Supporting Information

Primary Trifluoroborate-Iminiums Enable Facile Access to Chiral α-Aminoboronic Acids via Ru-Catalyzed Asymmetric Hydrogenation and Simple Hydrolysis of Trifluoroborate Moiety

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1. General Information

All reagents were purchased from commercial vendors (Merck-Sigma Aldrich, TCI, Acros Organics, abcr, Janssen, Fluka, STREM, Alfa Aesar) and were used as supplied unless noted otherwise. 1-Diol resin was purchased from Iris Biotech GmbH. Syringes for solid-phase peptide syntheses were purchased from Carl Roth. Commercial samples of optically pure ixazomib (catalog number HY-10453/CS-1657, lot number 43698, batch HYBE0008634) and bortezomib (catalog number HY-10227/CS-1039, lot number 45613, batch HYY00020087) were purchased from MedChemExpress. Dry THF was distilled from a benzophenone-ketyl/sodium still and kept over 4 Å molecular sieves under argon. Dry MeOH was purchased from Acros Organics. For TLC, Merck silica plates (60 F_{254}, 0.25 mm) were used and spots were detected under UV light (254 or 365 nm) or else visualized by ninhydrin or phosphomolybdate staining.

^{1}H, ^{11}B, ^{13}C and ^{19}F NMR spectra were recorded at the University of Ljubljana, Faculty of Pharmacy with a Bruker AVANCE III 400 at 400, 128, 101 and 376 MHz, respectively, using acetone-d_6, methanol-d_4 or DMSO-d_6 as solvents. All chemical shifts are reported in ppm, with ^{1}H and ^{13}C resonances referenced to the residual solvent signal as internal standard. Coupling constants *J* are reported in Hz. The resonances for boron-bound carbon nuclei were broadened and often suppressed in ^{13}C spectra. In such cases, they were extracted from ^{1}H–^{13}C *gs*-HMBC spectra for pTIMs **2** and ^{1}H–^{13}C HSQC spectra for pTAMs **3** and α-aminoboronic acids **4**.

Melting points were determined on a Reichelt hot-stage apparatus and are uncorrected. Attenuated total reflectance (ATR) infrared spectra were recorded on a FT-IR Thermo Nicolet spectrometer. High-resolution mass measurements (HRMS) were performed on a Thermo Scientific Q Exactive Plus mass spectrometer. Chiral HPLC analyses were performed on a Waters 2695 system equipped with Separations Module and Waters 2487 Dual Absorbance Detector. The columns, mobile phases and other parameters are reported for each analyzed compound in Section 4.3.1. Specific rotations were determined on a Perkin-Elmer 241MC polarimeter.

2. Preparation of Potassium Acyltrifluoroborates (KATs)

KATs **1a**–**1h**[S1] and **1k–1o**[S2] were synthesized according to the literature procedure with some modifications also published in literature.[S3] The following KATs were already synthesized and described in literature (**1a**[S4], **1b**[S5], **1c**[S5], **1d**[S5], **1e**[S1], **1f**[S4], **1g**[S3], **1h**[S3], **1k**[S2], **1l**[S2], **1m**[S3], **1n**[S2], **1o**[S2]). Their spectroscopic data corresponded to those that had been reported previously and are not repeated here. KATs **1i, 1j**, and **1p** were purchased from Sigma Aldrich. While **1m** was first synthesized by our group,[S3] an improved synthetic procedure was developed during this work and is reported below.

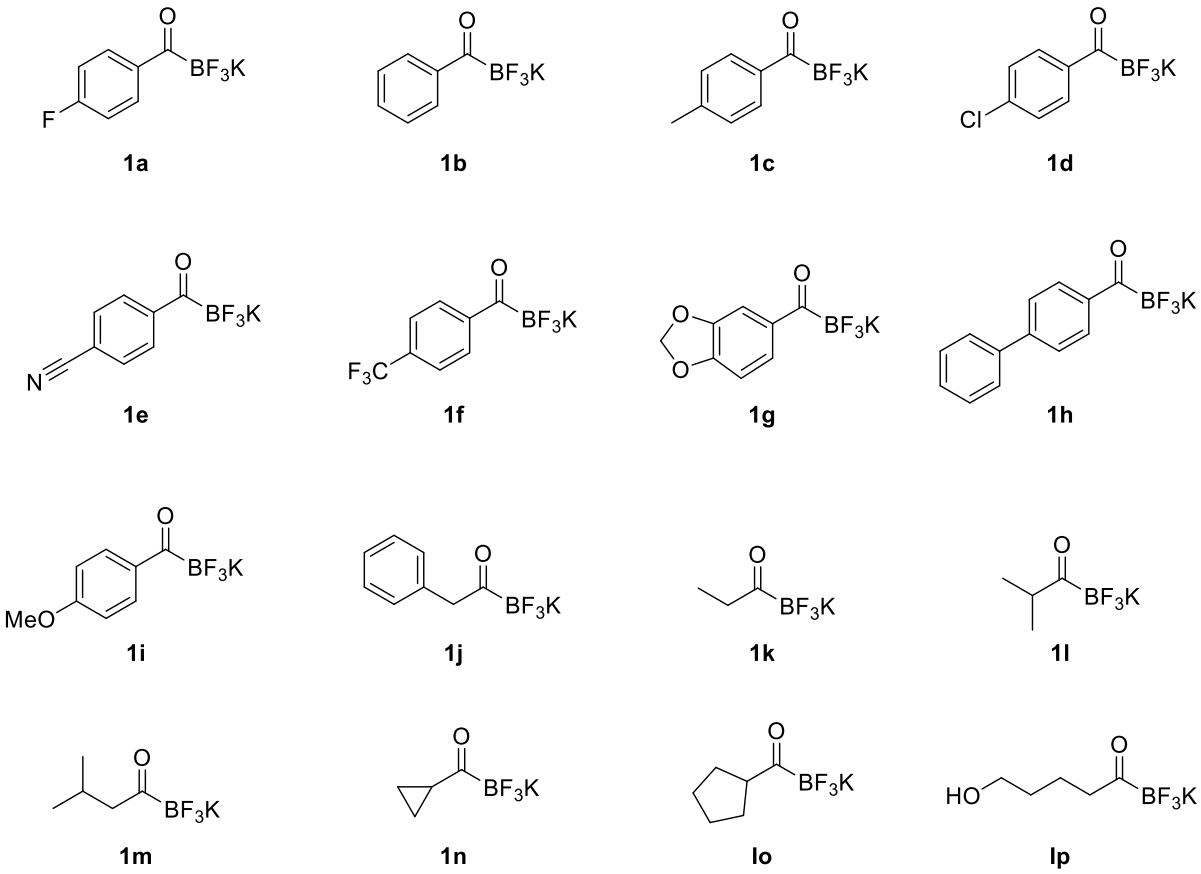
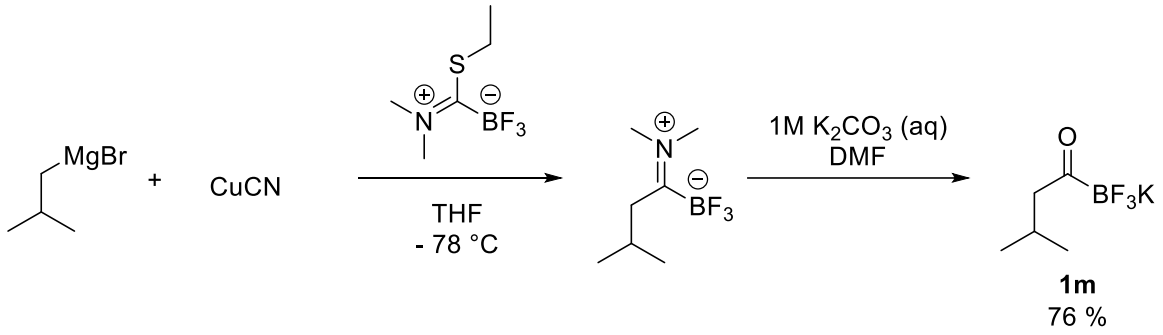


Figure S1. List of KATs used in this study.

Potassium (3-methylbutanoyl)trifluoroborate (1m)



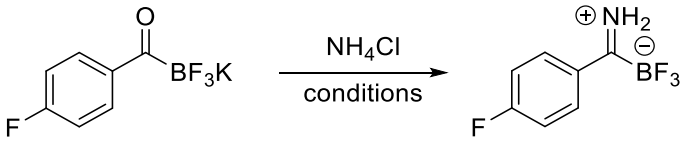
Scheme S1. Improved synthesis of **1m**.

Synthesized according to a modified literature procedure.[S2,S3] In an oven-dried flask under argon atmosphere, CuCN (394 mg, 4.4 mmol, 1.1 eq.) was suspended in dry THF (30 mL). The suspension was cooled on an ice bath and then *iso*-butyl magnesium bromide (2 M in Et_2O, 4.8 mL, 9.6 mmol, 2.4 eq.) was added. The reaction mixture, which turned grey shortly after the described addition, was stirred on ice bath for 1 h. Then, it was transferred into an acetone bath at – 80 °C and stirred for 10 minutes, followed by the addition of a solid (ethylthio-trifluoroborate)-methane dimethyliminium zwitterion in one portion. The reaction mixture was stirred at – 80 °C for 2 h, quenched with acetone (0.5 mL) and then the volatiles were removed under reduced pressure. The solids were suspended in EtOAc (100 mL), filtered and washed with EtOAc. The filtrate was evaporated under reduced pressure to afford the intermediate tertiary TIM ((1-(dimethyliminio)-3-methylbutyl)trifluoroborate) which was used directly in the next step without additional purification.

(1-(Dimethyliminio)-3-methylbutyl)trifluoroborate was dissolved in DMF (30 mL), to which 1 M K_2CO_3 (aq, 15 mL) was added. The reaction mixture was stirred for 2 h and then DMF and water were removed under reduced pressure. The dry residue was suspended in acetone, filtered and washed with acetone. The filtrate was concentrated under reduced pressure to cca. 2 mL then and Et_2O (20 mL) was added, upon which a white precipitate formed. The precipitate was filtered off and washed with Et_2O to afford pure **1m** as a white solid (584 mg, 76 % yield). The spectral data fully corresponded to those we published previously [S3] and are not reported here.

3. Preparation of Primary Trifluoroborate-Iminiums (pTIMs)

3.1. Reaction Optimization



1a **2a**

Scheme S2. Optimization of the synthesis of **2a**.

Table S1. Optimization of the synthesis of pTIM **2a**.

Entry	NH_4Cl [eq]	Solvent	Concentration	T [°C]	Time [h]	Conversion [%][a]
1	2	MeCN	0.2 M	RT	1; 20	0; 0
2	2	DMF	0.2 M	RT	1; 20	0; 0
3	2	DMF	0.2 M	60	1; 20	0; 0
4	2	MeOH	0.2 M	RT	1; 3; 20	16; 21; 38
5	2	MeOH	0.05 M	RT	1; 3; 20	14; 32; 62
6	2	MeOH	0.2 M	40	1; 3; 5; 7; 20	40; 69; 84; 90; 100[b]
7	2	MeOH	0.05 M	40	1; 3; 20	35; 59; 100[b]
8	1	MeOH	0.05 M	40	1; 3; 20	33; 55; 100[b]
9	5	MeOH	0.05 M	40	1; 3; 4	71; 94; 100 [88][c]
10[d]	5	MeOH	0.08 M	40	1; 3; 4	69; 93; 100 [94][c]

Reactions were performed with 0.2 mmol (46 mg) of starting material **1a** in an oven-dried flask equipped with 3 Å molecular sieves (100 mg) under argon atmosphere. [a]: Conversion determined by ^1H and ^{19}F NMR analysis, conversions at time points set in the Time column are separated by semicolons. [b]: Unidentified side product observed in ^1H NMR spectra in 5-10%. [c]: Isolated yield. [d]: No molecular sieves used, larger scale (764 mg of **1a**).

The model substrate **1a** was chosen for its favorable properties that allowed us to trace the reaction by TLC and ^{19}F NMR in addition to ^1H NMR, and also because of its ready synthetic availability. The reaction in MeCN and DMF (entries 1–3) gave no conversion, although these two solvents have been used for formation of secondary or tertiary TIMs.[S3, S6] However, when conducting the reaction in MeOH (entry 4), the formation of the desired product **2a** was observed in NMR spectra. By diluting to 0.05 M (entry 5) a higher conversion was reached, due to better solubility of NH_4Cl, and by heating the reaction mixture at 40 °C (entry 6), all starting material was consumed after 20 h. However, an

unidentified side product was observed in both cases in 5-10% in NMR spectra after 20 h. Setting the concentration at 0.05 M and temperature at 40 °C (entry 7) also gave full conversion in 20 h but still the side product was formed. Then, the effect of different quantities of NH_4Cl was studied. Performing the reaction with 1 eq of NH_4Cl led to similar conversions as with 2 eq (compare entry 8 vs. entry 7). By increasing the quantity of NH_4Cl to 5 eq, full conversion was reached already in 4 h and the reaction proceeded in a fully chemoselective fashion with no discernible side products in ^{1}H and ^{19}F NMR spectra.

Due to the full and clean conversion of the starting material, the isolation of the product was achieved in a very simple fashion. First, the solvent was evaporated under reduced pressure, the dry residue was suspended in EtOAc, and then followed by filtration and evaporation of the filtrate to afford the desired product **2a** in 88% isolated yield. However, we considered this yield unsatisfactory with regard to the 100% NMR yield and straightforward isolation procedure. We hypothesized that the molecular sieves bind the product to some extent, so a reaction without molecular sieves was performed on a larger scale and at a slightly higher concentration (entry 10). Gratifyingly, the reaction proceeded similarly as with sieves (entry 9), also giving full conversion after 4 h and affording the product **2a** in an excellent isolated yield of 94%.

3.2. General Procedure for the Synthesis of pTIMs

In an oven-dried flask under argon atmosphere, KAT **1** (1 eq) and NH_4Cl (5 eq) were dissolved in dry MeOH (0.08 M) and stirred at 40 °C. The conversion of starting material was followed by ^{1}H NMR. The reaction was typically complete in 3-4 h for aromatic substrates and 1 h for aliphatic substrates. When all starting material had been consumed, the solvent was evaporated under reduced pressure and dry residue was suspended in EtOAc. The suspension was filtered, washed with EtOAc, and the filtrate was evaporated under reduced pressure to afford pTIM **2** which required no additional purification.

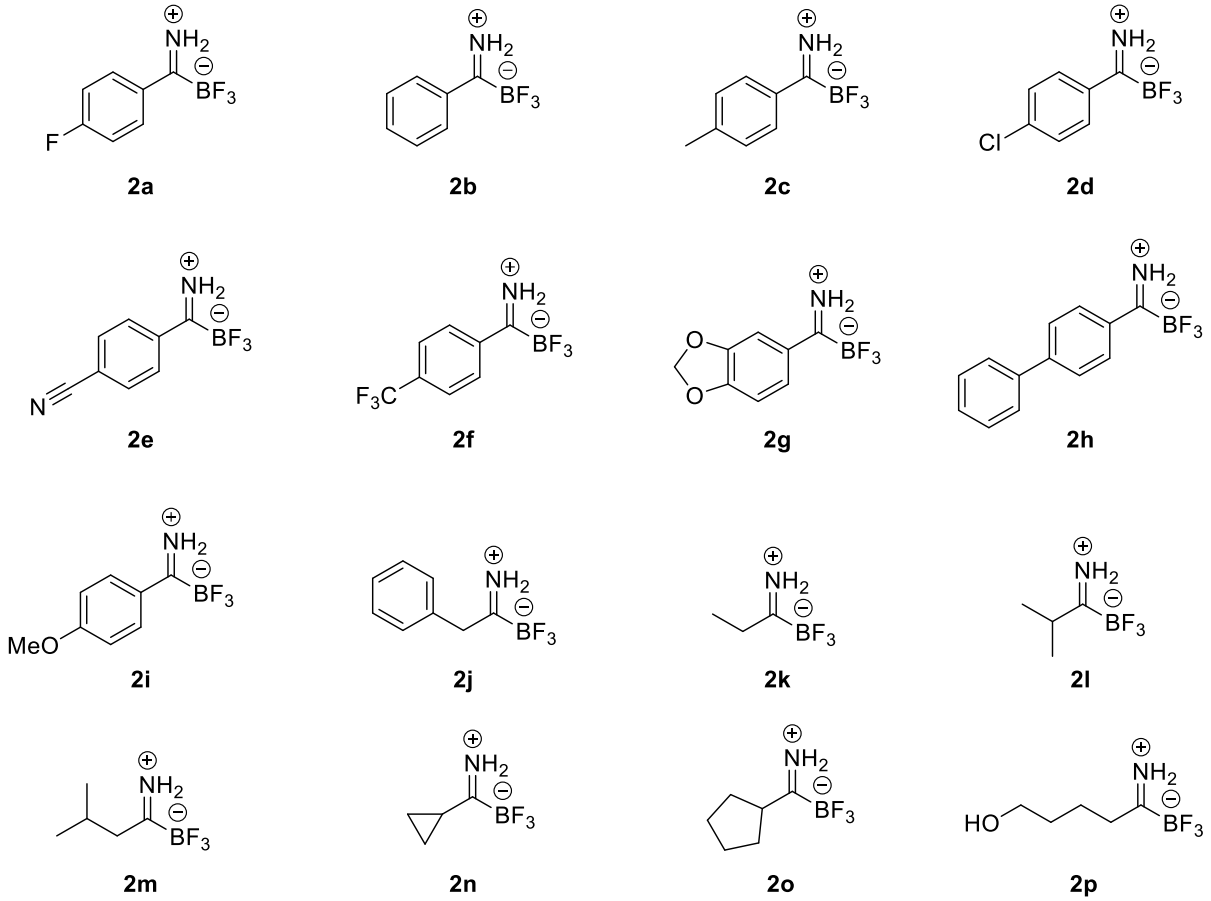
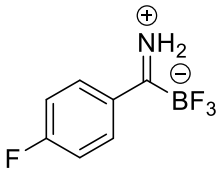


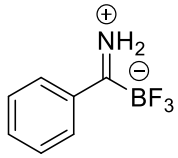
Figure S2. List of synthesized pTIMs.

((4-Fluorophenyl)(iminio)methyl)trifluoroborate (2a)



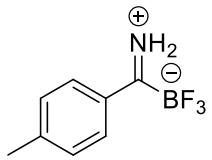
Synthesized from **1a** (764 mg, 3.32 mmol) and NH_4Cl (888 mg, 16.6 mmol) according to the General Procedure to afford **2a** as a white crystalline solid (596 mg, 94% yield). **m.p.** > 147 °C (decomp.) **^{1}H NMR** (400 MHz, Acetone-d_6) δ 7.38 – 7.45 (m, 2H, Ar-H), 8.31 – 8.37 (m, 2H, Ar-H), 10.68 (1:1:1 br t, J = 63 Hz, 1H, NH_{2a}), 11.06 (1:1:1 br t, J = 62 Hz, 1H, NH_{2b}). **^{11}B NMR** (128 MHz, Acetone-d_6) δ 0.03 (q, J = 39.0 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 117.17 (d, $^2J_{CF}$ = 22.4 Hz), 130.02, 134.48 (d, $^3J_{CF}$ = 10.0 Hz), 167.63 (d, $^1J_{CF}$ = 255.9 Hz), 205 (br m, extracted from ^{1}H-^{13}C *gs*-HMBC spectrum). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -145.75 (dd, J = 78.0, 38.5 Hz), -103.60. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 793, 851, 887, 955, 1001, 1514, 1601, 1668, 3241, 3368. **HRMS** (ESI^-): calc. for $C_7H_5NBF_4$ $[M-H]^-$: 190.0457, found: 190.0451.

(Iminio(phenyl)methyl)trifluoroborate (2b)



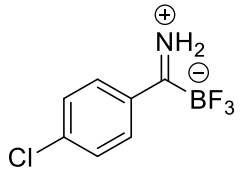
Synthesized from **1b** (107 mg, 0.505 mmol) and NH_4Cl (135 mg, 2.52 mmol) according to the General Procedure to afford **2b** as a white crystalline solid (84 mg, 96% yield). **m.p.** > 135 °C (decomp.) **^{1}H NMR** (400 MHz, Acetone-d_6) δ 7.60 – 7.66 (m, 2H, Ar-H), 7.72 – 7.79 (m, 1H, Ar-H), 8.20 – 8.25 (m, 2H, Ar-H), 10.26 – 11.30 (br m, 2H, NH_2^+). **^{11}B NMR** (128 MHz, Acetone-d_6) δ 0.07 (q, J = 39.1 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 129.95, 131.07, 133.61, 135.85, 205 (br m, extracted from ^{1}H-^{13}C *gs*-HMBC spectrum). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -145.88 (dd, J = 78.0, 38.9 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 742, 837, 890, 1035, 1450, 1598, 1665, 3242, 3368. **HRMS** (ESI$^-$): calc. for $C_7H_6NBF_3$ $[M-H]^-$: 172.0551, found: 172.0541.

(Iminio(*p*-tolyl)methyl)trifluoroborate (2c)



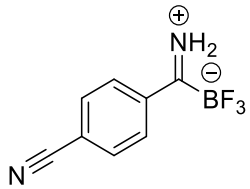
Synthesized from **1c** (405 mg, 1.79 mmol) and NH_4Cl (480 mg, 8.98 mmol) according to the General Procedure to afford **2c** as a white crystalline solid (302 mg, 90% yield). **m.p.** > 150 °C (decomp.) **^{1}H NMR** (400 MHz, Acetone-d_6) δ 2.45 (s, 3H, CH_3), 7.44 (d, J = 8.0 Hz, 2H, Ar-H), 8.17 – 8.12 (m, 2H, Ar-H), 10.14 – 11.18 (br m, 2H, NH_2^+). **^{11}B NMR** (128 MHz, Acetone-d_6) δ 0.10 (q, J = 39.5 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 21.76, 130.63, 130.70, 131.40, 147.48, 207 (br m, extracted from ^{1}H-^{13}C *gs*-HMBC spectrum). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -145.62 (dd, J = 78.8, 39.2 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 777, 847, 881, 955, 1002, 1035, 1609, 1654, 3243, 3333, 3376. **HRMS** (ESI$^-$): calc. for $C_8H_8NBF_3$ $[M-H]^-$: 186.0707, found: 186.0698.

((4-Chlorophenyl)(iminio)methyl)trifluoroborate (2d)



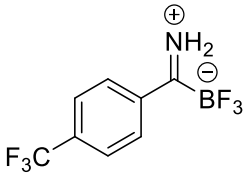
Synthesized from **1d** (874 mg, 3.55 mmol) and NH_4Cl (948 mg, 17.7 mmol) according to the General Procedure to afford **2d** as a white crystalline solid (711 mg, 97% yield). **m.p.** > 145 °C (decomp.) **^{1}H NMR** (400 MHz, Acetone-d_6) δ 7.67 – 7.74 (m, 2H, Ar-H), 8.21 – 8.28 (m, 2H, Ar-H), 10.52 – 11.44 (br m, 2H, NH_2^+). **^{11}B NMR** (128 MHz, Acetone-d_6) δ -0.01 (q, J = 38.8 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 130.22, 132.20, 132.84, 141.71, 206 (br m, extracted from ^{1}H-^{13}C *gs*-HMBC spectrum). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -145.99 (dd, J = 77.3, 38.3 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 919, 984, 1028, 1682, 2963, 3253, 3362. **HRMS** (ESI$^-$): calc. for $C_7H_5NBClF_3$ [M-H]$^-$: 206.0161, found: 240.0154.

((4-Cyanophenyl)(iminio)methyl)trifluoroborate (2e)



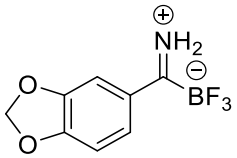
Synthesized from **1e** (948 mg, 4.0 mmol) and NH_4Cl (1070 mg, 20.0 mmol) according to the General Procedure to afford **2e** as a white crystalline solid (730 mg, 92% yield). **m.p.** > 153 °C (decomp.) **^{1}H NMR** (400 MHz, Acetone-d_6) δ 8.02 – 8.07 (m, 2H, Ar-H), 8.29 – 8.34 (m, 2H, Ar-H), 10.60 – 11.77 (br m, 2H, NH_2^+). **^{11}B NMR** (128 MHz, Acetone-d_6) δ -0.07 (q, J = 38.1 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 118.13, 118.38, 131.21, 133.61, 137.61, 207 (br m, extracted from ^{1}H-^{13}C *gs*-HMBC spectrum). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -146.38 (dd, J = 76.1, 37.7 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 541, 846, 1008, 1074, 1125, 1610, 1665, 2239, 3059, 3257, 3376. **HRMS** (ESI$^-$): calc. for $C_8H_5N_2BF_3$ [M-H]$^-$: 197.0503, found: 197.0496.

(Iminio(4-(trifluoromethyl)phenyl)methyl)trifluoroborate (2f)



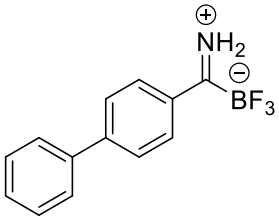
Synthesized from **1f** (250 mg, 0.89 mmol) and NH_4Cl (239 mg, 4.46 mmol) according to the General Procedure to afford **2f** as a white crystalline solid (209 mg, 97% yield). **m.p.** > 147 °C (decomp.) **^{1}H NMR** (400 MHz, Acetone-d_6) δ 7.99 (d, *J* = 8.2 Hz, 2H, Ar-H), 8.37 (d, *J* = 8.2 Hz, 2H, Ar-H), 10.72 – 11.75 (m, 2H, NH_2^+). **^{11}B NMR** (128 MHz, Acetone-d_6) δ -0.04 (q, *J* = 38.2 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 124.63 (q, $^1J_{CF}$ = 272.0 Hz), 126.82 (q, $^3J_{CF}$ = 4.1 Hz), 131.44, 135.57 (q, $^2J_{CF}$ = 32.8 Hz), 137.43, 206 (br m, extracted from ^{1}H-^{13}C *gs*-HMBC spectrum). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -146.51 (dd, *J* = 76.3, 38.0 Hz), -63.90. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 769, 842, 895, 966, 1004, 1136, 1171, 1320, 1672, 3238, 3366. **HRMS** (ESI$^-$): calc. for $C_8H_5NBF_6$ $[M-H]^-$: 240.0425, found: 240.0419.

(Benzo[*d*][1,3]dioxol-5-yl(iminio)methyl)trifluoroborate (2g)



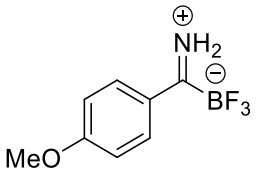
Synthesized from **1g** (110 mg, 0.43 mmol) and NH_4Cl (115 mg, 2.15 mmol) according to the General Procedure to afford **2g** as a white crystalline solid (91 mg, 98% yield). **m.p.** > 151 °C (decomp.) **^{1}H NMR** (400 MHz, Acetone-d_6) δ 6.21 (s, 2H, CH_2), 7.09 (d, *J* = 8.3 Hz, 1H, Ar-H), 7.70 (d, *J* = 1.8 Hz, 1H, Ar-H), 7.99 (dd, *J* = 8.3, 1.9 Hz, 1H, Ar-H), 9.99 – 10.88 (br m, 2H, NH_2^+). **^{11}B NMR** (128 MHz, Acetone-d_6) δ 0.06 (q, *J* = 39.1, Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 103.68, 108.72, 109.42, 127.14, 130.88, 149.59, 154.90, 231 (br m, extracted from ^{1}H-^{13}C *gs*-HMBC spectrum). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -145.25 (dd, *J* = 78.5, 38.9 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 816, 857, 924, 940, 994, 1020, 1067, 1247, 1449, 1492, 1503, 3259, 3394. **HRMS** (ESI$^-$): calc. for $C_8H_6O_2NBF_3$ $[M-H]^-$: 216.0449, found: 216.0443.

([1,1'-Biphenyl]-4-yl(iminio)methyl)trifluoroborate (2h)



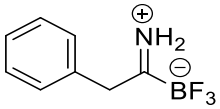
Synthesized from **1h** (630 mg, 2.19 mmol) and NH_4Cl (585 mg, 10.93 mmol) according to the General Procedure to afford **2h** as a white crystalline solid (524 mg, 96% yield). **m.p.** > 175 °C (decomp.) **^{1}H NMR** (400 MHz, Acetone-d_6) δ 7.44 – 7.49 (m, 1H, Ar-H), 7.50 – 7.56 (m, 2H, Ar-H), 7.77 – 7.83 (m, 2H, Ar-H), 7.91 – 7.96 (m, 2H, Ar-H), 8.31 – 8.37 (m, 2H, Ar-H), 10.36 – 11.29 (br m, 2H, NH_2^+). **^{11}B NMR** (128 MHz, Acetone-d_6) δ 0.12 (q, J = 39.4 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 128.13, 128.28, 129.65, 130.01 (2C), 132.00, 140.05, 148.19. Quaternary BF_3-bound carbon suppressed and could not be obtained even by ^{1}H-^{13}C *gs*-HMBC experiment. **^{19}F NMR** (376 MHz, Acetone-d_6) δ -145.77 (dd, J = 78.3, 38.3 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 745, 843, 855, 880, 1019, 1487, 1504, 1600, 1653, 3063, 3239, 3366. **HRMS** (ESI$^-$): calc. for $C_{13}H_{10}NBF_3$ $[M\text{-}H]^-$: 248.0864, found: 248.0860.

(Iminio(4-methoxyphenyl)methyl)trifluoroborate (2i)



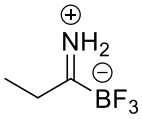
Synthesized from **1i** (1029 mg, 4.25 mmol) and NH_4Cl (1137 mg, 21.25 mmol) according to the General Procedure to afford **2i** as a white crystalline solid (812 mg, 94% yield). **m.p.** > 149 °C (decomp.) **^{1}H NMR** (400 MHz, Acetone-d_6) δ 3.94 (s, 3H, CH_3), 7.12 – 7.17 (m, 2H, Ar-H), 8.26 – 8.30 (m, 2H, Ar-H), 10.18 (1:1:1 br t, J = 65 Hz, 1H, NH_2^+), 10.63 (1:1:1 br t, 1H, J = 60 Hz, NH_2^+). **^{11}B NMR** (128 MHz, Acetone-d_6) δ 0.15 (q, J = 40.0 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 56.25, 115.37, 125.47, 134.29, 166.46, 204 (br m, extracted from ^{1}H-^{13}C *gs*-HMBC spectrum). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -145.23 (dd, J = 79.3, 39.0 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 844, 945, 1003, 1037, 1154, 1194, 1271, 1311, 1434, 1518, 1603, 1639, 3257, 3385. **HRMS** (ESI$^-$): calc. for $C_8H_8ONBF_3$ $[M\text{-}H]^-$: 202.0657, found: 202.0652.

(1-Iminio-2-phenylethyl)trifluoroborate (2j)



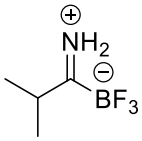
Synthesized from **1j** (1000 mg, 4.42 mmol) and NH_4Cl (1184 mg, 22.1 mmol) according to the General Procedure to afford **2j** as a pale yellow crystalline solid (817 mg, 99% yield). **m.p.** > 143 °C (decomp.) **^{1}H NMR** (400 MHz, Acetone-d_6) δ 4.13 (s, 2H, C$\underline{H}_2$), 7.25 – 7.46 (m, 5H, Ar-$\underline{H}$), 10.28 (1:1:1 br t, J = 63Hz, 1H, N$\underline{H}_{2a}^+$), 10.87 (1:1:1 br t, J = 64 Hz, 1H, N$\underline{H}_{2b}^+$). **^{11}B NMR** (128 MHz, Acetone-d_6) δ -0.48 (q, J = 36.6 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 43.33, 128.62, 129.96, 131.03, 132.99, 220.86 (br m). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -150.94 (dd, J = 77.5, 38.8 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 765, 836, 886, 923, 945, 1020, 1366, 1678, 3254, 3359. **HRMS** (ESI$^-$): calc. for $C_8H_8NBF_3$ [M-H]$^-$: 186.0707, found: 186.0701.

(1-Iminiopropyl)trifluoroborate (2k)



Synthesized from **1k** (294 mg, 1.79 mmol) and NH_4Cl (480 mg, 8.96 mmol) according to the General Procedure to afford **2k** as an off-white crystalline solid (218 mg, 97% yield). **m.p.** = 72 – 73 °C. **^{1}H NMR** (400 MHz, Acetone-d_6) δ 1.23 (t, J = 7.4 Hz, 3H, C$\underline{H}_3$), 2.78 (q, J = 7.7 Hz, 2H, C$\underline{H}_2$), 10.43 – 10.90 (br m, 2H, N$\underline{H}_2^+$). **^{11}B NMR** (128 MHz, Acetone-d_6) δ -0.59 (q, J = 39.4 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 8.81, 30.99, 223.68 (br m). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -151.19 (dd, J = 79.2, 39.3 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 996, 1189, 1420, 3216, 3321. **HRMS** (ESI$^-$): calc. for $C_3H_6NBF_3$ [M-H]$^-$: 124.0551, found: 124.0536.

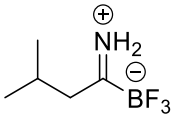
(1-Iminio-2-methylpropyl)trifluoroborate (2l)



Synthesized from **1l** (454 mg, 2.55 mmol) and NH_4Cl (682 mg, 12.75 mmol) according to the General Procedure to afford **2l** as an off-white crystalline solid (346 mg, 97% yield). **m.p.** = 117 – 119 °C. **^{1}H NMR** (400 MHz, Acetone-d_6) δ 1.26 (d, J = 6.9 Hz, 6H, (C$\underline{H}_3$)$_2$), 2.93 – 3.15 (m, 1H, C$\underline{H}$), 10.61 (1:1:1 br t, J = 65 Hz, 2H, N$\underline{H}_2^+$). **^{11}B NMR** (128 MHz, Acetone-d_6) δ -0.48 (q, J = 40.0 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 18.61, 37.17, 225.74 (br m). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -148.56 (dd, J = 80.1, 39.8

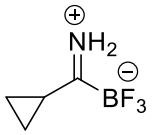
Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 795, 816, 925, 941, 996, 1020, 1066, 1248, 1449, 1492, 1503, 3260, 3395. **HRMS** (ESI$^-$): calc. for $C_4H_8NBF_3$ [M-H]$^-$: 138.0707, found: 138.0699.

(1-Iminio-3-methylbutyl)trifluoroborate (2m)



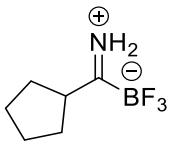
Synthesized from **1m** (388 mg, 2.02 mmol) and NH_4Cl (540 mg, 10.1 mmol) according to the General Procedure to afford **2m** as a white crystalline solid (302 mg, 98% yield). **m.p.** = 73 – 75 °C. **^{1}H NMR** (400 MHz, Acetone-d_6) δ 0.95 (d, J = 6.6 Hz, 6H, (C$\underline{H}_3$)$_2$), 2.42 (dh, J = 13.6, 6.5 Hz, 1H, C$\underline{H}$), 2.58 (d, J = 5.8 Hz, 2H, C$\underline{H}_2$), 10.33 – 11.24 (br m, 2H, N$\underline{H}_2^+$). **^{11}B NMR** (128 MHz, Acetone-d_6) δ -0.64 (q, J = 41.3 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 22.98, 26.02, 47.46, 224 (br m, extracted from ^{1}H-^{13}C *gs*-HMBC spectrum). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -150.75 (dd, J = 79.1, 39.4 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 840, 885, 901, 924, 972, 1042, 1669, 3265, 3358, 3388. **HRMS** (ESI$^-$): calc. for $C_5H_{10}NBF_3$ [M-H]$^-$: 152.0864, found: 152.0853.

(Cyclopropyl(iminio)methyl)trifluoroborate (2n)



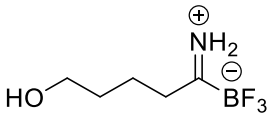
Synthesized from **1n** (121 mg, 0.69 mmol) and NH_4Cl (185 mg, 3.46 mmol) according to the General Procedure to afford **2n** as an off-white crystalline solid (90 mg, 96% yield). **m.p.** = 106 – 107 °C. **^{1}H NMR** (400 MHz, Acetone-d_6) δ 1.24 – 1.37 (m, 2H, C$\underline{H}_2$), 1.63 – 1.71 (m, 2H, C$\underline{H}_2$), 2.06 – 2.13 (m, 1H, C$\underline{H}$, partially concealed under residual NMR-solvent signal), 10.06 (1:1:1 br t, J = 67 Hz, 1H, N$\underline{H}_{2a}^+$), 10.69 (1:1:1 br t, J = 63 Hz, 1H, N$\underline{H}_{2b}^+$). **^{11}B NMR** (128 MHz, Acetone-d_6) δ -0.79 (q, J = 40.0 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 12.42, 12.45, 21.26, 220.09 (br m). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -148.09 (dd, J = 80.3, 39.8 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 858, 934, 1031, 1081, 1383, 1649, 3252, 3388. **HRMS** (ESI$^-$): calc. for $C_4H_6NBF_3$ [M-H]$^-$: 136.0551, found: 136.0538.

(Cyclopentyl(iminio)methyl)trifluoroborate (2o)



Synthesized from **1o** (491 mg, 2.41 mmol) and NH_4Cl (644 mg, 12.03 mmol) according to the General Procedure to afford **2o** as a white crystalline solid (376 mg, 95% yield). **m.p.** = 125 – 126 °C. **^{1}H NMR** (400 MHz, Acetone-d_6) δ 1.60 – 1.71 (m, 2H, C$\underline{H}_2$), 1.73 – 1.83 (m, 2H, C$\underline{H}_2$), 1.86 – 1.98 (m, 4H, C$\underline{H}_2$), 3.05 – 3.17 (m, 1H, C$\underline{H}$), 10.31 – 10.81 (br m, 2H, N$\underline{H}_2^+$). **^{11}B NMR** (128 MHz, Acetone-d_6) δ -0.48 (q, J = 40.2 Hz). **^{13}C NMR** (101 MHz, Acetone) δ 26.48, 30.37, 48.77, 224.06 (br m). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -148.01 (dd, J = 80.3, 39.8 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 919, 984, 1028, 1682, 2963, 3253, 3362. **HRMS** (ESI$^-$): calc. for $C_6H_{10}NBF_3$ [M-H]$^-$: 164.0864, found: 164.0853.

(5-Hydroxy-1-iminiopentyl)trifluoroborate (2p)



Synthesized from **1p** (1167 mg, 5.61 mmol) and NH_4Cl (1501 mg, 28.05 mmol) according to the General Procedure to afford **2p** as a white crystalline solid (902 mg, 95% yield). **m.p.** = 55 – 56 °C. **^{1}H NMR** (400 MHz, Acetone-d_6) δ 1.53 – 1.64 (m, 2H, C$\underline{H}_2$), 1.79 (p, J = 7.5 Hz, 2H, C$\underline{H}_2$), 2.76 (t, J = 7.7 Hz, 2H, C$\underline{H}_2$), 3.58 (t, J = 6.3 Hz, 2H, C$\underline{H}_2$), 3.70 (s, 1H, O$\underline{H}$), 10.31 – 11.07 (br m, 2H, N$\underline{H}_2^+$). **^{11}B NMR** (128 MHz, Acetone-d_6) δ =-0.60 (q, J = 39.7 Hz). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 21.86, 32.93, 37.65, 61.78, 223.16 (br m). **^{19}F NMR** (376 MHz, Acetone-d_6) δ -150.97 (dd, J = 79.2, 39.2 Hz). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 930, 947, 1042, 1686, 2887, 2947, 3062, 3319, 3550. **HRMS** (ESI$^-$): calc. for $C_5H_{10}ONBF_3$ [M-H]$^-$: 168.0813, found: 168.0803.

4. Preparation of Enantioenriched Primary Trifluoroborate Ammoniums (pTAMs)

4.1. Conditions Screening and Reaction Optimization

4.1.1. List of Catalysts, Catalyst Precursors and Ligands Used

Where the catalyst was prepared *in situ* (see Procedure B below), one of the following catalyst precursors was used: $[Ru(p\text{-cymene})Cl_2]_2$, $[Ru(cod)Cl_2]_n$, $[Ir(cod)Cl]_2$ or $[Rh(cod)Cl]_2$, where cod = cyclooctadiene.

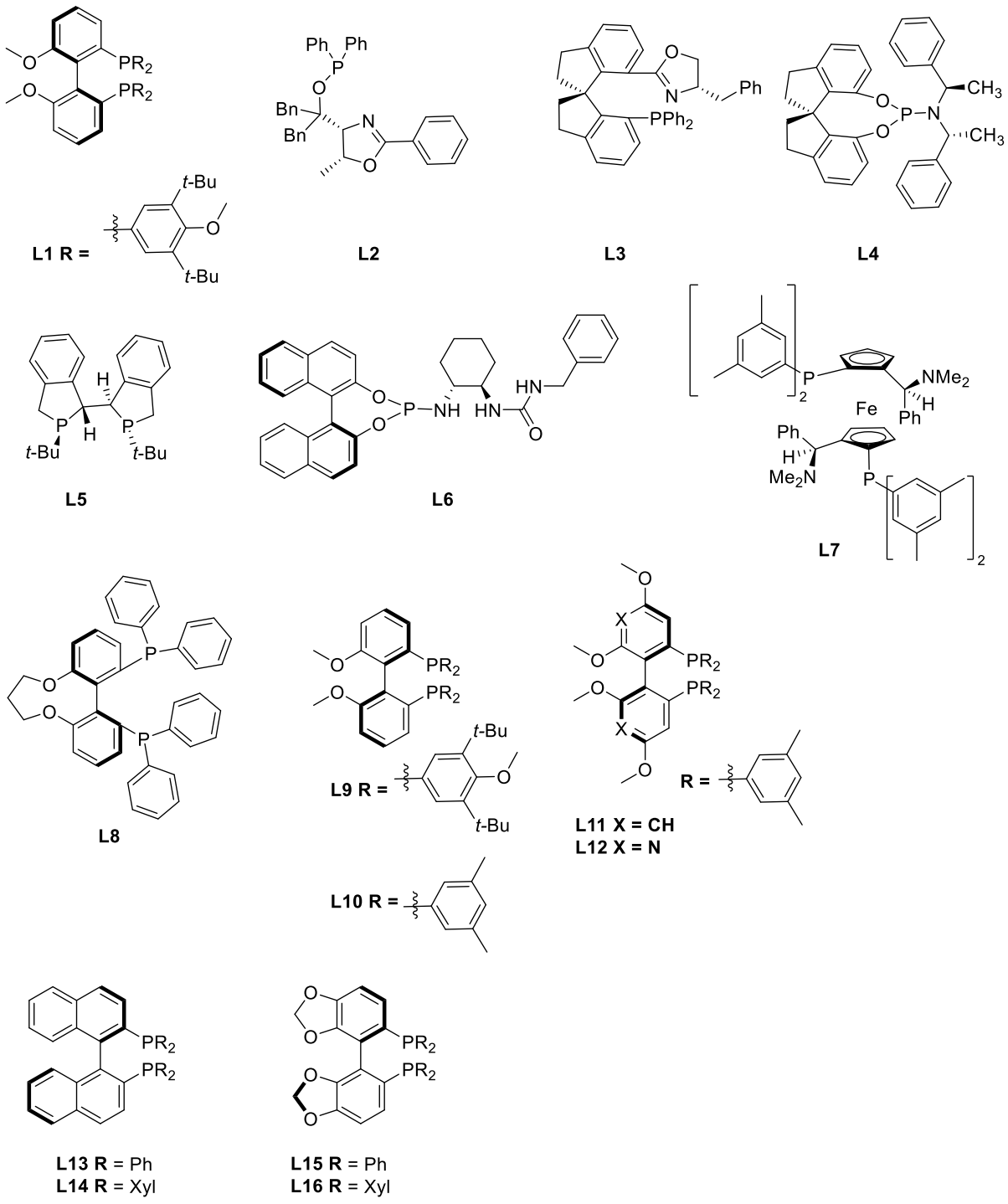


Figure S3. List of phosphine ligands used.

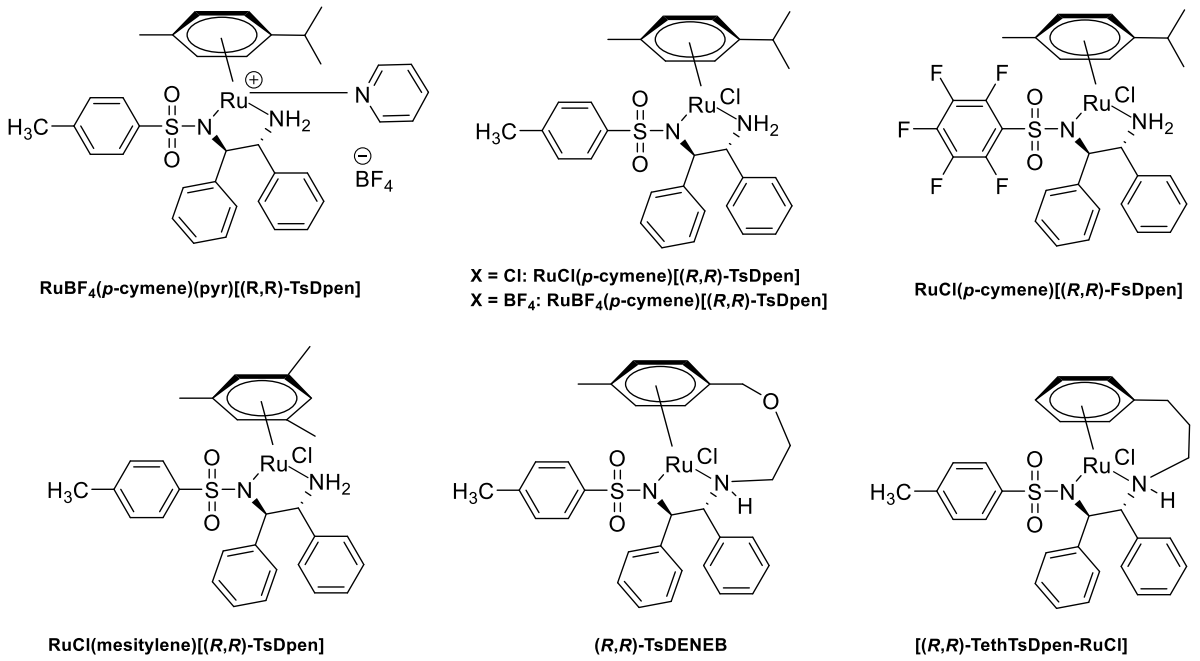
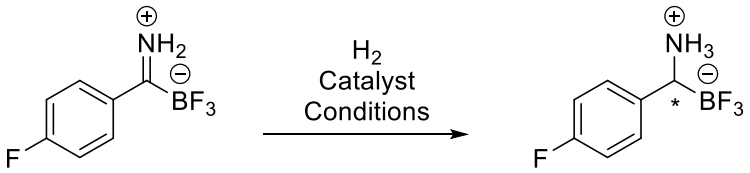


Figure S4. List of selected ruthenium catalysts used.

4.1.2. General Procedure for Reaction Optimization

Procedure A (pre-formed catalyst): In an oven-dried flask under argon atmosphere, catalyst (2 mol%) was dissolved in dry MeOH (2 mL). To this solution, **2a** (19 mg, 0.1 mmol) and the additive (if used) were added and the flask was transferred to a hydrogenation reactor. The reactor was purged with H_2 five times, after which the H_2 pressure was set to 20 bar and the reaction mixture was left to stir for 20 h. Then, the pressure was carefully released, the solvent evaporated under reduced pressure, and the crude dry residue was analyzed by NMR and HPLC.

Procedure B (*in situ* formation of catalyst): In an oven-dried flask under argon atmosphere, catalyst precursor (2 mol%, calculated based on the metal), and ligand (2 mol%) were dissolved in dry MeOH (2 mL). This mixture was left to stir for 10 min. The next steps closely followed Procedure A.



Scheme S3. Optimization of conditions for hydrogenation of **2a** to **3a**.

Table S2. Conversion and enantioselectivity outcomes for catalyst systems used in primary screening.

Entry	Catalyst	Additive	Procedure	Conversion	e.r.
1	[Ir(cod)]Cl/(*S*)-**L1**	*t*-BuOK	B	30 (**1a**)	n.a.
2	RuCl[(cod)]Cl/(*S*)-**L1**	*t*-BuOK	B	100 (decomp.)	n.a.

3	[Rh(cod)]Cl/(*S*)-**L1**	*t*-BuOK	B	28 (mostly **1a**)	n.a.
4	[Ir(cod)((*R*,*R*)-**L2**)BArF]	*t*-BuOK	A	30 (**1a**)	n.a.
5	RuCl[(*p*-cymene)]Cl/(*S*)-**L1**	*t*-BuOK	B	31 (**1a**)	n.a.
6	$RuBF_4$(*p*-cymene)(pyr)[(*R*,*R*)-TsDpen]	*t*-BuOK	A	27 (**1a**)	n.a.
7	[Ir(cod)]Cl/(*S*)-**L1**	/	B	0	n.a.
8	RuCl[(cod)Cl]/(*S*)-**L1**	/	B	0	n.a.
9	[Rh(cod)]Cl/(*S*)-**L1**	/	B	0	n.a.
10	[Ir(cod)((*R*,*R*)-**L2**)BArF]	/	A	0	n.a.
11	RuCl[(*p*-cymene)Cl]/(*S*)-**L1**	/	B	23 (100% **3a**)	50:50
12	$RuBF_4$(*p*-cymene)(pyr)[(*R*,*R*)-TsDpen]	/	A	89 (100% **3a**)	79:21

Since pTIMs have hitherto not been synthesized and no data were available regarding their stability and reactivity, a diverse range of catalysts was first assessed. In our previous study, secondary TIMs could only be hydrogenated with the addition of a strong base,[S3] therefore the same conditions were applied in the primary screening of pTIM hydrogenation (entries 1-6), namely 2 mol% catalyst and 1 eq of *t*-BuOK in MeOH. However, no formation of product occurred and only partial hydrolysis to parent KAT **1a** was observed, with the exception of RuCl[(cod)Cl]/(*S*)-**L1** (entry 2), where an unidentifiable mixture of decomposition products was obtained. These reactions were then repeated without the addition of *t*-BuOK (entries 7-12) and, gratifyingly, conversion to **3a** was observed when using RuCl[(*p*-cymene)Cl]/(*S*)-**L1** (entry 11) and $RuBF_4$(*p*-cymene)(pyr)[(*R*,*R*)-TsDpen] (entry 12). While the conversion was not full, the reaction appeared to proceed chemoselectively as no other peaks were observed in ^{1}H and ^{19}F NMR spectra. It appeared from these experiments that pTIMs are more susceptible to base-mediated hydrolysis than their secondary counterparts, therefore a different catalytic system was required, *i.e*. a ruthenium catalyst without any additives as opposed to an [Ir(cod)Cl]-based catalyst with 1 eq of strong base.

Having established that only ruthenium catalysts (either based on $[Ru(p\text{-cymene})Cl_2]_2$ as catalyst precursor, or the Noyori-Ikariya-type catalysts) without the addition of base can catalyze the hydrogenation of **2a**, we conducted an extensive screening of various ruthenium catalysts (Table S3).

Table S3. Conversion and enantioselectivity outcomes for ruthenium catalysts.

Entry	Catalyst	Procedure	Conversion [%]	e.r.
1	$RuBF_4$(*p*-cymene)(pyr)[(*R*,*R*)-TsDpen]	A	89	79:21
2	RuCl[(*p*-cymene)Cl]/(*S*)-**L1**	B	23	50:50
3	RuCl[(*p*-cymene)Cl]/(*S,S*)-**L3**	B	17	50:50
4	RuCl[(*p*-cymene)Cl]/(*S,R,R*)-**L4**	B	0	n.a.
5	RuCl[(*p*-cymene)(Cl]/(1*R*,1'*R*,2*S*,2'*S)*-**L5**	B	0	n.a.

6	RuCl[(*p*-cymene)Cl]/(*S,R,R*)-**L6**	B	trace	n.a.
7	RuCl[(*p*-cymene)Cl]/(*S,S*)-**L7**	B	0	n.a.
8	RuCl[(*p*-cymene)Cl]/(*S*)-**L8**	B	8	48:52
9	RuCl[(*p*-cymene)Cl]/(*R*)-**L9**	B	11	50:50
10	RuCl[(*p*-cymene)Cl]/(*R*)-**L10**	B	13	50:50
11	RuCl[(*p*-cymene)Cl]/(*R*)-**L11**	B	0	n.a.
12	RuCl[(*p*-cymene)Cl]/(*R*)-**L12**	B	0	n.a.
13	RuCl[(*p*-cymene)((*R*)-**L13**)Cl]	A	0	n.a.
14	RuCl[(*p*-cymene)Cl]/(*R*)-**L15**	B	0	n.a.
15	$RuOAc_2$-(*R*)-**L13**	A	20	70:30
16	$RuOAc_2$-(*R*)-**L16**	A	17	71:29
17	$RuCl_2$-(*R*)-**L14**-(*R,R*)-Dpen	A	15	80:20
18	$RuCl_2$-(*R*)-**L16**-(*R,R*)-Dpen	A	15	82:18
19	RUCY®-(*R*)-**L14**	A	0	n.a.
20	$RuCl_2$-(*R*)-**L14**-(*R,R*)-Daipen	A	trace	n.a.
21	$RuCl_2$-(*R*)-**L16**-(*R,R*)-Daipen	A	7	n.a.
22	RuCl-(*R*)-**L13**-(*R,R*)-Diaminocyclohexane-BF_4	A	4	n.a.
23	RuCl-(*R*)-**L13**-(*R,R*)-Diaminocyclohexane-$B(C_6F_5)_4$	A	11	70:30
24	$RuCl_2$-(*R*)-**L13**-(*S*)-Me-BIMAH	A	15	83:17
25	[(RuCl-(*R*)-**L13**)$_2$(μ-Cl)$_3$][NH_2Me_2]	A	52	70:30
26	[(RuCl-(*R*)-**L14**)$_2$(μ-Cl)$_3$][NH_2Me_2]	A	31	77:23
27	[(RuCl-(*R*)-**L15**)$_2$(μ-Cl)$_3$][NH_2Me_2]	A	25	69:31
28	RuCl(*p*-cymene)[(*R,R*)-TsDpen]	A	81	89:11
29	$RuBF_4$(*p*-cymene)[(*R,R*)-TsDpen]	A	100	89:11
30	[(*R,R*)-TethTsDpen-RuCl]	A	100	97:3
31	[(*S,S*)-TethTsDpen-RuCl]	A	100	5.5:94.5
32	(*R,R*)-TsDENEB®	A	88	92:8
33	RuCl(*p*-cymene)[(*R,R*)-FsDpen]	A	36	91:9
34	RuCl(mesitylene)[(*R,R*)-TsDpen]	A	40	88:12
35	$RuBF_4$(*p*-cymene)(pyr)[(*R,R*)-TsDpen]	A; 50 bar, 20 h	100	77:23
36	[(RuCl-(*R*)-**L13**)$_2$(μ-Cl)$_3$][NH_2Me_2]	A; 50 bar, 20 h	93	65:35
37	$RuCl_2$-(*R*)-**L14**-(*R,R*)-Dpen	A; 50 bar, 20 h	19	77:23
38	RuCl[(*p*-cymene)Cl]/(*S,S*)-**L3**	B; 50 bar, 20 h	17	50:50
39	$RuOAc_2$-(*R*)-**L13**	A; 50 bar, 20 h	44	68:32
40	$RuBF_4$(*p*-cymene)(pyr)[(*R,R*)-TsDpen]	A; 20 bar, 44 h	100	80:20
41	RuCl(*p*-cymene)[(*R,R*)-TsDpen]	A; 20 bar, 44 h	100	88:12
42	[(RuCl-(*R*)-**L13**)$_2$(μ-Cl)$_3$][NH_2Me_2]	A; 20 bar, 44 h	100	71:29
43	$RuOAc_2$-(*R*)-**L13**	A; 20 bar, 44 h	74	71:29

The study of ruthenium catalysts revealed that Ru-(*p*-cymene)-phosphine ligand complexes showed very low activity and no enantioselectivity in the hydrogenation of our substrate (entries 2-14). The $RuOAc_2$-phosphine complexes showed limited enantioselecivity and also low conversions (entries 15, 16), while the RuCl-diphosphine-diamine complexes performed slightly better in terms of enantioselecivity, but with similarly meagre conversions (entries 17-24). The dimethylamine adducts of RuCl-phosphine complexes were slightly more active but gave low enantioselectivity (entries 25-

27). In contrast to the above-mentioned experiments, the best conversions were achieved with the Noyori-Ikariya and Wills-type catalysts, and importantly, the e.r. values were good to excellent (entries 28-34), but only in several cases full conversions were reached. Subsequent experiments with higher pressure (entries 35-39) and longer reaction time (entries 40-43) indeed improved the conversions in reactions with selected catalysts, however we observed slight erosion of enantioselectivity if a higher H_2 pressure was applied (compare for example entries 1, 35 and 40; also entries 25, 36 and 42).

Based on these results, [(*R,R*)-TethTsDpen-RuCl] (entry 30) was chosen as the best catalyst since it showed the best enantioselectivity (e.r. = 97:3) of all the catalysts that were evaluated. Because of the full conversion and remarkable chemoselectivity, the NMR yield was quantitative. Its (*S,S*)-enantiomer (entry 31) gave a comparable e.r. in favor of the opposite enantiomer of the product (e.r. = 5.5:94.5). Having chosen the best catalyst, a targeted screening of solvents, concentration and catalyst loading was undertaken (Table S4).

Table S4. Solvent screening. For each reaction [(*R,R*)-TethTsDpen-RuCl] (2 mol%) was used and reactions were performed following the General Procedure for Reaction Optimization with the difference that those using water (entries 6-15) were not set up under argon atmosphere.

Entry	Solvent	Concentration [M]	Cat. loading [mol%]	ε of solvent	Conversion [%]	e.r.
1	MeOH	0.05	2	32.7	100	97:3
2	EtOH	0.05	2	24.5	43	89:11
3	*i*-PrOH	0.05	2	17.9	5	n.a.
4	TFE	0.05	2	8.55	10	88:12
5	MeCN	0.05	2	37.5	0	n.a.
6	MeOH (1% H_2O)	0.05	2	/	100	96:4
7	MeOH (10% H_2O)	0.05	2	/	100	95:5
8	MeOH : H_2O = 1:1	0.05	2	/	100 (**3a**:**1a** = 9:1)	96:4
9	H_2O	0.05	2	80.1	73 (**3a**:**2a**:**1a** = 1:5:13)	n.a.
10	MeOH (2% H_2O)	0.05	2	/	100	97:3
11	MeOH (2% H_2O)	0.025	2	/	100	93:7
12	MeOH (2% H_2O)	0.1	2	/	100	97:3
13	MeOH (2% H_2O)	0.05	1	/	100	95.5:4.5
14	MeOH (2% H_2O)	0.05	0.5	/	82	91.5:8.5
15	MeOH (2% H_2O)	0.05	0.1	/	9	89:11

As demonstrated by Noyori et al.,[S7] highly polar solvents are preferred in hydrogenation with Noyori-Ikariya-type catalysts. Using some less polar alcohols as solvents, the conversions drastically decreased along with a noticeable erosion of enantioselectivity (entries 2-4). However, the use of MeCN, which

has a higher dielectric constant than MeOH, gave no conversion at all (entry 5). Prompted by the hypothesis of solvent polarity-enhanced reactivity, reactions with the addition of water were performed (entries 6-10). With 10% water in MeOH, the reaction proceeded in the same fashion as with dry MeOH and notably, no hydrolysis of **2a** was observed, although a primary iminium is expected to be sensitive to the presence of water – and indeed hydrolyzed in presence of *t*-BuOK (*vide supra*). Using a 1:1 (V/V) mixture of MeOH and water, a 9:1 mixture of **3a** and parent KAT **1a** (hydrolysis product) was obtained with no deterring influence on the enantioselectivity, while in pure water, hydrolysis was the dominant reaction and only 5% of **3a** was formed. There was no significant difference in enantioselectivity between 10%, 2% and 1% water (entries 6, 7 and 10), so further reactions were undertaken with 2% water to prevent any possible hydrolysis in other substrates. The high value of these three experiments is in showing that the reaction can be set up in air in an aqueous medium (as much as 10% water in MeOH), which is especially remarkable since the substrate combines two moieties which are potentially highly labile in water: trifluoroborate and primary iminium.

With the optimal solvent chosen, the effects of concentration on conversion and enantioselectivity were studied (entries 10-12). While the concentration did not affect the conversions, a slight erosion of enantioselectivity was observed when the reaction was conducted at 0.025 M concentration (entry 11), while no difference between 0.05 and 0.1 M (entry 12) was observed. Then, we endeavored to establish the lowest feasible catalyst loading: at 1 mol% catalyst the reaction still proceeded to completion (entry 13), while lower loadings gave incomplete conversions with noticeable decrease in enantioselecivity (entries 14 and 15).

As a result of this extensive optimization study, optimal conditions were determined to be as follows: 20 bar H_2, [(*R,R*)-TethTsDpen-RuCl] (2 mol%), MeOH containing 2% water at 0.1 M concentration, RT, 20 h. As no difference was observed when comparing 0.1 M and 0.05 M concentrations, 0.1 M was chosen to use less solvent.

To showcase the remarkable chemoselectivity of this hydrogenation, a crude ^{1}H NMR spectrum of **3a** is enclosed here, recorded directly after the solvent was removed under reduced pressure (Figure S5; note that a peak for reaction solvent MeOH is still visible at 3.35 ppm).

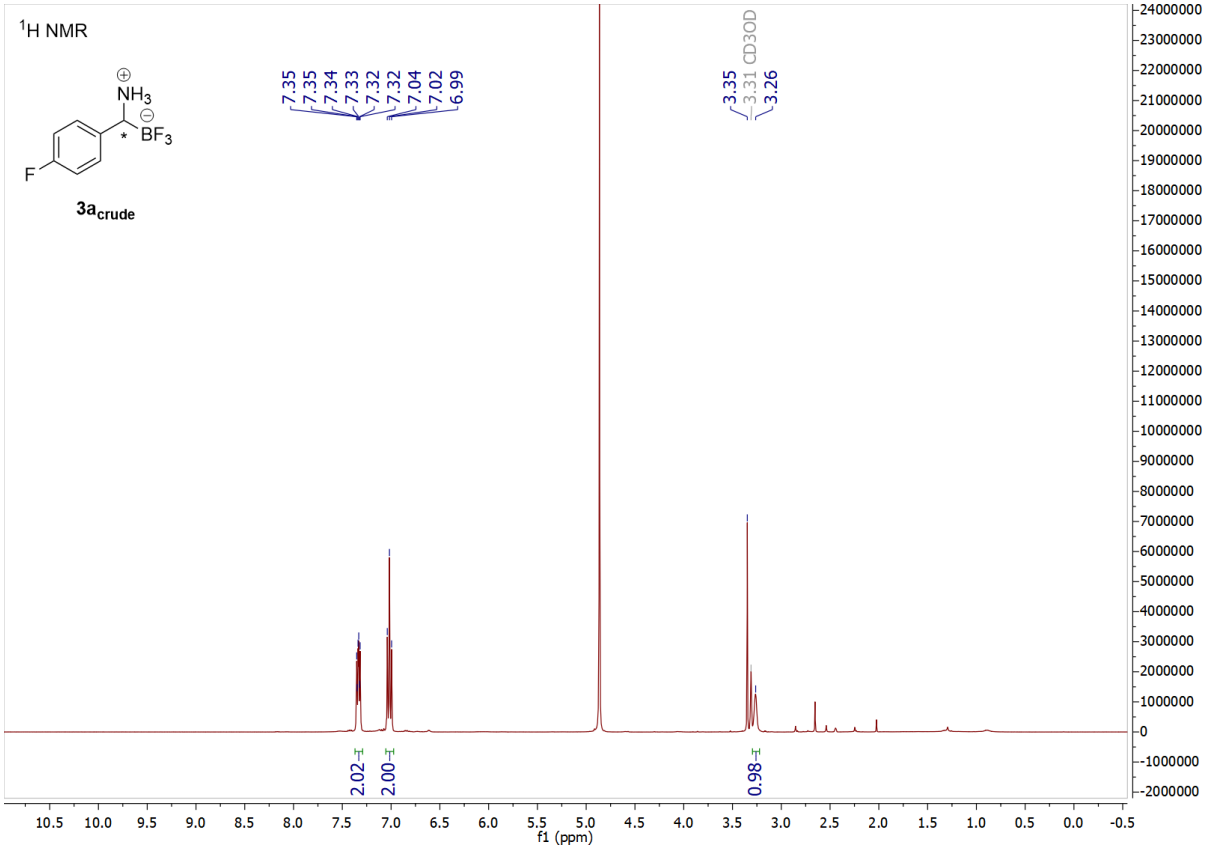
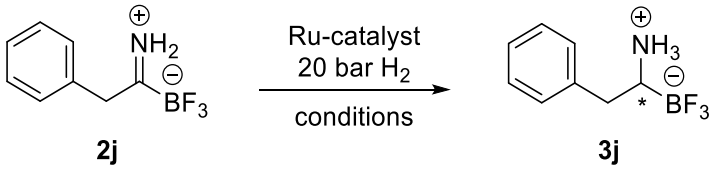


Figure S5. ^{1}H NMR spectrum of crude **3a** showing no apparent side product formation.

4.1.3. Reaction Optimization for Aliphatic Substrates

The hydrogenation of a model aliphatic substrate **2j** was undertaken under optimal conditions described above, but required some further optimization. (Table S5)



2j **3j**

Scheme S4. Optimization of conditions for hydrogenation of **2j** to **3j**.

Table S5. Reaction optimization for aliphatic substrate **2j**. Reactions performed at 0.1 M, 20 bar H_2, RT. [a]: signals too low for accurate integration; [b]: oven-dried glassware used, reaction set up under argon; [c]:additional peaks observed in HPLC, accurate integration of enantiomer peaks impossible.

Entry	Catalyst	Solvent	Time [h]	Conv. [%]	e.r.
1	[(*R,R*)-TethTsDpen-RuCl] 2%	MeOH (2% H_2O)	20	45	n.a.[a]
2[b]	[(*R,R*)-TethTsDpen-RuCl] 2%	MeOH (dry)	20	28	n.a.[a]
3	[(*R,R*)-TethTsDpen-RuCl] 2%	MeOH (2% H_2O)	72	90	94:6
4	[(*R,R*)-TethTsDpen-RuCl] 4%	MeOH (2% H_2O)	72	100	94:6
5	(*R,R*)-TsDENEB® 4%	MeOH (2% H_2O)	72	100	93:7
6	RuCl(*p*-cymene)[(*R,R*)-FsDpen] 4%	MeOH (2% H_2O)	72	30	n.a.[a]
7	RuCl(mesitylene)[(*R,R*)-TsDpen] 4%	MeOH (2% H_2O)	72	52	86:14
8	RuCl(*p*-cymene)[(*R,R*)-TsDpen] 4%	MeOH (2% H_2O)	72	93	88:12
9	$RuBF_4$(*p*-cymene)(pyr)[(*R,R*)-TsDpen] 4%	MeOH (2% H_2O)	72	100	n.a.[c]
10	$RuOAc_2$-(*R*)-**L13** 4%	MeOH (2% H_2O)	72	36	52:48

Under the same conditions that were optimal for hydrogenation of **2a** (entry 1), only 45% conversion was reached. Interestingly, a reaction performed in dry MeOH under anhydrous conditions gave an

even lower conversion of 28% (entry 2). For this reason, all reactions were performed with 2% water as previously established. With reaction time of 72 h, conversion was increased to 90% (entry 3), so to ensure full conversion in 72 h, the catalyst loading had to be increased to 4% (entry 4). Since the reactivity of **2j** was different than that of **2a**, we screened some other catalysts that showed promising results in hydrogenation of **2a** (entries 5-10). This targeted screening showed that [(*R,R*)-TethTsDpen-RuCl] 2% was the optimal catalyst also for this substrate, since the only other catalysts that gave full conversion were (*R,R*)-TsDENEB® (entry 5) and $RuBF_4$(*p*-cymene)(pyr)[(*R,R*)-TsDpen] (entry 9); the former with a slightly lower enantioselectivity, and the latter at the cost of side reactions.

This targeted optimization study revealed that aliphatic substrate **2j** required a higher catalyst loading (4 mol%) along with a longer reaction time (72 h). Although the reaction time was longer, no hydrolysis to parent KAT **1j** was observed. Since water did not affect the enantioselectivites but its presence was proven to improve the reaction rate in the case of **2j**, aqueous solvent was used for hydrogenation of all pTIMs.

4.2. Synthesis of pTAMs

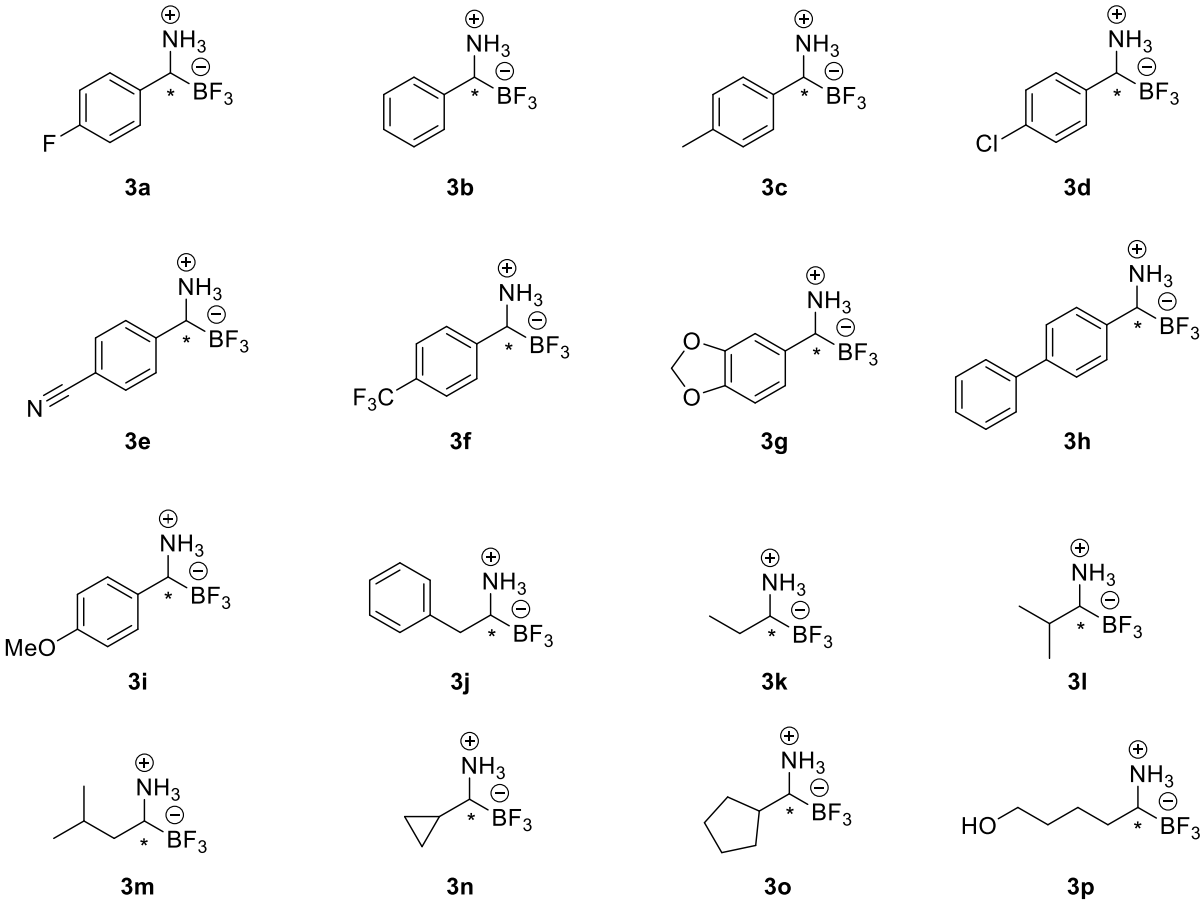


Figure S6. List of synthesized pTAMs.

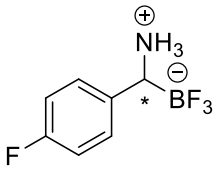
General procedure for the synthesis of aromatic pTAMs (3a – 3i)

pTIM **2** was dissolved in MeOH (containing 2 % V/V H_2O, 0.1 M unless stated otherwise) in a flask and [(*R,R*)-TethTsDpen-RuCl] (2 mol%) was added to the solution. No oven-dried glassware was used and the reaction was set up in air without flushing the flask with argon or nitrogen. The flask was transferred to a hydrogenation reactor. The reactor was purged with H_2 five times, after which the H_2 pressure was set to 20 bar and the reaction mixture was left to stir for 20 h. Then, the pressure was carefully released, the solvent evaporated under reduced pressure, and the crude dry residue was analyzed by NMR and HPLC to determine conversion and enantiomeric ratio. The crude product was suspended in CH_2Cl_2 (0.5 mL), filtered, and washed with *n*-hexane (2 × 5 mL) to afford the product which required no additional purification.

General procedure for the synthesis of aliphatic pTAMs (3j – 3p)

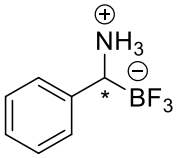
The reaction procedure followed the General procedure for aromatic pTAMs, apart from the catalyst loading (4 mol%) and reaction time (72 h). The crude product was suspended in CH_2Cl_2 (0.5 mL), filtered, and washed with CH_2Cl_2 (1 mL) and *n*-hexane (5 mL) to afford the product which required no additional purification.

(Ammonio(4-fluorophenyl)methyl)trifluoroborate (3a)



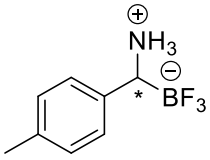
Synthesized according to the General Procedure from **2a** (57 mg, 0.3 mmol) to afford **3a** as a white solid (54 mg, 95% yield, 97:3 e.r.). **$[\alpha]_D^{24}$** -2.83 (*c* 0.05 M, MeOH). **m.p.** > 165 °C (decomp.) **^{1}H NMR** (400 MHz, MeOD) δ 3.25 (br s, 1H, C<u>H</u>), 6.97 – 7.06 (m, 2H, Ar-<u>H</u>), 7.28 – 7.38 (m, 2H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 2.56 (m). **^{13}C NMR** (101 MHz, MeOD) δ 50 (br m, extracted from ^{1}H-^{13}C HSQC spectrum), 115.71 (d, $^2J_{CF}$ = 21.3 Hz), 130.20 (d, $^3J_{CF}$ = 7.9 Hz), 137.58, 163.03 (d, $^1J_{CF}$ = 242.7 Hz). **^{19}F NMR** (376 MHz, MeOD) δ -151.67 (app. d, *J* = 76.1 Hz), -119.33 (m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 722, 830, 959, 1049, 1163, 1186, 1244, 1514, 1610, 3258. **HRMS** (ESI$^-$): calc. for $C_7H_7NBF_4$ [M-H]$^-$: 192.0613, found: 192.0606. **HPLC** Major enantiomer 11.0 min, minor enantiomer 12.0 min. Column: CHIRALPAK AD-H 250×4,6mm, 5 μm, T = 15 °C. Mobile phase: *n*-heptane/EtOH/methanesulfonic acid = 900/100/0.1 (V/V/V). Flow = 1.0 mL/min, injection volume = 10 μL.

(Ammonio(phenyl)methyl)trifluoroborate (3b)



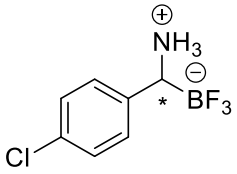
Synthesized according to the General Procedure from **2b** (52 mg, 0.3 mmol) to afford **3b** as a white solid (48 mg, 92% yield, e.r. = 93:7). **$[\alpha]_D^{24}$** -7.67 (*c* 0.01 M, MeOH). **m.p.** 161 – 162 °C. **^{1}H NMR** (400 MHz, MeOD) δ 3.29 (br s, 1H, C<u>H</u>), 7.16 – 7.23 (m, 1H, Ar-<u>H</u>), 7.26 – 7.34 (m, 4H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 2.66 (m). **^{13}C NMR** (101 MHz, MeOD) δ 51.18 (br m), 127.21, 128.08, 129.11, 141.53. **^{19}F NMR** (376 MHz, MeOD) δ -151.25 (m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 755, 954, 1038, 1482, 1599, 3252. **HRMS** (ESI$^-$): calc. for $C_7H_8NBF_3$ [M-H]$^-$: 174.0707, found: 174.0699. **HPLC** Major enantiomer 11.8 min, minor enantiomer 13.2 min. Column: CHIRALPAK AD-H 250×4,6mm, 5 μm, T = 15 °C. Mobile phase: *n*-heptane/EtOH/methanesulfonic acid = 900/100/0.1 (V/V/V). Flow = 1.0 mL/min, injection volume = 10 μL.

(Ammonio(*p*-tolyl)methyl)trifluoroborate (3c)



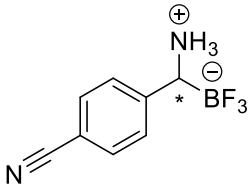
Synthesized according to the General Procedure from **2c** (56 mg, 0.3 mmol) to afford **3c** as a white solid (53 mg, 95% yield, 91:9 e.r.). **$[\alpha]_D^{24}$** -3.50 (*c* 0.1 M, MeOH). **m.p.** = 144 – 146 °C. **^{1}H NMR** (400 MHz, MeOD) δ 2.30 (s, 3H, C<u>H</u>$_3$), 3.22 (br s, 1H, C<u>H</u>), 7.11 (d, *J* = 8.0 Hz, 2H, Ar-<u>H</u>), 7.20 (d, *J* = 8.0 Hz, 2H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 2.67 (m). **^{13}C NMR** (101 MHz, MeOD) δ 21.06, 51 (br m, extracted from ^{1}H-^{13}C HSQC spectrum), 128.24, 129.76, 136.86, 138.49. **^{19}F NMR** (376 MHz, MeOD) δ -151.37 (m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 819, 924, 1031, 1263, 1479, 1600, 3160, 3253. **HRMS** (ESI$^-$): calc. for $C_8H_{10}NBF_3$ [M-H]$^-$: 188.0864, found: 188.0858. **HPLC** Major enantiomer 12.4 min, minor enantiomer 15.0 min. Column: CHIRALPAK AD-H 250×4,6mm, 5 μm, T = 15 °C. Mobile phase: *n*-heptane/EtOH/methanesulfonic acid = 900/100/0.1 (V/V/V). Flow = 1.0 mL/min, injection volume = 10 μL. Racemic compound is known in literature.[S3]

(Ammonio(4-chlorophenyl)methyl)trifluoroborate (3d)



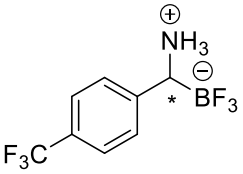
Synthesized according to the General Procedure from **2d** (62 mg, 0.3 mmol) to afford **3d** as a white solid (58 mg, 92% yield, 93:7 e.r.). **$[\alpha]_D^{24}$** -0.87 (*c* 0.1 M, MeOH). **m.p.** = 160 – 161 °C. **^{1}H NMR** (400 MHz, MeOD) δ 3.25 (br s, 1H, C<u>H</u>), 7.29 (app s, 4H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 2.51 (m). **^{13}C NMR** (101 MHz, MeOD) δ 50.81 (br m), 129.12, 129.74, 132.94, 140.47. **^{19}F NMR** (376 MHz, MeOD) δ -151.90 (m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 727, 824, 944, 973, 1039, 1089, 1243, 1480, 1597, 1613, 3150, 3264. **HRMS** (ESI$^-$): calc. for $C_7H_7NBClF_3$ [M-H]$^-$: 208.0318, found: 208.0313. **HPLC** Major enantiomer 11.5 min, minor enantiomer 14.2 min. Column: CHIRALPAK AD-H 250×4,6mm, 5 μm, T = 15 °C. Mobile phase: *n*-heptane/EtOH/methanesulfonic acid = 900/100/0.1 (V/V/V). Flow = 1.0 mL/min, injection volume = 10 μL.

(Ammonio(4-cyanophenyl)methyl)trifluoroborate (3e)



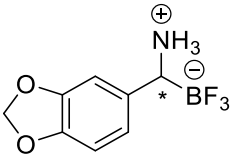
Synthesized according to the General Procedure from **2e** (40 mg, 0.2 mmol) to afford **3e** as a white solid (37 mg, 92% yield, 92:8 e.r.). **$[\alpha]_D^{24}$** -2.90 (*c* 0.01 M, MeOH). **m.p.** = 131 – 132 °C. **^{1}H NMR** (400 MHz, MeOD) δ 3.39 (s, 1H, C<u>H</u>), 7.44 (d, *J* = 8.3 Hz, 2H, Ar-<u>H</u>), 7.63 – 7.67 (m, 2H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 2.27 (m). **^{13}C NMR** (101 MHz, MeOD) δ 51 (br m, extracted from ^{1}H-^{13}C HSQC spectrum), 110.48, 119.98, 128.45, 132.91, 148.13. **^{19}F NMR** (376 MHz, MeOD) δ -151.92 (m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 840, 942, 1012, 1505, 1610, 2233, 2982, 3243. **HRMS** (ESI$^-$): calc. for $C_8H_7N_2BF_3$ [M-H]$^-$: 199.0660, found: 199.0654. **HPLC** Major enantiomer 17.1 min, minor enantiomer 23.4 min. Column: CHIRALPAK AD-H 250×4,6mm, 5 μm, T = 15 °C. Mobile phase: *n*-heptane/EtOH/methanesulfonic acid = 900/100/0.1 (V/V/V). Flow = 1.0 mL/min, injection volume = 10 μL.

(Ammonio(4-(trifluoromethyl)phenyl)methyl)trifluoroborate (3f)



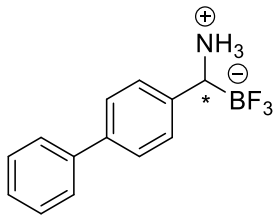
Synthesized according to the General Procedure from **2f** (72 mg, 0.3 mmol to afford **3f** as a white solid (68 mg, 93% yield, 97:3 e.r.). **$[\alpha]_D^{24}$** -2.77 (*c* 0.01 M, MeOH). **m.p.** = 163 – 164 °C. **^{1}H NMR** (400 MHz, MeOD) δ 3.41 (br s, 1H, C<u>H</u>), 7.47 (d, *J* = 8.1 Hz, 2H, Ar-<u>H</u>), 7.59 (d, *J* = 8.2 Hz, 2H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 2.46 (m). **^{13}C NMR** (101 MHz, MeOD) δ 50.91 (br m), 125.86 (q, $^3J_{CF}$ = 3.9 Hz), 125.87 (q, $^1J_{CF}$ = 270.3 Hz), 128.19, 129.18 (q, $^2J_{CF}$ = 32.2 Hz), 146.43. **^{19}F NMR** (376 MHz, MeOD) δ -151.45 (m), -63.78. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 723, 819, 929, 1039, 1263, 1478, 1516, 1600, 3162, 3252. **HRMS** (ESI$^-$): calc. for $C_8H_7NBF_6$ [M-H]$^-$: 242.0581, found: 242.0580. **HPLC** Major enantiomer 13.9 min, minor enantiomer 15.0 min. Column: CHIRALPAK AD-H 250×4,6mm, 5 μm, T = 30 °C. Mobile phase: *n*-heptane/*i*-PrOH/THF/methanesulfonic acid = 400/25/10/0.04 (V/V/V/V). Flow = 1.3 mL/min, injection volume = 5 μL.

(Ammonio(benzo[*d*][1,3]dioxol-5-yl)methyl)trifluoroborate (3g)



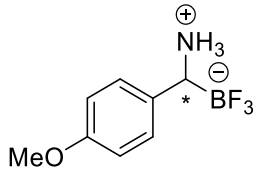
Synthesized according to the General Procedure from **2g** (65 mg, 0.3 mmol) with some minor changes in procedure. The reaction was conducted at 0.05M, namely in 6 mL MeOH (2% H_2O) instead of 3 mL: lower concentration was used due to poor solubility of **2g** in the reaction solvent. The isolation proceeded as per General Procedure to afford **3g** as a white solid (60 mg, 91% yield, 92:8 e.r.). **$[\alpha]_D^{24}$** -12.82 (*c* 0.05 M, MeOH). **m.p.** = 166 – 168 °C. **^{1}H NMR** (400 MHz, MeOD) δ 3.18 (br s, 1H, C<u>H</u>), 5.89 (s, 2H, C<u>H</u>$_2$), 6.74 (d, *J* = 8.0 Hz, 1H, Ar-<u>H</u>), 6.78 (d, *J* = 8.0 Hz, 1H, Ar-<u>H</u>), 6.89 (s, 1H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 2.59 (m). **^{13}C NMR** (101 MHz, MeOD) δ 51 (br m, extracted from ^{1}H-^{13}C HSQC spectrum), 102.12, 108.82, 109.22, 121.96, 135.33, 147.66, 148.97. **^{19}F NMR** (376 MHz, MeOD) δ -151.32 (m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 804, 927, 986, 1032, 1244, 1388, 1444, 1489, 2919, 3260. **HRMS** (ESI$^-$): calc. for $C_8H_8O_2NBF_3$ [M-H]$^-$: 218.0606, found: 218.0602. **HPLC** Major enantiomer 24.5 min, minor enantiomer 33.6 min. Column: CHIRALPAK AD-H 250×4,6mm, 5 μm, T = 15 °C. Mobile phase: *n*-heptane/EtOH/methanesulfonic acid = 900/100/0.1 (V/V/V). Flow = 1.0 mL/min, injection volume = 10 μL.

([1,1'-Biphenyl]-4-yl(ammonio)methyl)trifluoroborate (3h)



Synthesized according to the General Procedure from **2h** (25 mg, 0.1 mmol) with some minor changes in procedure. The reaction was conducted at 0.017 M, namely in 6 mL MeOH (2% H_2O) instead of 1 mL: lower concentration was used due to poor solubility of **2h** in the reaction solvent. After 20 h, the product had partially precipitated from the reaction mixture, which was concentrated under reduced pressure to 0.5 mL, filtered and washed with *n*-hexane to afford **3h** as a white solid (22 mg, 88% yield, 98:2 e.r.). **$[\alpha]_D^{24}$** -4.67 (*c* 0.01 M, MeOH). **m.p.** = 170 – 172 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 3.08 – 3.14 (m, 1H, C<u>H</u>), 7.28 – 7.37 (m, 3H, Ar-<u>H</u>), 7.42 – 7.52 (m, 4H, Ar-<u>H</u> + partially suppressed N<u>H</u>$_3^+$ overlapping), 7.53 – 7.57 (m, 2H, Ar-<u>H</u>), 7.62 – 7.66 (m, 2H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, DMSO-d_6) δ 2.60 (br s). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 49 (br m, extracted from ^{1}H-^{13}C HSQC spectrum), 125.92, 126.47, 127.09, 127.25, 128.90, 137.33, 140.30, 140.90. **^{19}F NMR** (376 MHz, DMSO-d_6) δ -145.50 (s). **HRMS** (ESI^-): calc. for $C_{13}H_{12}NBF_3$ $[M-H]^-$: 250.1020, found: 250.1021. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 761, 839, 960, 1005, 1050, 1484, 1597, 3167, 3211, 3276. **HPLC** Major enantiomer 12.7 min, minor enantiomer 11.6 min. Column: CHIRALPAK IA-3 250×4,6mm, 3 μm, T = 15 °C. Mobile phase: *n*-heptane/EtOH/methanesulfonic acid = 1000/180/0.12 (V/V/V). Flow = 1.0 mL/min, injection volume = 5 μL. Note that a different chiral column was used here (Chiralpak IA-3 since adequate resolution could not be obtained on Chiralpak AD-H), which caused that the major enantiomer eluted after the minor enantiomer. The absolute configuration of this compound is the same as in compounds **3a**–**3g** since all have a negative specific rotation. Compare with **3j** below, which has a positive specific rotation and its major enantiomer eluted as first on Chiralpak IA-3 column.

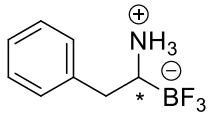
(Ammonio(4-methoxyphenyl)methyl)trifluoroborate (3i)



Synthesized according to the General Procedure from **2i** (82 mg, 0.4 mmol) with some minor changes in procedure. The reaction was conducted at 0.05 M, namely in 8 mL MeOH (2% H_2O) instead of 4 mL: lower concentration was used due to poor solubility of **2i** in the reaction solvent. The reaction mixture was left to stir for 44 h. The isolation proceeded as per General Procedure, which afforded **3i** as a

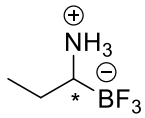
white solid (77 mg, 93% yield, 90:10 e.r.). **$[\alpha]_D^{24}$** -7.92 (*c* 0.05 M, MeOH). **m.p.** = 163 – 164 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 2.97 (br s, 1H, C<u>H</u>), 3.71 (s, 3H, C<u>H</u>$_3$), 6.78 – 6.85 (m, 2H, Ar-<u>H</u>), 7.11 – 7.20 (m, 2H, Ar-<u>H</u>), 7.37 (br s, 1.6H, N<u>H</u>$_3^+$, partially suppressed). **^{11}B NMR** (128 MHz, DMSO-d_6) δ 2.39 (br s). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 48 (br m, extracted from ^{1}H-^{13}C HSQC spectrum), 55.02, 113.11, 128.24, 133.29, 157.42. **^{19}F NMR** (376 MHz, DMSO-d_6) δ -145.48 (s). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 829, 951, 1020, 1110, 1180, 1250, 1304, 1474, 1514, 1608, 3277, 3613. **HRMS** (ESI$^-$): calc. for $C_8H_8ONBF_3$ [M-H]$^-$: 202.0657, found: 202.0652. **HPLC** Major enantiomer 18.7 min, minor enantiomer 23.2 min. Column: CHIRALPAK AD-H 250×4,6mm, 5 μm, T = 15 °C. Mobile phase: *n*-heptane/EtOH/methanesulfonic acid = 900/100/0.1 (V/V/V). Flow = 1.0 mL/min, injection volume = 10 μL.

(1-Ammonio-2-phenylethyl)trifluoroborate (3j)



Synthesized according to the General Procedure for aliphatic substrates from **2j** (56 mg, 0.3 mmol) to afford **3j** as a white solid (53 mg, 93% yield, 94:6 e.r.). **$[\alpha]_D^{24}$** +36.05 (*c* 0.1 M, MeOH). **m.p.** = 156 – 157 °C. **^{1}H NMR** (400 MHz, MeOD) 2.33 – 2.42 (m, 1H, C<u>H</u>-B), 2.63 (dd, *J* = 14.7, 11.2 Hz, 1H, C<u>H</u>$_{2a}$), 3.00 (dd, *J* = 14.7, 4.1 Hz, 1H, C<u>H</u>$_{2b}$), 7.18 – 7.35 (m, 5H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 2.85 (app. q, *J* = 49.4 Hz). **^{13}C NMR** (101 MHz, MeOD) δ 36.91, 48 (br m, extracted from ^{1}H-^{13}C HSQC spectrum), 127.41, 129.67, 130.06, 141.07. **^{19}F NMR** (376 MHz, MeOD) δ -152.73 (m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 925, 964, 994, 1494, 1602, 3172, 3204, 3275. **HRMS** (ESI$^-$): calc. for $C_8H_{10}NBF_3$ [M-H]$^-$: 188.0864, found: 188.0857. **HPLC** Major enantiomer 17.3 min, minor enantiomer 19.6 min. CHIRALPAK IA-3 250×4,6mm, 3 μm, T = 15 °C. Mobile phase: *n*-heptane/EtOH/methanesulfonic acid = 900/80/0.1 (V/V/V), flow = 1.0 mL/min, injection volume = 20 μL. Racemic compound is known in literature.[S3]

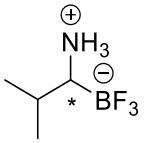
(1-Ammoniopropyl)trifluoroborate (3k)



Synthesized according to the General Procedure for aliphatic substrates from **2k** (25 mg, 0.2 mmol) to afford **3k** as a white solid (24 mg, 95% yield, 93:7 e.r.). **$[\alpha]_D^{24}$** +3.67 (*c* 0.05 M, MeOH). **m.p.** > 190 °C (decomp.) **^{1}H NMR** (400 MHz, MeOD) δ 0.98 (t, *J* = 7.5 Hz, 3H, C<u>H</u>$_3$), 1.42 – 1.54 (m, 1H, C<u>H</u>$_{2a}$), 1.59 – 1.72 (m, 1H, C<u>H</u>$_{2b}$), 1.99 (br s, 1H, C<u>H</u>-B). **^{11}B NMR** (128 MHz, MeOD) δ 2.91 (app. q, *J* = 53.9 Hz). **^{13}C NMR** (101 MHz, MeOD) δ 11.80, 23.95, 48 (br m, extracted from ^{1}H-^{13}C HSQC spectrum). **^{19}F NMR** (376

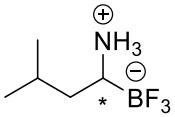
MHz, MeOD) δ -152.01 (m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 943, 1043, 1102, 2967, 3252. **HRMS** (ESI$^-$): calc. for $C_3H_8NBF_3$ [M-H]$^-$: 126.0707, found: 126.0696.

(1-Ammonio-2-methylpropyl)trifluoroborate (3l)



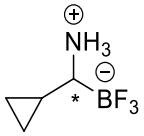
Synthesized according to the General Procedure for aliphatic substrates from **2l** (28 mg, 0.2 mmol) to afford **3l** as a white solid (25 mg, 89% yield, 93:7 e.r.). **[α]$_D^{24}$** +1.07 (*c* 0.05 M, MeOH). **m.p.** > 190 °C (decomp.) **^{1}H NMR** (400 MHz, MeOD) δ 0.99 (dd, *J* = 6.6, 3.8 Hz, 6H, (C$\underline{H}_3$)$_2$), 1.83 – 1.94 (m, 2H, C$\underline{H}$ + C$\underline{H}$-B, overlapping). **^{11}B NMR** (128 MHz, MeOD) δ 2.84 (m). **^{13}C NMR** (101 MHz, MeOD) δ 20.39, 20.57, 29.68, 53 (br m, extracted from ^{1}H-^{13}C HSQC spectrum). **^{19}F NMR** (376 MHz, MeOD) δ -148.42 (m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 943, 1016, 1491, 1602, 2945, 3279. **HRMS** (ESI$^-$): calc. for $C_4H_{10}NBF_3$ [M-H]$^-$: 140.0858, found: 140.0854. Racemic compound is known in literature.[S3]

(1-ammonio-3-methylbutyl)trifluoroborate (3m)



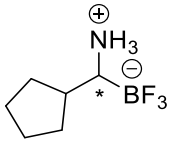
Synthesized according to the General Procedure for aliphatic substrates from **2m** (153 mg, 1.0 mmol) to afford **3m** as a white solid (148 mg, 95% yield, e.r. = 99:1). **[α]$_D^{24}$** +9.77 (*c* 0.2 M, MeOH). **m.p.** > 170 °C (decomp.) **^{1}H NMR** (400 MHz, MeOD) δ 0.91 (dd, *J* = 9.7, 6.5 Hz, 6H, (C$\underline{H}_3$)$_2$), 1.28 – 1.51 (m, 2H, C$\underline{H}_2$), 1.67 – 1.81 (m, 1H, (C$\underline{H}_3$)$_2$-C$\underline{H}$), 2.18 (s, 1H, C$\underline{H}$-NH$_3^+$). **^{11}B NMR** (128 MHz, MeOD) δ 2.96 (app. q, *J* = 52.3 Hz). **^{13}C NMR** (101 MHz, MeOD) δ 22.64, 23.43, 25.83, 40.40, 43.84 (br m). **^{19}F NMR** (376 MHz, MeOD) δ -152.51 (m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 816, 963, 1010, 1176, 1250, 1367, 1489, 1608, 2958, 3273. **HRMS** (ESI$^-$): calc. for $C_5H_{12}NBF_3$ [M-H]$^-$: 154.1020, found: 154.1011. Known compound.[S8]

(Ammonio(cyclopropyl)methyl)trifluoroborate (3n)



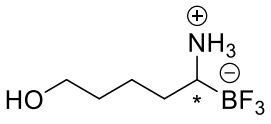
Synthesized according to the General Procedure for aliphatic substrates from **2n** (27 mg, 0.2 mmol) to afford **3n** as a white solid (25 mg, 90% yield, e.r. = 96:4). **$[\alpha]_D^{24}$** +28.79 (*c* 0.1 M, MeOH). **m.p.** > 200 °C (decomp.) **^{1}H NMR** (400 MHz, MeOD) δ 0.17 – 0.33 (m, 2H, C$\underline{H}_2$), 0.42 – 0.60 (m, 2H, C$\underline{H}_2$), 0.88 – 0.98 (m, 1H, C$\underline{H}$), 1.37 (br d, *J* = 9.6 Hz, 1H, CH-B). **^{11}B NMR** (128 MHz, MeOD) δ 2.77 (app. q, *J* = 55.6 Hz). **^{13}C NMR** (101 MHz, MeOD) δ 4.17, 4.68, 12.03, 52 (br m, extracted from ^{1}H-^{13}C HSQC spectrum). **^{19}F NMR** (376 MHz, MeOD) δ -151.61 (m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 897, 941, 1015, 1074, 1146, 1264, 1324, 1431, 3007, 3081, 3254. **HRMS** (ESI$^-$): calc. for $C_4H_8NBF_3$ [M-H]$^-$: 138.0702, found: 138.0697.

(Ammonio(cyclopentyl)methyl)trifluoroborate (3o)



Synthesized according to the General Procedure for aliphatic substrates from **2o** (33 mg, 0.2 mmol) to afford **3o** as a white solid (31 mg, 94% yield, e.r. = 99:1). **$[\alpha]_D^{24}$** +5.75 (*c* 0.02 M, MeOH). **m.p.** > 185 °C (decomp.) **^{1}H NMR** (400 MHz, DMSO-d_6) δ 1.06 – 1.23 (m, 2H, C$\underline{H}_2$), 1.34 – 1.59 (m, 4H, 2×C$\underline{H}_2$), 1.63 – 1.75 (m, 3H, C$\underline{H}_2$ + C$\underline{H}$-B), 1.77 – 1.90 (m, 1H, C$\underline{H}$), 6.73 (br s, 3H, N$\underline{H}_3^+$). **^{11}B NMR** (128 MHz, DMSO-d_6) δ 2.77 (br s). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 24.46, 24.62, 29.74, 30.52, 40.78, 48.5 (br m, extracted from ^{1}H-^{13}C HSQC spectrum). **^{19}F NMR** (376 MHz, DMSO-d_6) δ -143.77 (s). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 928, 961, 1040, 1490, 1600, 2869, 2945, 3275. **HRMS** (ESI$^-$): calc. for $C_6H_{12}NBF_3$ [M-H]$^-$: 166.1020, found: 166.1012. Racemic compound is known in literature.[S3]

(1-Ammonio-5-hydroxypentyl)trifluoroborate (3p)



Synthesized according to the General Procedure from **2p** (84.5 mg, 0.5 mmol) to afford **3p** as a white solid (82 mg, 96% yield, e.r. = 96:4). **$[\alpha]_D^{24}$** +7.94 (*c* 0.1 M, MeOH). **m.p.** > 140 °C (decomp.) **^{1}H NMR** (400 MHz, MeOD) δ 1.36 – 1.69 (m, 6H, 3×C$\underline{H}_2$), 2.07 (br s, 1H, C$\underline{H}$), 3.56 (t, *J* = 6.5 Hz, 2H, C$\underline{H}_2$-OH). **^{11}B NMR** (128 MHz, MeOD) δ 2.92 (m). **^{13}C NMR** (101 MHz, MeOD) δ 24.12, 30.83, 33.63, 46.16 (br m),

62.82. **^{19}F NMR** (376 MHz, MeOD) δ -152.23 (m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 729, 945, 1015, 1061, 1491, 1603, 2893, 2944, 3279. **HRMS** (ESI$^-$): calc. for $C_5H_{12}ONBF_3$ [M-H]$^-$: 170.0969, found: 170.0962.

4.3. Determination of Optical Purity of pTAMs

General procedure for the synthesis of racemic pTAMs (3a$_{rac}$ – 3p$_{rac}$)

A racemic standard for each pTAM was synthesized using a modification of the literature method.[S6] In an oven-dried flask under argon atmosphere, pTIM **2** (0.3 mmol) was dissolved in MeCN (4 mL) and MeOH (1 mL). The flask was transferred to an ice bath and solid $NaBH_4$ (6 mg, 0.16 mmol, 0.53 eq) was added to the solution. Then, the ice bath was removed and the reaction mixture was stirred at RT until all the starting material was consumed (30 min – 1 h), monitored by TLC or NMR. After the reaction was completed, 1 M aqueous HCl (600 μL, 2 eq) was added, the reaction mixture was stirred for five more minutes, and then evaporated to dryness. The dry residue was suspended in CH_2Cl_2:MeOH = 5:1 (10 mL) for aromatic compounds (**3a**$_{rac}$ – **3i**$_{rac}$) and EtOAc:MeOH = 5:1 for aliphatic compounds (**3j**$_{rac}$ – **3p**$_{rac}$), filtered, and washed with the same solvent mixture. The filtrate was evaporated under reduced pressure to afford crude racemic pTAM **3**$_{rac}$. The spectral data of these compounds corresponded fully to those of the enantioenriched pTAMs (*vide supra*) and are not repeated here.

It should be noted, however, that both spectra and chromatograms of crude racemic pTAMs obtained with $NaBH_4$ contained more impurities and additional signals in comparison to the spectra of crude enantioenriched pTAMs obtained by asymmetric hydrogenation. While the purity of crude racemic pTAMs was sufficient for them to serve as racemic standards in HPLC analyses, this observation showcases that the ruthenium-catalyzed hydrogenation of pTIMs is markedly superior to the borohydride reduction not only because it is enantioselective, but also in terms of chemoselectivity. The chromatograms can be compared directly in the section below.

4.3.1. Chromophore-Bearing Compounds (3a – 3j)

Chiral HPLC analysis of compounds **3a**-**3j** was performed to determine the e.r. for each compound. For each compound, an HPLC chromatogram of its racemic standard was obtained, followed by the analysis of the crude sample from the enantioselective reaction. The following methods were used:

3a-**3e**, **3g**, **3i**

Column: CHIRALPAK AD-H, 250×4,6mm, 5 μm, T = 15 °C

Mobile phase: *n*-heptane/EtOH/methanesulfonic acid = 900/100/0,1 (V/V/V)

Flow = 1.0 mL/min

Injection volume = 10 μL

3f

Column: CHIRALPAK AD-H, 250×4,6mm, 5 μm, T = 30 °C

Mobile phase: *n*-heptane/*i*-PrOH/THF/methanesulfonic acid = 400/25/10/0.04 (V/V/V/V)

Flow = 1.3 mL/min

Injection volume = 5 μL

3h

Column: CHIRALPAK IA-3, 250×4,6mm, 3 μm, T = 15 °C

Mobile phase: *n*-heptane/EtOH/methanesulfonic acid = 1000/180/0.12 (V/V/V)

Flow = 1.0 mL/min

Injection volume = 5 μL

3j

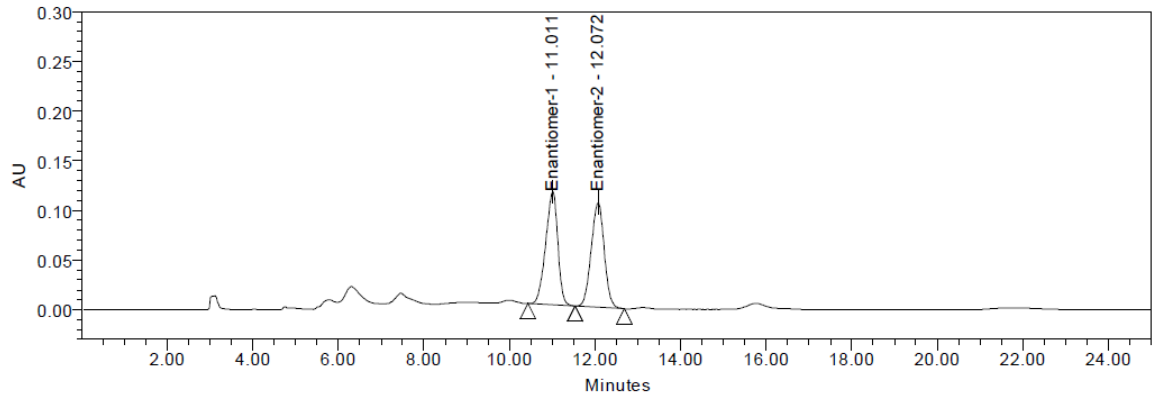
Column: CHIRALPAK IA-3, 250×4,6mm, 3 μm, T = 15 °C.

Mobile phase: *n*-heptane/EtOH/methanesulfonic acid = 900/80/0,1 (V/V/V)

Flow = 1.0 mL/min

Injection volume = 20 μL

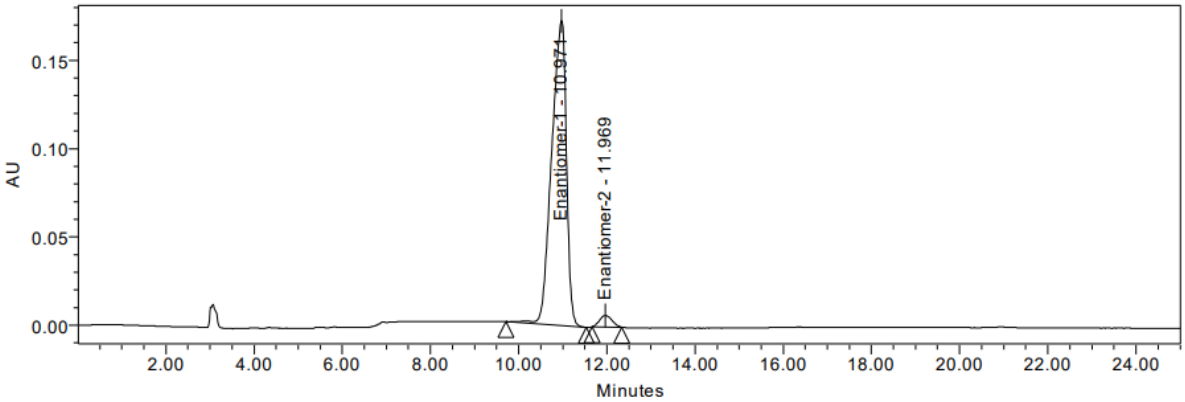
3a*rac*



Sample Name: Racemat amin

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	26	Enantiomer-1	11.011	2252701	50.41			8.856080e-001
2	26	Enantiomer-2	12.072	2216438	49.59		2.0	1.006566e+000

3a

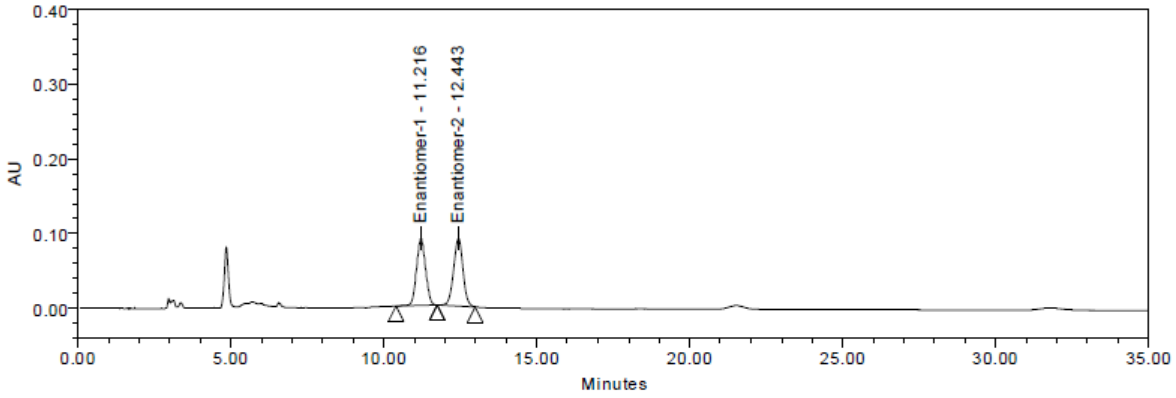


Sample Name: CAS-917

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	76	Enantiomer-1	10.971	3996517	96.98			7.933400e-001
2	76	Enantiomer-2	11.969	124346	3.02		1.7	1.097964e+000

e.r. = 97:3

3b$_{rac}$

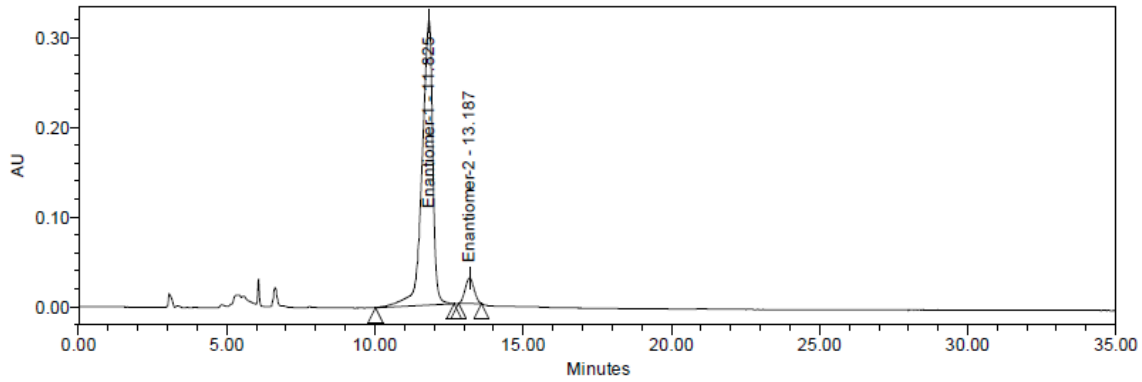


SampleName Racemat 1245; Vial 2; Injection 1; Date Acquired Wednesday, September 1, 2021 2:26:09 PM CEST; Date Processe
Thursday, September 2, 2021 10:47:44 AM CEST

Sample Name: Racemat 1245

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	2	Enantiomer-1	11.216	1874891	49.35			1.028670e+000
2	2	Enantiomer-2	12.443	1924539	50.65		2.2	1.004224e+000

3b



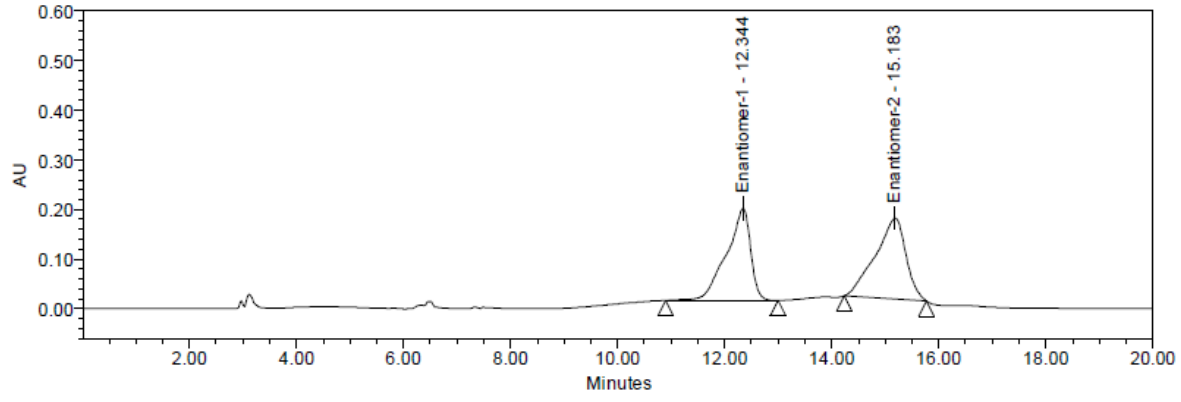
SampleName CAS-1409; Vial 67; Injection 1; Date Acquired Wednesday, October 13, 2021 9:22:41 AM CEST; Date Processe
Thursday, November 11, 2021 8:38:48 AM CET

Sample Name: CAS-1409

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	67	Enantiomer-1	11.825	7898416	92.88			7.708439e-001
2	67	Enantiomer-2	13.187	605640	7.12		2.3	1.064043e+000

e.r. = 93:7

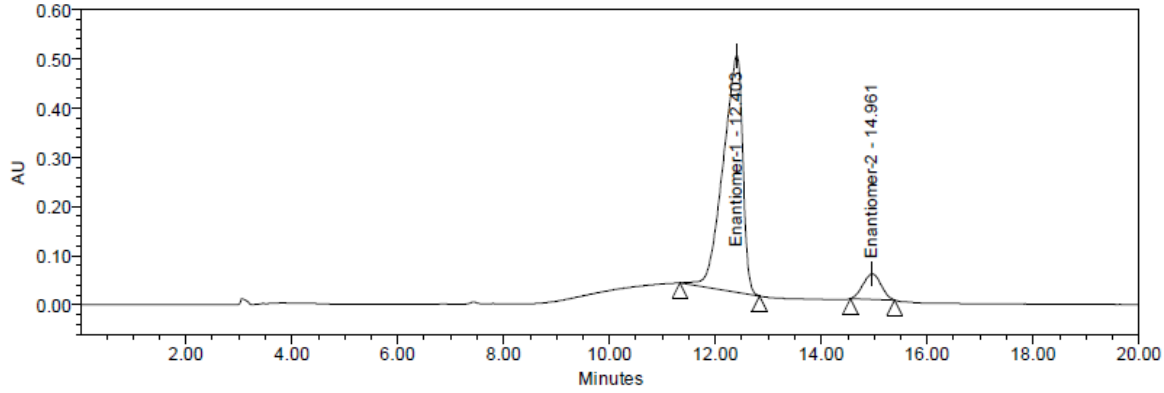
3c$_{rac}$



Sample Name: RR-1246

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	4	Enantiomer-1	12.344	5812909	47.26			7.261218e-001
2	4	Enantiomer-2	15.183	6486228	52.74		3.1	7.966051e-001

3c

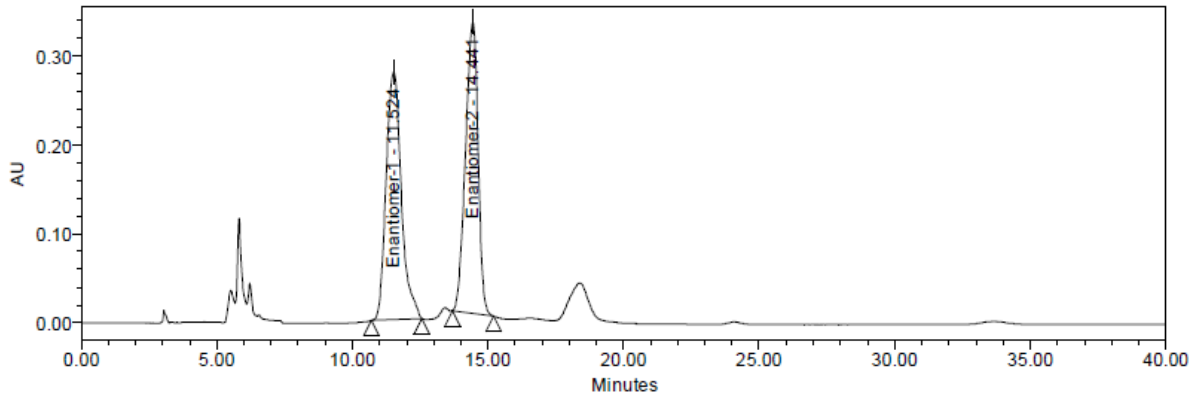


Sample Name: CAS-1398

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	68	Enantiomer-1	12.403	12374827	91.00			7.375484e-001
2	68	Enantiomer-2	14.961	1223166	9.00		3.9	1.009308e+000

e.r. = 91:9

3d$_{rac}$

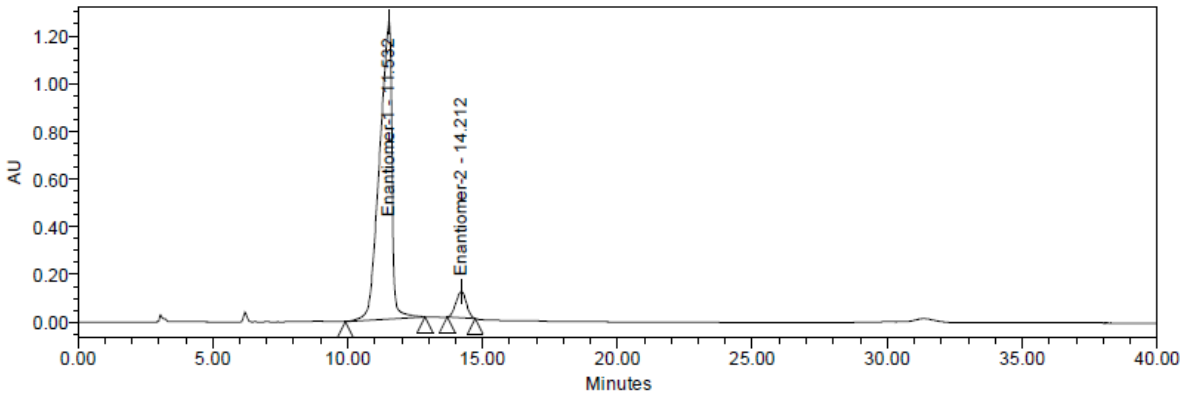


SampleName Racemat-1249-2; Vial 22; Injection 1; Date Acquired Wednesday, September 8, 2021 7:18:10 AM CEST; Date Processe
Friday, October 22, 2021 9:25:08 AM CEST

Sample Name: Racemat-1249-2

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	22	Enantiomer-1	11.524	10837617	50.65			1.243330e+000
2	22	Enantiomer-2	14.441	10561191	49.35		3.1	8.914956e-001

3d



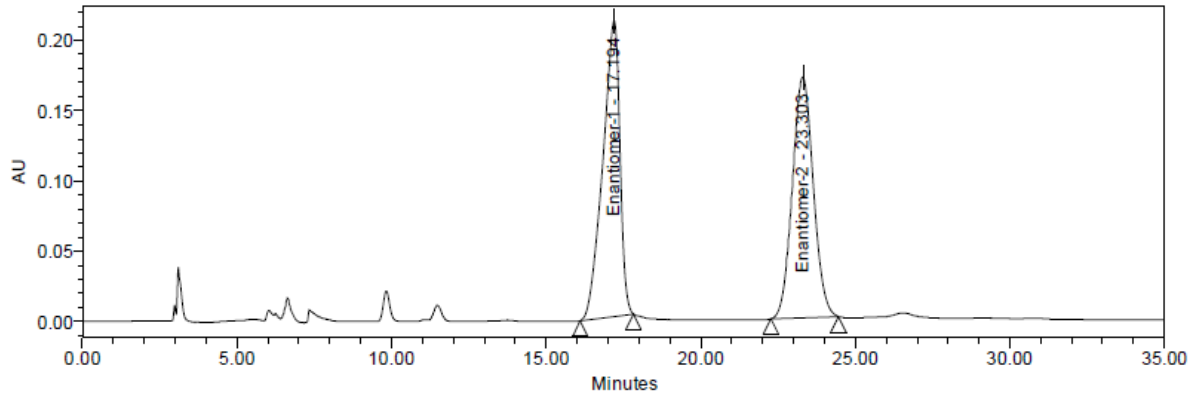
SampleName CAS 1329; Vial 41; Injection 1; Date Acquired Monday, September 20, 2021 3:32:20 PM CEST; Date Processed Tuesday
September 21, 2021 10:06:07 AM CEST

Sample Name: CAS 1329

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	41	Enantiomer-1	11.532	39980822	93.05			6.636979e-001
2	41	Enantiomer-2	14.212	2988427	6.95		3.4	9.886558e-001

e.r. = 93:7

3e$_{rac}$

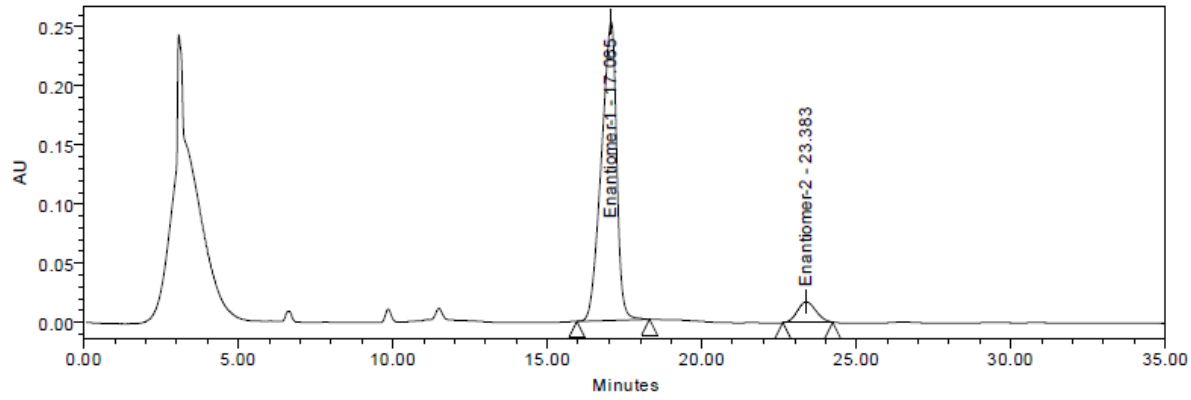


SampleName RR-1238; Vial 6; Injection 1; Date Acquired Tuesday, October 5, 2021 1:28:08 PM CEST; Date Processed Wednesday, October 6, 2021 6:34:13 AM CEST

Sample Name: RR-1238

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	6	Enantiomer-1	17.194	8002997	49.67			7.619686e-001
2	6	Enantiomer-2	23.303	8109105	50.33		5.4	1.041212e+000

3e



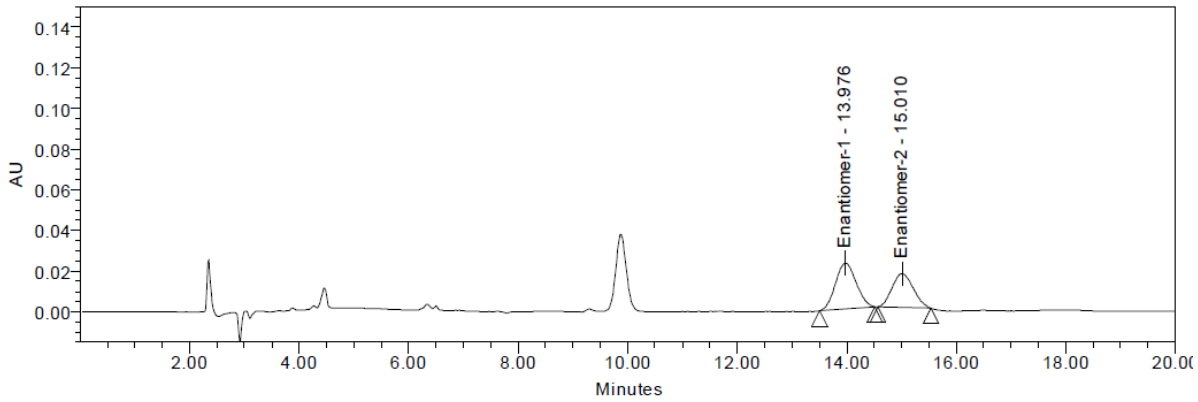
SampleName CAS-1365; Vial 59; Injection 1; Date Acquired Thursday, September 30, 2021 5:27:20 PM CEST; Date Processed Friday, October 1, 2021 6:41:33 AM CEST

Sample Name: CAS-1365

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	59	Enantiomer-1	17.065	8606262	92.17			8.091328e-001
2	59	Enantiomer-2	23.383	730660	7.83		6.3	1.074391e+000

e.r. = 92:8

3f$_{rac}$

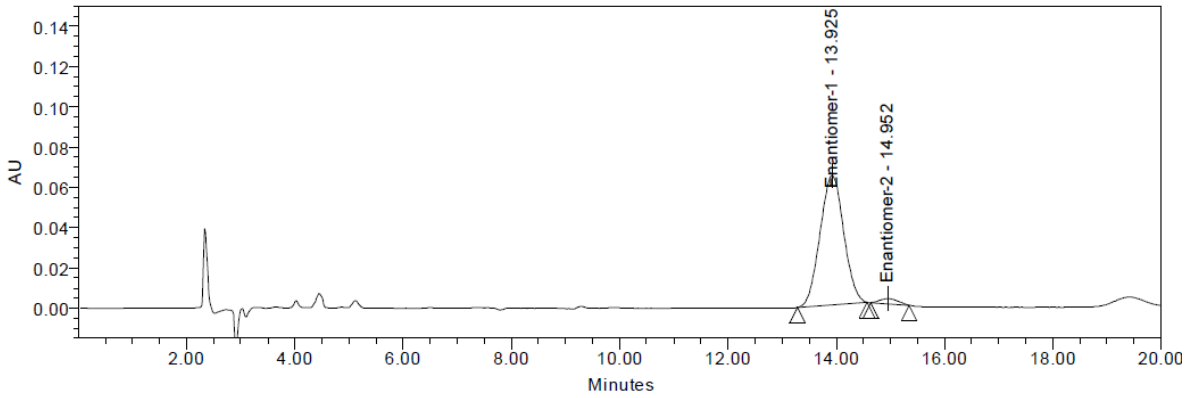


SampleName RR 1250; Vial 54; Injection 1; Date Acquired Monday, October 18, 2021 12:18:14 PM CEST; Date Processed Wednesda
January 19, 2022 8:36:14 AM CET

Sample Name: RR 1250

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	54	Enantiomer-1	13.976	590955	57.07			1.07
2	54	Enantiomer-2	15.010	444557	42.93		1.4	1.12

3f



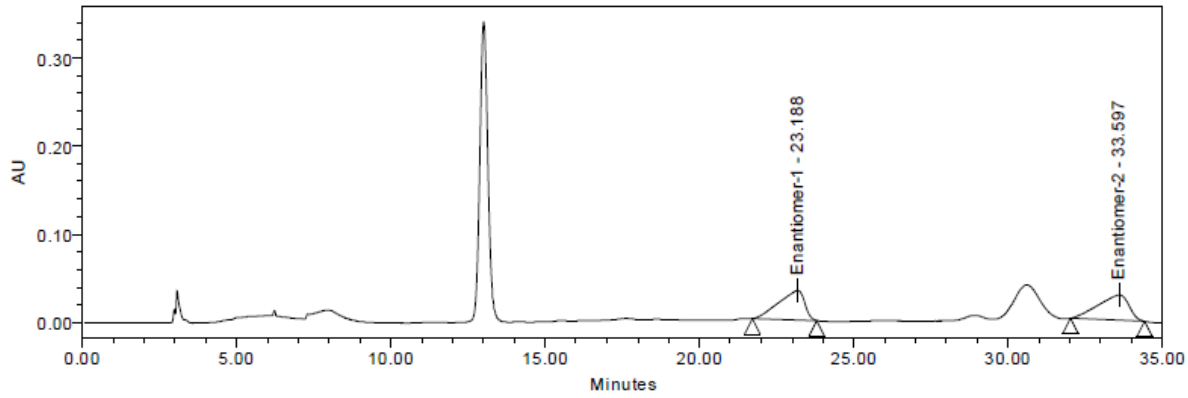
SampleName CAS 1367; Vial 55; Injection 1; Date Acquired Monday, October 18, 2021 12:39:06 PM CEST; Date Processe
Wednesday, January 19, 2022 8:38:18 AM CET

Sample Name: CAS 1367

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	55	Enantiomer-1	13.925	1957006	96.96			1.01
2	55	Enantiomer-2	14.952	61255	3.04		1.4	1.13

e.r. = 97:3

3g$_{rac}$

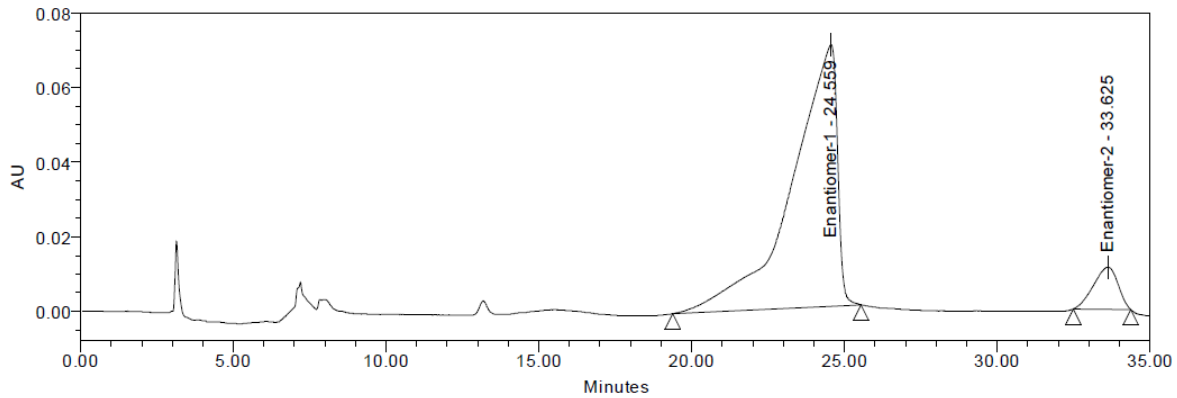


SampleName RR-1239; Vial 10; Injection 1; Date Acquired Thursday, September 30, 2021 1:14:05 PM CEST; Date Processed Friday October 1, 2021 6:34:44 AM CEST

Sample Name: RR-1239

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	10	Enantiomer-1	23.188	1949346	49.71			6.906352e-001
2	10	Enantiomer-2	33.597	1972102	50.29		5.9	7.406169e-001

3g



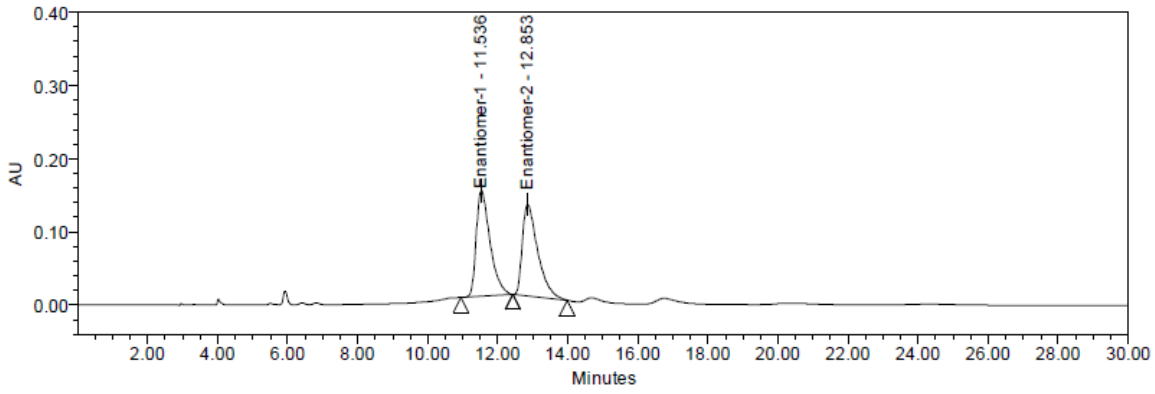
SampleName CAS-1470; Vial 69; Injection 1; Date Acquired Tuesday, November 9, 2021 9:46:03 AM CET; Date Processed Wednesday November 10, 2021 7:58:36 AM CET

Sample Name: CAS-1470

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	69	Enantiomer-1	24.559	7154811	91.91			0.56
2	69	Enantiomer-2	33.625	630091	8.09		4.5	0.83

e.r. = 92:8

3h$_{rac}$

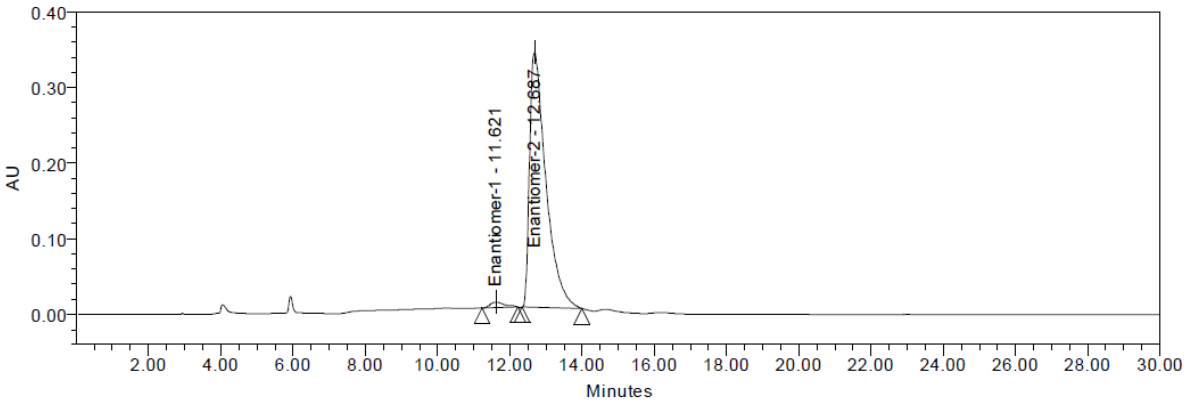


SampleName RR-1389; Vial 62; Injection 1; Date Acquired Wednesday, October 6, 2021 8:55:59 AM CEST; Date Processe
Wednesday, October 6, 2021 11:02:17 AM CEST

Sample Name: RR-1389

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	62	Enantiomer-1	11.536	3971949	50.86			1.554555e+000
2	62	Enantiomer-2	12.853	3837084	49.14		1.8	1.871571e+000

3h



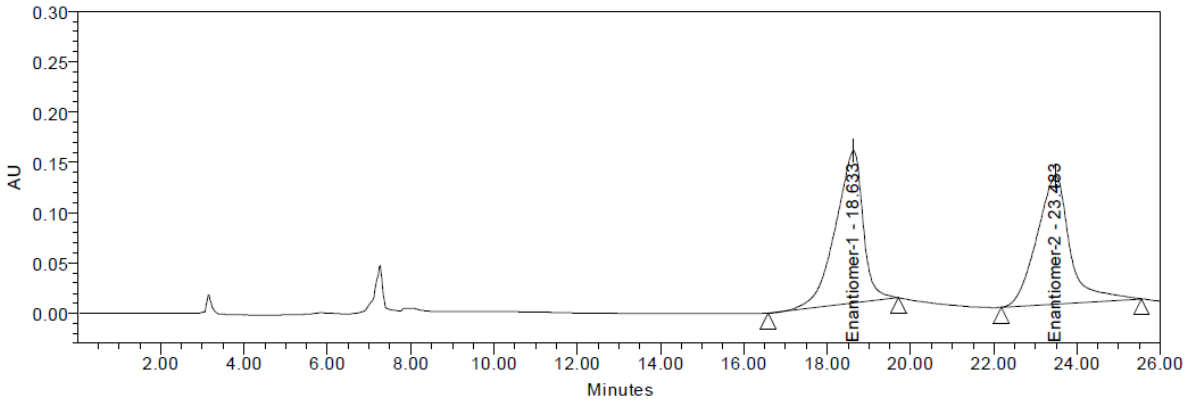
SampleName CAS-1244; Vial 52; Injection 1; Date Acquired Wednesday, October 6, 2021 9:31:54 AM CEST; Date Processe
Wednesday, January 19, 2022 9:07:26 AM CET

Sample Name: CAS-1244

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	52	Enantiomer-1	11.621	209715	1.95			1.39
2	52	Enantiomer-2	12.687	10569457	98.05		1.4	2.20

e.r. = 98:2

3i$_{rac}$

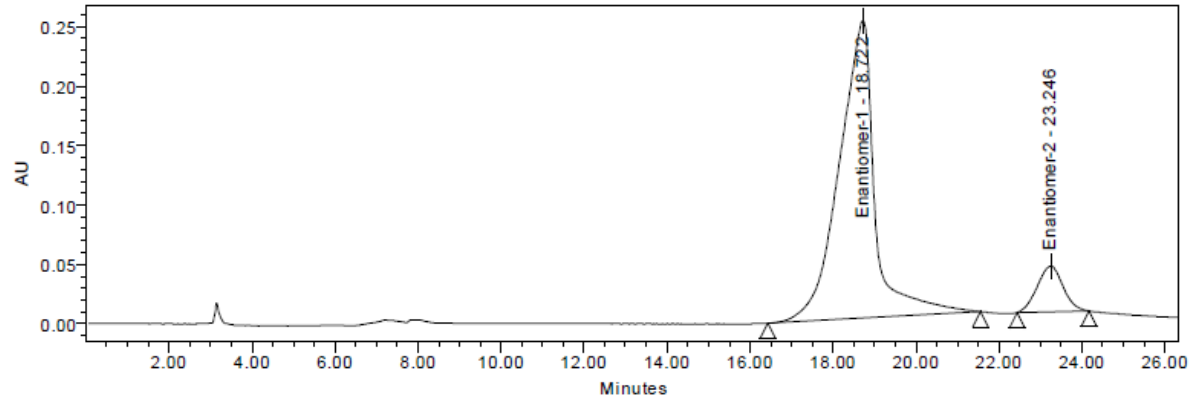


SampleName CAS-1494; Vial 70; Injection 1; Date Acquired Tuesday, November 9, 2021 10:26:55 AM CET; Date Processe
Wednesday, November 10, 2021 7:56:42 AM CET

Sample Name: CAS-1494

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	70	Enantiomer-1	18.633	7000433	49.90			0.73
2	70	Enantiomer-2	23.483	7028271	50.10		3.9	1.06

3i



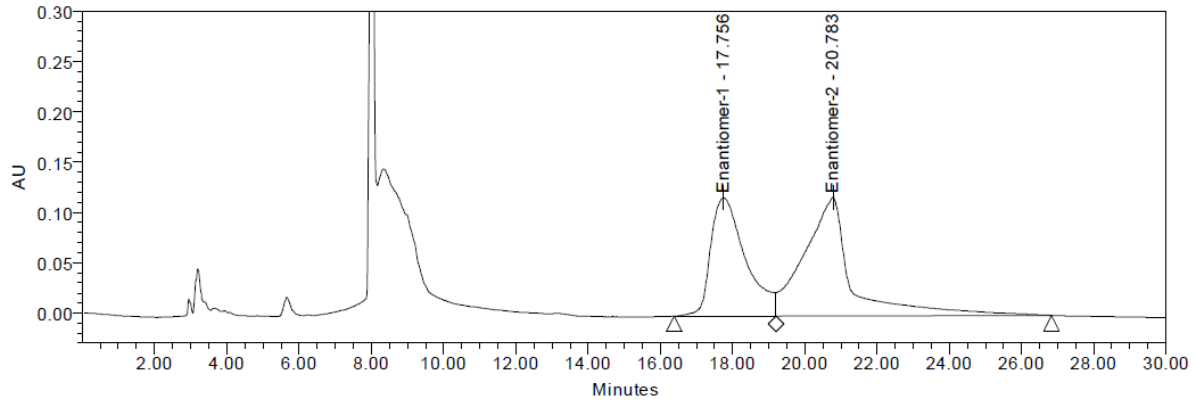
SampleName CAS-1486; Vial 71; Injection 1; Date Acquired Tuesday, November 9, 2021 11:07:50 AM CET; Date Processe
Wednesday, November 10, 2021 11:46:44 AM CET

Sample Name: CAS-1486

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	71	Enantiomer-1	18.722	14990718	90.01			8.981202e-001
2	71	Enantiomer-2	23.246	1663057	9.99		3.5	1.020718e+000

e.r. = 90:10

3j$_{rac}$

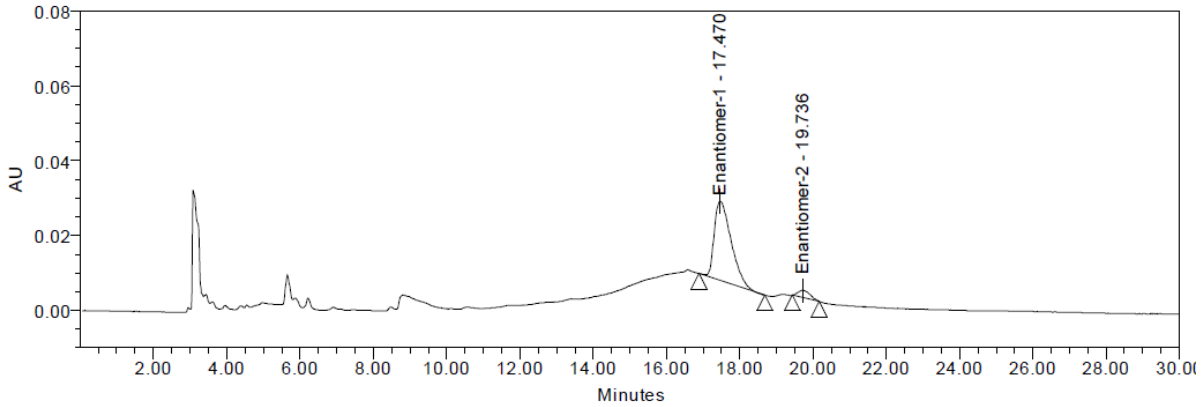


SampleName Racemat 1241; Vial 14; Injection 1; Date Acquired Tuesday, September 21, 2021 12:57:04 PM CEST; Date Processe
Wednesday, September 22, 2021 6:09:07 AM CEST

Sample Name: Racemat 1241

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	14	Enantiomer-1	17.756	7853411	42.39			
2	14	Enantiomer-2	20.783	10673139	57.61		1.7	

3j



SampleName CAS 1332; Vial 43; Injection 1; Date Acquired Tuesday, September 21, 2021 1:38:20 PM CEST; Date Processe
Wednesday, January 19, 2022 12:09:33 PM CET

Sample Name: CAS 1332

	Vial	Name	Retention Time (min)	Area (µV*sec)	% Area	EP s/n	Resolution	USP Tailing
1	43	Enantiomer-1	17.470	684441	93.73			2.03
2	43	Enantiomer-2	19.736	45792	6.27		2.9	1.24

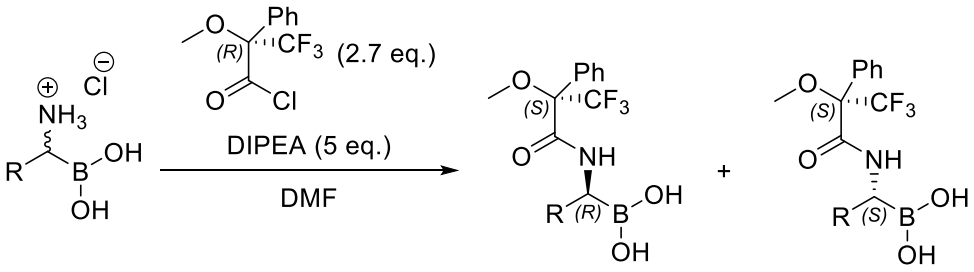
e.r. = 94:6

4.3.2. Substrates Without Chromophores (3k – 3p)

For compounds **3k**-**3p**, the conventional HPLC analysis coupled with a UV/VIS detector was not feasible, since these compounds contain no chromophores. The development of a method for the

resolution of enantiomers was attempted on a HPLC system coupled with an MS detector, but to no avail, despite several different normal-phase and reverse-phase chiral columns were tested with various mobile phases. Since TAMs are zwitterionic compounds and therefore highly stable towards most derivatization reactions, we were not able to derivatize them directly. For this reason, they were first transformed into α-aminoboronic acids **4k**-**4p** (*vide infra*: synthetic protocol described in Section 5.2.). A racemic standard for each α-aminoboronic acid was first prepared: racemic pTAMs **3k$_{rac}$**-**3p$_{rac}$** were synthesized by $NaBH_4$-mediated reduction of pTIMs **2k**-**2p** as described for aromatic racemic pTAMs. Then, the racemic pTAMs were converted to racemic α-aminoboronic acid **4k$_{rac}$**-**4p$_{rac}$** and acylated with (*R*)-(-)-MTPA-Cl (Mosher's acid chloride) according to the General Procedure below.

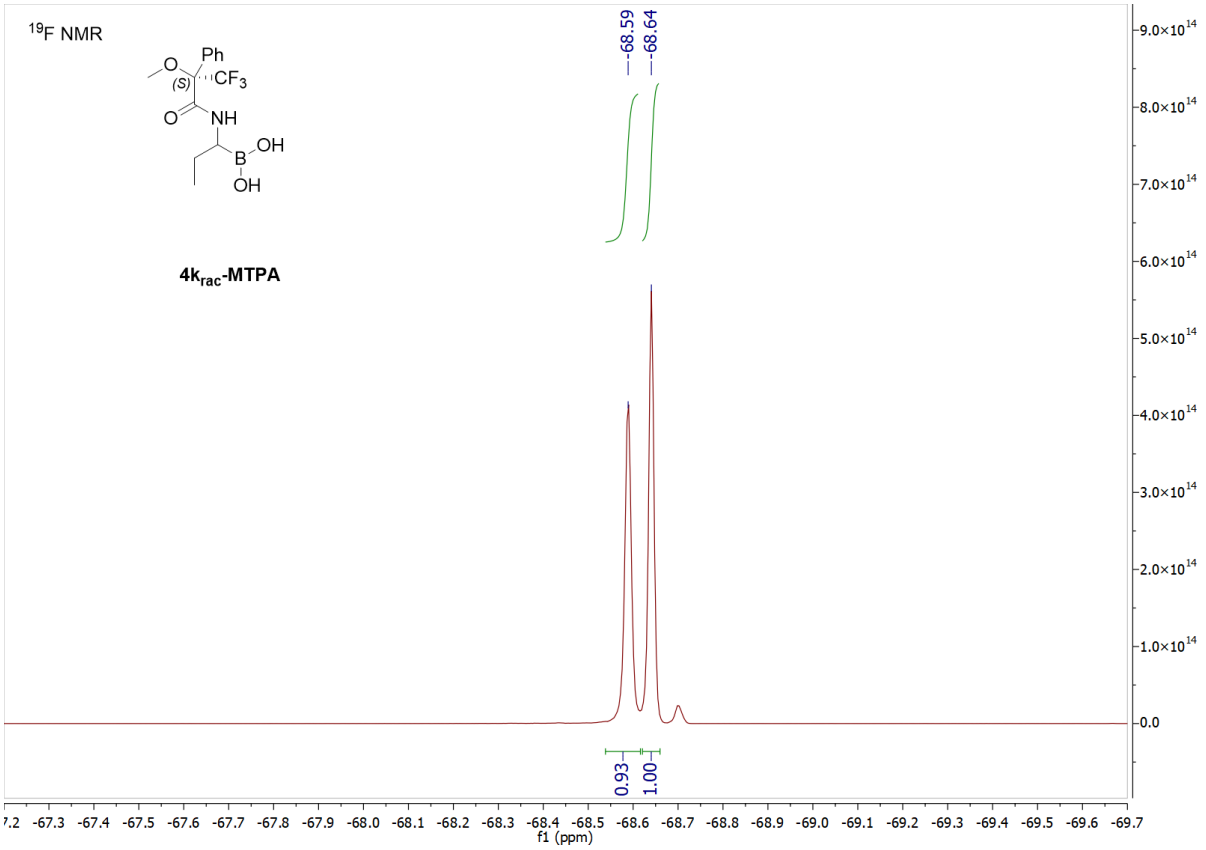
General Procedure for e.r. Determination in α-Aminoboronic Acids 4k-4p

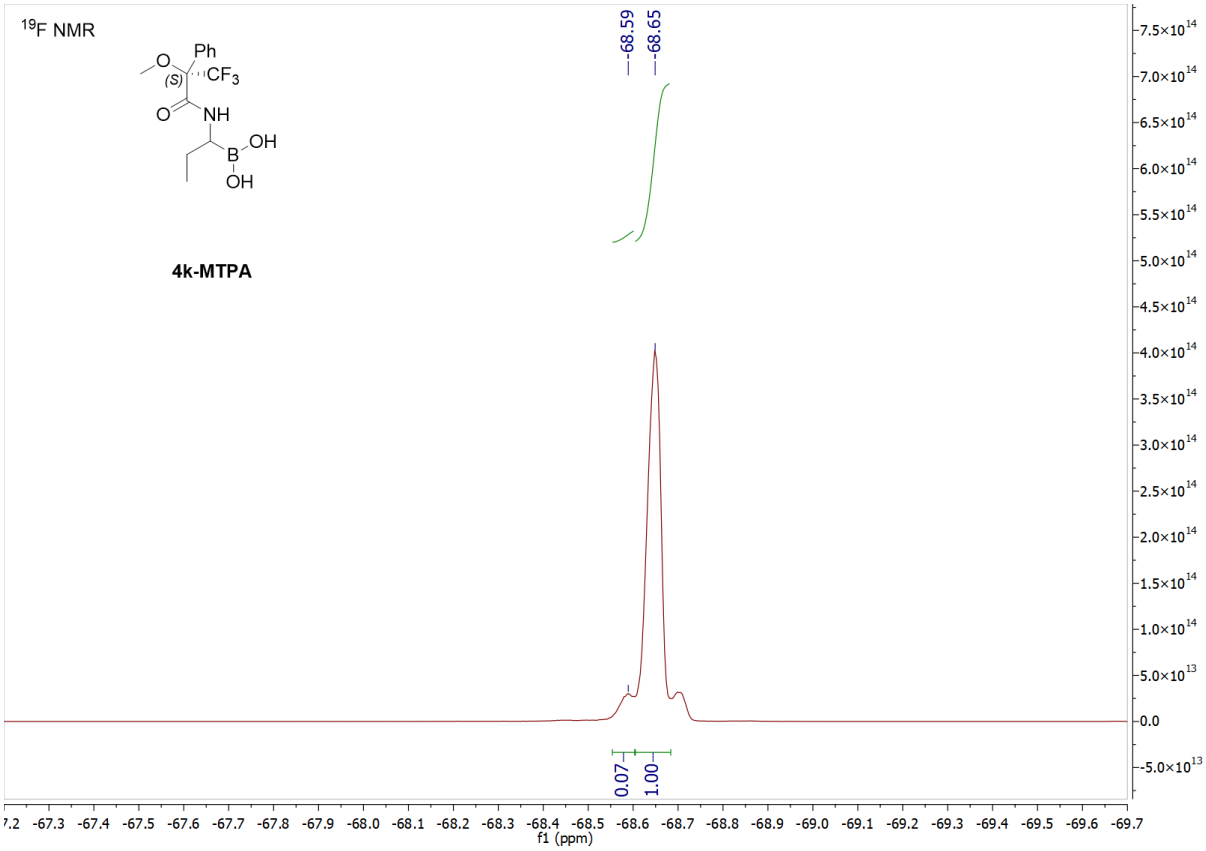


Scheme S5. Derivatization of aminoboronic acids **4** by Mosher's acid chloride.

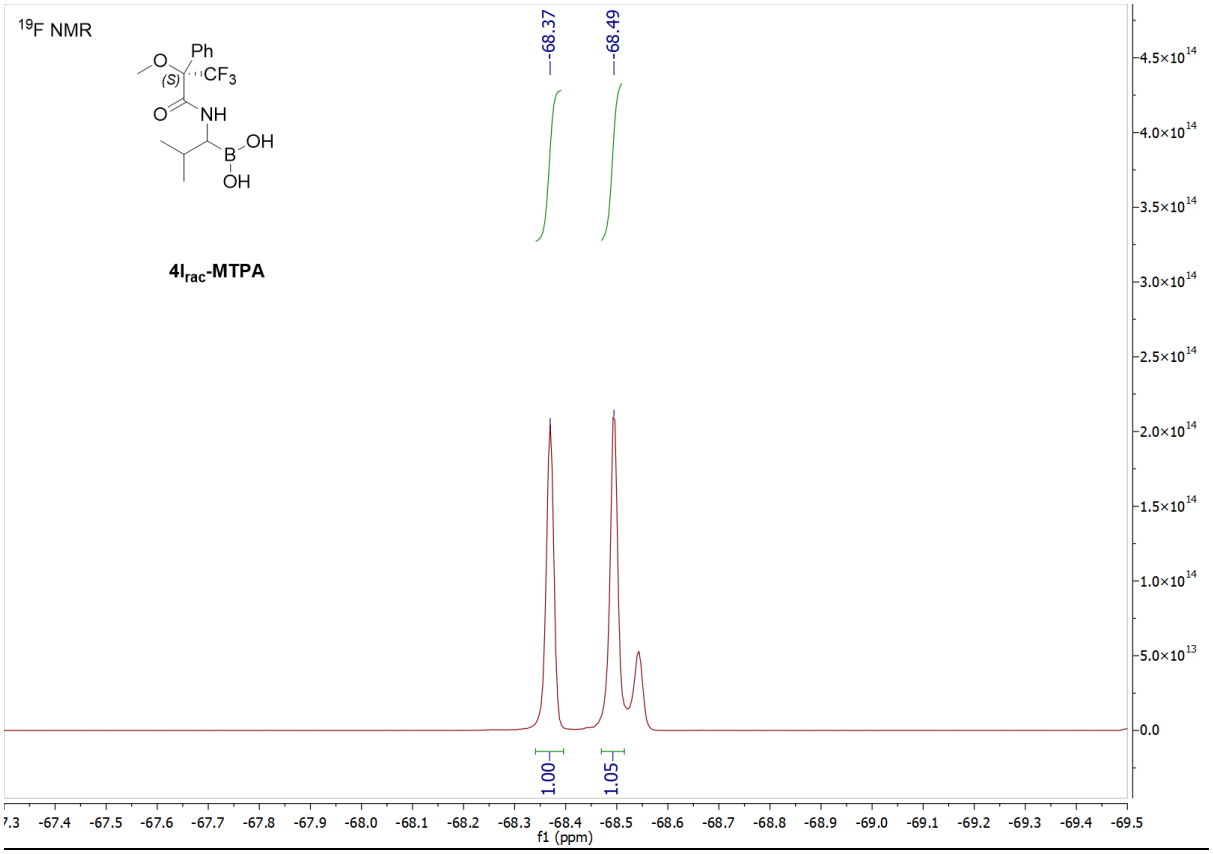
For each compound, a racemic standard **4k$_{rac}$**-**4p$_{rac}$** and the actual sample **4k**-**4p** were separately subjected to this procedure. In an oven-dried flask under argon atmosphere, aminoboronic acid **4** (0.02 mmol – typically 3-4 mg) was dissolved in dry DMF (0.5 mL) and the solution was stirred in an ice bath. Then, optically pure (*R*)-(-)-MTPA-Cl (10 μL, 2.7 eq.) was added to the solution, followed by the addition of DIPEA (17 μL, 5 eq.). After 1 h, the ice bath was removed and the reaction mixture was stirred for additional hour at RT. Then, a sample (150 μL) was taken directly from the flask, diluted with DMSO-d_6 (400 μL), and a ^{19}F NMR was recorded. The signals for the diastereotopic CF_3 moiety, one belonging to the (*S*,*S*) and the other to the (*S,R*)-diastereomer, were integrated. From this, the e.r. of **4k**-**4p** and consequently of **3k**-**3p** was inferred.

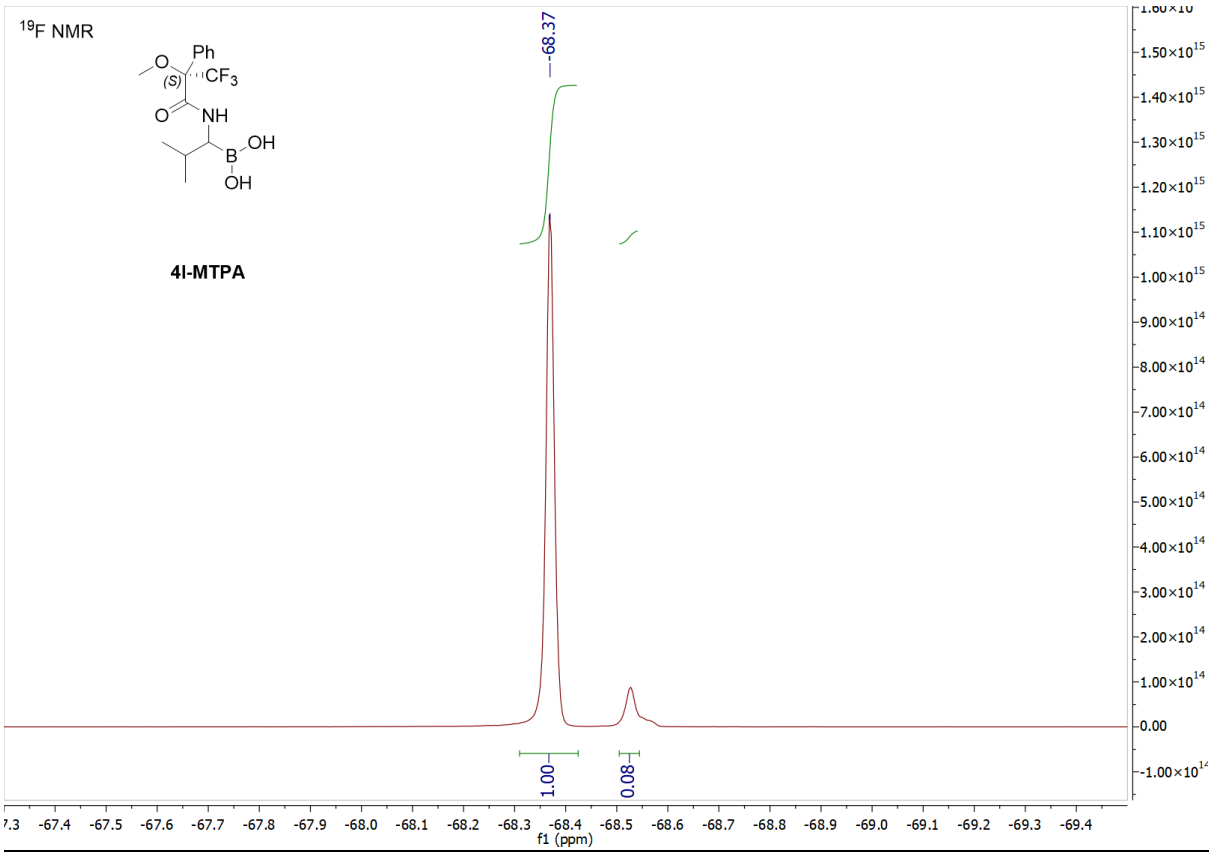
(Note that according to the Cahn-Ingold-Prelog rules, the priorities at the Mosher's chiral center change when -COCl moiety is converted to -CONH-, meaning that the same absolute stereochemistry is assigned the (*R*)-configuration in the acyl chloride and (*S*)-configuration in the amide.)



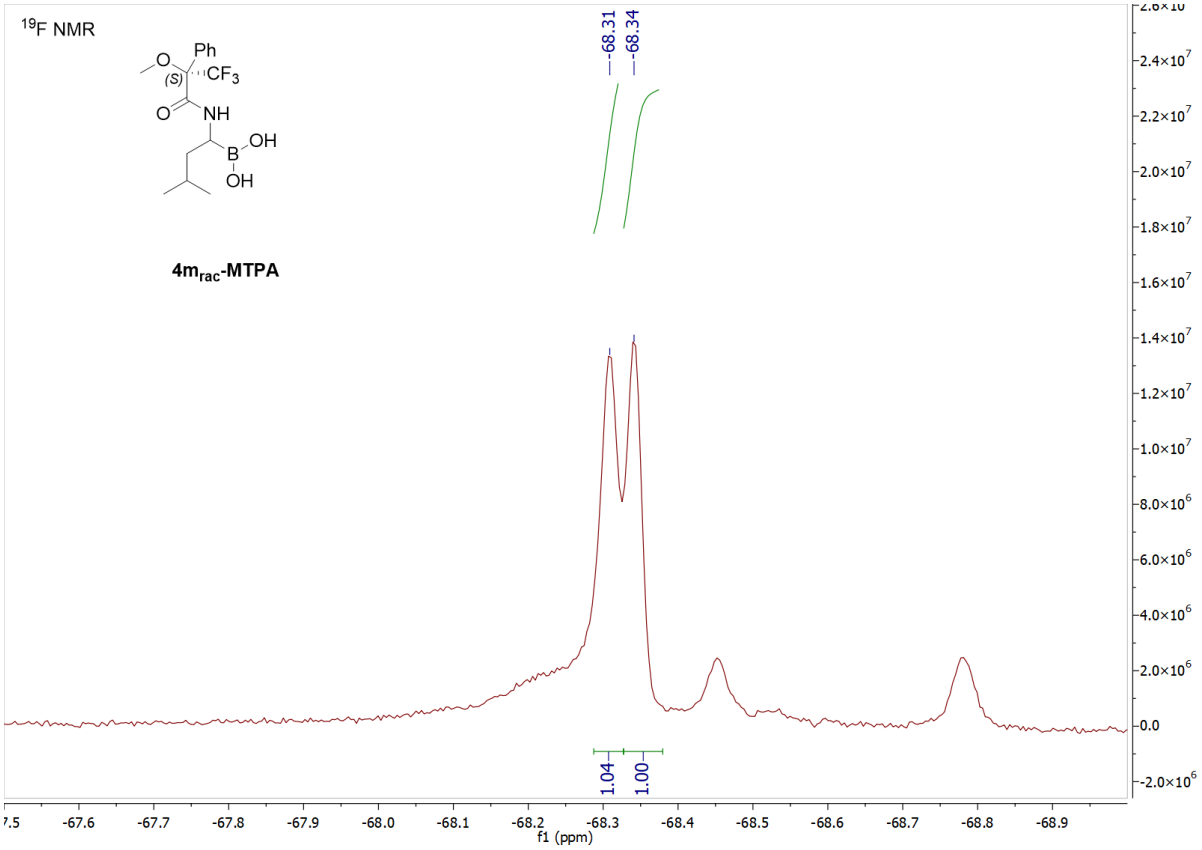


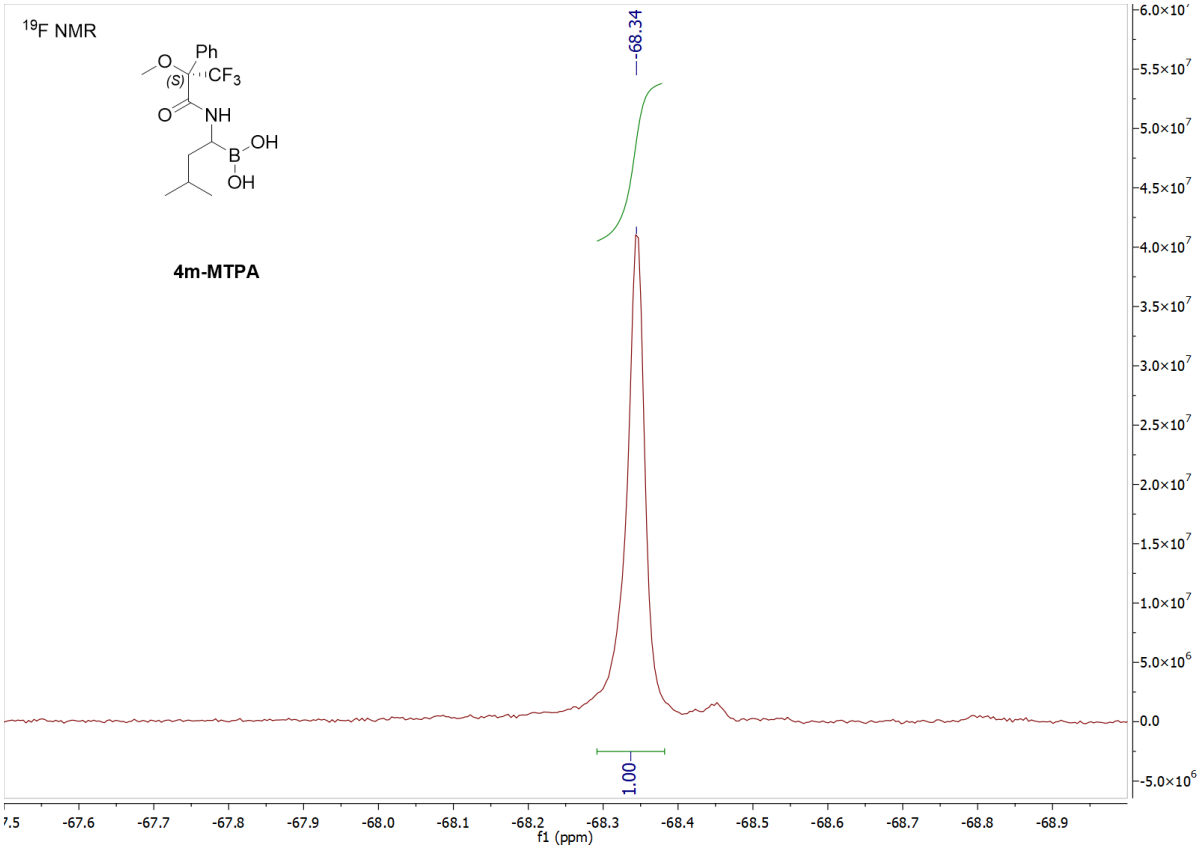
$$e.r. = \frac{1.00}{1.00 + 0.07} : \frac{0.07}{1.00 + 0.07} = 93:7$$



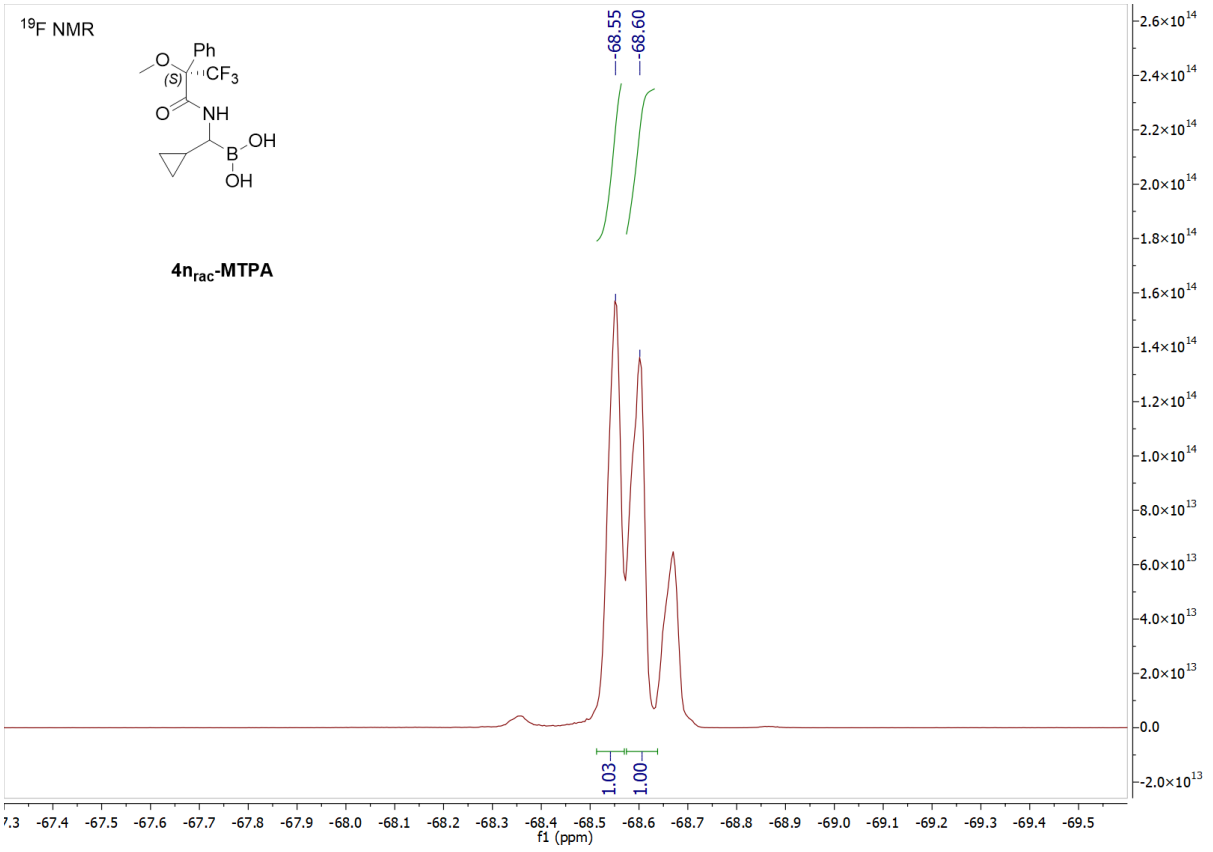


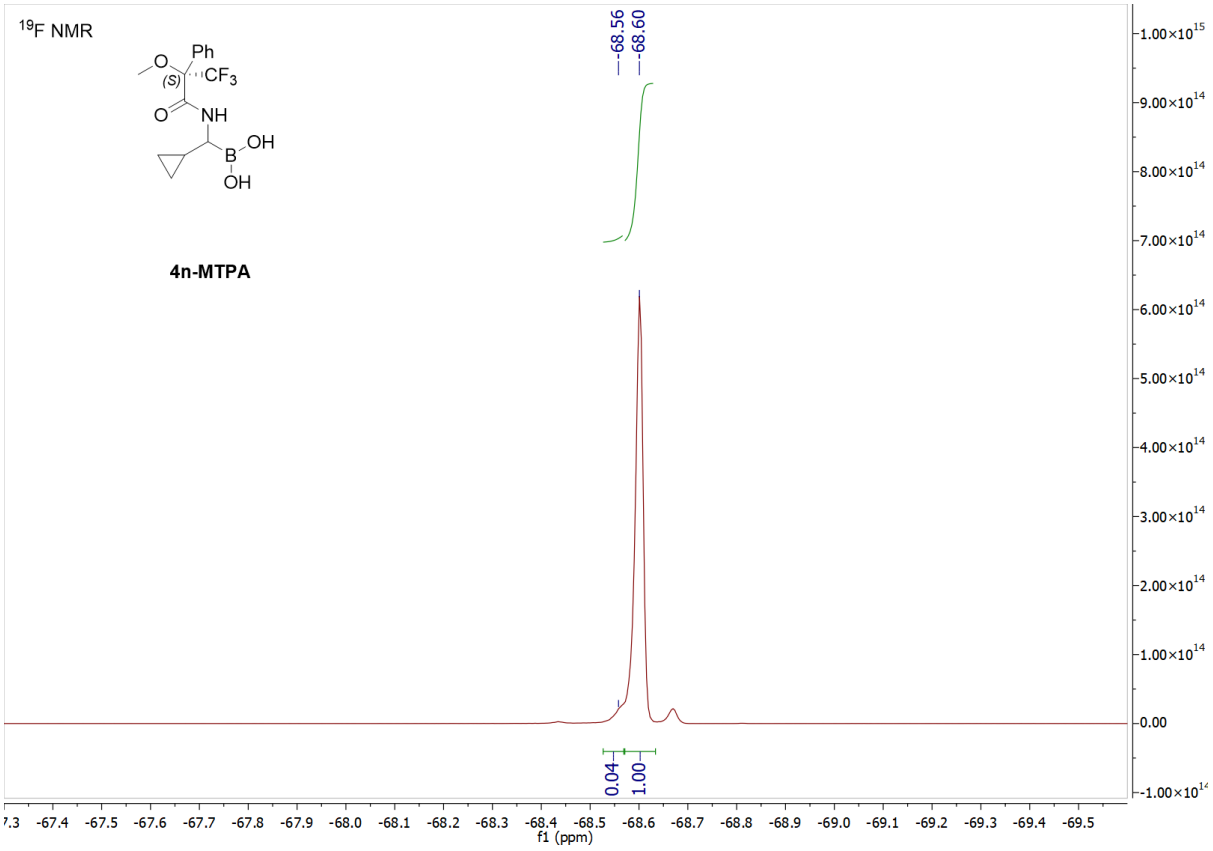
$$e.r. = \frac{1.00}{1.00 + 0.07} : \frac{0.07}{1.00 + 0.07} = 93:7$$


19F NMR
Ph
O
(S)
CF3
O
NH
B
OH
OH
4mrac-MTPA
-68.31
-68.34
1.04
1.00
f1 (ppm)

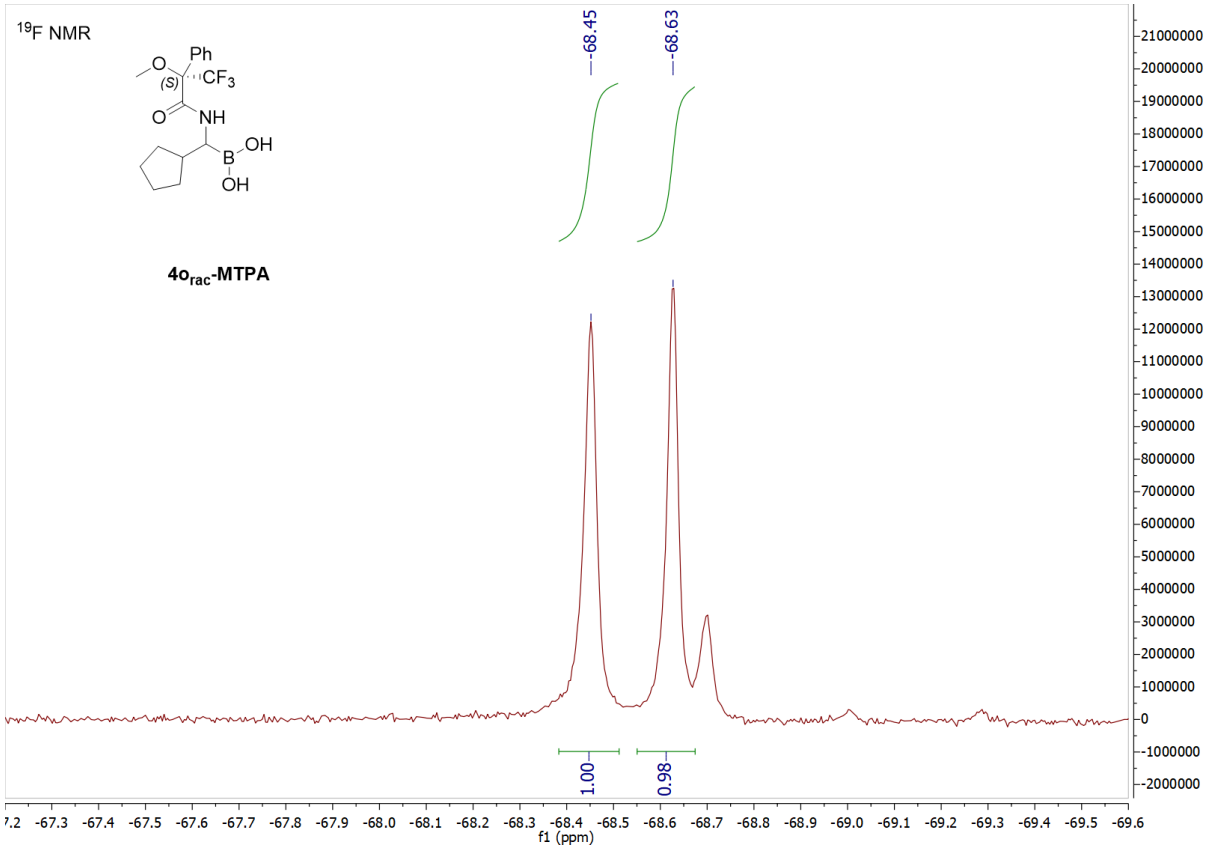

19F NMR
Ph
O
(S)
CF3
O
NH
B
OH
OH
4m-MTPA
-68.34
1.00
f1 (ppm)

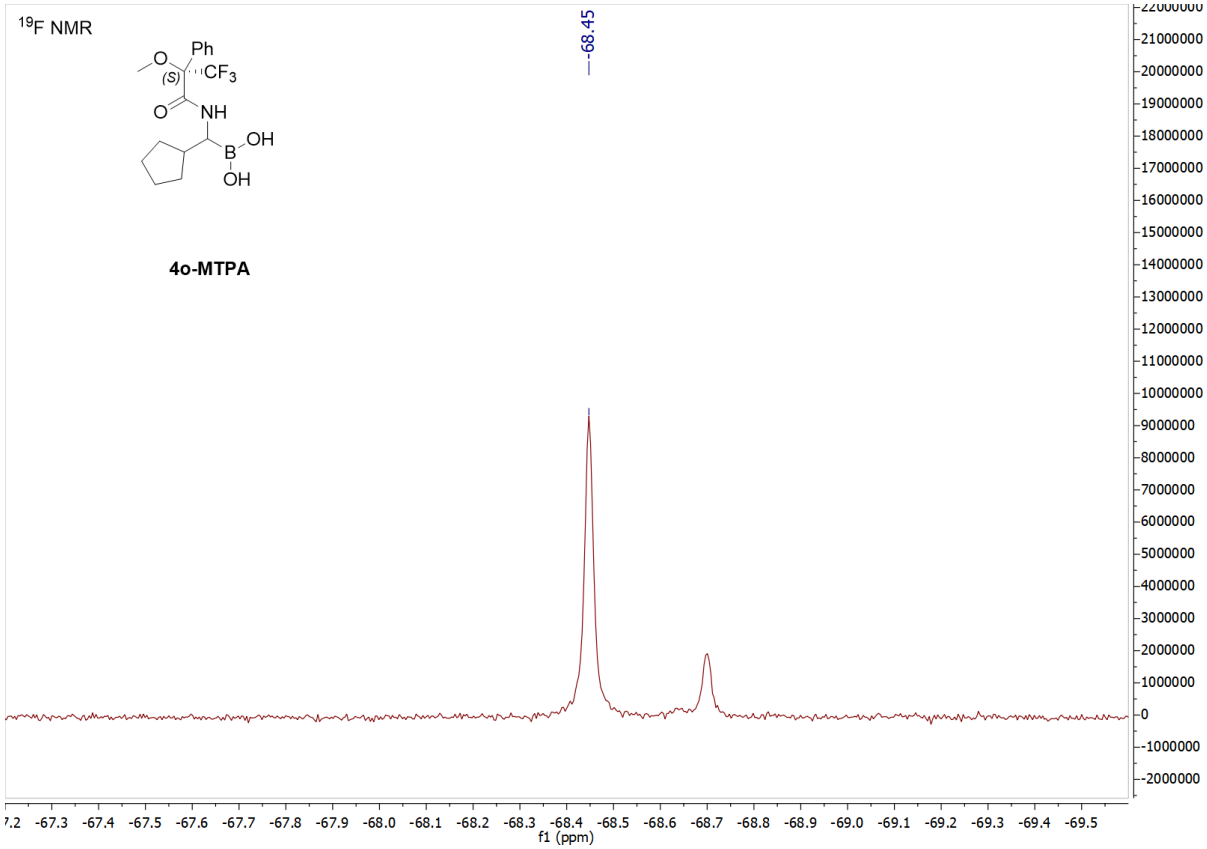
$e.r. = 99:1$



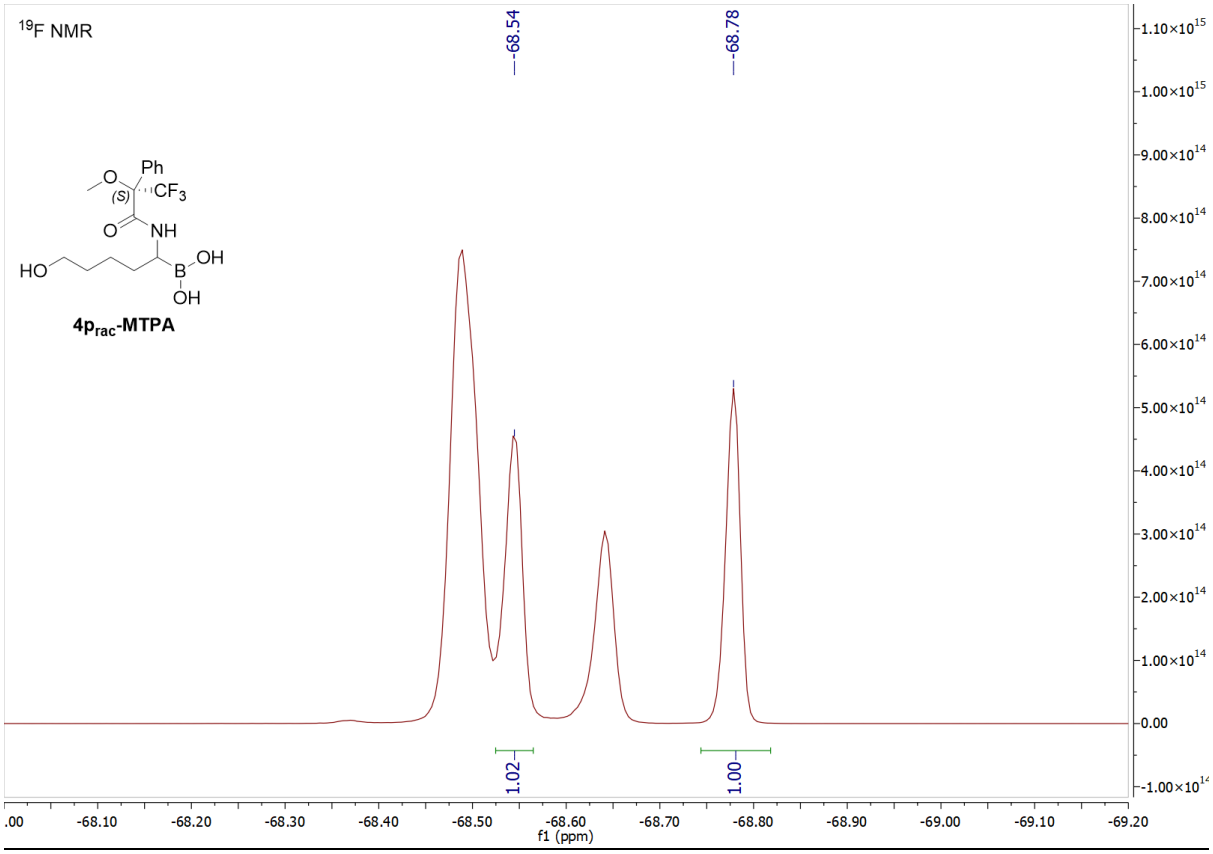


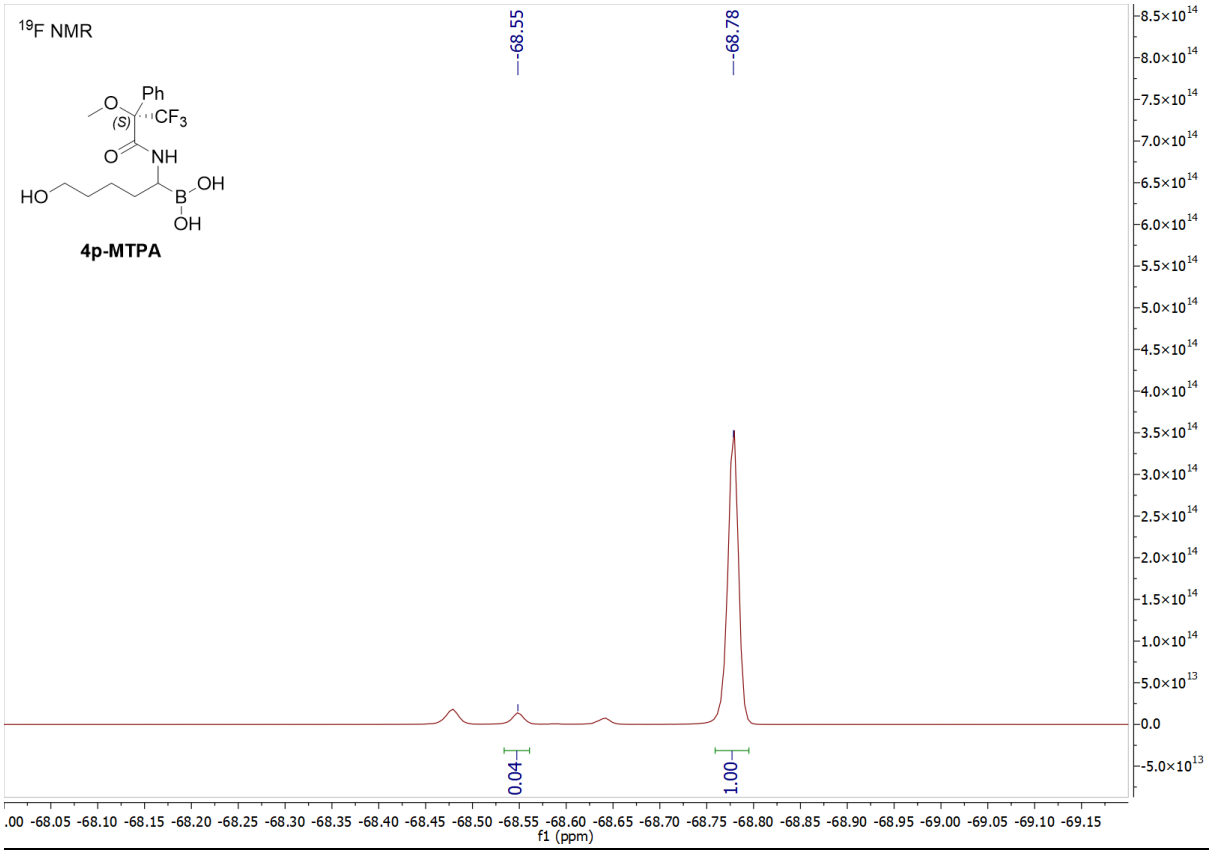
$$e.r. = \frac{1.00}{1.00 + 0.04} : \frac{0.04}{1.00 + 0.04} = 96:4$$


19F NMR
Ph
O
(S)
CF3
O
NH
B
OH
OH
4o-racMTPA
-68.45
-68.63
1.00
0.98
f1 (ppm)


19F NMR
Ph
O
(S)
CF3
O
NH
B
OH
OH
4o-MTPA
-68.45
f1 (ppm)

$e.r. = 99:1$

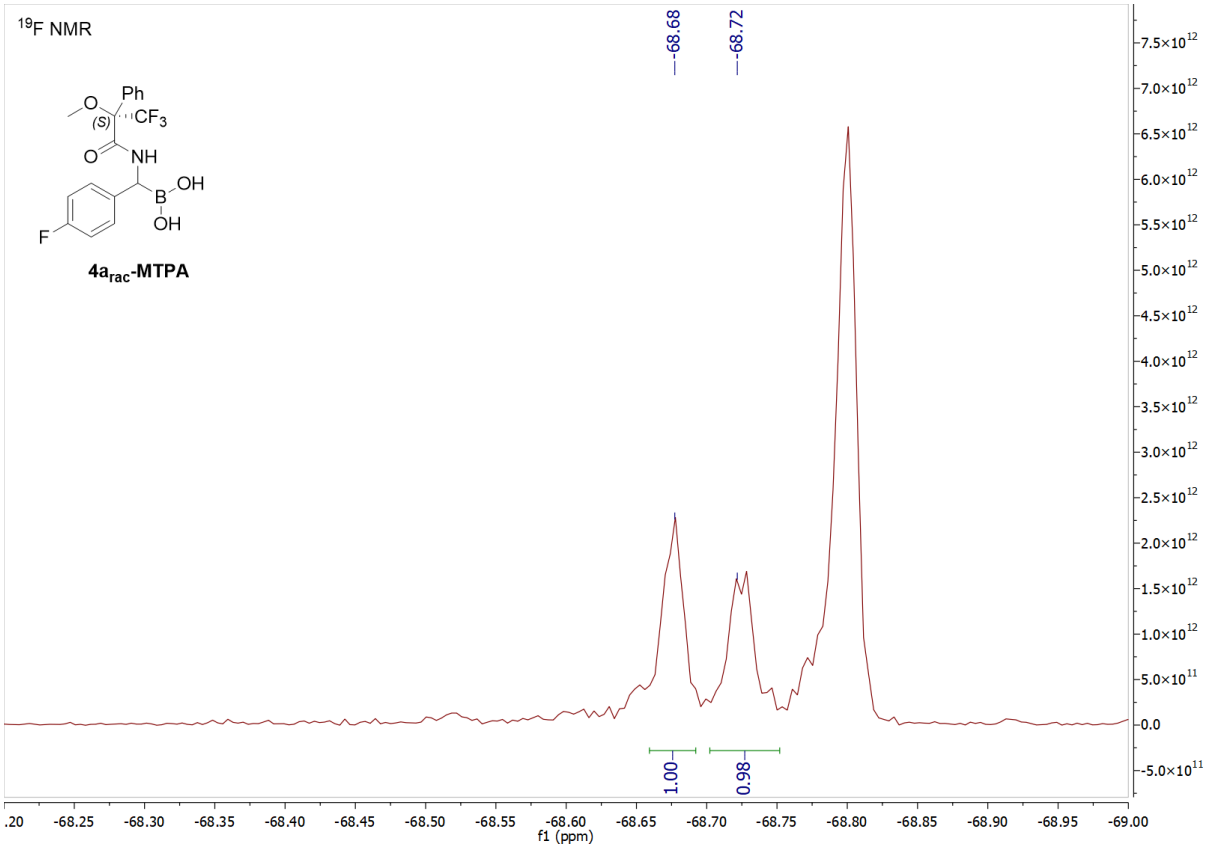


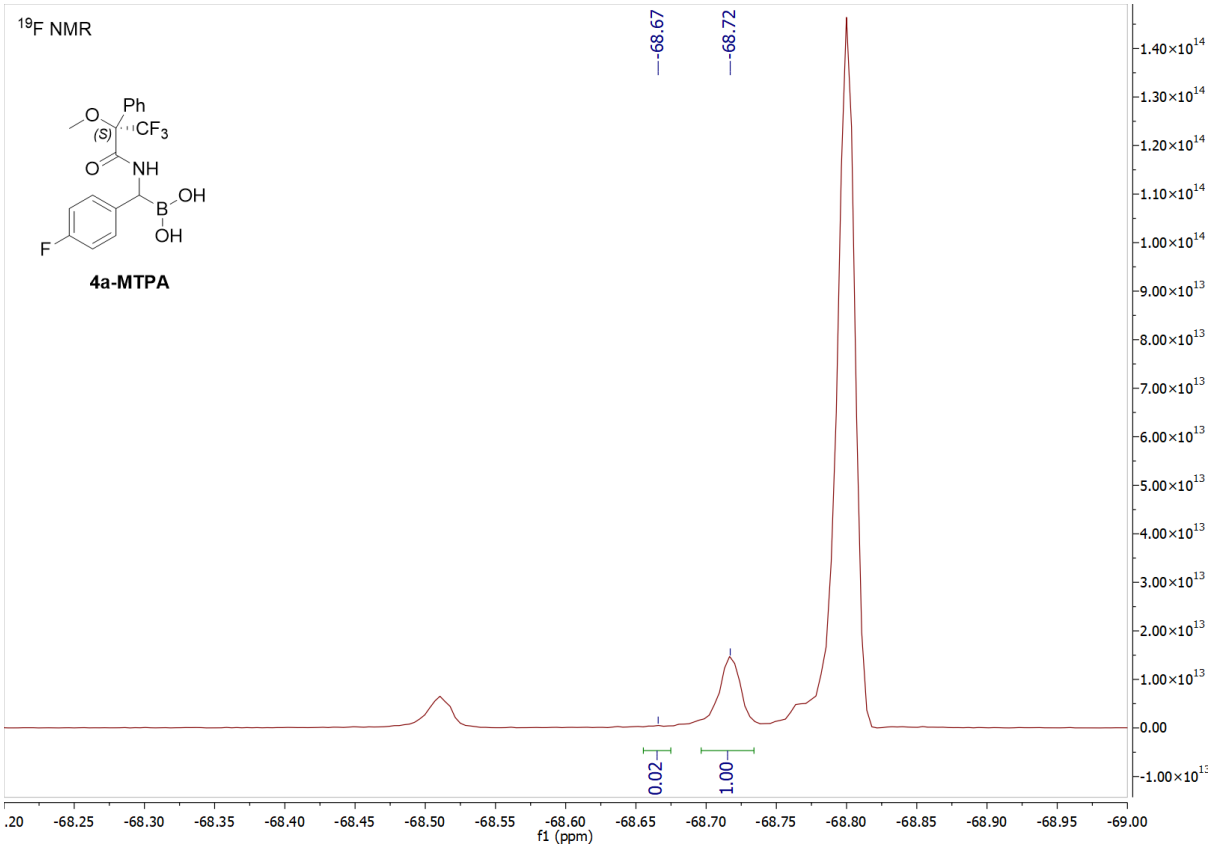


$$e.r. = \frac{1.00}{1.00 + 0.04} : \frac{0.04}{1.00 + 0.04} = 96:4$$

Validation of the Method for e.r. Determination

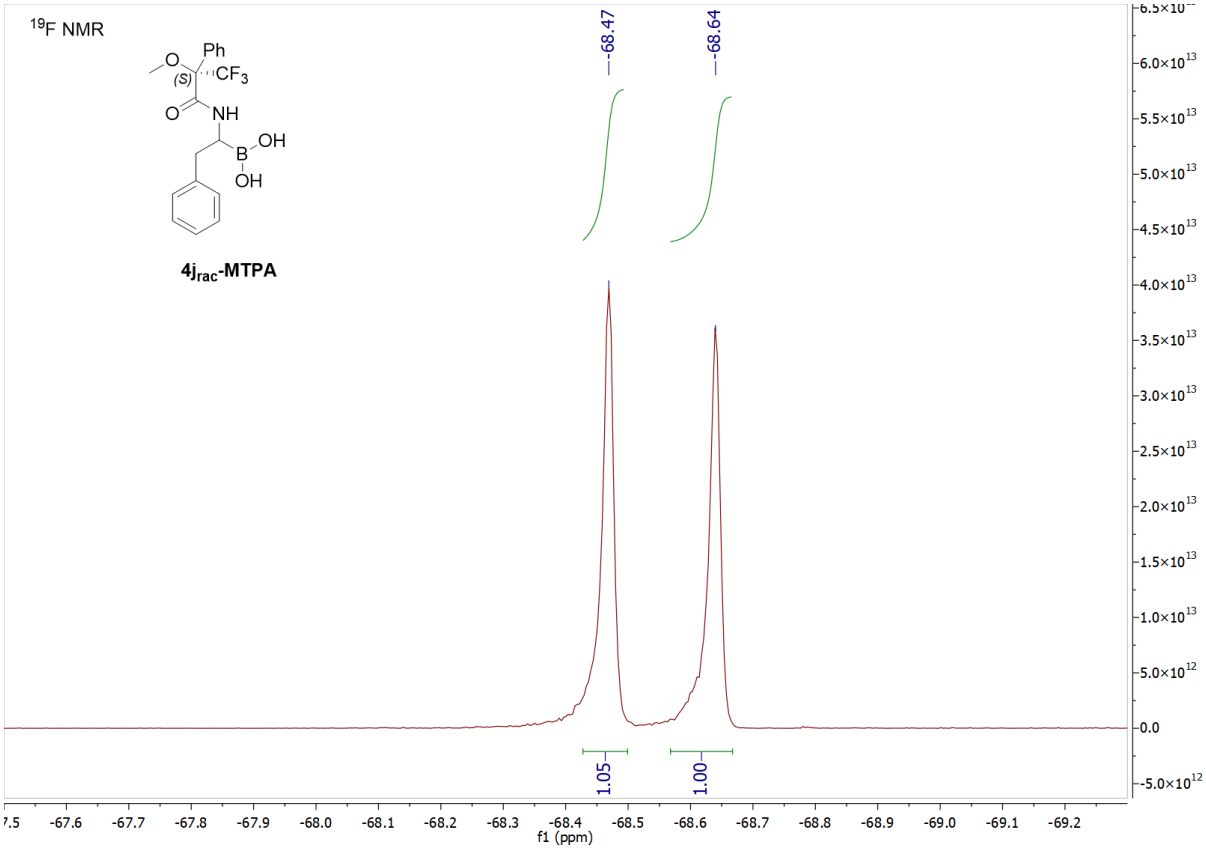
This method was validated by subjecting two chromophore-bearing pTAMs, namely **3a** and **3j**, to the same procedure. The e.r. for these two compounds had already been determined by chiral HPLC, so the results could be compared directly. When this method was attempted with aromatic aminoboronic acids **4b**-**4i**, a messy reaction was observed and integration of peaks in ^{19}F NMR was not possible. The reactions of **4a** and **4j** with (*R*)-(-)-MTPA-Cl validate that no epimerization occurs under the reaction conditions and that this method gives reliable e.r. values that can be extrapolated to compounds **3**. Compare e.r. of **3a** = 97:3 (determined by chiral HPLC in Section 4.3.1.) vs. e.r of **4a** = 98:2, and e.r. of **3j** = 94:6 (determined by chiral HPLC in Section 4.3.1.) vs. e.r. of **4j** = 94:6 as seen just below. For this reason, e.r. in compounds **4b**-**4i** was not determined.

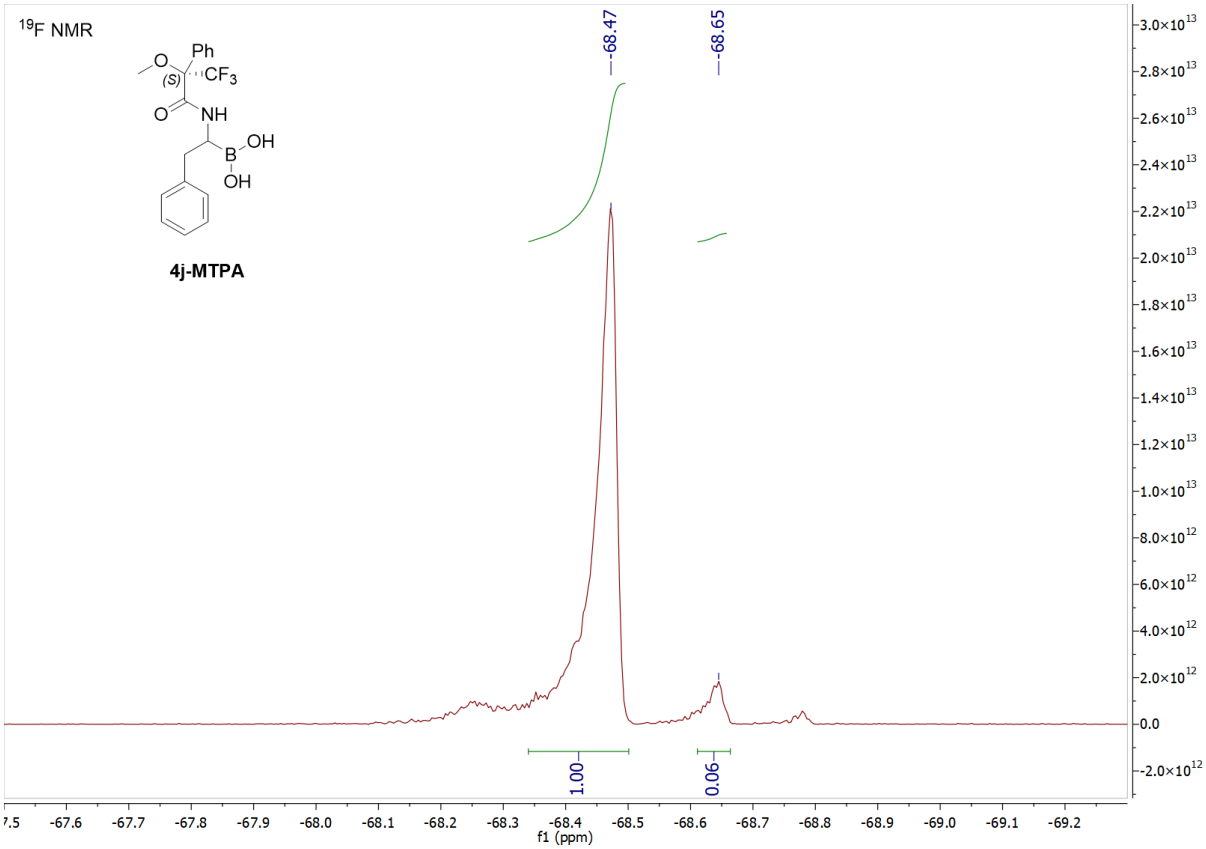




$$e.r. = \frac{1.00}{1.00 + 0.02} : \frac{0.02}{1.00 + 0.02} = 98:2$$

This corresponds to the HPLC-determined e.r. = 97:3.





$$e.r. = \frac{1.00}{1.00 + 0.06} : \frac{0.06}{1.00 + 0.06} = 94:6$$

This corresponds to the HPLC-determined e.r. = 94:6.

5. Synthesis of α-Aminoboronic Acids

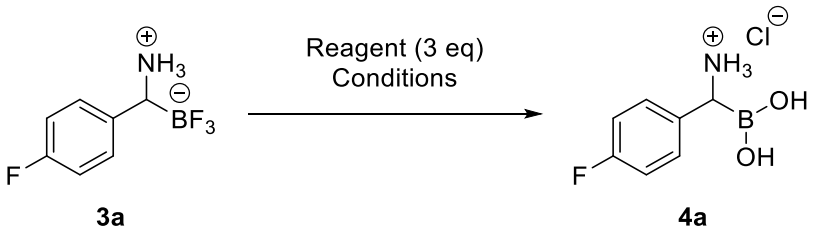
5.1. Development of a Novel Method to Convert pTAMs to α-Aminoboronic Acids

The hydrolysis of trifluoroborates to boronic acids has been well studied and several methods exist to effect this transformation.[S9] In Suzuki coupling of trifluoroborates, hydrolysis is usually achieved simply by the addition of Cs_2CO_3 and water, which generate the boronic acid *in situ*, however, there are vast differences in hydrolysis rates among structurally different substrates and parameters such as stirring bar size and flask shape have a significant effect.[S9f,h]

In contrast, the conversion of the trifluoroborate moiety in TAMs to boronic acids has been proved to be challenging, since none of the established methods (TMS-Cl/H_2O[S9a,b], silica gel[S9c], $FeCl_3$[S9d], alumina[S9e], Cs_2CO_3 [S9f]) worked in previous studies.[S3,S6] The only feasible method required a large excess (10 – 15 eq) of $SiCl_4$ under anhydrous conditions, followed by the addition of aqueous HCl.[S3, S6] While giving full conversions also in pTAMs, the paramagnetic salts that are generated as a side product were difficult to separate from the highly polar primary α-aminoboronic acids, resulting in significant line broadening in ^{1}H NMR spectra.[S3] For this reason, we sought to develop a more convenient and possibly milder and greener method.

General procedure for conditions screening

pTAM **3a** (19 mg, 0.1 mmol) was dissolved in the chosen solvent (0.05 M) and required reagents (3 eq.) and additives were added. Dry solvent was used in all cases, even when water was added to it – this was to ensure that water content was indeed as stated, since *pro analysis*-quality solvents can contain some water especially if the bottle has been opened before. The reaction mixture was left to stir at RT and was followed by ^{11}B NMR. The product was identified by a characteristic broad peak at approx. 28 ppm.



3a **4a**

Scheme S6. Optimization of conditions for conversion of **3a** to **4a**.

Table S6. Conditions screening for the synthesis of α-aminoboronic acids from pTAMs. Reactions conducted at 0.05 M concentration. [a]: side reaction, most probably protodeboronation observed *in situ* (5-10%). [b]: full conversion reached in 3 h.

Entry	Reagent	Additive	Solvent	Conversion (24 h) [%]
1	/	Cs_2CO_3 (1 eq.)	MeOH	0
2	/	Cs_2CO_3 (1 eq.)	MeOH (5% H_2O)	0
3	Silica gel	Cs_2CO_3 (1 eq.)	MeOH	0
4	Silica gel	Cs_2CO_3 (1 eq.)	MeOH (5% H_2O)	0
5	TMS-Cl	Cs_2CO_3 (1 eq.)	MeOH	Trace
6	TMS-Cl	Cs_2CO_3 (1 eq.)	MeOH (5% H_2O)	100[a]
7	HMDSO	Cs_2CO_3 (1 eq.)	MeOH (5% H_2O)	100 (decomp.)
8	HMDSO	2 M HCl (aq, 4 eq.)	MeOH	100 (pure **4a**)[b]
9	HMDSO	2 M HCl (aq, 2 eq.)	MeOH	100[a]

We hypothesized that the resistance of TAMs to established methods is due to their zwitterionic nature. For this reason, we conducted a series of experiments using Cs_2CO_3 (1 eq) as an additive to deprotonate the pTAM. Using only Cs_2CO_3 in MeOH or MeOH/water, no conversion was observed (entries 1 and 2), as well as there was no conversion when silica gel was added (entries 3 and 4, without and with water). When TMS-Cl was used as a reagent in dry MeOH, only trace amounts of the product were observed (entry 5). When conducting the same reaction with 5% water, full conversion of starting material was observed (entry 6). However, a small peak at cca. 18 ppm was observed in ^{11}B NMR spectrum, possibly indicating a low degree of base-mediated C-N migration/protodeboronation. In addition, TMS-Cl reacts with water, so we hypothesized that a hydrolysis product of TMS-Cl is actually responsible for the conversion, especially since only traces of **4a** were observed when the reaction was conducted in dry MeOH (entry 5). The most probable hydrolysis product at these conditions is hexamethyldisiloxane (HMDSO). A reaction with HMDSO and Cs_2CO_3 only resulted in decomposition of the starting material (entry 7), which can be attributed to the instability of α-aminoboronic acids in their free form, which is a well-known phenomenon.[S10] However, conducting the reaction with 2 M HCl (aq) instead of base, which can stabilize the amino moiety by trapping it as a hydrochloride salt, resulted in clean formation of the product **4a** (entry 8). If 2 eq. were used instead of 4 eq., signals indicative of protodeboronation were observed in NMR spectra *in situ* (entry 9). When TMS-Cl was used, it served also as a source of HCl, but not in a sufficient amount to fully prevent protodeboronation.

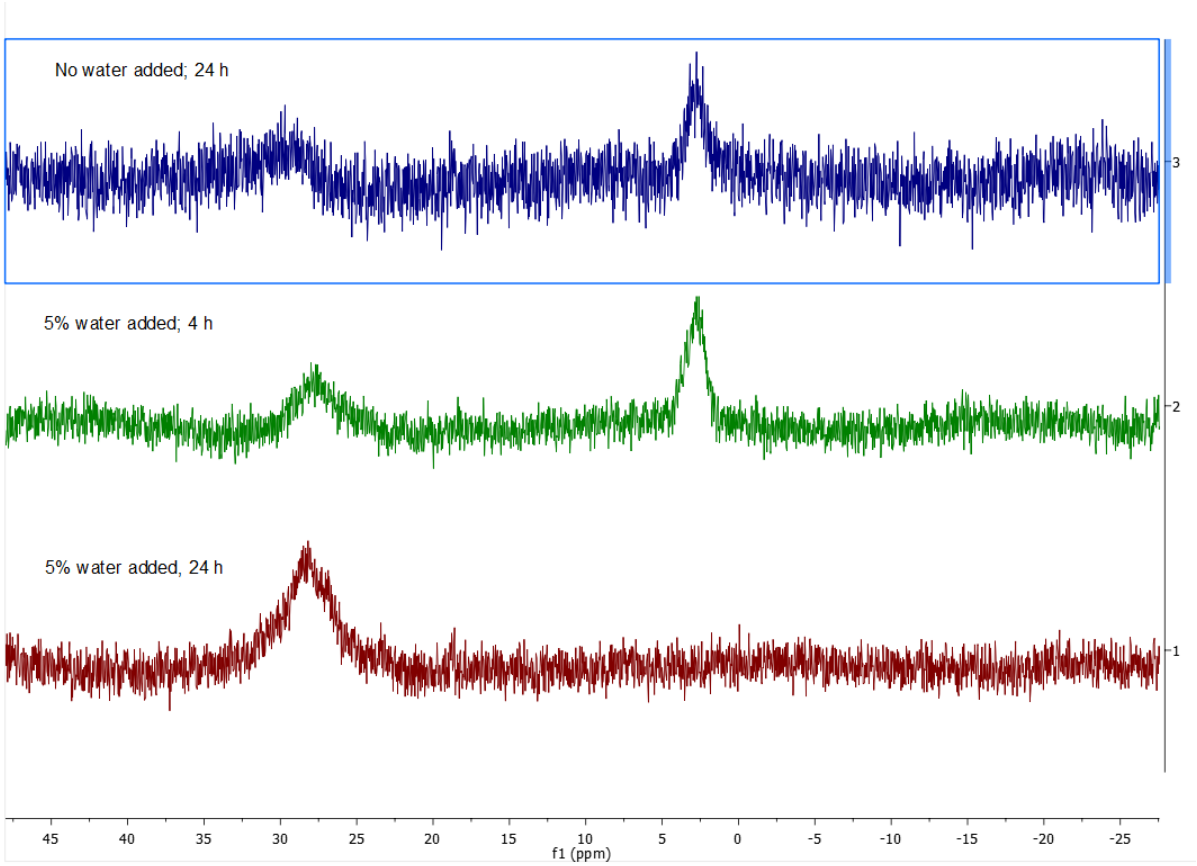


Figure S7. ^{11}B NMR spectra of reaction mixture for the reaction with TMS-Cl. Without water, only a slight peak for **4a** is observed (Table S6, entry 5). Upon the addition of water, **4a** is being formed after 4 h and full conversion is observed 24 h after the addition (Table S6, entry 6). Note a slight peak at cca. 18 ppm.

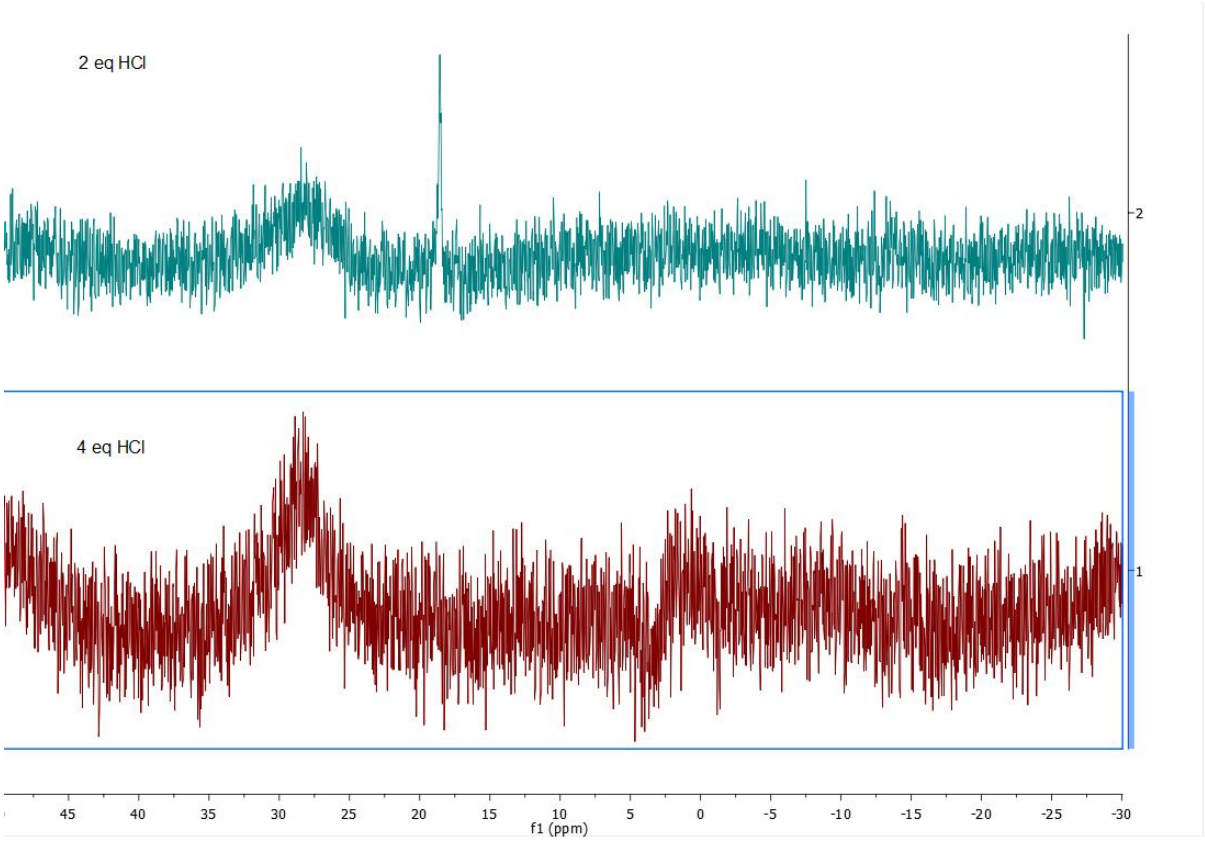


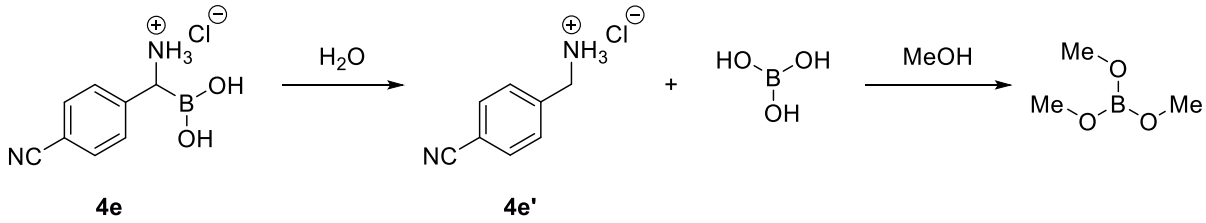
Figure S8. ^{11}B NMR spectra of reaction mixture for the reaction with HMDSO. The spectrum above represents the reaction conducted with 2 eq HCl (Table S6, entry 9) and the spectrum below the reaction with 4 eq HCl (Table S6, entry 8). In the latter case, **4a** is formed chemoselectively.

Under the optimized reaction conditions (3 eq. HMDSO, 4 eq. 2 M HCl, MeOH), the product required no purification besides the removal of volatiles on rotary evaporator, since all reagents and side products (most probably TMS-F and TMS-OH) are volatile and the reaction proceeded in a 100% chemoselective fashion. The isolation by evaporation only is highly desirable with small, highly polar and potentially unstable compounds such as α-aminoboronic acids, which cannot be easily separated even from inorganic salts. This operationally simple method is broad in scope, conducted in a green solvent (MeOH/water) and is even more valuable because it avoids the use of excess amounts of corrosive $SiCl_4$ or toxic TMS-Cl. Instead, it relies on the non-toxic HMDSO, which is known to have been injected into living mammals serving as an MRI probe without any apparent toxic effects.[S11]

With the optimized conditions in hand, all pTAMs **3a**-**3p** were subjected to this procedure. Quantitative yields were achieved in all cases as the reactions proceeded quickly (2 – 4 h), chemoselectively, and no purification was required besides evaporation. The only exception was the substrate **3e**, which underwent protodeboronation even when 10 eq. HCl were used, furnishing *p*-cyanobenzylammonium chloride **4e'**. This is most probably due to the inherent instability of

compound **4e**, since *in situ* ^{11}B NMR revealed the formation of a low peak at cca. 27 ppm (corresponding to **4e**) along with a high, sharp peak at cca. 18 ppm at 1 h reaction time. In 3 h, the peak at 27 ppm disappeared, leaving only the peak at 18 ppm, and upon evaporation, no signal was observed in ^{11}B NMR.

The compound which gives a signal at 18 ppm in ^{11}B NMR, but disappears upon solvent evaporation, is most probably trimethylborate. It is a volatile product of boric acid, which is formed upon protodeboronation, and MeOH, which is the reaction solvent. The reported spectral data for trimethylborate align with our hypothesis.[S12]



4e **4e'**

Scheme S7. Protodeboronation of **4e** and the probable fate of boron-containing moiety.

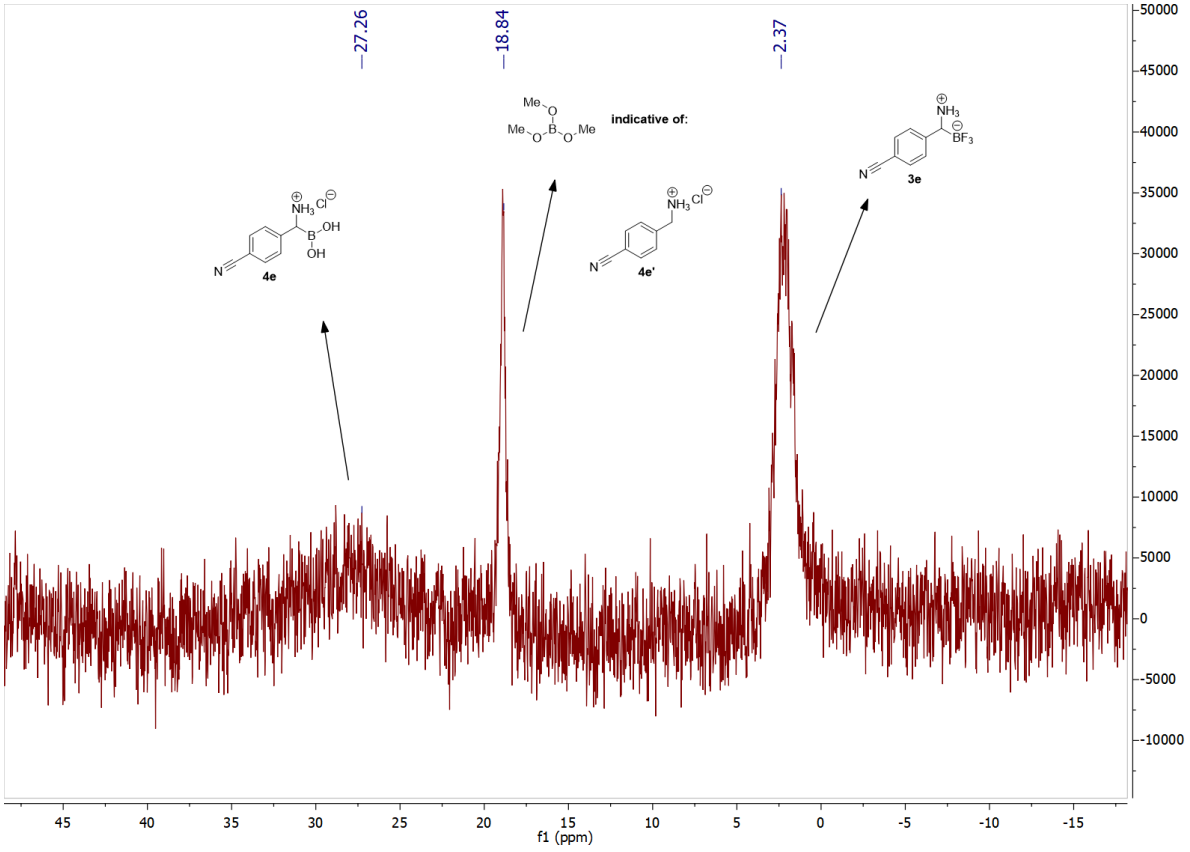


Figure S9. Attempted synthesis of **4e**, ^{11}B NMR spectrum recorded *in situ* at 1 h reaction time showing the formation of **4e** and at the same time its protodeboronation while the reaction is not complete yet.

5.2. General Procedure for the Synthesis of α-Aminoboronic Acids

pTAM **3** was dissolved in MeOH (0.05 M). To this solution, HCl (2 M aq, 4 eq) and HMDSO (3 eq) were added and the solution was left to stir at RT until the reaction was complete (monitored by ^{11}B NMR of crude reaction mixture – a 200 μL sample was diluted with 300 μL MeOD), typically 2 – 4 h. Then, the volatiles were removed under reduced pressure, taking care not to heat the flask over 30 °C. The residue was evaporated to dryness on an oil pump (0.02 mbar, RT, 30 min), to afford the α-aminoboronic acid **4** as a hydrochloride salt. Note that all spectra below are recorded directly after evaporation and that no further purification was necessary. In some cases, a partially suppressed signal for the $N\underline{H}_3^+$ protons can be seen even though the spectra were recorded in MeOD. This occured especially when the ^{1}H NMR spectrum was recorded immediately after the dissolution in MeOD and the H-D exchange with the protic $N\underline{H}_3^+$ moiety was not yet complete.

While α-aminoboronic acids are known to be labile compounds, they were stable enough to allow full characterization. However, when stored on benchtop or in a solution, they began to decompose and signs indicative of protodeboronation were observed in NMR spectra. For this reason, they should be stored at -20 °C, where no decomposition occurred when analyzed after two months.

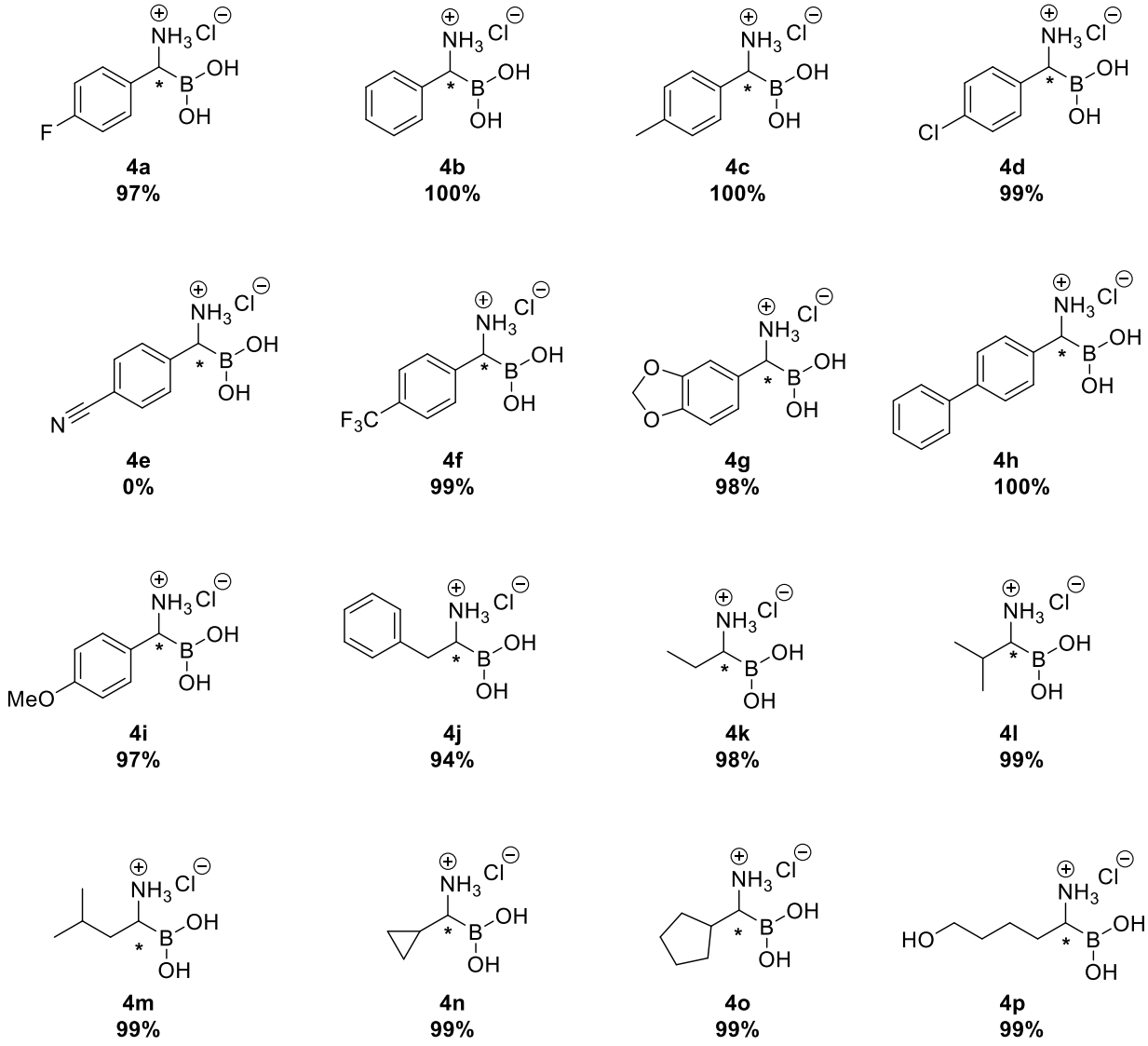
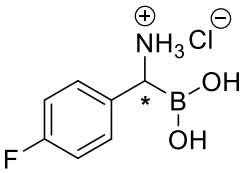


Figure S10. List of synthesized α-aminoboronic acids. **4e** could not be synthesized, 4-cyanobenzylamine was isolated instead in 95% yield.

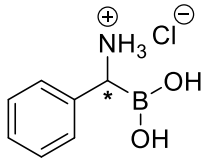
Borono(4-fluorophenyl)methanaminium chloride (4a)



Synthesized according to the General Procedure from **3a** (19 mg, 0.1 mmol) to afford **4a** after 3 h as a white foam-like solid (20 mg, 97% yield). **^{1}H NMR** (400 MHz, MeOD) δ 4.00 (br s, 1H, C<u>H</u>), 7.14 – 7.21 (m, 2H, Ar-<u>H</u>), 7.42 – 7.49 (m, 2H, Ar-<u>H</u>), 7.99 (br s, 0.5H, partially suppressed N<u>H</u>$_3^+$). **^{11}B NMR** (128 MHz, MeOD) δ 28.17. **^{13}C NMR** (101 MHz, MeOD) δ 117.28 (d, $^{2}J_{CF}$ = 21.9 Hz), 132.30, 132.60 (d, $^{3}J_{CF}$ =

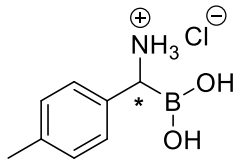
6.9 Hz), 164.34 (d, $^{1}J_{CF}$ = 247.2 Hz). **^{19}F NMR** (376 MHz, MeOD) δ -114.52. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 1229, 1394, 1513, 3046, 3385. **HRMS** (ESI^{+}): calc. for $C_7H_{10}O_2NB$ [M-Cl]$^{+}$: 170.0783, found: 170.0782.

Borono(phenyl)methanaminium chloride (4b)



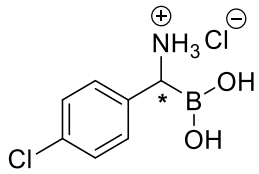
Synthesized according to the General Procedure from **3b** (17.5 mg, 0.1 mmol) to afford **4b** after 3 h as a white foam-like solid (19 mg, 100% yield). **^{1}H NMR** (400 MHz, MeOD) δ 4.00 (s, 1H, C<u>H</u>), 7.36 – 7.48 (m, 5H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 28.20. **^{13}C NMR** (101 MHz, MeOD) δ 46 (br m, extracted from ^{1}H-^{13}C HSQC spectrum), 129.85, 130.27, 130.47, 136.30. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 1002, 1292, 1309, 1333, 1374, 1399, 1454, 1494, 2894, 2990, 3140, 3197. **HRMS** (ESI^{+}): calc. for $C_7H_{11}O_2NB$ [M-Cl]$^{+}$: 152.0877, found: 152.0877.

Borono(4-tolyl)methanaminium chloride (4c)



Synthesized according to the General Procedure from **3c** (19 mg, 0.1 mmol) to afford **4c** after 3 h as a white foam-like solid (20 mg, 100% yield). **^{1}H NMR** (400 MHz, MeOD) δ 2.35 (s, 3H, C<u>H</u>$_3$), 3.98 (br s, 1H, C<u>H</u>), 7.26 (d, *J* = 7.9 Hz, 2H, Ar-<u>H</u>), 7.31 (d, *J* = 8.0 Hz, 2H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 27.97. **^{13}C NMR** (101 MHz, MeOD) δ 21.16, 45.28 (br m), 130.38, 131.14, 132.94, 140.16. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 813, 1043, 1158, 1227, 1271, 1300, 1321, 1400, 3000, 3012. **HRMS** (ESI^{+}): calc. for $C_8H_{13}O_2NB$ [M-Cl]$^{+}$: 166.1034, found: 166.1033.

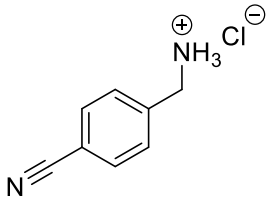
Borono(4-chlorophenyl)methanaminium chloride (4d)



Synthesized according to the General Procedure from **3d** (21 mg, 0.1 mmol) to afford **4d** after 4 h as a white foam-like solid (22 mg, 99% yield). **^{1}H NMR** (400 MHz, MeOD) δ 3.96 (br s, 1H, C<u>H</u>), 7.39 – 7.46 (m, 4H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 28.12. **^{13}C NMR** (101 MHz, MeOD) δ 45.37 (br m), 130.47,

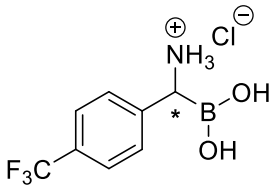
131.84, 135.36, 135.71. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 822, 1014, 1093, 1224, 1294, 1317, 1411, 1494, 3035. **HRMS** (ESI$^+$): calc. for $C_7H_{10}O_2NBCl$ [M-Cl]$^+$: 186.0488, found: 186.0487.

4-cyanobenzylammonium chloride (4e')



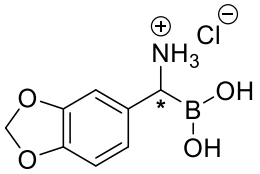
Obtained in an attempt to synthesize **4e** from **3e** (20 mg, 0.1 mmol) according to the General Procedure. Upon evaporation of volatiles, **4e'** was obtained as an off-white solid (16 mg, 95 % yield). **^{1}H NMR** (400 MHz, MeOD) δ 4.24 (s, 2H, C$\underline{H}_2$), 7.67 – 7.71 (m, 2H), Ar-$\underline{H}$), 7.79 – 7.85 (m, 2H, Ar-$\underline{H}$). No signal in ^{11}B NMR spectrum. **HRMS** (ESI$^+$): calc. for $C_8H_9N_2$ [M-Cl]$^+$: 133.0760, found: 133.0761. Known compound.[S13]

Borono(4-(trifluoromethyl)phenyl)methanaminium chloride (4f)



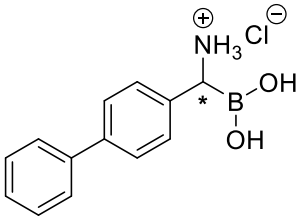
Synthesized according to the General Procedure from **3f** (24 mg, 0.1 mmol) to afford **4f** after 4 h as a white foam-like solid (25 mg, 99% yield). **^{1}H NMR** (400 MHz, MeOD) δ 4.10 (s, 1H), 7.64 (d, *J* = 8.1 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 2H). **^{11}B NMR** (128 MHz, MeOD) δ 27.79. **^{13}C NMR** (101 MHz, MeOD) δ 45.60 (br m), 125.42 (q, $^1J_{CF}$ = 271.4 Hz), 127.17 (q, $^3J_{CF}$ = 3.8 Hz), 130.67, 131.62 (q, $^2J_{CF}$ = 32.4 Hz), 141.14. **^{19}F NMR** (376 MHz, MeOD) δ -64.19. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 845, 1016, 1068, 1112, 1165, 1324, 1408, 1619, 2949. **HRMS** (ESI$^+$): calc. for $C_8H_{10}O_2NBF_3$ [M-Cl]$^+$: 220.0751, found: 220.0748.

(Benzo[*d*][1,3]dioxol-5-yl)boronomethanaminium chloride (4g)



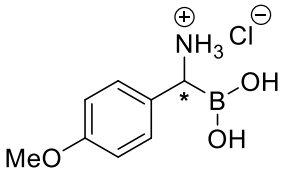
Synthesized according to the General Procedure from **3g** (22 mg, 0.1 mmol) to afford **4g** after 3 h as a white foam-like solid (23 mg, 98% yield). **^{1}H NMR** (400 MHz, MeOD) δ 3.94 (br s, 1H, C<u>H</u>), 5.99 (s, 2H, C<u>H</u>$_2$), 6.84 – 6.94 (m, 3H, Ar-<u>H</u>), 7.87 (br s, 1H, partially suppressed N<u>H</u>$_3^+$). **^{11}B NMR** (128 MHz, MeOD) δ 28.07. **^{13}C NMR** (101 MHz, MeOD) δ 45 (br m, extracted from ^{1}H-^{13}C HSQC spectrum), 102.93, 109.91, 110.41, 124.33, 129.53, 149.63, 149.91. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 811, 914, 1037, 1089, 1245, 1386, 1441, 1485, 1655, 2983. **HRMS** (ESI$^+$): calc. for $C_8H_{11}O_4NB$ [M-Cl]$^+$: 196.0776, found: 196.0776.

[1,1'-Biphenyl]-4-yl(borono)methanaminium chloride (4h)



Synthesized according to the General Procedure from **3h** (21 mg, 0.1 mmol) to afford **4h** after 3 h as a white foam-like solid (22 mg, 100% yield). Note: **3h** is not completely soluble under the reaction conditions, but dissolves within 1 h as it converts to the product, which is well soluble. **^{1}H NMR** (400 MHz, MeOD) δ 4.08 (br s, 1H, C<u>H</u>), 7.33 – 7.39 (m, 1H, Ar-<u>H</u>), 7.42 – 7.48 (m, 2H, Ar-<u>H</u>), 7.49 – 7.54 (m, 2H, Ar-<u>H</u>), 7.59 – 7.66 (m, 2H, Ar-<u>H</u>), 7.68 – 7.75 (m, 2H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 29.28. **^{13}C NMR** (101 MHz, MeOD) δ 45.79 (br m), 127.95, 128.79, 128.86, 129.99, 130.58, 141.45, 142.88. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 760, 839, 1006, 1487, 1603, 2926. **HRMS** (ESI$^+$): calc. for $C_{13}H_{15}O_2NB$ [M-Cl]$^+$: 228.1190, found: 228.1190.

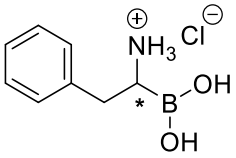
Borono(4-methoxyphenyl)methanaminium chloride (4i)



Synthesized according to the General Procedure from **3i** (20 mg, 0.1 mmol) to afford **4i** after 4 h as a white foam-like solid (20.5 mg, 97% yield). **^{1}H NMR** (400 MHz, MeOD) δ 3.81 (s, 3H, C<u>H</u>$_3$), 3.96 (br s, 1H, CH), 6.95 – 7.02 (m, 2H, Ar-<u>H</u>), 7.31 – 7.37 (m, 2H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 28.54. **^{13}C**

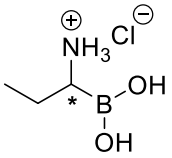
NMR (101 MHz, MeOD) δ 44.96 (br m), 55.82, 115.85, 127.72, 131.92, 161.65. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 830, 1027, 1179, 1248, 1403, 1515, 1612, 2839, 3006. **HRMS** (ESI$^+$): calc. for $C_8H_{10}O_3B$ [M-NH_2Cl]$^+$: 165.0718, found: 165.0719.

1-Borono-2-phenylethan-1-aminium chloride (4j)



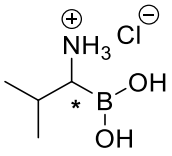
Synthesized according to the General Procedure from **3j** (19 mg, 0.1 mmol) to afford **4j** after 3 h as a white foam-like solid (19 mg, 94% yield). **^{1}H NMR** (400 MHz, MeOD) δ 2.91 – 3.10 (m, 3H, C<u>H</u>-B + C<u>H_2</u> overlapping), 7.25 – 7.31 (m, 3H, Ar-<u>H</u>), 7.33 – 7.38 (m, 2H, Ar-<u>H</u>). **^{11}B NMR** (128 MHz, MeOD) δ 28.60. **^{13}C NMR** (101 MHz, MeOD) δ 36.72, 42.50 (br m), 128.34, 130.01, 130.16, 138.07. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 698, 1155, 1234, 1279, 1423, 3028, 3349. **HRMS** (ESI$^+$): calc. for $C_8H_{13}O_2NB$ [M-Cl]$^+$: 166.1034, found: 166.1035.

1-Borono-propan-1-aminium chloride (4k)



Synthesized according to the General Procedure from **3k** (13 mg, 0.1 mmol) to afford **4k** after 2h as a white foam-like solid (14 mg, 98% yield). **^{1}H NMR** (400 MHz, MeOD) δ 1.02 (t, *J* = 7.5 Hz, 3H, C<u>H_3</u>), 1.67 – 1.85 (m, 2H, C<u>H_2</u>), 2.78 (br s, 1H, C<u>H</u>), 7.50 (s, 1.2H, N<u>H_3^+</u>, partially suppressed). **^{11}B NMR** (128 MHz, MeOD) δ 28.74. **^{13}C NMR** (101 MHz, MeOD) δ 11.23, 23.59, 42 (br m, extracted from ^{1}H-^{13}C HSQC spectrum). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 1325, 1410, 1615, 2958, 3064. **HRMS** (ESI$^+$): calc. for $C_3H_{11}O_2NB$ [M-Cl]$^+$: 104.0877, found: 104.0882.

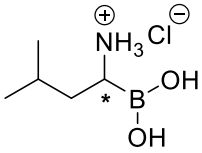
1-Borono-2-methylpropan-1-aminium chloride (4l)



Synthesized according to the General Procedure from **3l** (14 mg, 0.1 mmol) to afford **4l** after 2h as a white foam-like solid (15 mg, 99% yield). **^{1}H NMR** (400 MHz, MeOD) δ 1.04 (t, *J* = 5.9 Hz, 6H, (C<u>H_3</u>)$_2$),

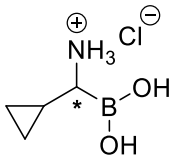
2.07 (h, *J* = 6.8 Hz, 1H, C<u>H</u>), 2.66 (br d, *J* = 112.0 Hz, 1H, C<u>H</u>-B). **^{11}B NMR** (128 MHz, MeOD) δ 28.64. **^{13}C NMR** (101 MHz, MeOD) δ 19.74, 20.15, 29.92, 45 – 48 (br m, extracted from ^{1}H-^{13}C HSQC spectrum). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 1043, 1248, 1297, 1387, 1413, 1464, 2963, 3131. **HRMS** (ESI^{+}): calc. for $C_4H_{13}O_2NB$ [M-Cl]$^{+}$: 118.1034, found: 118.1037.

1-Borono-3-methylbutan-1-aminium chloride (4m)



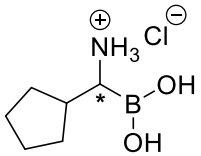
Synthesized according to the General Procedure from **3m** (15 mg, 0.1 mmol) to afford **4m** after 2h as a white foam-like solid (16 mg, 99% yield). **^{1}H NMR** (400 MHz, MeOD) δ 0.97 (dd, *J* = 6.6, 1.2 Hz, 6H, (C<u>H</u>$_3$)$_2$), 1.46 – 1.63 (m, 2H, C<u>H</u>$_2$), 1.72 (dh, *J* = 8.6, 6.4 Hz, 1H, C<u>H</u>), 2.85 (br s, 1H, C<u>H</u>-B). **^{11}B NMR** (128 MHz, MeOD) δ 29.06. **^{13}C NMR** (101 MHz, MeOD) δ 21.94, 23.36, 25.86, 39 (br m, extracted from ^{1}H-^{13}C HSQC spectrum) 39.45. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 1043, 1248, 1298, 1387, 1413, 1464, 2963, 3130. **HRMS** (ESI^{+}): calc. for $C_5H_{15}O_2NB$ [M-Cl]$^{+}$: 132.1190, found: 132.1190. Known compound.[S14a]

Borono(cyclopropyl)methanaminium chloride (4n)



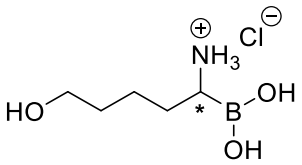
Synthesized according to the General Procedure from **3n** (14 mg, 0.1 mmol) to afford **4n** after 2h as a white foam-like solid (15 mg, 99% yield). **^{1}H NMR** (400 MHz, MeOD) δ 0.36 – 0.54 (m, 2H, C<u>H</u>$_2$), 0.62 – 0.73 (m, 2H, C<u>H</u>$_2$), 0.95 – 1.06 (m, 1H, C<u>H</u>), 2.27 (br d, *J* = 10.0 Hz, 1H, C<u>H</u>-B), 7.59 (br s, 0.3H, partially suppressed N<u>H</u>$_3^{+}$). **^{11}B NMR** (128 MHz, MeOD) δ 28.33. **^{13}C NMR** (101 MHz, MeOD) δ 4.77, 5.11, 11.64, 45.85 (br m). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 1028, 1219, 1293, 1398, 3080, 3337. **HRMS** (ESI^{+}): calc. for $C_4H_{11}O_2NB$ [M-Cl]$^{+}$: 116.0877, found: 116.0881.

Borono(cyclopentyl)methanaminium chloride (4o)



Synthesized according to the General Procedure from **3o** (17 mg, 0.1 mmol) to afford **4o** after 2h as a white foam-like solid (19 mg, 99% yield). Note: **3o** is not completely soluble under the reaction conditions, but dissolves within 30 min as it converts to the product, which is well soluble. **^{1}H NMR** (400 MHz, MeOD) δ 1.24 – 1.38 (m, 2H, C$\underline{H}_2$), 1.54 – 1.91 (m, 6H, 3×C$\underline{H}_2$), 2.05 – 2.17 (m, 1H, C$\underline{H}$), 2.73 (br s, 1H, C$\underline{H}$-B). **^{11}B NMR** (128 MHz, MeOD) δ 28.64. **^{13}C NMR** (101 MHz, MeOD) δ 25.70, 25.91, 30.61, 31.13, 41.98. Signal for the boron-bound carbon broadened and suppressed and could not be obtained even through ^{1}H-^{13}C HSQC experiment. **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 1066, 1156, 1216, 1272, 1410, 2951, 3287. **HRMS** (ESI^{+}): calc. for $C_6H_{15}O_2NB$ [M-Cl]$^{+}$: 144.1190, found: 144.1191.

1-Borono-5-hydroxypentan-1-aminium chloride (4p)



Synthesized according to the General Procedure from **3p** (17 mg, 0.1 mmol) to afford **4p** after 2h as a white foam-like solid (18 mg, 99% yield). **^{1}H NMR** (400 MHz, MeOD) δ 1.48 – 1.98 (m, 6H, 3×C$\underline{H}_2$), 2.78 – 2.92 (m, 1H, C$\underline{H}$-B), 3.75 – 4.10 (m, 2H, C$\underline{H}_2$-OH), 7.56 (br s, 1.6H, N$\underline{H}_3^{+}$, partially suppressed). **^{11}B NMR** (128 MHz, MeOD) δ 29.35. **^{13}C NMR** (101 MHz, MeOD) δ 30.18, 30.23, 30.28, 32.36, 41 (br m, extracted from ^{1}H-^{13}C HSQC spectrum). **IR** (ν/cm^{-1}, ATR): $\nu_{max.}$ = 1033, 1401, 1616, 2942, 3240. **HRMS** (ESI^{+}): calc. for $C_5H_{15}O_3NB$ [M-Cl]$^{+}$: 148.1140, found: 148.1138.

6. Synthesis of Boron-Containing Peptidomimetics (Bortezomib, Ixazomib)

To scientists who intend to use α-aminoboronic acids for their integration in boron-containing peptidomimetics, we suggest the following procedure. Subject the required pTAM to the transformation described in Section 5, and once full conversion has been determined directly by ^{11}B NMR of the reaction mixture, evaporate to dryness under reduced pressure. The dry residue can be then dissolved in DMF and used directly in solid-phase peptide synthesis.

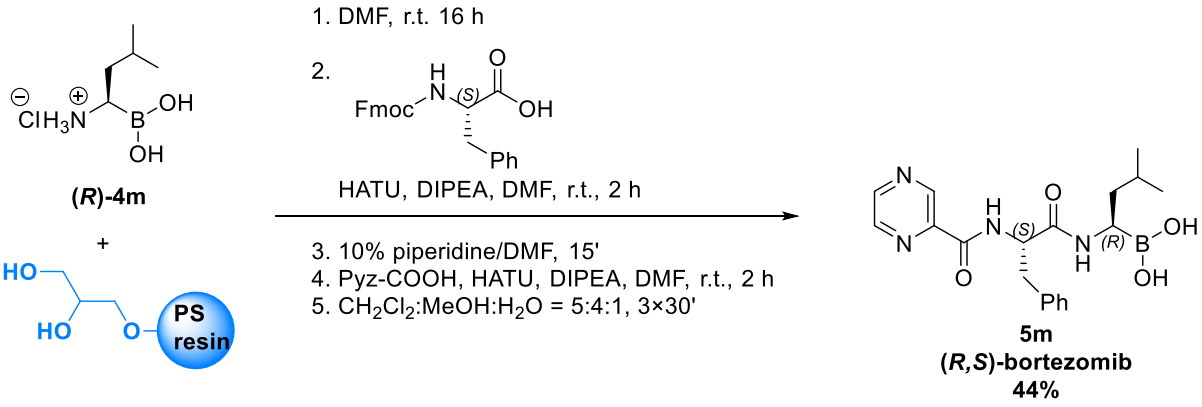
For the synthesis of bortezomib and ixazomib, we used a procedure based on literature method,[S14] however, with an important modification that no Fmoc-protection of the α-aminoboronic acid was employed. When loading the hydrochloride salt of α-aminoboronic acid to the diol resin, Daniels and Stivala[S14a] used CH_2Cl_2 and required the addition of DIPEA to dissolve the compound in this solvent.

Because aminoboronic acids are unstable in their free form, the compound was concurrently *N*-protected with Fmoc-Cl and then deprotected after binding to the resin.

Since we used DMF, in which compounds **4** are soluble, no protection was needed as the compound was stable in its hydrochloride salt form. This allowed us to shorten the procedure by two steps, altogether avoiding the use of piperidine in the synthesis of ixazomib and giving an appreciably more pure product. Interestingly, when synthesis of bortezomib was attempted with *N*-(pyrazin-2-oyl)-L-Phe-OH instead of Fmoc-L-Phe-OH, complete epimerization at the phenylalanine chiral center was observed and a mixture of (*R*,*S*)- and (*R*,*R*)-bortezomib was obtained. Amino acids are known to epimerize upon HATU activation, especially if bearing an *N*-acyl substituent, as opposed to an *N*-carbamate substituent. For this reason, the synthesis of bortezomib could not be shortened to one coupling step but had to be conducted in the same way as described in literature, namely coupling the aminoboronic acid with Fmoc-L-Phe-OH first, followed by Fmoc-deprotection, and finally coupling with pyrazine-2-carboxylic acid.[S14] When using Fmoc-L-Phe-OH, no epimerization was observed.

Compound **(*R*)-4m** used for the synthesis of bortezomib **5m** and ixazomib **6m** was prepared according to the General Procedures described in sections 4.2. and 5.2. Firstly, **2m** (61 mg, 0.4 mmol) was hydrogenated according to the General Procedure for aliphatic TAMs described in Section 4.2., using [(*S*,*S*)-TethTsDpen-RuCl], to afford **(*R*)-3m** (59 mg, 95% yield). Then, **(*R*)-3m** (15 mg, 0.1 mmol) was subjected to the General Procedure described in Section 5.2. to afford **(*R*)-4m** (16 mg, 99% yield, 99:1 e.r.). Spectral data of **(*R*)-3m** and **(*R*)-4m** corresponded to those of **(*S*)-3m** and **(*S*)-4m**, respectively, and are not repeated here.

Synthesis of bortezomib (5m)



Scheme S8. Solid-phase synthesis of bortezomib

Step 1

In a 5 mL PP syringe equipped with a PE-frit, 1-diol resin (167 mg, 0.6 mmol/g binding capacity, 1 eq) was suspended in CH_2Cl_2 (2 mL) and shaken for 30 min. CH_2Cl_2 was pushed out and the swelled resin was dried by vacuum filtration.

Step 2

Freshly prepared **(*R*)-4m** (17 mg, 0.1 mmol, 1 eq) was dissolved in DMF (2 mL) and the solution was transferred to the syringe with the resin. The syringe was shaken overnight.

Step 3

The syringe was emptied of the solvent and washed with DMF (6×1.5 mL). In a separate flask, Fmoc-L-Phe-OH (116 mg, 3 eq), HATU (114 mg, 3 eq) and DIPEA (87 μL, 5 eq) were dissolved in DMF (2 mL). The yellow solution was stirred in the flask for 5 minutes and then transferred to the syringe, which was shaken for 2 h.

Step 4

The syringe was emptied of the solvent and washed with DMF (3×1.5 mL), CH_2Cl_2 (3×1.5 mL) and again DMF (3×1.5 mL). Piperidine (10% in DMF, 1.5 mL) was added to the syringe, which was shaken for 10 min, emptied and the procedure was repeated, shaking for 5 min. The syringe was washed with DMF (3×1.5 mL), CH_2Cl_2 (3×1.5 mL) and again DMF (3×1.5 mL).

Step 5

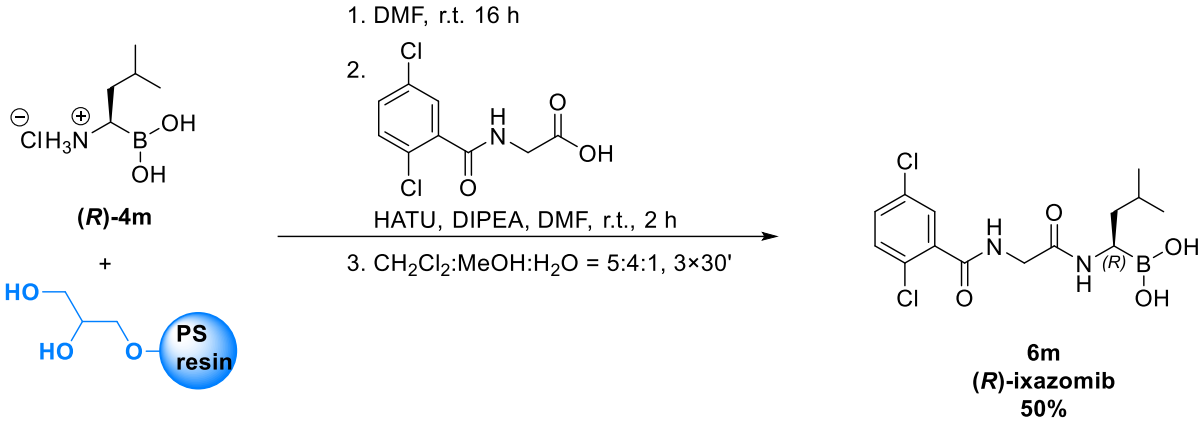
In a separate flask, pyrazine-2-carboxylic acid (37 mg, 3 eq), HATU (114 mg, 3 eq) and DIPEA (70 μL, 4 eq) were dissolved in DMF (2 mL). The red solution was stirred in the flask for 5 minutes and then transferred to the syringe, which was shaken for 2 h.

Step 6

The syringe was emptied of the solvent and washed with DMF (6×1.5 mL) and CH_2Cl_2 (9×1.5 mL). Then CH_2Cl_2:MeOH:H_2O = 5:4:1 (2 mL) was added and the syringe was shaken for 30 min. The procedure was repeated 3 times. The filtrate was collected and the solvent was removed under reduced pressure. The crude product was triturated with EtOAc:hexanes = 1:4 to remove residual DMF and filtered to afford bortezomib as a white solid (17 mg, 44% yield). **$[\alpha]_D^{24}$** -47.8 (*c* 0.02 M, MeOH) **^{1}H NMR** (400 MHz, MeOD) δ 0.85 (dd, *J* = 6.6, 4.9 Hz, 6H, ($C\underline{H}_3$)$_2$), 1.17 – 1.22 (m, 2H, $C\underline{H}_2$), 1.40 (hept, *J* = 13.4, 6.9 Hz, 1H, C<u>H</u>), 2.68 (t, *J* = 7.7 Hz, 1H, C<u>H</u>-B), 3.20 – 3.29 (m, 2H, $C\underline{H}_2$-Ph), 5.04 (t, *J* = 7.7 Hz, 1H, C<u>H</u>-Bn), 7.20 – 7.26 (m, 1H, Ar-<u>H</u>), 7.27 – 7.32 (m, 4H, Ar-<u>H</u>), 8.70 (dd, *J* = 2.5, 1.5 Hz, 1H, Ar-<u>H</u>), 8.80 (d, *J* = 2.5

Hz, 1H, Ar-H), 9.18 (d, *J* = 1.5 Hz, 1H, Ar-H). **^{11}B NMR** (128 MHz, MeOD) δ 14.02. **HRMS** (ESI^-): calc. for $C_{19}H_{24}O_4N_4B$ $[M-H]^-$: 383.1896, found: 383.1902. In full accordance with the commercial sample (see Section 6.1. for its ^{1}H NMR spectrum) which is a known compound.[S14]

Synthesis of ixazomib (6m)



Scheme S9. Solid-phase synthesis of ixazomib

Step 1

Same as for bortezomib.

Step 2

Same as for bortezomib, 0.1 mmol (*R*)-**4m** used.

Step 3

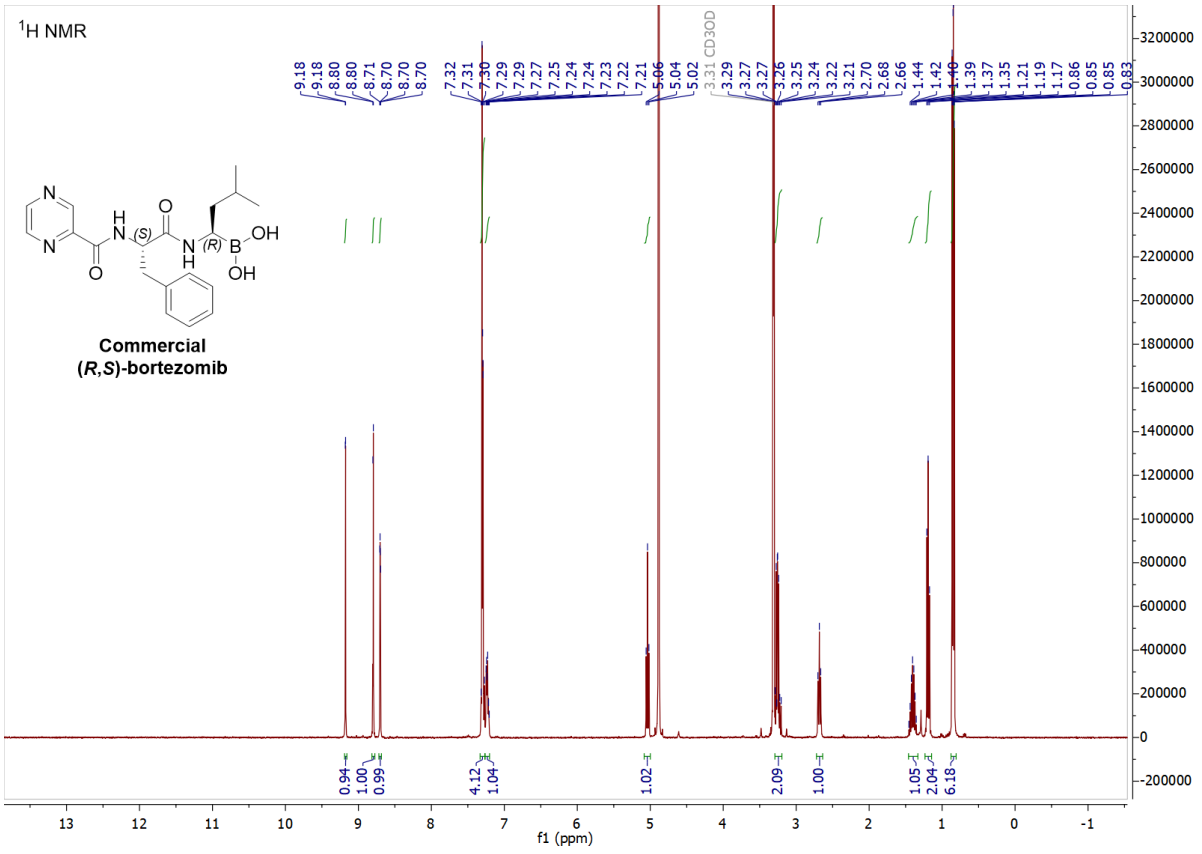
The syringe was emptied of the solvent and washed with DMF (6×1.5 mL). In a separate flask, *N*-(2,5-dichlorobenzoyl)glycine (74 mg, 3 eq), HATU (114 mg, 3 eq) and DIPEA (87 μL, 5 eq) were dissolved in DMF (2 mL). The yellow solution was stirred in the flask for 5 minutes and then transferred to the syringe, which was shaken for 2 h.

Step 4

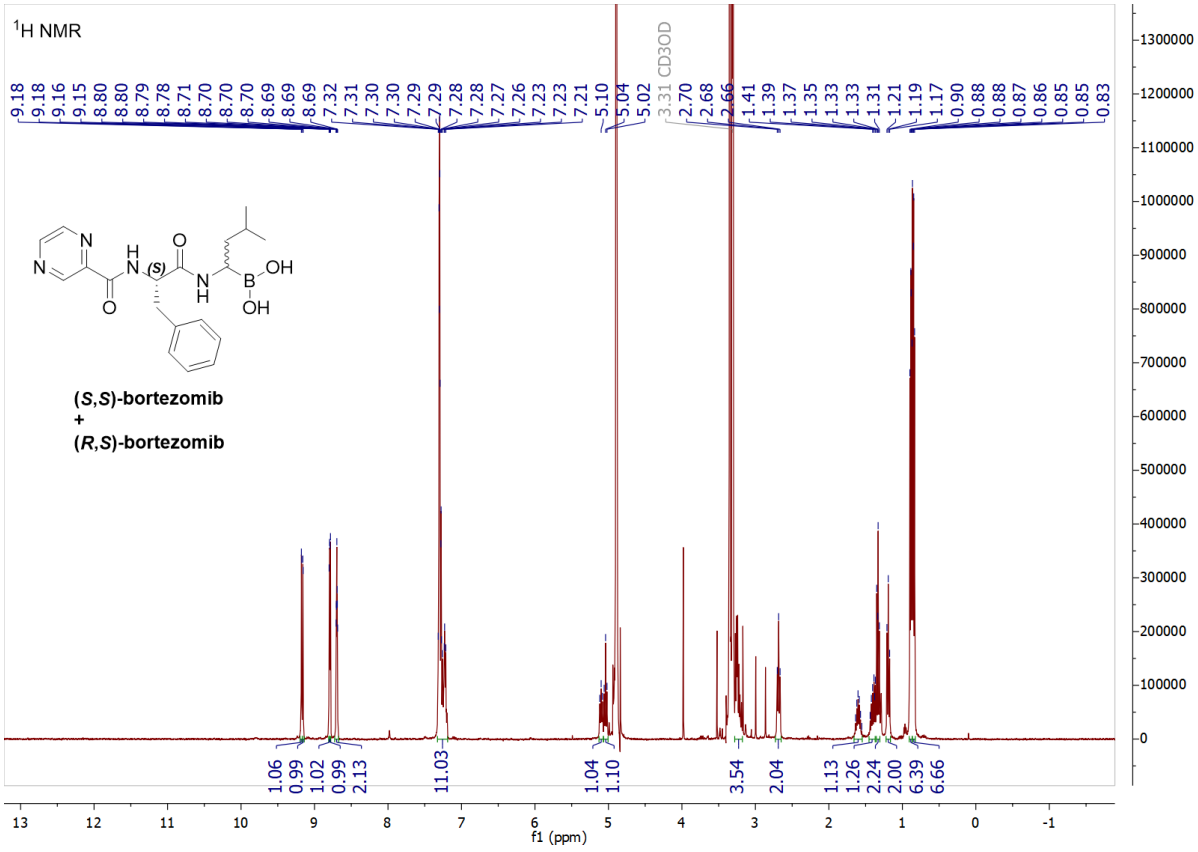
Same as Step 6 for bortezomib to afford ixazomib as a white solid (18 mg, 50 % yield). **$[\alpha]_D^{24}$** -40.5 (*c* 0.02 M, MeOH). **^{1}H NMR** (400 MHz, MeOD) δ 0.94 (dd, *J* = 6.6, 0.9 Hz, 6H, $(CH_3)_2$), 1.33 – 1.41 (m, 2H, CH_2), 1.62 – 1.74 (m, 1H, CH), 2.74 – 2.82 (m, 1H, CH-B), 4.24 (s, 2H CH_2), 7.49 (d, *J* = 1.5 Hz, 2H, Ar-H), 7.61 (t, *J* = 1.5 Hz, 1H, Ar-H). **^{11}B NMR** (128 MHz, MeOD) δ 13.81. **^{13}C NMR** (101 MHz, MeOD) δ 22.40, 23.75, 27.05, 40.14, 40.94, 130.15, 130.74, 132.47, 132.70, 134.00, 137.97, 168.81, 175.62. **HRMS** (ESI^-): calc. for $C_{14}H_{20}O_4N_2BCl_2$ $[M-H]^-$: 361.0888, found: 361.0873. In full accordance with the commercial sample which is a known compound.[S14]

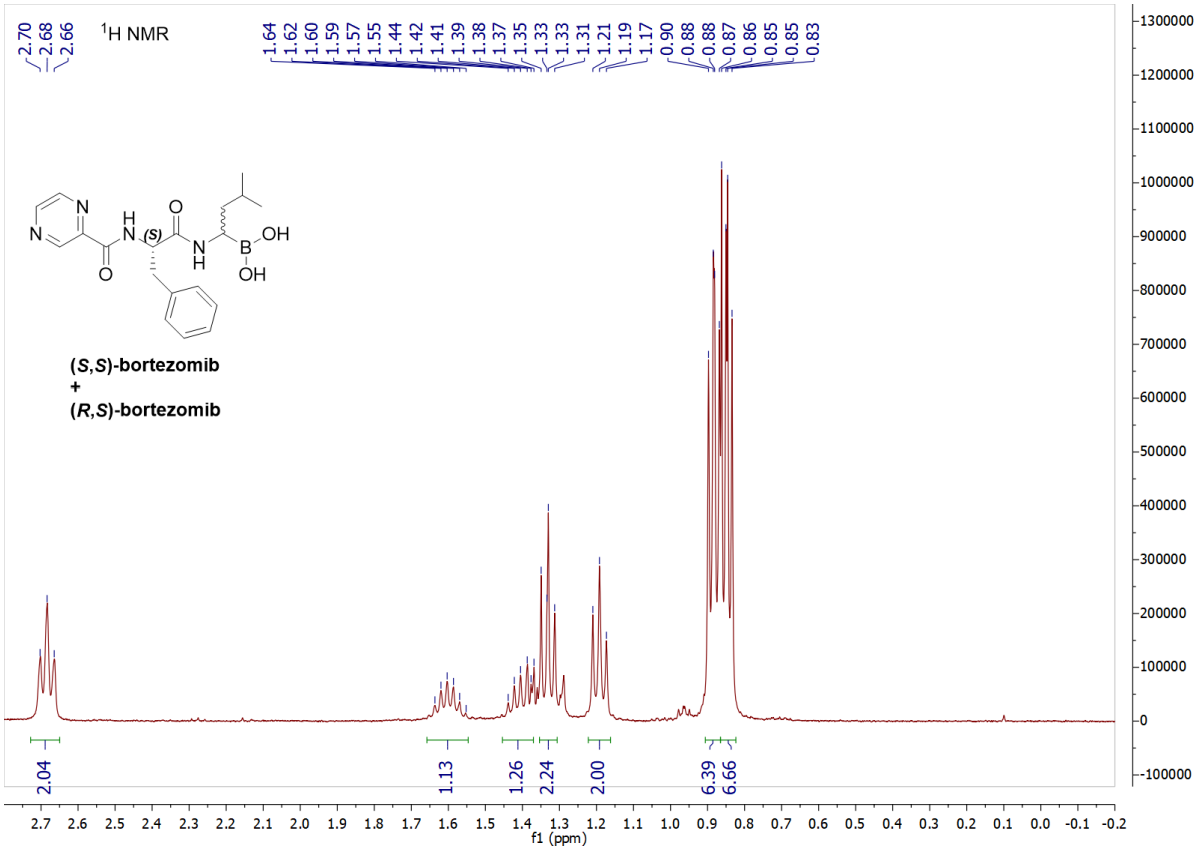
6.1. Determination of Absolute Configuration of **4m**

Bortezomib has two stereogenic centers, one in the phenylalanine residue and one in the boro-leucine residue. If the absolute configuration of the phenylalanine residue is known, one is able to determine the absolute configuration at the boro-leucine stereogenic center through NMR. An ^{1}H NMR spectrum of a commercial, optically pure sample of (*R*,*S*)-bortezomib was obtained to serve as a reference. **$[\alpha]_D^{24}$** -48.4 (*c* 0.02 M, MeOH). **^{1}H NMR** (400 MHz, MeOD) δ 0.85 (dd, *J* = 6.6, 5.0 Hz, 6H, (CH_3)$_2$), 1.16 – 1.22 (m, 2H, CH_2), 1.40 (hept, *J* = 13.3, 6.7 Hz, 1H, CH), 2.68 (t, *J* = 7.7 Hz, 1H CH-B), 3.20 – 3.29 (m, 2H, CH_2-Ph), 5.04 (t, *J* = 7.6 Hz, 1H, CH-Bn), 7.19 – 7.26 (m, 1H, Ar-H), 7.27 – 7.33 (m, 4H, Ar-H), 8.70 (dd, *J* = 2.5, 1.5 Hz, 1H, Ar-H), 8.80 (d, *J* = 2.5 Hz, 1H, Ar-H), 9.18 (d, *J* = 1.5 Hz, 1H, Ar-H).

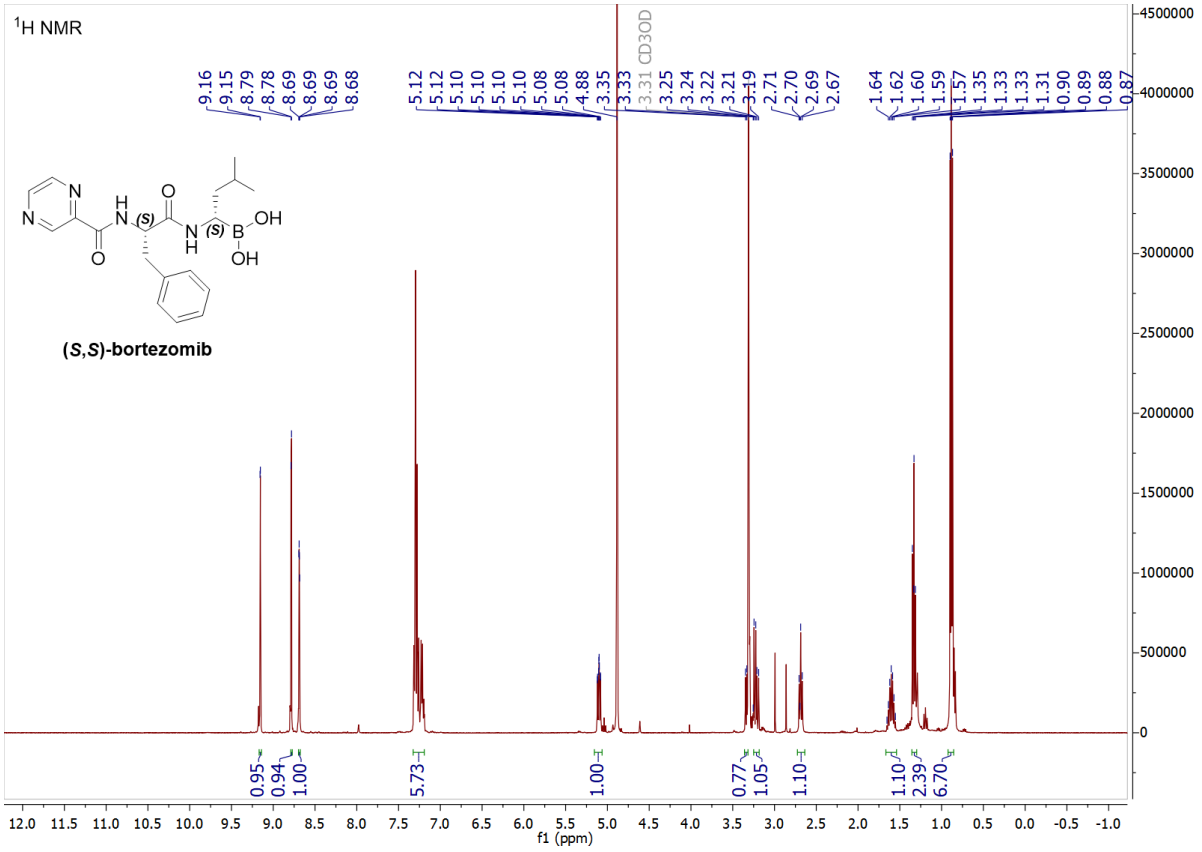


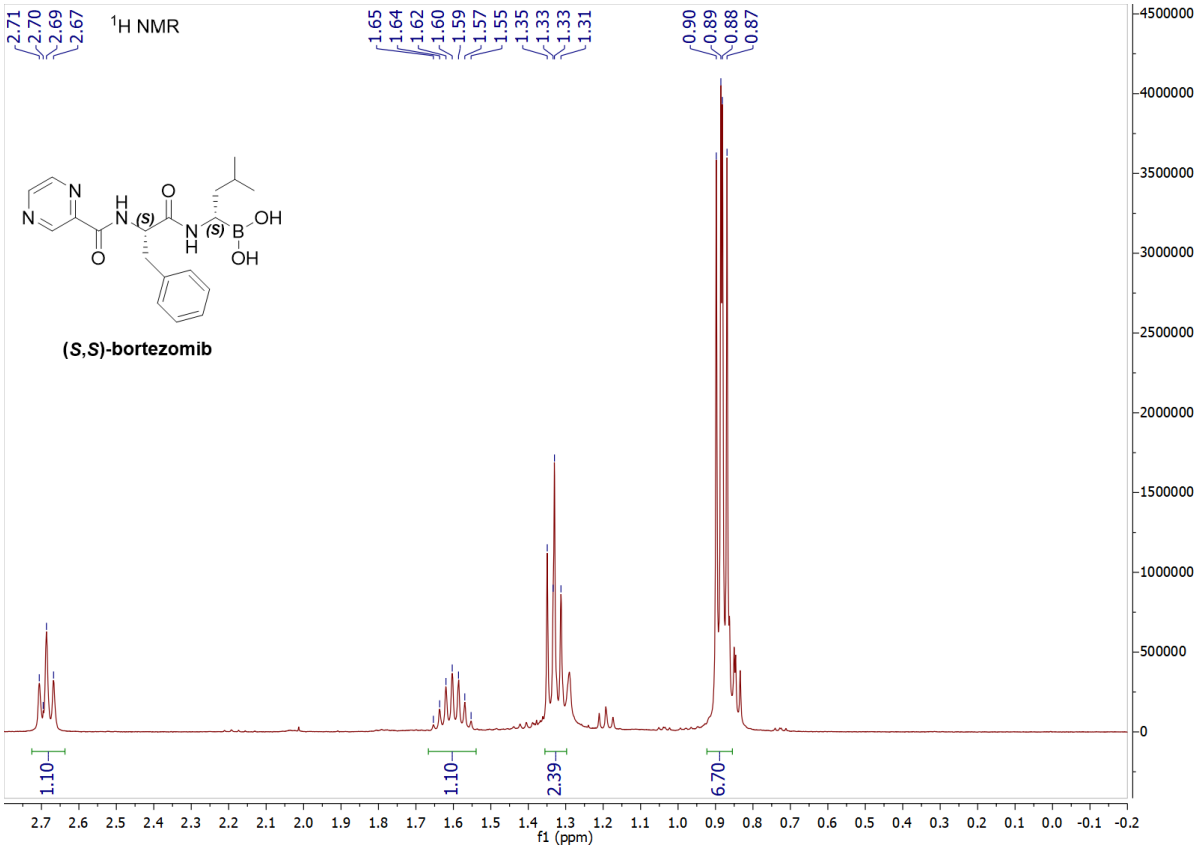
According to the procedure for the synthesis of bortezomib described above, **$4m_{rac}$** (racemic, synthesized with $NaBH_4$) was used. The product gave two sets of signals, one corresponding to (*R*,*S*)-bortezomib and the other to (*S*,*S*)-bortezomib. The signals for diastereotopic protons were well discernible, especially the CH heptet (1.60 ppm for (*S*,*S*)-bortezomib vs. 1.40 ppm for (*R*,*S*)-bortezomib) and the CH_2 triplet-like multiplet (1.30 – 1.35 ppm for (*S*,*S*)-bortezomib vs. 1.16 – 1.22 ppm for (*R*,*S*)-bortezomib).


1H NMR
(S,S)-bortezomib
+
(R,S)-bortezomib
f1 (ppm)

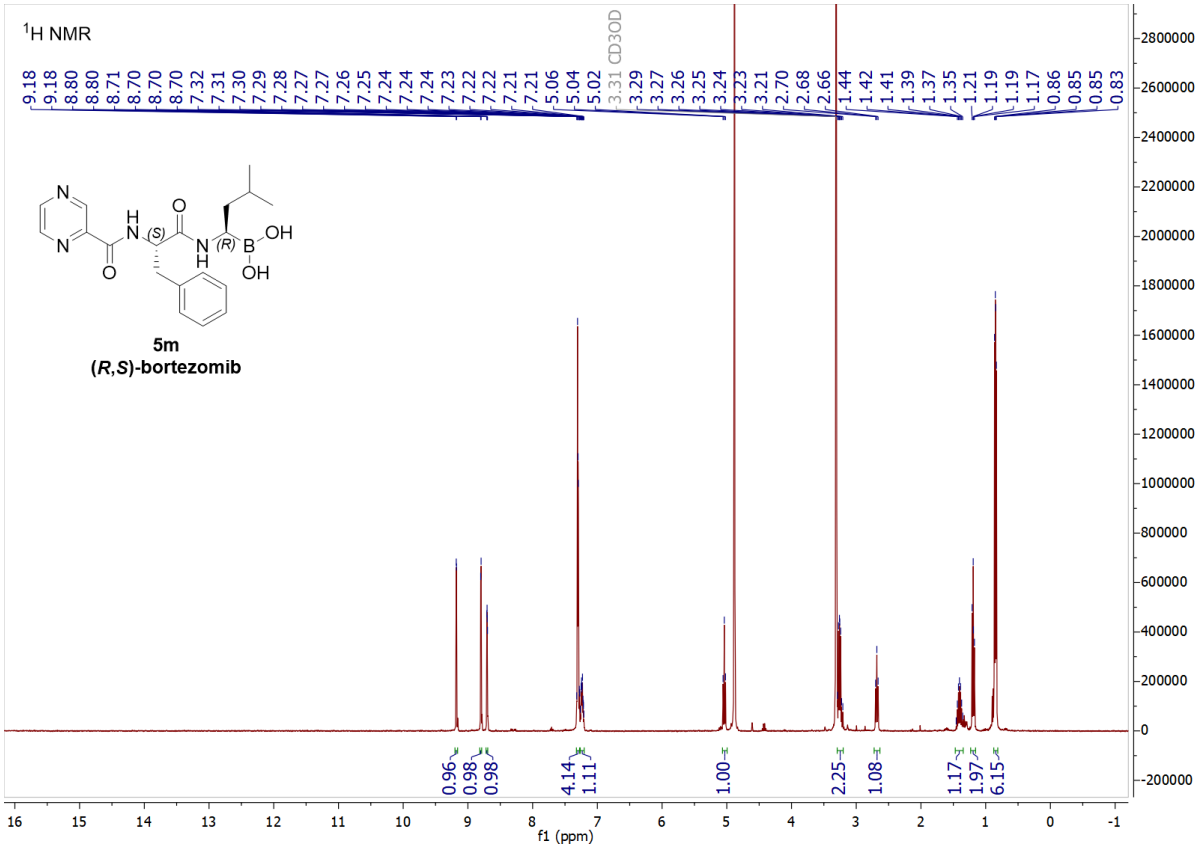

1H NMR
(S,S)-bortezomib
+
(R,S)-bortezomib
f1 (ppm)

Next, bortezomib was synthesized using **4m** (synthesized with [(*R,R*)-TethTsDpen-RuCl]) and gave the set of signals corresponding to (*S,S*)-bortezomib, confirming that [(*R,R*)-TethTsDpen-RuCl] affords **(*S*)-4m**. **^{1}H NMR** (400 MHz, MeOD) δ 0.88 (dd, *J* = 6.6, 4.9 Hz, 6H, (C$\underline{H}_3$)$_2$), 1.30 – 1.37 (m, 2H, C$\underline{H}_2$), 1.60 (hept, *J* = 13.4, 6.7 Hz, 1H, C$\underline{H}$), 2.69 (t, *J* = 7.6 Hz, 1H, C$\underline{H}$-B), 3.22 (dd, *J* = 13.8, 8.4 Hz, 1H, C$\underline{H}_{2a}$-Ph), 3.31 – 3.36 (m, 1H, C$\underline{H}_{2b}$-Ph), 5.08 – 5.13 (m, 1H, C$\underline{H}$-Bn), 7.15 – 7.33 (m, 5H, Ar-$\underline{H}$), 8.69 (dd, *J* = 2.5, 1.5 Hz, 1H, Ar-$\underline{H}$), 8.78 (d, *J* = 2.5 Hz, 1H, Ar-$\underline{H}$), 9.16 (d, *J* = 1.5 Hz, 1H, Ar-$\underline{H}$).





When the reaction was repeated using **(*R*)-4m** (synthesized with [(*S,S)*-TethTsDpen-RuCl]), the resulting ^{1}H NMR spectrum was in full accordance with the commercial (*R*,*S*)-bortezomib.



The absolute configuration of **4m** was further confirmed by the synthesis of ixazomib. In a commercial sample of (*R*)-ixazomib, we measured a specific rotation of -41.4 (*c* 0.02 M, MeOH). When ixazomib was synthesized with **4m** (synthesized with [(*R,R*)-TethTsDpen-RuCl]), it had a specific rotation of +40.0 (*c* 0.02 M, MeOH). When **4m** (synthesized with [(*S,S)*-TethTsDpen-RuCl]) was used, the product had a specific rotation of -40.5 (*c* 0.02 M, MeOH).

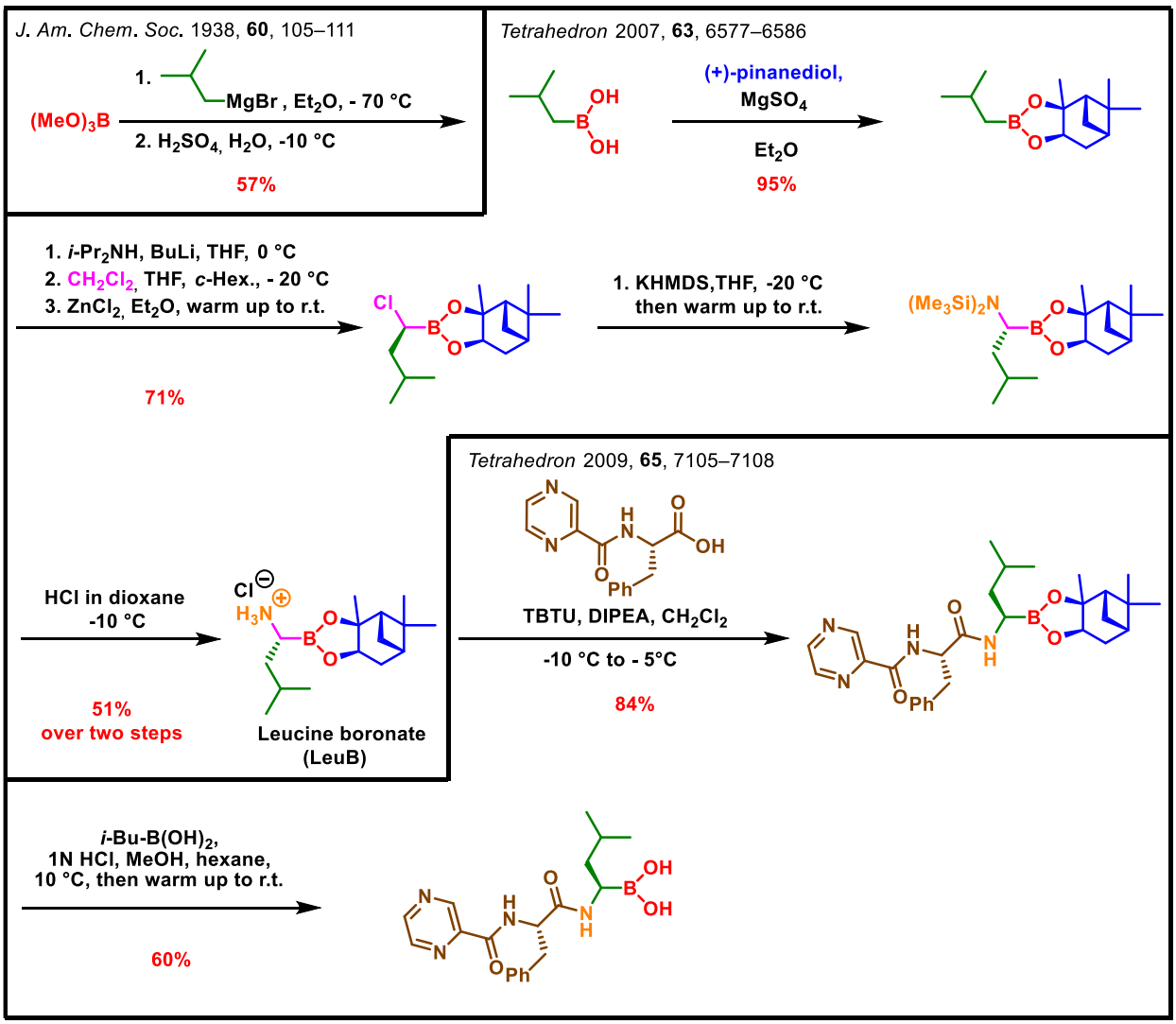
We can therefore conclude that the reaction with [(*R,R*)-TethTsDpen-RuCl] affords (*S*)-pTAMs for aliphatic compounds (**3j**-**3p**), since **(*S*)-3m** exhibits positive specific rotation and the same is true for the other aliphatic compounds, so their absolute configuration can be assigned by correlation to **(*S*)-3m**. Conversely, aromatic compounds (**3a**-**3i**) synthesized with the same catalyst have negative specific rotation and can by correlation to **(*S*)-3m** be assigned as (*R*)-pTAMs.

6.2. Overview of Synthetic Procedures Towards Bortezomib

Comparison of synthetic routes towards bortezomib.

Introduction of boron into the organic residue or key chirality elements were taken into consideration for determination of the starting point for each synthetic route.

Scheme S10. Matteson's homologation methodology approach towards bortezomib.



OVERALL YIELD = 9.9%

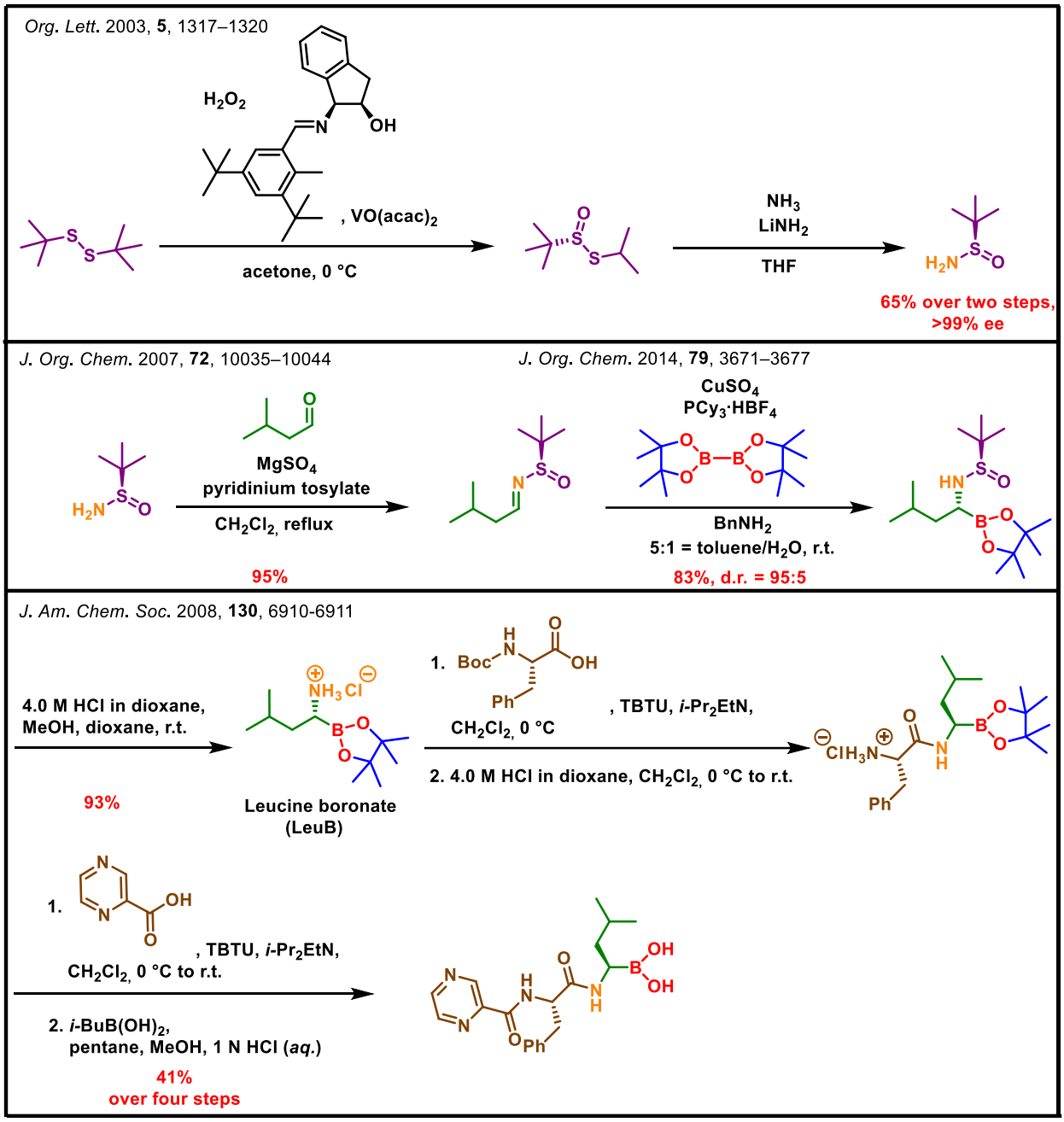
References:

S15. H. R. Snyder, J. A. Kuck, J. R. Johnson, *J. Am. Chem. Soc.* 1938, **60**, 105–111.

S16. F. Debaene, J. A. Da Silva, Z. Pianowski, F. J. Duran, N. Winssinger, *Tetrahedron* 2007, **63**, 6577–6586.

S17. A. S. Ivanov, A. A. Zhalnina, S. V. Shishkov, *Tetrahedron* 2009, **65**, 7105–7108.

Scheme S11. Ellman's borylation methodology approach towards bortezomib.



OVERALL YIELD = 19.5%

References:

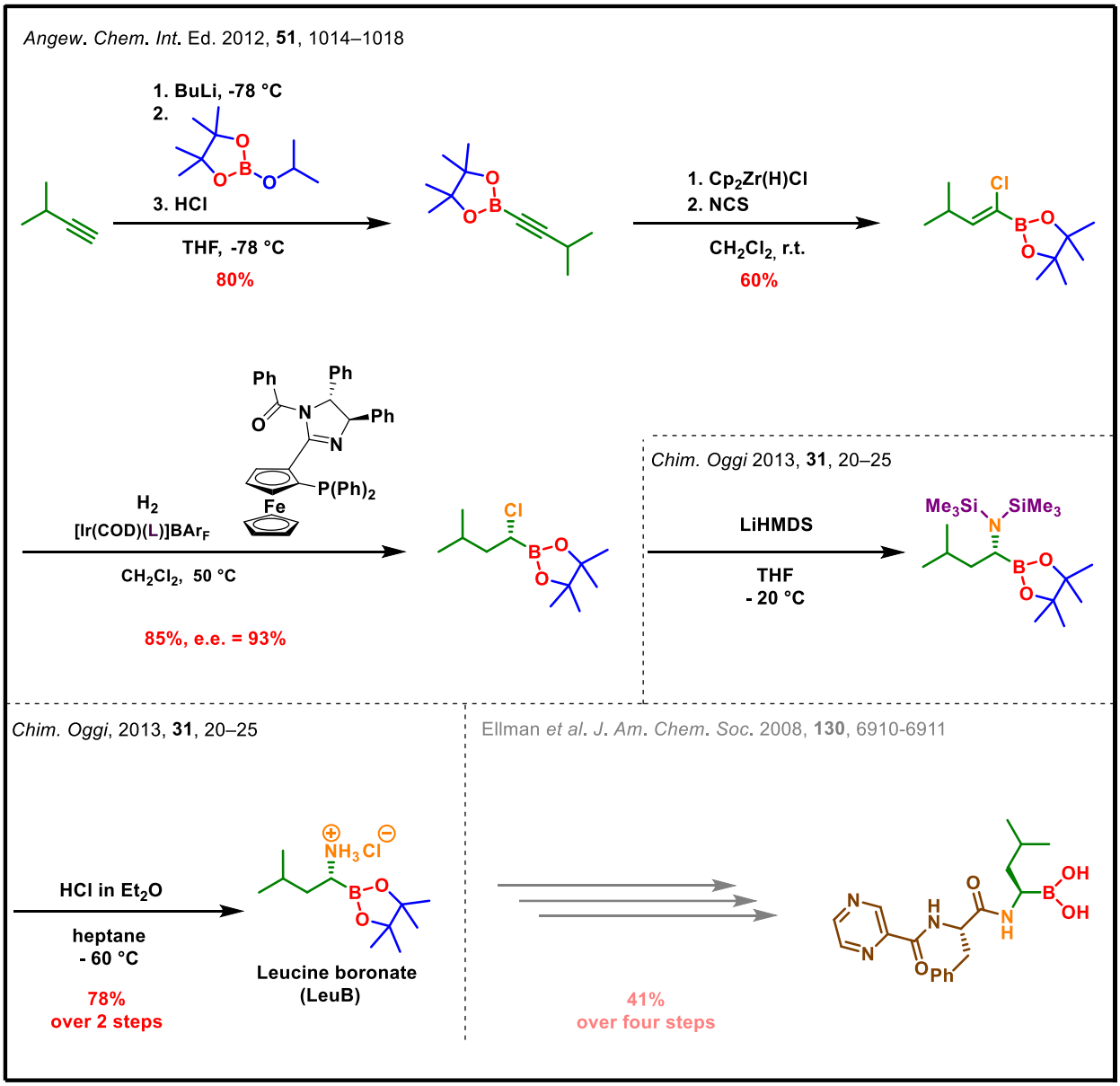
S18. D. J. Weix, J. A. Ellman, *Org. Lett.* 2003, **5**, 1317–1320.

S19. L. Nielsen, K. B. Lindsay, J. Faber, N. C. Nielsen, T. Skrydstrup, *J. Org. Chem.* 2007, **72**, 10035–10044.

S20. A. W. Buesking, V. Bacauanu, I. Cai, J. A. Ellman, *J. Org. Chem.* 2014, **79**, 3671–3677.

S21. M. A. Beenen, C. An, J. A. Ellman, *J. Am. Chem. Soc.* 2008, **130**, 6910–6911.

Scheme S12. Časar's asymmetric hydrogenation methodology approach towards bortezomib.



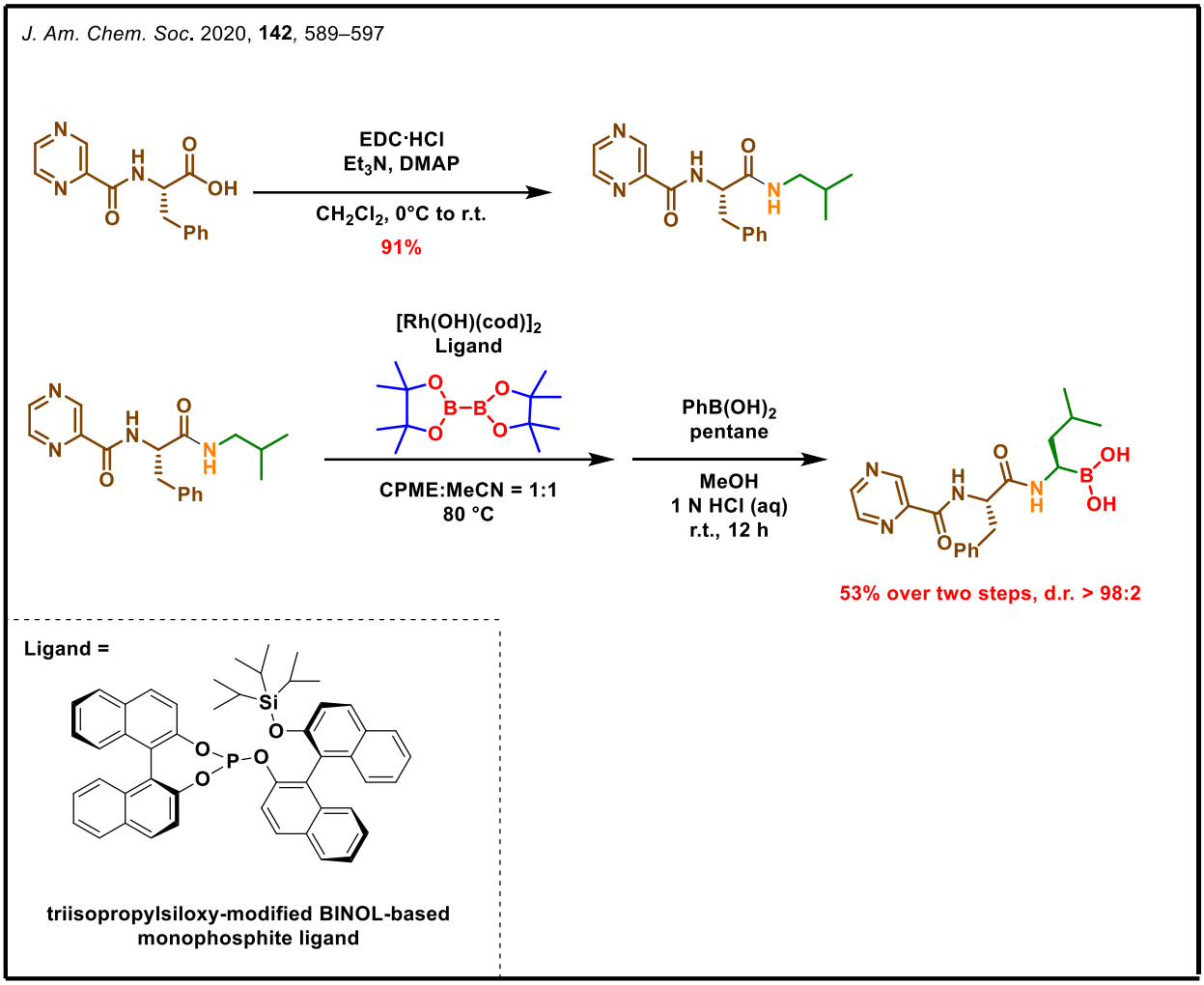
OVERALL YIELD = 13.0%

References:

S22. I. Gazić Smilović, E. Casas-Arcé, S. J. Roseblade, U. Nettekoven, A. Zanotti-Gerosa, M. Kovačevič, Z. Časar, *Angew. Chem. Int. Ed.* 2012, **51**, 1014–1018.

S23. I. Gazić Smilović, Z. Časar, *Chim. Oggi* 2013, **31**, 20–25.

Scheme S13. Sawamura's direct borylation approach towards bortezomib

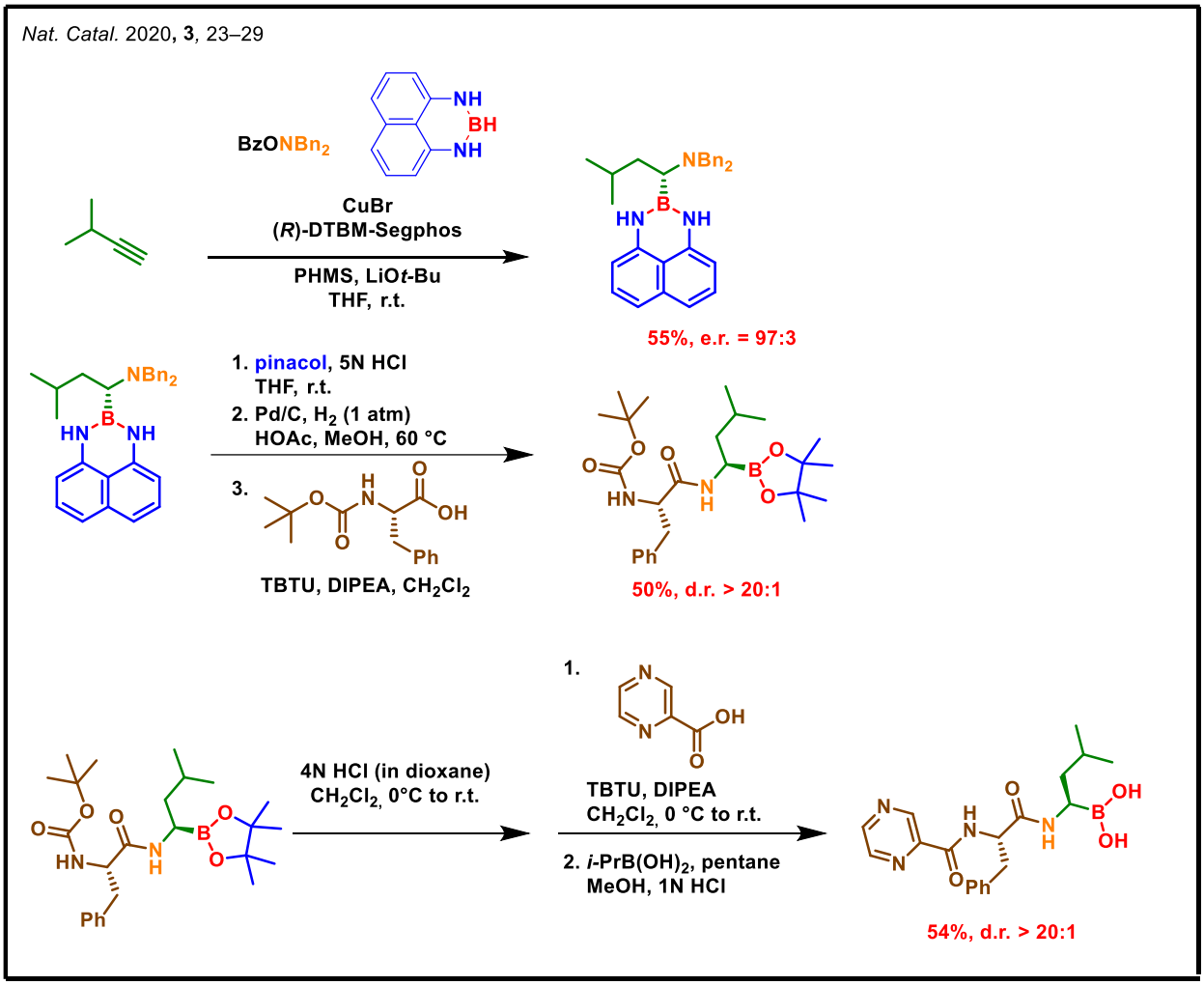


OVERALL YIELD = 48.2%

Reference:

S24. R. L. Reyes, M. Sato, T. Iwai, M. Sawamura, *J. Am. Chem. Soc.* 2020, **142**, 589–597.

Scheme S14. Engle's approach towards bortezomib via aminoboration of alkynes

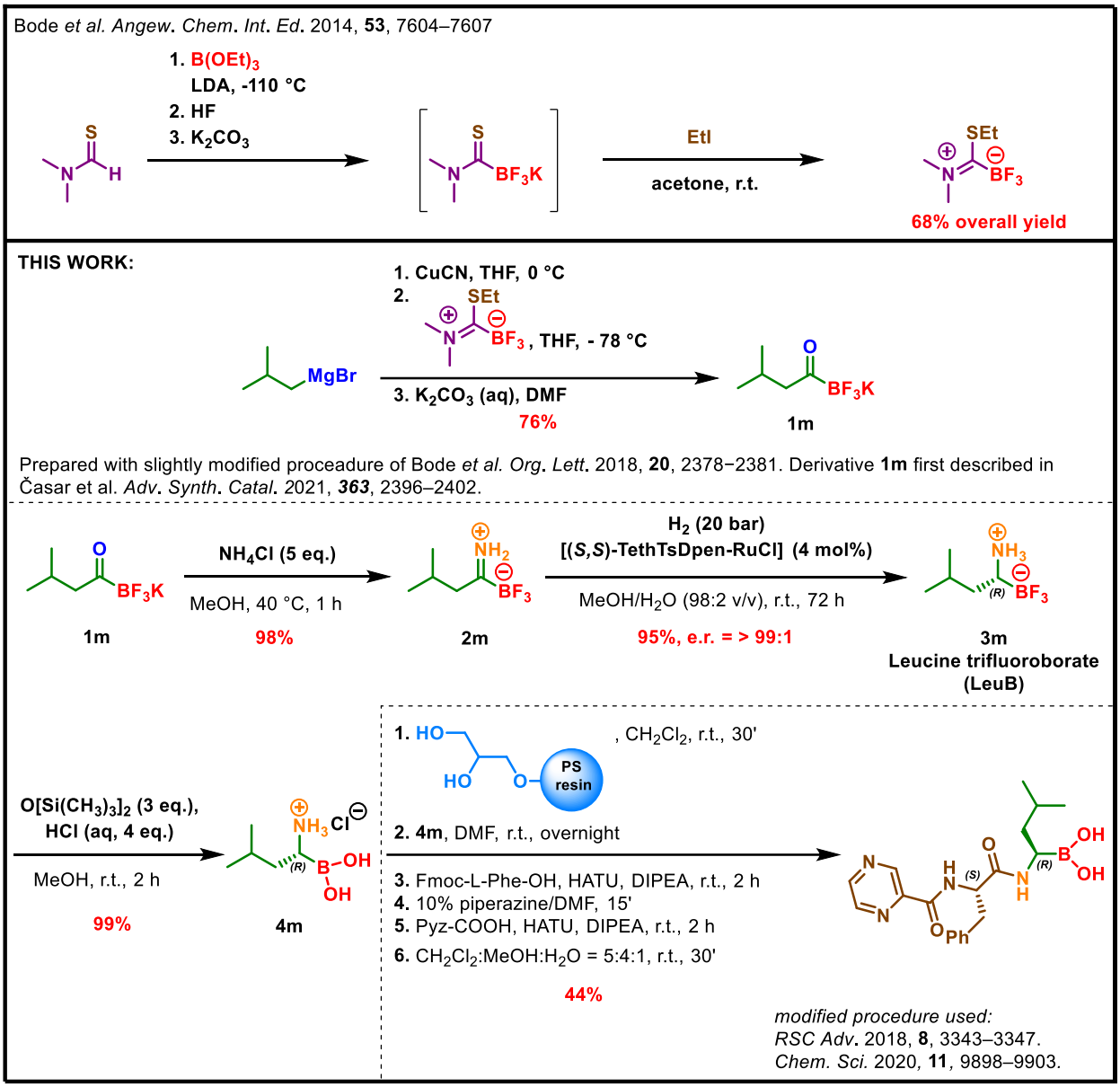


OVERALL YIELD = 14.9%

Reference:

S25. D. W. Gao, Y. Gao, H. Shao, T. Z. Qiao, X. Wang, B. B. Sanchez, J. S. Chen, P. Liu, K. M. Engle, *Nat. Catal.* 2020, **3**, 23–29.

Scheme S15. Present pTIM asymmetric hydrogenation methodology approach towards bortezomib.



OVERALL YIELD = 21.0%

References:

S1. G. Erős, Y. Kushida, J. W. Bode, *Angew. Chem. Int. Ed.* 2014, **53**, 7604–7607.
S2. S. M. Liu, D. Wu, J. W. Bode, *Org. Lett.* 2018, **20**, 2378–2381.
S3. A. Šterman, J. Košmrlj, N. Žigart, S. Gobec, I. Sosič, Z. Časar, *Adv. Synth. Catal.* 2021, ***363***, 2396–2402.
S14. a) B. E. Daniels, C. E. Stivala, *RSC Adv.* 2018, **8**, 3343–3347; b) S. P. A. Hinkes, S. Kämmerer, C. D. P. Klein, *Chem. Sci.* 2020, ***11***, 9898–9903.

7. References

S1. G. Erős, Y. Kushida, J. W. Bode, *Angew. Chem. Int. Ed.* 2014, **53**, 7604–7607.

S2. S. M. Liu, D. Wu, J. W. Bode, *Org. Lett.* 2018, **20**, 2378–2381.

S3. A. Šterman, J. Košmrlj, N. Žigart, S. Gobec, I. Sosič, Z. Časar, *Adv*. *Synth*. *Catal*. 2021, **363**, 2396–2402.

S4. J. Taguchi, T. Takeuchi, R. Takahashi, F. Masero, H. Ito, *Angew. Chem. Int. Ed.* 2019, **58**, 7299–7303.

S5. A. M. Dumas, J. W. Bode, *Org. Lett.* 2012, **14**, 2138–2141.

S6. T. Shiro, A. Schuhmacher, M. K. Jackl, J. W. Bode, *Chem. Sci.* 2018, **9**, 5191–5196.

S7. T. Ohkuma, N. Utsumi, K. Tsutsumi, K. Murata, C. Sandoval, R. Noyori, *J. Am. Chem. Soc.* 2006, **128**, 8724–8725.

S8. Y. Lou, J. Wang, G. Gong, F. Guan, J. Lu, J. Wen and X. Zhang, *Chem. Sci.* 2020, **11**, 851–855.

S9. a) A. K. L. Yuen, C. A. Hutton, *Tetrahedron Lett.* 2005, **46**, 7899–7903; b) Q. I. Churches, J. F. Hooper, C. A. Hutton, *J. Org. Chem.* 2015, **80**, 5428–5435; c) G. A. Molander, L. N. Cavalcanti, B. Canturk, P.-S. Pan, L. E. Kennedy, *J. Org. Chem.* 2009, **74**, 7364–7369; d) D. W. Blevins, M.-L. Yao, L. Yong, G. W. Kabalka, *Tetrahedron Lett.* 2011, **52**, 6534–6536; e) G. W. Kabalka, V. Coltuclu, *Tetrahedron Lett.* 2009, **50**, 6271–6272; f) A. J. J. Lennox, G. C. Lloyd-Jones, *J. Am. Chem. Soc.* 2012, **134**, 7431–7441; g) S. R. Inglis, E. C. Y. Woon, A. L. Thompson, C. J. Schofield, *J. Org. Chem.* 2010, **75**, 468–471; h) I. Omari, L. P. E. Yunker, J. Penafiel, D. Gitaari, A. San Roman, J. S. McIndoe, *Chem. Eur. J.* 2021, **27**, 3812–3816.

S10. a) V. M. Dembitsky, M. Srebnik, in *Amino Acids, Peptides and Proteins in Organic Chemistry* (Ed. A. B. Hughes). Wiley-VCH, 2010, pp 145–187; b) K. Duncan, W. S. Faraci, D. S. Matteson, C. T. Walsh, *Biochemistry* 1989, **28**, 3541–3549; c) D. S. Matteson, K. M. Sadhu, *Organometallics* 1984, **3**, 614–618.

S11. a) V. D. Kodibagkar, W. Cui, M. E. Merritt, R. P. Mason, *Magn. Reson. Med.* 2006, **55**, 743–748; b) P. K. Gulaka, U. Rastogi, M. A. McKay, X. Wang, R. P. Mason, V. D. Kodibagkar, *NMR Biomed.* 2011, **24**, 1226–1234.

S12. ^{11}B NMR signal for trimethylborate reported as sharp singlet at 18.69: J. Kupai, M. Razali, S. Buyuktiryaki, R. Kecili, G. Szekely, *Polym. Chem.* 2017, **8**, 666–673.

S13. 4-cyanobenzylamine reported here: N. Kühl, D. Graf, J. Bock, M. A. M. Behnam, M.-M. Leuthold, C. D. Klein, *J. Med. Chem.* 2020, **63**, 8179–8197.

S14. a) B. E. Daniels, C. E. Stivala, *RSC Adv*. 2018, **8**, 3343–3347; b) S. P. A. Hinkes, S. Kämmerer, C. D. P. Klein, *Chem*. *Sci*. 2020, **11**, 9898–9903.

S15. H. R. Snyder, J. A. Kuck, J. R. Johnson, *J. Am. Chem. Soc.* 1938, **60**, 105–111.

S16. F. Debaene, J. A. Da Silva, Z. Pianowski, F. J. Duran, N. Winssinger, *Tetrahedron* 2007, **63**, 6577–6586.

S17. A. S. Ivanov, A. A. Zhalnina, S. V. Shishkov, *Tetrahedron* 2009, **65**, 7105–7108.

S18. D. J. Weix, J. A. Ellman, *Org. Lett.* 2003, **5**, 1317–1320.

S19. L. Nielsen, K. B. Lindsay, J. Faber, N. C. Nielsen, T. Skrydstrup, *J*. *Org*. *Chem*. 2007, **72**, 10035–10044.

S20. A. W. Buesking, V. Bacauanu, I. Cai, J. A. Ellman, *J*. *Org*. *Chem*. 2014, **79**, 3671–3677.

S21. M. A. Beenen, C. An, J. A. Ellman, *J*. *Am*. *Chem*. *Soc*. 2008, **130**, 6910–6911.

S22. I. Gazić Smilović, E. Casas-Arcé, S. J. Roseblade, U. Nettekoven, A. Zanotti-Gerosa, M. Kovačevič, Z. Časar, *Angew. Chem. Int. Ed.* 2012, **51**, 1014–1018.

S23. I. Gazić Smilović, Z. Časar, *Chim*. *Oggi* **2013**, *31*, 20–25.

S24. R. L. Reyes, M. Sato, T. Iwai, M. Sawamura, *J*. *Am*. *Chem*. *Soc*. 2020, **142**, 589–597.

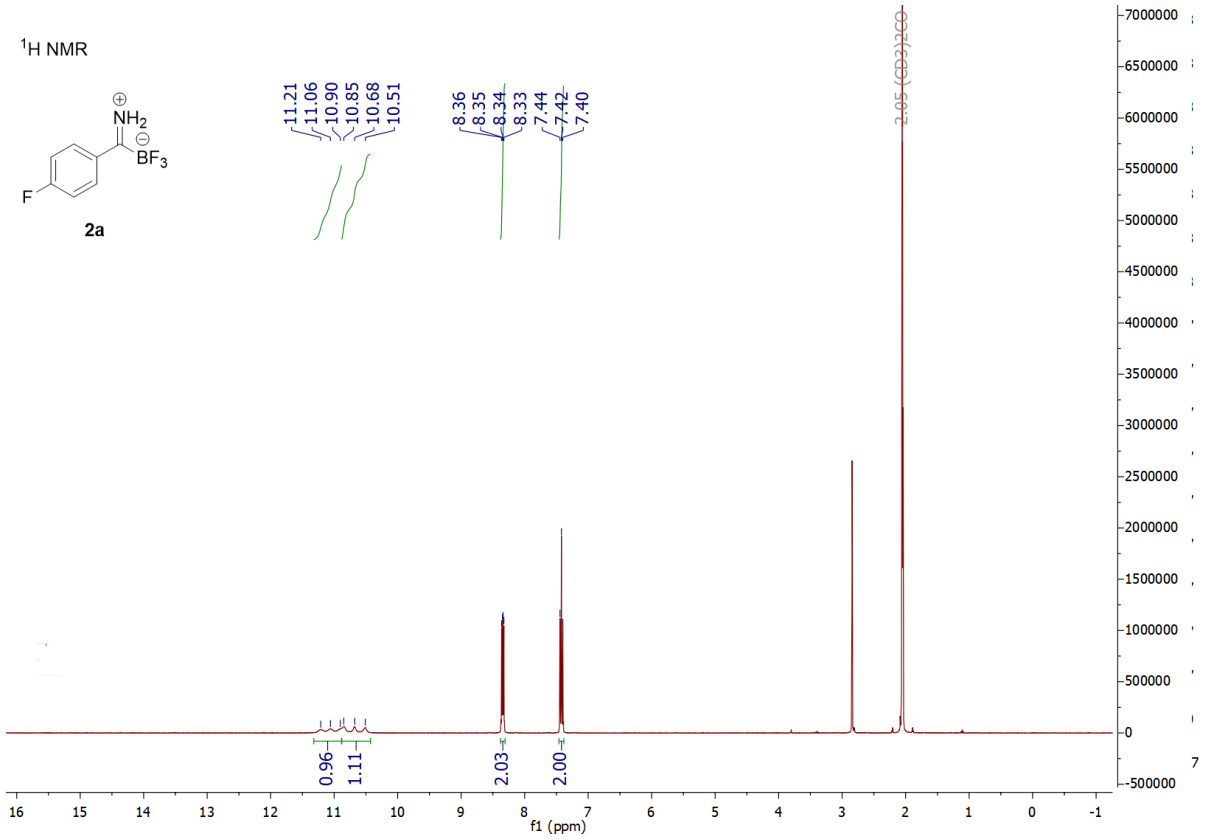
S25. D. W. Gao, Y. Gao, H. Shao, T. Z. Qiao, X. Wang, B. B. Sanchez, J. S. Chen, P. Liu, K. M. Engle, *Nat*. *Catal*. 2020, **3**, 23–29.

8. NMR Spectra

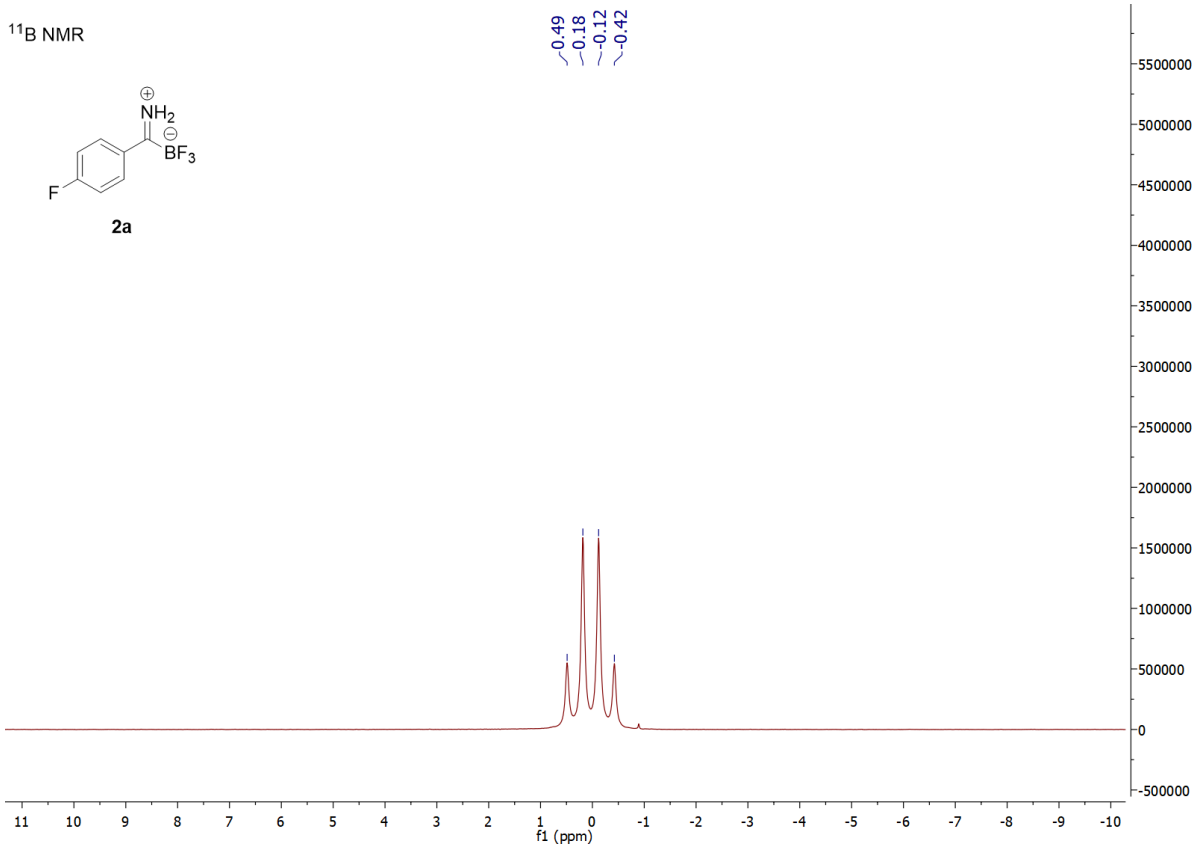
8.1. NMR Spectra of pTIMs 2

((4-Fluorophenyl)(iminio)methyl)trifluoroborate (2a)

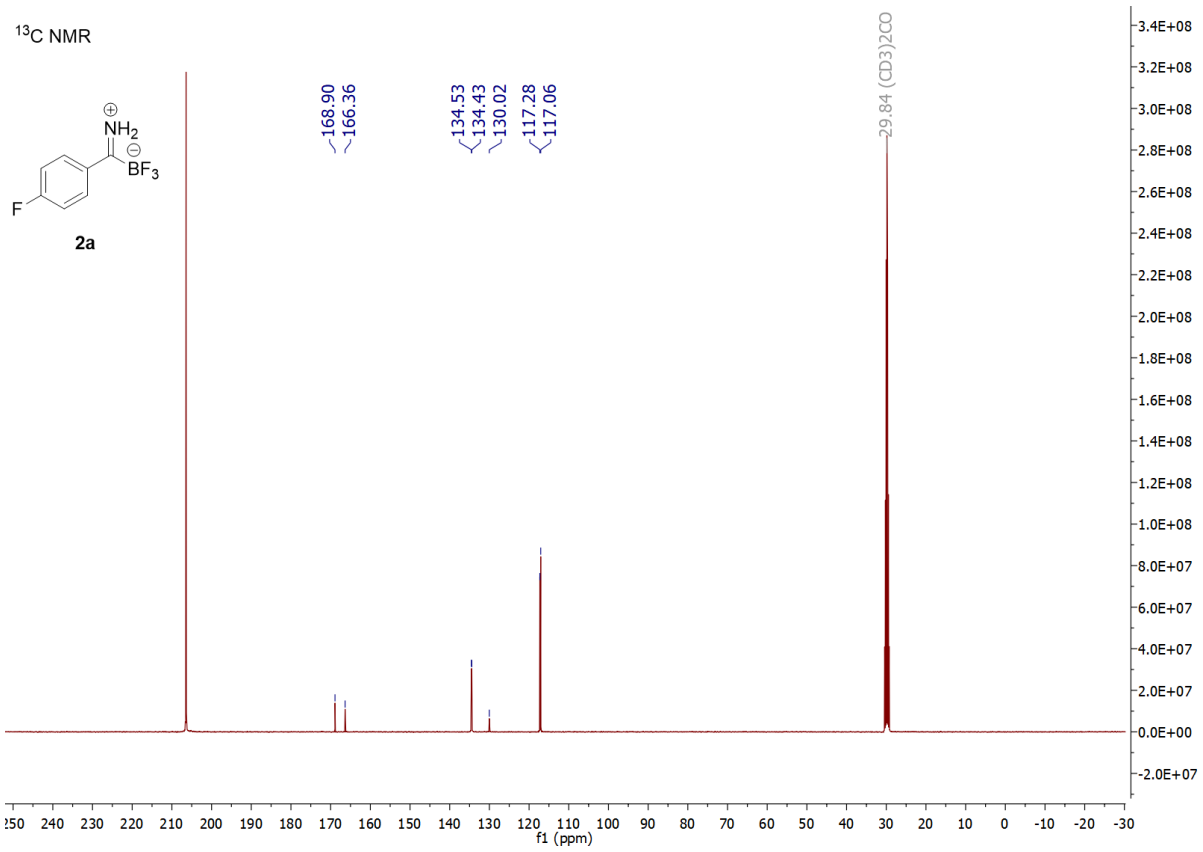
^{1}H-NMR (400 MHz, Acetone-d_6) of **2a**:



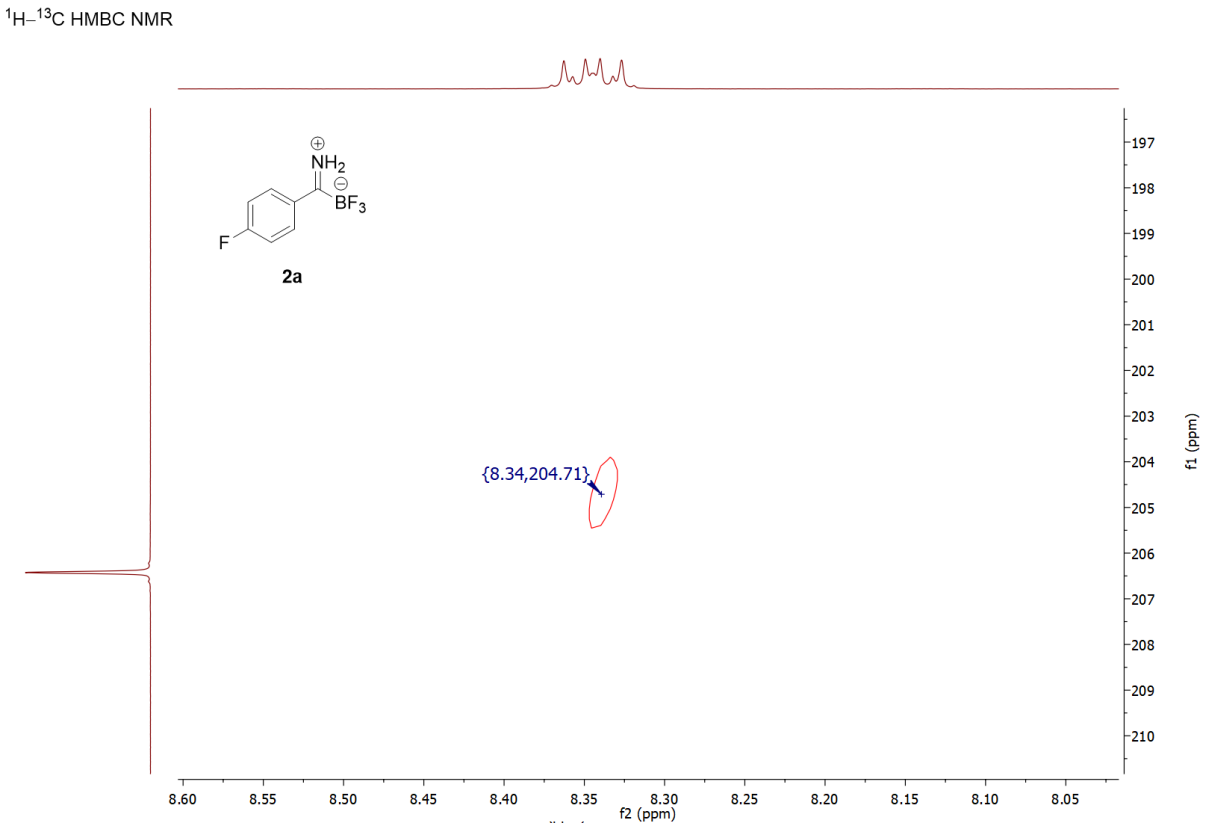
^{11}B-NMR (128 MHz, Acetone-d_6) of **2a**:



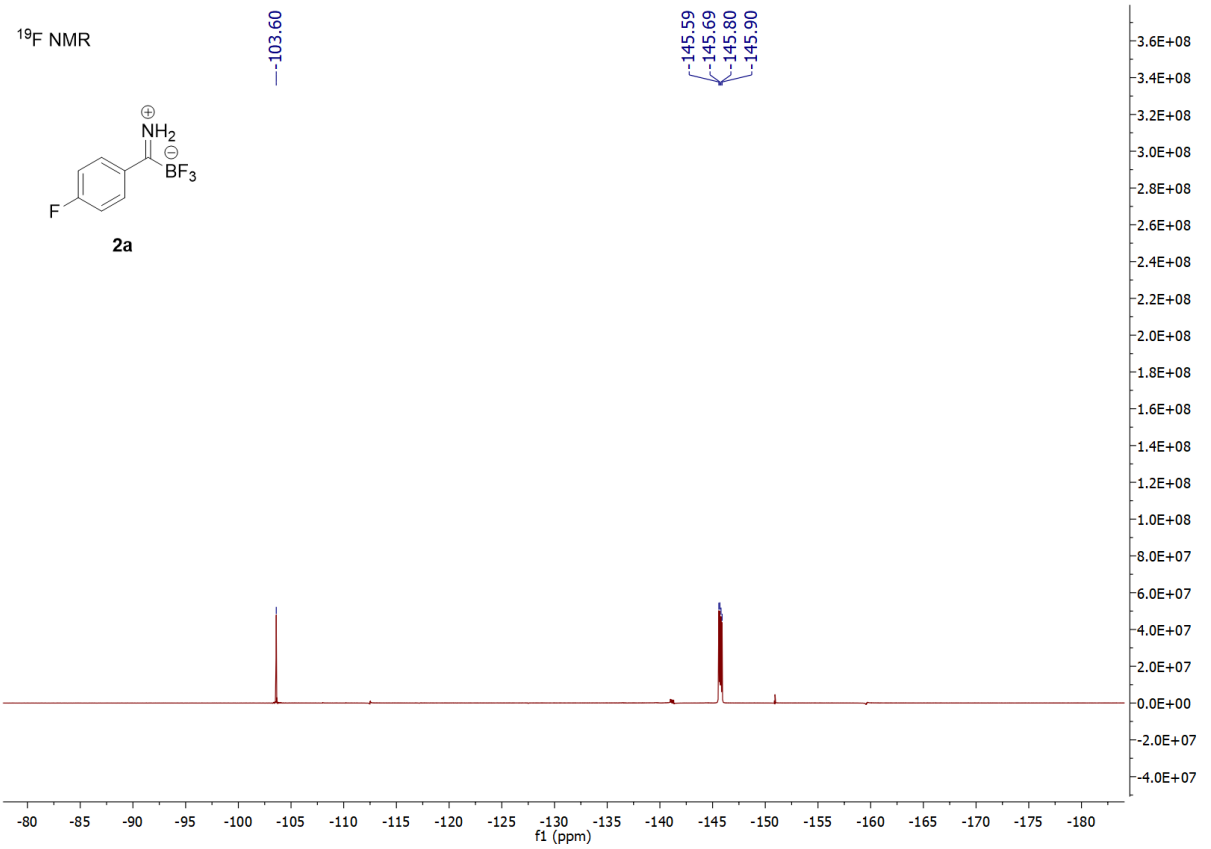
^{13}C-NMR (101 MHz, Acetone-d_6) of **2a**:



^{1}H-^{13}C -HMBC NMR (Acetone-d_6) of **2a**:

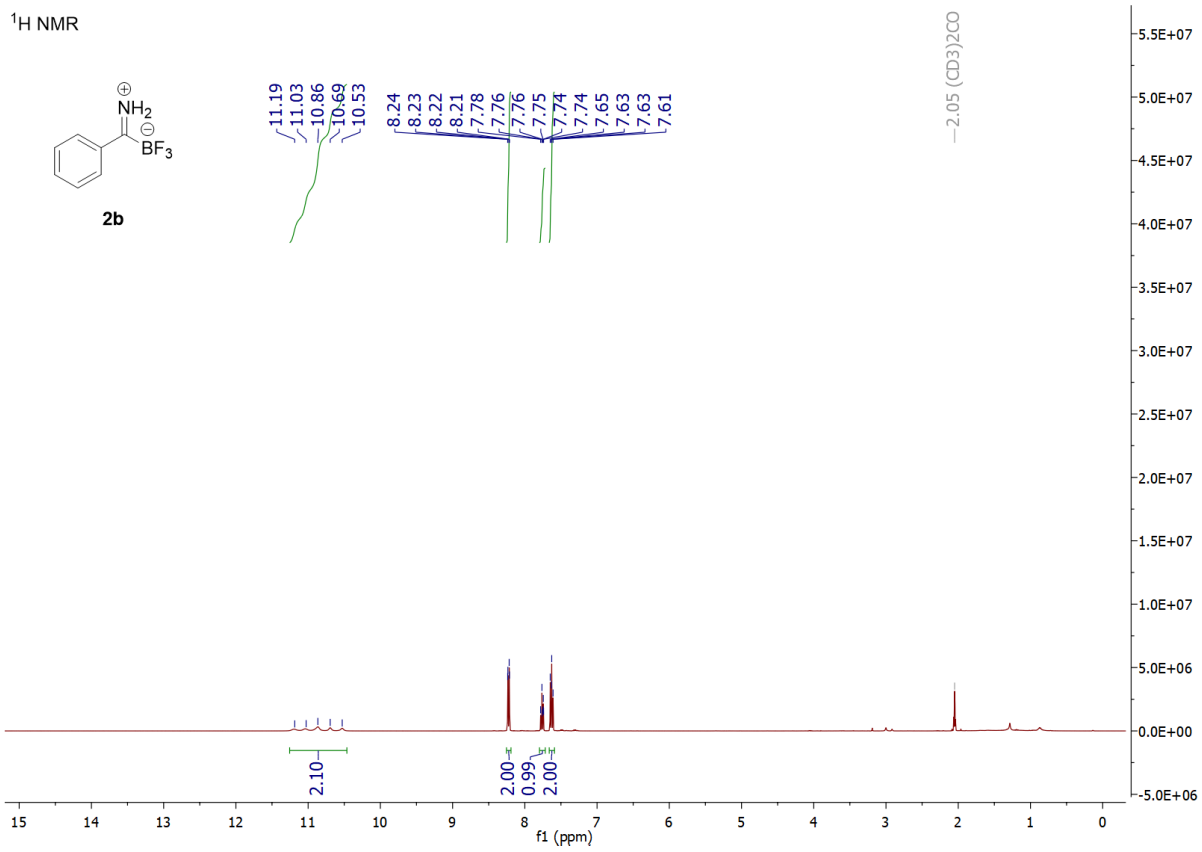


^{19}F-NMR (376 MHz, Acetone-d_6) of **2a**:

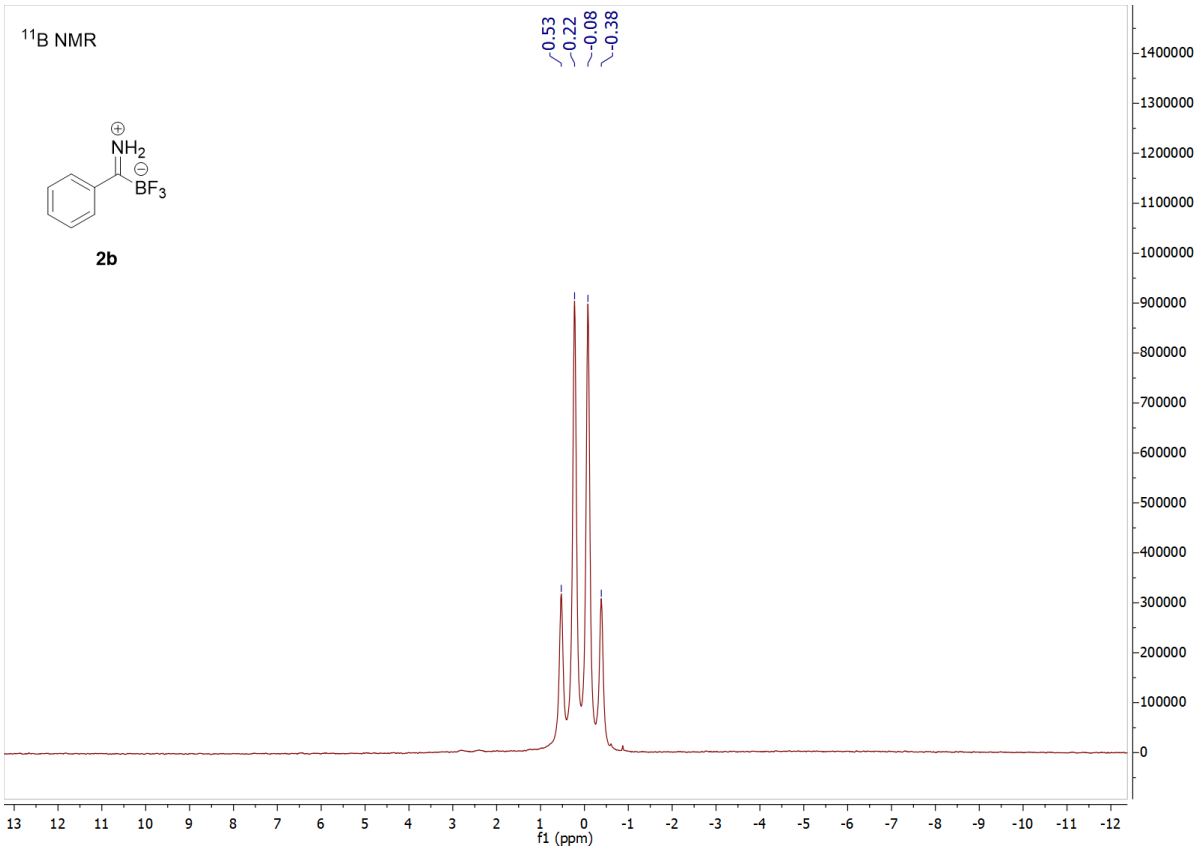


(Iminio(phenyl)methyl)trifluoroborate (2b)

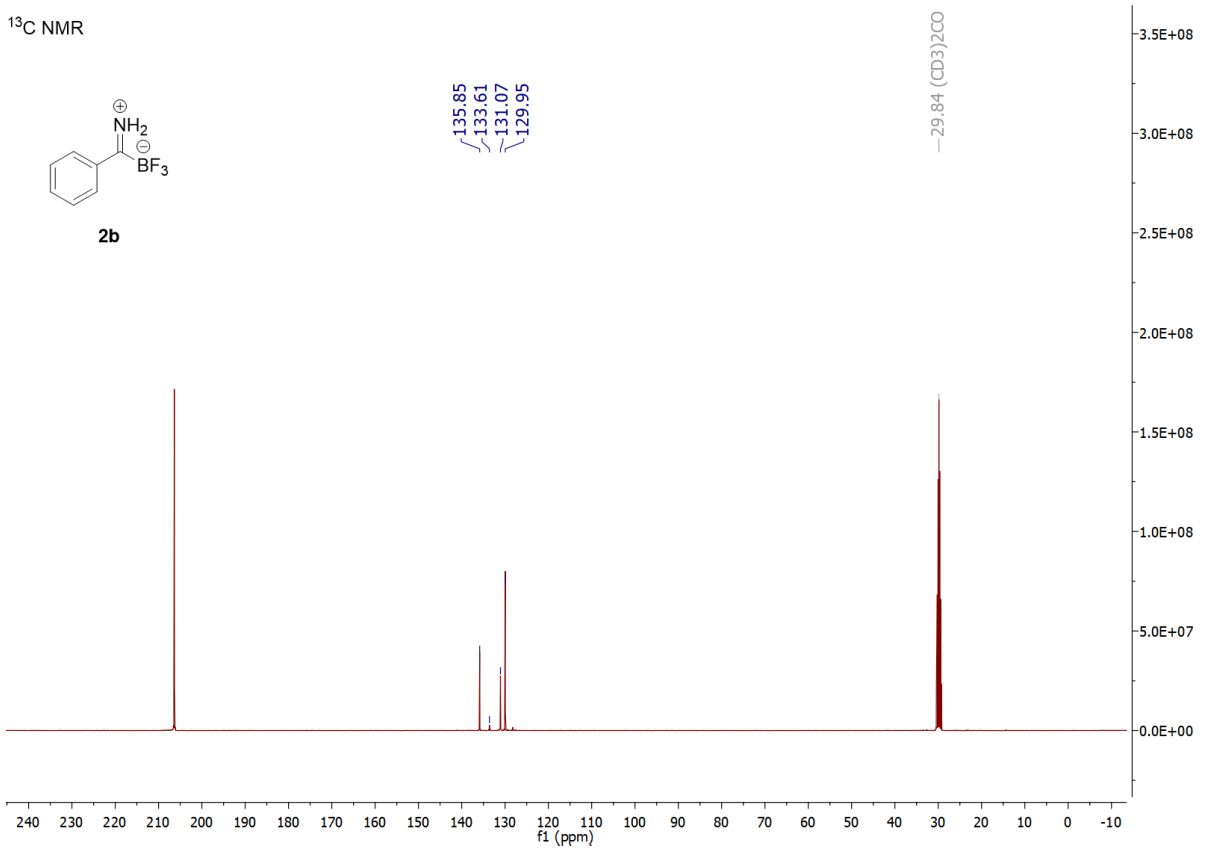
^{1}H-NMR (400 MHz, Acetone-d_6) of **2b**:



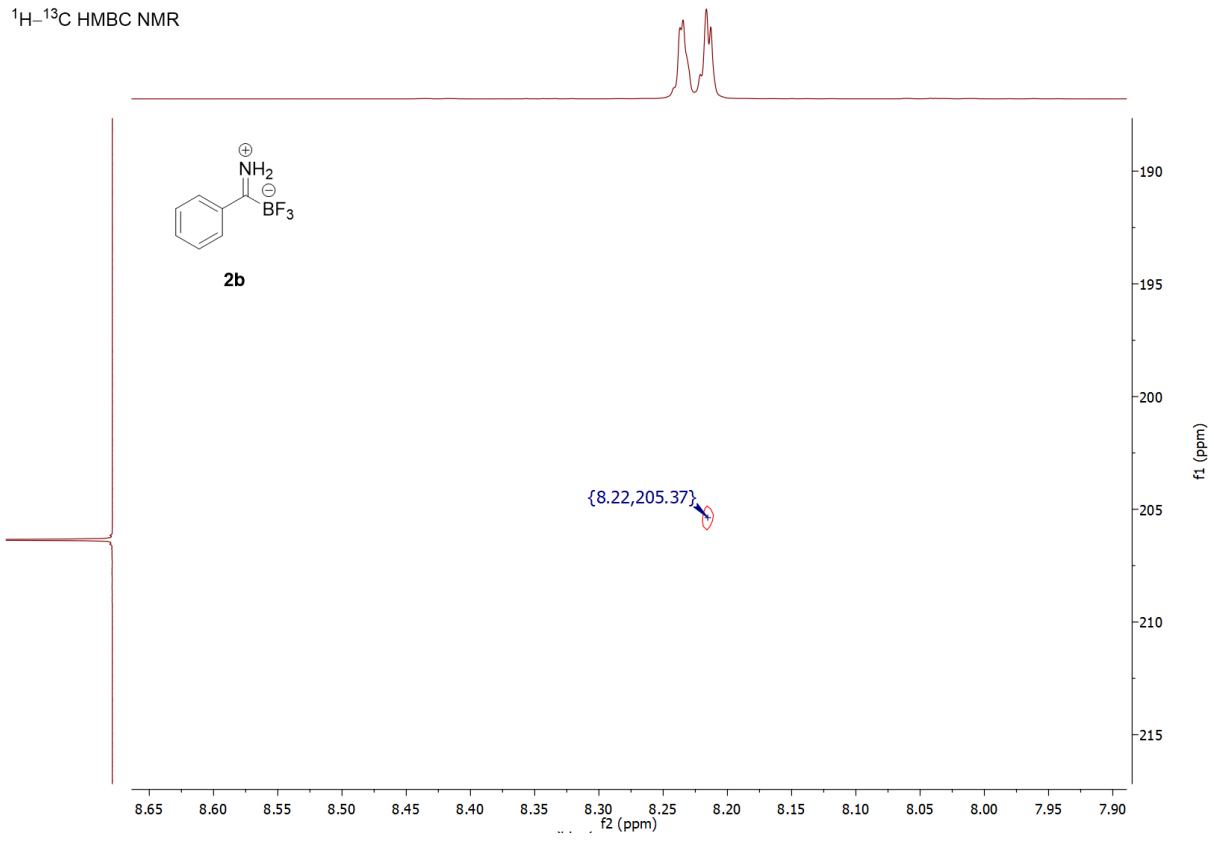
^{11}B-NMR (128 MHz, Acetone-d_6) of **2b**:



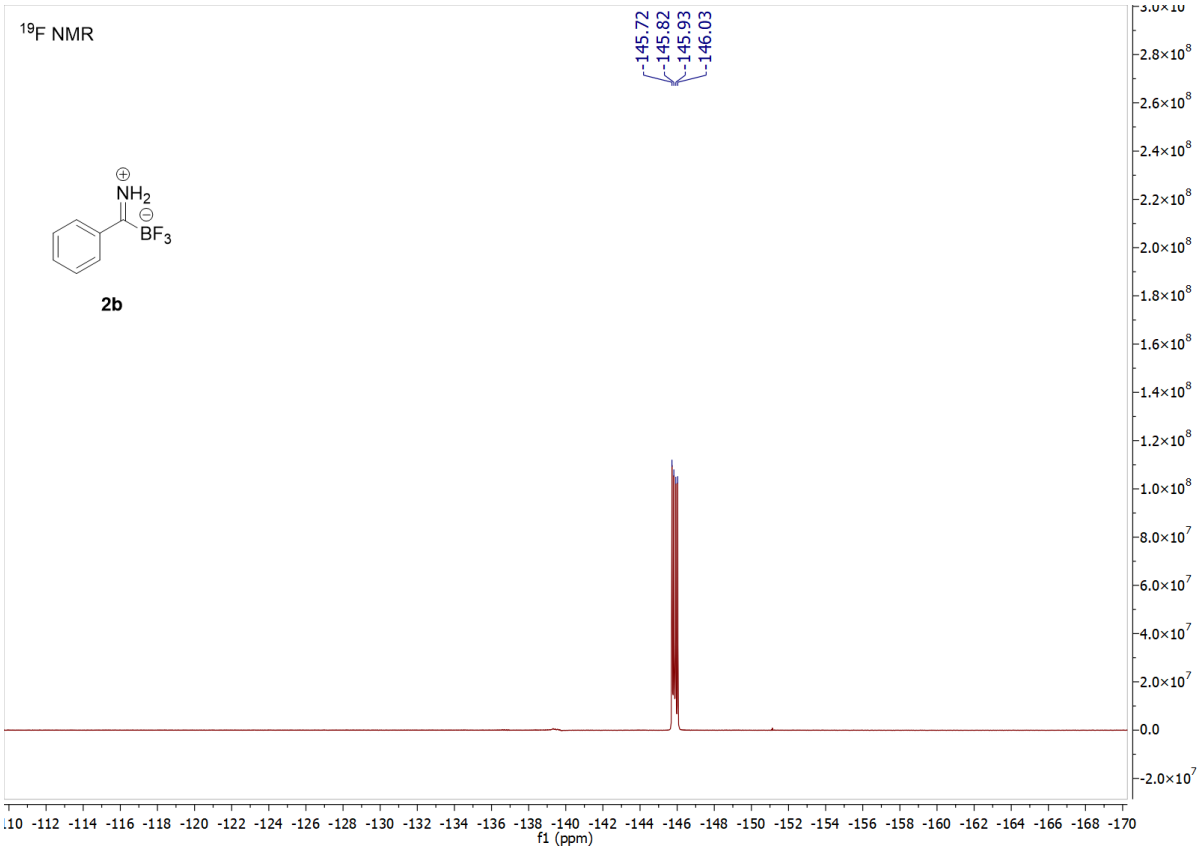
^{13}C-NMR (101 MHz, Acetone-d_6) of **2b**:



^{1}H-^{13}C-HMBC NMR (Acetone-d_6) of **2b**:

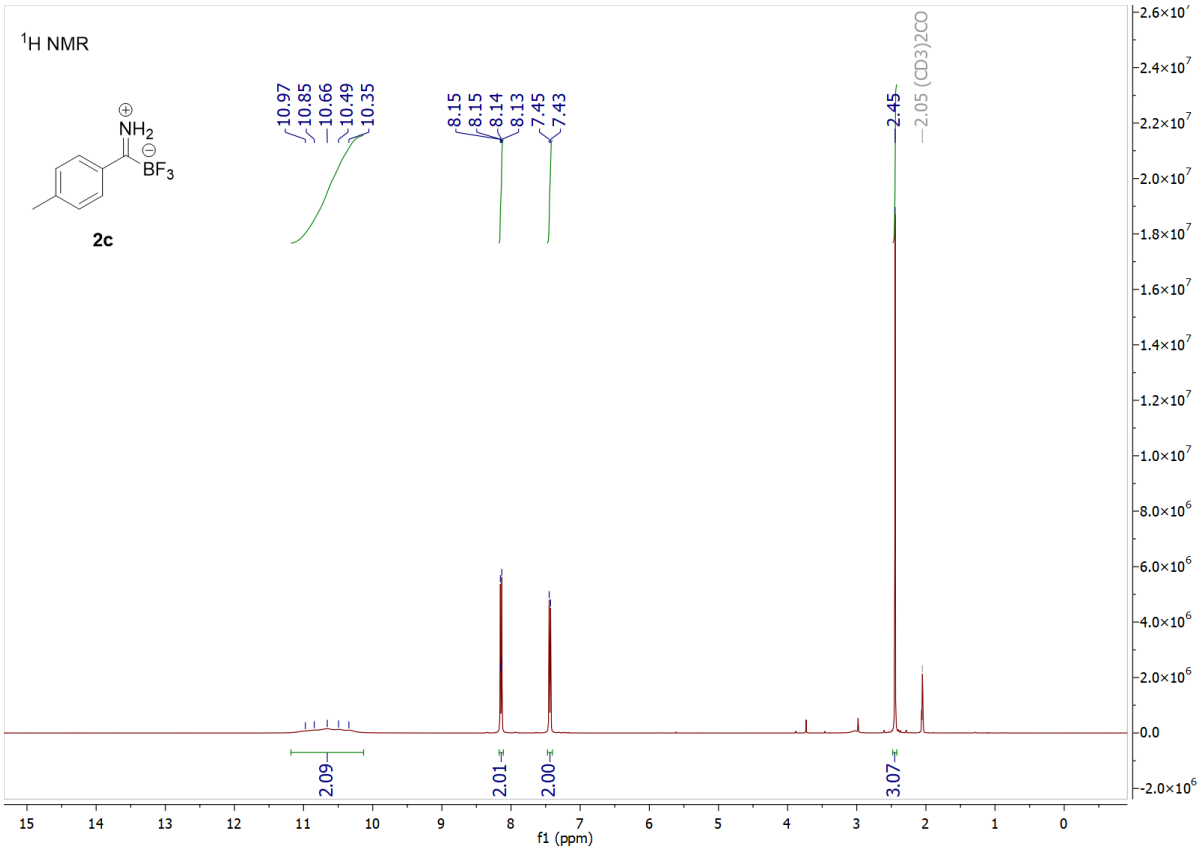


^{19}F-NMR (376 MHz, Acetone-d_6) of **2b**:

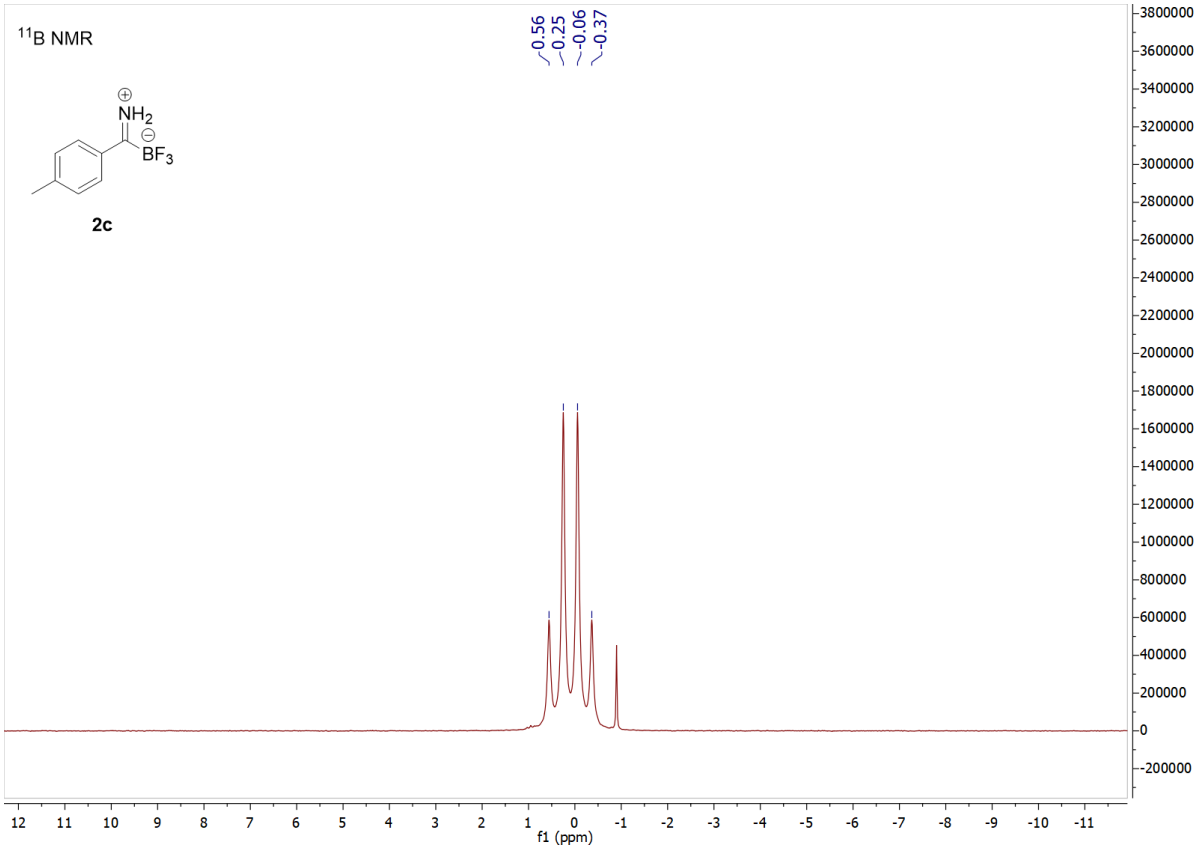


(Iminio(*p*-tolyl)methyl)trifluoroborate (2c)

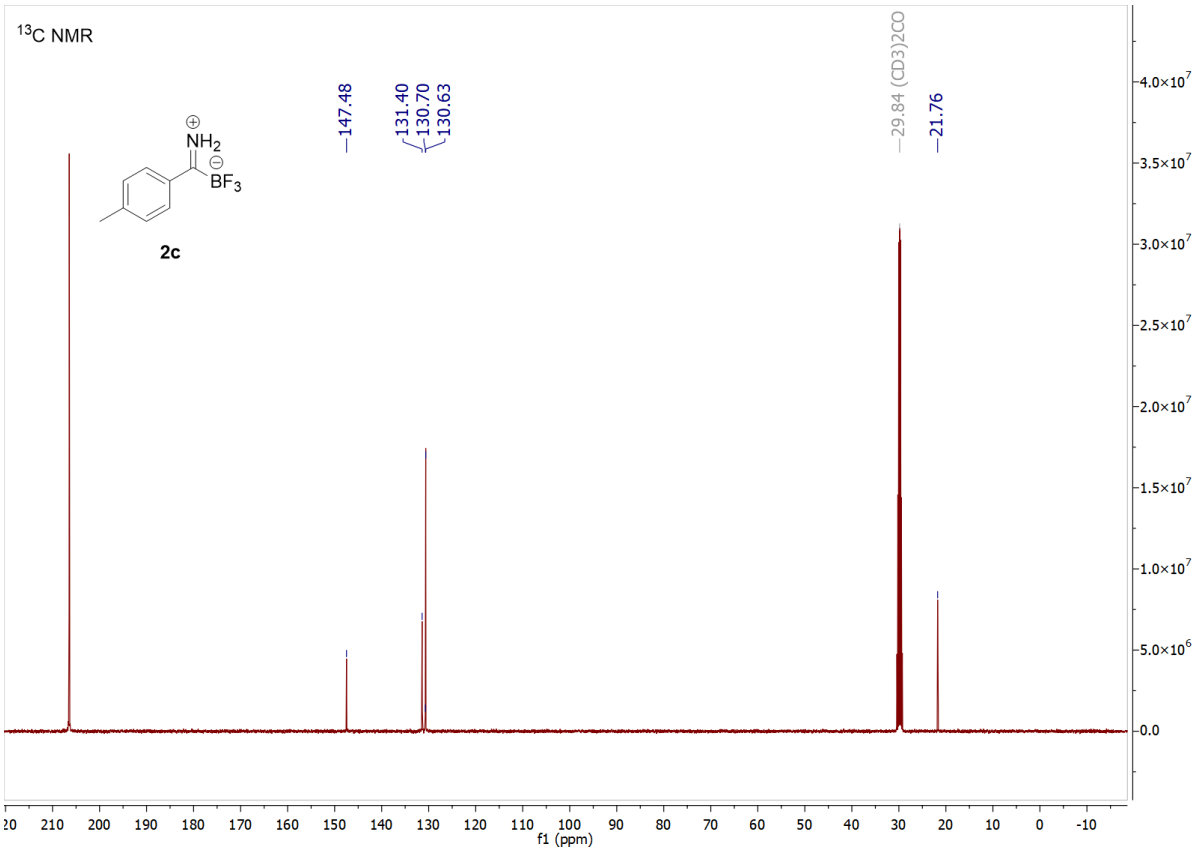
^{1}H-NMR (400 MHz, Acetone-d_6) of **2c**:



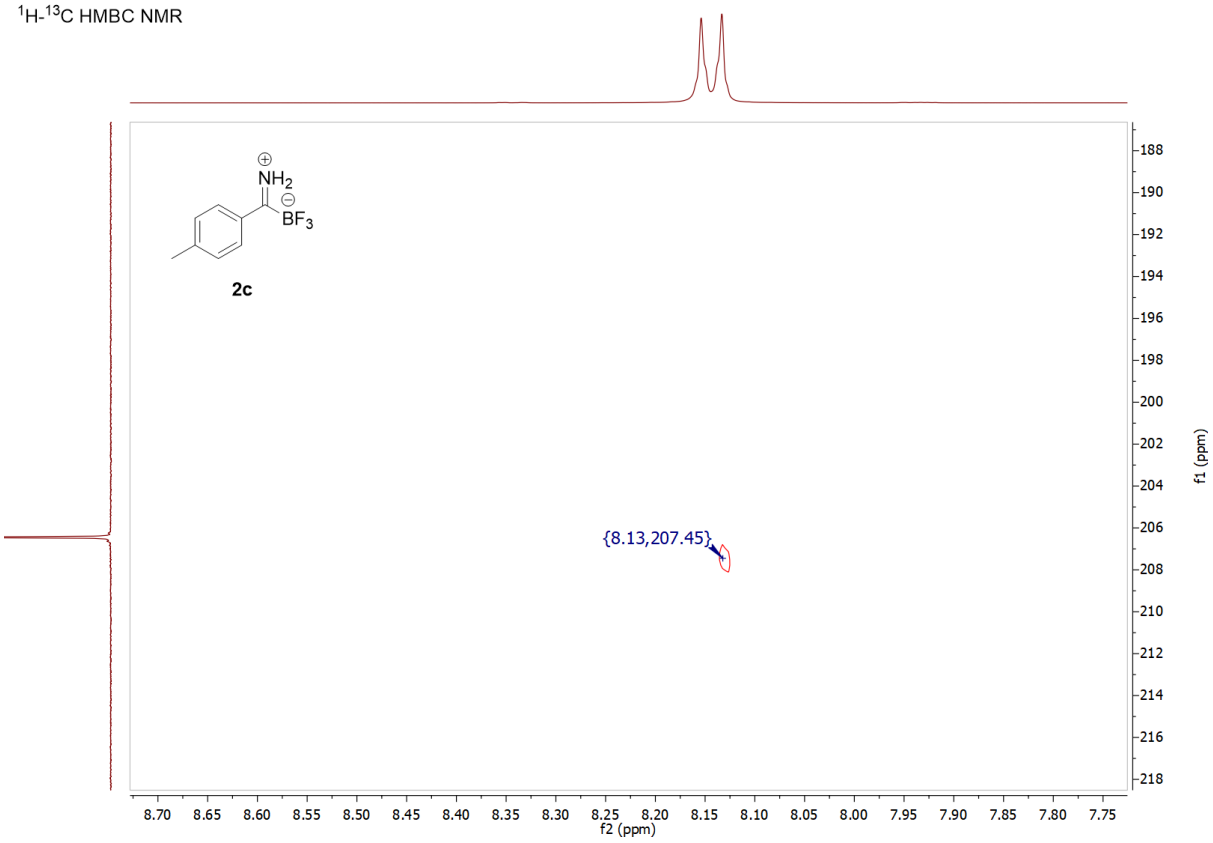
^{11}B-NMR (128 MHz, Acetone-d_6) of **2c**:



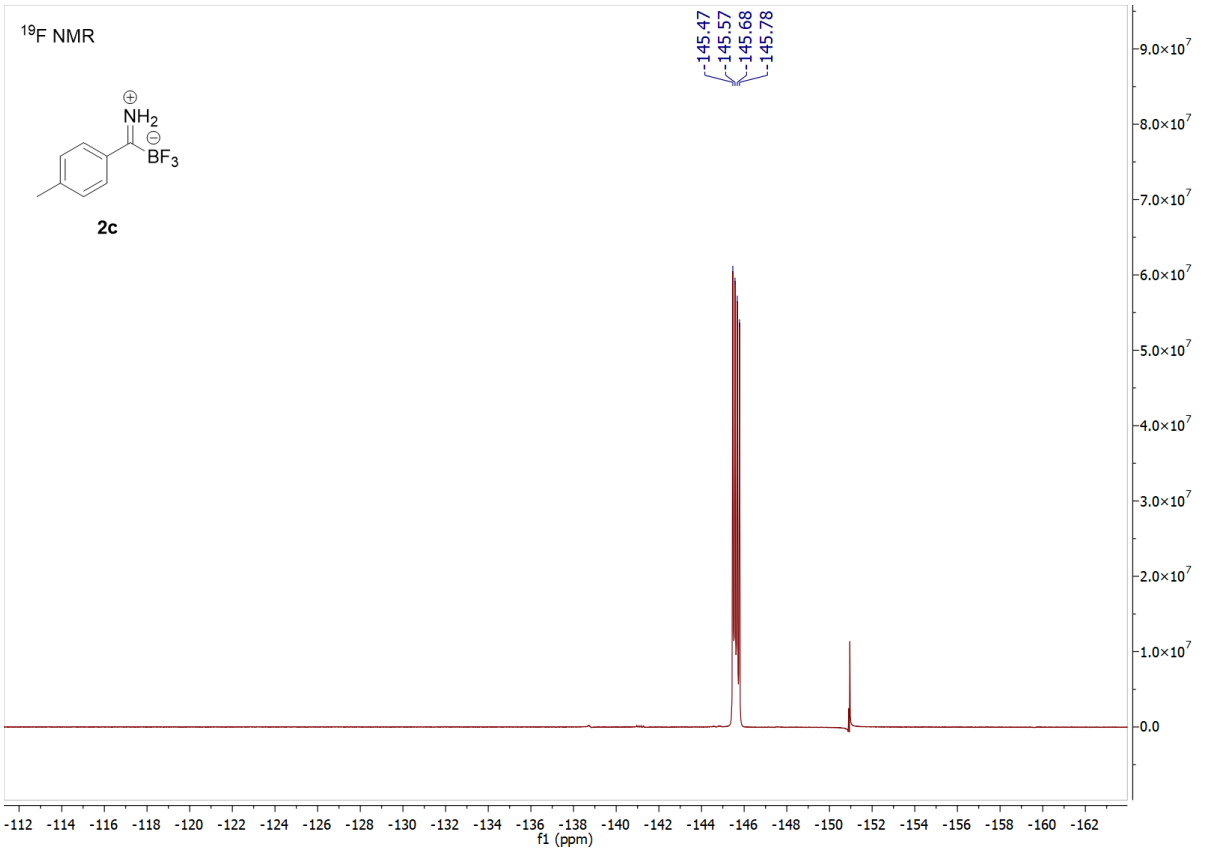
^{13}C-NMR (101 MHz, Acetone-d_6) of **2c**:



^{1}H-^{13}C-HMBC NMR (Acetone-d_6) of **2c**:

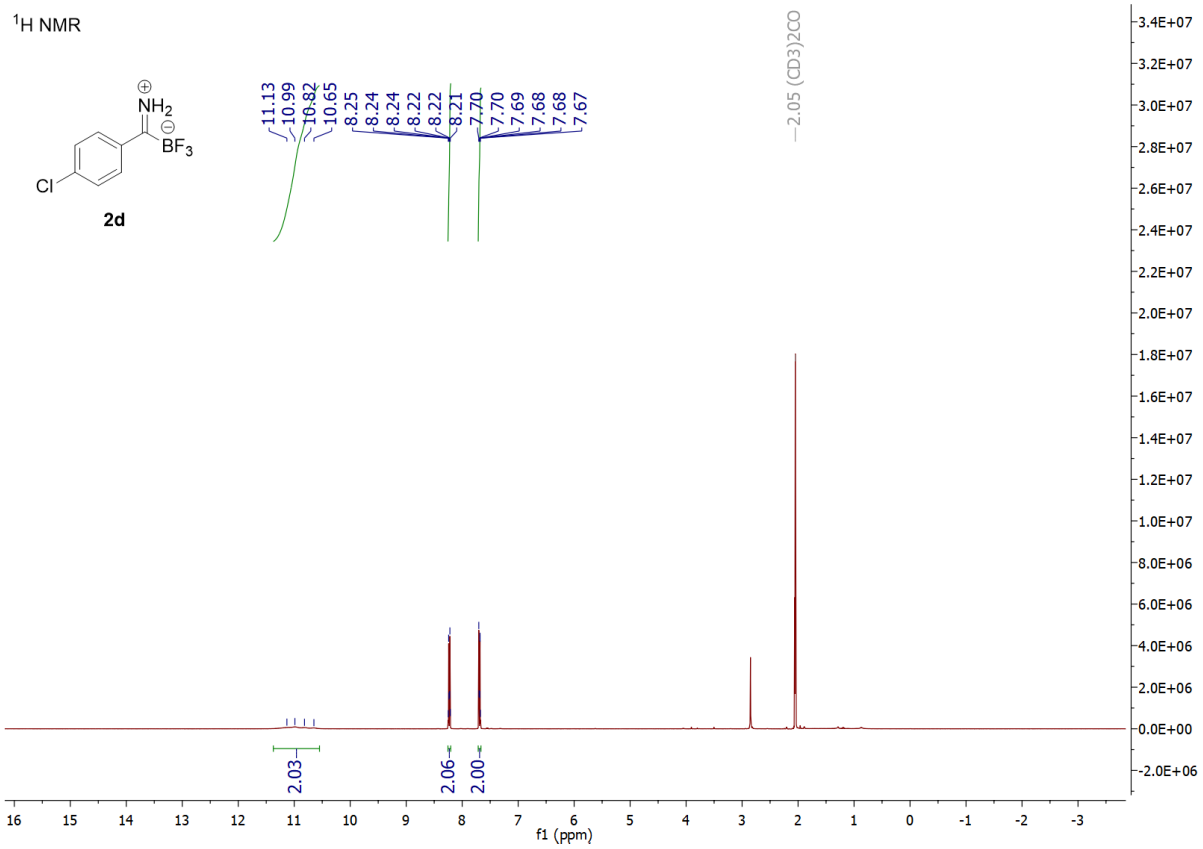


^{19}F-NMR (376 MHz, Acetone-d_6) of **2c**:

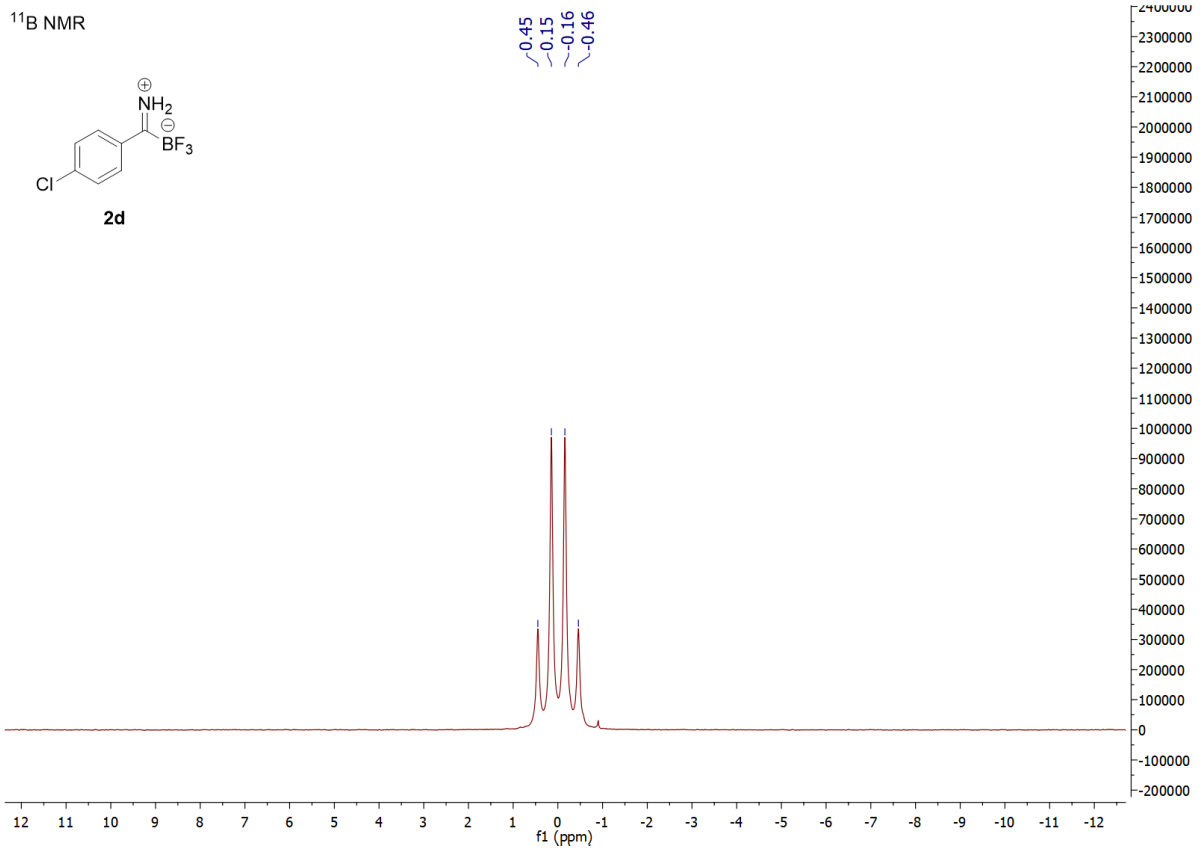


((4-Chlorophenyl)(iminio)methyl)trifluoroborate (2d)

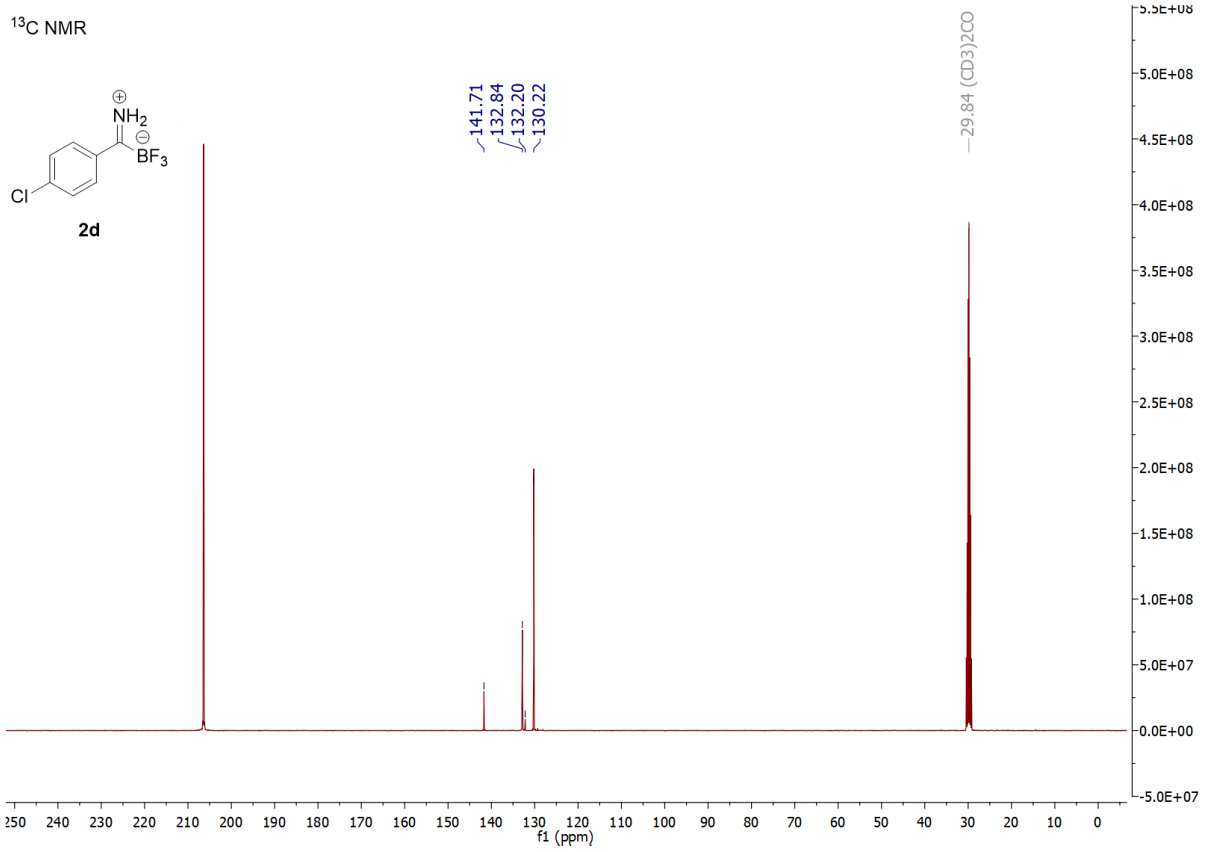
^{1}H-NMR (400 MHz, Acetone-d_6) of **2d**:



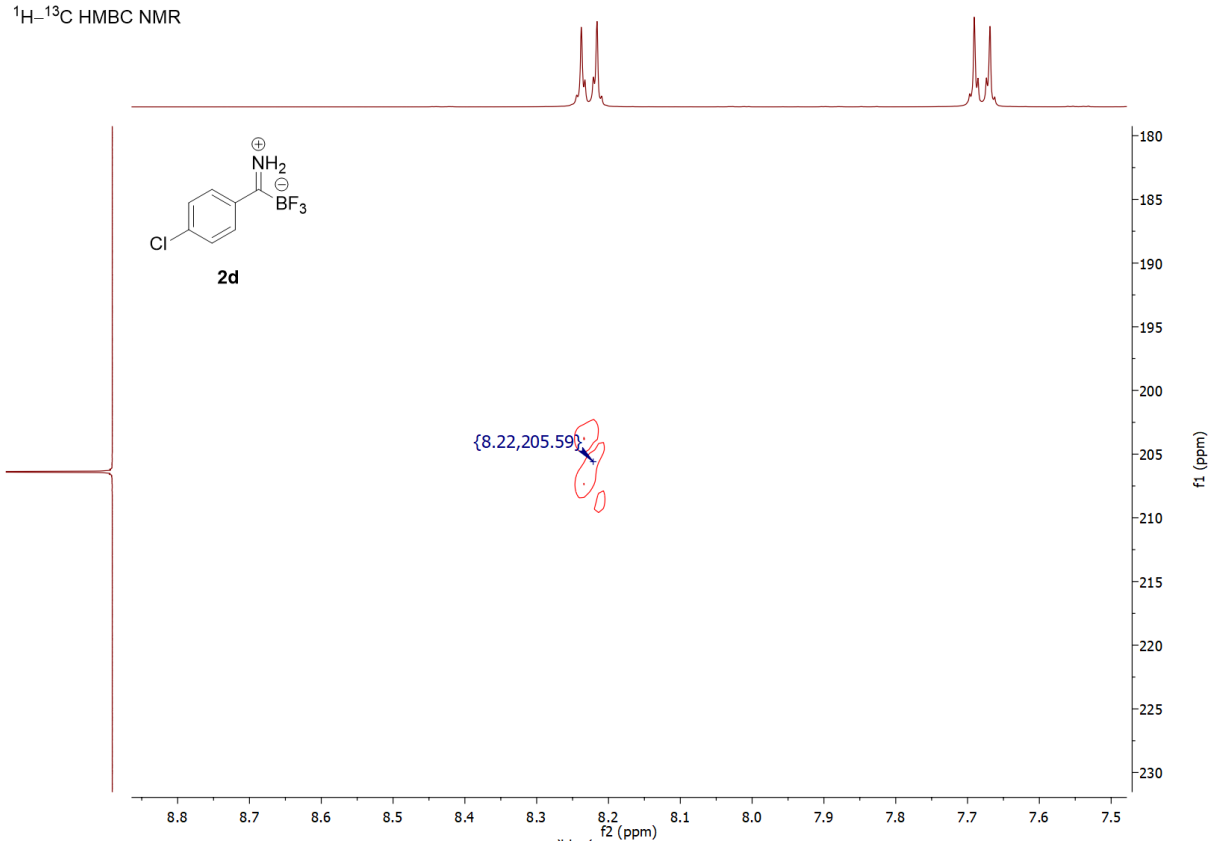
^{11}B-NMR (128 MHz, Acetone-d_6) of **2d**:



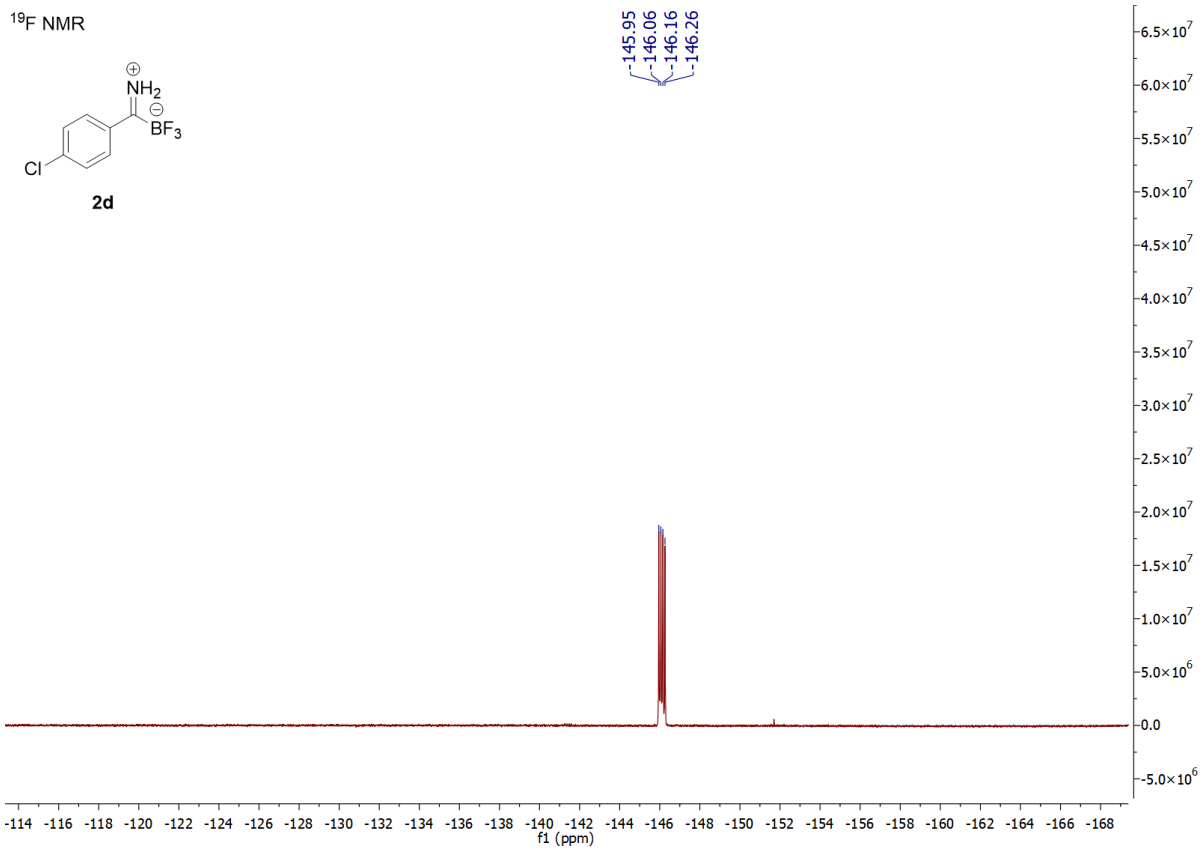
^{13}C-NMR (101 MHz, Acetone-d_6) of **2d**:



^{1}H-^{13}C-HMBC NMR (Acetone-d_6) of **2d**:

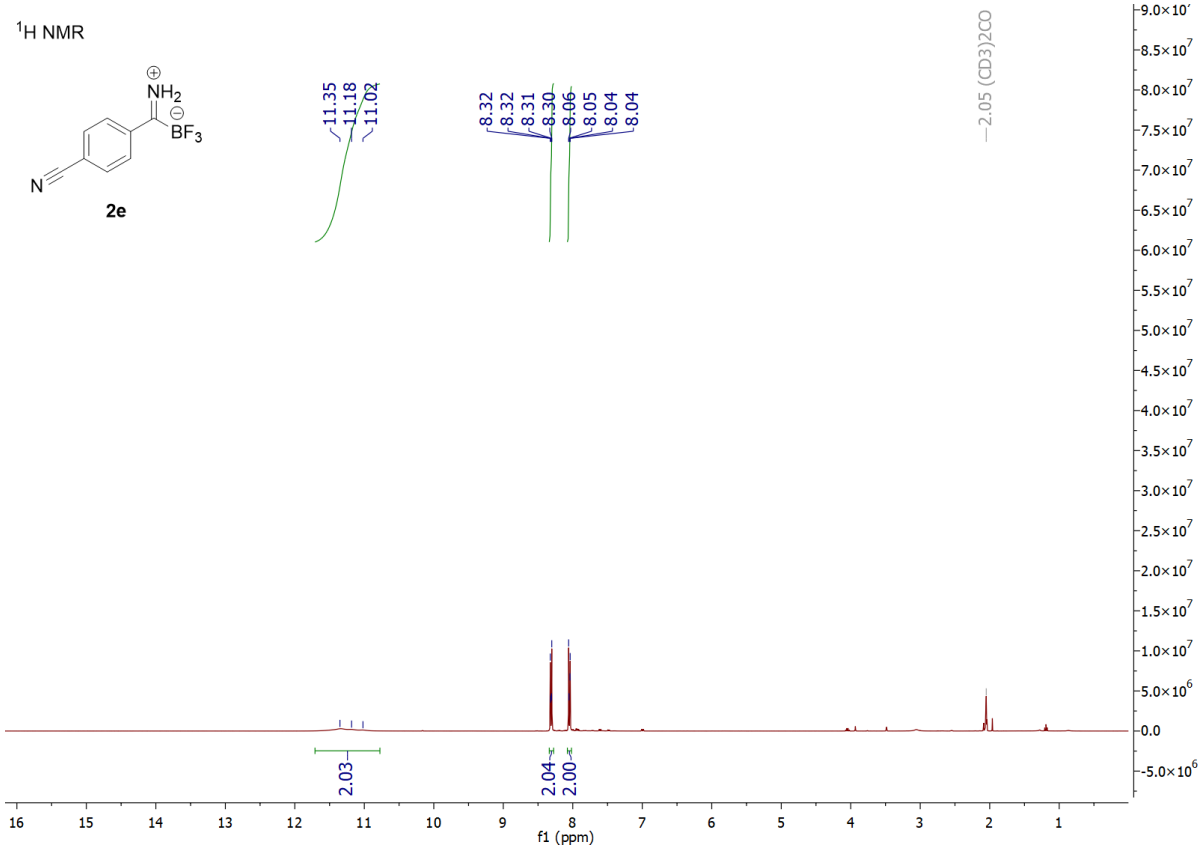


^{19}F-NMR (376 MHz, Acetone-d_6) of **2d**:

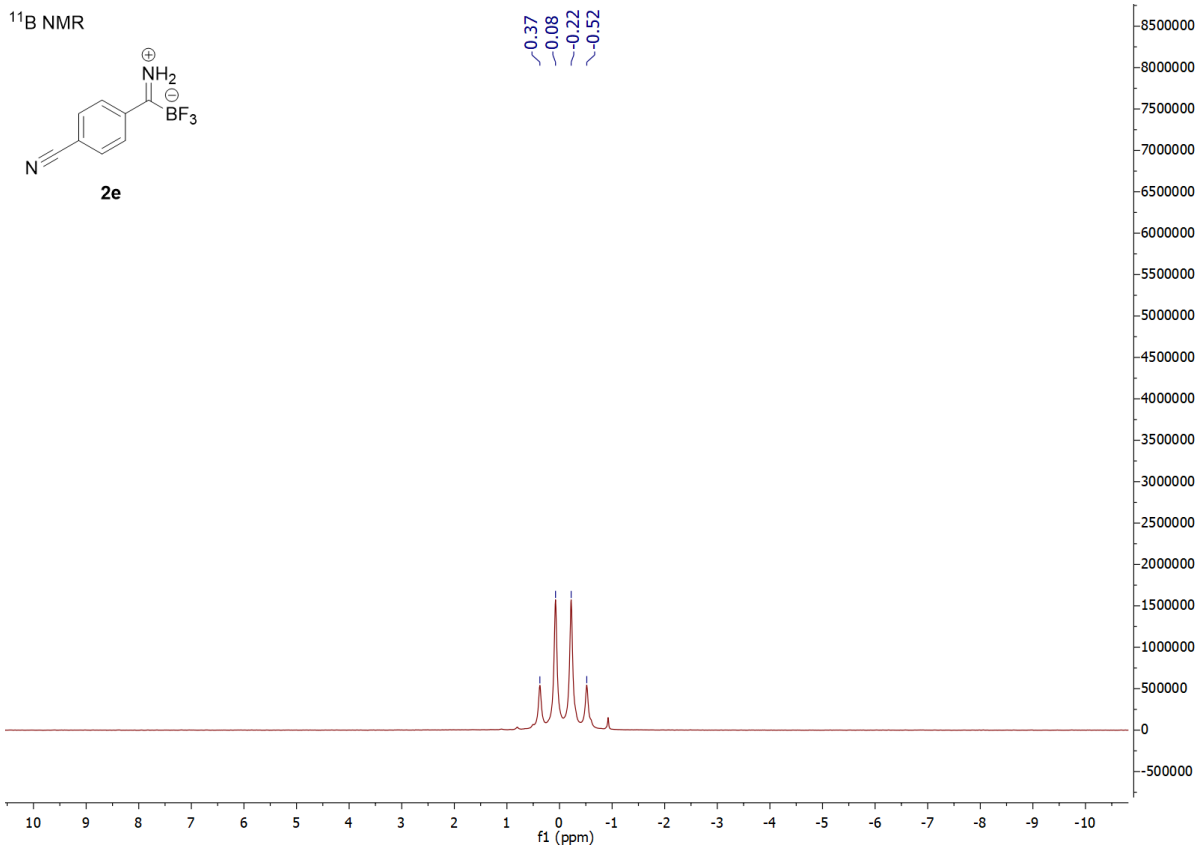


((4-Cyanophenyl)(iminio)methyl)trifluoroborate (2e)

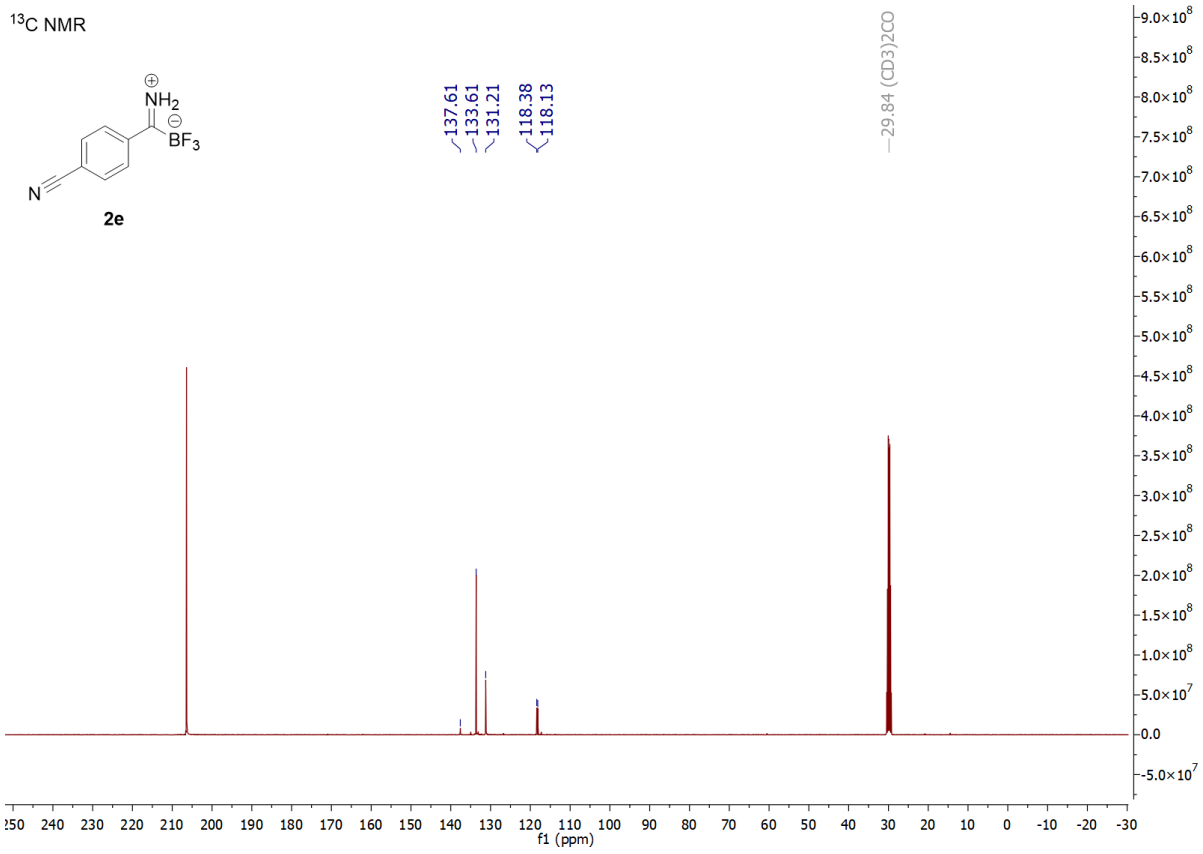
^{1}H-NMR (400 MHz, Acetone-d_6) of **2e**:



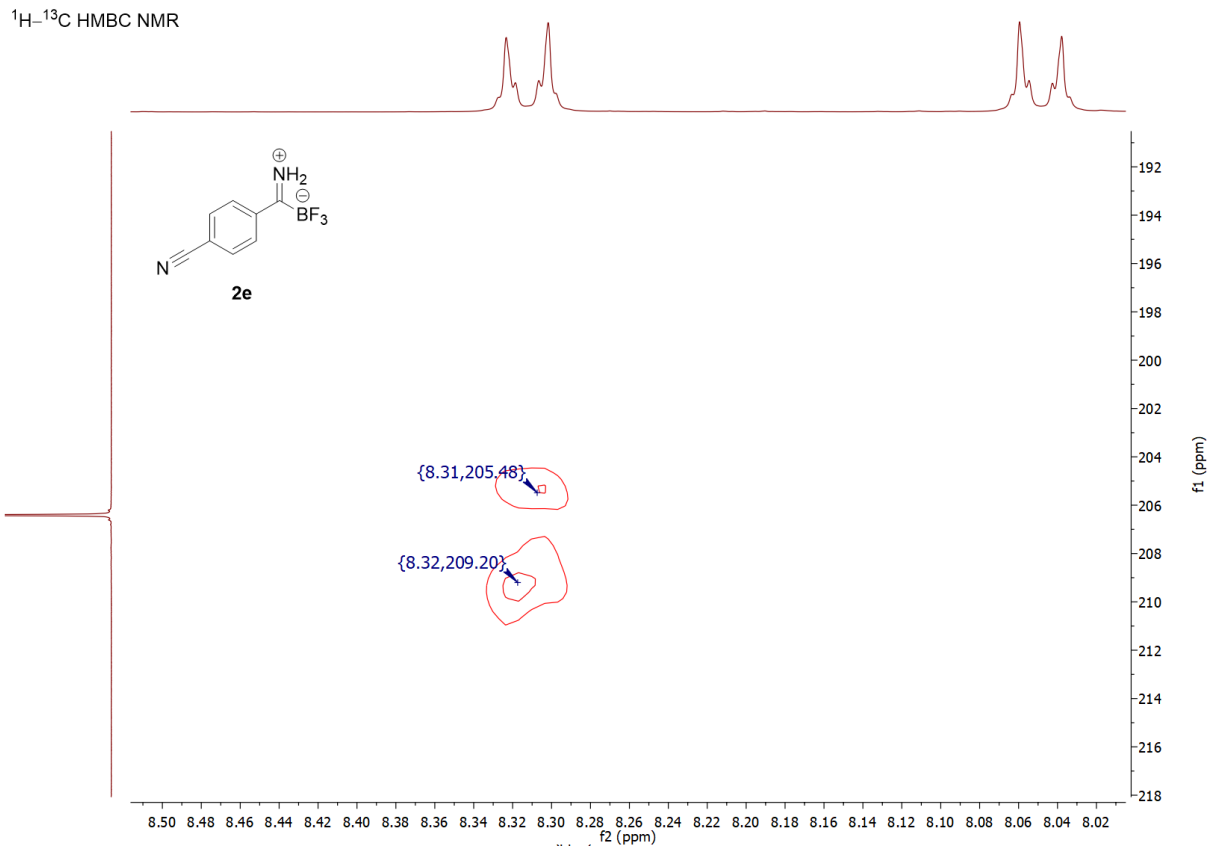
^{11}B-NMR (128 MHz, Acetone-d_6) of **2e**:



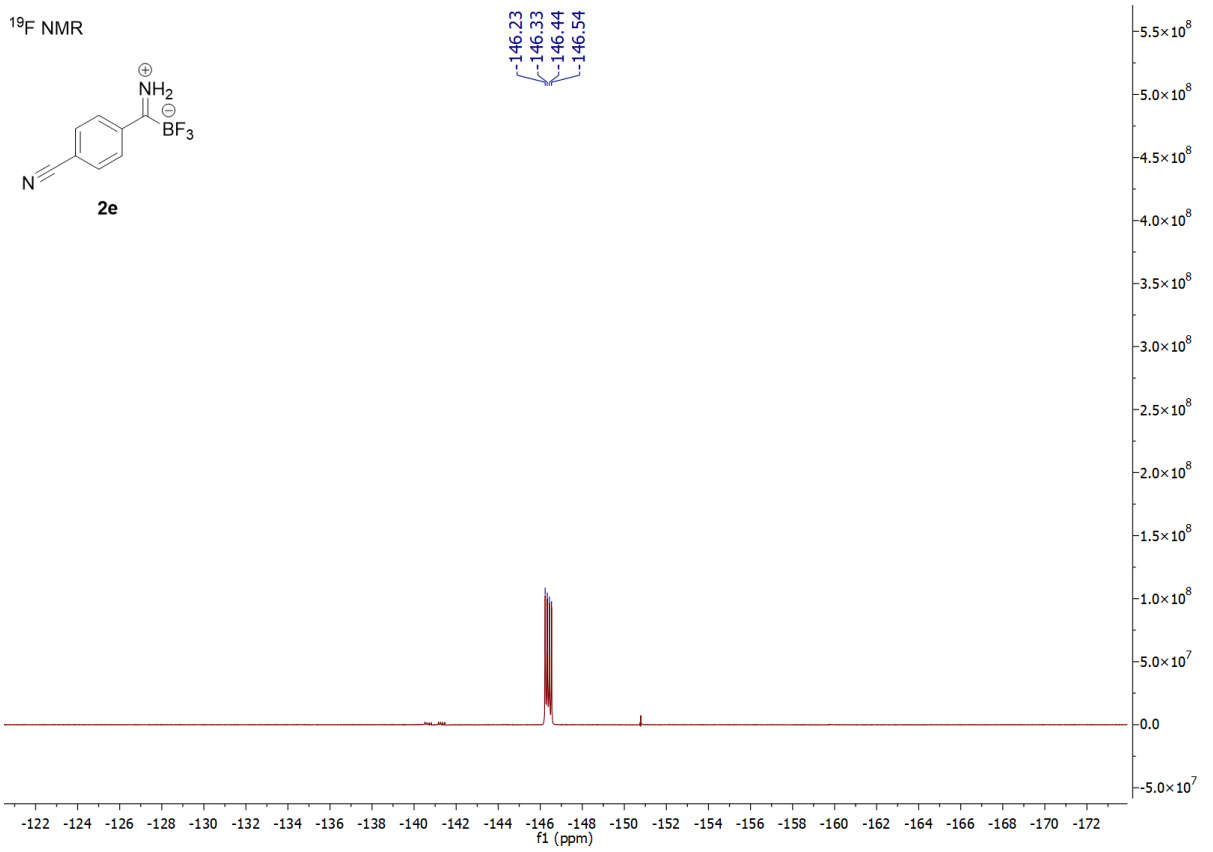
^{13}C-NMR (101 MHz, Acetone-d_6) of **2e**:



^{1}H-^{13}C-HMBC NMR (Acetone-d$_6$) of **2e**:

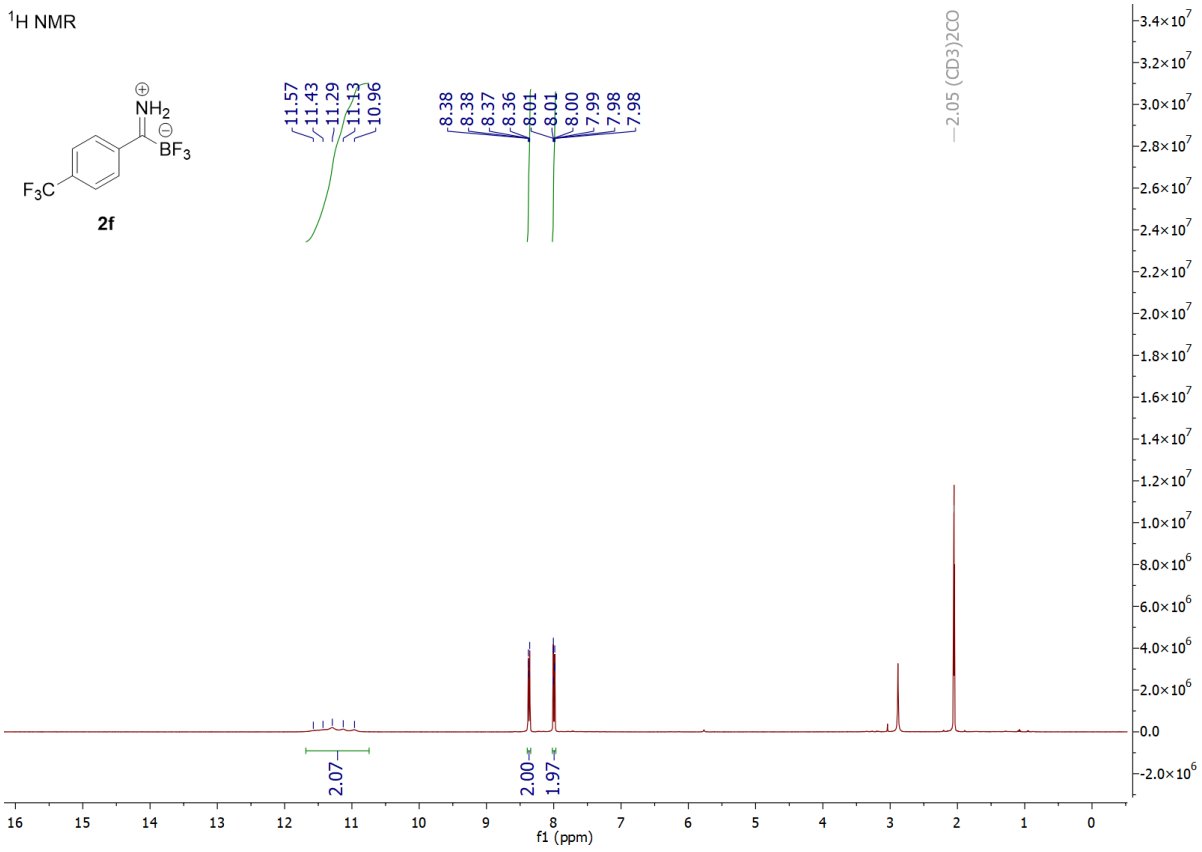


^{19}F-NMR (376 MHz, Acetone-d$_6$) of **2e**:

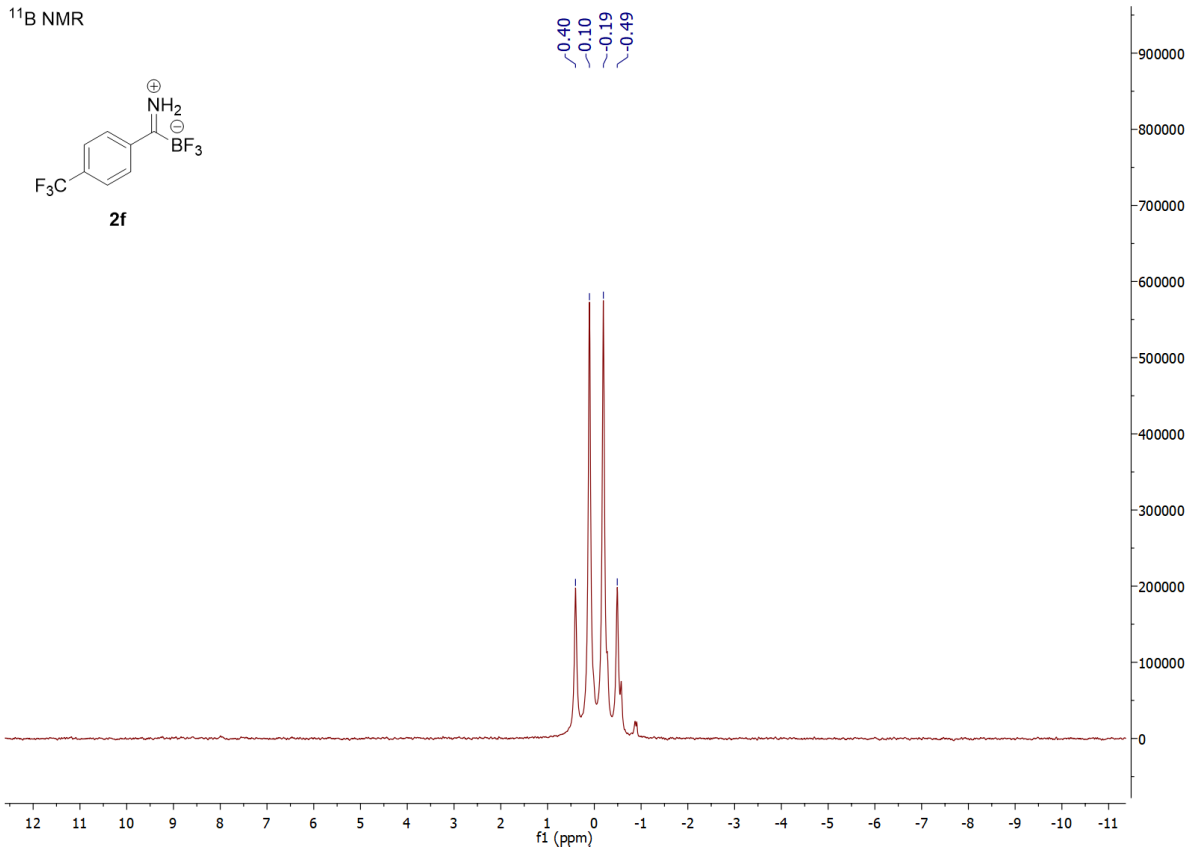


(Iminio(4-(trifluoromethyl)phenyl)methyl)trifluoroborate (2f)

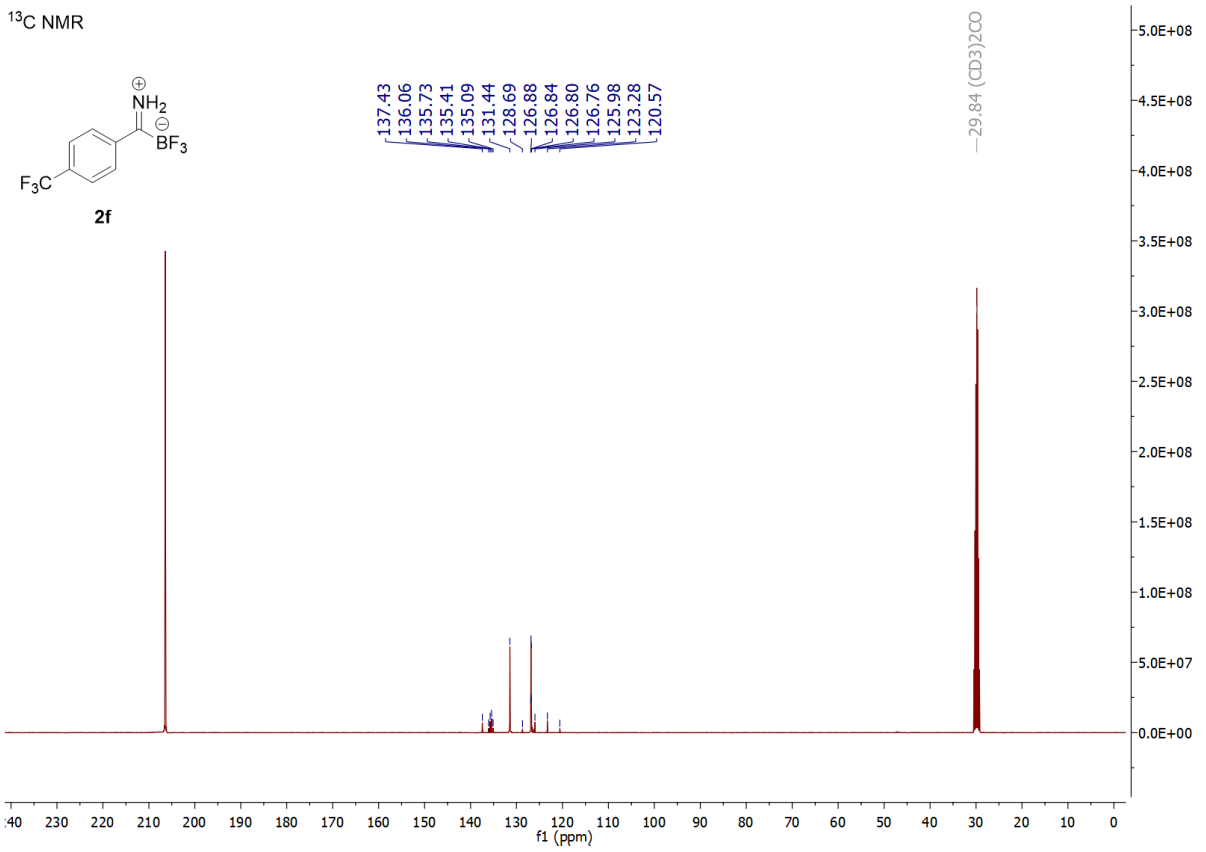
^{1}H-NMR (400 MHz, Acetone-d_6) of **2f**:



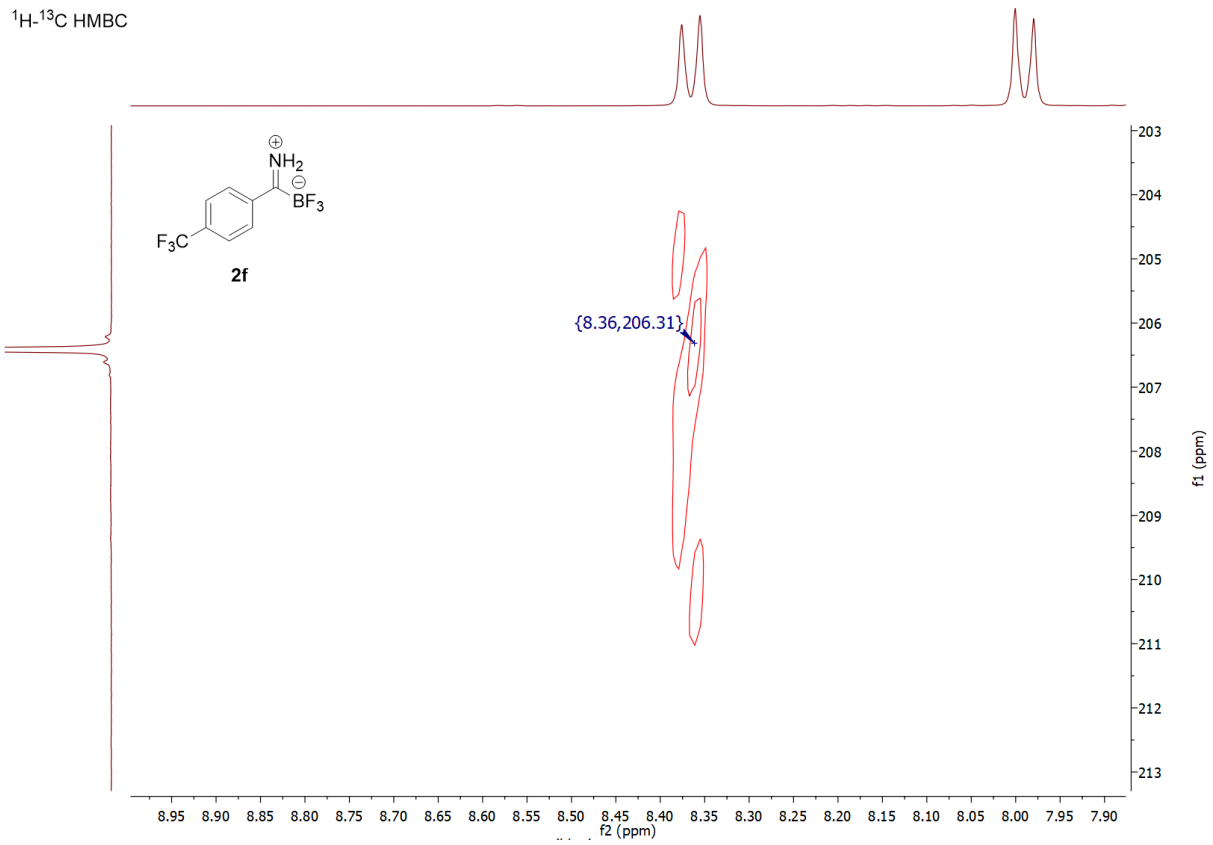
^{11}B-NMR (128 MHz, Acetone-d_6) of **2f**:



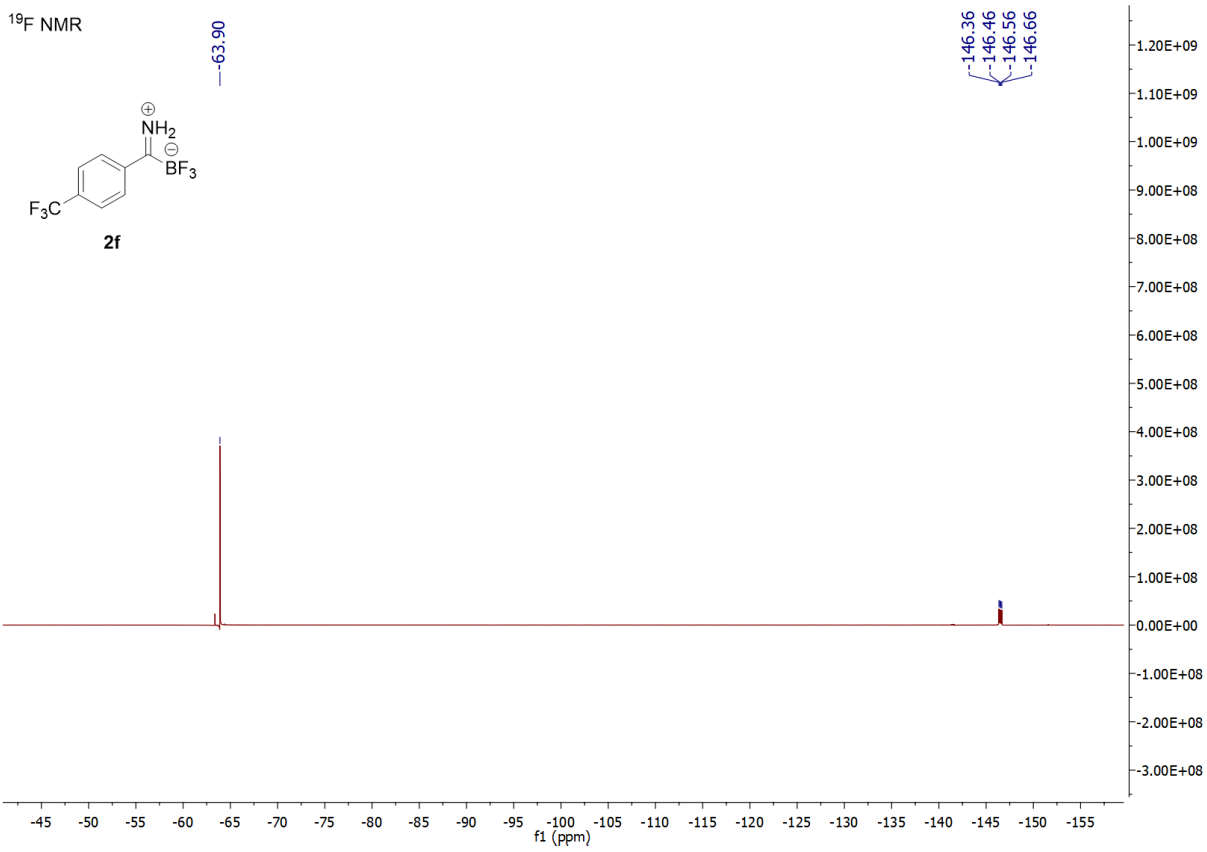
^{13}C-NMR (101 MHz, Acetone-d_6) of **2f**:



^{1}H-^{13}C-HMBC NMR (Acetone-d_6) of **2f**:

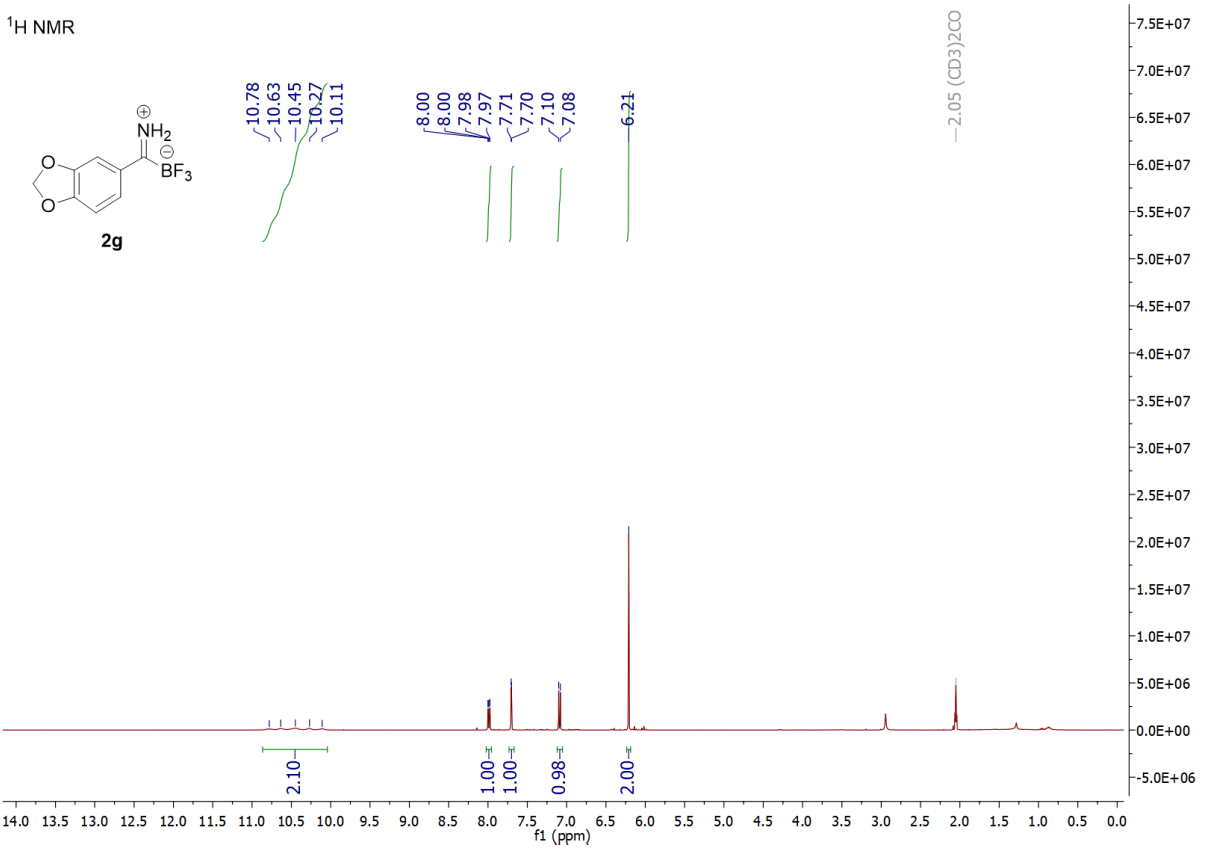


^{19}F-NMR (376 MHz, Acetone-d_6) of **2f**:

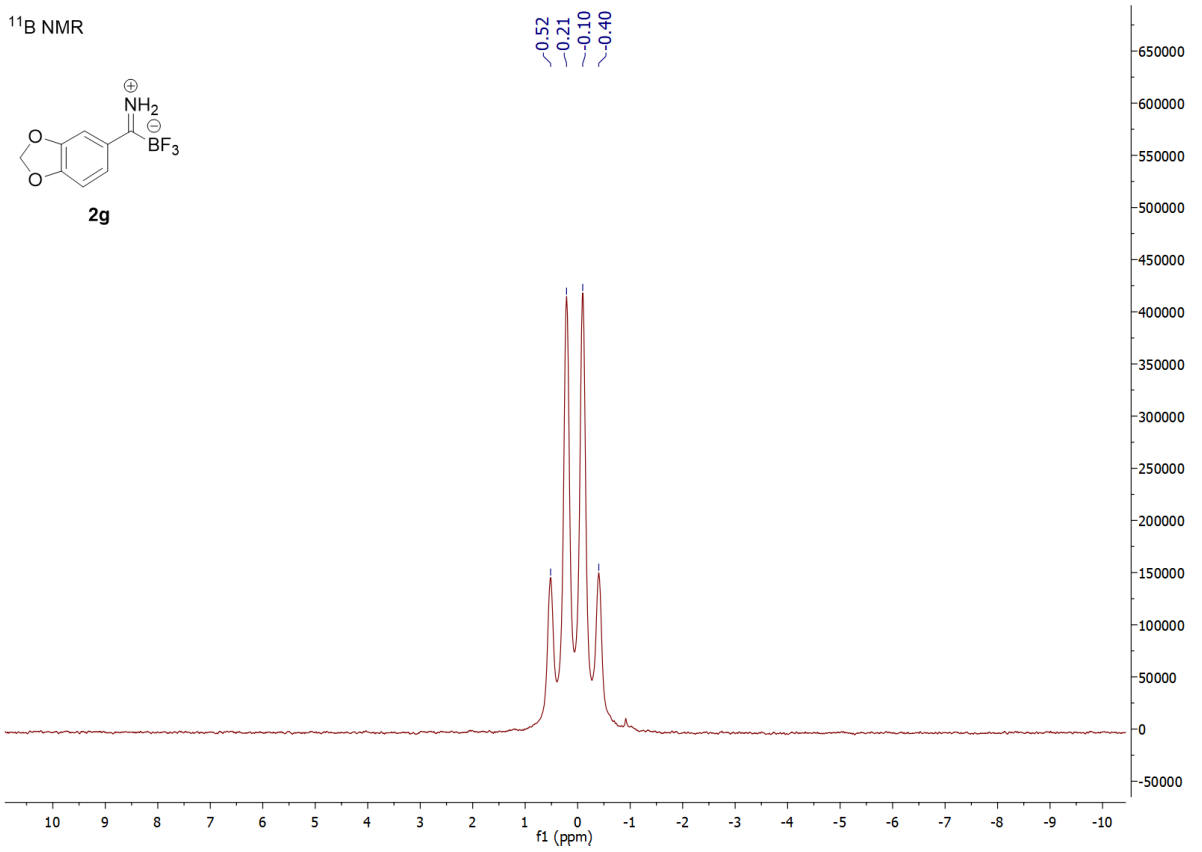


(Benzo[*d*][1,3]dioxol-5-yl(iminio)methyl)trifluoroborate (2g)

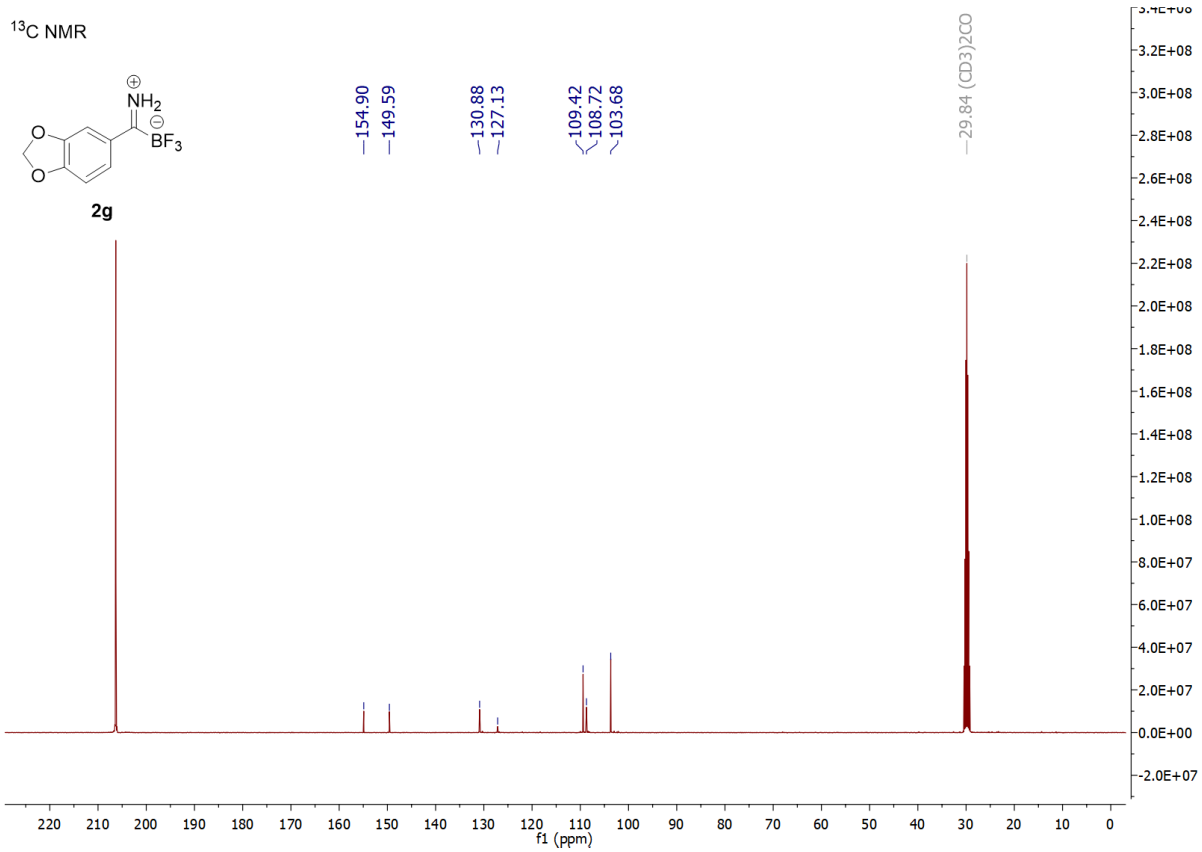
^{1}H-NMR (400 MHz, Acetone-d_6) of **2g**:



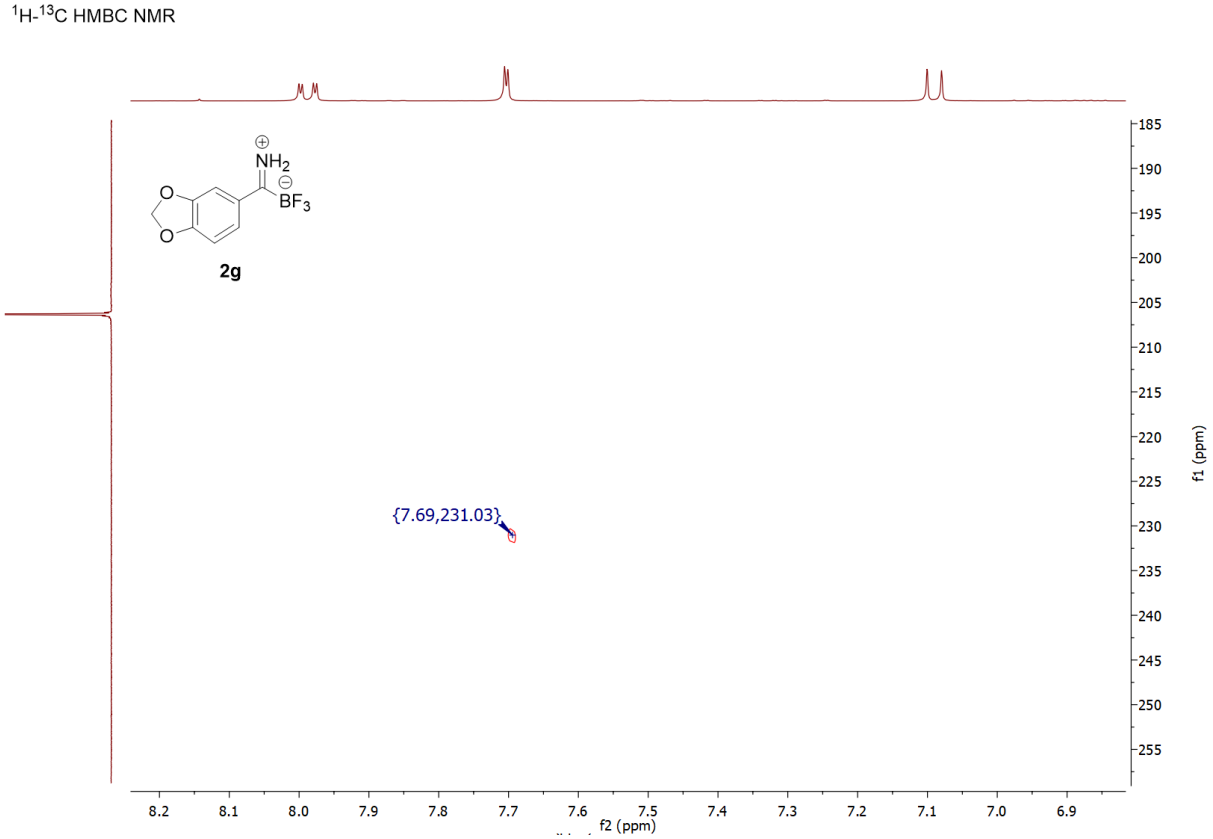
^{11}B-NMR (128 MHz, Acetone-d_6) of **2g**:



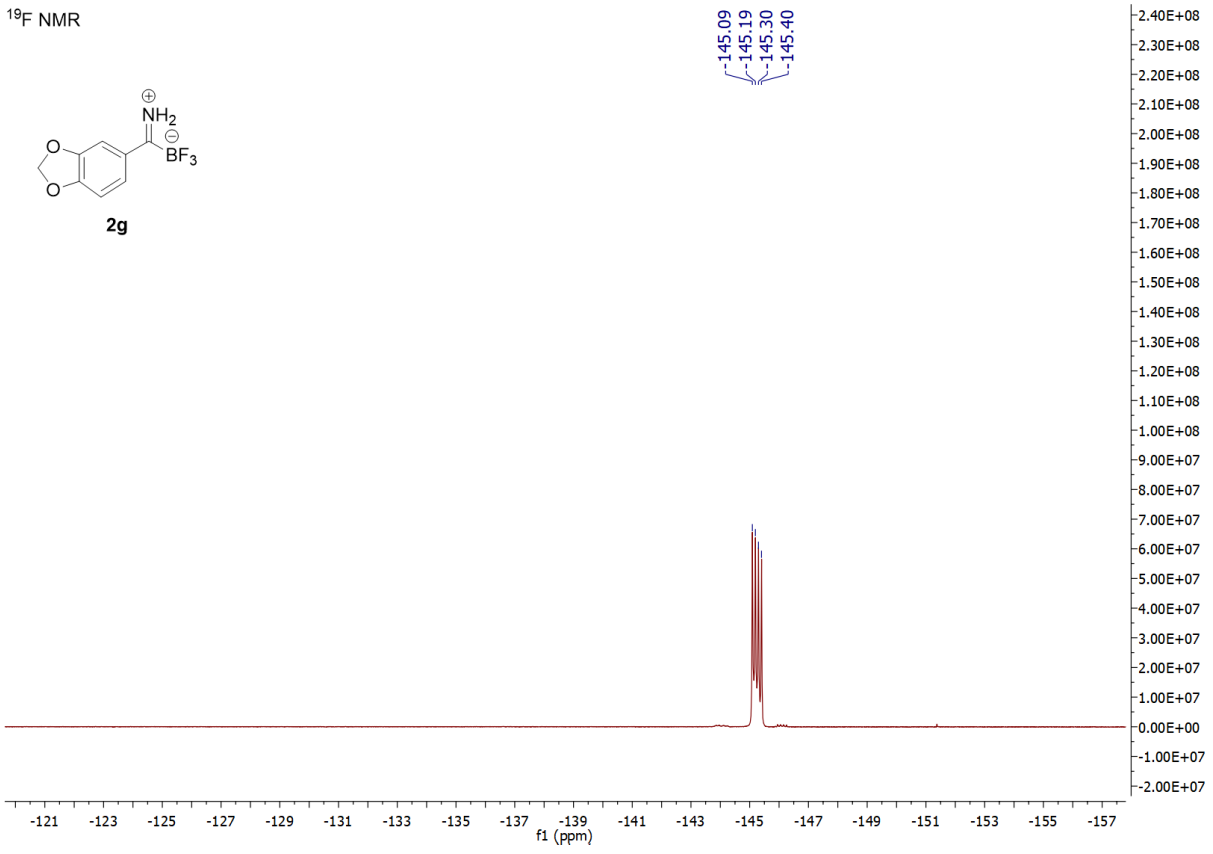
^{13}C-NMR (101 MHz, Acetone-d_6) of **2g**:



^{1}H-^{13}C-HMBC NMR (Acetone-d_6) of **2g**:

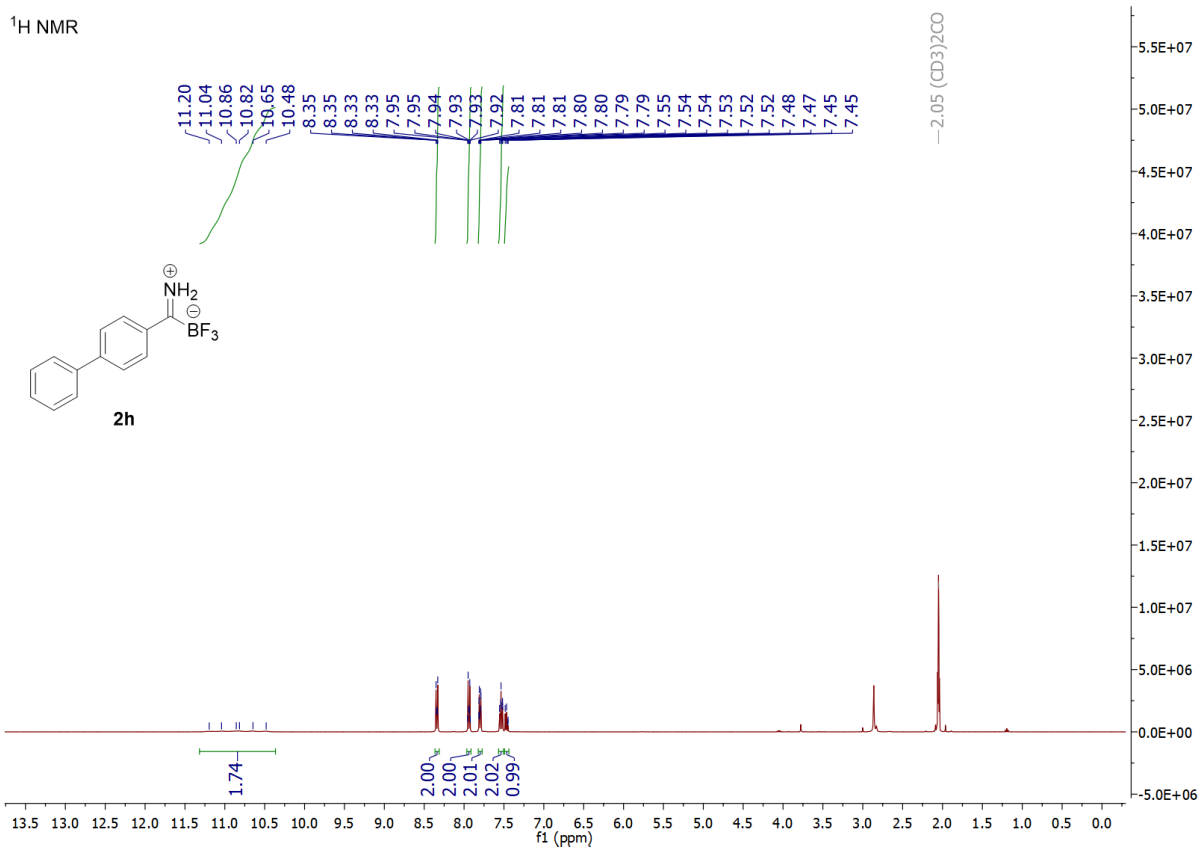


^{19}F-NMR (376 MHz, Acetone-d_6) of **2g**:

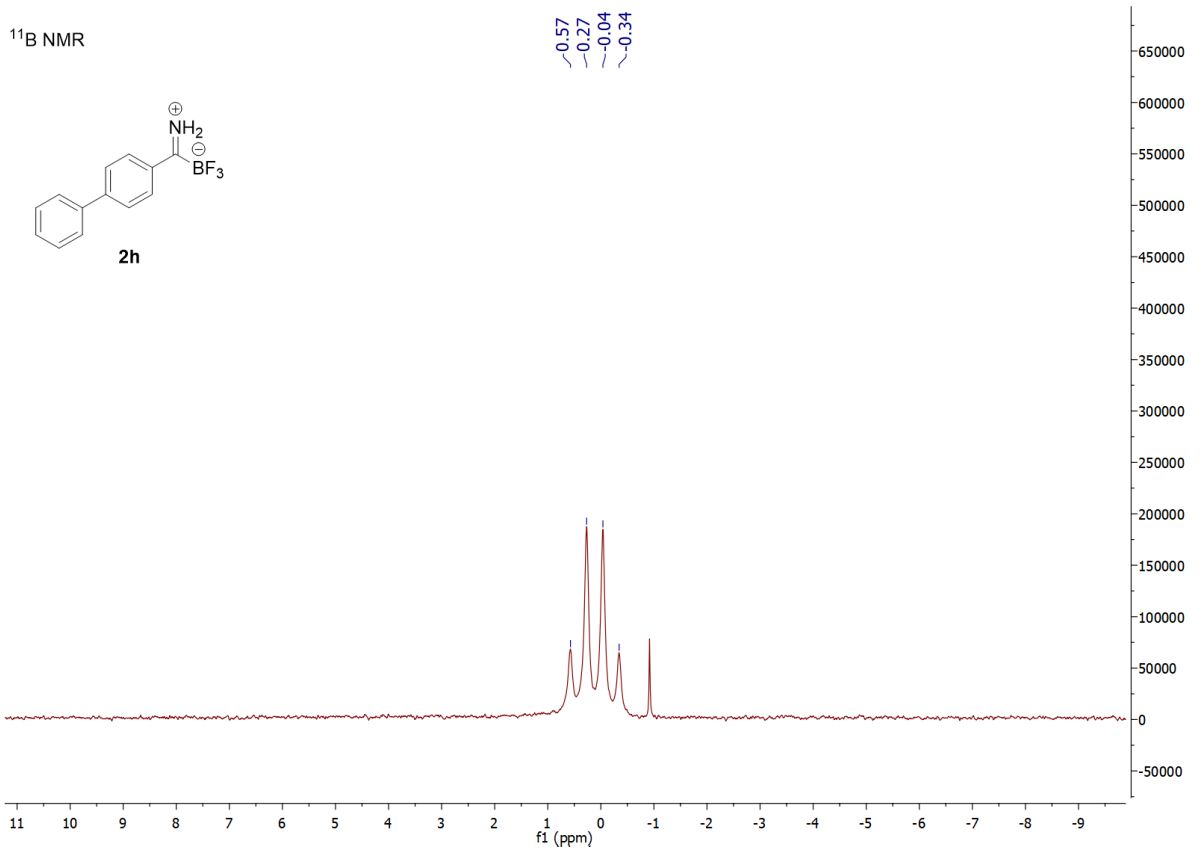


([1,1'-Biphenyl]-4-yl(iminio)methyl)trifluoroborate (2h)

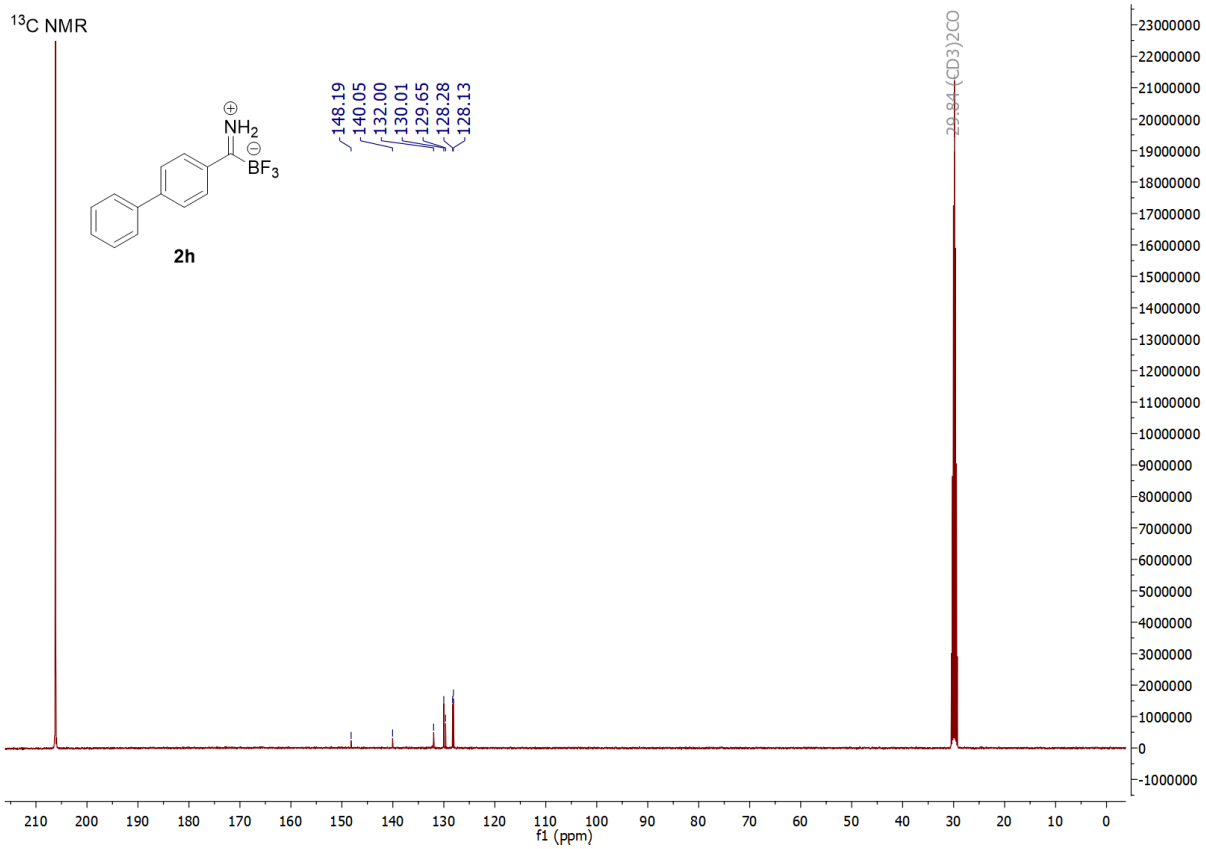
^{1}H-NMR (400 MHz, Acetone-d_6) of **2h**:



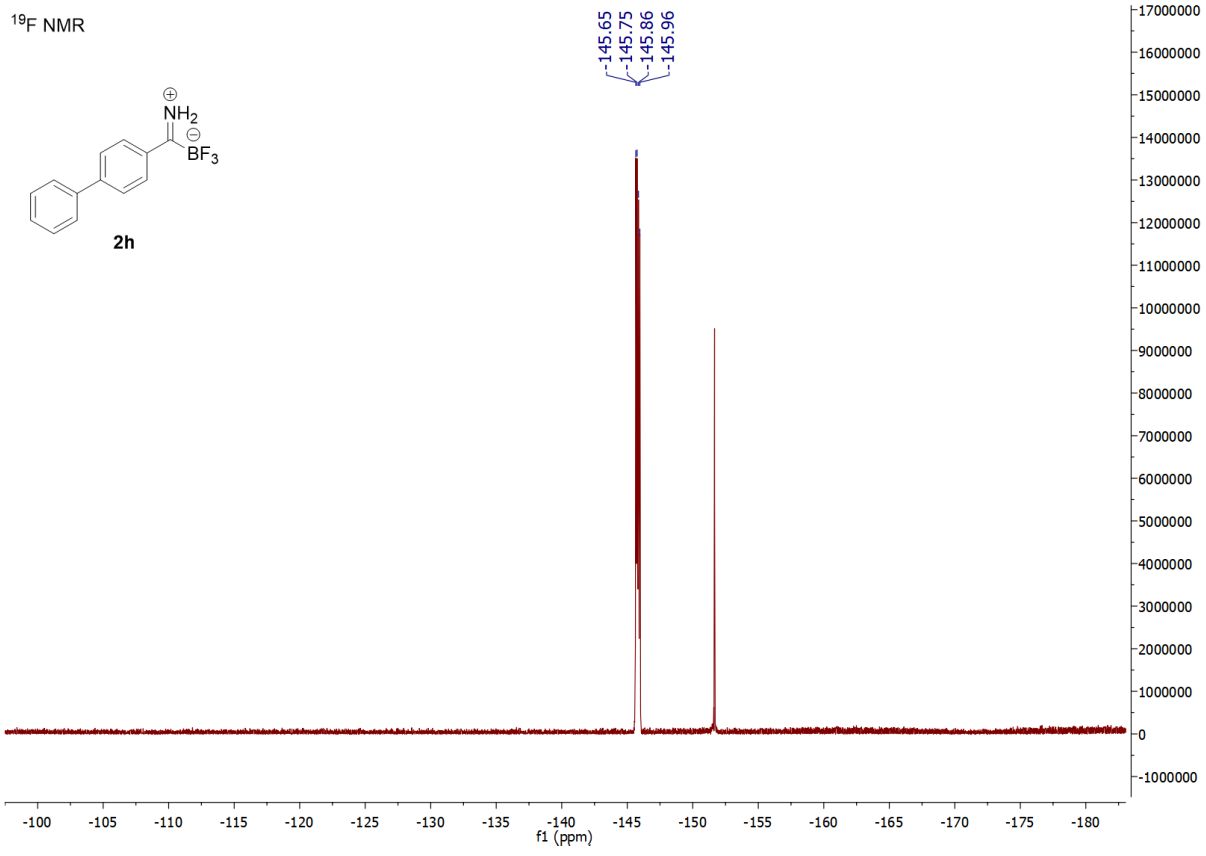
^{11}B-NMR (128 MHz, Acetone-d_6) of **2h**:



^{13}C-NMR (101 MHz, Acetone-d_6) of **2h**:

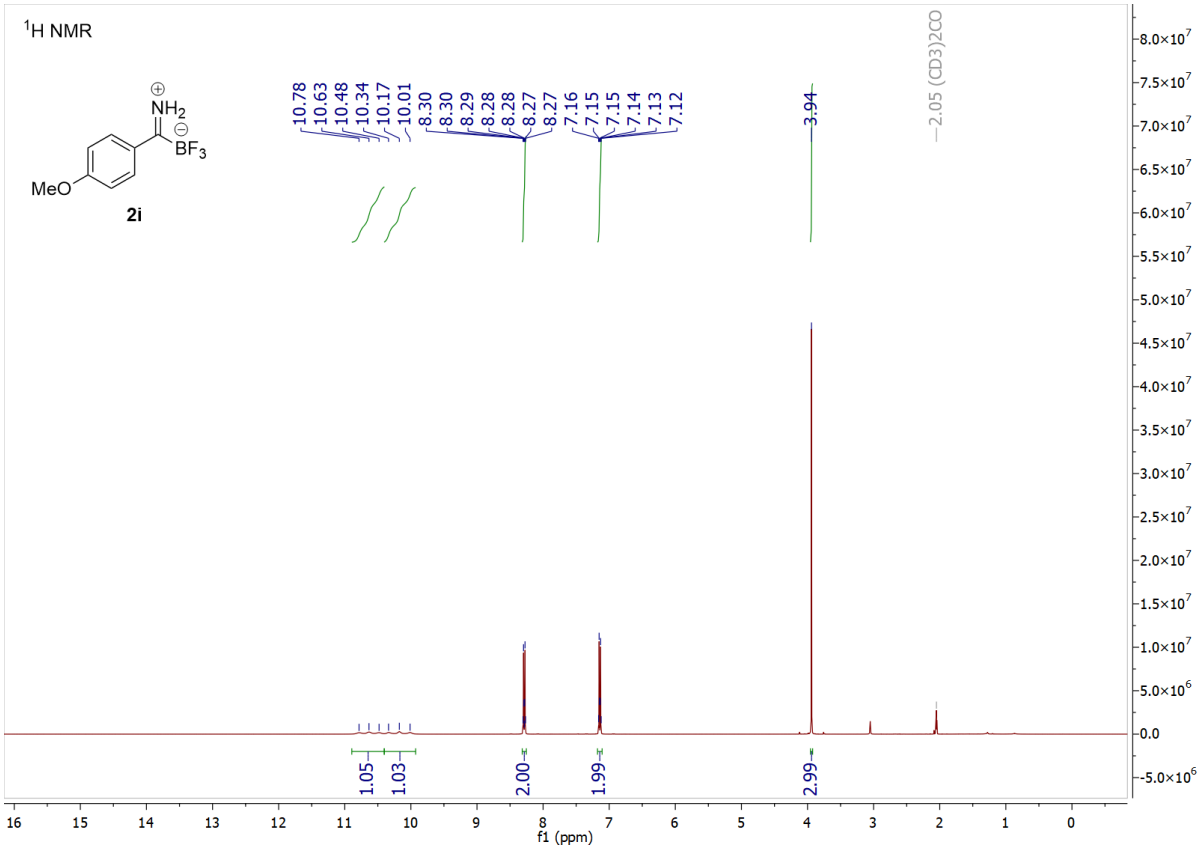


^{19}F-NMR (376 MHz, Acetone-d_6) of **2h**:

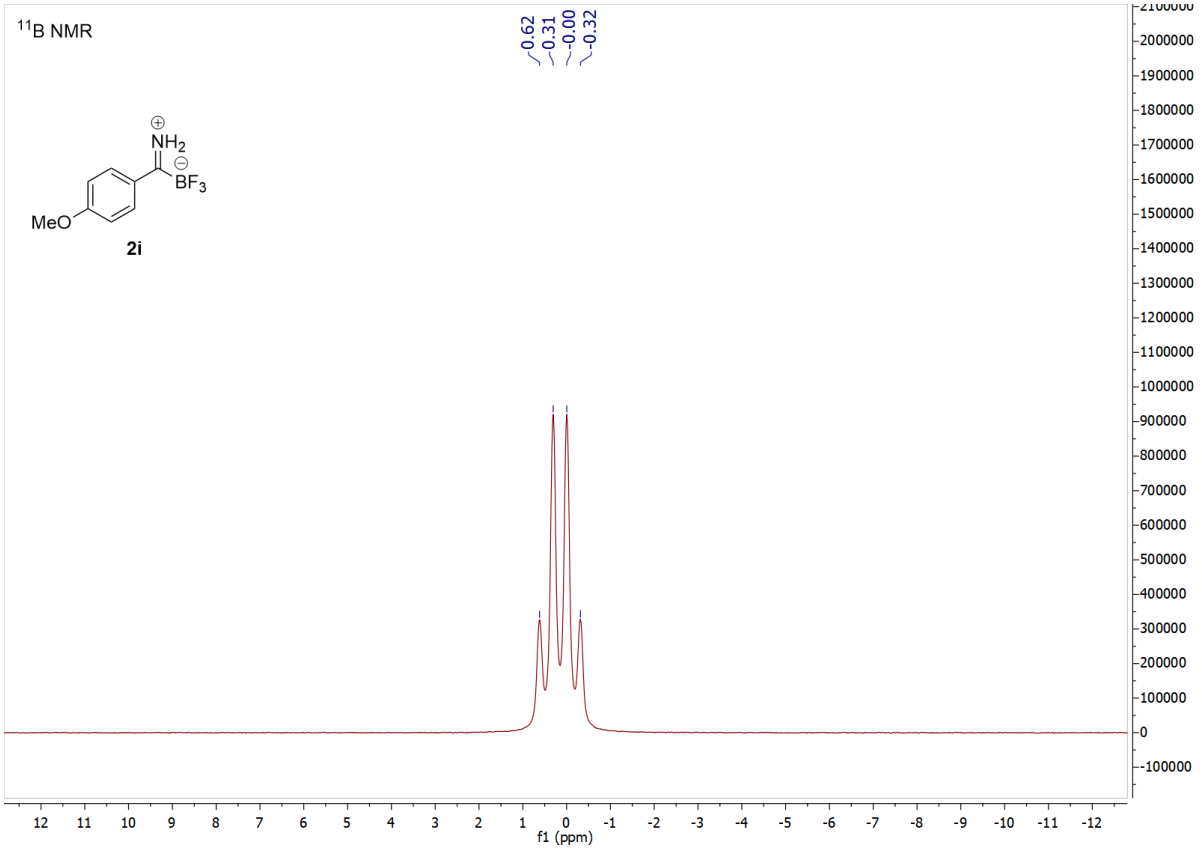


(Iminio(4-(methoxyphenyl)methyl)trifluoroborate (2i)

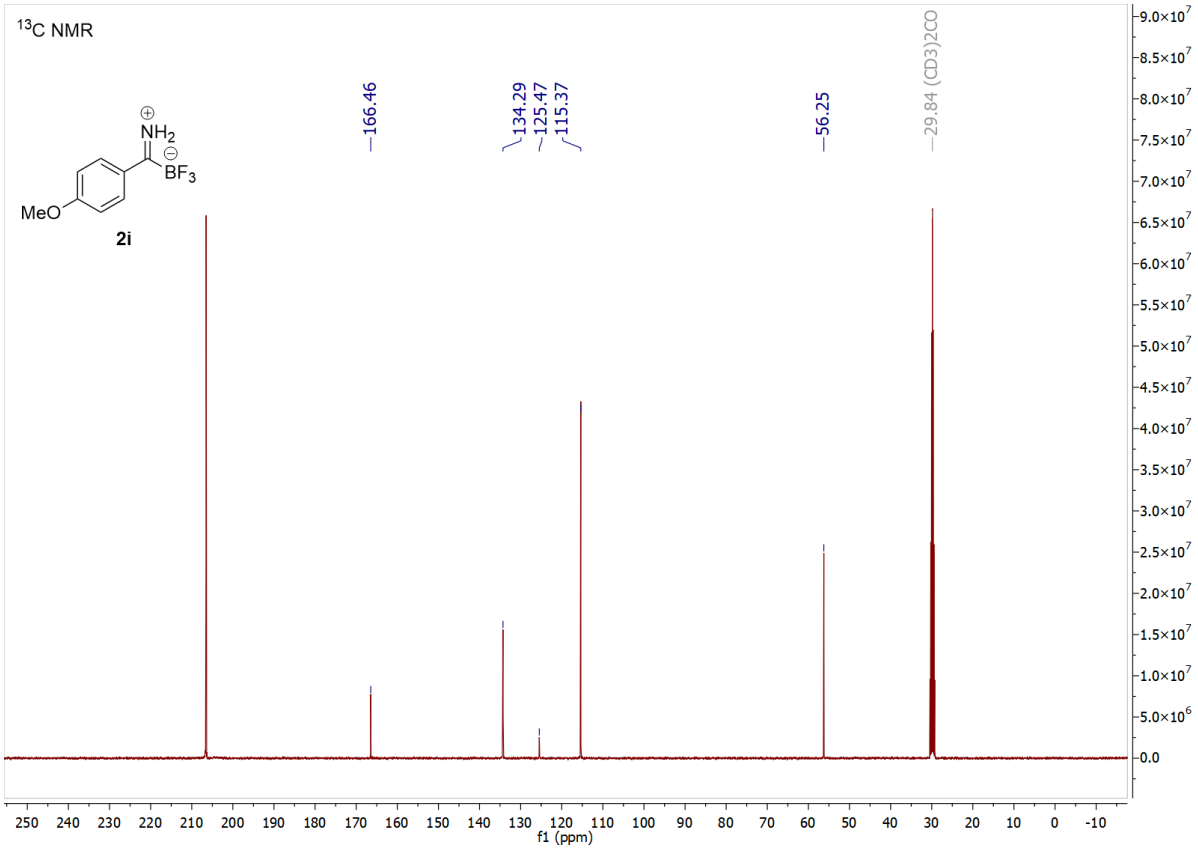
^{1}H-NMR (400 MHz, Acetone-d_6) of **2i**:



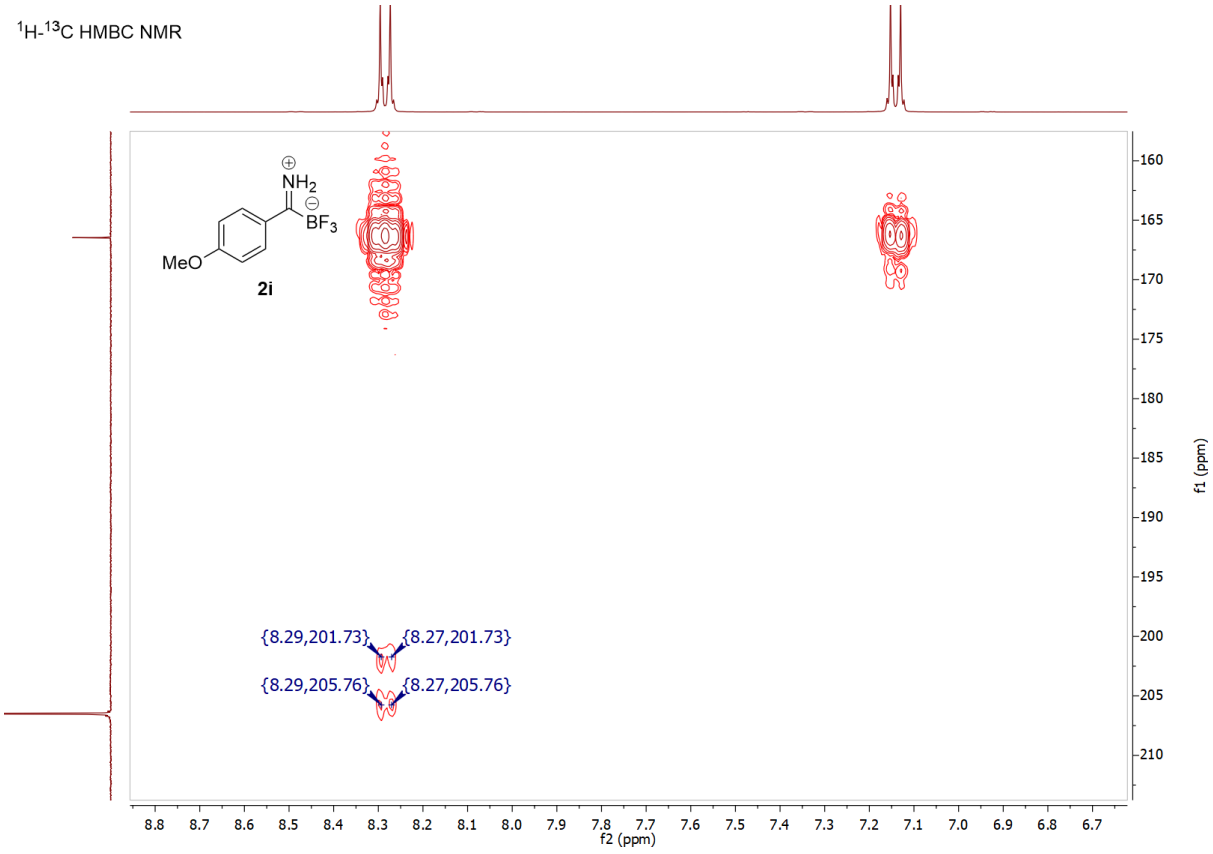
^{11}B-NMR (128 MHz, Acetone-d_6) of **2i**:



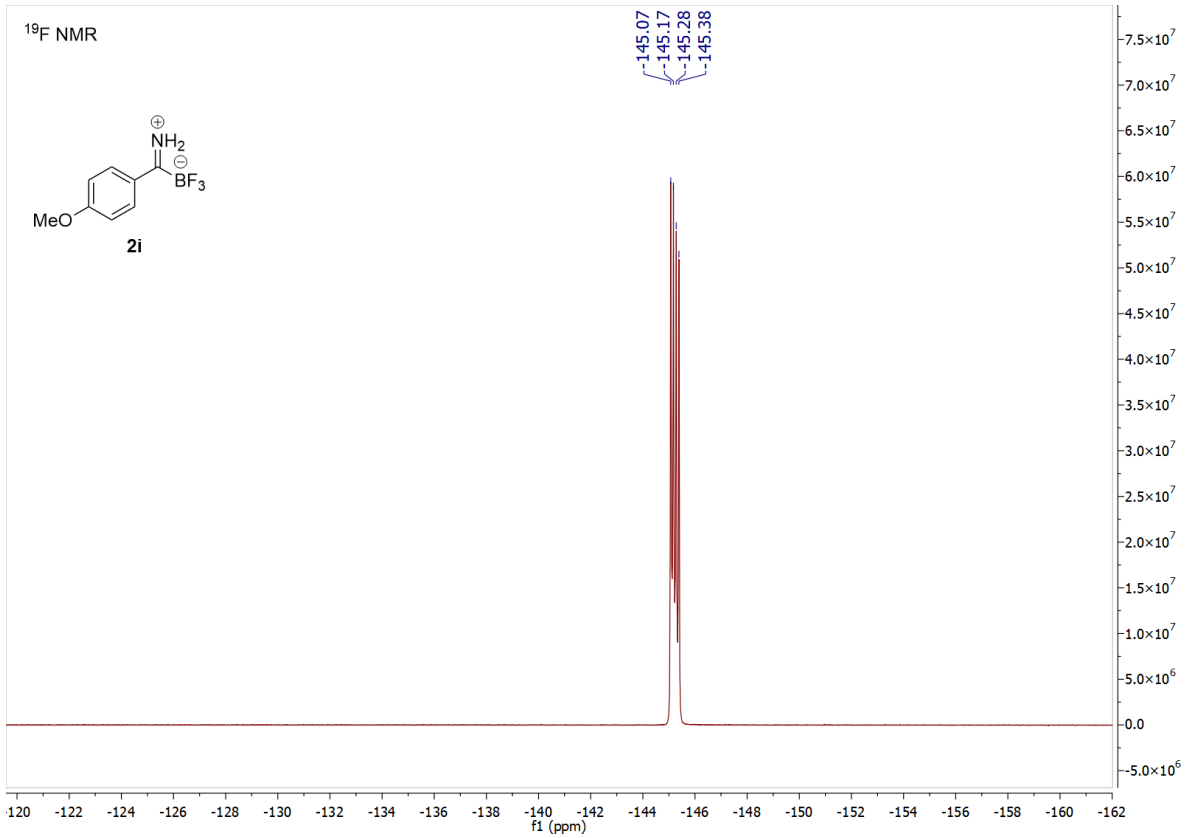
^{13}C-NMR (101 MHz, Acetone-d_6) of **2i**:



^{1}H-^{13}C-HMBC NMR (Acetone-d_6) of **2i**:

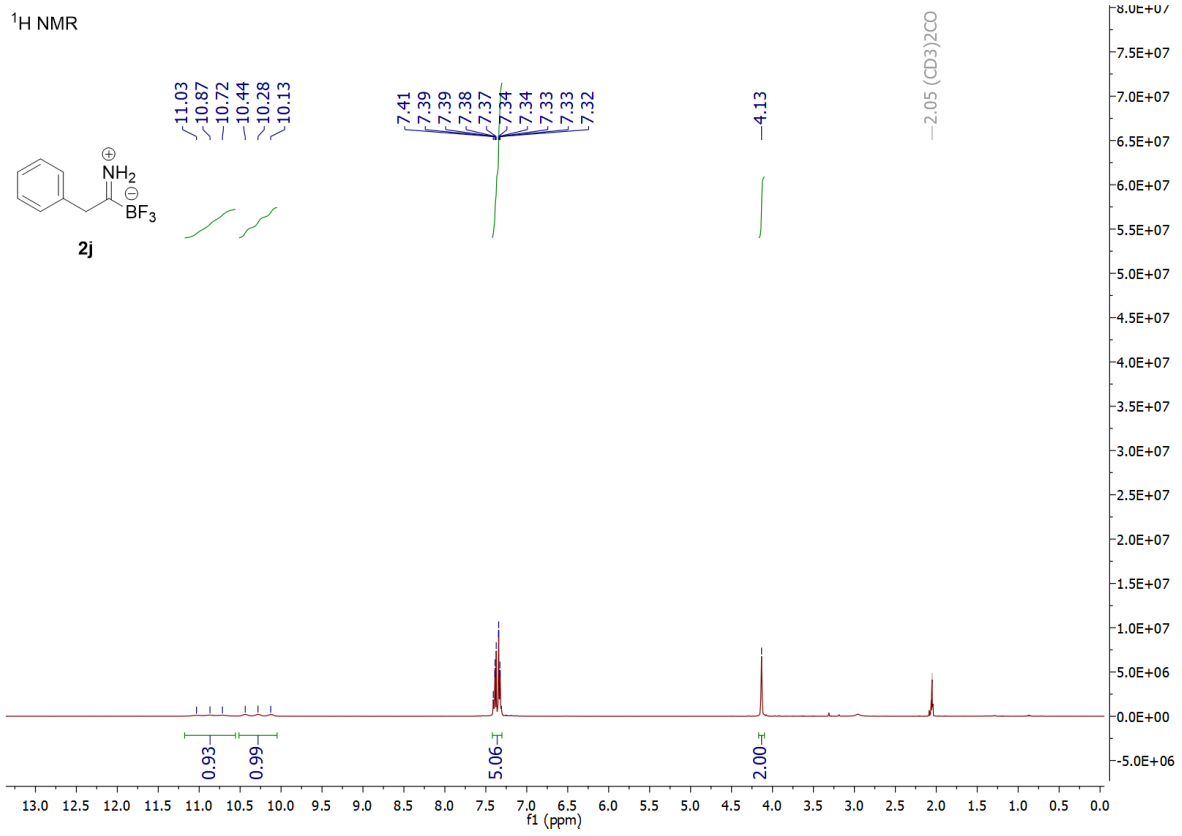


^{19}F-NMR (376 MHz, Acetone-d_6) of **2i**:

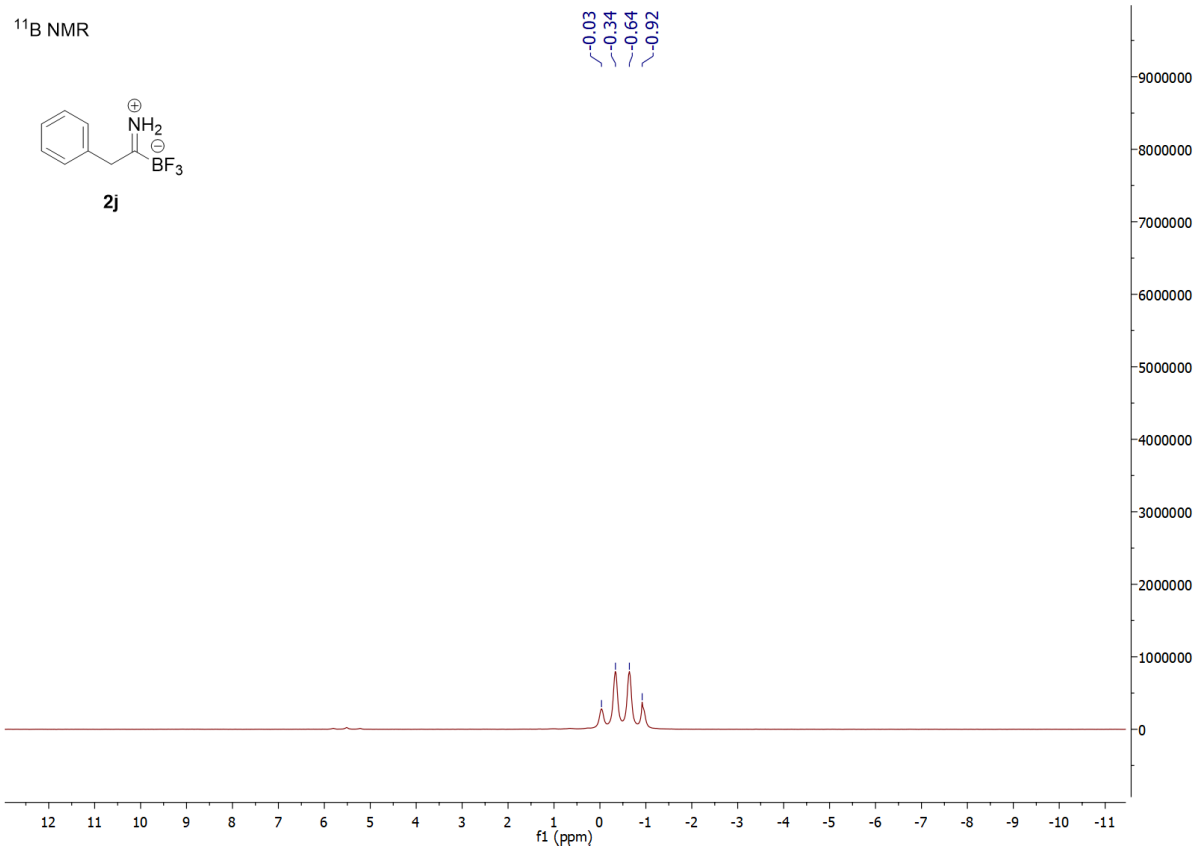


(1-Iminio-2-phenylethyl)trifluoroborate (2j)

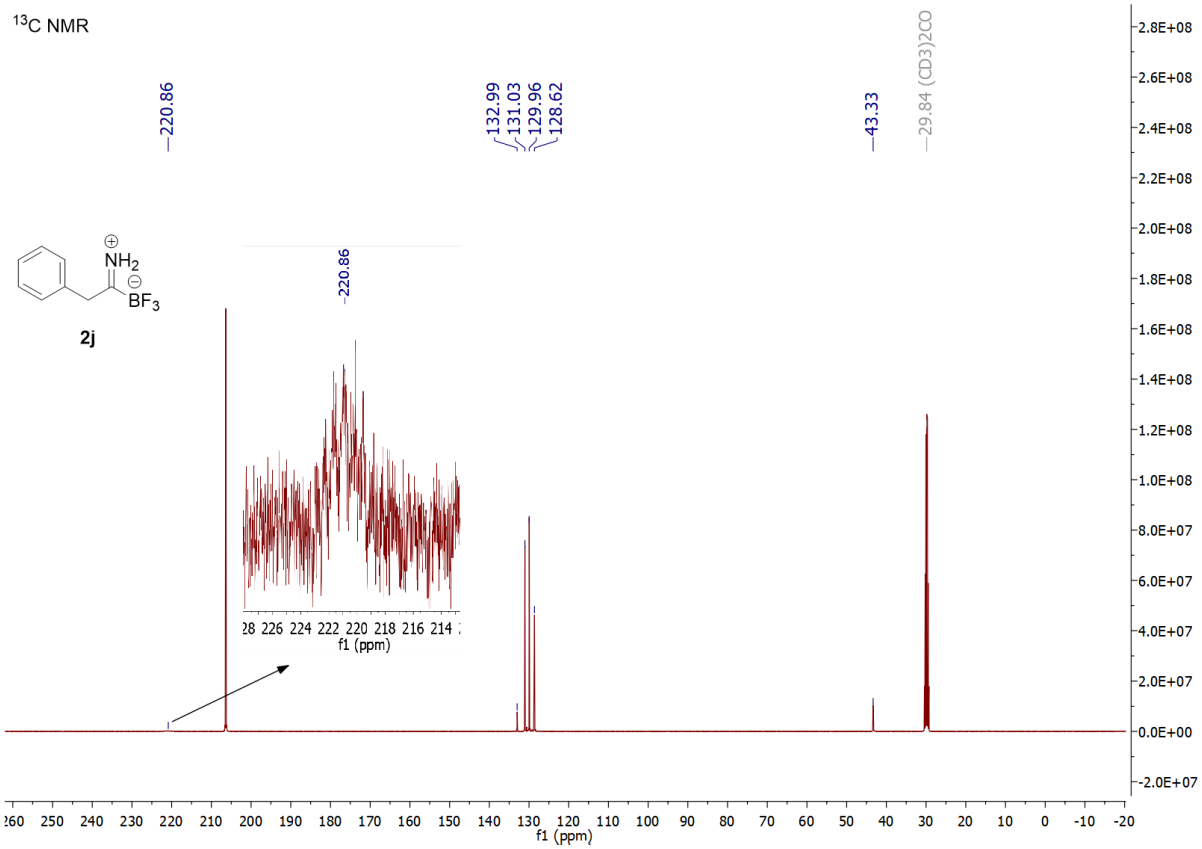
^{1}H-NMR (400 MHz, Acetone-d_6) of **2j**:



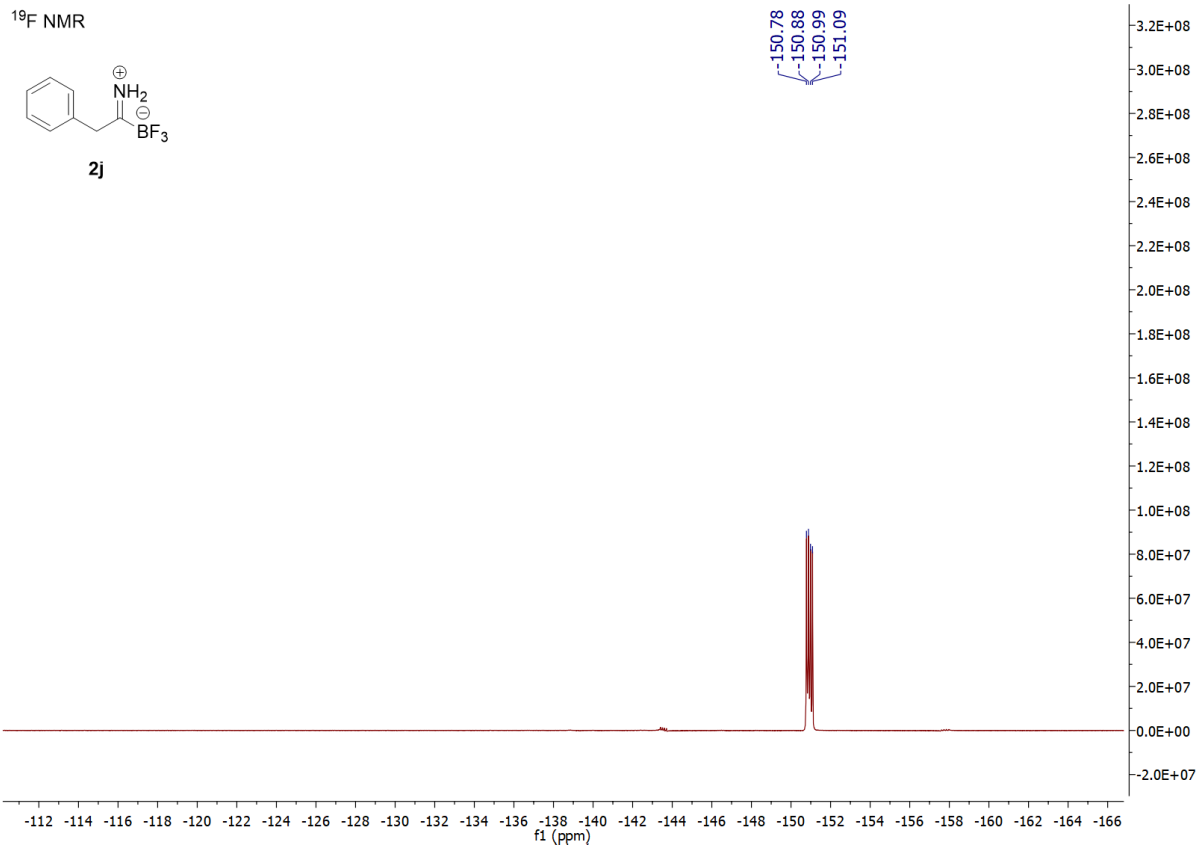
^{11}B-NMR (128 MHz, Acetone-d_6) of **2j**:



^{13}C-NMR (101 MHz, Acetone-d_6) of **2j**:

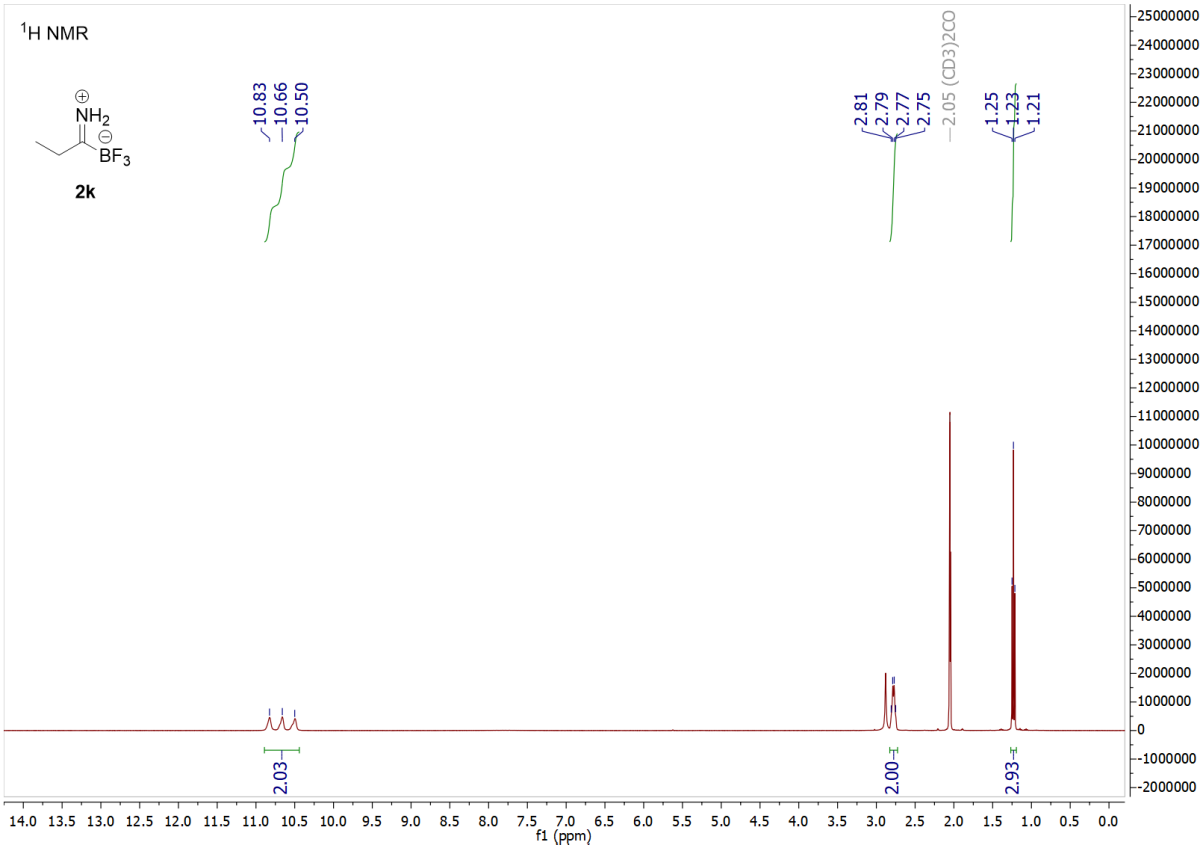


^{19}F-NMR (376 MHz, Acetone-d_6) of **2j**:

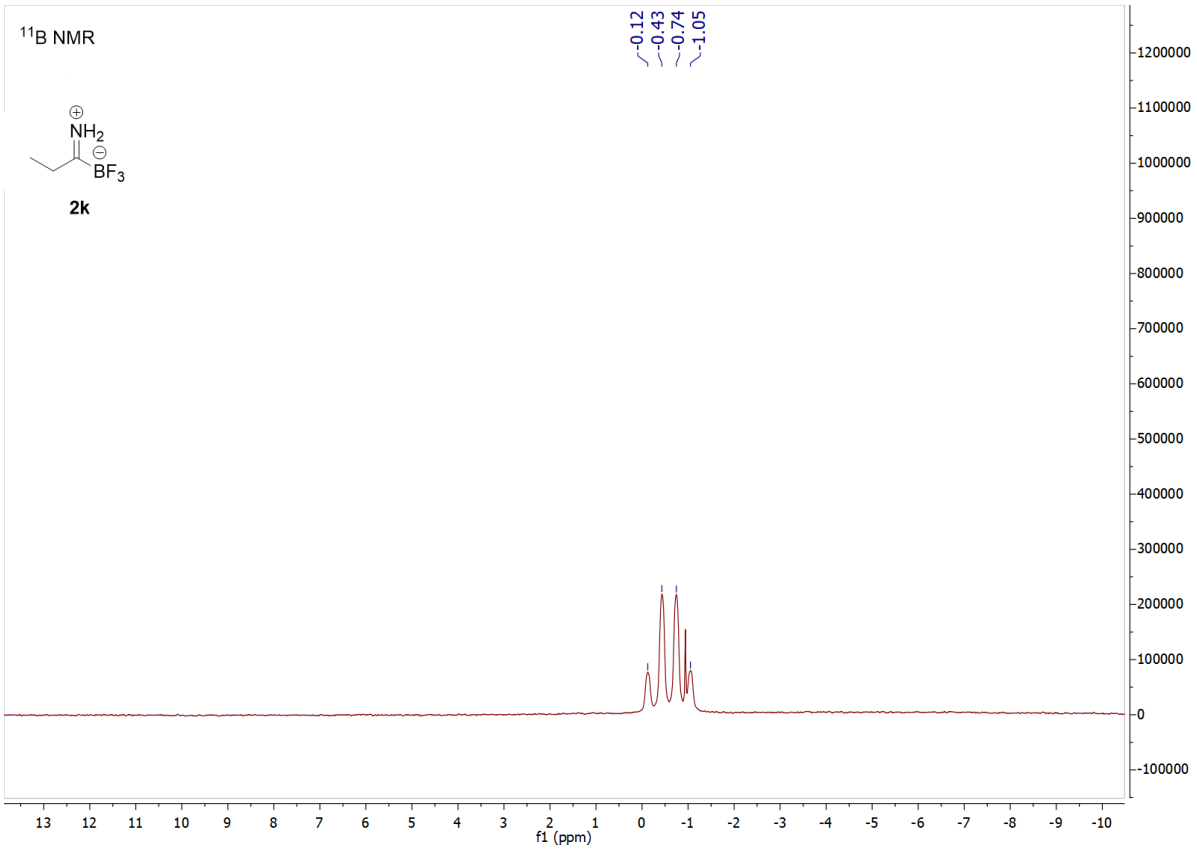


(1-Iminiopropyl)trifluoroborate (2k)

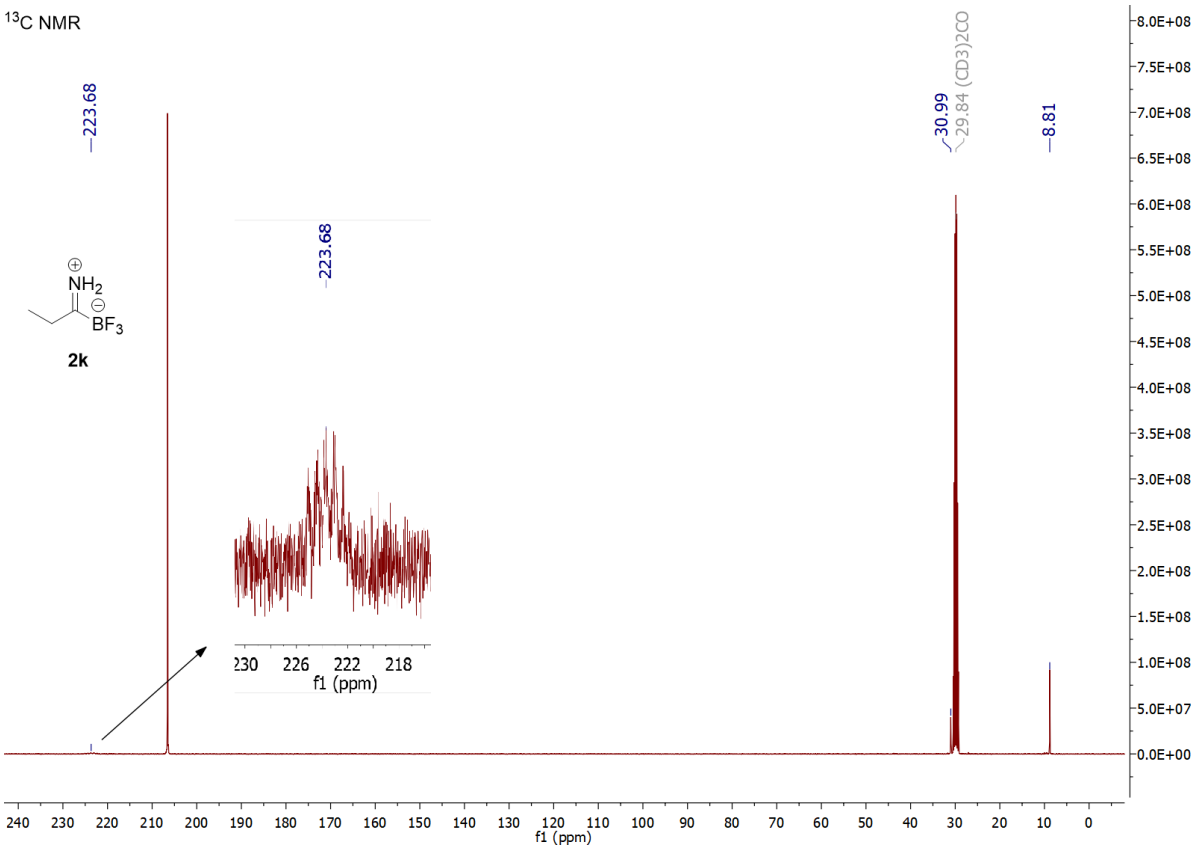
^{1}H-NMR (400 MHz, Acetone-d_6) of **2k**:



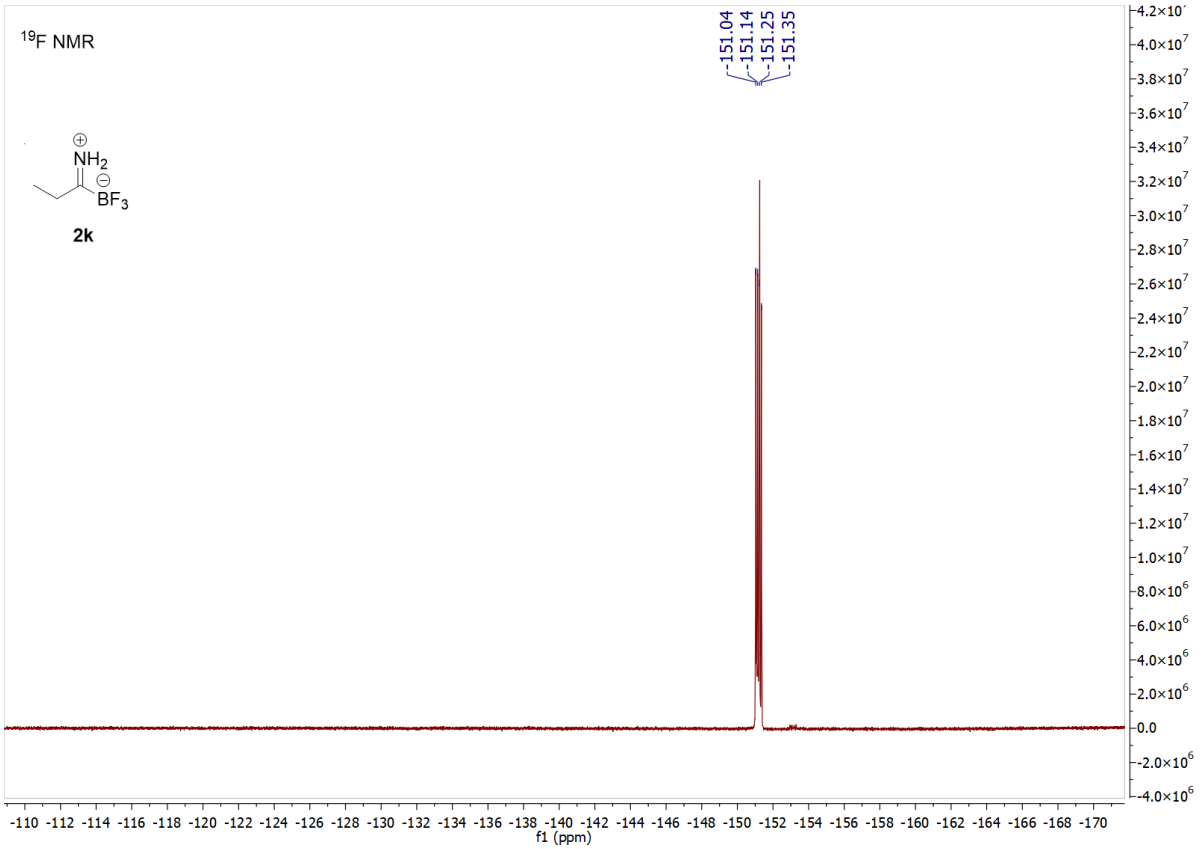
^{11}B-NMR (128 MHz, Acetone-d_6) of **2k**:



^{13}C-NMR (101 MHz, Acetone-d_6) of **2k**:

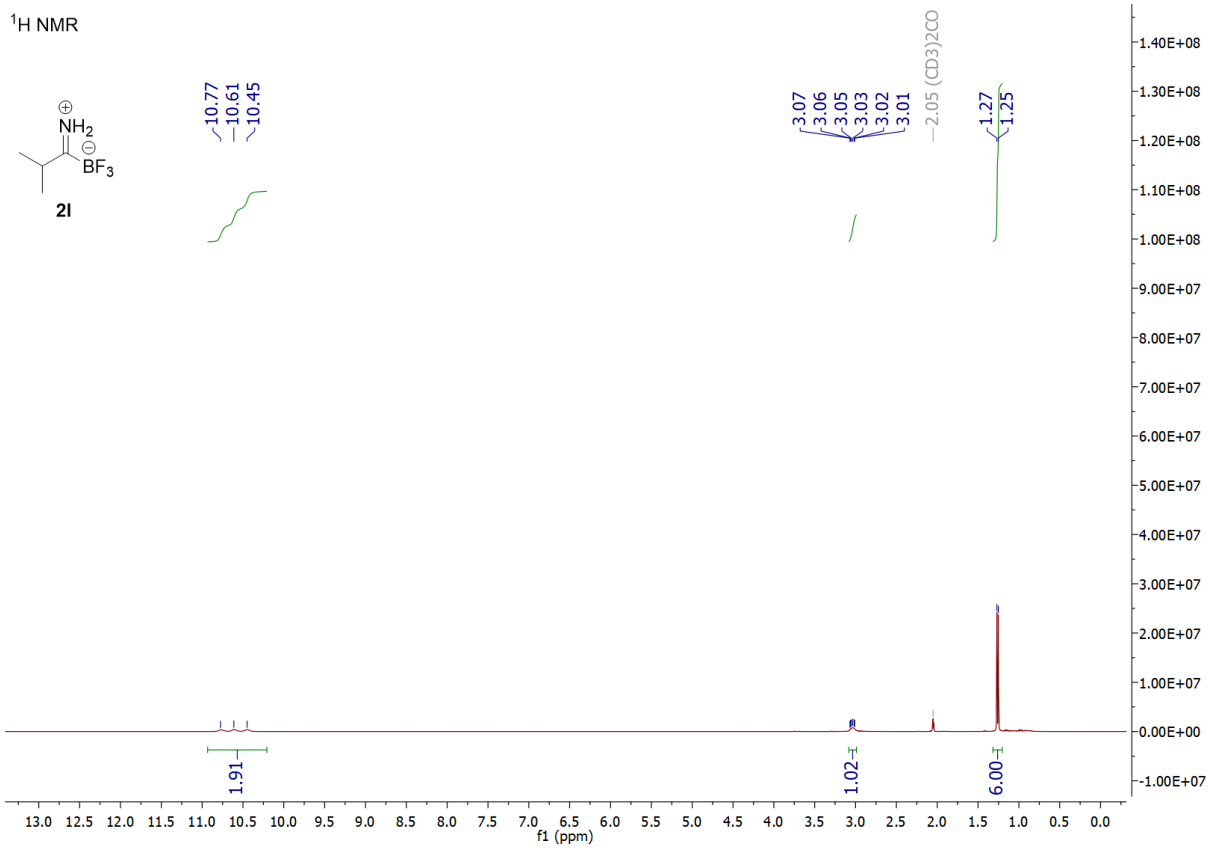


^{19}F-NMR (376 MHz, Acetone-d_6) of **2k**:

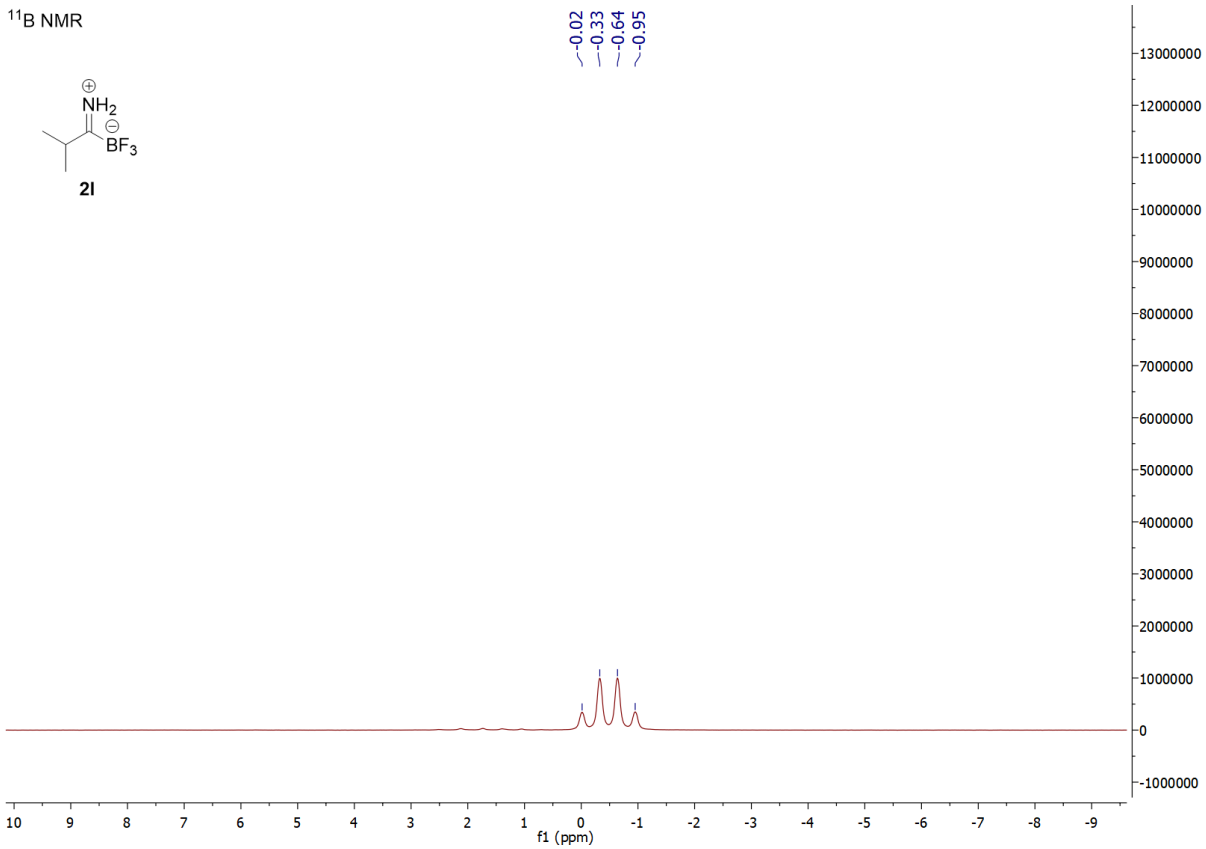


(1-Iminio-2-methylpropyl)trifluoroborate (2l)

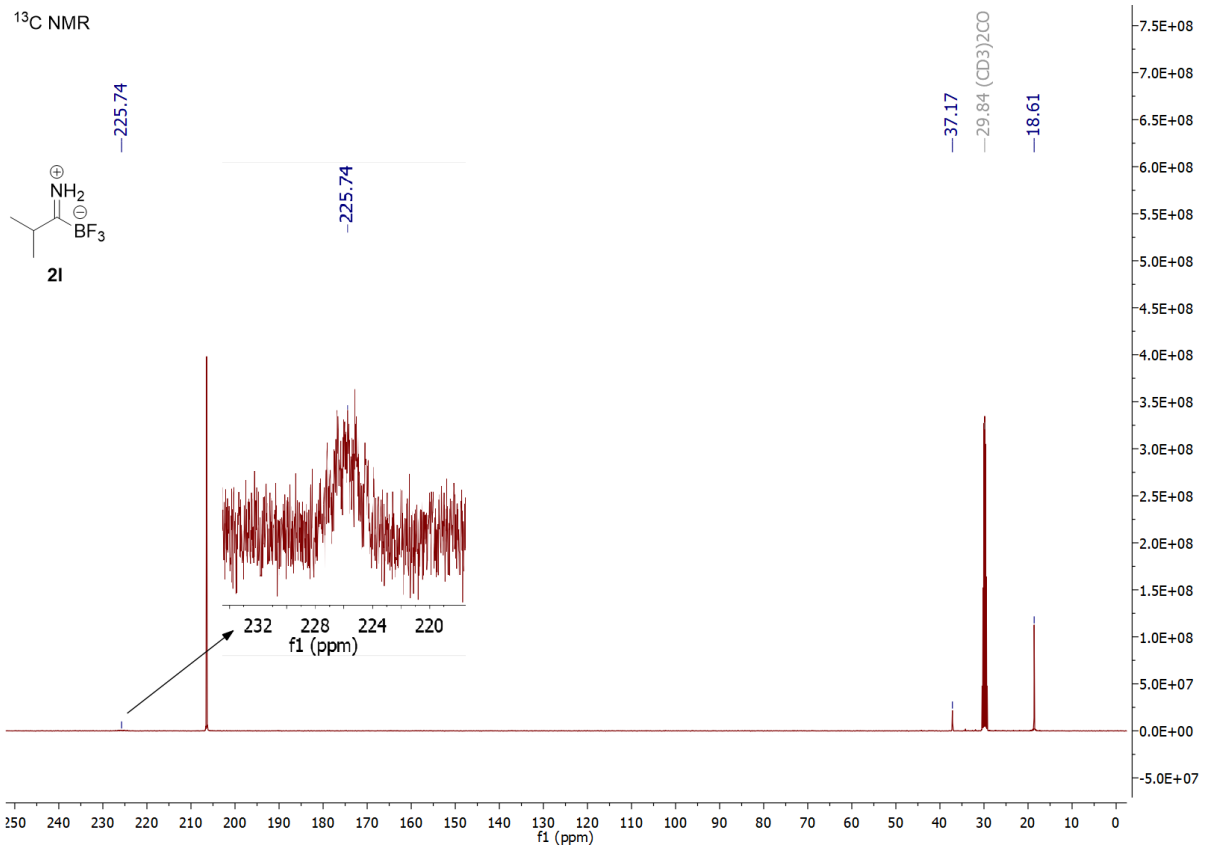
^{1}H-NMR (400 MHz, Acetone-d_6) of **2l**:



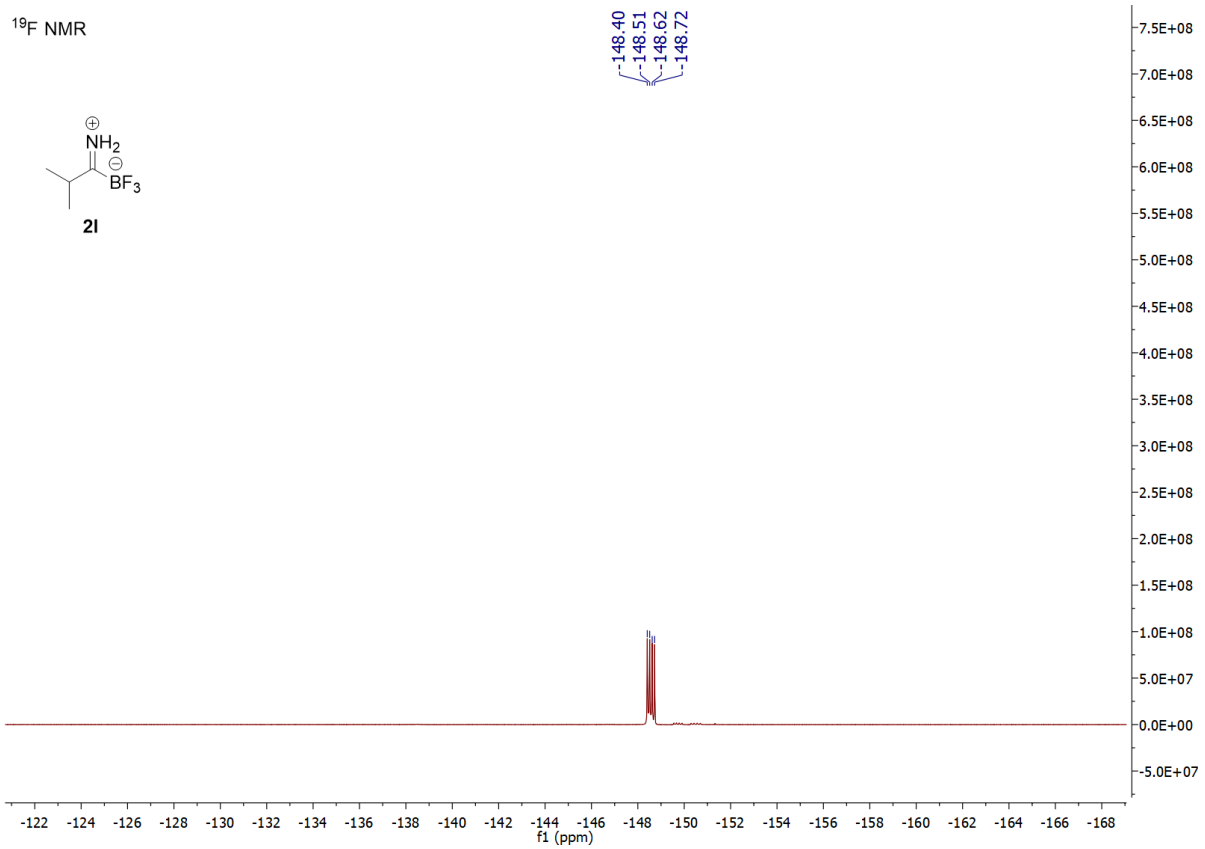
^{11}B-NMR (128 MHz, Acetone-d_6) of **2l**:



^{13}C-NMR (101 MHz, Acetone-d_6) of **2l**:

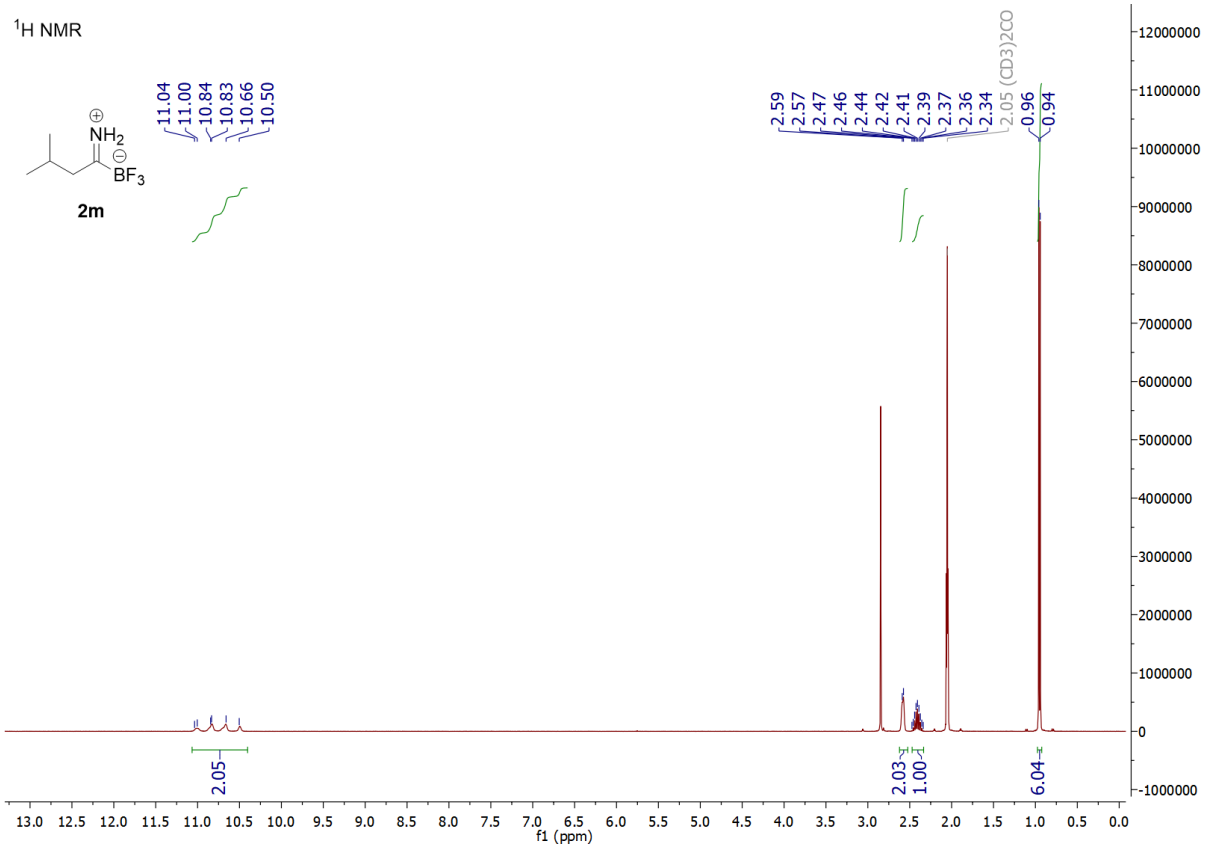


^{19}F-NMR (376 MHz, Acetone-d_6) of **2l**:

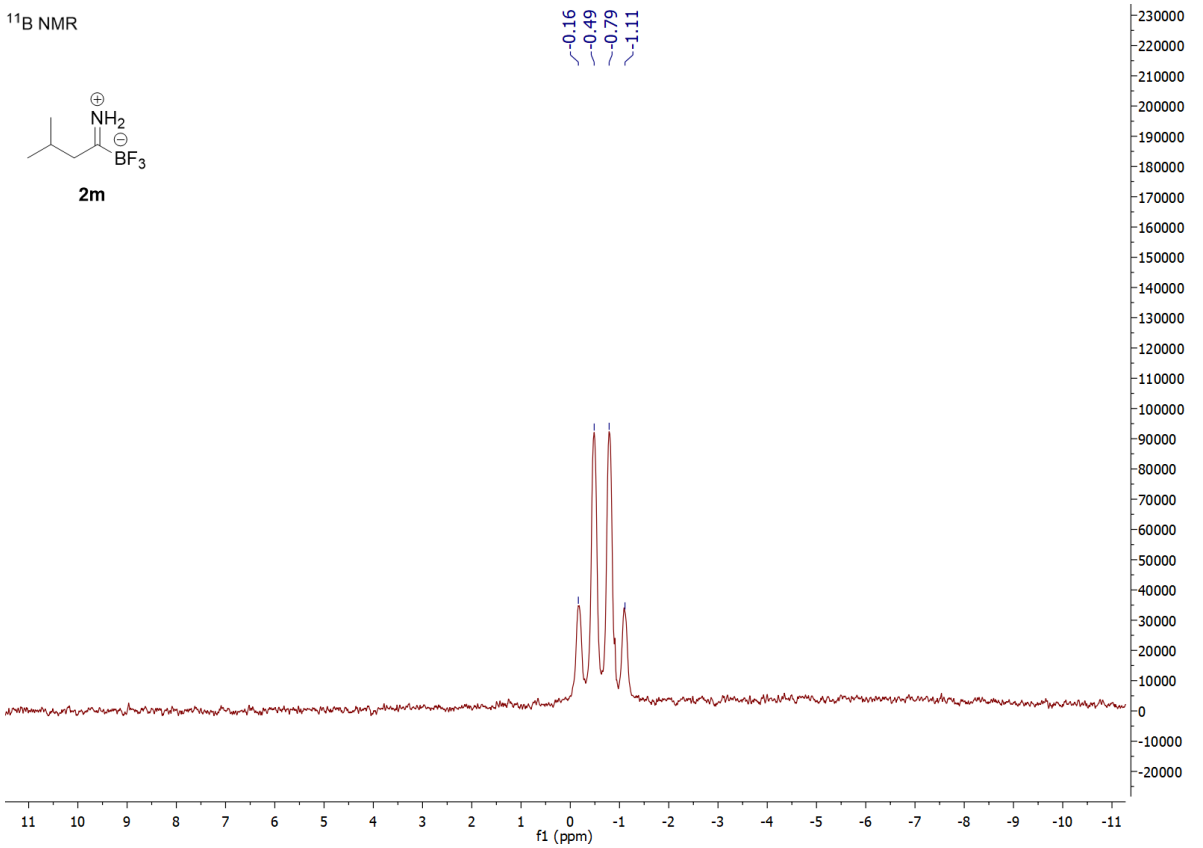


(1-Iminio-3-methylbutyl)trifluoroborate (2m)

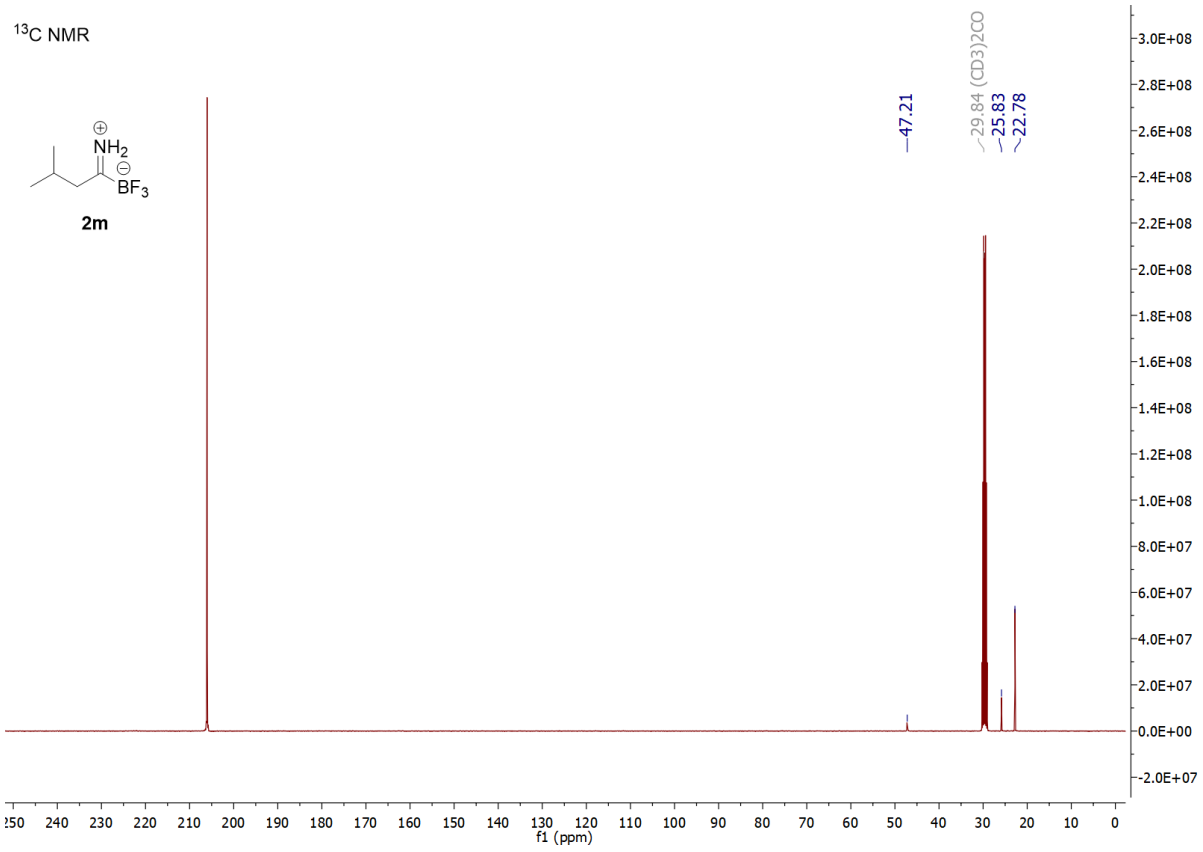
^{1}H-NMR (400 MHz, Acetone-d_6) of **2m**:



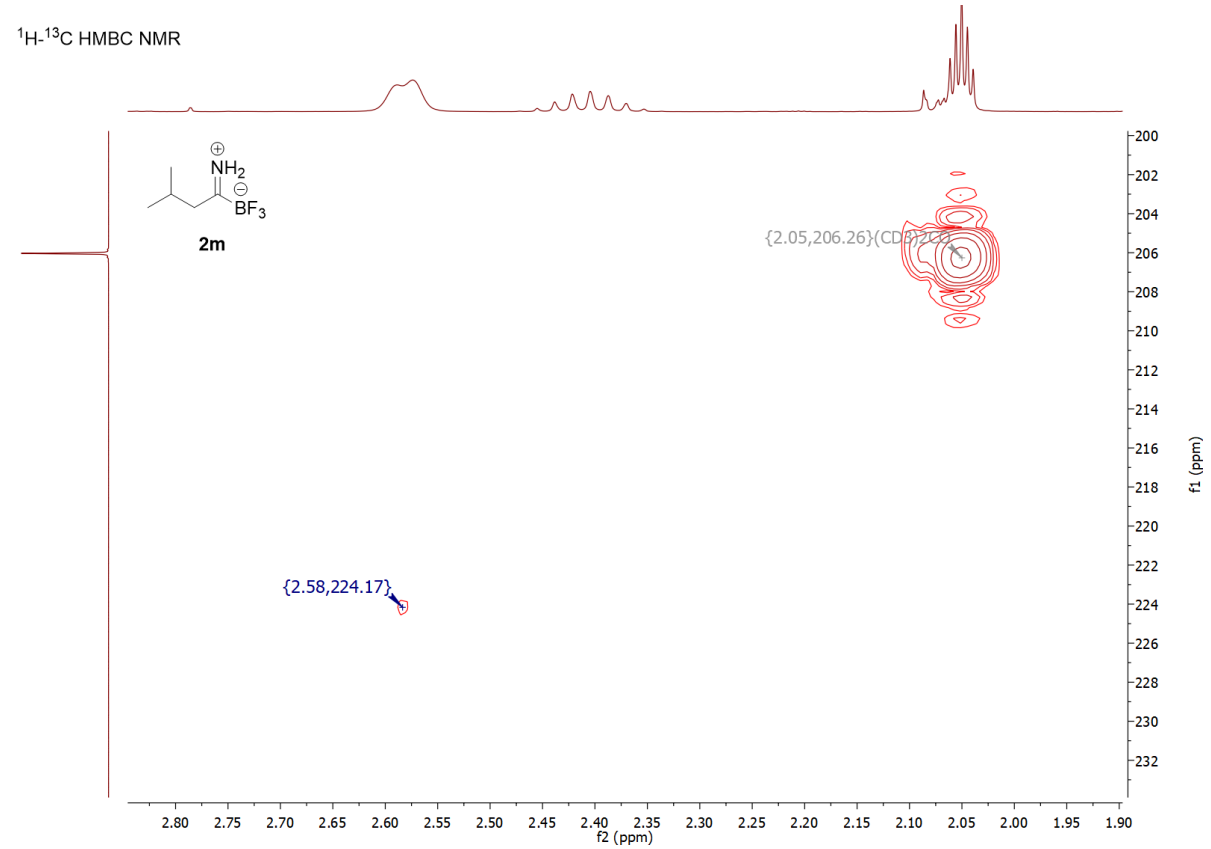
^{11}B-NMR (128 MHz, Acetone-d_6) of **2m**:



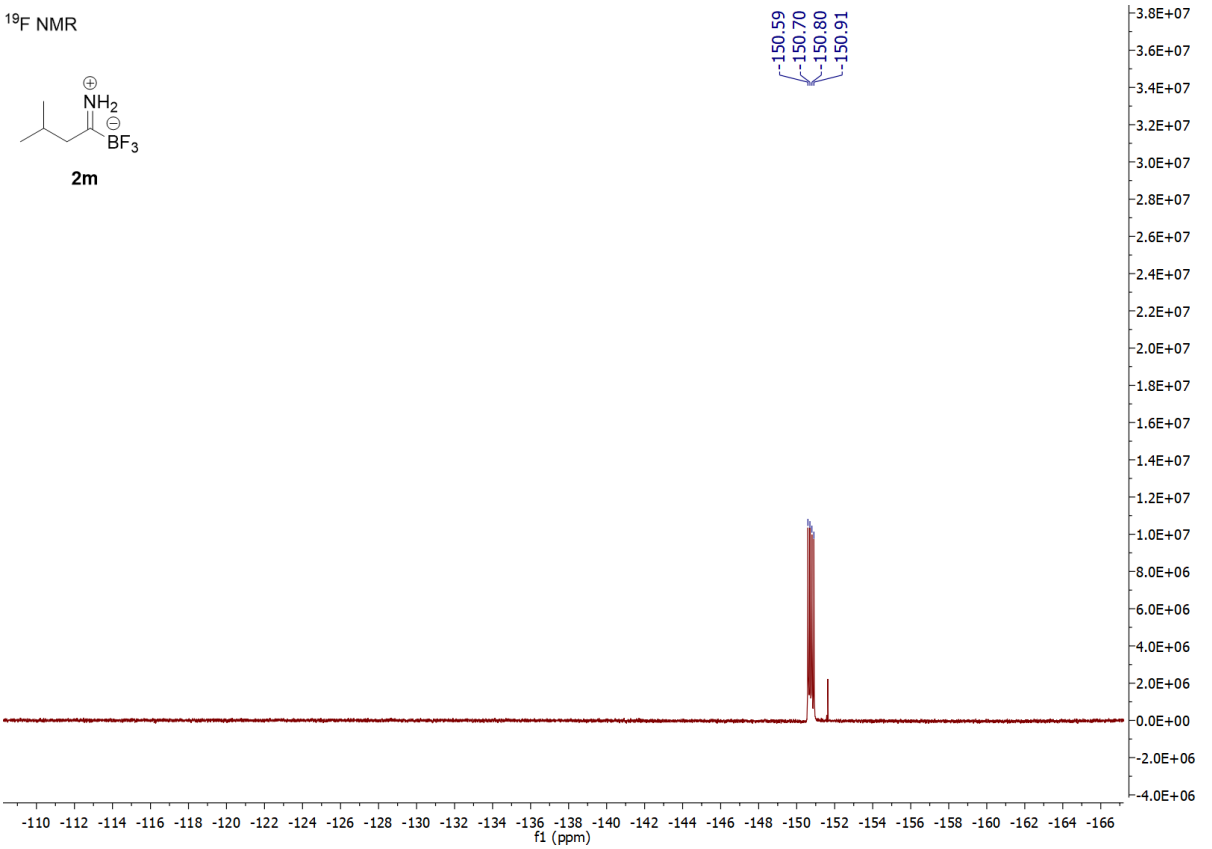
^{13}C-NMR (101 MHz, Acetone-d_6) of **2m**:



^{1}H-^{13}C-HMBC NMR (Acetone-d_6) of **2m**:

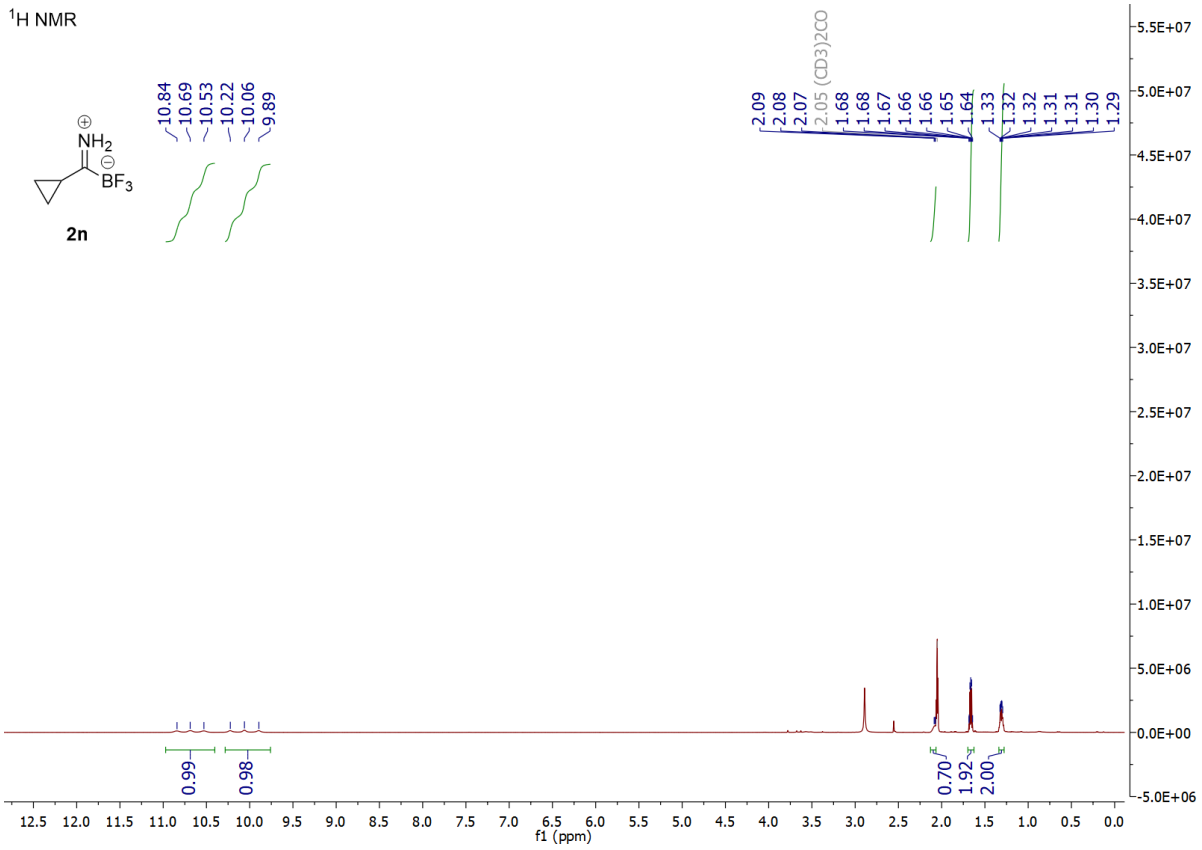


^{19}F-NMR (376 MHz, Acetone-d_6) of **2m**:

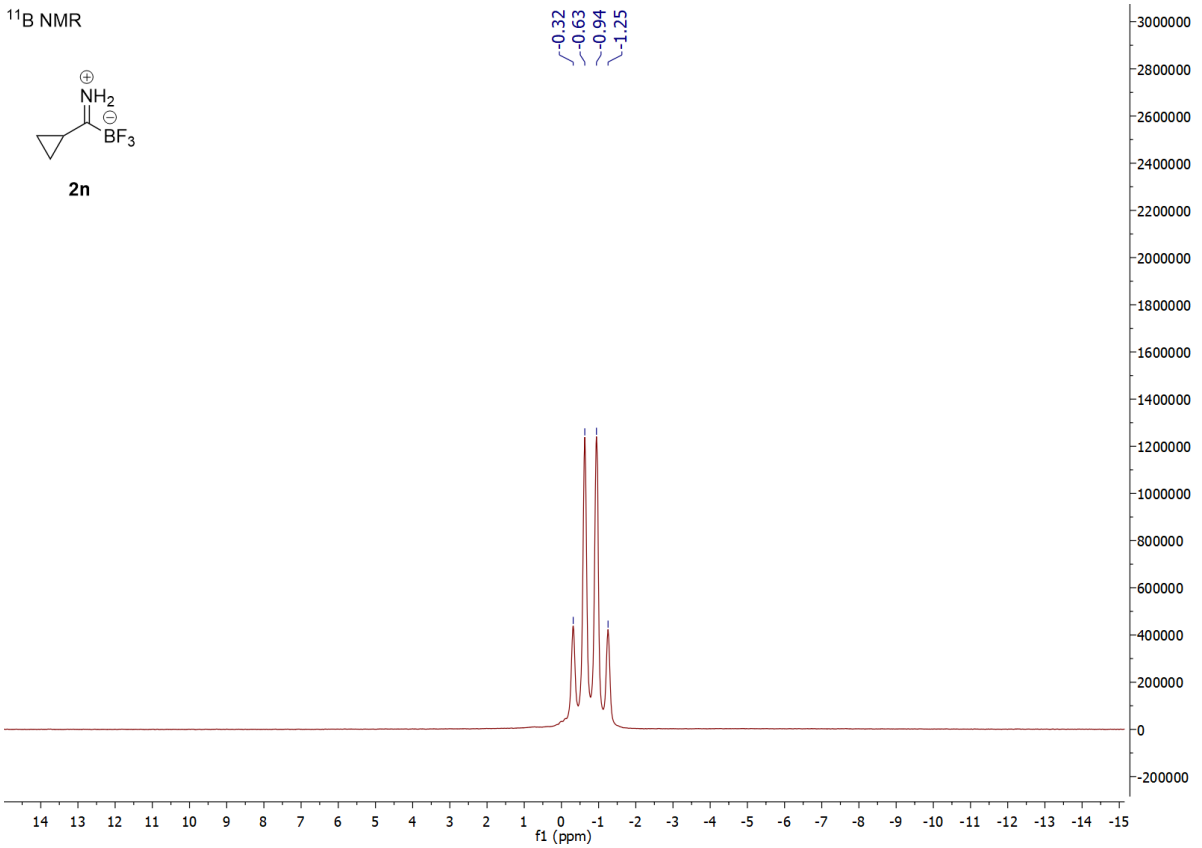


(Cyclopropyl(iminio)methyl)trifluoroborate (2n)

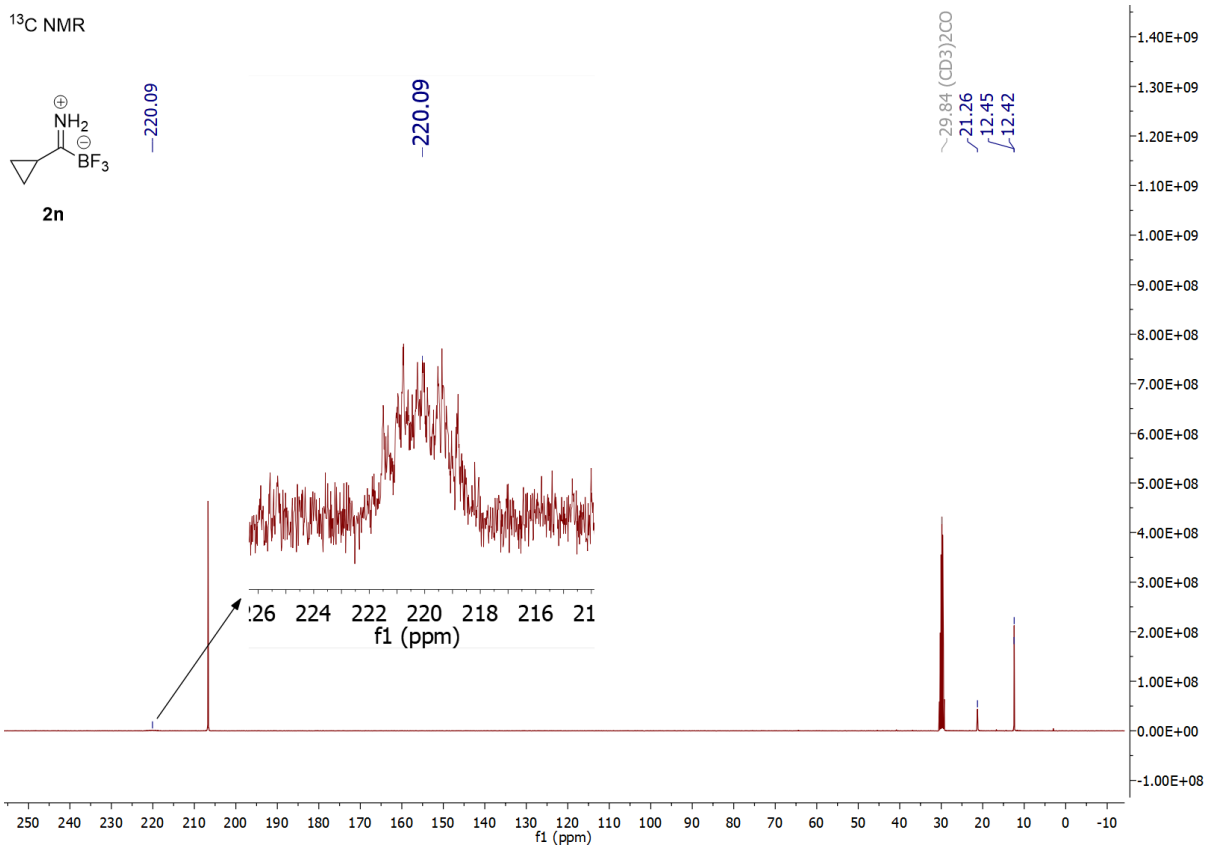
^{1}H-NMR (400 MHz, Acetone-d_6) of **2n**:



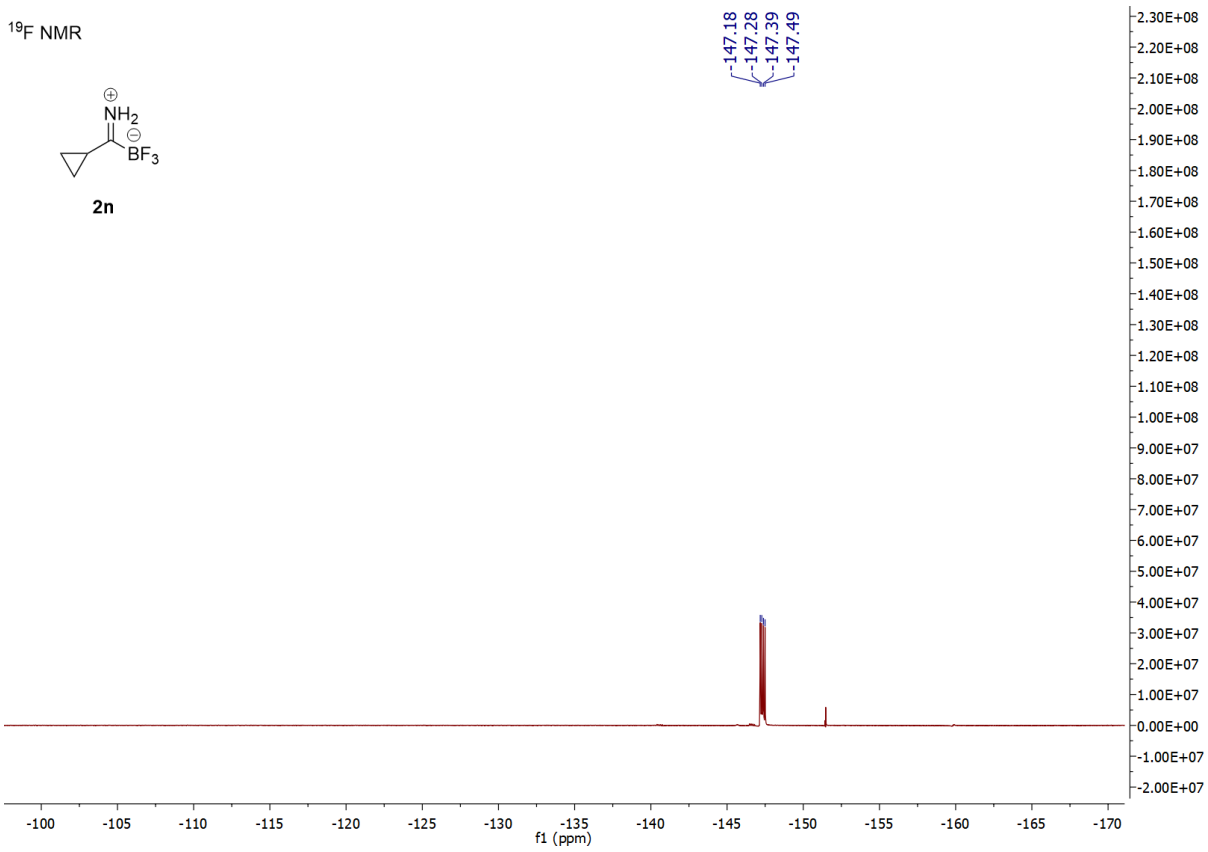
^{11}B-NMR (128 MHz, Acetone-d_6) of **2n**:



^{13}C-NMR (101 MHz, Acetone-d_6) of **2n**:

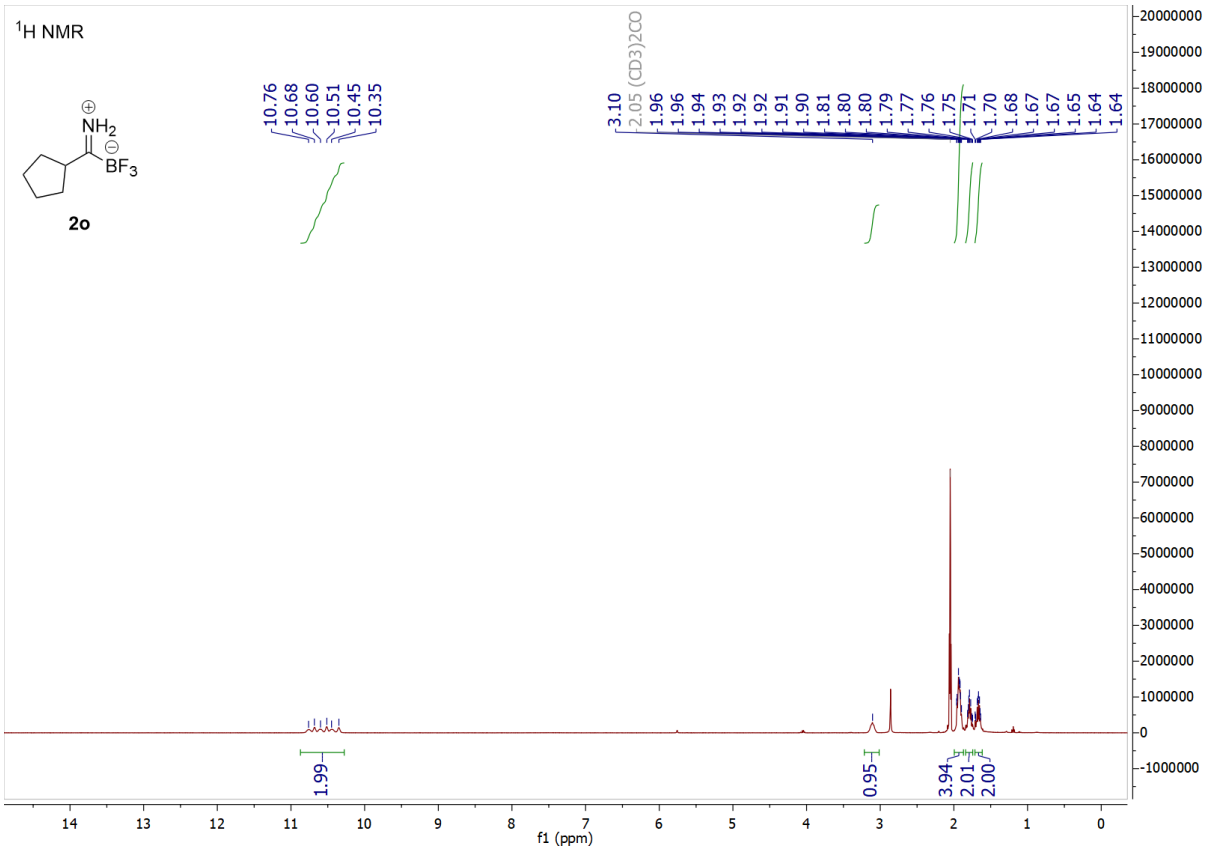


^{19}F-NMR (376 MHz, Acetone-d_6) of **2n**:

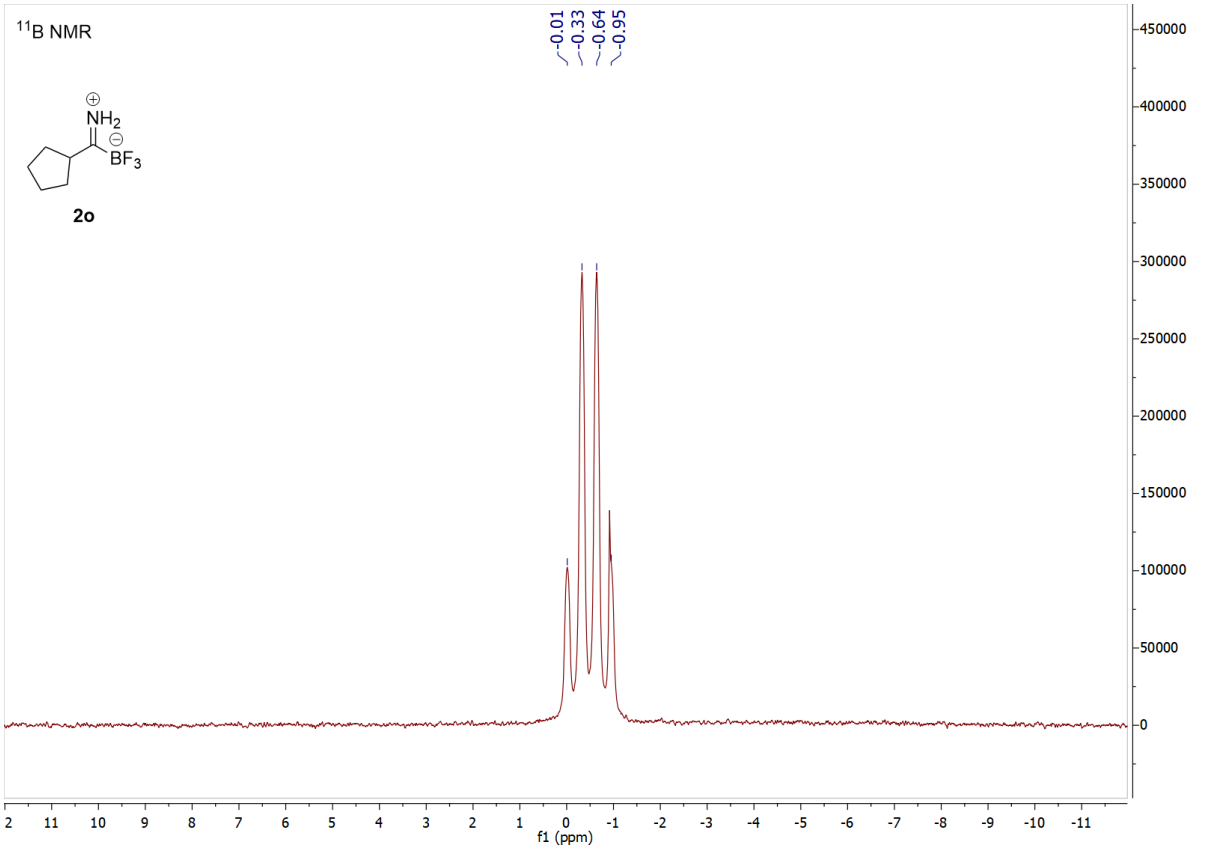


(Cyclopentyl(iminio)methyl)trifluoroborate (2o)

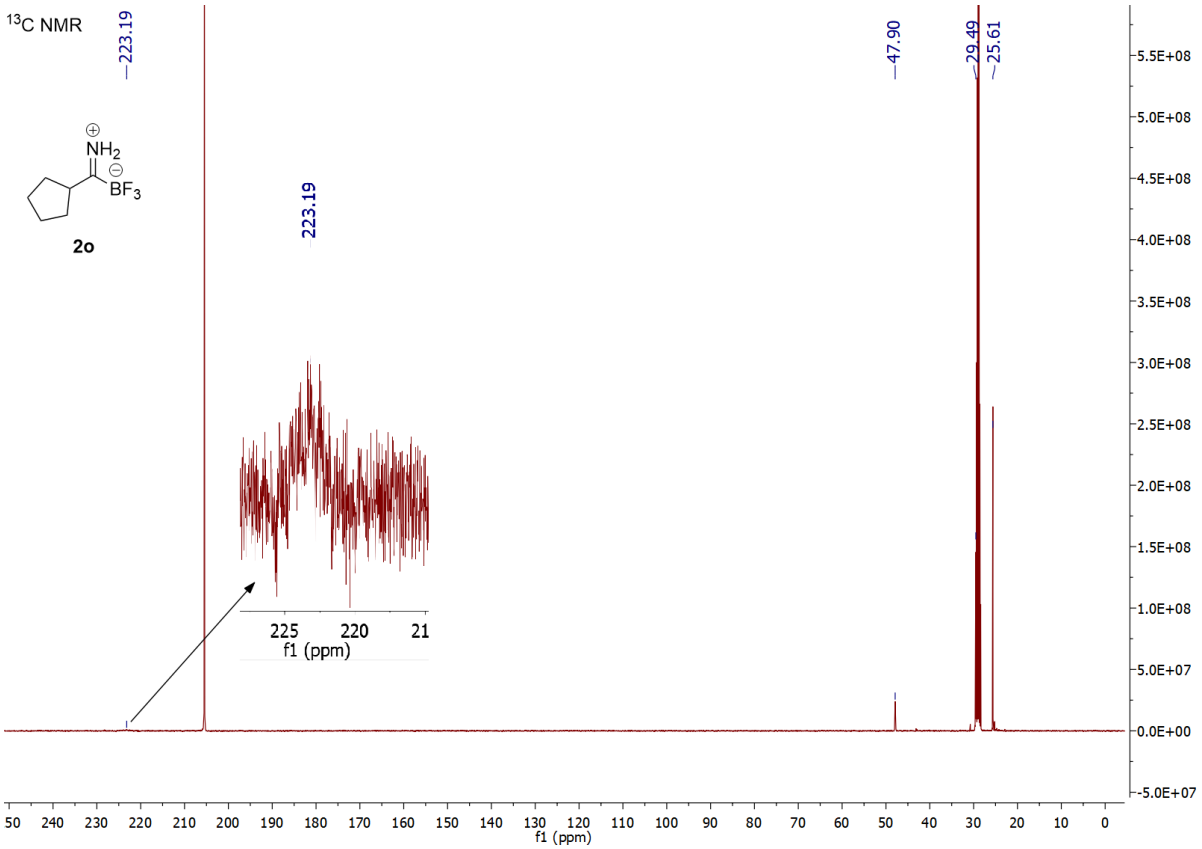
^{1}H-NMR (400 MHz, Acetone-d_6) of **2o**:



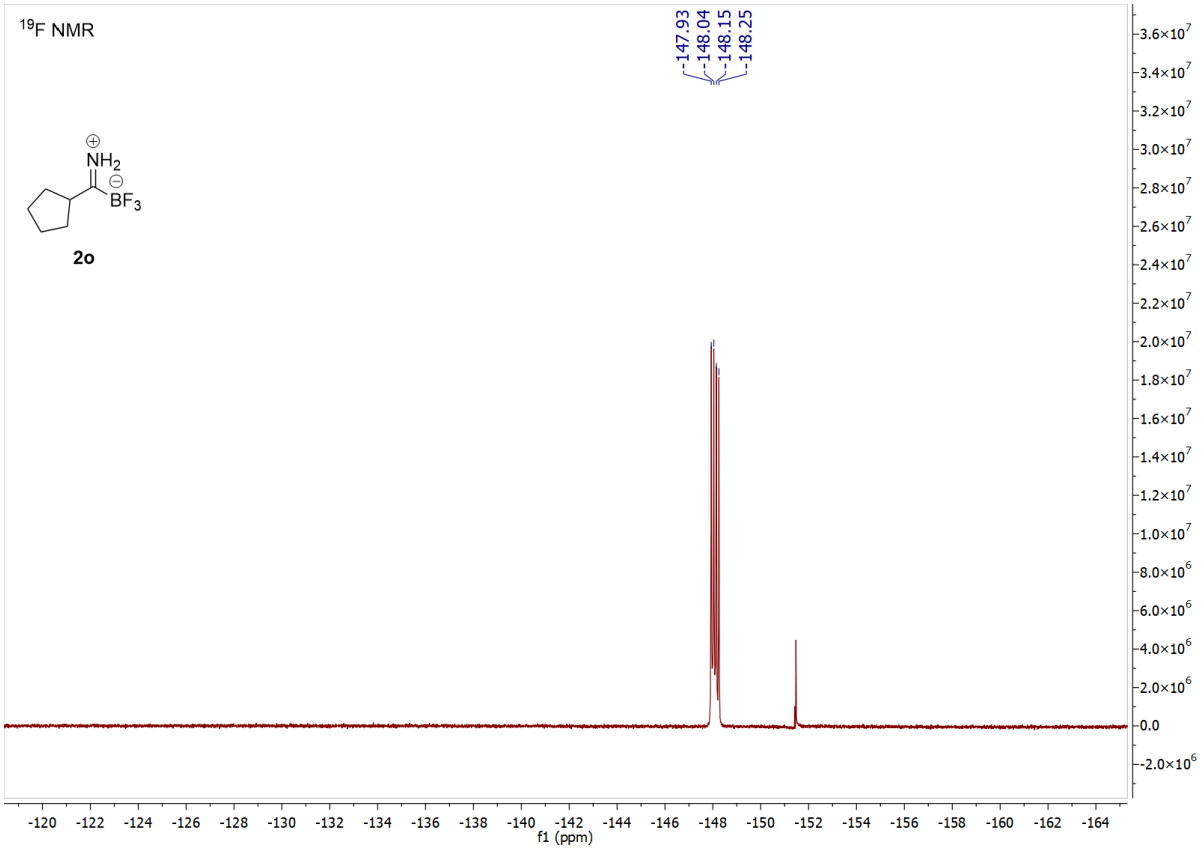
^{11}B-NMR (128 MHz, Acetone-d_6) of **2o**:



^{13}C-NMR (101 MHz, Acetone-d_6) of **2o**:

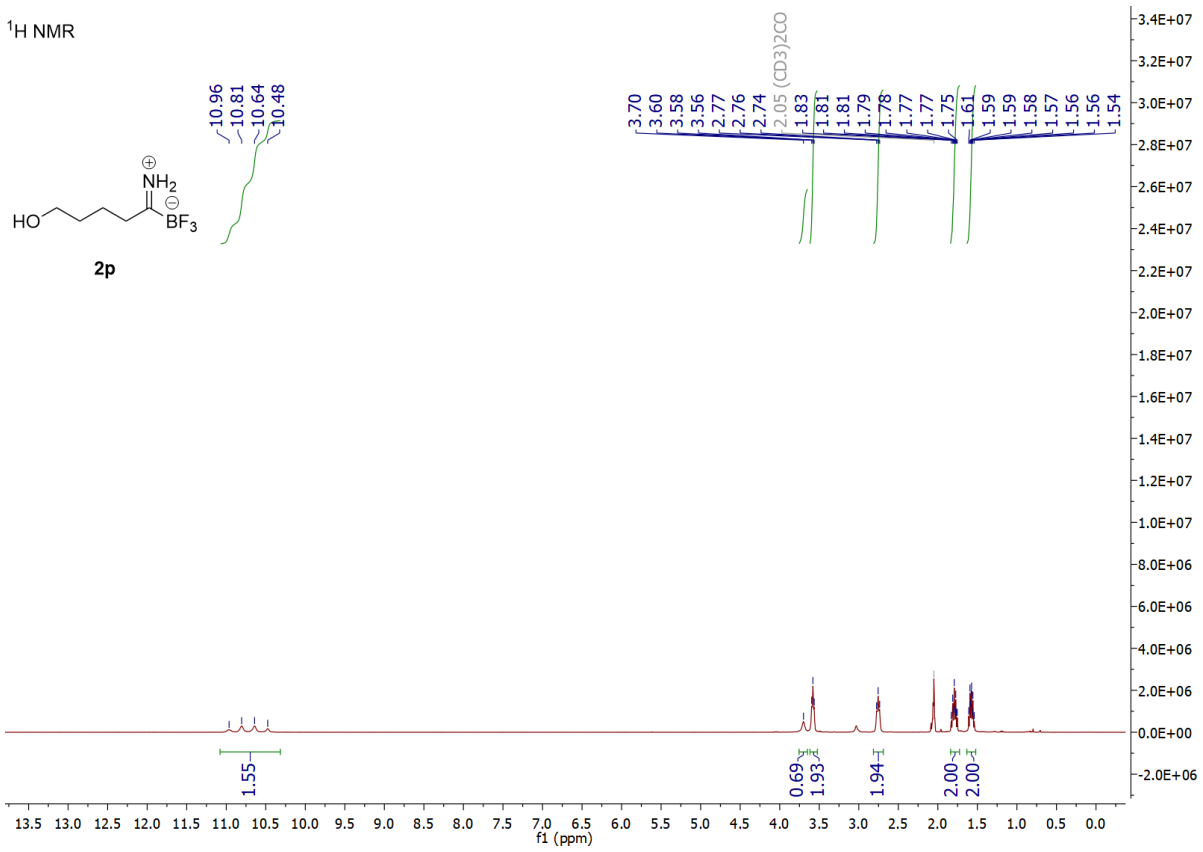


^{19}F-NMR (376 MHz, Acetone-d_6) of **2o**:

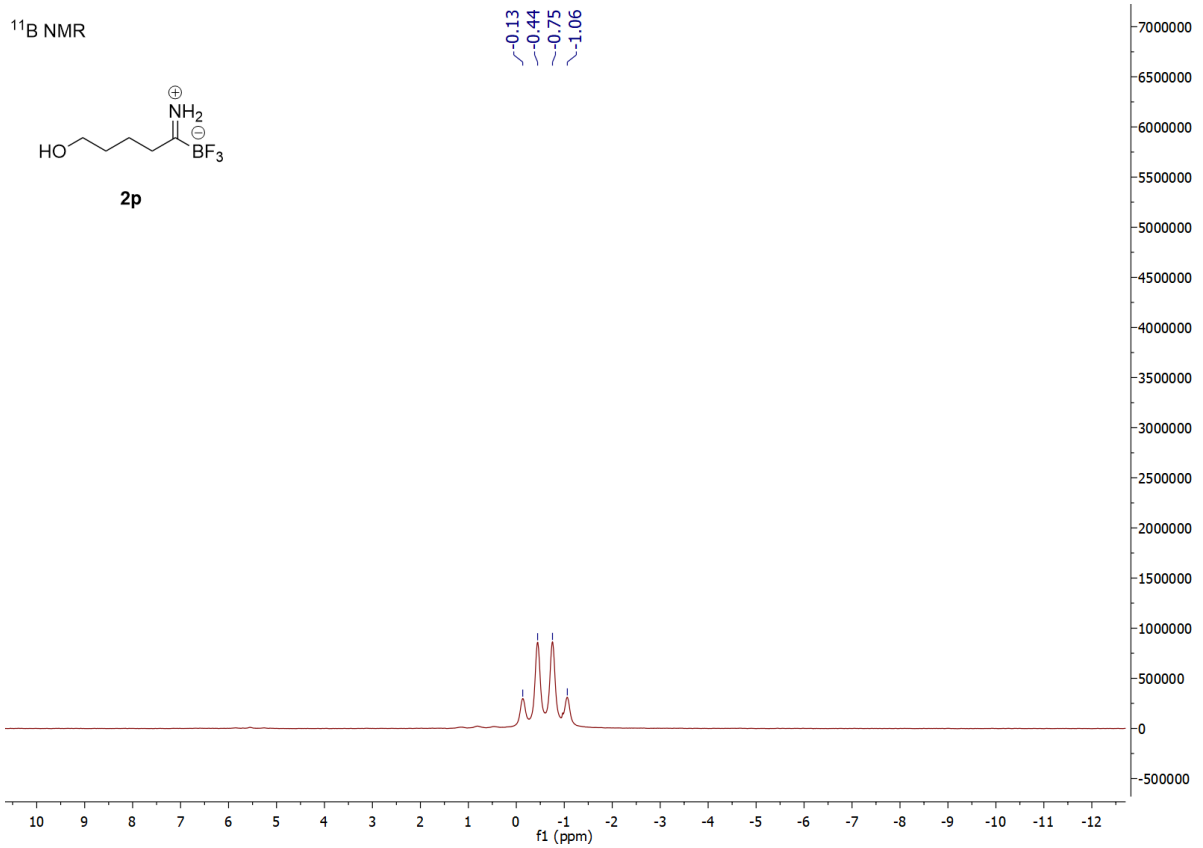


(5-Hydroxy-1-iminiopentyl)trifluoroborate (2p)

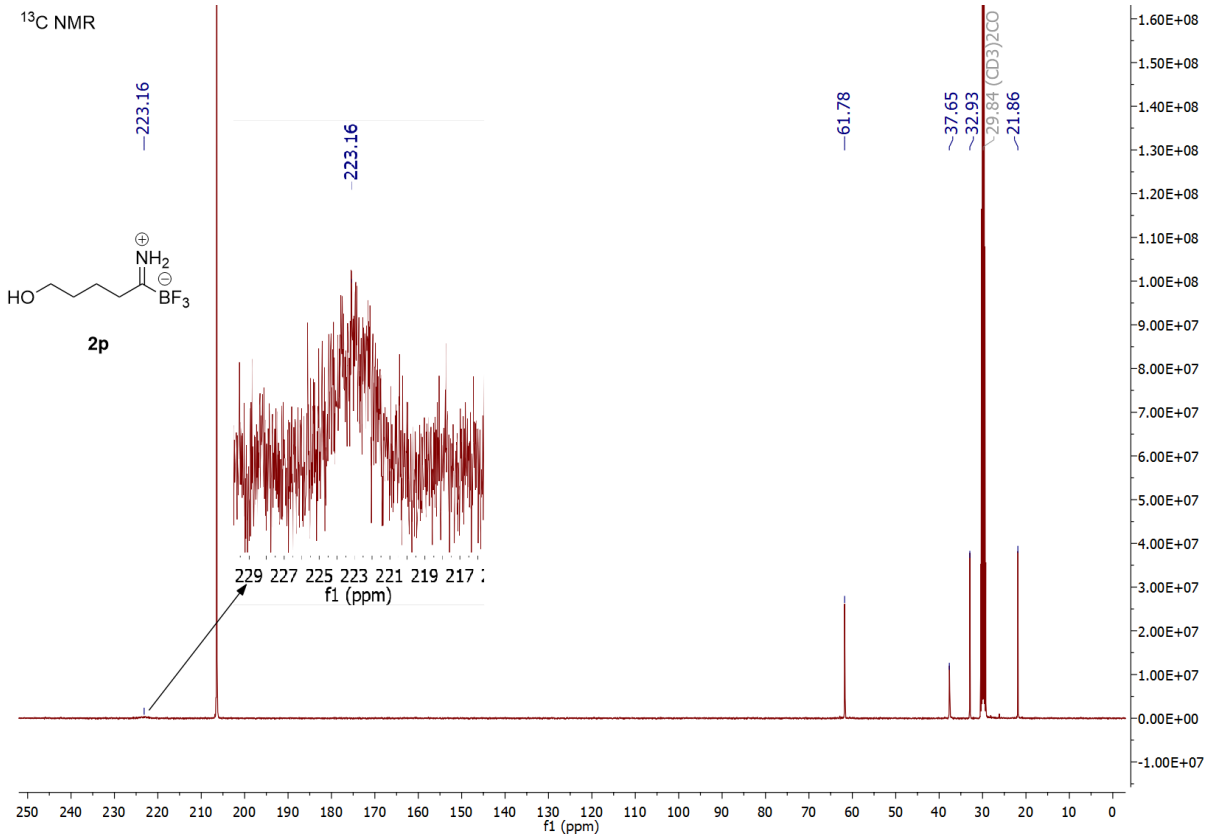
^{1}H-NMR (400 MHz, Acetone-d_6) of **2p**:



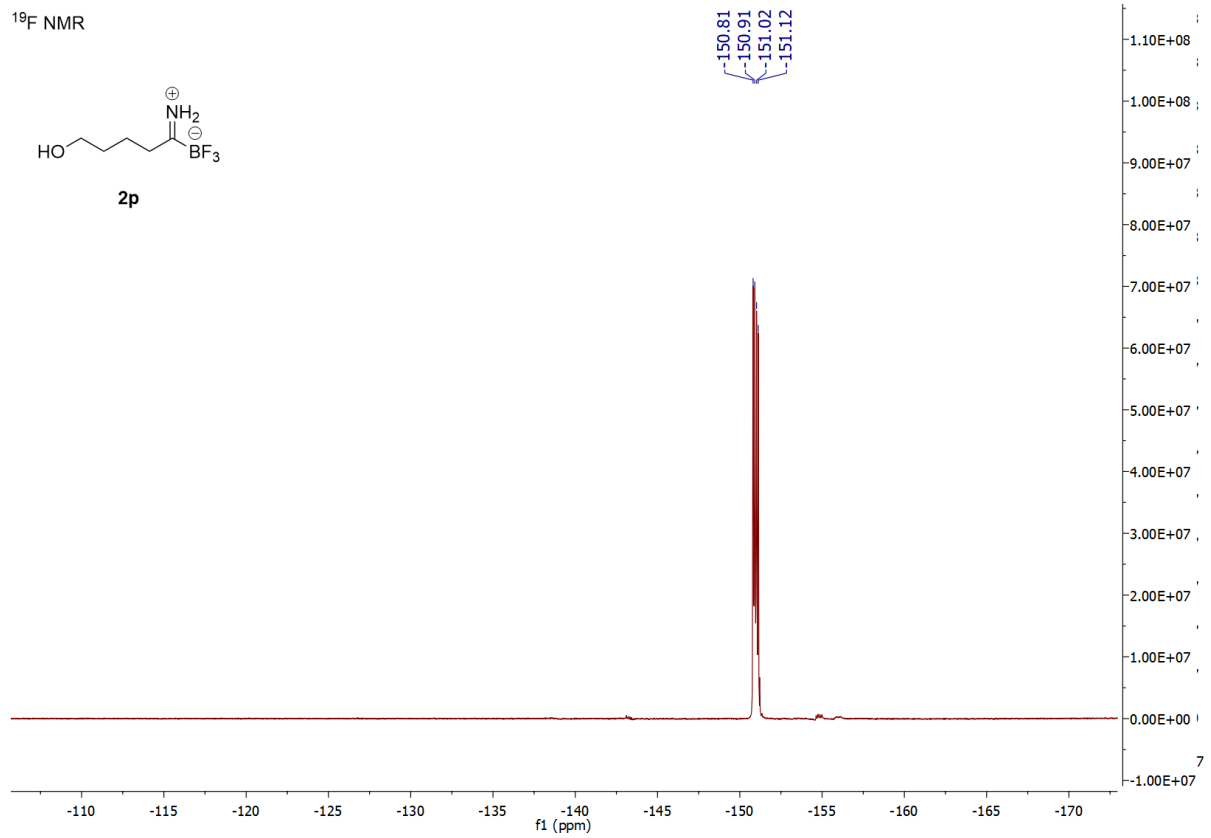
^{11}B-NMR (128 MHz, Acetone-d_6) of **2p**:



^{13}C-NMR (101 MHz, Acetone-d_6) of **2p**:



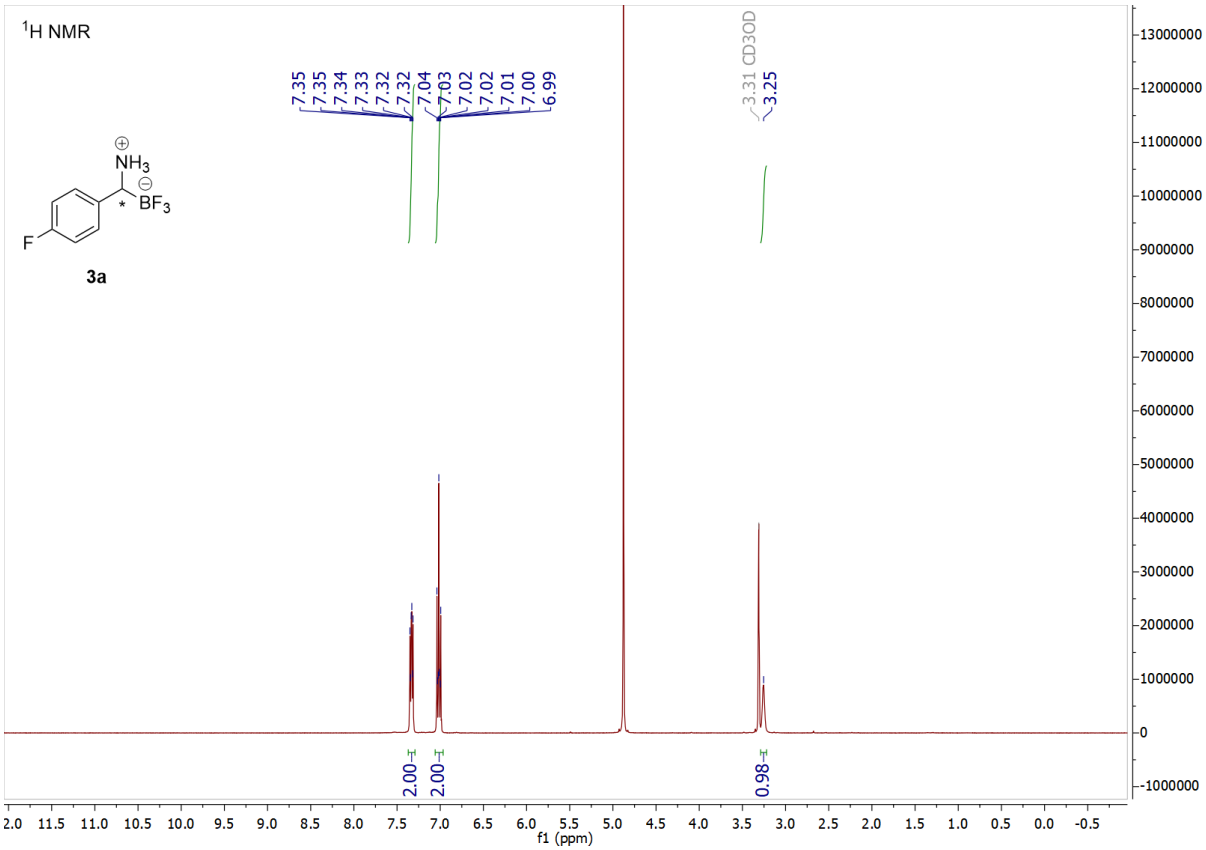
^{19}F-NMR (376 MHz, Acetone-d_6) of **2p**:



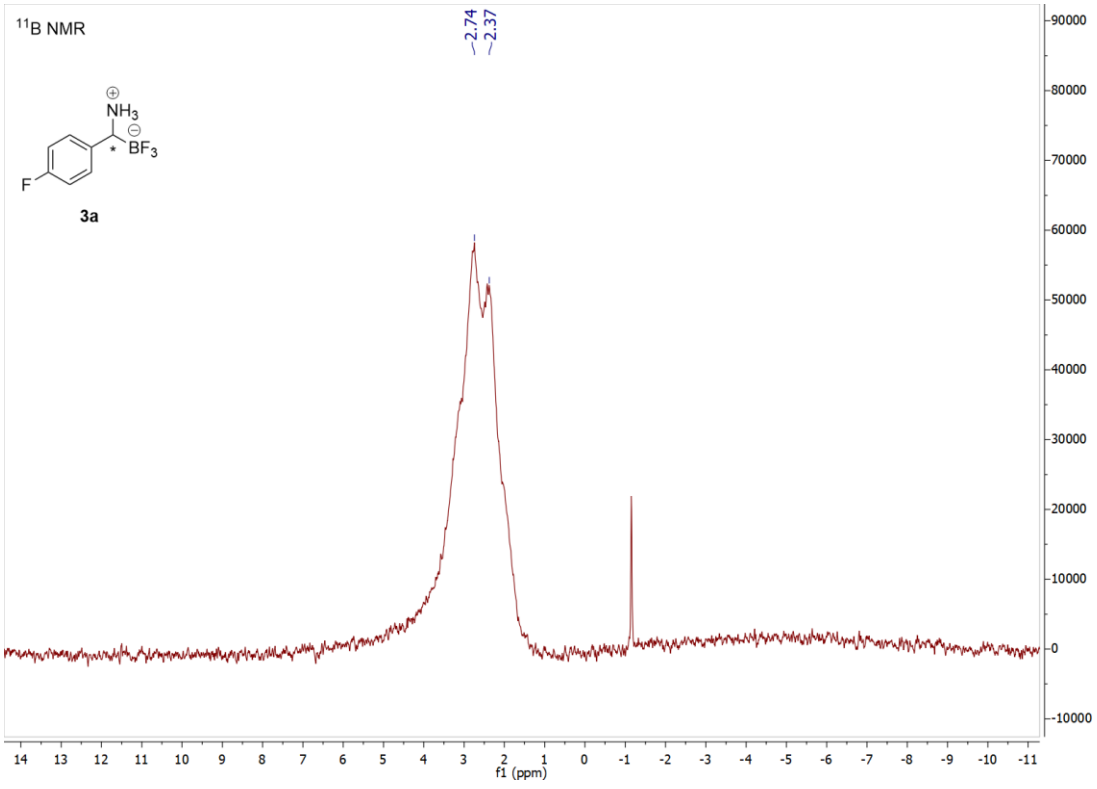
8.2. NMR Spectra of pTAMs **3**

(Ammonio(4-fluorophenyl)methyl)trifluoroborate (3a)

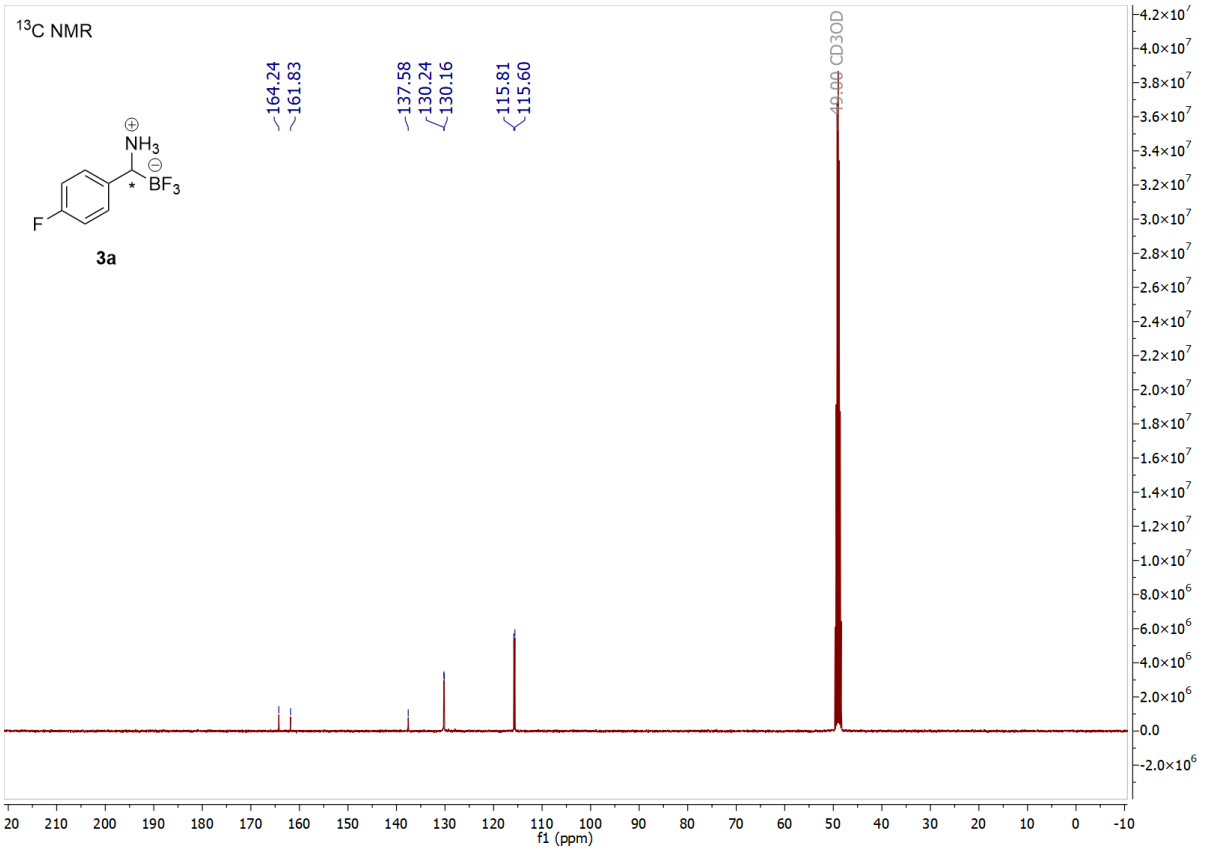
^{1}H-NMR (400 MHz, CD_3OD) of **3a**:



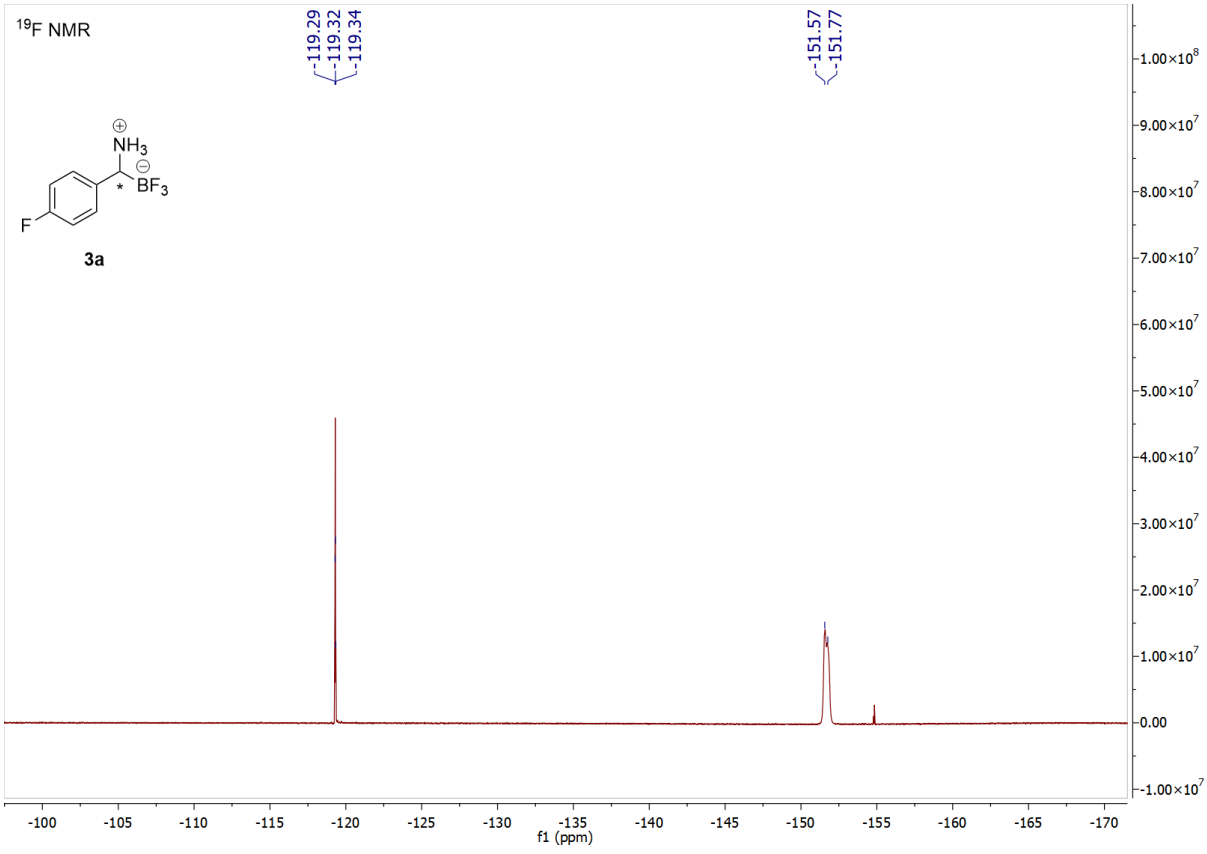
^{11}B-NMR (128 MHz, CD_3OD) of **3a**:



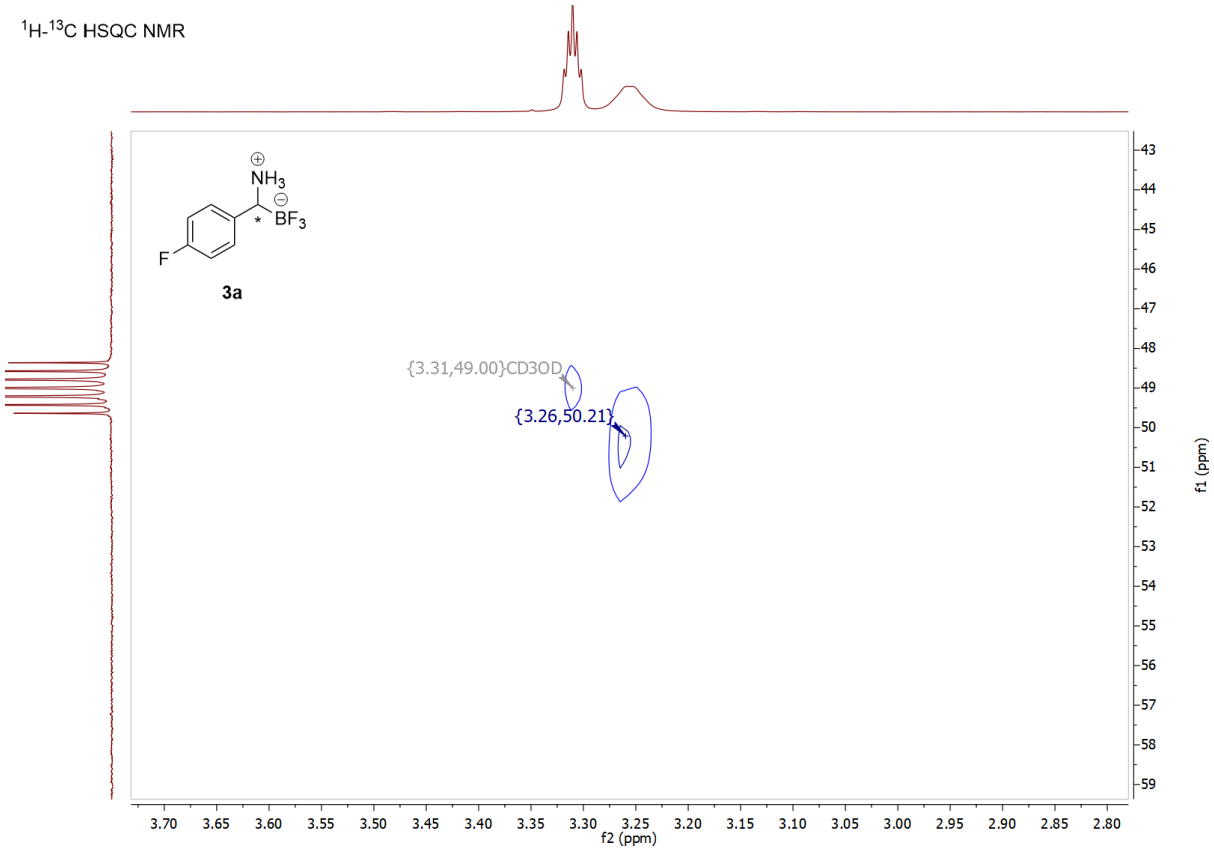
^{13}C-NMR (101 MHz, CD_3OD) of **3a**:



^{19}F-NMR (376 MHz, CD_3OD) of **3a**:

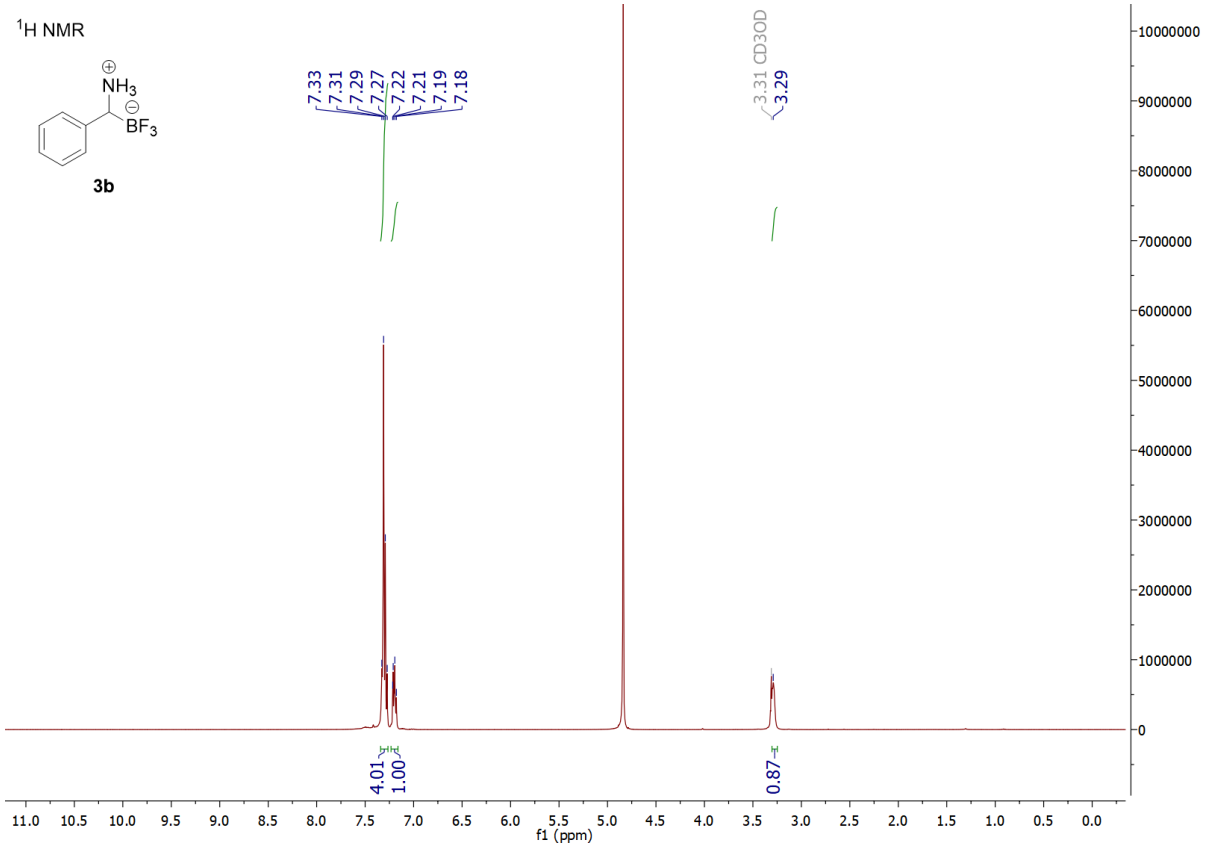


^{1}H-^{13}C-HSQC NMR (CD_3OD) of **3a**:

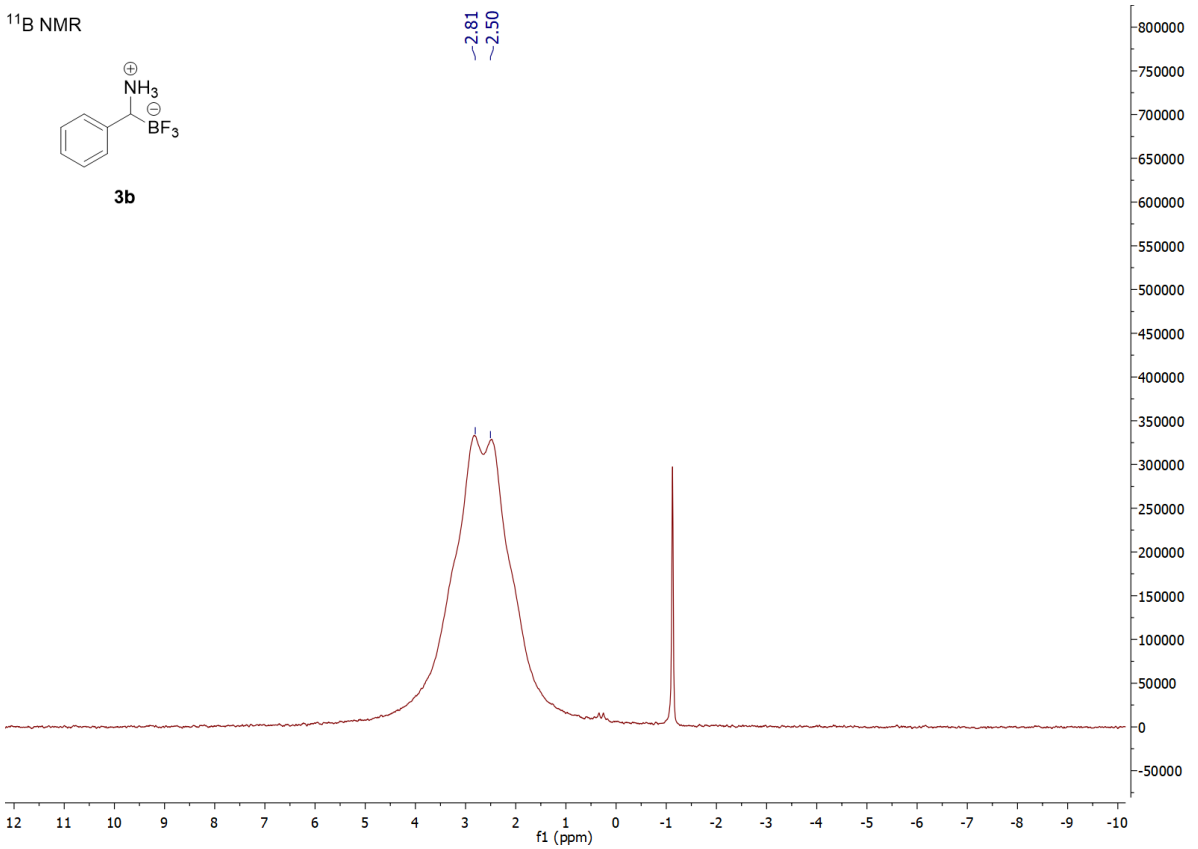


(Ammonio(phenyl)methyl)trifluoroborate (3b)

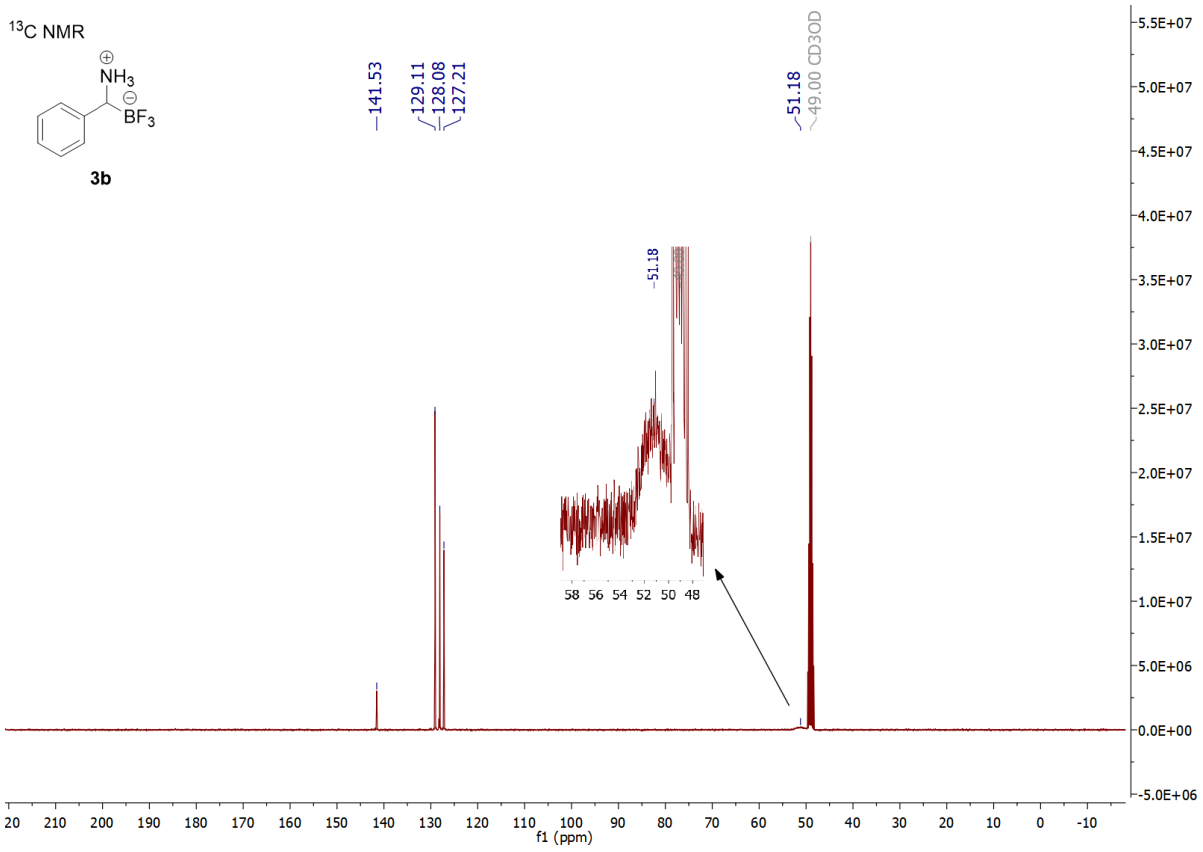
^{1}H-NMR (400 MHz, CD_3OD) of **3b**:



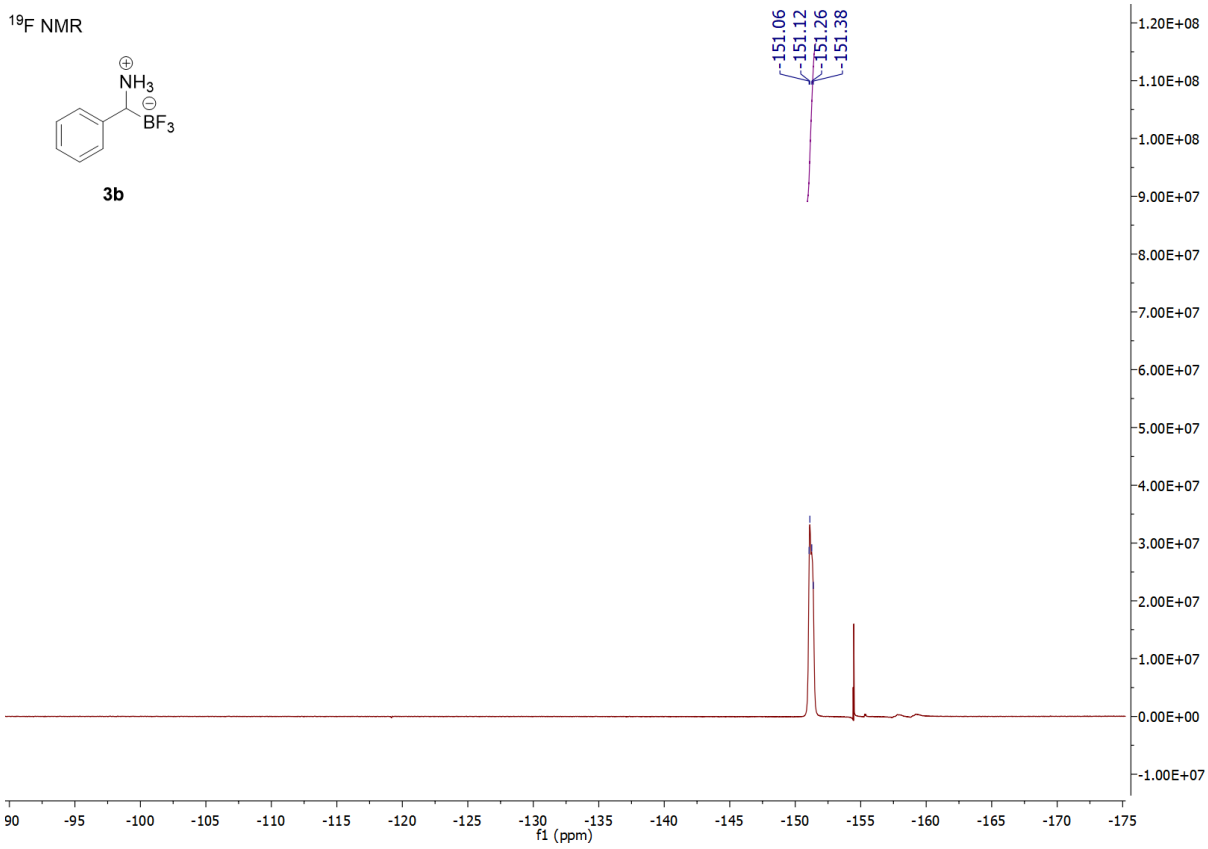
^{11}B-NMR (128 MHz, CD_3OD) of **3b**:



^{13}C-NMR (101 MHz, CD_3OD) of **3b**:

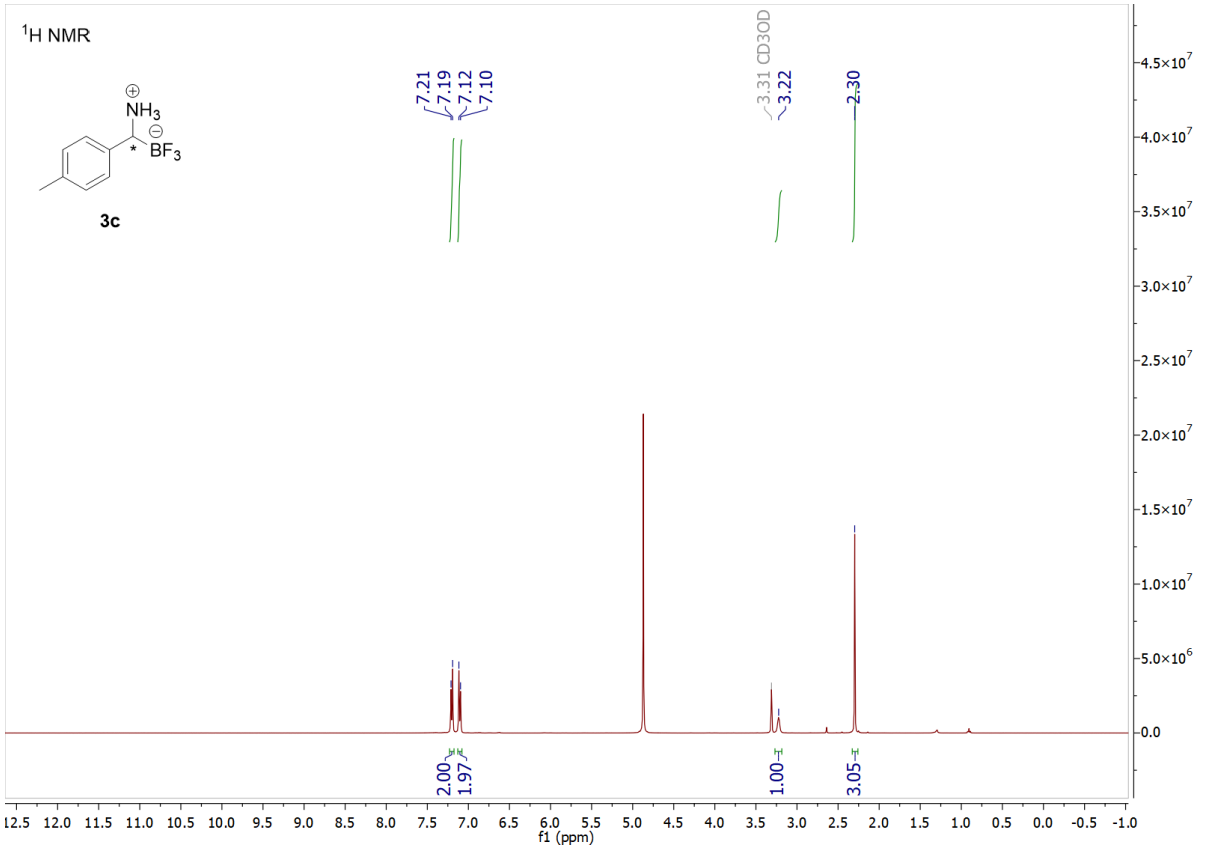


^{19}F-NMR (376 MHz, CD_3OD) of **3b**:

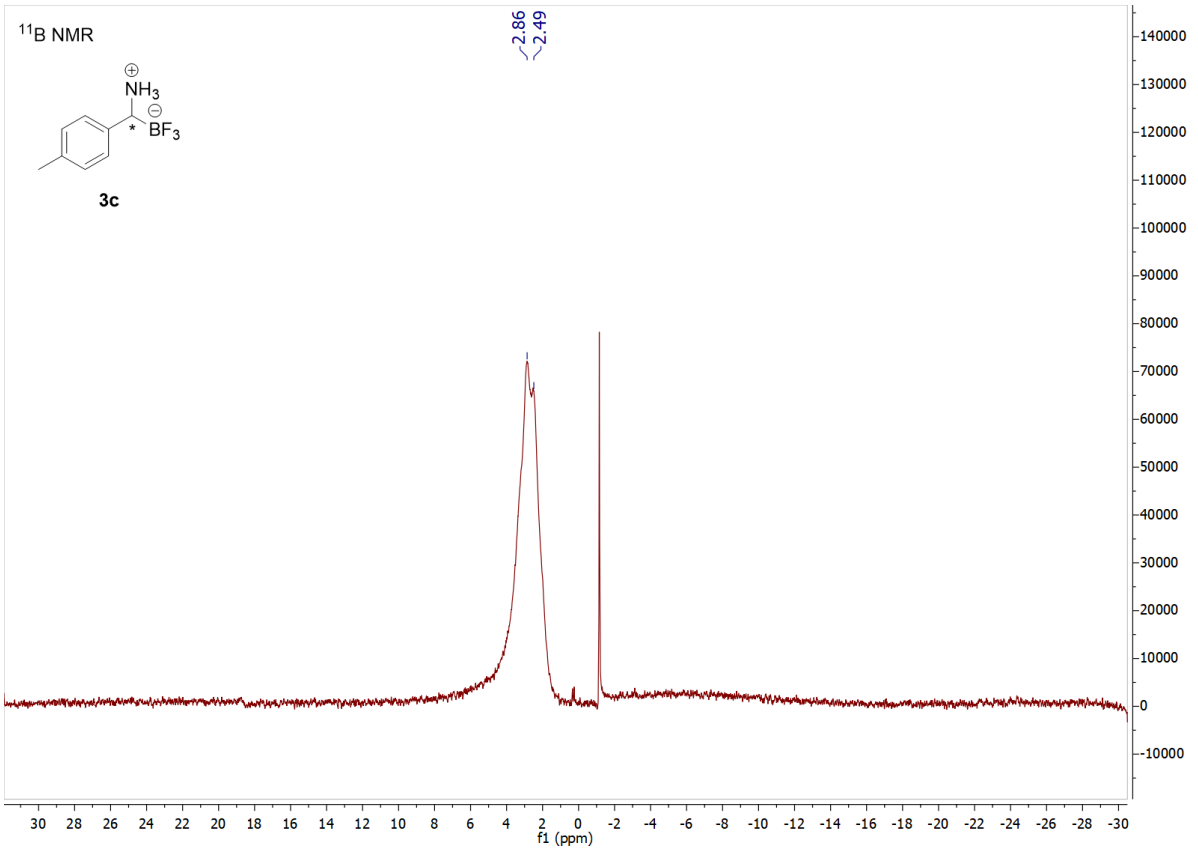


(Ammonio(*p*-tolyl)methyl)trifluoroborate (3c)

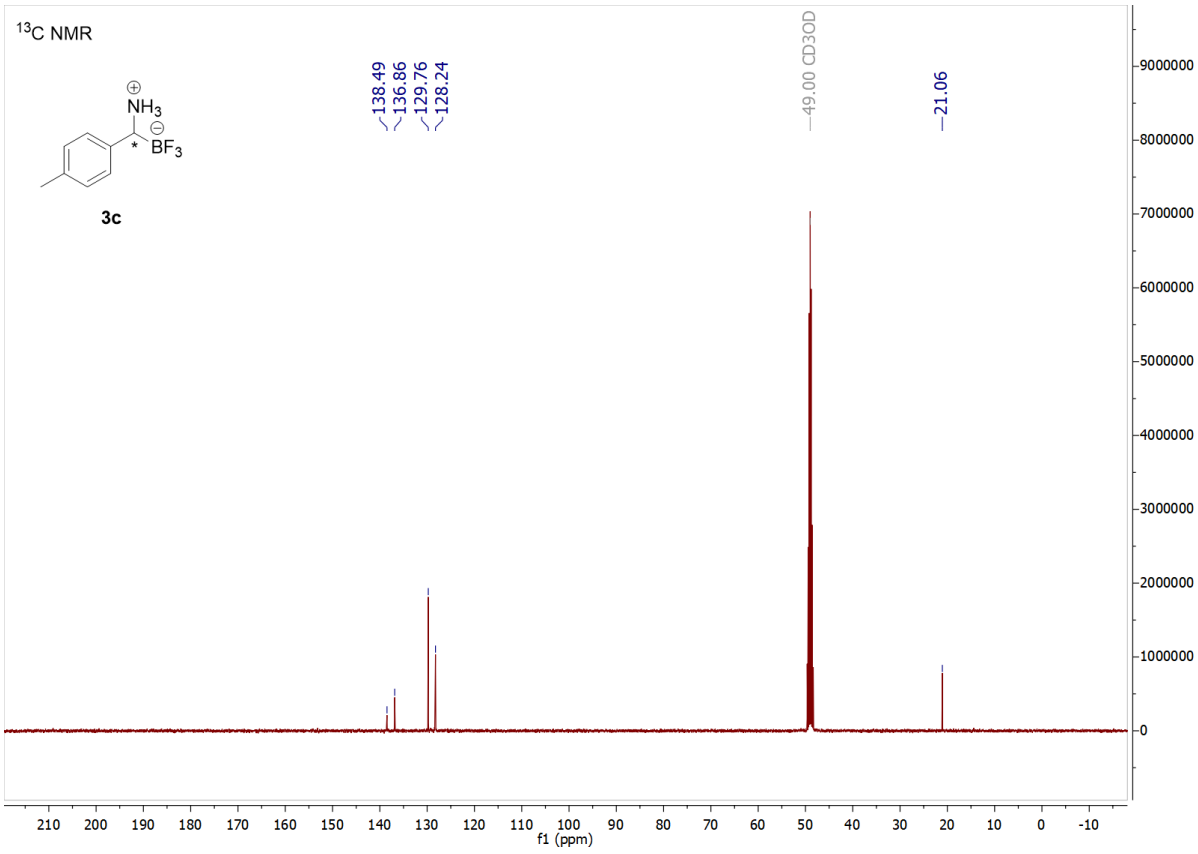
^{1}H-NMR (400 MHz, CD_3OD) of **3c**:



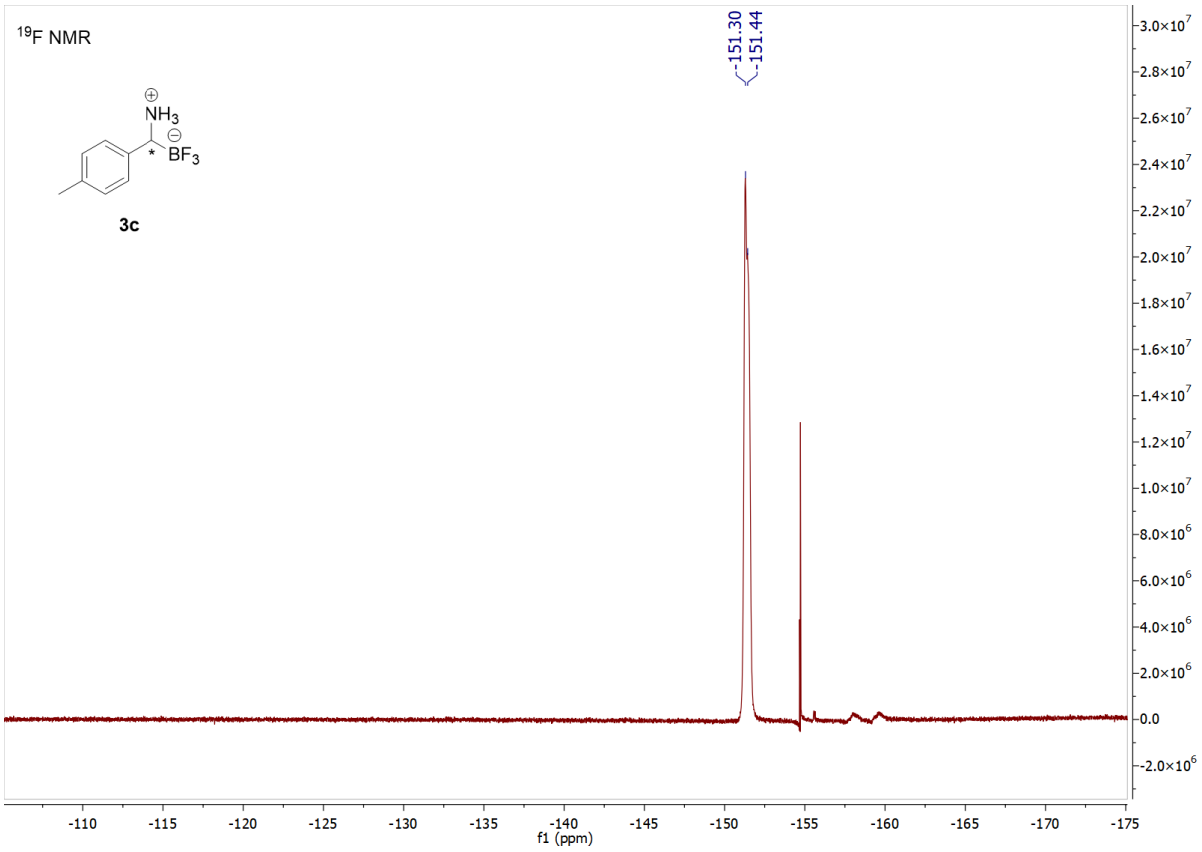
^{11}B-NMR (128 MHz, CD_3OD) of **3c**:



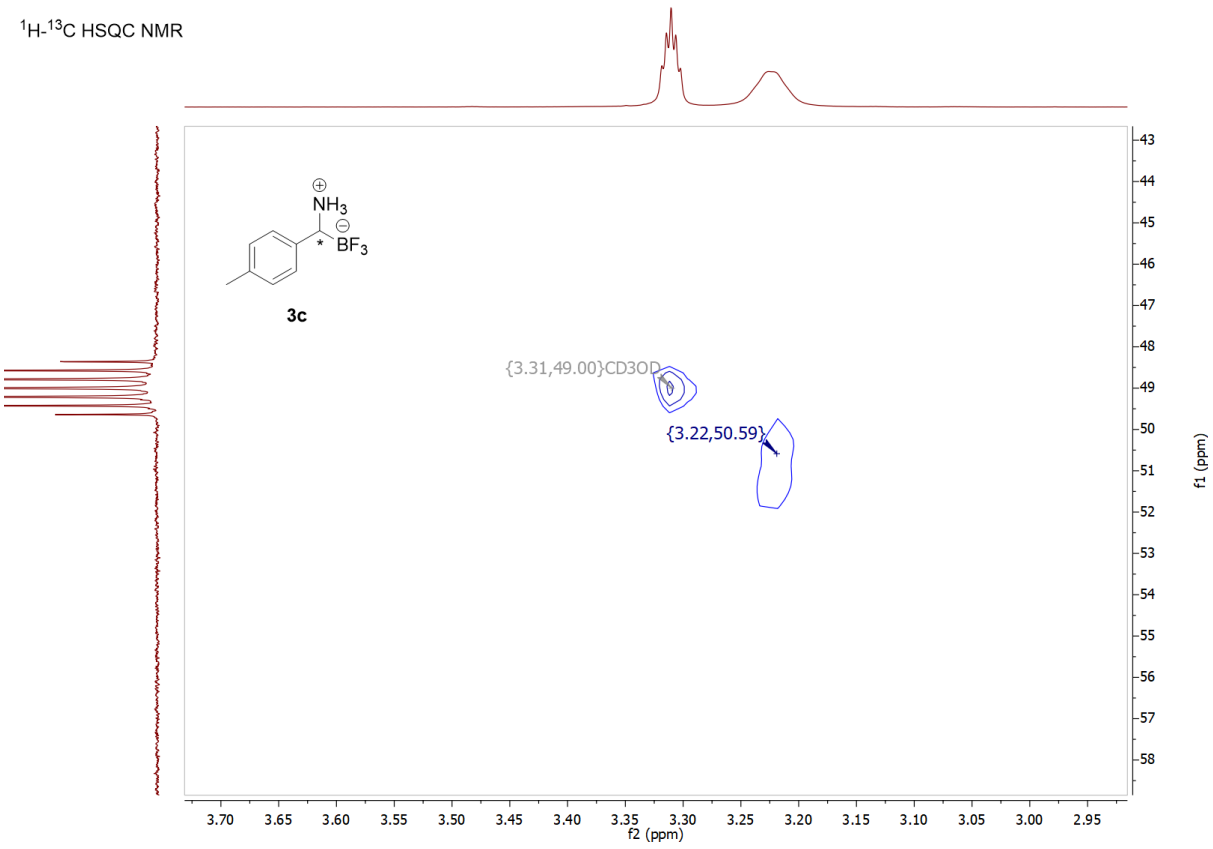
^{13}C-NMR (101 MHz, CD_3OD) of **3c**:



^{19}F-NMR (376 MHz, CD_3OD) of **3c**:

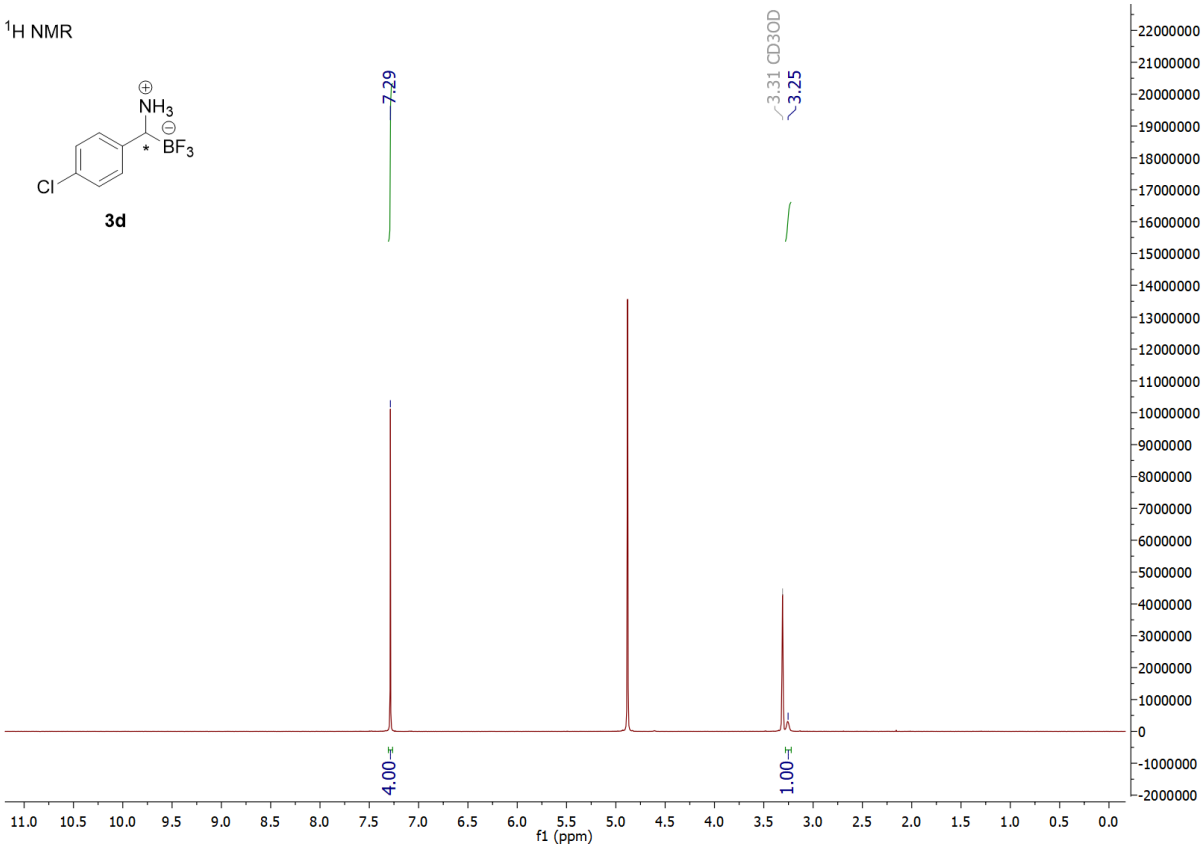


^{1}H-^{13}C-HSQC NMR (CD_3OD) of **3c**:

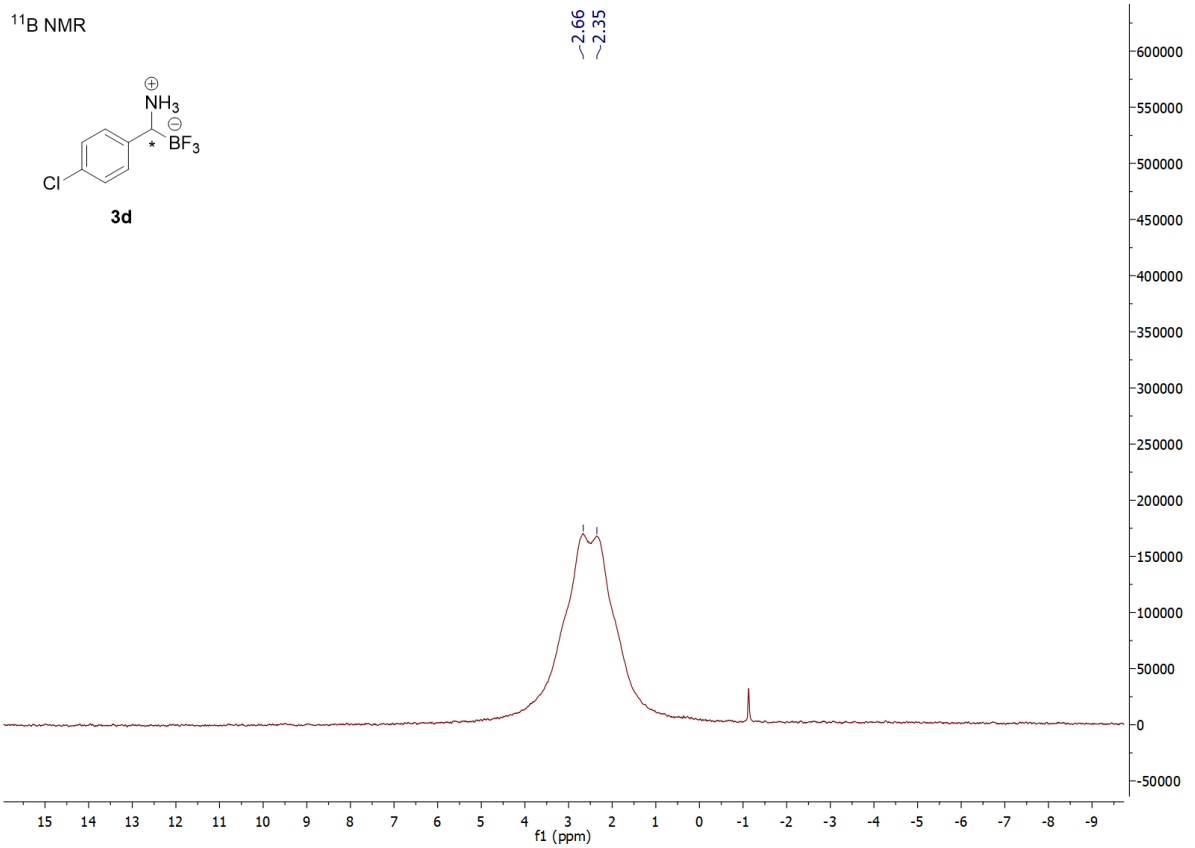


(Ammonio(4-chlorophenyl)methyl)trifluoroborate (3d)

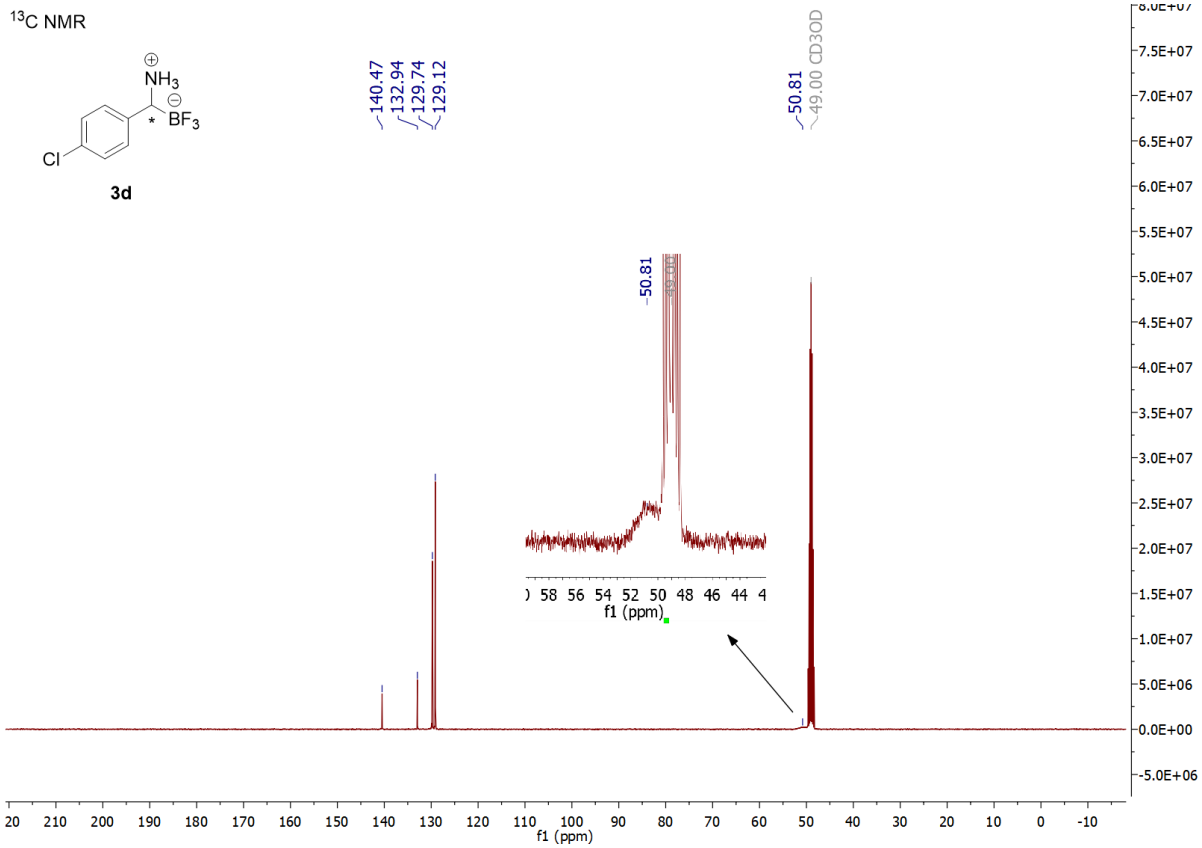
^{1}H-NMR (400 MHz, CD_3OD) of **3d**:



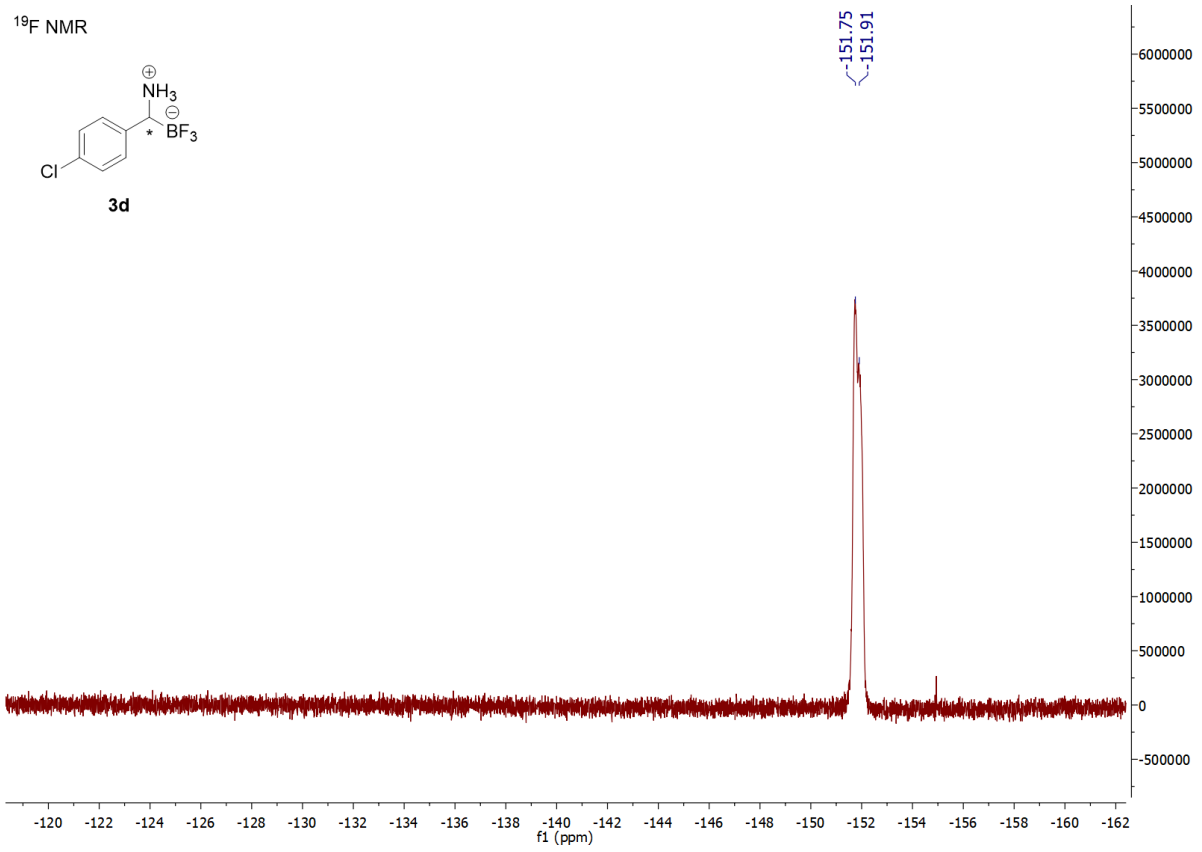
^{11}B-NMR (128 MHz, CD_3OD) of **3d**:



^{13}C-NMR (101 MHz, CD_3OD) of **3d**:

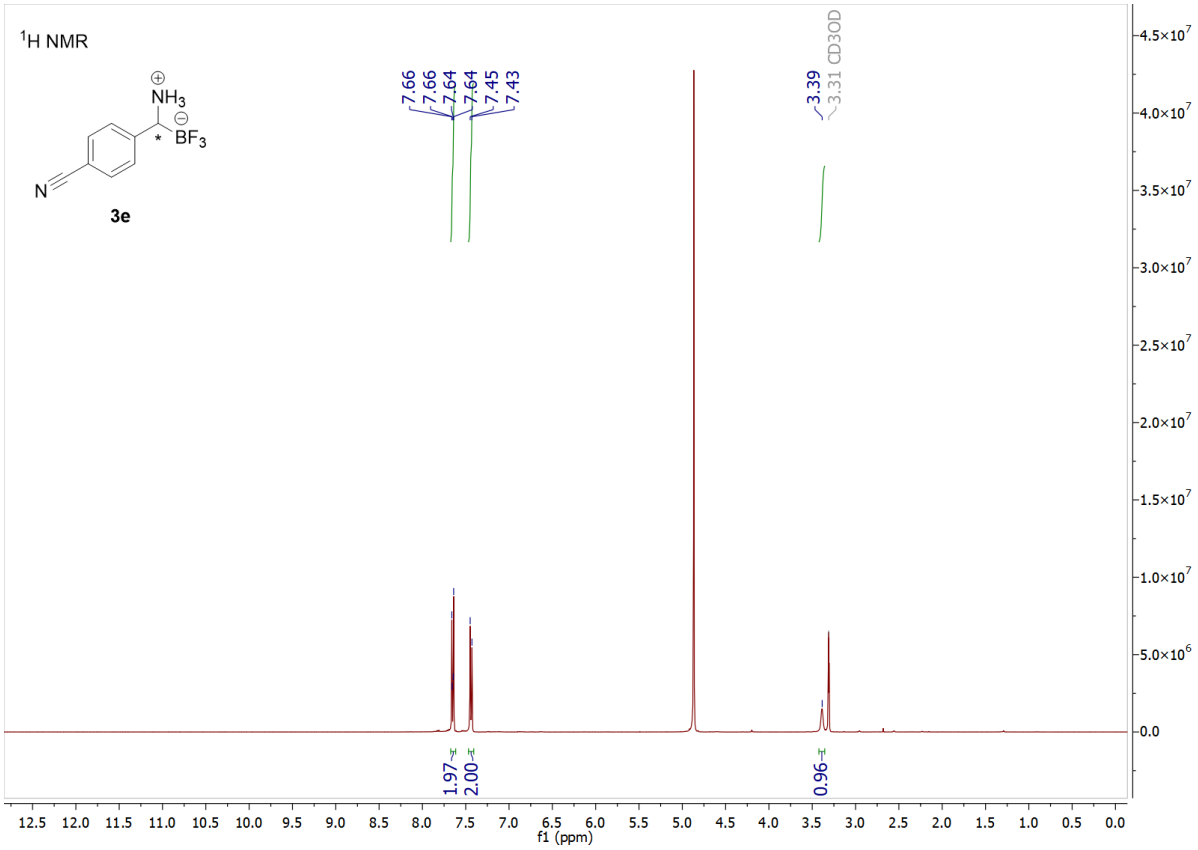


^{19}F-NMR (376 MHz, CD_3OD) of **3d**:

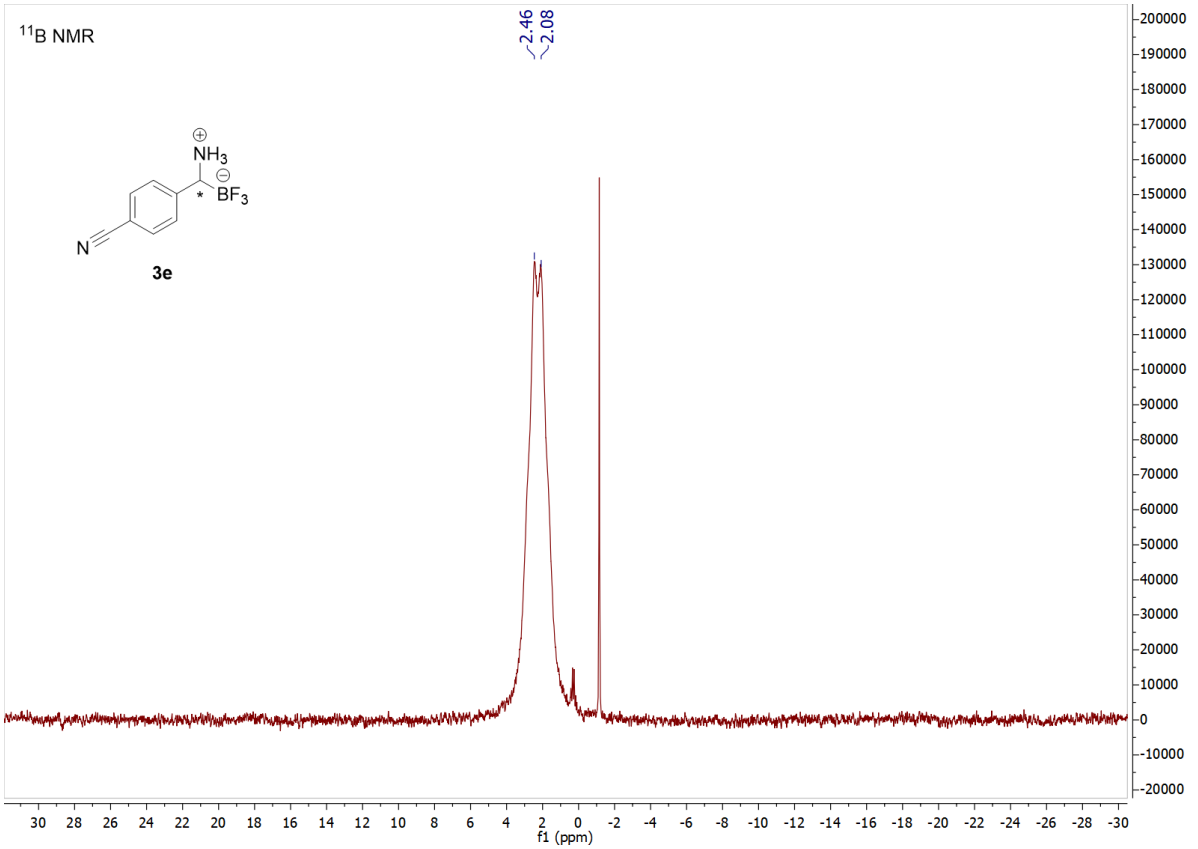


(Ammonio(4-cyanophenyl)methyl)trifluoroborate (3e)

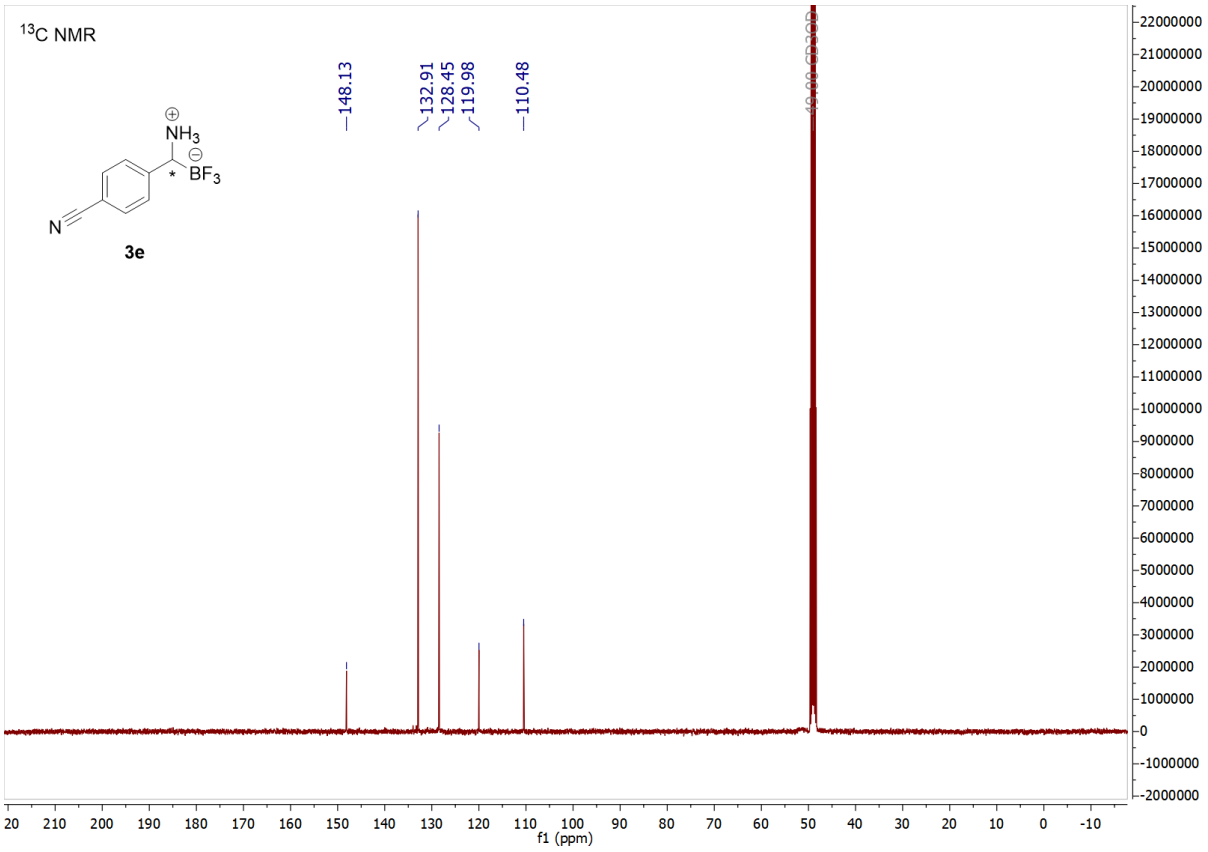
^{1}H-NMR (400 MHz, CD_3OD) of **3e**:



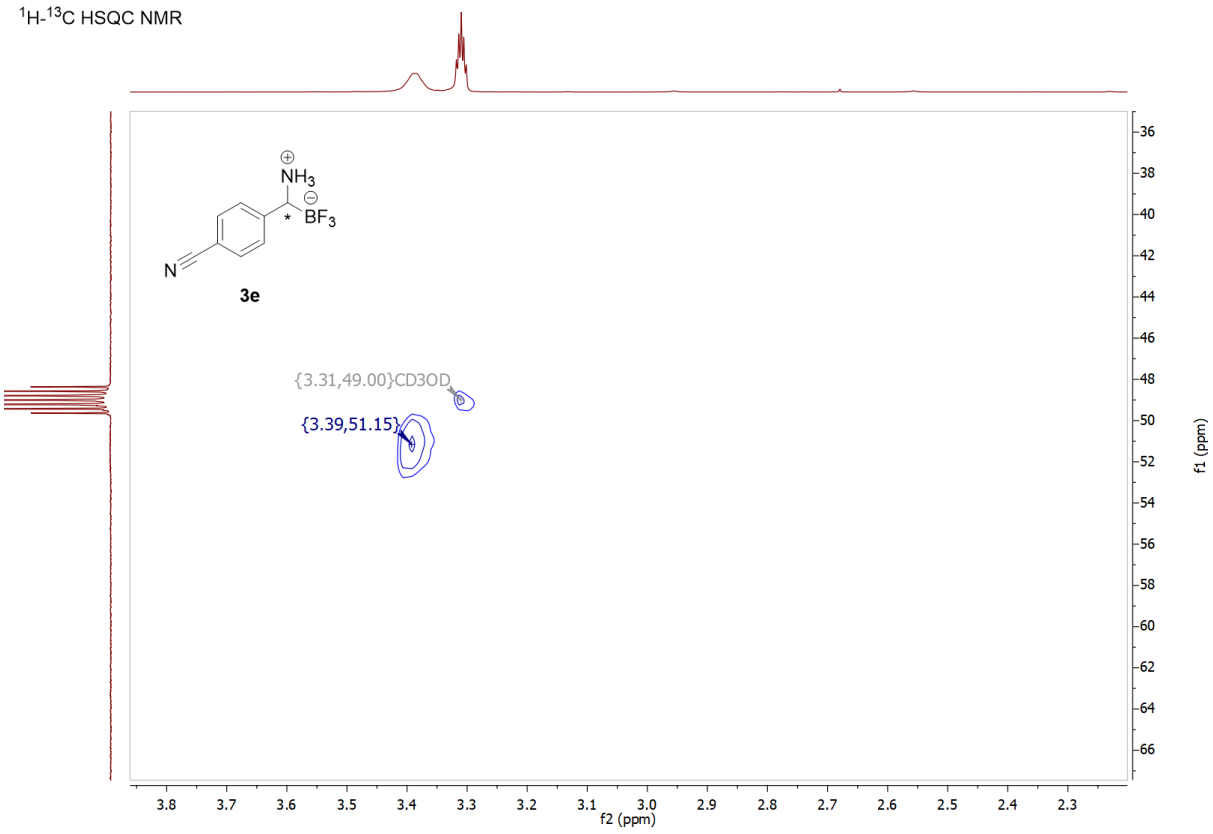
^{11}B-NMR (128 MHz, CD_3OD) of **3e**:



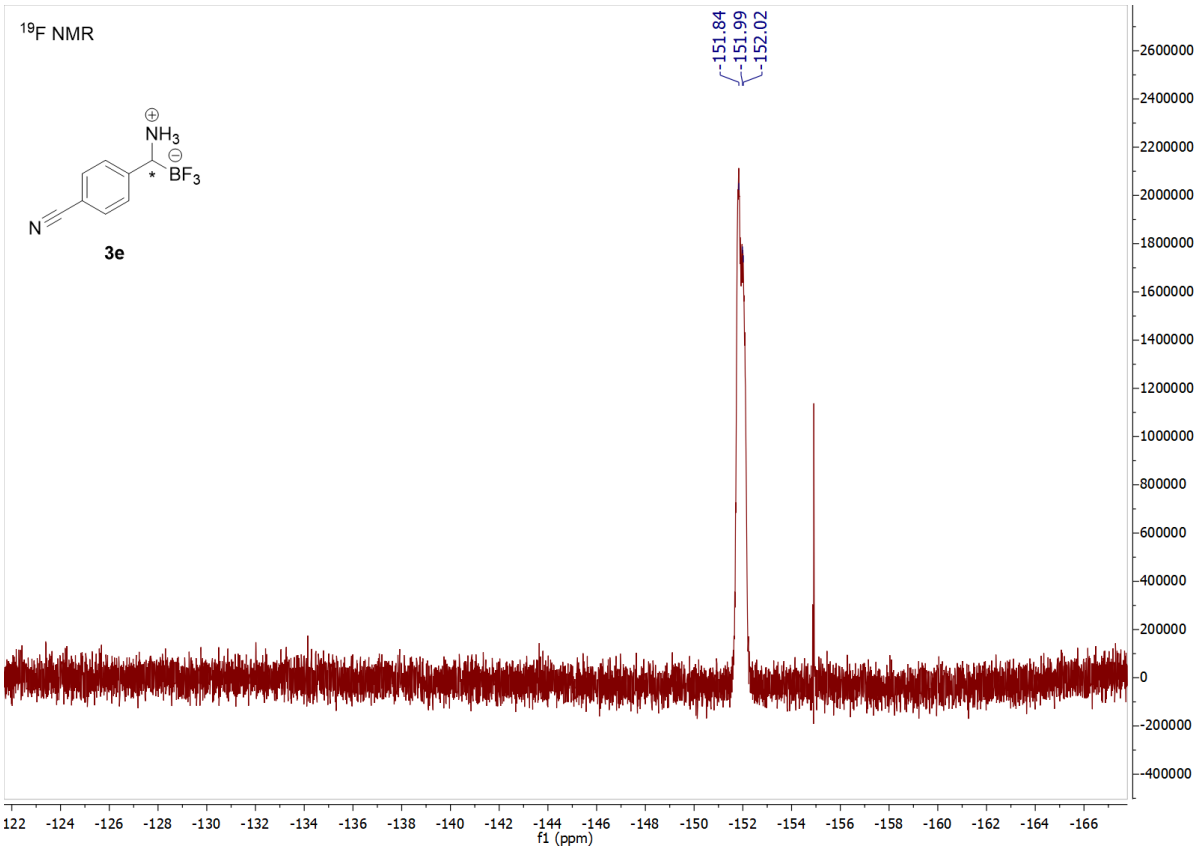
^{13}C-NMR (101 MHz, CD_3OD) of **3e**:



^{1}H-^{13}C-HSQC NMR (CD_3OD) of **3e**:

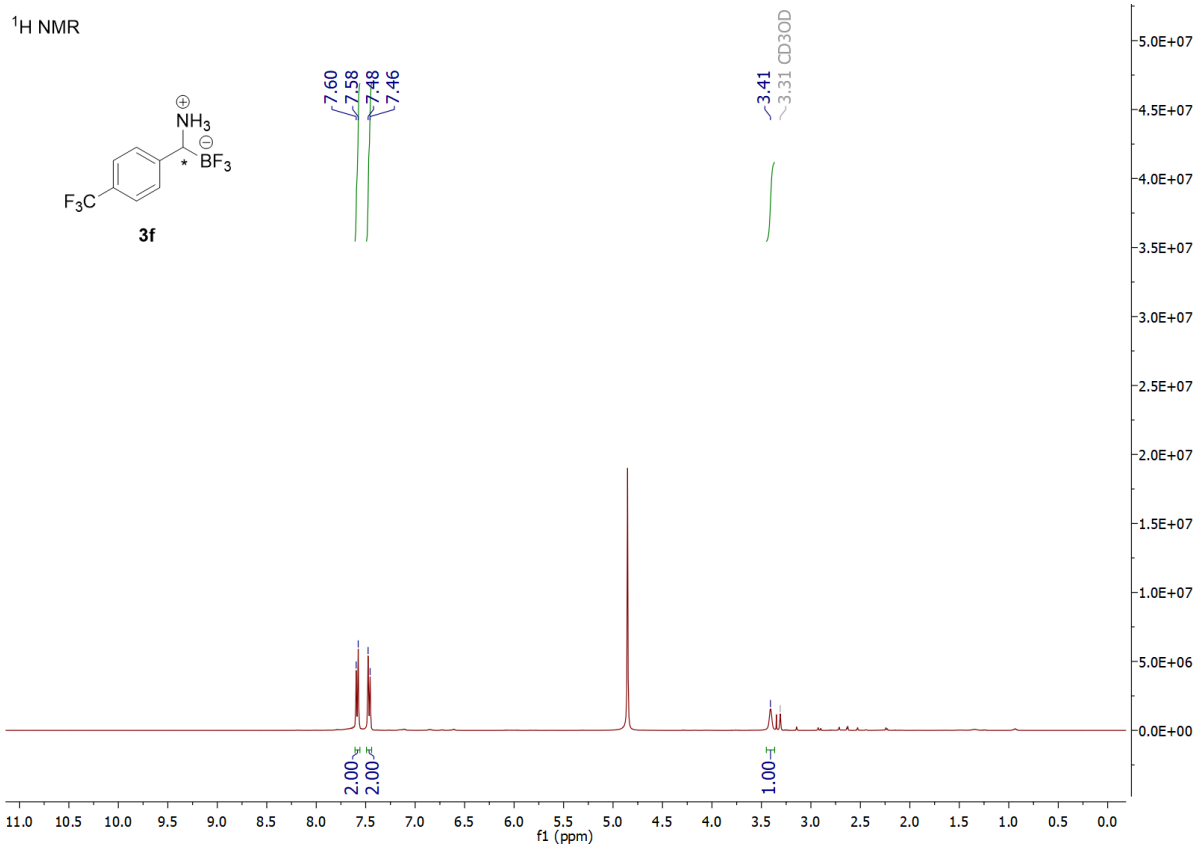


^{19}F-NMR (376 MHz, CD_3OD) of **3e**:

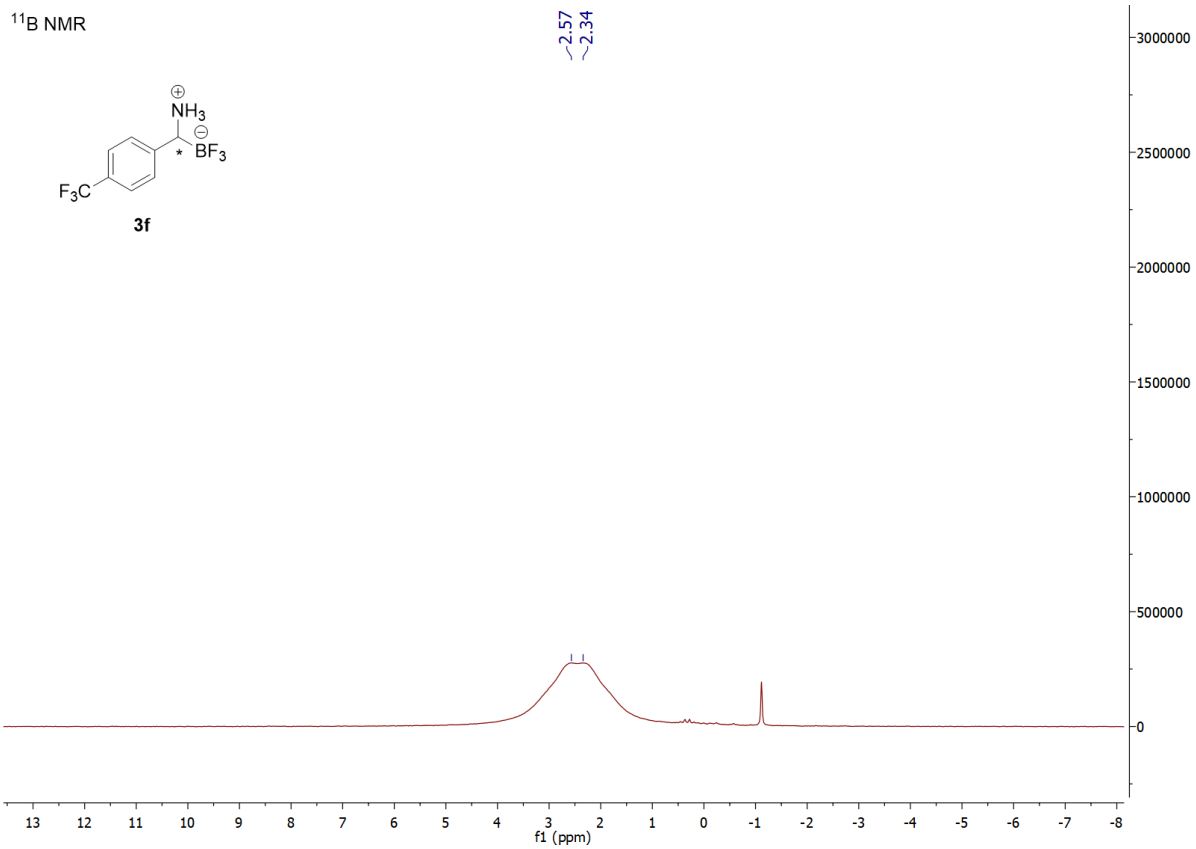


(Ammonio(4-(trifluoromethyl)phenyl)methyl)trifluoroborate (3f)

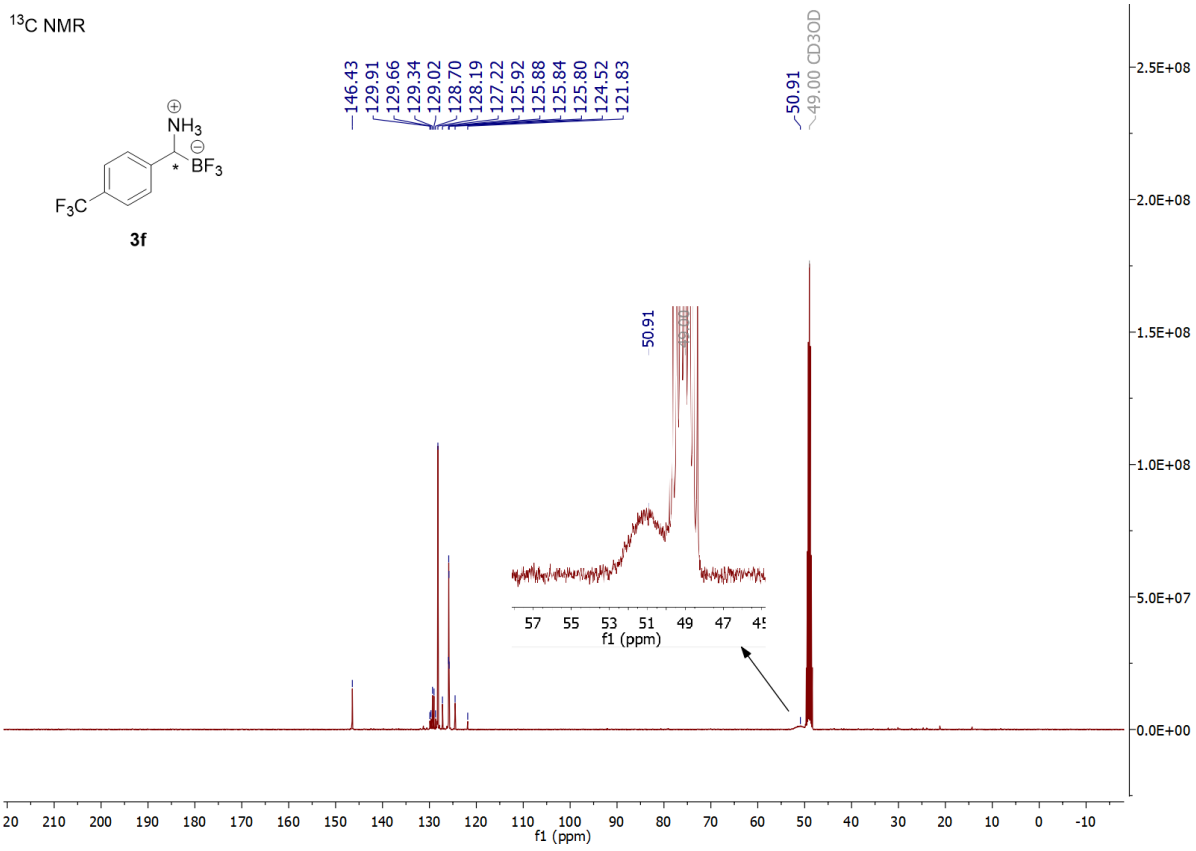
^{1}H-NMR (400 MHz, CD_3OD) of **3f**:



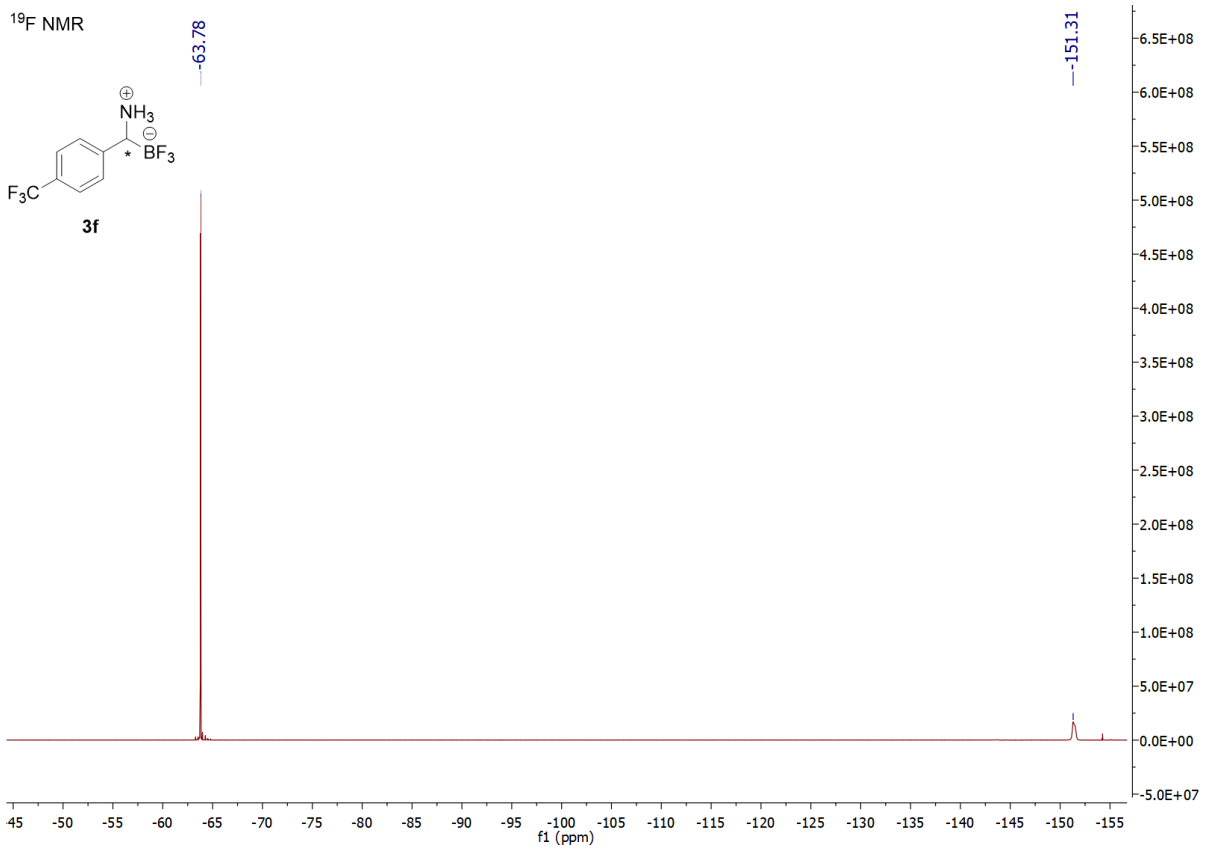
^{11}B-NMR (128 MHz, CD_3OD) of **3f**:



^{13}C-NMR (101 MHz, CD_3OD) of **3f**:

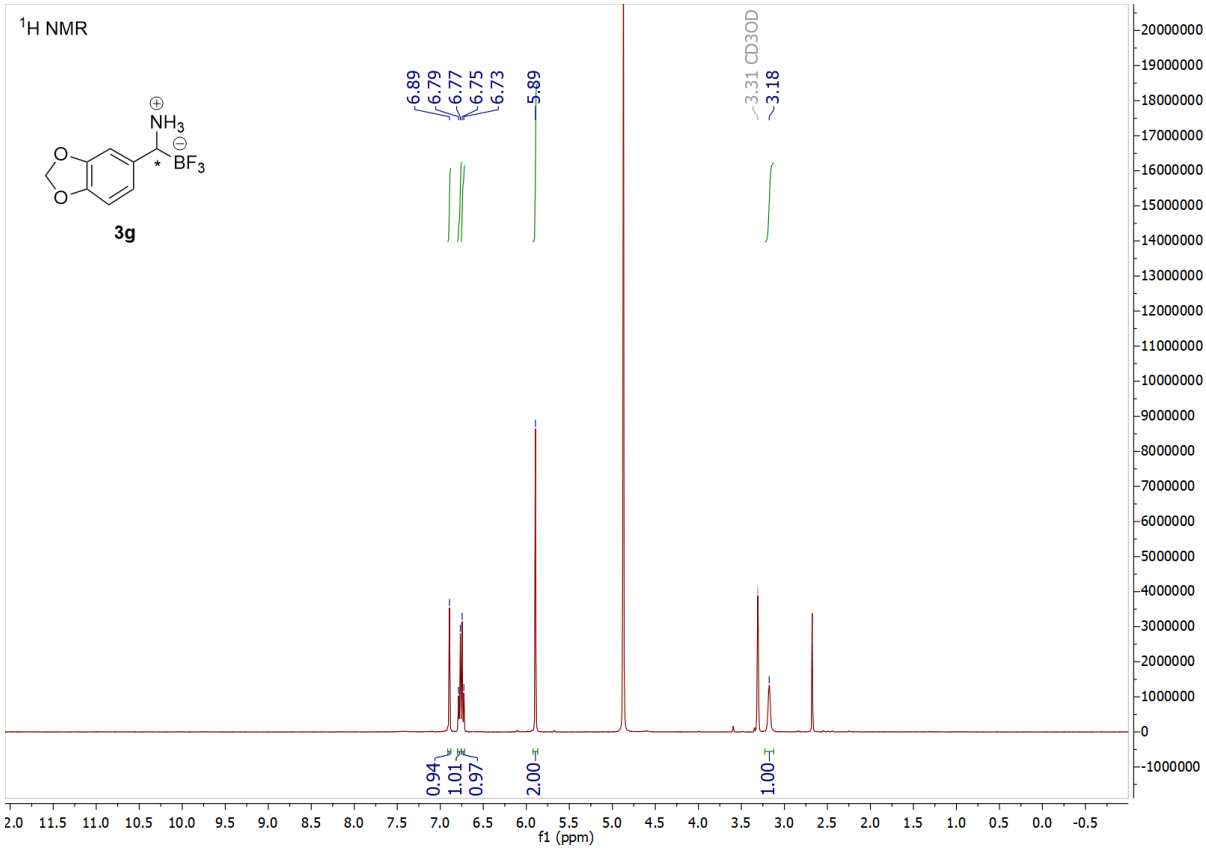


^{19}F-NMR (376 MHz, CD_3OD) of **3f**:

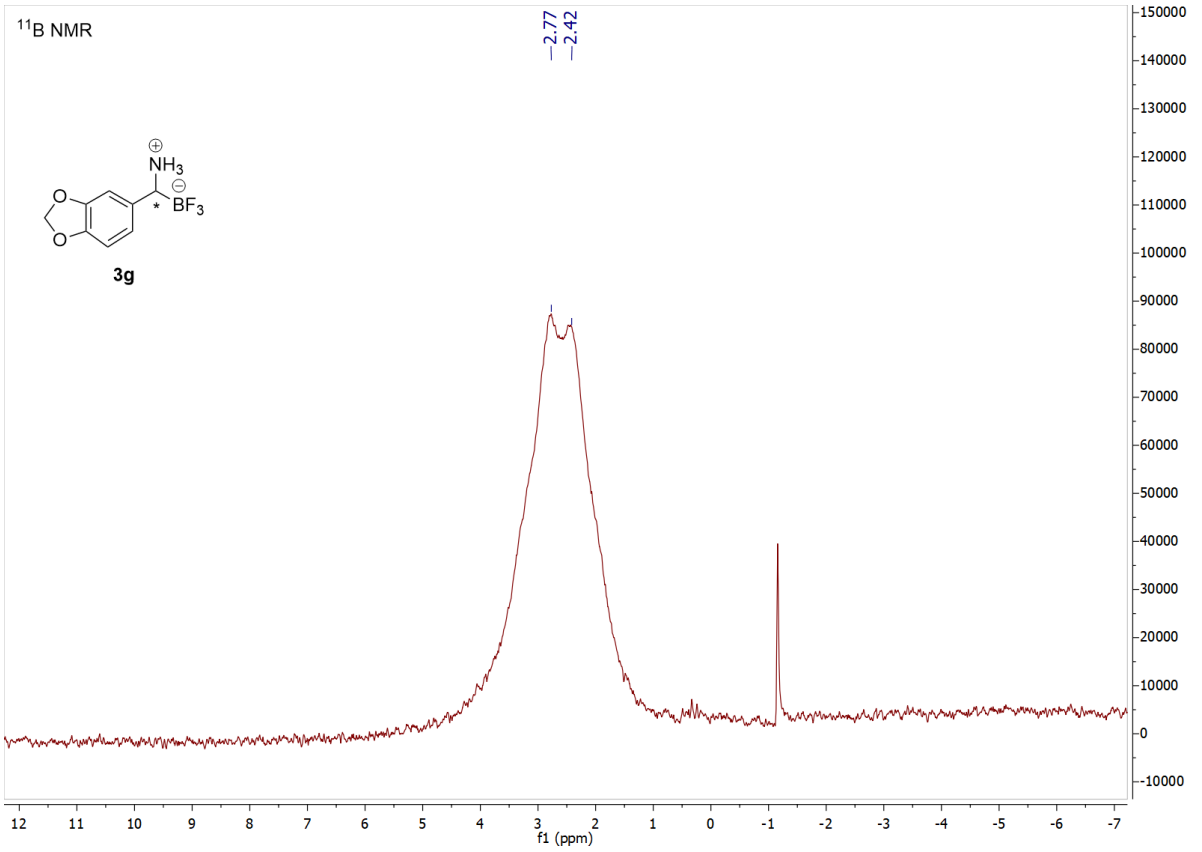


(Ammonio(benzo[*d*][1,3]dioxol-5-yl)methyl)trifluoroborate (3g)

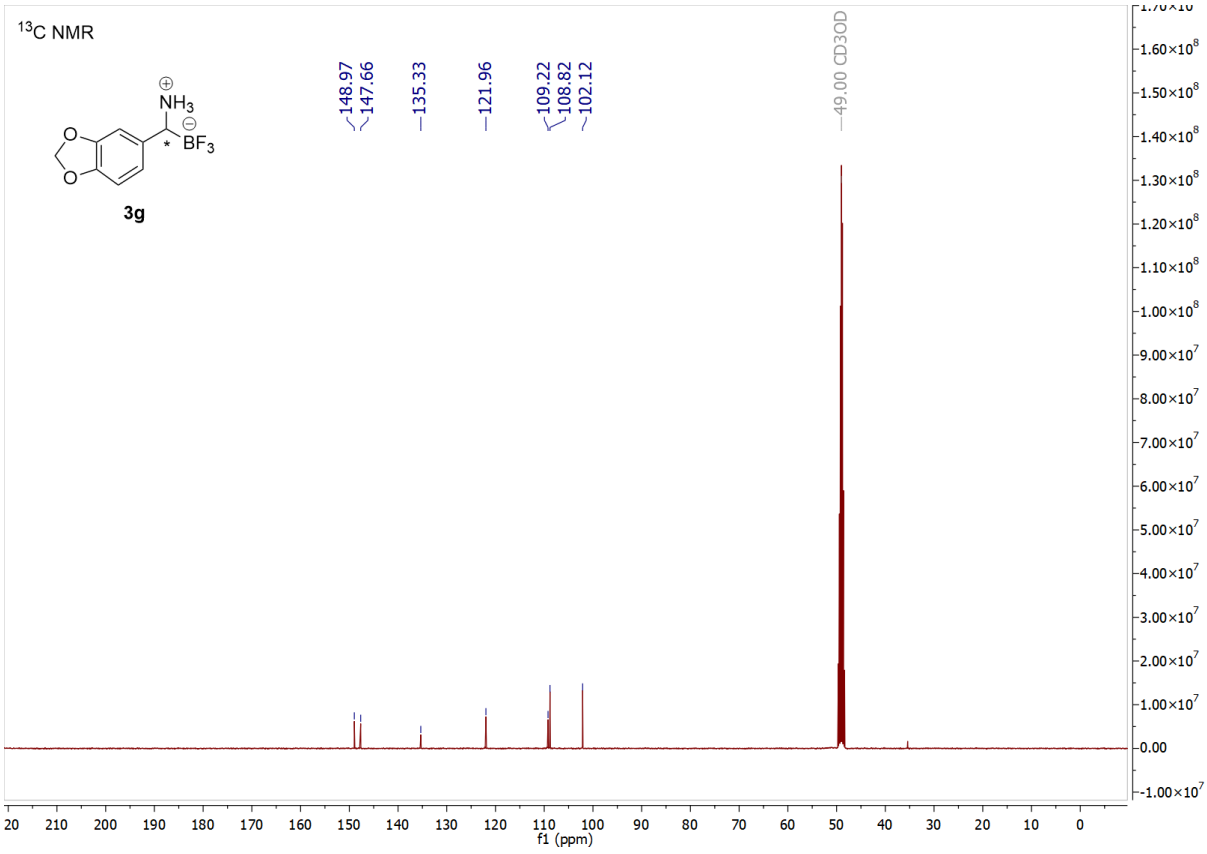
^{1}H-NMR (400 MHz, CD_3OD) of **3g**:



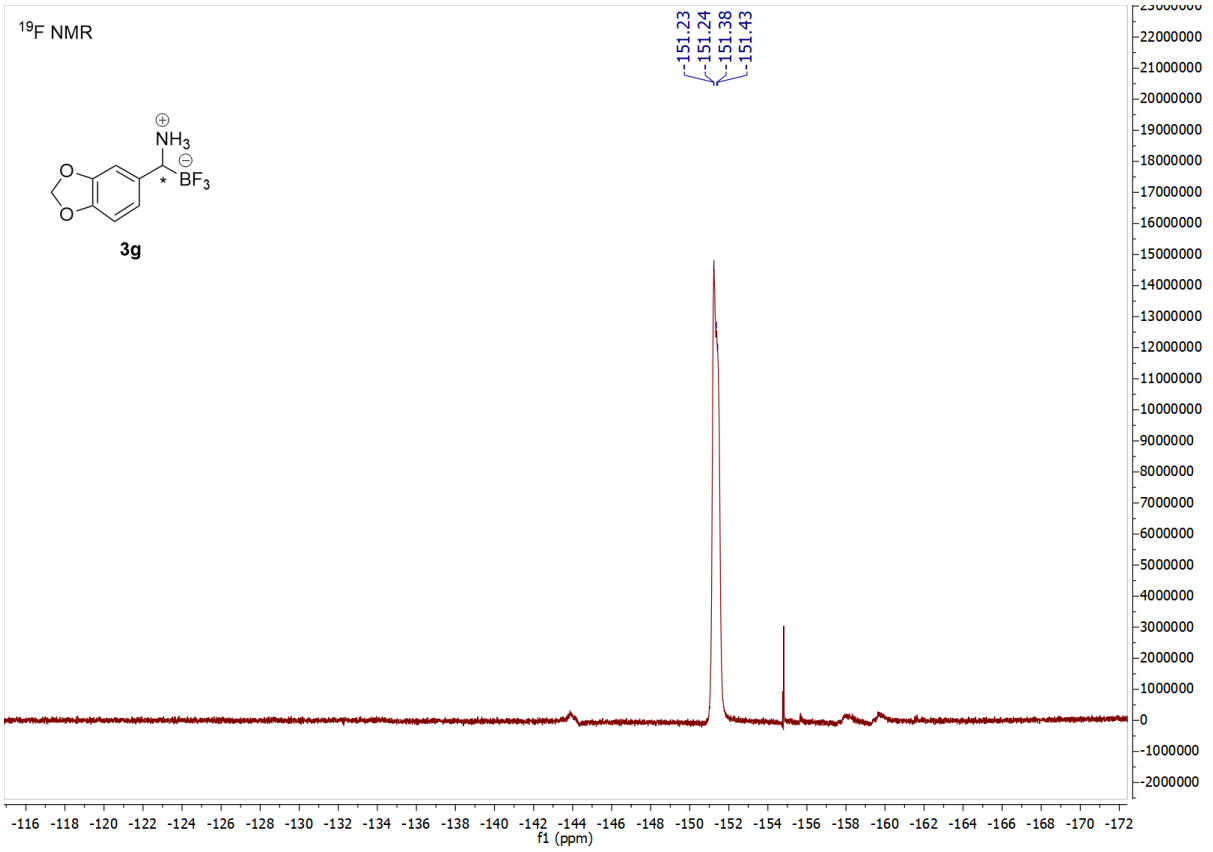
^{11}B-NMR (128 MHz, CD_3OD) of **3g**:



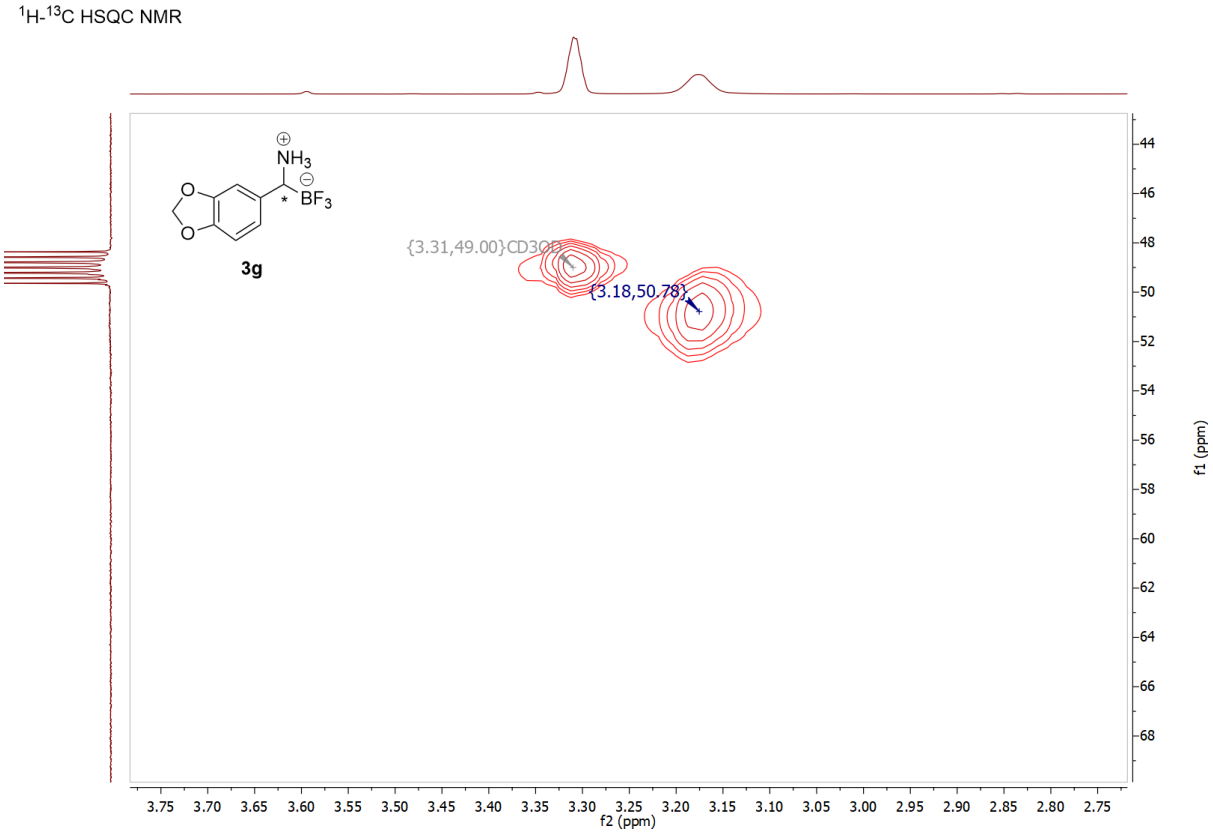
^{13}C-NMR (101 MHz, CD_3OD) of **3g**:



^{19}F-NMR (376 MHz, CD_3OD) of **3g**:

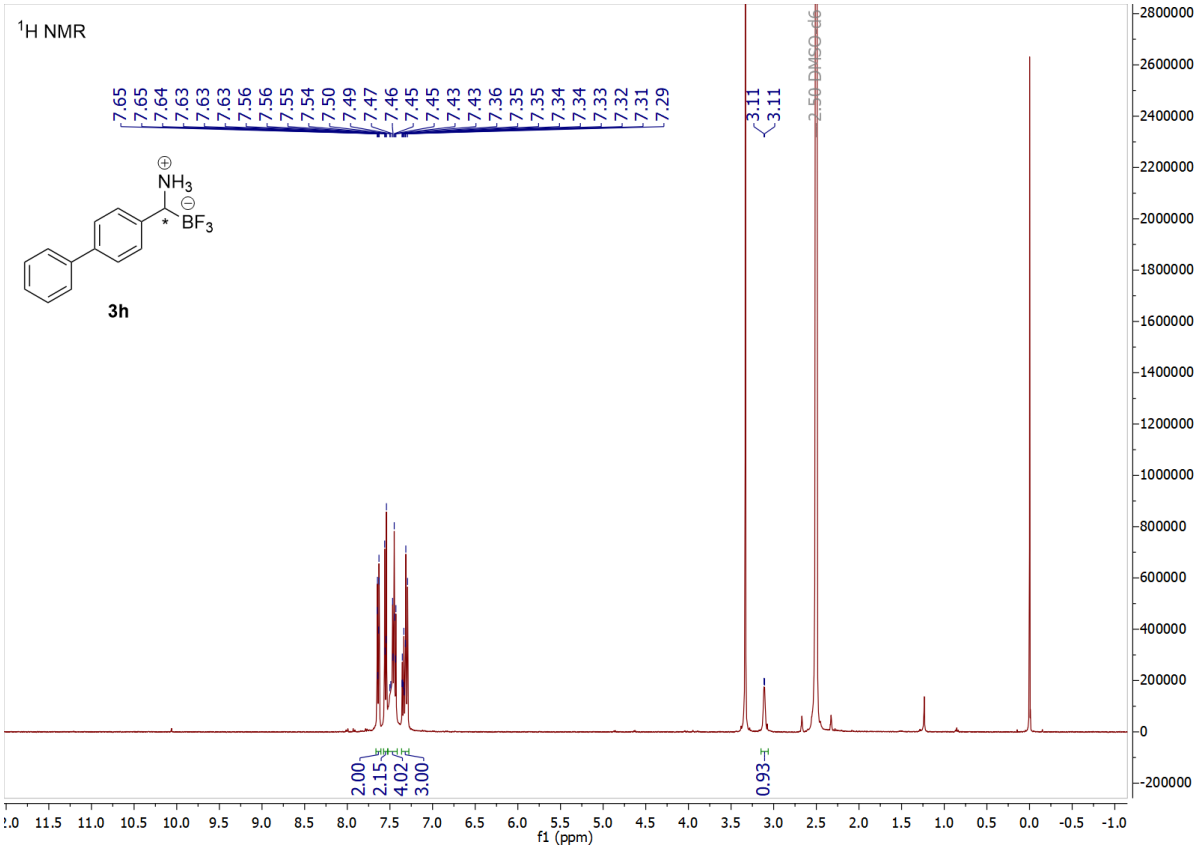


^{1}H-^{13}C-HSQC NMR (CD_3OD) of **3g**:

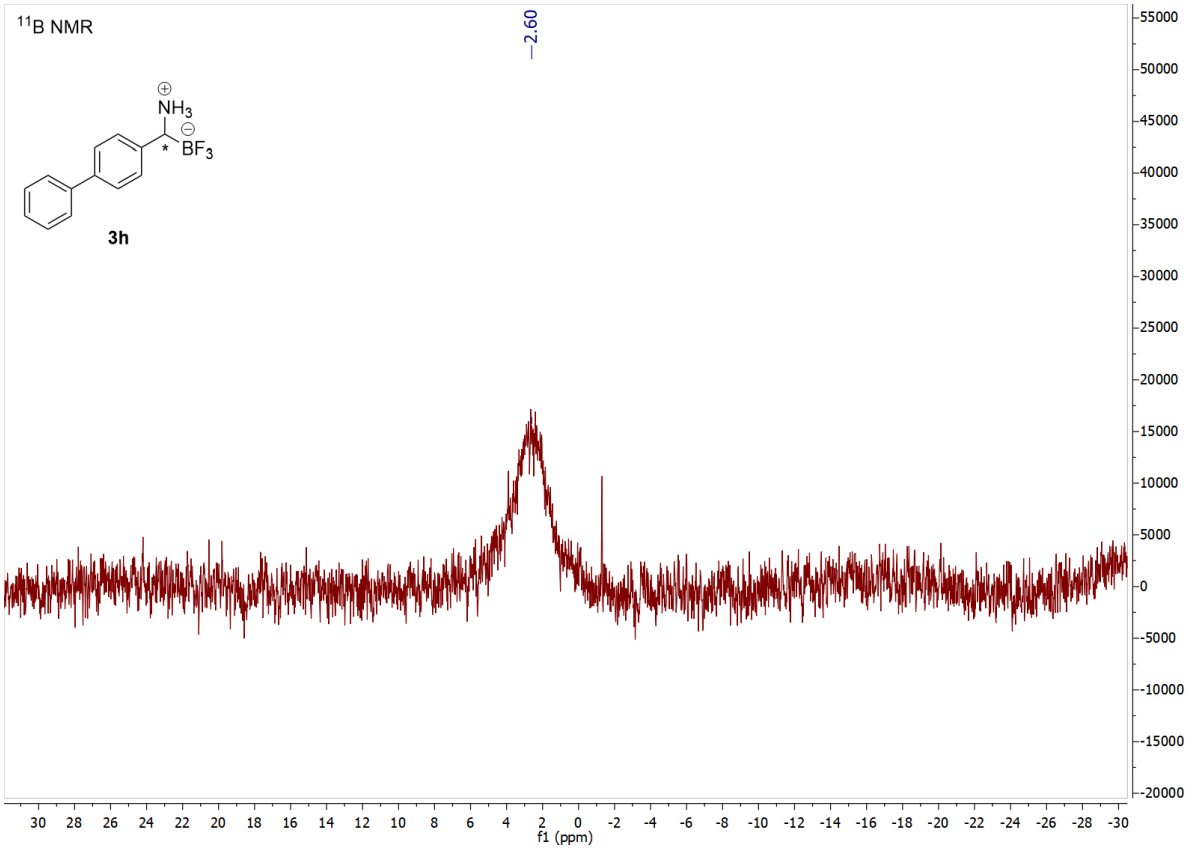


([1,1'-Biphenyl]-4-yl(ammonio)methyl)trifluoroborate (3h)

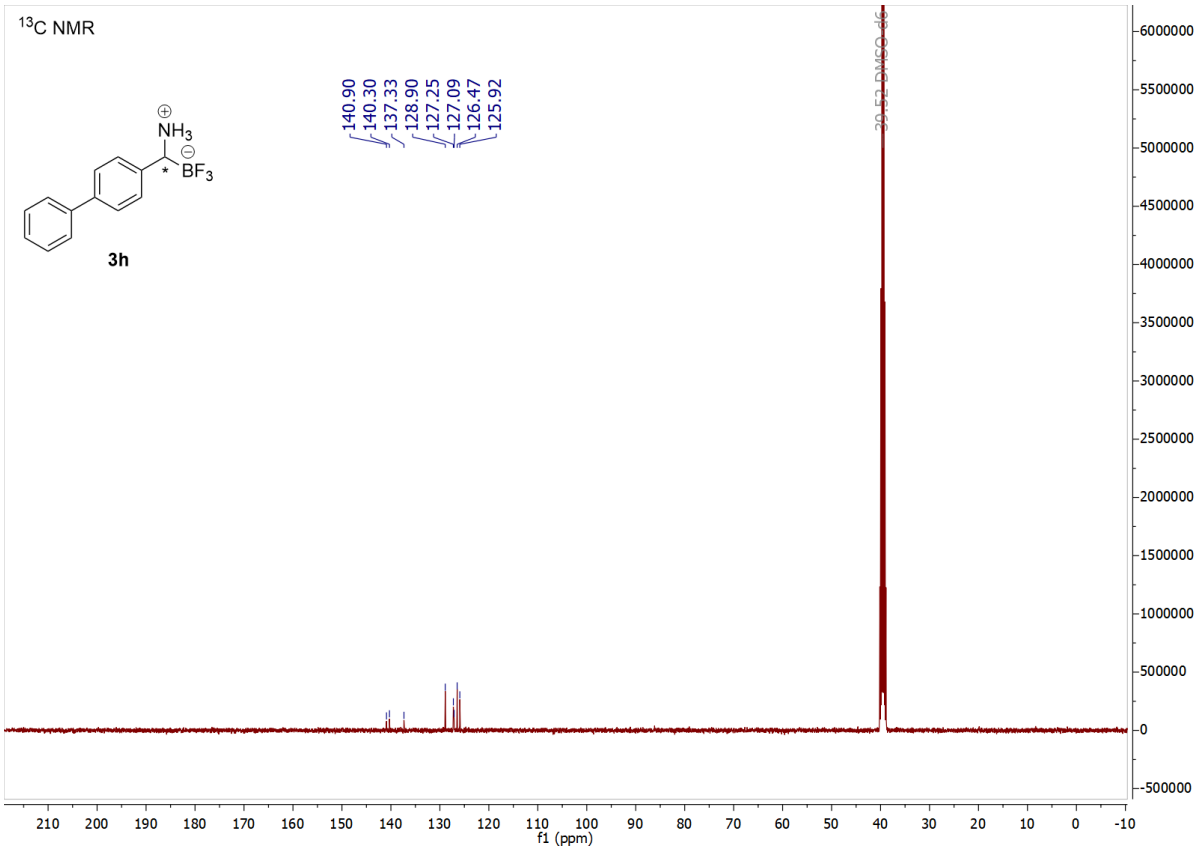
^{1}H-NMR (400 MHz, DMSO-d_6) of **3h**:



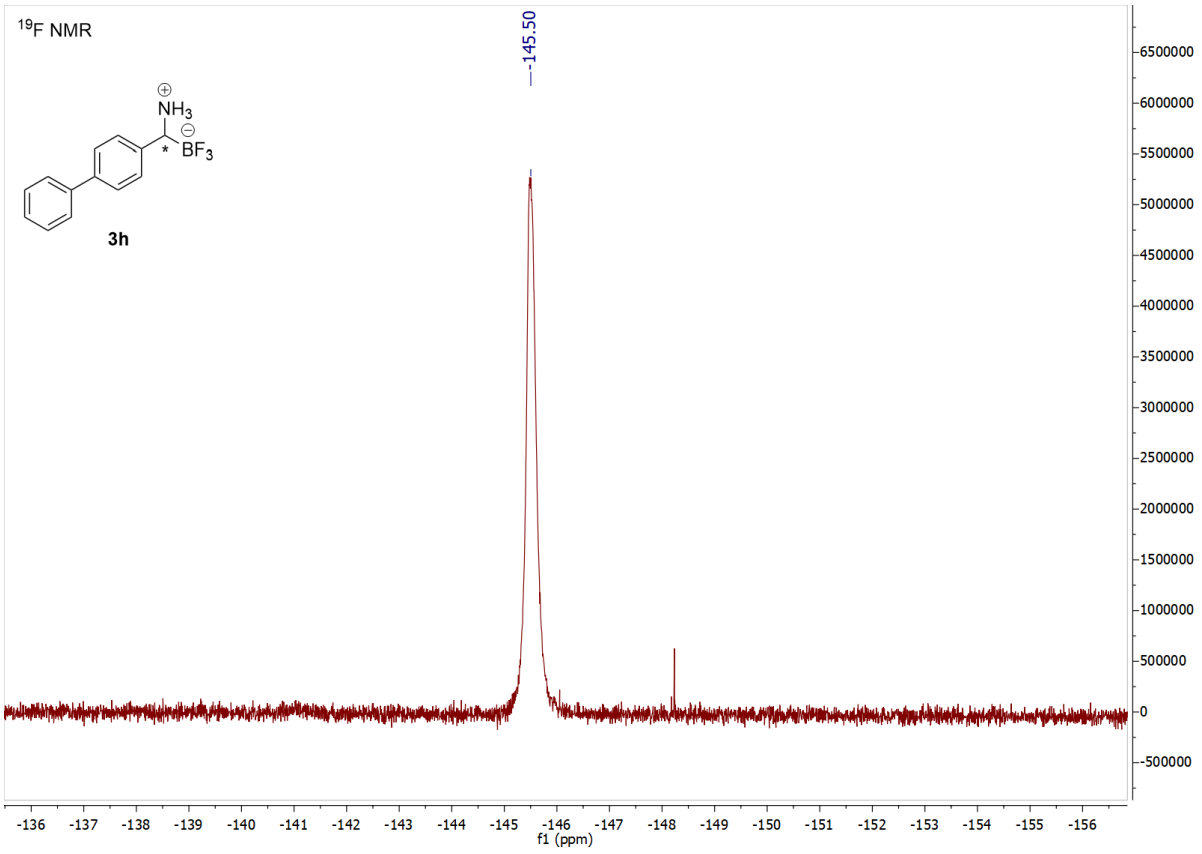
^{11}B-NMR (128 MHz, DMSO-d_6) of **3h**:



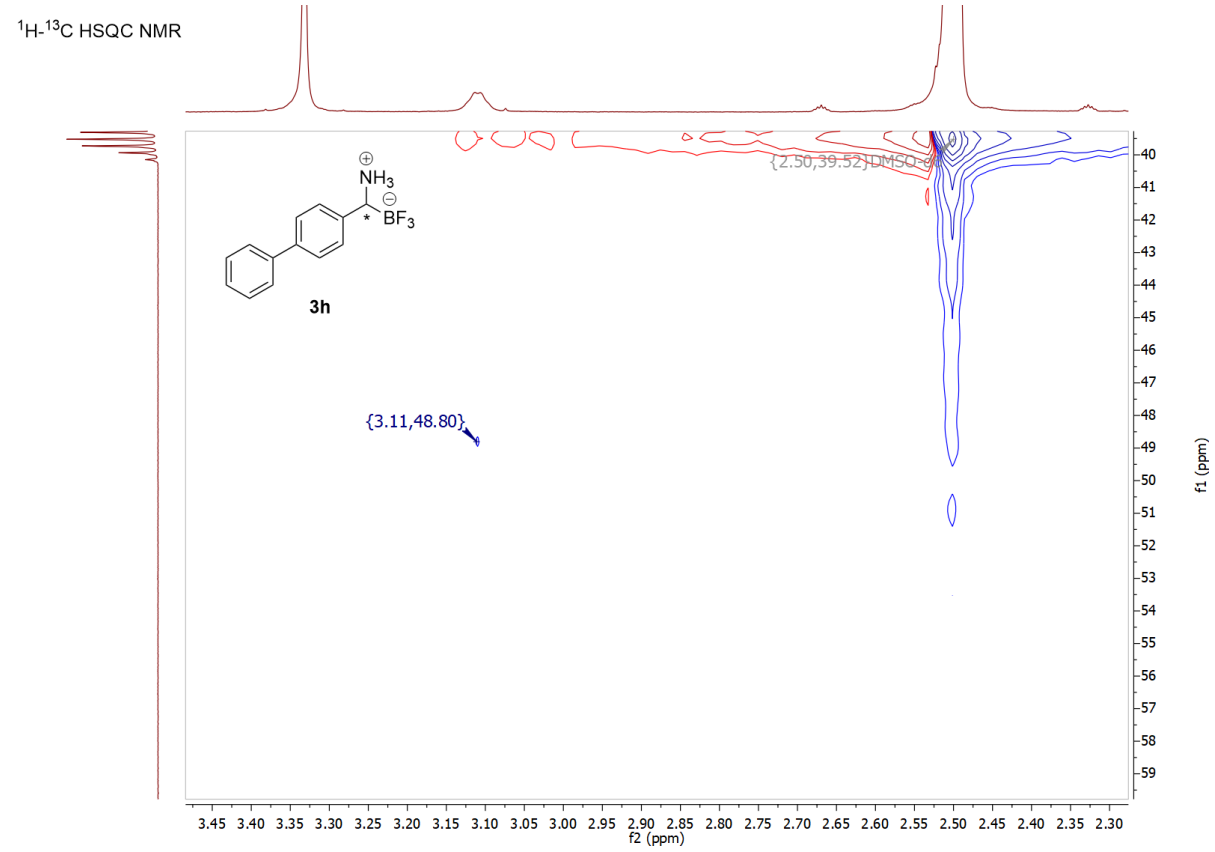
^{13}C-NMR (101 MHz, DMSO-d_6) of **3h**:



^{19}F-NMR (376 MHz, DMSO-d_6) of **3h**:

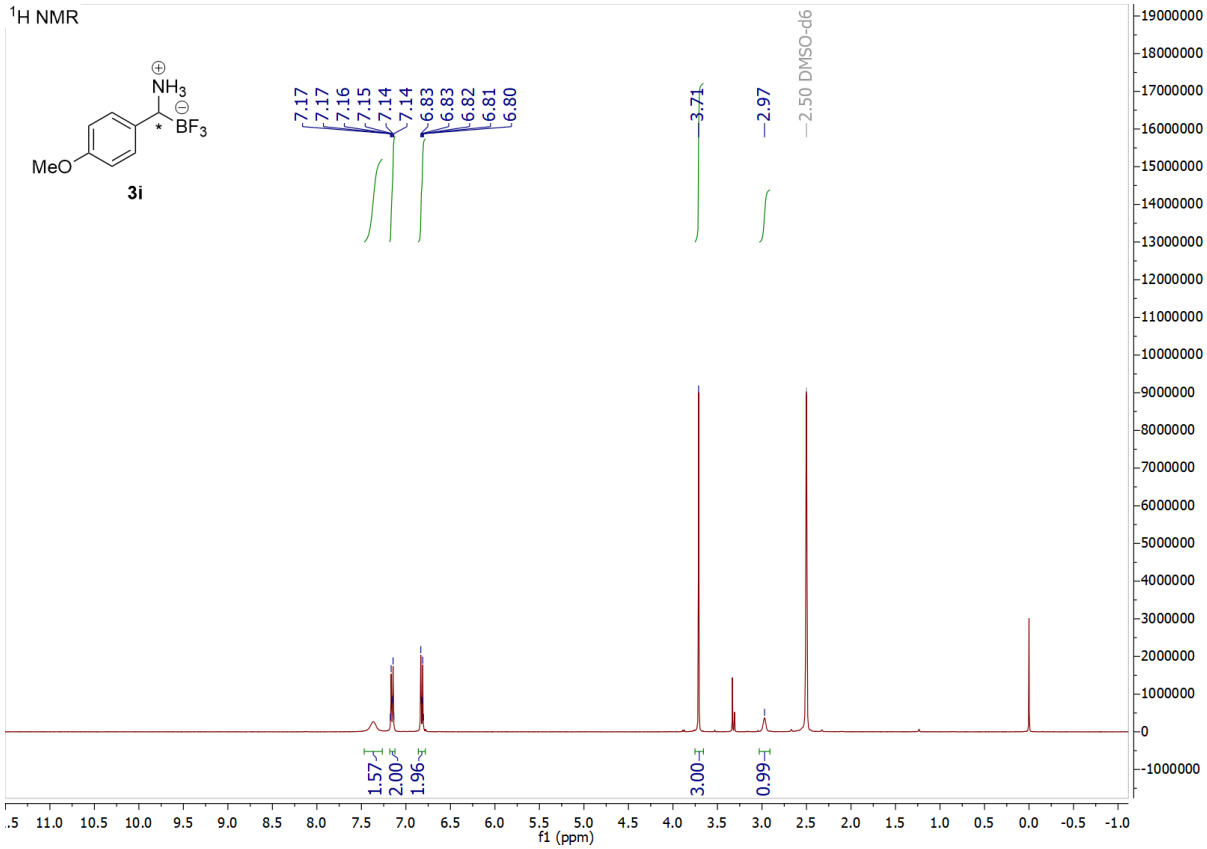


^{1}H-^{13}C-HSQC NMR (DMSO-d_6) of **3h**:

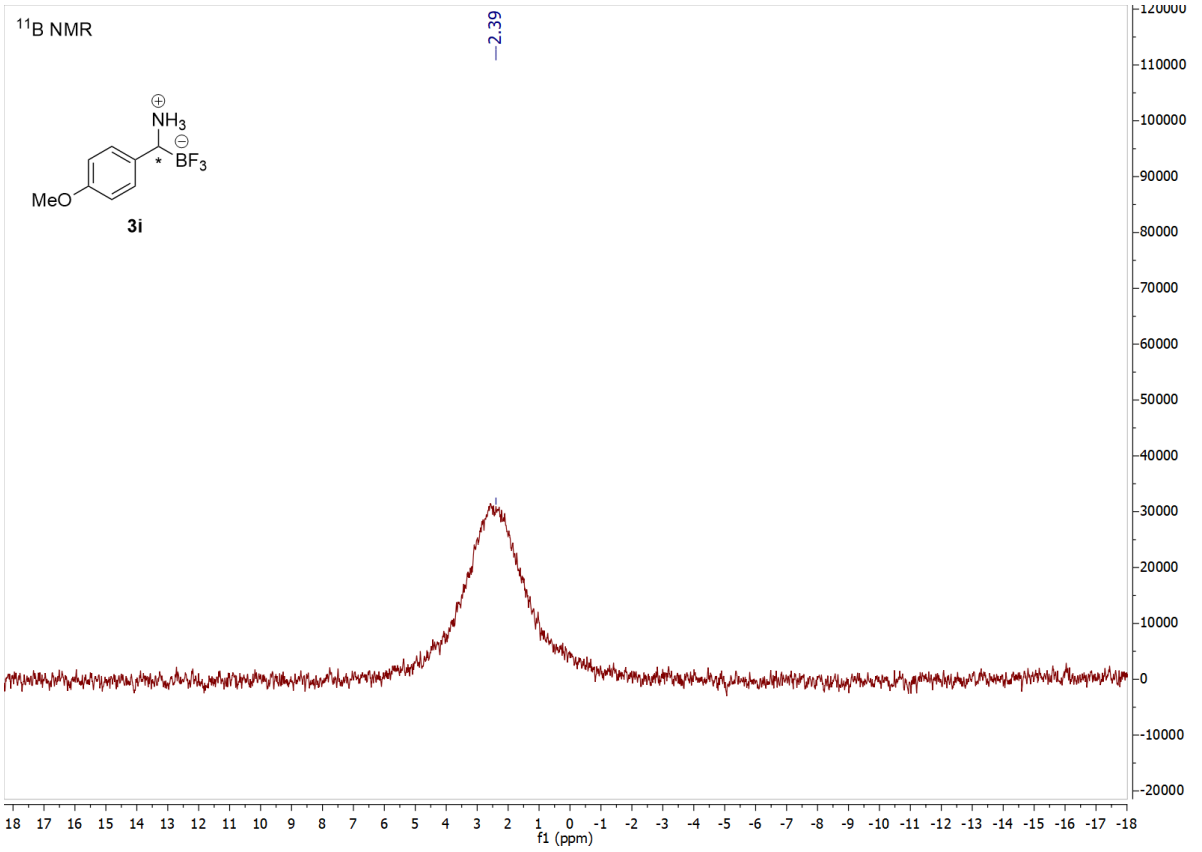


(Ammonio(4-methoxyphenyl)methyl)trifluoroborate (3i)

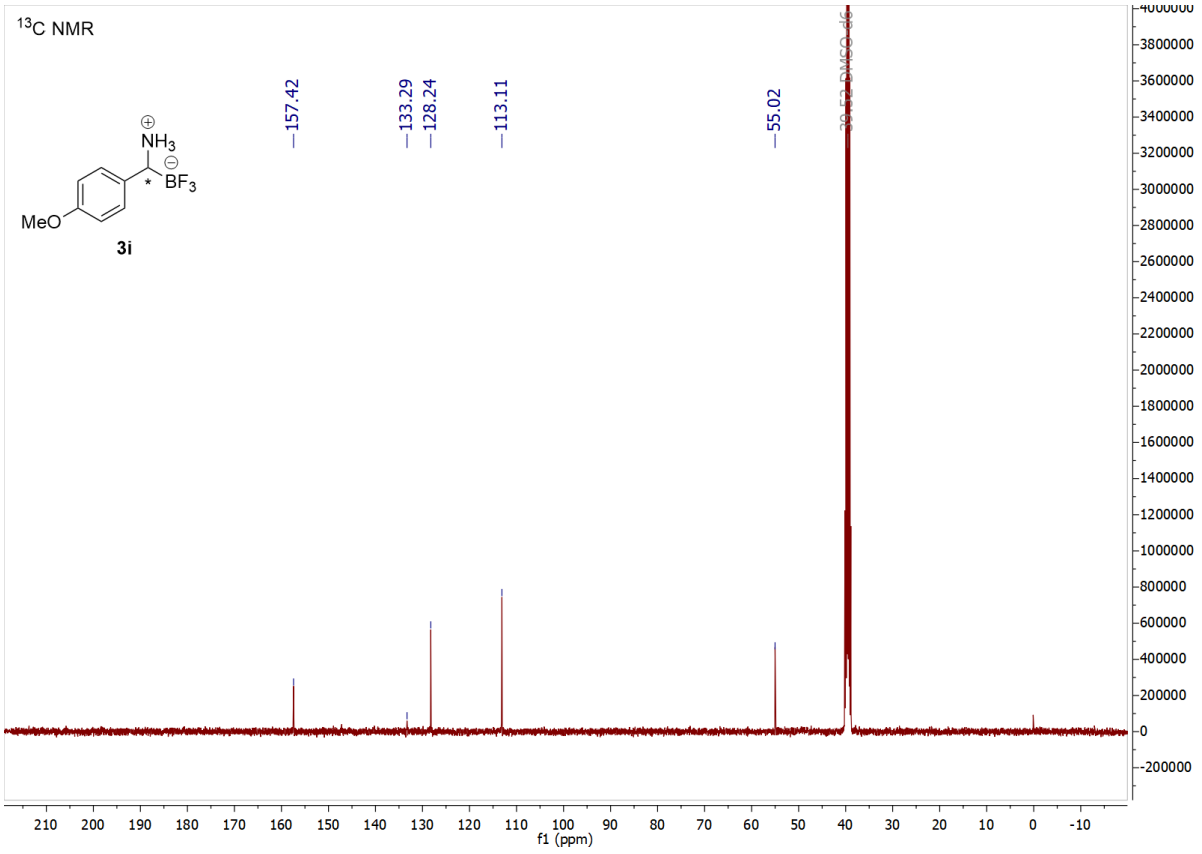
^{1}H-NMR (400 MHz, DMSO-d_6) of **3i**:



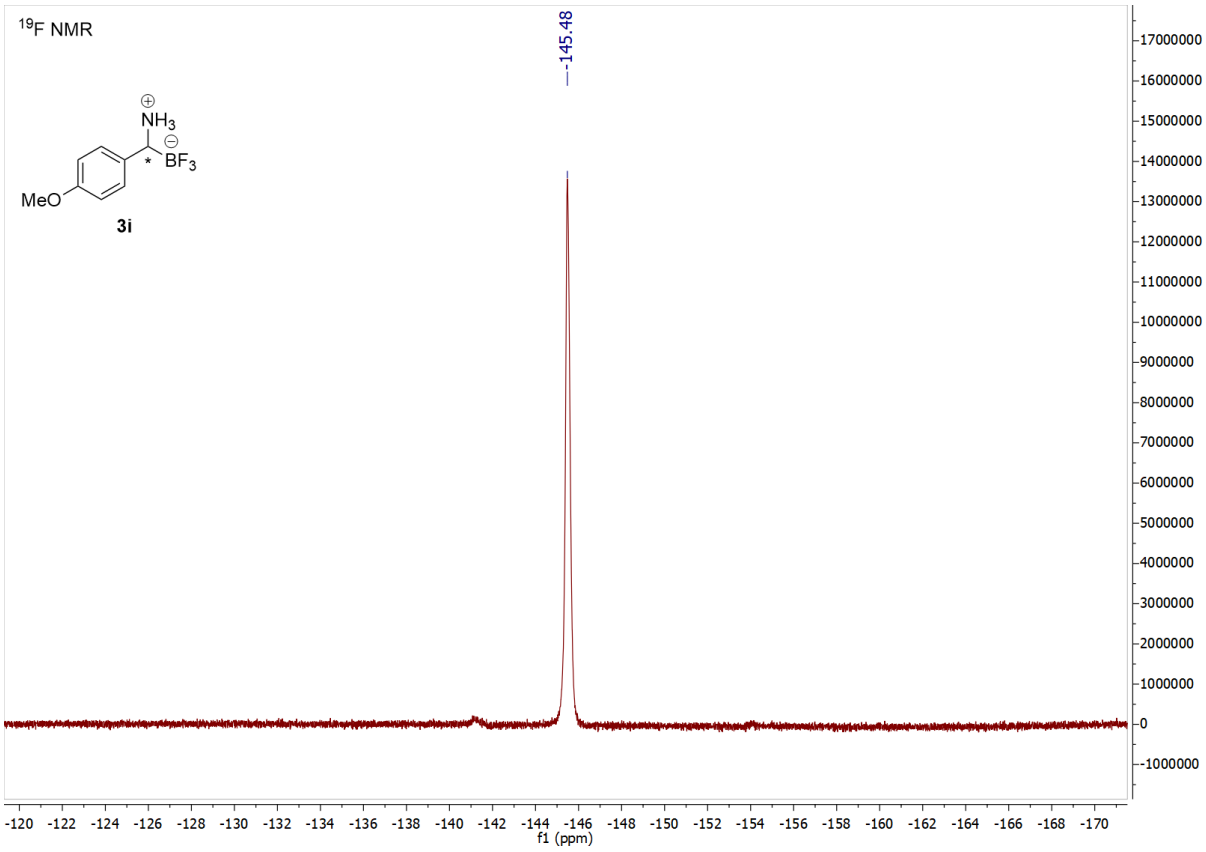
^{11}B-NMR (128 MHz, DMSO-d_6) of **3i**:



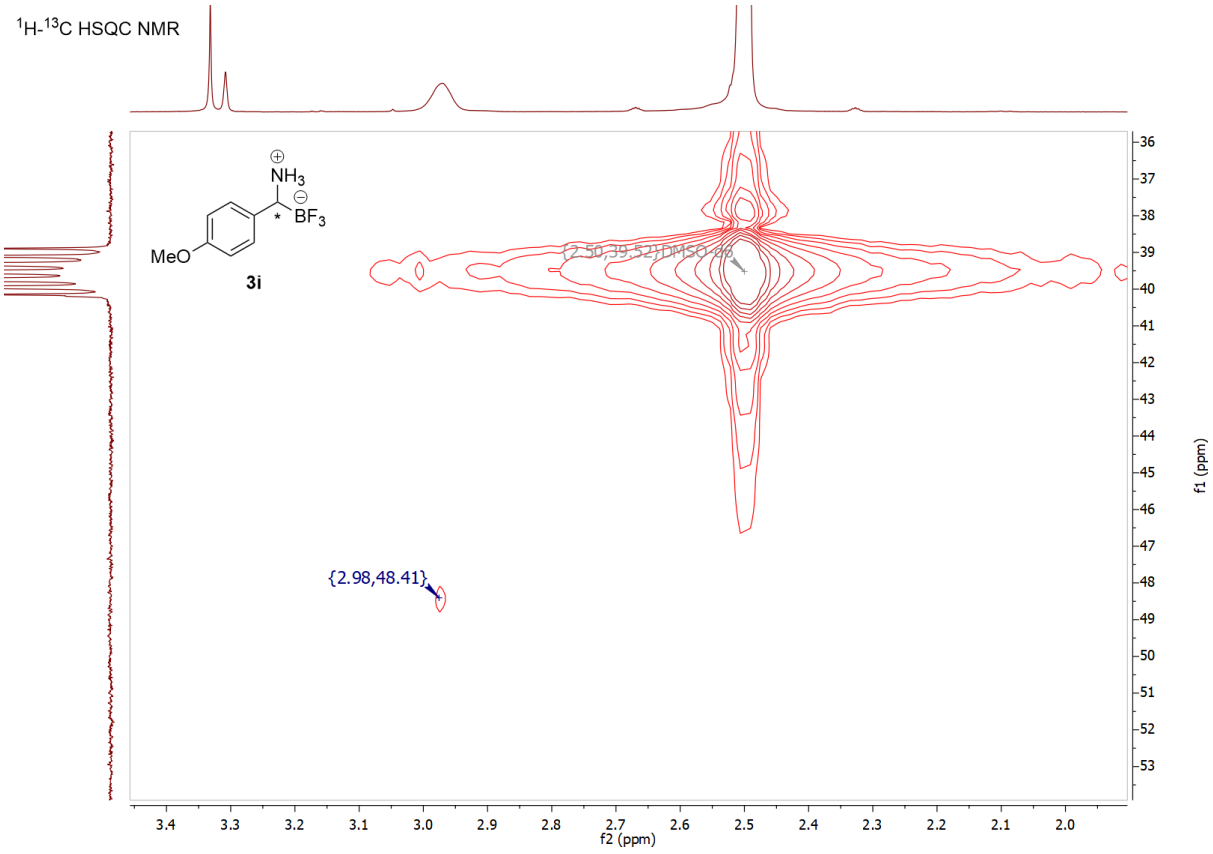
^{13}C-NMR (101 MHz, DMSO-d_6) of **3i**:



^{19}F-NMR (376 MHz, DMSO-d_6) of **3i**:

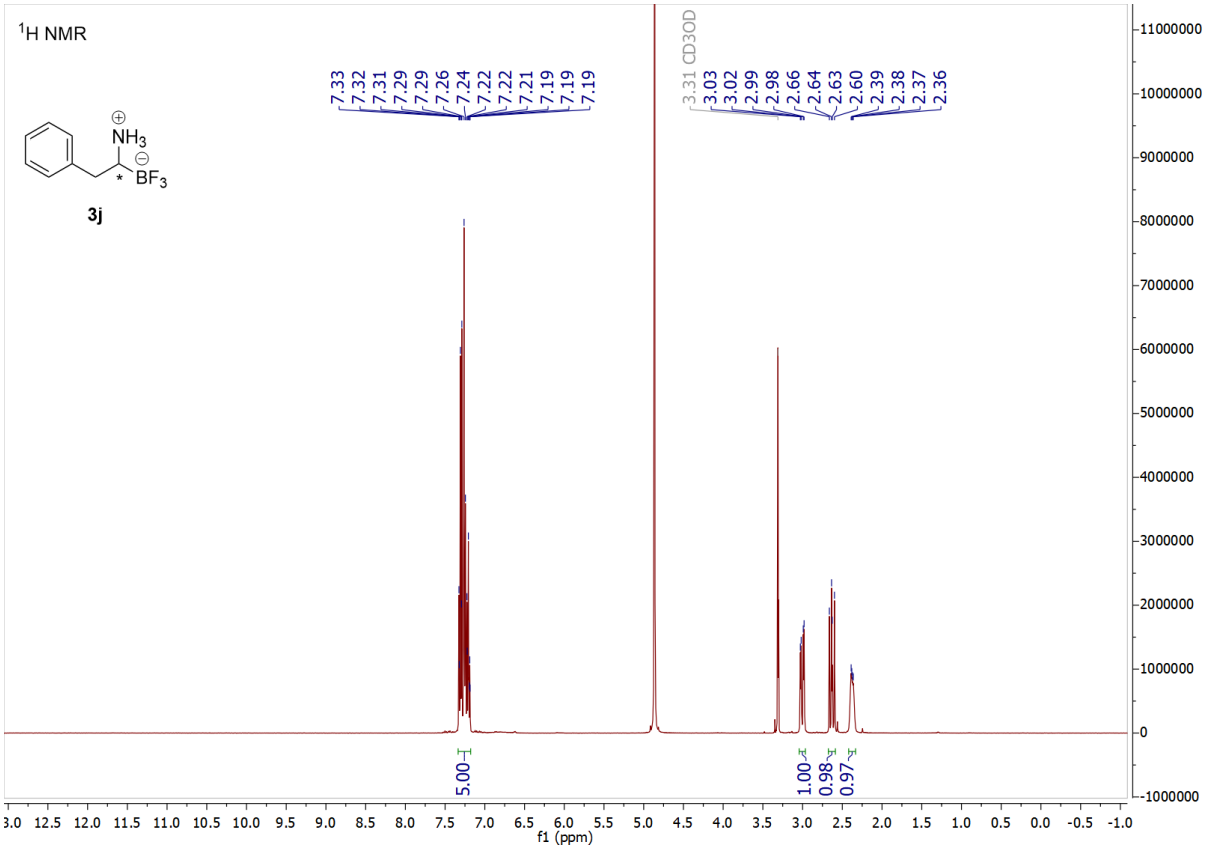


^{1}H-^{13}C-HSQC NMR (DMSO-d_6) of **3i**:

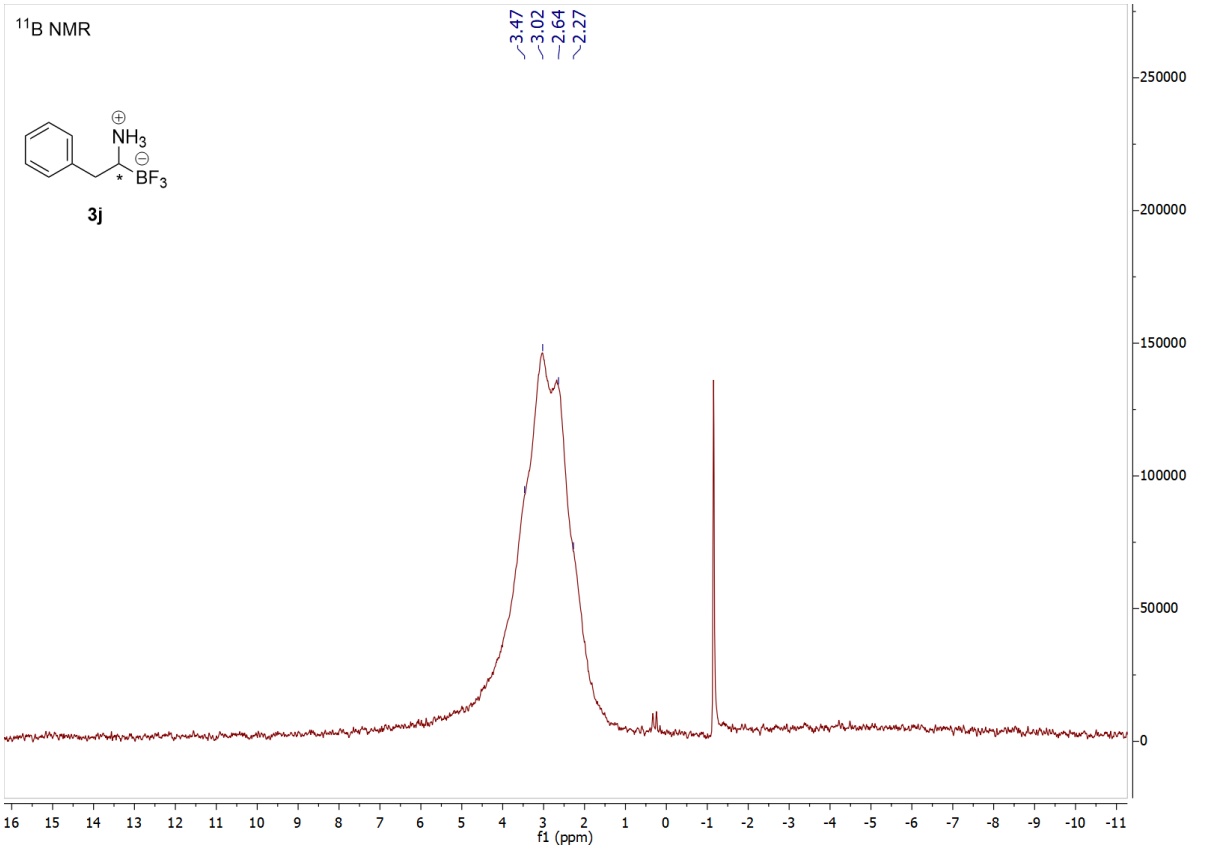


(1-Ammonio-2-phenylethyl)trifluoroborate (3j)

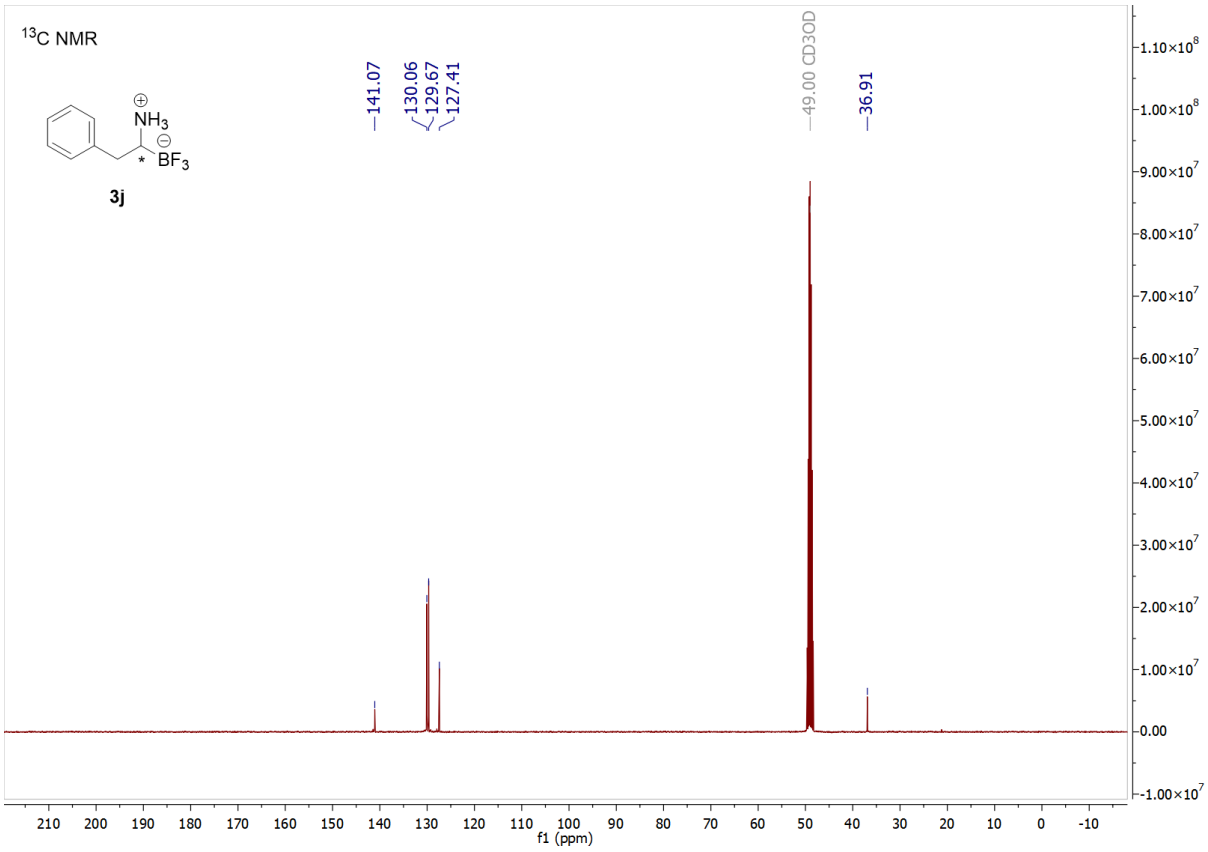
^{1}H-NMR (400 MHz, CD_3OD) of **3j**:



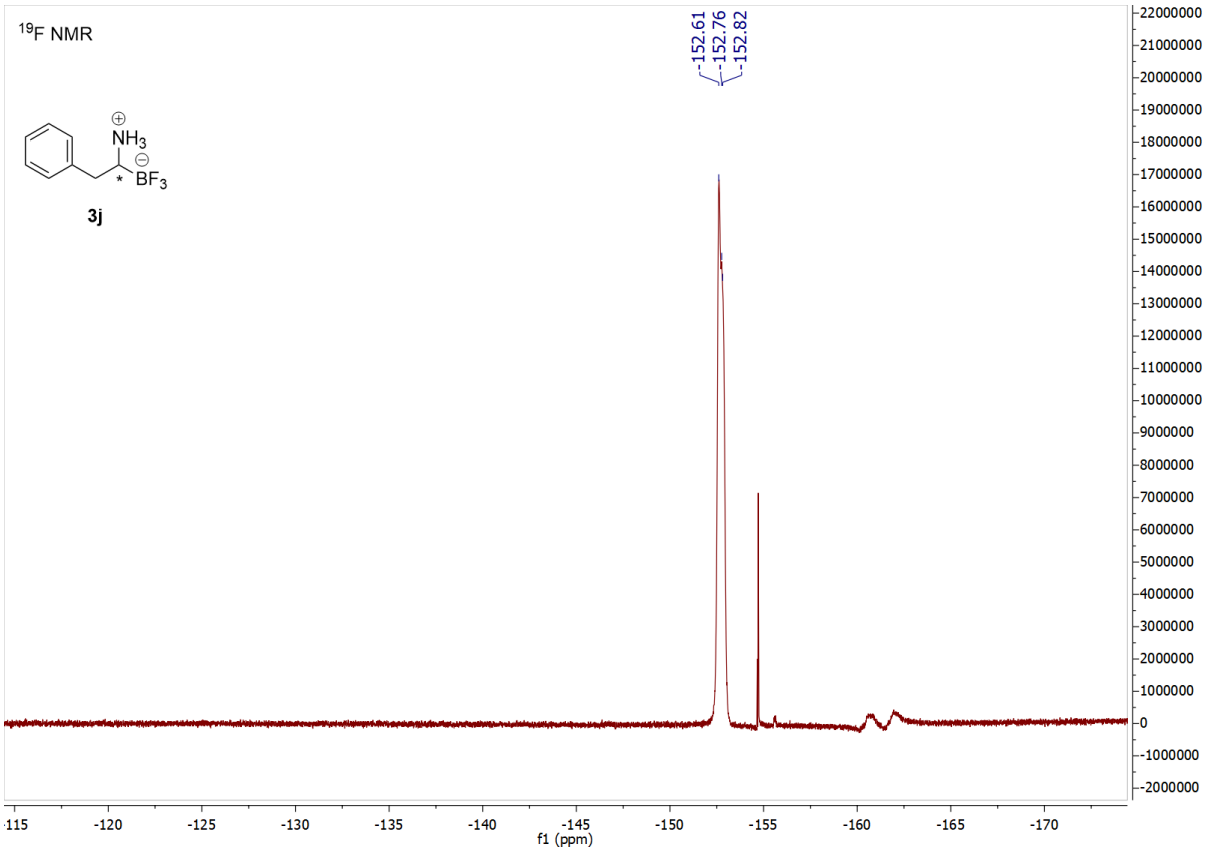
^{11}B-NMR (128 MHz, CD_3OD) of **3j**:



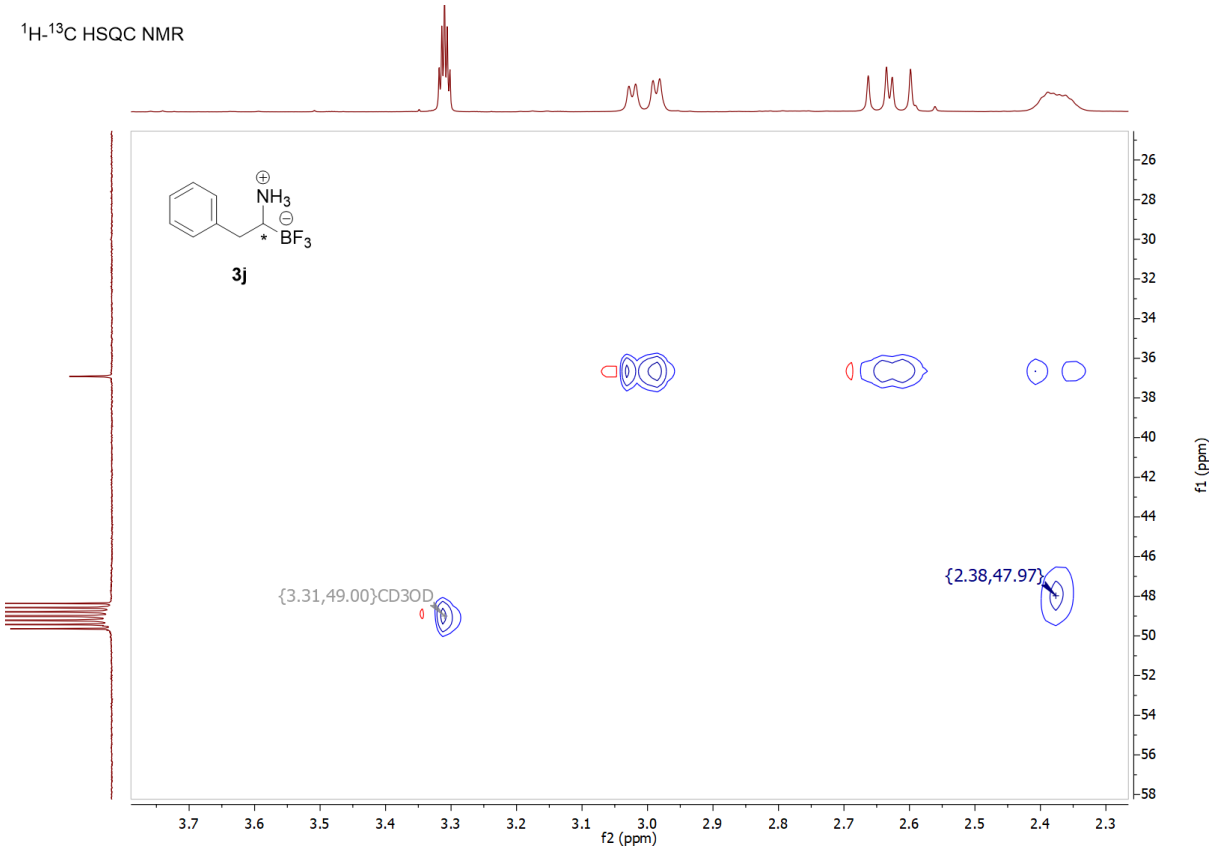
^{13}C-NMR (101 MHz, CD_3OD) of **3j**:



^{19}F-NMR (376 MHz, CD_3OD) of **3j**:

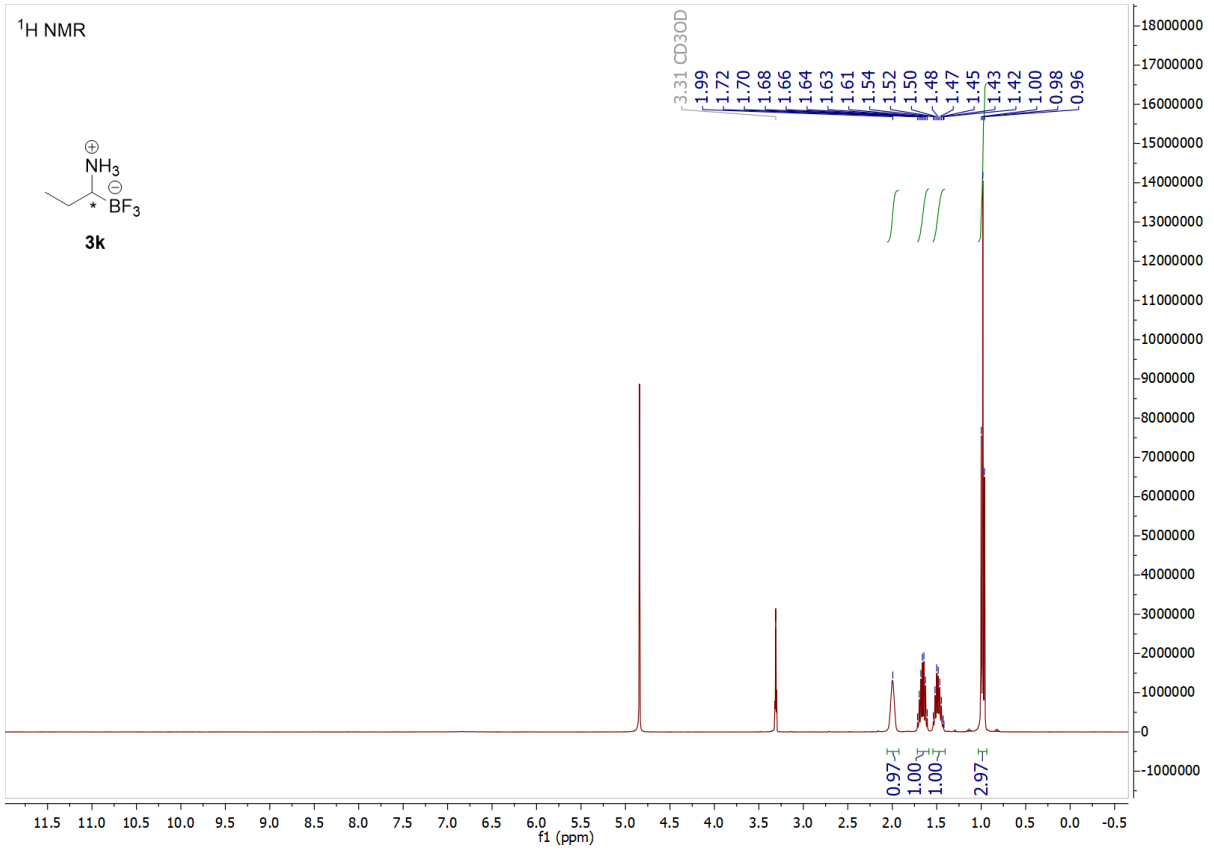


^{1}H-^{13}C-HSQC NMR (CD_3OD) of **3j**:

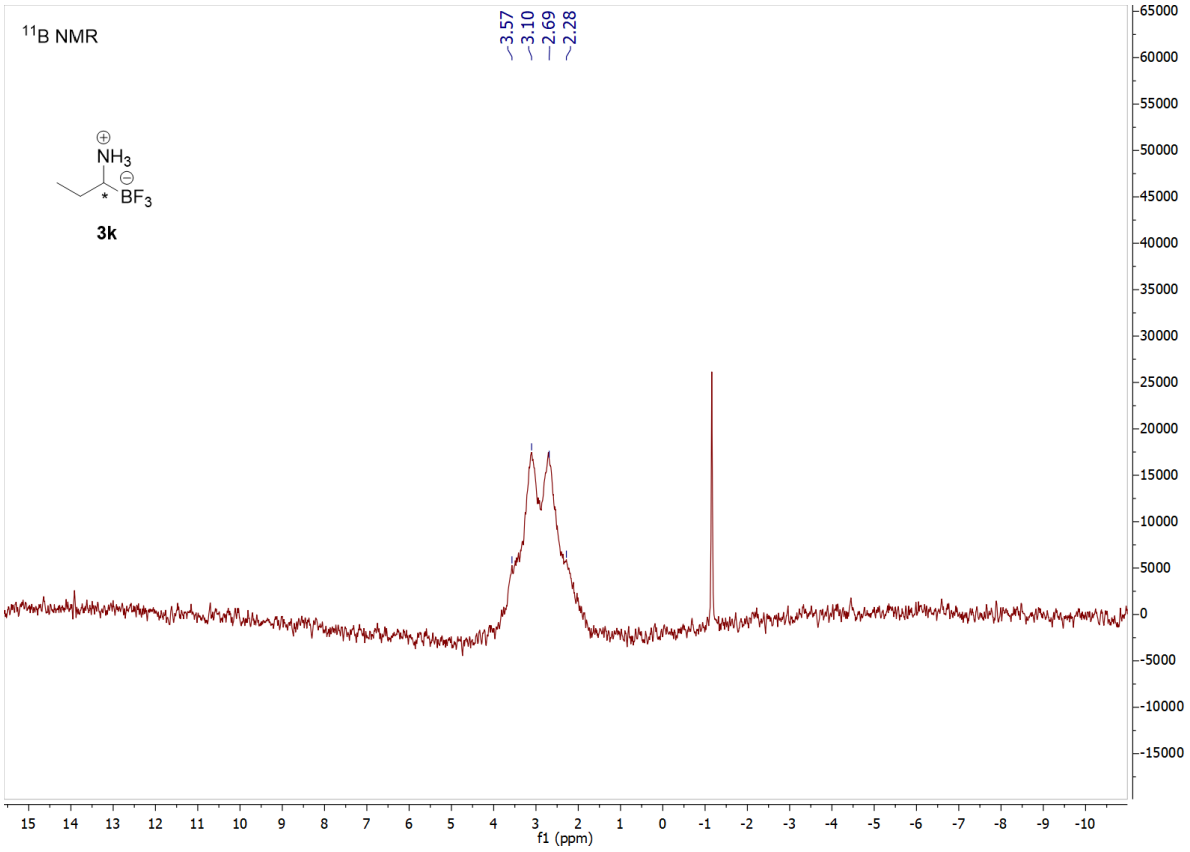


(1-Ammoniopropyl)trifluoroborate (3k)

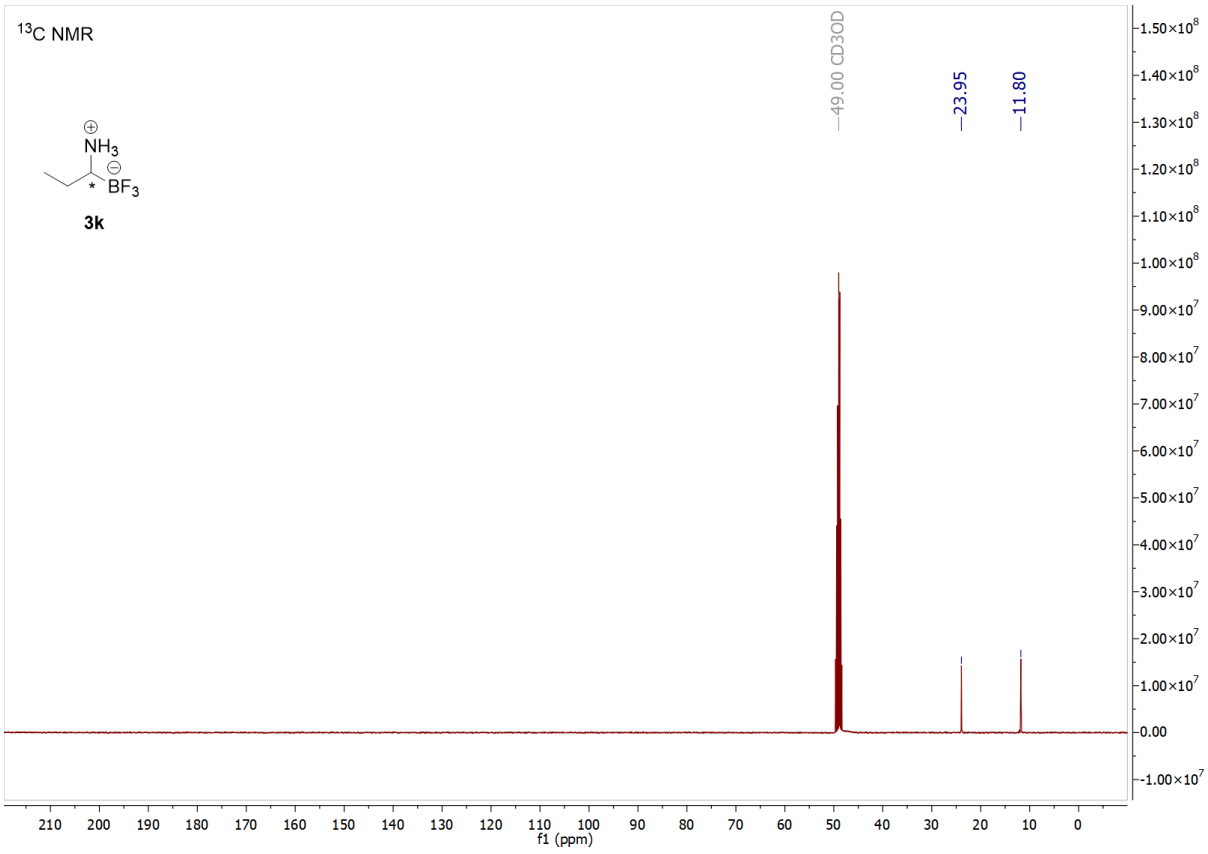
^{1}H-NMR (400 MHz, CD_3OD) of **3k**:



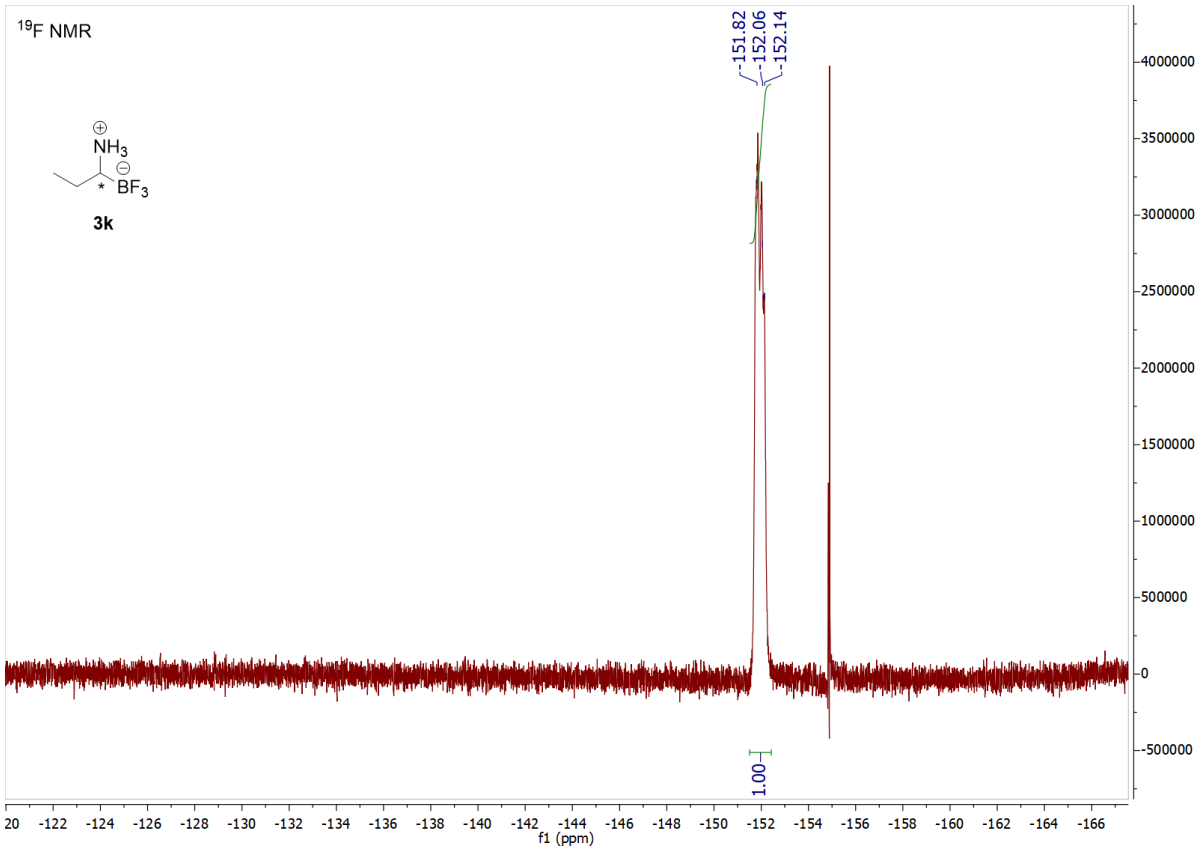
^{11}B-NMR (128 MHz, CD_3OD) of **3k**:



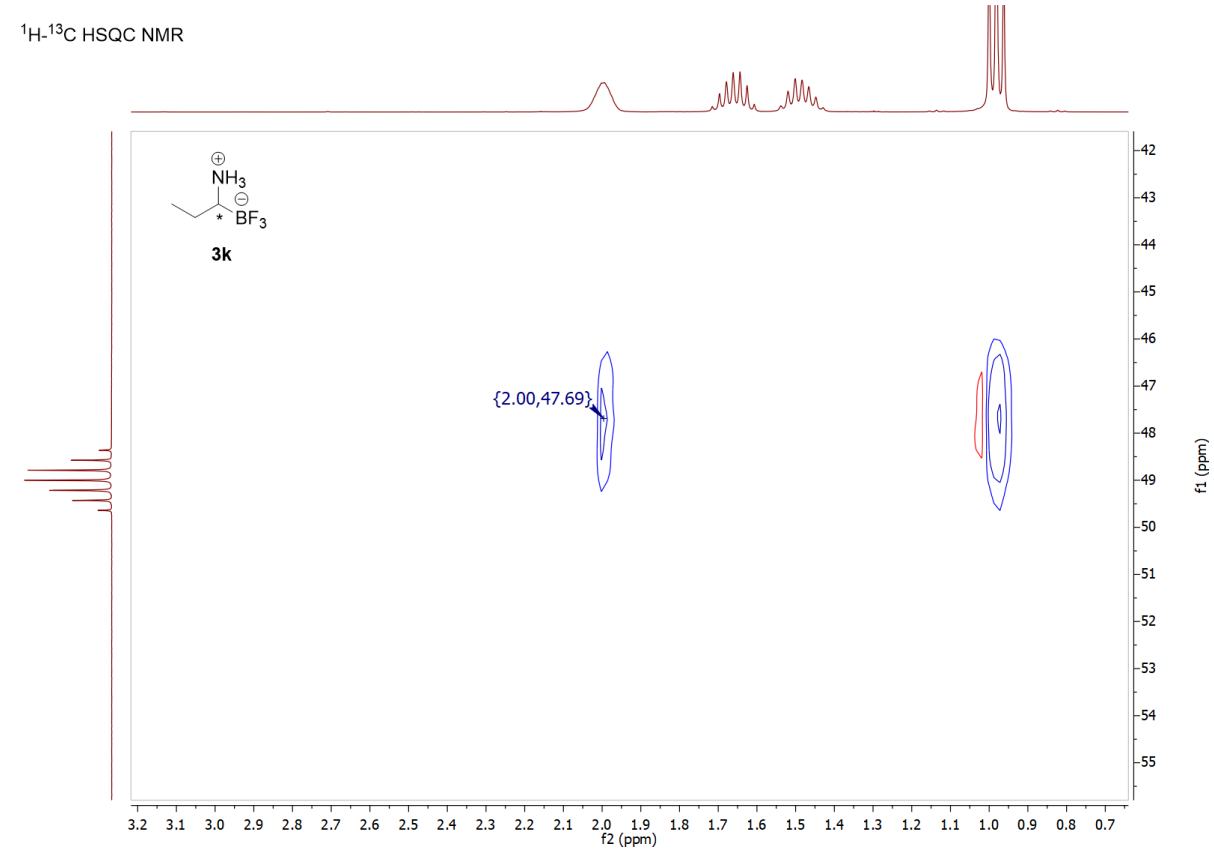
^{13}C-NMR (101 MHz, CD_3OD) of **3k**:



^{19}F-NMR (376 MHz, CD_3OD) of **3k**:

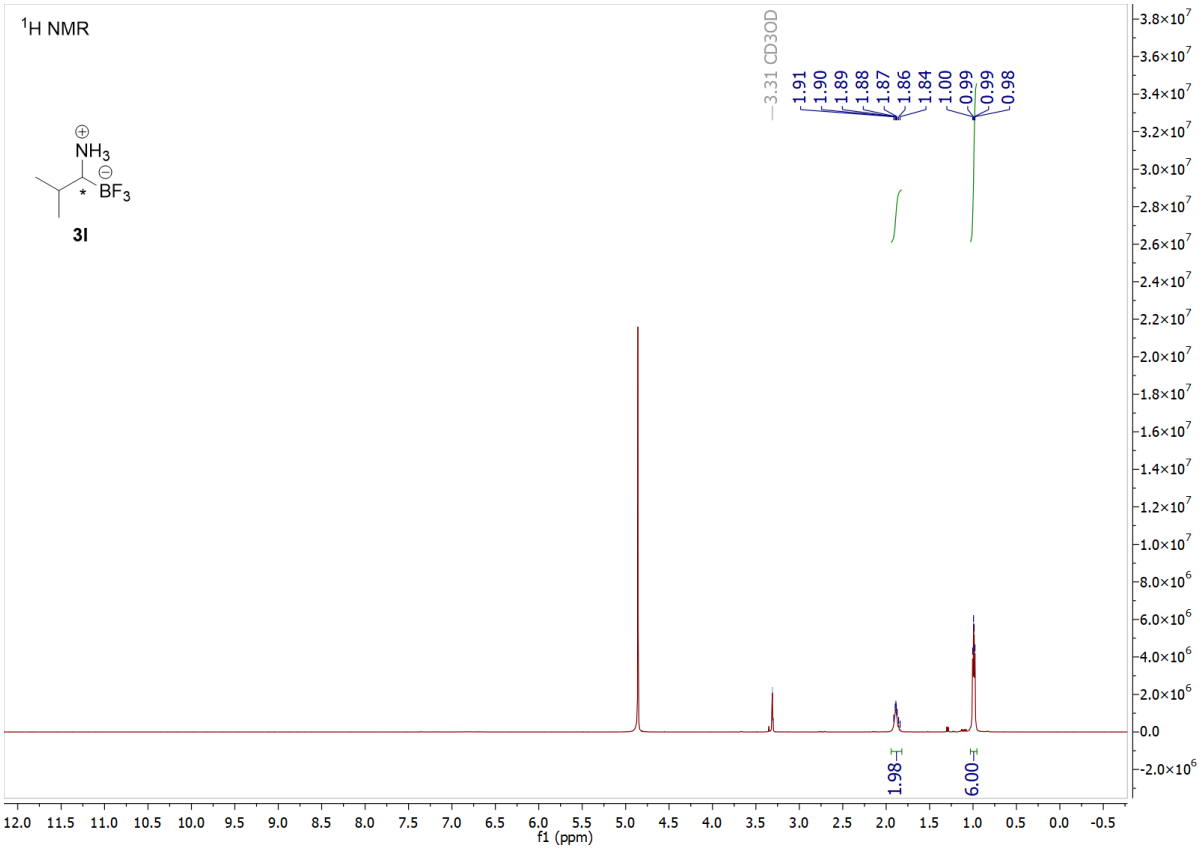


^{1}H-^{13}C-HSQC NMR (CD_3OD) of **3k**:

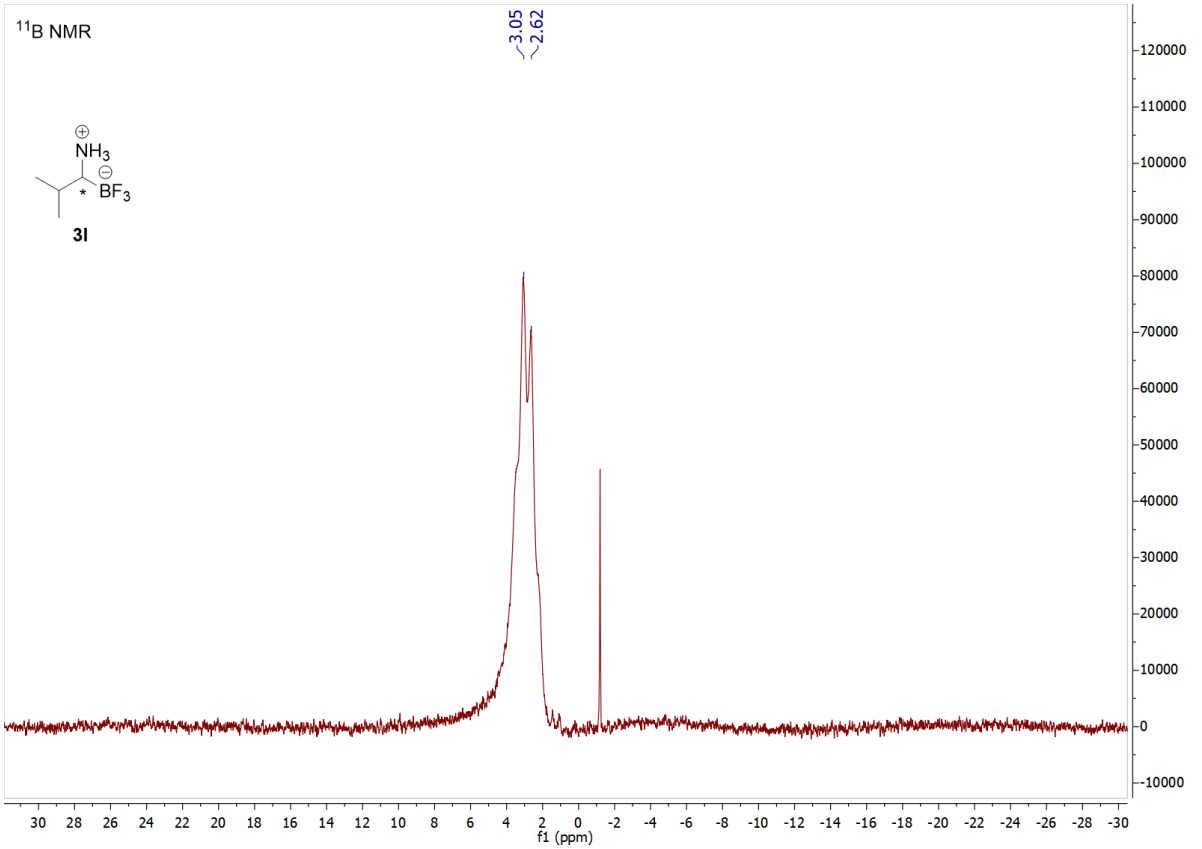


(1-Ammonio-2-methylpropyl)trifluoroborate (3l)

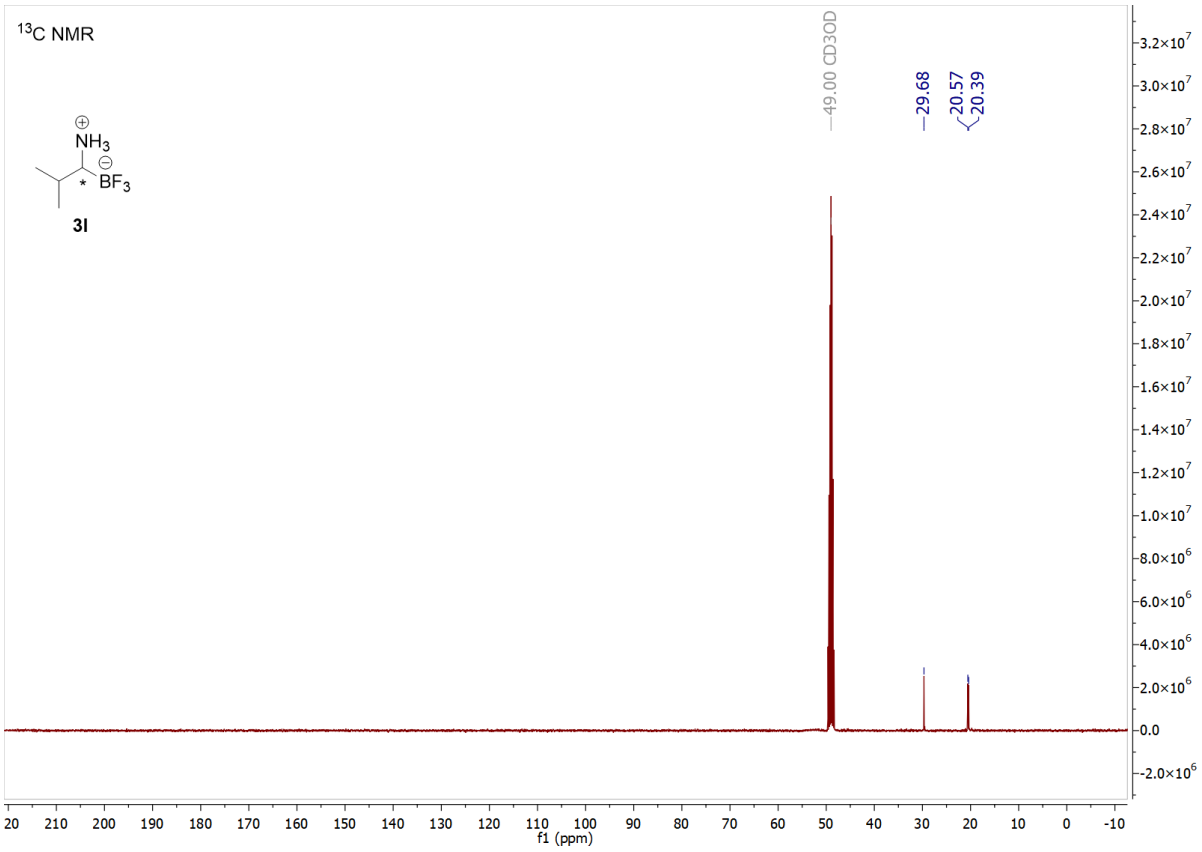
^{1}H-NMR (400 MHz, CD_3OD) of **3l**:



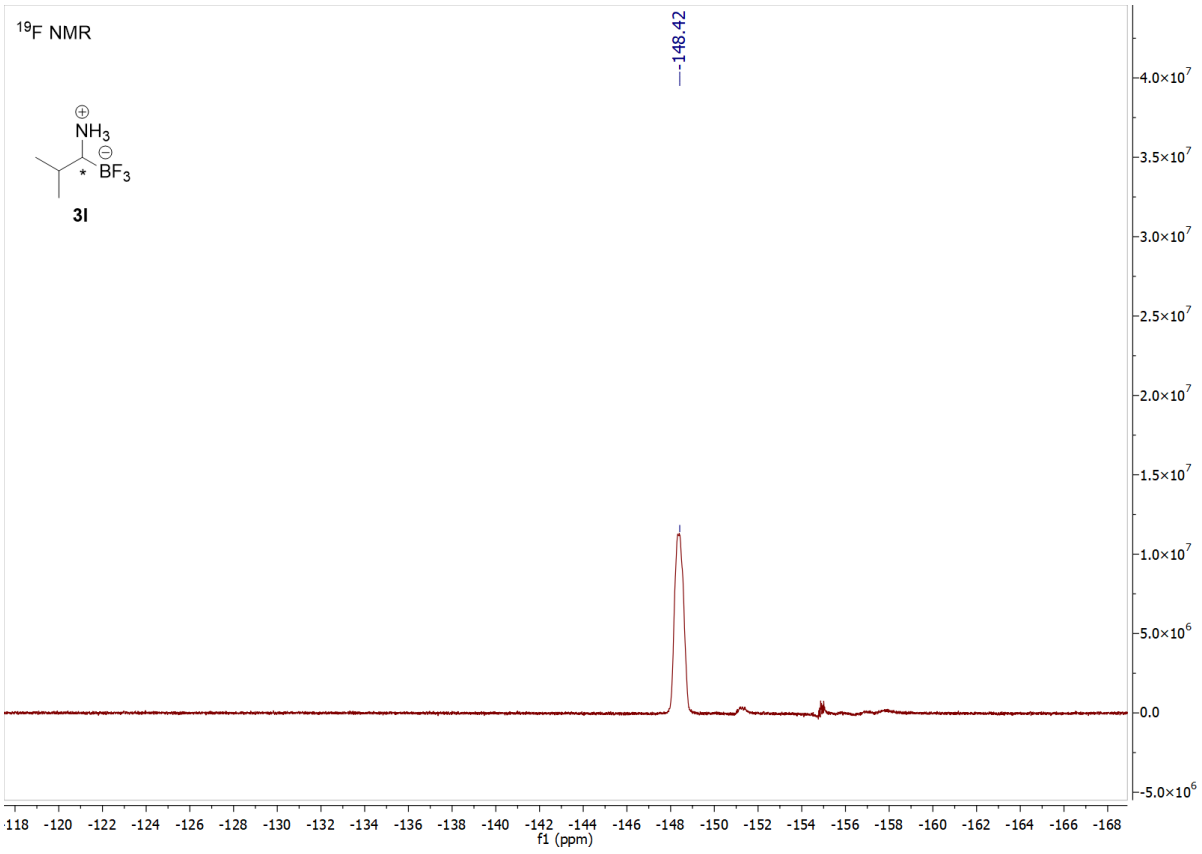
^{11}B-NMR (128 MHz, CD_3OD) of **3l**:



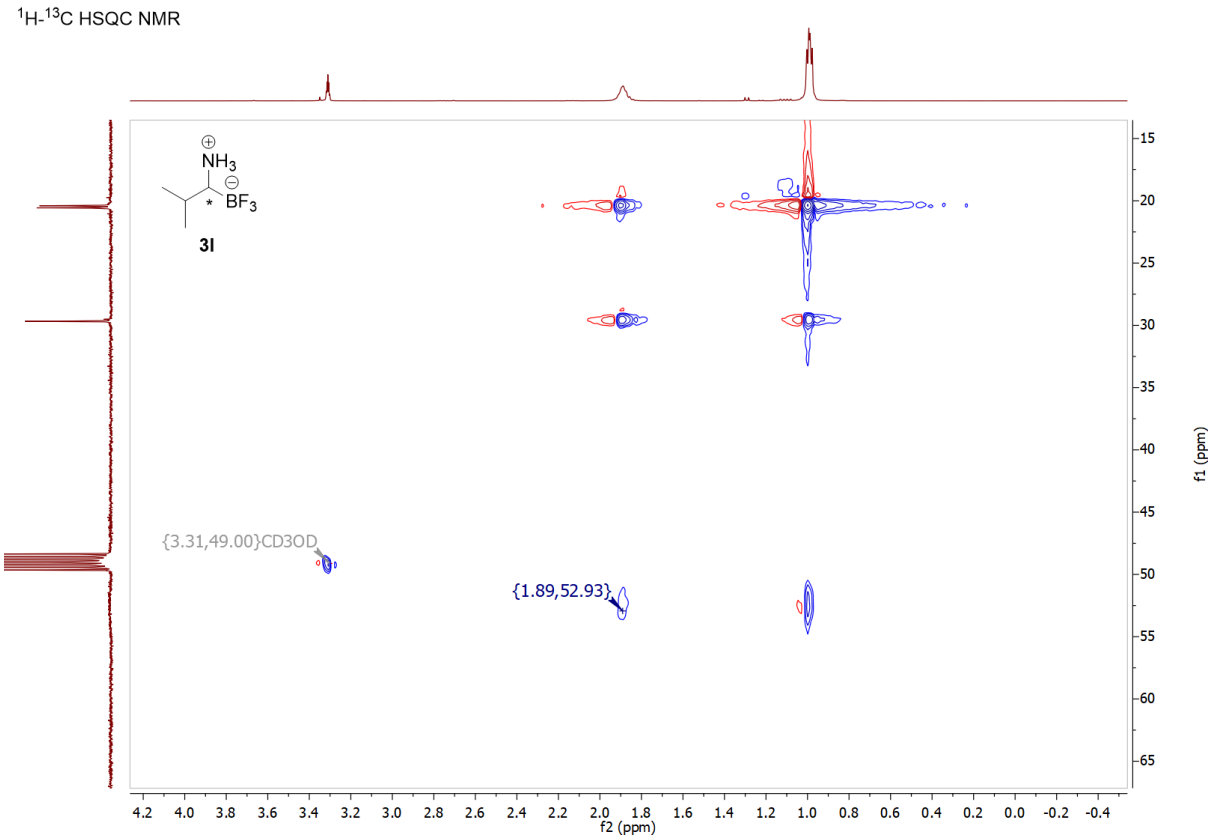
^{13}C-NMR (101 MHz, CD_3OD) of **3l**:



^{19}F-NMR (376 MHz, CD_3OD) of **3l**:

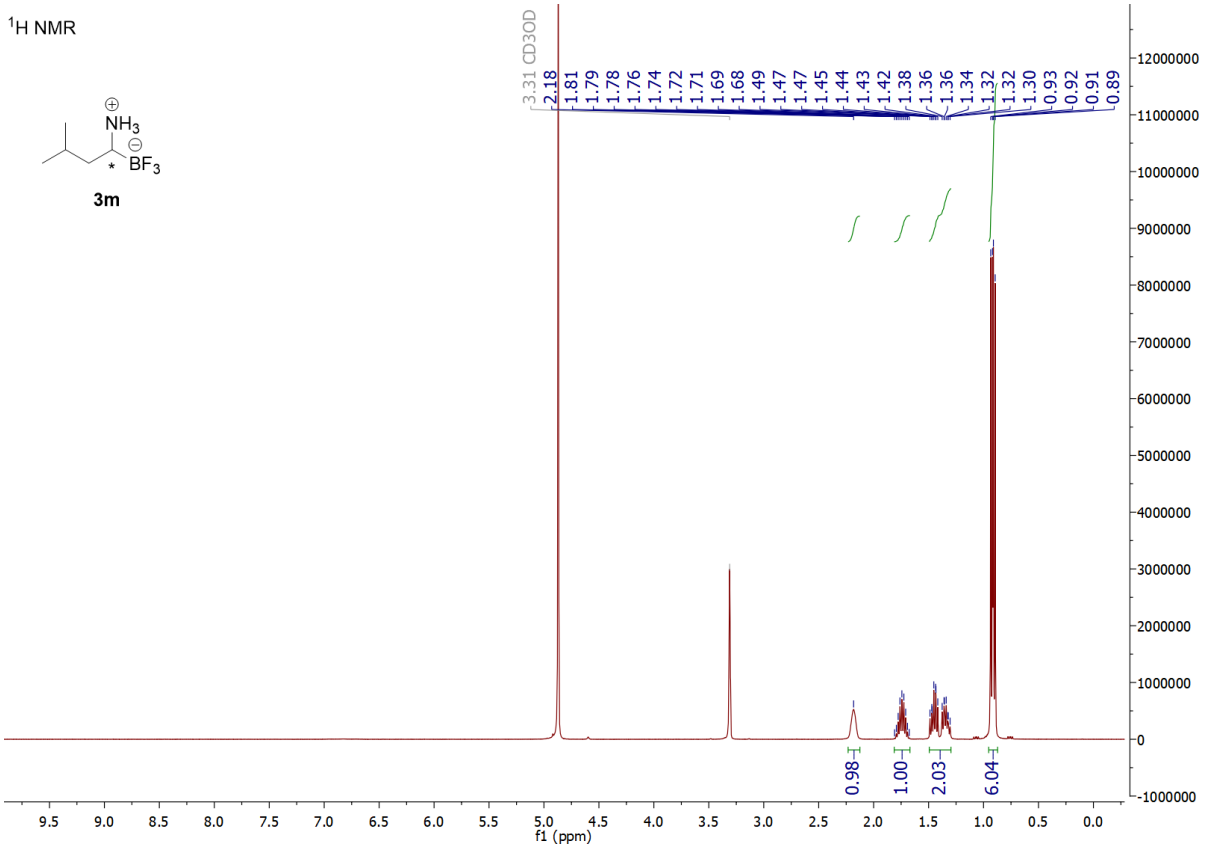


^{1}H-^{13}C-HSQC NMR (CD_3OD) of **3l**:

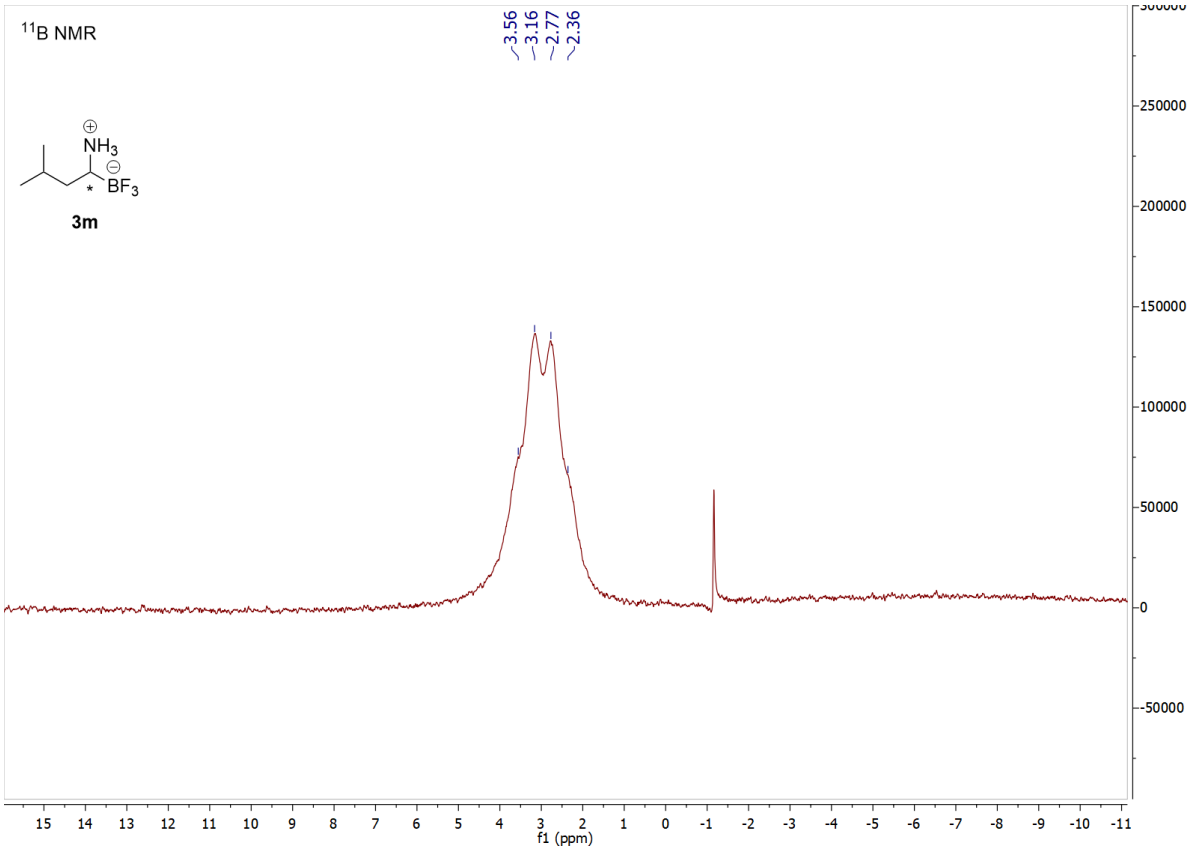


(1-ammonio-3-methylbutyl)trifluoroborate (3m)

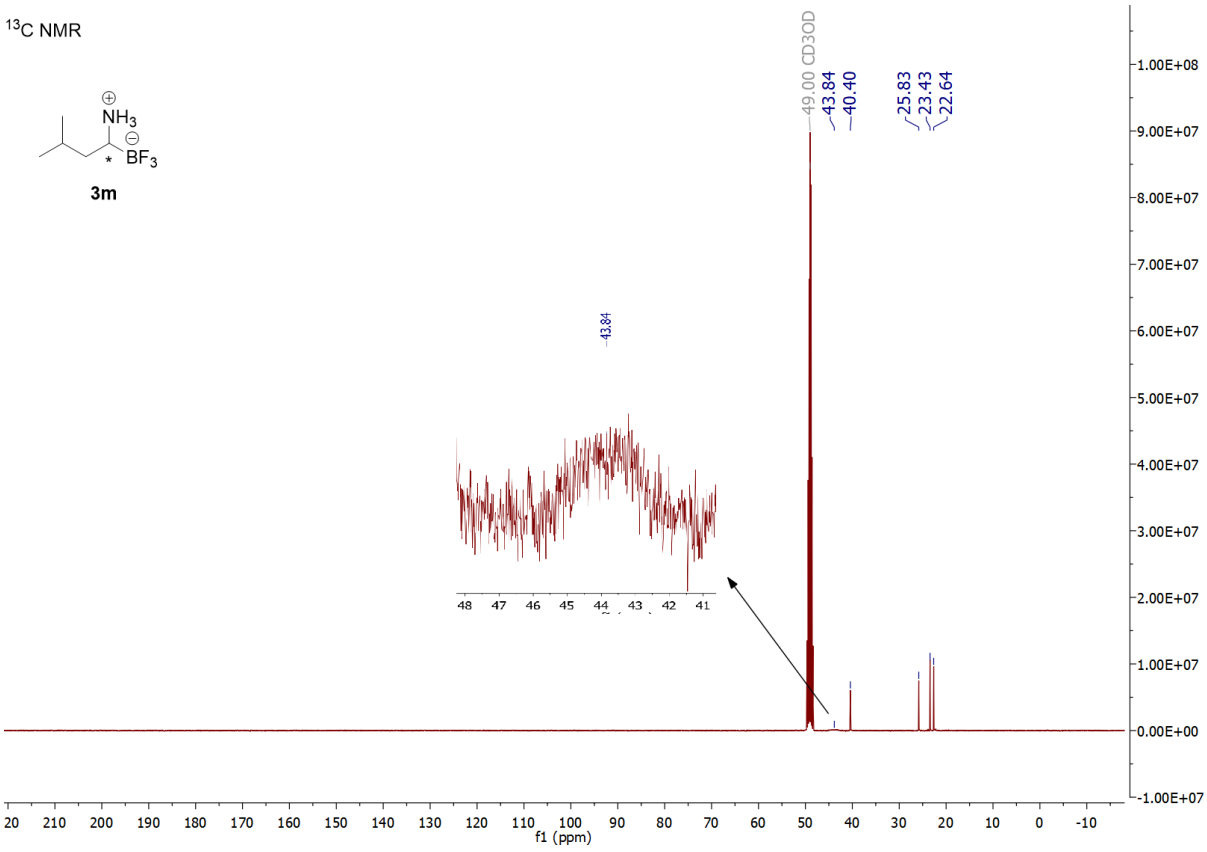
^{1}H-NMR (400 MHz, CD_3OD) of **3m**:



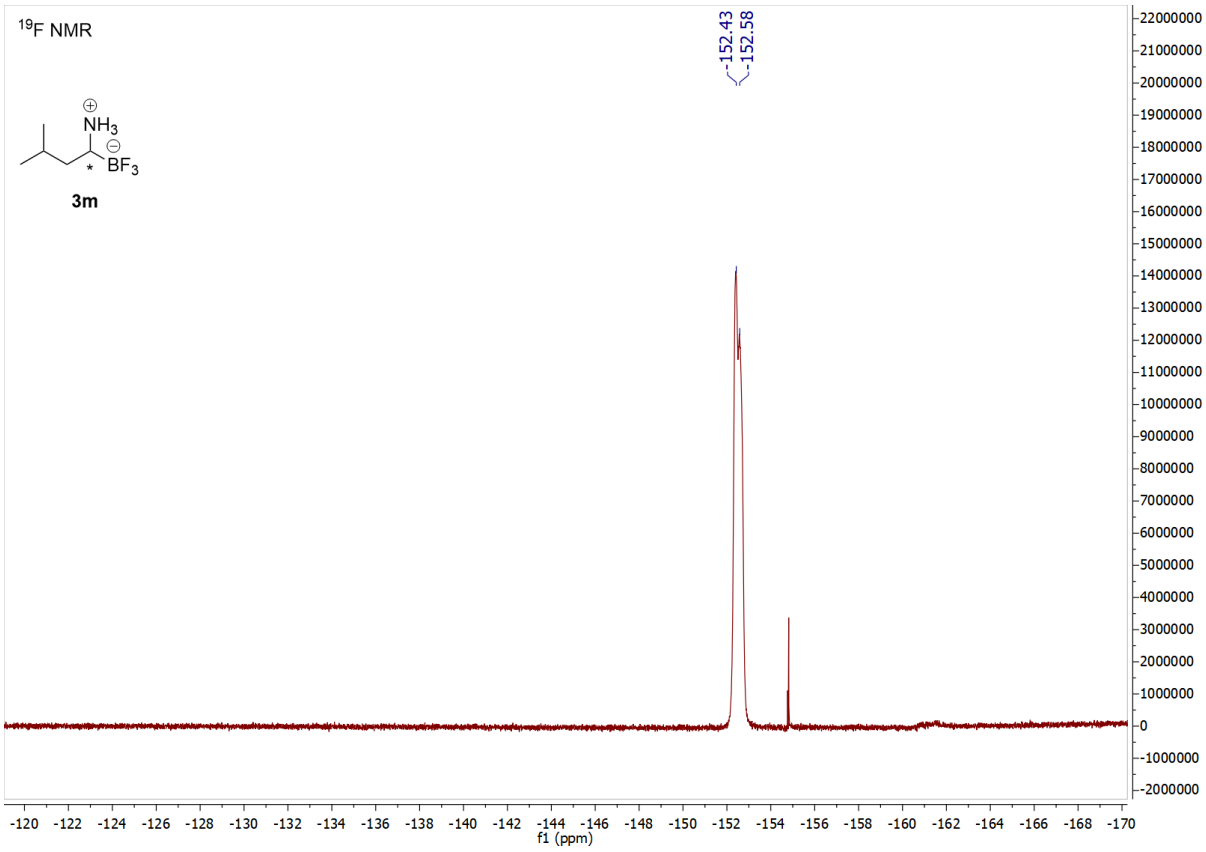
^{11}B-NMR (128 MHz, CD_3OD) of **3m**:



^{13}C-NMR (101 MHz, CD_3OD) of **3m**:

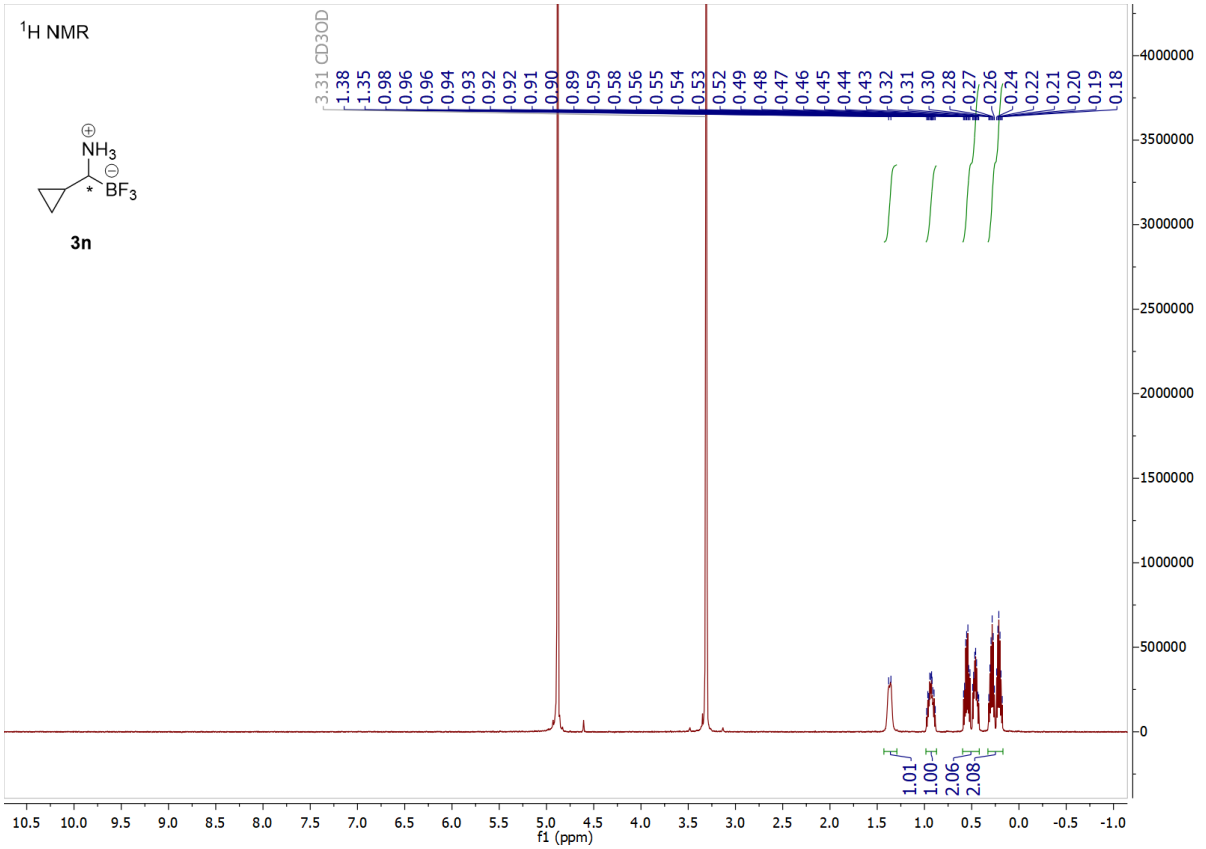


^{19}F-NMR (376 MHz, CD_3OD) of **3m**:

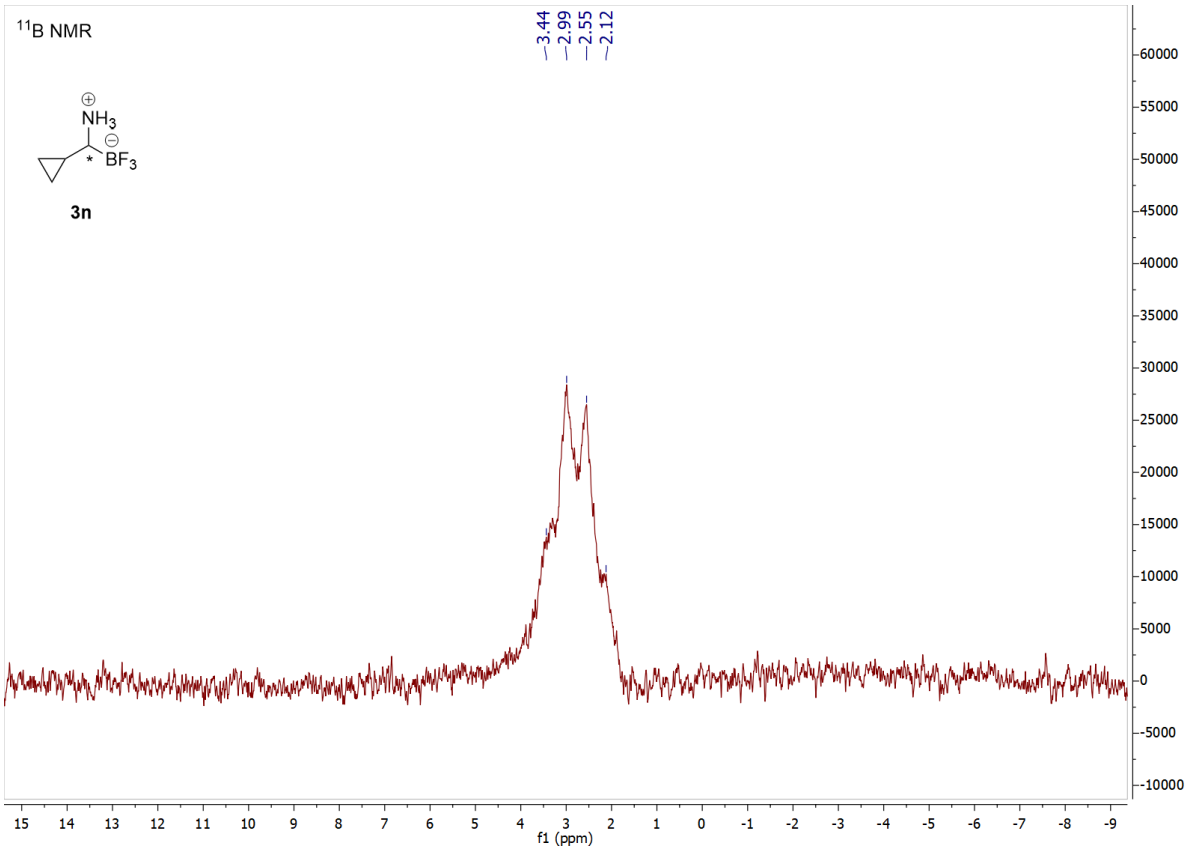


(Ammonio(cyclopropyl)methyl)trifluoroborate (3n)

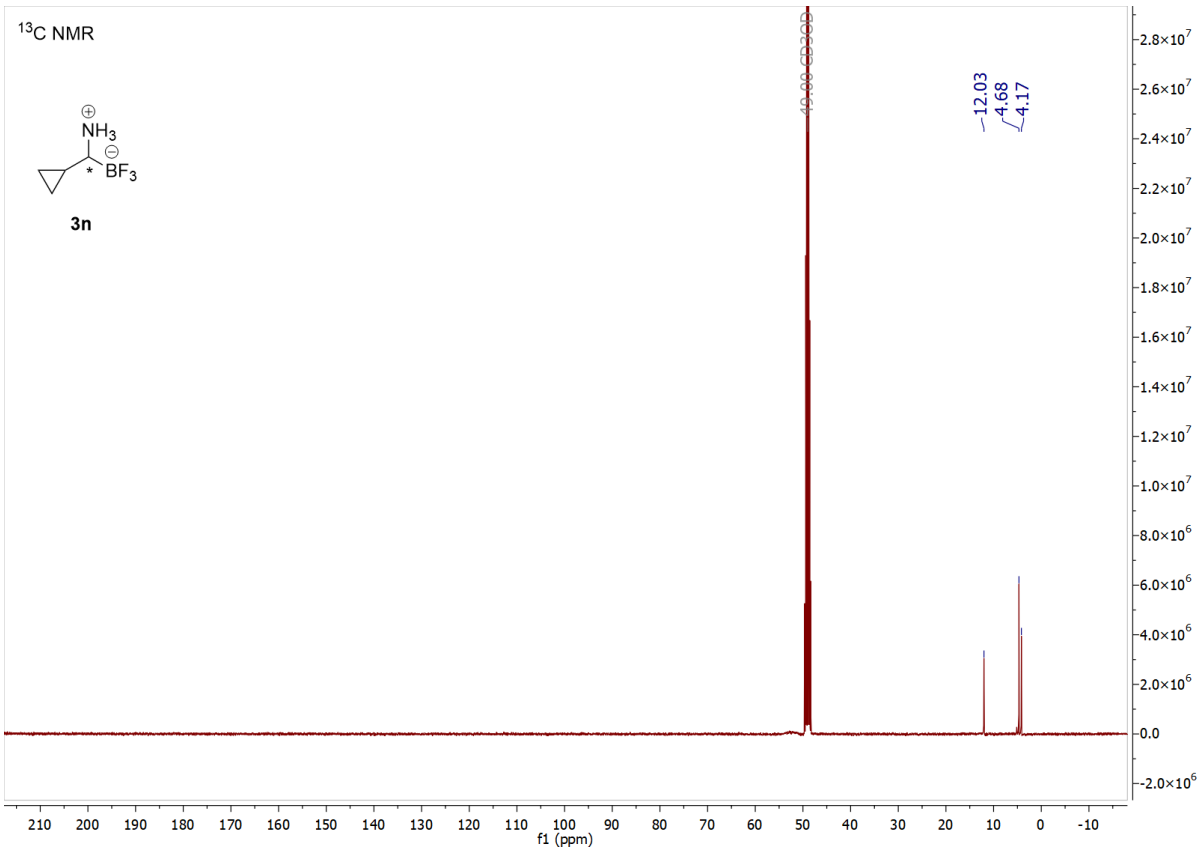
^{1}H-NMR (400 MHz, CD_3OD) of **3n**:



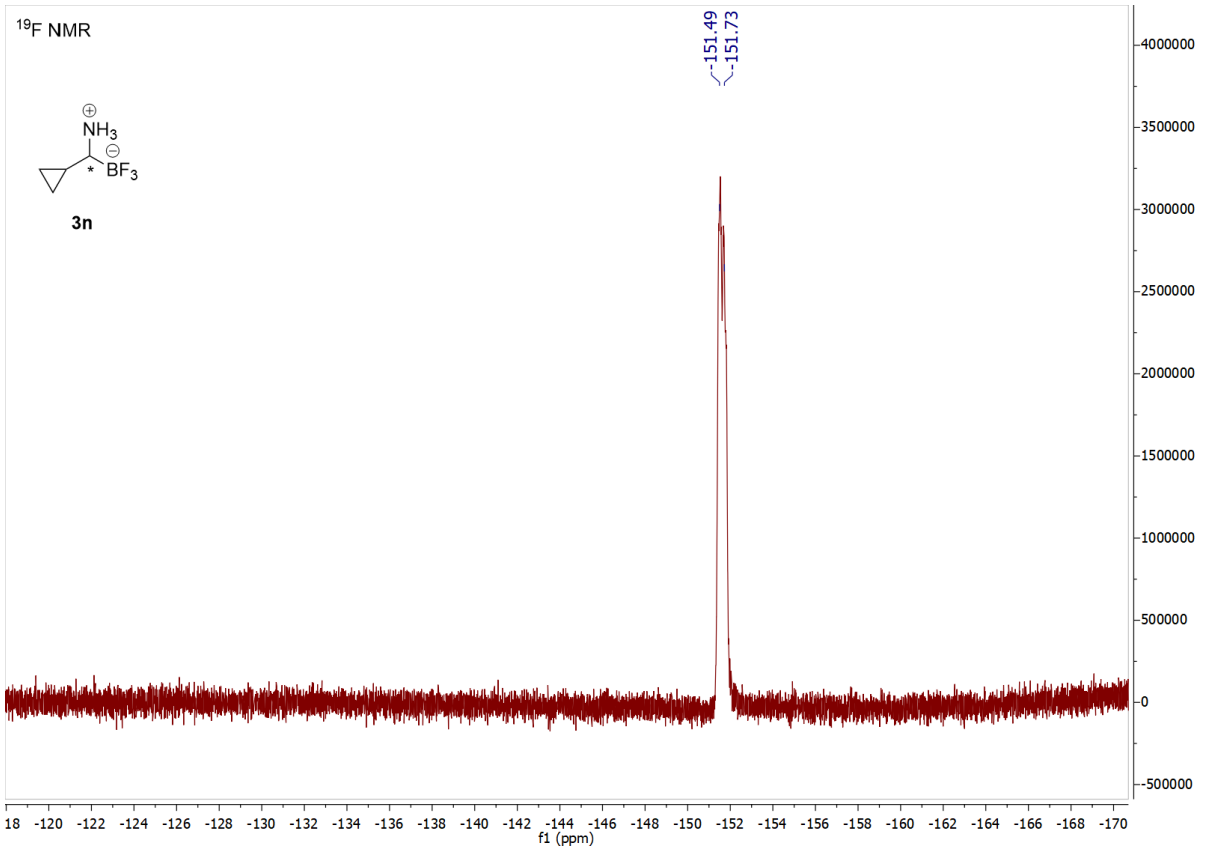
^{13}B-NMR (128 MHz, CD_3OD) of **3n**:



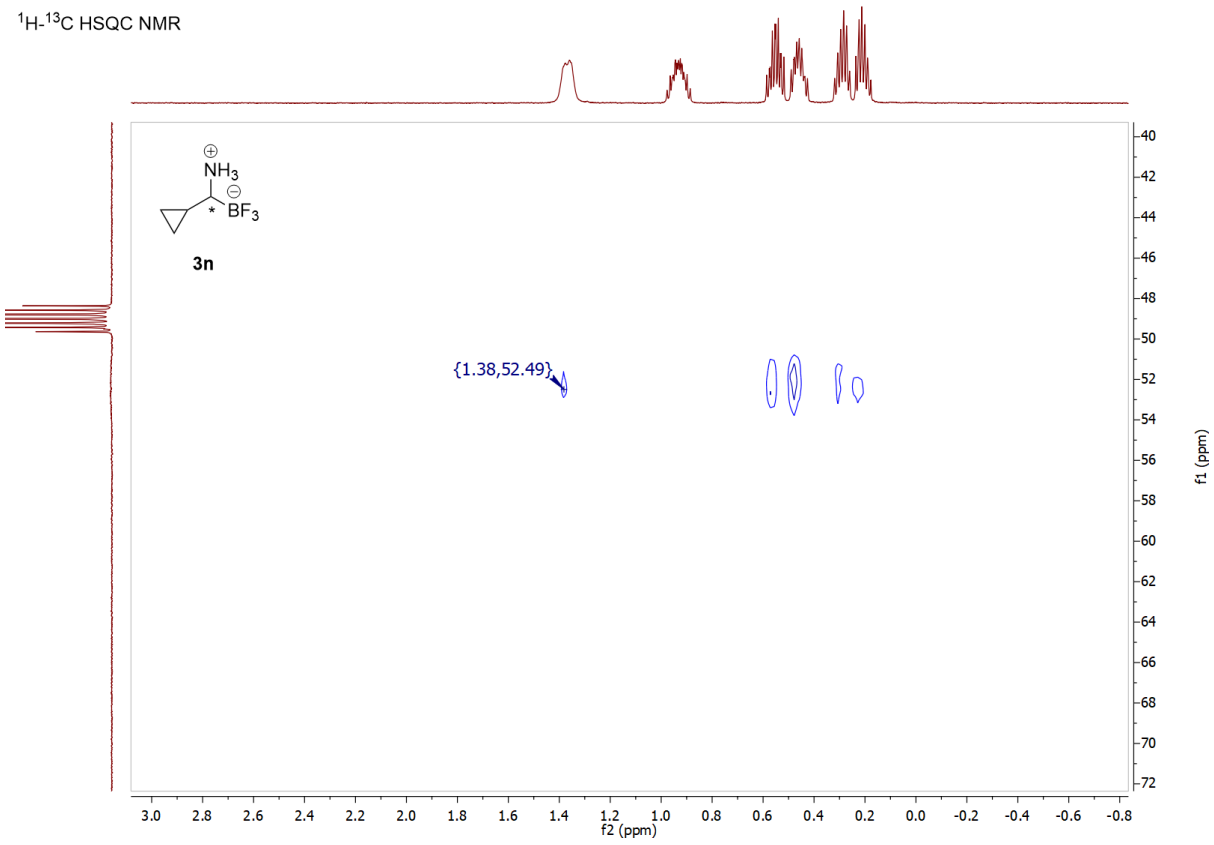
^{13}C-NMR (101 MHz, CD_3OD) of **3n**:



^{19}F-NMR (376 MHz, CD_3OD) of **3n**:

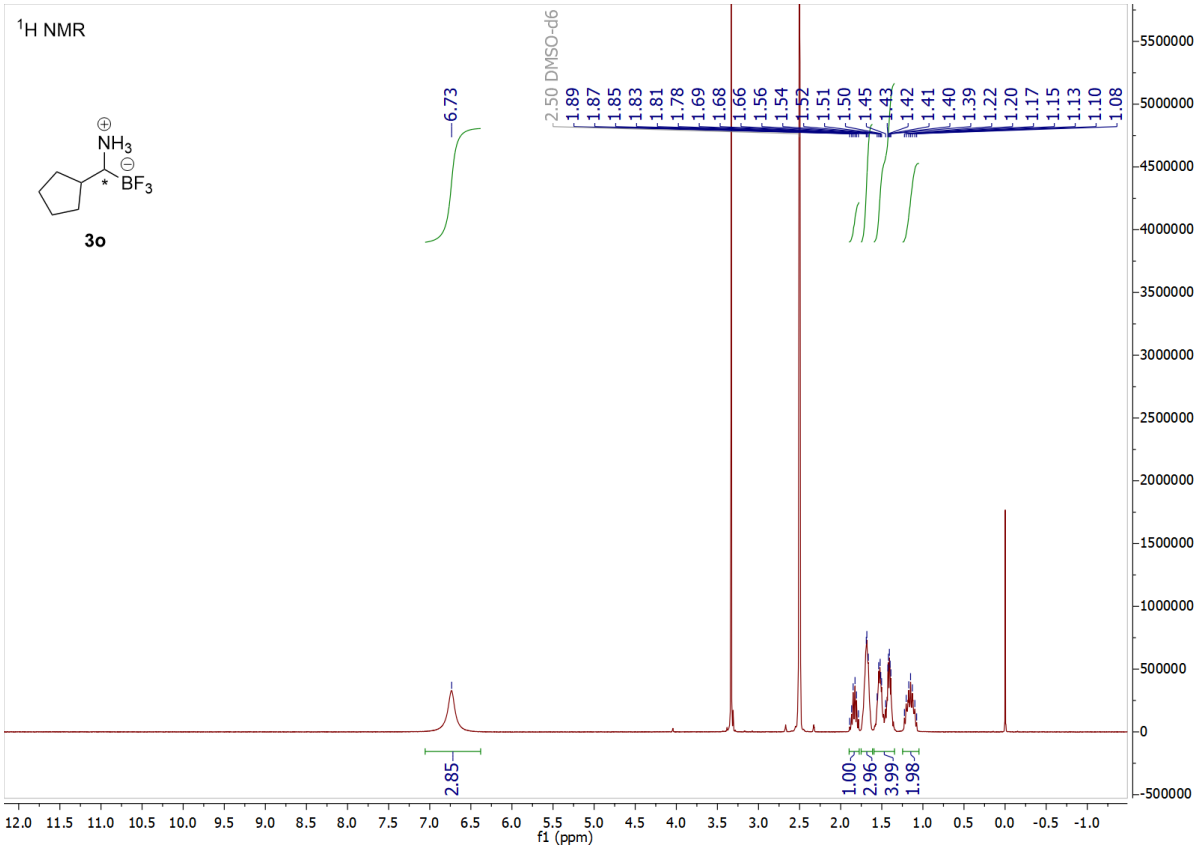


^{1}H-^{13}C-HSQC NMR (CD_3OD) of **3n**:

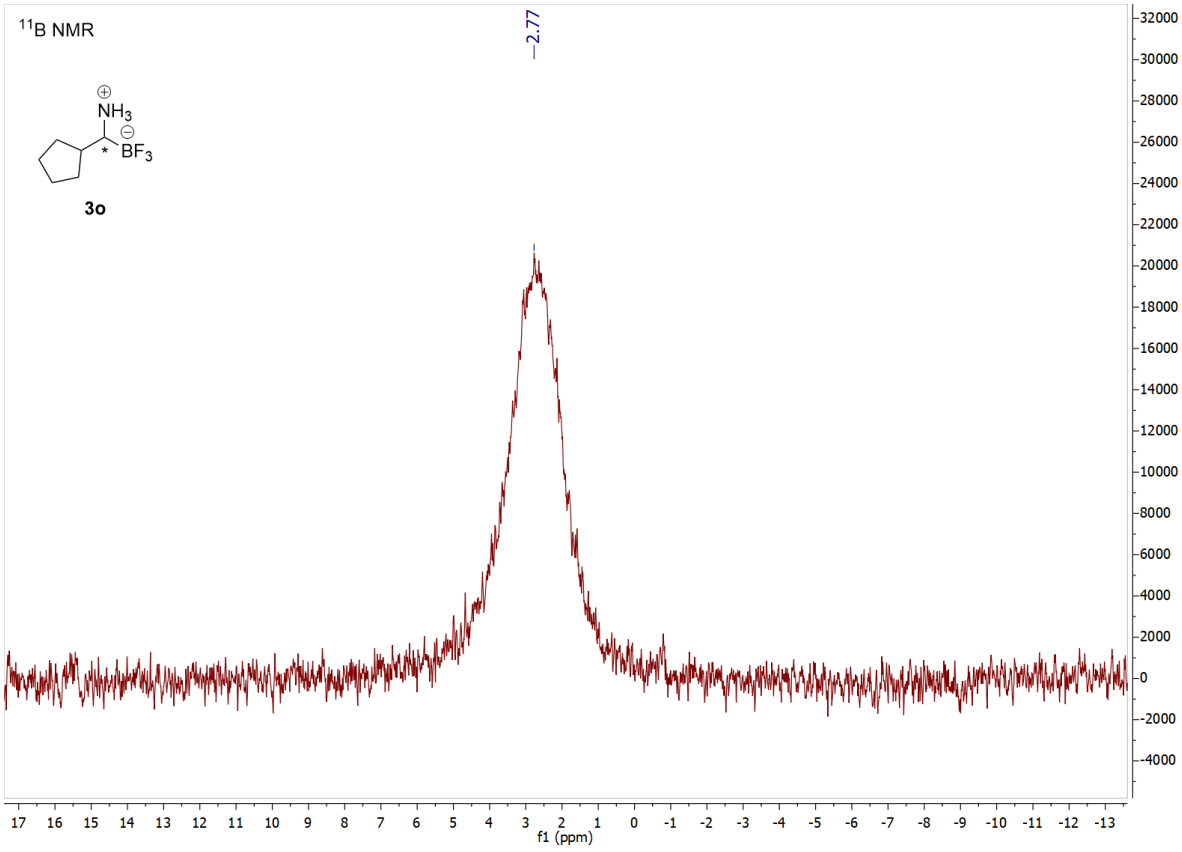


(Ammonio(cyclopentyl)methyl)trifluoroborate (3o)

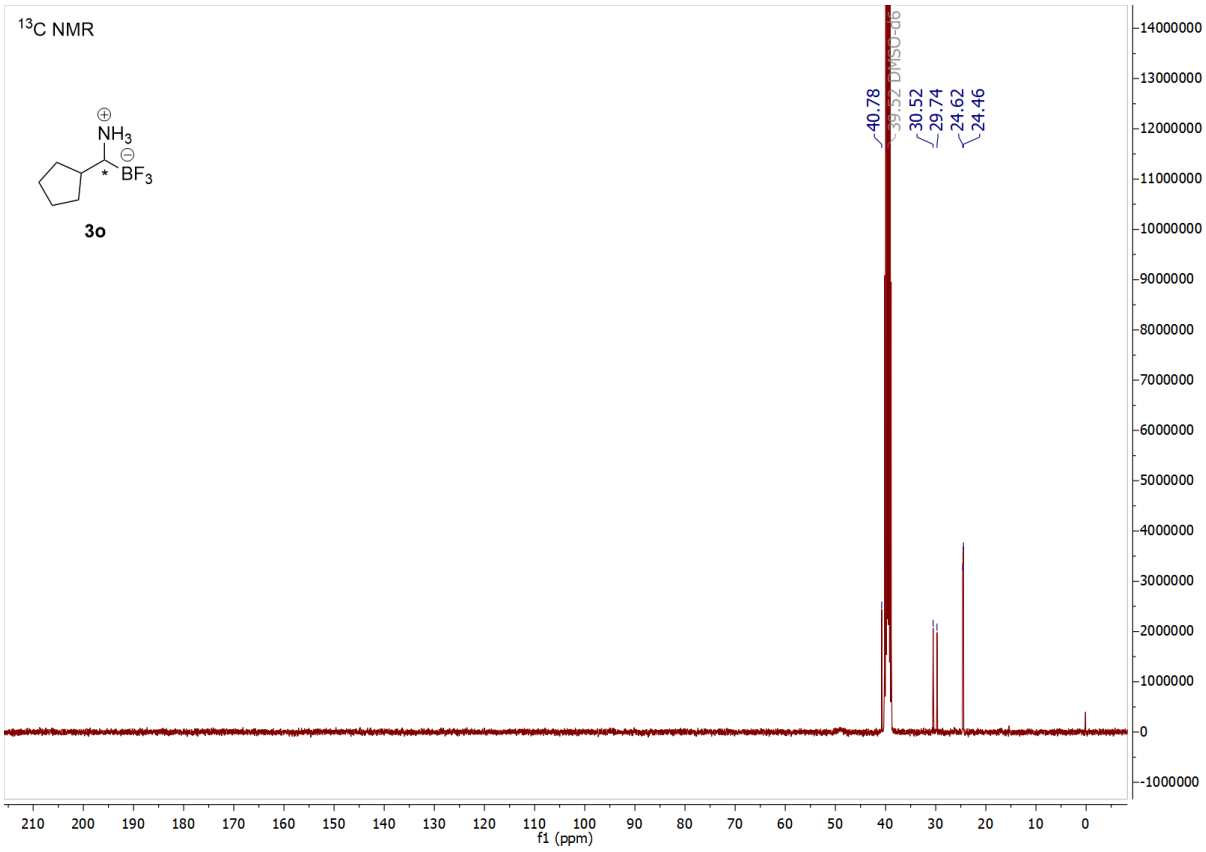
^{1}H-NMR (400 MHz, DMSO-d$_6$) of **3o**:



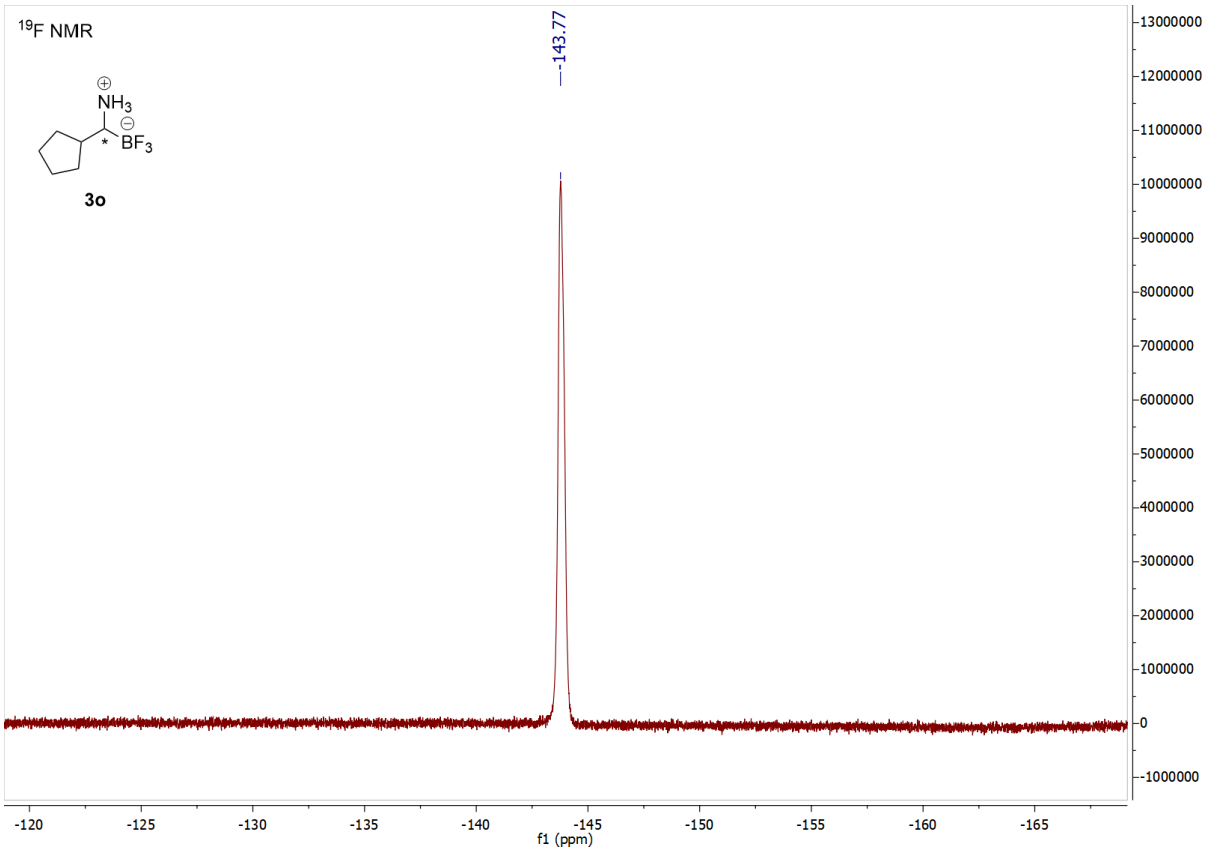
^{11}B-NMR (128 MHz, DMSO-d$_6$) of **3o**:



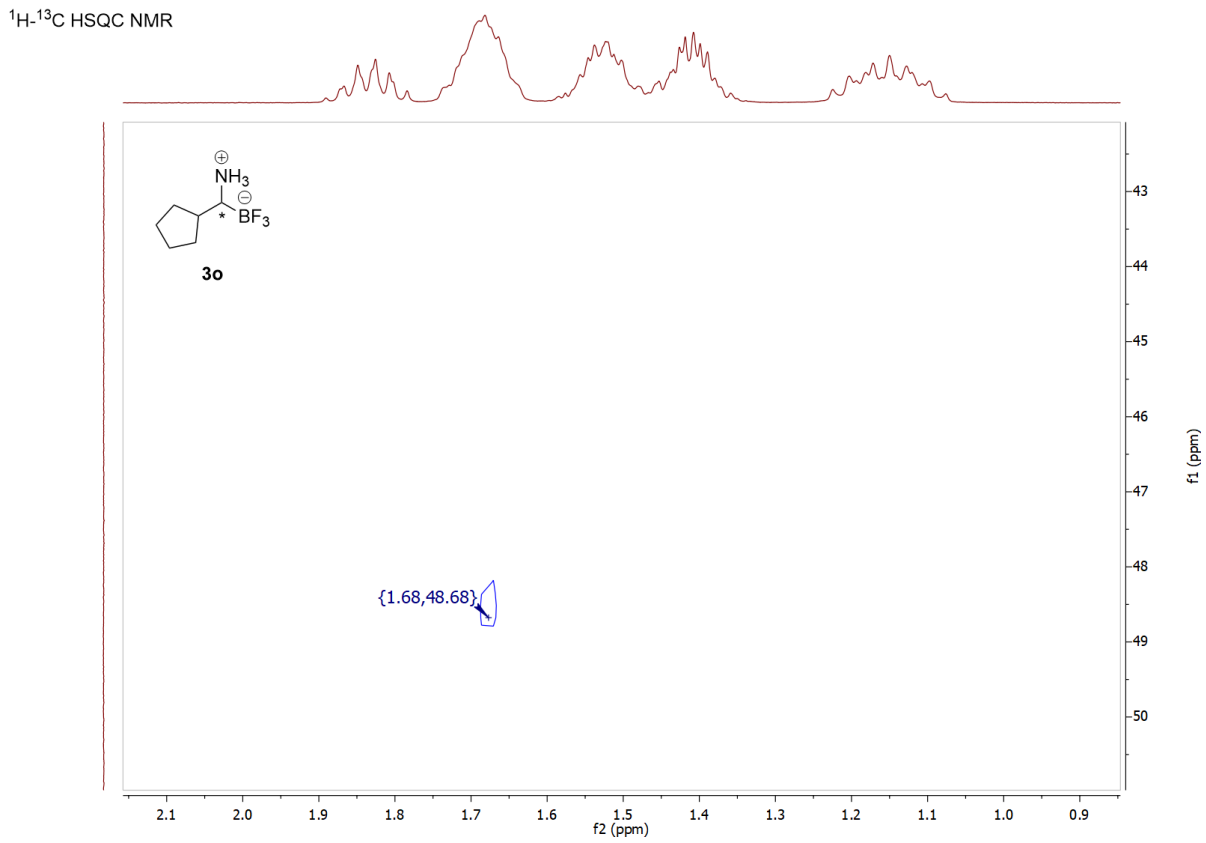
^{13}C-NMR (101 MHz, DMSO-d_6) of **3o**:



^{19}F-NMR (376 MHz, DMSO-d_6) of **3o**:

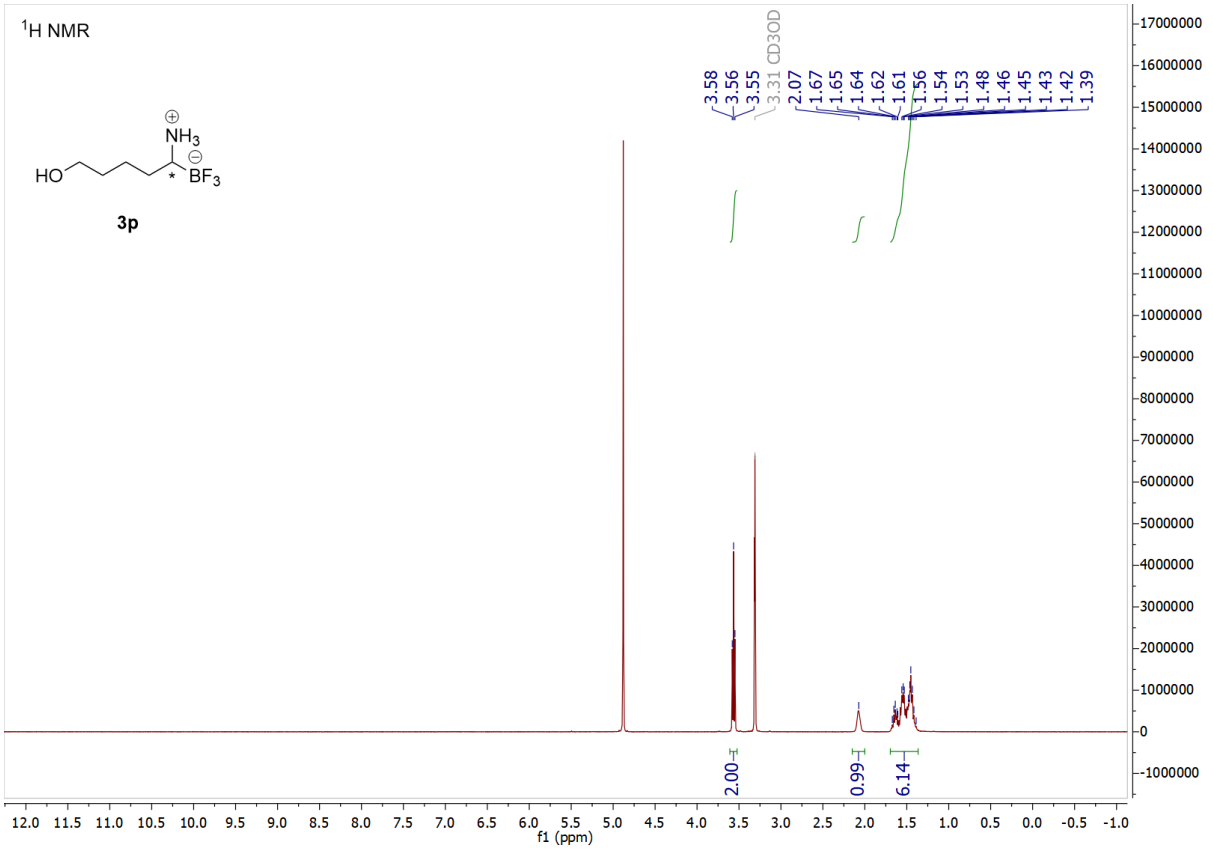


^{1}H-^{13}C-HSQC NMR (DMSO-d_6) of **3o**:

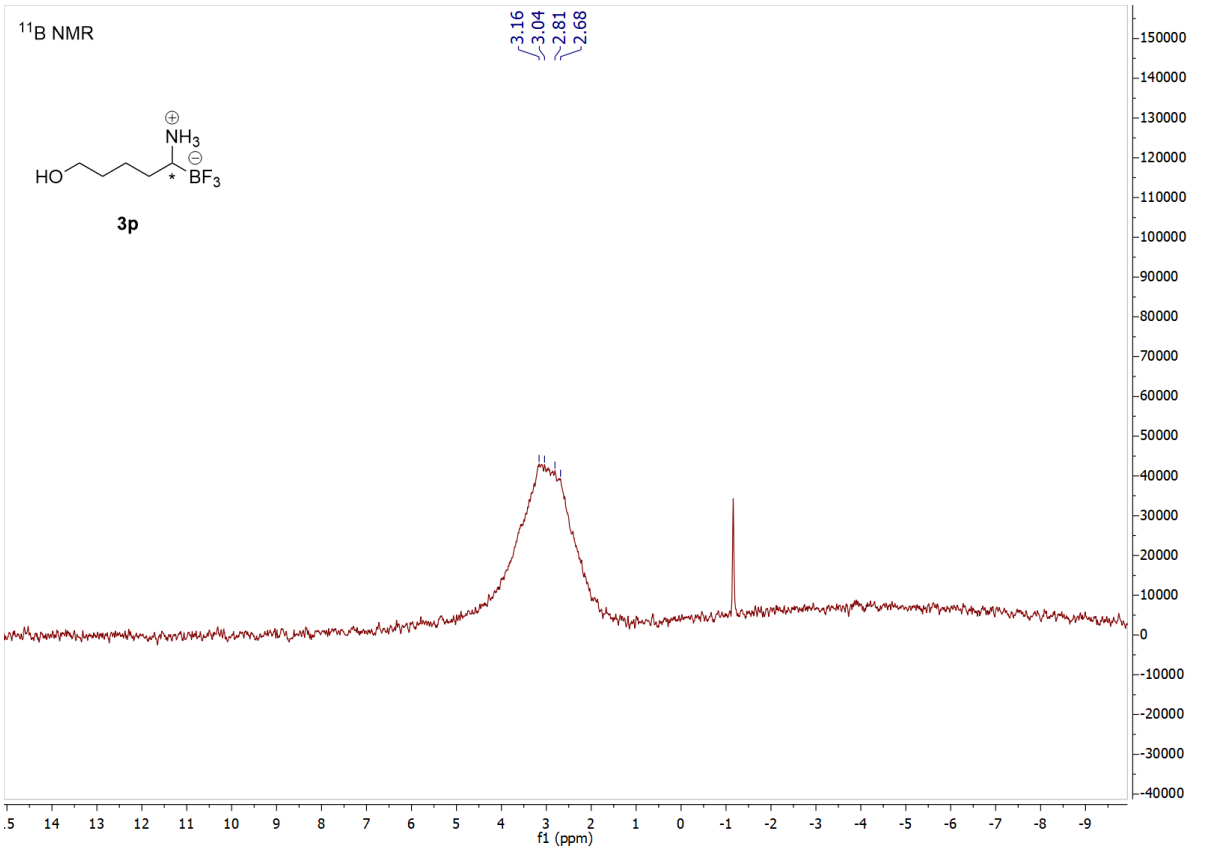


(1-Ammonio-5-hydroxypentyl)trifluoroborate (3p)

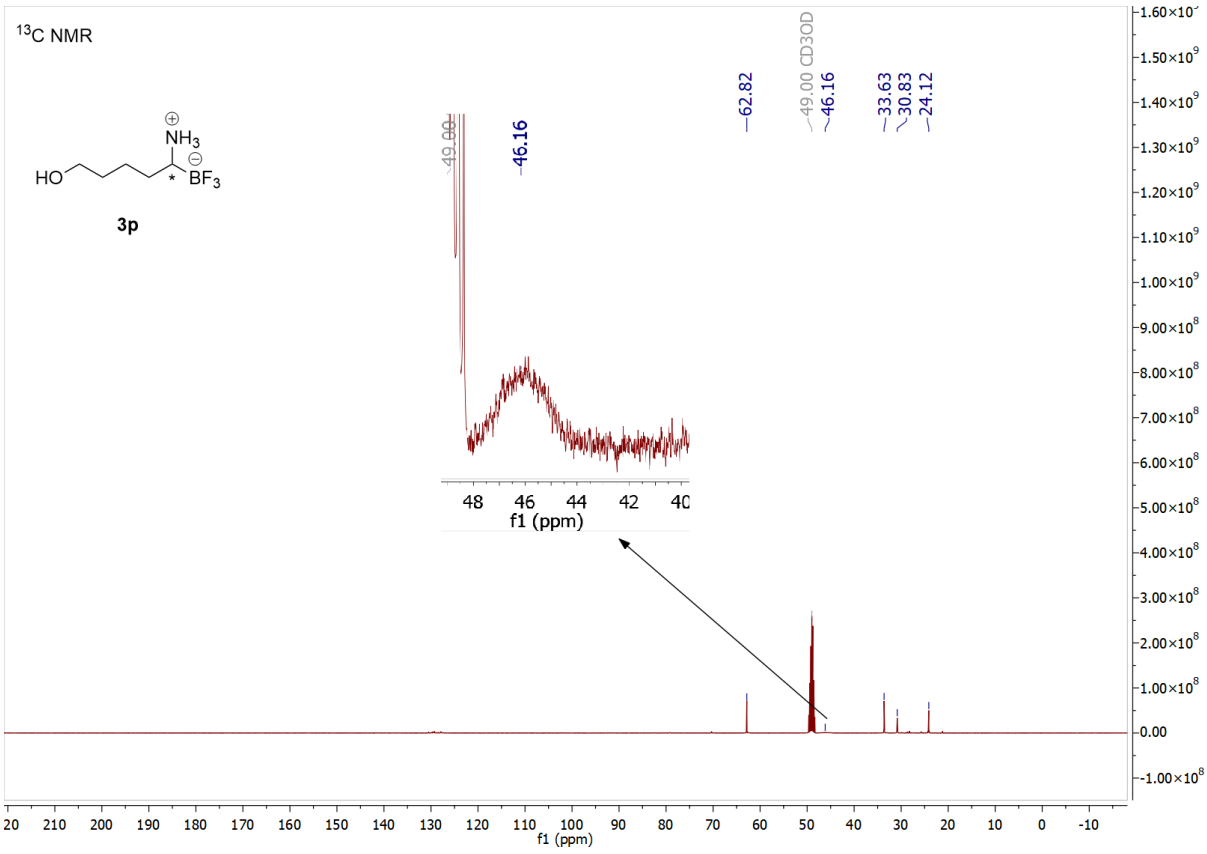
^{1}H-NMR (400 MHz, CD_3OD) of **3p**:



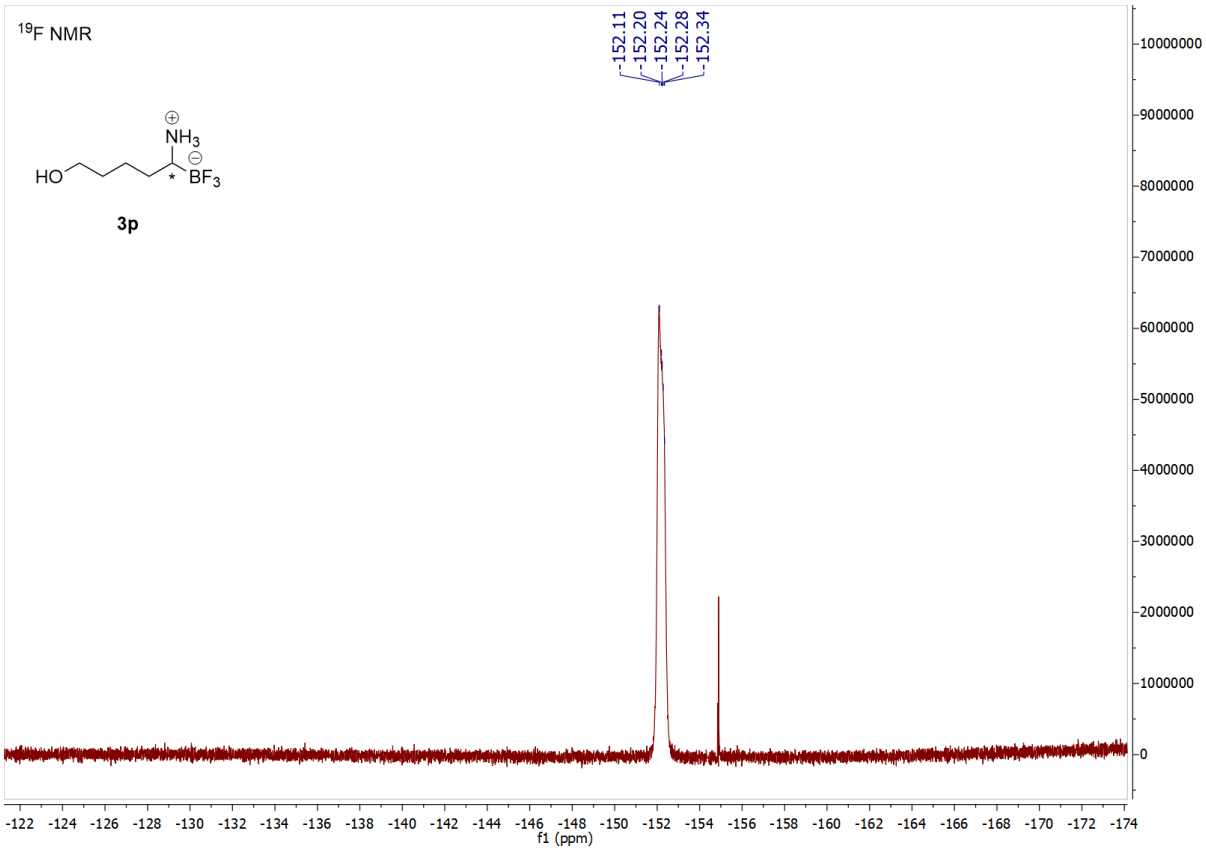
^{11}B-NMR (128 MHz, CD_3OD) of **3p**:



^{13}C-NMR (101 MHz, CD_3OD) of **3p**:



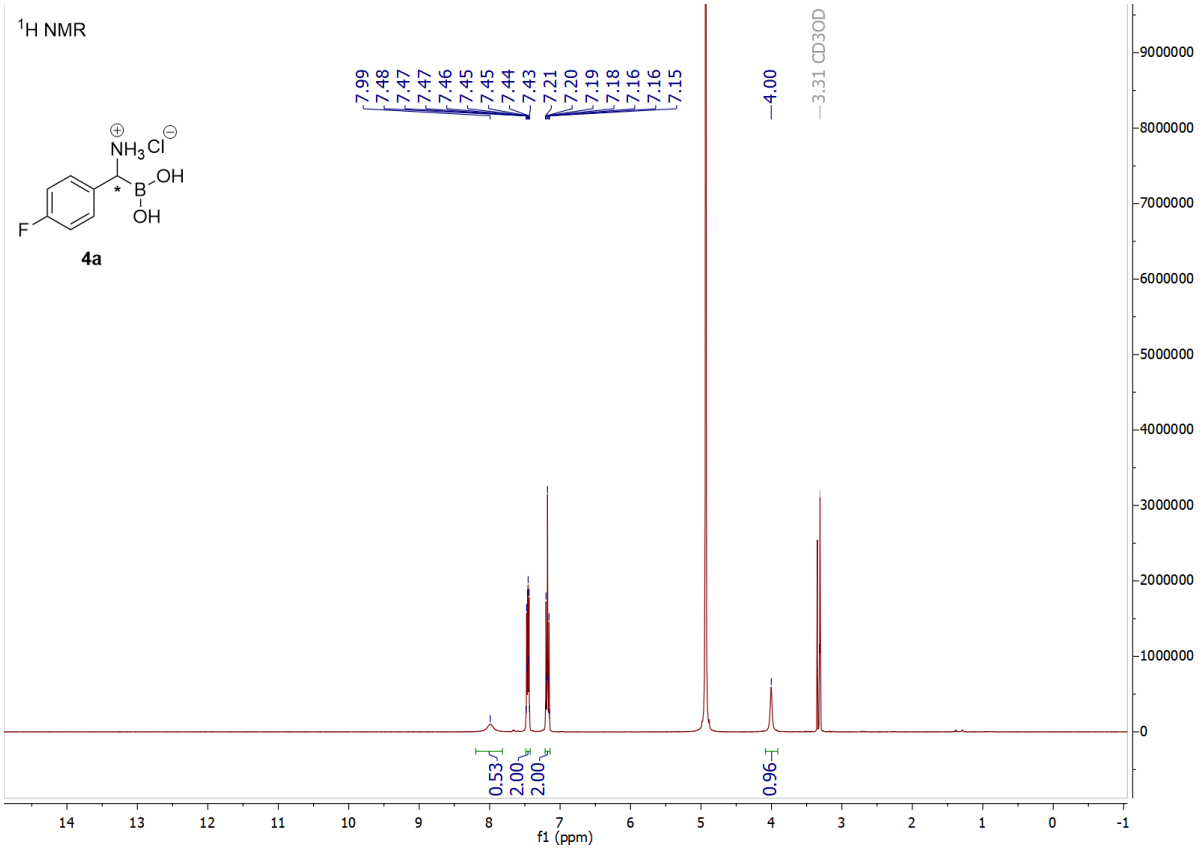
^{19}F-NMR (376 MHz, CD_3OD) of **3p**:



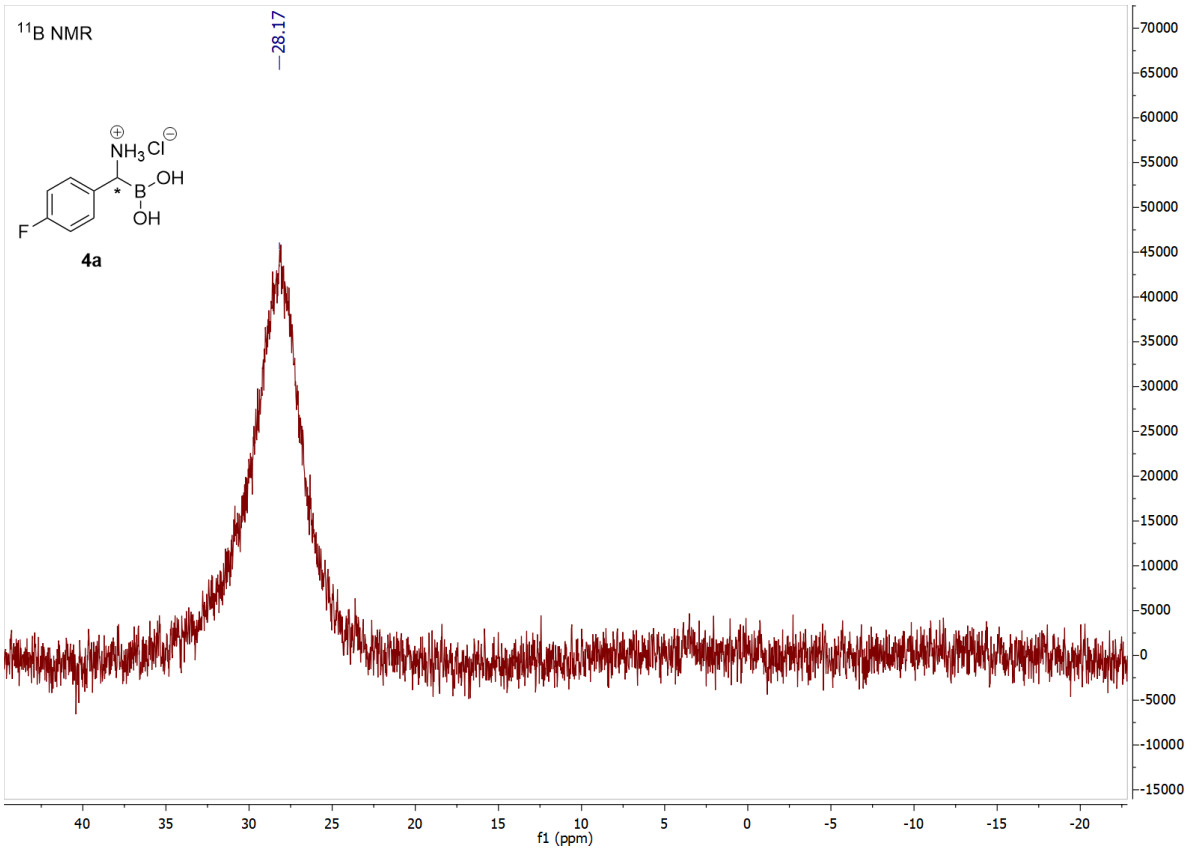
8.3. NMR Spectra of α-Aminoboronic Acids **4**

Borono(4-fluorophenyl)methanaminium chloride (4a)

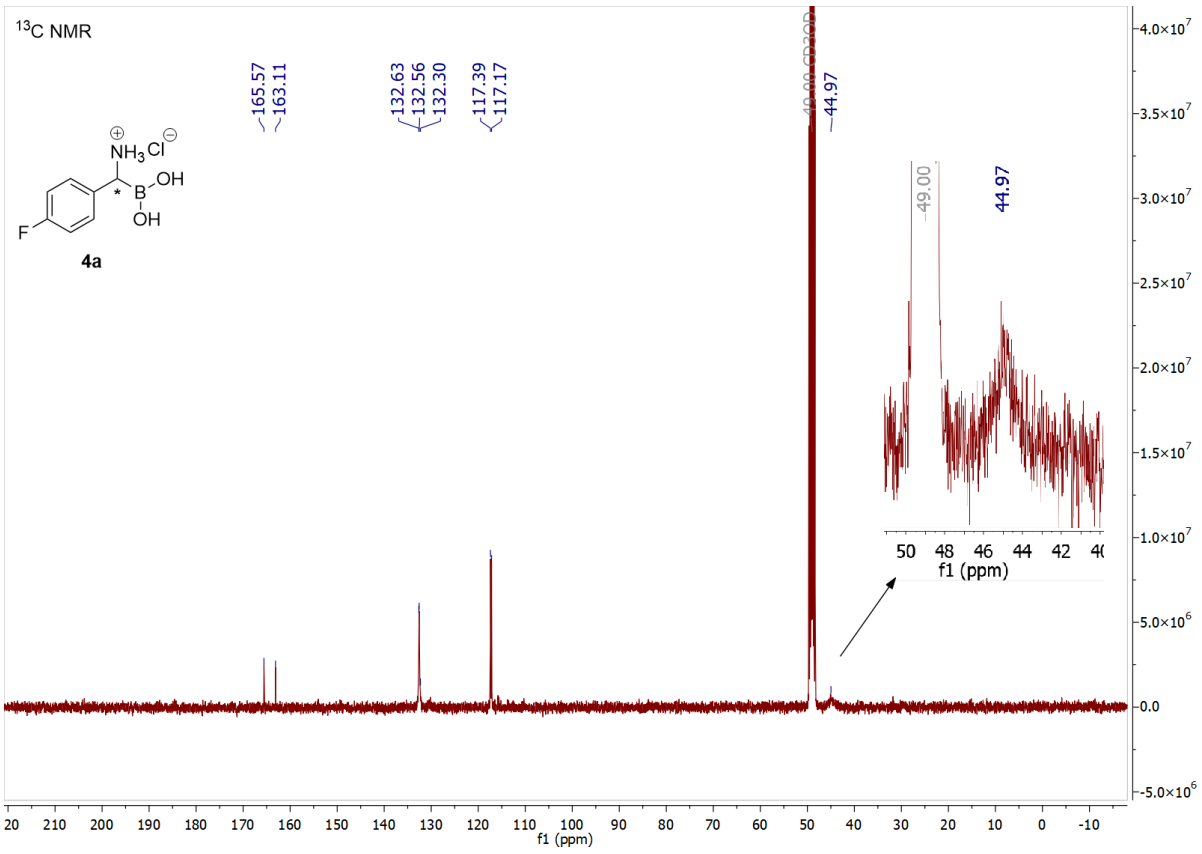
^{1}H-NMR (400 MHz, CD_3OD) of **4a**:



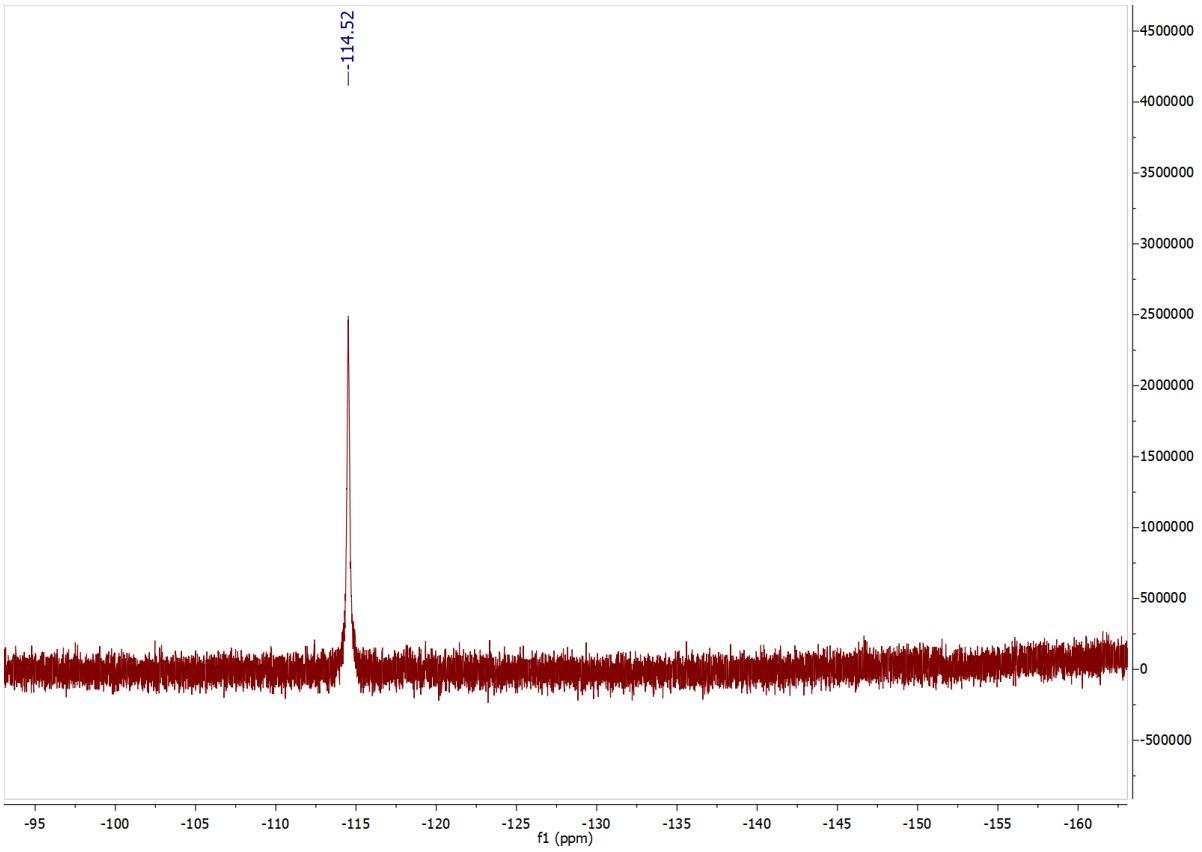
^{11}B-NMR (128 MHz, CD_3OD) of **4a**:



^{13}C-NMR (101 MHz, CD_3OD) of **4a**:

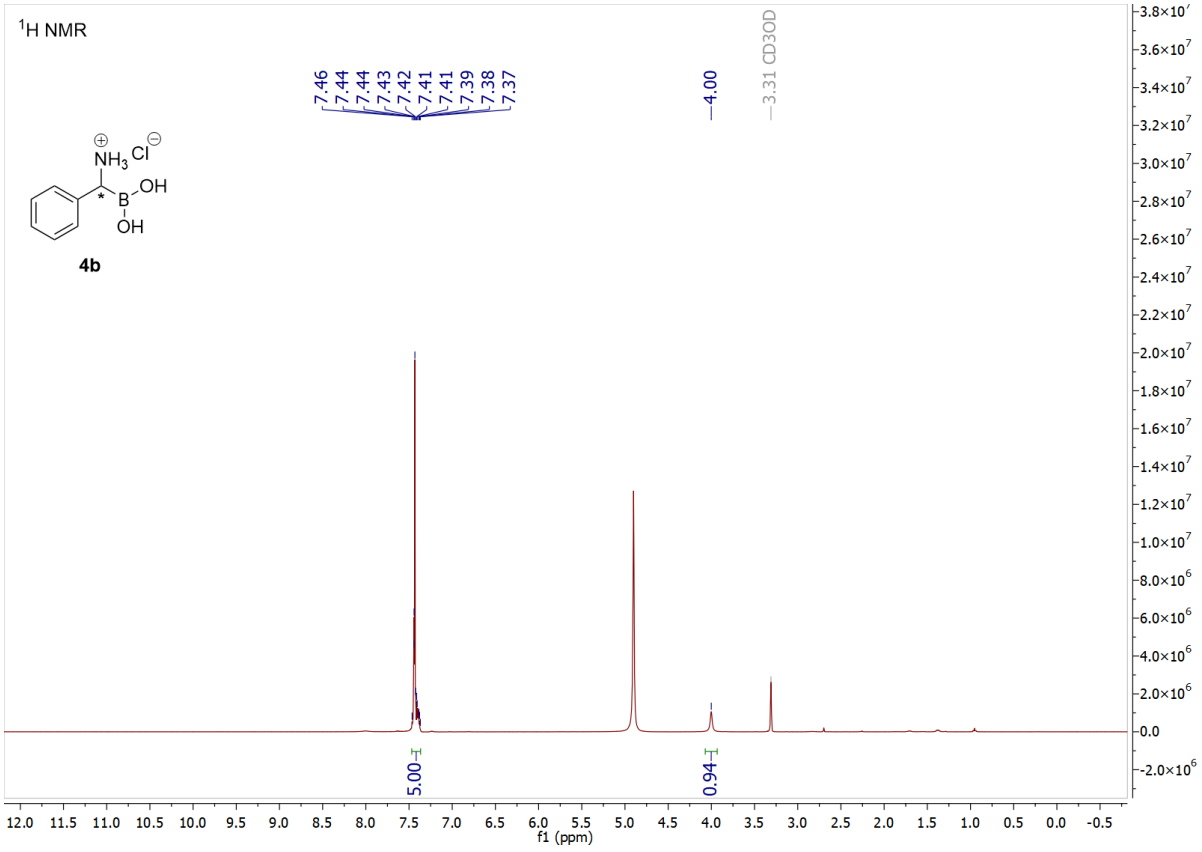


^{19}F-NMR (376 MHz, CD_3OD) of **4a**:

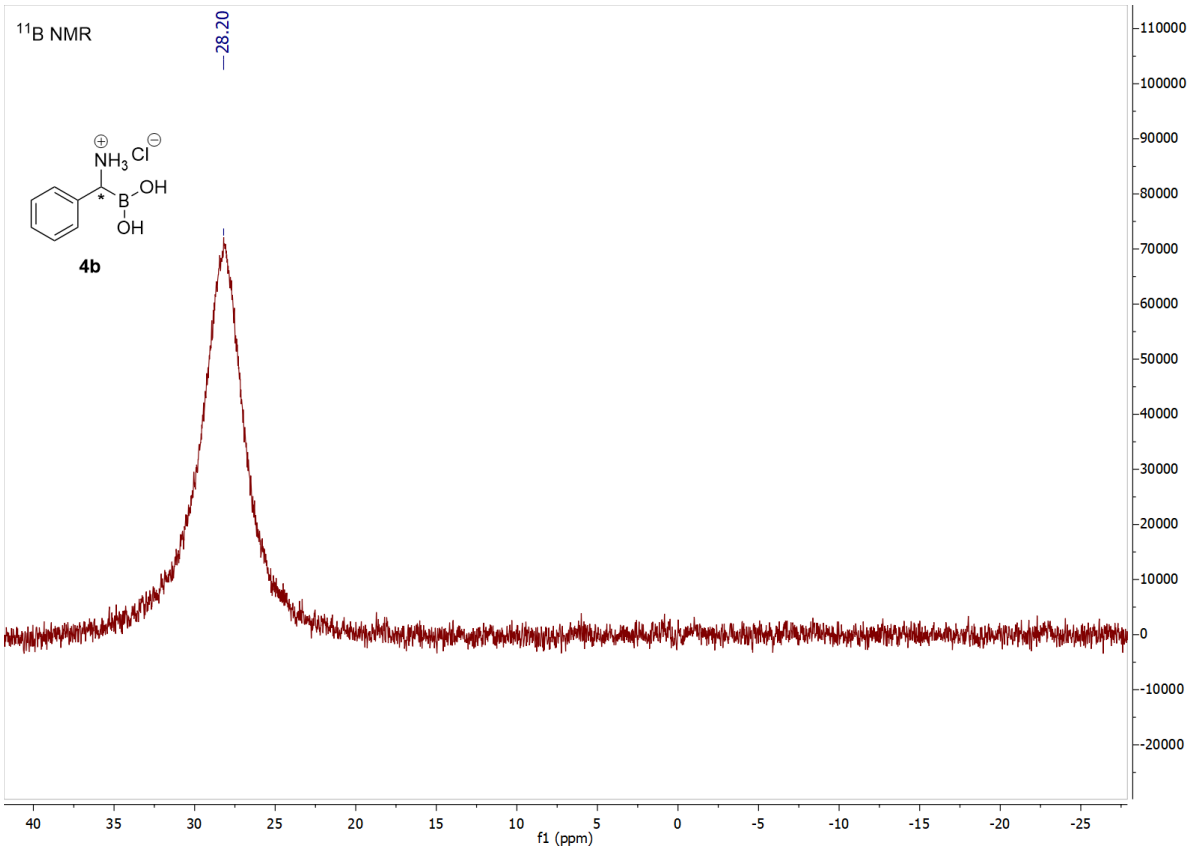


Borono(phenyl)methanaminium chloride (4b)

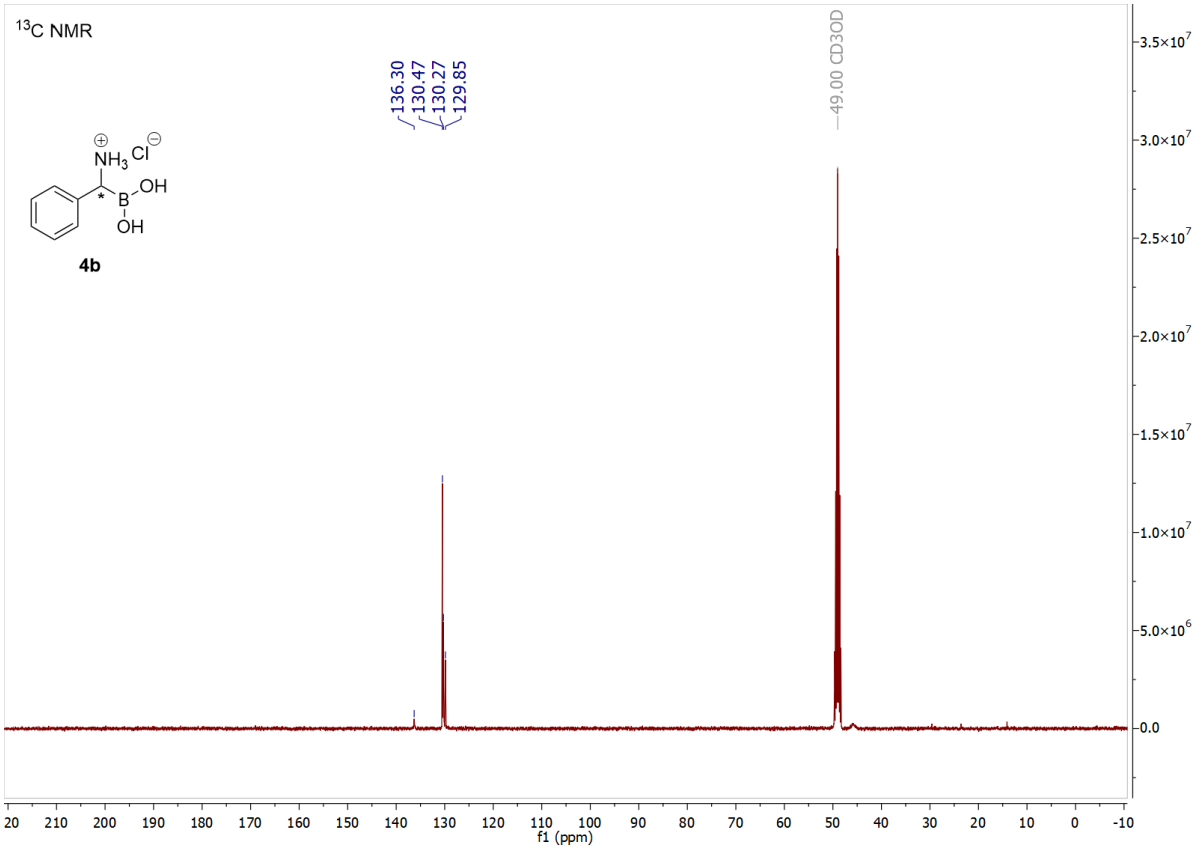
^{1}H-NMR (400 MHz, CD_3OD) of **4b**:



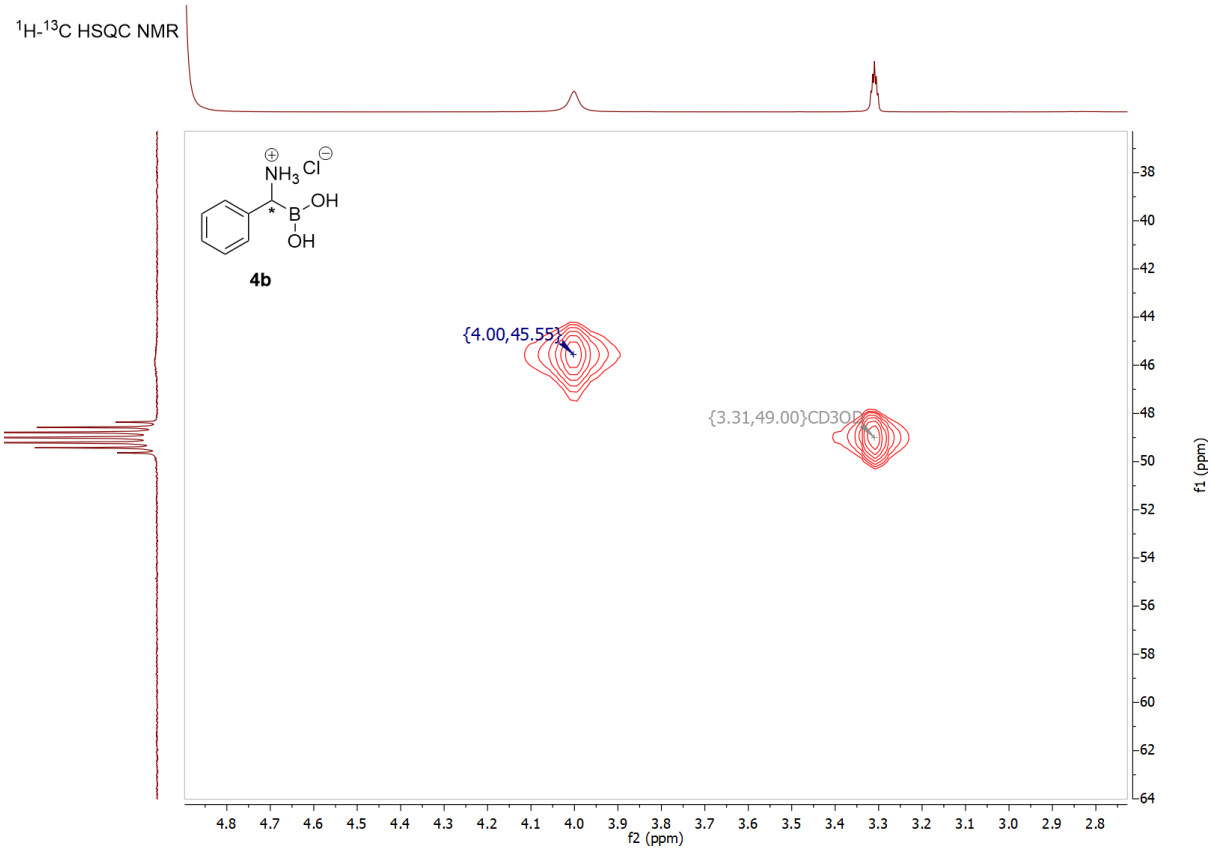
^{11}B-NMR (128 MHz, CD_3OD) of **4b**:



^{13}C-NMR (101 MHz, CD_3OD) of **4b**:

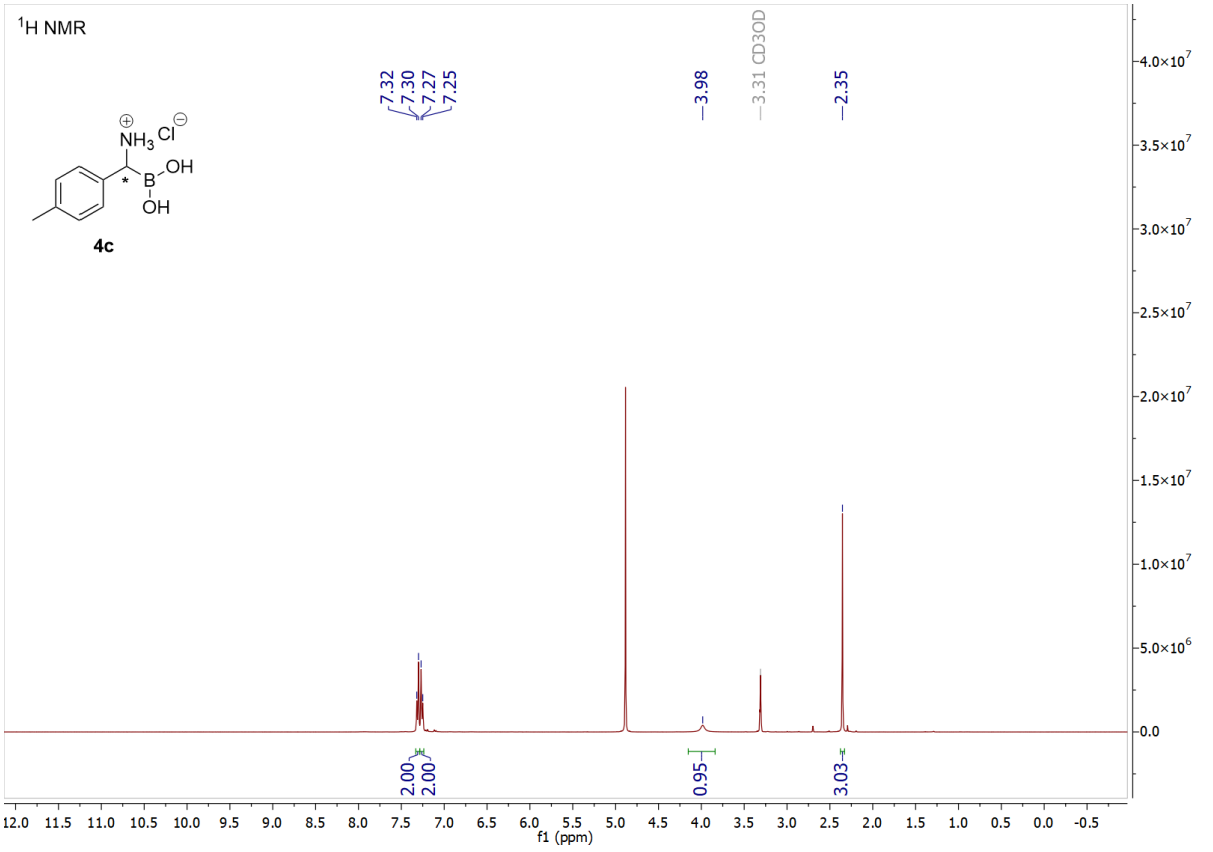


^{1}H-^{13}C HSQC-NMR (CD_3OD) of **4b**:

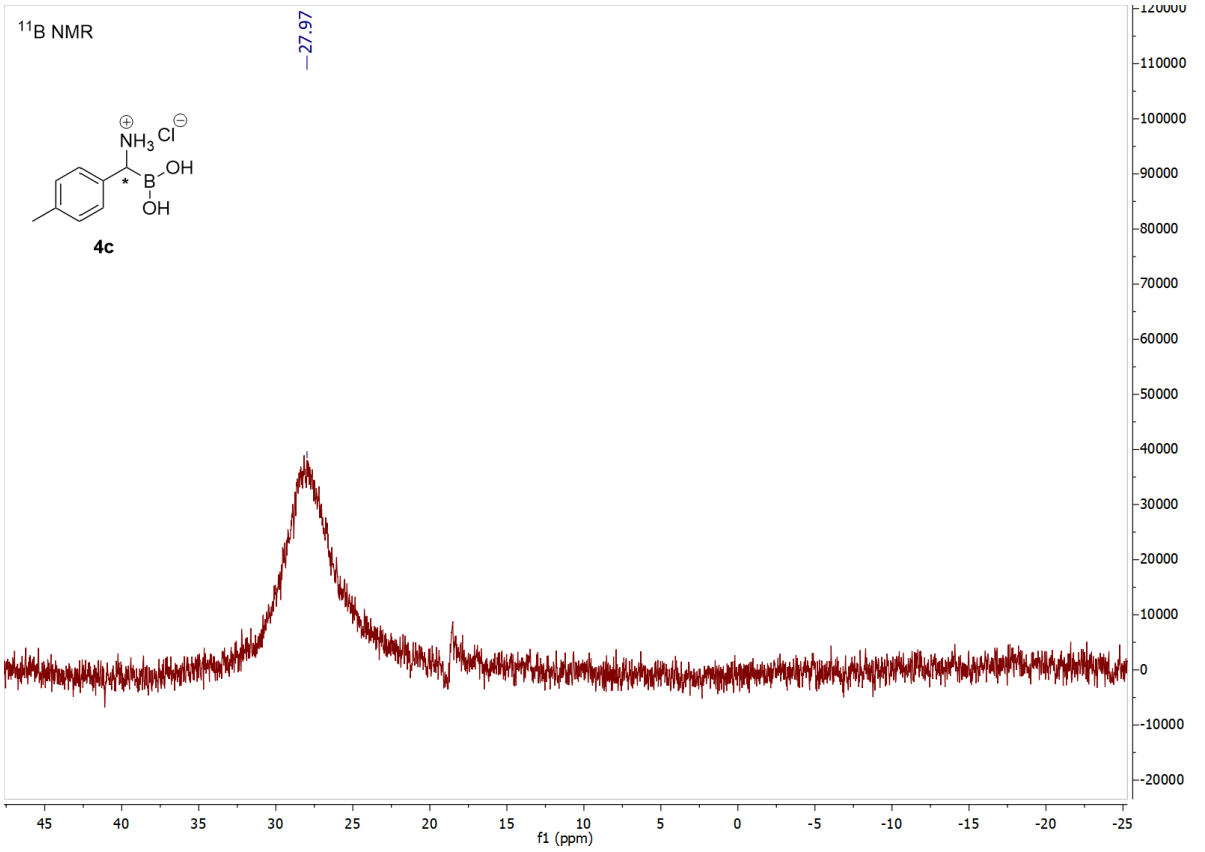


Borono(4-tolyl)methanaminium chloride (4c)

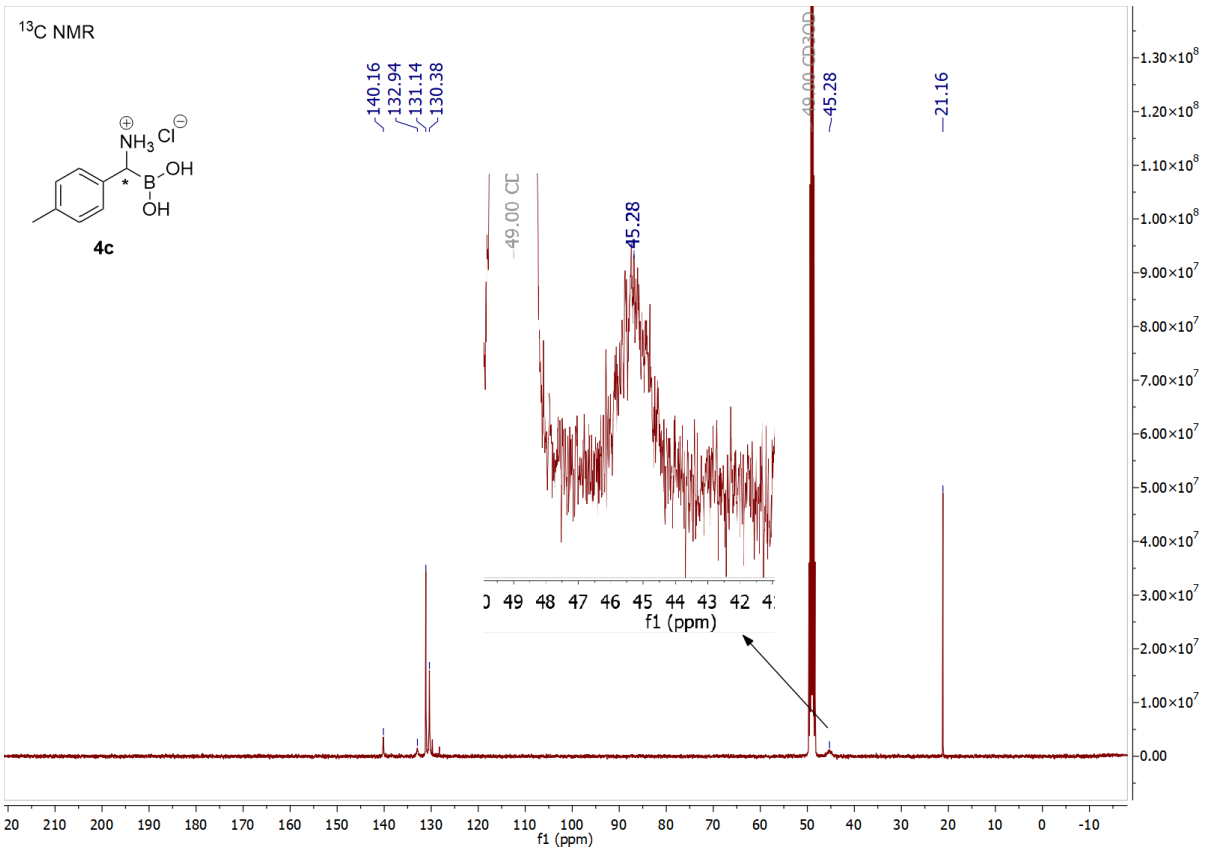
^{1}H-NMR (400 MHz, CD_3OD) of **4c**:



^{11}B-NMR (128 MHz, CD_3OD) of **4c**:

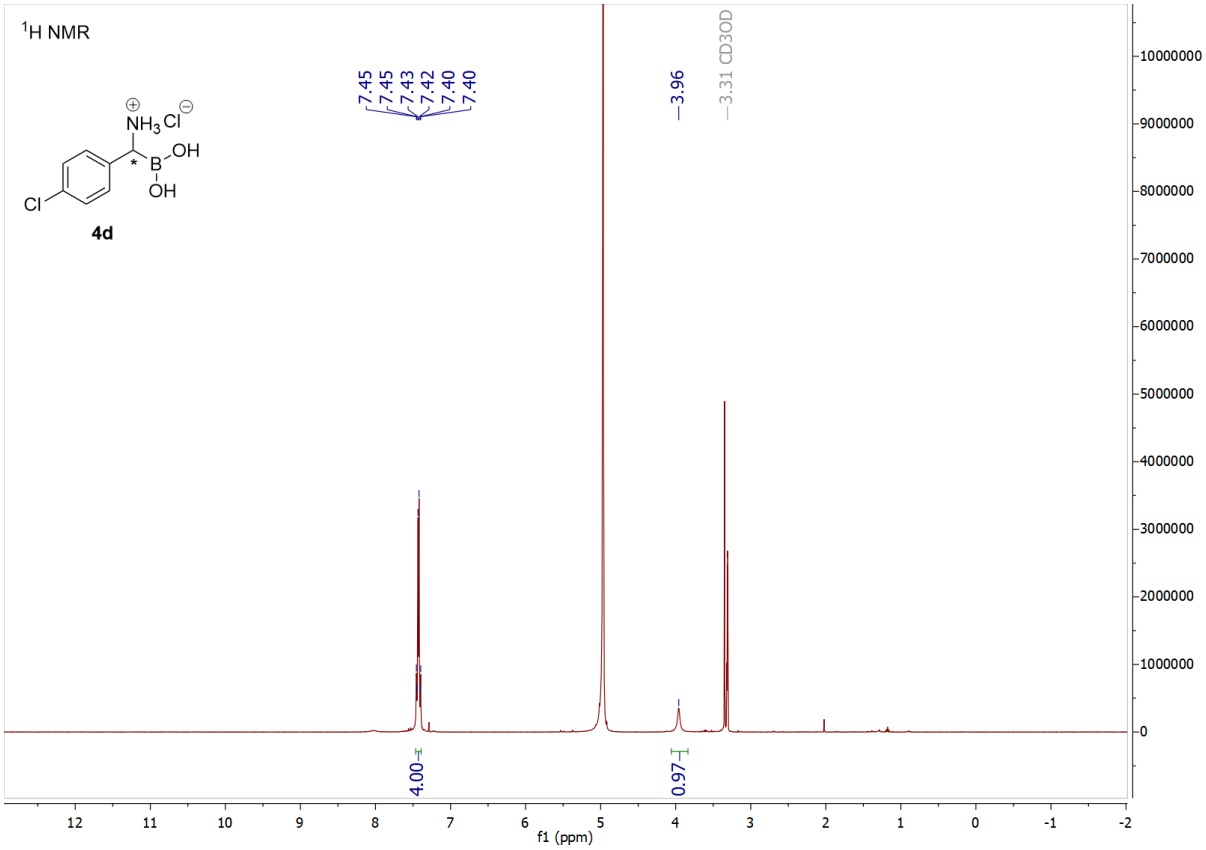


^{13}C-NMR (101 MHz, CD_3OD) of **4c**:

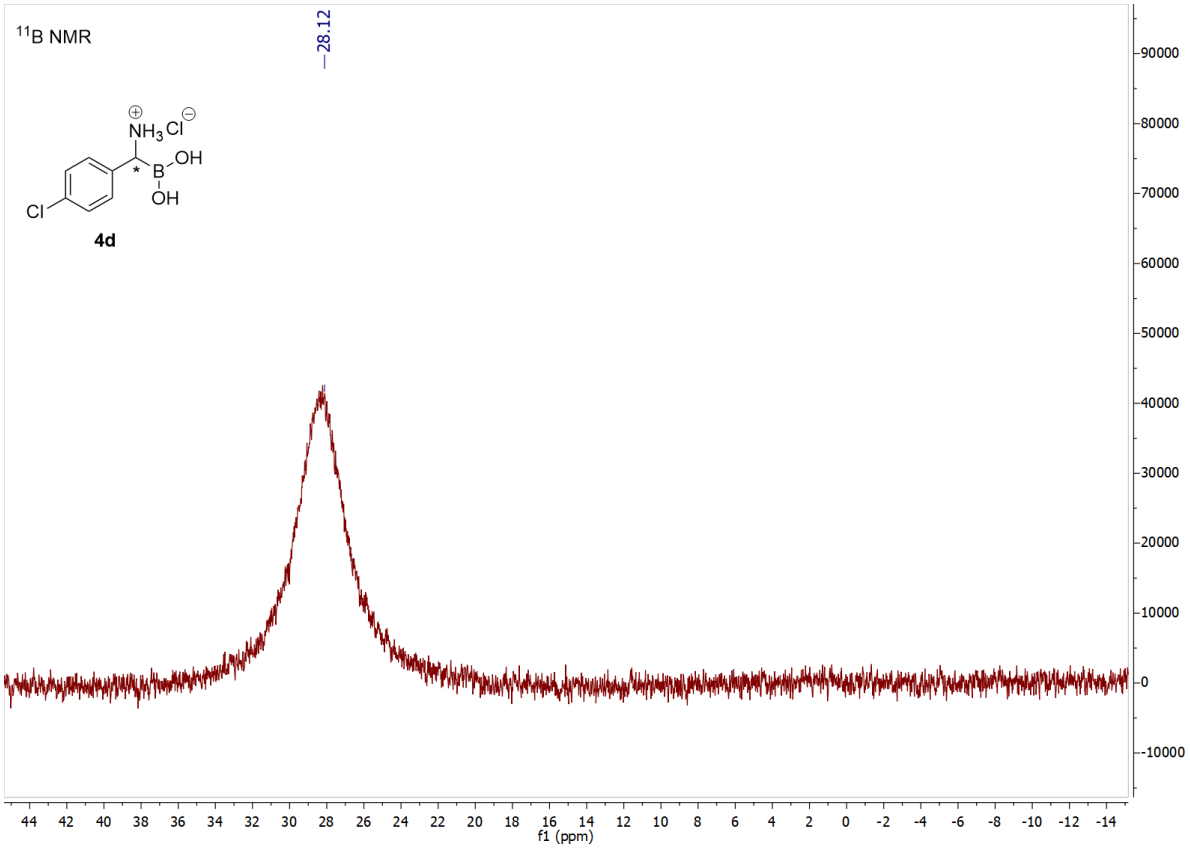


Borono(4-chlorophenyl)methanaminium chloride (4d)

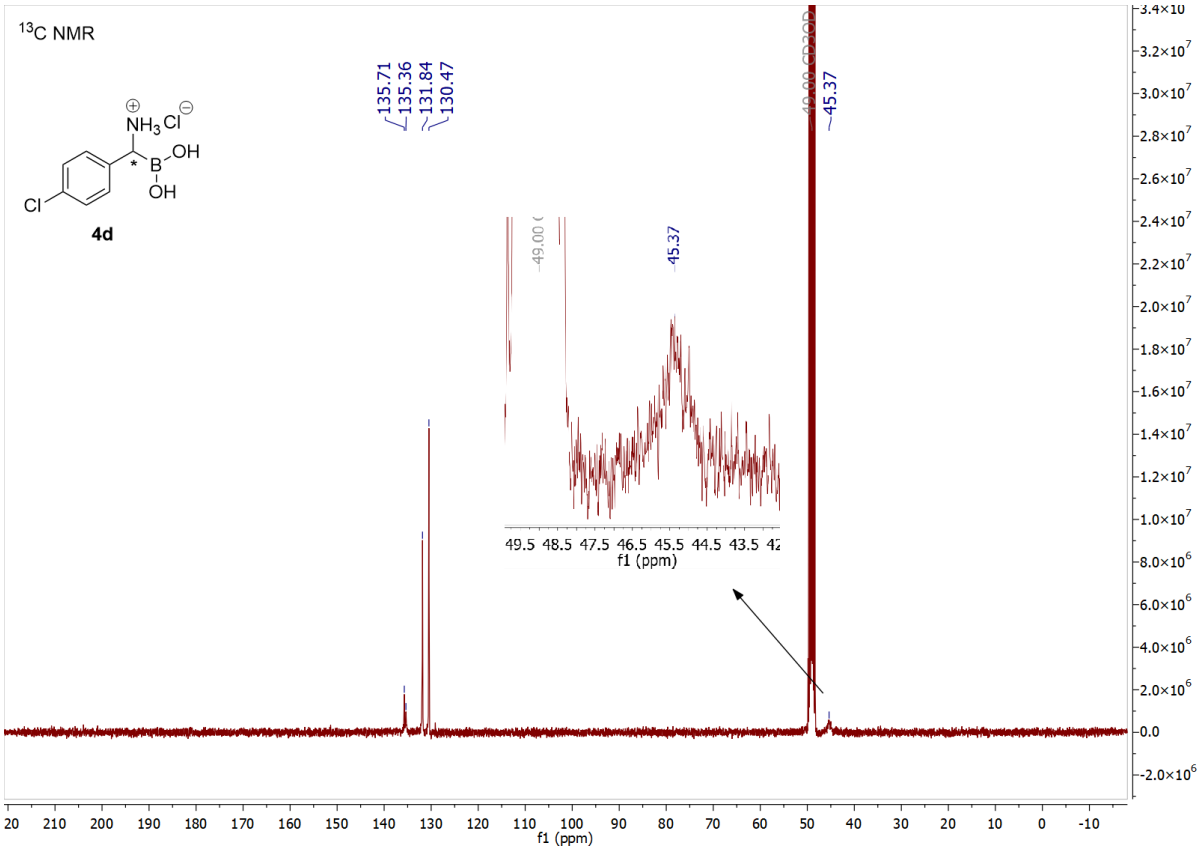
^{1}H-NMR (400 MHz, CD_3OD) of **4d**:



^{11}B-NMR (128 MHz, CD_3OD) of **4d**:

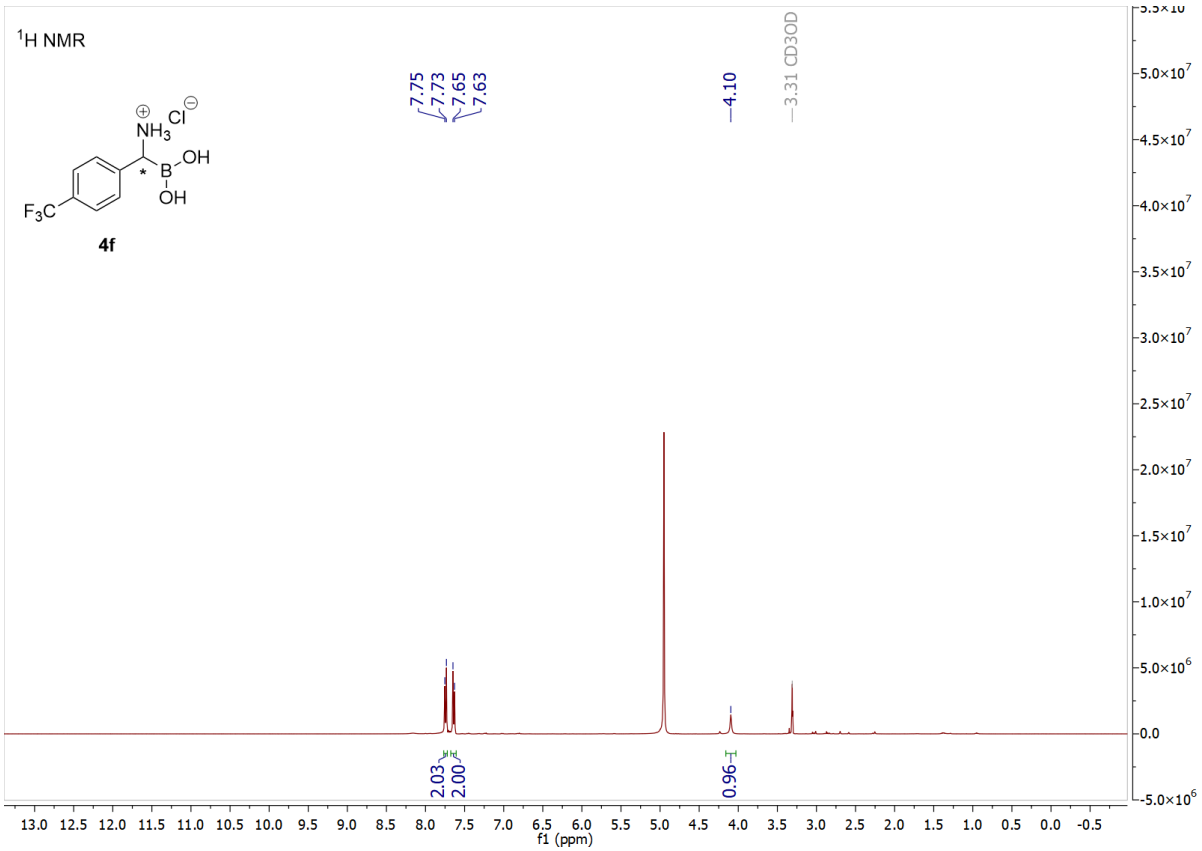


^{13}C-NMR (101 MHz, CD_3OD) of **4d**:

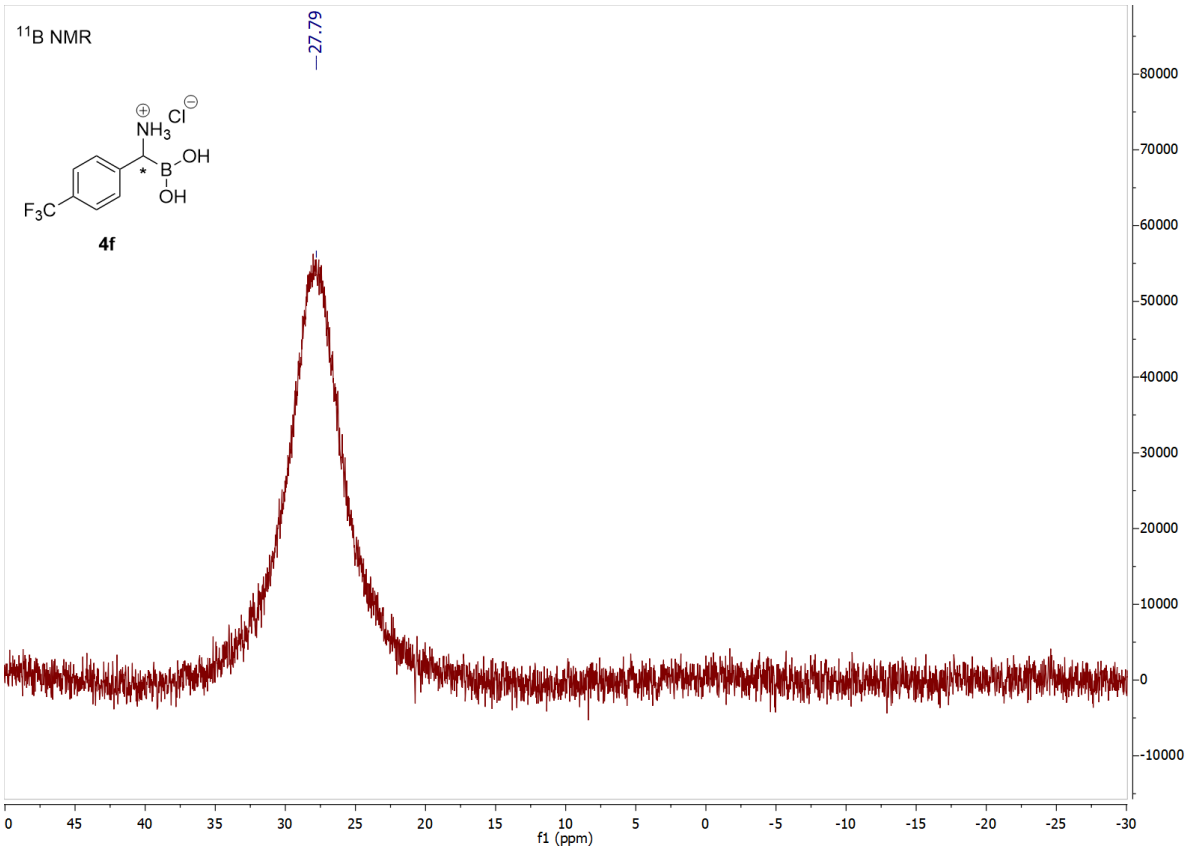


Borono(4-(trifluoromethyl)phenyl)methanaminium chloride (4f)

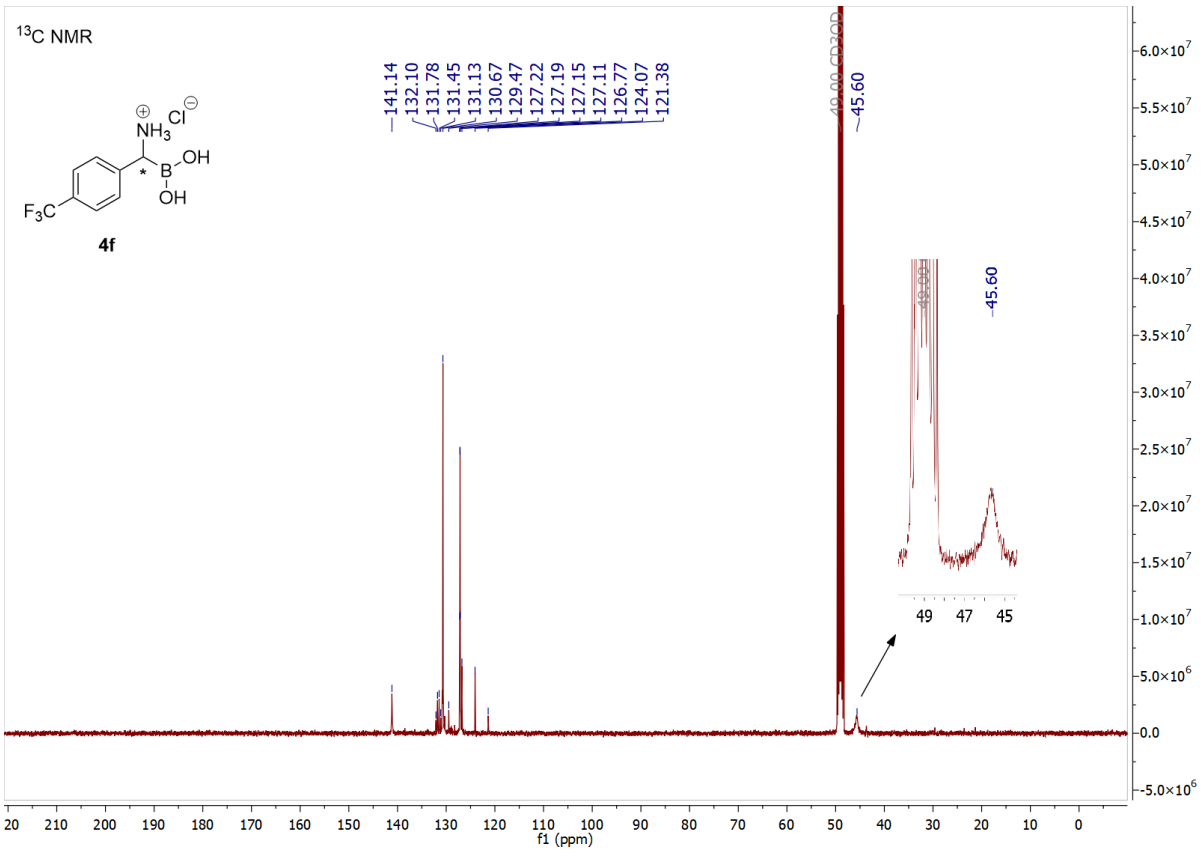
^{1}H-NMR (400 MHz, CD_3OD) of **4f**:



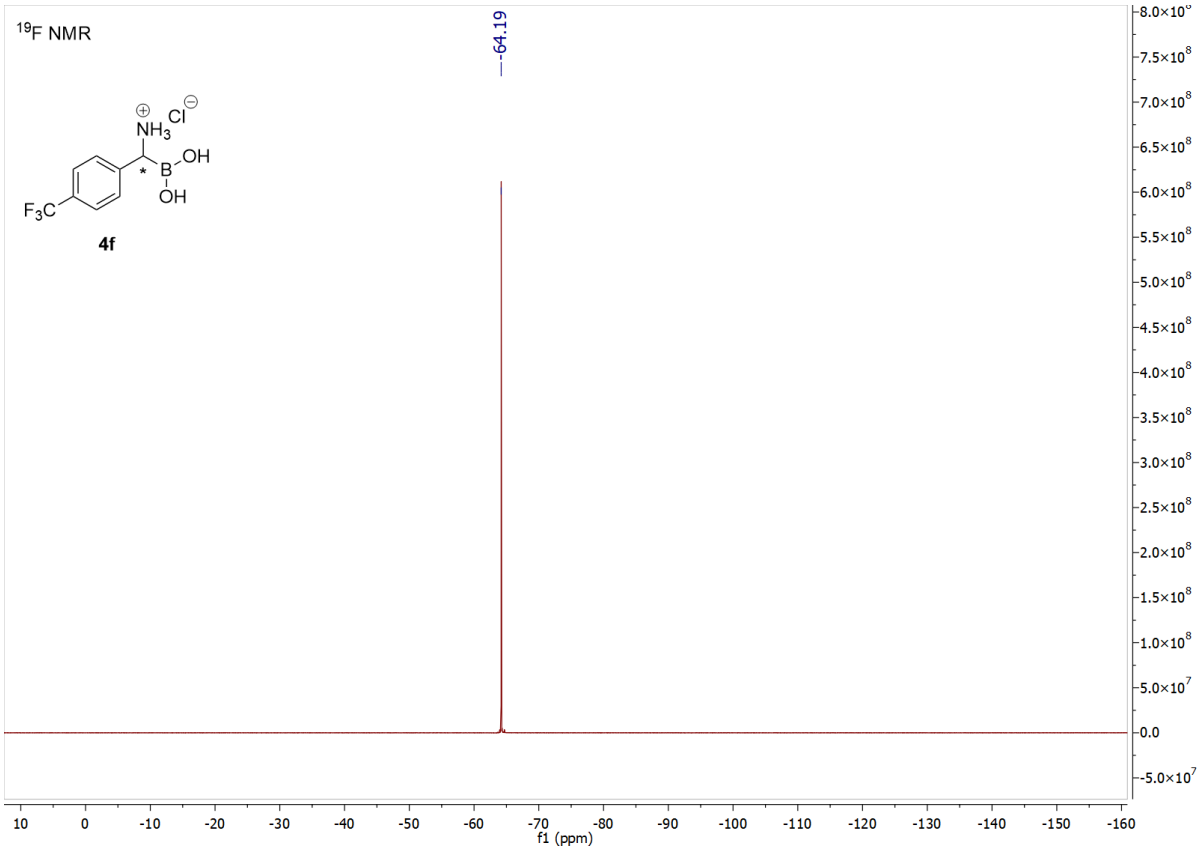
^{11}B-NMR (128 MHz, CD_3OD) of **4f**:



^{13}C-NMR (101 MHz, CD_3OD) of **4f**:

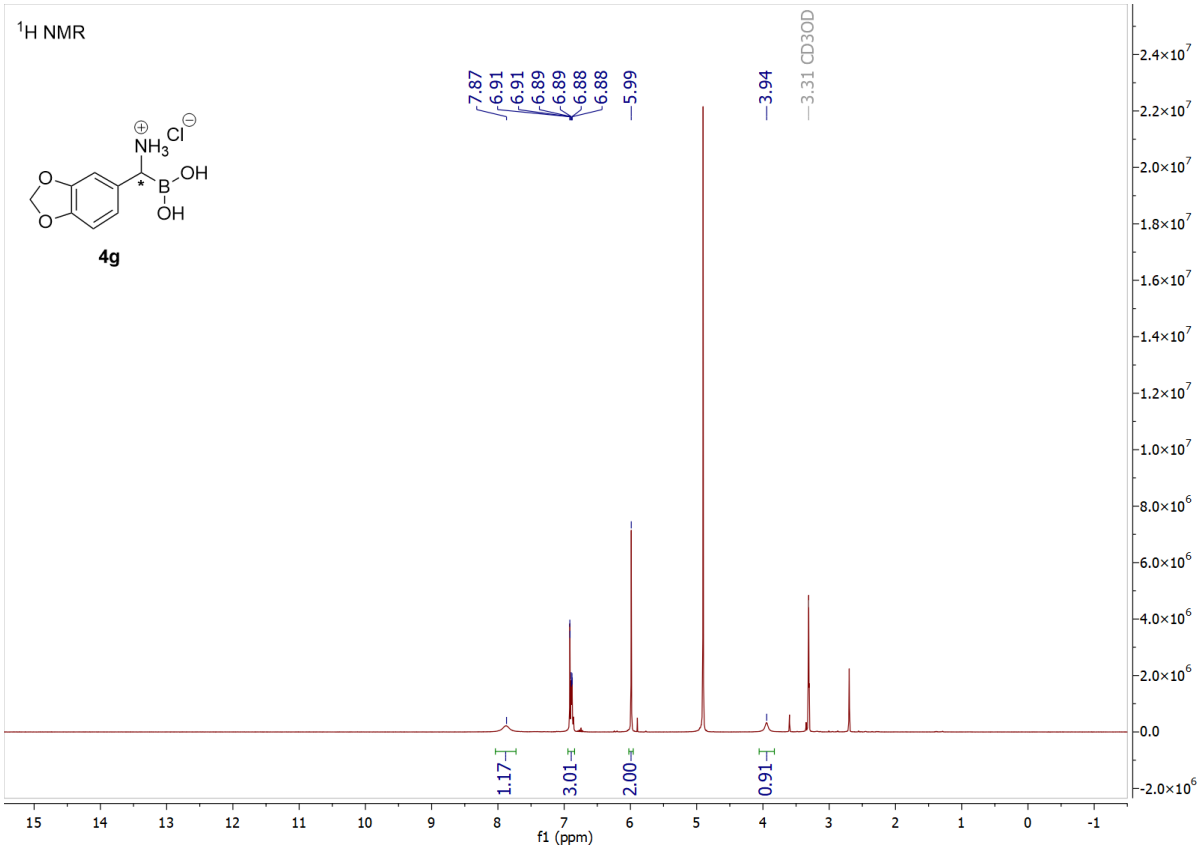


^{19}F-NMR (376 MHz, CD_3OD) of **4f**:

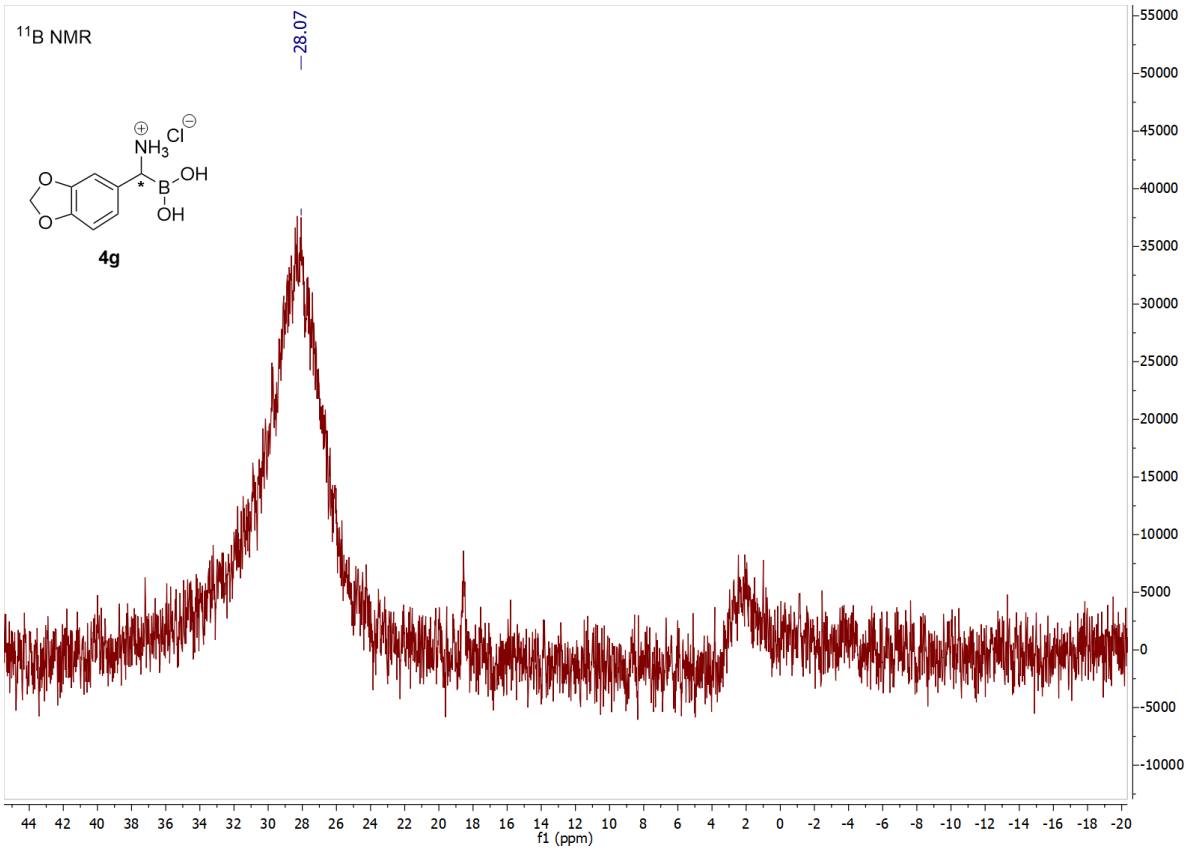


(Benzo[*d*][1,3]dioxol-5-yl)boronomethanaminium chloride (4g)

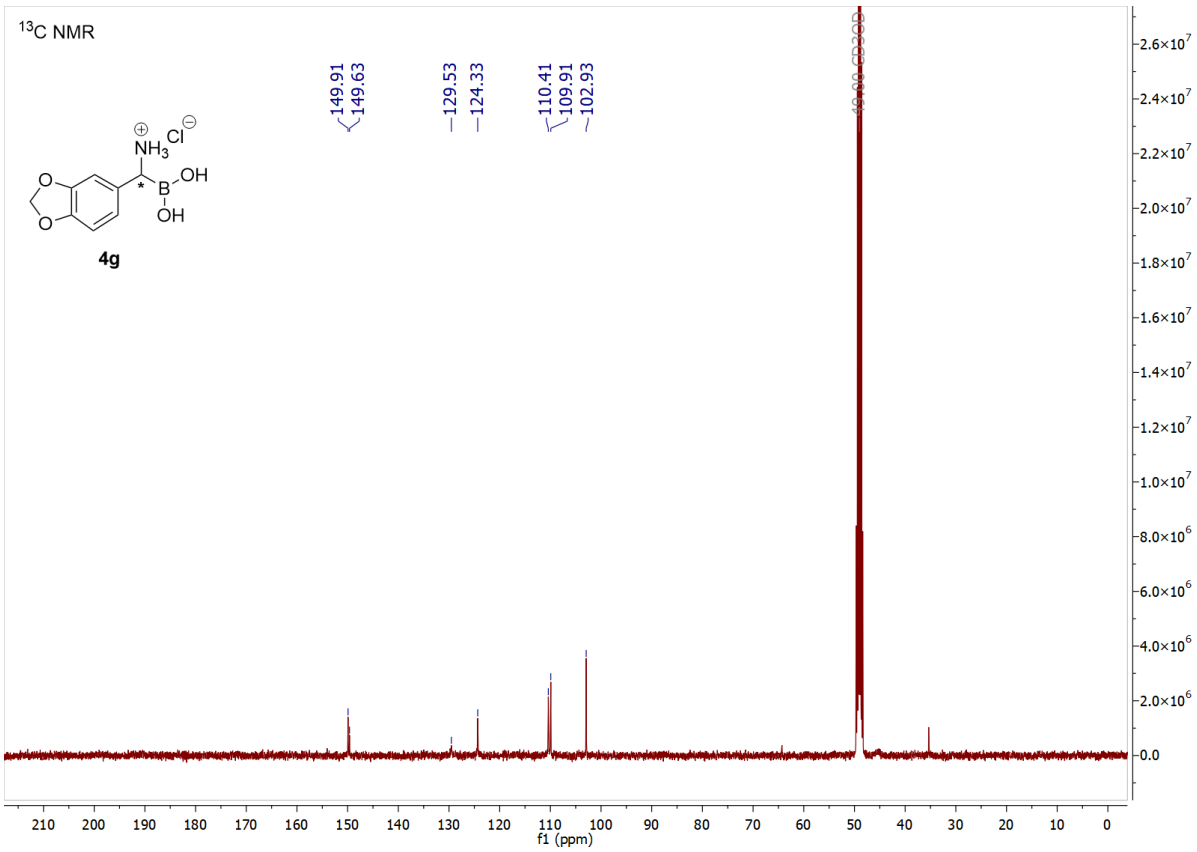
^{1}H-NMR (400 MHz, CD_3OD) of **4g**:



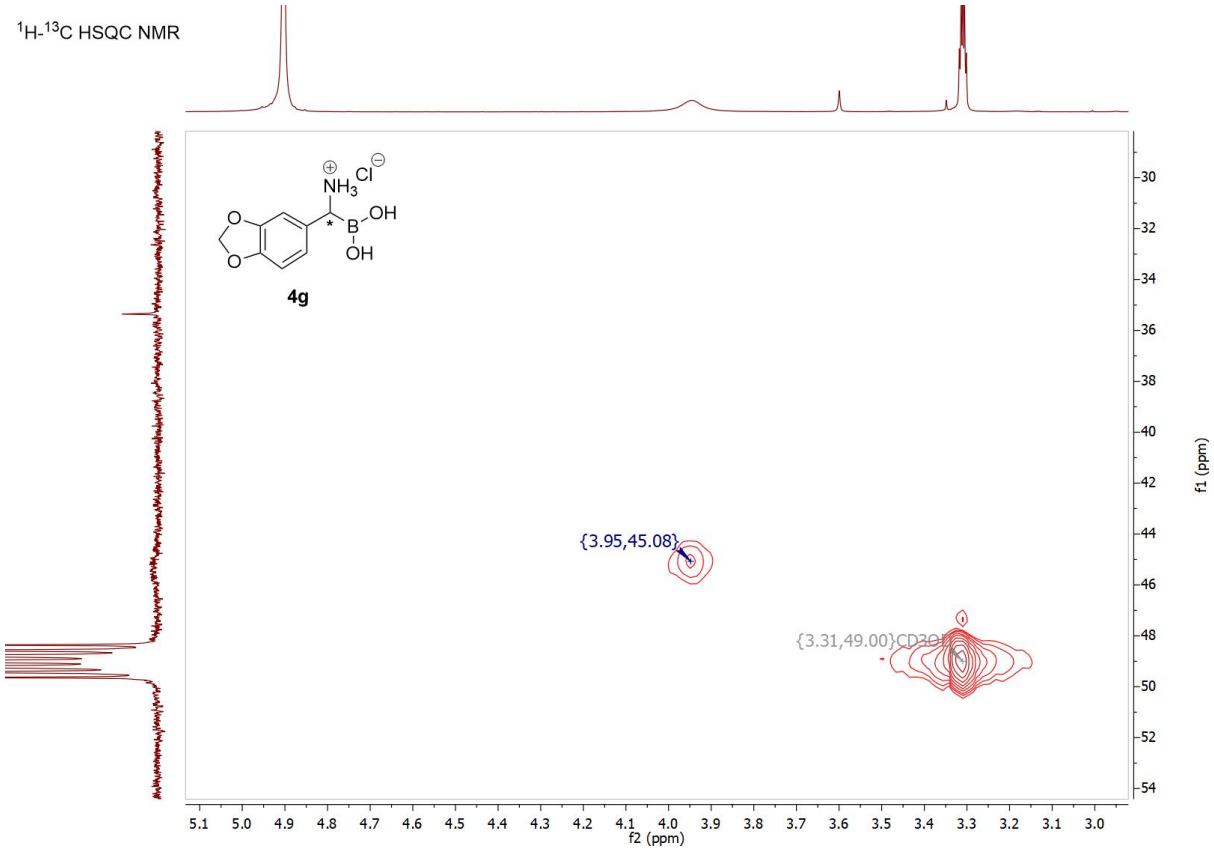
^{11}B-NMR (128 MHz, CD_3OD) of **4g**:



^{13}C-NMR (101 MHz, CD_3OD) of **4g**:

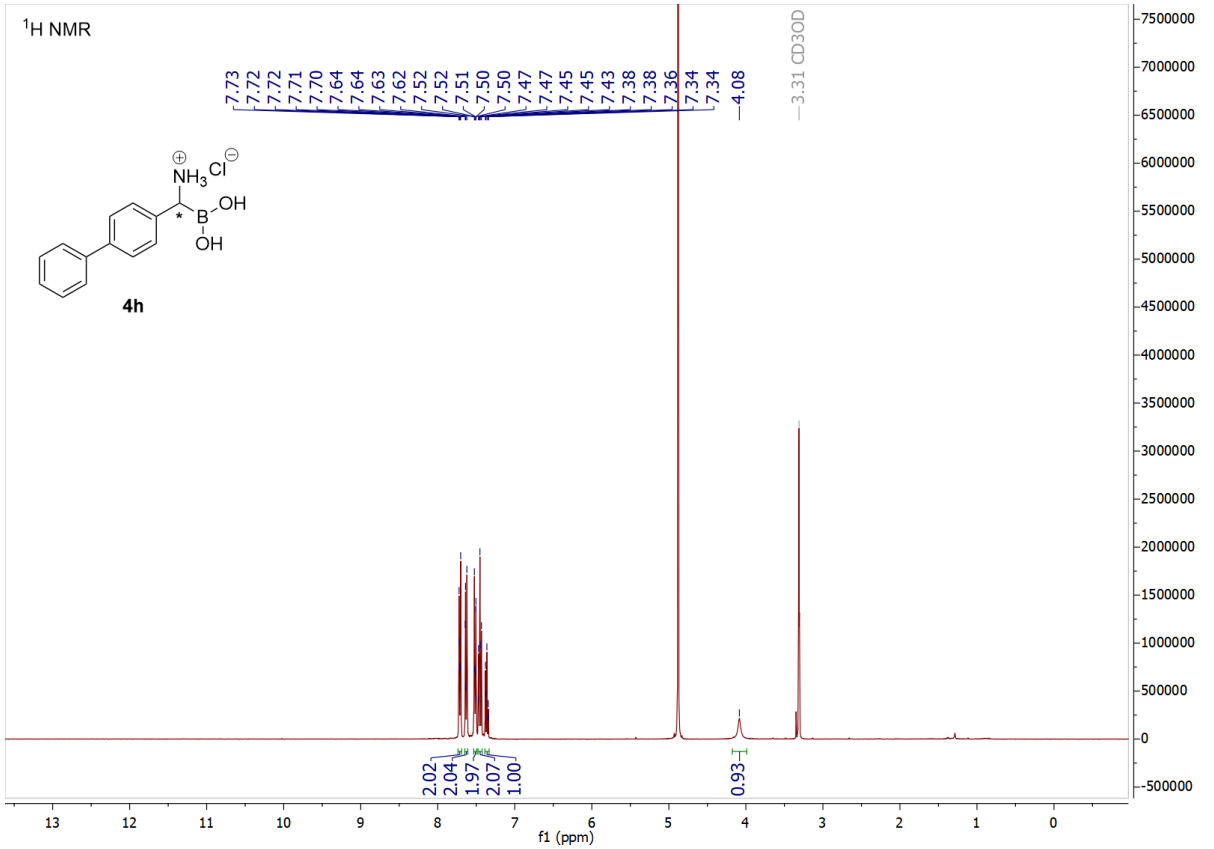


^{1}H-^{13}C HSQC-NMR (CD_3OD) of **4g**:

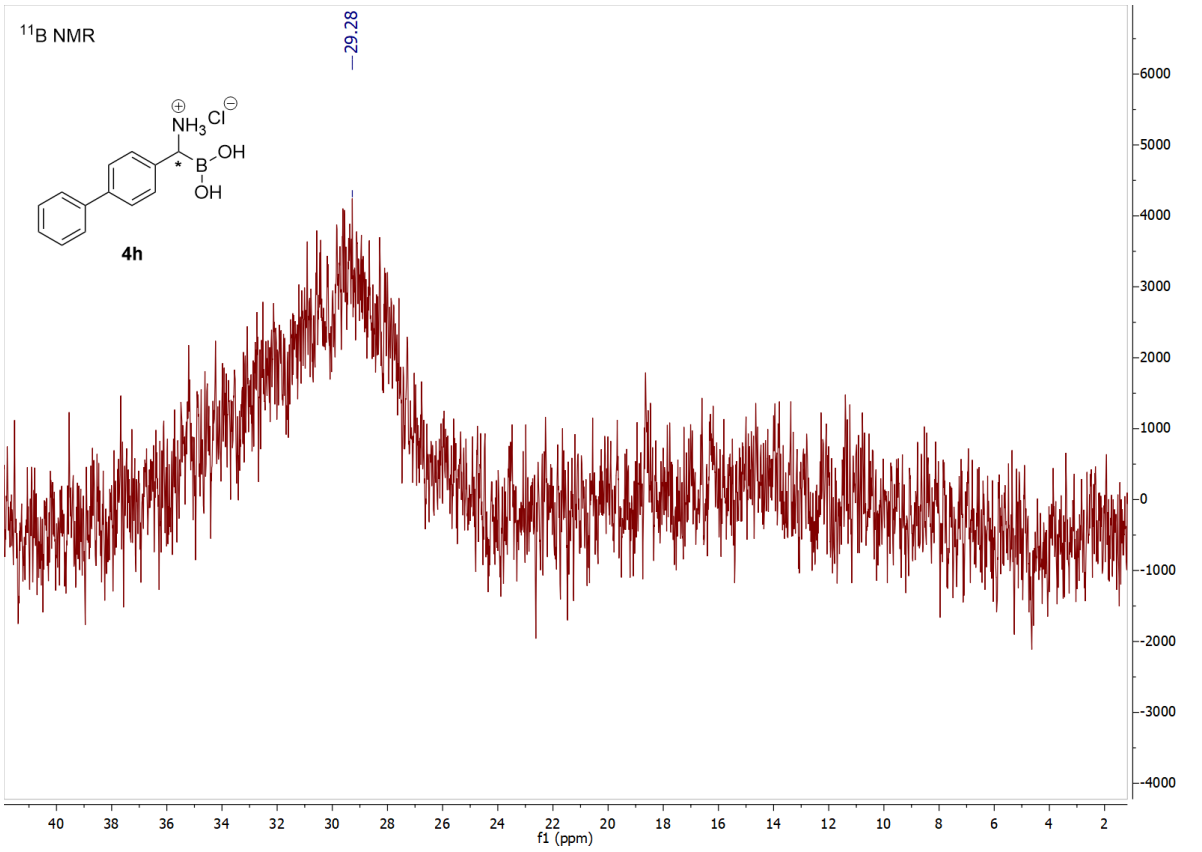


[1,1'-Biphenyl]-4-yl(borono)methanaminium chloride (4h)

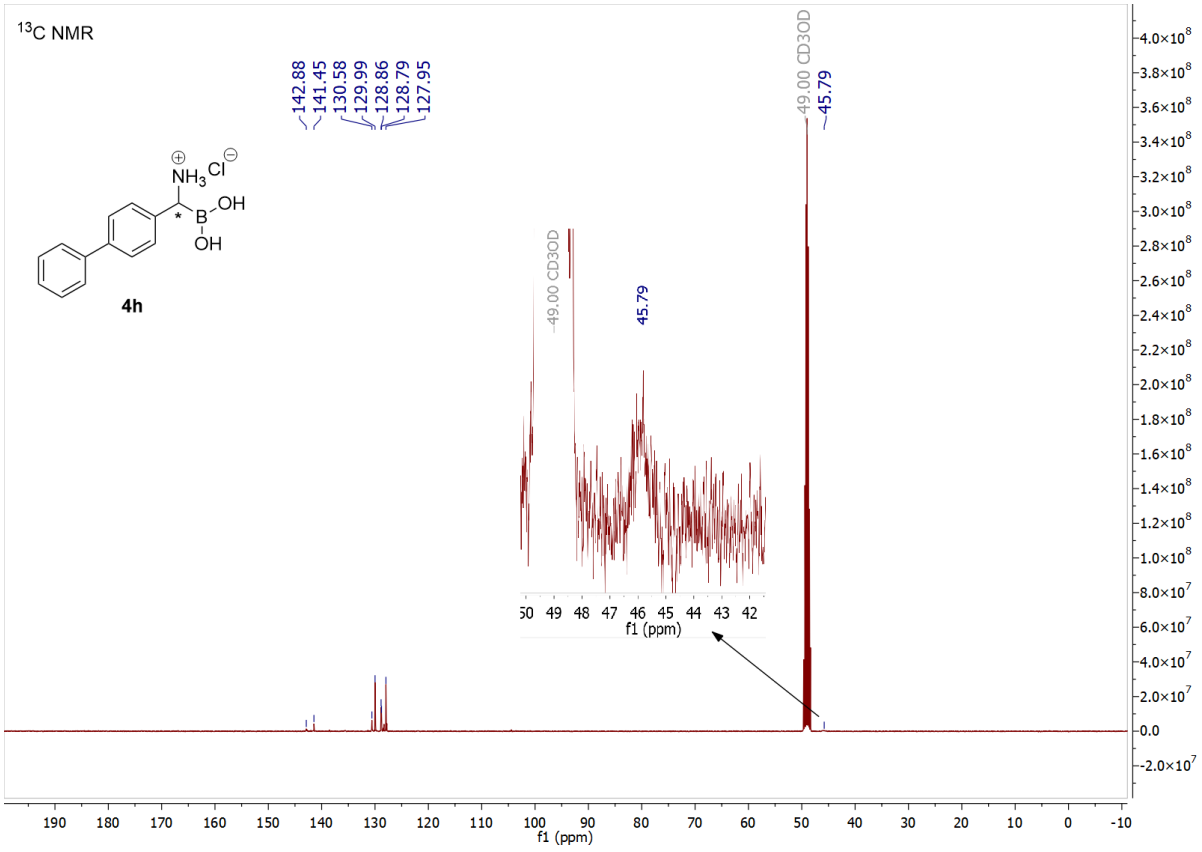
^{1}H-NMR (400 MHz, CD_3OD) of **4h**:



^{11}B-NMR (128 MHz, CD_3OD) of **4h**:

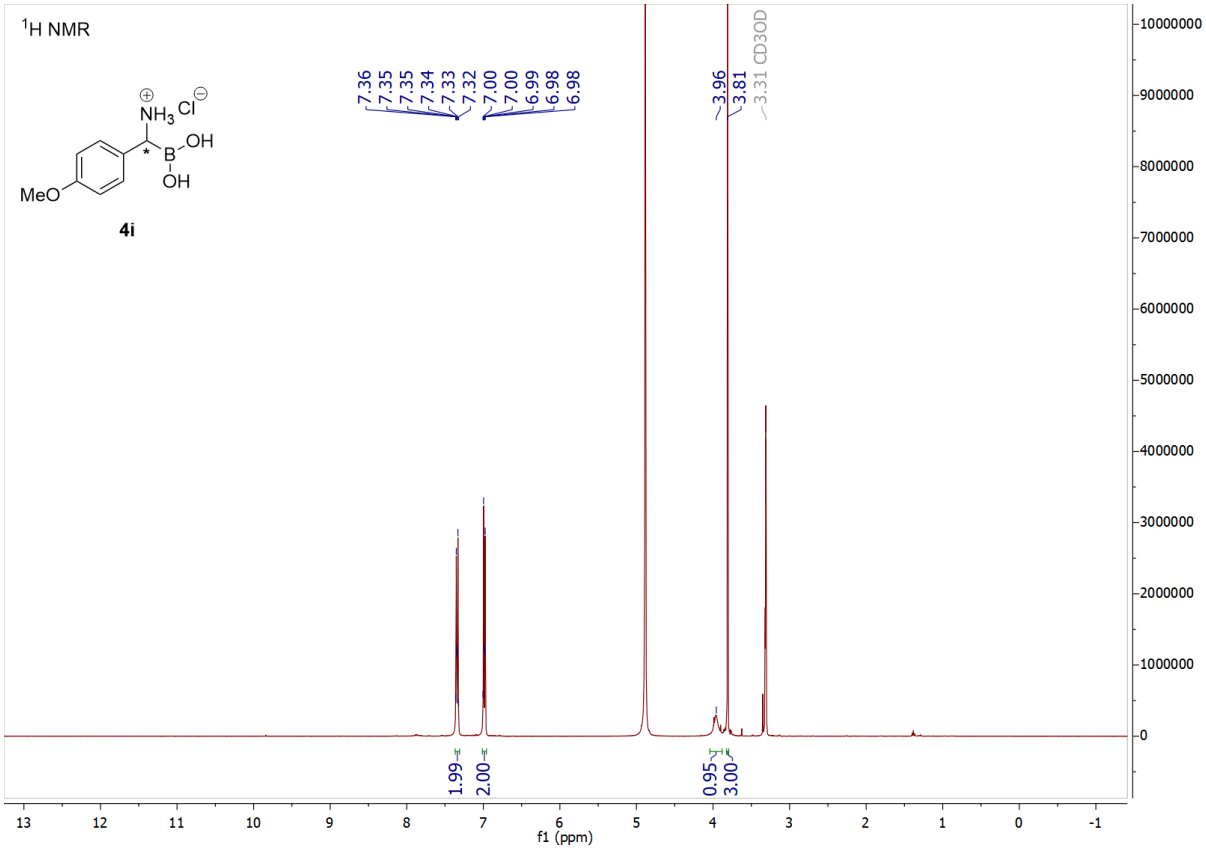


^{13}C-NMR (101 MHz, CD_3OD) of **4h**:

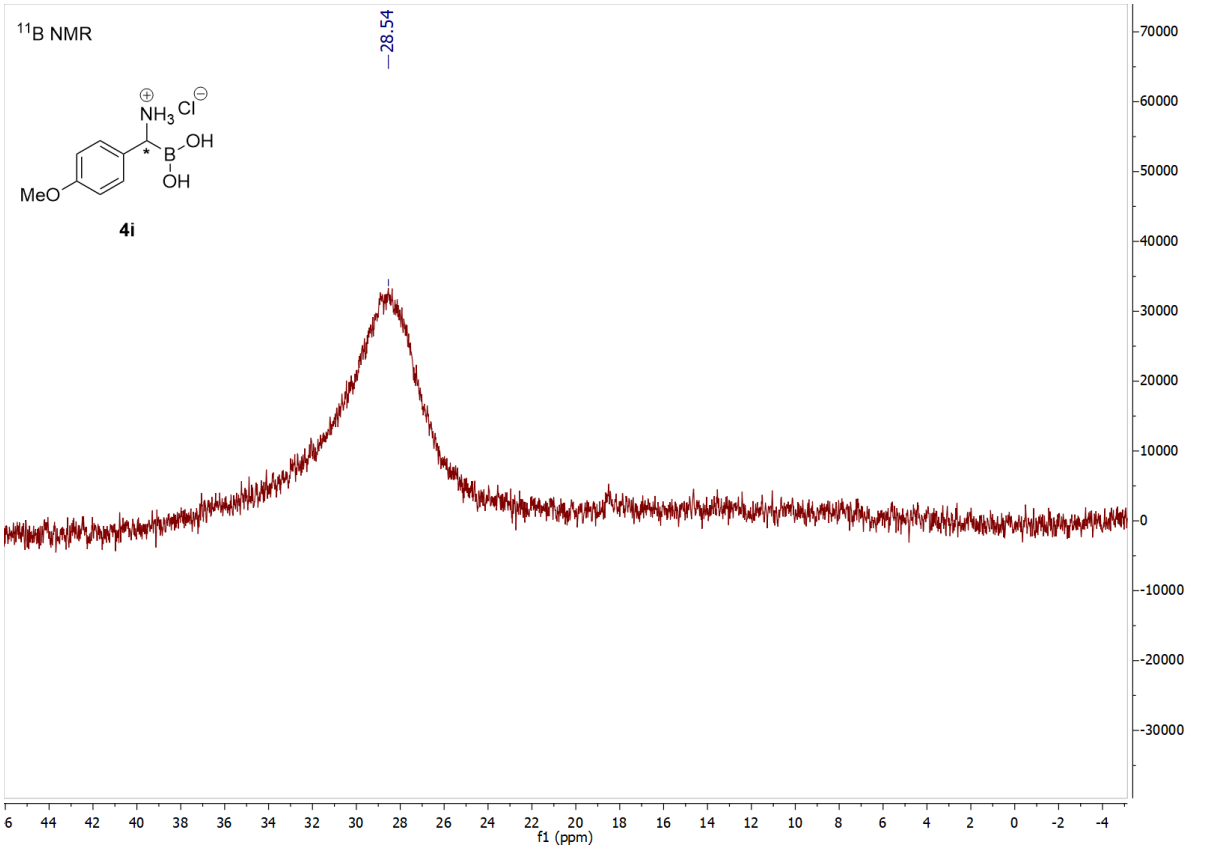


Borono(4-methoxyphenyl)methanaminium chloride (4i)

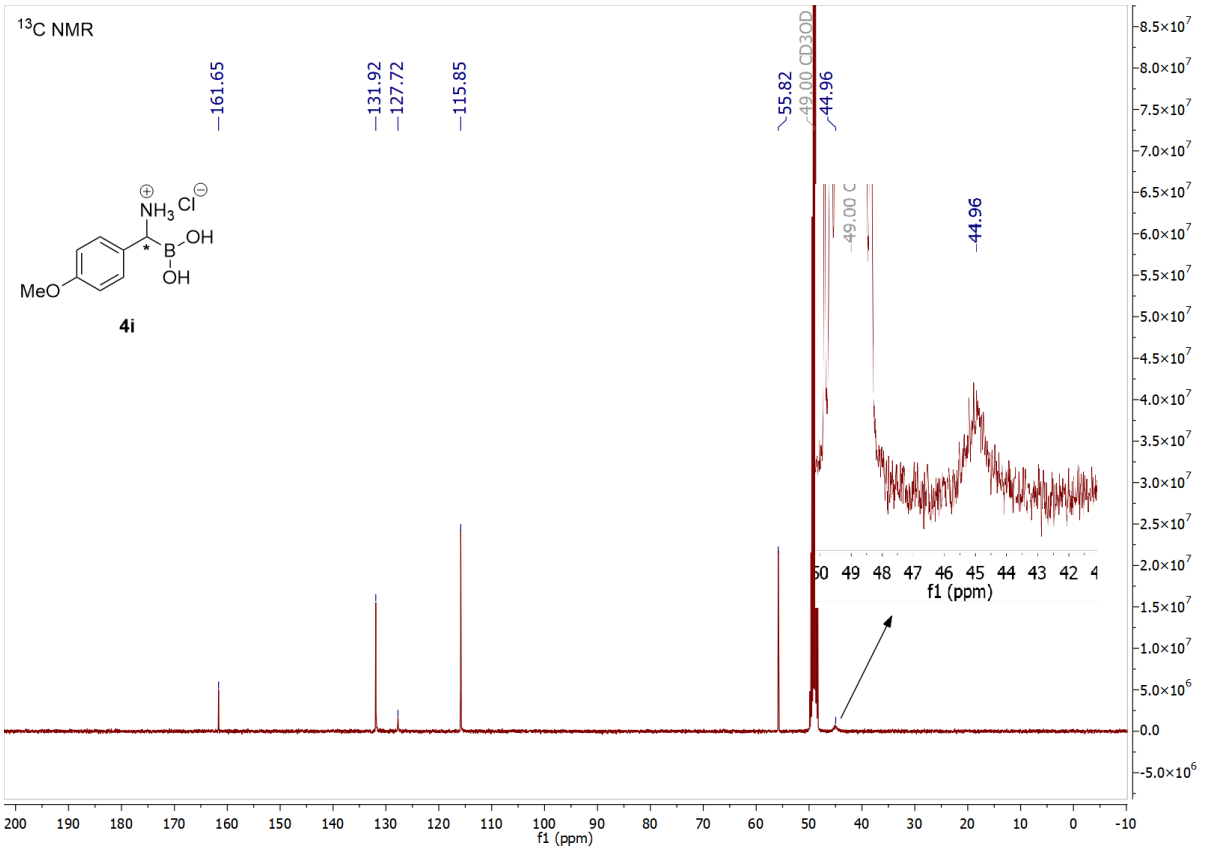
^{1}H-NMR (400 MHz, CD_3OD) of **4i**:



^{11}B-NMR (128 MHz, CD_3OD) of **4i**:

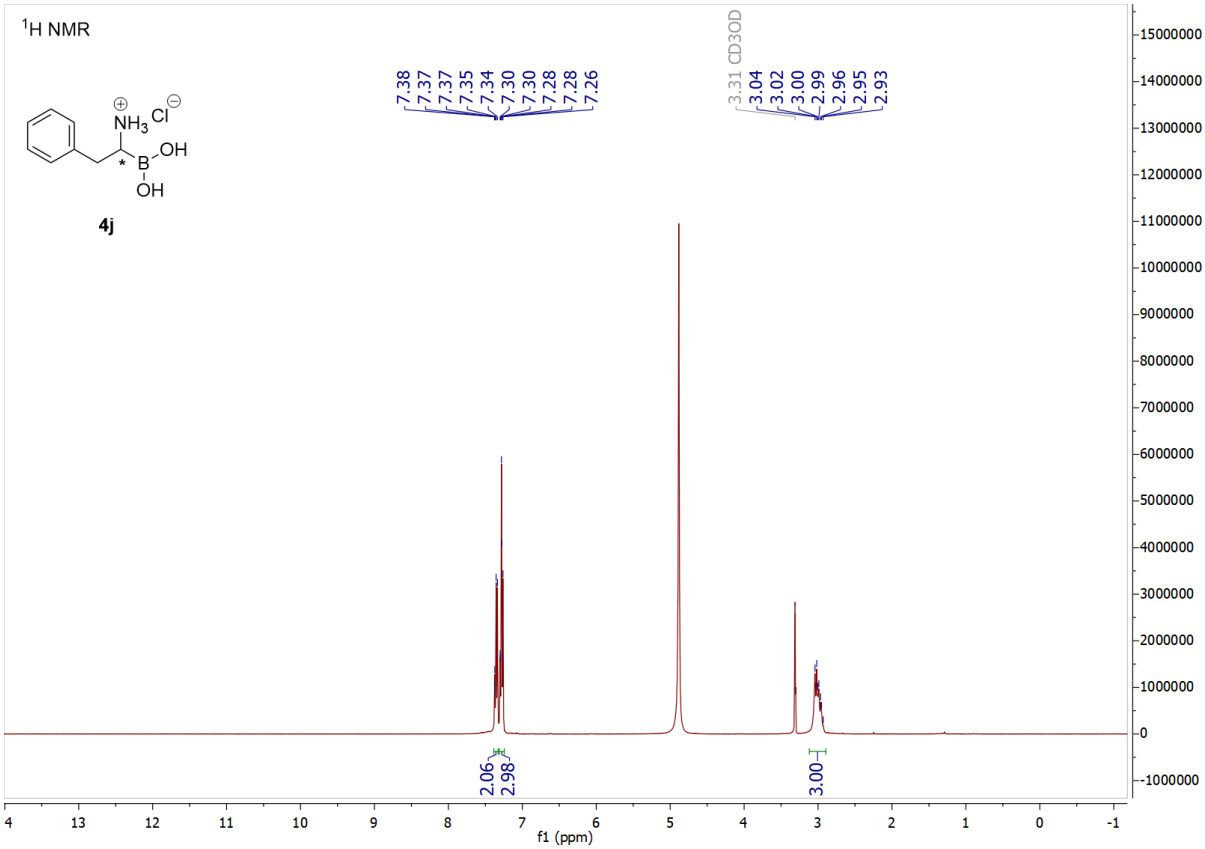


^{13}C-NMR (101 MHz, CD_3OD) of **4i**:

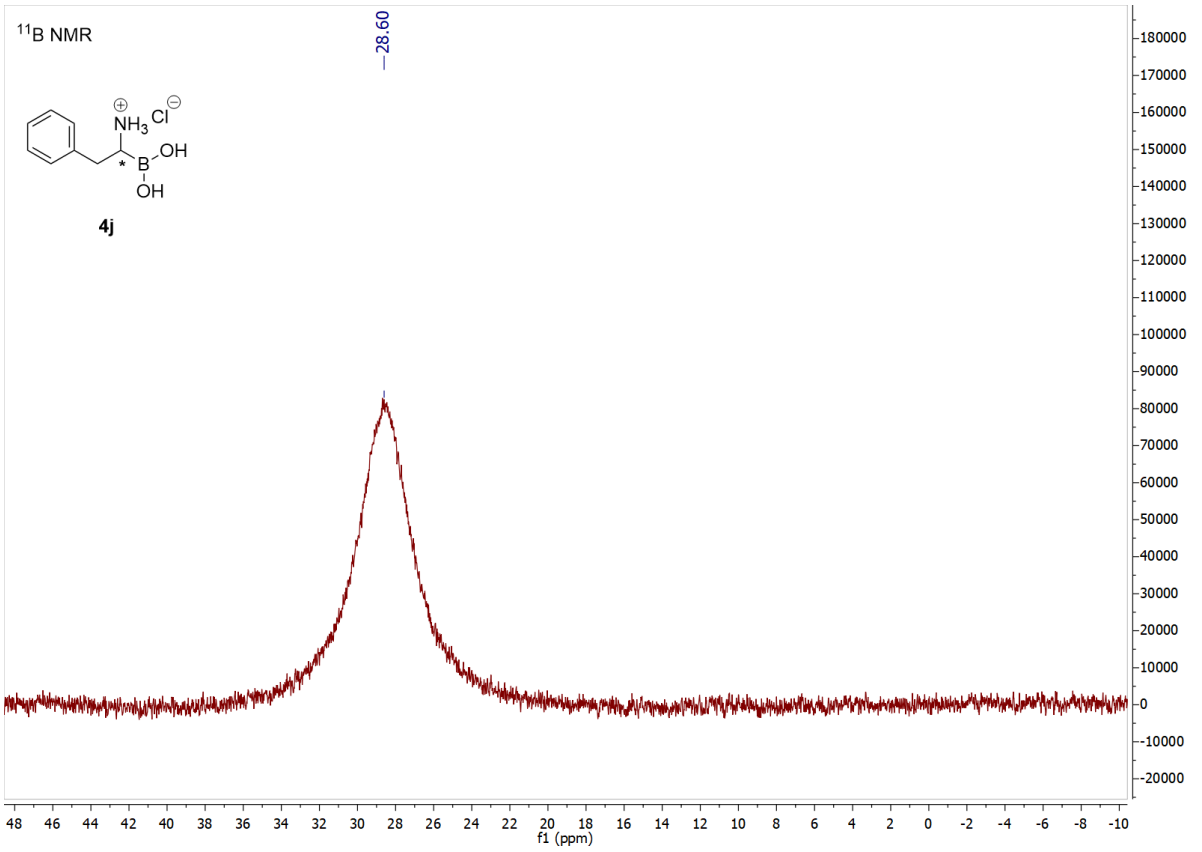


1-Borono-2-phenylethan-1-aminium chloride (4j)

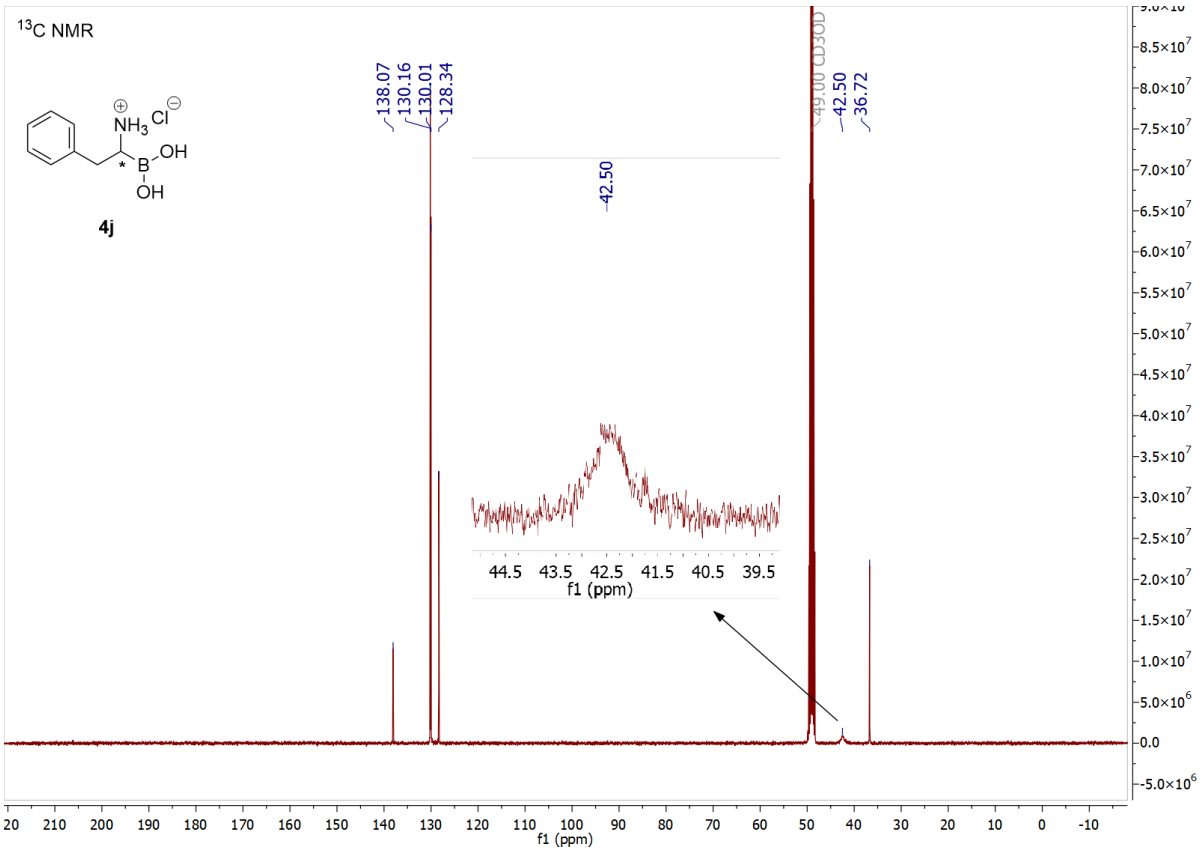
^{1}H-NMR (400 MHz, CD_3OD) of **4j**:



^{11}B-NMR (128 MHz, CD_3OD) of **4j**:

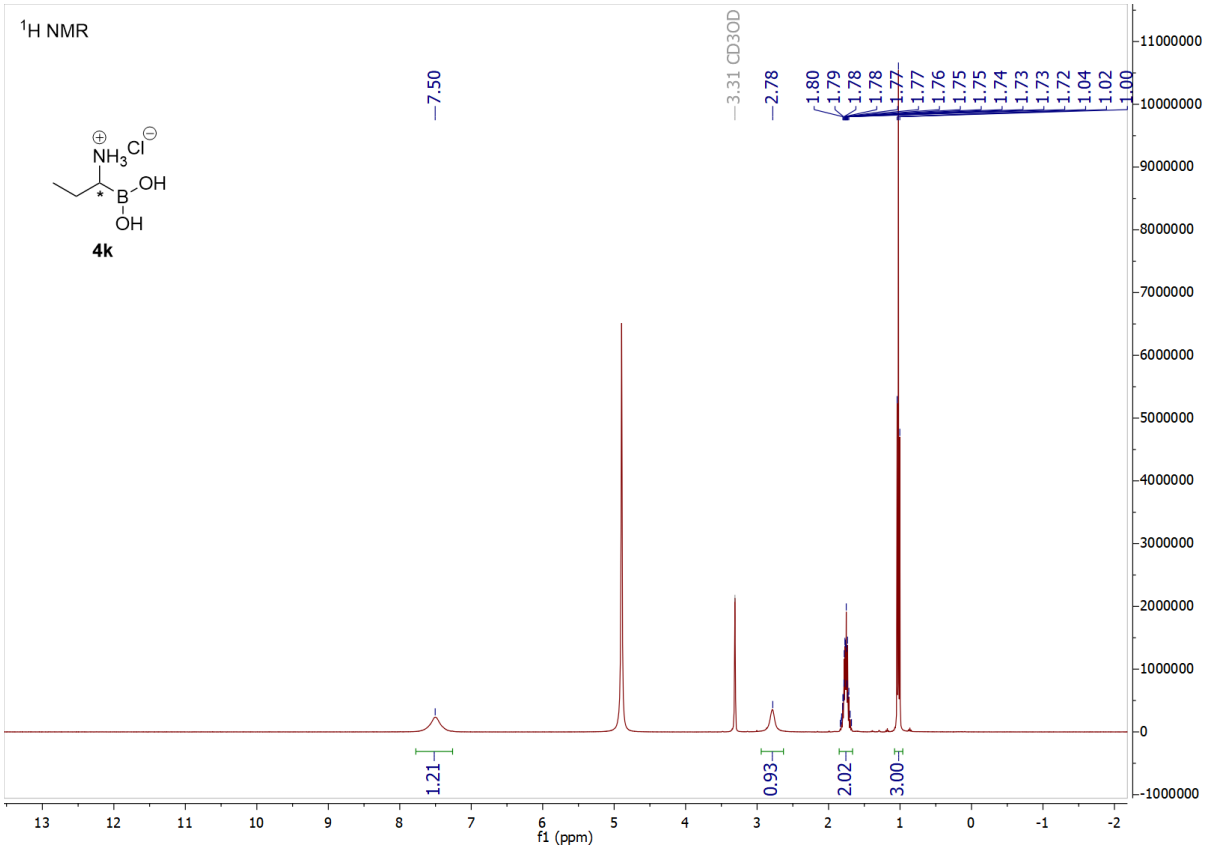


^{13}C-NMR (101 MHz, CD_3OD) of **4j**:

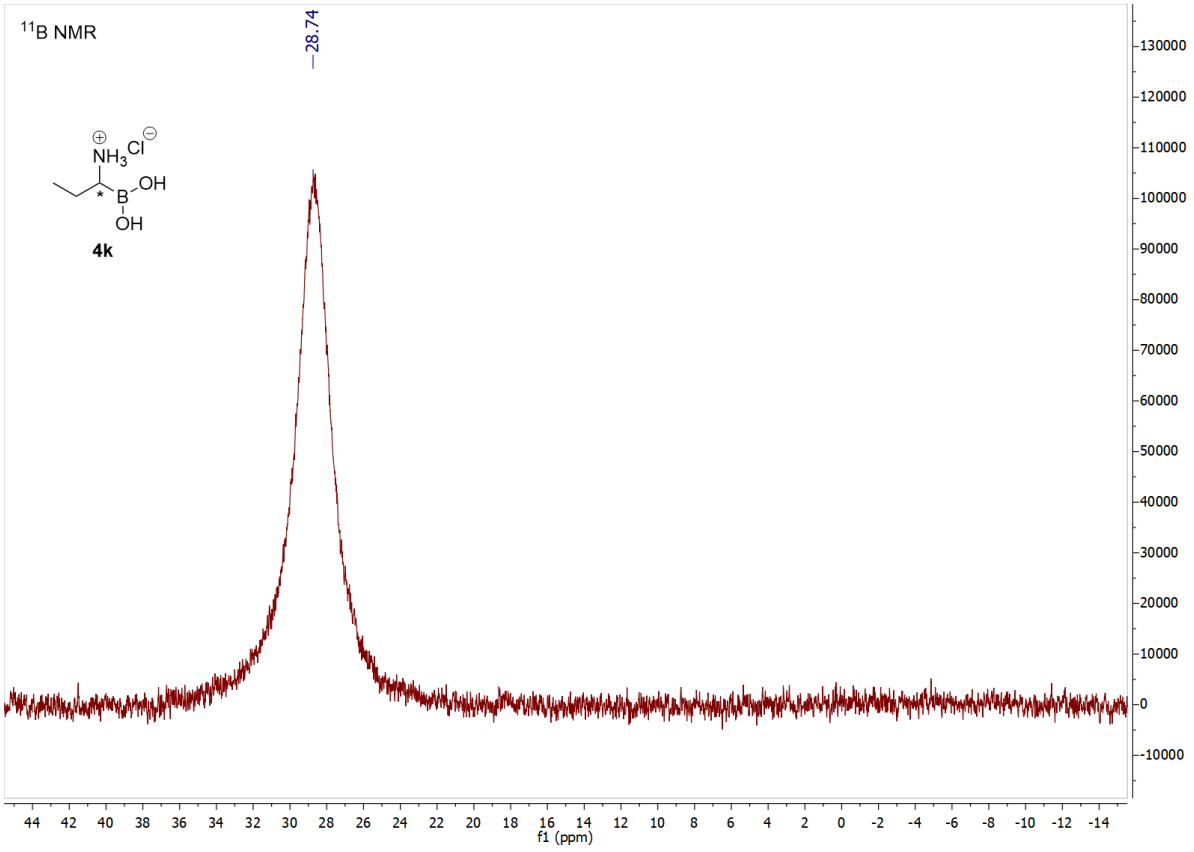


1-Borono-propan-1-aminium chloride (4k)

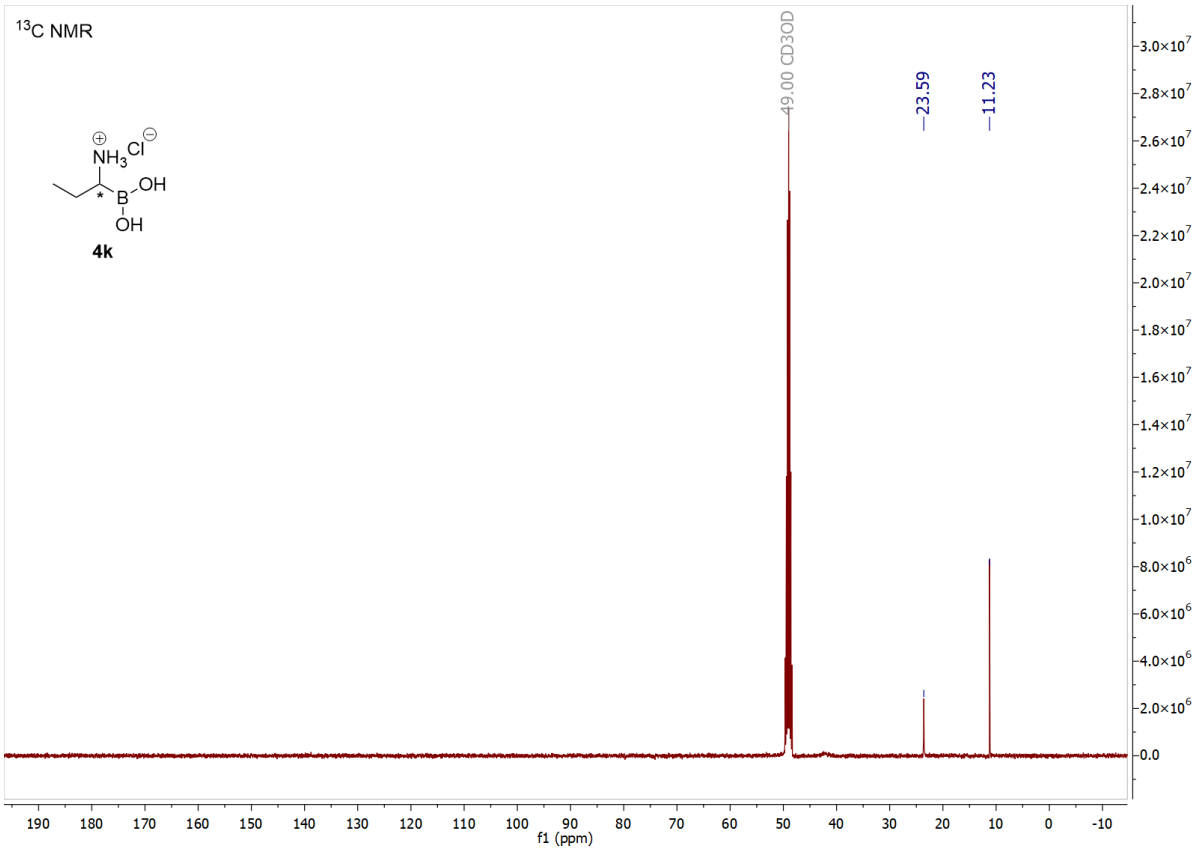
^{1}H-NMR (400 MHz, CD_3OD) of **4k**:



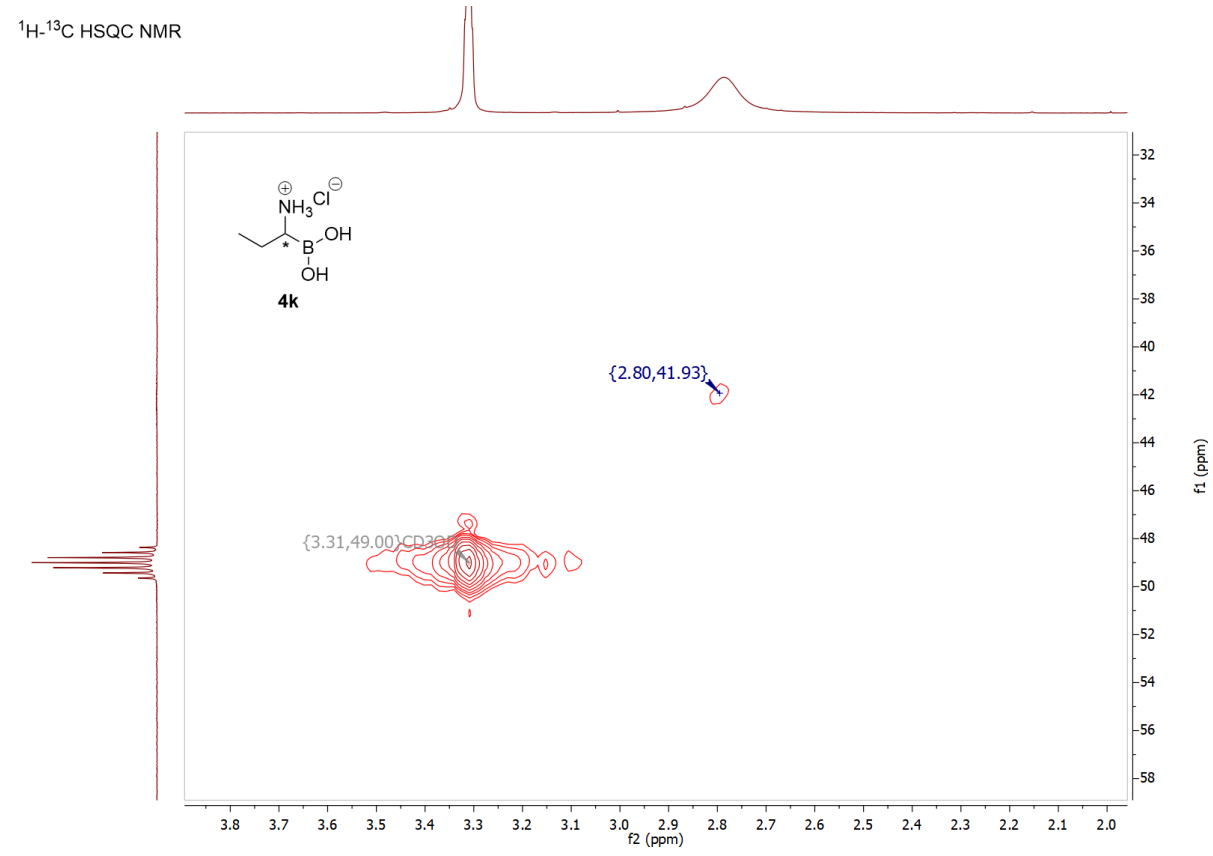
^{11}B-NMR (128 MHz, CD_3OD) of **4k**:



^{13}C-NMR (101 MHz, CD_3OD) of **4k**:

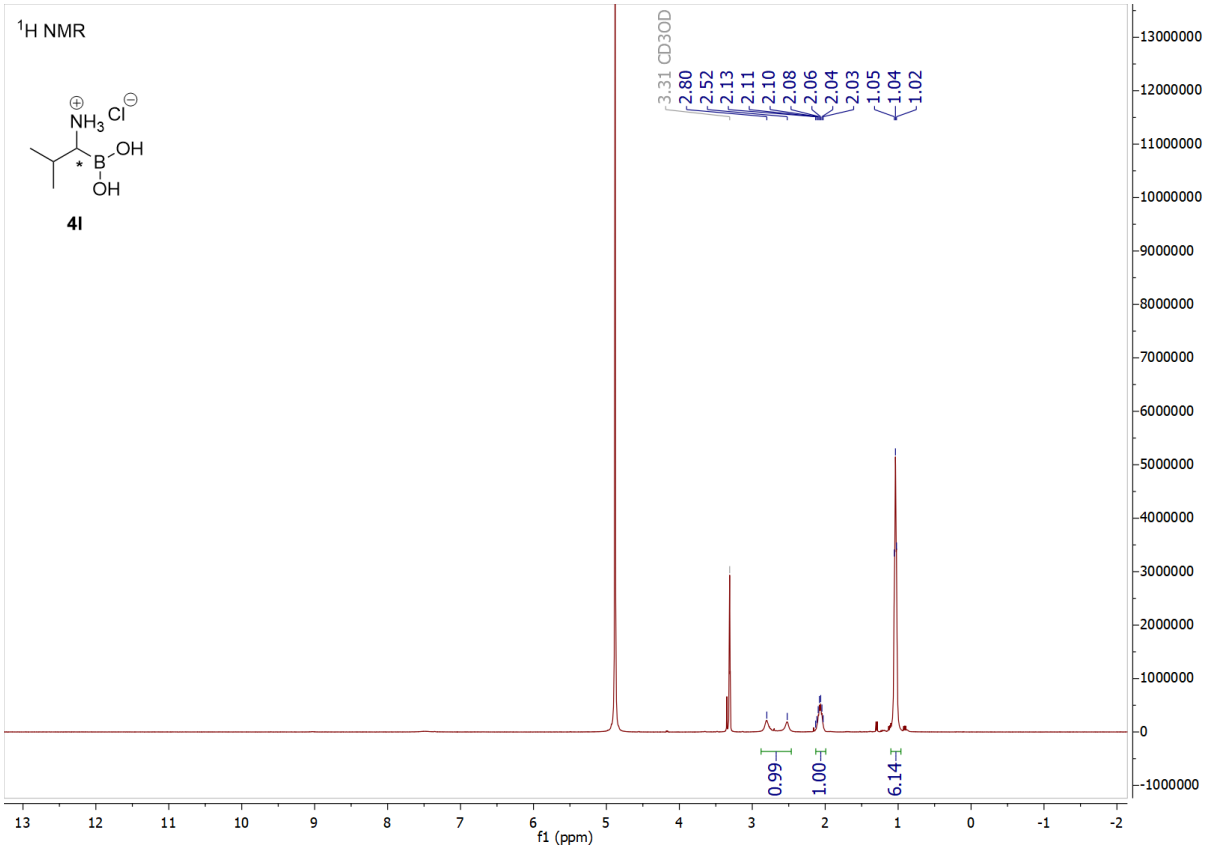


^{1}H-^{13}C HSQC-NMR (CD_3OD) of **4k**:

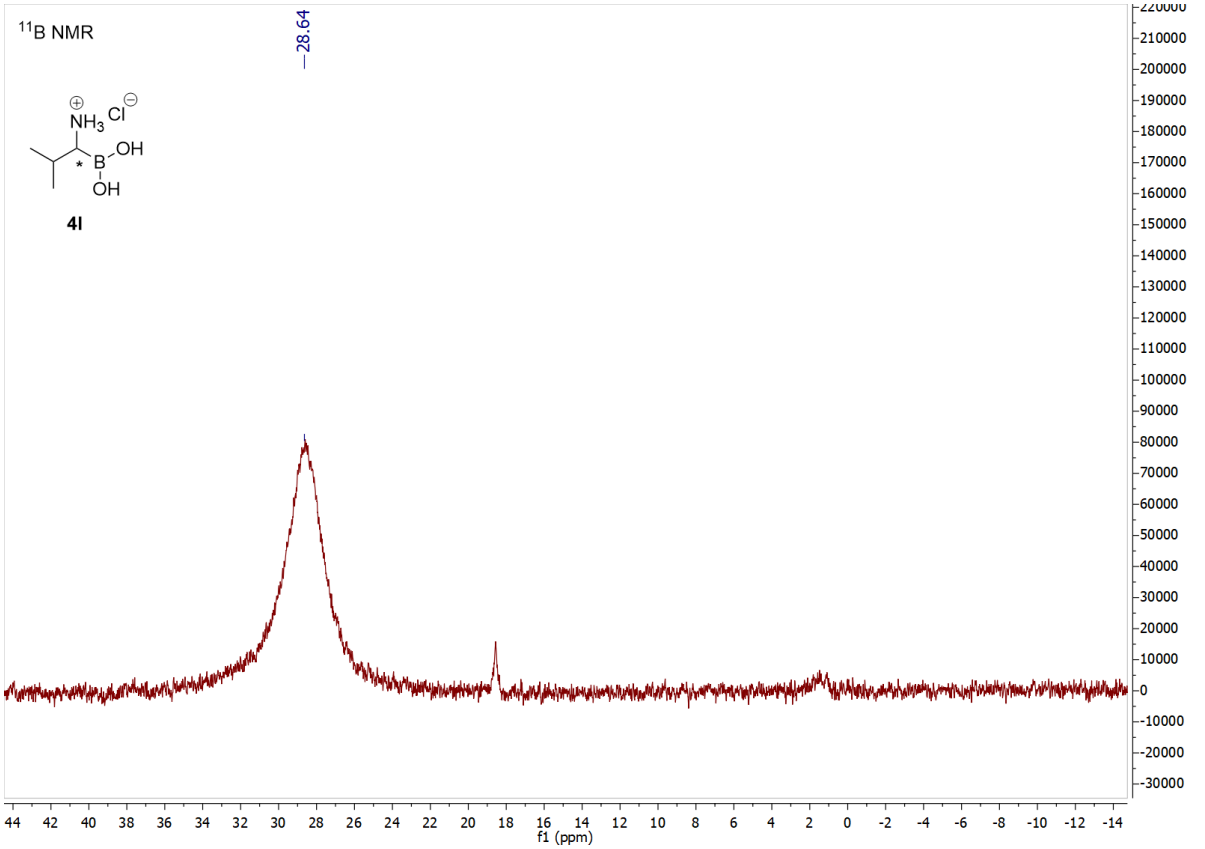


1-Borono-2-methylpropan-1-aminium chloride (4l)

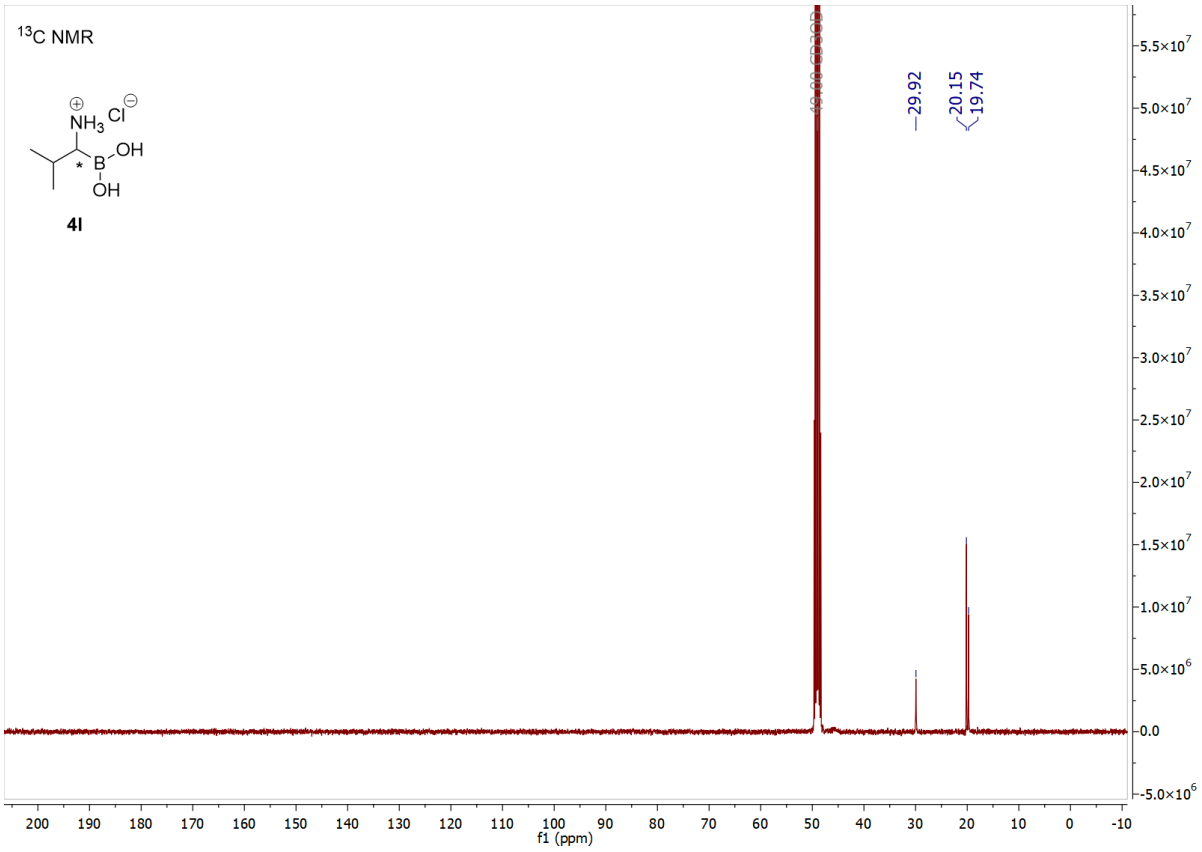
^{1}H-NMR (400 MHz, CD_3OD) of **4l**:



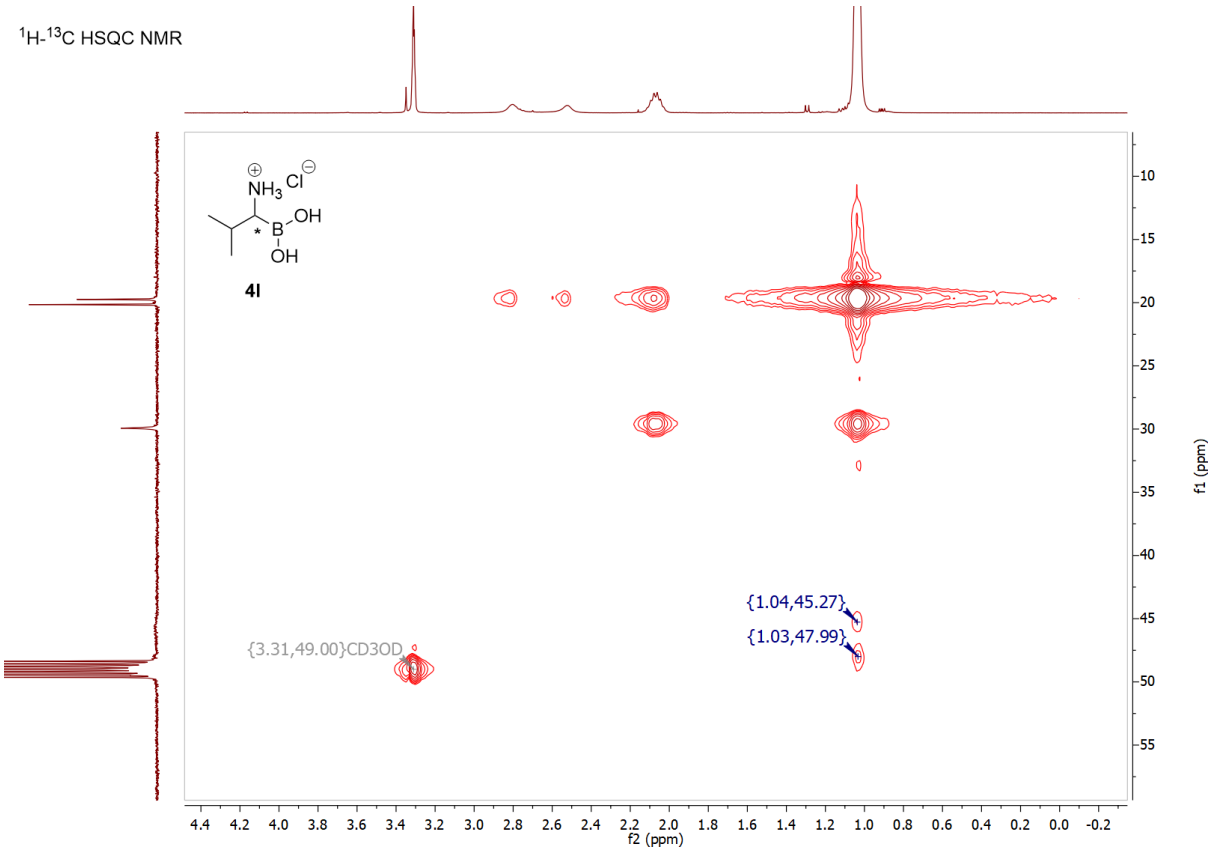
^{11}B-NMR (128 MHz, CD_3OD) of **4l**:



^{13}C-NMR (101 MHz, CD_3OD) of **4l**:

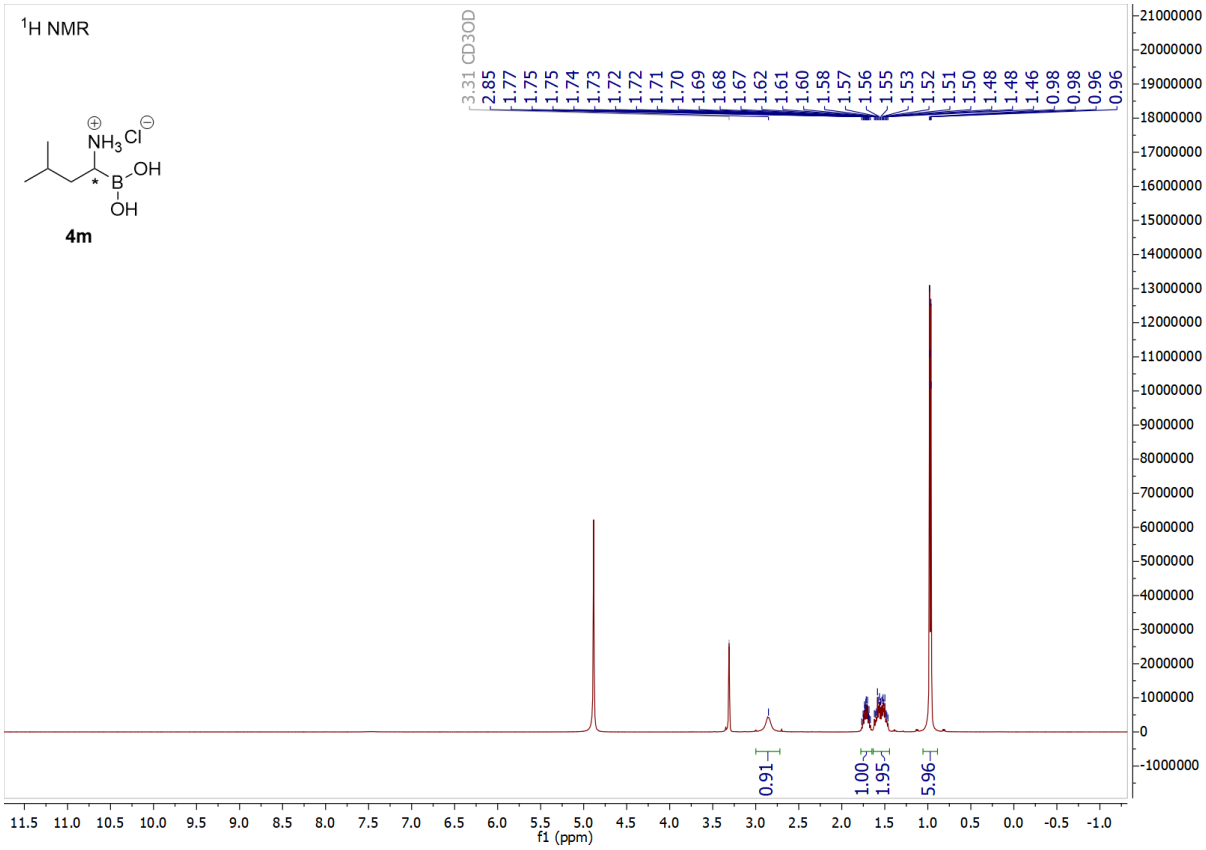


^{1}H-^{13}C HSQC-NMR (CD_3OD) of **4l**:

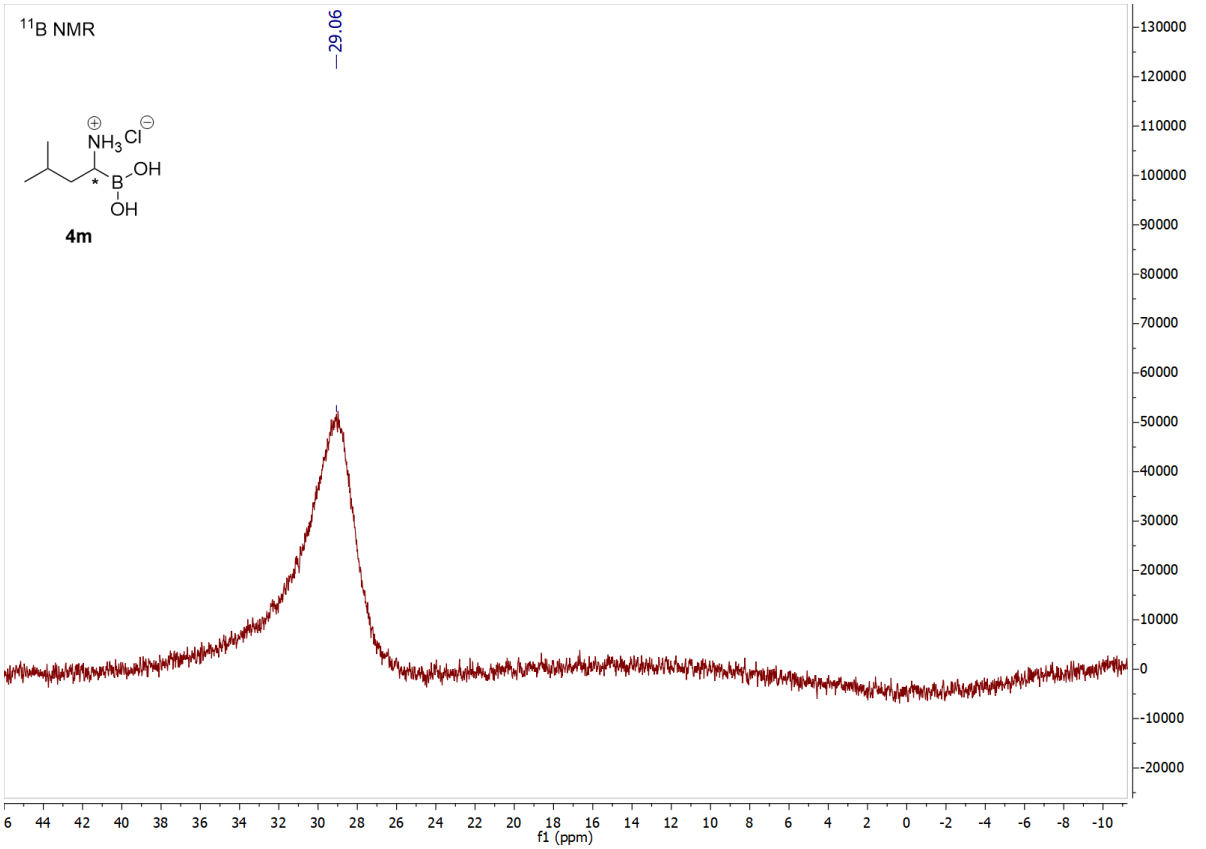


1-Borono-3-methylbutan-1-aminium chloride (4m)

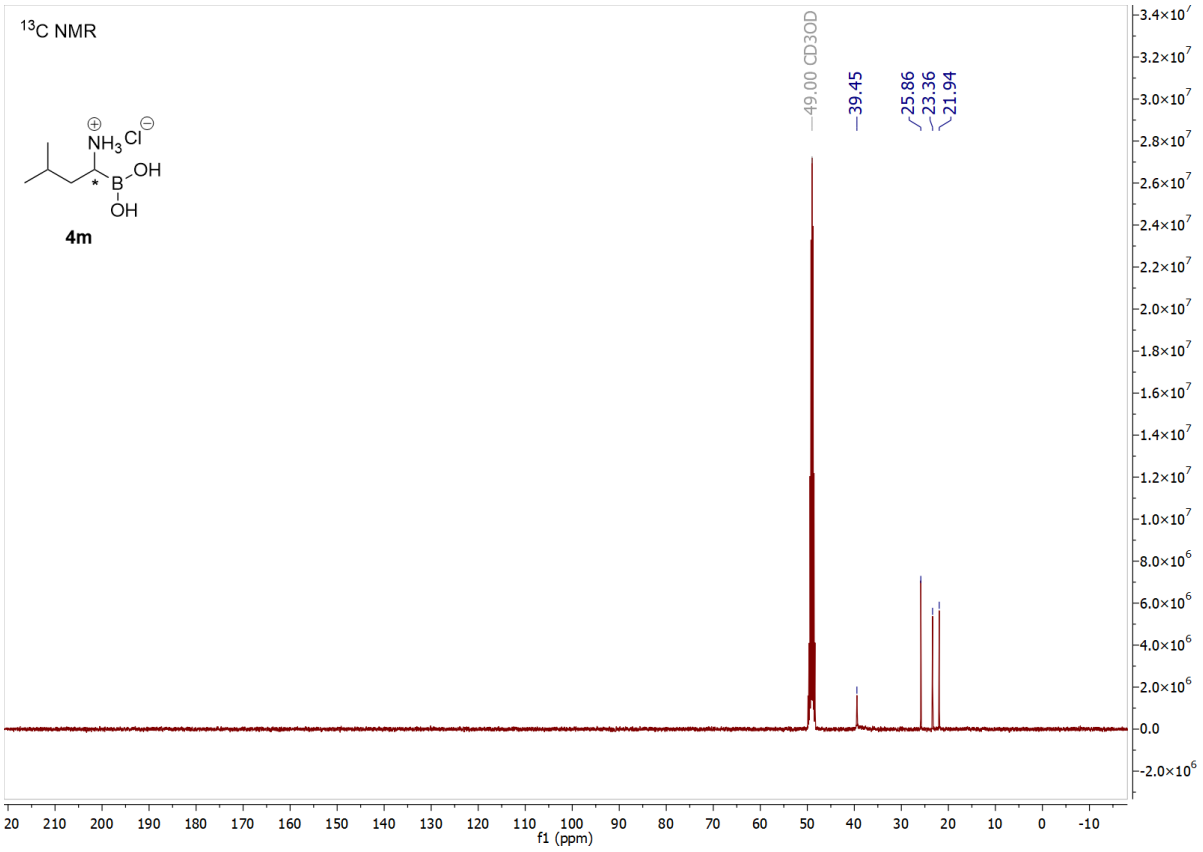
^{1}H-NMR (400 MHz, CD_3OD) of **4m**:



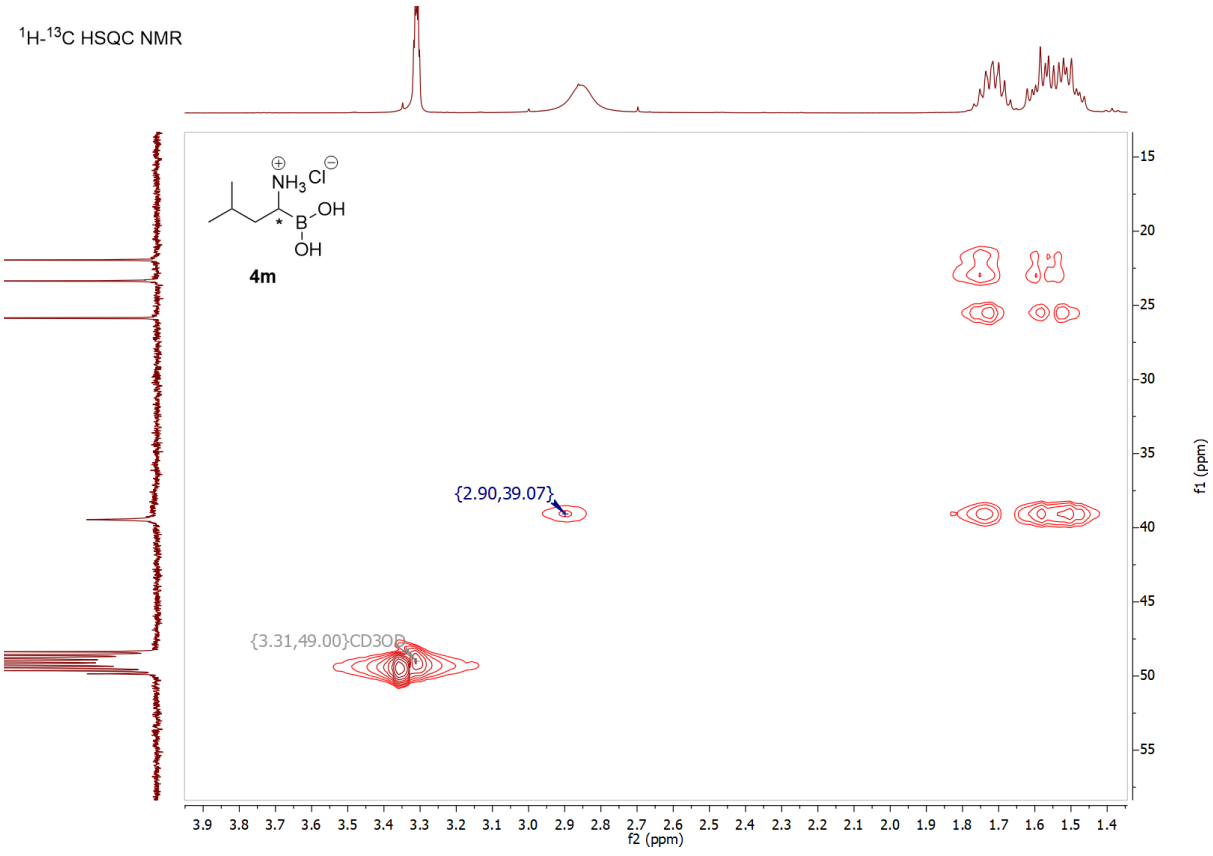
^{11}B-NMR (128 MHz, CD_3OD) of **4m**:



^{13}C-NMR (101 MHz, CD_3OD) of **4m**:

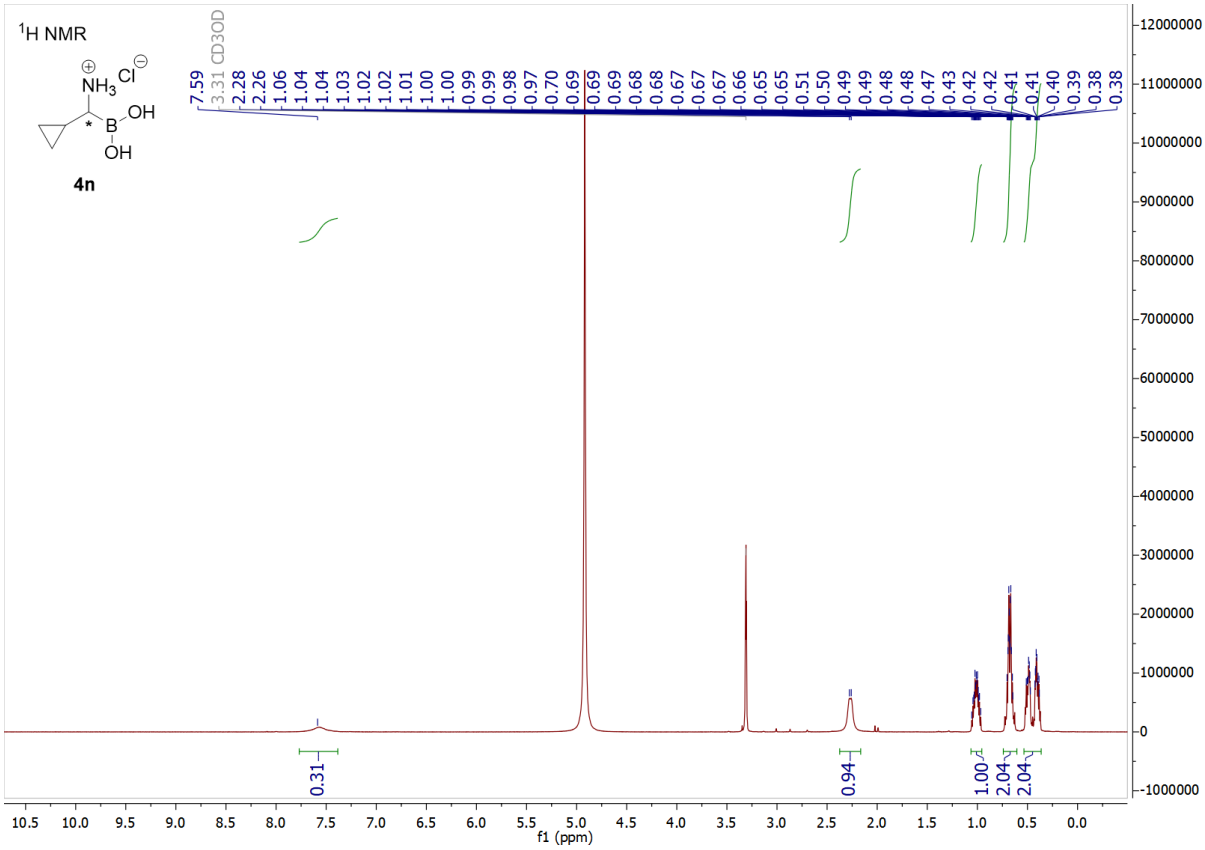


^{1}H-^{13}C HSQC-NMR (CD_3OD) of **4m**:

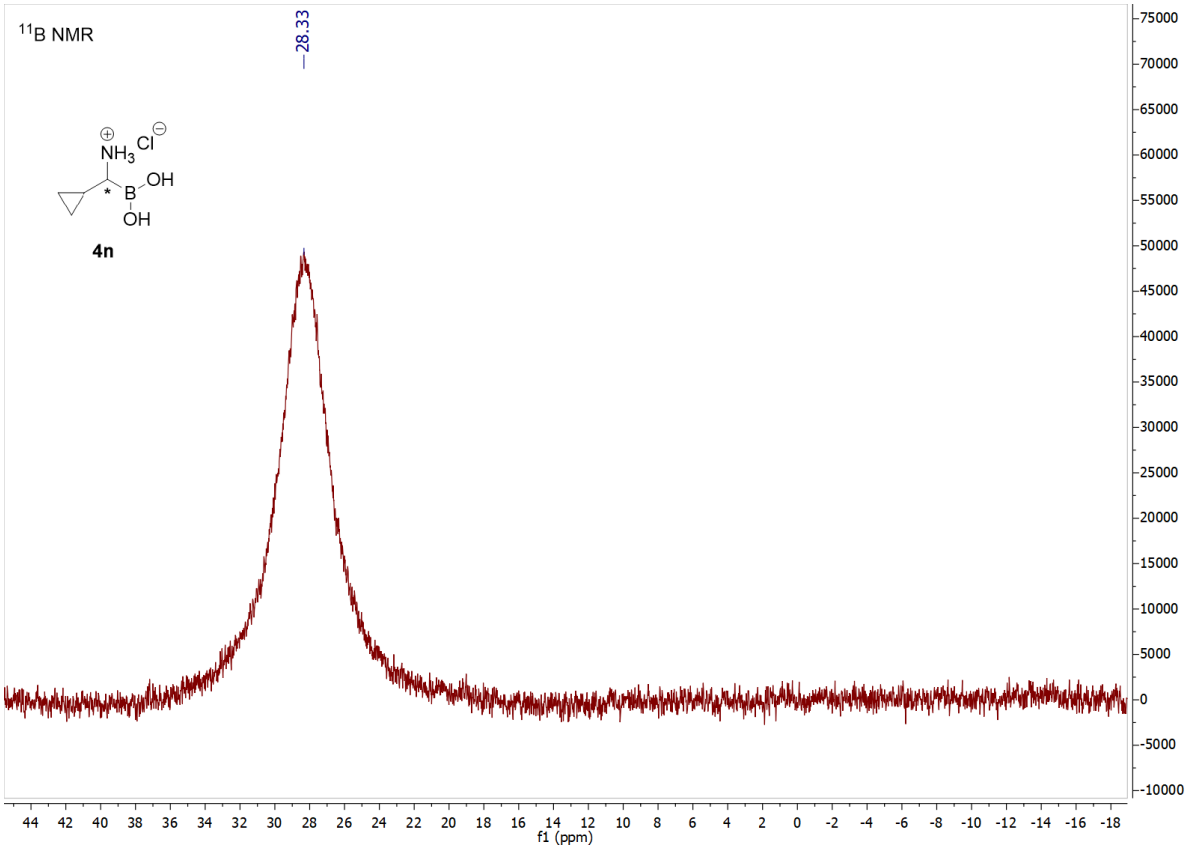


Borono(cyclopropyl)methanaminium chloride (4n)

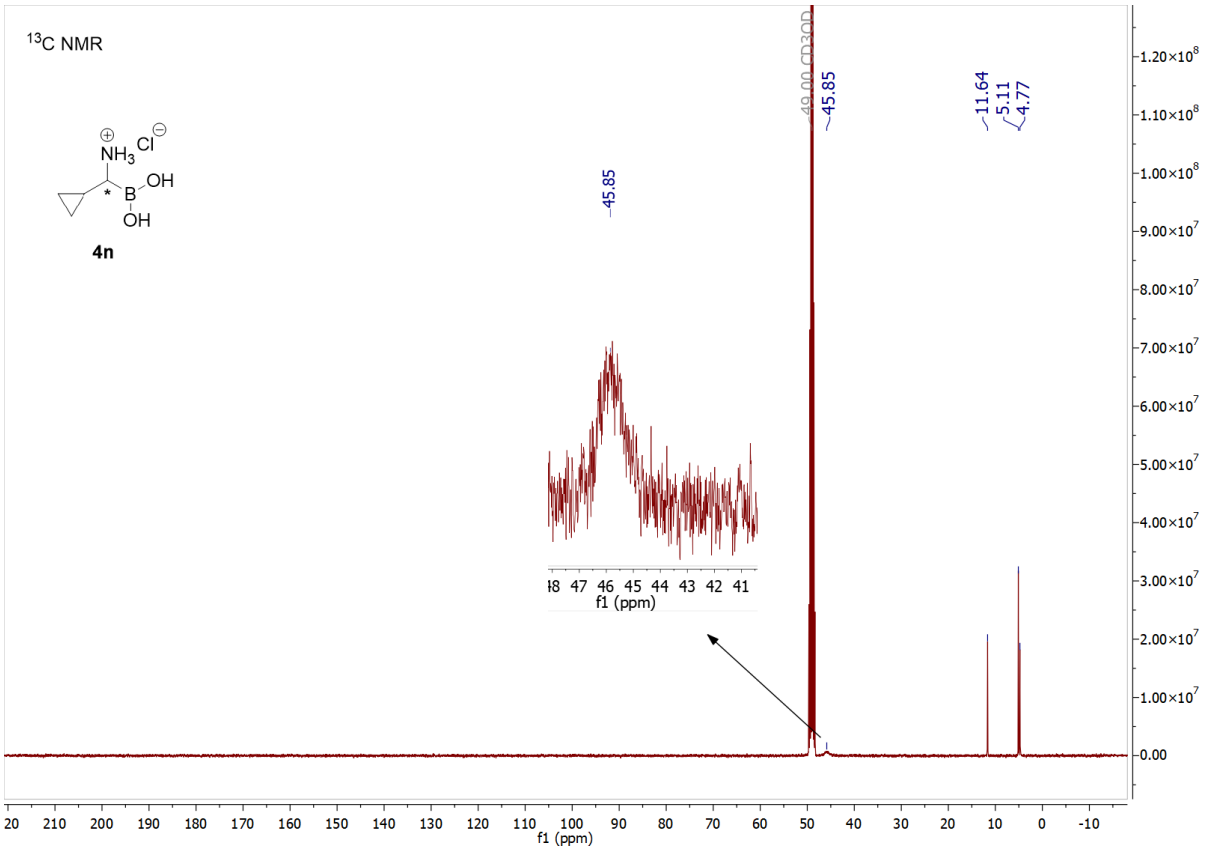
^{1}H-NMR (400 MHz, CD_3OD) of **4n**:



^{11}B-NMR (128 MHz, CD_3OD) of **4n**:

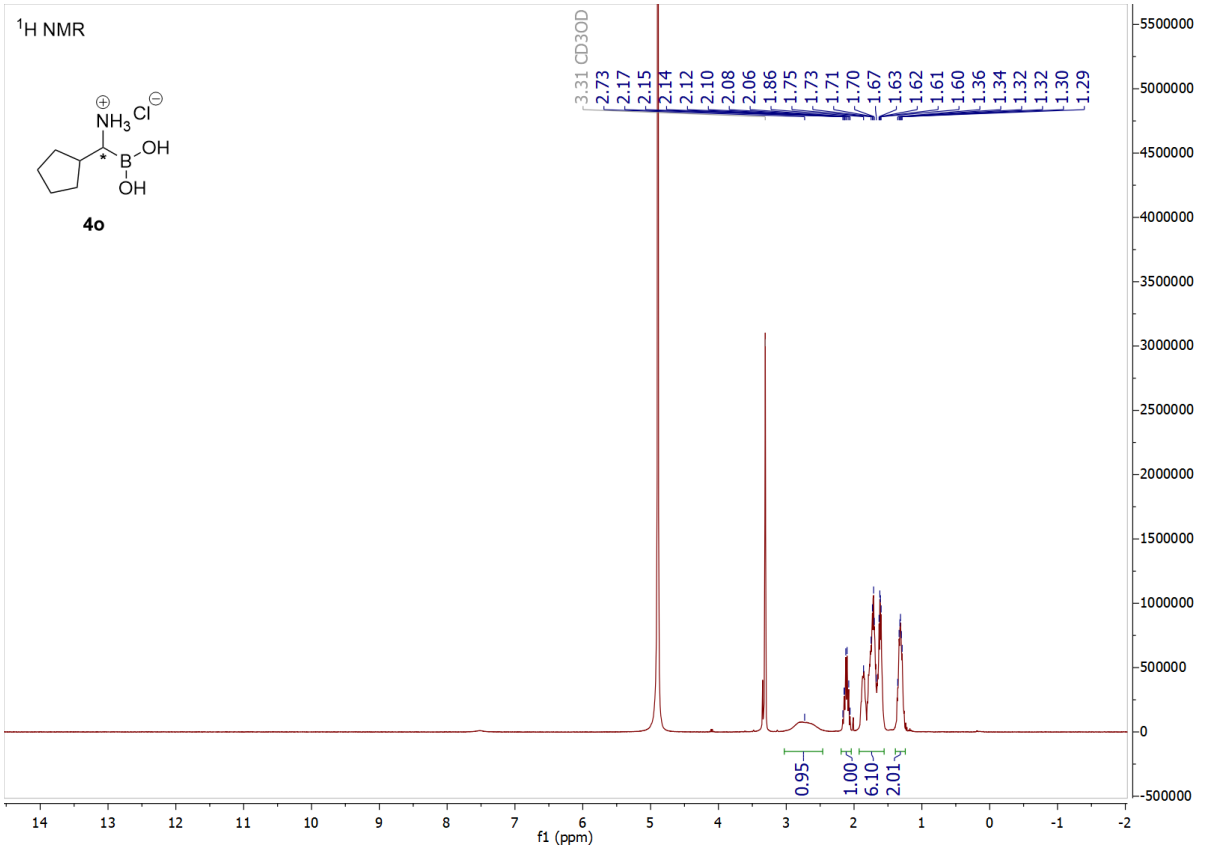


^{13}C-NMR (101 MHz, CD_3OD) of **4n**:

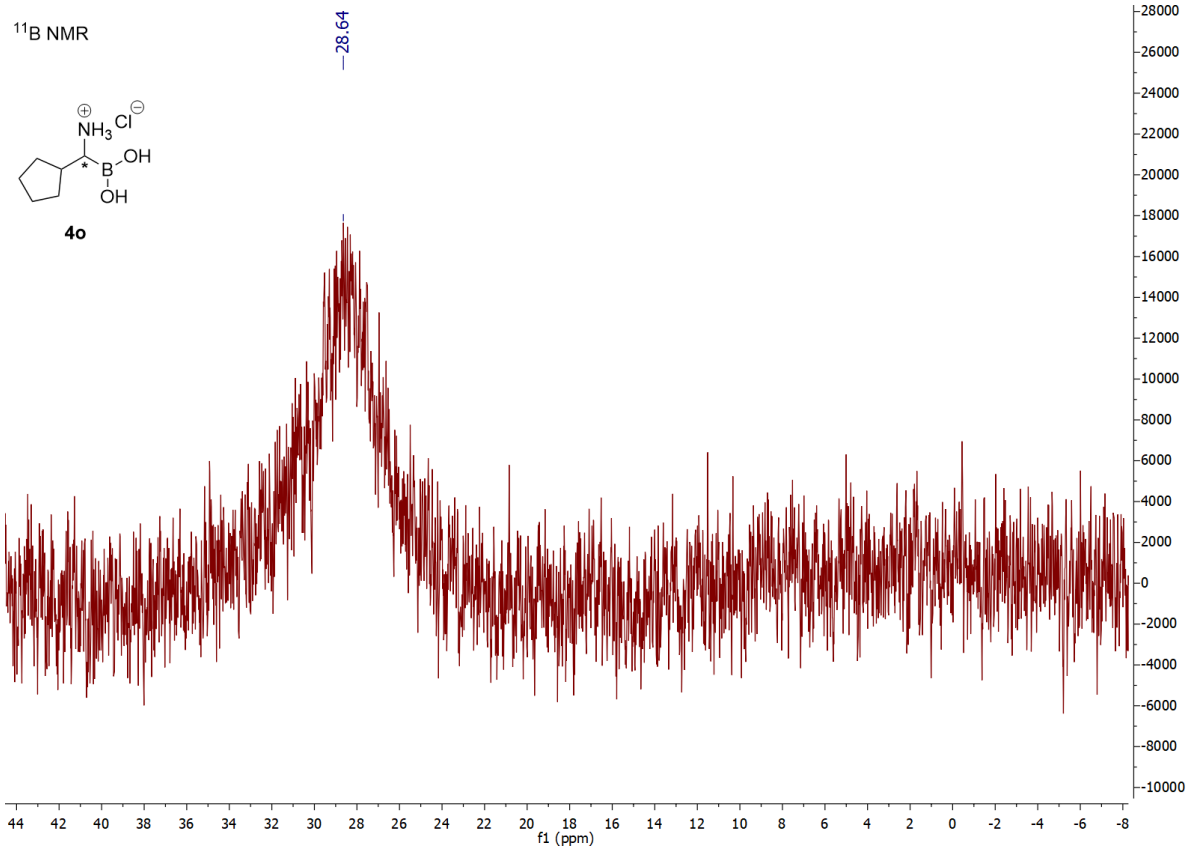


Borono(cyclopentyl)methanaminium chloride (4o)

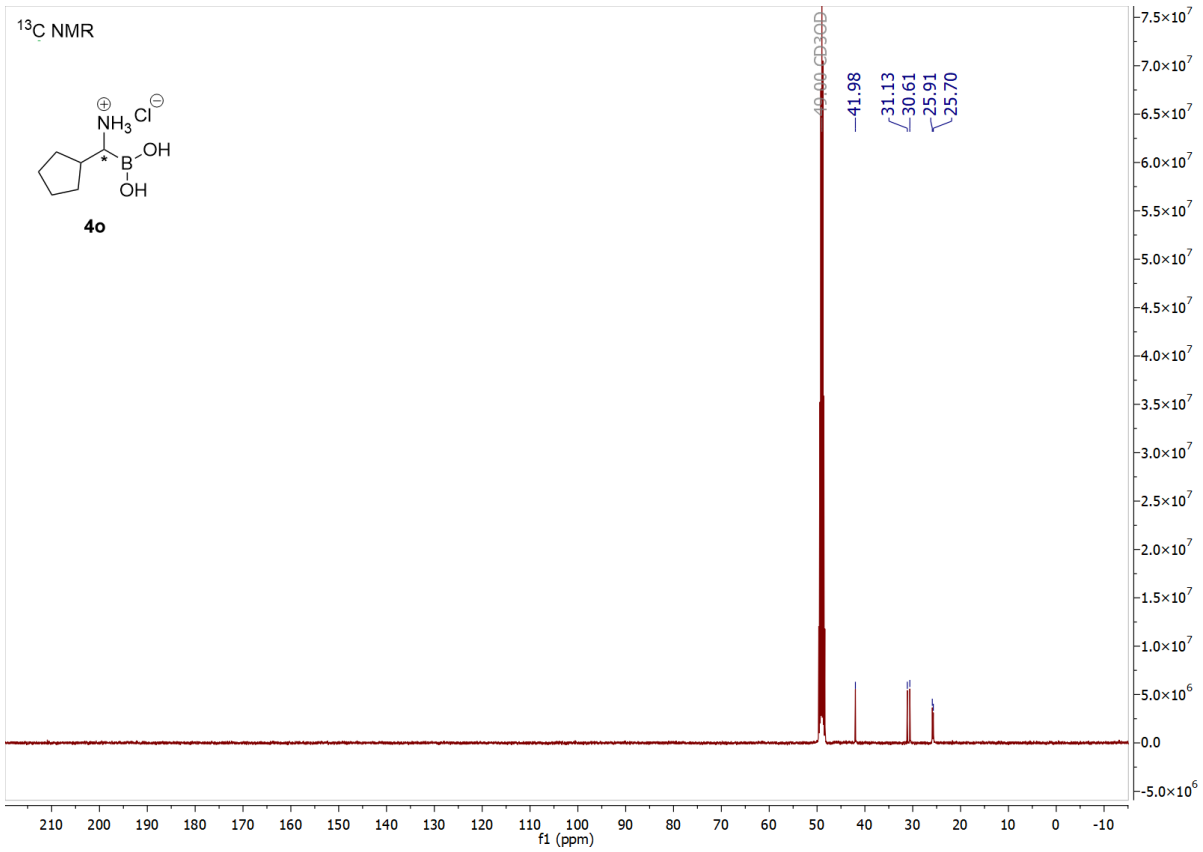
^{1}H-NMR (400 MHz, CD_3OD) of **4o**:



^{11}B-NMR (128 MHz, CD_3OD) of **4o**:

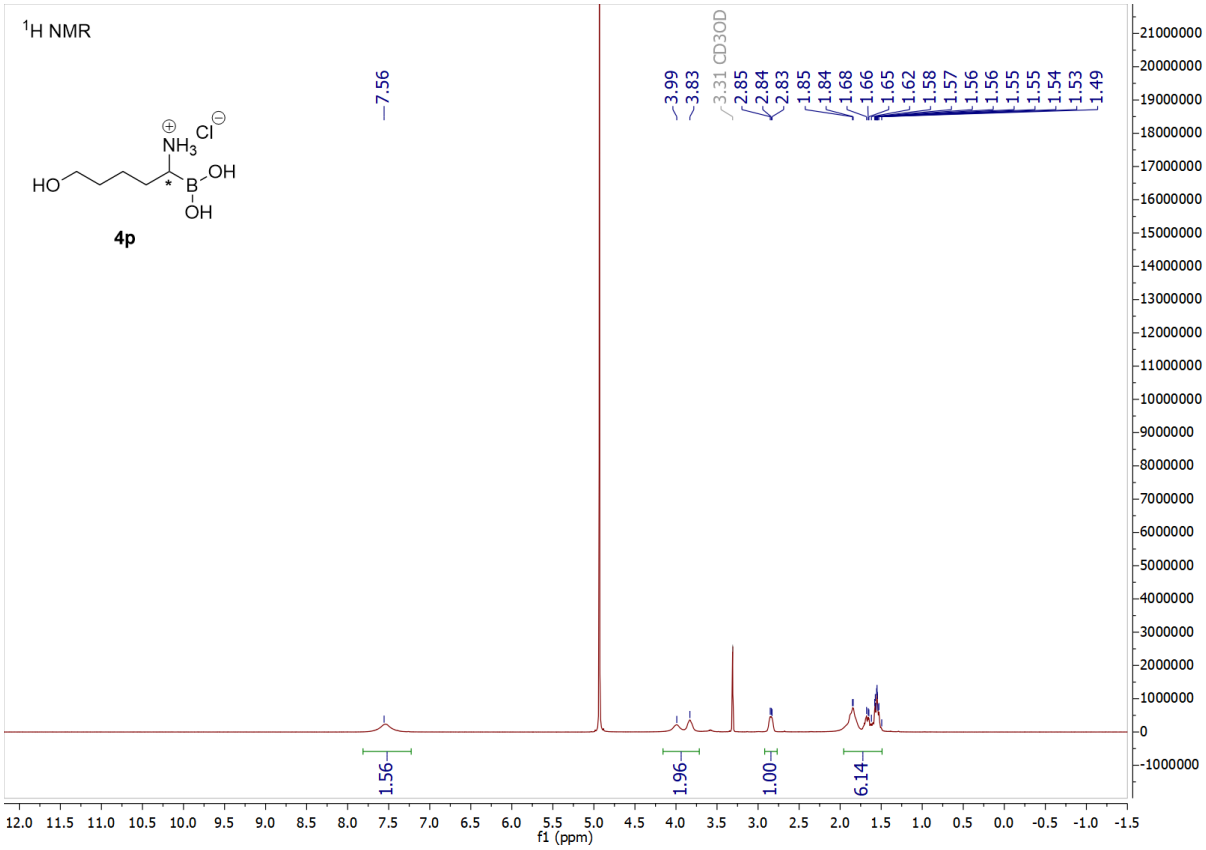


^{13}C-NMR (101 MHz, CD_3OD) of **4o**:

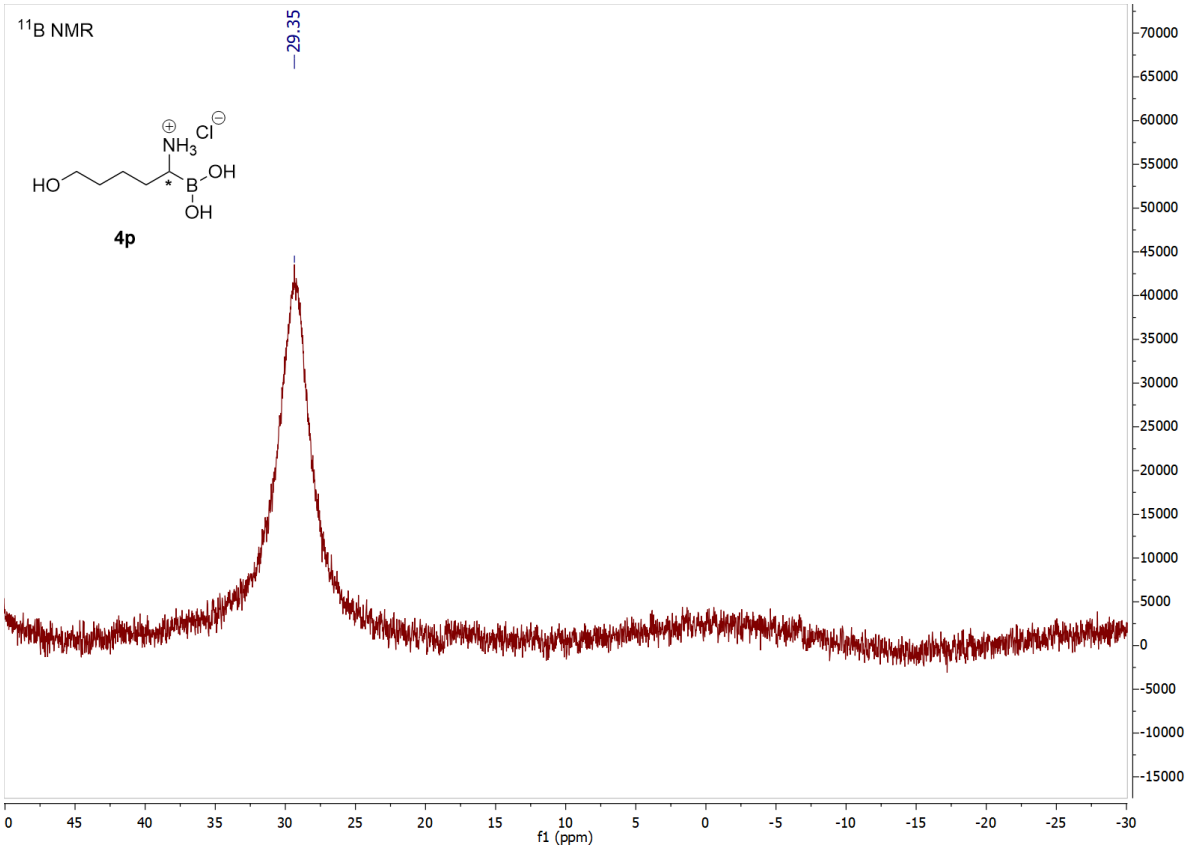


1-Borono-5-hydroxypentan-1-aminium chloride (4p)

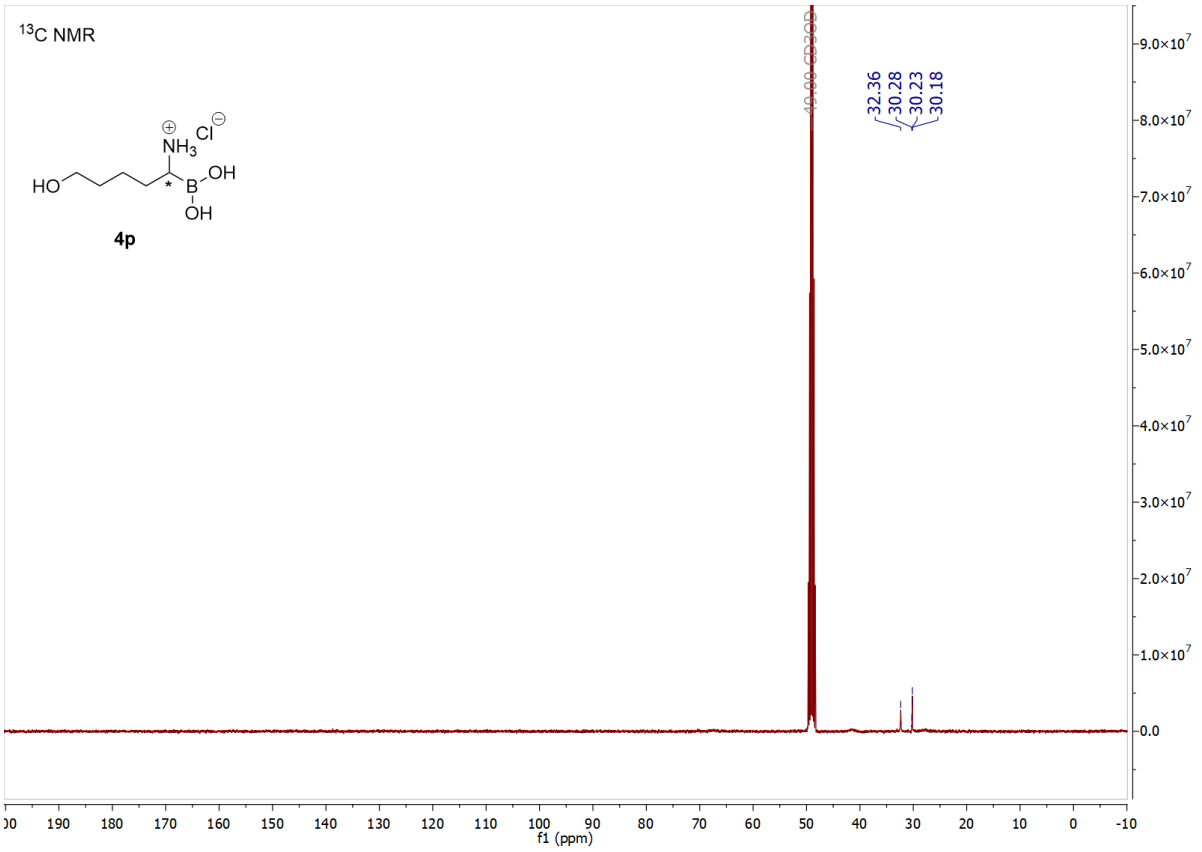
^{1}H-NMR (400 MHz, CD_3OD) of **4p**:



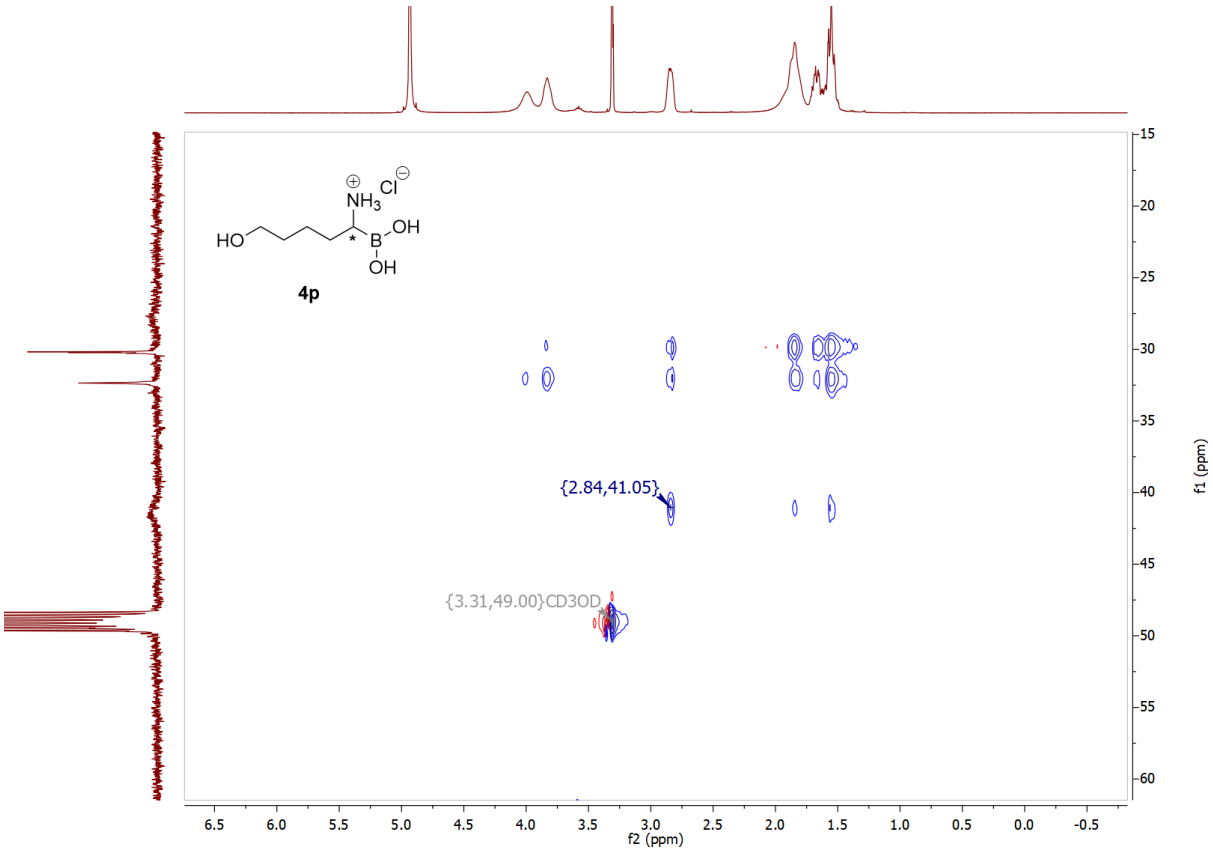
^{11}B-NMR (128 MHz, CD_3OD) of **4p**:



^{13}C-NMR (101 MHz, CD_3OD) of **4p**:



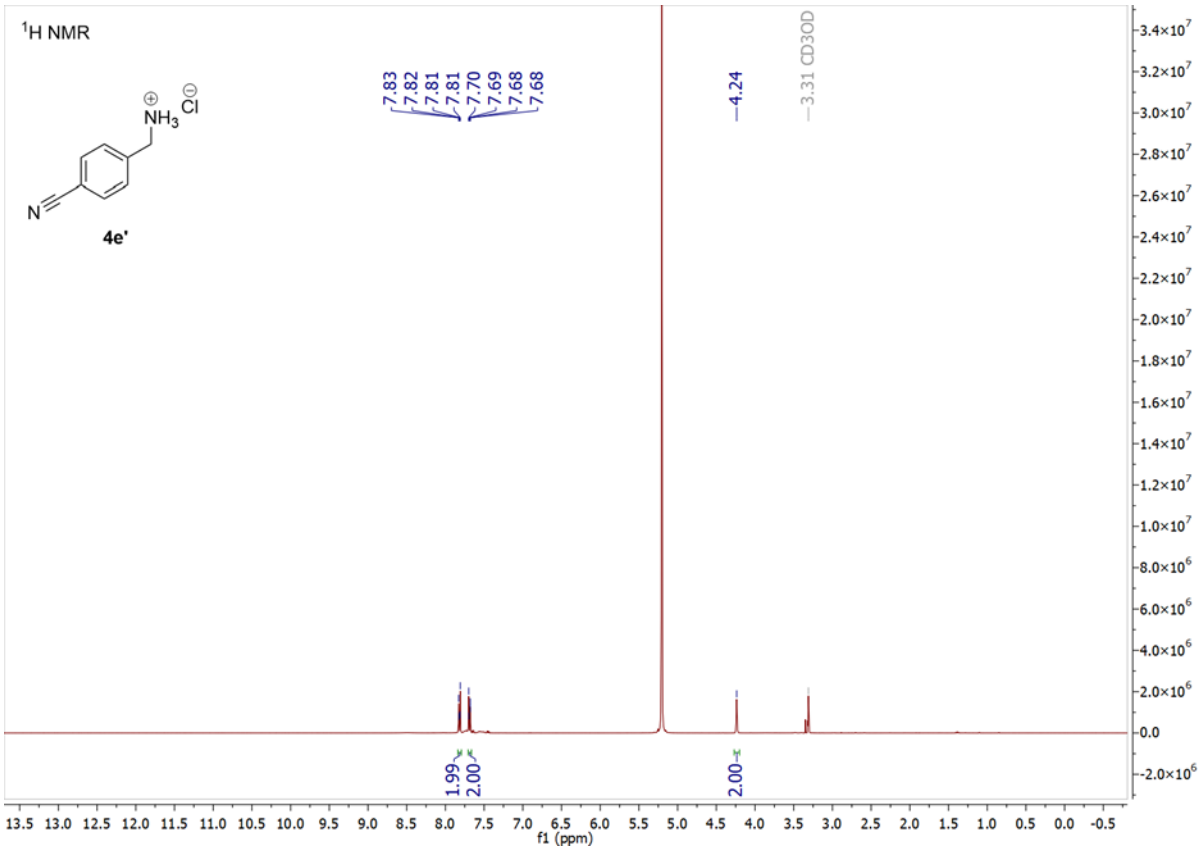
^{1}H-^{13}C HSQC-NMR (CD_3OD) of **4p**:



8.4. Other NMR Spectra

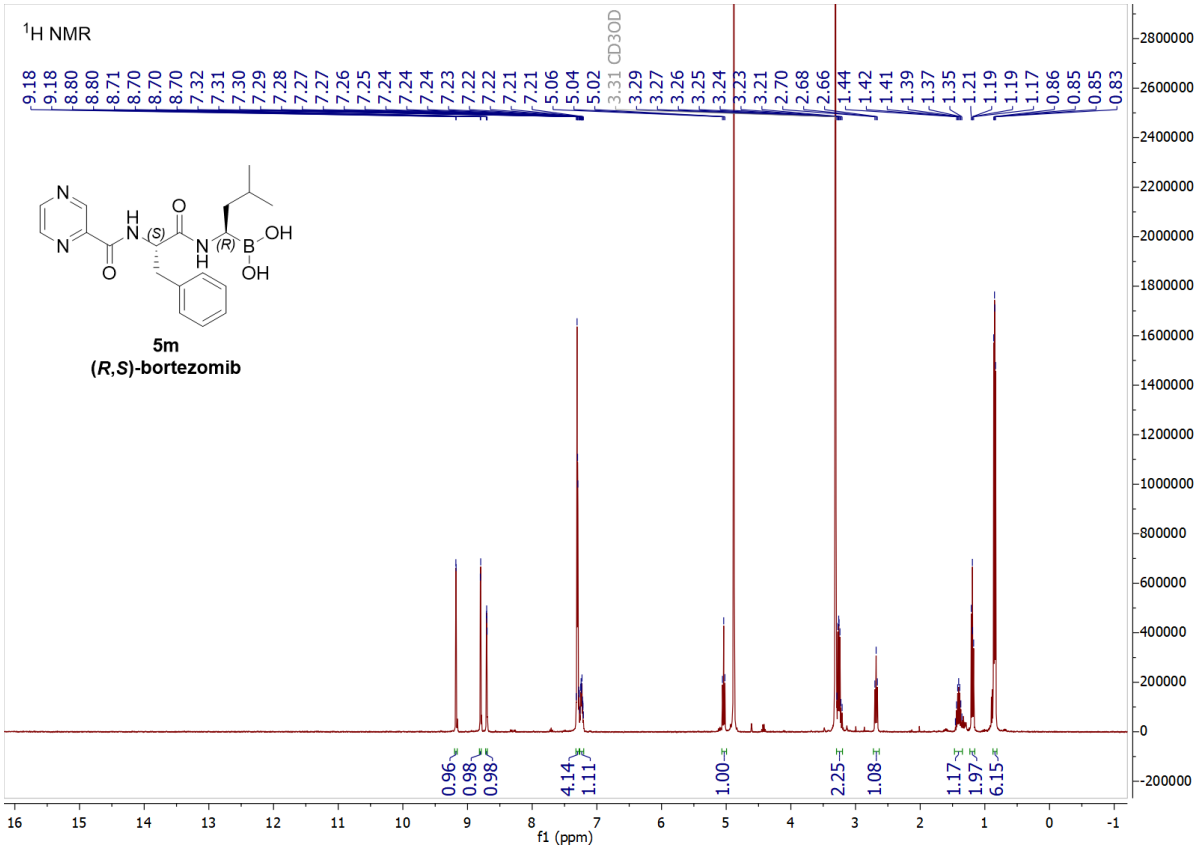
4-cyanobenzylammonium chloride (4e')

^{1}H-NMR (400 MHz, CD_3OD) of **4e'**:

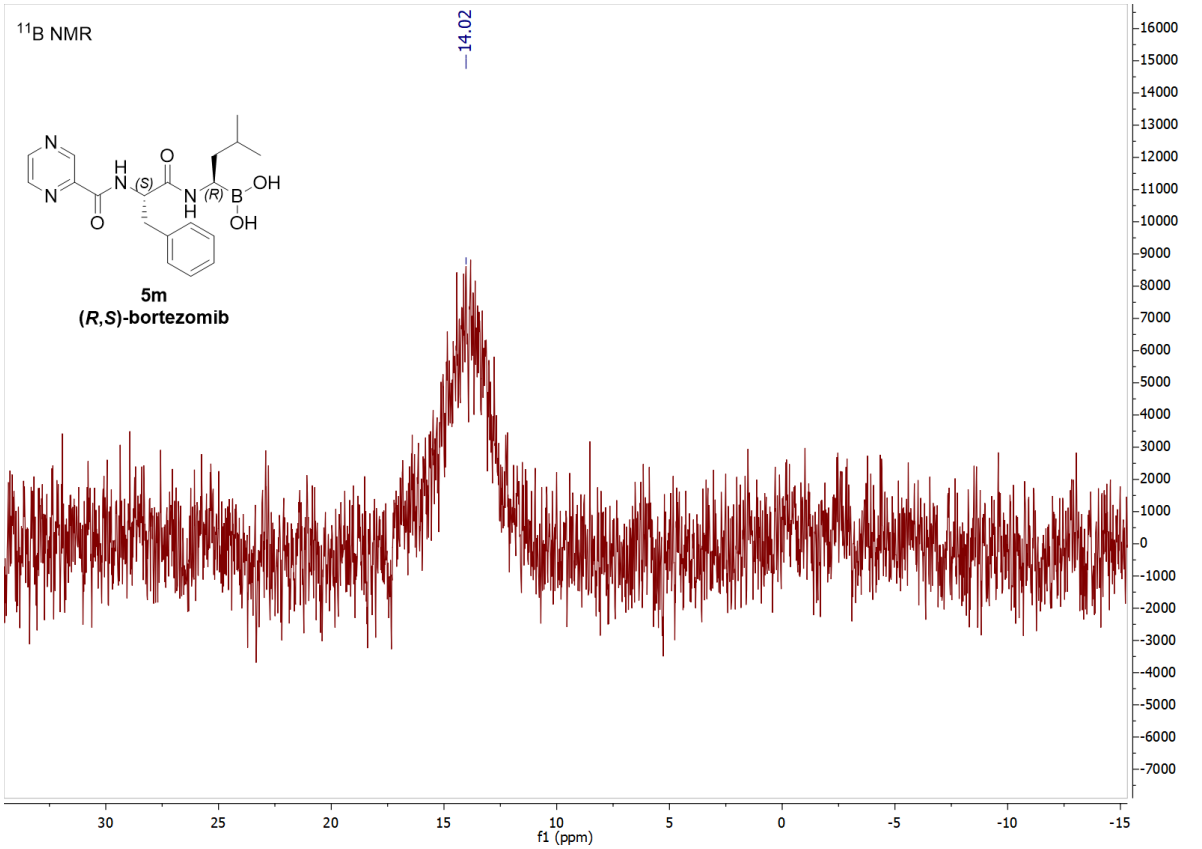


(*R*,*S*)-Bortezomib (5m)

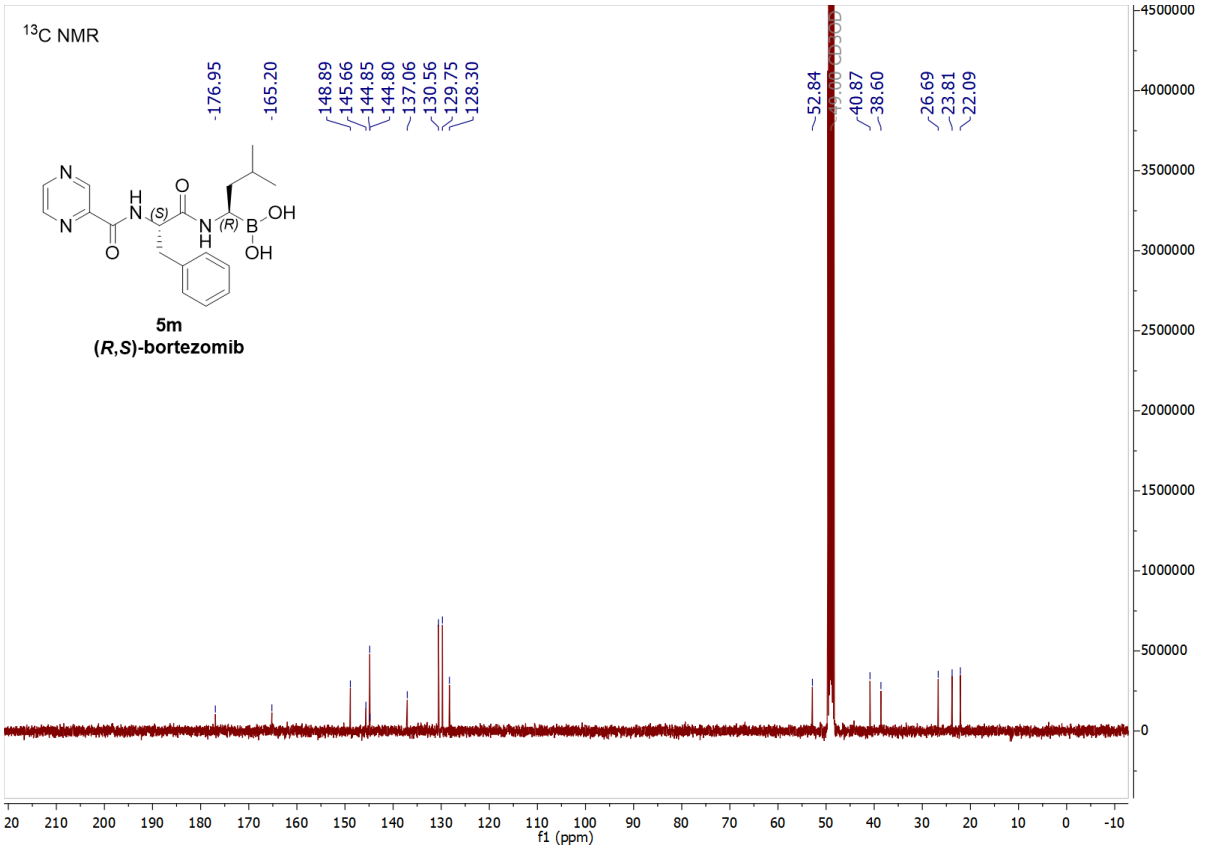
^{1}H-NMR (400 MHz, CD_3OD) of **5m**:



^{11}B-NMR (128 MHz, CD_3OD) of **5m**:

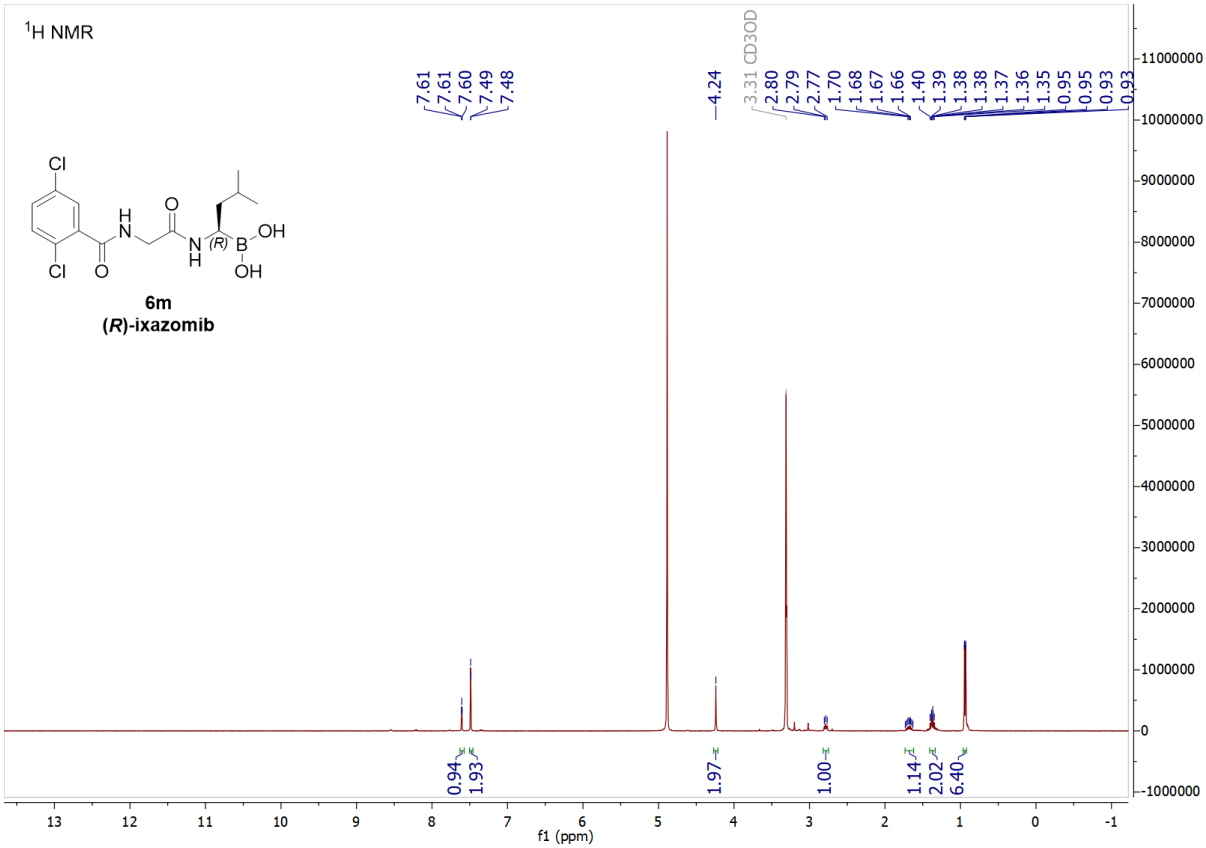


^{13}C-NMR (101 MHz, CD_3OD) of **5m**:

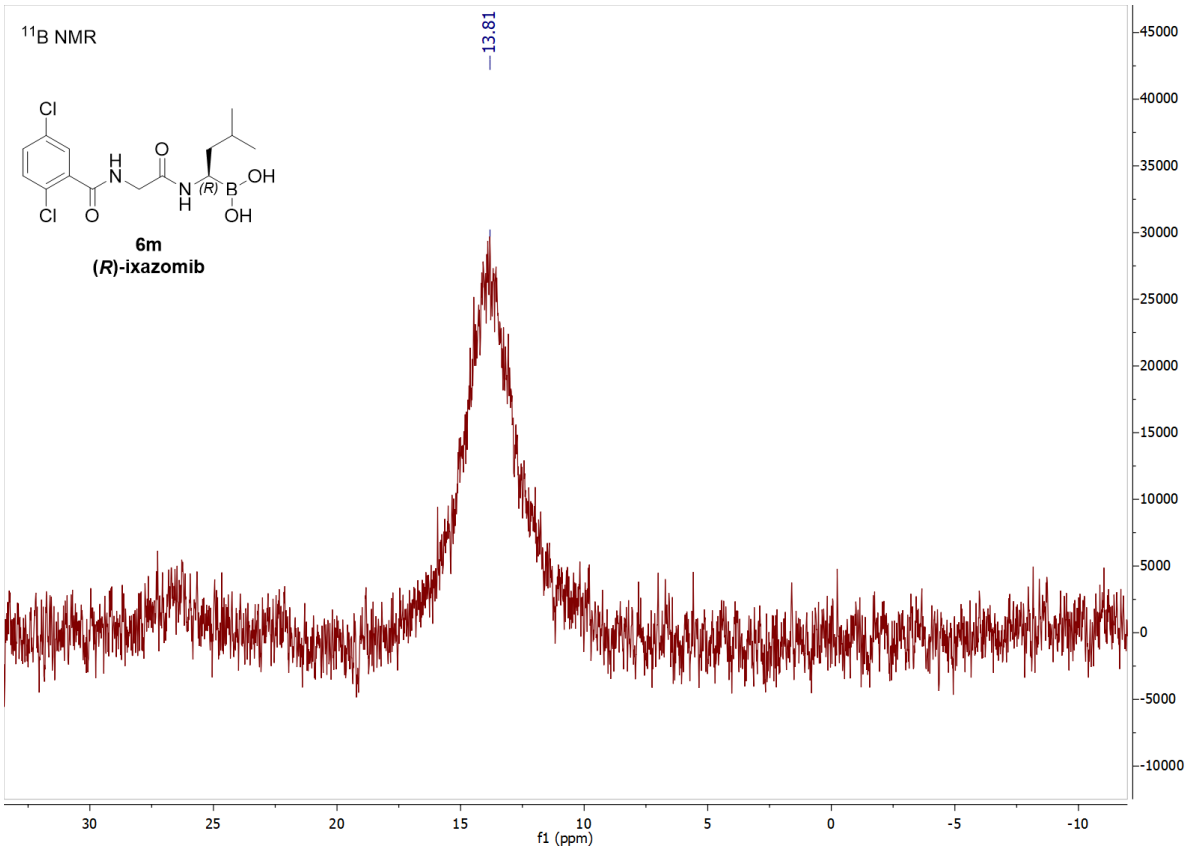


(*R*)-Ixazomib (6m)

^{1}H-NMR (400 MHz, CD_3OD) of **6m**:



^{11}B-NMR (128 MHz, CD_3OD) of **6m**:



^{13}C-NMR (101 MHz, CD_3OD) of **6m**: