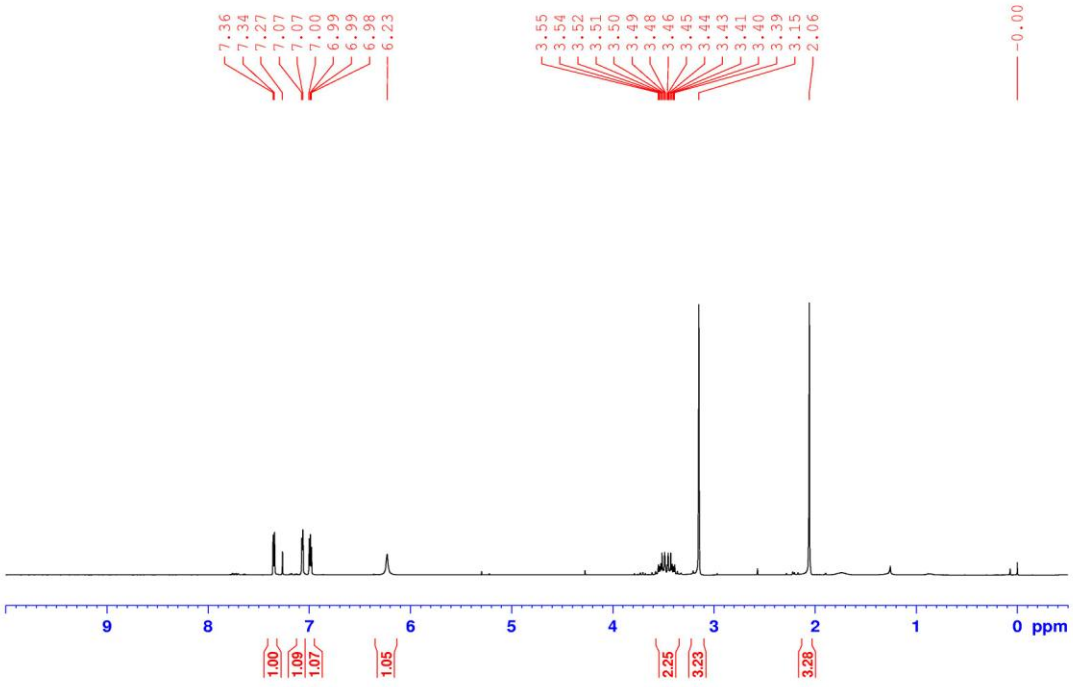
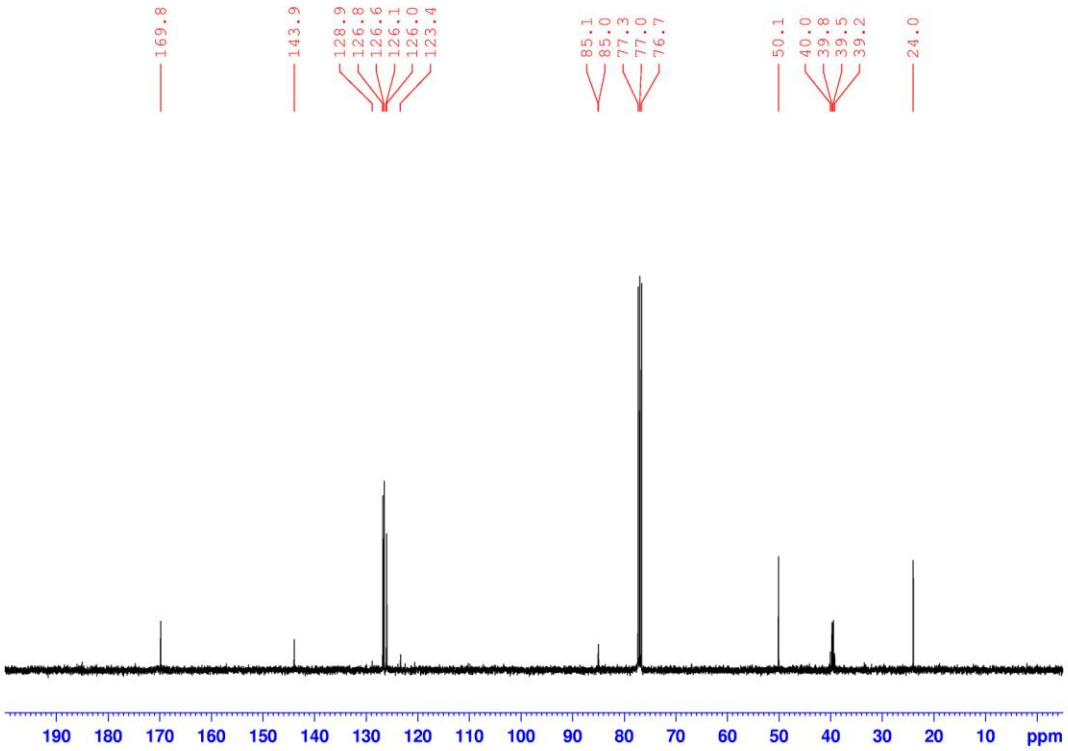
136.4
133.2
132.8
128.8
128.4
127.6
126.9
126.6
125.5
123.2
86.7
86.6
77.3
77.0
76.7
50.1
40.3
40.0
39.7
39.5
24.2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

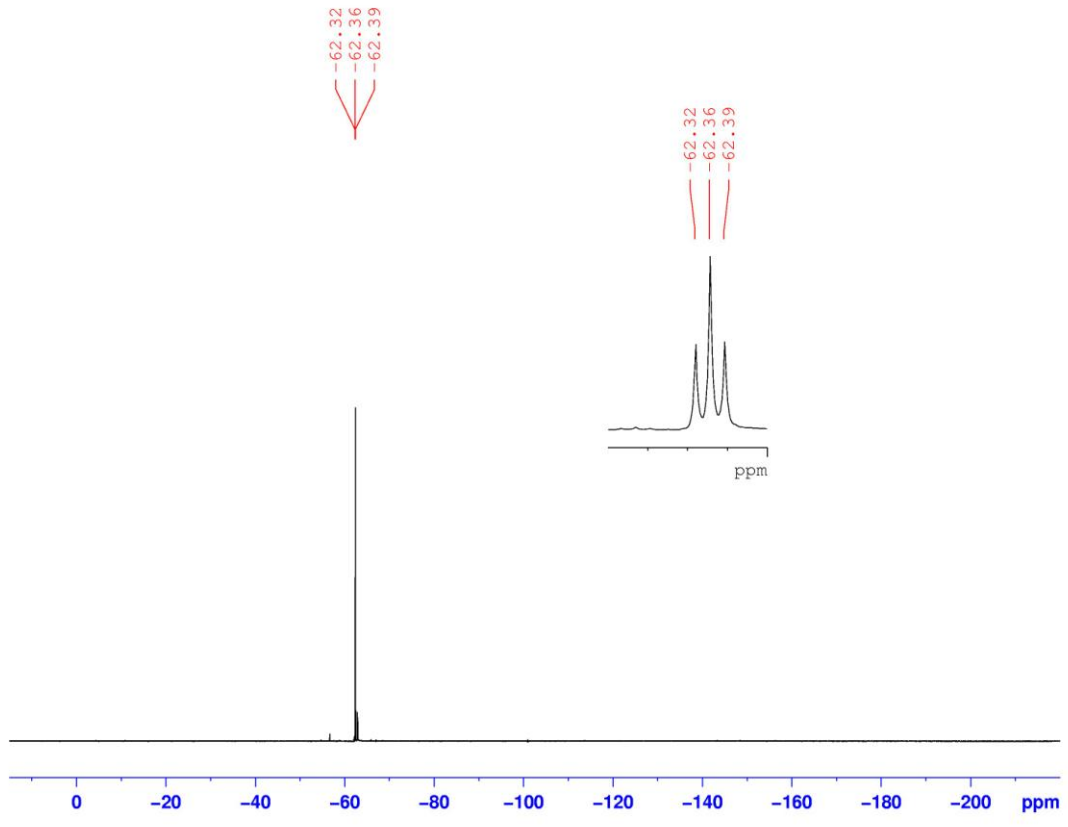


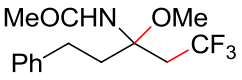


4p

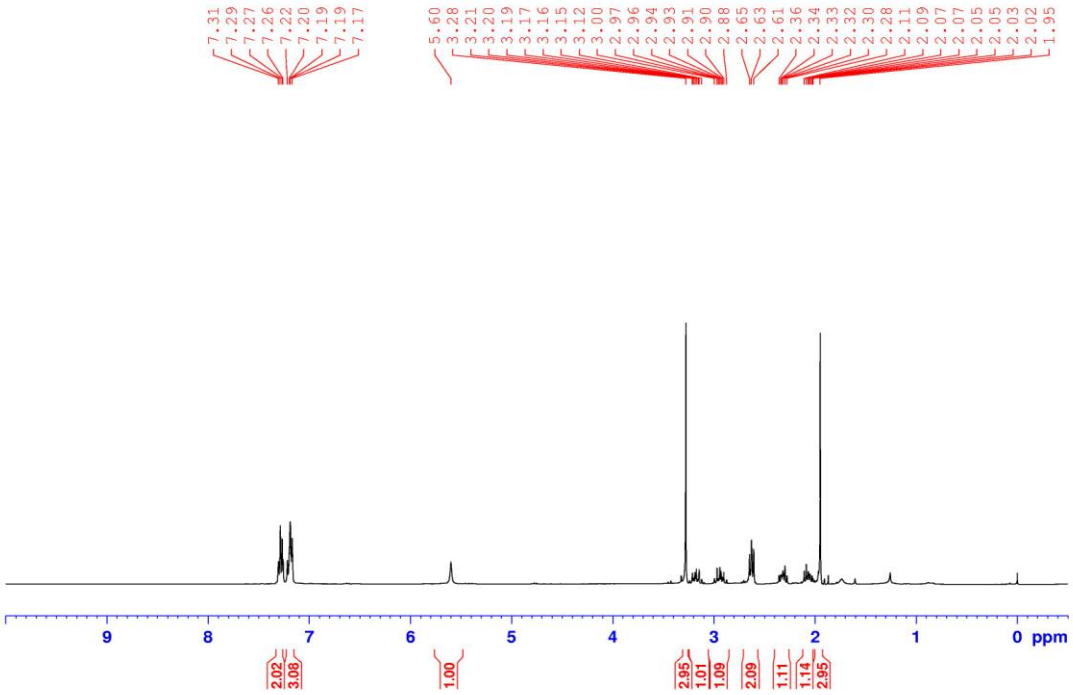


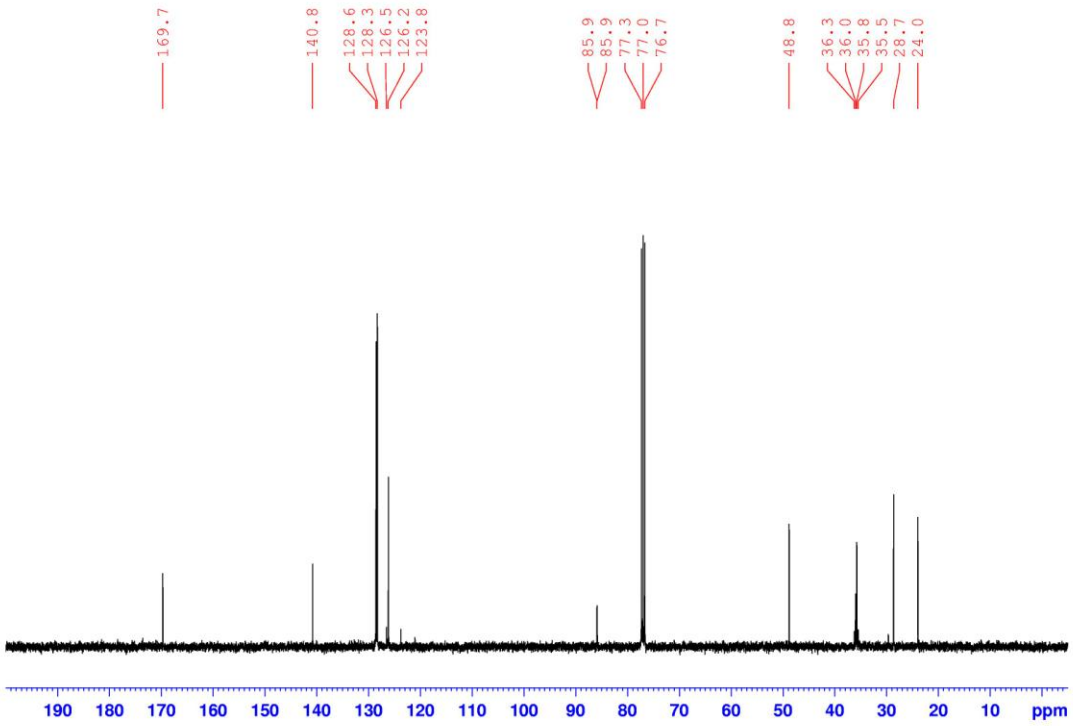


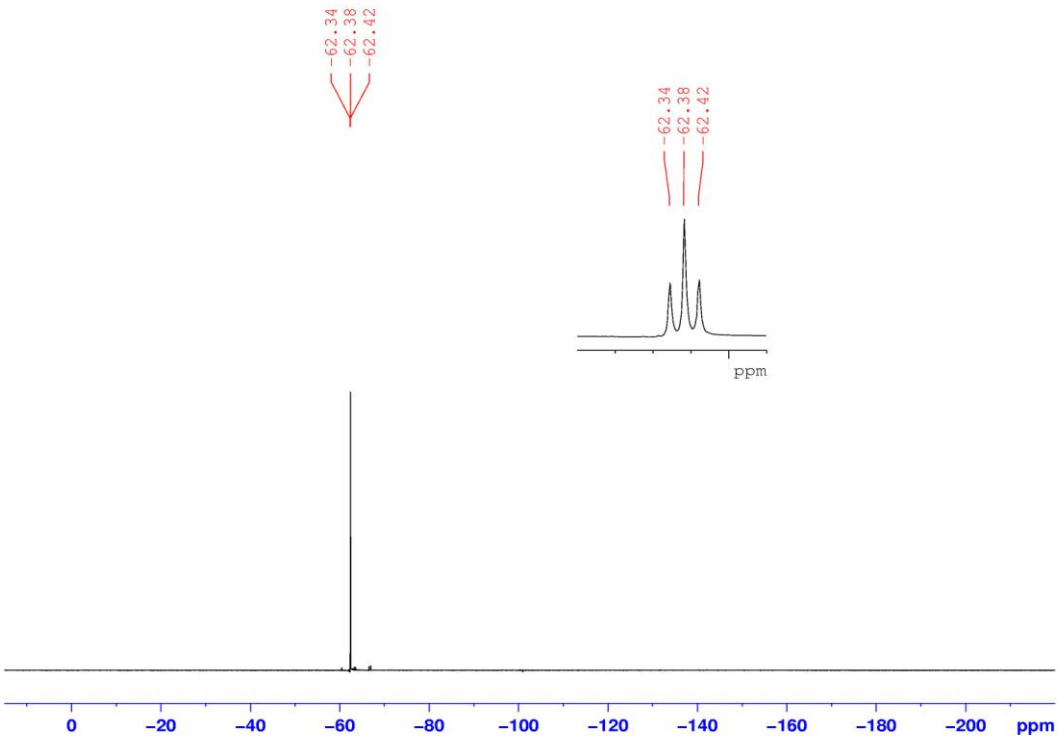




4s



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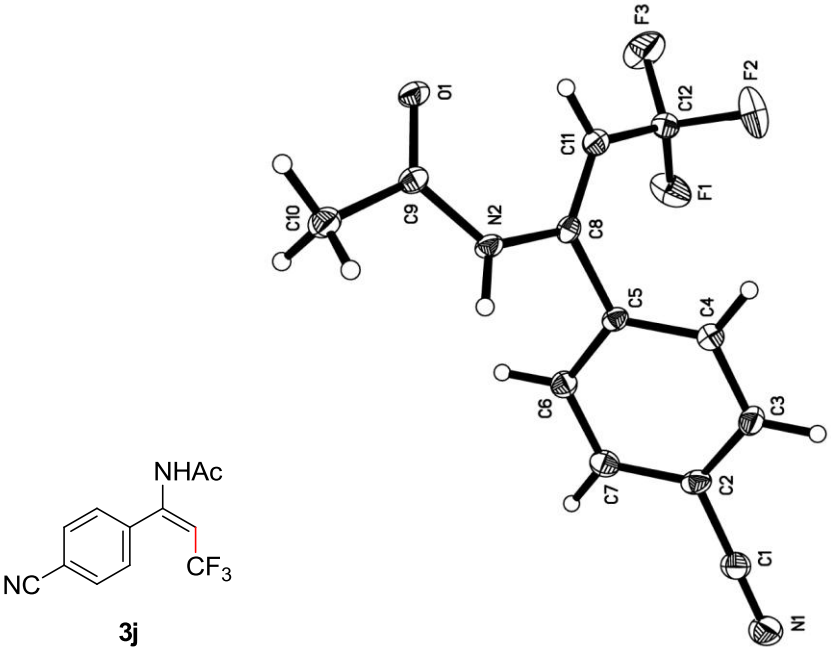
-62.34
-62.38
-62.42
ppm
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

X-ray data



3j

Table 1. Crystal data and structure refinement for ltp230s.

Identification code	ltp230s	
Empirical formula	C12 H9 F3 N2 O	
Formula weight	254.21	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 6.2648(2) Å	α= 90°.
	b = 8.9839(3) Å	β= 95.4600(10)°.
	c = 20.5622(5) Å	γ = 90°.
Volume	1152.04(6) $Å^3$	
Z	4	
Density (calculated)	1.466 Mg/m^3	
Absorption coefficient	0.128 mm^{-1}	
F(000)	520	
Crystal size	0.40 x 0.38 x 0.10 mm^3	
Theta range for data collection	1.99 to 29.64°.	
Index ranges	-6<=h<=8, -12<=k<=12, -28<=l<=28	
Reflections collected	9979	
Independent reflections	3206 [R(int) = 0.0299]	
Completeness to theta = 29.64°	98.2 %	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9873 and 0.9504
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3206 / 0 / 164
Goodness-of-fit on F^2	1.088
Final R indices [I>2sigma(I)]	R1 = 0.0454, wR2 = 0.1258
R indices (all data)	R1 = 0.0588, wR2 = 0.1427
Largest diff. peak and hole	0.436 and -0.477 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for ltp230s. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	2335(2)	3918(2)	5049(1)	20(1)
C(2)	1971(2)	2700(2)	4591(1)	17(1)
C(3)	3519(2)	2363(2)	4171(1)	18(1)
C(4)	3119(2)	1225(2)	3719(1)	16(1)
C(5)	1197(2)	445(2)	3682(1)	13(1)
C(6)	-345(2)	795(2)	4105(1)	16(1)
C(7)	46(2)	1913(2)	4564(1)	17(1)
C(8)	742(2)	-714(2)	3167(1)	13(1)
C(9)	-2167(2)	-1271(2)	2293(1)	14(1)
C(10)	-4101(2)	-586(2)	1926(1)	20(1)
C(11)	1903(2)	-1950(2)	3114(1)	16(1)
C(12)	3654(2)	-2471(2)	3597(1)	18(1)
F(1)	3469(2)	-2072(1)	4214(1)	29(1)
F(2)	5610(2)	-1995(2)	3469(1)	35(1)
F(3)	3757(2)	-3957(1)	3586(1)	39(1)
N(1)	2606(2)	4890(2)	5404(1)	27(1)
N(2)	-1036(2)	-347(1)	2730(1)	14(1)
O(1)	-1653(2)	-2569(1)	2212(1)	17(1)

Table 3. Bond lengths [Å] and angles [°] for ltp230s.

C(1)-N(1)	1.141(2)
C(1)-C(2)	1.448(2)
C(2)-C(3)	1.391(2)
C(2)-C(7)	1.395(2)
C(3)-C(4)	1.388(2)
C(3)-H(3)	0.9500
C(4)-C(5)	1.390(2)
C(4)-H(4)	0.9500
C(5)-C(6)	1.3962(19)
C(5)-C(8)	1.4927(18)
C(6)-C(7)	1.384(2)
C(6)-H(6)	0.9500
C(7)-H(7)	0.9500
C(8)-C(11)	1.338(2)
C(8)-N(2)	1.4020(17)
C(9)-O(1)	1.2255(18)
C(9)-N(2)	1.3699(18)
C(9)-C(10)	1.498(2)
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-C(12)	1.483(2)
C(11)-H(11)	0.9500
C(12)-F(1)	1.3348(17)
C(12)-F(3)	1.3368(18)
C(12)-F(2)	1.3469(18)
N(2)-H(2)	0.8800

N(1)-C(1)-C(2)	179.10(18)
C(3)-C(2)-C(7)	121.12(13)
C(3)-C(2)-C(1)	119.49(14)
C(7)-C(2)-C(1)	119.36(13)
C(4)-C(3)-C(2)	118.92(14)
C(4)-C(3)-H(3)	120.5
C(2)-C(3)-H(3)	120.5
C(3)-C(4)-C(5)	120.56(13)

C(3)-C(4)-H(4)	119.7
C(5)-C(4)-H(4)	119.7
C(4)-C(5)-C(6)	119.94(13)
C(4)-C(5)-C(8)	119.80(12)
C(6)-C(5)-C(8)	120.18(12)
C(7)-C(6)-C(5)	120.06(13)
C(7)-C(6)-H(6)	120.0
C(5)-C(6)-H(6)	120.0
C(6)-C(7)-C(2)	119.38(13)
C(6)-C(7)-H(7)	120.3
C(2)-C(7)-H(7)	120.3
C(11)-C(8)-N(2)	123.20(13)
C(11)-C(8)-C(5)	124.64(12)
N(2)-C(8)-C(5)	112.14(12)
O(1)-C(9)-N(2)	122.68(13)
O(1)-C(9)-C(10)	122.17(13)
N(2)-C(9)-C(10)	115.15(13)
C(9)-C(10)-H(10A)	109.5
C(9)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
C(9)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(8)-C(11)-C(12)	125.46(13)
C(8)-C(11)-H(11)	117.3
C(12)-C(11)-H(11)	117.3
F(1)-C(12)-F(3)	106.95(13)
F(1)-C(12)-F(2)	105.23(12)
F(3)-C(12)-F(2)	105.50(13)
F(1)-C(12)-C(11)	115.27(12)
F(3)-C(12)-C(11)	109.77(12)
F(2)-C(12)-C(11)	113.46(12)
C(9)-N(2)-C(8)	127.41(13)
C(9)-N(2)-H(2)	116.3
C(8)-N(2)-H(2)	116.3

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for ltp230s. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	19(1)	20(1)	21(1)	-4(1)	-4(1)	3(1)
C(2)	20(1)	14(1)	16(1)	-2(1)	-4(1)	3(1)
C(3)	15(1)	16(1)	23(1)	-2(1)	-3(1)	-2(1)
C(4)	15(1)	14(1)	18(1)	-1(1)	2(1)	0(1)
C(5)	15(1)	10(1)	13(1)	0(1)	-1(1)	0(1)
C(6)	16(1)	14(1)	17(1)	1(1)	2(1)	-1(1)
C(7)	19(1)	18(1)	15(1)	0(1)	3(1)	2(1)
C(8)	13(1)	12(1)	13(1)	1(1)	1(1)	-3(1)
C(9)	17(1)	12(1)	14(1)	0(1)	2(1)	-2(1)
C(10)	22(1)	16(1)	21(1)	-3(1)	-6(1)	3(1)
C(11)	16(1)	14(1)	19(1)	-2(1)	0(1)	0(1)
C(12)	17(1)	15(1)	21(1)	0(1)	2(1)	2(1)
F(1)	32(1)	37(1)	18(1)	2(1)	0(1)	14(1)
F(2)	15(1)	54(1)	34(1)	13(1)	1(1)	-1(1)
F(3)	41(1)	15(1)	55(1)	-2(1)	-21(1)	8(1)
N(1)	24(1)	26(1)	30(1)	-10(1)	-6(1)	5(1)
N(2)	16(1)	8(1)	17(1)	-1(1)	-2(1)	1(1)
O(1)	20(1)	11(1)	21(1)	-3(1)	0(1)	0(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for ltp230s.

	x	y	z	U(eq)
H(3)	4829	2902	4194	22
H(4)	4169	979	3432	19
H(6)	-1663	266	4078	19
H(7)	-987	2141	4859	21
H(10A)	-4505	-1166	1529	30
H(10B)	-3771	438	1805	30
H(10C)	-5292	-582	2202	30
H(11)	1581	-2544	2735	19
H(2)	-1475	582	2737	17