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# SUPPORTING INFORMATION

## Visible-light mediated carbonyl trifluoromethylative amination as a practical method for the synthesis of β-trifluoromethyl tertiary alkylamines

Kavoos Kolahdouzan, Roopender Kumar & Matthew J. Gaunt*

*Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, CB2 1EW, United Kingdom.*

*To whom correspondence should be addressed:
mjg32@cam.ac.uk

**Materials & Methods**

All reactions were run under an inert atmosphere ($N_2$) unless otherwise stated, with oven-dried glassware, using standard techniques. Commercial anhydrous solvents were used for all reactions. Powdered 4Å molecular sieves (MS) were activated prior to use by prolonged heating (250 qC) under high-vacuum and stored under $N_2$ in a round-bottom flask. Aldehydes were distilled prior to usage. Amines were similarly purified via distillation or column chromatography prior to usage. The Ritter Trifluoroiodomethane-DMSO reagent was purchased from Sigma Aldrich. All other commercial reagents were used as supplied unless otherwise stated.

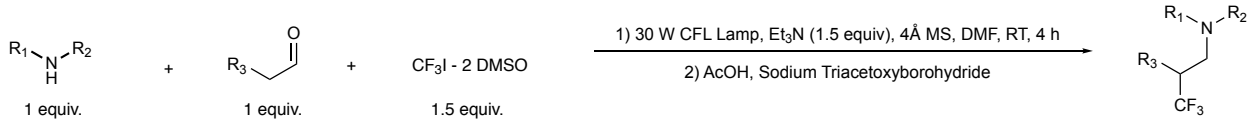
Irradiation of the reaction mixture for the $CF_3$ reactions was achieved via the use of a single 30 W CFL bulb. Clear microwave vials were used as the standard reaction vessel.

Analytical thin-layer chromatography (TLC) was performed on Merck Kieselgel 60 F254 0.20 mm precoated, glass backed silica gel plates. Visualization of the developed chromatogram was performed via UV absorbance and/or by aqueous $KMnO_4$. Flash column chromatography was performed using silica gel (Merck Geduran Si 60 [40-63 μm] with the suitable solvent system.

Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker DPX 400 or DPX 600 spectrometer. Chemical shifts (δ) for $^1H$ NMR spectra are recorded in ppm from TMS with the solvent resonance as the internal standard. Data is reported as follows: chemical shift [integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, spt = septet, m = multiplet, br = broad), coupling constant]. $^{13}C$ NMR spectra are reported in ppm from TMS with the solvent resonance as the internal standard. $^{19}F$ NMR spectra are reported in ppm from $CFCl_3$ and are uncorrected.

Infrared spectra (FT-IR) were recorded using a Perkin-Elmer Paragon 1000 Fourier transform Spectrometer equipped with ATR and analyzed as thin films, with absorption maxima being quoted in wavenumbers ($cm^{-1}$) and characteristic peaks being defined (s = strong, br = broad). High Resolution Mass spectrometry (HRMS) was conducted by the Cambridge chemistry department.

## General Procedure for Synthesis of β-Trifluoromethylated Tertiary Alkylamines

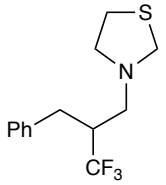



## General Procedure

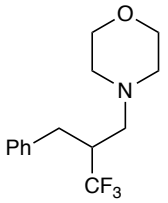
**E.g. for a 0.1 mmol scale reaction:** an oven dried vial (Biotage Microwave Process Vial 10 mL, equipped with gas-tight septa) was charged with a stir bar and pre-activated 4Å MS (100 mg). The vial was sealed, evacuated and backfilled three times with 1 atm of $N_2$. To this was added dry dimethylformamide (200 µL, 0.5 M) followed by addition of amine (0.1 mmol, 1 equiv.), aldehyde (1 equiv.), trifluoroiodomethane-DMSO reagent (1.5 equiv.) and triethylamine (1.5 equiv.) via microsyringe. The reaction mixture was irradiated using two 30 W CFL bulbs with vigorous stirring for 4 h at room temperature. Similar levels of reaction performance were achieved via the use of a single 40 W blue LED lamp (Kessil A160WE Tuna Blue) with an overhead fan. After the irradiation, the reaction vial was opened, followed by the addition of acetic acid (3 equiv.), sodium triacetoxyborohydride (2 equiv.) and dichloromethane (1 mL). To ensure completion, the solution mixture was stirred overnight at rapid stirring. After the completion of reductive amination, the reaction mixture was diluted with saturated $Na_2CO_3$ and diethylether within the reaction vial. The solution was filtered and transferred to a separating funnel, followed by extraction by diethyl ether (3x 10 mL). The organic phase was dried over anhydrous $MgSO_4$ and the solvent removed *in vacuo*. The crude material was purified by flash column chromatography with the suitable solvent system.

**From amine hydrochloride salts:** If amine hydrochloride salts are used, an additional equivalent of triethylamine was added to the reaction prior to irradiation.

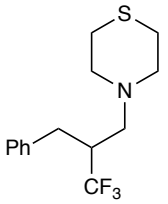
### Alkylamine substrate scope



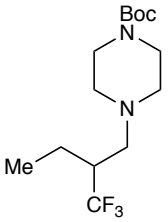

**3-(2-benzyl-3,3,3-trifluoropropyl)thiazolidine (3a).** The title compound was prepared according to the general procedure using thiazolidine (8 µL, 0.10 mmol), hydrocinnamaldehyde (13 µL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 µL, 0.15 mmol), triethylamine (21 µL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 µL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-20% ethyl acetate in 40°–60° petroleum ether) to afford the product as a pale yellow oil (19 mg, 67%). $^1$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.32-7.21 (m, 5H), 4.00 (d, $J$ = 9.4 Hz, 1H), 3.92 (d, $J$ = 9.4 Hz, 1H), 3.05-2.70 (m, 6H), 2.63 (dd, $J$ = 16.1, 5.1 Hz, 1H), 2.53 (m, 1H), 2.43 (dd, $J$ = 16.1, 6.4 Hz, 1H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 138.3, 129.2, 128.5, 127.8 (q, $J$ = 280.7 Hz), 126.7, 61.3, 58.3, 51.2 (q, $J$ = 2.6 Hz), 45.9 (q, $J$ = 23.9 Hz), 32.7 (q, $J$ = 2.5), 29.6, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.4; IR (film, cm$^{-1}$): 3029, 2948, 2871, 1604, 1497, 1455, 1395, 1314, 1254, 1214, 1180, 1163, 1117, 1053, 997, 929, 700, 667; HRMS (NSI+): *m/z* calcd for $C_{13}H_{17}F_3NS$, $[M+H]^+$, 276.1034; found, 276.1037.




**4-(2-benzyl-3,3,3-trifluoropropyl)morpholine (3b).** The title compound was prepared according to the general procedure using morpholine (9 μL, 0.10 mmol), hydrocinnamaldehyde (13 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-5% methanol in dichloromethane) to afford the product as a colorless oil (19 mg, 71%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.32-7.21 (m, 5H), 3.65 (m, 4H), 2.95 (dd, $J$ = 14.2, 5.6 Hz, 1H), 2.90 (dd, $J$ = 14.2, 6.4 Hz, 1H), 2.65-2.55 (m, 2H), 2.42-2.32 (m, 5H). $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 138.7, 129.2, 128.3, 127.8 (q, $J$ = 280.7 Hz), 126.4, 66.9, 56.5 (q, $J$ = 2.5 Hz), 53.6, 44.9, 43.0 (q, $J$ = 23.9 Hz), 33.0 (q, $J$ = 2.4), $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.5; IR (film, cm$^{-1}$): 2958, 2856, 2809, 1681, 1604, 1497, 1456, 1407, 1377, 1257, 1213, 1175, 1141, 1081, 1034, 1008, 978, 941, 916, 868, 743, 699, 667; HRMS (NSI+): *m/z* calcd for $C_{14}H_{19}NOF_3$, $[M+H]^+$, 274.1418; found, 274.1419.

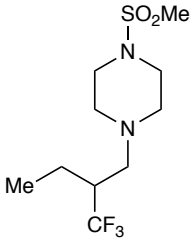



**4-(2-benzyl-3,3,3-trifluoropropyl)thiomorpholine (3c).** The title compound was prepared according to the general procedure using thiomorpholine (10 μL, 0.10 mmol), hydrocinnamaldehyde (13 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-10% ethyl acetate in 40°–60° petroleum ether) to afford the product as a colorless oil (21 mg, 71%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.35-7.20 (m, 5H), 2.98 (dd, $J$ = 14.8, 4.7 Hz), 2.48 (dd, $J$ = 14.8, 6.5 Hz), 2.72-2.52 (m, 10H), 2.40 (m, 1H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 138.7, 129.2, 128.3, 127.8 (q, $J$ = 280.7 Hz), 126.4, 56.8 (q, $J$ = 2.5 Hz), 55.1, 43.4 (q, $J$ = 23.7 Hz), 33.1 (q, $J$ = 2.5), 27.9, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.6; IR (film, cm$^{-1}$): 2931, 2812, 1381, 1255, 1214, 1174, 1159, 1130, 1104, 958, 700, 667; HRMS (NSI+): *m/z* calcd for $C_{14}H_{19}F_3NS$, $[M+H]^+$, 290.1190; found, 290.1181.

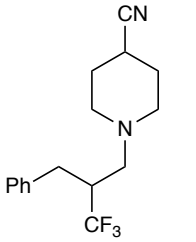



***Tert*-butyl 4-(2-(trifluoromethyl)*butyl*)piperazine-1-carboxylate (3d).** The title compound was prepared according to the general procedure using 1-Boc-piperazine (18.6 mg, 0.10 mmol), butyraldehyde (9 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-20% ethyl acetate in 40°–60° petroleum

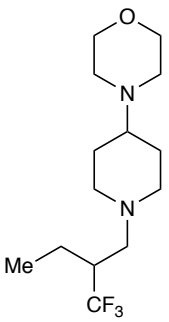
ether) to afford the product as a pale yellow oil (23 mg, 76%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 3.41 (br m, 4H), 2.54 (dd, $J$ = 17.6, 4.7 Hz, 1H), 2.48-2.30 (m, 5H), 2.18 (m, 1H), 1.68 (m, 2H), 1.48 (s, 9H), 1.02 (t, $J$ = 7.6 Hz, 2H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 154.7, 127.8 (q, $J$ = 280.7 Hz), 79.6, 56.3 (q, $J$ = 2.8 Hz), 53.3, 43.5, 42.3 (q, $J$ = 24.0 Hz), 28.4, 20.3 (q, $J$ = 2.4), 11.4, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.4; IR (film, cm$^{-1}$): 2977, 2939, 2800, 1693, 1458, 1418, 1392, 1366, 1296, 1243, 1214, 1120, 1044, 1004, 867, 762, 665; HRMS (NSI+): *m/z* calcd for $C_{14}H_{26}F_3N_2O_2$, $[M+H]^+$, 311.1946; found, 311.1950.



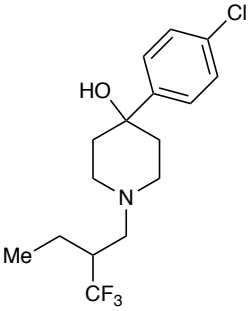

**1-(methylsulfonyl)-4-(2-(trifluoromethyl)butyl)piperazine (3e).** The title compound was prepared according to the general procedure using 1-Methanesulfonylpiperazine (16.4 mg, 0.10 mmol), butyraldehyde (9 µL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 µL, 0.15 mmol), triethylamine (21 µL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 µL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-10% ethyl acetate in 40°–60° petroleum ether) to afford the product as a yellow oil (17 mg, 58%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 3.25 (t, $J$ = 4.8 Hz, 4H), 2.81 (s, 3H), 2.65-2.50 (m, 5H), 2.43 (dd, $J$ = 13.0, 8.0 Hz, 1H), 2.20 (m, 1H), 1.72-1.55 (m, 2H), 1.03 (t, $J$ = 7.6, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 127.8 (q, $J$ = 280.7 Hz, $C_4$), 55.9 (q, $J$ = 2.8 Hz, $C_5$), 52.7, 45.8, 42.4 (q, $J$ = 24.0 Hz), 34.2, 20.2 (q, $J$ = 2.4), 11.4; IR (film, cm$^{-1}$): 2940, 2855, 1458, 1376, 1344, 1325, 1255, 1214, 1118, 1068, 1044, 961, 880, 777, 667; $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.3; HRMS (NSI+): *m/z* calcd for $C_{10}H_{20}N_2SO_2F_3$, $[M+H]^+$, 289.1198; found, 289.1184.



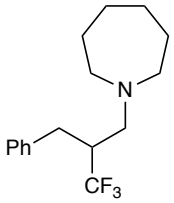

**1-(2-benzyl-3,3,3-trifluoropropyl)piperidine-4-carbonitrile (3f).** The title compound was prepared according to the general procedure using piperidine-4-carbonitrile (11 µL, 0.10 mmol), hydrocinnamaldehyde (13 µL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 µL, 0.15 mmol), triethylamine (21 µL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 µL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-10% ethyl actetate in 40°–60° petroleum ether) to afford the product as a pale yellow oil (22 mg, 71%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.35-7.20 (m, 5H), 2.98 (dd, $J$ = 19.4, 5.3 Hz, 1H), 2.82 (dd, $J$ = 19.4, 6.7 Hz, 1H), 2.64-2.50 (m, 5H), 2.42-2.22 (m, 3H), 1.92-1.70 (m, 4H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 138.7, 129.1, 128.4, 127.8 (q, $J$ = 280.7 Hz), 126.5, 121.6, 56.2 (q, $J$ = 2.6 Hz), 51.6, 51.2, 43.4 (q, $J$ = 23.9 Hz), 33.2 (q, $J$ = 2.5), 28.8, 28.7, 26.0, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.6; IR (film, cm$^{-1}$): 2952, 2797, 2161, 1257, 1214, 1159, 1109, 668; HRMS (NSI+): *m/z* calcd for $C_{16}H_{20}F_3N_2$, $[M+H]^+$, 297.1579; found, 297.1578.



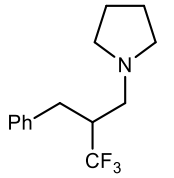

**4-(1-(2-(trifluoromethyl)butyl)piperidin-4-yl)morpholine (3g)**. The title compound was prepared according to the general procedure using 4-(Piperidin-4-yl)-morpholine (17 mg, 0.10 mmol), butyraldehyde (9 µL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 µL, 0.15 mmol), triethylamine (21 µL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 µL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-5% methanol in dichloromethane) to afford the product as a pale yellow oil (22 mg, 75%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 3.73 (t, $J$ = 4.6, 4H), 2.95 (dd, $J$ = 14.2, 5.6, Hz 1H), 2.89 (m, 2H), 2.55 (t, $J$ = 4.6, 4H), 2.47 (dd, $J$ = 12.8, 4.5 Hz, 1H), 2.36 (dd, $J$ = 12.8, 8.7 Hz, 1H), 2.25-2.05 (m, 3H), 1.95-1.76 (m, 3H), 1.63 (quint, $J$ = 7.6, 2H), 1.60-1.50 (m, 2H), 1.0 (t, $J$ = 7.6, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 128.1 (q, $J$ = 280.5 Hz), 67.1, 62.0, 56.1 (q, $J$ = 2.7 Hz), 54.4, 52.3, 49.8, 42.6 (q, $J$ = 23.6 Hz), 28.3, 28.1, 20.3 (q, $J$ = 2.4 Hz), 11.5, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.4; IR (film, cm$^{-1}$): 2950, 2854, 2803, 1452, 1372, 1333, 1254, 1215, 1170, 1043, 981, 878, 850, 750, 667; HRMS (NSI+): *m/z* calcd for $C_{14}H_{26}F_3N_2O$, $[M+H]^+$, 295.1992; found, 295.1984.



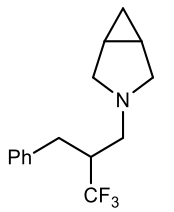

**4-(4-chlorophenyl)-1-(2-(trifluoromethyl)butyl)piperidin-4-ol (3h).** The title compound was prepared according to the general procedure using 4-(Chlorophenyl)-4-hydroxypiperidine (21 mg, 0.10 mmol), butyraldehyde (9 µL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 µL, 0.15 mmol), triethylamine (21 µL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 µL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-10% ethyl acetate in 40°–60° petroleum ether) to afford the product as a colorless crystalline solid (17 mg, 52%). NMR (400 MHz; $CDCl_3$): $\delta$ 7.47 (dt, $J$ = 8.7, 2.0 Hz, 2H), 7.33 (dt, $J$ = 8.7, 2.0 Hz, 2H), 2.75 (m, 2H), 2.66-2.55 (m, 2H), 2.50-2.39 (m, 2H), 2.31-2.05 (m, 3H), 1.80-1.62 (m, app. 5H), 1.06 (t, $J$ = 7.4, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 146.8, 132.8, 128.4, 127.8 (q, $J$ = 280.7 Hz), 126.1, 71.0, 56.4 (q, $J$ = 2.8 Hz), 50.6, 48.9, 42.5 (q, $J$ = 23.7 Hz), 38.6, 38.5, 20.5 (q, $J$ = 1.8), 11.5, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.4; IR (film, cm$^{-1}$): 3807-3379 (br peak), 2947, 2826, 1492, 1469, 1384, 1256, 1215, 1171, 1096, 1043, 1012, 991, 827, 667; HRMS (NSI+): *m/z* calcd for $C_{16}H_{22}ClF_3NO$, $[M+H]^+$, 336.1329; found, 336.1329.



**1-(2-benzyl-3,3,3-trifluoropropyl)azepane (3i).** The title compound was prepared according to the general procedure using azepane (11.3 μL, 0.10 mmol), hydrocinnamaldehyde (13 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-2% methanol in dichloromethane) to afford the product as a colorless oil (19 mg, 65%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.35-7.21 (m, 5H), 3.00 (dd, $J$ = 14.2, 5.1 Hz, 1H), 2.92 (dd, $J$ = 14.2, 6.2 Hz, 1H), 2.80-2.40 (m, 7H), 1.80-1.50 (br m, 8H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 138.3, 129.2, 128.3, 127.8 (q, $J$ = 280.7 Hz), 126.2, 55.8 (q, $J$ = 2.7 Hz), 55.6, 44.8 (q, $J$ = 23.0 Hz), 32.9 (q, $J$ = 2.5), 28.5, 27.0, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.1; IR (film, cm$^{-1}$): 2928, 2853, 1605, 1497, 1455, 1380, 1256, 1141, 1110, 1080, 699. HRMS (NSI+): *m/z* calcd for $C_{16}H_{23}F_3N$, $[M+H]^+$, 286.1783; found, 286.1782.

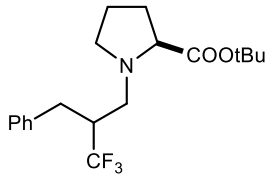


**1-(2-Benzyl-3,3,3-trifluoropropyl)pyrrolidine (3j).** The title compound was prepared according to the general procedure using pyrrolidine (8 μL, 0.10 mmol), hydrocinnamaldehyde (13 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-20% ethyl acetate in 40°–60° petroleum ether) to afford the product as a colorless oil (14.4 mg, 56%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.32-7.21 (m, 5H), 3.00 (dd, $J$ = 16.1, 5.1 Hz, 1H), 2.93 (dd, $J$ = 16.1, 6.4 Hz, 1H), 2.65 (m, 3H), 2.48 (m, 4H), 1.79 (m, 4H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 138.9, 129.2, 128.3, 127.8 (q, $J$ = 280.7 Hz), 126.3, 54.1, 53.7 (q, $J$ = 2.6 Hz), 44.7 (q, $J$ = 23.9 Hz), 32.8 (q, $J$ = 2.5), 23.7, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.4; IR (film, cm$^{-1}$): 2960, 2786, 1497, 1455, 1364, 1252, 1168, 1129, 1098, 742, 698. HRMS (NSI+): *m/z* calcd for $C_{14}H_{19}NF_3$, $[M+H]^+$, 258.1470; found, 258.1476.

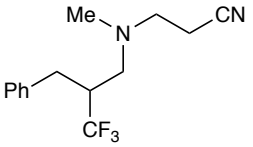


**3-(2-Benzyl-3,3,3-trifluoropropyl)-3-azabicyclo[3.1.0]hexane (3k).** The title compound was prepared according to the general procedure using 3-azabicyclo[3.1.0]hexane hydrochloride (12 mg, 0.10 mmol), hydrocinnamaldehyde (13 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (35 μL, 0.25 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-20% ethyl acetate in 40°–60° petroleum ether) to afford the product as a colorless oil (11.5 mg, 43%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.32-7.21 (m, 5H), 3.00-2.85 (m, 4H), 2.65-2.45 (m, 3H), 2.38 (m, 1H), 2.22 (m, 1H), 1.99

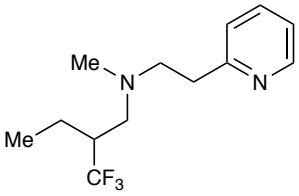
(m, 2H), 0.65 (m, 1H), 0.35 (m, 1H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 139.0, 129.3, 128.3, 127.8 (q, $J$ = 280.7 Hz), 126.3, 55.7, 54.0, 52.3 (q, $J$ = 2.6 Hz), 44.6 (q, $J$ = 23.9 Hz), 32.6 (q, $J$ = 2.1), 15.3, 15.1, 6.7, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.3; IR (film, cm$^{-1}$): 2949, 2891, 2787, 1497, 1455, 1344, 1251, 1106, 1082, 743, 699. HRMS (NSI+): *m/z* calcd for $C_{15}H_{19}NF_3$, $[M+H]^+$, 270.1470; found, 270.1476.



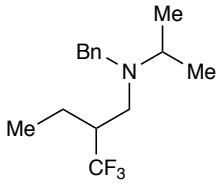

***tert*-Butyl (2-benzyl-3,3,3-trifluoropropyl)-L-prolinate (3l).** The title compound was prepared according to the general procedure using tert-butyl L-prolinate (17 mg, 0.10 mmol), hydrocinnamaldehyde (13 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (20-50% dichloromethane in 40°–60° petroleum ether) to afford the product as a colorless oil (18.5 mg, 52%). $^1$H NMR (400 MHz; $CDCl_3$) for major diastereoisomer: $\delta$ 7.32-7.21 (m, 5H), 3.15 (m, 2H), 2.96 (m, 1H), 2.86 (m, 2H), 2.71 (dd, $J$ = 16.1, 5.1 Hz, 1H), 2.6 (m, 1H), 2.35 (q, $J$ = 8.0 Hz, 1H), 2.10-1.70 (m, 4H), 1.49 (s, 9H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 173.0, 139.8, 129.2, 128.3, 127.8 (q, $J$ = 280.7 Hz), 126.1, 80.8, 66.3, 53.0, 52.4, 45.0 (q, $J$ = 23.9 Hz), 32.7 (q, $J$ = 2.5), 29.0, 28.0, 23.2, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.4; IR (film, cm$^{-1}$): 2976, 1735, 1455, 1367, 1252, 1148, 1104, 1081, 743, 699. HRMS (NSI+): *m/z* calcd for $C_{19}H_{27}NO_2F_3$, $[M+H]^+$, 358.1994; found, 358.2004.



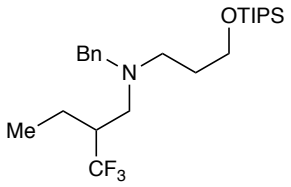

**3-((2-benzyl-3,3,3-trifluoropropyl)(methyl)amino)propanenitrile (3m).** The title compound was prepared according to the general procedure using 3-(methylamino)propanenitrile (9 μL, 0.10 mmol), hydrocinnamaldehyde (13 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-10% ethyl acetate in 40°–60° petroleum ether) to afford the product as a yellow oil (22 mg, 81%). $\delta$ 7.37-7.23 (m, 5H), 2.99 (dd, $J$ = 14.3, 5.9 Hz, 1H), 2.99 (dd, $J$ = 14.3, 6.6 Hz, 1H), 2.76-2.30 (m, 7H), 2.22 (s, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 138.4, 129.2, 128.4, 128.0 (q, $J$ = 280.8 Hz), 126.6, 118.6, 55.1 (q, $J$ = 2.6 Hz), 53.3, 44.2 (q, $J$ = 23.5 Hz), 41.5, 32.9 (q, $J$ = 2.6 Hz), 16.0, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.4; IR (film, cm$^{-1}$): 2956, 2853, 2243, 1604, 1497, 1465, 1377, 1255, 1211, 1164, 1138, 1081, 1048, 947, 747, 701, 668; HRMS (NSI+): *m/z* calcd for $C_{14}H_{18}F_3N_2$, $[M+H]^+$, 271.1422; found, 271.1422.



***N*-methyl-*N*-(2-(pyridin-2-yl)ethyl)-2-(trifluoromethyl)butan-1-amine (3n).** The title compound was prepared according to the general procedure using *N*-Methyl-*N*-(2-pyridin-2-ylethyl)amine (13.8 μL, 0.10 mmol), butyraldehyde (9 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-5% methanol in dichloromethane) to afford the product as a colorless oil (16 mg, 62%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 8.54 (dq, $J$ = 4.9, 1.0 Hz, 1H), 7.62 (td, $J$ = 9.5, 1.9 Hz, 1H), 7.20 (dt, $J$ = 7.8, 1.0 Hz, 1H), 7.10 (ddd, $J$ = 7.8, 4.9, 1.0 Hz, 1H), 3.00-2.70 (m, 4H), 2.58 (dd, $J$ = 12.8, 4.5 Hz, 1H), 2.44 (dd, $J$ = 12.8, 8.8 Hz, 1H), 2.32 (s, 3H), 2.12 (m, 1H), 1.58 (m, 2H), 0.94 (t, $J$ = 7.6 Hz, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 160.4, 149.2, 136.2, 128.2 (q, $J$ = 280.2 Hz), 123.3, 121.4, 58.0, 55.7 (q, $J$ = 2.9 Hz), 43.0 (q, $J$ = 23.5 Hz), 42.3, 36.0, 21.0 (q, $J$ = 2.3 Hz), 11.4, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.2; IR (film, cm$^{-1}$): 2958, 2818, 1591, 1570, 1473, 1435, 1363, 1169, 1129, 1097, 1046, 992, 876, 750, 667; HRMS (NSI+): *m/z* calcd for $C_{13}H_{20}F_3N_2$, $[M+H]^+$, 261.1573; found, 261.1566.

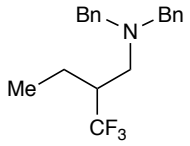



***N*-benzyl-*N*-isopropyl-2-(trifluoromethyl)butan-1-amine (3o).** The title compound was prepared according to the general procedure using N-Isopropylbenzylamine (17 μL, 0.10 mmol), butyraldehyde (9 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (2-5% ethyl actetate in 40°–60° petroleum ether) to afford the product as a colorless oil (19 mg, 70%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.40-7.20 (m, 5H, $H_{8\text{-}9\text{-}10}$), 3.65 (d, $J$ = 14.2 Hz, 1H, $H_{6a}$), 3.55 (d, $J$ = 14.2 Hz, 1H), 2.92 (spt, $J$ = 6.6 Hz, 1H), 2.65 (dd, $J$ = 17.5, 4.3 Hz, 1H), 2.46 (dd, $J$ = 17.5, 9.1 Hz, 1H), 2.02 (m, 1H), 1.78-1.50 (m, 2H), 1.08 (d, $J$ = 6.6 Hz, 2H), 1.02 (d, $J$ = 6.6 Hz, 2H), 0.94 (t, $J$ = 8.5 Hz, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 140.6, 128.4, 128.2, 128.0 (q, $J$ = 280.8 Hz), 126.7, 54.7, 50.1, 47.8 (q, $J$ = 3.0 Hz), 43.6 (q, $J$ = 23.0 Hz), 19.8 (q, $J$ = 2.3 Hz), 19.2, 15.9, 11.5, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –68.9; IR (film, cm$^{-1}$): 2967, 2938, 2882, 1604, 1495, 1453, 1286, 1365, 1323, 1252, 1123, 1093, 1043, 952, 908, 871, 760, 734, 698, 667; HRMS (NSI+): *m/z* calcd for $C_{15}H_{23}F_3N$, $[M+H]^+$, 274.1783; found, 274.1786.



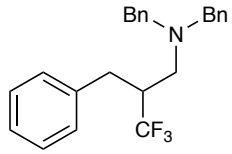

***N*-benzyl-2-(trifluoromethyl)-*N*-(3-((triisopropylsilyl)oxy)propyl)butan-1-amine (3p).** The title compound was prepared according to the general procedure using *N*-benzyl-3-((triisopropylsilyl)oxy)propan-1-amine (32.1 mg, 0.10 mmol), butyraldehyde (9 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-50% dichloromethane in 40°–60° petroleum ether) to afford the product as a colorless oil (28 mg, 62%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.35-7.25 (m, 5H), 3.72 (m, 3H), 3.46 (d, $J$ = 13.7, 1H), 2.70-2.60 (m, 2H), 2.55-2.45 (m, 2H), 2.20 (m, 1H), 1.80-1.55 (m, 4H), 1.15-1.02 (m, 21H), 0.94 (t, $J$ = 7.6 Hz, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 139.3, 128.8, 128.2 (q, $J$ = 280.2 Hz), 128.1, 126.9, 61.4, 59.2, 52.4 (q, $J$ = 2.9 Hz), 50.9, 43.1 (q, $J$ = 23.4 Hz), 30.3, 20.0 (q, $J$ = 2.3 Hz), 18.0, 11.9, 11.3, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –68.9; IR (film, cm$^{-1}$): 2941,

2866, 1495, 1463, 1367, 1253, 1171, 1122, 1041, 1013, 995, 967, 915, 882, 803, 738, 698, 680, 658; HRMS (NSI+): *m/z* calcd for $C_{24}H_{43}F_3NOSi$, $[M+H]^+$, 446.3066; found, 446.3053.

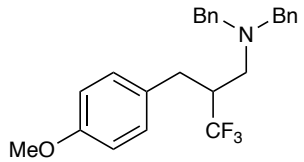



***N*,*N*-dibenzyl-2-(trifluoromethyl)butan-1-amine (3q).** The title compound was prepared according to the general procedure using dibenzylamine (19 μL, 0.10 mmol), butyraldehyde (9 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-30% dichloromethane in 40°–60° petroleum ether) to afford the product as a colorless oil (26 mg, 80%). $^1$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.40-7.25 (m, 10H), 3.69 (d, $J$ = 13.6 Hz, 2H), 3.45 (d, $J$ = 13.6, 2H), 2.65 (dd, $J$ = 13.0, 4.6, Hz 1H), 2.56 (dd, $J$ = 13.0, 4.6 Hz, 1H2.23 (m, 1H), 1.61 (m, 2H), 0.87 (t, $J$ = 7.6 Hz, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 138.9, 129.0, 128.3, 128.0 (q, $J$ = 280.8 Hz), 127.1, 59.0, 51.9 (q, $J$ = 2.9 Hz), 42.9 (q, $J$ = 23.5 Hz), 19.9 (q, $J$ = 2.3 Hz), 11.1, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –68.8; IR (film, cm$^{-1}$): 3064, 3029, 2938, 2798, 1495, 1453, 1401, 1369, 1327, 1252, 1169, 1113, 1076, 1041, 1028, 964, 914, 881, 865, 746, 667; HRMS (NSI+): *m/z* calcd for $C_{19}H_{23}F_3N$, $[M+H]^+$, 322.1783; found, 322.1797.

**Aldehyde substrate scope**

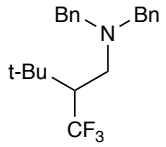



***N*,*N*,2-tribenzyl-3,3,3-trifluoropropan-1-amine (3r).** The title compound was prepared according to the general procedure using dibenzylamine (19 μL, 0.10 mmol), hydrocinnamaldehyde (13 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-30% dichloromethane in 40°–60° petroleum ether) to afford the product as a colorless oil (31 mg, 80%). $^1$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.40-7.10 (m, 15H), 3.65 (d, $J$ = 13.6 Hz, 2H), 3.46 (d, $J$ = 13.6 Hz, 2H), 2.88 (dd, $J$ = 14.5, 5.4 Hz, 1H), 2.78-2.52 (m, 4H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 139.0, 138.7, 129.1, 129.0, 128.4, 128.3, 127.8 (q, $J$ = 280.7 Hz), 127.2, 126.3, 58.9, 52.4 (q, $J$ = 2.6 Hz), 43.9 (q, $J$ = 23.5 Hz), 33.1 (q, $J$ = 2.4), $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –68.9; IR (film, cm$^{-1}$): 2920, 2865, 1603, 1452, 1355, 1133, 1074, 907, 733, 695; HRMS (NSI+): *m/z* calcd for $C_{24}H_{25}F_3N$, $[M+H]^+$, 384.1939; found, 384.1946.

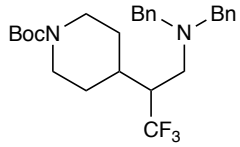



***N*,*N*-dibenzyl-3,3,3-trifluoro-2-(4-methoxybenzyl)propan-1-amine (3s).** The title compound was prepared according to the general procedure using dibenzylamine (19 μL, 0.10 mmol), 3-(4-Methoxyphenyl)propionaldehyde (15.8 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-20% dichloromethane in 40°–60° petroleum ether) to afford the product as a colorless oil (31

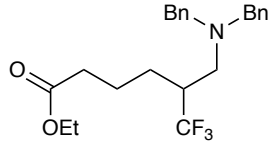
mg, 76%). $^1$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.40-7.28 (m, 10 H), 7.03 (d, $J$ = 8.5 Hz, 2H), 6.84 (d, $J$ = 8.5 Hz, 2H), 3.85 (s, 3H), 3.67 (d, $J$ = 13.6 Hz, 2H), 3.49 (d, $J$ = 13.6 Hz, 2H), 2.83 (dd, $J$ = 14.4, 5.3 Hz, 1H), 2.81-2.55 (m, 4H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 158.2, 138.7, 130.6, 130.2, 129.1, 128.3, 127.8 (q, $J$ = 280.7 Hz), 127.2 , 129.8, 113.7, 58.9, 55.1, 52.4 (q, $J$ = 2.5 Hz), 42.0 (q, $J$ = 23.7 Hz), 33.1 (q, $J$ = 2.4), $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –68.7; IR (film, cm$^{-1}$): 2935, 2838, 1612, 1585, 1513, 1494, 1453, 1366, 1301, 1166, 1129, 1097, 1077, 1037, 973, 829, 748, 699, 667; HRMS (NSI+): *m/z* calcd for $C_{25}H_{27}F_3NO$, $[M+H]^+$, 414.2045; found, 414.2047.



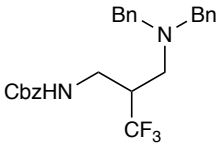

***N*,*N*-dibenzyl-3,3-dimethyl-2-(trifluoromethyl)butan-1-amine (3t).** The title compound was prepared according to the general procedure using dibenzylamine (19 μL, 0.10 mmol), 3,3-dimethylbutyraldehyde (12.6 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-30% dichloromethane in 40°–60° petroleum ether) to afford the product as a colorless oil (26 mg, 81%). $^1$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.37-7.25 (m, 10H), 3.62 (d, $J$ = 13.7 Hz, 2H), 3.48 (d, $J$ = 13.7 Hz, 2H), 2.72-2.60 (m, 2H), 2.10 (m, 1H), 0.95 (s, 9H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 138.9, 129.1, 128.1, 127.8 (q, $J$ = 280.7 Hz), 127.0, 58.6, 51.2 (q, $J$ = 2.6 Hz), 50.8 (q, $J$ = 21.3 Hz), 32.7, 28.6 (q, $J$ = 2.0), $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –62.2; IR (film, cm$^{-1}$): 2959, 2877, 1603, 1495, 1453, 1372, 1292, 1253, 1217, 1194, 1156, 1118, 1093, 1057, 1027, 968, 912, 872, 845, 747; HRMS (NSI+): *m/z* calcd for $C_{21}H_{27}F_3N$, $[M+H]^+$, 350.2090; found, 350.2079.



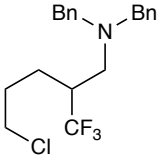

***Tert*-butyl 4-(3-(dibenzylamino)-1,1,1-trifluoropropan-2-yl)piperidine-1-carboxylate (3u).** The title compound was prepared according to the general procedure using dibenzylamine (19 μL, 0.10 mmol), *N*-boc-piperidineacetaldehyde (22.8 mg, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-20% ethyl acetate in 40°–60° petroleum ether) to afford the product as a colorless oil (30 mg, 62%). $^1$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.37-7.25 (m, 10H), 3.62 (d, $J$ = 13.7 Hz, 2H), 3.48 (d, $J$ = 13.7 Hz, 2H), 2.72-2.60 (m, 2H), 2.10 (m, 1H), 0.95 (s, 9H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 154.6, 138.9, 129.1, 128.3, 127.8 (q, $J$ = 280.7 Hz), 127.3, 79.4, 59.3, 49.7 (q, $J$ = 2.9 Hz), 46.1 (q, $J$ = 22.8 Hz), 44.5 (br s), 34.8, 30.3, 28.5, 27.2, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –64.8; IR (film, cm$^{-1}$): 2925, 2851, 1688, 1495, 1452, 1423, 1365, 1252, 1235, 1214, 1165, 1141, 1119, 1075, 1055, 1028, 972, 867, 699, 567. HRMS (NSI+): *m/z* calcd for $C_{27}H_{36}F_3N_2O_2$ $[M+H]^+$, 477.2729; found, 477.2718.



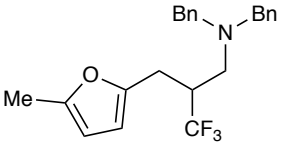
**Ethyl 5-((dibenzylamino)methyl)-6,6,6-trifluorohexanoate (3v).** The title compound was prepared according to the general procedure using dibenzylamine (19 μL, 0.10 mmol), ethyl 6-oxohexanoate (15.8 mg, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-50% dichloromethane in 40°–60° petroleum ether) to afford the product as a colorless oil (33 mg, 82%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.40-7.25 (m, 10H), 4.15 (q, $J$ = 7.1 Hz, 2H), 3.72 (d, $J$ = 13.5 Hz, 2H), 3.41 (d, $J$ = 13.5 Hz, 2H), 2.64 (dd, $J$ = 15.3, 4.6 Hz, 1H), 2.53 (dd, $J$ = 13.6, 9.0 Hz, 1H), 2.23 (m, 3H), 1.65-1.45 (m, 4H), 1.28 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 173.1, 138.8, 136.5, 129.1, 128.3, 127.8 (q, $J$ = 280.7 Hz), 127.1, 60.3, 59.1, 52.3 (q, $J$ = 2.9 Hz), 41.4 (q, $J$ = 24.0 Hz), 34.4, 26.5 (q, $J$ = 2.1 Hz), 22.0, 14.3, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.1; IR (film, cm$^{-1}$): 2941, 1734, 1495, 1453, 1369, 1257, 1214, 1161, 1126, 1103, 1028, 699, 567. HRMS (NSI+): *m/z* calcd for $C_{23}H_{29}F_3NO_2$, $[M+H]^+$, 408.2150; found, 408.2137.



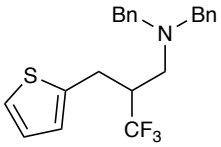

**Benzyl (2-((dibenzylamino)methyl)-3,3,3-trifluoropropyl)carbamate (3w).** The title compound was prepared according to the general procedure using dibenzylamine (19 μL, 0.10 mmol), benzyl 3-oxopropylcarbamate (20.7 mg, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-50% dichloromethane in 40°–60° petroleum ether) to afford the product as a colorless oil (26 mg, 80%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.45-7.25 (m, 15H), 5.55 (br s, 1H), 5.16 (d, $J$ = 12.1, 1H), 5.13 (d, $J$ = 12.1, 1H), 3.84 (d, $J$ = 13.5 Hz, 2H), 3.41 (m, 2H), 3.33 (d, $J$ = 13.3 Hz, 2H), 2.68 (m, 2H), 2.51 (m, 1H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 156.0, 138.0, 136.5, 129.1, 128.56, 128.5, 128.1, 128.05, 127.5, 126.8 (q, $J$ = 280.7 Hz), 66.8, 59.1, 50.9 (br s), 41.6 (q, $J$ = 23.4 Hz), 39.0 (br s), $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.4; IR (film, cm$^{-1}$): 3029, 2934, 2802, 1721, 1516, 1496, 1453, 1303, 1369, 1336, 1245, 1173, 1146, 1105, 1073, 1027, 969, 913, 825, 747, 668; HRMS (NSI+): *m/z* calcd for $C_{26}H_{27}F_3N_2O_2$, $[M+H]^+$, 457.2103; found, 457.2101.



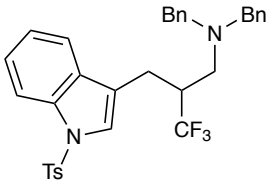

***N*,*N*-dibenzyl-5-chloro-2-(trifluoromethyl)pentan-1-amine (3x).** The title compound was prepared according to the general procedure using dibenzylamine (19 μL, 0.10 mmol), 5-chloropentanal (12 mg, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-30% dichloromethane in 40°–60° petroleum ether) to afford the product as a colorless oil (30 mg, 80%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.45-7.30 (m, 10H), 3.81 (d, $J$ = 13.4 Hz, 2H), 3.55-3.40 (m, 4H), 2.69 (br d, $J$ = 13.6 Hz, 1H), 2.60 (br d, $J$ = 13.6 Hz, 1H), 2.30 (m, 1H), 1.90-1.60 (m, 4H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 138.8, 129.1, 128.3, 127.8 (q, $J$ = 280.7 Hz), 127.3, 59.3, 52.1 (q, $J$ = 2.8 Hz), 44.9, 41.3 (q, $J$ = 24.0 Hz), 29.4, 24.4 (q, $J$ = 1.8), $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.0; IR (film, cm$^{-1}$): 3029, 2932, 2803, 1602, 1495, 1453, 1401, 1365, 1256, 1214, 1158, 1120, 1102, 1073, 1027, 968, 904, 853, 746, 657. HRMS (NSI+): *m/z* calcd for $C_{20}H_{24}ClF_3N$, $[M+H]^+$, 370.1549; found, 370.1536.




***N*,*N*-dibenzyl-3,3,3-trifluoro-2-((5-methylfuran-2-yl)methyl)propan-1-amine (3y).** The title compound was prepared according to the general procedure using dibenzylamine (19 μL, 0.10 mmol), 3-(5-methyl-2-furyl)propionaladehyde (13.5 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-50% dichloromethane in 40°–60° petroleum ether) to afford the product as a colorless oil (23s mg, 60%).$^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.40-7.27 (m, 10H), 5.90-5.83 (m, 2H), 3.69 (d, $J$ = 13.5 Hz, 2H), 3.50 (d, $J$ = 13.5 Hz, 2H), 2.90 (m, 1H), 2.85-2.70 (m, 3H), 2.60 (m, 1H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 150.8, 150.3, 138.8, 129.1, 128.3, 127.8 (q, $J$ = 280.7 Hz), 127.1, 107.4, 106.1, 60.3, 58.7, 52.1 (q, $J$ = 2.6 Hz), 41.4 (q, $J$ = 23.8 Hz), 25.6 (q, $J$ = 2.7 Hz), 13.5, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.6; IR (film, cm$^{-1}$): 2965, 2865, 1454, 1214, 1168, 1121, 1028, 667. 1603, 1452, 1355, 1133, 1074, 907, 733, 695; HRMS (NSI+): *m/z* calcd for $C_{23}H_{25}F_3NO$, $[M+H]^+$, 388.1888; found, 388.1875.



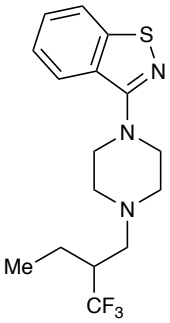

***N*,*N*-dibenzyl-3,3,3-trifluoro-2-(thiophen-2-ylmethyl)propan-1-amine (3z).** The title compound was prepared according to the general procedure using dibenzylamine (19 μL, 0.10 mmol), 3-(thiophen-2-yl)propanal (14 mg, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-50% dichloromethane in 40°–60° petroleum ether) to afford the product as a colorless oil (23 mg, 60%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.40-7.23 (m, 11H), 6.81 (m, 2H), 3.68 (d, $J$ = 13.6 Hz, 2H), 3.46 (d, $J$ = 13.6 Hz, 2H), 2.90 (dd, $J$ = 14.9, 5.0 Hz, 1H), 2.80 (dd, $J$ = 14.9, 5.8 Hz, 1H), 2.71 (m, 1H), 2.57 (m, 2H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 138.8, 138.7, 129.0, 128.3, 127.8 (q, $J$ = 280.9 Hz), 127.2, 125.4, 121.9, 59.0, 52.3 (q, $J$ = 2.5 Hz), 43.4 (q, $J$ = 23.6 Hz), 27.4 (q, $J$ = 2.5), $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.0; IR (film, cm$^{-1}$): 2934, 2804, 1602, 1494, 1452, 1366, 1317, 1245, 1215, 1192, 1165, 1123, 1098, 1078, 1027, 968, 918, 853, 833, 746, 665. HRMS (NSI+): *m/z* calcd for $C_{22}H_{23}F_3NS$, $[M+H]^+$, 390.1498; found, 390.1491.



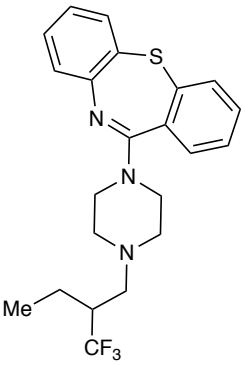

***N*,*N*-dibenzyl-3,3,3-trifluoro-2-((1-tosyl-1*H*-indol-3-yl)methyl)propan-1-amine (3aa).** The title compound was prepared according to the general procedure using dibenzylamine (19 μL, 0.10 mmol), 3-(1-tosyl-1H-indol-3- yl)propanal (33 mg, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 μL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-50% dichloromethane in 40°–60° petroleum ether) to afford the product as a colorless oil (47 mg, 81%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 8.0 (d, $J$ = 8.3, 1H), 7.72 (d, $J$ = 8.3, 2H), 7.43 (d, $J$ = 7.7, 1H), 7.35-7.18 (m, 15H),

3.65 (d, $J$ = 13.6, 2H), 3.45 (d, $J$ = 13.6, 2H), 2.90 (dd, $J$ = 15.4, 4.9 Hz, 1H), 2.76 (m, 2H), 2.59 (m, 2H), 2.33 (s, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 144.8, 138.5, 135.3, 135.2, 130.6, 129.8, 128.9, 128.3, 127.3, 126.7, 124.7, 124.1, 123.2, 119.7, 119.2, 113.9, 59.1, 52.9 (q, $J$ = 2.5 Hz), 42.0 (q, $J$ = 23.7 Hz), 22.7 (q, $J$ = 2.4), 21.5, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.1; IR (film, cm$^{-1}$): 2915, 2808, 1598, 1494, 1448, 1369, 1250, 1214, 1172, 1120, 1095, 1019, 976, 701, 667; HRMS (NSI+): *m/z* calcd for $C_{33}H_{32}F_3N_2O_2S$, $[M+H]^+$, 577.2137; found, 577.2127.

**Drugs and Drug building blocks substrate scope**

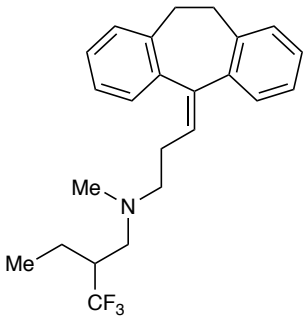



**3-(4-(2-(trifluoromethyl)butyl)piperazin-1-yl)benzo[*d*]isothiazole (3ab).** The title compound was prepared according to the general procedure using 3-Piperazin-1-yl-benzo[d]isothiazole (22 mg, 0.10 mmol), butyraldehyde (9 µL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 µL, 0.15 mmol), triethylamine (21 µL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 µL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-20% ethyl acetate in 40°–60° petroleum ether) to afford the product as a colorless oil (23 mg, 68%). $^1$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.93 (d, $J$ = 8.2 Hz, 1H), 7.83 (d, $J$ = 8.1 Hz, 1H), 7.48 (t, $J$ = 7.0 Hz, 1H), 7.38 (t, $J$ = 7.0 Hz, 1H), 3.55 (t, $J$ = 4.4 Hz, 4H), 2.75 (m, 2H), 2.65 (m, 3H), 2.50 (dd, $J$ = 12.8, 8.6 Hz, 1H), 1.72 (quint, $J$ = 7.6, 2H), 1.08 (t, $J$ = 7.5, 3H). $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 163.9, 153.3, 128.1, 127.8 (q, $J$ = 280.7 Hz), 127.5, 123.9, 123.8, 120.6, 56.4 (q, $J$ = 2.9 Hz), 53.3, 50.1, 42.3 (q, $J$ = 21.3 Hz), 20.0 (q, $J$ = 2.4 Hz), 11.5, $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –69.4; IR (film, cm$^{-1}$): 2945, 2882, 2842, 1592, 1562, 1494, 1451, 1381, 1303, 1119, 1045, 908, 806, 773, 738, 699, 666; HRMS (NSI+): *m/z* calcd for $C_{16}H_{22}F_3N_3S_2$, $[M+H]^+$, 344.1408; found, 344.1405.

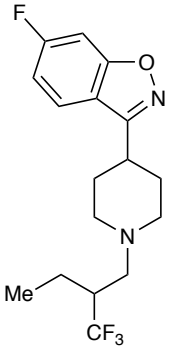



**11-(4-(2-(trifluoromethyl)butyl)piperazin-1-yl)dibenzo[*b*,*f*][1,4]thiazepine (3ac).** The title compound was prepared according to the general procedure using 11-piperazin-1-yl-dibenzo[b,f][1,4]thiazepine (29.5 mg, 0.10 mmol), butyraldehyde (9 µL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 µL, 0.15 mmol), triethylamine (21 µL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 µL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-2% methanol in dichloromethane) to afford the product as a colorless oil (21 mg, 50%). $^1$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.55-7.51 (m, 1H), 7.42 (dd, $J$ = 7.7, 1.5 Hz, 1H), 7.38-7.28 (m, 3H), 7.19 (ddd, $J$ = 8.0, 7.2, 1.6 Hz,

1H), 7.10 (dd, $J$ = 8.3, 1.6 Hz, 1H), 6.92 (td, $J$ = 7.5 Hz, 1.5 Hz, 1H), 3.50 (br s, 4H), 2.70-2.40 (m, 6H), 2.25 (m, 1H), 1.70 (quin, $J$ = 7.6 Hz, 2H), 1.03 (t, $J$ = 7.6, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 160.9, 148.8, 139.9, 134.2, 132.3, 132.2, 130.8, 129.1, 128.9, 128.3, 128.1 (q, $J$ = 280.7 Hz), 128.0, 125.3, 122.8, 128.1, 127.8 (q, $J$ = 280.7 Hz), 127.5, 123.9, 123.8, 120.6, 56.4 (q, $J$ = 2.9 Hz), 53.3, 47.0, 42.3 (q, $J$ = 23.8 Hz), 20.3 (q, $J$ = 2.4 Hz), 11.5, $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –69.4; IR (film, cm$^{-1}$): 3055, 2957, 2871, 1600, 1576, 1409, 1305, 1256, 1214, 1171, 1119, 1015, 666; HRMS (NSI+): *m/z* calcd for $C_{22}H_{25}F_3N_3S$, $[M+H]^+$, 420.1721; found, 420.1702.

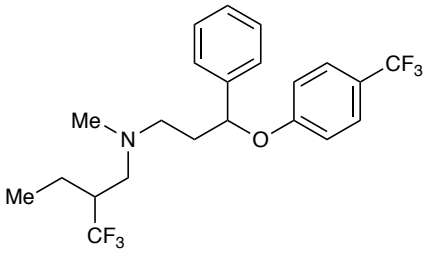



***N*-(3-(10,11-dihydro-5*H*-dibenzo[*a*,*d*][7]annulen-5-ylidene)propyl)-*N*-methyl-2-(trifluoromethyl)butan-1-amine (3ad).** The title compound was prepared according to the general procedure using nortriptyline (26.5 mg, 0.10 mmol), butyraldehyde (9 µL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 µL, 0.15 mmol), triethylamine (21 µL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 µL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-10% ethyl acetate in 40°–60° petroleum ether) to afford the product as a colorless oil (28 mg, 70%). $^1$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.32-7.08 (m, 8H), 5.89 (t, $J$ = 7.4 Hz, 1H), 3.50-3.20 (m, 2H), 3.10-2.70 (m, 2H), 2.60-2.27 (m, 6H), 2.18 (s, 3H), 2.12 (m, 1H), 1.70-1.60 (m, 2H), 0.99 (t, $J$ = 7.4 Hz, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 143.6, 141.3, 140.1, 139.3, 137.0, 130.0, 129.3, 128.5, 128.1, 128.0, 127.8 (q, $J$ = 280.7 Hz), 127.4, 127.0, 126.0, 125.7, 57.7, 55.6 (q, $J$ = 2.9 Hz), 43.0 (q, $J$ = 23.5 Hz), 42.3, 33.7, 32.0, 27.2, 20.2 (q, $J$ = 2.4 Hz), 11.4, $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –69.2; IR (film, cm$^{-1}$): 3022, 1941, 2850, 1485, 1454, 1363, 1199, 1169, 1123, 1096, 1044, 875, 768, 755, 719; HRMS (NSI+): *m/z* calcd for $C_{24}H_{29}F_3N$, $[M+H]^+$, 388.2252; found, 388.2236.

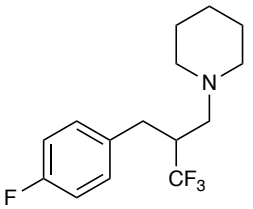



**6-fluoro-3-(1-(2-(trifluoromethyl)butyl)piperidin-4-yl)benzo[*d*]isoxazole (3ae).** The title compound was prepared according to the general procedure using 6-Fluoro-3-(4-piperidyl)-1,2-benzisoxazole hydrochloride (25.6 mg, 0.10 mmol), butyraldehyde (9 µL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 µL, 0.15 mmol), triethylamine (35 µL, 0.25 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 µL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-5% methanol in dichloromethane) to afford the product as a pale yellow oil (21 mg, 60%). $^1$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.67 (dd, $J$ = 8.7, 5.1 Hz, 1H), 7.27 (dd, $J$ = 8.5, 2.1 Hz), 7.08 (td, $J$ = 8.8, 2.1 Hz, 1H), 3.14-2.95 (m, 3H), 2.57 (dd, $J$ = 12.8, 4.8 Hz, 1H), 2.45 (dd, $J$ = 12.8, 8.7 Hz, 1H), 2.35-2.20 (m, 2H), 2.15-

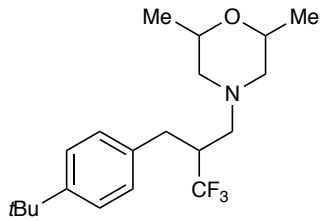
2.00 (m, 5H), 1.70 (quint, $J$ = 7.5 Hz, 2H), 1.06 (t, $J$ = 7.5 Hz, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 164.2 (d, $J$ = 250.6 Hz), 163.9 (d, $J$ = 13.6 Hz), 161.1, 128.0 (q, $J$ = 280.9 Hz), 122.5 (d, $J$ = 11.1 Hz), 117.3, 112.4 (d, $J$ = 25.3 Hz), 97.5 (d, $J$ = 26.7), 56.5 (q, $J$ = 2.8 Hz), 54.8, 52.9, 42.5 (q, $J$ = 23.6 Hz), 34.4, 30.7, 30.4, 20.4 (q, $J$ = 2.4 Hz), 11.5, $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –69.4, -109.6; IR (film, cm$^{-1}$): 2935, 1617, 1495, 1416, 1385, 1255, 1215, 1170, 1122, 1046, 956, 841, 815, 667; HRMS (NSI+): *m/z* calcd for $C_{17}H_{21}F_4N_2O$, $[M+H]^+$, 345.1585; found, 345.1579.



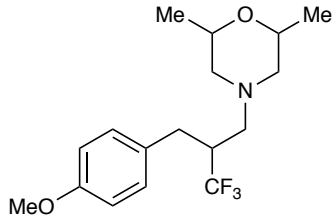

***N*-methyl-*N*-(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)-2-(trifluoromethyl)butan-1-amine (3af).** The title compound was prepared according to the general procedure using Fluoxetine hydrochloride (34.5 mg, 0.10 mmol), butyraldehyde (9 µL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 µL, 0.15 mmol), triethylamine (35 µL, 0.25 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The reduction was carried out with acetic acid (17 µL, 0.30 mmol), sodium triacetoxyborohydride (42 mg, 0.2 mmol) and an additional 1 mL of dichloromethane. The crude reaction mixture was purified by flash column chromatography (0-5% ethyl acetate in 40°–60° petroleum ether) to afford the mixture of diastereomers as a pale yellow oil (30 mg, 70%); $^1$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.45 (d, $J$ = 9.0 Hz, 2H), 7.40-7.25 (m, 5H), 6.92 (d, $J$ = 8.6 Hz, 2H), 5.39-5.32 (m, 1H), 2.70-2.30 (m, 4H), 2.27 (d, $J$ = 8.3 Hz, 3H), 2.15 (m, 2H), 1.99 (m, 1H), 1.65-1.50 (m, 2H), 0.95 (q, $J$ = 7.5 Hz, 3H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 160.74, 160.63, 141.27, 141.20, 128.76, 163.9 (d, $J$ = 13.6 Hz), 161.1, 128.78, 128.76, 128.1 (q, $J$ = 280.5 Hz), 128.0 (q, $J$ = 280.5 Hz), 127.83, 127.80, 126.80 (m), 125.80, 124.60 (q, $J$ = 271.1 Hz), 122.70 (q, J = 32.5 Hz), 122.66 (q, J = 32.5 Hz), 115.68, 115.66, 77.93, 77.87, 56.1 (q, J = 2.6 Hz), 55.9 (q, J = 2.6 Hz), 54.3, 53.8, 42.9 (q, $J$ = 23.6 Hz), 42.8 (q, $J$ = 23.6 Hz), 42.5, 42.1, 36.55, 36.45, 20.3 (br s), 11.35, 11.25; IR (film, cm$^{-1}$): 2962, 1615, 1517, 1455, 1328, 1214, 1163, 1119, 1068, 1045, 1009, 835, 754, 701, 569; HRMS (NSI+): *m/z* calcd for $C_{22}H_{27}F_6NO$, $[M+H]^+$, 434.1913; found, 434.1909.



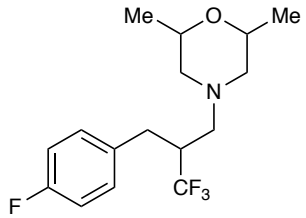

**1-(3,3,3-trifluoro-2-(4-fluorobenzyl)propyl)piperidine (4a).** The title compound was prepared according to the general procedure using piperidine (10 µL, 0.10 mmol), 3-(4-Fluorophenyl)propionaldehyde (15 mg, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 µL, 0.15 mmol), triethylamine (21 µL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The crude reaction mixture was purified by flash column chromatography (0-10% ethyl acetate in 40°–60° petroleum ether) to afford the product as a colorless oil (22 mg, 75%). $^1$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.20 (m, 2H), 6.99 (m, 2H), 2.93 (m, 2H), 2.60-2.20 (m, 7H), 1.60-1.39 (m, 6H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 161.6 (d, $J$ = 244.6 Hz), 134.4 (d, $J$ = 3.3 Hz), 130.7 (d, $J$ = 7.8 Hz), 127.8 (q, $J$ = 280.9 Hz), 115.0 (d, $J$ = 21.2 Hz), 56.6 (q, $J$ = 2.7 Hz), 54.7, 43.4 (q, $J$ = 23.8 Hz), 32.2 (q, $J$ = 2.4 Hz), 26.0, 24.3, $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –69.2, -117.0 IR (film, cm$^{-1}$): 2920, 2865, 1603, 1452, 1355, 1133, 1074, 907, 733, 695; HRMS (NSI+): *m/z* calcd for $C_{15}H_{20}F_4N$, $[M+H]^+$, 290.1532; found, 290.1525.




**4-(2-(4-(*tert*-butyl)benzyl)-3,3,3-trifluoropropyl)-2,6-dimethylmorpholine (4b).** The title compound was prepared according to the general procedure using cis-2,6-dimethylmorpholine (12 μL, 0.10 mmol), Bourgeonal (19 mg, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The crude reaction mixture was purified by flash column chromatography (0-10% ethyl acetate in 40°–60° petroleum ether) to afford the product as a colorless oil (25 mg, 71%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.34 (d, $J$ = 8.6, 2H), 7.17 (d, $J$ = 8.6 Hz, 2H), 3.65-3.45 (m, 2H), 2.98 (dd, $J$ = 11.6, 5.3 Hz, 1H), 2.82 (dd, $J$ = 11.6, 6.7 Hz, 1H), 2.63-2.38 (m, 5H), 1.73 (t, $J$ = 10.7 Hz, 1H), 1.65 (t, $J$ = 10.7 Hz, 1H), 1.35 (s, 9H), 1.14 (dd, $J$ = 8.2, 6.3 Hz, 6H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 149.3, 135.7, 129.8, 127.8 (q, $J$ = 280.9 Hz), 125.5, 71.6, 71.5, 60.1, 58.6, 56.1 (q, $J$ = 2.6 Hz), 43.0 (q, $J$ = 23.8 Hz), 34.4, 32.6 (q, $J$ = 2.5 Hz), 31.4, 19.1, 19.0, $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –69.7, IR (film, cm$^{-1}$): 2920, 2865, 1603, 1452, 1355, 1133, 1074, 907, 733, 695; HRMS (NSI+): *m/z* calcd for $C_{20}H_{31}F_3NO$, $[M+H]^+$, 358.2358; found, 358.2365.

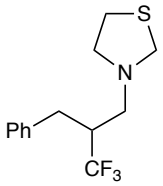



**2,6-dimethyl-4-(3,3,3-trifluoro-2-(4-methoxybenzyl)propyl)morpholine (4c).** The title compound was prepared according to the general procedure using cis-2,6-dimethylmorpholine (12 μL, 0.10 mmol), 3-(4-Methoxyphenyl)propionaldehyde (16 μL, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The crude reaction mixture was purified by flash column chromatography (0-10% ethyl acetate in 40°–60° petroleum ether) to afford the product as a colorless oil (23 mg, 70%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.14 (d, $J$ = 8.6 Hz, 2H), 6.85 (d, $J$ = 8.6 Hz, 2H), 3.82 (s, 3H), 3.62 (m, 2H), 2.93 (dd, $J$ = 14.3, 5.6 Hz, 1H), 2.83 (dd, $J$ = 14.3, 6.1 Hz, 1H), 2.63-2.45 (m, 5H), 1.75 (t, $J$ = 10.5 Hz, 1H), 1.68 (t, $J$ = 10.5 Hz, 1H), 1.14 (dd, $J$ = 6.3, 2.7 Hz, 6H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 158.2, 130.6, 130.2, 127.8 (q, $J$ = 280.9 Hz), 113.7, 71.6, 71.5, 60.2, 58.8, 55.9 (q, $J$ = 2.6 Hz), 55.2, 43.2 (q, $J$ = 23.6 Hz), 32.1 (q, $J$ = 2.5 Hz), 19.1, 19.0, $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –69.3, IR (film, cm$^{-1}$): 2920, 2865, 1603, 1452, 1355, 1133, 1074, 907, 733, 695; HRMS (NSI+): *m/z* calcd for $C_{17}H_{25}F_3NO_2$, $[M+H]^+$, 332.1837; found, 332.1841.




**2,6-dimethyl-4-(3,3,3-trifluoro-2-(4-fluorobenzyl)propyl)morpholine (4d).** The title compound was prepared according to the general procedure using cis-2,6-dimethylmorpholine (12 μL, 0.10 mmol), 3-(4-Fluorophenyl)propionaldehyde (15 mg, 0.10 mmol), Ritter's Trifluoroiodomethane-DMSO solution (34 μL, 0.15 mmol), triethylamine (21 μL, 0.15 mmol) and 4Å MS (100 mg) in 0.2 mL of dimethylformamide. The crude reaction mixture was purified by flash column chromatography (0-10% ethyl acetate in 40°–60° petroleum ether) to afford the product as a colorless oil (23 mg, 72%). $^{1}$H NMR (400 MHz; $CDCl_3$): $\delta$ 7.19 (m, 2H), 7.00 (m, 2H,

$H_2$), 3.70-3.50 (m, 2H), 2.95 (dd, $J$ = 14.5, 5.9 Hz, 1H), 2.89 (dd, $J$ = 14.5, 5.9 Hz, 1H), 2.63-2.35 (m, 5H), 1.75 (t, $J$ = 10.4 Hz, 1H), 1.68 (t, $J$ = 10.4 Hz, 1H), 1.15 (dd, $J$ = 6.3, 4.3 Hz, 6H), $^{13}$C NMR (101 MHz; $CDCl_3$): $\delta$ 161.6 (d, $J$ = 244.6 Hz), 134.4 (d, $J$ = 3.3 Hz), 130.7 (d, $J$ = 7.8 Hz), 127.8 (q, $J$ = 280.9 Hz), 115.0 (d, $J$ = 21.2 Hz), 71.6, 71.5, 60.4, 58.6, 55.9 (q, $J$ = 2.6 Hz), 43.0 (q, $J$ = 23.8 Hz), 32.2 (q, $J$ = 2.4 Hz), 19.1, 19.0, $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –69.3, -116.7 IR (film, $cm^{-1}$): 2920, 2865, 1603, 1452, 1355, 1133, 1074, 907, 733, 695; HRMS (NSI+): *m/z* calcd for $C_{18}H_{23}F_4N$, $[M+H]^+$, 320.1628; found, 320.1638.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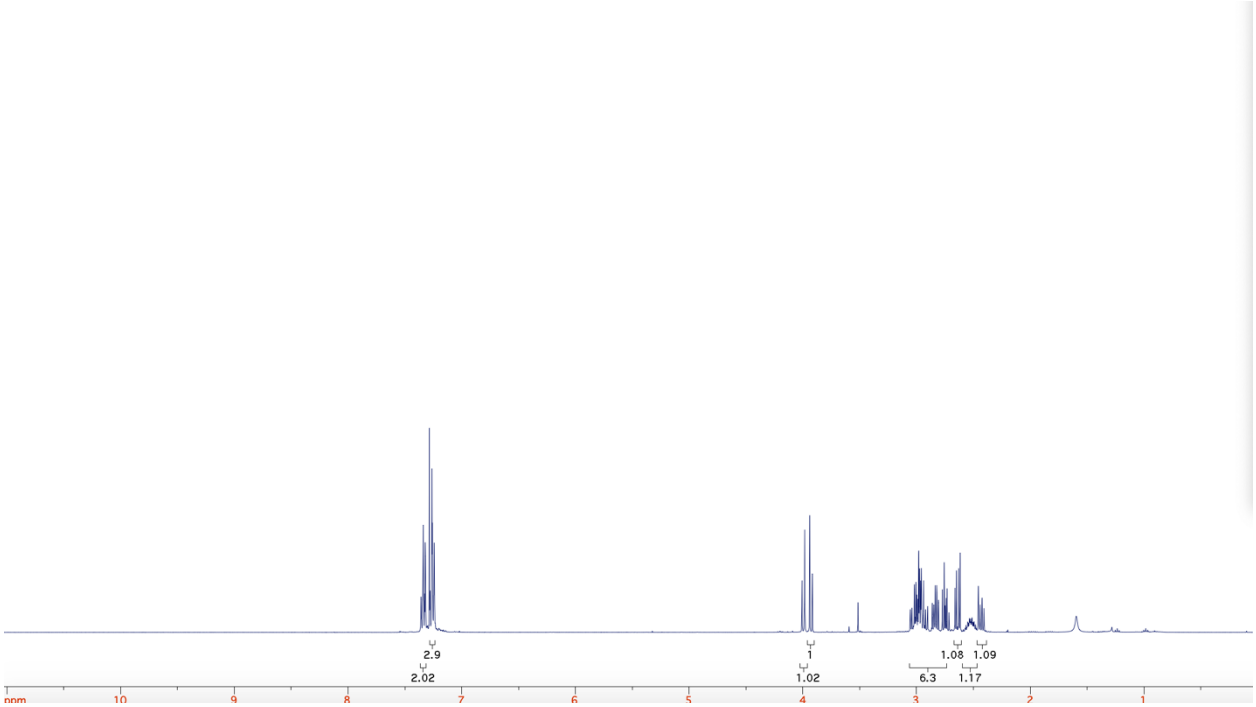
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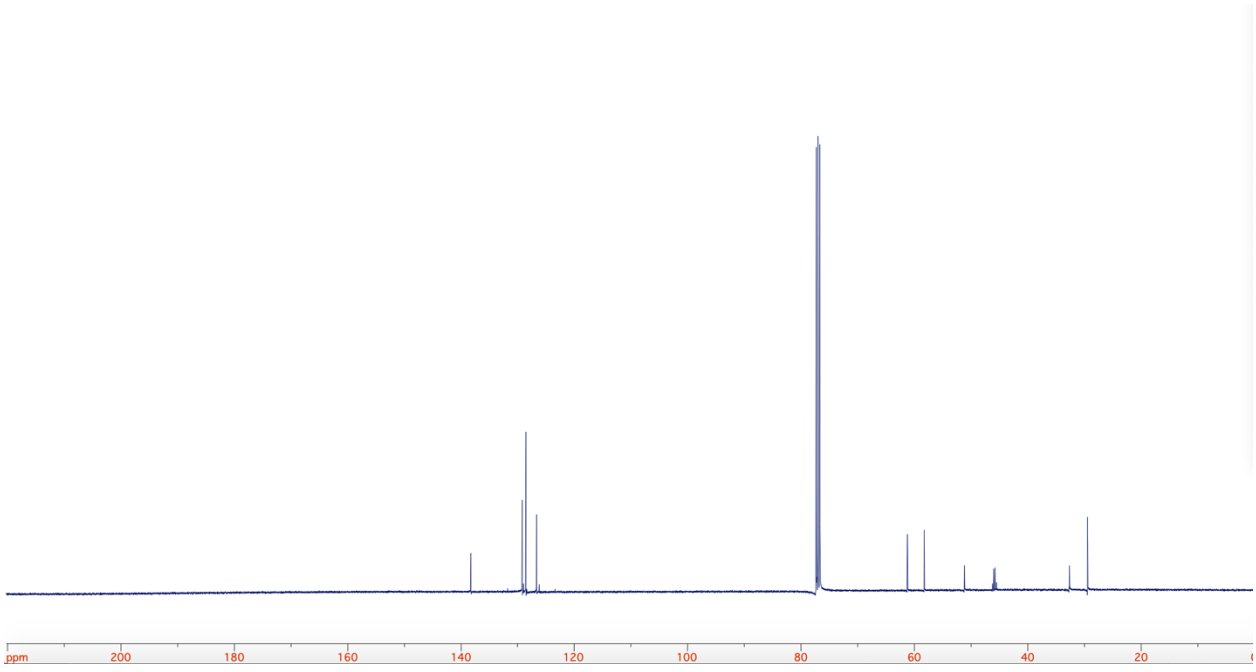
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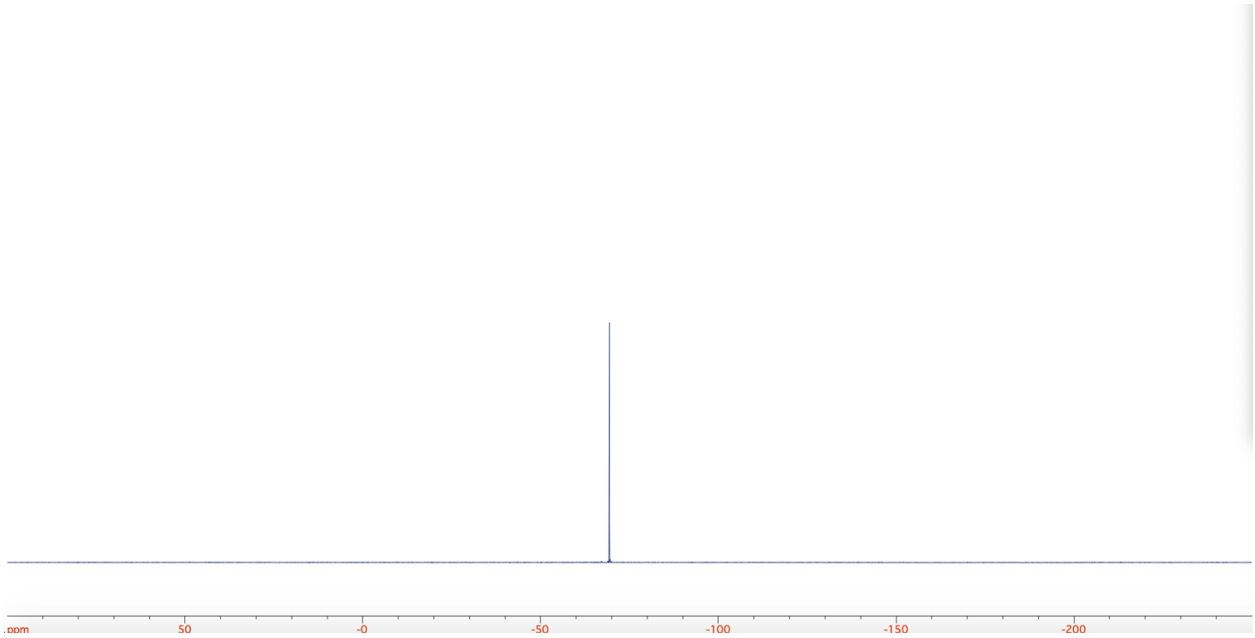
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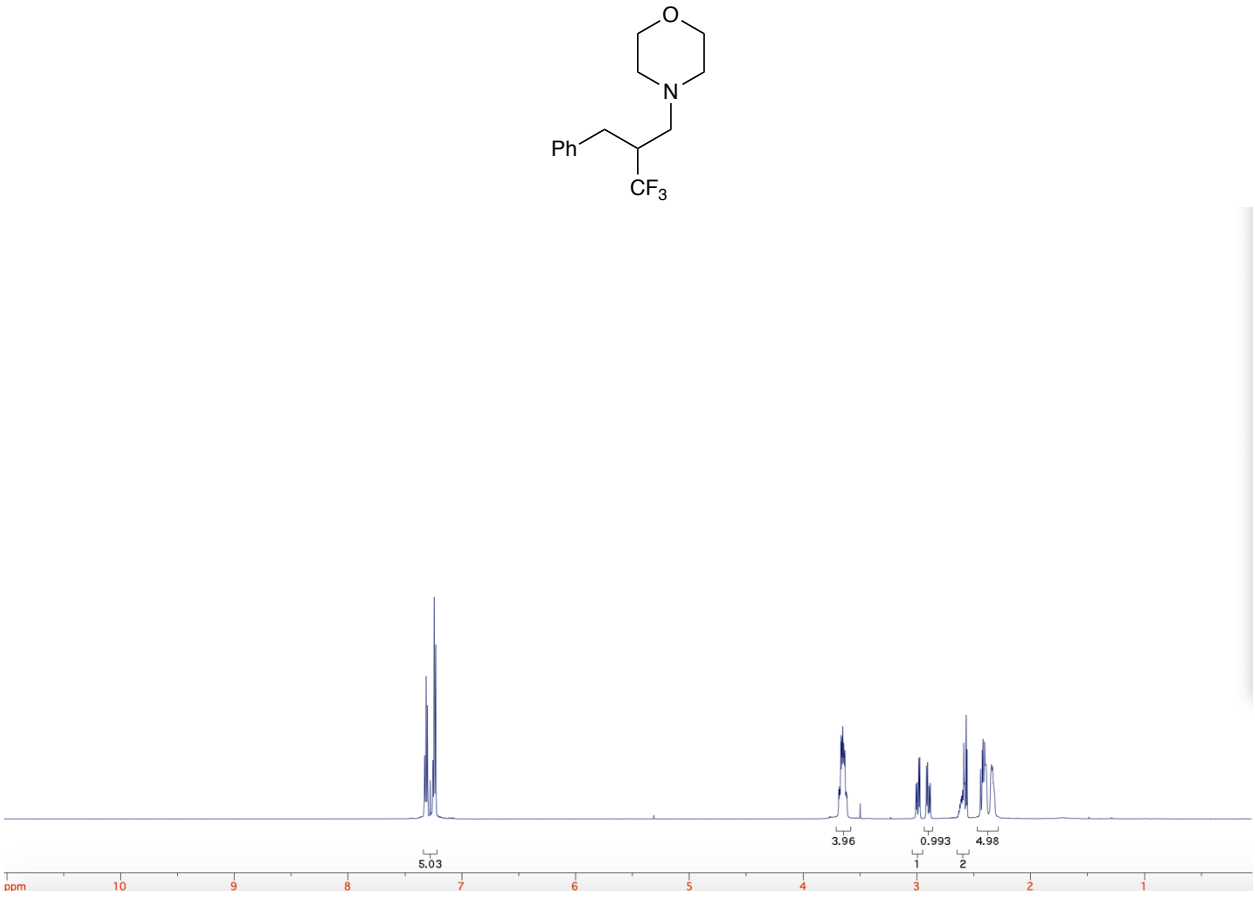
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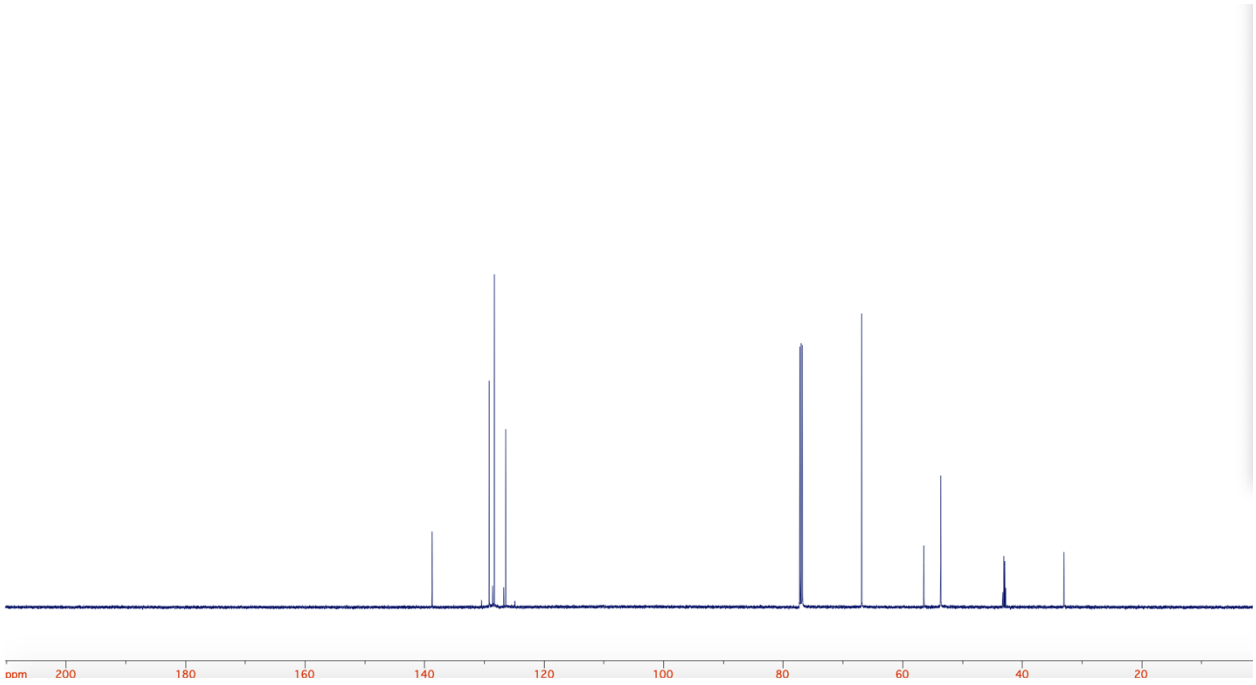
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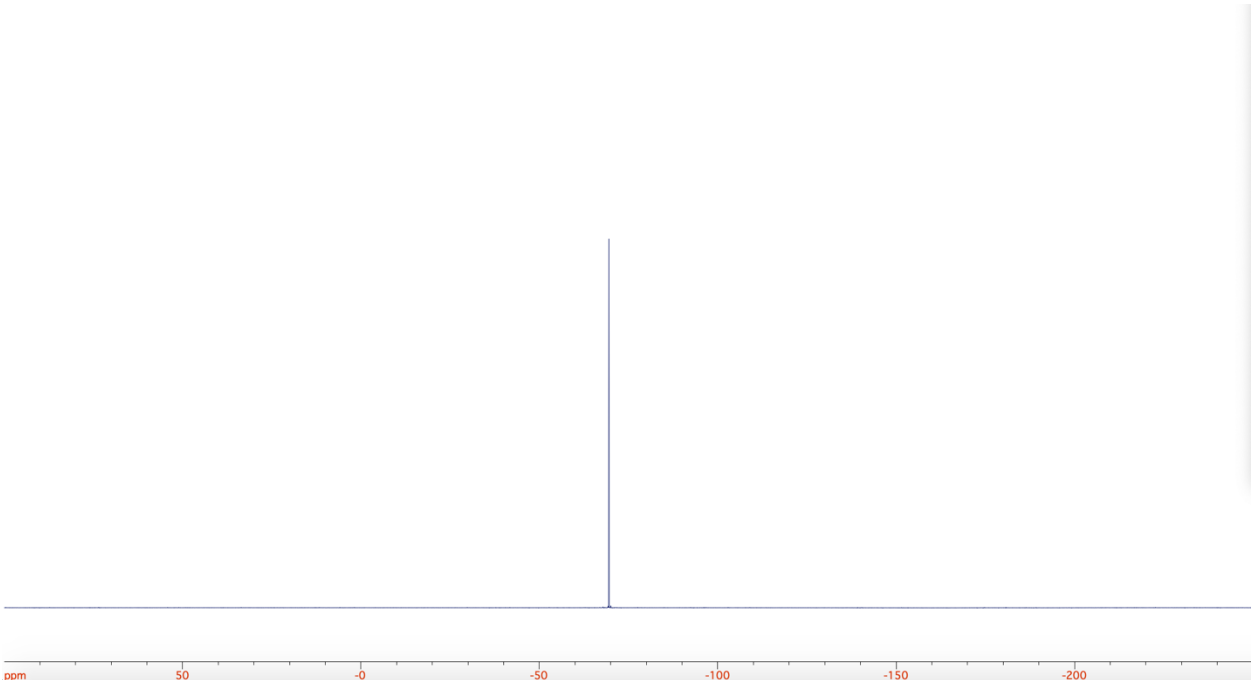
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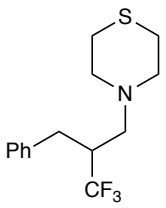
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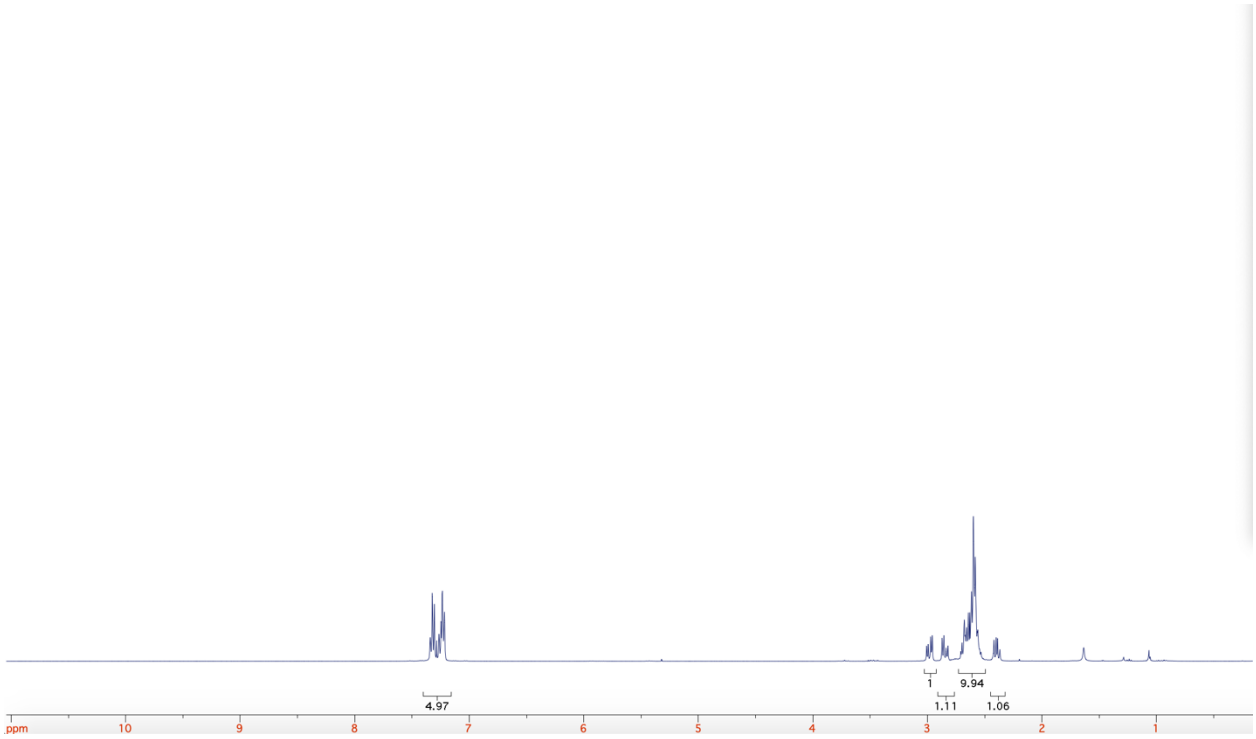
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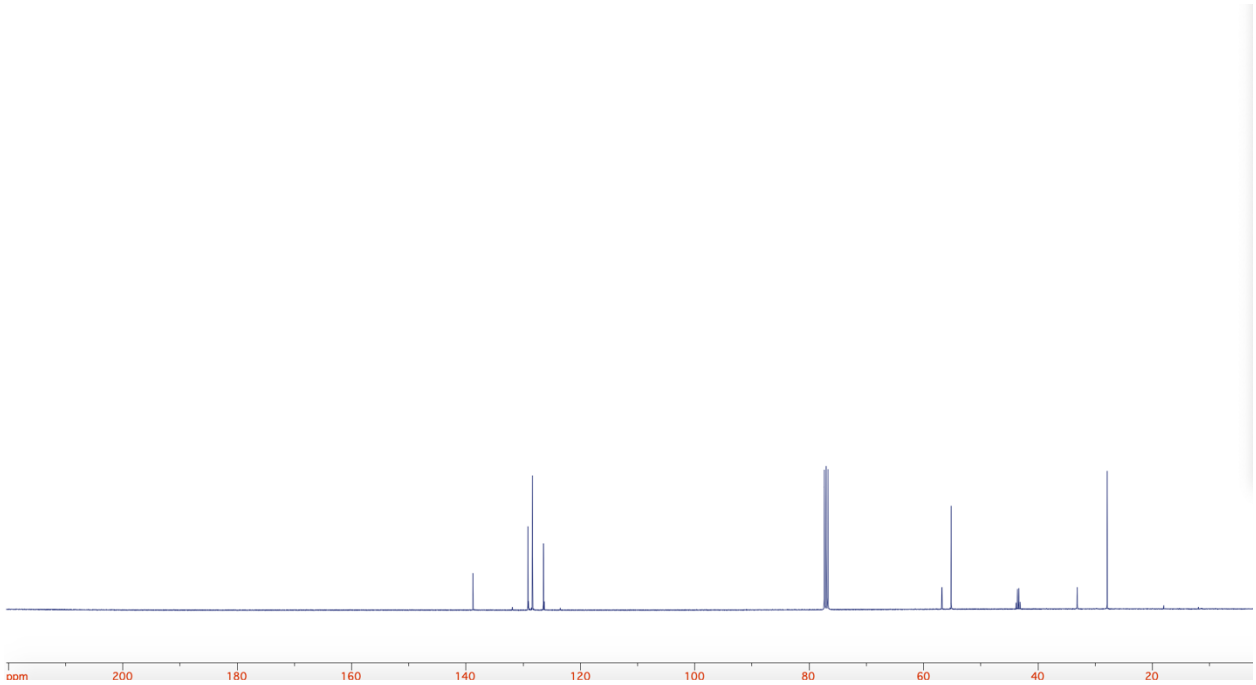
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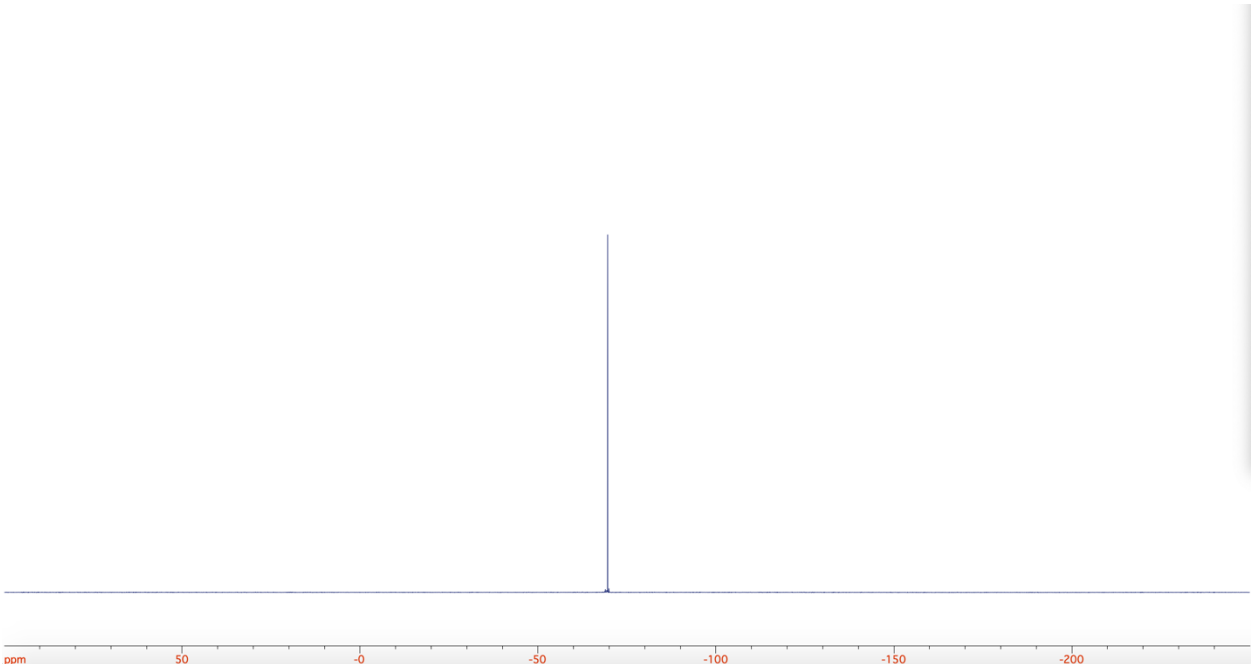
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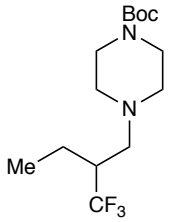
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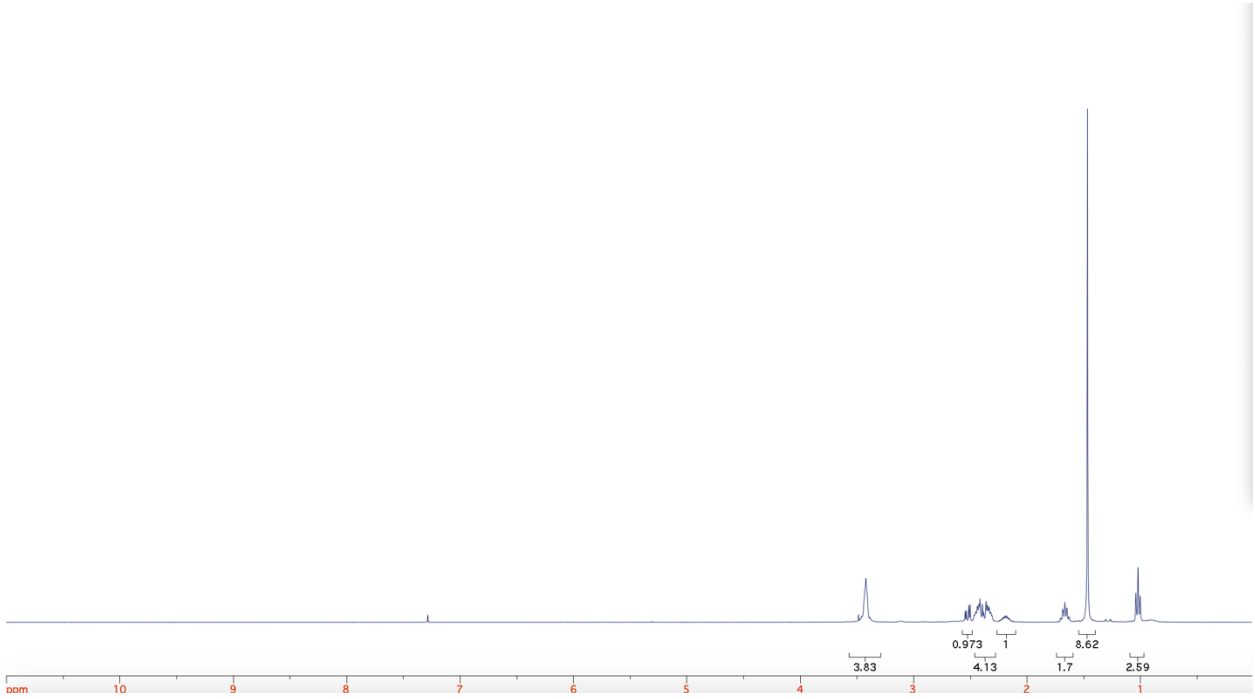
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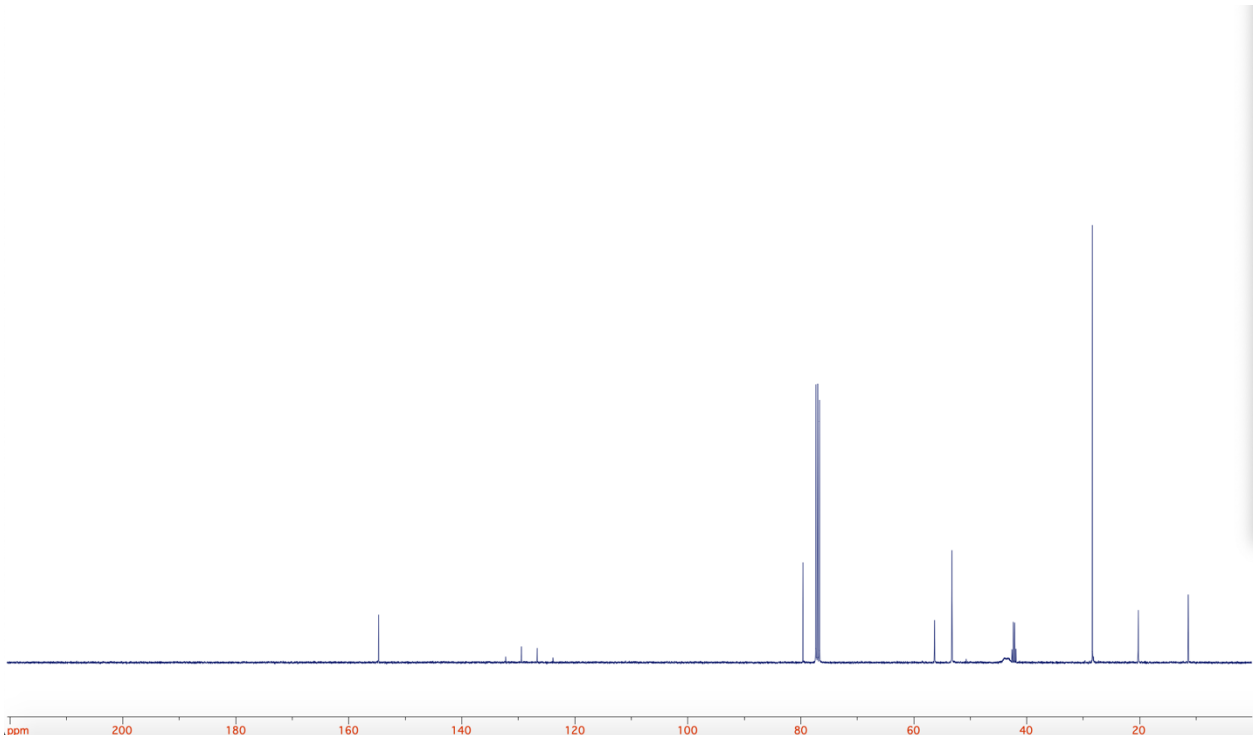
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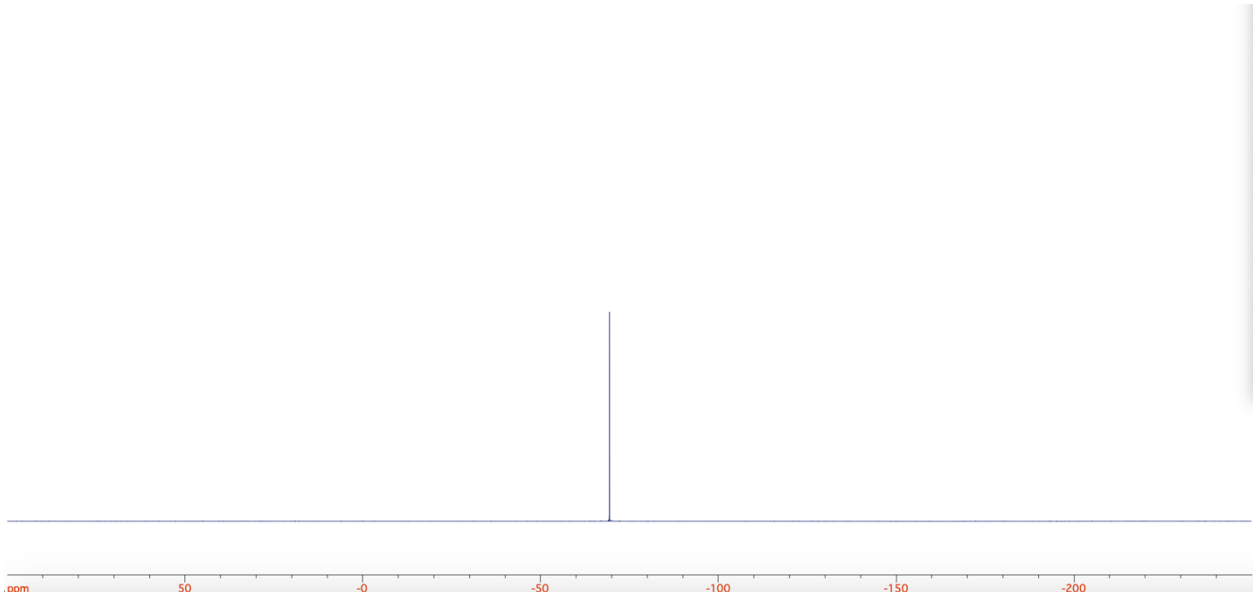
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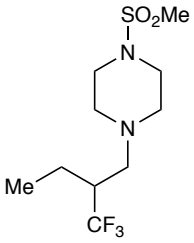
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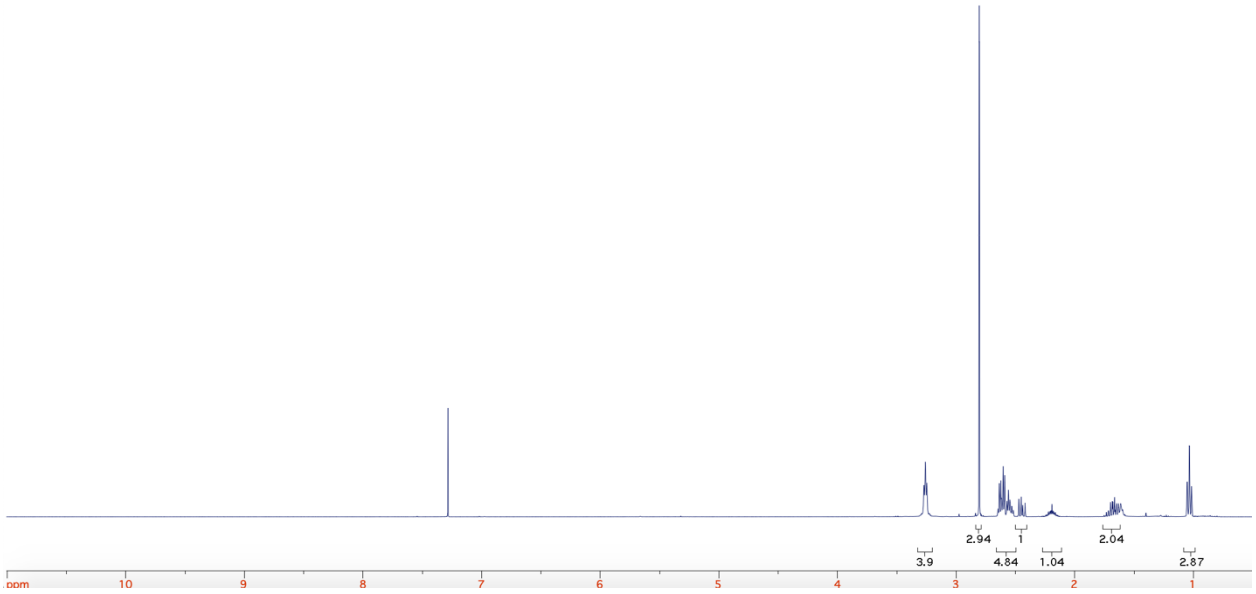
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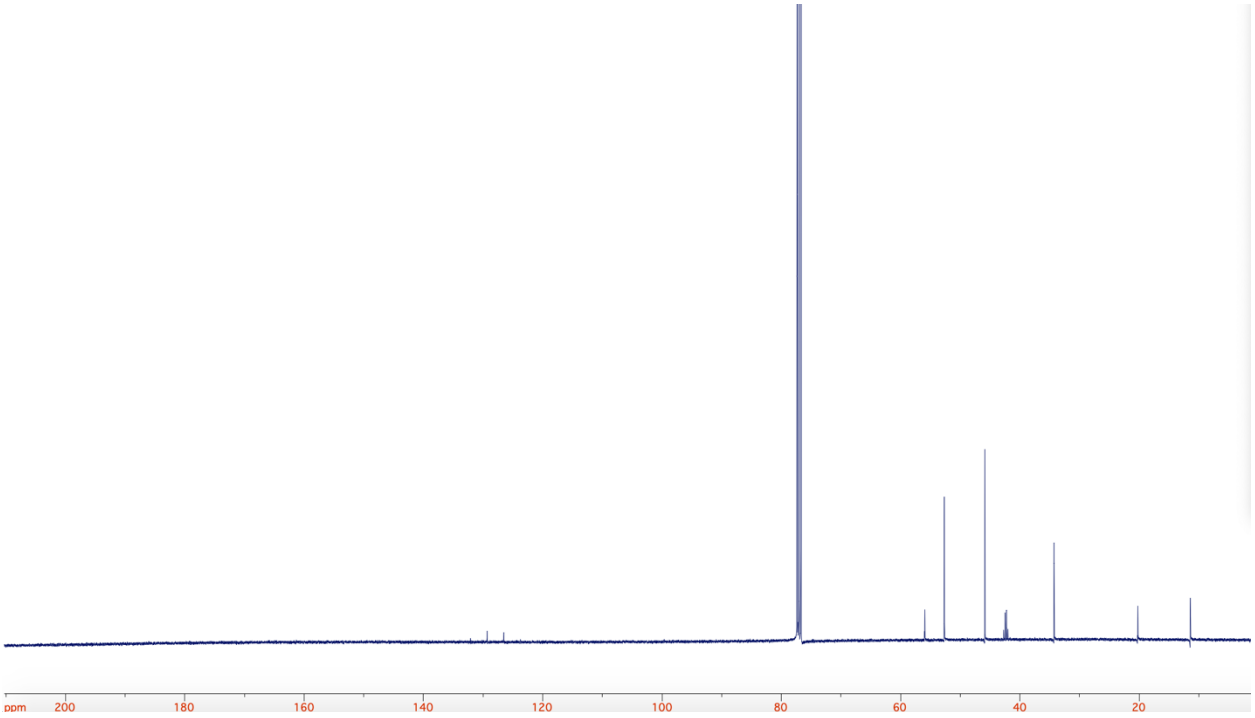
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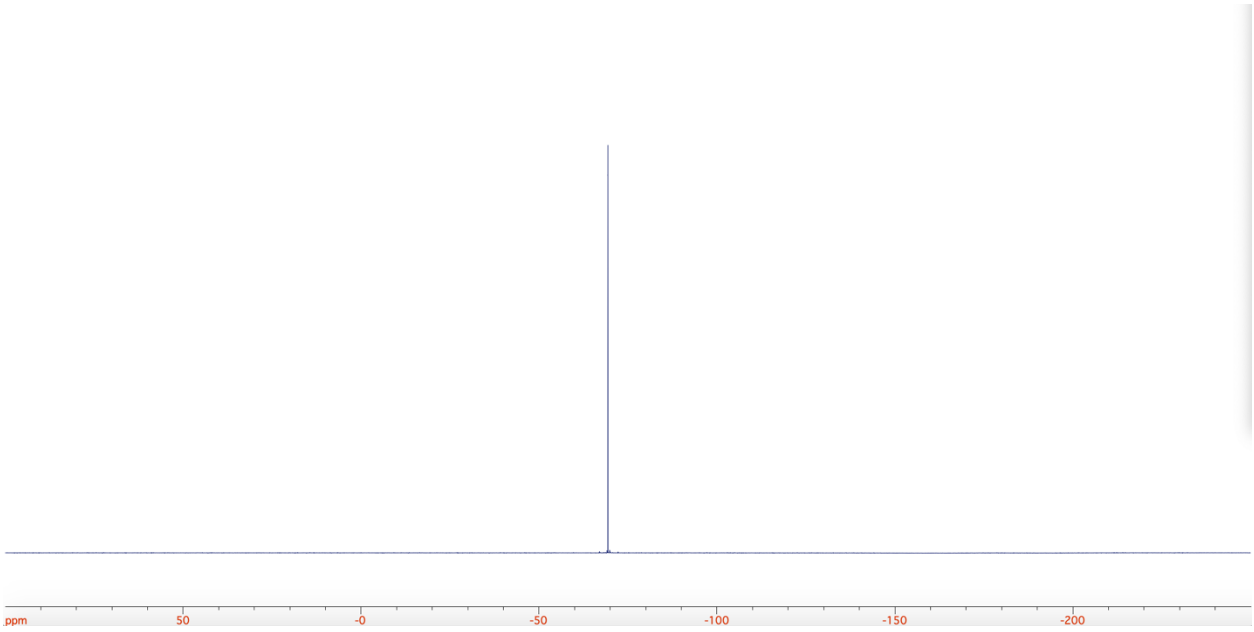
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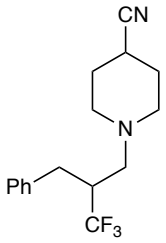
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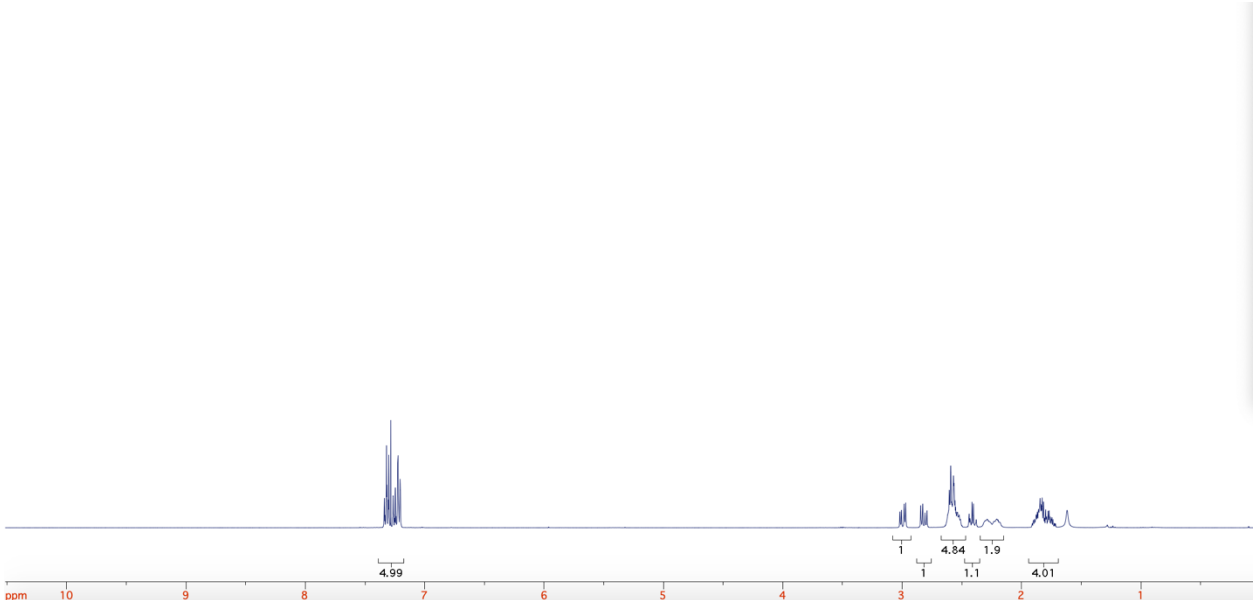
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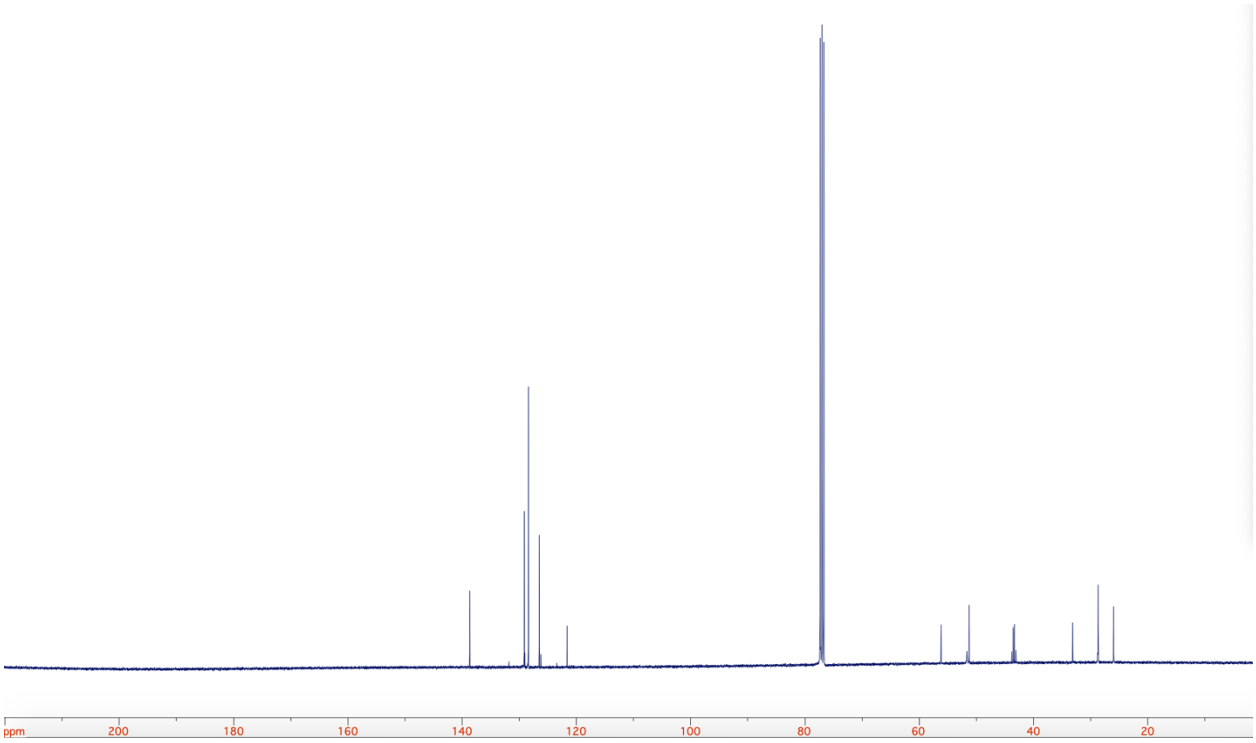
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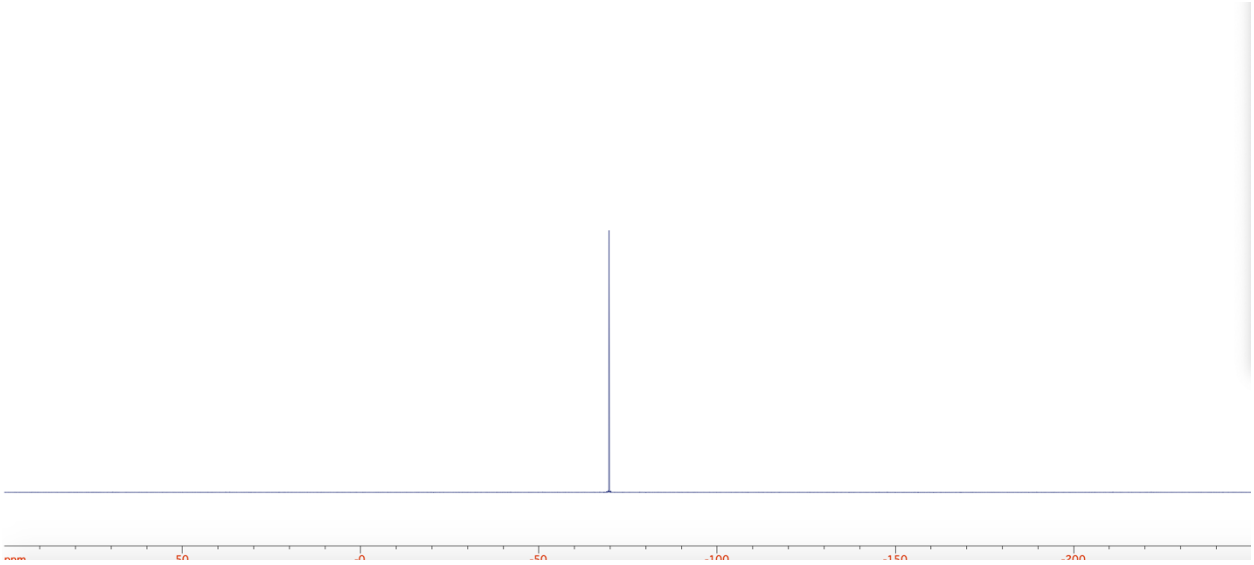
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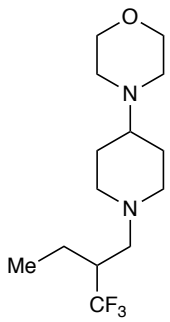
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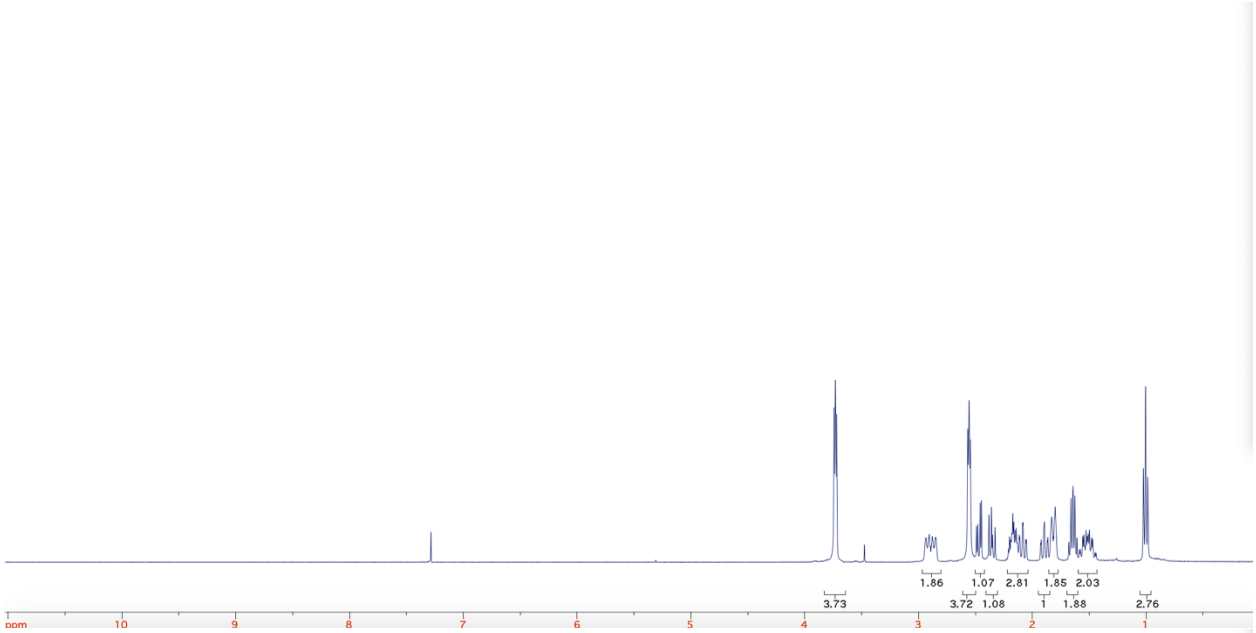
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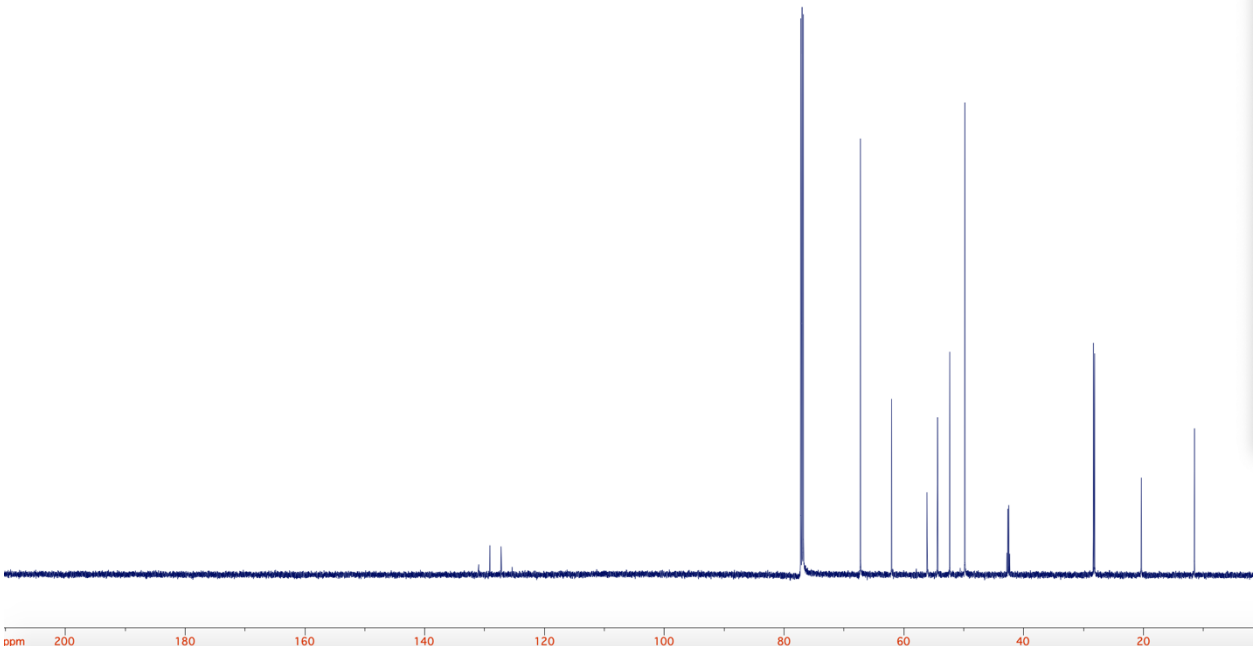
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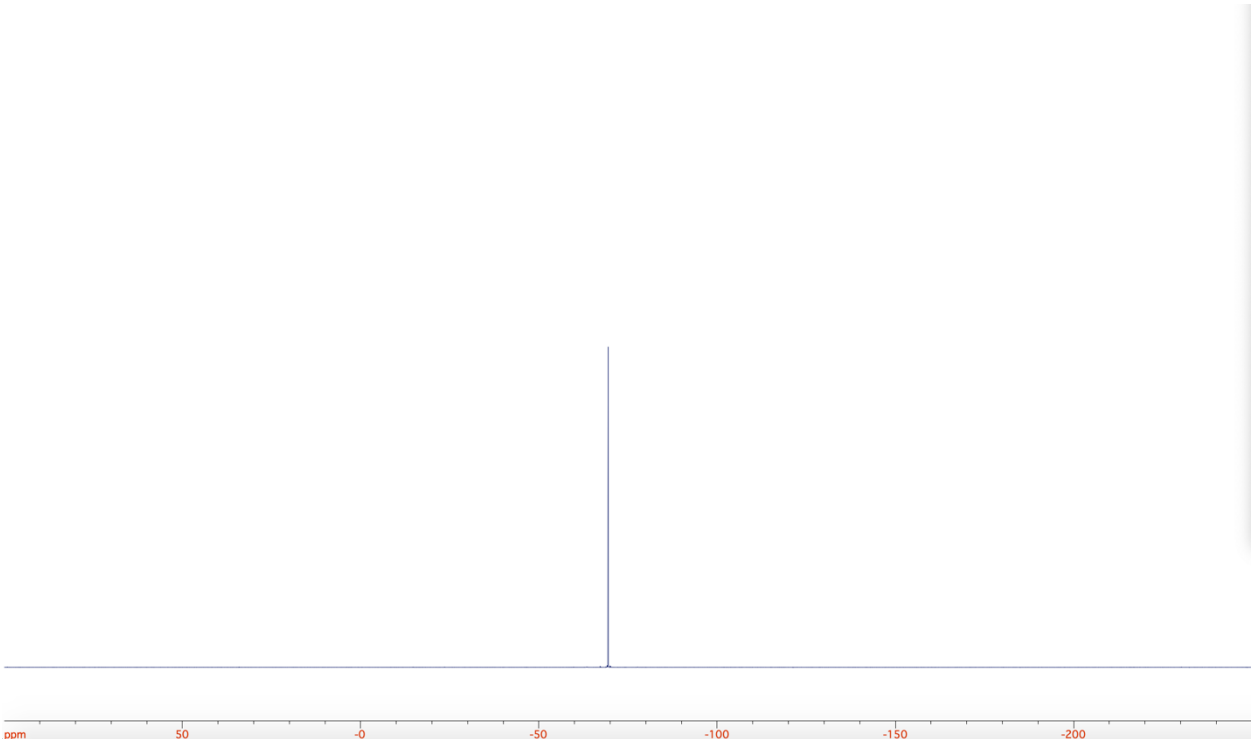
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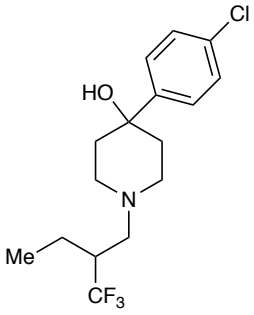
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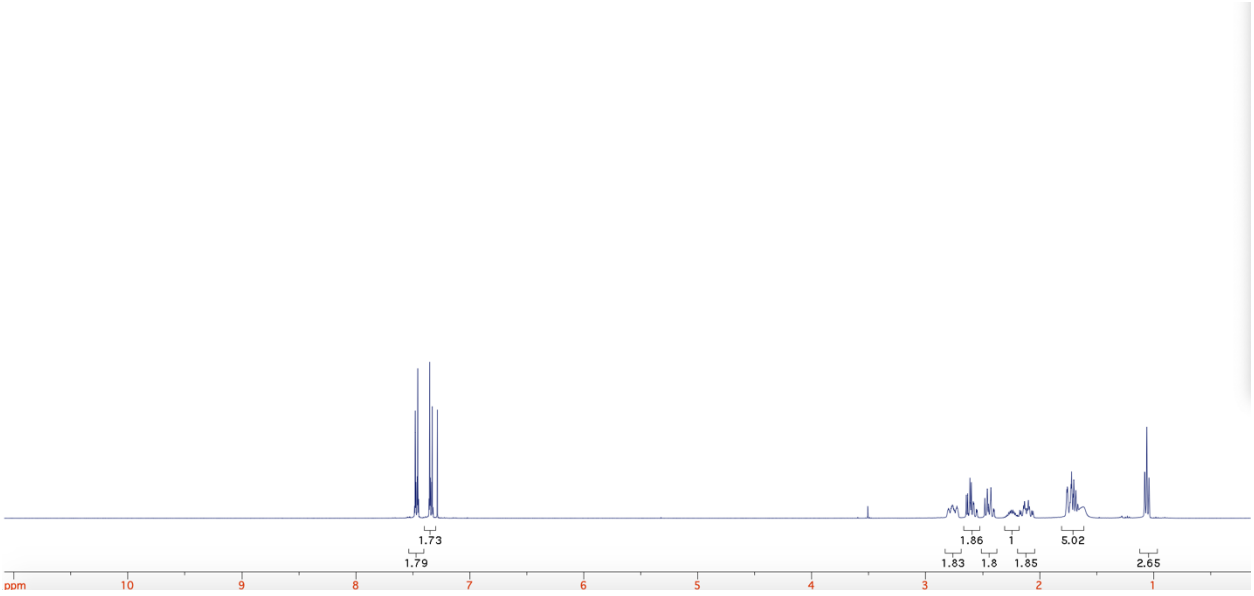
CF3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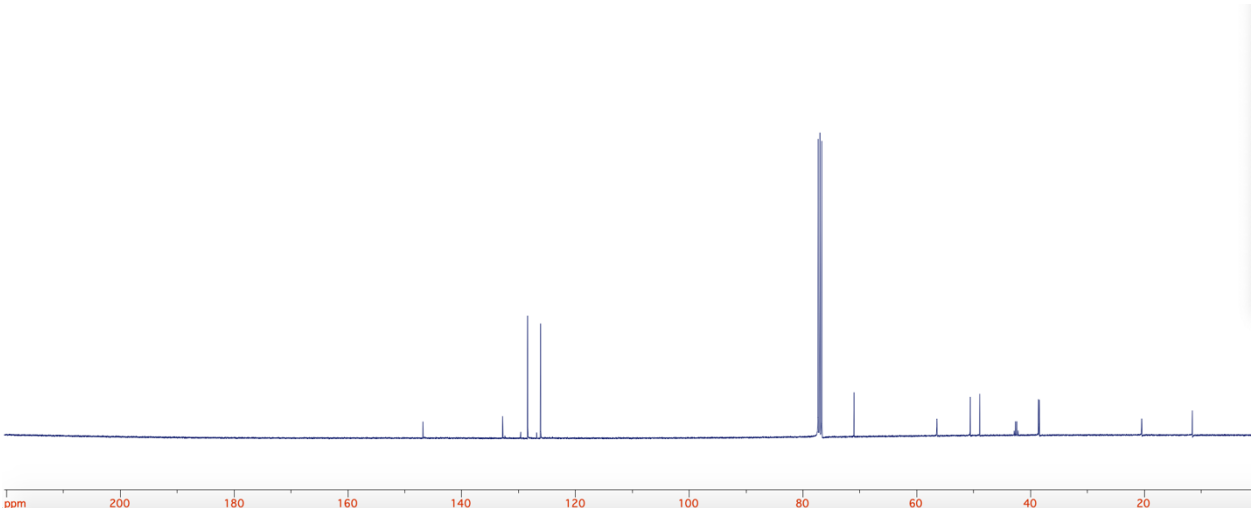
4
3
2
1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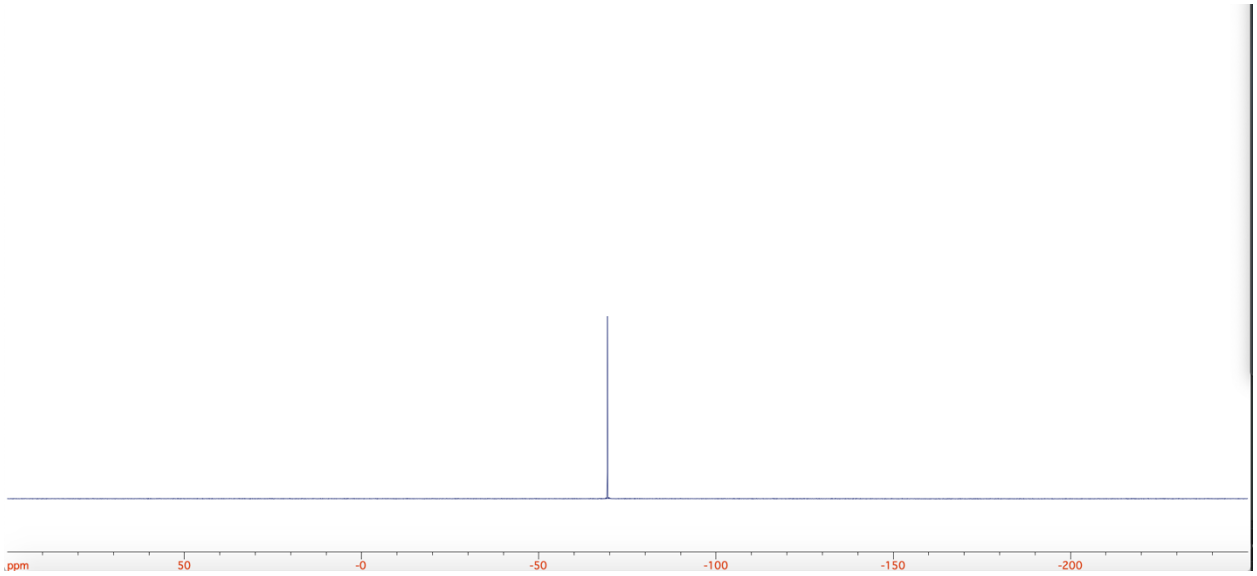
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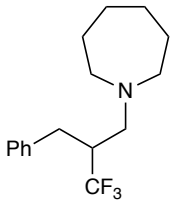
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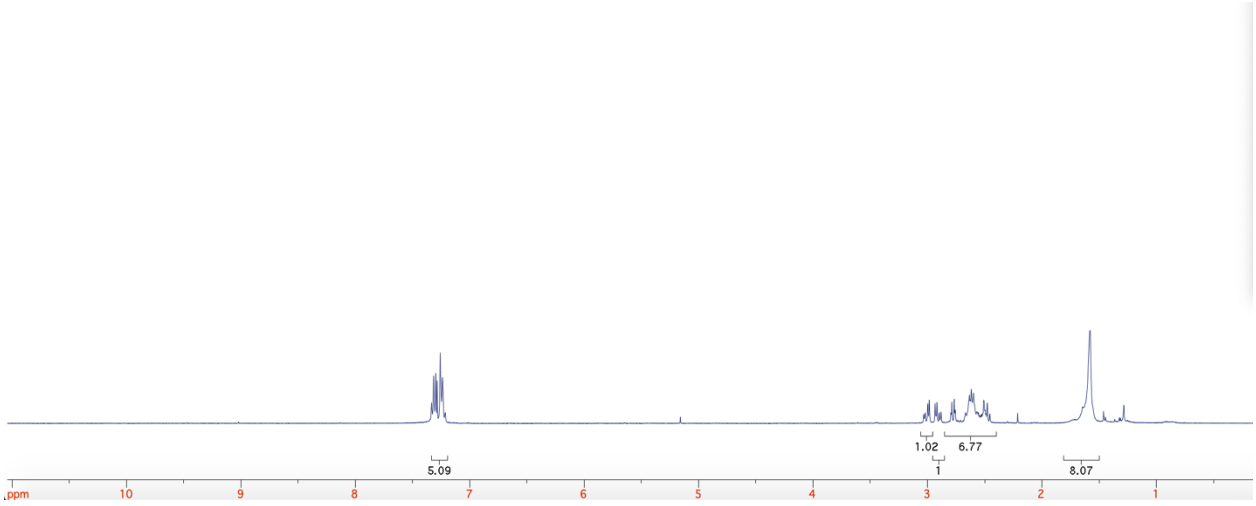
Ph
CF3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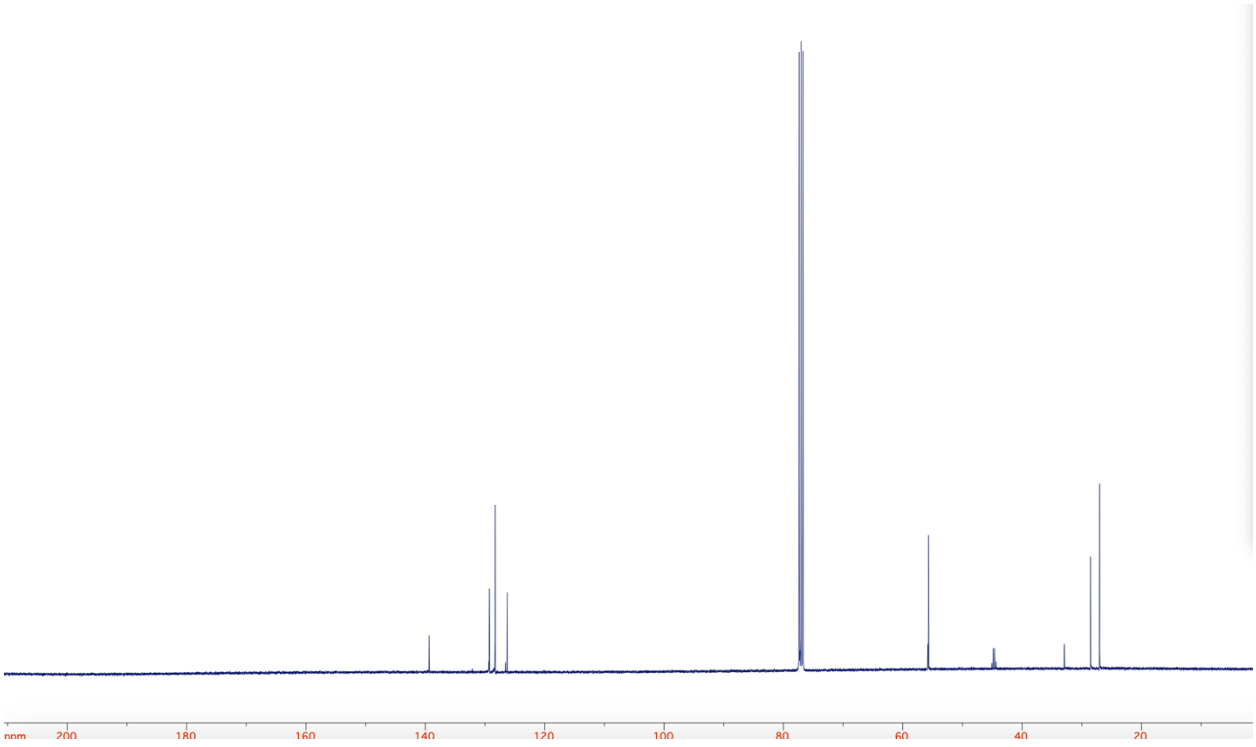
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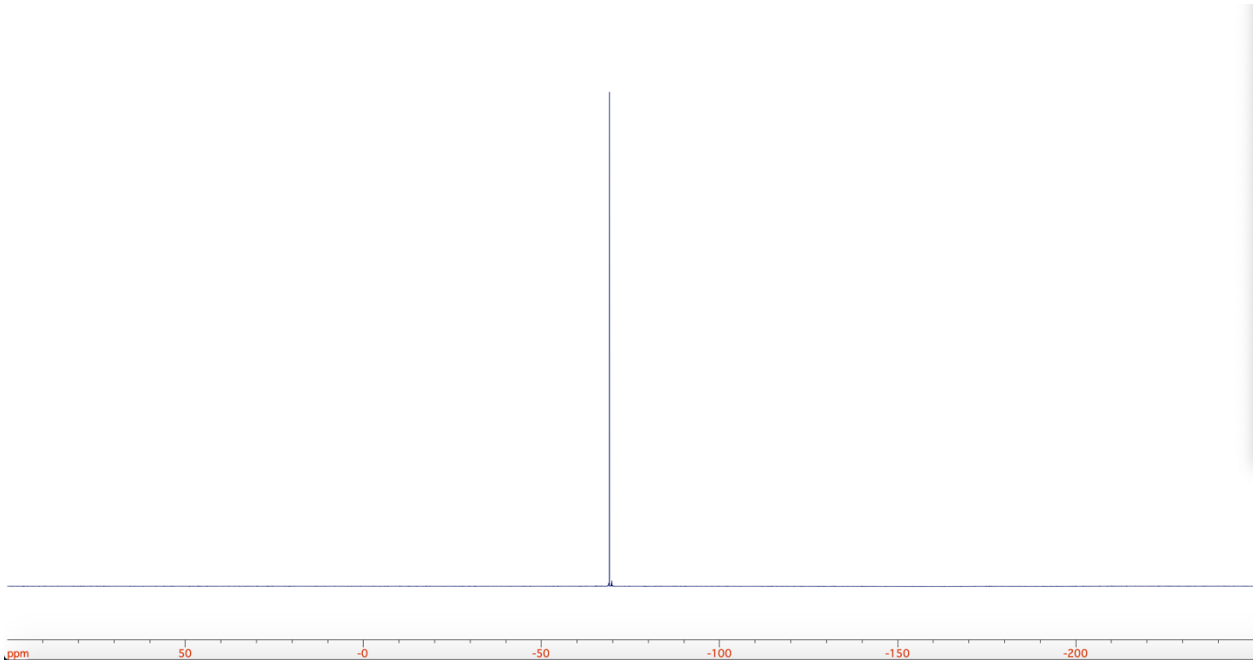
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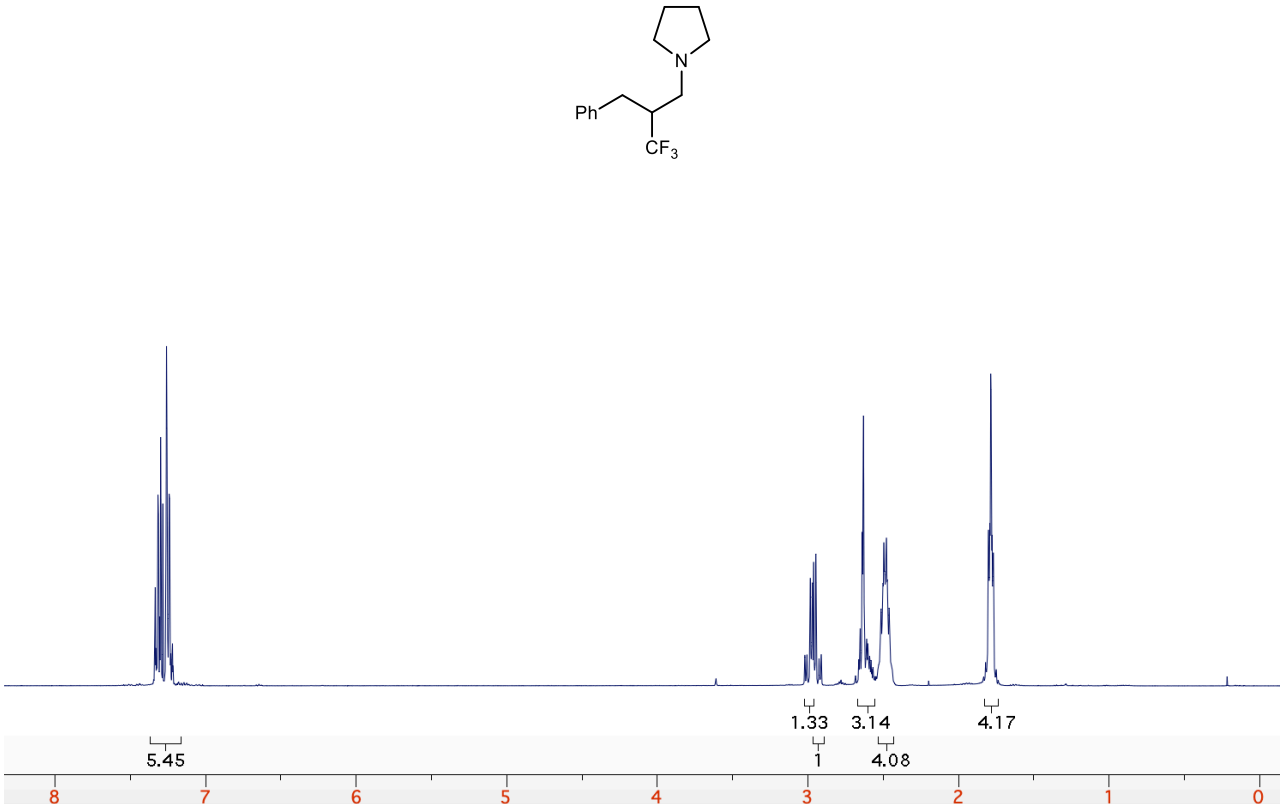
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Ph
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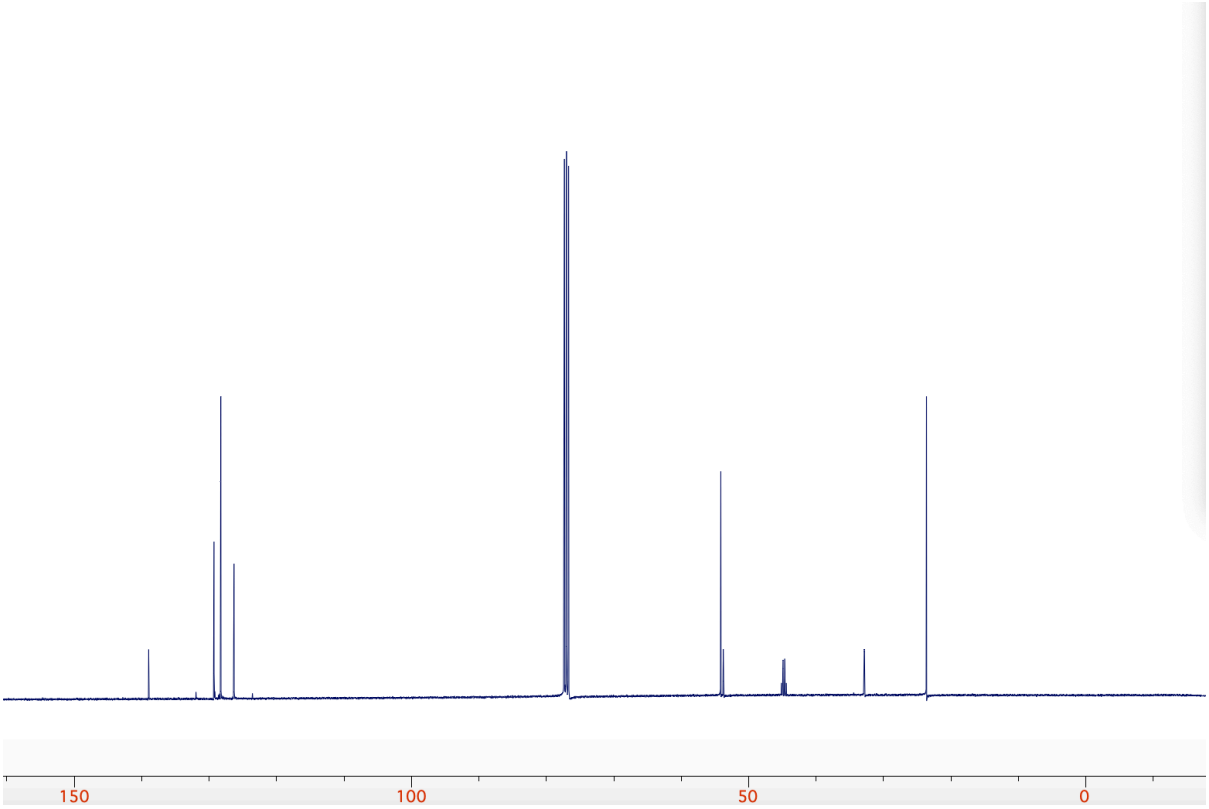
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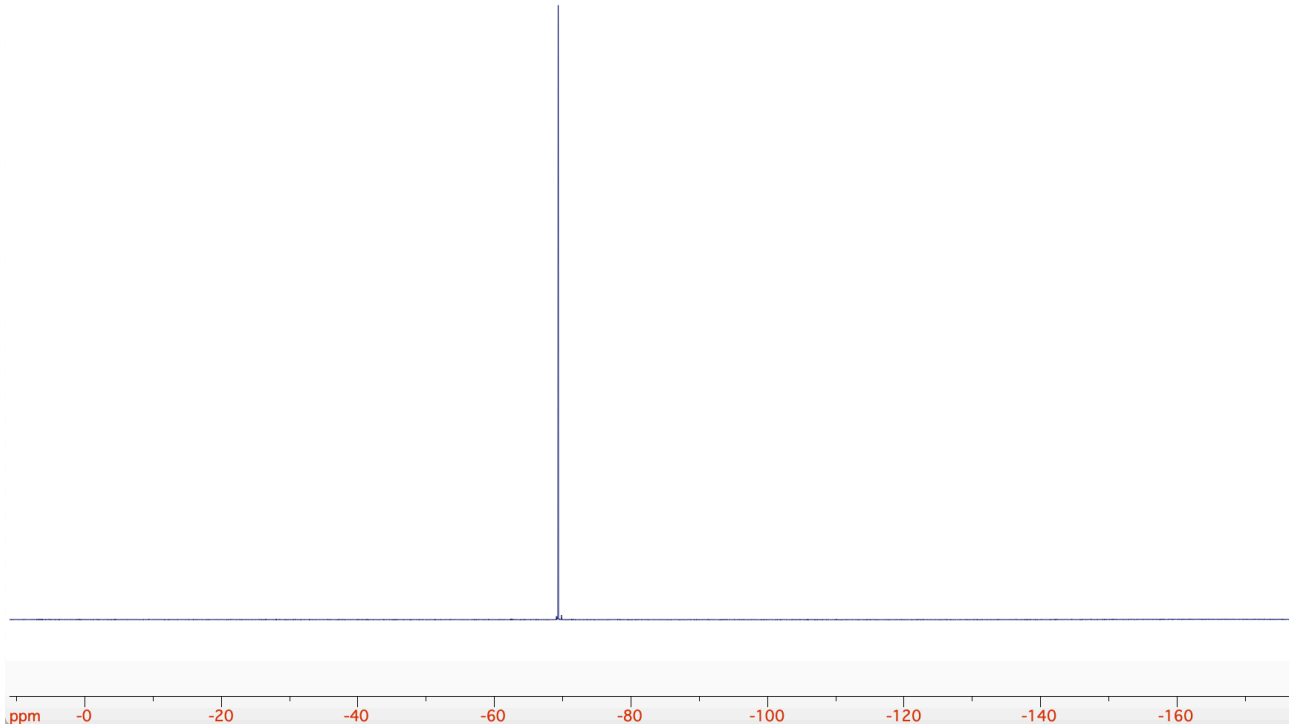
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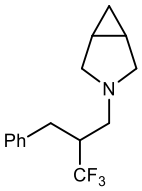
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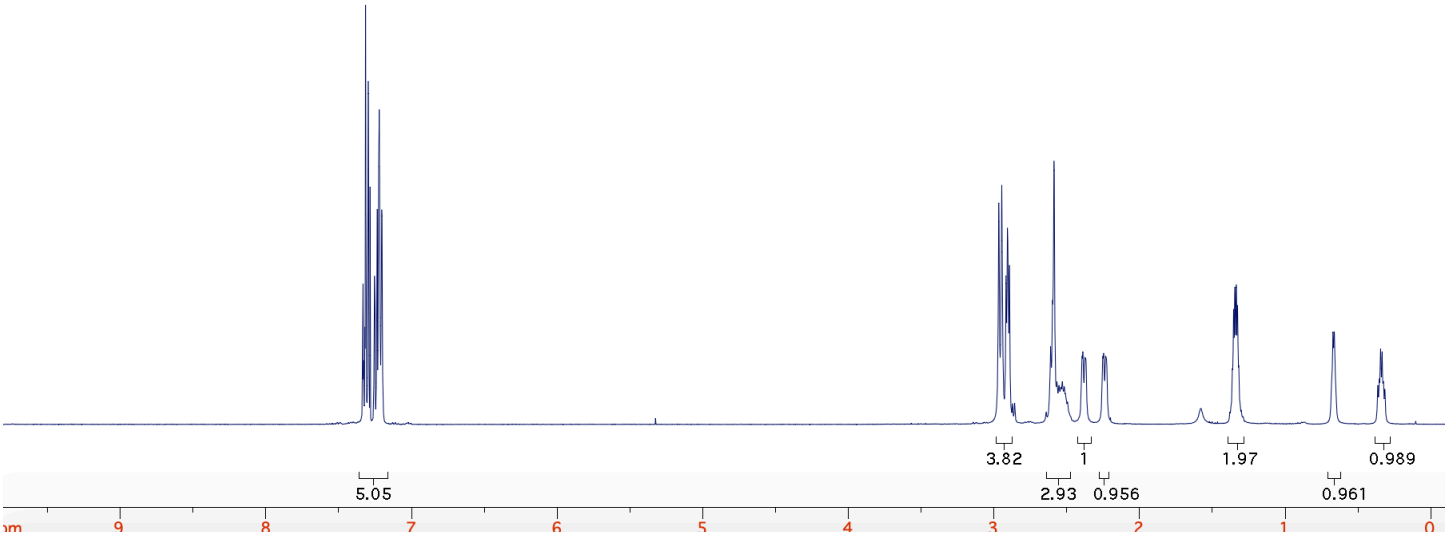
CF3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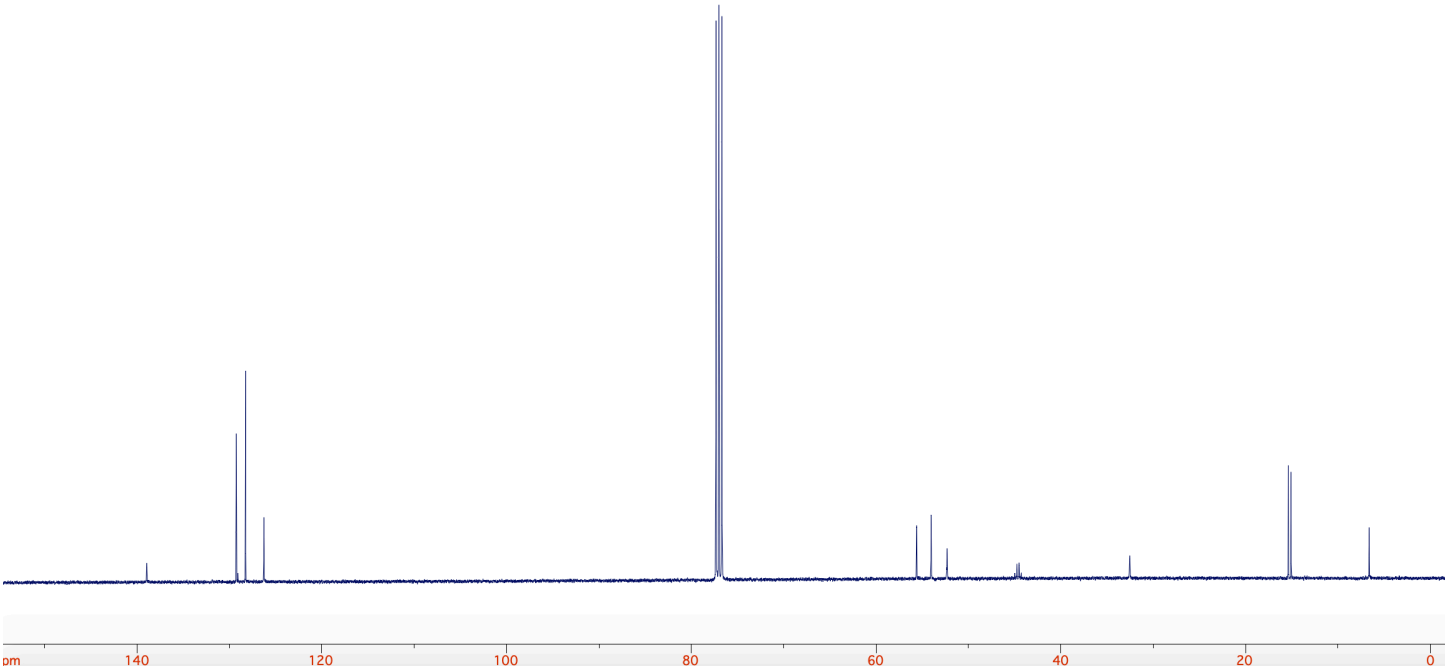
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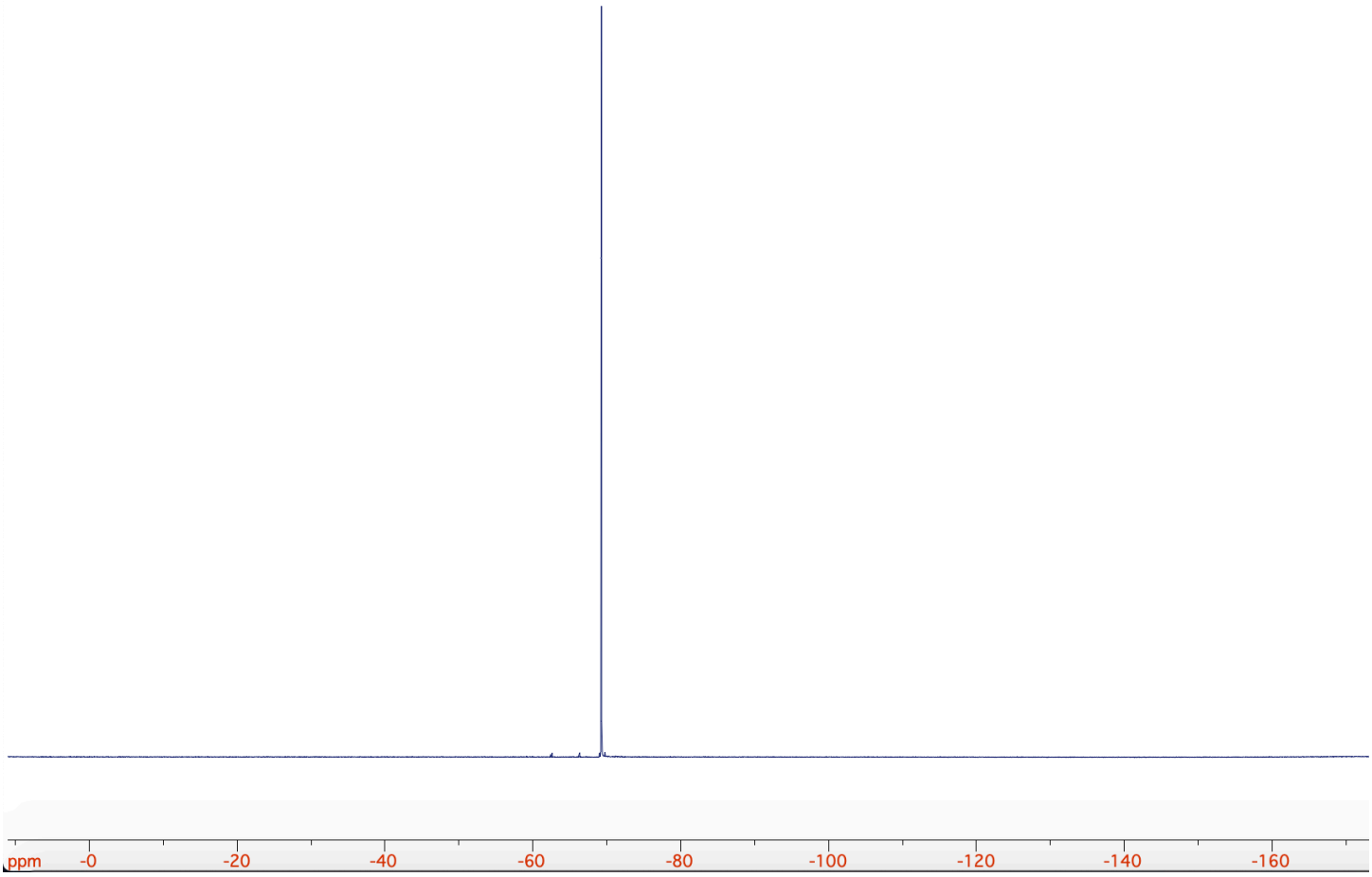
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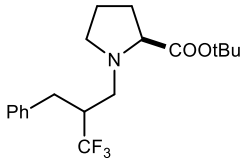
COOtBu
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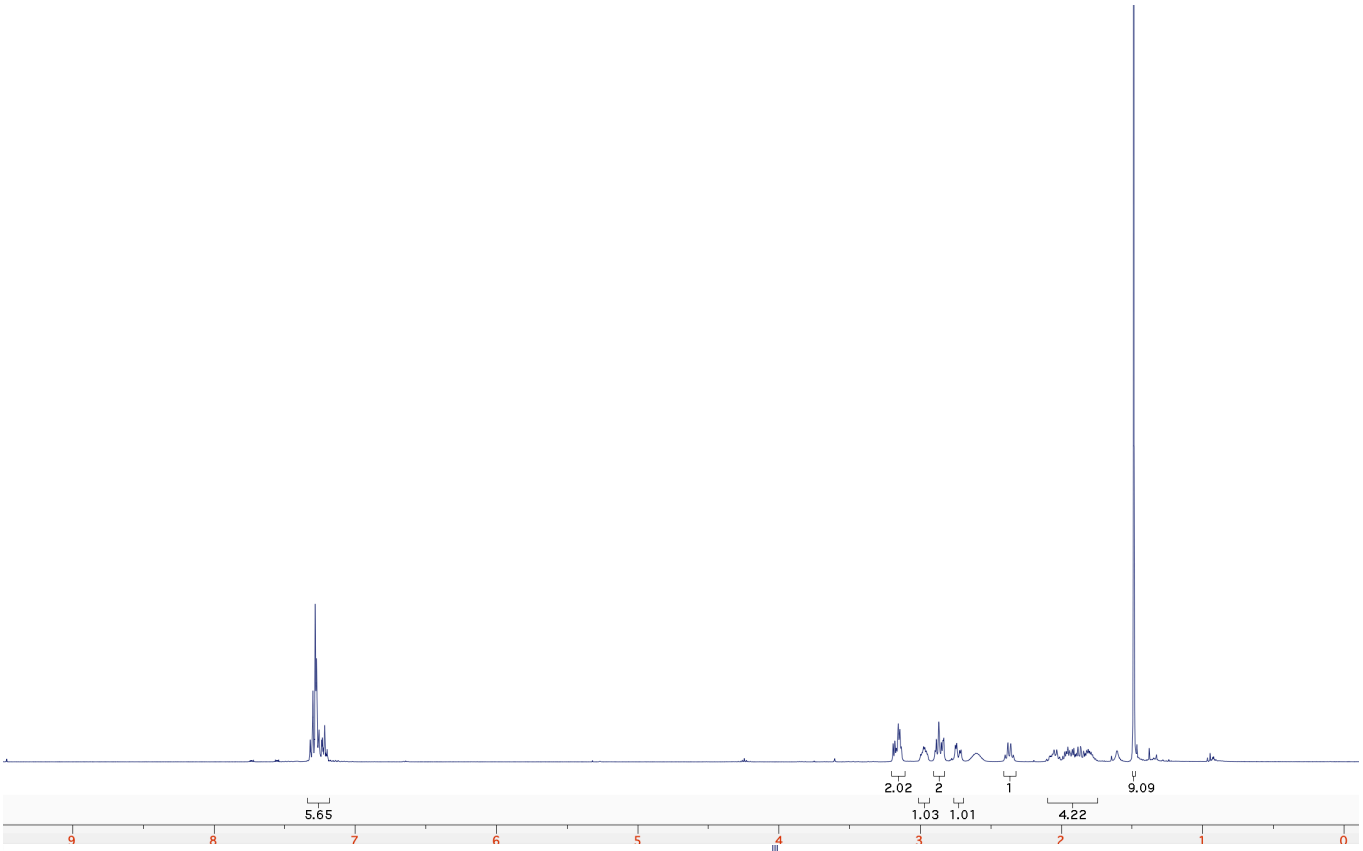
Ph
CF3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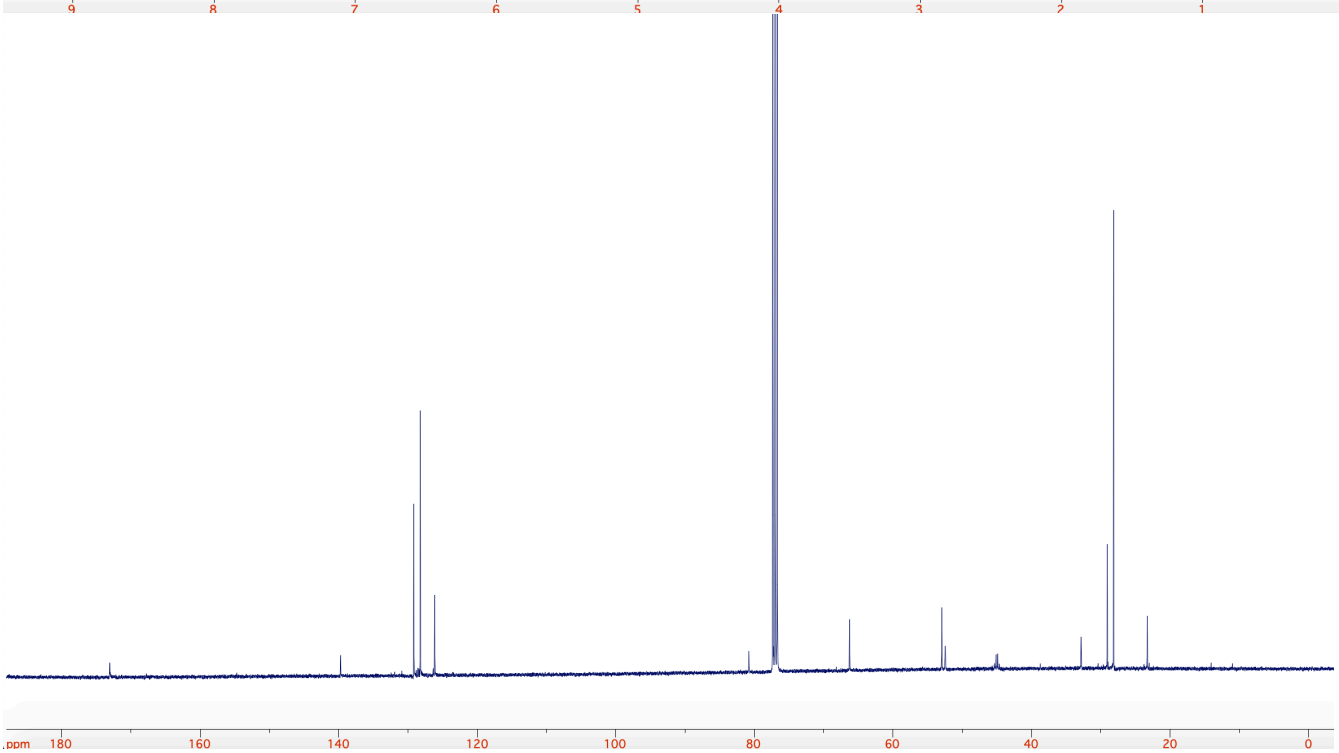
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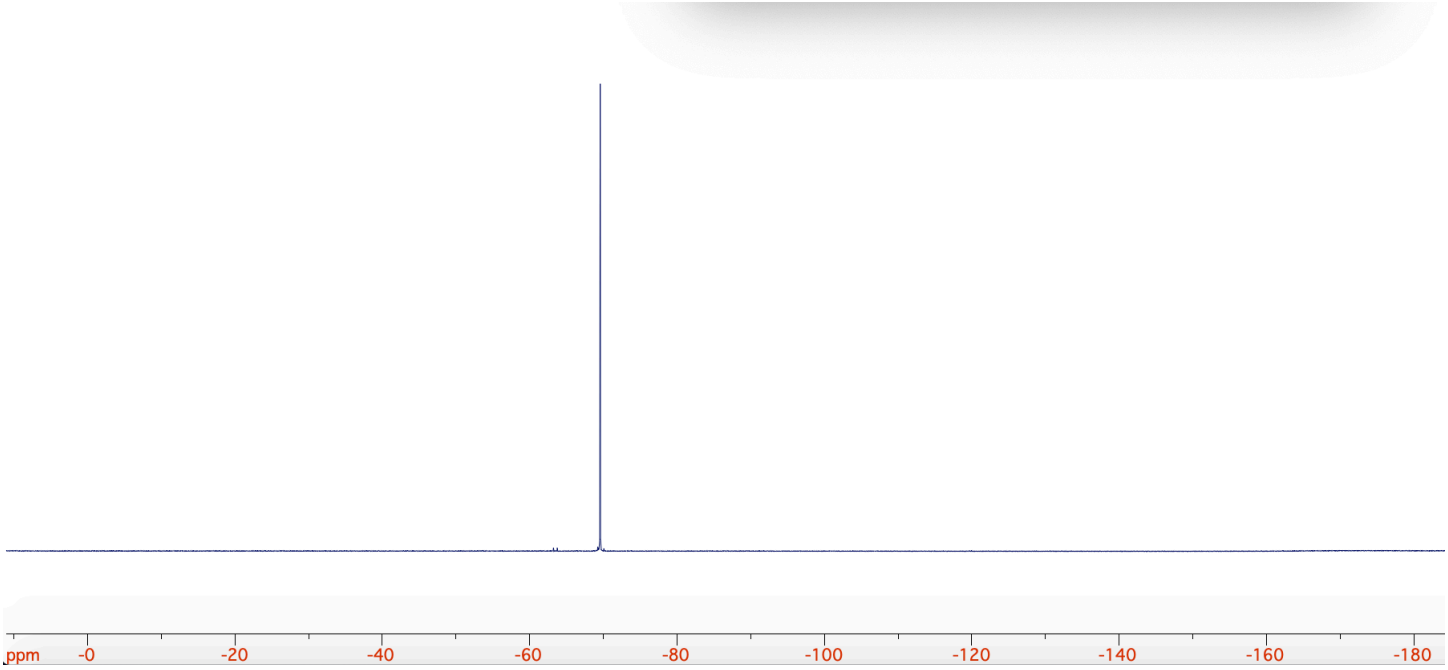
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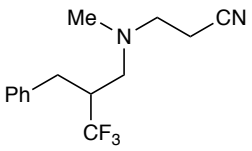
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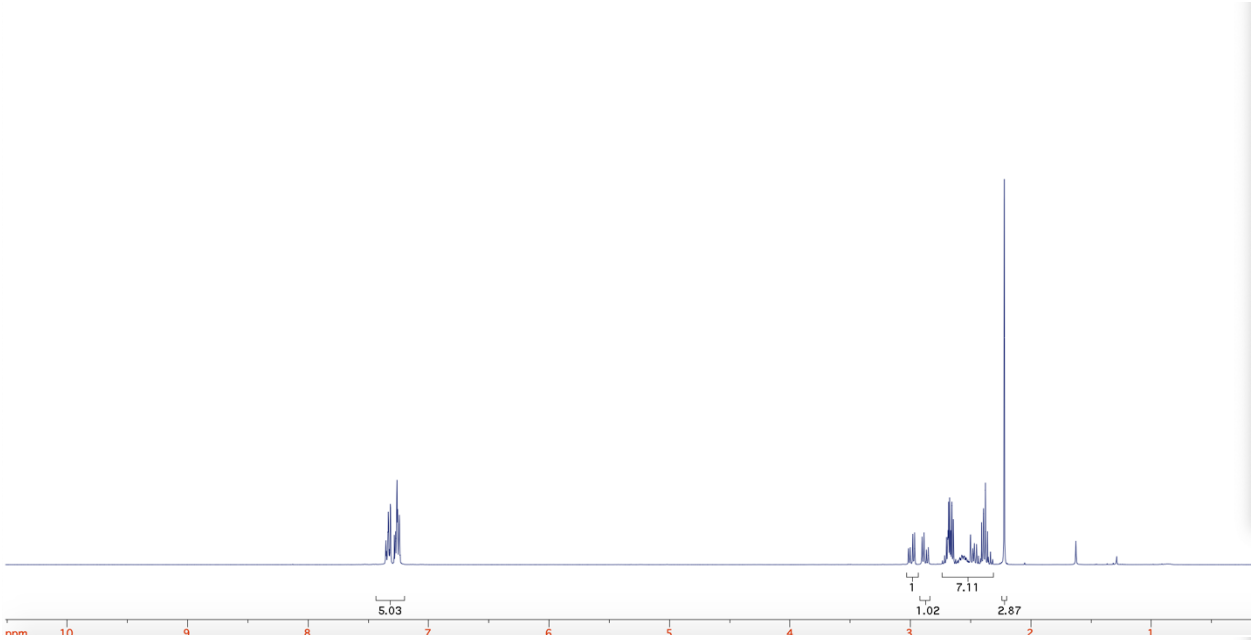
CF3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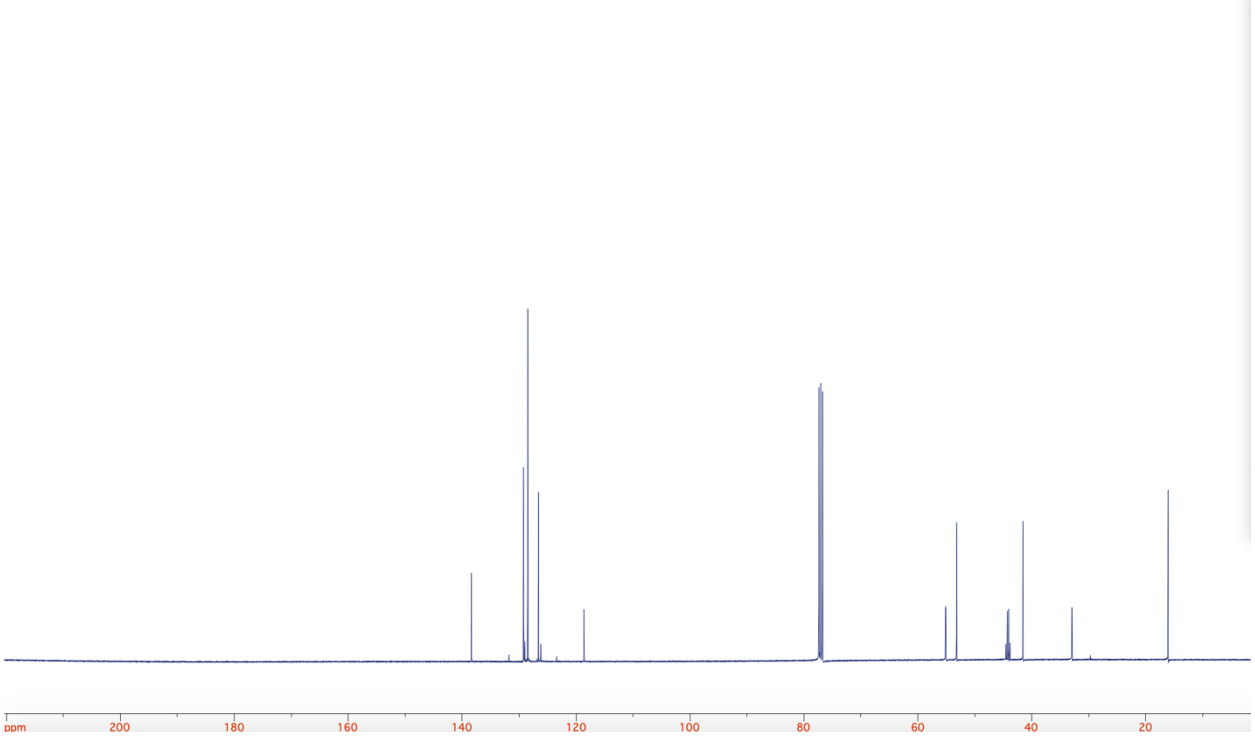
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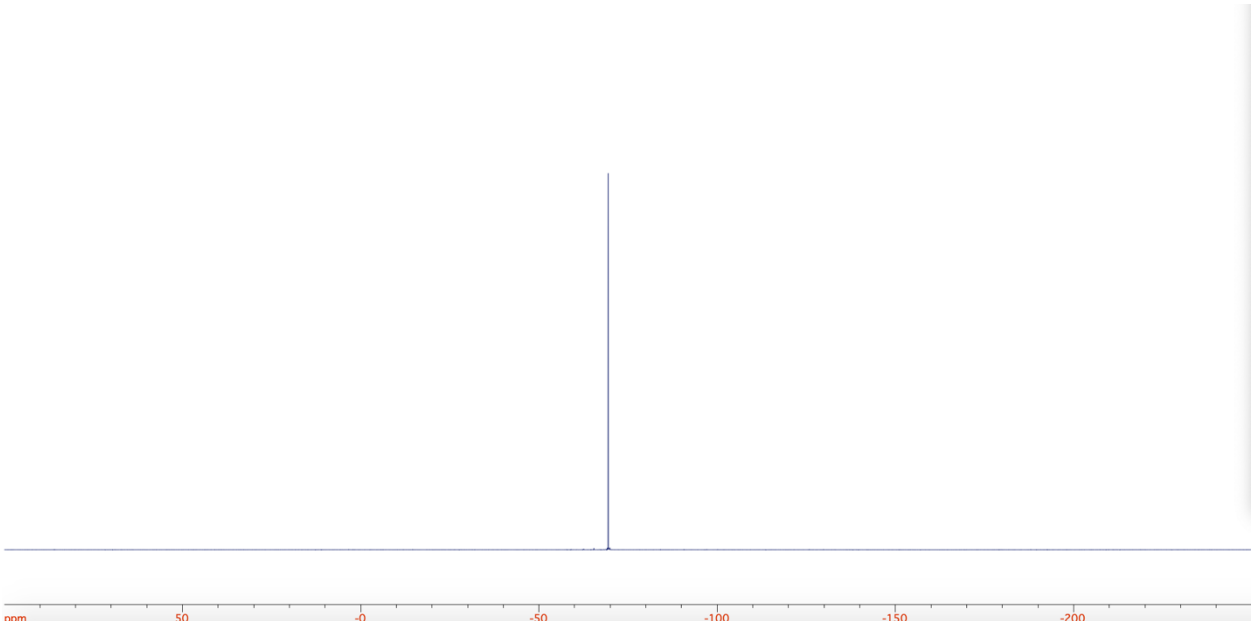
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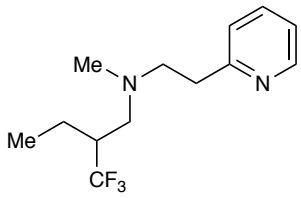
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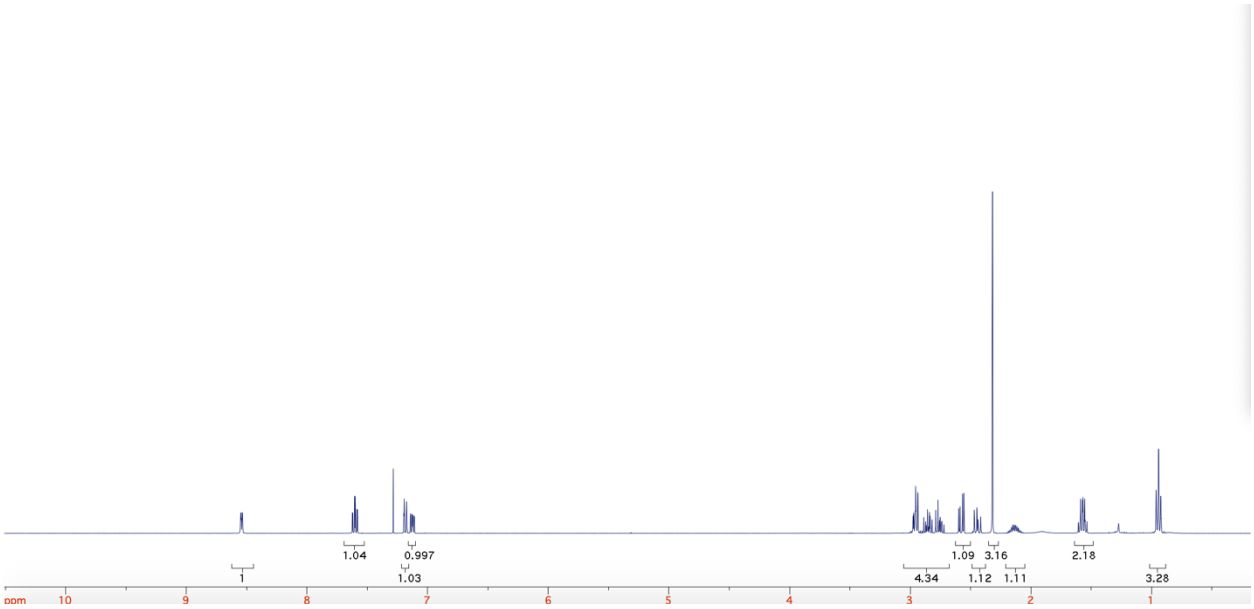
CF3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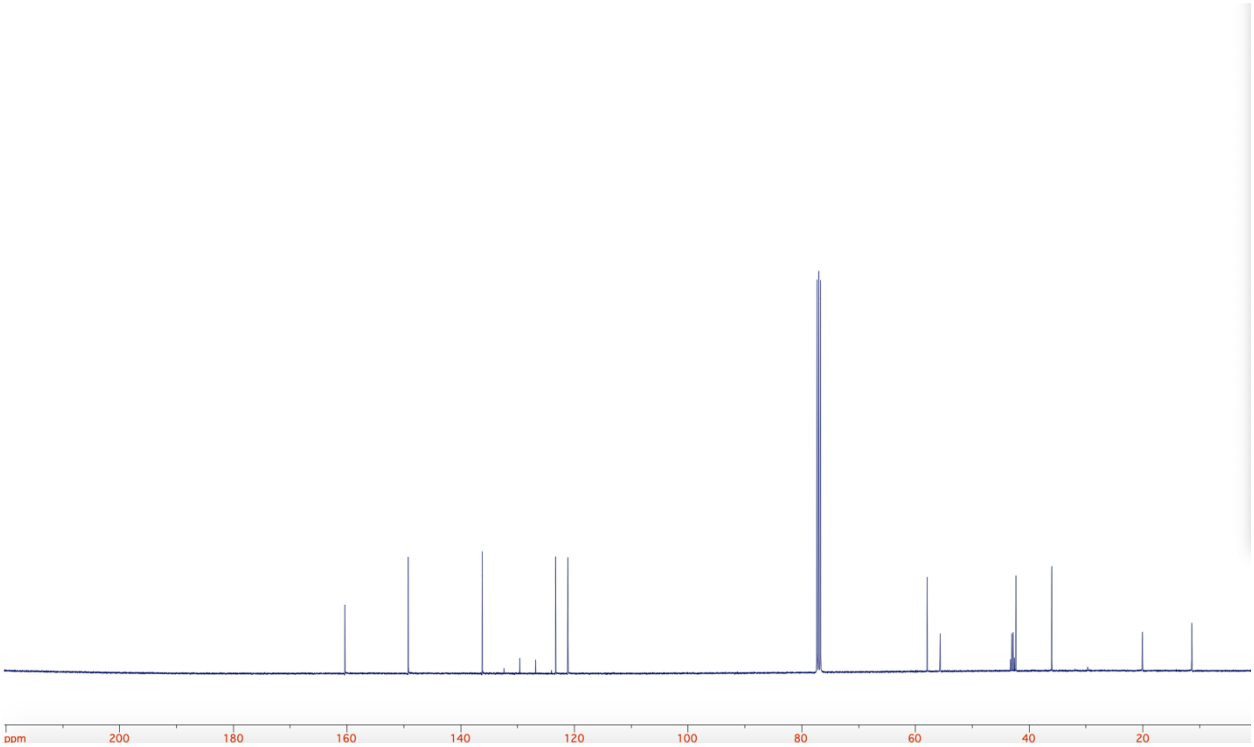
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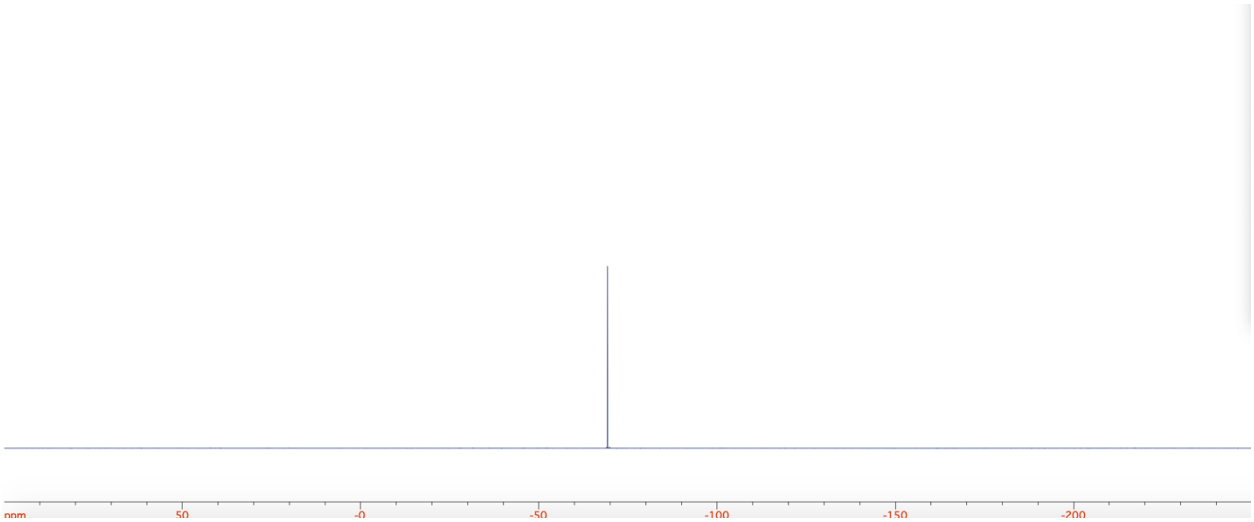
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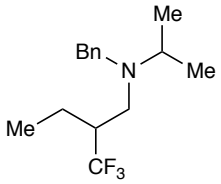
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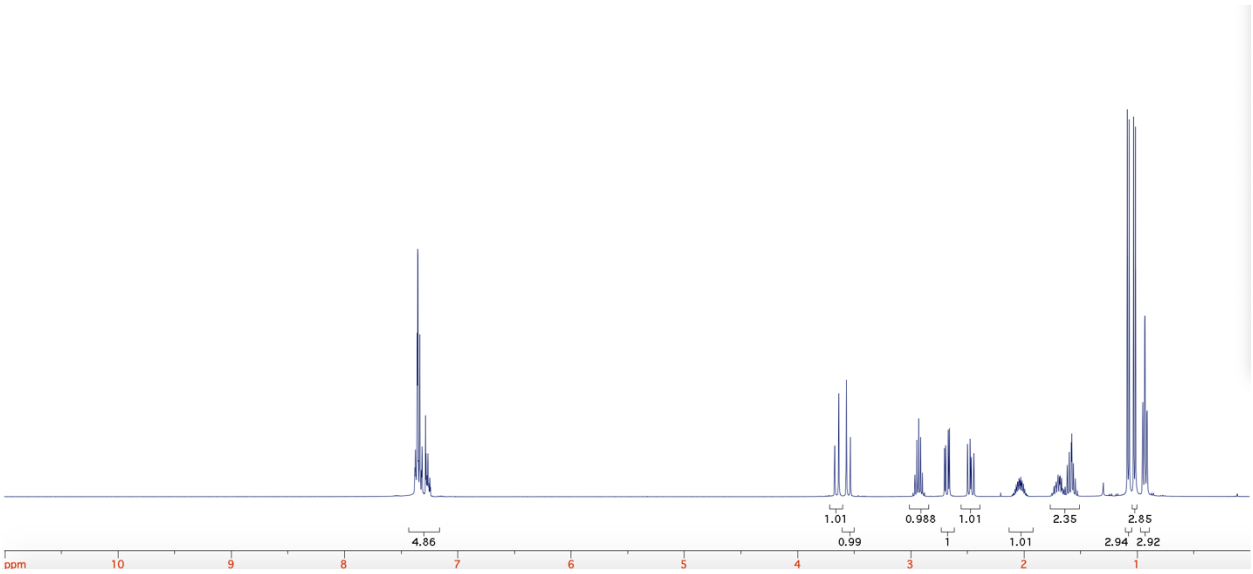
Bn
N
Me
Me
CF3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2
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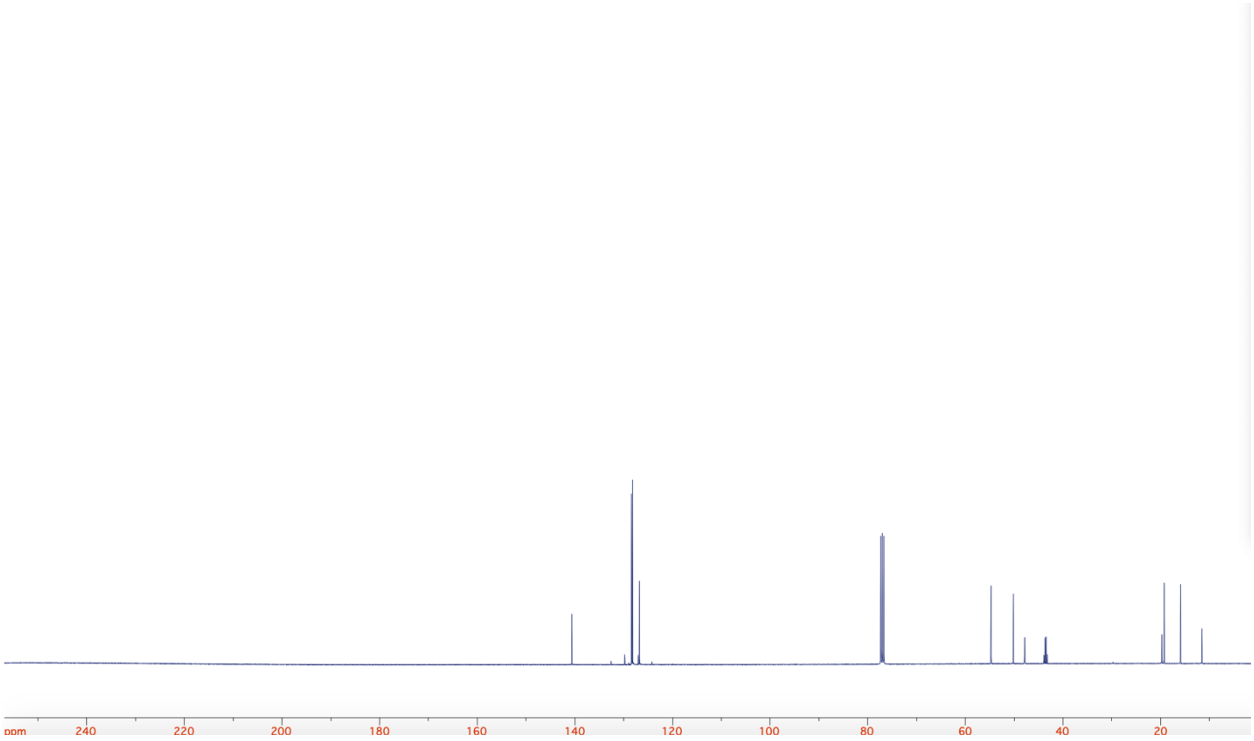
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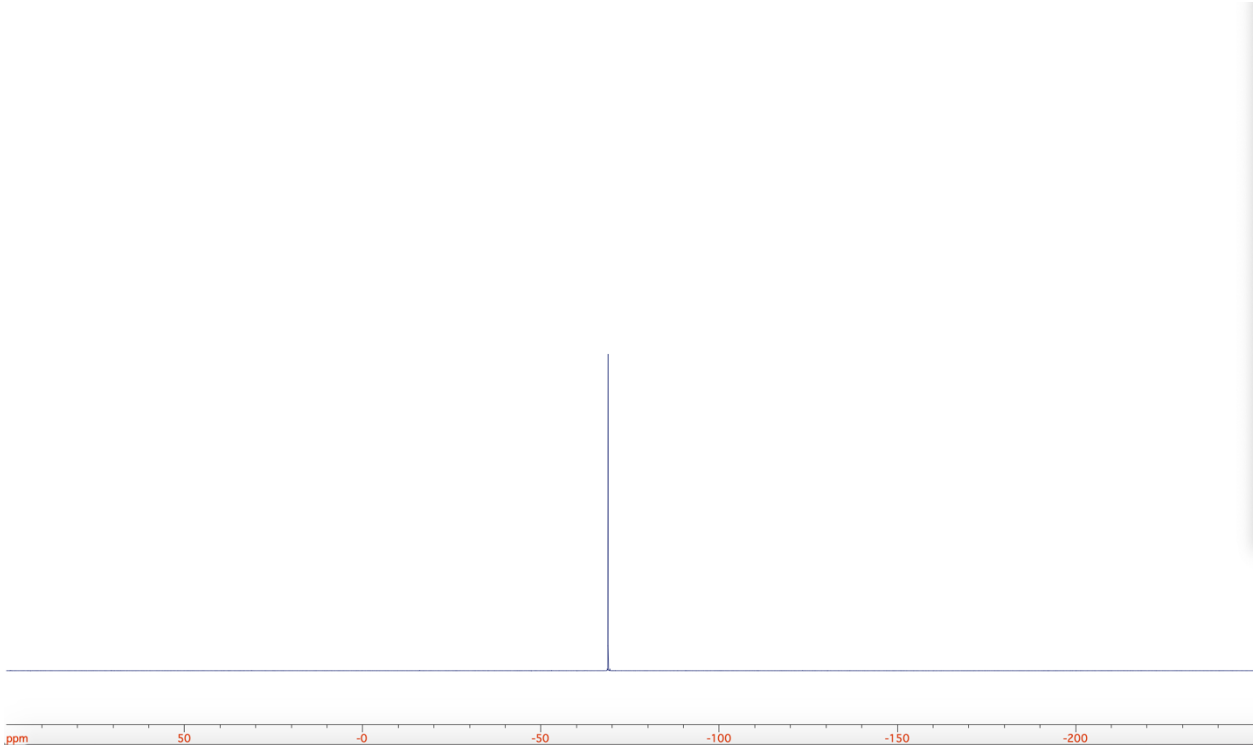
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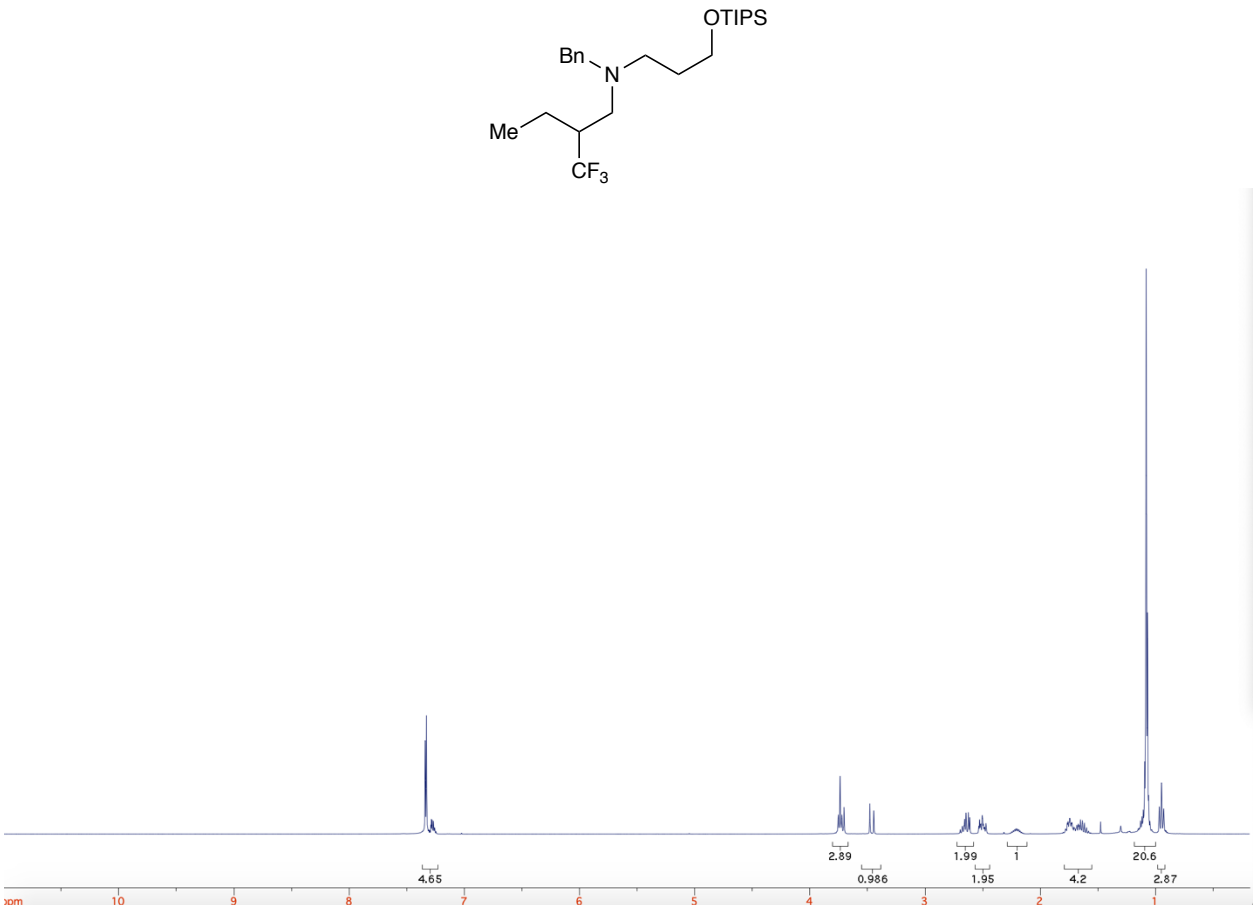
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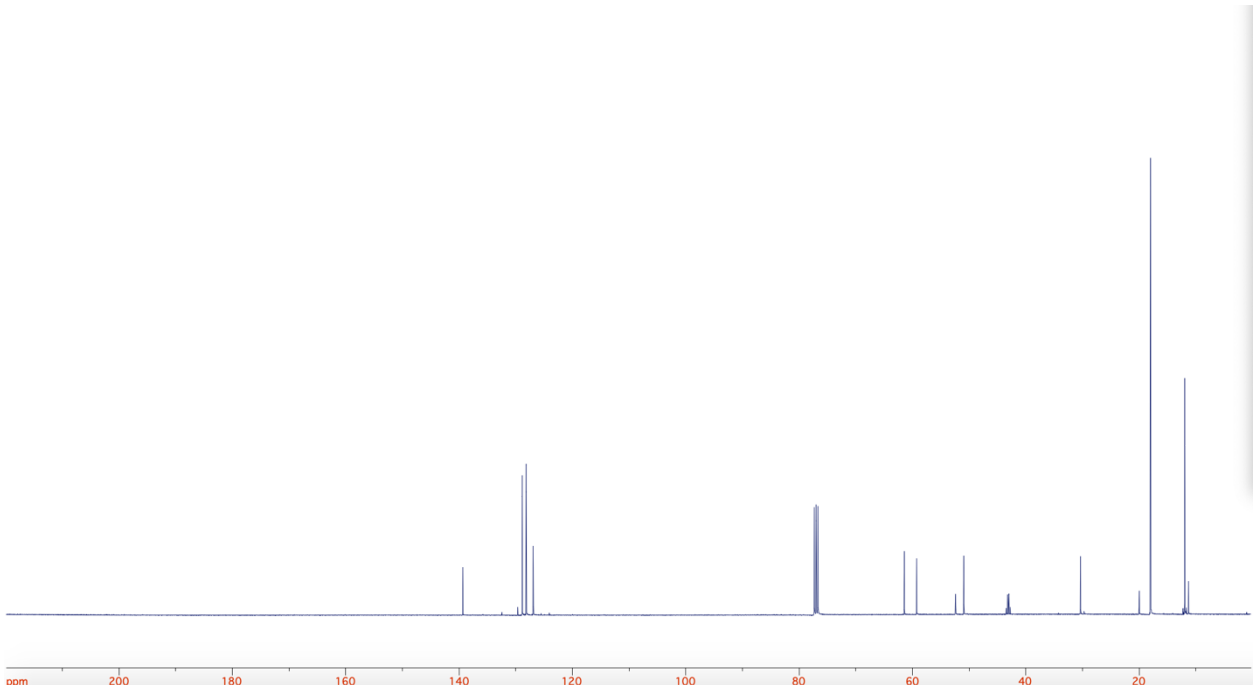
2
1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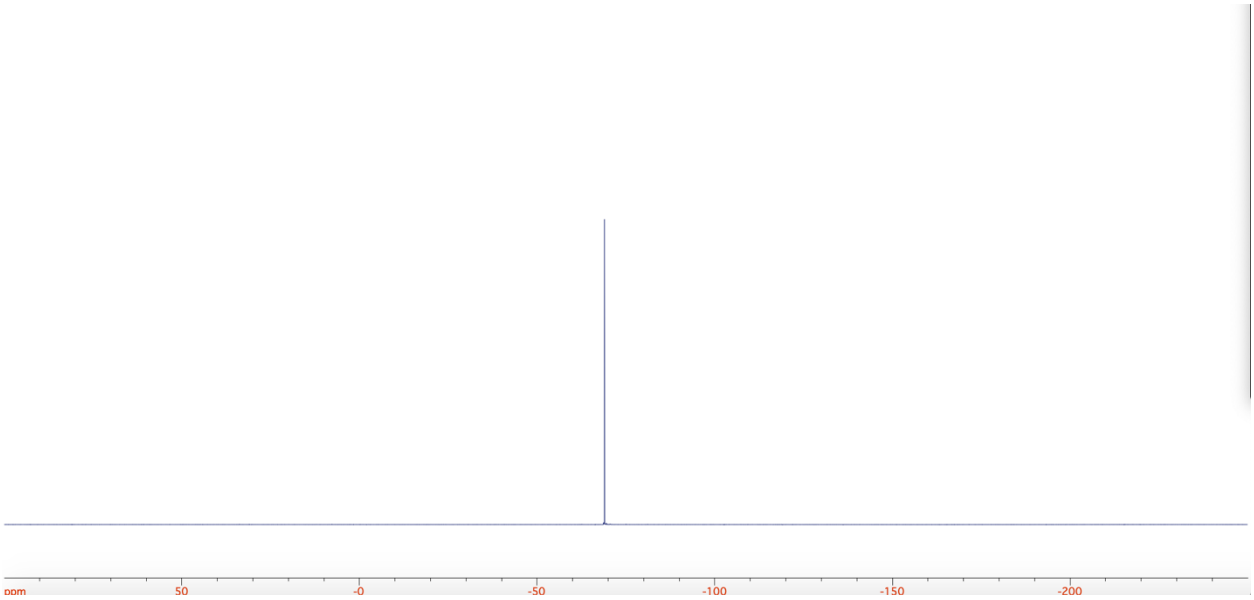
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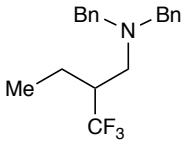
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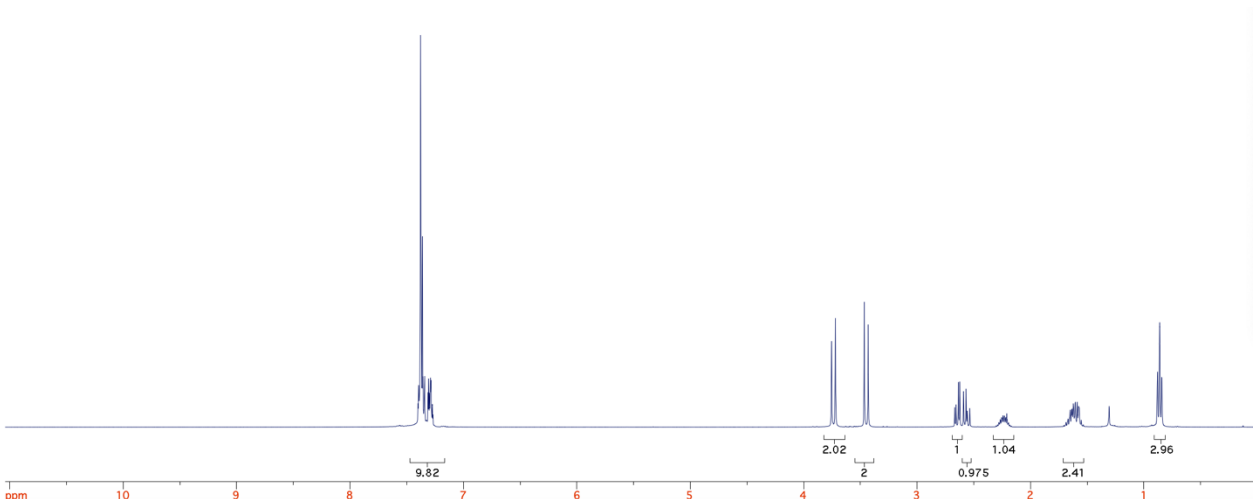
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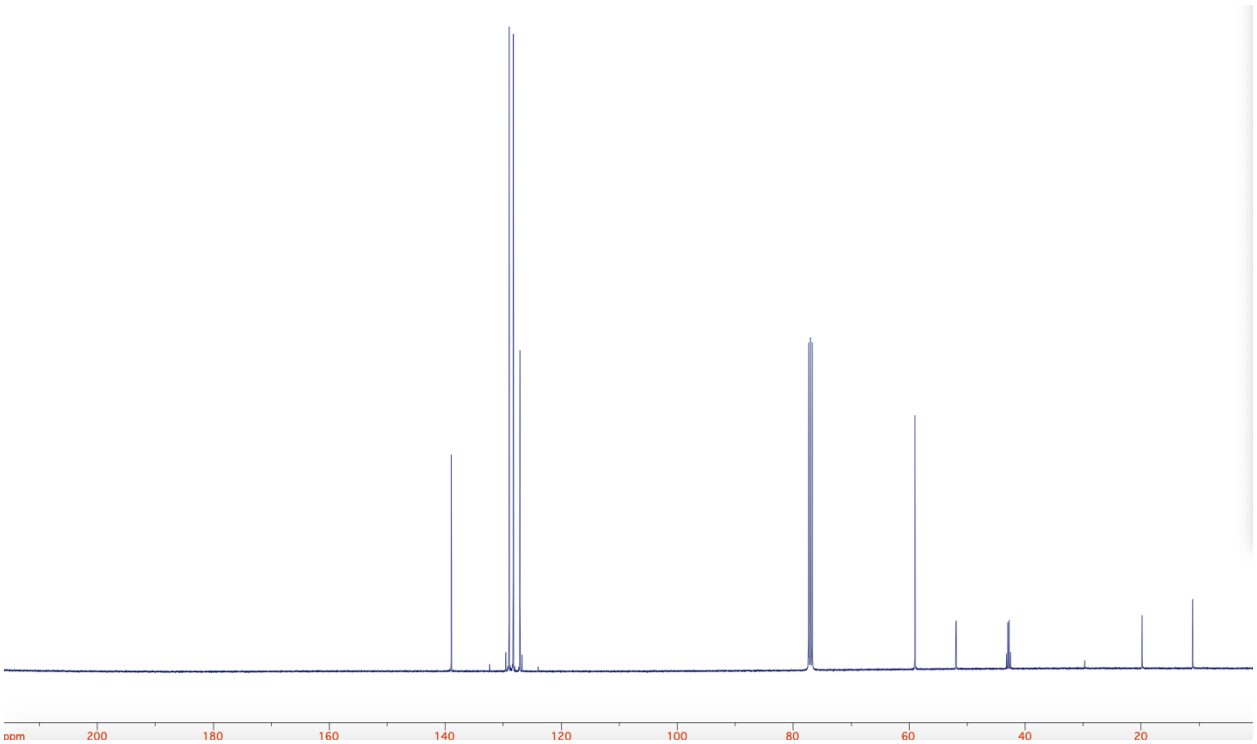
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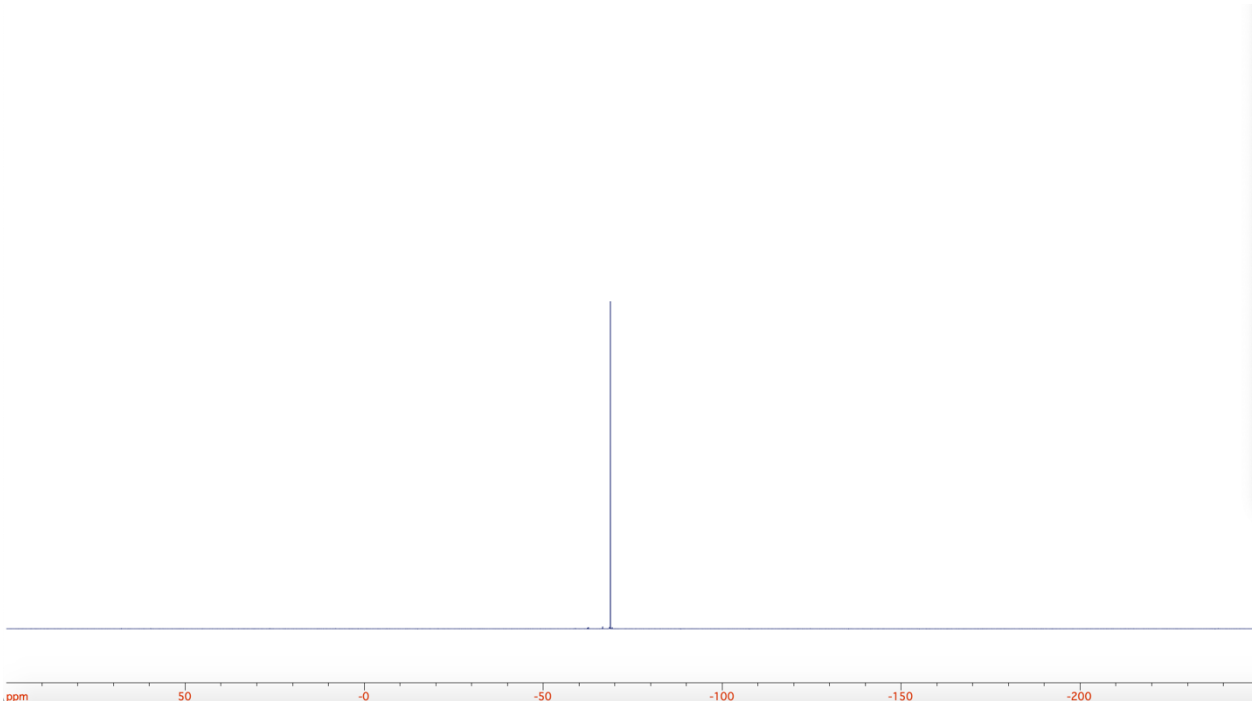
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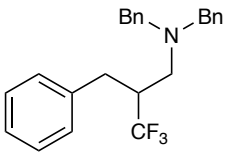
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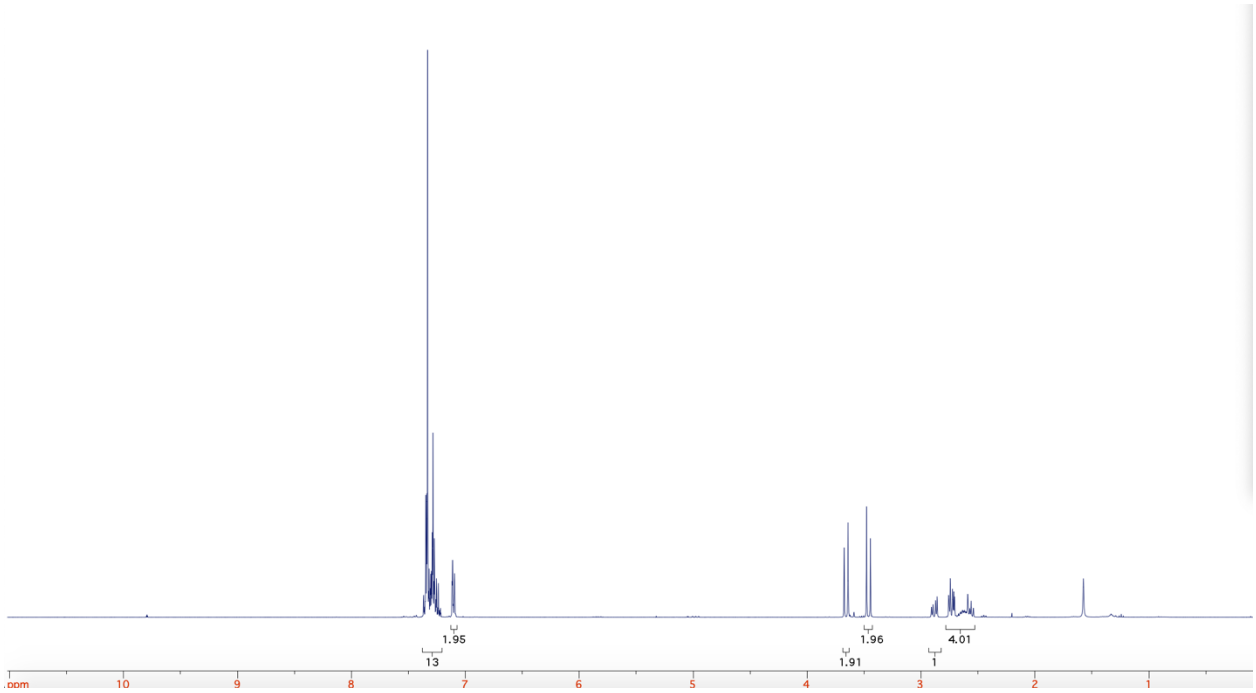
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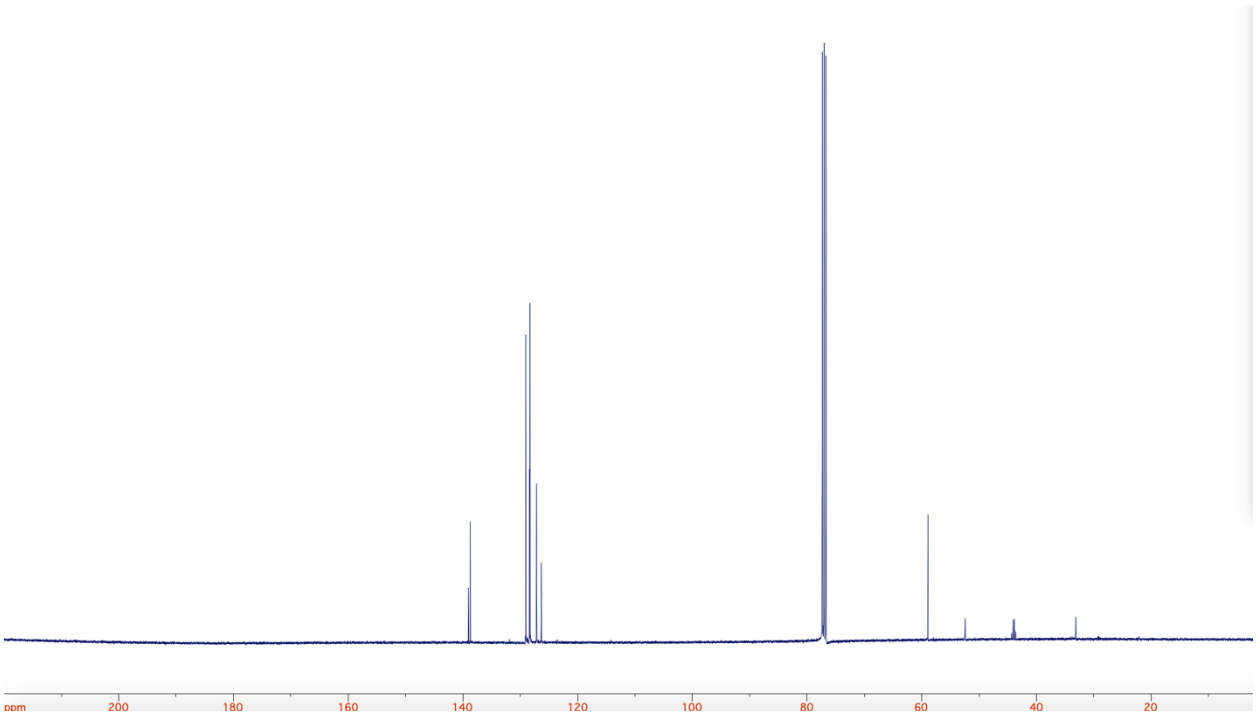
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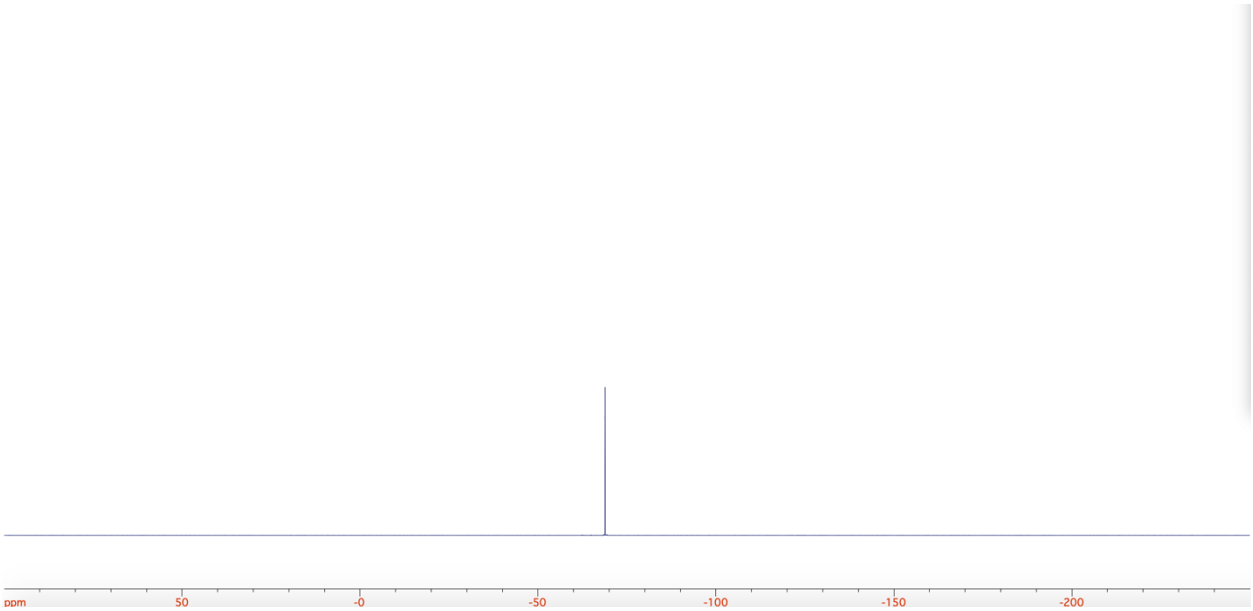
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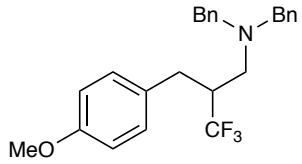
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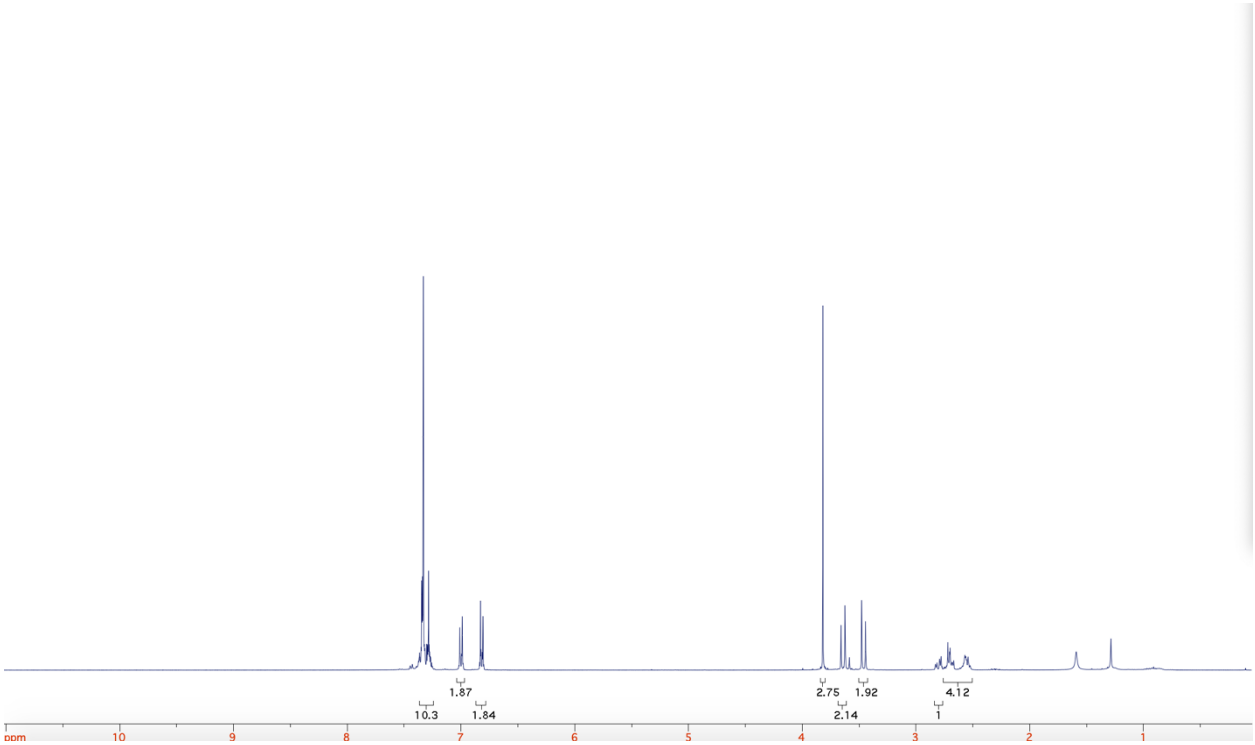
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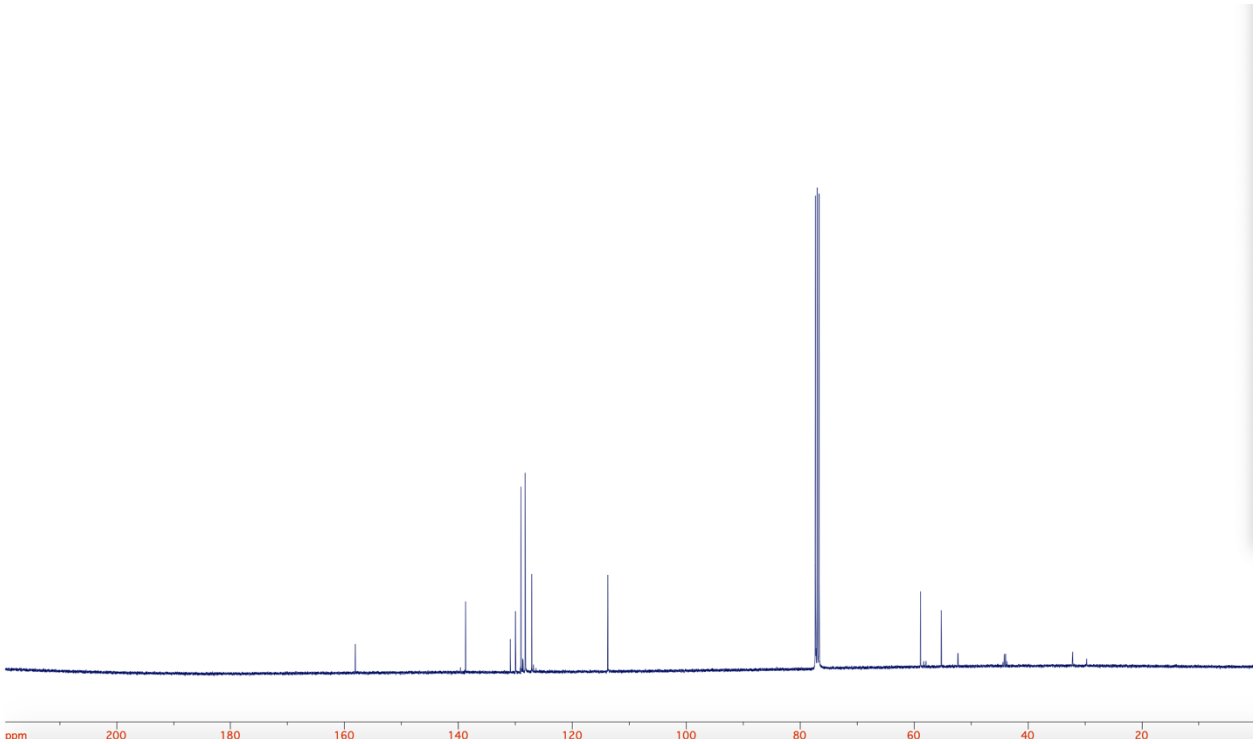
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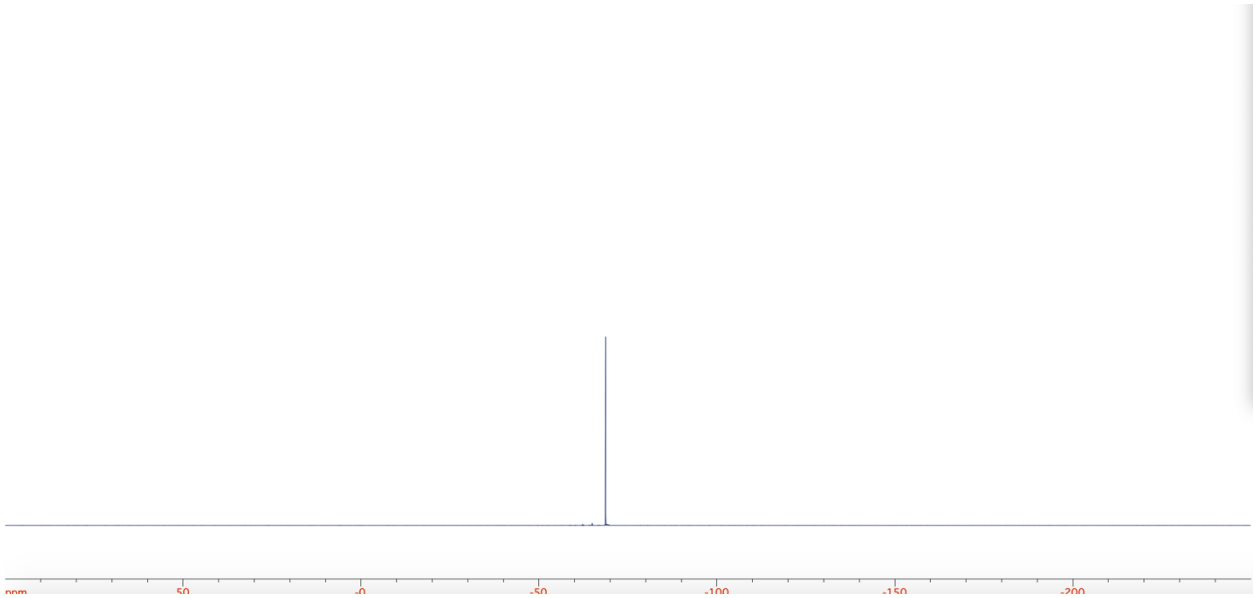
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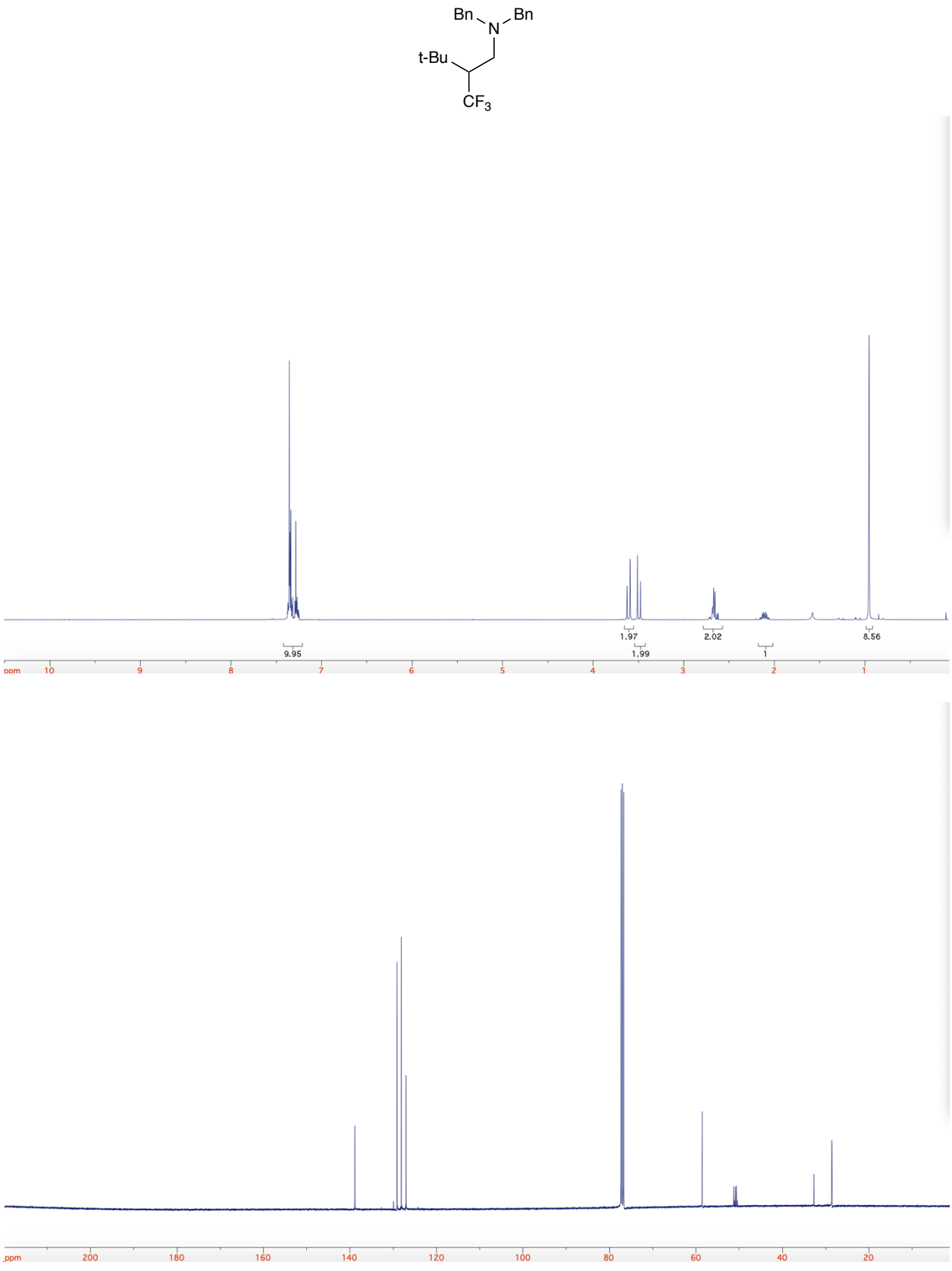
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Bn
t-Bu
CF3
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1.99
2.02
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8.56
ppm
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1
ppm
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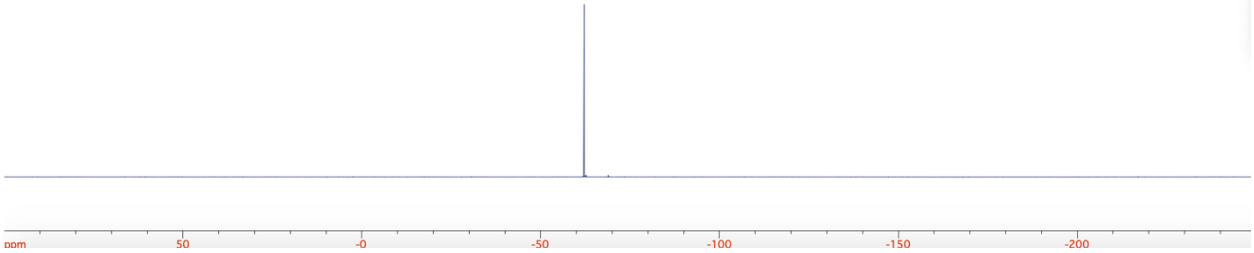
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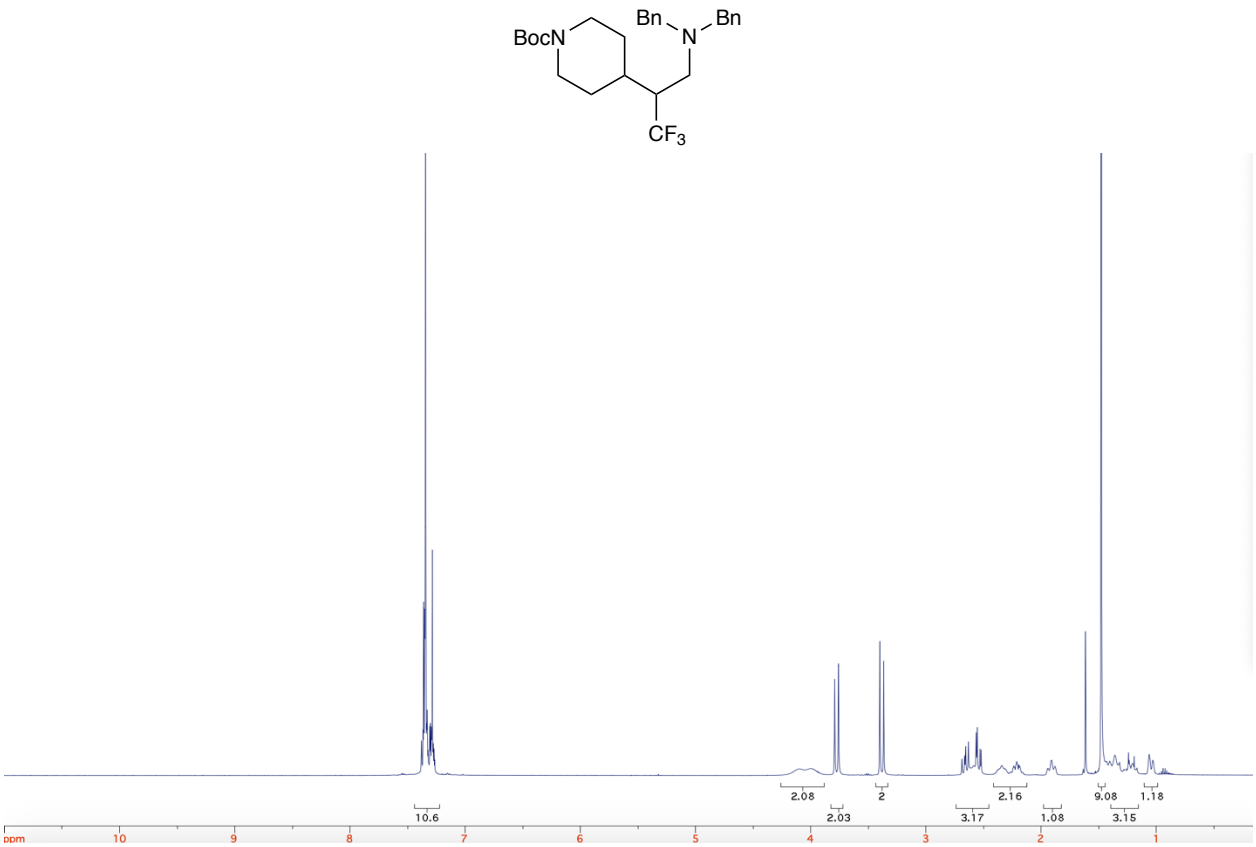
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Bn
N
Bn
CF3
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2
2.16
9.08
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10.6
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3.15
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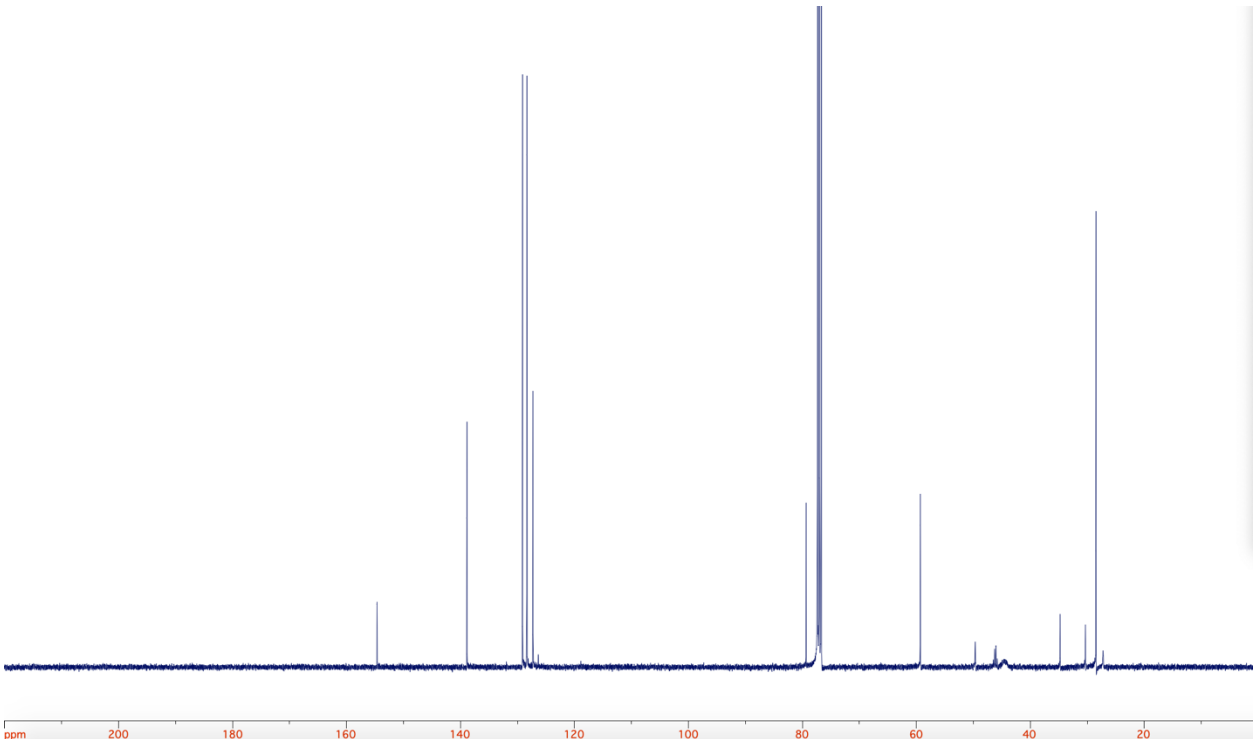
3
2
1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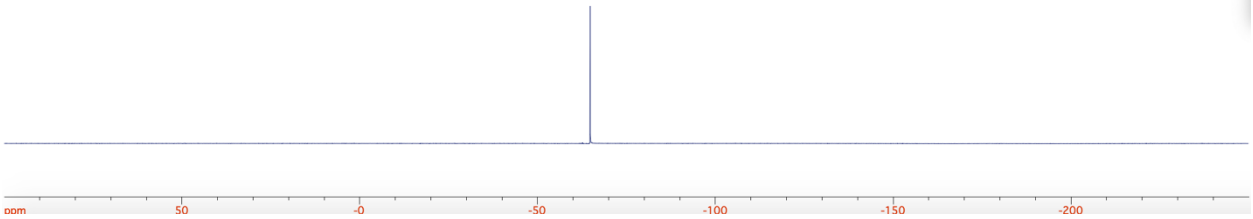
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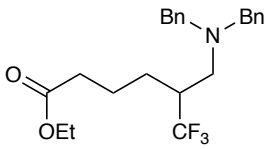
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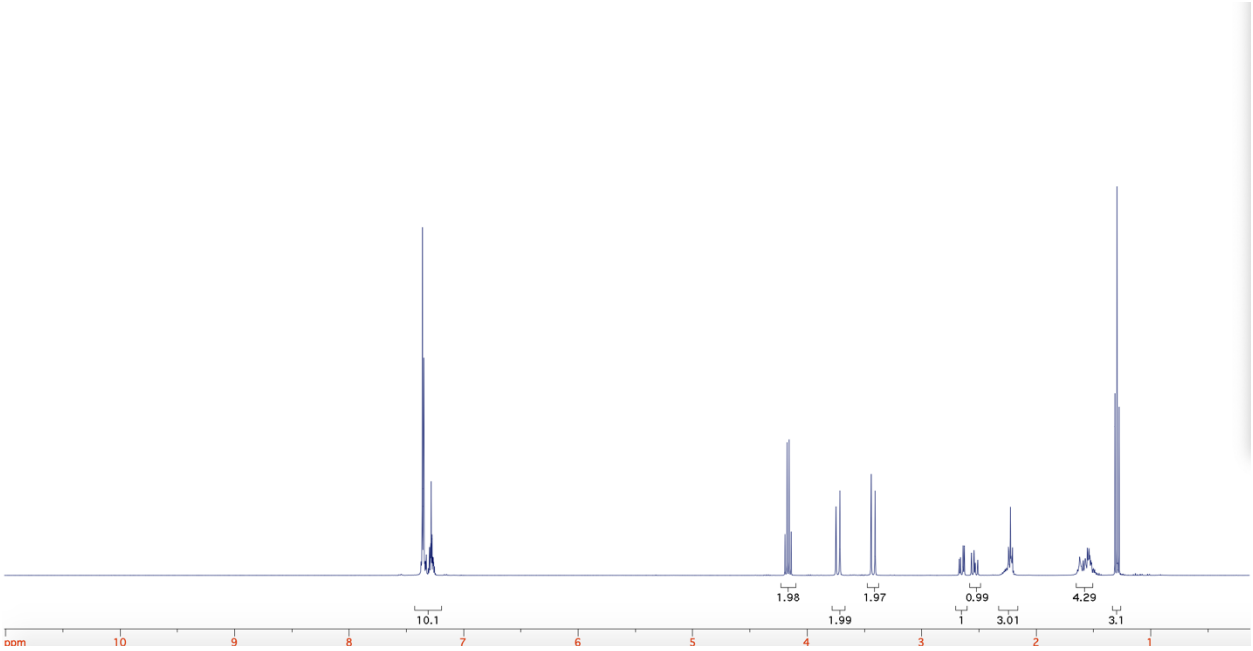
N
Bn
O
OEt
CF3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ppm
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2
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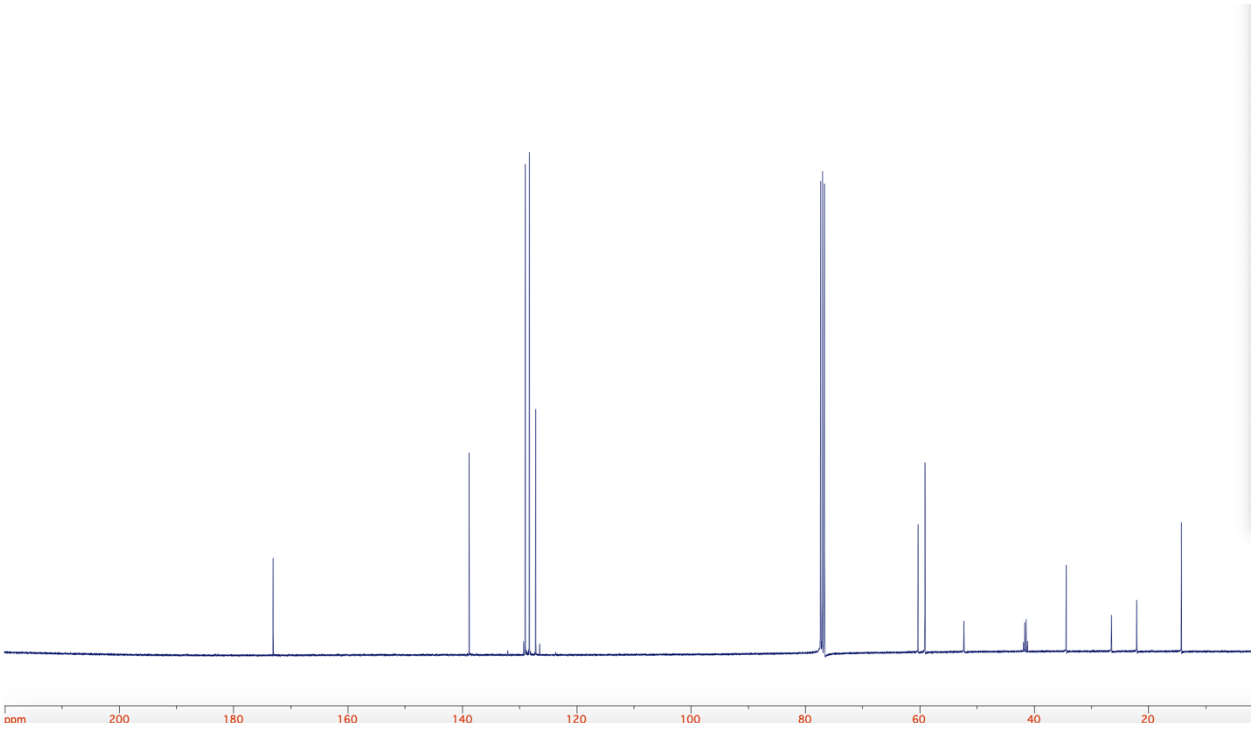
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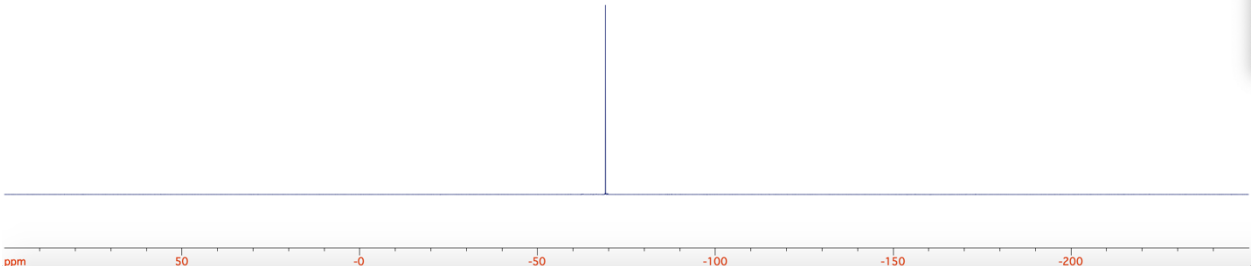
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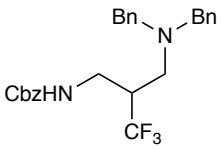
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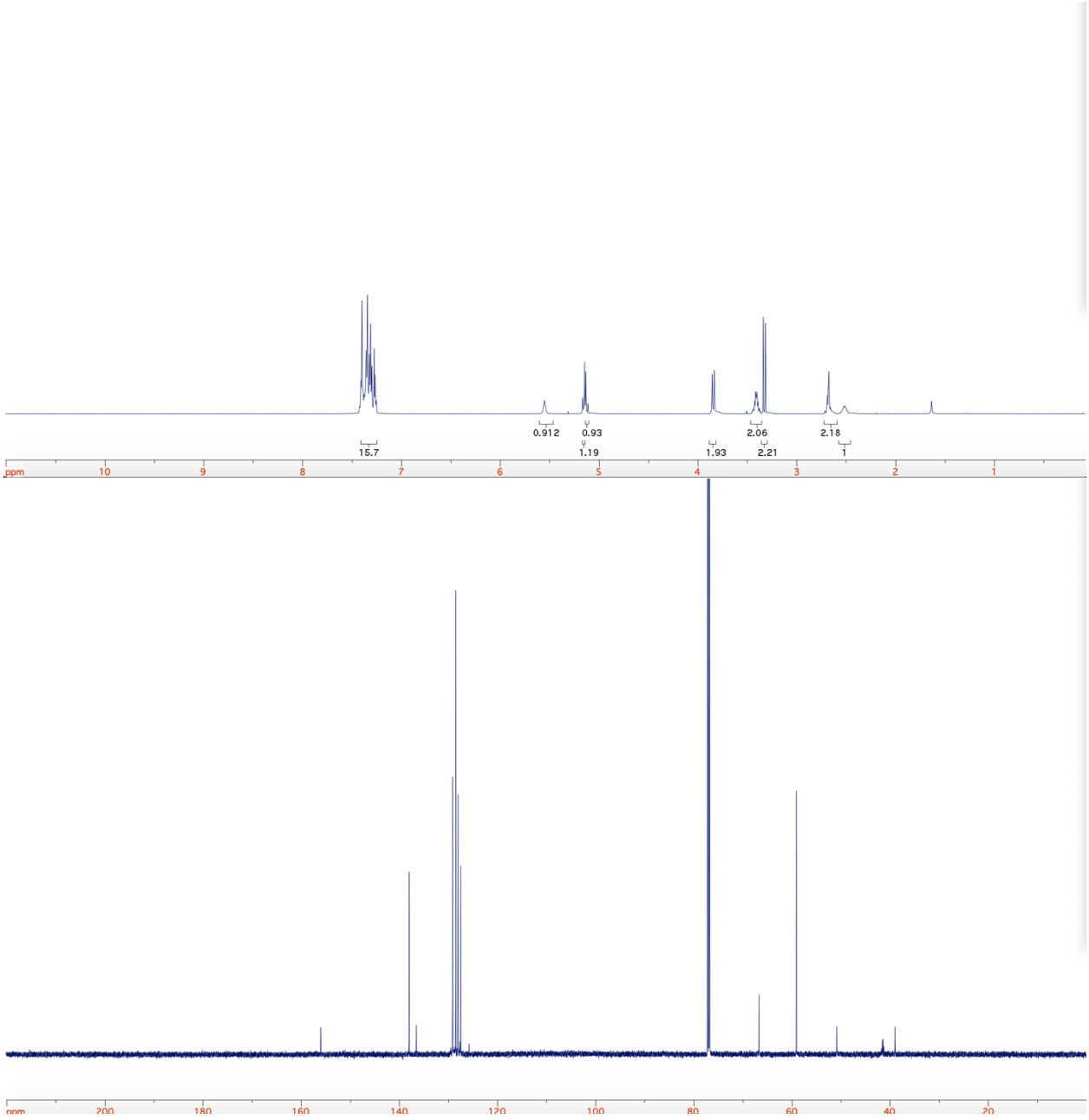
CF3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1.93
2.21
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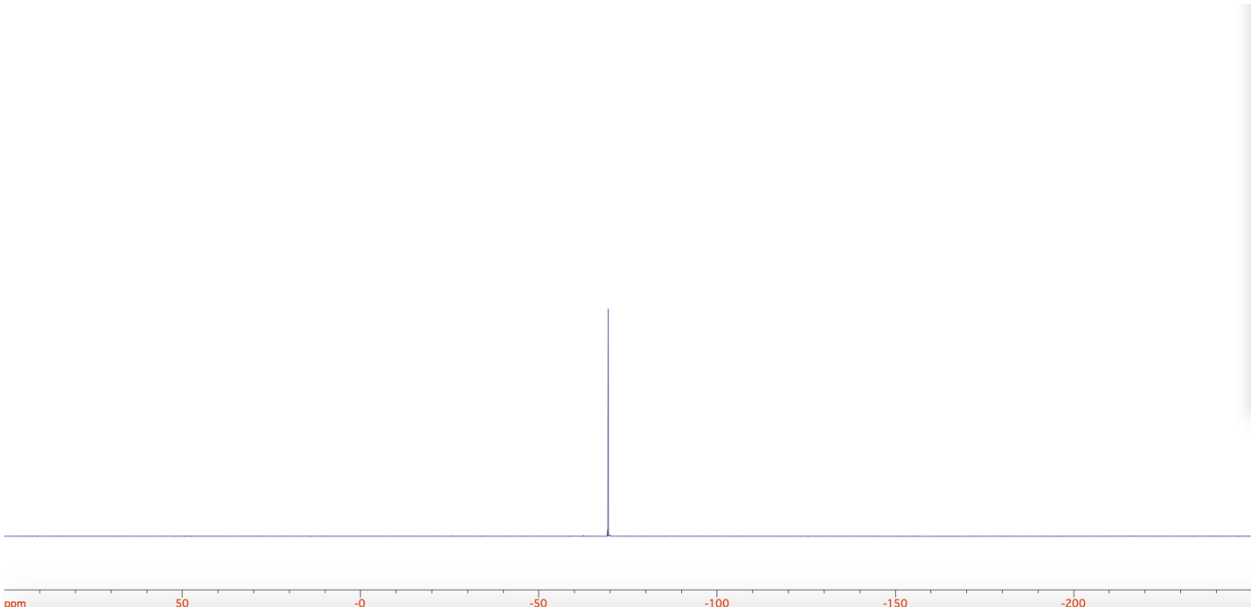
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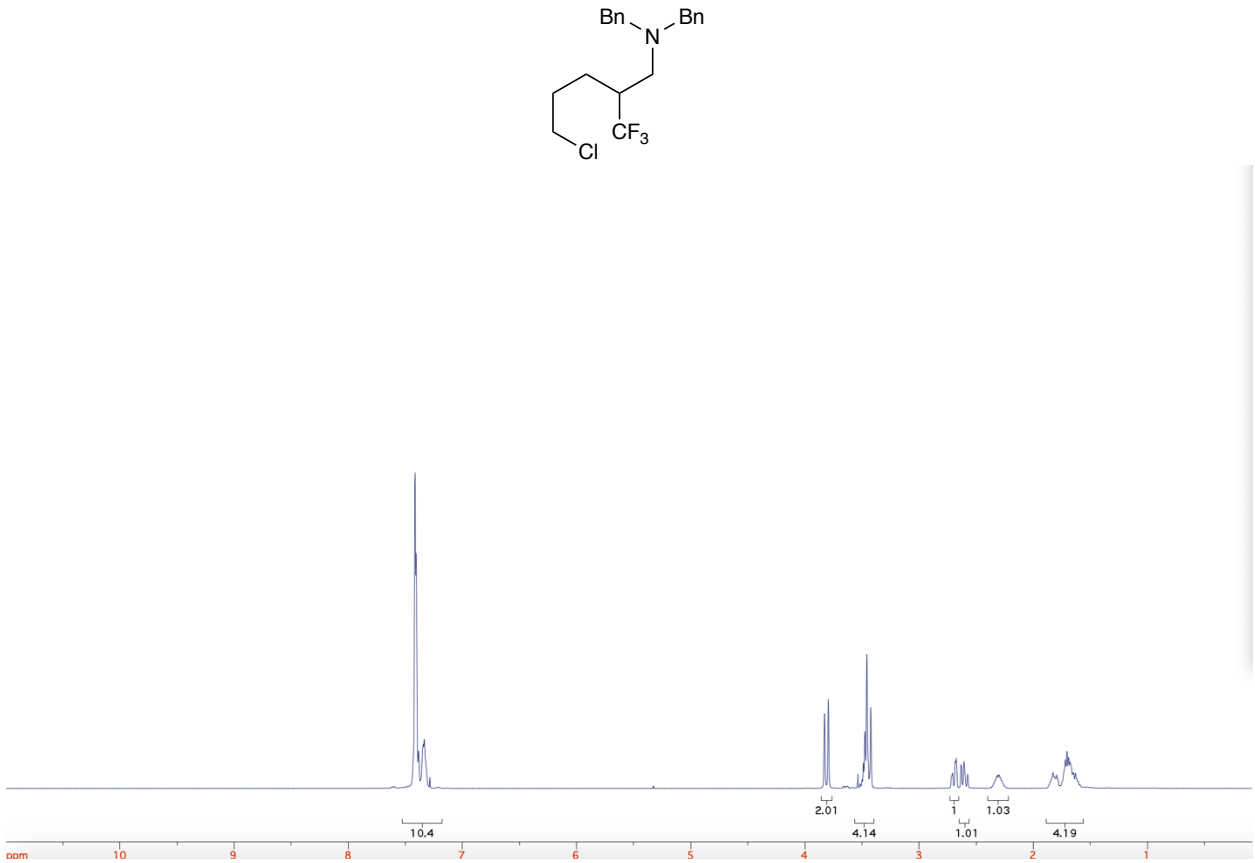
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Bn
CF3
Cl
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4.19
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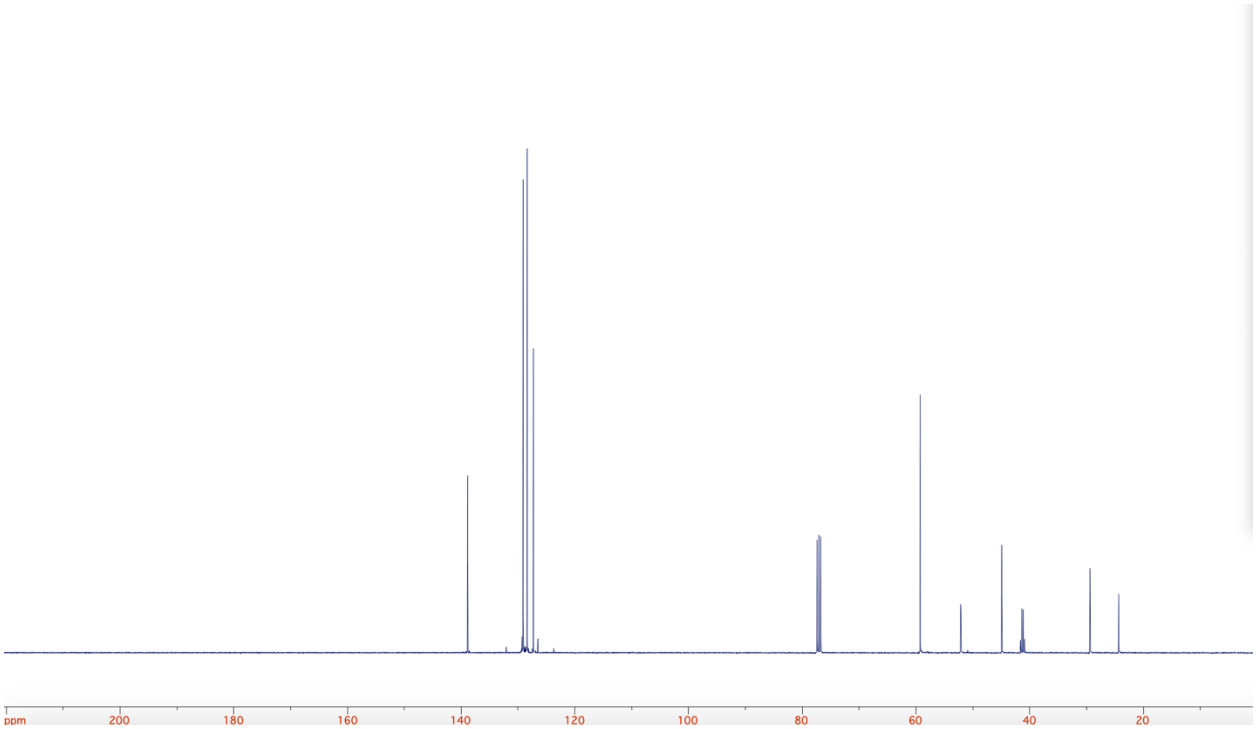
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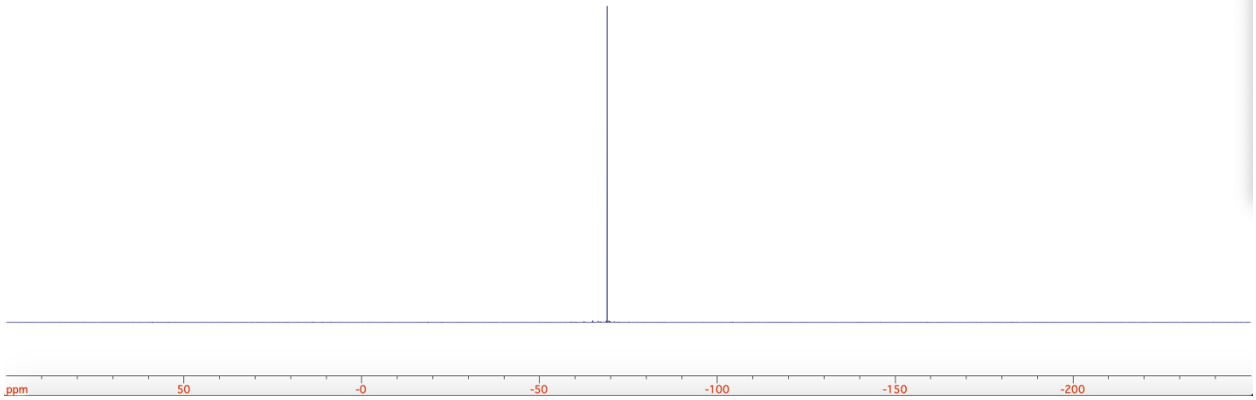
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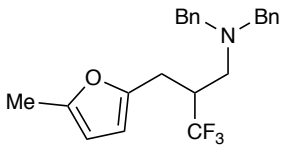
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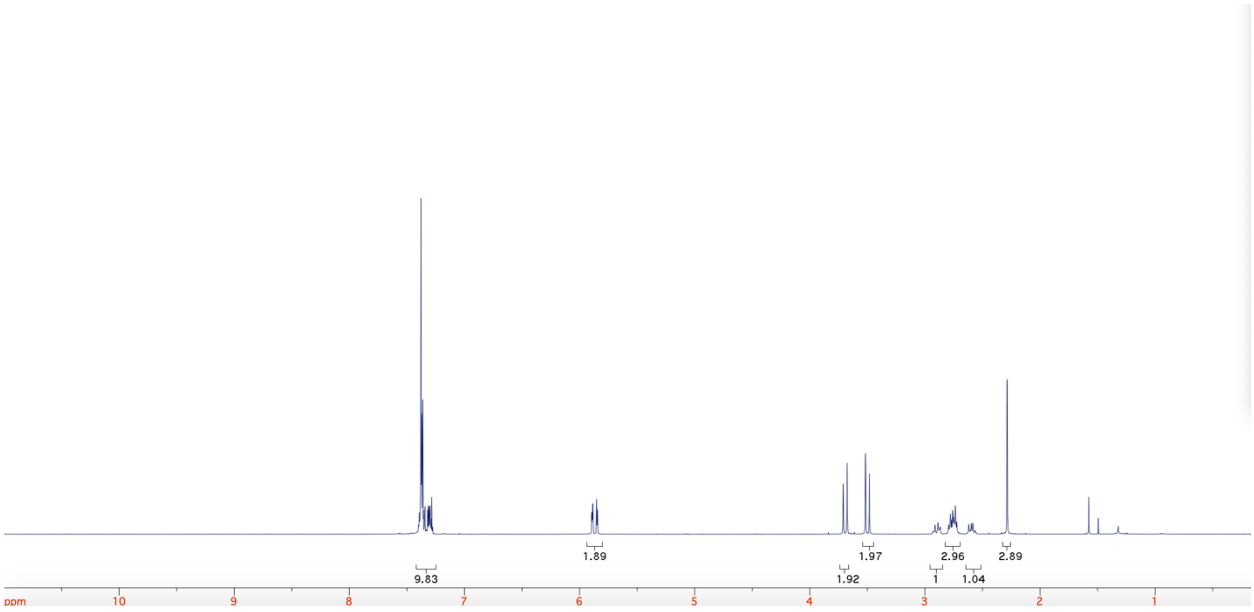
Bn
O
Me
CF3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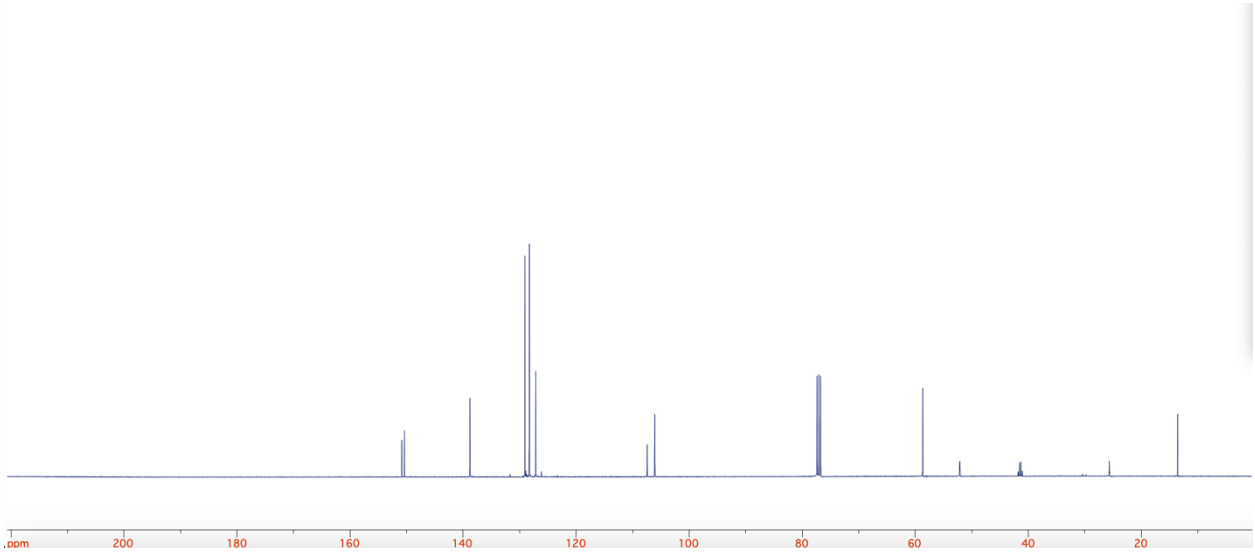
1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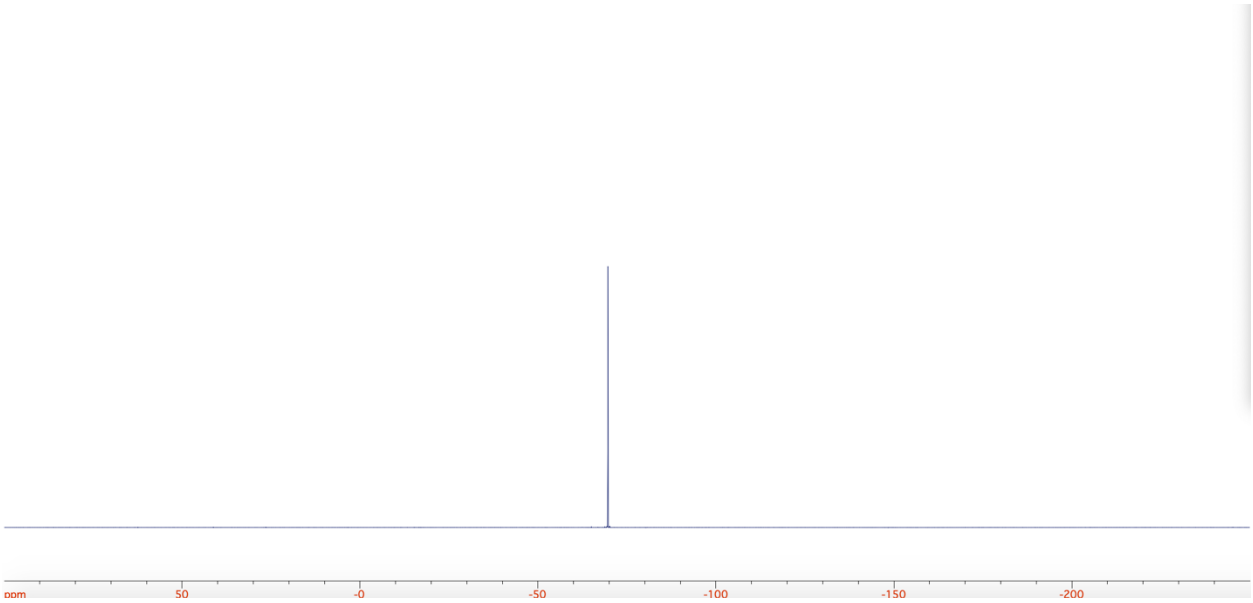
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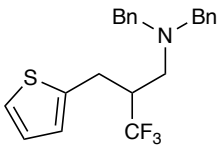
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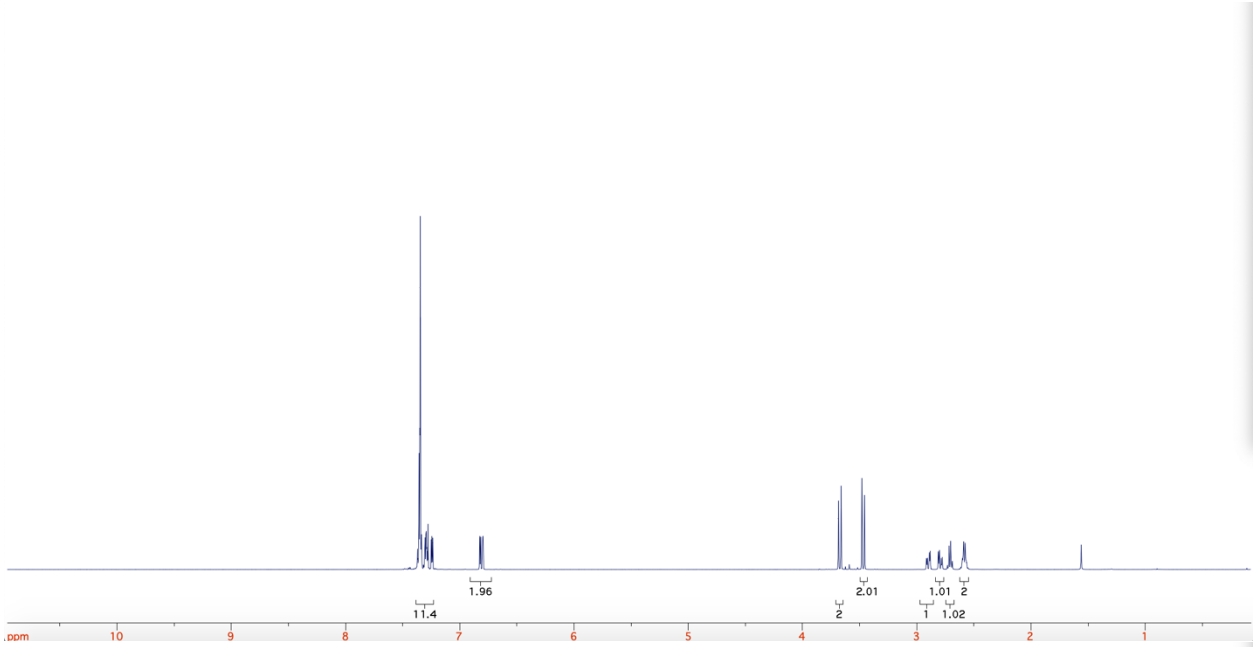
Bn
S
CF3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1.01
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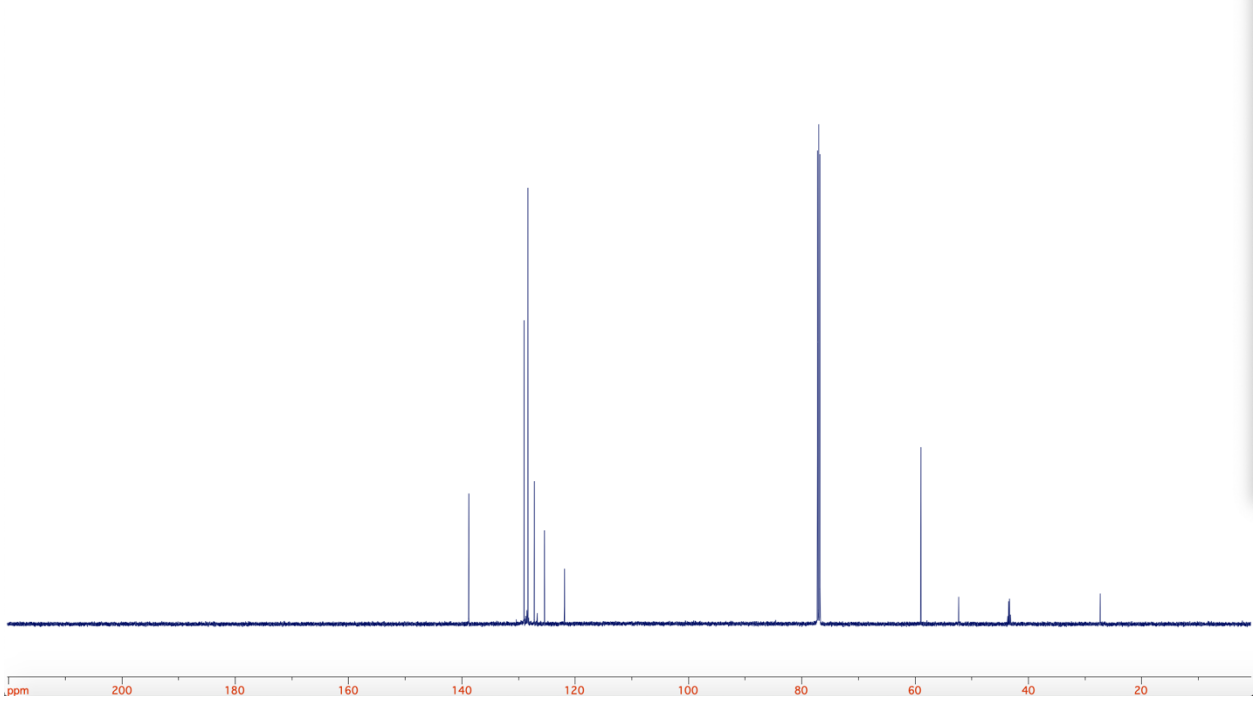
4
3
2
1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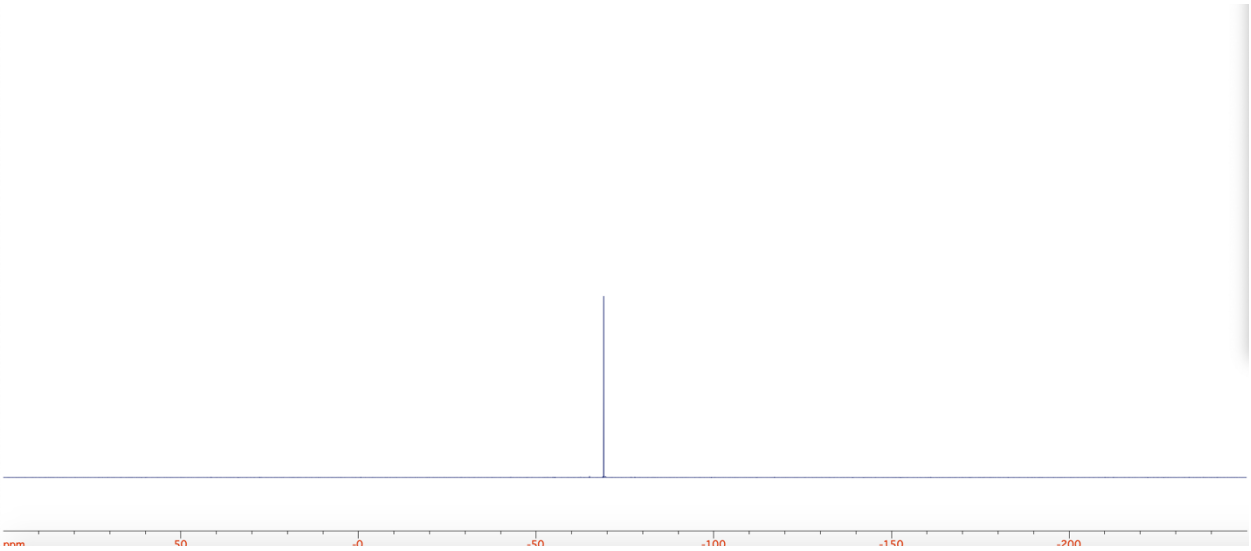
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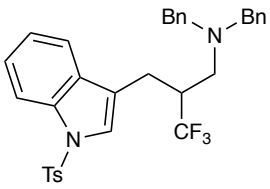
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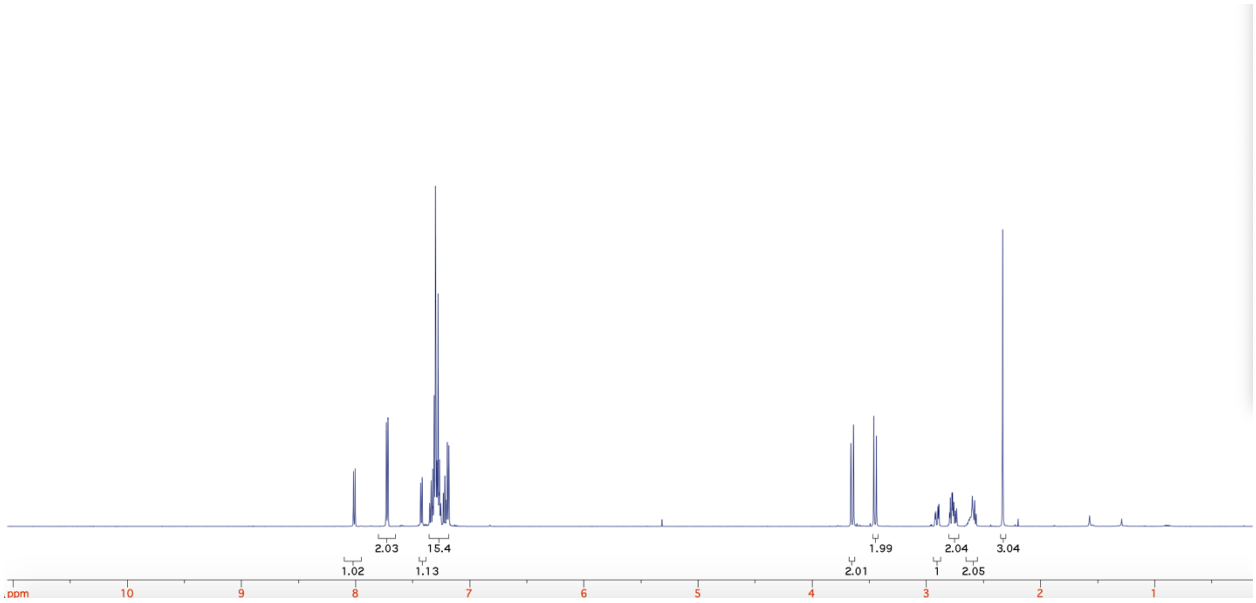
Bn
N
Ts
CF3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1.02
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1
2.05
ppm
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8
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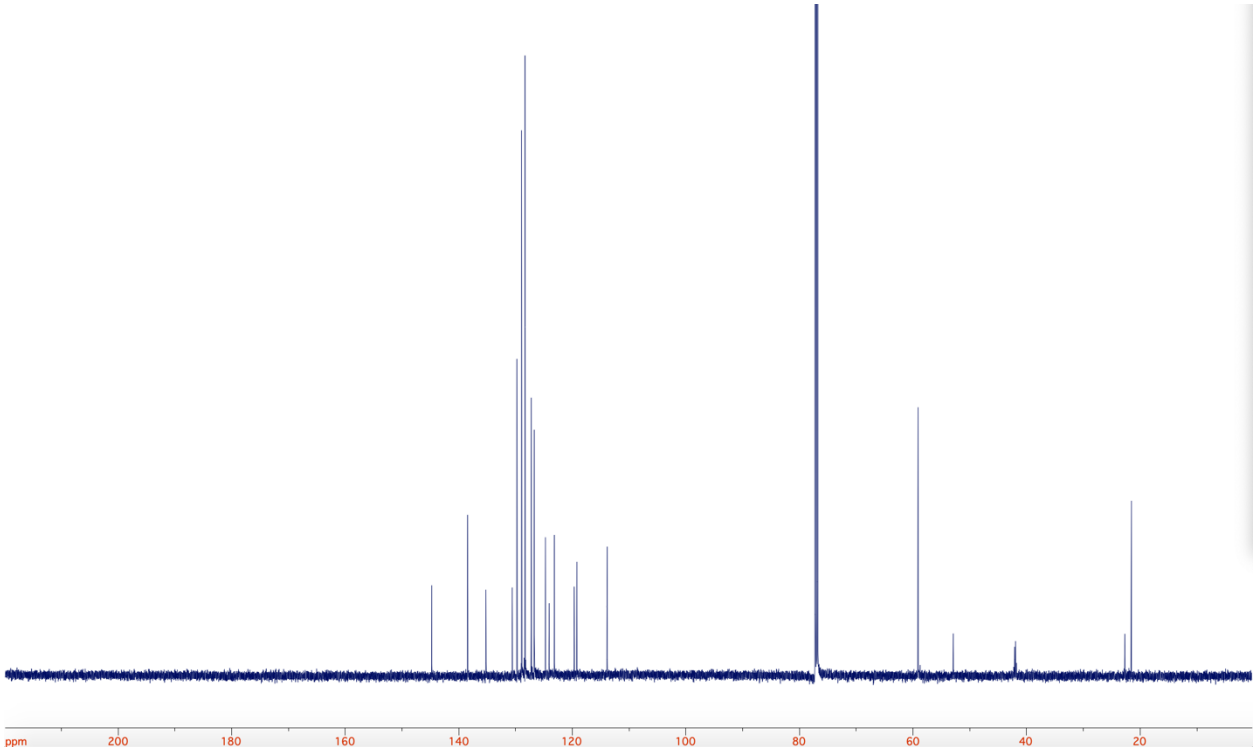
4
3
2
1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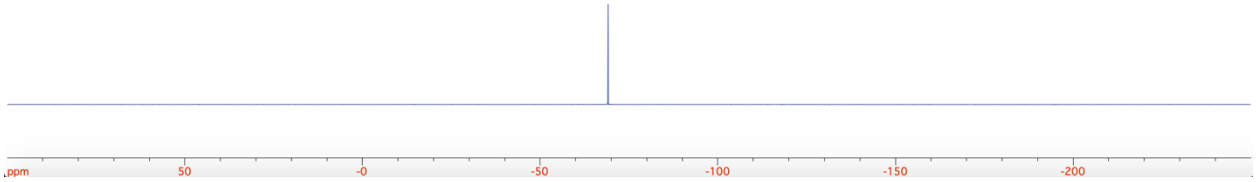
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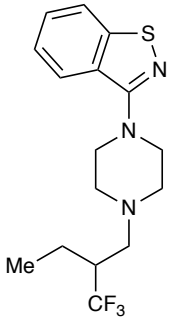
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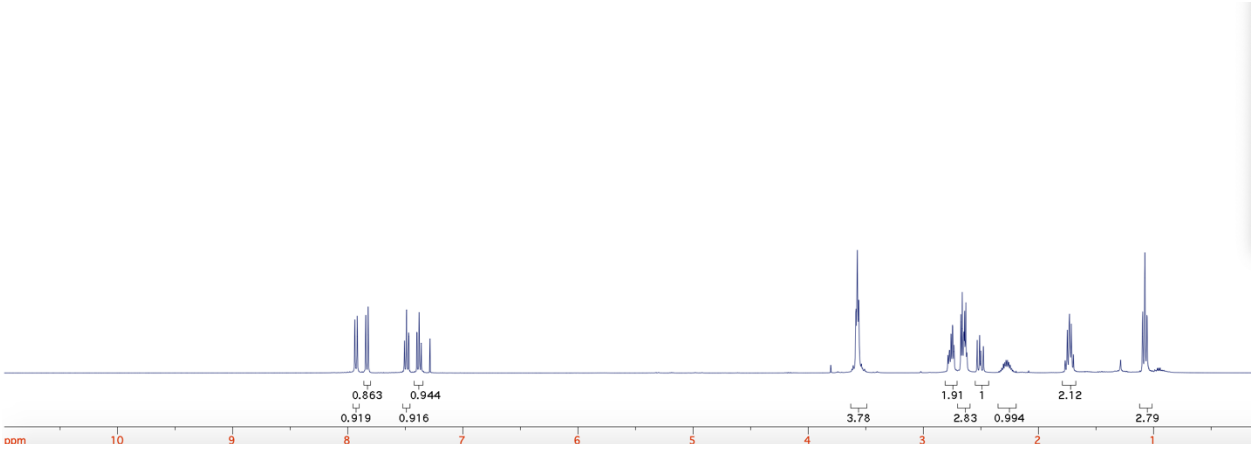
N
N
N
Me
CF3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0.916
3.78
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0.994
2.12
2.79
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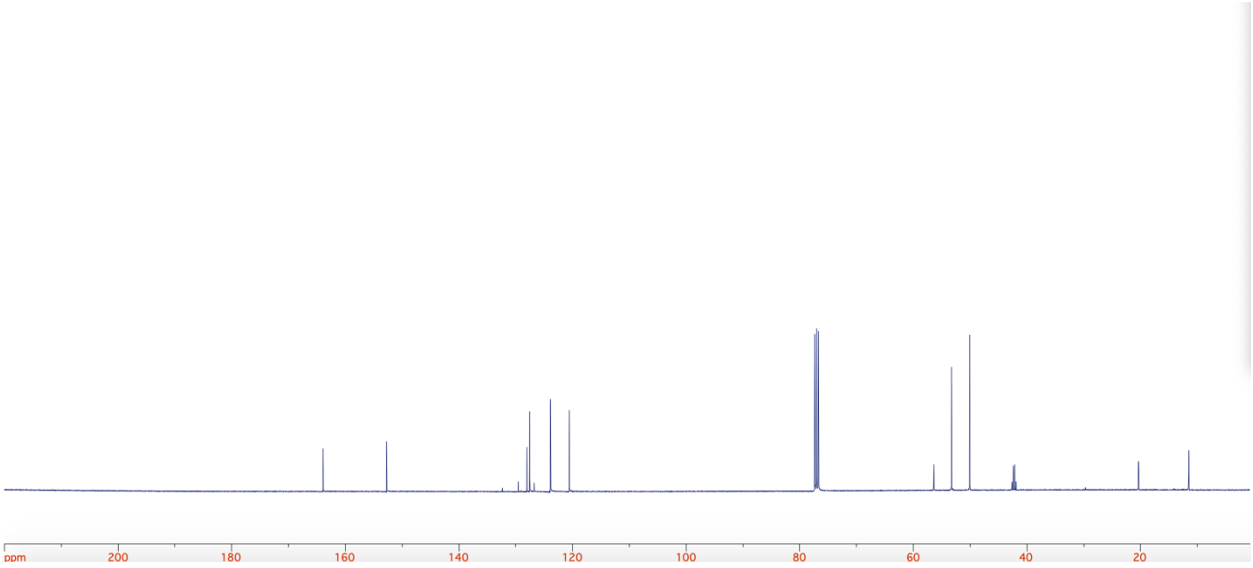
4
3
2
1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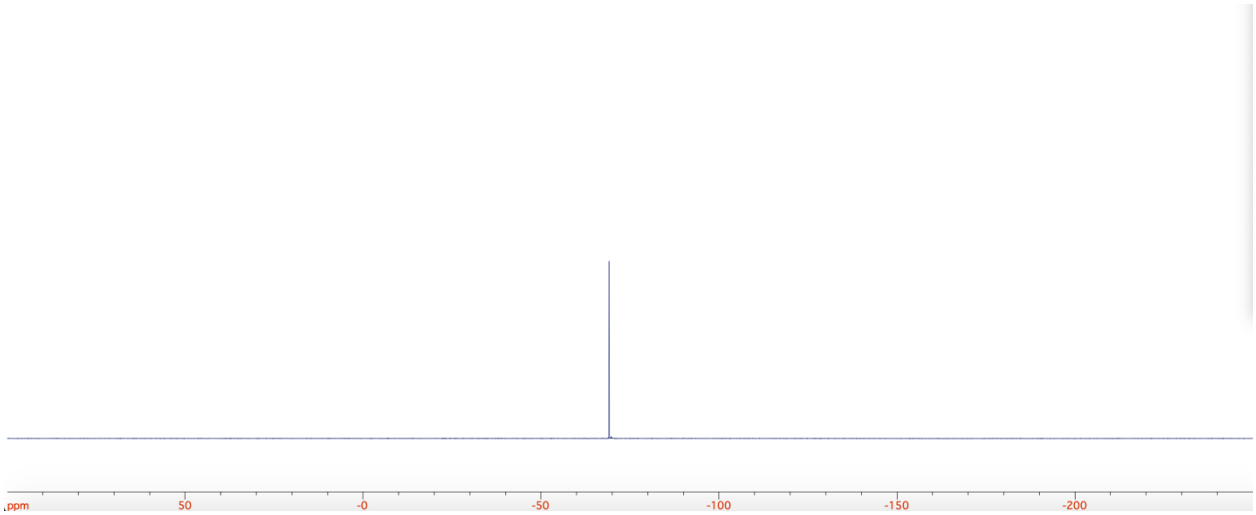
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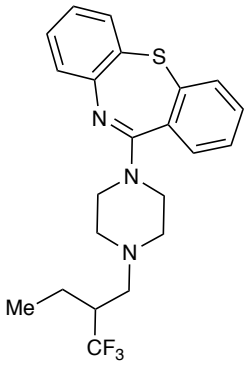
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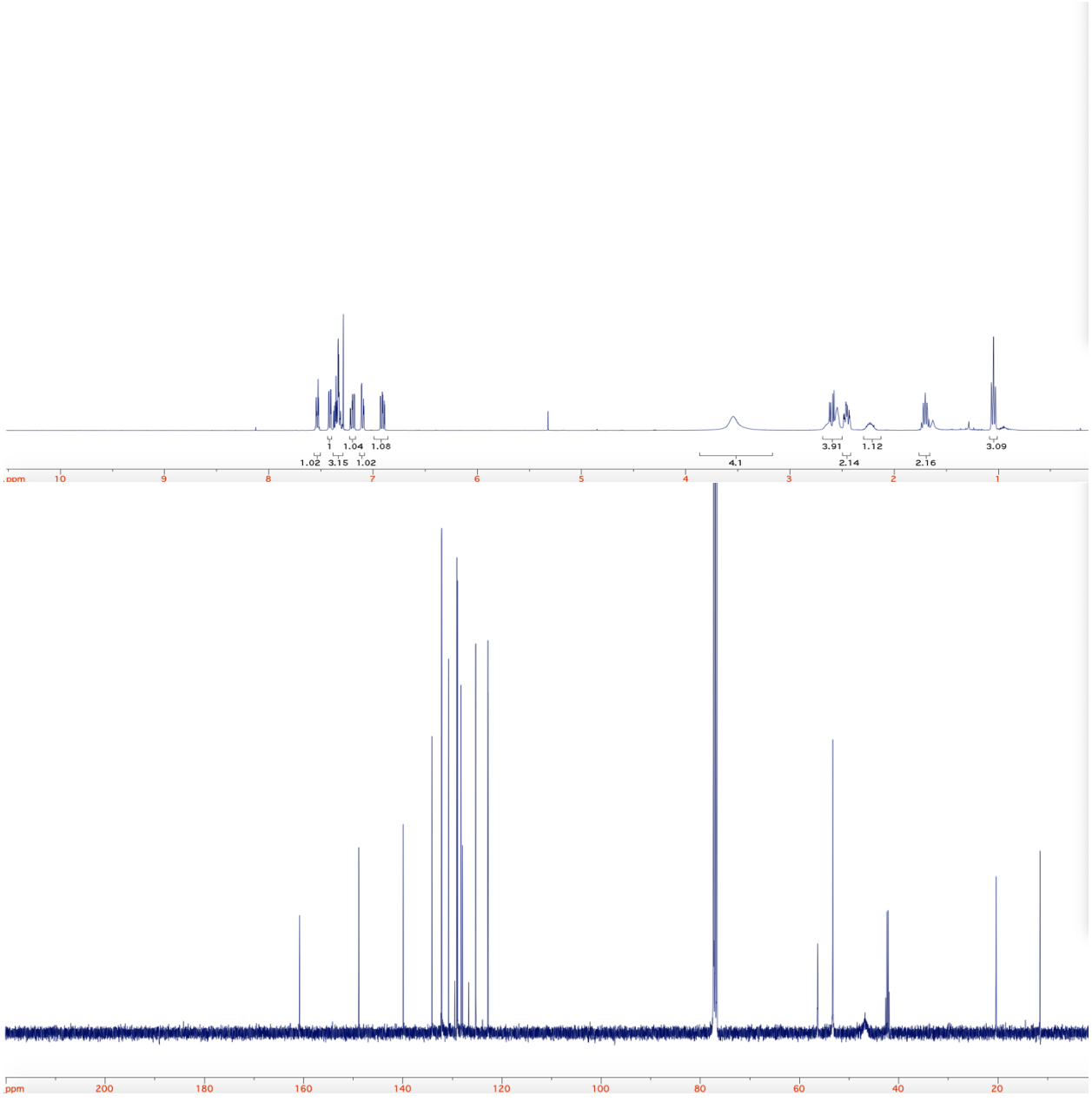
N
N
Me
CF3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1.08
1.02
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1.02
4.1
3.91
1.12
2.14
2.16
3.09
ppm
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8
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5
4
3
2
1
ppm
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80
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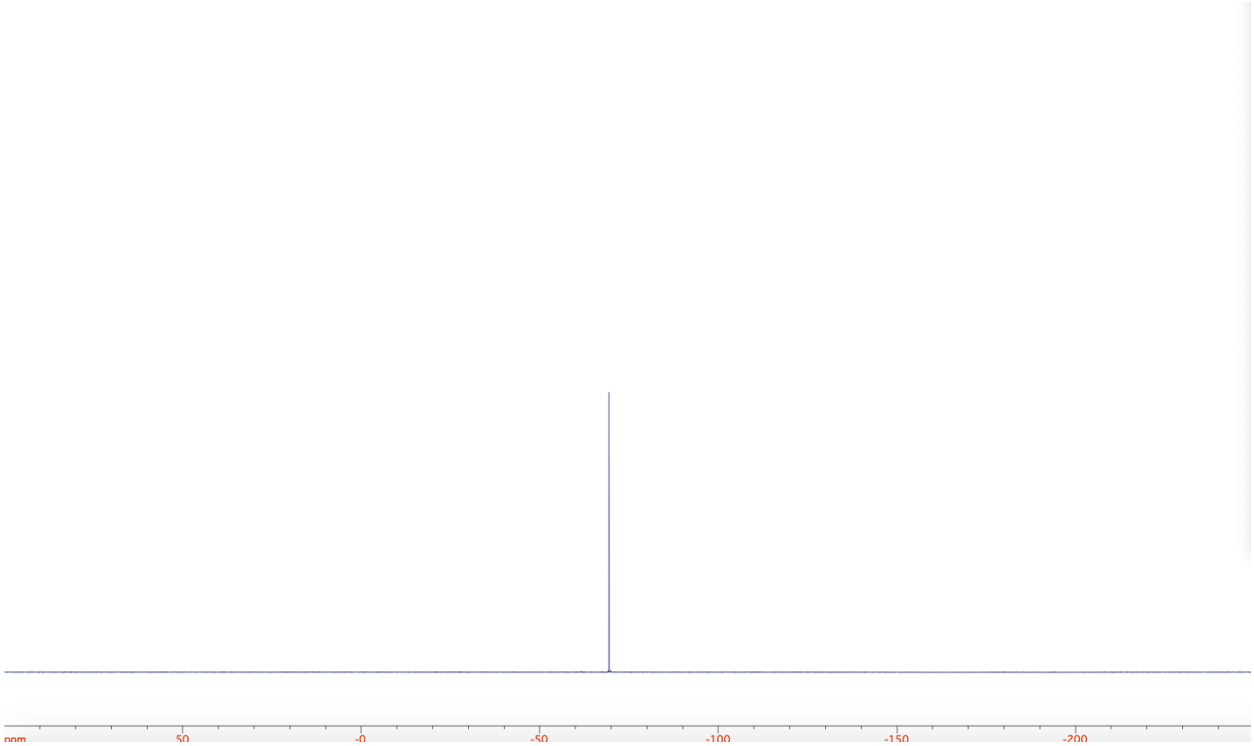
40
20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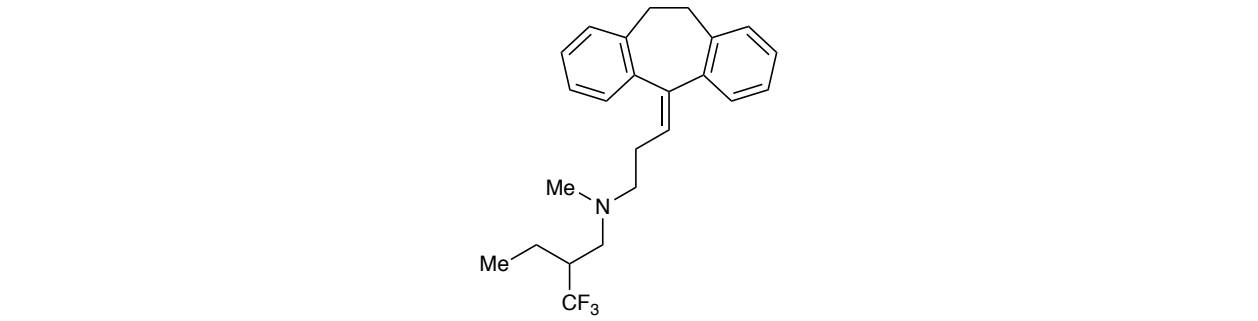
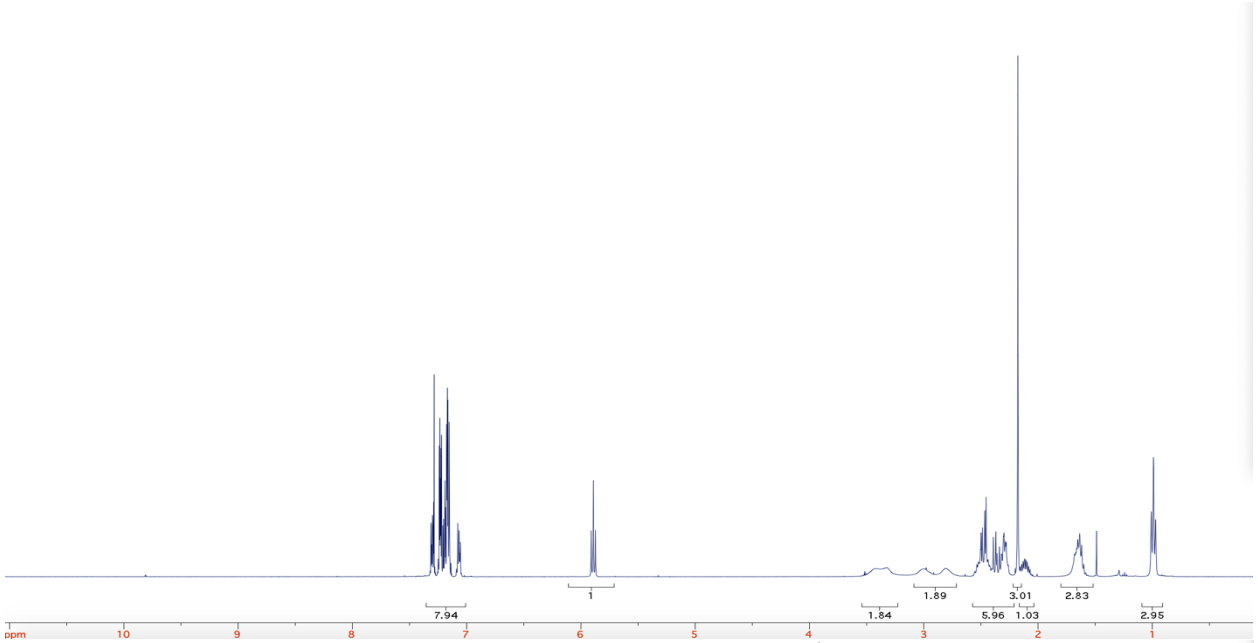

Me
N
Me
CF3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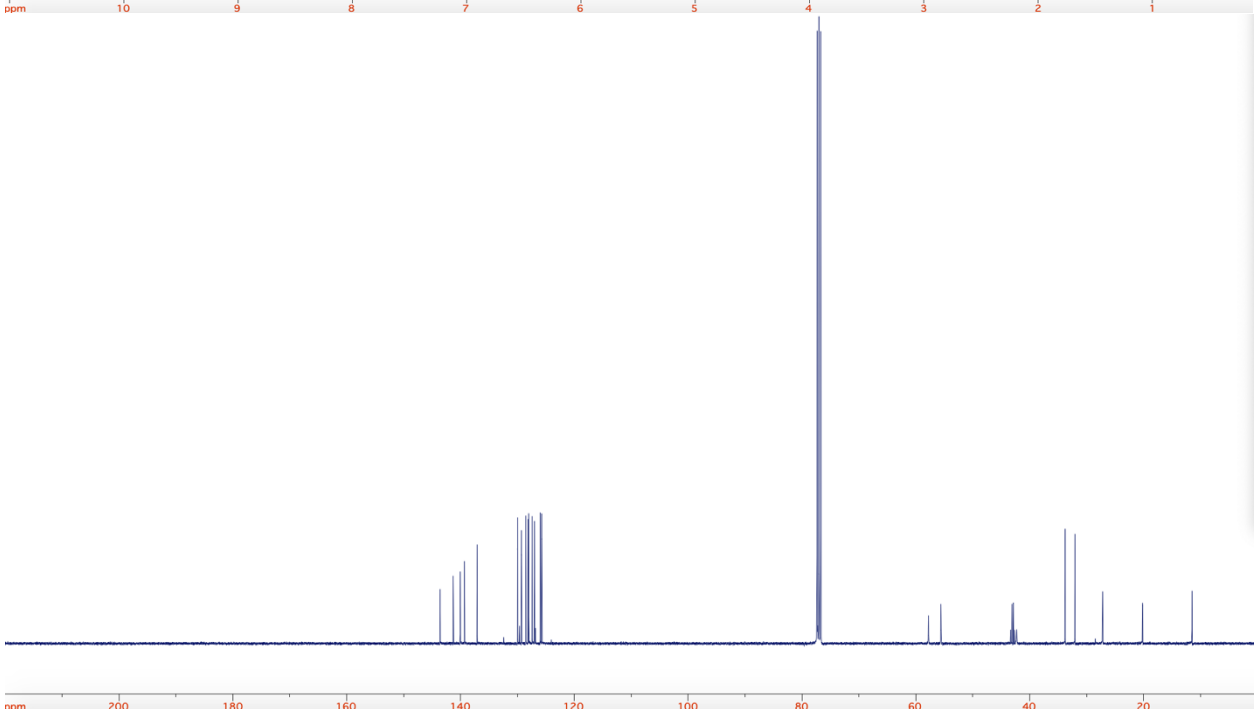
1
1.84
1.89
5.96
3.01
1.03
2.83
2.95
ppm
10
9
8
7
6
5
4
3
2
1


ppm
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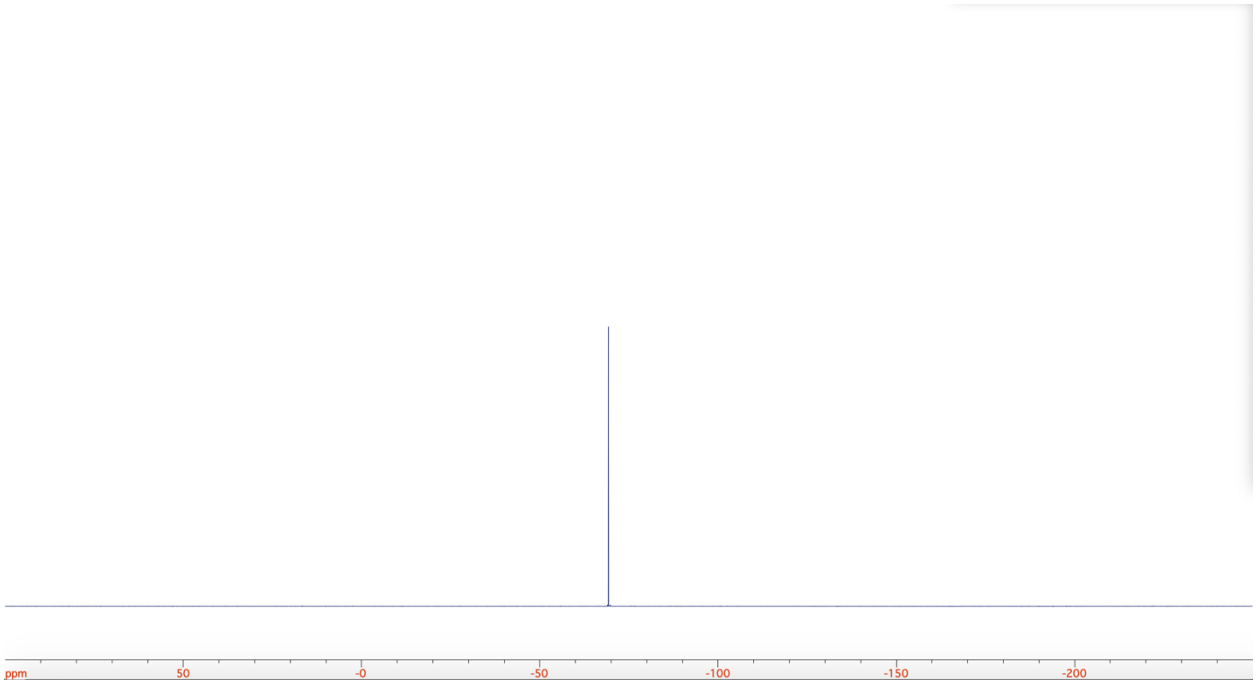
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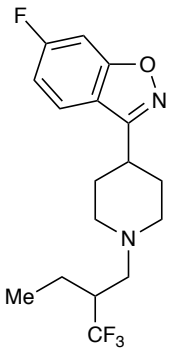
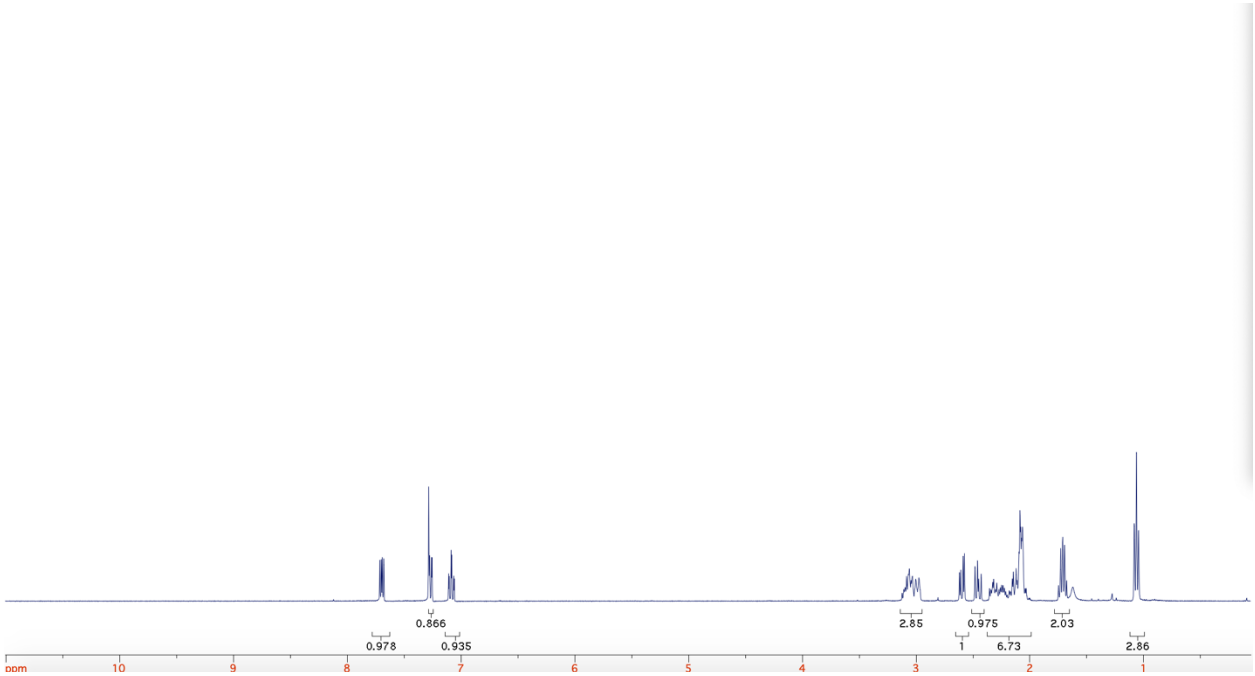
-200


F
O
N
N
Me
CF3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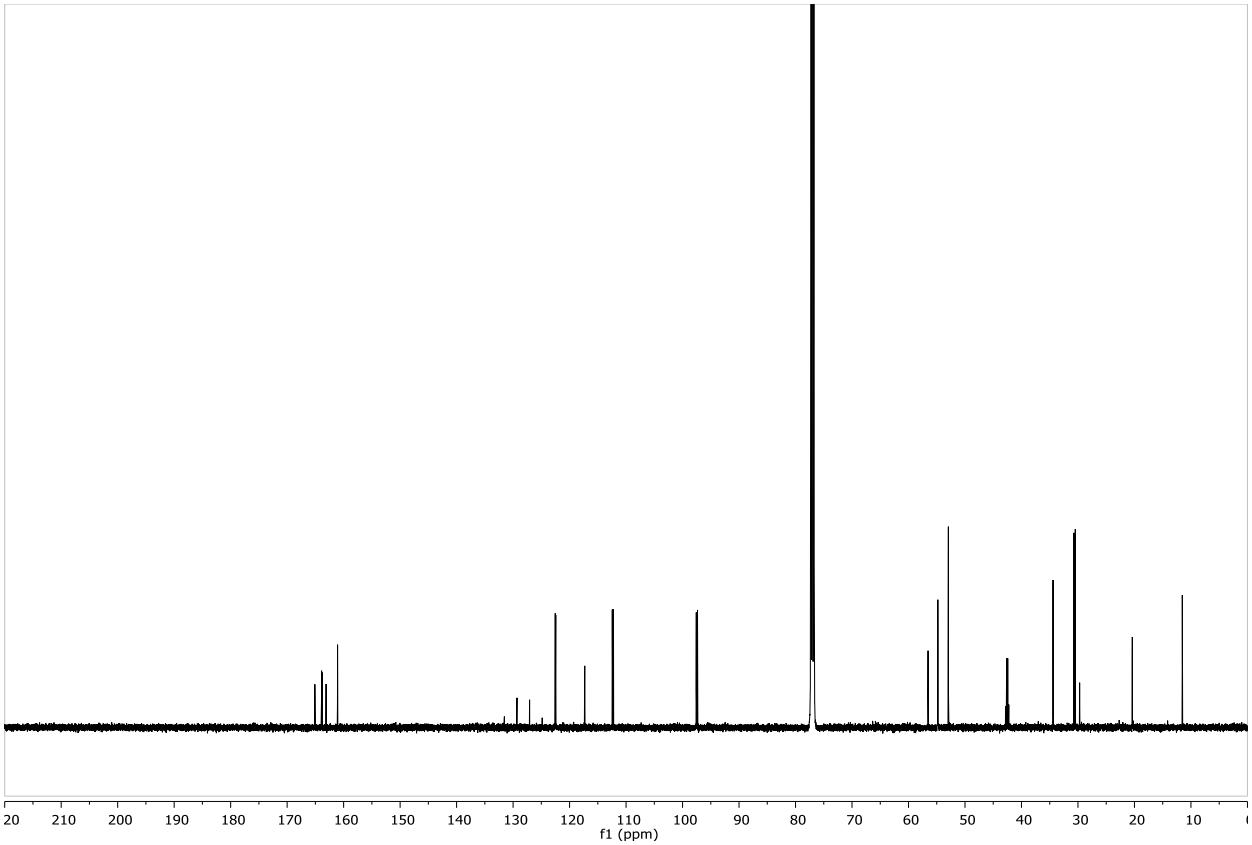
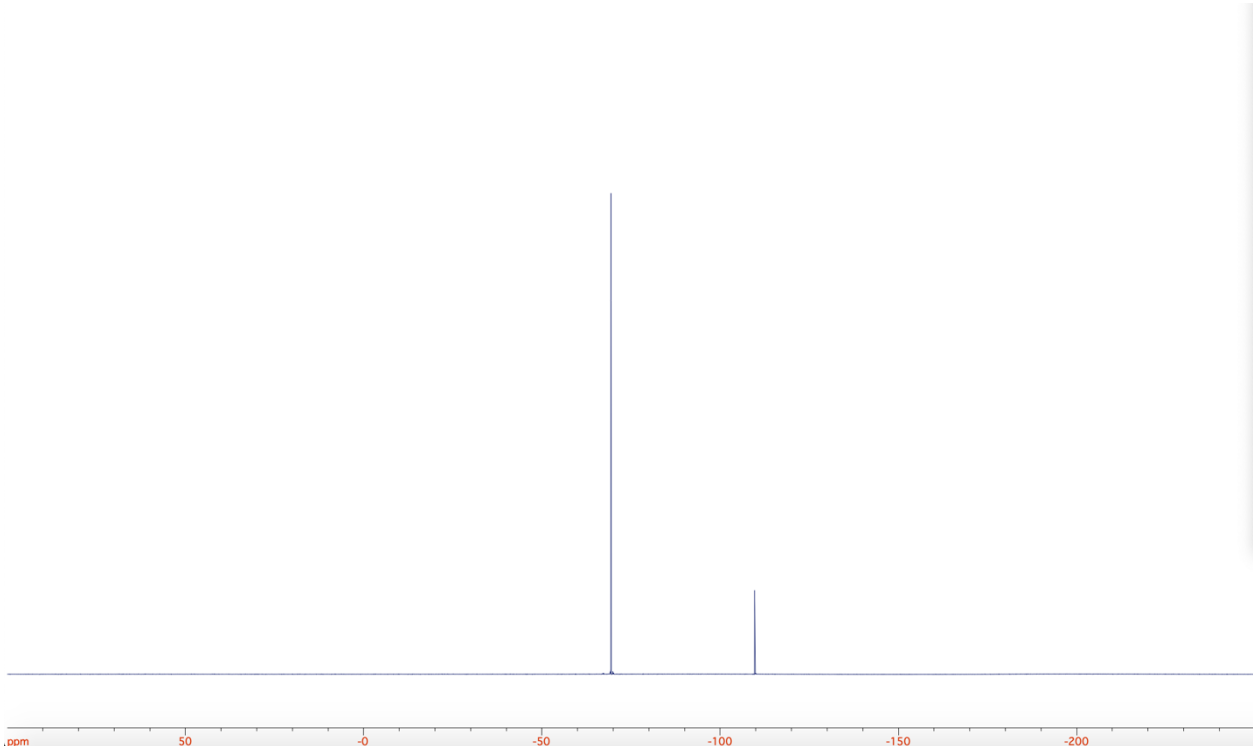
0.935
2.85
1
0.975
6.73
2.03
2.86
ppm
10
9
8
7
6
5
4
3
2
1


20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


ppm
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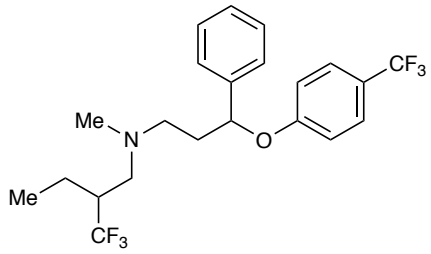
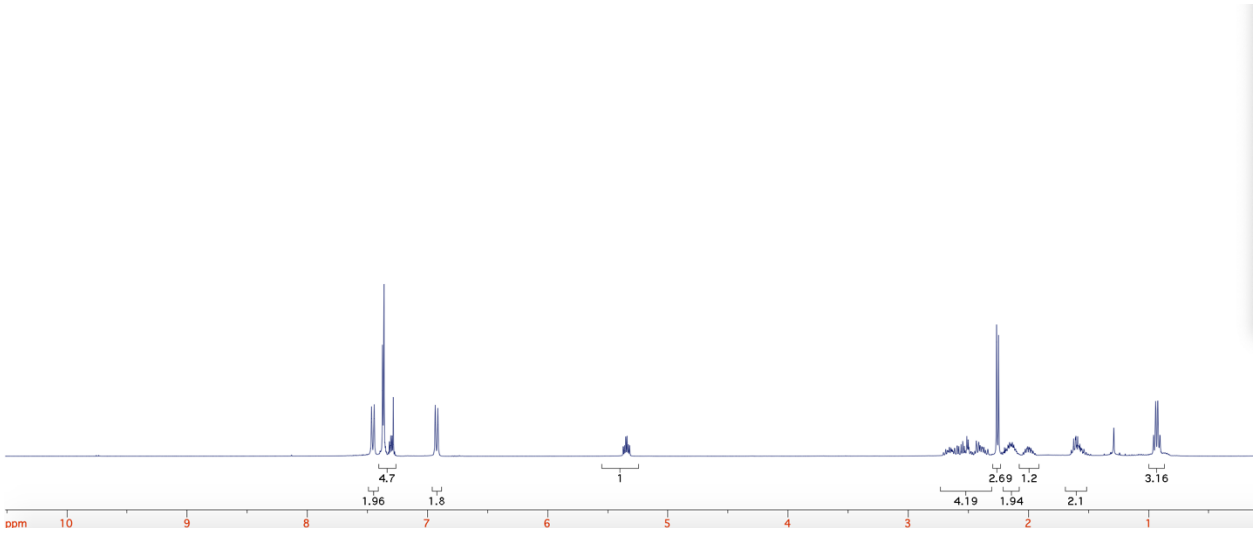
-100
-150
-200


Me
N
O
CF3
Me
CF3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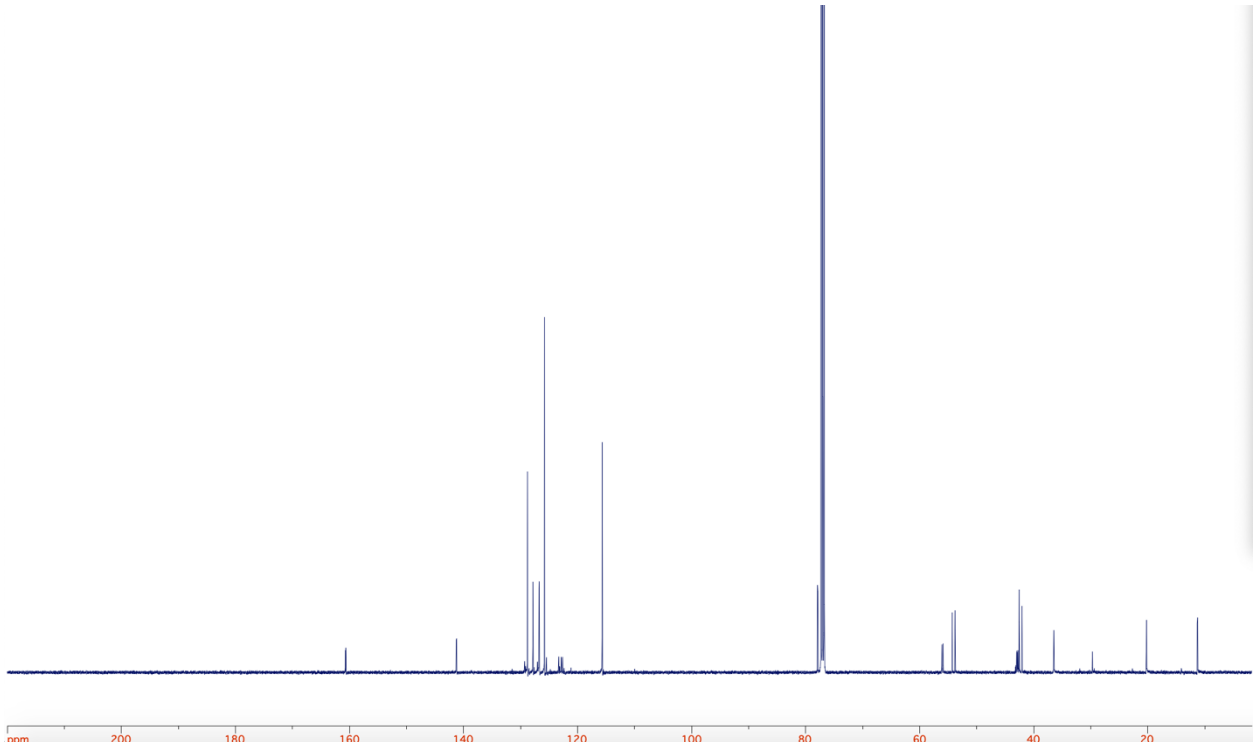
1.96
1.8
1
2.69
1.2
4.19
1.94
2.1
3.16
ppm
10
9
8
7
6
5
4
3
2
1


ppm
200
180
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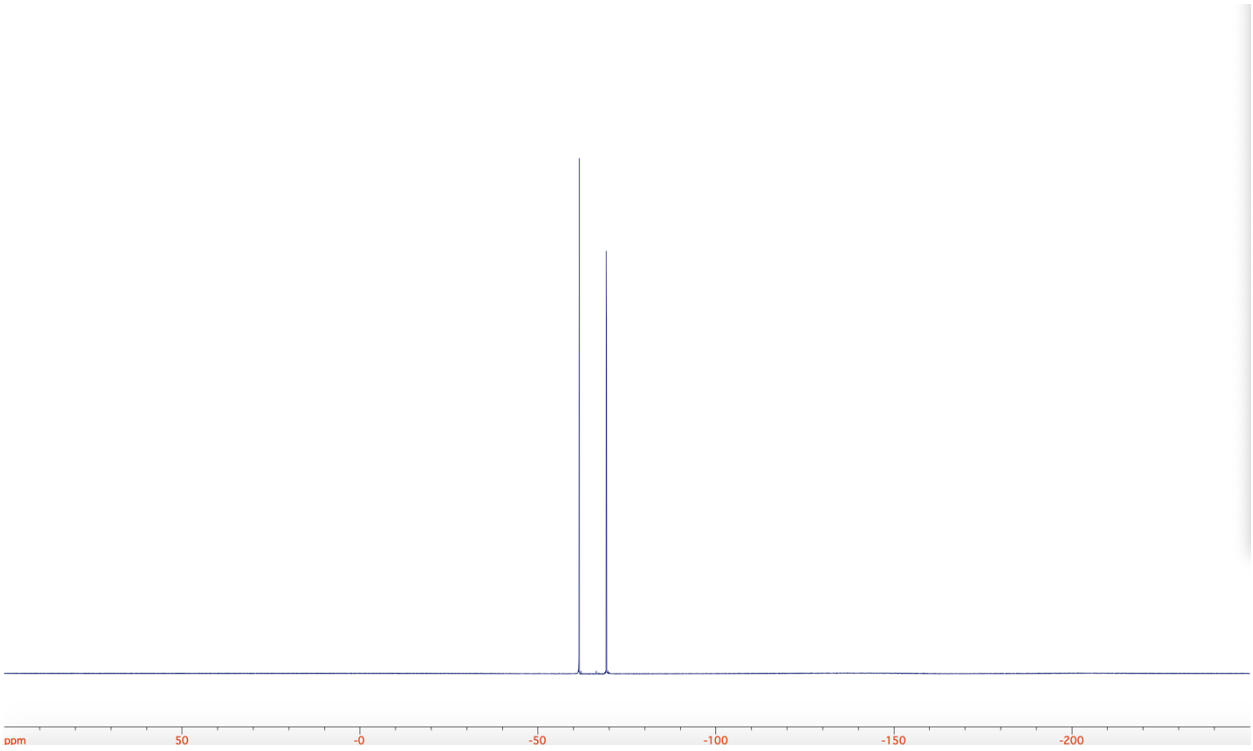
140
120
100
80
60
40
20


ppm
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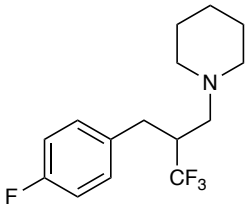
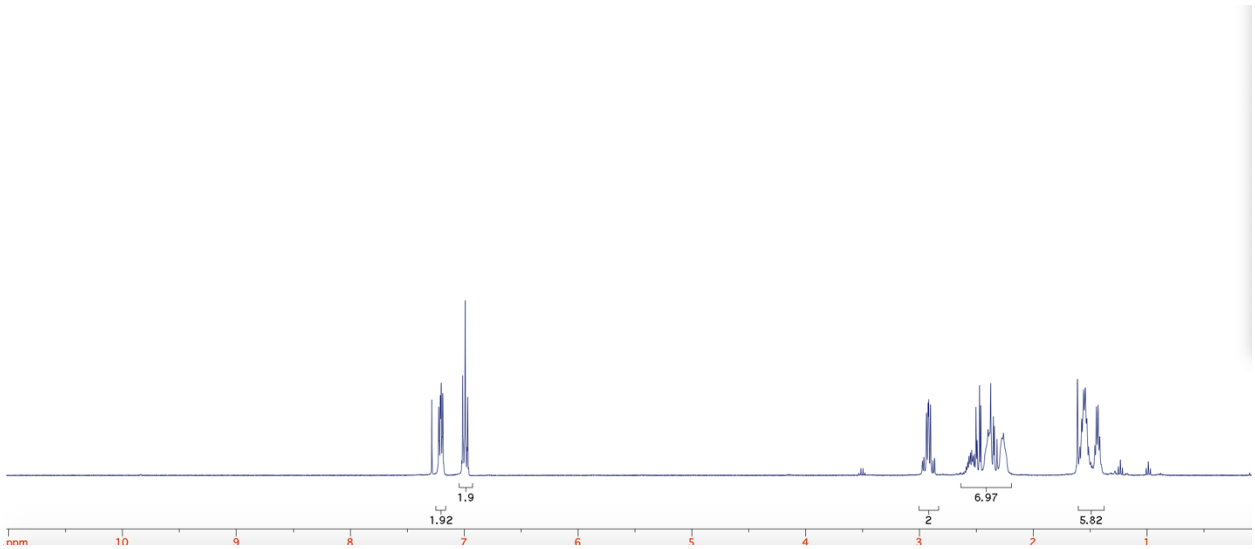
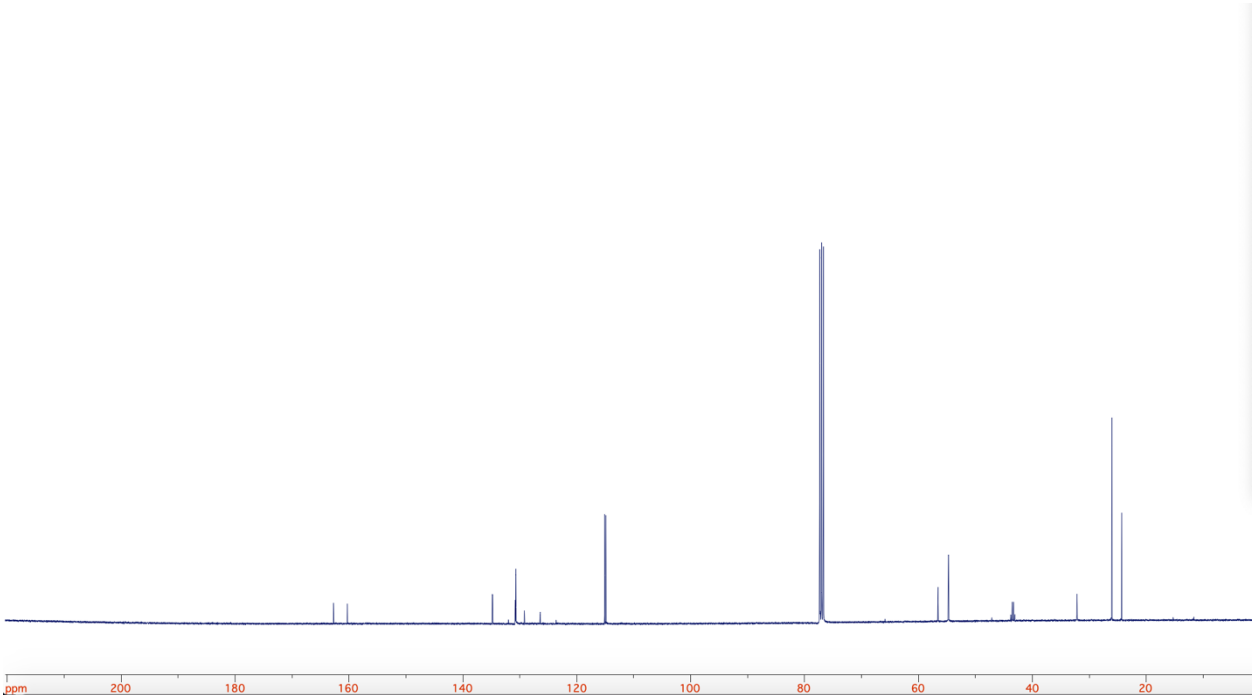
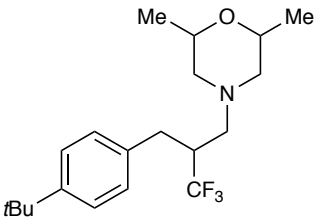
-100
-150
-200

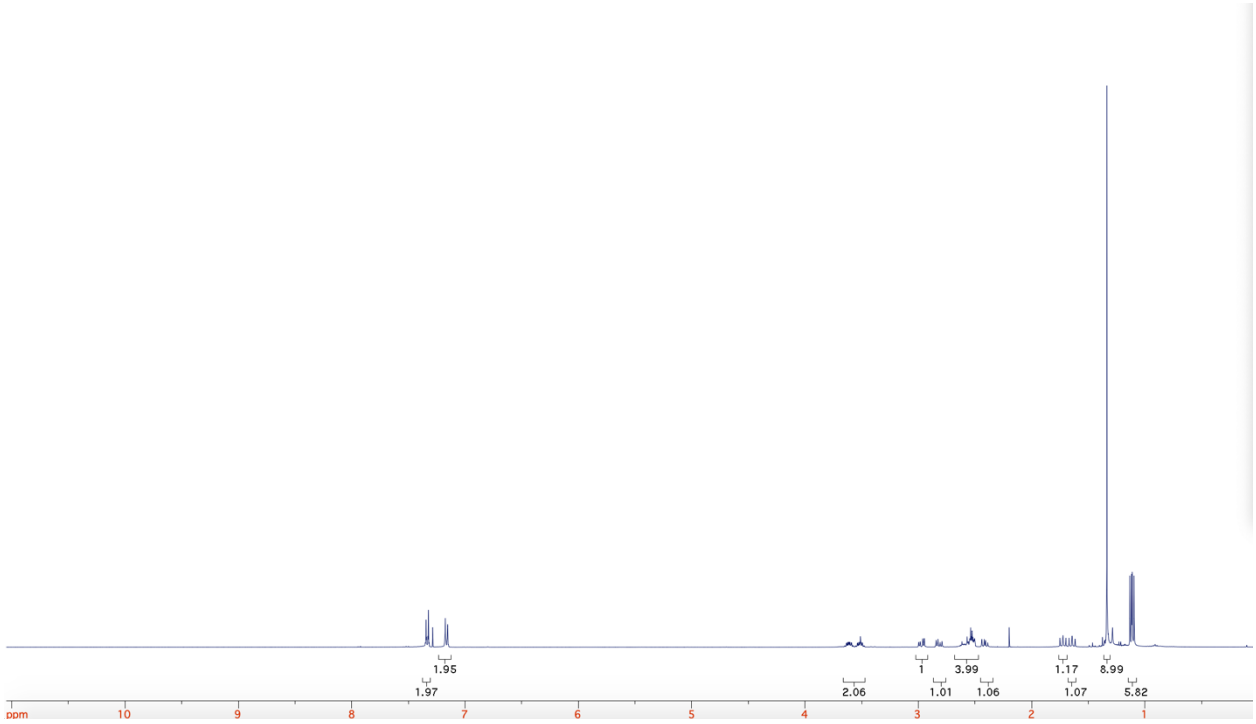

N
F
CF3

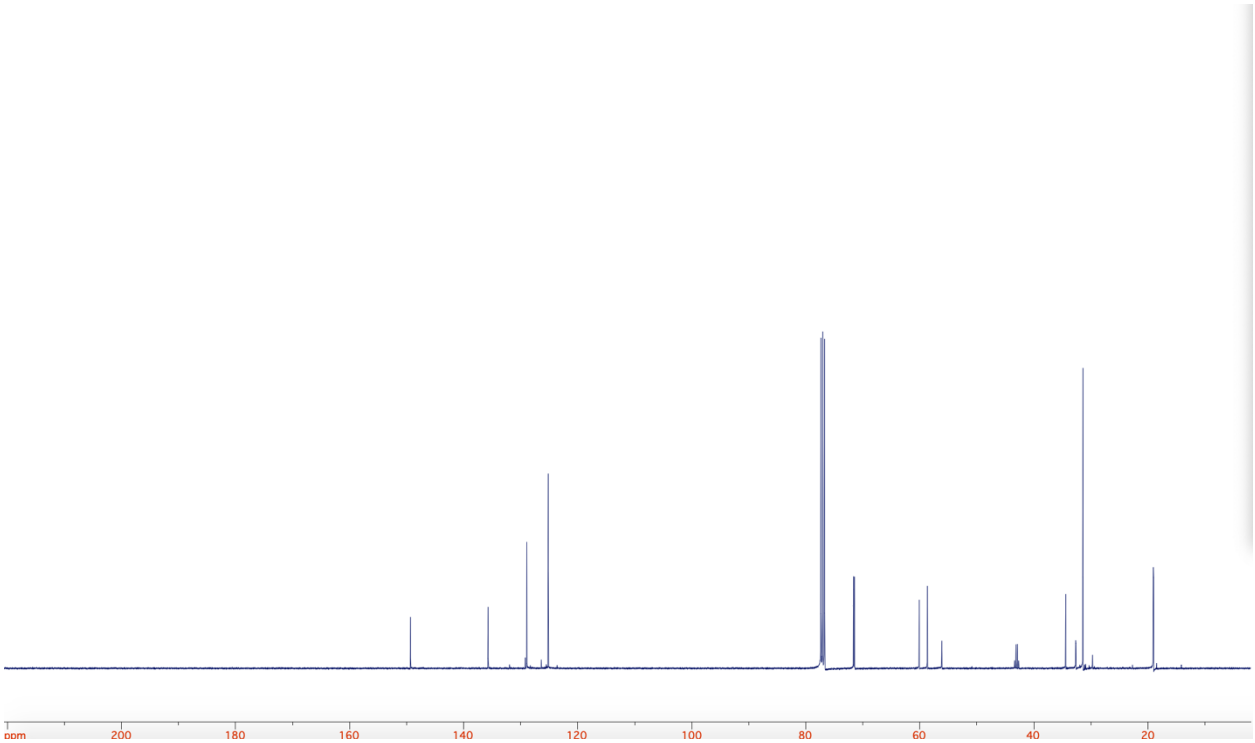

1.9
1.92
6.97
2
5.82
ppm
10
9
8
7
6
5
4
3
2
1

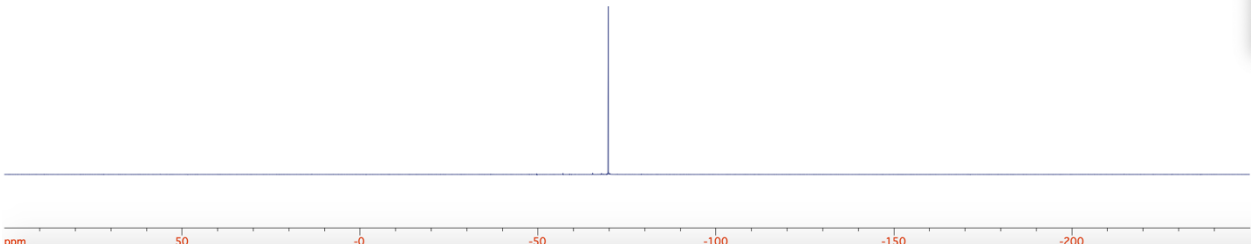

ppm
200
180
160
140
120
100
80
60
40
20


ppm
50
0
-50
-100
-150
-200


Me
O
Me
N
tBu
CF3


1.95
1.97
2.06
1
1.01
3.99
1.06
1.17
1.07
8.99
5.82
ppm
10
9
8
7
6
5
4
3
2
1


ppm
200
180
160
140
120
100
80
60
40
20


ppm
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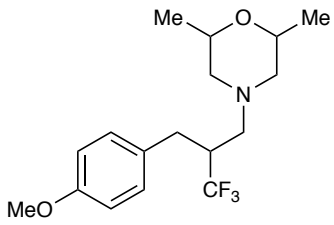
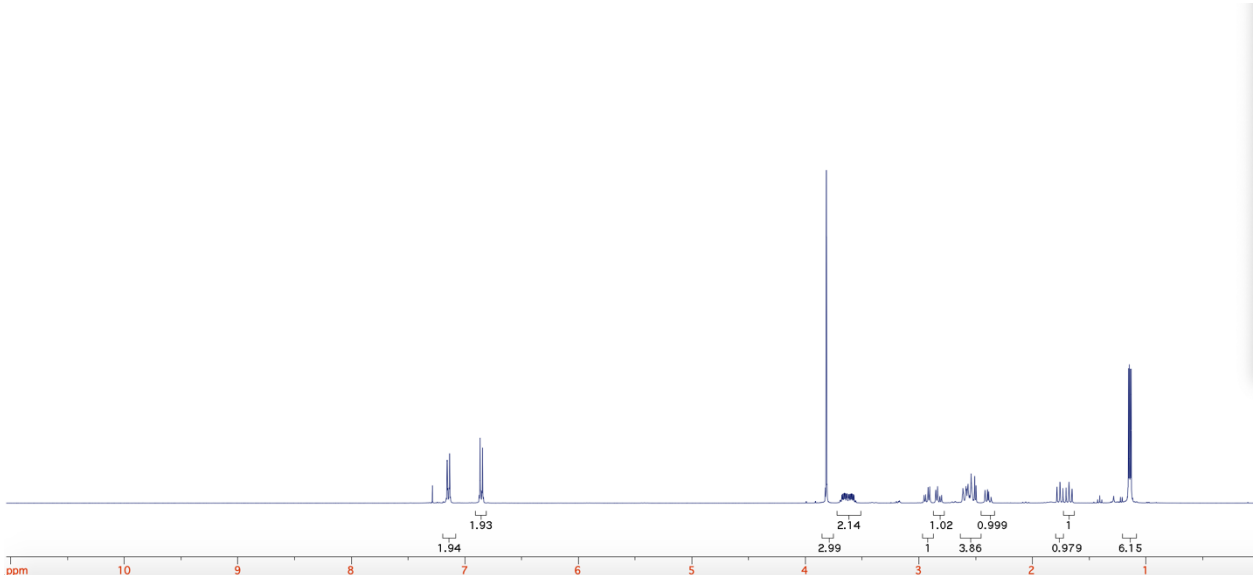
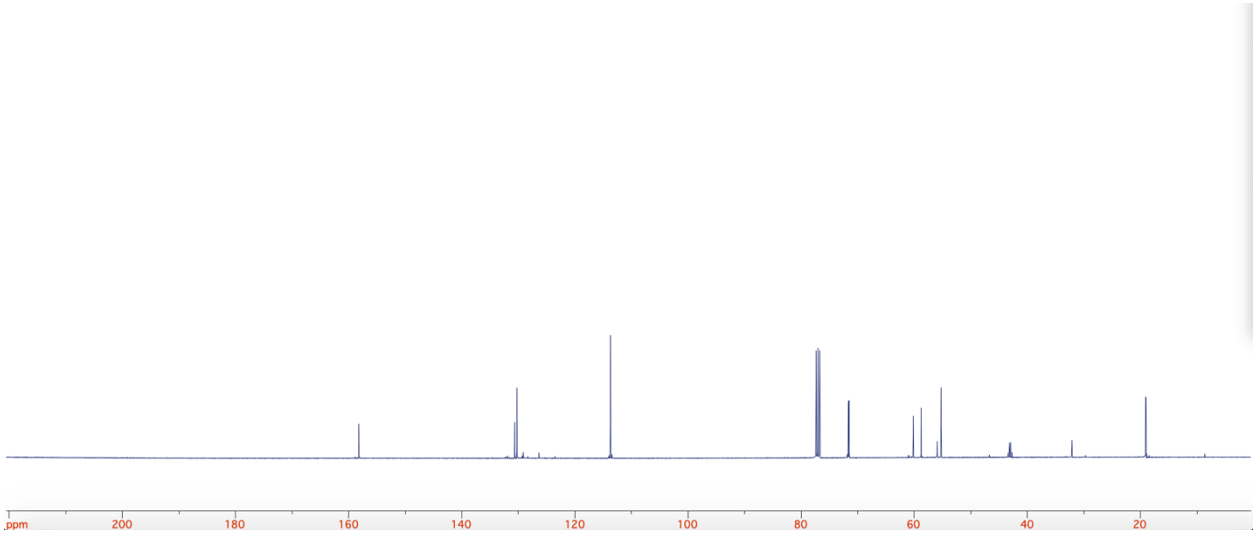
-50
-100
-150
-200


Me
O
Me
N
MeO
CF3


1.94
1.93
2.99
2.14
1
1.02
3.86
0.999
0.979
1
6.15
ppm
10
9
8
7
6
5
4
3
2
1


ppm
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180
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140
120
100
80
60
40
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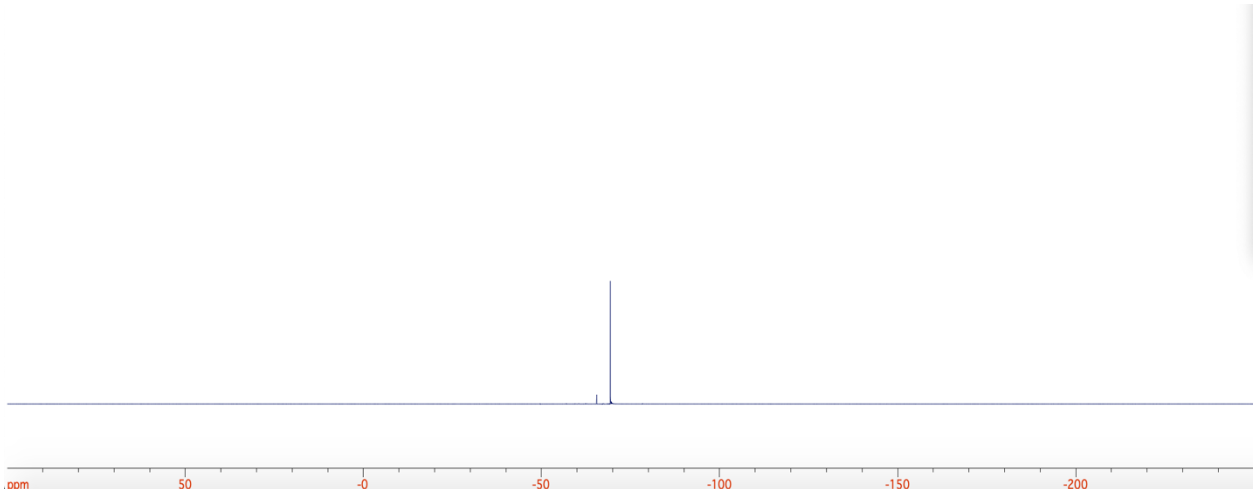
ppm
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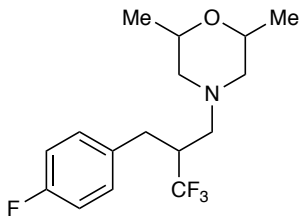
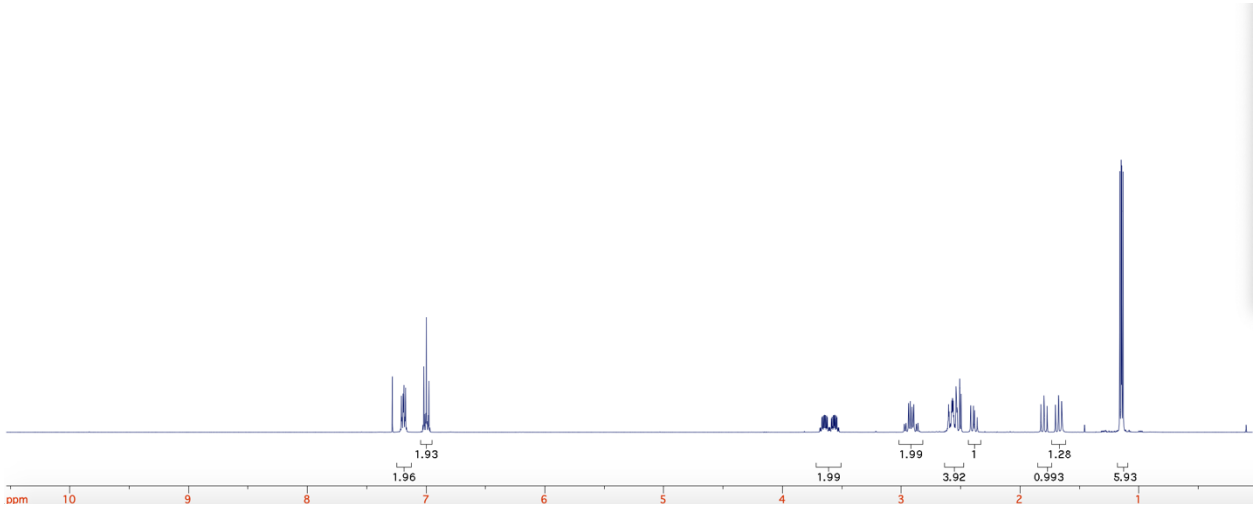
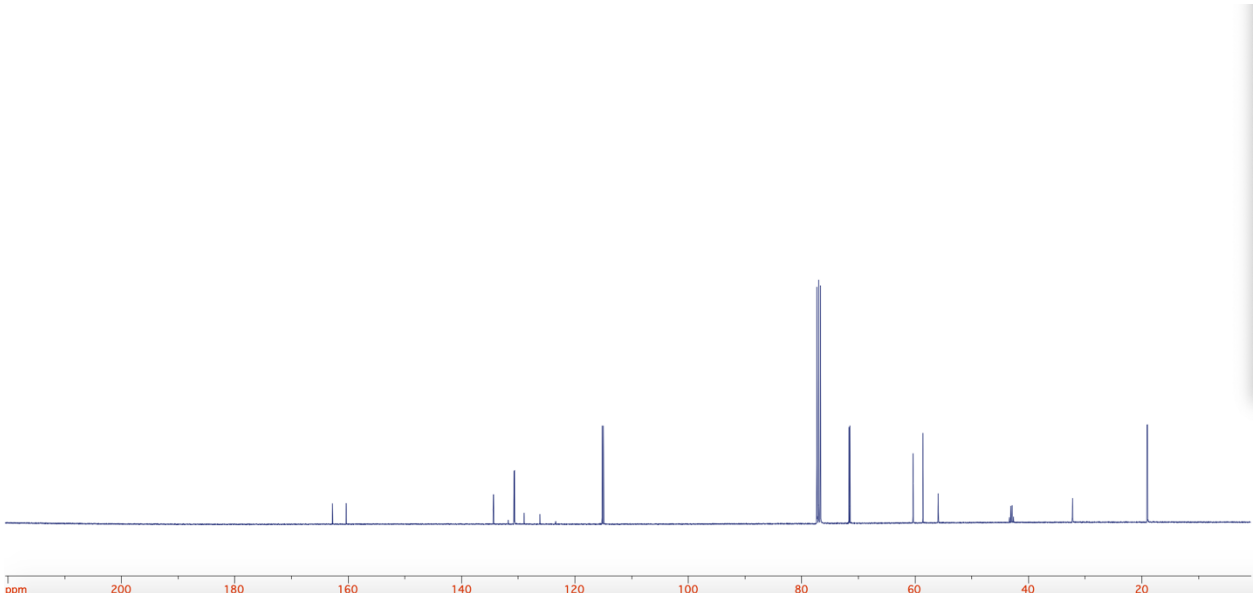
-100
-150
-200


Me
O
Me
N
F
CF3


1.93
1.96
1.99
1.99
1
3.92
1.28
0.993
5.93
ppm
10
9
8
7
6
5
4
3
2
1


ppm
200
180
160
140
120
100
80
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40
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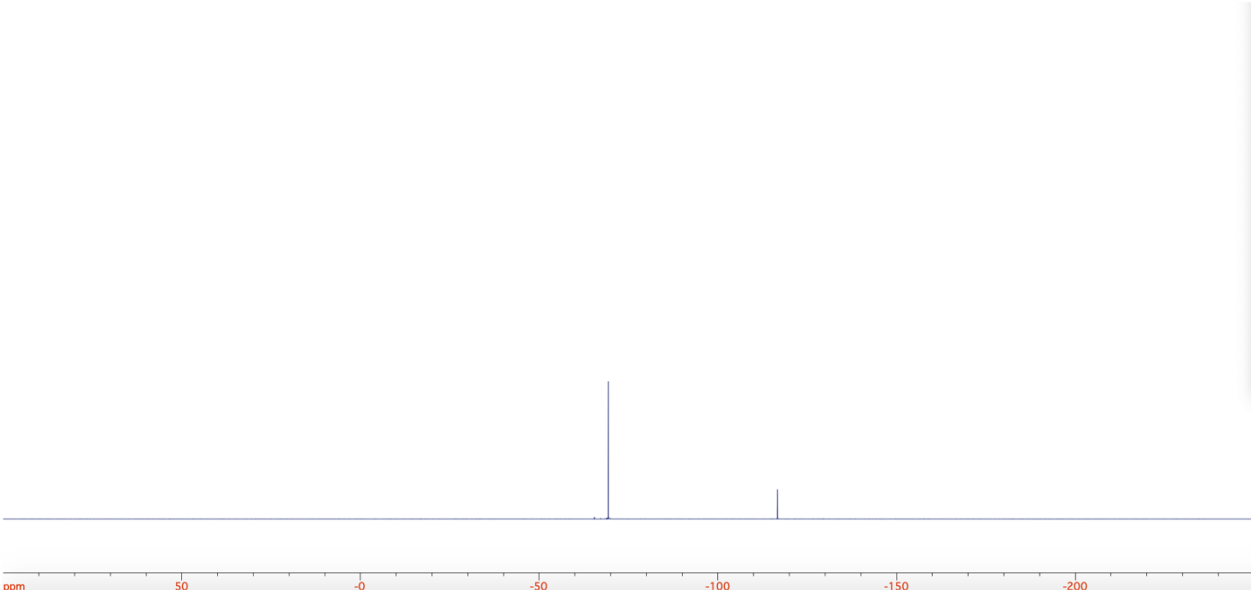
ppm
50
-0
-50
-100
-150
-200