

Supporting Information

Linchpin Synthons: Metallation of Aryl Halides Bearing a Proximal Trifluoroborate Moiety

Gary A. Molander and Noel M. Ellis*

Roy and Diana Vagelos Laboratories, Department of Chemistry, University of
Pennsylvania,

Philadelphia, Pennsylvania 19104-6323

Contents:

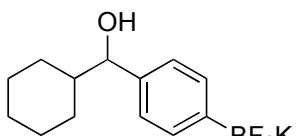
General Experimental Procedure	S2
Compound Characterization	S3
NMR spectra	S10

General. *n*-BuLi was used as a 2.5 M solution in hexanes purchased commercially and stored at 3 °C. All boronic acids and aldehydes were obtained from commercial sources and used without further purification. Solvents were distilled from sodium/benzophenone prior to use. Standard benchtop techniques were employed for handling air-sensitive reagents. Melting points (°C) were determined using a Thomas-Hoover melting point apparatus and are uncorrected. ¹H, ¹³C, and ¹⁹F NMR spectra were recorded on a 500 MHz spectrometer. ¹¹B NMR spectra were recorded on a 400 MHz spectrometer with appropriate decoupling accessories. Compounds **1**², **2**¹, and **23**² were prepared according to known literature procedures. They are also commercially available.

General Experimental Procedure for the Lithium-Halogen Exchange of Potassium Bromoaryl Trifluoroborates. Preparation of Potassium 4-(1-Hydroxypropyl)phenyl Trifluoroborate. To an oven-dried round bottom flask (50 mL) was added *p*-bromophenyl trifluoroborate (262 mg, 1.0 mmol). The flask was evacuated and back-filled with N₂ three times before adding freshly distilled THF (10 mL). A Dry Ice/ acetone bath was then used to cool the reaction to –78 °C and *n*-BuLi (1.0 mmol) was added dropwise. The reaction was then left to stir at –78 °C for 1 h, during which time an insoluble salt precipitated. Next, neat propionaldehyde (58 mg, 1.0 mmol) was added dropwise, and stirring was continued for an additional 10 min at –78 °C. After warming to rt, the reaction was stirred for 30 min, then sat. KHF₂ (aq) (390 mg, 5.0 mmol) was added, and the reaction was stirred at rt for an additional 10 min. Evaporation of the

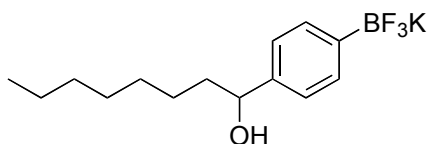
solvent *in vacuo* was followed by drying at 0.05 torr for a minimum of 6 h. Acetone extraction (3 x 20 mL) and filtration of the solids gave a solution of the product trifluoroborate in acetone. Reduction of the solvent followed by dropwise addition of Et₂O led to precipitation of the product. The product was then filtered, collected, and dried overnight at 0.05 torr to afford potassium 4-(1-hydroxypropyl)phenyl trifluoroborate (212 mg, 88%).

Compound Characterization:



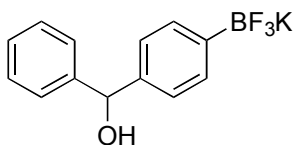
4-(Cyclohexyl(hydroxy)methyl)phenyl Trifluoroborate (4).

According to the general procedure, the product was obtained in 84% yield (250 mg, 0.84 mmol) as a white crystalline solid after acetone/Et₂O precipitation. mp > 250 °C. ¹H-NMR (500 MHz, DMSO-*d*₆): 7.27 (d, *J* = 7.9 Hz, 2H), 6.96 (d, *J* = 7.9 Hz, 2H), 4.77 (d, *J* = 4.4 Hz, 1H), 4.13 (dd, *J* = 6.8, 4.4 Hz, 1H), 1.86 (d, *J* = 12.8 Hz, 1H), 1.66 (d, *J* = 12.5 Hz, 1H), 1.57 (s, 2H), 1.44 (m, 1H), 1.35 (d, *J* = 12.3 Hz, 1H), 1.13 (m, 3H), 0.93 (m, 2H); ¹³C-NMR (125.8 MHz, DMSO-*d*₆): 141.1, 130.6, 124.6, 77.6, 45.0, 29.1, 28.5, 26.2, 25.8, 25.7; ¹⁹F-NMR (471 MHz, DMSO-*d*₆): -139.1; ¹¹B-NMR (128.37 MHz, DMSO-*d*₆): 4.07; IR (KBr) = 3539, 2914, 2852 cm⁻¹; HRMS (ESI) calcd. for C₁₃H₁₇BF₃O (M⁺) 257.1324, found 257.1340.



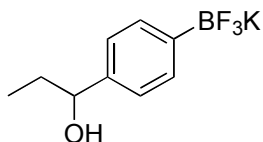
4-(1-Hydroxyoctyl)phenyl Trifluoroborate (6).

According to the general procedure, the product was obtained in 87% yield (270 mg, 0.87 mmol) as a white crystalline solid after acetone/Et₂O precipitation. mp > 250 °C. ¹H-NMR (500 MHz, DMSO-*d*₆): 7.26 (d, *J* = 7.9 Hz, 2H), 7.02 (d, *J* = 7.9 Hz, 2H), 4.79 (d, *J* = 4 Hz, 1H), 4.37 (m, 1H), 1.58 (m, 1H), 1.65 (m, 1H), 1.23 (m, 10 H), 0.88 (t, *J* = 6.6 Hz, 3H); ¹³C-NMR (125.8 MHz, DMSO-*d*₆): 142.6, 130.9, 123.9, 72.8, 39.5, 31.3, 29.1, 28.8, 25.5, 22.1, 13.9; ¹⁹F-NMR (471 MHz, DMSO-*d*₆): -139.1; ¹¹B-NMR (128.37 MHz, DMSO-*d*₆): 3.78 ; IR (KBr) = 3392, 2924, 2854 cm⁻¹; HRMS (ESI) calcd. for C₁₄H₂₁BF₃O (M⁺) 273.1638, found 273.1638.



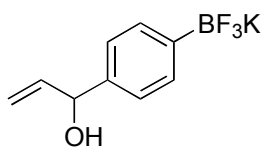
4-(Hydroxy(phenyl)methyl)phenyl Trifluoroborate (8).

According to the general procedure, the product was obtained in 69% yield (200 mg, 0.69 mmol) as a white crystalline solid after acetone/Et₂O precipitation. mp > 250 °C. ¹H-NMR (500 MHz, DMSO-*d*₆): 7.36 (d, *J* = 7.7 Hz, 2H), 7.26 (m, 4H), 7.17 (m, 1H), 7.08 (d, *J* = 7.7 Hz, 2H), 5.61 (d, *J* = 4 Hz, 1H), 5.59 (d, *J* = 4 Hz, 1H); ¹³C-NMR (125.8 MHz, acetone-*d*₆): 146.4, 142.0, 131.0, 127.8, 126.3, 126.2, 124.4, 74.7; ¹⁹F-NMR (471 MHz, DMSO-*d*₆): -139.3; ¹¹B-NMR (128.37 MHz, DMSO-*d*₆): 2.82; IR (KBr) = 3527, 3032, 2891 cm⁻¹; HRMS (ESI) calcd. for C₁₃H₁₁BF₃O (M⁺) 251.0855, found 251.0858.

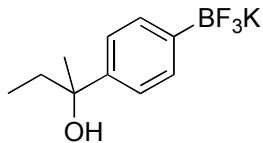


4-(1-Hydroxypropyl)phenyl Trifluoroborate (10). According to the general procedure, the product was obtained in 88% yield (212 mg, 0.88 mmol) as a white crystalline solid after acetone/Et₂O precipitation. mp > 250 °C. ¹H-NMR (500 MHz, DMSO-*d*₆): 7.26 (d, *J* =

7.8 Hz, 2H), 7.0 (d, *J* = 7.8 Hz, 2H), 4.82 (m, 1H), 4.31 (m, 1H), 1.58 (m, 2H), 0.80 (t, *J* = 7 Hz, 3H); ¹³C-NMR (125.8 MHz, DMSO-*d*₆): 142.3, 130.9, 123.9, 74.2, 32.1, 10.3; ¹⁹F-NMR (471 MHz, DMSO-*d*₆): -139.2 ; ¹¹B-NMR (128.37 MHz, DMSO-*d*₆): 3.37 ; IR (KBr) = 3403, 2964 cm⁻¹; HRMS (ESI) calcd. for C₉H₁₁OBF₃ (M⁻) 203.0855, found 203.0845.

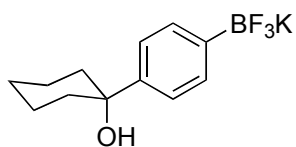


4-(1-Hydroxyallyl)phenyl Trifluoroborate (12). According to the general procedure, the product was obtained in 94% yield (225 mg, 0.94 mmol) as a white crystalline solid that was 95% pure after acetone/Et₂O precipitation. mp > 250 °C. ¹H-NMR (500 MHz, acetone-*d*₆): 7.45 (d, *J* = 8 Hz, 2H), 7.12 (d, *J* = 8 Hz, 2H), 5.99 (ddd, *J* = 16.5, 10.3, 5.7 Hz, 1H), 5.25 (m, 1H), 5.06 (s, 1H), 5.00 (m, 1H), 4.16 (d, *J* = 4.5 Hz, 1H); ¹³C-NMR (125.8 MHz, acetone-*d*₆): 142.5, 140.8, 131.5, 124.5, 112.1, 74.9; ¹⁹F-NMR (471 MHz, acetone-*d*₆): -142.6 ; ¹¹B-NMR (128.37 MHz, acetone-*d*₆): 3.77 ; IR (KBr) = 3394, 3017, 2874, 1939 cm⁻¹; HRMS (ESI) calcd. for C₉H₉BF₃O (M⁻) 201.0698, found 201.0697.



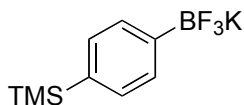
4-(2-Hydroxy-2-butanyl)phenyl Trifluoroborate (14). According to the general procedure, the product was obtained in 83% yield (212 mg, 0.83 mmol) as a white crystalline solid after acetone/Et₂O precipitation. mp > 250 °C. ¹H-NMR (500 MHz, DMSO-*d*₆): 7.25 (d, *J* = 7.34 Hz, 2H), 7.13 (d, *J* = 7.34 Hz, 2H), 4.51 (s, 1H), 1.65 (m, 2H), 1.36 (s, 3H), 0.68 (t, *J* = 7.34 Hz, 3H); ¹³C-NMR (125.8 MHz, DMSO-*d*₆): 145.1, 130.6, 122.9, 72.9, 36.6,

29.8, 8.5; ¹⁹F-NMR (471 MHz, DMSO-*d*₆): -139.6; ¹¹B-NMR (128.37 MHz, DMSO-*d*₆): 3.80; IR (KBr) = 3430, 2974, 2937 cm⁻¹; HRMS (ESI) calcd. for C₁₀H₁₃BF₃O (M⁺) 217.1011, found 217.1014.

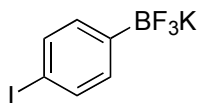


4-(Hydroxycyclohexyl)phenyl Trifluoroborate (16). According to the general procedure, the product was obtained in 65% yield (183 mg, 0.65 mmol) as a white crystalline solid in 95% purity after acetone/Et₂O precipitation. mp > 250 °C. ¹H-NMR (500 MHz, acetone-*d*₆): 7.41 (d, *J* = 7.9 Hz, 2H), 7.26 (d, *J* = 7.9 Hz, 2H), 3.26 (s, 1H), 1.80 (m, 4H), 1.68 (m, 3H), 1.52 (m, 2H), 1.29 (m, 1H); ¹³C-NMR (125.8 MHz, acetone-*d*₆): 148.0, 132.2, 123.5, 72.9, 40.0, 26.7, 23.1; ¹⁹F-NMR (471 MHz, acetone-*d*₆): -142.7; ¹¹B-NMR (128.37 MHz, acetone-*d*₆): 3.94; IR (KBr) = 3434, 2930, 2858 cm⁻¹; HRMS (ESI)

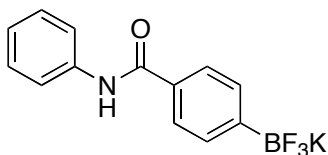
calcd. for $C_{12}H_{15}BF_3O$ (M^-) 243.1168, found 243.1178.



4-(Trimethylsilyl)phenyl Trifluoroborate (18). According to the general procedure, the product was obtained in 68% yield (172 mg, 0.68 mmol) as a white crystalline solid after acetone/ Et_2O precipitation. mp > 250 °C. 1H -NMR (500 MHz, acetone- d_6): 7.47 (d, J = 7.3 Hz, 2H), 7.29 (d, J = 7.3 Hz, 2H), 0.20 (s, 9H); ^{13}C -NMR (125.8 MHz, acetone- d_6): 136.2, 132.2, 132.1, -0.8; ^{19}F -NMR (471 MHz, acetone- d_6): -143.1; ^{11}B -NMR (128.37 MHz, acetone- d_6): 3.59; IR (KBr) = 3638, 3054, 2959 cm^{-1} ; HRMS (ESI) calcd. for $C_9H_{13}BF_3Si$ (M^-) 217.0831, found 217.0835.

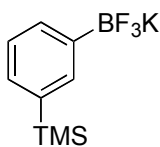


4-Iodophenyl Trifluoroborate (20). According to the general procedure, the product was obtained in 64% yield (198 mg, 0.64 mmol) as a white crystalline solid that was 90% pure after acetone/ Et_2O precipitation. mp > 250 °C. 1H -NMR (500 MHz, DMSO- d_6): 7.45 (d, J = 7.6 Hz, 2H), 7.14 (d, J = 7.6 Hz, 2H); ^{13}C -NMR (125.8 MHz, DMSO- d_6): 134.9, 133.9, 91.4; ^{19}F -NMR (471 MHz, acetone- d_6): -140.1; ^{11}B -NMR (128.37 MHz, acetone- d_6): 3.50; IR (KBr) = 3660, 3030, 2926 cm^{-1} ; HRMS (ESI) calcd. for $C_6H_4BF_3I$ (M^-) 270.9402, found 270.9390.



4-(Phenylcarbamoyl)phenyl Trifluoroborate (22). According

to the general procedure, the product was obtained in 68% yield (208 mg, 0.68 mmol) as a white crystalline solid after acetone/Et₂O precipitation. mp > 250 °C. ¹H-NMR (500 MHz, DMSO-*d*₆): 10.01 (s, 1H), 7.79 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 7.7 Hz, 2H), 7.47 (d, *J* = 7.7 Hz, 2H), 7.33 (m, 2H), 7.07 (m, 1H); ¹³C-NMR (125.8 MHz, DMSO-*d*₆): 166.9, 140.0, 132.1, 131.6, 129.0, 126.1, 123.7, 120.7; ¹⁹F-NMR (471 MHz, DMSO-*d*₆): -140.0; ¹¹B-NMR (128.37 MHz, DMSO-*d*₆): 3.66 ; IR (KBr) = 3057, 1944 cm⁻¹; HRMS (ESI) calcd. for C₁₃H₁₀BF₃NO (M⁺) 264.0808, found 264.0817.



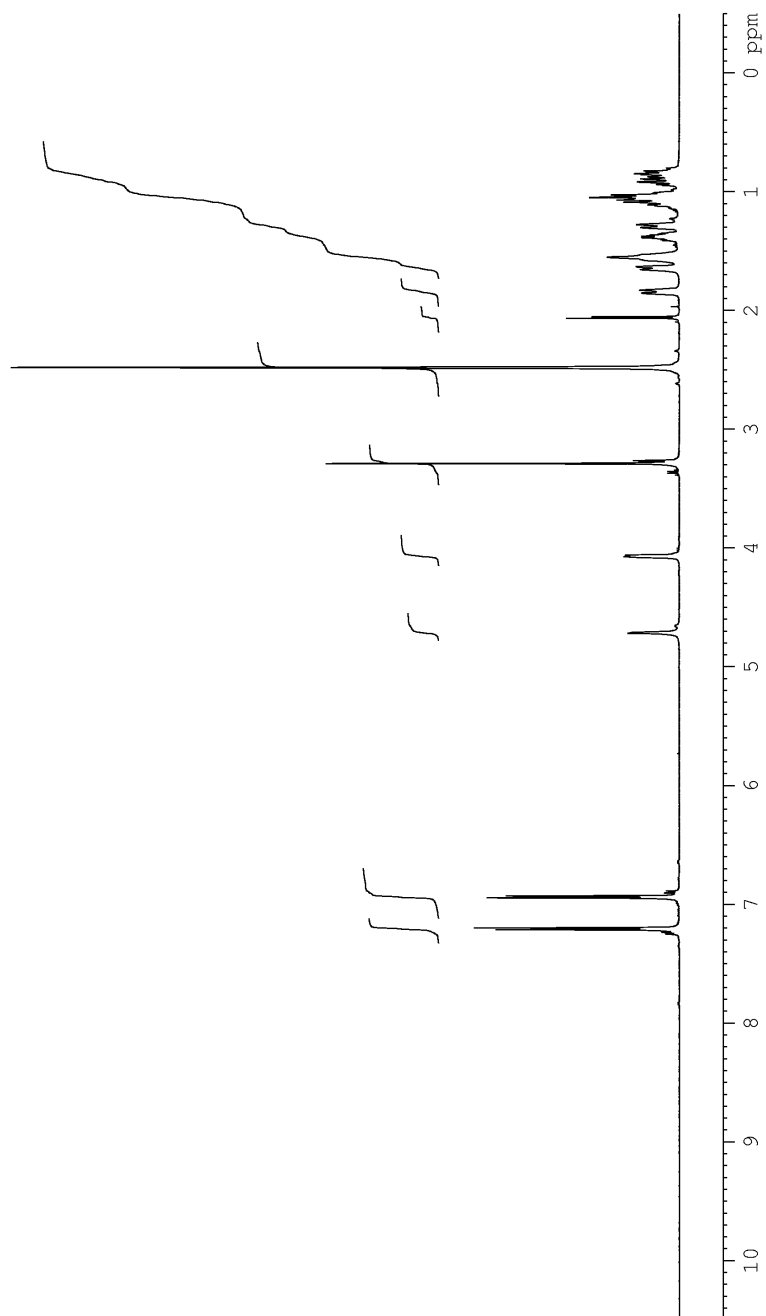
3-(Trimethylsilyl)phenyl Trifluoroborate (24). To a stirring solution of *m*-

bromophenyl trifluoroborate (262 mg, 1.0 mmol) in THF at -78 °C was added dropwise a solution of *t*-BuLi in pentane (2.0 mmol). The mixture was stirred for 10 minutes, at which point neat TMSCl (109 mg, 1 mmol) was added dropwise and the reaction was allowed to warm to rt. After stirring for 30 minutes, a saturated solution of KHF₂ (aq) (390 mg, 5.0 mmol) was added and the mixture was kept stirring for 10 minutes before removing the solvents *in vacuo* and subjecting the resulting solids to a vacuum of 0.05 torr for a minimum of 6 h. Acetone extraction (3 x 20 mL) and filtration of the solids gave a solution of the product trifluoroborate in acetone. Reduction of the acetone followed by dropwise addition of Et₂O led to precipitation of the product. The product was obtained in 81% yield (208 mg, 0.81 mmol) as a white crystalline solid upon filtration. mp > 250 °C. ¹H-NMR (500 MHz, acetone-*d*₆): 7.72 (s, 1H), 7.48 (d, *J* = 7.15 Hz, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 0.21 (s, 9H); ¹³C-NMR (125.8

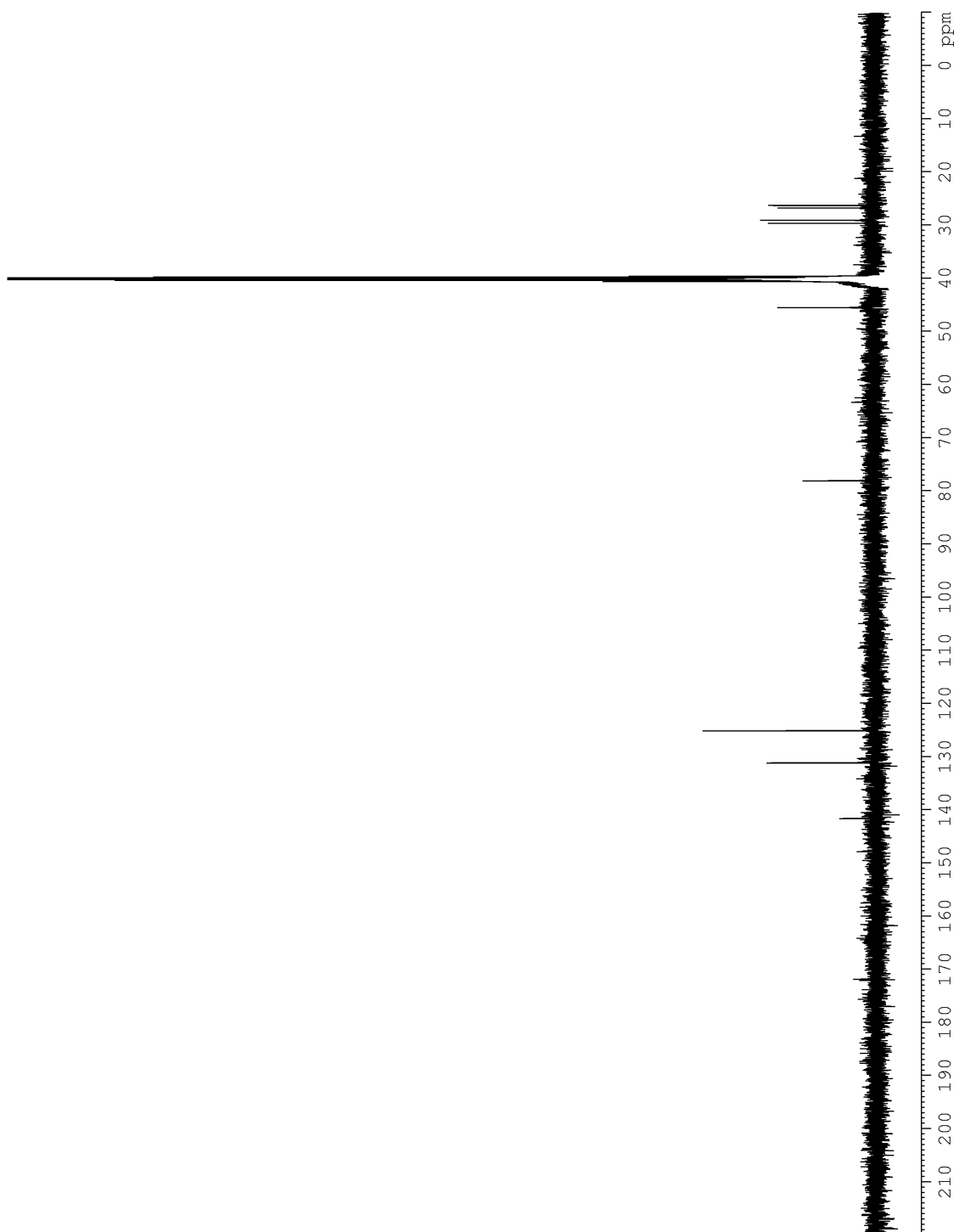
MHz, acetone- d_6): 136.7, 132.5, 130.1, 125.7; ^{19}F -NMR (471 MHz, acetone- d_6): -142.9;
 ^{11}B -NMR (128.37 MHz, acetone- d_6): 3.72; IR (KBr) = 2958, 2896 cm^{-1} ; HRMS (ESI)
calcd. for $\text{C}_9\text{H}_{13}\text{BF}_3\text{Si}(\text{M})^-$ 217.0832, found 217.0826.

References:

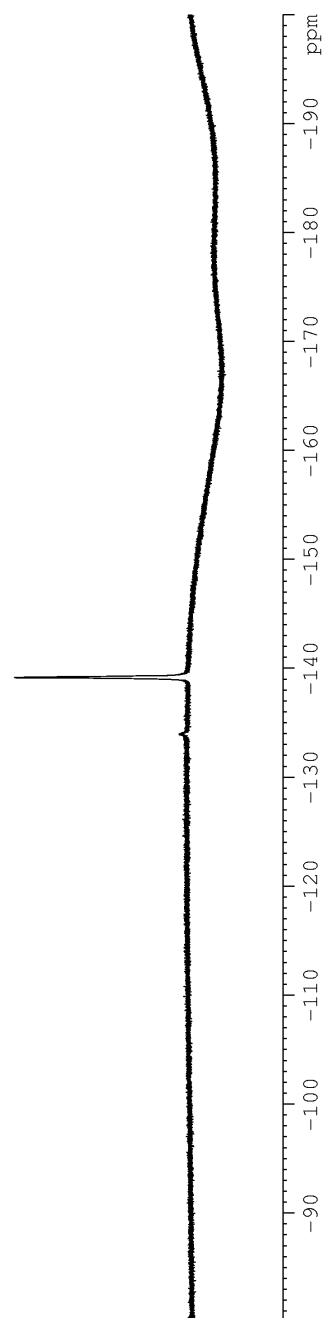
- (1) Vedejs, E.; Chapman, R. W.; Fields, S.C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, 60, 3020-3027.
- (2) Darses, S.; Michaud, G.; Genêt, J-P. *Eur. J. Org. Chem.* **1999**, 1875-1883.



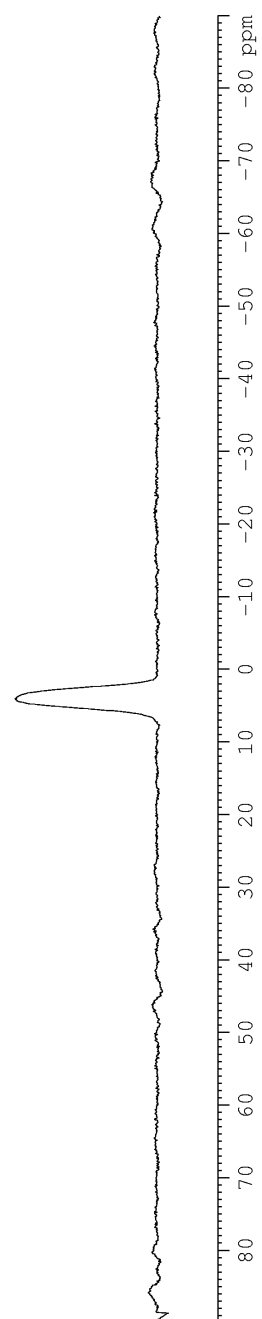
^1H NMR Spectrum of 4-(Cyclohexyl(hydroxy)methyl)phenyl Trifluoroborate (**4**)



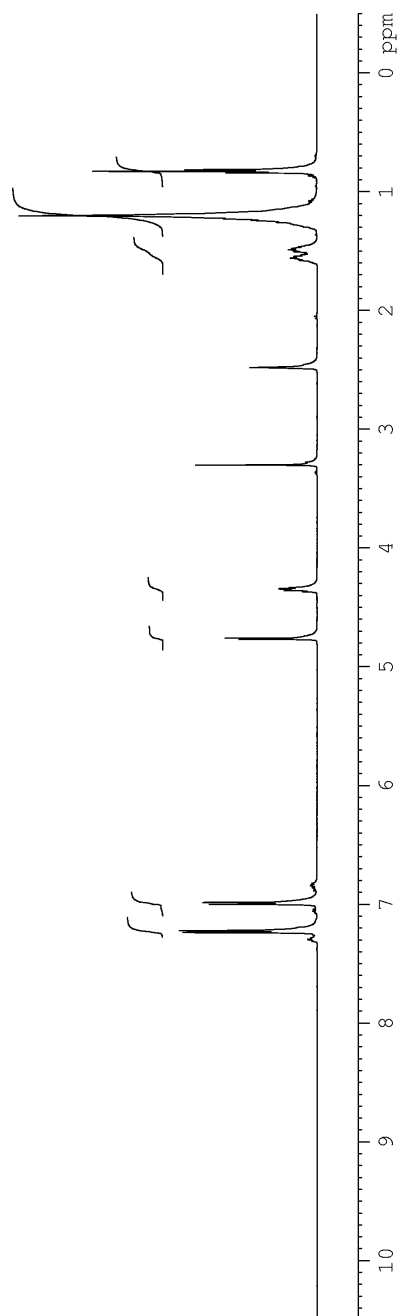
^{13}C NMR Spectrum of 4-(Cyclohexyl(hydroxy)methyl)phenyl Trifluoroborate (4)



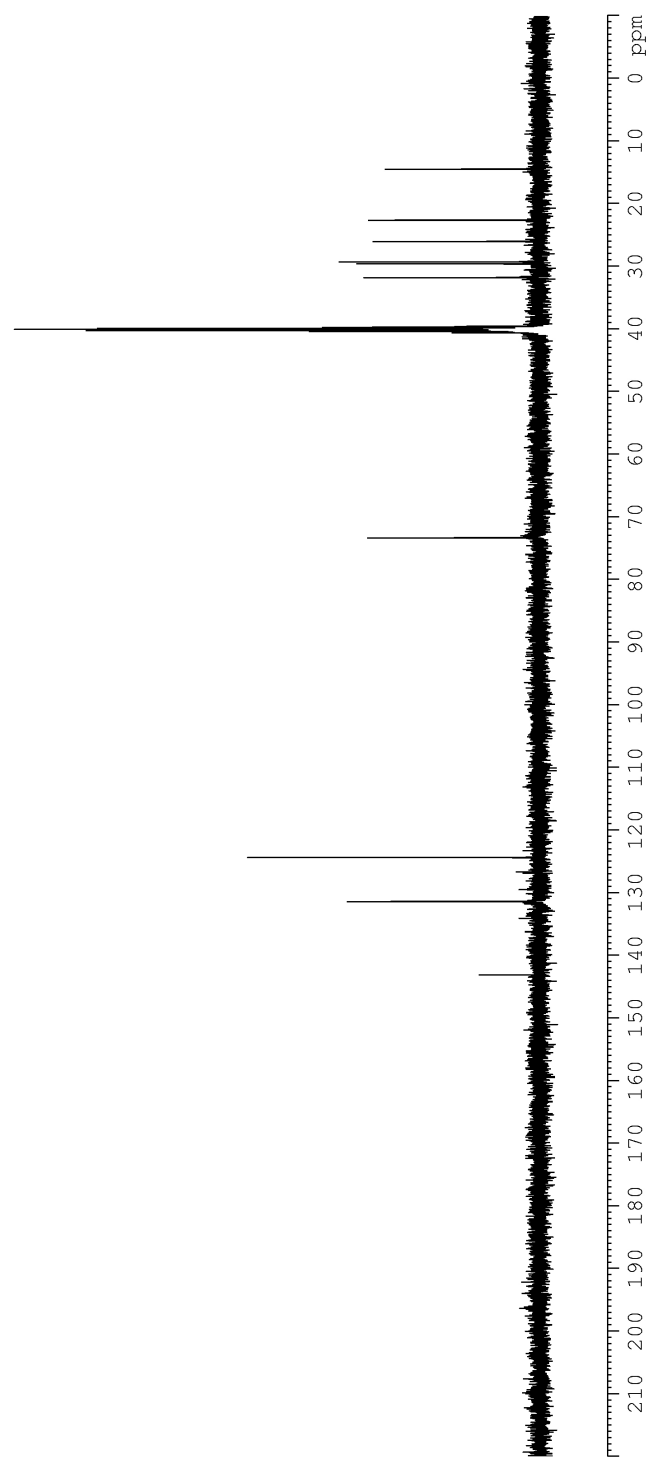
^{19}F NMR Spectrum of 4-(Cyclohexyl(hydroxy)methyl)phenyl Trifluoroborate (**4**)



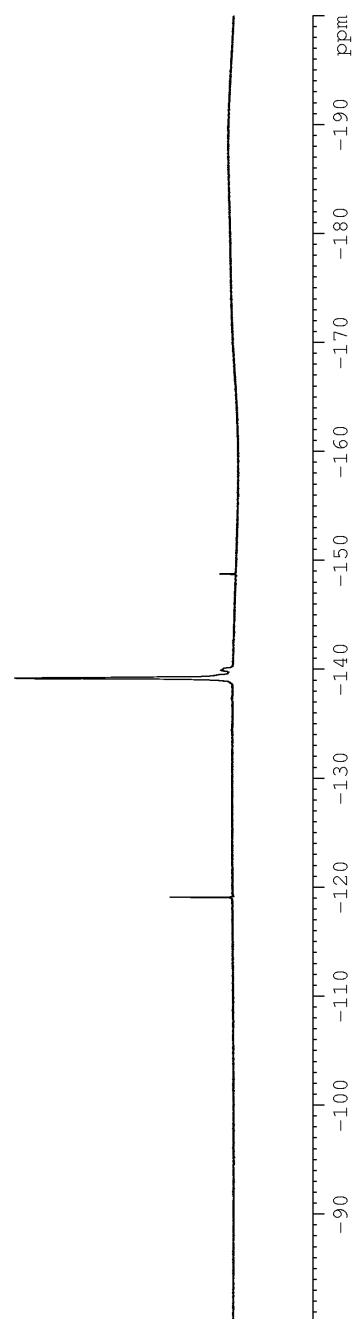
^{11}B NMR Spectrum of 4-(Cyclohexyl(hydroxy)methyl)phenyl Trifluoroborate (**4**)



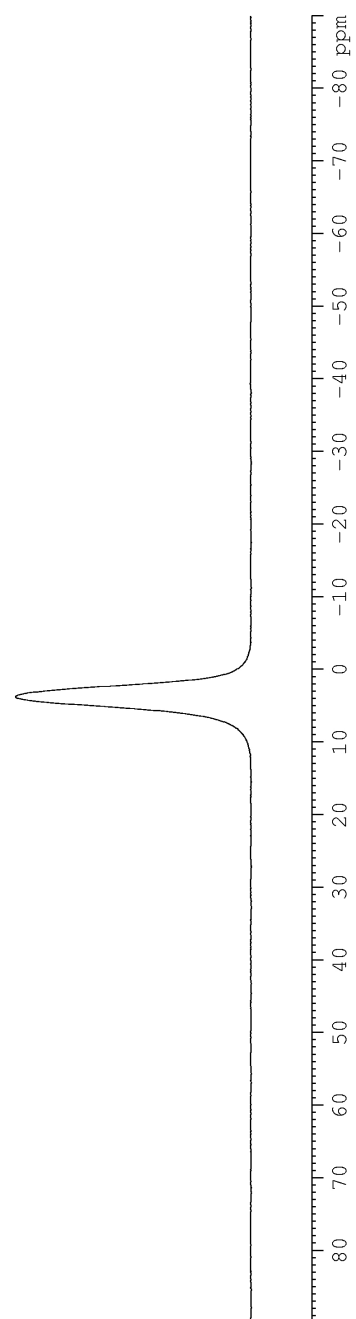
^1H NMR Spectrum of 4-(1-Hydroxyoctyl)phenyl Trifluoroborate (**6**)



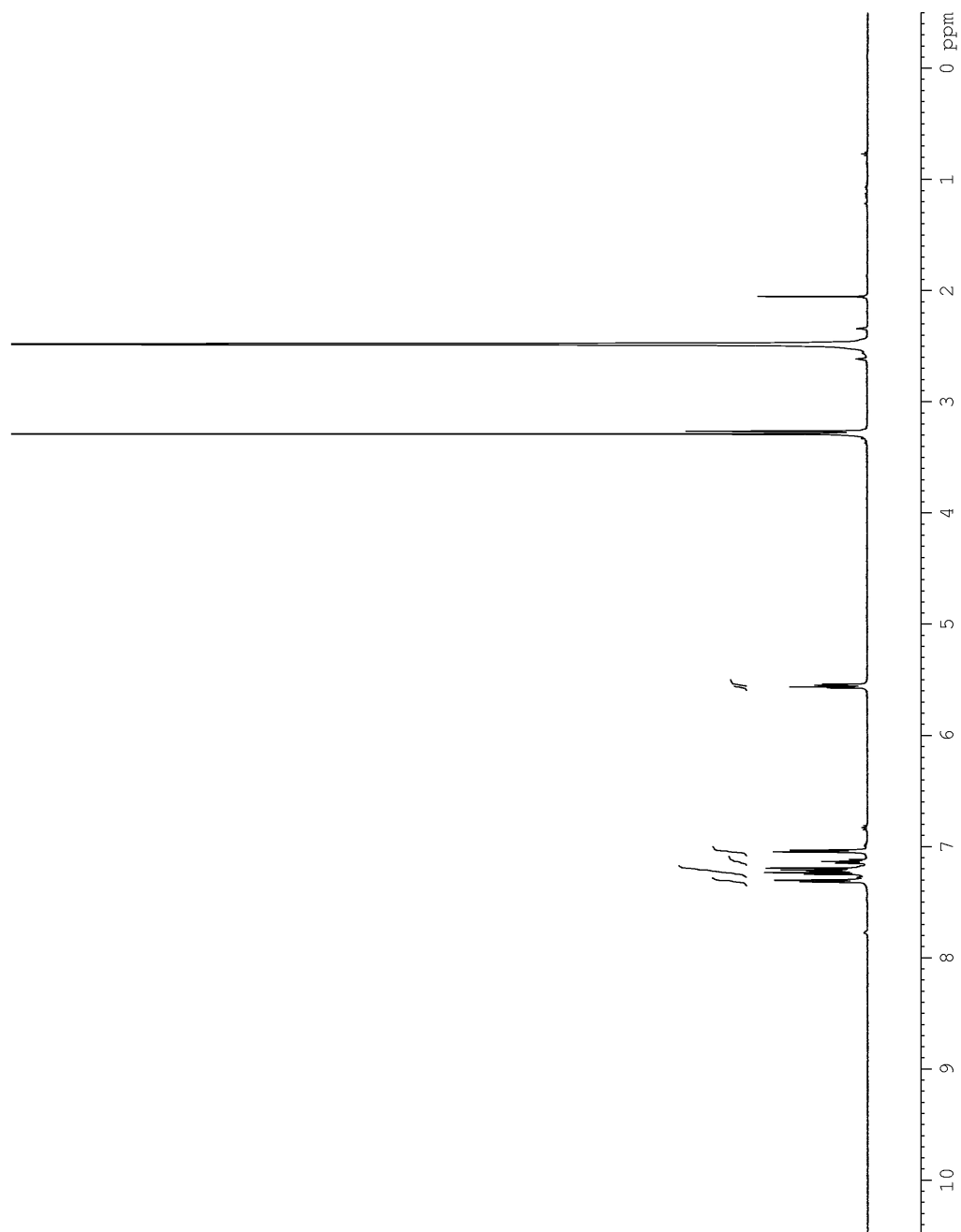
^{13}C NMR Spectrum of 4-(1-Hydroxyoctyl)phenyl Trifluoroborate (**6**)



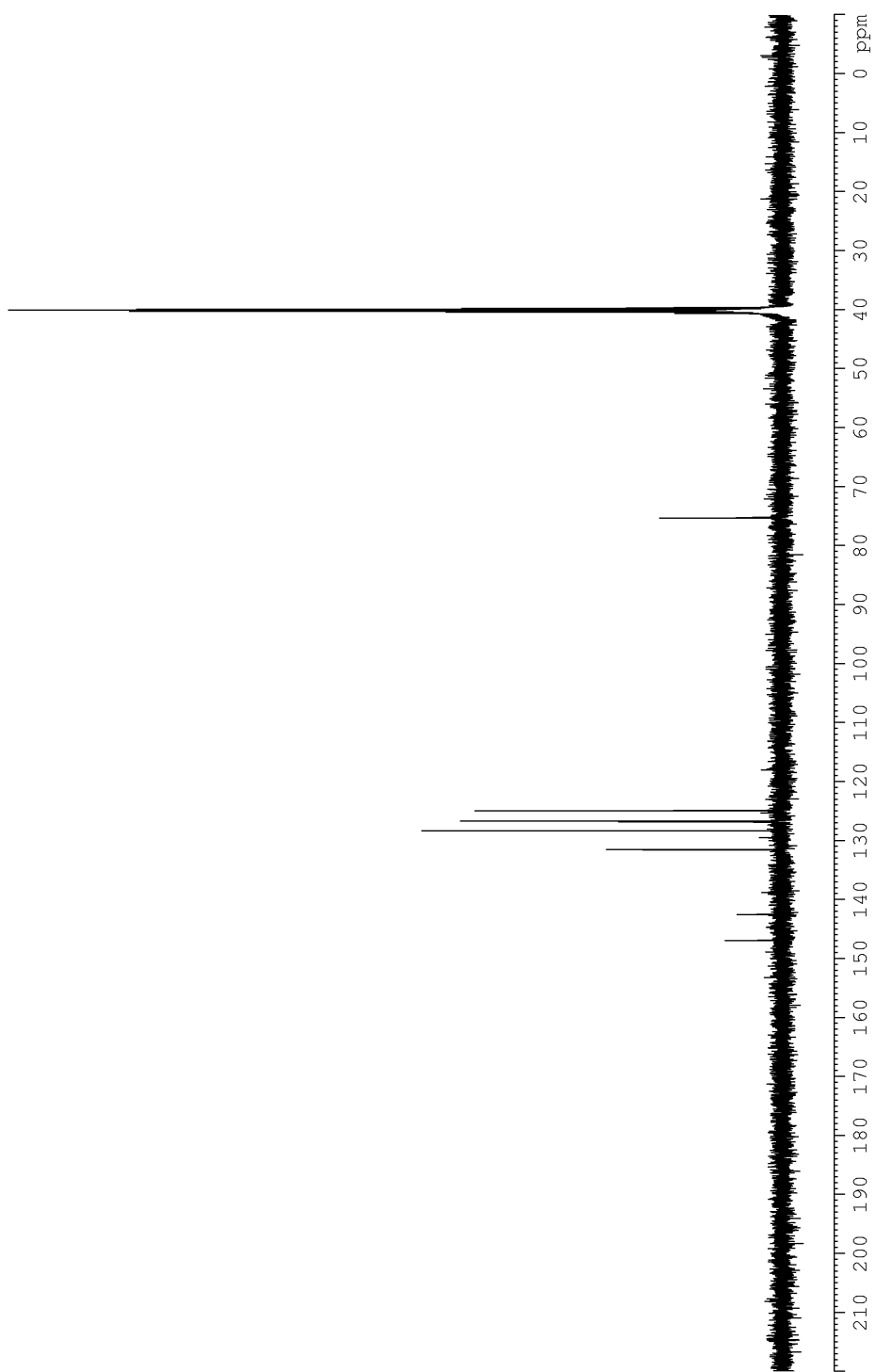
^{19}F NMR Spectrum of 4-(1-Hydroxyoctyl)phenyl Trifluoroborate (**6**)



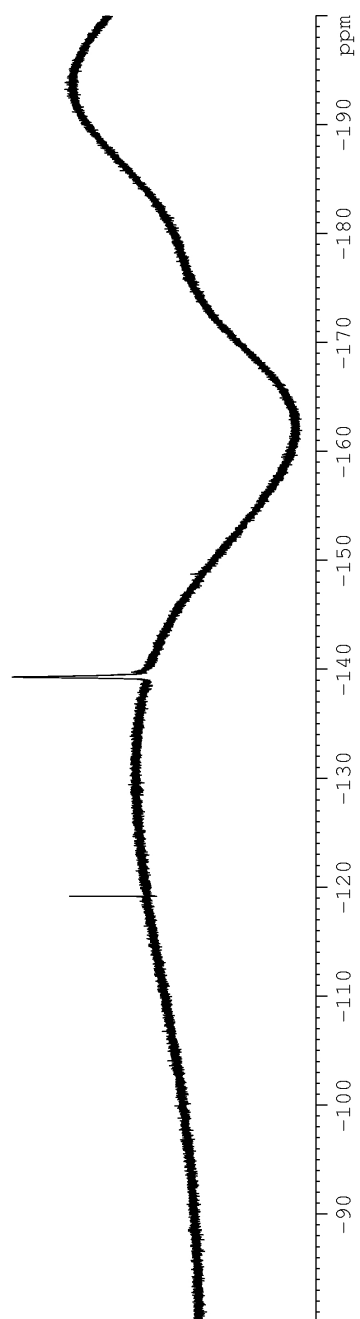
^{11}B NMR Spectrum of 4-(1-Hydroxyoctyl)phenyl Trifluoroborate (**6**)



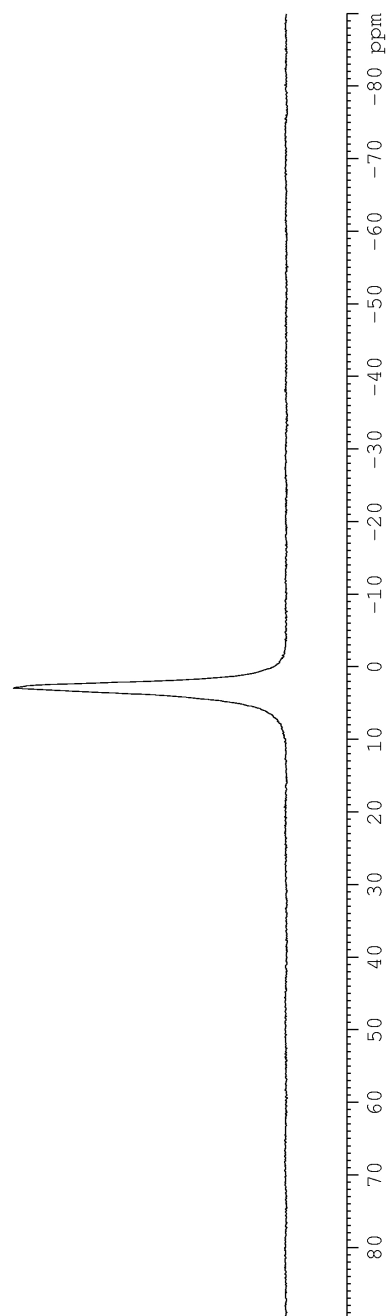
^1H NMR spectrum of 4-(Hydroxy(phenyl)methyl)phenyl Trifluoroborate (**8**)



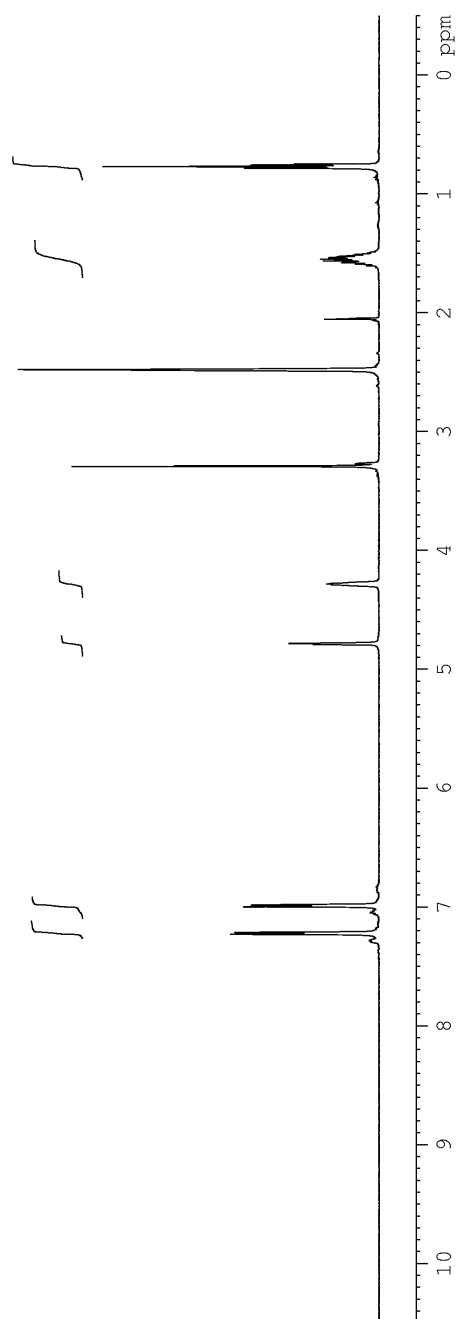
^{13}C NMR spectrum of 4-(Hydroxy(phenyl)methyl)phenyl Trifluoroborate (**8**)



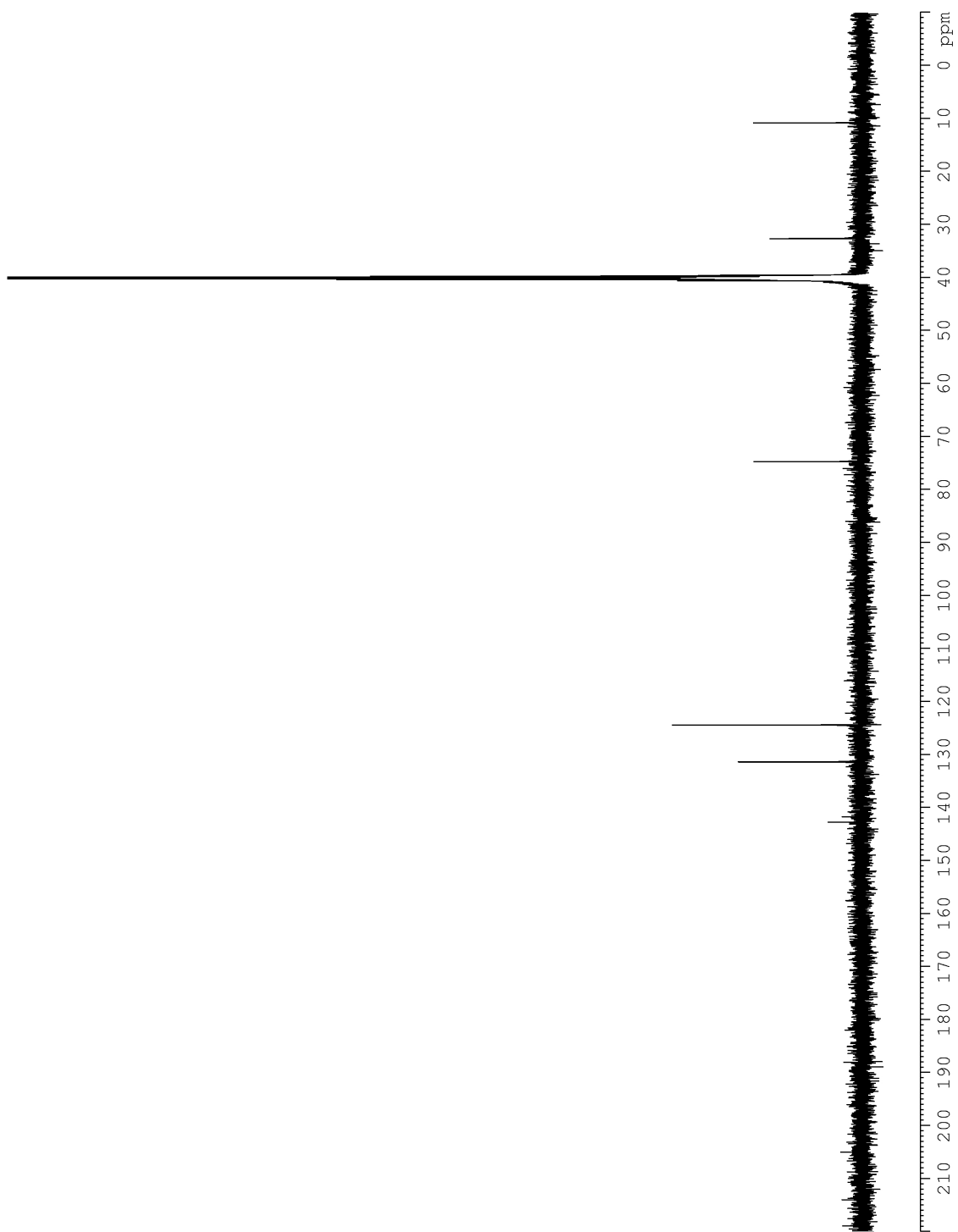
^{19}F NMR spectrum of 4-(Hydroxy(phenyl)methyl)phenyl Trifluoroborate (**8**)



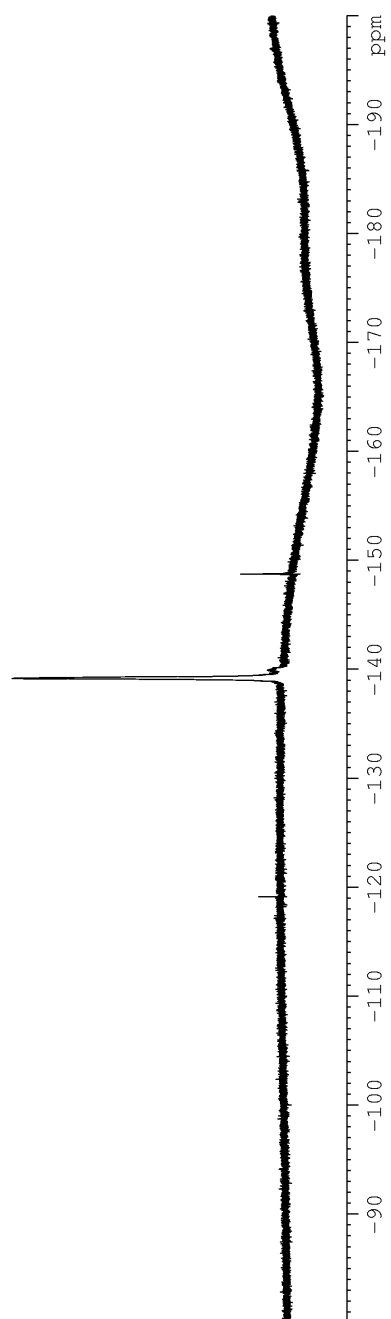
^{11}B NMR spectrum of 4-(Hydroxy(phenyl)methyl)phenyl Trifluoroborate (**8**)



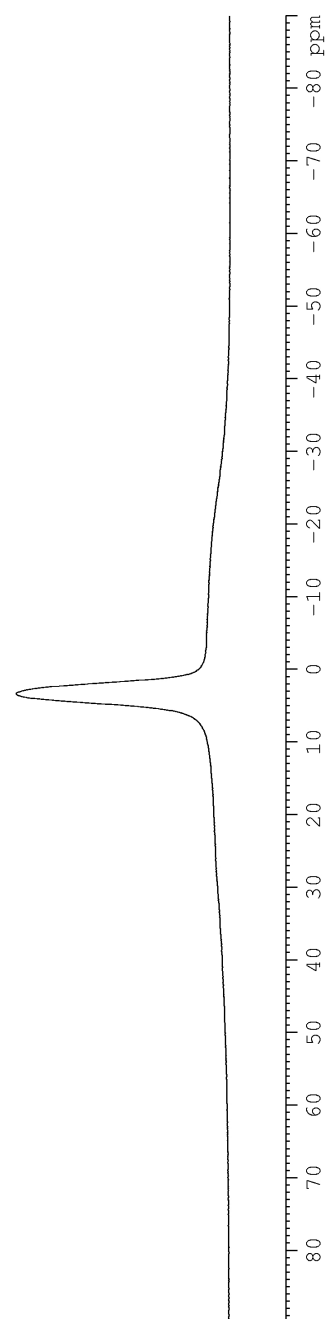
^1H NMR spectrum of 4-(1-Hydroxypropyl)phenyl Trifluoroborate (**10**)



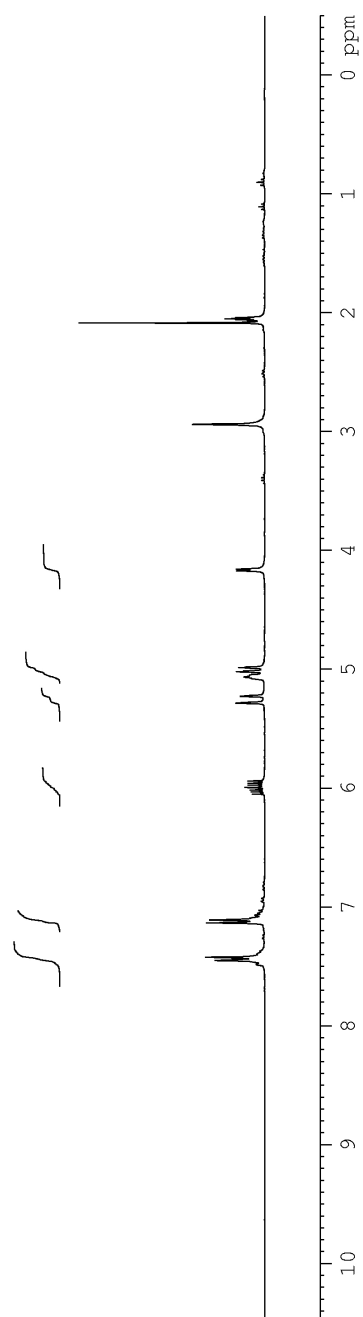
^{13}C NMR spectrum of 4-(1-Hydroxypropyl)phenyl Trifluoroborate (**10**)



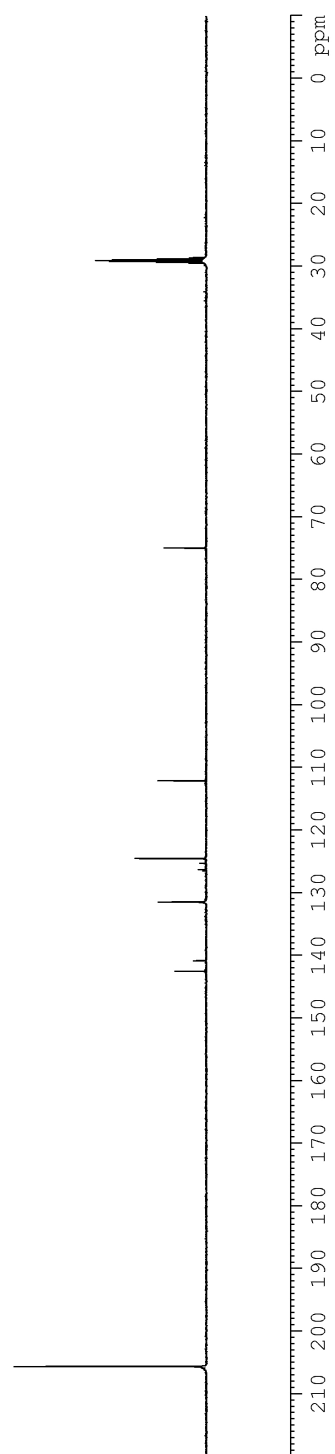
^{19}F NMR spectrum of 4-(1-Hydroxypropyl)phenyl Trifluoroborate (**10**)



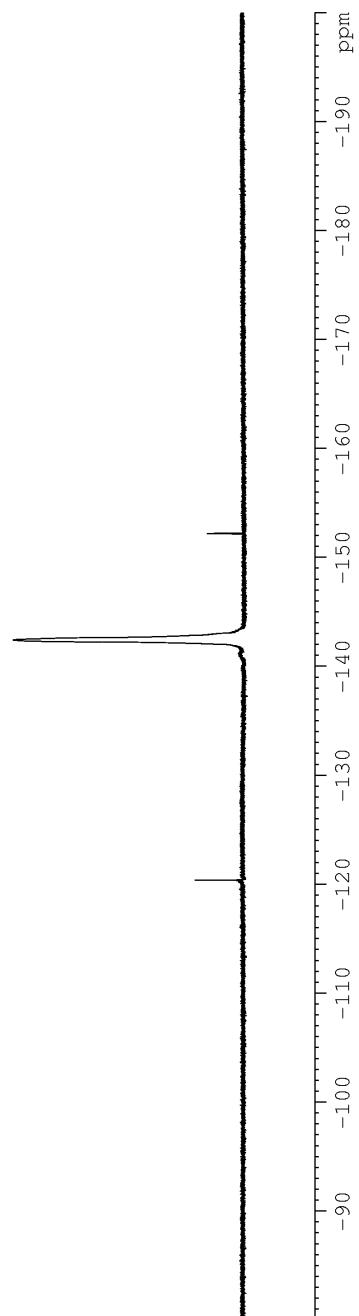
^{11}B NMR spectrum of 4-(1-Hydroxypropyl)phenyl Trifluoroborate (**10**)



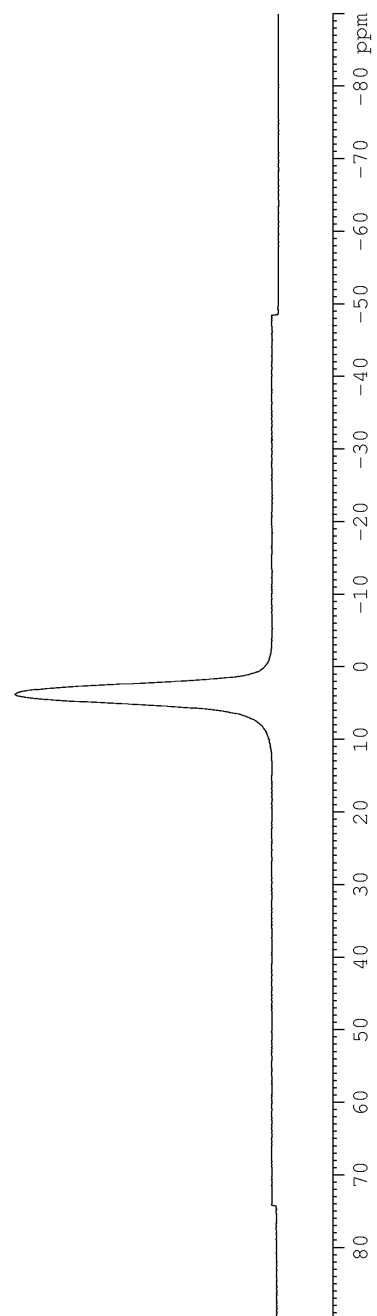
^1H NMR spectrum of 4-(1-Hydroxyallyl)phenyl Trifluoroborate (**12**)



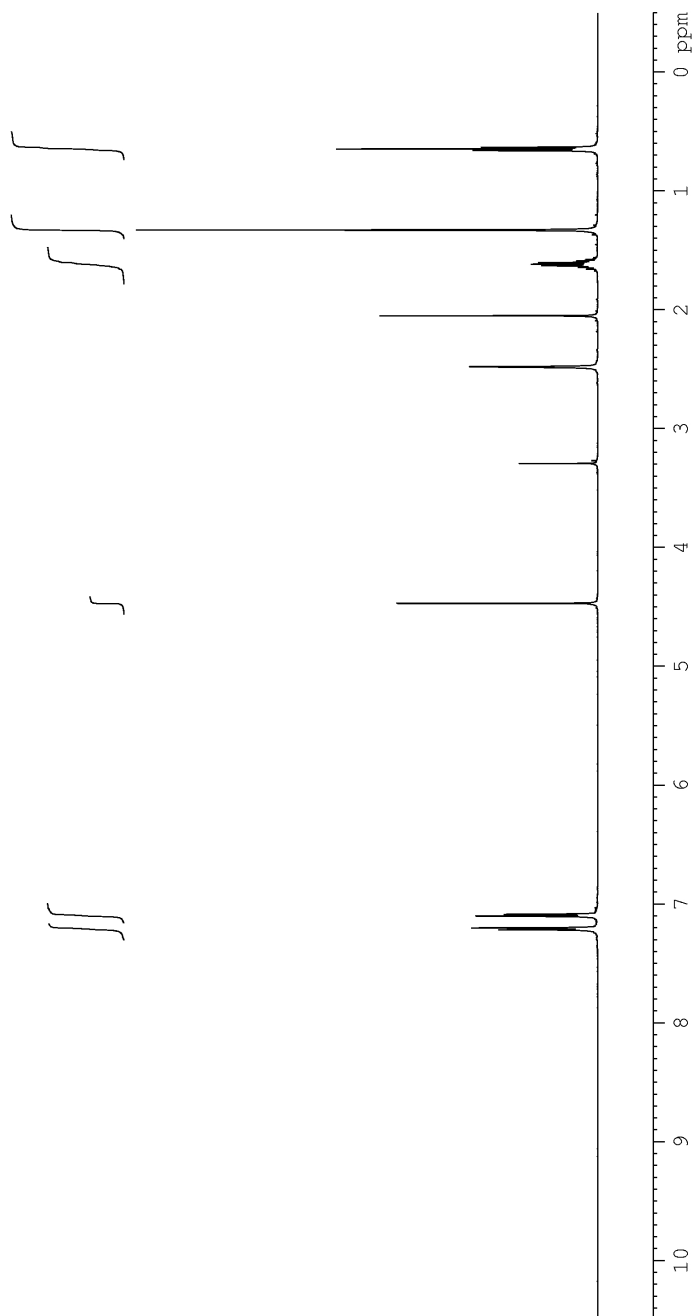
^{13}C NMR spectrum of 4-(1-Hydroxyallyl)phenyl Trifluoroborate (**12**)



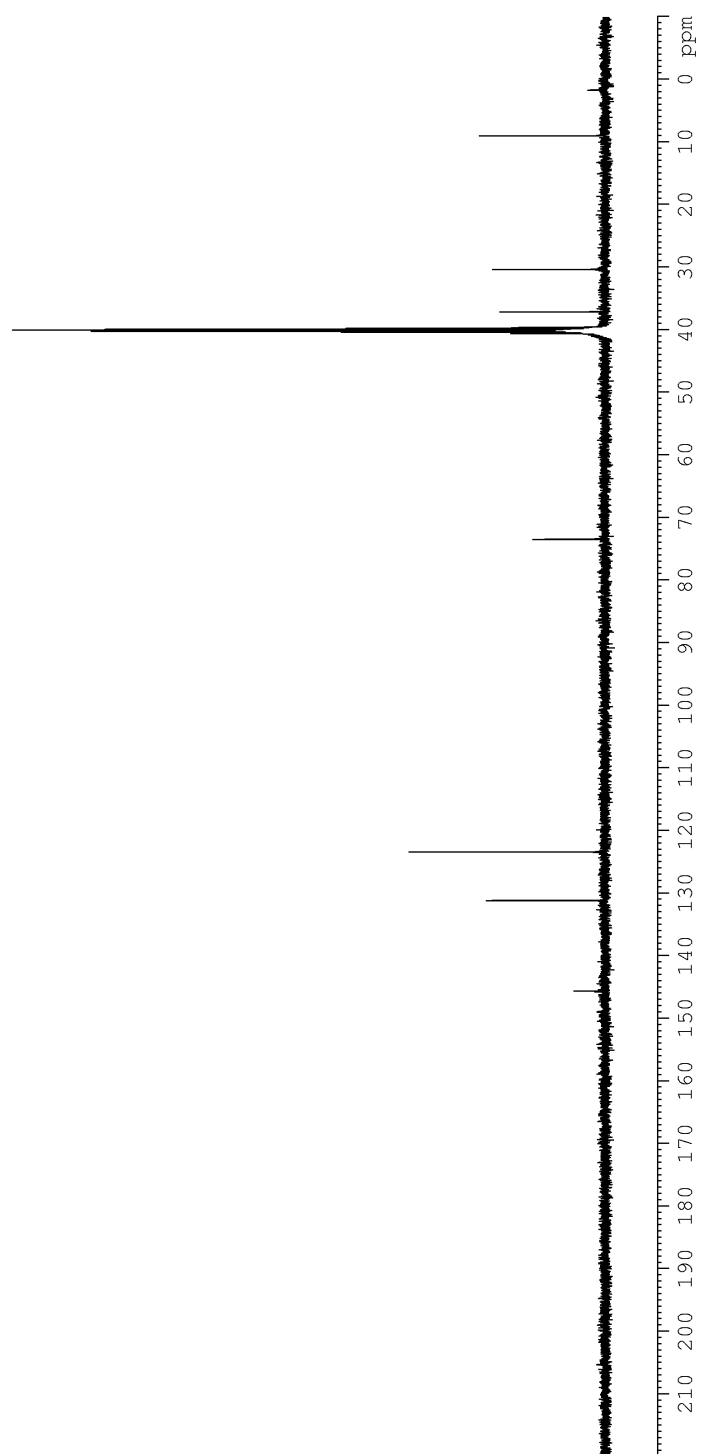
^{19}F NMR spectrum of 4-(1-Hydroxyallyl)phenyl Trifluoroborate (**12**)



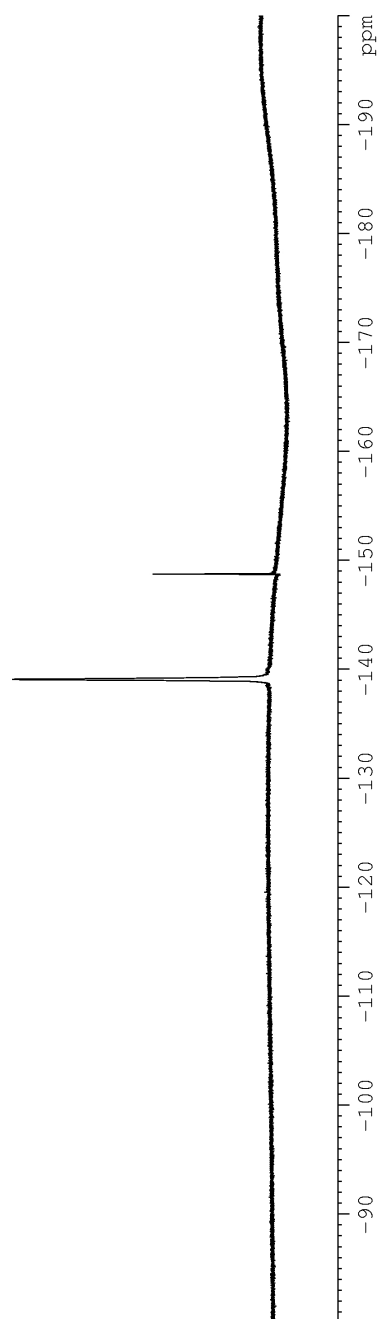
^{11}B NMR spectrum of 4-(1-Hydroxyallyl)phenyl Trifluoroborate (**12**)



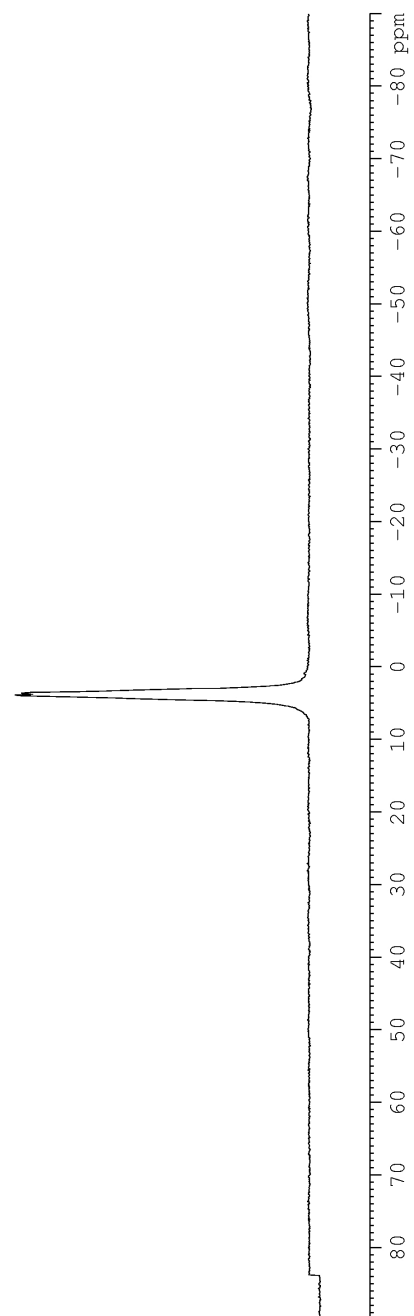
^1H NMR spectrum of 4-(2-Hydroxy-2-butanyl)phenyl Trifluoroborate (**14**)



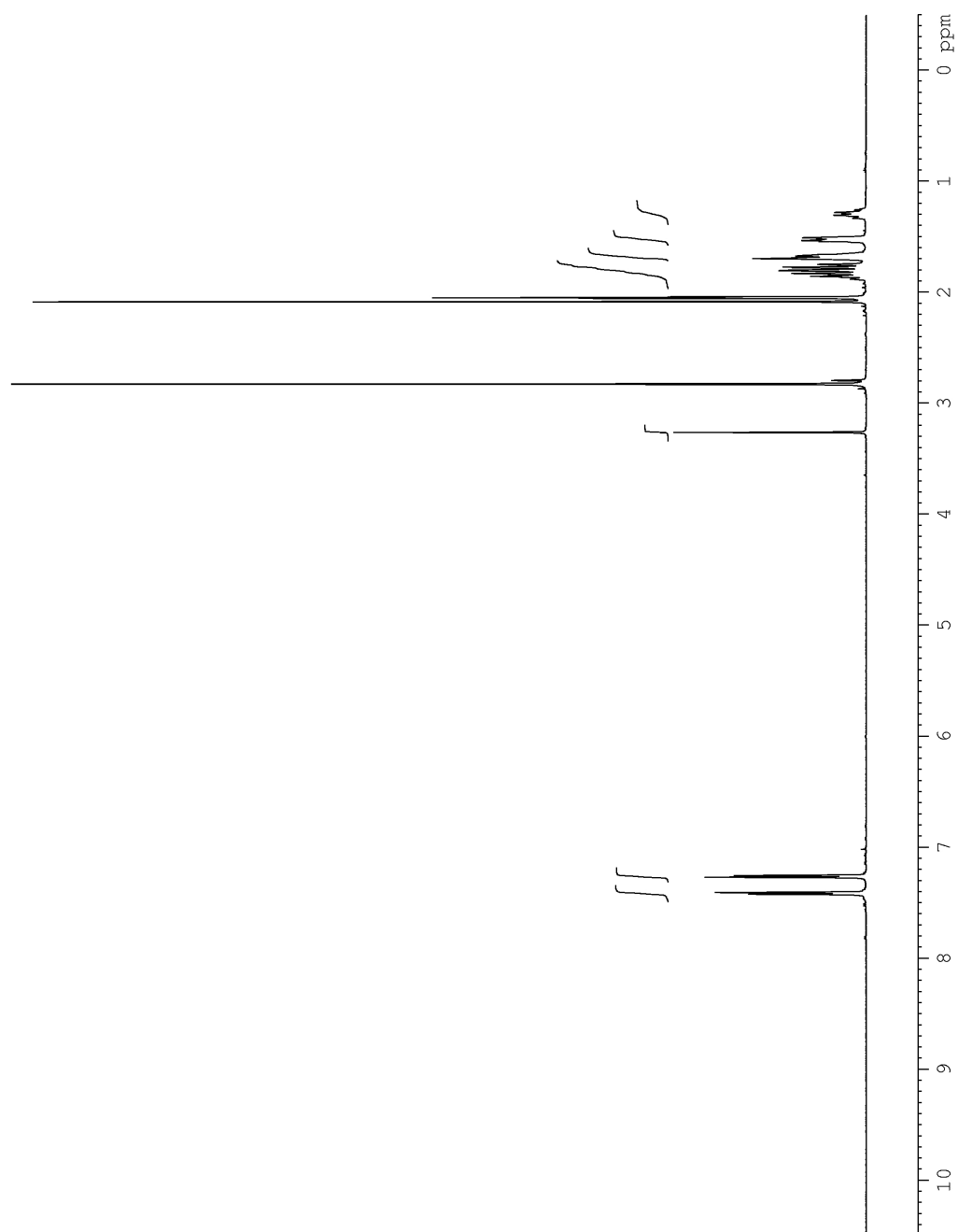
^{13}C NMR spectrum of 4-(2-Hydroxy-2-butanyl)phenyl Trifluoroborate (**14**)



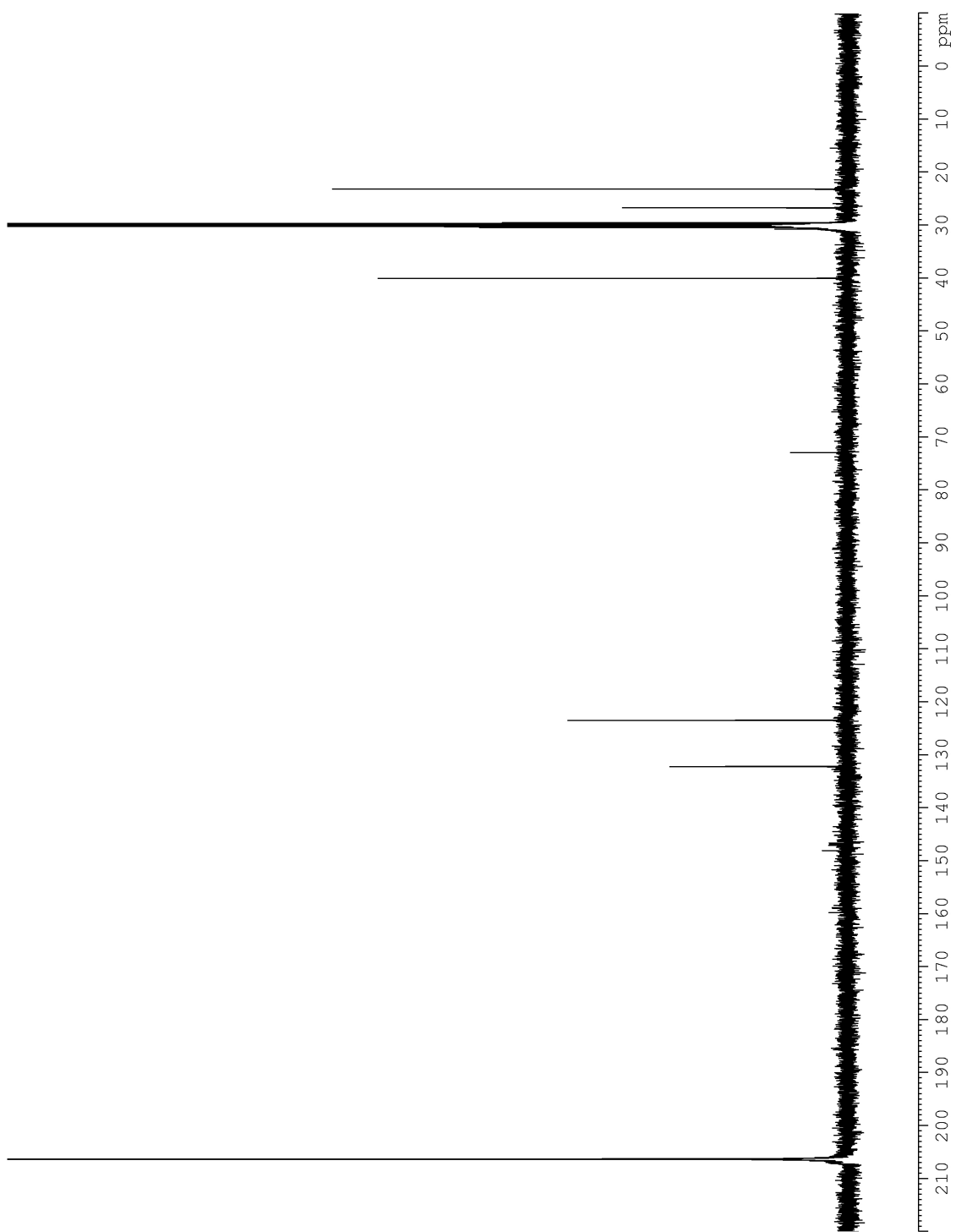
^{19}F NMR spectrum of 4-(2-Hydroxy-2-butanyl)phenyl Trifluoroborate (**14**)



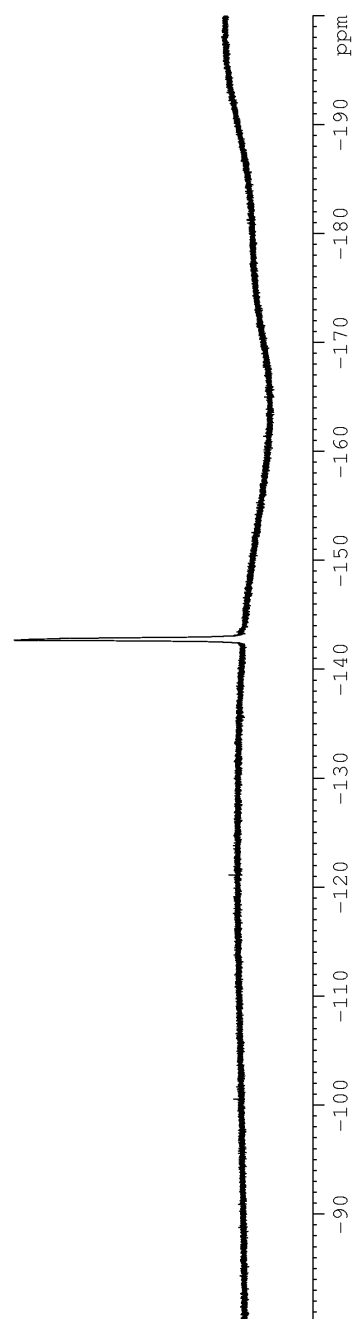
^{11}B NMR spectrum of 4-(2-Hydroxy-2-butanyl)phenyl Trifluoroborate (**14**)



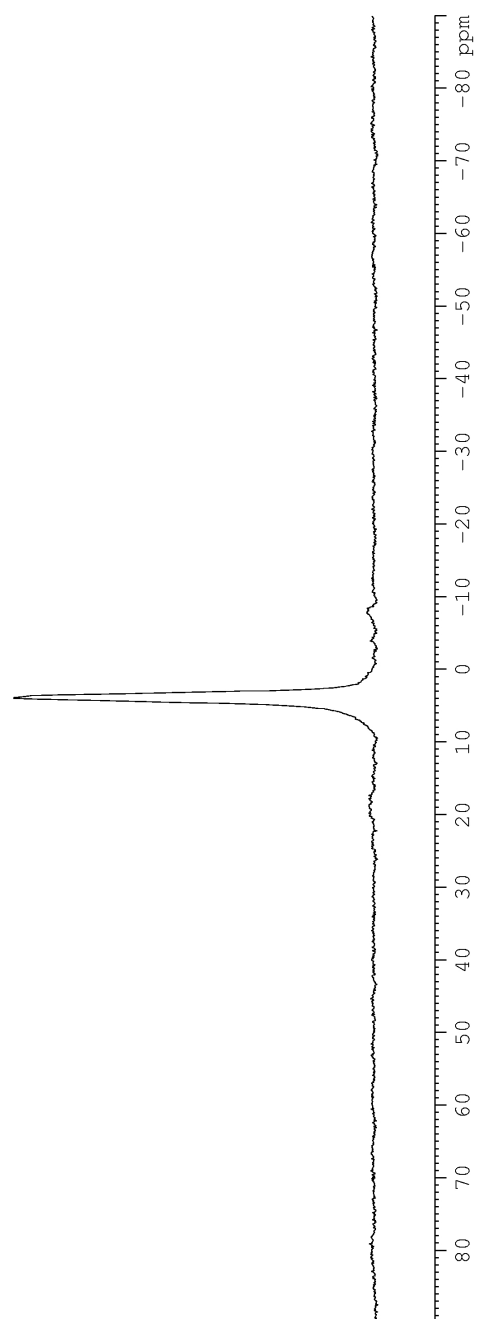
^1H NMR spectrum of 4-(Hydroxycyclohexyl)phenyl Trifluoroborate (**16**)



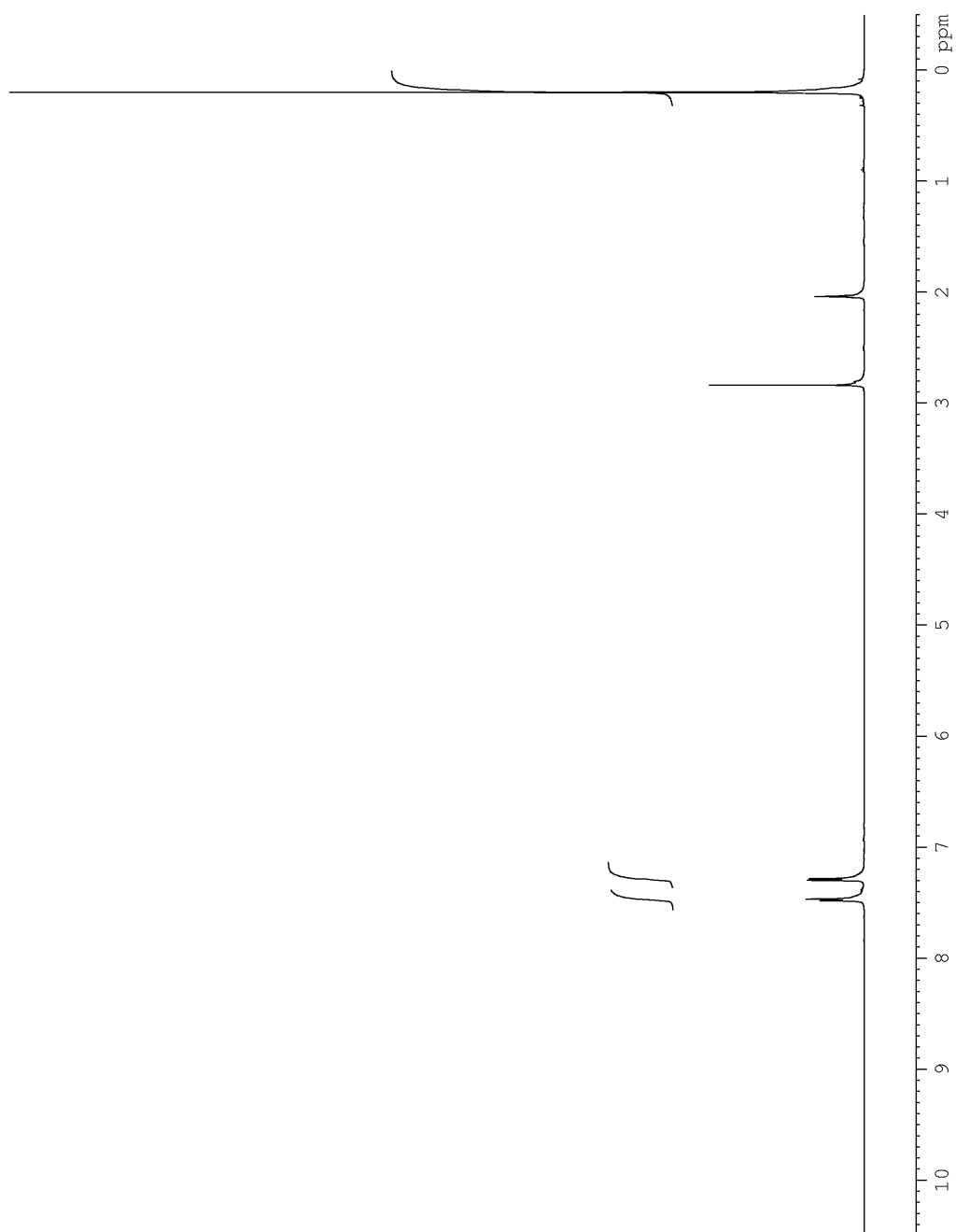
^{13}C NMR spectrum of 4-(Hydroxycyclohexyl)phenyl Trifluoroborate (**16**)



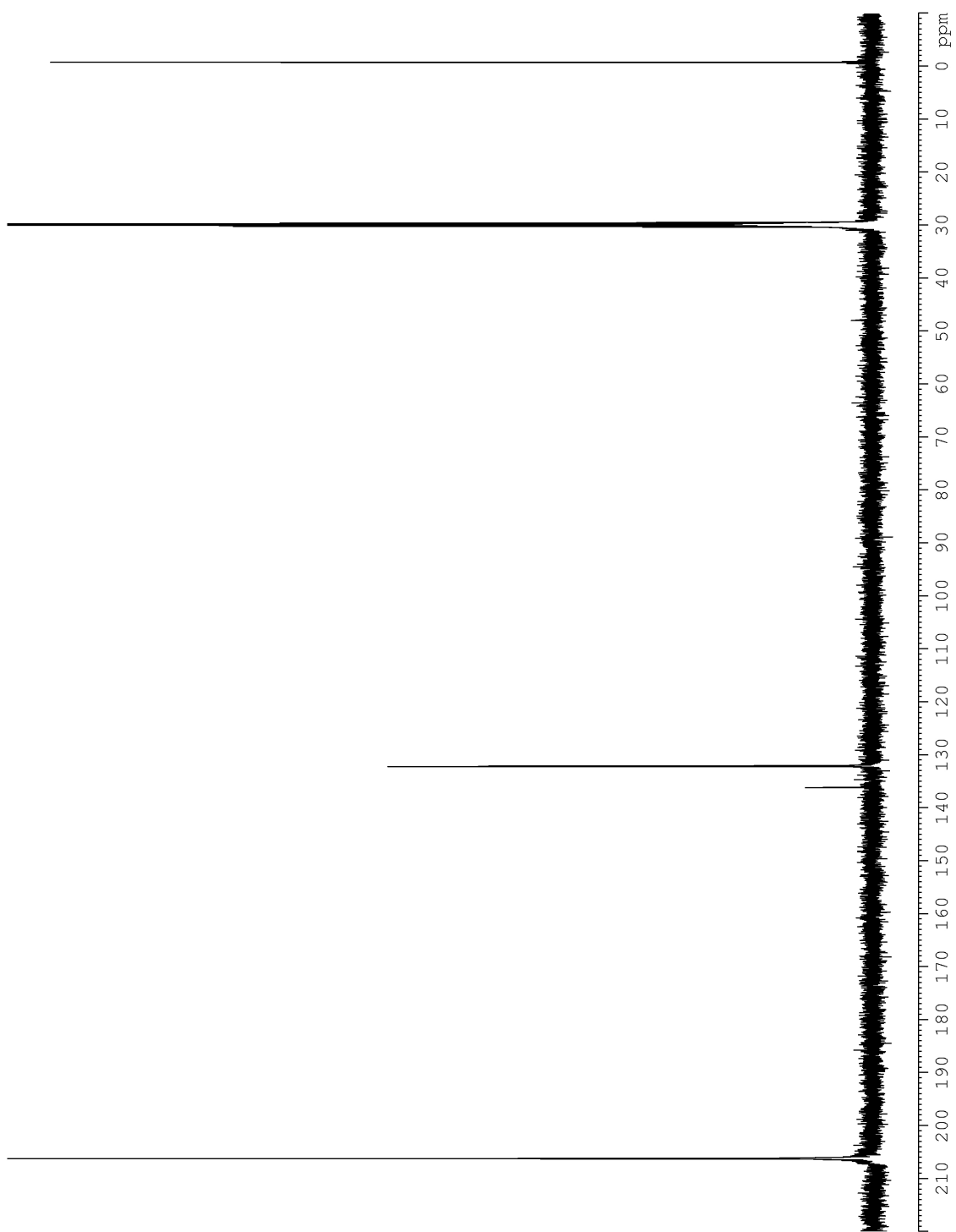
^{19}F NMR spectrum of 4-(Hydroxycyclohexyl)phenyl Trifluoroborate (**16**)



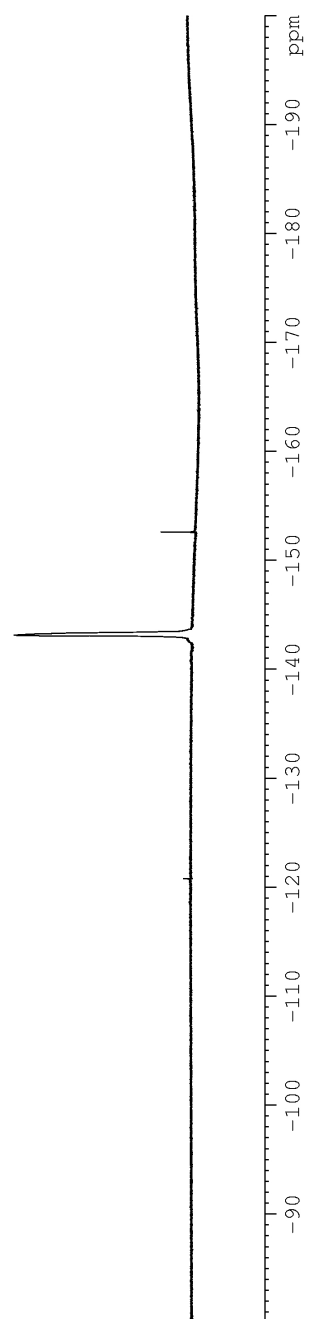
^{11}B NMR spectrum of 4-(Hydroxycyclohexyl)phenyl Trifluoroborate (**16**)



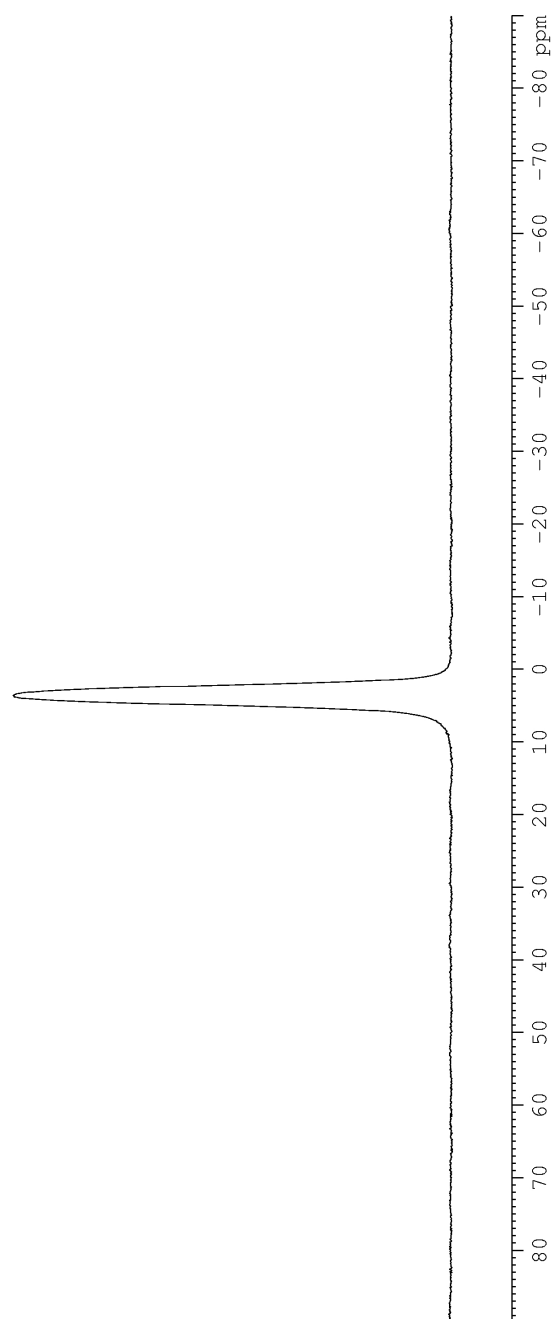
^1H NMR spectrum of 4-(Trimethylsilyl)phenyl Trifluoroborate (**18**)



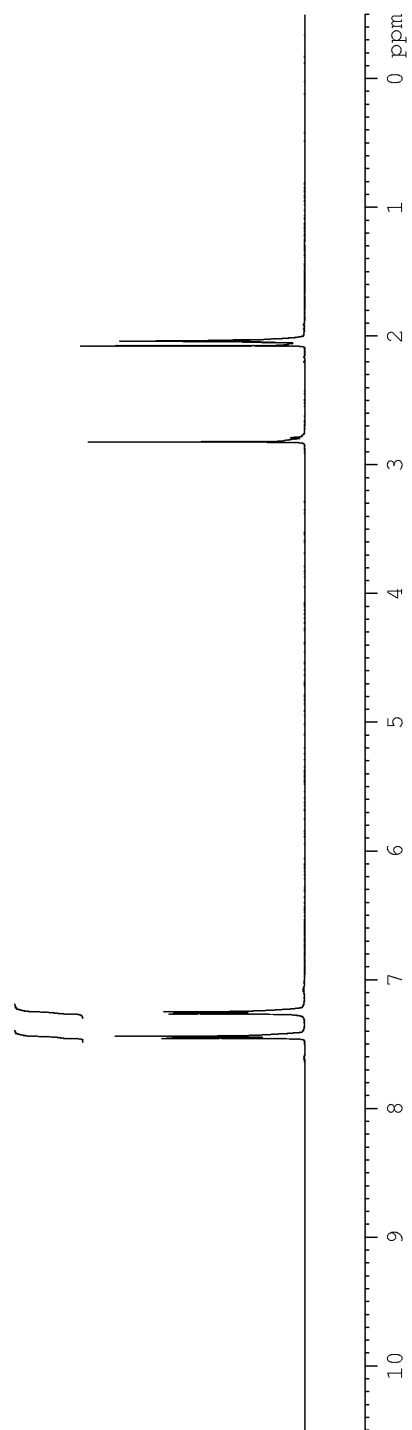
^{13}C NMR spectrum of 4-(Trimethylsilyl)phenyl Trifluoroborate (**18**)



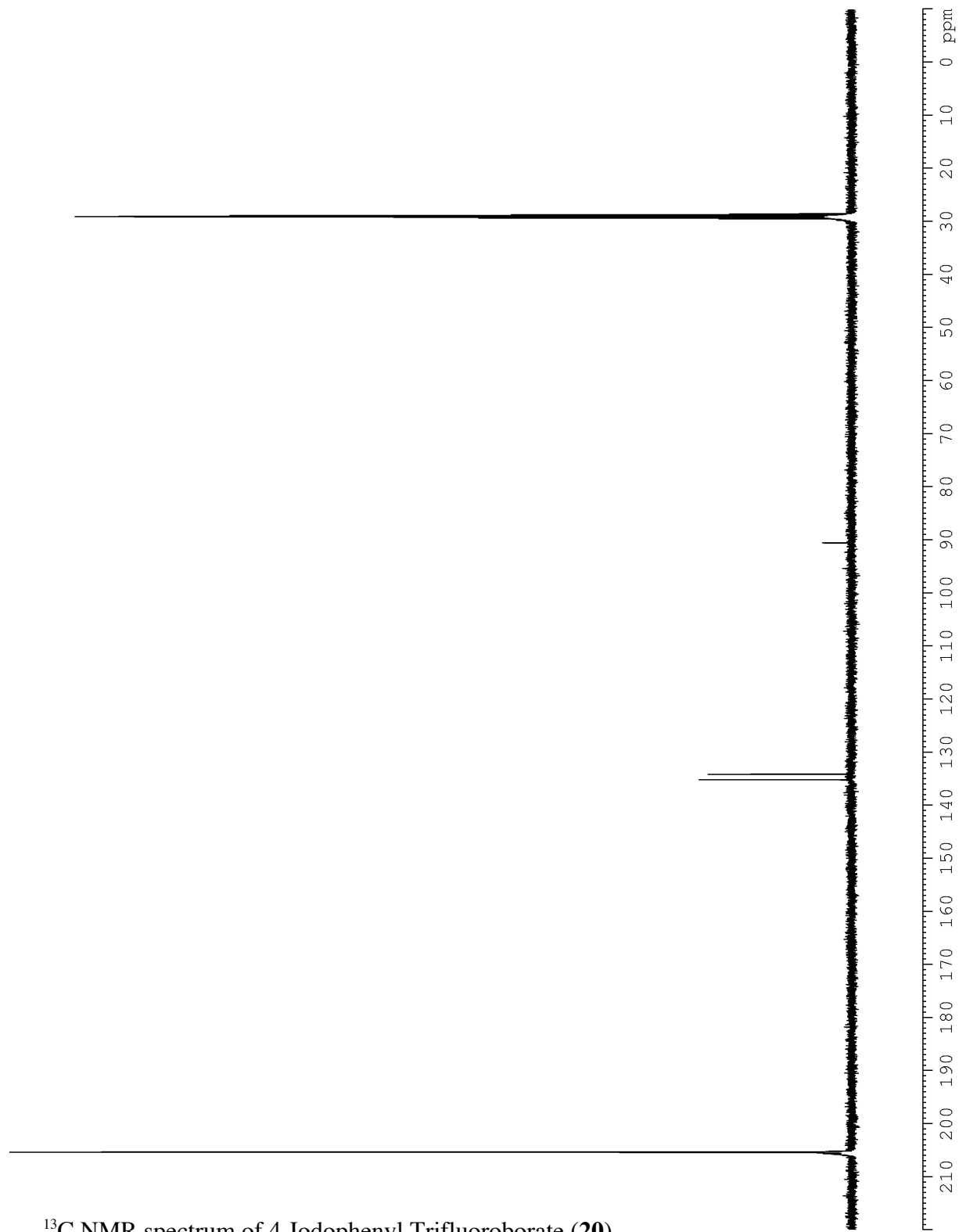
^{19}F NMR spectrum of 4-(Trimethylsilyl)phenyl Trifluoroborate (**18**)



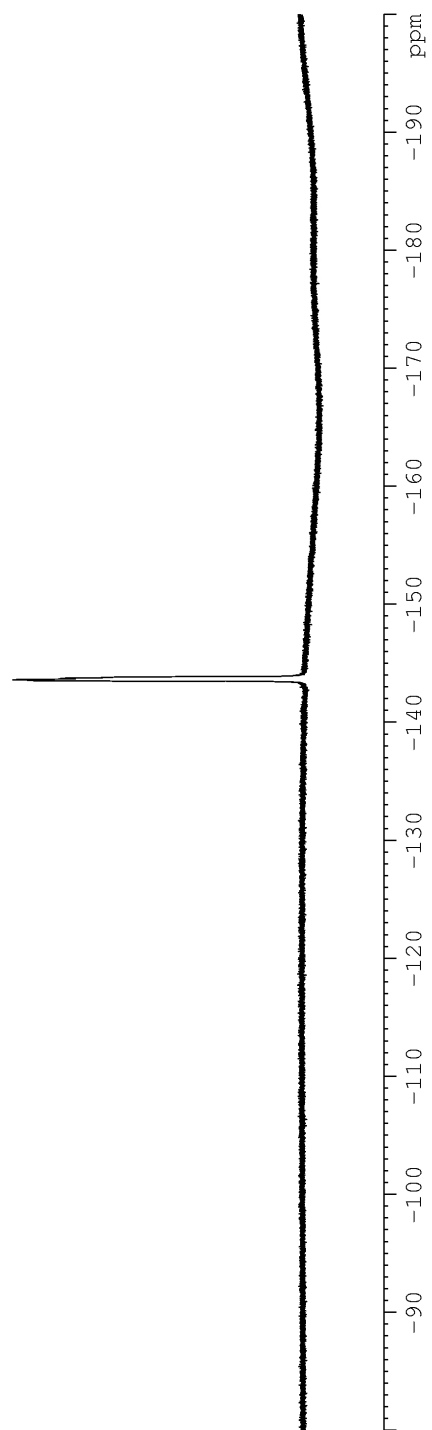
^{11}B NMR spectrum of 4-(Trimethylsilyl)phenyl Trifluoroborate (**18**)

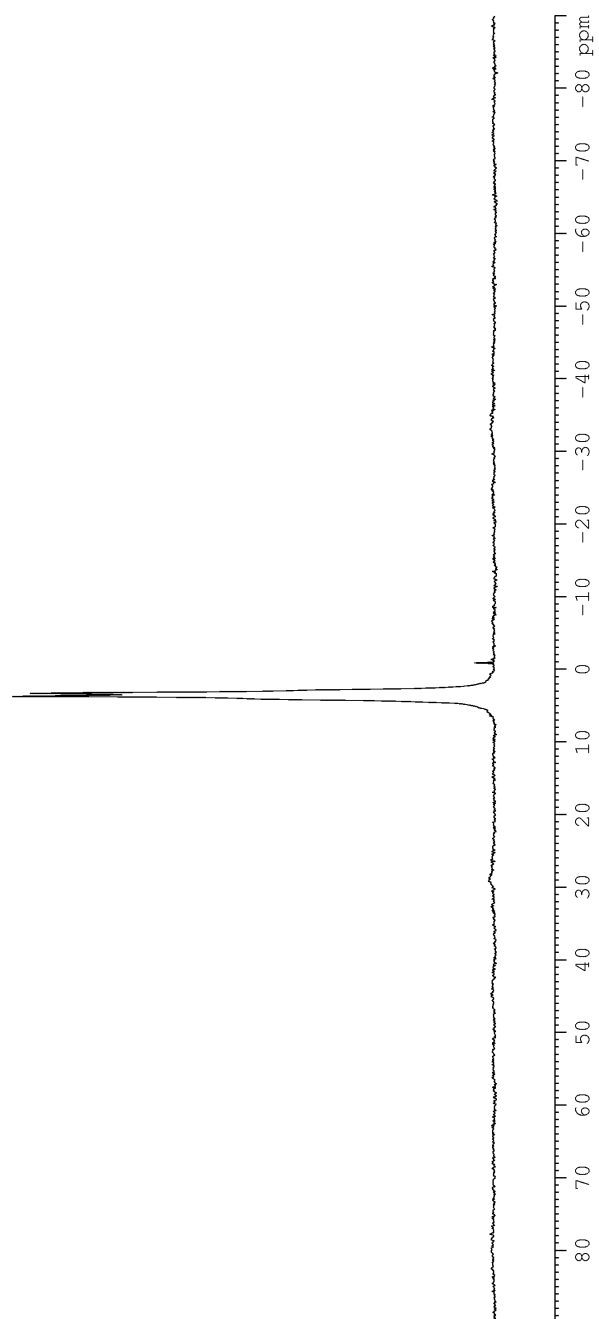


^1H NMR spectrum of 4-Iodophenyl Trifluoroborate (**20**)

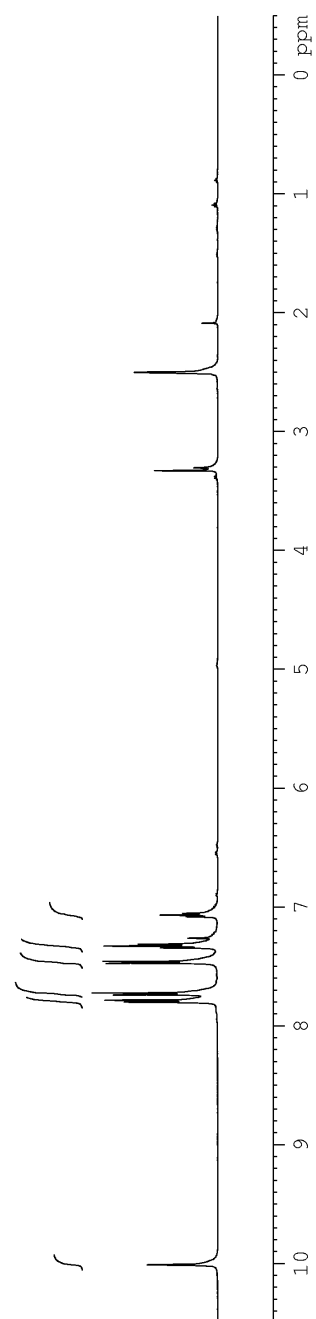


^{19}F NMR spectrum of 4-Iodophenyl Trifluoroborate (**20**)

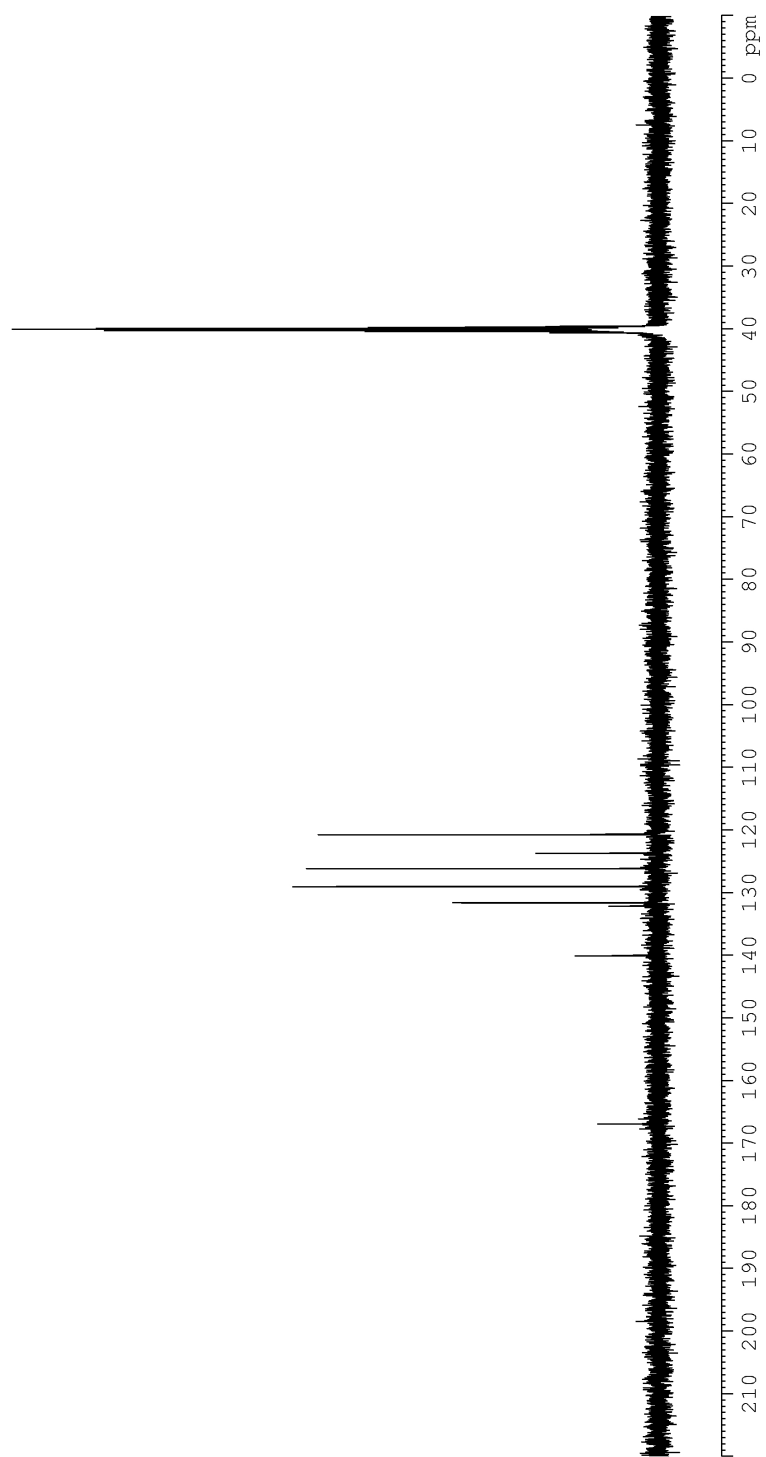




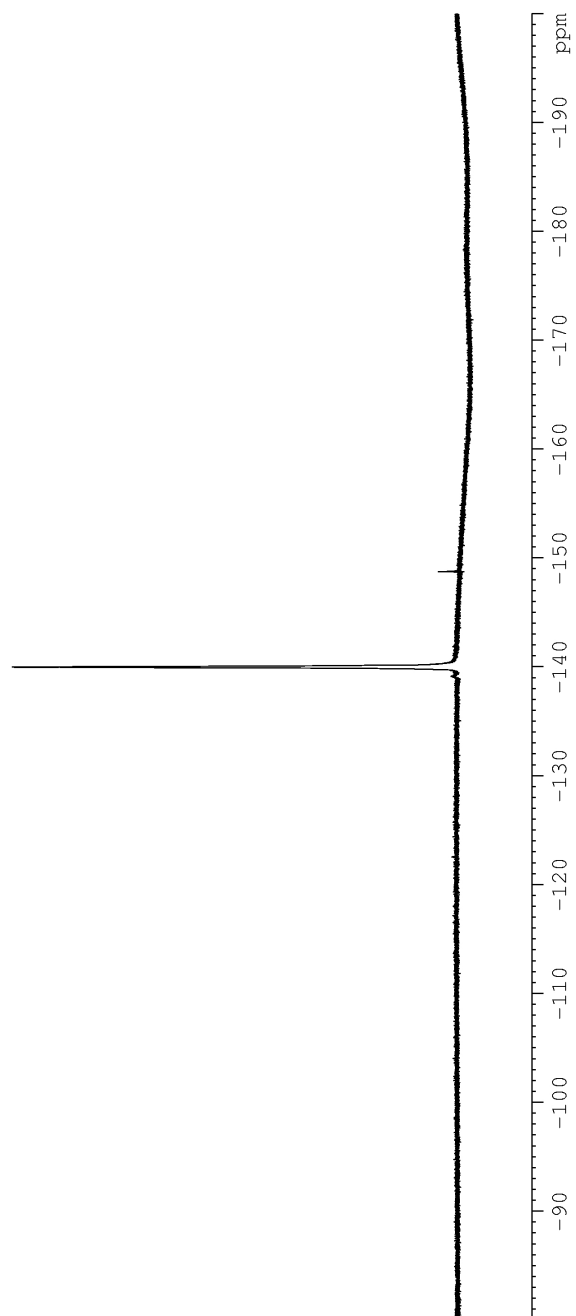
^{11}B NMR spectrum of 4-Iodophenyl Trifluoroborate (**20**)



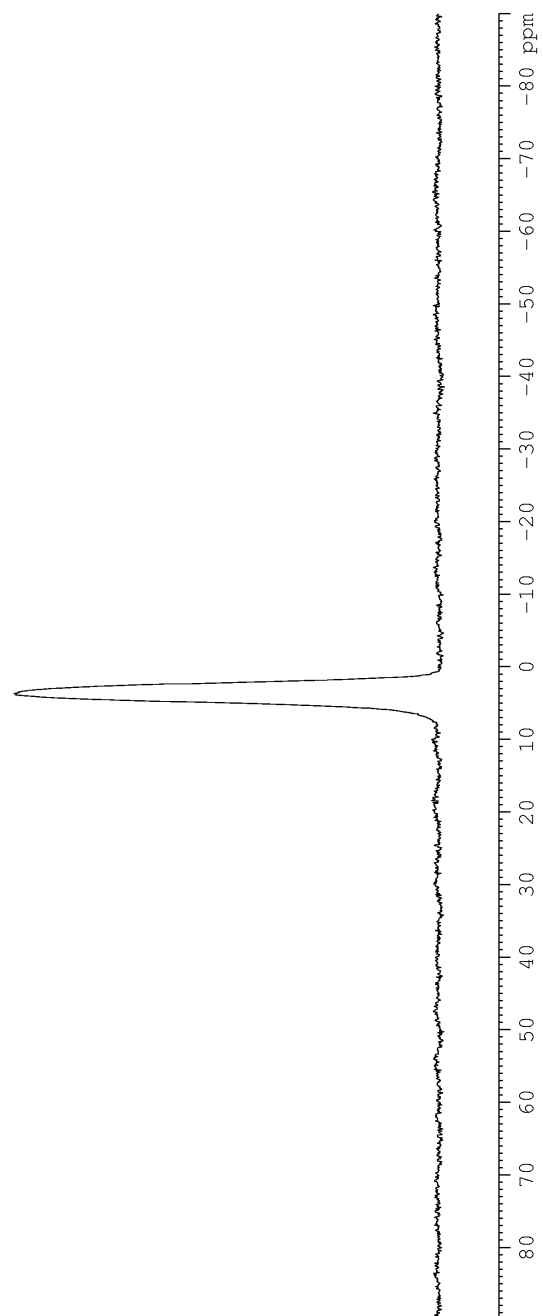
^1H NMR spectrum of 4-(Phenylcarbamoyl)phenyl Trifluoroborate (**22**)



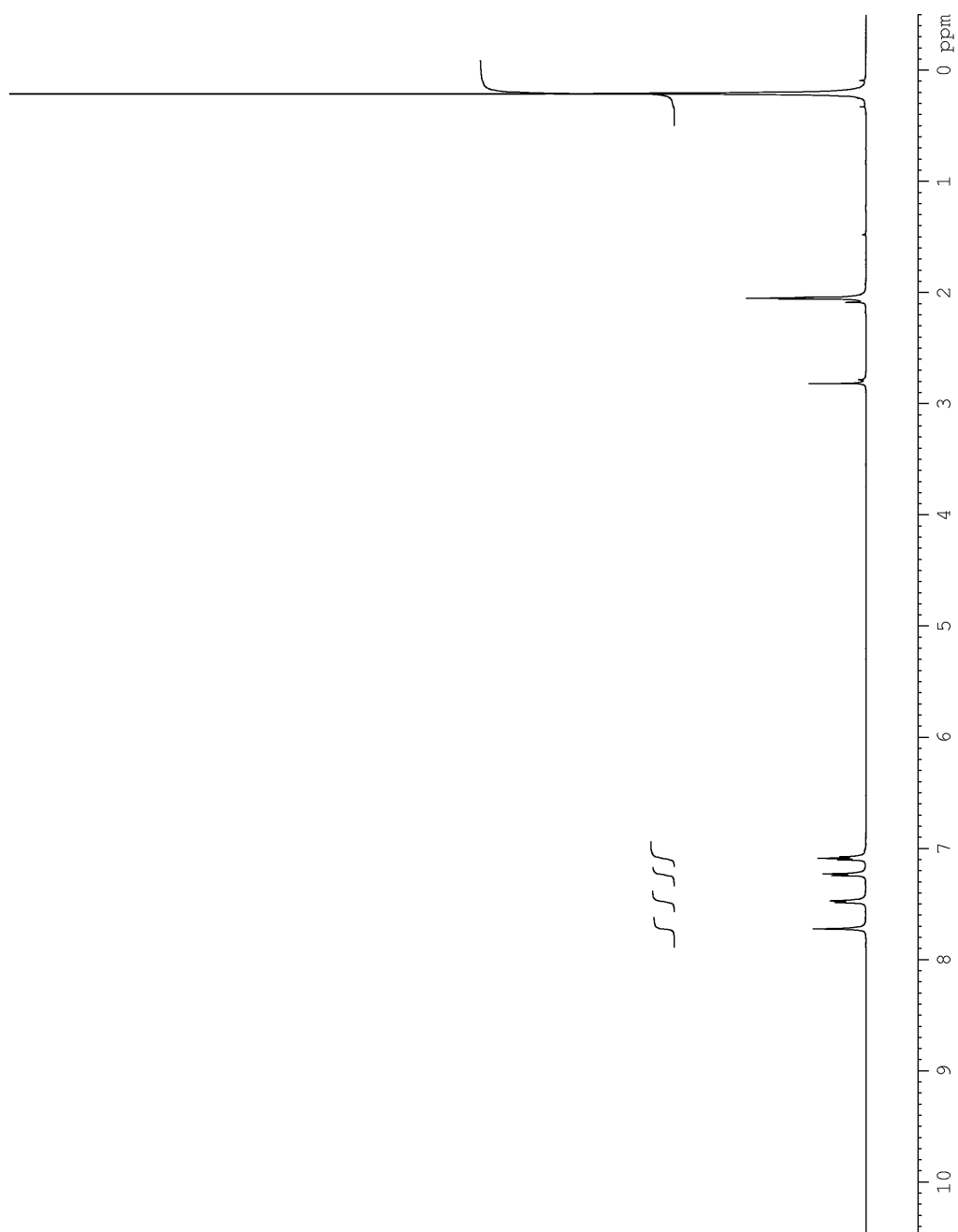
^{13}C NMR spectrum of 4-(Phenylcarbamoyl)phenyl Trifluoroborate (**22**)



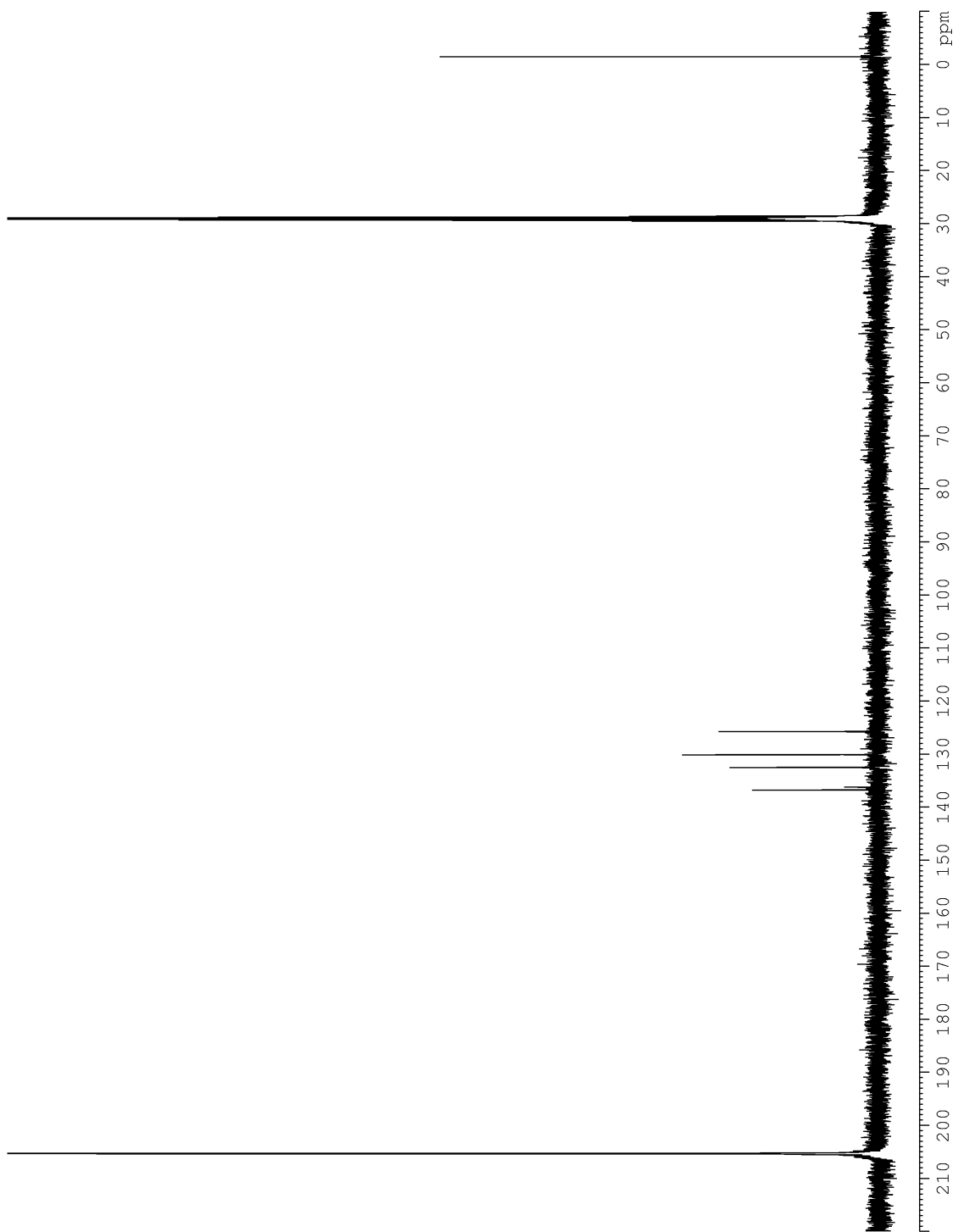
^{19}F NMR spectrum of 4-(Phenylcarbamoyl)phenyl Trifluoroborate (**22**)



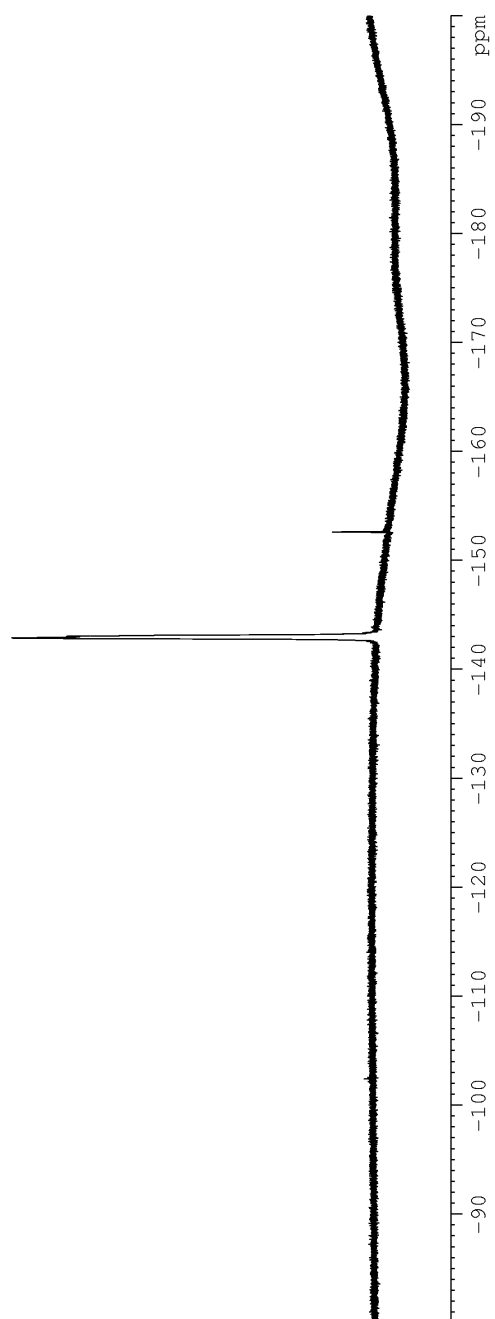
^{11}B NMR spectrum of 4-(Phenylcarbamoyl)phenyl Trifluoroborate (**22**)



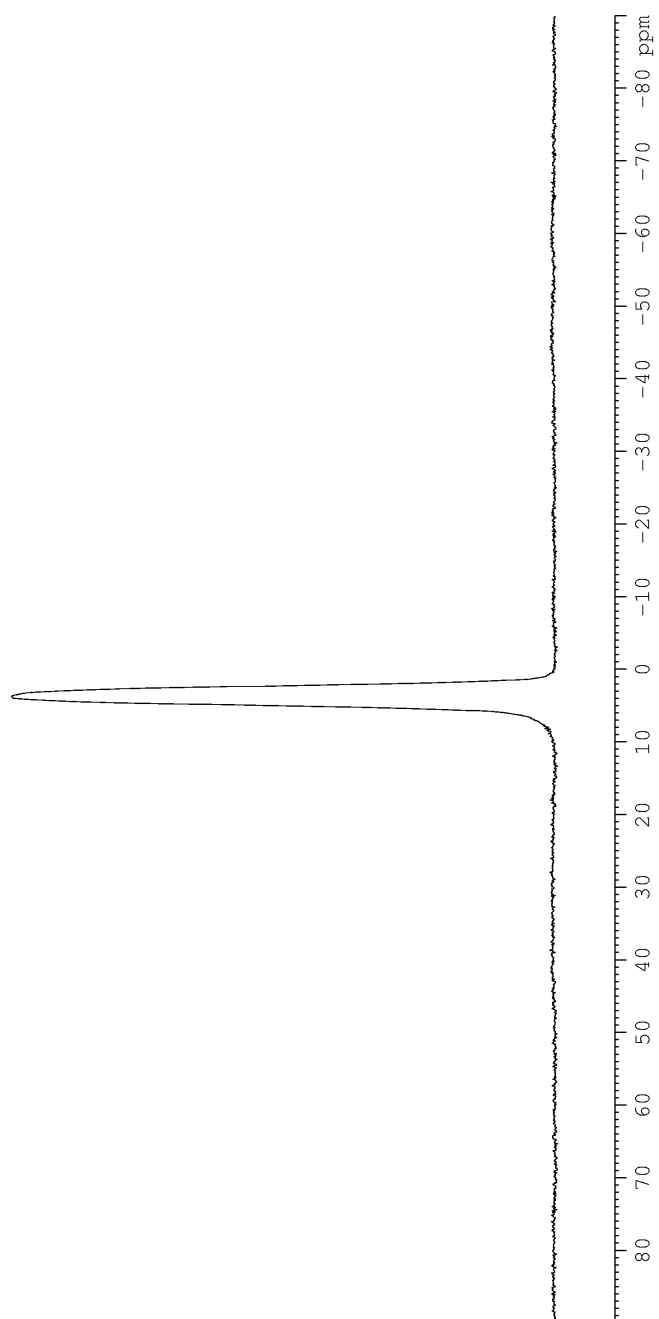
^1H NMR spectrum of 3-(Trimethylsilyl)phenyl Trifluoroborate (**24**)



^{13}C NMR spectrum of 3-(Trimethylsilyl)phenyl Trifluoroborate (**24**)



^{19}F NMR spectrum of 3-(Trimethylsilyl)phenyl Trifluoroborate (**24**)



^{11}B NMR spectrum of 3-(Trimethylsilyl)phenyl Trifluoroborate (**24**)