Total Synthesis and Characterization of 7-Hypoquinuclidonium Tetrafluoroborate and 7-Hypoquinuclidone BF_3 Complex

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Table of Contents

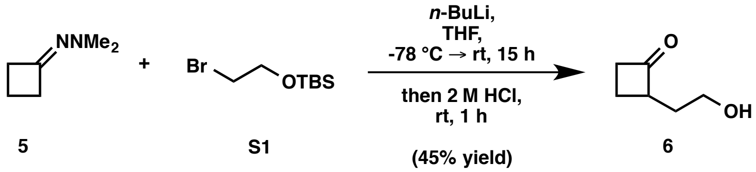
Materials and Methods

Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. All commercially obtained reagents were used as received unless specified otherwise. Triethylamine was distilled from calcium hydride prior to use. Reaction temperatures were controlled using an IKAmag temperature modulator. Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 pre-coated plates (0.25 mm) and visualized using UV at 254 nm or potassium permanganate. TLC data include R_f and eluent. ICN silica gel (particle size 0.032-0.063 mm), SilliaFlash P60 Academic silica gel (0.040-0.063 mm), or Florisil (Aldrich) was used for flash column chromatography. All NMR spectra were recorded on Varian 400, 500 or 600 MHz spectrometers or on a Bruker 400 MHz spectrometer with a Prodigy broadband cryoprobe. ^{1}H NMR spectra are reported relative to the residual solvent peak (δ 7.26 ppm for $CDCl_3$ and 1.94 ppm for CD_3CN). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. ^{13}C NMR spectra are reported relative to the residual solvent peak (δ 77.0 ppm for $CDCl_3$ and 1.32 ppm for CD_3CN). ^{11}B NMR spectra are reported relative to $BF_3•OEt_2$ (δ 0.0 ppm). ^{19}F NMR spectra are reported relative to $CFCl_3$ (δ 0.0 ppm). ^{14}N NMR spectra are reported relative to $(CH_3)_4NI$ (δ 0.0 ppm). ^{15}N NMR spectra are reported relative to ammonia NH_3 (δ 0.0 ppm). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad, app = apparent. IR spectra were recorded on a Perkin Elmer Spectrum BXII spectrometer or on a Fourier transform infrared ATR spectrometer (Thermo Scientific Nicolet iS5) with diamond ATR crystal (utilized iD5 ATR insert) and are reported in frequency of absorption (cm^{-1}). High resolution mass spectra (HRMS) were acquired with an Agilent 6200 Series TOF with Agilent G1978A Multimode source in mixed ionization mode

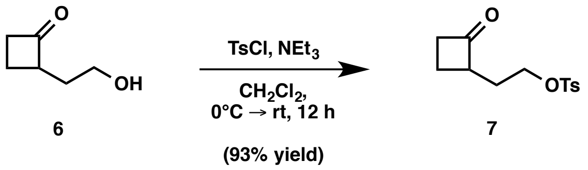
(MM: ESI/APCI) or with a JEOL JMS-600H double-focusing magnetic sector mass spectrometer by fast atom bombardment (FAB) in the positive ion mode using thioglycerol as FAB matrix. The FAB$^+$-MS was externally calibrated with PEG polymer in the Voltage scan mode. A drop of sample (kept in vial) was added to the probe tip and analyzed immediately. Samples for low resolution LTQ-MS were dissolved in anhydrous acetonitrile and analyzed by direct infusion electrospray ionization (ESI) using an LTQ linear ion trap mass spectrometer (Thermo) in the positive ion mode. Collision-induced-dissociation (CID) was performed on ions of interest. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected.

MacSPARTAN 10 was used to perform all DFT calculations at the 6-311+G** level.

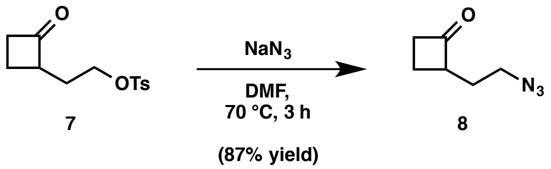
Preparative Procedures



Hydroxy ketone 6. To a solution of cyclobutanone *N*,*N*-dimethylhydrazone[1] (**5**) (200 mg, 1.78 mmol, 1.0 equiv) in THF (3 mL) was added at 0 °C *n*-BuLi (0.78 mL, 1.96 mmol, 1.1 equiv, 2.5 M solution in hexanes). After stirring for 1 h at that temperature, a yellow suspension was formed. Then, a solution of 2-bromo-1-tert-butyldimethylsilyloxy ethane[2] (**S1**) (469 mg, 1.96 mmol, 1.1 equiv) in THF (2.0 mL) was added dropwise at -78 °C. After stirring for 15 min at 0 °C, the reaction mixture was allowed to warm slowly to rt in the ice bath over 15 h. Then, 2 M HCl (3.6 mL) was added at rt. After stirring vigorously for 1 h at rt, Et_2O (25 mL) and water (10 mL) were added and the layers were separated. The aqueous layer was extracted with Et_2O (2 x 25 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography (pentane/Et_2O, 1:1 → 1:2 → 1:3 → Et_2O) to afford 2-(2-hydroxyethyl) cyclobutanone (**6**) (93.4 mg, 45%) as a colorless liquid.[3] $R_f = 0.39$ (Et_2O); ^1H NMR (500 MHz, $CDCl_3$): δ 3.81-3.56 (m, 2H), 3.52-3.29 (m, 1H), 3.17-2.99 (m, 1H), 2.99-2.83 (m, 1H), 2.57 (brs, 1H), 2.33-2.12 (m, 1H), 2.00-1.56 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 212.9, 60.8, 58.1, 44.2, 32.5, 16.5; IR (NaCl): 3418br, 2931, 2880, 1771, 1393, 1287, 1243, 1202, 1057, 941 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_6H_{10}O_2$ $[M+H]^+$: 115.0759, found 115.0767.

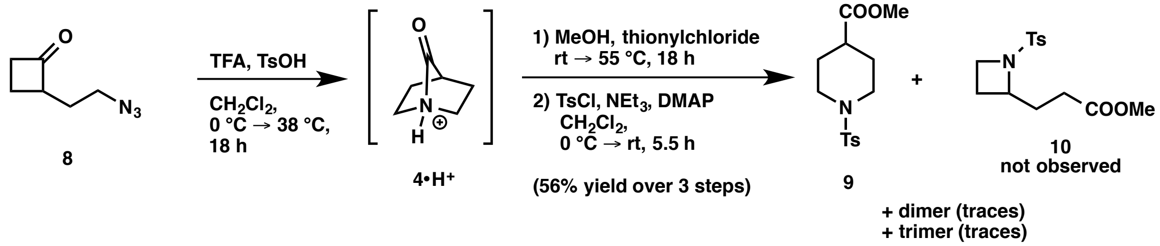


Tosylate 7. To a solution of alcohol **6** (93.0 mg, 0.81 mmol, 1.0 equiv) in CH_2Cl_2 (1 mL) was added at 0 °C triethylamine (0.17 mL, 1.22 mmol, 1.5 equiv) followed by *p*-toluenesulfonyl chloride (171 mg, 0.90 mmol, 1.1 equiv). After stirring for 12 h at rt, the heterogeneous reaction mixture was quenched with 1 M NaOH (10 mL) and diluted with CH_2Cl_2 (15 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc, 4:1 → 2:1) to afford **7** (204 mg, 93%) as a colorless liquid. R_f = 0.35 (hexane/EtOAc, 2:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 4.17-4.04 (m, 2H), 3.44-3.31 (m, 1H), 3.08 (dddd, *J* = 17.7, 10.7, 8.2, 2.6 Hz, 1H), 2.90 (dddd, *J* = 17.6, 9.5, 4.8, 2.7 Hz, 1H), 2.46 (s, 3H), 2.21 (app qd, *J* = 10.7, 4.8 Hz, 1H), 2.04 (app dq, *J* = 14.5, 6.3 Hz, 1H), 1.86 (ddt, *J* = 14.7, 8.5, 6.5 Hz, 1H), 1.66 (ddt, *J* = 11.2, 9.6, 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 209.8, 144.9, 132.8, 129.9, 127.9, 68.1, 56.3, 44.9, 28.7, 21.7, 16.8; IR (NaCl): 3534, 2960, 2927, 1778, 1598, 1495, 1455, 1354, 1307, 1293, 1177, 1097, 1032, 943, 817, 773 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_{13}H_{16}O_4S$ $[M+H]^+$: 269.0848, found 269.0844.



Azide 8. To a solution of tosylate **7** (1.375 g, 5.12 mmol, 1.0 equiv) in dry DMF (10 mL) was added at rt sodium azide (366 mg, 5.64 mmol, 1.1 equiv). After stirring for 3 h at 70 °C, the reaction mixture was diluted with Et_2O (50 mL) and filtered over Celite. The filter cake was washed with Et_2O (3 x 40 mL). The combined organic filtrates were washed with water (3 x 25 mL), brine (25 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure.

The residue was purified by column chromatography (hexane/Et$_2$O, 4:1 → 3:1) to afford azide **8** (623 mg, 87%) as a colorless liquid. R$_f$ = 0.59 (hexane/EtOAc, 2:1); ^{1}H NMR (500 MHz, CDCl$_3$): δ 3.48-3.32 (m, 3H), 3.11 (dddd, *J* = 17.7, 10.7, 8.1, 2.6 Hz, 1H), 2.96 (dddd, *J* = 17.5, 9.6, 4.9, 2.7 Hz, 1H), 2.27 (app qd, *J* = 10.6, 4.9 Hz, 1H), 1.99 (app dq, *J* = 13.6, 6.8 Hz, 1H), 1.79 (ddt, *J* = 14.1, 8.3, 7.1 Hz, 1H), 1.71 (ddt, *J* = 11.2, 9.6, 7.8 Hz, 1H); ^{13}C NMR (126 MHz, CDCl$_3$): δ 210.4, 57.4, 49.2, 44.8, 28.8, 16.8; IR (NaCl): 3535, 3334, 2932, 2877, 2516, 2098, 1776, 1456, 1393, 1348, 1259, 1202, 1122, 1086, 1036, 905 cm^{-1}; HRMS (FAB+) m/z calc'd for $C_6H_9N_3O$ [M+H]$^+$: 140.0824, found 140.0833.



***N*-Tosyl piperidine 4-carboxylic acid methyl ester 9.** To a solution of azide **8** (20.0 mg, 0.14 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (1.2 mL) was added at 0 °C a predried stock solution of trifluoroacetic acid (0.26 mL, calcd. 16.5 µL, 0.22 mmol, 1.5 equiv) in CH$_2$Cl$_2$ (over 4Å molecular sieves, 0.1 mL TFA was dissolved in 1.5 mL CH$_2$Cl$_2$). After stirring for 30 min, neither conversion of the starting material was observed according to TLC nor evolution of nitrogen. Then, a predried stock solution of triflic acid (0.25 mL, calcd. 14.1 µL, 0.22 mmol, 1.5 equiv) in CH$_2$Cl$_2$ (over 4Å molecular sieves, 0.1 mL TfOH was dissolved in 1.2 mL CH$_2$Cl$_2$) was added at rt and stirring was continued for 30 min at rt and for 1 h at 38 °C. Since keto azide **8** was still not fully consumed, more of the triflic acid stock solution (0.25 mL, calcd. 14.1 µL, 0.22 mmol, 1.5 equiv) was added. After stirring for 16 h at 38 °C, the solvent had evaporated. The orange residue was redissolved in CH$_2$Cl$_2$ (1.2 mL). The starting material was fully consumed and a new polar spot was observed according to TLC (*n*-BuOH/H_2O/EtOAc/AcOH, 1:1:1:1, blue/purple with ninhydrin, the intermediate will be hydrolyzed by the water in the TLC solvent mixture to the corresponding amino acid). MeOH (1.2 mL) was added at rt to the reaction mixture and stirring was continued for 1 h at that temperature. Since it was unclear according to TLC, if the intermediate **4•H**$^+$ was hydrolyzed with MeOH and, moreover, if the corresponding amino acid had been formed in the reaction mixture with traces of water as well, thionyl chloride (42.0 µL, 0.57 mmol, 4.0 equiv) was added dropwise at 0 °C in order to assure acid catalyzed esterification of the amino acid mediated by *in situ* formed dry HCl. The reaction mixture was stirred at 55 °C for 17 h, concentrated under reduced pressure and the residue was dried under high vacuum (TLC *n*-BuOH/H_2O/EtOAc/AcOH, 1:1:1:1, dark purple spot with ninhydrin).

To a solution of the orange/red crude residue in CH_2Cl_2 (2.4 mL) was added at rt triethylamine (0.40 mL, 2.87 mmol, 20 equiv), DMAP (1.8 mg, 10 mol%) followed by TsCl (82.2 mg, 0.43 mmol, 4.0 equiv). After stirring at rt for 5.5 h, the reaction mixture was quenched with sat. $NaHCO_3$ (10 mL) and extracted with EtOAc (3 x 20 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc, 5:1 → 4:1 → 3:1 → 2:1 → 1:1) to afford **9** (24.1 mg, 56%) as a beige, crystalline solid.[4] X-ray quality crystals were obtained at rt by slow diffusion of heptane (with a few drops of benzene) into a solution of **9** in EtOAc. R_f = 0.11 (hexane/EtOAc, 4:1); R_f = 0.55 (hexane/EtOAc, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 3.66 (s, 3H), 3.63 (dt, *J* = 11.9, 4.0 Hz, 2H), 2.50-2.39 (m, 2H), 2.44 (s, 3H), 2.26 (tt, *J* = 10.7, 4.0 Hz, 1H), 2.02-1.92 (m, 2H), 1.81 (dtd, *J* = 14.4, 10.8, 4.0 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 174.3, 143.6, 133.0, 129.6, 127.6, 51.9, 45.4, 39.9, 27.4, 21.5; IR (KBr): 2932, 2845, 1726, 1596, 1437, 1350, 1336, 1291, 1250, 1204, 1161, 1120, 1094, 1043, 986, 933, 818, 730 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{14}H_{19}NO_4S$ $[M+H]^+$: 298.1108, found 298.1094; mp 127-128 °C; LC-MS (ESI+): m/z: 298.1 $[M+H]^+$, 320.1 $[M+Na]^+$. The X-ray structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC) under the deposition number 1435049.

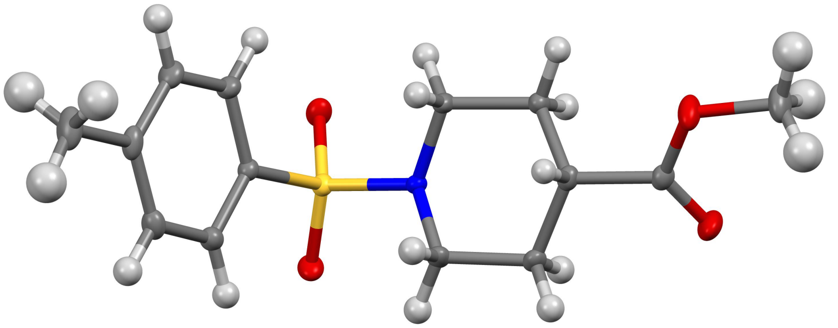
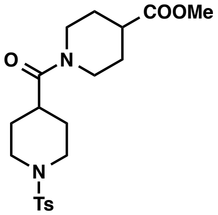
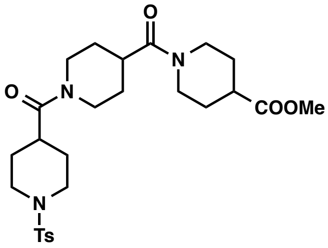


Figure 1: X-ray structure of **9** (ellipsoids, 50% probability level).

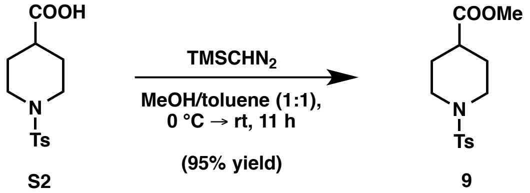
Dimer: LC-MS (ESI+): m/z calc'd and found for $C_{20}H_{28}N_2O_5S$: 409.2 $[M+H]^+$, 431.2 $[M+Na]^+$.



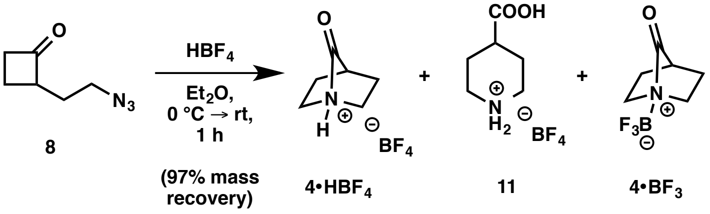
Trimer: LC-MS (ESI+): m/z calc'd and found for $C_{26}H_{37}N_3O_6S$: 520.3 $[M+H]^+$, 542.3 $[M+Na]^+$.



Structural confirmation of 9 by chemical synthesis:



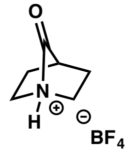
***N*-Tosyl piperidine 4-carboxylic acid methyl ester 9.** To a solution of 1-tosyl-4-piperidine-carboxylic acid[5] (**S2**) (202 mg, 0.71 mmol, 1.0 equiv) in a 1:1 mixture of toluene (3.0 mL) and MeOH (3.0 mL) was added dropwise at 0 °C TMS diazomethane (1.07 mL, 2.14 mmol, 3.0 equiv). After stirring for 11 h at rt, the colorless reaction mixture was quenched with a few drops of a 10:1 mixture of MeOH/AcOH until the solution discolored completely. The reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc, 3:1 → 1:1) to afford **9** (201 mg, 95%) as a colorless, crystalline solid. The analytical data were identical to those reported above (*vide supra*). R*f* = 0.55 (hexane/EtOAc, 1:1).



7-Hypoquinuclidone tetrafluoroborate 4•HBF$_4$ and 7-hypoquinuclidone BF$_3$ complex 4•BF$_3$. To a solution of keto azide **8** (52.0 mg, 0.37 mmol, 1.0 equiv) in Et$_2$O (0.75 mL) was added at 0 °C HBF$_4$ (0.10 mL, 0.71 mmol, 1.9 equiv, 50-54% wt/wt in Et$_2$O). Gas evolution was observed immediately. After stirring for 1 h at rt, the starting material was fully consumed and a colorless precipitate was formed. The solvent was decanted off with a syringe under argon. The solids were washed with Et$_2$O (3 x 0.8 mL) and dried under high vacuum to afford **4•HBF$_4$**

(72.0 mg, 97% mass recovery) as a colorless solid. When solid **4•HBF$_4$** was dissolved in dry CD$_3$CN, a mixture of **4•HBF$_4$** / **11** / **4•BF$_3$** in a ratio of 77%/15%/12% was observed by ^{1}H-NMR spectroscopy. Slow diffusion of Et$_2$O into a solution of **4•HBF$_4$** in acetonitrile at -40 °C over four weeks yielded one single crystal of 7-hypoqunuclidone BF$_3$ complex **4•BF$_3$** (2.0 mg, 3%) as a colorless needle.

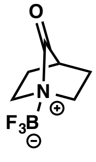
Analytical data for **4•HBF$_4$**:



4•HBF$_4$

^{1}H NMR (400 MHz, CD$_3$CN): δ 7.76 (t, $^1J_{1H14N}$ = 63 Hz, 1H), 3.85-3.68 (m, 2H), 3.41 (td, J = 11.2, 5.1 Hz, 2H), 2.87 (brs, 1H), 2.37 (m$_c$, 2H), 2.07 (td, J = 11.7, 5.3 Hz, 2H); ^{1}H{^{14}N} NMR (500 MHz, CD$_3$CN): δ 7.76 (s, 1H), 3.88-3.71 (m, 2H), 3.52-3.37 (m, 2H), 2.89 (brs, 1H), 2.46-2.34 (m, 2H), 2.09 (td, J = 11.8, 5.6 Hz, 2H); ^{13}C NMR (126 MHz, CD$_3$CN): δ 174.7, 47.8, 32.3, 22.8; ^{11}B NMR (128 MHz, CD$_3$CN): δ −1.2 (s); ^{19}F NMR (376 MHz, CD$_3$CN): δ −151.3 (s); ^{14}N NMR (36 MHz, CD$_3$CN): δ 34.8 (d, $^1J_{14N1H}$ = 62.8 Hz); ^{14}N{^{1}H} NMR (36 MHz, CD$_3$CN): δ 34.8 (s); ^{15}N NMR (41 MHz, CD$_3$CN): δ 78.6 (J_{1H15N} = ~88 Hz); ^{15}N{^{1}H} NMR (41 MHz, CD$_3$CN): δ 78.6; IR (ATR): 3224, 1877 (C=O), 1493, 1472, 1363, 1288, 1180, 1125, 1031br (B-F), 992, 966, 868, 783, 679, 606, 520, 475 cm^{-1}; HRMS (EF FAB+)[6] m/z calc'd for C$_6$H$_9$NO [M+H$_2$O+H]$^+$: 130.0868, found 130.0862; HRMS (EF FAB+)[6] m/z calc'd for C$_6$H$_9$NO [M+H]$^+$: 112.0762, found 112.0764.

Analytical data for **4•BF$_3$**:



4•BF$_3$

^{1}H NMR (400 MHz, CD$_3$CN): δ 3.55 (td, *J* = 11.3, 5.6 Hz, 2H), 3.18 (td, *J* = 11.4, 5.0 Hz, 2H), 2.70 (t, *J* = 4.6 Hz, 1H), 2.24 (m$_c$, 2H), 1.96-1.83 (m, 2H, overlapping with CD$_3$CN); ^{13}C NMR (101 MHz, CD$_3$CN): δ 179.8, 49.2, 34.3, 22.7; ^{11}B NMR (128 MHz, CD$_3$CN): δ −0.3 (q, $^1J_{11B19F}$ = 13.8 Hz); ^{19}F NMR (376 MHz, CD$_3$CN): δ −154.93 (q, $^1J_{19F11B}$ = 13.9 Hz); ^{14}N NMR (36 MHz, CD$_3$CN): δ 39.3 (s); IR (ATR): 2990, 1860 (C=O), 1467, 1278, 1191, 1174, 1160, 1129, 1118, 1084, 1020, 948, 924, 884, 870, 813, 715, 667, 629, 548 cm^{-1}; HRMS (EF FAB+)[7] m/z calc'd for $C_6H_9BF_3NO$ [M−BF$_3$+H$_2$O+H]$^+$: 130.0868, found 130.0898; HRMS (EF FAB+)[7] m/z calc'd for $C_6H_9BF_3NO$ [M−BF$_3$+H]$^+$: 112.0762, found 112.0762; LTQ-CID-MS (ESI+): m/z 130.08 [M+H]$^+$, 112.08 [M−H$_2$O+H]$^+$, 84.08 [M−H$_2$O−CO +H]$^+$. The X-ray structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC) under the deposition number 1435048.

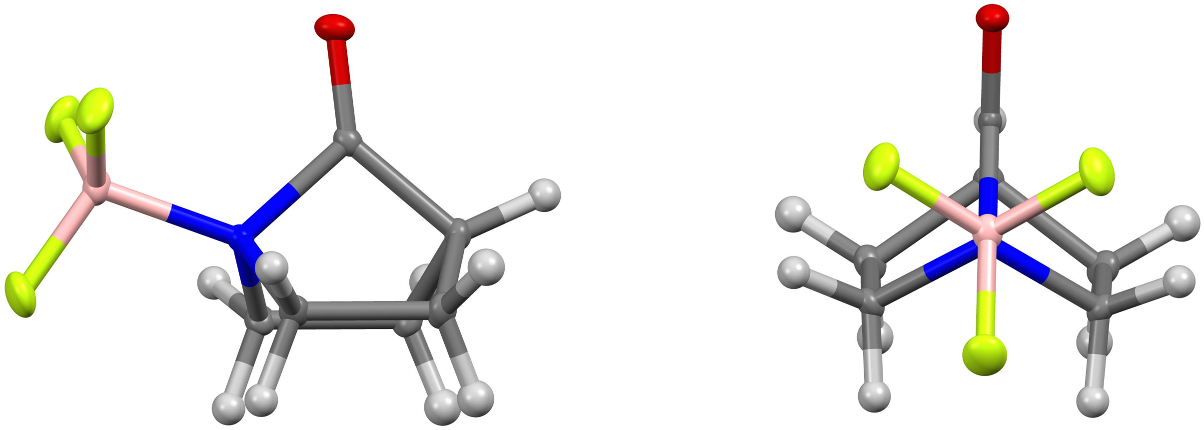
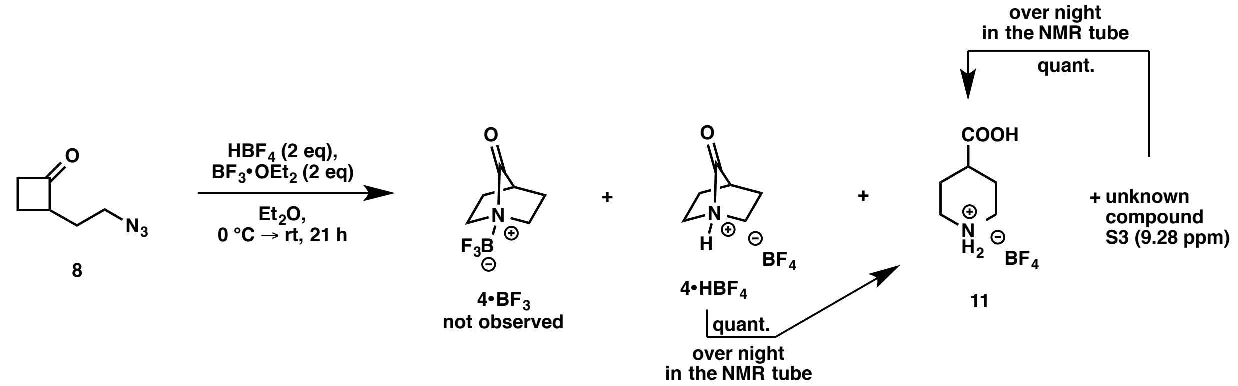
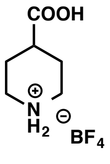


Figure 2: X-ray structure of **4•BF$_3$** (ellipsoids, 50% probability level, side view and view along the B-N-C-O axis).



Isonipecotic acid tetrafluoroborate 11. To a solution of keto azide **8** (67.7 mg, 0.49 mmol, 1.0 equiv) in Et_2O (1.0 mL) was added at 0 °C boron trifluoride diethyletherate (0.12 mL, 0.97 mmol, 2.0 equiv). After stirring for 2 h at rt, neither evolution of nitrogen nor formation of a precipitate was observed. Then, a catalytic amount of HBF_4 (0.02 mL, 0.14 mmol, 0.29 equiv, 50-54% wt/wt in Et_2O) was added at 0 °C, which led to immediate gas evolution and precipitation of a colorless solid. After stirring for 1 h at rt, there was still a lot of unreacted starting material present according to TLC. Therefore, more HBF_4 (0.06 mL, 0.43 mmol, 0.87 equiv, 50-54% wt/wt in Et_2O) was added at 0 °C (again gas evolution observed). After stirring for another hour at rt, the starting material was still not fully consumed (apparently a stoichiometric amount of acid is necessary, even more than 1 equivalent). Another portion of HBF_4 (0.05 mL, 0.36 mmol, 0.73 equiv, 50-54% wt/wt in Et_2O) was added at rt (gas evolution continued) and stirring was continued over night at rt (15 h). The starting material was fully consumed according to TLC and a colorless solid had precipitated. The solvent was removed with a syringe. The residue was washed with Et_2O (3 x 1.0 mL) and dried under high vacuum to afford the amino acid **11** along with **4•HBF_4** and an unknown compound **S3** (the ratio of **11** / **4•HBF_4** / **S3** is 73%/15%/12%; the BF_3 complex **4•BF_3** was not observed at all) as a colorless solid. When the crude product was dissolved in acetonitrile and stored over night at rt, compounds **4•HBF_4** and **S3** fully converted to isonipecotic acid tetrafluoroborate **11**. The solvent was removed under reduced pressure to give **11** (91.4 mg, 87%) as a yellow oil.[8] Two X-ray quality crystals were grown by overlaying a solution of **11** in CD_3CN with an excess of Et_2O in the NMR tube followed by slow evaporation of the solvents at rt over 2 month (closed NMR tube with a cap).

Analytical data for **11**:



11

^{1}H NMR (500 MHz, CD_3CN): δ 6.90-6.12 (m, $^1J_{1H14N}$ = ~55 Hz, 1H), 3.40 (dt, *J* = 13.1, 3.5 Hz, 2H), 3.05 (m_c, 2H), 2.84 (tt, *J* = 10.7, 4.0 Hz, 1H), 2.17 (dd, *J* = 14.8, 4.0 Hz, 2H), 1.96-1.83 (m, 2H, overlapping with CD_3CN); ^{1}H{^{14}N} NMR (500 MHz, CD_3CN): δ 6.72-6.58 (m, 1H), 6.50-6.35 (m, 1H), 3.41 (dt, *J* = 13.2, 3.5 Hz, 2H), 3.06 (m_c, 2H), 2.85 (tdd, *J* = 10.9, 5.8, 2.5 Hz, 1H), 2.17 (dd, *J* = 14.8, 4.0 Hz, 2H), 1.96-1.84 (m, 2H, overlapping with CD_3CN); ^{13}C NMR (126 MHz, CD_3CN): δ 169.7, 44.4, 39.6, 24.7; ^{11}B NMR (128 MHz, CD_3CN): δ −1.2 (s); ^{19}F NMR (376 MHz, CD_3CN): δ −151.2 (s); ^{14}N NMR (36 MHz, CD_3CN): δ −4.9 (m, $^1J_{14N1H}$ coupling not resolved); ^{14}N{^{1}H} NMR (36 MHz, CD_3CN): δ −5.0 (s); ^{15}N NMR (41 MHz, CD_3CN): δ 38.8 ($^1J_{1H15N}$ = ~77 Hz, $^2J_{1H1H}$ = 10.8 Hz); ^{15}N{^{1}H} NMR (41 MHz, CD_3CN): δ 38.8; IR (NaCl): 3625, 3233, 2952, 2814, 2725, 2502, 1814 (C=O), 1738, 1600, 1456, 1428, 1314, 1286, 1069br (B-F), 1021br (B-F), 958, 908, 844, 766 cm^{-1}; mp 124-138 °C; HRMS (MM: ESI-APCI+) m/z calc'd for $C_6H_{11}NO_2$ $[M+H]^+$: 130.0863, found 130.0864; HRMS (EF FAB+)[9] m/z calc'd for $C_6H_{11}NO_2$ $[M+H]^+$: 130.0868, found 130.0872; HRMS (EF FAB+)[9] m/z calc'd for $C_6H_{11}NO_2$ $[M-H_2O+H]^+$: 112.0762, found 112.0758; LTQ-CID-MS (ESI+): m/z 130.08 $[M+H]^+$, 112.08

$[M{-}H_2O{+}H]^+$, 84.08 $[M{-}H_2O{-}CO\ {+}H]^+$. The X-ray structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC) under the deposition number 1435047.

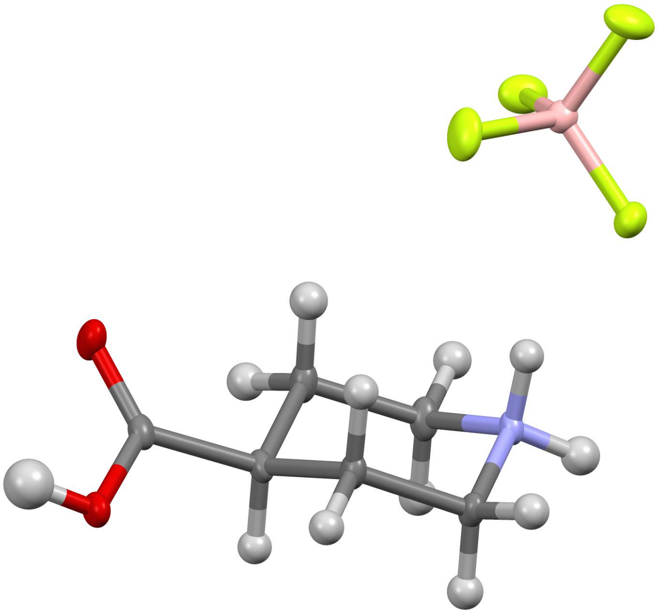
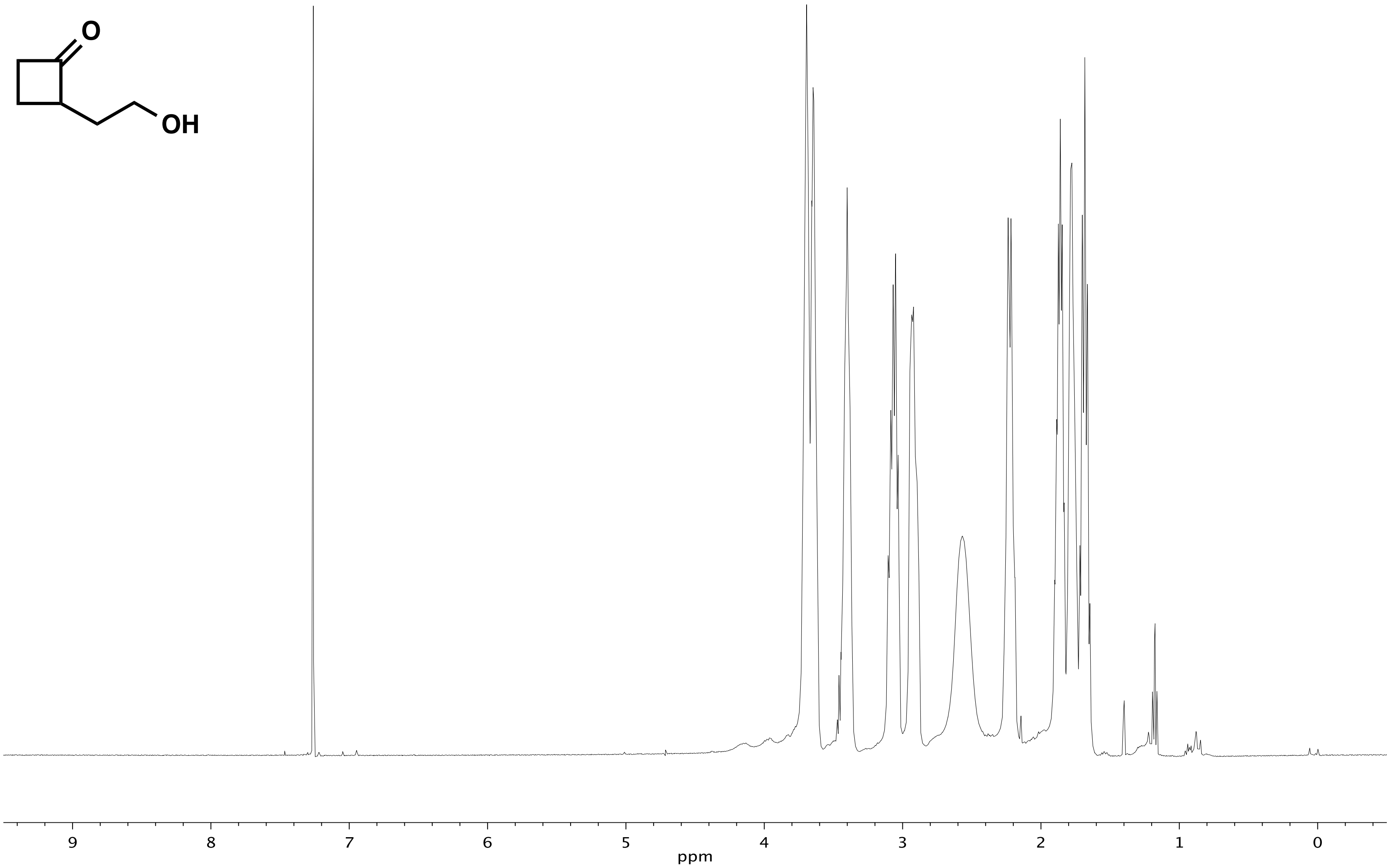
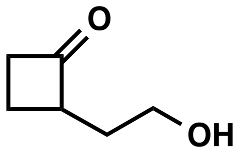
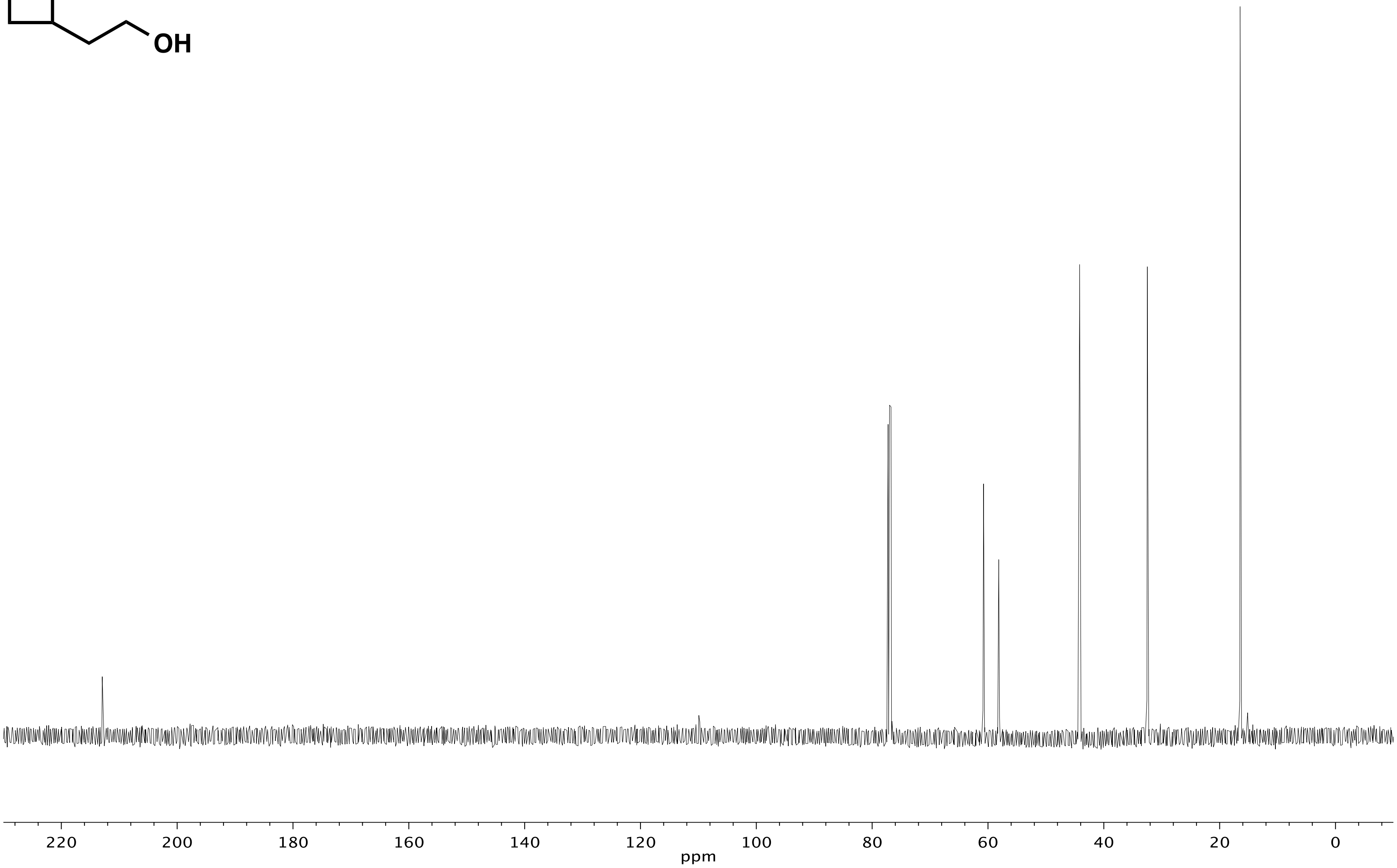


Figure 3: X-ray structure of **11** (ellipsoids, 50% probability level).

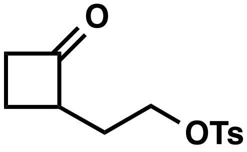
NMR Spectra

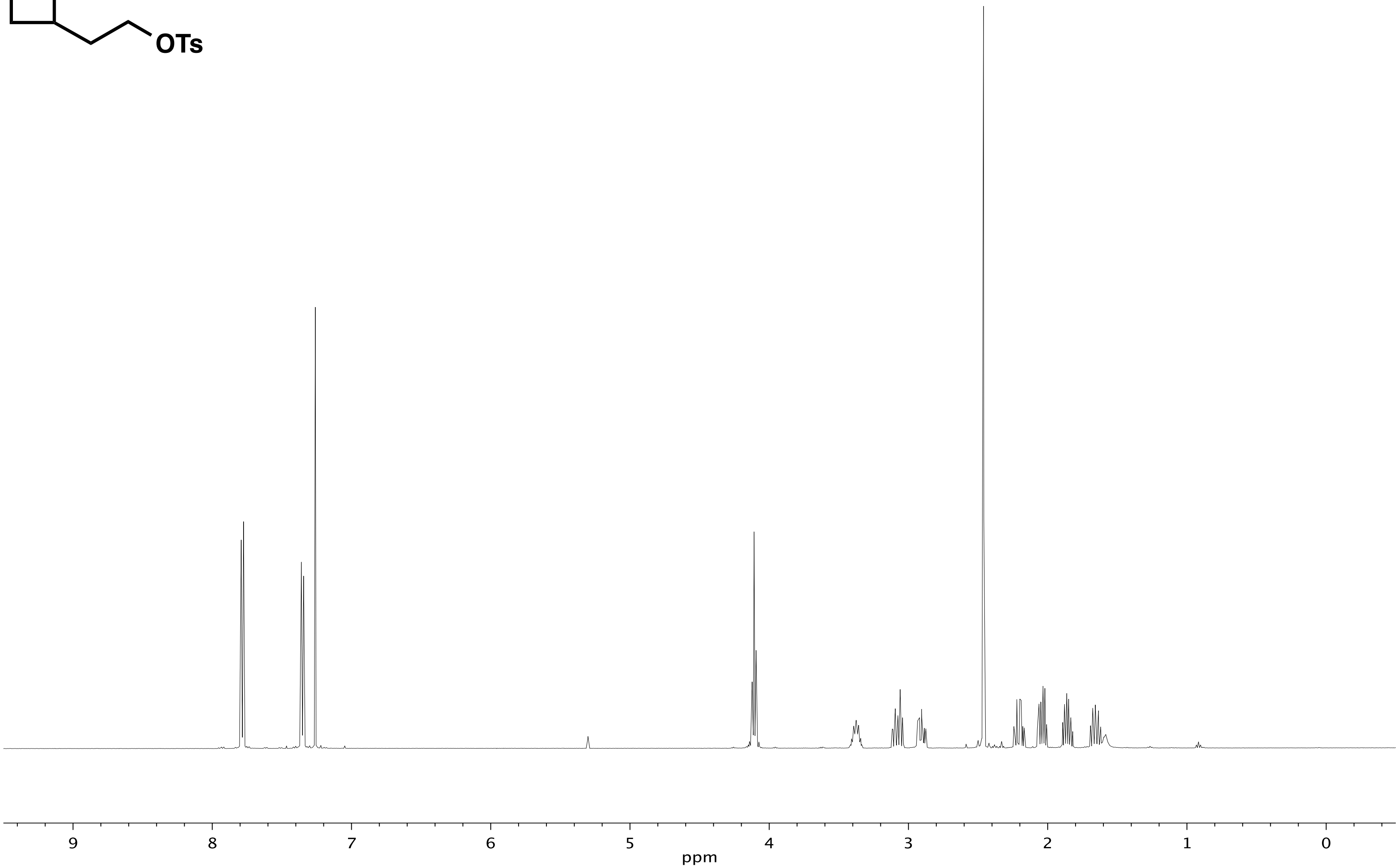




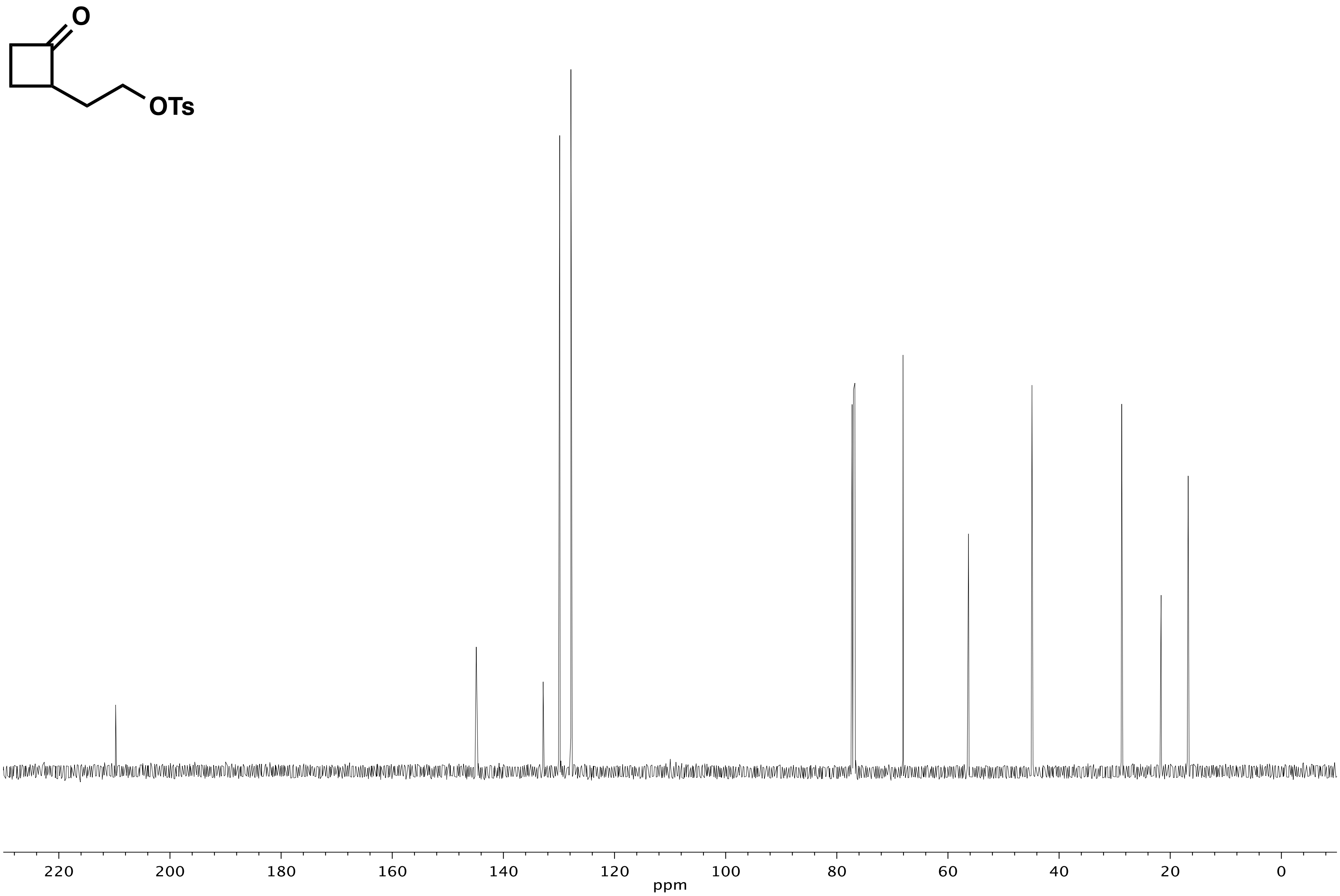


^{13}C NMR (126 MHz, CDCl$_3$) of compound **6.**

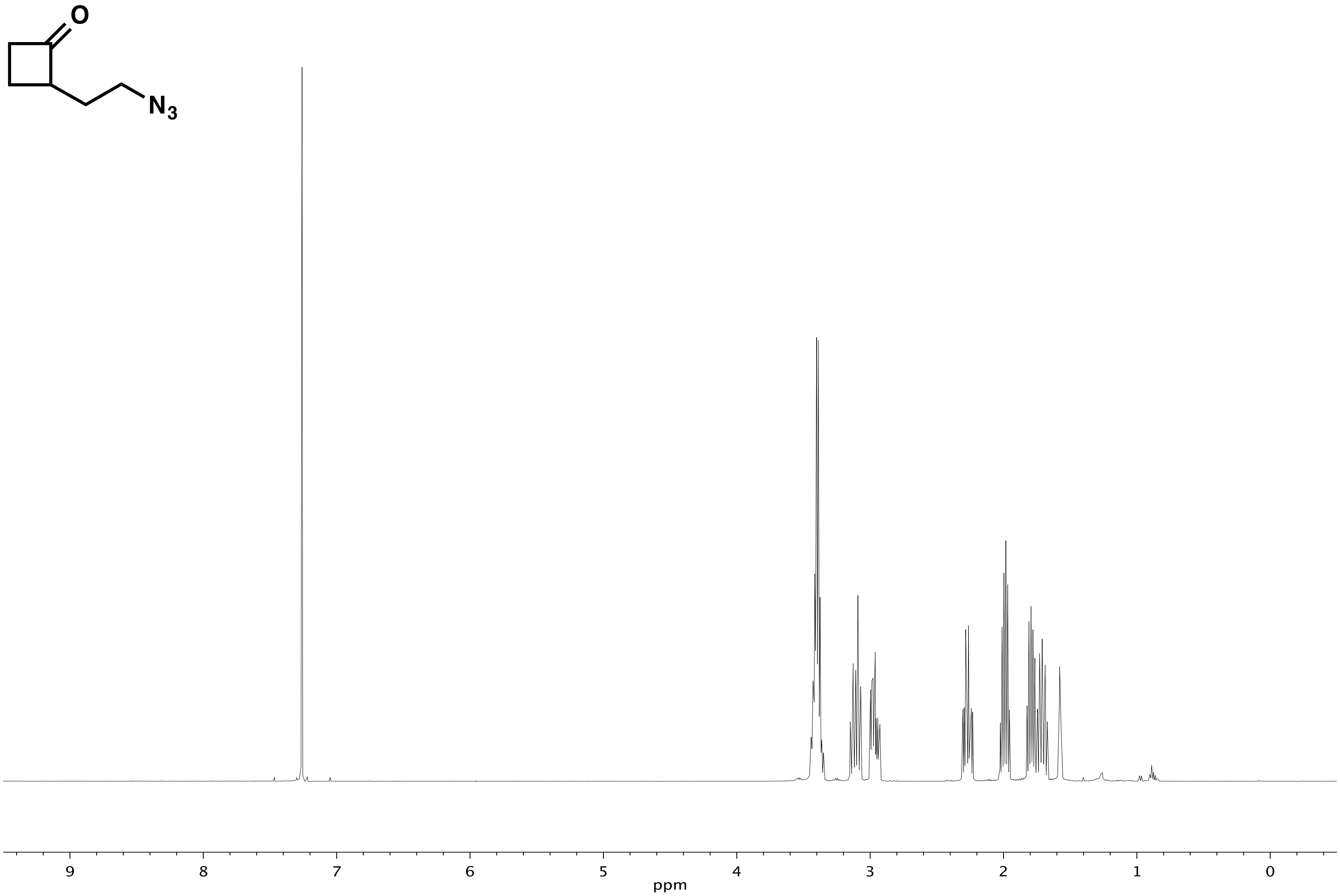




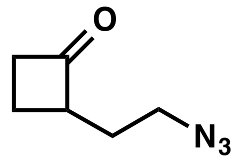
^{1}H NMR (500 MHz, CDCl$_3$) of compound **7**.

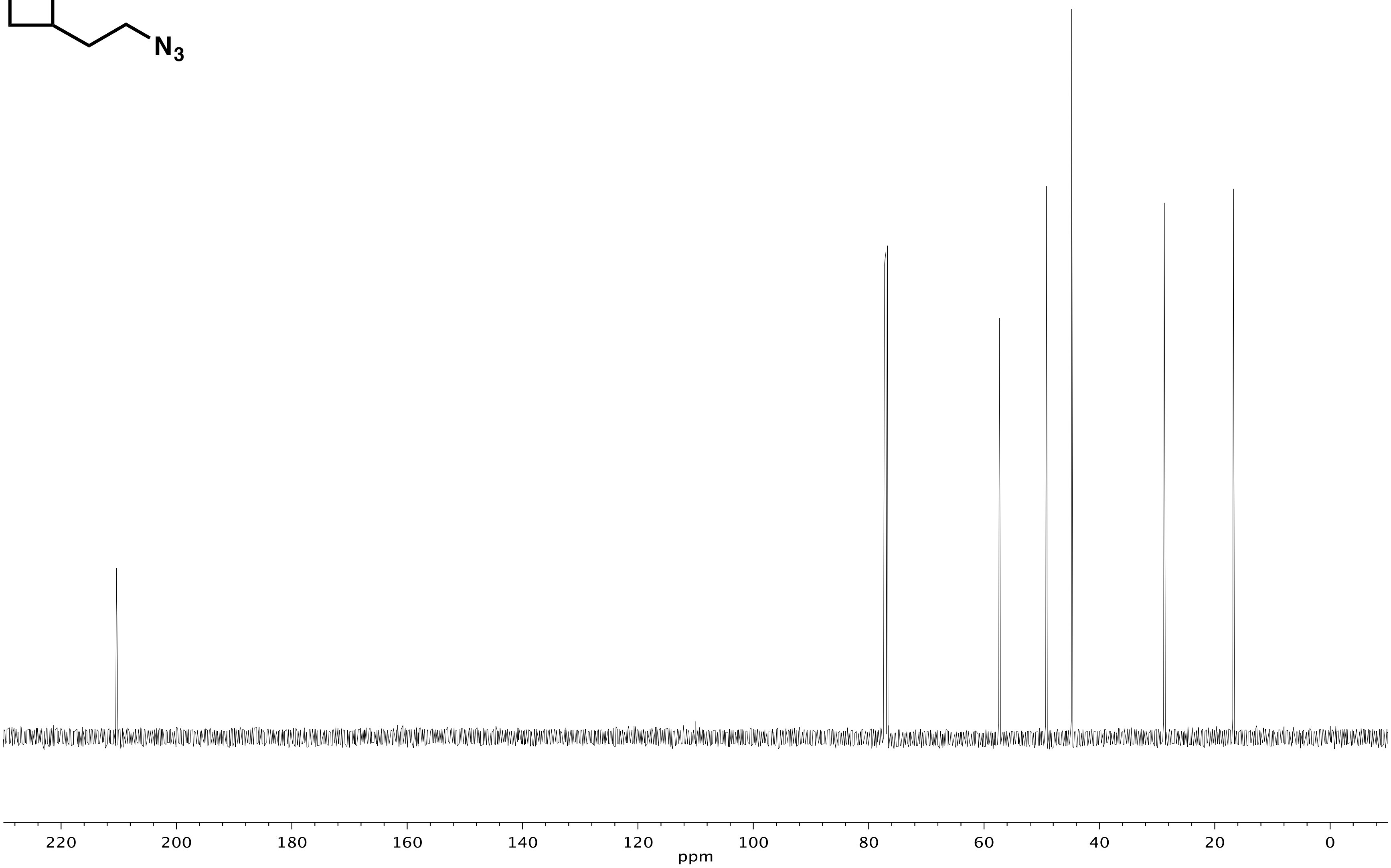


^{13}C NMR (126 MHz, CDCl$_3$) of compound **7.**

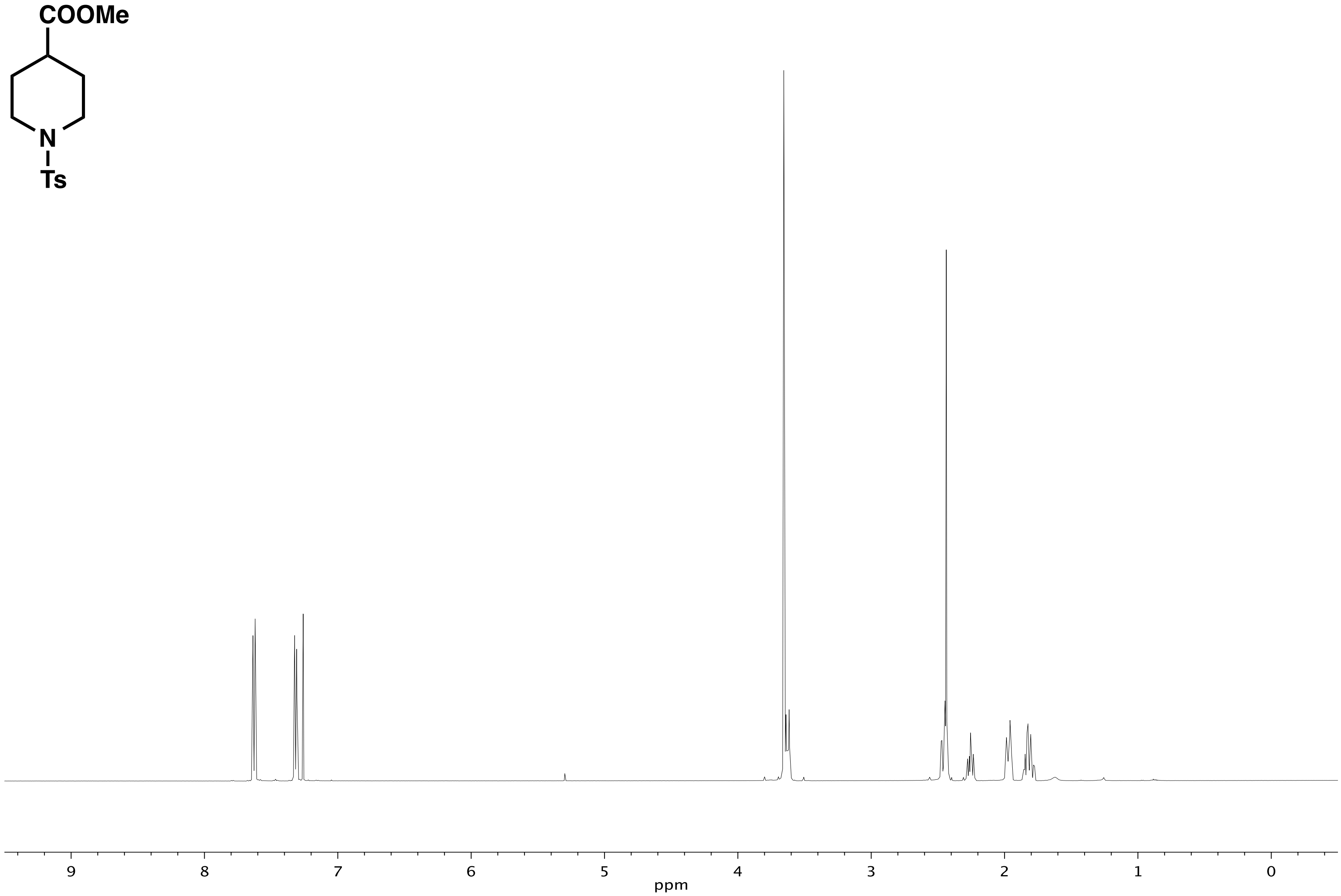


^{1}H NMR (500 MHz, CDCl$_3$) of compound **8**.

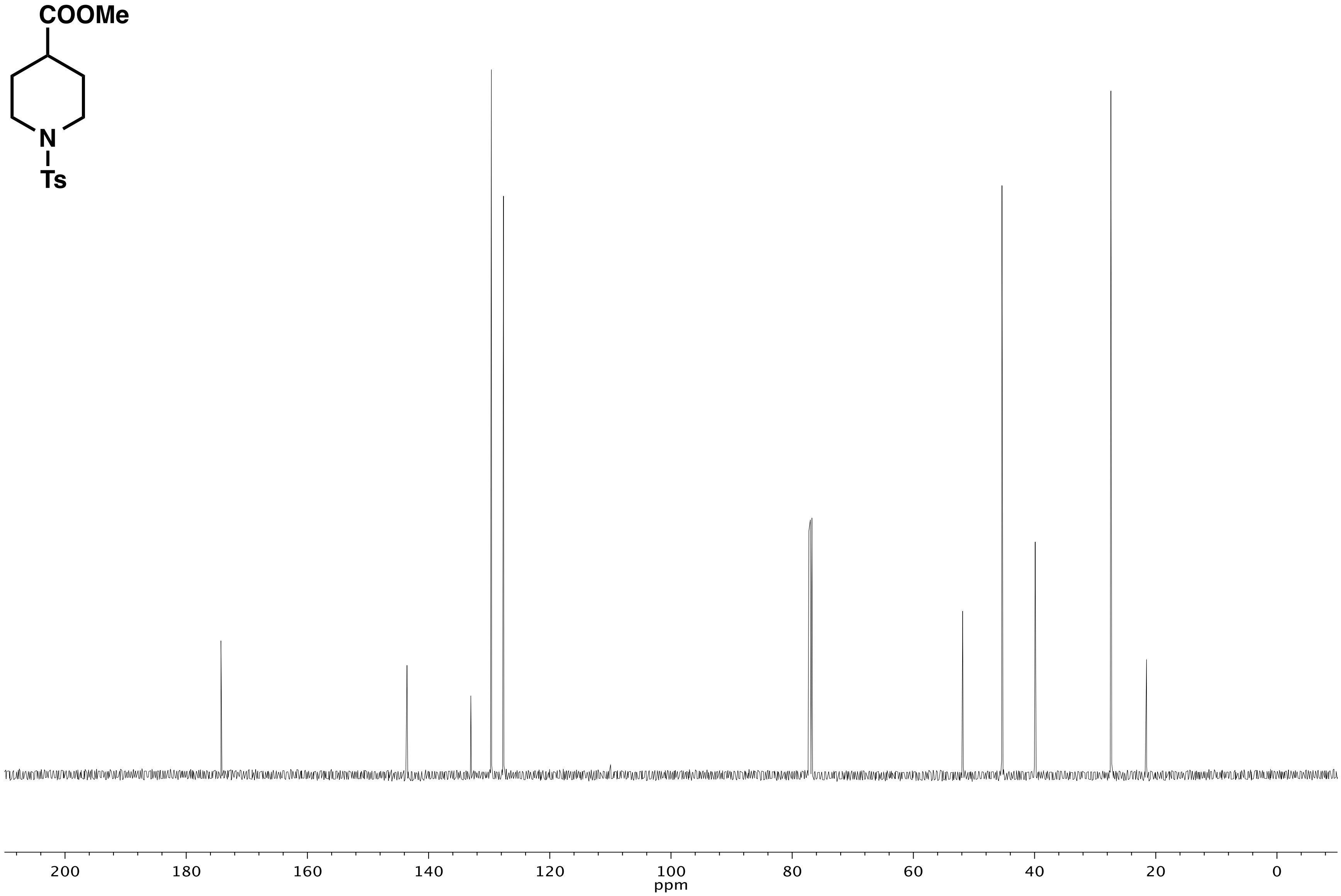




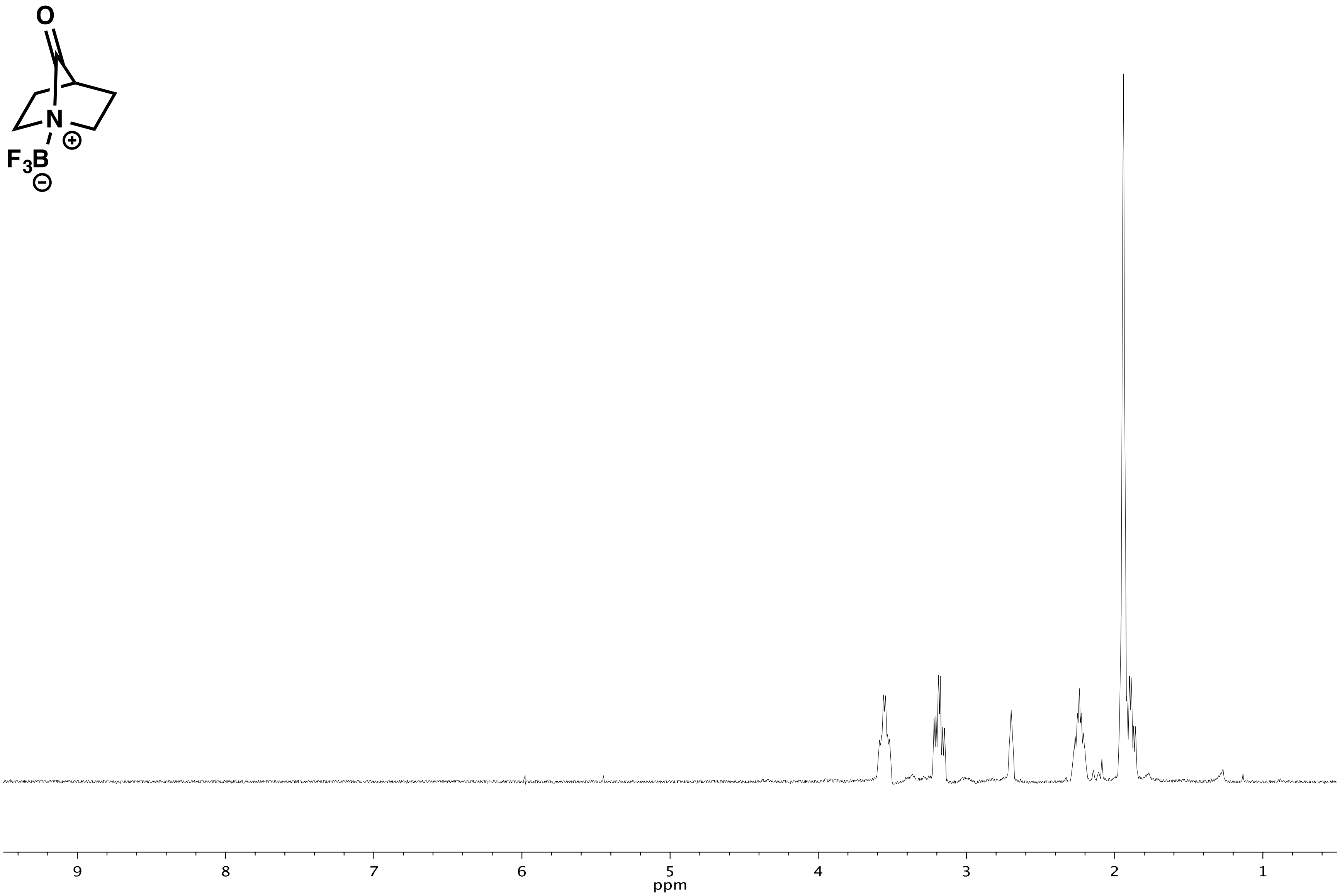
^{13}C NMR (126 MHz, CDCl$_3$) of compound **8.**



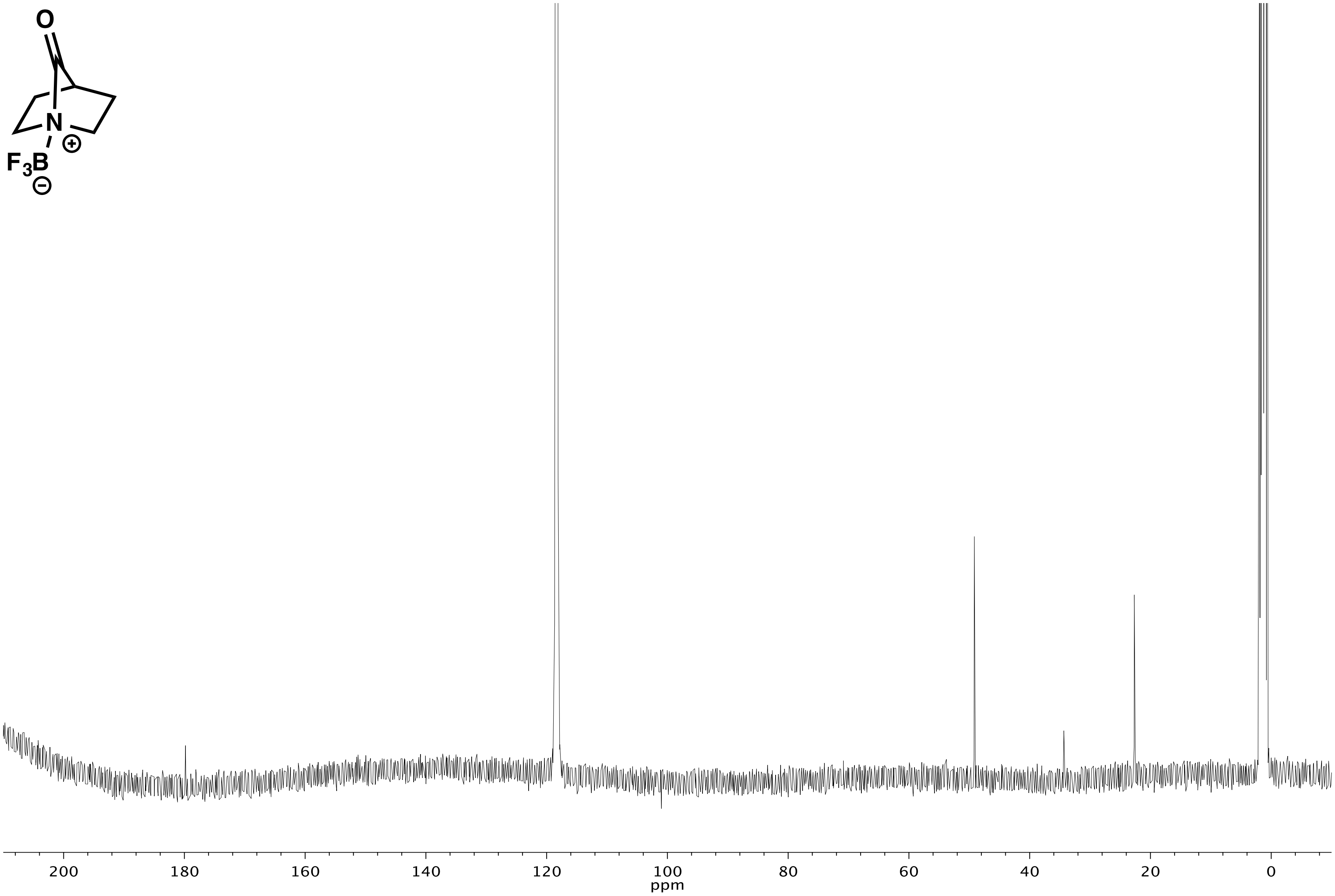
^{1}H NMR (500 MHz, CDCl$_3$) of compound **9**.



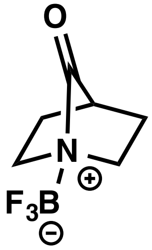
^{13}C NMR (126 MHz, CDCl$_3$) of compound **9.**

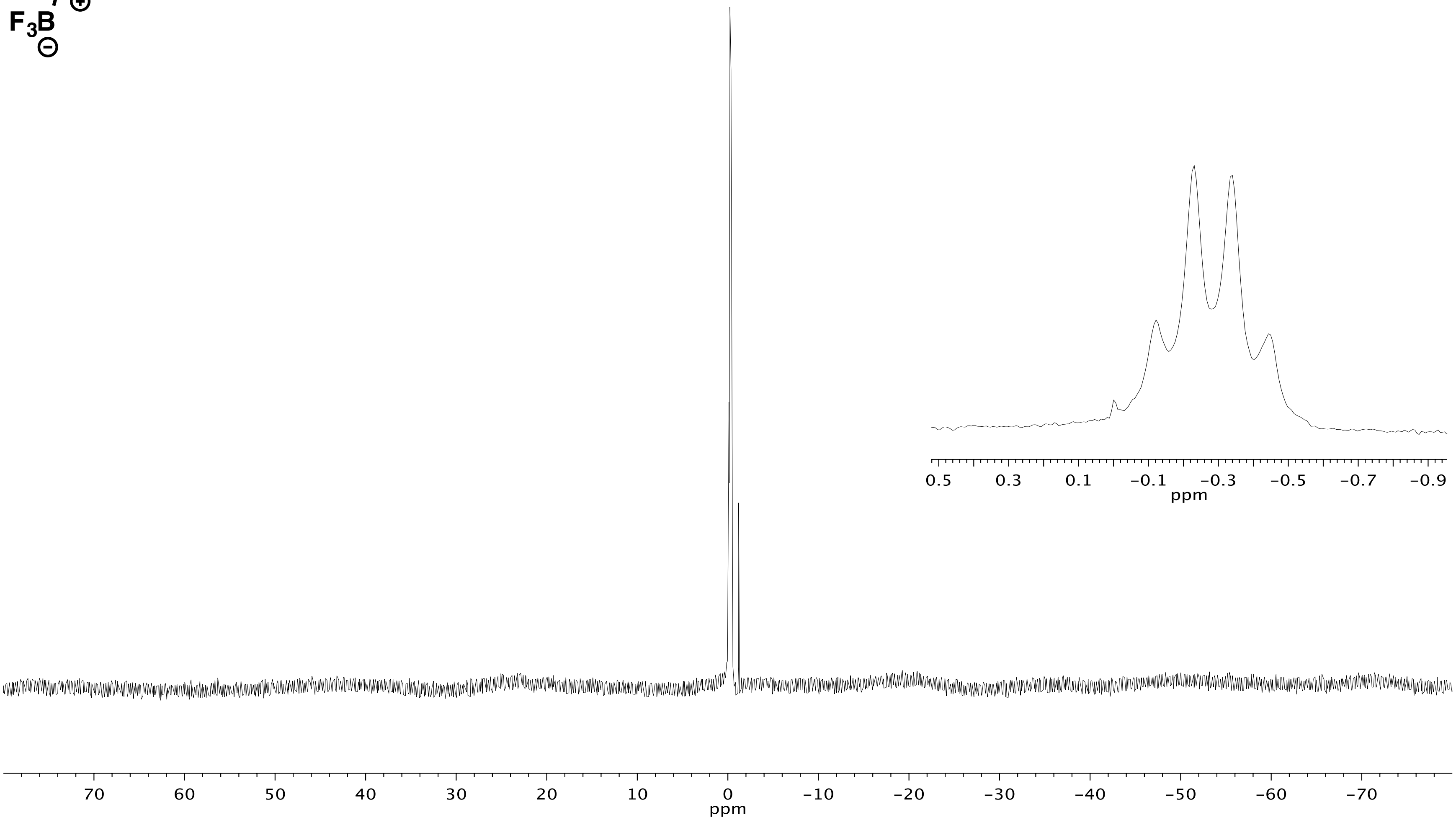


^{1}H NMR (400 MHz, CD_3CN) of compound **4•BF$_3$**.

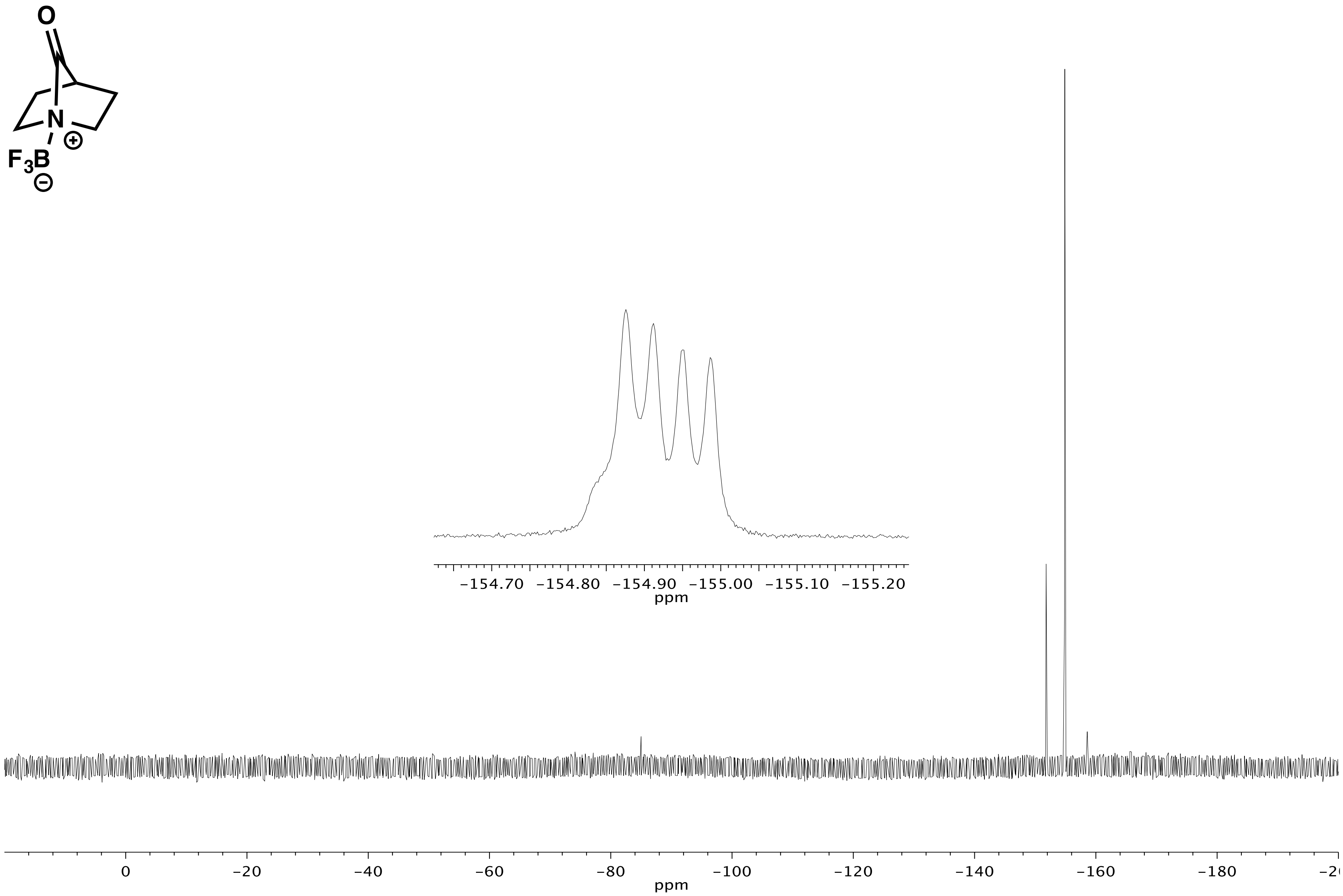


^{13}C NMR (101 MHz, CD$_3$CN) of compound **4•BF$_3$**.

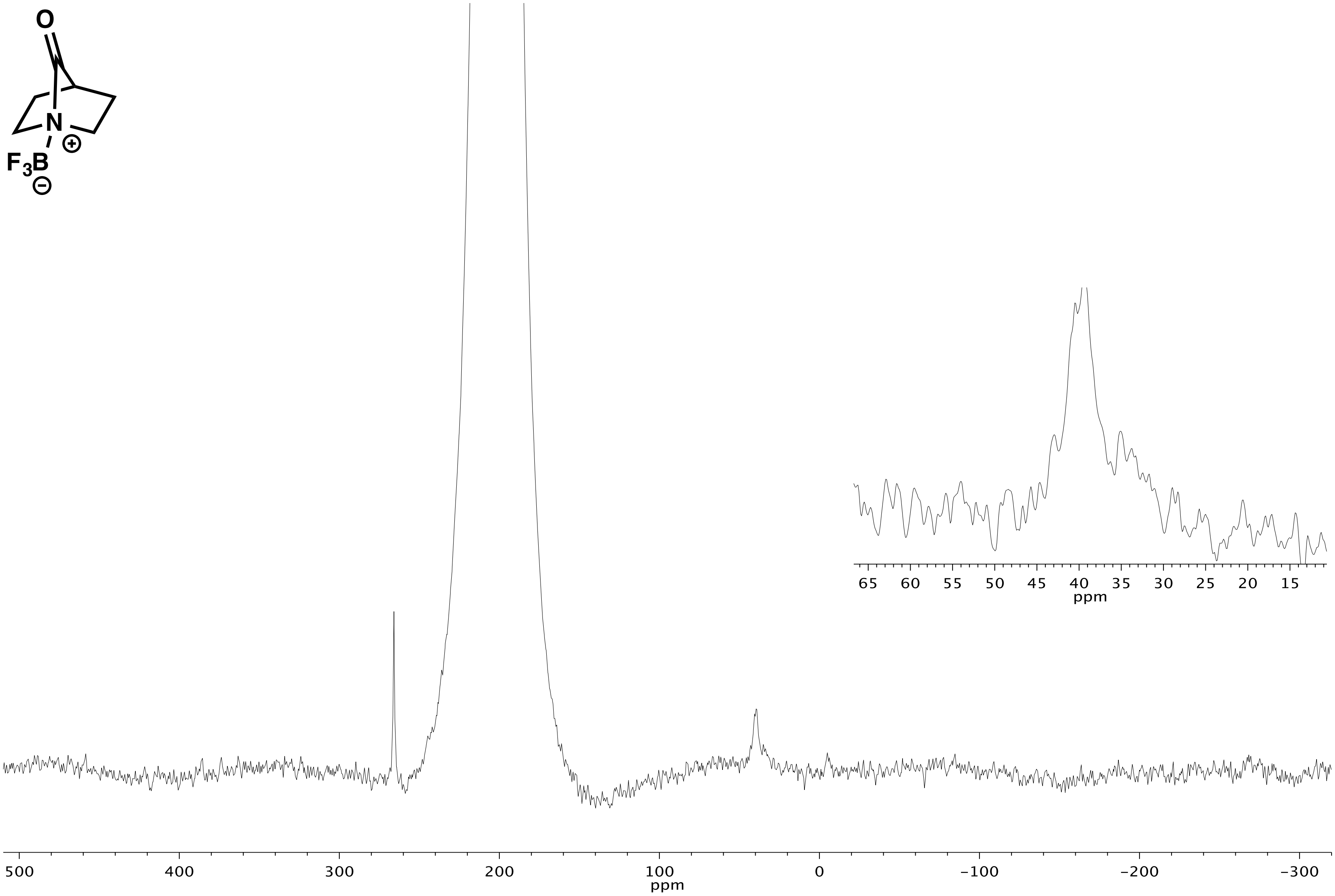




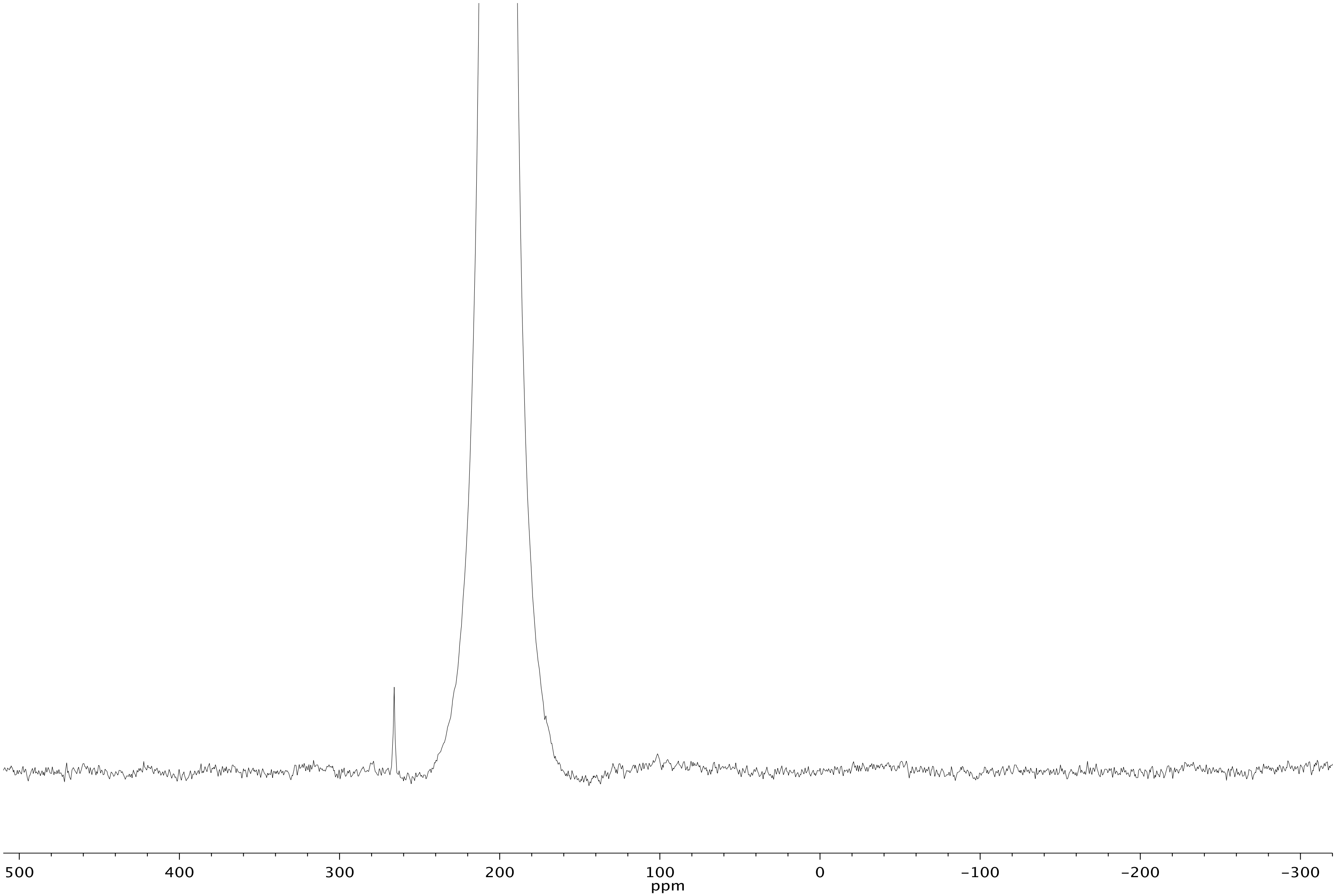
^{11}B NMR (128 MHz, CD$_3$CN) of compound **4•BF$_3$**.



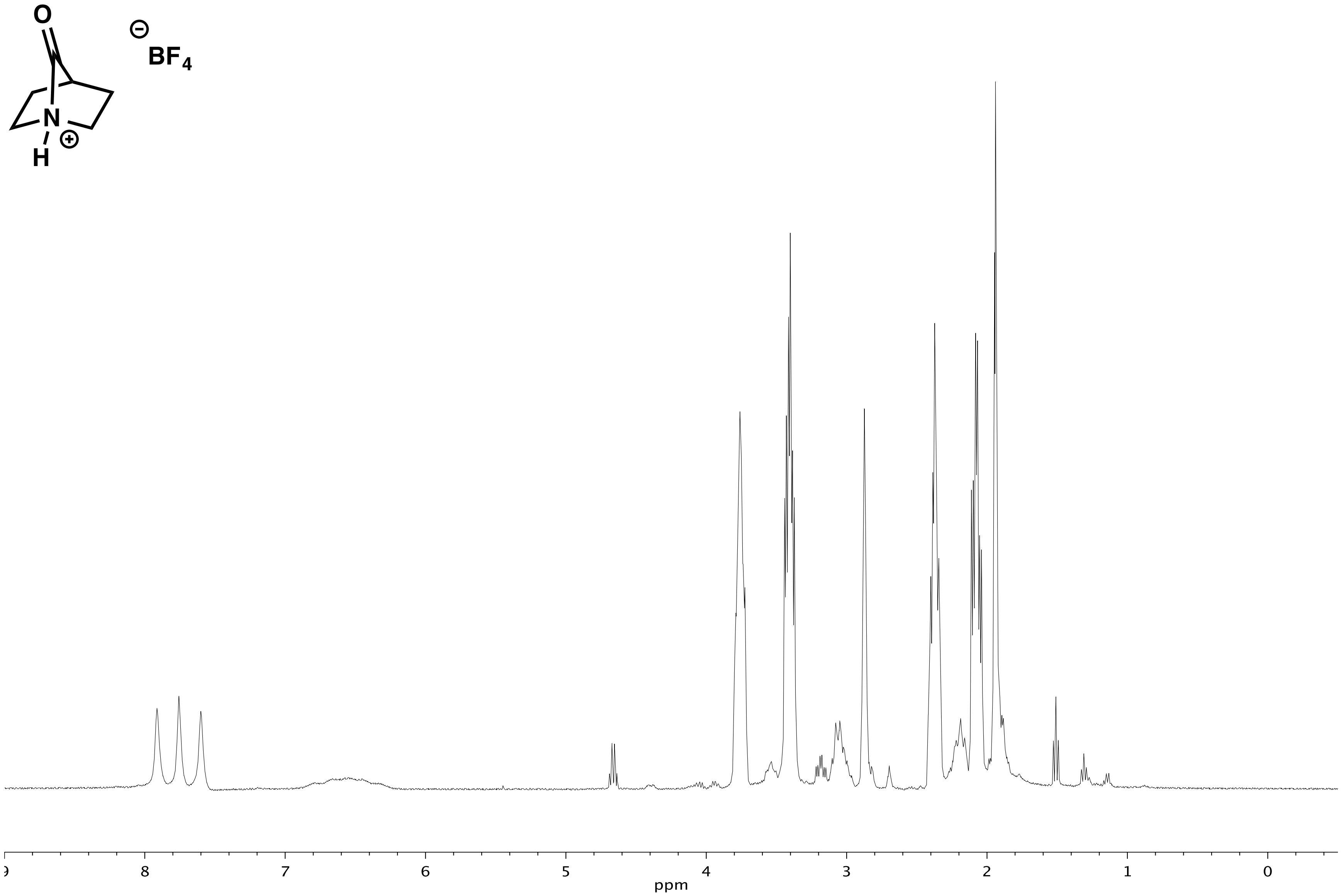
^{19}F NMR (376 MHz, CD_3CN) of compound **4•BF$_3$**.



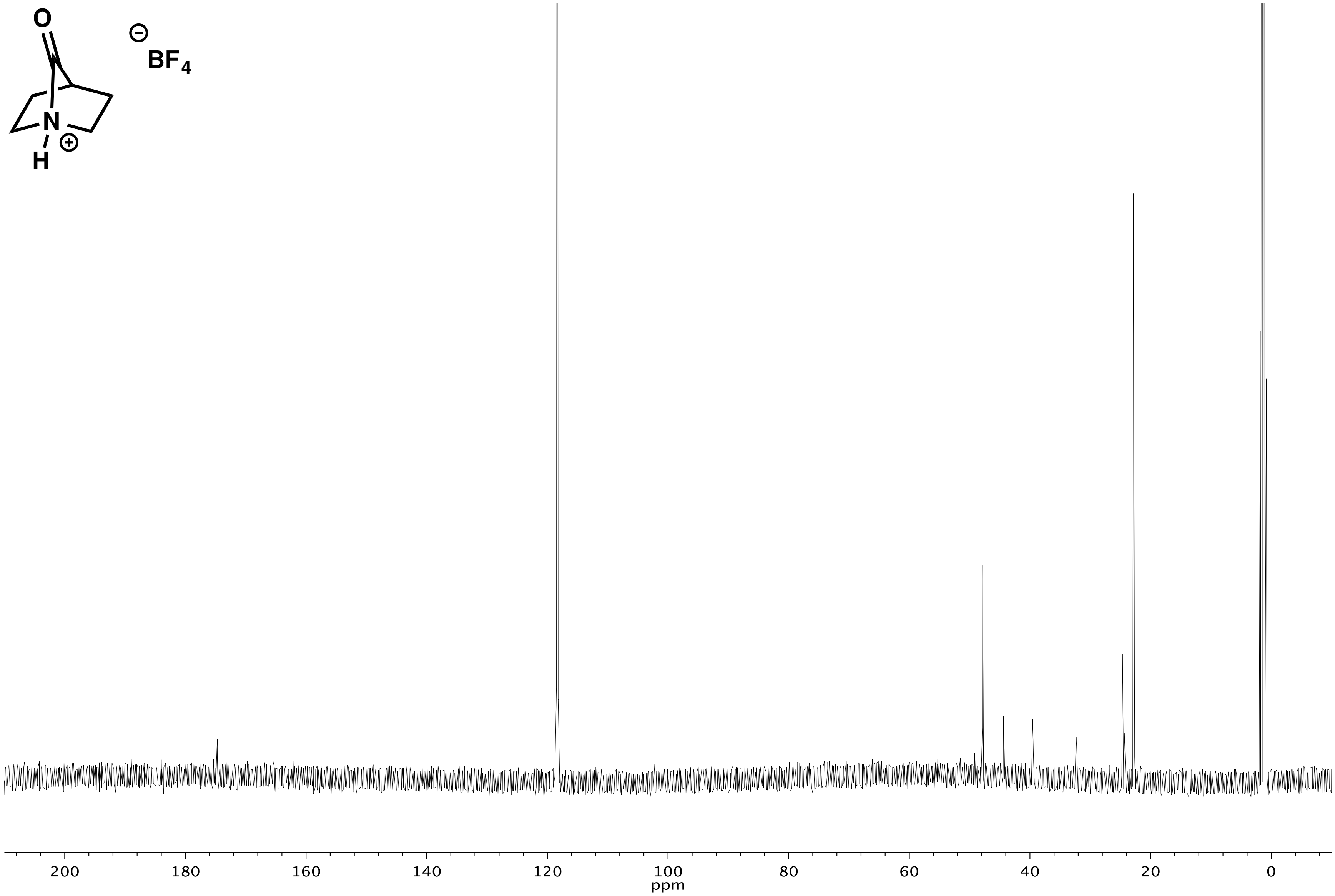
^{14}N NMR (36 MHz, CD$_3$CN) of compound **4•BF$_3$**.



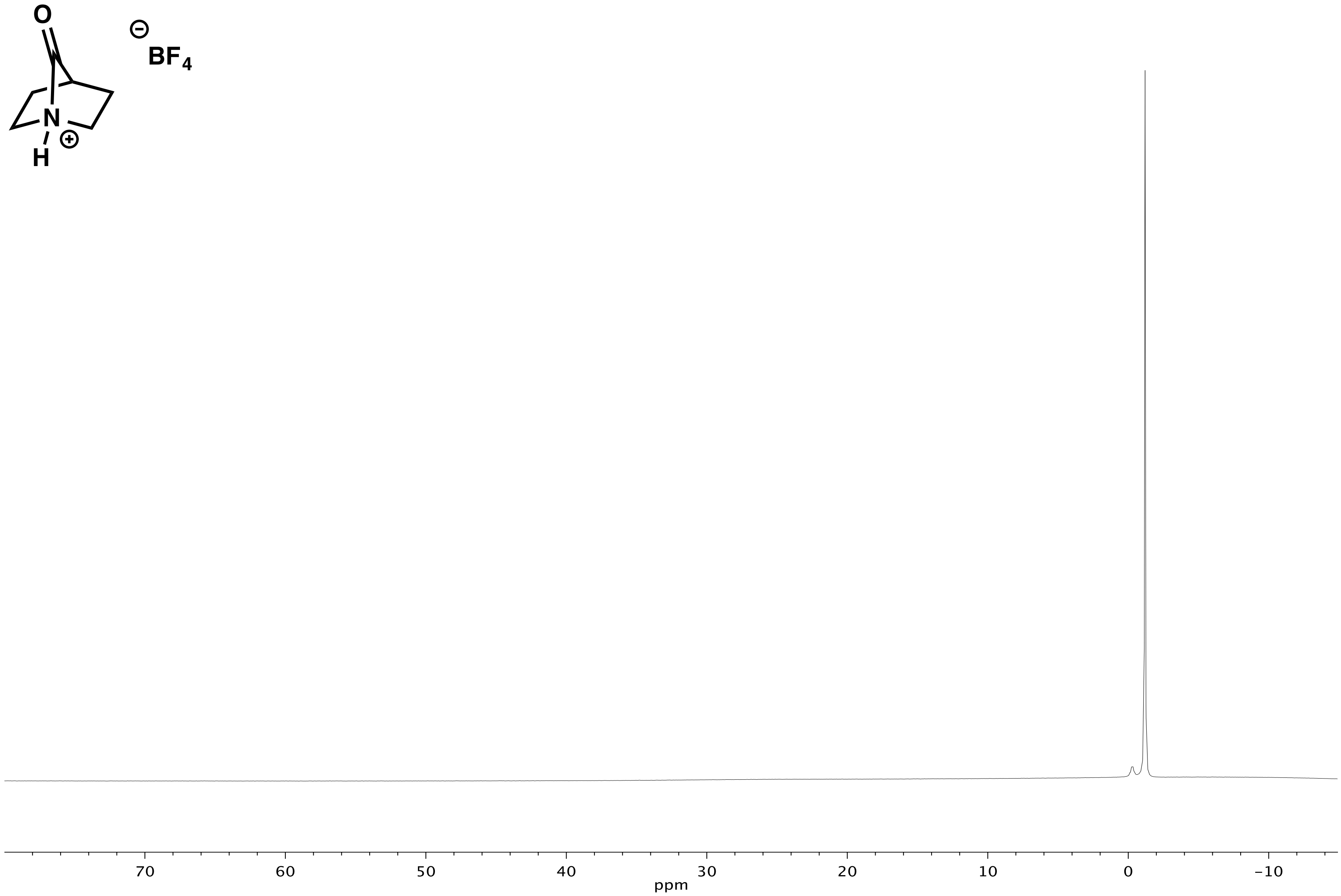
^{14}N NMR (36 MHz, CD_3CN) of blank CD_3CN.



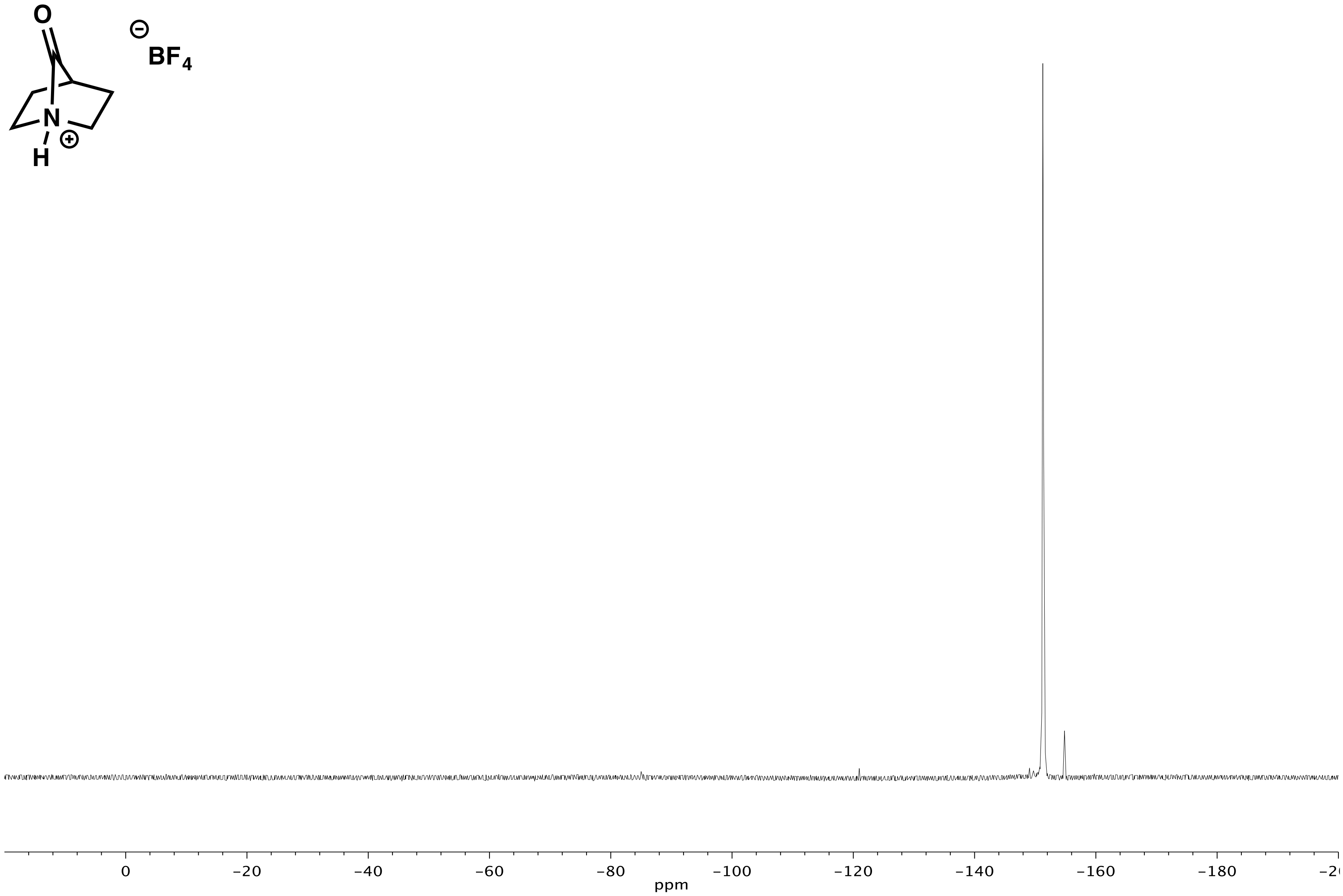
^{1}H NMR (400 MHz, CD$_3$CN) of compound **4•HBF$_4$**.



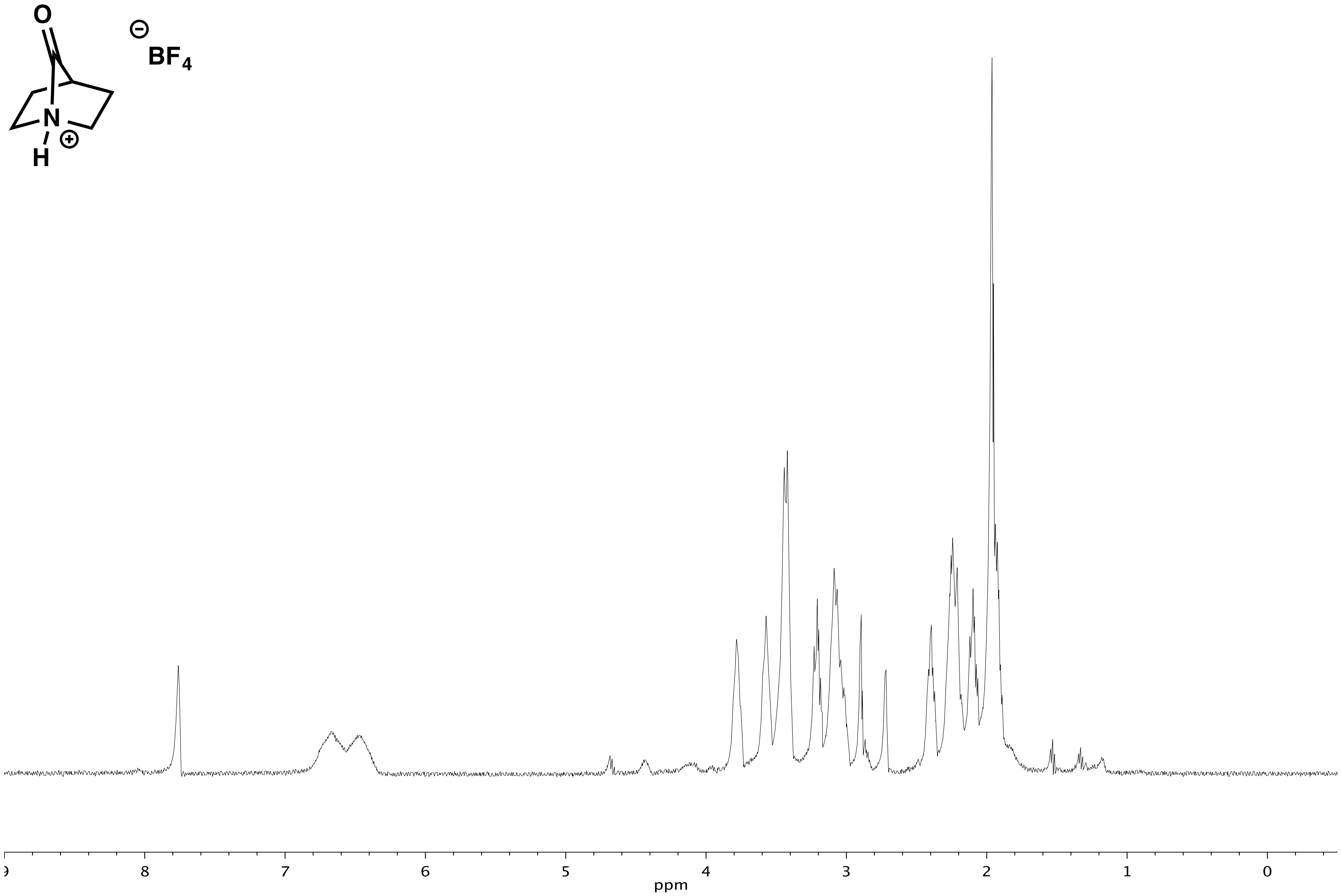
^{13}C NMR (126 MHz, CD$_3$CN) of compound **4•HBF$_4$**.



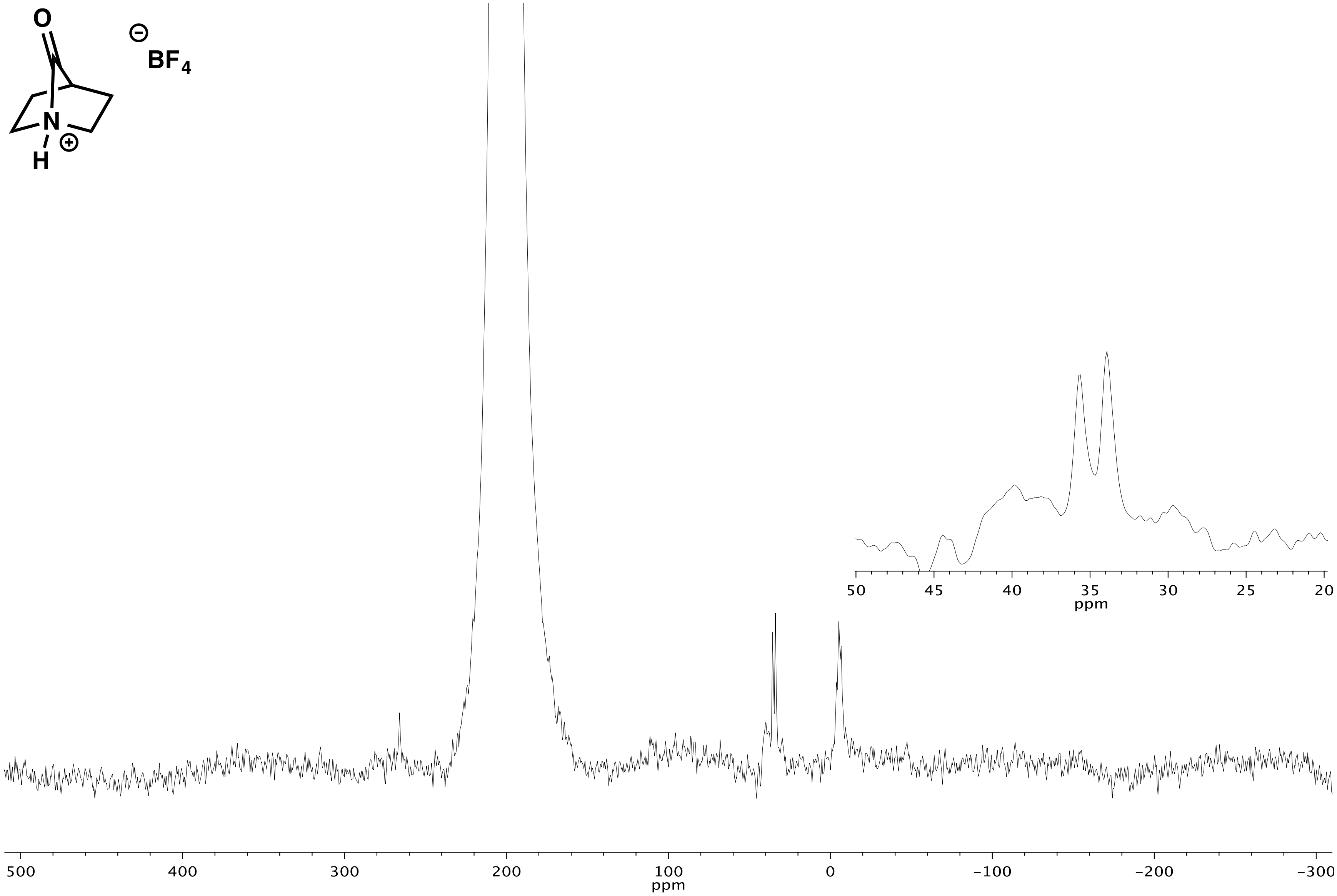
^{11}B NMR (128 MHz, CD$_3$CN) of compound **4•HBF$_4$**.



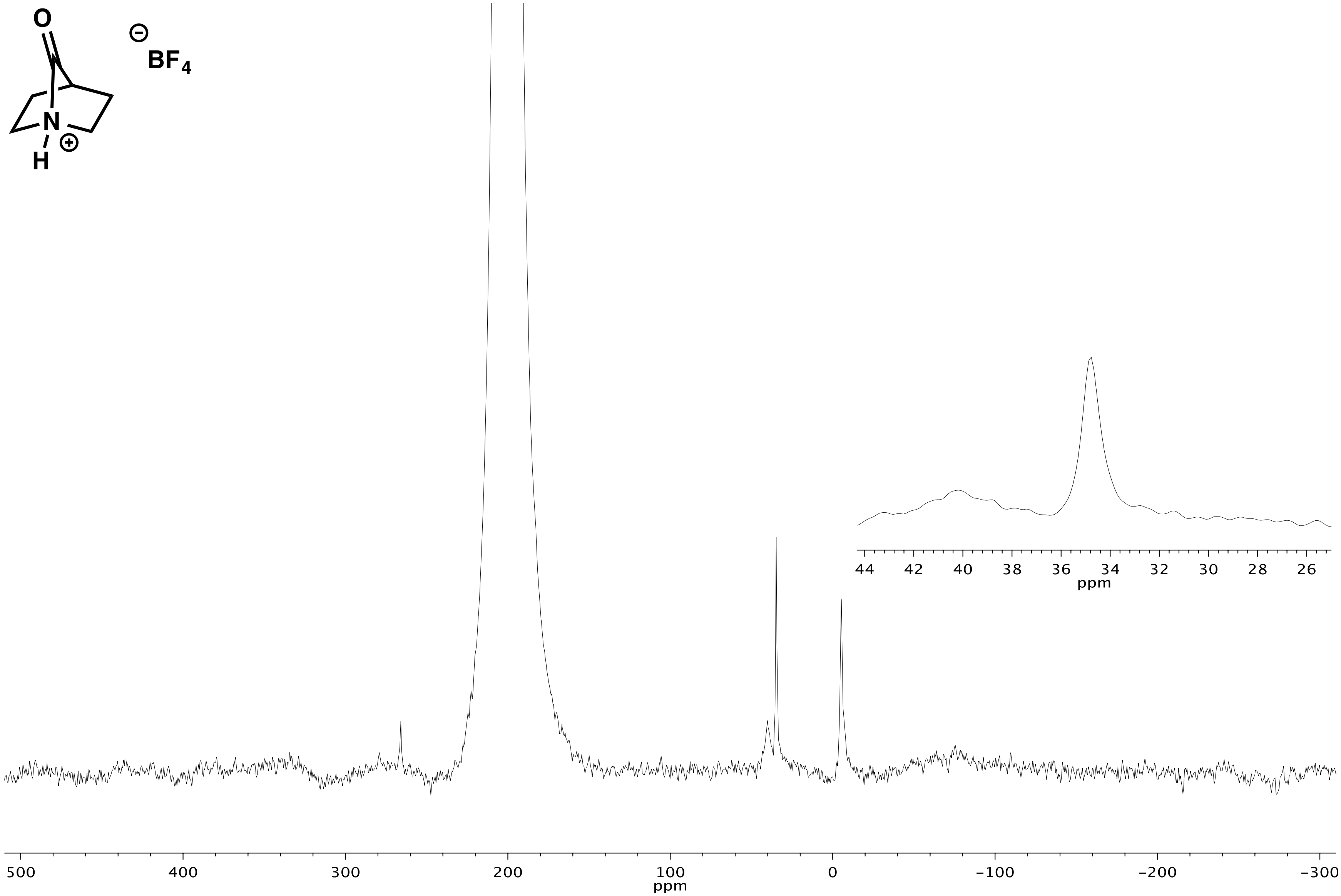
^{19}F NMR (376 MHz, CD_3CN) of compound **4• HBF_4**.



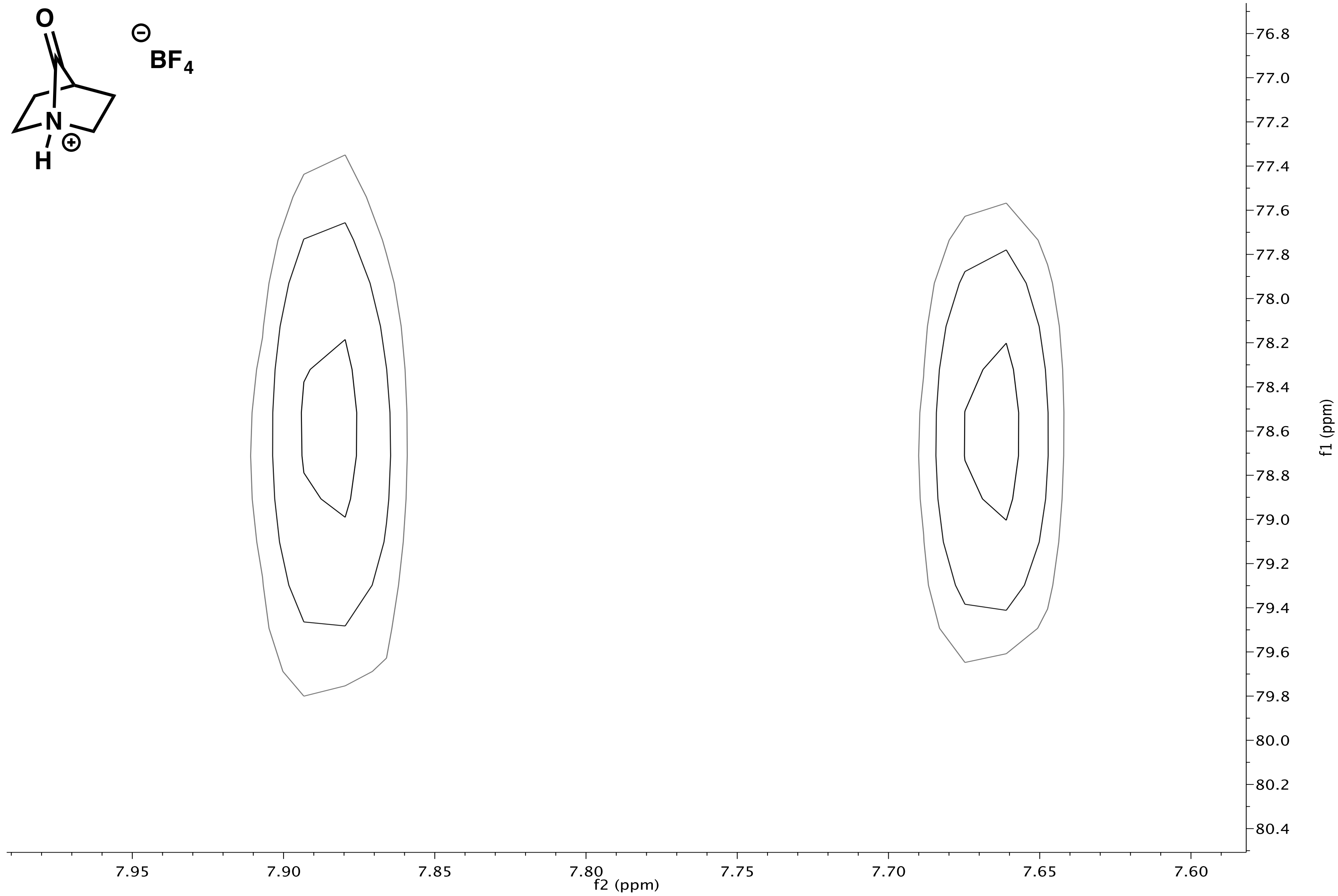
$^{1}H\{^{14}N\}$ NMR (500 MHz, CD_3CN) of compound **4•HBF$_4$**.



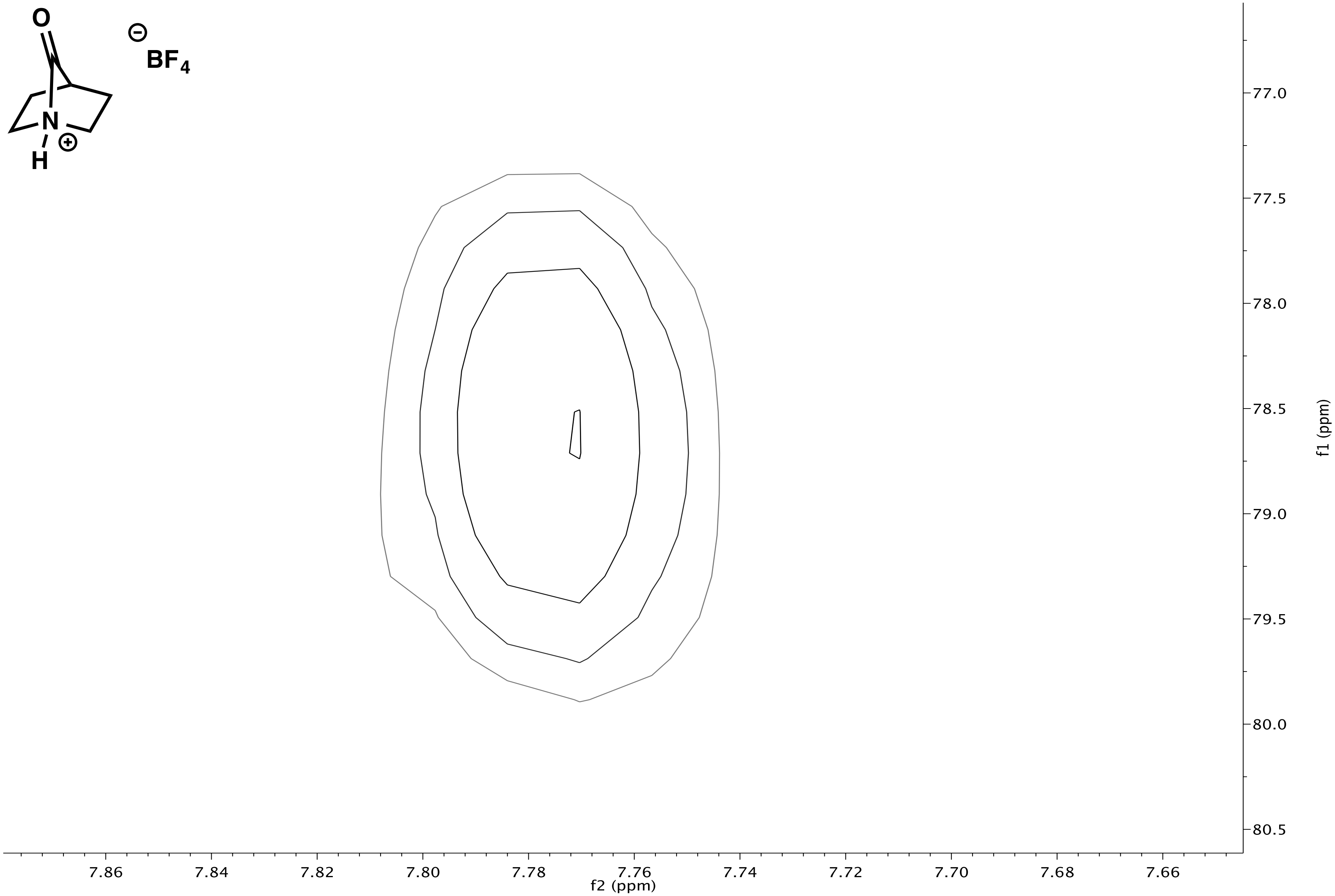
^{14}N NMR (36 MHz, CD$_3$CN) of compound **4•HBF$_4$**.



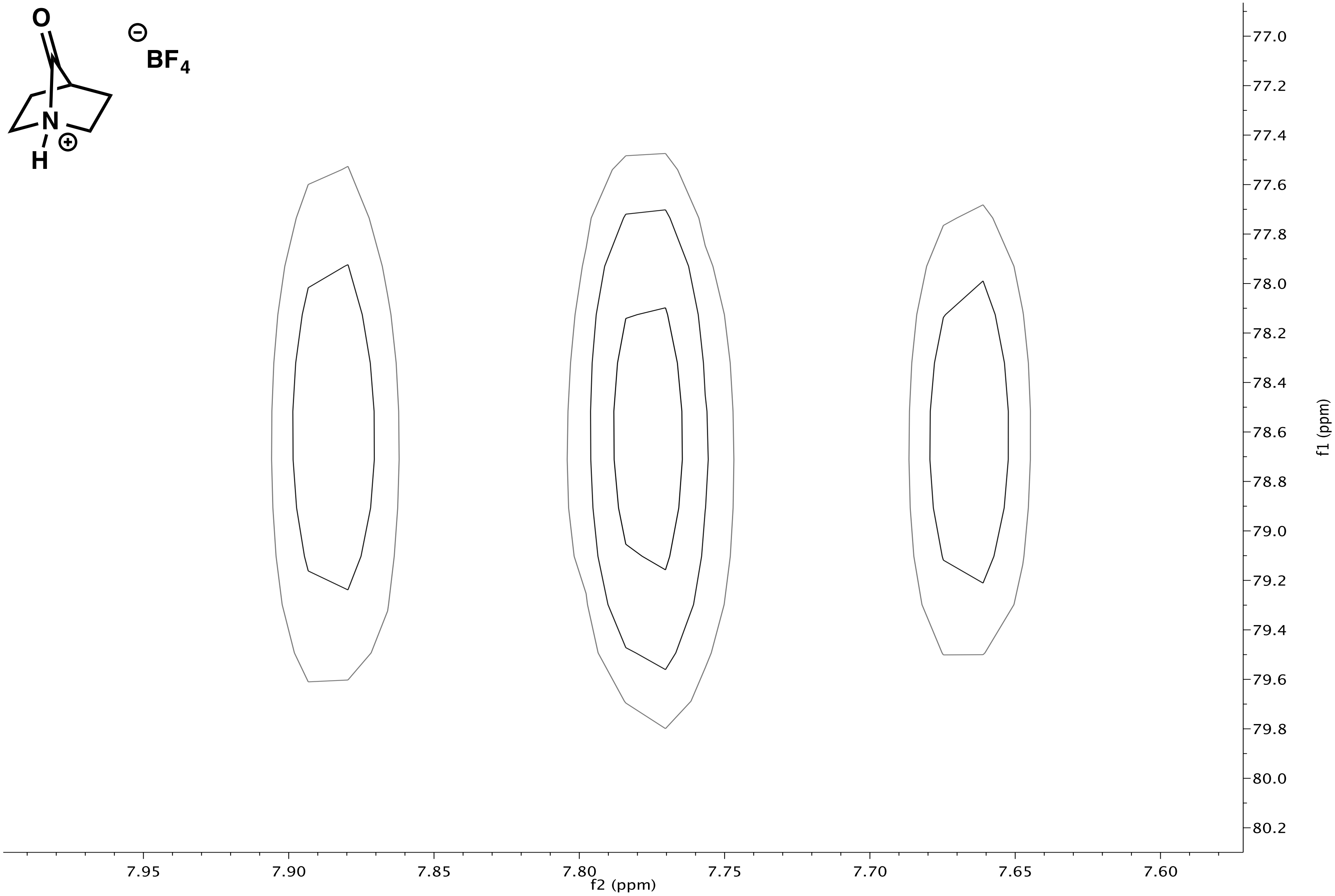
^{14}N{^{1}H} NMR (36 MHz, CD_3CN) of compound **4•HBF$_4$**.



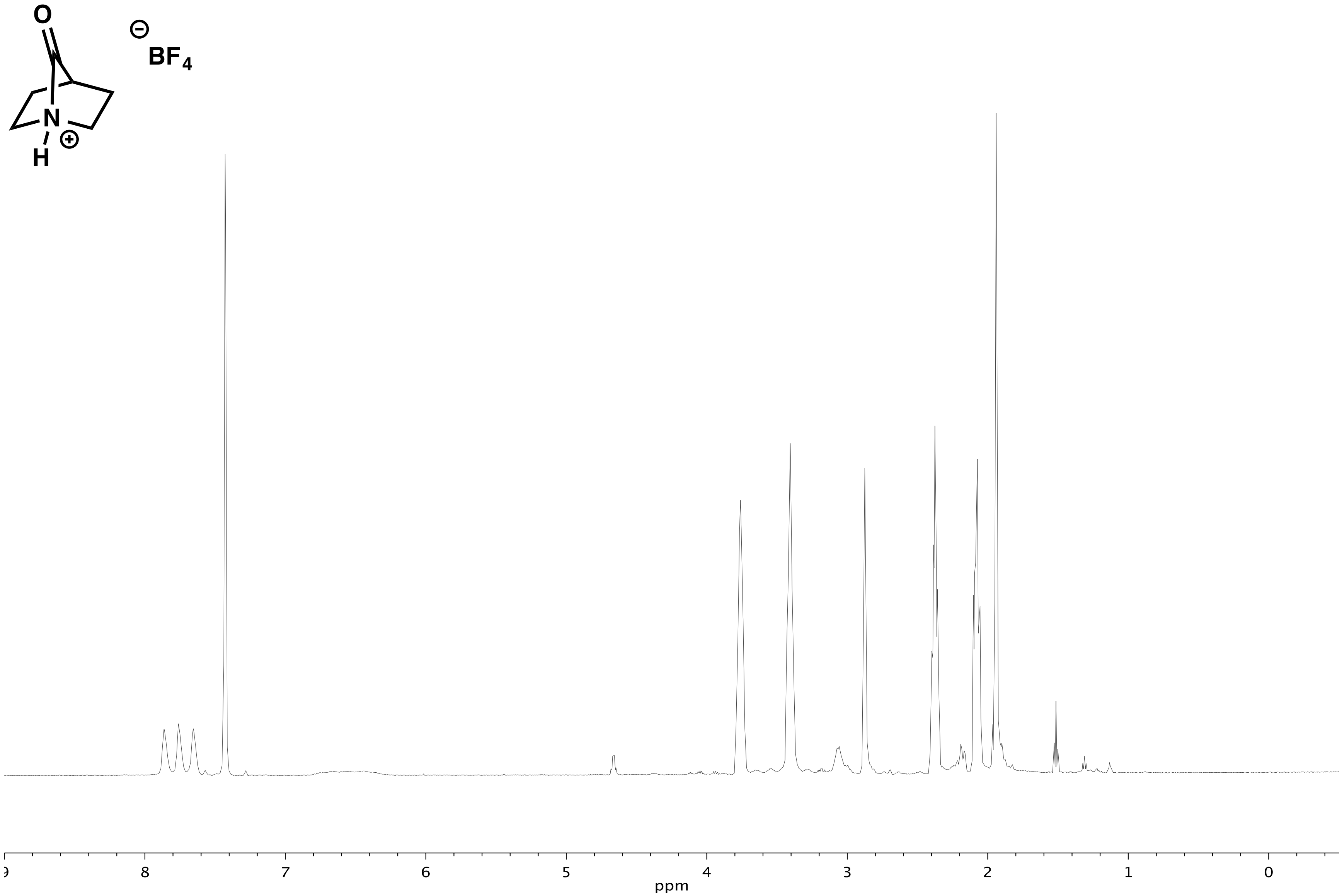
^{1}H-^{15}N hsqc (400 MHz and 41 MHz, CD$_3$CN) of compound **4•HBF$_4$**.



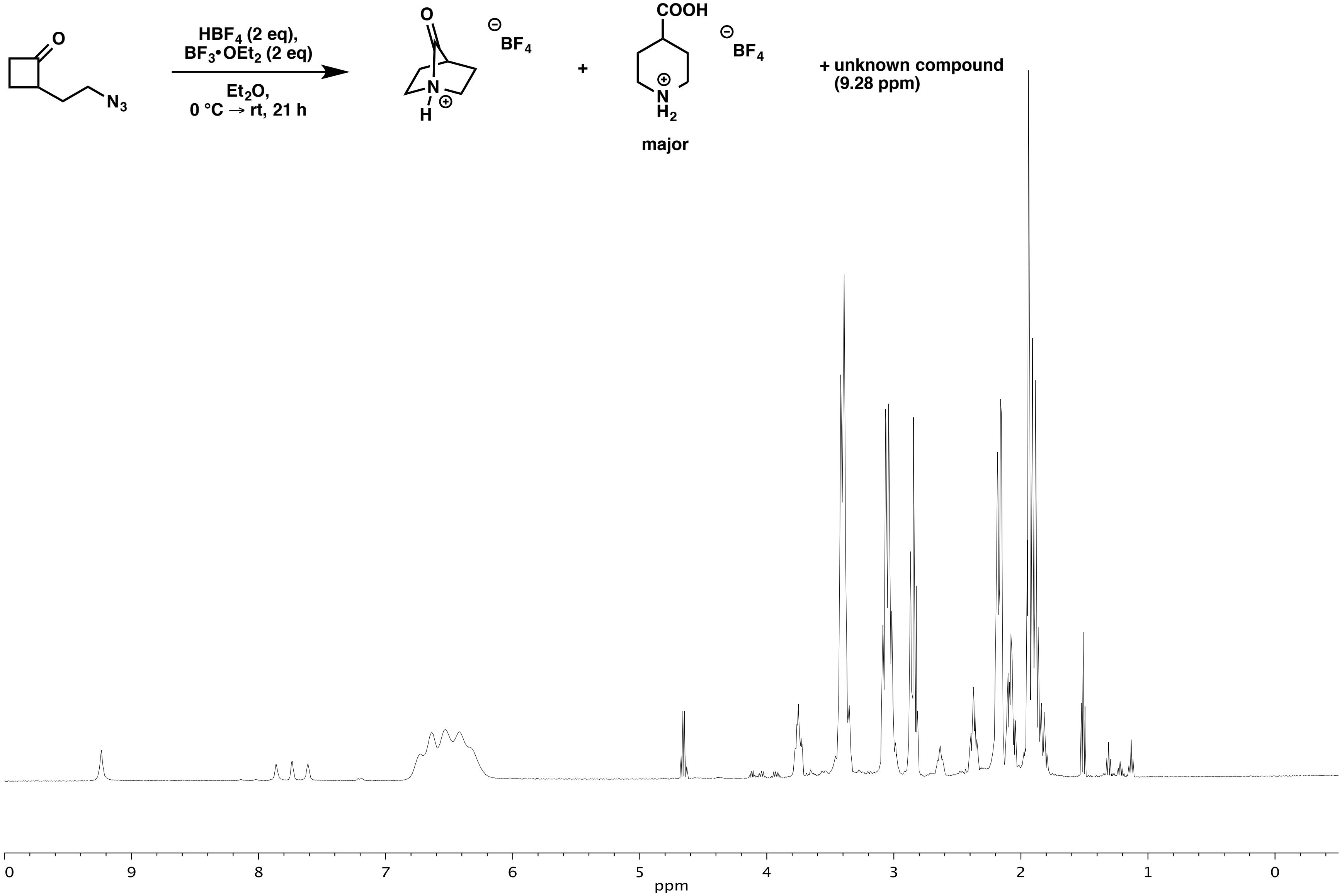
$^{1}H\{^{15}N\}$-^{15}N hsqc (400 MHz and 41 MHz, CD_3CN) of compound **4•HBF**$_4$.



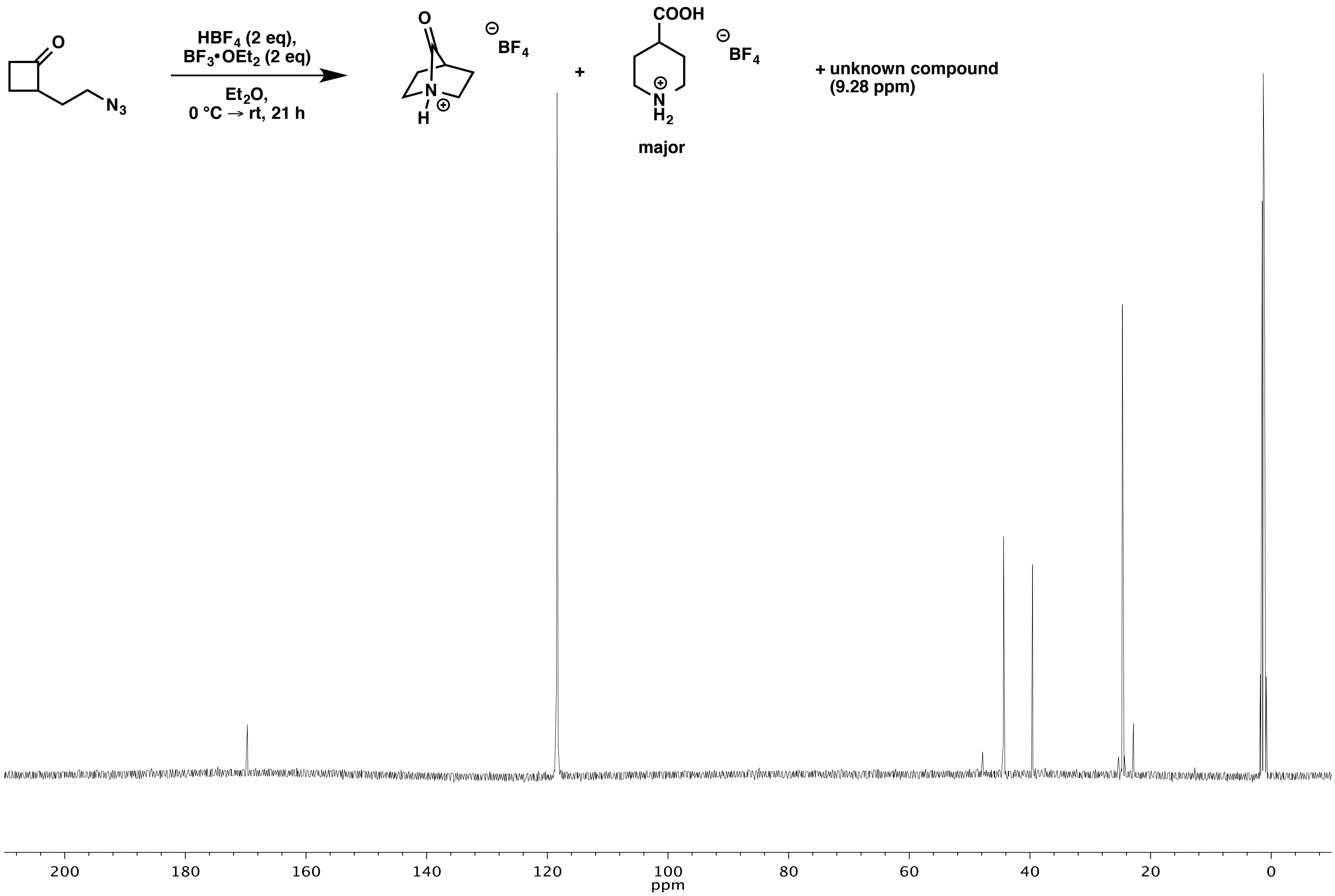
Superimposed ^{1}H-^{15}N hsqc and ^{1}H{^{15}N}-^{15}N hsqc (400 MHz and 41 MHz, CD_3CN) of compound **4•HBF$_4$**.



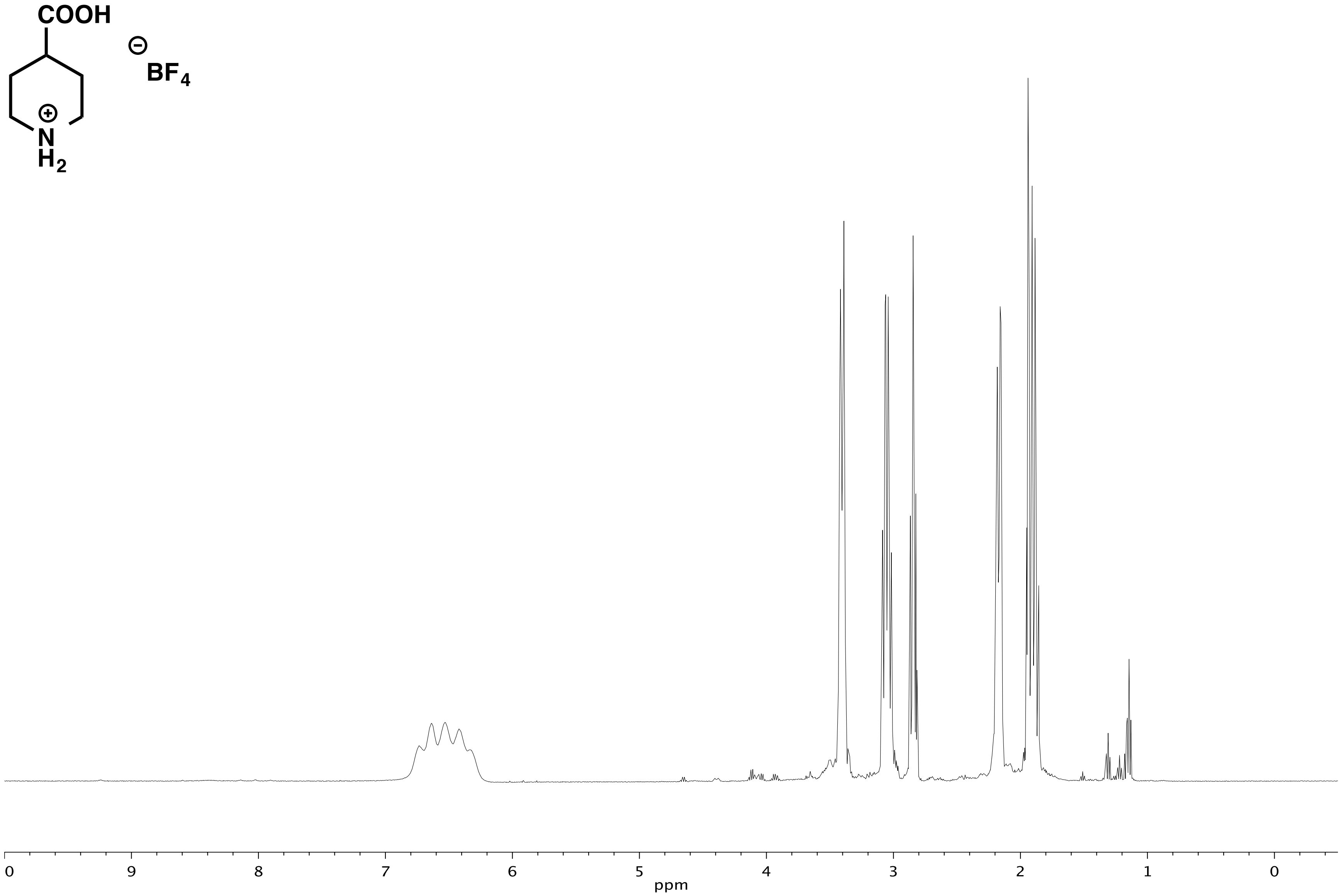
^{1}H NMR (600 MHz, CD$_3$CN) of compound **4•HBF$_4$** with 1,3,5-trichlorobenzene (internal standard).



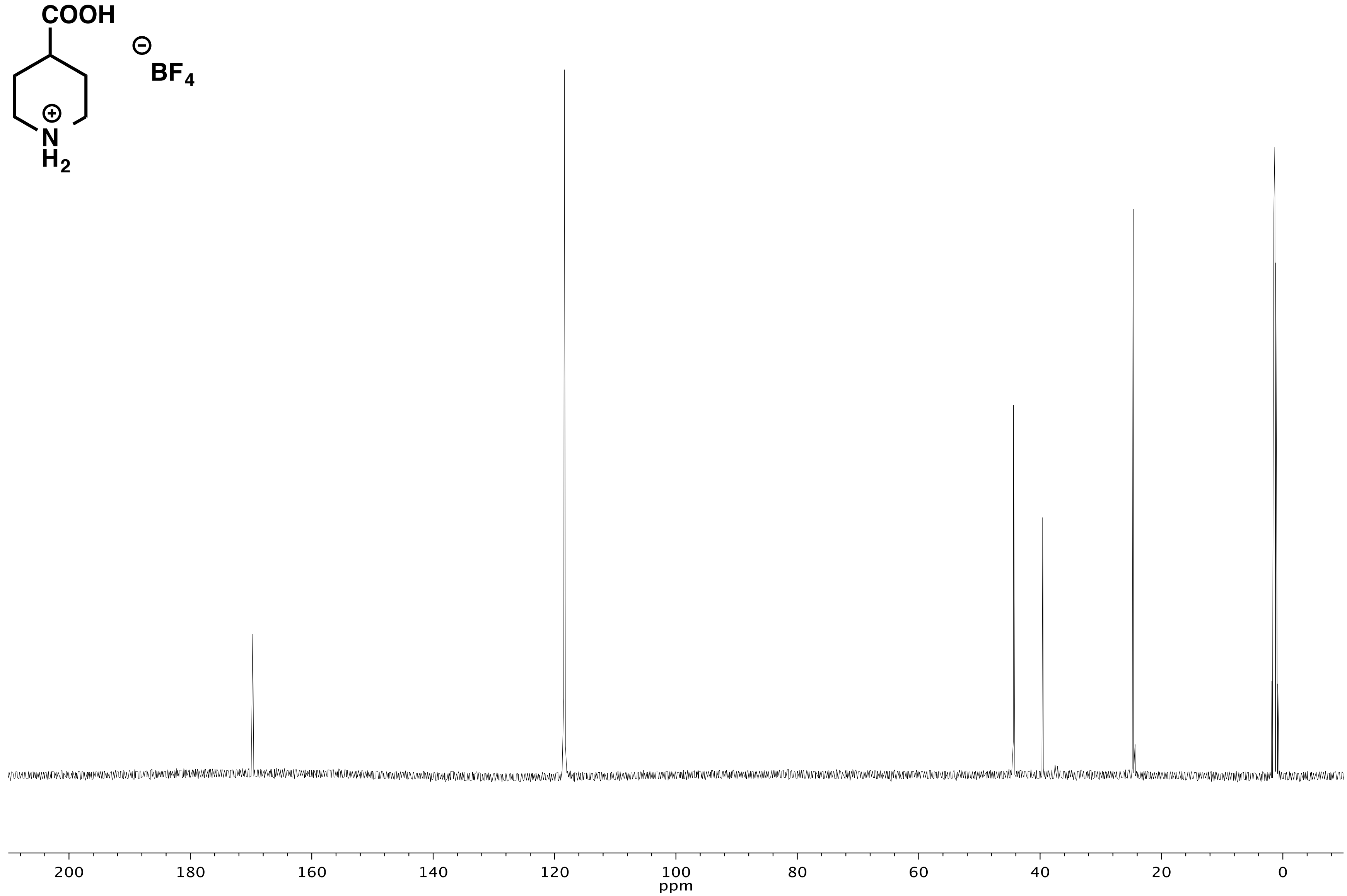
Crude ^{1}H NMR (500 MHz, CD$_3$CN) of compound **11**.



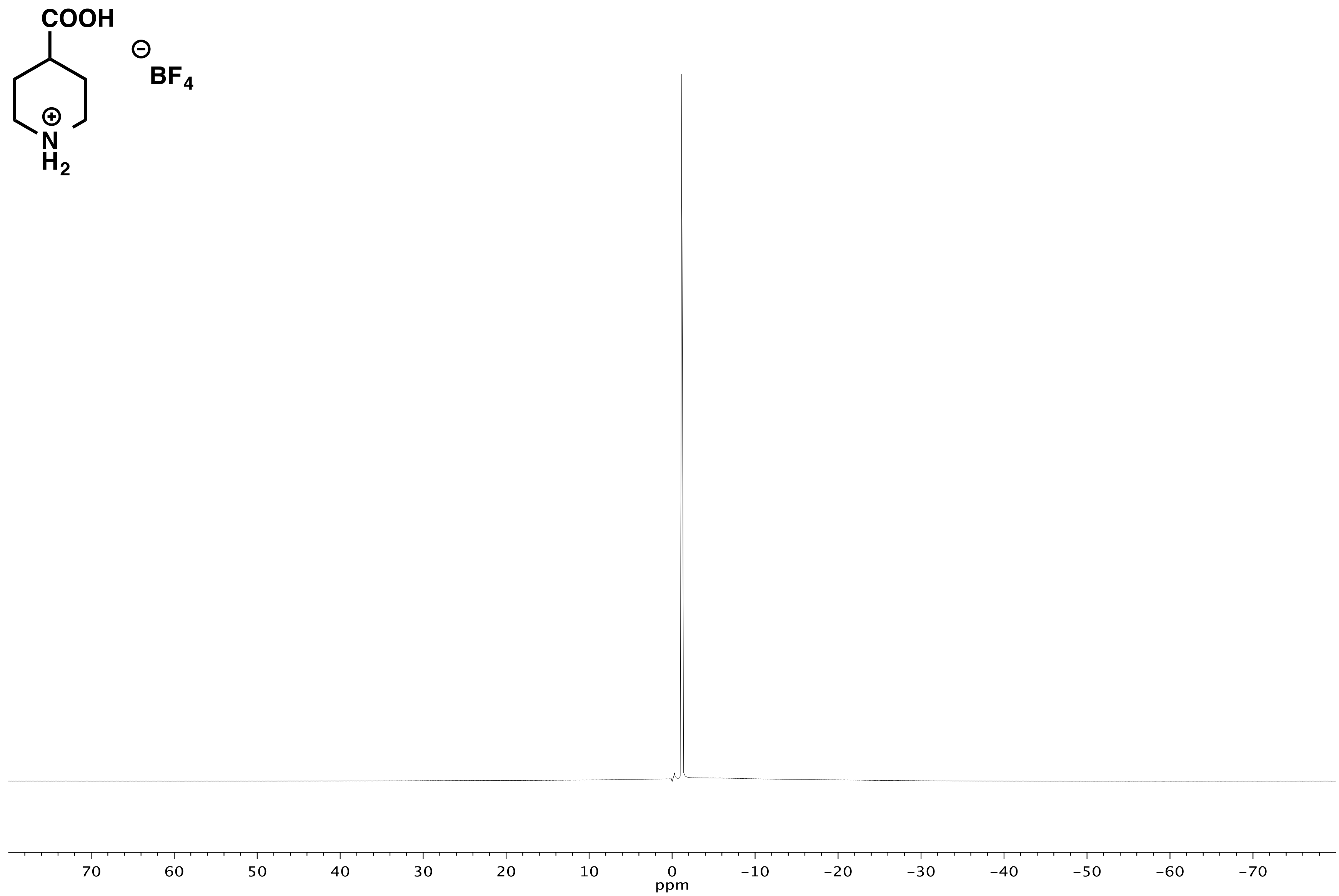
Crude ^{13}C NMR (126 MHz, CD_3CN) of compound **11**.



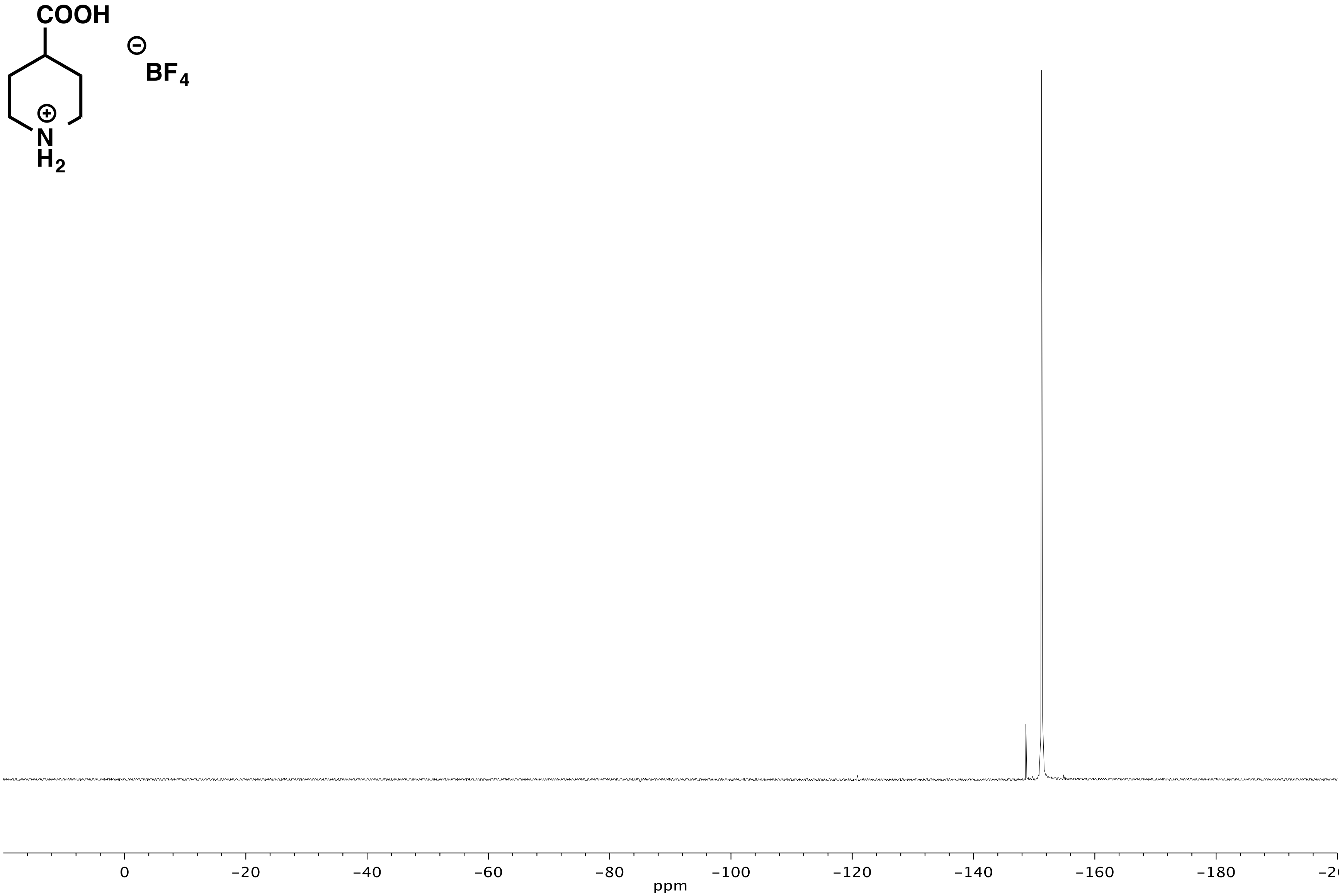
^{1}H NMR (500 MHz, CD$_3$CN) of compound **11**.



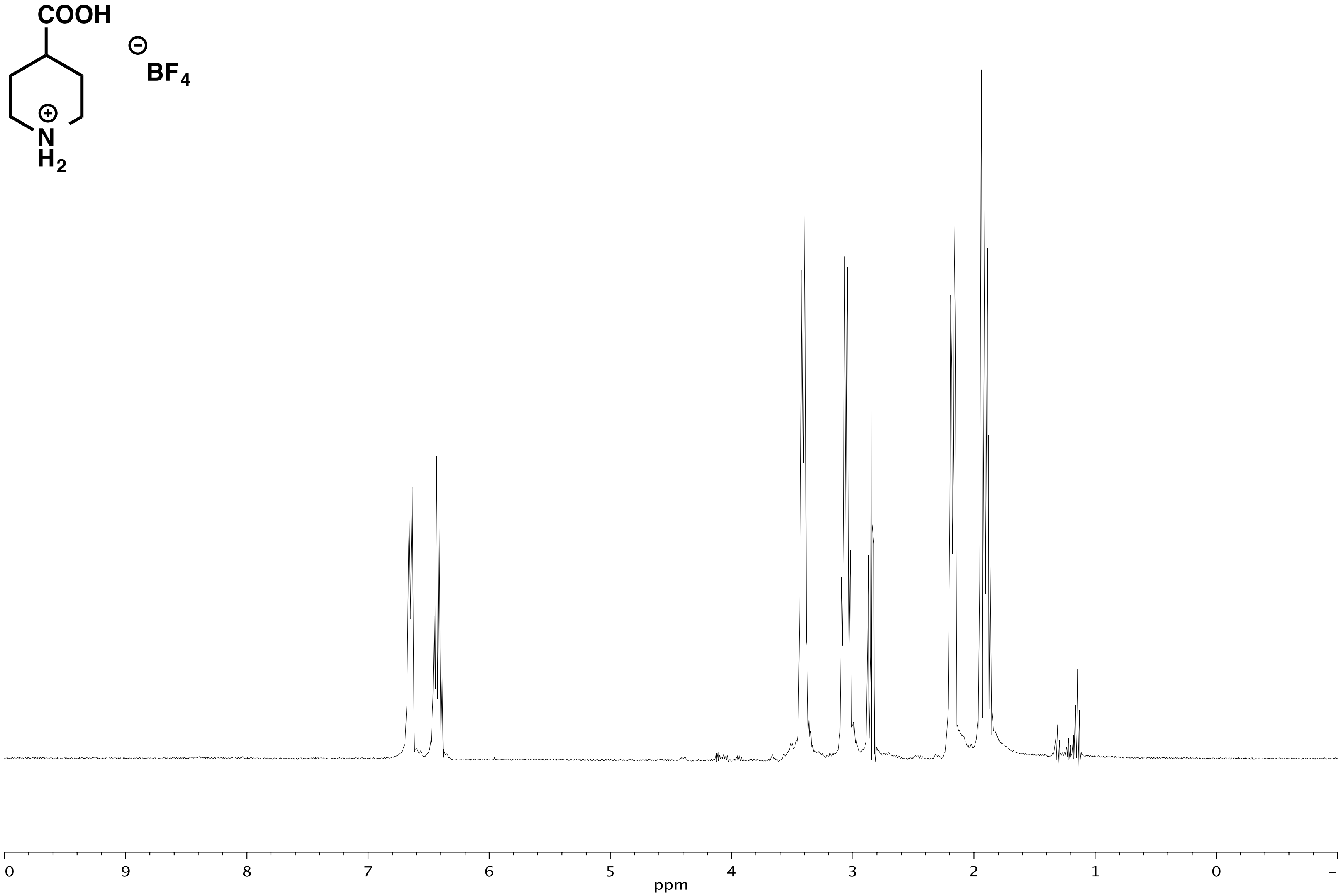
^{13}C NMR (126 MHz, CD$_3$CN) of compound **11**.



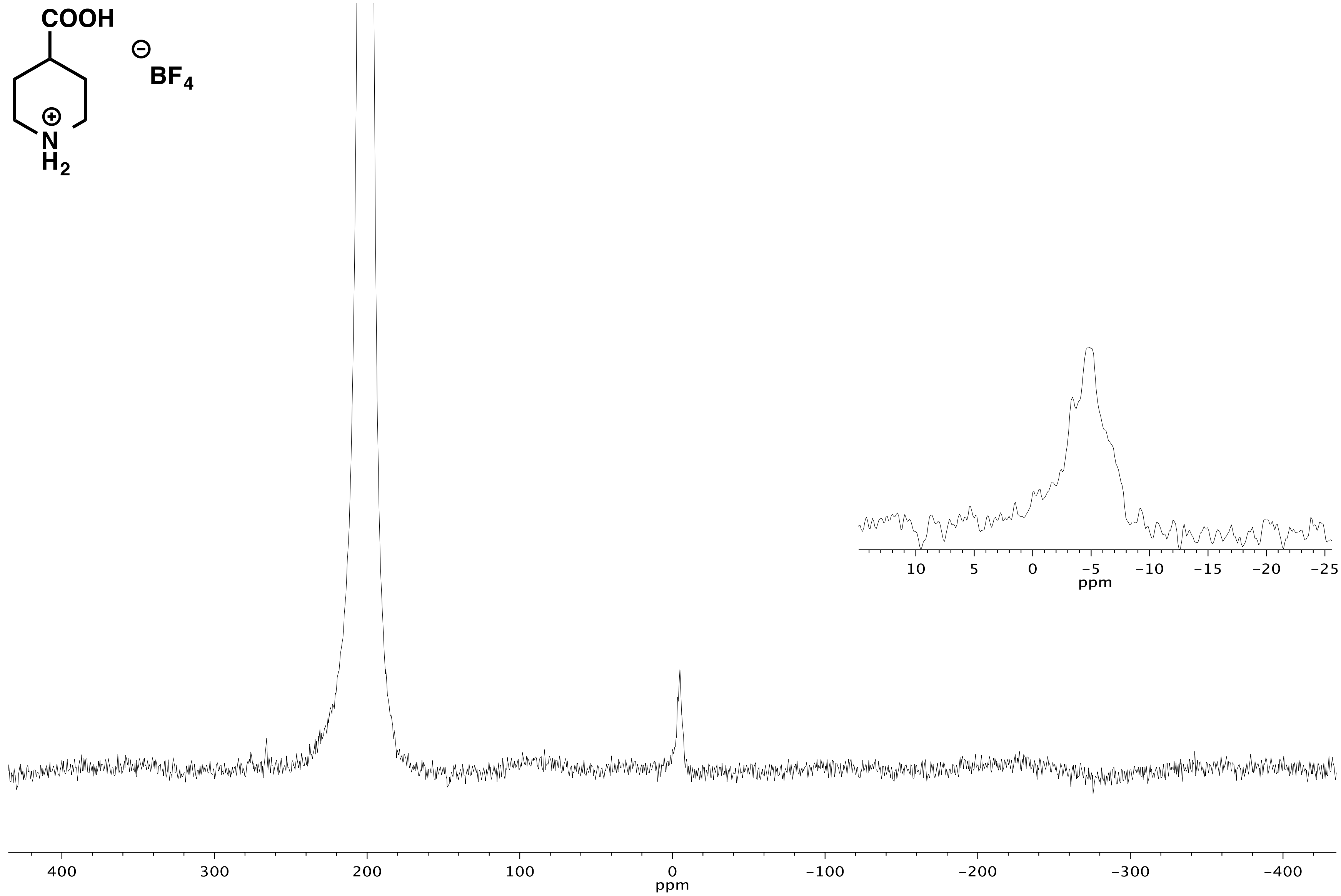
^{11}B NMR (128 MHz, CD$_3$CN) of compound **11**.



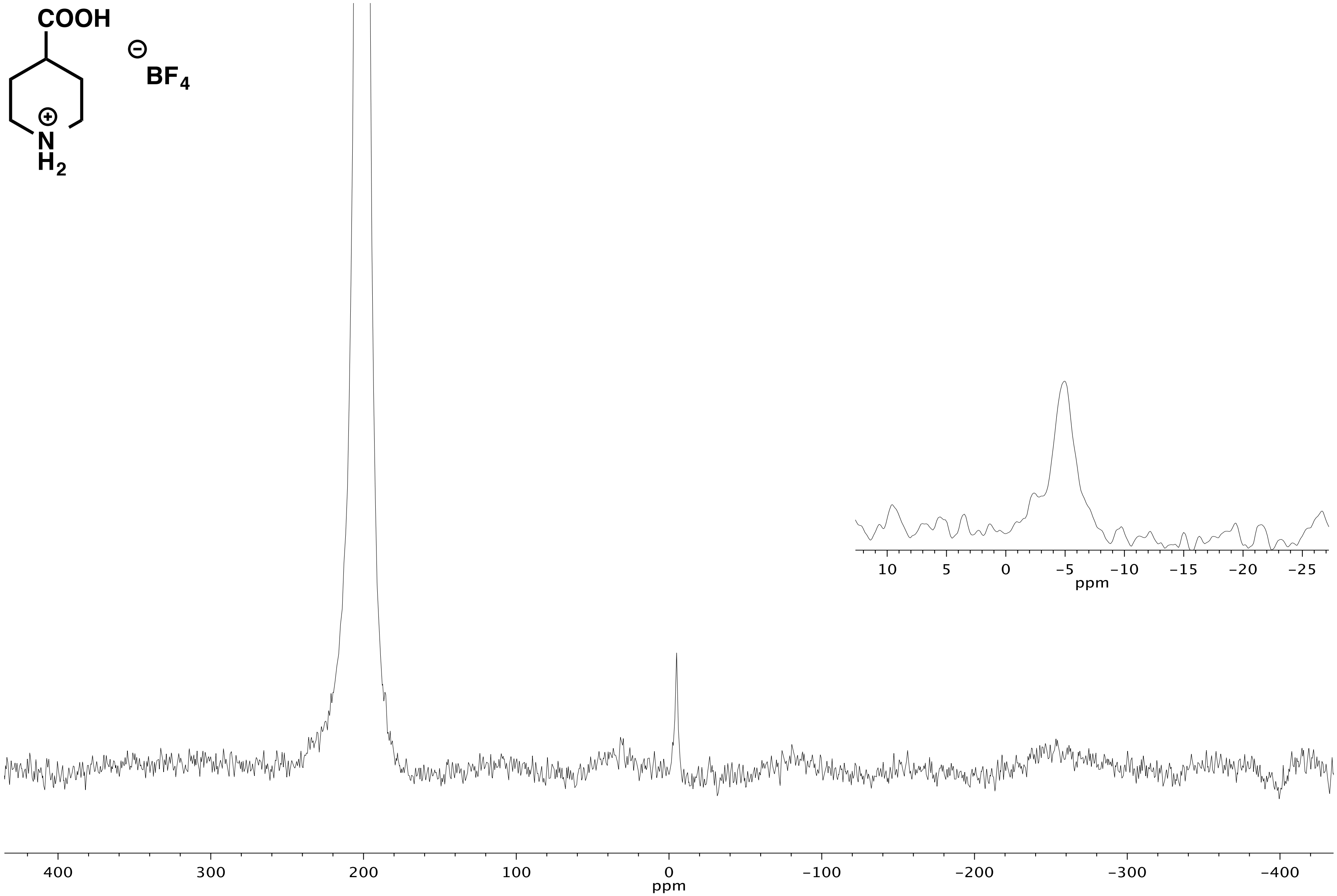
^{19}F NMR (376 MHz, CD$_3$CN) of compound **11**.



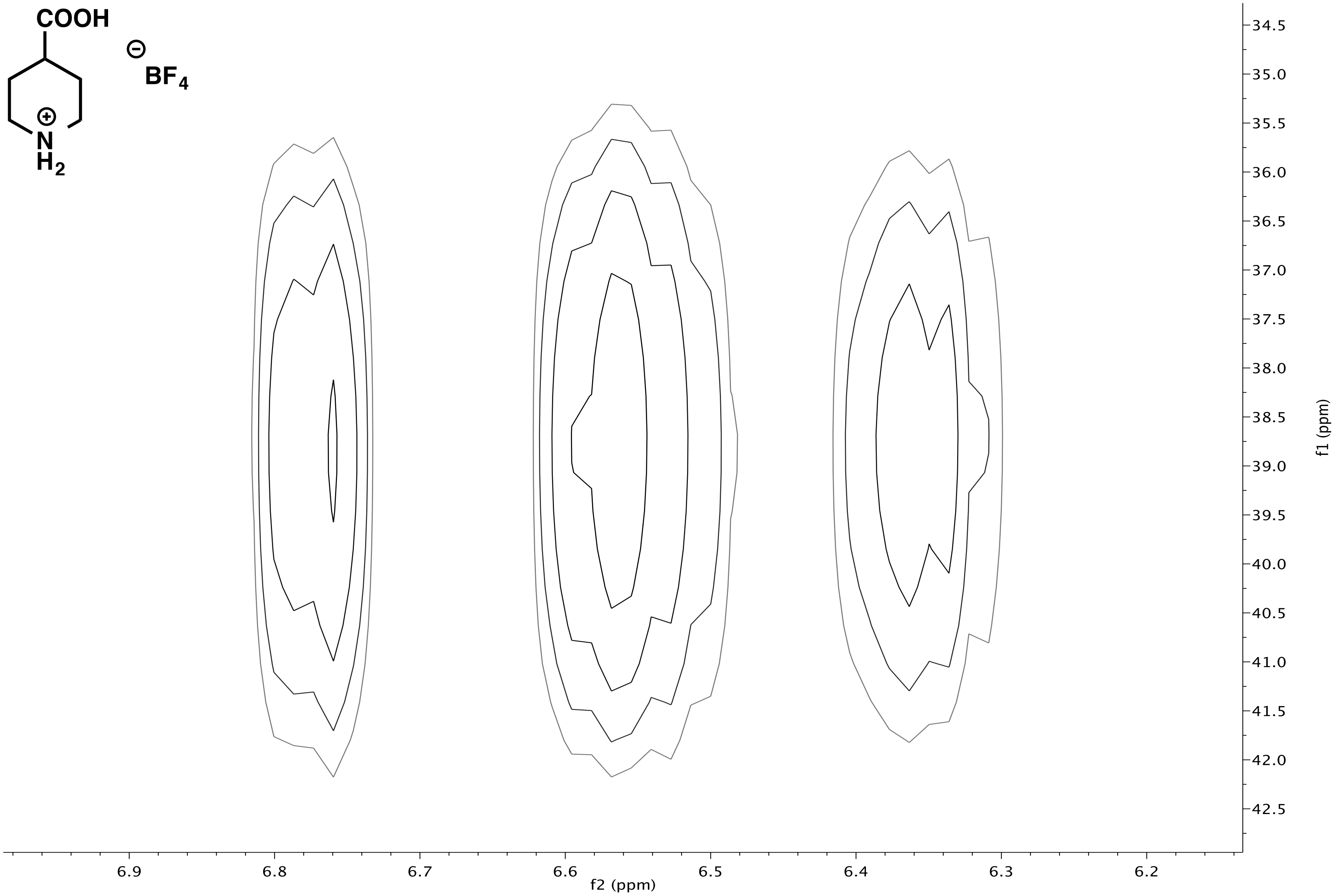
^{1}H{^{14}N} NMR (500 MHz, CD$_3$CN) of compound **11**.



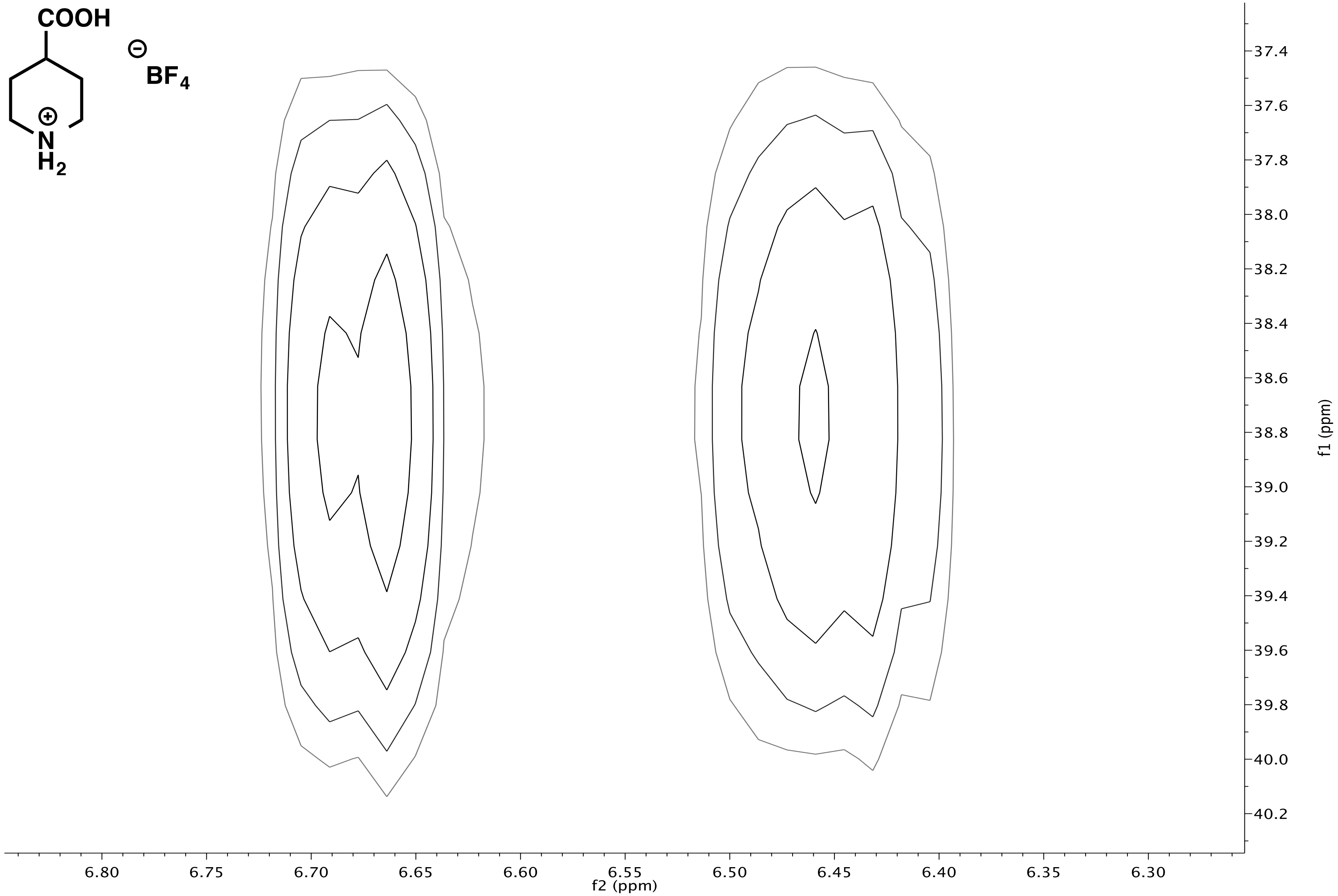
^{14}N NMR (36 MHz, CD$_3$CN) of compound **11**.



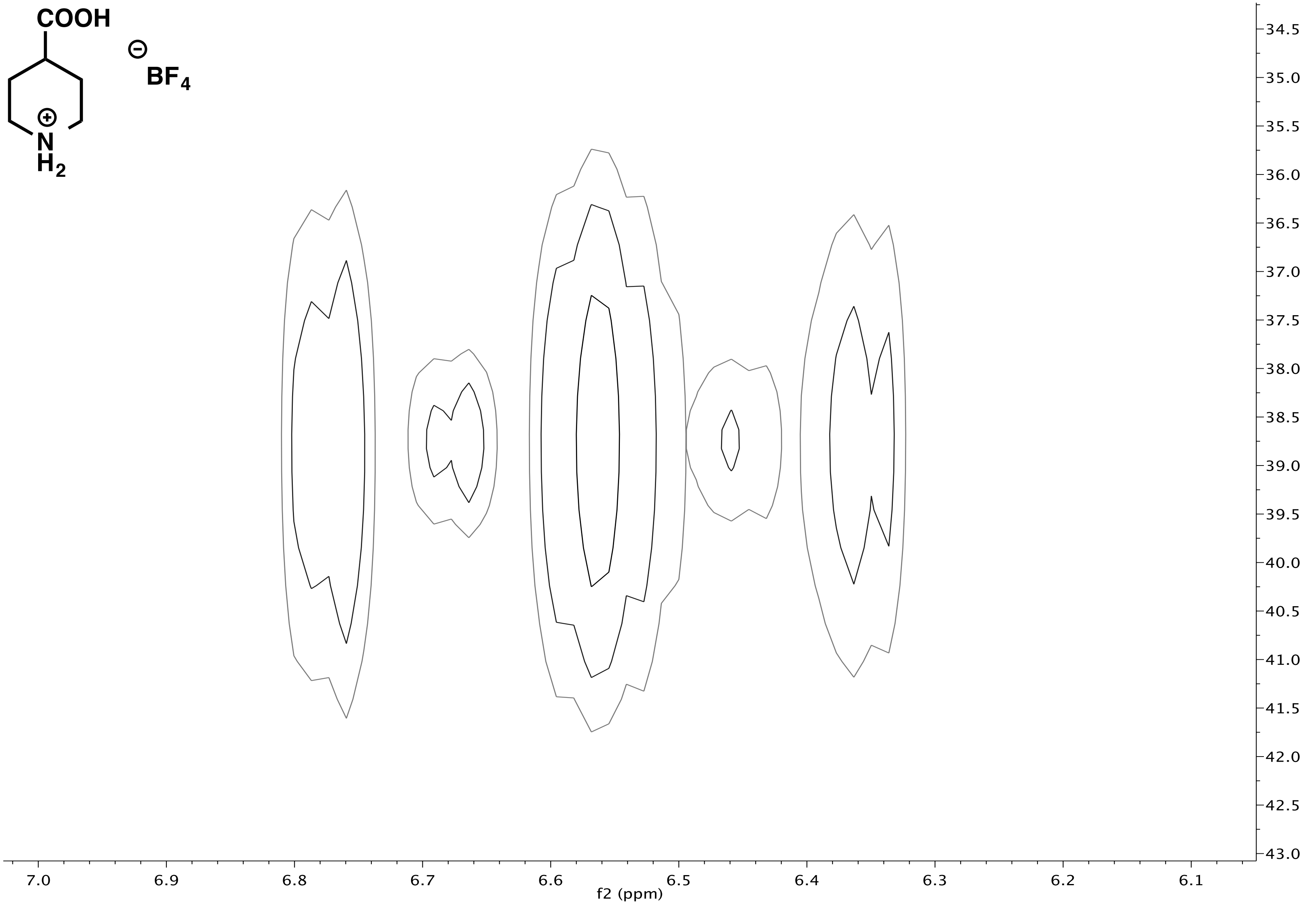
$^{14}N\{^1H\}$ NMR (36 MHz, CD_3CN) of compound **11**.



^{1}H-^{15}N hsqc (400 MHz and 41 MHz, CD_3CN) of compound **11**.

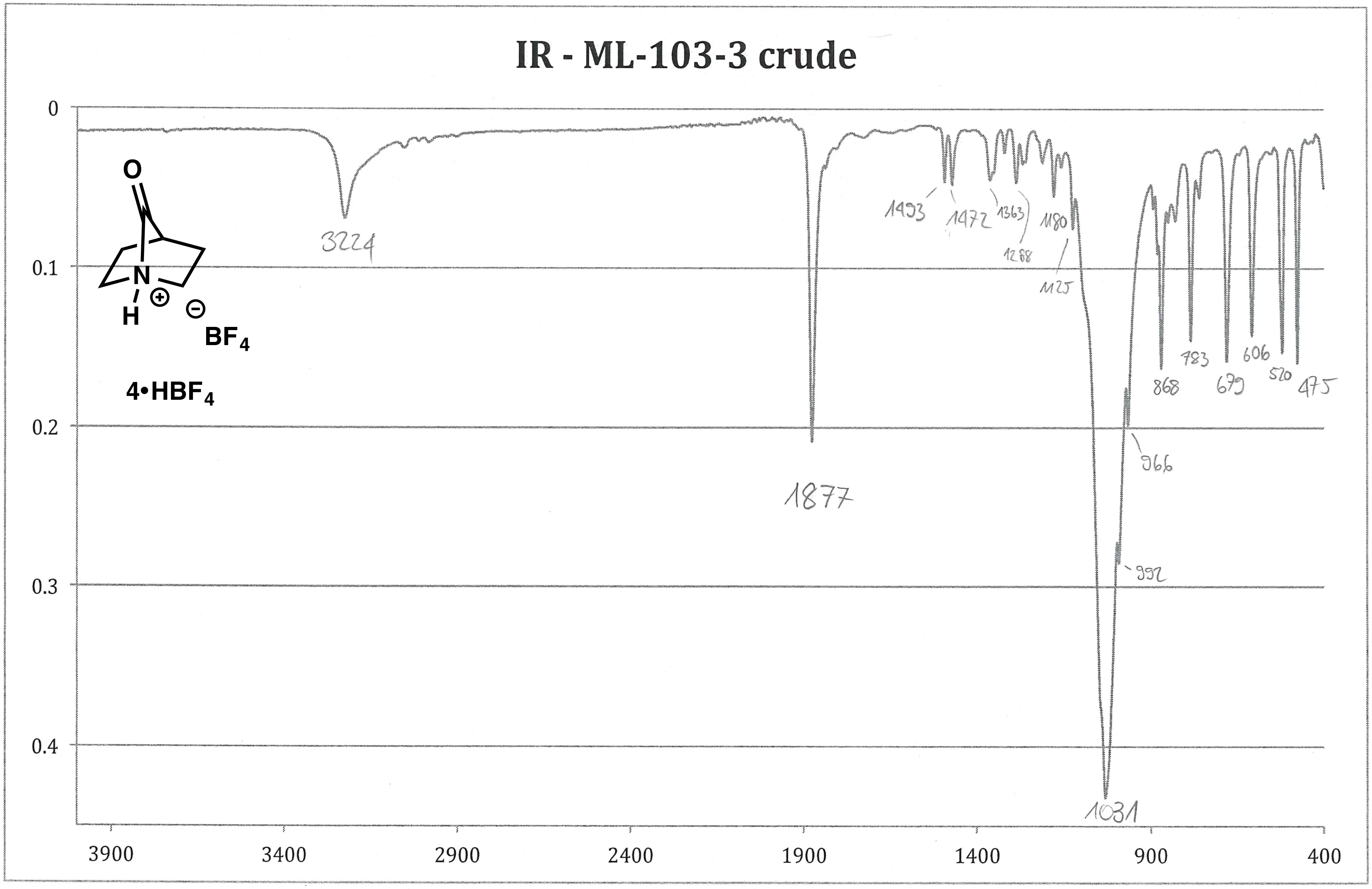


$^{1}H\{^{15}N\}$-^{15}N hsqc (400 MHz and 41 MHz, CD_3CN) of compound **11**.



Superimposed ^{1}H-^{15}N hsqc and ^{1}H{^{15}N}-^{15}N hsqc (400 MHz and 41 MHz, CD_3CN) of compound **11**.

IR Spectra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0.4
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2900
2400
1900
1400
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400
O
N
H
BF4
4•HBF4
3224
1877
1493
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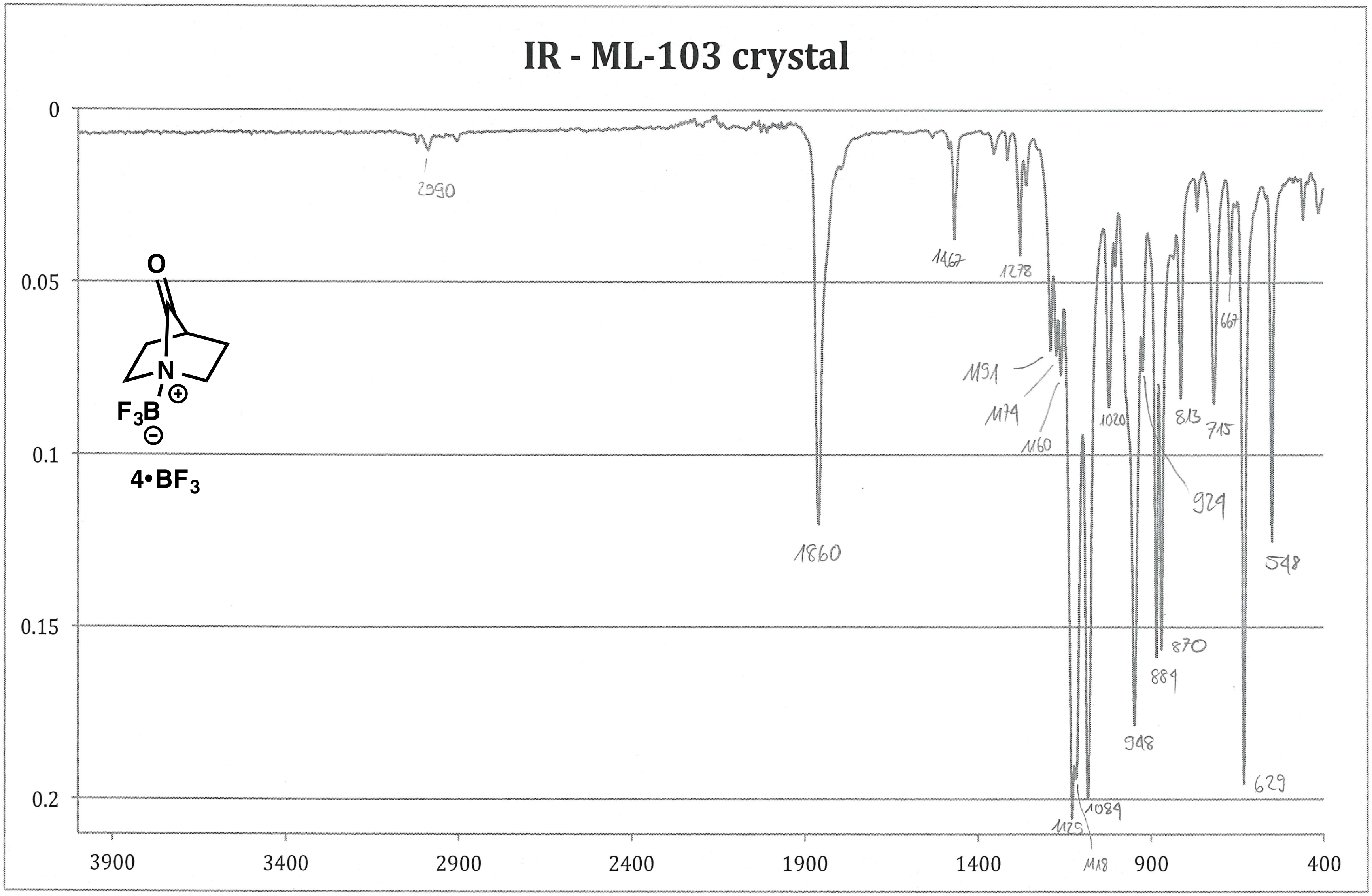
966
868
783
679
606
520
475


IR - ML-103 crystal
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2400
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1400
900
400
2990
1860
1467
1278
1191
1174
1160
1125
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715
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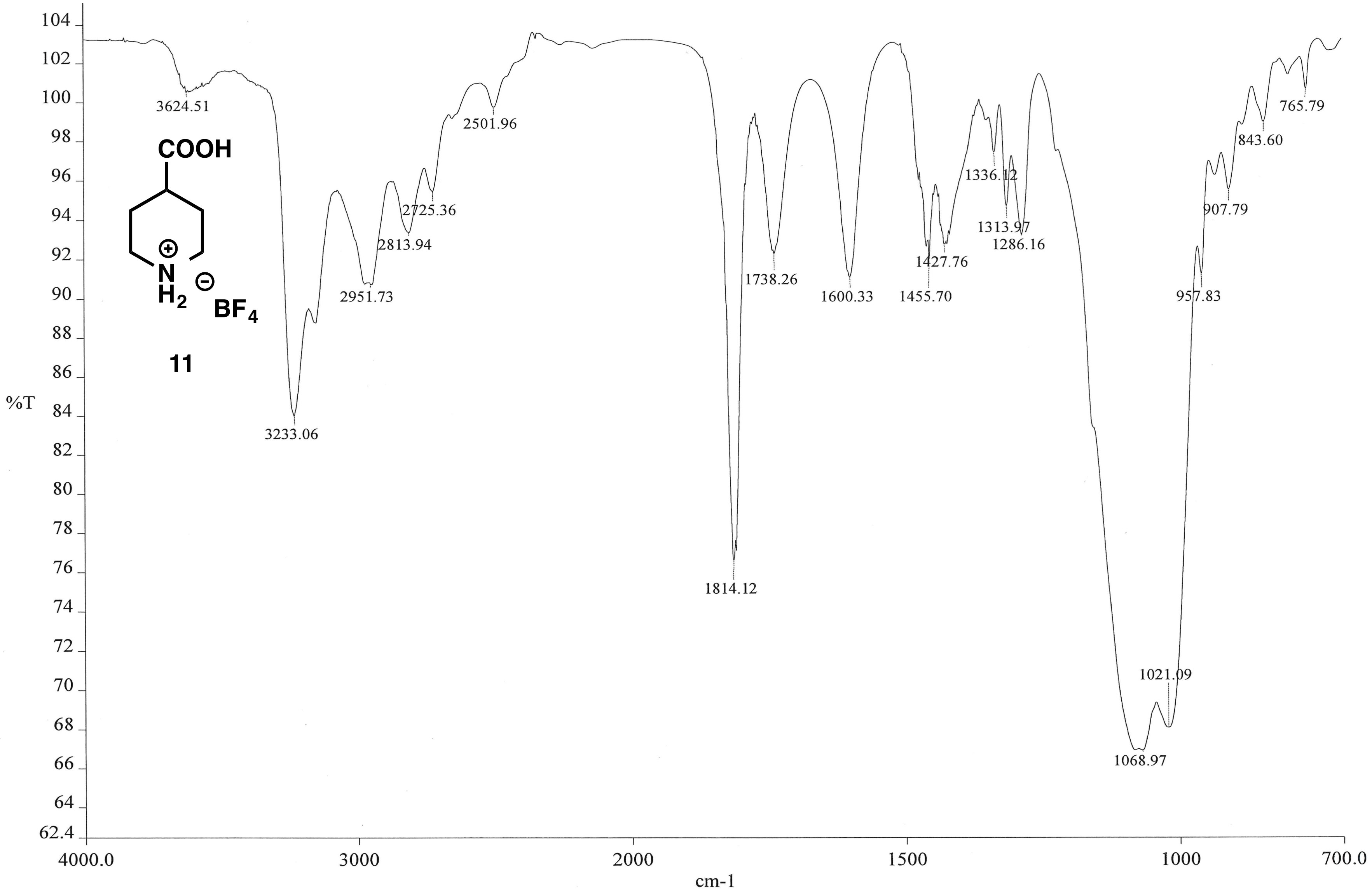
O
N
F3B
4•BF3

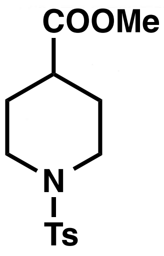


_____ c:\pel_data\spectra\stoltz\marc\ml-103-1 isonipecoticacid hbf4-p.sp - ML-103-1 isonipecoticacid HBF4 salt

mp = 124–138°C

NaCl

Mass Spectra



9

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    Acq. Instrument  : INSTRUMENT 1                   Location : Vial 89
    Injection Date   : 12/15/2014 2:00:47 PM
                                                    Inj Volume : 5.000 µl
    Acq. Method      : C:\CHEM32\1\METHODS\PES7AX.M
    Last changed     : 12/15/2014 1:59:58 PM by Marc Liniger
                       (modified after loading)
    Analysis Method  : C:\CHEM32\1\METHODS\PES10BX.M
    Last changed     : 12/15/2014 2:09:45 PM by chen xu
                       (modified after loading)
    Method Info      : PES10BX: 5-95 ACN (1 mL/min, 10 min) 190 to 800 AMU NO PRINT

    Sample Info      : Easy-Access Method: 'PES7AX'
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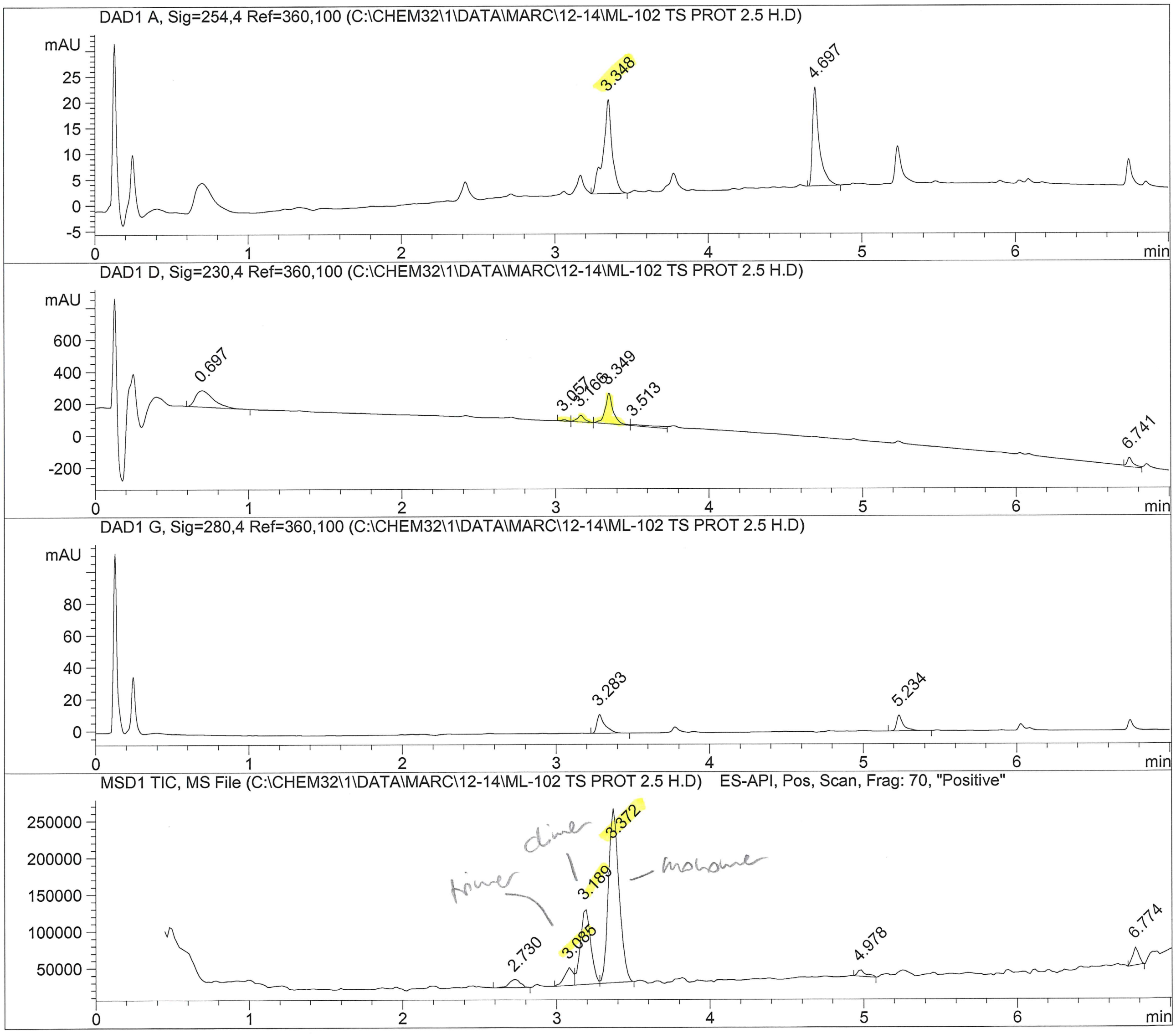

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INSTRUMENT 1 12/15/2014 2:27:46 PM chen xu                      Page   1 of 4
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Sample Name: ML-102 Ts prot 2.5 h

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        Spectra averaged over upper half of peaks.
        Noise Cutoff: 1000 counts.
        Reportable Ion Abundance: > 30%.
    LC Signal: DAD1 A, Sig=254,4 Ref=360,100
        Peak matching window: 0.1  min

    Retention                  Retention                  Mol. Weight
    Time (LC)      LC Area      Time (MS)      MS Area      or Ion
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                                                             141.10 I
                                                             111.05 I
                                                             105.10 I
                                                             102.10 I

        -              -          3.085          93201       521.30 I
                                                             520.30 I
                                                             141.10 I
                                                             105.10 I
                                                             102.10 I

        -              -          3.189         472570       409.20 I

       3.348          75          3.372        1147989       298.10 I

       4.697          59           -              -

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                                                             105.10 I

        -              -          6.774          70654       141.15 I
                                                             105.10 I
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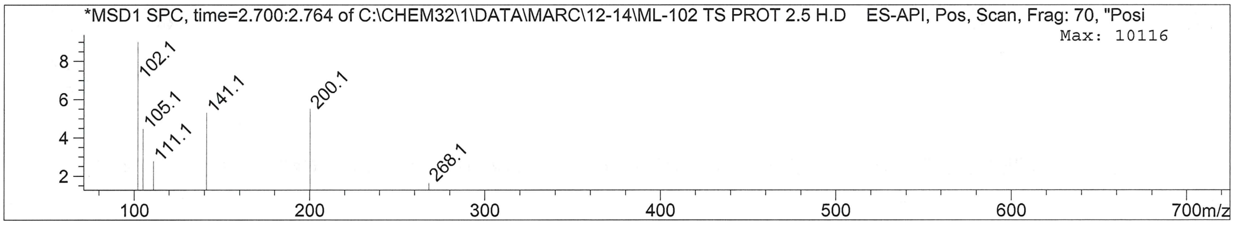

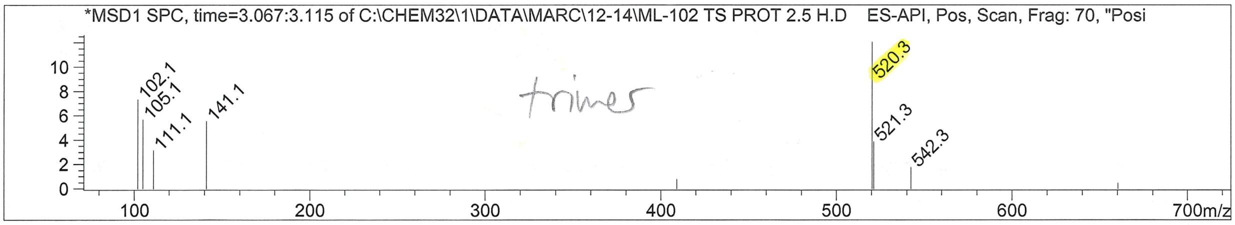

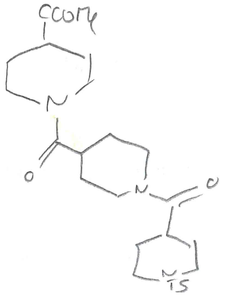

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INSTRUMENT 1 12/15/2014 2:27:46 PM chen xu                          Page    3 of 4
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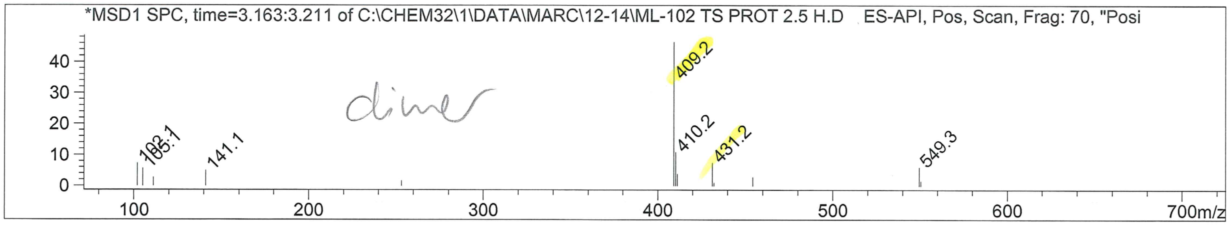
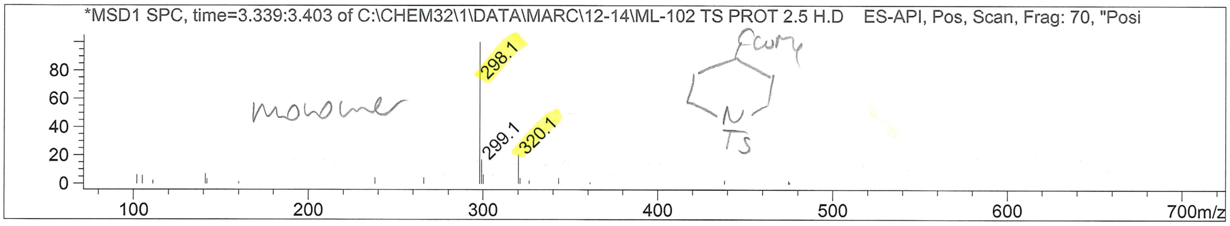
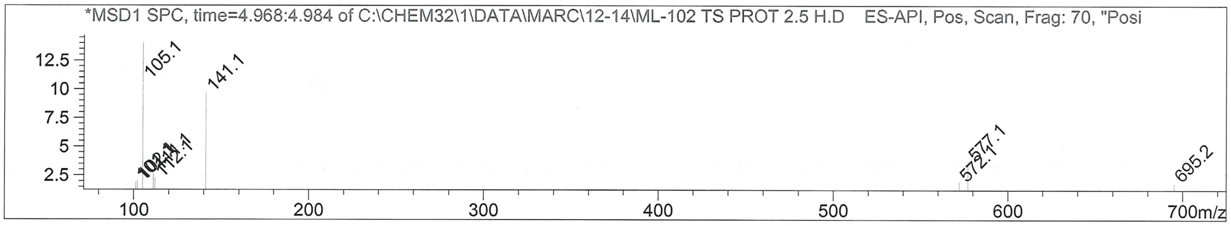
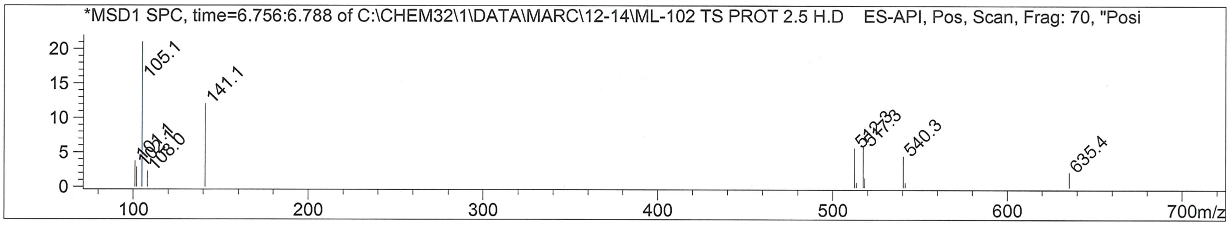
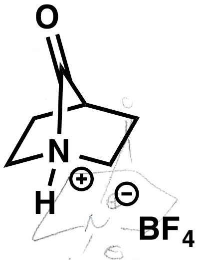










4•HBF$_4$

Marc Liniger.

CALTECH
3/13/2015

Page 1

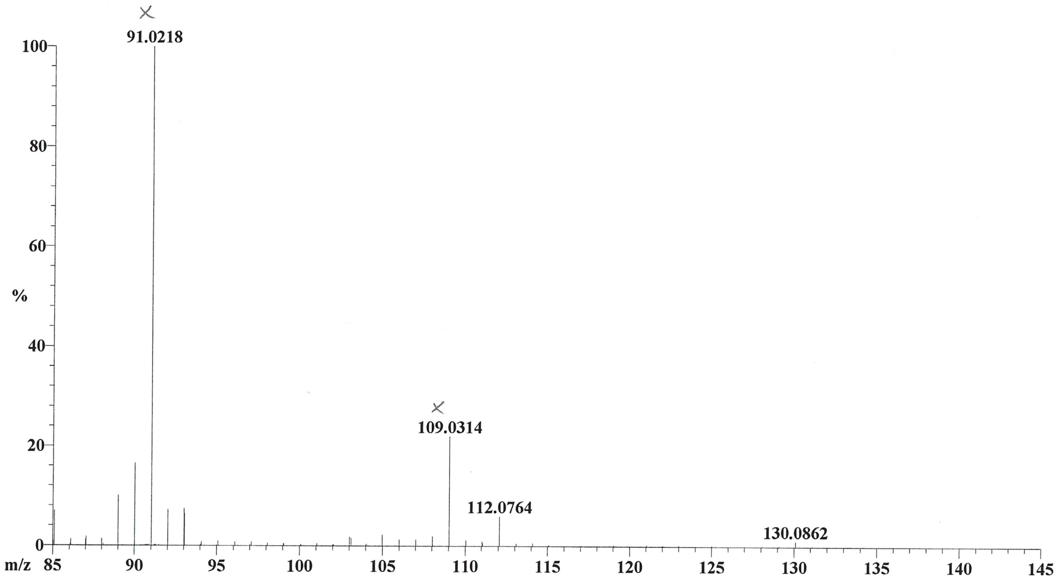
File: 031315-03 crude **Date Run: 03-13-2015 (12:35:48)**
Sample: ML-103-3 m/z 130/112 HR FAB thio EF scan
Instrument: JEOL MSRoute **Ionization mode: FAB+**
Marc Liniger

Scan: 17-24 **Base: m/z 91; 100%FS** **TIC: 2289622 (Max Inten : 1048560)**

Selected Isotopes : C H $N_{0-2}O_{0-3}$ **Error Limit : 5 ppm**

Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
112.0764	5.9%	$C_6H_{10}NO$	112.0762	1.4
130.0862	1.1%	$C_6H_{12}NO_2$	130.0868	-4.6

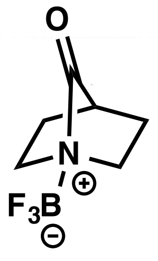
Scan: 17-24 **Base: m/z 91; 100%FS**
TIC: 2289622 (Max Inten : 1048560)



× thioglycerol

ML-103 crystal

CALTECH
3/5/2015



$4\cdot BF_3$

Page 1

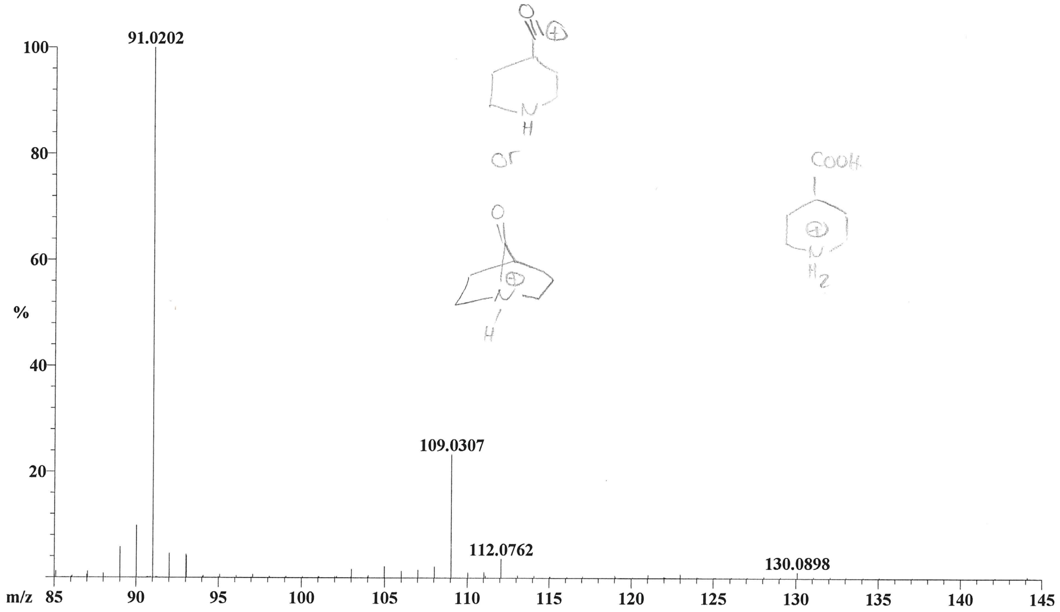
File: 030515-09 **Date Run: 03-05-2015 (12:13:56)**
Sample: m/z 112 HR EF FAB thio
Instrument: JEOL MSRoute **Ionization mode: FAB+**
Marc Liniger

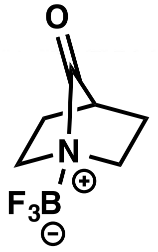
Scan: 6-12 **Base: m/z 91; 87.3%FS** **TIC: 1725665 (Max Inten : 915490)**

Selected Isotopes : C H $N_{0-2}O_{0-2}$ **Error Limit : 5 ppm**

Measured Mass	***% Base***	***Formula***	***Calculated Mass***	***Error***
112.0762	3.6%	$C_6H_{10}NO$	112.0762	-0.4

Scan: 6-12 **Base: m/z 91; 87.3%FSTIC: 1725665 (Max Inten : 915490)**





4•BF$_3$

ML-103 crystal

CALTECH
3/5/2015

Page 1

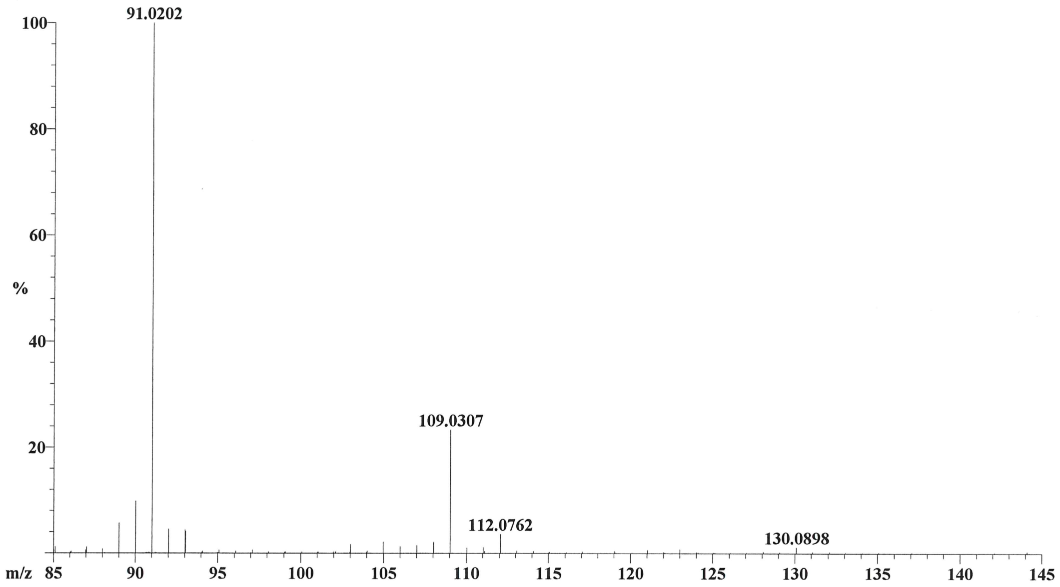
File: 030515-09 **Date Run: 03-05-2015 (12:13:56)**
Sample: m/z 112 HR EF FAB thio
Instrument: JEOL MSRoute **Ionization mode: FAB+**
Marc Liniger

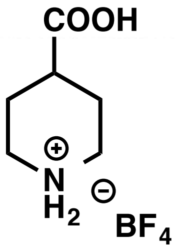
Scan: 6-12 **Base: m/z 91; 87.3%FS** **TIC: 1725665 (Max Inten : 915490)**

Selected Isotopes : C H N$_{0-2}$O$_{0-2}$ **Error Limit : 5 mmu**

Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
130.0898	1.1%	$C_6H_{12}NO_2$	130.0868	3.0

Scan: 6-12 **Base: m/z 91; 87.3%FSTIC: 1725665 (Max Inten : 915490)**





11

Marc Linige

CALTECH
3/5/2015

Page 1

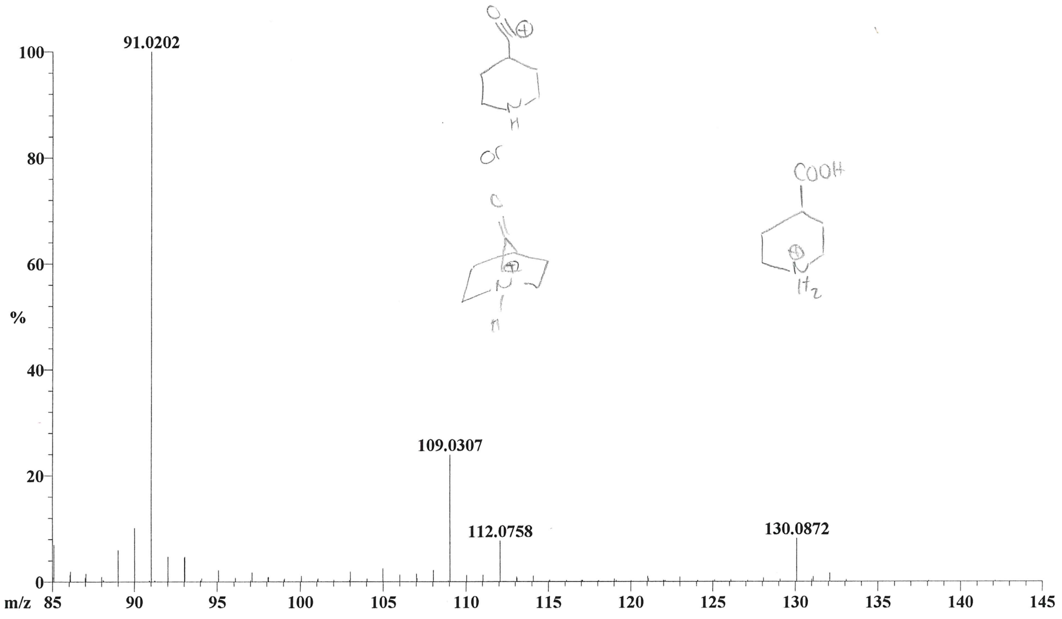
File: 030515-11 **Date Run: 03-05-2015 (12:29:53)**
Sample: ML103-1 m/z 130 HR EF FAB thio
Instrument: JEOL MSRoute **Ionization mode: FAB+**
Marc Liniger

Scan: 19-24 **Base: m/z 91; 61%FS** **TIC: 1444170 (Max Inten : 640101)**

Selected Isotopes : C H $N_{0-2}O_{0-2}$ **Error Limit : 5 ppm**

Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
112.0758	7.7%	$C_6H_{10}NO$	112.0762	-3.9
130.0872	8.1%	$C_6H_{12}NO_2$	130.0868	3.1

Scan: 19-24 **Base: m/z 91; 61%FS TIC: 1444170 (Max Inten : 640101)**



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ESILowFlow041014

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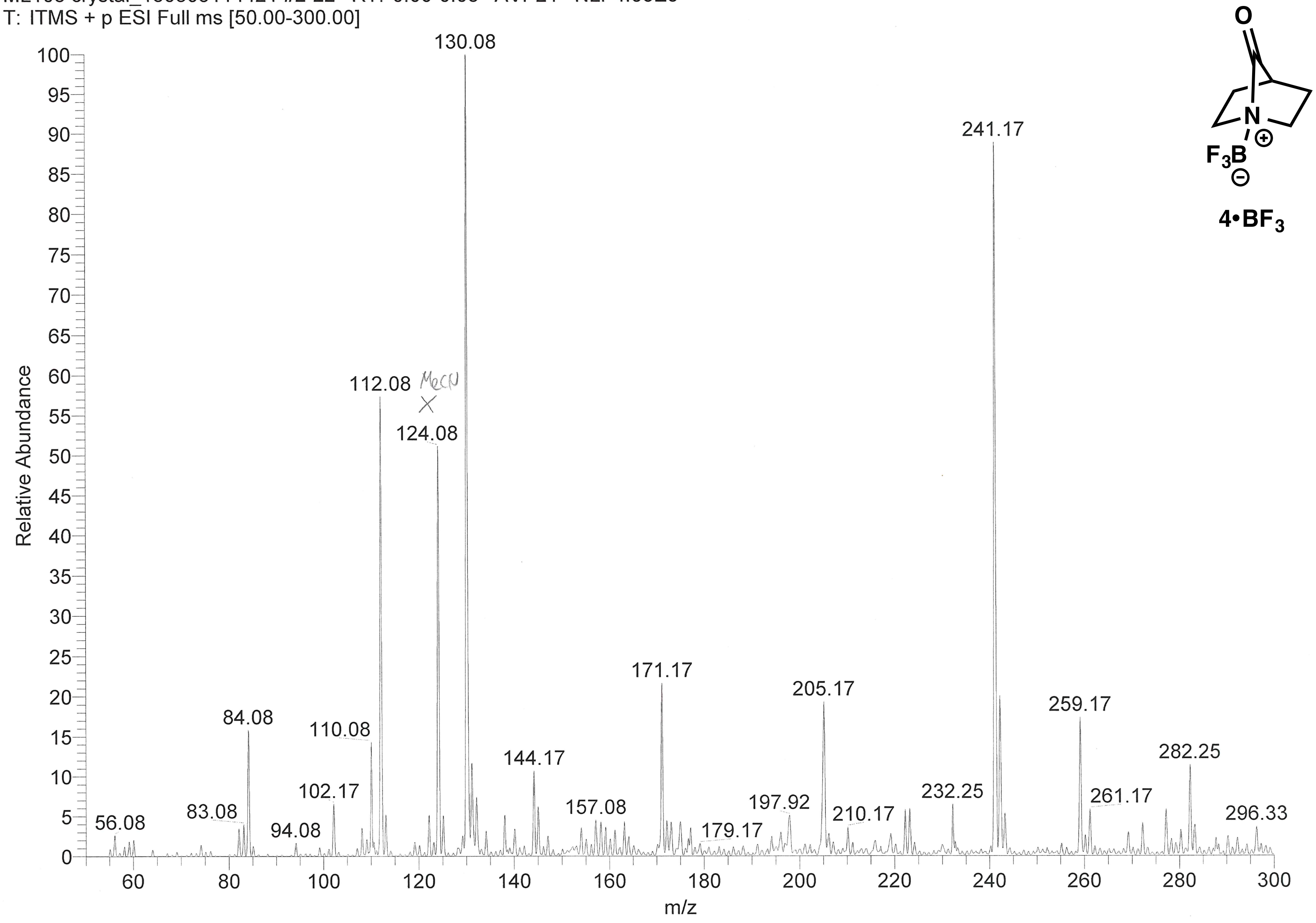

$4\cdot BF_3$

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ESILowFlow041014

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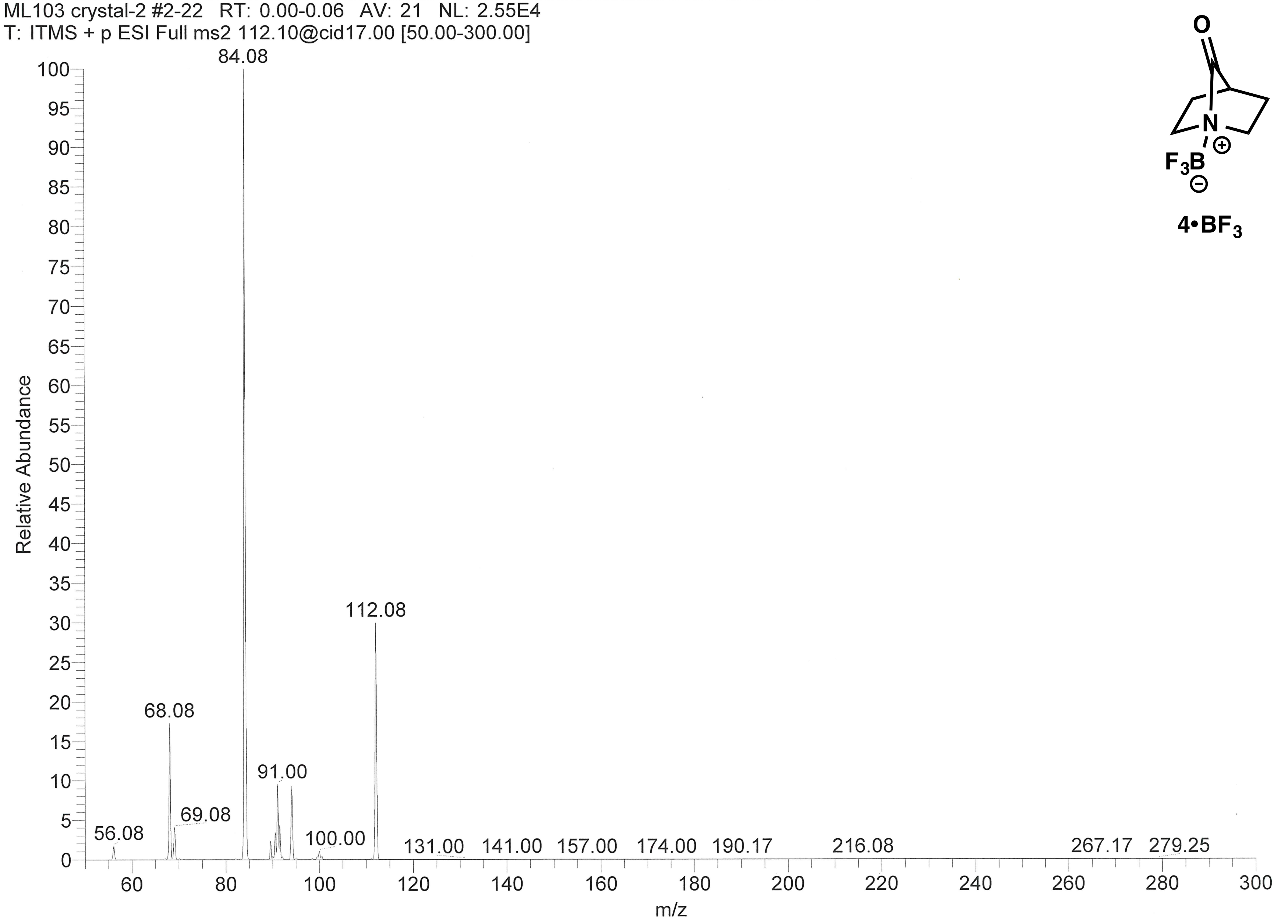
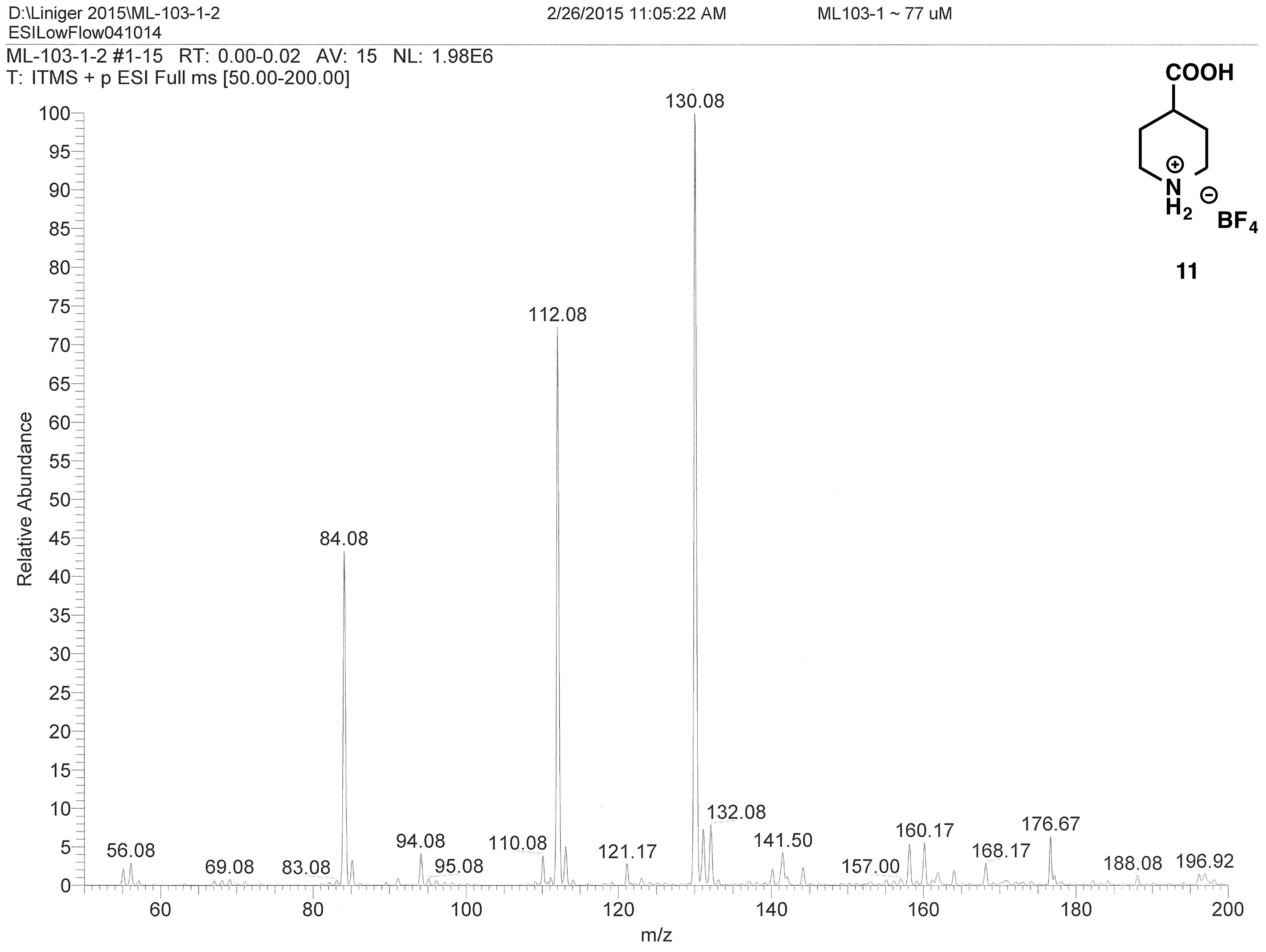


4•BF$_3$



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2/26/2015 11:05:22 AM
ML103-1 ~ 77 uM

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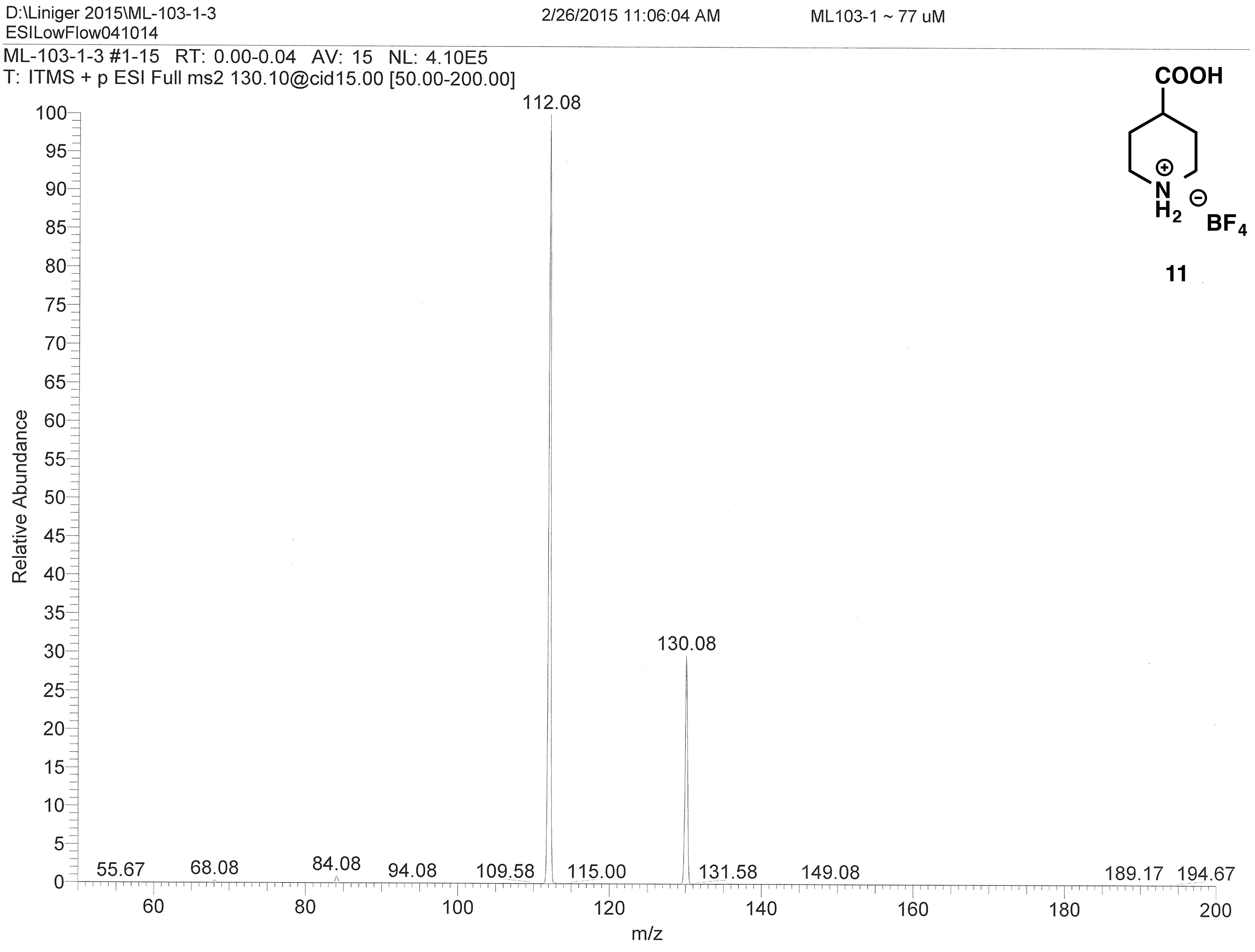
11



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2/26/2015 11:06:04 AM
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ML-103-1-3 #1-15 RT: 0.00-0.04 AV: 15 NL: 4.10E5
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11

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ESILowFlow041014

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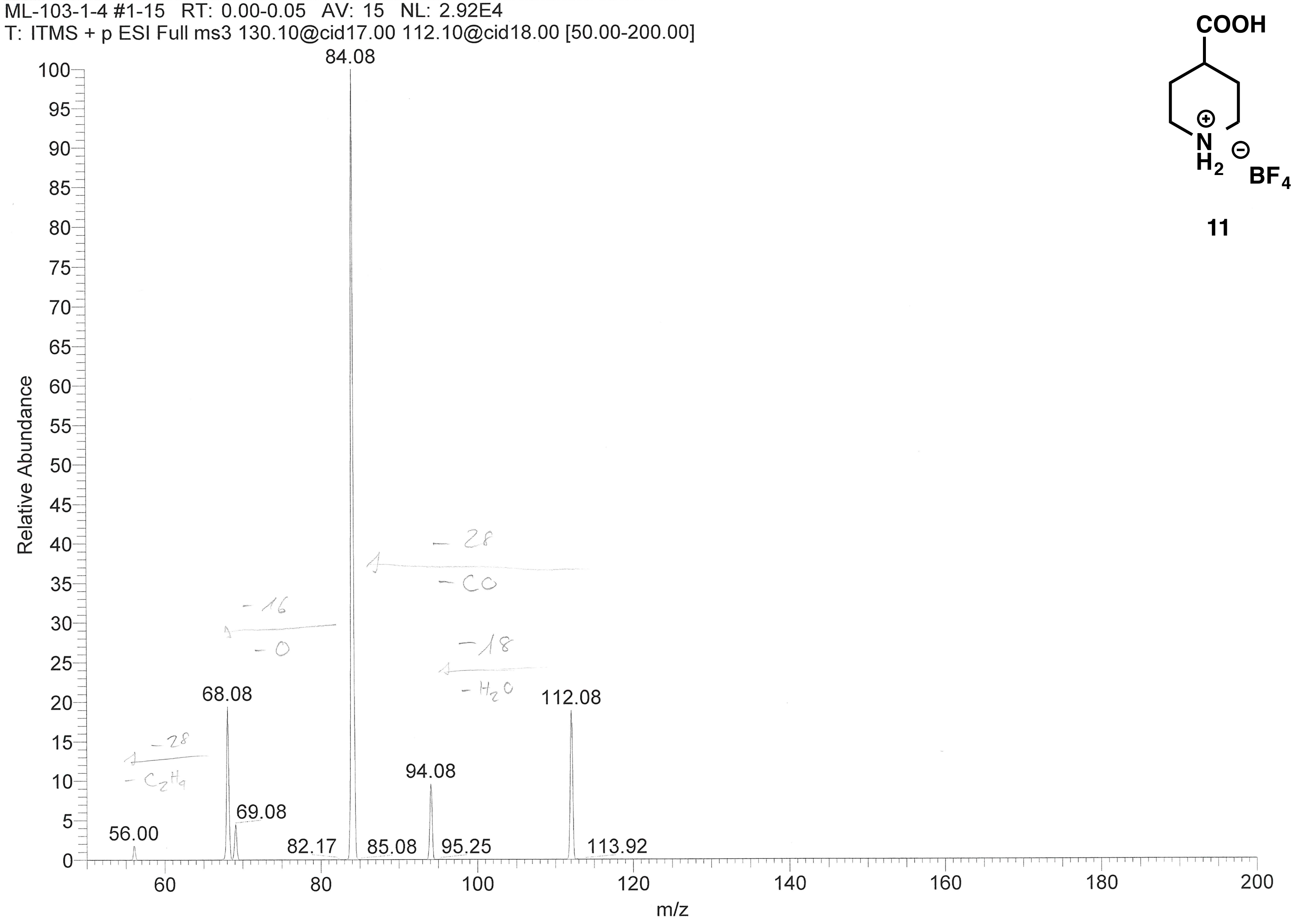
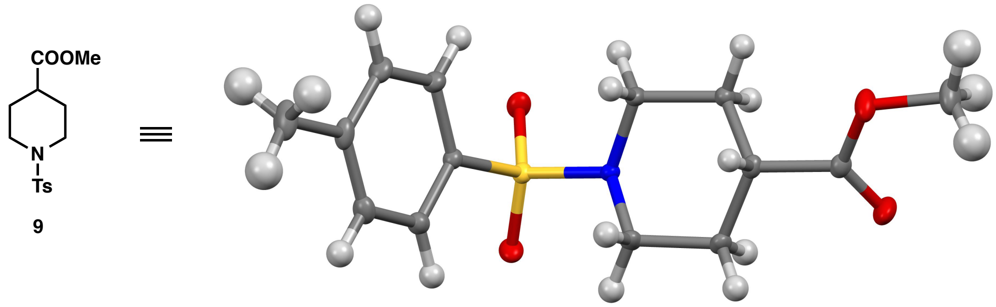


11

X-ray Structure Determination

Low-temperature diffraction data (ϕ-and ω-scans) were collected on a Bruker Kappa diffractometer coupled to an Apex II CCD detector with graphite monochromated Mo Kα radiation (λ = 0.71073 Å) for the structure of compound **9** and on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON 100 CMOS detector with Mo Kα radiation (λ = 0.71073 Å) or Cu Kα radiation (l = 1.54178 Å) from an IμS micro-source for the structure of compounds **4•BF$_3$** and **11**, respectively. The structure was solved by direct methods using SHELXS[10] and refined against F^2 on all data by full-matrix least squares with SHELXL-2013[11] using established refinement techniques.[12] All non-hydrogen atoms were refined anisotropically. Unless otherwise noted, all hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the *U* value of the atoms they are linked to (1.5 times for methyl groups).



9

Compound **9** crystallizes in the monoclinic space group $P2_1/n$ with one molecule in the asymmetric unit.

Table 1. Crystal data and structure refinement for **9**.

Identification code	A15032	
CCDC Deposition Number	1435049	
Empirical formula	C14 H19 N O4 S	
Formula weight	297.36	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 5.9734(4) Å	α = 90°.
	b = 31.405(2) Å	β = 104.610(3)°.
	c = 8.2426(5) Å	γ = 90°.
Volume	1496.27(17) Å^3	
Z	4	
Density (calculated)	1.320 Mg/m^3	
Absorption coefficient	0.228 mm^{-1}	
F(000)	632	
Crystal size	0.200 x 0.200 x 0.100 mm^3	
Theta range for data collection	2.594 to 36.390°.	
Index ranges	-9<=h<=9, -52<=k<=51, -13<=l<=12	
Reflections collected	28938	
Independent reflections	7196 [R(int) = 0.0400]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7471 and 0.6913	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7196 / 0 / 183	
Goodness-of-fit on F2	1.033	
Final R indices [I>2sigma(I)]	R1 = 0.0442, wR2 = 0.1024	
R indices (all data)	R1 = 0.0621, wR2 = 0.1096	

Extinction coefficient	n/a
Largest diff. peak and hole	0.552 and -0.392 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **9**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	6517(2)	5806(1)	9516(1)	20(1)
O(2)	9855(1)	5958(1)	8316(1)	18(1)
S(1)	7424(1)	5989(1)	8219(1)	13(1)
N(1)	6826(2)	6499(1)	8176(1)	13(1)
C(1)	4456(2)	6618(1)	8220(1)	17(1)
C(2)	4462(2)	7082(1)	8772(1)	18(1)
C(3)	5358(2)	7371(1)	7586(1)	15(1)
O(3)	5386(2)	7960(1)	9478(1)	28(1)
C(6)	5482(2)	7831(1)	8117(1)	16(1)
C(7)	6080(3)	8535(1)	7305(2)	28(1)
O(4)	5824(2)	8086(1)	6902(1)	25(1)
C(4)	7763(2)	7221(1)	7483(1)	16(1)
C(5)	7702(2)	6755(1)	6973(1)	16(1)
C(11)	5916(2)	5772(1)	6285(1)	13(1)
C(12)	6923(2)	5791(1)	4929(1)	16(1)
C(13)	5735(2)	5626(1)	3389(1)	20(1)
C(14)	3562(2)	5441(1)	3180(1)	19(1)
C(17)	2300(3)	5261(1)	1512(2)	29(1)
C(15)	2588(2)	5429(1)	4547(1)	20(1)
C(16)	3738(2)	5595(1)	6104(1)	17(1)

Table 3. Bond lengths [Å] and angles [°] for **9**.

O(1)-S(1)	1.4341(8)
O(2)-S(1)	1.4370(8)
S(1)-N(1)	1.6385(8)
S(1)-C(11)	1.7595(10)
N(1)-C(5)	1.4722(12)

N(1)-C(1)	1.4731(13)
C(1)-C(2)	1.5274(14)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-C(3)	1.5256(14)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(6)	1.5075(14)
C(3)-C(4)	1.5344(14)
C(3)-H(3)	1.0000
O(3)-C(6)	1.2066(13)
C(6)-O(4)	1.3370(13)
C(7)-O(4)	1.4486(14)
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(4)-C(5)	1.5201(13)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(11)-C(16)	1.3876(15)
C(11)-C(12)	1.3975(13)
C(12)-C(13)	1.3884(15)
C(12)-H(12)	0.9500
C(13)-C(14)	1.3923(17)
C(13)-H(13)	0.9500
C(14)-C(15)	1.3928(16)
C(14)-C(17)	1.5024(15)
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(15)-C(16)	1.3949(15)
C(15)-H(15)	0.9500
C(16)-H(16)	0.9500
O(1)-S(1)-O(2)	119.82(5)
O(1)-S(1)-N(1)	106.59(4)
O(2)-S(1)-N(1)	106.28(4)
O(1)-S(1)-C(11)	108.47(5)

O(2)-S(1)-C(11)	107.63(5)
N(1)-S(1)-C(11)	107.47(4)
C(5)-N(1)-C(1)	112.64(8)
C(5)-N(1)-S(1)	115.88(6)
C(1)-N(1)-S(1)	116.92(7)
N(1)-C(1)-C(2)	108.61(8)
N(1)-C(1)-H(1A)	110.0
C(2)-C(1)-H(1A)	110.0
N(1)-C(1)-H(1B)	110.0
C(2)-C(1)-H(1B)	110.0
H(1A)-C(1)-H(1B)	108.3
C(3)-C(2)-C(1)	110.57(8)
C(3)-C(2)-H(2A)	109.5
C(1)-C(2)-H(2A)	109.5
C(3)-C(2)-H(2B)	109.5
C(1)-C(2)-H(2B)	109.5
H(2A)-C(2)-H(2B)	108.1
C(6)-C(3)-C(2)	112.56(8)
C(6)-C(3)-C(4)	109.35(8)
C(2)-C(3)-C(4)	109.76(8)
C(6)-C(3)-H(3)	108.4
C(2)-C(3)-H(3)	108.4
C(4)-C(3)-H(3)	108.4
O(3)-C(6)-O(4)	123.28(10)
O(3)-C(6)-C(3)	125.45(10)
O(4)-C(6)-C(3)	111.21(8)
O(4)-C(7)-H(7A)	109.5
O(4)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
O(4)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(6)-O(4)-C(7)	115.96(9)
C(5)-C(4)-C(3)	110.62(8)
C(5)-C(4)-H(4A)	109.5
C(3)-C(4)-H(4A)	109.5
C(5)-C(4)-H(4B)	109.5
C(3)-C(4)-H(4B)	109.5
H(4A)-C(4)-H(4B)	108.1
N(1)-C(5)-C(4)	109.19(8)

N(1)-C(5)-H(5A)	109.8
C(4)-C(5)-H(5A)	109.8
N(1)-C(5)-H(5B)	109.8
C(4)-C(5)-H(5B)	109.8
H(5A)-C(5)-H(5B)	108.3
C(16)-C(11)-C(12)	120.83(9)
C(16)-C(11)-S(1)	120.31(7)
C(12)-C(11)-S(1)	118.85(8)
C(13)-C(12)-C(11)	119.39(10)
C(13)-C(12)-H(12)	120.3
C(11)-C(12)-H(12)	120.3
C(12)-C(13)-C(14)	120.95(10)
C(12)-C(13)-H(13)	119.5
C(14)-C(13)-H(13)	119.5
C(13)-C(14)-C(15)	118.57(10)
C(13)-C(14)-C(17)	120.51(11)
C(15)-C(14)-C(17)	120.92(11)
C(14)-C(17)-H(17A)	109.5
C(14)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(14)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(14)-C(15)-C(16)	121.62(10)
C(14)-C(15)-H(15)	119.2
C(16)-C(15)-H(15)	119.2
C(11)-C(16)-C(15)	118.64(10)
C(11)-C(16)-H(16)	120.7
C(15)-C(16)-H(16)	120.7

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for **9**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	31(1)	18(1)	12(1)	2(1)	8(1)	-2(1)
O(2)	14(1)	18(1)	19(1)	-1(1)	1(1)	3(1)

S(1)	16(1)	13(1)	10(1)	0(1)	3(1)	0(1)
N(1)	13(1)	13(1)	14(1)	0(1)	6(1)	0(1)
C(1)	14(1)	16(1)	24(1)	-3(1)	9(1)	-2(1)
C(2)	15(1)	17(1)	24(1)	-3(1)	9(1)	1(1)
C(3)	14(1)	14(1)	14(1)	-2(1)	2(1)	2(1)
O(3)	46(1)	20(1)	24(1)	-6(1)	19(1)	-1(1)
C(6)	15(1)	16(1)	16(1)	-1(1)	2(1)	3(1)
C(7)	46(1)	14(1)	23(1)	1(1)	6(1)	1(1)
O(4)	44(1)	14(1)	16(1)	1(1)	6(1)	2(1)
C(4)	17(1)	13(1)	19(1)	-1(1)	8(1)	0(1)
C(5)	19(1)	14(1)	17(1)	0(1)	10(1)	0(1)
C(11)	15(1)	12(1)	12(1)	0(1)	4(1)	1(1)
C(12)	19(1)	18(1)	14(1)	-1(1)	6(1)	0(1)
C(13)	26(1)	20(1)	12(1)	-1(1)	5(1)	2(1)
C(14)	24(1)	13(1)	16(1)	-2(1)	-3(1)	4(1)
C(17)	38(1)	22(1)	19(1)	-4(1)	-8(1)	4(1)
C(15)	16(1)	17(1)	23(1)	-2(1)	0(1)	0(1)
C(16)	16(1)	16(1)	19(1)	-1(1)	6(1)	-1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **9**.

	x	y	z	U(eq)
H(1A)	3919	6432	9016	21
H(1B)	3392	6582	7094	21
H(2A)	2872	7169	8782	21
H(2B)	5458	7113	9924	21
H(3)	4281	7348	6443	17
H(7A)	4632	8645	7493	43
H(7B)	6451	8689	6372	43
H(7C)	7332	8575	8321	43
H(4A)	8291	7397	6652	19
H(4B)	8878	7259	8587	19
H(5A)	6683	6719	5832	19
H(5B)	9276	6659	6962	19
H(12)	8407	5916	5060	20
H(13)	6414	5640	2465	23
H(17A)	1950	5490	679	44

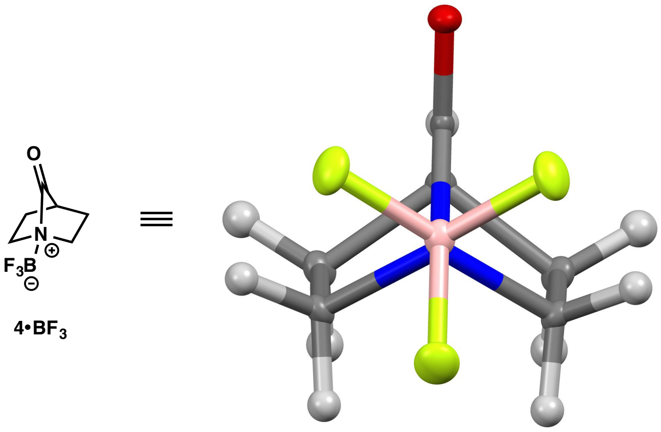
H(17B)	855	5128	1611	44
H(17C)	3272	5046	1159	44
H(15)	1104	5304	4416	23
H(16)	3044	5587	7021	20

Table 6. Torsion angles [°] for **9**.

O(1)-S(1)-N(1)-C(5)	177.31(7)
O(2)-S(1)-N(1)-C(5)	48.44(8)
C(11)-S(1)-N(1)-C(5)	-66.57(8)
O(1)-S(1)-N(1)-C(1)	-46.13(8)
O(2)-S(1)-N(1)-C(1)	-175.00(7)
C(11)-S(1)-N(1)-C(1)	69.99(8)
C(5)-N(1)-C(1)-C(2)	-61.35(11)
S(1)-N(1)-C(1)-C(2)	160.73(7)
N(1)-C(1)-C(2)-C(3)	57.90(11)
C(1)-C(2)-C(3)-C(6)	-177.81(9)
C(1)-C(2)-C(3)-C(4)	-55.77(11)
C(2)-C(3)-C(6)-O(3)	15.13(16)
C(4)-C(3)-C(6)-O(3)	-107.14(12)
C(2)-C(3)-C(6)-O(4)	-167.71(9)
C(4)-C(3)-C(6)-O(4)	70.02(11)
O(3)-C(6)-O(4)-C(7)	0.00(17)
C(3)-C(6)-O(4)-C(7)	-177.23(10)
C(6)-C(3)-C(4)-C(5)	179.18(8)
C(2)-C(3)-C(4)-C(5)	55.25(11)
C(1)-N(1)-C(5)-C(4)	61.13(11)
S(1)-N(1)-C(5)-C(4)	-160.49(7)
C(3)-C(4)-C(5)-N(1)	-56.91(11)
O(1)-S(1)-C(11)-C(16)	21.84(10)
O(2)-S(1)-C(11)-C(16)	152.85(8)
N(1)-S(1)-C(11)-C(16)	-93.05(9)
O(1)-S(1)-C(11)-C(12)	-159.84(8)
O(2)-S(1)-C(11)-C(12)	-28.82(9)
N(1)-S(1)-C(11)-C(12)	85.28(9)
C(16)-C(11)-C(12)-C(13)	-0.73(15)
S(1)-C(11)-C(12)-C(13)	-179.05(8)
C(11)-C(12)-C(13)-C(14)	-0.22(16)

C(12)-C(13)-C(14)-C(15)	0.65(16)
C(12)-C(13)-C(14)-C(17)	-179.47(10)
C(13)-C(14)-C(15)-C(16)	-0.16(16)
C(17)-C(14)-C(15)-C(16)	179.96(10)
C(12)-C(11)-C(16)-C(15)	1.21(15)
S(1)-C(11)-C(16)-C(15)	179.50(8)
C(14)-C(15)-C(16)-C(11)	-0.76(16)

Symmetry transformations used to generate equivalent atoms: none



4•BF$_3$

Compound **4•BF$_3$** crystallizes in the orthorhombic space group *Pnma* with half a molecule in the asymmetric unit.

Table 7. Crystal data and structure refinement for **4•BF$_3$**.

Identification code	P15025
CCDC Deposition Number	1435048
Empirical formula	C6 H9 B F3 N O
Formula weight	178.95
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	Pnma

Unit cell dimensions	a = 11.4731(4) Å	α = 90°.
	b = 8.2140(2) Å	β = 90°.
	c = 7.6132(3) Å	γ = 90°.
Volume	717.47(4) $Å^3$	
Z	4	
Density (calculated)	1.657 Mg/m^3	
Absorption coefficient	0.160 mm^{-1}	
F(000)	368	
Crystal size	0.350 x 0.350 x 0.350 mm^3	
Theta range for data collection	3.211 to 36.320°.	
Index ranges	-19<=h<=18, -12<=k<=13, -12<=l<=12	
Reflections collected	17613	
Independent reflections	1826 [R(int) = 0.0355]	
Completeness to theta = 25.242°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7471 and 0.6989	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1826 / 0 / 64	
Goodness-of-fit on F2	1.038	
Final R indices [I>2sigma(I)]	R1 = 0.0317, wR2 = 0.0824	
R indices (all data)	R1 = 0.0404, wR2 = 0.0863	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.421 and -0.261 e.$Å^{-3}$	

Table 8. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **4•BF$_3$**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
B(1)	3589(1)	7500	3777(1)	12(1)
F(1)	4102(1)	8894(1)	3124(1)	19(1)
F(2)	2397(1)	7500	3477(1)	20(1)

N(1)	3755(1)	7500	5872(1)	9(1)
C(1)	4987(1)	7500	6625(1)	9(1)
C(2)	4675(1)	7500	8549(1)	11(1)
O(1)	5855(1)	7500	5778(1)	14(1)
C(3)	3881(1)	9010(1)	8616(1)	13(1)
C(4)	3274(1)	8993(1)	6792(1)	11(1)

Table 9. Bond lengths [Å] and angles [°] for **4•BF$_3$**.

B(1)-F(1)#1	1.3803(7)
B(1)-F(1)	1.3803(7)
B(1)-F(2)	1.3857(12)
B(1)-N(1)	1.6065(12)
N(1)-C(4)	1.5160(7)
N(1)-C(4)#1	1.5161(7)
N(1)-C(1)	1.5258(11)
C(1)-O(1)	1.1862(11)
C(1)-C(2)	1.5082(12)
C(2)-C(3)#1	1.5401(8)
C(2)-C(3)	1.5401(8)
C(2)-H(2)	1.0000
C(3)-C(4)	1.5538(9)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
F(1)#1-B(1)-F(1)	112.07(8)
F(1)#1-B(1)-F(2)	111.20(5)
F(1)-B(1)-F(2)	111.20(5)
F(1)#1-B(1)-N(1)	107.89(5)
F(1)-B(1)-N(1)	107.89(5)
F(2)-B(1)-N(1)	106.30(8)
C(4)-N(1)-C(4)#1	107.99(6)
C(4)-N(1)-C(1)	99.44(4)
C(4)#1-N(1)-C(1)	99.44(4)
C(4)-N(1)-B(1)	114.54(4)
C(4)#1-N(1)-B(1)	114.53(4)

C(1)-N(1)-B(1)	118.86(7)
O(1)-C(1)-C(2)	136.64(8)
O(1)-C(1)-N(1)	125.06(8)
C(2)-C(1)-N(1)	98.30(6)
C(1)-C(2)-C(3)#1	99.96(5)
C(1)-C(2)-C(3)	99.96(5)
C(3)#1-C(2)-C(3)	107.31(7)
C(1)-C(2)-H(2)	115.8
C(3)#1-C(2)-H(2)	115.8
C(3)-C(2)-H(2)	115.8
C(2)-C(3)-C(4)	103.18(5)
C(2)-C(3)-H(3A)	111.1
C(4)-C(3)-H(3A)	111.1
C(2)-C(3)-H(3B)	111.1
C(4)-C(3)-H(3B)	111.1
H(3A)-C(3)-H(3B)	109.1
N(1)-C(4)-C(3)	104.89(5)
N(1)-C(4)-H(4A)	110.8
C(3)-C(4)-H(4A)	110.8
N(1)-C(4)-H(4B)	110.8
C(3)-C(4)-H(4B)	110.8
H(4A)-C(4)-H(4B)	108.8

Symmetry transformations used to generate equivalent atoms:
#1 x,-y+3/2,z

Table 10. Anisotropic displacement parameters (Å^2 x 10^3) for **4•BF$_3$**. The anisotropic displacement factor exponent takes the form: -2p^2[h^2 a*^{2}U^{11} + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
B(1)	16(1)	11(1)	10(1)	0	-2(1)	0
F(1)	28(1)	16(1)	13(1)	4(1)	0(1)	-4(1)
F(2)	18(1)	24(1)	18(1)	0	-9(1)	0
N(1)	9(1)	8(1)	9(1)	0	-1(1)	0
C(1)	9(1)	7(1)	12(1)	0	-1(1)	0
C(2)	12(1)	12(1)	9(1)	0	-2(1)	0
O(1)	10(1)	14(1)	18(1)	0	3(1)	0
C(3)	16(1)	13(1)	11(1)	-3(1)	-1(1)	2(1)

C(4)	12(1)	10(1)	12(1)	-1(1)	0(1)	3(1)

Table 11. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for **4•BF**$_3$.

	x	y	z	U(eq)
H(2)	5347	7500	9385	13
H(3A)	4342	10017	8781	16
H(3B)	3303	8920	9577	16
H(4A)	2417	8913	6924	13
H(4B)	3462	9993	6123	13

Table 12. Torsion angles [°] for **4•BF**$_3$.

F(1)#1-B(1)-N(1)-C(4)	177.85(6)
F(1)-B(1)-N(1)-C(4)	56.58(9)
F(2)-B(1)-N(1)-C(4)	-62.78(5)
F(1)#1-B(1)-N(1)-C(4)#1	-56.58(9)
F(1)-B(1)-N(1)-C(4)#1	-177.85(6)
F(2)-B(1)-N(1)-C(4)#1	62.78(5)
F(1)#1-B(1)-N(1)-C(1)	60.64(6)
F(1)-B(1)-N(1)-C(1)	-60.64(6)
F(2)-B(1)-N(1)-C(1)	180.000(1)
C(4)-N(1)-C(1)-O(1)	-124.91(4)
C(4)#1-N(1)-C(1)-O(1)	124.91(4)
B(1)-N(1)-C(1)-O(1)	0.000(1)
C(4)-N(1)-C(1)-C(2)	55.09(4)
C(4)#1-N(1)-C(1)-C(2)	-55.09(4)
B(1)-N(1)-C(1)-C(2)	180.000(1)
O(1)-C(1)-C(2)-C(3)#1	-125.14(4)
N(1)-C(1)-C(2)-C(3)#1	54.86(4)
O(1)-C(1)-C(2)-C(3)	125.14(4)
N(1)-C(1)-C(2)-C(3)	-54.86(4)
C(1)-C(2)-C(3)-C(4)	33.32(6)
C(3)#1-C(2)-C(3)-C(4)	-70.48(7)

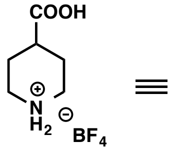
C(4)#1-N(1)-C(4)-C(3)	69.51(7)
C(1)-N(1)-C(4)-C(3)	-33.72(6)
B(1)-N(1)-C(4)-C(3)	-161.57(6)
C(2)-C(3)-C(4)-N(1)	0.55(6)

Symmetry transformations used to generate equivalent atoms:
#1 x,-y+3/2,z

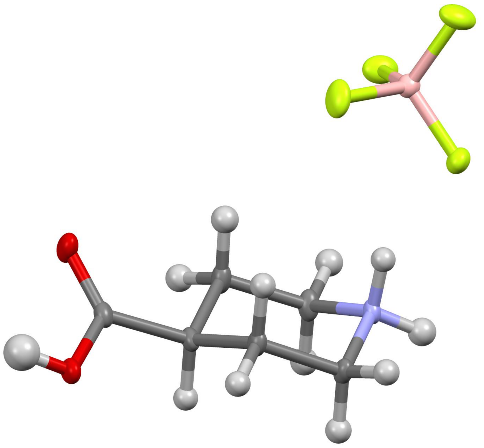
Table 13. Hydrogen bonds for **4•BF$_3$** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(3)-H(3A)...F(1)#2	0.99	2.47	3.1741(8)	128.0
C(4)-H(4B)...O(1)#2	0.99	2.64	3.6227(8)	174.3

Symmetry transformations used to generate equivalent atoms:
#1 x,-y+3/2,z #2 -x+1,-y+2,-z+1



11



Compound **11** crystallizes in the triclinic space group *P*-1 with one molecule in the asymmetric unit. The coordinates for the hydrogen atoms bound to N1 and O2 were located in the difference Fourier synthesis and refined semi-freely with the help of a restraint on the N-H and O-H distances (0.91(4) and 0.84(4) Å, respectively).

Table 14. Crystal data and structure refinement for **11**.

Identification code	P15095	
CCDC Deposition Number	1435047	
Empirical formula	C6 H12 B F4 N O2	
Formula weight	216.98	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 5.4701(2) Å	α = 103.512(2)°.
	b = 7.6337(3) Å	β = 91.167(2)°.
	c = 11.2184(4) Å	γ = 98.484(2)°.
Volume	449.76(3) Å^3	
Z	2	
Density (calculated)	1.602 Mg/m^3	
Absorption coefficient	1.495 mm^{-1}	
F(000)	224	
Crystal size	0.150 x 0.050 x 0.050 mm^3	
Theta range for data collection	4.059 to 74.488°.	
Index ranges	-6<=h<=6, -9<=k<=9, -14<=l<=13	
Reflections collected	6970	
Independent reflections	1825 [R(int) = 0.0537]	
Completeness to theta = 67.679°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7538 and 0.6051	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1825 / 3 / 139	
Goodness-of-fit on F2	1.043	
Final R indices [I>2sigma(I)]	R1 = 0.0378, wR2 = 0.0918	
R indices (all data)	R1 = 0.0451, wR2 = 0.0965	

Extinction coefficient	n/a
Largest diff. peak and hole	0.266 and -0.339 e.Å^{-3}

Table 15. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **11**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1)	-67(2)	3792(2)	6555(1)	13(1)
C(1)	342(3)	4840(2)	7868(1)	17(1)
C(2)	2125(3)	4014(2)	8553(1)	16(1)
C(3)	1208(3)	1996(2)	8446(1)	13(1)
O(1)	4957(2)	1959(2)	9585(1)	19(1)
O(2)	2065(2)	-536(2)	9164(1)	16(1)
C(4)	839(3)	974(2)	7082(1)	14(1)
C(5)	-981(3)	1806(2)	6428(1)	15(1)
C(6)	2939(3)	1146(2)	9123(1)	14(1)
B(1)	5206(3)	7199(2)	6208(2)	14(1)
F(1)	2724(2)	6740(1)	5764(1)	19(1)
F(2)	6692(2)	7557(1)	5272(1)	25(1)
F(3)	5469(2)	8718(1)	7184(1)	23(1)
F(4)	5875(2)	5721(1)	6602(1)	26(1)

Table 16. Bond lengths [Å] and angles [°] for **11**.

N(1)-C(5)	1.4969(19)
N(1)-C(1)	1.4975(19)
N(1)-H(1N1)	0.904(15)
N(1)-H(1N2)	0.902(15)
C(1)-C(2)	1.522(2)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-C(3)	1.524(2)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(6)	1.509(2)

C(3)-C(4)	1.540(2)
C(3)-H(3)	1.0000
O(1)-C(6)	1.224(2)
O(2)-C(6)	1.3135(19)
O(2)-H(2O)	0.872(16)
C(4)-C(5)	1.519(2)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
B(1)-F(3)	1.3843(19)
B(1)-F(2)	1.393(2)
B(1)-F(4)	1.397(2)
B(1)-F(1)	1.4021(19)
C(5)-N(1)-C(1)	112.63(12)
C(5)-N(1)-H(1N1)	107.8(13)
C(1)-N(1)-H(1N1)	108.3(13)
C(5)-N(1)-H(1N2)	109.1(12)
C(1)-N(1)-H(1N2)	111.7(12)
H(1N1)-N(1)-H(1N2)	107.1(18)
N(1)-C(1)-C(2)	110.29(12)
N(1)-C(1)-H(1A)	109.6
C(2)-C(1)-H(1A)	109.6
N(1)-C(1)-H(1B)	109.6
C(2)-C(1)-H(1B)	109.6
H(1A)-C(1)-H(1B)	108.1
C(1)-C(2)-C(3)	111.08(13)
C(1)-C(2)-H(2A)	109.4
C(3)-C(2)-H(2A)	109.4
C(1)-C(2)-H(2B)	109.4
C(3)-C(2)-H(2B)	109.4
H(2A)-C(2)-H(2B)	108.0
C(6)-C(3)-C(2)	112.11(13)
C(6)-C(3)-C(4)	110.62(12)
C(2)-C(3)-C(4)	109.79(12)
C(6)-C(3)-H(3)	108.1
C(2)-C(3)-H(3)	108.1
C(4)-C(3)-H(3)	108.1
C(6)-O(2)-H(2O)	109.5(16)

C(5)-C(4)-C(3)	109.78(12)
C(5)-C(4)-H(4A)	109.7
C(3)-C(4)-H(4A)	109.7
C(5)-C(4)-H(4B)	109.7
C(3)-C(4)-H(4B)	109.7
H(4A)-C(4)-H(4B)	108.2
N(1)-C(5)-C(4)	110.19(12)
N(1)-C(5)-H(5A)	109.6
C(4)-C(5)-H(5A)	109.6
N(1)-C(5)-H(5B)	109.6
C(4)-C(5)-H(5B)	109.6
H(5A)-C(5)-H(5B)	108.1
O(1)-C(6)-O(2)	123.82(14)
O(1)-C(6)-C(3)	122.68(14)
O(2)-C(6)-C(3)	113.50(13)
F(3)-B(1)-F(2)	110.06(13)
F(3)-B(1)-F(4)	109.67(13)
F(2)-B(1)-F(4)	109.81(13)
F(3)-B(1)-F(1)	109.61(13)
F(2)-B(1)-F(1)	109.55(13)
F(4)-B(1)-F(1)	108.10(13)

Symmetry transformations used to generate equivalent atoms:

Table 17. Anisotropic displacement parameters (Å^2 x 10^3) for **11**. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	16(1)	13(1)	11(1)	5(1)	1(1)	5(1)
C(1)	25(1)	14(1)	12(1)	1(1)	-2(1)	8(1)
C(2)	22(1)	14(1)	13(1)	3(1)	-3(1)	6(1)
C(3)	15(1)	16(1)	12(1)	7(1)	2(1)	6(1)
O(1)	21(1)	18(1)	21(1)	8(1)	-6(1)	3(1)
O(2)	16(1)	17(1)	18(1)	9(1)	0(1)	6(1)
C(4)	17(1)	11(1)	14(1)	4(1)	-3(1)	4(1)
C(5)	16(1)	12(1)	16(1)	5(1)	-4(1)	2(1)
C(6)	18(1)	16(1)	10(1)	5(1)	3(1)	7(1)
B(1)	15(1)	14(1)	14(1)	2(1)	1(1)	3(1)

F(1)	15(1)	23(1)	19(1)	7(1)	-2(1)	4(1)
F(2)	25(1)	25(1)	22(1)	2(1)	11(1)	-1(1)
F(3)	23(1)	19(1)	21(1)	-5(1)	6(1)	2(1)
F(4)	32(1)	24(1)	25(1)	8(1)	-1(1)	17(1)

Table 18. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for **11**.

	x	y	z	U(eq)
H(1N1)	-1230(30)	4250(30)	6190(18)	21(5)
H(1N2)	1320(30)	3910(30)	6140(17)	16(5)
H(1A)	-1259	4817	8265	20
H(1B)	1029	6128	7905	20
H(2A)	2296	4671	9430	20
H(2B)	3776	4160	8211	20
H(3)	-436	1883	8818	16
H(2O)	3160(40)	-970(30)	9540(20)	35(6)
H(4A)	2446	1057	6692	17
H(4B)	200	-330	7013	17
H(5A)	-1182	1168	5548	18
H(5B)	-2617	1653	6785	18

Table 19. Torsion angles [°] for **11**.

C(5)-N(1)-C(1)-C(2)	56.22(18)
N(1)-C(1)-C(2)-C(3)	-55.56(18)
C(1)-C(2)-C(3)-C(6)	-179.72(12)
C(1)-C(2)-C(3)-C(4)	56.90(17)
C(6)-C(3)-C(4)-C(5)	177.91(13)
C(2)-C(3)-C(4)-C(5)	-57.84(17)
C(1)-N(1)-C(5)-C(4)	-57.86(17)
C(3)-C(4)-C(5)-N(1)	57.83(17)
C(2)-C(3)-C(6)-O(1)	-7.2(2)
C(4)-C(3)-C(6)-O(1)	115.71(16)
C(2)-C(3)-C(6)-O(2)	172.77(13)
C(4)-C(3)-C(6)-O(2)	-64.32(17)

Symmetry transformations used to generate equivalent atoms:

Table 20. Hydrogen bonds for **11** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1N1)...F(1)#1	0.904(15)	2.239(18)	2.8676(15)	126.2(16)
N(1)-H(1N1)...F(4)#2	0.904(15)	2.072(18)	2.8338(16)	141.2(17)
N(1)-H(1N2)...F(1)	0.902(15)	2.318(18)	2.8566(16)	118.2(15)
N(1)-H(1N2)...F(2)#3	0.902(15)	2.134(17)	2.8984(16)	141.9(16)
C(1)-H(1B)...O(2)#4	0.99	2.58	3.4679(19)	149.0
C(2)-H(2B)...F(4)	0.99	2.58	3.380(2)	137.3
O(2)-H(2O)...O(1)#5	0.872(16)	1.769(17)	2.6349(15)	172(2)
C(4)-H(4B)...F(3)#6	0.99	2.61	3.1969(19)	118.3
C(5)-H(5A)...F(1)#1	0.99	2.62	3.1110(17)	110.6
C(5)-H(5B)...F(3)#6	0.99	2.47	3.1139(19)	122.1

Symmetry transformations used to generate equivalent atoms:
#1 -x,-y+1,-z+1 #2 x-1,y,z #3 -x+1,-y+1,-z+1
#4 x,y+1,z #5 -x+1,-y,-z+2 #6 x-1,y-1,z

Kinetic Experiments

The NMR spectra for kinetic experiments were recorded on Varian 600 MHz spectrometer in CD_3CN with at least 30 seconds relaxation delay. The NMR data were processed with MestReNova v8.1.4. using the advanced data analysis tool and Microsoft Excel 2011 for Mac. The following, non-overlapping signals were used for quantitative integration (in ppm): standard (7.60-7.29), **4•BF$_3$** (3.65-3.49), **4•HBF$_4$** (3.84-3.72), **11** (3.45-3.31 or 2.70-2.61).

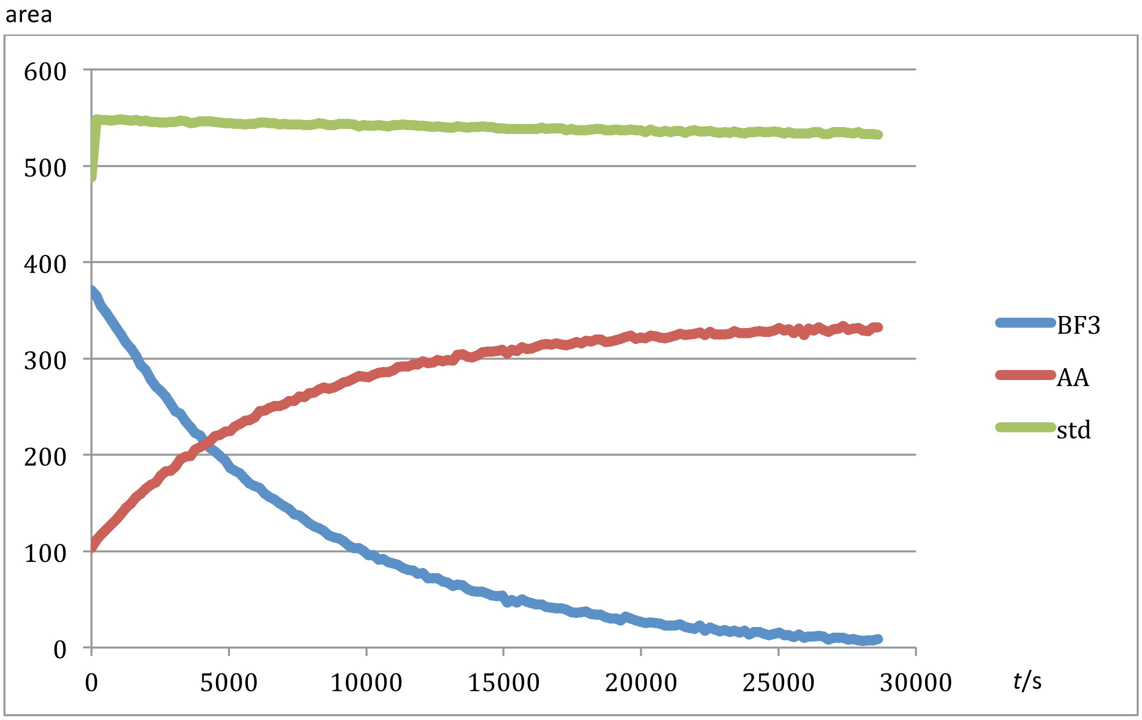
Procedure for hydrolysis study of 4•BF$_3$ by ^{1}H-NMR (9.6 equiv D_2O; CD_3CN; 10.6 μM; internal standard: 1,3,5-trichlorobenzene): A piece of the crystal of **4•BF$_3$** (<2.0 mg, calcd. with standard 1.04 mg) was dissolved in dry CD_3CN (0.45 mL, distilled over CaH_2 under argon prior to use) and transferred into a J. Young NMR-tube. After all spectral data were recorded (^{1}H, ^{13}C, ^{19}F, ^{11}B, ^{14}N, ^{15}N), a stock solution of 1,3,5-trichlorobenzene in CD_3CN (50 μL, 1.0 mg, 5.51 μmol, 11.0 mg dissolved in 0.55 mL CD_3CN) was added by a micro-syringe in the glove box and the content of the tube was vigorously shaken. After the first ^{1}H-NMR spectrum was recorded (to check the peak intensity of the internal standard), a stock solution of D_2O in CD_3CN (50 μL, 8.8 equiv, 10 μL D_2O dissolved in 0.49 mL CD_3CN) was added to the NMR sample by a micro-syringe in air. After vigorous shaking of the sample, a series of 160 single scan ^{1}H-NMR spectra was recorded as quickly as possible (every 3 minutes over 8 h). The calculated concentration c_0 of the NMR solution at $t = 0$ was 10.6 μM (1.04 mg in 0.55 mL, rel. to internal standard). The calculated half-life $t_{1/2}$ for the hydrolysis was 87 minutes (9.6 equiv D_2O, rel. to 1.04 mg substrate according to internal standard).

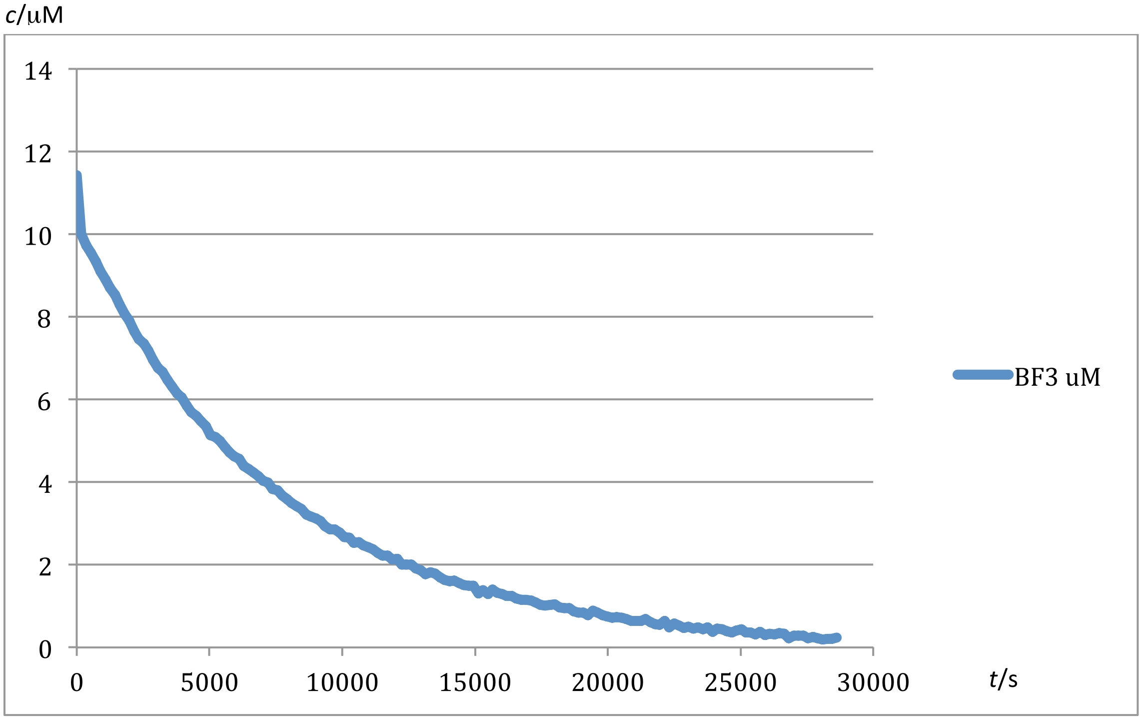
$\ln(c) = -0.0239*t+2.3616$; $R^2 = 0.99697$

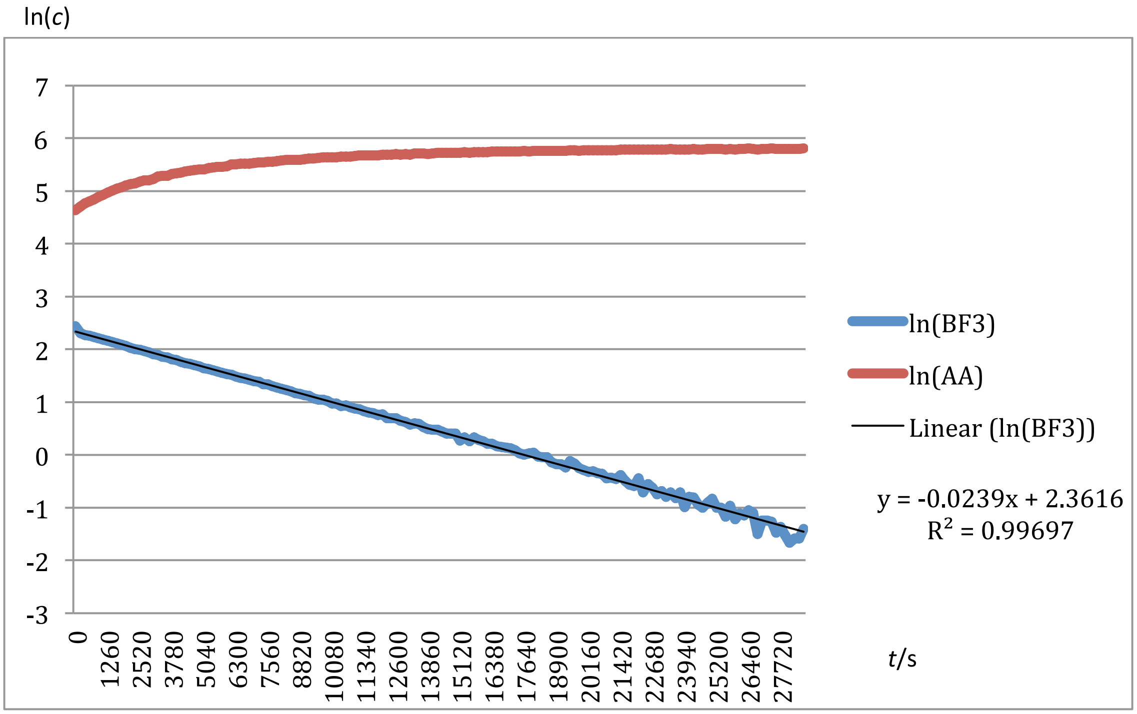
$t_{1/2} = (\ln(2)/0.0239) * 180\text{ s} = 5220\text{ s} = 87\text{ min}$

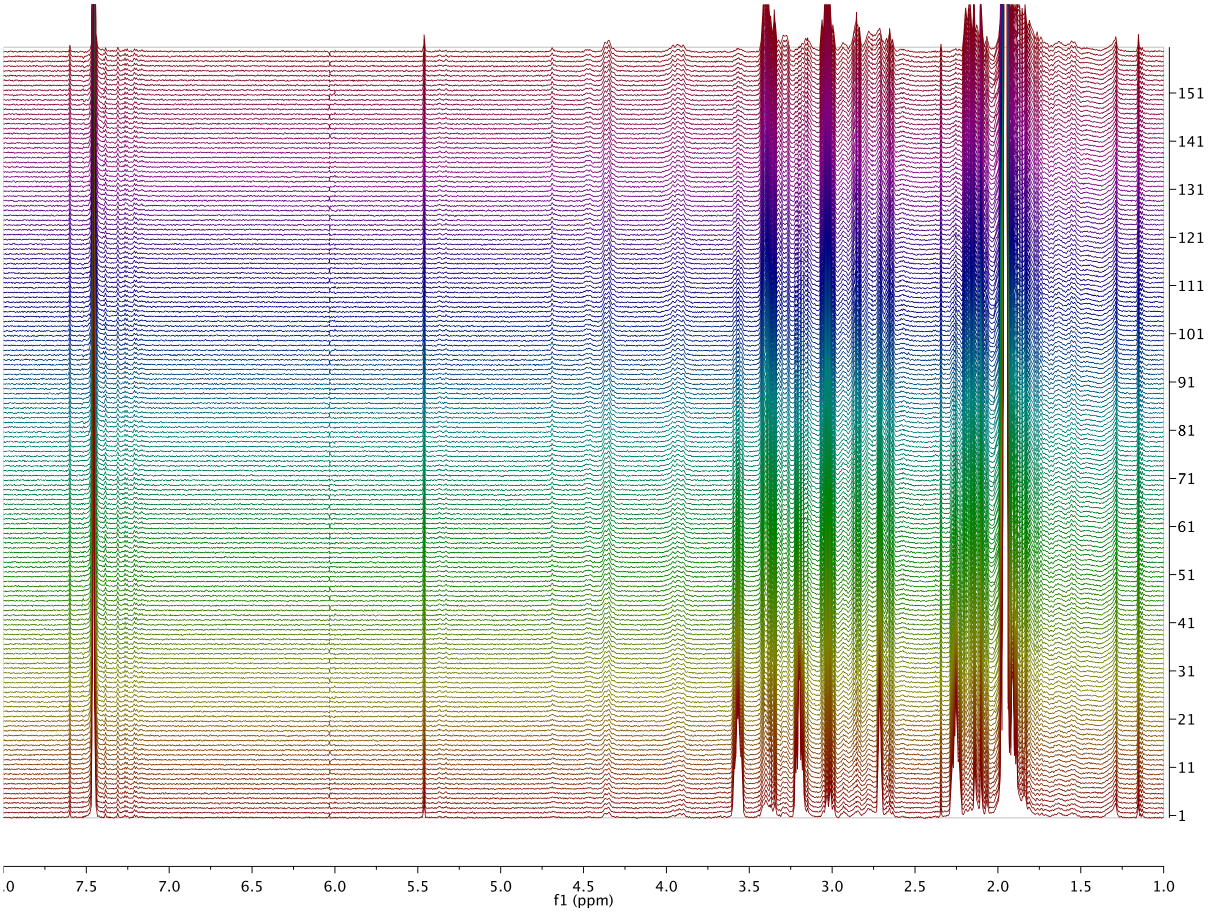
$c_0 = e^{2.3616} = 10.6$ μM.

Hydrolysis of 4•BF$_3$:
(9.6 equiv D$_2$O, 10.6 μM, $t_{1/2}$ = 87 min)

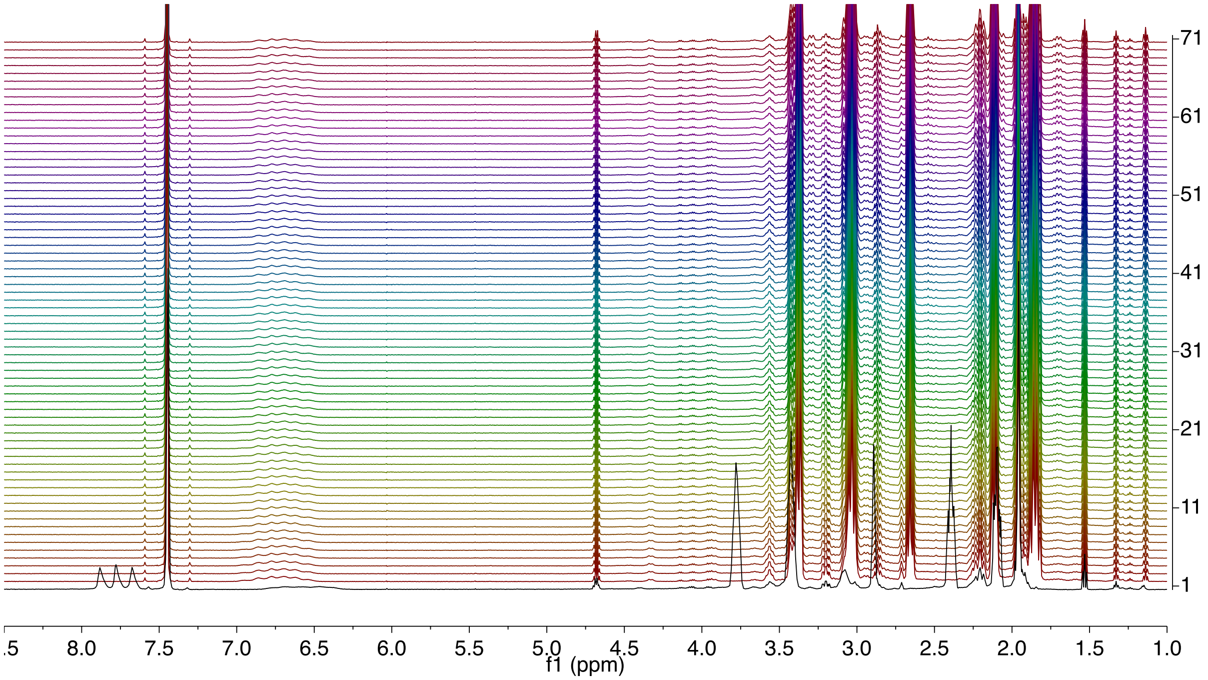




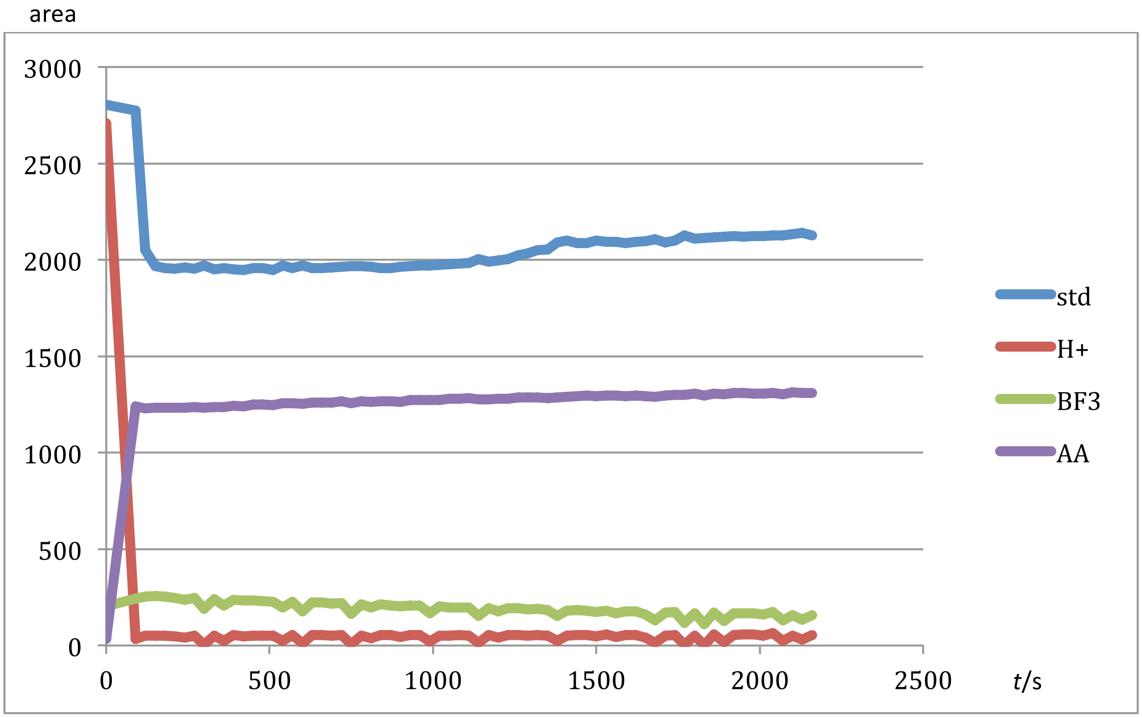

ln(c)
7
6
5
4
3
2
1
0
-1
-2
-3
0
1260
2520
3780
5040
6300
7560
8820
10080
11340
12600
13860
15120
16380
17640
18900
20160
21420
22680
23940
25200
26460
27720
t/s
ln(BF3)
ln(AA)
Linear (ln(BF3))
y = -0.0239x + 2.3616
R² = 0.99697

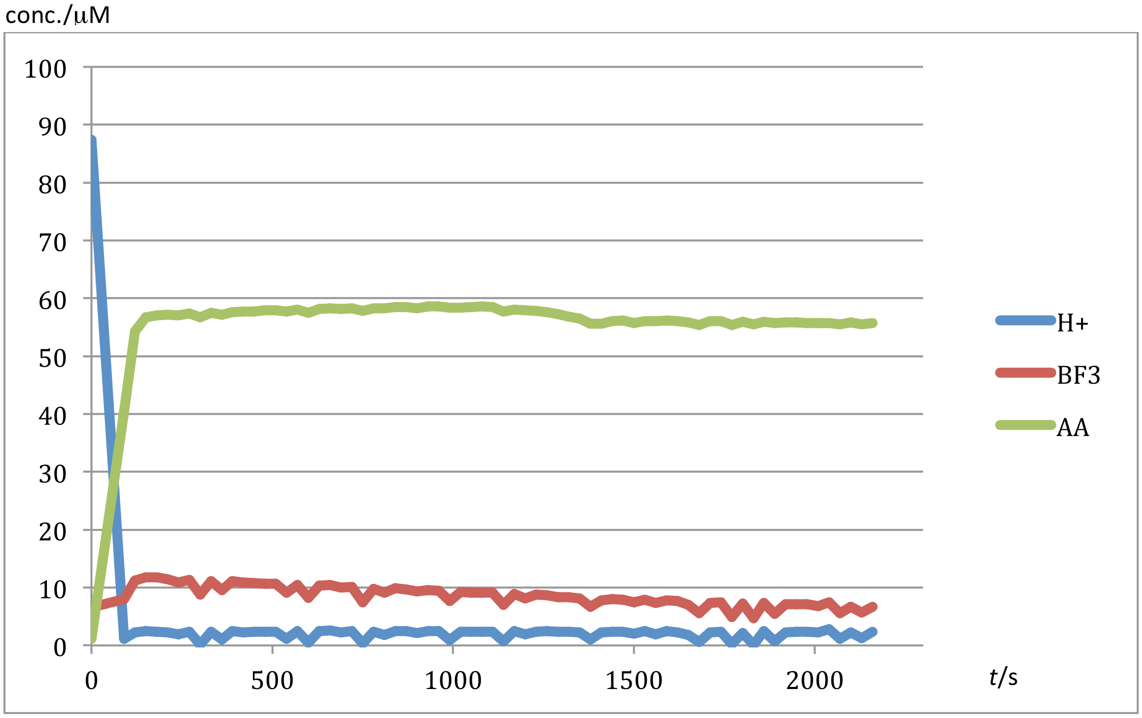

151
141
131
121
111
101
91
81
71
61
51
41
31
21
11
1
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

Procedure for hydrolysis study of 4•HBF$_4$ by ^{1}H-NMR (4.9 equiv D_2O; CD_3CN; 87.4 µM; internal standard: 1,3,5-trichlorobenzene): A solution of **4•HBF$_4$** (20.0 mg) and 1,3,5-trichlorobenzene (9.2 mg) in dry CD_3CN (0.6 mL, distilled over CaH_2 under argon prior to use) was transferred to a J. Young NMR-tube in a nitrogen-filled glove box. After recording the first ^{1}H-NMR spectrum and calculating the actual amount of protonated amide **4•HBF$_4$** present (14.6 mg of **4•HBF$_4$**, rel. to the standard), the concentration of the NMR solution was adjusted with dry CD_3CN (0.24 mL, conc. of **4•HBF$_4$** 87.4 µM) and D_2O (6.5 µL, 4.9 equiv) was added by a micro-syringe. After vigorous shaking and shimming of the sample (the time was measured = 90 seconds), a series of single scan ^{1}H-NMR spectra was recorded as quickly as possible (every 30 seconds). The calculated concentration c_0 of the NMR solution at t = 0 was 87.4 µM (14.6 mg in 0.84 mL, rel. to internal standard). The calculated half-life $t_{1/2}(H_2O)$ for the hydrolysis of **4•HBF$_4$** was less than one minute <1 min (4.9 equiv D_2O relative to **4•HBF$_4$**, 87.4 µM, with internal standard), since not even traces of **4•HBF$_4$** were visible in the ^{1}H-NMR spectrum after adding water and shimming of the sample (3 minutes).



Hydrolysis of 4•HBF$_4$:
(4.9 equiv D$_2$O, 87.4 µM, $t_{1/2}$ < 1 min)



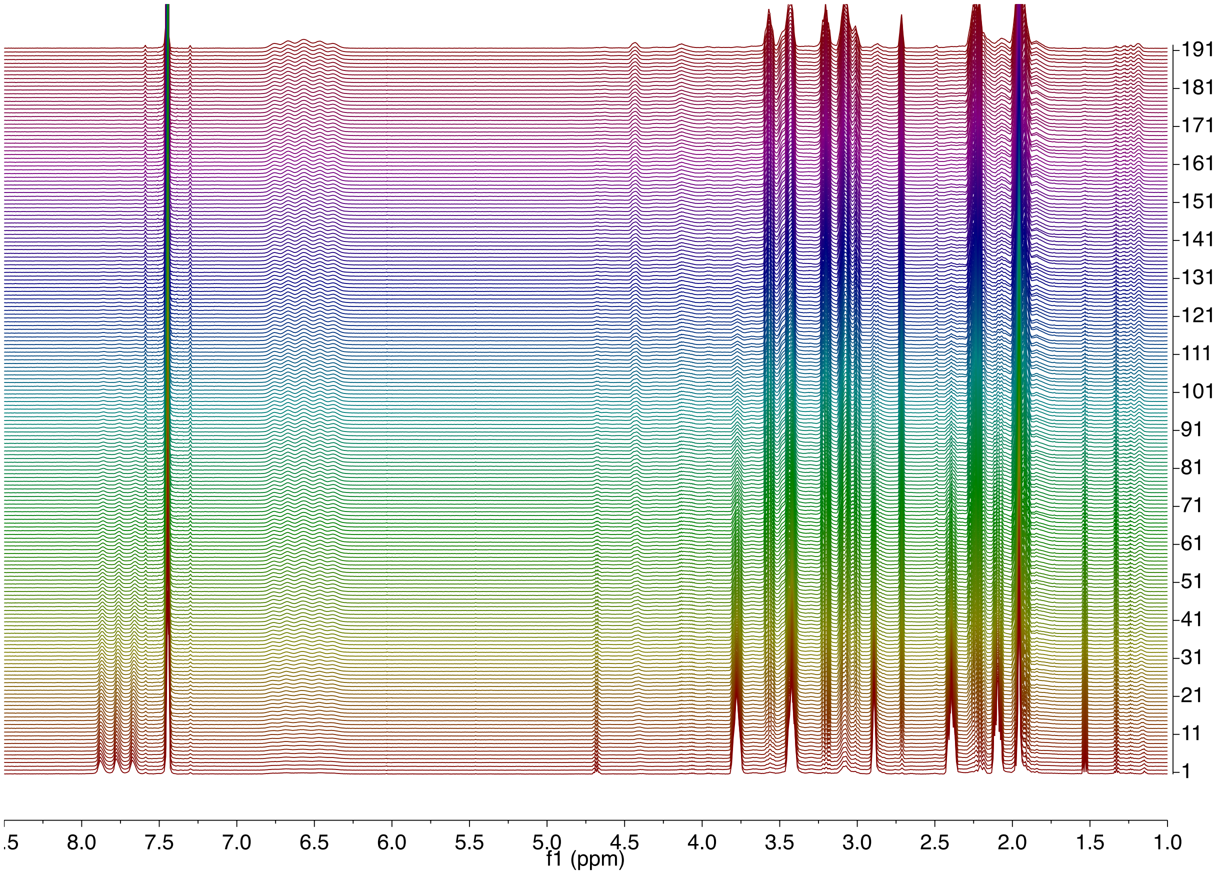


Procedure for decomposition study of 4•HBF$_4$ by ^{1}H-NMR (dry CD$_3$CN; 117 µM; internal standard: 1,3,5-trichlorobenzene): A solution of **4•HBF$_4$** (20.0 mg) and 1,3,5-trichlorobenzene (12.3 mg) in dry CD$_3$CN (0.84 mL, distilled over CaH$_2$ under argon prior to use) was transferred to a J. Young NMR-tube in a nitrogen-filled glovebox. Then, a series of single scan ^{1}H-NMR spectra were recorded every 5 minutes over 16 h. The calculated concentration of **4•HBF$_4$** in the NMR solution at $t = 0$ was 117 µM (19.5 mg in 0.84 mL, rel. to internal standard). The calculated half-life $t_{1/2}$(CD$_3$CN) for the decomposition of **4•HBF$_4$** in dry CD$_3$CN was 119 min = 1 h 59 min (117 µM, with internal standard).

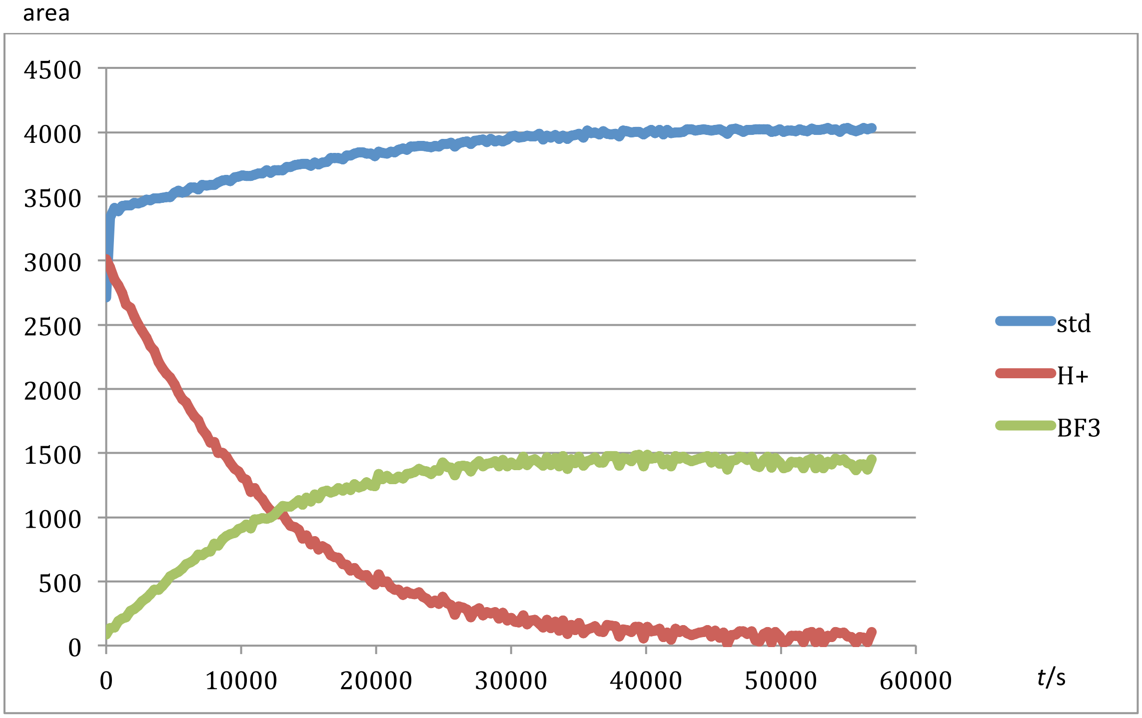
$\ln(c) = -0.0288*t+4.7608$; $R^2 = 0.99605$

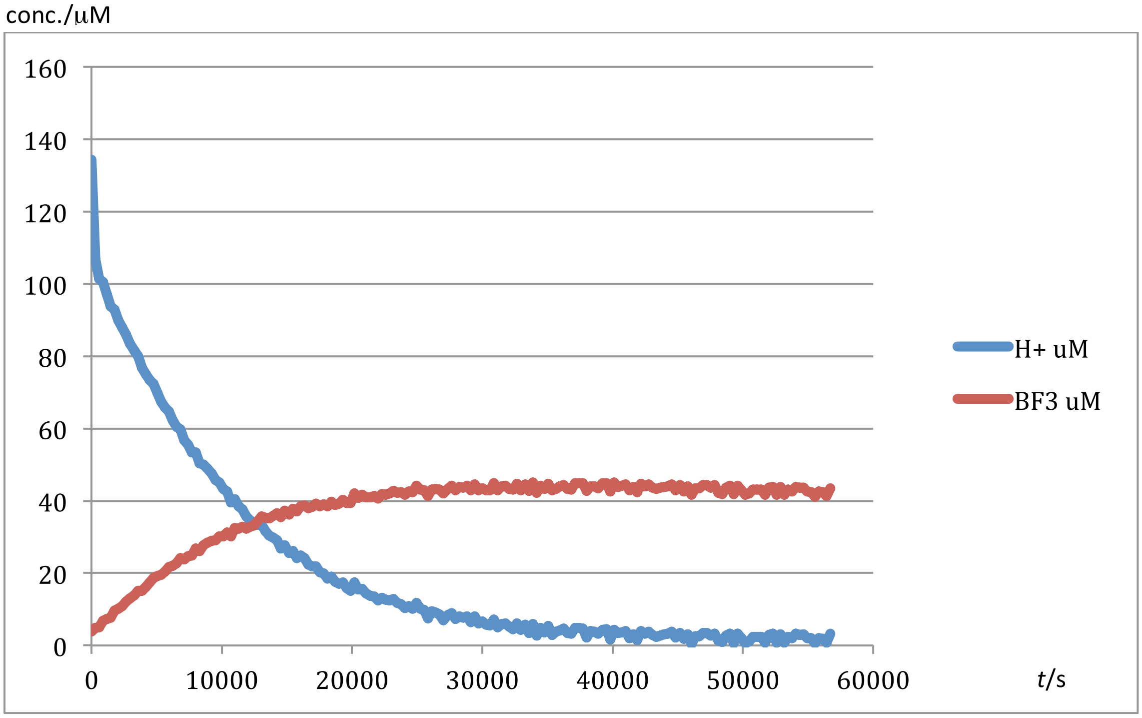
$t_{1/2} = (\ln(2)/0.0288) * 297\ \text{s} = 7148\ \text{s} = 119\ \text{min} = 1\ \text{h}\ 59\ \text{min}$

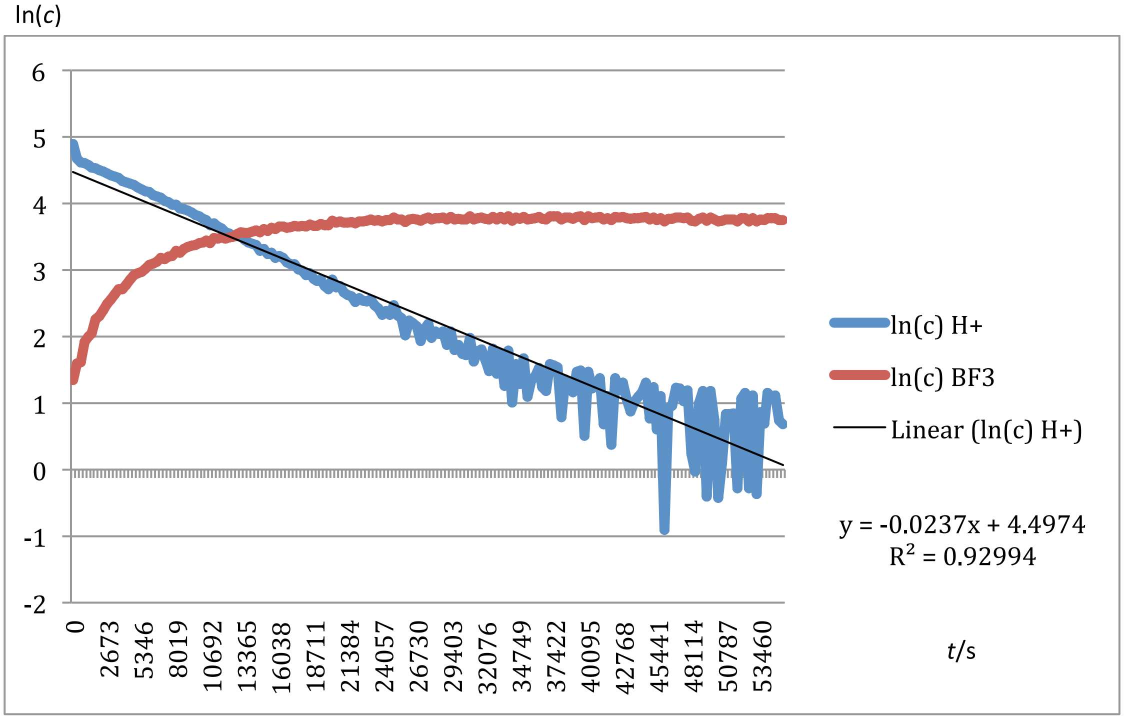
$c_0 = e^{4.7608} = 116.8\ \mu\text{M}$

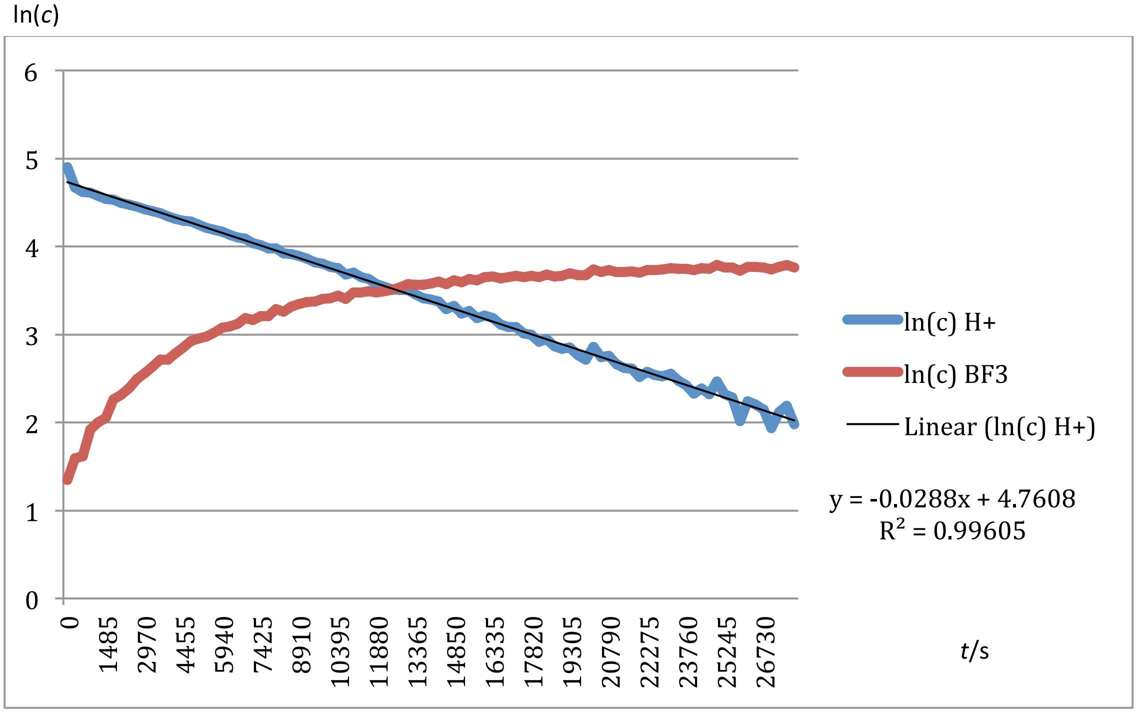


Decomposition of 4•HBF$_4$
(dry CD$_3$CN, 117 µM, $t_{1/2}$ = 119 min)



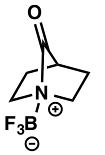


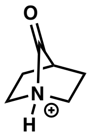

ln(c)
6
5
4
3
2
1
0
-1
-2
0
2673
5346
8019
10692
13365
16038
18711
21384
24057
26730
29403
32076
34749
37422
40095
42768
45441
48114
50787
53460
ln(c) H+
ln(c) BF3
Linear (ln(c) H+)
y = -0.0237x + 4.4974
R² = 0.92994
t/s

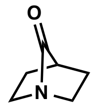

ln(c)
6
5
4
3
2
1
0
0
1485
2970
4455
5940
7425
8910
10395
11880
13365
14850
16335
17820
19305
20790
22275
23760
25245
26730
ln(c) H+
ln(c) BF3
Linear (ln(c) H+)
y = -0.0288x + 4.7608
R² = 0.99605
t/s

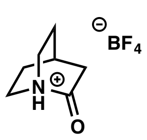
DFT Calculations

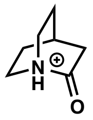
Table 21.

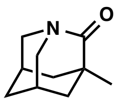

4•BF$_3$

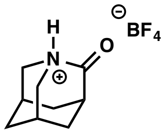

4•H$^+$


4


1


1•H$^+$


S3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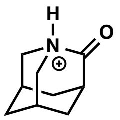
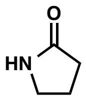
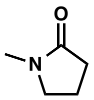
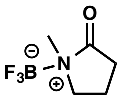
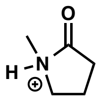
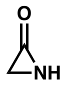

2•H$^+$


S4


S5


S5•BF$_3$


S5•H$^+$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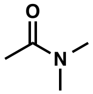
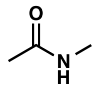
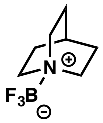

S7


S8


S9

	hypo*BF$_3$ **4•BF$_3$** X-ray	hypo*BF$_3$ **4•BF$_3$** DFT[a]	hypo*H+ **4•H$^+$** DFT[a]	hypo **4** DFT[a]	quinuc*HBF$_4$ **1** X-ray[b]	quinuc*HBF$_4$ **1'** X-ray[b]	quinuc*H+ **1•H$^+$** DFT[a]	Me-adamant **S3** X-ray[c]	Me-adamant **S3** DFT[a]	adamant-HBF$_4$ **2** X-ray[c]	adamant-H+ **2•H$^+$** DFT[a]
X_C	0.0°	0.0°	0.0°	0.0°	0.2°	–2.4°	0.0°	0.0°	0.0°	1.47°	0.0°
X_N	–69.8°	–69.4°	–66.3°	–70.3°	–59.5°	–58.9	–58.2°	–61.8°	–60.0°	–58.0°	–57.4°
τ	90.0°	90.0°	90.0°	90.0°	89.1°	89.2°	90.0°	90.0°	90.0°	91.9°	90.0°
bending[e] ξ	5.8°	4.5°	9.5°	2.5°	5.8°	5.6°	7.4°	2.0°	2.75°	6.3°	8.0°
Σ angles at N	306.8°	307.7°	311.5°	306.2°	328.5°	331.0°	329.7°	325.6°	328.1°	330.3°	330.8°
N-C(O) (Å)	1.526	1.534	1.613	1.475	1.524	1.483	1.560	1.448	1.455	1.508	1.565
C=O (Å)	1.186	1.179	1.168	1.193	1.192	1.168	1.180	1.201	1.202	1.186	1.182
N-B (Å)	1.606	1.664	-	-	-	-	-	-	-	-	-

	γ-lactam **S4** DFT[a]	Me-γ-lactam **S5** DFT[a]	Me-γ-lactam*BF$_3$ **S5•BF$_3$** DFT[a]	Me-γ-lactam*H+ **S5•H$^+$** DFT[a]	α-lactam **S6** DFT[a]	Me$_2$-acetamide **S7** DFT[a]	Me-acetamide **S8** DFT[a]	formamide (planar) DFT[b]	formamide (perpendicular) DFT[b]	quinuclidine*BF$_3$ **S9** X-ray[d]
X_C	0.9°	1.2°	2.4°	0.2°	5.5°	0.3°	0.6°	0.0°	0.0°	-
X_N	14.7°	12.0°	56.0°	54.9°	–67.2°	–5.2°	–5.7°	0.0°	63.4°	-
τ	1.5°	1.3°	3.9°	35.7°	30.9°	0.6°	1.2°	0.0°	90.0°	-
bending[e] ξ	0.7°	0.5°	3.4°	8.5°	3.4°	–0.7°	0.1°	-	-	-
Σ angles at N	358.2°	358.8°	330.9°	330.9°	308.0°	359.8°	359.8°	360°	-	-
N-C(O) (Å)	1.370	1.371	1.489	1.608	1.358	1.374	1.365	1.349	1.423	-
C=O (Å)	1.215	1.218	1.192	1.173	1.195	1.224	1.221	1.193	1.179	-
N-B (Å)	-	-	1.761	-	-	-	-	-	-	1.601

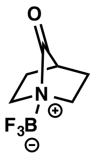
[a] DFT RB3LYP 6-311+G** calculations

[b] Tani, K.; Stoltz, B. M. *Nature* **2006**, *441*, 731.

[c] Kamarov, I. V.; Yanik, S.; Ishchenko, A. Y.; Davies, J. E.; Goodman, J. M.; Kirby, A. J. *J. Am. Chem. Soc.* **2015**, *137*, 926.

[d] Banks, R. E.; Besheesh, M. K.; Pritchard, R. G.; Sharif*, I. Acta Cryst.* **1993**, *C49*, 1804.

[e] definition: ξ = ((360°-CCN)/2)-OCN; CCN = bond path angle of C-C-N; OCN = bond path angle of O-C-N.



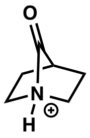
4•BF$_3$

```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Reason for exit: Successful completion
Mechanics CPU Time : .04
Mechanics Wall Time: .26
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
Number of shells: 108
Number of basis functions: 318
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
Optimization:
Step Energy Max Grad. Max Dist.
1 -688.656221 0.408451 0.261502
2 -688.751896 0.173798 0.164331
3 -688.780015 0.123197 0.208810
4 -688.795022 0.025896 0.211679
5 -688.793019 0.032840 0.117793
6 -688.798577 0.008058 0.041223
7 -688.798994 0.004691 0.015330
8 -688.799076 0.000671 0.006070
9 -688.799080 0.000272 0.002090
10 -688.799081 0.000059 0.000585
Reason for exit: Successful completion
Quantum Calculation CPU Time : 1:11:57.07
Quantum Calculation Wall Time: 1:15:23.90
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
Properties CPU Time : 1.24
Properties Wall Time: 1.43
molecule M0001 terminated normally
End- molecule "M0001" Thu Jan 15 17:08:17 2015
```

xyz coordinates:

N	0.091165	-0.196059	0.000000
C	-1.981641	-0.467673	1.254298
C	-1.981641	-0.467673	-1.254298
C	-2.123156	0.422995	0.000000
C	-0.473371	-0.877215	-1.224015
C	-0.473371	-0.877215	1.224015
H	-2.646305	-1.331473	1.204497

H	-2.646305	-1.331473	-1.204497
H	0.081173	-0.507027	-2.084004
H	0.081173	-0.507027	2.084004
H	-2.216770	0.088792	2.162880
H	-2.216770	0.088792	-2.162880
H	-2.958855	1.116644	0.000000
H	-0.303728	-1.947619	-1.130495
H	-0.303728	-1.947619	1.130495
C	-0.757188	1.081620	0.000000
O	-0.356302	2.190888	0.000000
B	1.750600	-0.074010	0.000000
F	2.180159	-1.396771	0.000000
F	2.075910	0.595728	1.160970
F	2.075910	0.595728	-1.160970



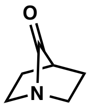
4•H$^+$

```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Reason for exit: Successful completion
Mechanics CPU Time : .04
Mechanics Wall Time: .14
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
Number of shells: 88
Number of basis functions: 236
Charge : +1
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
Optimization:
Step Energy Max Grad. Max Dist.
1 -364.452896 0.040618 0.142176
2 -364.466803 0.015862 0.091710
3 -364.469917 0.005157 0.046188
4 -364.470626 0.002549 0.034528
5 -364.470768 0.000721 0.012846
6 -364.470785 0.000086 0.003574
7 -364.470784 0.000034 0.000515
Reason for exit: Successful completion
Quantum Calculation CPU Time : 21:54.43
Quantum Calculation Wall Time: 23:26.35
```

```
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0000
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -223.033
Memory Used: 769.81 Kb
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .03
Semi-Empirical Program Wall Time: .11
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
Properties CPU Time : .76
Properties Wall Time: .86
molecule M0000 terminated normally
End- molecule "M0000" Mon Jan 19 00:38:15 2015

xyz coordinates:

C        0.550974     -0.890757     -1.244599
C        0.879832      0.637545     -1.261696
C        0.167200      1.192396      0.000000
C        0.879832      0.637545      1.261696
C        0.550974     -0.890757      1.244599
N       -0.289982     -1.052410      0.000000
C       -1.076392      0.355456      0.000000
O       -2.241749      0.434876      0.000000
H       -0.049125     -1.201906     -2.098964
H        1.426352     -1.533688     -1.169158
H        1.951862      0.823761     -1.209809
H        0.498385      1.104629     -2.169610
H       -0.020390      2.261841      0.000000
H        1.951862      0.823761      1.209809
H        0.498385      1.104629      2.169610
H        1.426352     -1.533688      1.169158
H       -0.049125     -1.201906      2.098964
H       -0.903825     -1.867396      0.000000
```



4

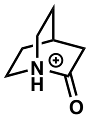
```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Reason for exit: Successful completion
Mechanics CPU Time : .04
Mechanics Wall Time: .15
```

```
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
Number of shells: 84
Number of basis functions: 230
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
Optimization:
Step Energy Max Grad. Max Dist.
1 -364.090560 0.035020 0.139826
2 -364.098450 0.005637 0.079748
3 -364.098739 0.000930 0.003240
4 -364.098745 0.000777 0.012519
5 -364.098757 0.000045 0.001441
6 -364.098757 0.000025 0.000323
Reason for exit: Successful completion
Quantum Calculation CPU Time : 15:38.18
Quantum Calculation Wall Time: 16:41.82
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0001
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -36.911
Memory Used: 716.53 Kb
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .03
Semi-Empirical Program Wall Time: .13
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
Properties CPU Time : .65
Properties Wall Time: .75
molecule M0001 terminated normally
End- molecule "M0001" Mon Jan 19 00:33:28 2015
```

```
xyz coordinates:

H       -0.237490      1.204140      2.086549
C       -0.723227      0.783274      1.204871
C       -0.723227      0.783274     -1.204871
C        0.105993     -1.140973      0.000000
C       -0.730148     -0.793225     -1.250191
C       -0.730148     -0.793225      1.250191
N        0.071509      1.166991      0.000000
H       -1.721509      1.215201     -1.129361
H        0.588037     -2.115033      0.000000
H       -0.260790     -1.165806     -2.163111
H       -0.260790     -1.165806      2.163111
H       -1.721509      1.215201      1.129361
H       -0.237490      1.204140     -2.086549
```

```
H       -1.736907     -1.212167     -1.192406
H       -1.736907     -1.212167      1.192406
C        1.052203      0.065379      0.000000
O        2.241385      0.155122      0.000000
```



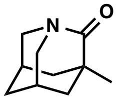
1•H$^+$

```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Reason for exit: Successful completion
Mechanics CPU Time : .04
Mechanics Wall Time: .17
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
Number of shells: 102
Number of basis functions: 270
Charge : +1
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
Optimization:
Step Energy Max Grad. Max Dist.
1 -403.800652 0.043444 0.126902
2 -403.812023 0.017612 0.073096
3 -403.813261 0.002635 0.022037
4 -403.813408 0.001191 0.009905
5 -403.813440 0.000201 0.003838
6 -403.813438 0.000054 0.000508
Reason for exit: Successful completion
Quantum Calculation CPU Time : 24:49.32
Quantum Calculation Wall Time: 26:21.81
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0001
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -216.994
Memory Used: 1.028 Mb
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .03
Semi-Empirical Program Wall Time: .13
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
```

```
Properties CPU Time : .98
Properties Wall Time: 1.11
molecule M0001 terminated normally
End- molecule "M0001" Tue Jan 20 10:47:57 2015

xyz coordinates:

H       -0.379959     -1.049165      2.104260
C        0.303664     -1.065746      1.255203
C        0.303664     -1.065746     -1.255203
C        1.096504      0.977518      0.000000
C        1.308056      0.112304     -1.258227
C        1.308056      0.112304      1.258227
N       -0.551473     -0.974068      0.000000
H        0.788719     -2.042030     -1.226859
H        1.800033      1.809801      0.000000
H        1.171301      0.711824     -2.159932
H        1.171301      0.711824      2.159932
H        0.788719     -2.042030      1.226859
H       -0.379959     -1.049165     -2.104260
H        2.329454     -0.270034     -1.280007
H        2.329454     -0.270034      1.280007
H       -1.267670     -1.705038      0.000000
C       -1.322101      0.382149      0.000000
C       -0.345415      1.522004      0.000000
H       -0.561186      2.144823      0.875259
H       -0.561186      2.144823     -0.875259
O       -2.501654      0.343121      0.000000
```



S3

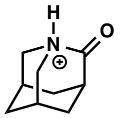
```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Reason for exit: Successful completion
Mechanics CPU Time : .05
Mechanics Wall Time: .15
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
Number of shells: 132
Number of basis functions: 354
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
```

```
Optimization:
Step Energy Max Grad. Max Dist.
1 -520.209046 0.025272 0.140462
2 -520.212622 0.004689 0.062347
3 -520.212915 0.001060 0.003240
4 -520.212926 0.000720 0.009921
5 -520.212933 0.000022 0.000437
Reason for exit: Successful completion
Quantum Calculation CPU Time : 48:24.97
Quantum Calculation Wall Time: 50:28.04
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0001
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -27.982
Memory Used: 1.916 Mb
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .08
Semi-Empirical Program Wall Time: .32
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
Properties CPU Time : 1.91
Properties Wall Time: 2.05
molecule M0001 terminated normally
End- molecule "M0001" Fri Mar 20 12:22:58 2015
```

xyz coordinates:

```
H       -0.780184     -0.734683     -2.163840
C       -0.252092     -1.052494     -1.257765
C        1.929767     -0.996983      0.000000
C       -0.252092     -1.052494      1.257765
C        1.183723     -0.500230      1.253164
C       -1.026384     -0.561927      0.000000
C        1.183723     -0.500230     -1.253164
H        1.987535     -2.091556      0.000000
H       -0.248656     -2.149136      1.256914
H       -0.248656     -2.149136     -1.256914
H        2.959442     -0.620227      0.000000
H       -0.780184     -0.734683      2.163840
H        1.708953     -0.819637      2.160057
H        1.708953     -0.819637     -2.160057
C        1.105118      1.035971     -1.214498
H        2.102728      1.486536     -1.210384
H        0.576974      1.423538     -2.091055
C        1.105118      1.035971      1.214498
H        2.102728      1.486536      1.210384
H        0.576974      1.423538      2.091055
N        0.396194      1.509581      0.000000
C       -0.956729      0.973100      0.000000
O       -1.918777      1.694423      0.000000
C       -2.468841     -1.060474      0.000000
```

```
H       -2.489368     -2.154914      0.000000
H       -3.008844     -0.704553     -0.880368
H       -3.008844     -0.704553      0.880368
```



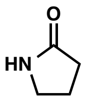
2•H$^+$

```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Reason for exit: Successful completion
Mechanics CPU Time : .06
Mechanics Wall Time: .21
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
Number of shells: 122
Number of basis functions: 326
Charge : +1
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
Optimization:
Step Energy Max Grad. Max Dist.
1 -481.253033 0.038813 0.113296
2 -481.264135 0.010341 0.071157
3 -481.265536 0.002857 0.026175
4 -481.265770 0.001112 0.008223
5 -481.265800 0.000240 0.004239
6 -481.265799 0.000037 0.001203
Reason for exit: Successful completion
Quantum Calculation CPU Time : 56:08.41
Quantum Calculation Wall Time: 58:47.46
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0001
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -206.317
Memory Used: 1.581 Mb
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .05
Semi-Empirical Program Wall Time: .20
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
```

```
Properties CPU Time : 1.65
Properties Wall Time: 1.77
molecule M0001 terminated normally
End- molecule "M0001" Thu Mar 19 16:30:05 2015

xyz coordinates:

H        2.532550     -1.178395      0.000000
C        1.990618     -0.227491      0.000000
C        0.374079      1.244044     -1.273760
C        0.374079      1.244044      1.273760
C       -0.506536      1.383420      0.000000
C        1.103263     -0.112554      1.256079
C        1.103263     -0.112554     -1.256079
H        1.097037      2.063187     -1.282791
H        1.097037      2.063187      1.282791
H        2.744508      0.563844      0.000000
H       -0.238828      1.349465     -2.173301
H       -0.238828      1.349465      2.173301
H       -1.058125      2.323995      0.000000
H        1.708073     -0.219249      2.159923
H        1.708073     -0.219249     -2.159923
C        0.071169     -1.242738      1.258546
H       -0.609357     -1.189090      2.110630
H        0.527303     -2.234244      1.232845
C        0.071169     -1.242738     -1.258546
H       -0.609357     -1.189090     -2.110630
H        0.527303     -2.234244     -1.232845
N       -0.778085     -1.109506      0.000000
C       -1.509315      0.273678      0.000000
O       -2.691049      0.254626      0.000000
H       -1.525745     -1.809074      0.000000
```



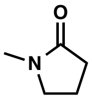
S4

```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Reason for exit: Successful completion
Mechanics CPU Time : .04
Mechanics Wall Time: .13
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
Number of shells: 64
Number of basis functions: 174
```

```
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
Optimization:
Step Energy Max Grad. Max Dist.
1 -286.715877 0.019677 0.088005
2 -286.718703 0.005065 0.114454
3 -286.718981 0.001039 0.003240
4 -286.718980 0.000980 0.074524
5 -286.719001 0.000090 0.008802
6 -286.719001 0.000027 0.002854
Reason for exit: Successful completion
Quantum Calculation CPU Time : 6:06.04
Quantum Calculation Wall Time: 6:40.61
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0001
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -30.366
Memory Used: 393.70 Kb
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .02
Semi-Empirical Program Wall Time: .13
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
Properties CPU Time : .38
Properties Wall Time: .47
molecule M0001 terminated normally
End- molecule "M0001" Mon Jan 19 14:29:36 2015
```

xyz coordinates:

N	0.100299	-1.096707	-0.061089
C	-1.315441	-0.818669	0.145775
C	-1.407178	0.687698	-0.189405
C	-0.000063	1.223901	0.122371
C	0.914565	0.004125	-0.010681
H	-1.614160	-1.017326	1.183354
H	-1.940319	-1.430660	-0.508783
H	-1.625987	0.809740	-1.253148
H	-2.198518	1.184503	0.373229
H	0.086253	1.588211	1.151679
H	0.335116	2.024028	-0.537504
H	0.500400	-2.021573	-0.007568
O	2.129001	-0.004460	-0.048226



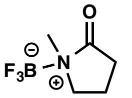
S5

```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Reason for exit: Successful completion
Mechanics CPU Time : .05
Mechanics Wall Time: .15
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
Number of shells: 78
Number of basis functions: 208
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
Optimization:
Step Energy Max Grad. Max Dist.
1 -326.036531 0.015778 0.081400
2 -326.039284 0.003119 0.121733
3 -326.039581 0.002056 0.117139
4 -326.039703 0.001005 0.052845
5 -326.039714 0.000225 0.012030
6 -326.039716 0.000082 0.006654
7 -326.039716 0.000066 0.003160
Reason for exit: Successful completion
Quantum Calculation CPU Time : 12:30.85
Quantum Calculation Wall Time: 13:30.79
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0001
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -22.935
Memory Used: 584.71 Kb
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .02
Semi-Empirical Program Wall Time: .12
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
Properties CPU Time : .53
Properties Wall Time: .61
molecule M0001 terminated normally
End- molecule "M0001" Mon Jan 19 14:37:23 2015
```

xyz coordinates:

N	0.582361	0.426356	0.038640

```
C       -0.479620      1.400128     -0.179070
C       -1.761855      0.613193      0.162212
C       -1.373125     -0.851695     -0.088803
C        0.148747     -0.874234      0.042343
H       -0.477716      1.748493     -1.222354
H       -0.339452      2.276275      0.461367
H       -2.010847      0.759485      1.216005
H       -2.615226      0.944760     -0.430594
H       -1.620815     -1.180647     -1.103783
H       -1.824060     -1.563122      0.603223
O        0.859595     -1.860922      0.113844
C        1.983360      0.784987     -0.020983
H        2.232052      1.509991      0.760355
H        2.239226      1.220455     -0.994661
H        2.569808     -0.121316      0.127252
```



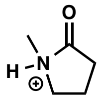
S5•BF$_3$

```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Reason for exit: Successful completion
Mechanics CPU Time : .05
Mechanics Wall Time: .14
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
Number of shells: 102
Number of basis functions: 296
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
Optimization:
Step Energy Max Grad. Max Dist.
1 -650.570751 0.362821 0.211931
2 -650.672118 0.145027 0.144661
3 -650.700803 0.062322 0.178539
4 -650.700877 0.053256 0.151135
5 -650.707315 0.018114 0.209833
6 -650.704052 0.041649 0.150719
7 -650.709580 0.008856 0.116683
8 -650.709331 0.008370 0.061109
9 -650.710146 0.001300 0.054352
10 -650.710195 0.000590 0.056754
11 -650.710213 0.000372 0.019776
```

```
12 -650.710217 0.000072 0.003276
13 -650.710217 0.000035 0.000314
Reason for exit: Successful completion
Quantum Calculation CPU Time : 1:08:18.52
Quantum Calculation Wall Time: 1:11:51.92
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
Properties CPU Time : 1.05
Properties Wall Time: 1.16
molecule M0001 terminated normally
End- molecule "M0001" Mon Jan 19 21:13:45 2015

xyz coordinates:

H       -2.059828      0.677133      1.701954
C       -2.078968      0.373672      0.654008
C       -1.655457      1.482184     -0.322943
C       -0.717255      0.772892     -1.315201
N       -0.065017     -0.328305     -0.527198
C       -1.098459     -0.761134      0.453953
H       -3.077201     -0.023842      0.449259
H       -1.123528      2.273532      0.201437
H       -2.503292      1.927119     -0.844653
H       -1.282166      0.311763     -2.130854
H        0.051200      1.416967     -1.735906
O       -1.109955     -1.855695      0.924854
C        0.425061     -1.456529     -1.368369
H       -0.384828     -1.825543     -2.001013
H        0.775052     -2.249178     -0.713657
H        1.247355     -1.093744     -1.981928
B        1.318342      0.301234      0.361410
F        0.786230      1.186810      1.274241
F        1.901336     -0.796637      0.927112
F        2.071432      0.904349     -0.619698
```



S5•H$^+$

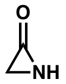
```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Reason for exit: Successful completion
Mechanics CPU Time : .04
Mechanics Wall Time: .13
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
```

```
Number of shells: 82
Number of basis functions: 214
Charge : +1
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
Optimization:
Step Energy Max Grad. Max Dist.
1 -326.354723 0.038528 0.096480
2 -326.369219 0.019246 0.099789
3 -326.371825 0.004837 0.086474
4 -326.372381 0.002230 0.066343
5 -326.372503 0.000370 0.059369
6 -326.372528 0.000256 0.039343
7 -326.372532 0.000200 0.023732
8 -326.372532 0.000063 0.004995
Reason for exit: Successful completion
Quantum Calculation CPU Time : 17:49.88
Quantum Calculation Wall Time: 19:14.52
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0001
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -226.600
Memory Used: 631.34 Kb
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .02
Semi-Empirical Program Wall Time: .19
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
Properties CPU Time : .62
Properties Wall Time: .72
molecule M0001 terminated normally
End- molecule "M0001" Mon Jan 19 20:19:25 2015

xyz coordinates:

C       -0.284695     -1.006024     -0.027035
N       -0.603523      0.513625     -0.446110
C        0.746284      1.176805     -0.582054
C        1.662365      0.391920      0.368807
C        1.187872     -1.062488      0.250709
H        1.059683      1.067249     -1.621382
H        0.659073      2.236142     -0.347221
H        1.556362      0.749792      1.395192
H        2.707182      0.514352      0.087498
H        1.363244     -1.681477      1.132236
H        1.652477     -1.580513     -0.598309
O       -1.169984     -1.774808      0.000464
C       -1.537358      1.146454      0.551008
H       -1.820675      2.132659      0.186204
```

H	-1.025606	1.233190	1.508302
H	-2.415957	0.510961	0.650578
H	-1.088533	0.466994	-1.344907



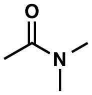
S6

```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Reason for exit: Successful completion
Mechanics CPU Time : .03
Mechanics Wall Time: .37
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
Number of shells: 36
Number of basis functions: 106
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
Optimization:
Step Energy Max Grad. Max Dist.
1 -207.977677 0.045213 0.202673
2 -207.987275 0.022160 0.219514
3 -207.991937 0.009886 0.267435
4 -207.993352 0.009322 0.211538
5 -207.993416 0.007629 0.226694
6 -207.994186 0.002621 0.039125
7 -207.994152 0.003671 0.016393
8 -207.994255 0.000954 0.016815
9 -207.994260 0.000730 0.010114
10 -207.994265 0.000247 0.005924
11 -207.994267 0.000201 0.005100
12 -207.994269 0.000096 0.003533
13 -207.994269 0.000013 0.000224
Reason for exit: Successful completion
Quantum Calculation CPU Time : 3:10.19
Quantum Calculation Wall Time: 3:44.37
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0001
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -44.187
Memory Used: 140.20 Kb
```

```
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .01
Semi-Empirical Program Wall Time: .17
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
Properties CPU Time : .14
Properties Wall Time: .24
molecule M0001 terminated normally
End- molecule "M0001" Mon Jan 19 19:14:45 2015
```

xyz coordinates:

H	-1.177306	1.068295	1.048292
C	-0.911919	0.686118	0.064964
C	0.401517	0.029306	-0.059199
N	-0.665741	-0.809240	-0.094377
H	-1.436154	1.135630	-0.771122
H	-0.869214	-1.487950	0.632335
O	1.596140	0.070749	-0.041247



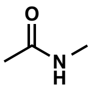
S7

```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Adjusted 2 (out of 45) low frequency modes
Reason for exit: Successful completion
Mechanics CPU Time : .04
Mechanics Wall Time: .13
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
Number of shells: 72
Number of basis functions: 186
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
Optimization:
Step Energy Max Grad. Max Dist.
1 -287.916395 0.017863 0.087772
2 -287.918255 0.002996 0.126031
3 -287.918375 0.001549 0.065520
4 -287.918409 0.000731 0.098062
5 -287.918422 0.000453 0.066447
6 -287.918429 0.000374 0.035908
```

```
7 -287.918431 0.000108 0.024404
8 -287.918432 0.000065 0.008245
Reason for exit: Successful completion
Quantum Calculation CPU Time : 11:25.83
Quantum Calculation Wall Time: 12:30.12
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0001
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -19.876
Memory Used: 468.84 Kb
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .02
Semi-Empirical Program Wall Time: .12
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
Properties CPU Time : .49
Properties Wall Time: .59
molecule M0001 terminated normally
End- molecule "M0001" Mon Jan 19 00:46:02 2015
```

```
xyz coordinates:

C         0.729378      0.287472     -0.036109
N        -0.596941     -0.071653     -0.011676
O         1.082083      1.459491     -0.057324
C        -1.618677      0.966520      0.037442
H        -2.331421      0.832676     -0.782995
H        -1.138006      1.937188     -0.052583
H        -2.168843      0.922427      0.984755
C        -1.092073     -1.435612      0.076722
H        -0.297314     -2.158007     -0.086187
H        -1.862106     -1.602253     -0.684147
H        -1.540831     -1.630800      1.059127
C         1.763418     -0.830623     -0.044140
H         1.665520     -1.467268     -0.927505
H         1.683984     -1.465815      0.841884
H         2.744546     -0.361074     -0.056100
```



S8

```
MacSPARTAN '10 MECHANICS PROGRAM: x86/Darwin 1.1.0
Frequency Calculation
Adjusted 2 (out of 36) low frequency modes
Reason for exit: Successful completion
```

```
Mechanics CPU Time : .04
Mechanics Wall Time: .18
MacSPARTAN '10 Quantum Mechanics Program: (x86/Darwin) build 1.1.0v4
Job type: Geometry optimization.
Method: RB3LYP
Basis set: 6-311+G**
Number of shells: 58
Number of basis functions: 152
Multiplicity: 1
SCF model:
A restricted hybrid HF-DFT SCF calculation will be
performed using Pulay DIIS + Geometric Direct Minimization
Optimization:
Step Energy Max Grad. Max Dist.
1 -248.604092 0.013606 0.099298
2 -248.605651 0.004238 0.078626
3 -248.605823 0.001355 0.003240
4 -248.605825 0.001309 0.209313
5 -248.605879 0.000449 0.128534
6 -248.605890 0.000652 0.029002
7 -248.605896 0.000300 0.024043
8 -248.605895 0.000067 0.001590
Reason for exit: Successful completion
Quantum Calculation CPU Time : 5:04.62
Quantum Calculation Wall Time: 5:41.51
MacSPARTAN '10 Semi-Empirical Program: (x86/Darwin) build 1.1.0
Semi-empirical Property Calculation
M0001
Guess from Archive
Energy Due to Solvation
Solvation Energy SM5.4/A -28.653
Memory Used: 304.39 Kb
Reason for exit: Successful completion
Semi-Empirical Program CPU Time : .01
Semi-Empirical Program Wall Time: .16
MacSPARTAN '10 Properties Program: (x86/Darwin) build 1.1.0
Reason for exit: Successful completion
Properties CPU Time : .28
Properties Wall Time: .38
molecule M0001 terminated normally
End- molecule "M0001" Mon Jan 19 13:54:29 2015
```

xyz coordinates:

```
C        0.483374     -0.146587     -0.052371
N       -0.628505      0.641110      0.033356
H       -0.517070      1.641260      0.047232
C       -1.971735      0.082965     -0.017290
H       -2.009267     -0.824275      0.585926
H       -2.266776     -0.176254     -1.039089
H       -2.676994      0.812071      0.383448
O        0.414389     -1.362778     -0.141050
C        1.814753      0.584046     -0.016795
```

H	2.396709	0.206415	0.826232
H	1.719047	1.668372	0.073574
H	2.367928	0.349429	-0.928595

References

[1] Cyclobutanone *N*,*N*-dimethylhydrazone (bp 150 °C, 1 atm) was prepared according to: Mino, T.; Masuda, S.; Nishio, M.; Yamashita, M. *J. Org. Chem.* **1997**, *62*, 2633-2635.

[2] 2-Bromo-1-tert-butyldimethylsilyloxy ethane was prepared according to: Kuwabe, S.; Torraca, K. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 12202-12206

[3] 2-(2-Hydroxyethyl) cyclobutanone was synthesized previously by hydroboration of 2-vinylcyclobutanone dimethylacetal: Fadel, A.; Salaun, J. *Tetrahedron* **1985**, *41*, 413-420.

[4] Procedure adapted from: MacLeod, F.; Lang, S.; Murphy, J. A. *Synlett* **2010**, 529-534.

[5] 1-Tosyl-4-piperidinecarboxylic acid is commercially available (*e.g.* from abcr, Germany; CAS 147636-36-0).

[6] EF: electric field scan.

[7] EF: electric field scan.

[8] Isonipecotic acid tetrafluoroborate (**11**) was isolated as a colorless oil under air moisture. However, slow diffusion of Et_2O into a solution of **11** in CH_3CN at -40 °C over 2 weeks led to precipitation of the salt as a colorless, fluffy solid.

[9] EF: electric field scan.

[10] Sheldrick, G. M. *Acta Cryst.* **1990**, A46, 467-473.

[11] Sheldrick, G. M. *Acta Cryst.* **2008**, A64, 112-122.

[12] Müller, P. *Crystallography Reviews* **2009**, *15*, 57-83.