Functional Group Compatibility of the Oxidation-Resistant Benzoxaborolone Pharmacophore

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Abbreviations

Abs	absorbance
aq.	aqueous
B_2Pin_2	bis(pinacolato)diboron
B(O*i*Pr)	triisopropyl borate
BOL	benzoxaborolone
°C	degrees Celsius
cat.	catalytic
cLog*P*	calculated logarithm of the partition coefficient
conc.	concentrated
Da	Dalton
DART	direct analysis in real time
DCM	dichloromethane
δ	NMR chemical shift
DMAP	4-(dimethylamino)pyridine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
equiv	equivalents
ESI	electrospray ionization
ESIPT	excited-state intramolecular proton transfer
Et_3N	triethylamine
EW	electron-withdrawing
ED	electron-donating
h	hour
HBQ	10-hydroxybenzo[*h*]quinolone
HCl	hydrochloric acid
HRMS	high-resolution mass spectrometry
*i*PrMg·LiCl	isopropylmagnesium chloride lithium chloride complex (Turbo Grignard)
k_{ox}	second-order rate constant for oxidation
KOAc	potassium acetate
k_{rel}	relative second-order rate constant for oxidation
LDA	lithium diisopropylamide
M	molar (moles/liter)
MeOH	methanol
min	minutes
mM	millimolar (millimoles/liter)
MHz	megahertz
m/*z*	mass-to-charge ratio
4-nitro-PBA	(4-nitrophenyl)boronic acid
N	normal (equiv/liter)
NMR	nuclear magnetic resonance
o/n	overnight
PBA	phenylboronic acid
$PdCl_2$(dppf)	1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II)
Q-TOF	quadrupole time-of-flight

quant.	quantitative yield
ROS	reactive oxygen species
rt	room temperature
s	seconds or solid
sat. aq.	saturated aqueous
SE	standard error
SD	standard deviation
t-BuOH	*tert*-butyl alcohol
t-BuOK	potassium *tert*-butoxide
THF	tetrahydrofuran
TLC	thin-layer chromatography
TMS-Cl	trimethylsilyl chloride
TOF	time-of-flight
UV	ultraviolet
vis	visible

Materials and Methods

General. Commercial reagents were used without further purification. 2-Carboxy-5-fluorophenylboronic acid (CAS 874290-62-7) and 2-borono-5-fluorobenzoic acid (CAS 874290-63-8), 2-carboxy-4-chlorophenylboronic acid (CAS 850568-07-9), and 4-nitrophenylboronic acid (CAS 24067-17-2) were from Combi-Blocks (San Diego, CA). 2-Carboxy-5-chlorophenylboronic acid (CAS 874290-67-2) was from AK Scientific (Union City, CA). All salicylic acids were from TCI (Portland, OR), Sigma–Aldrich (St. Louis, MO), AmBeed (Buffalo Grove, IL), and Oakwood Chemical (Estill, SC). 10-Hydroxybenzo[*h*]quinoline (HBQ) was from Alfa Aesar (Haverhill, MA). All other reagents used in chemical synthesis were from Sigma–Aldrich or Fisher Scientific (Hampton, NH). Methacrylate cuvettes were from Fisher Scientific.

The phrase "concentrated under reduced pressure" refers to the removal of solvents and other volatile materials using a rotary evaporator at water aspirator pressure (<20 Torr) while maintaining the water-bath temperature at 30–40 °C. Residual solvent was removed from samples by the vacuum (<0.1 Torr) achieved by a mechanical belt-drive oil pump. NMR samples that are reported with mixed solvents (*e.g.*, D_2O/CD_3CN) were typically dissolved in ~500 μL of organic or aqueous deuterated solvent to afford some solubility. The other phase solvent was then titrated into the mixture until solubility was achieved, often at a ratio between 3:1 D_2O/CD_3CN and 1:1 D_2O/CD_3CN.

Instrumentation. NMR spectra were obtained with an Avance Neo 400.17 MHz or an Avance Neo 500.34 MHz spectrometer from Bruker (Billerica, MA). High-resolution mass spectra were obtained with an AccuTOF-DART 4G from JEOL (Peabody, MA) by helium DART ionization or with a 6545A QTOF mass spectrometer coupled to an Infinity 1260 LC system from Agilent (Santa Clara, CA). The pH of buffers was determined with an Accumet XL50 pH meter from Fisher Scientific. Column chromatography was performed on a Selekt flash chromatography system from Biotage (Uppsala, Sweden) using prepacked Sfar Duo silica gel columns for normal-phase purification or Sfar Duo C18 columns for reversed-phase purification. UV–vis measurements were

obtained using a Cary 60 UV–vis spectrophotometer from Agilent Technologies (Santa Clara, CA). Melting point measurements were obtained using an MPA100 automated melting point apparatus from Stanford Research Systems (Sunnyvale, CA). Data analyses were performed using Microsoft Excel and Prism GraphPad.

pH Measurements. pH measurements were performed using a Fisher Scientific accumet® LX500 Dual Channel pH/mV/Ion/Conductivity Meter. The Instrument was standardized before every measurement using Buffer Reference Standard solutions of pH 4.00, 7.00, and 10.00 from VWR Chemicals.

^{11}B NMR Spectroscopy. ^{11}B NMR spectra were obtained on samples in borosilicate NMR tubes. ^{11}B NMR spectra were acquired with or without background suppression, and a background signal from NMR tubes was often observed even with background suppression. Variability in ^{11}B NMR chemical shifts can be induced by solvent type as well as the chemical identity of the boron species. Common chemical shifts for trigonal (sp^2) alkyl and aryl boronic acids were ~30 ± 5 ppm. Boric acid was typically observed with a chemical shift of ~19–20 ppm. Depending on the pK_a of the boronic acid (Figure S1), a sufficiently aqueous environment can produce a tetrahedral (sp^3) boron species and associated shift. Mixtures of D_2O and an organic solvent, such as CD_3CN, can lead to variability (in ppm) of the sp^3 chemical shift. This variability is particularly evident if the instrument locks onto the CD_3CN in one sample mixture and D_2O in another sample mixture. Also, the carbon bonded directly to the boron might not be observed due to quadrupolar broadening.

Caution! The commonly used ^{11}B NMR standard, $BF_3{\cdot}OEt_2$, cannot be used when preparing compounds in aqueous NMR solvent, as this molecule will rapidly decompose into boric acid and fluoroboric acid, producing highly toxic and corrosive hydrogen fluoride as an intermediate.

TLC Staining for Benzoxaborolones. A 4 mM solution of HBQ was prepared in methanol and used as a benzoxaborolone stain after thin-layer chromatography (TLC). In brief, the silica TLC plate was dipped in the solution of HBQ, air-dried, and then heated until the silica turned pale yellow. Upon exposure to long-wavelength (365 nm) ultraviolet light (UV), spots containing boronic acids that can complex with HBQ appear cyan (495 nm) due to the interruption of the excited-state intramolecular proton transfer (ESIPT) of 10-hydroxybenzo[*h*]quinolone, as reported previously.[1]

Melting Point Measurements. When possible, the melting points of newly synthesized and experimentally tested boronic acid derivatives were obtained. In an initial experiment, a rough estimate of the melting point was obtained by heating from 40 to 350 °C at a rate of 20 °C/min. The experiment was then repeated, starting at a temperature 25 °C below the estimated melting point from the previous experiment and increasing the temperature at a rate of 5 °C/min to determine the true melting point range.

cLog*P* values. Log*P* values were calculated with Chemicalize software from ChemAxon (https://chemicalize.com).

Conditions. All procedures were performed in air at ambient temperature (~23 °C) and pressure (1.0 atm) unless indicated otherwise. Reactions requiring heat were heated with a silicon oil bath.

Safety Statement. H_2O_2 (30% v/v in water) is a strong oxidizer and should not be combined with other organic waste streams. Stock solutions were stored at 4 °C in a secondary container and protected from light. All solutions containing H_2O_2 were quenched with MnO_2, which catalyzes the decomposition of H_2O_2 into O_2(g) and water, in a fume hood. Once the reaction had finished (*i.e.*, no more effervescence was observed), the solutions were disposed of in a separate waste container. No other unexpected or unusually high safety hazards were encountered in this work.

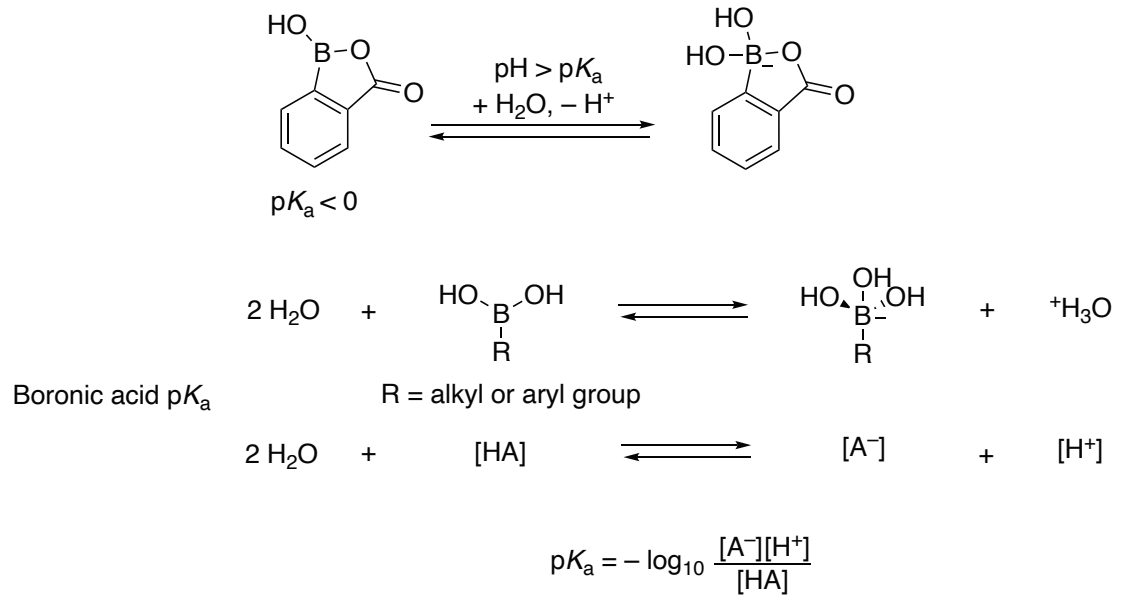


Figure S1. sp^2–sp^3 Boron equilibrium. Trigonal (sp^2) to tetrahedral (sp^3) configuration equilibrium of the boron in benzoxaborolone as a function of pK_a. The pK_a of benzoxaborolone is from ref 3.

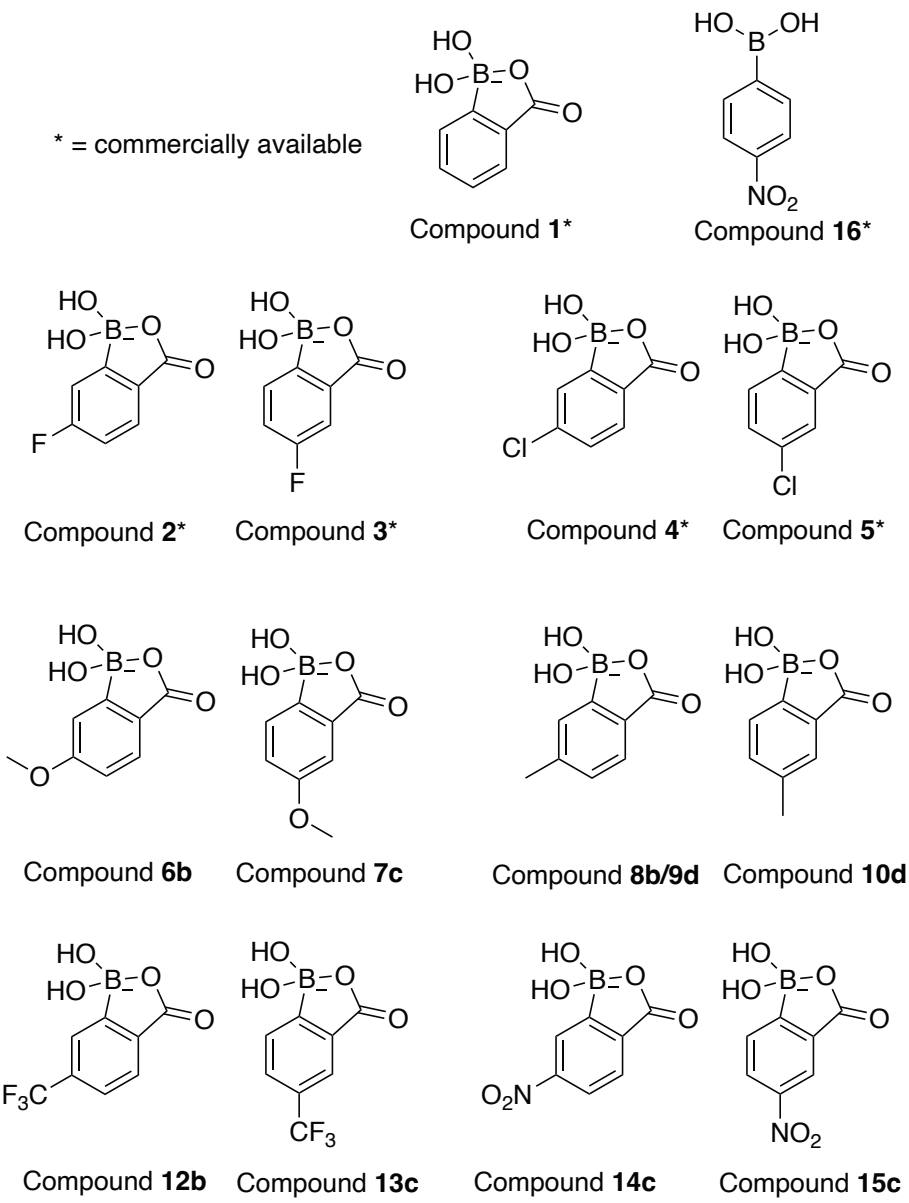
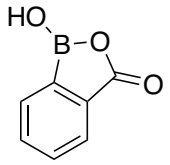
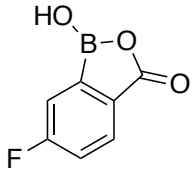


Figure S2. Panel of chemical compounds used in this study.

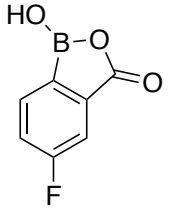
Chemical Synthesis



Compound 1
Compound name: 1-Hydroxy-2,1-benzoxaborol-3-one
Compound obtained from Combi-Blocks. NMR and HRMS data obtained for compound confirmation and purity analysis.
^{1}H NMR (500 MHz, D_2O, δ): 7.56 (d, J = 7.7 Hz, 1H), 7.49–7.41 (m, 2H), 7.30 (t, J = 7.3 Hz, 1H). **^{13}C{^{1}H} NMR** (126 MHz, D_2O, δ): 175.5, 133.9, 133.3, 128.7, 128.4, 125.0. Note: The carbon bonded directly to the boron is not observed due to quadrupolar broadening. **^{11}B{^{1}H} NMR** (160 MHz, D_2O, δ): 11.14. **^{11}B{^{1}H} NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ): 11.47. **HRMS** (DART–TOF) (m/z): $[M + H]^+$ calculated for $C_7H_6BO_3$, 149.0404; found, 149.0412.
Melting point: 162 °C (reported); found, 159–160 °C.

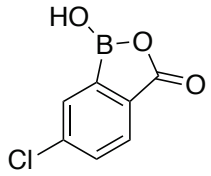


Compound 2
Compound name: 1-Hydroxy-6-(fluoro)-2,1-benzoxaborol-3-one
Compound obtained from Combi-Blocks. NMR and HRMS data obtained for compound confirmation and purity analysis.
^{1}H NMR (500 MHz, CD_3CN/D_2O, δ): 7.58 (dd, J = 8.3, 4.7 Hz, 1H), 7.11 (d, J = 9.0 Hz, 1H), 6.99–6.92 (m, 1H). **^{13}C{^{1}H} NMR** (126 MHz, CD_3CN/D_2O, δ): 174.6, 166.9, 164.9, 131.5, 126.6, 126.5, 118.2, 114.6, 114.4, 114.3, 0.9, 0.7, 0.6, 0.4, 0.2, 0.1, -0.1. **^{11}B{^{1}H} NMR** (160 MHz, CD_3CN/D_2O, δ): 7.93. **^{11}B{^{1}H} NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ): 7.87. **^{19}F{^{1}H} NMR** (471 MHz, CD_3CN/D_2O, δ): −109.80. **HRMS** (DART–TOF) (m/z): $[M + H]^+$ calculated for $C_7H_5BFO_3$, 167.0318; found, 167.0320.



Compound 3
Compound name: 1-Hydroxy-5-(fluoro)-2,1-benzoxaborol-3-one
Compound obtained from Combi-Blocks. NMR and HRMS data obtained for compound confirmation and purity analysis.
^{1}H NMR (500 MHz, CD_3CN/D_2O, δ): 7.44 (ddd, J = 24.2, 8.2, 4.0 Hz, 1H), 7.33–7.25 (m, 1H), 7.20 (ddd, J = 10.4, 8.0, 2.4 Hz, 1H). **^{13}C{^{1}H} NMR** (126 MHz, CD_3CN/D_2O, δ): 174.2, 163.6, 161.7, 137.5, 130.4, 119.4, 119.2, 110.4, 110.2, 1.0, 0.8, 0.6, 0.4, 0.3, 0.1, −0.0. **^{11}B{^{1}H} NMR**

(160 MHz, CD_3CN/D_2O, δ): 9.24. **$^{11}B\{^1H\}$ NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ): 8.84. **$^{19}F\{^1H\}$ NMR** (471 MHz, CD_3CN/D_2O, δ): −110.93, −114.21, −115.93, −116.79, −117.06. **HRMS** (DART–TOF) (*m*/*z*): $[M + H]^+$ calculated for $C_7H_5BFO_3$, 167.0318; found, 167.0319.

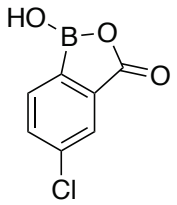


Compound 4

Product name: 1-Hydroxy-6-(chloro)-2,1-benzoxaborol-3-one

Compound obtained from Combi-Blocks. NMR and HRMS data obtained for compound confirmation and purity analysis.

^1H NMR (500 MHz, D_2O, δ): 7.58 (d, J = 1.8 Hz, 1H), 7.46 (dd, J = 9.8, 8.0 Hz, 2H). **$^{13}C\{^1H\}$ NMR** (126 MHz, D_2O, δ): 175.8, 136.7, 132.8, 132.6, 129.7, 123.7. Note: The carbon bonded directly to the boron is not observed due to quadrupolar broadening.**$^{11}B\{^1H\}$ NMR** (160 MHz, D_2O, δ): 7.86. **$^{11}B\{^1H\}$ NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ): 12.35. **HRMS** (DART–TOF) (*m*/*z*): $[M + H]^+$ calculated for $C_7H_5BClO_3$, 183.0015; found, 183.0020.

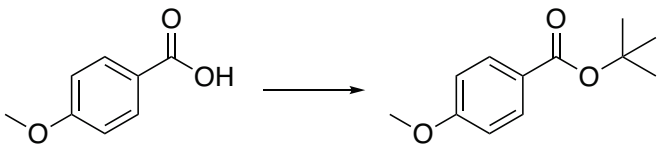


Compound 5

Product name: 1-Hydroxy-5-(chloro)-2,1-benzoxaborol-3-one

Compound obtained from Combi-Blocks. NMR and HRMS data obtained for compound confirmation and purity analysis.

^1H NMR (500 MHz, CD_3CN/D_2O, δ): 7.55 (d, J = 1.8 Hz, 1H), 7.46–7.41 (m, 2H). **$^{13}C\{^1H\}$ NMR** (126 MHz, CD_3CN/D_2O, δ): 176.4, 137.8, 133.6, 133.4, 130.7, 124.5, 120.0, 1.8, 1.6, 1.5, 1.2, 1.0, 0.8. Note: The carbon bonded directly to the boron is not observed due to quadrupolar broadening. **$^{11}B\{^1H\}$ NMR** (160 MHz, CD_3CN/D_2O, δ): 5.27. **$^{11}B\{^1H\}$ NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ): 8.23. **HRMS** (DART–TOF) (*m*/*z*): $[M + H]^+$ calculated for $C_7H_5BClO_3$, 183.0015; found, 183.0019.

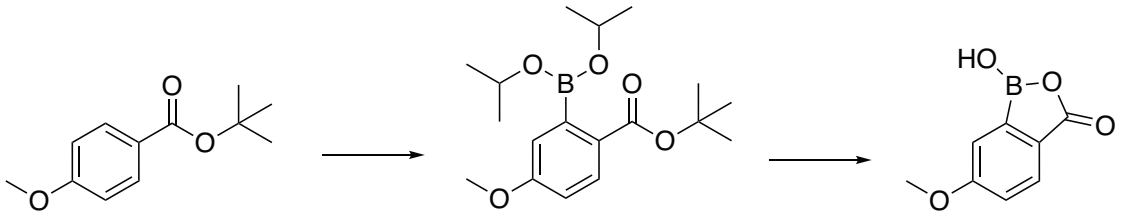


Compound 6a

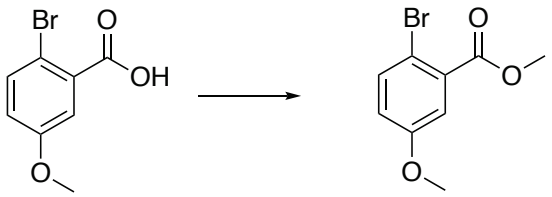
Product name: *tert*-Butyl 4-methoxybenzoate

Procedure: 4-Methoxybenzoic acid (23.3 mmol, 3.5440 g) was dissolved in 50 mL of anhydrous dichloromethane containing a catalytic amount of dimethylformamide. $SOCl_2$ (4.1580 g, 35.0 mmol, 1.5 equiv) was added, and the reaction mixture was stirred overnight. Only 50% conversion was observed based on TLC, so 3 more equiv of $SOCl_2$ and additional catalytic dimethylformamide

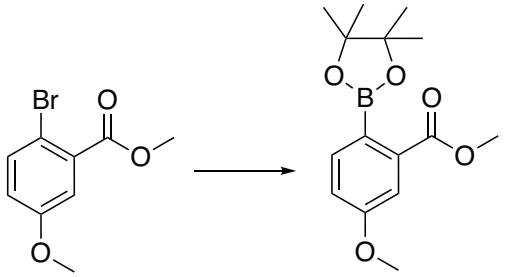
were added, and the reaction mixture was stirred again overnight. The reaction appeared to reach completion by TLC, and the reaction mixture was concentrated under reduced pressure. The residue was dissolved in 25 mL of tetrahydrofuran. Potassium *tert*-butoxide (35.0 mL, 35.0 mmol, 1.5 equiv) in a 1 M solution in tetrahydrofuran was added slowly, followed by *tert*-butanol (2.5942 g, 35.0 mmol, 1.5 equiv). The reaction mixture was stirred for 48 h. The reaction mixture was then diluted in 100 mL of 1 N HCl and extracted three times with ethyl acetate. The organic layer was washed once with water, once with brine, dried on anhydrous Na_2SO_4(s), and concentrated under reduced pressure. The mixture was purified on silica with flash chromatography[2] in hexanes and ethyl acetate. The product was isolated as a pale-yellow liquid (2.2320 g, 23.3 mmol, 46%).
Caution! *$SOCl_2$ is highly corrosive and toxic.*
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.99–7.90 (m, 2H), 6.93–6.85 (m, 2H), 3.83 (s, 3H), 1.59 (s, 9H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, δ): 165.6, 163.0, 131.4, 124.5, 113.4, 80.4, 77.4, 77.1, 76.8, 55.3, 28.2. **HRMS** (DART–TOF) (*m*/*z*): $[M + H]^+$ calculated for $C_{12}H_{17}O_3$, 209.1183; found, 209.1185.



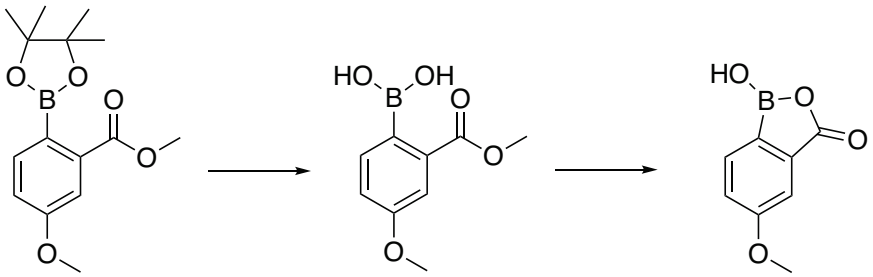
Compound 6b
Product name: 1-Hydroxy-6-(methoxy)-2,1-benzoxaborol-3-one
Procedure: *tert*-Butyl 4-methoxybenzoate (1.1037 g, 5.3 mmol) was dissolved in 15 mL of anhydrous tetrahydrofuran and cooled to 0 °C, then isopropyl borate (2.5954 g, 13.8 mmol, 2.6 equiv) was added. Lithium diisopropylamide (LDA) (4.2 mL, 8.48 mmol, 1.6 equiv of a 2 M solution in 50:28:13 tetrahydrofuran/heptane/ethylbenzene from Fisher Scientific (Product Number AC268831000), added dropwise, and the mixture was stirred at 0 °C for 3 h, then quenched with sat. aq. NH_4Cl. The reaction mixture was extracted three times with ethyl acetate, washed once with brine, dried on Na_2SO_4(s), and concentrated under reduced pressure. The product was then separated on silica with flash chromatography in methanol and dichloromethane. The borylation product was confirmed via TLC stained with HBQ. The residue was then stirred in a mixture of 5 mL of dichloromethane and 3 mL of trifluoroacetic acid (TFA) for 1 h, then concentrated under reduced pressure and further dried on high vacuum overnight. The product was purified via reversed-phase flash chromatography. The product was isolated as a white solid (0.1040 g, 0.58 mmol, 11%, 2 steps).
Caution! *Triisopropyl borate solution is highly flammable. LDA solution is highly flammable and corrosive.*
^{1}H NMR (400 MHz, CD_3CN/D_2O, δ): 7.37 (d, J = 7.9 Hz, 1H), 7.11 (d, J = 2.4 Hz, 1H), 7.03 (dd, J = 7.9, 2.5 Hz, 1H), 3.76 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, CD_3CN/D_2O, δ): 160.0, 138.0, 130.4, 120.5, 119.3, 108.5, 56.1, 1.9, 1.7, 1.5, 1.5, 1.3, 1.3, 1.1, 1.1, 0.9, 0.7. Note: The carbon bonded directly to the boron is not observed due to quadrupolar broadening. There is an overlapping peak between the solvent peak and aromatic carbon peak at 119 ppm. **^{11}B{^{1}H} NMR** (128 MHz, CD_3CN/D_2O, δ): 7.63. **^{11}B{^{1}H} NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ): 9.95. **HRMS** (DART–TOF) (*m*/*z*): $[M - H]^-$ calculated for $C_8H_8BO_4$: 177.0365, found 177.0383. **Melting point** 175–175 °C.



Compound: 7a
Product name: Methyl 2-bromo-5-methoxybenzoate
Procedure: 2-Bromo-5-methoxybenzoic acid (0.9980 g, 4.32 mmol) was dissolved in 10% v/v H_2SO_4 in methanol, and the resulting solution was stirred for 24 h. The reaction mixture was concentrated under reduced pressure. The residue was diluted with sat. aq. $NaHCO_3$ and extracted three times with dichloromethane. The organic layer was washed once with water and once with brine, then dried on Na_2SO_4(s) and concentrated under reduced pressure. The product was isolated as a pale-yellow liquid (1.0576 g, 4.31 mmol, quant.).
Caution! *H_2SO_4 is highly corrosive.*
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.53 (d, J = 8.8 Hz, 1H), 7.32 (d, J = 3.1 Hz, 1H), 6.89 (dd, J = 8.8, 3.1 Hz, 1H), 3.94 (s, 3H), 3.82 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, δ): 166.5, 158.5, 135.0, 132.7, 119.0, 116.2, 111.9, 77.4, 77.1, 76.8, 55.6, 52.5.



Compound: 7b
Product name: Methyl 5-methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate
Procedure: Methyl 2-bromo-5-methoxybenzoate (0.3500 g, 1.43 mmol) was added to an oven-dried round-bottom flask. Bis(pinacolato)diboron (0.3630 g, 1.43 mmol, 1 equiv), potassium acetate (0.4211g, 4.29 mmol, 3 equiv), and Pd(dppf)Cl_2·CH_2Cl_2 complex (0.2336 g, 0.29 mmol, 0.2 equiv) were added to the round-bottom flask. The flask was evacuated and refilled with N_2(g) three times. Anhydrous 1,4-dioxane (15 mL) was added to the flask, and the reaction mixture was heated to 80 °C under N_2(g) and stirred for 16 h. The reaction mixture was then cooled and filtered through a silica plug with 1:1 hexanes/ethyl acetate. The flow-through was collected and concentrated under reduced pressure. The product was separated on silica with flash chromatography in hexanes and ethyl acetate. The product was isolated as an orange-brown oil (0.1800 g, 0.62 mmol, 43%).
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.49–7.42 (m, 2H), 7.06 (dd, J = 8.1, 2.6 Hz, 1H), 3.91 (s, 3H), 3.84 (s, 3H), 1.41 (s, 12H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, δ): 168.4, 160.3, 135.6, 133.9, 118.0, 113.7, 83.8, 83.5, 77.4, 77.0, 76.7, 55.3, 52.3, 25.0, 24.8. **^{11}B{^{1}H} NMR** (128 MHz, $CDCl_3$, δ): 31.22.



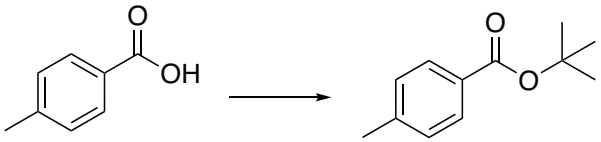
Compound: 7c

Product name: 1-Hydroxy-5-(methoxy)-2,1-benzoxaborol-3-one

Procedure: Methyl 5-methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (0.1632 g, 0.56 mmol) was dissolved in 4:1 tetrahydrofuran/water and stirred with $NaIO_4$ (0.3594 g, 1.68 mmol, 3 equiv) for 30 min. HCl (0.39 mL, 0.39 mmol, 0.7 equiv from a 1 N solution) was added, and the reaction mixture was stirred overnight. The mixture was concentrated under reduced pressure, then resuspended in methanol. White precipitate formed and was filtered through filter paper. The filtrate was concentrated under reduced pressure and resuspended in dichloromethane before being filtered through filter paper to remove precipitate. The filtrate was dried on Na_2SO_4(s) and concentrated under reduced pressure. The deprotected boronic acid is confirmed via TLC with minimal movement in hexanes/ethyl acetate and a streak in dichloromethane/methanol, showing a bright spot under long-wavelength UV light after HBQ staining and heating. The residue was resuspended in a few milliliters of sat. aq. $NaHCO_3$, and the resulting solution was stirred overnight to remove the methyl ester protecting group. The reaction mixture was acidified with 1 N HCl, purified on reversed-phase flash chromatography, and lyophilized. The product was isolated as a white solid (0.0220 g, 0.12 mmol, 22%, 2 steps).

Caution! *$NaIO_4$ is a strong oxidizer and highly corrosive.*

^{1}H NMR (500 MHz, D_2O, δ): 7.41 (d, J = 8.0 Hz, 1H), 7.14 (d, J = 2.3 Hz, 1H), 7.12–7.06 (m, 1H), 3.77 (d, J = 0.6 Hz, 3H), 1.82 (d, J = 0.6 Hz, 2H). **^{13}C{^{1}H} NMR** (126 MHz, D_2O, δ): 176.8, 158.8, 136.4, 129.4, 120.1, 107.9, 55.4, 55.4, 55.4. **^{11}B{^{1}H} NMR** (160 MHz, D_2O, δ): 7.98. **^{11}B{^{1}H} NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ) 8.38.



Compound: 8a

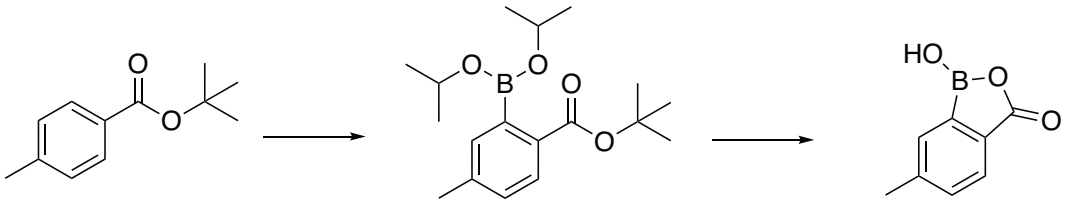
Product name: *tert*-Butyl 4-methylbenzoate

Procedure: $MgSO_4$ (14.155 g, 118 mmol, 4 equiv) was suspended in 100 mL of dichloromethane. Concentrated H_2SO_4 (2.8835 g, 29.4 mmol, 1 equiv) was added, and the resulting solution was stirred for 15 min. 4-Methylbenzoic acid (4.0028 g, 29.4 mmol) was added, followed by *tert*-butanol (10.996 g, 147 mmol, 5 equiv). The reaction mixture was stirred overnight, then slowly quenched with sat. aq. $NaHCO_3$ until all the $MgSO_4$ dissolved in the aqueous layer. The mixture was extracted two times with dichloromethane, washed once with water, once with brine, dried on Na_2SO_4(s), and concentrated under reduced pressure. The product was isolated as colorless liquid (1.4160 g, 7.36 mmol, 25% yield).

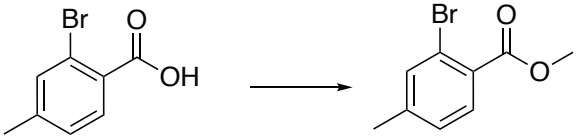
Caution! *H_2SO_4 is highly corrosive.*

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.91 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 7.9 Hz, 2H), 2.42 (s, 3H), 1.62 (s, 9H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$, δ): 165.9, 142.9, 129.4, 129.3, 128.9, 80.6, 77.3,

77.1, 76.8, 28.2, 21.6. **HRMS** (DART–TOF) (*m*/*z*): $[M + H]^+$ calculated for $C_{12}H_{16}O_2$, 193.1223; found, 193.1220.

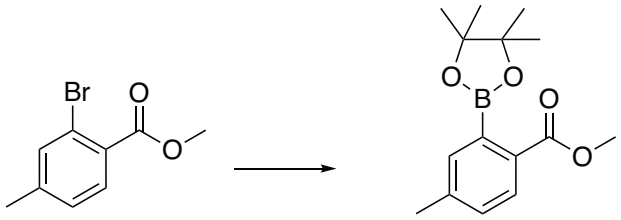


Compound: 8b
Product name: 1-Hydroxy-6-(methyl)-2,1-benzoxaborol-3-one
Procedure: *tert*-Butyl 4-methylbenzoate (1.3070 g, 6.8 mmol) was dissolved in 15 mL of tetrahydrofuran, and the resulting solution was cooled to 0 °C. Triisopropyl borate (3.3251 g, 17.7 mmol, 2.6 equiv) was added, followed by LDA (4.1 mL, 8.2 mmol, 1.2 equiv of a 2 M solution in 50:28:13 tetrahydrofuran/heptane/ethylbenzene from Fisher Scientific (Product Number AC268831000) dropwise. The reaction mixture was stirred for 3 h at 0 °C. The reaction mixture was quenched with sat. aq. NH_4Cl, extracted three times with ethyl acetate, washed once with water, and once with brine. The organic layer was dried with Na_2SO_4(s) and concentrated under reduced pressure. The isopropyl borate product was separated on silica with flash chromatography in methanol and dichloromethane, and the isopropylborate product was confirmed via TLC. The product was then stirred in a mixture of 5 mL of dichloromethane and 3 mL of trifluoroacetic acid for 1 h and concentrated under reduced pressure. The product was separated with reversed-phase flash chromatography and lyophilized. The product was isolated as a white powder (0.1433 g, 0.88 mmol, 13%, 2 steps).
Caution! *Triisopropyl borate solution is highly flammable. LDA solution is highly flammable and corrosive.*
^{1}H NMR (500 MHz, D_2O/CD_3CN, δ): 7.64 (d, J = 7.9 Hz, 1H), 7.28 (s, 1H), 7.19 (d, J = 7.9 Hz, 1H), 2.33 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz, D_2O/CD_3CN, δ): 173.7, 144.3, 131.6, 131.1, 129.8, 127.4, 119.3, 21.7, 1.7, 1.5, 1.2, 1.0, 0.8, 0.7.**^{11}B{^{1}H} NMR** (160 MHz, D_2O/CD_3CN, δ): 13.73. **^{11}B{^{1}H} NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ): 9.09. **HRMS** (DART–TOF) (*m*/*z*): $[M + H]^+$ calculated for $C_8H_8BO_3$, 163.0572; found, 163.0573. **Melting point:** 139–140 °C.



Compound 9a
Product name: Methyl 2-bromo-4-methylbenzoate
Procedure: 2-Bromo-4-methylbenzoic acid (1.5032 g, 6.99 mmol) was dissolved in 10 mL 10% v/v H_2SO_4 in methanol, and the resulting solutions was heated at reflux (60 °C) overnight. The reaction mixture was concentrated and resuspended in sat. aq. $NaHCO_3$ and dichloromethane. The mixture was extracted three times with dichloromethane, washed once with water, and once with brine. The organic layer was dried on Na_2SO_4(s) and concentrated under reduced pressure. The product was separated on silica with flash chromatography in hexanes and ethyl acetate. The product was isolated as a pale-yellow liquid (1.1370 g, 4.96 mmol, 71% yield).
Caution! *H_2SO_4 is highly corrosive.*

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.68 (d, J = 7.9 Hz, 1H), 7.43 (s, 1H), 7.13–7.06 (m, 1H), 3.87 (s, 3H), 2.30 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, δ): 166.3, 143.6, 134.9, 131.4, 128.8, 127.9, 121.8, 77.5, 77.2, 76.9, 52.2, 21.0. **HRMS** (DART–TOF) (m/z): $[M + H]^+$ calculated for $C_9H_{10}BrO_2$, 228.9859; found, 228.9869.

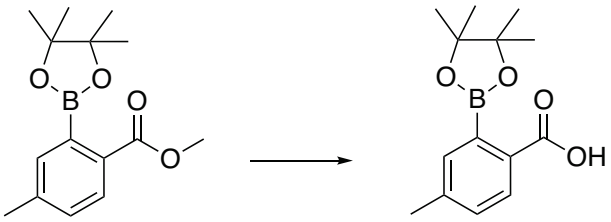


Compound: 9b

Product name: Methyl 4-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate

Procedure: Methyl 2-bromo-4-methoxybenzoate (0.3275 g, 1.43 mmol) was added to an oven-dried round-bottom flask. Bis(pinacolato)diboron (0.7263 g, 2.86 mmol, 2 equiv), potassium acetate (0.4211 g, 4.29 mmol, 3 equiv), and $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ complex (0.2346 g, 0.29 mmol, 0.2 equiv) were added to the round-bottom flask. The flask was evacuated and refilled with N_2(g) three times. Anhydrous 1,4-dioxane (22 mL) was added to the flask, and the reaction mixture was heated to 80 °C under N_2(g) flow and stirred for 16 h. The reaction mixture was then cooled, and filtered through celite with 1:1 hexanes/ethyl acetate, then filtered through a silica plug with 1:1 hexanes/ethyl acetate. The flow-through was concentrated under reduced pressure. The product was separated on silica with flash chromatography in hexanes and ethyl acetate. The product was isolated as a dark yellow oil (0.1580 g, 0.57 mmol, 40%).

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.83 (d, J = 8.0 Hz, 1H), 7.29 (d, J = 1.8 Hz, 1H), 7.20 (dd, J = 8.3, 1.5 Hz, 1H), 3.89 (s, 3H), 2.37 (s, 3H), 1.42 (s, 12H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, δ): 168.5, 142.3, 132.8, 130.6, 129.6, 128.9, 84.0, 77.4, 77.0, 76.7, 52.1, 24.9, 21.5. **^{11}B{^{1}H} NMR** (128 MHz, $CDCl_3$, δ): 31.45. **HRMS** (DART–TOF) (m/z): $[M + H]^+$ calculated for $C_{15}H_{22}BO_4$, 277.1606; found, 277.1616.

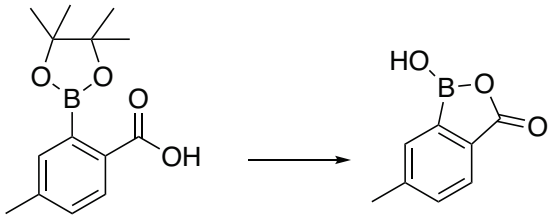


Compound: 9c

Product name: 4-Methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid

Procedure: Methyl 4-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (0.1510 g, 0.55 mmol) was dissolved in 4 mL of sat. aq. $NaHCO_3$ and stirred for 24 h. Then, the reaction mixture was acidified with 1 N HCl. The product was separated with reversed-phase flash chromatography and lyophilized. The product was isolated as a white solid (0.1126 g, 0.43 mmol, 79%).

^{1}H NMR (400 MHz, DMSO, δ): 7.73 (d, J = 7.9 Hz, 1H), 7.26 (dd, J = 8.2, 1.8 Hz, 1H), 7.21 (d, J = 1.8 Hz, 1H), 2.35 (s, 3H), 1.29 (s, 12H). **^{13}C{^{1}H} NMR** (101 MHz, DMSO, δ): 168.8, 141.5, 131.9, 131.2, 129.1, 128.0, 82.8, 39.9, 39.7, 39.5, 39.3, 39.1, 38.9, 38.7, 24.4, 20.8.**^{11}B{^{1}H} NMR** (128 MHz, $CDCl_3$, δ): 31.12.



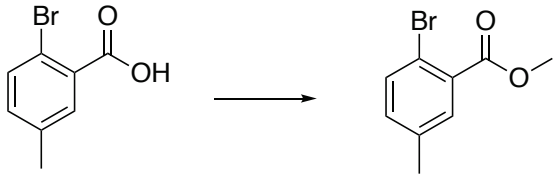
Compound: 9d

Product name: 1-Hydroxy-6-(methyl)-2,1-benzoxaborol-3-one

Procedure: 4-Methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid (0.0996 g, 0.38 mmol) was dissolved in 5 mL of 5% v/v trifluoroacetic acid in DCM. $CH_3B(OH)_2$ (0.1140 g, 1.90 mmol, 5 equiv) was added, forming a cloudy white solution. The reaction mixture was stirred for 16 h. Then, the mixture was concentrated under reduced pressure, purified with reversed-phase flash chromatography, and lyophilized. The product was isolated as a white powder (0.0340 g, 0.21 mmol, 54%).

Caution! *TFA is highly corrosive.*

^{1}H NMR (400 MHz, D_2O/CD_3CN, δ): 7.60 (d, J = 7.9 Hz, 1H), 7.28 (s, 1H), 7.22–7.15 (m, 1H), 2.32 (s, 3H).**^{13}C{^{1}H} NMR** (101 MHz, D_2O/ CD_3CN, δ): 174.8, 144.3, 131.2, 129.8, 129.4, 125.7, 119.2, 21.1. Note: The carbon bonded directly to the boron is not observed due to quadrupolar broadening. **^{11}B{^{1}H} NMR** (128 MHz, D_2O/ CD_3CN, δ): 13.81. **HRMS** (DART–TOF) (m/z): [M + H]$^+$ calculated for $C_8H_8BO_3$, 163.0561; found, 163.0566. **Melting point:** 176–177 °C.



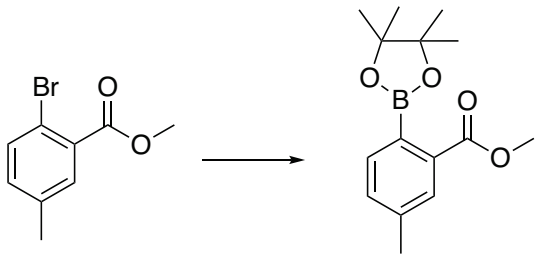
Compound 10a

Product name: Methyl 2-bromo-5-methylbenzoate

Procedure: 2-Bromo-5-methyl benzoic acid (2.0043 g, 9.32 mmol) was dissolved in 10% v/v H_2SO_4, and the resulting solution was heated at reflux (60 °C) overnight. The reaction mixture was concentrated and resuspended in sat. aq. $NaHCO_3$ and dichloromethane. The mixture was extracted three times with dichloromethane, washed once with water, and once with brine. The organic layer was dried on Na_2SO_4(s) and concentrated under reduced pressure. The product was separated on silica with flash chromatography in hexanes and ethyl acetate. The product was isolated as a pale-yellow liquid (1.6217 g, 7.08 mmol, 76%).

Caution! *H_2SO_4 is highly corrosive.*

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.59 (d, J = 2.3 Hz, 1H), 7.50 (d, J = 8.2 Hz, 1H), 7.11 (dd, J = 8.2, 2.3 Hz, 1H), 3.92 (s, 3H), 2.32 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, δ): 167.1, 137.6, 134.4, 133.8, 132.2, 132.1, 118.6, 77.8, 77.5, 77.2, 52.7, 21.1.

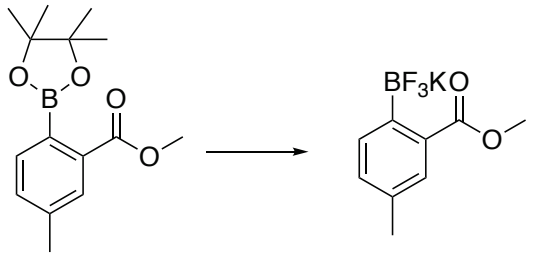


Compound 10b

Product name: Methyl 5-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate

Procedure: Methyl 2-bromo-5-methoxybenzoate (0.8820 g, 3.85 mmol**)** was added to an oven-dried round-bottom flask. Bis(pinacolato)diboron (0.97770 g, 3.85 mmol, 1 equiv), potassium acetate (1.1346 g, 11.56 mmol, 3 equiv), and $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ complex (0.4737 g, 0.58 mmol, 0.15 equiv) were added to the round-bottom flask. The flask was evacuated and refilled with N_2(g) three times. 22 mL of anhydrous 1,4-dioxane was added to the flask and the reaction mixture was heated to 80 °C under N_2(g) flow and stirred for 16 h. The reaction mixture was then cooled and filtered through celite with 1:1 hexanes/ethyl acetate, then filtered through a silica plug with 1:1 hexanes/ethyl acetate. The flow-through was concentrated under reduced pressure. The product was separated on silica with flash chromatography in hexanes and ethyl acetate. The product was isolated as a light-yellow liquid (0.5531 g, 2.02 mmol, 52%).

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.77 (dt, J = 1.7, 0.7 Hz, 1H), 7.42 (d, J = 7.4 Hz, 1H), 7.33 (ddd, J = 7.5, 1.7, 0.8 Hz, 1H), 3.91 (s, 3H), 2.39 (s, 3H), 1.42 (s, 12H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, δ): 168.6, 139.0, 133.7, 132.5, 132.3, 129.4, 83.9, 83.7, 77.4, 77.1, 76.8, 52.2, 24.9, 24.6, 21.3. **^{11}B{^{1}H} NMR** (128 MHz, $CDCl_3$, δ): 31.57. **HRMS** (DART–TOF) (m/z): $[M + H]^+$ calculated for $C_{15}H_{22}BO_4$, 277.1606; found, 277.1616.



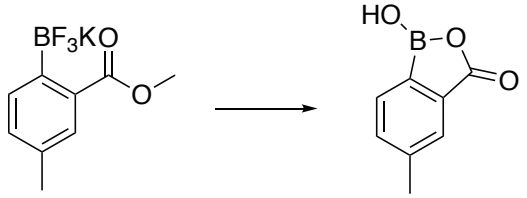
Compound: 10c

Product name: Methyl 5-methyl-2-(trifluoro-λ^4-boraneyl)benzoate, potassium salt

Procedure: Methyl 5-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (0.9941 g, 3.60 mmol) was dissolved in 8 mL/mmol methanol, and KHF_2 (3.6 mL, 16.2 mmol, 4.5 equiv of a 4.5 M aqueous solution) was added slowly to the resulting solution. The reaction mixture was stirred for 30 min and then concentrated under reduced pressure. The residue was stirred in acetone overnight and then filtered the following day while rinsing with hot acetone. The filtrate was concentrated under reduced pressure. The product was isolated as a white solid (0.5070 g, 1.98 mmol, 55%).

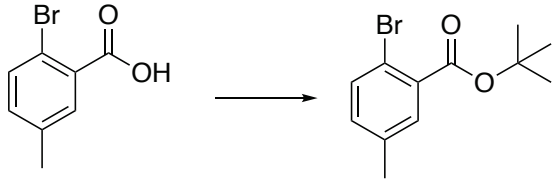
Caution! *KHF_2 is highly corrosive and toxic.*

^{1}H NMR (500 MHz, DMSO, δ): 7.36 (d, J = 7.5 Hz, 1H), 7.06–6.98 (m, 2H), 3.66 (s, 3H), 2.23 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz, DMSO, δ): 172.4, 136.6, 133.7, 133.0, 129.2, 126.5, 51.4, 40.2, 40.0, 39.9, 39.7, 39.5, 39.4, 39.2, 20.8. **^{11}B{^{1}H} NMR** (160 MHz, DMSO, δ): 2.74. **^{19}F{^{1}H} NMR** (471 MHz, DMSO, δ): −137.08.



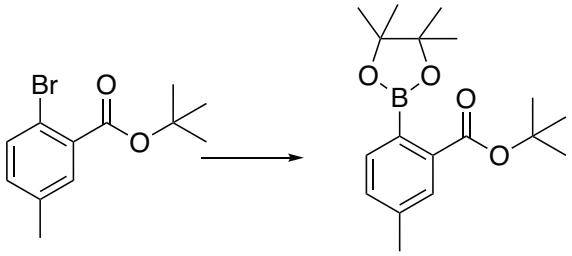
Compound 10d
Product name: 1-Hydroxy-5-(methyl)-2,1-benzoxaborol-3-one
Procedure: Methyl 5-methyl-2-(trifluoro-λ^4-boraneyl)benzoate, potassium salt (0.4610 g, 1.8 mmol) was resuspended in 10 mL of acetonitrile. Trimethylsilyl chloride (0.5867 g, 5.40 mmol, 3 equiv) and water (0.0972 g, 5.40 mmol, 3 equiv) were added, and the reaction mixture was stirred for 1 h before concentrating under reduced pressure. The residue was resuspended in 3 mL of sat. aq. $NaHCO_3$ and stirred for 1 h. The reaction mixture was acidified until clear with 1 N HCl. The solution was lyophilized, then resuspended in water and purified with reversed-phase flash chromatography. The product was lyophilized. The product was isolated as a white powder (0.0940 g, 0.58 mmol, 32%)
Caution! *Trimethylsilyl chloride is highly corrosive and flammable.*
^{1}H NMR (500 MHz, D_2O/CD_3CN, δ): 7.58 (s, 1H), 7.35 (t, J = 9.5 Hz, 2H), 2.31 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz, D_2O/CD_3CN, δ): 174.1, 139.5, 135.0, 134.6, 130.9, 128.0, 119.6, 21.5, 2.0, 1.8, 1.7, 1.6, 1.2, 1.00. **^{11}B NMR** (160 MHz, D_2O/CD_3CN, δ): 18.86. **^{11}B{^{1}H} NMR** (128 MHz, D_2O/CD_3CN, δ): 19.72, 15.88 (with 20 mg of boric acid added as a reference). **^{11}B{^{1}H} NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ): 7.43. **HRMS** (DART–TOF) (m/z): $[M - H]^-$ calculated for $C_8H_6BO_3$, 161.0405; found, 161.0419. **Melting point:** 139–140 °C.

Compounds **11a** and **11b** were included to demonstrate the synthetic compatibility of a *tert*-butyl-protected *ortho* carboxylic acid with the Miyaura borylation synthetic strategy, as the methyl ester protecting group was used for all other compounds subjected to Miyaura borylation herein.



Compound 11a
Product name: *tert*-Butyl 2-bromo-5-methylbenzoate
Procedure: Anhydrous $MgSO_4$ (27.990 g, 232.5 mmol, 4 equiv) was added to a round-bottom flask, followed by 200 mL of dichloromethane. Concentrated H_2SO_4 (5.7015 g, 58.13 mmol, 1 equiv) was added to the flask, and the resulting solution was stirred for 15 min. 2-Bromo-5-methylbenzoic acid (12.501 g, 58.13 mmol) was added to the flask, followed by *tert*-butanol (21.543 g, 290.7 mmol, 5 equiv). The reaction mixture was stirred overnight. sat. aq. $NaHCO_3$ (100 mL) was added slowly until the $MgSO_4$ had dissolved completely in the aqueous layer. The mixture was extracted three times with dichloromethane. The organic layers were combined and washed once with water, once with brine, dried on Na_2SO_4(s), and concentrated under reduced pressure. The product was separated on silica with flash chromatography in hexanes and ethyl acetate. The product was isolated as a light-yellow oil (10.273 g, 37.20 mmol, 64%).
Caution! *H_2SO_4 is highly corrosive.*

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.53–7.46 (m, 2H), 7.14–7.06 (m, 1H), 2.34 (s, 3H), 1.63 (s, 9H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, δ): 165.9, 137.2, 134.1, 133.7, 132.7, 131.3, 117.5, 82.5, 77.4, 77.0, 76.7, 28.2, 20.8. **HRMS** (DART–TOF) (*m*/*z*): $[M + H]^+$ calculated for $C_{12}H_{16}BrO_2$, 271.0354; found, 271.0328.

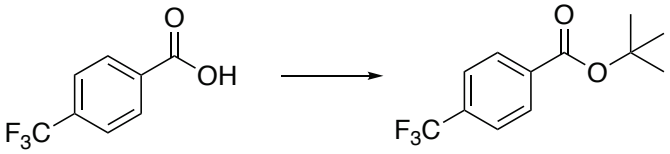


Compound 11b

Product name: *tert*-Butyl 5-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate

Procedure: *tert*-Butyl 2-bromo-5-methylbenzoate (1.8363 g, 6.65 mmol) was added to an oven-dried round-bottom flask. Bis(pinacolato)diboron (1.6887 g, 6.65 mmol, 1 equiv), potassium acetate (1.9630 g, 20.0 mmol, 3 equiv), and $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ complex (0.8150 g, 1.00 mmol, 0.15 equiv) were added to the round-bottom flask. The flask was evacuated and refilled with N_2(g) three times. Anhydrous 1,4-dioxane (30 mL) was added to the flask, and the reaction mixture was heated to 80 °C under N_2(g) flow and stirred for 16 h. The reaction mixture was then cooled and filtered through celite with 1:1 hexanes/ethyl acetate, then filtered through a silica plug with 1:1 hexanes/ethyl acetate. The flow-through concentrated under reduced pressure. The product was separated on silica with flash chromatography in hexanes and ethyl acetate. The product was isolated as a light-orange oil (0.9196 g, 3.39 mmol, 51%).

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.61 (s, 1H), 7.39 (d, J = 7.3 Hz, 1H), 7.32–7.25 (m, 1H), 2.37 (s, 3H), 1.42 (s, 12H), 1.28 (s, 9H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, δ): 167.8, 138.6, 136.4, 134.8, 133.2, 132.0, 132.0, 128.7, 83.8, 83.6, 81.2, 77.5, 77.2, 76.8, 28.3, 25.1, 24.9, 21.4. **^{11}B{^{1}H} NMR** (128 MHz, $CDCl_3$, δ): 30.83.



Compound 12a

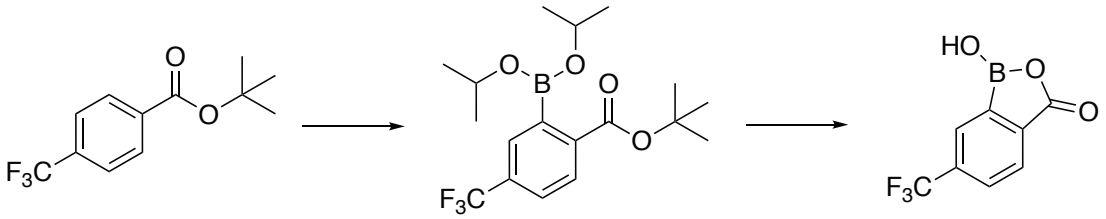
Product name: *tert*-Butyl 4-(trifluoromethyl)benzoate

Procedure: A solution of 4-trifluoromethyl benzoic acid (3.2130 g, 16.9 mmol) in $SOCl_2$ (20.106 g, 169 mmol, 10 equiv) was heated at reflux for 4 h. The reaction mixture was concentrated under reduced pressure. The residue was dissolved in 30 mL anhydrous tetrahydrofuran. Triethylamine (11.77 mL, 8.5506 g, 84.5 mmol, 5 equiv), 4-dimethylaminopyridine (DMAP) (0.4130 g, 3.38 mmol, 0.2 equiv), and *tert*-butanol (12.5262 g, 169 mmol, 10 equiv) were added, and the reaction mixture was stirred overnight. The reaction mixture was diluted with 100 mL of 4 N HCl and extracted three times with dichloromethane. The organic layer was washed once with water, once with brine, dried on Na_2SO_4(s), and concentrated under reduced pressure. The product was isolated as a light-yellow liquid (2.8713 g, 11.70 mmol, 69%) and used without further purification.

Caution! *DMAP is highly toxic.*

^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.12 (d, J = 8.2 Hz, 2H), 7.70 (d, J = 8.2 Hz, 2H), 1.63 (s, 9H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, δ): 193.3, 164.5, 135.2, 134.4, 134.1, 133.8, 133.6, 130.6, 129.8, 125.2, 125.2, 125.2, 125.2, 122.7, 82.0, 77.3, 77.0, 76.8, 28.1. **^{19}F{^{1}H} NMR** (471 MHz, $CDCl_3$, δ): −63.04. **HRMS** (DART–TOF) (*m*/*z*): $[M + H]^+$ calculated for $C_{12}H_{14}F_3O_2$, 247.0940; found, 247.0943.



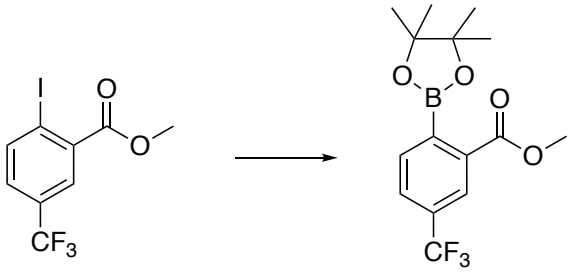
Compound 12b

Product name: 1-Hydroxy-6-(trifluoromethyl)-2,1-benzoxaborol-3-one

Procedure: *tert*-Butyl 4-(trifluoromethyl)benzoate (1.1340 g, 4.6 mmol) was dissolved in 15 mL of anhydrous tetrahydrofuran, and the resulting solution was cooled to 0 °C. Triisopropyl borate (2.2568 g, 12.0 mmol, 2.6 equiv) was added, followed by the dropwise addition of lithium diisopropylamide (LDA) (2.76 mL, 5.52 mmol, 1.2 equiv of 2 M solution in 50:28:13 tetrahydrofuran/heptane/ethylbenzene from Fisher Scientific (Product Number AC268831000). The reaction mixture was stirred for 30 min at 0 °C. The reaction mixture was quenched with sat. aq. NH_4Cl, extracted three times with ethyl acetate, washed once with water, and washed once with brine. The organic layer was dried on Na_2SO_4(s) and concentrated under reduced pressure. The isopropyl borate product was separated on silica with flash chromatography in methanol and dichloromethane, and the isopropyl borate product was confirmed via TLC. The residue was then stirred for 1 h in a mixture of 5 mL of dichloromethane and 3 mL of trifluoroacetic acid and concentrated under reduced pressure. The product was separated with reversed-phase flash chromatography and lyophilized. The product was isolated as a white solid (0.5571 g, 2.58 mmol, 56%, 2 steps).

Caution! *Triisopropyl borate solution is highly flammable. LDA solution is highly flammable and corrosive.*

^{1}H NMR (400 MHz, D_2O/CD_3CN, δ): 7.79–7.57 (m, 3H). **^{13}C{^{1}H} NMR** (126 MHz, D_2O/CD_3CN, δ): 175.4, 138.7, 134.5, 134.3, 126.3, 126.2, 126.2, 126.2, 126.2, 126.1, 125.8, 124.1, 120.0, 65.1, 28.6, 24.6, 1.8, 1.6, 1.5, 1.2, 1.0, 0.8. **^{11}B{^{1}H} NMR** (128 MHz, D_2O/CD_3CN, δ): 9.18. **^{11}B{^{1}H} NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ): 12.09. **^{19}F{^{1}H} NMR** (376 MHz, D_2O/CD_3CN, δ): −63.05. **HRMS** (DART–TOF) (*m*/*z*): $[M + H]^+$ calculated for $C_8H_5BF_3O_3$, 217.0289; found, 217.0273.



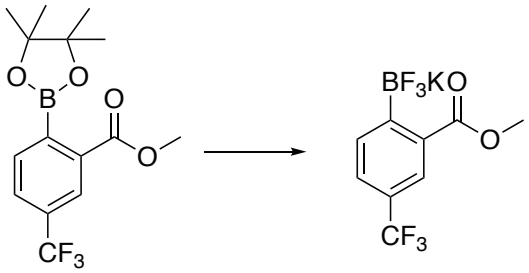
Compound 13a

Product name: Methyl 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)-5(trifluoromethyl) benzoate

Procedure: Methyl 2-iodo-5-(trifluoromethyl)benzoate (1.5182 g, 4.6 mmol) and 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.9415 g, 5.06 mmol, 1.1 equiv) were dissolved in 6 mL of tetrahydrofuran, and the resulting solution was cooled to 0 °C. Isopropylmagnesium chloride lithium chloride complex solution (6.72 mL, 8.74 mmol, 1.9 equiv of a 1.3 M in tetrahydrofuran) were added dropwise over 5 min. The reaction mixture was stirred for an additional 10 min, then quenched with sat. aq. NH_4Cl. The mixture was extracted three times with ethyl acetate, washed once with sat. aq. NH_4Cl, and dried on Na_2SO_4(s). The organic layer was concentrated under reduced pressure. The residue was resuspended in dichloromethane and purified on silica with flash chromatography in dichloromethane. The product was isolated as a yellow crystalline solid (1.2742 g, 3.86 mmol, 84%).

Caution! *Isopropylmagnesium chloride lithium chloride complex solution is highly flammable and corrosive.*

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.22 (s, 1H), 7.77 (d, J = 6.9 Hz, 1H), 7.64 (d, J = 7.7 Hz, 1H), 3.96 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, δ): 167.2, 134.2, 132.8, 132.5, 132.4, 131.9, 131.5, 131.2, 130.9, 128.2, 128.2, 128.2, 128.2, 125.5, 125.5, 125.4, 125.4, 125.0, 84.5, 77.4, 77.0, 76.7, 52.7, 24.8. **^{11}B{^{1}H} NMR** (128 MHz, $CDCl_3$, δ): 30.23. **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$, δ): −63.00.



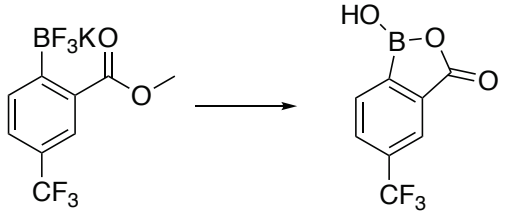
Compound 13b

Product name: Methyl 2-(trifluoro-λ^4-boraneyl)-5-(trifluoromethyl)benzoate, potassium salt

Procedure: Methyl 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)-5(trifluoromethyl) benzoate (1.2544 g, 3.8 mmol) was dissolved in methanol (8 mL/mmol), and KHF_2 (3.80 mL, 17.1 mmol, 4.5 equiv of a 4.5 M aqueous solution) was added slowly. The reaction mixture was stirred for 30 min and then concentrated under reduced pressure. The residue was resuspended in acetone and stirred overnight. The following day, the solid was removed by filtration and rinsed with hot acetone. The filtrate was concentrated under reduced pressure. The product was isolated as a white solid (0.7434 g, 2.43 mmol, 64%) and was used without further purification.

Caution! *KHF_2 is highly corrosive and toxic.*

^{1}H NMR (500 MHz, DMSO, δ): 7.68 (d, J = 7.8 Hz, 1H), 7.63–7.54 (m, 1H), 7.51–7.47 (m, 1H), 3.72 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz, DMSO, δ): 170.9, 137.3, 133.7, 126.1, 125.9, 124.5, 123.4, 122.2, 51.7, 40.0, 39.8, 39.7, 39.5, 39.4, 39.2, 39.0. **^{11}B{^{1}H} NMR** (160 MHz, DMSO, δ): 2.33. **^{19}F{^{1}H} NMR** (471 MHz, DMSO, δ): −60.83, −138.12.



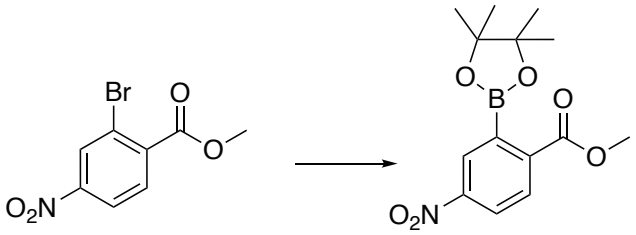
Compound 13c

Product name: 1-Hydroxy-5-(trifluoromethyl)-2,1-benzoxaborol-3-one

Procedure: Methyl 2-(trifluoro-λ⁴-boraneyl)-5-(trifluoromethyl)benzoate, potassium salt (0.4341g, 1.4 mmol) was resuspended in 10 mL of acetonitrile. Trimethylsilyl chloride (0.4563 g, 4.2 mmol, 3 equiv) and water (0.0756 g, 4.2 mmol, 3 equiv) were added, and the reaction mixture was stirred for 1 h before being concentrated under reduced pressure. The residue was resuspended in 4 mL of sat. aq. $NaHCO_3$, and the suspension was stirred for 2 h. The reaction mixture was acidified with 1 N HCl until clear. The solution was frozen and lyophilized prior to resuspending in water and purifying with reversed-phase flash chromatography. The product was lyophilized. The product was isolated as a white powder (0.1000 g, 0.46 mmol, 33%).

Caution! *Trimethylsilyl chloride is highly corrosive and flammable.*

^{1}H NMR (500 MHz, D_2O/CD_3CN, δ): 7.86 (s, 1H), 7.73 (d, J = 7.6 Hz, 1H), 7.61 (d, J = 7.6 Hz, 1H). **^{13}C{^{1}H} NMR** (126 MHz, D_2O, δ): 173.1, 136.3, 131.0, 129.8, 126.3, 124.15, 122.8, 121.6, 119.3. **^{11}B{^{1}H} NMR** (160 MHz, D_2O/CD_3CN, δ): 15.98. **^{11}B{^{1}H} NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ): 12.36. **^{19}F{^{1}H} NMR** (471 MHz, D_2O/CD_3CN, δ): −62.17. **HRMS** (DART–TOF) (m/z): $[M + H]^+$ calculated for $C_8H_5BF_3O_3$, 217.0278; found, 217.0285. **Melting point** 172–175 °C.

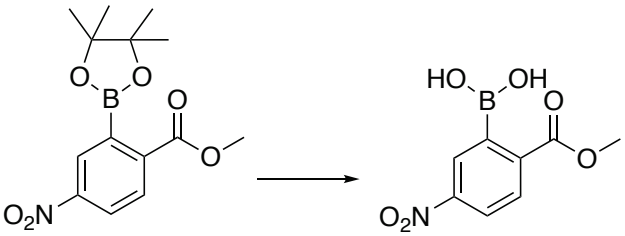


Compound 14a

Product name: Methyl 4-nitro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate

Procedure: Methyl 2-bromo-4-nitrobenzoate (1.0142 g, 3.90 mmol), bis(pinacolato)diboron (1.9810 g, 7.80 mmol, 2 equiv), potassium acetate (1.1484 g, 11.7 mmol, 3 equiv), and $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ complex (0.6369 g, 0.78 mmol, 0.2 equiv) were added to an oven-dried round-bottom flask. The flask was evacuated and refilled with N_2(g) three times. Anhydrous 1,4-dioxane (20 mL) was added to the flask, and the reaction mixture was heated to 80 °C under N_2(g) flow and stirred for 24 h. The reaction mixture was then cooled and filtered through celite with 1:1 hexanes/ethyl acetate, then filtered through a silica plug with 1:1 hexanes/ethyl acetate. The flow-through was concentrated under reduced pressure. The product was separated on silica with flash chromatography in hexanes and ethyl acetate twice. The product was isolated as a golden oil (0.4551 g, 1.48 mmol, 38%).

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.78 (d, J = 2.2 Hz, 1H), 8.37 (dd, J = 8.1, 2.2 Hz, 1H), 7.69 (d, J = 8.1 Hz, 1H), 4.00 (s, 3H), 1.46 (s, 12H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, δ): 166.5, 148.5, 135.1, 133.4, 126.0, 123.4, 84.8, 77.4, 77.0, 76.7, 53.0, 24.8. **^{11}B{^{1}H} NMR** (128 MHz, $CDCl_3$, δ): 31.02. **HRMS** (DART–TOF) (m/z): $[M + H]^+$ calculated for $C_{14}H_{19}BNO_6$, 308.1311; found, 308.1318.

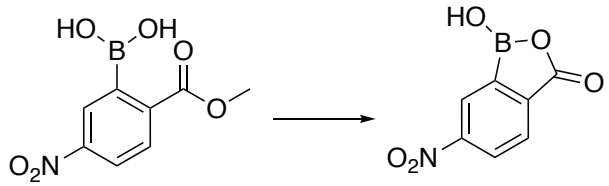


Compound 14b

Product name: (2-(Methoxycarbonyl)-5-nitrophenyl)boronic acid

Procedure: Methyl 4-nitro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (0.1465 g, 0.477 mmol) was dissolved in 4:1 tetrahydrofuran/water and stirred with $NaIO_4$ (3 equiv) for 30 min. 1 N HCl (0.3060 g, 1.43 mmol, 0.7 equiv) was added, and the reaction mixture was stirred overnight. The mixture was concentrated under reduced pressure, then resuspended in methanol. A white precipitate formed and was removed by filtration. The filtrate was concentrated under reduced pressure and resuspended in dichloromethane before being filtered through filter paper to remove a precipitate. The filtrate was dried on Na_2SO_4(s) and concentrated under reduced pressure. The product was separated with reversed-phase flash chromatography, and lyophilized. The product was isolated as a white powder (0.0687 g, 0.31 mmol, 64%).

^{1}H NMR (500 MHz, CD_3CN, δ): 8.63 (d, J = 2.3 Hz, 1H), 8.33 (dd, J = 8.1, 2.2 Hz, 1H), 7.68 (d, J = 8.1 Hz, 1H), 3.91 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz, CD_3CN, δ): 166.7, 147.9, 133.6, 132.8, 126.3, 126.2, 123.14, 123.10, 117.8, 52.6, 52.5. **^{11}B{^{1}H} NMR** (160 MHz, CD_3CN, δ): 29.29.

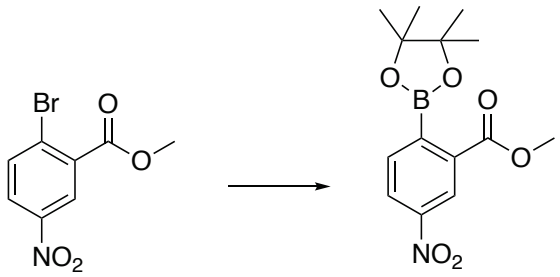


Compound 14c

Product name: 1-Hydroxy-6-(nitro)-2,1-benzoxaborol-3-one

Procedure: (2-(Methoxycarbonyl)-5-nitrophenyl)boronic acid (0.0676 g, 0.30 mmol) was dissolved in 3 mL of sat. aq. $NaHCO_3$, and the resulting solution was stirred for 2.5 h. The reaction mixture changed from white and cloudy to yellow and cloudy over the course of 20 min. The reaction mixture was acidified with 2 N HCl until the solution became clear and colorless. The reaction mixture was lyophilized, resuspended in 1 mL of water, and purified with reversed-phase flash chromatography. The product was isolated as a white solid (0.0110 g, 0.06 mmol, 19%).

^{1}H NMR (400 MHz, CD_3CN/D_2O, δ): 8.31 (s, 1H), 8.26 (dd, J = 7.9, 2.0 Hz, 1H), 7.65 (d, J = 7.9 Hz, 1H). **^{13}C{^{1}H} NMR** (101 MHz, CD_3CN/D_2O, δ): 175.3, 149.0, 137.6, 130.6, 128.2, 120.1, 120.0, 2.2, 1.9, 1.7, 1.5, 1.3, 1.1, 0.9. Note: The carbon bonded directly to the boron is not observed due to quadrupolar broadening. **^{11}B{^{1}H} NMR** (128 MHz, CD_3CN/D_2O, δ): 5.12. **^{11}B{^{1}H} NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ): 8.30. **HRMS** (DART–TOF) (m/z): $[M - H]^-$ calculated for $C_7H_3BNO_5$, 192.0099; found, 192.0114

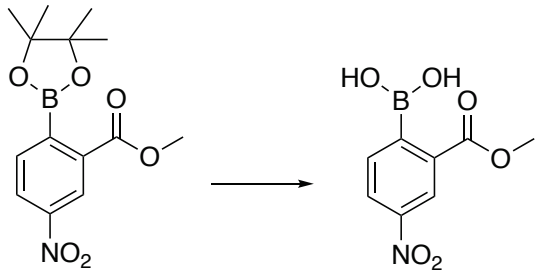


Compound 15a

Product name: methyl 5-nitro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate

Procedure: Methyl 2-bromo-5-nitrobenzoate (0.7385 g, 2.84 mmol), bis(pinacolato)diboron (1.4424 g, 5.68 mmol, 2 equiv), potassium acetate (0.8362 g, 8.52 mmol, 3 equiv), and Pd(dppf)Cl_2·CH_2Cl_2 complex (0.4641 g, 0.57 mmol, 0.2 equiv) were added to an oven-dried round-bottom flask. The flask was evacuated and refilled with N_2(g) three times. Anhydrous 1,4-dioxane (20 mL) was added to the flask, and the reaction mixture was heated to 80 °C under N_2(g) flow and stirred for 24 h. The reaction mixture was then cooled and filtered through celite with 1:1 hexanes/ethyl acetate, then filtered through a silica plug with 1:1 hexanes/ethyl acetate. The flow-through was concentrated under reduced pressure. The product was separated on silica with flash chromatography in hexanes and ethyl acetate. The product was isolated as a red-orange oil (0.6357 g, 2.07 mmol, 73%).

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.35 (d, J = 2.4 Hz, 1H), 8.27 (dd, J = 8.6, 2.3 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 3.99 (s, 3H), 1.46 (s, 12H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, δ): 166.8, 149.6, 139.0, 129.8, 127.2, 124.1, 84.8, 77.4, 77.0, 76.7, 53.0, 24.9. **^{11}B{^{1}H} NMR** (128 MHz, $CDCl_3$, δ): 30.76. **HRMS** (DART–TOF) (m/z): $[M + H]^+$ calculated for $C_{14}H_{19}BNO_6$, 308.1311; found, 308.1321.

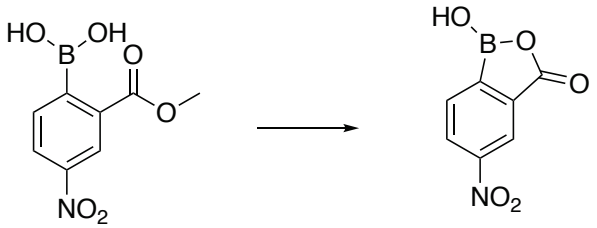


Compound 15b

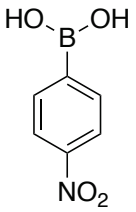
Product name: (2-(Methoxycarbonyl)-4-nitrophenyl)boronic acid

Procedure: Methyl 5-nitro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (0.6326 g, 2.06 mmol) was dissolved in 4:1 tetrahydrofuran/water. $NaIO_4$ (1.3224 g, 6.18 mmol, 3 equiv) was added, and the reaction mixture was stirred for 30 min. 1 N HCl (1.44 mL, 1.44 mmol, 0.7 equiv) was added, and the resulting reaction mixture was stirred overnight. The solution was initially light yellow and cloudy, and became orange and cloudy by the following day. The mixture was concentrated under reduced pressure, resuspended in methanol, and filtered through filter paper. The filtrate was concentrated under reduced pressure and resuspended in dichloromethane, before being filtered again through filter paper. The filtrate was dried on Na_2SO_4(s) and concentrated under reduced pressure. The residue was resuspended in 1 mL of 1:1 water/acetonitrile, purified with reversed-phase flash chromatography, and lyophilized. The product was isolated as a white solid (0.1807 g, 0.80 mmol, 39%).

Caution! *$NaIO_4$ is a strong oxidizer and highly corrosive.*
^{1}H NMR (400 MHz, CD_3CN, δ): 8.67 (d, J = 2.3 Hz, 1H), 8.37 (dd, J = 8.1, 2.3 Hz, 1H), 7.73 (d, J = 8.1 Hz, 1H), 3.96 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, CD_3CN, δ): 166.6, 148.0, 133.8, 132.9, 126.2, 123.1, 117.4, 52.5, 0.9, 0.7, 0.5, 0.3, 0.1, −0.1, −0.3. **^{11}B{^{1}H} NMR** (128 MHz, CD_3CN, δ): 29.31.



Compound 15c
Product name: 1-Hydroxy-5-(nitro)-2,1-benzoxaborol-3-one
Procedure: (2-(Methoxycarbonyl)-4-nitrophenyl)boronic acid (0.1807 g, 0.80 mmol) was dissolved in 5 mL of sat. aq. $NaHCO_3$ and 5 mL of water. The resulting solution was stirred overnight. The reaction mixture was acidified with 2 N HCl until clear and then lyophilized. The residue was resuspended in 1 mL of 1:1 water/acetonitrile and purified with reversed-phase flash chromatography, then lyophilized. The product was isolated as a white solid (0.0803 g, 0.42 mmol, 52%).
^{1}H NMR (400 MHz, D_2O, δ): 8.36 (s, 1H), 8.30 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H).**^{13}C{^{1}H} NMR** (101 MHz, D_2O, δ): 174.8, 147.9, 136.2, 129.3, 127.3, 119.1. **^{11}B{^{1}H} NMR** (128 MHz, D_2O, δ): 7.70. **^{11}B{^{1}H} NMR** (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, δ): 8.08. **HRMS** (DART–TOF) (m/z): $[M - H]^-$ calculated for $C_7H_3BNO_5$, 192.0109; found, 192.0200.



Compound 16
Product name: 4-Nitrophenylboronic acid
Compound obtained from Sigma–Aldrich. NMR and HRMS data obtained for compound confirmation and purity analysis.
^{1}H NMR (400 MHz, CD_3CN, δ): 8.20–8.13 (m, 2H), 8.02–7.95 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, CD_3CN, δ): 150.4, 136.0, 123.2, 118.7, 1.9, 1.7, 1.5, 1.3, 1.1, 0.9, 0.7. **^{11}B{^{1}H} NMR** (128 MHz, CD_3CN, δ): 28.01. Note: The carbon bonded directly to the boron is not observed due to quadrupolar broadening. **HRMS** (DART–TOF) (m/z): $[M + H]^+$ calculated for $C_6H_7BNO_4$, 168.0474; found, 168.0476.

UV–vis Assay of Oxidation of Boronic Acid Derivatives by Hydrogen Peroxide

Oxidation experiments were performed, as described previously.[3] Briefly, solutions (10 mL) of each boronic acid derivative and each corresponding salicylic acid were prepared at a concentration of 1 mM in 0.10 M sodium phosphate buffer, pH 7.45. Some boronic acid derivatives required 5–10 min of sonication to dissolve. The final pH of the reaction mixture was confirmed not to change by more than 0.1 pH units. All stock solutions were prepared on the day of use.

UV absorbance oxidation experiments were performed in 1-mL UV-transparent single-use cuvettes on a Cary 60 UV–vis spectrophotometer. For each boronic acid derivative and salicylic acid pair, a UV–vis scan was performed to determine the wavelength of maximum separation with optimal signal-to-noise ratios that would be used for single-wavelength kinetic assays. The selected wavelengths ranged between 290–350 nm. The oxidation of 4-nitrophenylboronic acid (compound **16**) was measured at 400 nM, which offered the largest change in absorbance between the boronic acid and the oxidized product, 4-nitrophenol (Figure 2).

Single-read measurements at the wavelength determined in the previous scan were taken for each boronic acid and salicylic acid pair with 4 to 5 serial dilutions starting at 1 mM for the boronic acid and 250 μM for the salicylic acid. The mean absorbance (± SD) for each compound was plotted against the corresponding concentration. A linear regression analysis was performed to determine the slope of the absorbance versus concentration curve, giving the molar extinction coefficient according to Beer's Law, and its corresponding standard error of the mean. Example linear regression plots for 2-carboxyphenylboronic acid and salicylic acid are shown in Figures S3 and S4. Extinction coefficients for the oxidation of boronic acid derivatives were calculated as the difference in absorbance between the product and the starting materials with the equation: $\Delta\varepsilon_{\text{oxidation}} = \varepsilon_{\text{phenol}} - (\varepsilon_{\text{boronic acid}} + \varepsilon_{\text{hydrogen peroxide}})$ and are listed in Table S1.

Kinetic experiments were performed in triplicate for each boronic acid. Briefly, a 10 mM solution of H_2O_2 (30% solution from Sigma–Aldrich) was prepared fresh daily in cold 0.10 M sodium phosphate buffer pH 7.45. The solution was kept on ice and protected from light for the duration of the experiment. Any remaining H_2O_2 solution was quenched with MnO_2. H_2O_2 (10 μL of a 10 mM solution) was added to a cuvette. Boronic acid derivative (990 μL of 1.0 mM solution) was then added to the cuvette, and the solutions were mixed by pipetting. The cuvette was then placed in the spectrophotometer, and the absorbance was read continuously at the wavelength previously determined for the boronic acid derivative and salicylic acid pair. Each experiment was allowed to run for at least 10 min before starting another replicate. From each measurement, the slope and standard deviation of the absorbance versus time curve was calculated. For the fastest reaction (which was the oxidation of 4-nitrophenylboronic acid), the slope from the first 10% of the reaction was calculated. This slope value was then converted to the slope of the change in molar concentration of the boronic acid derivative versus time by dividing by the difference in extinction coefficients between the salicylic acid and boronic acid derivative pair. These reactions were previously determined to be first-order with respect to both the boronic acid derivative and H_2O_2.[3] The second-order rate constant (M^{-1} s^{-1}) for each reaction was determined with the equation $k_{\text{obs}} = v_o/([\text{boronic acid}][\text{hydrogen peroxide}])$. Second-order rate constant and standard error values are listed in Table S2.

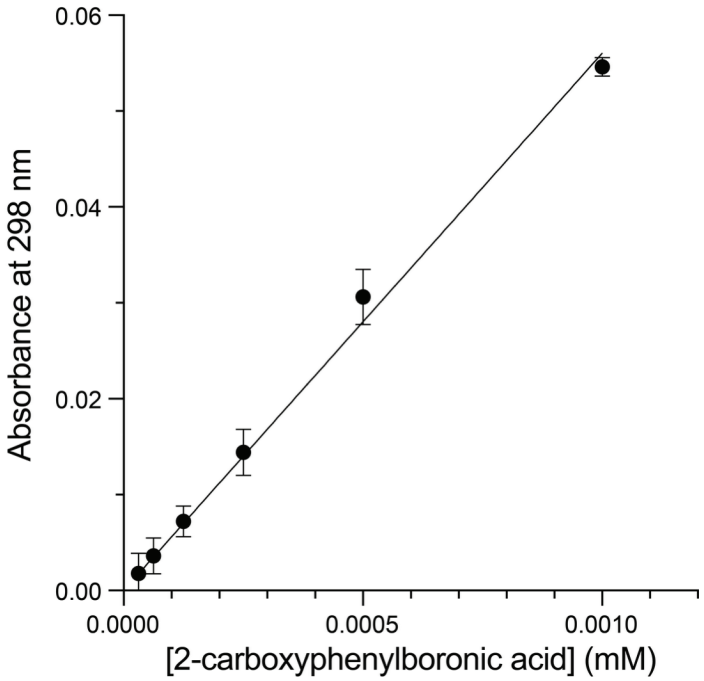


Figure S3. Linear regression analysis for determining the extinction coefficient of 2-carboxyphenylboronic acid in 0.10 M sodium phosphate buffer, pH 7.45. ε = 56.03 ± 1.16 M^{-1} cm^{-1}.

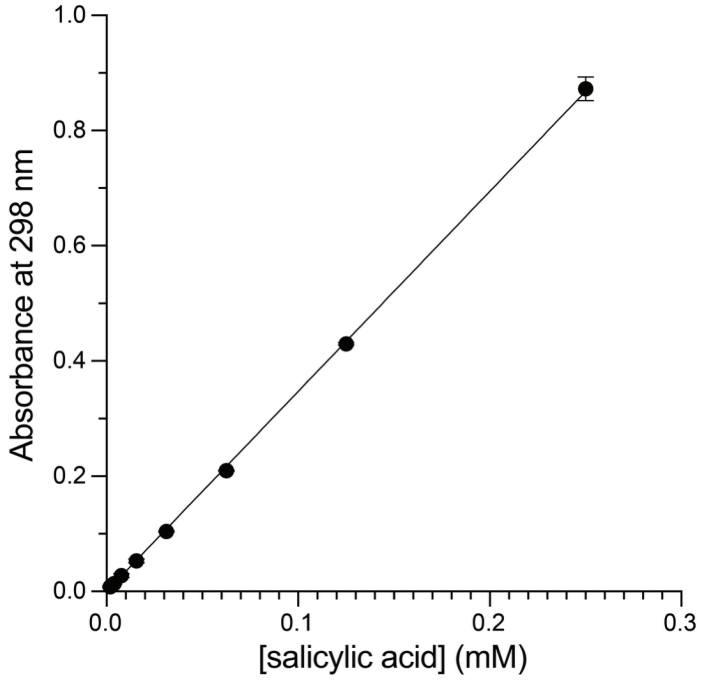


Figure S4. Linear regression analysis for determining the extinction coefficient of salicylic acid in 0.10 M sodium phosphate buffer, pH 7.45. ε = 3422 ± 12 M^{-1} cm^{-1}.

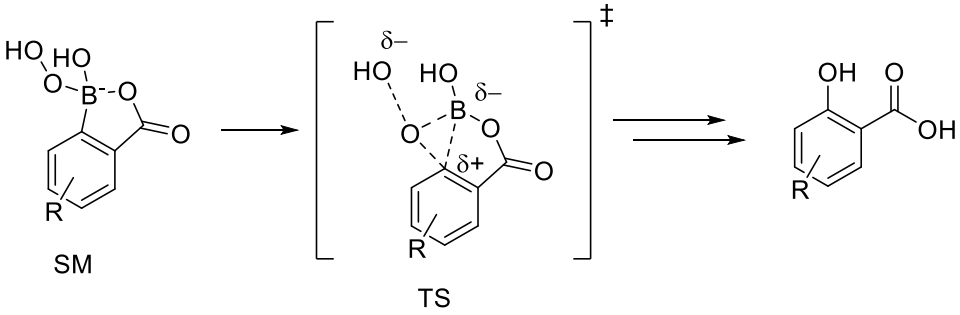
Table S1. Second-Order Rate Constants for the Oxidation of Boronic Acid Derivatives by H_2O_2 in 0.10 M Sodium Phosphate Buffer, pH 7.45

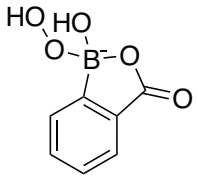
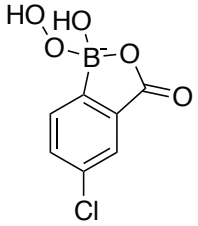
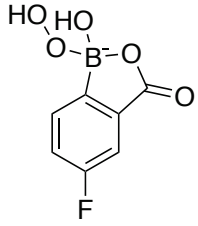
Boronic Acid	$\Delta\varepsilon$ (M^{-1} cm^{-1})	λ (nm)	k_2 (M^{-1} s^{-1})
1	3366 ± 12	298	$(1.73 \pm 0.09) \times 10^{-4}$
2	2517 ± 12	290	$(1.9 \pm 0.3) \times 10^{-5}$
3	3893 ± 10	310	$(1.28 \pm 0.03) \times 10^{-4}$
4	4047 ± 5	301	$(6.2 \pm 0.5) \times 10^{-5}$
5	3487 ± 14	311	$(9.7 \pm 0.5) \times 10^{-5}$
6b	4227 ± 13	298	$(2.6 \pm 0.1) \times 10^{-4}$
7c	3579 ± 14	328	$(3.77 \pm 0.07) \times 10^{-4}$
8b	2006 ± 11	300	$(7.3 \pm 0.3) \times 10^{-4}$
10d	3192 ± 21	309	$(3.86 \pm 0.03) \times 10^{-4}$
12b	4084 ± 41	303	$(8.1 \pm 0.3) \times 10^{-5}$
13c	2955 ± 42	294	$(8.5 \pm 0.4) \times 10^{-5}$
14c	2690 ± 2	348	$(1.28 \pm 0.04) \times 10^{-4}$
15c	6183 ± 44	344	$(6.9 \pm 0.9) \times 10^{-5}$
16	12770 ± 18	400	$(5.7 \pm 0.1) \times 10^{-1}$

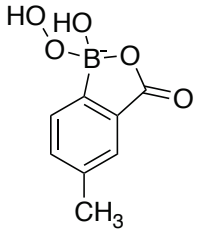
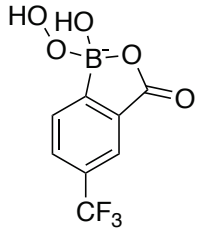
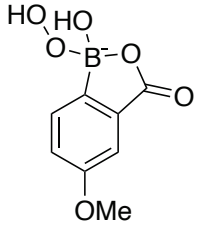
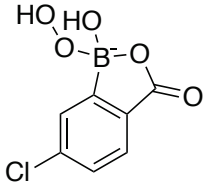
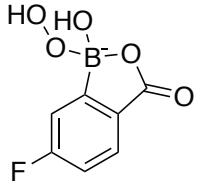
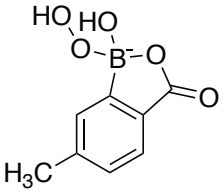
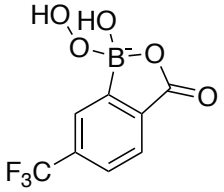
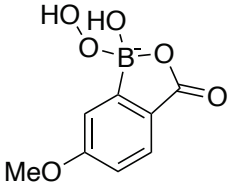
Computational Analysis of Benzoxaborolone Oxidation by Hydrogen Peroxide

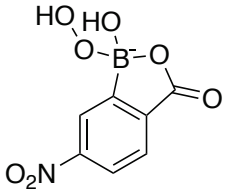
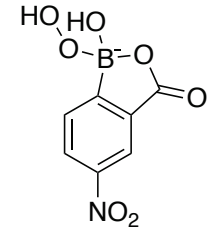
Structure optimizations were performed with Gaussian 09 software from Gaussian at the M06-2X/6-311+G(d,p) level of theory and employing the IEFPCM solvation model for water.[4-6] Frequency calculations were performed to confirm each stationary point as a minimum or first-order saddle point. Natural Bonding Orbital (NBO) analysis of the optimized structures was conducted with NBO 6.0 software.[7]

Table S2. Calculated Free Energies of Activation and Relative Rate Constants for the Rate-Limiting Step in the Oxidation of Benzoxaborolones by Hydrogen Peroxide



Boronic Acid	SM	$\Delta G^{‡}$ (kcal/mol)	k_{rel}
1		35.18505714	1
5		36.43819261	0.121
3		36.12318309	0.205

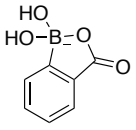
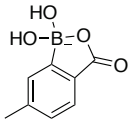
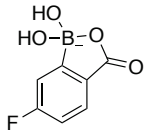
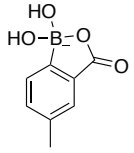
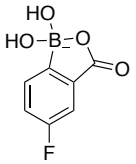
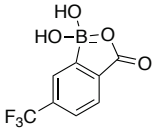
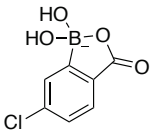
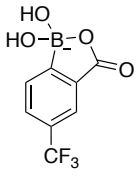
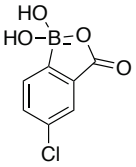
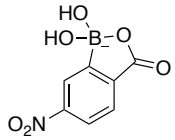
10d		34.74517333	2.10
13c		36.28696294	0.156
7c		34.8612625	1.73
4		36.22734959	0.172
2		36.20350425	0.179
8b		34.4571467	3.42
12b		36.54486914	0.101
6b		35.16434934	1.04

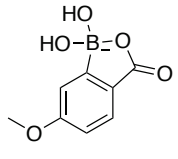
14c		37.20187106	0.0332
15c		37.22822644	0.0318

^{11}B NMR Analysis of Benzoxaborolones in a Buffered Solvent System

0.010 M phosphate buffer, pD 7.2, containing 0.0027 M KCl and 0.137 M NaCl was prepared in D_2O with pre-made tablets from Sigma–Aldrich (#P4417). Each compound (15–20 mg) was dissolved in 700 µL of 1:1 phosphate-buffered D_2O/CD_3CN, the exception being compound **14c**, which required 100% phosphate-buffered D_2O. Boric acid (2–3 mg) was added to each sample as a reference standard, with no change in observed pD. A proton decoupled ^{11}B NMR with background suppression was obtained at 160 MHz with a D_2O lock. In each analysis, the boric acid signal, which is observed at 19–20 ppm, was fixed to 20 ppm. All spectra are included with their corresponding compound in the NMR Spectra section below.

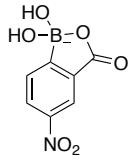
Table S3. Proton Decoupled ^{11}B NMR Analysis of Compounds Prepared in 1:1 Phosphate-Buffered D_2O/CD_3CN

Compound	^{11}B{^{1}H} NMR (δ) (ppm)	Compound	^{11}B{^{1}H} NMR (δ) (ppm)
 Compound **1**	11.47	 Compound **8b/9d**	9.09
 Compound **2**	7.87	 Compound **10d**	7.43
 Compound **3**	8.84	 Compound **12b**	12.09
 Compound **4**	12.35	 Compound **13c**	12.36
 Compound **5**	8.23	 Compound **14c**	8.30



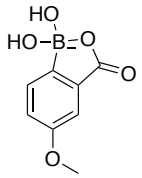
Compound **6b**

9.95



Compound **15c**

8.08



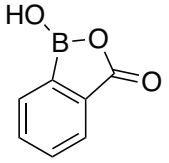
Compound **7c**

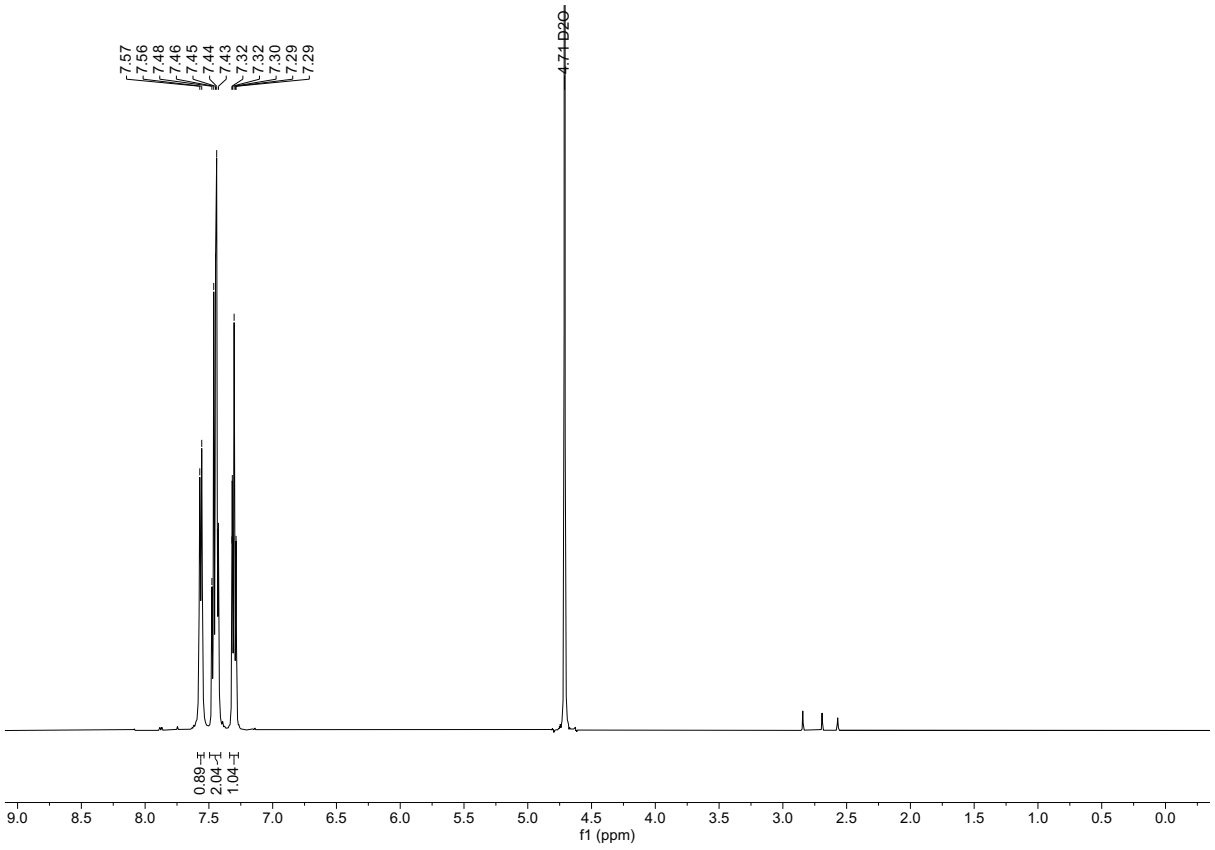
8.38

NMR Spectra

Compound 1

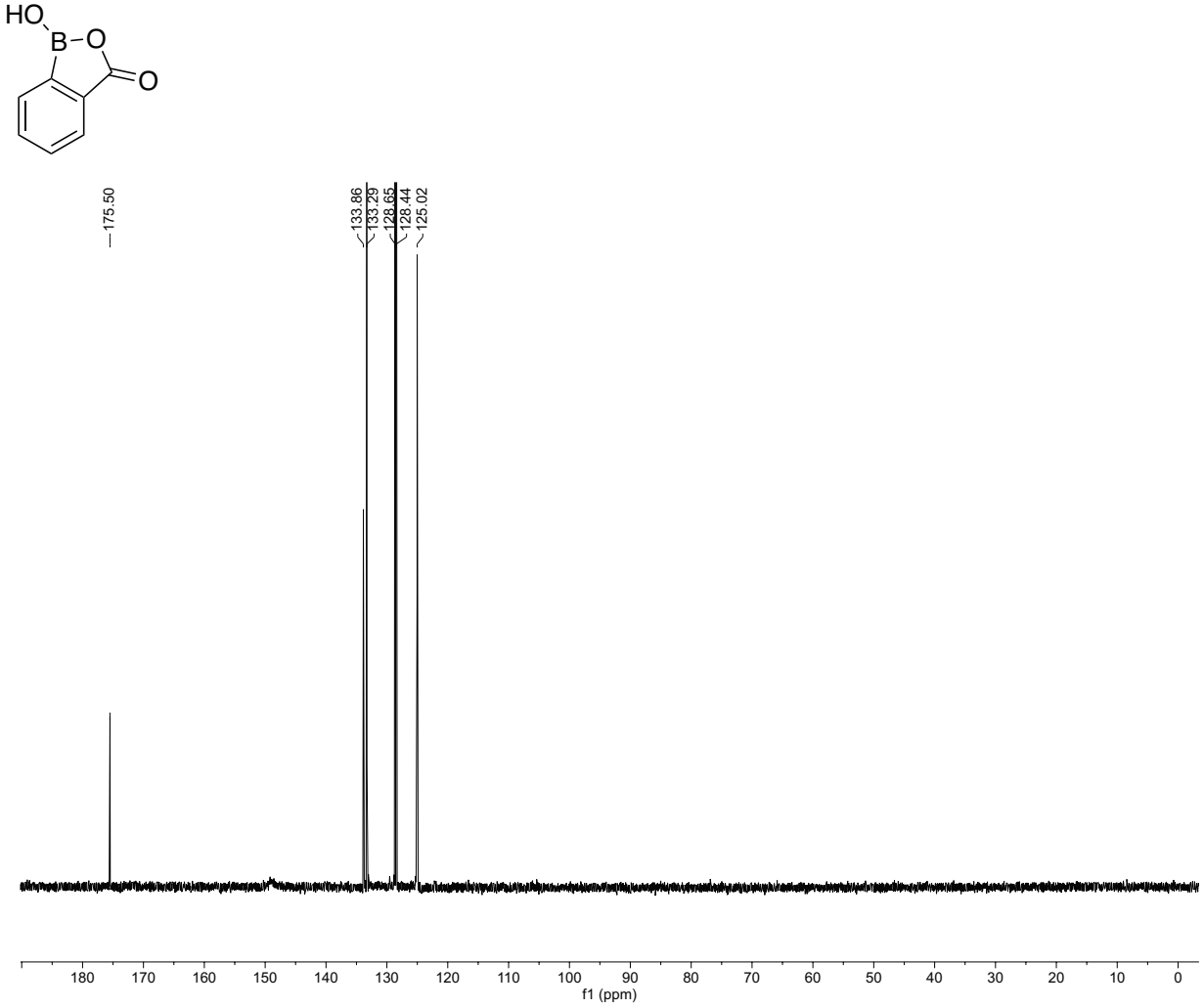
^{1}H NMR (500 MHz, D_2O)





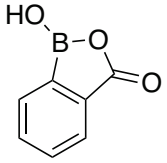
Compound 1

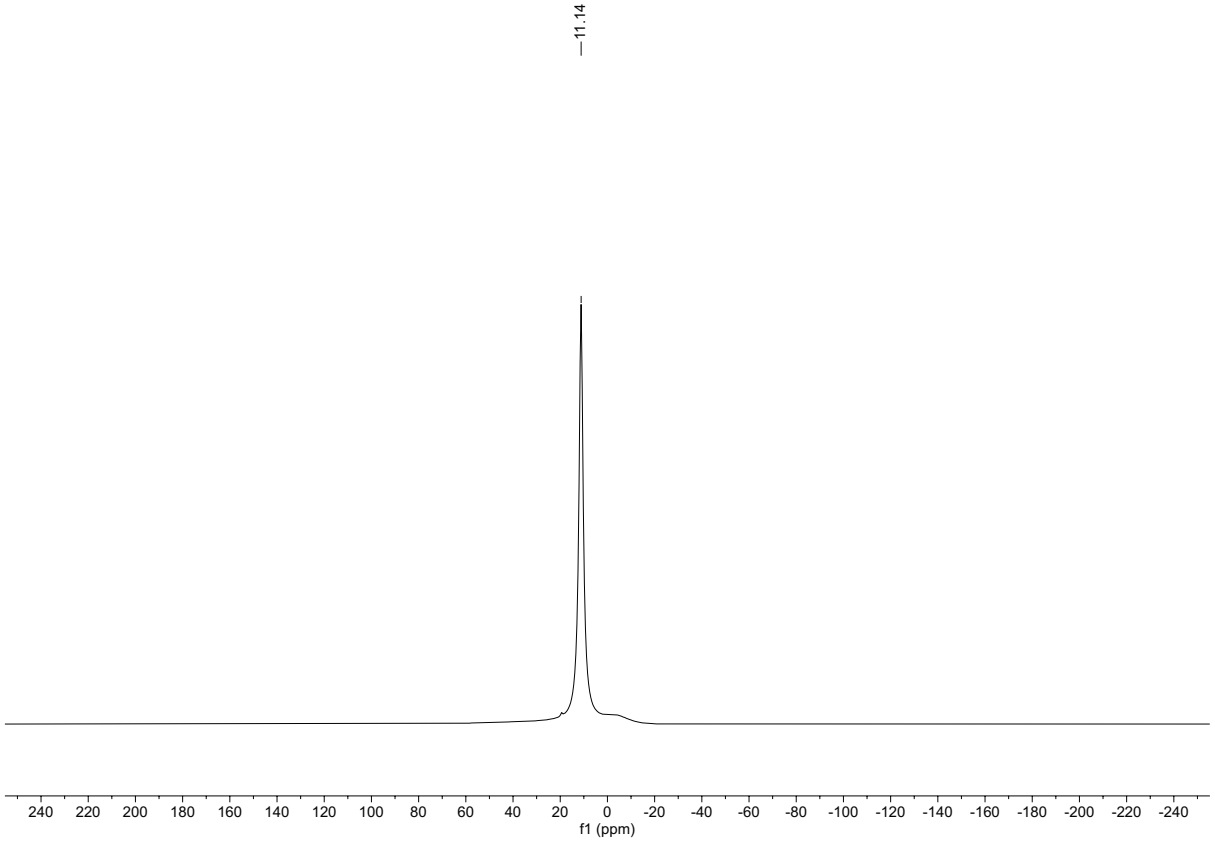
$^{13}C\{^{1}H\}$ NMR (126 MHz, D_2O)



Compound 1

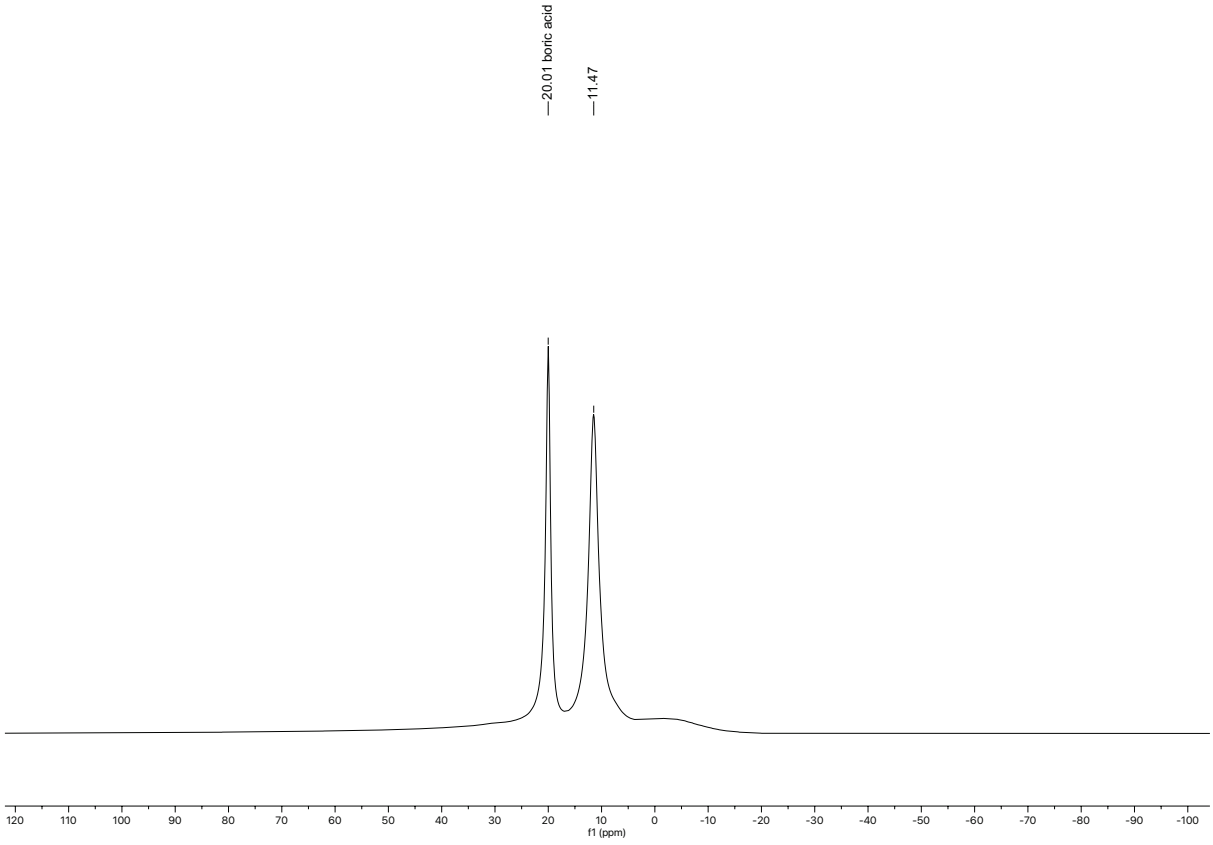
$^{11}B\{^{1}H\}$ NMR (160 MHz, D_2O)





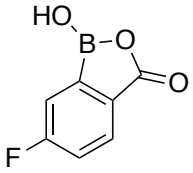
Compound 1

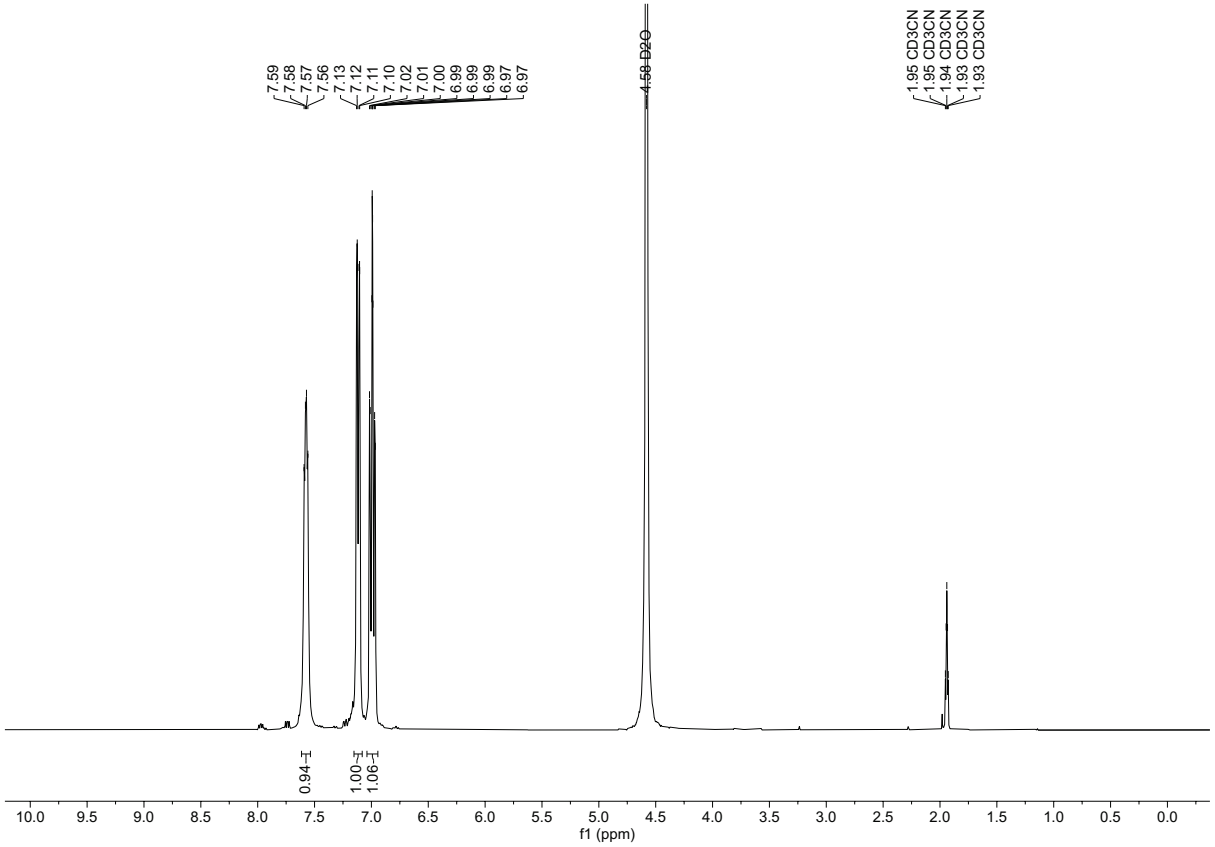
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 2

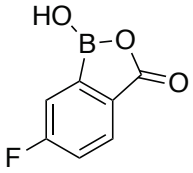
^{1}H NMR (500 MHz, CD_3CN/D_2O)

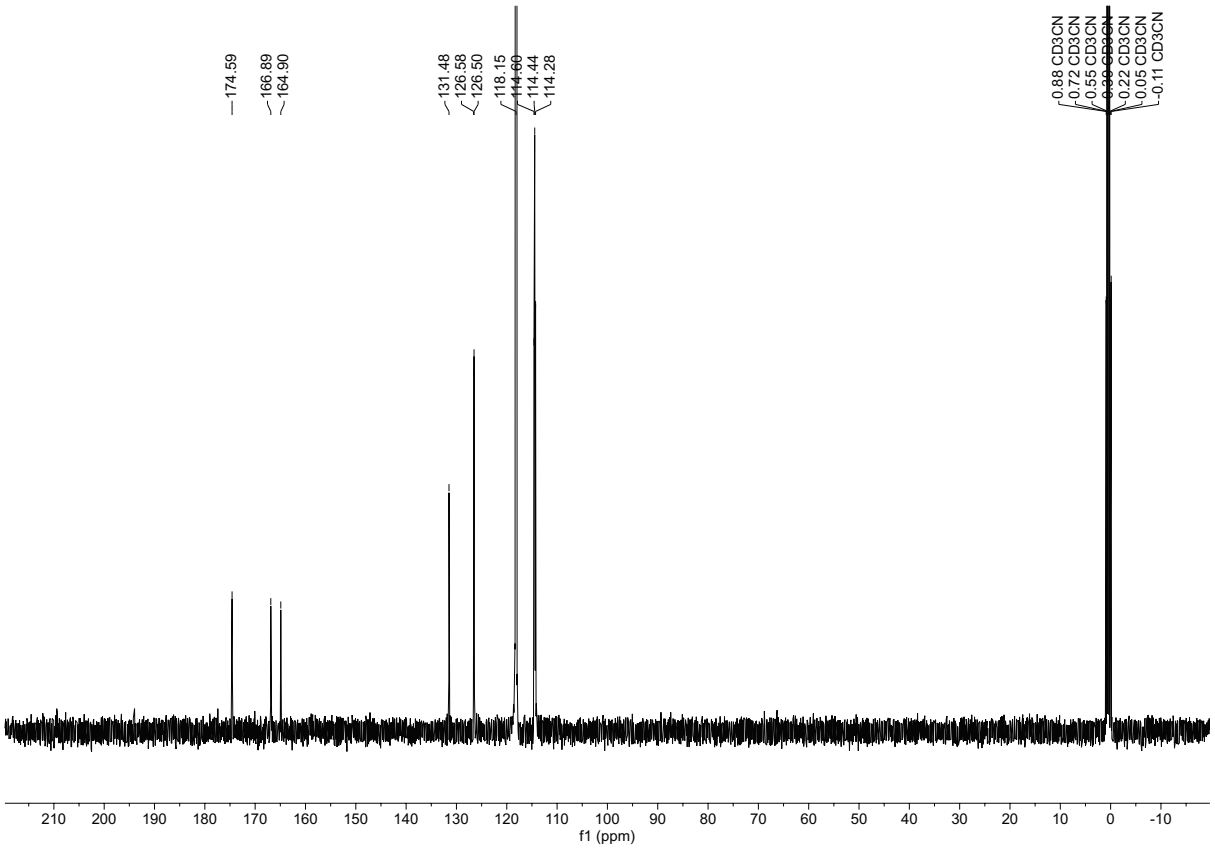




Compound 2

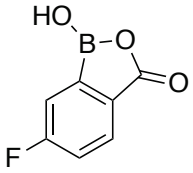
$^{13}C\{^{1}H\}$ NMR (126 MHz, CD_3CN/D_2O)

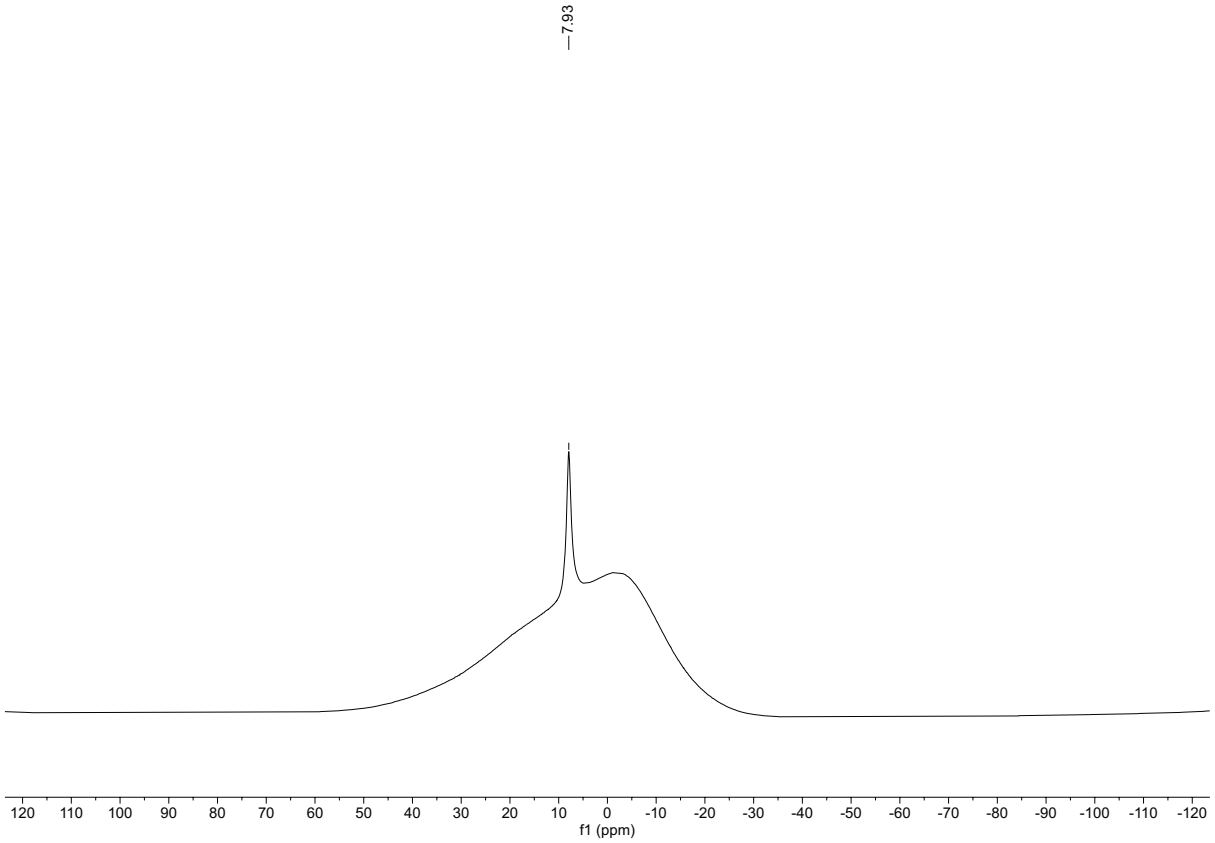




Compound 2

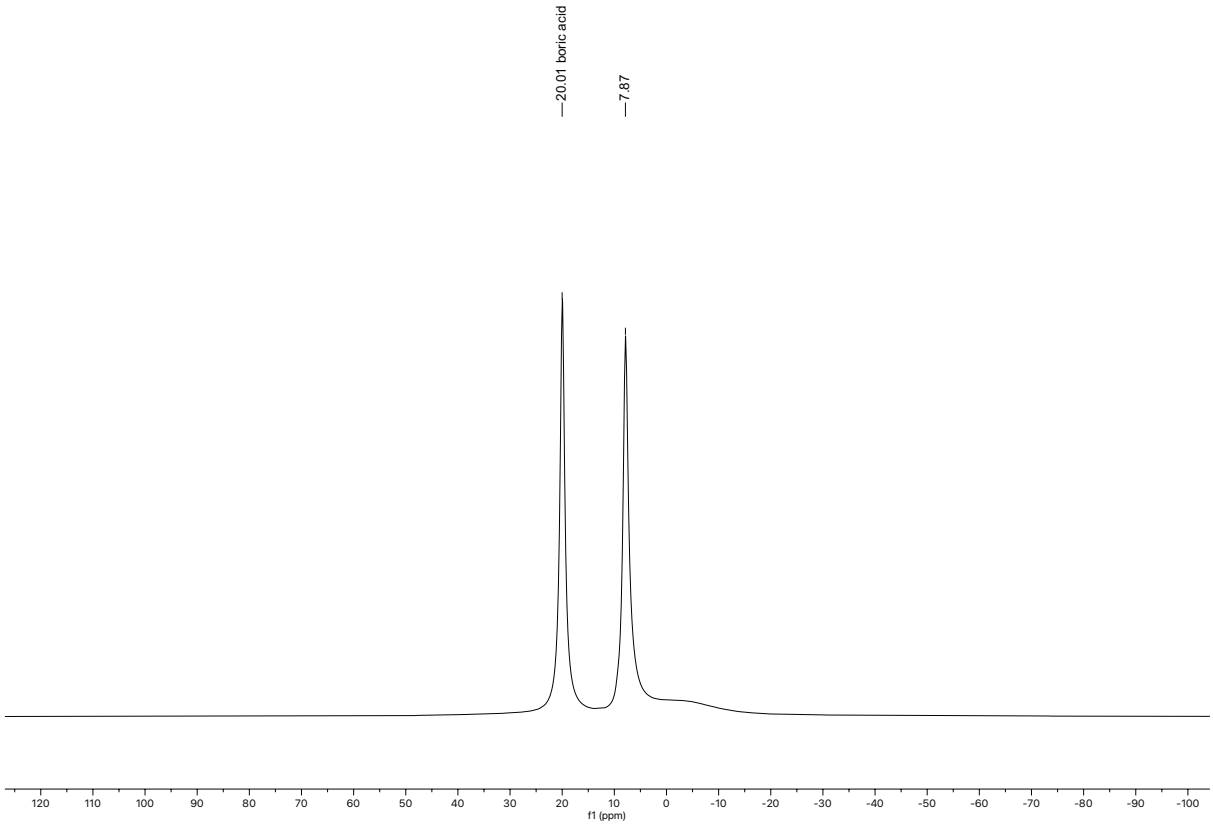
$^{11}B\{^{1}H\}$ NMR (160 MHz, CD_3CN/D_2O)





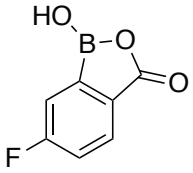
Compound 2

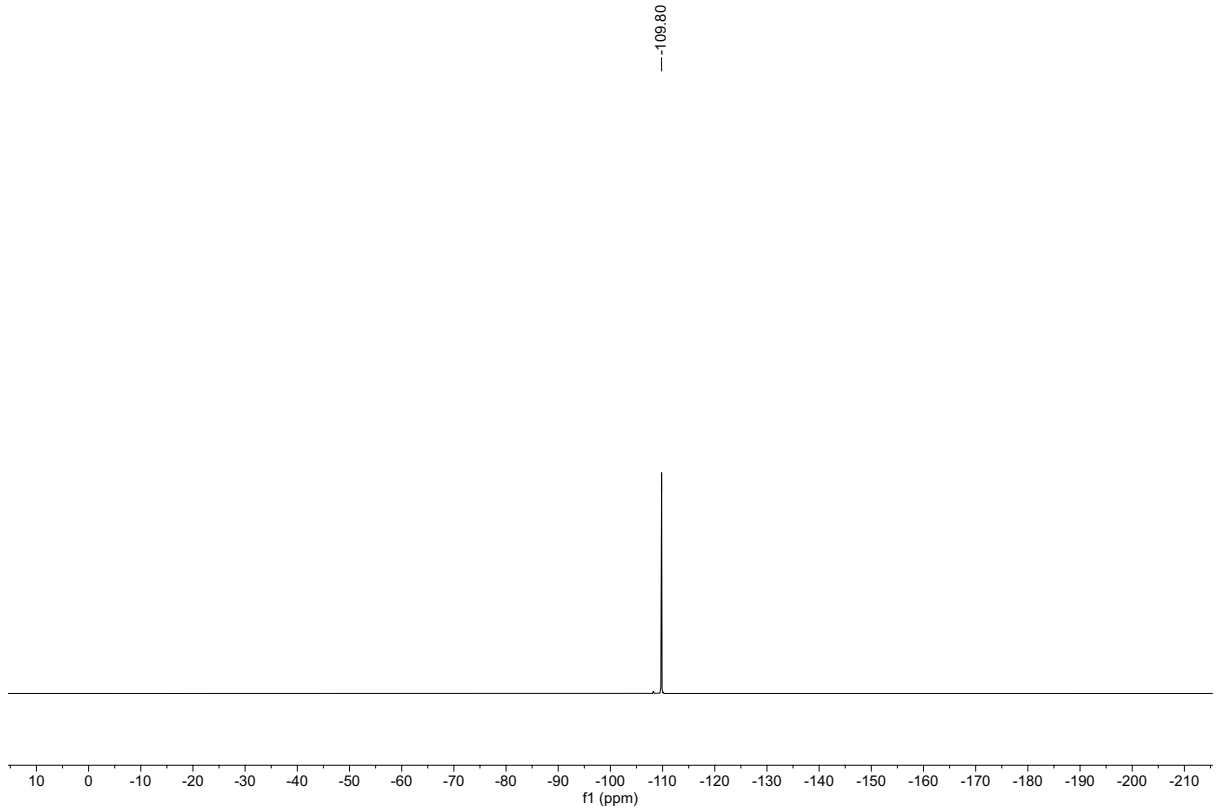
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 2

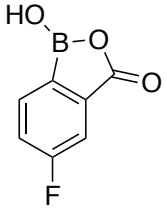
$^{19}F\{^{1}H\}$ NMR (471 MHz, CD_3CN/D_2O)

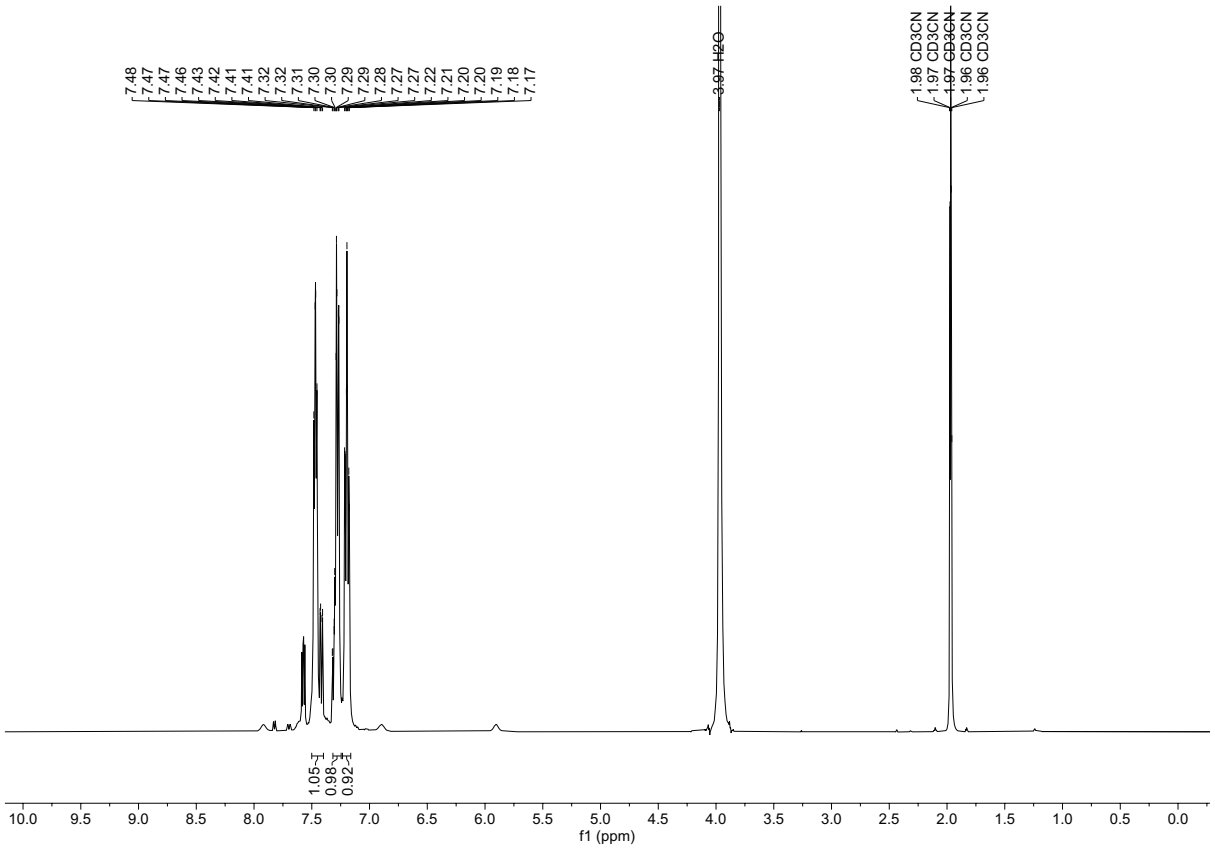




Compound 3

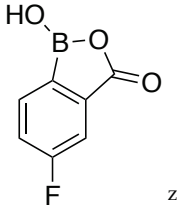
^{1}H NMR (500 MHz, CD_3CN/D_2O)





Compound 3

$^{13}C\{^{1}H\}$ NMR (126 MHz, CD_3CN/D_2O)



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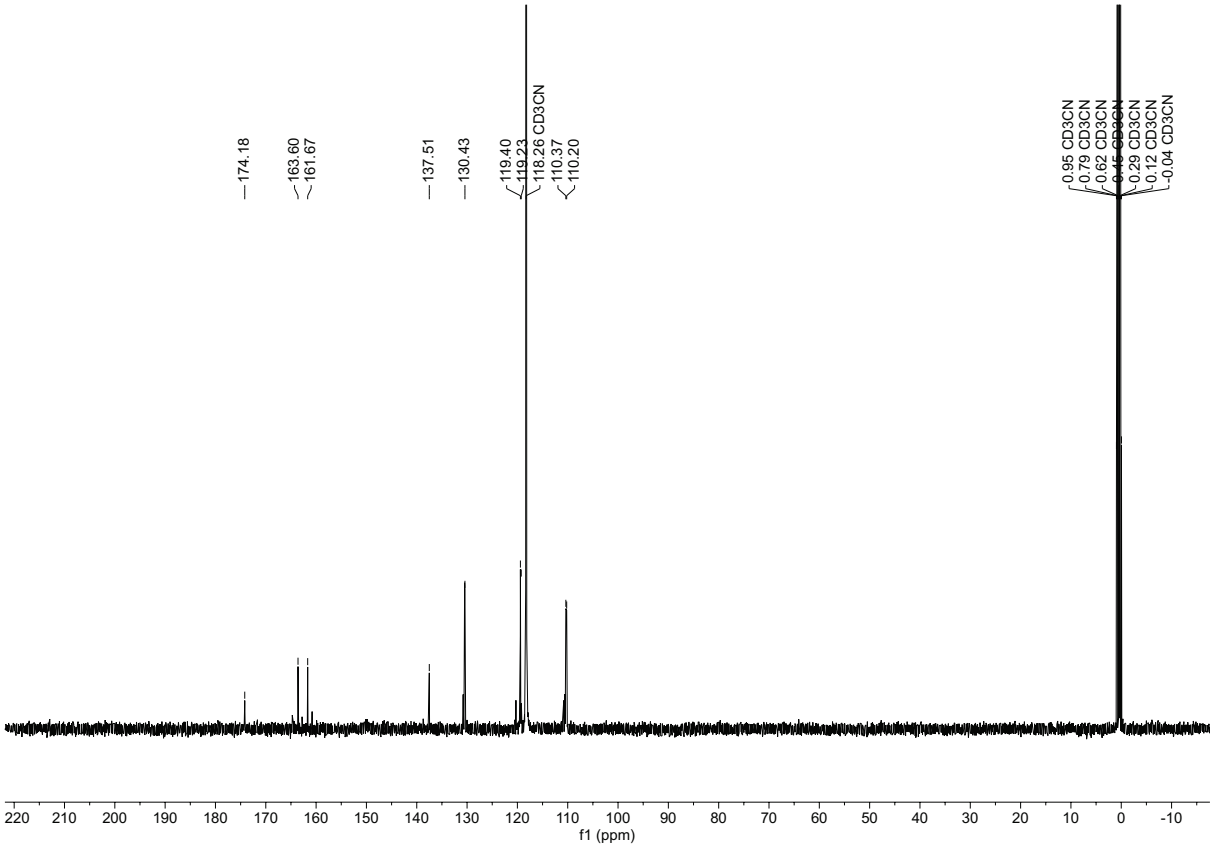
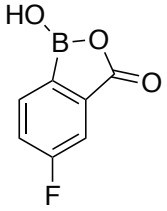
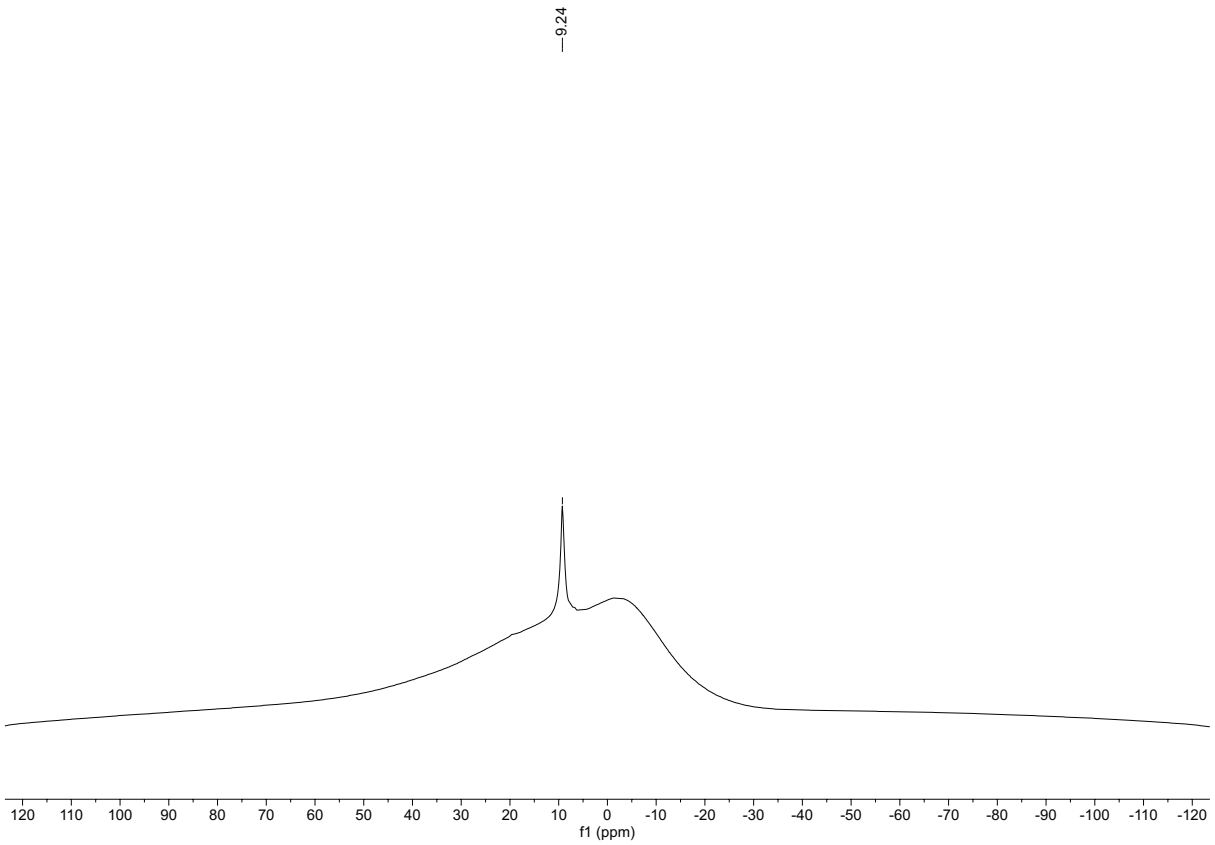


Compound 3

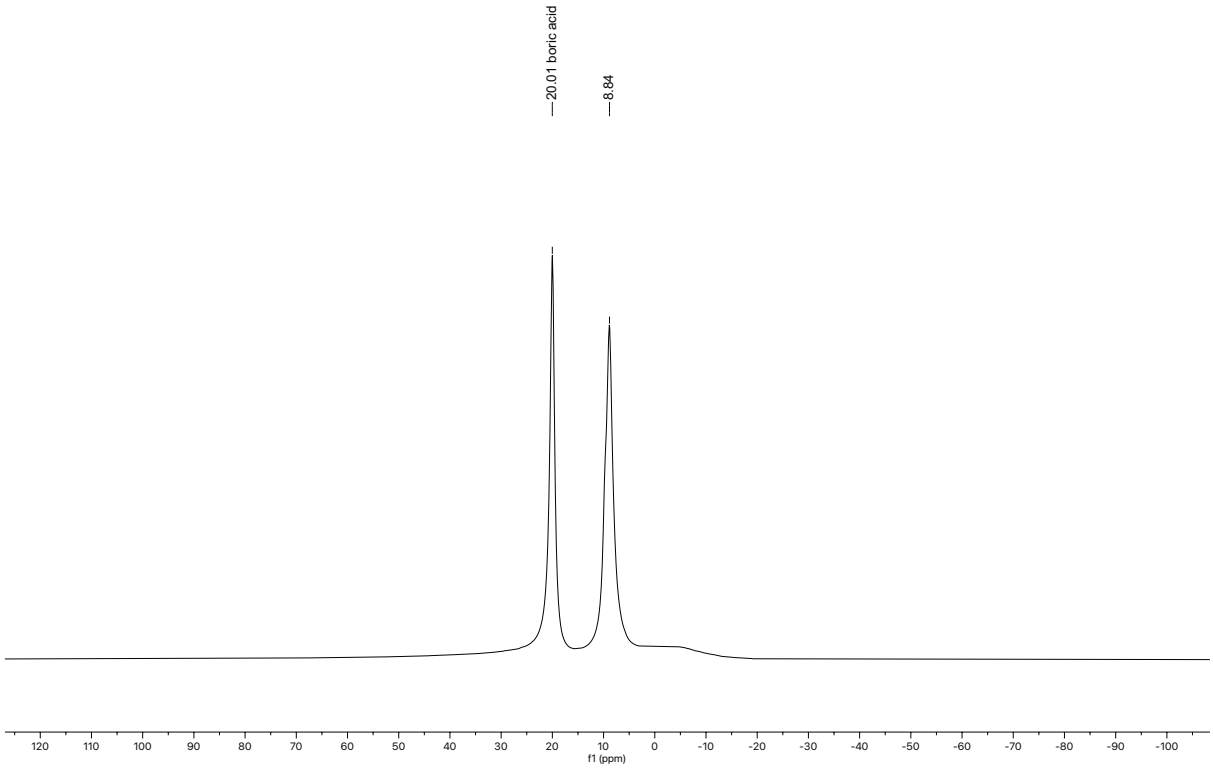
$^{11}B\{^{1}H\}$ NMR (160 MHz, CD_3CN/D_2O)





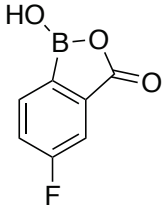
Compound 3

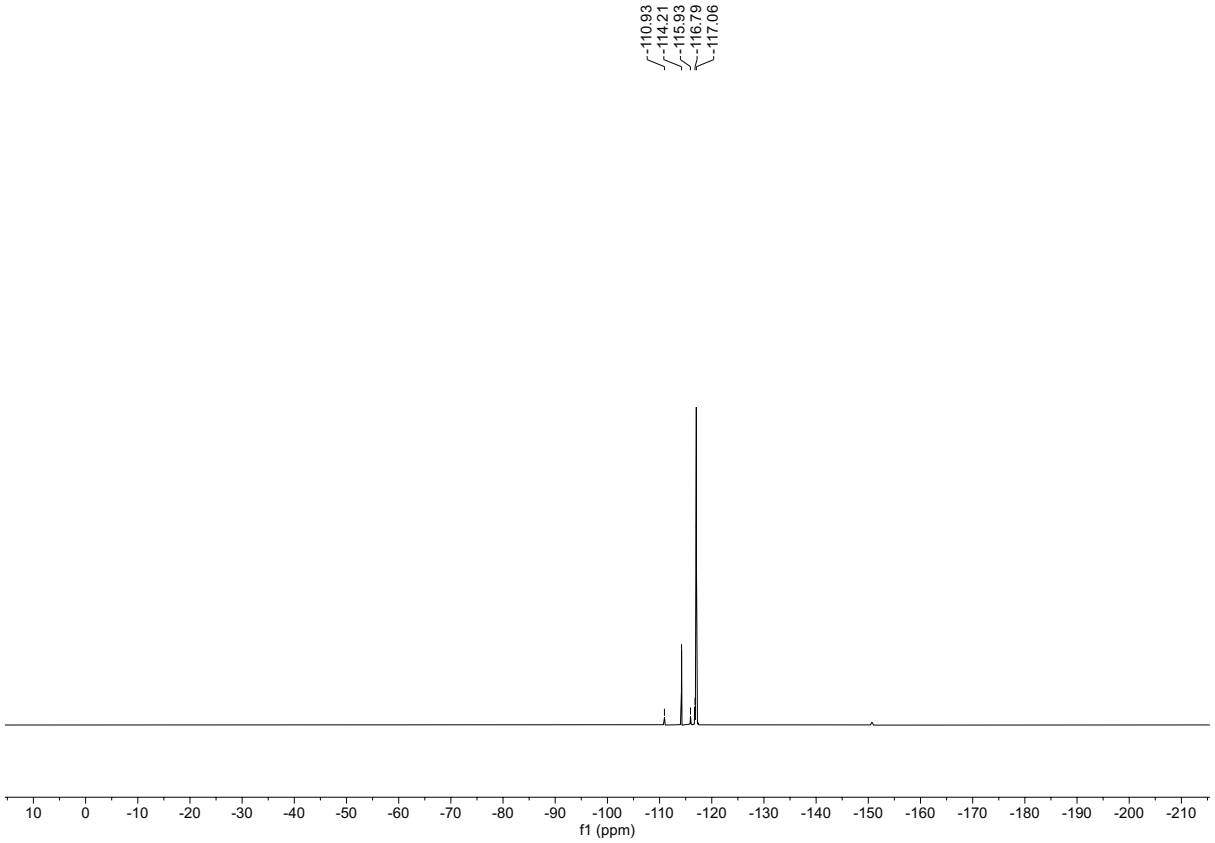
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 3

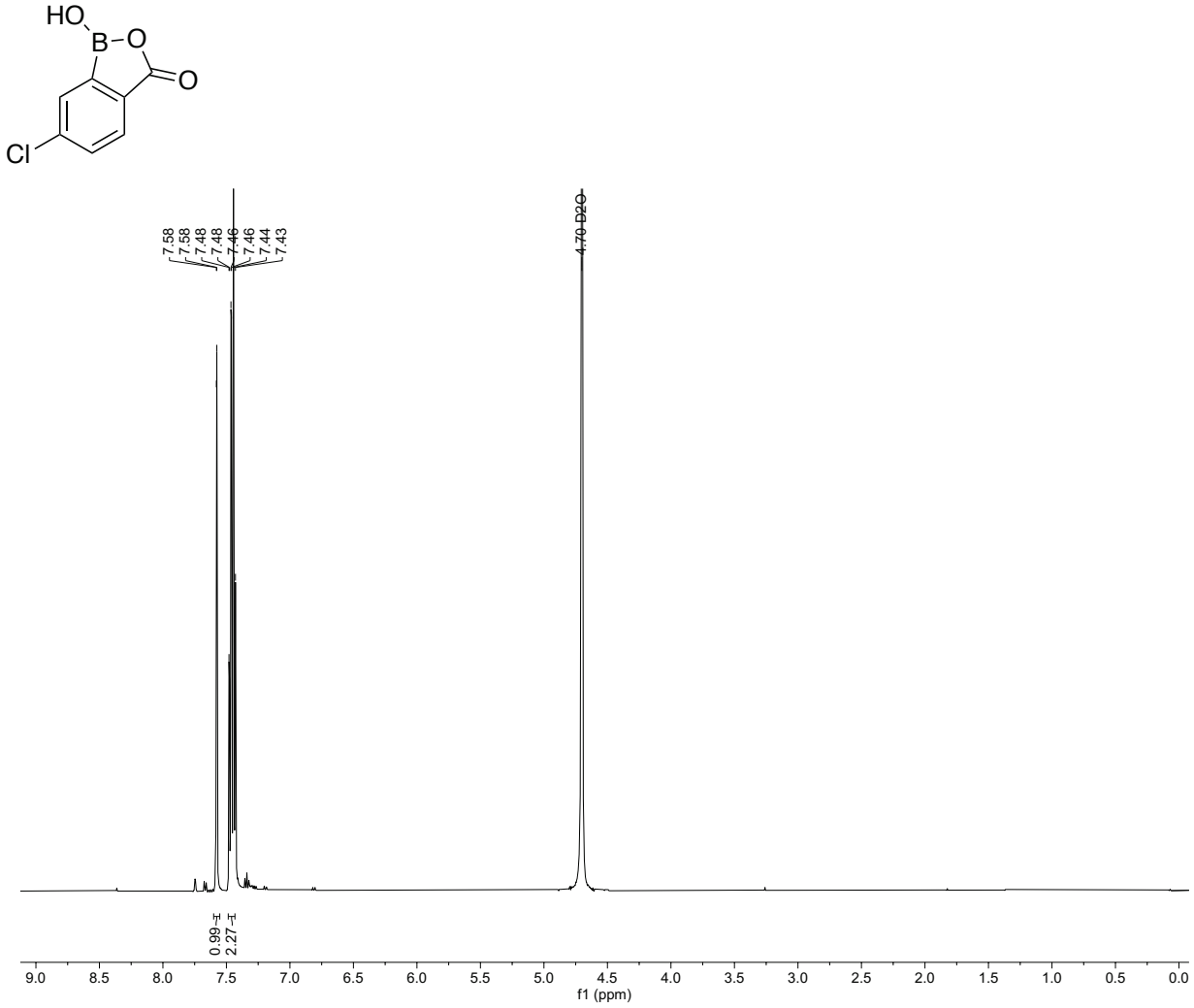
$^{19}F\{^{1}H\}$ NMR (471 MHz, CD_3CN/D_2O)





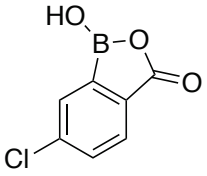
Compound 4

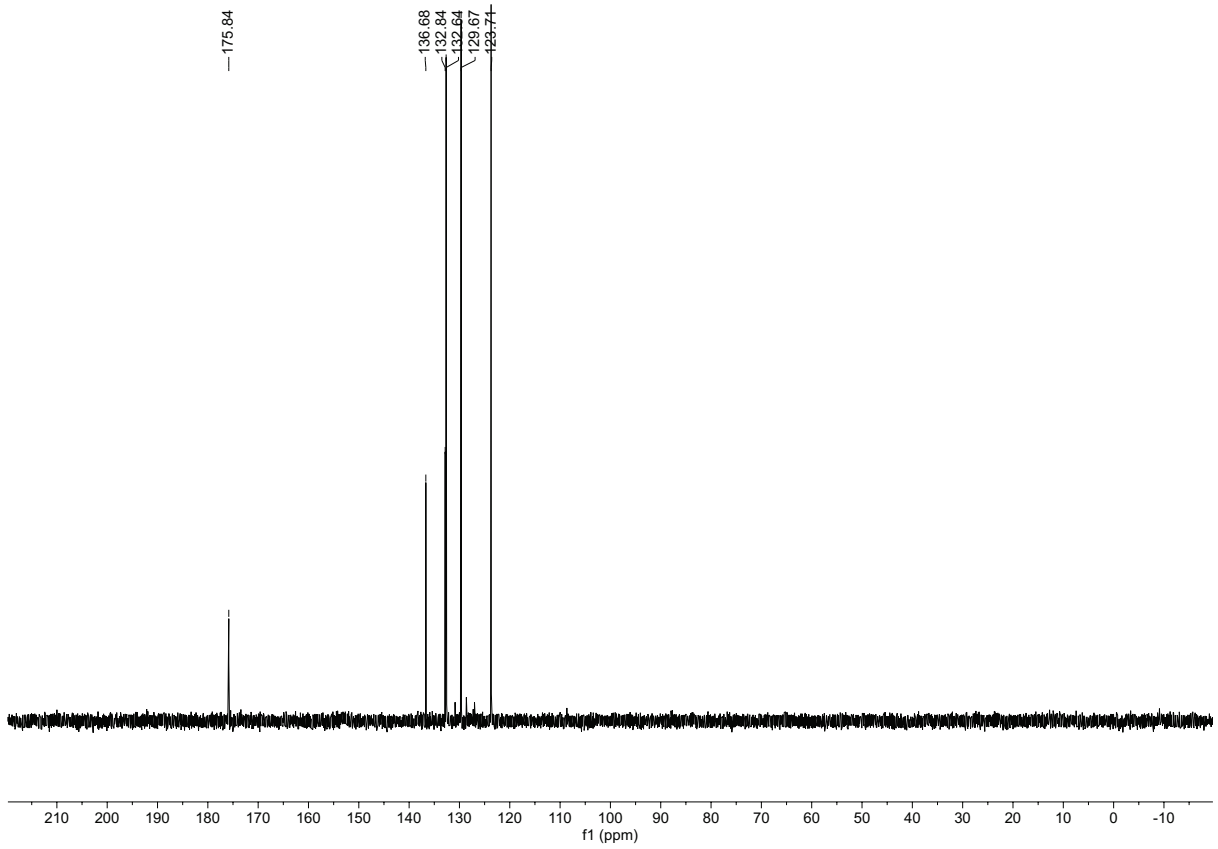
^{1}H NMR (500 MHz, D_2O)



Compound 4

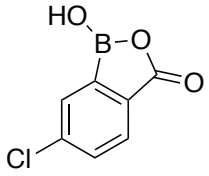
$^{13}C\{^{1}H\}$ NMR (126 MHz, D_2O)

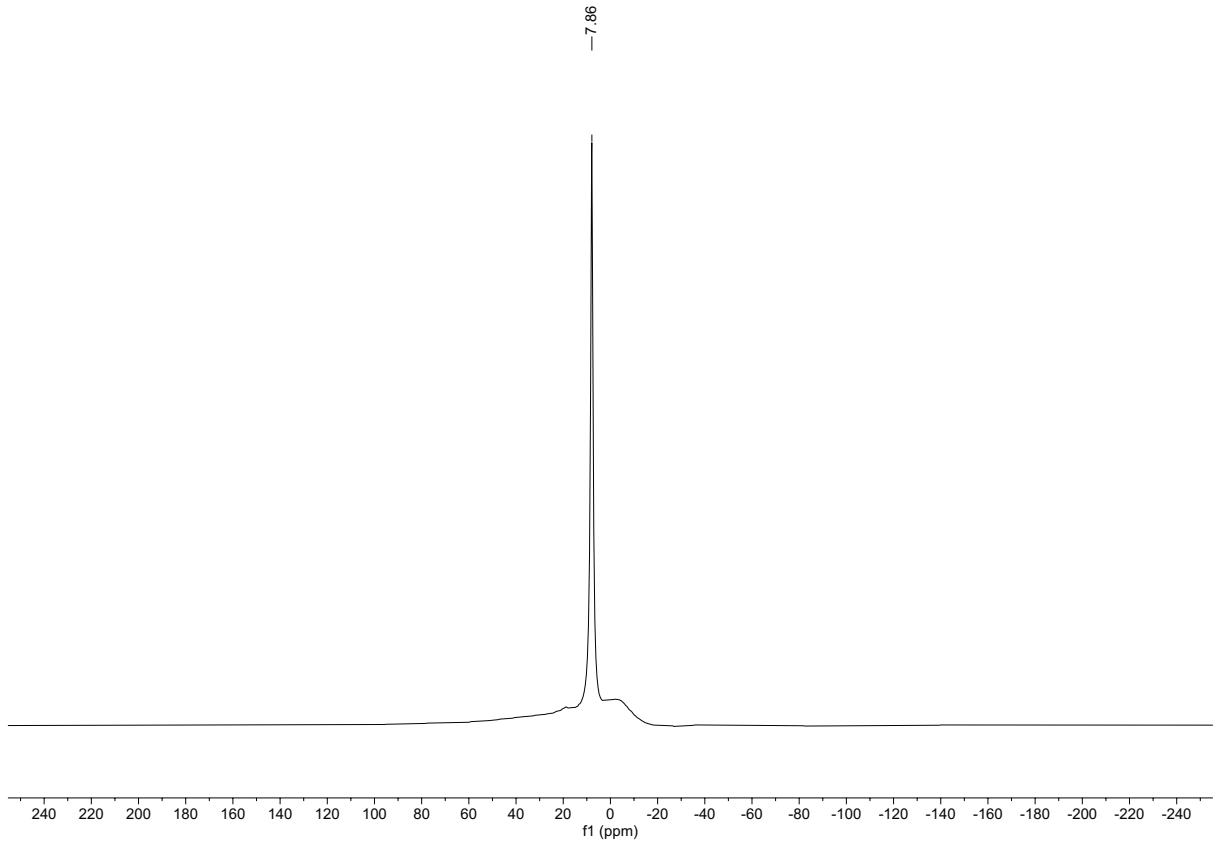




Compound 4

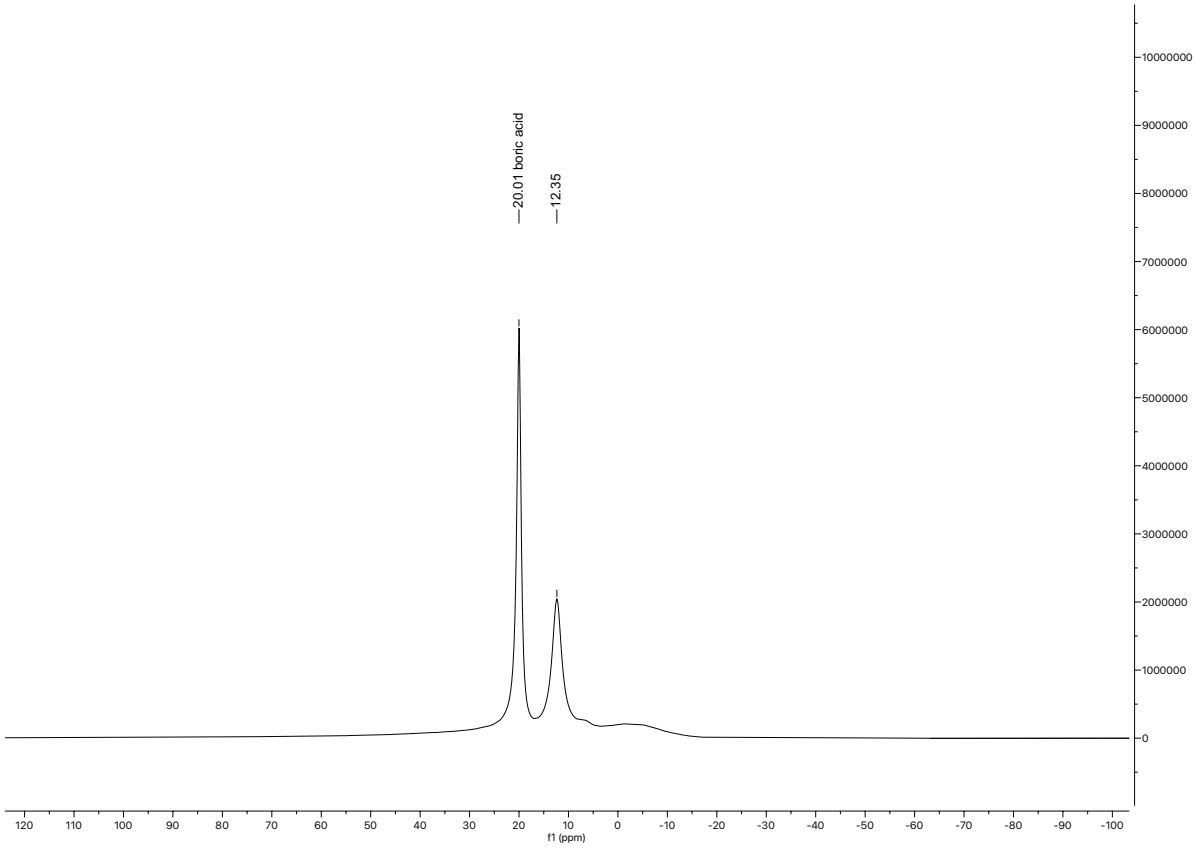
$^{11}B\{^{1}H\}$ NMR (160 MHz, D_2O)





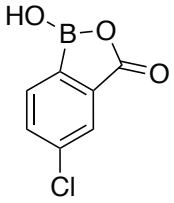
Compound 4

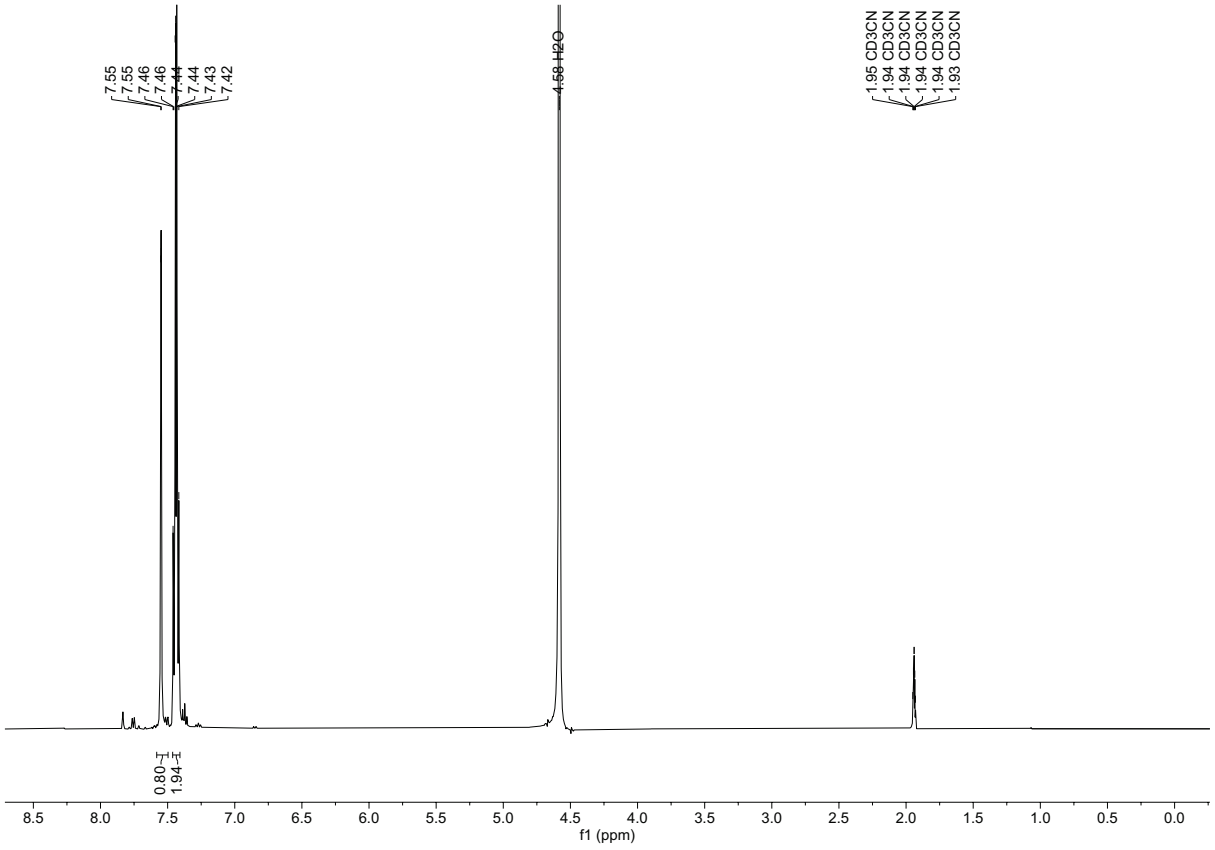
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 5

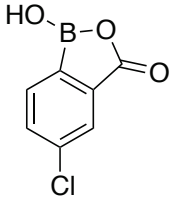
^{1}H NMR (500 MHz, CD_3CN/D_2O)

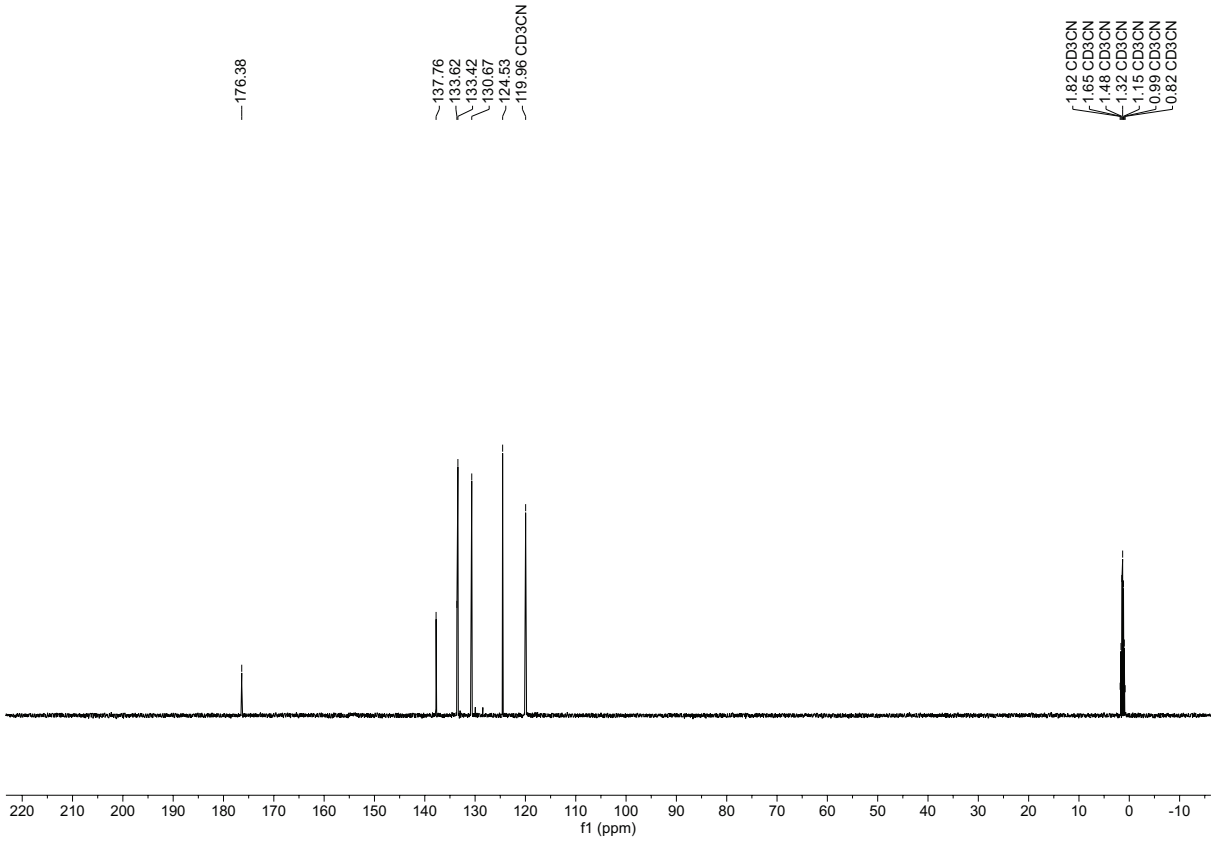




Compound 5

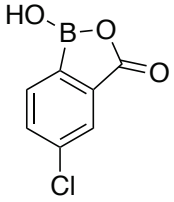
$^{13}C\{^{1}H\}$ NMR (126 MHz, CD_3CN/D_2O)

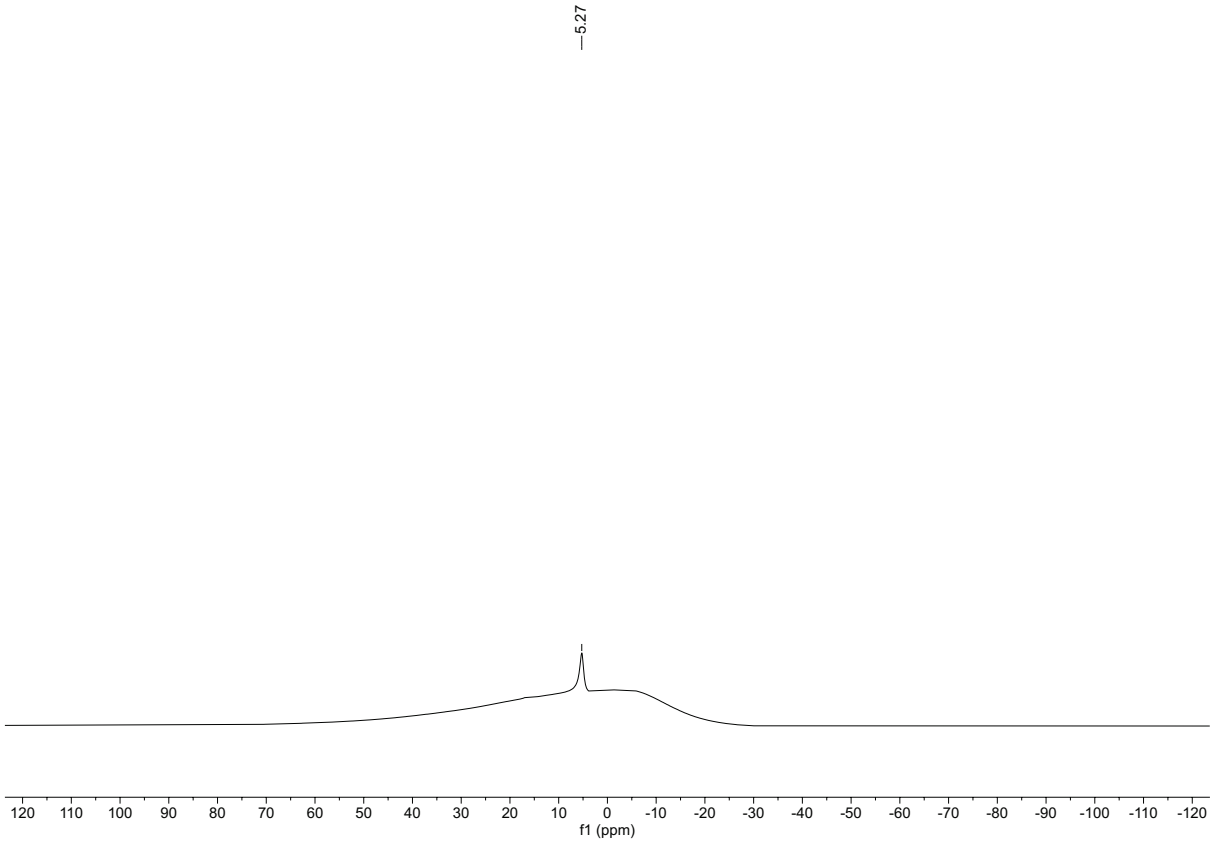




Compound 5

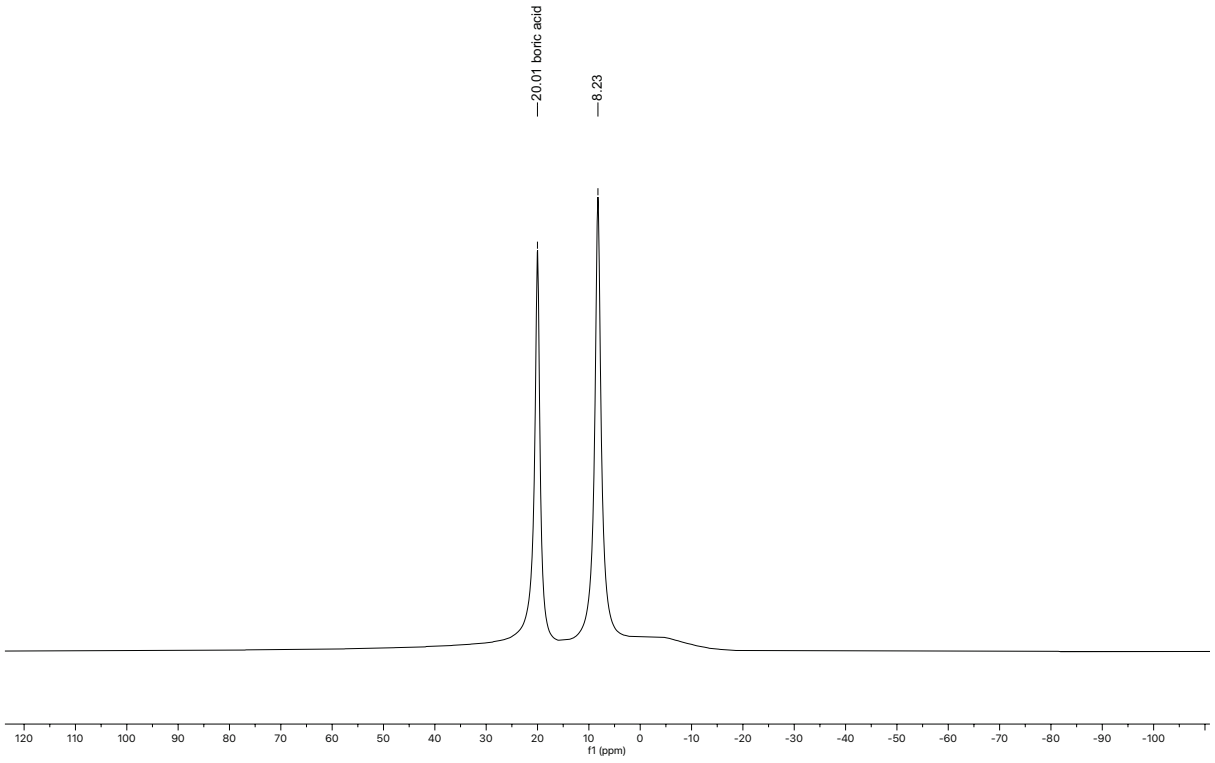
$^{11}B\{^{1}H\}$ NMR (160 MHz, CD_3CN/D_2O)





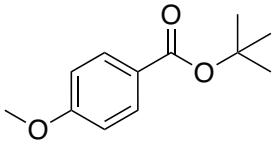
Compound 5

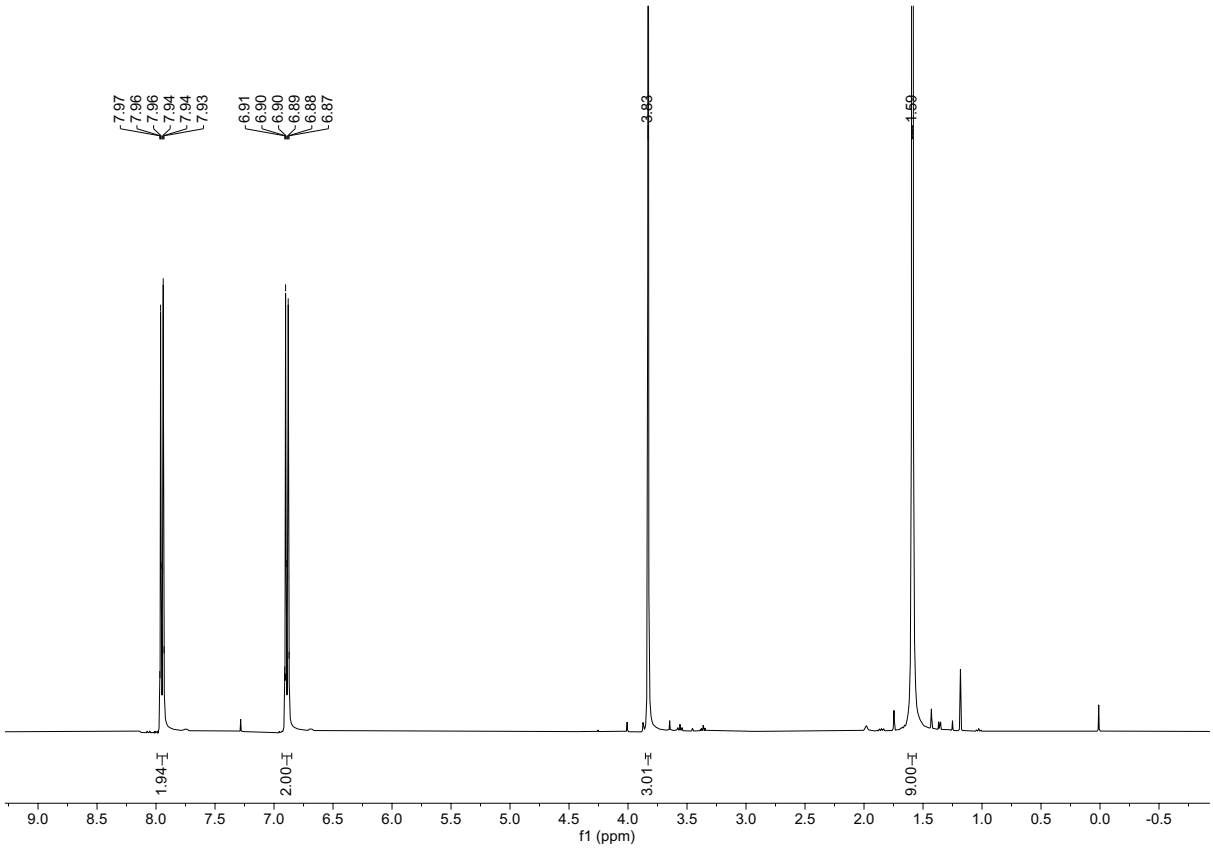
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 6a

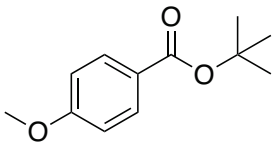
^{1}H NMR (400 MHz, $CDCl_3$)

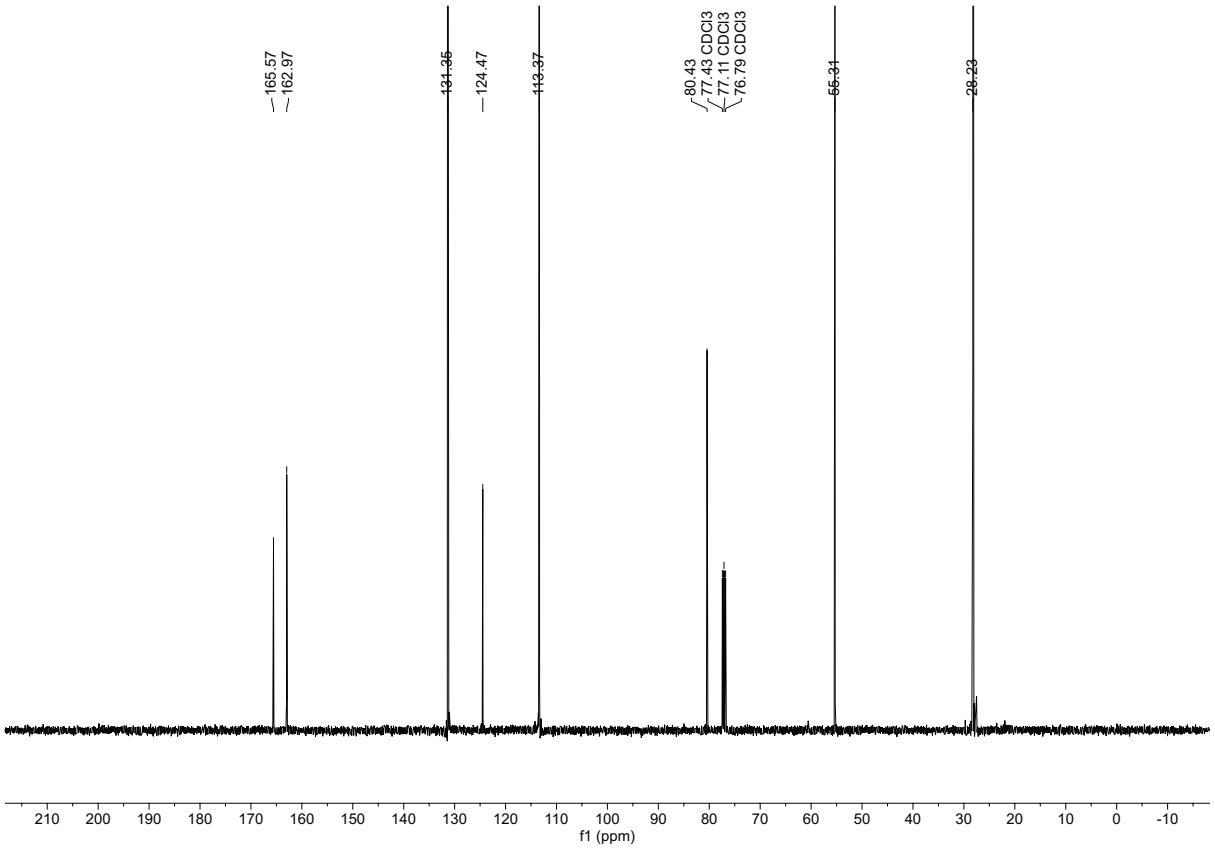




Compound 6a

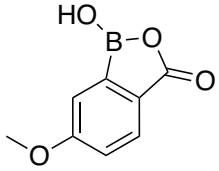
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

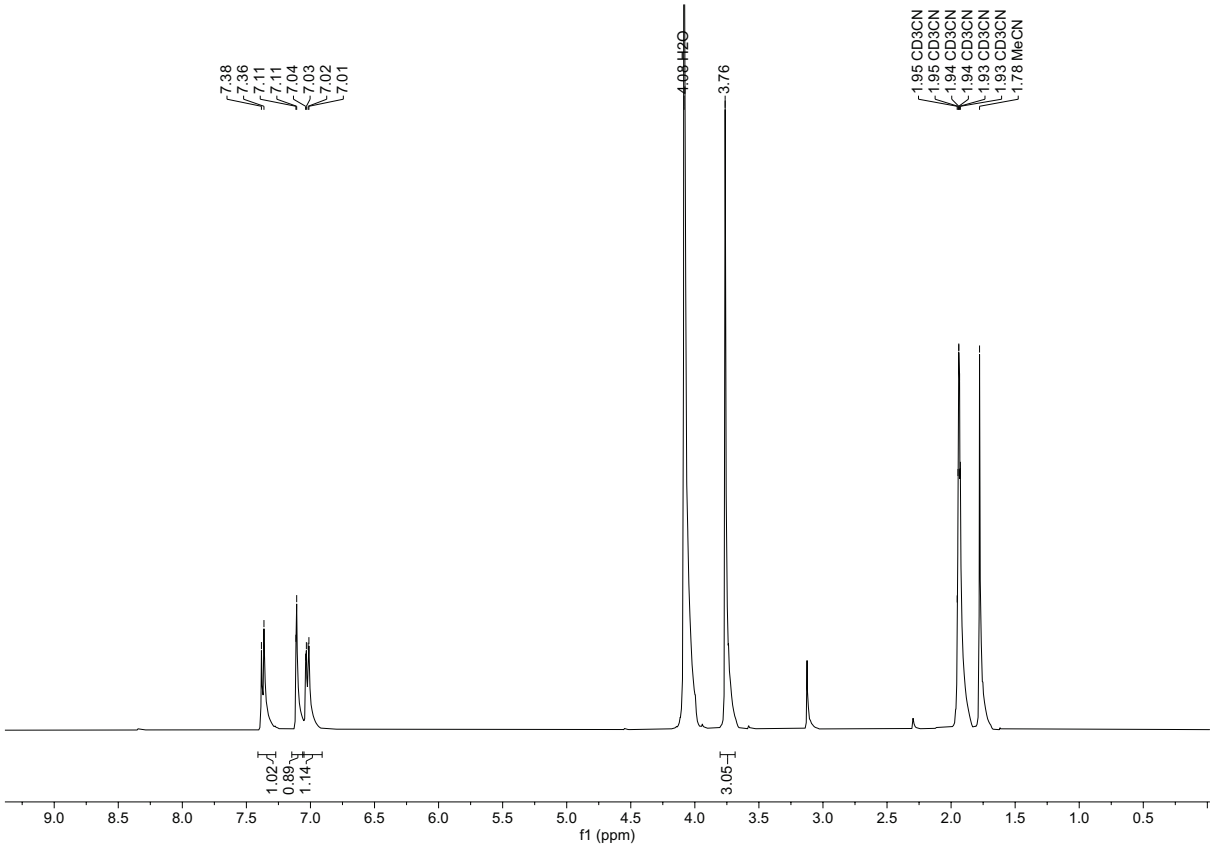




Compound 6b

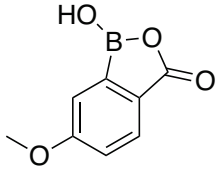
^{1}H NMR (400 MHz, CD_3CN/D_2O)

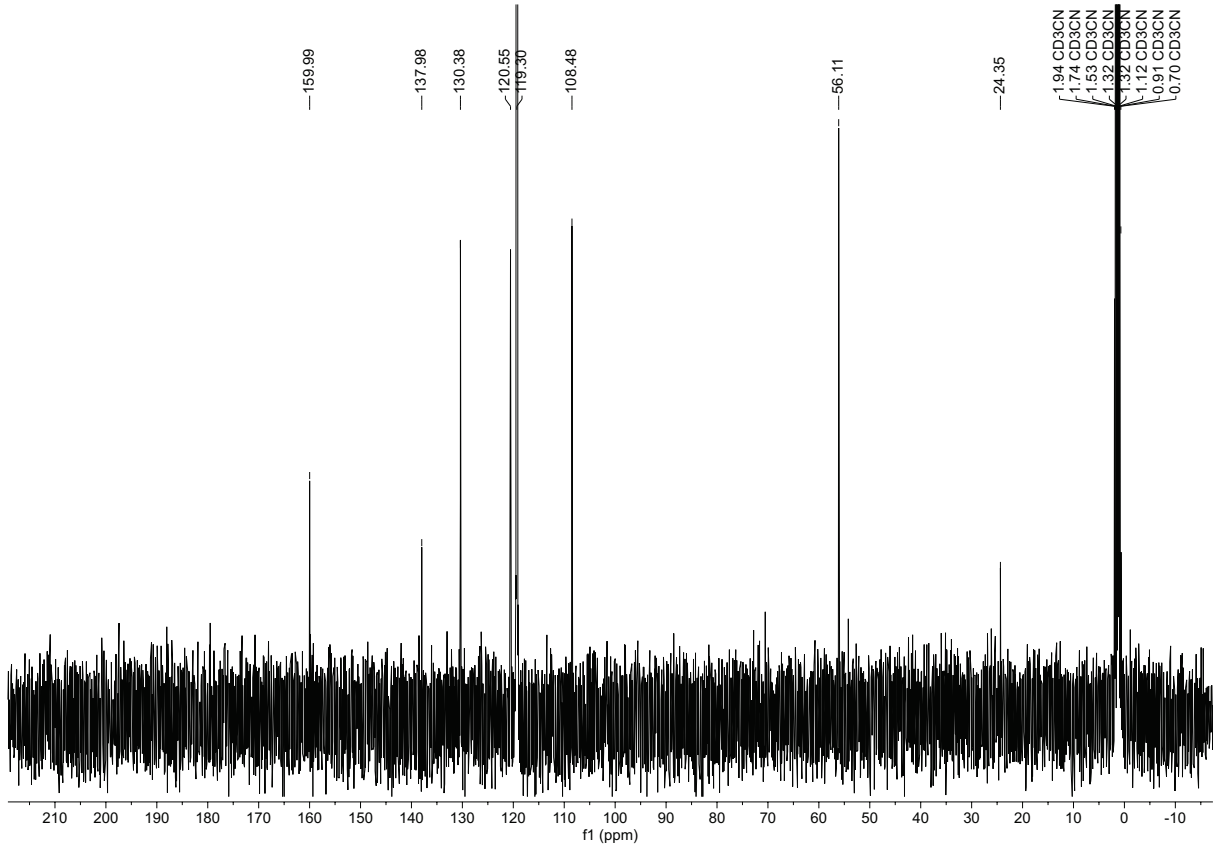




Compound 6b

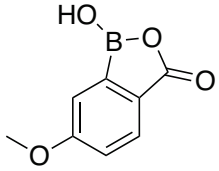
$^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3CN/D_2O)

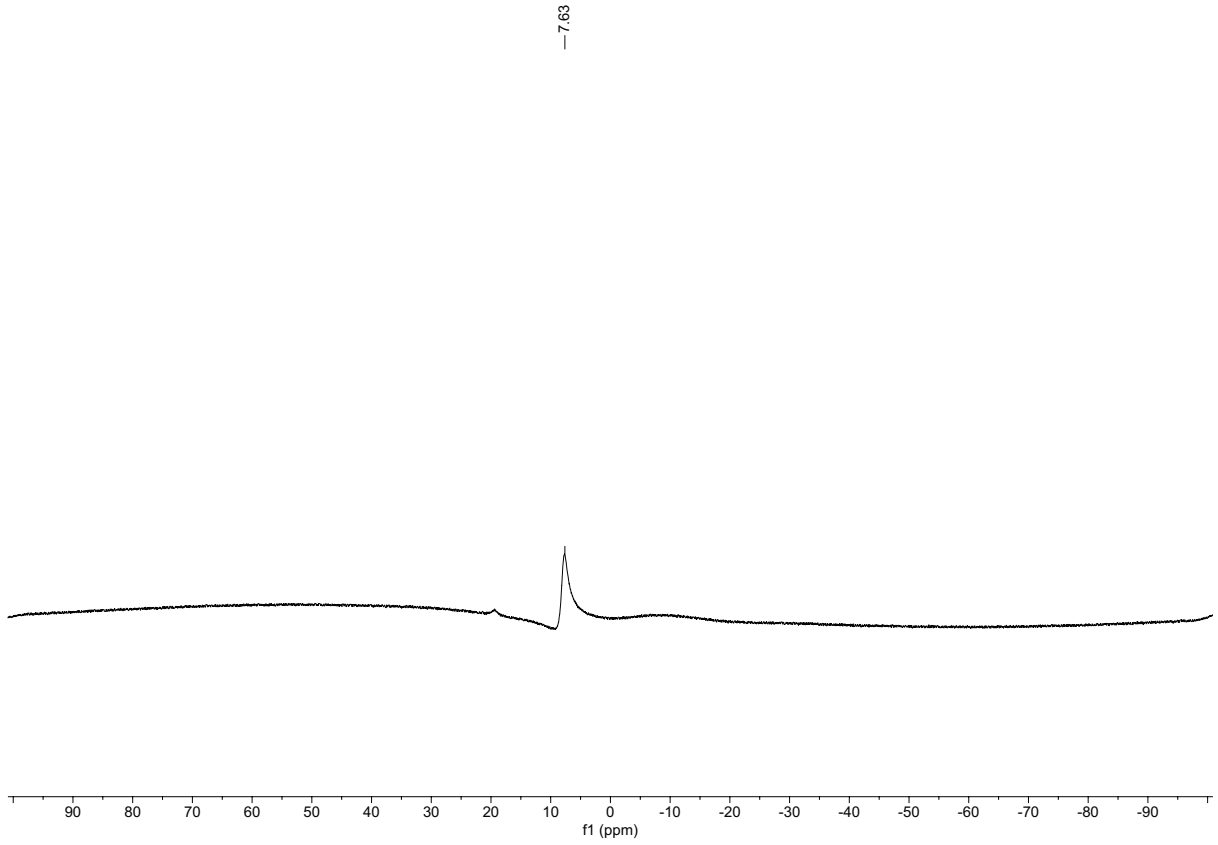




Compound 6b

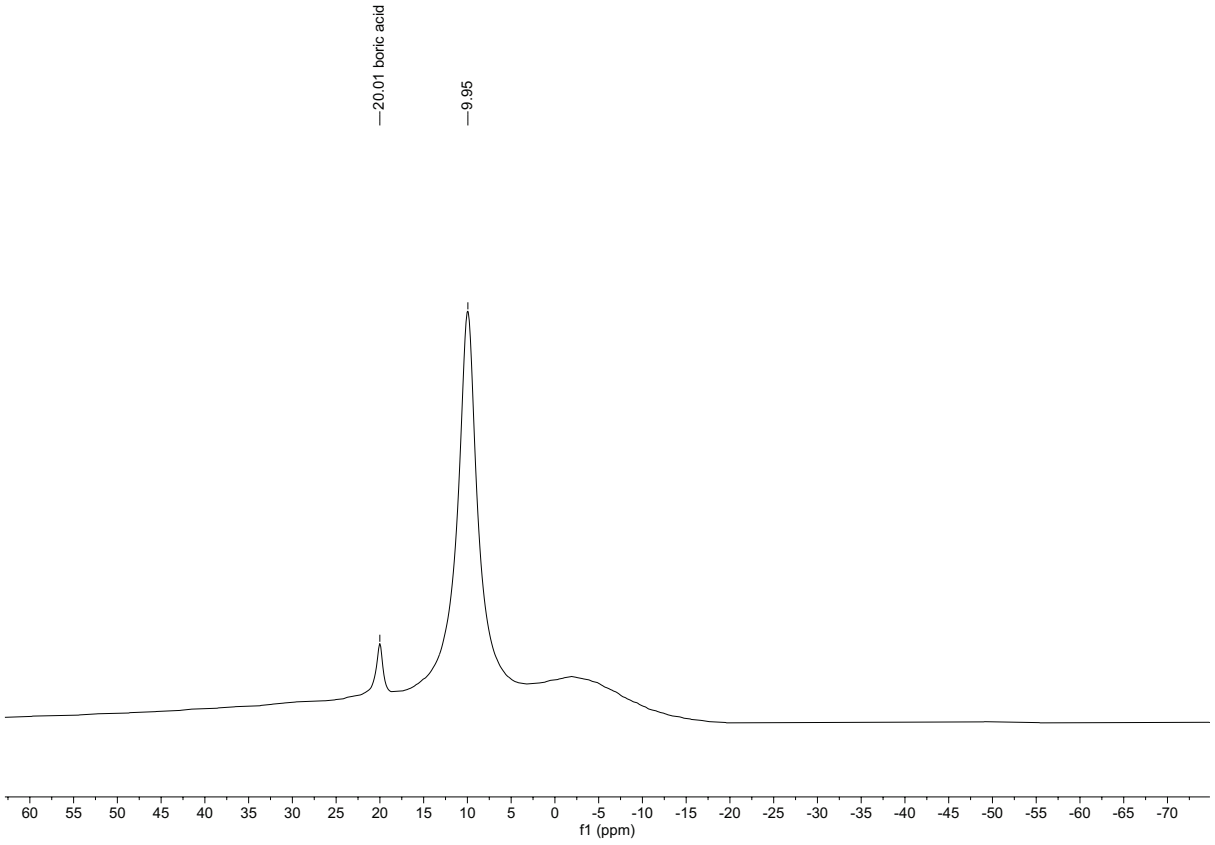
$^{11}B\{^{1}H\}$ NMR (128 MHz, CD_3CN/D_2O)





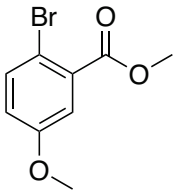
Compound 6b

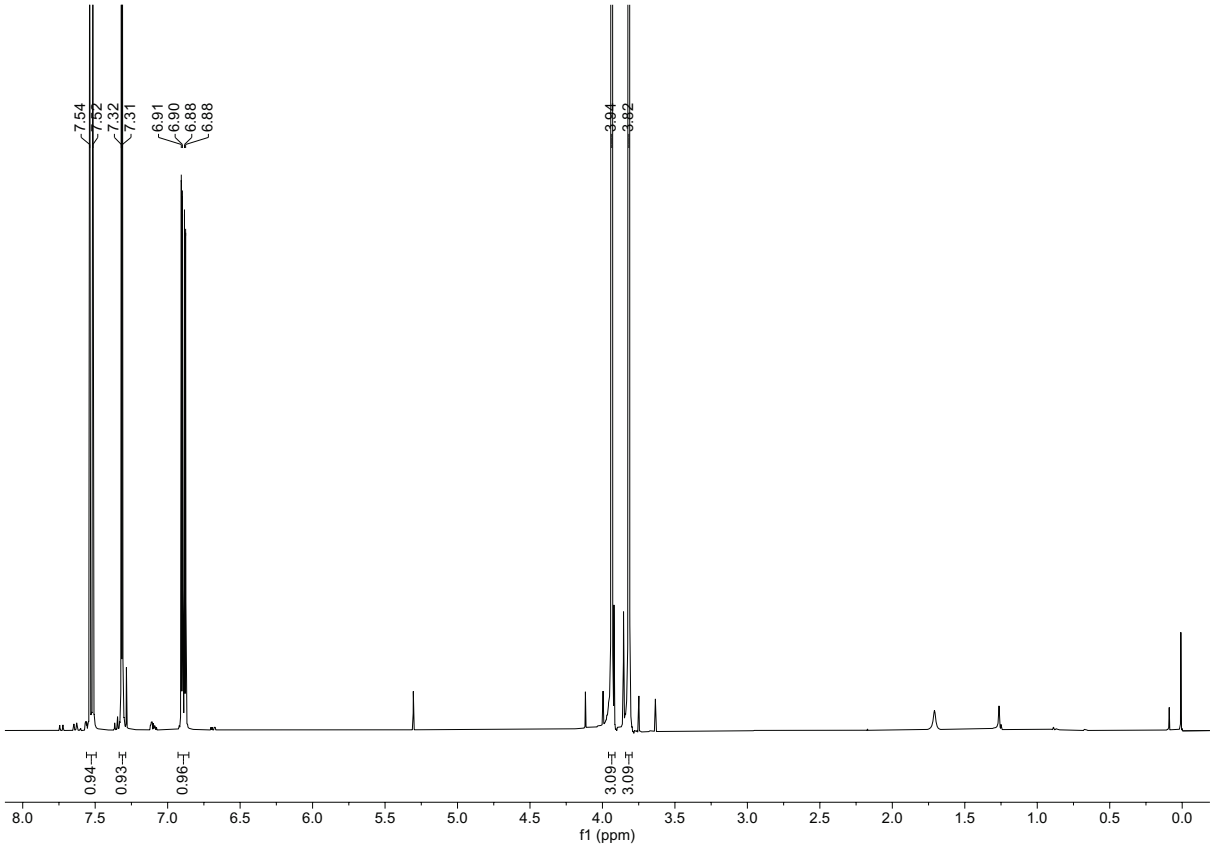
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 7a

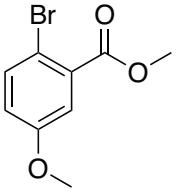
^{1}H NMR (400 MHz, $CDCl_3$)

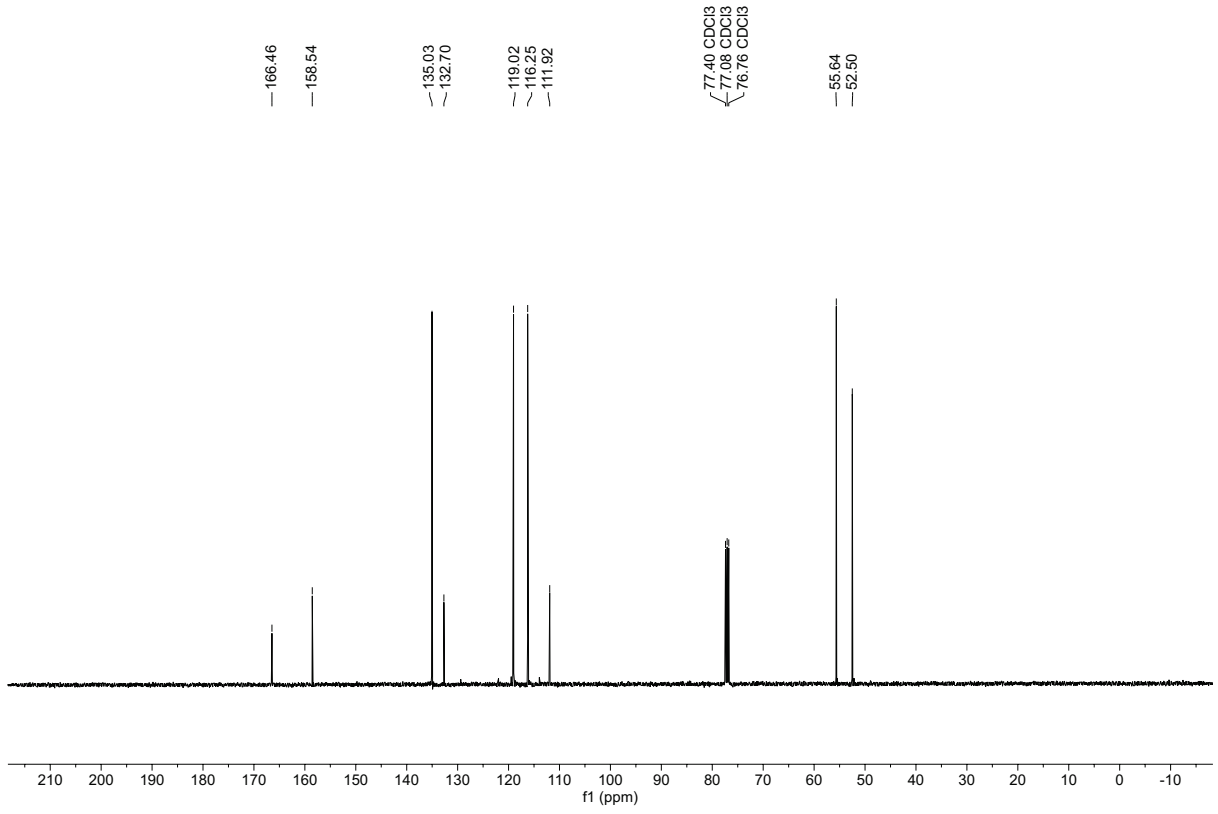




Compound 7a

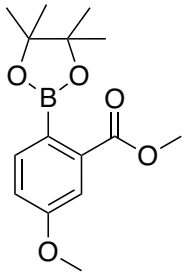
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

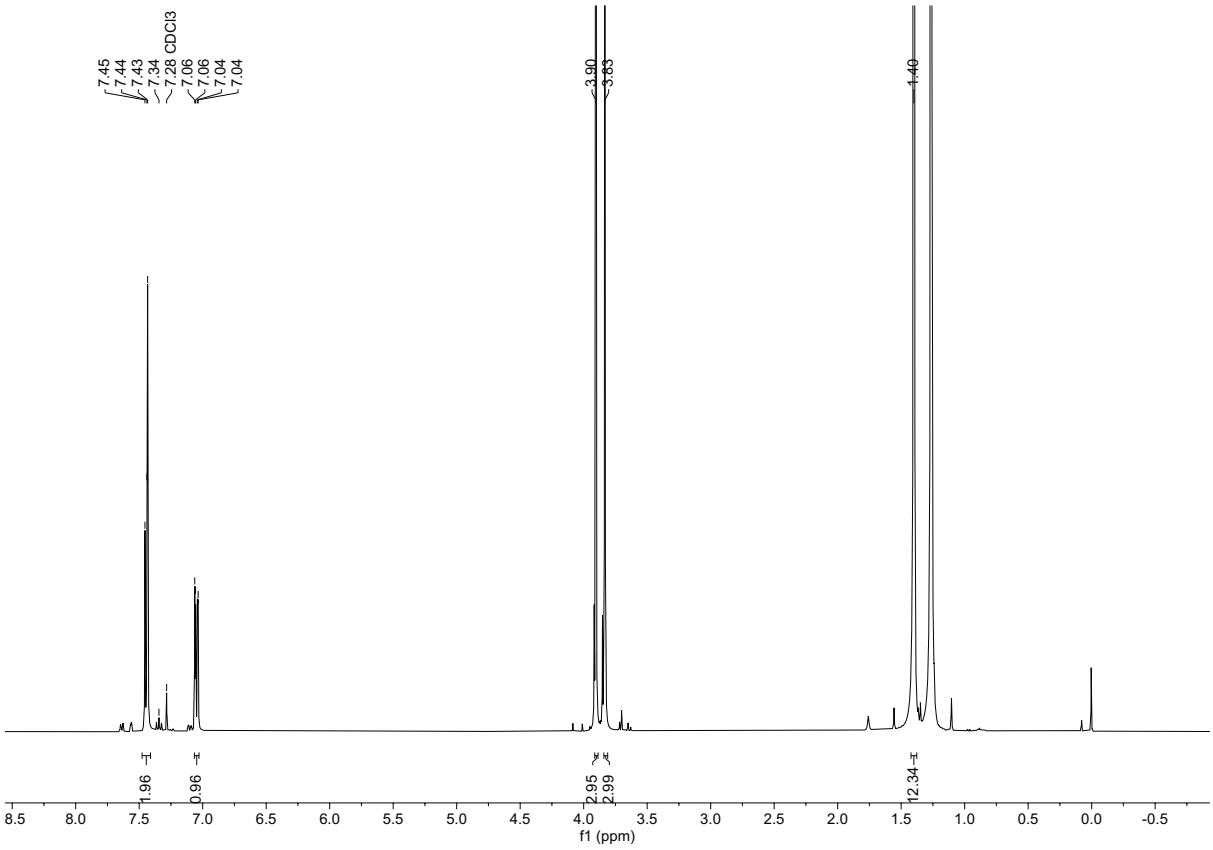




Compound 7b

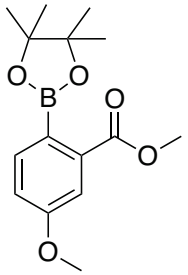
^{1}H NMR (400 MHz, $CDCl_3$)

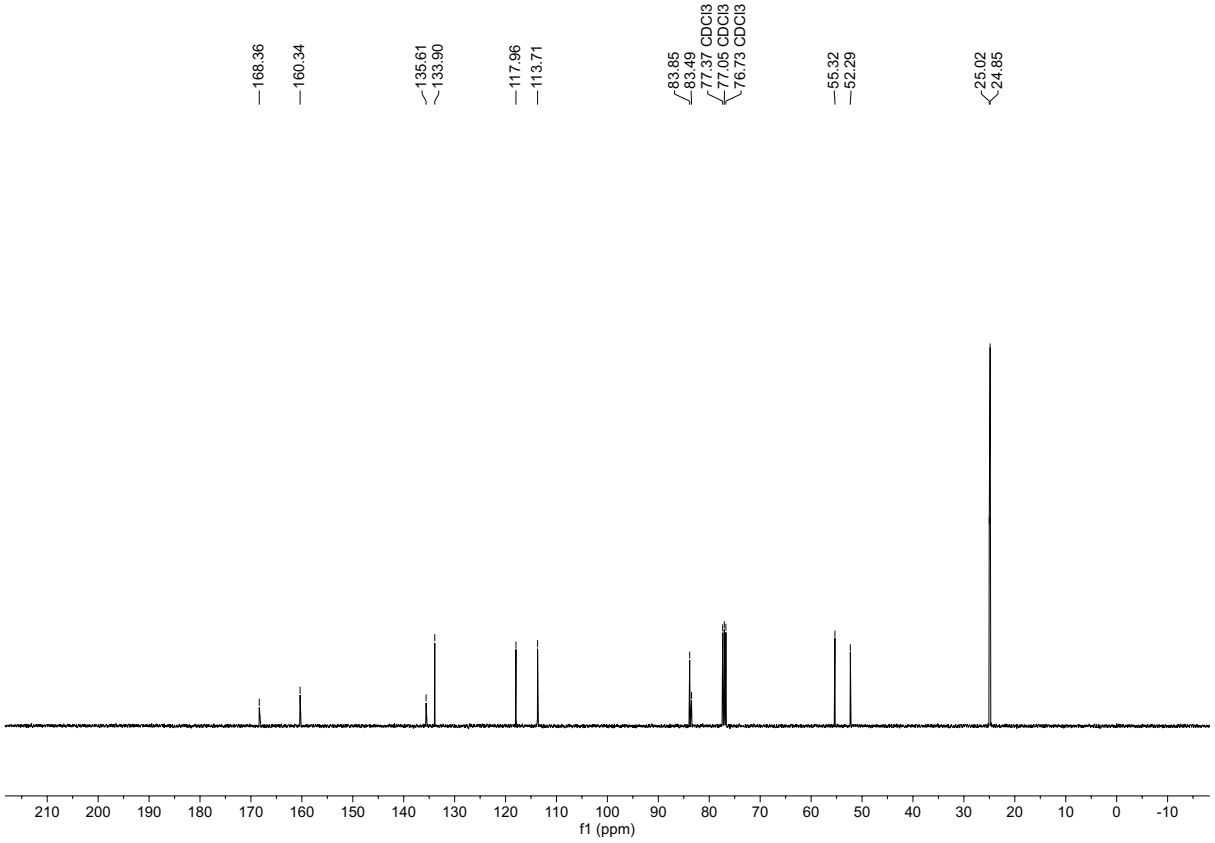




Compound 7b

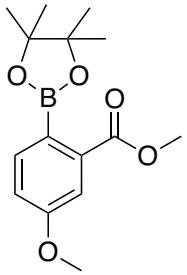
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

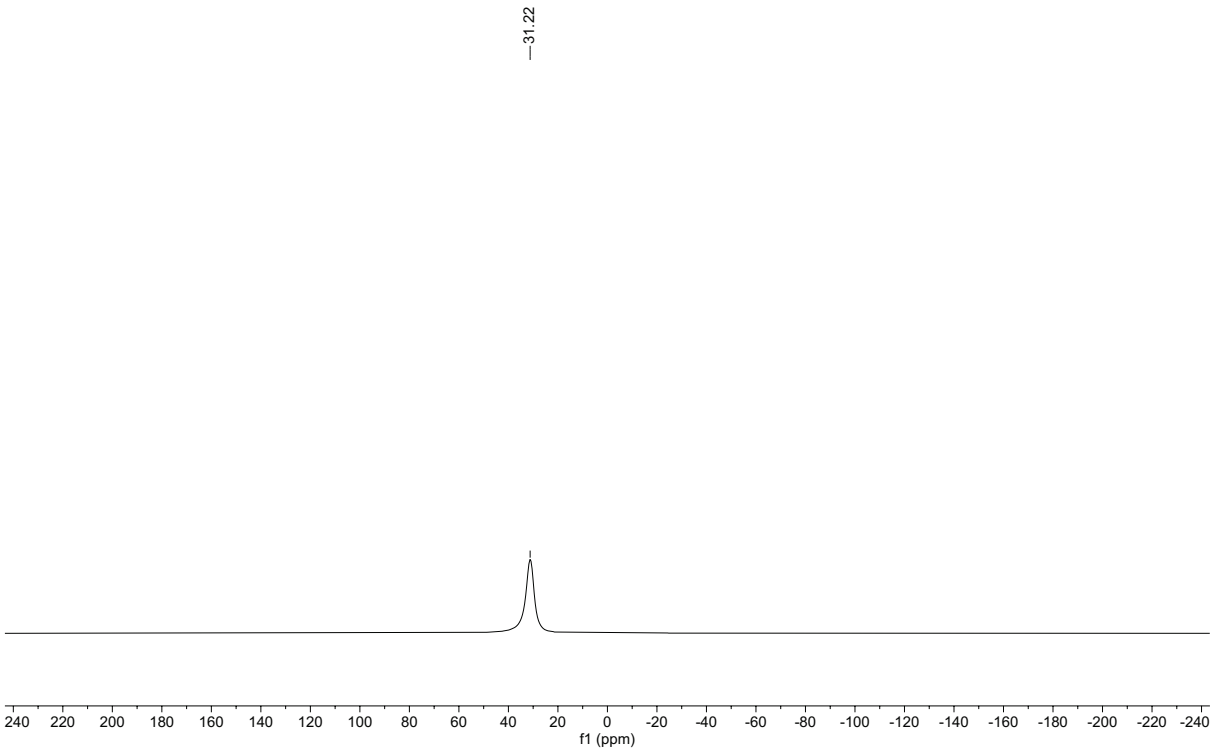




Compound 7b

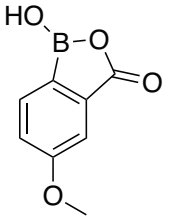
$^{11}B\{^{1}H\}$ NMR (128 MHz, $CDCl_3$)

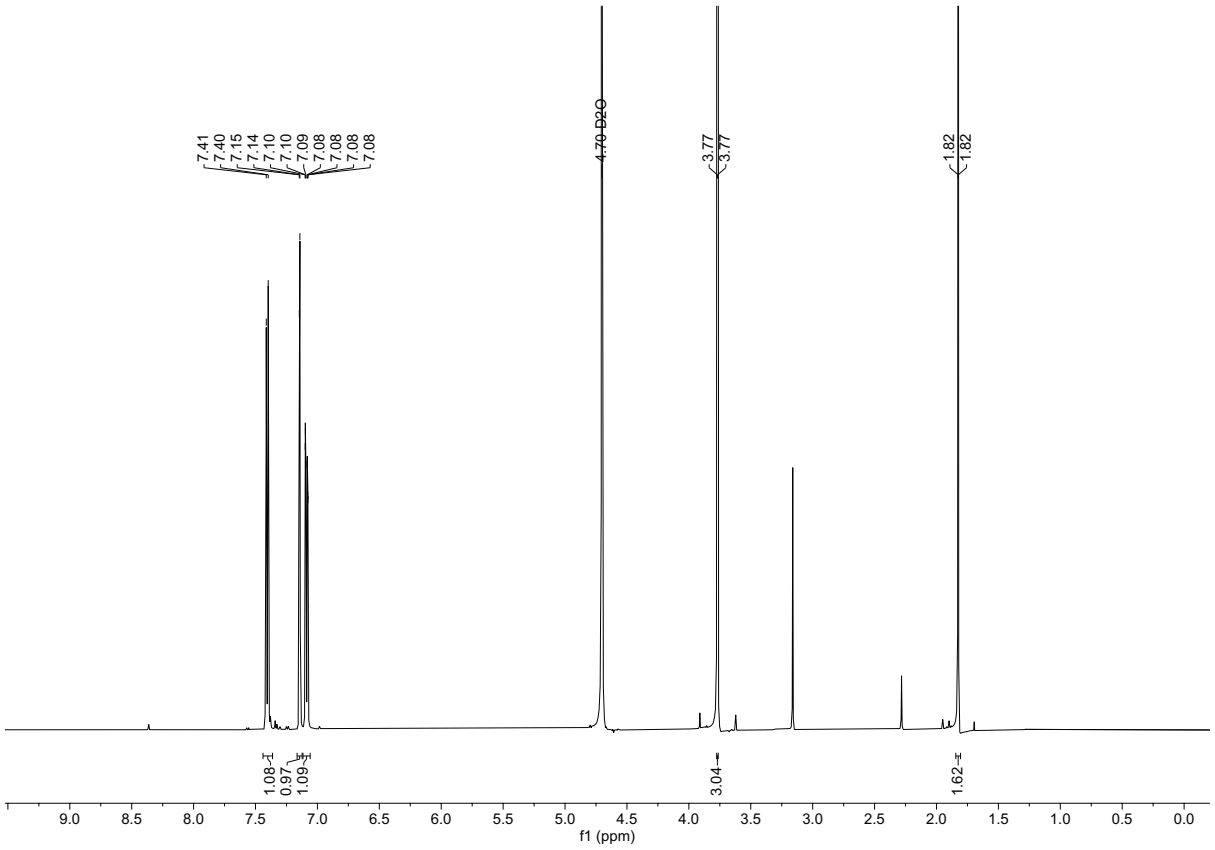




Compound 7c

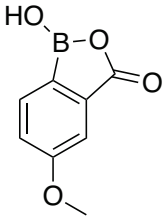
^{1}H NMR (500 MHz, D_2O)

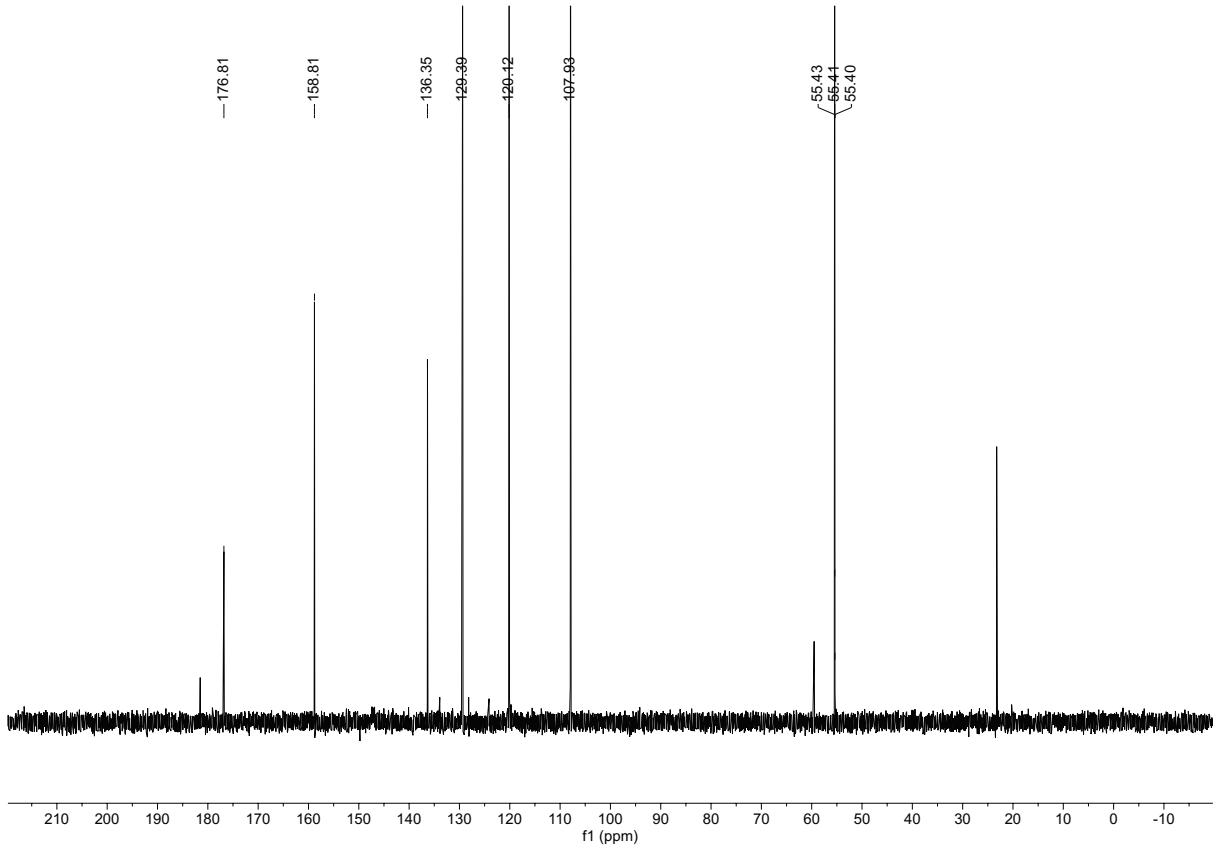




Compound 7c

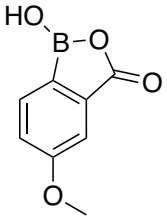
$^{13}C\{^{1}H\}$ NMR (126 MHz, D_2O)

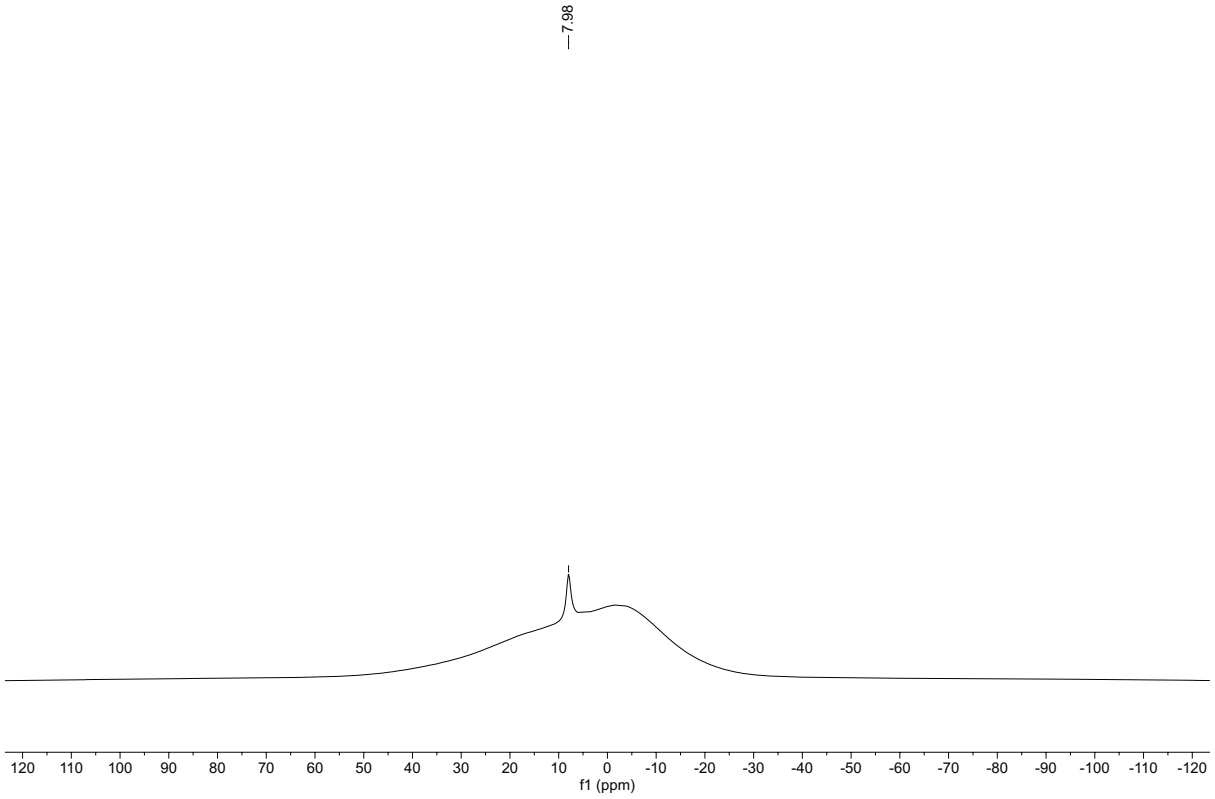




Compound 7c

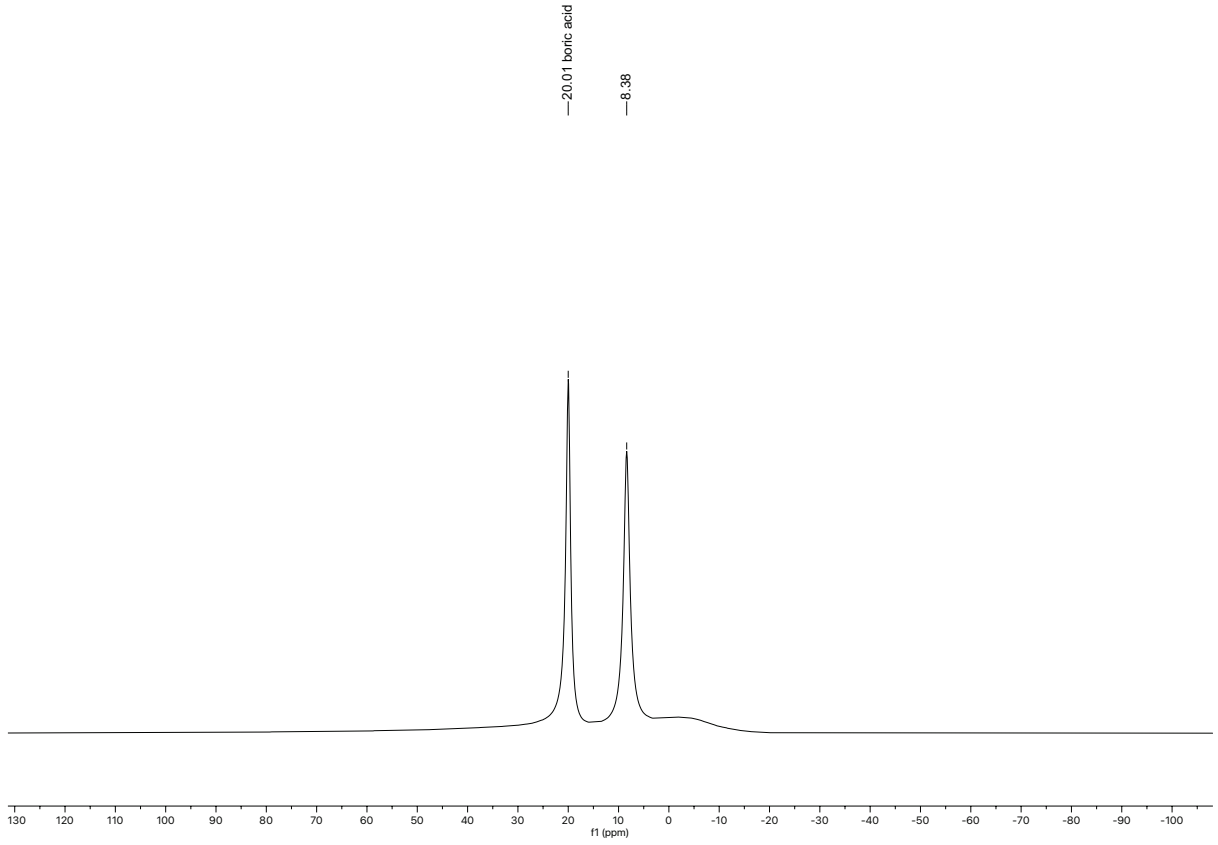
$^{11}B\{^{1}H\}$ NMR (160 MHz, D_2O)





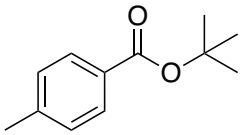
Compound 7c

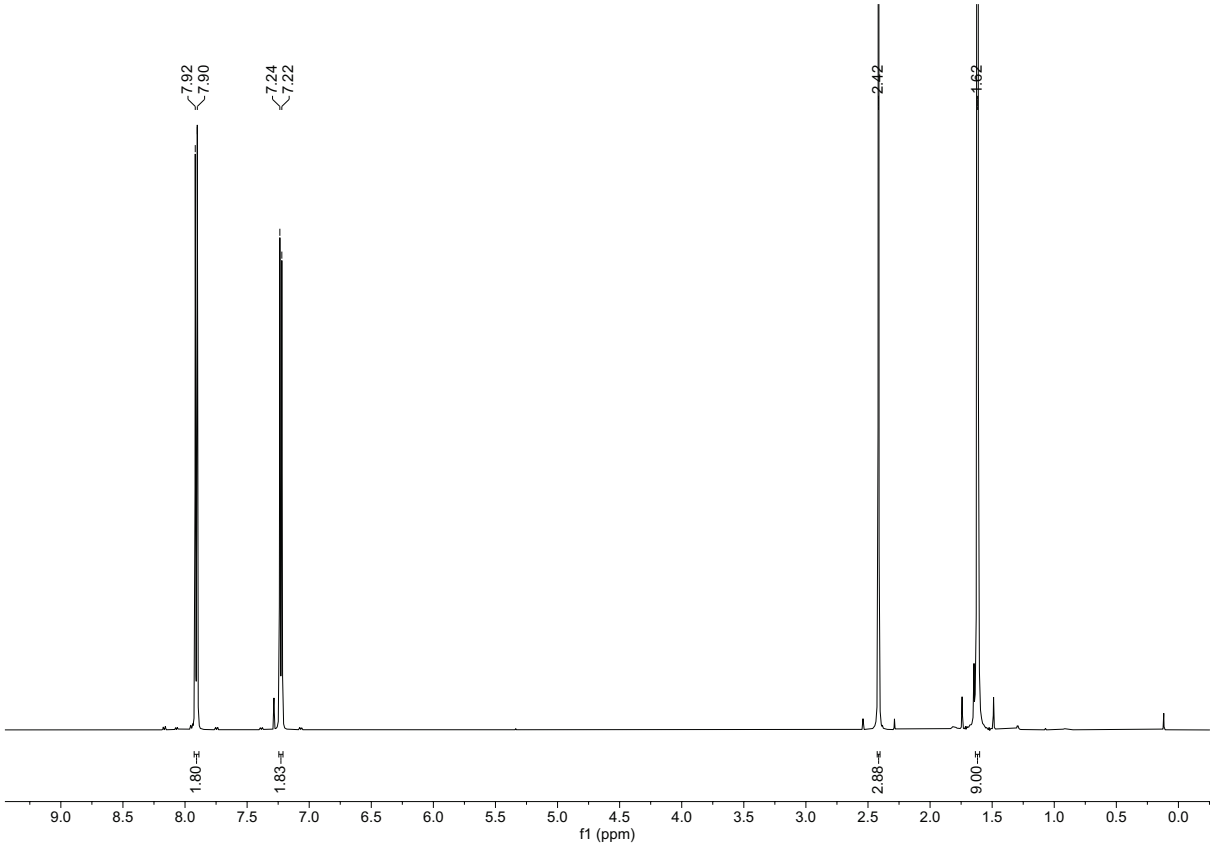
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 8a

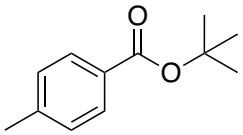
^{1}H NMR (500 MHz, $CDCl_3$)

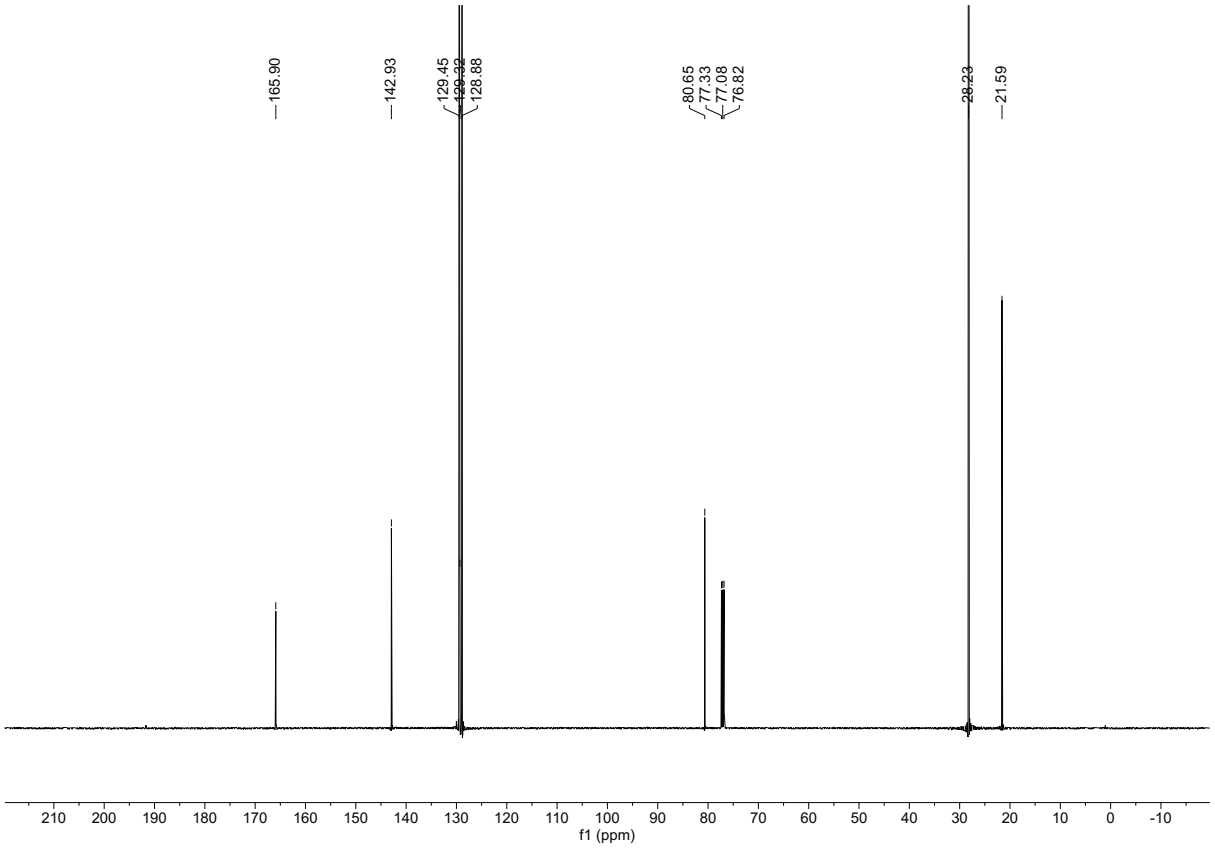




Compound 8a

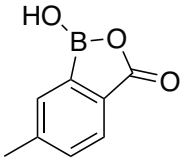
$^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$)

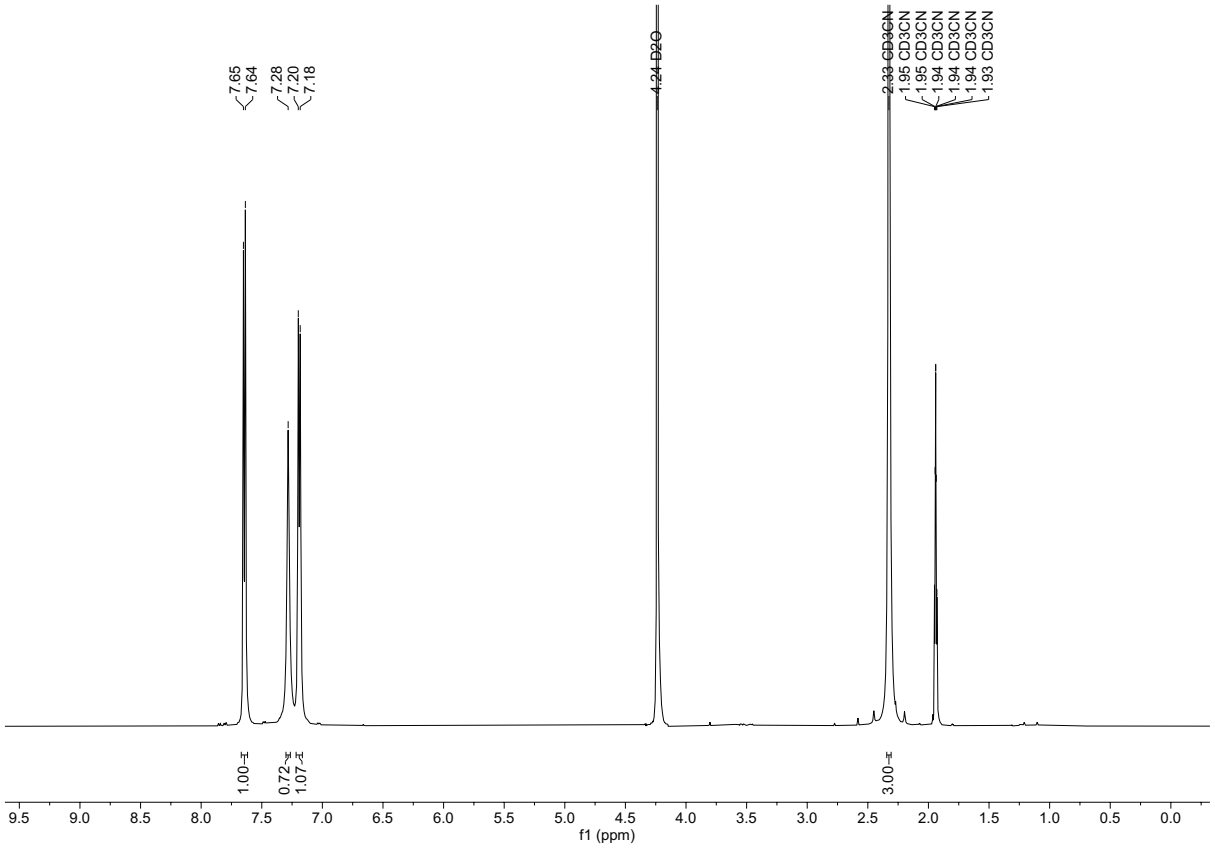




Compound 8b

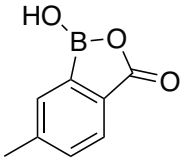
^{1}H NMR (500 MHz, D_2O/CD_3CN)

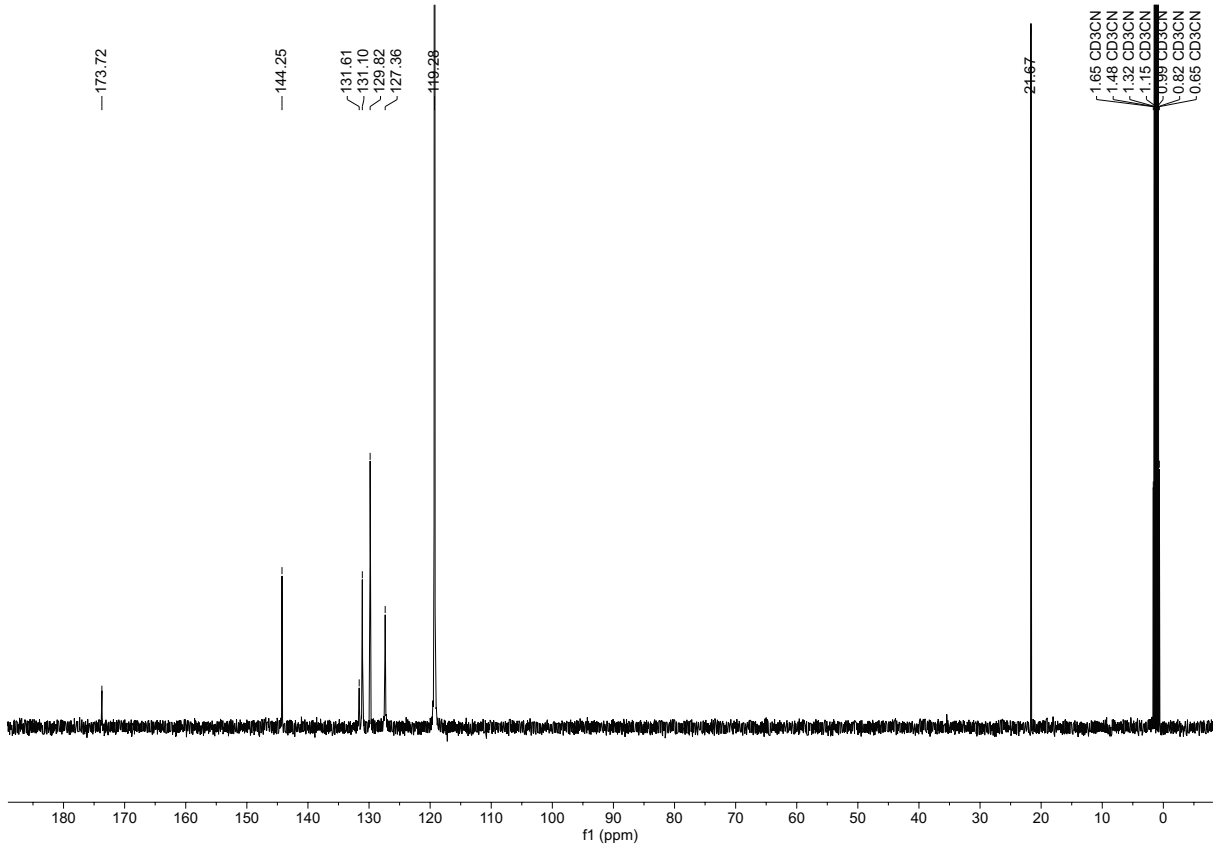




Compound 8b

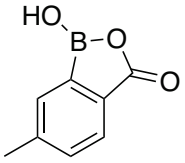
$^{13}C\{^{1}H\}$ NMR (126 MHz, D_2O/CD_3CN)

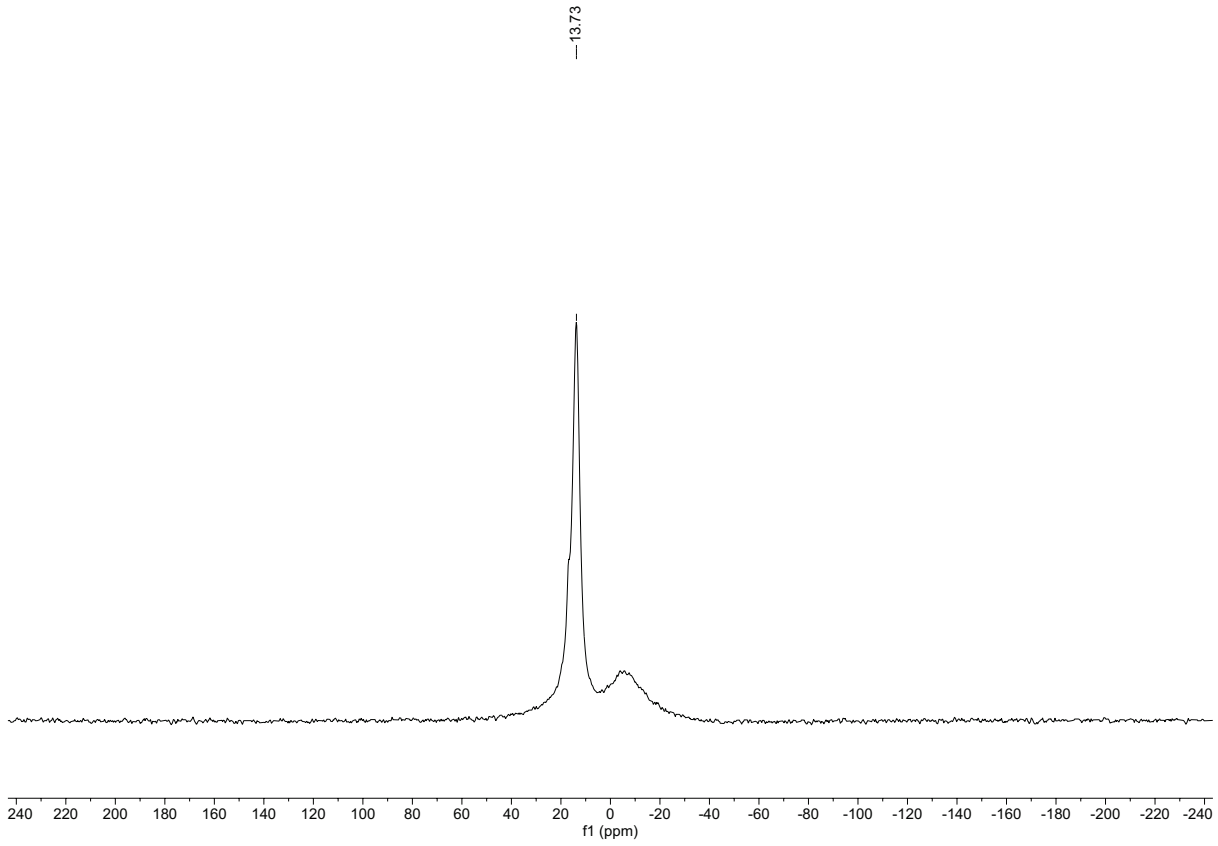




Compound 8b

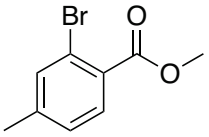
$^{11}B\{^{1}H\}$ NMR (160 MHz, D_2O/CD_3CN)

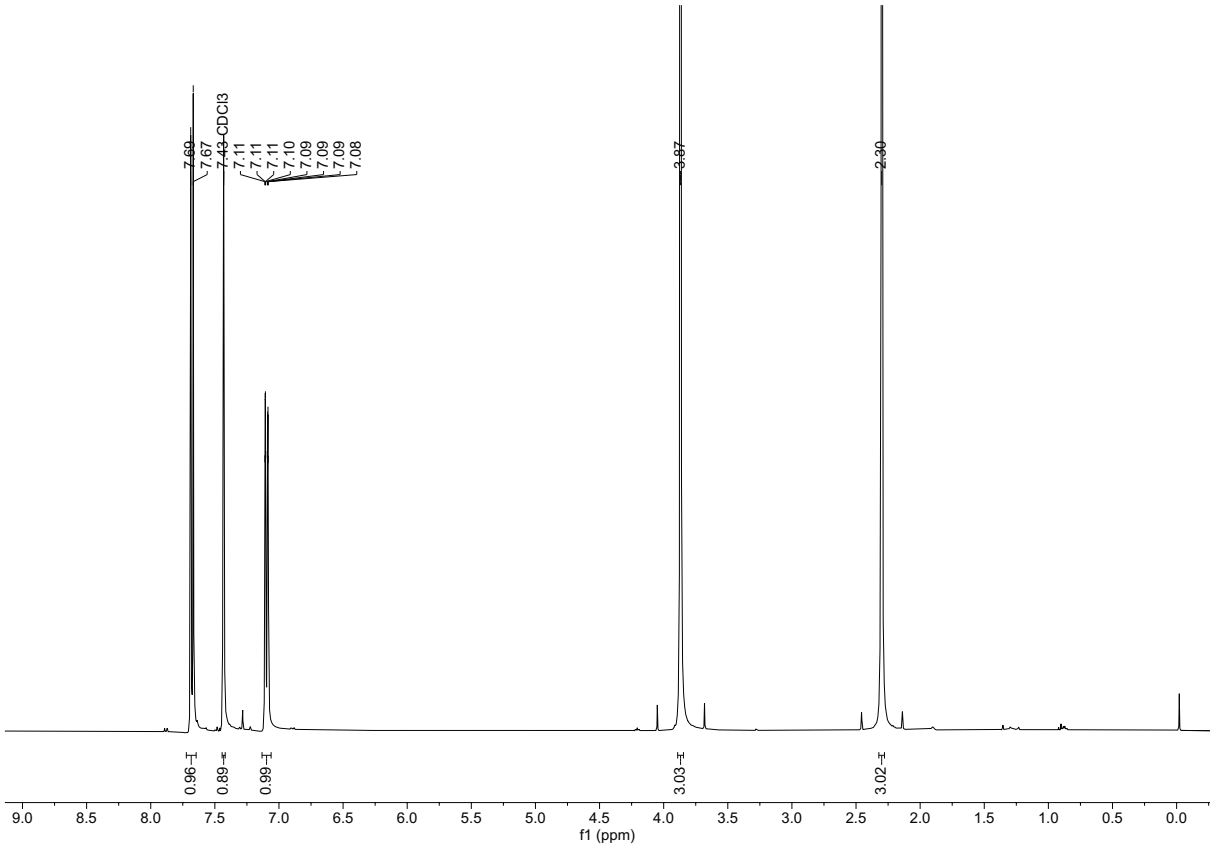




Compound 9a

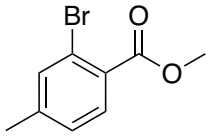
^{1}H NMR (400 MHz, $CDCl_3$)

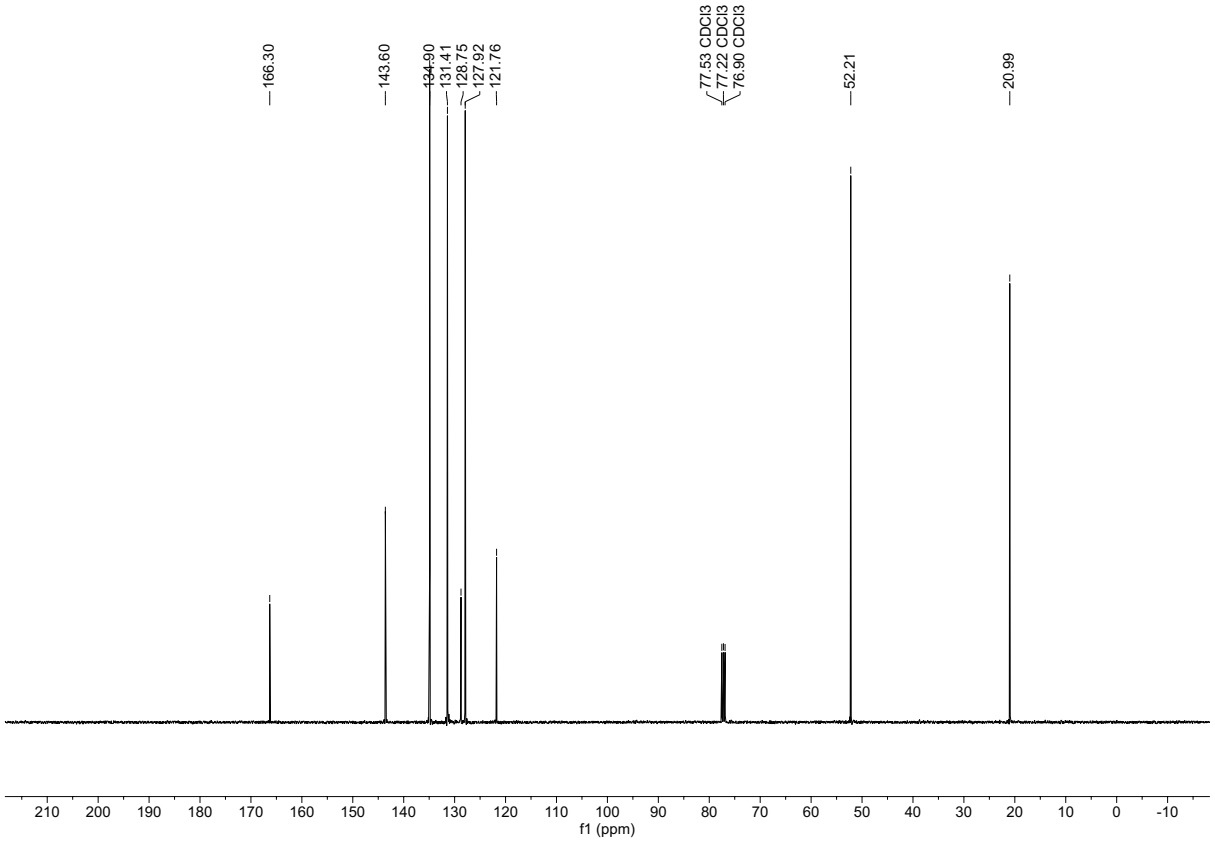




Compound 9a

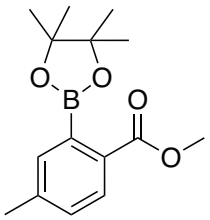
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

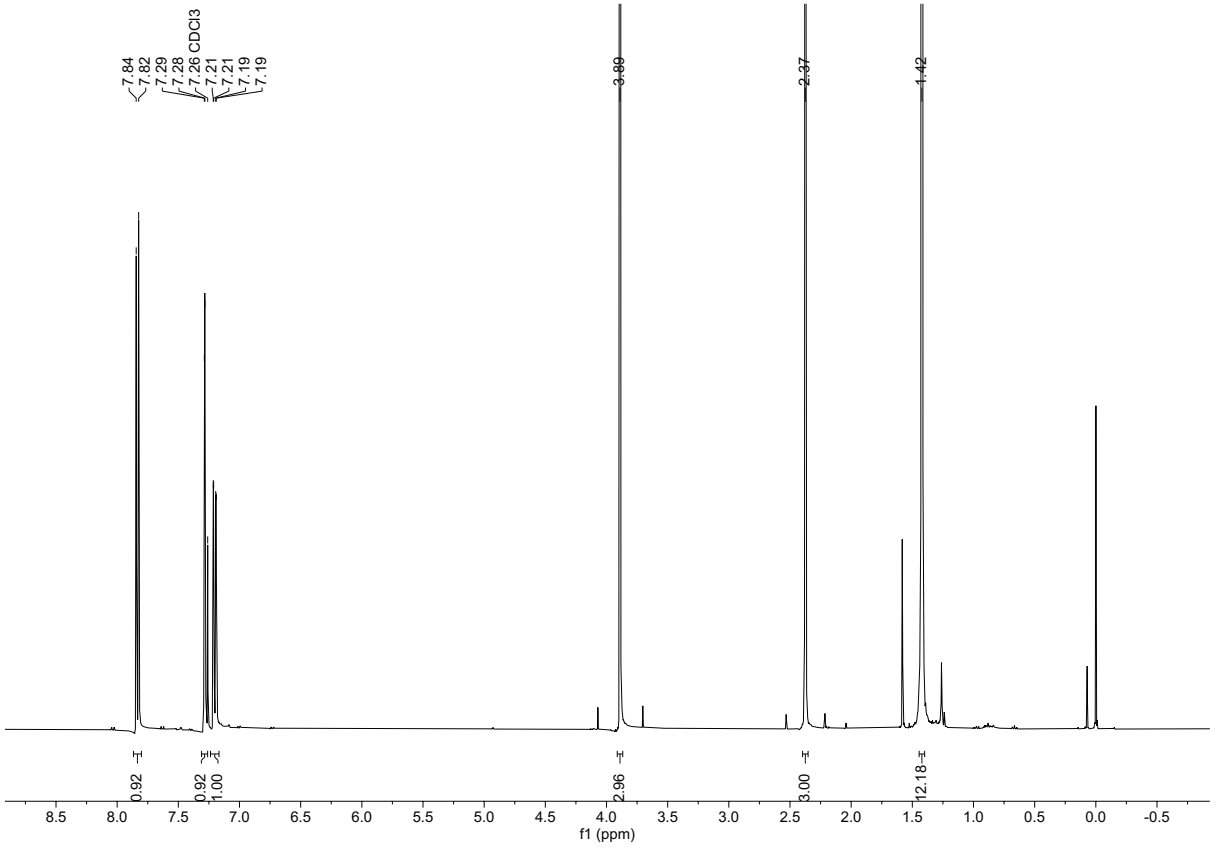




Compound 9b

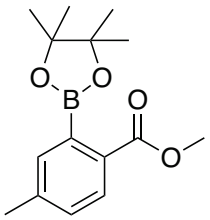
^{1}H NMR (400 MHz, $CDCl_3$)

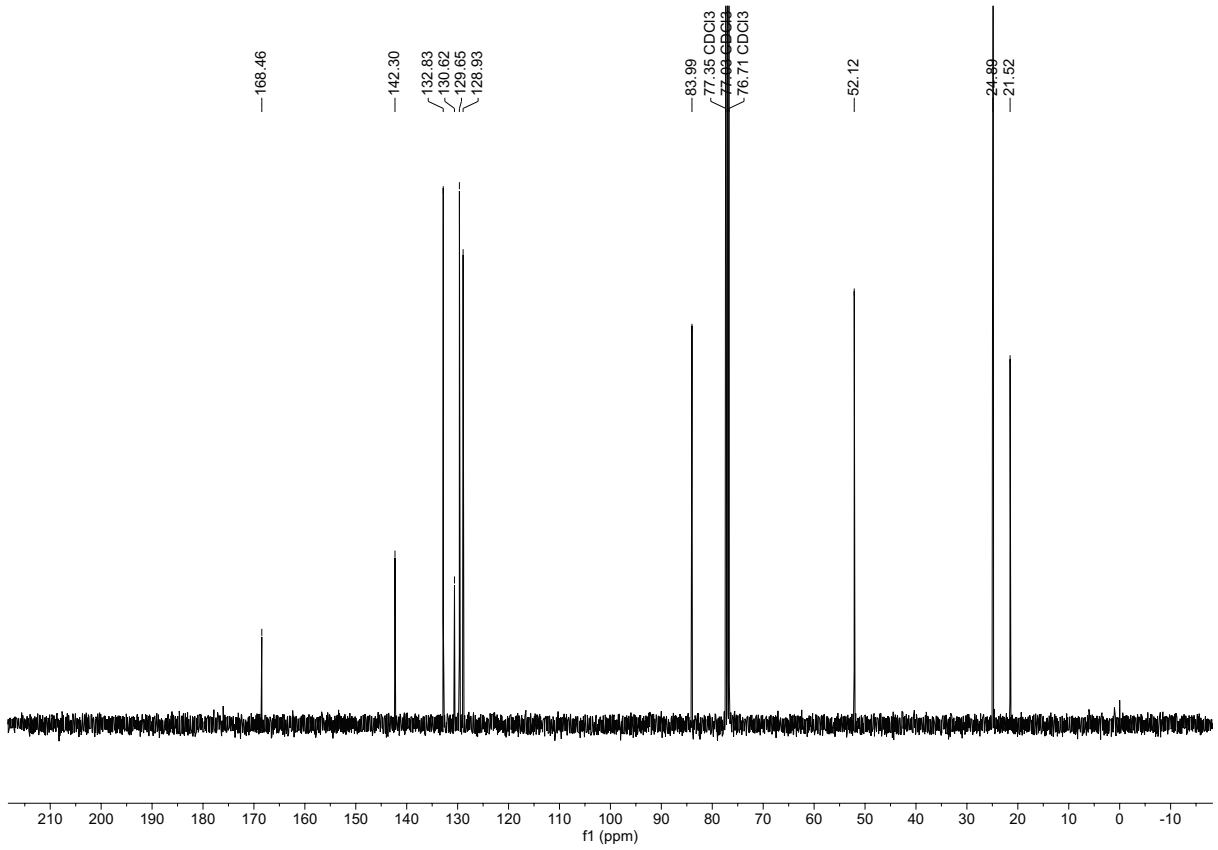




Compound 9b

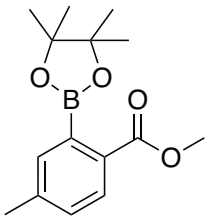
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

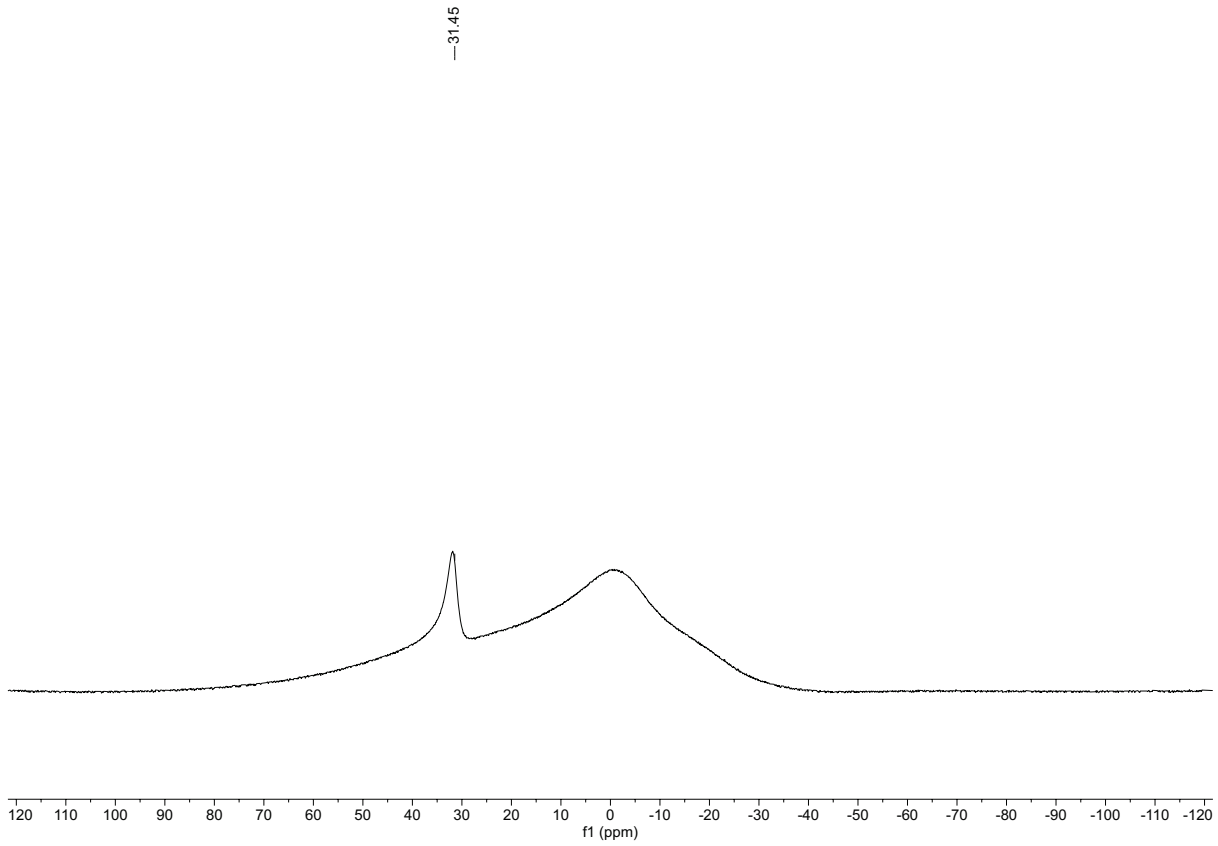




Compound 9b

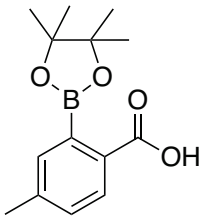
$^{11}B\{^{1}H\}$ NMR (128 MHz, $CDCl_3$)

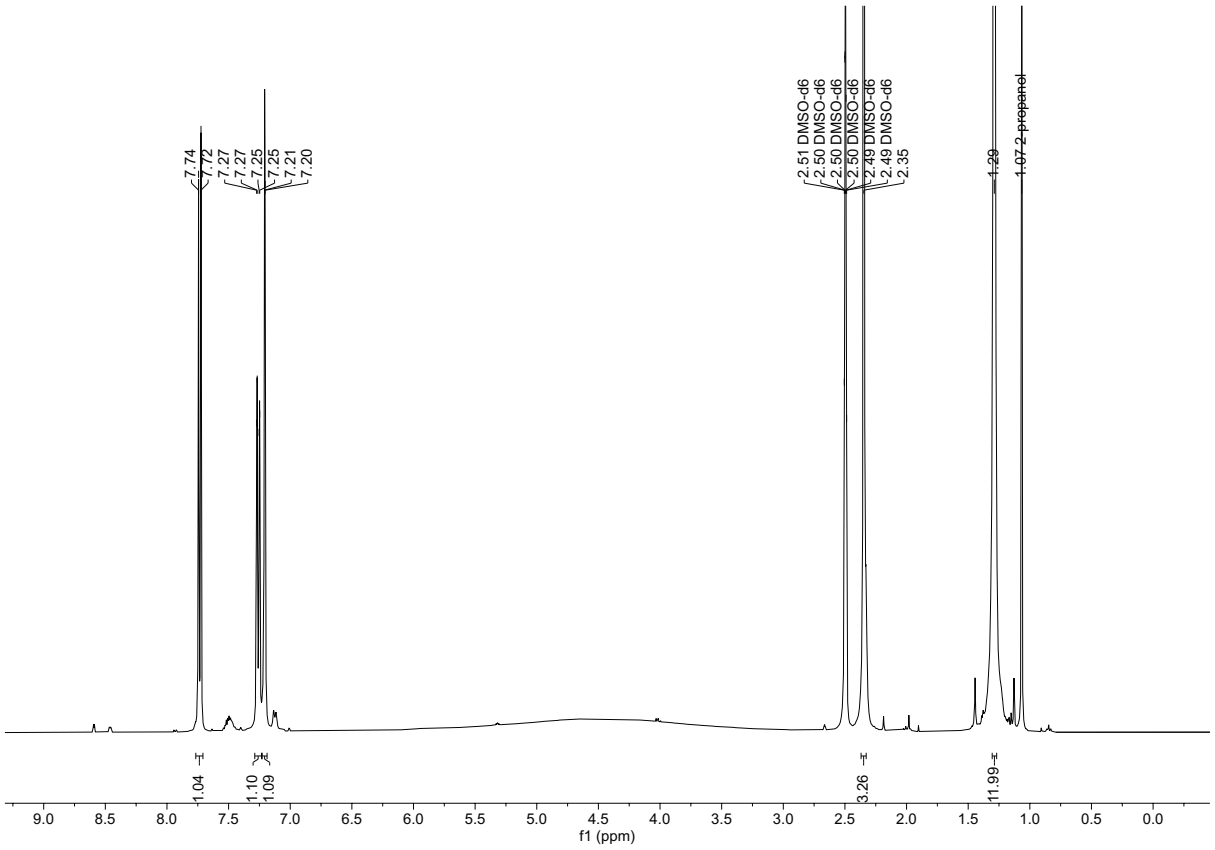




Compound 9c

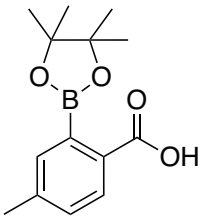
^{1}H NMR (400 MHz, DMSO)

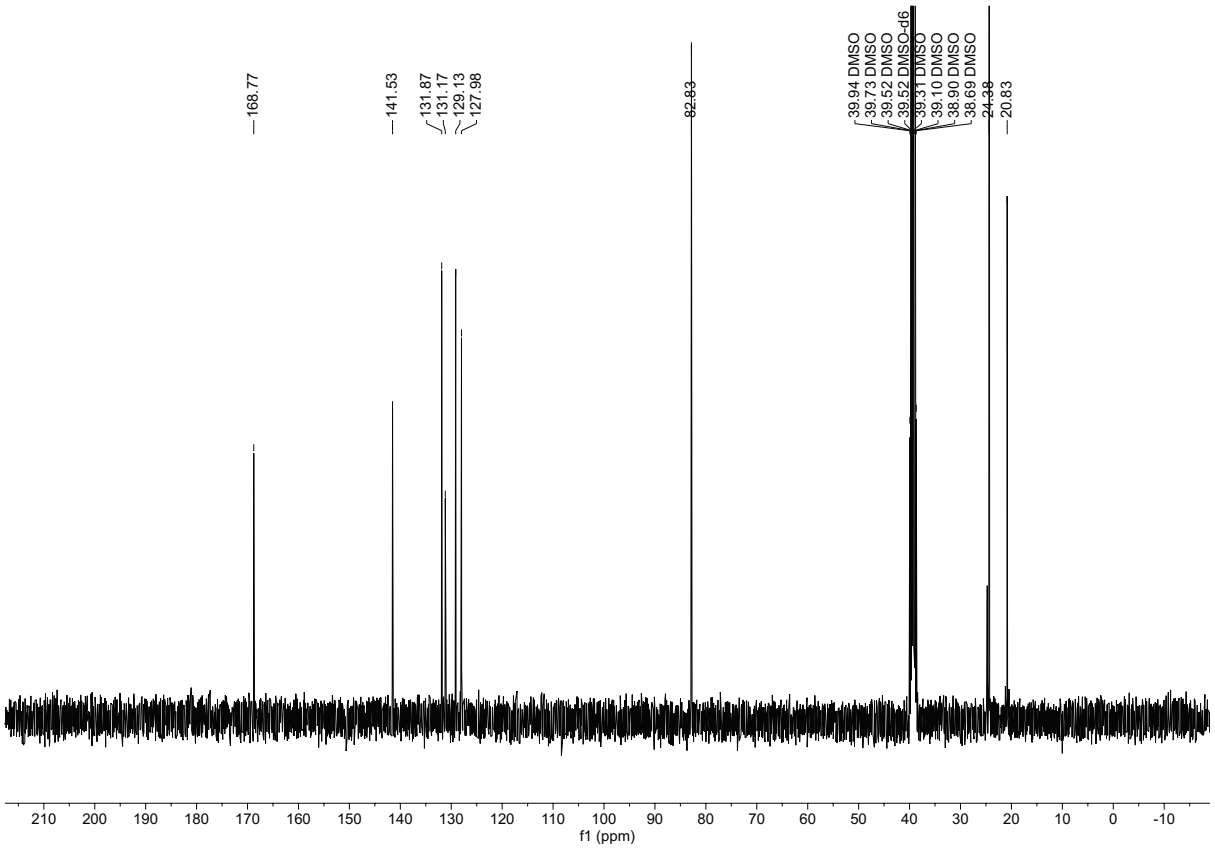




Compound 9c

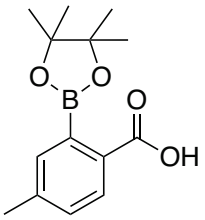
$^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO)

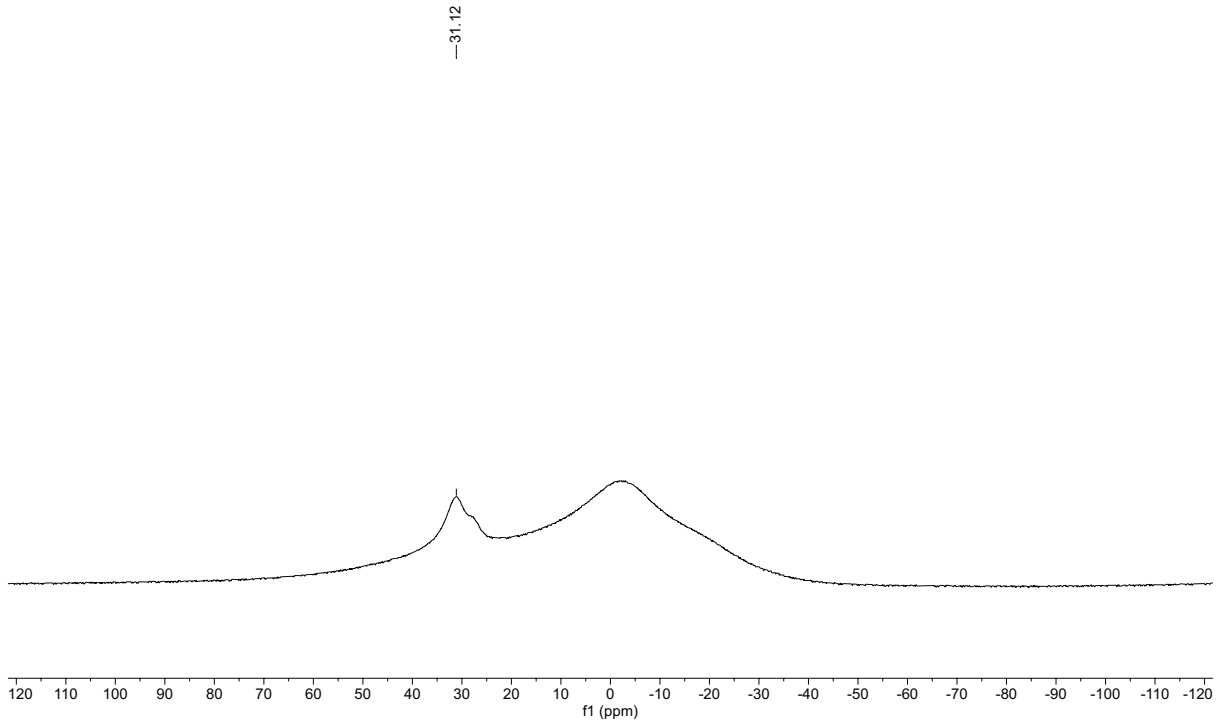




Compound 9c

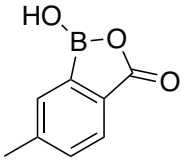
$^{11}B\{^{1}H\}$ NMR (128 MHz, $CDCl_3$)

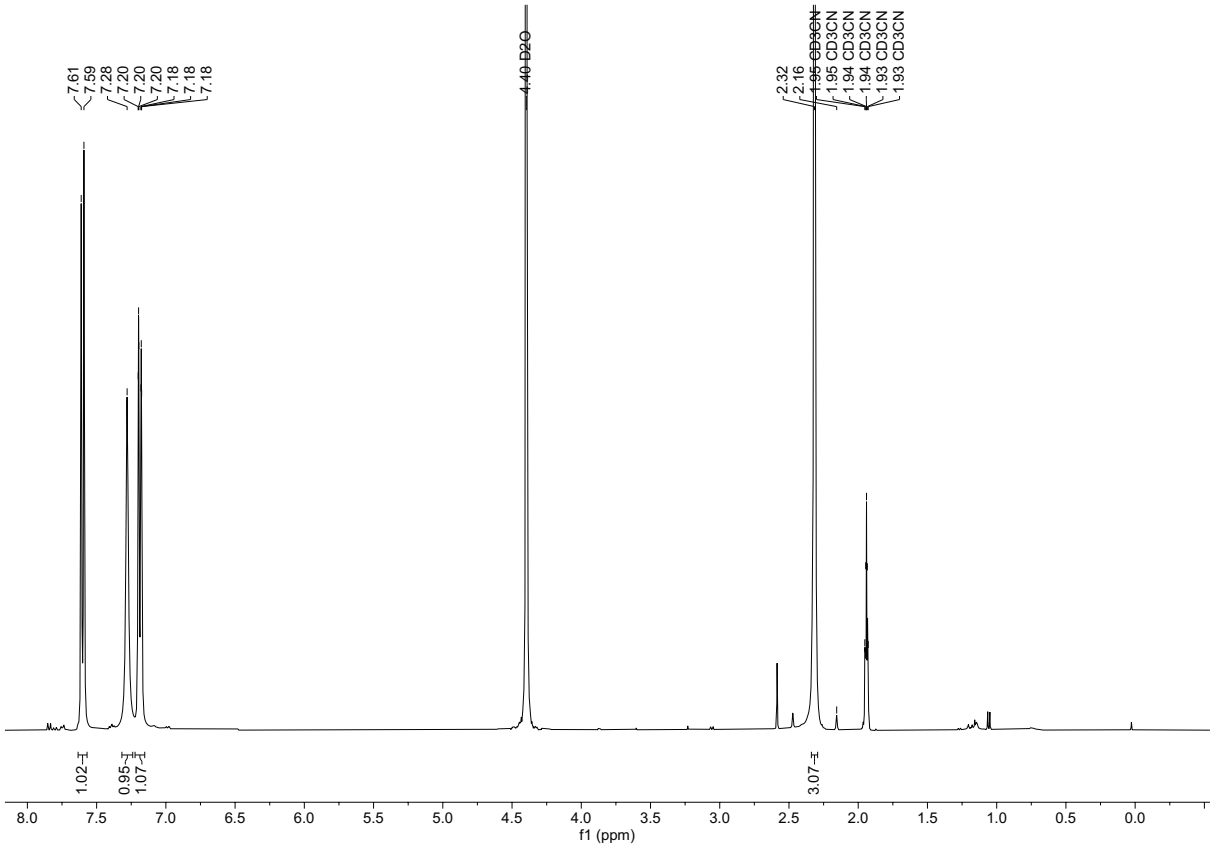




Compound 9d

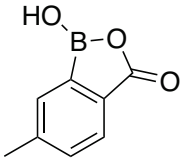
^{1}H NMR (400 MHz, D_2O)

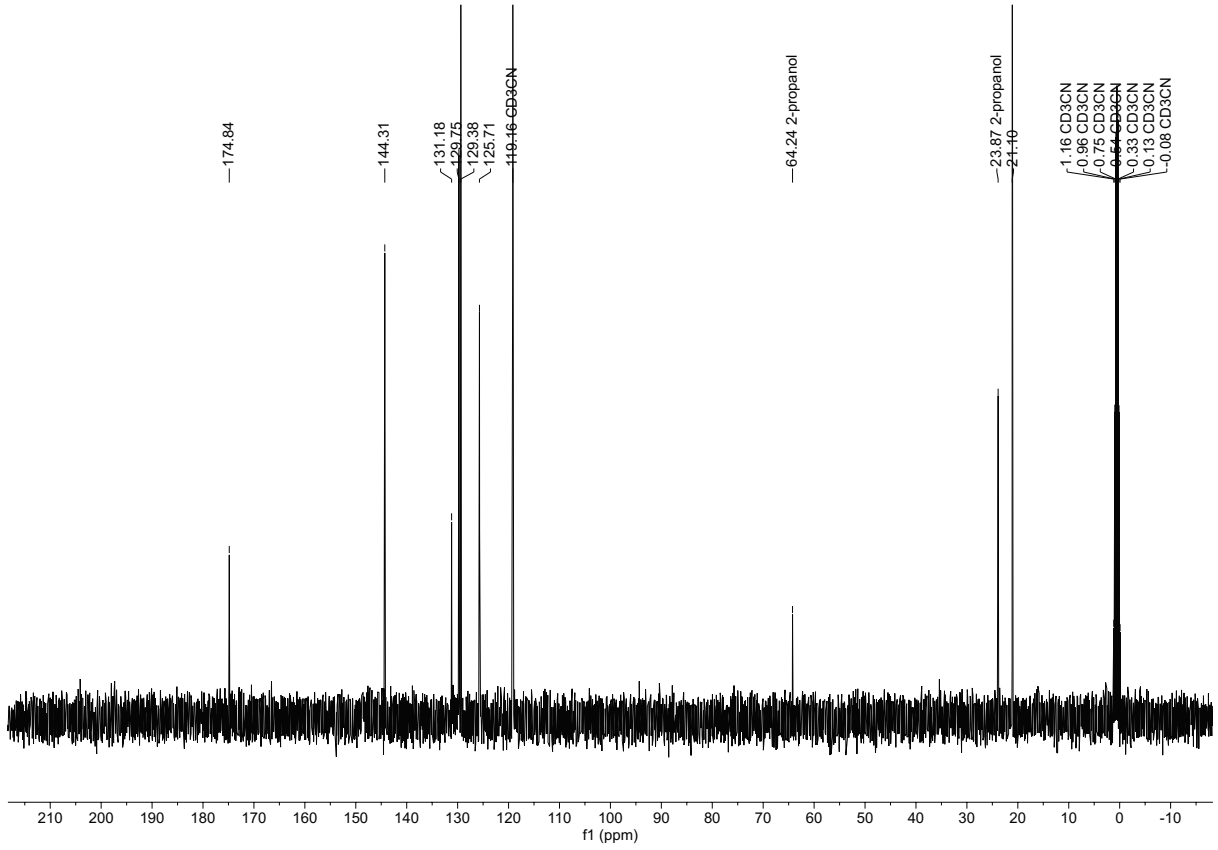




Compound 9d

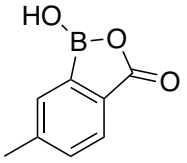
$^{13}C\{^{1}H\}$ NMR (101 MHz, D_2O)

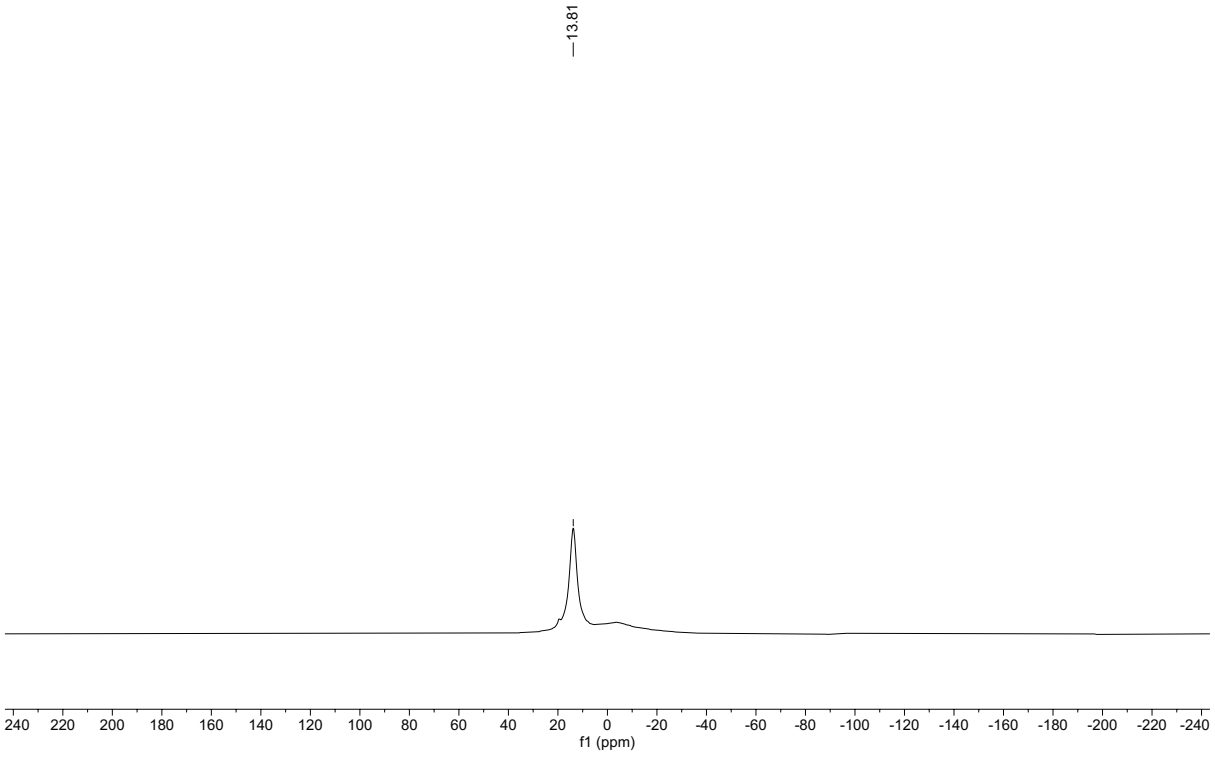




Compound 9d

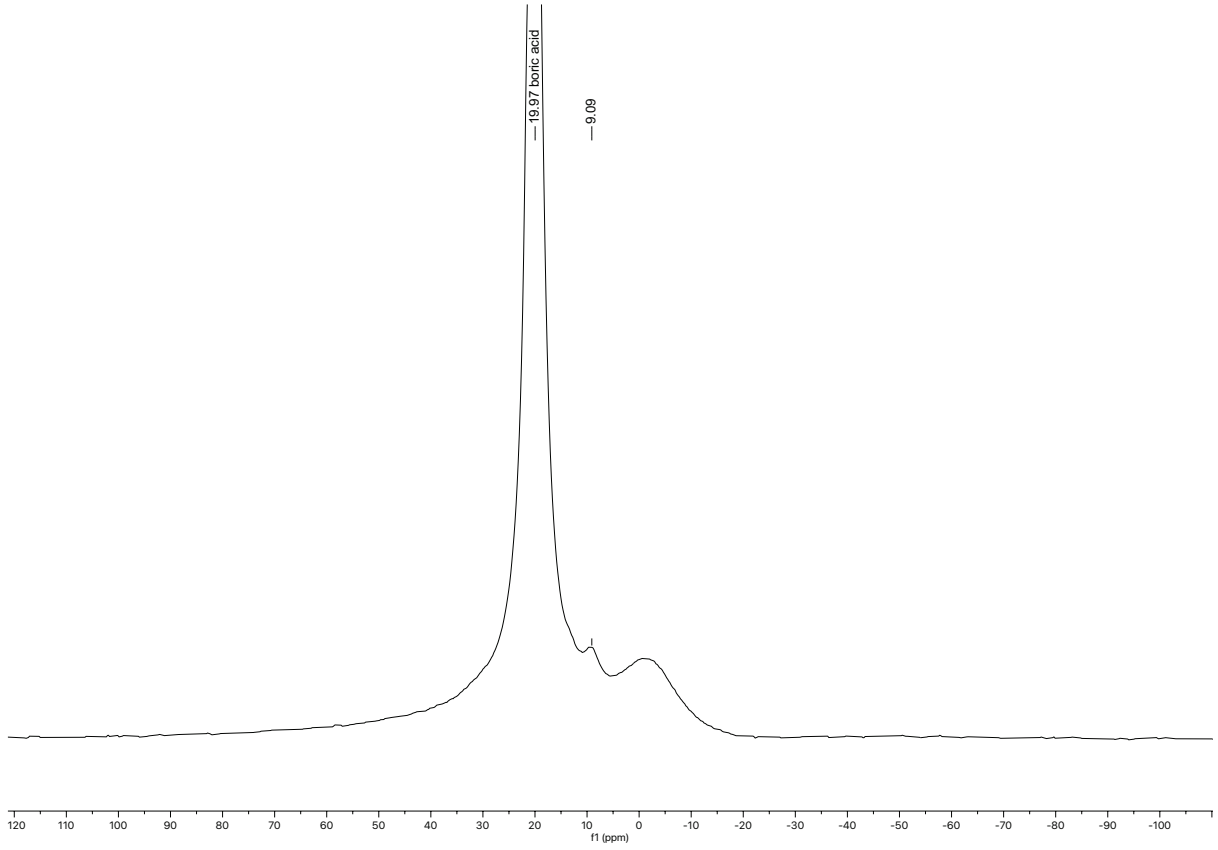
$^{11}B\{^{1}H\}$ NMR (128 MHz, D_2O)





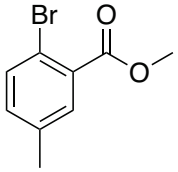
Compound 9d

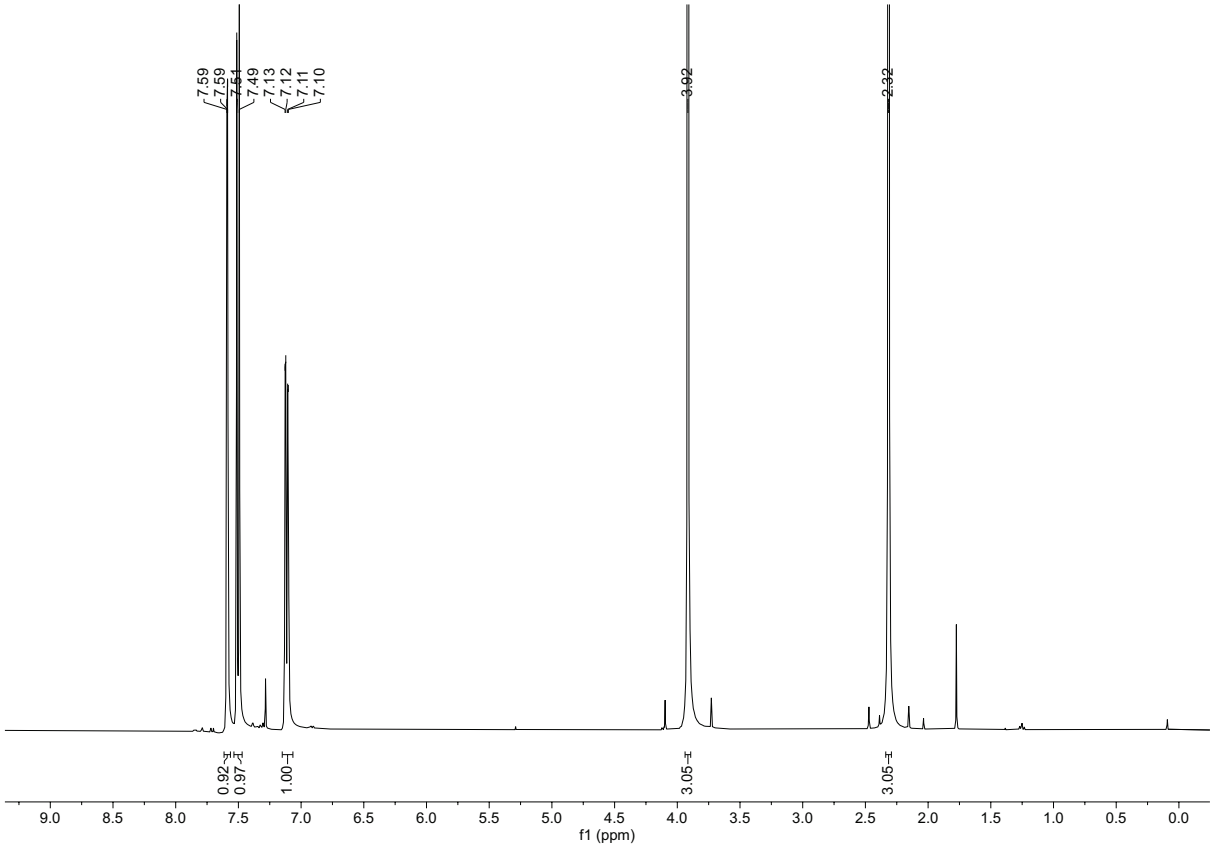
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 10a

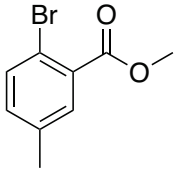
^{1}H NMR (400 MHz, $CDCl_3$)

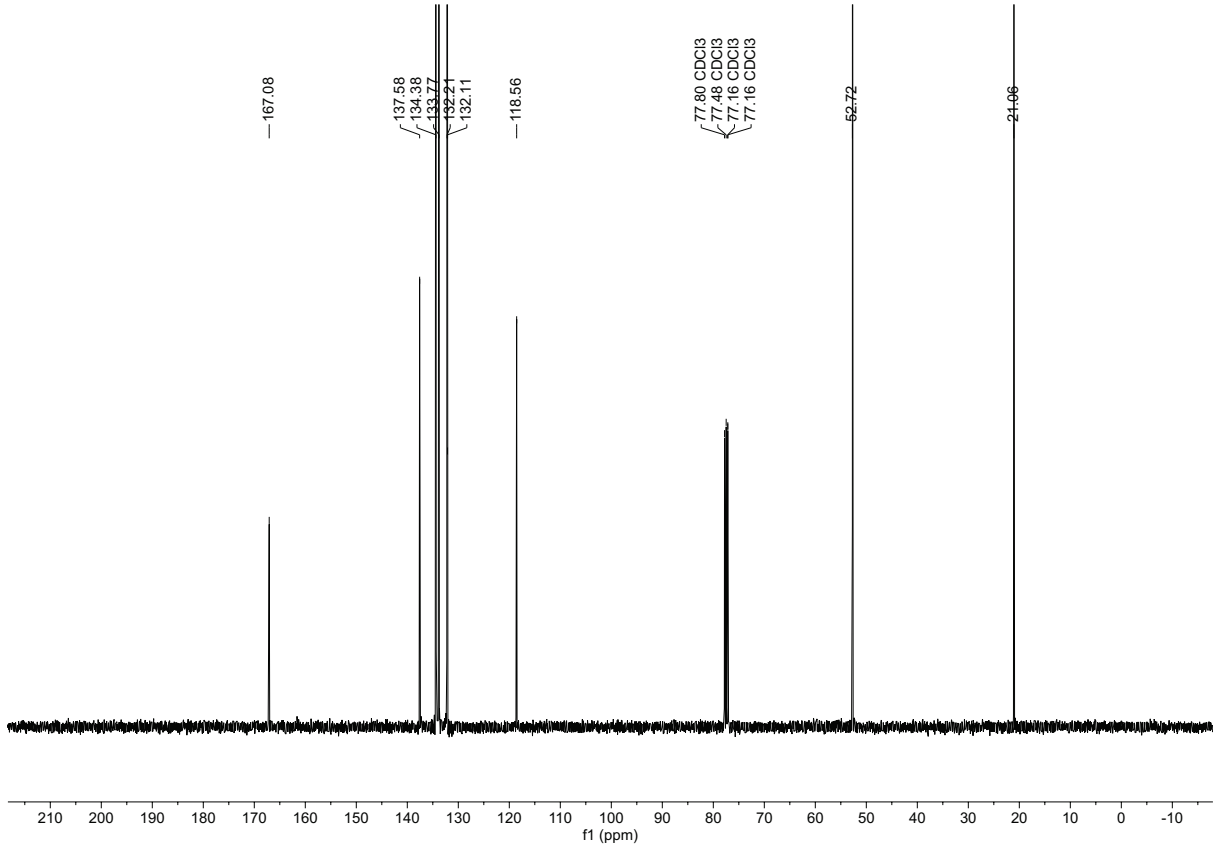




Compound 10a

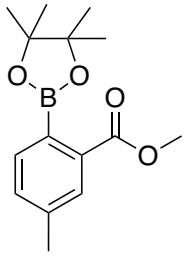
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

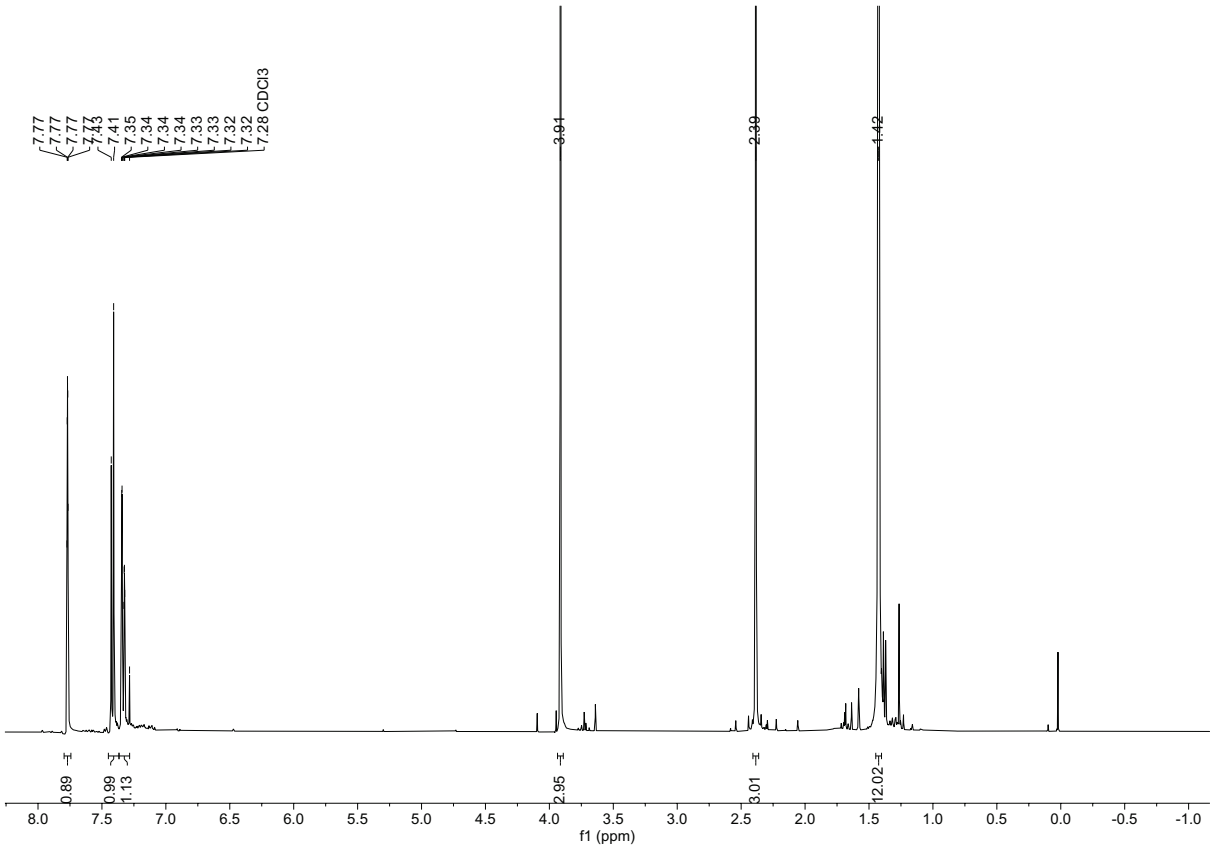




Compound 10b

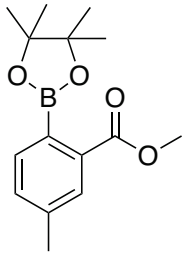
^{1}H NMR (400 MHz, $CDCl_3$)

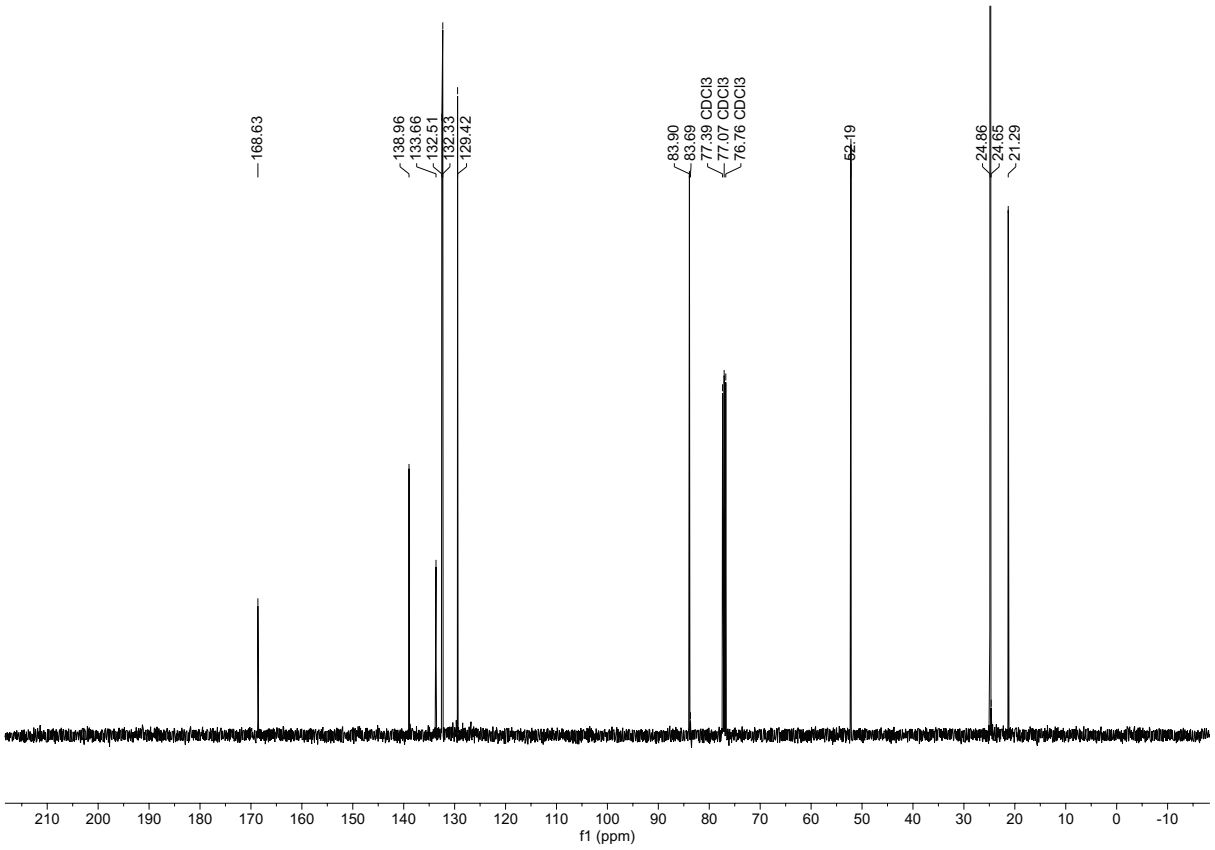




Compound 10b

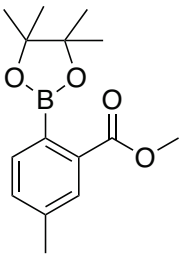
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

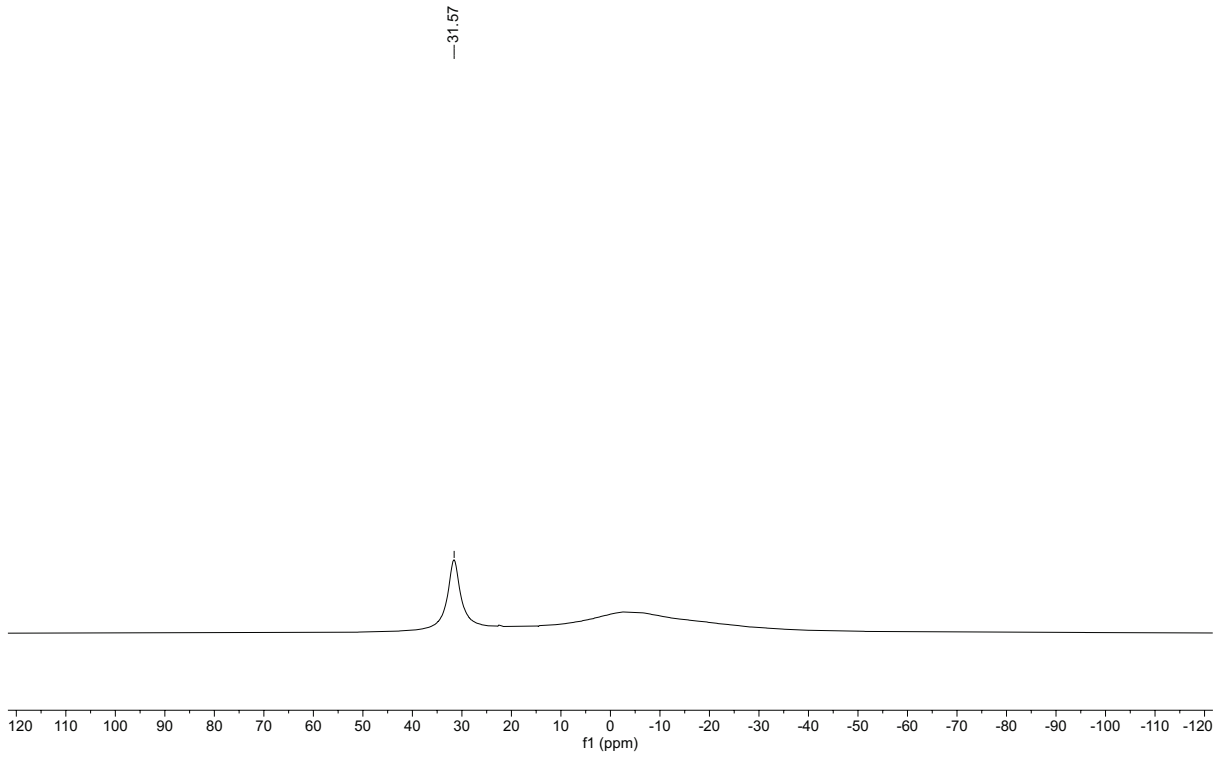




Compound 10b

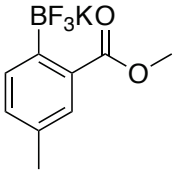
$^{11}B\{^{1}H\}$ NMR (128 MHz, $CDCl_3$)

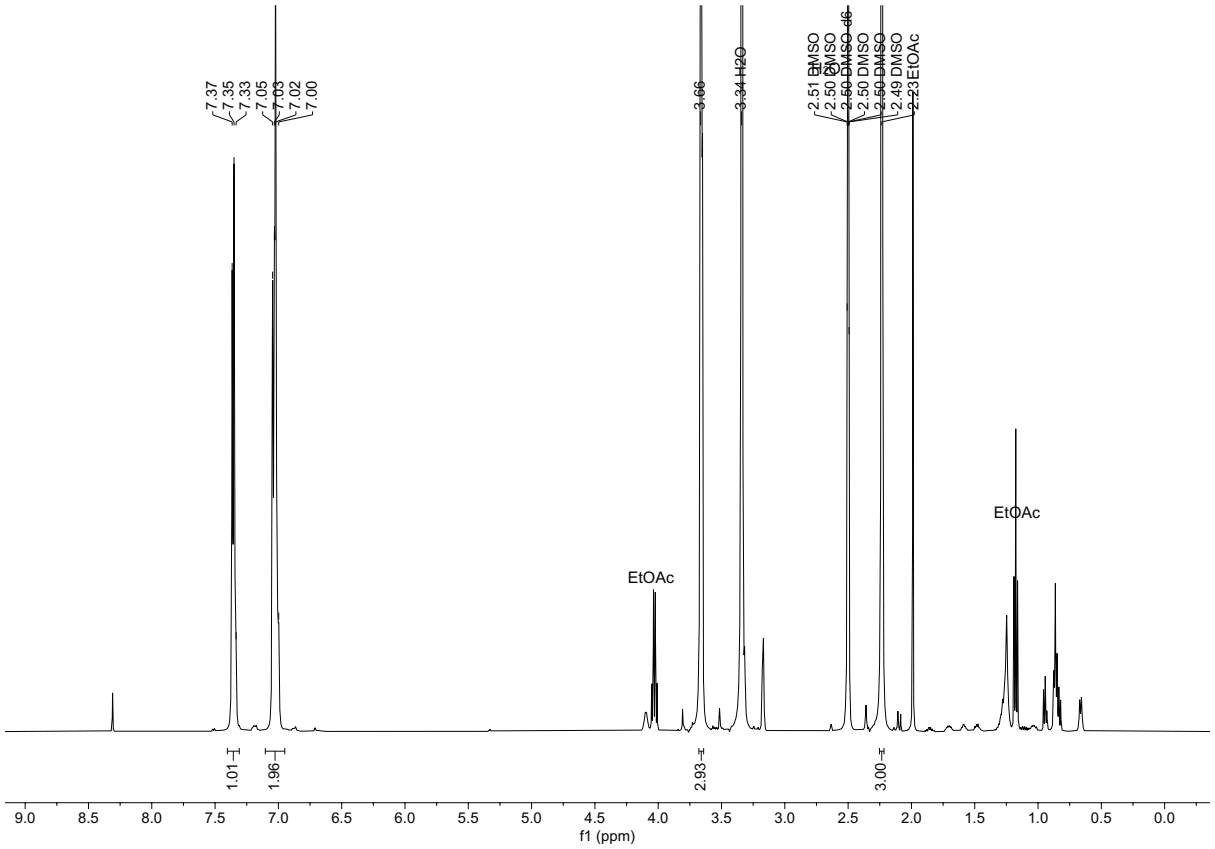




Compound 10c

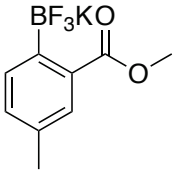
^{1}H NMR (500 MHz, DMSO)

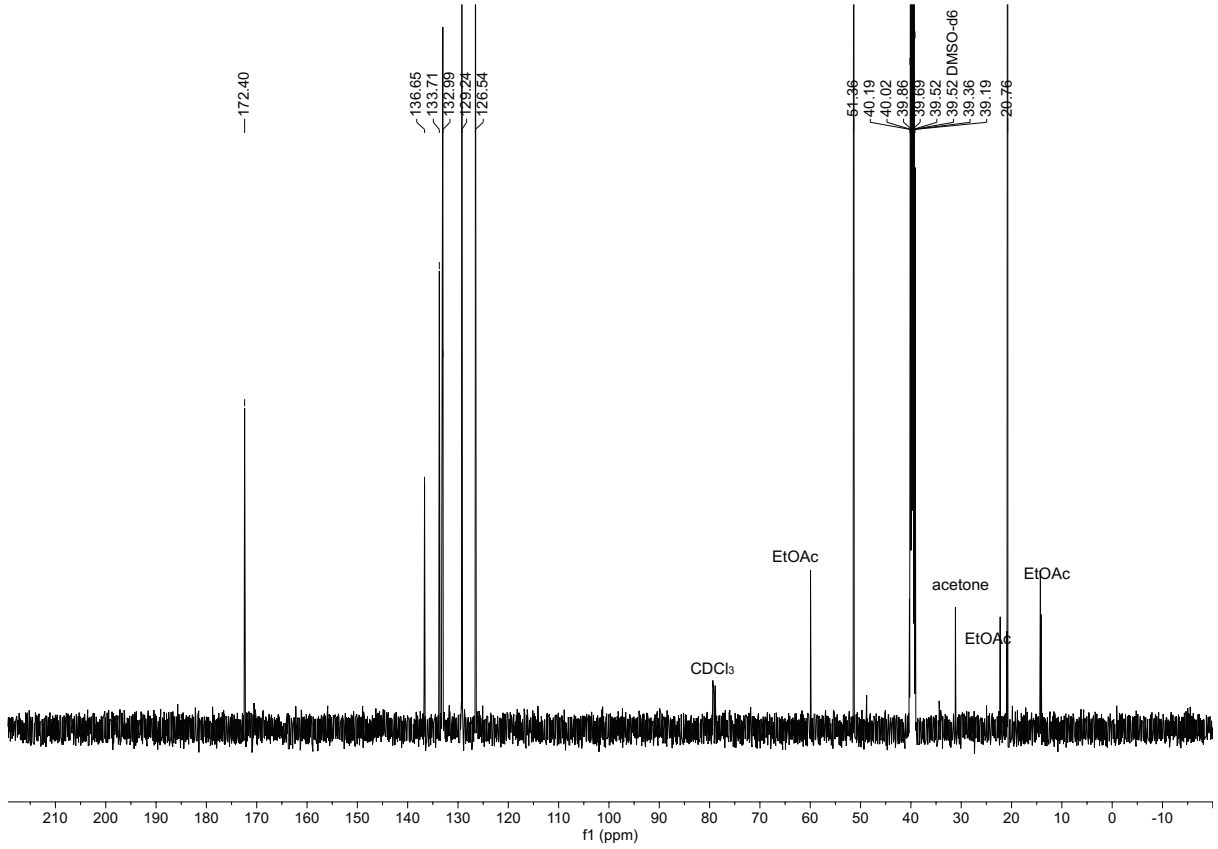




Compound 10c

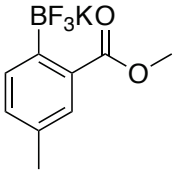
$^{13}C\{^{1}H\}$ NMR (126 MHz, DMSO)

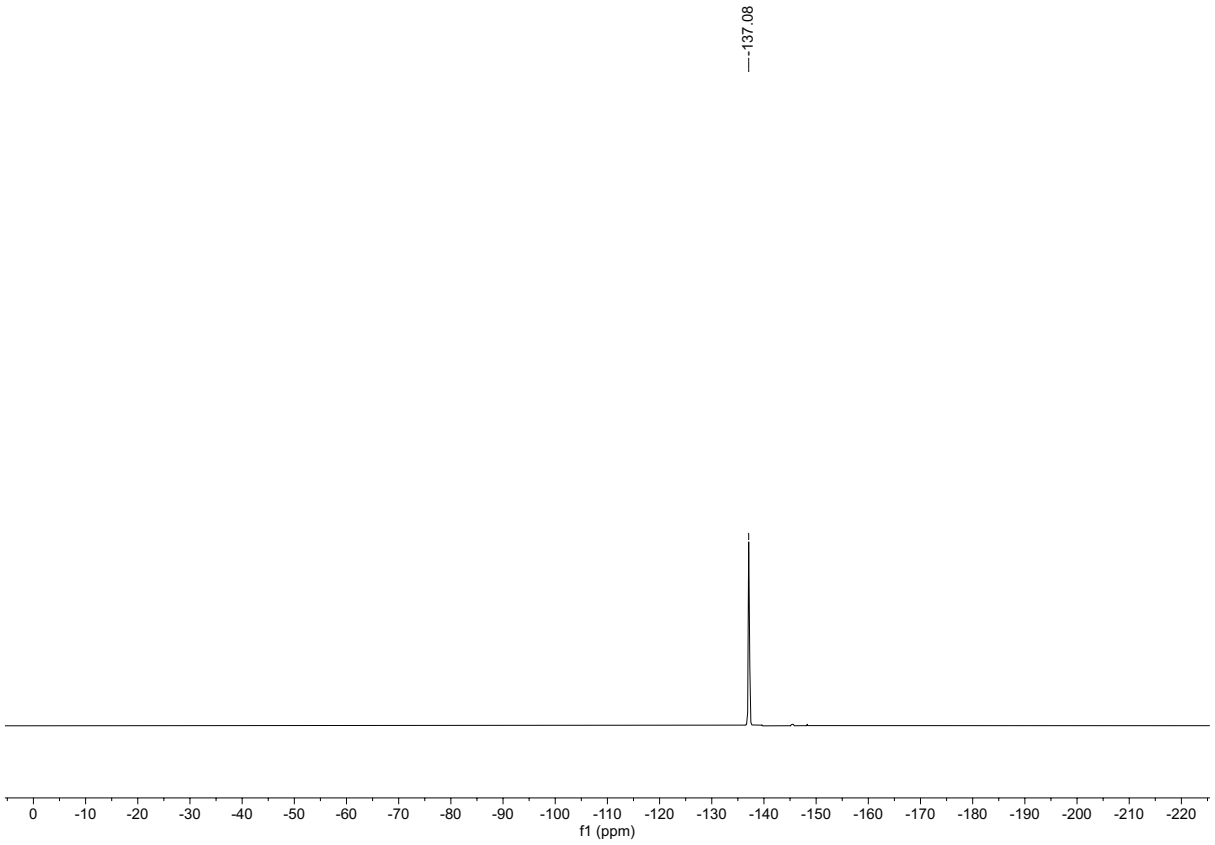




Compound 10c

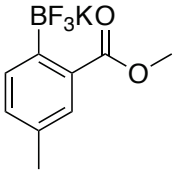
$^{19}F\{^{1}H\}$ NMR (471 MHz, DMSO)

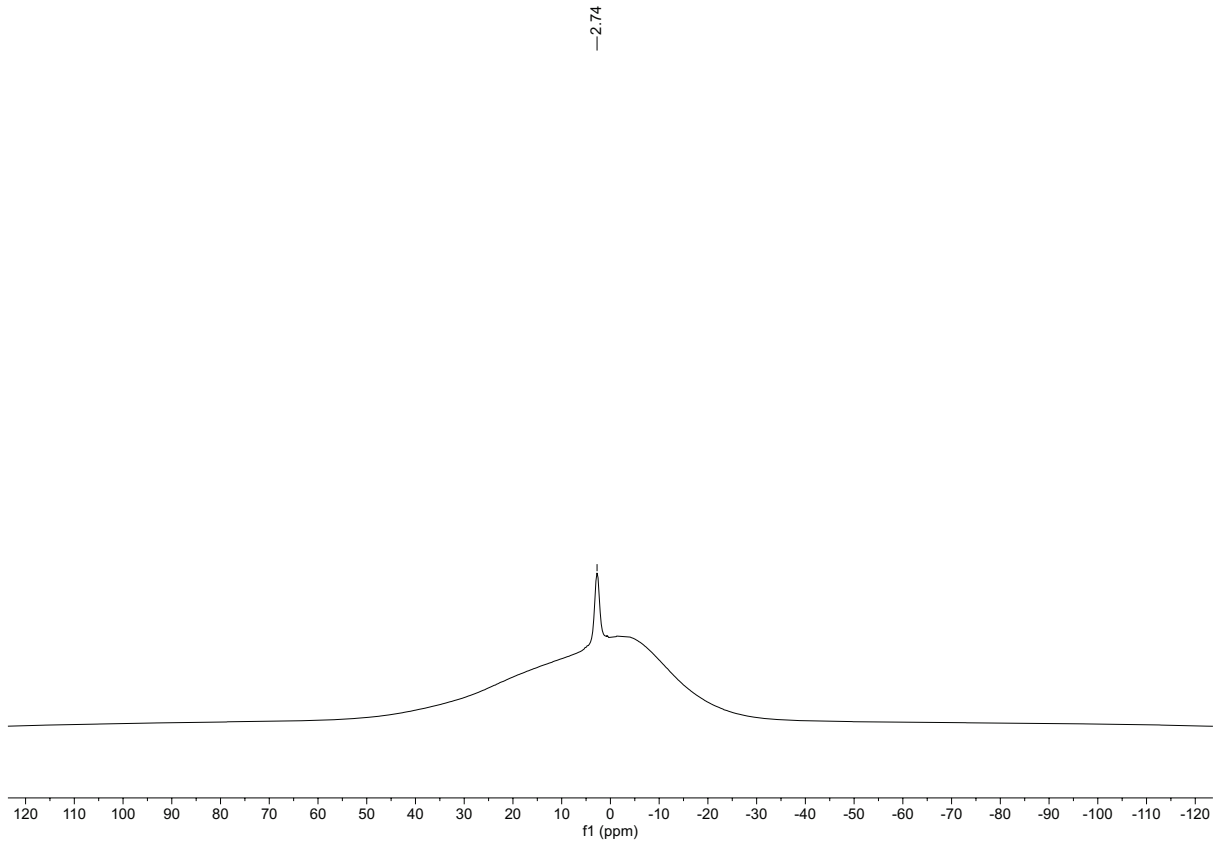




Compound 10c

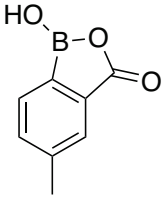
$^{11}B\{^{1}H\}$ NMR (160 MHz, DMSO)

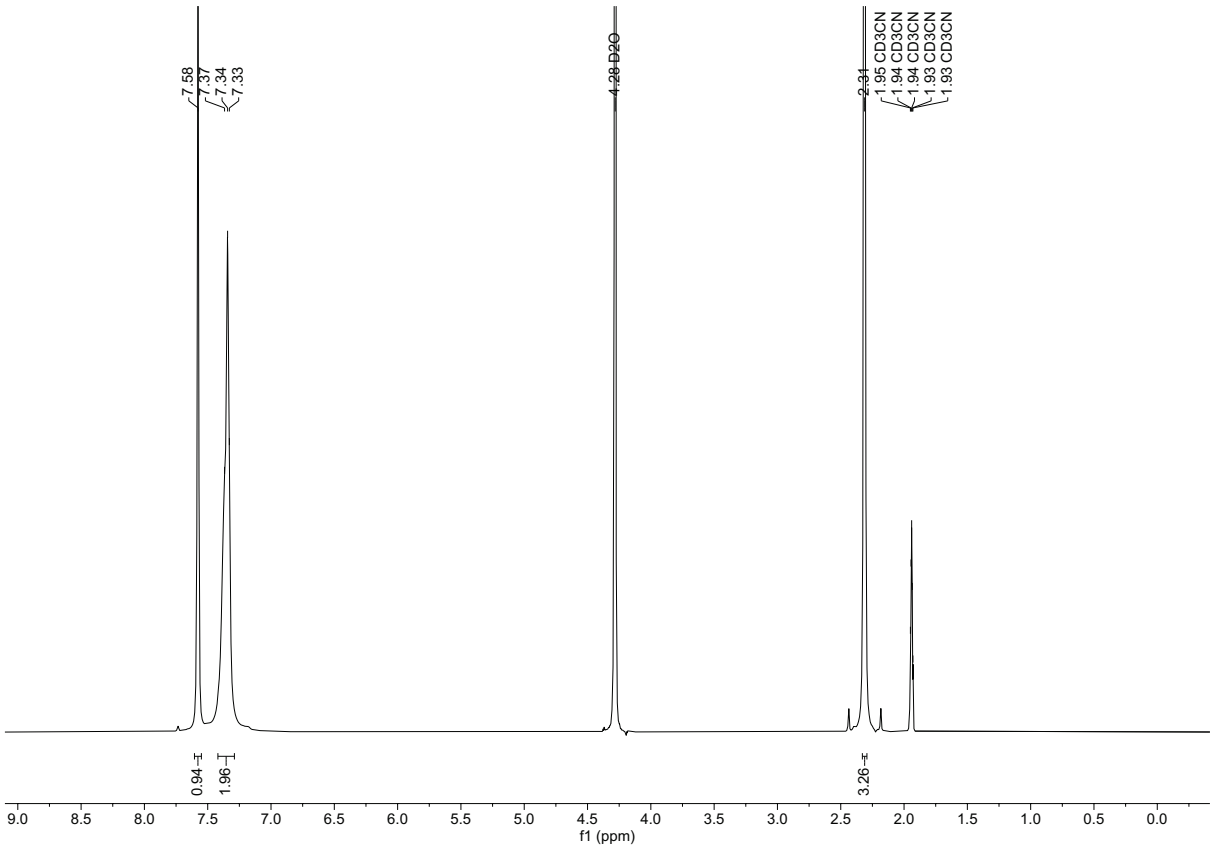




Compound 10d

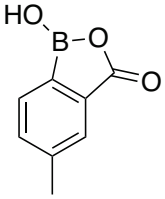
^{1}H NMR (500 MHz, D_2O/CD_3CN)

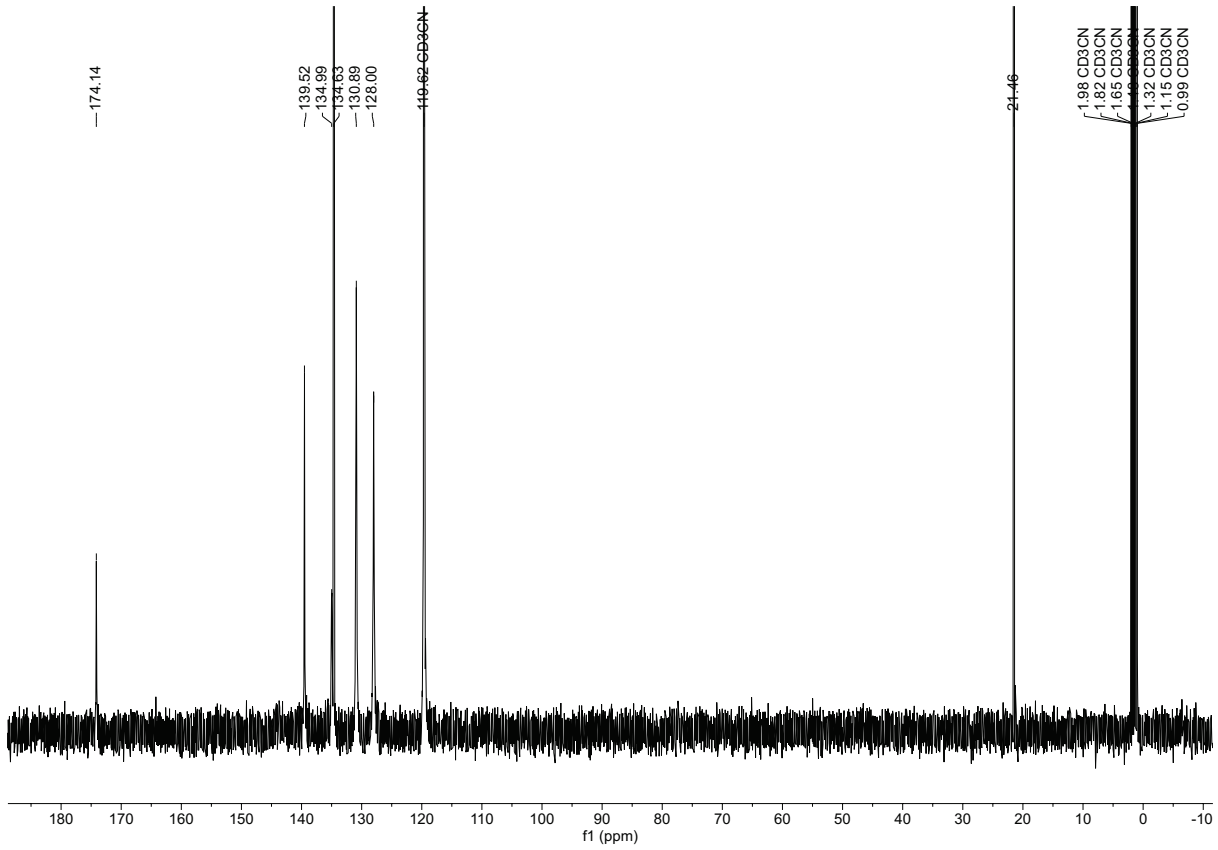




Compound 10d

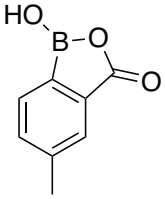
$^{13}C\{^{1}H\}$ NMR (126 MHz, D_2O/CD_3CN)

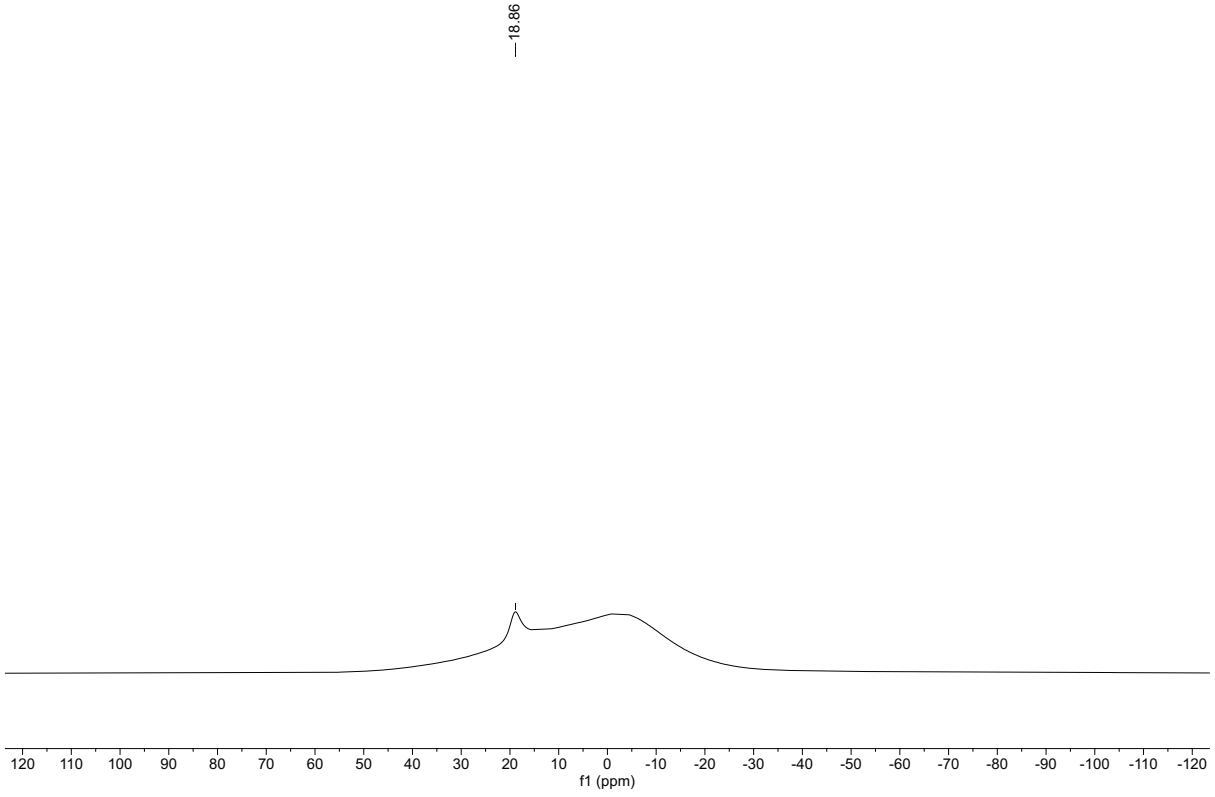




Compound 10d

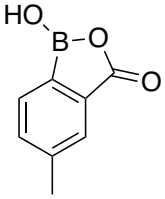
$^{11}B\{^{1}H\}$ NMR (160 MHz, D_2O/CD_3CN)



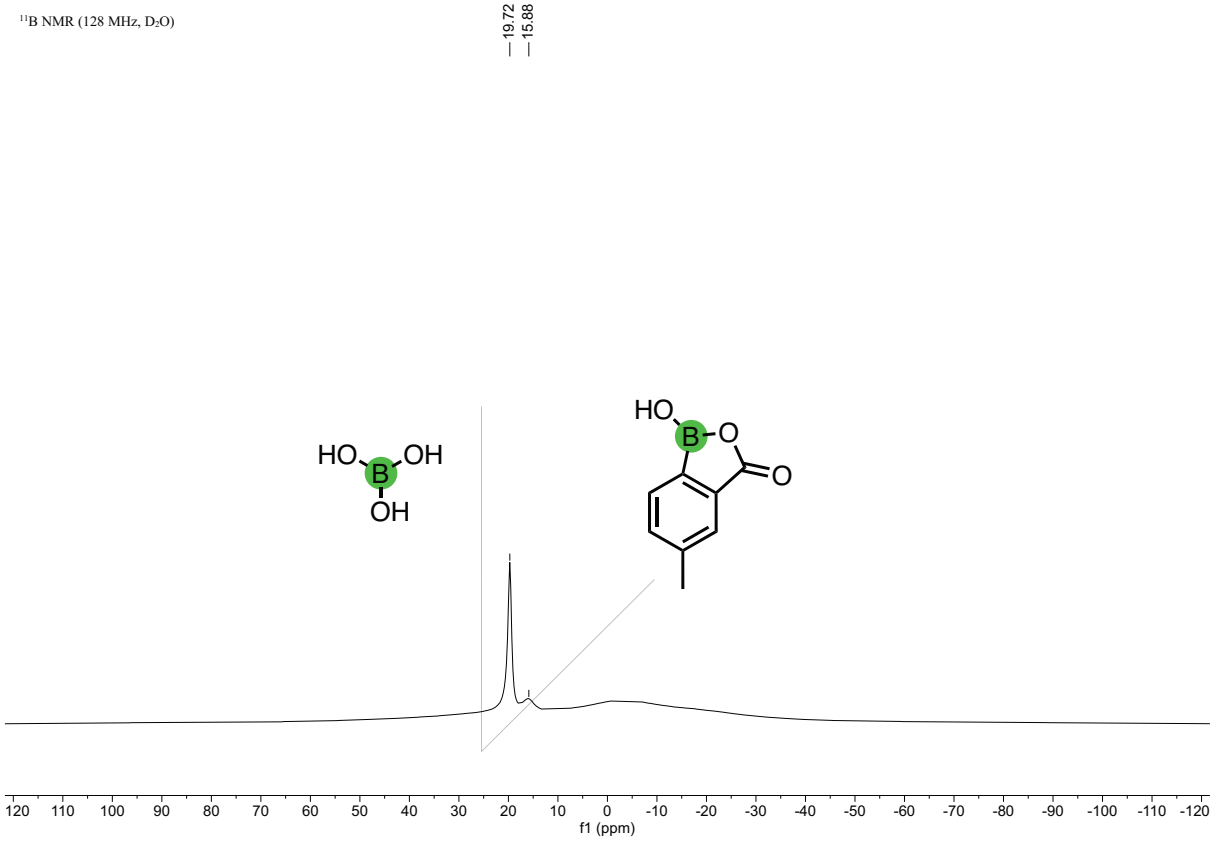


Compound 10d

$^{11}B\{^{1}H\}$ NMR (128 MHz, D_2O/CD_3CN)

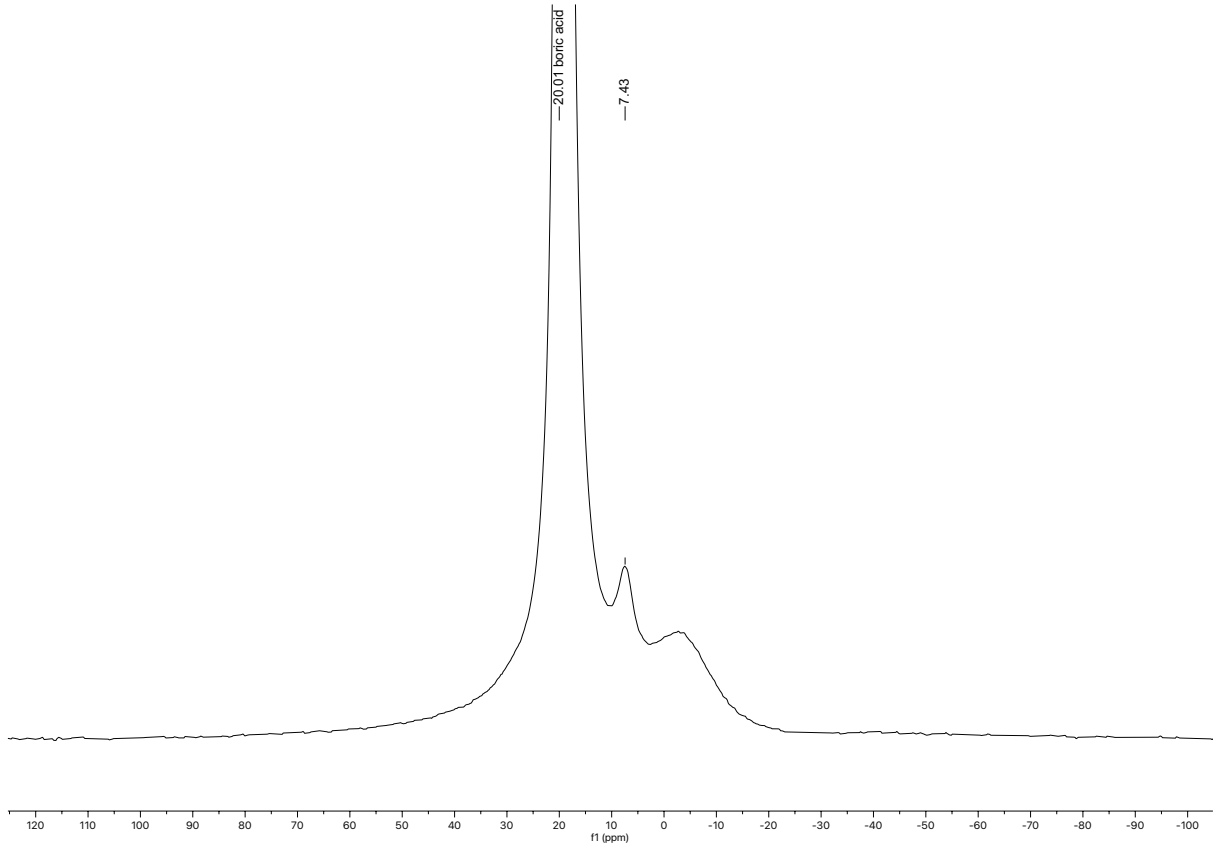


(including 20 mg of boric acid as a ^{11}B NMR reference)



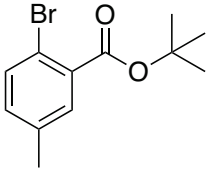
Compound 10d

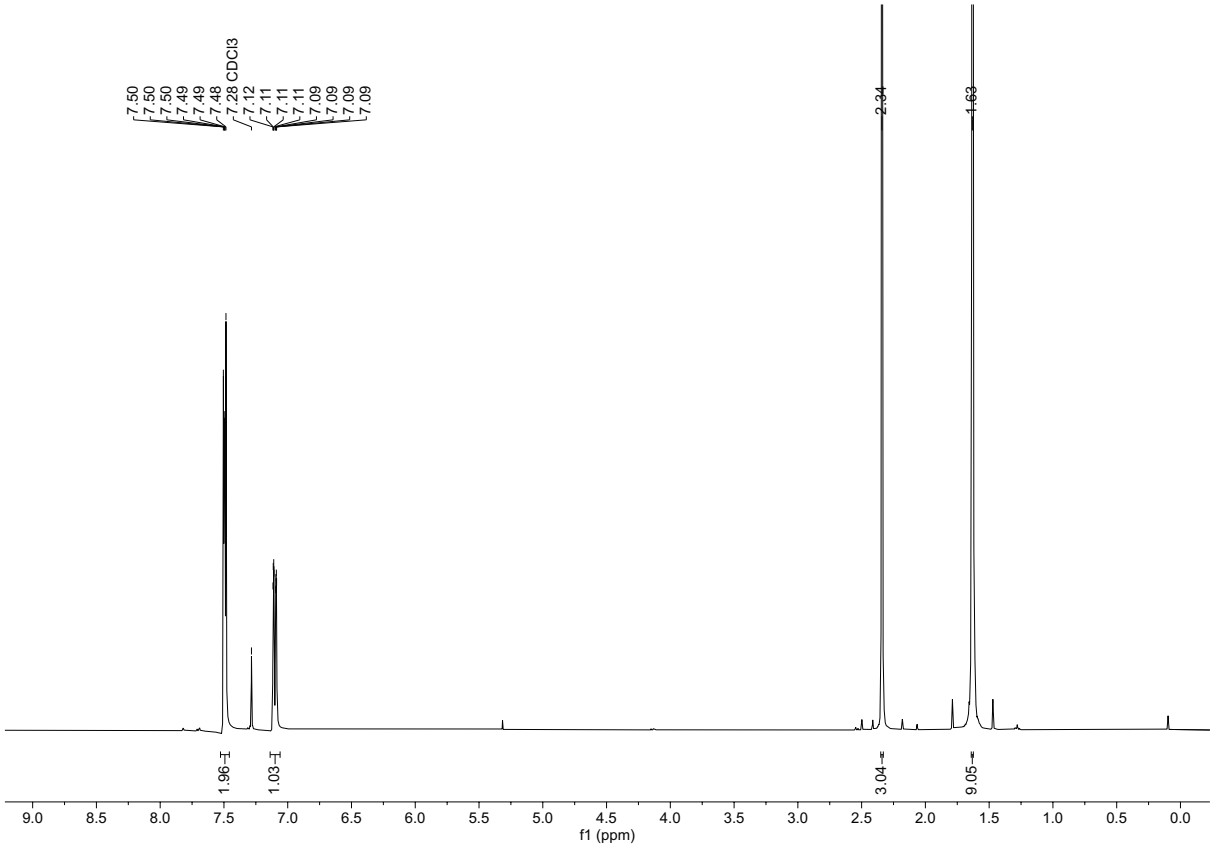
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 11a

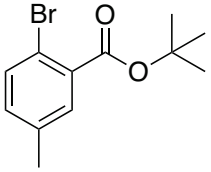
^{1}H NMR (400 MHz, $CDCl_3$)

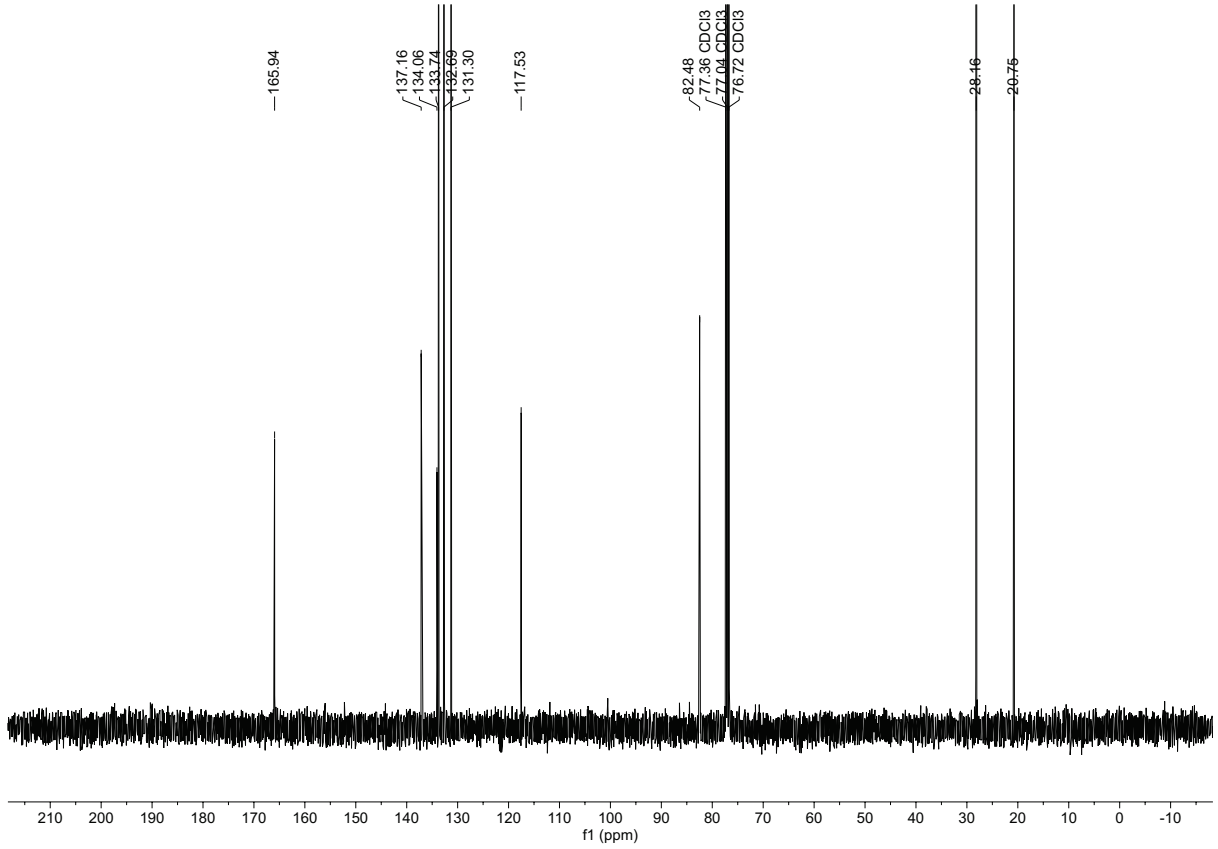




Compound 11a

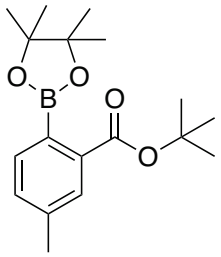
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

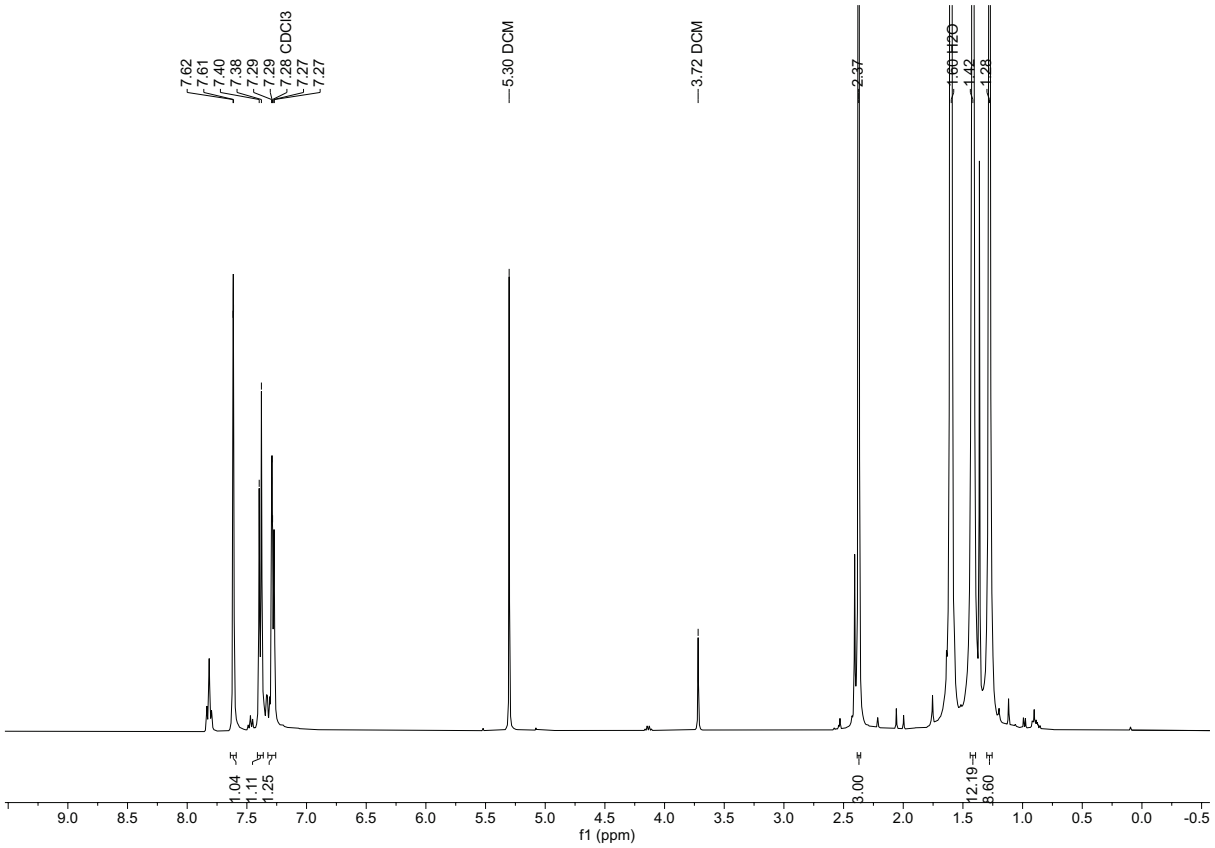




Compound 11b

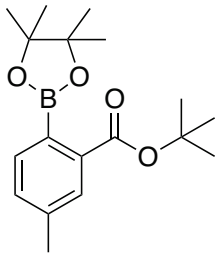
^{1}H NMR (400 MHz, $CDCl_3$)

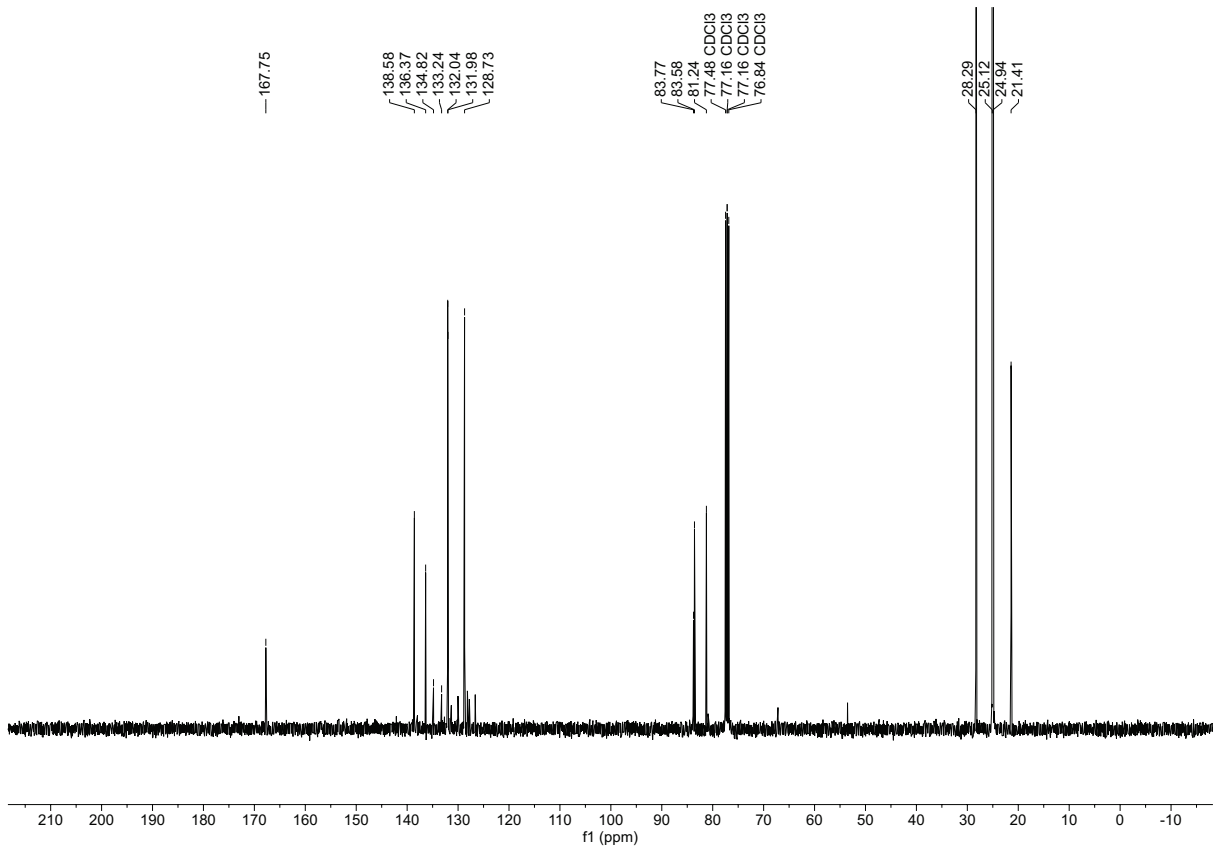




Compound 11b

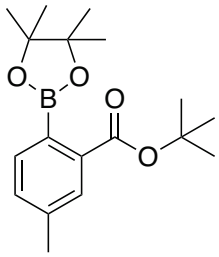
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

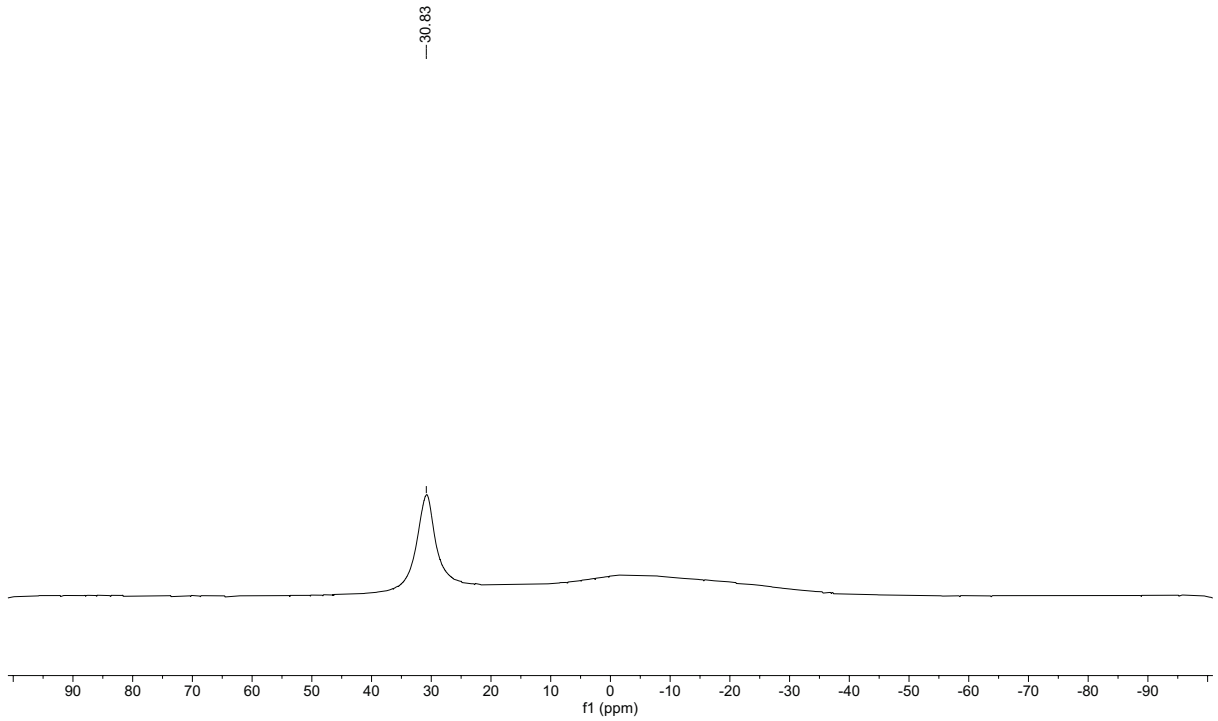




Compound 11b

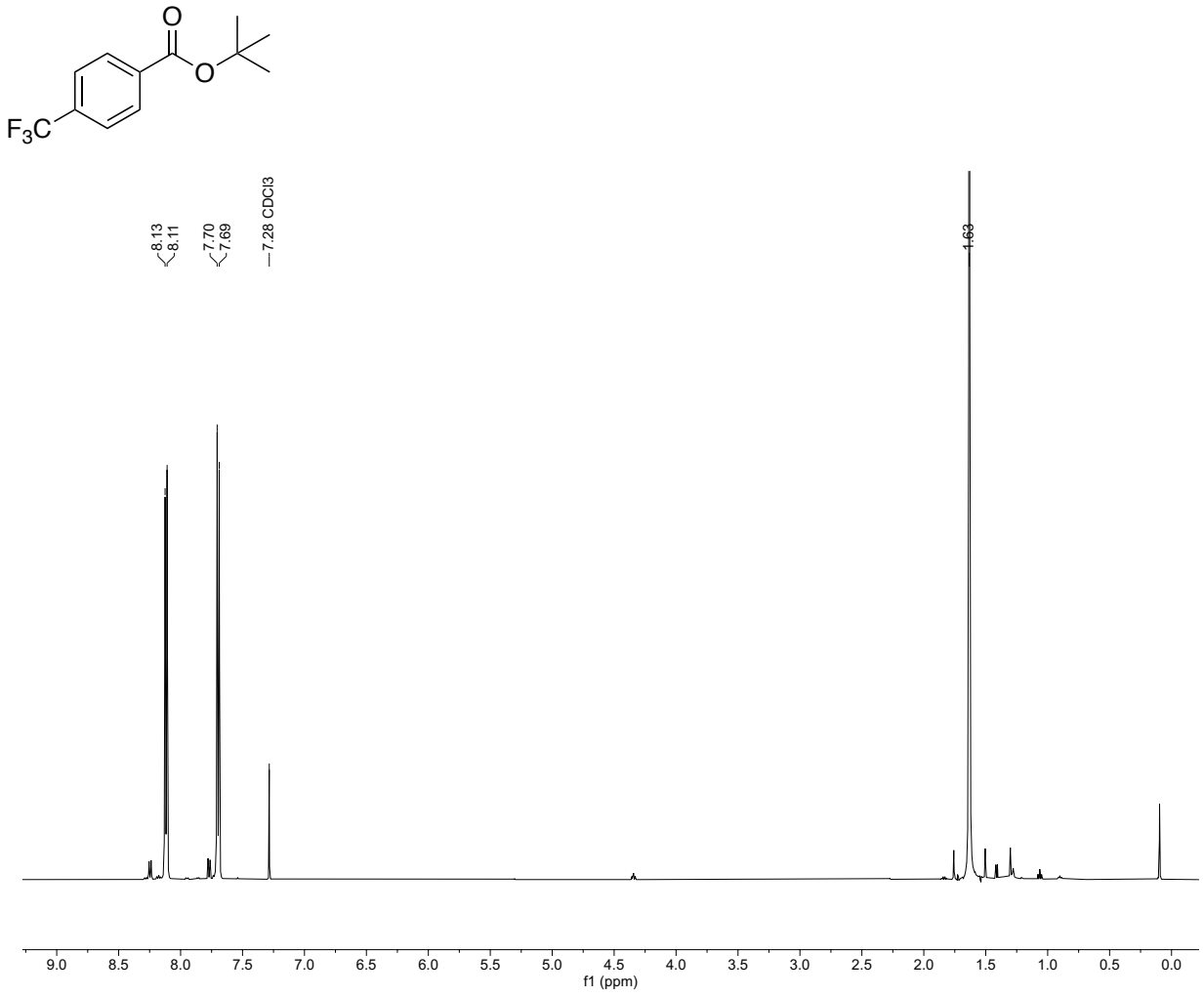
$^{11}B\{^{1}H\}$ NMR (128 MHz, $CDCl_3$)





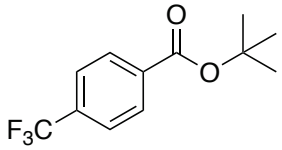
Compound 12a

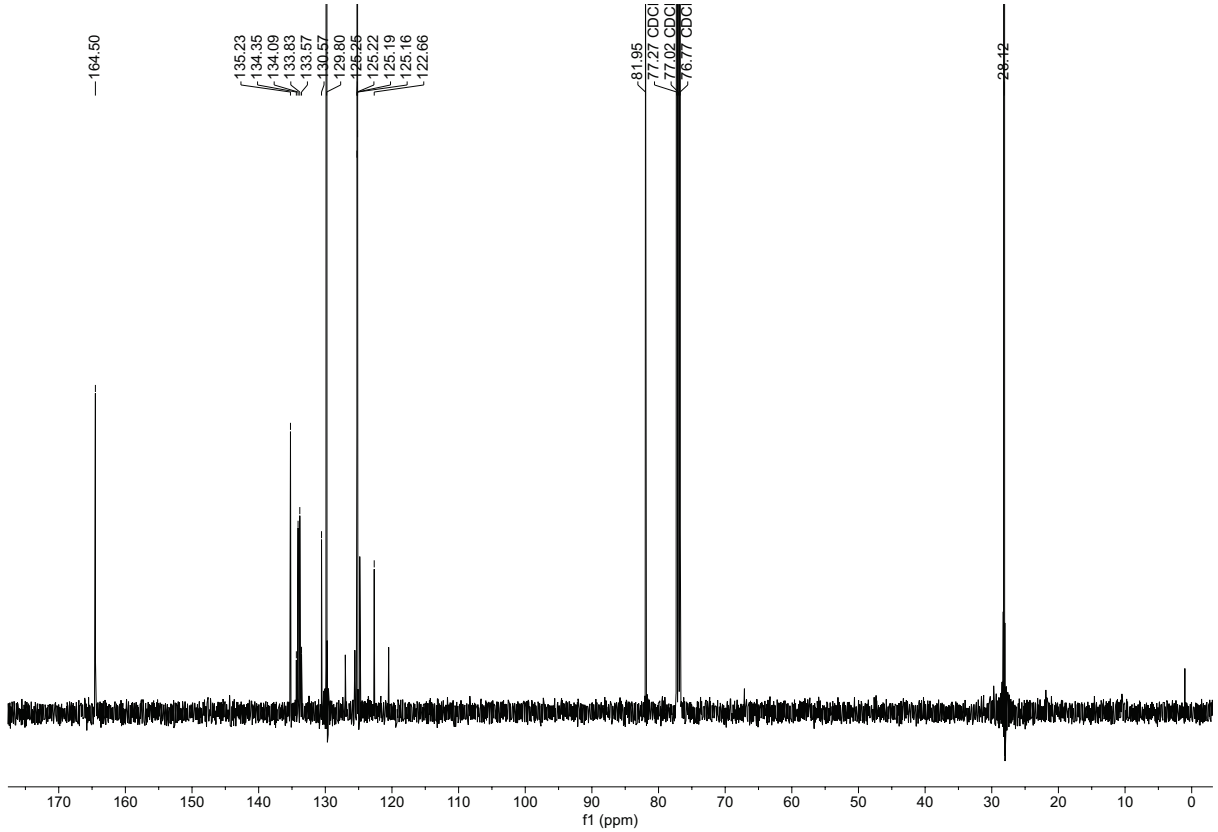
^{1}H NMR (500 MHz, $CDCl_3$)



Compound 12a

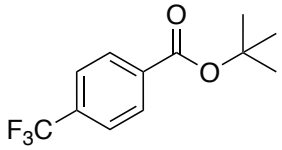
$^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$)

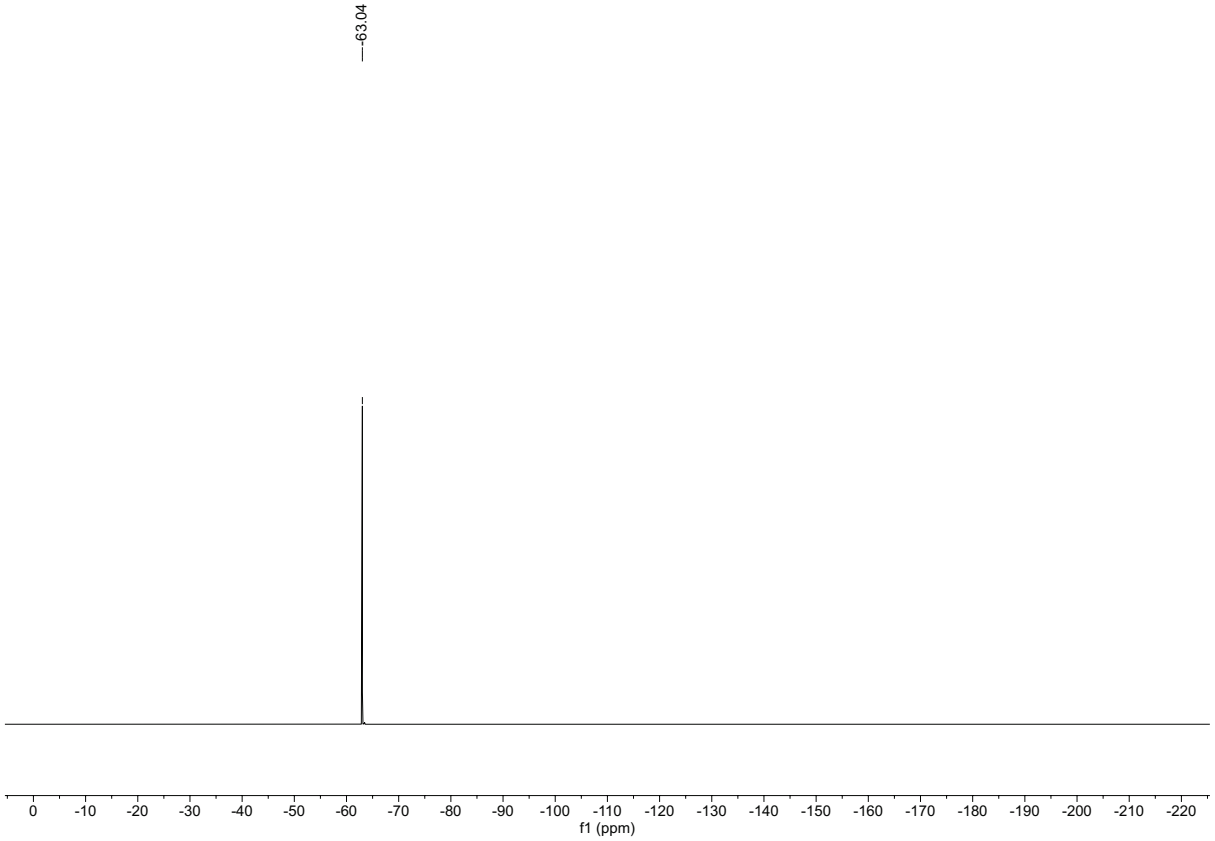




Compound 12a

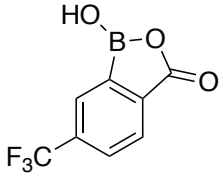
$^{19}F\{^{1}H\}$ NMR (471 MHz, $CDCl_3$)

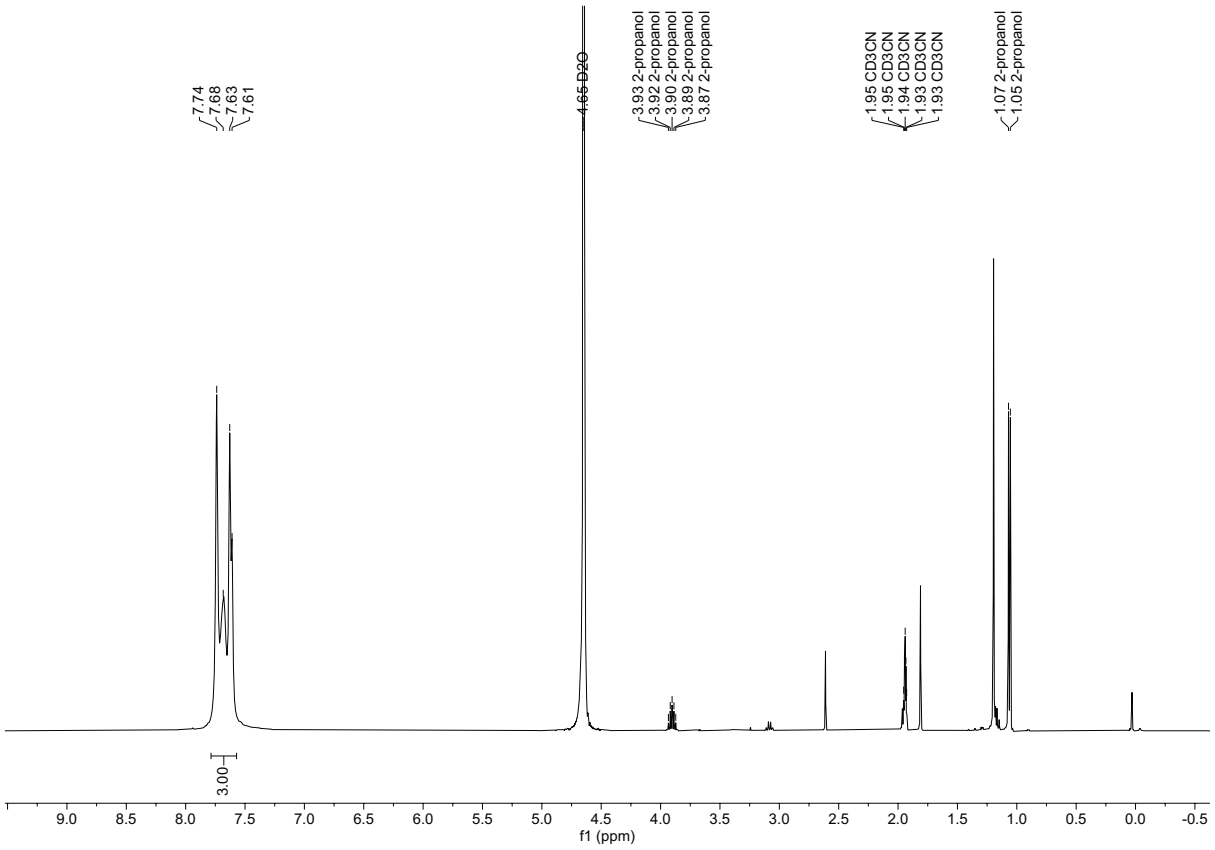




Compound 12b

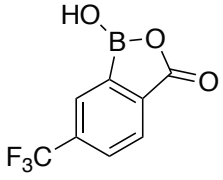
^{1}H NMR (400 MHz, D_2O/CD_3CN)

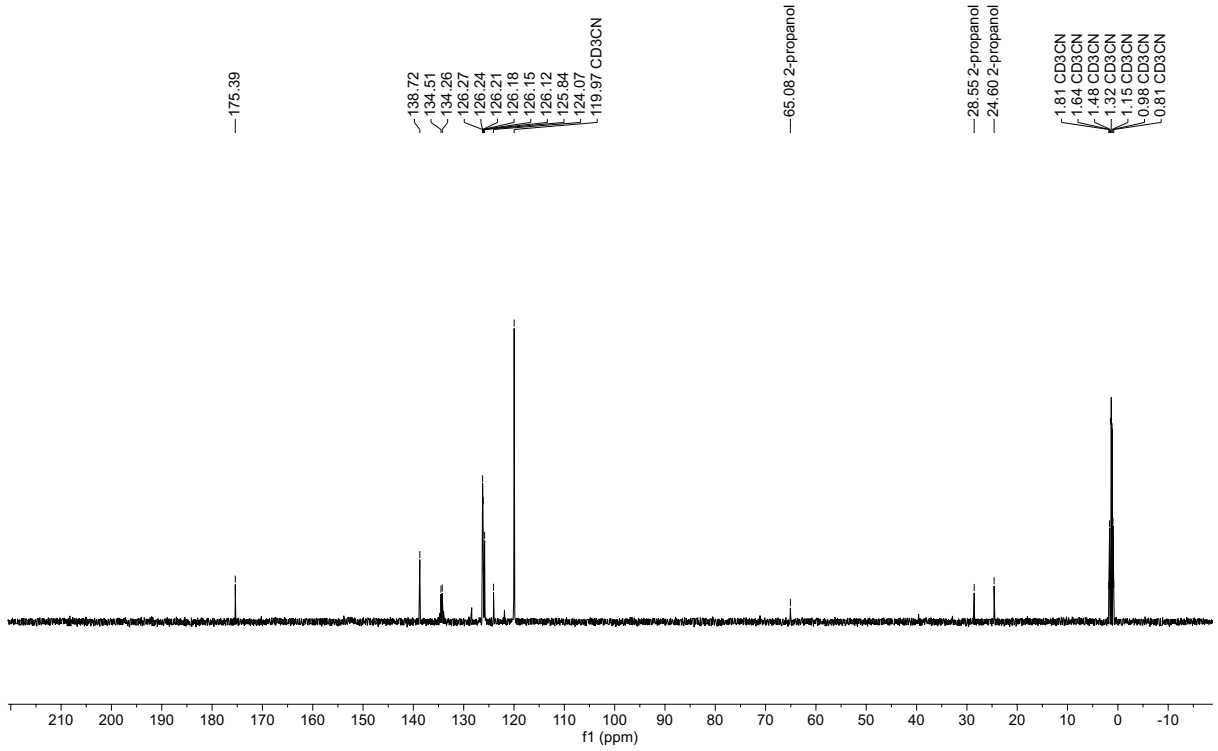




Compound 12b

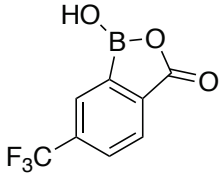
$^{13}C\{^{1}H\}$ NMR (126 MHz, D_2O/CD_3CN)

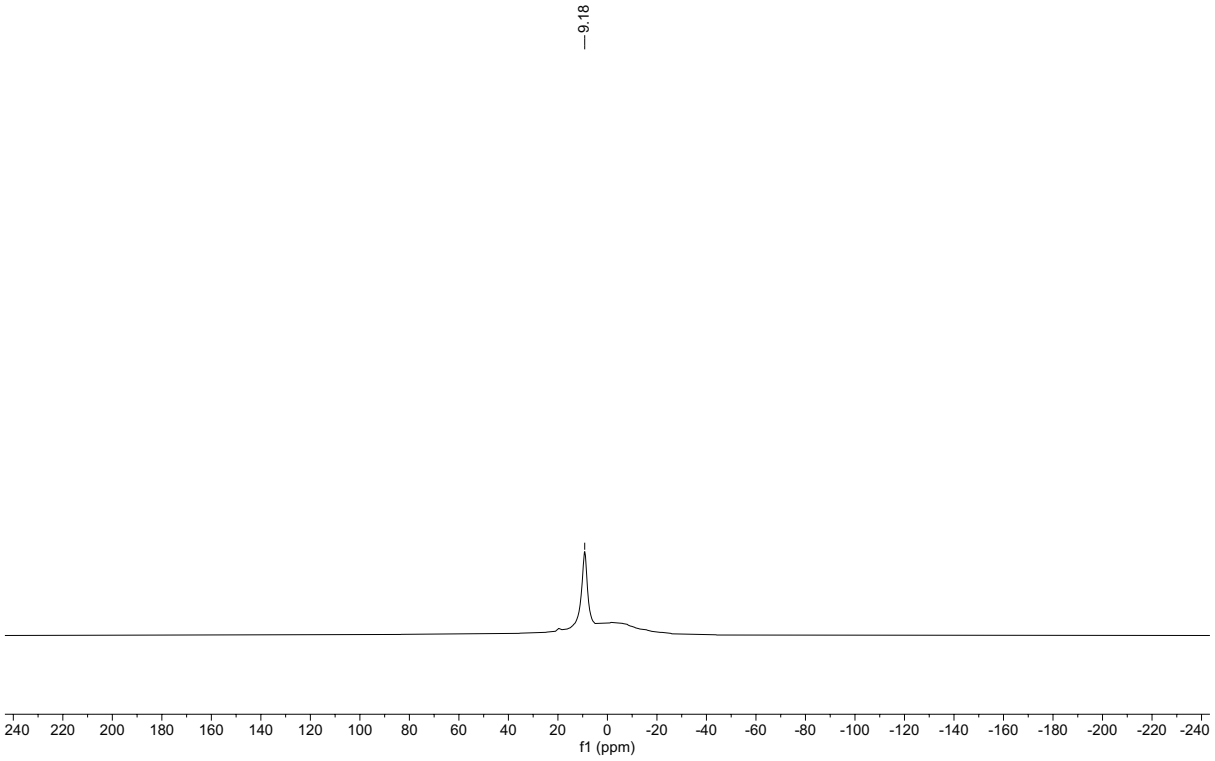




Compound 12b

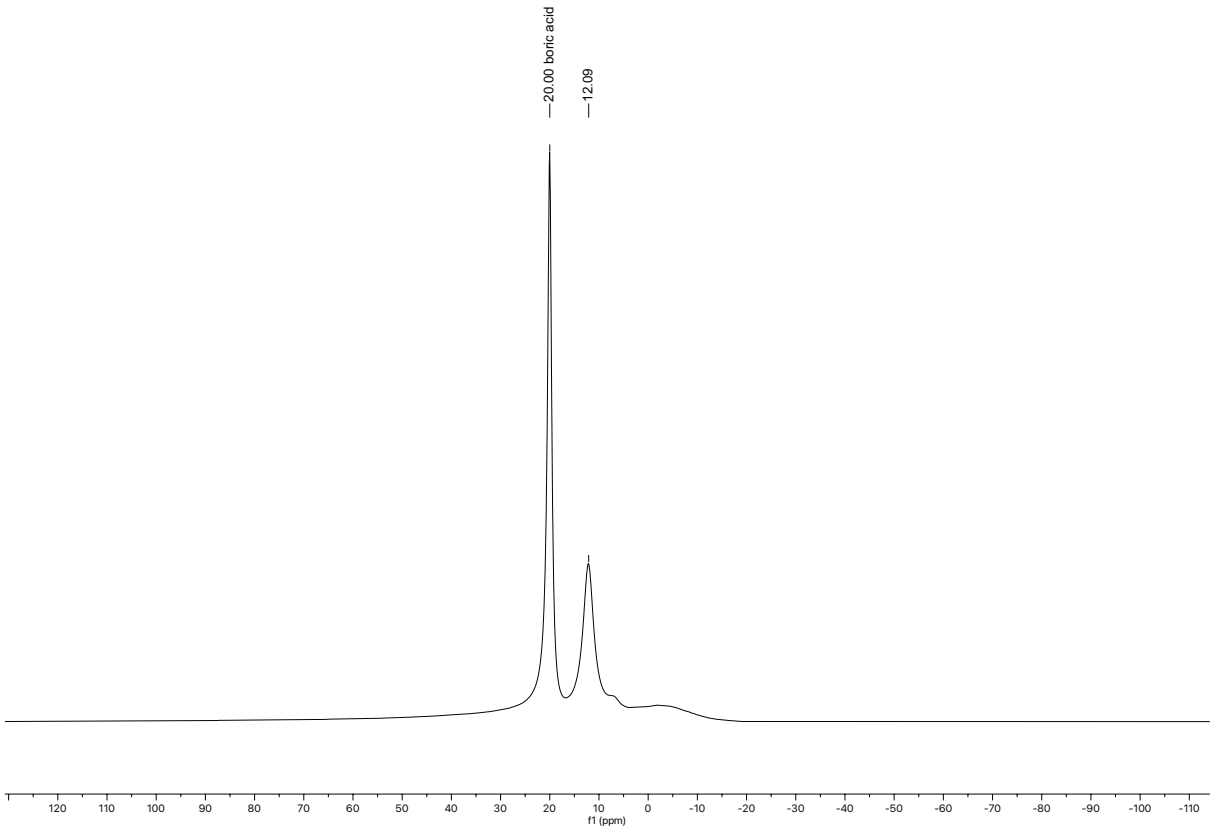
$^{11}B\{^{1}H\}$ NMR (128 MHz, D_2O/CD_3CN)





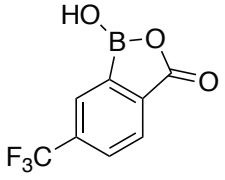
Compound 12b

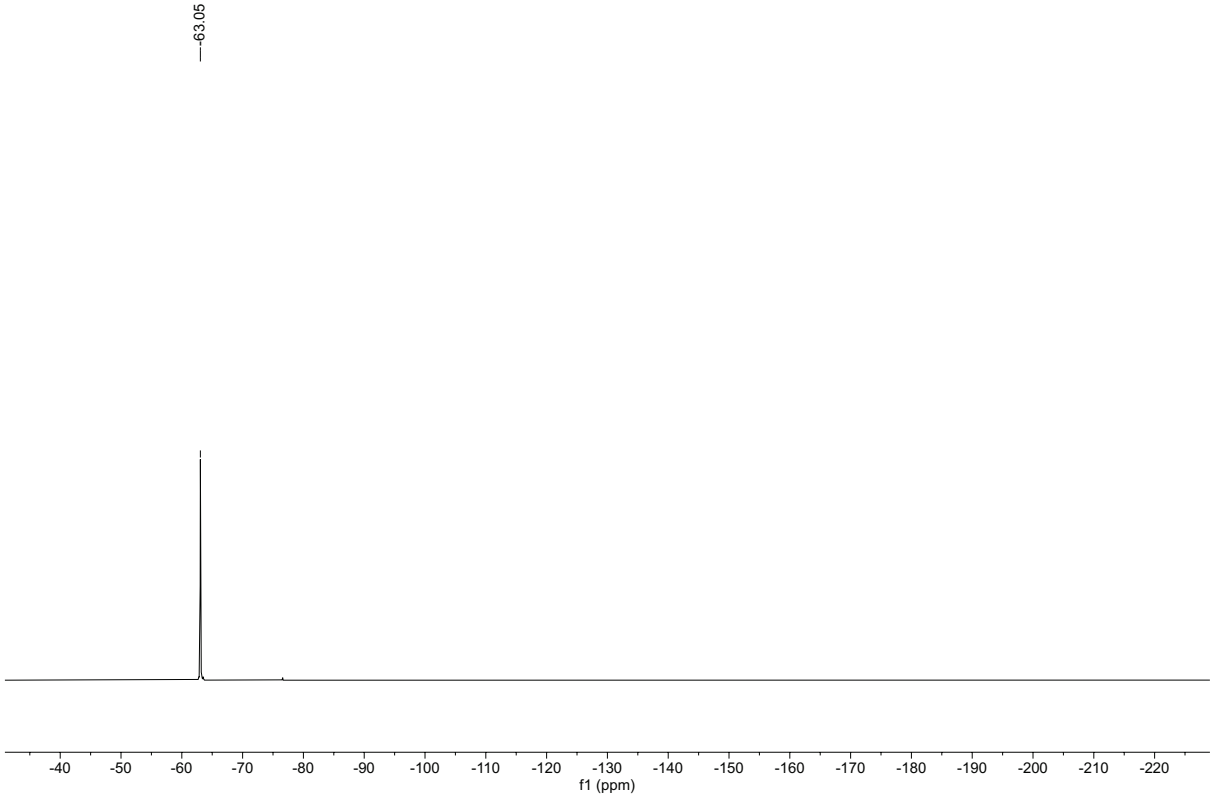
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 12b

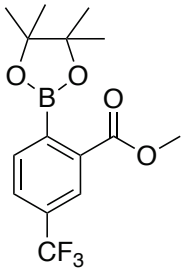
$^{19}F\{^{1}H\}$ NMR (376 MHz, D_2O/CD_3CN)

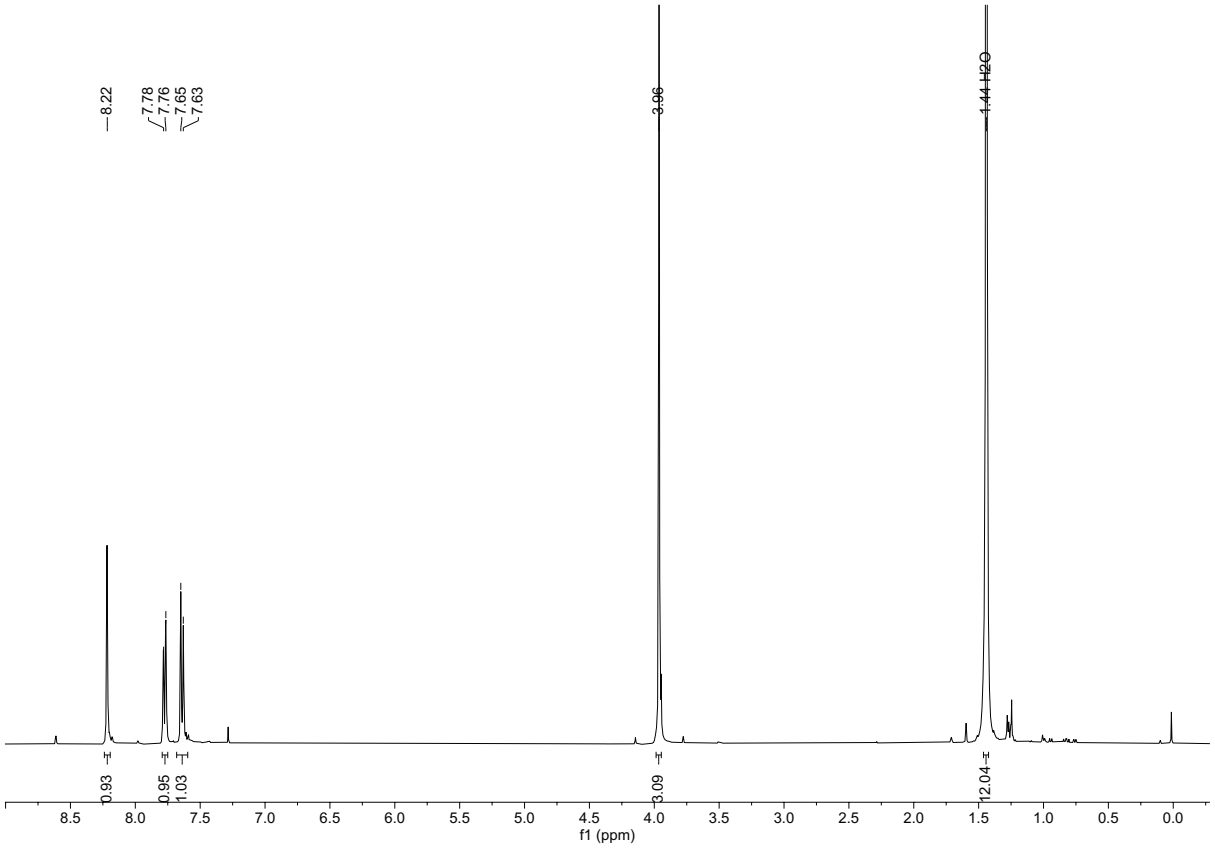




Compound 13a

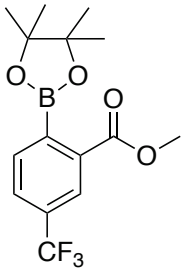
^{1}H NMR (400 MHz, $CDCl_3$)

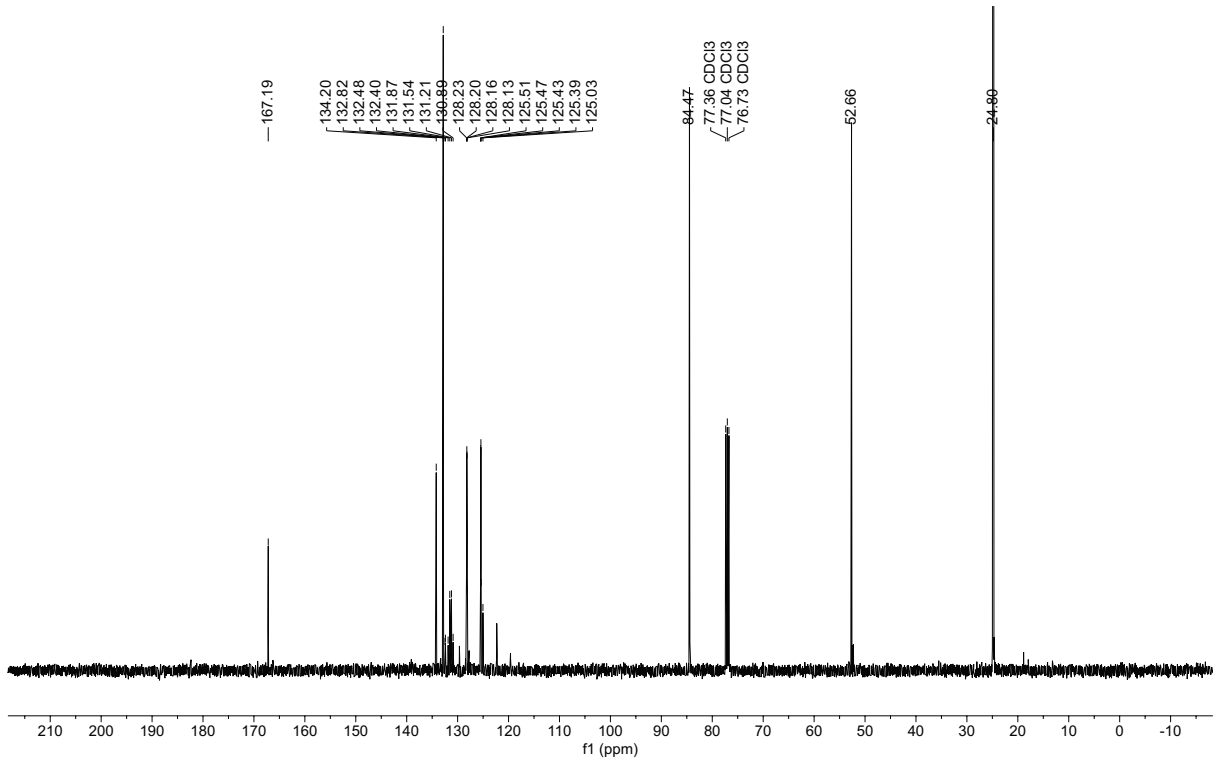




Compound 13a

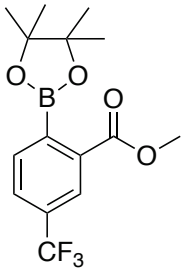
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

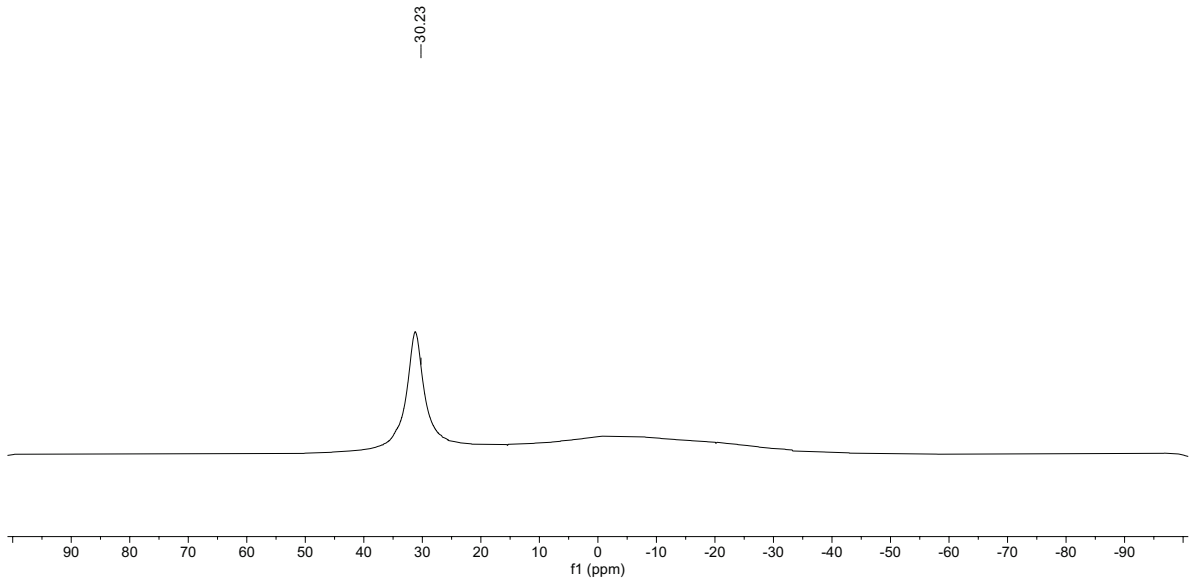




Compound 13a

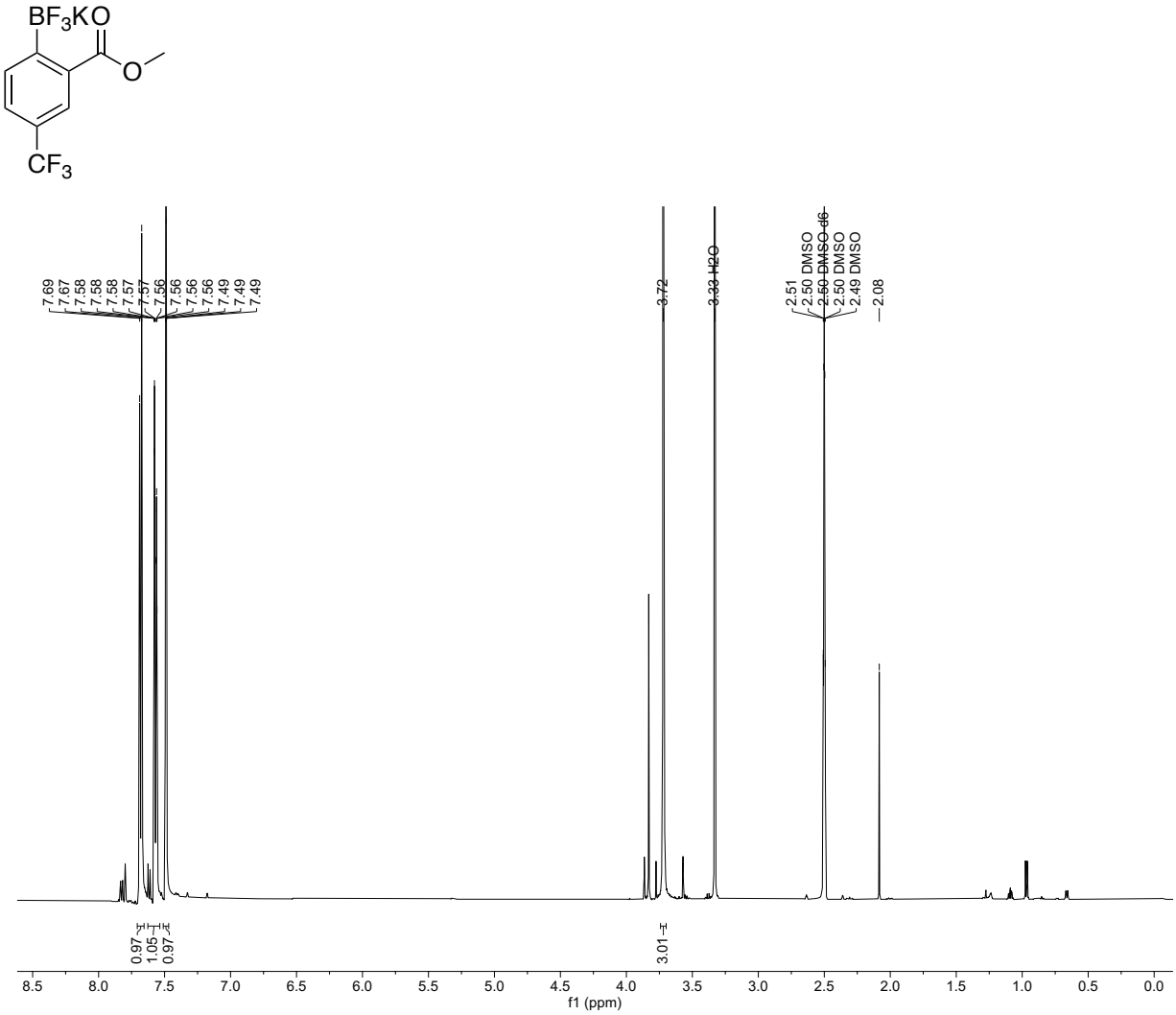
$^{11}B\{^{1}H\}$ NMR (128 MHz, $CDCl_3$)





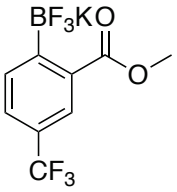
Compound 13b

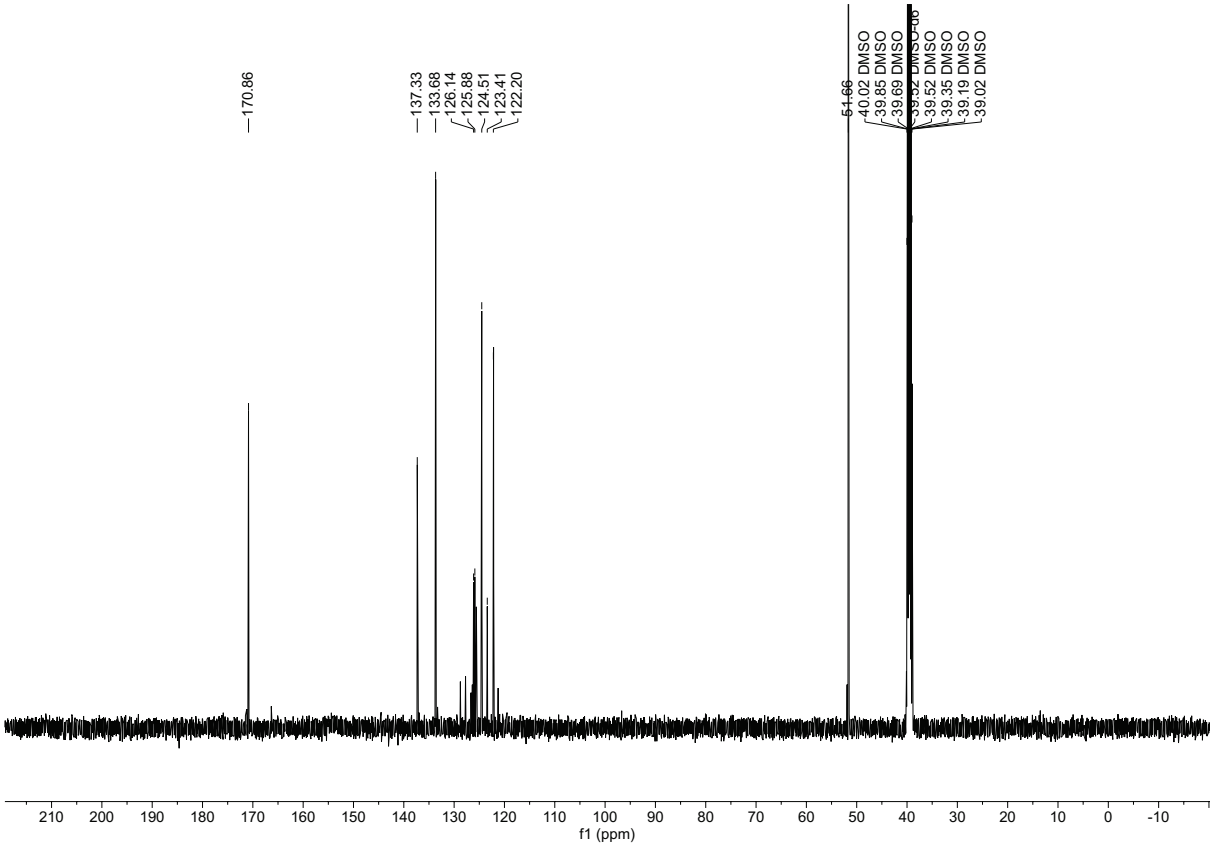
^{1}H NMR (500 MHz, DMSO)



Compound 13b

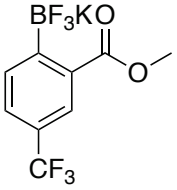
$^{13}C\{^{1}H\}$ NMR (126 MHz, DMSO)

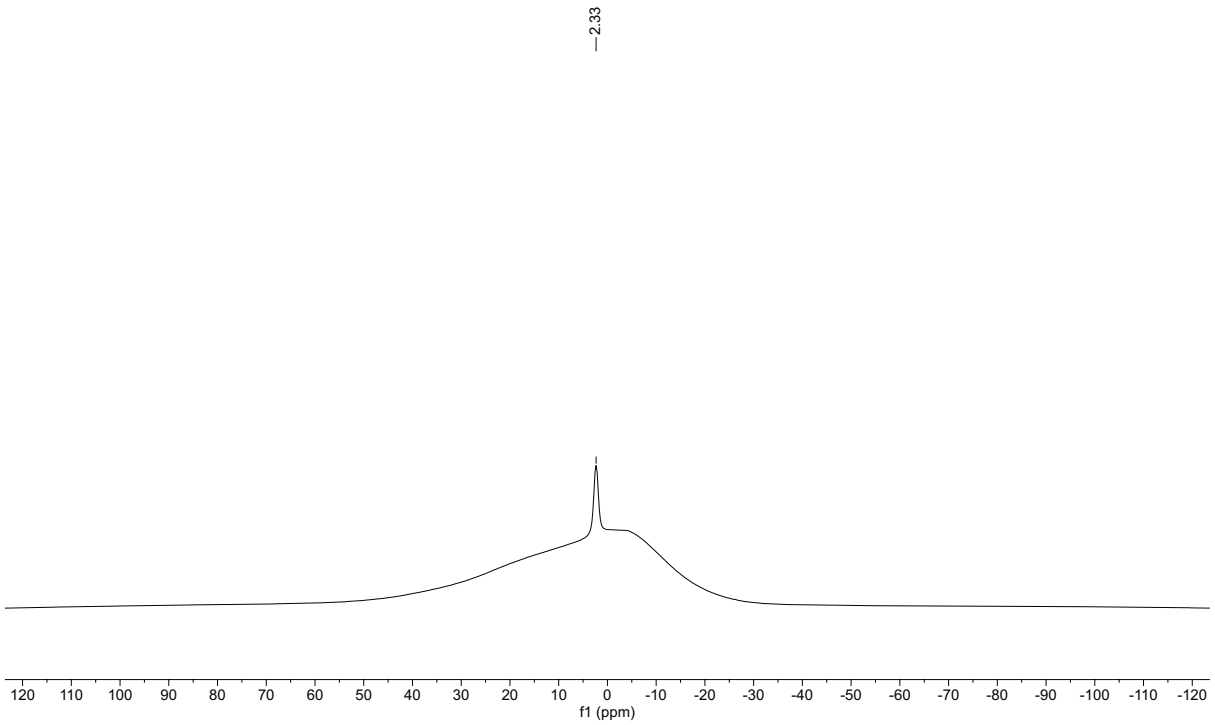




Compound 13b

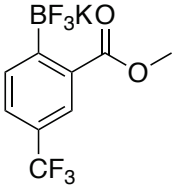
$^{11}B\{^{1}H\}$ NMR (160 MHz, DMSO)

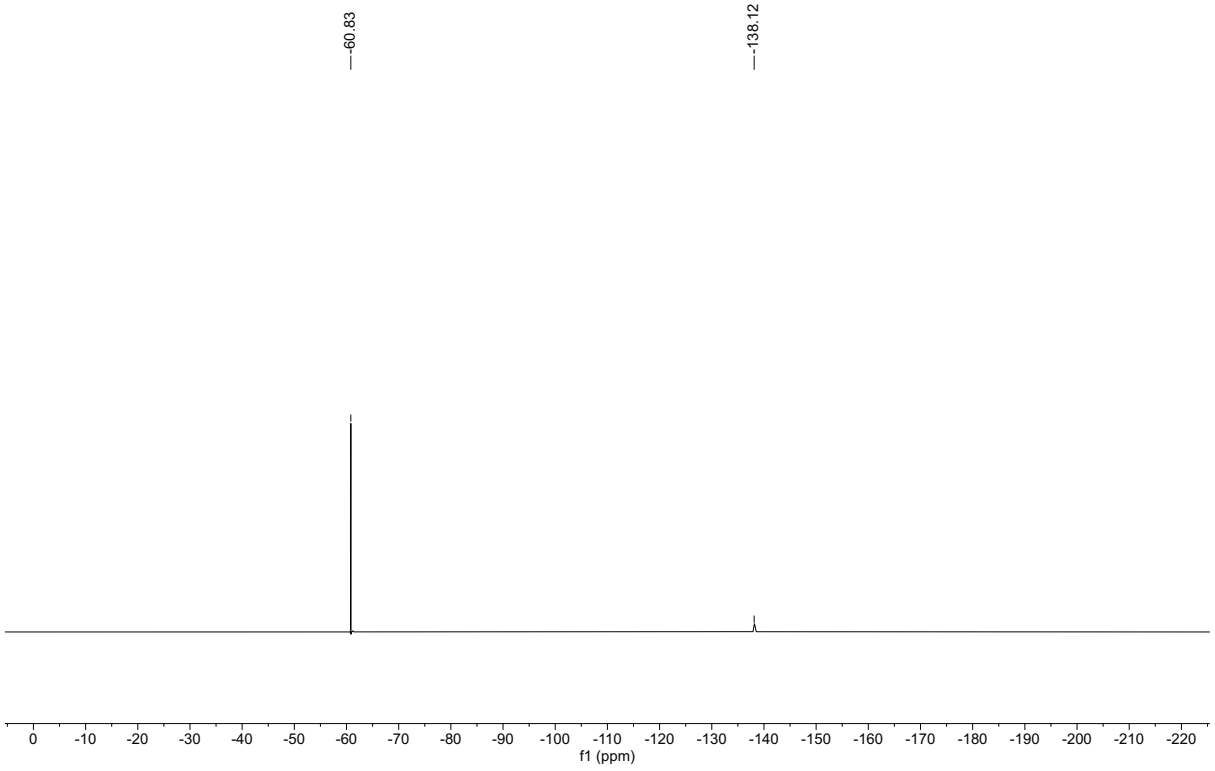




Compound 13b

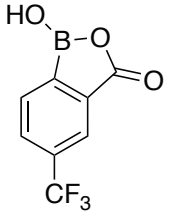
$^{19}F\{^{1}H\}$ NMR (471 MHz, DMSO)

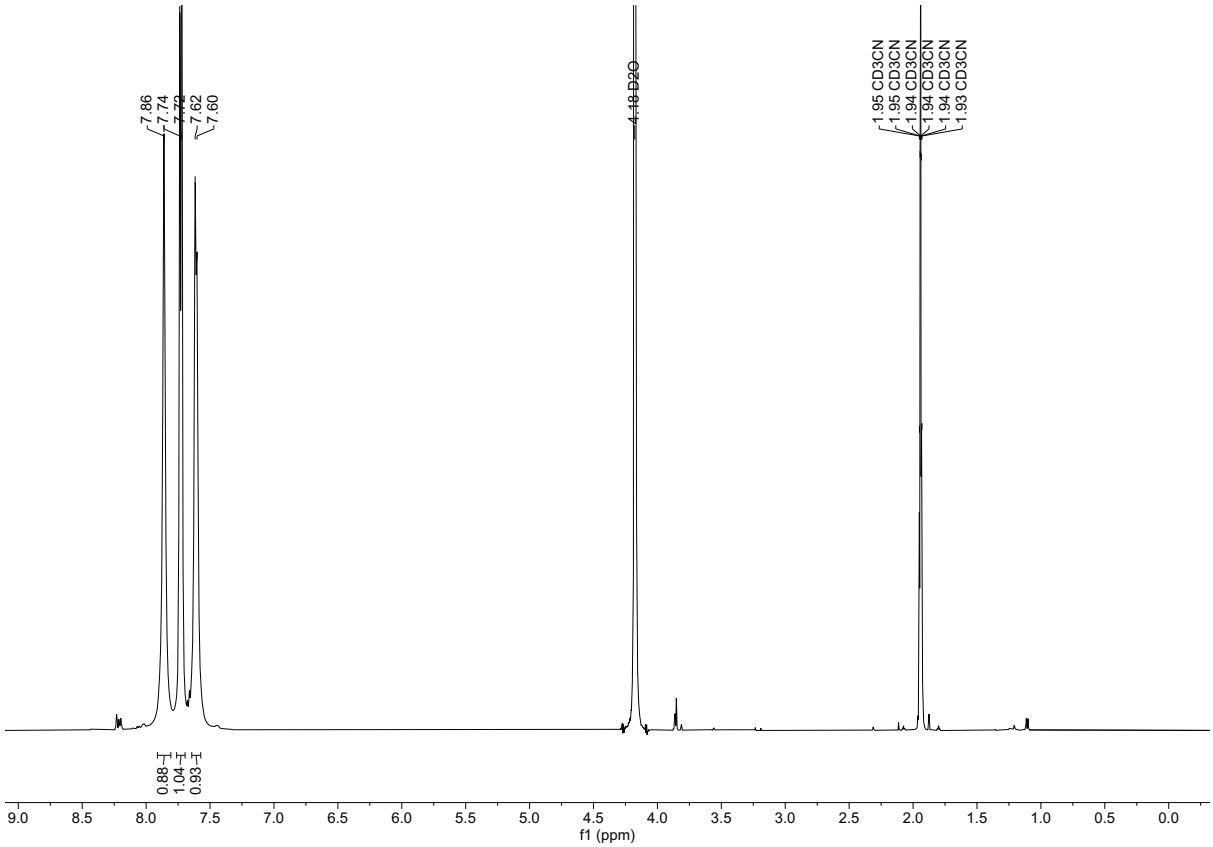




Compound 13c

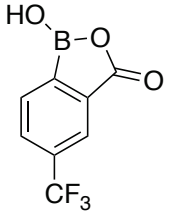
^{1}H NMR (500 MHz, D_2O/CD_3CN)

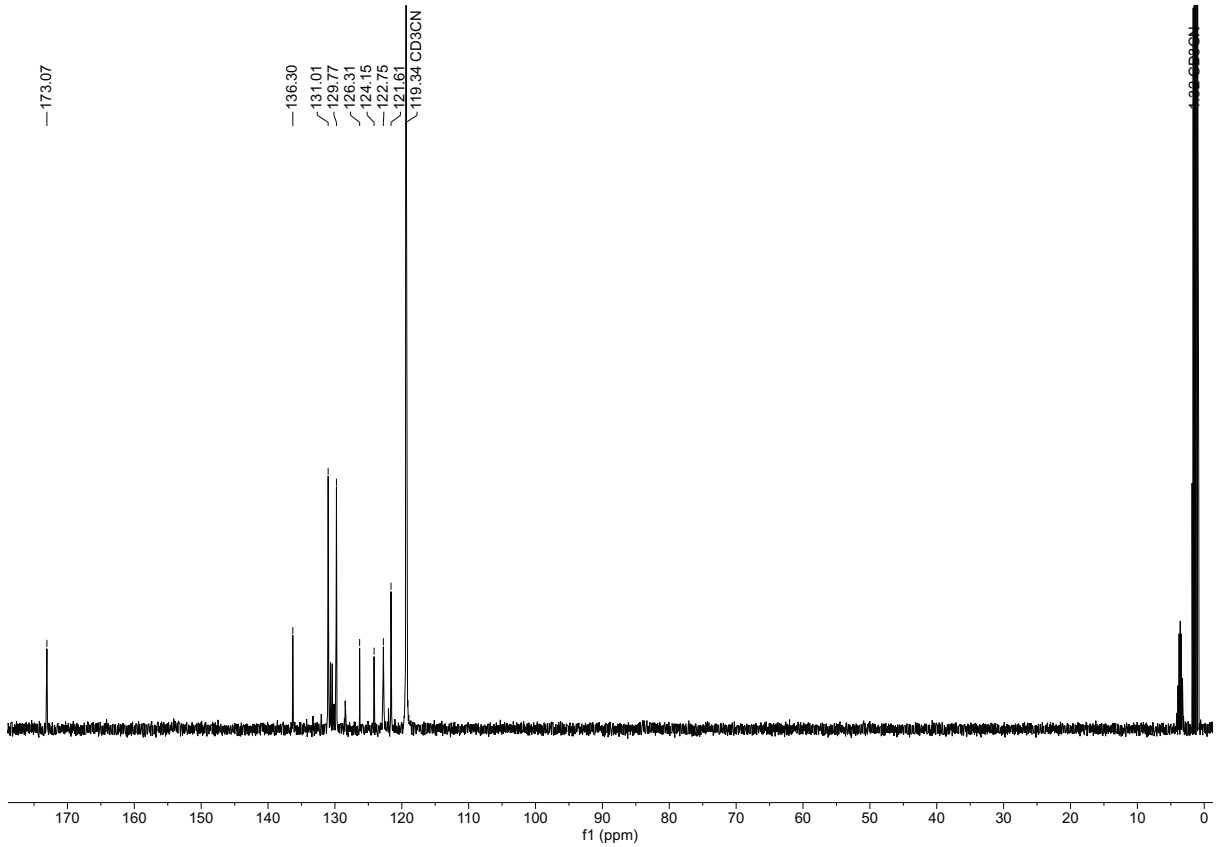




Compound 13c

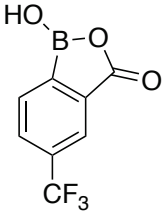
$^{13}C\{^{1}H\}$ NMR (126 MHz, D_2O/CD_3CN)

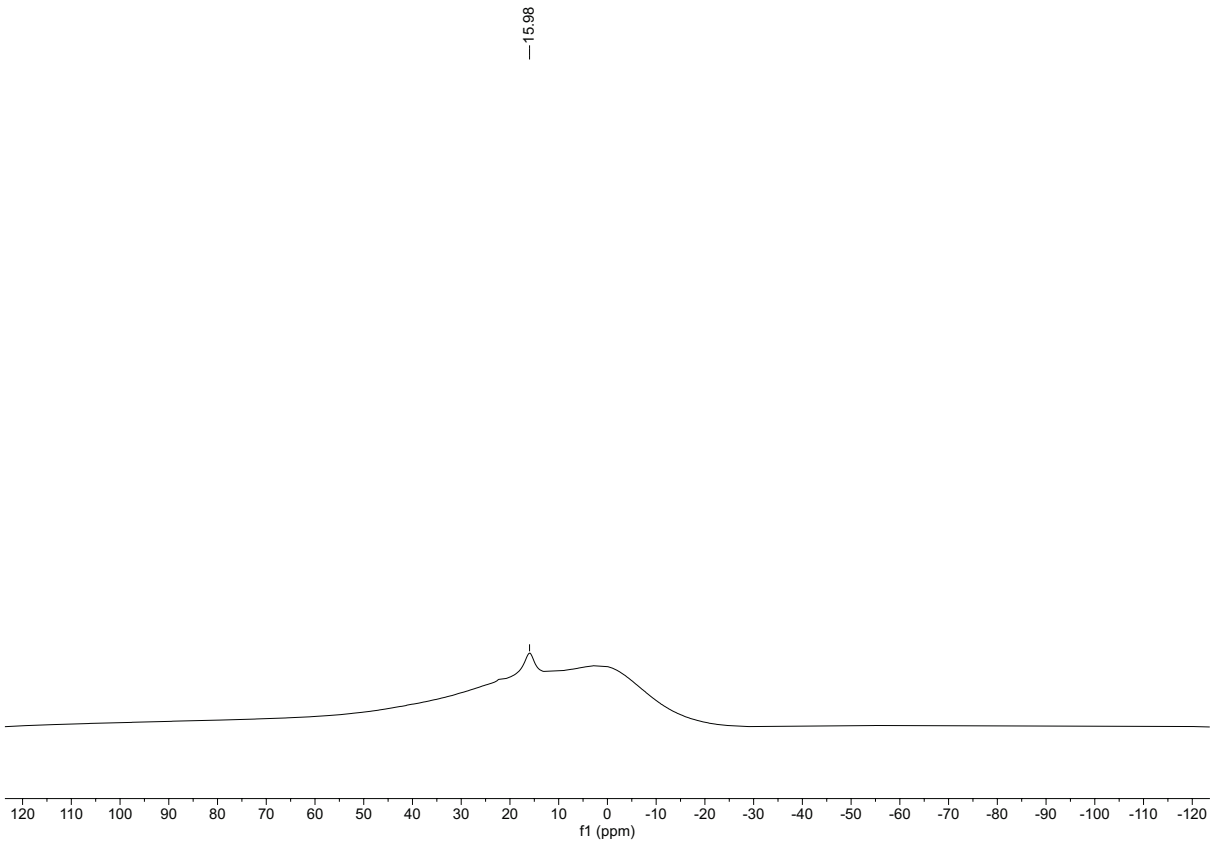




Compound 13c

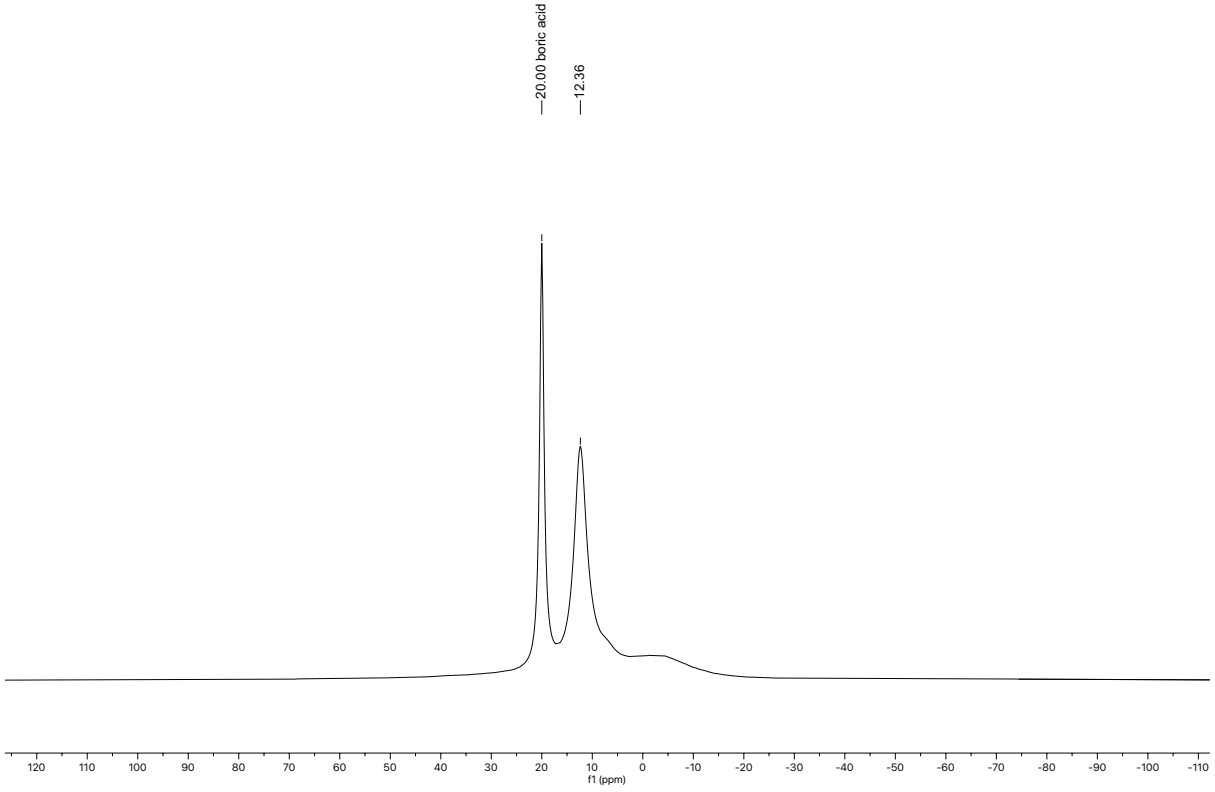
$^{11}B\{^{1}H\}$ NMR (160 MHz, D_2O/CD_3CN)





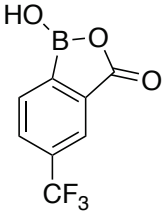
Compound 13c

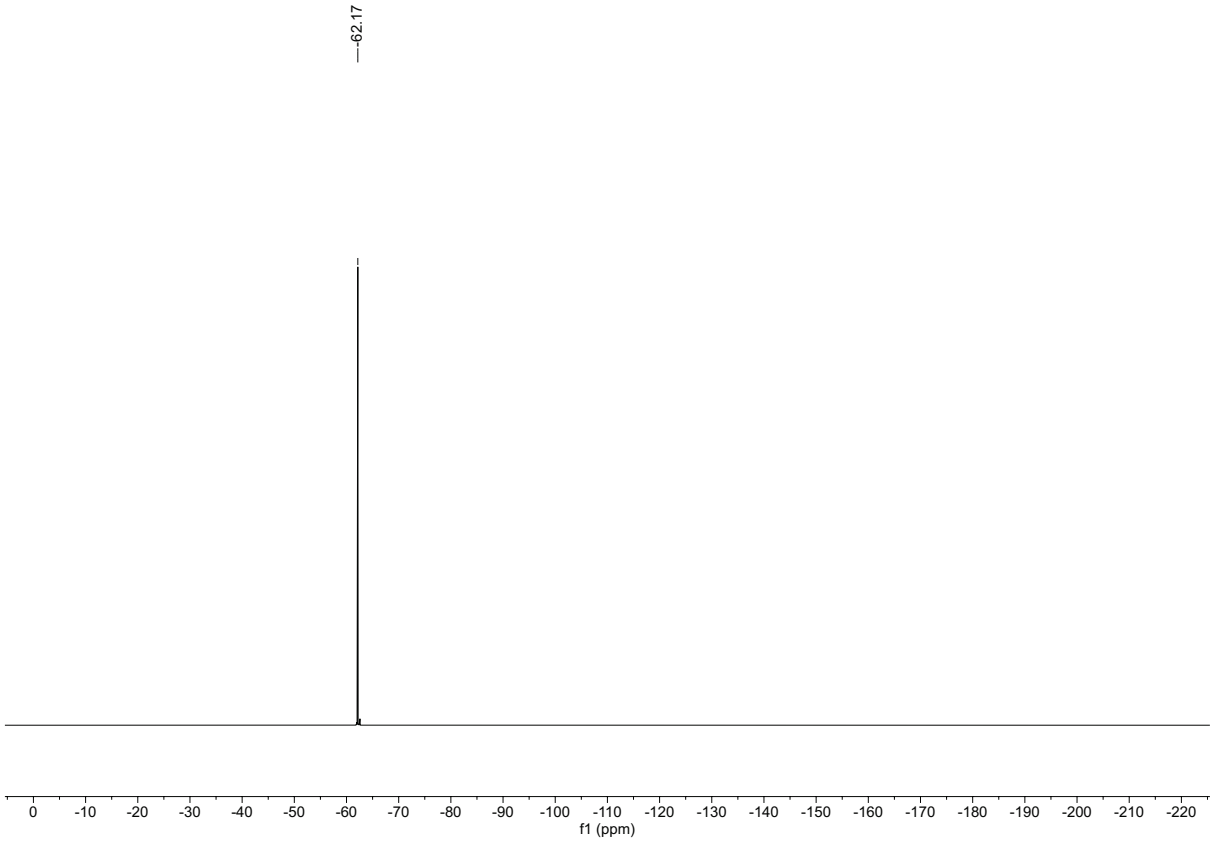
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 13c

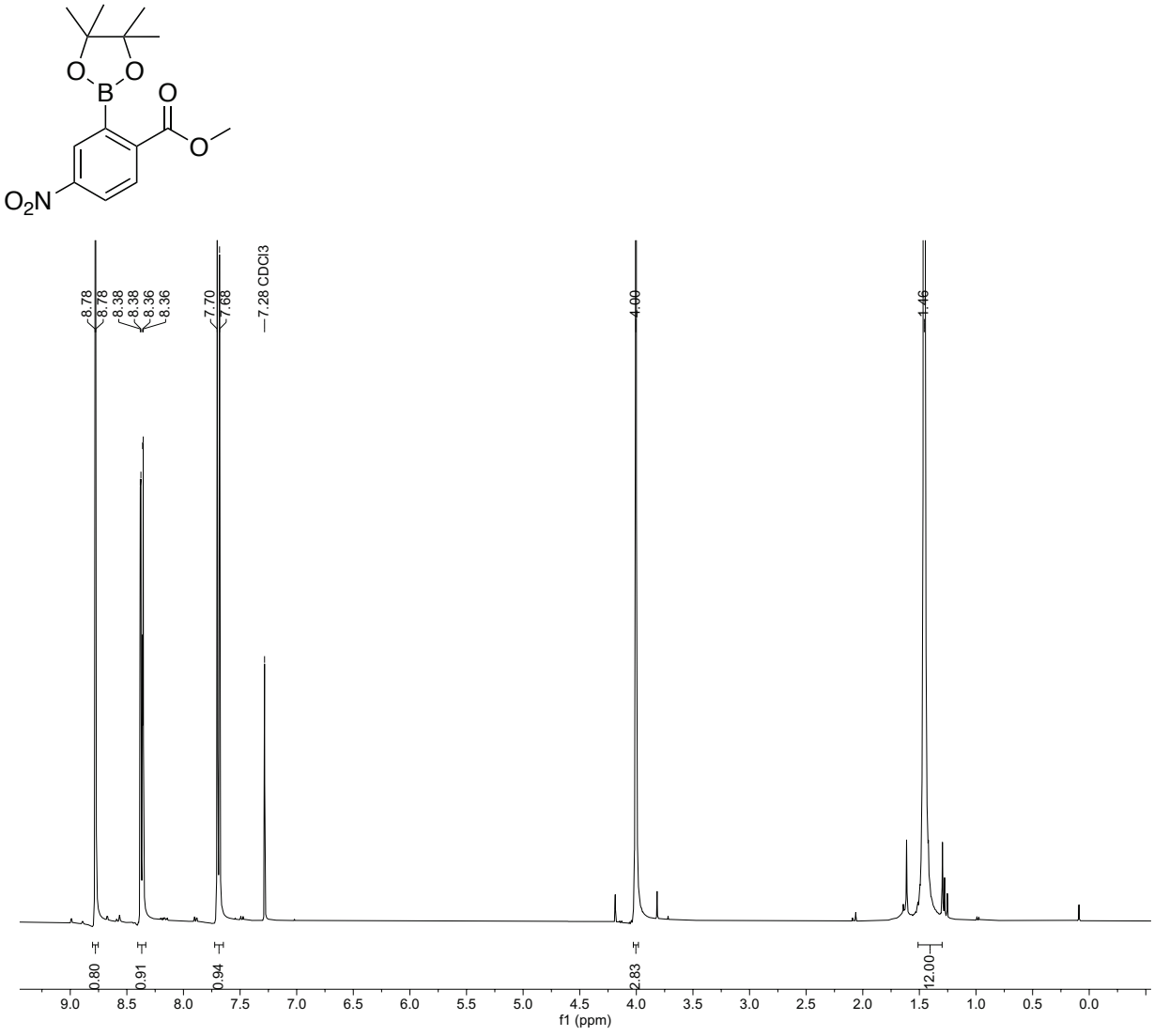
$^{19}F\{^{1}H\}$ NMR (471 MHz, D_2O/CD_3CN)





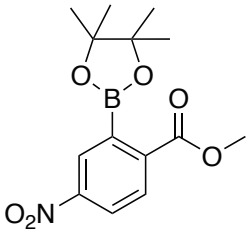
Compound 14a

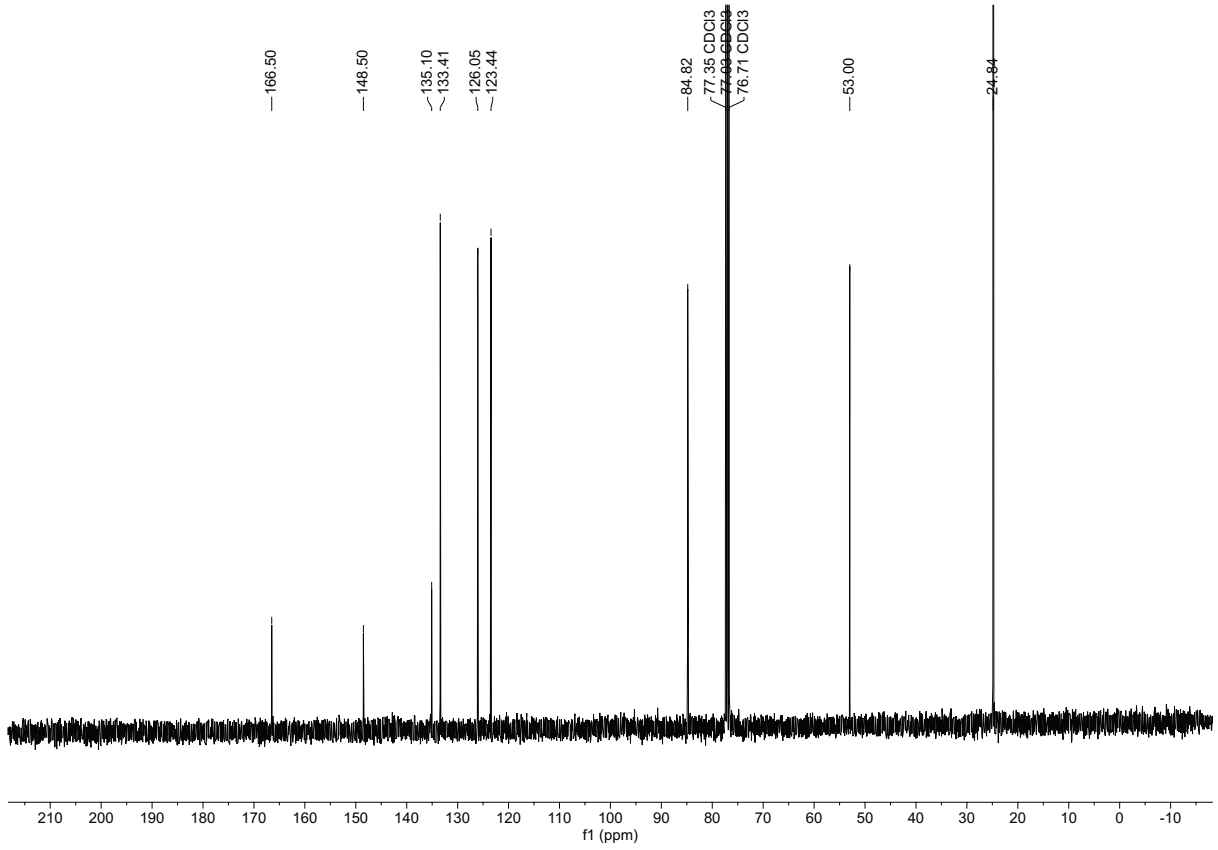
^{1}H NMR (400 MHz, $CDCl_3$)



Compound 14a

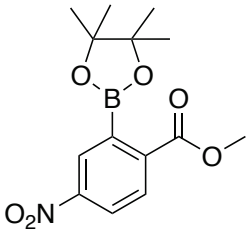
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

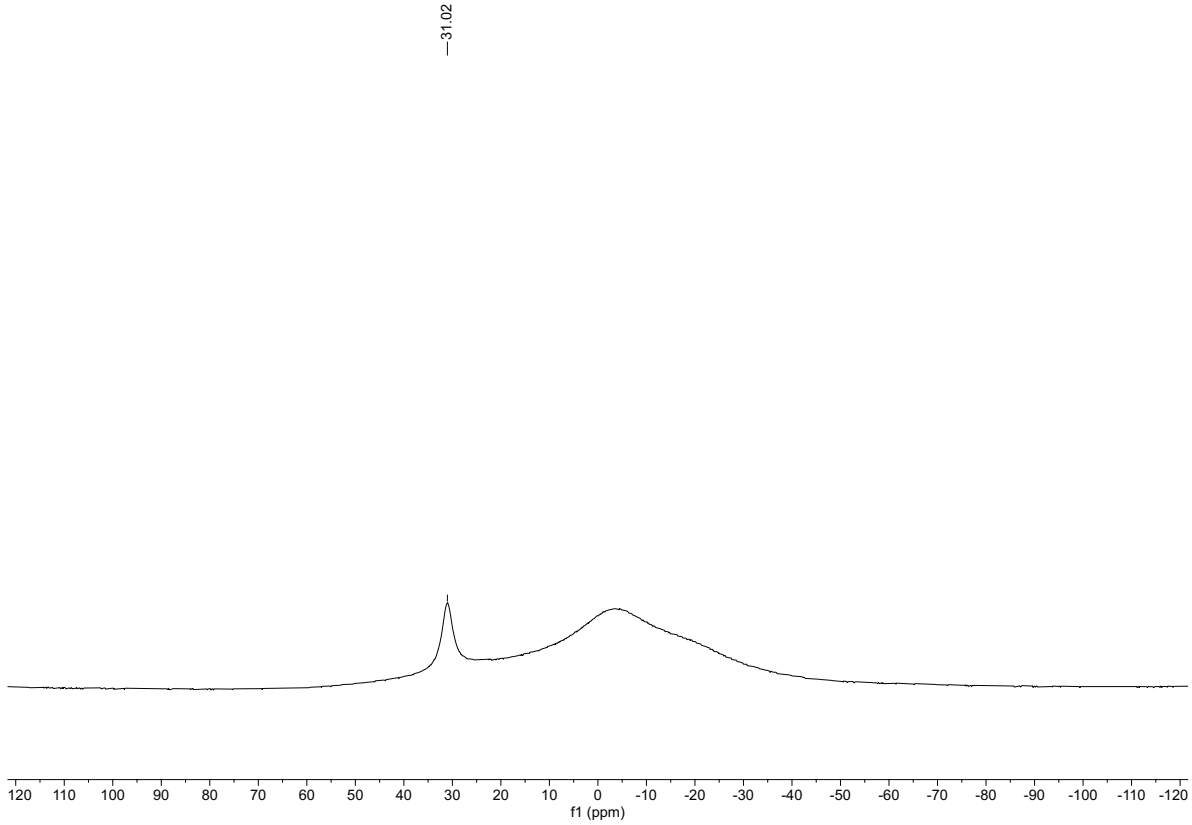




Compound 14a

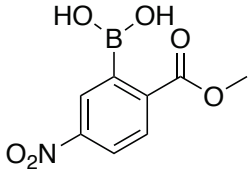
$^{11}B\{^{1}H\}$ NMR (128 MHz, $CDCl_3$)

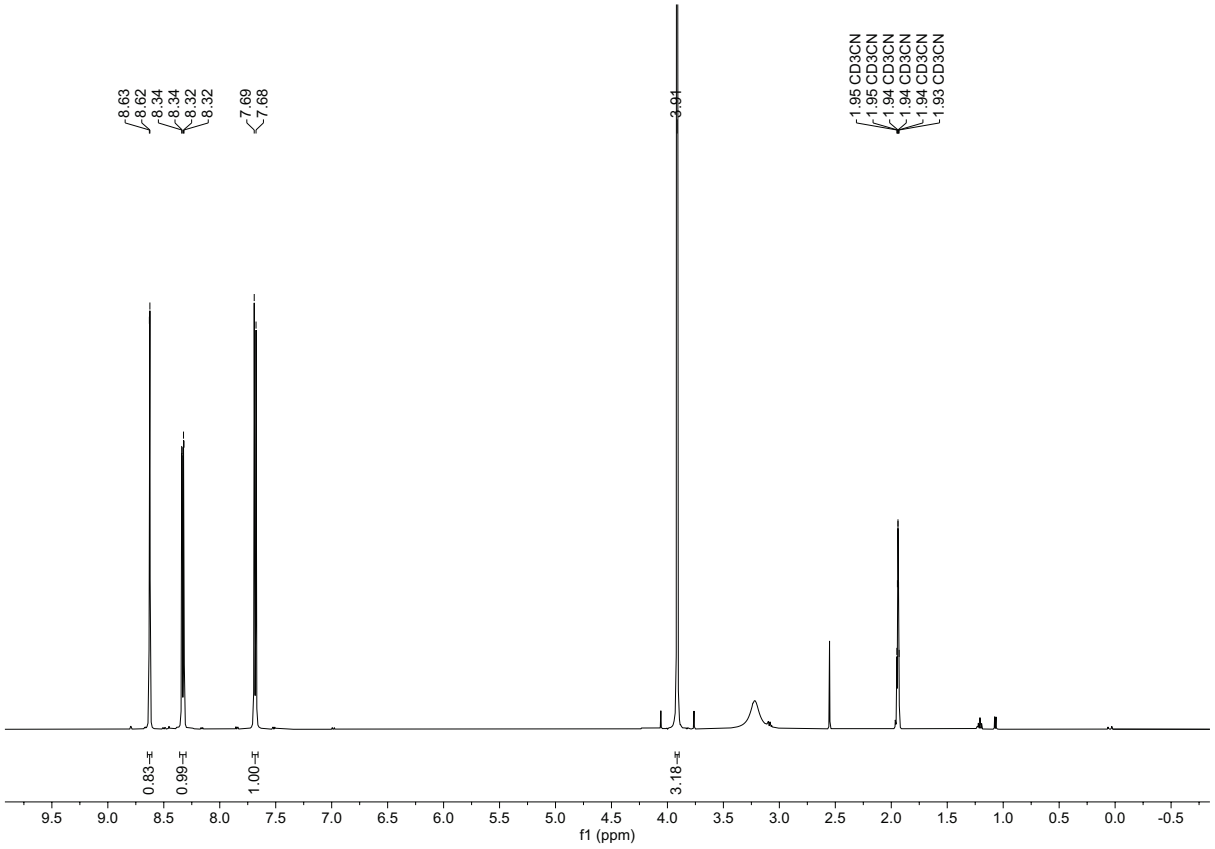




Compound 14b

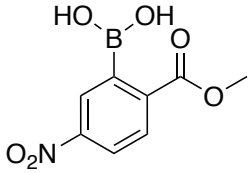
^{1}H NMR (500 MHz, CD_3CN)

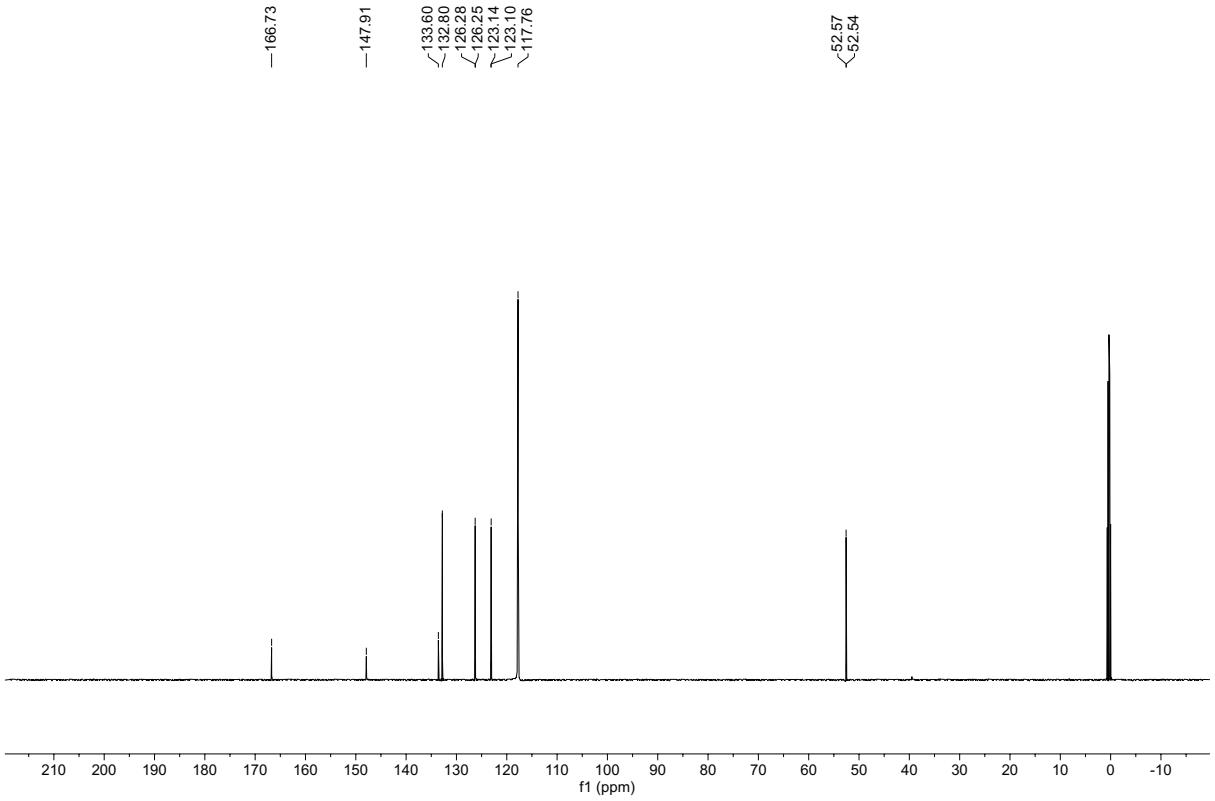




Compound 14b

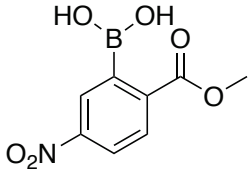
$^{13}C\{^{1}H\}$ NMR (126 MHz, CD_3CN)

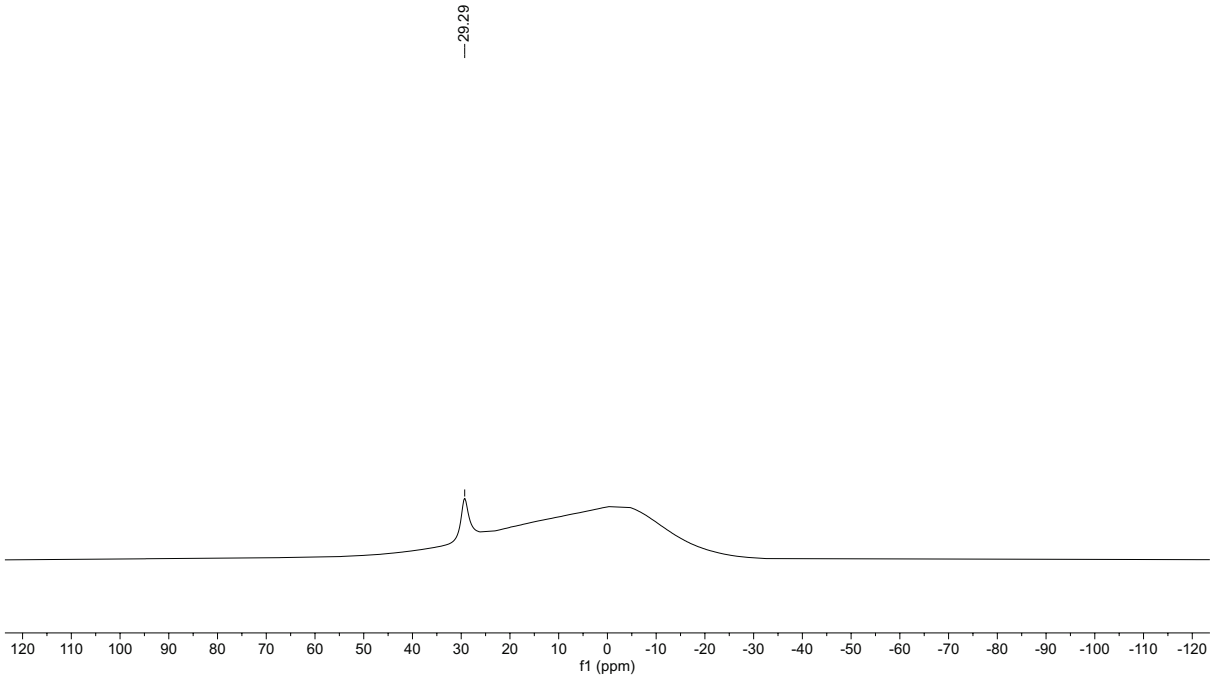




Compound 14b

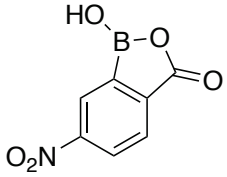
$^{11}B\{^{1}H\}$ NMR (160 MHz, CD_3CN)

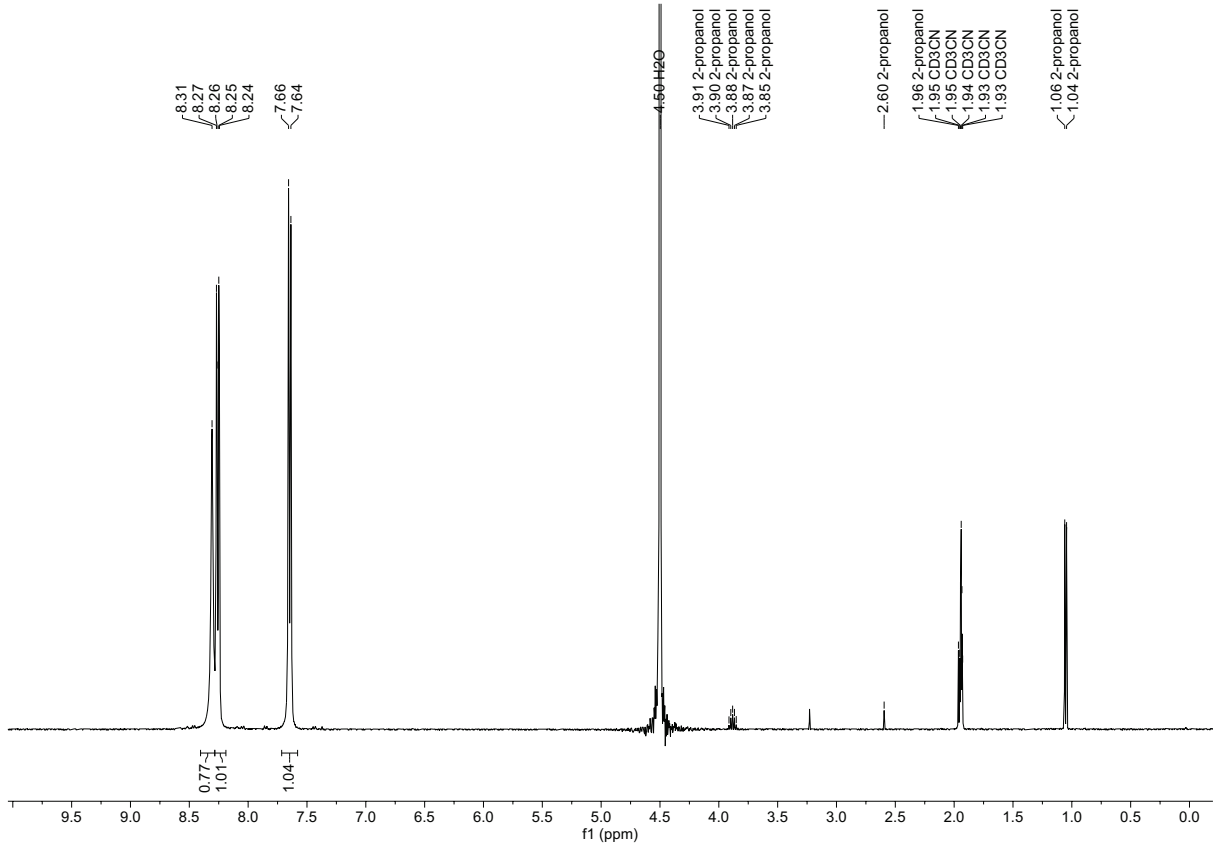




Compound 14c

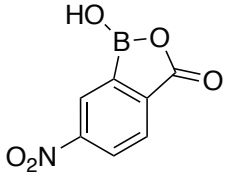
^{1}H NMR (400 MHz, CD_3CN/D_2O)

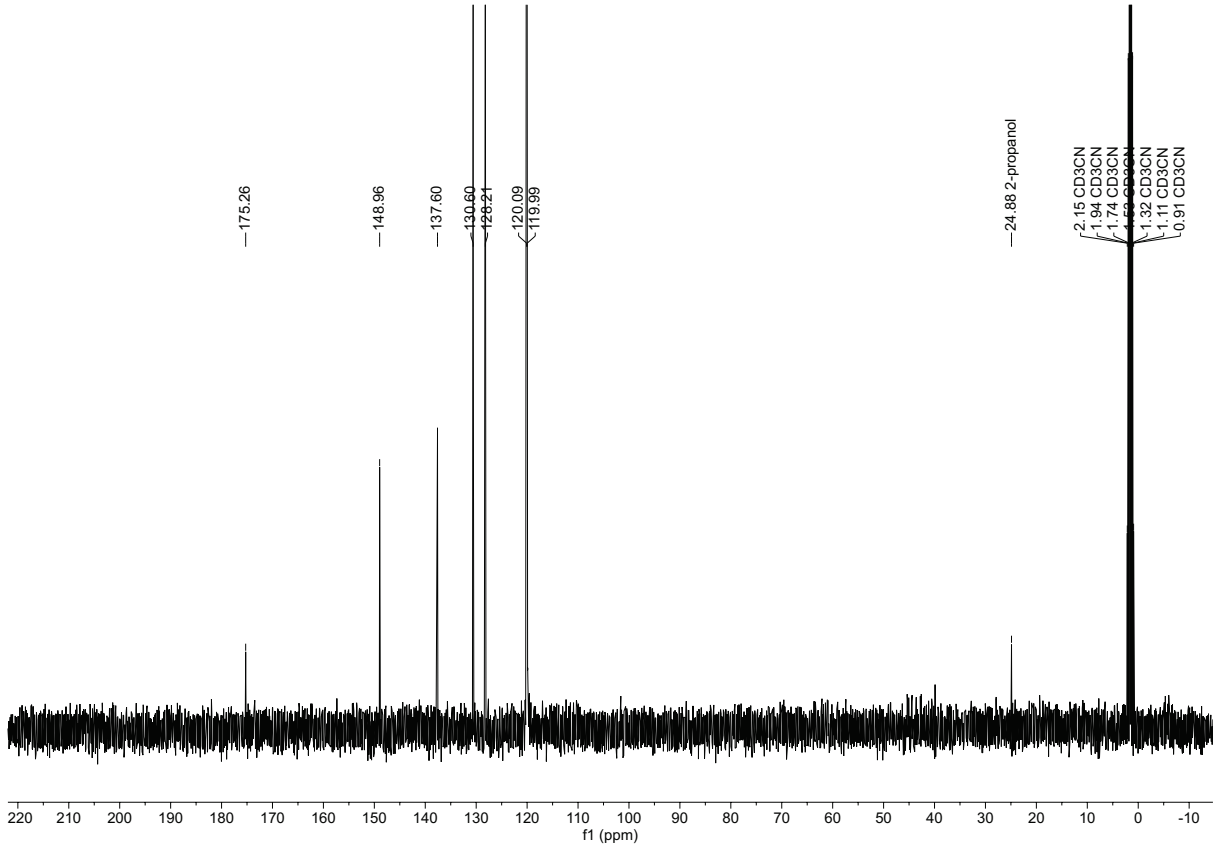




Compound 14c

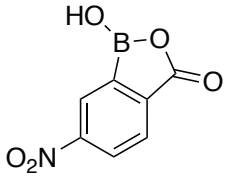
$^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3CN/D_2O)

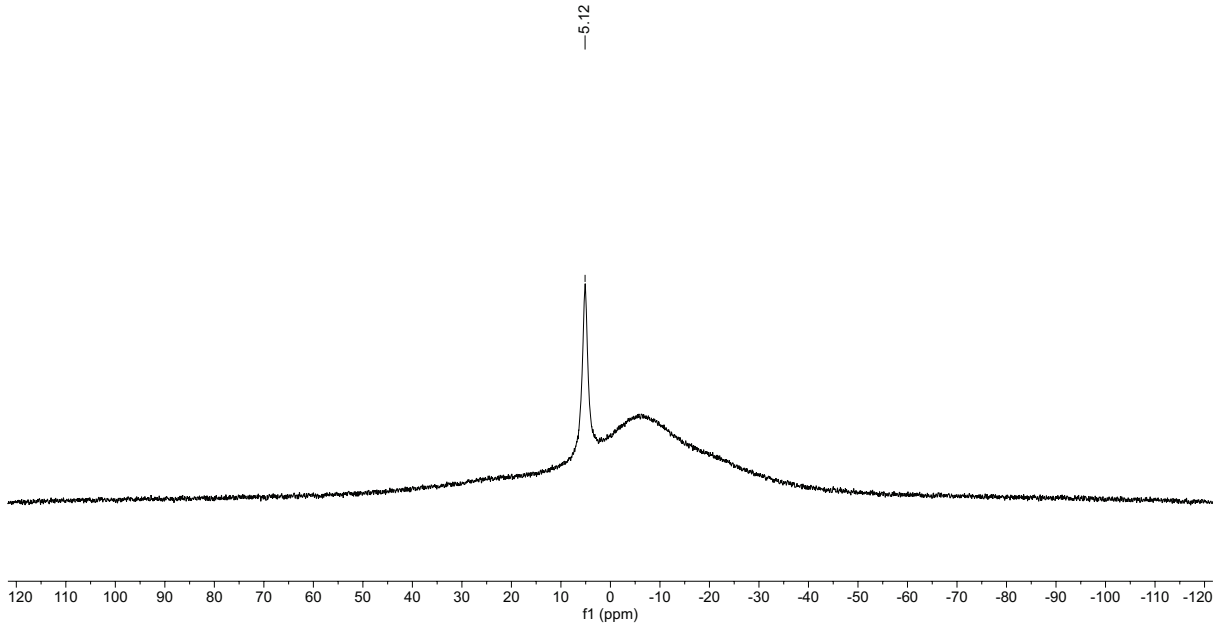




Compound 14c

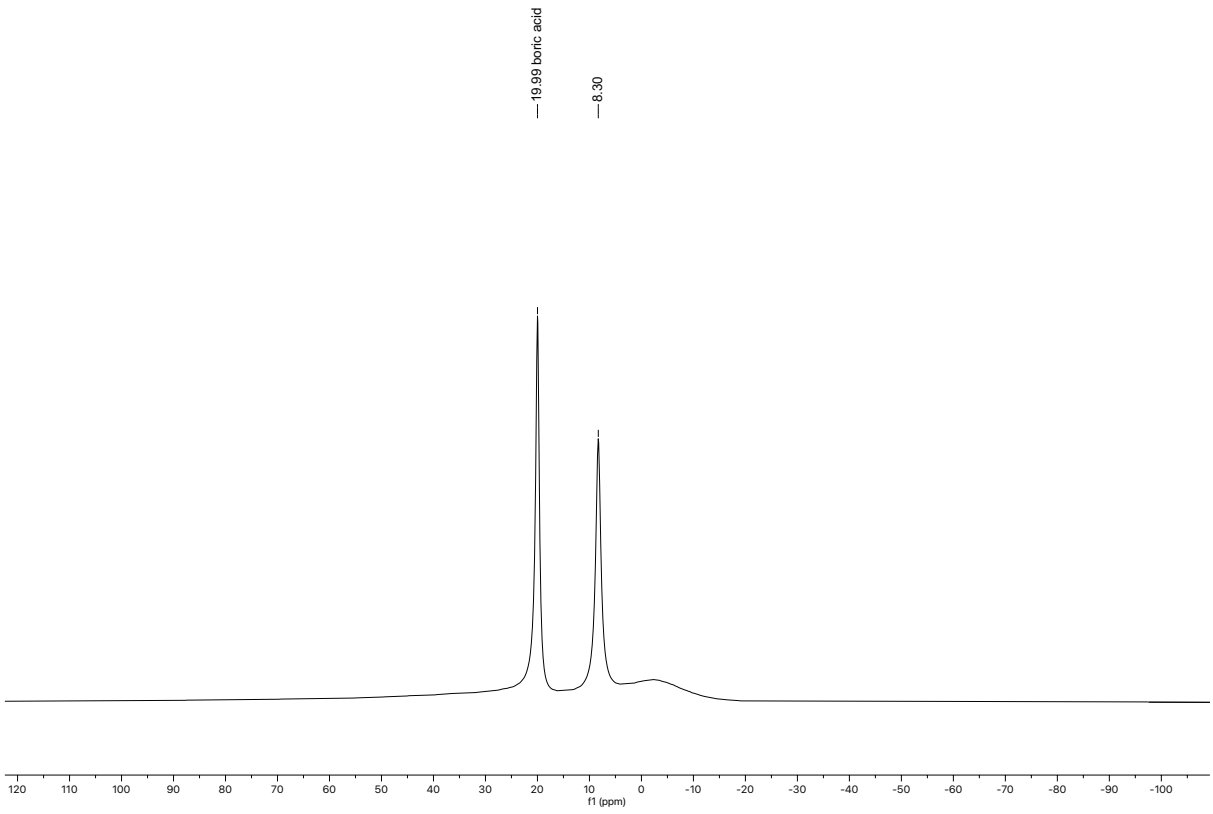
$^{11}B\{^{1}H\}$ NMR (128 MHz, CD_3CN/D_2O)





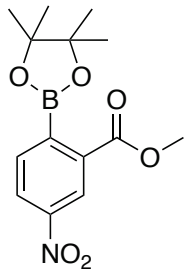
Compound 14c

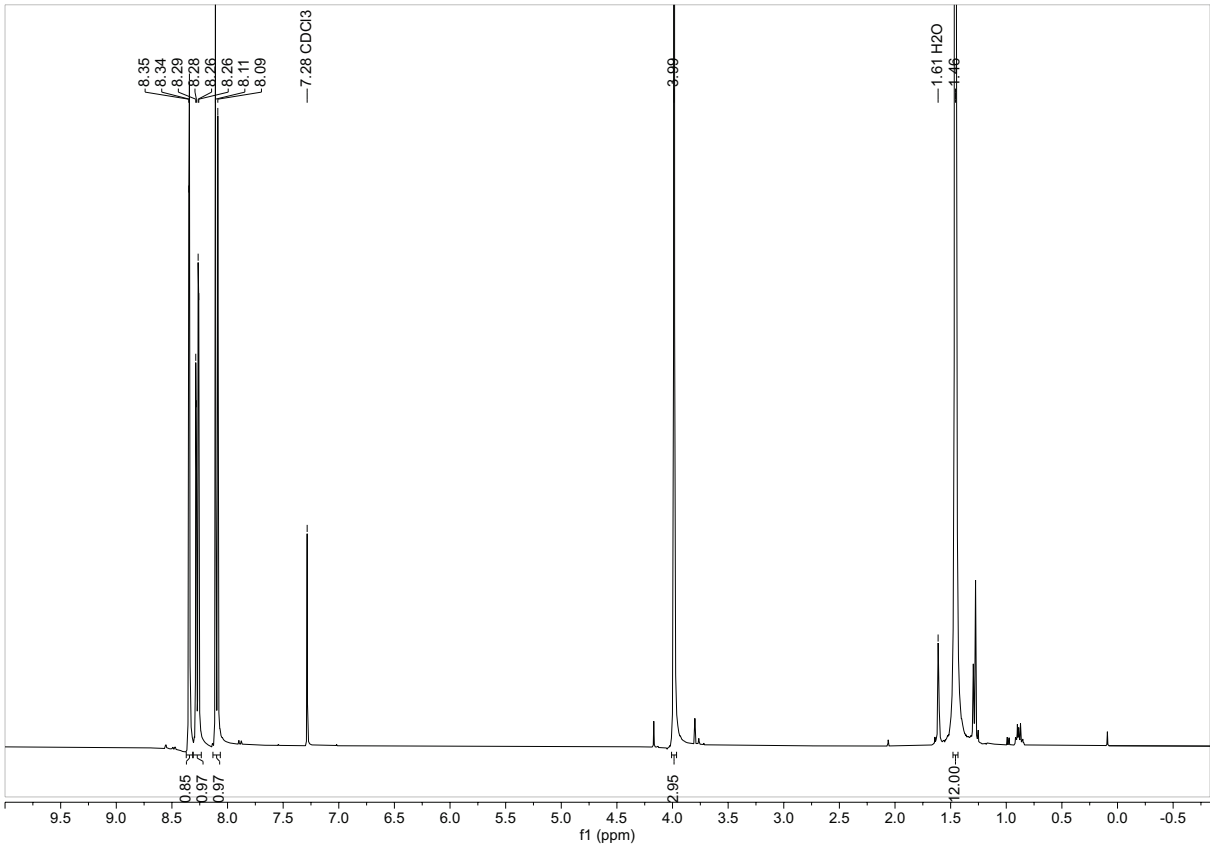
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 15a

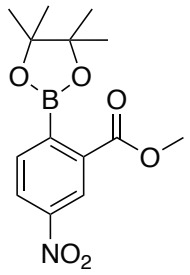
^{1}H NMR (400 MHz, $CDCl_3$)

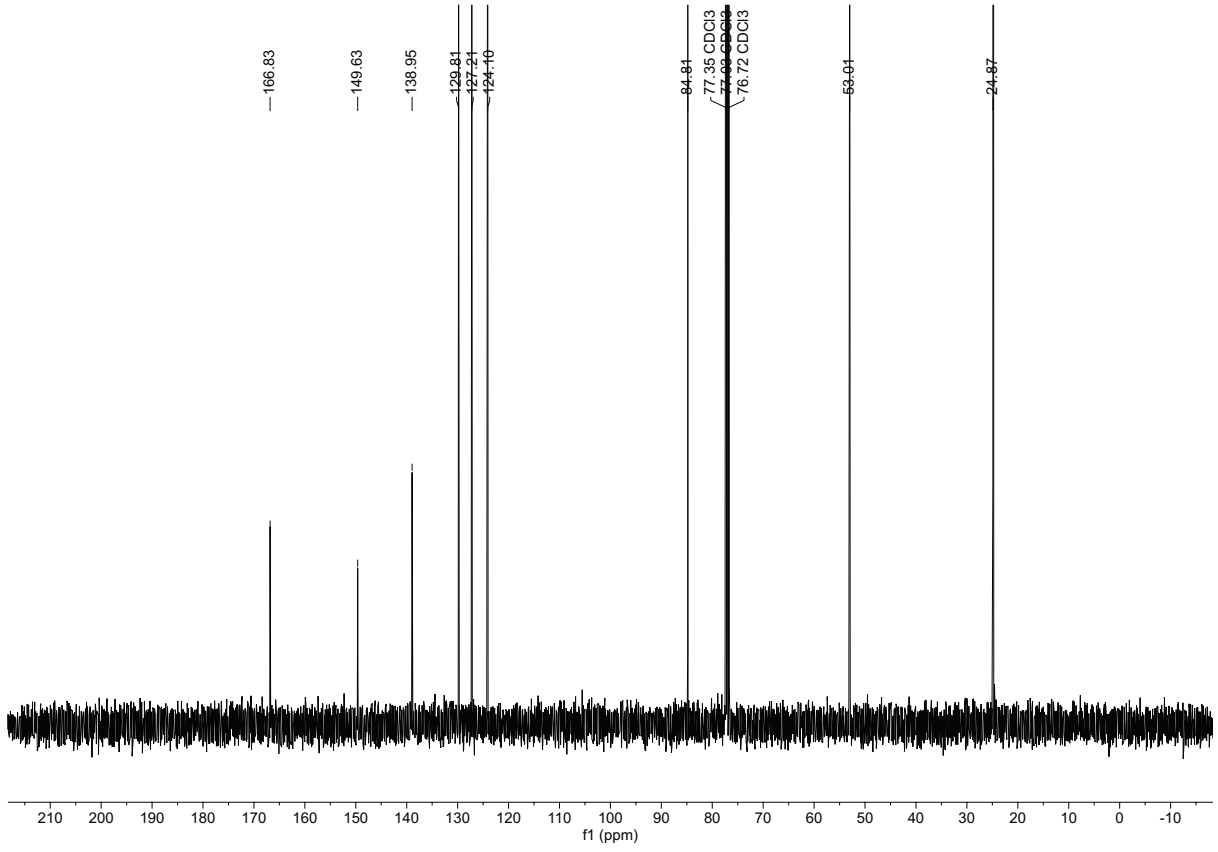




Compound 15a

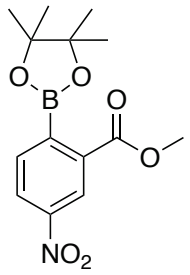
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

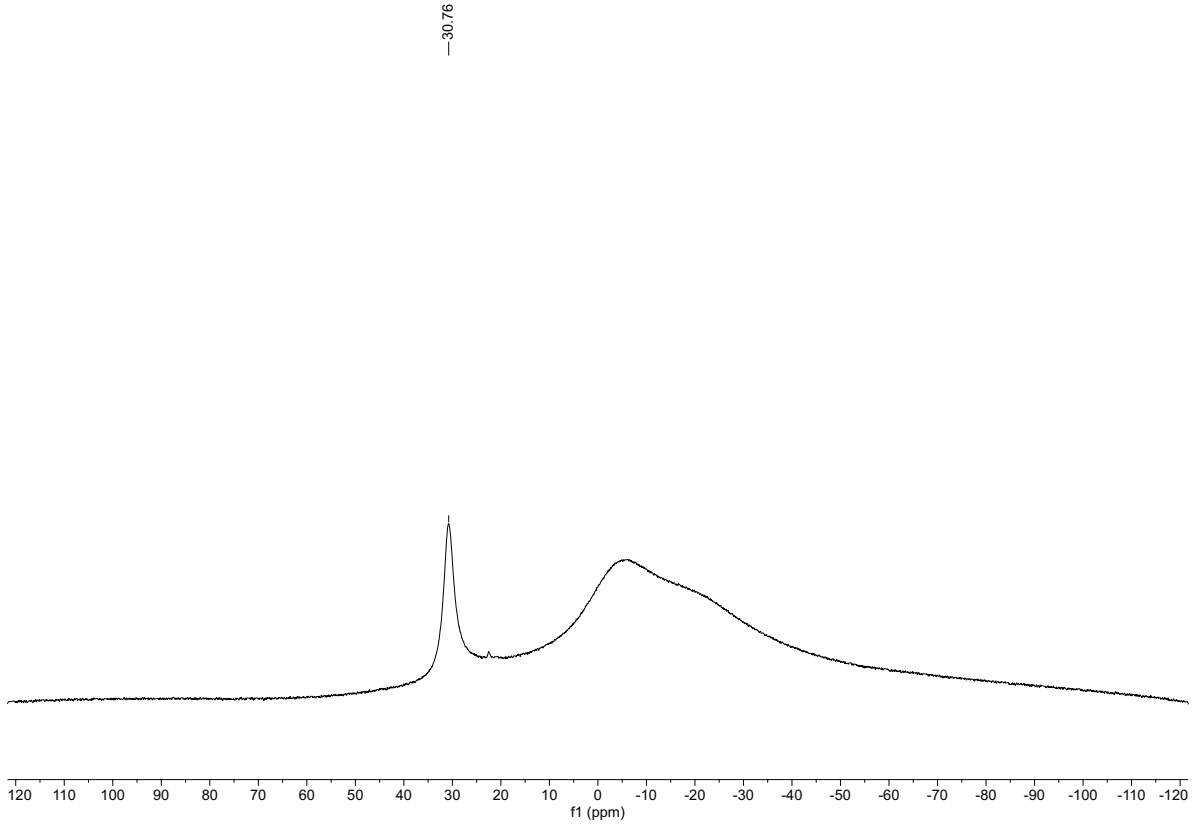




Compound 15a

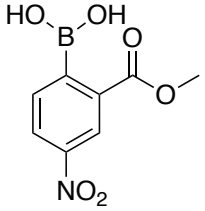
$^{11}B\{^{1}H\}$ NMR (128 MHz, $CDCl_3$)

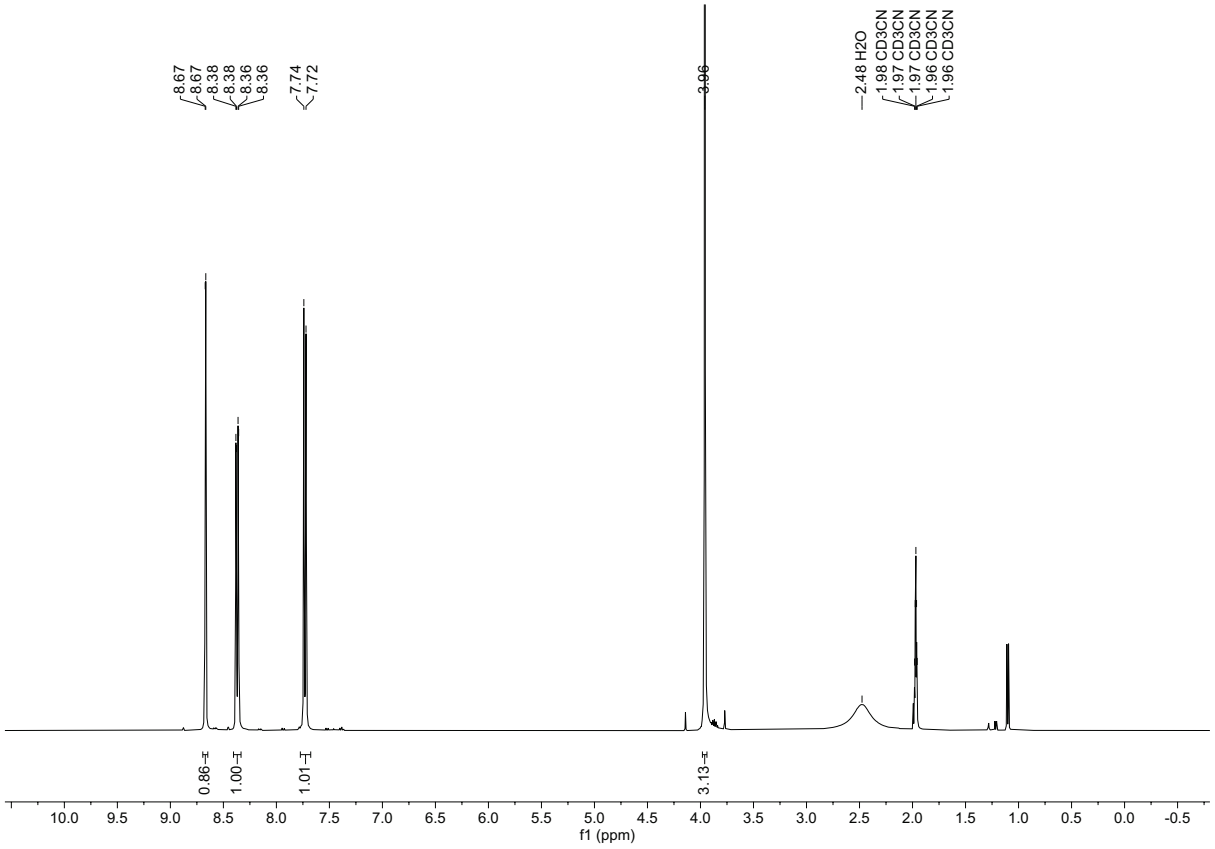




Compound 15b

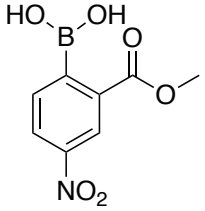
^{1}H NMR (400 MHz, CD_3CN)

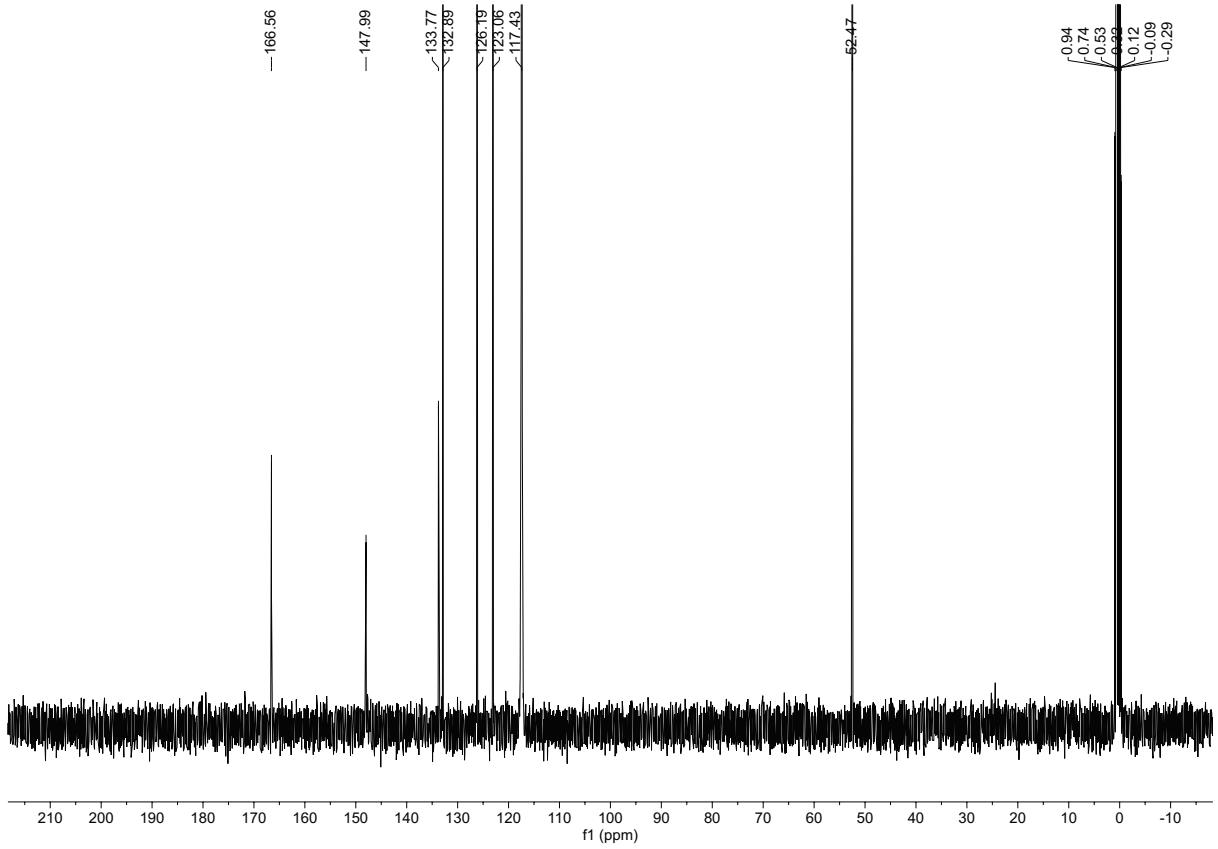




Compound 15b

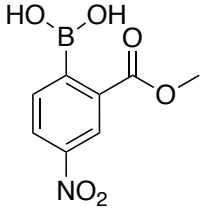
$^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3CN)

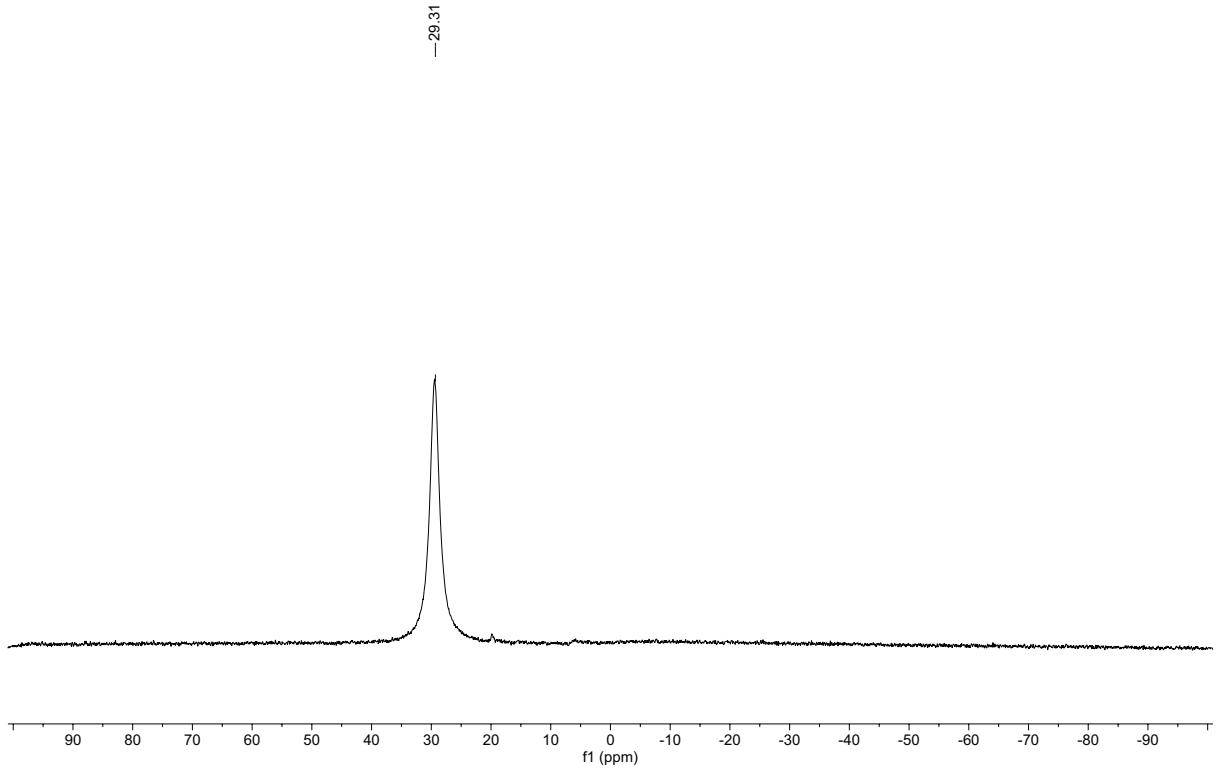




Compound 15b

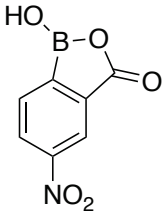
$^{11}B\{^{1}H\}$ NMR (128 MHz, CD_3CN)

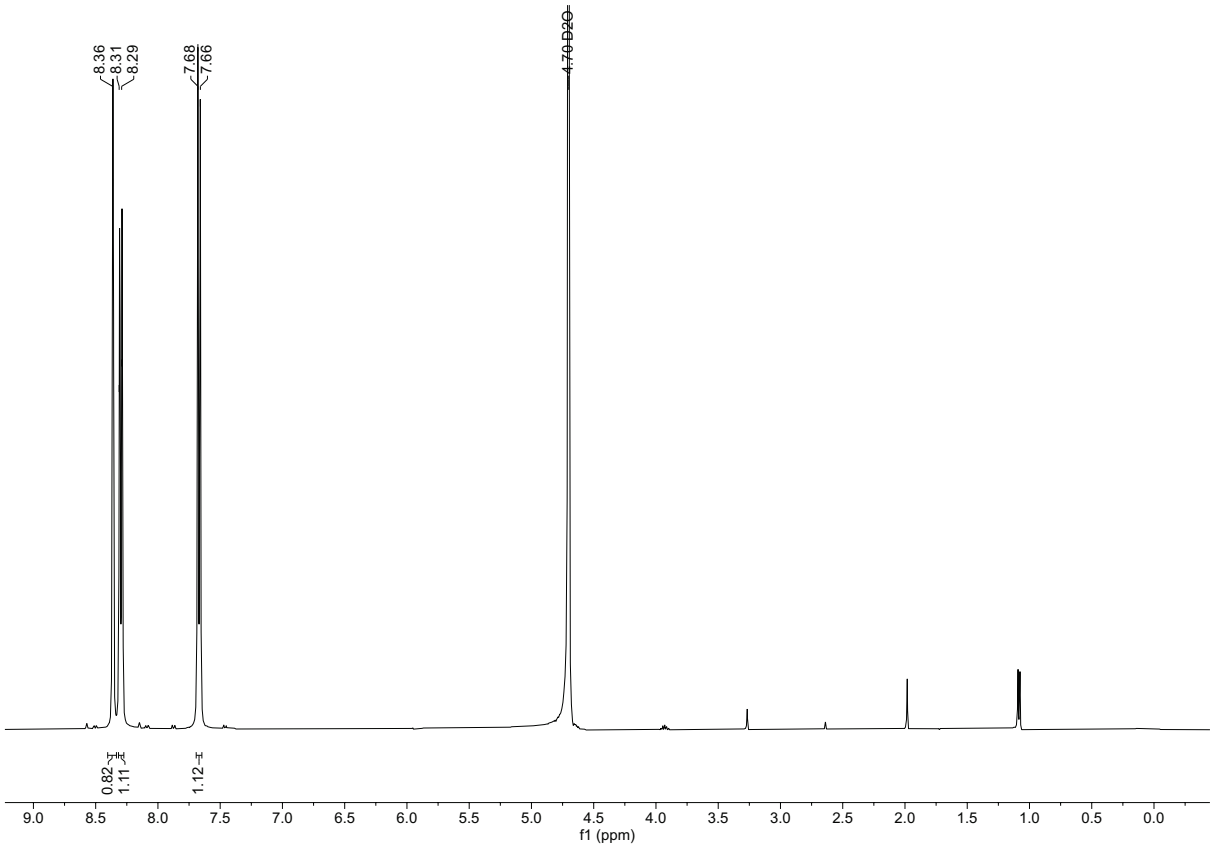




Compound 15c

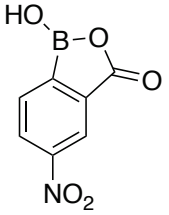
^{1}H NMR (400 MHz, D_2O)

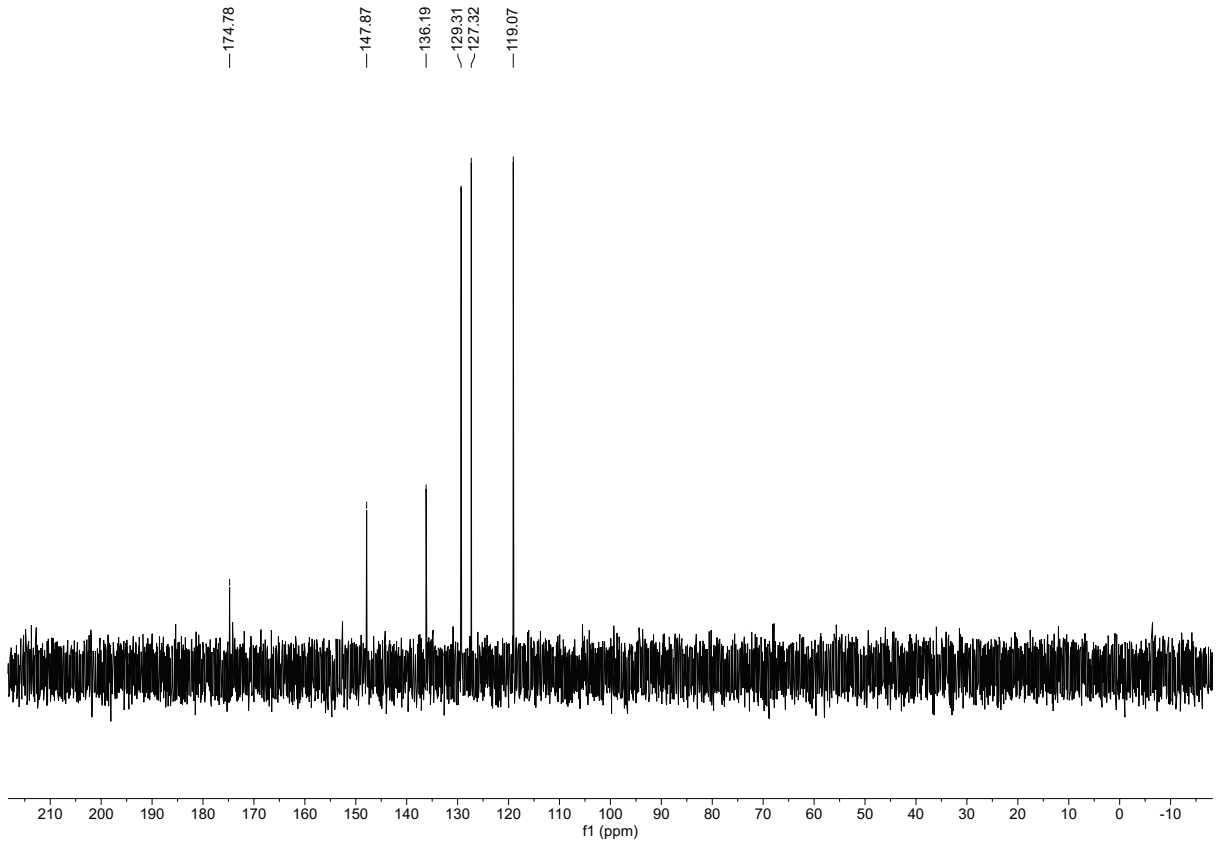




Compound 15c

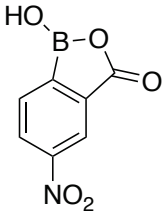
$^{13}C\{^{1}H\}$ NMR (101 MHz, D_2O)

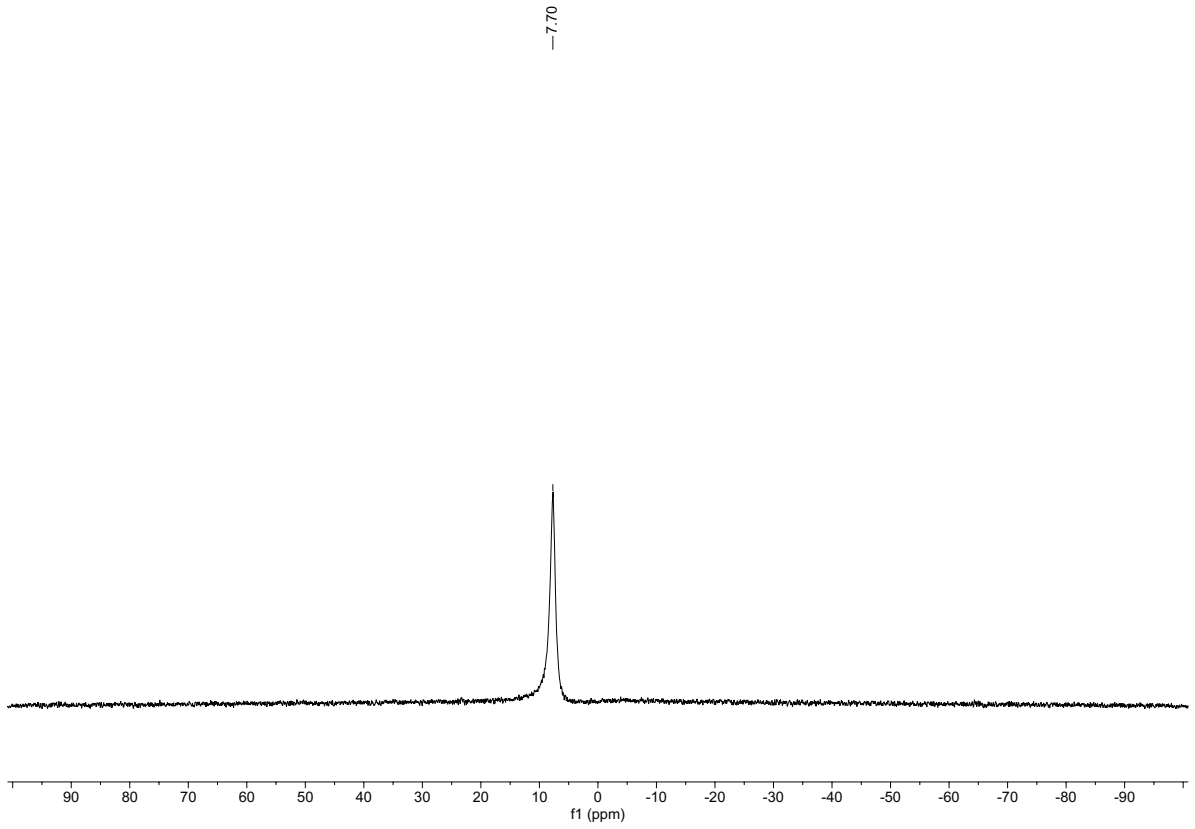




Compound 15c

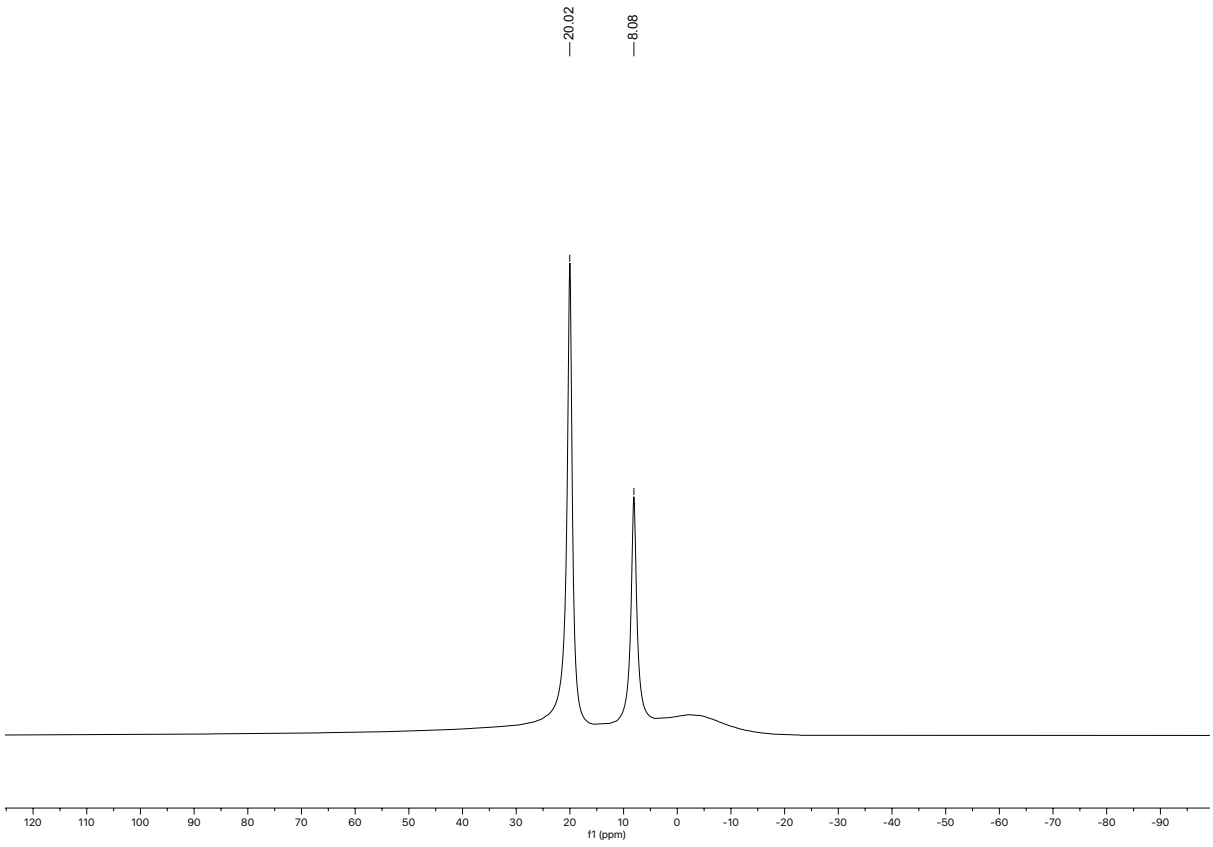
$^{11}B\{^{1}H\}$ NMR (128 MHz, D_2O)





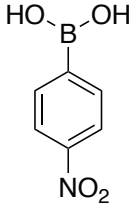
Compound 15c

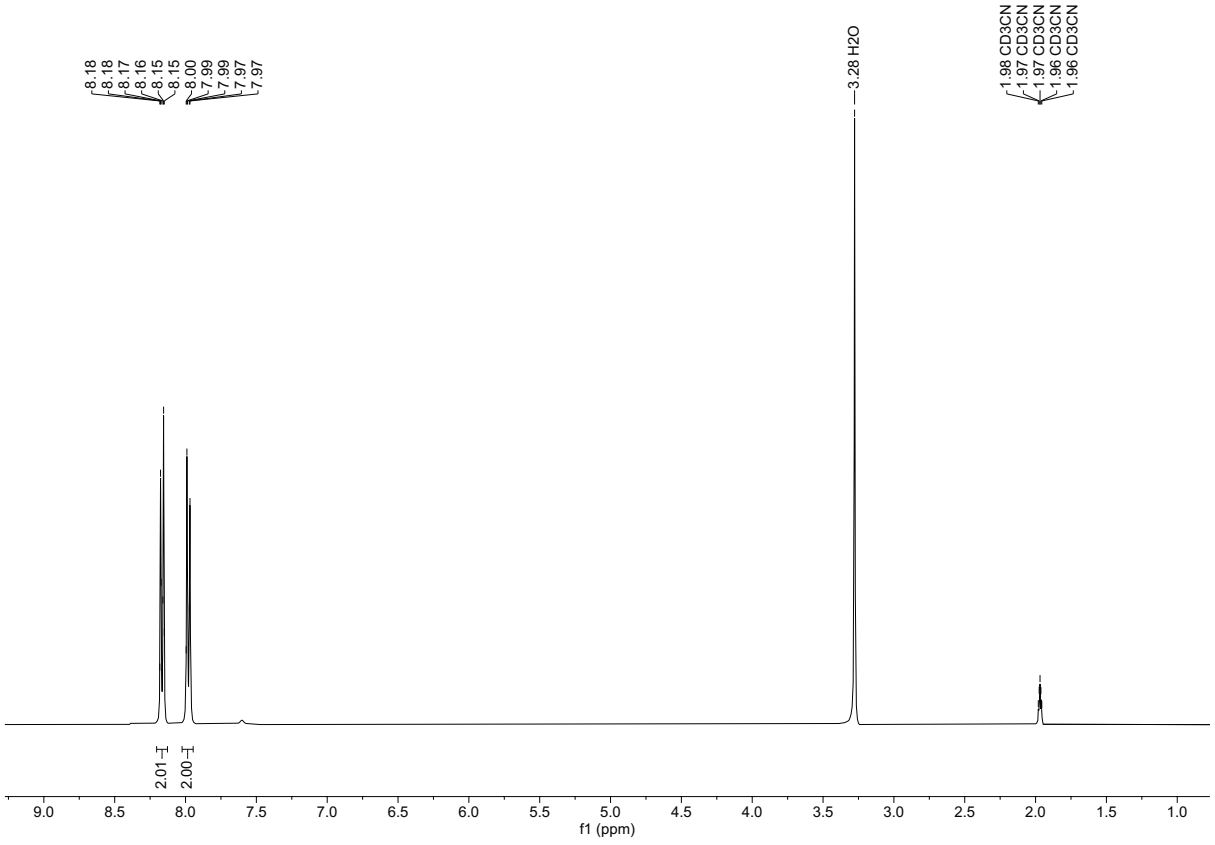
$^{11}B\{^{1}H\}$ NMR (160 MHz, 1:1 phosphate-buffered D_2O/CD_3CN, boric acid added as reference)



Compound 16

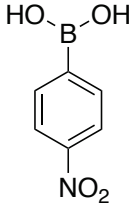
^{1}H NMR (400 MHz, CD_3CN)

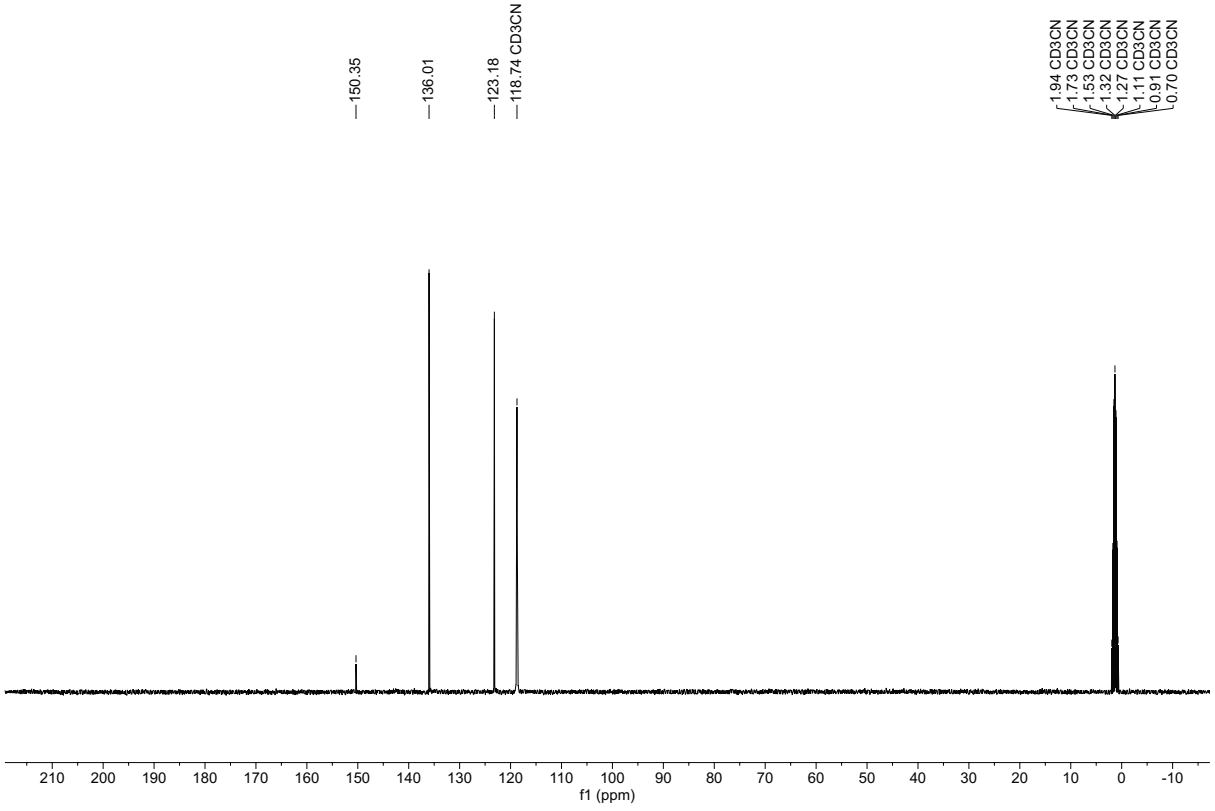




Compound 16

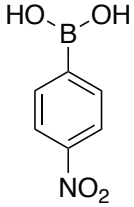
$^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3CN)

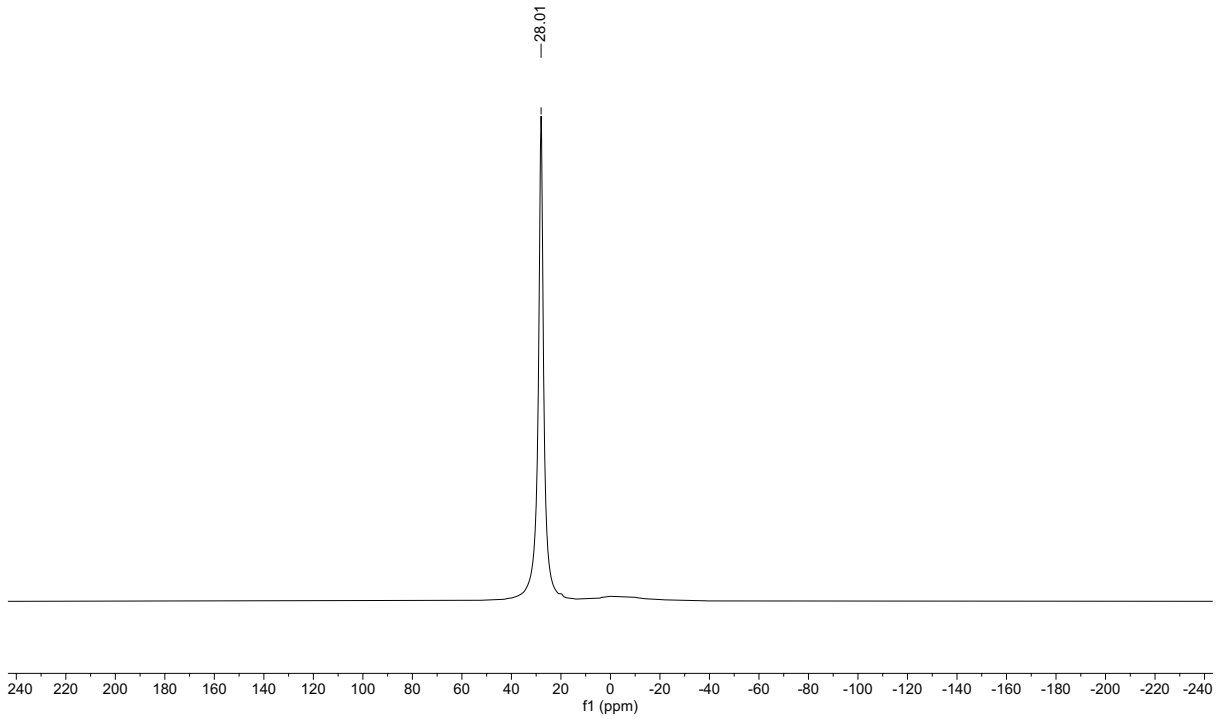




Compound 16

$^{11}B\{^{1}H\}$ NMR (128 MHz, CD_3CN)





Computational Gibbs Free Energies and Optimized Cartesian Coordinates

Compound 1 SM

Energy −671.397301

C	0.378251	-0.621931	0.101771
C	1.032505	0.601791	-0.020832
C	2.411236	0.721927	-0.152602
C	3.165301	-0.447793	-0.161339
C	2.534827	-1.690381	-0.040013
C	1.148485	-1.783639	0.089995
H	2.879197	1.695846	-0.245218
H	4.243258	-0.399677	-0.261591
H	3.137371	-2.592111	-0.048167
H	0.683641	-2.760248	0.181969
B	-1.203577	-0.30874	0.229665
O	-1.178349	1.236802	0.183477
O	-1.882818	-0.862858	-0.939595
O	-1.932968	-0.727631	1.409893
H	-1.768162	-0.148835	2.156702
O	-3.292917	-0.605642	-0.838668
H	-3.458022	-0.784255	0.101785
C	0.038298	1.717024	0.020845
O	0.292949	2.903203	-0.072703

Compound 1 TS

Energy (*G*) −671.34123

Negative vibration −757.58

C	0.326815	-0.633684	0.083892
C	0.944491	0.600817	-0.097921
C	2.32595	0.710009	-0.203507
C	3.089105	-0.451743	-0.12777
C	2.470713	-1.691919	0.055505
C	1.083511	-1.794227	0.15131
H	2.788362	1.683135	-0.32554
H	4.168048	-0.396154	-0.204713
H	3.07942	-2.586777	0.116257
H	0.606075	-2.760628	0.265471
B	-1.355833	-0.129434	0.477621
O	-1.218045	1.336439	0.324964
O	-1.359102	-0.903994	-0.651983
O	-2.011467	-0.514547	1.641982
H	-2.047573	0.197931	2.28496
O	-3.136578	-0.898891	-1.316641
H	-3.393205	-1.722224	-0.890705
C	-0.011192	1.744158	-0.056642
O	0.250401	2.897423	-0.306203

Compound 5 SM

Energy (*G*) −1131.010867

C	-0.322354	-0.587098	0.138332
C	0.275996	0.664184	0.032741
C	1.648562	0.86084	-0.053618
C	2.437932	-0.279328	-0.030845
C	1.887371	-1.556713	0.072357
C	0.504258	-1.709191	0.155997
H	2.081451	1.85081	-0.133763
H	2.543371	-2.41864	0.086347
H	0.090274	-2.708849	0.235757
B	-1.921755	-0.347404	0.216335
O	-1.964153	1.198999	0.164174
O	-2.535588	-0.932801	-0.971295
O	-2.663087	-0.795519	1.375368
H	-2.547384	-0.208696	2.125249
O	-3.956917	-0.733716	-0.918364
H	-4.148762	-0.926791	0.013996
C	-0.769405	1.735667	0.036857
O	-0.560109	2.929252	-0.056312
Cl	4.179676	-0.114747	-0.133455

Compound 5 TS

Energy (*G*) −1130.952799

Negative vibration −763.91

C	-0.359196	-0.60409	0.115906
C	0.200423	0.657779	-0.053401
C	1.574089	0.847635	-0.124176
C	2.37627	-0.280777	-0.022114
C	1.837999	-1.556573	0.148613
C	0.45713	-1.722493	0.207451
H	1.99864	1.838066	-0.237094
H	2.500404	-2.409779	0.226924
H	0.03309	-2.714068	0.312836
B	-2.082258	-0.177478	0.459006
O	-2.004634	1.291849	0.304744
O	-1.996177	-0.955204	-0.664962
O	-2.759159	-0.591823	1.59722
H	-2.854972	0.116953	2.238357
O	-3.749906	-1.035583	-1.389468
H	-3.993924	-1.852189	-0.94344
C	-0.810733	1.756451	-0.04553
O	-0.592935	2.917428	-0.294781
Cl	4.11145	-0.099559	-0.098537

Compound 3 SM

Energy (*G*) −770.649375

C	0.042688	-0.592189	0.125743
C	0.650502	0.654119	0.012711
C	2.024328	0.839699	-0.092357
C	2.788673	-0.311144	-0.079842
C	2.241695	-1.583722	0.029525
C	0.858423	-1.723291	0.131824
H	2.47956	1.819101	-0.178521
H	2.904054	-2.441189	0.032731
H	0.434392	-2.718219	0.216702
B	-1.552494	-0.33901	0.223285
O	-1.583182	1.208519	0.174539
O	-2.187338	-0.916007	-0.958126
O	-2.28638	-0.782417	1.389663
H	-2.153564	-0.200313	2.140336
O	-3.606686	-0.707458	-0.885305
H	-3.786118	-0.897291	0.050255
C	-0.385346	1.734078	0.031638
O	-0.166678	2.926206	-0.062685
F	4.133386	-0.200342	-0.177562

Compound 3 TS

Energy (*G*) −770.591809

Negative vibration −759.69

C	0.000462	-0.605498	0.106332
C	0.568341	0.652312	-0.068689
C	1.943033	0.832124	-0.154215
C	2.720924	-0.307771	-0.060854
C	2.188504	-1.579431	0.114911
C	0.807068	-1.732666	0.189006
H	2.390432	1.812127	-0.269635
H	2.858704	-2.427625	0.183034
H	0.373253	-2.719481	0.298055
B	-1.710958	-0.170057	0.467578
O	-1.628074	1.300612	0.314762
O	-1.647897	-0.943675	-0.66094
O	-2.378932	-0.581387	1.613251
H	-2.458516	0.126557	2.257452
O	-3.414529	-1.013373	-1.361838
H	-3.656083	-1.830468	-0.915472
C	-0.435424	1.757501	-0.048132
O	-0.212138	2.917395	-0.298647
F	4.060235	-0.182981	-0.134908

Compound 10d SM

Energy (*G*) −710.679409

C	0.006986	-0.594824	0.125567
C	0.619113	0.648911	0.015572
C	1.996239	0.821576	-0.082763
C	2.814034	-0.306759	-0.072075
C	2.210543	-1.570226	0.037439
C	0.829192	-1.722083	0.134146
H	2.423974	1.816144	-0.165131
H	2.848273	-2.44963	0.046197
H	0.407247	-2.718956	0.217102
B	-1.586327	-0.340281	0.219048
O	-1.616883	1.205966	0.169257
O	-2.224603	-0.91862	-0.961901
O	-2.326259	-0.781818	1.385393
H	-2.189531	-0.200359	2.135802
O	-3.644182	-0.707936	-0.887882
H	-3.819851	-0.884358	0.051102
C	-0.414393	1.728106	0.0312
O	-0.200522	2.92274	-0.061937
C	4.313792	-0.191735	-0.175312
H	4.624327	0.851654	-0.237654
H	4.799842	-0.641901	0.693432
H	4.683914	-0.711647	-1.062172

Compound 10d TS

Energy (*G*) −710.624039

Negative vibration −752.10

C	-0.029522	-0.62136	0.123387
C	0.522268	0.643036	-0.053115
C	1.896147	0.830367	-0.149474
C	2.743078	-0.27553	-0.073017
C	2.175433	-1.547541	0.102459
C	0.799078	-1.733415	0.190307
H	2.298828	1.831412	-0.268514
H	2.833879	-2.408681	0.161265
H	0.383222	-2.728951	0.295977
B	-1.735433	-0.2203	0.490572
O	-1.682401	1.254745	0.344551
O	-1.684688	-0.981839	-0.646822
O	-2.392751	-0.645256	1.641292
H	-2.466271	0.058751	2.290332
O	-3.456724	-1.051733	-1.326774
H	-3.223715	-0.630389	-2.158969
C	-0.496521	1.730898	-0.021913
O	-0.29832	2.898093	-0.267854

C	4.238814	-0.119719	-0.154684
H	4.512532	0.880165	-0.491636
H	4.696187	-0.284927	0.824249
H	4.668923	-0.848367	-0.844419

Compound 13c SM

Energy (*G*) −1008.454225

C	-0.894293	-0.576928	0.144994
C	-0.314995	0.683287	0.038966
C	1.0546	0.892556	-0.045746
C	1.866772	-0.234855	-0.024444
C	1.320956	-1.518748	0.082297
C	-0.056923	-1.692338	0.165411
H	1.468797	1.890496	-0.129452
H	1.981986	-2.378396	0.09402
H	-0.4632	-2.694832	0.243661
B	-2.499323	-0.360192	0.217405
O	-2.563406	1.183876	0.159835
O	-3.094872	-0.96125	-0.970523
O	-3.233008	-0.816575	1.376434
H	-3.147053	-0.213843	2.117707
O	-4.519095	-0.784781	-0.92749
H	-4.715394	-0.985657	0.00223
C	-1.376454	1.73851	0.035753
O	-1.184314	2.934398	-0.060057
C	3.357205	-0.094191	-0.067447
F	3.916986	-0.265601	1.148015
F	3.750846	1.111929	-0.500756
F	3.930815	-1.006984	-0.871646

Compound 13c TS

Energy (*G*) −1008.396398

Negative vibration −769.71

C	-0.923113	-0.600528	0.128568
C	-0.383711	0.670005	-0.038294
C	0.988354	0.875891	-0.091492
C	1.812854	-0.235538	0.031429
C	1.281894	-1.518812	0.199685
C	-0.094321	-1.709197	0.238944
H	1.393042	1.874871	-0.204387
H	1.950533	-2.366569	0.298832
H	-0.508713	-2.704157	0.34784
B	-2.666924	-0.190429	0.4566
O	-2.60238	1.275182	0.291199
O	-2.547173	-0.979622	-0.65605
O	-3.340659	-0.604454	1.594308

H	-3.462195	0.111318	2.223333
O	-4.278445	-1.08439	-1.415207
H	-4.462344	-1.975982	-1.104497
C	-1.409832	1.753926	-0.046792
O	-1.204702	2.916408	-0.297794
C	3.302331	-0.08319	-0.049315
F	3.69952	1.184592	0.12168
F	3.78347	-0.481159	-1.243158
F	3.935279	-0.824285	0.875681

Compound 7c SM

Energy (*G*) −785.882342

C	-0.301185	-0.527623	0.141655
C	0.193139	0.771083	0.024018
C	1.53913	1.079965	-0.06716
C	2.451601	0.022468	-0.040615
C	1.994472	-1.296145	0.07508
C	0.624796	-1.563745	0.164851
H	1.892715	2.100952	-0.156635
H	2.696624	-2.119209	0.095887
H	0.30387	-2.596959	0.253465
B	-1.910928	-0.425054	0.218253
O	-2.086098	1.114382	0.151682
O	-2.482522	-1.068619	-0.962735
O	-2.621005	-0.920625	1.380944
H	-2.534939	-0.329886	2.131612
O	-3.916379	-0.989643	-0.9037
H	-4.084492	-1.172898	0.035335
C	-0.939936	1.74858	0.021338
O	-0.837135	2.956864	-0.079035
O	3.765456	0.366789	-0.13195
C	4.727792	-0.675493	-0.11301
H	5.697324	-0.190921	-0.19744
H	4.680759	-1.236791	0.82399
H	4.58538	-1.356739	-0.956073

Compound 7c TS

Energy (*G*) −785.826787

Negative vibration −748.36

C	-0.335433	-0.545745	0.11484
C	0.113459	0.762804	-0.067508
C	1.457296	1.071702	-0.147643
C	2.385842	0.027747	-0.053797
C	1.948451	-1.291598	0.12353
C	0.584413	-1.57726	0.195458
H	1.799856	2.094153	-0.258621

H	2.661061	-2.101831	0.198841
H	0.256693	-2.605007	0.302667
B	-2.060088	-0.293211	0.463743
O	-2.134871	1.184797	0.324698
O	-1.940168	-1.039224	-0.680221
O	-2.699629	-0.779619	1.60111
H	-2.835948	-0.090893	2.256312
O	-3.703423	-1.270357	-1.369141
H	-3.886301	-2.07565	-0.875998
C	-0.996499	1.761654	-0.041094
O	-0.8955	2.940262	-0.288916
O	3.687658	0.388794	-0.137347
C	4.672944	-0.630597	-0.039358
H	5.632177	-0.127792	-0.129025
H	4.614052	-1.138448	0.926529
H	4.563472	-1.357937	-0.847451

Compound 4 SM

Energy (*G*) −1131.011639

C	-0.051617	-0.200248	0.109345
C	-0.021323	1.185571	-0.018121
C	1.155582	1.912691	-0.145269
C	2.358727	1.216028	-0.144951
C	2.33339	-0.172684	-0.017751
C	1.152787	-0.897982	0.108617
H	1.141081	2.992268	-0.242104
H	3.305295	1.732215	-0.24069
H	1.190749	-1.977311	0.204054
B	-1.607347	-0.637781	0.232488
O	-2.280091	0.75188	0.172953
O	-1.949052	-1.445961	-0.933677
O	-2.067051	-1.331809	1.415226
H	-2.199559	-0.734861	2.154255
O	-3.324051	-1.850834	-0.843732
H	-3.397524	-2.093758	0.093798
C	-1.412883	1.730744	0.011769
O	-1.718869	2.902943	-0.090016
Cl	3.860096	-1.03436	-0.018802

Compound 4 TS

Energy (*G*) −1130.953907

Negative vibration −765.03

C	-0.071662	-0.241992	0.062891
C	-0.138078	1.138148	-0.100258
C	1.013421	1.906346	-0.220534
C	2.249076	1.271285	-0.177126

C	2.295984	-0.113013	-0.009642
C	1.1506	-0.893801	0.103006
H	0.946711	2.982628	-0.331026
H	3.168576	1.835011	-0.264648
H	1.219687	-1.969864	0.205454
B	-1.798669	-0.623114	0.48417
O	-2.379494	0.727113	0.354125
O	-1.4176	-1.28445	-0.653863
O	-2.166357	-1.291742	1.641935
H	-2.546825	-0.699388	2.295439
O	-2.977744	-2.121881	-1.330908
H	-2.79386	-2.984764	-0.947686
C	-1.527371	1.67307	-0.031601
O	-1.860069	2.810371	-0.264092
Cl	3.857492	-0.894329	0.051978

Compound 2 SM

Energy (*G*) −770.650682

C	0.226498	-0.350538	0.106672
C	0.511531	1.007388	-0.018522
C	1.802369	1.507097	-0.147137
C	2.856938	0.601456	-0.15034
C	2.565321	-0.751751	-0.025242
C	1.281656	-1.258469	0.102325
H	1.983862	2.571521	-0.242053
H	3.888027	0.917504	-0.24584
H	1.137547	-2.329337	0.194791
B	-1.382984	-0.492088	0.232198
O	-1.787587	0.996636	0.179573
O	-1.871527	-1.218538	-0.936025
O	-1.960911	-1.095713	1.413607
H	-1.97031	-0.490838	2.157978
O	-3.297779	-1.360539	-0.843787
H	-3.413143	-1.591054	0.092616
C	-0.753925	1.798637	0.016219
O	-0.840832	3.007688	-0.083243
F	3.601743	-1.619618	-0.029258

Compound 2 TS

Energy (*G*) −770.592988

Negative vibration −766.67

C	0.200904	-0.373176	0.066796
C	0.392068	0.995651	-0.101108
C	1.667288	1.538809	-0.212678
C	2.764276	0.687818	-0.157145
C	2.541117	-0.673579	0.014141

C	1.28093	-1.239768	0.119865
H	1.798858	2.608744	-0.325764
H	3.779303	1.055082	-0.235684
H	1.166096	-2.311754	0.225658
B	-1.56764	-0.425007	0.47876
O	-1.89016	1.007324	0.334304
O	-1.312061	-1.156844	-0.650804
O	-2.055558	-1.003989	1.641052
H	-2.320885	-0.345219	2.287797
O	-2.999589	-1.705175	-1.317759
H	-2.974059	-2.58056	-0.919876
C	-0.873318	1.777831	-0.045275
O	-0.989528	2.956694	-0.281964
F	3.61383	-1.485205	0.074207

Compound 8b SM

Energy (*G*) −710.679451

C	0.217466	-0.31637	0.107792
C	0.43678	1.052065	-0.020704
C	1.70778	1.60291	-0.144826
C	2.794398	0.736961	-0.139786
C	2.616052	-0.650308	-0.014839
C	1.321689	-1.166132	0.109728
H	1.84509	2.674688	-0.238987
H	3.801096	1.132017	-0.230981
H	1.192074	-2.240476	0.211712
B	-1.380716	-0.533119	0.230501
O	-1.859973	0.935125	0.173111
O	-1.839731	-1.285375	-0.935621
O	-1.939296	-1.159056	1.4134
H	-1.975469	-0.55112	2.154401
O	-3.258218	-1.493537	-0.839311
H	-3.361046	-1.709157	0.10226
C	-0.862935	1.783709	0.010958
O	-1.009246	2.988181	-0.089854
C	3.814464	-1.564201	-0.037193
H	3.565366	-2.550242	0.356354
H	4.178882	-1.693398	-1.060127
H	4.635138	-1.151224	0.552285

Compound 8b TS

Energy (*G*) −710.62454

Negative vibration −755.77

C	0.19837	-0.34742	0.072219
C	0.29861	1.02961	-0.098593
C	1.540213	1.642501	-0.227229

C	2.679813	0.84866	-0.186131
C	2.594886	-0.541726	-0.010727
C	1.336194	-1.139182	0.104378
H	1.608857	2.718511	-0.34344
H	3.657829	1.307154	-0.285447
H	1.253669	-2.216413	0.206626
B	-1.538979	-0.520524	0.502665
O	-1.970208	0.89023	0.370314
O	-1.28223	-1.230398	-0.639505
O	-1.972764	-1.131473	1.674958
H	-2.251649	-0.487552	2.330612
O	-2.955002	-1.882793	-1.252279
H	-2.886934	-1.44618	-2.106184
C	-1.01267	1.727869	-0.019803
O	-1.211932	2.898765	-0.248189
C	3.850885	-1.36936	0.062221
H	3.63562	-2.426936	-0.091172
H	4.575207	-1.046921	-0.687597
H	4.321582	-1.259403	1.042868

Compound 12b SM

Energy (*G*) −1008.453161

C	-0.580629	-0.107653	0.124944
C	-0.687921	1.272548	-0.013743
C	0.405805	2.120086	-0.135607
C	1.672682	1.549732	-0.116126
C	1.801341	0.165399	0.02631
C	0.691922	-0.671345	0.142565
H	0.275459	3.190911	-0.239606
H	2.557068	2.169095	-0.203001
H	0.832256	-1.741328	0.251593
B	-2.083991	-0.701586	0.236026
O	-2.894139	0.61483	0.163216
O	-2.331132	-1.541588	-0.930362
O	-2.482794	-1.434638	1.416065
H	-2.662293	-0.855159	2.159051
O	-3.657638	-2.085999	-0.85134
H	-3.713897	-2.335553	0.085588
C	-2.131671	1.674716	0.001623
O	-2.549267	2.810043	-0.110889
C	3.175627	-0.434774	-0.009509
F	3.245974	-1.60038	0.651556
F	3.579451	-0.689449	-1.27122
F	4.104374	0.374998	0.525218

Compound 12b TS

Energy (*G*) −1008.394923

Negative vibration −767.25

C	-0.598194	-0.167728	0.040461
C	-0.784304	1.202078	-0.108757
C	0.289401	2.074208	-0.237171
C	1.575383	1.54849	-0.212597
C	1.756334	0.171152	-0.061785
C	0.680055	-0.704048	0.057449
H	0.121291	3.139817	-0.339636
H	2.435644	2.199064	-0.309661
H	0.837794	-1.772478	0.144769
B	-2.277414	-0.702584	0.485536
O	-2.975662	0.594176	0.375669
O	-1.855005	-1.315843	-0.664204
O	-2.566688	-1.407653	1.642742
H	-2.985167	-0.854953	2.307687
O	-3.342711	-2.294511	-1.316756
H	-3.034073	-3.149979	-1.003675
C	-2.218671	1.612464	-0.018202
O	-2.649817	2.716934	-0.241997
C	3.157044	-0.365309	0.020323
F	3.648267	-0.281853	1.271702
F	3.232595	-1.655142	-0.335114
F	4.006734	0.312416	-0.766491

Compound 6b SM

Energy (*G*) −785.883788

C	-0.12276	-0.266397	0.119368
C	-0.002351	1.119457	-0.012805
C	1.224864	1.75265	-0.132651
C	2.3824	0.977633	-0.120488
C	2.279376	-0.414527	0.011722
C	1.027559	-1.03683	0.130489
H	1.28933	2.830505	-0.234333
H	3.347181	1.457053	-0.212332
H	1.000979	-2.11734	0.229632
B	-1.704816	-0.593628	0.22866
O	-2.28361	0.835785	0.162914
O	-2.095603	-1.380691	-0.939461
O	-2.227277	-1.253525	1.409015
H	-2.339825	-0.640644	2.138206
O	-3.49654	-1.689397	-0.857389
H	-3.593694	-1.908606	0.084001
C	-1.347693	1.754469	0.005957
O	-1.582434	2.944906	-0.098739

O	3.352869	-1.244753	0.034441
C	4.646787	-0.672557	-0.084178
H	5.346975	-1.502976	-0.043271
H	4.757177	-0.14773	-1.036488
H	4.847618	0.015895	0.740553

Compound 6b TS

Energy (*G*) −785.82775

Negative vibration −761.90

C	-0.145993	-0.304008	0.066875
C	-0.106435	1.081047	-0.105978
C	1.107997	1.741399	-0.215909
C	2.292446	1.011971	-0.157243
C	2.24427	-0.378389	0.019995
C	1.013875	-1.045639	0.121523
H	1.134407	2.819521	-0.330249
H	3.238665	1.527737	-0.241176
H	1.004338	-2.124456	0.226299
B	-1.889169	-0.545598	0.475058
O	-2.370945	0.843664	0.336549
O	-1.578241	-1.247784	-0.659463
O	-2.311098	-1.176185	1.640434
H	-2.636258	-0.547501	2.289635
O	-3.206531	-1.963197	-1.316856
H	-3.108577	-2.818574	-0.888114
C	-1.442578	1.72197	-0.042134
O	-1.691823	2.883642	-0.270202
O	3.341921	-1.16308	0.096867
C	4.61913	-0.547534	-0.01086
H	5.345304	-1.351449	0.074374
H	4.732101	-0.051895	-0.977983
H	4.773331	0.173228	0.795667

Compound 14c SM

Energy (*G*) −875.895100

C	-0.266869	-0.155766	0.109096
C	-0.296231	1.231178	-0.002648
C	0.840257	2.022007	-0.120175
C	2.074997	1.387492	-0.126375
C	2.105291	-0.000904	-0.012187
C	0.968772	-0.793935	0.104056
H	0.767467	3.099663	-0.203859
H	2.998434	1.942310	-0.214125
H	1.066866	-1.868770	0.187035
B	-1.801918	-0.667496	0.222195
O	-2.534437	0.695090	0.182159
O	-2.102264	-1.467082	-0.958592
O	-2.229271	-1.398350	1.391103
H	-2.378037	-0.824283	2.145071
O	-3.457937	-1.933397	-0.882737
H	-3.521829	-2.209364	0.046164
C	-1.717043	1.713583	0.033199
O	-2.067317	2.872559	-0.054730
N	3.425065	-0.663508	-0.016366
O	3.460935	-1.864780	0.157006
O	4.411065	0.023528	-0.192522

Compound 14c TS

Energy (*G*) −875.835815

Negative vibration −773.4437

C	-0.284579	-0.207451	0.056303
C	-0.403547	1.171978	-0.080538
C	0.707508	1.999006	-0.188665
C	2.063926	0.039976	-0.012061
C	0.965293	-0.803930	0.085368
H	0.586894	3.071776	-0.280105
H	1.092283	-1.875201	0.167619
B	-2.004999	-0.666090	0.471806
O	-2.628894	0.666659	0.372490
O	-1.581341	-1.278489	-0.678169
O	-2.349635	-1.375068	1.608254
H	-2.757353	-0.816922	2.275494
O	-3.105242	-2.160289	-1.382005
H	-2.898301	-3.022270	-1.008349
C	-1.819431	1.650027	-0.002540
O	-2.190424	2.776198	-0.220710
C	1.970359	1.421658	-0.156779
H	2.867921	2.018809	-0.232466
N	3.412929	-0.564516	0.028674

O	4.368259	0.164012	-0.139421
O	3.493012	-1.758239	0.228504

Compound 15c SM

Energy −875.895568

C	-0.554345	-0.584052	0.141099
C	0.033577	0.675043	0.045050
C	1.401210	0.878805	-0.033456
C	2.185478	-0.266053	-0.011498
C	0.271892	-1.707652	0.157924
H	1.838567	1.865891	-0.107357
H	-0.143390	-2.706390	0.230516
B	-2.159844	-0.355201	0.213223
O	-2.210479	1.189514	0.166219
O	-2.753482	-0.944198	-0.979916
O	-2.893248	-0.815385	1.368202
H	-2.805561	-0.219321	2.114709
B	-4.175820	-0.755744	-0.941817
H	-4.380645	-0.973019	-0.017748
C	-1.021413	1.738747	0.048886
O	-0.818135	2.932487	-0.036515
C	1.651682	-1.550784	0.082391
H	2.317678	-2.403036	0.094484
N	3.646889	-0.116927	-0.090439
O	4.328453	-1.122447	-0.070630
O	4.102194	1.006529	-0.171798

Compound 15c TS

Energy (*G*) −875.836241

Negative vibration −774.9456

C	-0.588727	-0.612397	0.115419
C	-0.043177	0.660235	-0.035375
C	1.325470	0.862956	-0.102527
C	2.125372	-0.267241	-0.010831
C	1.610332	-1.553452	0.144015
C	0.233350	-1.729367	0.195932
H	1.751171	1.852942	-0.203933
H	2.286556	-2.394620	0.215073
H	-0.186910	-2.722996	0.290436
B	-2.335905	-0.190349	0.463062
O	-2.254002	1.275264	0.328162
O	-2.208532	-0.959967	-0.663326
O	-3.013934	-0.623417	1.587867
H	-3.137242	0.079290	2.231291
O	-3.927717	-1.034105	-1.442282
H	-4.117566	-1.934546	-1.161837

C	-1.062594	1.751868	-0.015469
O	-0.850053	2.915412	-0.249756
N	3.585681	-0.097762	-0.067634
O	4.280220	-1.086433	0.052219
O	4.021965	1.023294	-0.232870

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