Aminodifluorosulfinium Tetrafluoroborate Salts as Stable and Crystalline Deoxofluorination Reagents

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General Methods. The ^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on a Varian oxford 300 spectrometer. Differential scanning calorimetry data were collected using a DSC (TA instruments, model Q1000) under the following parameters: 50 mL/ min. purge gas (N_2); scan range 40 to 300 °C, scan rate 10 °C/ min. The isothermal experiments were performed at 90 °C for extended period of time. Melting points were obtained from a Büchi B-545 capillary apparatus and are uncorrected. Column chromatography purifications were carried out on Sorbent technologies silica gel 40-63 µm flash chromatography packing (60 Á pore diameter). Dialkylaminosulfur trifluoride were purchased from Apollo scientific, with the exception of dimethylaminosulfur trifluoride which was bought from Aldrich.

General Procedure for the preparation of dialkylaminodifluorosulfinium tetrafluoroborate salts: To an ice-cold solution of dialkylaminosulfur trifluoride (62 mmol) in anhydrous diethyl ether (100 mL) was added, dropwise and under nitrogen, neat borontrifluoride etherate (62 mmol) over a period of 15 min, while keeping the reaction temperature below 5˚C. The resulting suspension was stirred for an additional hour at the same temperature, then allowed to warm to room temperature and filtered under a blanket of nitrogen. The solid material was rinsed twice with diethyl ether (2x50 mL), then dried under vacuum to provide the dialkylaminodifluorosulfinium tetrafluoroborate.

Diethylaminodifluorosulfinium tetrafluoroborate (4): The titled compound was prepared according to the general procedure above using diethylaminosulfur trifluoride yielding (11.9g, 84%) as a off-white hygroscopic solid; (5.0 g of the crude salt was re-crystallized in 50 mL of boiling 1,2-dichloroethane with gradual cooling to r.t. over an hour to provide 4.6 g (92%) of white crystals flakes; m.p. 83-84 ˚C); ^{1}H NMR (CD_3CN) 3.87 (m (br), 4H), 1.35 (t, J = 7.2 Hz, 6H); ^{19}F NMR (CD_3CN) 12.91 (m, J = 5.1 Hz, 2F), -151.14 (s, 4F); ^{13}C NMR (CD_3CN) 45.49, 12.56.

Morpholinodifluorosulfinium tetrafluoroborate (6): The titled compound was prepared according to the general procedure using morpholinosulfur trifluoride yielding (13.9g, 92%) as a white solid ; m.p. 122-125 ˚C; ^{1}H NMR (CD_3CN) 3.90-3.85 (m, 8H); ^{19}F NMR (CD_3CN) 10.16 (s, 2F), -151.27 (s, 4H); ^{13}C NMR (CD_3CN) 65.71, 48.32 (br).

Bis(2-methoxyethyl)aminodifluorosulfinium tetrafluoroborate (11): The titled compound was prepared according to the general procedure above using bis(2-methoxyethyl)aminosulfur trifluoride yielding (14.0g, 78%) off-white hygroscopic solid; m.p. 35-38 ˚C; ^{1}H NMR (CD_3CN) 4.07 (m, 4H), 3.60 (m, 4H), 3.43 (s, 6H); ^{19}F NMR (CD_3CN) 10.22 (s, 2F), -151.47 (s, 4F); ^{13}C NMR (CD_3CN) 67.08, 58.92, 51.53.

General Procedure for deoxofluorinations. To a stirred suspension of diethylaminodifluorosulfinium tetrafluoroborate (4.0 mmol) in dichloromethane (25 mL) at room temperature was added the substrate (2.67 mmol) and triethylamine trihydrofluoride (4.0 mmol). The resulting mixture was stirred under nitrogen over the prescribed amount of time. The reaction was then quenched at room temperature with a 5% sodium bicarbonate aqueous solution, stirred for 15 minutes, and the resulting mixture was extracted twice using dichloromethane. The organic phases were combined, dried over magnesium sulfate, filtered and concentrated. The residual oil was purified by SiO_2 chromatography.

1-Fluoro-3-phenylpropane. The titled compound was prepared according to the foregoing procedure using 3-phenylpropanol (reaction time = 4h). Column chromatography (pentane) of the residual material yielded 1-fluoro-3-phenylpropane (314mg, 85%) as a clear liquid. 1H NMR (CDCl3) 7.4-7.1 (m, 5H), 4.47 (dt, J = 47.3, 5.9 Hz, 2H), 2.76 (t, 7.3 Hz, 2H), 2.1-1.9 (m, 2H); ^{19}F NMR ($CDCl_3$) -220.56 (m, 1F); ^{13}C NMR ($CDCl_3$) 141.21, 128.59, 128.57, 126.13, 83.25 (d, 164.5 Hz), 32.15 (d, 19.6 Hz), 31.42 (d, 5.7 Hz).

1,1-Difluoro-3-phenylpropane. The titled compound was prepared according to the foregoing procedure using 3-phenylpropionaldehyde (reaction time = 4h). Column chromatography (pentane) of the residual material yielded 1,1-difluoro-3-phenylpropane (346mg, 83%) as a clear liquid. ^{1}H NMR ($CDCl_3$) 7.4-7.2 (m, 5H), 5.65 (tt, J = 56.7, 4.4 Hz, 1H), 2.82 (t, J = 7.7 Hz, 2H), 2.20 (m, 2H). ^{19}F NMR ($CDCl_3$) -117.45 (dt, J = 16.9, 56.9 Hz, 1F); ^{13}C NMR ($CDCl_3$) 140.20, 128.93, 128.61, 126.68, 117.00 (d, 238.9 Hz), 35.95 (t, 20.5 Hz), 28.67 (d, 6.1 Hz).

1,1-Difluoro-4-*tert*-butylcyclohexane. The titled compound was prepared according to the foregoing procedure using 4-*tert*-butylcyclohexanone (reaction time = 16h). Column chromatography (pentane) of the residual material yielded 1,1-difluoro-4-*tert*-butylcyclohexane (400mg, 85%) as a clear liquid admixed with 4% of 1-fluoro-4-*tert*-butylcyclohex-1-ene. ^{1}H NMR ($CDCl_3$) 2.2-2.0 (m, 2H), 1.7-1.5 (m, 4H), 1.4-1.2

(m, 2H), 1.2-1.0 (m, 1H) 0.88 (s, 9H). ^{19}F NMR ($CDCl_3$) -91.94 (d, J = 231.8 Hz, 1F), 103.50(dtt, 234.9, 36.7, 12.1 Hz, 1F); ^{13}C NMR ($CDCl_3$) 124.01 (t, 238.9Hz), 46.79, 41.58, 34.41 (dd, J = 25.4, 21.8 Hz), 32.50, 27.83, 24.01 (d, J = 9.8 Hz).

Fluorooctane. The titled compound was prepared according to the foregoing procedure using cyclooctanol (reaction time = 16h). Column chromatography of the crude material (10% CH_2Cl_2/pentane) yielded a 77/23 mixture of fluorooctane and cyclooctene (292mg, 84%) as a clear liquid. ^{1}H NMR ($CDCl_3$) 4.63 (dm, J = 45.9 Hz, 1H), 2.0-1.3 (m, 16H); ^{19}F NMR ($CDCl_3$) -159.65 (s, 1F); ^{13}C NMR ($CDCl_3$) 94.98 (d, J = 162.9 Hz), 32.30 (d, J = 21.9 Hz), 27.37, 25.31, 22.23 (d, J = 9.7 Hz).

3-Phenylpropanoyl fluoride. The titled compound was prepared according to the foregoing procedure using 3-phenylpropanoic acid (reaction time = 4h). Column chromatography (pentane) of the residual material yielded 3-phenylpropanoyl fluoride (382mg, 94%) as a clear liquid. ^{1}H NMR ($CDCl_3$) 7.1-7.3 (m, 5H), 2.96 (t, J = 7.6 Hz, 2H), 2.79 (t, J = 7.6 Hz, 2H); ^{19}F NMR ($CDCl_3$) 44.78 (s, 1F); ^{13}C NMR ($CDCl_3$) 161.82 (d, J = 180.2 Hz), 139.1, 128.97, 128.46, 127.02, 34.72 (d, J = 50.7 Hz), 30.15.

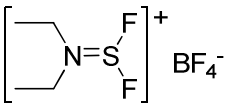
Benzoyl fluoride. The titled compound was prepared according to the foregoing procedure using benzoic acid (reaction time = 4h). Column chromatography (pentane) of the residual material yielded benzoyl fluoride (292mg, 88%) as a clear liquid. ^{1}H NMR ($CDCl_3$) 7.94 (d, J = 7.8, 2H), 7.62 (t, J = 7.3 Hz, 2H), 7.43 (t, J = 8.2 Hz, 2H); ^{19}F NMR ($CDCl_3$) 17.54 (s, 1F); ^{13}C NMR ($CDCl_3$) 157.53 (d, J = 344.3 Hz), 135.49, 131.52 (d, J = 4 Hz), 129.20, 125.03 (d, J = 60.4 Hz).

(±)-Benzyl 3-fluoropyrrolidine-1-carboxylate. The titled compound was prepared according to the foregoing procedure using (±)-benzyl 3-hydroxypyrrolidine-1-carboxylate (reaction time = 16 h). Column chromatography of the crude material (25% EtOAc/Hexanes) yielded (±)-benzyl 3-fluoropyrrolidine-1-carboxylate (290mg, 49%) as a clear liquid. ^{1}H NMR ($CDCl_3$) 7.5-7.2 (m, 5H), 5.15 (d, J = 52.5 Hz, 1H), 5.08 (s, 2H) 3.9-3.5 (m, 4H), 2.4-1.8 (m, 2H); ^{19}F NMR ($CDCl_3$) -177.79 (m, 1F); ^{13}C NMR ($CDCl_3$) 154.88, 136.94, 128.67, 128.19, 128.10, 93.03 (d, J = 176.8 Hz), 92.2 (d, J = 176.2 Hz), 67.08, 53.04 (d, J = 27.1 Hz), 52.73 (d, J = 27.1 Hz), 44.16, 43.80, 32.40 (d, J = 57.6 Hz), 32.11 (d, J = 57.6 Hz). Benzyl 3-dehydropyrrolidine-1-carboxylate was also isolated (58 mg, 11%) as a clear liquid. ^{1}H NMR ($CDCl_3$) 7.3-

7.1 (m, 5H), 5.8-5.6 (m, 2H), 5.08 (s, 2H) 4.2-4.0 (m, 4H); ^{13}C NMR ($CDCl_3$) 154.76, 137.01, 128.61, 128.16, 128.08, 128.01, 125.92, 125.81, 66.90, 53.56, 53.09

Benzyl 3,3-difluoropyrrolidine-1-carboxylate. The titled compound was prepared according to the foregoing procedure using benzyl pyrrolidin-3-one-1-carboxylate (reaction time = 16 h). Column chromatography of the crude material (10% EtOAc/Hexanes) yielded benzyl 3,3-difluoropyrrolidine-1-carboxylate (340mg, 53%) as a clear liquid. ^{1}H NMR ($CDCl_3$) 7.3-7.2 (m, 5H), 5.08 (s, 2H), 3.7-3.5 (m, 4H), 2.3-2.2 (m, 2H); ^{19}F NMR ($CDCl_3$) -102.71 (dq, J = 198.2, 12.1 Hz, 2F); ^{13}C NMR ($CDCl_3$) 154.60, 136.51, 129.29 (t, J = 124.4 Hz), 128.69 (t, J = 124.4 Hz), 128.71, 128.48, 128.36, 128.20, 67.42, 52.99 (d, J = 32.2 Hz), 52.86 (d, J = 32.2 Hz), 43.85, 34.33 (d, J = 24.2 Hz), 33.68 (d, J = 24.2 Hz).

8,8-Difluoro-1,4-dioxaspiro[4,5]decane (13). To a stirred solution of Bis(2-methoxyethyl)aminodifluorosulfinium tetrafluoroborate (**11**) (997mg, 12.8 mmol) in dichloromethane (10 mL) at room temperature was added 1,4-dioxaspiro[4,5]decan-8-one (**12**) (3.69g, 6.4 mmol) and triethylamine trihydrofluoride (1.04mL, 12.8 mmol) The resulting mixture was stirred under nitrogen over 18 hrs. The reaction was quenched at room temperature with a 5% sodium bicarbonate aqueous solution, stirred for 15 minutes, and the resulting mixture was extracted twice using dichloromethane. Organic phases were combined, washed with 10% aqueous HCl, dried over magnesium sulfate and filtered. Solvents were evaporated and the resulting oil was purified by column chromatography (10% EtOAc/Hexanes) yielding the title compound **13** (340mg, 53%) as a colorless solid. ^{1}H NMR ($CDCl_3$) 3.92 (s, 4H), 2.1-1.9 (m, 4H), 1.8-1.6 (m, 4H); ^{19}F NMR ($CDCl_3$) -100.19 (s, 2F); ^{13}C NMR ($CDCl_3$) 123.00 (t, J = 240.4 Hz), 107.35, 64.61, 31.54 (t, J = 25.0 Hz), 31.22 (t, J = 5.4 Hz).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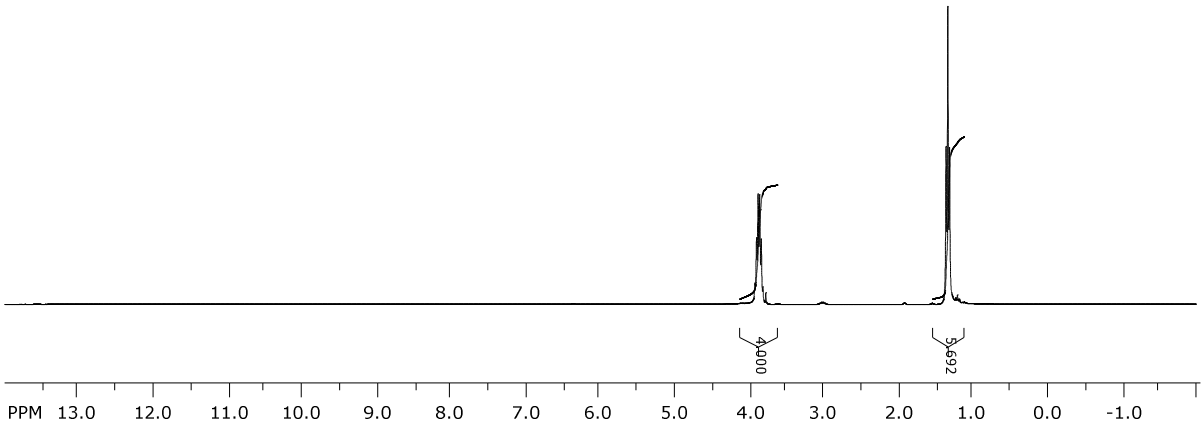
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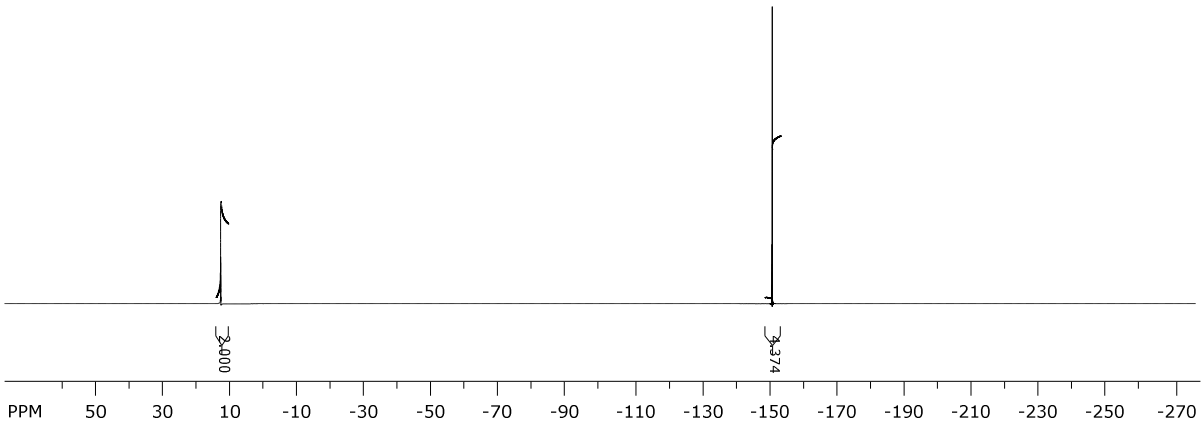
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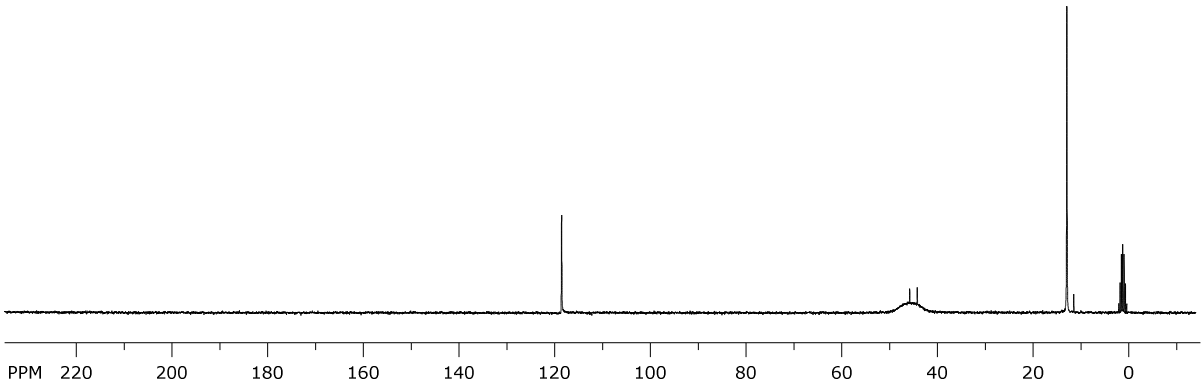
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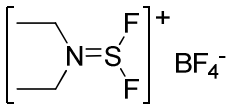
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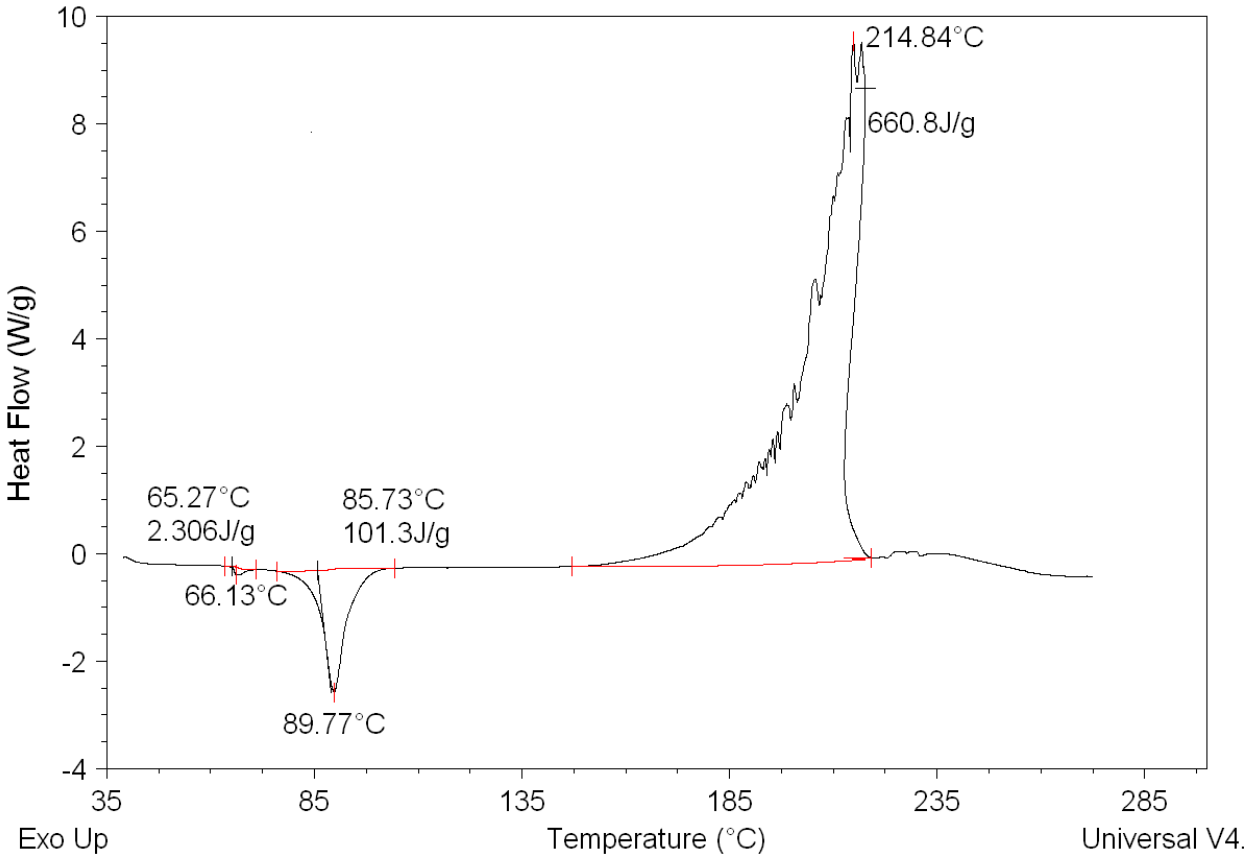
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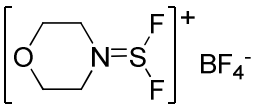
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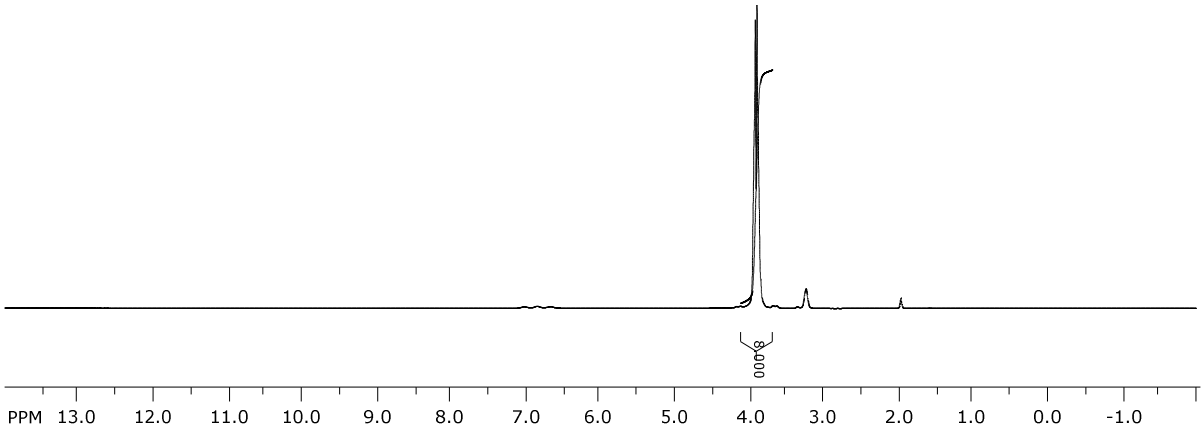
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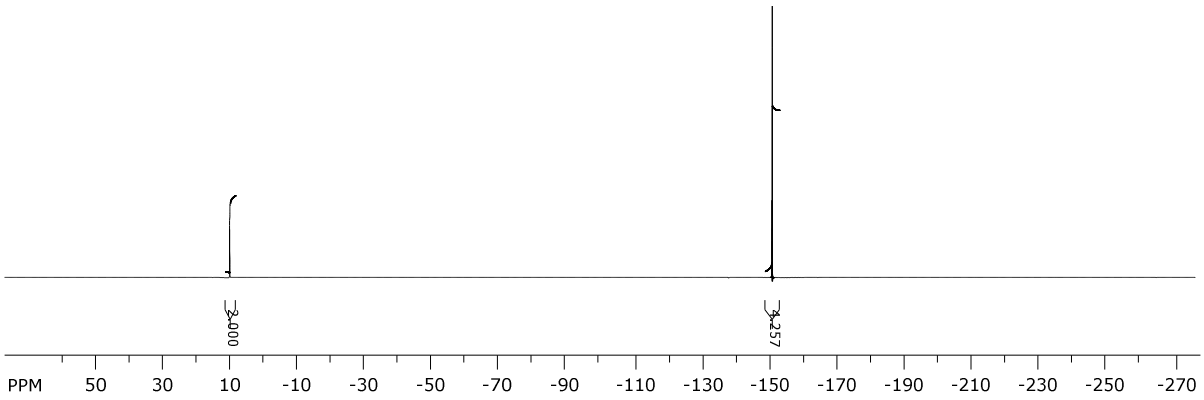
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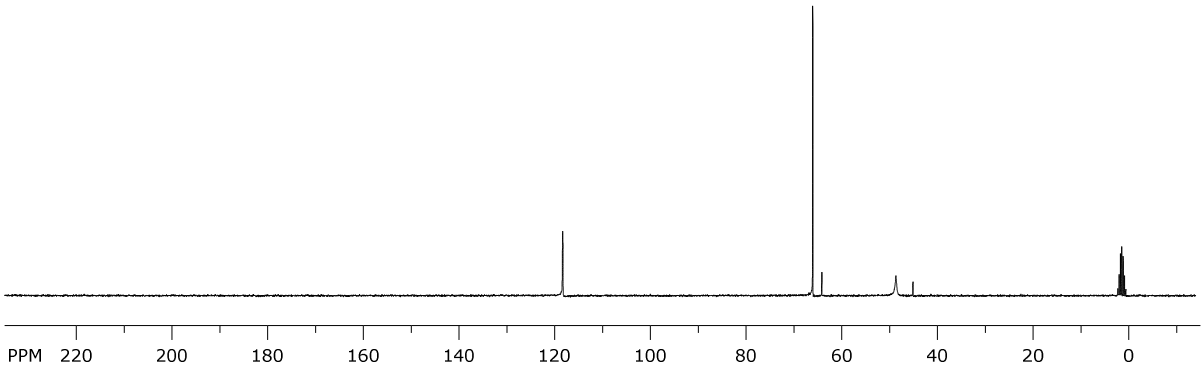
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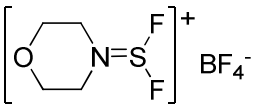
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+
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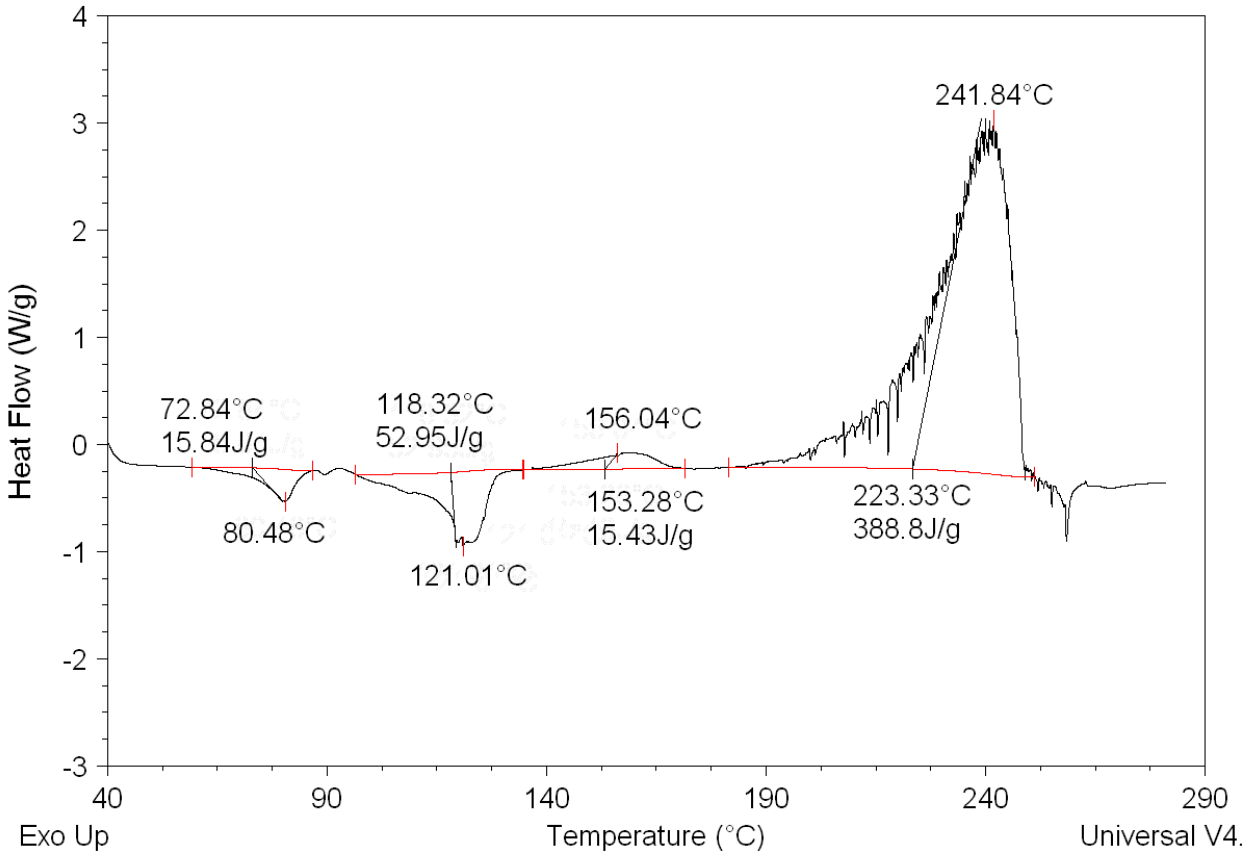
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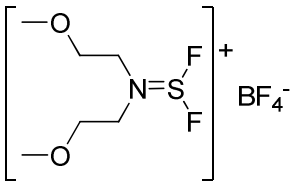
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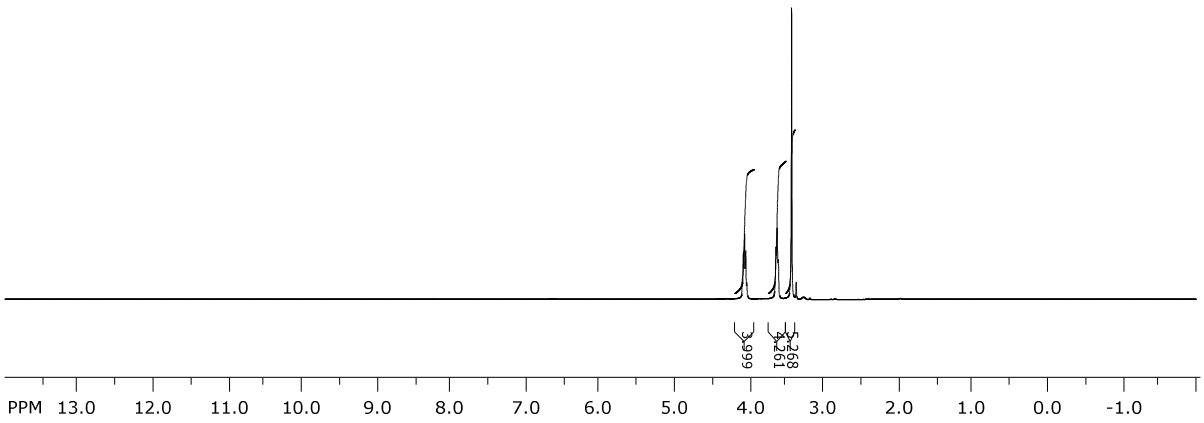
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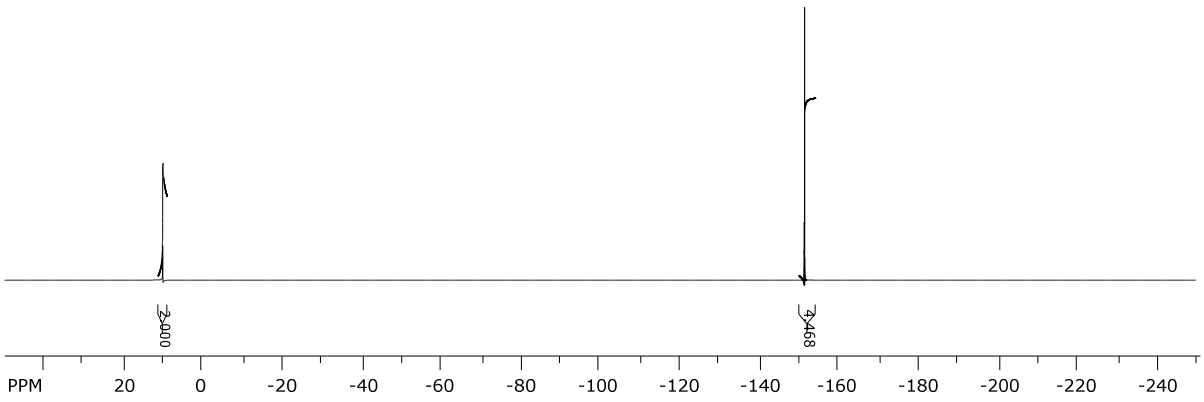
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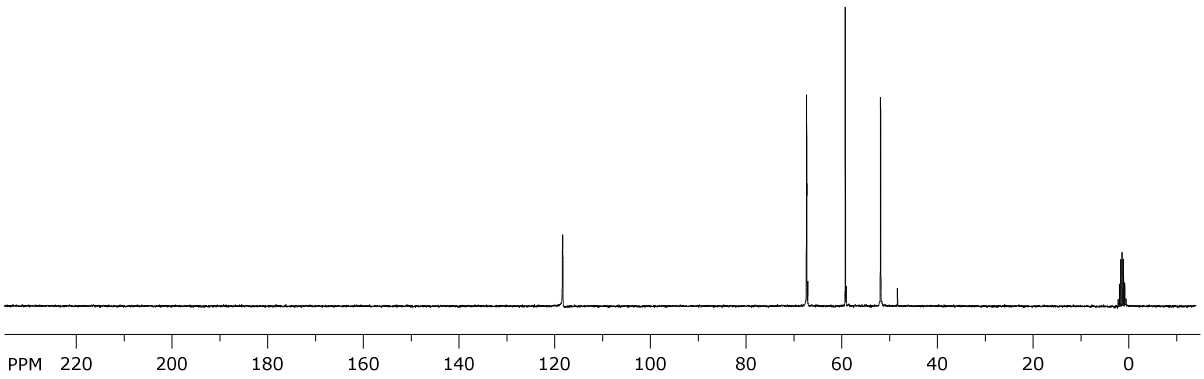
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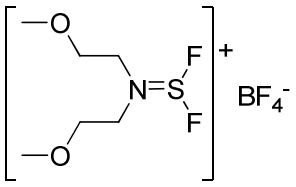
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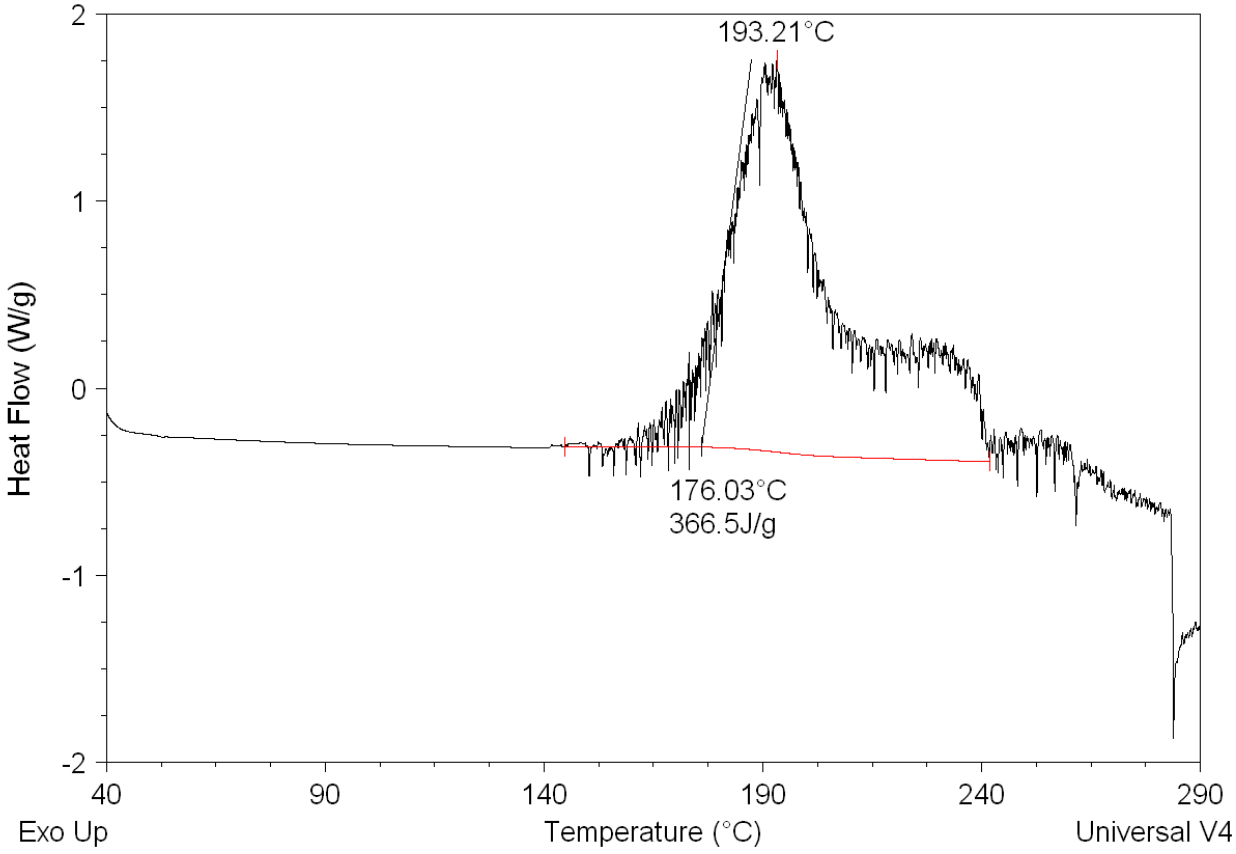
11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Temperature (°C)
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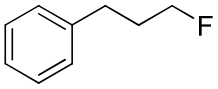

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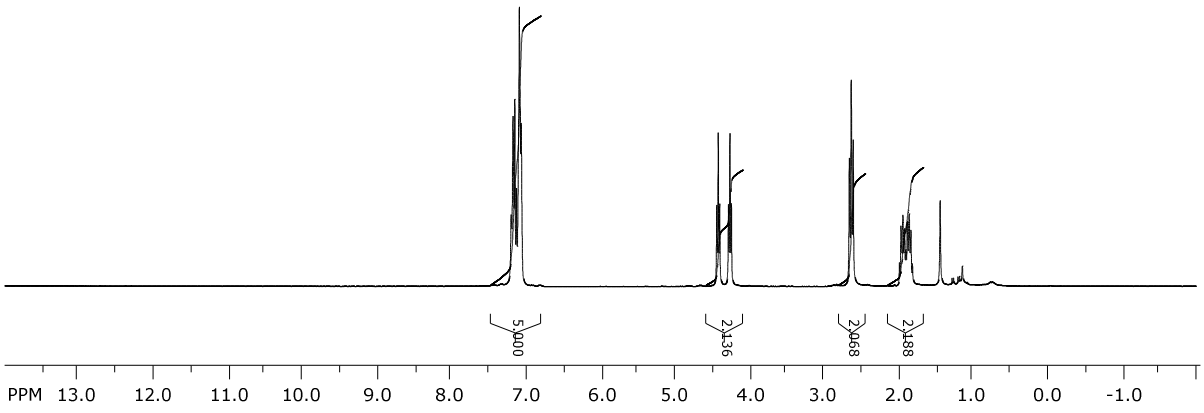

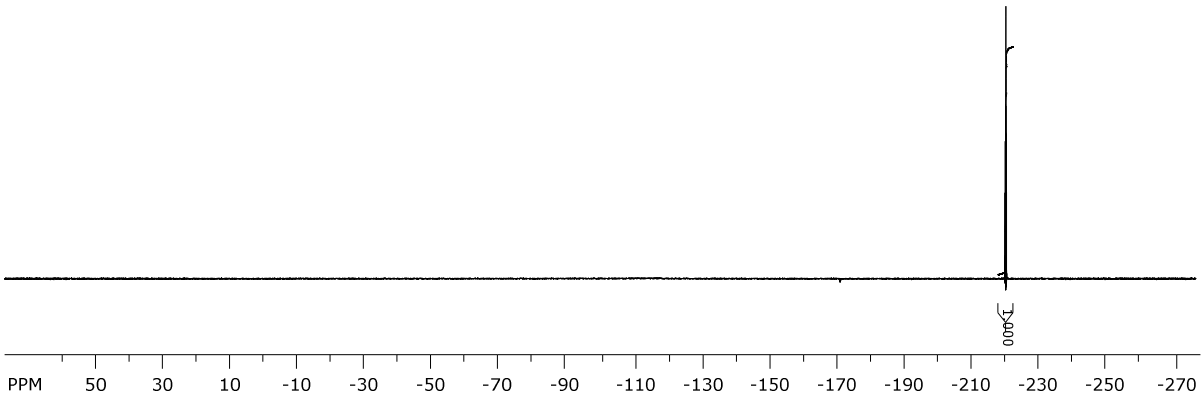

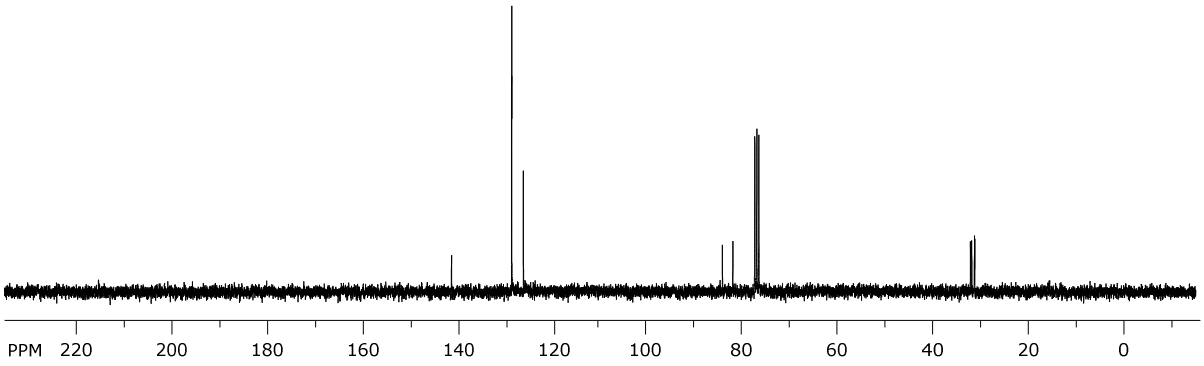

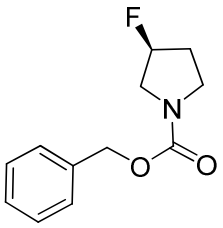

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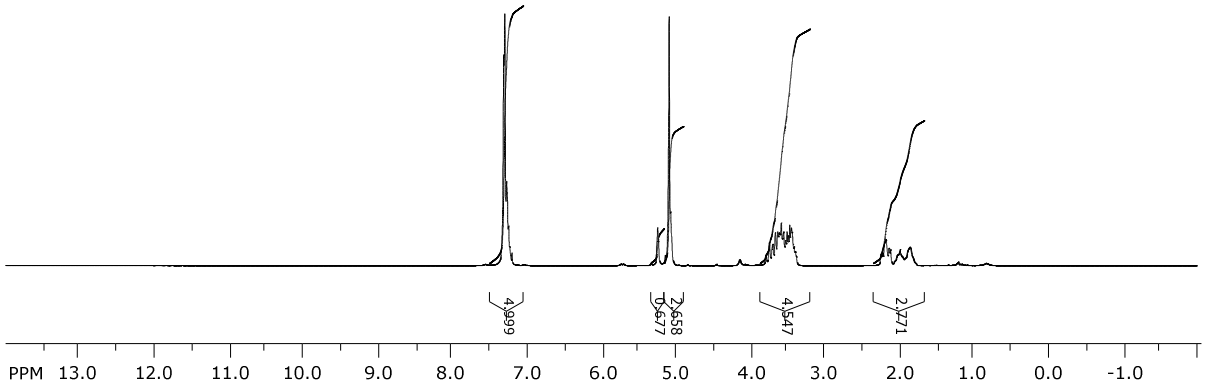

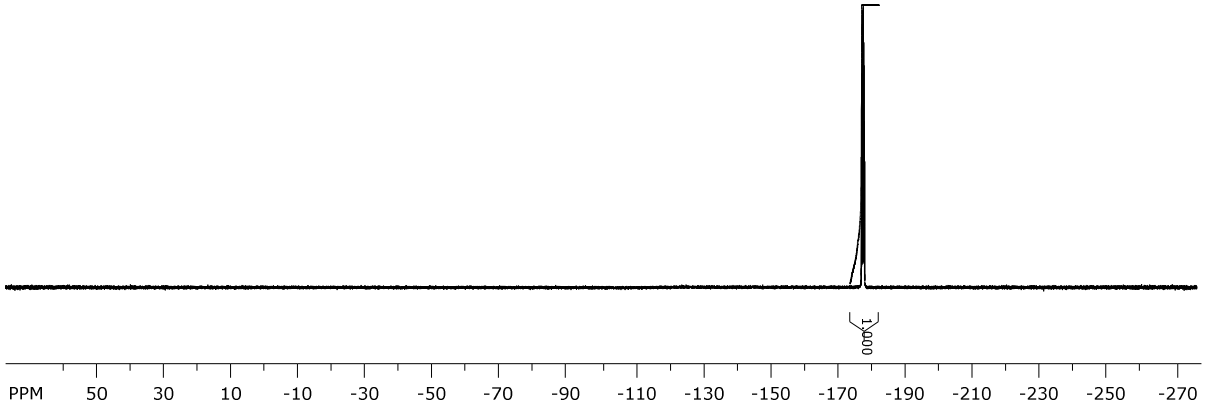

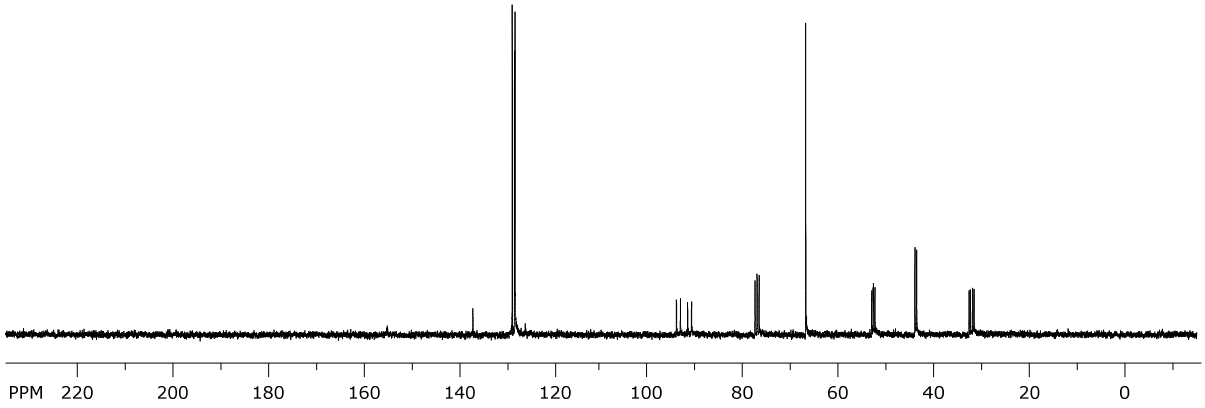

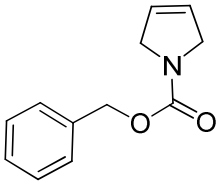

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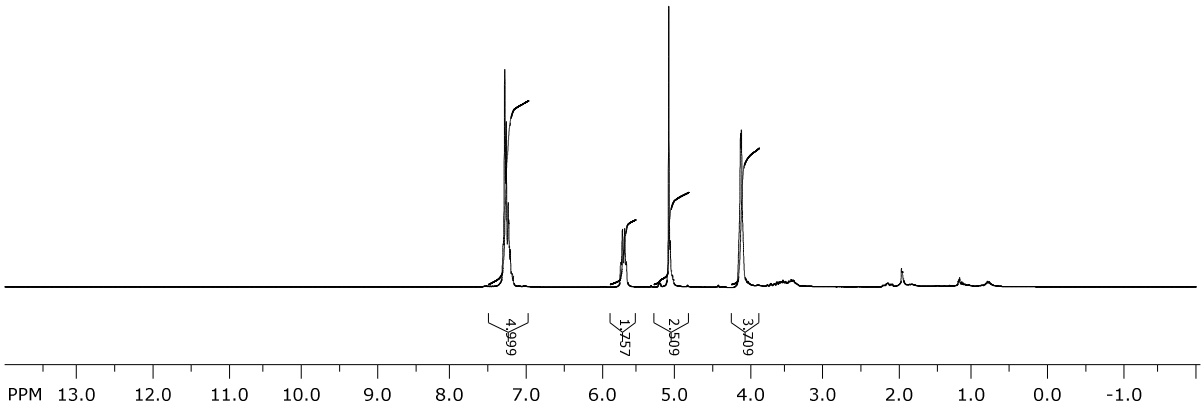

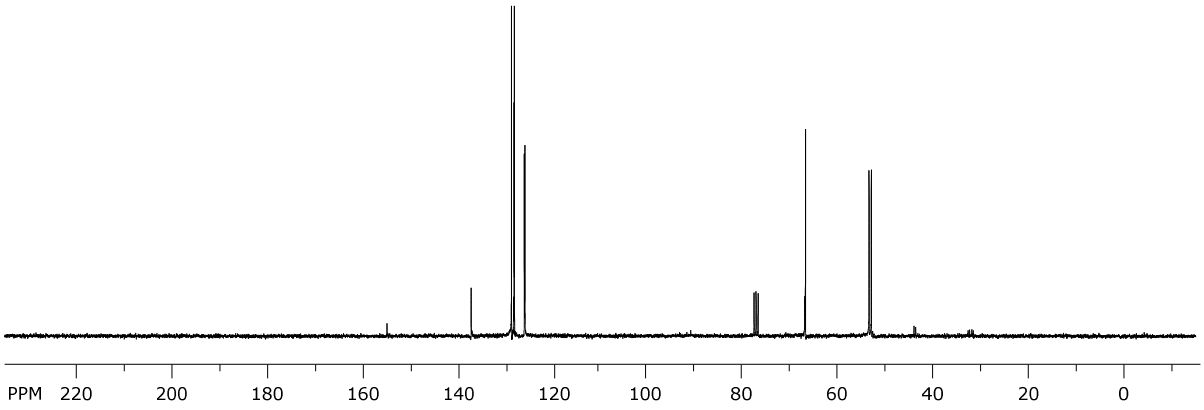

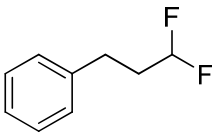

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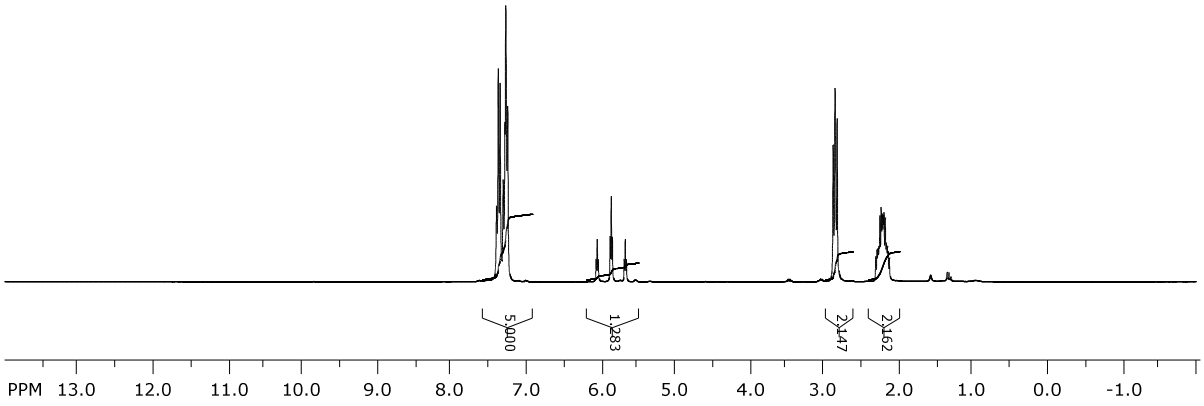

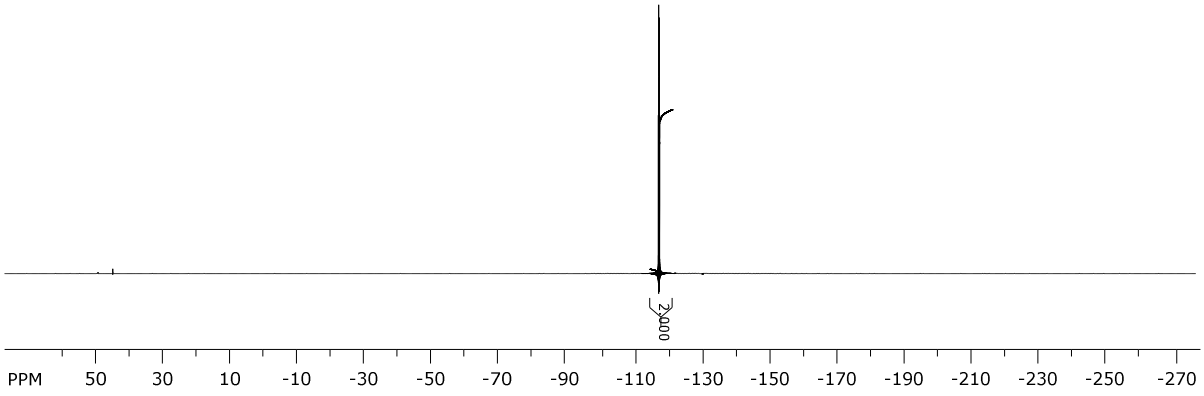

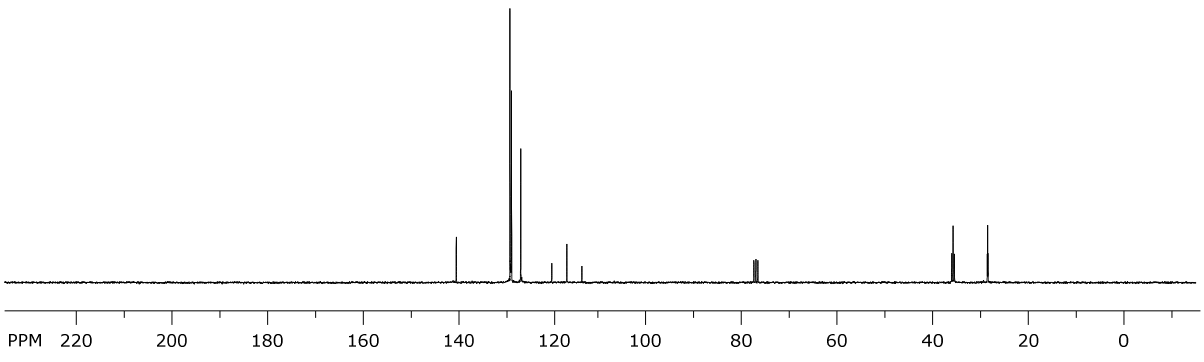

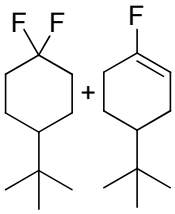

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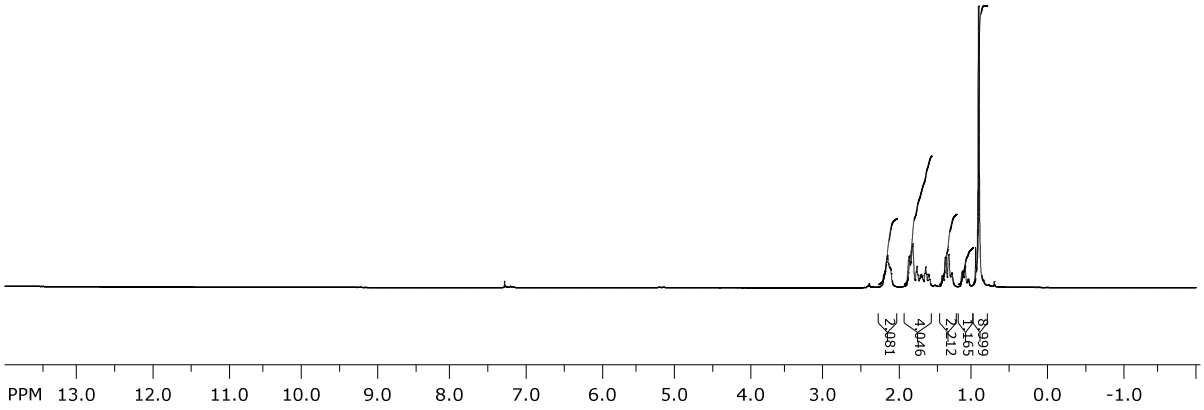

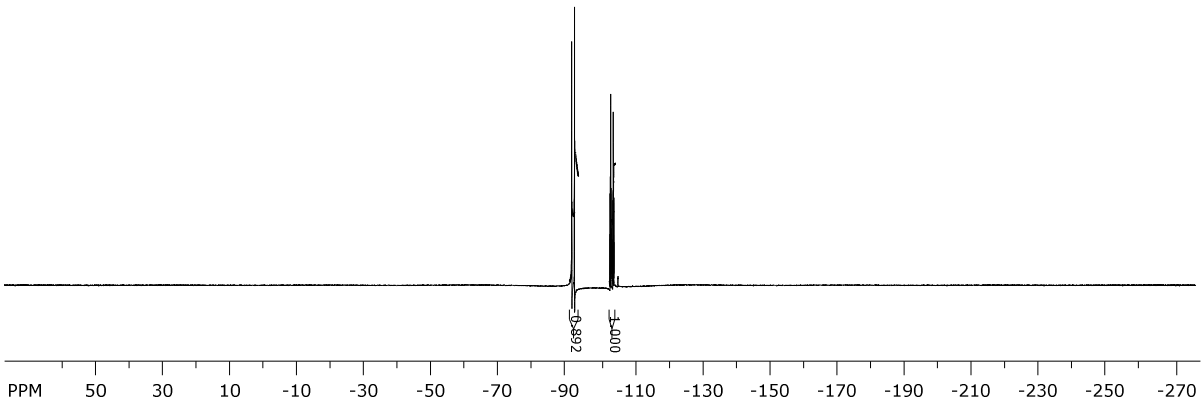

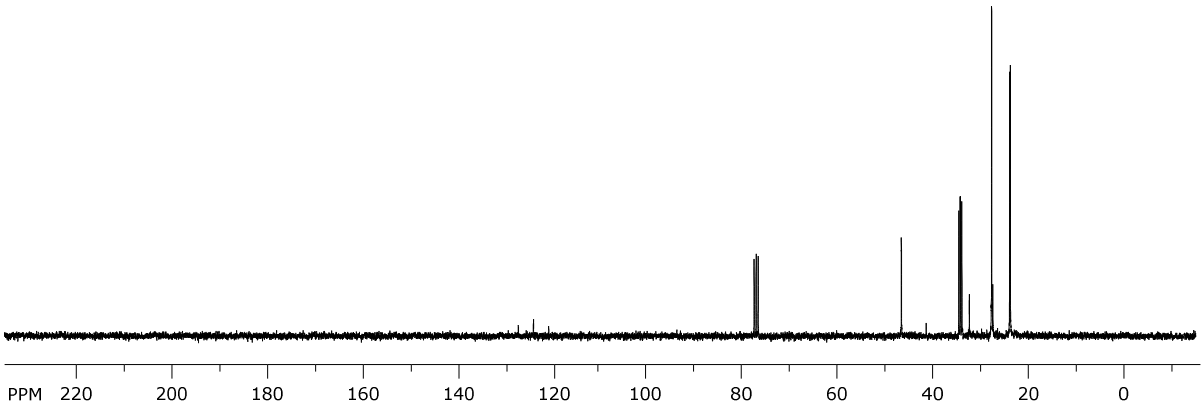

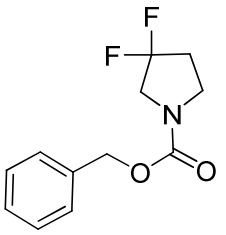

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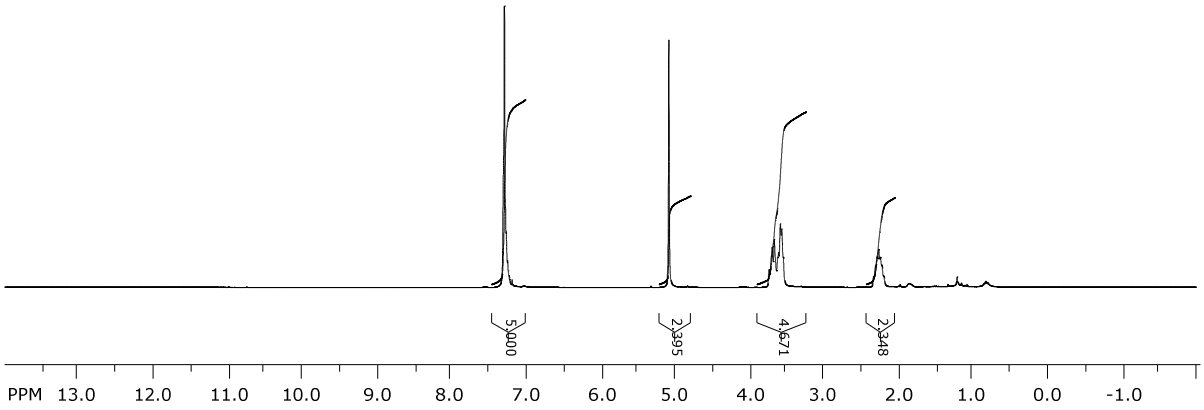

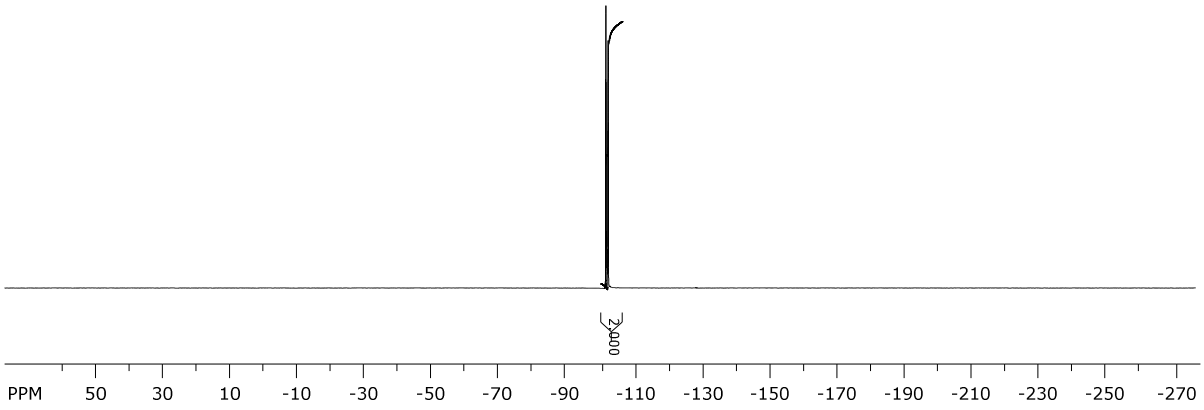

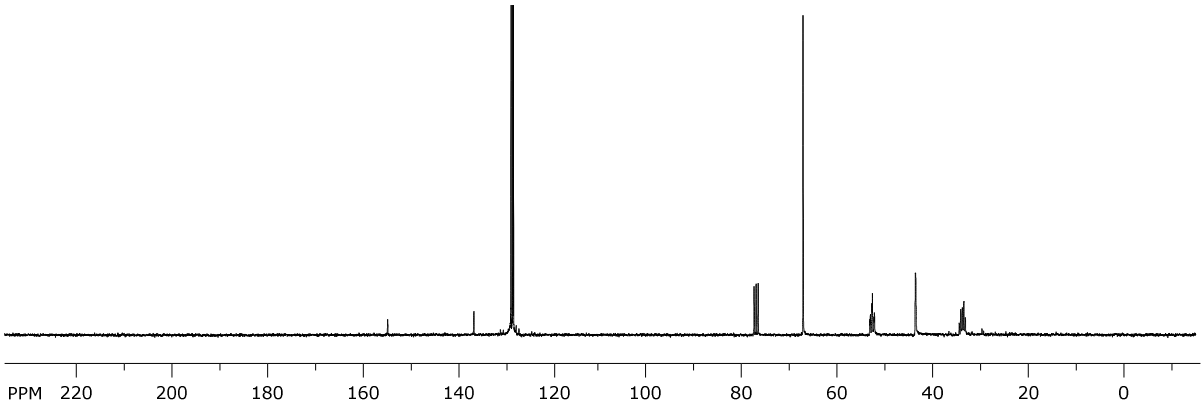

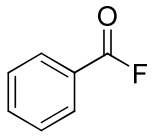

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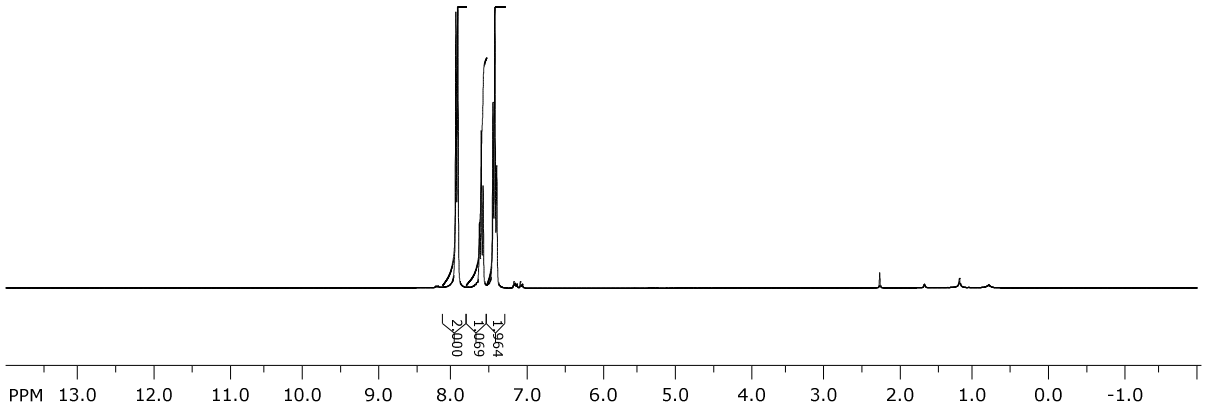

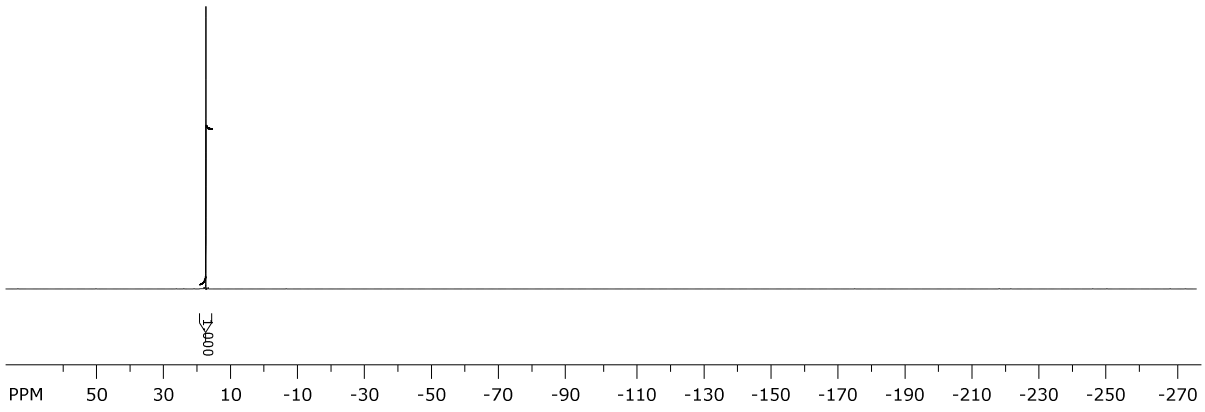

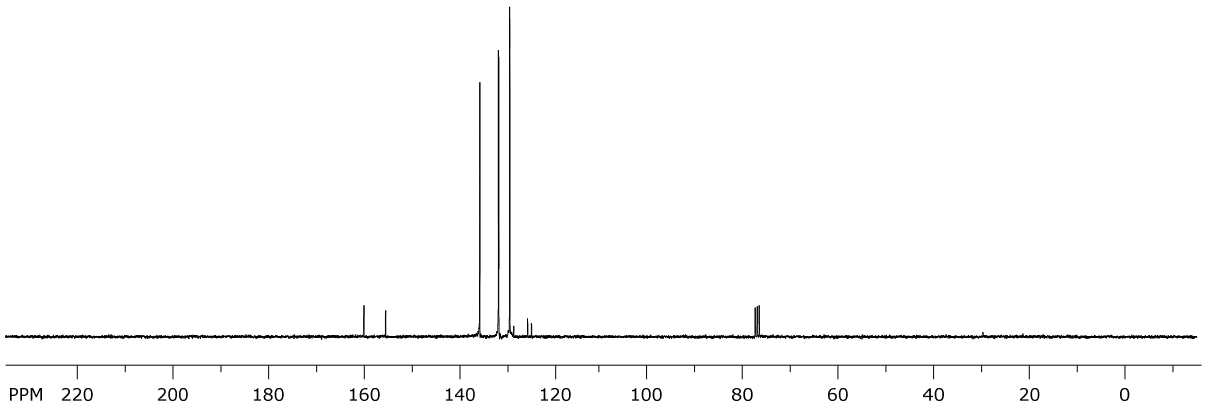

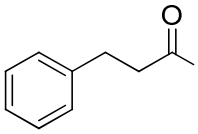

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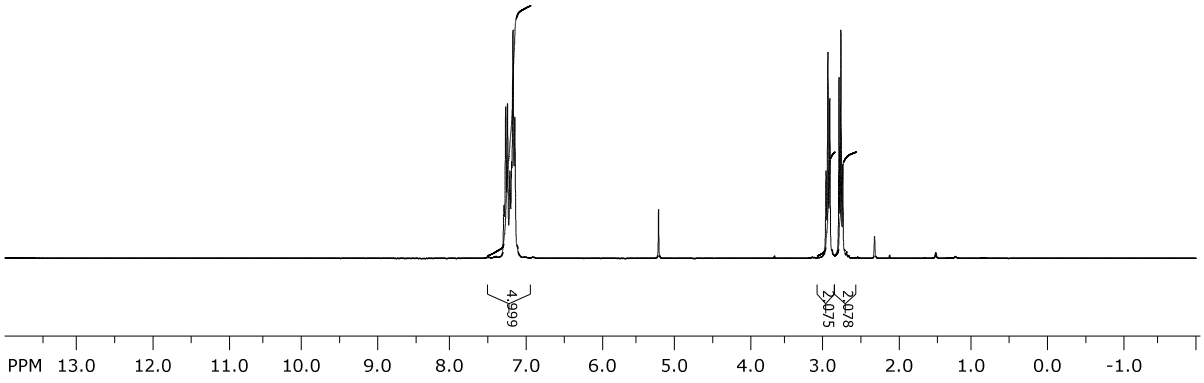

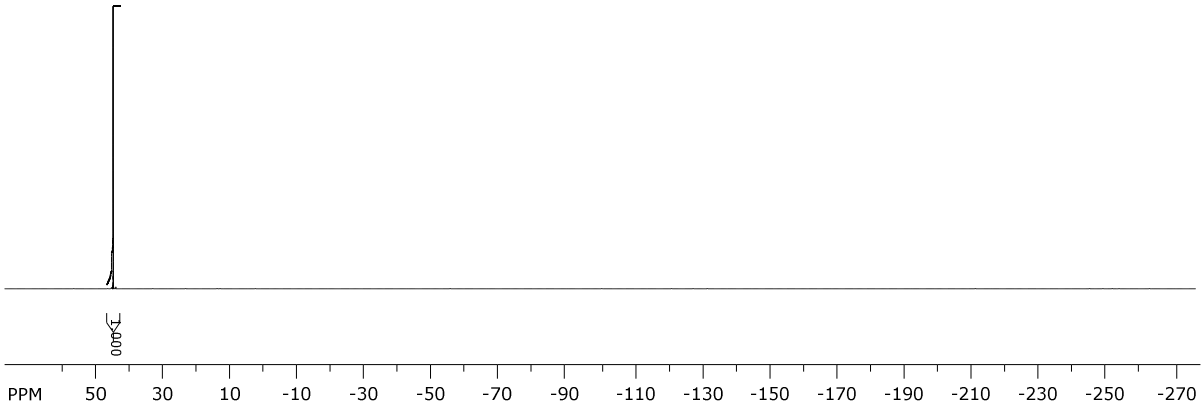

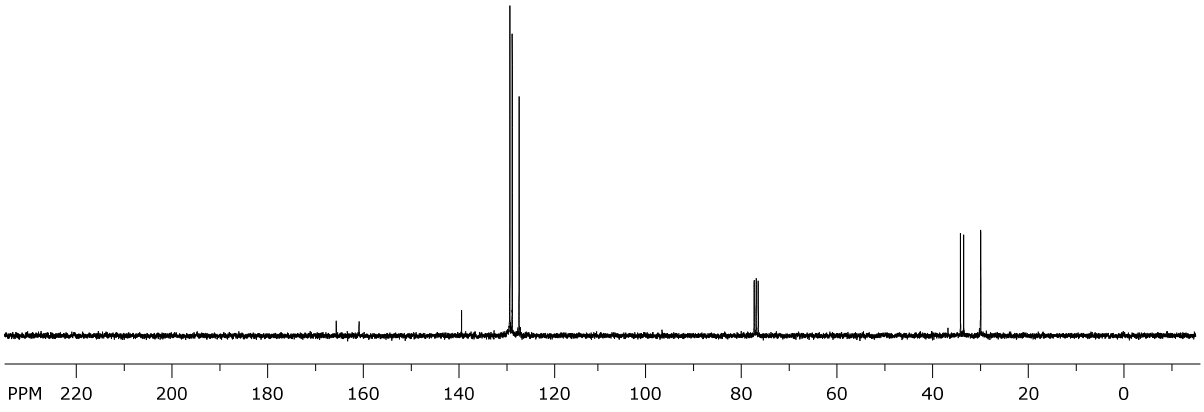

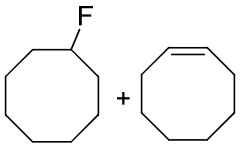

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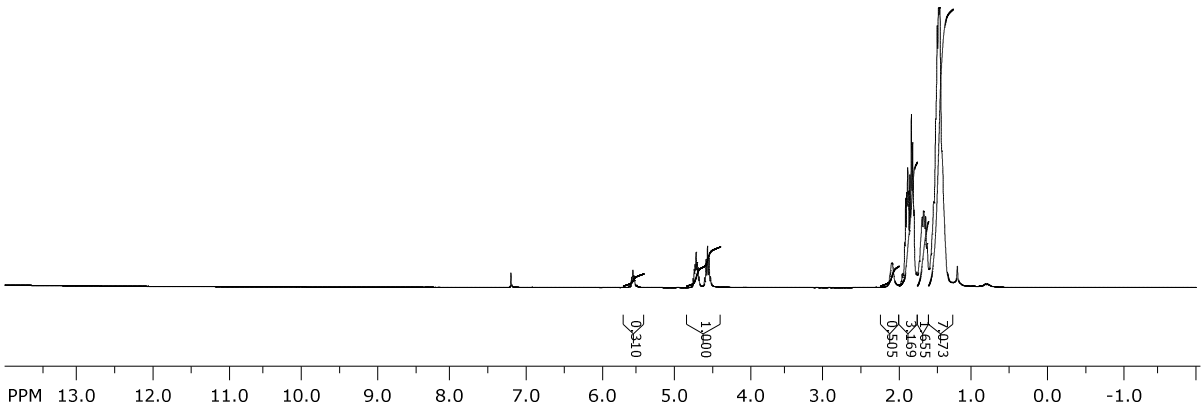

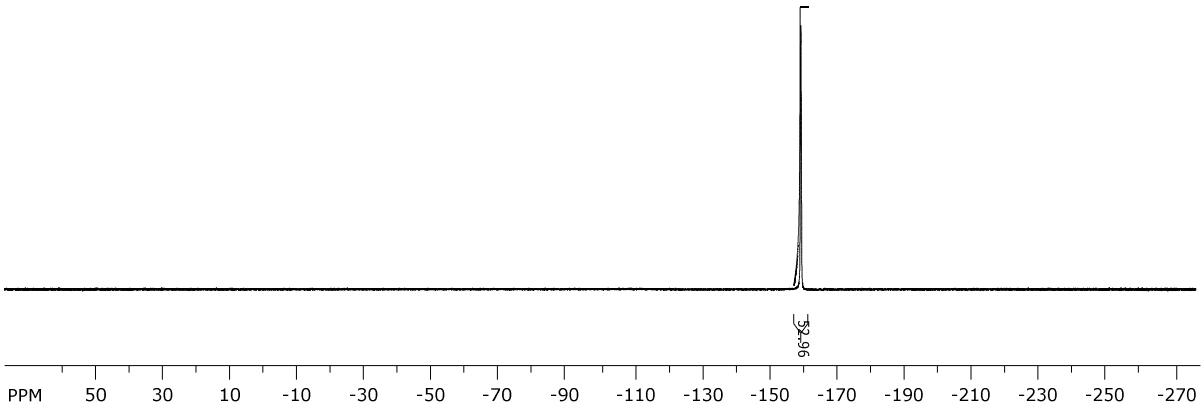

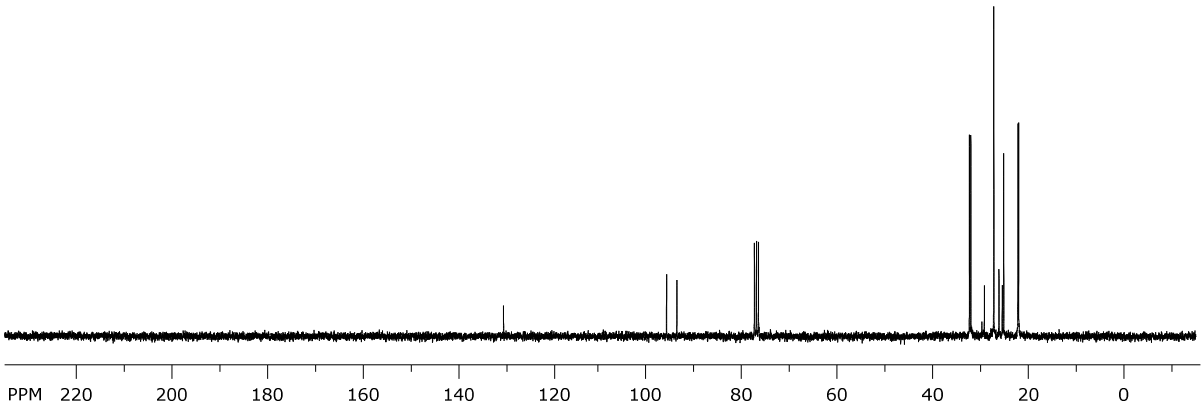

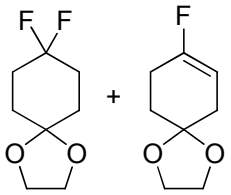
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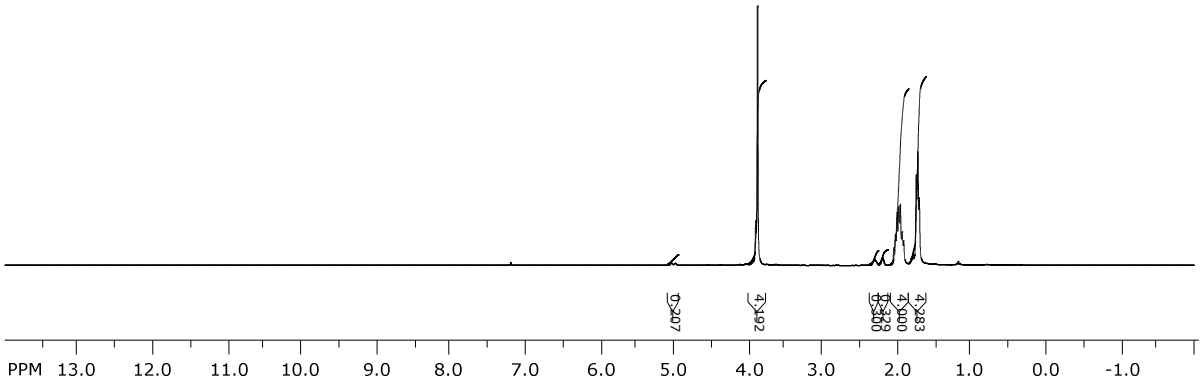
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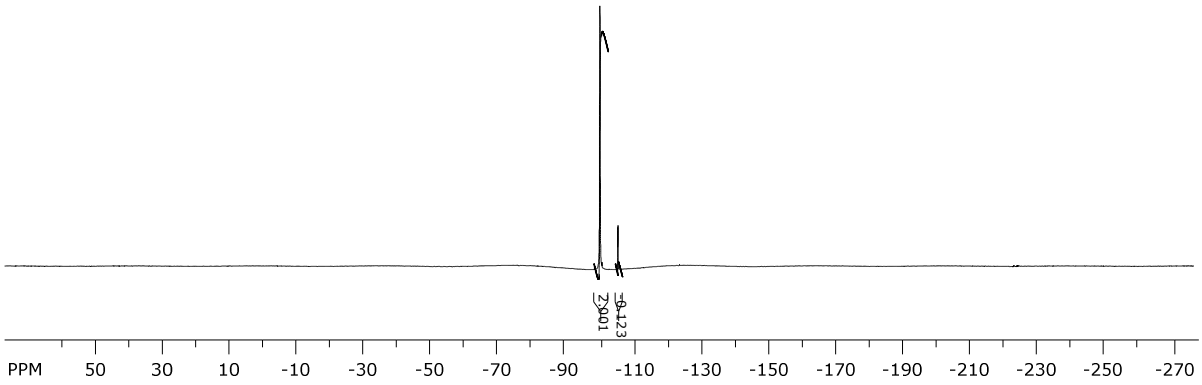
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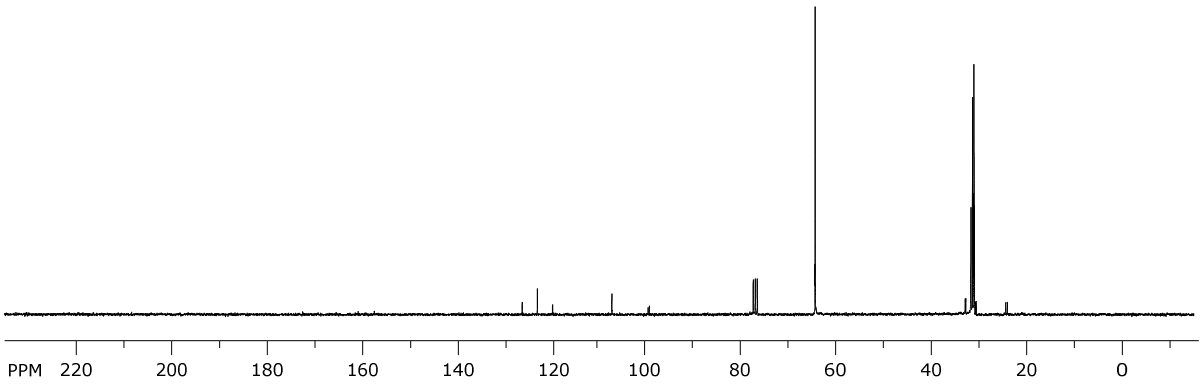
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