Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.


# Supporting Information

*for*

## Highly diastereoselective entry to chiral oxindole-based β-amino boronic acids and spiro derivatives

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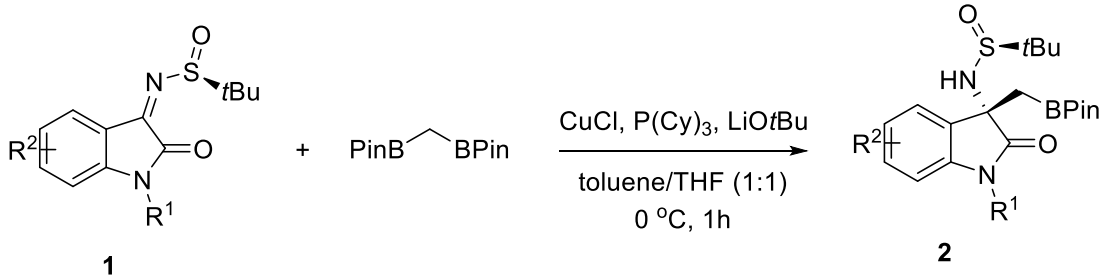
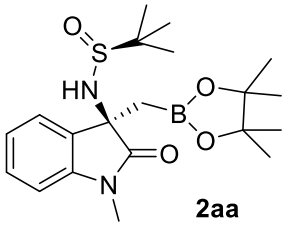
# General Information

All commercial materials (Fluorochem, Merck, TCI) were used without further purification. All solvents were of reagent grade or HPLC grade. All reactions were carried out under a nitrogen atmosphere, unless otherwise noted. All reactions were monitored by thin layer chromatography (TLC) on precoated silica gel 60 F254; spots were visualized with UV light. All reactions involving a boron-containing molecule were followed by TLC using a curcumin solution, as reported in literature.[1] Column chromatography were performed by Flash Chromatography (FC) using Merck Silica gel 60 (230–400 mesh).
$^{1}$H NMR,$^{13}$C NMR and $^{11}$B NMR spectra were recorded using a Bruker AV 400 Ultrashield spectrometer. $^{1}$H NMR and $^{13}$C NMR chemical shifts were reported in parts per million (ppm) downfield from tetramethylsilane,$^{11}$B NMR chemical shifts were determined relative to $BF_3 \cdot Et_2O$ and spectra were recorded using quartz NMR tubes.$^{19}$F NMR spectra were decoupled from $^{1}$H and chemical shifts were determined relative to $CFCl_3$. Coupling constants (*J*) were reported in Hertz (Hz). The residual solvent peaks were used as internal references: $^{1}$H NMR ($CD_3CN$ 1.98 ppm, acetone d-6 2.07 ppm, DMSO d-6 2.51 ppm) $^{13}$C NMR ($CD_3CN$ 0.3 ppm, 117.3 ppm; acetone d-6 29.0 ppm, 205.4 ppm; DMSO d-6 40.0 ppm). To overcame solubility problems and not losing information about exchangeable protons, in few cases a drop of water was added to the solvent (signal of water in: acetone d-6 4.14 ppm; DMSO-d6 3.35 ppm). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, sept = septet, m = multiplet, br = broad. High-resolution MS spectra were recorded with a Waters Micromass Q-ToF micro TM mass spectrometer, equipped with an ESI source.
N-Substituted isatins[2] and the corresponding ketimines are synthetized according to the previous literature.[3,4]

# General procedure for the copper-catalysed synthesis of oxindole-based β-amino boronic esters (compounds 2)



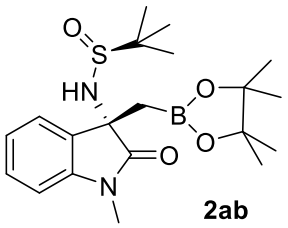

In a flame-dried round-bottom flask, CuCl (2.0 mg, 0.02 mmol, 0.1 eq) and $PCy_3$ (11.2 mg, 0.04 mmol, 0.2 eq) were placed under nitrogen. Dry toluene (1.0 mL) and dry THF (0.4 mL) were added. Under vigorous stirring, *t*BuOLi (1M in THF, 0.6 mL, 0.6 mmol, 3.0 eq) was added and the reaction was stirred for 30 minutes at room temperature. After that, bis[(pinacolato)boryl]methane (80.4 mg, 0.3 mmol, 1.5 eq) was added and the reaction was stirred at room temperature for 2h. Then the reaction was cooled to 0°C and the proper N-substituted-ketimine **1** (0.2 mmol) was added. After stirring at 0°C for 1h (monitoring by TLC), the reaction was diluted with dichloromethane and washed with saturated aqueous $NH_4Cl$ and brine. The organic phase was dried over $NaSO_4$ and the solvents were removed under reduced pressure. The crude product was purified by FC with EtOAc / Hexane to obtain compound **2**.



**2aa**

***(S)*-2-methyl-N-((*R*)-1-methyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)propane-2-sulfinamide (2aa)** (*minor diastereoisomer*)
Purified by FC (EtOAc / Hexane 7:3 to 9:1) to afford a pale-yellow foam (yield < 5%). $^{1}$H NMR (400 MHz, $CD_3CN$) δ 7.38 (t, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 7.3 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 5.12 (s, 1H), 3.15 (s, 3H), 1.55 (d, *J* = 14.9 Hz, 1H), 1.34 (d, *J* = 14.9 Hz, 1H), 1.17

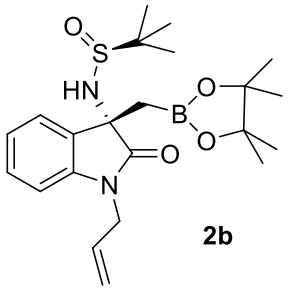
(s, 9H), 1.16 (s, 6H), 1.14 (s, 6H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 22.5 (3C), 24.4 (2C), 24.8 (2C), 26.4 (1C), 56.0 (1C), 62.2 (1C), 84.1 (2C), 109.2 (1C), 123.0 (1C), 125.5 (1C), 129.9 (1C), 130.2 (1C), 144.9 (1C), 178.3 (1C) (*due to the quadrupolar nature of $^{11}$B, the C signal of the carbon atom linked to boron was not observed, 22.4 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 32.1. HRMS (ESI) *m/z*: 429.2081 $[M+Na]^+$, calcd for $C_{20}H_{31}BN_2O_4SNa^+$ 429.2098. $[\alpha]_D$ = - 13.3 (c 0.9, $CHCl_3$).



**2ab**

***(S)*-2-methyl-N-(*(S)*-1-methyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)propane-2-sulfinamide (2ab)** (*major diastereoisomer*)

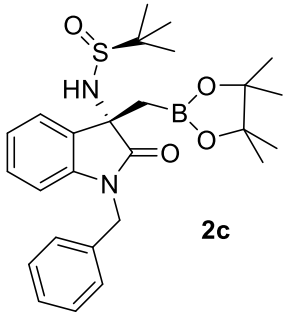
Purified by FC (EtOAc / Hexane 7:3 to 9:1) to afford a yellow foam (yield 92%). $^1$H NMR (400 MHz, $CD_3CN$) δ 7.45 (d, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.7 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 7.8 Hz, 1H), 4.94 (s, 1H), 3.17 (s, 3H), 1.59 (d, *J* = 14.9 Hz, 1H), 1.50 (d, *J* = 14.9 Hz, 1H), 1.15 (s, 9H), 1.11 (s, 6H), 1.07 (s, 6H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 22.4 (3C), 24.4 (2C), 24.8 (2C), 26.4 (1C), 55.7 (1C), 62.9 (1C), 84.1 (2C), 109.2 (1C), 123.0 (1C), 125.2 (1C), 130.0 (1C), 131.7 (1C), 144.4 (1C), 177.1 (1C), (*due to the quadrupolar nature of $^{11}$B, the C signal of the carbon atom linked to boron was not observed, 22.7 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 32.0. HRMS (ESI) *m/z*: 429.2103 $[M+Na]^+$, calcd for $C_{20}H_{31}BN_2O_4SNa^+$ 429.2098. $[\alpha]_D$ = - 5.9 (c 1.0, $CHCl_3$).



**2b**

***(S)*-N-(*(S)*-1-allyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)-2-methylpropane-2-sulfinamide (2b)**

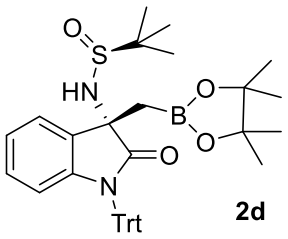
Purified by FC (EtOAc / Hexane 8:2) to afford a yellow foam (yield 66%). $^1$H NMR (400 MHz, $CD_3CN$) δ 7.44 (d, *J* = 6.8 Hz, 1H), 7.32 (t, *J* = 6.6 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.9 Hz, 1H), 5.91 (m, 1H), 5.22 (m, 1H), 5.00 (s, 1H), 4.40 (br d, 1H), 4.21 (br d, 1H), 1.59 (d, *J* = 15.0 Hz, 1H), 1.49 (d, *J* = 15.0, 1H), 1.13 (s, 9H), 1.12 (s, 6H), 1.06 (s, 6H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 22.4 (3C), 24.3 (2C), 24.8 (2C), 42.5 (1C), 56.4 (1C), 62.9 (1C), 84.3 (2C), 109.9 (1C), 116.9 (1C), 123.0 (1C), 125.4 (1C), 129.9 (1C), 131.7 (1C), 132.6 (1C), 143.5 (1C), 177.0 (1C), *(due to the quadrupolar nature of $^{11}$B, the C signal of the carbon atom linked to boron was not observed, 21.9 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 32.3. HRMS (ESI) *m/z*: 455.2131 $[M+Na]^+$, calcd for $C_{22}H_{33}BN_2O_4SNa^+$ 455.2152. $[\alpha]_D$ = - 10.0 (c 1.0, $CHCl_3$).



**2c**

***(S)*-N-(*(S)*-1-benzyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)-2-methylpropane-2-sulfinamide (2c)**

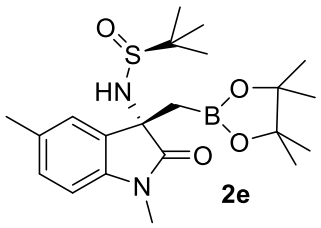
Purified by FC (EtOAc / Hexane 6:4 to 7:3) to afford a pale-yellow solid (yield 76%). $^{1}$H NMR (400 MHz, $CD_3CN$) δ 7.46 (d, *J* = 7.4 Hz, 1H), 7.39-7.29 (m, 5H), 7.24 (t, *J* = 7.7 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 5.09 (d, *J* = 15.8 Hz, 1H), 5.08 (s, 1H), 4.70 (d, *J* = 15.9 Hz, 1H), 1.63 (d, *J* = 15.0 Hz, 1H), 1.52 (d, *J* = 15.0, 1H), 1.15 (s, 9H), 1.14 (s, 6H), 1.08 (s, 6H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 22.4 (3C), 24.4 (2C), 24.9 (2C), 43.9 (1H), 56.4 (1C), 63.1 (1C), 84.3 (2C), 109.8 (1C), 123.2 (1C), 125.6 (1C), 127.8 (2C), 128.2 (1C), 129.3 (2C), 129.9 (1C), 131.7 (1C), 137.1 (1C), 143.2 (1C), 177.7 (1C), *(due to the quadrupolar nature of $^{11}$B, the C signal of the carbon atom linked to boron was not observed, 22.6 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 32.3. HRMS (ESI) *m/z*: 483.2456 $[M+H]^+$, calcd for $C_{27}H_{35}BN_2O_4S^+$ 483.2483. $[\alpha]_D$ = - 9.5 (c 0.7, $CHCl_3$).




**2d**

***(S)*-2-methyl-N-(*(S)*-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-1-tritylindolin-3-yl)propane-2-sulfinamide (2d)**

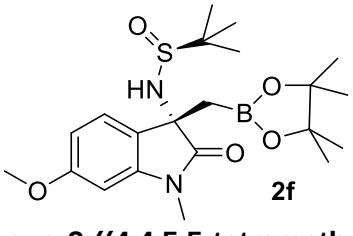
Purified by FC (EtOAc / Hexane 8:2) to afford a yellow foam (yield 91%). $^{1}$H NMR (400 MHz, $CD_3CN$) δ 7.56 (br d, *J* = 7.3 Hz, 6H), 7.41 (d, *J* = 7.2 Hz, 1H), 7.32-7.21 (m, 9H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 1H), 6.35 (d, *J* = 7.6 Hz, 1H), 4.98 (s, 1H), 1.62 (d, *J* = 15.5 Hz, 1H), 1.58 (d, *J* = 15.5 Hz, 1H), 1.24 (s, 6H), 1.18 (s, 6H), 1.08 (s, 9H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 21.8 (3C), 24.0 (2C), 24.1 (2C), 55.9 (1C), 62.3 (1C), 74.1 (1C), 83.9 (2C), 115.7 (1C), 122.1 (1C), 124.8 (1C), 126.7 (3C), 127.5 (7C), 128.2 (1C), 129.1 (6C), 131.8 (1C), 142.6 (3C), 178.2 (1C), *(due to the quadrupolar nature of $^{11}$B, the C signal of the carbon atom linked to boron was not observed, 23.0 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 32.5. HRMS (ESI) *m/z*: 635.3117 $[M+H]^+$, calcd for $C_{38}H_{44}BN_2O_4S^+$ 635.3109. $[\alpha]_D$ = - 12.1 (c 0.9, $CHCl_3$).




**2e**

***(S)*-N-(*(S)*-1,5-dimethyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)-2-methylpropane-2-sulfinamide (2e)**

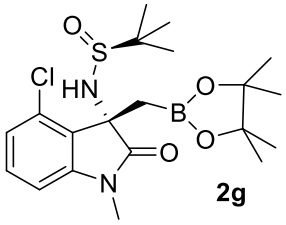
Purified by FC (EtOAc / Hexane 8:2) to afford a pale-yellow foam (yield 74%). $^{1}$H NMR (400 MHz, $CD_3CN$) δ 7.26 (s, 1H), 7.16 (d, *J* = 7.9 Hz, 1H), 6.84 (d, *J* = 7.9 Hz, 1H), 4.90 (s, 1H), 3.13 (s, 3H), 2.33 (s, 3H), 1.54 (d, *J* = 14.8 Hz, 1H), 1.44 (d, *J* = 15.5 Hz, 1H), 1.14 (s, 9H), 1.10 (s, 6H), 1.07 (s, 6H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 20.8 (1C), 22.4 (3C), 24.4 (2C), 24.8 (2C), 26.4 (1C), 56.4 (1C), 62.7 (1C), 84.0 (2C), 108.9 (1C), 125.9 (1C), 130.1 (1C), 131.8 (1C), 132.4 (1C), 142.0 (1C), 177.1 (1C), *(due to the quadrupolar nature of $^{11}$B, the C signal of the carbon atom linked to boron was not observed, 23.3 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 32.3. HRMS (ESI) *m/z*: 421.2335 $[M+H]^+$, calcd for $C_{21}H_{34}BN_2O_4S^+$ 421.2327. $[\alpha]_D$ = - 5.4 (c 0.4, $CHCl_3$).




**2f**

***(S)*-N-(*(S)*-6-methoxy-1-methyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)-2-methylpropane-2-sulfinamide (2f)**

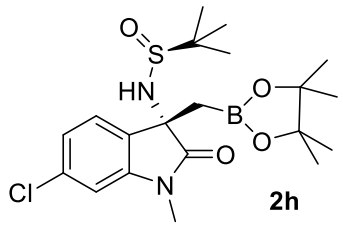
Purified by FC (EtOAc / Hexane 8:2) to afford a pale-yellow foam (yield 78%). $^{1}$H NMR (400 MHz, acetone d-6) δ 7.37 (d, *J* = 7.6 Hz, 1H), 6.63 (br d, 1H), 6.60 (s, 1H), 5.09 (s, 1H), 3.85 (s, 3H), 3.18 (s, 3H), 1.57 (d, *J* = 15.0 Hz, 1H), 1.47 (d, *J* = 15.0 Hz, 1H), 1.15 (s, 6H), 1.13 (s, 9H), 1.12 (s, 6H). $^{13}$C NMR (101 MHz, acetone d-6) δ 22.5 (3C), 24.6 (2C), 25.0 (2C), 26.2 (1C), 55.6 (1C), 56.0 (1C), 62.5 (1C), 83.9 (2C), 94.5 (1C), 106.9 (1C), 123.4 (1C), 126.4 (1C), 145.8 (1C), 161.9 (1C), 177.6 (1C), *(due to the quadrupolar nature of $^{11}$B, the C signal of the carbon atom linked to boron was not observed, 23.6 ppm from HSQC*). $^{11}$B NMR (128 MHz, acetone d-6) δ 32.3. HRMS (ESI) *m/z*: 459.2096 $[M+Na]^+$, calcd for $C_{21}H_{33}BN_2O_5SNa^+$ 459.2101. $[\alpha]_D$ = - 7.1 (c 1.0, $CHCl_3$).




**2g**

***(S)*-N-(*(S)*-4-chloro-1-methyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)-2-methylpropane-2-sulfinamide (2g)**

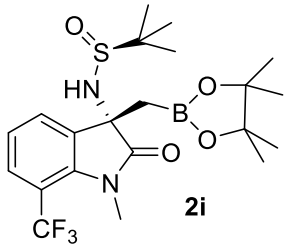
Purified by FC (EtOAc / Hexane 8:2) to afford a pale-yellow solid (yield 61%). $^{1}$H NMR (400 MHz, $CD_3CN$) δ 7.23 (t, *J* = 8.0 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 6.85 (d, *J* = 7.9 Hz, 1H), 4.82 (s, 1H), 3.10 (s, 3H), 1.82 (d, *J* = 14.6 Hz, 1H), 1.65 (d, *J* = 14.6 Hz, 1H), 1.05 (s, 9H), 0.92 (s, 6H), 0.86 (s, 6H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 22.3 (3C), 24.3 (2C), 24.7 (2C), 26.7 (1C), 56.7 (1C), 63.8 (1C), 83.9 (2C), 107.9 (1C), 123.8 (1C), 128.2 (1C), 131.4 (1C), 131.8 (1C), 146.5 (1C), 176.0 (1C), *(due to the quadrupolar nature of $^{11}$B, the C signal of the carbon atom linked to boron was not observed, 20.1 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 32.2. HRMS (ESI) *m/z*: 463.1615 $[M+Na]^+$, calcd for $C_{20}H_{30}BN_2O_4SClNa^+$ 463.1606. $[\alpha]_D$ = - 10.7 (c 0.8, $CHCl_3$).




**2h**

***(S)*-N-(*(S)*-6-chloro-1-methyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)-2-methylpropane-2-sulfinamide (2h)**

Purified by FC (EtOAc / Hexane 8:2) to afford a pale-yellow foam (yield 79%). $^{1}$H NMR (400 MHz, $CD_3CN$) δ 7.39 (d, *J* = 7.9 Hz, 1H), 7.10 (dd, $J_3$=7.9 Hz, $J_4$=2.2 Hz, 1H), 7.03 (d, *J* = 1.8 Hz, 1H), 4.89 (s, 1H), 3.15 (s, 3H), 1.58 (d, *J* = 15.0 Hz, 1H), 1.50 (d, *J* = 15.0 Hz, 1H), 1.14 (s, 9H), 1.11 (s, 6H), 1.05 (s, 6H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 21.7 (3C), 23.7 (2C), 24.1 (2C), 25.9 (1C), 62.0 (1C), 67.7 (1C), 83.6 (1C), 109.1 (1C), 121.9 (1C), 125.7 (1C), 130.0 (1C), 134.4 (1C), 145.3 (1C), 176.4 (1C), *(due to the quadrupolar nature of $^{11}$B, the C signal of the carbon atom linked to boron was not observed, 21.9 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 32.1. HRMS (ESI) *m/z*: 463.1599 $[M+Na]^+$, calcd for $C_{20}H_{30}BN_2O_4SClNa^+$ 463.1606. $[\alpha]_D$ = - 6.8 (c 1.7, $CHCl_3$).

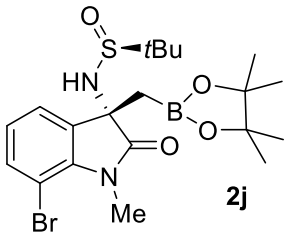



**2i**

***(S)*-2-methyl-N-(*(S)*-1-methyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-7-(trifluoromethyl)indolin-3-yl)propane-2-sulfinamide (2i)**

Purified by FC (EtOAc / Hexane 8:2) to afford a yellow foam (yield 60%). $^{1}$H NMR (400 MHz, $CD_3CN$) δ 7.63 (d, *J* = 7.4 Hz, 1H), 7,58 (d, *J* = 7.5 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 5.12 (s, 1H), 3.29 (q, *J* = 2.4 Hz, 3H), 1.62 (d, *J* = 15.0 Hz, 1H), 1.58 (d, *J* = 15 Hz, 1H), 1.05 (s, 9H), 0.97 (s, 6H), 0.91 (s,

6H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 22.3 (3C), 24.3 (2C), 24.7 (2C), 29.2 (1C), 56.6 (1C), 61.2 (1C), 84.2 (1C), 122.7 (1C), 124.6 (q, *J* = 271.1 Hz, 1C), 127.55 (1C), 129.1 (1C), 134.8 (1C), 142.3 (1C), 178.1 (1C), *(due to the quadrupolar nature of $^{11}$B, the C signal of the carbon atom linked to boron was not observed, 22.2 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 31.9. $^{19}$F NMR (300 MHz, $CD_3CN$) δ -53.90 (s, 3F). HRMS (ESI) *m/z*: 497.1878 $[M+Na]^+$, calcd for $C_{21}H_{30}BF_3N_2O_4SNa^+$ 497.1869. $[\alpha]_D$ = - 9.2 (c 0.9, $CHCl_3$).



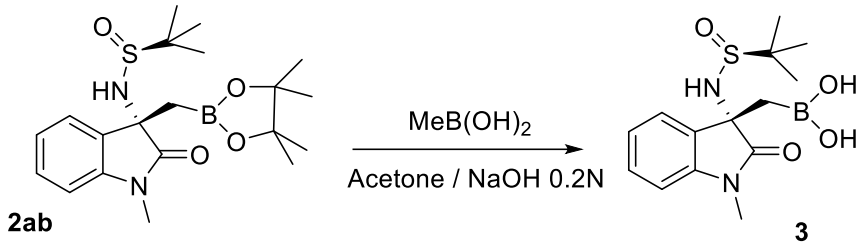

**2j**

***(S)*-N-(*(S)*-7-bromo-1-methyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)-2-methylpropane-2-sulfinamide (2j)**

Purified by FC (EtOAc / Hexane 7:3) to afford a brown foam (yield 58%). $^1$H NMR (400 MHz, $CD_3CN$) δ 7.47 (d, *J* = 8.2 Hz, 1H), 7.38 (d, *J* = 7.3 Hz, 1H), 6.99 (t, *J* = 7.8 Hz, 1H), 4.83 (s, 1H), 3.53 (s, 3H), 1.61 (d, *J* = 14.9 Hz, 1H), 1.50 (d, *J* = 14.8 Hz, 1H), 1.14 (s, 9H), 1.08 (s, 6H), 1.03 (s, 6H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 22.3 (3C), 24.3 (2C), 24.8 (2C), 30.0 (1C), 62.5 (1C), 84.2 (2C), 102.6 (1C), 124.5 (2C), 135.2 (1C), 135.4 (1C), 141.6 (1C), 177.7 (1C), *(due to the quadrupolar nature of $^{11}$B, the C signal of the carbon atom linked to boron was not observed, 23.3 ppm from HSQC; $C_q$(tBu) missed*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 32.1. HRMS (ESI) *m/z*: 485.1268 $[M+H]^+$, calcd for $C_{20}H_{31}BN_2O_4SBr^+$ 485.1275. $[\alpha]_D$ = - 23.1 (c 0.8, $CHCl_3$).

## Post transformation reactions

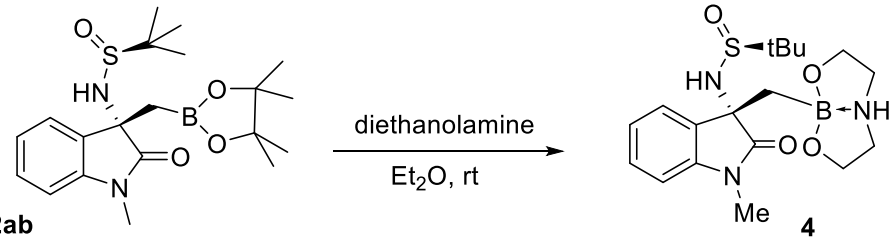
### ((3-(((*S*)-tert-butylsulfinyl)amino)-1-methyl-2-oxoindolin-3-yl)methyl)boronic acid (3)




**2ab** **3**

Compound **2ab** (60 mg, 0.123 mmol, 1 eq) and methyl boronic acid (73 mg, 1.23 mmol, 10 eq) were dissolved in a 1:1 solution of acetone and NaOH 0.2 N (2 mL, 0.06 M) and stirred overnight at room temperature. The solvents were evaporated under reduced pressure with a 45 °C bath to complete the reaction. The reaction was diluted with water (3 mL) and carefully neutralized using HCl 0.1 N, then the solution was lyophilized to dryness. The solid was washed with hot acetone (3 x 8 mL) and filtered off. The acetone was evaporated under reduced pressure to afford **3** as a white solid. Yield 92% (37 mg). $^{1}$H NMR (400 MHz, acetone d-6) δ 7.55-7.50 (m, 3H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 7.8 Hz, 1H), 5.37 (s, 1H), 3.23 (s, 3H), 1.58 (d, *J* = 16.0 Hz, 1H), 1.34 (d, *J* = 16.0 Hz, 1H), 1.14 (s, 9H). $^{13}$C NMR (101 MHz, acetone d-6) δ 22.4 (3C), 26.3 (1C), 56.5 (1C), 63.8 (1C), 109.1 (1C), 123.3 (1C), 125.1 (1C), 129.4 (1C), 133.7 (1C), 143.0 (1C), 178.4 (1C), *(due to the quadrupolar nature of 11B, the C signal of the carbon atom linked to boron was not observed, 26.7 ppm from HSQC*). $^{11}$B NMR (128 MHz, acetone d-6) δ 30.8. HRMS (ESI) *m/z*: 375.1518 $[M(OMe)_2+Na]^+$, calcd for $C_{16}H_{25}BN_2O_4SNa^+$ 375.1526. $[\alpha]_D$ = - 13.4 (c 0.4, $CHCl_3$).

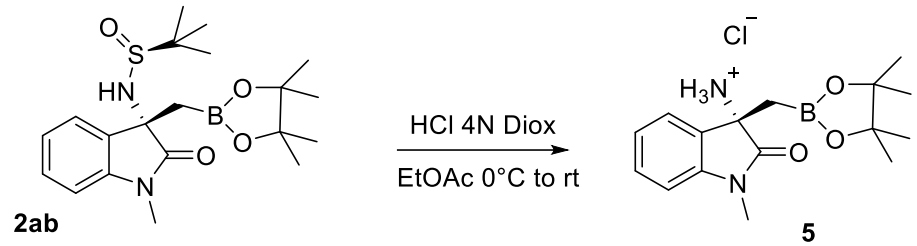
### (*S*,*S*) DEA-Protected oxindole-β-amino boronic ester (4)




**2ab** **4**

Compound **2ab** (54 mg, 0.133 mmol, 1 eq) was dissolved in $Et_2O$ (1.5 mL 0.09 M). Diethanolamine (14 µL, 0.148 mmol, 1.1 eq) was added and the reaction was stirred vigorously for 3h. The brown slurry was filtered and washed with $Et_2O$ / isopropanol 10:1 (2 x 3 mL) and dried under reduced pressure to afford **4** as a white gum. Yield 69% (36 mg). $^{1}$H NMR (400 MHz, $CD_3CN$) δ 7.47 (d, *J* = 7.3 Hz, 1H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 7.3 Hz, 1H), 6.95 (d, *J* = 7.7 Hz, 1H), 6.86 (s, 1H), 6.61 (br s, 1H), 3.96-3.90 (m, 2H), 3.86-3.78 (m, 1H), 3.64-3.57 (m, 1H), 3.41-3.31 (m, 1H), 3.28-3.19 (m, 1H), 3.17 (s, 3H), 2.93-2.81 (m, 2H), 1.23 (d, *J* = 15.1 Hz, 1H), 1.11 (s, 9H), 0.78 (d, *J* = 15.1 Hz, 1H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 21.8 (3C), 25.8 (1C), 51.0 (1C), 51.1 (1C), 55.0 (1C), 62.6 (1C), 62.8 (1C), 64.3 (1C), 108.3 (1C), 122.7 (1C), 125.1 (1C), 128.7 (1C), 133.6 (1C), 142.8 (1C), 180.6 (1C), *(due to the quadrupolar nature of 11B, the C signal of the carbon atom linked to boron was not observed, 26.8 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 11.1. HRMS (ESI) *m/z*: 394.1959 $[M+H]^+$, calcd for $C_{18}H_{29}BN_3O_4S^+$ 394.1966. $[\alpha]_D$ = - 3.1° (c 0.9, $CHCl_3$).

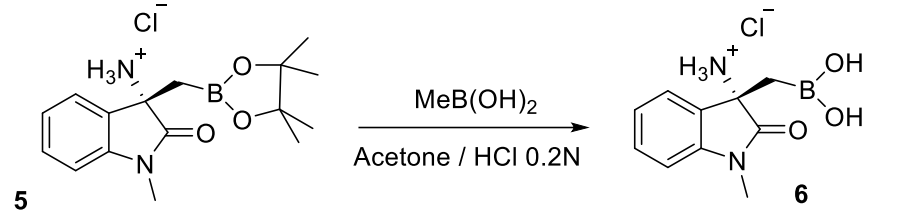
### *(S)*-1-methyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-ammonium chloride (5)




**2ab** **5**

Compound **2ab** (290 mg, 0.71 mmol) was dissolved in EtOAc (5 mL, 0,14 M) and stirred at 0 °C for 5 minutes. HCl (4N in dioxane, 0.67 mL, 2.68 mmol) was added dropwise and the reaction was stirred at 0 °C for 10 minutes. After warming to room temperature, the reaction was stirred until precipitation of product **5** (approximatively 30 minutes). The solid was filtered, washed with cold EtOAc (2 x 10 mL) and dried, to afford pure **5**, as a light brown powder. Yield: 97% (234 mg). $^{1}$H NMR (400 MHz, DMSO d-6) δ 9.12 (br s, 3H), 7.75 (d, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.15-7.10 (m, 2H), 3.16 (s, 3H), 1.89 (d, *J* = 14.4 Hz, 1H), 1.61 (d, *J* = 14.4 Hz, 1H), 0.88 (s, 6H), 0.81 (s, 6H). $^{13}$C NMR (101 MHz, DMSO d-6) δ 25.0 (2C), 25.4 (2C), 27.4 (1C), 58.8 (1C), 84.3 (2C), 110.2 (1C), 123.8 (1C), 125.6 (1C), 127.6 (1C), 131.7 (1C), 145.0 (1C), 174.2 (1C), *(due to the quadrupolar nature of $^{11}$B, the C signal of the carbon atom linked to boron was not observed, 20.1 ppm from HSQC*). $^{11}$B NMR (128 MHz, DMSO d-6) δ 32.2. HRMS (ESI) *m/z*: 303.1881 $[M+H]^+$, calcd for $C_{16}H_{24}BN_2O_3^+$ 303.1874. $[\alpha]_D$ = + 1.7 (c 0.8, DMSO).

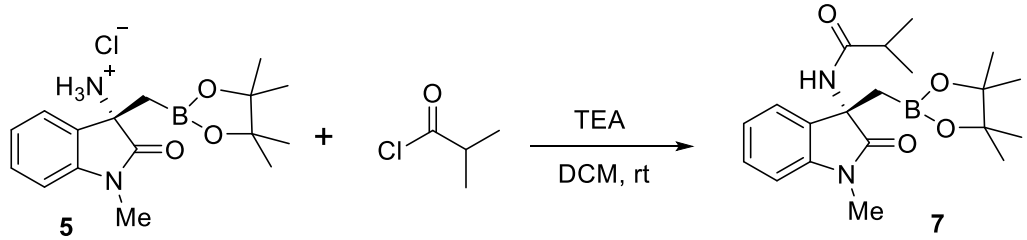
### *(S)*-3-(boronomethyl)-1-methyl-2-oxoindolin-3-ammonium chloride (6)




**5** **6**

Compound **5** (120 mg, 0.396 mmol, 1 eq) and methyl boronic acid (237 mg, 3.96 mmol, 10 eq) were dissolved in a 1:1 solution of acetone and HCl 0.2 N (6.6 mL, 0.06 M) and stirred overnight at room temperature. The solvents were evaporated under reduced pressure with a 45 °C bath to complete the reaction, diluted with HCl 0.2 N (3 mL) and evaporated again. The sticky residue was diluted with water (3 mL) and lyophilized to afford **6** as a dark yellow gum. Yield 98% (99 mg). $^{1}$H NMR (400 MHz, DMSO d-6) δ 8.85 (s, 3H), 7.84 (br s, 2H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 1H), 7.14-7.06 (m, 2H), 3.14 (s, 3H), 1.71 (d, *J* = 15.5 Hz, 1H), 1.49 (d, *J* = 15.5 Hz, 1H). $^{13}$C NMR (101 MHz, DMSO d-6) δ 26.8 (1C), 58.7 (1C), 109.4 (1C), 122.8 (1C), 124.7 (1C), 127.9 (1C), 130.6 (1C), 144.5 (1C), 174.3 (1C), *(due to the quadrupolar nature of 11B, the C signal of the carbon atom linked to boron was not observed, 17.7 ppm from HSQC*). $^{11}$B NMR (128 MHz, DMSO d-6) δ 32.6. HRMS (ESI) *m/z*: 249.1389 $[M(OMe)_2 + H]^+$, calcd for $C_{12}H_{18}BN_2O_3^+$ 249.1405. $[\alpha]_D$ = + 1.3° (c 0.8, DMSO).

### *(S)*-N-(1-methyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)isobutyramide (7)

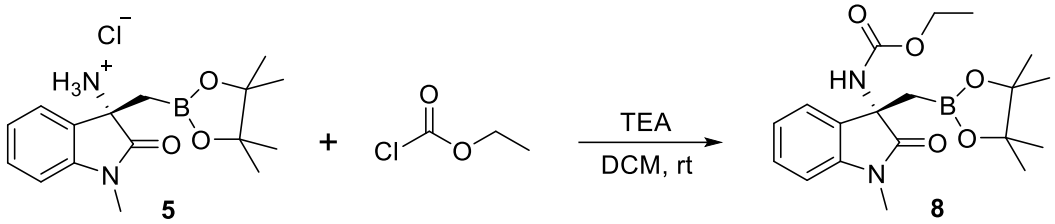



**5** **7**

Compound **5** (35 mg, 0.104 mmol, 1 eq) was suspended in dry dichloromethane (3 mL, 0.03 M) and stirred for 10 minutes. Freshly distilled triethylamine (36 µL, 0.260 mmol, 2.5 eq) and isobutyryl chloride (12 µL, 0.110 mmol, 1.05 eq) were added sequentially and the reaction was stirred at room temperature overnight. The reaction was diluted with dichloromethane (15 mL) and washed with 5% aqueous solution of citric acid, $NaHCO_{3\ sat}$ and brine. Then the organic phase was dried over

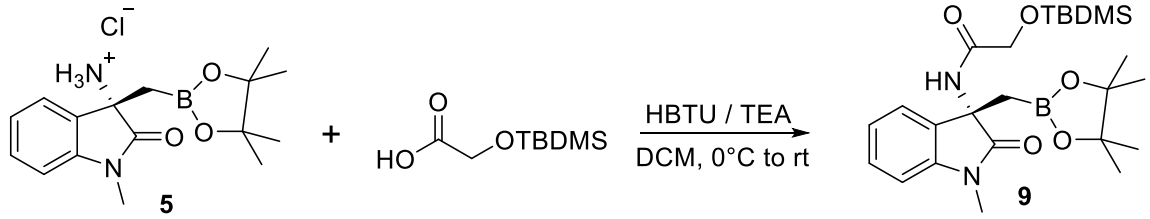
anhydrous $NaSO_4$. The solvent was evaporated under reduced pressure and the crude mixture purified by FC (EtOAc / Hexane 9:1) to afford **7** as a yellow foam. Yield 94% (36 mg). $^1$H NMR (400 MHz, $CD_3CN$) δ 7.28 (t, *J* = 7.7 Hz, 1H), 7.22 (d, *J* = 6.6 Hz, 1H), 7.05-6.99 (m, 2H), 6.89 (d, *J* = 7.8, 1H), 3.17 (s, 3H), 2.39 (sept, *J* = 6.9 Hz, 1H), 1.45 (d, *J* = 14.6 Hz, 1H), 1.31 (d, *J* = 14.6 Hz, 1H), 1.10 (s, 6H), 1.08 (s, 6H), 1.03 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 18.4 (1C), 18.7 (1C), 23.9 (2C), 24.1 (2C), 25.7 (1C), 33.9 (1C), 58.8 (1C), 83.5 (2C), 107.9 (1C), 121.6 (1C), 121.9 (1C), 128.3 (1C), 132.2 (1C), 144.0 (1C), 175.2 (1C), 176.5 (1C), *(due to the quadrupolar nature of 11B, the C signal of the carbon atom linked to boron was* not observed, 20.5 ppm from HSQC). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 32.0. HRMS (ESI) *m/z*: 395.2127 $[M+Na]^+$, calcd for $C_{20}H_{29}BN_2O_4Na^+$ 395.2118. $[\alpha]_D$ = - 29.7 (c 0.9, $CHCl_3$).

***(S)*-ethyl (1-methyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)carbamate (8)**




Compound **5** (100 mg, 0.296 mmol, 1 eq) was suspended in dry dichloromethane (9 mL, 0.03 M) and stirred for 10 minutes. Freshly distilled triethylamine (103 µL, 0.740 mmol, 2.5 eq) and ethyl-chloroformate (30 µL, 0.310 mmol, 1.05 eq) were added sequentially and the reaction was stirred at room temperature overnight. The reaction was diluted with dichloromethane (15 mL) and washed with 5% aqueous solution of citric acid, $NaHCO_{3\ sat}$ and brine. The organic phase was dried over anhydrous $NaSO_4$. The solvent was evaporated under reduced pressure and the crude mixture purified by FC (EtOAc / Hexane 9:1) to afford **8** as a pale-yellow foam. Yield 96% (106 mg). $^1$H NMR (400 MHz, $CD_3CN$) δ 7.33-7.26 (m, 2H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.7 Hz, 1H), 6.27 (br s, 1H), 3.90 (br m, 2H), 3.17 (s, 3H), 1.47 (d, *J* = 14.6 Hz, 1H), 1.34 (d, *J* = 14.6 Hz, 1H), 1.12 (br m, 3H), 1.06 (s, 6H), 1.05 (s, 6H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 13.8 (1C), 23.8 (2C), 24.0 (2C), 25.7 (1C), 59.2 (1C), 60.5 (1C), 83.5 (2C), 108.0 (1C), 122.0 (2C), 128.6 (1C), 131.9 (1C), 143.9 (1C), 154.3 (1C), 176.6 (1C), *(due to the quadrupolar nature of 11B, the C signal of the carbon atom linked to boron was not observed, 21.7 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 31.7. HRMS (ESI) *m/z*: 397.1919 $[M+Na]^+$, calcd for $C_{19}H_{27}BN_2O_5Na^+$ 397.1911. $[\alpha]_D$ = - 32.9 (c 1.0, $CHCl_3$).

***(S)*-2-((tert-butyldimethylsilyl)oxy)-N-(2-((1-methyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)amino)-2-oxoethyl)acetamide (9)**

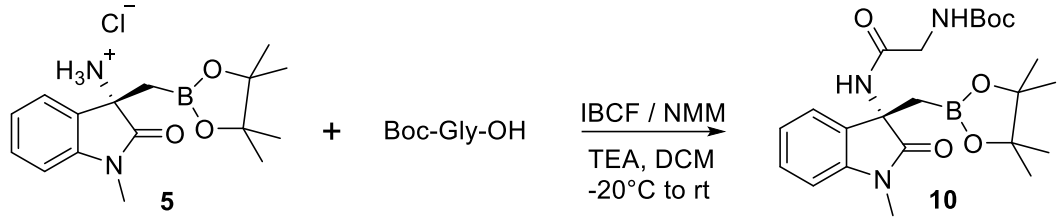



The TBDMS-protected glycolic acid was synthetized in a two-step procedure, as reported in literature.[5]

TBDMS-protected glycolic acid (84 mg, 0.442 mmol, 1.5 eq) was dissolved in dry dichloromethane (4.4 mL, 0.1M in TBDMS-glycolic acid) and cooled to 0 °C. HBTU (672 mg, 1.78 mmol, 6 eq) and freshly distilled triethylamine (360 µL, 2.96 mmol, 10 eq) were added sequentially and the reaction stirred at 0 °C for 1h. Compound **5** (100 mg, 0.296 mmol, 1 eq) and triethylamine (140 µL, 1.18 mmol, 4 eq) were added, then the ice bath was removed and the reaction stirred until competition (approximatively 2h, monitored by TLC). The reaction was diluted with dichloromethane (15 mL) and washed with an aqueous phosphate buffer (x2) and brine. Then the organic phase was dried over anhydrous $NaSO_4$. The solvent was removed under reduced pressure and the crude mixture was purified by FC (EtOAc / Hexane 7:3) to afford **9** as a light-yellow foam. Yield 71% (100 mg). $^1$H NMR (400 MHz, $CD_3CN$) δ 7.58 (br s, 1H), 7.31 (t, *J* = 7.7 Hz, 1H), 7.28 (d, *J* = 7.1 Hz, 1H), 7.04 (t, *J* =

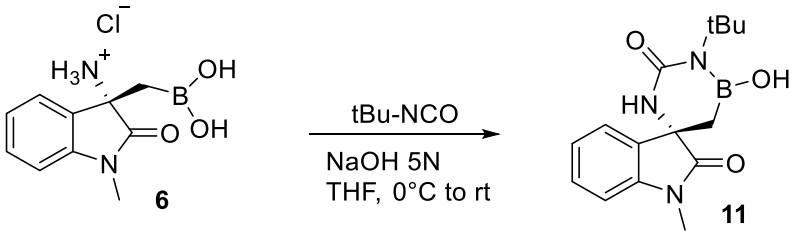
7.5 Hz, 1H), 6.92 (d, *J* = 7.8 Hz, 1H), 4.01 (d, *J* = 15.8 Hz, 1H), 3.96 (d, *J* = 15.8 Hz, 1H), 3.18 (s, 3H), 1.49 (d, *J* = 14.8 Hz, 1H), 1.30 (d, *J* = 14.8 Hz, 1H), 1.16 (s, 6H), 1.15 (s, 6H), 1.02 (s, 9H), 0.19 (s, 6H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ -6.2 (2C), 18.0 (1C), 24.0 (2C), 24.2 (2C), 25.3 (3C), 25.8 (1C), 58.5 (1C), 63.0 (1C), 83.8 (2C), 108.0 (1C), 122.1 (2C), 128.6 (1C), 131.7 (1C), 143.8 (1C), 169.6 (1C), 176.2 (1C), *(due to the quadrupolar nature of 11B, the C signal of the carbon atom linked to boron was not observed, 20.8 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 32.0. HRMS (ESI) *m/z*: 497.2628 $[M+Na]^+$, calcd for $C_{24}H_{39}BN_2O_5SiNa^+$ 497.2619. $[\alpha]_D$ = - 37.1 (c 0.9, $CHCl_3$).

**(*S*)-tert-butyl (2-((1-methyl-2-oxo-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)indolin-3-yl)amino)-2-oxoethyl)carbamate (10)**




Boc-Gly-OH (535 mg, 3.05 mmol, 7.7 eq) was dissolved in dry dichloromethane (9 mL 0.04 M) and cooled to – 20 °C. N-methyl morpholine (409 µL, 3.72 mmol, 9.4 eq) and isobutyl chloroformate (351 µL, 2.73 mmol, 6.9 eq) were added sequentially and the reaction was stirred at – 20 °C for 5h. Compound **5** (135 mg, 0.396 mmol, 1 eq) and freshly distilled triethylamine (107 µL, 0.79 mmol, 2 eq) were added, then the cooling bath was removed and the reaction stirred overnight. The reaction was diluted with dichloromethane (15 mL) and washed with 5% aqueous solution of citric acid, $NaHCO_{3\ sat}$ and brine. Then the organic phase was dried over anhydrous $NaSO_4$. The solvent was evaporated under reduced pressure and the crude mixture purified by FC (EtOAc / Hexane 9:1) to afford **10** as a yellow foam. Yield 96% (175 mg). $^1$H NMR (400 MHz, $CD_3CN$) δ 7.37 (br s, 1H), 7.29 (td, $J_3$ = 7.7 Hz, $J_4$ = 1.3 Hz, 1H), 7.24 (d, *J* = 7.1 Hz, 1H), 7.03 (td, $J_3$ = 7.5 Hz, $J_4$ = 1.0 Hz, 1H), 6.91 (d, *J* = 7.8 Hz, 1H), 5.55 (br s, 1H), 3.68-3.51 (m, 2H), 3.17 (s, 3H), 1.49 (d, *J* = 14.7, 1H), 1.45 (s, 9H), 1.31 (d, *J* = 14.9 Hz, 1H), 1.11 (s, 6H), 1.09 (s, 6H). $^{13}$C NMR (101 MHz, $CD_3CN$) δ 23.9 (2C), 24.2 (2C), 25.7 (1C), 27.5 (3C), 43.1 (1C), 58.8 (1C), 79.1 (1C), 83.6 (2C), 108.0 (1C), 121.9 (1C), 122.0 (1C), 128.5 (1C), 131.6 (1C), 143.9 (1C), 168.3 (1C), 176.1 (2C), *(due to the quadrupolar nature of 11B, the C signal of the carbon atom linked to boron was not observed, 20.4 ppm from HSQC*). $^{11}$B NMR (128 MHz, $CD_3CN$) δ 31.9. HRMS (ESI) *m/z*: 460.2628 $[M+H]^+$, calcd for $C_{23}H_{35}BN_3O_6^+$ 460.2613. $[\alpha]_D$ = - 34.5 (c 1.1, $CHCl_3$).

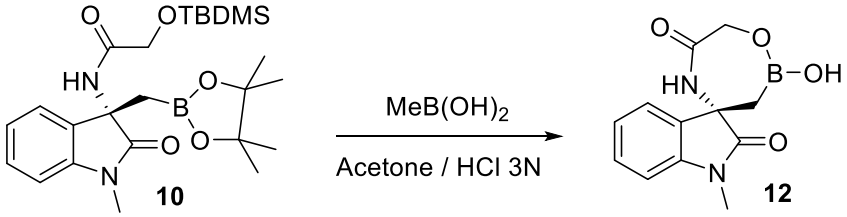
**(*S*)-1'-(tert-butyl)-2'-hydroxy-1-methylspiro[indoline-3,4'-[1,5,2]diazaborinane]-2,6'-dione (11)**




Compound **6** (93 mg, 0.361 mmol, 1 eq) was suspended in THF (7 mL, 0.05 M) and cooled to 0 °C. NaOH 5N (72 µL, 0.361 mmol, 1 eq) was added dropwise and the reaction was stirred for 10 minutes at 0° C. Tert-butyl isocyanate (46 µL, 0.397 mmol, 1.1 eq) was added and the reaction was stirred overnight at room temperature. The solvent was evaporated under reduced pressure and the solid was washed with hot acetone (x3) and filtered off. The solvent was evaporated under reduced pressure and the crude was purified by reverse-phase FC ($CH_3CN$ / $H_2O$ 5:95 to 20:80) to afford **11** as a white-off powder. Yield 86% (92 mg). $^1$H NMR (400 MHz, acetone d-6) δ 7.71 (br s, 1H), 7.24 (m, 2H), 7.01 (t, *J* = 7.4 Hz, 1H), 6.94 (d, *J* = 7.6 Hz, 1H), 6.23 (br s, 1H), 5.67 (br s, 1H), 3.22 (s, 3H), 1.39 (d, *J* = 16.4 Hz, 1H), 1.17 (s, 9H), 1.12 (d, *J* = 16.4 Hz, 1H). $^{13}$C NMR (101 MHz, acetone d-6) δ 25.8 (1C), 28.7 (3C), 49.4 (1C), 59.3 (1C), 108.0 (1C), 121.2 (1C), 122.3 (1C), 127.7 (1C), 135.3 (1C), 142.8 (1C), 155.8 (1C), 180.2 (1C), *(due to the quadrupolar nature of 11B, the C signal*

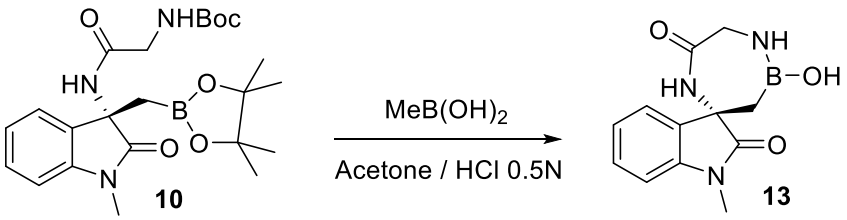
*of the carbon atom linked to boron was not observed, 25.0 ppm from HSQC*). $^{11}$B NMR (128 MHz, acetone d-6) δ 31.8. HRMS (ESI) *m/z*: 370.1925 [M(B-OMe)·MeOH+Na]$^+$, calcd for $C_{17}H_{26}BN_3O_4Na^+$ 370.1914. $[\alpha]_D$ = + 0.9 (c 0.5, acetone).

**(*S*)-2'-hydroxy-1-methylspiro[indoline-3,4'-[1,5,2]oxazaborepane]-2,6'-dione (12)**




Compound **10** (66 mg, 0.140 mmol, 1 eq) and methyl boronic acid (75 mg, 1.25 mmol, 9 eq) were dissolved in a 1:1 solution of acetone / HCl 3N (4 mL, 0.03 M) and stirred overnight at room temperature. The solvents were evaporated under reduced pressure with a 45 °C bath, then the reaction was diluted with water (5 mL) and lyophilized. The solid was purified by reverse-phase FC ($CH_3CN$ / $H_2O$ 5:95 to 10:90) to afford **12** as a white gum. Yield 94% (34 mg). $^1$H NMR (400 MHz, acetone d-6) δ 7.31 (d, *J* = 7.4 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 3.91 (d, *J* = 16.4 Hz, 1H), 3.78 (d, *J* = 16.4 Hz, 1H), 3.18 (s, 3H), 1.42 (d, *J* = 15.6 Hz, 1H), 1.16 (d, *J* = 15.6 Hz, 1H*), two exchangeable protons missed*. $^{13}$C NMR (101 MHz, acetone d-6) δ 26.6 (1C), 59.7 (1C), 61.8 (1C), 109.2 (1C), 122.8 (1C), 123.4 (1C), 129.2 (1C), 133.0 (1C), 143.7 (1C), 172.6 (1C), 179.4 (1C), *(due to the quadrupolar nature of 11B, the C signal of the carbon atom linked to boron was not observed, 24.8 ppm from HSQC*). $^{11}$B NMR (128 MHz, acetone d-6) δ 30.8. HRMS (ESI) *m/z*: 329.1292 [M(BOMe)·MeOH+Na]$^+$, calcd for $C_{14}H_{19}BN_2O_5Na^+$ 329.1285. $[\alpha]_D$ = + 1.3 (c 0.3, acetone).

**(*S*)-2'-hydroxy-1-methylspiro[indoline-3,4'-[1,5,2]diazaborepane]-2,6'-dione (13)**




Compound **10** (70 mg, 0.152 mmol, 1 eq) and methyl boronic acid (91 mg, 1.52 mmol, 10 eq) were dissolved in a 1:1 mixture of acetone and HCl 0.5 N (4.6 mL, 0.03 M) and stirred overnight at room temperature. The solvents were removed under reduced pressure with a 45 °C bath, then the reaction was diluted with water (5 mL) and carefully neutralized with NaOH 0.2N. The solvent was removed under reduced pressure and the solid was washed with hot acetone (x3) and filtered off. Acetone was evaporated under reduced pressure and the crude product was purified by reverse-phase FC ($CH_3CN$ / $H_2O$ 5:95 to 15:85) to afford **13** as a colourless gum. Yield 90% (35 mg). $^1$H NMR (400 MHz, DMSO d-6) δ 9.08 (br s, 1H), 7.84 (br s, 2H), 7.49 (br s, 1H), 7.26-7.20 (m, 2H), 7.00-6.92 (m, 2H), 3.53 (d, *J* = 16.4 Hz, 1H, *only detected at 100 °C, due to overlapping of water signal*), 3.47 (d, *J* = 16.3 Hz, 1H, *only detected at 150 °C, due to overlapping of water signal*), 3.11 (s, 3H), 1.32 (d, *J* = 15.3 Hz, 1H), 1.18 (d, *J* = 15.3 Hz, 1H). $^{13}$C NMR (101 MHz, DMSO d-6) δ 25.4 (1C), 27.3 (1C), 41.2 (1C, *from HSQC*), 60.3 (1C), 109.0 (1C), 123.0 (1C), 123.1 (1C), 129.2 (1C), 133.1 (1C), 144.5 (1C), 166.1 (1C), 178.0 (1C). $^{11}$B NMR (128 MHz, DMSO d-6) δ 31.9. HRMS (ESI) *m/z*: 328.1454 [M(B-OMe)·MeOH+Na]$^+$, calcd for $C_{14}H_{20}BN_3O_4Na^+$ 328.1445. $[\alpha]_D$ = + 1.1 (c 0.4, acetone).

## Assignment of the C-3 configuration by NMR studies (Mosher method)[1]

The two methoxy-α-trifluoromethyl-α-phenylacetic acid (MTPA) amide derivatives of compound **5** (unknown C-3 configuration) were obtained from the corresponding optically pure (*R*)- and *(S)*-MTPA chlorides, following the well-known literature procedure.[2] It is noteworthy that, following the CIP rules of priority, the *(S)*-MTPA chloride gives the (*R*)-MTPA amide and vice versa.
The NMR spectra of the two derivatives are then recorded (using $CD_3CN$ as solvent) and the differences in the chemical shifts ($\Delta\delta SR$) are evaluated. According to the general model proposed by Mosher, for which the most-relevant conformer would be the one in which the $CF_3$, the carbonyl and the NH-C bond are in the same plane, with the $CF_3$ and the carbonyl units in a *syn*-periplanar disposition, we assumed an arbitrary *(S)*-configuration at C-3 and considered the models reported in Figure 1.

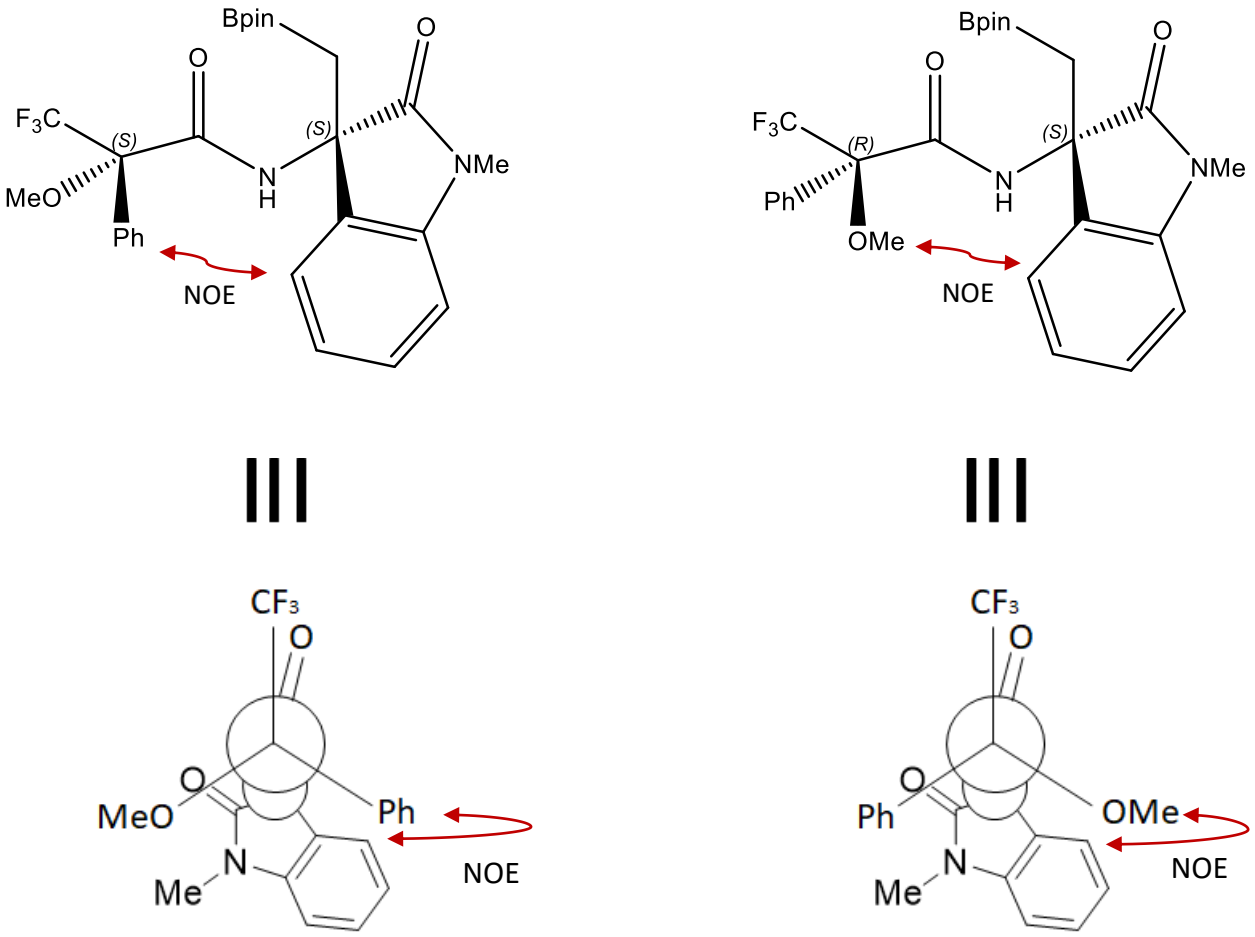



**Figure 1**. *(S)*- and (*R*)-methoxy-α-trifluoromethyl-α-phenylacetic acid (MTPA) amides from compound **5** (arbitrary (*S*)-configuration) in their assumed preferred conformation (the red arrows point out NOE contacts).

[1] (a) J. M. Seco, E. Quiñoá and R. Riguera, The Assignment of Absolute Configuration by NMR. *Chem. Rev.*, 2004, **104**, 17. (b) R. J. Wehrle, D. R. Powell and D. S. Masterson, Direct determination of absolute stereochemistry of α-methylselenocysteine using the Mosher method. *Results in Chemistry,* 2021, **3**, 100114.
[2] D. A. Allen, A. E. Tomaso Jr., O. P. Priest, D. F. Hindson and J. L. Hurlburt, Mosher Amides: Determining the Absolute Stereochemistry of Optically-Active Amines. *J. Chem. Educ*., 2008, **85**, 698.

In accordance with these models, a shielding effect is expected for the oxindole aromatic protons in the *(S)*-MTPA derivative, due to the anisotropic effect of the MTPA Ph moiety. On the other hand, in the (*R*)-MTPA derivative the shielding effect due to the MTPA Ph should affect the oxindole N-Me, while the anisotropy of the oxindole phenyl ring should have a shielding effect on the MTPA OMe signal (*if the C-3 would have the opposite (R)-configuration, such shielding effects would be exchanged*).

In Figures 2 and 3, significant expansions of $^{1}$H NMR spectra for both *(S)*- and (*R*)-MTPA derivatives are reported.

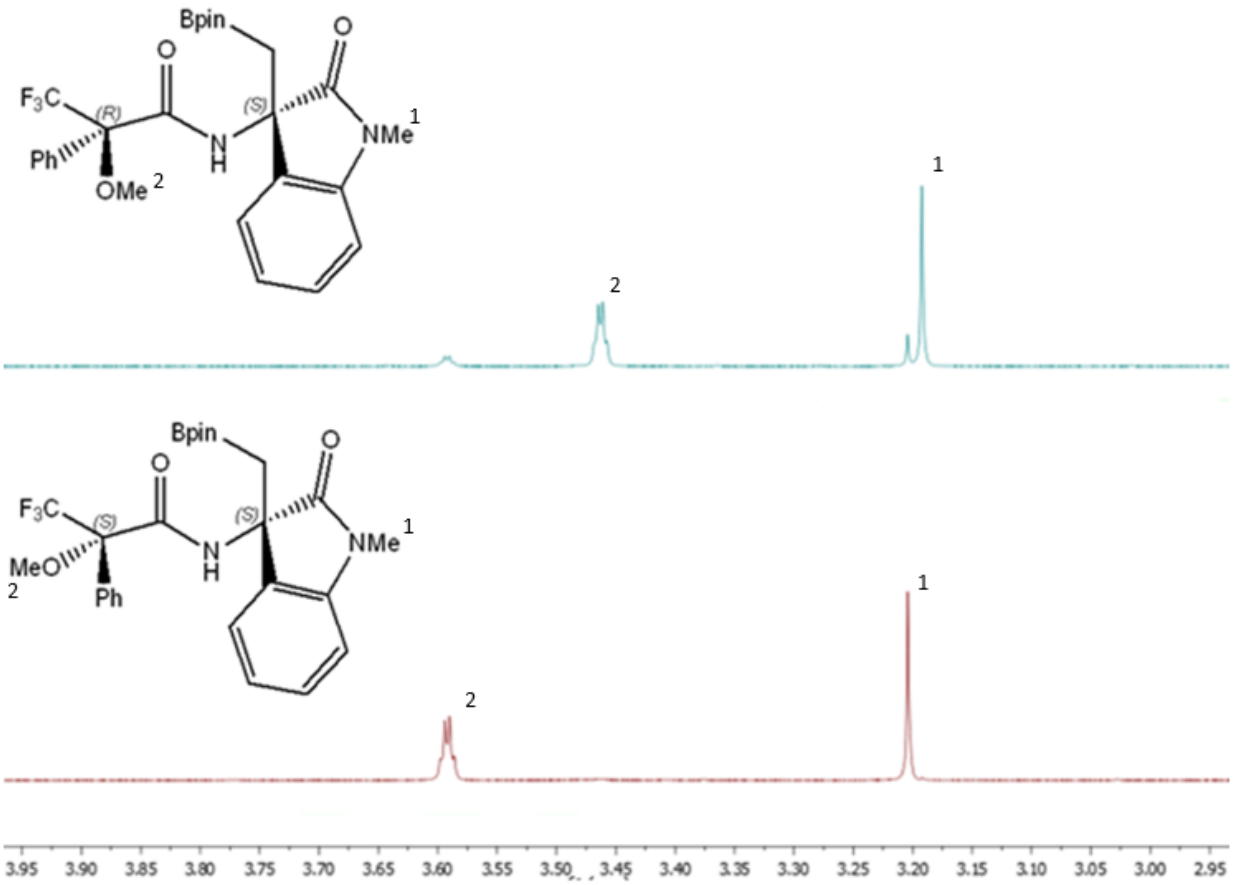



**Figure 2**. $^{1}$H NMR (expansion zone) of (*R*)-MTPA derivative (blue) and *(S)*-MTPA derivative (red). As predicted from models, in the (*R*)-derivative both the N-Me and OMe signals are shielded with respect to the same signals of the *(S)*-derivative.

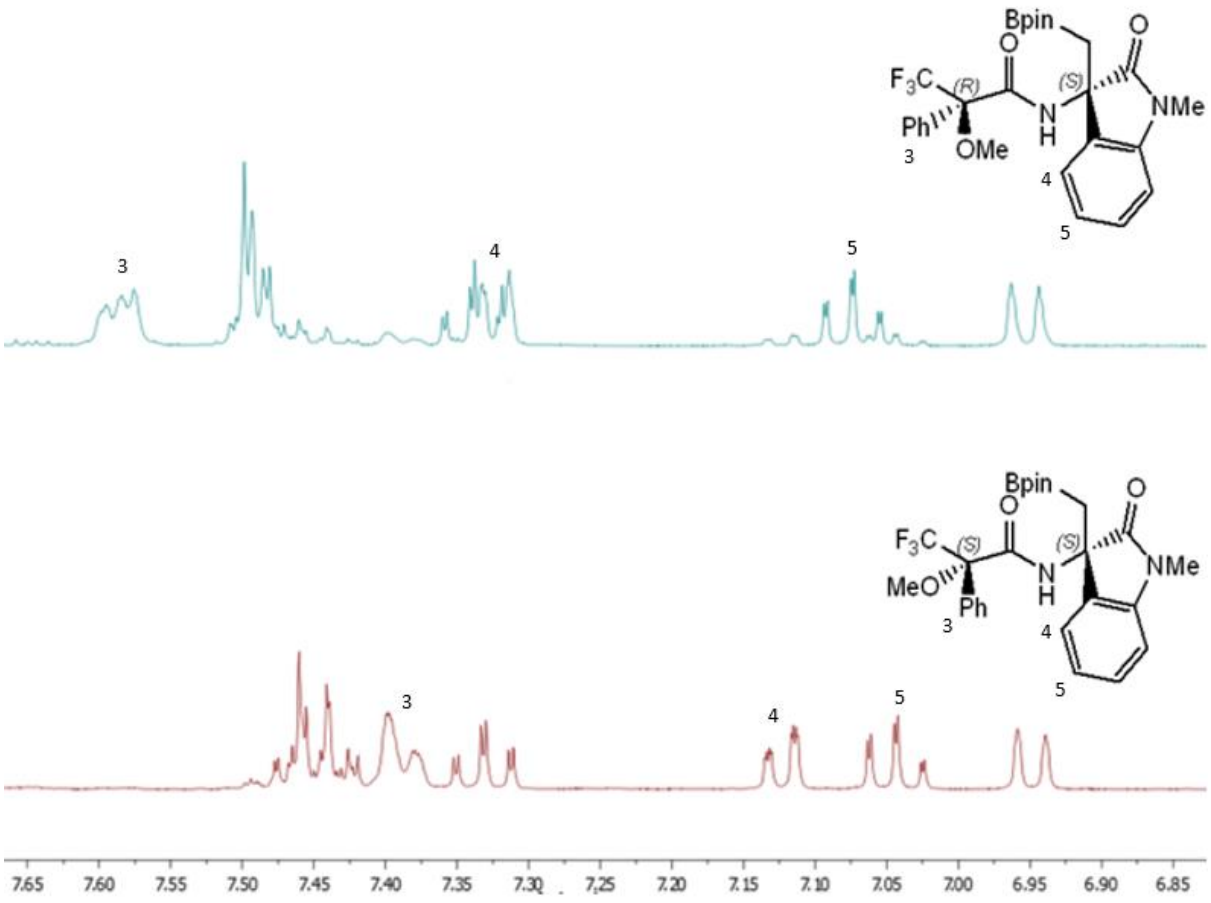
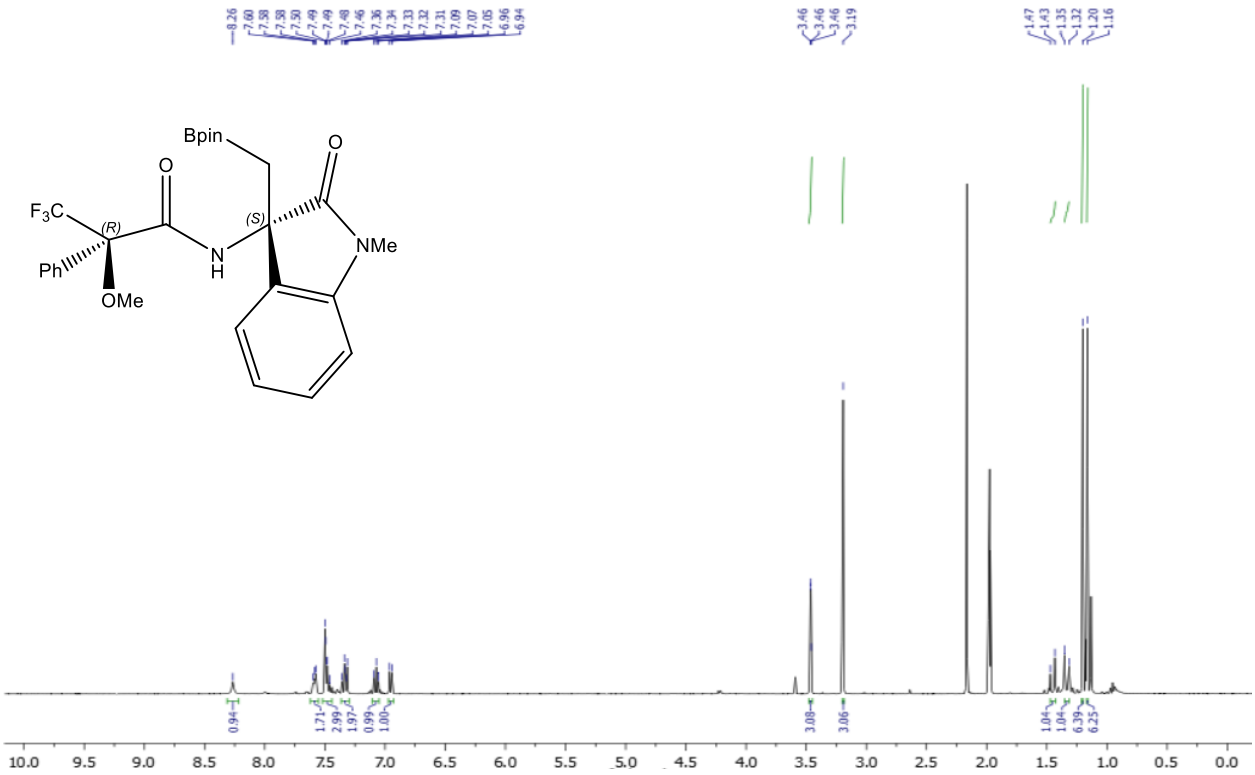


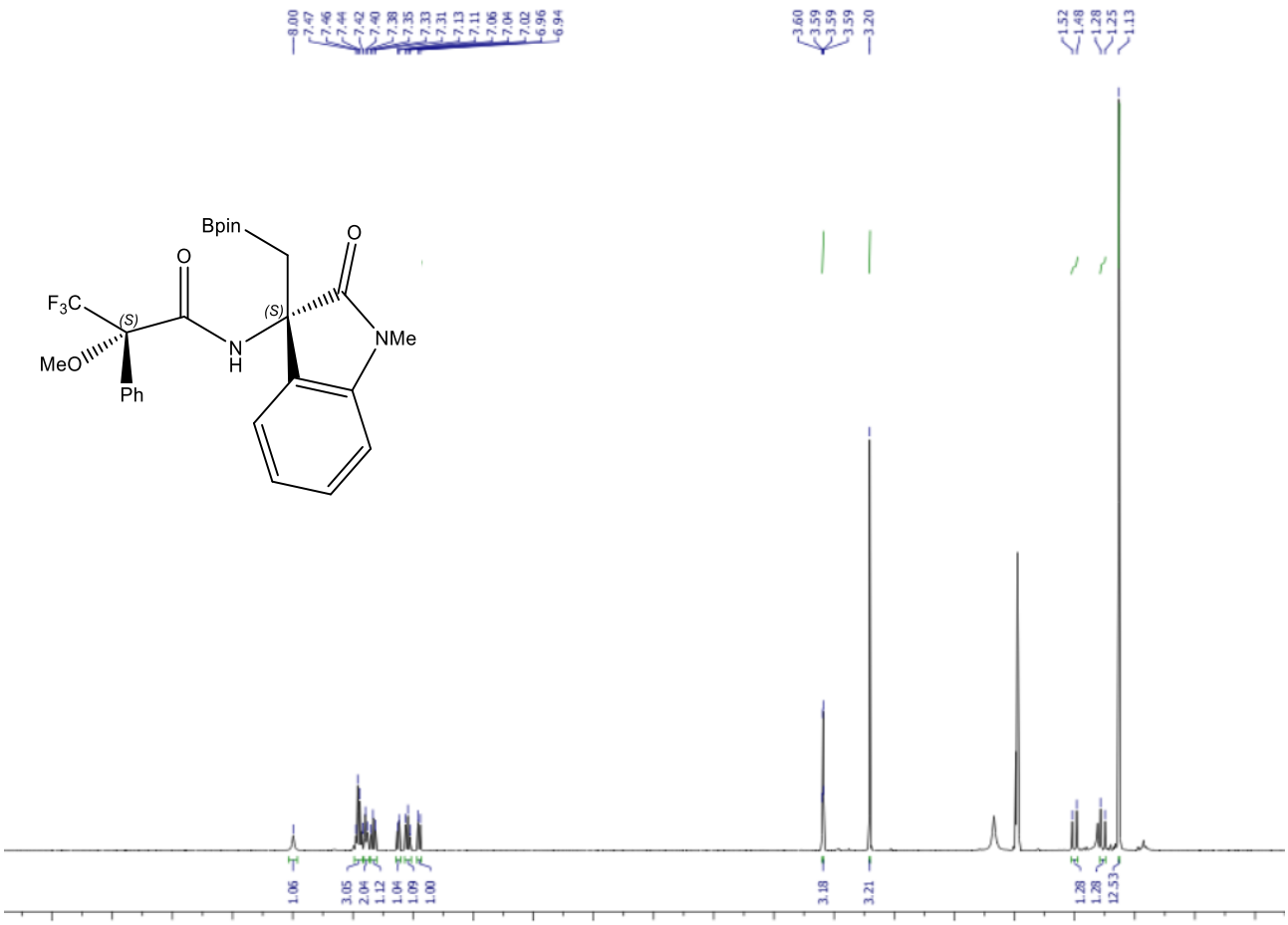

**Figure 3**. $^{1}$H NMR (expansion zone) of (*R*)-MTPA derivative (blue) and *(S)*-MTPA derivative (red). As predicted from models, in the *(S)*-derivative the signals ascribed to both the phenyl rings are shielded by a mutual anisotropic effect. Such effect is particularly evident for the oxindole H-4, which shifts from 7.33 ppm in the (*R*)-derivative to 7.13 ppm in the *(S)*-one.

From experimental NMR data ($\Delta\delta SR$ signs), the *(S)*-configuration can be unambiguously ascribed to compound **5** oxindole C-3 stereocentre.

$^{1}$H NMR spectrum of the (*R*)-MTPA derivative (400 MHz, $CD_3CN$)

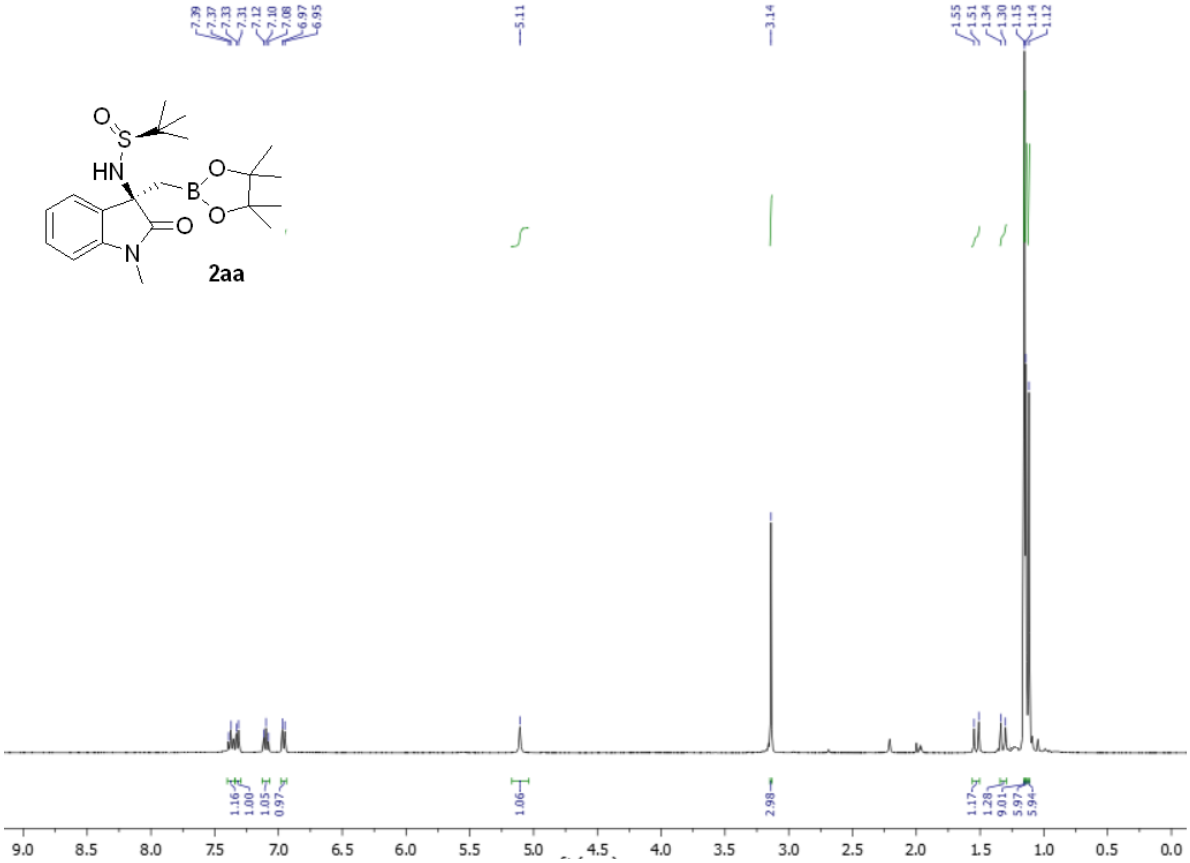



$^{1}$H NMR spectrum of the *(S)*-MTPA derivative (400 MHz, $CD_3CN$)

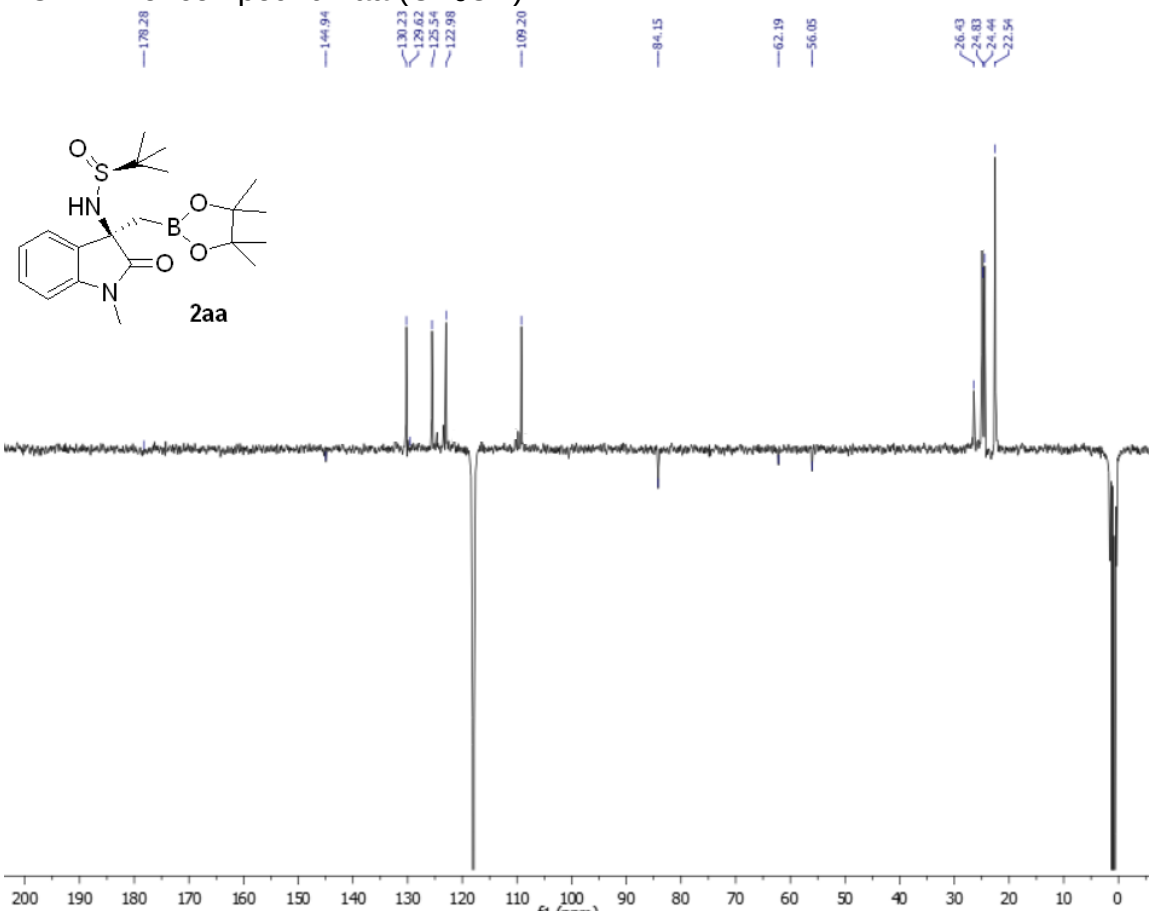


## Copies of $^{1}$H NMR,$^{13}$C NMR and $^{11}$B NMR Spectra

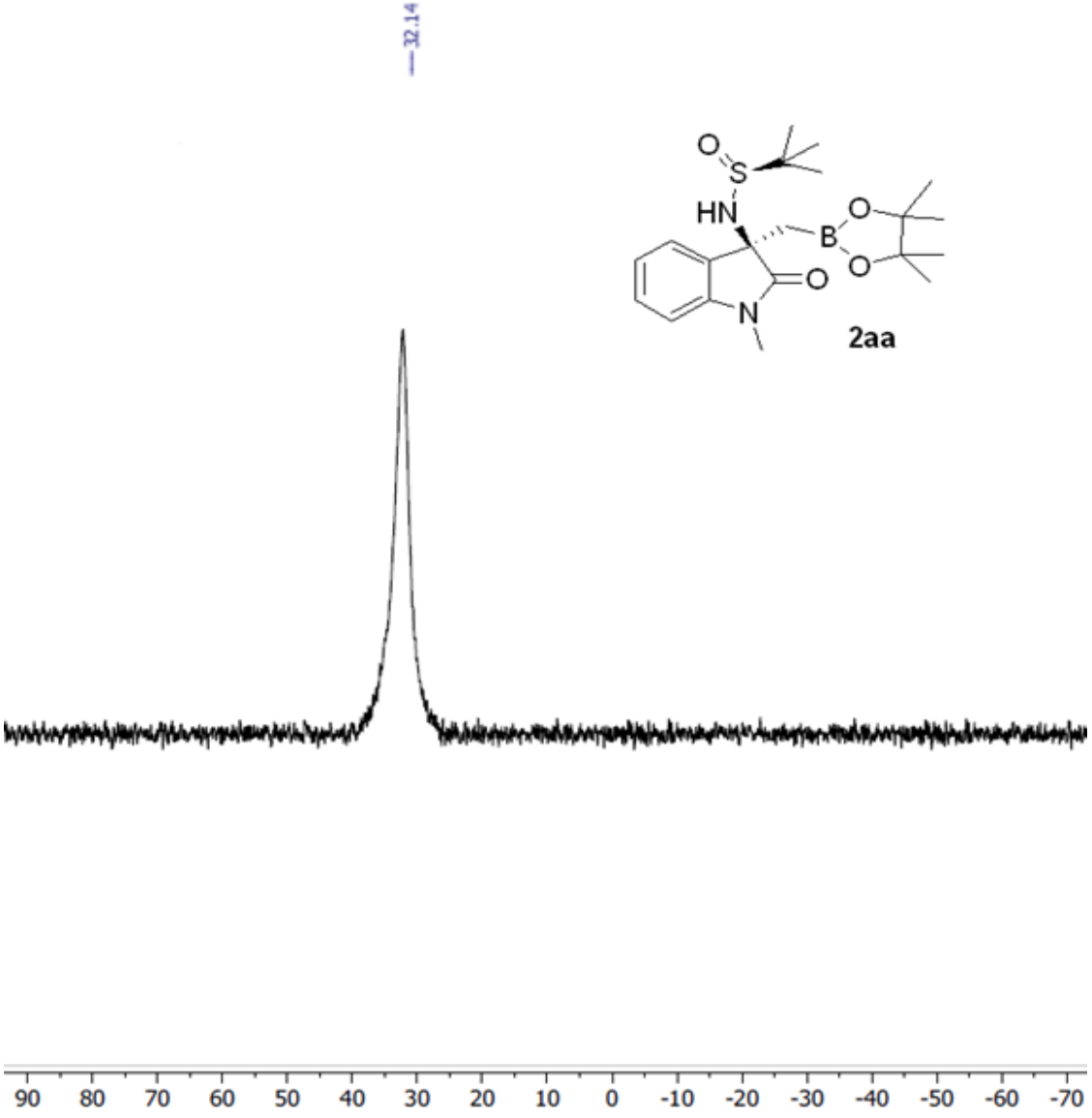
$^{1}$H NMR of compound **2aa** ($CD_3CN$)



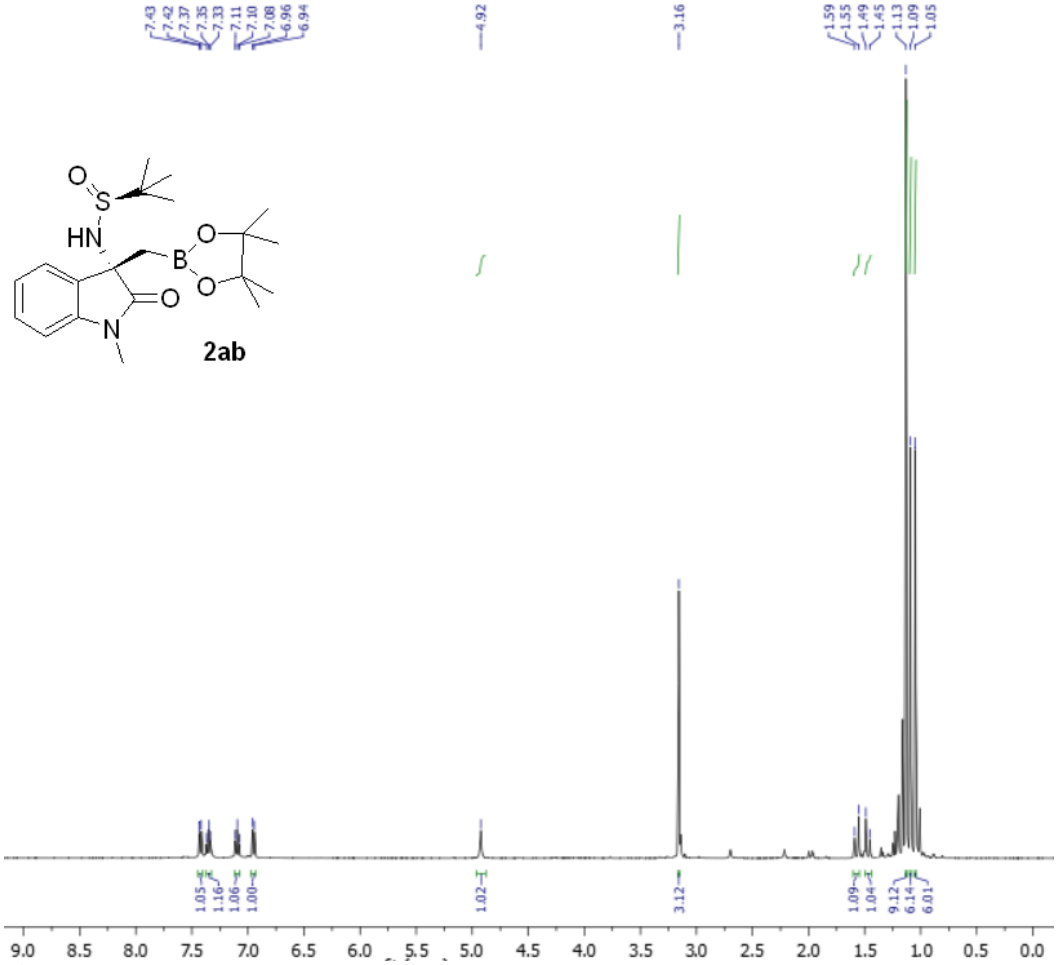

$^{13}$C NMR of compound **2aa** ($CD_3CN$)



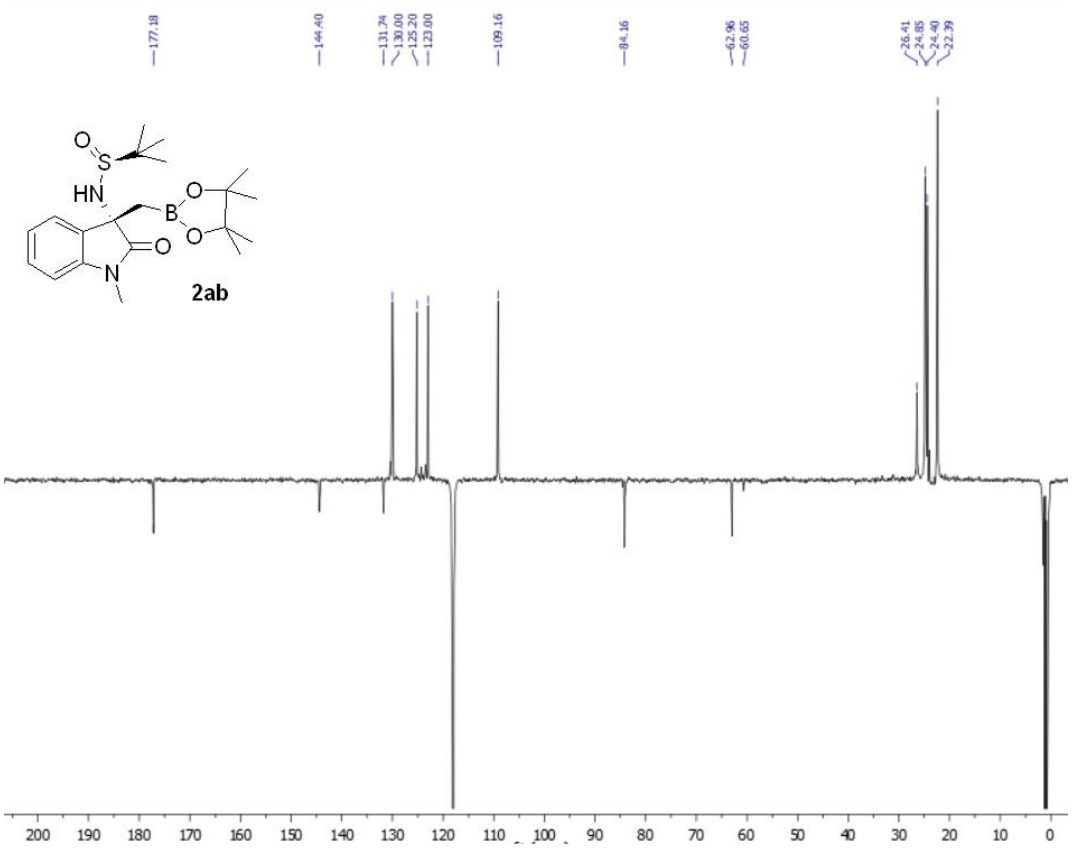
$^{11}$B NMR of compound **2aa** ($CD_3CN$)



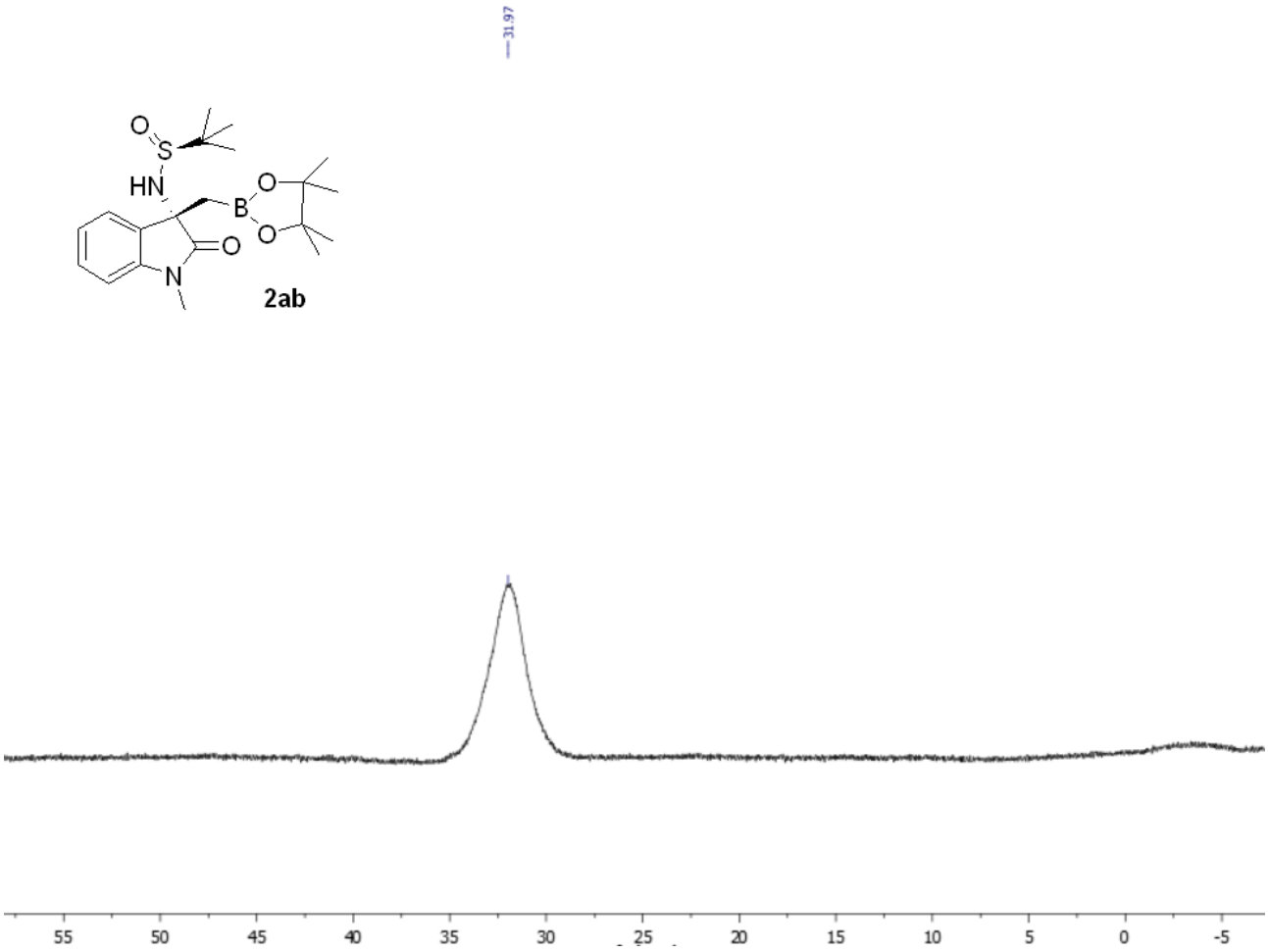
$^{1}$H NMR of compound **2ab** ($CD_3CN$)



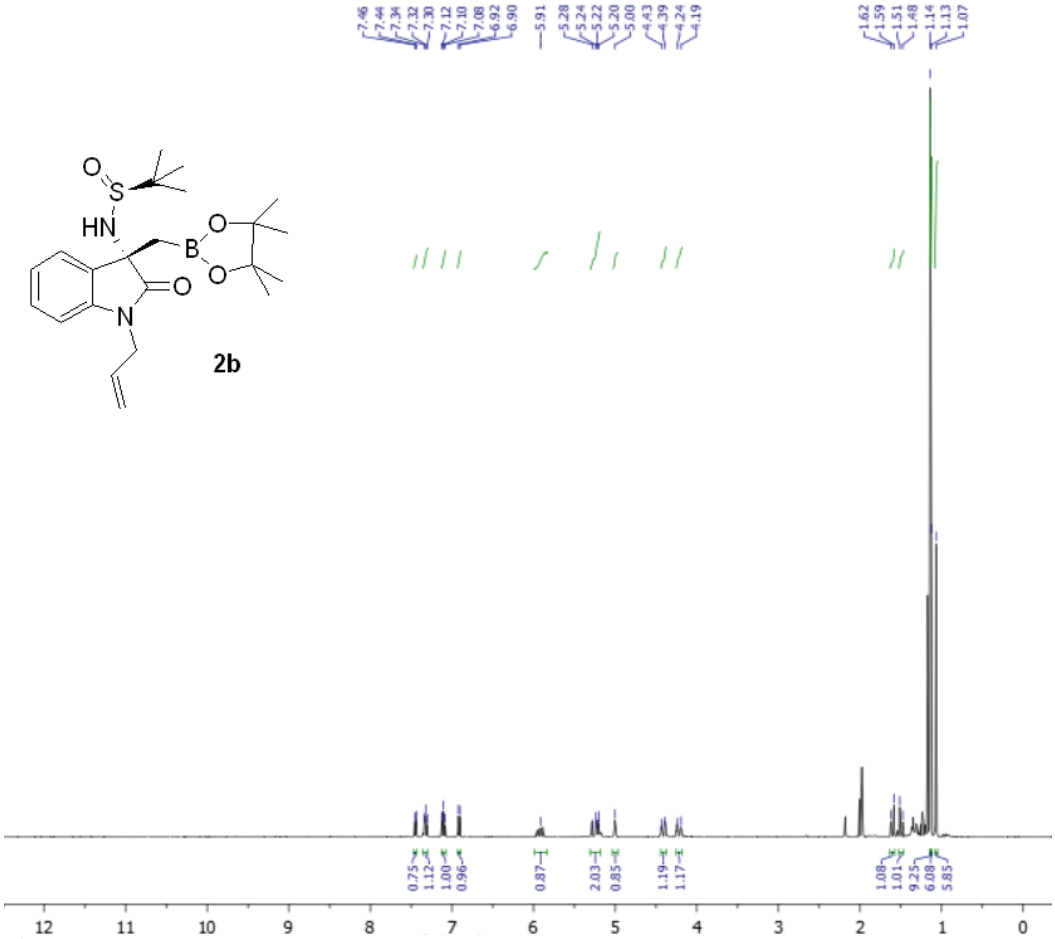

$^{13}$C NMR of compound **2ab** ($CD_3CN$)



$^{11}$B NMR of compound **2ab** ($CD_3CN$)



$^{1}$H NMR of compound **2b** ($CD_3CN$)

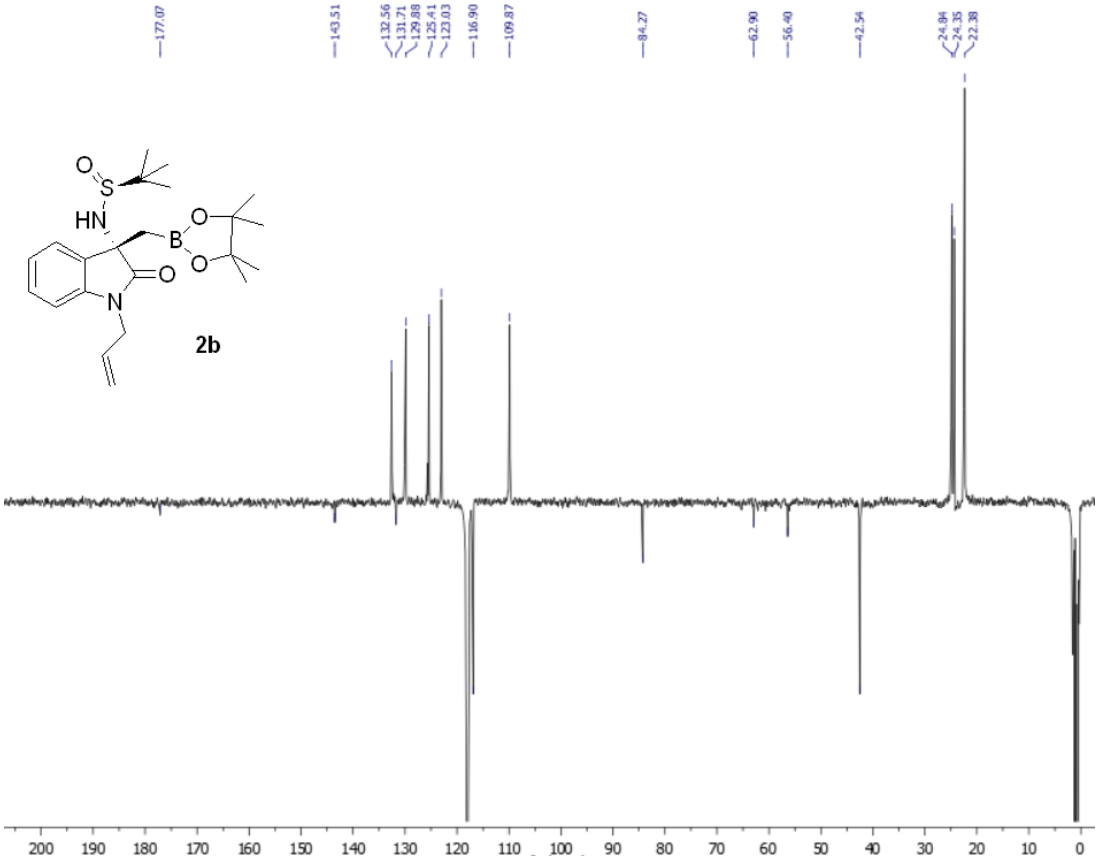






**2b**

$^{13}$C NMR of compound **2b** ($CD_3CN$)

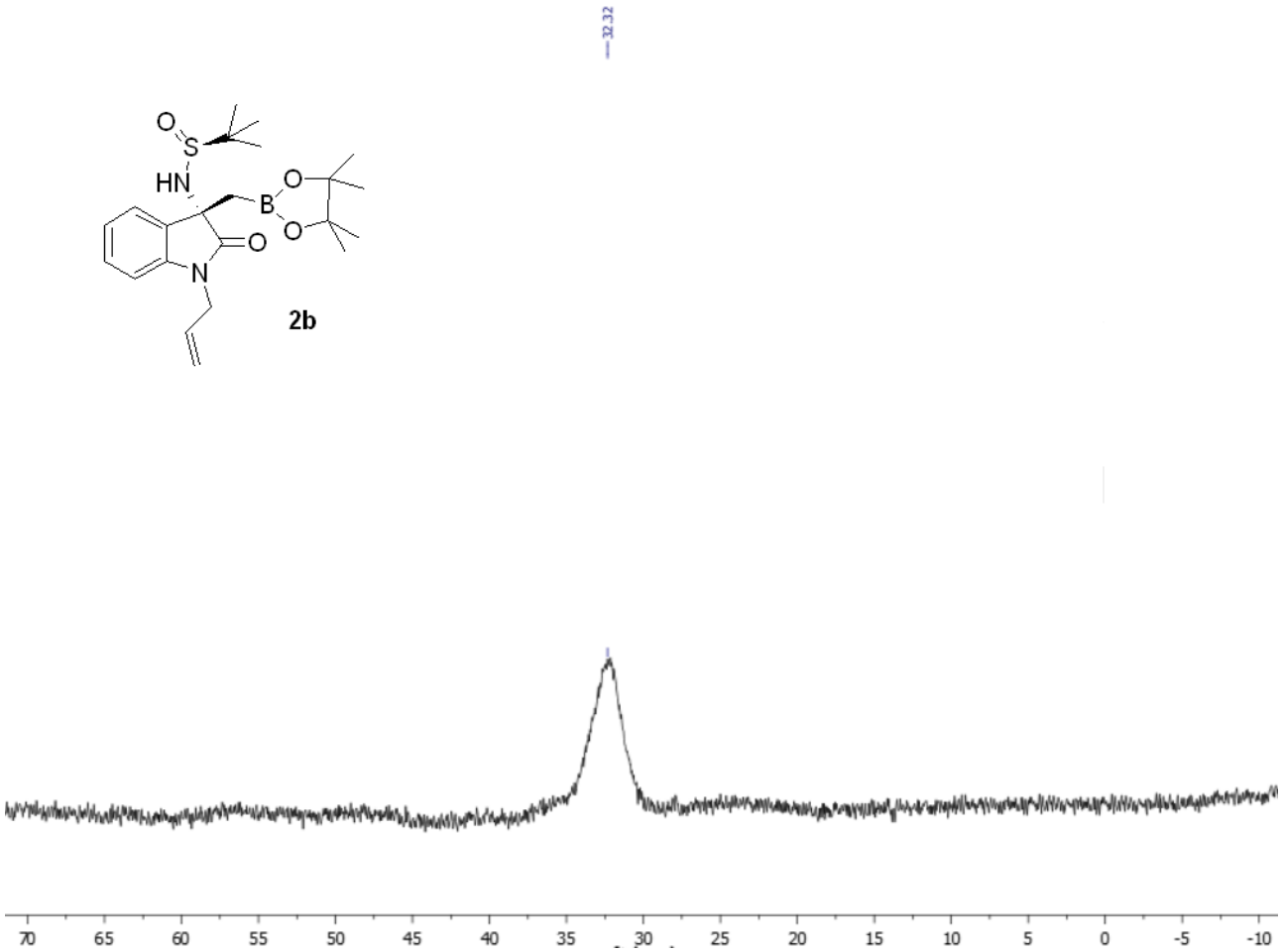




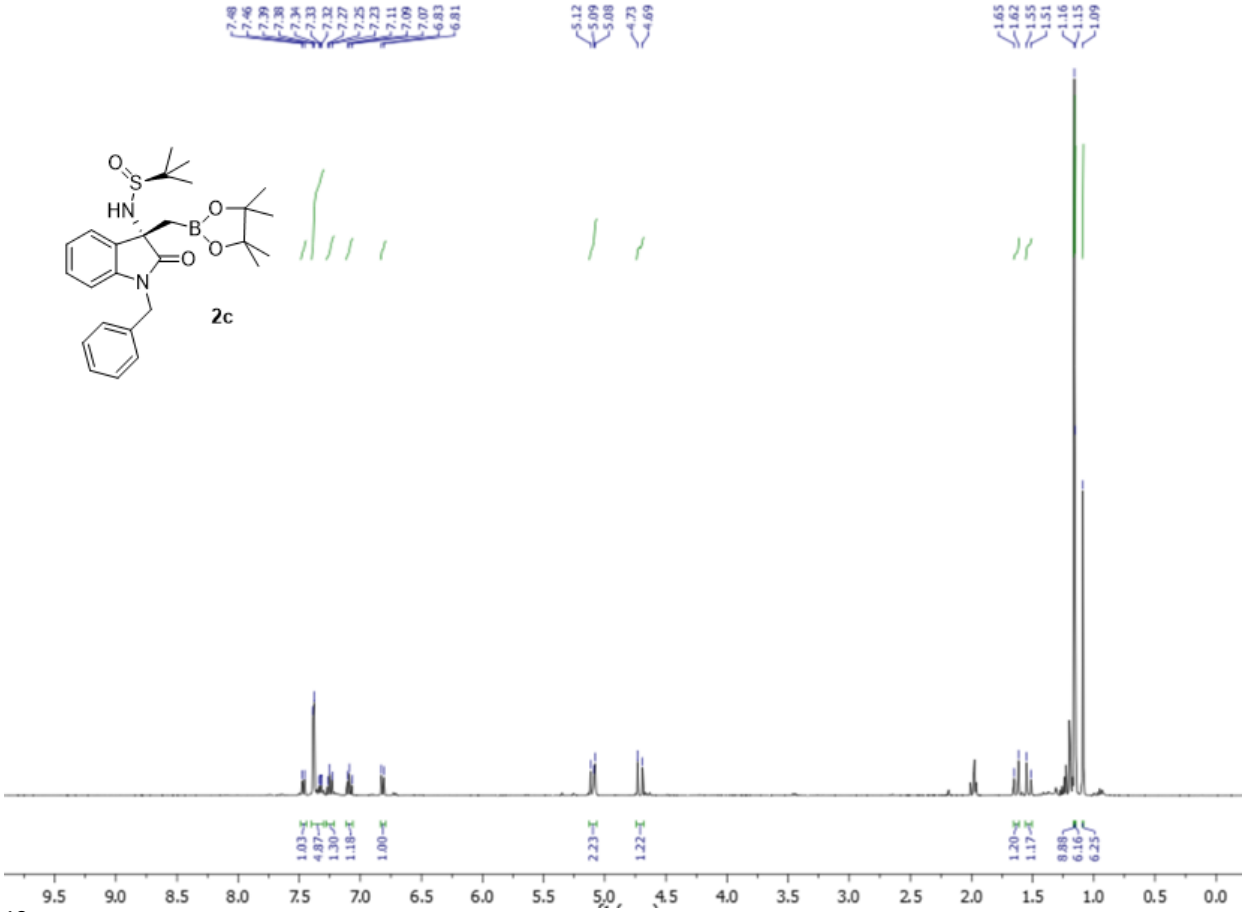


**2b**

$^{11}$B NMR of compound **2b** ($CD_3CN$)



$^{1}$H NMR of compound **2c** ($CD_3CN$)

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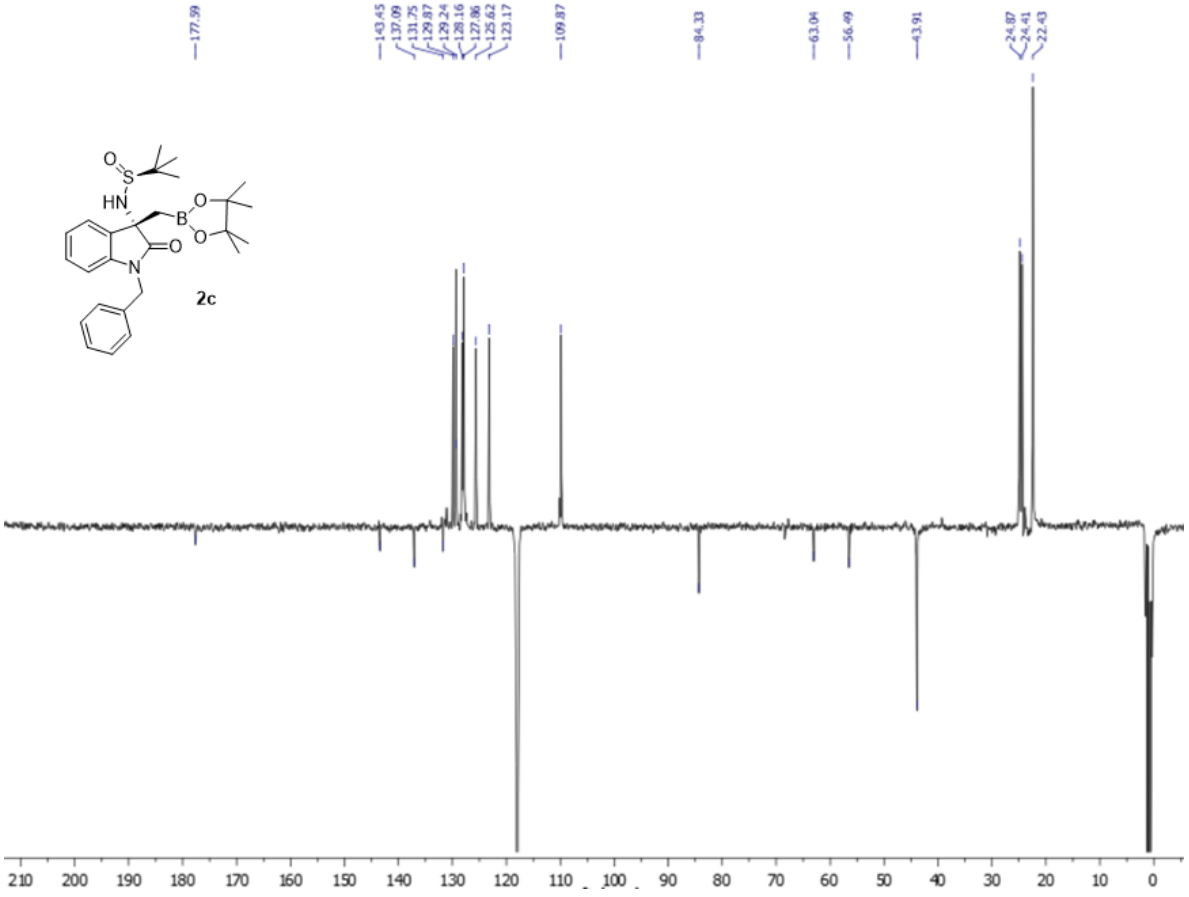
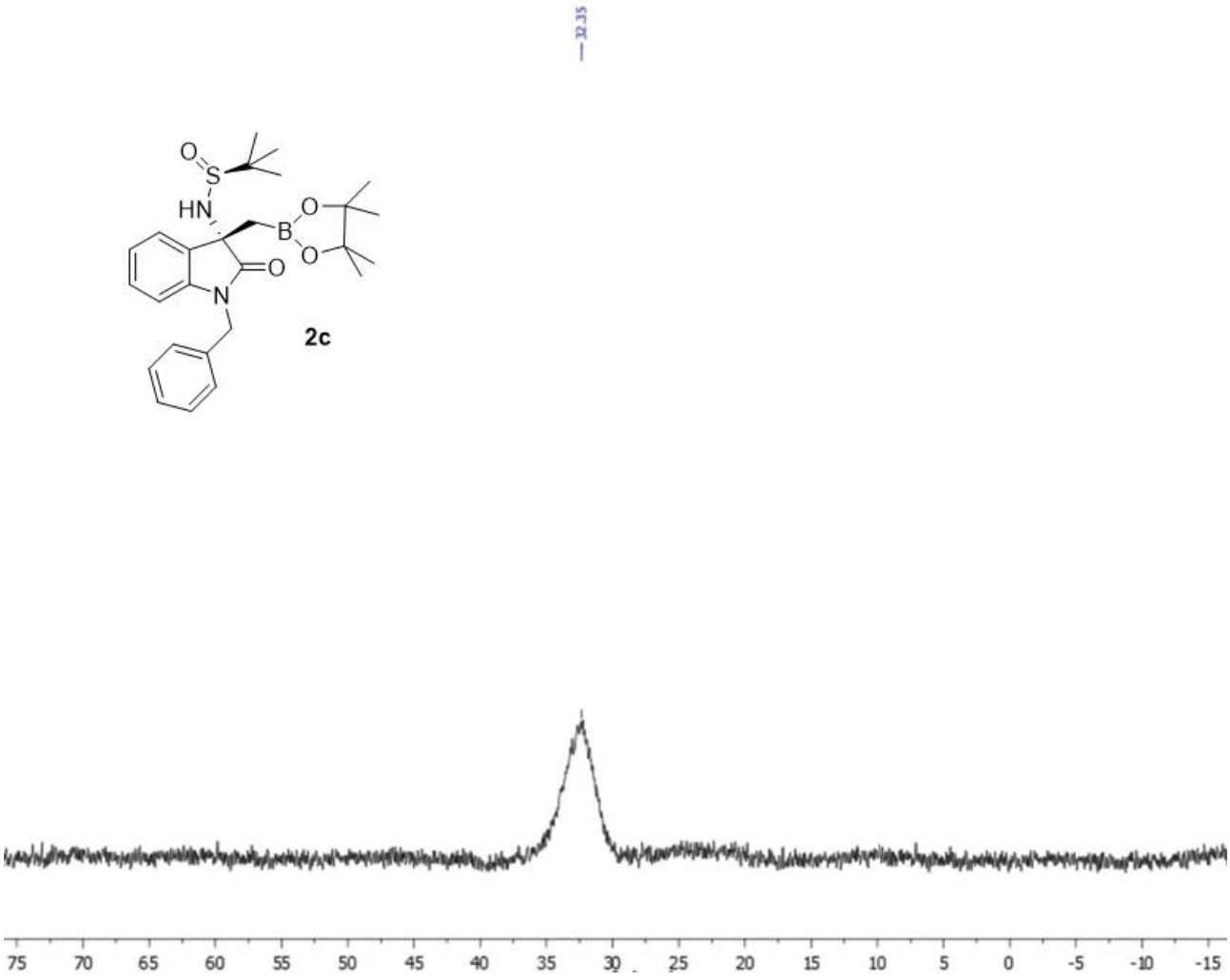
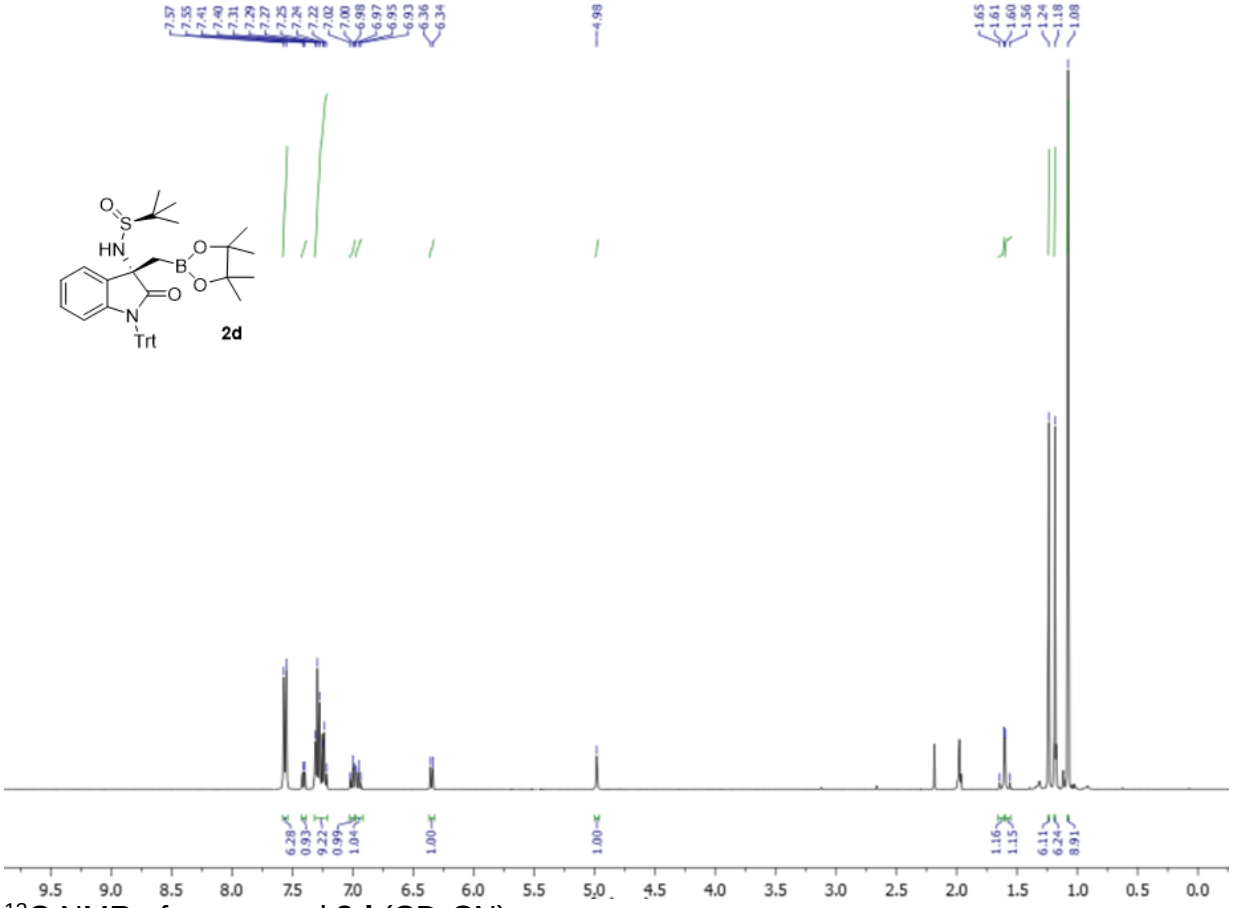


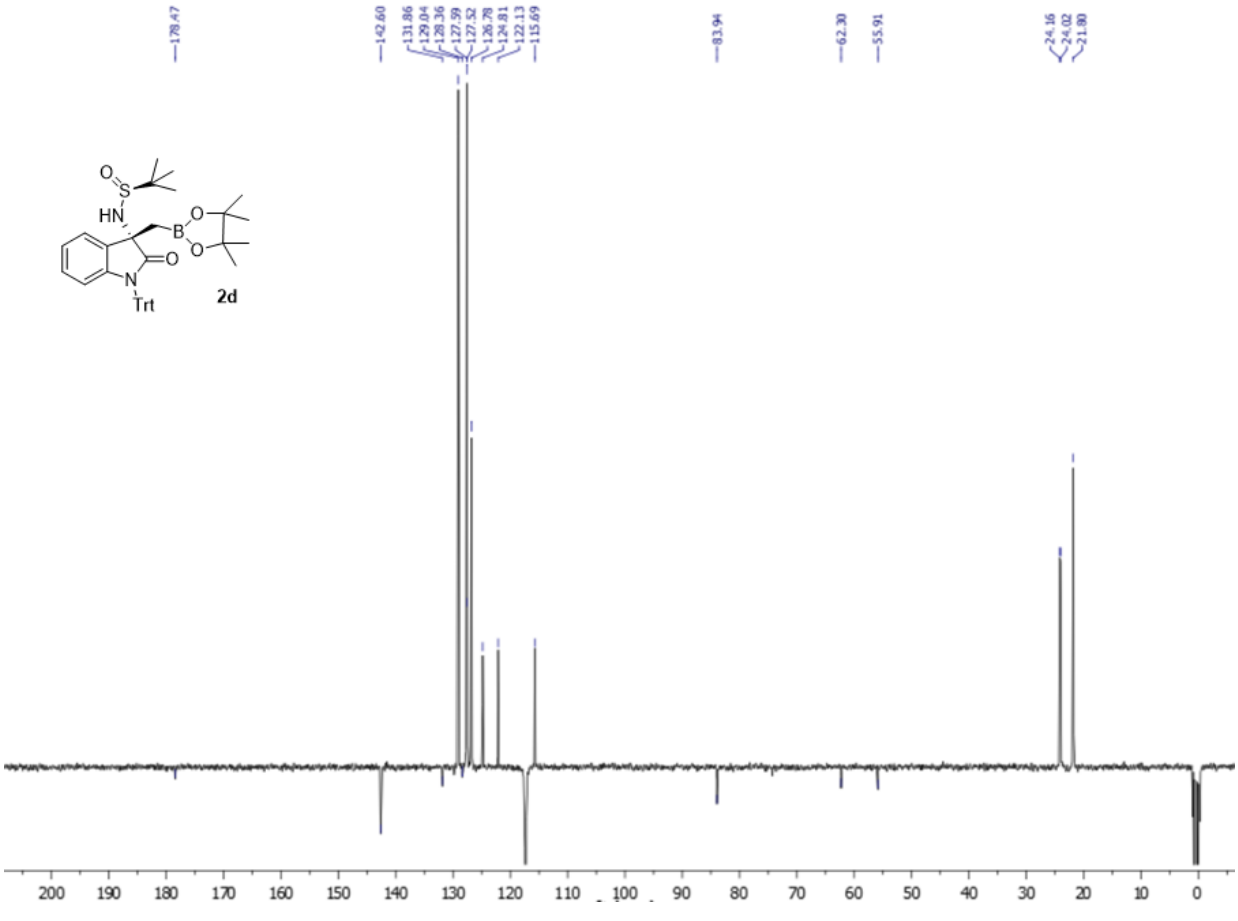
$^{11}$B NMR of compound **2c** ($CD_3CN$)



$^{1}$H NMR of compound **2d** ($CD_3CN$)




$^{13}$C NMR of compound **2d** ($CD_3CN$)



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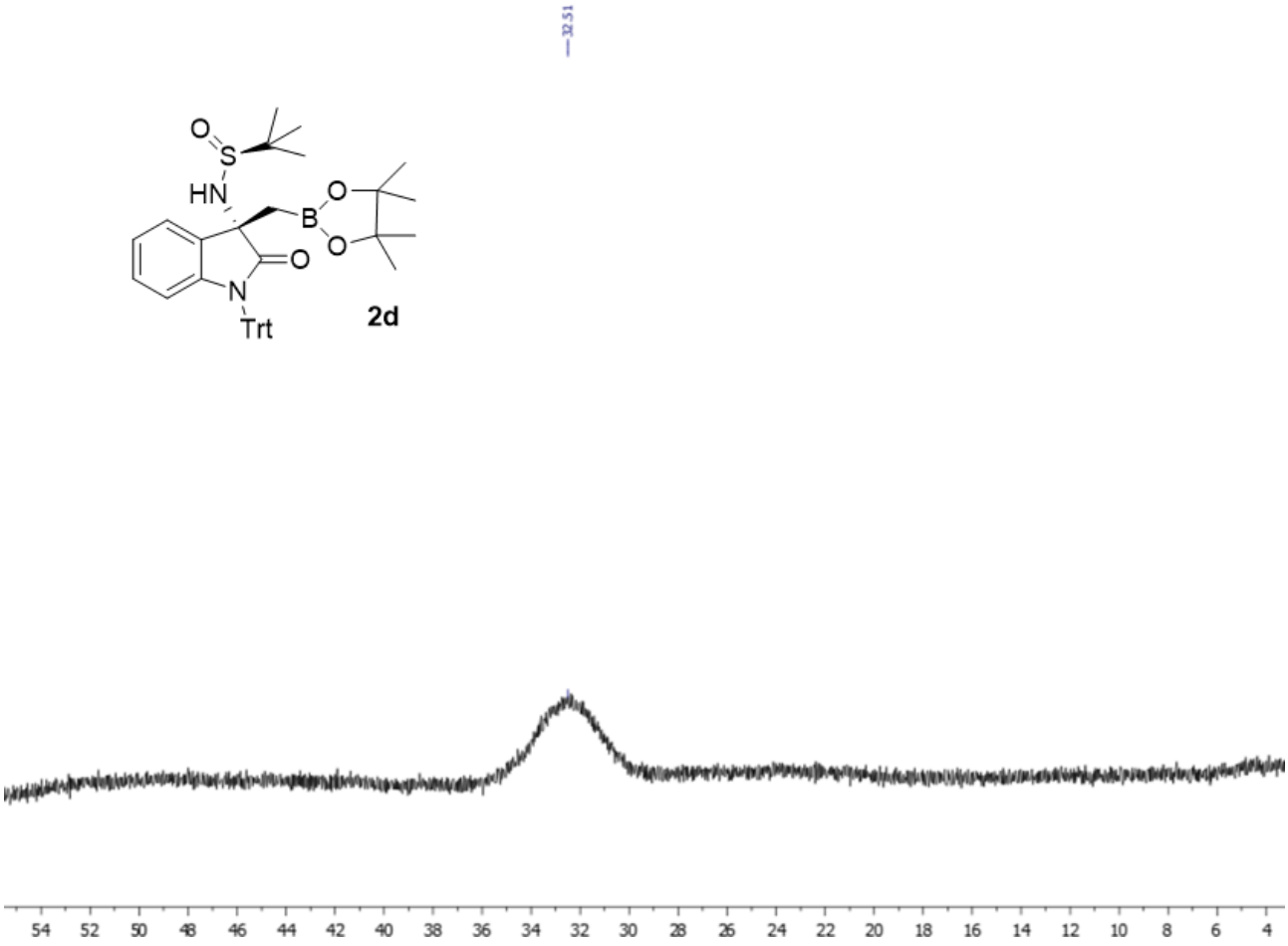
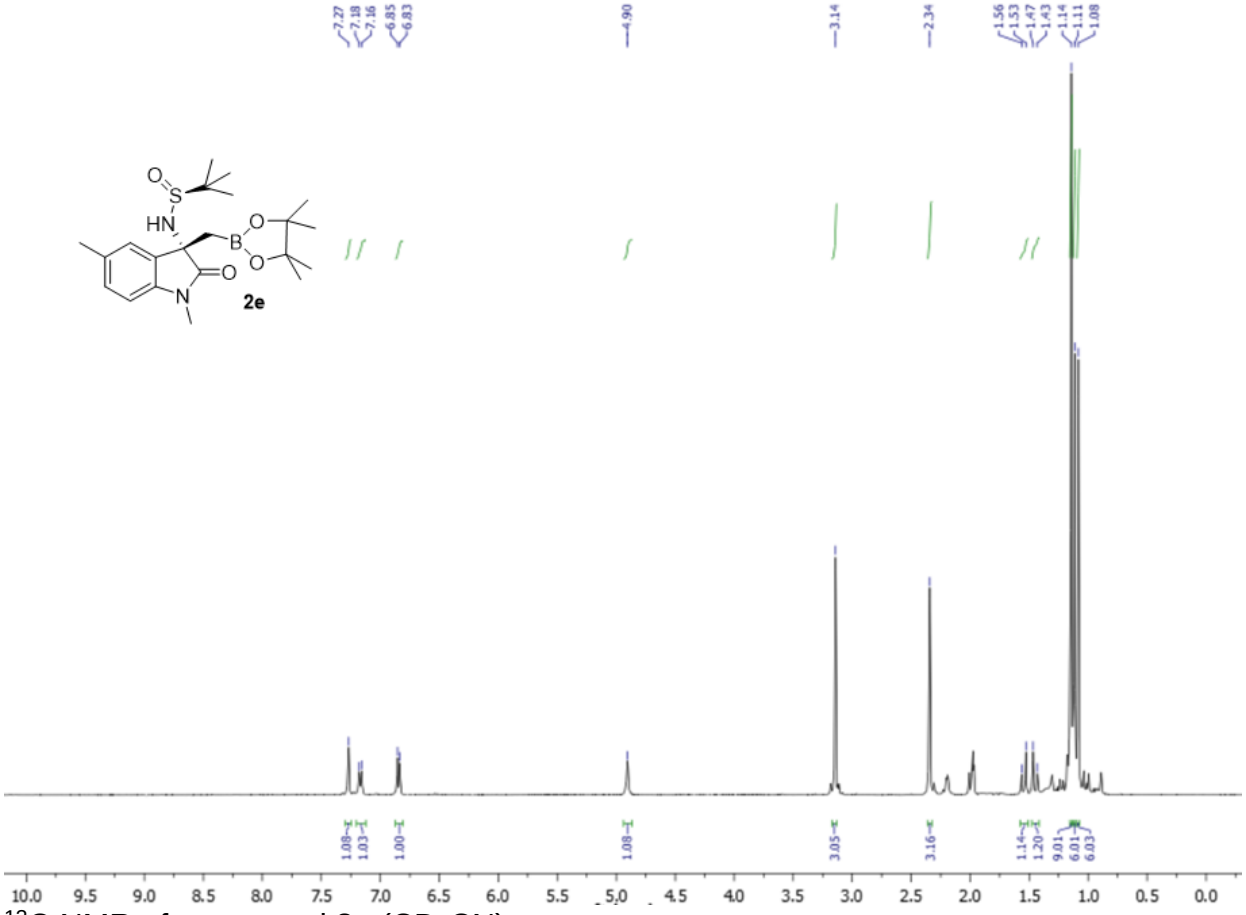
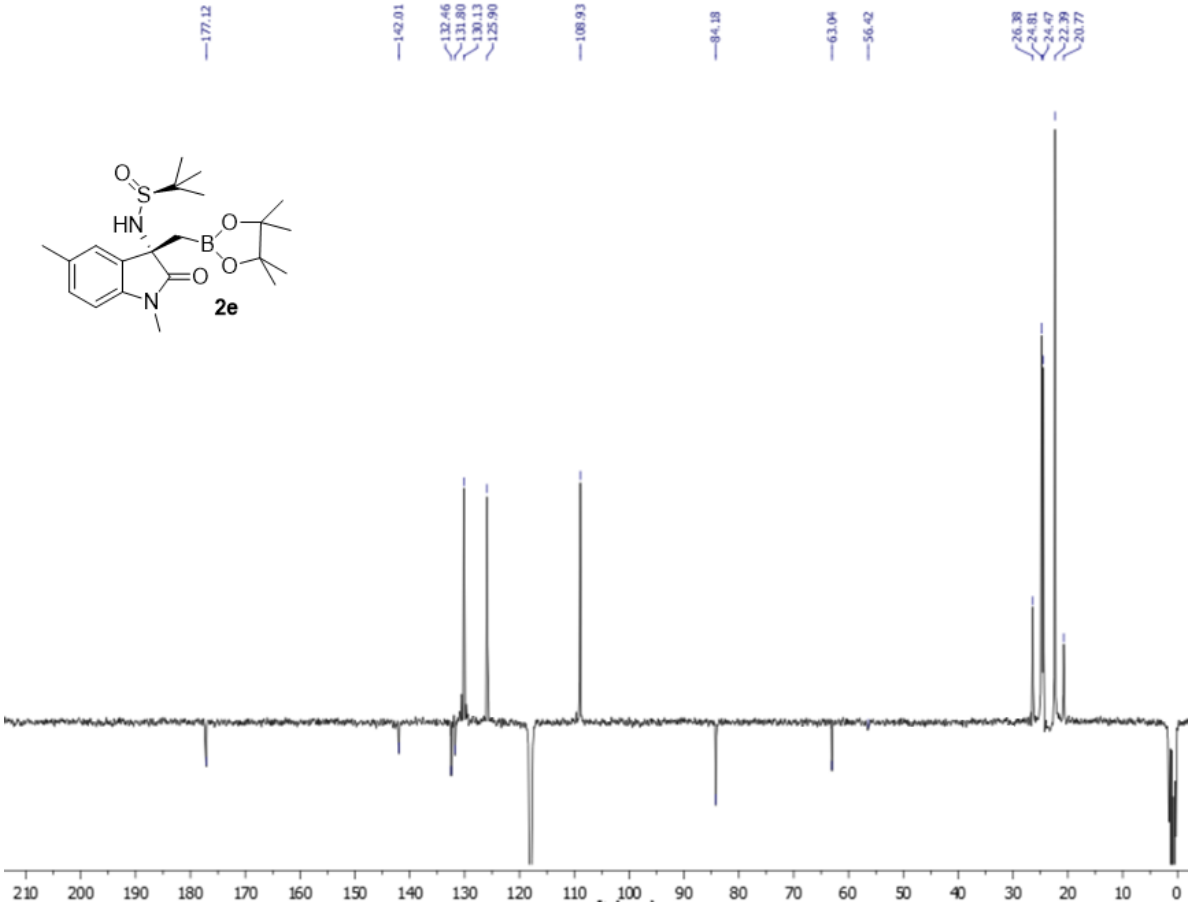


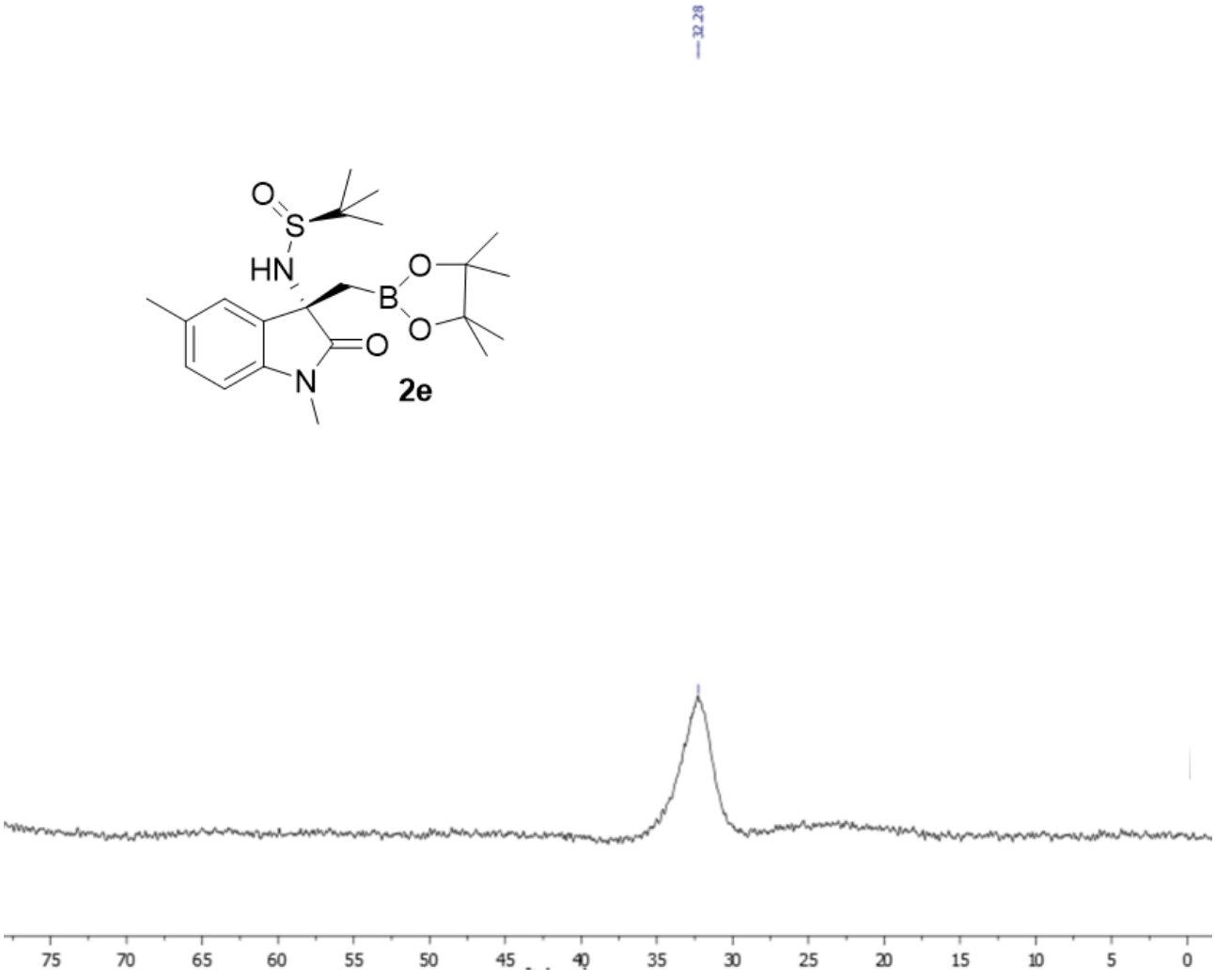
$^{1}$H NMR of compound **2e** ($CD_3CN$)



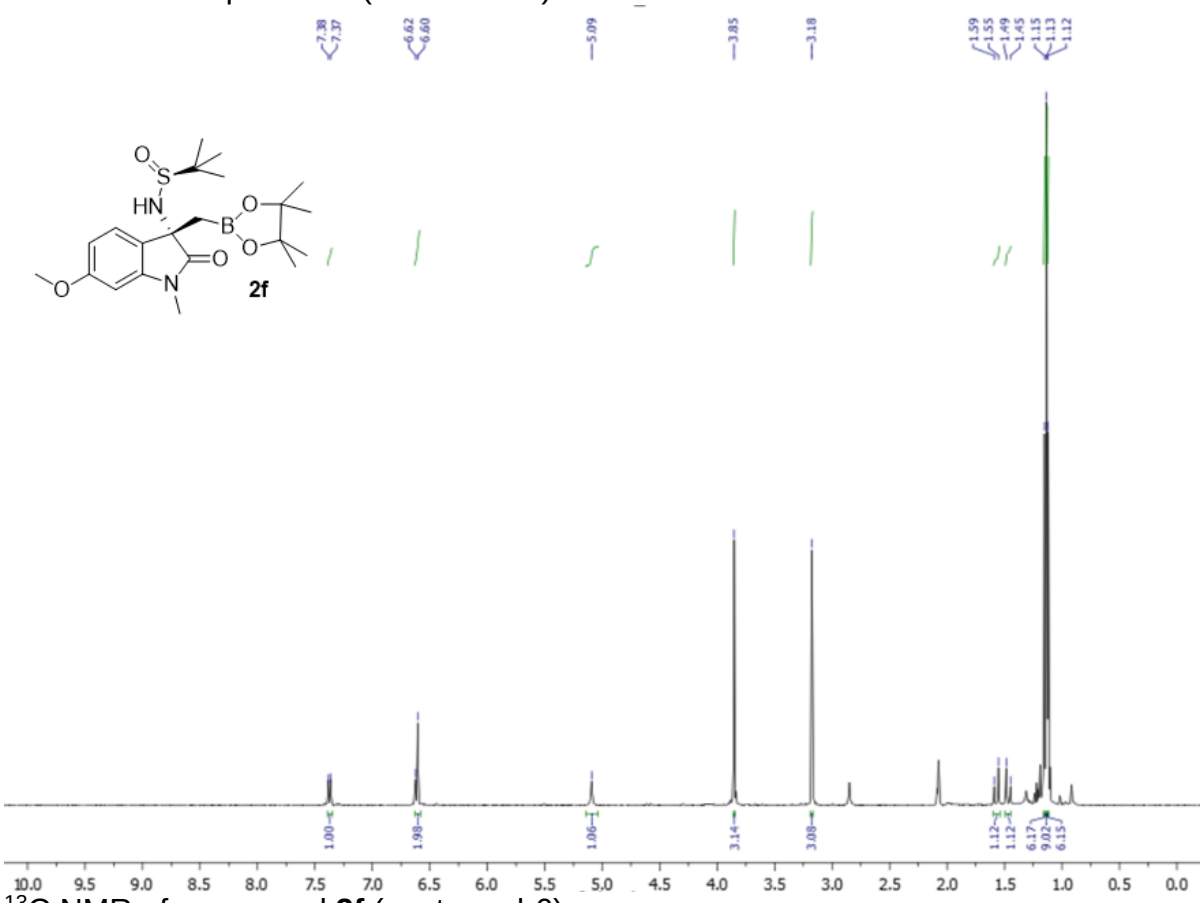

$^{13}$C NMR of compound **2e** ($CD_3CN$)



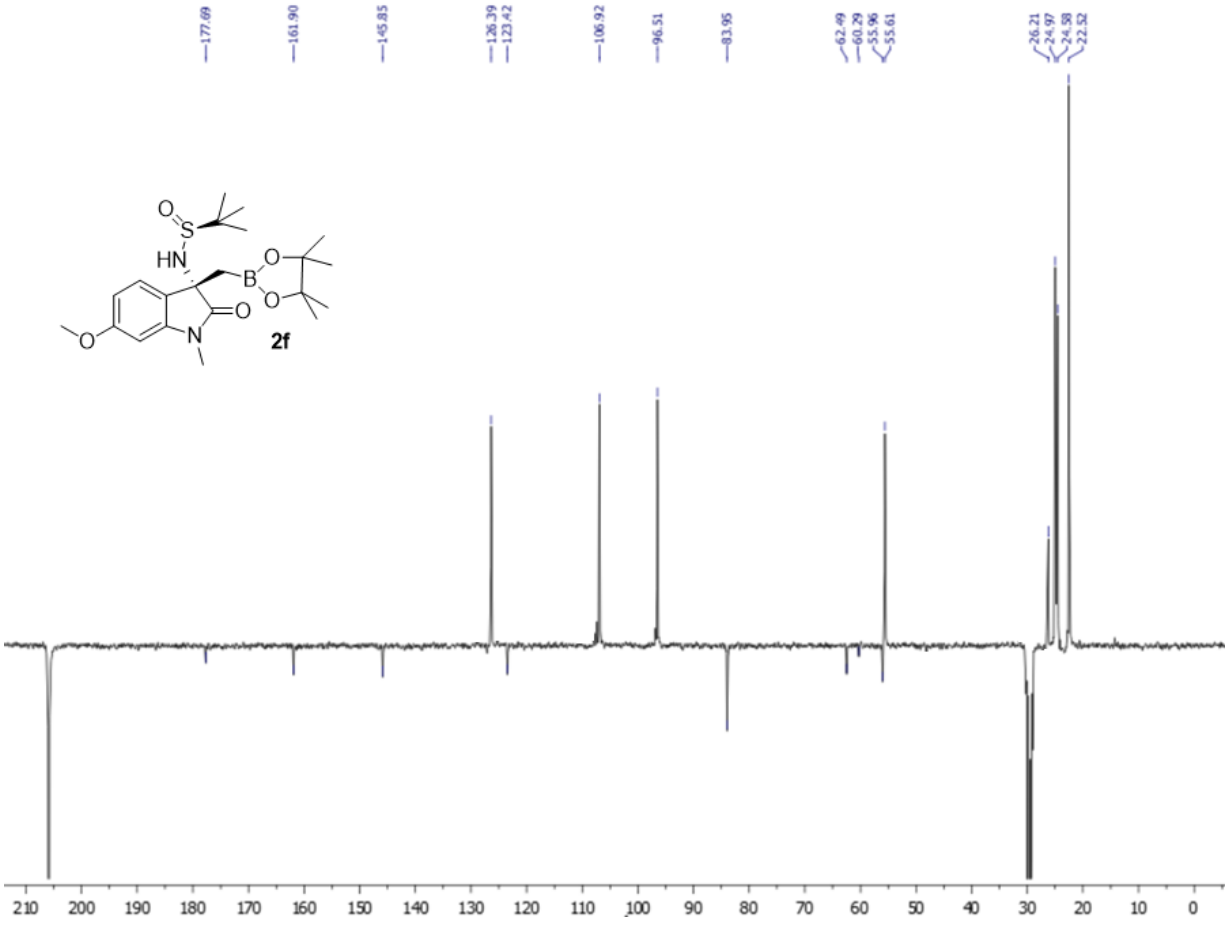
$^{11}$B NMR of compound **2e** ($CD_3CN$)



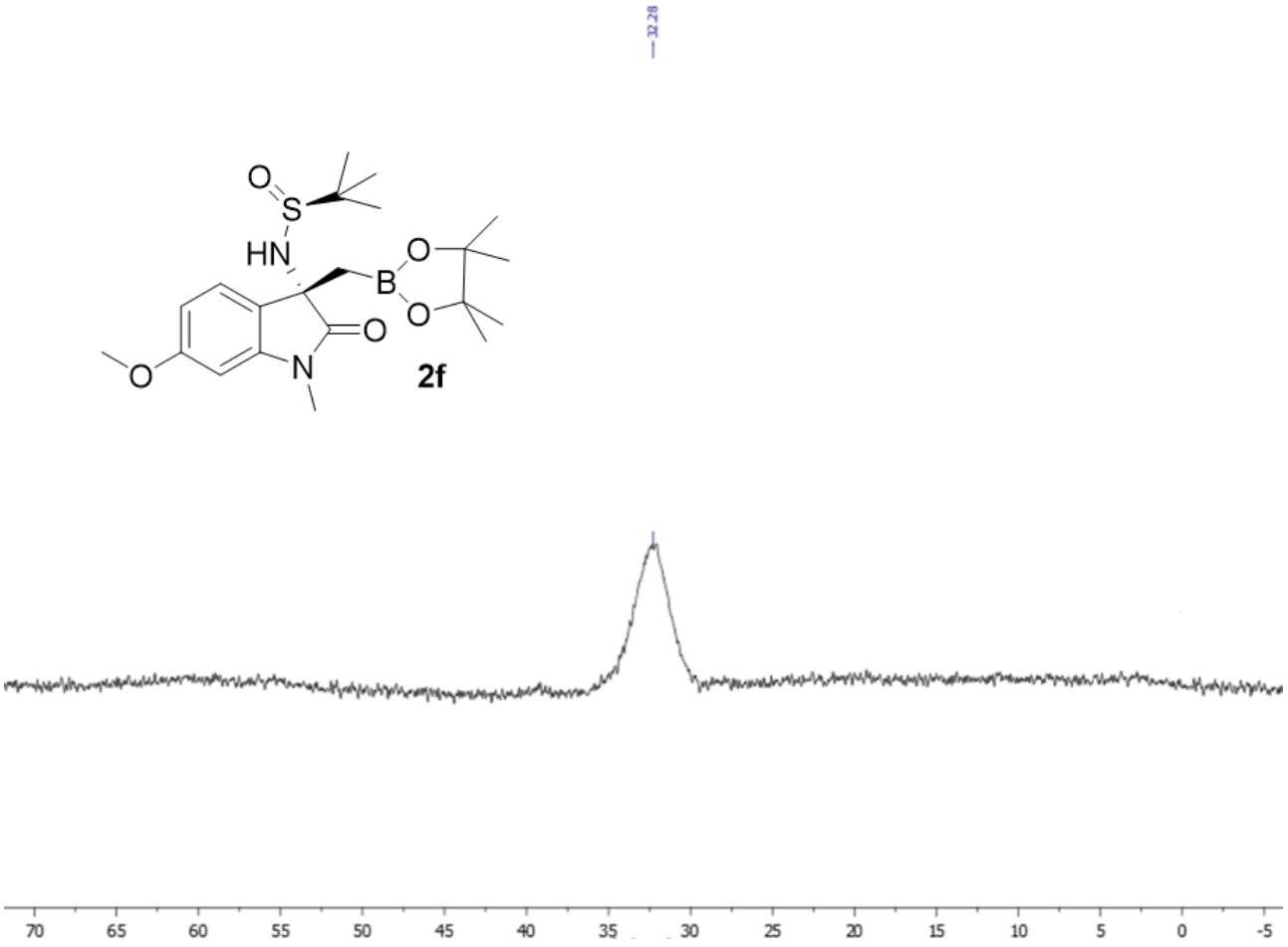
$^{1}$H NMR of compound **2f** (acetone d-6)



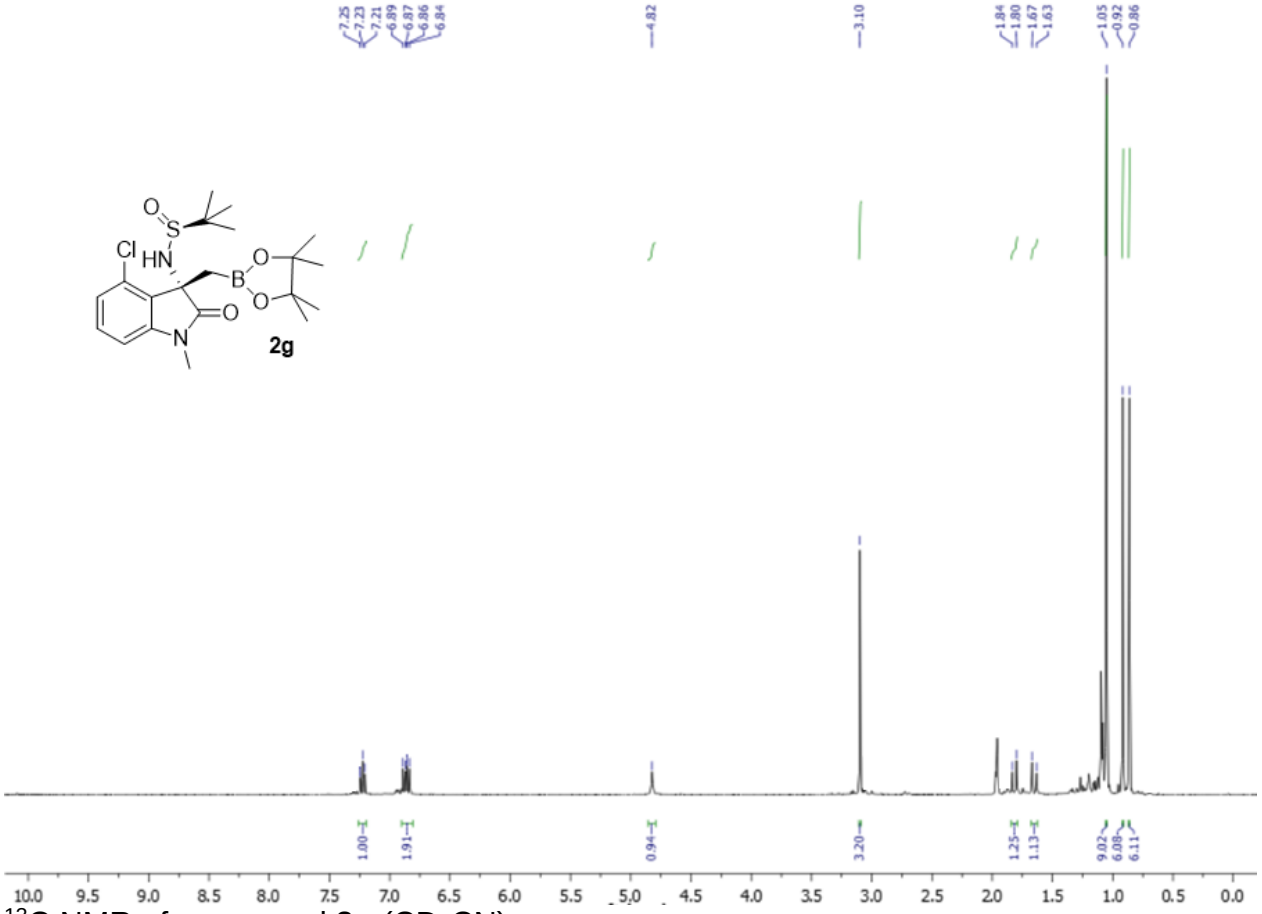

$^{13}$C NMR of compound **2f** (acetone d-6)



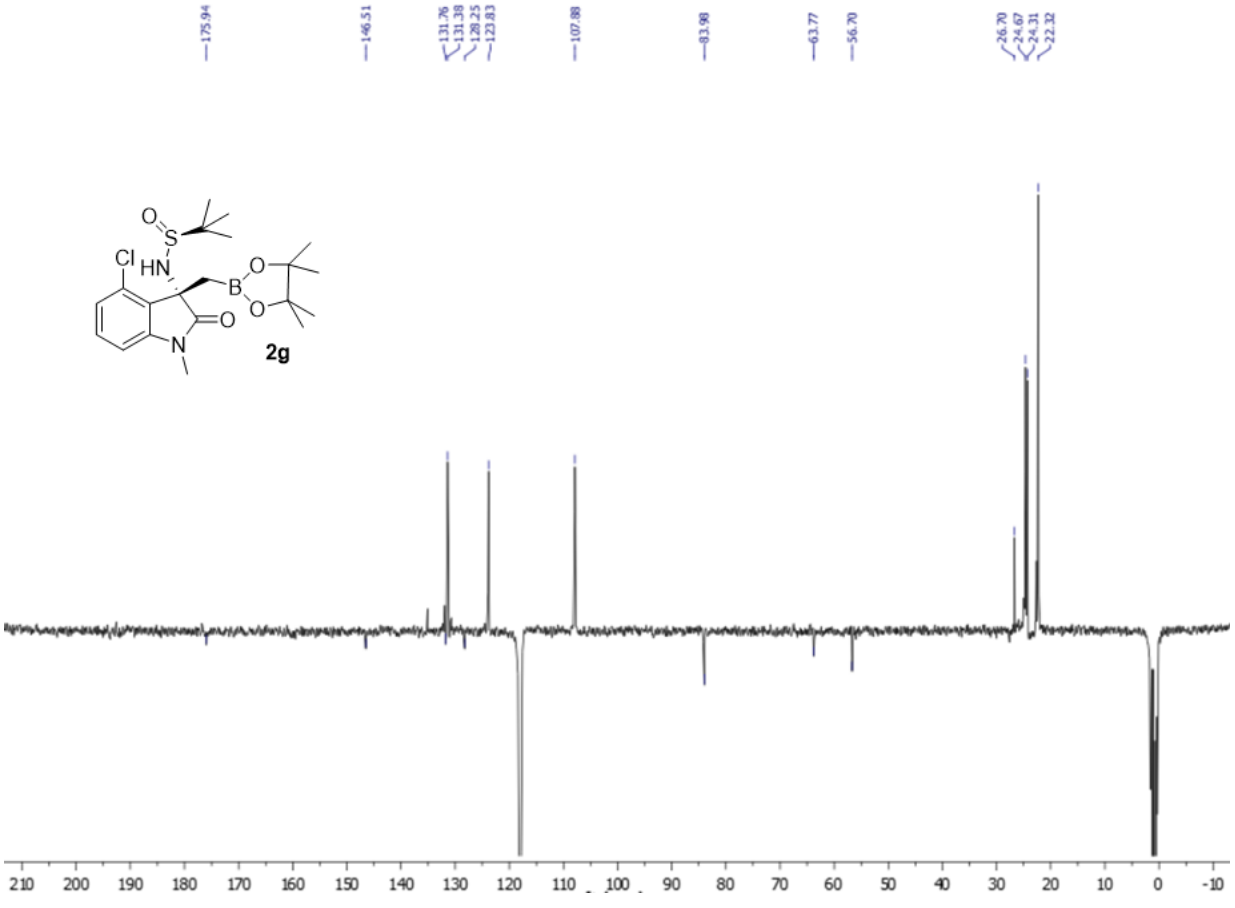
$^{11}$B NMR of compound **2f** (acetone d-6)



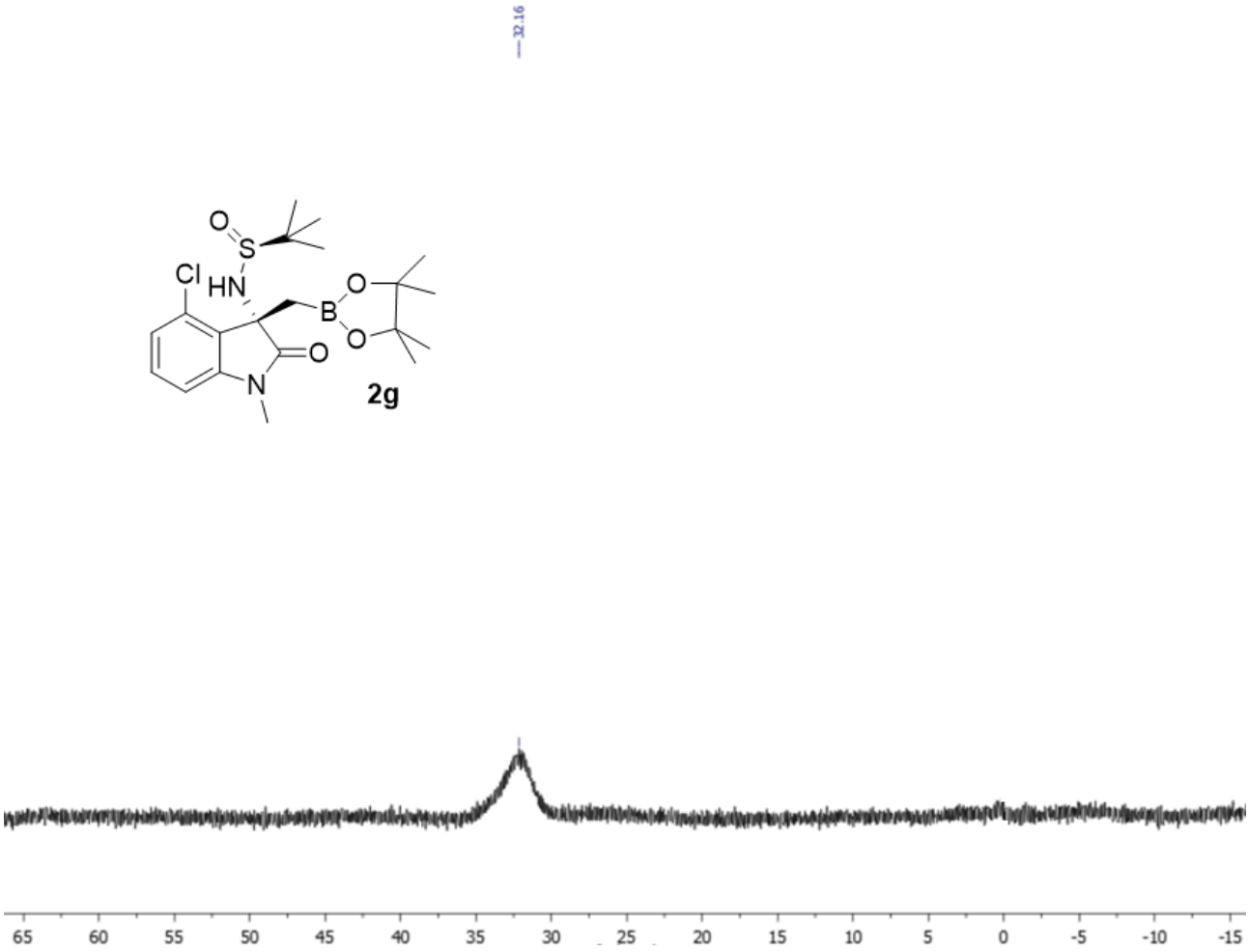
$^{1}$H NMR of compound **2g** ($CD_3CN$)



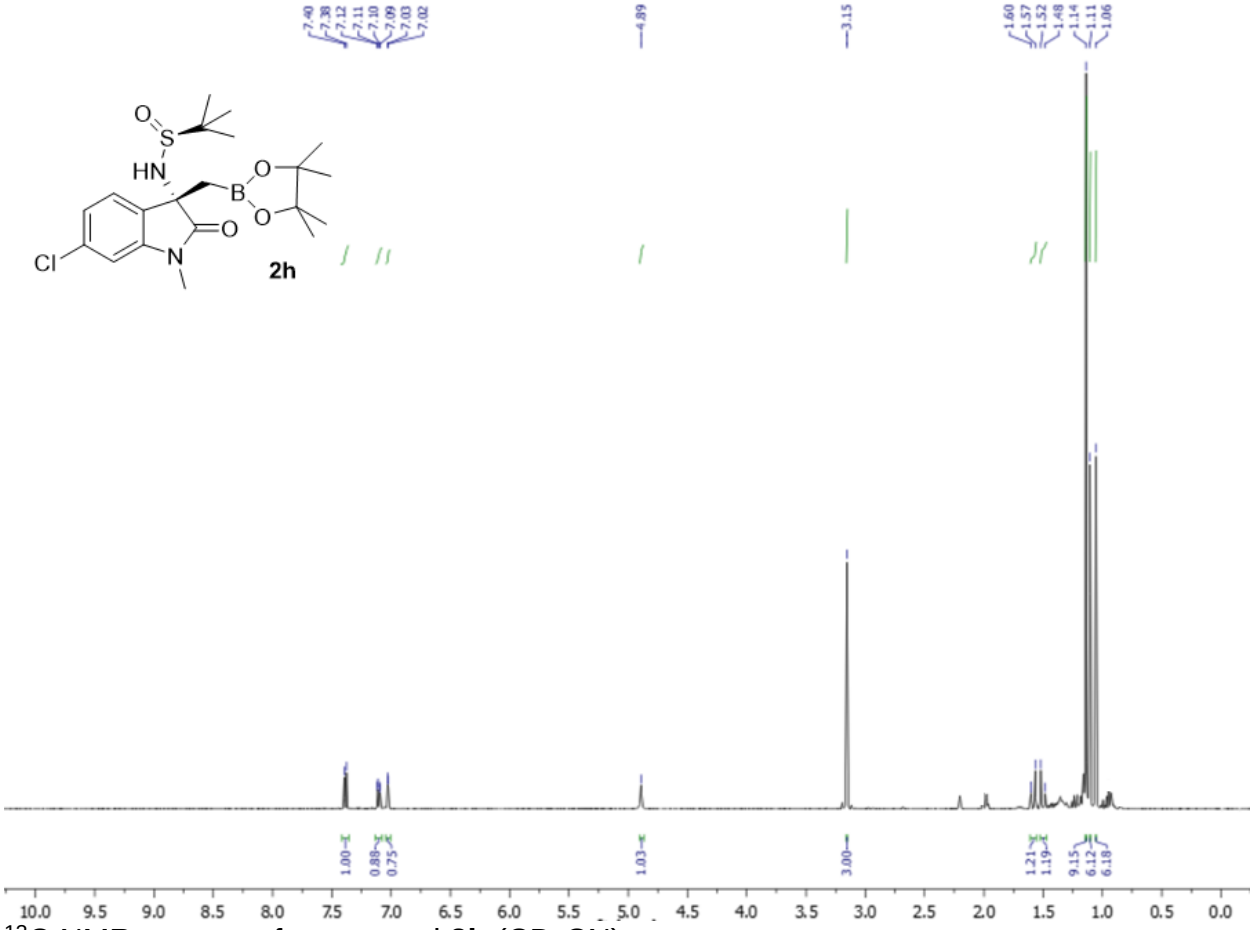

$^{13}$C NMR of compound **2g** ($CD_3CN$)



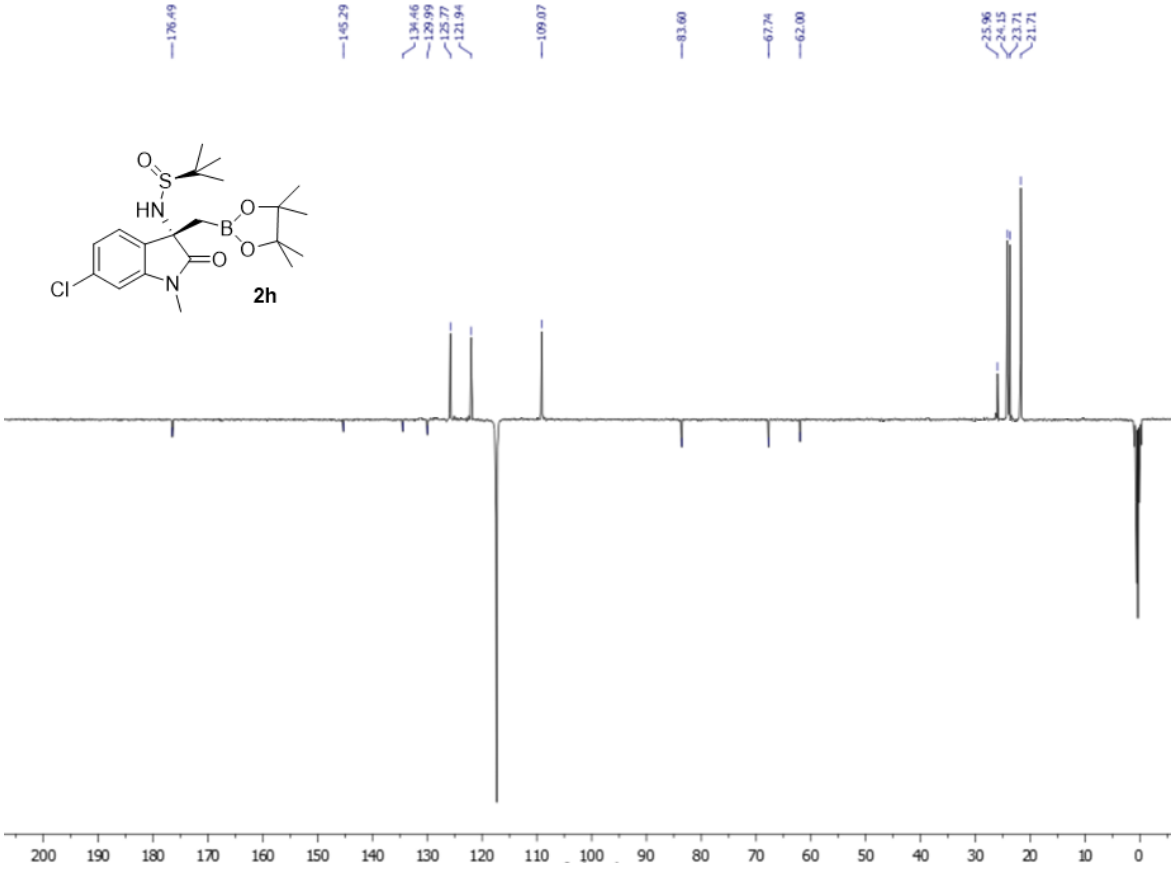
$^{11}$B NMR of compound **2g** ($CD_3CN$)



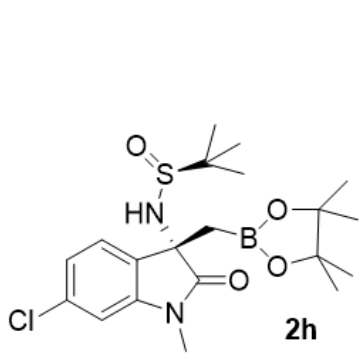
$^{1}$H NMR of compound **2h** ($CD_3CN$)



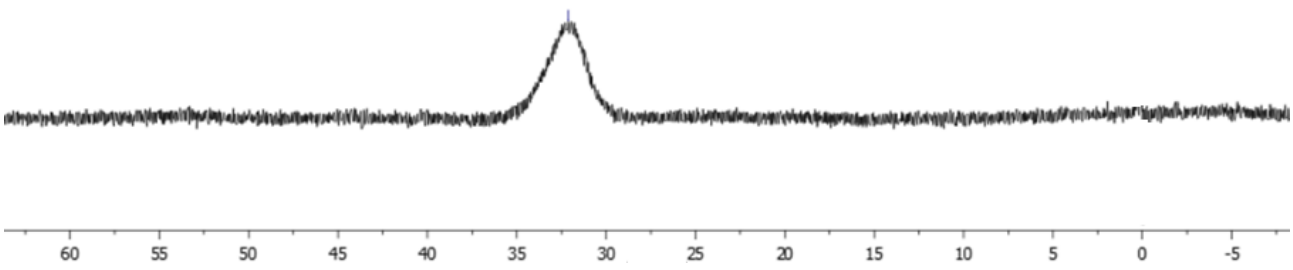

$^{13}$C NMR spectra of compound **2h** ($CD_3CN$)



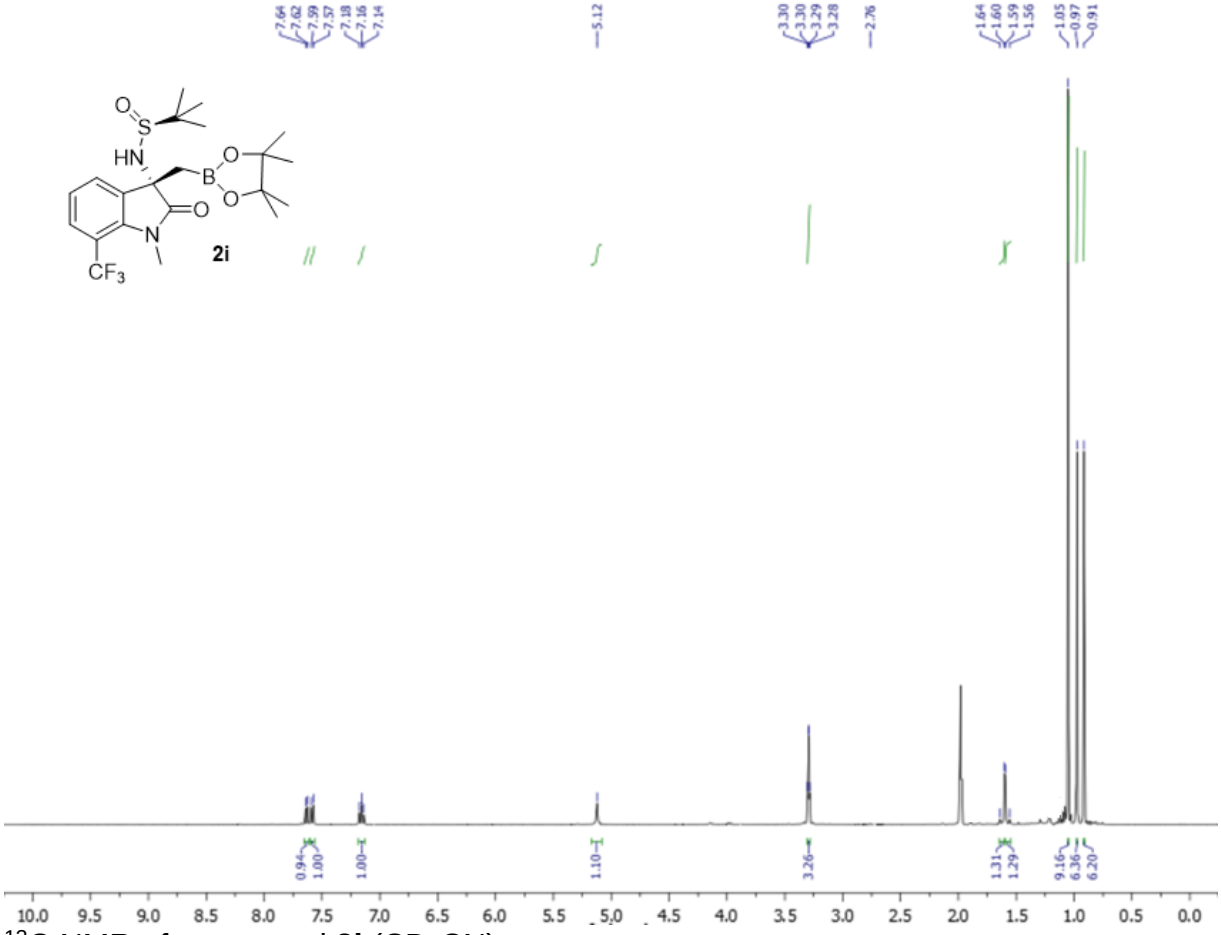
$^{11}$B NMR spectra of compound **2h** ($CD_3CN$)



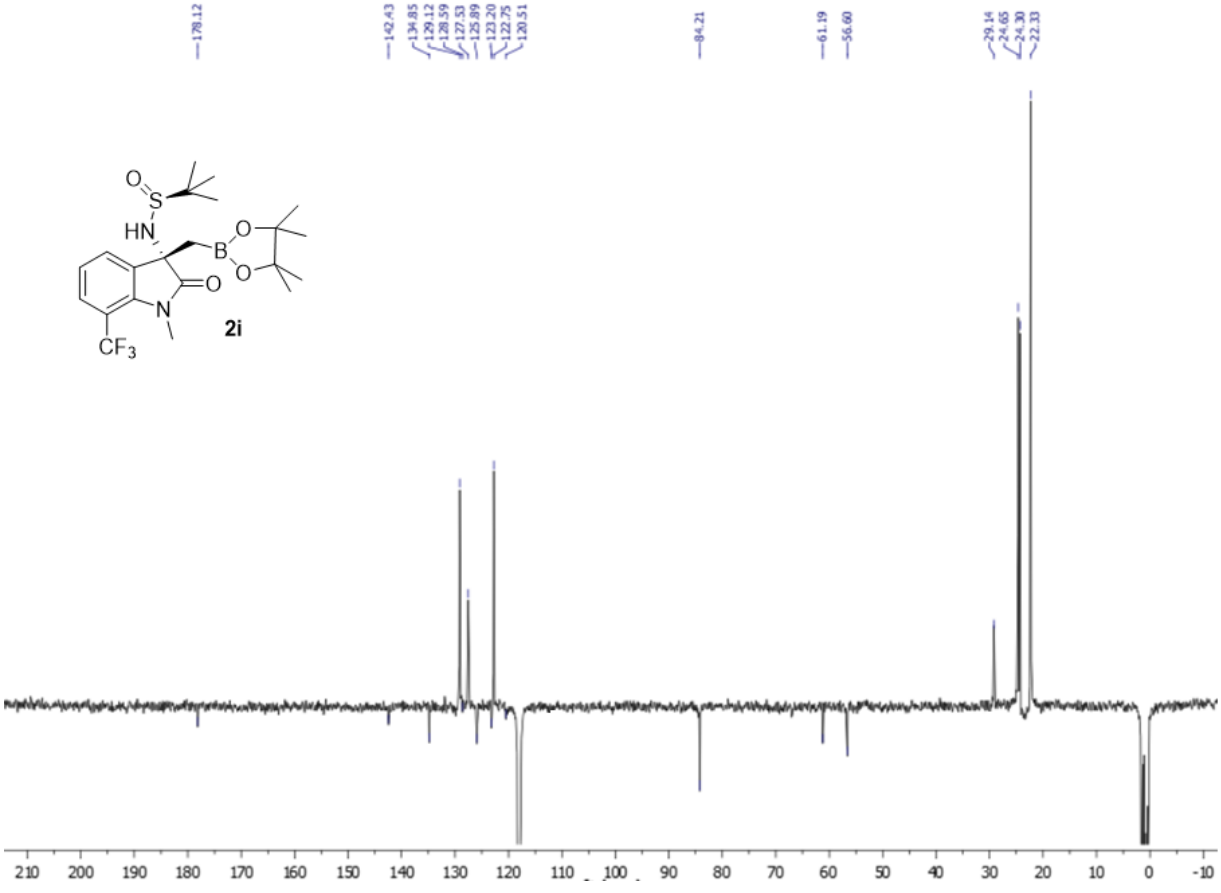

**2h**



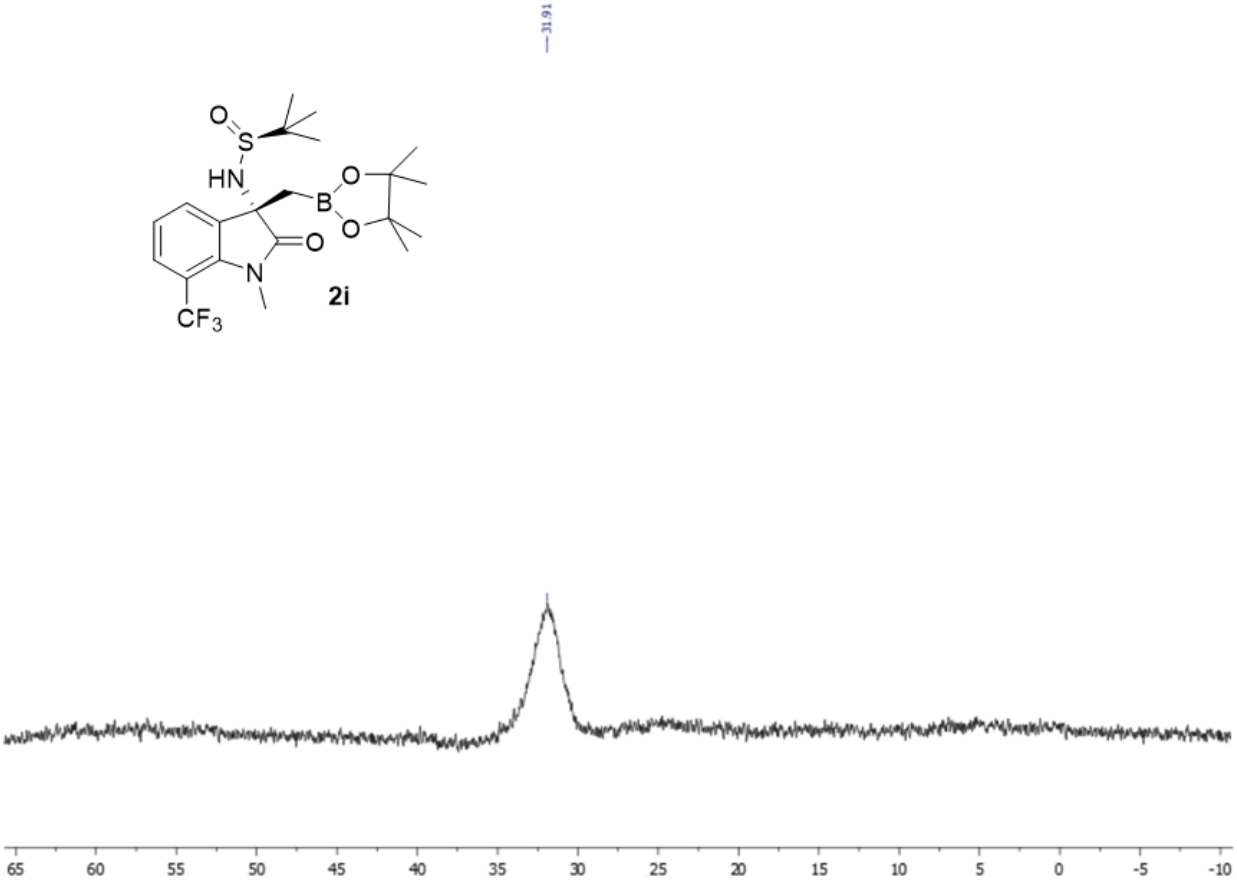
$^{1}$H NMR of compound **2i** ($CD_3CN$)



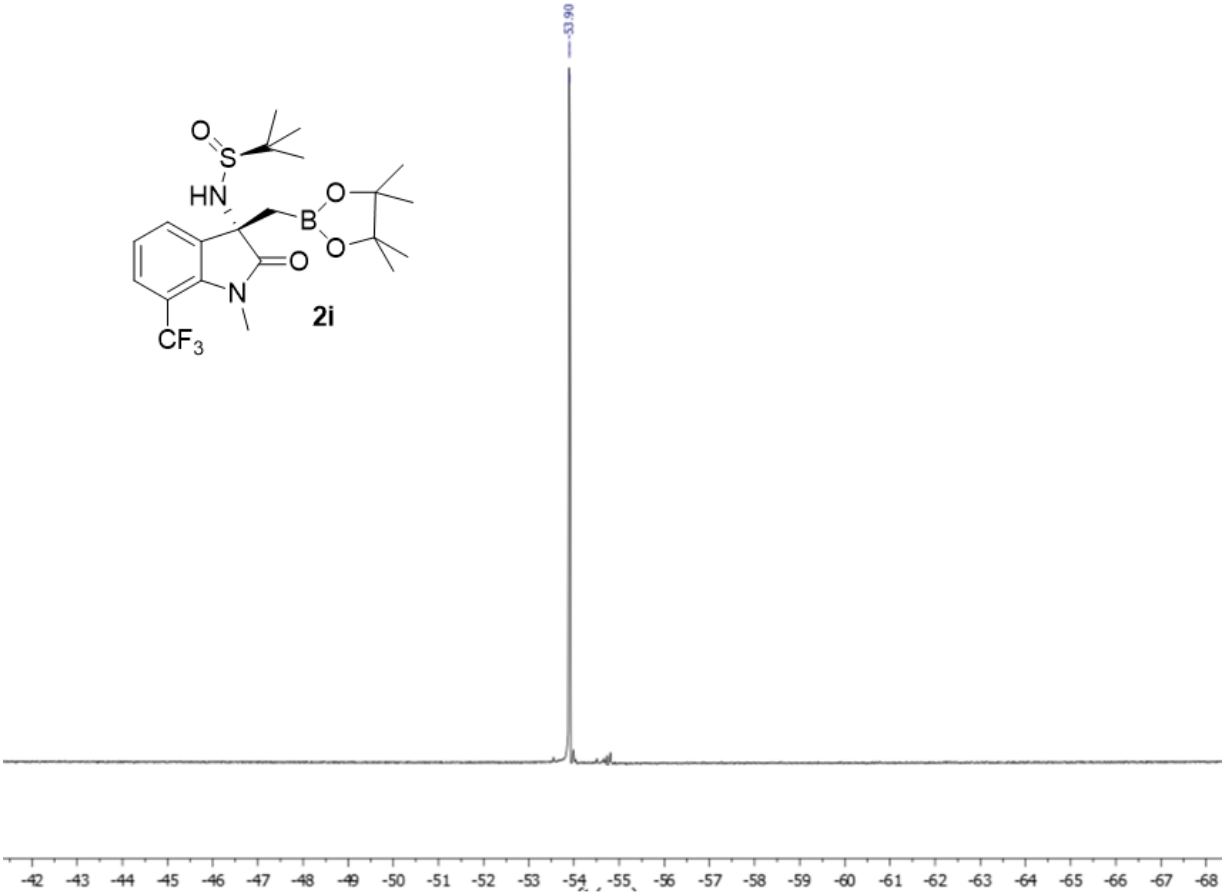

$^{13}$C NMR of compound **2i** ($CD_3CN$)



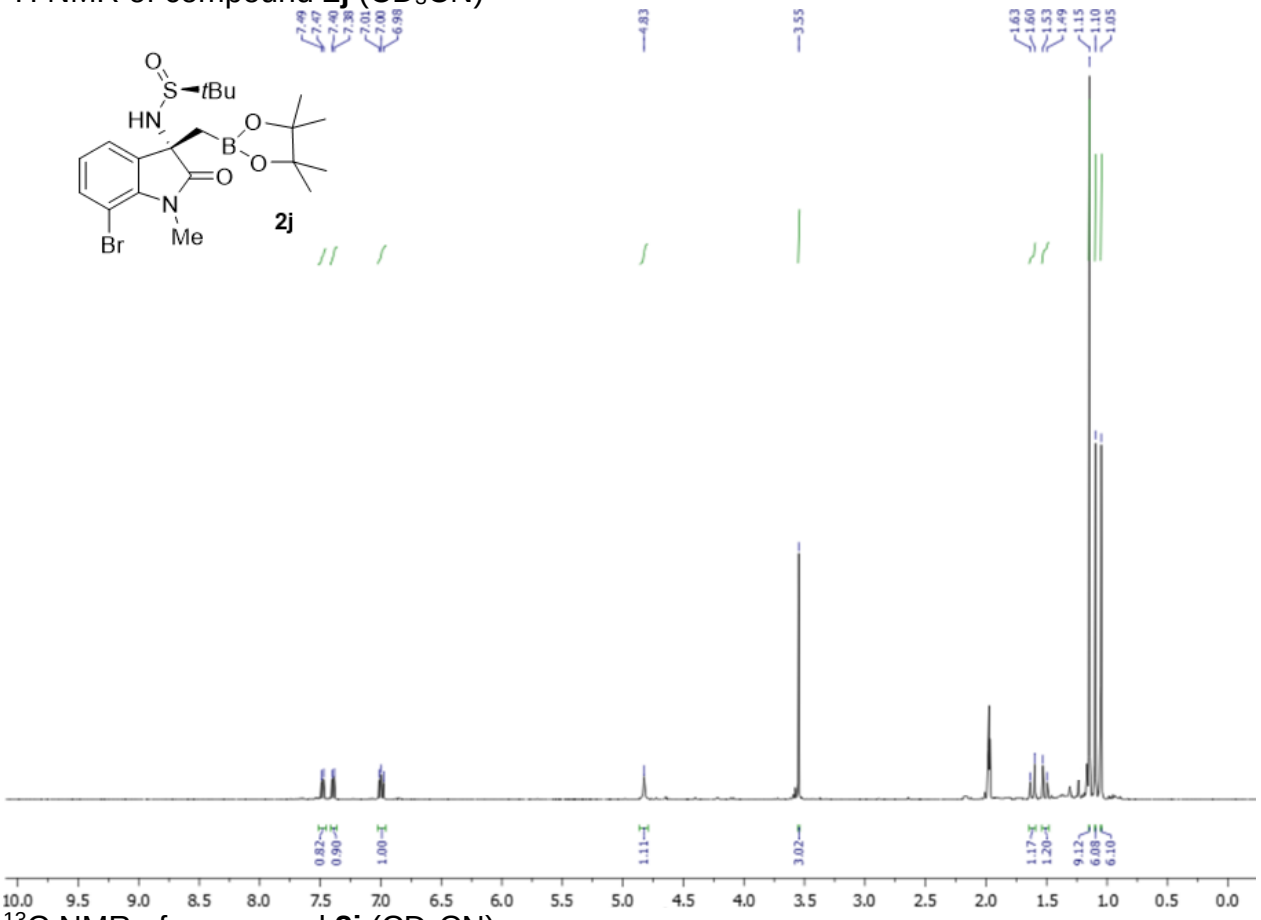
$^{11}$B NMR of compound **2i** ($CD_3CN$)



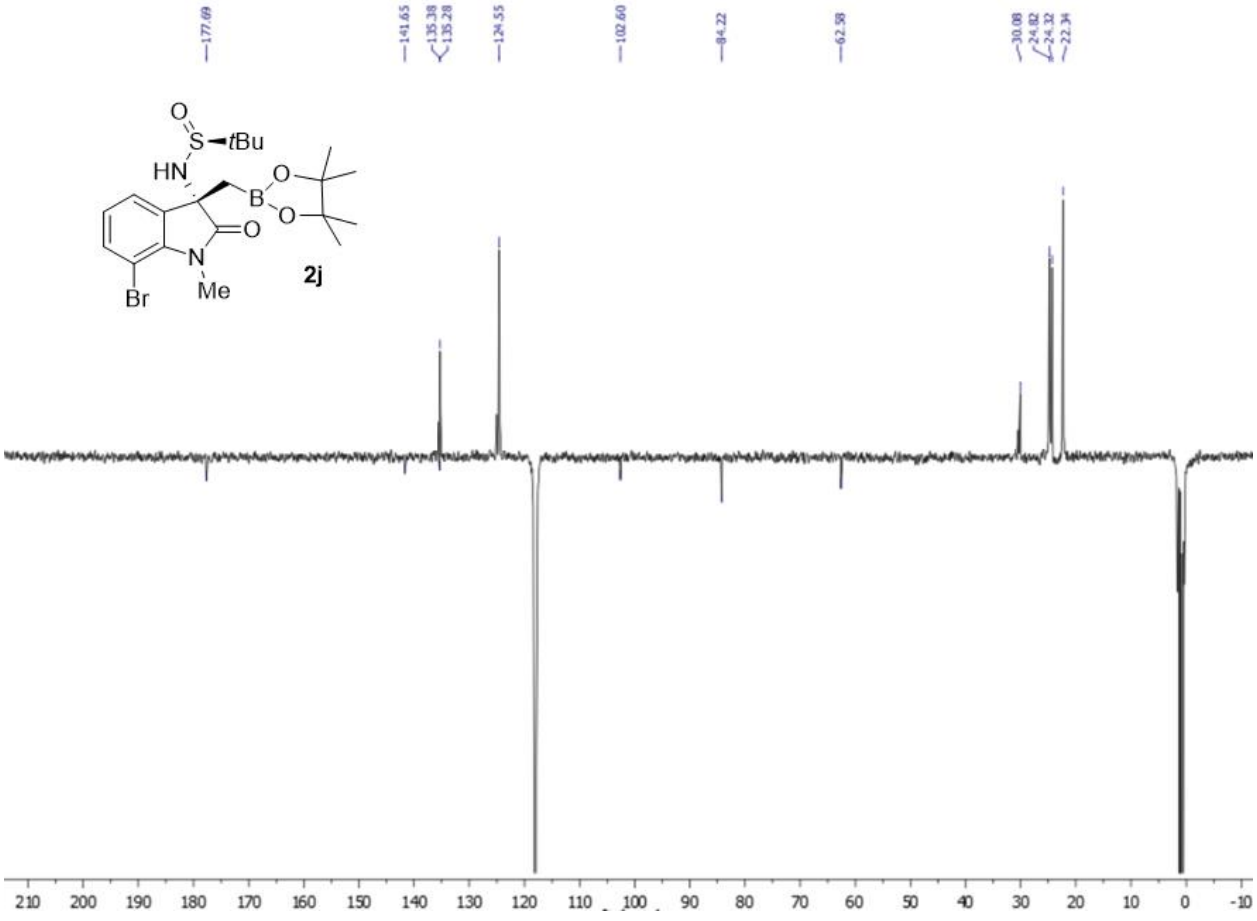

$^{19}$F NMR of compound **2i** ($CD_3CN$)



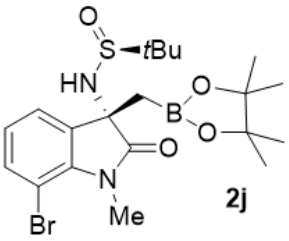
$^{1}$H NMR of compound **2j** ($CD_3CN$)



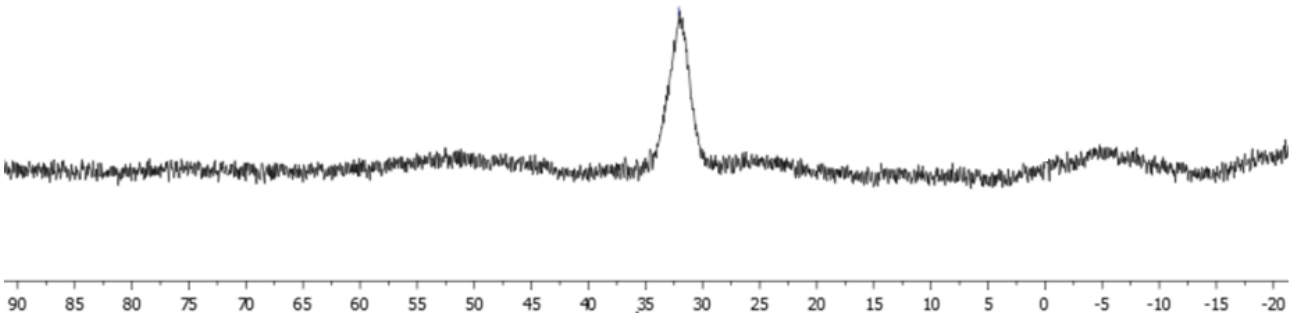

$^{13}$C NMR of compound **2j** ($CD_3CN$)



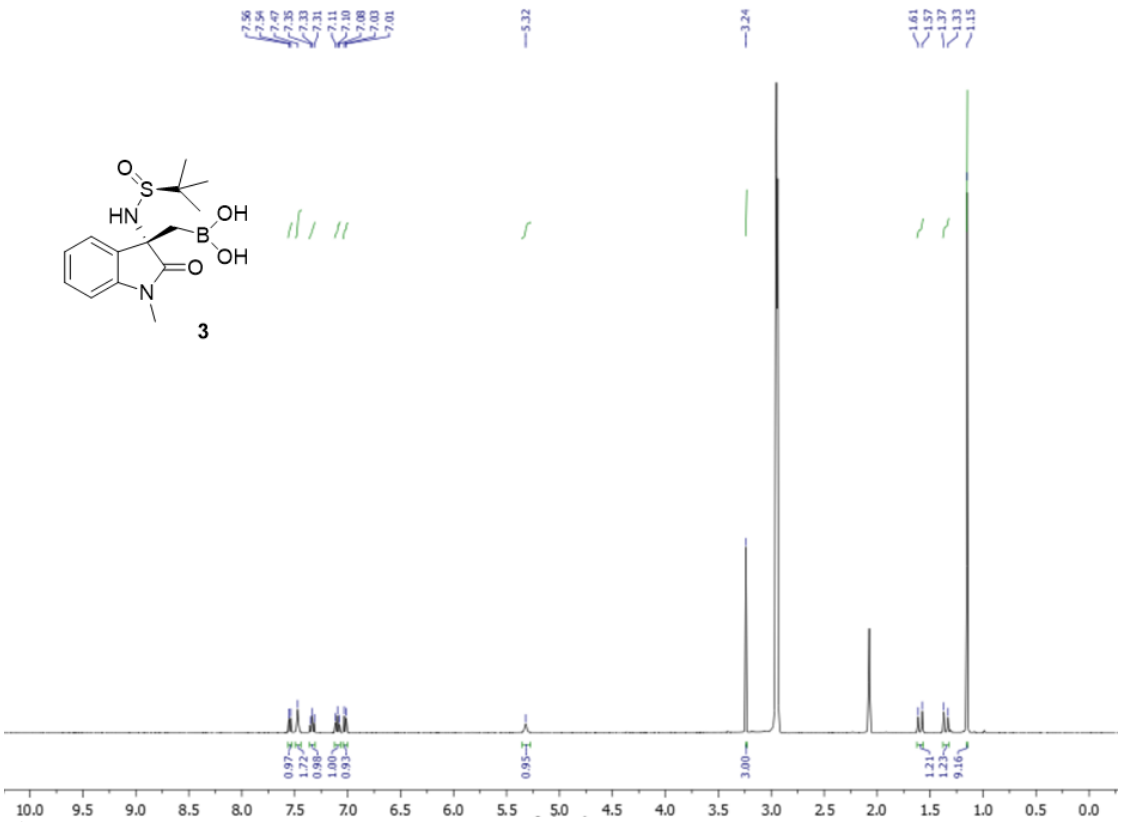
$^{11}$B NMR of compound **2j** ($CD_3CN$)




**2j**



$^{1}$H NMR of compound **3** (acetone d-6 + 1 drop of $H_2O$)

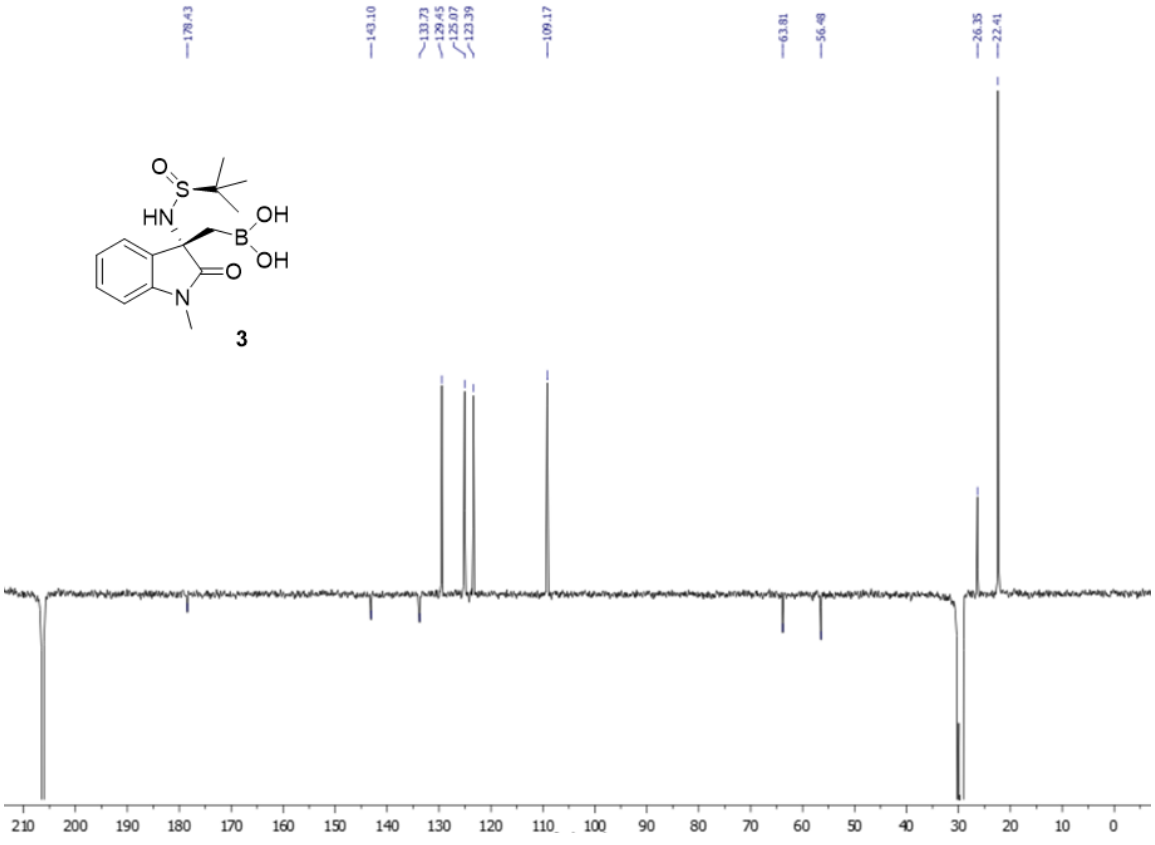






**3**

$^{13}$C NMR of compound **3** (acetone d-6 + 1 drop of $H_2O$)

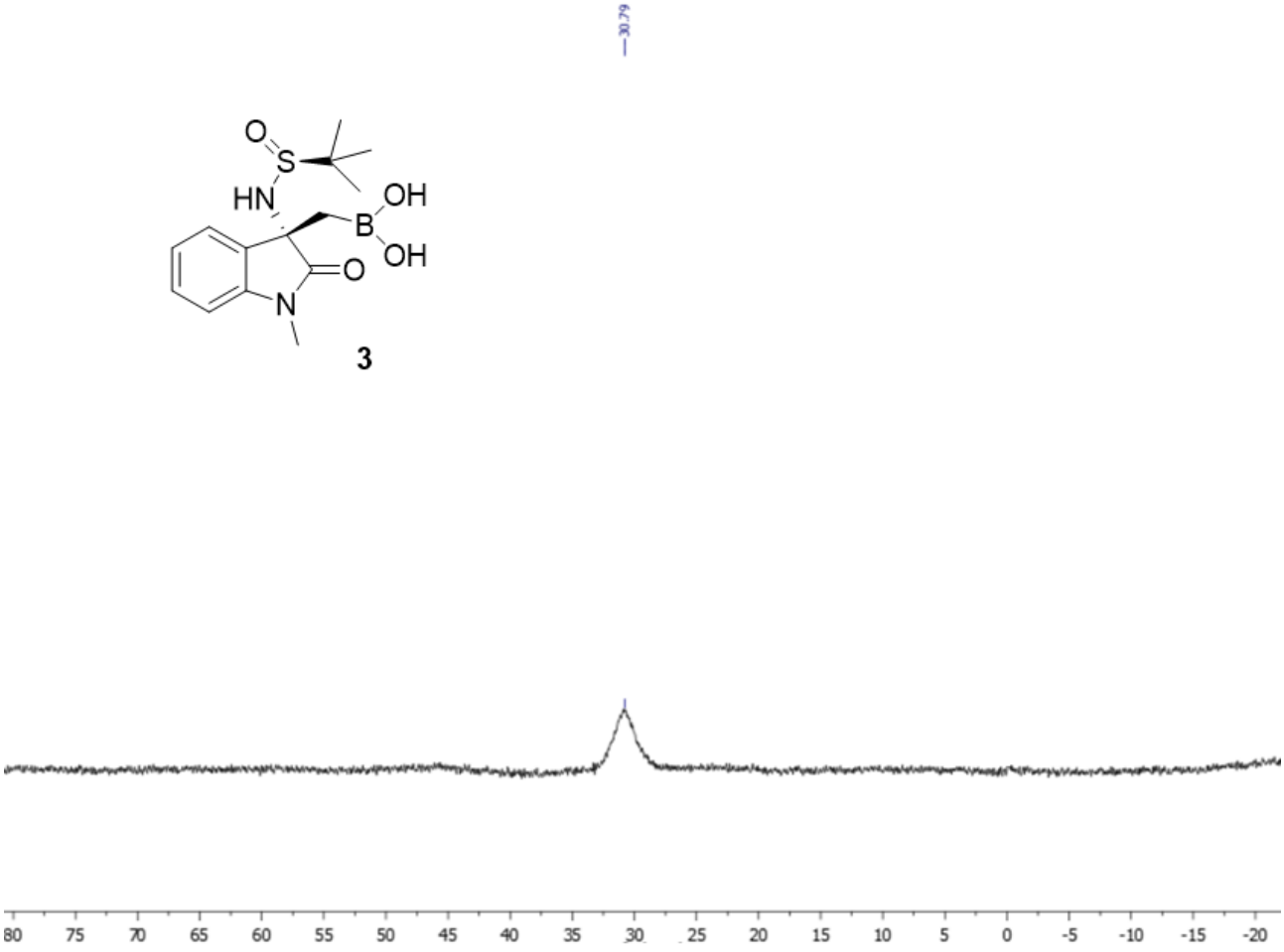






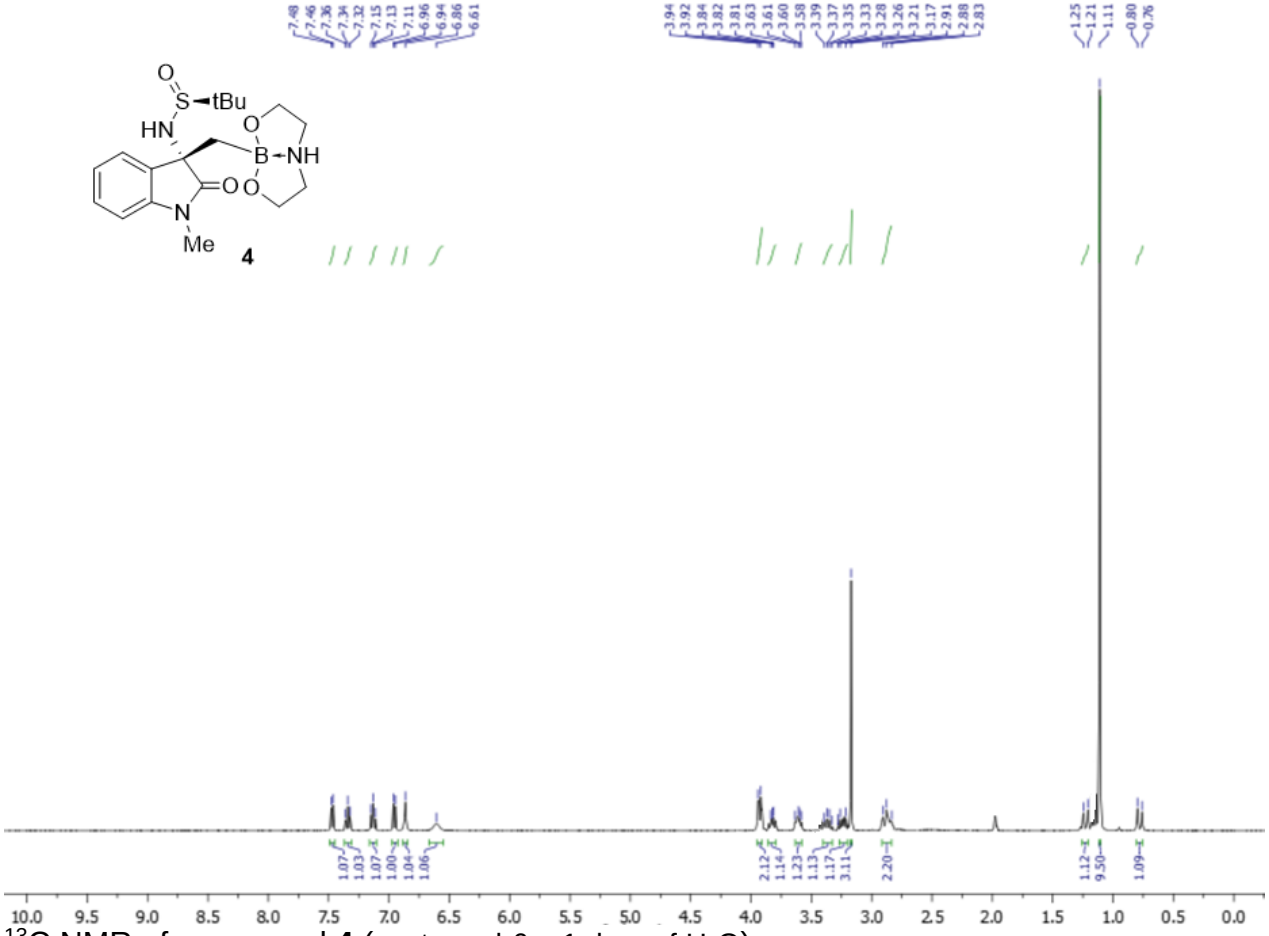
**3**

$^{11}$B NMR of compound **3** (acetone d-6 + 1 drop of $H_2O$)

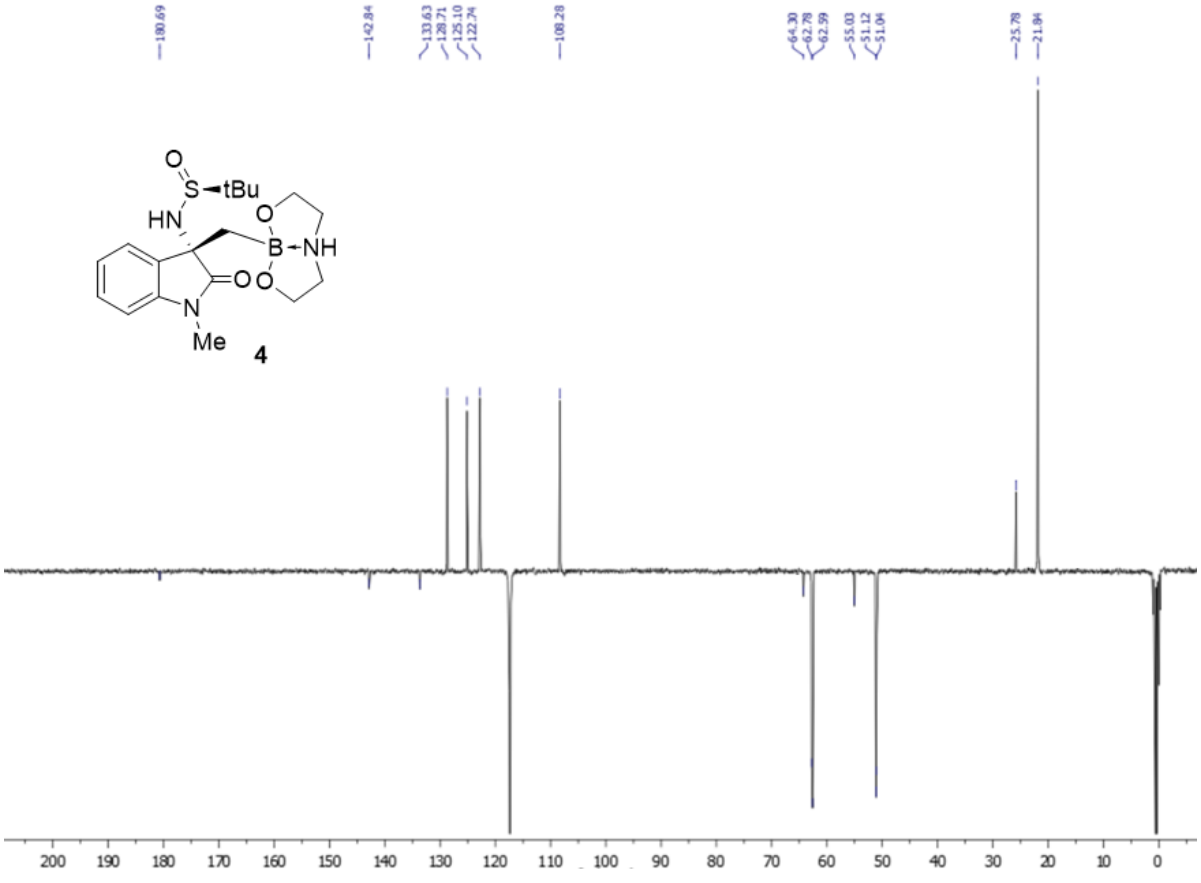



**3**

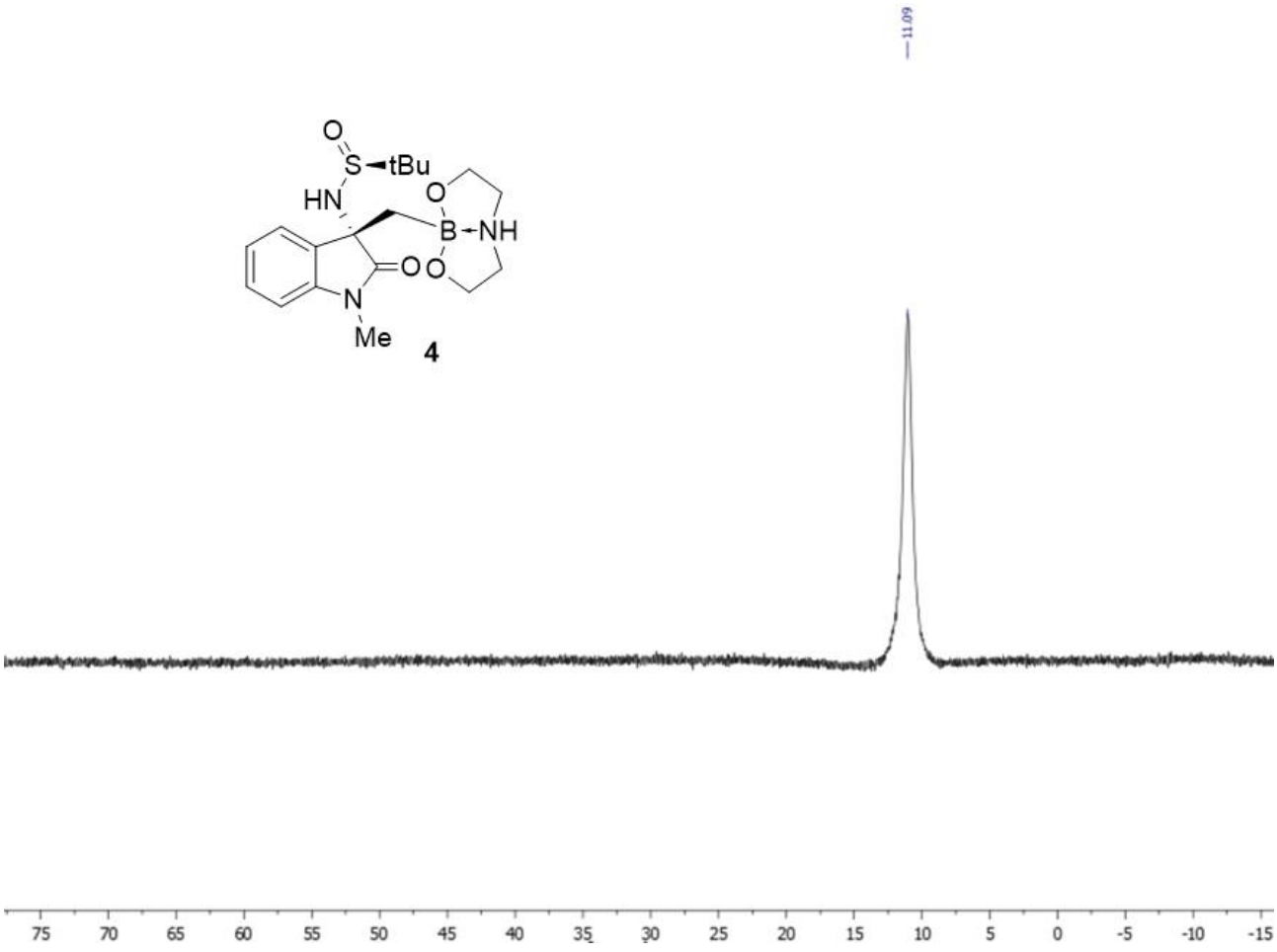
$^{1}$H NMR of compound **4** (acetone d-6 + 1 drop of $H_2O$)



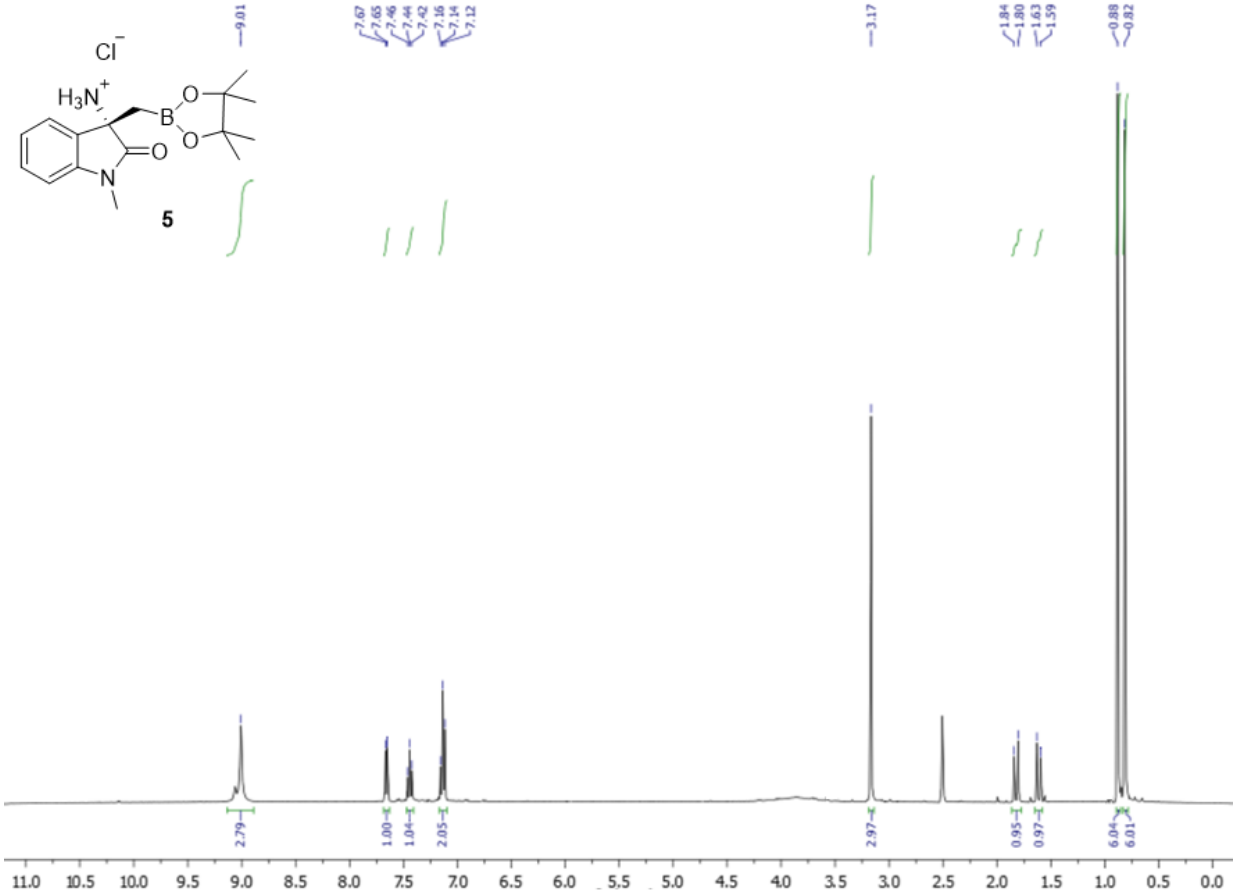

$^{13}$C NMR of compound **4** (acetone d-6 + 1 drop of $H_2O$)



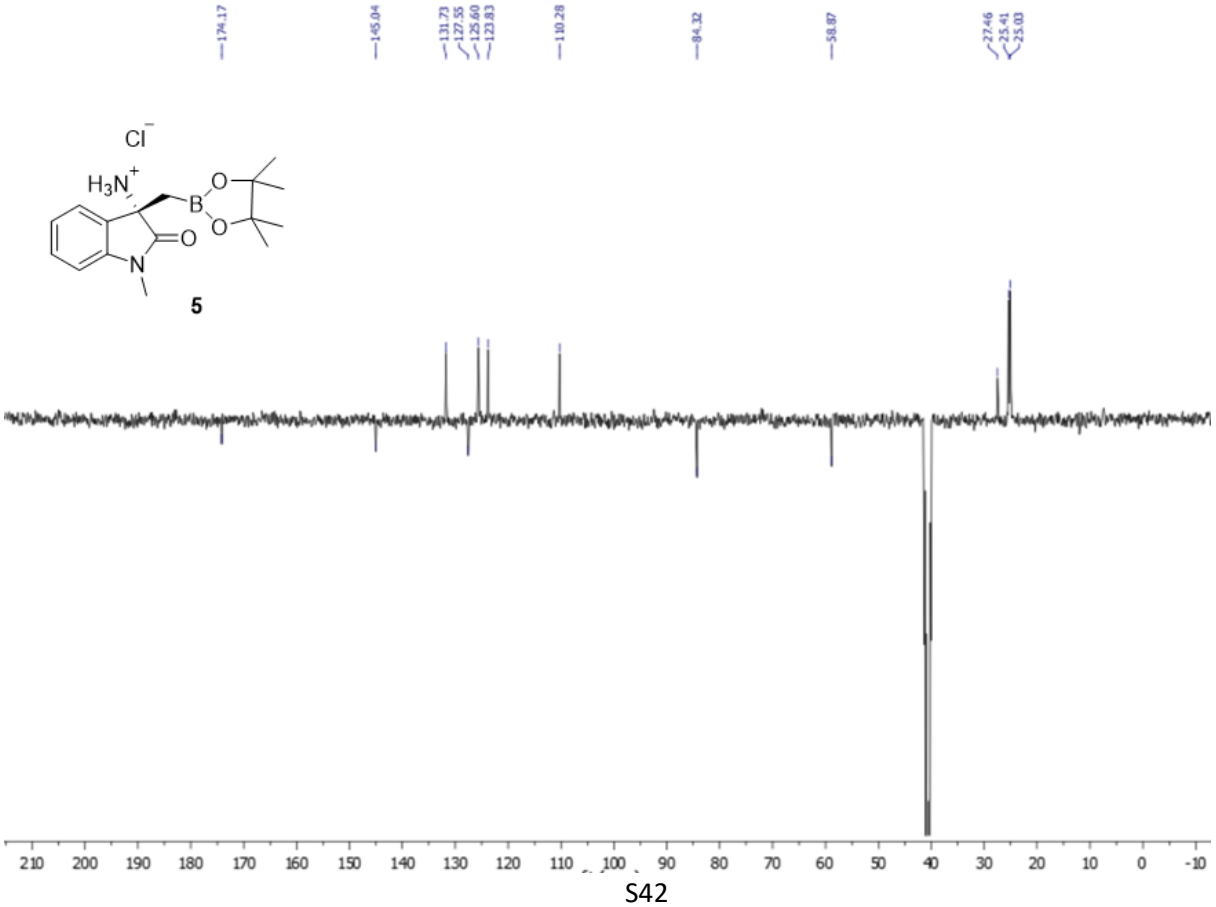
$^{11}$B NMR of compound **4** (acetone d-6 + 1 drop of $H_2O$)



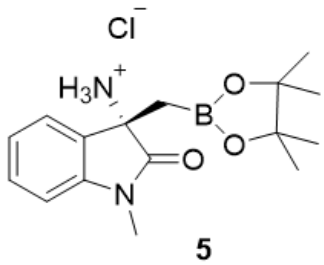
$^{1}$H NMR of compound **5** (DMSO d-6)




$^{13}$C NMR of compound **5** (DMSO d-6)

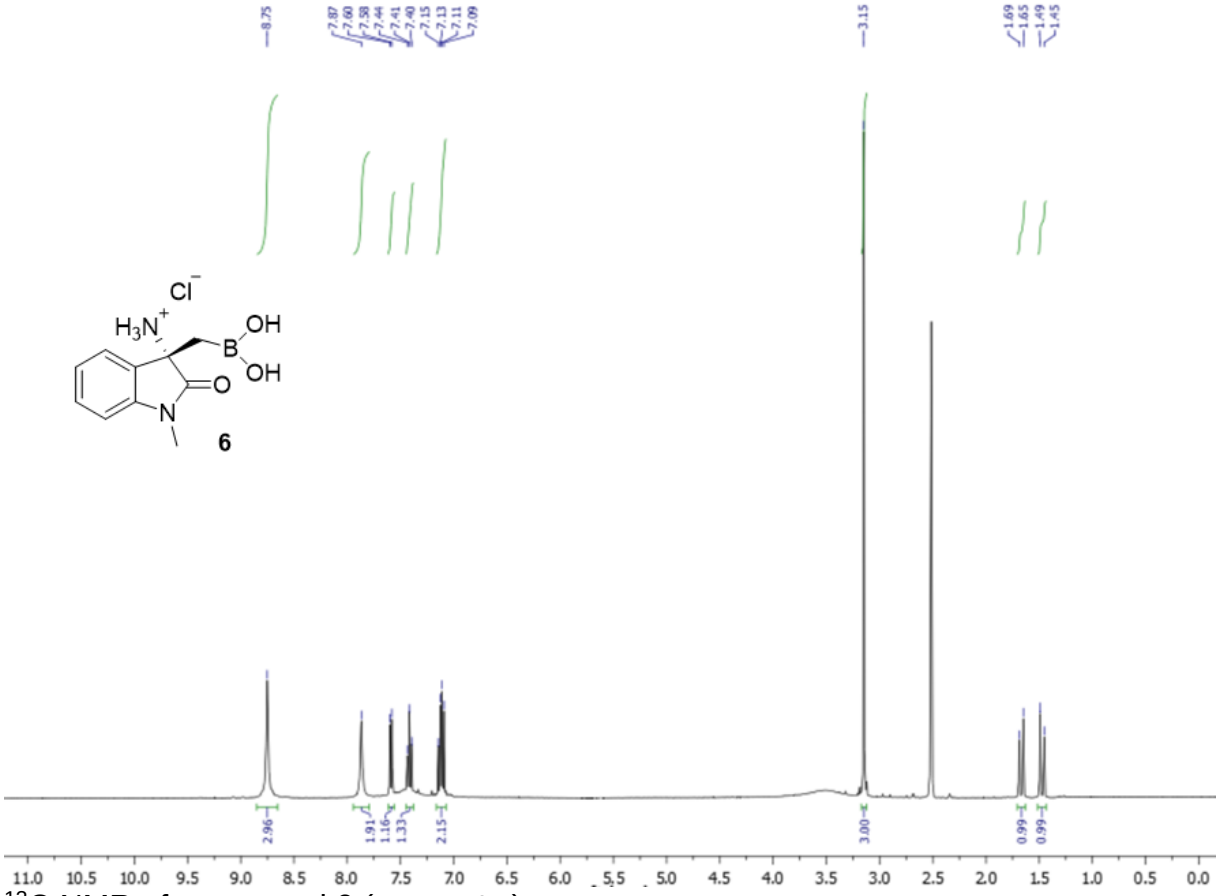


$^{11}$B NMR of compound **5** (DMSO d-6)

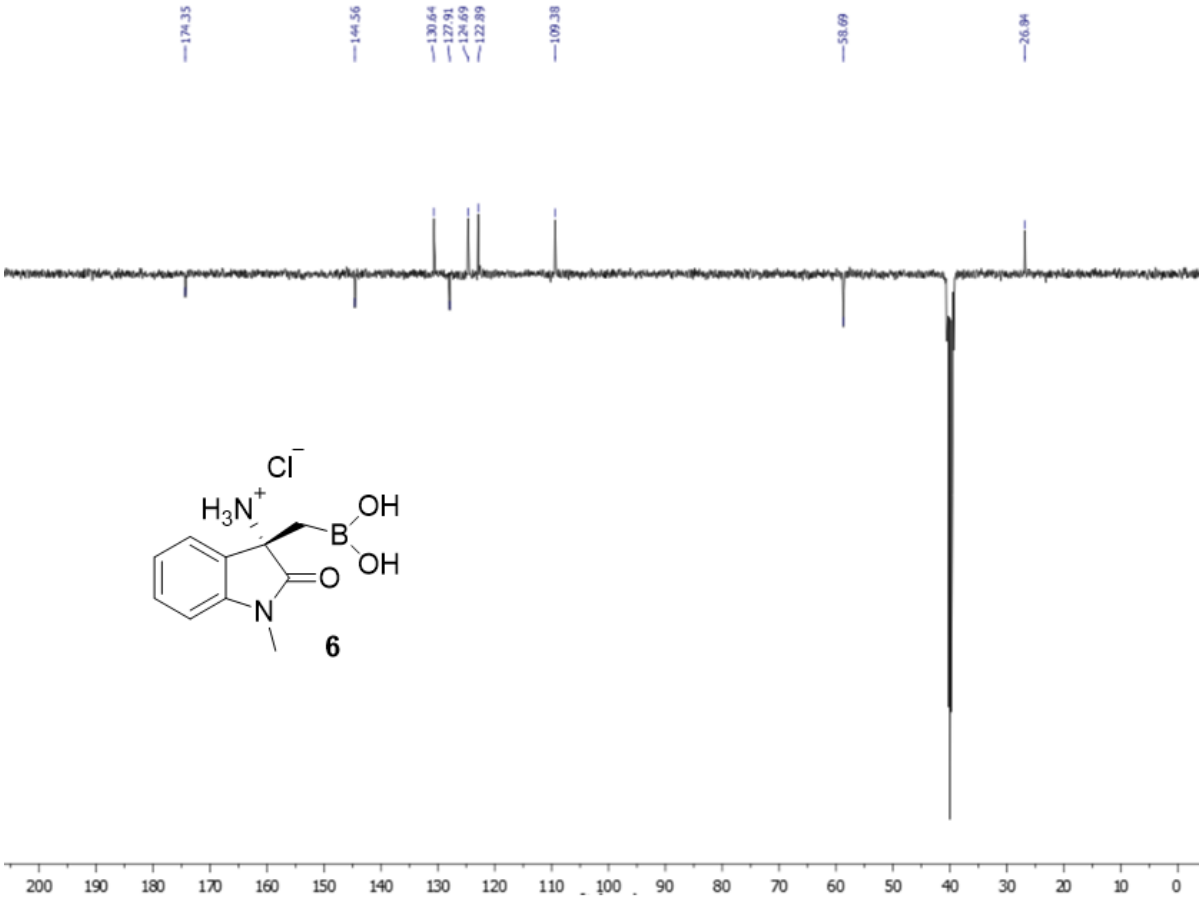



**5**

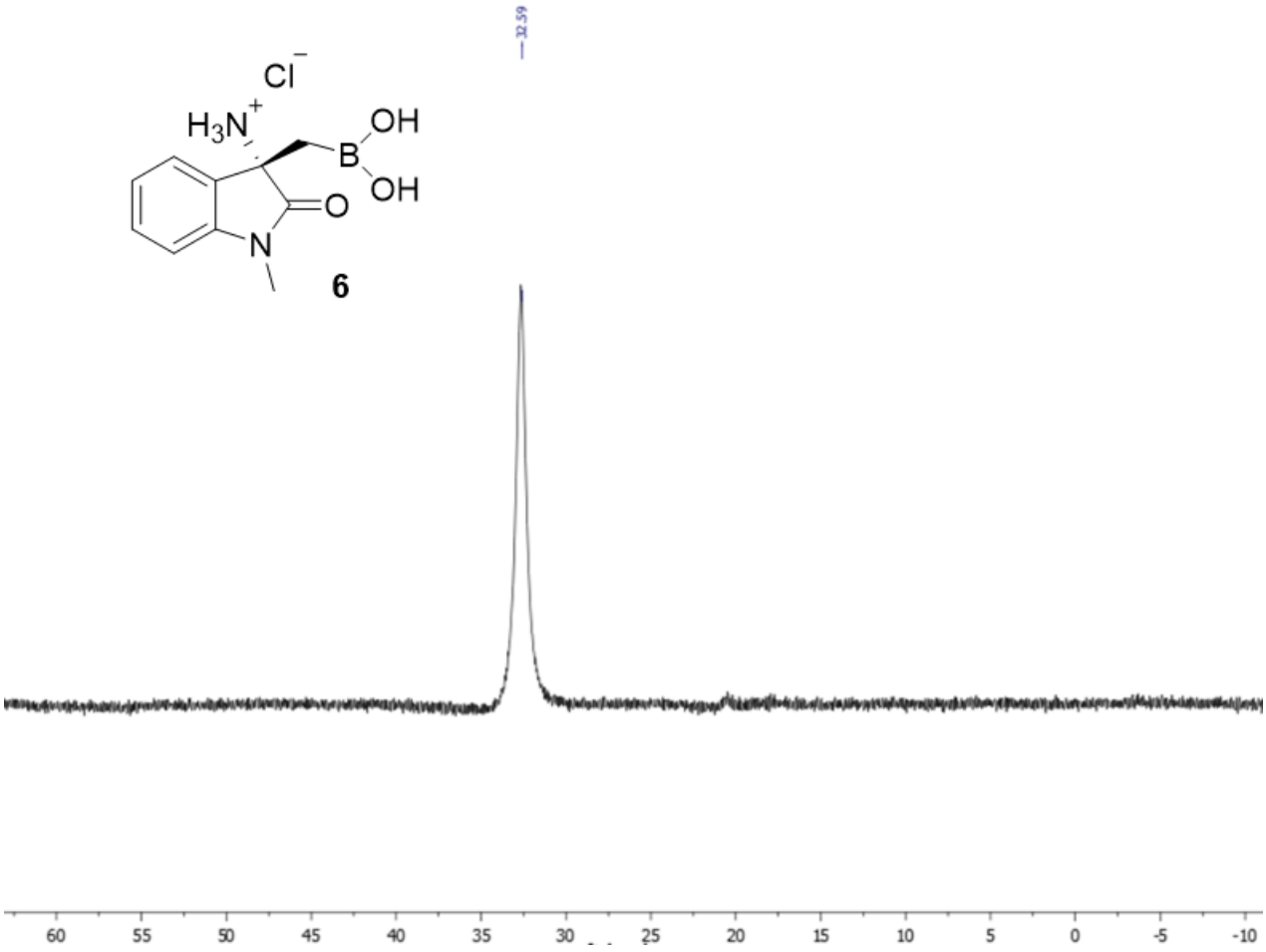
$^{1}$H NMR of compound **6** (DMSO d-6)



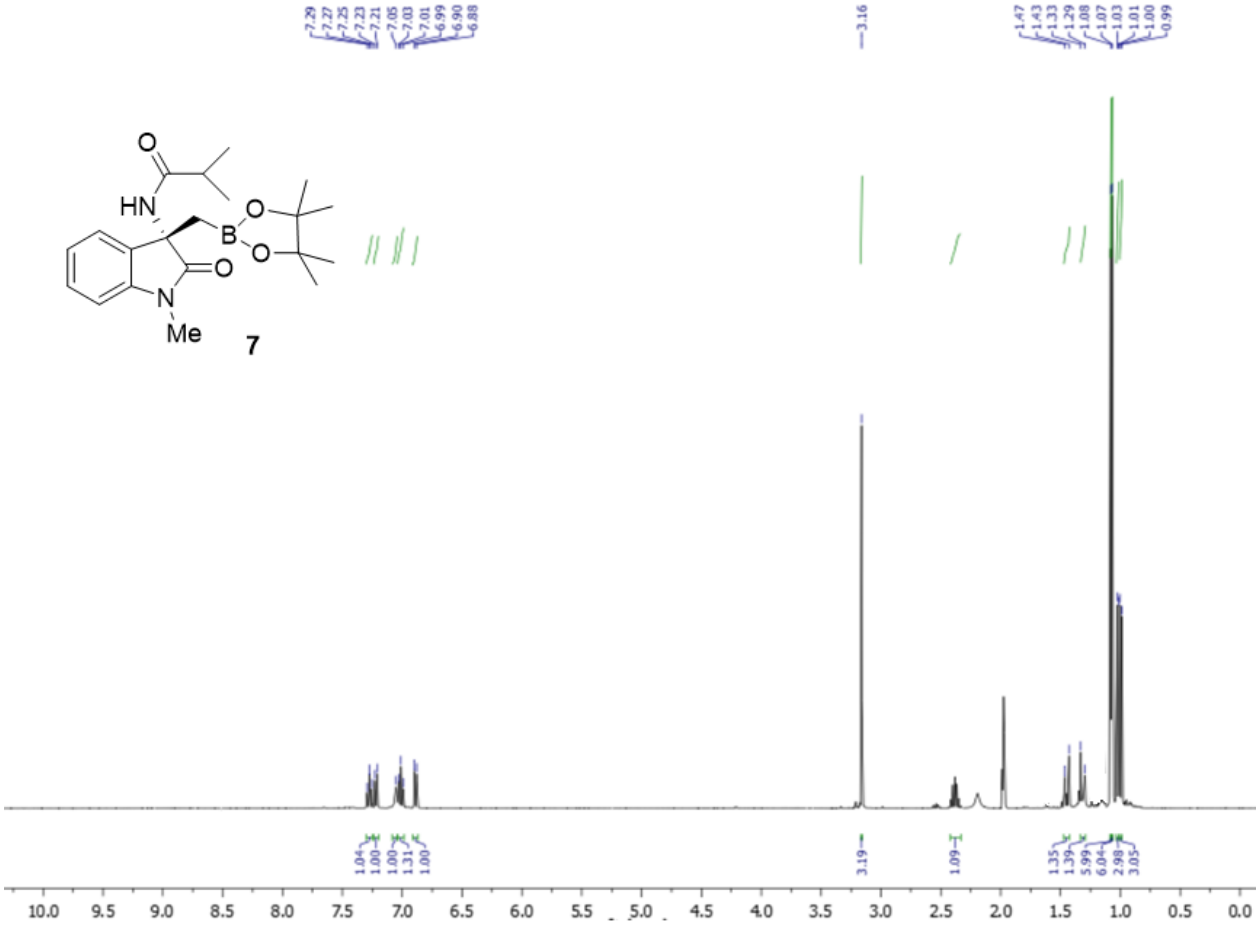

$^{13}$C NMR of compound **6** (DMSO d-6)



$^{11}$B NMR of compound **6** (DMSO d-6)



$^{1}$H NMR of compound **7** ($CD_3CN$)

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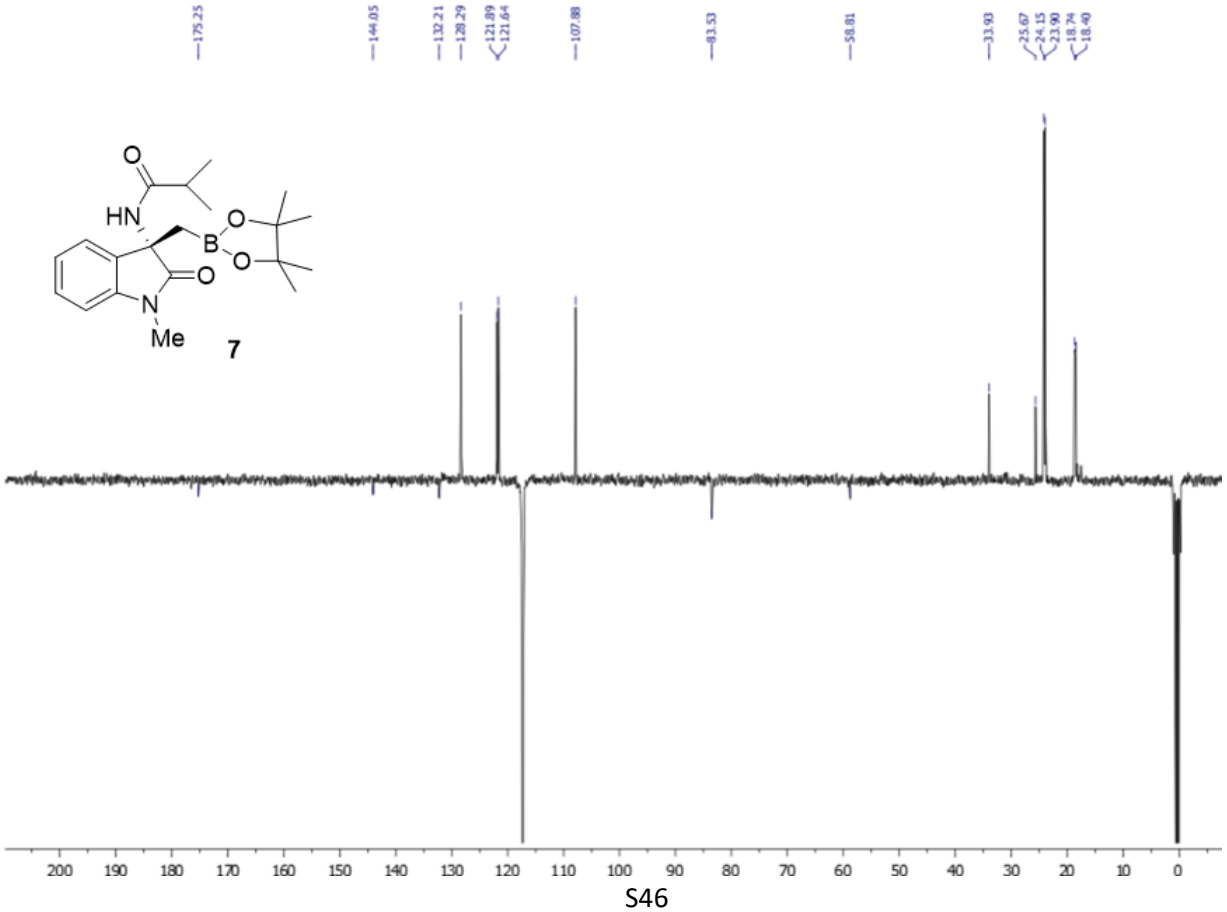
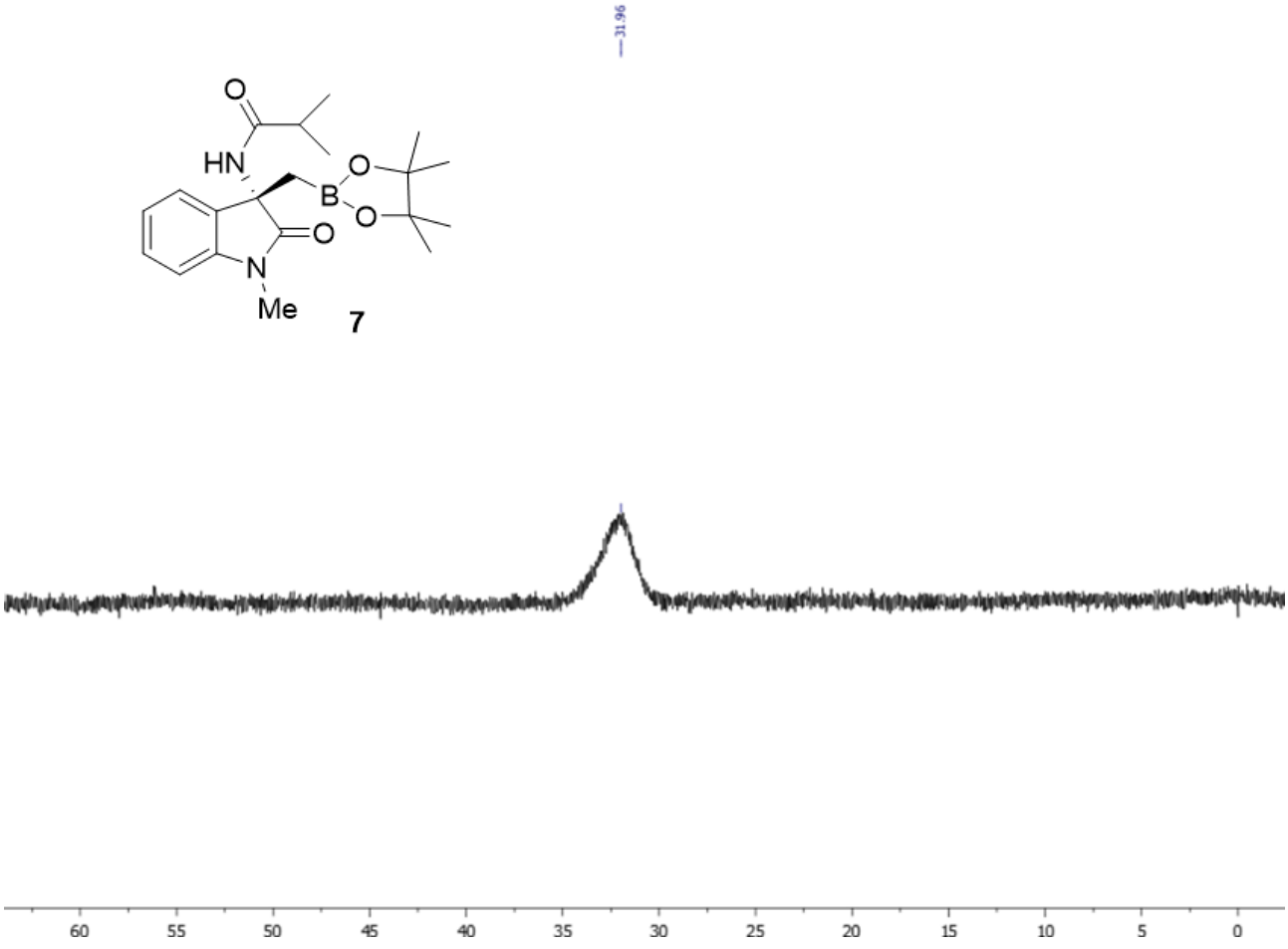
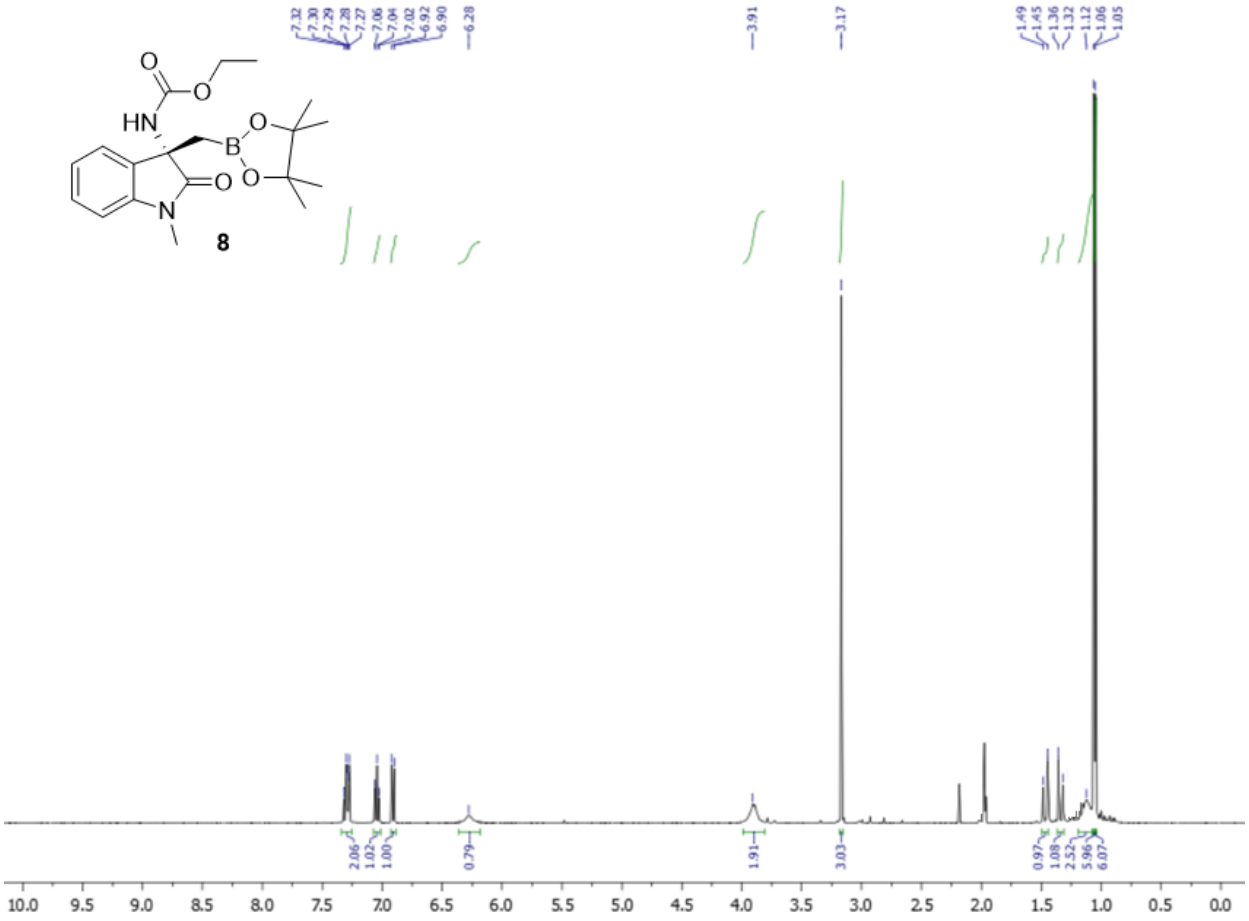


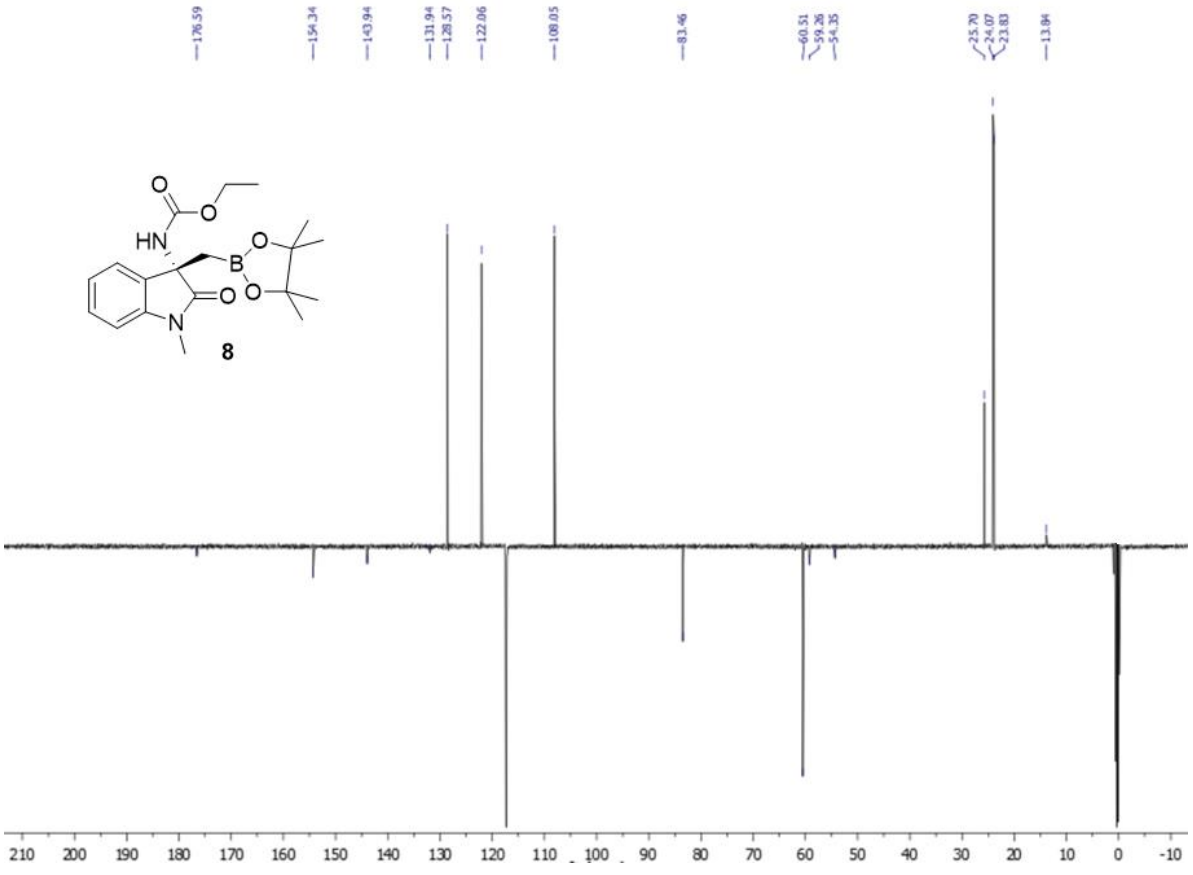
$^{11}$B NMR of compound **7** ($CD_3CN$)



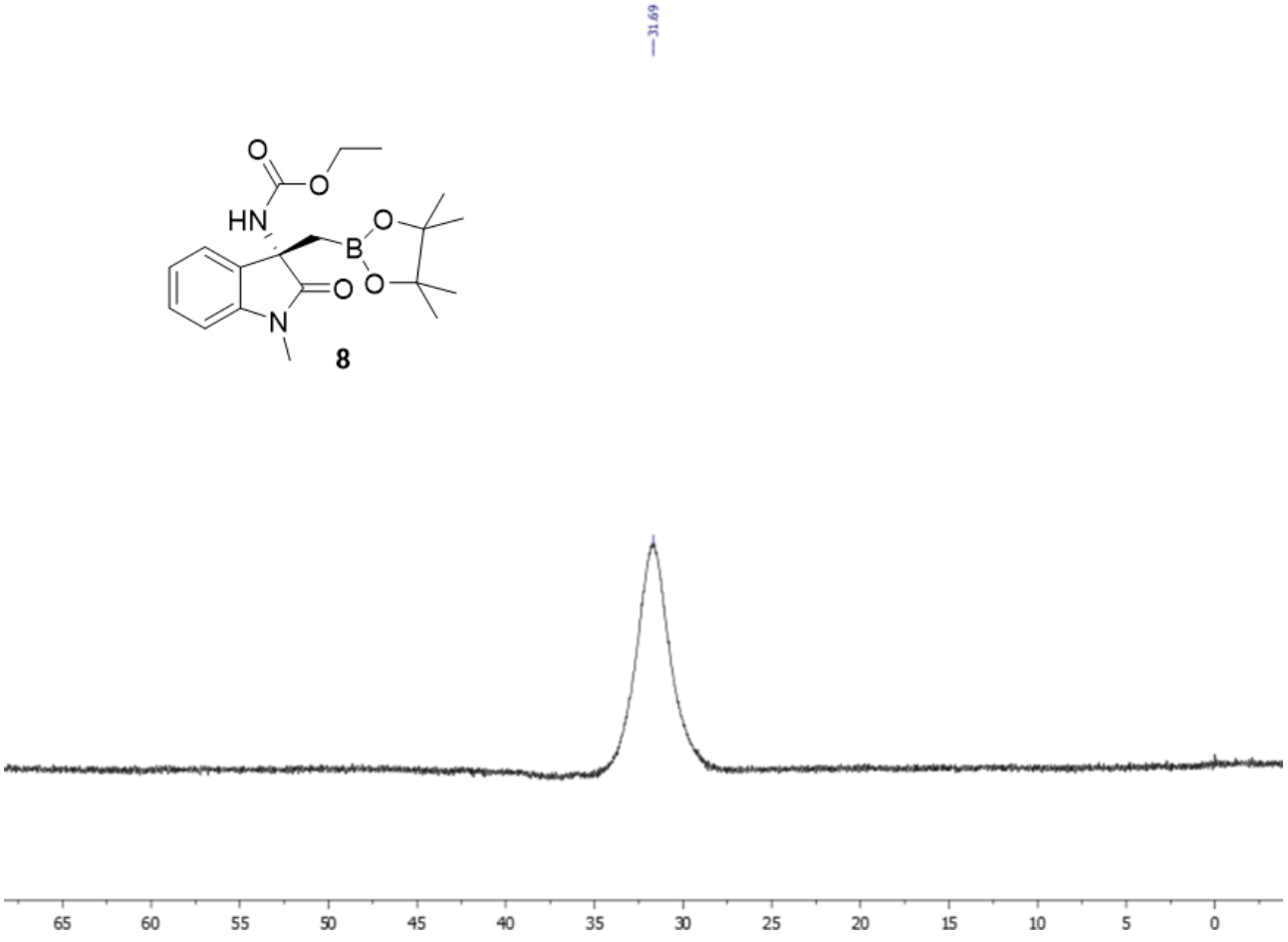
$^{1}$H NMR of compound **8** ($CD_3CN$)



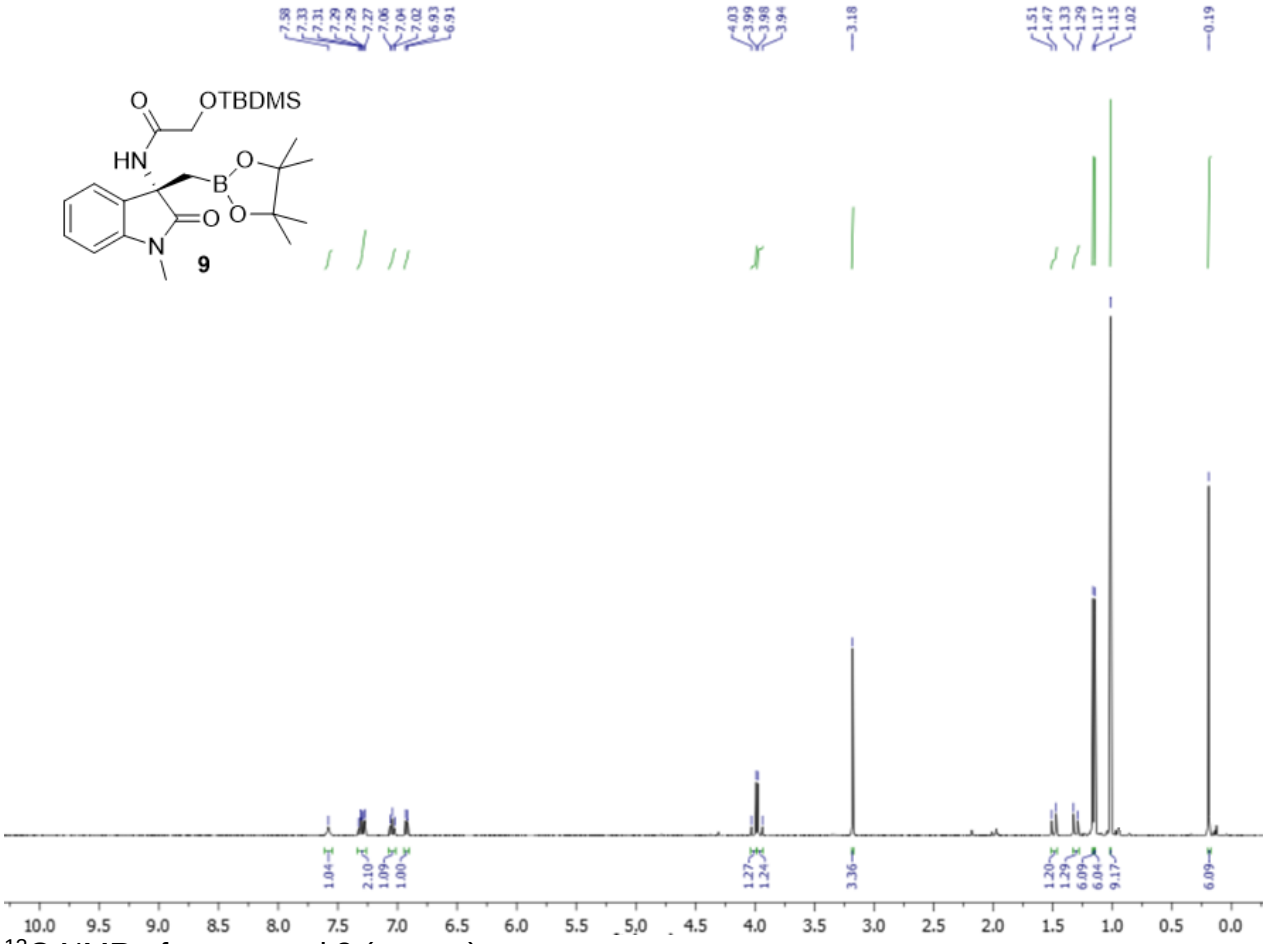

$^{13}$C NMR of compound **8** ($CD_3CN$)



$^{11}$B NMR of compound **8** ($CD_3CN$)



$^{1}$H NMR of compound **9** ($CD_3CN$)

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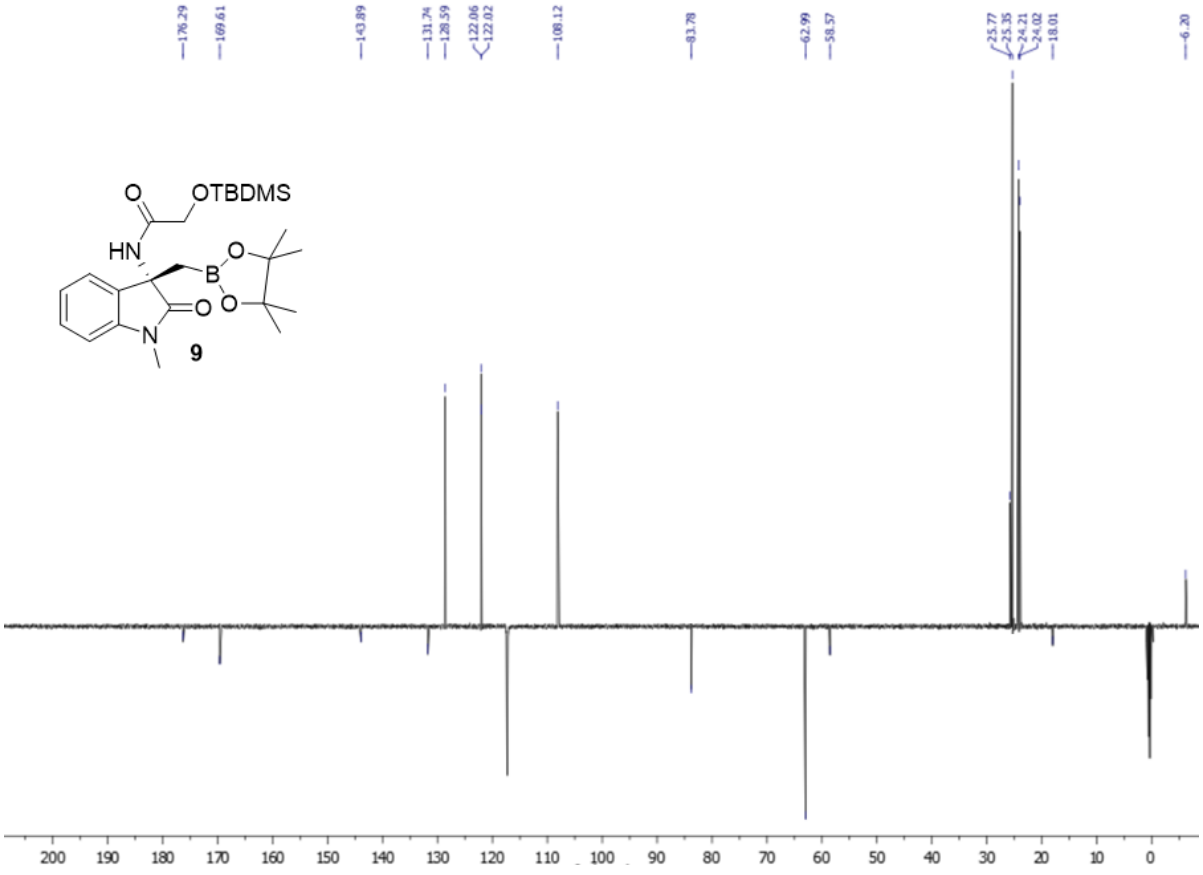
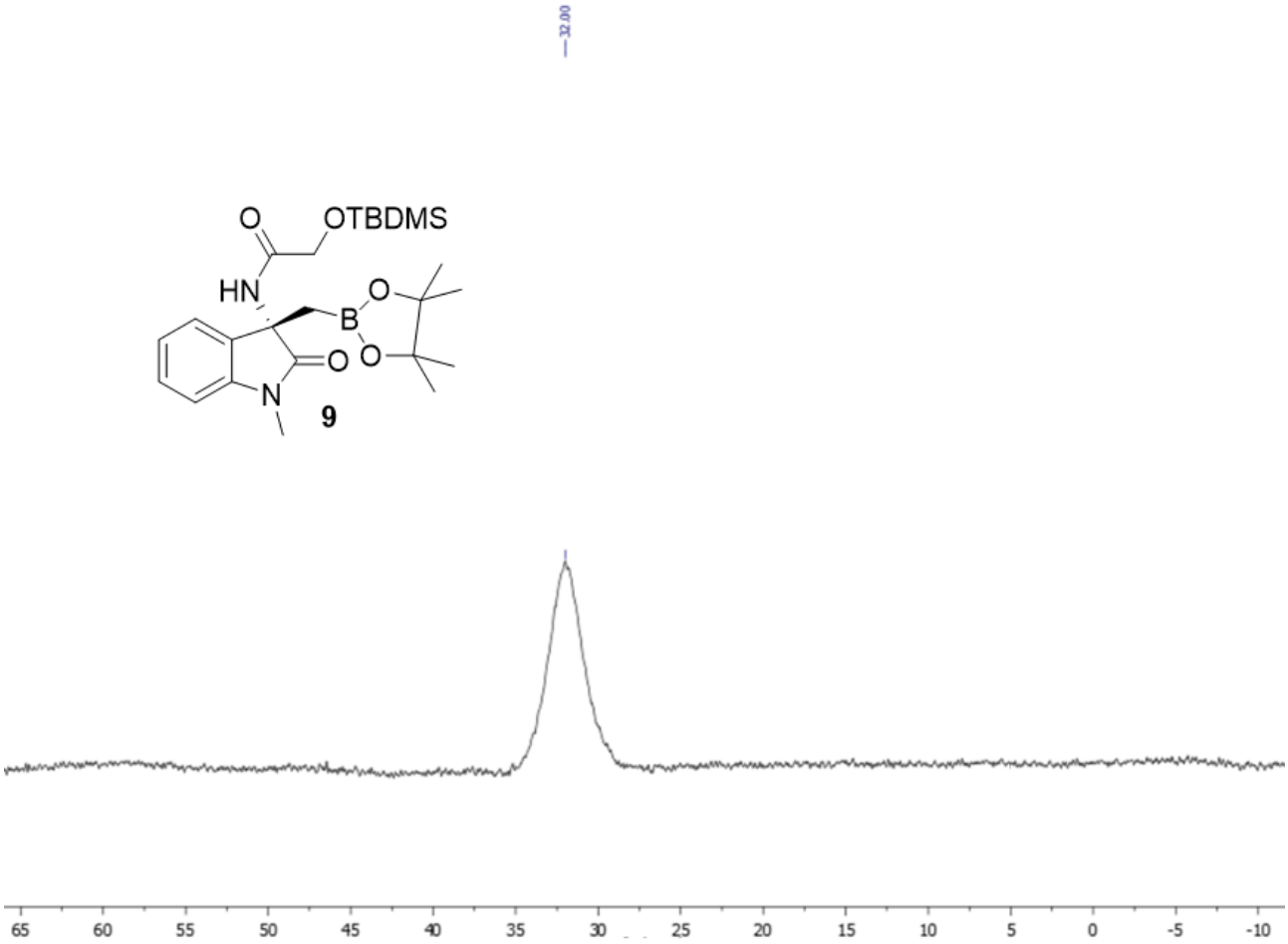
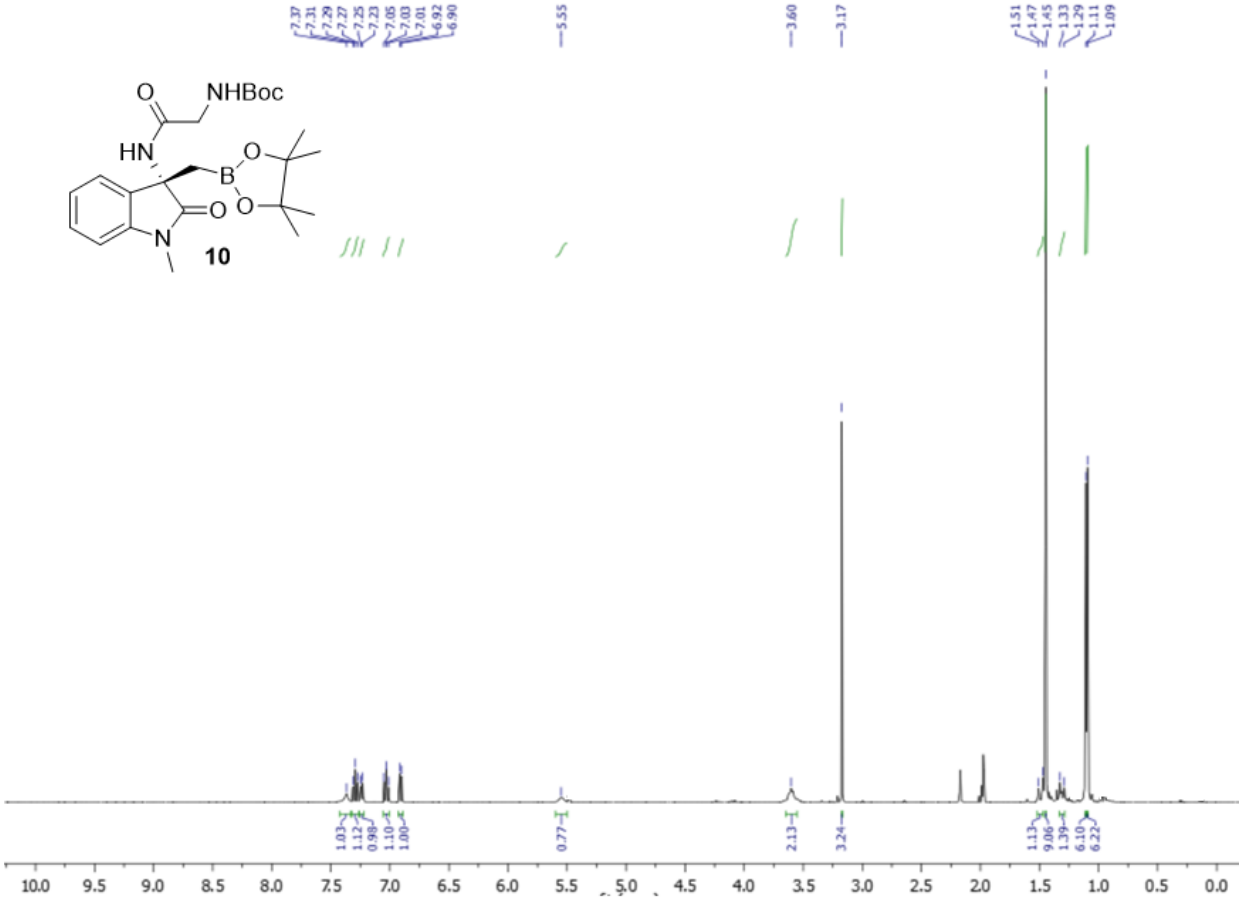


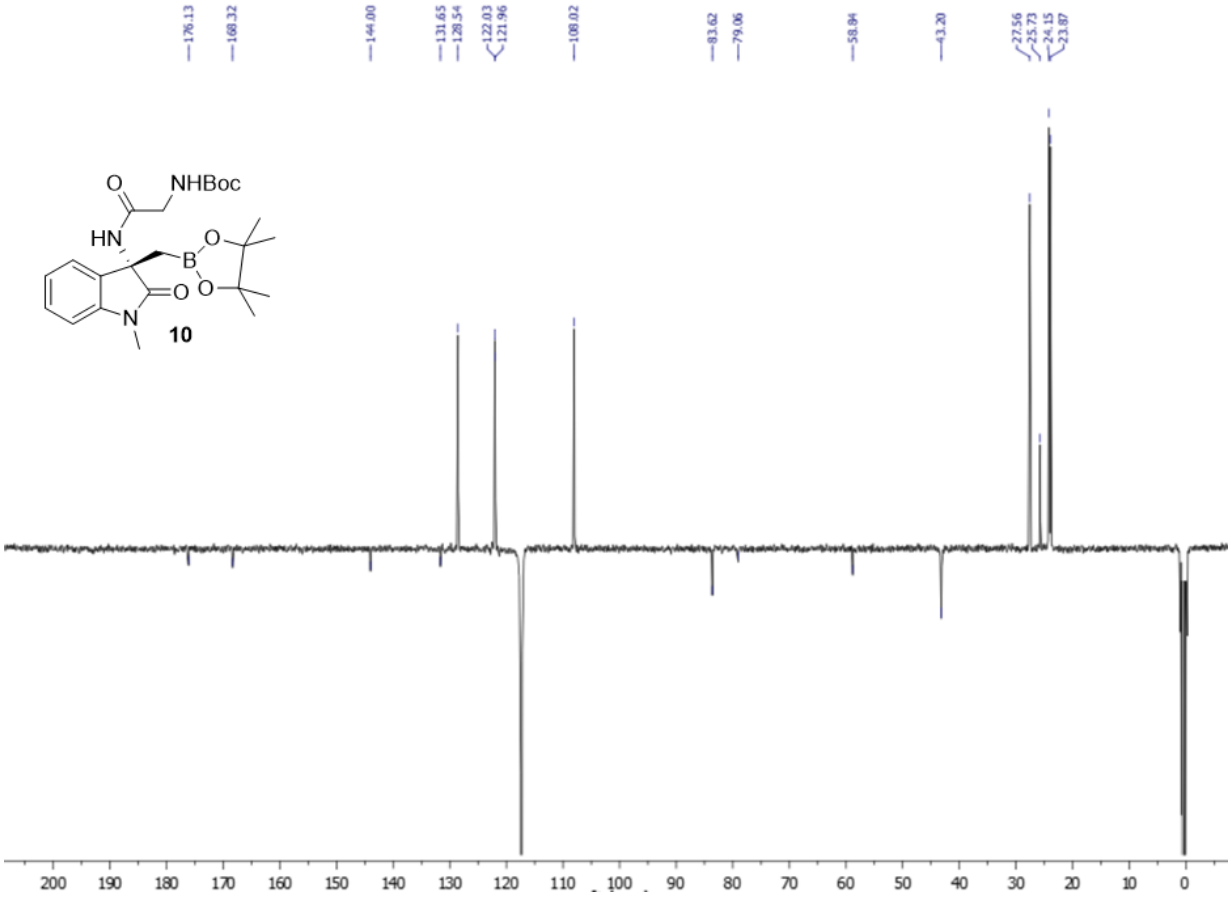
$^{11}$B NMR of compound **9** ($CD_3CN$)



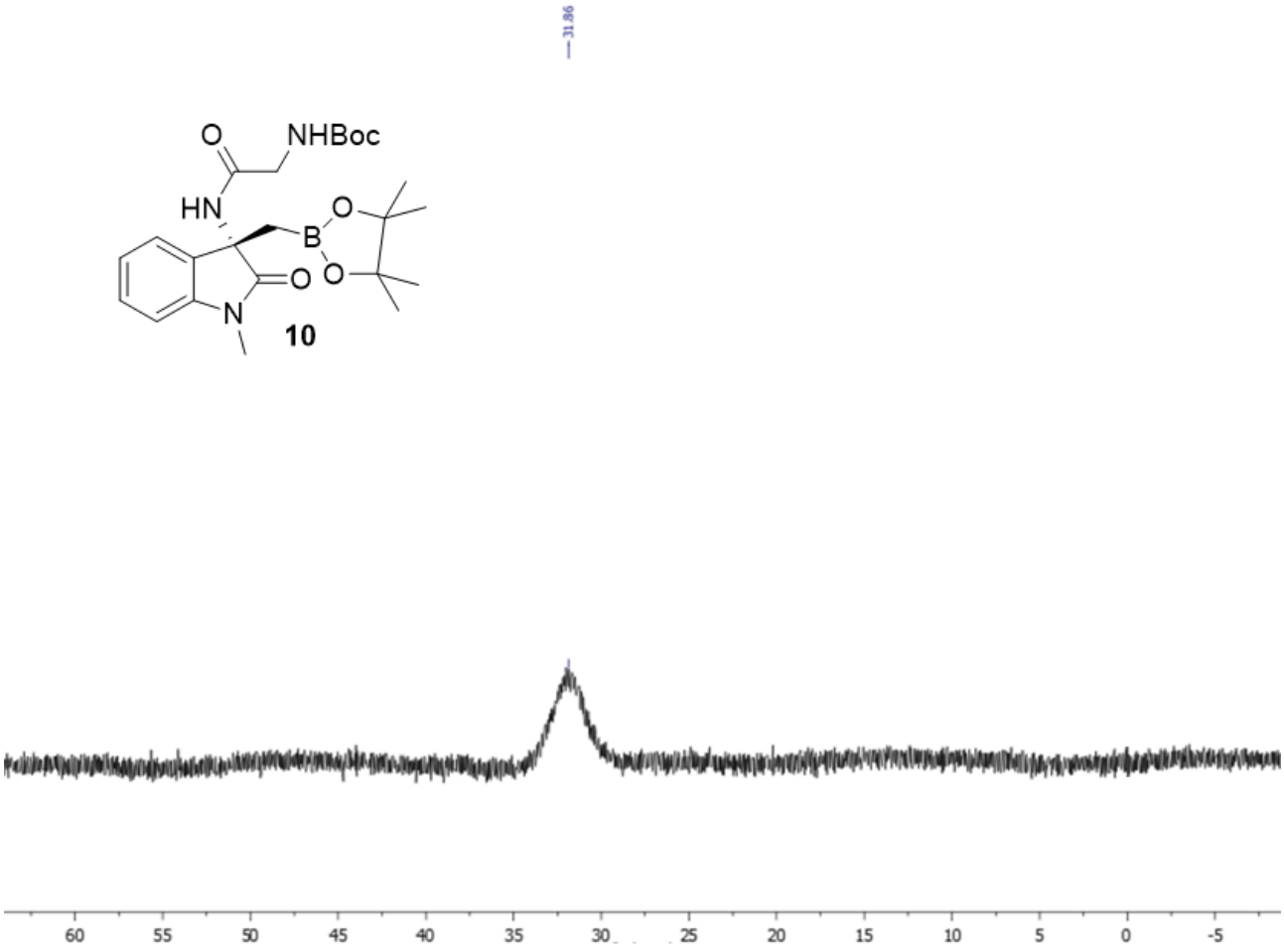
$^{1}$H NMR of compound **10** ($CD_3CN$)



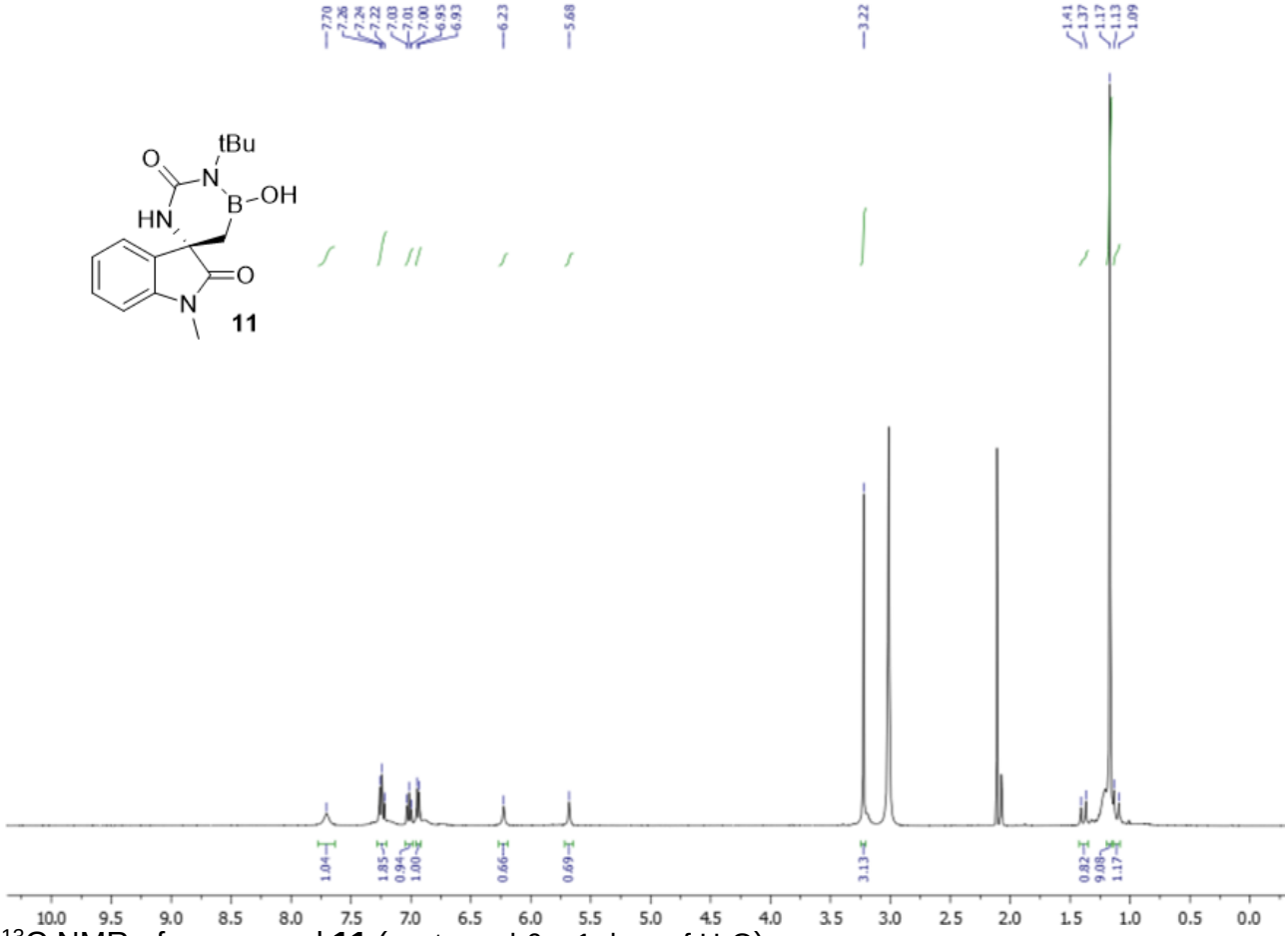

$^{13}$C NMR of compound **10** ($CD_3CN$)



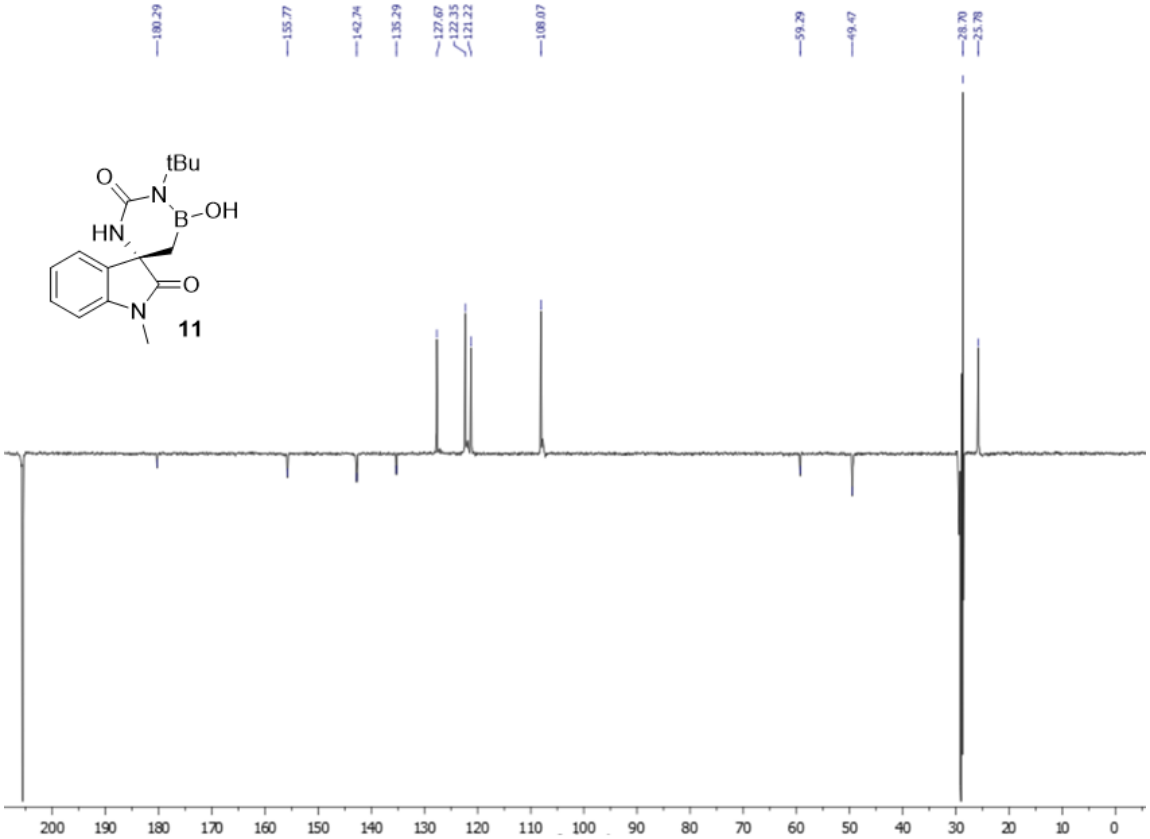
$^{11}$B NMR of compound **10** ($CD_3CN$)



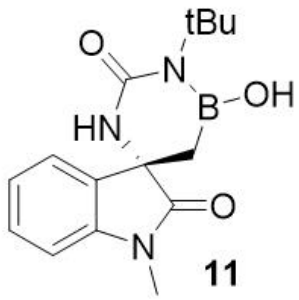
$^{1}$H NMR of compound **11** (acetone d-6 + 1 drop of $H_2O$)




$^{13}$C NMR of compound **11** (acetone d-6 + 1 drop of $H_2O$)

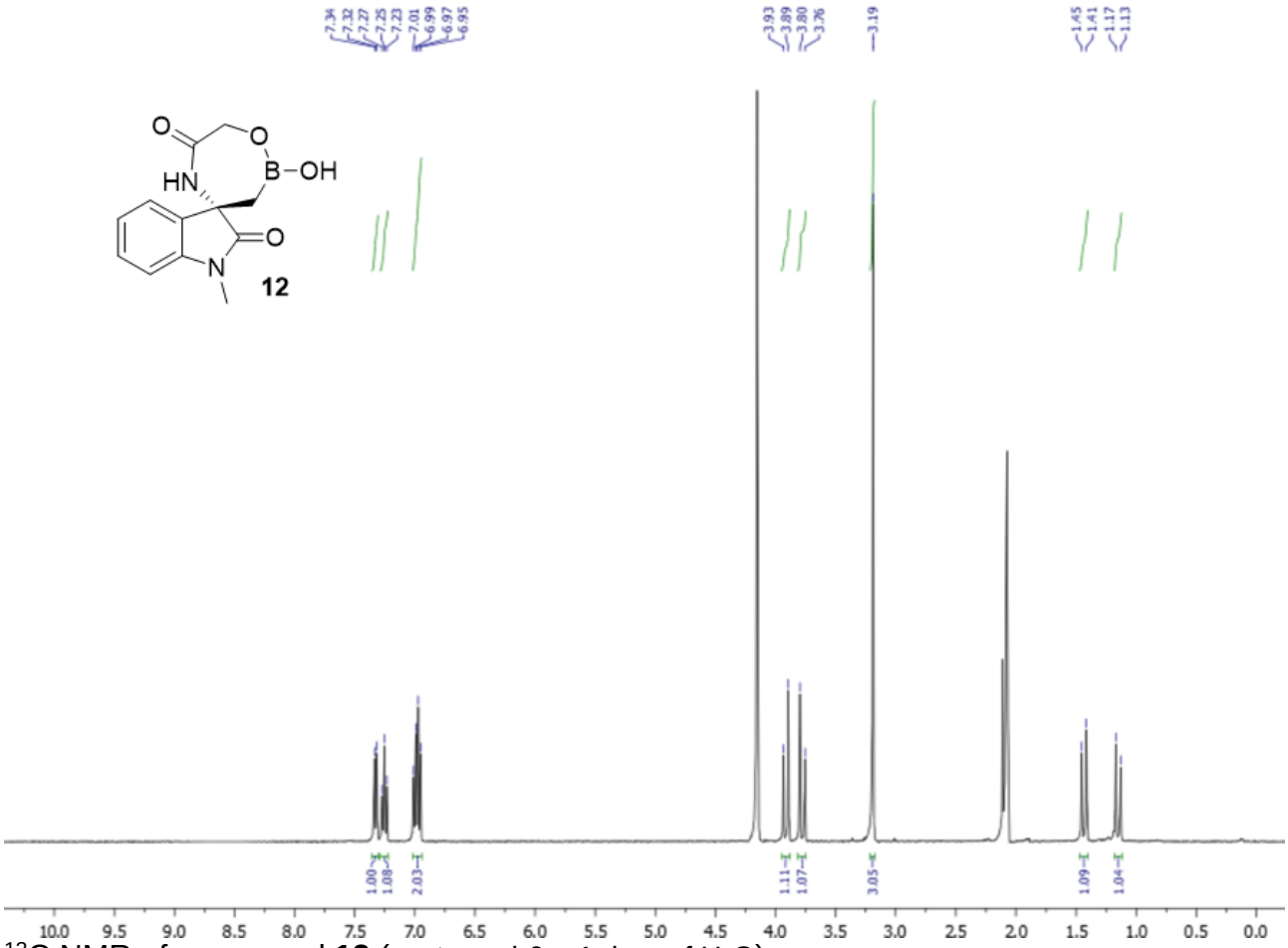


$^{11}$B NMR of compound **11** (acetone d-6 + 1 drop of $H_2O$)

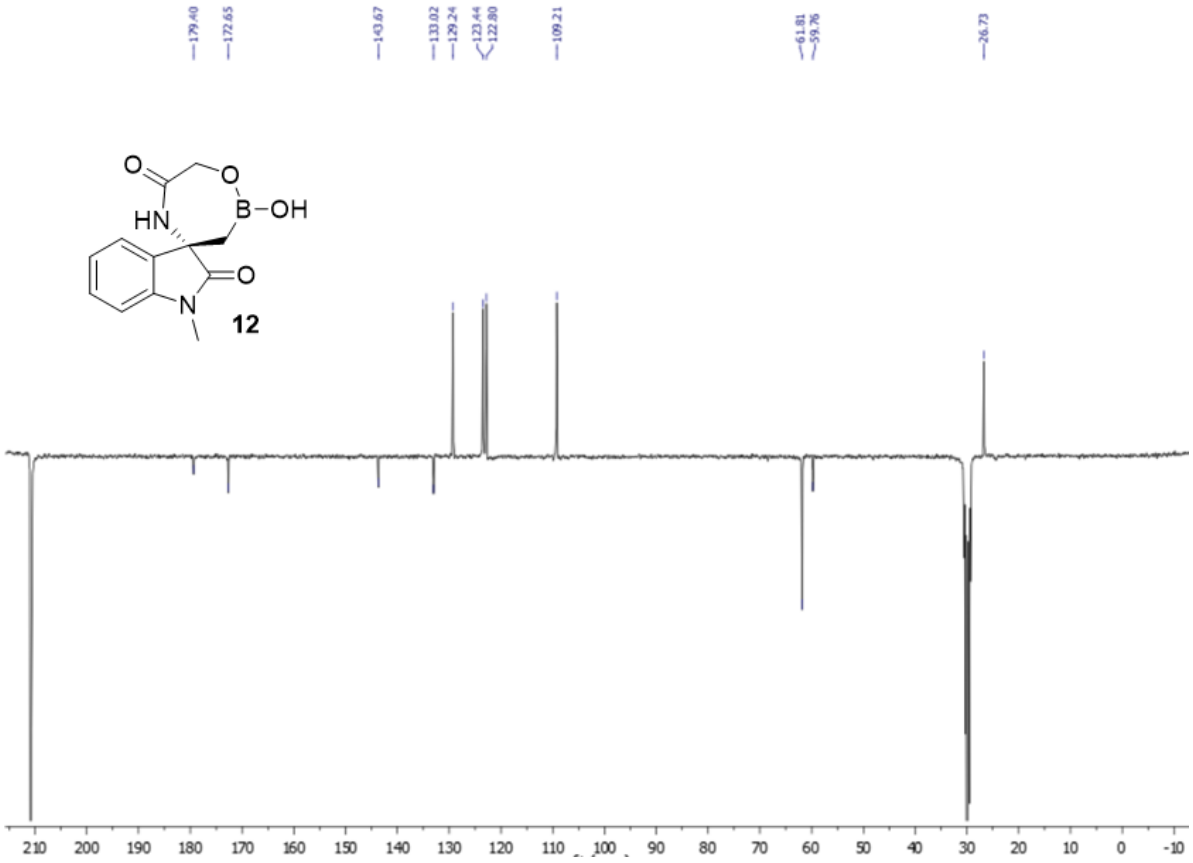



**11**

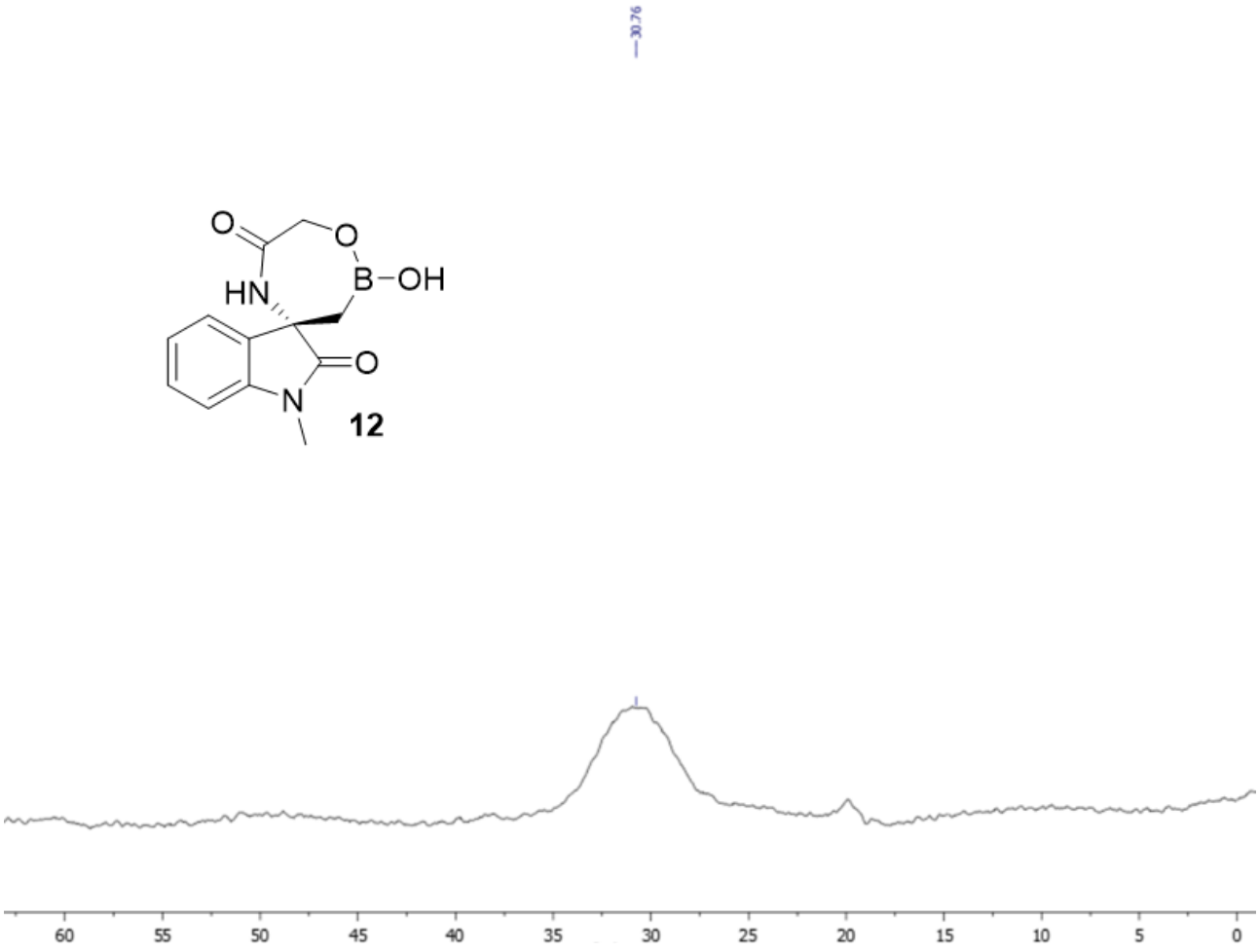
$^{1}$H NMR of compound **12** (acetone d-6 + 1 drop of $H_2O$)



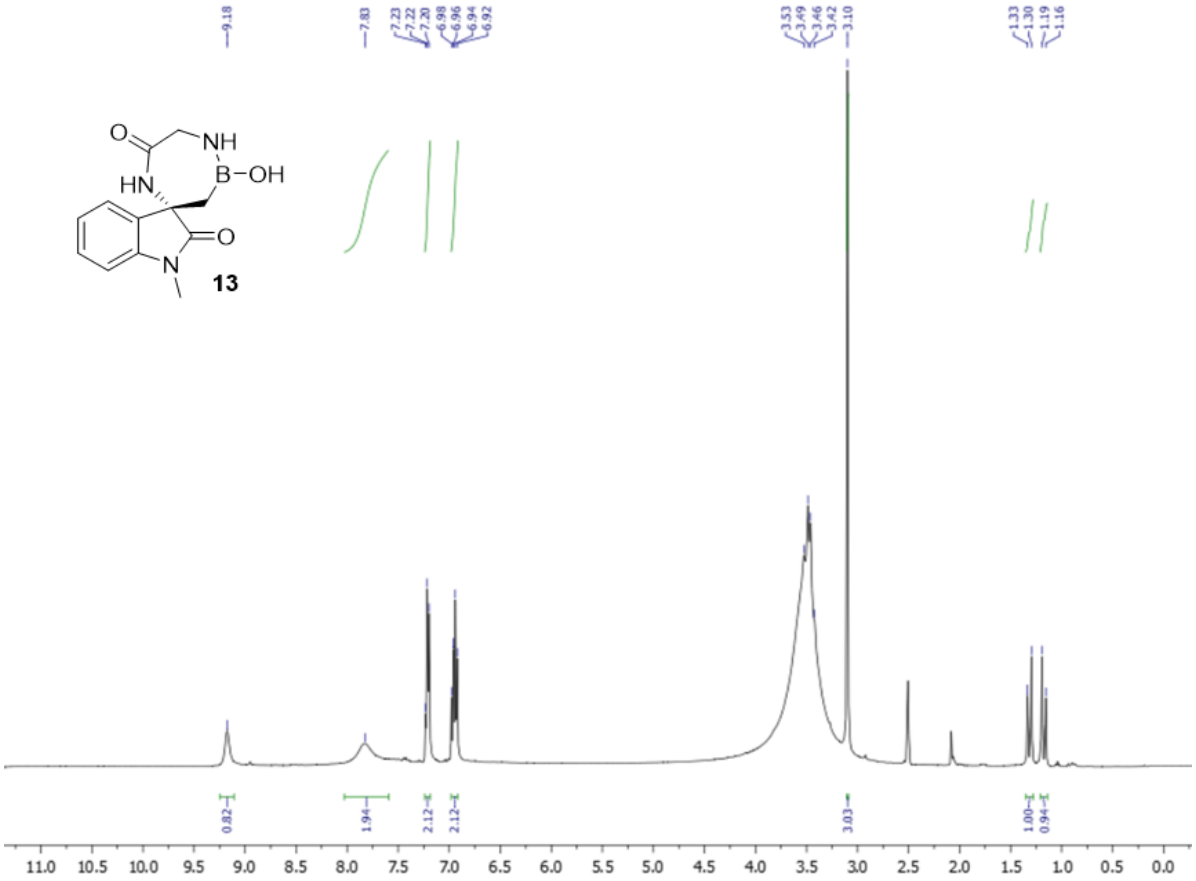

$^{13}$C NMR of compound **12** (acetone d-6 + 1 drop of $H_2O$)



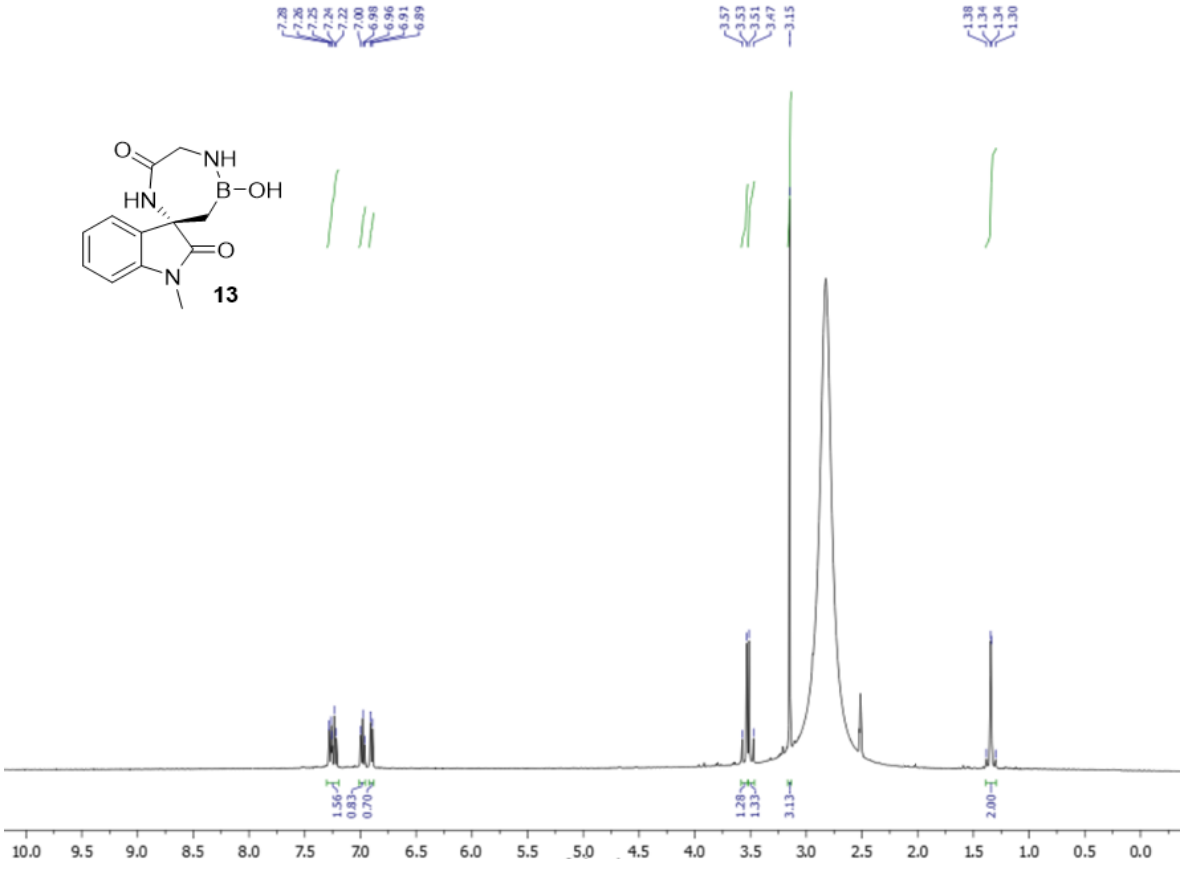
$^{11}$B NMR of compound **12** (acetone d-6 + 1 drop of $H_2O$)



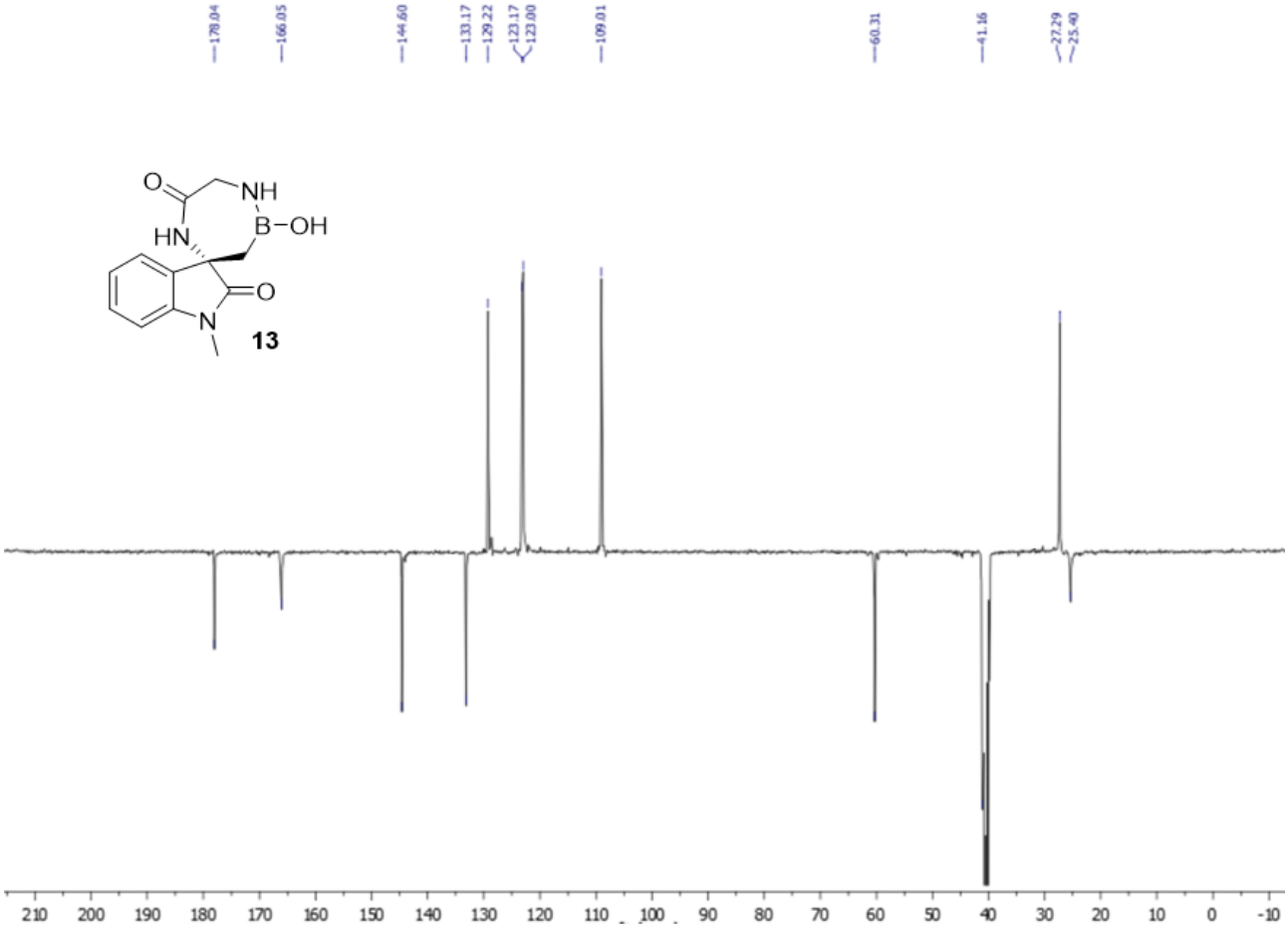
$^1$H NMR of compound **13** (acetone d-6 + 1 drop of $H_2O$)



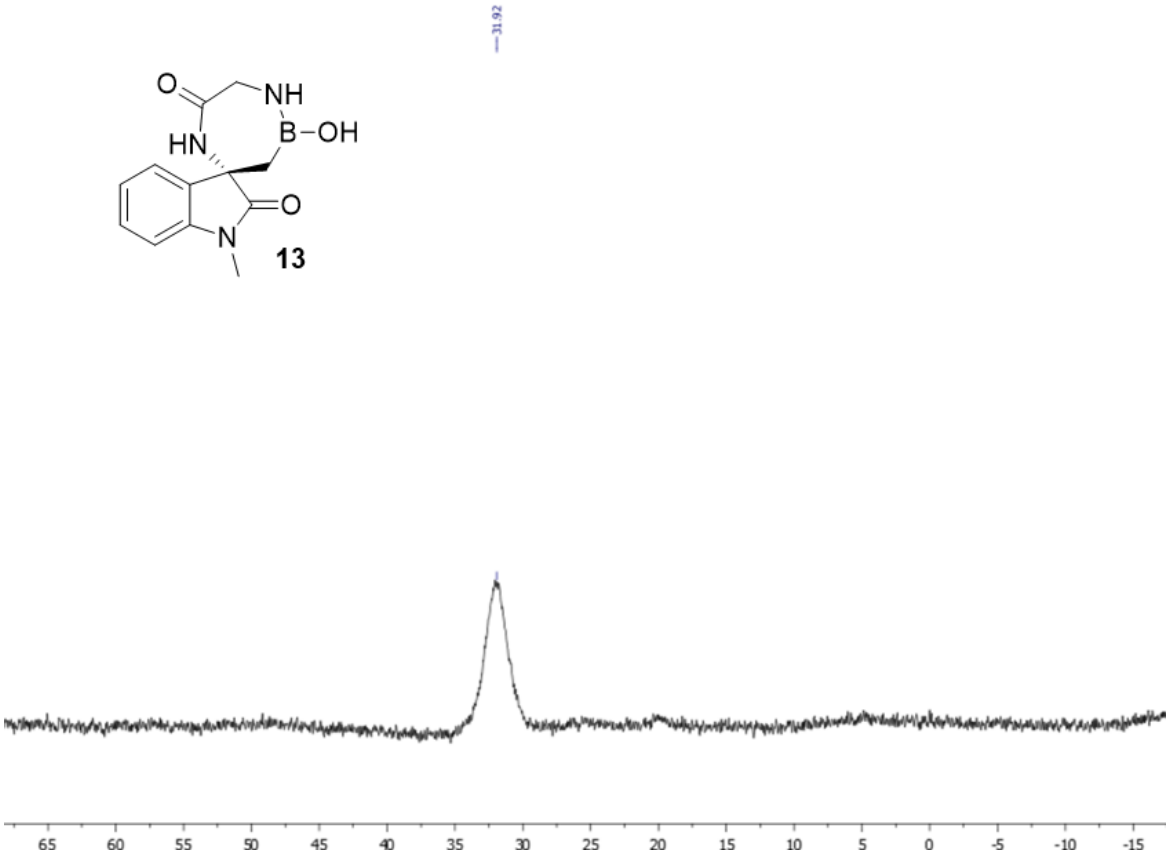

$^1$H NMR of compound **13** (acetone d-6 + 1 drop of $H_2O$, 150°C)



$^{13}$C NMR of compound **13** (acetone d-6 + 1 drop of $H_2O$)



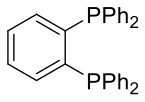

$^{11}$B NMR of compound **13** (Acetone d-6 + 1 drop of $H_2O$)



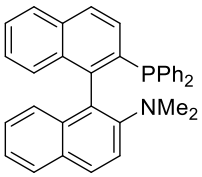
## Notes and References

*Abbreviations were used for ligands, during the survey of the reaction conditions (Table 1). Ligands' chemical structures are:*

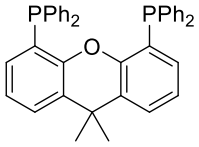
1,2-bis(diphenylphosphino)benzene (DPPBn):



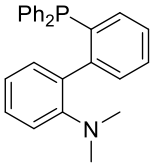

2'-(diphenylphosphino)-N,N-dimethyl[1,1'-binaphtalen]-2-amine (rac-MAP):



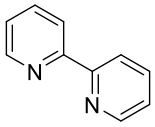

Xantphos:



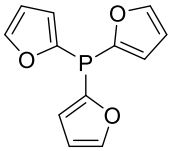

PhDavePhos:



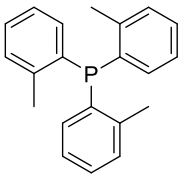

2,2'-bipyridine (bipy):



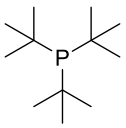

Tri(2-furyl)phosphine (TFP):



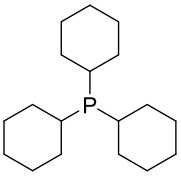

Tris(o-tolyl)phosphine (TTP):



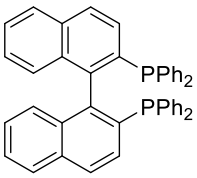

Tri-tert-butylphosphine ($P(tBu)_3$):




Tricyclohexylphosphine ($P(Cy)_3$):




(+/-)-BINAP:




[1] K. Lawrence, S.E. Flower, G. Kociok-Kohn, C.G. Frost and T.D. James, A simple and effective colorimetric technique for the detection of boronic acids and their derivatives, *Anal. Methods,* 2012, **4**, 2215.

[2] S. Elderwish, A. Audebrand, C.G. Nebigil and L. Dèsaubry, Discovery of 3,3'-pyrrolidinyl-spirooxindoles as cardioprotectant prohibitin ligands, *Eur. J. Med. Chem.,* 2020, **186,** 111859.

[3] W. Yan, D. Wang, J. Feng, P. Li, R. Wang, Zinc-mediated diastereoselective synthesis of 3-amino oxindoles by addition of methyl and terminal alkynes to N-tert-butanesulfinyl ketimines, *J. Org. Chem.,* 2012, **77**, 3311.

[4] G. Rainoldi, M. Faltracco, C. Spatti, A. Silvani and G. Lesma, Organocatalytic access to enantioenriched spirooxindole-based 4-methyleneazetidines, *Molecules,* 2017, **22**, 2016.

[5] L.S. Mills, J. Graham, P. Patel and S.A. Rousseaux, Ni-catalyzed reductive cyanation of aryl halides and phenol derivatives via transnitrilation, *J. Am. Chem. Soc.,* 2019, **141**, 19257.