Practical synthesis of 6-amino-1-hydroxy-2,1-benzoxaborolane: a key intermediate of DNDI-6148

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GENERAL METHODS

Reagents and solvents were obtained from commercial suppliers and used as received unless otherwise indicated. Reactions were carried out in oven-dried (120 °C) glassware, that was assembled while hot, and cooled to ambient temperature under an inert atmosphere. All reactions were carried out under inert atmosphere (N_2) unless otherwise noted. Reactions were monitored by TLC (precoated silica gel 60 F254 plates, EMD Chemicals), HPLC or LC/MS using various methods. TLC was visualized with UV light or by treatment with Phosphomolybdic acid (PMA), ninhydrin, and/or $KMnO_4$. Flash chromatography was performed on a Teledyne ISCO Combi-Flash NEXTGEN 300+ and/or a Biotage Isolera using solvents as indicated. HRMS was recorded using Perkin Elmer Axion 2 ToF MS, ionization mode: positive with scan range: 100 - 1000 m/z, flight tube voltage: 8 kV, spray voltage: 3.5 kV, solvent: methanol.^{1}HNMR and ^{13}CNMR spectra were routinely recorded on Bruker Avance III HD Ascend 600 MHz spectrometer. The NMR solvents used were $CDCl_3$, CD_3OD or DMSO-d_6 as indicated. Tetramethylsilane (TMS) was used as an internal standard. Coupling constants *J* are reported in hertz (Hz). The following abbreviations were used to designate signal multiplicity: s, singlet; d, doublet; t, triplet; q, quartet, p, pentet; dd, doublet of doublets; ddd, doublet of doublet of doublets; dt, double of triplets; ddt, doublet of doublet of triplets; m, multiplet; br, broad. 1,3,5-trimethoxybenzene and/or triphenylmethane, were used as internal standards for quantitative ^{1}H-NMR.

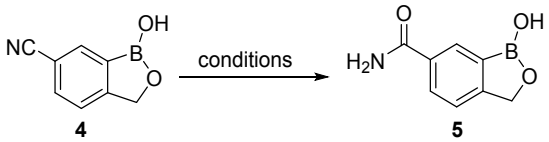
HPLC/LCMS Method

LC with UV detection was used for the analysis of reaction mixtures and isolated product and intermediates. An Agilent 1100 series LC equipped with a diode array detector was used with the parameters shown below.

Column	Phenomenex Kinetex Phenyl Hexyl (150 x 4.6 mm; 5 µm)
Flow Rate	2.0 mL/min
Column Temperature	40 °C
Injection Volume	1 µL
Mobile Phase A	0.1% H_3PO_4 in water*
Mobile Phase B	Methanol

Gradient Table	Time (min)	%A	%B
	0.0	80%	20%
	9.0	25%	75%
	12.0	25%	75%
Post-Run Equilibration	2 min		
Detection Wavelength	210 nm		

Table S1. Synthesis of amide 5 by hydrolysis of nitrile 4.

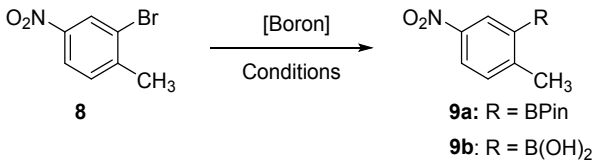


4 **5**

Entry	Conditions	Isolated yield of **5**
1 (**4**: 1 g)	NaOH, iPrOH, 90 ˚C, 16h	~18 A%
2 (**4**: 1 g)	LiOH, iPrOH, 90 ˚C, 16h	NR
3 (**4**: 1 g)	KOH, iPrOH, 90 ˚C, 16h	~60 A% (failed to isolate)
4 (**4**: 1 g)	H_2SO_4, 90 ˚C, 1h	49%
5 (**4**: 10 g)	H_2SO_4, 90 ˚C, 1h	53%
6 (**4**: 1 g)	MsOH, 90 ˚C, 16h	72%
7 (**4**: 10 g)	MsOH, 90 ˚C, 16h	78%
8 (**4**: 1 g)	TFA, 90 ˚C, 16h	31%
9 (**4**: 1 g)	TfOH, 90 ˚C, 16h	5%[a]
10 (**4**: 1 g)	H_2SO_4, 90 ˚C, 16h	0[a]
11 (**4**: 1 g)	HCl, 90 ˚C, 16h	12[b]
11 (**4**: 1 g)	$NaHSO_4$, 90 ˚C, 16h	NR
11 (**4**: 1 g)	$NaHSO_3$, 90 ˚C, 16h	NR

[a]SM was consumed. Decomposition occurred. [b]76 A% carboxylic acid was formed.

Table S2. Condition screening for the borylation of 2-bromo-1-methyl-4-nitrobenzene (8).



8

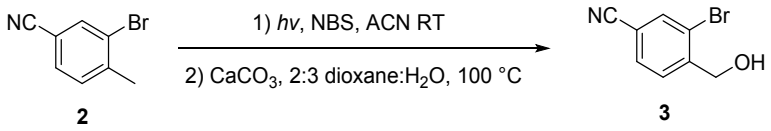
9a: R = BPin

9b: R = $B(OH)_2$

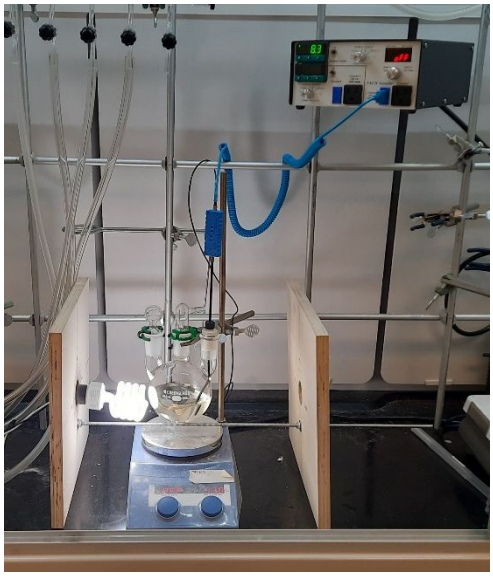
Entry[a]	[Boron]	Conditions	Solvent	Temp /°C	A%[b]
1	$B(OMe)_3$	iPrMgCl-LiCl	THF	-78	ND
2	$B(OiPr)_3$	iPrMgCl-LiCl	THF	-78	ND
3	$B(OiPr)_3$	n-BuLi	THF	-78	ND
4	iPrO-BPin	n-BuLi	THF	-78	ND
5	BH_3-$NH(iPr)_2$	Mg, PhLi	THF	70	ND
6	$B(OiPr)_3$	Mg	THF	-78	NR
7	B_2Pin_2	5 mol% $Pd(PPh_3)Cl_2$, PPh_3, KOAc	1,4-Dioxane	100	20
8	B_2Pin_2	5 mol% $Pd(OAc)_2$, PPh_3, KOAc	1,4-Dioxane	100	ND
9	B_2Pin_2	5 mol% $Pd(OAc)_2$, Xphos,, KOAc	EtOH	80	10
10	B_2Pin_2	5 mol% $Pd(dppf)Cl_2$, KOAc	1,4-Dioxane	100	>90
11	B_2Pin_2	1% Pd(dppf)Cl2, KOAc	1,4-Dioxane	100	~30
12	B_2Pin_2	1% Pd(OAc)2, dppf, KOAc	1,4-Dioxane	100	~56
13	B_2Pin_2	0.1% Pd(dppf)Cl2, KOAc	1,4-Dioxane	100	~7
14	B_2Pin_2	10 mol% Pd(OAc)2	1,4-Dioxane	100	ND
15	B_2Pin_2	10 mol% PdCl2	1,4-Dioxane	100	ND
16	B_2Pin_2	10 mol% Pd/C	1,4-Dioxane	100	ND
17	$B_2(OH)_4$	5 mol% Pd(PPh3)Cl_2, PPh_3, KOAc	EtOH	80	ND
18	$B_2(OH)_4$	5 mol/% Pd(OAc)2, Xphos,, KOAc	EtOH	80	20
19	$B_2(OH)_4$	5 mol% Pd(dppf)Cl2, KOAc	EtOH	80	ND
20	$B_2(OH)_4$	5 mol% Xphos-Pd-G2, KOAc	EtOH	80	ND

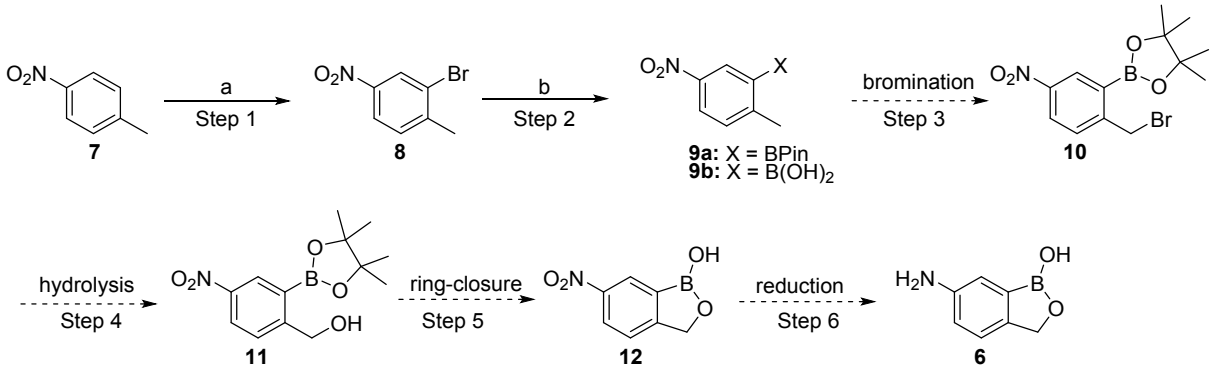
[a]Reaction conditions: For metal-halo exchange borylation: organometal (1.5 eq) and/or Mg (2 eq), 2-bromo-1-methyl-4-nitrobenzene (1.0 eq.), [Boron] (2 eq.), Solvent (10V); For Pd-borylation: Pd-Catalyst (X mol%), 2-bromo-1-methyl-4-nitrobenzene (1.0 eq.), [Boron] (1.1 eq.), potassium acetate (2.0 eq.), Solvent (10V). [b]Yields were calculated using HPLC A% at 210 nm.

Setup for synthesis of 3-bromo-4-(hydroxymethyl)benzonitrile (3) from 3-bromo-4-methylbenzonitrile (2)



2 **3**

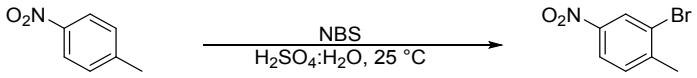




7 **8** **10** **11** **12** **6**

Reagents and conditions: (a) NBS, H_2SO_4, rt, 92%; (b) B_2Pin_2, 5 mol% $Pd(dppf)Cl_2$, KOAc, toluene, 100 °C, 90%.

Synthesis of 2-Bromo-4-nitrotoluene (8)[1]



7 **8**

To a round bottom flask equipped with a magnetic stir bar, a mixture of p-nitrotoluene **7** (10.0 g, 1.0 eq. 72.9 mmol) and aqueous sulfuric acid (80 mL, 1:1 ratio by volume of conc. H_2SO_4 and water) were added. The flask was wrapped with aluminum foil so that darkness might prevent competitive radical reactions. The mixture was stirred for 10 minutes, then N-bromosuccinimide (15.5 g, 1.2 eq. 87.5 mmol)

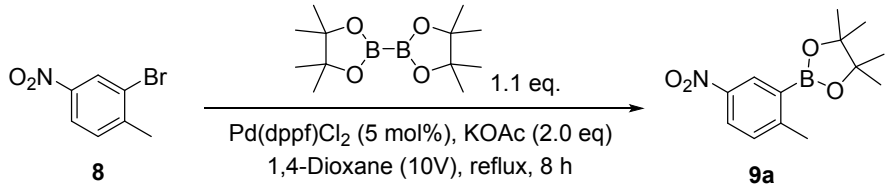
was added slowly (portion wise, over 20 minutes). The mixture was stirred at room temperature for 24 h. After completion (monitored by HPLC), the product was extracted by EtOAc (50 mL x 3). The combined organic phase was washed with brine and dried over anhydrous sodium sulfate. Solvent was removed to afford 2-Bromo-4-nitrotoluene **8** (14.42 g, 92% yield) as a yellow solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ/ppm: 8.37 (s, 1H), 8.05 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 8.2 Hz, 1H), 2.49 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ/ppm: 146.7, 146.0, 131.2, 127.5, 125.1, 122.3, 23.4.

Melting Point 74-76 °C.

Synthesis of 4,4,5,5-tetramethyl-2-(2-methyl-5-nitrophenyl)-1,3,2-dioxaborolane (9a):



A mixture of $Pd(dppf)Cl_2$ (0.34 g, 5 mol%, 462.9 µmol), 2-bromo-1-methyl-4-nitrobenzene **8** (2.0 g, 1.0 eq, 9.2 mmol), bis(pinacolato)diboron (2.58 g, 1.1 eq, 10.2 mmol), and potassium acetate (1.82 g, 2.0 eq, 18.5 mmol) in 1,4-dioxane (20 mL) was degassed with N_2 at rt for 5 min, then the mixture was refluxed under nitrogen for 8 h. After completion (monitored by HPLC), the mixture was extracted with EtOAc (20 mL x 3). The organic layers were combined and washed sequentially with water and brine. The organic [1]phase was separated and dried over anhydrous Na_2SO_4, and evaporated to dryness by rotary evaporation. The residue was stirred in hexanes (20 mL) for 30 min at rt, then the solid was collected by filtration and washed with hexanes (10 mL x 3) to afford a pure compound **9a**, 2.1 g, 86% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ/ppm: 8.59 (d, *J* = 2.6 Hz, 1H), 8.12 (dd, *J* = 8.4, 2.6 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 2.62 (s, 3H), 1.35 (s, 12H).

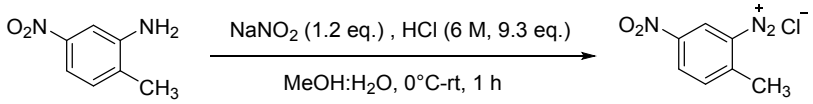
^{13}C NMR (150 MHz, $CDCl_3$) δ/ppm: 152.9, 145.8, 130.8, 125.5, 84.4, 25.0, 22.6.

MS (m/z) (M+H): calc. for $C_{13}H_{19}BNO_4$ 264, found 264.

Melting Point 89-92 °C.

[1]Wagner, P. J.; Wang, L. Electronic Effects of Ring Substituents on Triplet Benzylic Biradicals. *Org. Lett.* **2006**, *8*, 645–647.

General procedure for the synthesis of diazonium salt (14) for DSC/TGA studies



13 **14**

To an ice-cold solution of 2-methyl-5-nitroaniline **13** (1.0 g, 1.0 eq, 6.8 mmol) in methanol (20 mL) was added aq. HCl (10.2 mL, 6. 0 M, 9.3 eq, 61.1 mmol). To this mixture was added a solution of sodium nitrite (0.59 g, 1.3 eq, 8.5 mmol) in water (10 mL) dropwise using addition funnel. The resulting mixture was stirred at 0 °C for 1h (Monitored by TLC, HPLC). After completion, the solid was collected by filtration and washed with methanol to get the pure diazonium salt as a brown solid **14** (1.29g, 98%).

^{1}H NMR (600 MHz, CD_3OD) δ/ppm: 9.64 (d, *J* = 2.3 Hz, 1H), 8.93 (dd, *J* = 8.7, 2.3 Hz, 1H), 8.15 (d, *J* = 8.7 Hz, 1H), 2.98 (s, 3H).

^{13}C NMR (150 MHz, CD_3OD) δ/ppm: 141.9, 138.1, 126.1, 125.9, 119.4, 109.3, 9.6.

HRMS (ESI) *m/z*: $[M]^+$ Calcd for $C_7H_6N_3O_2^+$ 164.0455; Found 164.0456.

Melting Point 94-96 °C.

DSC and TGA studies of Diazonium salt 14:

Instrument: TA SDT 650
Sample holder: TA Alumina 90 uL sample cup
Scan temperature range: 30 ˚C to 250 ˚C
Scan rate: 10 ˚C/min
Purge: Nitrogen, 100 mL/min

For the DSC-TGA analysis, samples were analyzed as received in alumina 90 µL sample cups. Approximately 5 mg of sample was added to the sample cup after tearing. The thermogram ran from 30-250 ˚C at a ramp of 10 ˚C/min.

DSC **TGA**

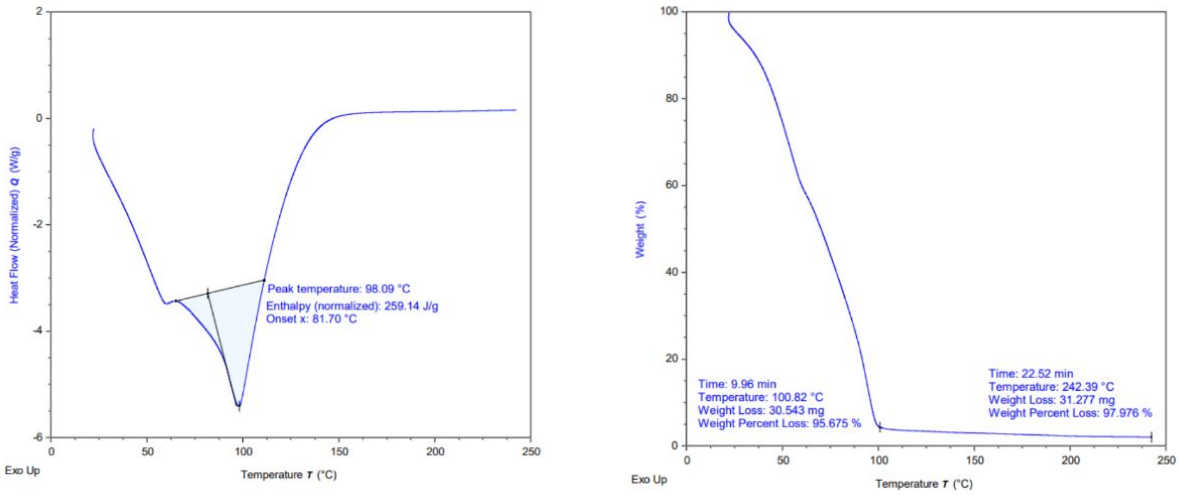


Figure S1. DSC (left) and TGA (right) results of the diazonium salt collected directly from a reaction mixture.

DSC **TGA**

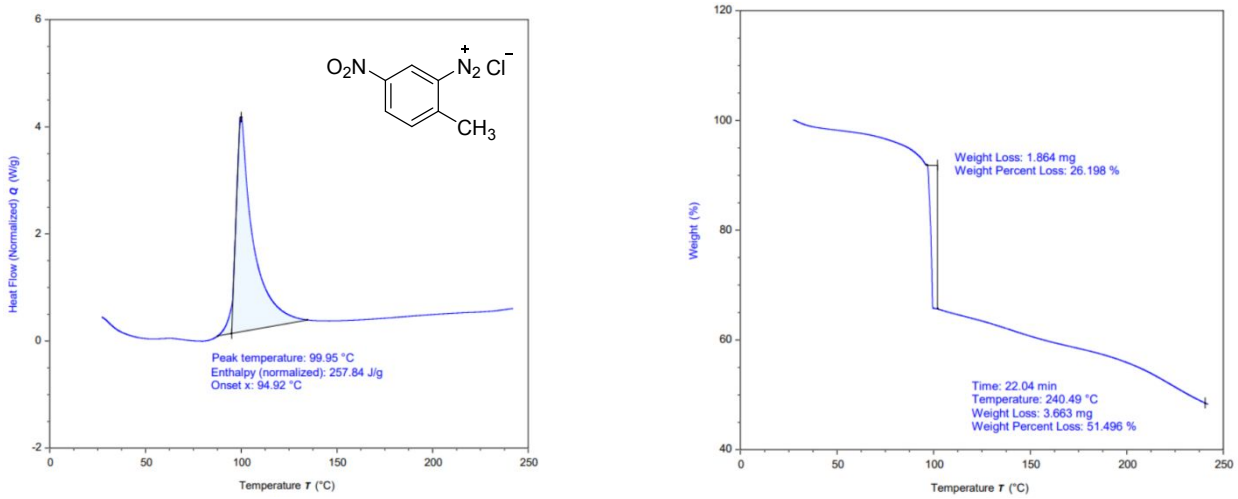
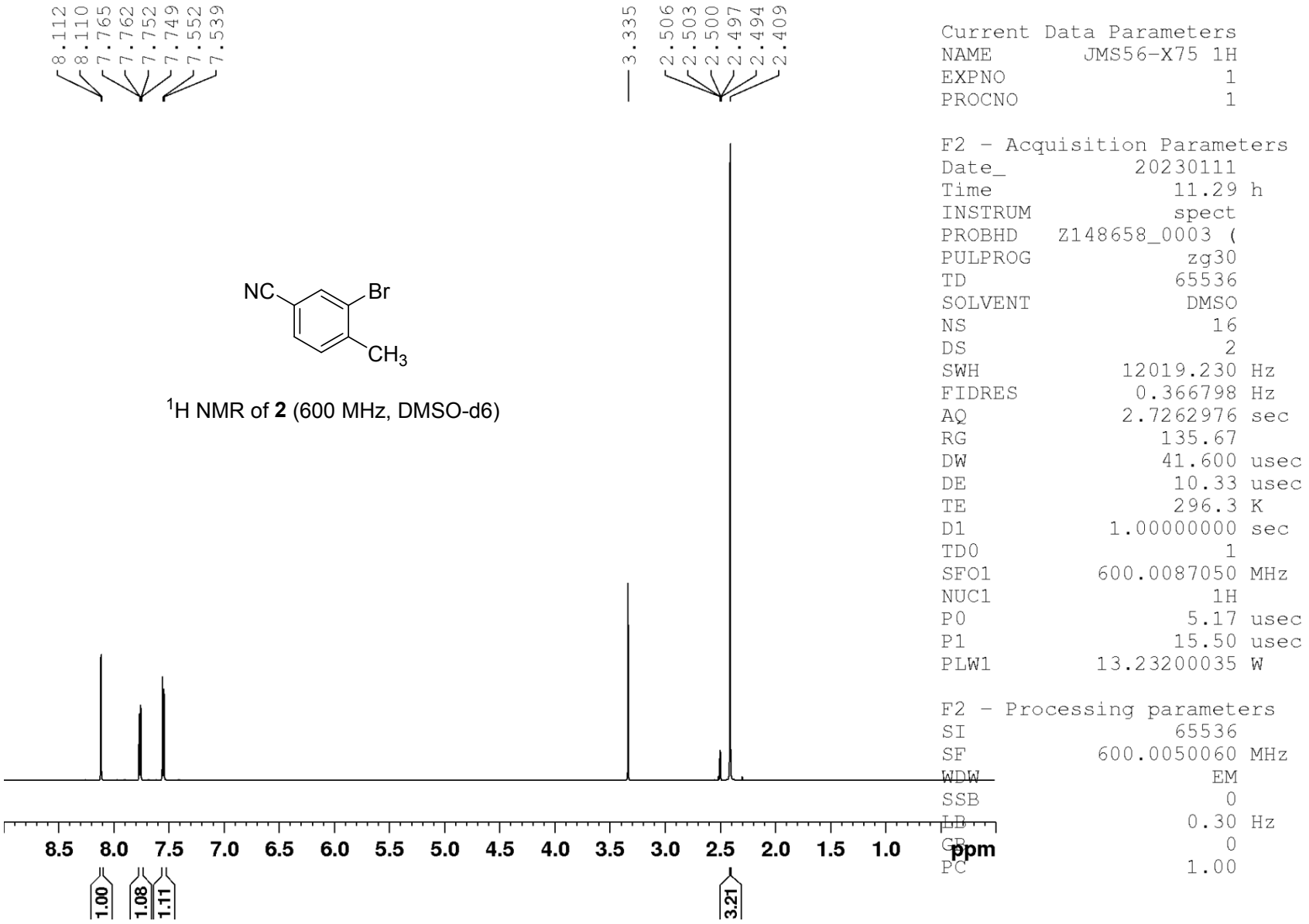


Figure S2. DSC (left) and TGA (right) results of the purified diazonium salt **14**.

^{1}H and ^{13}C NMR Spectra of all compounds



^{1}H NMR of **2** (600 MHz, DMSO-d6)

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PROCNO                1

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PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  16
DS                   2
SWH           12019.230 Hz
FIDRES         0.366798 Hz
AQ            2.7262976 sec
RG               135.67
DW                41.600 usec
DE                10.33 usec
TE                296.3 K
D1           1.00000000 sec
TD0                  1
SFO1        600.0087050 MHz
NUC1                1H
P0                 5.17 usec
P1                15.50 usec
PLW1        13.23200035 W

F2 - Processing parameters
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SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
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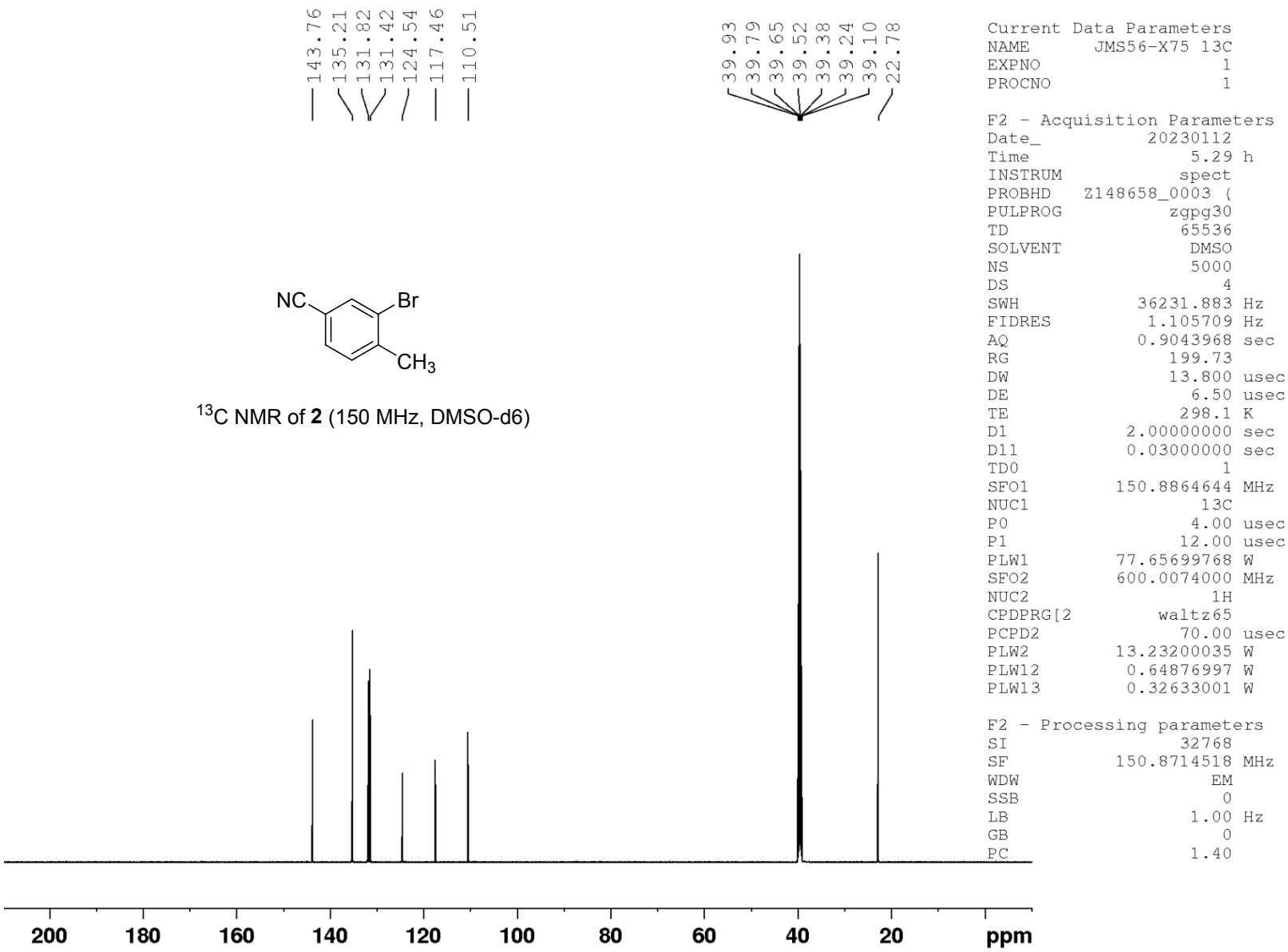

^{13}C NMR of **2** (150 MHz, DMSO-d6)

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PROCNO               1

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TD                65536
SOLVENT            DMSO
NS                 5000
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ            0.9043968 sec
RG               199.73
DW               13.800 usec
DE                6.50 usec
TE                298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1
SFO1        150.8864644 MHz
NUC1               13C
P0                4.00 usec
P1               12.00 usec
PLW1        77.65699768 W
SFO2        600.0074000 MHz
NUC2               1H
CPDPRG[2        waltz65
PCPD2            70.00 usec
PLW2        13.23200035 W
PLW12        0.64876997 W
PLW13        0.32633001 W

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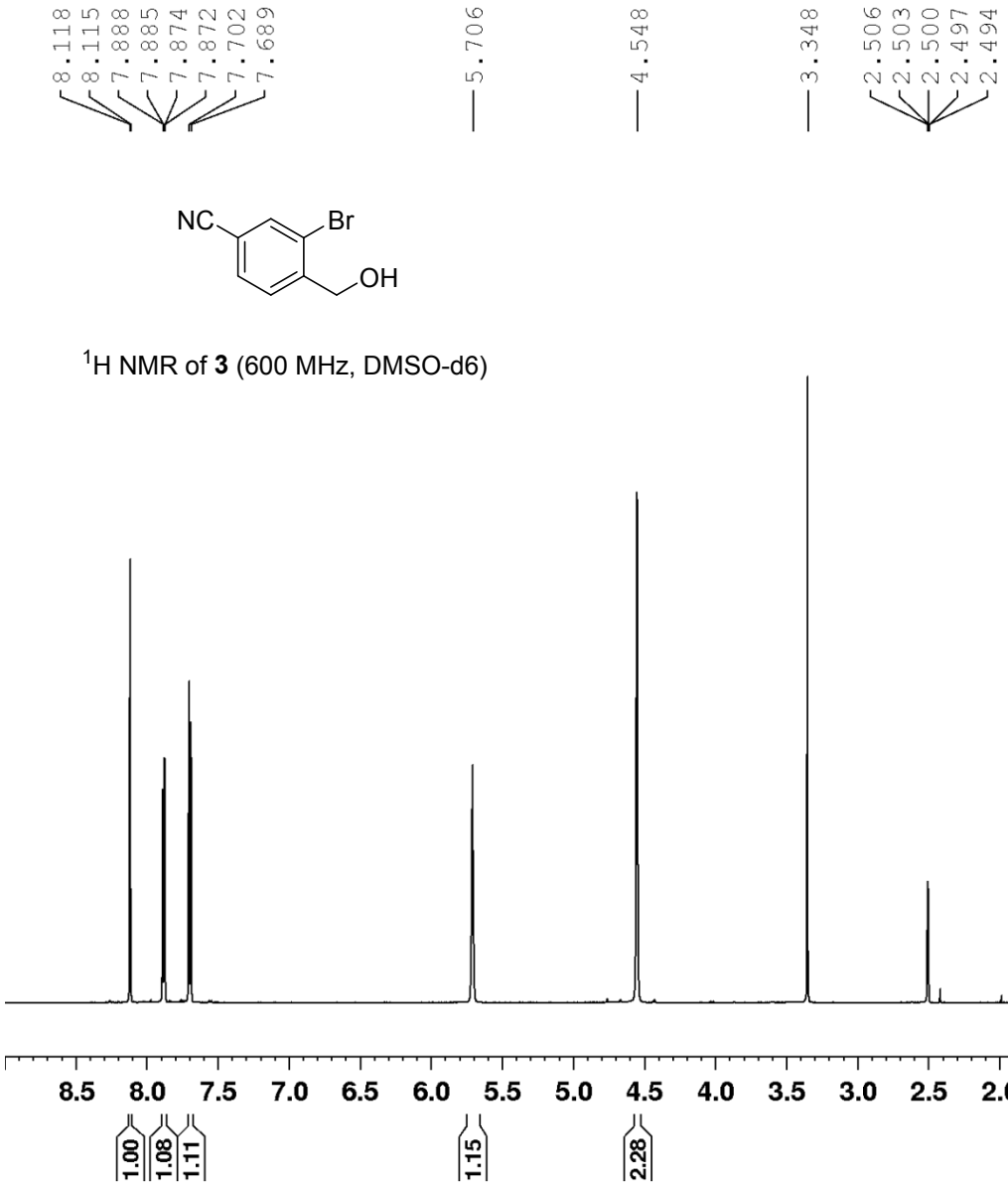

^{1}H NMR of **3** (600 MHz, DMSO-d6)

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PROCNO                1

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PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  16
DS                   2
SWH           12019.230 Hz
FIDRES         0.366798 Hz
AQ            2.7262976 sec
RG               135.67
DW               41.600 usec
DE               10.33 usec
TE               296.4 K
D1           1.00000000 sec
TD0                  1
SFO1        600.0087050 MHz
NUC1                1H
P0                5.17 usec
P1               15.50 usec
PLW1        13.23200035 W

F2 - Processing parameters
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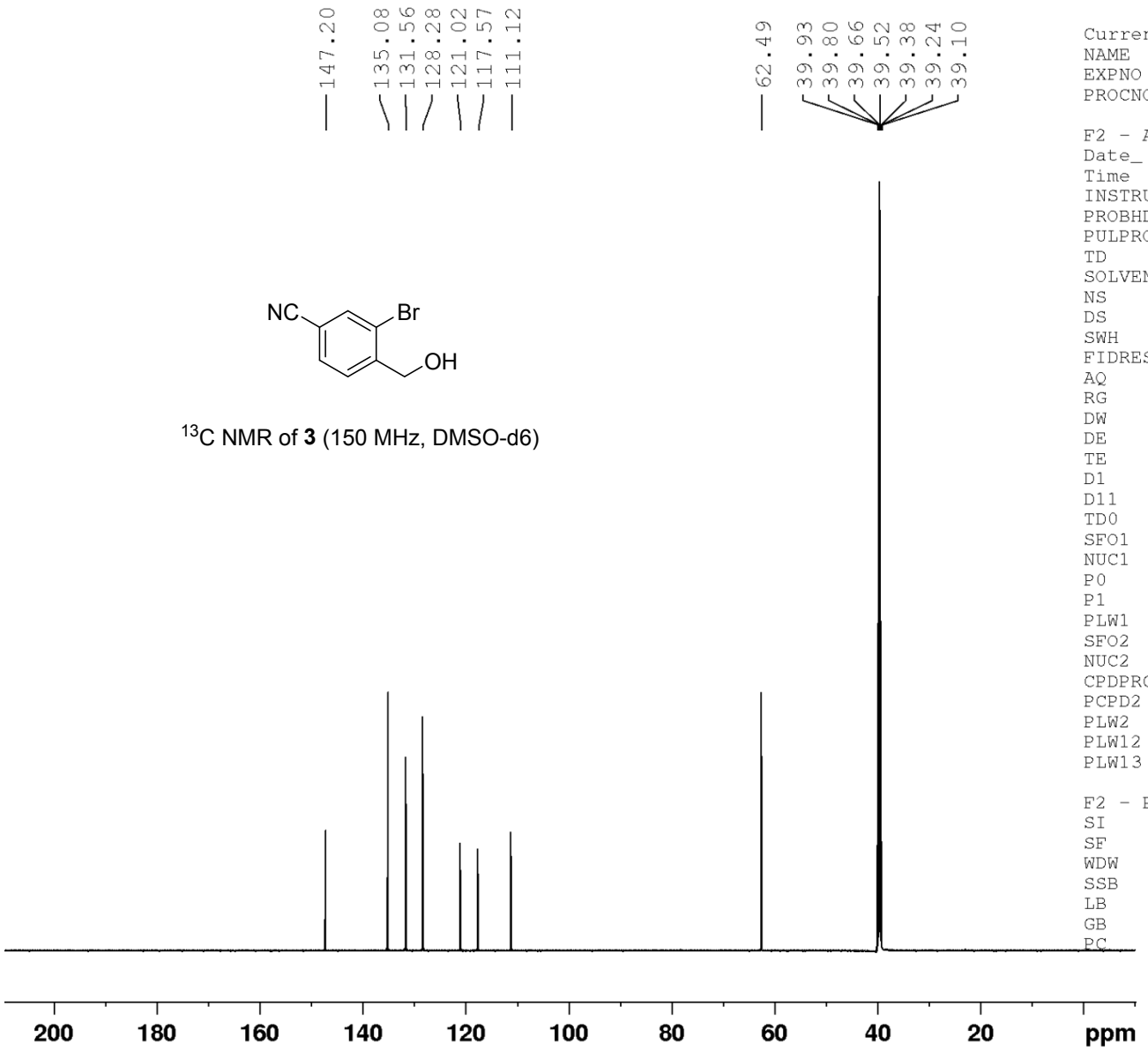

^{13}C NMR of **3** (150 MHz, DMSO-d6)

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PROCNO               1

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PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                5000
DS                   4
SWH          36231.883 Hz
FIDRES        1.105709 Hz
AQ           0.9043968 sec
RG              199.73
DW              13.800 usec
DE               6.50 usec
TE              297.6 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1
SFO1       150.8864644 MHz
NUC1               13C
P0               4.00 usec
P1              12.00 usec
PLW1       77.65699768 W
SFO2       600.0074000 MHz
NUC2               1H
CPDPRG[2        waltz65
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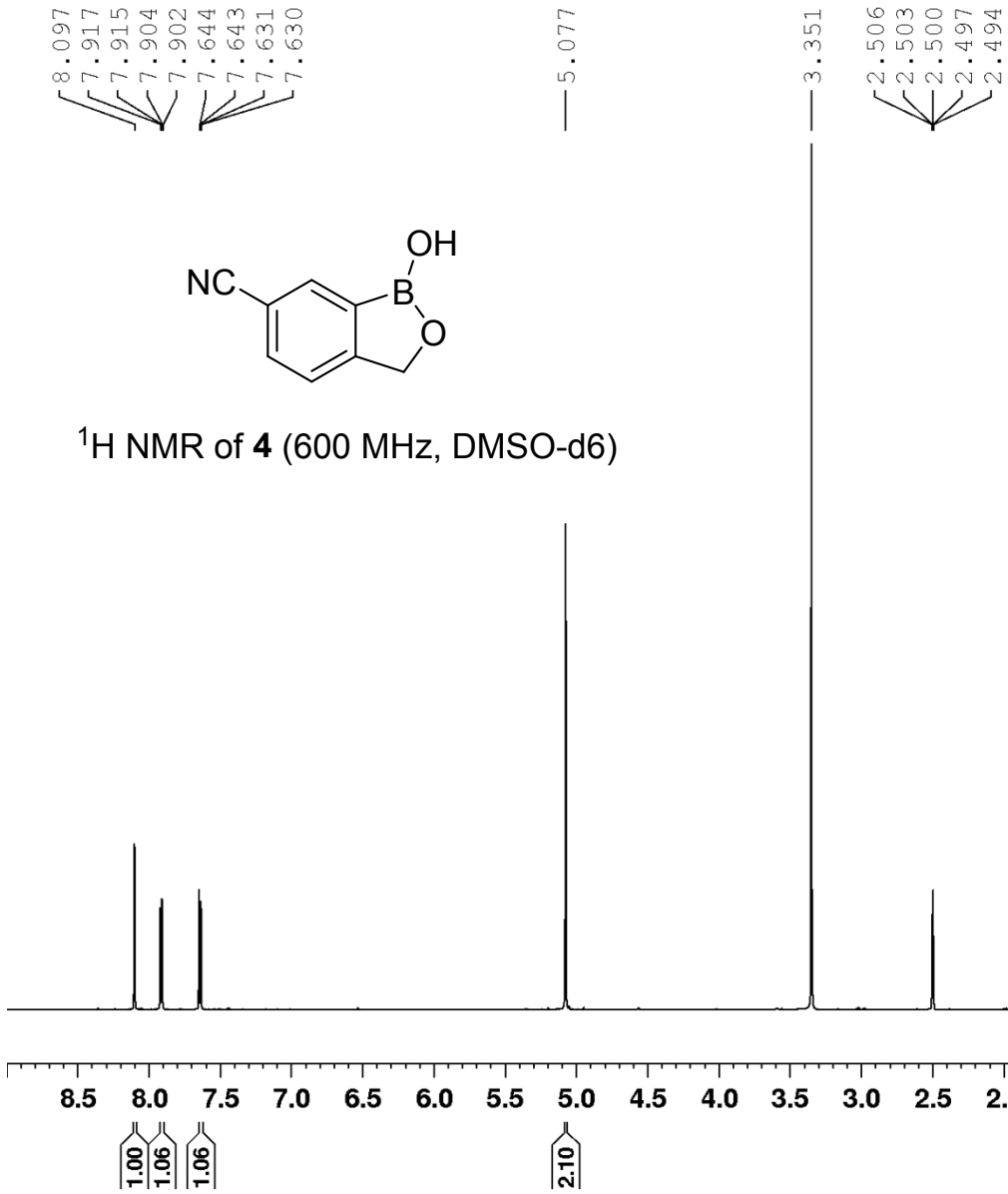

^{1}H NMR of **4** (600 MHz, DMSO-d6)

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PROCNO                1

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TD               65536
SOLVENT           DMSO
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DS                   2
SWH           12019.230 Hz
FIDRES         0.366798 Hz
AQ            2.7262976 sec
RG               199.73
DW               41.600 usec
DE               10.33 usec
TE               296.4 K
D1           1.00000000 sec
TD0                  1
SFO1         600.0087050 MHz
NUC1                1H
P0                5.17 usec
P1               15.50 usec
PLW1         13.23200035 W

F2 - Processing parameters
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LB                0.30 Hz
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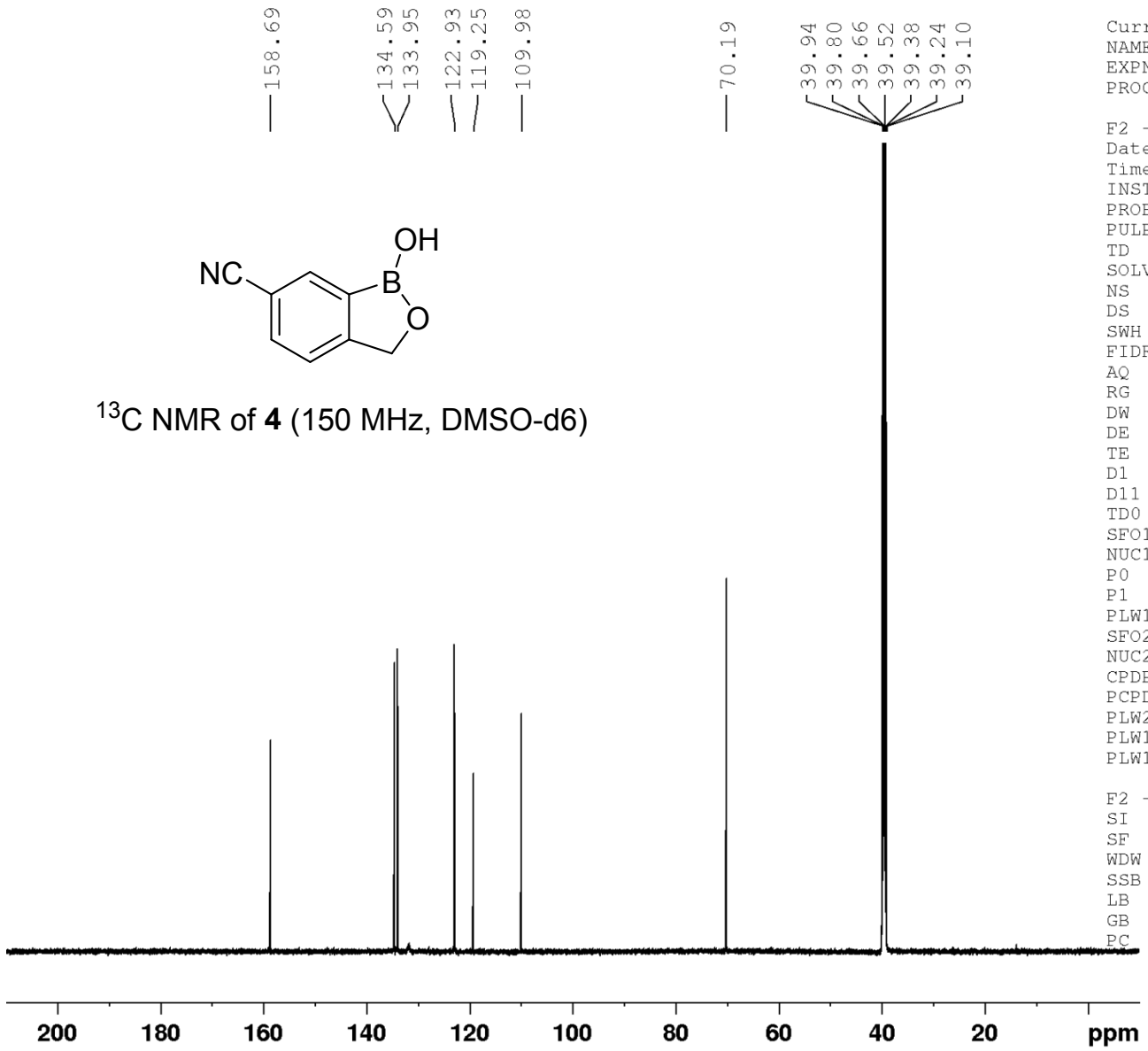

^{13}C NMR of **4** (150 MHz, DMSO-d6)

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PROCNO               1

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NS                5000
DS                   4
SWH          36231.883 Hz
FIDRES        1.105709 Hz
AQ           0.9043968 sec
RG              199.73
DW              13.800 usec
DE               6.50 usec
TE              297.1 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0                  1
SFO1       150.8864644 MHz
NUC1              13C
P0               4.00 usec
P1              12.00 usec
PLW1       77.65699768 W
SFO2       600.0074000 MHz
NUC2              1H
CPDPRG[2       waltz65
PCPD2            70.00 usec
PLW2       13.23200035 W
PLW12       0.64876997 W
PLW13       0.32633001 W

F2 - Processing parameters
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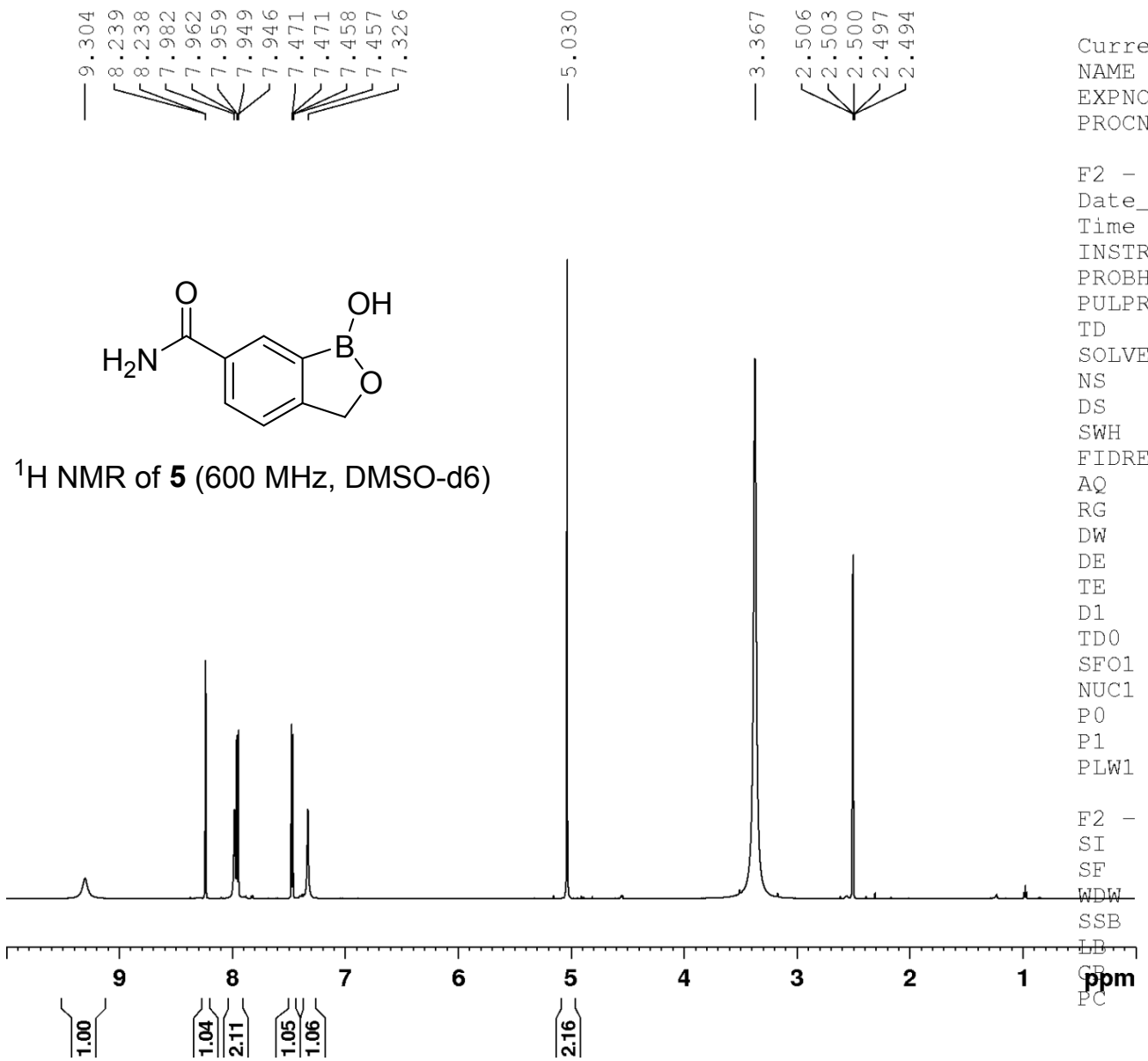
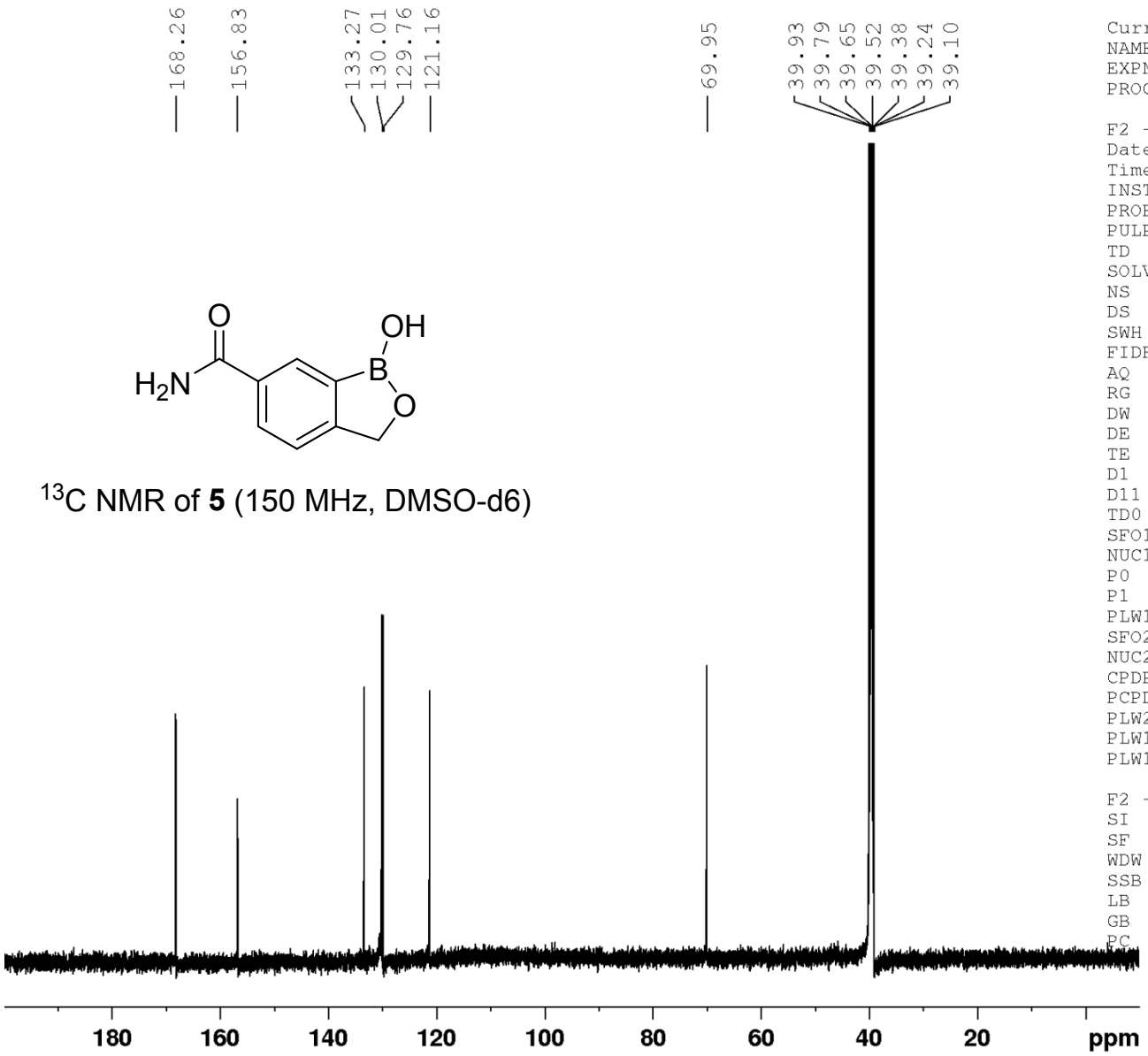


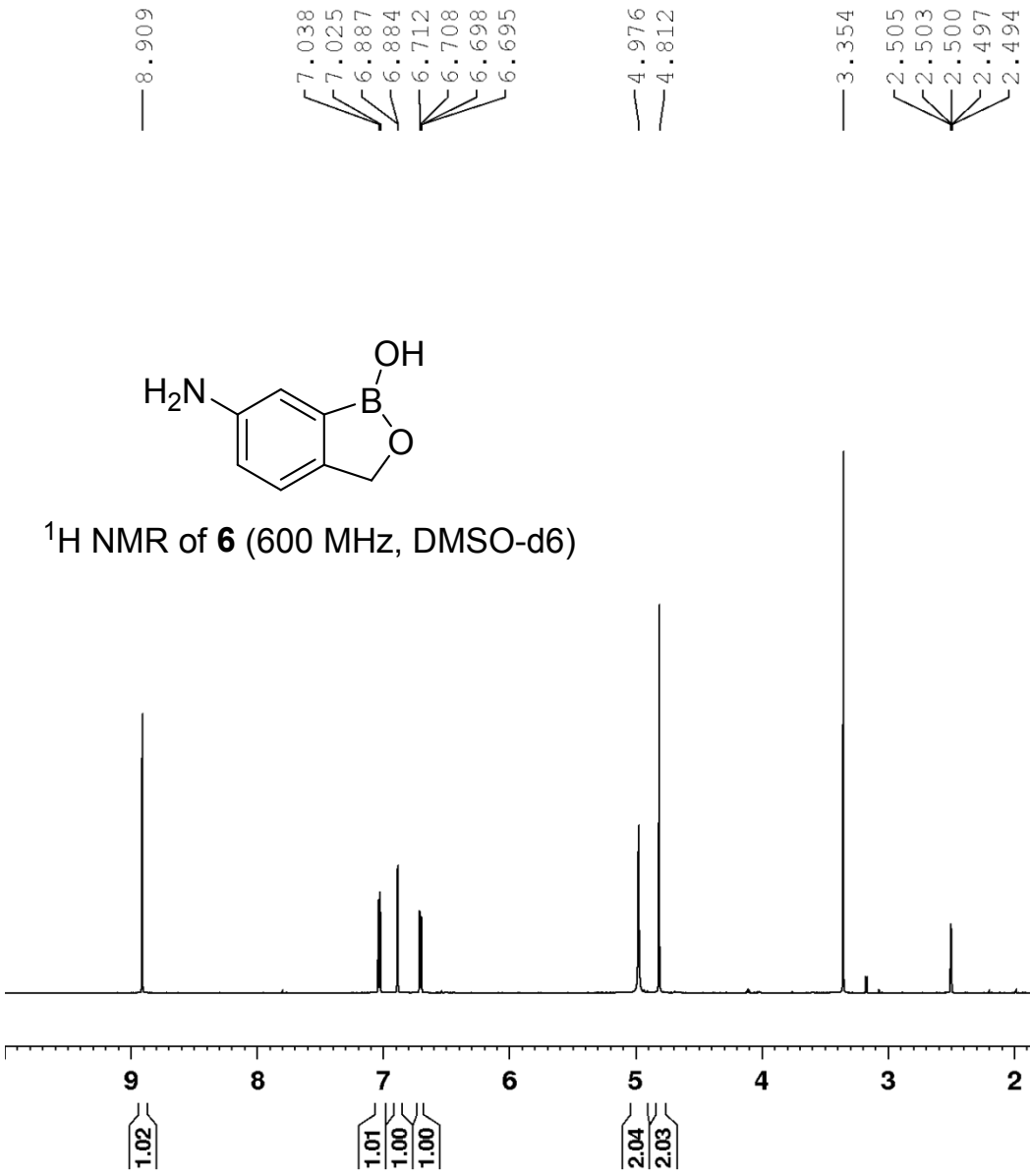
^{1}H NMR of **5** (600 MHz, DMSO-d6)

```
Current Data Parameters
NAME        JMS56-X81 1H
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20230228
Time               12.31 h
INSTRUM             spect
PROBHD   Z855801_0105 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ             2.7262976 sec
RG                110.56
DW                41.600 usec
DE                10.93 usec
TE                295.1 K
D1           1.00000000 sec
TD0                    1
SFO1         599.9587047 MHz
NUC1                  1H
P0                 4.00 usec
P1                12.00 usec
PLW1         15.77700043 W

F2 - Processing parameters
SI                 65536
SF           599.9550063 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



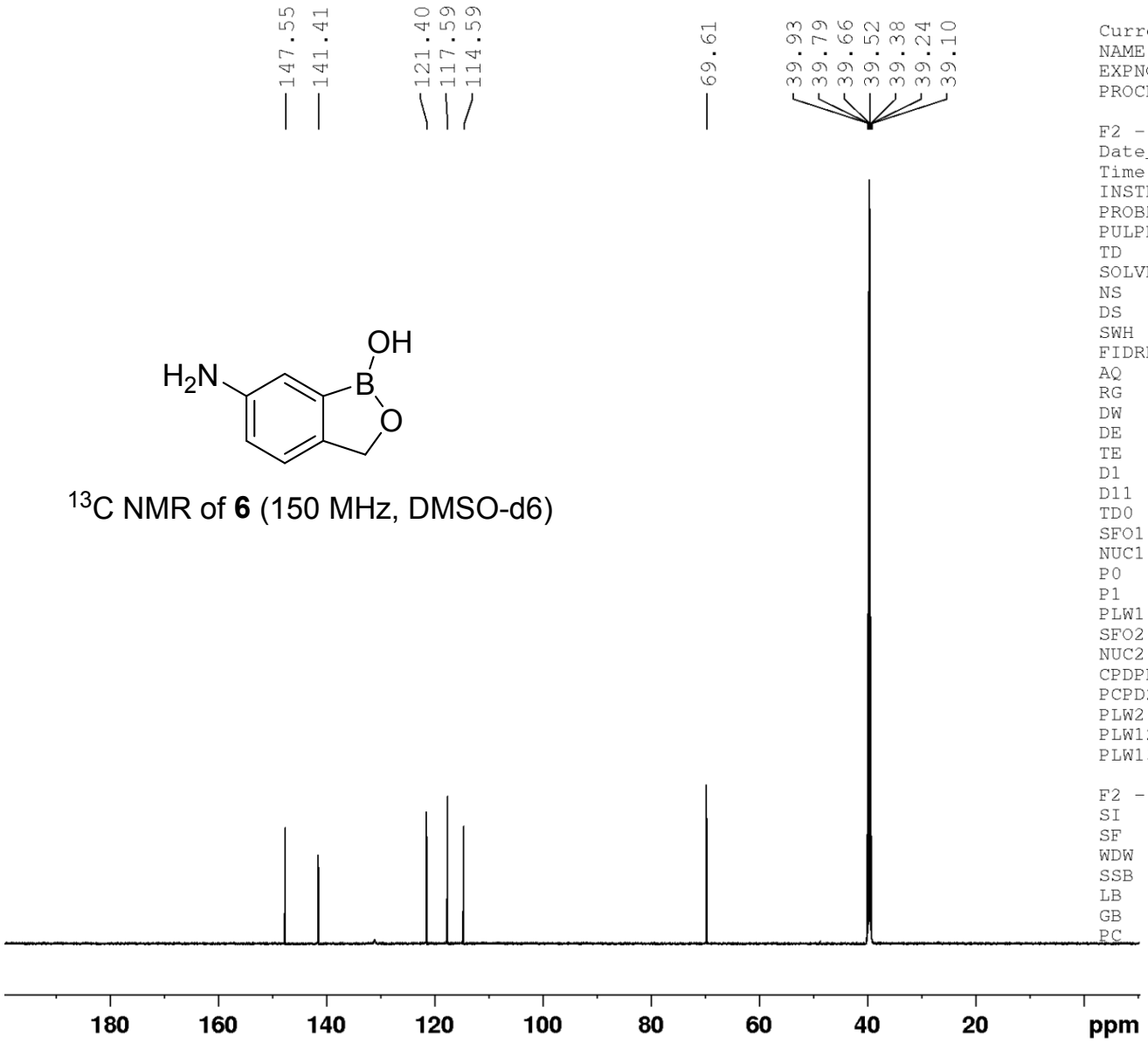
^{13}C NMR of **5** (150 MHz, DMSO-d6)

```
Current Data Parameters
NAME      JMS56-X81 13C
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20230302
Time               2.52 h
INSTRUM           spect
PROBHD   Z855801_0105 (
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                5000
DS                   4
SWH          36231.883 Hz
FIDRES        1.105709 Hz
AQ           0.9043968 sec
RG              194.75
DW              13.800 usec
DE               6.50 usec
TE              296.6 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1
SFO1       150.8738906 MHz
NUC1               13C
P0               3.67 usec
P1              11.00 usec
PLW1      178.30999756 W
SFO2       599.9573998 MHz
NUC2               1H
CPDPRG[2       waltz65
PCPD2            70.00 usec
PLW2       15.77700043 W
PLW12       0.46366000 W
PLW13       0.23322000 W

F2 - Processing parameters
SI               32768
SF         150.8588751 MHz
WDW                EM
SSB                 0
LB               1.00 Hz
GB                  0
PC               1.40
```



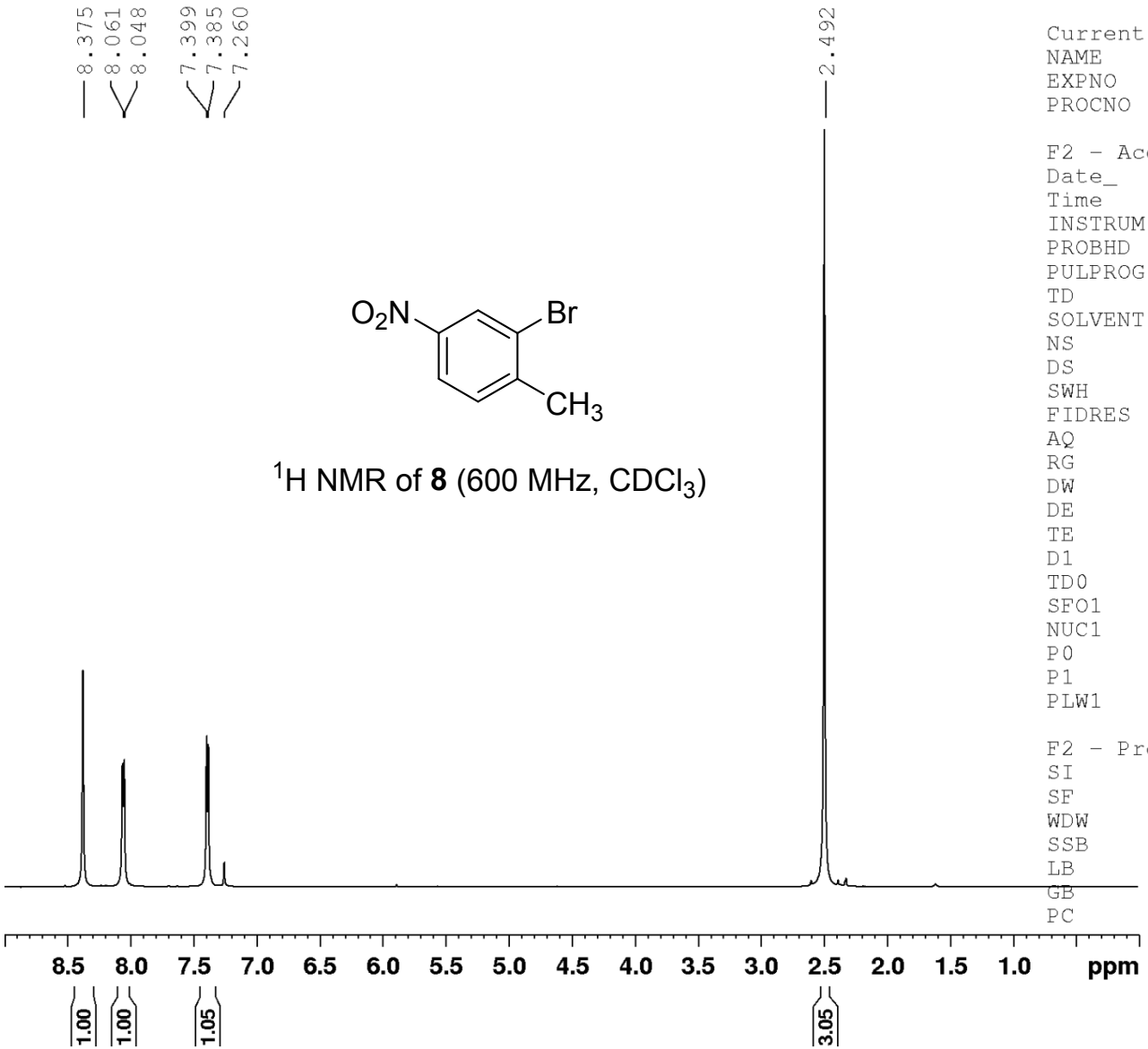
^{1}H NMR of **6** (600 MHz, DMSO-d6)

```
Current Data Parameters
NAME        JMS56-X74 1H
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20230221
Time              13.18 h
INSTRUM           spect
PROBHD   Z148658_0003 (
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  16
DS                   2
SWH          12019.230 Hz
FIDRES        0.366798 Hz
AQ           2.7262976 sec
RG              199.73
DW              41.600 usec
DE              10.33 usec
TE              296.2 K
D1           1.00000000 sec
TD0                  1
SFO1        600.0087050 MHz
NUC1                1H
P0               5.17 usec
P1              15.50 usec
PLW1        13.23200035 W

F2 - Processing parameters
SI                65536
SF          600.0050061 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```



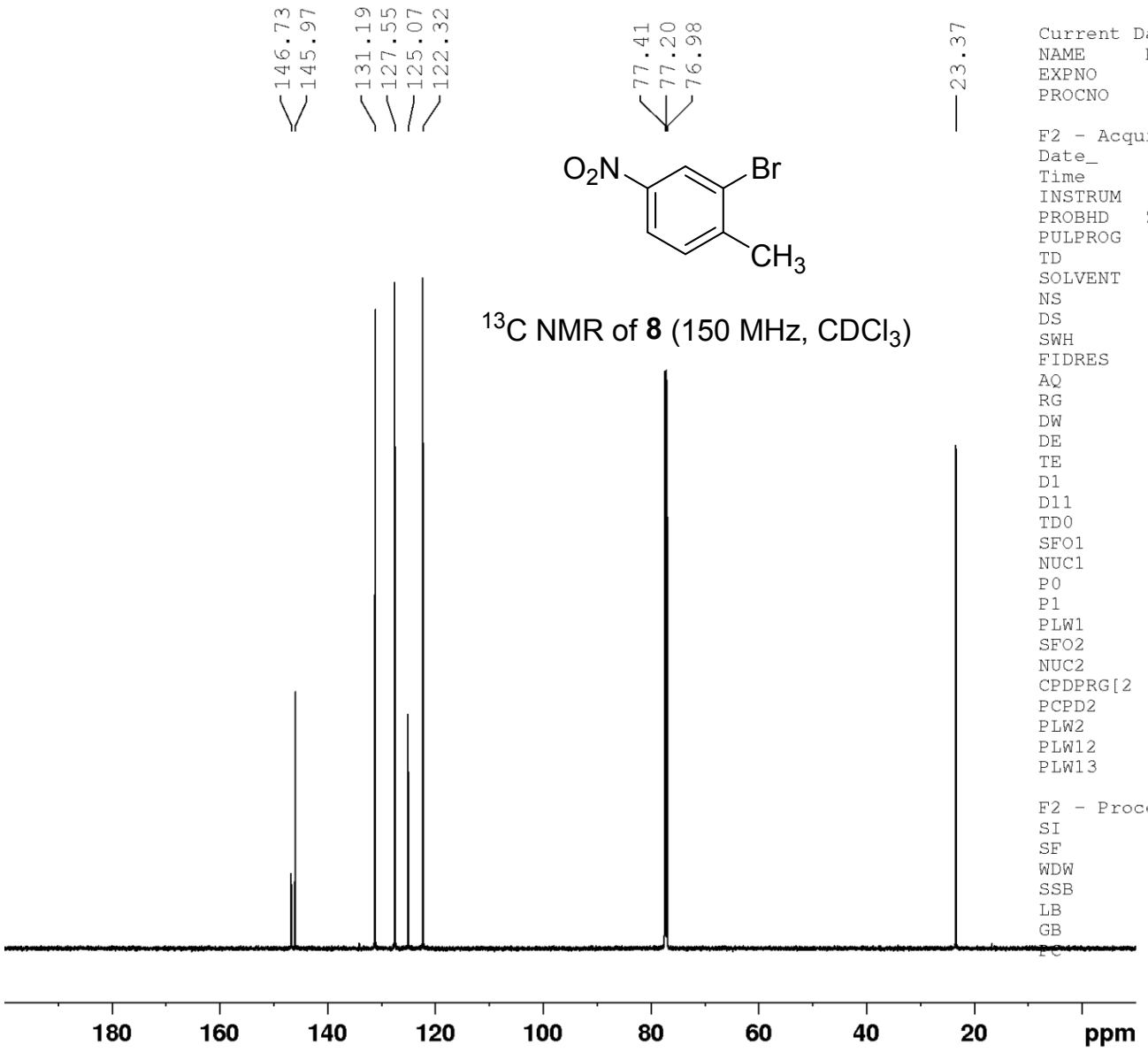
^{13}C NMR of **6** (150 MHz, DMSO-d6)

```
Current Data Parameters
NAME      JMS56-X74 13C
EXPNO                 4
PROCNO                1

F2 - Acquisition Parameters
Date_          20230302
Time               7.05 h
INSTRUM           spect
PROBHD   Z855801_0105 (
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                5000
DS                   4
SWH          36231.883 Hz
FIDRES        1.105709 Hz
AQ           0.9043968 sec
RG              194.75
DW              13.800 usec
DE               6.50 usec
TE              296.9 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0                  1
SFO1       150.8738906 MHz
NUC1               13C
P0               3.67 usec
P1              11.00 usec
PLW1      178.30999756 W
SFO2       599.9573998 MHz
NUC2               1H
CPDPRG[2       waltz65
PCPD2            70.00 usec
PLW2       15.77700043 W
PLW12       0.46366000 W
PLW13       0.23322000 W

F2 - Processing parameters
SI                32768
SF         150.8588756 MHz
WDW                EM
SSB                 0
LB               1.00 Hz
GB                  0
PC               1.40
```

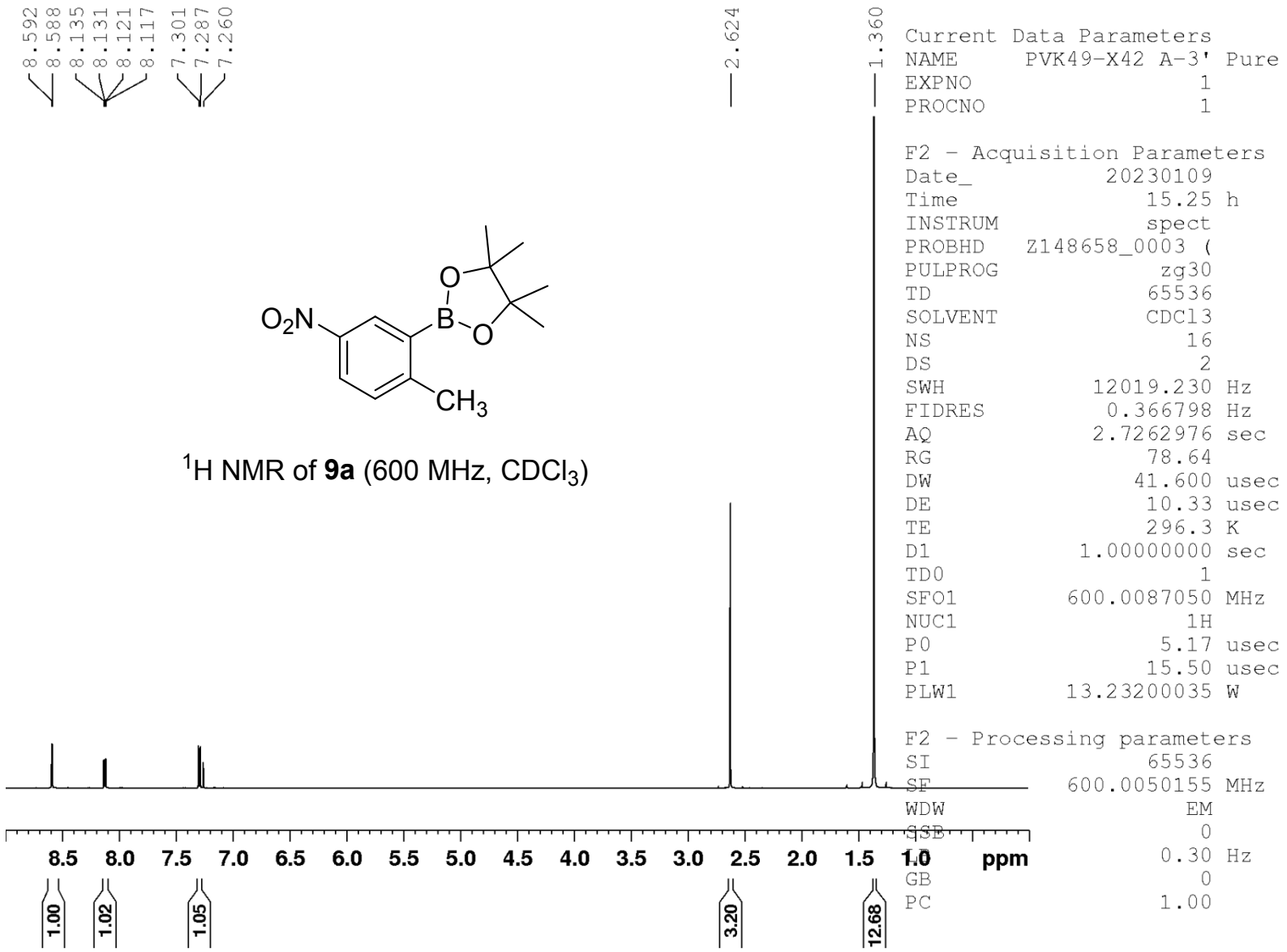


^{1}H NMR of **8** (600 MHz, $CDCl_3$)

```
Current Data Parameters
NAME      PVK49-X8 Product Pure 2nd
EXPNO                1
PROCNO               1

F2 - Acquisition Parameters
Date_          20230106
Time              17.35 h
INSTRUM           spect
PROBHD   Z148658_0003 (
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           12019.230 Hz
FIDRES         0.366798 Hz
AQ            2.7262976 sec
RG                89.69
DW               41.600 usec
DE                10.33 usec
TE                296.8 K
D1           1.00000000 sec
TD0                  1
SFO1        600.0087050 MHz
NUC1                 1H
P0                5.17 usec
P1               15.50 usec
PLW1        13.23200035 W

F2 - Processing parameters
SI                65536
SF          600.0050160 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

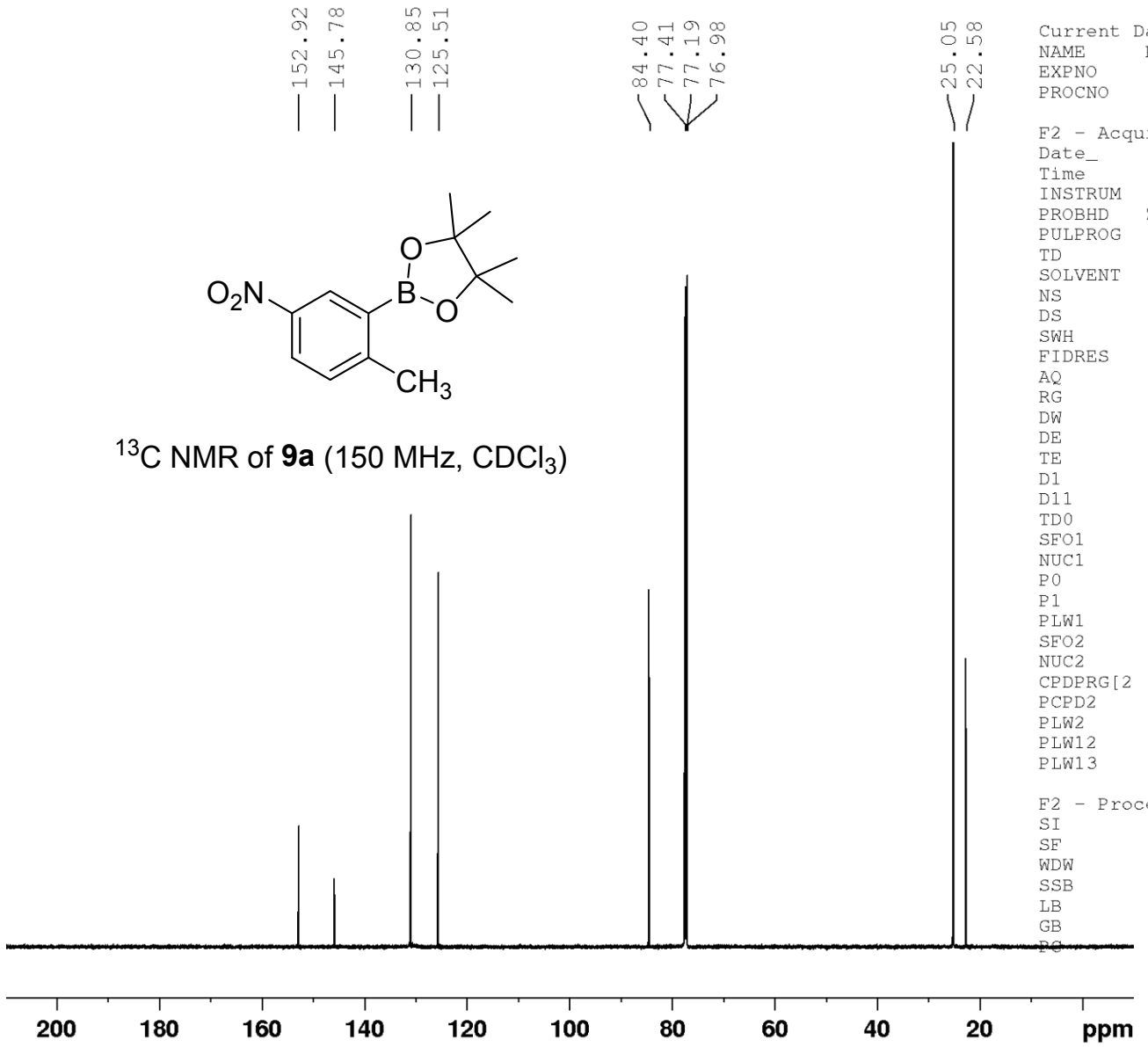



```
Current Data Parameters
NAME      PVK49-X8 Product Pure 2nd
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20230106
Time              18.27 h
INSTRUM           spect
PROBHD   Z148658_0003 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ            0.9043968 sec
RG               199.73
DW               13.800 usec
DE                 6.50 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        150.8864644 MHz
NUC1               13C
P0                4.00 usec
P1               12.00 usec
PLW1        77.65699768 W
SFO2        600.0074000 MHz
NUC2               1H
CPDPRG[2        waltz65
PCPD2            70.00 usec
PLW2        13.23200035 W
PLW12        0.64876997 W
PLW13        0.32633001 W

F2 - Processing parameters
SI                32768
SF          150.8713585 MHz
WDW                EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```



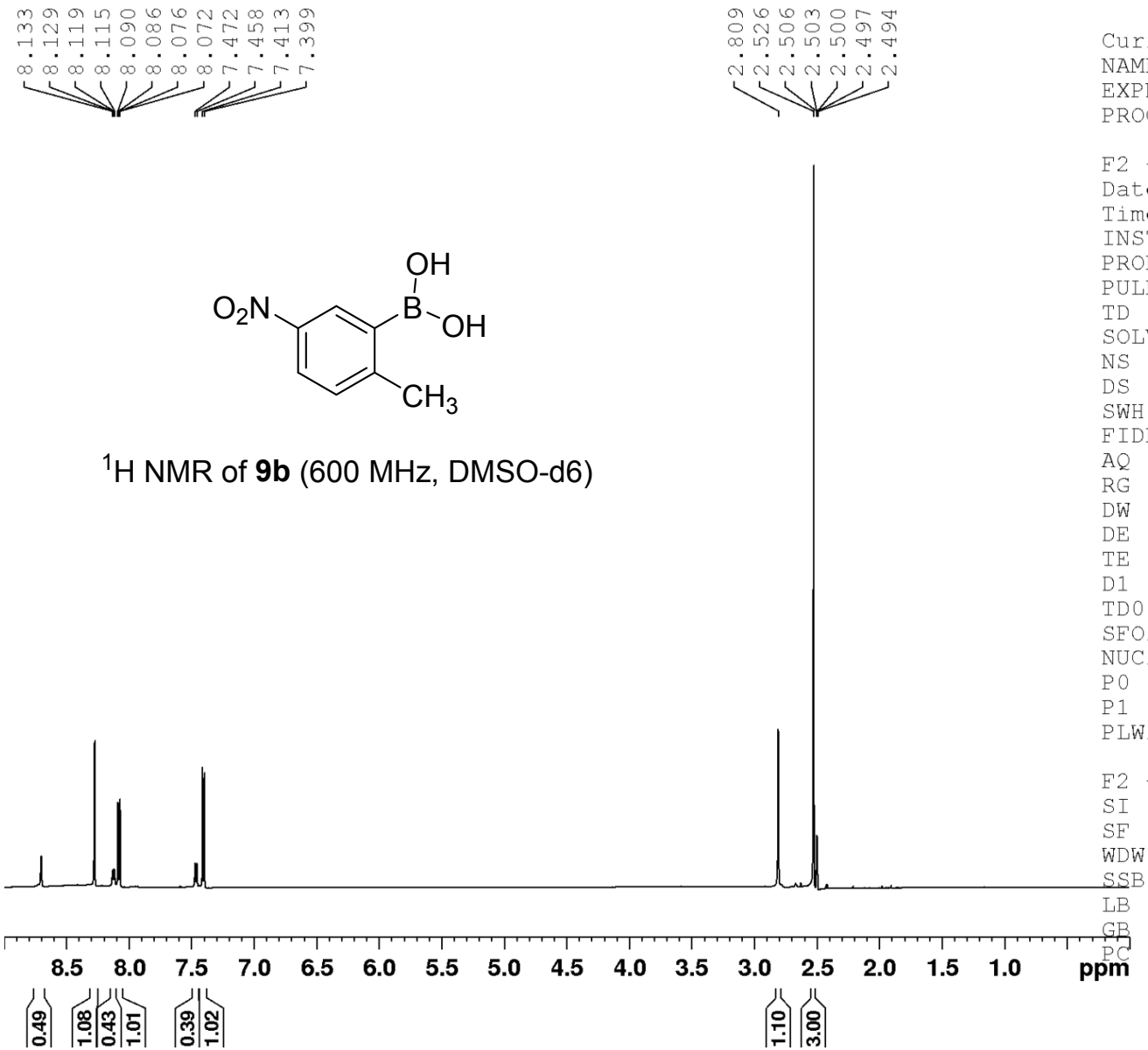
^{1}H NMR of **9a** (600 MHz, $CDCl_3$)

```
Current Data Parameters
NAME      PVK49-X42 A-3' Pure
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230109
Time               15.25 h
INSTRUM             spect
PROBHD   Z148658_0003 (
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ             2.7262976 sec
RG                 78.64
DW                41.600 usec
DE                10.33 usec
TE                296.3 K
D1             1.00000000 sec
TD0                     1
SFO1         600.0087050 MHz
NUC1                   1H
P0                  5.17 usec
P1                 15.50 usec
PLW1         13.23200035 W

F2 - Processing parameters
SI                  65536
SF           600.0050155 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```



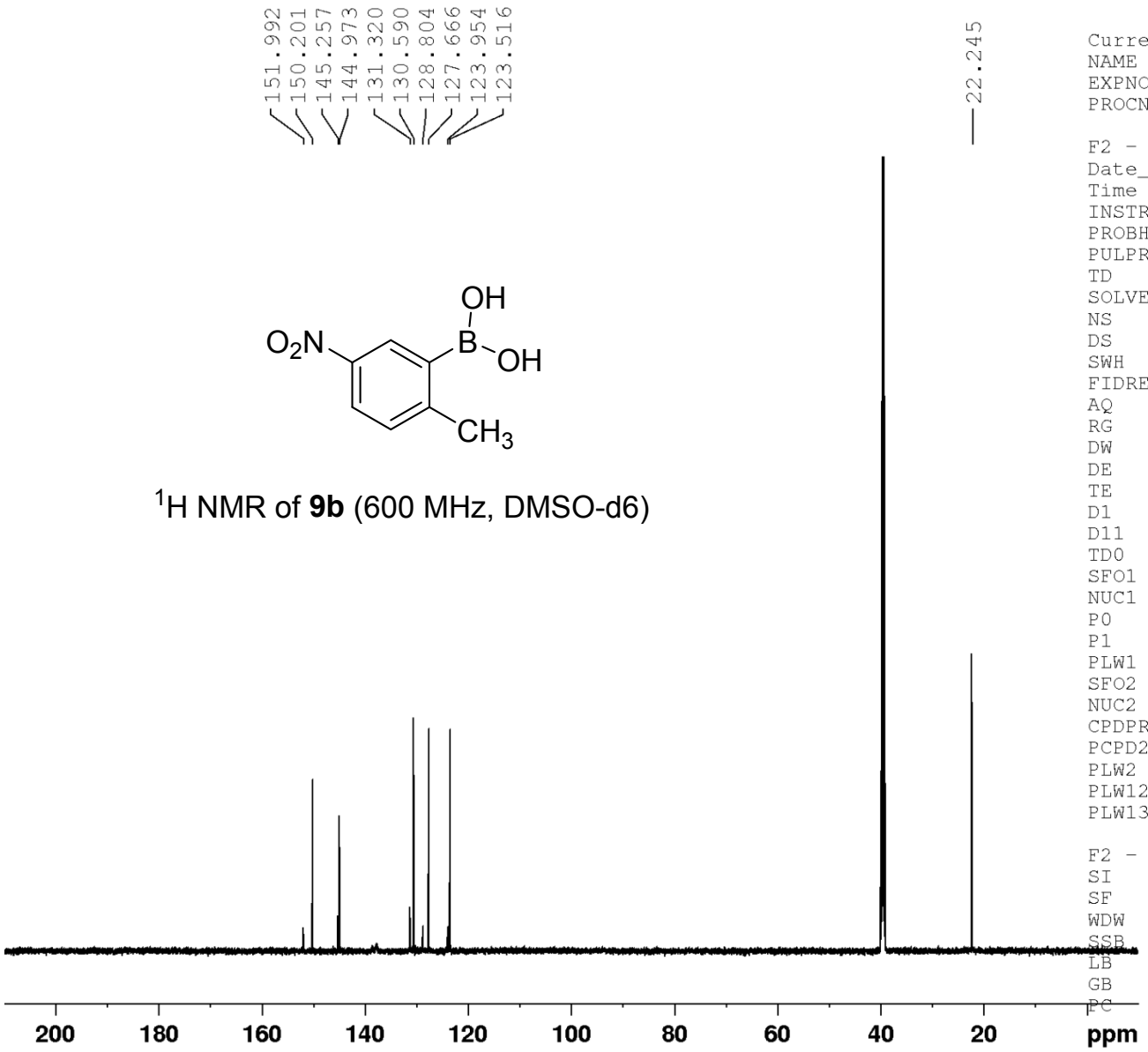
^{13}C NMR of **9a** (150 MHz, $CDCl_3$)

```
Current Data Parameters
NAME      PVK49-X42 A-3' Pure
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230109
Time              16.17 h
INSTRUM            spect
PROBHD   Z148658_0003 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ            0.9043968 sec
RG               199.73
DW               13.800 usec
DE                6.50 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        150.8864644 MHz
NUC1                13C
P0                4.00 usec
P1               12.00 usec
PLW1        77.65699768 W
SFO2        600.0074000 MHz
NUC2                1H
CPDPRG[2         waltz65
PCPD2            70.00 usec
PLW2        13.23200035 W
PLW12        0.64876997 W
PLW13        0.32633001 W

F2 - Processing parameters
SI                32768
SF          150.8713540 MHz
WDW                EM
SSB                 0
LB               1.00 Hz
GB                  0
PC                1.40
```



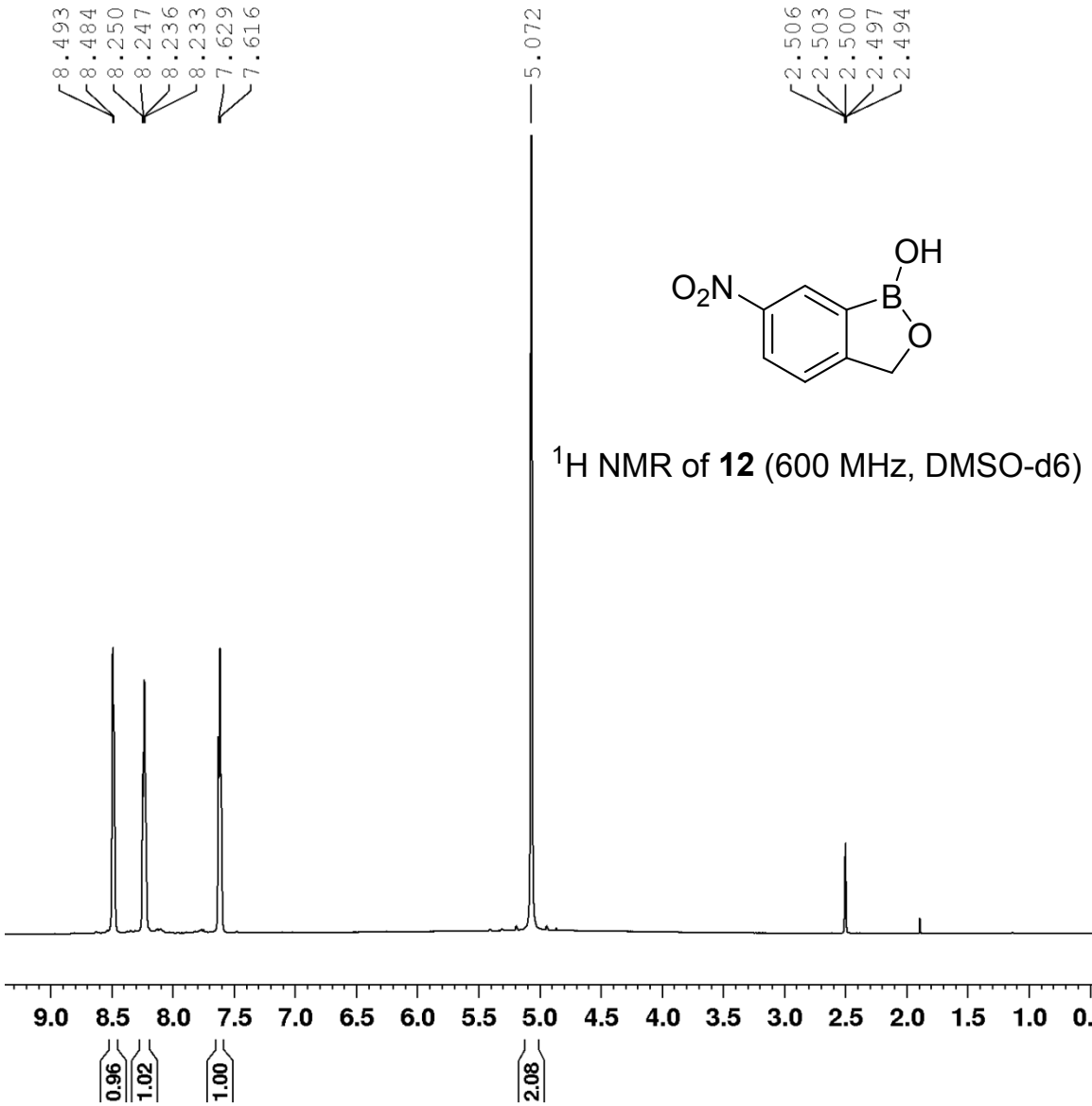
^{1}H NMR of **9b** (600 MHz, DMSO-d6)

```
Current Data Parameters
NAME      PVK49-X65 A3 Pure
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230306
Time               13.18 h
INSTRUM             spect
PROBHD   Z855801_0105 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ              2.7262976 sec
RG                 63.39
DW                41.600 usec
DE                10.93 usec
TE                295.0 K
D1             1.00000000 sec
TD0                    1
SFO1         599.9587047 MHz
NUC1                  1H
P0                 4.00 usec
P1                12.00 usec
PLW1         15.77700043 W

F2 - Processing parameters
SI                 65536
SF           599.9550061 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



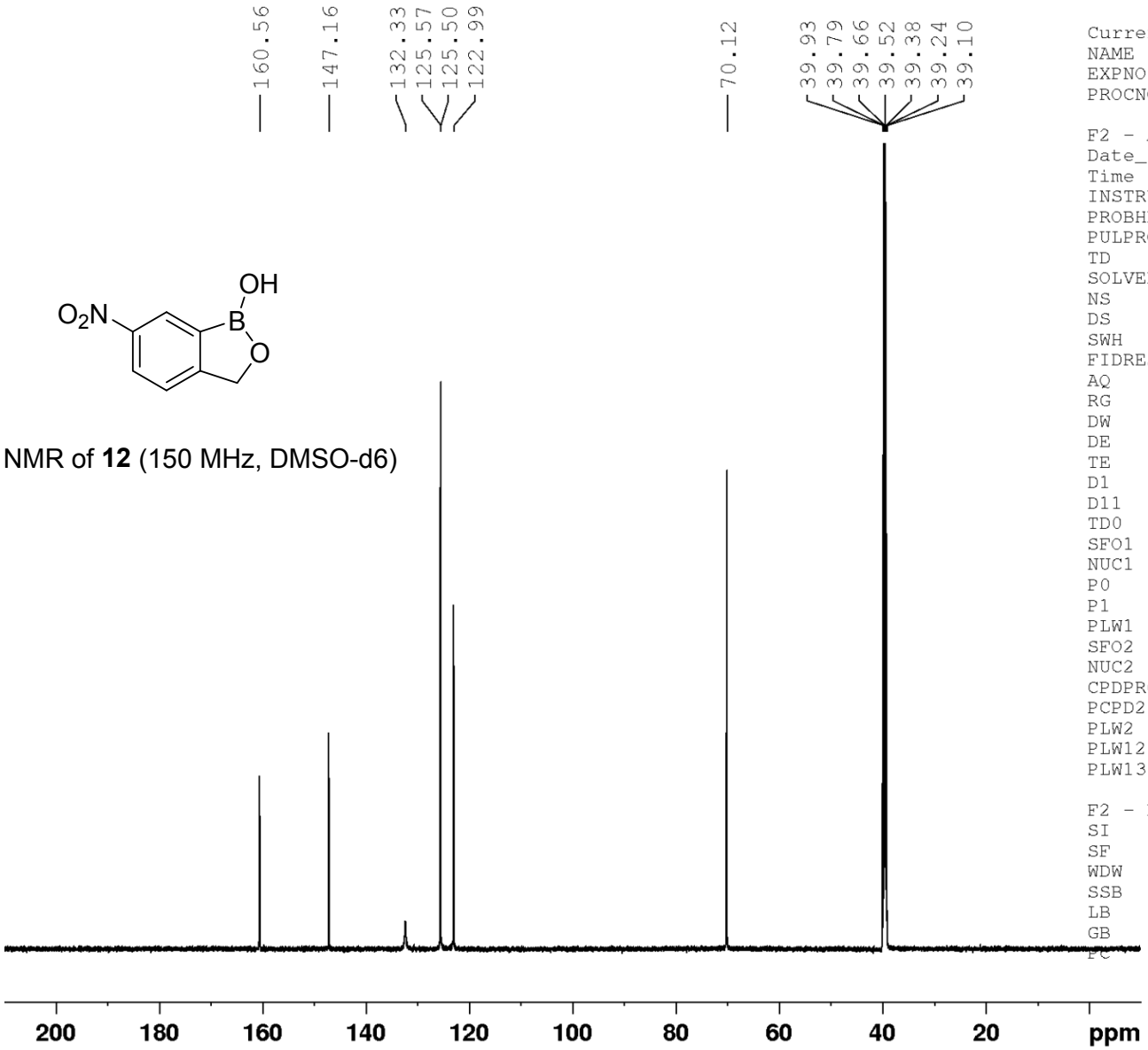
^{1}H NMR of **9b** (600 MHz, DMSO-d6)

```
Current Data Parameters
NAME      PVK49-X65 A3 Pure
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230306
Time              14.10 h
INSTRUM             spect
PROBHD   Z855801_0105 (
PULPROG           zgpg30
TD                65536
SOLVENT            DMSO
NS                 1024
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ            0.9043968 sec
RG               194.75
DW               13.800 usec
DE                6.50 usec
TE               296.8 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        150.8738906 MHz
NUC1               13C
P0                3.67 usec
P1               11.00 usec
PLW1       178.30999756 W
SFO2        599.9573998 MHz
NUC2               1H
CPDPRG[2        waltz65
PCPD2            70.00 usec
PLW2        15.77700043 W
PLW12        0.46366000 W
PLW13        0.23322000 W

F2 - Processing parameters
SI                32768
SF          150.8588758 MHz
WDW                EM
SSB                0
LB              1.00 Hz
GB                 0
PC              1.40
```



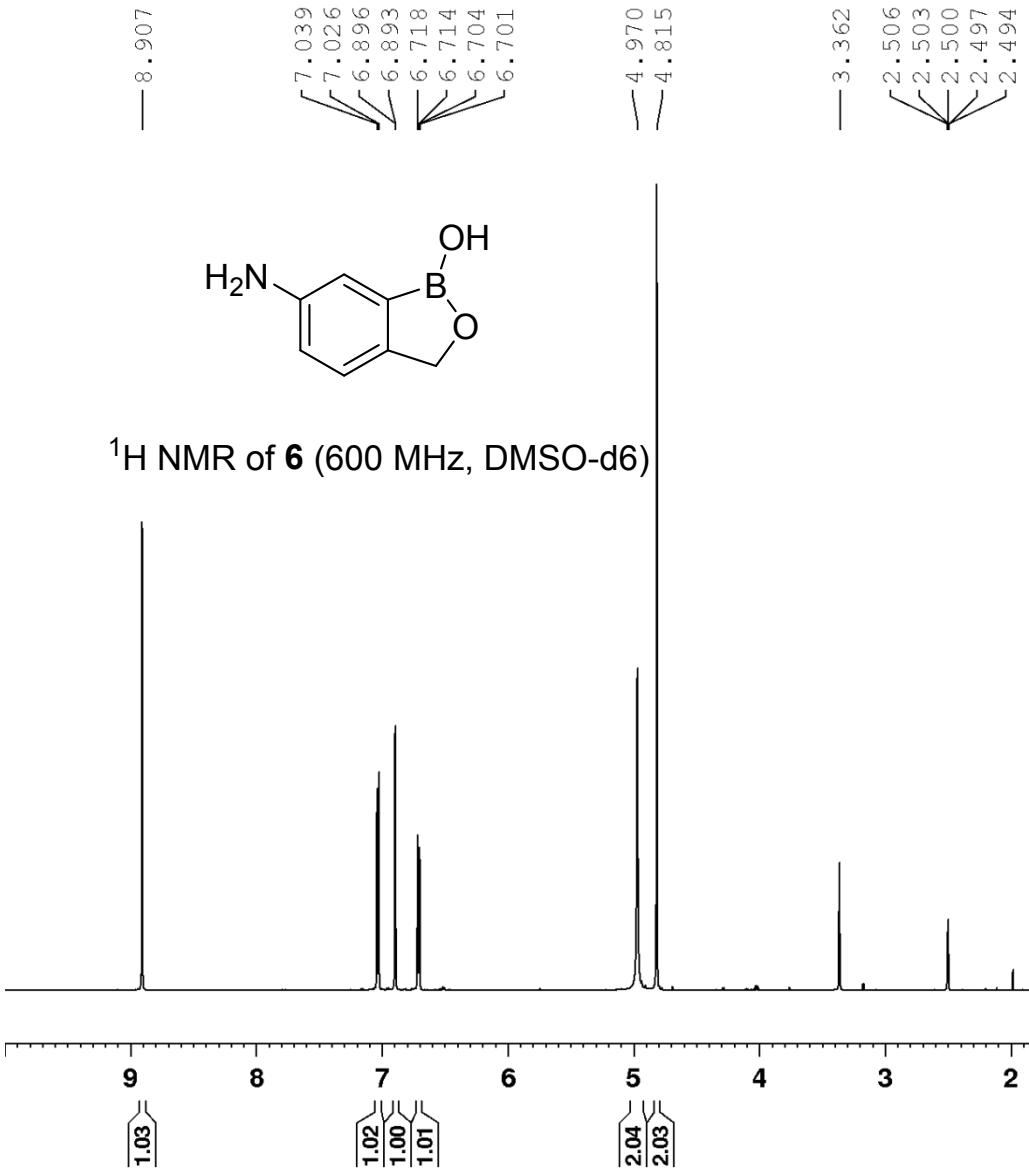
^{1}H NMR of **12** (600 MHz, DMSO-d6)

```
Current Data Parameters
NAME      PVK49-X68 Pure A-4
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230110
Time               15.19 h
INSTRUM             spect
PROBHD   Z148658_0003 (
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ             2.7262976 sec
RG                     61
DW                41.600 usec
DE                10.33 usec
TE                296.2 K
D1            1.00000000 sec
TD0                     1
SFO1         600.0087050 MHz
NUC1                   1H
P0                  5.17 usec
P1                 15.50 usec
PLW1         13.23200035 W

F2 - Processing parameters
SI                  65536
SF         600.0050064 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```



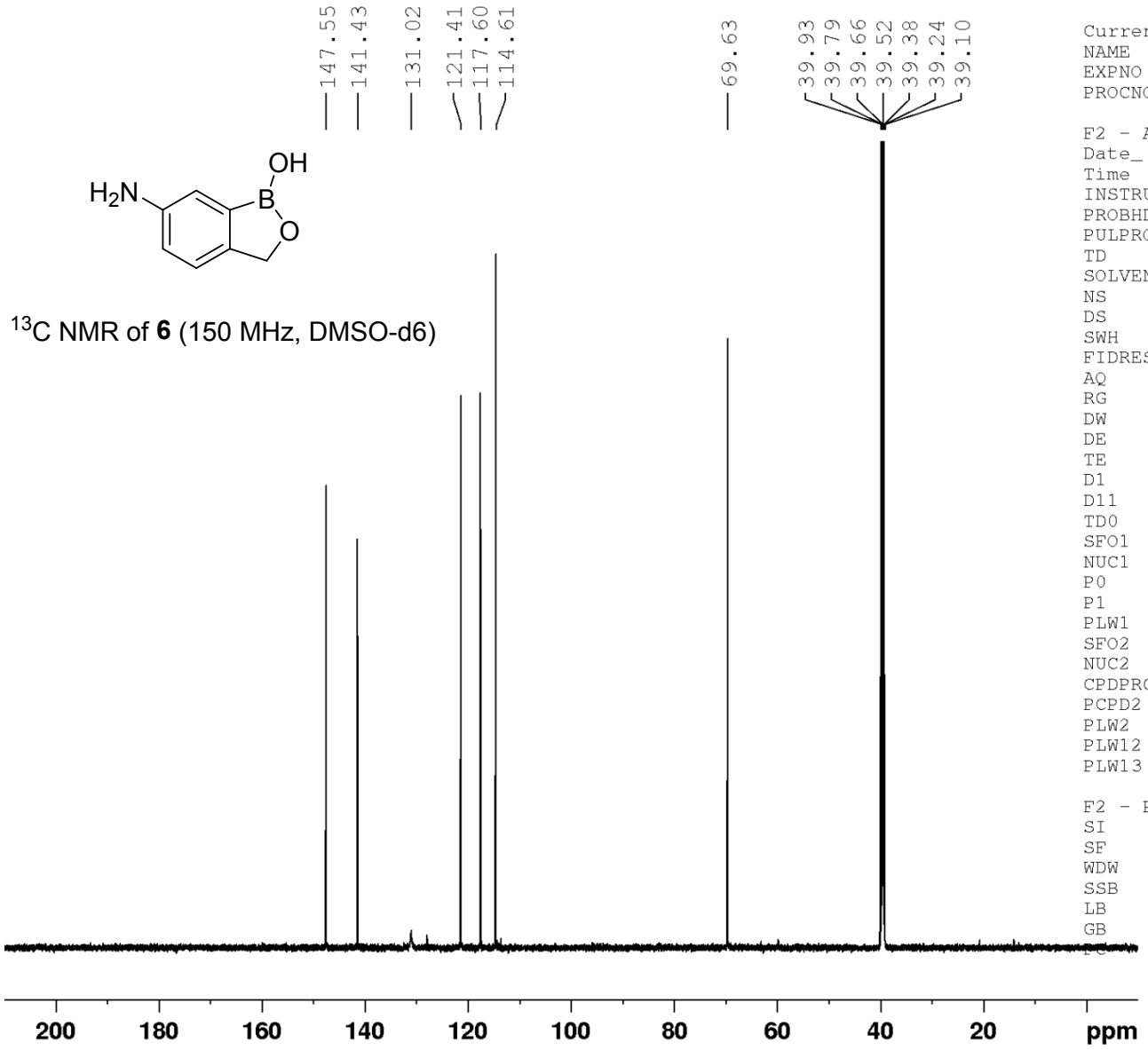
^{13}C NMR of **12** (150 MHz, DMSO-d6)

```
Current Data Parameters
NAME      PVK49-X68 Pure A-4
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230110
Time              16.11 h
INSTRUM            spect
PROBHD   Z148658_0003 (
PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                 1024
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ            0.9043968 sec
RG               199.73
DW               13.800 usec
DE                6.50 usec
TE               298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        150.8864644 MHz
NUC1               13C
P0                4.00 usec
P1               12.00 usec
PLW1        77.65699768 W
SFO2        600.0074000 MHz
NUC2               1H
CPDPRG[2        waltz65
PCPD2             70.00 usec
PLW2        13.23200035 W
PLW12        0.64876997 W
PLW13        0.32633001 W

F2 - Processing parameters
SI                32768
SF          150.8714319 MHz
WDW                EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                1.40
```



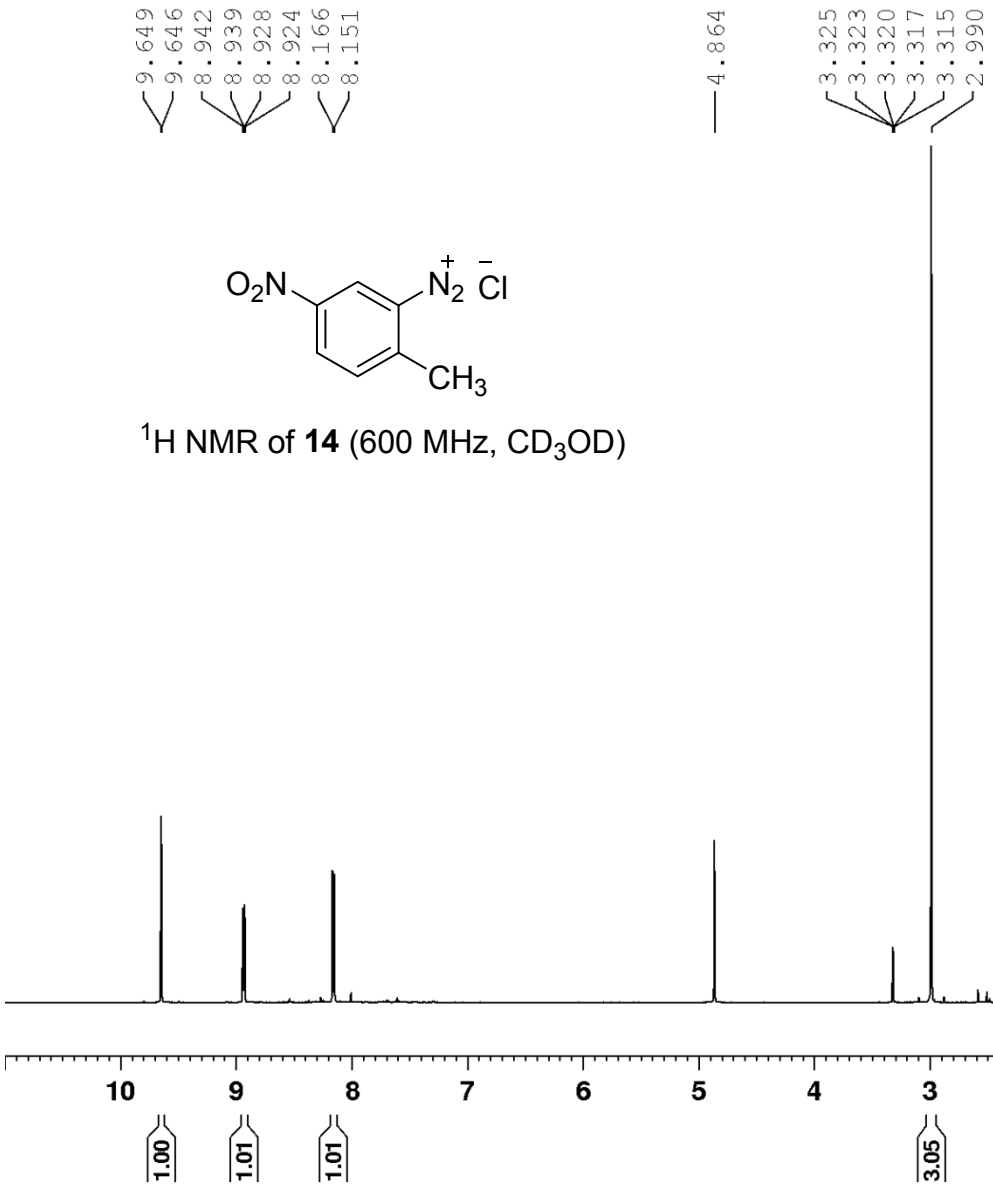
^{1}H NMR of **6** (600 MHz, DMSO-d6)

```
Current Data Parameters
NAME      PVK49-X78 A-5 Pure_2
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230111
Time               16.33 h
INSTRUM            spect
PROBHD   Z148658_0003 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ             2.7262976 sec
RG                 106.9
DW                41.600 usec
DE                10.33 usec
TE                298.0 K
D1             1.00000000 sec
TD0                    1
SFO1         600.0087050 MHz
NUC1                  1H
P0                 5.17 usec
P1                15.50 usec
PLW1         13.23200035 W

F2 - Processing parameters
SI                 65536
SF           600.0050063 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



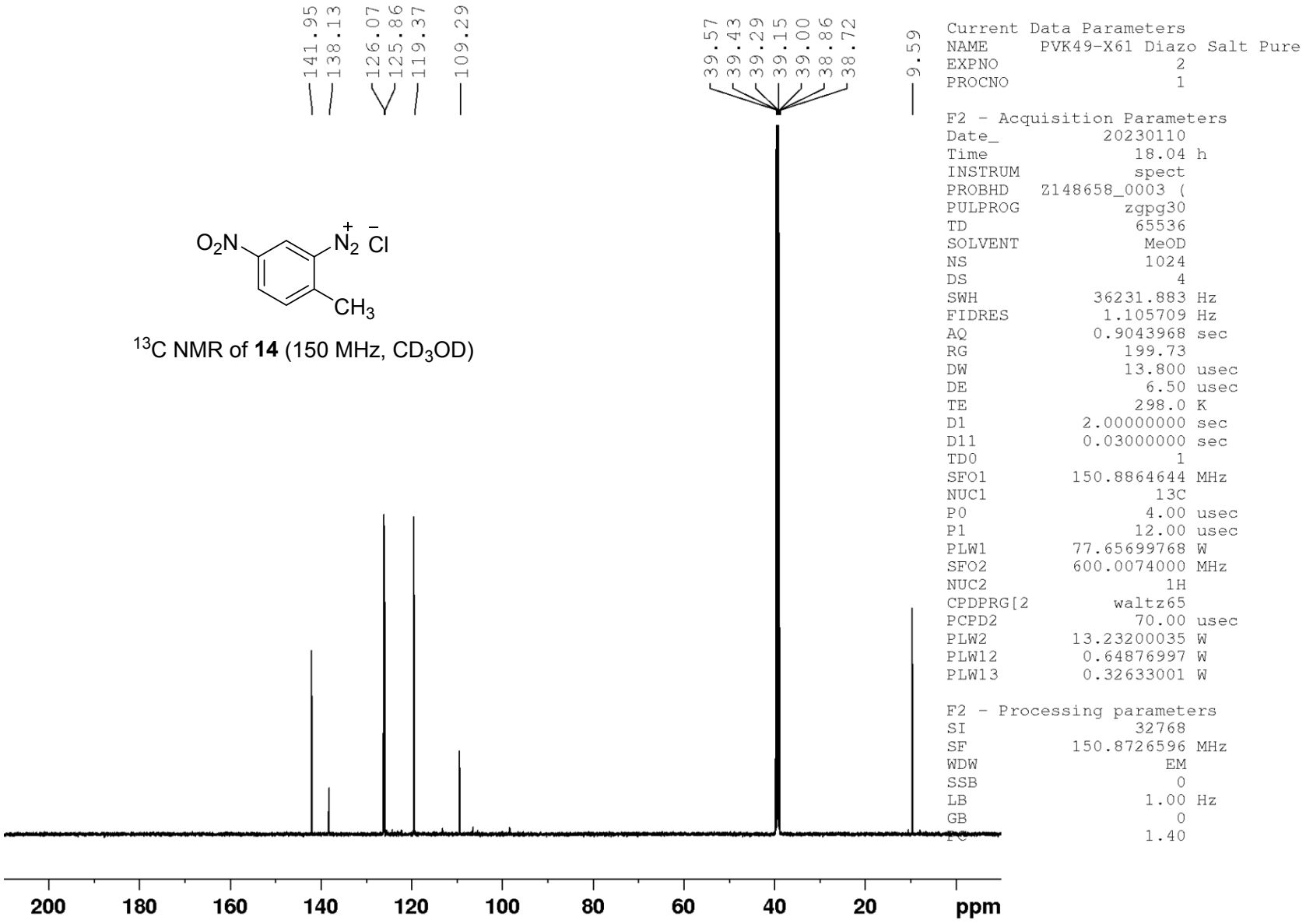
^{13}C NMR of **6** (150 MHz, DMSO-d6)

```
Current Data Parameters
NAME      PVK49-X78 A-5 Pure
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_           20230111
Time              17.25 h
INSTRUM             spect
PROBHD   Z148658_0003 (
PULPROG           zgpg30
TD                 65536
SOLVENT             DMSO
NS                  1024
DS                     4
SWH            36231.883 Hz
FIDRES          1.105709 Hz
AQ             0.9043968 sec
RG                199.73
DW                13.800 usec
DE                 6.50 usec
TE                298.7 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1         150.8864644 MHz
NUC1                13C
P0                 4.00 usec
P1                12.00 usec
PLW1         77.65699768 W
SFO2         600.0074000 MHz
NUC2                1H
CPDPRG[2         waltz65
PCPD2             70.00 usec
PLW2         13.23200035 W
PLW12         0.64876997 W
PLW13         0.32633001 W

F2 - Processing parameters
SI                 32768
SF           150.8714473 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
                   1.40
```



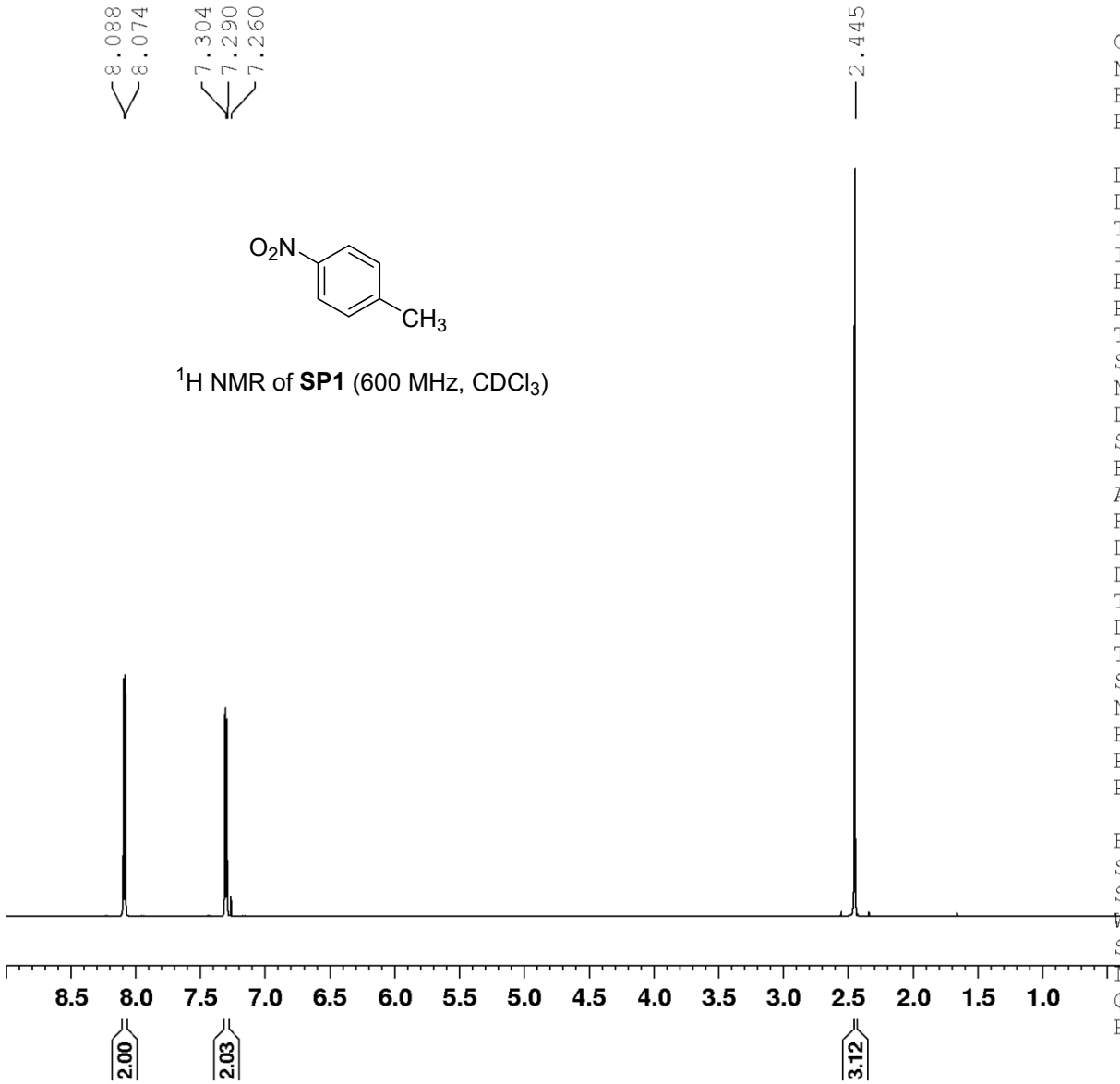
^{1}H NMR of **14** (600 MHz, CD_3OD)

```
Current Data Parameters
NAME      PVK49-X61 Diazo Salt Pure
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20230110
Time              17.12 h
INSTRUM           spect
PROBHD   Z148658_0003 (
PULPROG            zg30
TD                65536
SOLVENT            MeOD
NS                   16
DS                    2
SWH           12019.230 Hz
FIDRES         0.366798 Hz
AQ             2.7262976 sec
RG                157.38
DW                41.600 usec
DE                10.33 usec
TE                296.6 K
D1           1.00000000 sec
TD0                   1
SFO1        600.0087050 MHz
NUC1                1H
P0                 5.17 usec
P1                15.50 usec
PLW1        13.23200035 W

F2 - Processing parameters
SI                65536
SF          600.0050056 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```



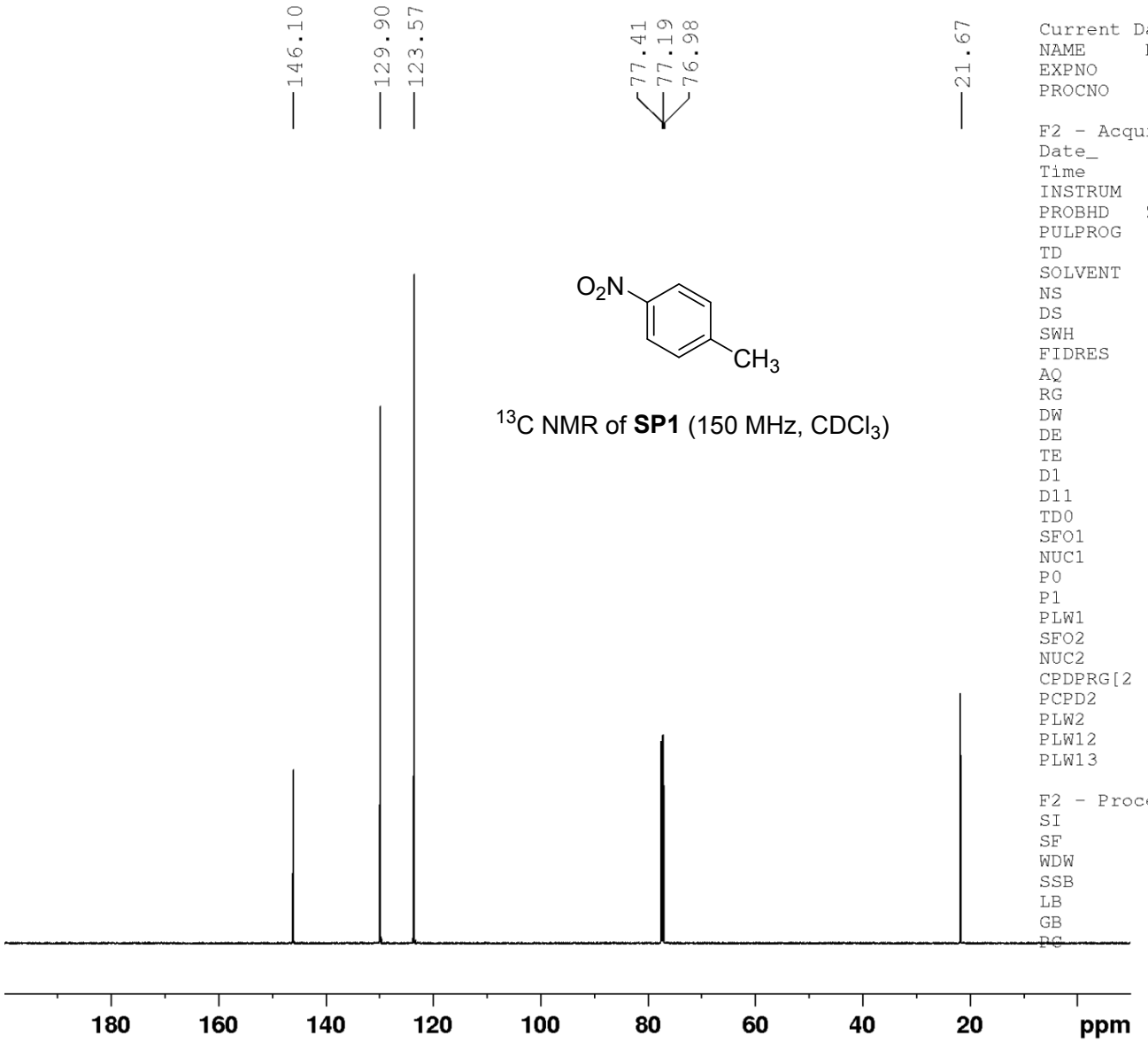
^{13}C NMR of **14** (150 MHz, CD_3OD)

```
Current Data Parameters
NAME      PVK49-X61 Diazo Salt Pure
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20230110
Time             18.04 h
INSTRUM           spect
PROBHD   Z148658_0003 (
PULPROG         zgpg30
TD               65536
SOLVENT            MeOD
NS                 1024
DS                    4
SWH          36231.883 Hz
FIDRES        1.105709 Hz
AQ           0.9043968 sec
RG              199.73
DW              13.800 usec
DE               6.50 usec
TE              298.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        150.8864644 MHz
NUC1                13C
P0                4.00 usec
P1               12.00 usec
PLW1        77.65699768 W
SFO2        600.0074000 MHz
NUC2                1H
CPDPRG[2         waltz65
PCPD2             70.00 usec
PLW2        13.23200035 W
PLW12        0.64876997 W
PLW13        0.32633001 W

F2 - Processing parameters
SI                32768
SF          150.8726596 MHz
WDW                EM
SSB                 0
LB               1.00 Hz
GB                  0
PC                1.40
```



^{1}H NMR of **SP1** (600 MHz, $CDCl_3$)

```
Current Data Parameters
NAME      PVK49-X8 S.M Pure
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230106
Time                15.42 h
INSTRUM             spect
PROBHD   Z148658_0003 (
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ             2.7262976 sec
RG                  55.05
DW                 41.600 usec
DE                 10.33 usec
TE                 296.3 K
D1             1.00000000 sec
TD0                     1
SFO1         600.0087050 MHz
NUC1                   1H
P0                  5.17 usec
P1                 15.50 usec
PLW1         13.23200035 W

F2 - Processing parameters
SI                  65536
SF           600.0050153 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```



^{13}C NMR of **SP1** (150 MHz, $CDCl_3$)

```
Current Data Parameters
NAME      PVK49-X8 S.M Pure
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230106
Time               16.34 h
INSTRUM             spect
PROBHD   Z148658_0003 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ            0.9043968 sec
RG               199.73
DW               13.800 usec
DE                6.50 usec
TE                298.3 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        150.8864644 MHz
NUC1                13C
P0                 4.00 usec
P1                12.00 usec
PLW1        77.65699768 W
SFO2        600.0074000 MHz
NUC2                1H
CPDPRG[2         waltz65
PCPD2             70.00 usec
PLW2        13.23200035 W
PLW12        0.64876997 W
PLW13        0.32633001 W

F2 - Processing parameters
SI                32768
SF          150.8713629 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```