
Supplementary information

Continuous collective analysis of chemical reactions

In the format provided by the
authors and unedited

Supplementary Materials for

Continuous collective analysis of chemical reaction mixtures

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1. Materials and general methods	4
1.1 Reagents and solvents	4
1.2 Liquid Chromatography-Mass Spectrometry (LC-MS).....	4
1.3 Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS).....	4
1.4 Preparative Liquid Chromatography Mass Spectrometry.....	5
1.5 Neutral Loss-Acoustic Droplet Ejection-Mass Spectrometry (<i>NL</i> -ADE-MS)	5
Table S1 Parameters for fragmentation of starting materials	7
Table S1 Continued... ..	8
1.6 Neutral Loss-Liquid Chromatography-Tandem Mass Spectrometry (<i>NL</i> -LC-MS/MS).....	9
1.7 Selection of 100 diverse compounds (Extended Data Fig. 3a-c).....	9
1.8 Selection of 96 diverse amines from the St. Jude collection (Fig. 4)	9
2. Synthesis	11
2.1 Synthesis of TIDA boronate building blocks.....	11
2.2 Synthesis of clarithromycin derivative (5).....	17
2.3 Synthesis of THP protected alcohol (9)	18
2.4 Synthesis of 60 TIDA boronate test set (Extended Data Fig. 1a)	19
3. Neutral Loss-Acoustic Droplet Ejection-Mass Spectrometry (<i>NL</i> -ADE-MS) method optimization and validation	36
3.1 Concentration series for 60 TIDA boronate testing set (Extended Data Fig 2c)	36
3.2 Variation of collision energy (CE) on signal intensity (Extended Data Fig 3f).....	36
3.3 Mass range (Extended Data Fig 3g).....	36
3.4 Carryover (Extended Data Fig 3h).....	37
3.5 Matrix effects (Extended Data Fig 3i)	37
3.6 Systematic error (Extended Data Fig 3j)	37
4. High throughput miniaturized reaction.....	38
4.1 Buchwald-Hartwig C-N coupling reaction	38
4.2 Suzuki-Miyaura C-C coupling reaction	39

4.3 C-O coupling reaction.....	40
4.4 Reductive amination reaction	41
4.5 Amidation reaction.....	42
4.6 <i>N</i> -alkylation reaction.....	43
4.7 384-Well plate data processing example.....	44
4.8 Individual 384-well plate experiments.....	45
4.8.1 TIDA 1 Buchwald-Hartwig C-N coupling reaction	45
4.8.2 TIDA 1 Suzuki–Miyaura C-C coupling reaction.....	47
4.8.3 TIDA 1 C-O coupling reaction	49
4.8.4 TIDA 2 reductive amination reaction	51
4.8.5 TIDA 3 amidation reaction	52
4.8.6 TIDA 4 <i>N</i> -alkylation reaction	53
4.8.7 Clarithromycin derivative 5 Buchwald-Hartwig C-N coupling reaction	55
4.8.8 Clarithromycin derivative 5 Suzuki–Miyaura C-C coupling reaction.....	57
4.8.9 Amphotericin B 6 amidation reaction.....	59
4.8.10 Boc amine 7 Buchwald-Hartwig C-N coupling reaction.....	60
4.8.11 Boc amine 7 Suzuki–Miyaura C-C coupling reaction.....	62
4.8.12 Boc-L-proline 8 amidation reaction	63
4.8.13 THP alcohol 9 Buchwald-Hartwig C-N coupling reaction.....	65
4.8.14 THP alcohol 9 Suzuki–Miyaura C-C coupling reaction.....	67
4.8.15 (+)-JQ1 10 Buchwald-Hartwig C-N coupling reaction	68
4.8.16 (+)-JQ1 10 Suzuki–Miyaura C-C coupling reaction	70
4.8.17 Indomethacin 11 Buchwald-Hartwig C-N coupling reaction.....	71
4.8.18 Indomethacin 11 Suzuki–Miyaura C-C coupling reaction	73
4.8.19 C5-Lenalidomide 12 reductive amination reaction	74
4.8.20 C5-Lenalidomide 12 amidation reaction	76
4.8.21 Lenalidomide-5-Br 13 Buchwald-Hartwig C-N coupling reaction.....	78
4.9 High-throughput experimentation spanning 12,288 reactions (Fig. 4).....	79
4.10 Quantitative analysis (Extended Data Fig. 10a-f).....	81
4.11 Reaction kinetics under native conditions (Extended Data Fig 10g).....	82
4.12 Neutral loss-LC-MS (<i>NL</i> -LC-MS) (Extended Data Fig 10h).....	82

4.13 Supplementary Figures	83
Figure S1 Amine selection for high-throughput experimentation.	83
Figure S2 Starting materials define fragmentation barcodes for downstream products.....	84
Figure S3 Starting materials define fragmentation barcodes for downstream products.....	85
Figure S4 Head to head comparison of <i>NL</i> -ADE-MS and LC-MS.....	86
Figure S5 Head to head comparison of <i>NL</i> -ADE-MS and LC-MS.....	87
Figure S6 Head to head comparison of <i>NL</i> -ADE-MS and LC-MS.....	88
Figure S7 Head to head comparison of <i>NL</i> -ADE-MS and LC-MS.....	89
Figure S8 Structures for 100 compounds (S111-S210) used as test set	90
Figure S8 continued.....	91
Figure S9 Structures of 96 amines used in Fig. 4.....	92
Figure S9 continued.....	93
4.14 CID spectra for 60 TIDA boronates.....	94
4.15 CID spectra for starting materials	124
5. References	131
6. NMR Spectra.....	132

1. Materials and general methods

1.1 Reagents and solvents

Air- and moisture-sensitive reactions were carried out in the nitrogen filled glovebox. Chemicals were purchased from Oakwood chemical, Acros Organics, Alfa Aesar, Frontier Scientific, Combi-Blocks, Enamine, Matrix Scientific, or Sigma Aldrich and were used as received unless otherwise mentioned. Anhydrous DMF, DMSO, NMP, and DMAc were purchased from Sigma Aldrich and stored in the glovebox. Amines were selected from St Jude chemical inventory and used directly. Methanol and acetonitrile (LC-MS grade) were acquired from Fisher Scientific (Waltham, MA). Milli-Q water (Millipore, Molsheim Cedex, France) was used as produced. ^1H , ^{13}C , and ^{19}F Nuclear Magnetic Resonance (NMR) spectra were recorded in DMSO-d₆ solvent on Bruker Ascend 500 with Avance III HD Console (at 500 MHz, 126 MHz, and 471 Hz). Chemical shifts (δ_{H} , δ_{C}) are calibrated to the residual protio solvent signals of DMSO-d₆ (2.50 ppm, 39.5 ppm). Coupling constants are quoted in parts per million (ppm) and refer to apparent multiplicities. Data are listed as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, sept = septet, m = multiplet, dd = doublet of doublet, etc.), coupling constant, integration, and assignment.

1.2 Liquid Chromatography-Mass Spectrometry (LC-MS)

The chromatographic system utilized was a Waters Acquity I class ultra-performance liquid chromatography (UPLC) system, comprising a binary pump, integrated degasser, column oven, autosampler, and sample organizer, all sourced from Waters Corporation (Milford, MA, USA). Separation was carried out on an Acquity UPLC BEH C18 1.7 μm , 2.1 x 50 mm column from Waters Corporation (Milford, MA, USA). Data acquisition utilized Masslynx v. 4.2, with analysis conducted using the Openlynx software suite. UV data within the 220-350 nm range was captured using an Acquity photodiode array detector. The flow was evenly split, with one half directed to an evaporative light scattering detector (ELSD) and the other to a single quadrupole (SQ) mass spectrometer. The total flow rate was maintained at 1 mL/min, with a sample injection volume of 4 μL . The UPLC column temperature was set at 63 °C, and the gradient program began at 90% A (0.1 % formic acid in MilliQ H₂O), transitioning to 70% A over 0.2 minutes, then to 95% B (0.1 % formic acid in acetonitrile) over 1.4 minutes, holding for 0.35 minutes, before returning to 90% A over 0.05 minutes. Positive-ion mode electrospray ionization was employed for the mass spectrometer, with the following parameters: capillary voltage of 3.5 kV, cone voltage of 30 V, source temperature of 150 °C, desolvation temperature of 350 °C, desolvation gas flow of 750 L/hr, and cone gas flow of 25 L/hr. Mass spectrometry data acquisition involved a full scan range from m/z = 50–1200 Da within a 0.2 s timeframe. Single ion recording mass spectrometry was utilized for sample quantification of each compound.

1.3 Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

The multiple reaction monitoring (MRM) transitions of each compound were monitored using a SCIEX ExionLC/Qtrap 6500 plus triple-quadrupole mass spectrometer system from SCIEX (Forster City, CA), equipped with an electrospray ion (Turbo Ionspray) interface. The SCIEX

ExionLC featured two pumps, an integrated degasser, column oven, autosampler, and sample organizer. Nitrogen served as curtain, nebulizer, and collision gas. Analytes were dissolved individually in 30% aqueous acetonitrile and were introduced into the ion source of the mass spectrometer by an autosampler. The following solvent series of was used to introduce the sample and wash the system: The isocratic program had a runtime of 2 minutes at 25% A (0.1 % formic acid in MilliQ H₂O) and 75% B (0.1 % formic acid in acetonitrile). The flow rate started at 0.4 mL/min, held for 0.3 minutes, transitioned to 0.05 mL/min over 0.01 minutes, changed to 0.03 mL/min over 1.39 minutes, then returned to 0.5 mL/min over 0.01 minutes, and held for 0.29 minutes. MRM transitions and compound-dependent parameters (including declustering potential (DP), entrance potential (EP), collision energy (CE), and collision cell exit potential (CXP)) for each tested compound were selected using Discovery Quant Software (version 3.0.2). The temperature was set at 300 °C, employing high collision gas, and using a 30 µL injection volume. The two most abundant fragments of the parent ion were documented. Scan step size was 0.1 amu, with Q3 scan at 200 amu/s. Compounds were acquired in positive mode, and negative mode if required. Data acquisition was performed with Analyst 1.7.3 (SCIEX).

1.4 Preparative Liquid Chromatography Mass Spectrometry

Samples were purified using an Agilent auto-scaling preparative liquid chromatography mass spectrometry system comprising of a preparative pump, analytical quaternary pump, single quadrupole mass spectrometer, preparative variable wavelength detector, an analytical diode array detector, a column management featuring 4 valves [1. analytical column selection 2. preparative column selection 3. Integration of an open bed fraction collector sampler into the analytical and preparative flow paths 4. a flow splitter to accommodate preparative scale MS analysis.], an open bed fraction collector/sampler. Using the Agilent auto-purification software suite analytical data were collected on a reverse phase column of known dimensions and particle size, these data were used to generate customized preparative purification profiles for each target product based on the retention times for specific targets and observation of MS + UV signals. Thresholds were manually inspected before executing preparative runs and adjusted if required. Individual pure fractions were transferred to pre-weighed tubes and concentrated using a Genevac centrifugal evaporator.

1.5 Neutral Loss-Acoustic Droplet Ejection-Mass Spectrometry (NL-ADE-MS)

Samples were prepared in 384-well PP plates (001-14615) or 1536-well COC plates (001-6969), at the indicated concentrations. Acoustic transfer of solutions from 384-well COC plates (001-12782) was the typical method used to generate these samples from reaction mixtures or stock solutions. Prior to loading into the NL-ADE-MS system, the source microplates containing the sample cosolvent underwent centrifugation (at 537 RCF for 5 min) to eliminate gas bubbles and ensure a uniform fluid meniscus shape. Sample collection was facilitated using the Sciex OS-MQ Analytics Software (version 2.1.6.59781) from Sciex (Forster City, CA), to control an ADE-MS system operating in neutral loss mode. This system comprised an externalized transducer assembly from an ADE-MS autosampler, an open port interface (OPI) connected to a carrier solvent pump, and a transfer capillary leading to a standard IonDrive Turbo V ESI source of an AB Sciex Triple

Quad 6500+ system. The carrier liquid utilized was methanol supplemented with 1 mM ammonium fluoride, flowing at a rate of 350 μ L or 500 μ L/min, generating a stable vortex at the OPI inlet for optimized signal performance. Contactless sampling involved ejecting of 2.5 nL (if not otherwise mentioned) directly from the microtiter plate wells into the carrier liquid vortex of the OPI, at a frequency of 3 seconds per well or 1.2 seconds per well. The electrospray ionization (ESI) source of the triple quadrupole MS instrument operated in positive ionization mode, with nebulizer gas (GS1) set to 90 psi, heater gas (GS2) to 70 psi, curtain gas and collision-activated dissociation (CAD) gas to 20 psi and 9 units, respectively. The mass scan range was set according to samples being studied. For analyte measurements, the following MS parameters were employed: ion source temperature: 500 °C; spray voltage: 5500 V; dwell time: 0.1 s; pause time: 5 ms; Q1 operated at unit resolution. The following parameters are defined in **Table S1** on a per-starting material basis - declustering potential (DP), entrance potential (EP), collision energy (CE), and collision cell exit potential (CXP), and neutral loss. *These details can also be found in Extended Tabular Data Sheet 1 and CID spectra can be found at the end of this document.* After acquiring sample batches, data processing was conducted using an in-house-built R script.

Table S1 Parameters for fragmentation of starting materials

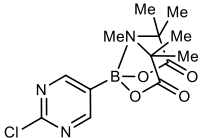
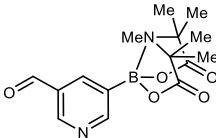
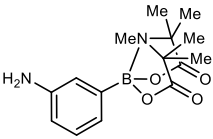
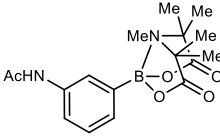
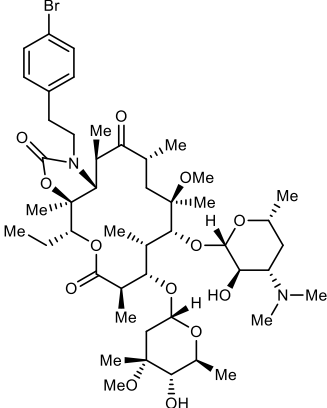
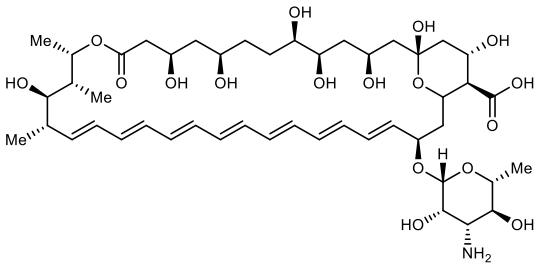
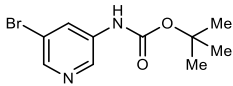
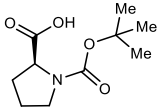
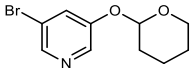
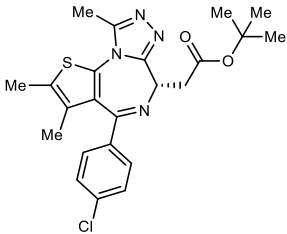
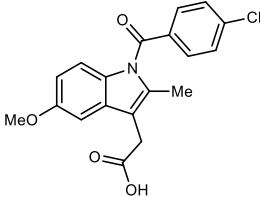
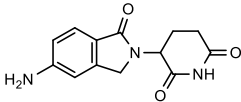
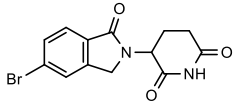
ID	Molecule	NL (Da)	CE (V)	DP (V)	EP (V)	CXP
1		86	31	100	10	13
2		86	30	100	10	14
3		86	32	100	10	16
4		86	23	110	10	13
5		158	32	50	10	16
6		181	29	60	10	11

Table S1 Continued...

ID	Molecule	NL (Da)	CE (V)	DP (V)	EP (V)	CXP
7		56	15	80	10	3
8		56	11	70	10	9
9		84	22	70	10	10
10		56	23	100	10	12
11		219	29	90	10	9
12		111	25	90	10	10
13		111	26	90	10	14

1.6 Neutral Loss-Liquid Chromatography-Tandem Mass Spectrometry (NL-LC-MS/MS)

Liquid chromatography tandem mass spectrometry (LC-MS/MS) using the neutral loss method was monitored by a Waters Acquity UPLC (Milford, MA) coupled with a Sciex 6500 triple-quadrupole mass spectrometer system (Foster City, CA). 2 μ L of samples were separated on an Acquity UPLC BEH C18 1.7 μ m, 2.1 x 50 mm column from Waters Corporation (Milford, MA, USA). Data acquisition utilized Analyst Software (AB Sciex, version 1.6.3) and with analysis conducted using MultiQuant Software (AB Sciex, version 3.0.3). The inlet method for these samples utilized a flow rate of 0.9 mL/min. The UPLC column temperature was set at 60 $^{\circ}$ C, and the gradient program began at 90% A (0.1 % formic acid in MilliQ H₂O), transitioning to 70% A over 0.2 minutes, then to 95% B (0.1 % formic acid in acetonitrile) over 1.4 minutes, holding for 0.35 minutes, before returning to 90% A over 0.05 minutes. The first 0.1 min of eluate was desalted to waste using an integrated Valco valve. Neutral loss of 86 Da was used to quantify each compound based on a full scan in the range of 370-520 Da. The mass spectrometer was operated in positive ion mode with electrospray ionization. Reaction monitoring parameters were as follows: ion source gas 1 pressure of 50 psi, ion source gas 2 pressure of 50 psi, curtain gas pressure of 40 psi, collision gas pressure of 8 psi, ion spray voltage of 5.5 kV, source temperature of 500 $^{\circ}$ C, declustering potential (DP) of 100 V, entrance potential (EP) of 10 V, collision energy (CE) of 31 V, and collision cell exit potential (CX) of 13 V.

1.7 Selection of 100 diverse compounds (Extended Data Fig. 3a-c)

Data pipelining and RDKit molecular calculations were conducted within Konstanz Information Miner (KNIME) version 4.7.6¹ 698K unique Compounds in our internal collection² which had at least one 384 REMP 10 μ L sample tube at 10 mM served as the starting point as candidate for selections. The following additional filters were applied to reduce the set: Samples with <6 REMP samples were removed to preserve compounds with low availability. (192K); Samples which were not commercially sourced from a vendor were removed. (139K); Samples were selected from general diversity sources. (125K); From this curated subset SlogP, TPSA, and AMW descriptors were calculated using RDkit³. Compounds were further selected with a free-base AMW between 249.99 and 650. (123K); Compounds passing all PAINS⁴, BRENK⁵, NIH^{6,7}, and ZINC⁸ filters were selected (89.5K); Additional SMARTS filters were utilized to remove electrophiles such as aldehydes, anhydrides, esters, alkyl chlorides, epoxides, and aromatic/heteroaromatic ketones. (75.6K); From this curated set a Morgan 3 fingerprint calculated in RDKit was used in the RDKit Diversity Picker to select the most diverse 9K compounds. These 9K diverse compounds were placed into 100 bins by molecular weight and a random member of each bin was selected as a representative. The SlogP, TPSA, and AMW distribution for the selected are shown in **Extended Data Fig 3a-c**. NL-ADE-MS data were collected on these compounds using the following parameters compound concentration 2 μ M using collisional parameters for the neutral loss of 86 defined by compound 1.

1.8 Selection of 96 diverse amines from the St. Jude collection (Fig. 4)

From 125K+ unique available reagents in the St. Jude inventory a subset of 1062 molecules which contained a single aromatic amine functional group and a maximum molecular weight of

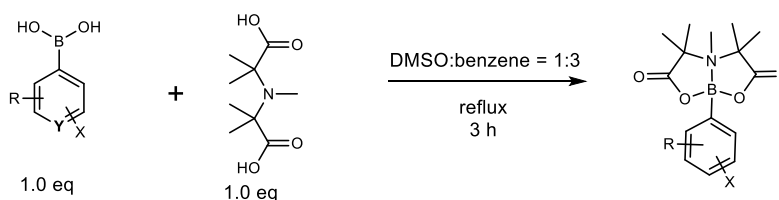
300 were selected. This molecule subset was further tailored for the Buchwald cross coupling. Utilizing SMARTS⁹ string matching amidine, secondary amines (aryl and aromatic), carbamates, aryl / heteroaryl halides (Cl, Br, I), aryl boronic acids, alkyl halides, thiols, ureas, and heterocycles containing tautomeric hydrogen such as pyradinone and pyrazoles were removed. Finally, molecules containing isotopes (i.e. N15, H2, H3) or transition metals (i.e. Pd) were removed leaving 628 aromatic amines.

The final amine set was clustered using a python implementation of the Taylor-Butina algorithm¹⁰ with a radius 3 Morgan fingerprint set to 2048 bits and similarity threshold 0.6. This resulted in 116 clusters and 177 singletons. Where physical availability allowed a cluster representative from each cluster was selected followed by backfilling with singleton compounds. After the final reagents were secured, the final products were enumerated utilizing the combinatorial library module in CCG MOE¹¹. The exact mass descriptor was calculated in RDKit³ for mass analysis. Visual representation of the amine set was achieved by plotting the t-sne¹² as implemented within *Konstanz Information Miner (KNIME)* version 4.7.6¹ derived from the RDKit radius 3 morgan fingerprint set to 2048 bits as shown in Extended Data Fig. 6a. Settings for t-sne: 2 dimensions, 5000 iterations, Theta 0.2, 7 threads.

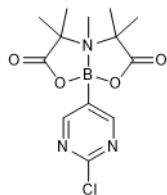
2. Synthesis

2.1 Synthesis of TIDA boronate building blocks

General procure 1 (GP1) Synthesis of TIDA boronate building blocks



TIDA boronates were prepared directly from commercial halo-boronic acids *via* dehydrative condensation with the free TIDA ligand. Boronic acid (25 mmol, 1 equiv.) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (25 mmol, 1 equiv.) were suspended in 1:2 DMSO/benzene (125:250 mL). A Dean-Stark apparatus fitted with a reflux condenser was attached and the mixture was heated to reflux for 3 h, periodically draining the collection trap a total of 3 times. The reaction mixture was cooled to room temperature, diluted with EtOAc (500 mL), transferred to a separatory funnel, washed with 50% of brine (3 x 500 mL), dried over Na₂SO₄, filtered through cotton, and concentrated *in vacuo*. The residue was suspended in acetone (5 mL) and 1:1 hexanes/Et₂O (500 mL) was added causing precipitation of the TIDA boronate product which was collected by vacuum filtration onto a medium porosity fritted funnel. ¹H, ¹⁹F, and ¹³C NMR data were collected, and product identity and purity were further characterized by QC and HRMS (see *Extended Tabular Data Sheet 60*).



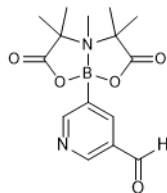
1

(2-chloropyrimidin-5-yl)boronic acid TIDA ester (**1**)

Prepared according to **GP1** using (2-chloropyrimidin-5-yl)boronic acid (12 g, 74 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (15 g, 74 mmol) in 54% yield (13 g).

^1H NMR (500 MHz, DMSO) δ 1.41 (s, 6H), 1.68 (s, 6H), 2.70 (s, 3H), 8.76 (s, 2H).

^{13}C NMR (126 MHz, DMSO) δ 36.5, 54.9, 161.1, 164.8, 174.3.



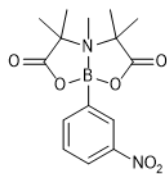
2

(5-formylpyridin-3-yl)boronic acid TIDA ester (**2**)

Prepared according to **GP1** using (5-formylpyridin-3-yl)boronic acid (1 g, 5 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (0.75 g, 5 mmol) in 45% yield (0.71 g).

^1H NMR (500 MHz, DMSO) δ 1.43 (s, 6H), 1.69 (s, 6H), 2.67 (s, 3H), 8.32 (s, 1H), 8.89 (s, 1H), 9.05 (s, 1H), 10.13 (s, 1H).

^{13}C NMR (126 MHz, DMSO) δ 36.7, 130.5, 141.4, 151.4, 158.9, 174.5, 192.9.



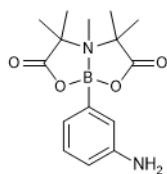
S109

3-nitrophenyl)boronic acid TIDA ester (**S109**)

Prepared according to **GP1** using 3-nitrophenyl)boronic acid (2 g, 10 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (1.7 g, 10 mmol) in 90% yield (3.0 g) of 3-nitrophenyl)boronic acid TIDA ester.

^1H NMR (500 MHz, DMSO) δ 1.43 (s, 6H), 1.69 (s, 6H), 2.65 (s, 3H), 7.66 (t, J = 7.8 Hz, 2H), 7.94 (d, J = 7.6 Hz, 1H), 8.22 (d, J = 8.7 Hz, 1H), 8.29 (s, 1H).

^{13}C NMR (126 MHz, DMSO) δ 36.8, 123.8, 127.7, 129.3, 140.2, 147.5, 174.6.



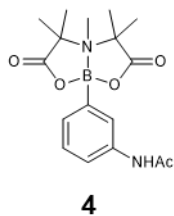
3

(3-aminophenyl)boronic acid TIDA ester (**3**)

Then 3-nitrophenyl)boronic acid TIDA ester **S109** and Pd/C (0.6 g, 0.3 mmol) were suspended in DMF (133 mL) and sparged with N_2 . The mixture was sparged with H_2 and kept under a positive pressure of H_2 for 36 h at room temperature and heat at 45 °C overnight to complete conversion. 55% yield (1.5 g) of (3-aminophenyl)boronic acid TIDA ester was obtained.

^1H NMR (500 MHz, DMSO) δ 1.45 (s, 6H), 1.65 (s, 6H), 2.52 (s, 3H), 4.92 (s, 2H), 6.52 (d, J = 7.6 Hz, 1H), 6.61 (d, J = 7.3 Hz, 1H), 6.71 (s, 1H), 6.98 (t, J = 7.6 Hz, 1H).

^{13}C NMR (126 MHz, DMSO) δ 37.3, 114.3, 121.4, 127.9, 147.7, 175.0.

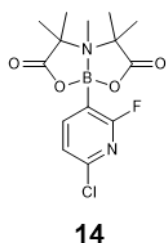


N-(3-(dihydroxymethyl)phenyl)acetamide (**4**)

Prepared according to **GP1** using N-(3-(dihydroxymethyl)phenyl)acetamide (2 g, 10 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (1.8 g, 10 mmol) in 90% yield (3.1 g).

^1H NMR (500 MHz, DMSO) δ 1.44 (s, 6H), 1.67 (s, 6H), 2.01 (s, 3H), 2.53 (s, 3H), 7.14 (d, J = 7.3 Hz, 1H), 7.26 (t, J = 7.8 Hz, 1H), 7.50 (s, 1H), 7.73 (d, J = 7.9 Hz, 1H), 9.90 (s, 1H).

^{13}C NMR (126 MHz, DMSO) δ 23.9, 37.2, 119.6, 124.3, 127.8, 128.4, 138.6, 168.2, 174.8.



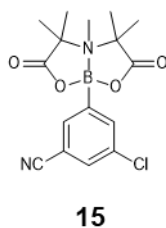
(6-chloro-2-fluoropyridin-3-yl)boronic acid TIDA ester (**14**)

Prepared according to **GP1** using (6-chloro-2-fluoropyridin-3-yl)boronic acid (1.0 g, 5.7 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (1.2 g, 5.7 mmol) in 74% yield (1.4 g).

^1H NMR (500 MHz, DMSO) δ 1.43 (s, 6H), 1.68 (s, 6H), 2.65 (s, 3H), 7.49 (dd, J = 7.7, 1.6 Hz, 1H), 8.00 (m, 1H).

^{13}C NMR (126 MHz, DMSO) δ 36.6, 36.6, 122.1 (d, J = 4.5 Hz), 148.6 (d, J = 15.0 Hz), 150.3 (d, J = 7.7 Hz), 164.2 (d, J = 244.3 Hz), 174.2.

^{19}F NMR (471 MHz, DMSO) δ -57.02.

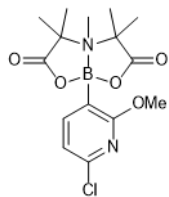


(3-chloro-5-cyanophenyl)boronic acid TIDA ester (**15**)

Prepared according to **GP1** using (3-chloro-5-cyanophenyl)boronic acid (0.9 g, 5 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (1.0 g, 5 mmol) in 77% yield (1.3 g).

^1H NMR (500 MHz, DMSO) δ 1.41 (s, 6H), 1.67 (s, 6H), 2.68 (s, 3H), 7.81 (s, 1H), 7.89 (s, 1H), 8.03 (s, 1H).

^{13}C NMR (126 MHz, DMSO) δ 36.6, 112.9, 117.8, 132.0, 133.7, 135.9, 137.8, 174.4.



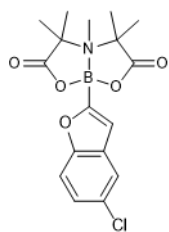
16

(6-chloro-2-methoxypyridin-3-yl)boronic acid TIDA ester (**16**)

Prepared according to **GP1** using (6-chloro-2-methoxypyridin-3-yl)boronic acid (1.0 g, 5.3 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (1.1 g, 5.3 mmol) in 66% yield (1.2 g).

^1H NMR (500 MHz, DMSO) δ 1.42 (s, 6H), 1.65 (s, 6H), 2.60 (s, 3H), 3.81 (s, 3H), 7.08 (d, $J = 7.6$ Hz, 1H), 7.73 (d, $J = 7.6$ Hz, 1H).

^{13}C NMR (126 MHz, DMSO) δ 36.9, 53.8, 116.4, 147.8, 148.4, 165.9, 174.4.



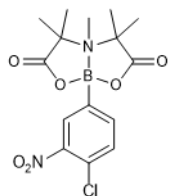
17

(5-chlorobenzofuran-2-yl)boronic acid TIDA ester (**17**)

Prepared according to **GP1** using (5-chlorobenzofuran-2-yl)boronic acid (1.0 g, 5 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (1.0 g, 5 mmol) in 83% yield (1.5 g).

^1H NMR (500 MHz, DMSO) δ 1.54 (s, 6H), 1.69 (s, 6H), 2.64 (s, 3H), 7.13 (s, 1H), 7.32 (dd, $J = 8.7, 2.2$ Hz, 1H), 7.62 (d, $J = 8.7$ Hz, 1H), 7.72 (d, $J = 2.2$ Hz, 1H).

^{13}C NMR (126 MHz, DMSO) δ 37.2, 112.8, 115.2, 120.7, 124.5, 126.9, 129.5, 155.1, 174.4.



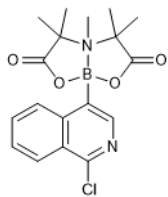
18

(4-chloro-3-nitrophenyl)boronic acid TIDA ester (**18**)

Prepared according to **GP1** using (4-chloro-3-nitrophenyl)boronic acid (1.0 g, 5 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (1.0 g, 5 mmol) in 79% yield (1.5 g).

^1H NMR (500 MHz, DMSO) δ 1.42 (s, 6H), 1.67 (s, 6H), 2.65 (s, 3H), 7.74 (d, $J = 8.0$ Hz, 1H), 7.78 (d, $J = 8.2$ Hz, 1H), 8.12 (s, 1H).

^{13}C NMR (126 MHz, DMSO) δ 36.7, 125.5, 130.2, 130.9, 138.7, 147.4, 174.5.



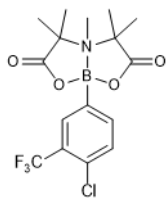
19

(1-chloroisoquinolin-4-yl)boronic acid TIDA ester (**19**)

Prepared according to **GP1** using (1-chloroisoquinolin-4-yl)boronic acid (1.0 g, 5 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (1.0 g, 5 mmol) in 64% yield (1.2 g).

^1H NMR (500 MHz, DMSO) δ 1.50 (s, 6H), 1.73 (s, 6H), 2.63 (s, 3H), 7.80 (t, J = 7.6 Hz, 1H), 7.89 (m, 1H), 8.16 (s, 1H), 8.36 (d, J = 9.2 Hz, 2H).

^{13}C NMR (126 MHz, DMSO) δ 37.4, 125.8, 126.5, 128.4, 131.7, 140.6, 148.9, 152.9, 174.6.



20

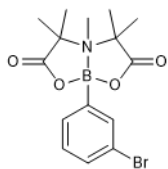
(4-chloro-3-(trifluoromethyl)phenyl)boronic acid TIDA ester (**20**)

Prepared according to **GP1** using (4-chloro-3-(trifluoromethyl)phenyl)boronic acid (1.1 g, 5 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (1.0 g, 5 mmol) in 84% yield (1.6 g).

^1H NMR (500 MHz, DMSO) δ 1.41 (s, 6H), 1.67 (s, 6H), 2.64 (s, 3H), 7.71 (d, J = 8.1 Hz, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.86 (s, 1H).

^{13}C NMR (126 MHz, DMSO) δ 37.2, 123.6 (q, J = 273.0 Hz), 126.4 (q, J = 30.1 Hz), 131.4, 132.0, 132.7 (q, J = 5.0 Hz), 139.8, 175.1.

^{19}F NMR (471 MHz, DMSO) δ -60.85.



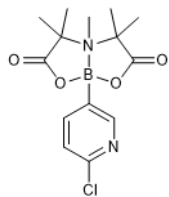
S1

(3-bromophenyl)boronic acid TIDA ester (**S1**)

Prepared according to **GP1** using (3-bromophenyl)boronic acid TIDA ester (2.0 g, 10 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (2.0 g, 10 mmol) in 76% yield (2.8 g).

^1H NMR (500 MHz, DMSO) δ 1.42 (s, 6H), 1.66 (s, 6H), 2.61 (s, 3H), 7.32 (t, J = 7.7 Hz, 1H), 7.47 (d, J = 7.4 Hz, 1H), 7.55 (dd, J = 7.9, 2.1 Hz, 1H), 7.63 (d, J = 2.1 Hz, 1H).

^{13}C NMR (126 MHz, DMSO) δ 36.9, 121.7, 130.0, 131.6, 132.4, 136.0, 174.7.



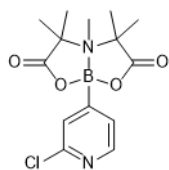
S2

(6-chloropyridin-3-yl)boronic acid TIDA ester (**S2**)

Prepared according to **GP1** using (6-chloropyridin-3-yl)boronic acid (3.9 g, 25 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (5.1 g, 25 mmol) in 83% yield (6.7 g).

^1H NMR (500 MHz, DMSO) δ 1.41 (s, 6H), 1.67 (s, 6H), 2.63 (s, 3H), 7.49 (d, J = 8.0 Hz, 1H), 7.90 (dd, J = 8.2, 2.2 Hz, 1H), 8.44 (d, J = 2.3 Hz, 1H).

^{13}C NMR (126 MHz, DMSO) δ 36.7, 123.6, 144.8, 151.1, 154.6, 174.5.



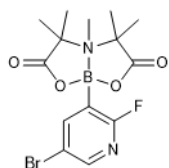
S3

(2-chloropyridin-4-yl)boronic acid TIDA ester (**S3**)

Prepared according to **GP1** using (2-chloropyridin-4-yl)boronic acid (3.9 g, 25 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (5.1 g, 25 mmol) in 80% yield (6.5 g).

^1H NMR (500 MHz, DMSO) δ 1.41 (s, 6H), 1.67 (s, 6H), 2.67 (s, 3H), 7.47 (d, J = 4.8 Hz, 1H), 7.55 (s, 1H), 8.39 (d, J = 4.8 Hz, 1H).

^{13}C NMR (126 MHz, DMSO) δ 36.7, 127.5, 128.7, 149.2, 150.2, 174.4.



S4

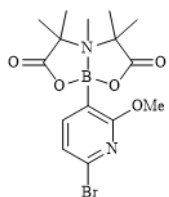
(5-bromo-2-fluoropyridin-3-yl)boronic acid TIDA ester (**S4**)

Prepared according to **GP1** using (5-bromo-2-fluoropyridin-3-yl)boronic acid (5.1 g, 23 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (4.7 g, 23 mmol) in 53% yield (4.7 g).

^1H NMR (500 MHz, DMSO) δ 1.43 (s, 6H), 1.68 (s, 6H), 2.68 (s, 3H), 8.07 (dd, J = 8.0, 2.7 Hz, 1H), 8.42 (d, J = 2.5 Hz, 1H).

^{13}C NMR (126 MHz, DMSO) δ 36.6, 36.6, 116.7 (d, J = 4.4 Hz), 149.1 (d, J = 8.2 Hz), 149.4 (d, J = 16.8 Hz), 164.5 (d, J = 238.2 Hz), 174.1.

^{19}F NMR (471 MHz, DMSO) δ -61.33.



S5

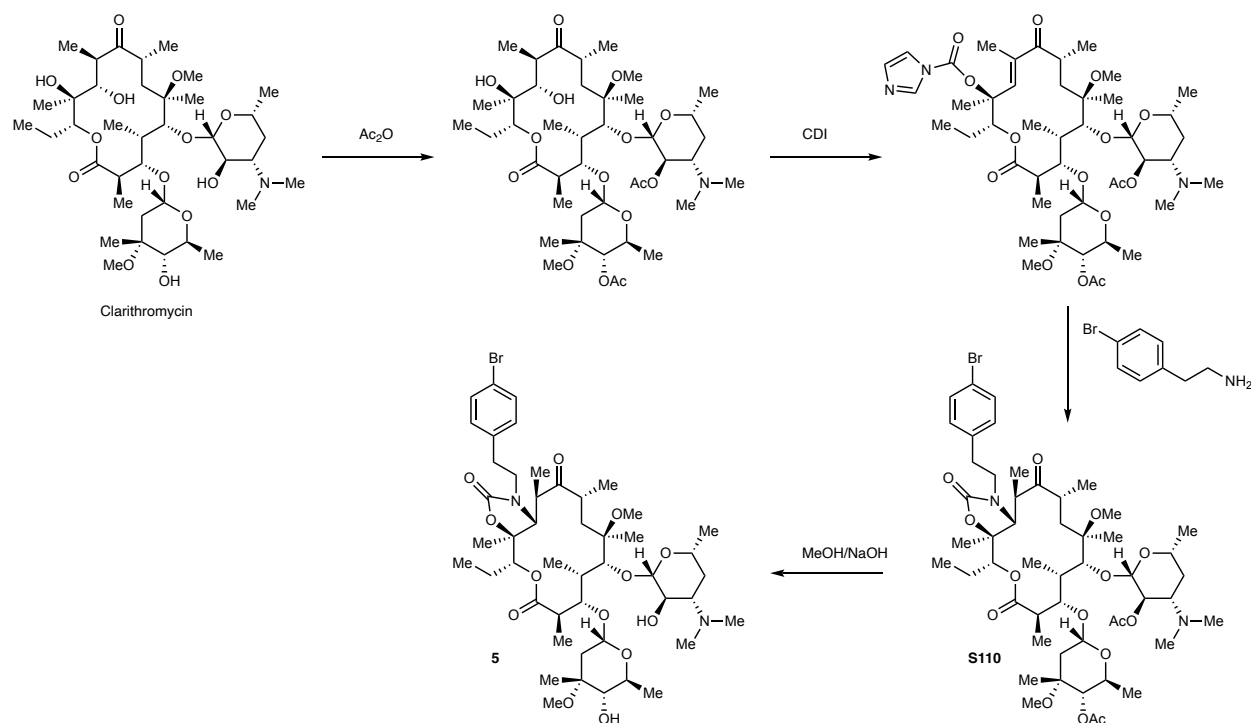
(6-bromo-2-methoxypyridin-3-yl)boronic acid TIDA ester (**S5**)

Prepared according to **GP1** using (6-bromo-2-methoxypyridin-3-yl)boronic acid (5.8 g, 25 mmol) and 2,2'-(methylazanediyl)bis(2-methylpropanoic acid) (5.1 g, 25 mmol) in 84% yield (8.4 g).

^1H NMR (500 MHz, DMSO) δ 1.42 (s, 6H), 1.65 (s, 6H), 2.60 (s, 3H), 3.81 (s, 3H), 7.22 (d, J = 7.5 Hz, 1H), 7.62 (d, J = 7.5 Hz, 1H).

^{13}C NMR (126 MHz, DMSO) δ 36.9, 53.9, 120.4, 139.3, 147.5, 165.8, 174.4.

2.2 Synthesis of clarithromycin derivative (5)

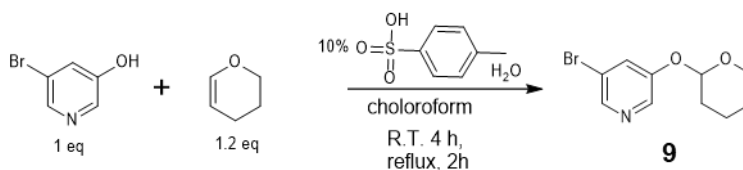


A solution of diacetylated clarithromycin imidazole-carbamate¹³ (700 mg, 0.77 mmol) and 2-(4-bromophenyl)ethan-1-amine (0.60 mL, 3.9 mmol) in DMF (2.5 mL) was heated to 35 °C for 48 h under inert atmosphere. Reaction was monitored by LC-MS and product was confirmed. Solution was cooled to 0 °C and water added. After addition of water, precipitated that formed was filtered, dissolved in dichloromethane (DCM), and dried over Na_2SO_4 . Solution was concentrated *in vacuo*, frozen, and left overnight in the lyophilizer to remove traces of DMF to provide **S110** which was carried forward into a deprotection step using $\text{NaOH}_{(\text{s})}$ (1 eq.) and MeOH (20 mL, 0.04 M) and refluxed for 1.5 h, TLC (10 % MeOH – DCM) and LC-MS showed formation of product. The reaction mixture was concentrated down to give **5** in 70% yield over two steps (518 mg).

^1H NMR (500 MHz, CDCl_3) δ 0.82 (t, $J = 7.3$ Hz, 3H), 1.02 (d, $J = 6.8$ Hz, 3H), 1.11 (d, $J = 7.5$ Hz, 3H), 1.15 (d, $J = 7.1$ Hz, 3H), 1.21 (d, $J = 7.1$ Hz, 3H), 1.23 – 1.26 (m, 6H), 1.30 (d, $J = 6.3$ Hz, 3H), 1.41 (d, $J = 11.6$ Hz, 6H), 1.48 – 1.55 (m, 1H), 1.58 (dd, $J = 15.5, 5.2$ Hz, 1H), 1.69 – 1.77 (m, 3H), 1.84 – 1.94 (m, 3H), 2.35 (s, 1H), 2.37 (s, 6H), 2.56 – 2.66 (m, 3H), 2.81 – 2.93 (m, 3H), 2.94 – 3.00 (m, 1H), 3.02 (d, $J = 9.3$ Hz, 1H), 3.06 (s, 3H), 3.11 (q, $J = 6.9$ Hz, 1H), 3.23 (t, $J = 8.8$ Hz, 1H), 3.33 (s, 3H), 3.47 – 3.53 (m, 1H), 3.66 (d, $J = 7.4$ Hz, 1H), 3.69 (s, 1H), 3.73 (d, $J = 9.5$ Hz, 1H), 3.79 – 3.86 (m, 2H), 4.00 (p, $J = 6.5$ Hz, 1H), 4.45 (d, $J = 7.1$ Hz, 1H), 4.88 – 4.94 (m, 2H), 7.21 (d, $J = 7.9$ Hz, 2H), 7.39 (d, $J = 7.9$ Hz, 2H).

^{13}C NMR (126 MHz, CDCl_3) δ 9.2, 10.4, 14.3, 14.4, 16.2, 18.8, 19.0, 20.3, 21.6, 21.6, 22.1, 29.1, 33.0, 35.0, 39.1, 39.2, 40.2, 45.1, 45.4, 45.7, 49.6, 50.8, 60.5, 65.6, 65.9, 68.7, 71.0, 72.8, 78.0, 78.1, 79.0, 80.5, 96.4, 103.0, 120.1, 130.9, 131.6, 138.0, 157.4, 176.6, 216.5.

2.3 Synthesis of THP protected alcohol (**9**)



3-bromo-5-((tetrahydro-2H-pyran-2-yl)oxy)pyridine (**9**)

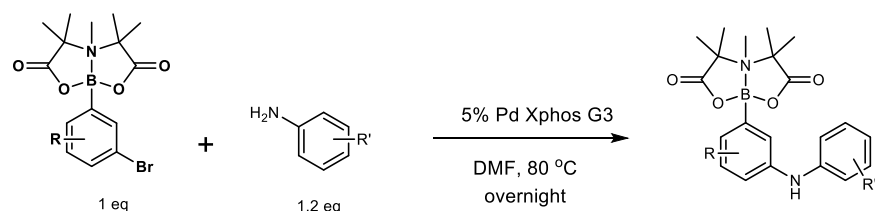
5-bromopyridin-3-ol (1.0 g, 5.7 mmol, 1 eq), 3,4-dihydro-2H-pyran (0.6 g, 6.9 mmol, 1.2 eq) and 4-methylbenzenesulfonic acid (0.1 g, 0.6 mmol, 10 %) were stirred in chloroform (10 mL) at room temperature for 4 hours. LC-MS analysis indicated incomplete conversion so the mixture was additionally heated at reflux for 2 hours. Upon completion the crude mixture was purified by column chromatography to afford **9** in 37% yield (550 mg).

^1H NMR (500 MHz, DMSO) δ 1.49 – 1.66 (m, 3H), 1.71 – 1.91 (m, 3H), 3.55 – 3.63 (m, 1H), 3.70 (ddd, J = 12.5, 9.5, 3.4 Hz, 1H), 5.66 (t, J = 3.0 Hz, 1H), 7.75 (t, J = 2.2 Hz, 1H), 8.33 (d, J = 1.9 Hz, 1H), 8.35 (d, J = 2.4 Hz, 1H).

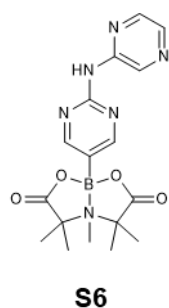
^{13}C NMR (126 MHz, DMSO) δ 18.1, 24.5, 29.3, 61.5, 96.1, 119.8, 125.9, 138.2, 143.0, 153.2.

2.4 Synthesis of 60 TIDA boronate test set (Extended Data Fig. 1a)

General procure 2 (GP2) Synthesis of TIDA boronates using Buchwald-Hartwig reactions



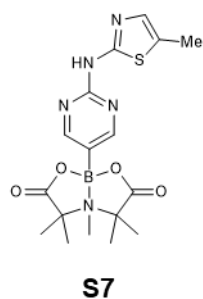
In a N₂ filled glovebox, aryl halide (1 eq, 0.2 mmol), aryl amine (1.2 eq, 0.24 mmol), PdXPhos G3 (5%, 10 μmol, 8.46 mg), and Cs₂CO₃ (2 eq, 0.4 mmol, 130 mg) were added to a dry screw-capped vial equipped with a magnetic stir bar, followed by anhydrous DMF (1 mL). The vial was sealed with a cap fitted with a PTFE septum and removed from the glovebox. The reaction mixture was stirred at 80 °C overnight. Crude reaction mixtures were filtered prior to automated preparative LC-MS purification using UV and mass spectrum signal monitoring. Only single pure tubes were collected for further utilization to obtain mg amounts and so no yields are reported post purification. ¹H NMR data were collected, and product identity and purity were further characterized by QC and HRMS (see *Extended Tabular Data Sheet 60*).



(2-(pyrazin-2-ylamino)pyrimidin-5-yl)boronic acid TIDA ester (**S6**)

Prepared according to **GP2** using TIDA boronate **1** (65.1 mg, 0.2 mmol) and pyrazin-2-amine (22.8 mg, 0.24 mmol).

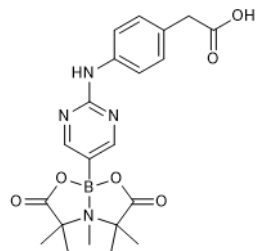
¹H NMR (500 MHz, DMSO) δ 1.45 (s, 6H), 1.68 (s, 6H), 2.68 (s, 3H), 8.22 (d, *J* = 2.6 Hz, 1H), 8.33 (t, *J* = 2.1 Hz, 1H), 8.58 (s, 2H), 9.52 (d, *J* = 1.5 Hz, 1H), 10.36 (s, 1H).



(2-((5-methylthiazol-2-yl)amino)pyrimidin-5-yl)boronic acid TIDA ester (**S7**)

Prepared according to **GP2** using TIDA boronate **1** (65.1 mg, 0.2 mmol) and 5-methylthiazol-2-amine (22.8 mg, 0.24 mmol).

¹H NMR (500 MHz, DMSO) δ 1.45 (s, 6H), 1.67 (s, 6H), 2.34 (s, 3H), 2.67 (s, 3H), 7.08 (d, *J* = 1.5 Hz, 1H), 8.56 (s, 2H), 11.52 (s, 1H).

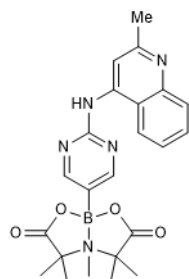


S8

2-(4-((5-boronopyrimidin-2-yl)amino)phenyl)acetic acid TIDA ester (**S8**)

Prepared according to **GP2** using TIDA boronate **1** (65.1 mg, 0.2 mmol) and 2-(4-aminophenyl)acetic acid (27.4 mg, 0.24 mmol).

¹H NMR (500 MHz, DMSO) δ 1.45 (s, 6H), 1.67 (s, 6H), 2.66 (s, 3H), 3.48 (s, 2H), 7.16 (m, 2H), 7.68 (m, 2H), 8.44 (s, 2H), 9.67 (s, 1H), 12.22 (s, 1H).

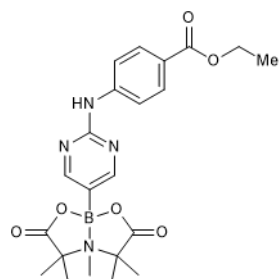


S9

2-(4-((5-boronopyrimidin-2-yl)amino)phenyl)acetic acid TIDA ester (**S9**)

Prepared according to **GP2** using TIDA boronate **1** (65.1 mg, 0.2 mmol) and 2-methylquinolin-4-amine (38.0 mg, 0.24 mmol).

¹H NMR (500 MHz, DMSO) δ 1.47 (s, 6H), 1.69 (s, 6H), 2.60 (s, 3H), 2.70 (s, 3H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 8.21 (s, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 8.61 (s, 2H), 9.99 (s, 1H).

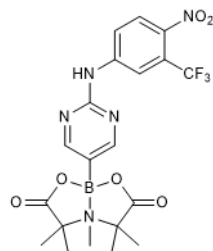


S10

(2-((4-(ethoxycarbonyl)phenyl)amino)pyrimidin-5-yl)boronic acid TIDA ester (**S10**)

Prepared according to **GP2** using TIDA boronate **1** (65.1 mg, 0.2 mmol) and ethyl 4-aminobenzoate (39.6 mg, 0.24 mmol).

¹H NMR (500 MHz, DMSO) δ 1.30 (t, *J* = 7.2 Hz, 3H), 1.46 (s, 6H), 1.68 (s, 6H), 2.68 (s, 3H), 4.27 (q, *J* = 7.2 Hz, 2H), 7.88 (m, 2H), 7.94 (m, 2H), 8.54 (s, 1H).

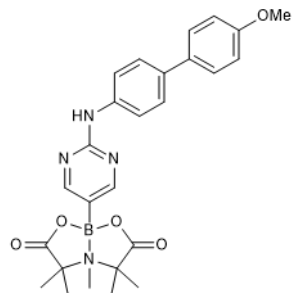


S11

(2-((4-nitro-3-(trifluoromethyl)phenyl)amino)pyrimidin-5-yl)boronic acid TIDA ester (**S11**)

Prepared according to **GP2** using TIDA boronate **1** (65.1 mg, 0.2 mmol) and 4-nitro-3-(trifluoromethyl)aniline (49.5 mg, 0.24 mmol).

¹H NMR (400 MHz, DMSO) δ 1.45 (s, 6H), 1.68 (s, 6H), 2.69 (s, 3H), 8.21 (d, *J* = 9.1 Hz, 1H), 8.27 (dd, *J* = 9.1, 2.3 Hz, 1H), 8.55 (d, *J* = 2.3 Hz, 1H), 8.64 (s, 2H), 10.76 (s, 1H).

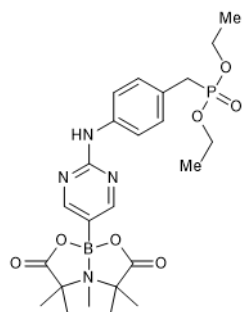


S12

(2-((4'-methoxy-[1,1'-biphenyl]-4-yl)amino)pyrimidin-5-yl)boronic acid TIDA ester (**S12**)

Prepared according to **GP2** using TIDA boronate **1** (65.1 mg, 0.2 mmol) and 4'-methoxy-[1,1'-biphenyl]-4-amine (47.8 mg, 0.24 mmol).

¹H NMR (500 MHz, DMSO) δ 1.46 (s, 6H), 1.68 (s, 6H), 2.67 (s, 3H), 3.78 (s, 3H), 6.99 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 8.6 Hz, 2H), 7.57 (d, J = 8.6 Hz, 2H), 7.84 (d, J = 8.6 Hz, 2H), 8.48 (s, 2H), 9.80 (s, 1H).

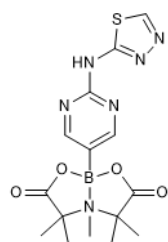


S13

(2-((4-((diethoxyphosphoryl)methyl)phenyl)amino)pyrimidin-5-yl)boronic acid TIDA ester (**S13**)

Prepared according to **GP2** using TIDA boronate **1** (65.1 mg, 0.2 mmol) and diethyl (4-aminobenzyl)phosphonate (58.4 mg, 0.24 mmol).

¹H NMR (500 MHz, DMSO) δ 1.17 (t, J = 7.0 Hz, 6H), 1.45 (s, 6H), 1.67 (s, 6H), 2.65 (s, 3H), 3.15 (d, J = 21.3 Hz, 2H), 3.93 (p, J = 7.3 Hz, 4H), 7.17 (dd, J = 8.7, 2.5 Hz, 2H), 7.69 (d, J = 8.3 Hz, 2H), 8.45 (s, 2H), 9.69 (s, 1H).

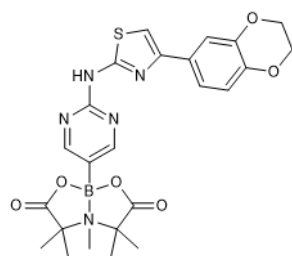


S14

(2-((1,3,4-thiadiazol-2-yl)amino)pyrimidin-5-yl)boronic acid TIDA ester (**S14**)

Prepared according to **GP2** using TIDA boronate **1** (65.1 mg, 0.2 mmol) and 1,3,4-thiadiazol-2-amine (24.3 mg, 0.24 mmol).

¹H NMR (500 MHz, DMSO) δ 1.45 (s, 6H), 1.68 (s, 6H), 2.69 (s, 3H), 8.64 (s, 2H), 9.08 (s, 1H), 12.18 (s, 1H).

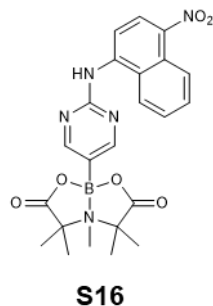


S15

(2-((4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thiazol-2-yl)amino)pyrimidin-5-yl)boronic acid TIDA ester (**S15**)

Prepared according to **GP2** using TIDA boronate **1** (65.1 mg, 0.2 mmol) and 4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thiazol-2-amine (56.2 mg, 0.24 mmol).

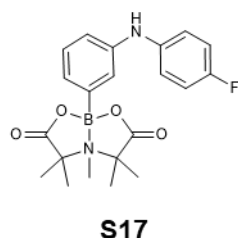
¹H NMR (400 MHz, DMSO) δ 1.46 (s, 6H), 1.68 (s, 6H), 2.69 (s, 3H), 4.27 (s, 4H), 6.89 (d, J = 8.3 Hz, 1H), 7.33 – 7.45 (m, 3H), 8.61 (s, 2H), 11.80 (s, 1H).



(2-((4-nitronaphthalen-1-yl)amino)pyrimidin-5-yl)boronic acid TIDA ester (**S16**)

Prepared according to **GP2** using TIDA boronate **1** (65.1 mg, 0.2 mmol) and 4-nitronaphthalen-1-amine (45.2 mg, 0.24 mmol).

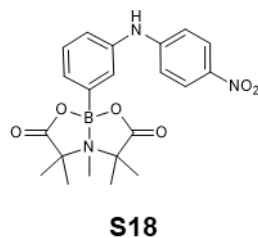
^1H NMR (400 MHz, DMSO) δ 1.47 (s, 6H), 1.68 (s, 6H), 2.69 (s, 3H), 7.69 (ddd, J = 8.3, 6.8, 1.2 Hz, 1H), 7.82 (ddd, J = 9.1, 7.5, 1.2 Hz, 1H), 8.26 (d, J = 8.7 Hz, 1H), 8.42 (d, J = 8.7 Hz, 1H), 8.49 (d, J = 8.6 Hz, 1H), 8.57 (s, 2H), 8.59 (m, 1H), 10.25 (s, 1H).



(3-((4-fluorophenyl)amino)phenyl)boronic acid TIDA ester (**S17**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 4-fluoroaniline (26.7 mg, 0.24 mmol).

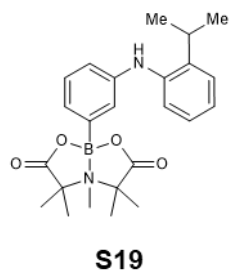
^1H NMR (500 MHz, DMSO) δ 1.46 (s, 6H), 1.66 (s, 6H), 2.57 (s, 3H), 6.93 (d, J = 7.3 Hz, 1H), 6.99 – 7.08 (m, 5H), 7.11 (m, 1H), 7.19 (t, J = 7.7 Hz, 1H), 8.07 (s, 1H).



(3-((4-nitrophenyl)amino)phenyl)boronic acid TIDA ester (**S18**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 4-nitroaniline (33.2 mg, 0.24 mmol).

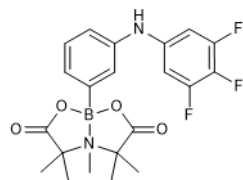
^1H NMR (500 MHz, DMSO) δ 1.47 (s, 6H), 1.67 (s, 6H), 2.61 (s, 3H), 7.01 (d, J = 9.2 Hz, 2H), 7.23 (d, J = 7.3 Hz, 1H), 7.27 (d, J = 6.0 Hz, 1H), 7.31 (d, J = 2.3 Hz, 1H), 7.37 (d, J = 7.6 Hz, 1H), 8.08 (d, J = 9.0 Hz, 2H), 9.32 (s, 1H).



(3-((2-isopropylphenyl)amino)phenyl)boronic acid TIDA ester (**S19**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 2-isopropylaniline (32.5 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.15 (d, J = 6.8 Hz, 6H), 1.46 (s, 6H), 1.66 (s, 6H), 2.56 (s, 3H), 3.25 (p, J = 6.9 Hz, 1H), 6.78 (dd, J = 8.0, 2.4 Hz, 1H), 6.84 (d, J = 7.3 Hz, 1H), 7.01 (dt, J = 10.5, 2.9 Hz, 2H), 7.08 (m, 1H), 7.12 (t, J = 7.7 Hz, 1H), 7.29 (d, J = 7.0 Hz, 1H), 7.31 (s, 1H).

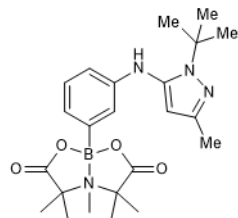


S20

(3-((3,4,5-trifluorophenyl)amino)phenyl)boronic acid TIDA ester (**S20**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 3,4,5-trifluoroaniline (35.3 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.46 (s, 6H), 1.67 (s, 6H), 2.59 (s, 3H), 6.73 (dd, $J = 10.7, 6.0$ Hz, 2H), 7.09 (d, $J = 7.4$ Hz, 1H), 7.18 (d, $J = 2.3$ Hz, 1H), 7.29 (s, 1H), 8.51 (s, 1H).

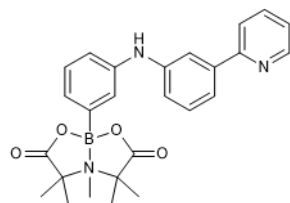


S21

(3-((1-(tert-butyl)-3-methyl-1H-pyrazol-5-yl)amino)phenyl)boronic acid TIDA ester (**S21**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 1-(tert-butyl)-3-methyl-1H-pyrazol-5-amine (36.8 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.44 (s, 6H), 1.50 (s, 9H), 1.65 (s, 6H), 2.09 (s, 3H), 2.52 (s, 3H), 5.76 (s, 1H), 6.58 (dd, $J = 7.8, 1.3$ Hz, 1H), 6.79 (d, $J = 7.3$ Hz, 1H), 6.88 (s, 1H), 7.09 (t, $J = 7.7$ Hz, 1H), 7.25 (s, 1H).

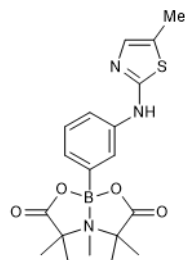


S22

(3-((3-(pyridin-2-yl)phenyl)amino)phenyl)boronic acid TIDA ester (**S22**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 3-(pyridin-2-yl)aniline (40.9 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.46 (s, 6H), 1.67 (s, 6H), 2.59 (s, 3H), 6.99 (d, $J = 7.3$ Hz, 1H), 7.06 (dd, $J = 8.1, 2.2$ Hz, 1H), 7.10 (m, 1H), 7.15 (dd, $J = 8.0, 2.3$ Hz, 1H), 7.24 (d, $J = 7.6$ Hz, 1H), 7.28 (d, $J = 7.8$ Hz, 1H), 7.34 (t, $J = 7.9$ Hz, 1H), 7.47 (dd, $J = 7.9, 4.8$ Hz, 1H), 7.99 (dt, $J = 8.0, 2.1$ Hz, 1H), 8.32 (s, 1H), 8.56 (dd, $J = 4.8, 1.6$ Hz, 1H), 8.80 (d, $J = 2.3$ Hz, 1H).

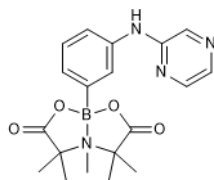


S23

(3-((5-methylthiazol-2-yl)amino)phenyl)boronic acid TIDA ester (**S23**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 5-methylthiazol-2-amine (27.4 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.46 (s, 6H), 1.67 (s, 6H), 2.27 (d, $J = 1.3$ Hz, 3H), 2.55 (s, 3H), 6.87 (d, $J = 1.5$ Hz, 1H), 7.03 (m, 1H), 7.25 (t, $J = 7.7$ Hz, 1H), 7.43 (t, $J = 1.7$ Hz, 1H), 7.80 (dd, $J = 8.1, 2.4$ Hz, 1H), 9.90 (s, 1H).

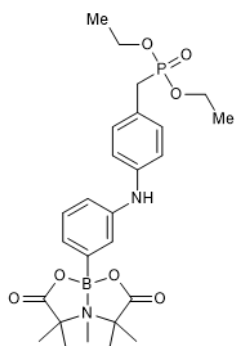


S24

(3-(pyrazin-2-ylamino)phenyl)boronic acid TIDA ester (**S24**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and pyrazin-2-amine (22.8 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.47 (s, 6H), 1.68 (s, 6H), 2.57 (s, 3H), 7.08 (dt, J = 7.4, 1.2 Hz, 1H), 7.28 (t, J = 7.8 Hz, 1H), 7.52 (dd, J = 2.1, 1.3 Hz, 1H), 7.88 (d, J = 2.8 Hz, 1H), 7.94 (ddd, J = 8.2, 2.4, 1.0 Hz, 1H), 8.07 (dd, J = 2.8, 1.4 Hz, 1H), 8.19 (d, J = 1.5 Hz, 1H), 9.46 (s, 1H).

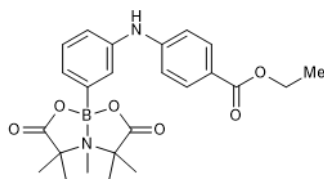


S25

(3-((4-((diethoxyphosphoryl)methyl)phenyl)amino)phenyl)boronic acid TIDA ester (**S25**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and diethyl (4-aminobenzyl)phosphonate (58.4 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.17 (t, J = 7.0 Hz, 6H), 1.47 (s, 6H), 1.66 (s, 6H), 2.57 (s, 3H), 3.09 (d, J = 20.9 Hz, 2H), 3.94 (p, J = 7.3 Hz, 4H), 6.93 (d, J = 7.4 Hz, 1H), 6.96 (d, J = 8.3 Hz, 2H), 7.06 (dd, J = 7.9, 2.3 Hz, 1H), 7.10 (dd, J = 8.6, 2.4 Hz, 2H), 7.16 (d, J = 2.4 Hz, 1H), 7.20 (t, J = 7.7 Hz, 1H), 8.09 (s, 1H).

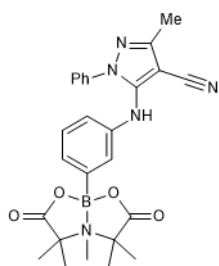


S26

(3-((4-(ethoxycarbonyl)phenyl)amino)phenyl)boronic acid TIDA ester (**S26**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and ethyl 4-aminobenzoate (39.6 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.29 (t, J = 7.1 Hz, 3H), 1.47 (s, 6H), 1.67 (s, 6H), 2.60 (s, 3H), 4.24 (q, J = 7.1 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 7.11 (dd, J = 7.4, 1.3 Hz, 1H), 7.19 (ddd, J = 8.0, 2.4, 1.0 Hz, 1H), 7.26 – 7.28 (m, 1H), 7.31 (t, J = 7.7 Hz, 1H), 7.78 (d, J = 8.8 Hz, 2H), 8.77 (s, 1H).

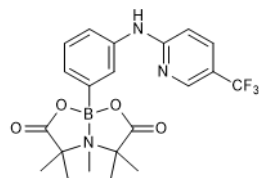


S27

(3-((4-cyano-3-methyl-1-phenyl-1H-pyrazol-5-yl)amino)phenyl)boronic acid TIDA ester (**S27**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 5-amino-3-methyl-1-phenyl-1H-pyrazole-4-carbonitrile (47.6 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.41 (s, 6H), 1.65 (s, 6H), 2.56 (s, 3H), 6.91 (dd, J = 7.9, 1.5 Hz, 3H), 7.01 – 7.09 (m, 2H), 7.20 (t, J = 7.5 Hz, 1H), 7.38 (t, J = 7.3 Hz, 2H), 7.47 (t, J = 8.1 Hz, 2H), 7.54 (d, J = 7.8 Hz, 1H), 8.75 (s, 1H).

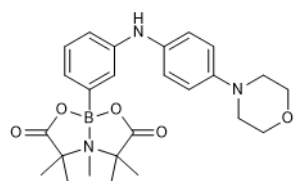


S28

(3-((5-(trifluoromethyl)pyridin-2-yl)amino)phenyl)boronic acid TIDA ester (**S28**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 5-(trifluoromethyl)pyridin-2-amine (38.9 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.47 (s, 6H), 1.68 (s, 6H), 2.58 (s, 3H), 6.89 (d, J = 8.8 Hz, 1H), 7.11 (d, J = 7.4 Hz, 1H), 7.30 (t, J = 7.7 Hz, 1H), 7.55 (t, J = 1.8 Hz, 1H), 7.82 (dd, J = 8.9, 2.6 Hz, 1H), 7.88 (dd, J = 8.1, 2.3 Hz, 1H), 8.43 (d, J = 2.5 Hz, 1H), 9.58 (s, 1H).

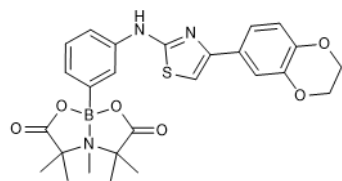


S29

(3-((4-morpholinophenyl)amino)phenyl)boronic acid TIDA ester (**S29**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 4-morpholinoaniline (42.8 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.47 (s, 6H), 1.66 (s, 6H), 2.56 (s, 3H), 2.93 – 3.06 (m, 4H), 3.72 (dd, J = 5.9, 3.5 Hz, 4H), 6.83 (d, J = 7.3 Hz, 1H), 6.86 (d, J = 8.9 Hz, 2H), 6.93 (dd, J = 8.0, 2.4 Hz, 1H), 6.96 (d, J = 8.9 Hz, 2H), 7.06 (d, J = 2.4 Hz, 1H), 7.13 (t, J = 7.7 Hz, 1H), 7.78 (s, 1H).

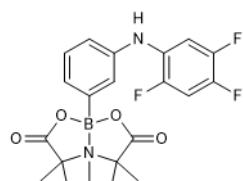


S30

(3-((4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thiazol-2-yl)amino)phenyl)boronic acid TIDA ester (**S30**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thiazol-2-amine (56.2 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.48 (s, 6H), 1.69 (s, 6H), 2.58 (s, 3H), 4.27 (s, 4H), 6.89 (d, J = 8.4 Hz, 1H), 7.08 (d, J = 7.4 Hz, 1H), 7.15 (s, 1H), 7.32 (t, J = 7.7 Hz, 1H), 7.36 (d, J = 2.1 Hz, 1H), 7.39 (dd, J = 8.3, 2.1 Hz, 1H), 7.66 (dd, J = 8.2, 2.3 Hz, 1H), 7.91 (d, J = 2.4 Hz, 1H), 10.19 (s, 1H).

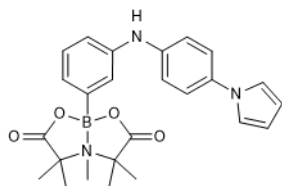


S31

(3-((2,4,5-trifluorophenyl)amino)phenyl)boronic acid TIDA ester (**S31**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 2,4,5-trifluoroaniline (35.3 mg, 0.24 mmol).

^1H NMR (400 MHz, DMSO) δ 1.46 (s, 6H), 1.66 (s, 6H), 2.58 (s, 3H), 7.01 (ddd, J = 10.4, 7.7, 1.8 Hz, 2H), 7.10 – 7.20 (m, 2H), 7.24 (t, J = 7.7 Hz, 1H), 7.52 (td, J = 10.9, 7.5 Hz, 1H), 8.02 (s, 1H).

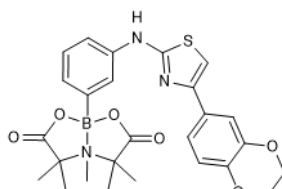


S32

(3-((4-(1H-pyrrol-1-yl)phenyl)amino)phenyl)boronic acid TIDA ester (**S32**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 4-(1H-pyrrol-1-yl)aniline (38.0 mg, 0.24 mmol).

^1H NMR (400 MHz, DMSO) δ 1.48 (s, 6H), 1.67 (s, 6H), 2.59 (s, 3H), 6.21 (t, J = 2.2 Hz, 2H), 6.97 (dt, J = 7.4, 1.2 Hz, 1H), 7.04 – 7.15 (m, 3H), 7.18 (dd, J = 2.4, 1.3 Hz, 1H), 7.20 – 7.27 (m, 3H), 7.36 – 7.43 (m, 2H), 8.21 (s, 1H).

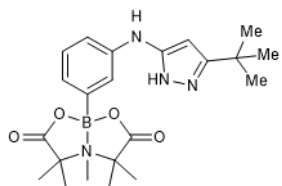


S33

(3-((4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thiazol-2-yl)amino)phenyl)boronic acid TIDA ester (**S33**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thiazol-2-amine (56.2 mg, 0.24 mmol).

^1H NMR (400 MHz, DMSO) δ 1.48 (s, 6H), 1.69 (s, 6H), 2.58 (s, 3H), 4.27 (s, 4H), 6.89 (d, J = 8.4 Hz, 1H), 7.08 (dt, J = 7.4, 1.2 Hz, 1H), 7.15 (s, 1H), 7.32 (t, J = 7.7 Hz, 1H), 7.34 – 7.43 (m, 2H), 7.66 (ddd, J = 8.1, 2.4, 1.1 Hz, 1H), 7.91 (dd, J = 2.4, 1.2 Hz, 1H), 10.19 (s, 1H).

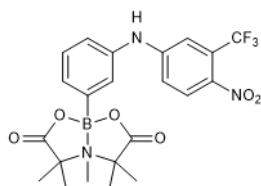


S34

(3-((3-(tert-butyl)-1H-pyrazol-5-yl)amino)phenyl)boronic acid TIDA ester (**S34**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 3-(tert-butyl)-1H-pyrazol-5-amine (33.4 mg, 0.24 mmol).

^1H NMR (400 MHz, DMSO) δ 1.24 (s, 9H), 1.46 (s, 6H), 1.66 (s, 6H), 2.54 (s, 3H), 5.53 (s, 1H), 6.80 (dt, J = 7.3, 1.2 Hz, 1H), 7.13 (t, J = 7.7 Hz, 1H), 7.32 (t, J = 1.3 Hz, 1H), 7.35 – 7.42 (m, 1H), 8.14 (s, 1H), 11.63 (s, 1H).

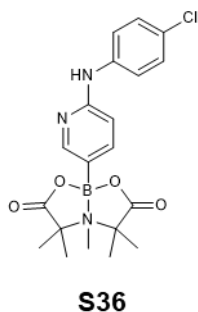


S35

(3-((4-nitro-3-(trifluoromethyl)phenyl)amino)phenyl)boronic acid TIDA ester (**S35**)

Prepared according to **GP2** using TIDA boronate **S1** (73.6 mg, 0.2 mmol) and 4-nitro-3-(trifluoromethyl)aniline (49.5 mg, 0.24 mmol).

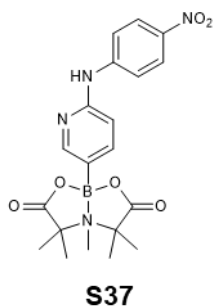
^1H NMR (400 MHz, DMSO) δ 1.46 (s, 6H), 1.68 (s, 6H), 2.62 (s, 3H), 7.20 (dd, J = 9.2, 2.5 Hz, 1H), 7.24 – 7.31 (m, 2H), 7.31 – 7.37 (m, 2H), 7.41 (t, J = 7.7 Hz, 1H), 8.12 (d, J = 9.1 Hz, 1H), 9.56 (s, 1H).



(6-((4-chlorophenyl)amino)pyridin-3-yl)boronic acid TIDA ester (**S36**)

Prepared according to **GP2** using TIDA boronate **S2** (64.9 mg, 0.2 mmol) and 4-chloroaniline (30.6 mg, 0.24 mmol), and purified by prep.

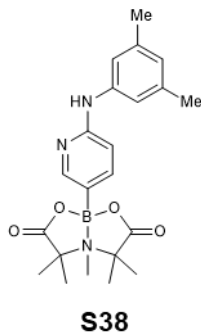
^1H NMR (500 MHz, DMSO) δ 1.44 (s, 6H), 1.66 (s, 6H), 2.58 (s, 3H), 6.80 (d, J = 8.3 Hz, 1H), 7.29 (d, J = 8.9 Hz, 2H), 7.60 (dd, J = 8.4, 2.2 Hz, 1H), 7.71 – 7.77 (m, 2H), 8.19 (d, J = 2.2 Hz, 1H), 9.23 (s, 1H).



(6-((4-nitrophenyl)amino)pyridin-3-yl)boronic acid TIDA ester (**S37**)

Prepared according to **GP2** using TIDA boronate **S2** (64.9 mg, 0.2 mmol) and 4-nitroaniline (33.2 mg, 0.24 mmol).

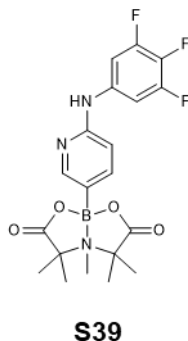
^1H NMR (500 MHz, DMSO) δ 1.45 (s, 6H), 1.67 (s, 6H), 2.61 (s, 3H), 6.96 (d, J = 8.3 Hz, 1H), 7.74 (dd, J = 8.4, 2.1 Hz, 1H), 7.95 (d, J = 9.3 Hz, 2H), 8.17 (d, J = 9.3 Hz, 2H), 8.31 (d, J = 2.1 Hz, 1H), 9.99 (s, 1H).



(6-((3,5-dimethylphenyl)amino)pyridin-3-yl)boronic acid TIDA ester (**S38**)

Prepared according to **GP2** using TIDA boronate **S2** (64.9 mg, 0.2 mmol) and 3,5-dimethylaniline (29.1 mg, 0.24 mmol).

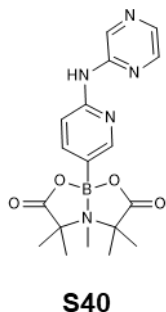
^1H NMR (500 MHz, DMSO) δ 1.45 (s, 6H), 1.66 (s, 6H), 2.22 (s, 6H), 2.59 (s, 3H), 6.53 (s, 1H), 6.78 (dd, J = 8.4, 0.8 Hz, 1H), 7.29 (d, J = 1.5 Hz, 2H), 7.55 (dd, J = 8.4, 2.2 Hz, 1H), 8.18 (d, J = 2.1 Hz, 1H), 8.89 (s, 1H).



(6-((3,4,5-trifluorophenyl)amino)pyridin-3-yl)boronic acid TIDA ester (**S39**)

Prepared according to **GP2** using TIDA boronate **S2** (64.9 mg, 0.2 mmol) and 3,4,5-trifluoroaniline (35.3 mg, 0.24 mmol).

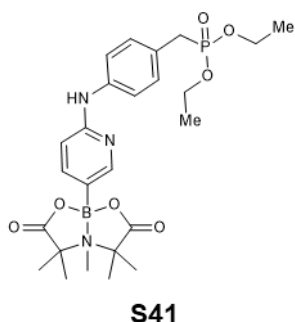
^1H NMR (500 MHz, DMSO) δ 1.44 (s, 6H), 1.67 (s, 6H), 2.59 (s, 3H), 6.80 (d, J = 8.4 Hz, 1H), 7.62 – 7.72 (m, 3H), 8.25 (d, J = 2.1 Hz, 1H), 9.50 (s, 1H).



(6-(pyrazin-2-ylamino)pyridin-3-yl)boronic acid TIDA ester (**S40**)

Prepared according to **GP2** using TIDA boronate **S2** (64.9 mg, 0.2 mmol) and pyrazin-2-amine (22.8 mg, 0.24 mmol).

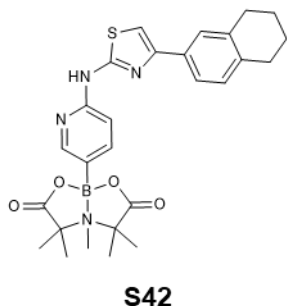
^1H NMR (500 MHz, DMSO) δ 1.45 (s, 6H), 1.67 (s, 6H), 2.61 (s, 3H), 7.69 (d, J = 8.4 Hz, 1H), 7.75 (dd, J = 8.4, 2.1 Hz, 1H), 8.07 (s, 1H), 8.23 (dd, J = 2.7, 1.5 Hz, 1H), 8.31 (d, J = 2.0 Hz, 1H), 9.03 (d, J = 1.5 Hz, 1H), 10.10 (s, 1H).



(6-((4-((diethoxyphosphoryl)methyl)phenyl)amino)pyridin-3-yl)boronic acid TIDA ester (**S41**)

Prepared according to **GP2** using TIDA boronate **S2** (64.9 mg, 0.2 mmol) and diethyl (4-aminobenzyl)phosphonate (58.4 mg, 0.24 mmol).

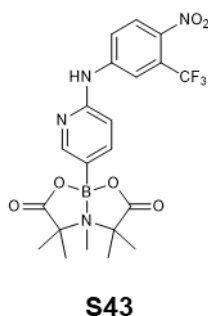
^1H NMR (500 MHz, DMSO) δ 1.17 (t, J = 7.0 Hz, 6H), 1.45 (s, 6H), 1.66 (s, 6H), 2.58 (s, 3H), 3.12 (d, J = 21.1 Hz, 2H), 3.93 (p, J = 7.2 Hz, 4H), 7.15 (dd, J = 8.7, 2.5 Hz, 2H), 7.57 (dd, J = 8.4, 2.2 Hz, 1H), 7.59 – 7.62 (m, 2H), 8.12 (dd, J = 8.0, 2.1 Hz, 1H), 8.48 (s, 1H), 9.04 (s, 1H).



(6-((4-(5,6,7,8-tetrahydronaphthalen-2-yl)thiazol-2-yl)amino)pyridin-3-yl)boronic acid TIDA ester (**S42**)

Prepared according to **GP2** using TIDA boronate **S2** (64.9 mg, 0.2 mmol) and 4-(5,6,7,8-tetrahydronaphthalen-2-yl)thiazol-2-amine (55.3 mg, 0.24 mmol).

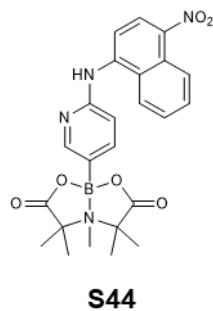
^1H NMR (400 MHz, DMSO) δ 1.45 (s, 6H), 1.67 (s, 6H), 1.76 (p, J = 3.1 Hz, 4H), 2.62 (s, 3H), 2.74 (m, 4H), 7.04 (d, J = 8.3 Hz, 1H), 7.08 (d, J = 7.9 Hz, 1H), 7.32 (s, 1H), 7.55 – 7.65 (m, 2H), 7.73 (dd, J = 8.4, 2.1 Hz, 1H), 8.32 (d, J = 2.1 Hz, 1H), 11.42 (s, 1H).



(6-((4-nitro-3-(trifluoromethyl)phenyl)amino)pyridin-3-yl)boronic acid TIDA ester (**S43**)

Prepared according to **GP2** using TIDA boronate **S2** (64.9 mg, 0.2 mmol) and 4-nitro-3-(trifluoromethyl)aniline (49.5 mg, 0.24 mmol).

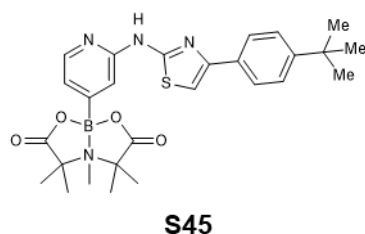
^1H NMR (400 MHz, DMSO) δ 1.45 (s, 6H), 1.67 (s, 6H), 2.62 (s, 3H), 6.96 (d, J = 8.4 Hz, 1H), 7.77 (dd, J = 8.3, 2.2 Hz, 1H), 8.18 (d, J = 2.4 Hz, 2H), 8.35 (d, J = 2.1 Hz, 1H), 8.47 (d, J = 1.9 Hz, 1H), 10.23 (s, 1H).



(6-((4-nitro-3-(trifluoromethyl)phenyl)amino)pyridin-3-yl)boronic acid TIDA ester (**S44**)

Prepared according to **GP2** using TIDA boronate **S2** (64.9 mg, 0.2 mmol) and 4-nitronaphthalen-1-amine (45.2 mg, 0.24 mmol).

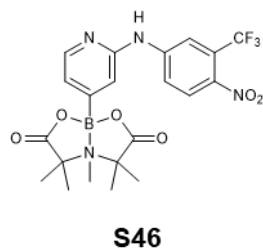
^1H NMR (400 MHz, DMSO) δ 1.47 (s, 6H), 1.68 (s, 6H), 2.64 (s, 3H), 7.32 (d, $J = 8.3$ Hz, 1H), 7.72 (ddd, $J = 8.3, 6.8, 1.3$ Hz, 1H), 7.76 – 7.87 (m, 2H), 8.34 (d, $J = 2.2$ Hz, 1H), 8.44 (d, $J = 3.1$ Hz, 2H), 8.58 (d, $J = 8.5$ Hz, 1H), 8.71 (dd, $J = 8.8, 1.2$ Hz, 1H), 9.71 (s, 1H).



(2-((4-(4-(tert-butyl)phenyl)thiazol-2-yl)amino)pyridin-4-yl)boronic acid TIDA ester (**S45**)

Prepared according to **GP2** using TIDA boronate **S3** (64.9 mg, 0.2 mmol) and 4-(4-(tert-butyl)phenyl)thiazol-2-amine (55.8 mg, 0.24 mmol).

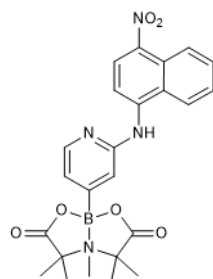
^1H NMR (400 MHz, DMSO) δ 1.31 (s, 9H), 1.46 (s, 6H), 1.69 (s, 6H), 2.61 (s, 3H), 6.99 (d, $J = 5.1$ Hz, 1H), 7.33 (s, 2H), 7.43 (d, $J = 8.4$ Hz, 2H), 7.82 (d, $J = 8.2$ Hz, 2H), 8.27 (d, $J = 5.1$ Hz, 1H), 11.24 (s, 1H).



(2-((4-nitro-3-(trifluoromethyl)phenyl)amino)pyridin-4-yl)boronic acid TIDA ester (**S46**)

Prepared according to **GP2** using TIDA boronate **S3** (64.9 mg, 0.2 mmol) and 4-nitro-3-(trifluoromethyl)aniline (49.5 mg, 0.24 mmol).

^1H NMR (400 MHz, DMSO) δ 1.46 (s, 6H), 1.69 (s, 6H), 2.63 (s, 3H), 7.07 (dd, $J = 5.1, 1.1$ Hz, 1H), 7.13 (s, 1H), 8.13 – 8.21 (m, 2H), 8.28 (d, $J = 5.0$ Hz, 1H), 8.38 (d, $J = 2.0$ Hz, 1H), 10.21 (s, 1H).

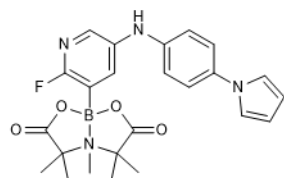


S47

(2-((4-nitronaphthalen-1-yl)amino)pyridin-4-yl)boronic acid TIDA ester (**S47**)

Prepared according to **GP2** using TIDA boronate **S3** (64.9 mg, 0.2 mmol) and 4-nitronaphthalen-1-amine (45.2 mg, 0.24 mmol).

^1H NMR (400 MHz, DMSO) δ 1.49 (s, 6H), 1.70 (s, 6H), 2.66 (s, 3H), 7.10 (dd, J = 5.0, 1.1 Hz, 1H), 7.58 (s, 1H), 7.71 (ddd, J = 8.4, 6.8, 1.3 Hz, 1H), 7.83 (ddd, J = 8.5, 6.8, 1.2 Hz, 1H), 8.29 (d, J = 5.0 Hz, 1H), 8.43 (d, J = 9.0 Hz, 1H), 8.52 (d, J = 9.0 Hz, 1H), 8.62 (d, J = 8.6 Hz, 1H), 8.73 (dd, J = 8.8, 1.2 Hz, 1H), 9.66 (s, 1H).

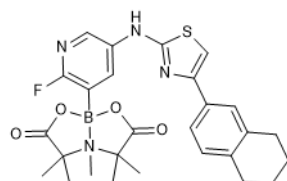


S48

(5-((4-(1H-pyrrol-1-yl)phenyl)amino)-2-fluoropyridin-3-yl)boronic acid TIDA ester (**S48**)

Prepared according to **GP2** using TIDA boronate **S4** (77.4 mg, 0.2 mmol) and 4-(1H-pyrrol-1-yl)aniline (38.0 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.49 (s, 6H), 1.68 (s, 6H), 2.67 (s, 3H), 6.22 (t, J = 2.1 Hz, 2H), 7.06 (d, J = 8.8 Hz, 2H), 7.23 (t, J = 2.2 Hz, 2H), 7.43 (d, J = 8.8 Hz, 2H), 7.62 (dd, J = 8.1, 3.0 Hz, 1H), 8.00 (dd, J = 3.2, 1.5 Hz, 1H), 8.36 (s, 1H).

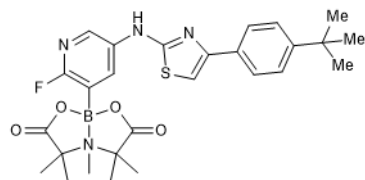


S49

(2-fluoro-5-((4-(5,6,7,8-tetrahydronaphthalen-2-yl)thiazol-2-yl)amino)pyridin-3-yl)boronic acid TIDA ester (**S49**)

Prepared according to **GP2** using TIDA boronate **S4** (77.4 mg, 0.2 mmol) and 4-(5,6,7,8-tetrahydronaphthalen-2-yl)thiazol-2-amine (55.3 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.50 (s, 6H), 1.71 (s, 6H), 1.76 (m, 4H), 2.67 (s, 3H), 2.73 (t, J = 5.3 Hz, 2H), 2.79 (t, J = 5.9 Hz, 2H), 7.12 (d, J = 7.9 Hz, 1H), 7.27 (s, 1H), 7.56 (d, J = 1.8 Hz, 1H), 7.61 (dd, J = 8.0, 1.9 Hz, 1H), 8.47 (d, J = 2.8 Hz, 1H), 8.57 (dd, J = 8.2, 3.0 Hz, 1H), 10.50 (s, 1H).

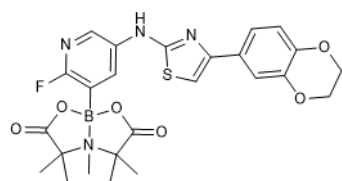


S50

(5-((4-(4-(tert-butyl)phenyl)thiazol-2-yl)amino)-2-fluoropyridin-3-yl)boronic acid TIDA ester (**S50**)

Prepared according to **GP2** using TIDA boronate **S4** (77.4 mg, 0.2 mmol) and 4-(4-(tert-butyl)phenyl)thiazol-2-amine (55.8 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.31 (s, 9H), 1.50 (s, 6H), 1.72 (s, 6H), 2.67 (d, J = 2.1 Hz, 3H), 7.31 (s, 1H), 7.46 (d, J = 8.5 Hz, 2H), 7.79 – 7.85 (m, 2H), 8.44 (dd, J = 3.1, 1.4 Hz, 1H), 8.71 (dd, J = 8.2, 2.9 Hz, 1H), 10.54 (s, 1H).

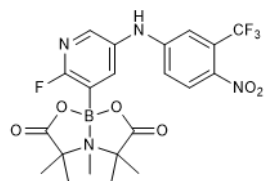


S51

(5-((4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thiazol-2-yl)amino)-2-fluoropyridin-3-yl)boronic acid TIDA ester (**S51**)

Prepared according to **GP2** using TIDA boronate **S4** (77.4 mg, 0.2 mmol) and 4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thiazol-2-amine (56.2 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.50 (s, 6H), 1.71 (s, 6H), 2.67 (s, 3H), 4.27 (s, 4H), 6.91 (d, J = 8.4 Hz, 1H), 7.23 (s, 1H), 7.36 (d, J = 2.1 Hz, 1H), 7.40 (dd, J = 8.3, 2.1 Hz, 1H), 8.47 (dd, J = 8.1, 2.9 Hz, 1H), 8.54 (dd, J = 3.0, 1.4 Hz, 1H), 10.48 (s, 1H).

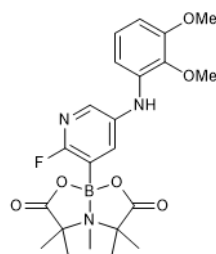


S52

(2-fluoro-5-((4-nitro-3-(trifluoromethyl)phenyl)amino)pyridin-3-yl)boronic acid TIDA ester (**S52**)

Prepared according to **GP2** using TIDA boronate **S4** (77.4 mg, 0.2 mmol) and 4-nitro-3-(trifluoromethyl)aniline (49.5 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.48 (s, 6H), 1.69 (s, 6H), 2.71 (s, 3H), 7.18 (dd, J = 9.1, 2.6 Hz, 1H), 7.29 (d, J = 2.5 Hz, 1H), 7.81 (dd, J = 8.0, 2.9 Hz, 1H), 8.11 (d, J = 9.1 Hz, 1H), 8.22 (dd, J = 3.0, 1.2 Hz, 1H), 9.56 (s, 1H).

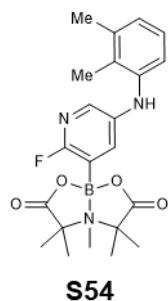


S53

(5-((2,3-dimethoxyphenyl)amino)-2-fluoropyridin-3-yl)boronic acid TIDA ester (**S53**)

Prepared according to **GP2** using TIDA boronate **S4** (77.4 mg, 0.2 mmol) and 2,3-dimethoxyaniline (36.8 mg, 0.24 mmol).

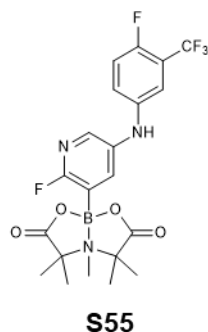
^1H NMR (500 MHz, DMSO) δ 1.48 (s, 6H), 1.67 (s, 6H), 2.65 (s, 3H), 3.67 (s, 3H), 3.79 (s, 3H), 6.58 (d, J = 8.3 Hz, 1H), 6.65 (d, J = 8.3 Hz, 1H), 6.90 (t, J = 8.2 Hz, 1H), 7.67 (dd, J = 8.1, 2.8 Hz, 1H), 7.76 (s, 1H), 7.95 (s, 1H).



(5-((2,3-dimethylphenyl)amino)-2-fluoropyridin-3-yl)boronic acid TIDA ester (**S54**)

Prepared according to **GP2** using TIDA boronate **S4** (77.4 mg, 0.2 mmol) and 2,3-dimethylaniline (29.1 mg, 0.24 mmol).

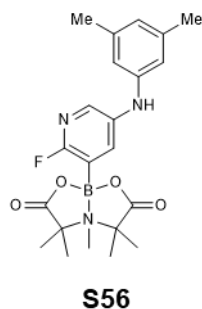
^1H NMR (500 MHz, DMSO) δ 1.47 (s, 6H), 1.67 (s, 6H), 2.09 (s, 3H), 2.25 (s, 3H), 2.65 (s, 3H), 6.85 (d, J = 7.4 Hz, 1H), 6.90 (d, J = 7.9 Hz, 1H), 6.98 (t, J = 7.7 Hz, 1H), 7.44 (dd, J = 8.1, 3.0 Hz, 1H), 7.57 (s, 1H), 7.67 (t, J = 2.2 Hz, 1H).



(2-fluoro-5-((4-fluoro-3-(trifluoromethyl)phenyl)amino)pyridin-3-yl)boronic acid TIDA ester (**S55**)

Prepared according to **GP2** using TIDA boronate **S4** (77.4 mg, 0.2 mmol) and 4-fluoro-3-(trifluoromethyl)aniline (43.0 mg, 0.24 mmol).

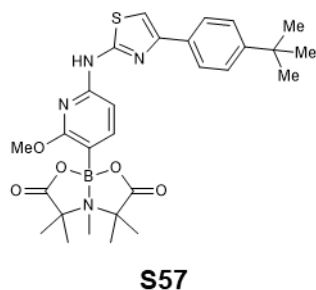
^1H NMR (500 MHz, DMSO) δ 1.47 (s, 6H), 1.68 (s, 6H), 2.67 (s, 3H), 7.21 (dd, J = 6.0, 2.9 Hz, 1H), 7.26 (dt, J = 8.9, 3.6 Hz, 1H), 7.37 (t, J = 9.7 Hz, 1H), 7.62 (dd, J = 8.0, 3.0 Hz, 1H), 7.98 – 8.04 (m, 1H), 8.57 (s, 1H).



(5-((3,5-dimethylphenyl)amino)-2-fluoropyridin-3-yl)boronic acid TIDA ester (**S56**)

Prepared according to **GP2** using TIDA boronate **S4** (77.4 mg, 0.2 mmol) and 3,5-dimethylaniline (29.1 mg, 0.24 mmol).

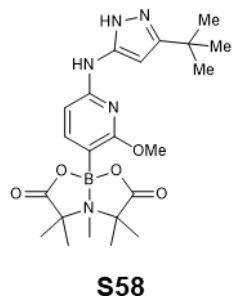
^1H NMR (500 MHz, DMSO) δ 1.49 (s, 6H), 1.68 (s, 6H), 2.17 (s, 6H), 2.66 (s, 3H), 6.49 (s, 1H), 6.59 (s, 2H), 7.62 (dd, J = 8.1, 3.0 Hz, 1H), 7.93 (m, 1H), 8.14 (s, 1H).



(6-((4-(4-(tert-butyl)phenyl)thiazol-2-yl)amino)-2-methoxypyridin-3-yl)boronic acid TIDA ester (**S57**)

Prepared according to **GP2** using TIDA boronate **S5** (79.8 mg, 0.2 mmol) and 4-(4-(tert-butyl)phenyl)thiazol-2-amine (55.7 mg, 0.24 mmol).

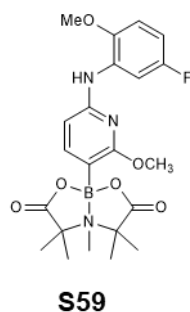
^1H NMR (500 MHz, DMSO) δ 1.30 (s, 9H), 1.44 (s, 3H), 1.65 (s, 6H), 2.60 (s, 3H), 4.01 (s, 3H), 6.63 (d, J = 7.9 Hz, 1H), 7.43 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 7.9 Hz, 1H), 7.83 (d, J = 8.6 Hz, 2H), 11.42 (s, 1H).



(6-((3-(tert-butyl)-1H-pyrazol-5-yl)amino)-2-methoxypyridin-3-yl)boronic acid TIDA ester (**S58**)

Prepared according to **GP2** using TIDA boronate **S5** (79.8 mg, 0.2 mmol) and 3-(tert-butyl)-1H-pyrazol-5-amine (33.4 mg, 0.24 mmol).

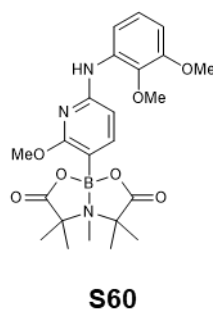
^1H NMR (500 MHz, DMSO) δ 1.26 (s, 9H), 1.43 (s, 6H), 1.63 (s, 6H), 2.56 (s, 3H), 3.80 (s, 3H), 6.27 (s, 1H), 6.64 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 8.0 Hz, 1H), 9.13 (s, 1H), 11.80 (s, 1H).



(6-((5-fluoro-2-methoxyphenyl)amino)-2-methoxypyridin-3-yl)boronic acid TIDA ester (**S59**)

Prepared according to **GP2** using TIDA boronate **S5** (79.8 mg, 0.2 mmol) and 5-fluoro-2-methoxyaniline (33.9 mg, 0.24 mmol).

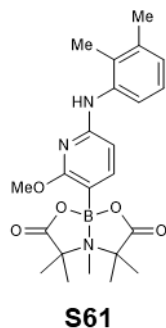
^1H NMR (500 MHz, DMSO) δ 1.44 (s, 6H), 1.64 (s, 6H), 2.59 (s, 3H), 3.82 (s, 3H), 3.85 (s, 3H), 6.67 (td, J = 8.5, 3.1 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 6.97 (dd, J = 8.9, 5.3 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 8.32 – 8.37 (m, 2H).



(6-((2,3-dimethoxyphenyl)amino)-2-methoxypyridin-3-yl)boronic acid TIDA ester (**S60**)

Prepared according to **GP2** using TIDA boronate **S5** (79.8 mg, 0.2 mmol) and 2,3-dimethoxyaniline (36.7 mg, 0.24 mmol).

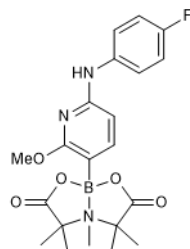
^1H NMR (500 MHz, DMSO) δ 1.44 (s, 6H), 1.64 (s, 6H), 2.58 (s, 3H), 3.73 (s, 3H), 3.79 (s, 3H), 3.80 (s, 3H), 6.64 (d, J = 8.2 Hz, 1H), 6.67 (d, J = 8.0 Hz, 1H), 6.98 (t, J = 8.3 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 8.23 (s, 1H).



(6-((2,3-dimethylphenyl)amino)-2-methoxypyridin-3-yl)boronic acid TIDA ester (**S61**)

Prepared according to **GP2** using TIDA boronate **S5** (79.8 mg, 0.2 mmol) and 2,3-dimethylaniline (29.1 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.43 (s, 6H), 1.63 (s, 6H), 2.25 (s, 3H), 2.56 (s, 3H), 3.68 (s, 3H), 6.15 (dd, J = 7.9, 1.5 Hz, 1H), 6.92 (d, J = 7.4 Hz, 1H), 7.04 (t, J = 7.7 Hz, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 8.17 (s, 1H).

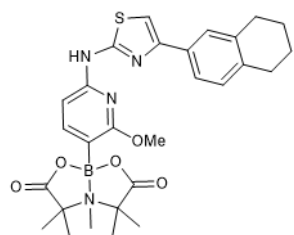


S62

(6-((4-fluorophenyl)amino)-2-methoxypyridin-3-yl)boronic acid TIDA ester (**S62**)

Prepared according to **GP2** using TIDA boronate **S5** (79.8 mg, 0.2 mmol) and 4-fluoroaniline (26.7 mg, 0.24 mmol).

^1H NMR (500 MHz, DMSO) δ 1.44 (s, 6H), 1.63 (s, 6H), 2.58 (s, 3H), 3.80 (s, 3H), 6.36 (d, J = 8.0 Hz, 1H), 7.10 (t, J = 8.8 Hz, 2H), 7.46 (d, J = 8.0 Hz, 1H), 7.68 (dd, J = 8.9, 4.9 Hz, 2H), 9.09 (s, 1H).

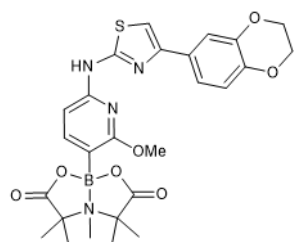


S63

(2-methoxy-5-((4-(5,6,7,8-tetrahydronaphthalen-2-yl)thiazol-2-yl)amino)phenyl)boronic acid TIDA ester (**S63**)

Prepared according to **GP2** using TIDA boronate **S5** (79.6 mg, 0.2 mmol) and 4-(5,6,7,8-tetrahydronaphthalen-2-yl)thiazol-2-amine (55.3 mg, 0.24 mmol).

^1H NMR (400 MHz, DMSO) δ 1.45 (s, 6H), 1.65 (s, 6H), 1.75 (m, 4H), 2.60 (s, 3H), 2.75 (m, 4H), 4.01 (s, 3H), 6.62 (d, J = 7.9 Hz, 1H), 7.08 (d, J = 7.9 Hz, 1H), 7.33 (s, 1H), 7.56 – 7.64 (m, 3H), 11.38 (s, 1H).

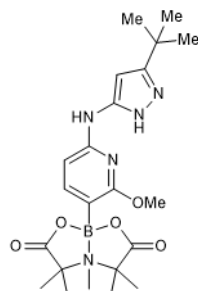


S64

(5-((4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thiazol-2-yl)amino)-2-methoxyphenyl)boronic acid TIDA ester (**S64**)

Prepared according to **GP2** using TIDA boronate **S5** (79.6 mg, 0.2 mmol) and 4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thiazol-2-amine (56.2 mg, 0.24 mmol).

^1H NMR (400 MHz, DMSO) δ 1.45 (s, 6H), 1.65 (s, 6H), 2.60 (s, 3H), 4.00 (s, 3H), 4.27 (s, 4H), 6.63 (d, J = 7.9 Hz, 1H), 6.88 (d, J = 8.3 Hz, 1H), 7.30 (s, 1H), 7.36 (d, J = 2.1 Hz, 1H), 7.39 (t, J = 2.0 Hz, 1H), 7.59 (d, J = 7.9 Hz, 1H), 11.34 (s, 1H).

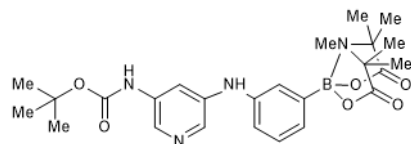


S65

(5-((3-(tert-butyl)-1H-pyrazol-5-yl)amino)-2-methoxyphenyl)boronic acid TIDA ester (**S65**)

Prepared according to **GP2** using TIDA boronate **S5** (79.6 mg, 0.2 mmol) and 3-(tert-butyl)-1H-pyrazol-5-amine (33.4 mg, 0.24 mmol).

^1H NMR (400 MHz, DMSO) δ 1.26 (s, 9H), 1.43 (s, 6H), 1.63 (s, 6H), 2.56 (s, 3H), 3.80 (s, 3H), 6.27 (s, 1H), 6.65 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 8.0 Hz, 1H), 9.12 (s, 1H), 11.78 (s, 1H).



S96

(3-((5-((tert-butoxycarbonyl)amino)pyridin-3-yl)amino)phenyl)boronic acid TIDA ester (**S96**)

Prepared according to **GP2** using TIDA boronate **3** (85.0 mg, 0.28 mmol) and tert-butyl (5-bromopyridin-3-yl)carbamate **7** (69.0 mg, 0.26 mmol).

^1H NMR (500 MHz, DMSO) δ 1.46 (s, 15H), 1.67 (s, 6H), 2.60 (s, 3H), 7.01 (d, $J = 7.3$ Hz, 1H), 7.07 – 7.13 (m, 1H), 7.25 (t, $J = 7.7$ Hz, 1H), 7.73 (s, 1H), 7.91 (d, $J = 2.4$ Hz, 1H), 8.00 (d, $J = 2.1$ Hz, 1H), 8.33 (s, 1H), 9.45 (s, 1H)

3. Neutral Loss-Acoustic Droplet Ejection-Mass Spectrometry (NL-ADE-MS) method optimization and validation

3.1 Concentration series for 60 TIDA boronate testing set (Extended Data Fig 2c)

Concentration series for the 60 TIDA boronate testing set was prepared in similar method to the above. To obtain final concentrations spanning from 0 to 11.5 μM in increments of 0.5 μM , droplet volumes from 0 nL to 57.5 nL in steps of 2.5 nL were added from 10 mM stock solutions in 384-well low dead volume COC plates (001-12782) by acoustic transfer into a 384-well PP plate (001-14615) with appropriate back fill with DMSO to a final volume of 57.5 nL. The samples were diluted with 50 μL of cosolvent (30% aqueous acetonitrile). Samples were grouped based on molecular weight and tested within its corresponding mass range. Mass range of 350 to 500 Da and CE 31 V were used for the first half samples, mass range of 450 to 600 Da with CE 42 V were used for second half of samples with neutral loss of 86 Da, flow rate of 500 $\mu\text{L}/\text{min}$, and 3 second per sample ejection frequency. (*Extended Tabular Data Sheet 3*).

3.2 Variation of collision energy (CE) on signal intensity (Extended Data Fig 3f)

Solutions of the entire 60 TIDA boronate test set (5 $\mu\text{M}/\text{each}$) were prepared by transferring 25 nL of 10 mM of DMSO stock solutions to a 384-well PP plate (001-14615). Five replicates were prepared in the same 384-well PP plate and data were averaged. The mass range was set from 380 to 555 Da and independent data were collected at CE 36 V and CE 42 V. For comparison samples were grouped in to four smaller groups and CEs were calculated. These individualized CE values (33, 36, 37, and 42 V) were used to create independent neutral loss profiles spanning the mass range 380 to 555 Da (380-400, 400-450, 450-500, and 500-555 Da). These profiles were used in a single analysis featuring four neutral loss scans. Flow rate of 500 $\mu\text{L}/\text{min}$ and 3 second per sample frequency was applied. Data were compared between CE 36 V, CE 42 V, and the collective output of the narrow ranges. (*Extended Tabular Data Sheet 7*).

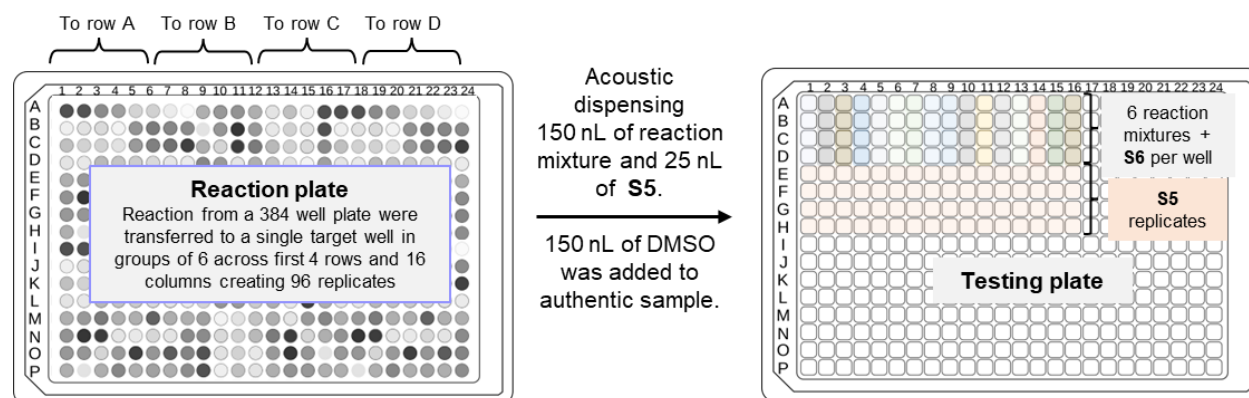
3.3 Mass range (Extended Data Fig 3g)

Prediluted solution of 5 μM of each individual member of our 60 TIDA test set was prepared in 30% aqueous acetonitrile, and loaded as 24 replicates of 50 μL in a row across four 384-well PP plates (001-14615). Samples were analyzed by NL-ADE-MS in the following way: Mass scan range 100 Da, three separate methods were used to span the full range of sixty compounds $\text{Mw} < 450$ (scan range 350-450 Da, CE 36 V), $\text{Mw} 450\text{-}550$ (scan range 450-550 Da, CE 42 V), $\text{Mw} > 520$ (scan range 500-600 Da, CE 42 V). Mass scan range 150 Da, two separate methods were used to span the full range of sixty compounds $\text{Mw} < 460$ (scan range 350-500 Da, CE 36 V), $\text{Mw} > 460$ (scan range 450-600 Da, CE 42 V). Mass scan range 200 Da, two separate methods were used to span the full range of sixty compounds $\text{Mw} < 460$ (scan range 350-550 Da, CE 36 V), $\text{Mw} > 460$ (scan range 450-650 Da, CE 42 V). Data were collected at a flow rate of 500 $\mu\text{L}/\text{min}$ and 3 second per sample frequency. Percentage coefficient of variation (%CV) was calculated to compare the precision for different mass ranges. (*Extended Tabular Data Sheet 8*).

3.4 Carryover (Extended Data Fig 3h)

Carryover samples were prepared with alternating sample and blank across 12 replicates in a 384-well PP plate (001-14615). TIDA **1** was prepared by adding 100 nL of 25 mM stock solution to achieve 50 μ M concentration upon dilution with 50 μ L of cosolvent (30% aqueous acetonitrile). For Boc **7** and THP **9**, a higher concentration was prepared by adding 500 nL stock solution to receive a 250 μ M concentration. Samples were tested by *NL*-ADE-MS method using the following parameters **1** (neutral loss of 86 Da, CE of 31 V, and mass range 320 to 330 Da); **7** (neutral loss 56 Da, CE 15 V, mass range 268 to 278 Da); **9** (neutral loss 84 Da, CE 24 V, mass range 252 to 262 Da). Flow rate was set to 350 μ L/min with 1.2 second per sample ejection frequency. (Extended Tabular Data Sheet 9).

3.5 Matrix effects (Extended Data Fig 3i)



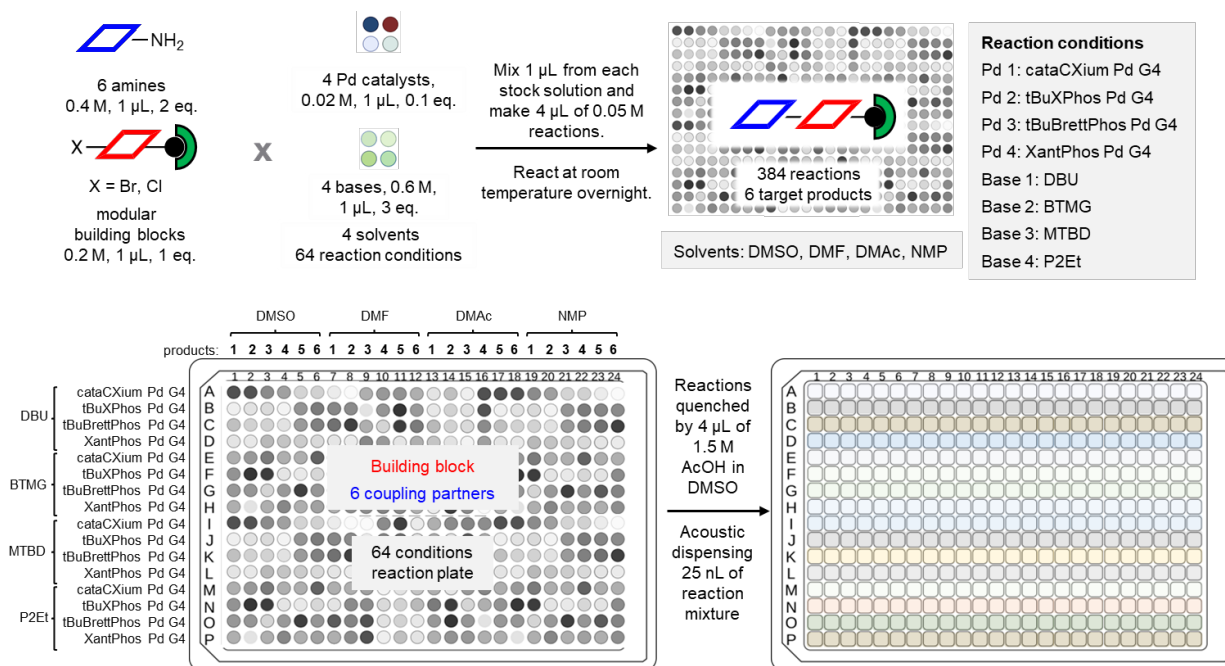
Matrix effects were tested by mixing authentic samples of 5 μ M TIDA boronate (**S5**) (acoustic transfer of 25 nL of stock solution at 10 mM) with reaction mixture components (150 nL total) derived from Buchwald-Hartwig coupling reactions across 96 wells of a 384-well PP plate (001-14615). A separate series of 96 wells on the same plate were filled with only **S5** (5 μ M, 25 nL of 10 mM stock) with an additional amount of DMSO (150 nL). The samples were diluted with 50 μ L of cosolvent (30% aqueous acetonitrile). Both sets of samples were tested using a single method by *NL*-ADE-MS (neutral loss 86 Da, mass range 262 to 272 Da, CE 31 V, flow rate of 350 μ L/min, and 1.2 second per sample). Signals for **S5** were extracted by an in-house-built R script and compared (Extended Tabular Data Sheet 10).

3.6 Systematic error (Extended Data Fig 3j)

To test the precision of *NL*-ADE-MS, a prediluted solution of **S2** (5 μ M in water) was replicated 384 times in a single 384-well PP plate (001-14615) (50 μ L per well). A *NL*-ADE-MS method was set up with a mass range from 320 to 330 Da, flow rate 500 μ L/min, and a 3 second per sample frequency. Injection volumes of 2.5 nL and 10 nL were collected separately, compared and %CV was calculated (Extended Tabular Data Sheet 11).

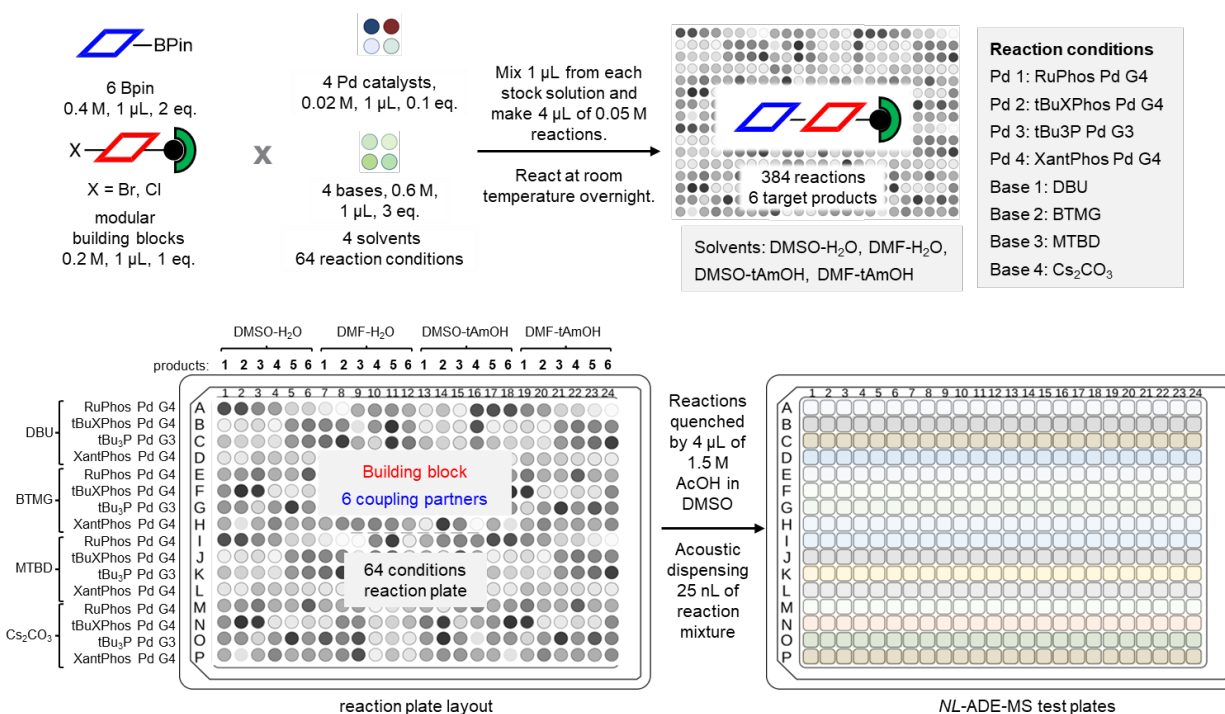
4. High throughput miniaturized reaction

4.1 Buchwald-Hartwig C-N coupling reaction



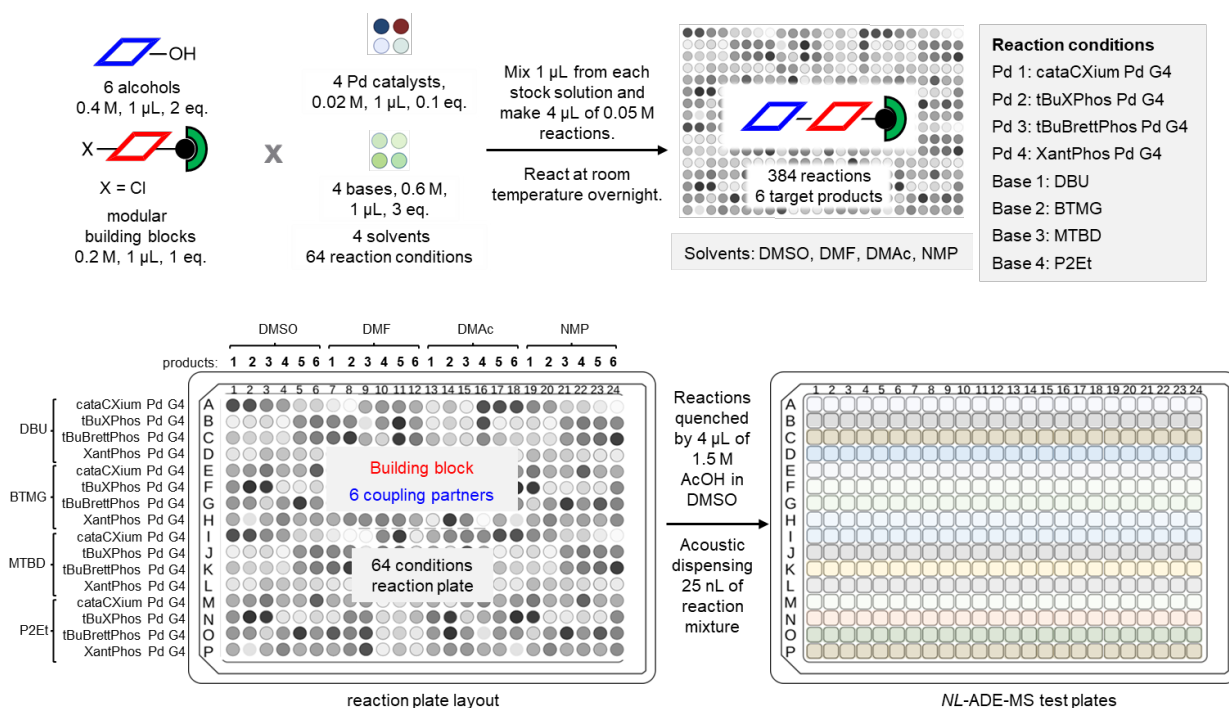
For Buchwald-Hartwig C-N coupling reaction, a building block with a unique fragmentation pattern was selected for reaction with 6 amine coupling partners to provide 6 potential products. 4 *Palladium* catalysts (cataCXium Pd G4, tBuXPhos Pd G4, tBuBrettPhos Pd G4, and XantPhos Pd G4), 4 bases (1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), Barton's base (BTMG), 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD), and phosphazene base P2Et), and 4 solvents (dimethyl sulfoxide (DMSO), dimethylformamide (DMF), dimethylacetamide (DMAc), N-methyl-2-pyrrolidone (NMP)) were selected to give 64 reaction conditions combinations. In the end, 384 unique reactions ($384 = 1 \times 6 \times 4 \times 4 \times 4$) were arranged in a 384 well plate.

4.2 Suzuki–Miyaura C-C coupling reaction



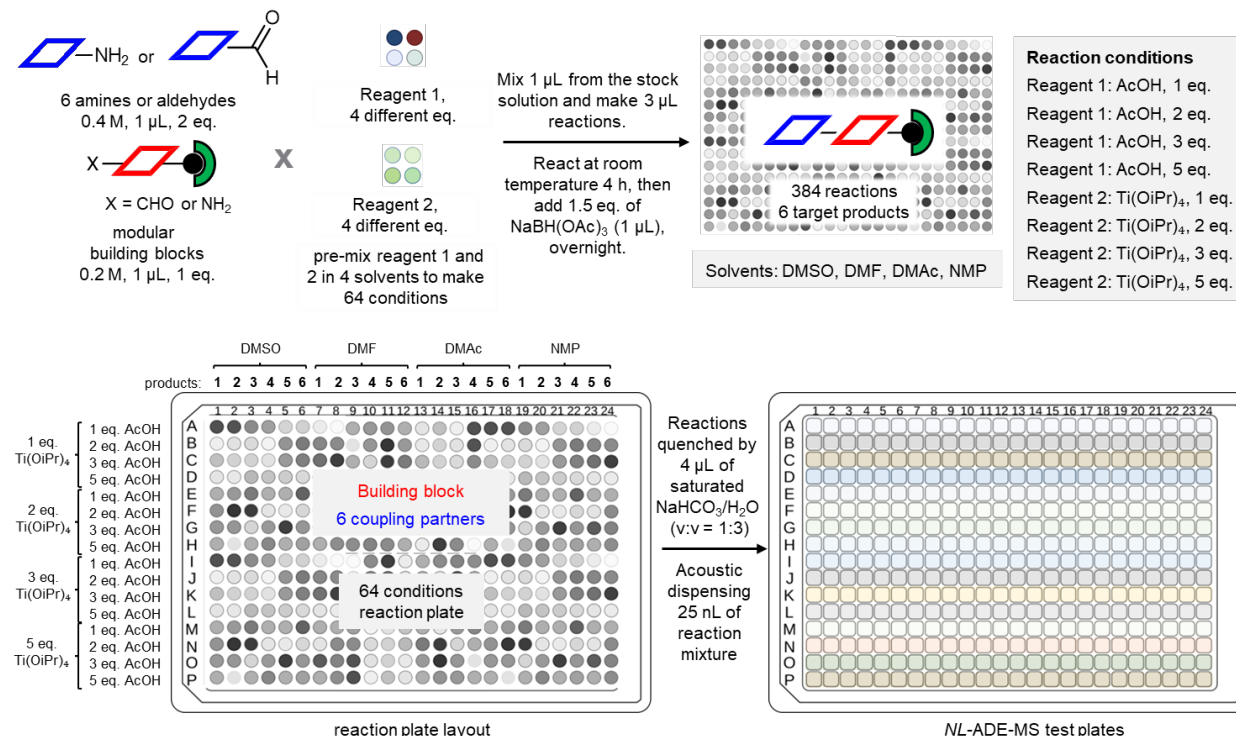
For Suzuki–Miyaura C-C coupling reaction, a building block with a unique fragmentation pattern was selected for reaction with 6 pinacol boronic esters (Bpin) coupling partners to provide 6 potential products. 4 *Palladium* catalysts (RuPhos Pd G4, tBuXPhos Pd G4, tBu3P Pd G3, and XantPhos Pd G4), 4 bases (DBU, BTMG, MTBD, and cesium carbonate (Cs₂CO₃), and 4 mixed solvents (DMSO+ H₂O (DMSO-H₂O = 3:1 (v:v), DMF + H₂O (DMF-H₂O = 3:1 (v:v), DMSO+ tert-amyl alcohol (tAmOH) (DMSO- tAmOH = 3:1 (v:v), DMF + tAmOH (DMF-tAmOH = 3:1 (v:v)) were selected to give 64 reaction conditions combinations. In the end, 384 unique reactions (384 = 1*6*4*4*4) were arranged in a 384 well plate.

4.3 C-O coupling reaction



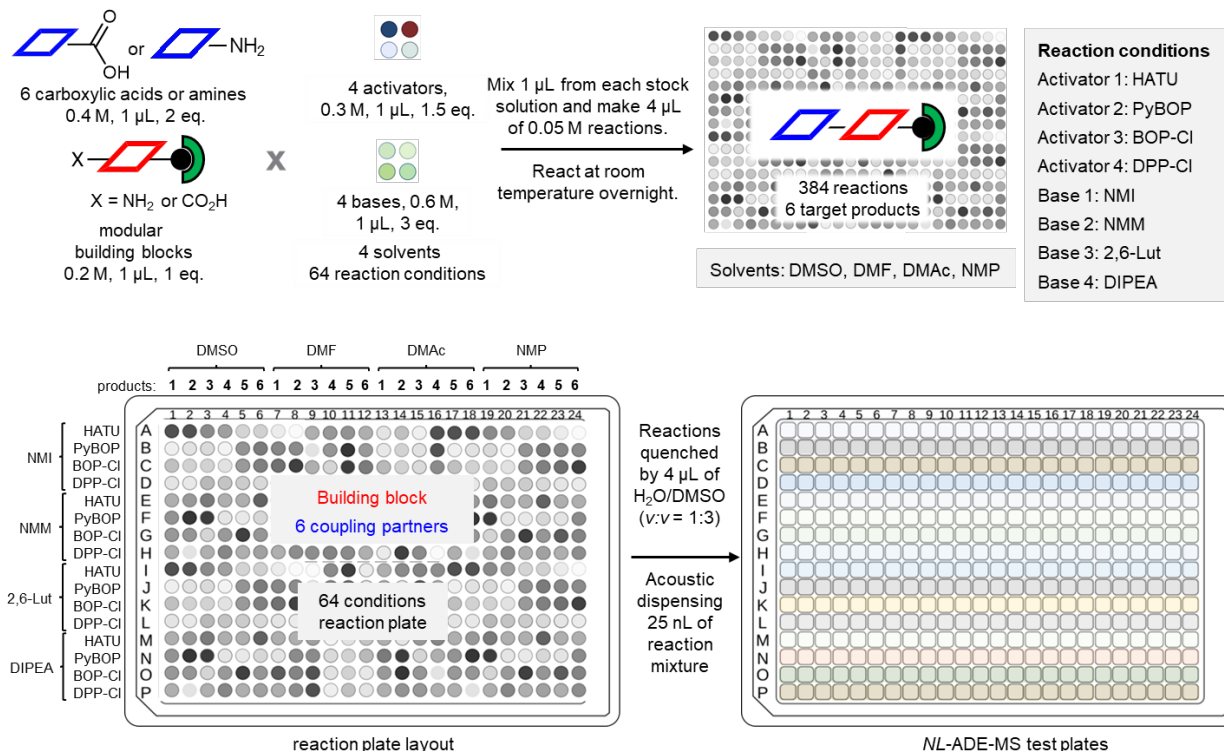
For C-O coupling reaction, a building block with a unique fragmentation pattern was selected for reaction with 6 amine coupling partners to provide 6 potential products. 4 *Palladium* catalysts (cataCXium Pd G4, tBuXPhos Pd G4, tBuBrettPhos Pd G4, and XantPhos Pd G4), 4 bases (DBU, BTMG, MTBD, and P2Et), and 4 solvents (DMSO, DMF, DMAc, and NMP) were selected to give 64 reaction conditions combinations. In the end, 384 unique reactions ($384 = 1 \times 6 \times 4 \times 4 \times 4$) were arranged in a 384 well plate.

4.4 Reductive amination reaction



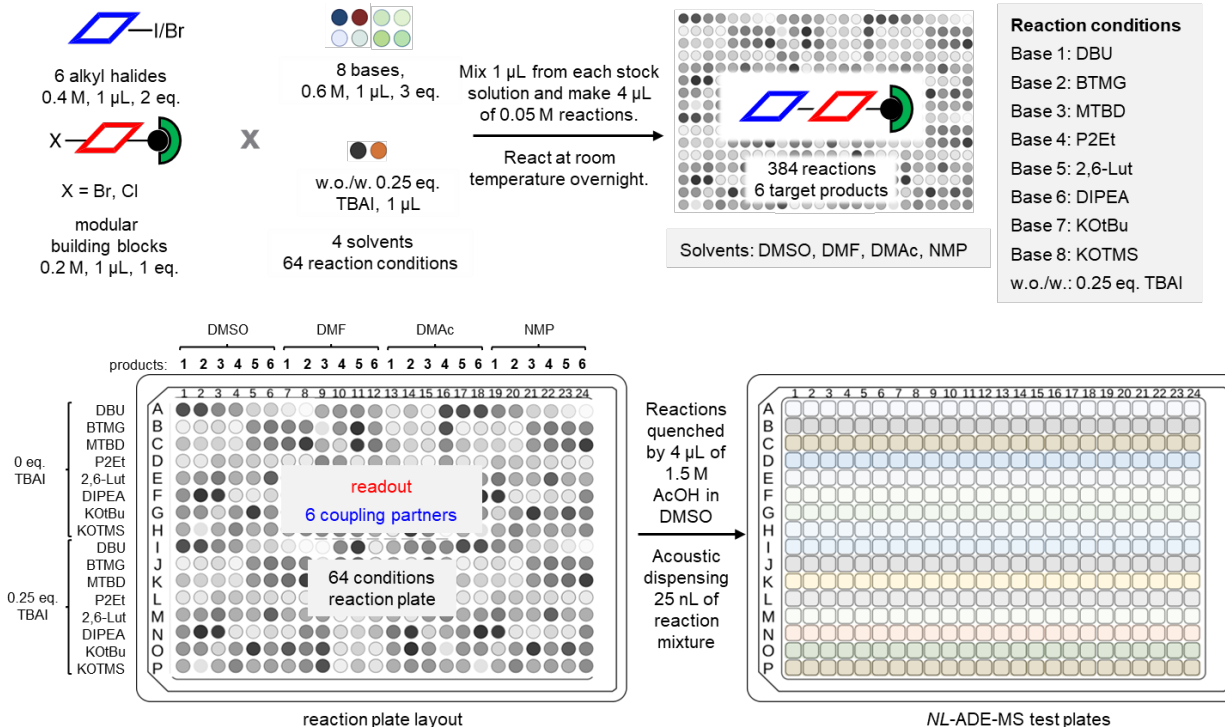
For reductive amination, building block with a unique fragmentation pattern (with aldehyde or amine as functional group) was selected for reaction with 6 coupling partners (amines and aldehydes respectively) to provide 6 potential products. Equivalents of AcOH (1 eq., 2 eq., 3 eq., and 5 eq.) and titanium isopropoxide (Ti(OiPr)₄, 1 eq., 2 eq., 3 eq., and 5 eq.) were varied across 4 solvents (DMSO, DMF, DMAc, and NMP) to give 64 reaction conditions combinations. In the end, 384 unique reactions ($384 = 1 \times 6 \times 4 \times 4 \times 4$) were arranged in a 384 well plate.

4.5 Amidation reaction



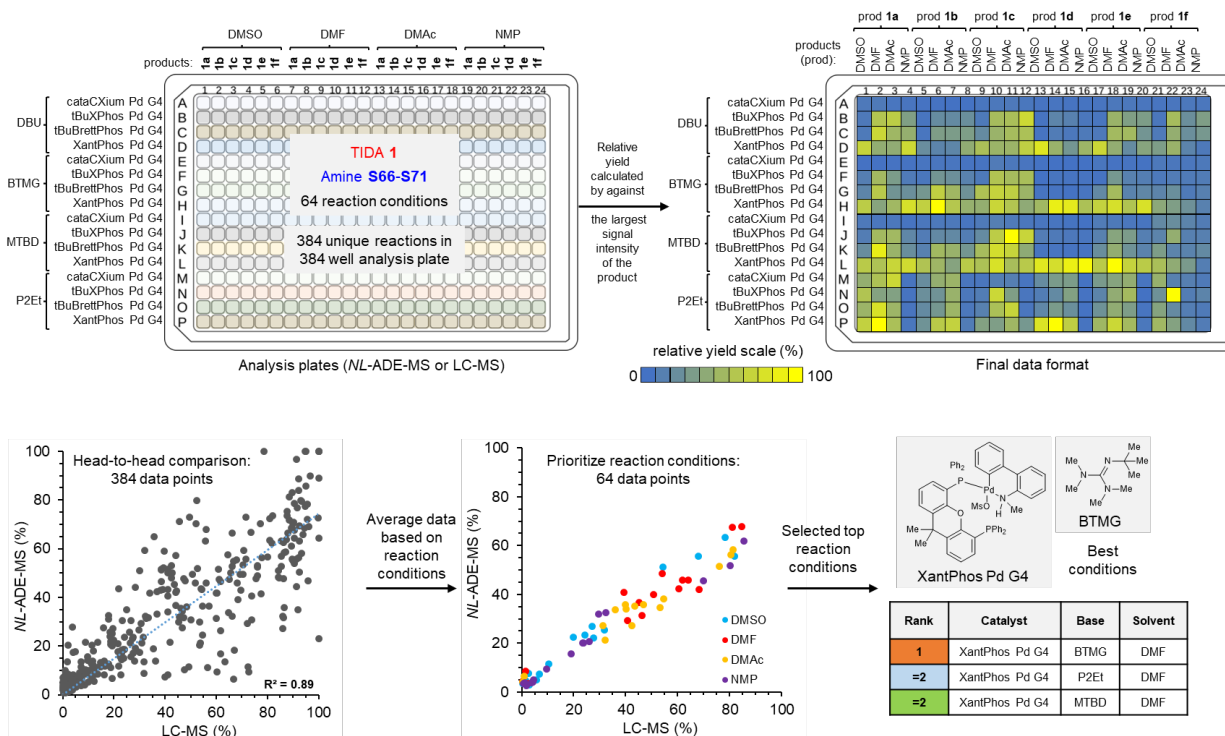
For amidation, a building block with a unique fragmentation pattern (amine or carboxylic acid as functional group) was selected for reaction with 6 coupling partners (carboxylic acids and amines respectively) to provide 6 potential products. 4 Activators (hexafluorophosphate azabenzotriazole tetramethyl uranium (HATU), benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate (PyBOP), bis(2-oxo-3-oxazolidinyl)phosphinic chloride (BOP-Cl), diphenylphosphinic chloride (DPP-Cl)), 4 bases (*N*-methylimidazole (NMI), *N*-methylmorpholine (NMM), 2,6-Lutidine (2,6-Lut), and *N,N*-diisopropylethylamine (DIPEA)), and 4 solvents (DMSO, DMF, DMAc, and NMP) were selected to give 64 reaction conditions combinations. In the end, 384 unique reactions ($384 = 1 \times 6 \times 4 \times 4 \times 4$) were arranged in a 384 well plate.

4.6 *N*-alkylation reaction



For alkylation, a building block with a unique fragmentation pattern was selected for reaction with 6 alkyl halide coupling partners to provide 6 potential products. 8 bases (DBU, BTMG, MTBD, P2Et, 2,6-Lut, DIPEA, potassium tert-butoxide (KOtBu), and potassium trimethylsilanolate (KOTMS)), tetra-*n*-butylammonium iodide (TBAI, without (w.o.) or with (w.) 0.25 eq.), and 4 solvents (DMSO, DMF, DMAc, and NMP) were selected to give 64 reaction conditions combinations. In the end, 384 unique reactions ($384 = 1 \times 6 \times 8 \times 2 \times 4$) were arranged in a 384 well plate.

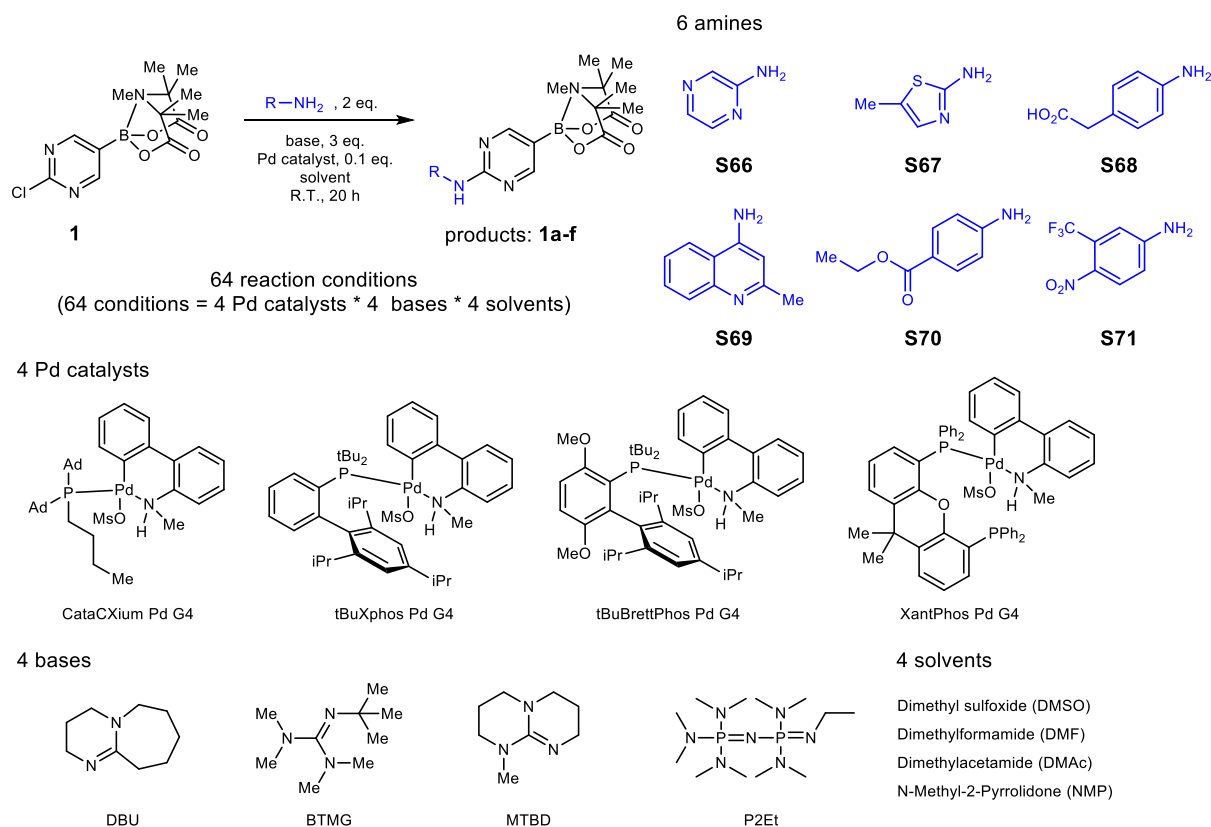
4.7 384-Well plate data processing example



Here data processing was demonstrated by using TIDA 1 in a Buchwald-Hartwig C-N coupling reaction. More specifically, TIDA 1 coupled with 6 amines S66-S71 give 6 target products 1a-1f. The analysis plates for NL-ADE-MS and LC-MS have the same layout as the reaction plate. After collecting the data, signal intensity was normalized based on the largest signal intensity of the corresponding product 1a-1f across all 64 conditions respectively. Data were reformatted to generate the heatmap shown top right, clustered by product identity and solvent (following DMSO, DMF, DMAc, and NMP). Each column represents 16 reaction conditions using a specific base and catalyst listed in the left (this is uniform across each row). Products from 1 to 6 listed in an order cross the column by solvent, i.e. product 1a can be found in column 1 (DMSO), column 2 (DMF), column 3 (DMAc), and column 4 (NMP). 384 Data points from conventional LC-MS and NL-ADE-MS were compared head to head and R^2 (coefficient of determination) was calculated assuming relative LC-MS data to be to ground truth for these crude reactions. Then, data were averaged based on reaction conditions to give 64 data points (average 6 data points from the corresponding 6 products, unless product was not formed under any conditions then it was excluded). Based on the average relative yield of all detected products, best reaction conditions or top 3 were listed and all corresponding data can be found in Extended Tabular Data. The specific data relating to this example are found on *Extended Tabular Data Sheet 12*.

4.8 Individual 384-well plate experiments

4.8.1 TIDA 1 Buchwald-Hartwig C-N coupling reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: **TIDA 1** (0.2 M in DMSO, DMF, DMAc, and NMP, 1 eq.). **Amines S66-S71** (0.4 M in DMSO, DMF, DMAc, and NMP, 2 eq.). **Palladium** catalysts cataCXium Pd G4, tBuXPhos Pd G4, tBuBrettPhos Pd G4, and XantPhos Pd G4 (0.02 M in DMSO, DMF, DMAc, and NMP, 0.1 eq.) **Bases** DBU, BTMG, MTBD, and P2Et (0.6 M in DMSO, DMF, DMAc, and NMP, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: **TIDA 1** was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, **amines S66-S71** were added to their respective columns following the same pattern of solvents, i.e. **S66** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **S67** column 2 (DMSO), column 8 (DMF), ... **Palladium** catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. cataCXium Pd G4 rows A, E, I, and M). **Bases** were distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of acetic acid (AcOH) in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

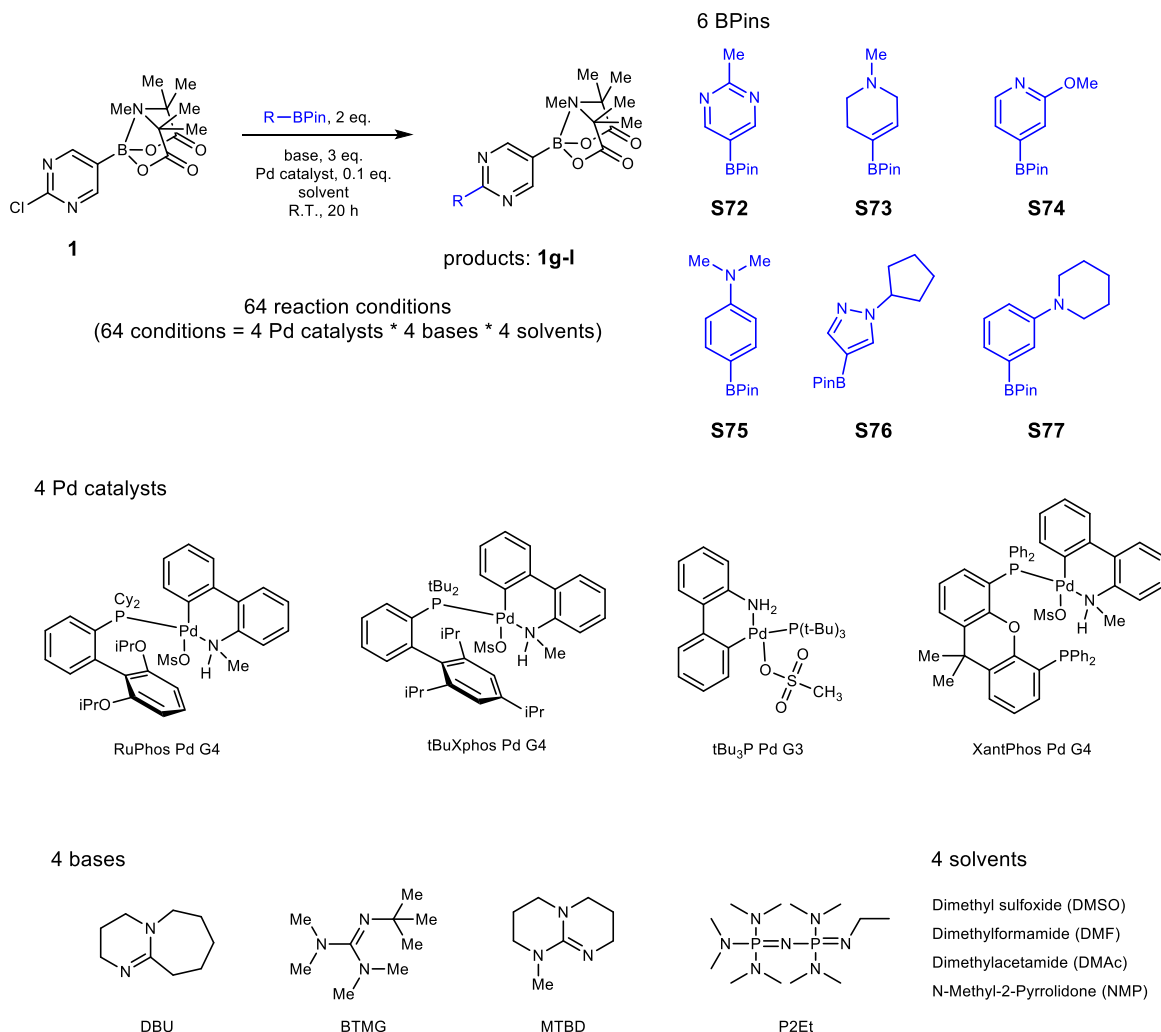
Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL*-ADE-MS analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 12.

4.8.2 TIDA 1 Suzuki–Miyaura C-C coupling reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: *TIDA 1* (0.2 M in DMSO and DMF, 1 eq.). *Boronic acid pinacol ester (Bpin)* **S72-S77** (0.4 M in DMSO and DMF, 2 eq.). *Palladium* catalysts RuPhos Pd G4, tBuXPhos Pd G4, tBu3P Pd G3, and XantPhos Pd G4 (0.02 M in DMSO and DMF, 0.1 eq.) *Bases* DBU, BTMG, MTBD, and Cs₂CO₃ (0.6 M in H₂O and tAmOH, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: *TIDA 1* was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMSO, columns 13-18; DMF, columns 19-24. Next, *boronic acid pinacol ester (Bpin)* **S72-S77** were added to their respective columns following the same pattern of solvents, i.e. **S72** column 1 (DMSO), column 7 (DMF), column 13 (DMSO), and column 19 (DMSO); **S77** column 2 (DMSO), column 8 (DMF), ... Palladium catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. RuPhos Pd G4 rows A, E, I, and M). Bases in H₂O were distributed to column 1 to 12 arrayed as identical blocks of 4 (i.e. DBU rows A-D). Bases in tAmOH were distributed to column 13 to 24 arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and

then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of AcOH in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

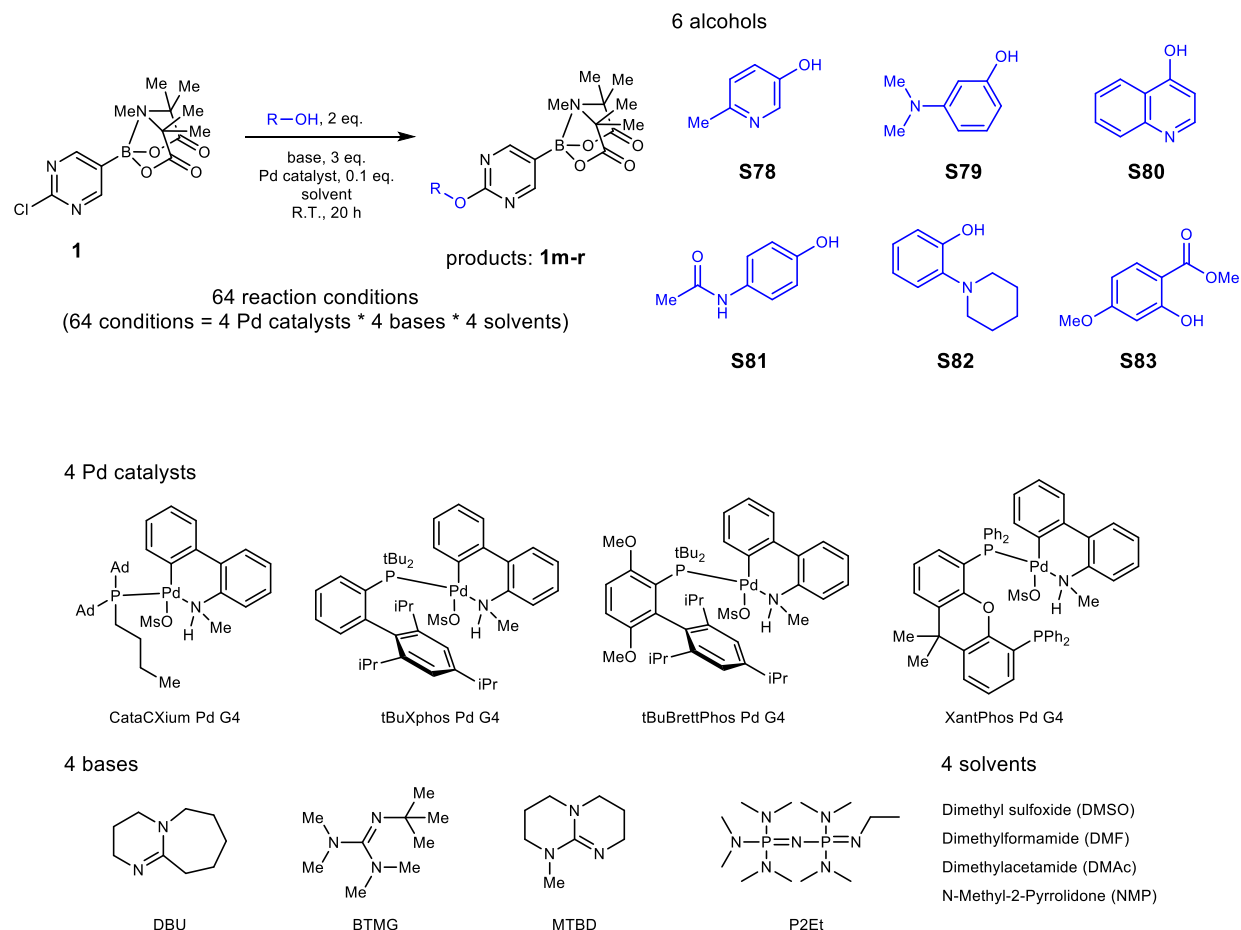
Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to NL-ADE-MS analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of S5 as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 13

4.8.3 TIDA 1 C-O coupling reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: **TIDA 1** (0.2 M in DMSO, DMF, DMAc, and NMP, 1 eq.). **Alcohols S78-S83** (0.4 M in DMSO, DMF, DMAc, and NMP, 2 eq.). **Palladium** catalysts cataCXium Pd G4, tBuXPhos Pd G4, tBuBrettPhos Pd G4, and XantPhos Pd G4 (0.02 M in DMSO, DMF, DMAc, and NMP, 0.1 eq.) **Bases** DBU, BTMG, MTBD, and P2Et (0.6 M in DMSO, DMF, DMAc, and NMP, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: **TIDA 1** was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, **alcohols S78-S83** were added to their respective columns following the same pattern of solvents, i.e. **S78** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **S79** column 2 (DMSO), column 8 (DMF), ... **Palladium** catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. cataCXium Pd G4 rows A, E, I, and M). **Bases** were distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed

from the glovebox and quenched through addition of AcOH in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

Analysis plates were generated as follows by acoustic liquid handling:

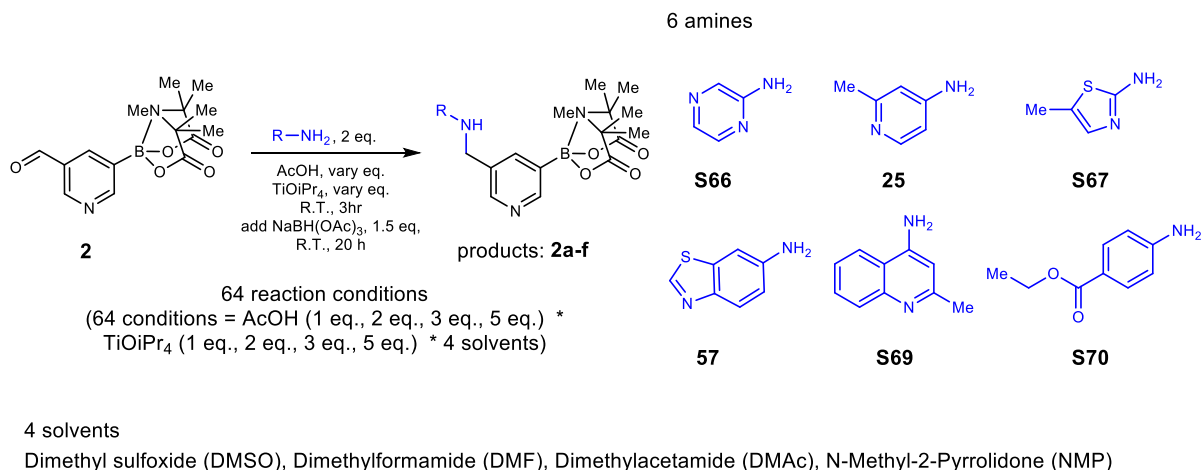
NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to NL-ADE-MS analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

NL-ADE-MS (multiplex) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) as groups of 6 spanning an individual reaction condition and solvent type: A1-A6 was pooled at 25 nL per source well into well A1 of the analysis plate, followed by A7-A12 to well A2 ...etc. Immediately prior to NL-ADE-MS analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 14.

4.8.4 TIDA 2 reductive amination reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: *TIDA 2* (0.2 M in DMSO, DMF, DMAc, and NMP, 1 eq.). *Amines S66, 25, S67, 57, S69, S70* (0.4 M in DMSO, DMF, DMAc, and NMP, 2 eq.). AcOH, 1 eq. (0.4 M), 2 eq. (0.8 M), 3 eq. (1.2 M), and 5 eq. (2 M) (in DMSO, DMF, DMAc, and NMP) and 2 Ti(OiPr)₄, 1 eq. (0.4 M), 2 eq. (0.8 M), 3 eq. (1.2 M), and 5 eq. (2 M) (in DMSO, DMF, DMAc, and NMP). *Reducing agent* sodium triacetoxyborohydride (NaBH(OAc)₃) (0.3 M in DMSO, DMF, DMAc, and NMP, 1.5 eq.). AcOH and Ti(OiPr)₄ were pre-mixed in the source plate right before preparing the reaction plate. AcOH was distributed by column to each solvent grouping arrayed every 4th row (i.e. 1 eq. AcOH rows A, E, I, and M). Ti(OiPr)₄ was distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. 1 eq. Ti(OiPr)₄ rows A-D). Using multi-channel pipetting 1 μ L of each of the three components were arrayed in the following manner: *TIDA 2* was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, *amines S66, 25, S67, 57, S69, S70* were added to their respective columns following the same pattern of solvents, i.e. *S66* column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); *25* column 2 (DMSO), column 8 (DMF), ... Mixed AcOH and Ti(OiPr)₄ were distributed by column to each solvent grouping (i.e. DMF column 1-6...). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). *Reducing agent* NaBH(OAc)₃ (1 μ L) added 3 h later and centrifuged for ~1 min at 1000 rpm before re-sealing. The mixtures were left to stand at room temperature for 20 h in total. Upon completion plates were removed from the glovebox and quenched through addition of saturated NaHCO₃/H₂O (v:v = 1:3, 4 μ L) using a Multidrop combi nL. 3 μ L of additional DMSO was added to the plate and centrifuged for 5 min at 1000 rpm. To avoid interference of solid precipitates 4 μ L of this solution was transferred to a separate 384-well COC plate (001-12782) to enable preparation of analysis plates.

Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS*

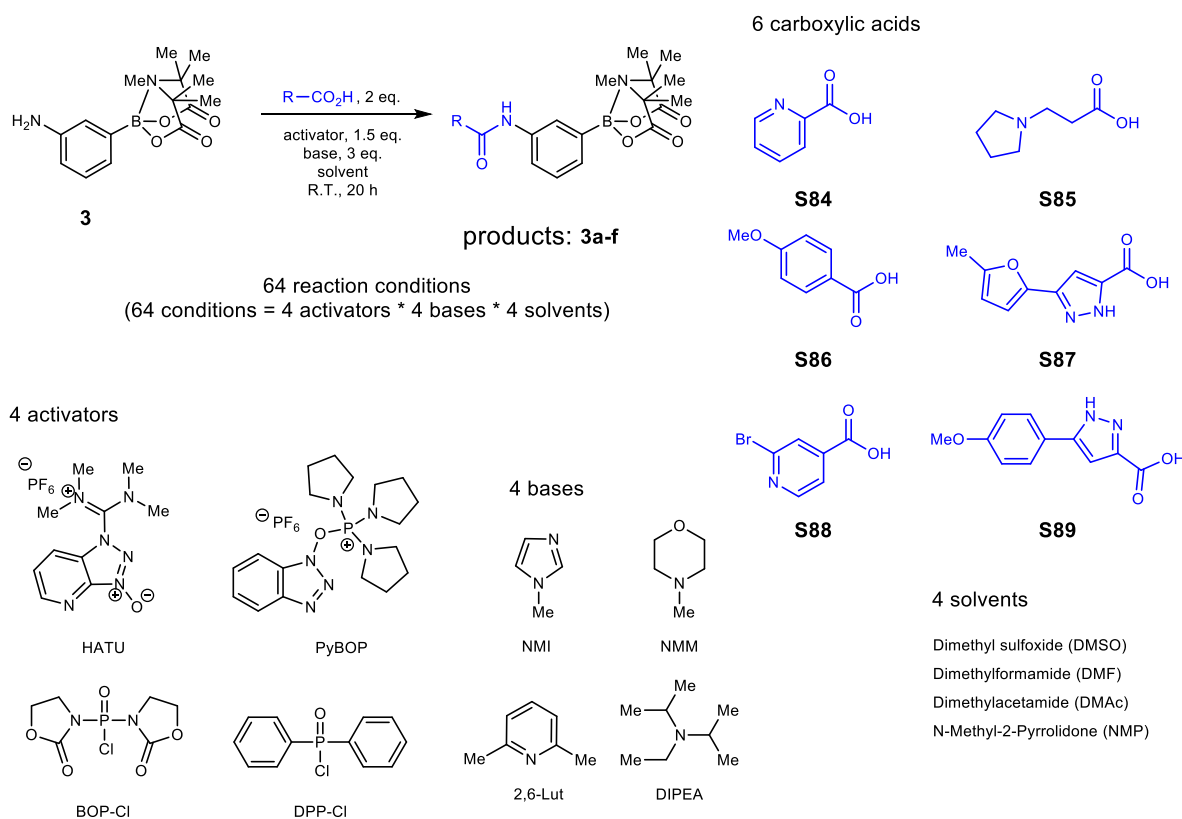
analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 9 μ M.

NL-ADE-MS (multiplex) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) as groups of 6 spanning an individual reaction condition and solvent type: A1-A6 was pooled at 25 nL per source well into well A1 of the analysis plate, followed by A7-A12 to well A2 ...etc. Immediately prior to NL-ADE-MS analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 9 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 18 μ M.

Data are found in Extended Tabular Data Sheet 15.

4.8.5 TIDA 3 amidation reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: **TIDA 3** (0.2 M in DMSO, DMF, DMAC, and NMP, 1 eq.). **Carboxylic acids S84-S89** (0.4 M in DMSO, DMF, DMAC, and NMP, 2 eq.). Activators HATU, PyBOP, BOP-Cl, DPP-Cl (0.3 M in DMSO, DMF, DMAC, and NMP, 1.5 eq.) **Bases** NMI, NMM, 2,6-Lut, and DIPEA (0.6 M in DMSO, DMF, DMAC, and NMP, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components

were arrayed in the following manner: *TIDA 3* was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, *carboxylic acids S84-S89* were added to their respective columns following the same pattern of solvents, i.e. **S84** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **S85** column 2 (DMSO), column 8 (DMF), ... Activators were distributed by column to each solvent grouping arrayed every 4th row (i.e. HATU rows A, E, I, and M). Bases were distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. NMI rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of H₂O/DMSO (v:v = 1:3, 4 μ L) using a Multidrop combi nL.

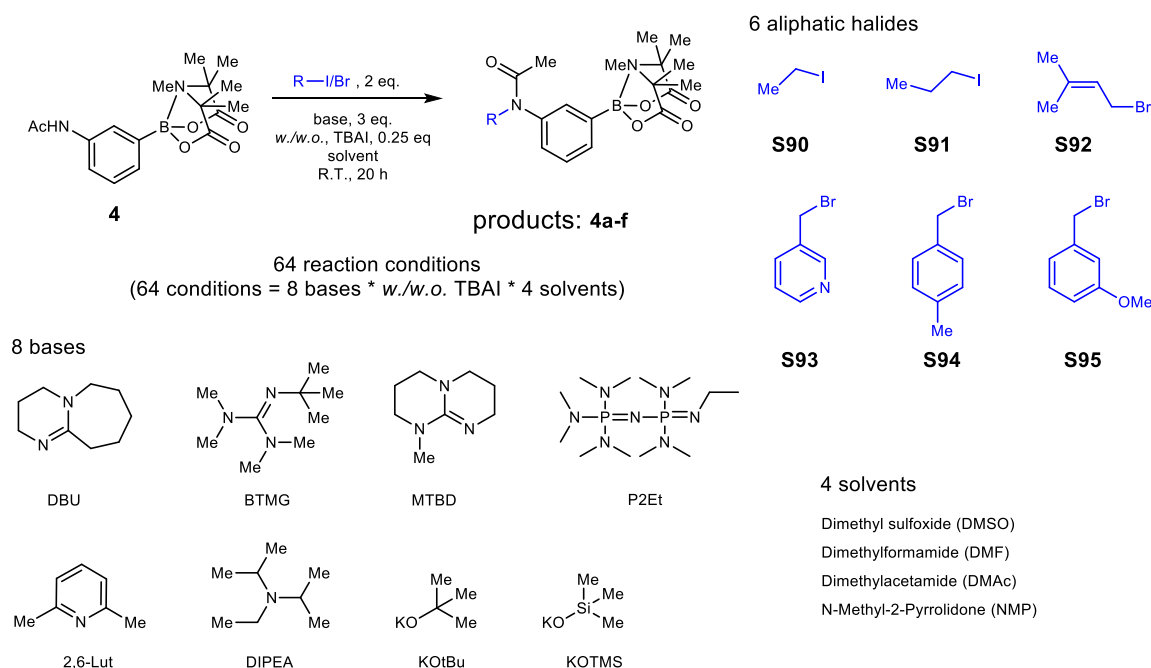
Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 50 μ M.

Data are found in Extended Tabular Data Sheet 16.

4.8.6 TIDA 4 *N*-alkylation reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: *TIDA 4* (0.2 M in DMSO, DMF, DMAc, and NMP, 1 eq.). *Alkyl halides S90-S95* (0.4 M in DMSO, DMF, DMAc, and NMP, 2 eq.). *Bases* DBU, BTMG, MTBD, P2Et, 2,6-Lut, DIPEA, KOTBu, and KOTMS (0.6 M in DMSO, DMF, DMAc, and NMP, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: *TIDA 4* was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, *alkyl halides S90-S95* were added to their respective columns following the same pattern of solvents, i.e. **S90** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **S91** column 2 (DMSO), column 8 (DMF), ... *Bases* were distributed by column to each solvent grouping arrayed every 8th row (i.e. DBU rows A and I). TBAI was distributed by column to each solvent grouping arrayed as 0 eq. of TBAI in row A-H, 0.25 eq. of TBAI in row I-P. Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of AcOH in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

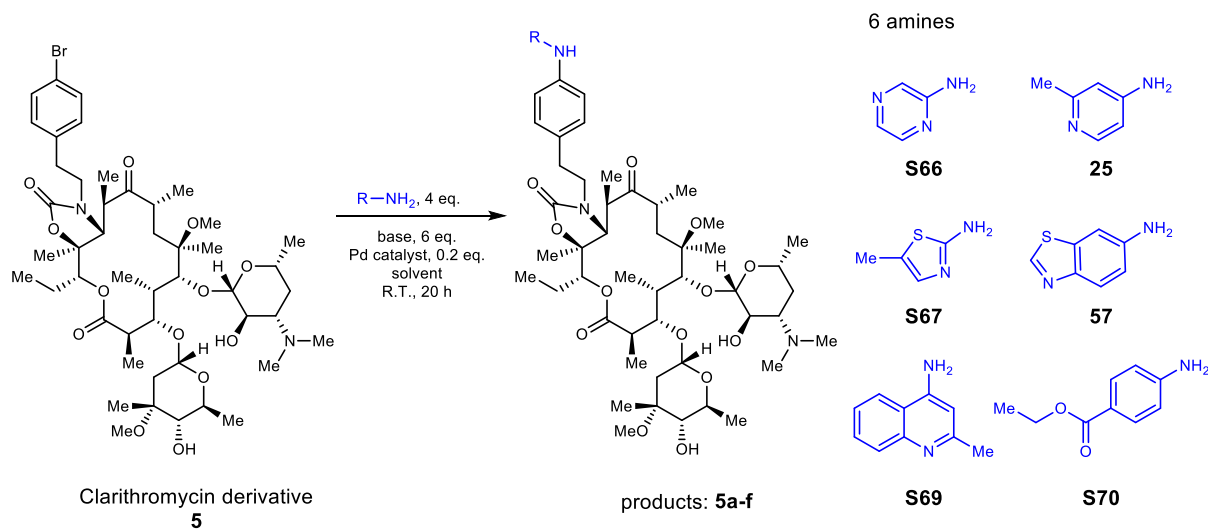
Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

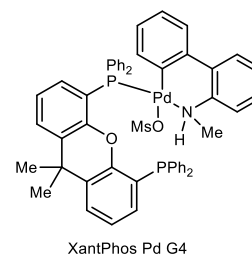
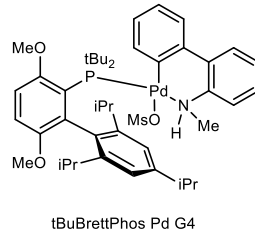
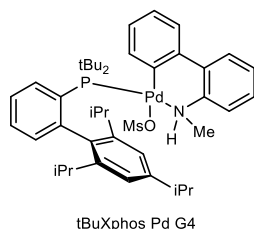
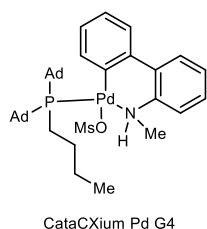
Data are found in Extended Tabular Data Sheet 17.

4.8.7 Clarithromycin derivative 5 Buchwald-Hartwig C-N coupling reaction

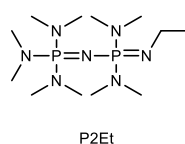
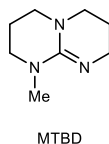
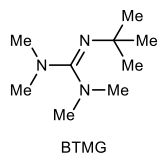
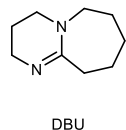


64 reaction conditions
(64 conditions = 4 Pd catalysts * 4 bases * 4 solvents)

4 Pd catalysts



4 bases



4 solvents

Dimethyl sulfoxide (DMSO)
Dimethylformamide (DMF)
Dimethylacetamide (DMAc)
N-Methyl-2-Pyrrolidone (NMP)

All stock solutions were prepared inside the glovebox using anhydrous solvents: *Clarithromycin derivative 5* (0.1 M in DMSO, DMF, DMAc, and NMP, 1 eq.). *Amines S66, 25, S67, 57, S69, S70* (0.4 M in DMSO, DMF, DMAc, and NMP, 4 eq.). *Palladium* catalysts cataCXium Pd G4, tBuXPhos Pd G4, tBuBrettPhos Pd G4, and XantPhos Pd G4 (0.02 M in DMSO, DMF, DMAc, and NMP, 0.2 eq.) *Bases* DBU, BTMG, MTBD, and P2Et (0.6 M in DMSO, DMF, DMAc, and NMP, 6 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: *TIDA 1* was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, *amines S66, 25, S67, 57, S69, S70* were added to their respective columns following the same pattern of solvents, i.e. **S66** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **25** column 2 (DMSO), column 8 (DMF), ... *Palladium* catalysts were distributed by column to each solvent grouping arrayed every 4th row

(i.e. cataCXium Pd G4 rows A, E, I, and M). Bases were distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of AcOH in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

Analysis plates were generated as follows by acoustic liquid handling:

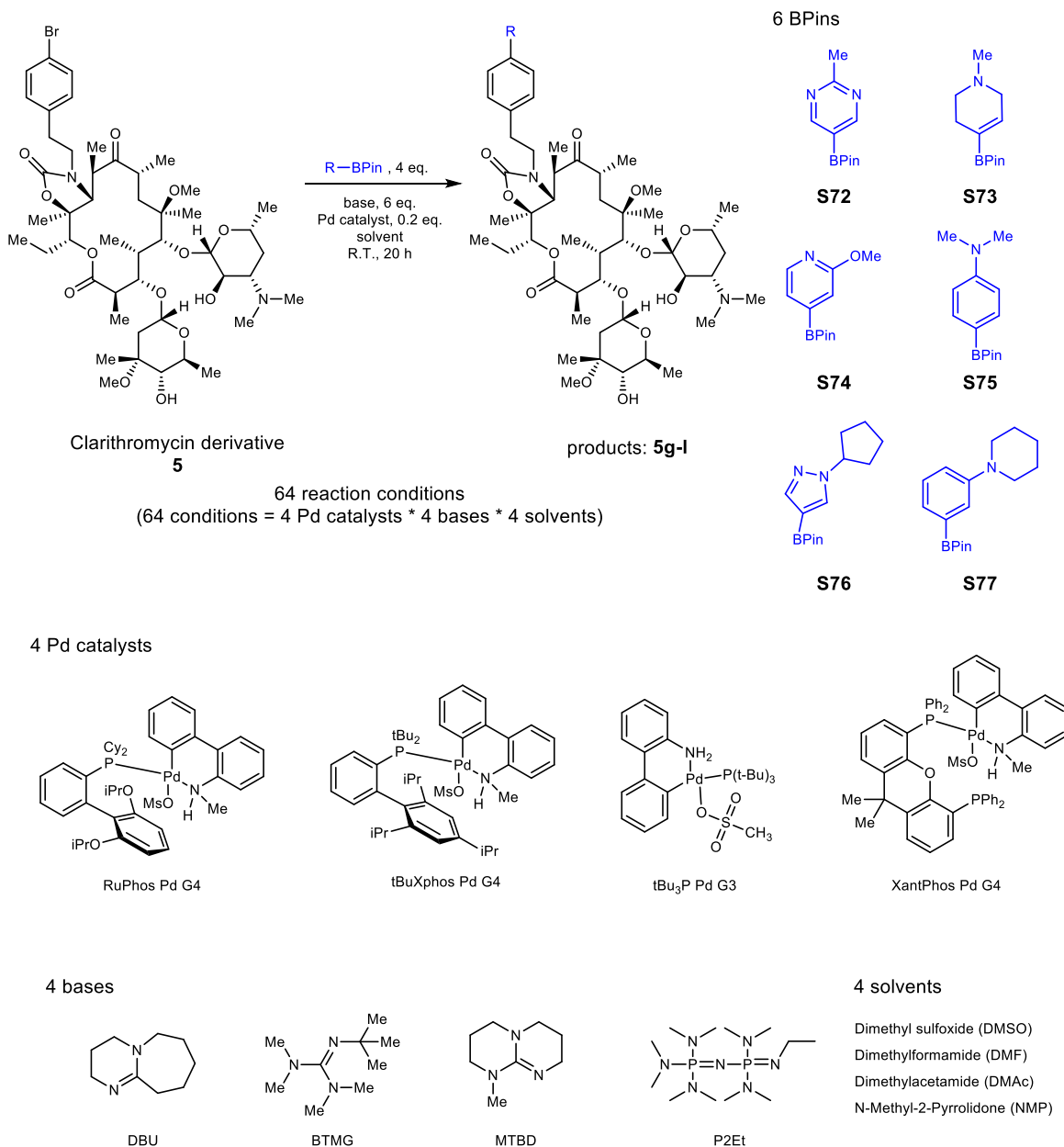
NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 6.25 μ M.

NL-ADE-MS (multiplex) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) as groups of 6 spanning an individual reaction condition and solvent type: A1-A6 was pooled at 25 nL per source well into well A1 of the analysis plate, followed by A7-A12 to well A2 ...etc. Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 6.25 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 12.5 μ M.

Data are found in Extended Tabular Data Sheet 20.

4.8.8 Clarithromycin derivative 5 Suzuki–Miyaura C-C coupling reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: *Clarithromycin derivative 5* (0.1 M in DMSO and DMF, 1 eq.). *Boronic acid pinacol ester (Bpin) S72–S77* (0.4 M in DMSO and DMF, 4 eq.). *Palladium* catalysts RuPhos Pd G4, tBuXPhos Pd G4, tBu₃P Pd G3, and XantPhos Pd G4 (0.02 M in DMSO and DMF, 0.2 eq.) *Bases* DBU, BTMG, MTBD, and Cs₂CO₃ (0.6 M in H₂O and tAmOH, 6 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: *TIDA 1* was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMSO, columns 13-18; DMF, columns 19-24. Next, *boronic acid pinacol ester (Bpin) S72–S77* were added to their respective columns following the same pattern of solvents,

i.e. **S72** column 1 (DMSO), column 7 (DMF), column 13 (DMSO), and column 19 (DMSO); **S77** column 2 (DMSO), column 8 (DMF), ... *Palladium* catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. RuPhos Pd G4 rows A, E, I, and M). *Bases* in H₂O were distributed to column 1 to 12 arrayed as identical blocks of 4 (i.e. DBU rows A-D). Bases in tAmOH were distributed to column 13 to 24 arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of AcOH in DMSO (4 µL, 1.5 M) using a Multidrop combi nL.

Analysis plates were generated as follows by acoustic liquid handling:

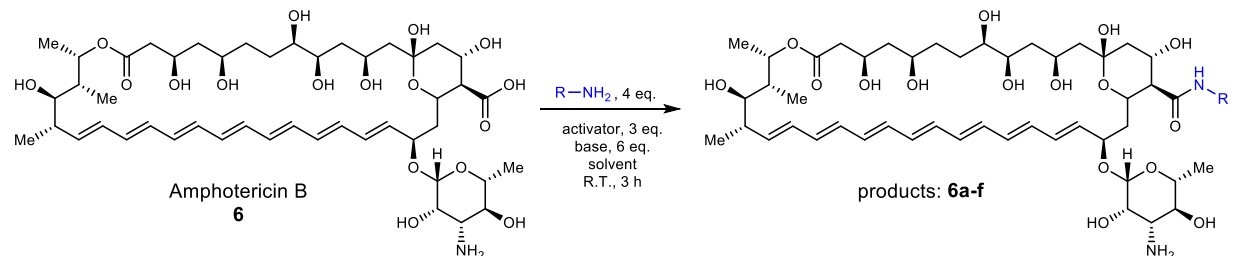
NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 µL) to provide a final maximum concentration of 6.25 µM.

NL-ADE-MS (multiplex) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) as groups of 6 spanning an individual reaction condition and solvent type: A1-A6 was pooled at 25 nL per source well into well A1 of the analysis plate, followed by A7-A12 to well A2 ...etc. Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 µL) to provide a final maximum concentration of 6.25 µM.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 µL with 50 µM of **S5** as an internal standard) to provide a final maximum concentration of 12.5 µM.

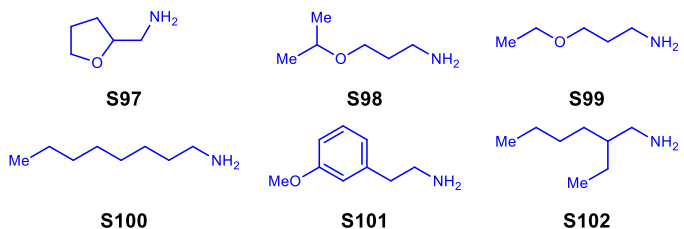
Data are found in Extended Tabular Data Sheet 21.

4.8.9 Amphotericin B amidation reaction



64 reaction conditions
(64 conditions = 4 activators * 4 bases * 4 solvents)

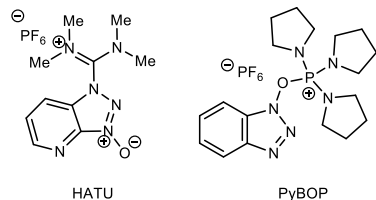
4 aliphatic amines



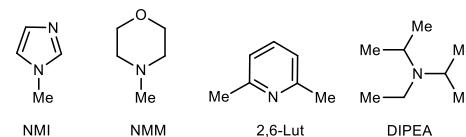
4 solvents

Dimethyl sulfoxide (DMSO), Dimethylformamide (DMF),
Dimethylacetamide (DMAc), N-Methyl-2-Pyrrolidone (NMP)

4 activators



4 bases



All stock solutions were prepared inside the glovebox using anhydrous solvents: *Amphotericin B* **6** (0.05 M in DMSO, DMF, DMAc, and NMP). *Amines S97-S102* (0.4 M in DMSO, DMF, DMAc, and NMP). *Activators* HATU, PyBOP, BOP-Cl, DPP-Cl (0.3 M in DMSO, DMF, DMAc, and NMP) *Bases* NMI, NMM, 2,6-Lut, and DIPEA (0.6 M in DMSO, DMF, DMAc, and NMP). Using multi-channel pipetting each of the four components were arrayed in the following manner: *Amphotericin B* (2 μ L, 1 eq.) was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, *amines S97-S102* (1 μ L, 4 eq.) were added to their respective columns following the same pattern of solvents, i.e. **S97** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **S98** column 2 (DMSO), column 8 (DMF), ... *Activators* (1 μ L, 3 eq.) were distributed by column to each solvent grouping arrayed every 4th row (i.e. HATU rows A, E, I, and M). *Bases* (1 μ L, 6 eq.) were distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. NMI rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 3 h. Upon completion plates were removed from the glovebox and quenched through addition of H₂O/DMSO (v:v = 1:3, 4 μ L) using a Multidrop combi nL.

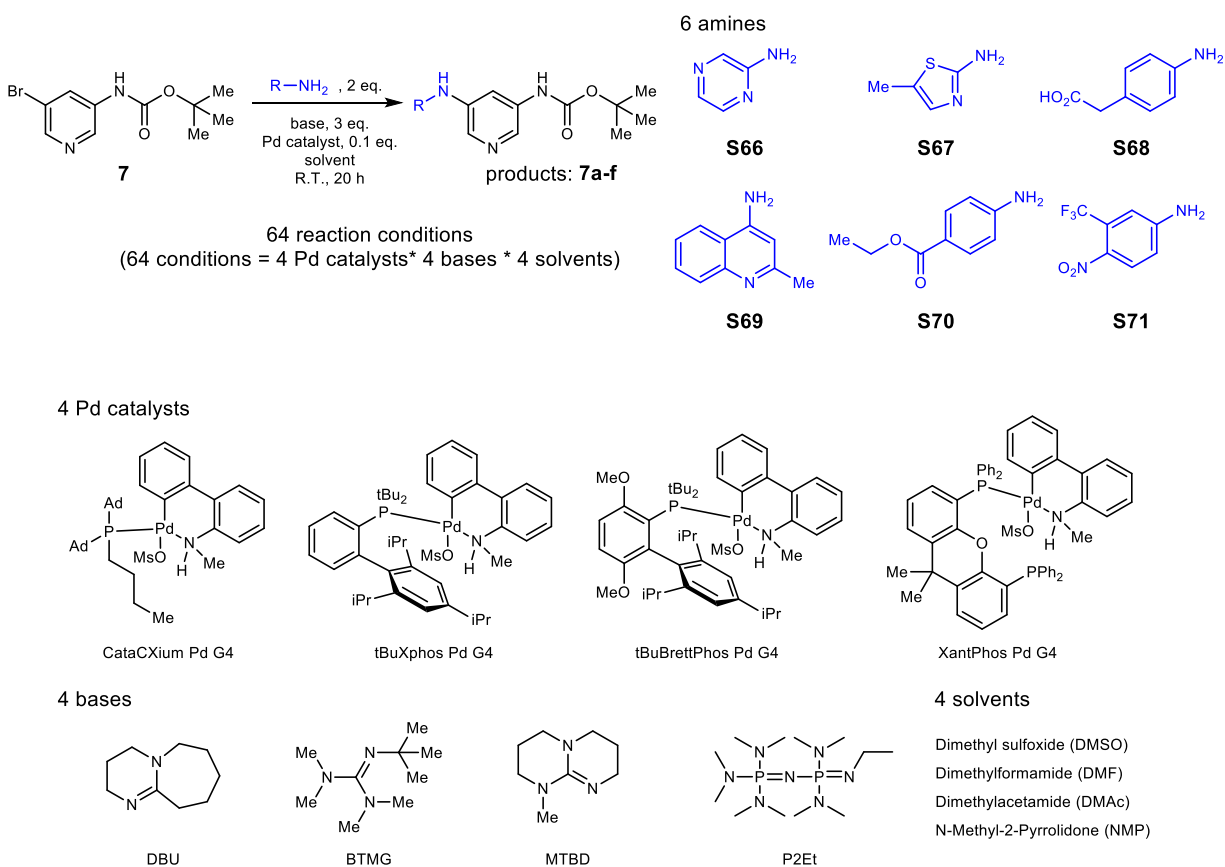
Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (250 nL per source well). Immediately prior to NL-ADE-MS analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 55.6 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 500 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 111.1 μ M.

Data are found in Extended Tabular Data Sheet 22.

4.8.10 Boc amine **7** Buchwald-Hartwig C-N coupling reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: *Boc amine 7* (0.2 M in DMSO, DMF, DMAc, and NMP, 1 eq.). *Amines S66-S71* (0.4 M in DMSO, DMF, DMAc, and NMP, 2 eq.). *Palladium* catalysts cataCXium Pd G4, tBuXPhos Pd G4, tBuBrettPhos Pd G4, and XantPhos Pd G4 (0.02 M in DMSO, DMF, DMAc, and NMP, 0.1 eq.) *Bases* DBU, BTMG, MTBD, and P2Et (0.6 M in DMSO, DMF, DMAc, and NMP, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: *Boc amine 7* was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18;

DMP, columns 19-24. Next, *amines* **S66-S71** were added to their respective columns following the same pattern of solvents, i.e. **S66** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **S67** column 2 (DMSO), column 8 (DMF), ... *Palladium* catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. cataCXium Pd G4 rows A, E, I, and M). *Bases* were distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of AcOH in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

Analysis plates were generated as follows by acoustic liquid handling:

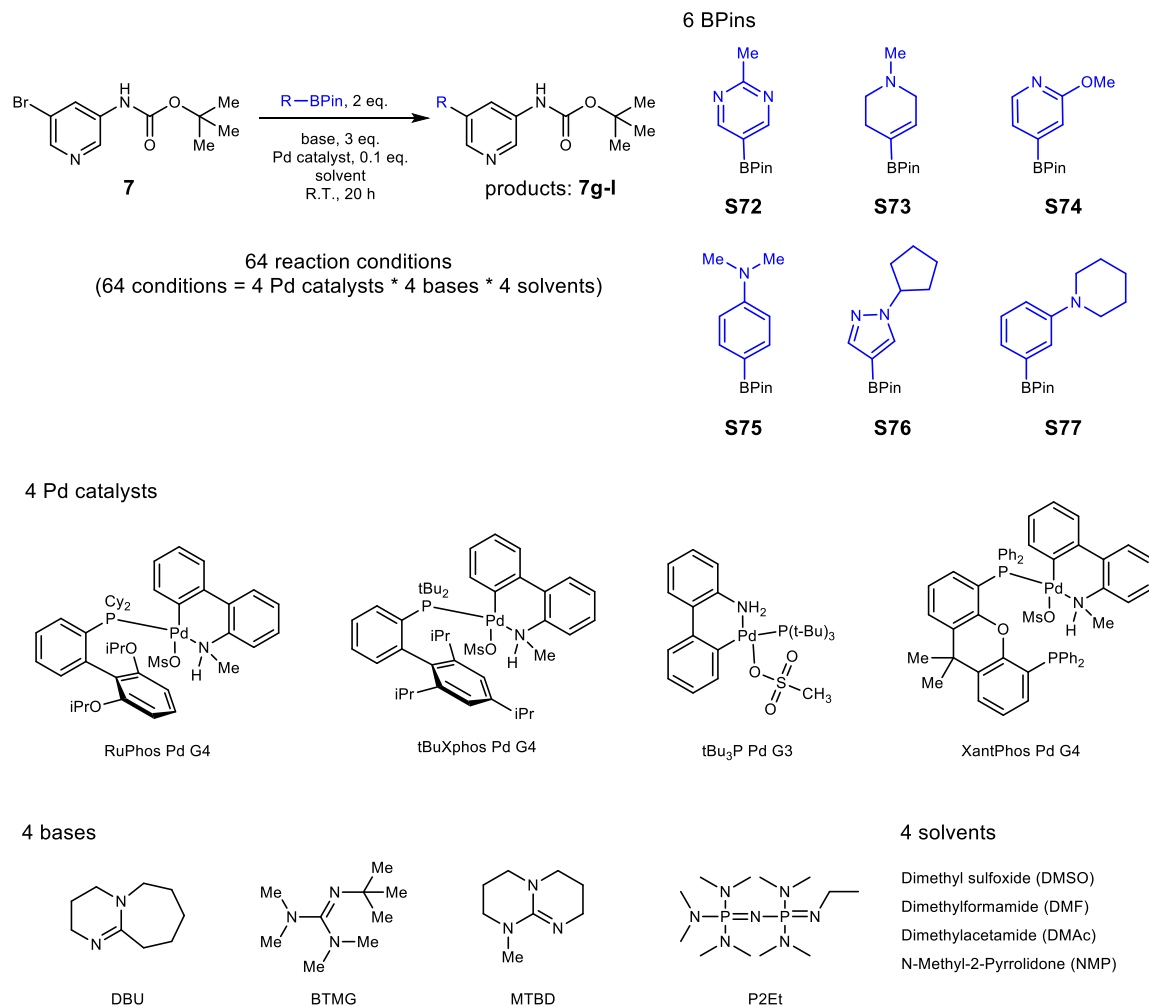
NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

NL-ADE-MS (multiplex) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) as groups of 6 spanning an individual reaction condition and solvent type: A1-A6 was pooled at 25 nL per source well into well A1 of the analysis plate, followed by A7-A12 to well A2 ...etc. Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 23.

4.8.11 Boc amine 7 Suzuki–Miyaura C-C coupling reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: *Boc amine* **7** (0.2 M in DMSO and DMF, 1 eq.). *Boronic acid pinacol ester* (*Bpin*) **S72-S77** (0.4 M in DMSO and DMF, 2 eq.). *Palladium* catalysts RuPhos Pd G4, tBuXPhos Pd G4, tBu3P Pd G3, and XantPhos Pd G4 (0.02 M in DMSO and DMF, 0.1 eq.) *Bases* DBU, BTMG, MTBD, and Cs₂CO₃ (0.6 M in H₂O and tAmOH, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: *Boc amine* **7** was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMSO, columns 13-18; DMF, columns 19-24. Next, *boronic acid pinacol ester* (*Bpin*) **S72-S77** were added to their respective columns following the same pattern of solvents, i.e. **S72** column 1 (DMSO), column 7 (DMF), column 13 (DMSO), and column 19 (DMSO); **S77** column 2 (DMSO), column 8 (DMF), ... *Palladium* catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. RuPhos Pd G4 rows A, E, I, and M). *Bases* in H₂O were distributed to column 1 to 12 arrayed as identical blocks of 4 (i.e. DBU rows A-D). Bases in tAmOH were distributed to column 13 to 24 arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm

and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of AcOH in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

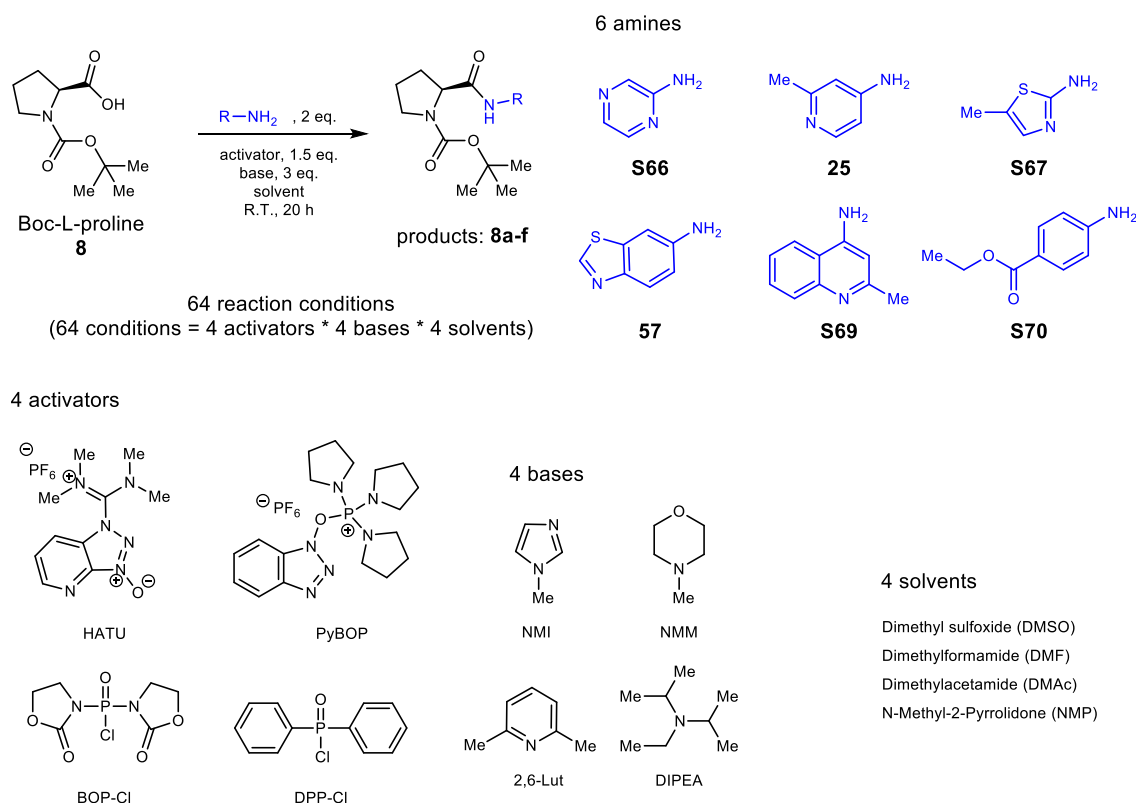
Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 24.

4.8.12 Boc-L-proline 8 amidation reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: *Boc-L-proline* **8** (0.2 M in DMSO, DMF, DMAc, and NMP, 1 eq.). *Amines* **S66**, **25**, **S67**, **57**, **S69**, **S70** (0.4 M in DMSO, DMF, DMAc, and NMP, 2 eq.). *Activators* HATU, PyBOP, BOP-Cl, DPP-Cl (0.3 M in DMSO, DMF, DMAc, and NMP, 1.5 eq.) *Bases* NMI, NMM, 2,6-Lut, and DIPEA (0.6 M in

DMSO, DMF, DMAc, and NMP, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: *Boc-L-proline* **8** was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, amines **S66**, **25**, **S67**, **57**, **S69**, **S70** were added to their respective columns following the same pattern of solvents, i.e. **S66** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **25** column 2 (DMSO), column 8 (DMF), ... Activators were distributed by column to each solvent grouping arrayed every 4th row (i.e. HATU rows A, E, I, and M). Bases were distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. NMI rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of H₂O/DMSO ($v:v = 1:3$, 4 μ L) using a Multidrop combi nL.

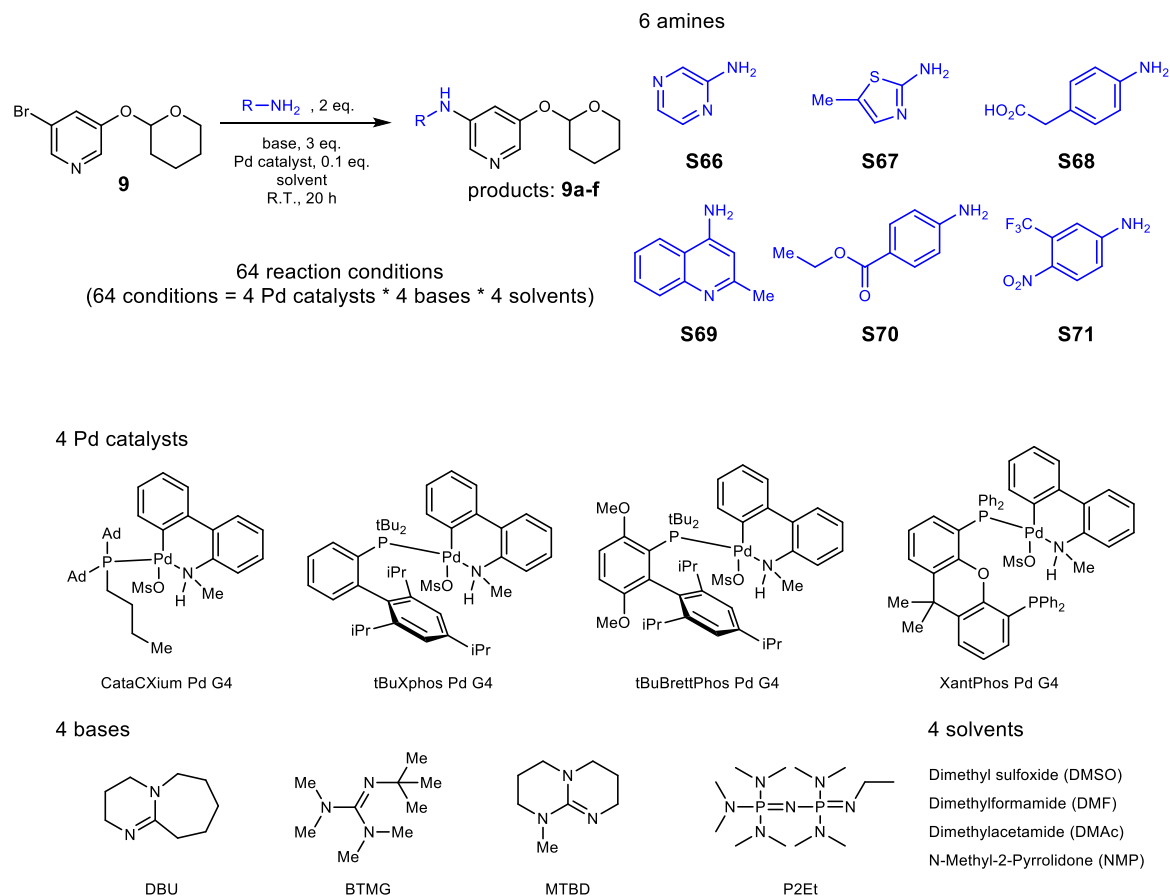
Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 25.

4.8.13 THP alcohol 9 Buchwald-Hartwig C-N coupling reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: *THP alcohol 9* (0.2 M in DMSO, DMF, DMAc, and NMP, 1 eq.). *Amines S66-S71* (0.4 M in DMSO, DMF, DMAc, and NMP, 2 eq.). *Palladium* catalysts cataCXium Pd G4, tBuXPhos Pd G4, tBuBrettPhos Pd G4, and XantPhos Pd G4 (0.02 M in DMSO, DMF, DMAc, and NMP, 0.1 eq.) *Bases* DBU, BTMG, MTBD, and P2Et (0.6 M in DMSO, DMF, DMAc, and NMP, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: *THP alcohol 9* was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, *amines S66-S71* were added to their respective columns following the same pattern of solvents, i.e. **S66** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **S67** column 2 (DMSO), column 8 (DMF), ... *Palladium* catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. cataCXium Pd G4 rows A, E, I, and M). *Bases* were distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of Acetic acid (AcOH) in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

Analysis plates were generated as follows by acoustic liquid handling:

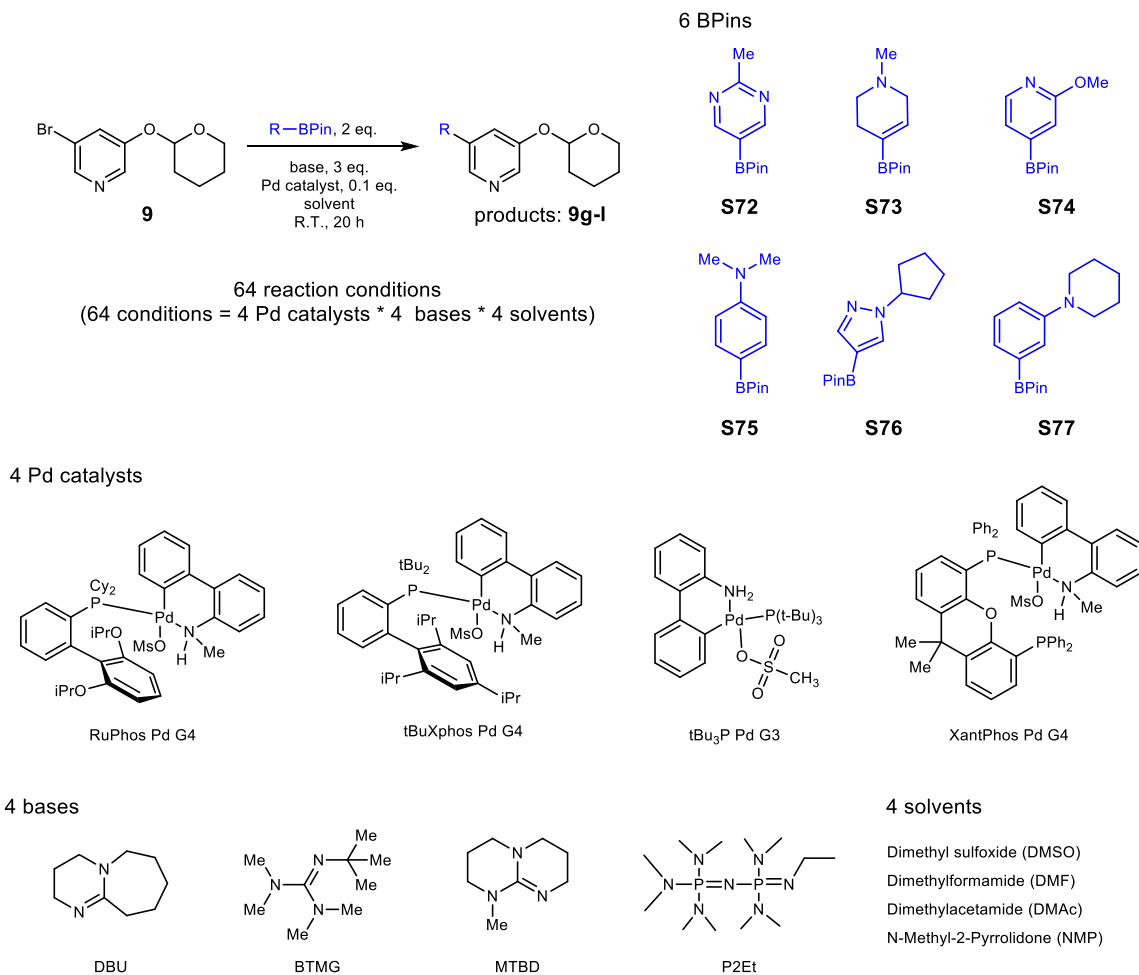
NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

NL-ADE-MS (multiplex) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) as groups of 6 spanning an individual reaction condition and solvent type: A1-A6 was pooled at 25 nL per source well into well A1 of the analysis plate, followed by A7-A12 to well A2 ...etc. Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 26.

4.8.14 THP alcohol **9** Suzuki–Miyaura C-C coupling reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: THP alcohol **9** (0.2 M in DMSO and DMF, 1 eq.). Boronic acid pinacol ester (Bpin) **S72-S77** (0.4 M in DMSO and DMF, 2 eq.). Palladium catalysts RuPhos Pd G4, tBuXPhos Pd G4, tBu₃P Pd G3, and XantPhos Pd G4 (0.02 M in DMSO and DMF, 0.1 eq.) Bases DBU, BTMG, MTBD, and Cs₂CO₃ (0.6 M in H₂O and tAmOH, 3 eq.). Using multi-channel pipetting 1 µL of each of the four components were arrayed in the following manner: THP alcohol **9** was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMSO, columns 13-18; DMF, columns 19-24. Next, boronic acid pinacol ester (Bpin) **S72-S77** were added to their respective columns following the same pattern of solvents, i.e. **S72** column 1 (DMSO), column 7 (DMF), column 13 (DMSO), and column 19 (DMSO); **S77** column 2 (DMSO), column 8 (DMF), ... Palladium catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. RuPhos Pd G4 rows A, E, I, and M). Bases in H₂O were distributed to column 1 to 12 arrayed as identical blocks of 4 (i.e. DBU rows A-D). Bases in tAmOH were distributed to column 13 to 24 arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were

left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of AcOH in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

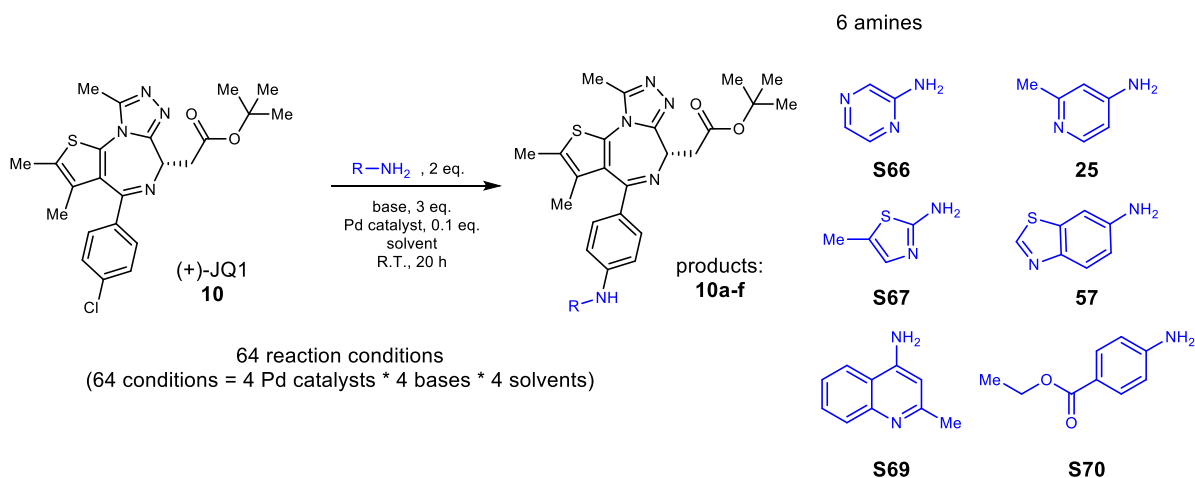
Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

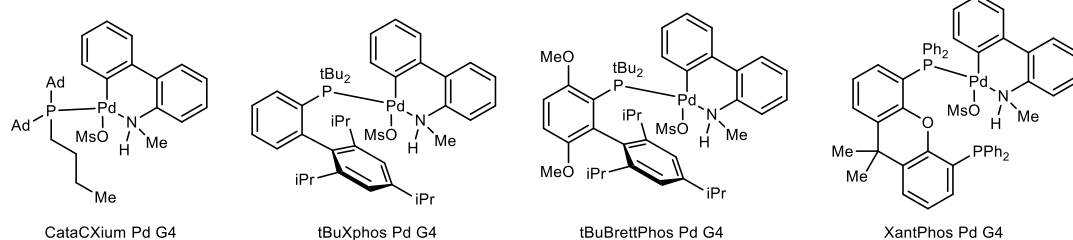
LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 27.

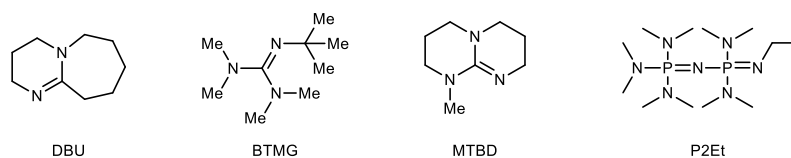
4.8.15 (+)-JQ1 10 Buchwald-Hartwig C-N coupling reaction



4 Pd catalysts



4 bases



4 solvents

Dimethyl sulfoxide (DMSO)
Dimethylformamide (DMF)
Dimethylacetamide (DMAc)
N-Methyl-2-Pyrrolidone (NMP)

All stock solutions were prepared inside the glovebox using anhydrous solvents: (+)-*JQI* **10** (0.2 M in DMSO, DMF, DMAc, and NMP, 1 eq.). *Amines* **S66**, **25**, **S67**, **57**, **S69**, **S70** (0.4 M in DMSO, DMF, DMAc, and NMP, 2 eq.). *Palladium* catalysts cataCXium Pd G4, tBuXPhos Pd G4, tBuBrettPhos Pd G4, and XantPhos Pd G4 (0.02 M in DMSO, DMF, DMAc, and NMP, 0.1 eq.) *Bases* DBU, BTMG, MTBD, and P2Et (0.6 M in DMSO, DMF, DMAc, and NMP, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: : (+)-*JQI* **10** was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, *amines* **S66**, **25**, **S67**, **57**, **S69**, **S70** were added to their respective columns following the same pattern of solvents, i.e. **S66** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **25** column 2 (DMSO), column 8 (DMF), ... *Palladium* catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. cataCXium Pd G4 rows A, E, I, and M). *Bases* were distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of AcOH in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

Analysis plates were generated as follows by acoustic liquid handling:

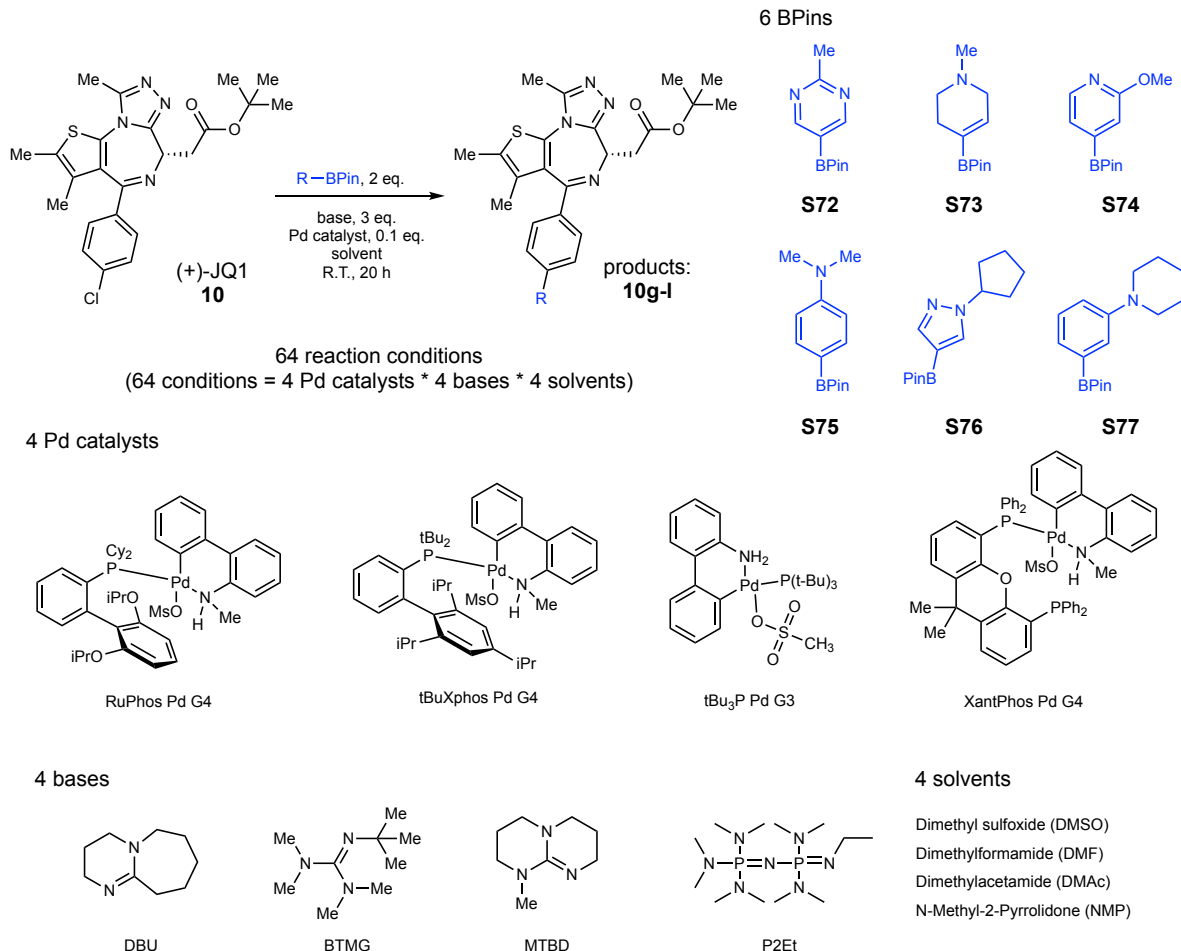
NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

NL-ADE-MS (multiplex) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) as groups of 6 spanning an individual reaction condition and solvent type: A1-A6 was pooled at 25 nL per source well into well A1 of the analysis plate, followed by A7-A12 to well A2 ...etc. Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 28.

4.8.16 (+)-JQ1 10 Suzuki–Miyaura C-C coupling reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: (+)-JQ1 **10** (0.2 M in DMSO and DMF, 1 eq.). Boronic acid pinacol ester (Bpin) **S72**–**S77** (0.4 M in DMSO and DMF, 2 eq.). Palladium catalysts RuPhos Pd G4, tBuXphos Pd G4, tBu3P Pd G3, and XantPhos Pd G4 (0.02 M in DMSO and DMF, 0.1 eq.) Bases DBU, BTMG, MTBD, and Cs₂CO₃ (0.6 M in H₂O and tAmOH, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: (+)-JQ1 **10** was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMSO, columns 13-18; DMF, columns 19-24. Next, boronic acid pinacol ester (Bpin) **S72**–**S77** were added to their respective columns following the same pattern of solvents, i.e. **S72** column 1 (DMSO), column 7 (DMF), column 13 (DMSO), and column 19 (DMSO); **S77** column 2 (DMSO), column 8 (DMF), ... Palladium catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. RuPhos Pd G4 rows A, E, I, and M). Bases in H₂O were distributed to column 1 to 12 arrayed as identical blocks of 4 (i.e. DBU rows A-D). Bases in tAmOH were distributed to column 13 to 24 arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left

to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of AcOH in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

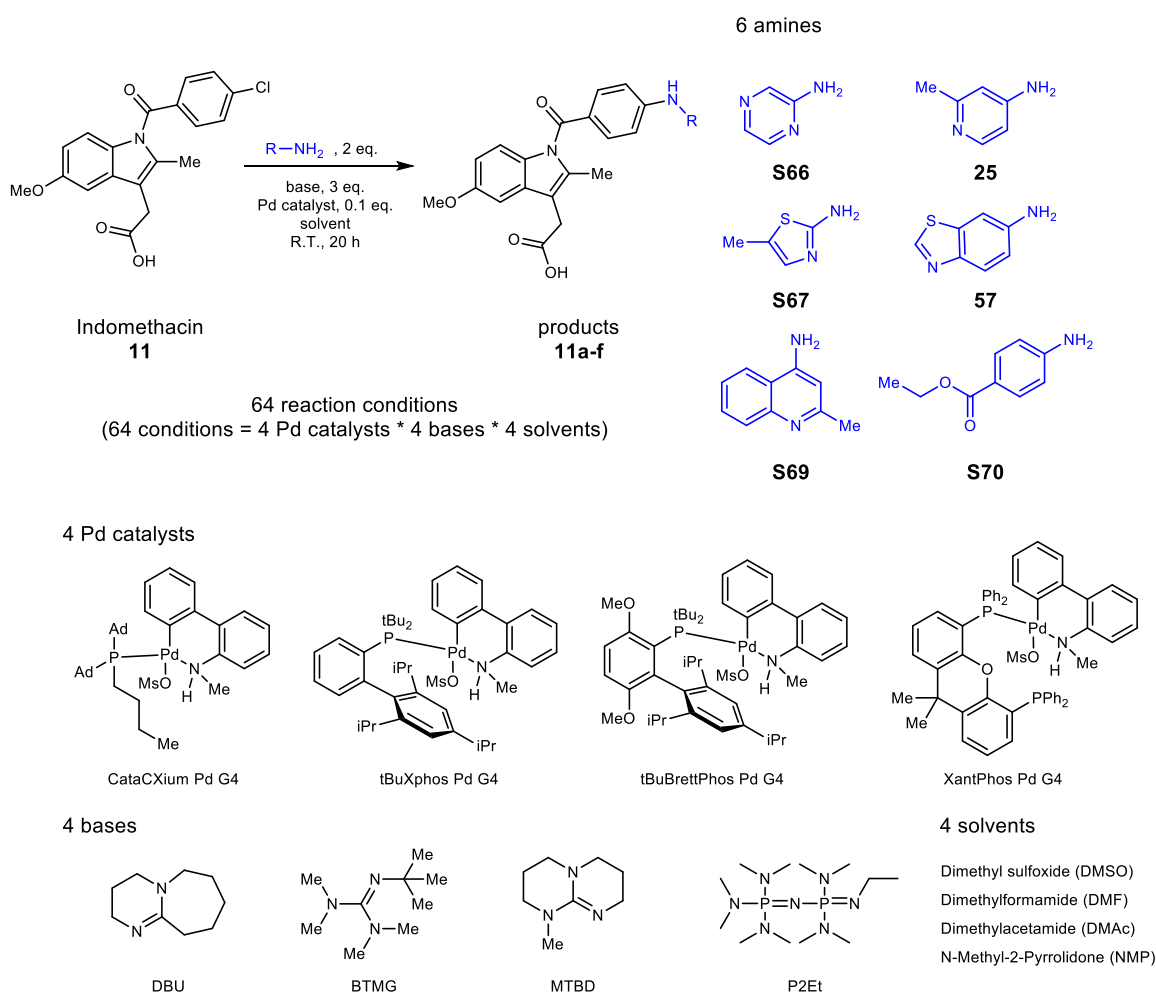
Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL*-ADE-MS analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 29.

4.8.17 Indomethacin 11 Buchwald-Hartwig C-N coupling reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: *Indomethacin* **11** (0.2 M in DMSO, DMF, DMAc, and NMP, 1 eq.). *Amines* **S66**, **25**, **S67**, **57**, **S69**, **S70** (0.4 M in DMSO, DMF, DMAc, and NMP, 2 eq.). *Palladium* catalysts cataCXium Pd G4, tBuXPhos Pd G4, tBuBrettPhos Pd G4, and XantPhos Pd G4 (0.02 M in DMSO, DMF, DMAc, and NMP, 0.1 eq.). *Bases* DBU, BTMG, MTBD, and P2Et (0.6 M in DMSO, DMF, DMAc, and NMP, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: *Indomethacin* **11** was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, *amines* **S66**, **25**, **S67**, **57**, **S69**, **S70** were added to their respective columns following the same pattern of solvents, i.e. **S66** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **25** column 2 (DMSO), column 8 (DMF), ... *Palladium* catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. cataCXium Pd G4 rows A, E, I, and M). *Bases* were distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of Acetic acid (AcOH) in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

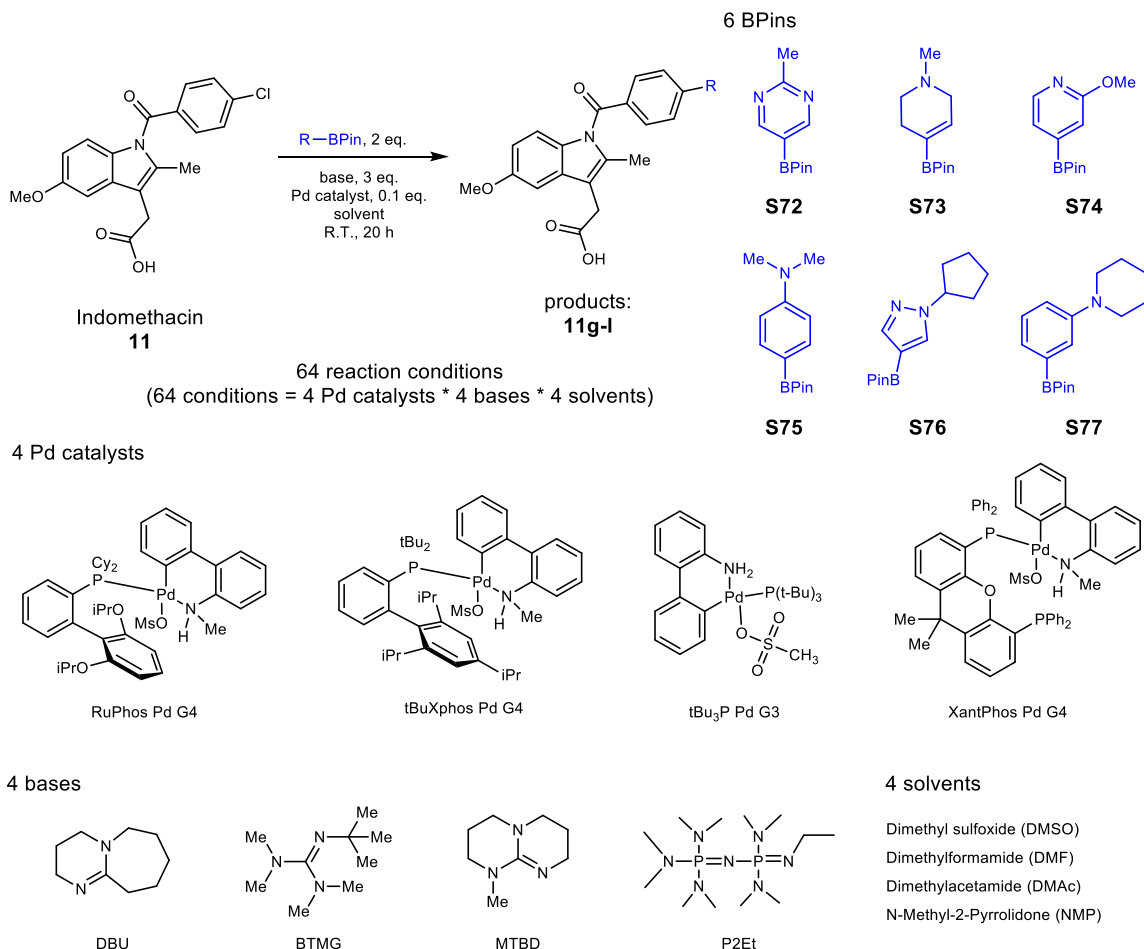
Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 30.

4.8.18 Indomethacin 11 Suzuki–Miyaura C-C coupling reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: *Indomethacin* **11** (0.2 M in DMSO and DMF, 1 eq.). *Boronic acid pinacol ester (Bpin)* **S72-S77** (0.4 M in DMSO and DMF, 2 eq.). *Palladium* catalysts RuPhos Pd G4, tBuXPhos Pd G4, tBu₃P Pd G3, and XantPhos Pd G4 (0.02 M in DMSO and DMF, 0.1 eq.) *Bases* DBU, BTMG, MTBD, and Cs₂CO₃ (0.6 M in H₂O and tAmOH, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: *Indomethacin* **11** was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMSO, columns 13-18; DMF, columns 19-24. Next, *boronic acid pinacol ester (Bpin)* **S72-S77** were added to their respective columns following the same pattern of solvents, i.e. **S72** column 1 (DMSO), column 7 (DMF), column 13 (DMSO), and column 19 (DMSO); **S77** column 2 (DMSO), column 8 (DMF), ... *Palladium* catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. RuPhos Pd G4 rows A, E, I, and M). *Bases* in H₂O were distributed to column 1 to 12 arrayed as identical blocks of 4 (i.e. DBU rows A-D). *Bases* in tAmOH were distributed to column 13 to 24 arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed

from the glovebox and quenched through addition of Acetic acid (AcOH) in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

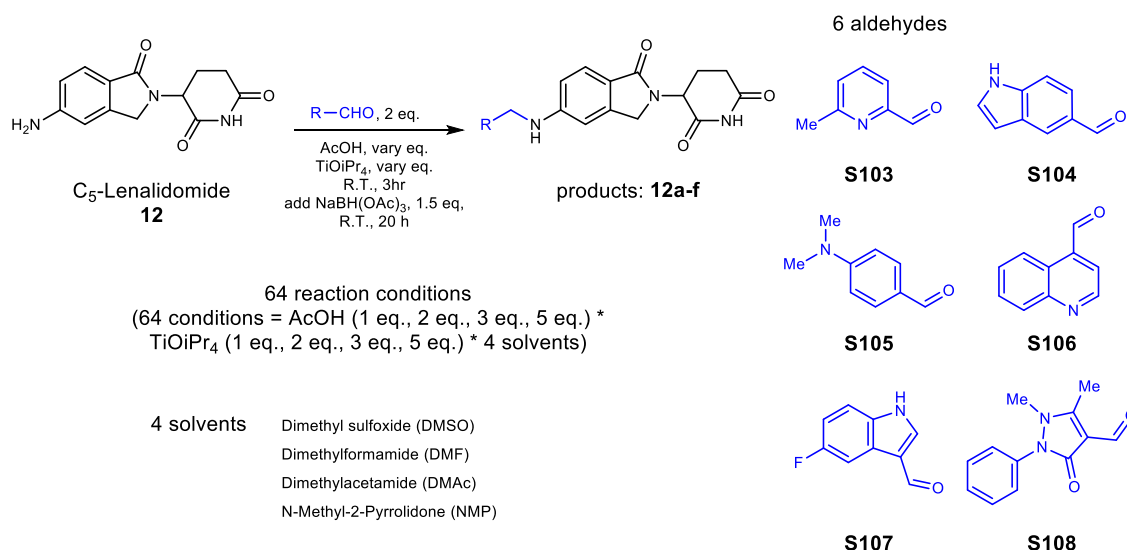
Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL*-ADE-MS analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 31.

4.8.19 C5-Lenalidomide **12** reductive amination reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: *C5-Lenalidomide 12* (0.2 M in DMSO, DMF, DMAc, and NMP, 1 eq.). *Aldehydes S103-S108* (0.4 M in DMSO, DMF, DMAc, and NMP, 2 eq.). AcOH, 1 eq. (0.4 M), 2 eq. (0.8 M), 3 eq. (1.2 M), and 5 eq (2 M) (in DMSO, DMF, DMAc, and NMP) and 2 $\text{Ti}(\text{OiPr})_4$, 1 eq. (0.4 M), 2 eq. (0.8 M), 3 eq. (1.2 M), and 5 eq (2 M) (in DMSO, DMF, DMAc, and NMP). *Reducing agent* sodium triacetoxyborohydride ($\text{NaBH}(\text{OAc})_3$) (0.3 M in DMSO, DMF, DMAc, and NMP, 1.5 eq.). AcOH and $\text{Ti}(\text{OiPr})_4$ were pre-mixed in the source plate right before preparing the reaction plate. AcOH was distributed by column to each solvent grouping arrayed every 4th row (i.e. 1 eq. AcOH rows A, E, I, and M). $\text{Ti}(\text{OiPr})_4$ was distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. 1 eq. $\text{Ti}(\text{OiPr})_4$ rows A-D). Using multi-channel pipetting 1 μ L of each of the three components were arrayed in the following manner: *C5-Lenalidomide 12* was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO,

columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, *aldehydes* **S103-S108** were added to their respective columns following the same pattern of solvents, i.e. **S103** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **S104** column 2 (DMSO), column 8 (DMF), ... Mixed AcOH and Ti(OiPr)₄ were distributed by column to each solvent grouping (i.e. DMF column 1-6...). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). *Reducing agent* NaBH(OAc)₃ (1 µL) added 3 h later and centrifuged for ~1 min at 1000 rpm before re-sealing. The mixtures were left to stand at room temperature for 20 h in total. Upon completion plates were removed from the glovebox and quenched through addition of saturated NaHCO₃/H₂O (v:v = 1:3, 4 µL) using a Multidrop combi nL. 3 µL of additional DMSO was added to the plate and centrifuged for 5 min at 1000 rpm. To avoid interference of solid precipitates 4 µL of this solution was transferred to a separate 384-well COC plate (001-12782) to enable preparation of analysis plates.

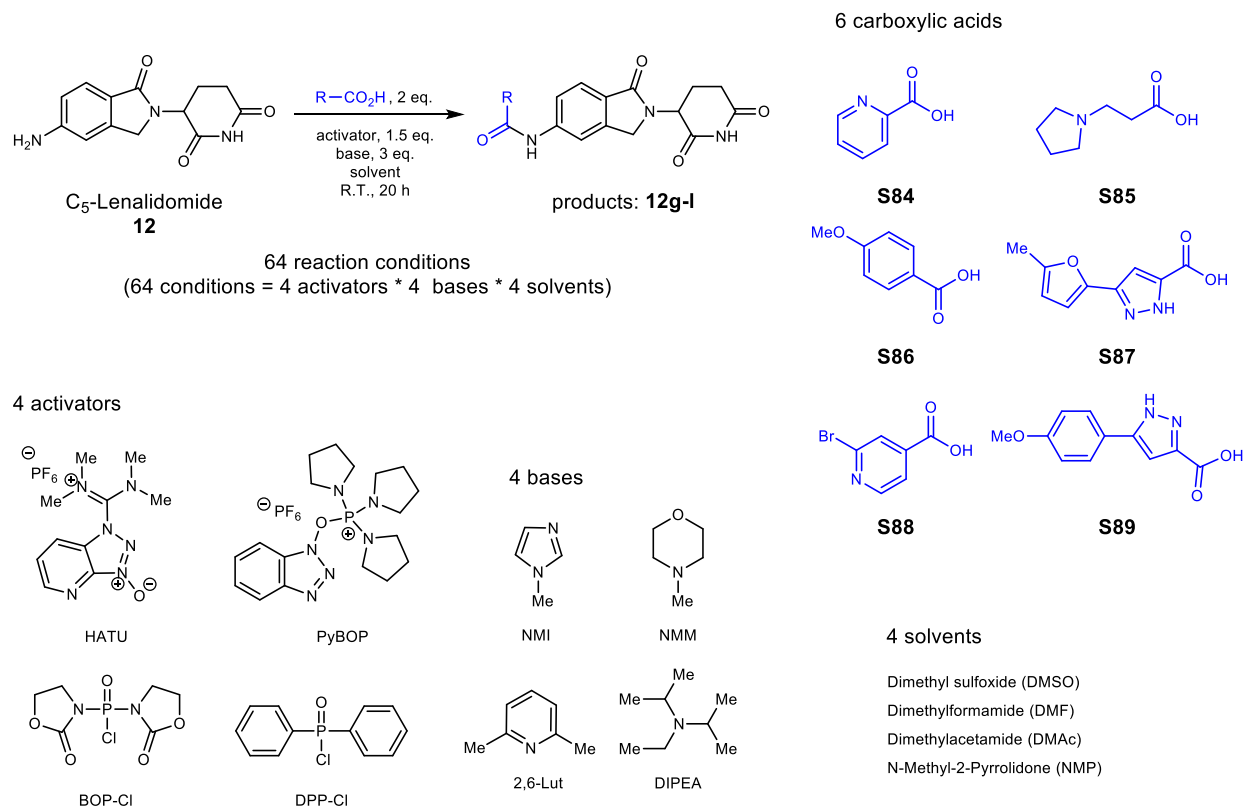
Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 µL) to provide a final maximum concentration of 9 µM.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 µL with 50 µM of **S5** as an internal standard) to provide a final maximum concentration of 18 µM.

Data are found in Extended Tabular Data Sheet 32.

4.8.20 C5-Lenalidomide 12 amidation reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: C5-Lenalidomide **12** (0.2 M in DMSO, DMF, DMAc, and NMP, 1 eq.). Carboxylic acids **S84-S89** (0.4 M in DMSO, DMF, DMAc, and NMP, 2 eq.). Activators HATU, PyBOP, BOP-Cl, DPP-Cl (0.3 M in DMSO, DMF, DMAc, and NMP, 1.5 eq.) Bases NMI, NMM, 2,6-Lut, and DIPEA (0.6 M in DMSO, DMF, DMAc, and NMP, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: C5-Lenalidomide **12** was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, carboxylic acids **S84-S89** were added to their respective columns following the same pattern of solvents, i.e. **S84** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **S85** column 2 (DMSO), column 8 (DMF), ... Activators were distributed by column to each solvent grouping arrayed every 4th row (i.e. HATU rows A, E, I, and M). Bases were distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. NMI rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of H₂O/DMSO (v:v = 1:3, 4 μ L) using a Multidrop combi nL.

Analysis plates were generated as follows by acoustic liquid handling:

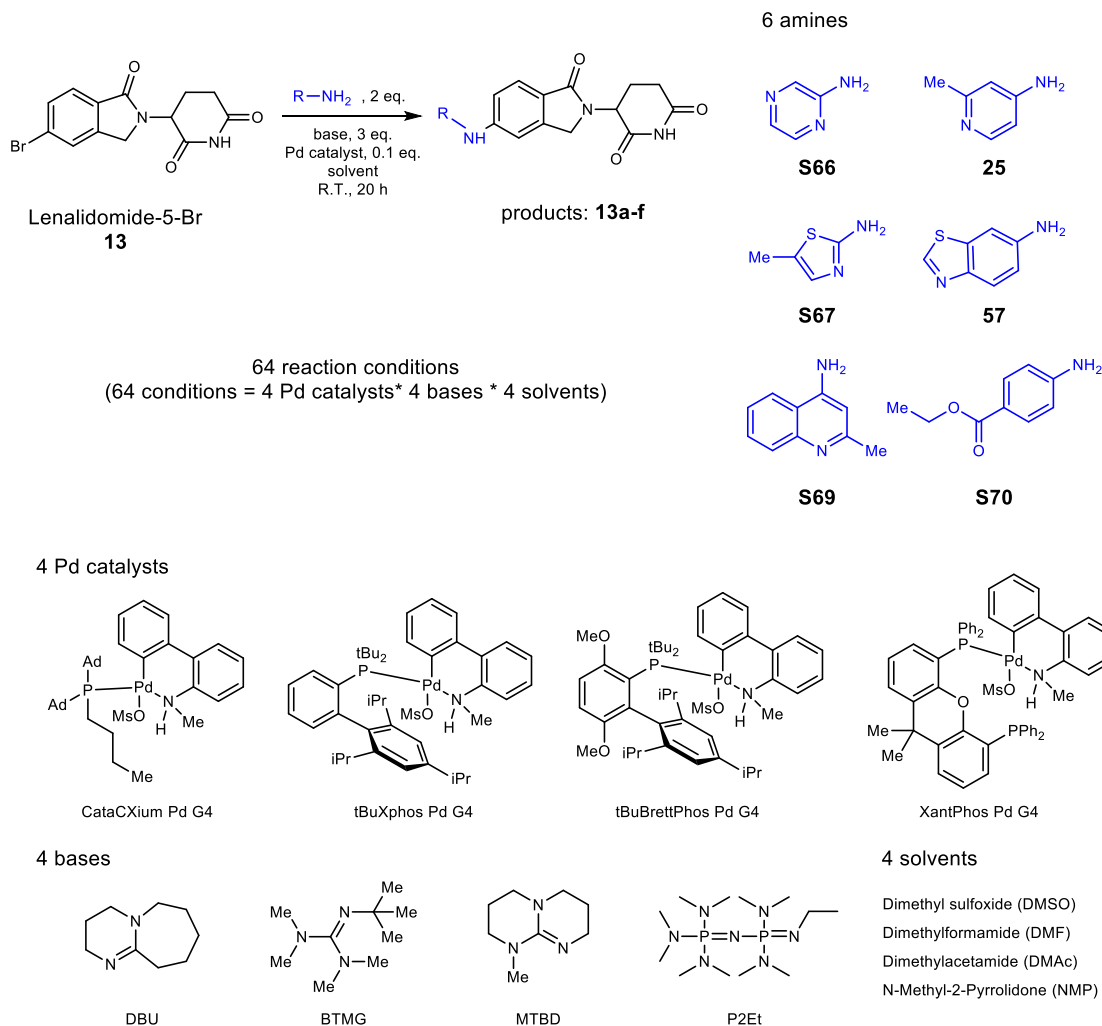
NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to NL-ADE-MS analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

NL-ADE-MS (multiplex) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) as groups of 6 spanning an individual reaction condition and solvent type: A1-A6 was pooled at 25 nL per source well into well A1 of the analysis plate, followed by A7-A12 to well A2 ...etc. Immediately prior to NL-ADE-MS analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 33.

4.8.21 Lenalidomide-5-Br 13 Buchwald-Hartwig C-N coupling reaction



All stock solutions were prepared inside the glovebox using anhydrous solvents: *Lenalidomide-5-Br* **13** (0.2 M in DMSO, DMF, DMAc, and NMP, 1 eq.). *Amines* **S66**, **25**, **S67**, **57**, **S69**, **S70** (0.4 M in DMSO, DMF, DMAc, and NMP, 2 eq.). *Palladium* catalysts cataCXium Pd G4, tBuXPhos Pd G4, tBuBrettPhos Pd G4, and XantPhos Pd G4 (0.02 M in DMSO, DMF, DMAc, and NMP, 0.1 eq.) *Bases* DBU, BTMG, MTBD, and P2Et (0.6 M in DMSO, DMF, DMAc, and NMP, 3 eq.). Using multi-channel pipetting 1 μ L of each of the four components were arrayed in the following manner: *Lenalidomide-5-Br* **13** was added across every well of a 384-well COC plate (001-12782) separated by solvent class DMSO, columns 1-6; DMF, columns 7-12; DMAc, columns 13-18; DMP, columns 19-24. Next, *amines* **S66**, **25**, **S67**, **57**, **S69**, **S70** were added to their respective columns following the same pattern of solvents, i.e. **S66** column 1 (DMSO), column 7 (DMF), column 13 (DMAc), and column 19 (NMP); **25** column 2 (DMSO), column 8 (DMF), ... Palladium catalysts were distributed by column to each solvent grouping arrayed every 4th row (i.e. cataCXium Pd G4 rows A, E, I, and M). Bases were distributed by column to each solvent grouping arrayed as identical blocks of 4 (i.e. DBU rows A-D). Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and then immediately sealed

with polyolefin sealing tape (Thermo 232701). The mixtures were left to stand at room temperature for 20 h. Upon completion plates were removed from the glovebox and quenched through addition of AcOH in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

Analysis plates were generated as follows by acoustic liquid handling:

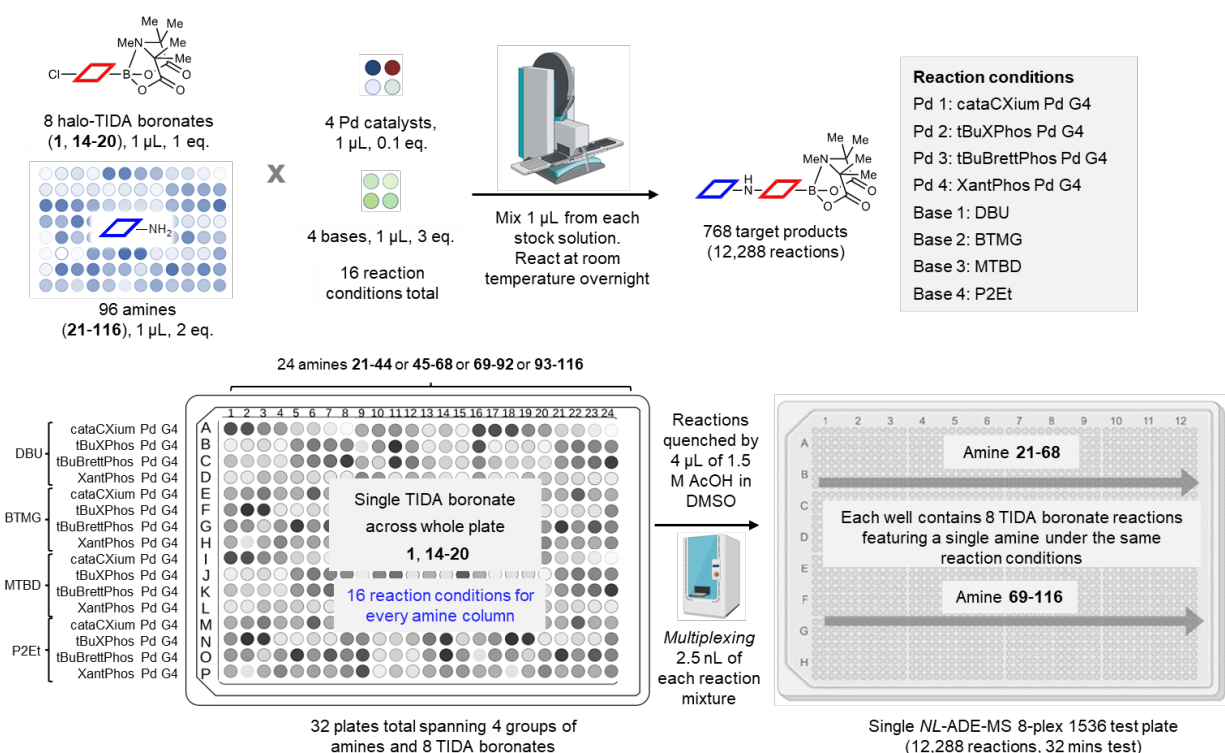
NL-ADE-MS (single) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) (25 nL per source well). Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

NL-ADE-MS (multiplex) – the 384-well COC reaction plate (001-12782) was directly copied a single 384-well PP plate (001-14615) as groups of 6 spanning an individual reaction condition and solvent type: A1-A6 was pooled at 25 nL per source well into well A1 of the analysis plate, followed by A7-A12 to well A2 ...etc. Immediately prior to *NL-ADE-MS* analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (50 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384-well plates (001-12782) by creating direct 1-1 copies through transfer of 50 nL to a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M.

Data are found in Extended Tabular Data Sheet 34.

4.9 High-throughput experimentation spanning 12,288 reactions (Fig. 4)



Using multichannel and single channel pipettes a series of source plates were created inside a nitrogen filled glovebox to enable generation of 12,288 chemical reaction mixtures. All stock solutions were prepared inside the glovebox using anhydrous solvent. *Boronates* **1** and **14-20** (15 μ L, 0.2 M in DMF (0.1 M for **19**)) were added individually to eight 384-well PP plates (Greiner 784201) *Amines* **21-116** (20 μ L, 0.4 M in DMF) were added to four plates 384-well PP plates (Greiner 784201) as singletons across each row A1->A24, B1->B24, ... following the order shown in Supplementary Tabular Data Sheet 26. *Palladium* catalysts cataCXium Pd G4, tBuXPhos Pd G4, tBuBrettPhos Pd G4, and XantPhos Pd G4 (50 μ L, 0.02 M in DMF) were distributed across every 4th row of a single 384-well PP plate, i.e. cataCXium Pd G4 on rows A, E, I, M; tBuXPhos Pd G4 rows B, F, J, N; ... *Bases* DBU, BTMG, MTBD, and P2Et (50 μ L, 0.6 M in DMF) were added to rows A-D, E-H, I-L, and M-P respectively of a single 384-well PP plate (Greiner 784201).

To generate reaction mixtures from these plates we used an Apricot PP-5 liquid handler (50 μ L, 384-tip head) located inside a nitrogen filled glovebox. This 5-position liquid handler allowed creation of 4 plate copies at a time from an individual source plate by using the single aspirate multi-dispense feature. A typical transfer would involve a pre-airgap (1 μ L) drawing liquid from all 384-wells of a source plate simultaneously (5 μ L), which would be transferred as 1 μ L volumes to the remaining 4 positions with appropriate bottom or side touching, the remaining volume was returned to the source plate. Tips were changed only when the source plate identity changed. To mitigate solvent evaporation all required equipment was transferred to a nitrogen filled glovebox, the circulator was then deactivated for the entire transfer process and a large volume of DMF was poured into an open container. Each of the eight *boronate* source plates were used to generate four copies into barcoded 384-well COC low-dead volume plates (001-12782) transferring 1 μ L ensuring effective transfer by using the bottom touch feature. The resulting 32 plates were separated into four stacks containing one of each of the eight boronates. The four *amine* source plates were distributed to one of each of these four stacks transferring 1 μ L at 50% well depth touching the left and right sides of the target wells to avoid cross-contamination. Next, the *palladium* source plate was used to transfer 1 μ L at 50% well depth across all 32 plates touching the front and back sides of the target wells to avoid cross-contamination. Finally, *base* source plate was used to transfer 1 μ L at 50% well depth across all 32 plates touching the front and back sides of the target wells. Upon completion of the transfers the plates were centrifuged for ~1 min at 1000 rpm and immediately sealed with polyolefin sealing tape (Thermo 232701). The glovebox circulator was reactivated, the DMF reservoir was emptied, and the mixtures were left to stand at room temperature for 20 h. Upon completion the 32 plates were removed from the glovebox and quenched through addition of AcOH in DMSO (4 μ L, 1.5 M) using a Multidrop combi nL.

Analysis plates were generated as follows by acoustic liquid handling:

NL-ADE-MS (single) – for each boronate there are four 384-well COC plates (001-12782) which span the full range of 96 amines. These four plates were directly copied into quadrants of single 1536-well COC plate (001-6969) (2.5 nL per source well). Immediately prior to NL-ADE-MS

analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (5 μ L) to provide a final maximum concentration of 12.5 μ M.

NL-ADE-MS (multiplex) – the 32 reaction plates were separated into 4 stacks. Each stack of eight 384-well COC plates (001-12782) arises from an individual set of 96 amines. These four stacks were directly copied into quadrants of single 1536-well COC plate (001-6969) (2.5 nL per source well) for a total of 8 transfers to each well of the target plate. Immediately prior to NL-ADE-MS analysis the plate was diluted using a Multidrop combi nL with 30% aqueous acetonitrile (5 μ L) to provide a final maximum concentration of 12.5 μ M.

LC-MS – individual plate copies when needed were generated from the 384 plates COC low-plates (001-12782) by creating direct 1-1 copies through transfer of 50 or 500 nL to a a costar 384-well plate (3657). The plate was diluted using a Multidrop combi nL with with DMSO (50 μ L with 50 μ M of **S5** as an internal standard) to provide a final maximum concentration of 25 μ M, 125 μ M, or 250 μ M.

Data are found in Extended Tabular Data Sheets 36-41.

4.10 Quantitative analysis (Extended Data Fig. 10a-f)

Quantitative analysis used similar format as mentioned above for single 384-well plate experiments, each selected building block was coupled with 6 coupling partners and products distributed across columns. One control column only contained the starting building block to establish 0% conversion signal intensity. Here, we tested *TIDA 1*, coupled with *amines S66-S71* (Buchwald-Hartwig C-N coupling reaction) in DMF (plate 1 column 1 to 7, column 7 is control), *boronic acid pinacol esters S72-S77* (Suzuki–Miyaura C-C coupling reaction) in DMF-H₂O (plate 1 column 9 to 15, column 15 is control), and *alcohols S78-S83* (C-N coupling reaction) in DMF (plate 1 column 17 to 23, column 23 is control). (+)-*JQ1 10*, coupled with *amines S66, 25, S67, 57, S69, S70* (Buchwald-Hartwig C-N coupling reaction) in DMF (plate 2 column 1 to 7, column 7 is control), *C5-Lenalidomide 12*, coupled with *carboxylic acid S84-S89* (amidation) in DMF (plate 2 column 9 to 15, column 15 is control), Clarithromycin derivative **5** coupled with *boronic acid pinacol esters S72-S77* (Suzuki–Miyaura C-C coupling reaction) in DMF-H₂O (plate 2 column 17 to 23, column 23 is control). One column was skipped in between different reactions. All the reagents and concentration are the same as mentioned for the 384-plate reactions described above. The reaction plate was prepared similarly as described for 384-well plate reactions, 3 μ L of blank DMF solvent was added into control column in place of solutions of reagents to dilute the respective starting material in those wells (i.e. **1**, **10**, **12**, and **5**). All wells were quenched after 20 h. The analysis plate was prepared as described above. The average signal intensity of the control column (16 data points) was used as starting point to define 0% conversion and starting material conversation was calculated against this measure. Product relative yield was calculated against the largest signal in each column as described above.

Data are found in Extended Tabular Data Sheets 51-56.

4.11 Reaction kinetics under native conditions (Extended Data Fig 10g)

A stock solution of 10 mM NaOH in 70:30 (v:v) water:acetonitrile was prepared. In 3 separate Eppendorf tubes were added TIDA boronates **1**, **S2** and **S5** (2 μ L, 0.2 μ mol, 100 mM in DMSO) which were immediately diluted with the NaOH stock solution (2 mL, 20 μ mol, 100 eq.). 50 μ L aliquots were then assembled in a 384-well COC reaction plate (001-12782) with 6 replicates per TIDA boronate. After brief centrifugation (3 minutes), the samples were immediately analyzed by *NL*-ADE-MS to track consumption of TIDA boronates over time. Data were collected at the following intervals (0, 3, 6, 9, 12, 15, 25, 35, 50, 60 minutes). Parameters for *NL*-ADE-MS were assigned based on product ion scans of **1** (CE 31 V, DP 100 V, EP 10 V, CXP 13), **S2** (CE 30 V, DP 100 V, EP 10 V, CXP 14), and **S5** (CE 33 V, DP 100 V, EP 10 V, CXP 10), mass range was set to ± 5 Da relative to the parent ion $[M+H]^+$ for each analysis. Data were then averaged across the six replicates for each time point. *Data are found in Extended Tabular Data Sheet 57.*

4.12 Neutral loss-LC-MS (*NL*-LC-MS) (Extended Data Fig 10h)

Neutral loss-LC-MS data was collected in the mass range of 370-520 Da, scan rate was 2000 Da/s. Neutral loss was set to 86 Da. The TIDA **1** Buchwald-Hartwig C-N coupling reaction in Section 4.8.2 was used for this experiment. Samples were prepared by transfer of 2.5 nL from the reaction plate to four 96-well waters 350 μ L plates (#186002643), diluted with 300 μ L of 50% aqueous acetonitrile (containing 500 nM of **S5** as internal standard) to achieve a sample concentration of 208 nM. The plate was then sealed using waters adhesive plate seals (#186006336) and centrifuged for 5 minutes at 2000 rpm. A 2 μ L injection volume was used and relative yields were calculated for products by comparison against the largest signal intensity for each product across all 64 conditions as described above. Reaction conditions were plotted as an average of 6 products. *Data are found in Extended Tabular Data Sheet 58.*

4.13 Supplementary Figures

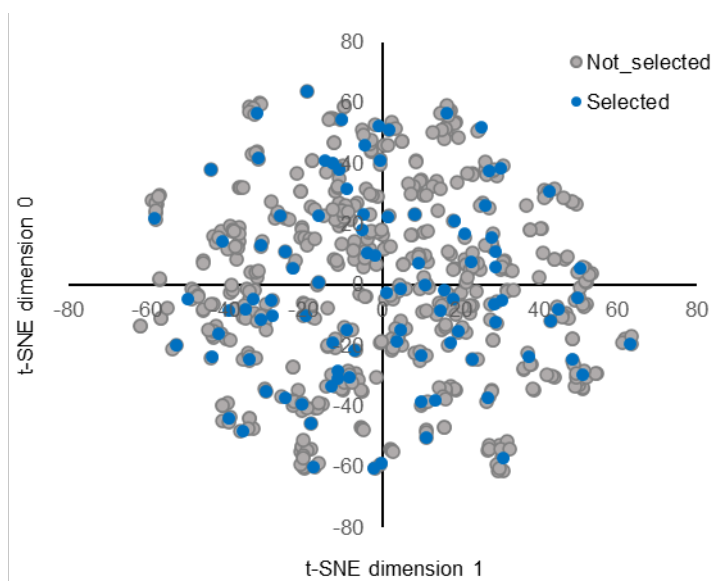


Figure S1 Amine selection for high-throughput experimentation. Representative t-SNE plot showing distribution of amines across structure property space for high-throughput experimentation. Selected amines shown in **blue**, non-selected cluster members in **gray** (see Figure S9 for compound structures).

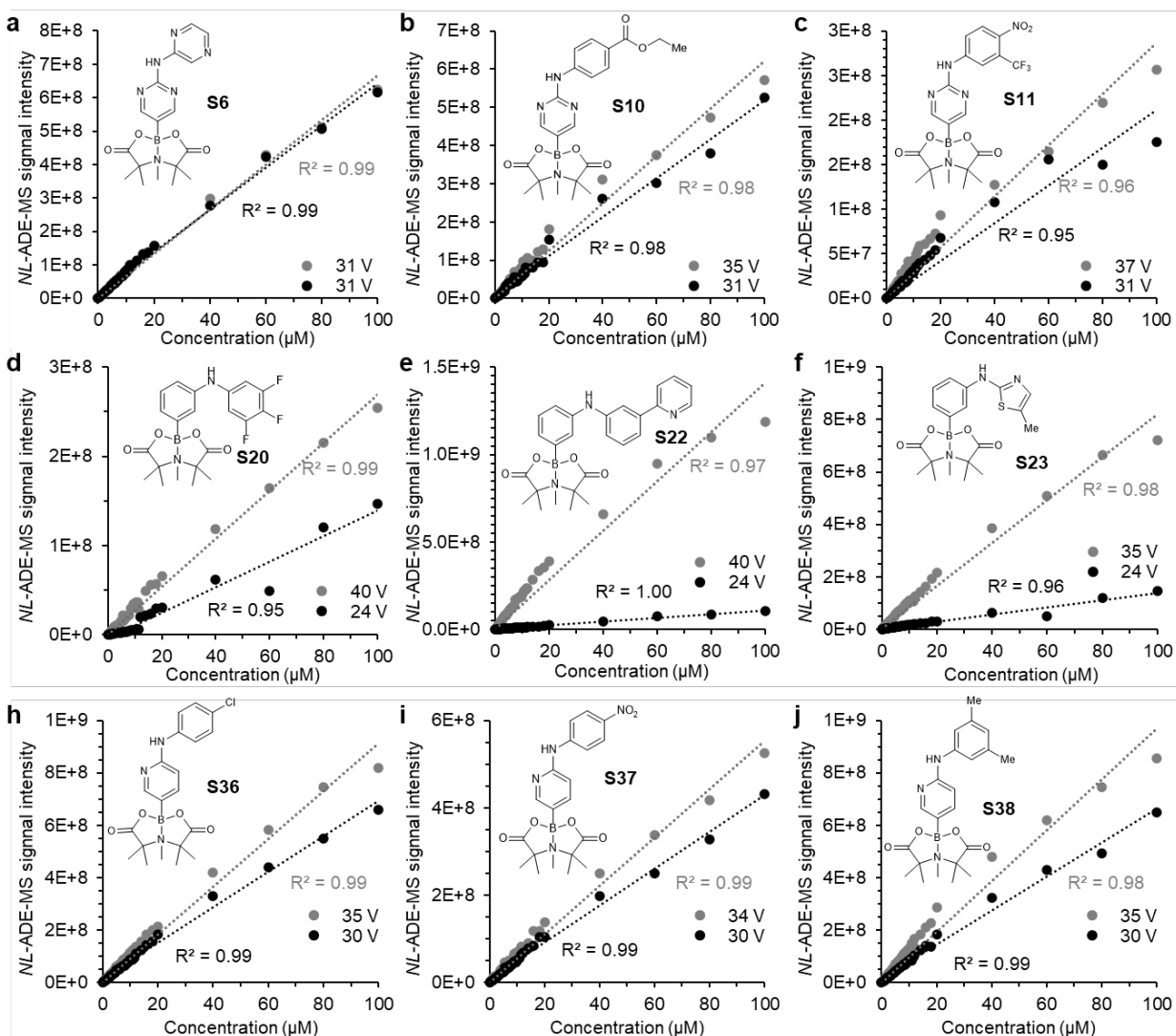


Figure S2 Starting materials define fragmentation barcodes for downstream products. NL-ADE-MS analysis of products arising from TIDA 1 (a, S6, b, S10, c, S11), TIDA S1 (d, S20, e, S22, f, S23), and TIDA S2 (h, S36, i, S37, j, S38) using both idealized (gray) and starting material (black) defined fragmentation parameters show that linear concentration responses are followed with the starting material defined collision energy over a wide concentration range. Data are found in Extended Tabular Data Sheet 18.

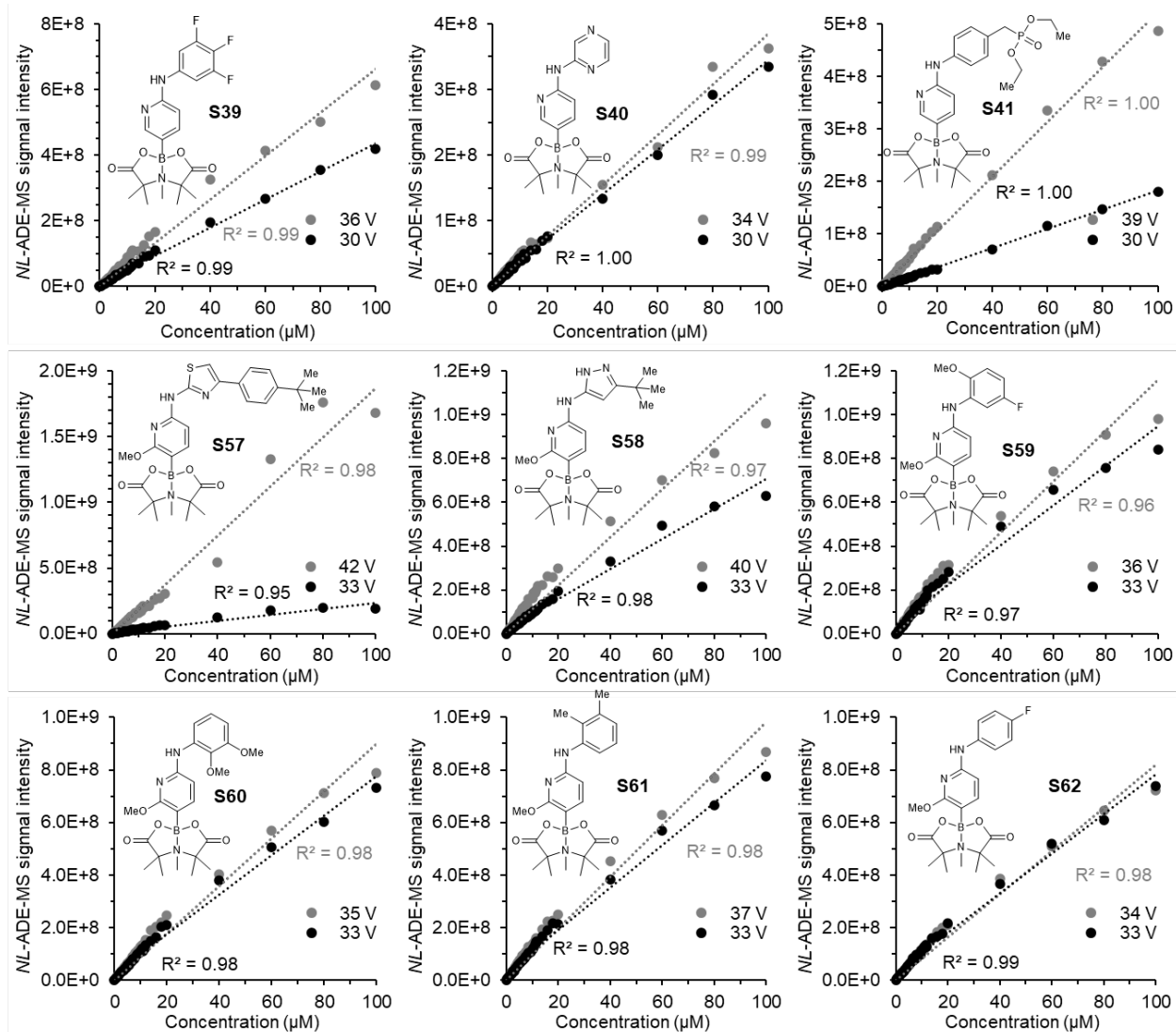


Figure S3 Starting materials define fragmentation barcodes for downstream products. NL-ADE-MS analysis of products arising from TIDA S2 (a, S39, b, S40, c, S41) and TIDA S5 (d, S57, e, S58, f, S59, h, S80, i, S61, j, S62) using both idealized (gray) and starting material (black) defined fragmentation parameters show that linear concentration responses are followed with the starting material defined collision energy over a wide concentration range. Data are found in Extended Tabular Data Sheet 18.

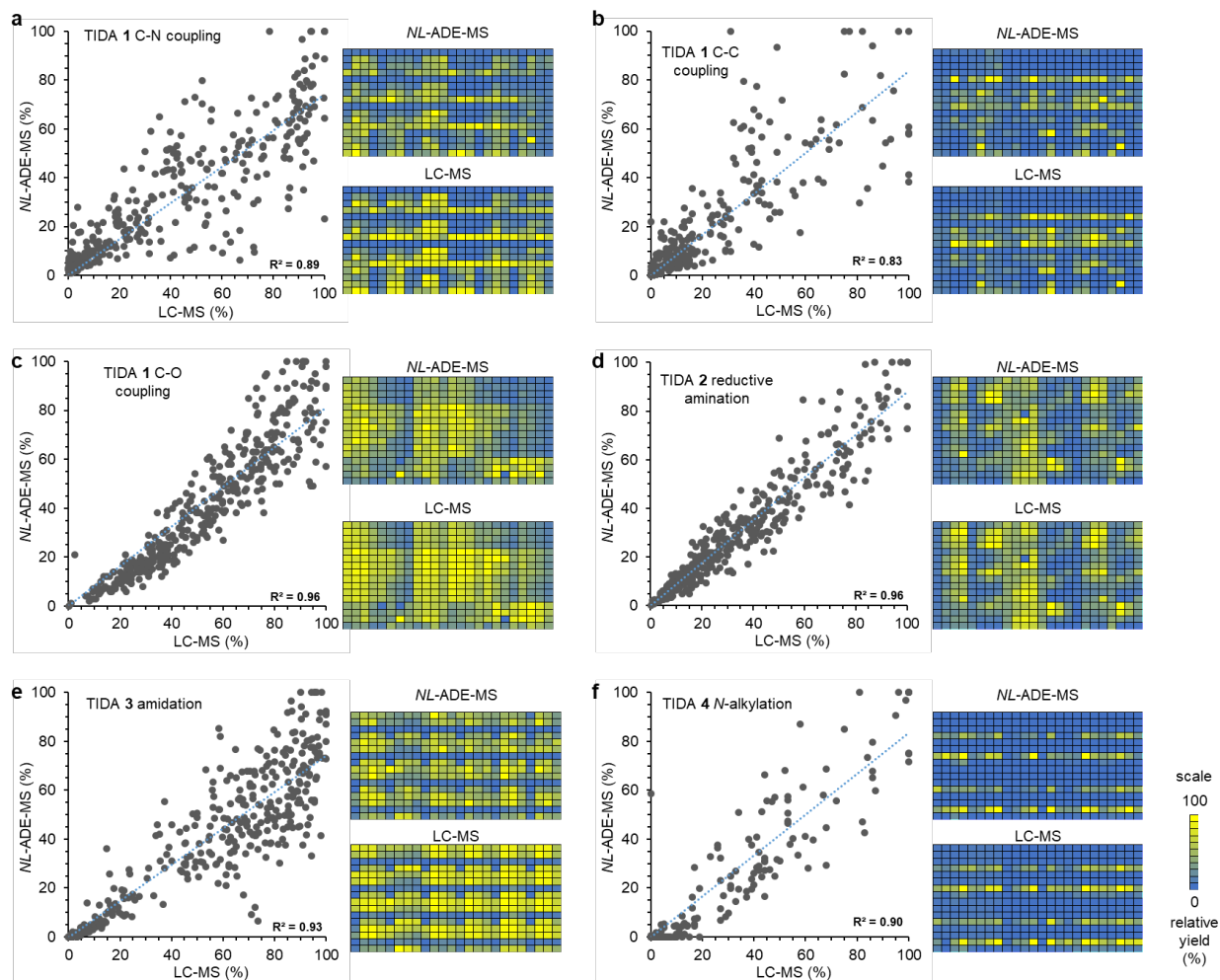


Figure S4 Head to head comparison of NL-ADE-MS and LC-MS. Relative product outputs were determined for products derived from building blocks **a**, TIDA 1 (Buchwald-Hartwig C-N coupling), **b**, TIDA 1 (Suzuki-Miyaura C-C coupling), **c**, TIDA 1 (C-O coupling), **d**, TIDA 2 (reductive amination), **e**, TIDA 3 (amidation), and **f**, TIDA 4 (N-alkylation) by both NL-ADE-MS and LC-MS. Data are found in Extended Tabular Data Sheet 12-17.

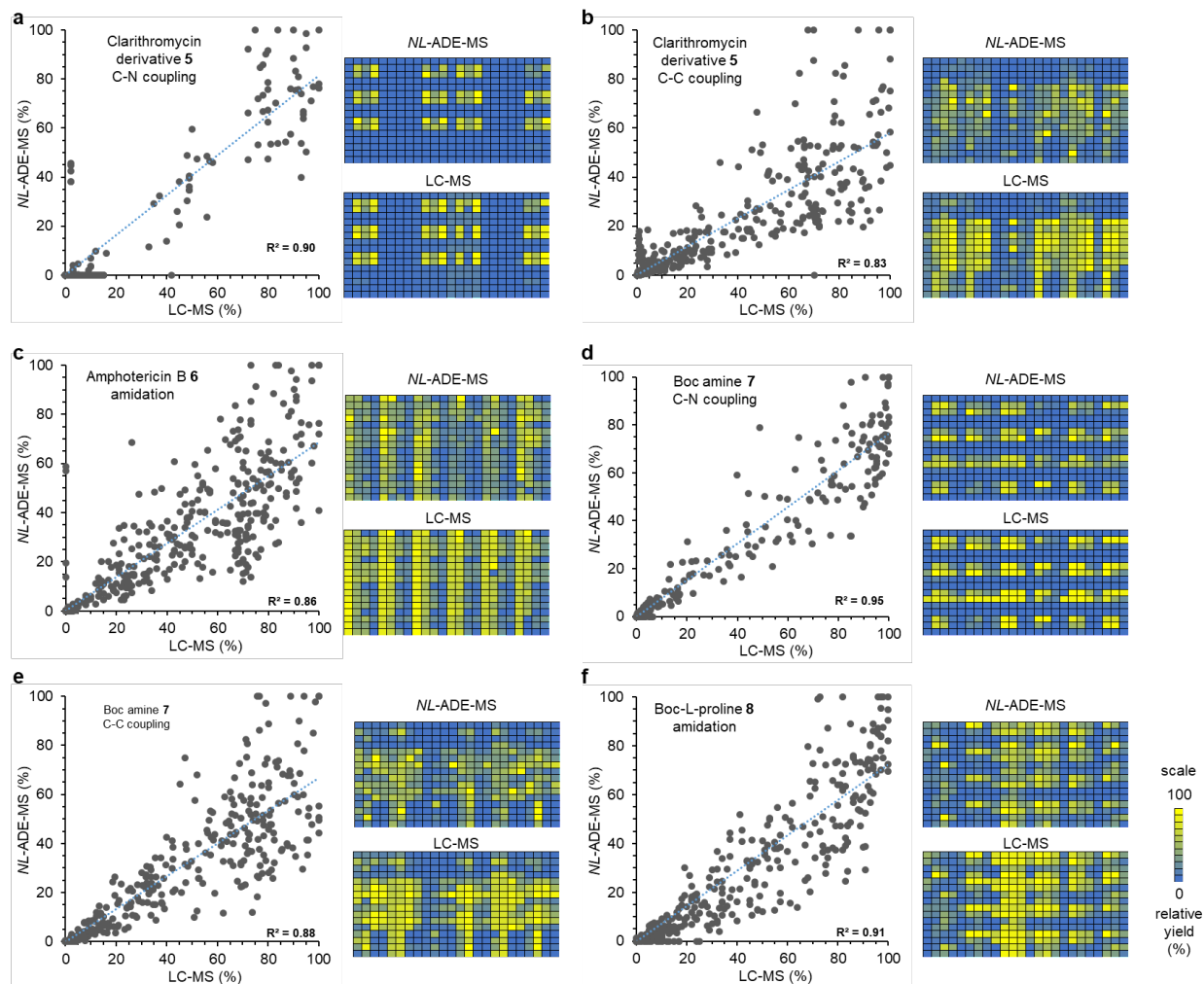


Figure S5 Head to head comparison of NL-ADE-MS and LC-MS. Relative product outputs were determined for products derived from building blocks **a**, Clarithromycin derivative **5** (Buchwald-Hartwig C-N coupling), **b**, Clarithromycin derivative **5** (Suzuki-Miyaura C-C coupling), **c**, Amphotericin B **6** (amidation), **d**, Boc amine **7** (Buchwald-Hartwig C-N coupling), **e**, Boc amine **7** (Suzuki-Miyaura C-C coupling), and **f**, Boc-L-proline **8** (amidation) by both NL-ADE-MS and LC-MS. Data are found in *Extended Tabular Data Sheet 20-25*.

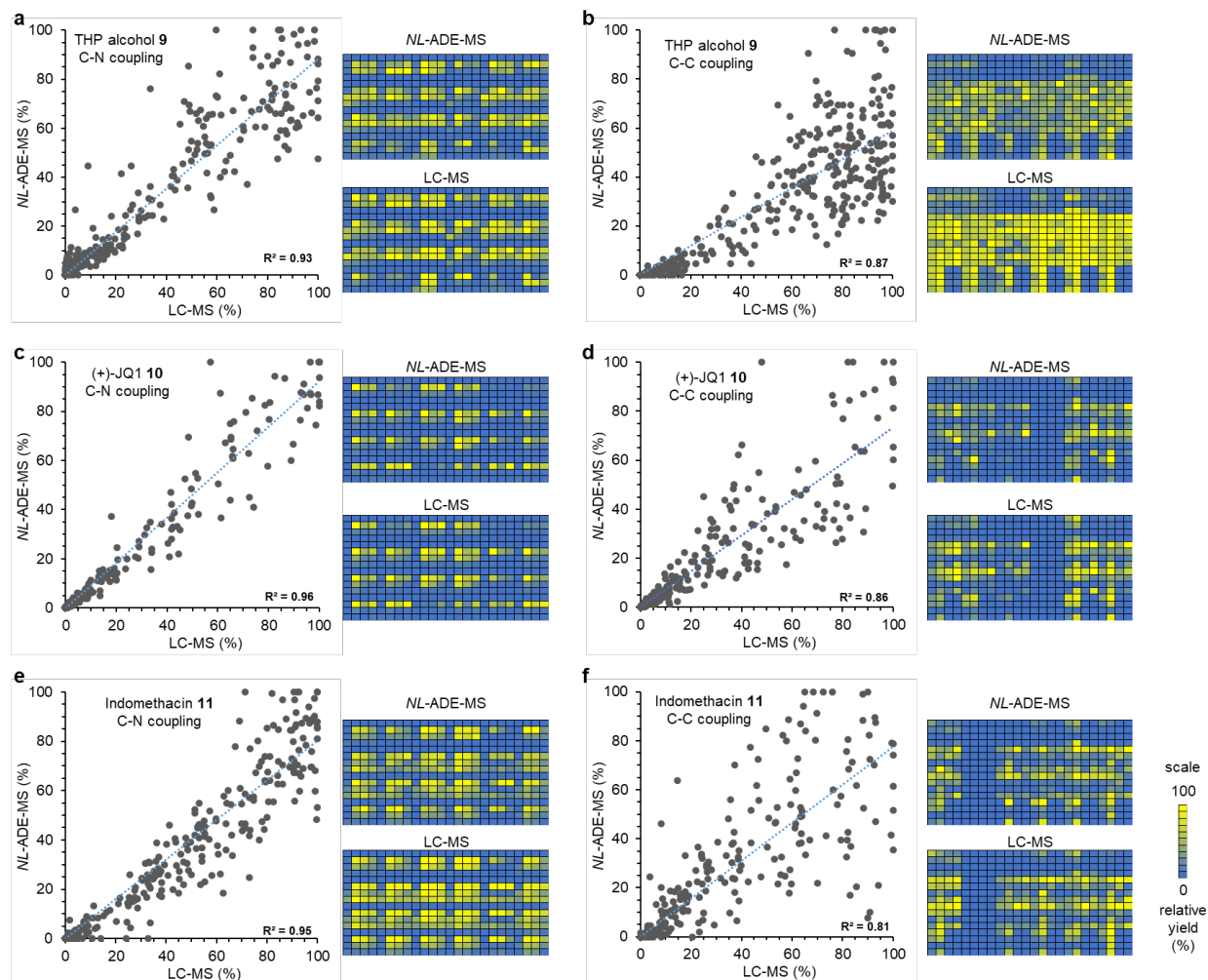


Figure S6 Head to head comparison of NL-ADE-MS and LC-MS. Head to head comparison of NL-ADE-MS and LC-MS. Relative product outputs were determined for products derived from building blocks **a**, THP alcohol **9** (Buchwald-Hartwig C-N coupling), **b**, THP alcohol **9** (Suzuki-Miyaura C-C coupling), **c**, (+)-JQ1 **10** (Buchwald-Hartwig C-N coupling), **d**, (+)-JQ1 **10** (Suzuki-Miyaura C-C coupling), **e**, Indomethacin **11** (Buchwald-Hartwig C-N coupling), and **f**, Indomethacin **11** (Suzuki-Miyaura C-C coupling) by both NL-ADE-MS and LC-MS. Data are found in *Extended Tabular Data Sheet 26-31*.

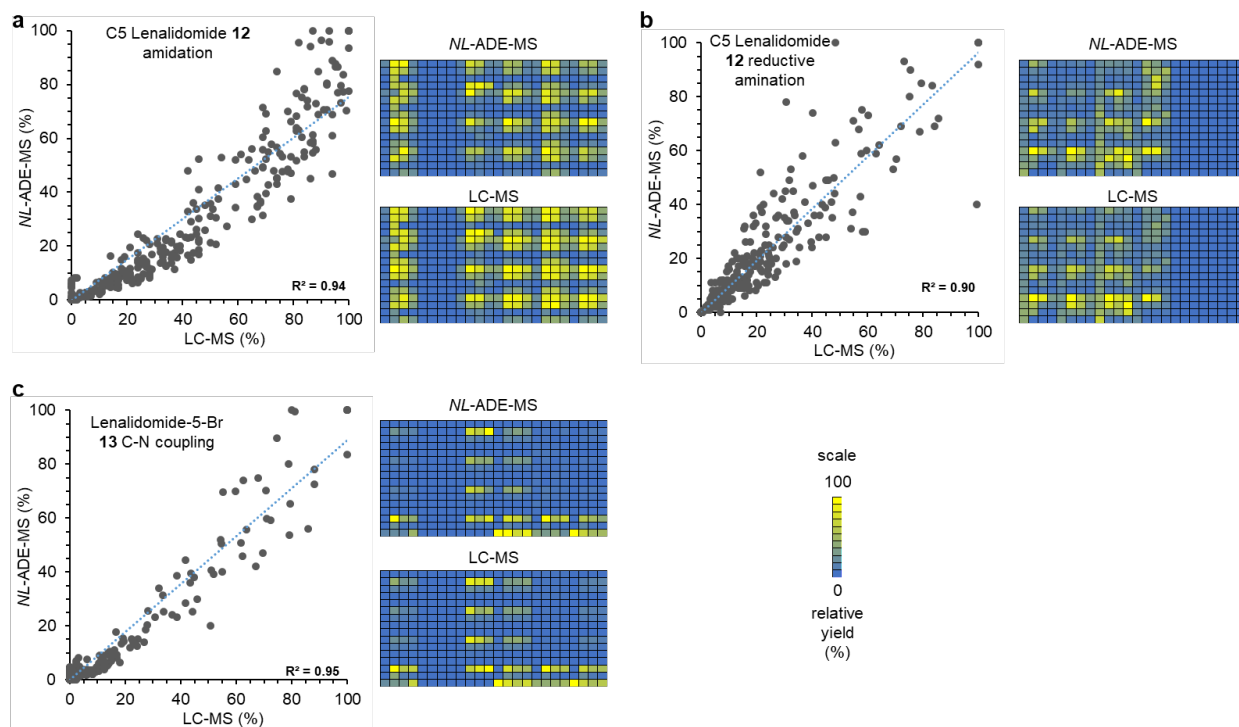


Figure S7 Head to head comparison of NL-ADE-MS and LC-MS. Head to head comparison of NL-ADE-MS and LC-MS. Relative product outputs were determined for products derived from building blocks **a**, C5 Lenalidomide **12** (amidation), **b**, C5 Lenalidomide **12** (reductive amination), **c**, Lenalidomide-5-Br **13** (Buchwald-Hartwig C-N coupling by both NL-ADE-MS and LC-MS). Data are found in *Extended Tabular Data Sheet 32-34*.

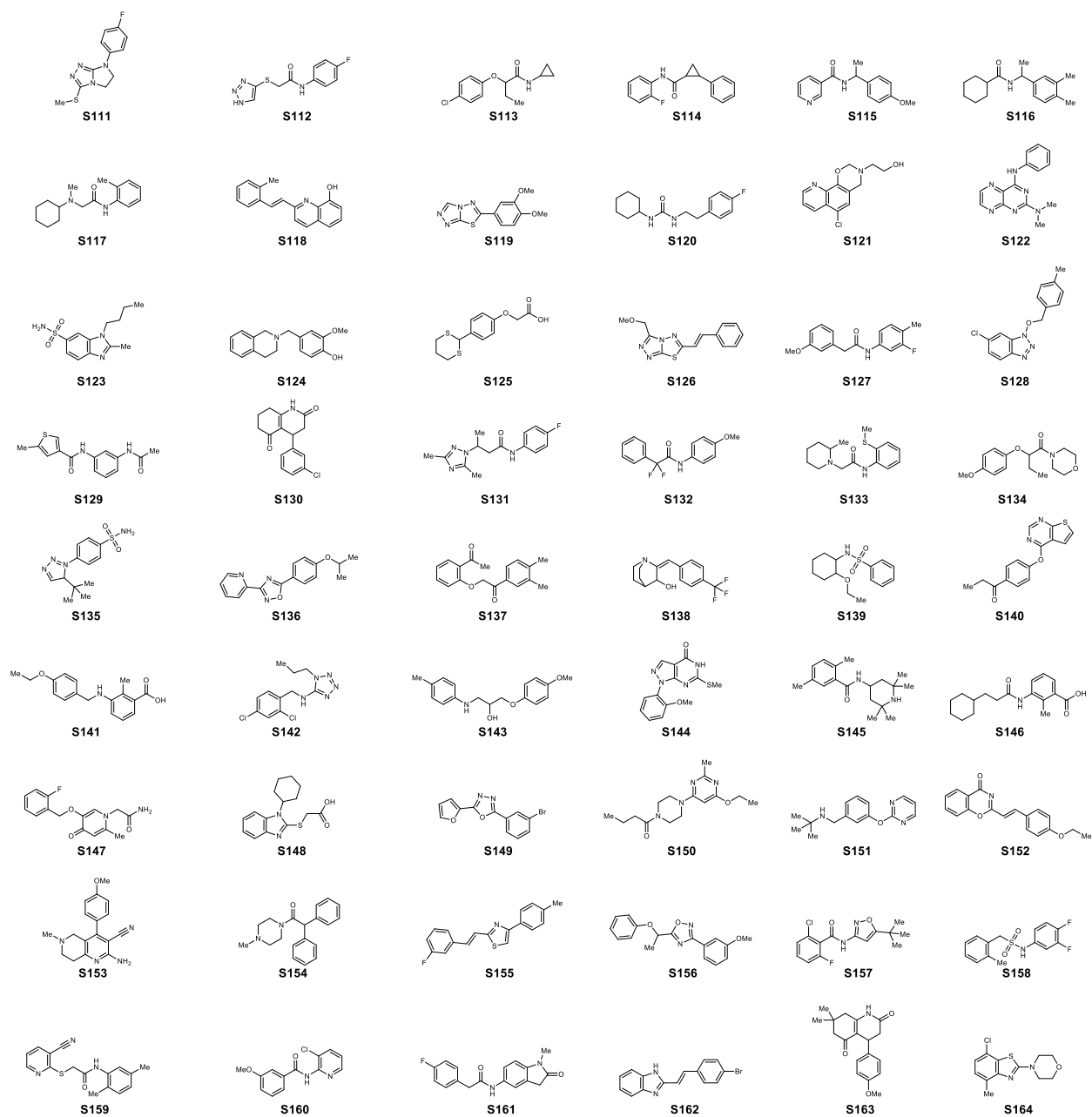


Figure S8 Structures for 100 compounds (S111-S210) used as test set



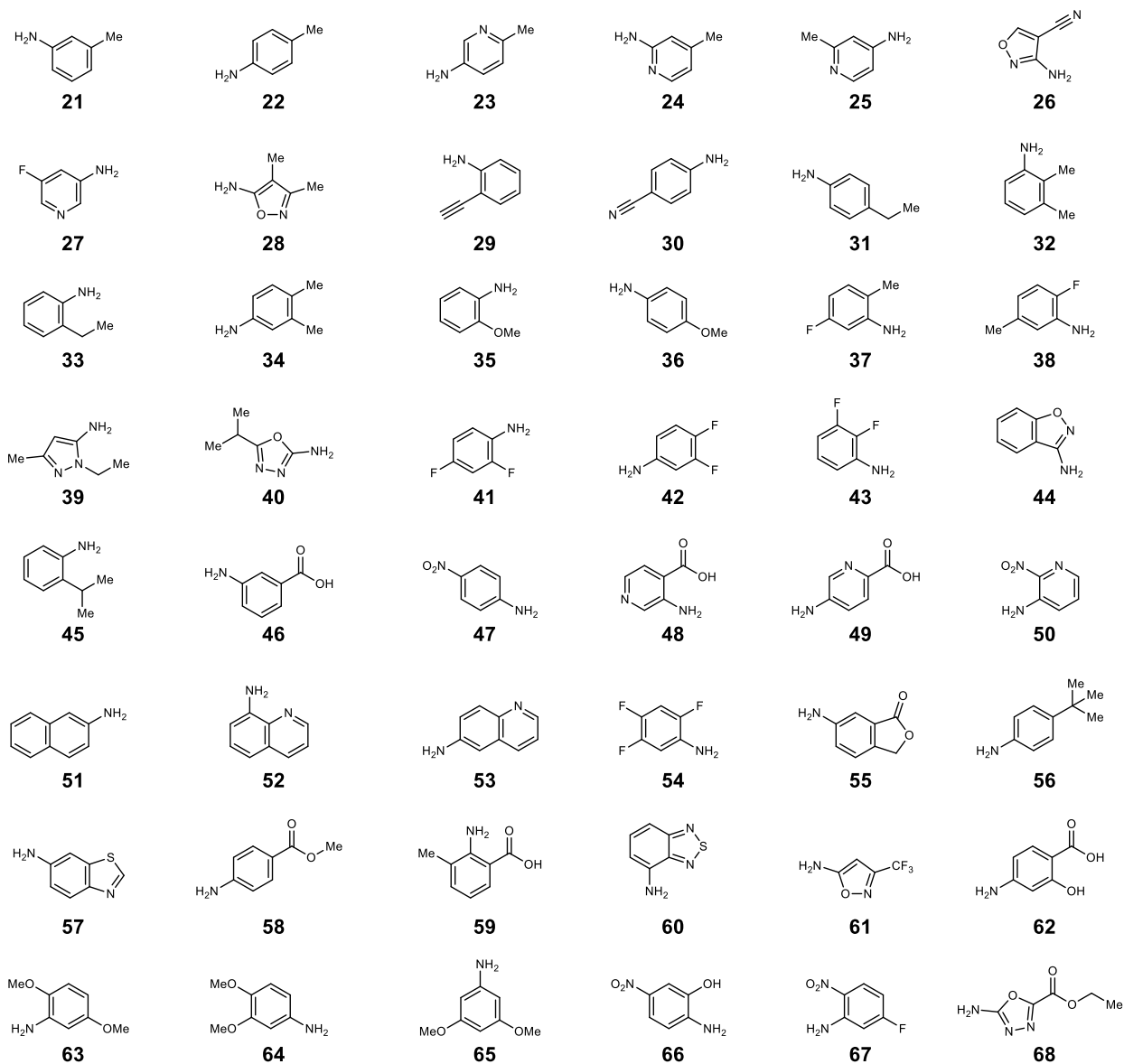


Figure S9 Structures of 96 amines used in Fig. 4

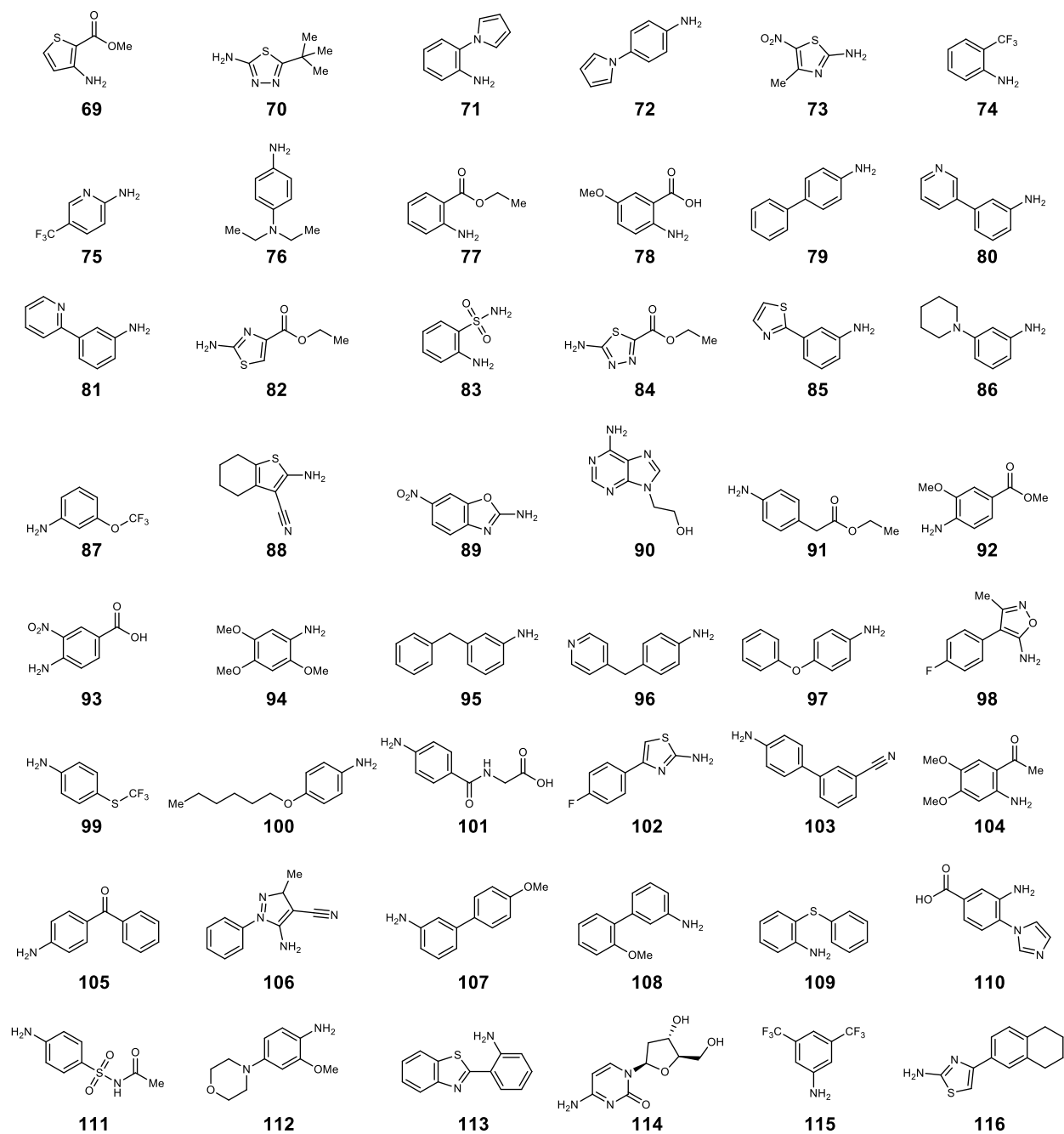
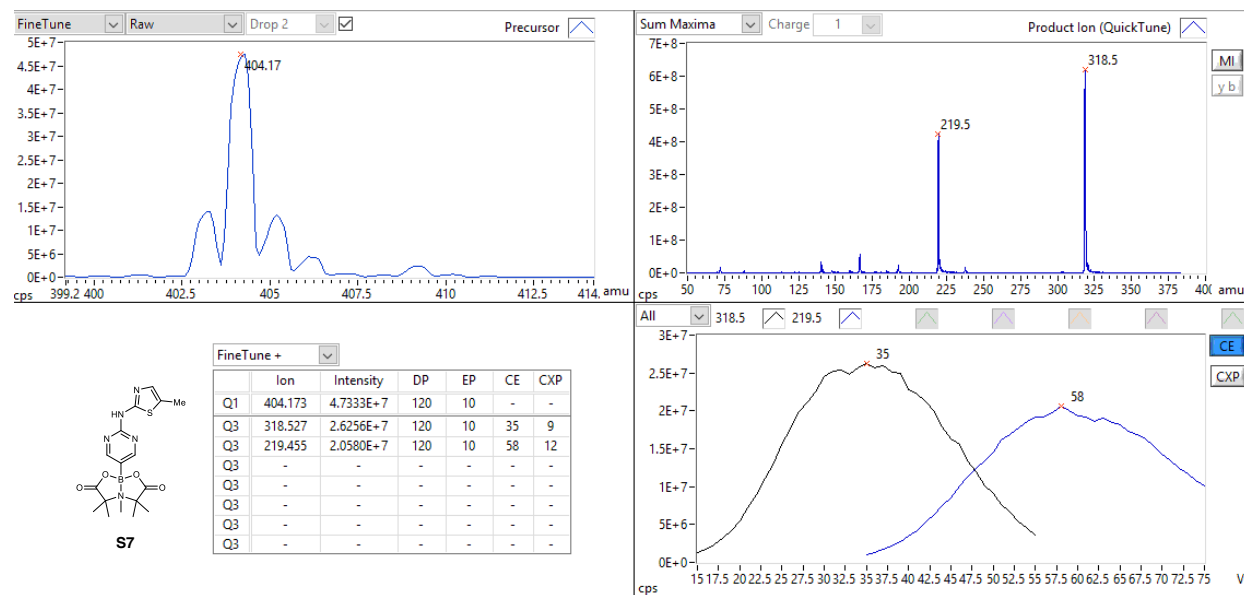
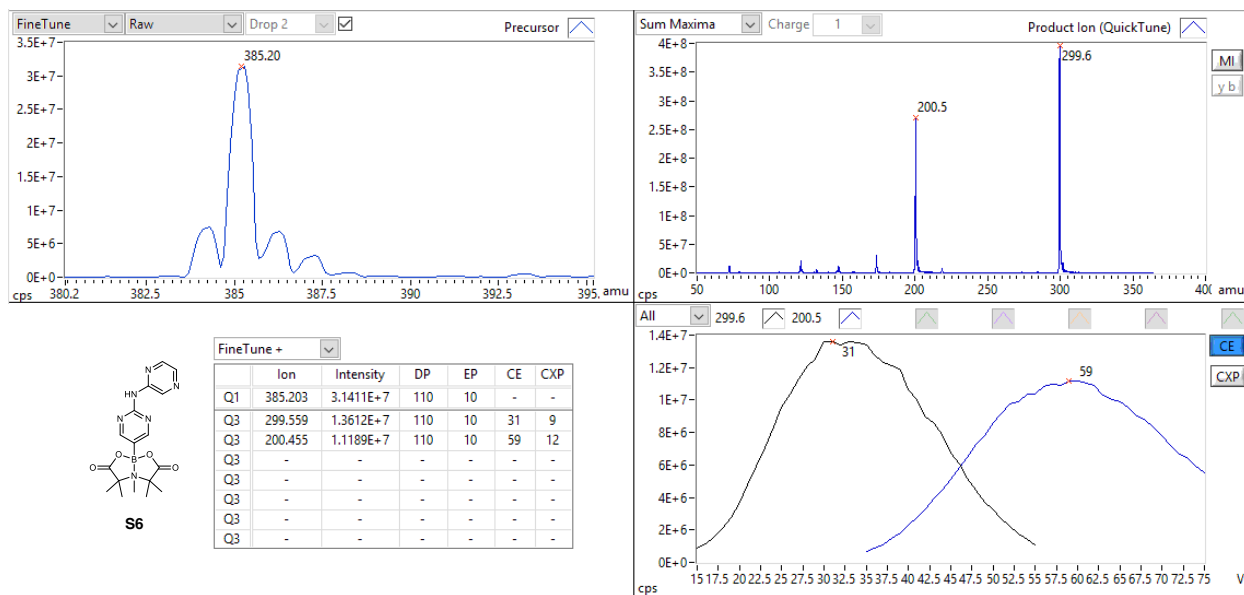
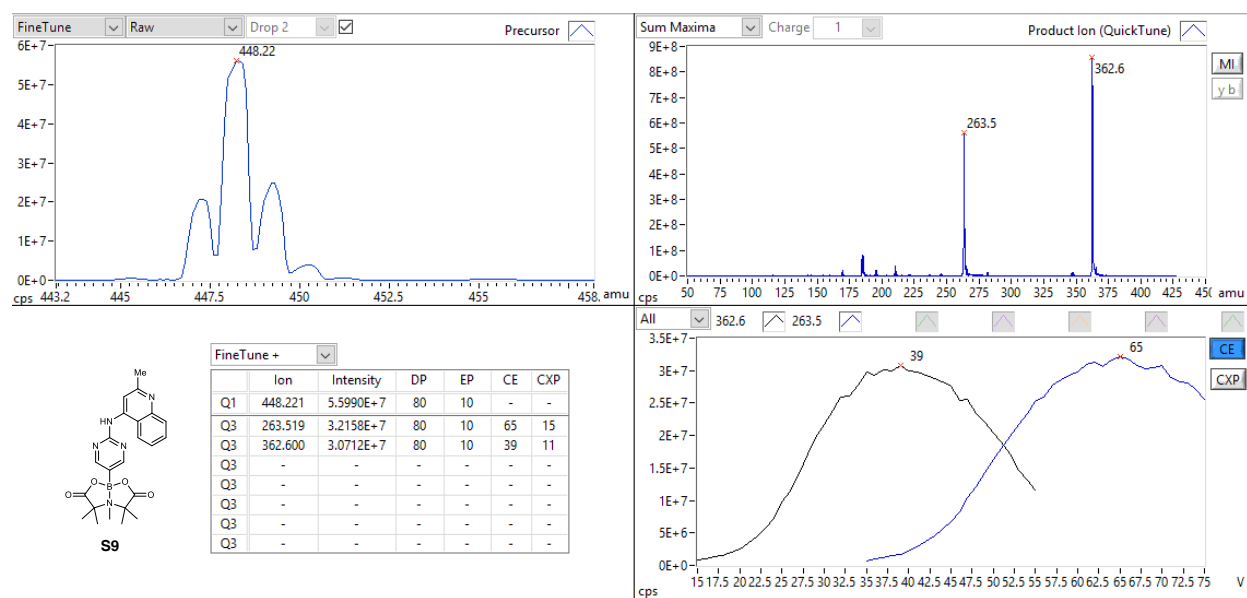
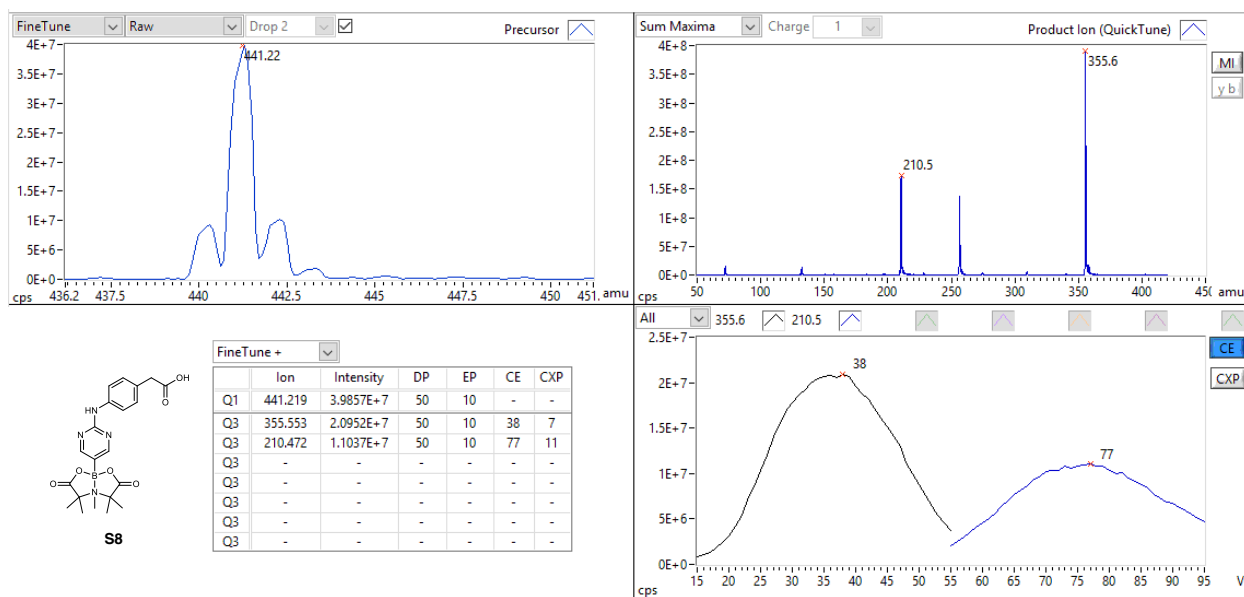


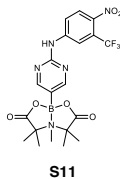
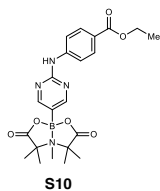
Figure S9 continued...

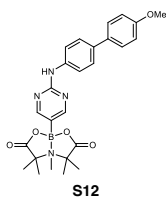
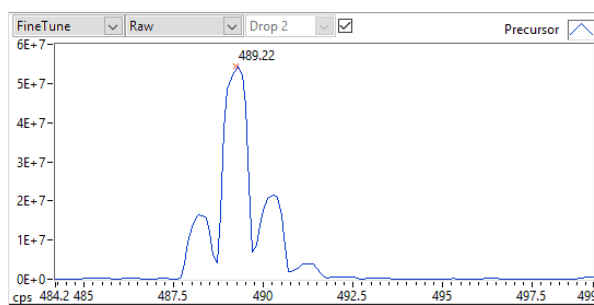
4.14 CID spectra for 60 TIDA boronates

Data can be found in Extended Tabular Data Sheet 1.

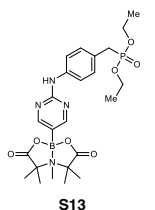
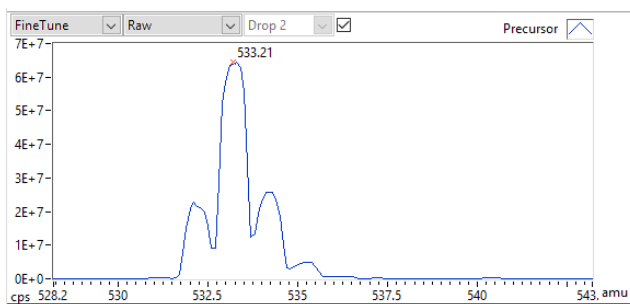
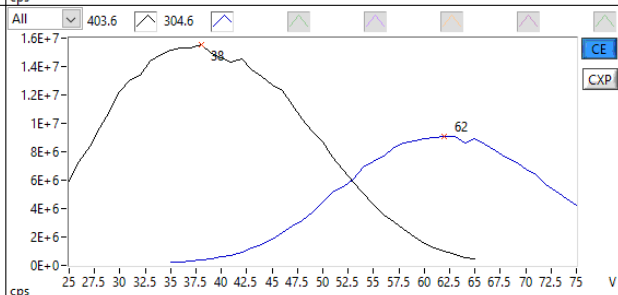
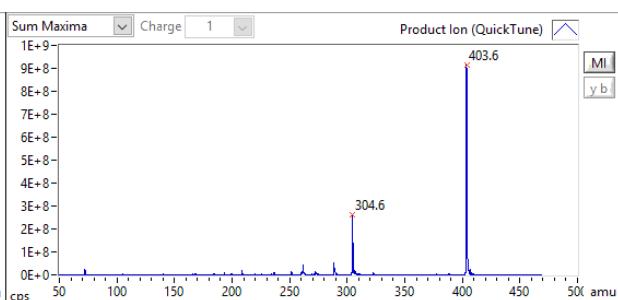




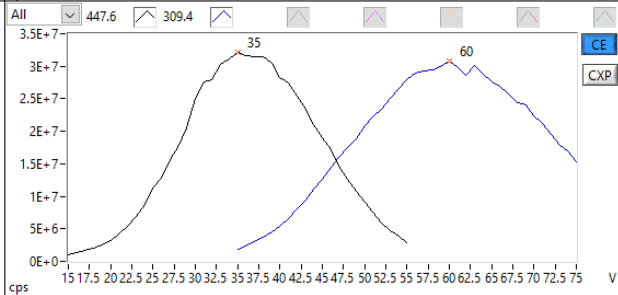
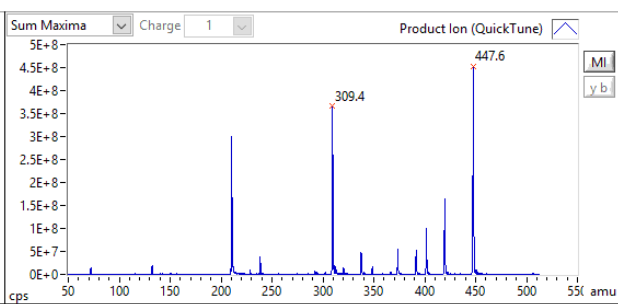


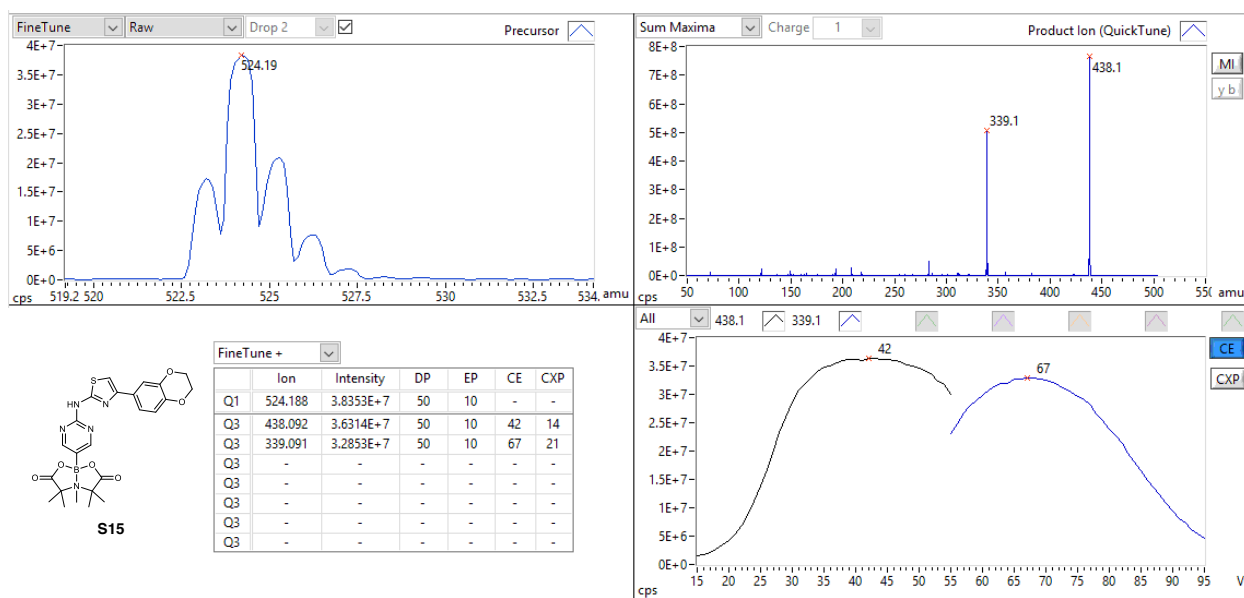
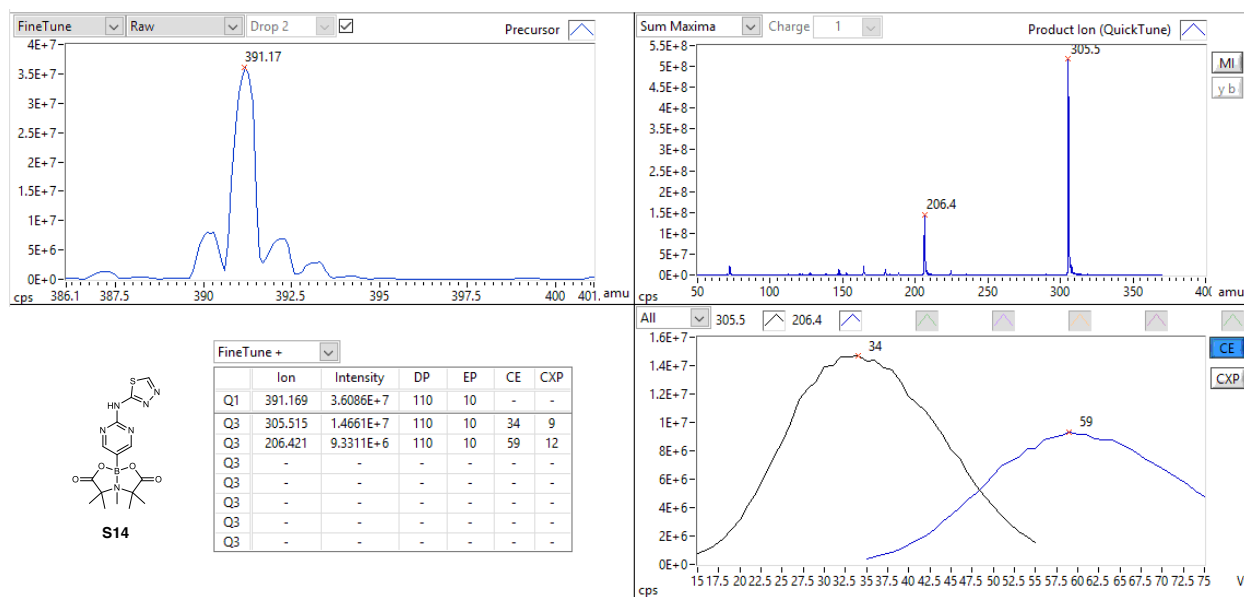


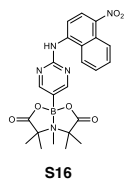
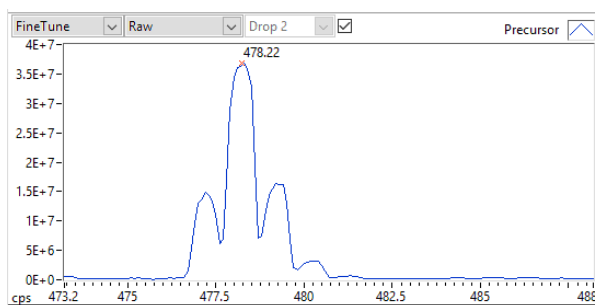
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Q3	403.647	1.5504E+7	80	10	38	12
Q3	304.553	9.0960E+6	80	10	62	9
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-



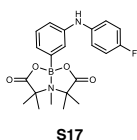
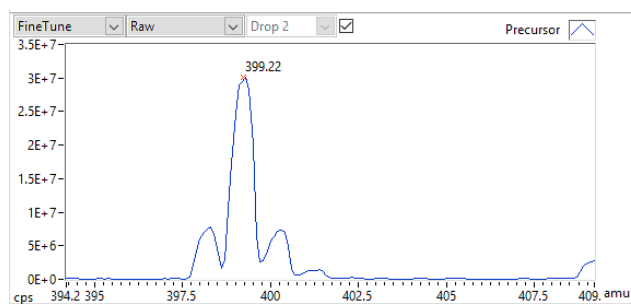
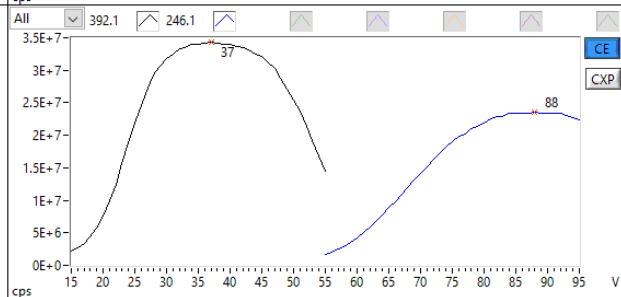
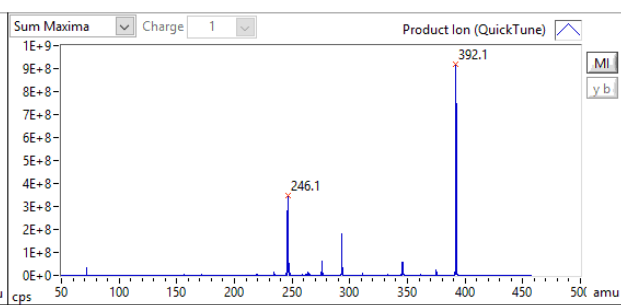
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Q1	533.214	6.4380E+7	50	10	-	-
Q3	447.603	3.2131E+7	50	10	35	13
Q3	309.449	3.0763E+7	50	10	60	9
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-



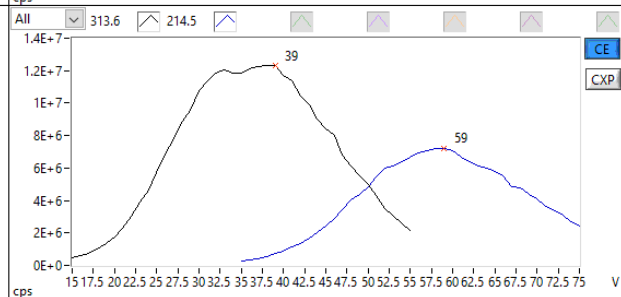
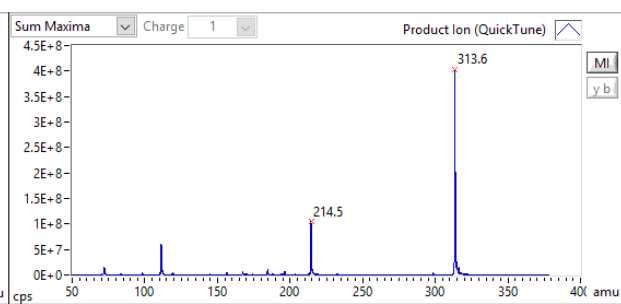


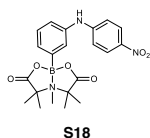
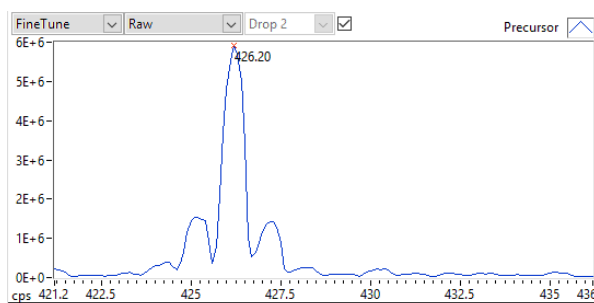


	Ion	Intensity	DP	EP	CE	CXP
Q1	478.218	3.6888E+7	50	10	-	-
Q3	392.141	3.4298E+7	50	10	37	13
Q3	246.118	2.3515E+7	50	10	88	14
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

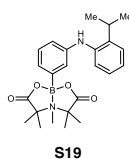
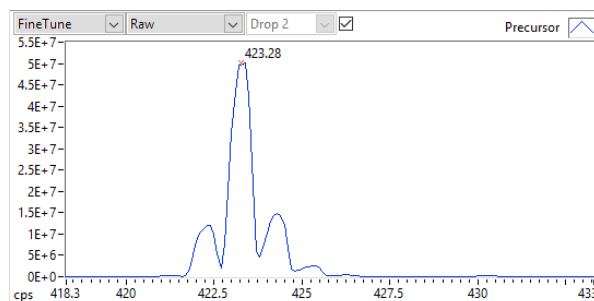
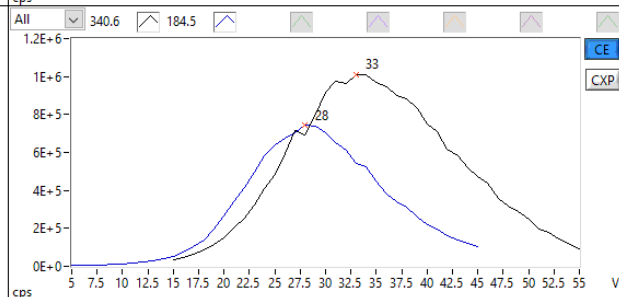
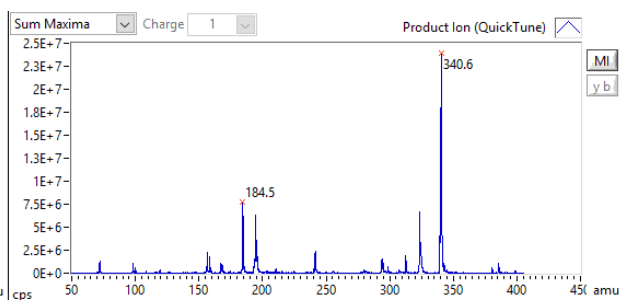


	Ion	Intensity	DP	EP	CE	CXP
Q1	399.223	3.0182E+7	120	10	-	-
Q3	313.562	1.2320E+7	120	10	39	9
Q3	214.471	7.2340E+6	120	10	59	14
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

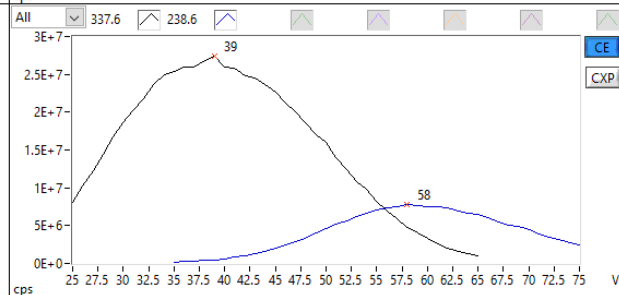
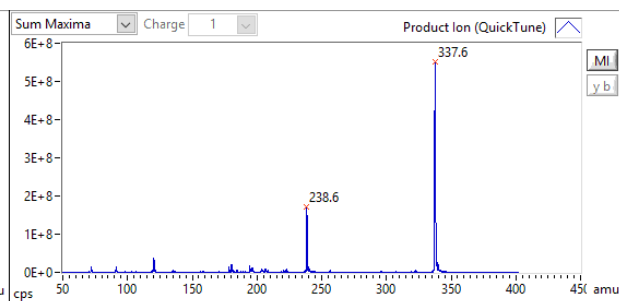


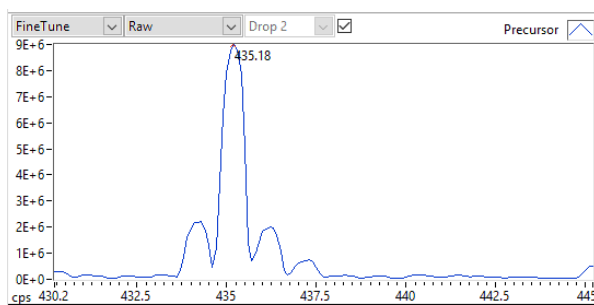


	Ion	Intensity	DP	EP	CE	CXP
Q1	426.199	5.9146E+6	110	10	-	-
Q3	340.564	1.0116E+6	110	10	33	10
Q3	184.514	7.4363E+5	110	10	28	10
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-



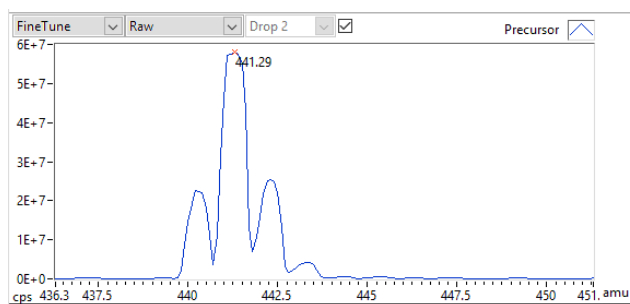
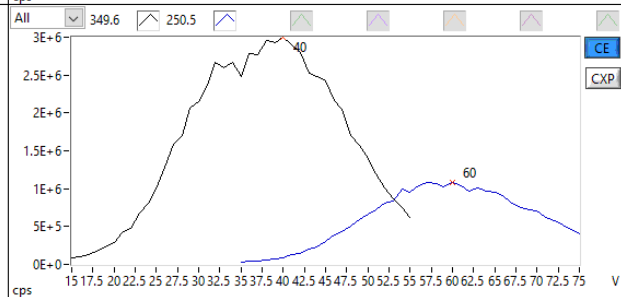
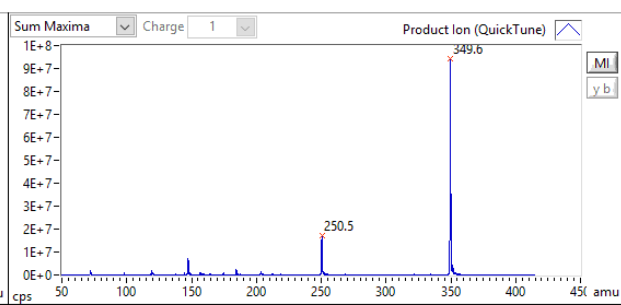
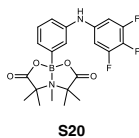
	Ion	Intensity	DP	EP	CE	CXP
Q1	423.277	5.0012E+7	120	10	-	-
Q3	337.607	2.7333E+7	120	10	39	10
Q3	238.563	7.7797E+6	120	10	58	14
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-





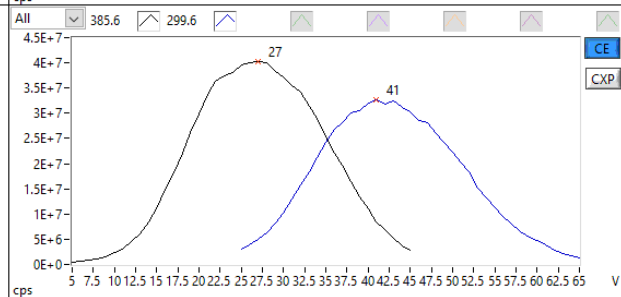
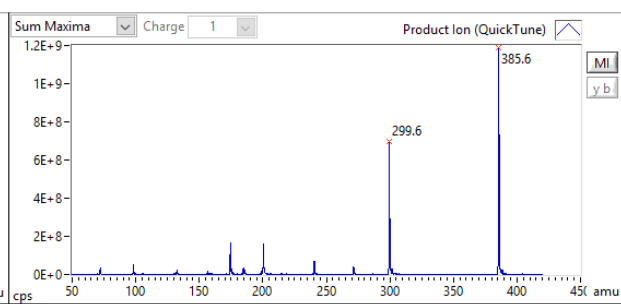
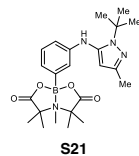
FineTune +

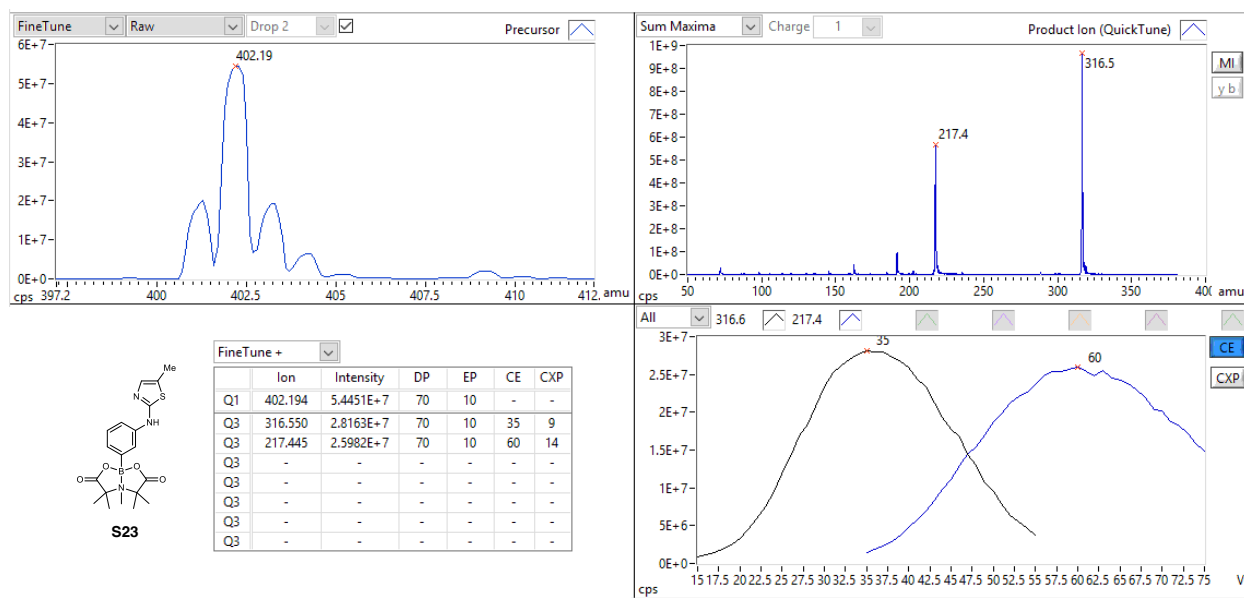
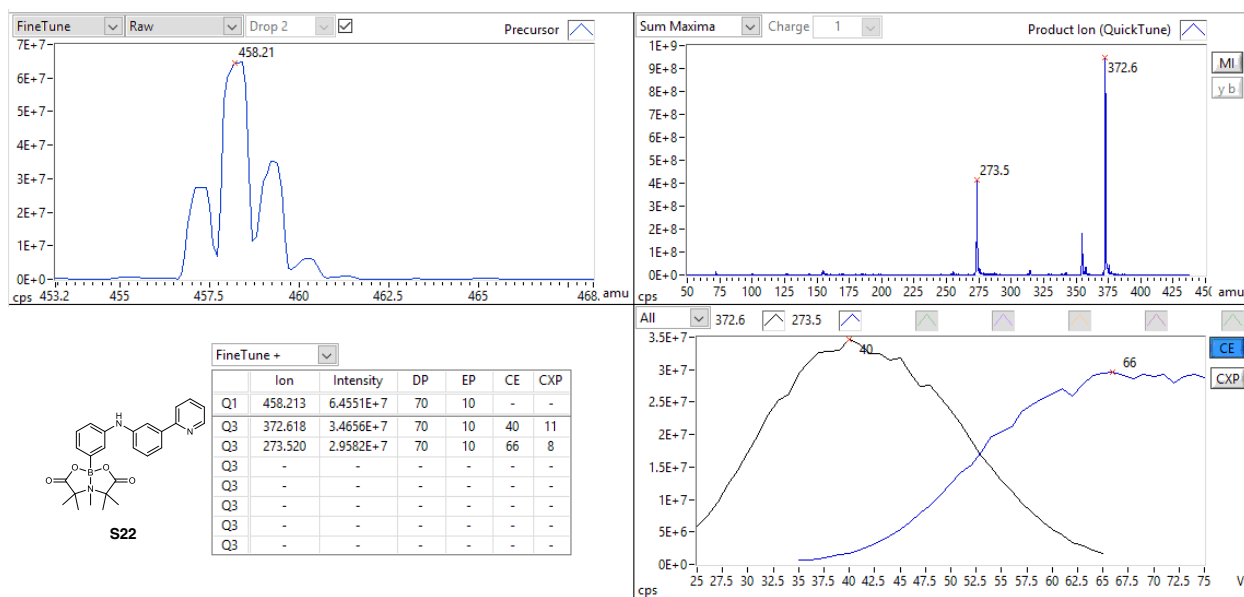
	Ion	Intensity	DP	EP	CE	CXP
Q1	435.183	8.9971E+6	100	10	-	-
Q3	349.550	2.9977E+6	100	10	40	11
Q3	250.484	1.0841E+6	100	10	60	20
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

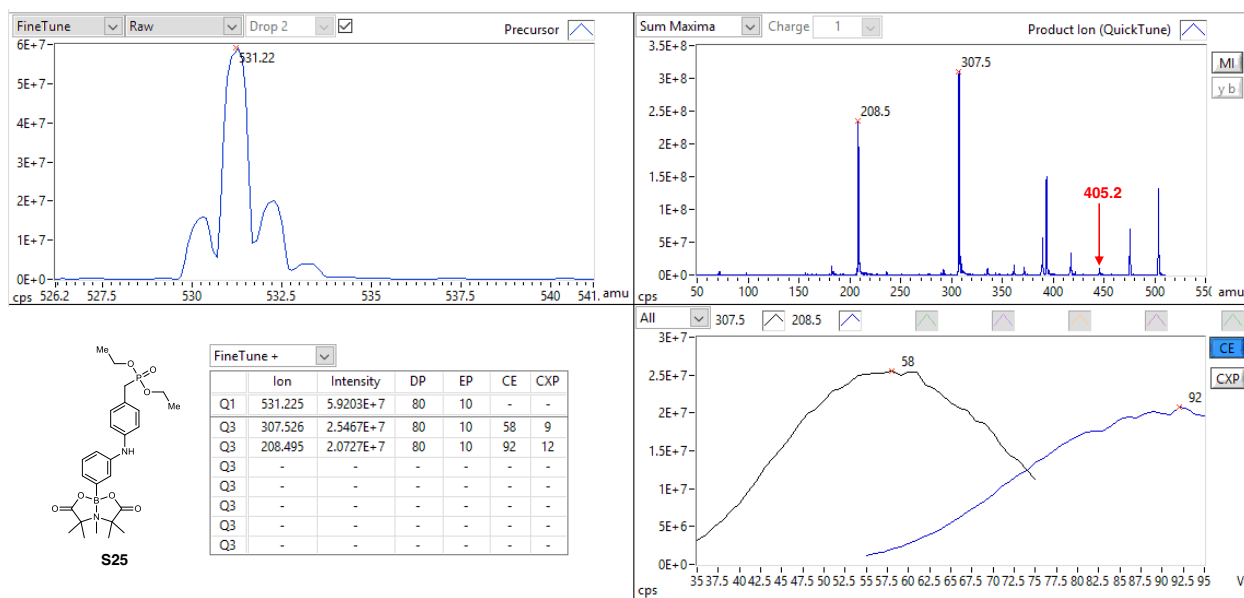
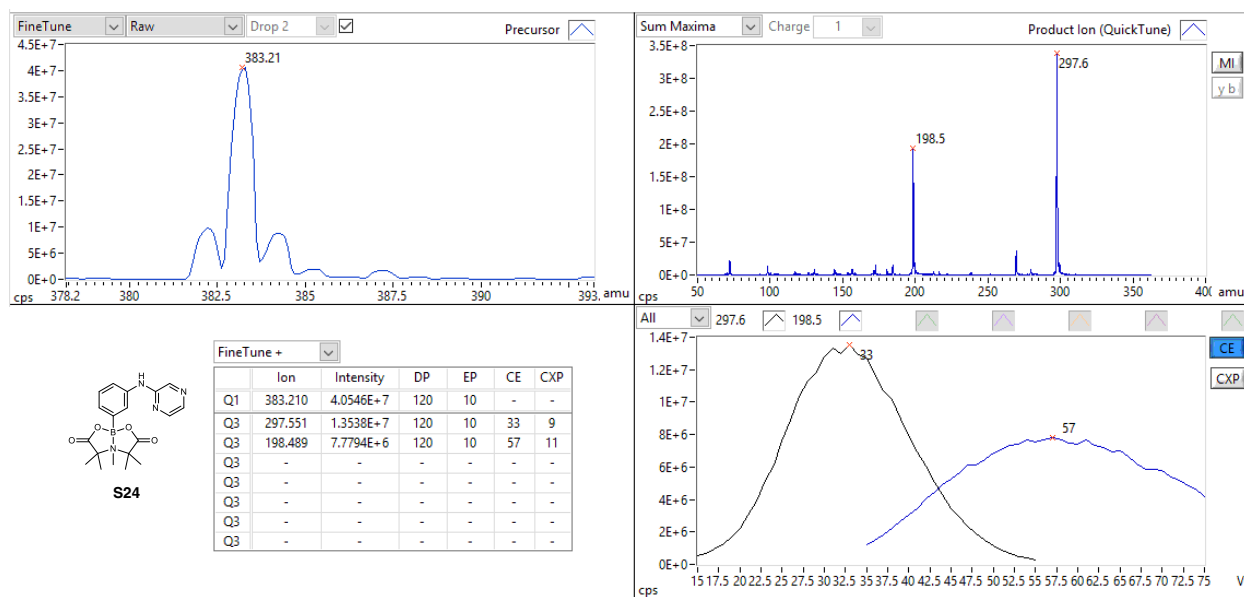


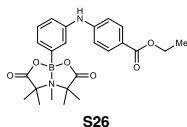
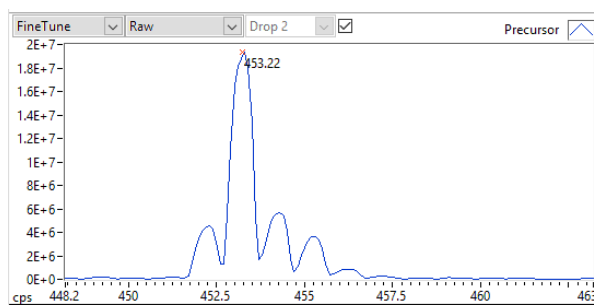
FineTune +

	Ion	Intensity	DP	EP	CE	CXP
Q1	441.287	5.8146E+7	100	10	-	-
Q3	385.612	4.0198E+7	100	10	27	8
Q3	299.558	3.2638E+7	100	10	41	9
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

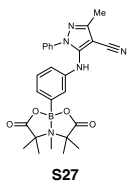
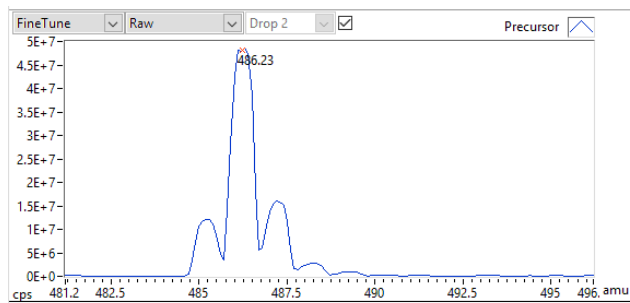
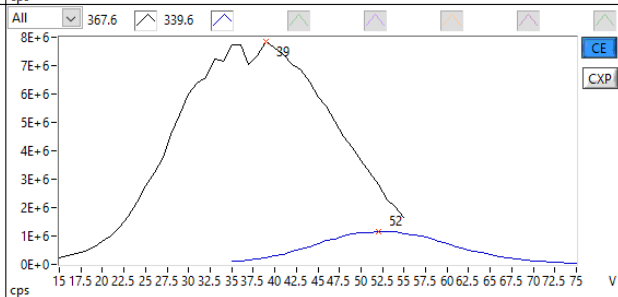
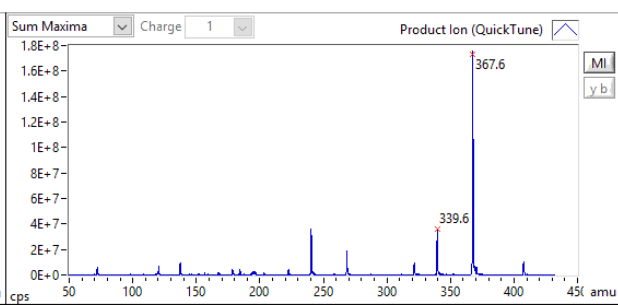




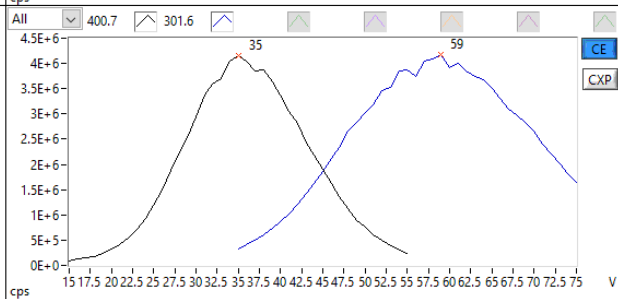
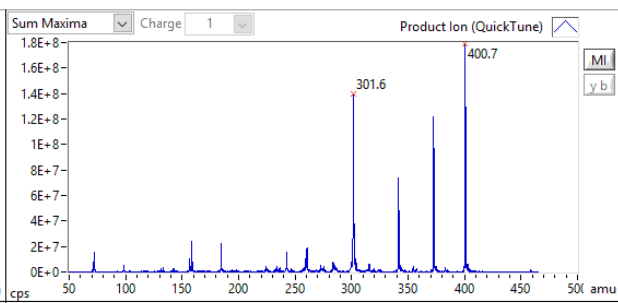


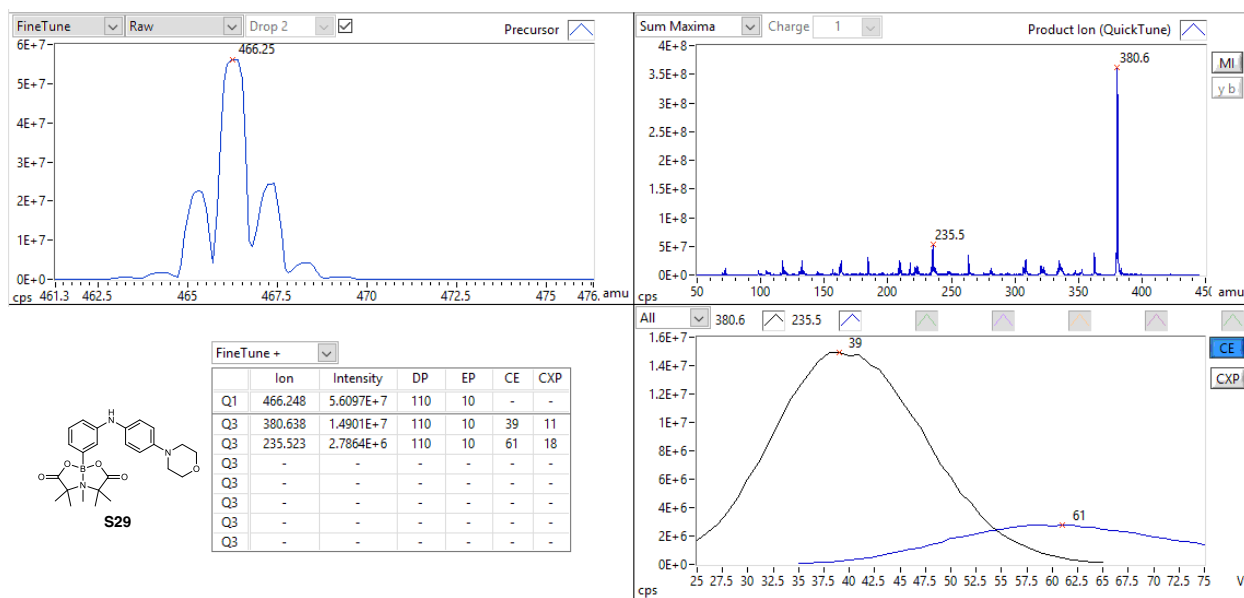
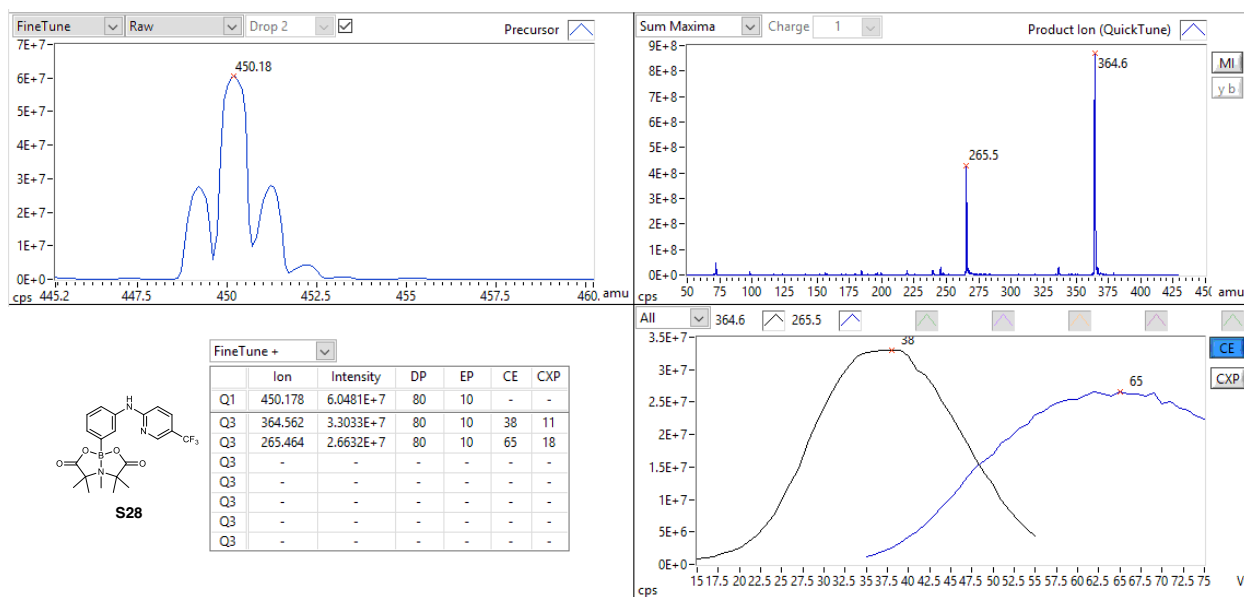


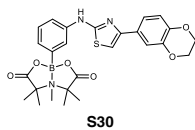
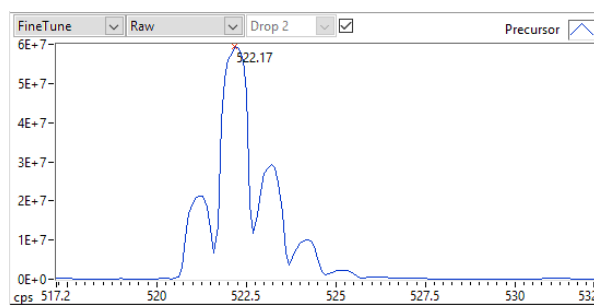
	Ion	Intensity	DP	EP	CE	CXP
Q1	453.223	1.9322E+7	110	10	-	-
Q3	367.586	7.8431E+6	110	10	39	10
Q3	339.578	1.1639E+6	110	10	52	10
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-



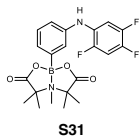
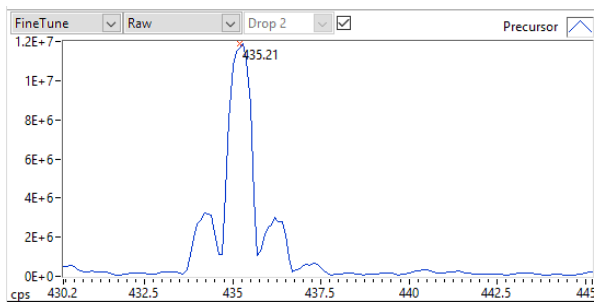
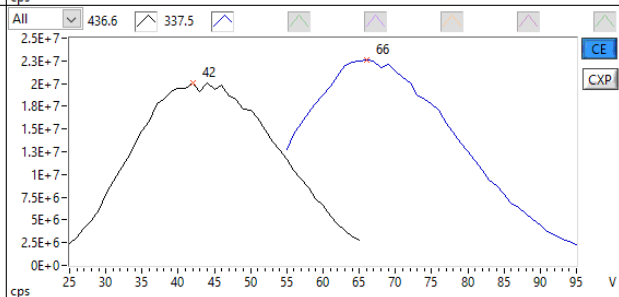
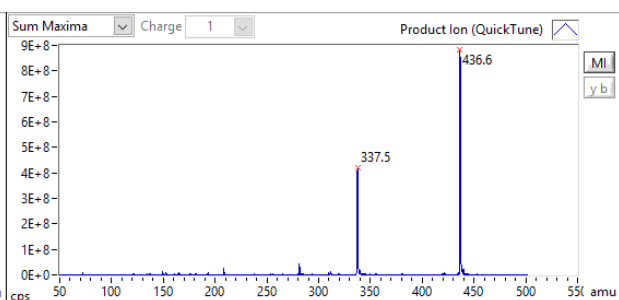
	Ion	Intensity	DP	EP	CE	CXP
Q1	486.232	4.8183E+7	70	10	-	-
Q3	301.561	4.1819E+6	70	10	59	24
Q3	400.665	4.1636E+6	70	10	35	12
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-



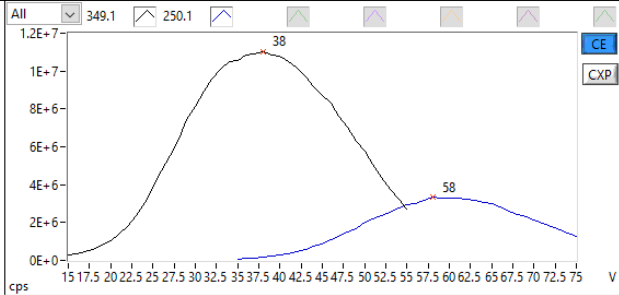
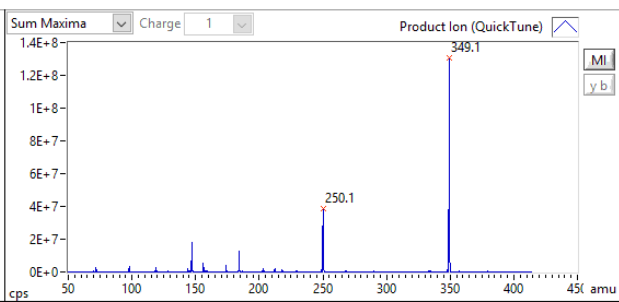


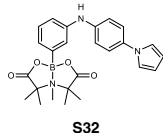
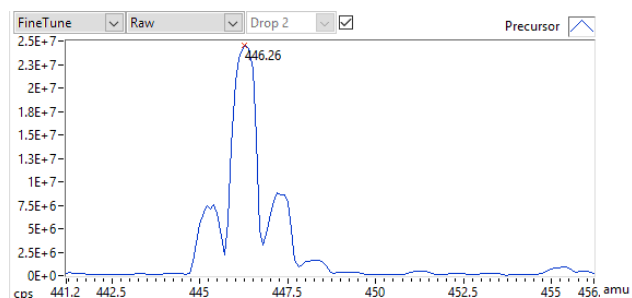


	Ion	Intensity	DP	EP	CE	CXP
Q1	522.172	5.9404E+7	100	10	-	-
Q3	337.484	2.2633E+7	100	10	66	10
Q3	436.592	2.0107E+7	100	10	42	13
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

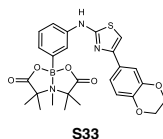
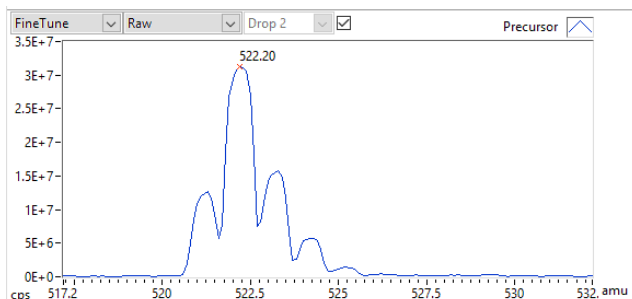
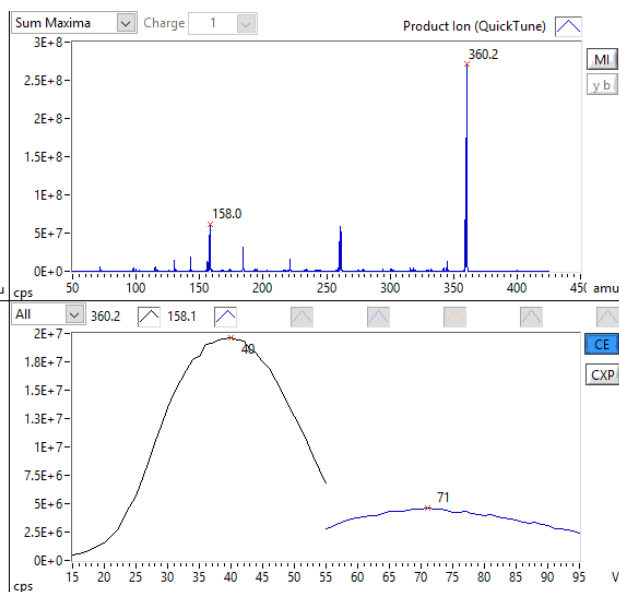


	Ion	Intensity	DP	EP	CE	CXP
Q1	435.210	1.1879E+7	130	10	-	-
Q3	349.141	1.1045E+7	130	10	38	11
Q3	250.126	3.3588E+6	130	10	58	14
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

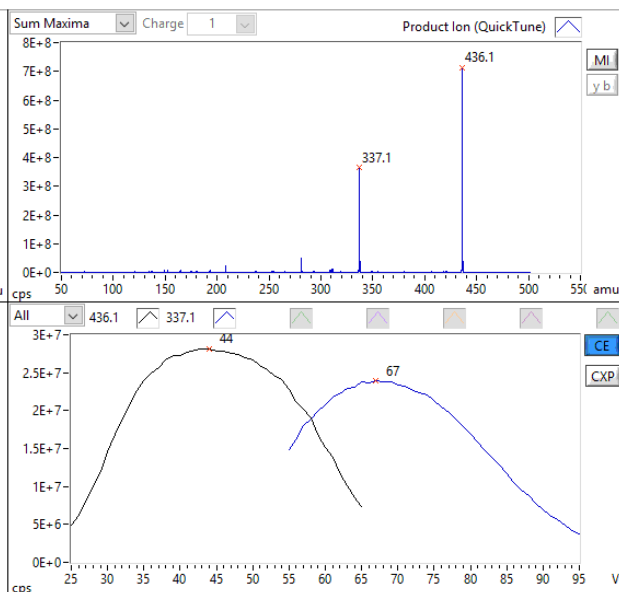


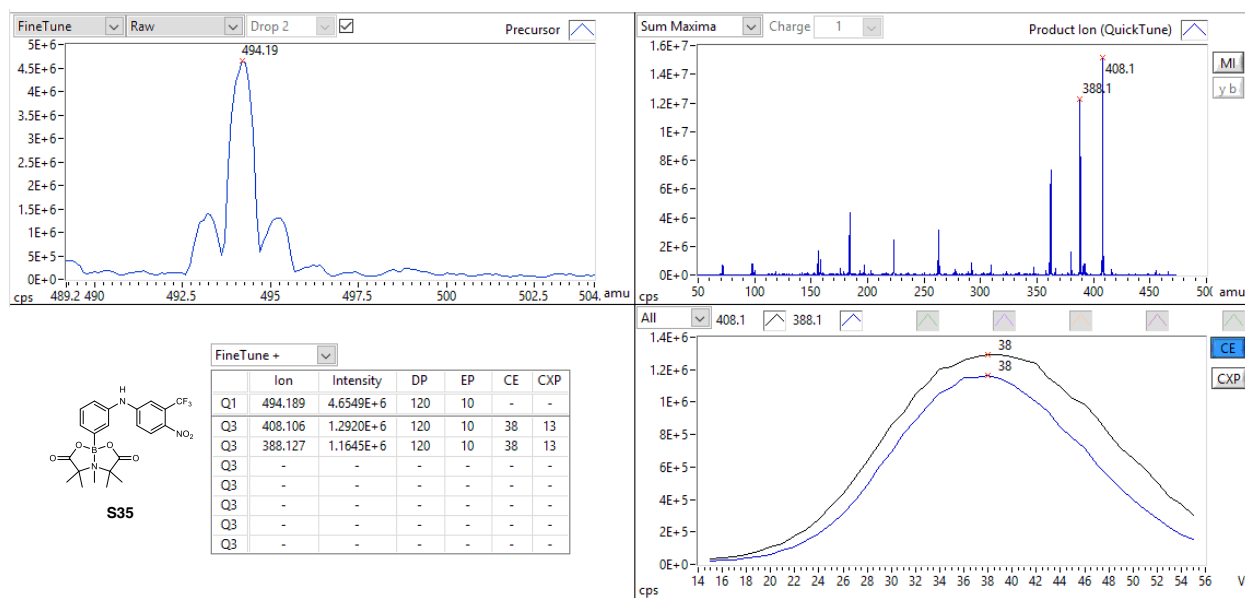
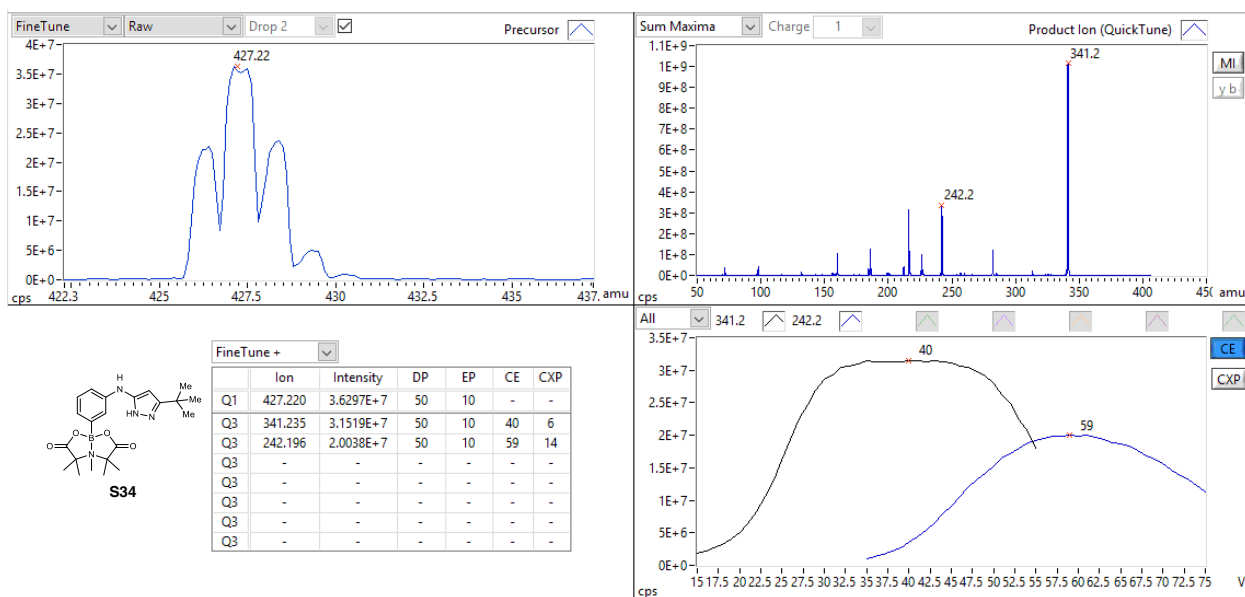


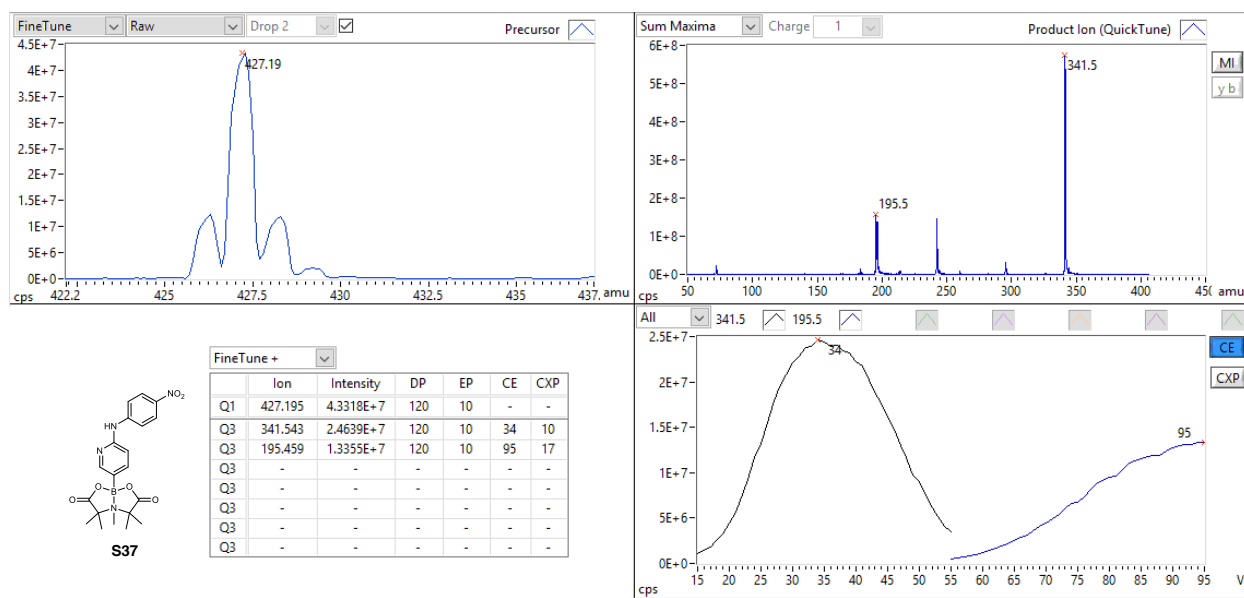
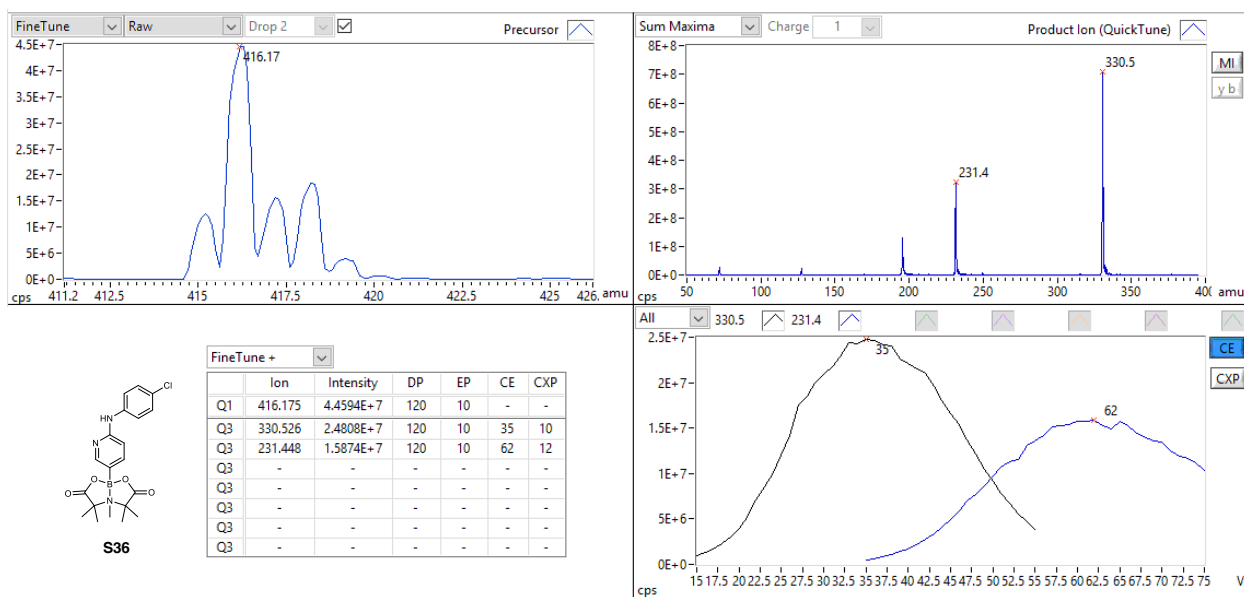
	Ion	Intensity	DP	EP	CE	CXP
Q1	446.262	2.4581E+7	90	10	-	-
Q3	360.201	1.9581E+7	90	10	40	12
Q3	158.048	4.6552E+6	90	10	71	9
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

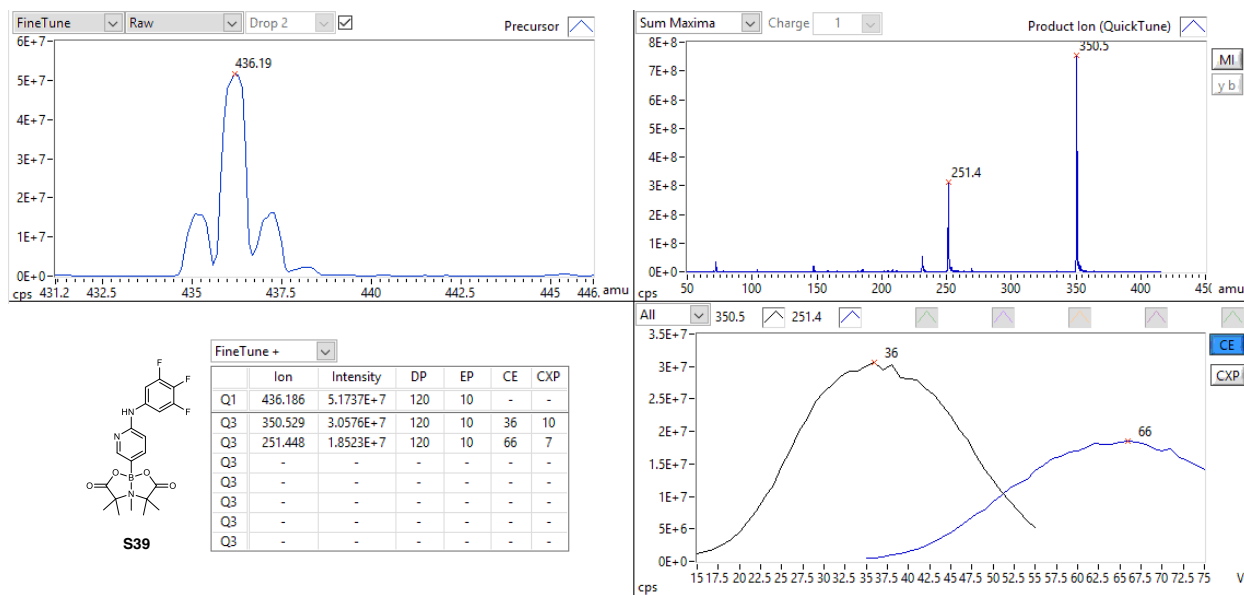
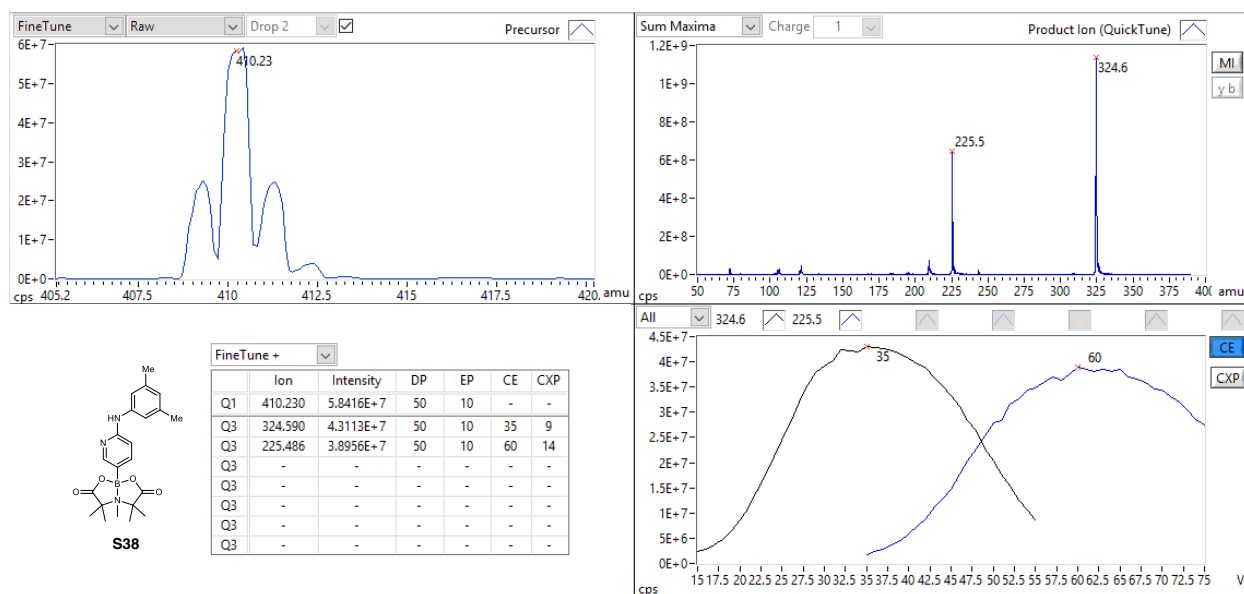


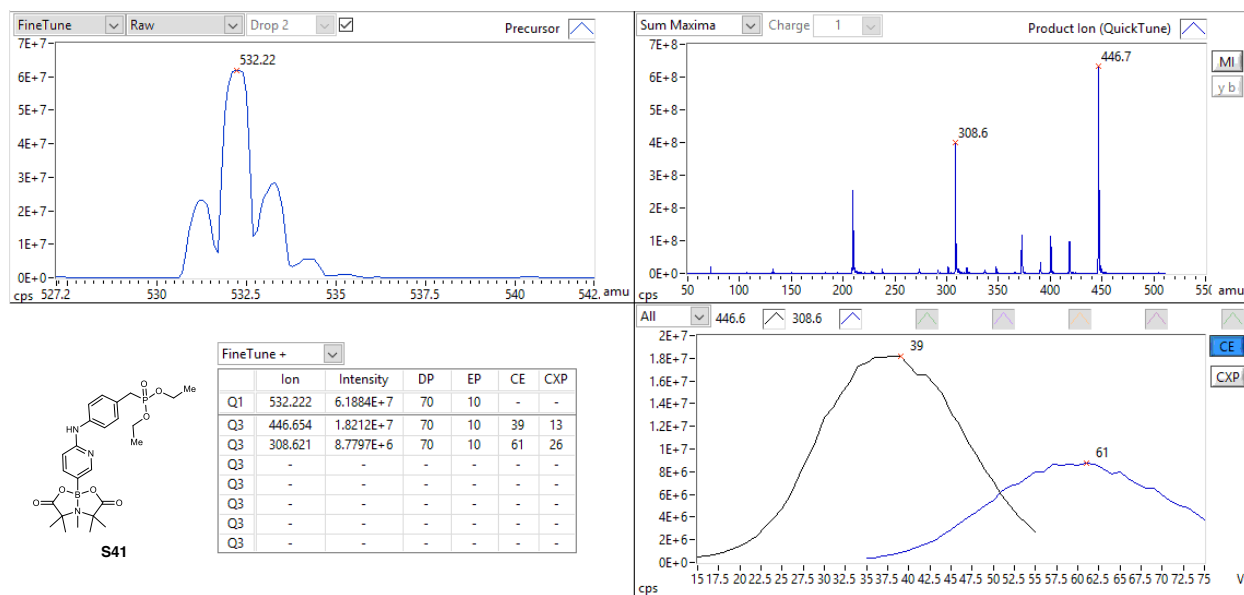
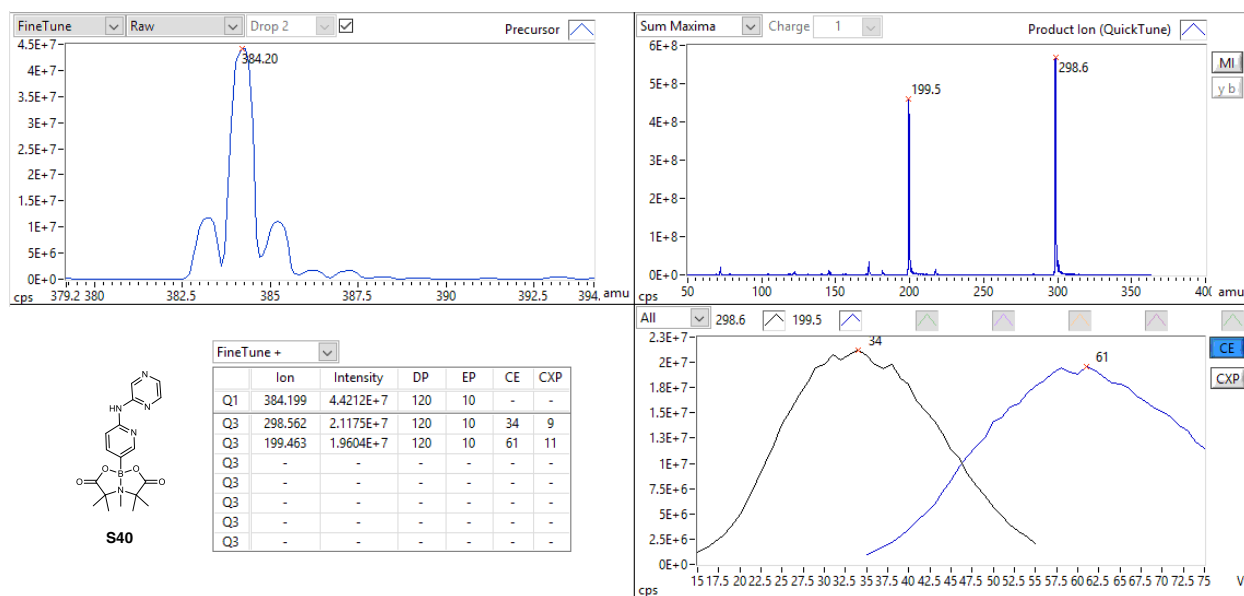
	Ion	Intensity	DP	EP	CE	CXP
Q1	522.202	3.1323E+7	50	10	-	-
Q3	436.112	2.8184E+7	50	10	44	14
Q3	337.095	2.3923E+7	50	10	67	18
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

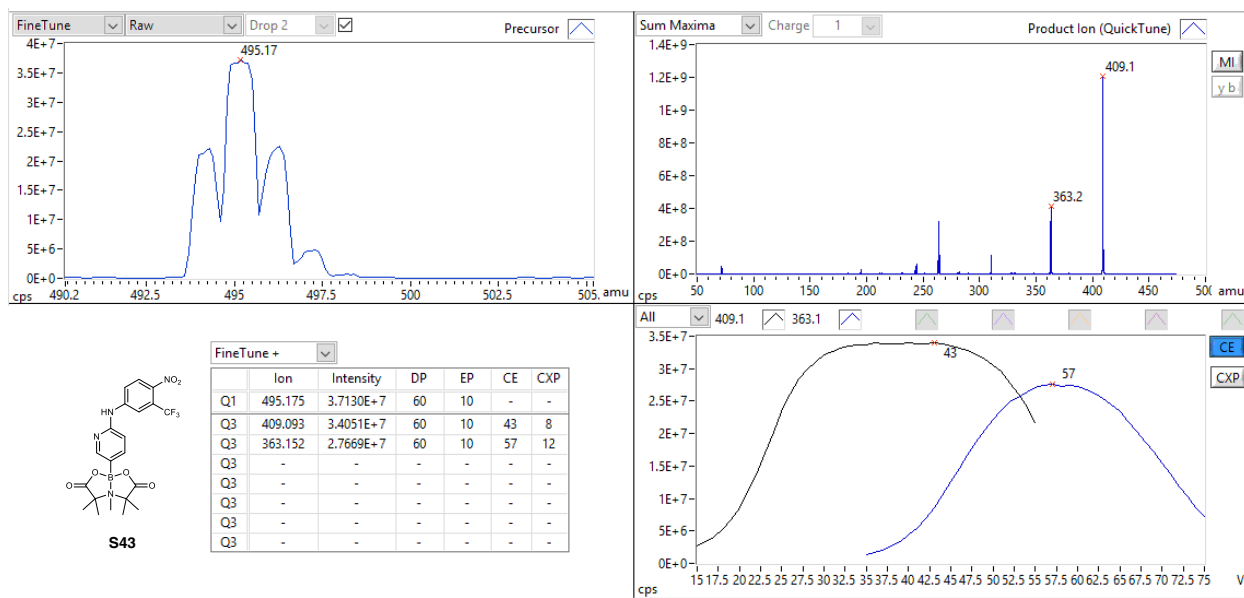
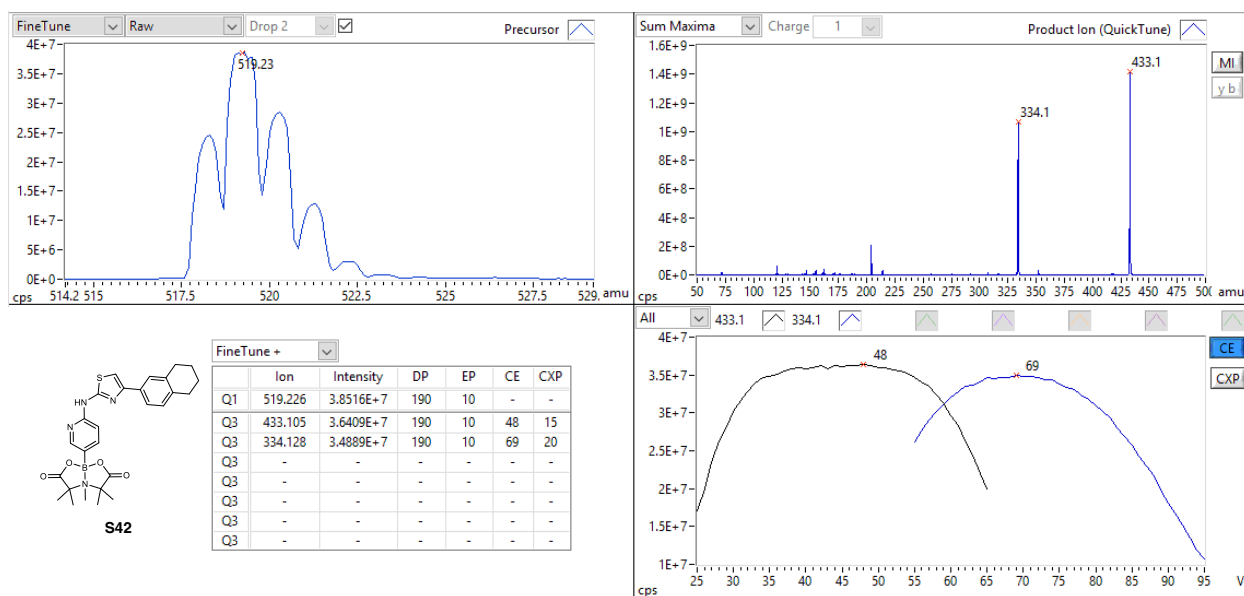


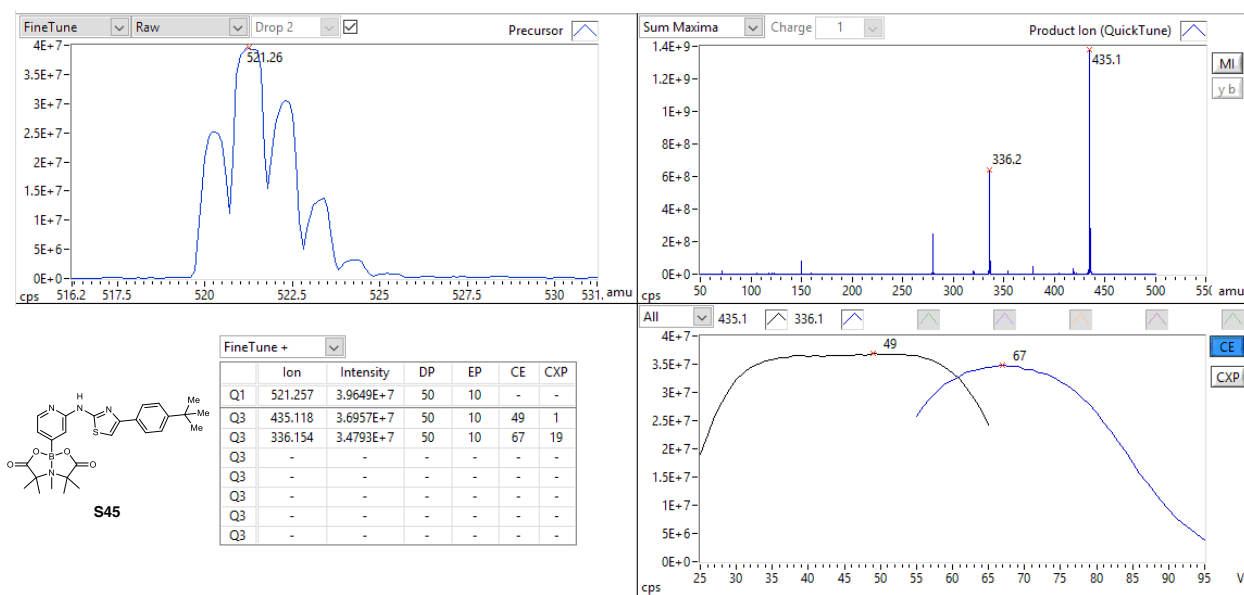
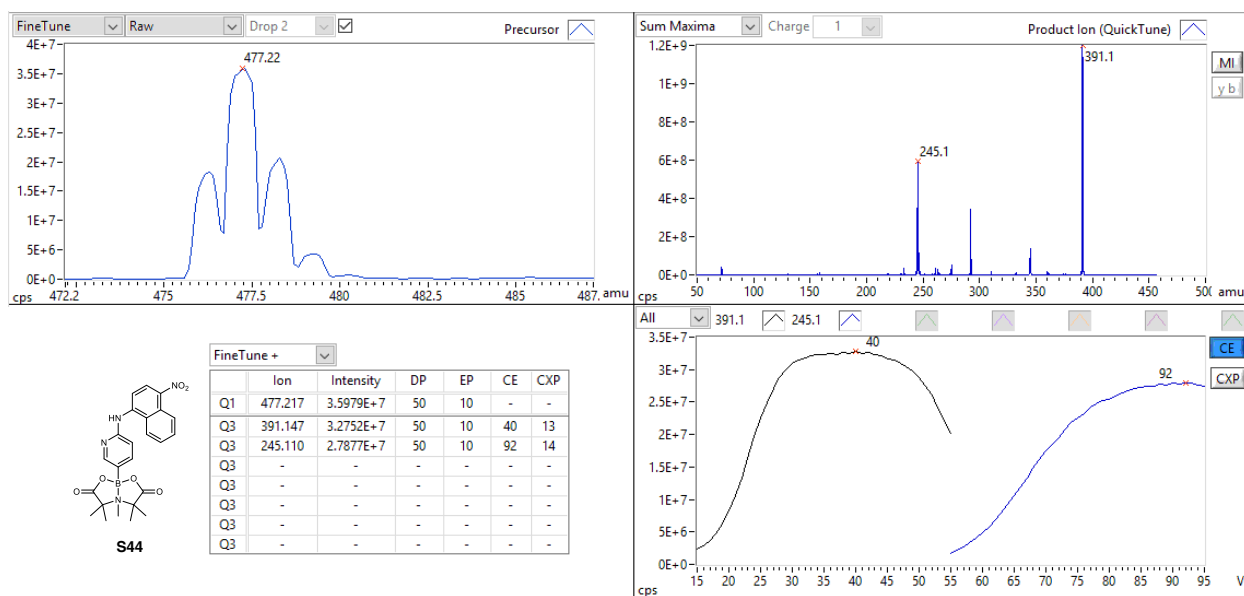


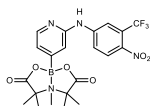
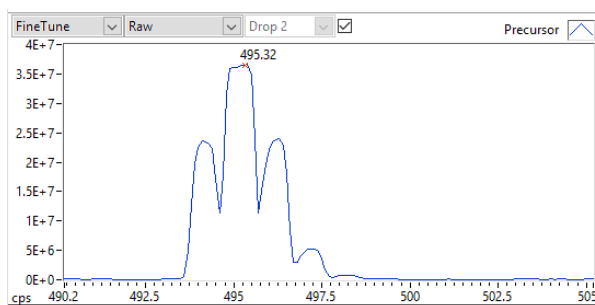






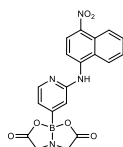
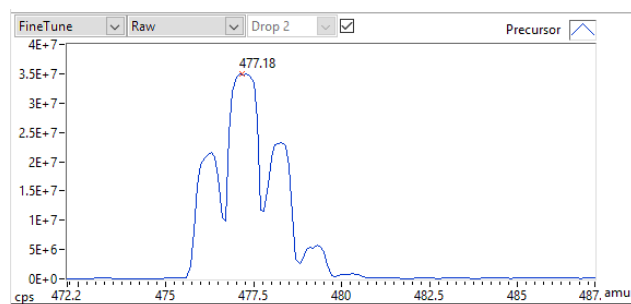
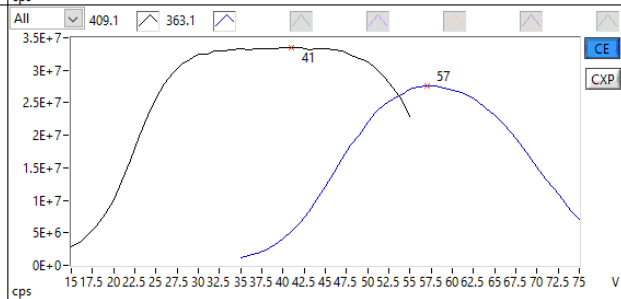
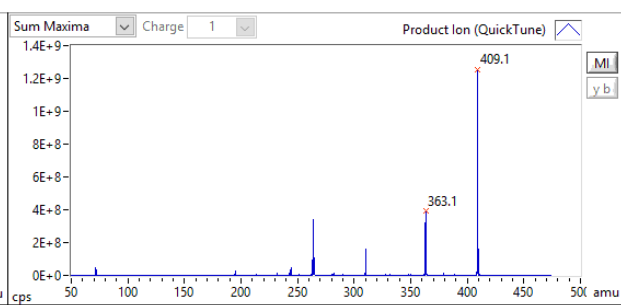






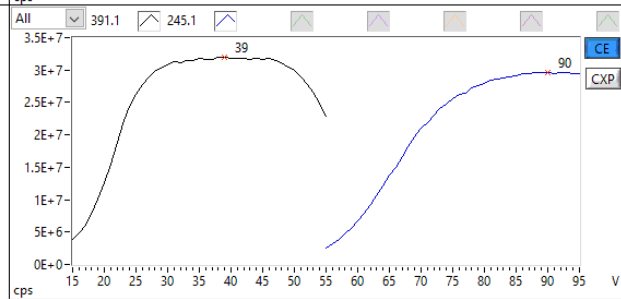
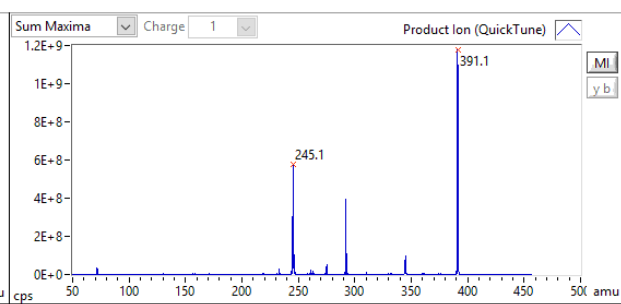
S46

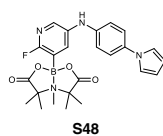
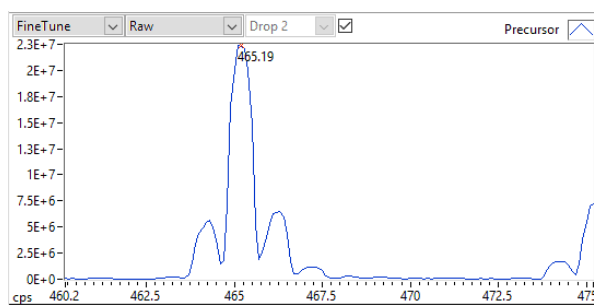
	Ion	Intensity	DP	EP	CE	CXP
Q1	495.316	3.6500E+7	50	10	-	-
Q3	409.072	3.3525E+7	50	10	41	1
Q3	363.149	2.7544E+7	50	10	57	12
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-



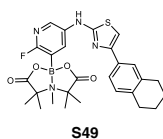
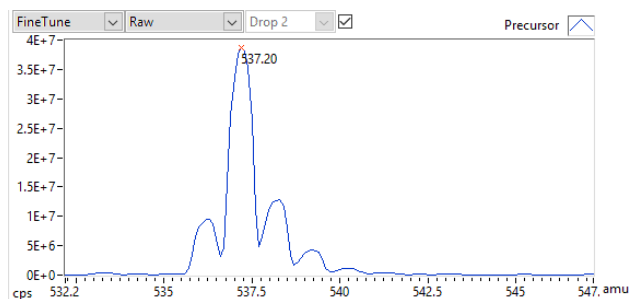
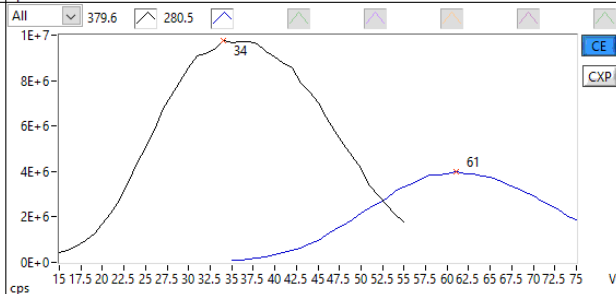
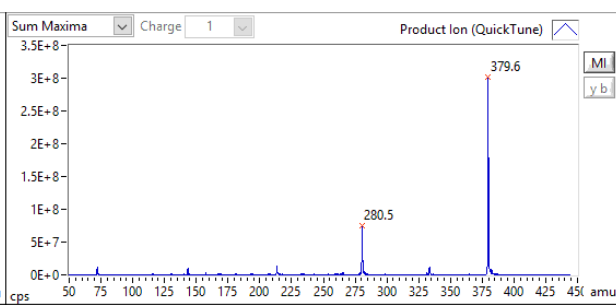
S47

	Ion	Intensity	DP	EP	CE	CXP
Q1	477.180	3.5050E+7	50	10	-	-
Q3	391.136	3.1958E+7	50	10	39	14
Q3	245.126	2.9648E+7	50	10	90	14
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

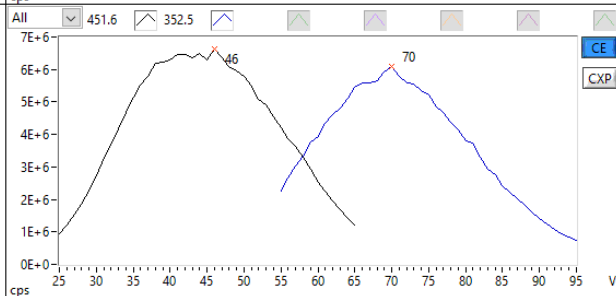
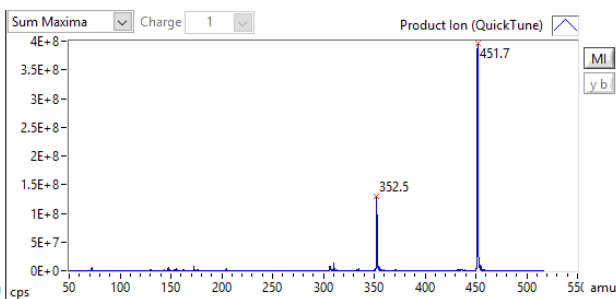


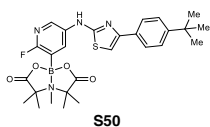
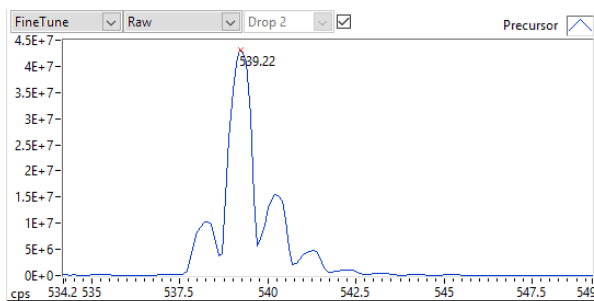


	Ion	Intensity	DP	EP	CE	CXP
Q1	465.191	2.2363E+7	120	10	-	-
Q3	379.582	9.7834E+6	120	10	34	11
Q3	280.492	3.9779E+6	120	10	61	8
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

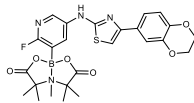
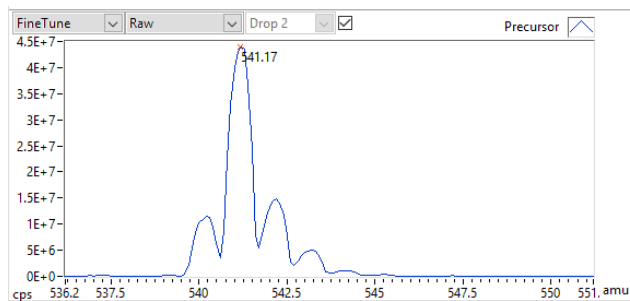
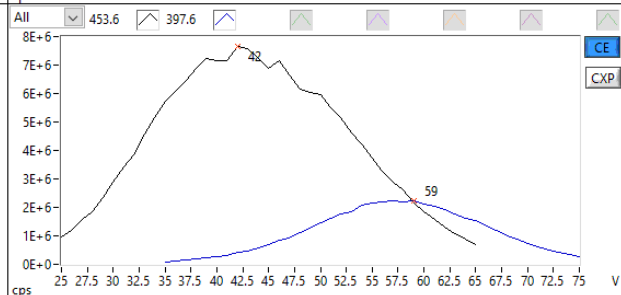
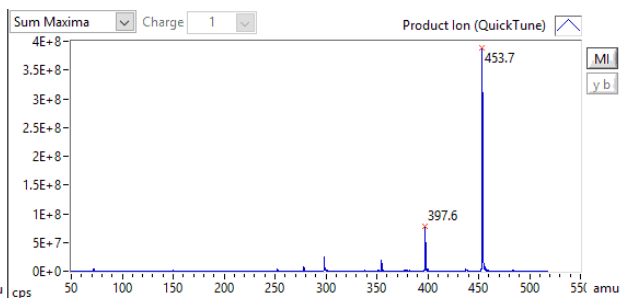


	Ion	Intensity	DP	EP	CE	CXP
Q1	537.201	3.8638E+7	110	10	-	-
Q3	451.651	6.6448E+6	110	10	46	14
Q3	352.545	6.0860E+6	110	10	70	10
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

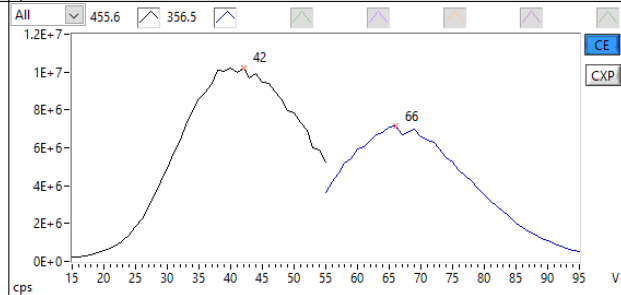
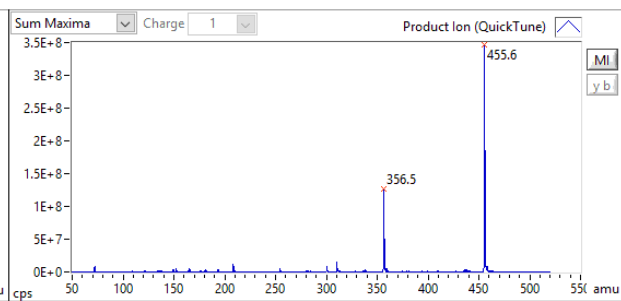


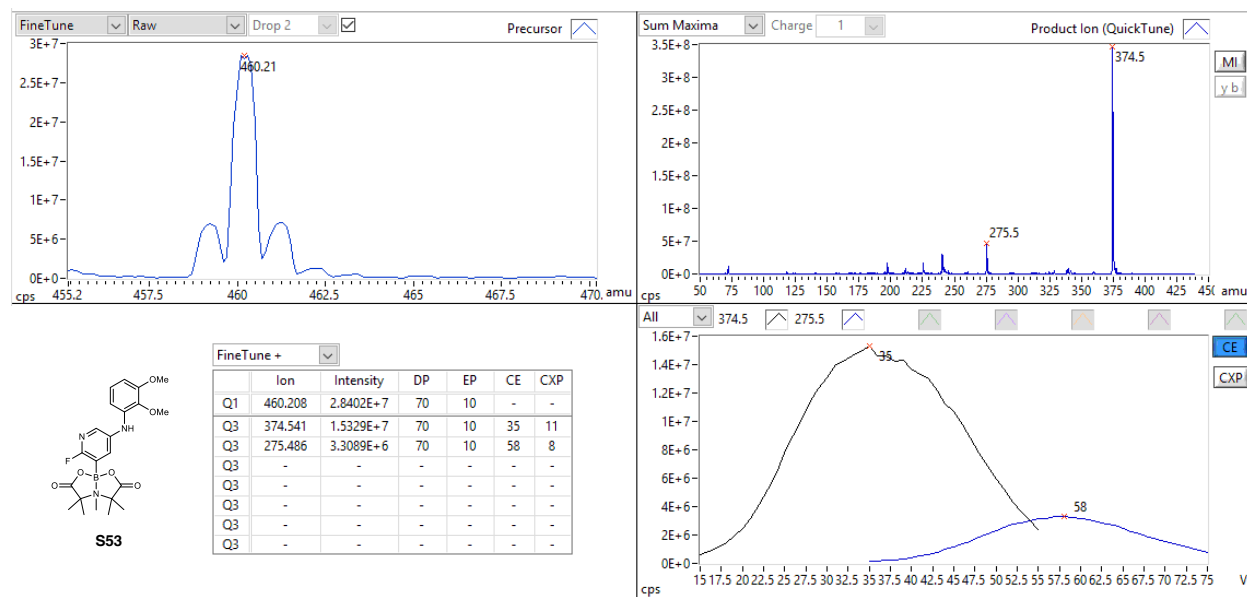
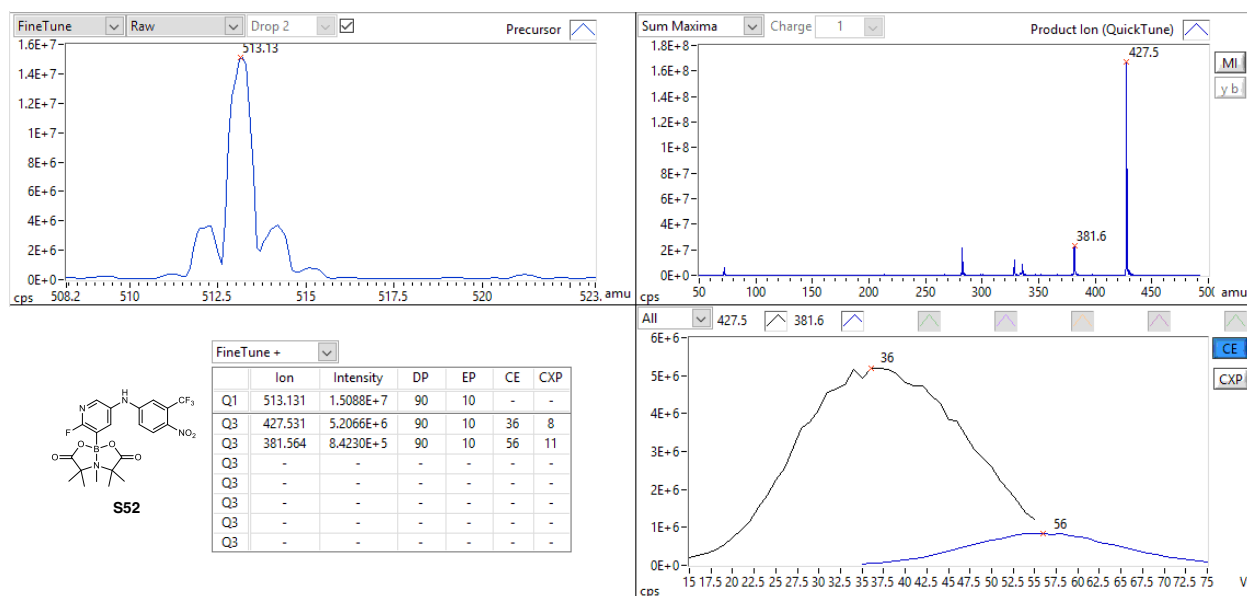


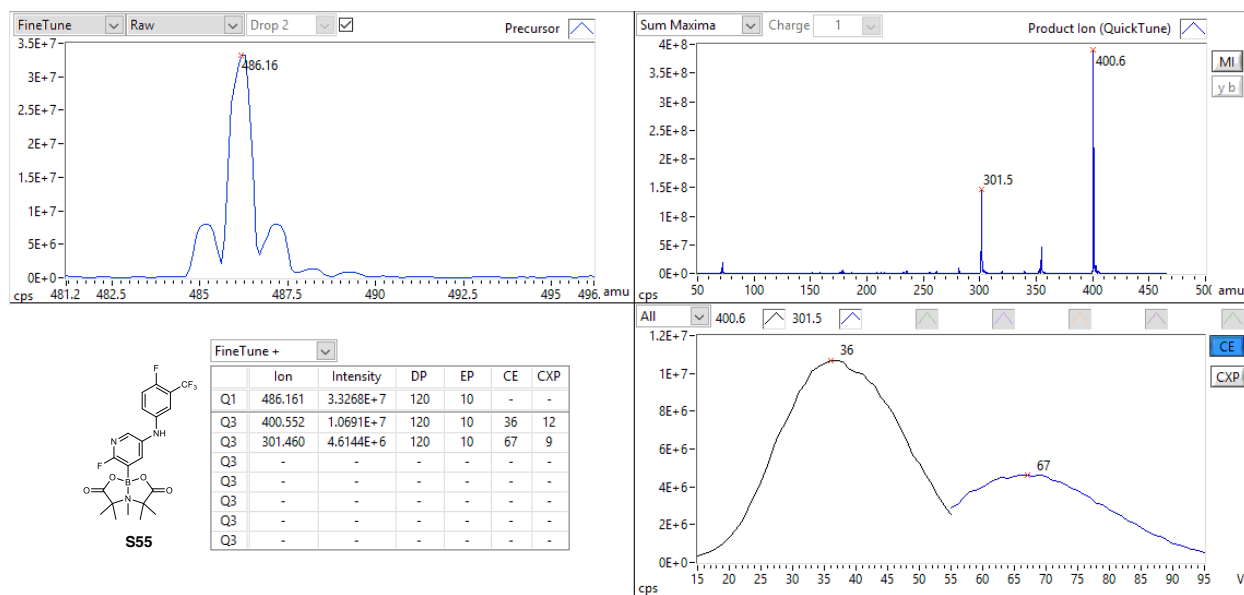
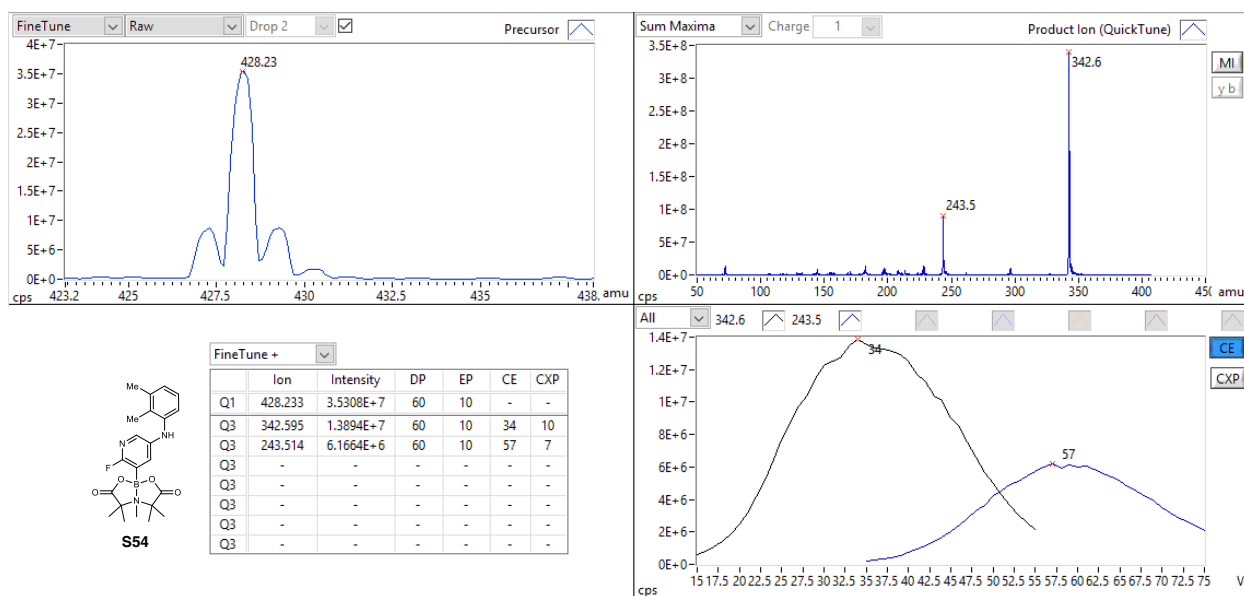
	Ion	Intensity	DP	EP	CE	CXP
Q1	539.224	4.3126E+7	100	10	-	-
Q3	453.655	7.6582E+6	100	10	42	14
Q3	397.619	2.2268E+6	100	10	59	12
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

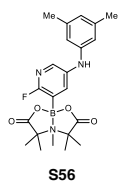
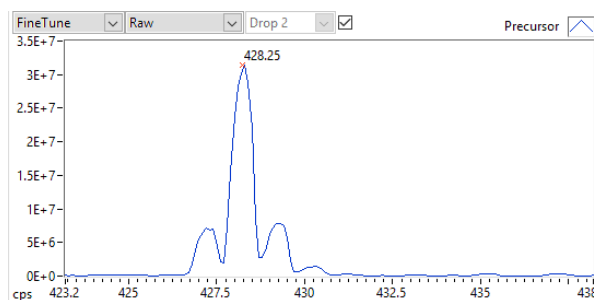


	Ion	Intensity	DP	EP	CE	CXP
Q1	541.169	4.4042E+7	100	10	-	-
Q3	455.584	1.0227E+7	100	10	42	14
Q3	356.496	7.1548E+6	100	10	66	11
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

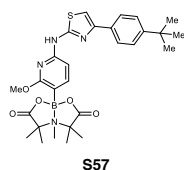
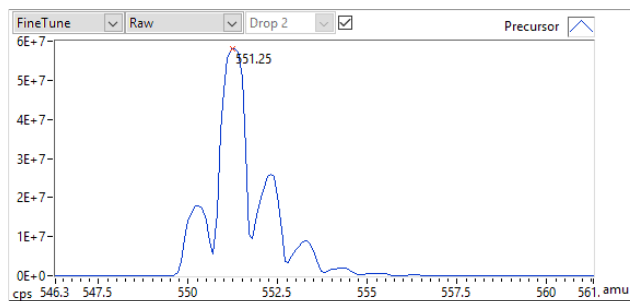
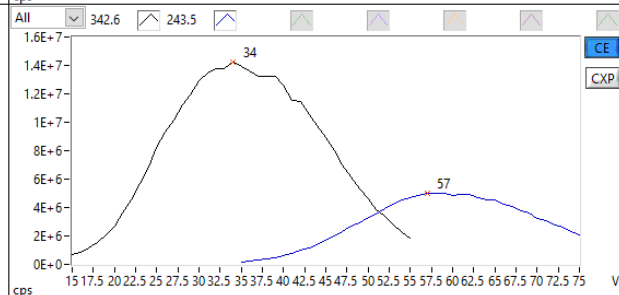
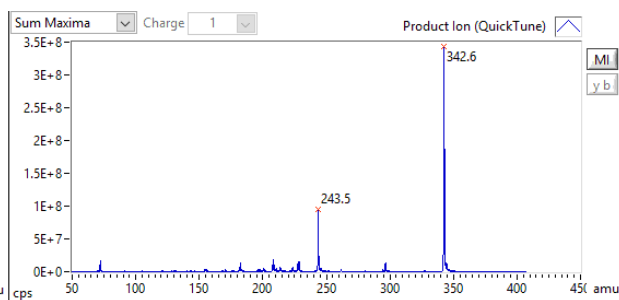




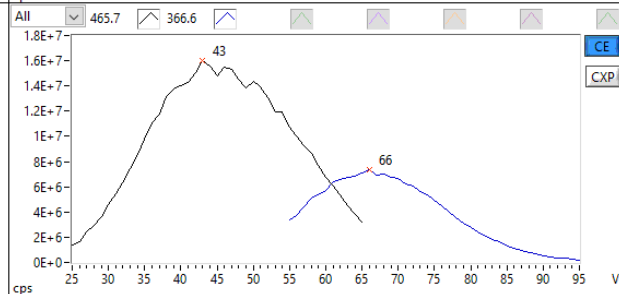
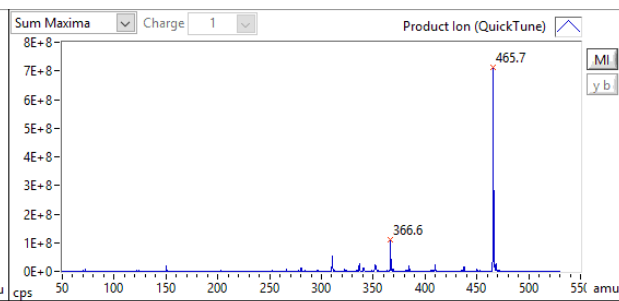


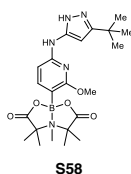
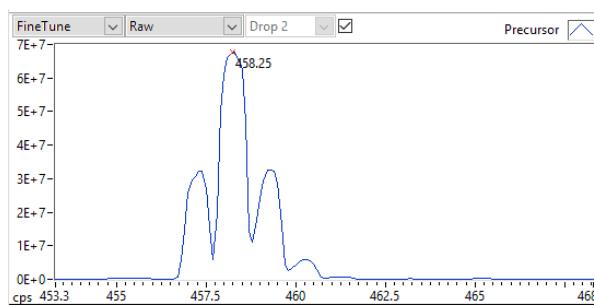


	Ion	Intensity	DP	EP	CE	CXP
Q1	428.245	3.1342E+7	120	10	-	-
Q3	342.588	1.4240E+7	120	10	34	10
Q3	243.537	5.0015E+6	120	10	57	14
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

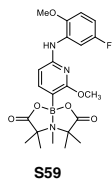
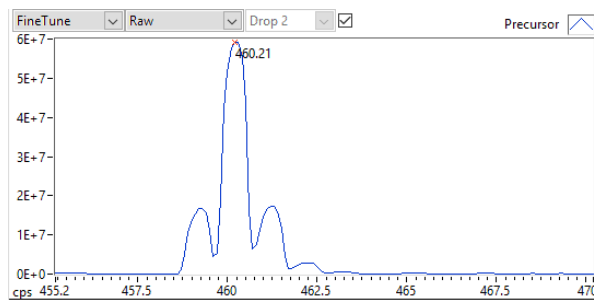
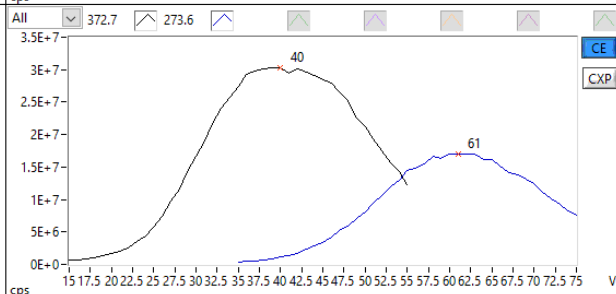
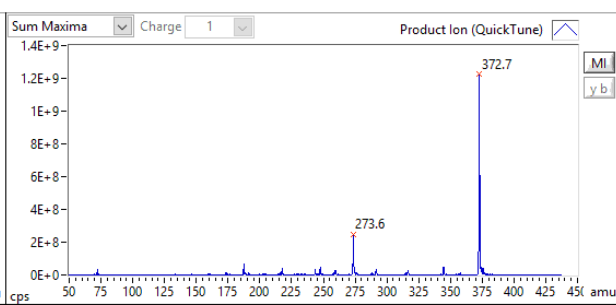


	Ion	Intensity	DP	EP	CE	CXP
Q1	551.246	5.8158E+7	90	10	-	-
Q3	465.665	1.6029E+7	90	10	43	14
Q3	366.571	7.3529E+6	90	10	66	11
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

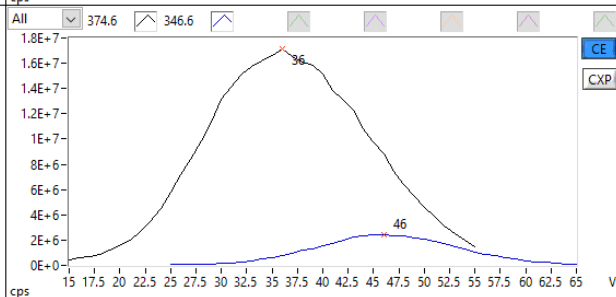
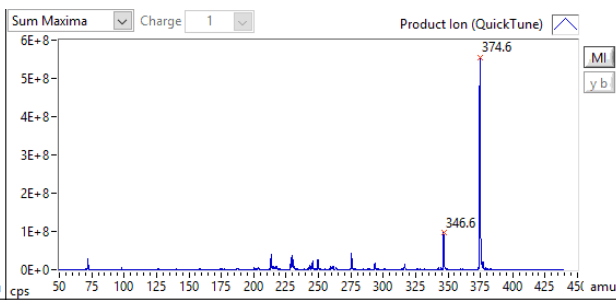


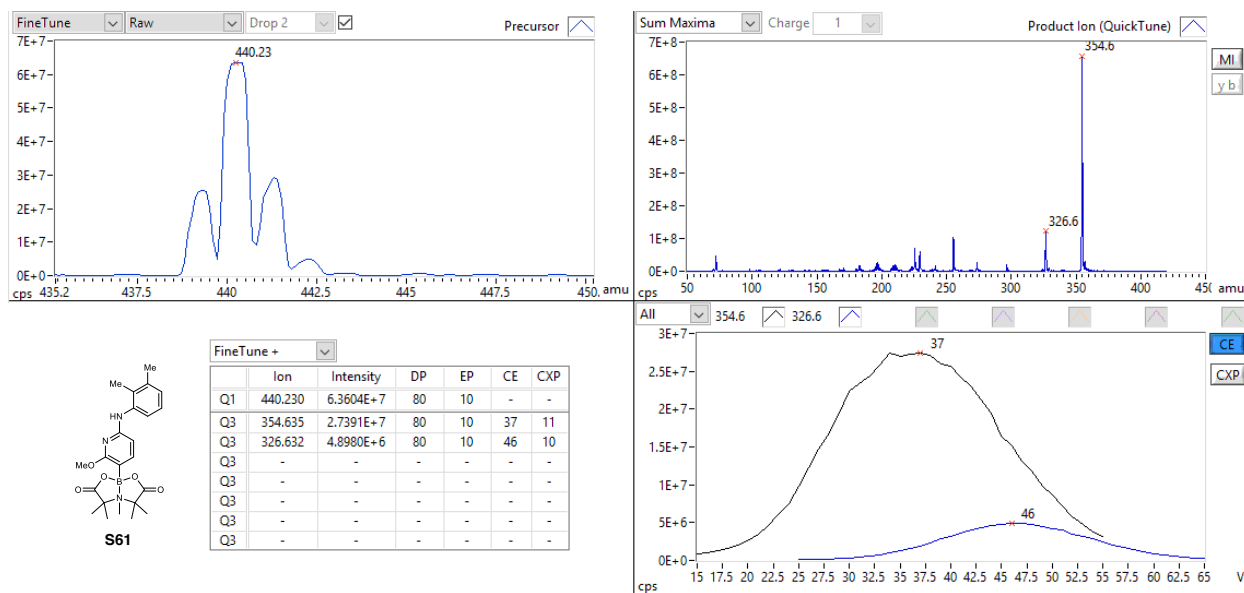
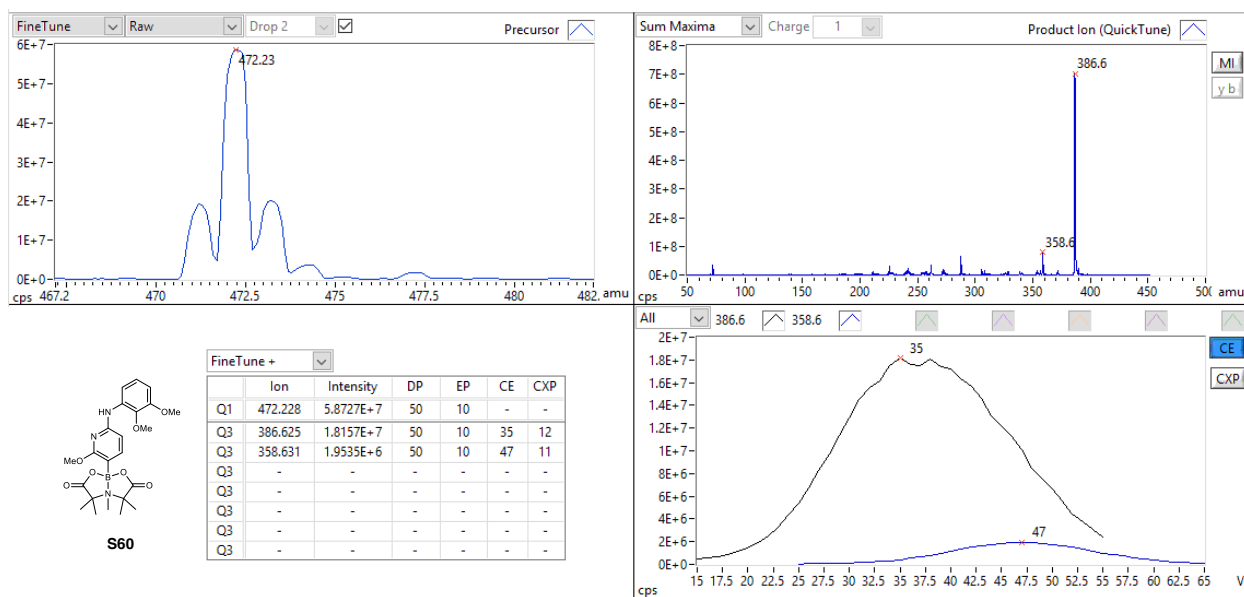


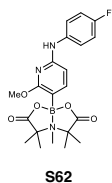
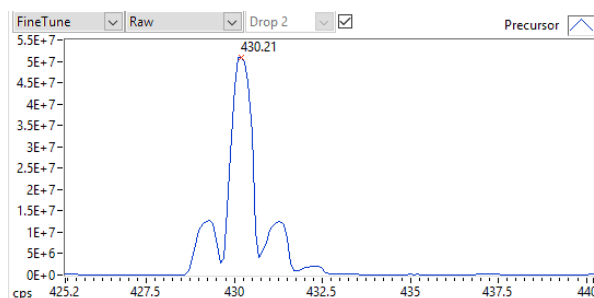
	Ion	Intensity	DP	EP	CE	CXP
Q1	458.246	6.7617E+7	90	10	-	-
Q3	372.673	3.0363E+7	90	10	40	11
Q3	273.551	1.7049E+7	90	10	61	8
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-



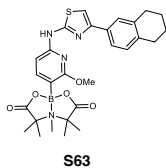
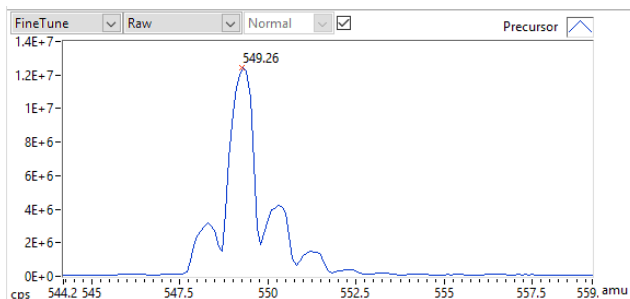
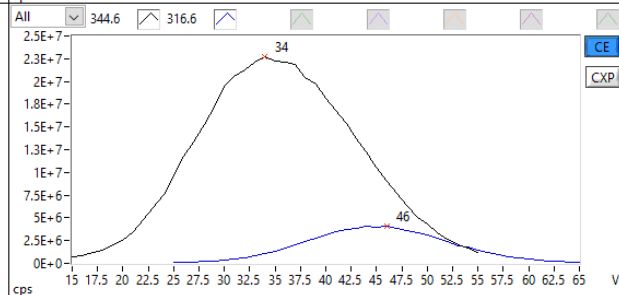
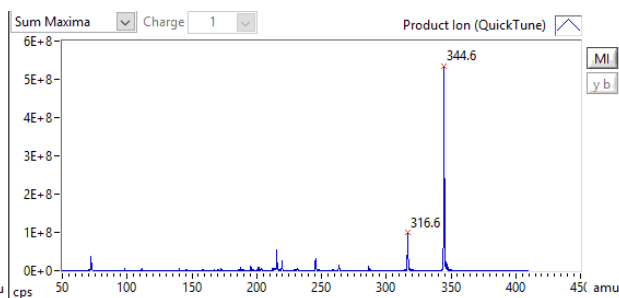
	Ion	Intensity	DP	EP	CE	CXP
Q1	460.209	5.9121E+7	80	10	-	-
Q3	374.608	1.7111E+7	80	10	36	11
Q3	346.637	2.4607E+6	80	10	46	19
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-



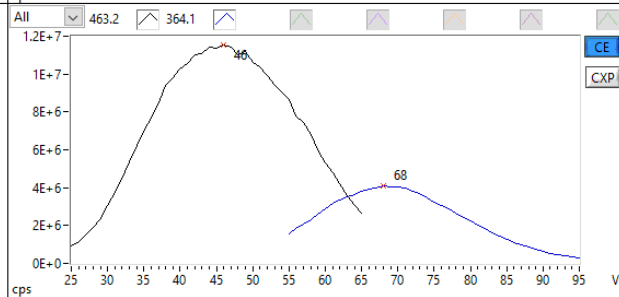
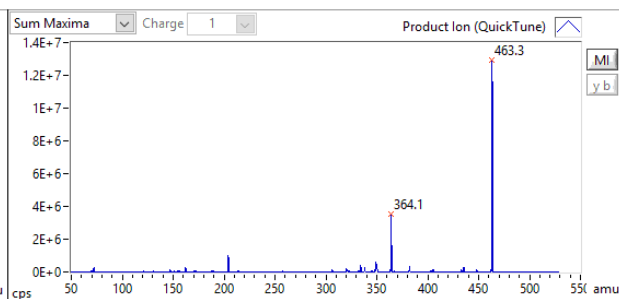


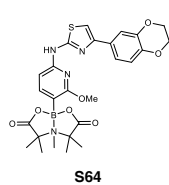


	Ion	Intensity	DP	EP	CE	CXP
Q1	430.213	5.0952E+7	120	10	-	-
Q3	344.558	2.2679E+7	120	10	34	10
Q3	316.585	4.0668E+6	120	10	46	10
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

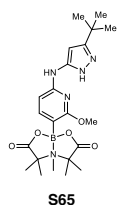
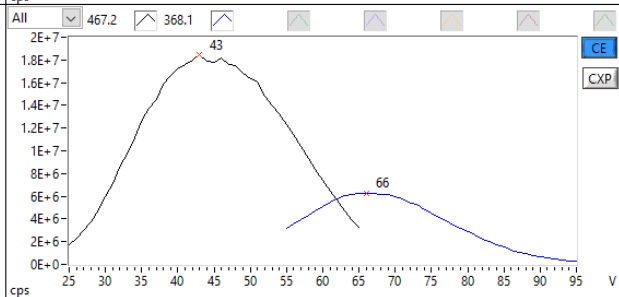


	Ion	Intensity	DP	EP	CE	CXP
Q1	549.259	1.2415E+7	50	10	-	-
Q3	463.252	1.1529E+7	50	10	46	15
Q3	364.149	4.1144E+6	50	10	68	12
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

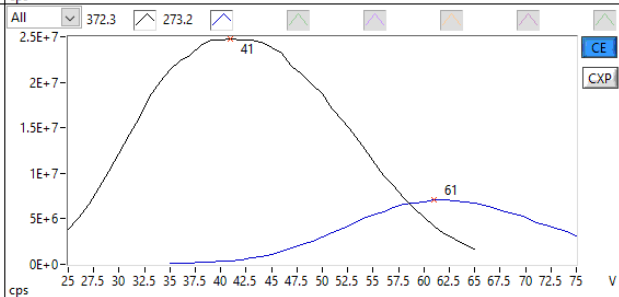




FineTune +						
	lon	Intensity	DP	EP	CE	CXP
Q1	553.221	2.0449E+7	50	10	-	-
Q3	467.224	1.8418E+7	50	10	43	10
Q3	368.126	6.2956E+6	50	10	66	12
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

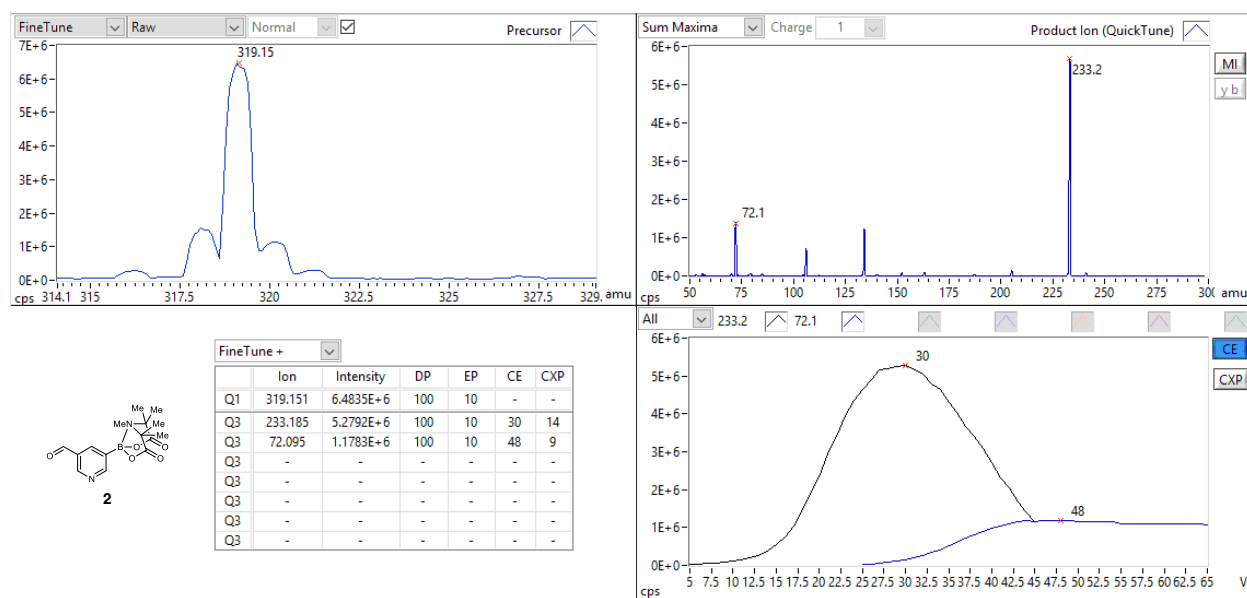
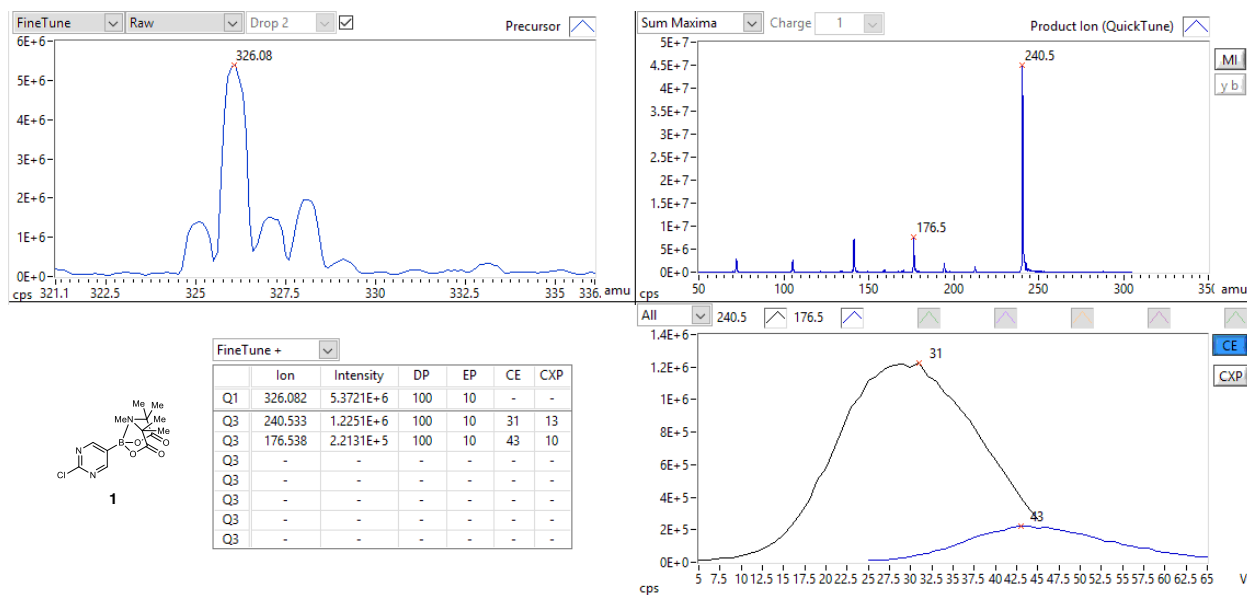


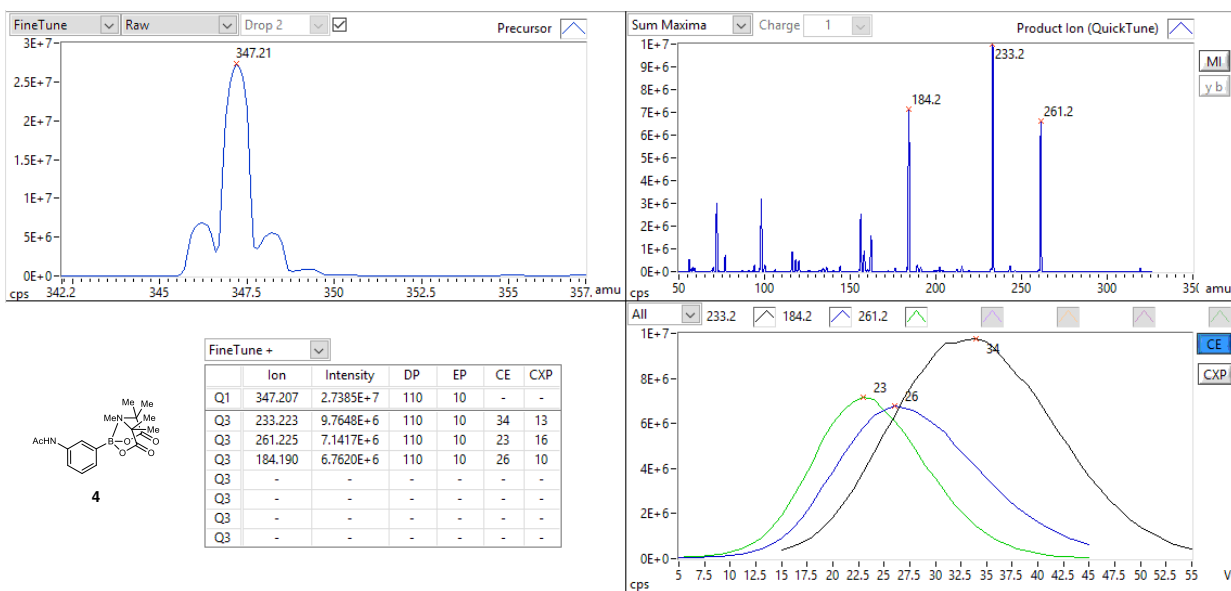
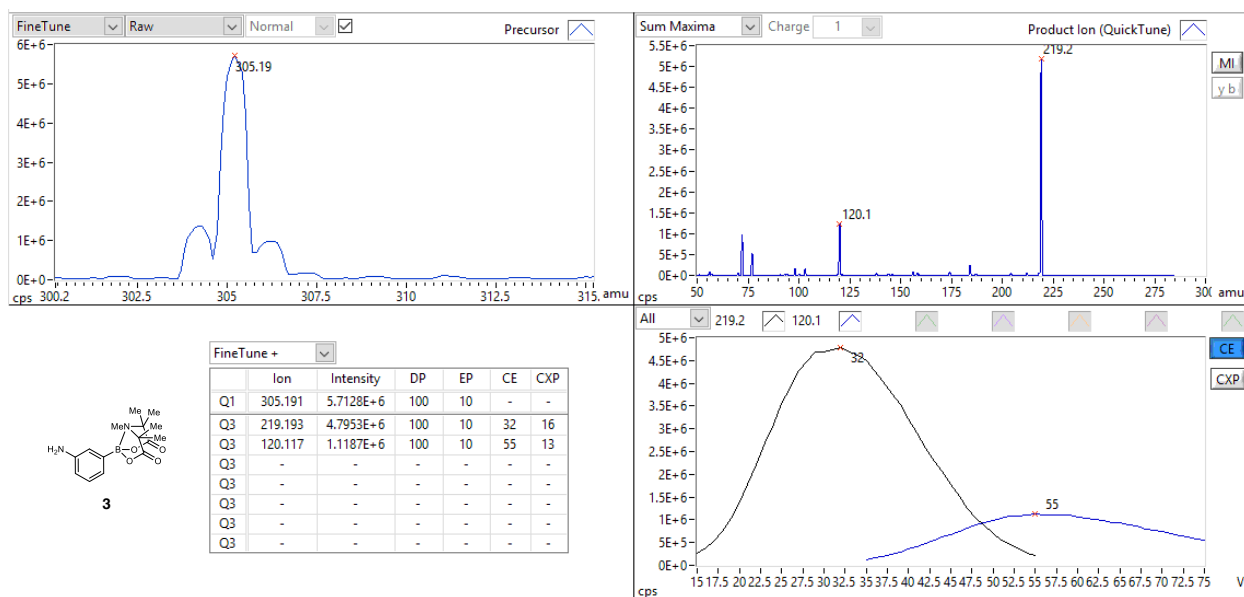
	lon	Intensity	DP	EP	CE	CXP
Q1	458.286	2.5884E+7	60	10	-	-
Q3	372.263	2.4809E+7	60	10	41	12
Q3	273.227	7.0815E+6	60	10	61	16
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

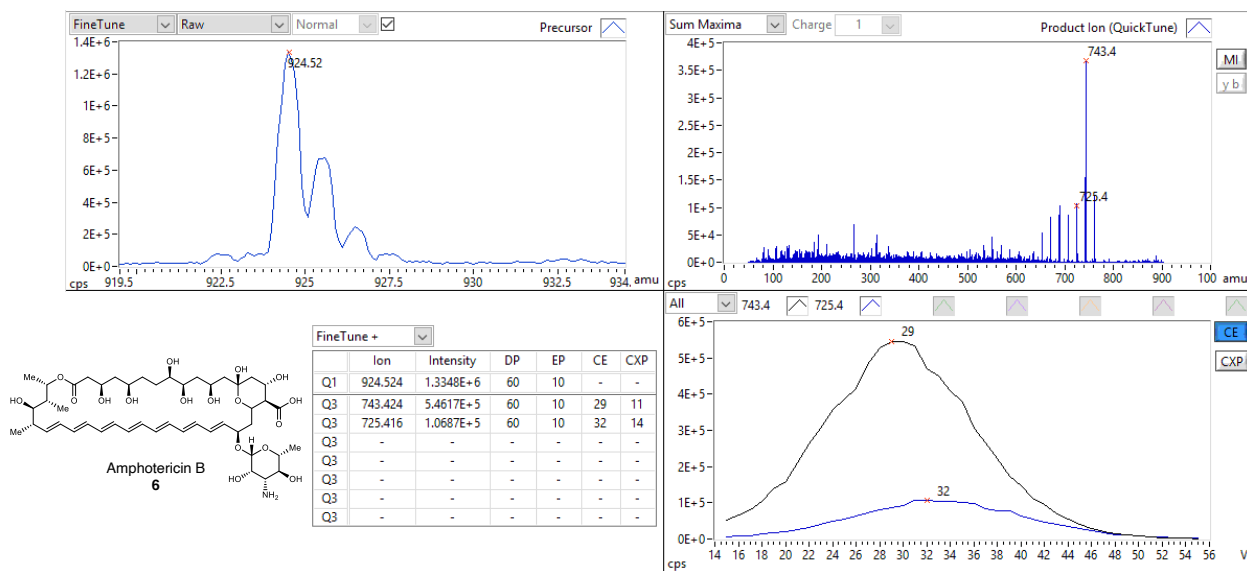
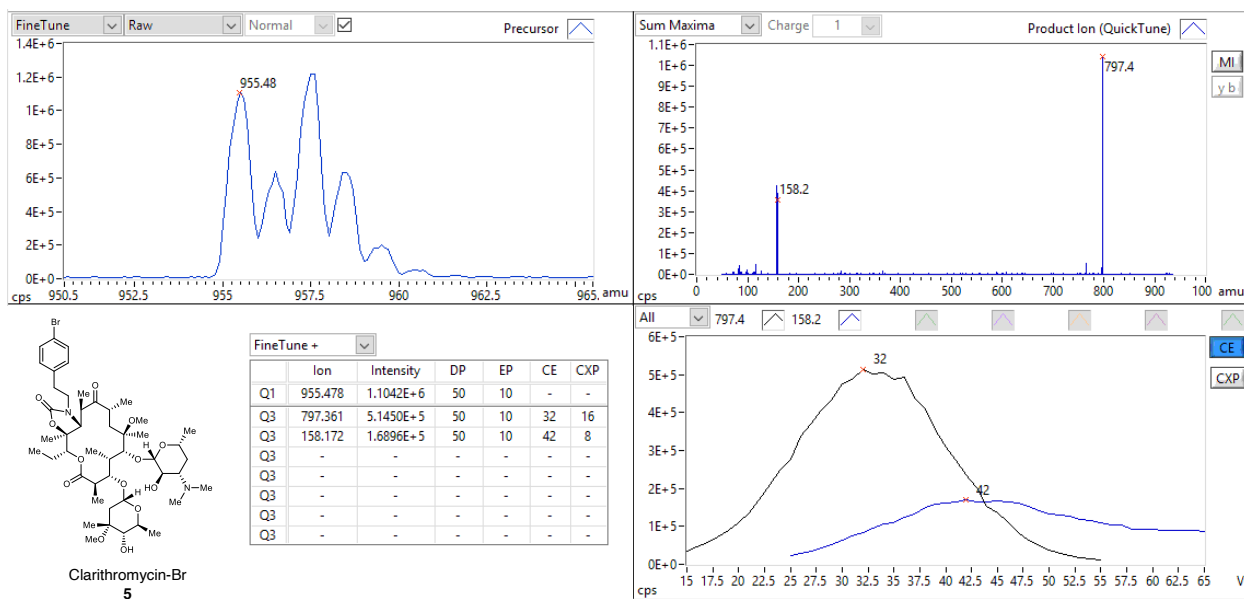


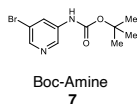
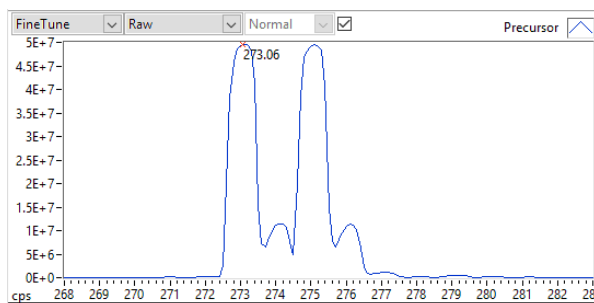
4.15 CID spectra for starting materials

Data can be found in *Extended Tabular Data Sheet 1*.

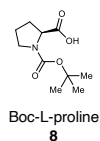
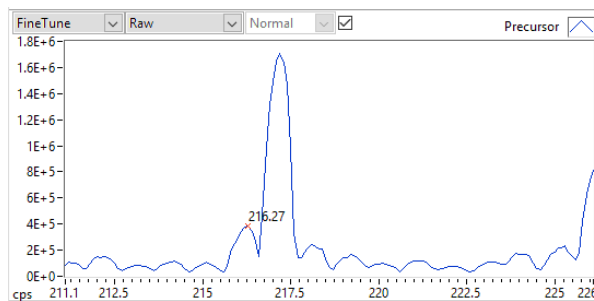
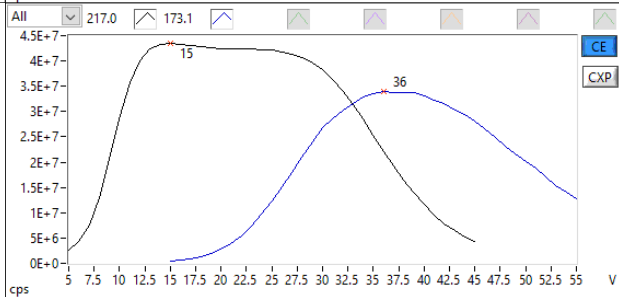
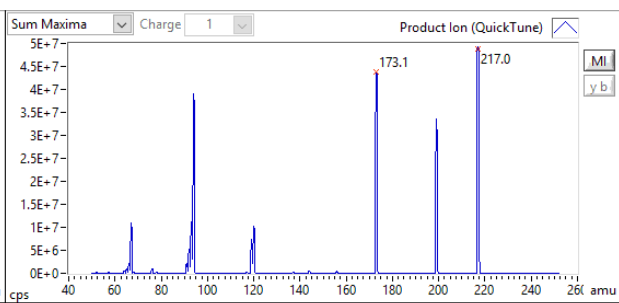




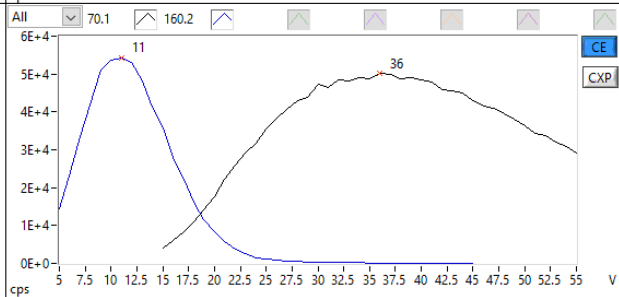
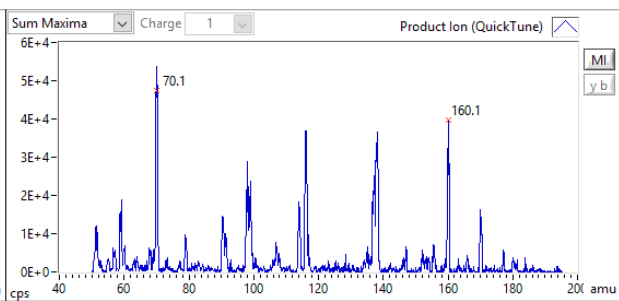


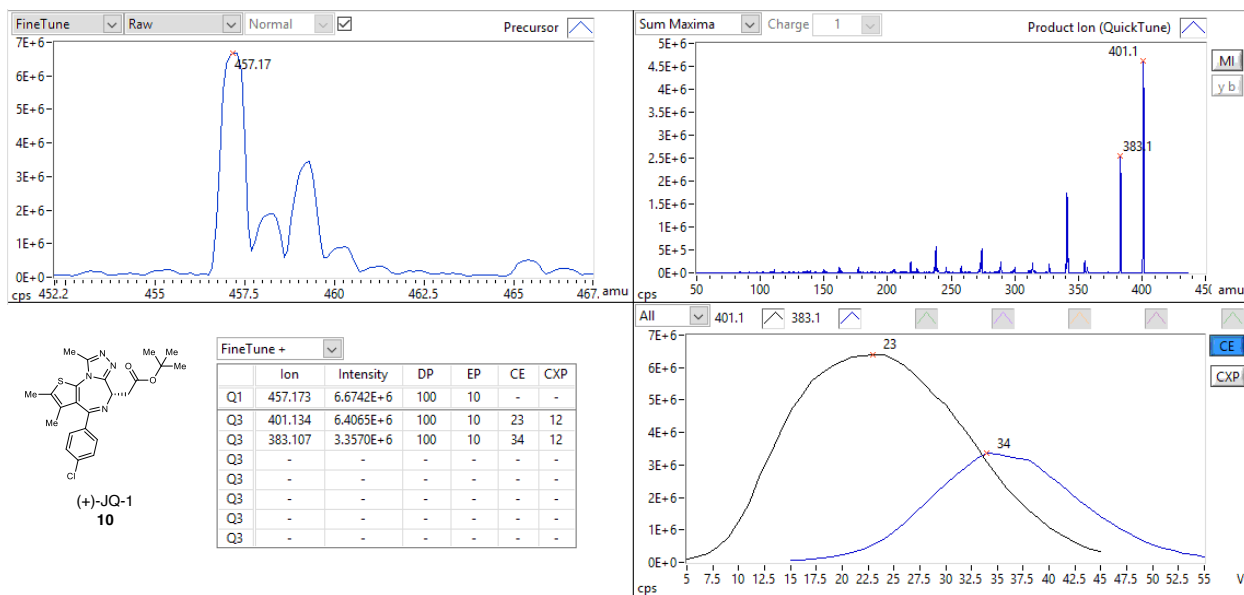
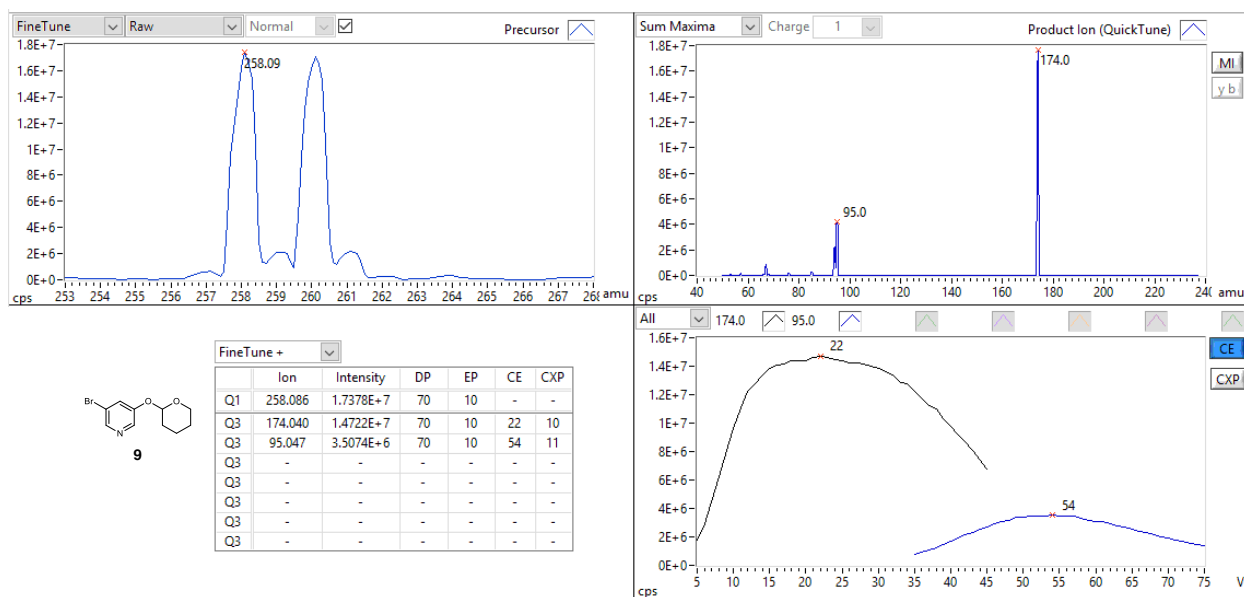


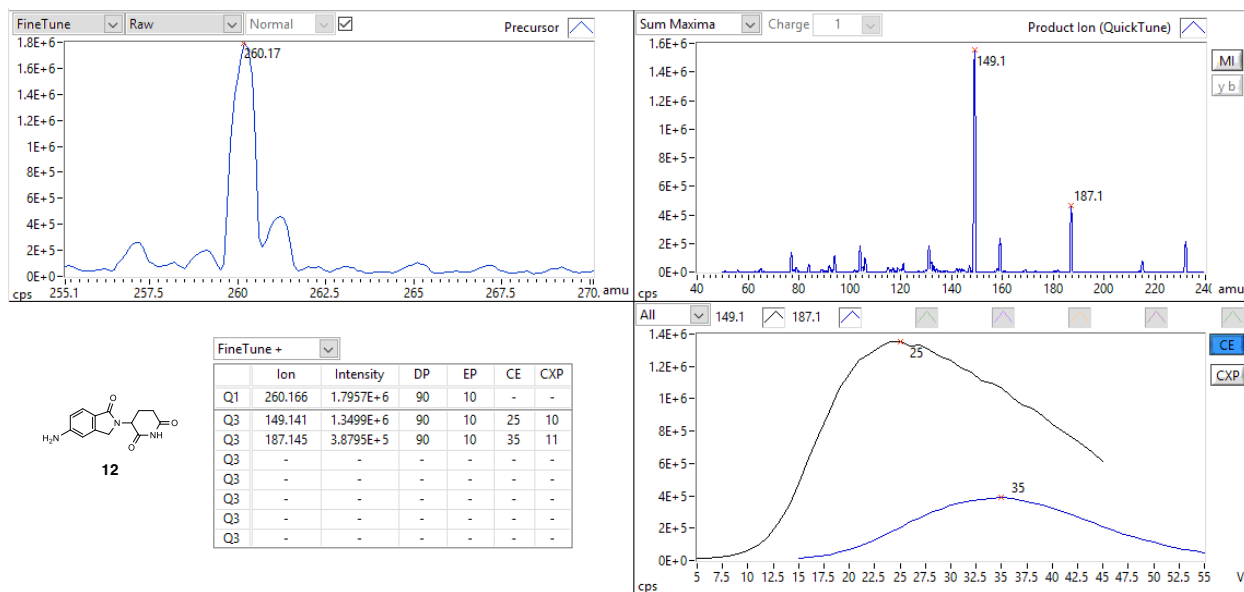
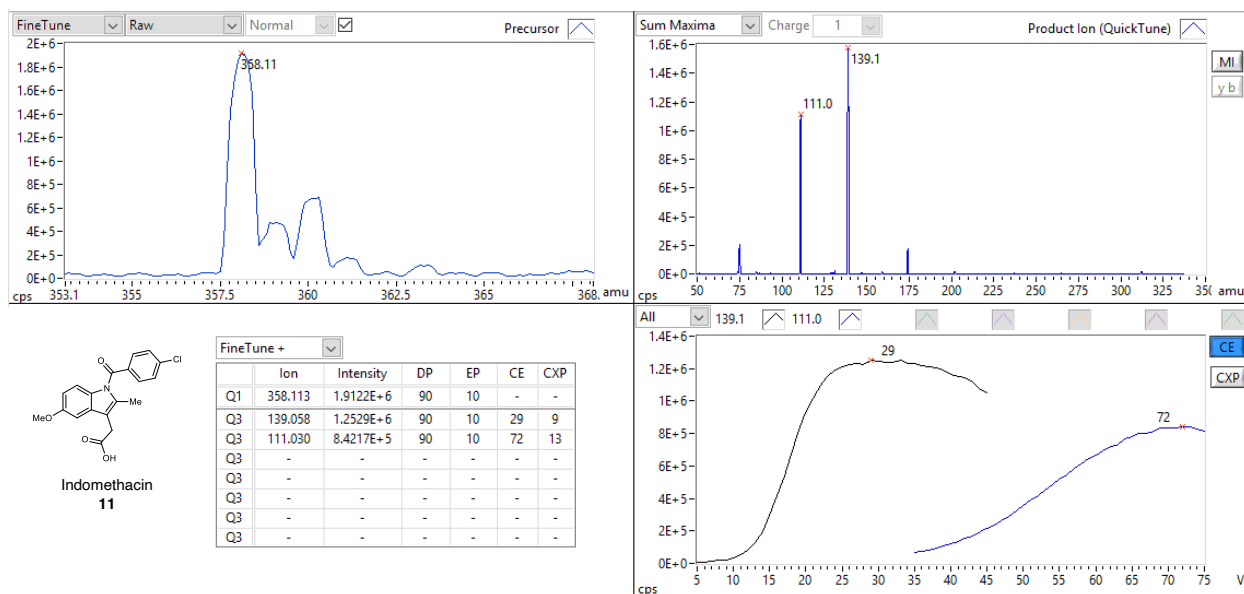
	Ion	Intensity	DP	EP	CE	CXP
Q1	273.061	4.9645E+7	80	10	-	-
Q3	217.020	4.3449E+7	80	10	15	3
Q3	173.060	3.3960E+7	80	10	36	10
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-

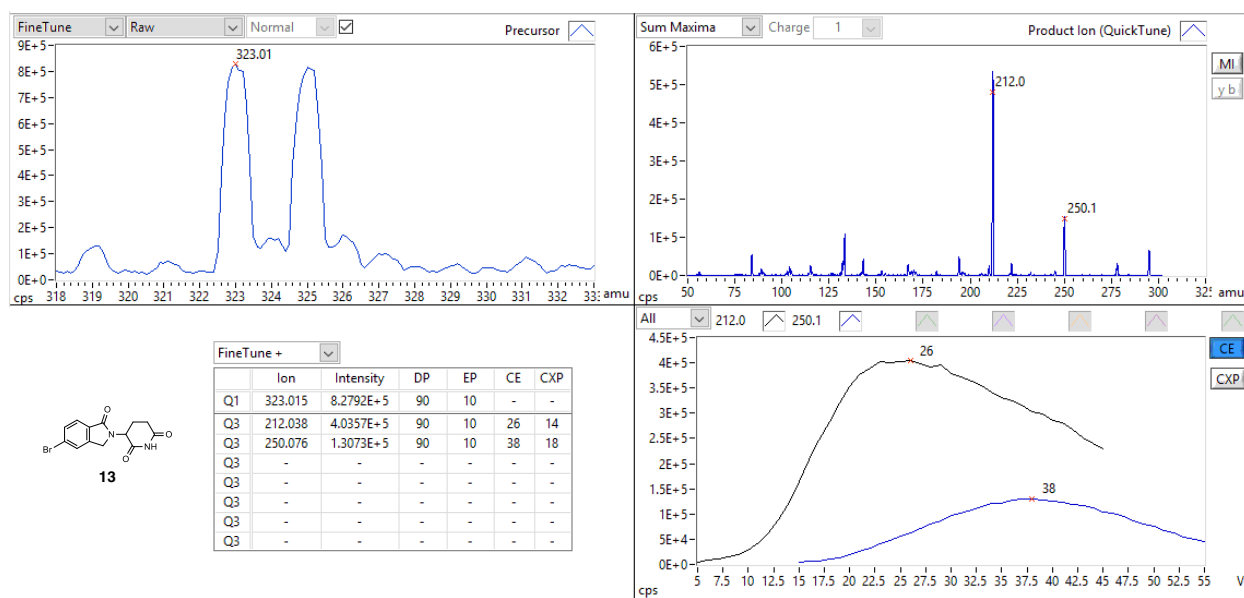


	Ion	Intensity	DP	EP	CE	CXP
Q1	216.275	1.7058E+6	50	10	-	-
Q3	160.146	5.4216E+4	50	10	11	10
Q3	70.069	5.0309E+4	50	10	36	8
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-
Q3	-	-	-	-	-	-





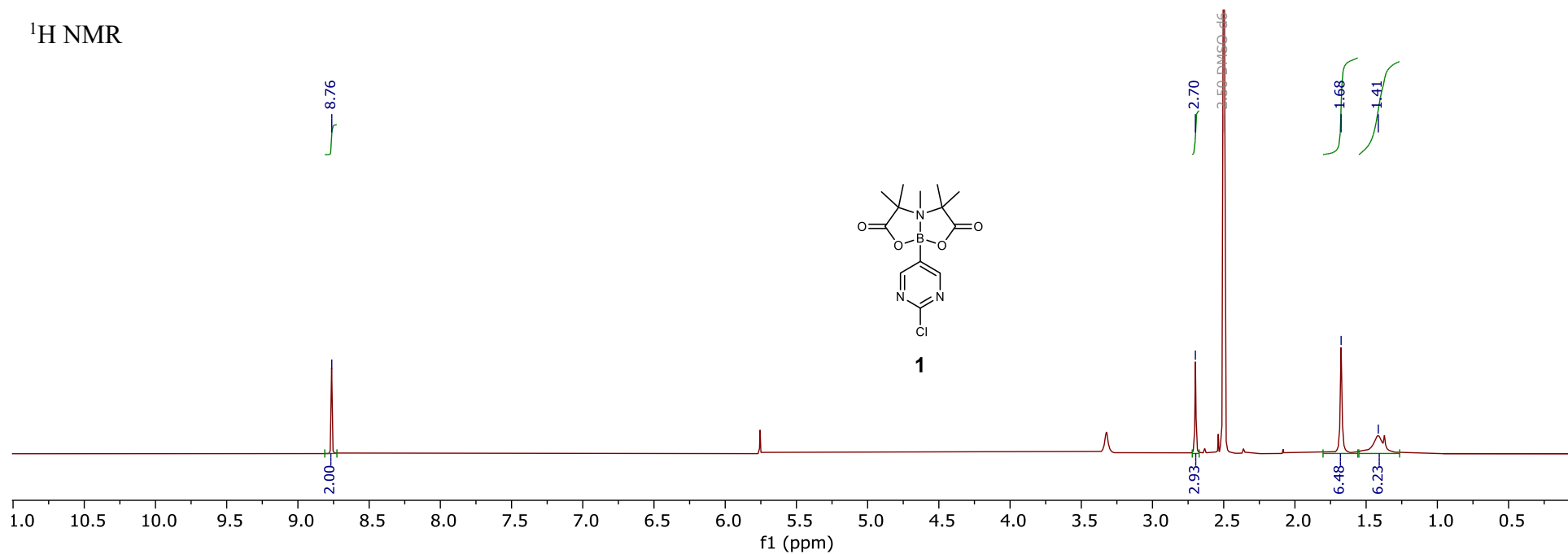




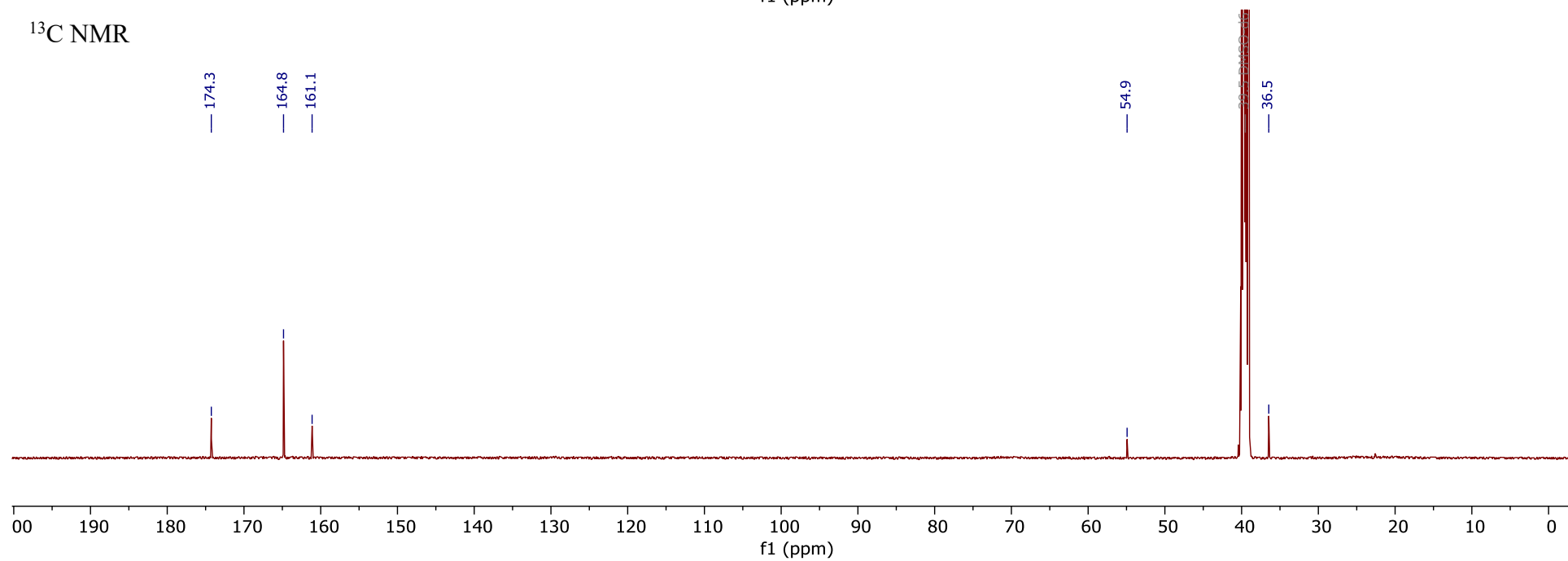
5. References

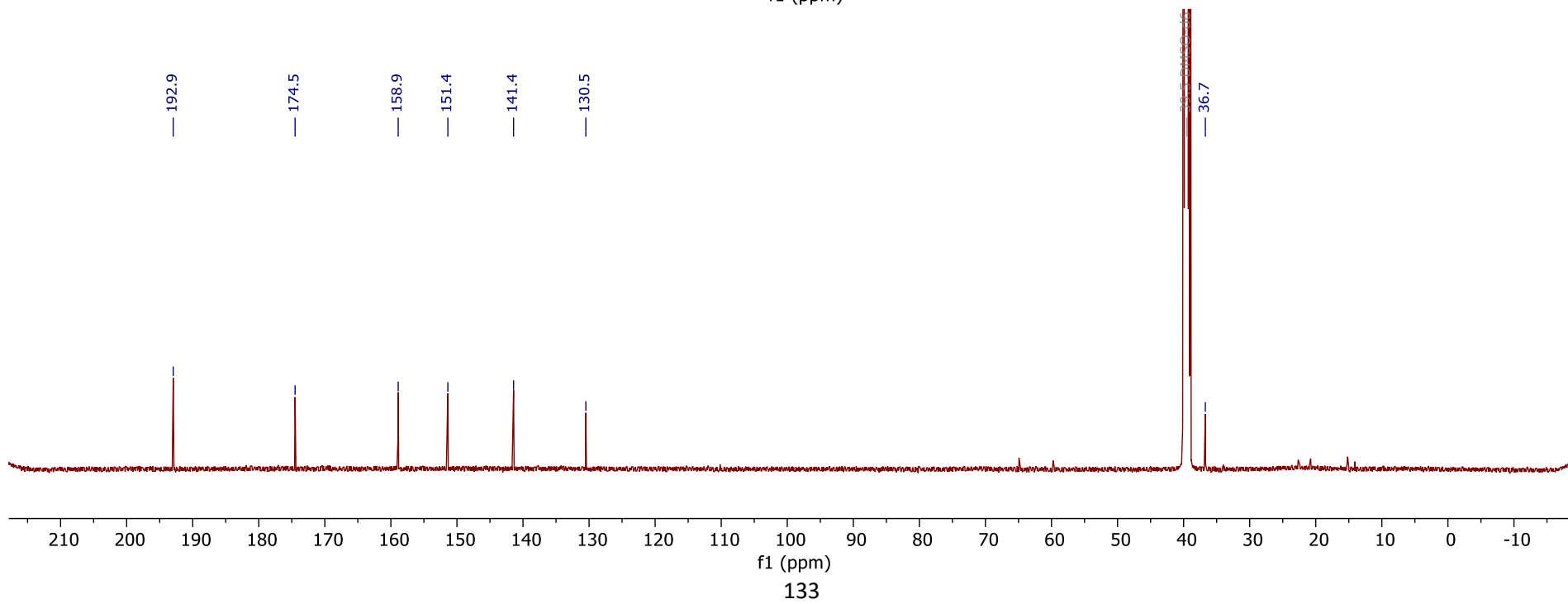
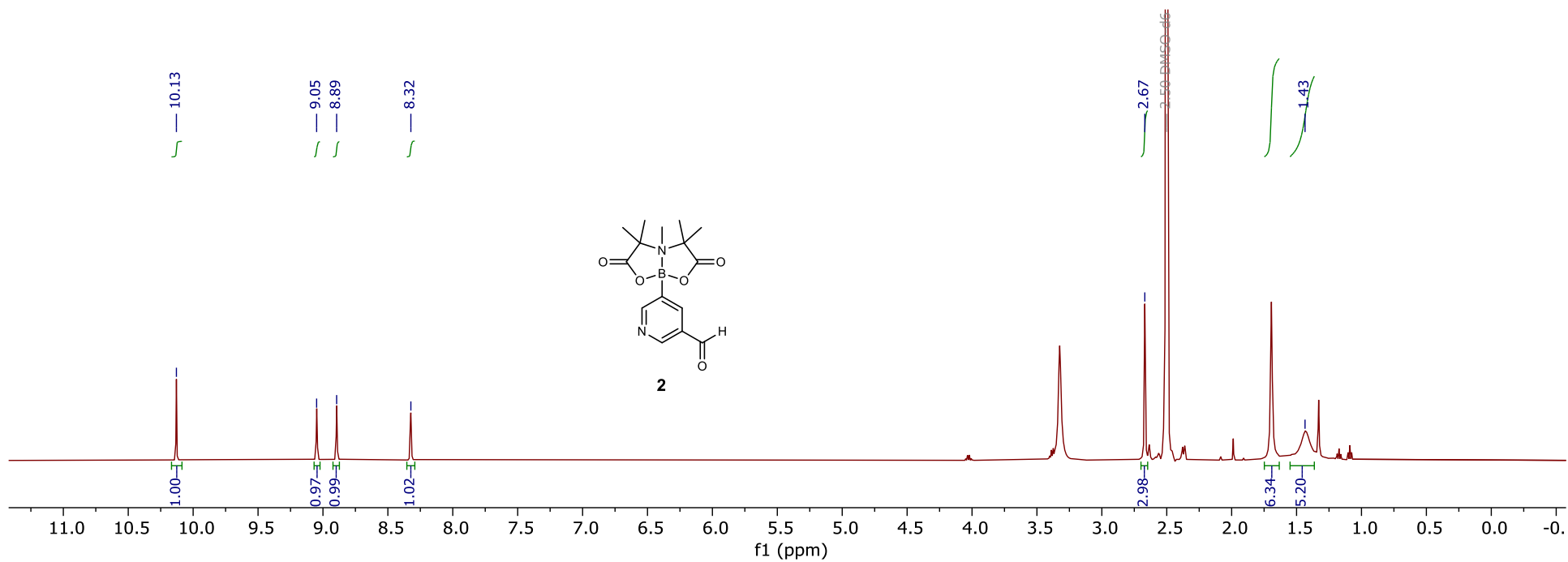
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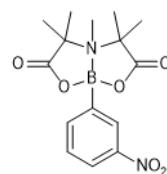
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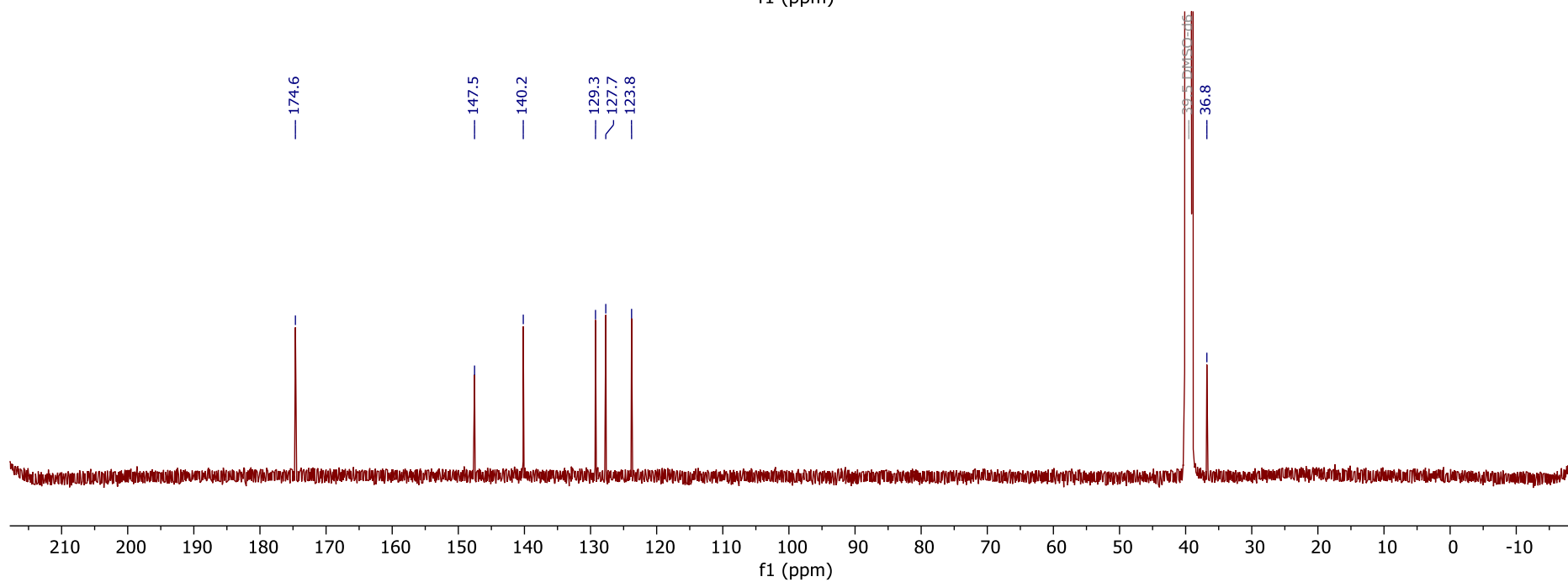
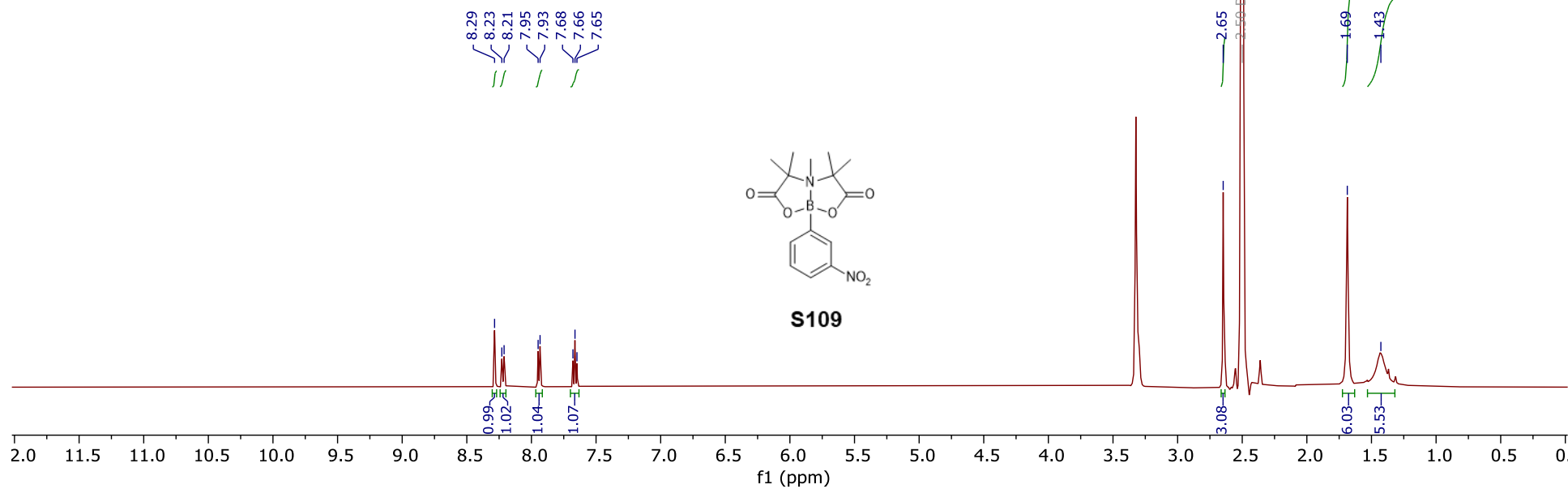
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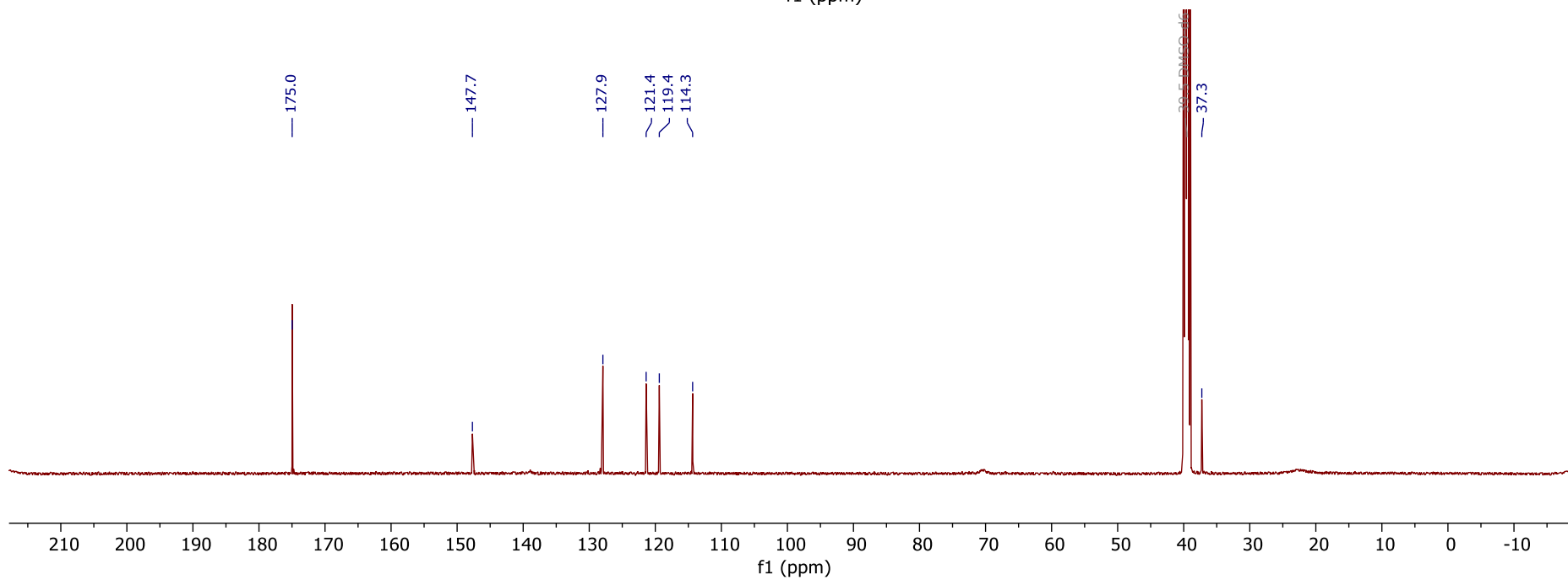
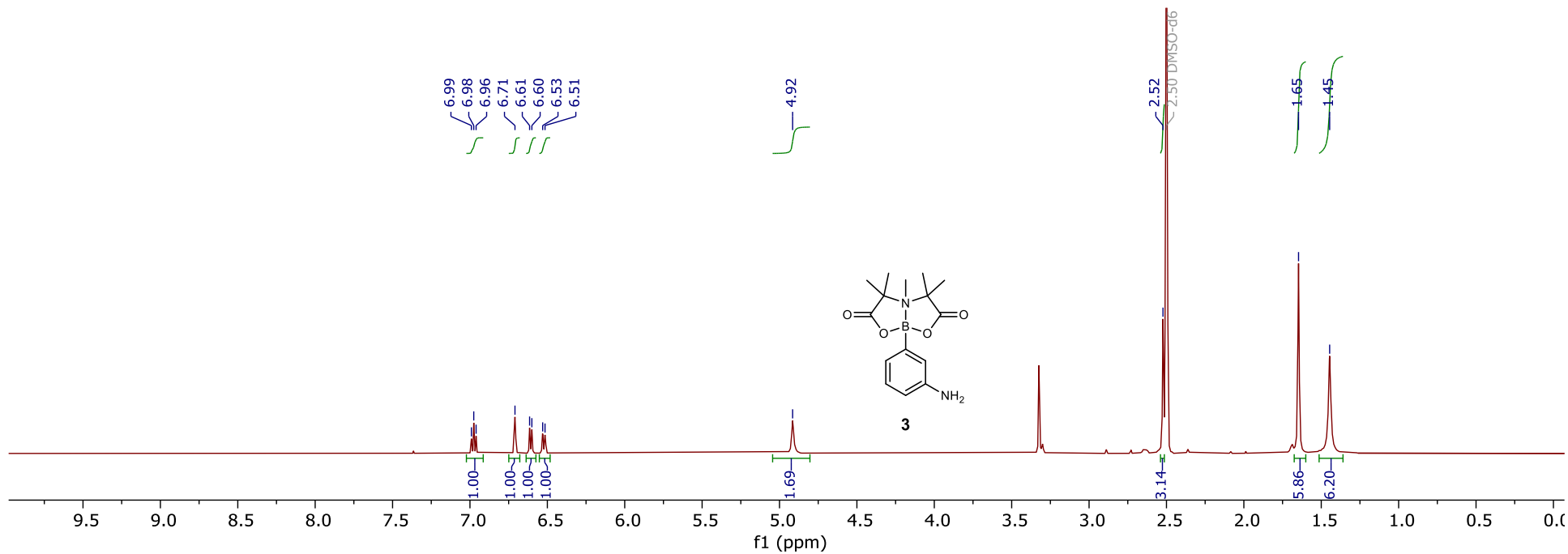


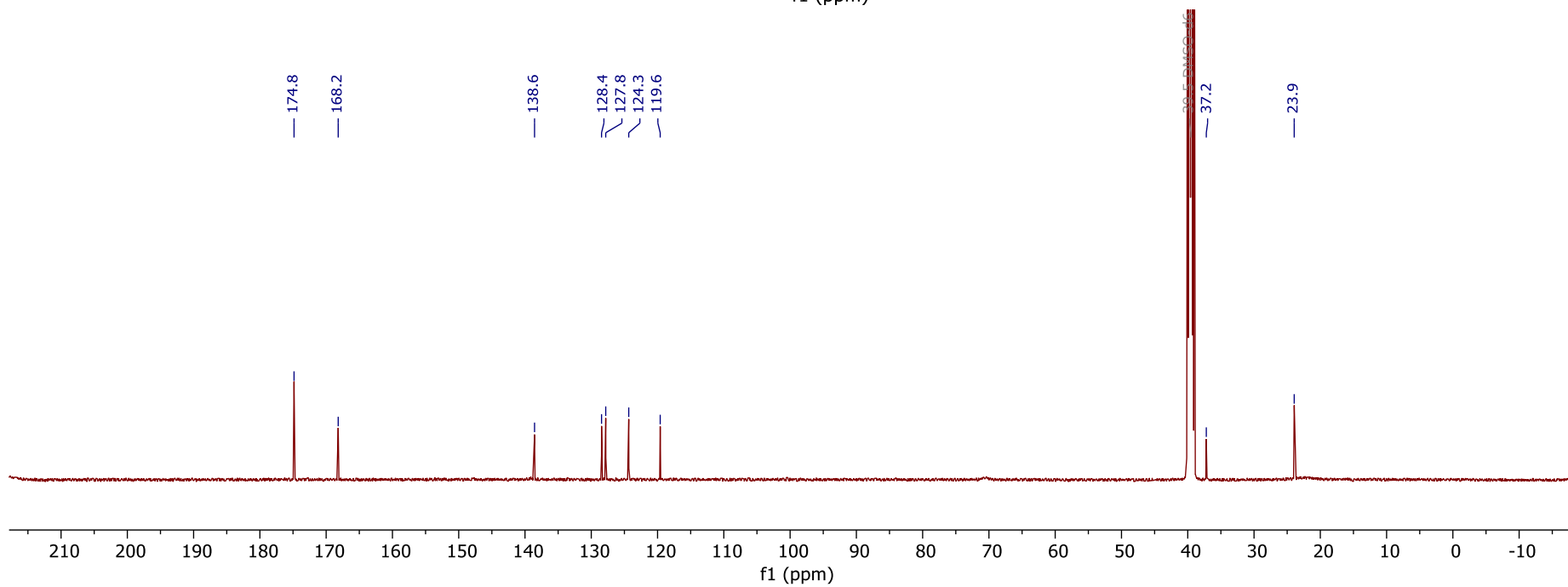
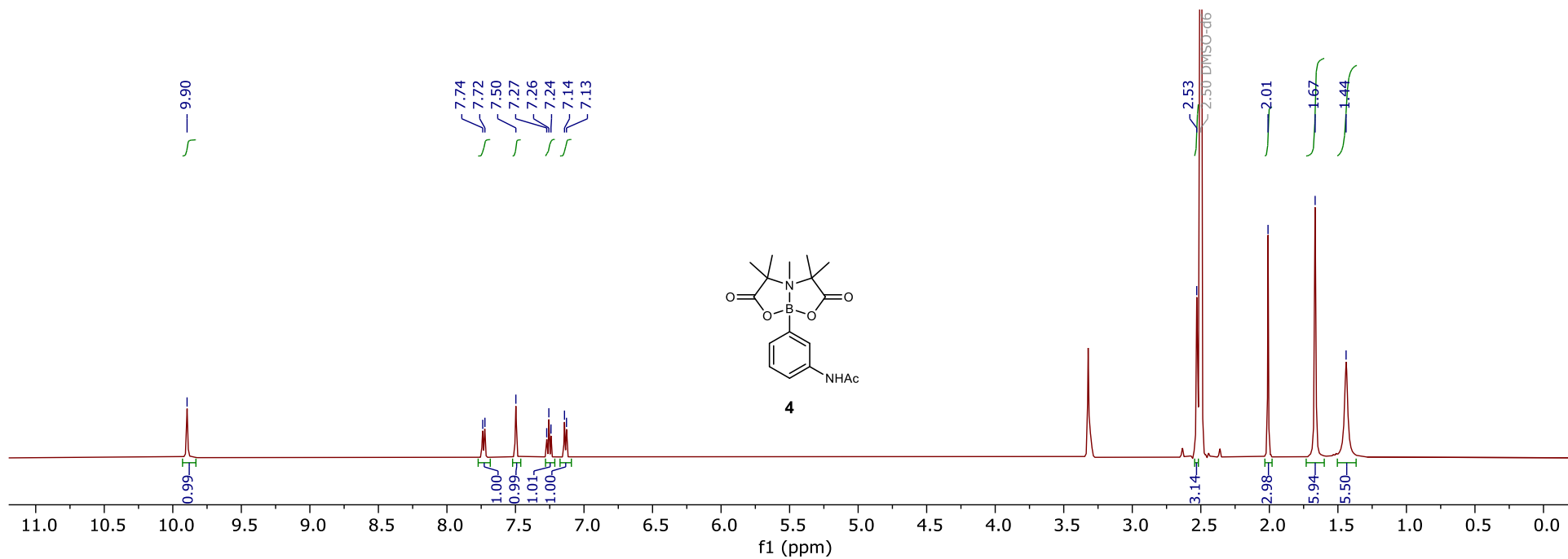


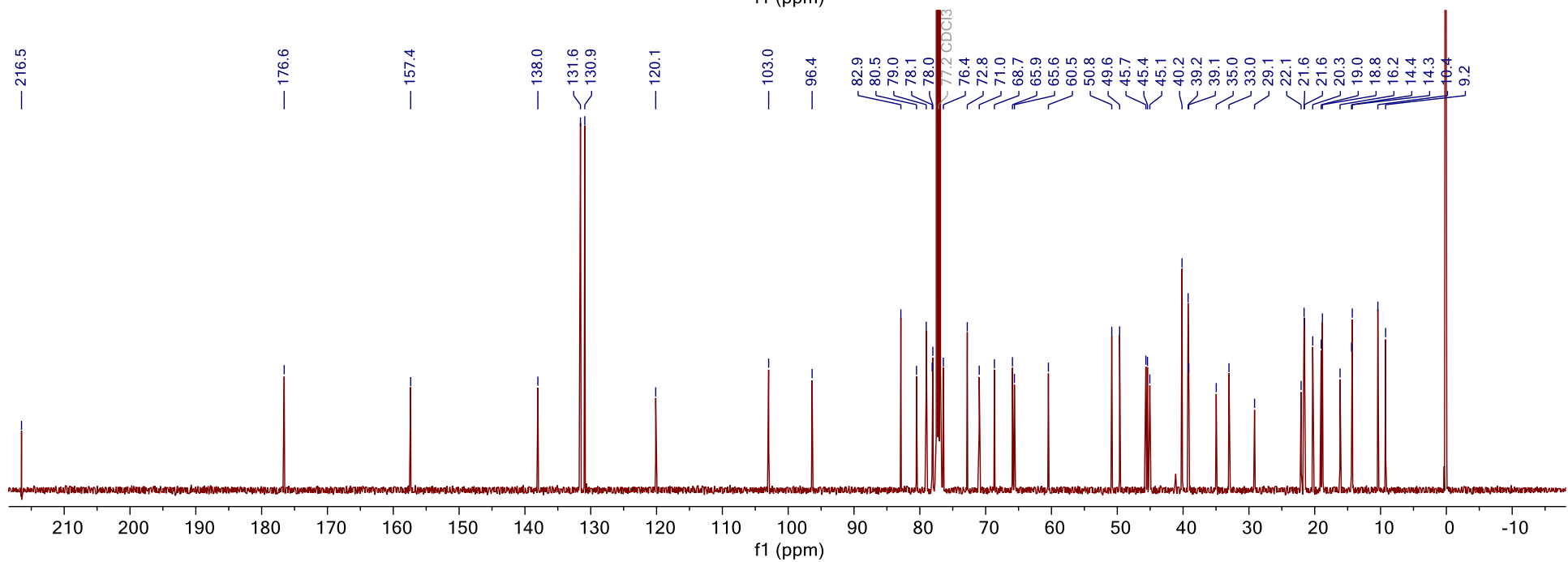
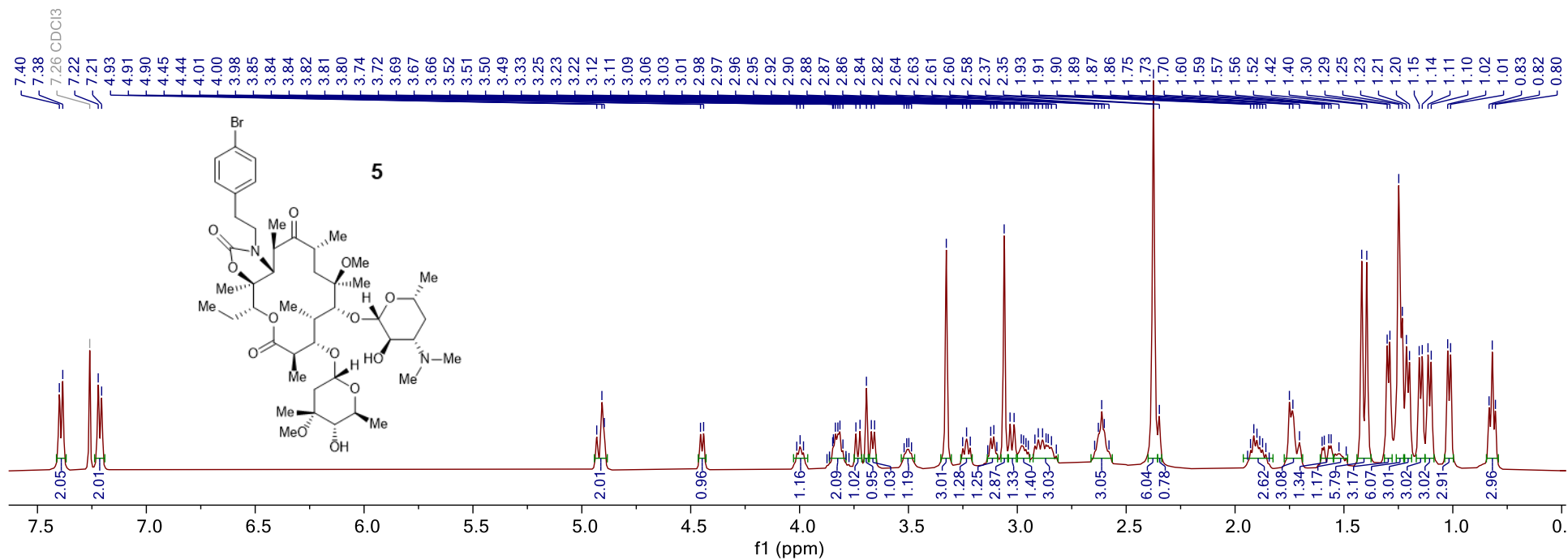


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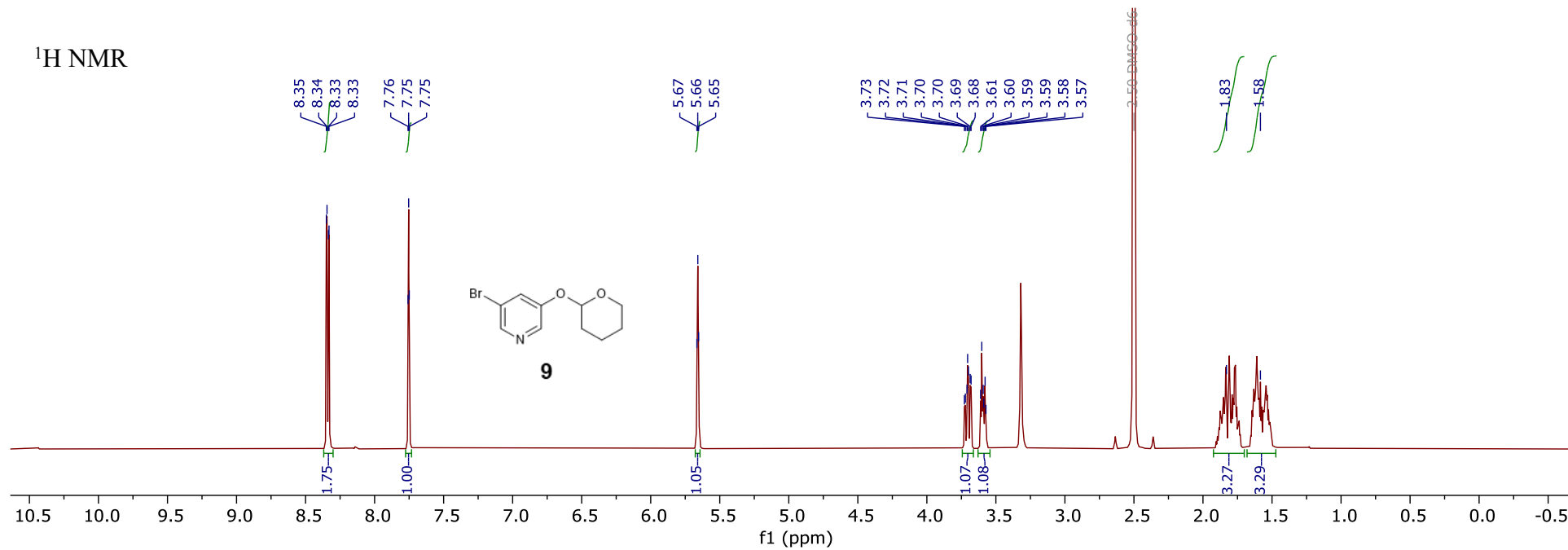




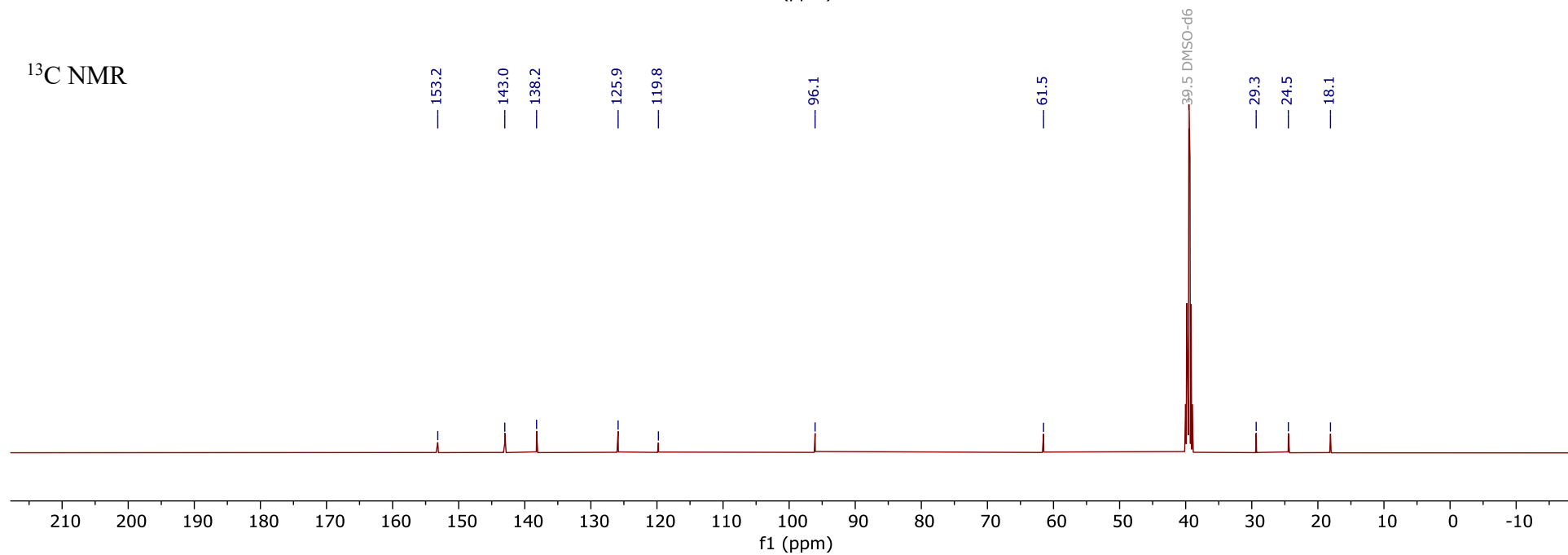




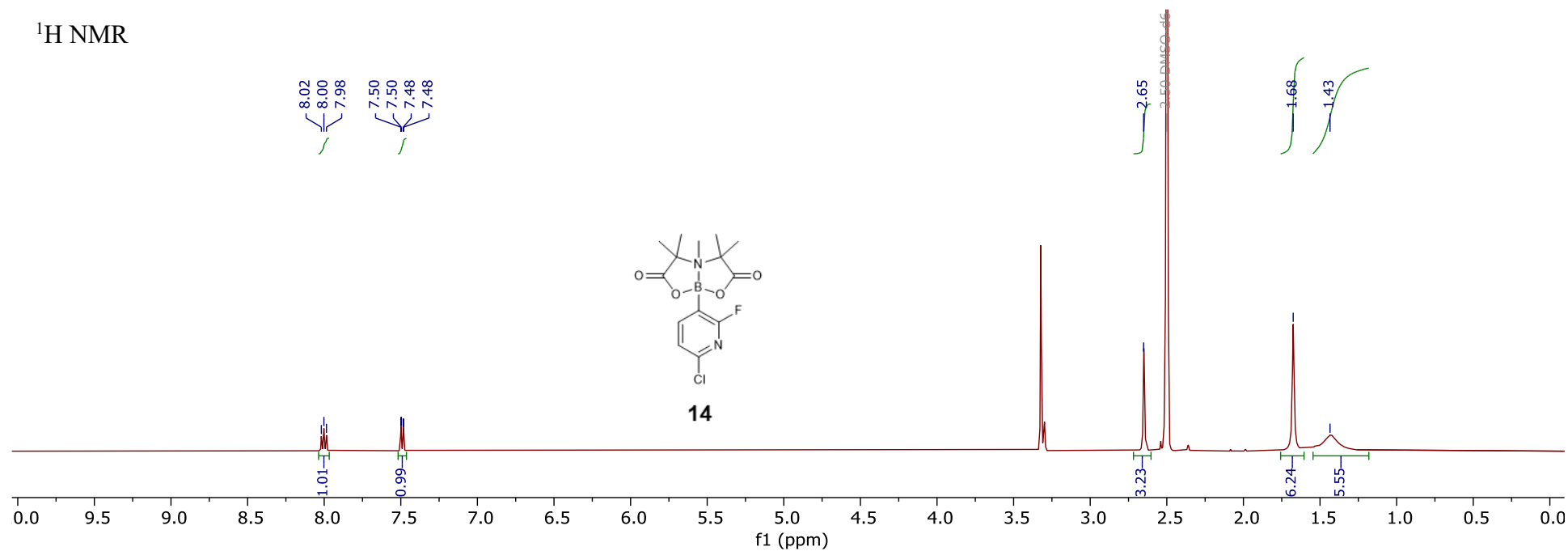
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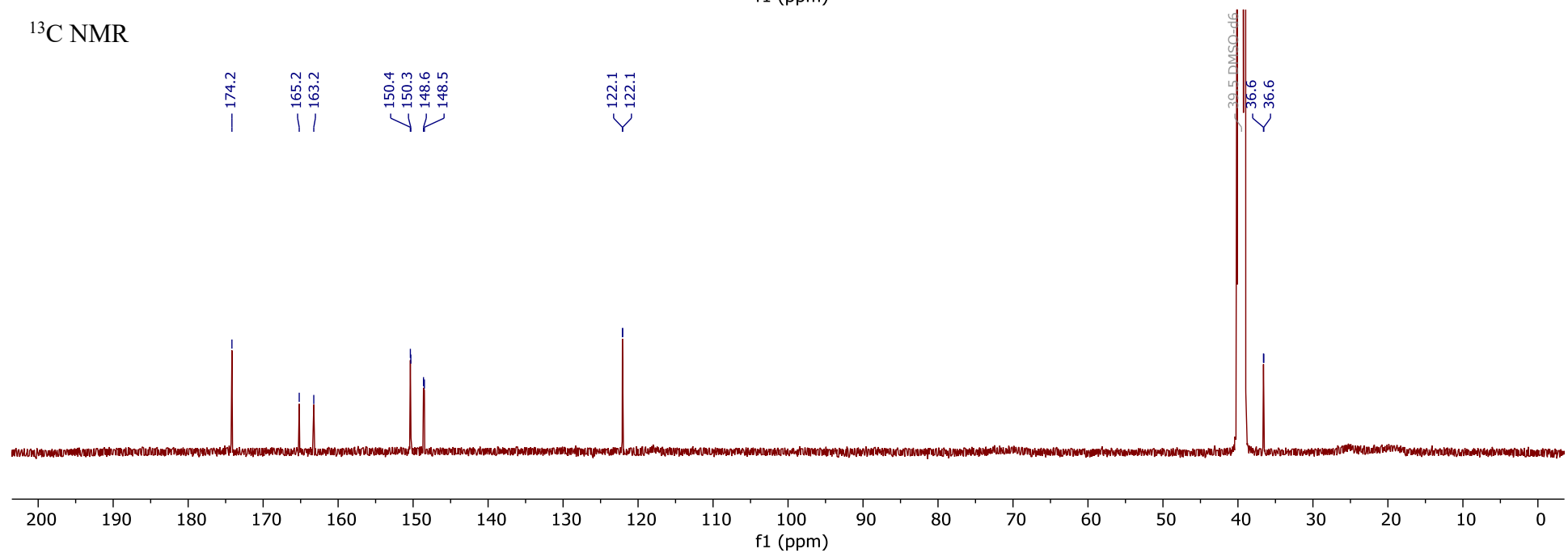
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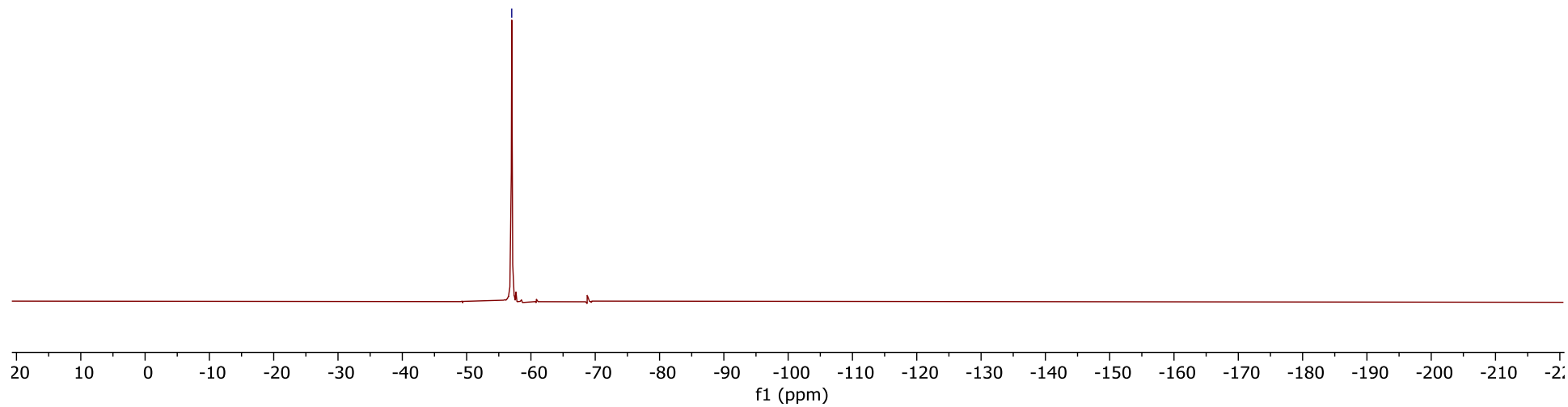


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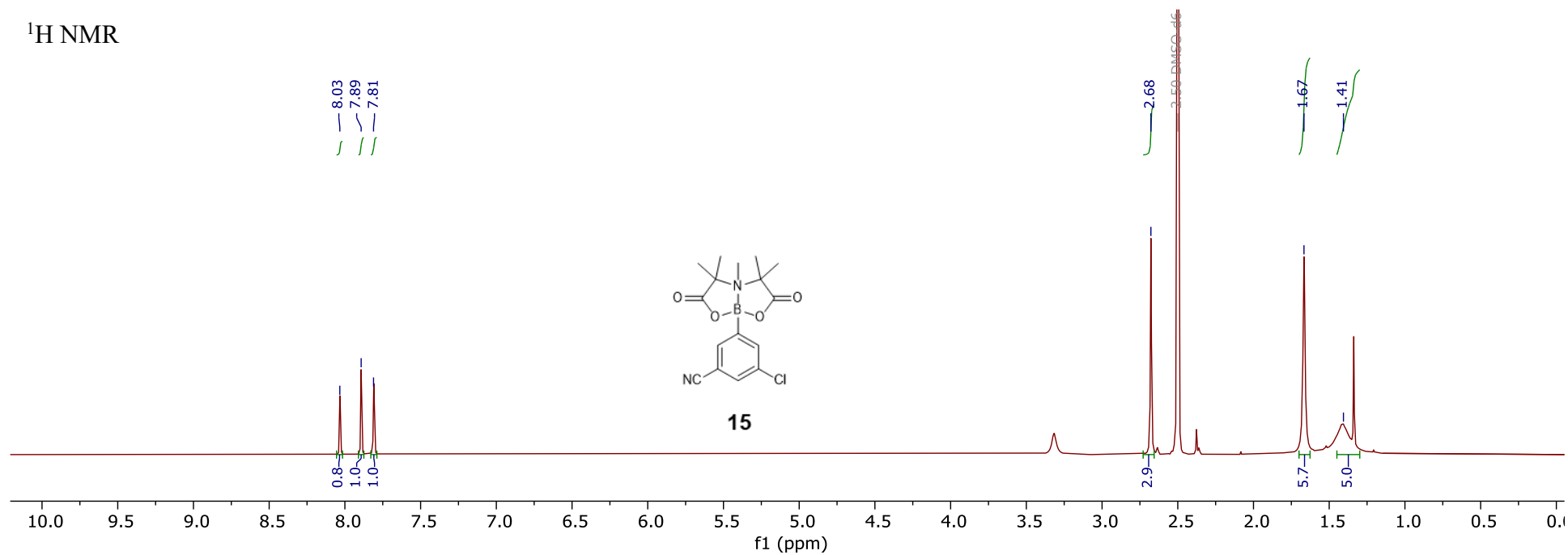


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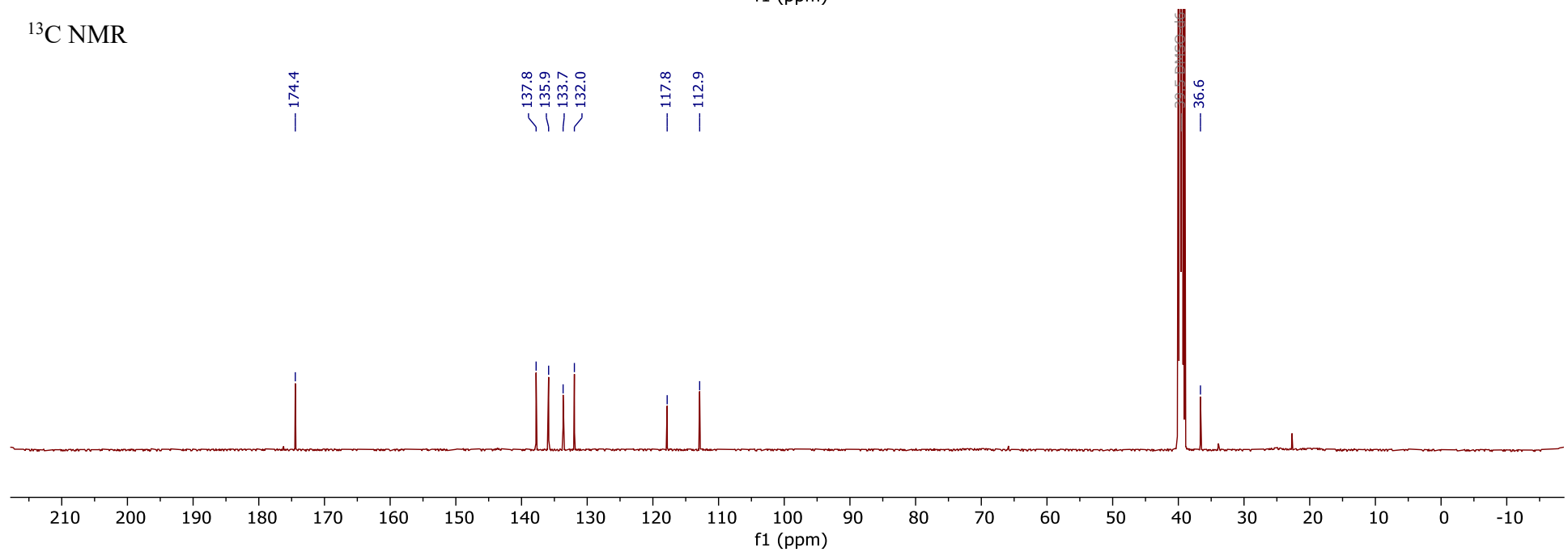
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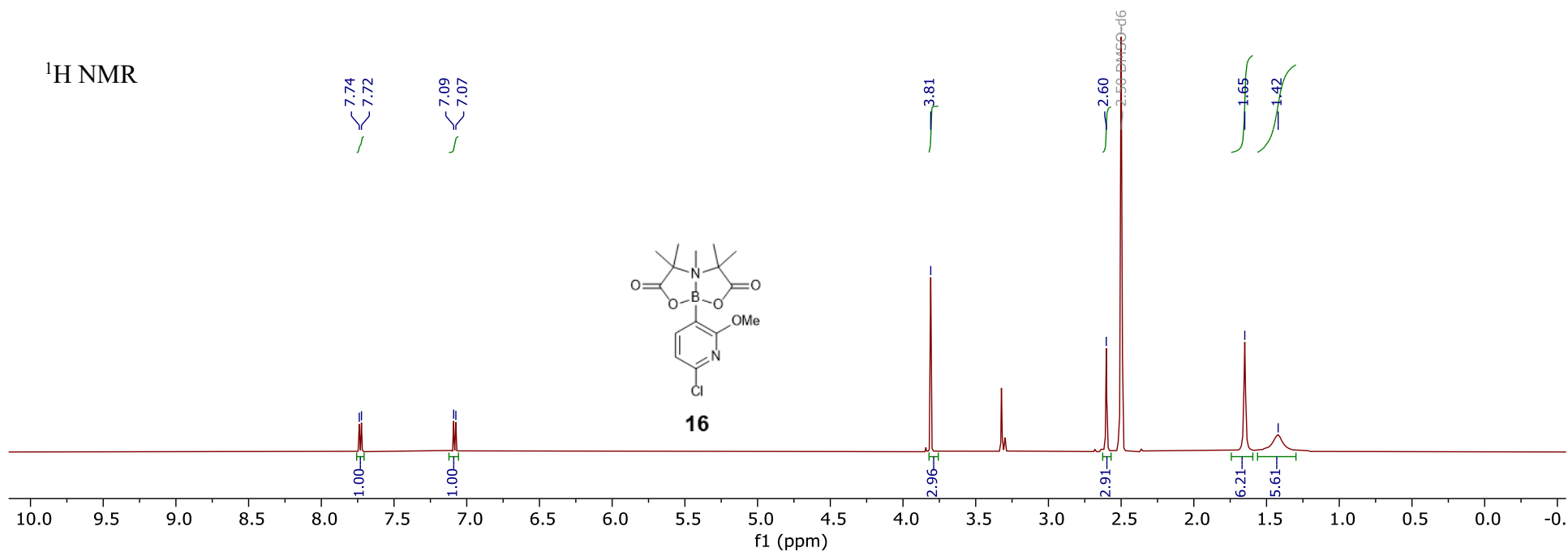
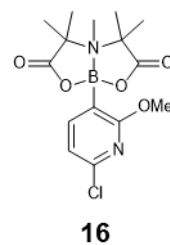
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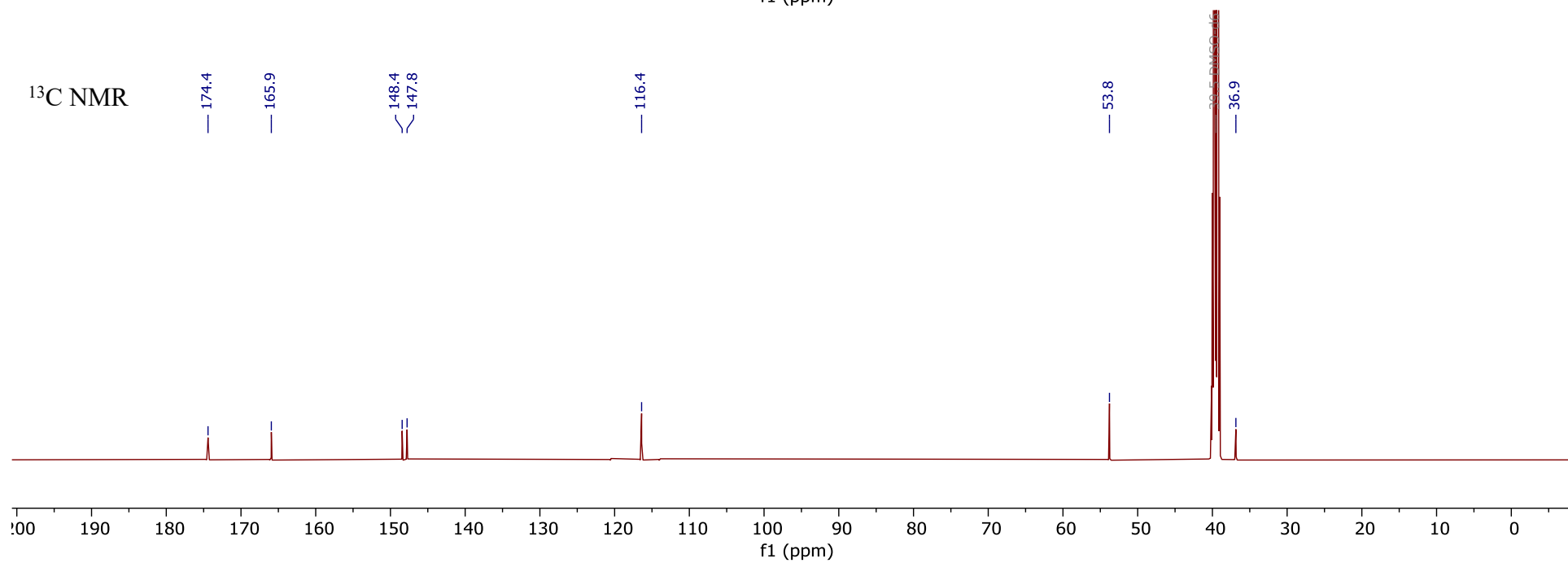
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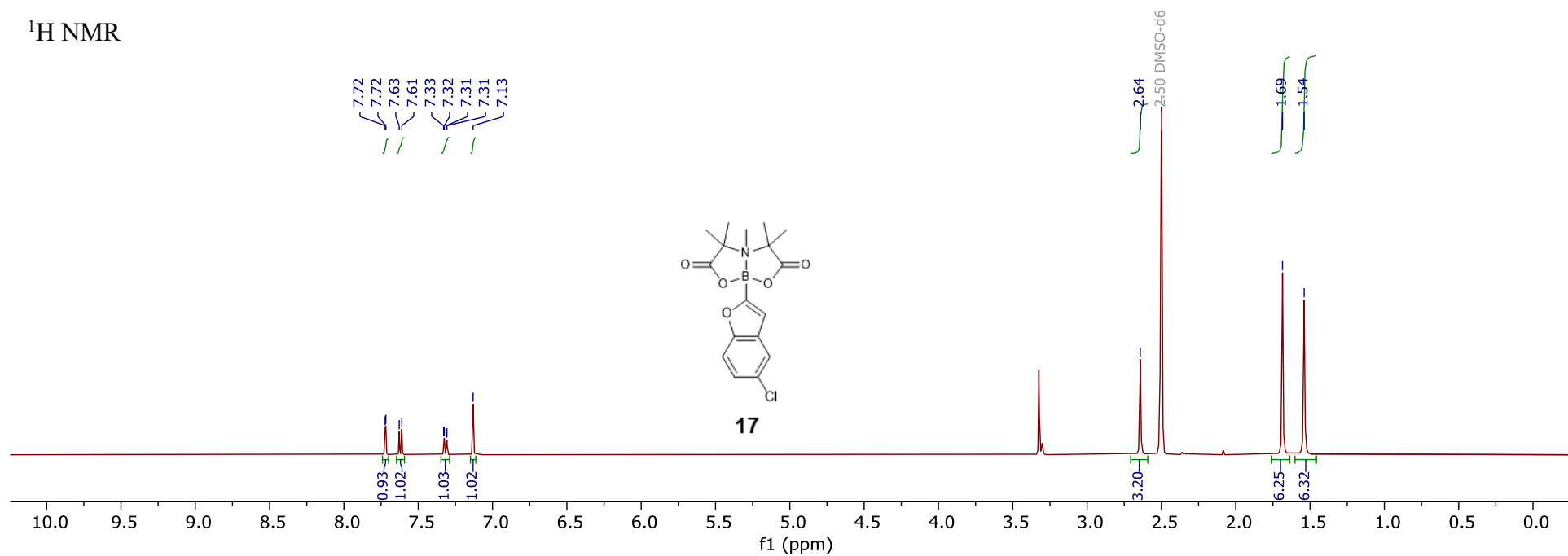
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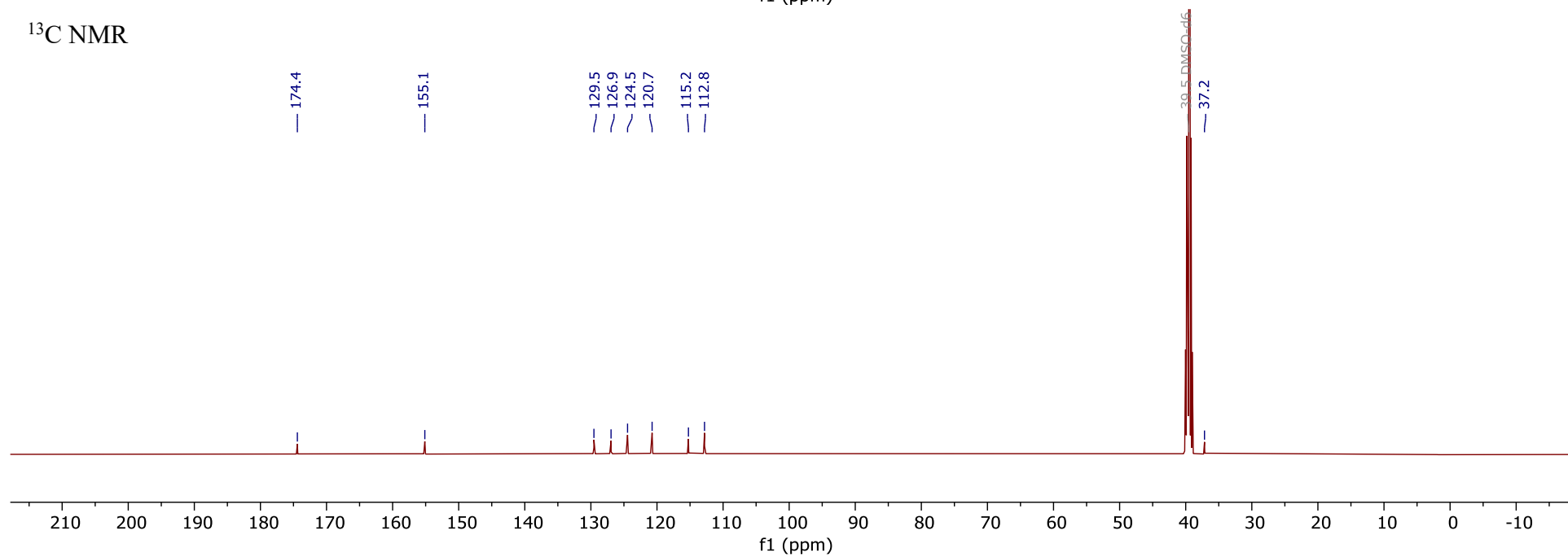
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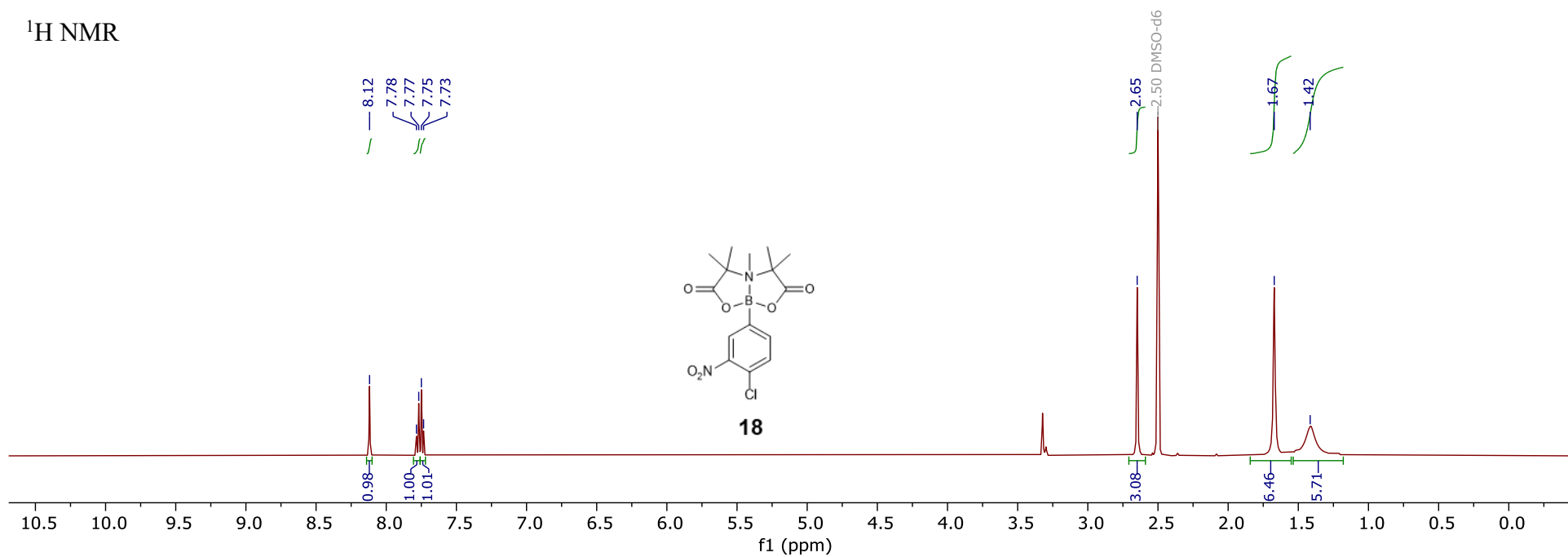
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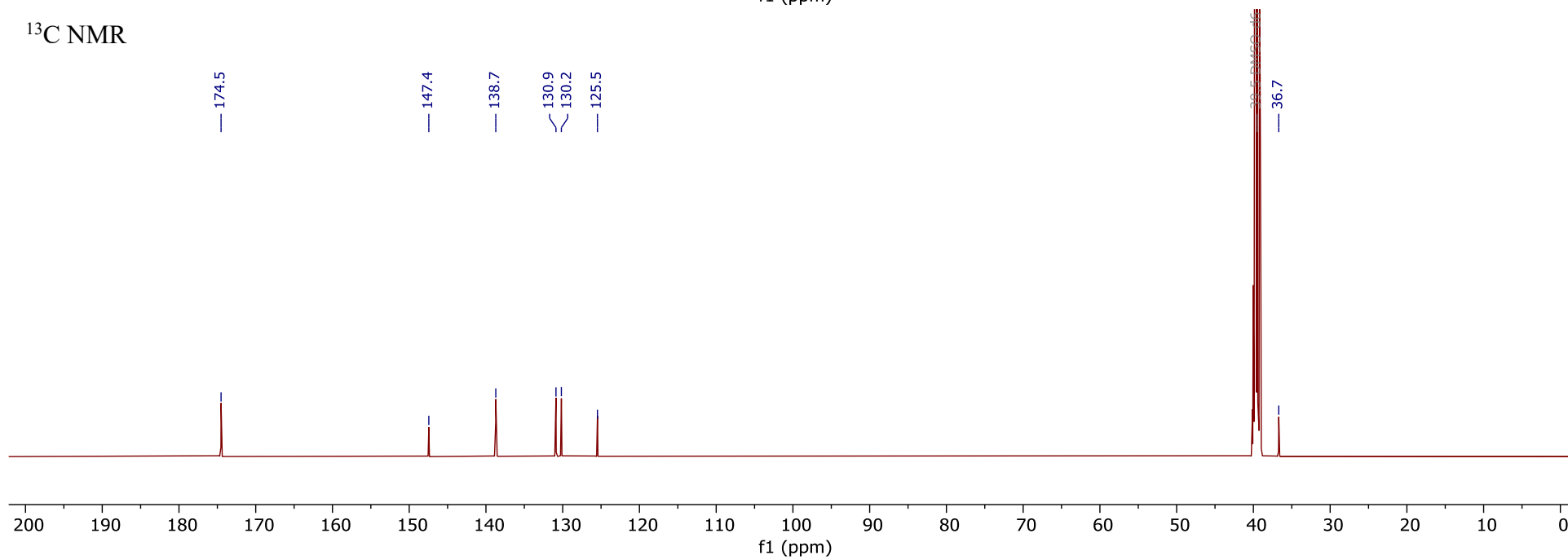
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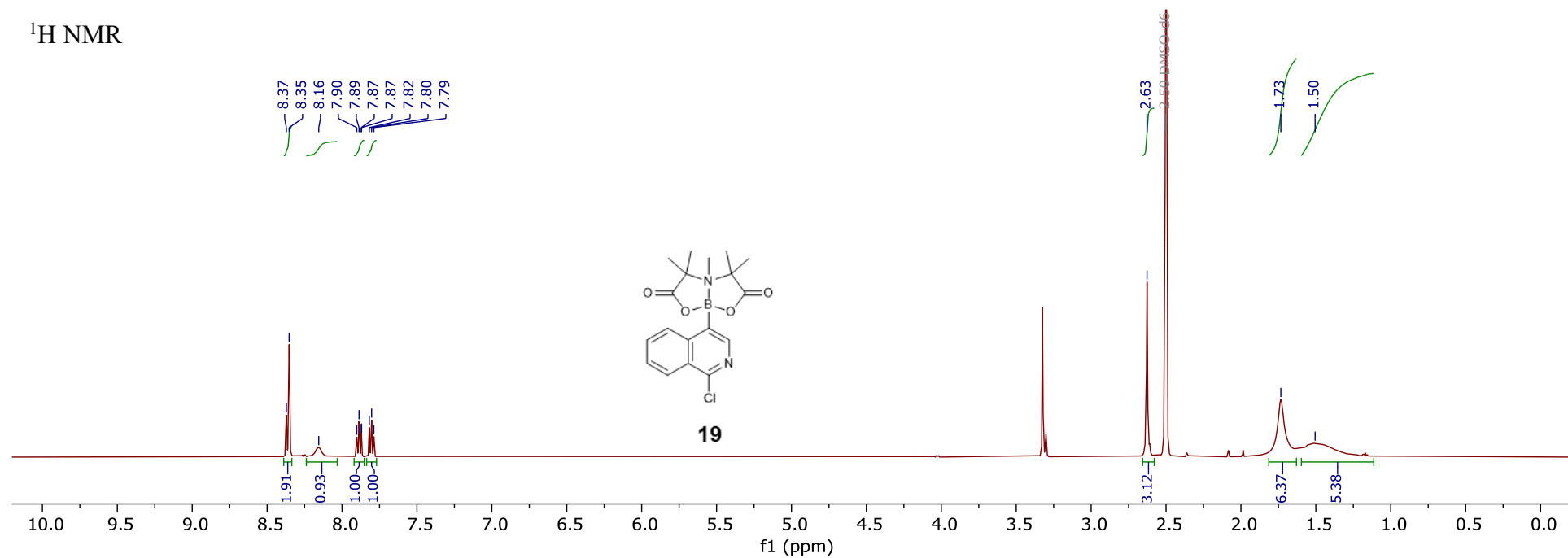
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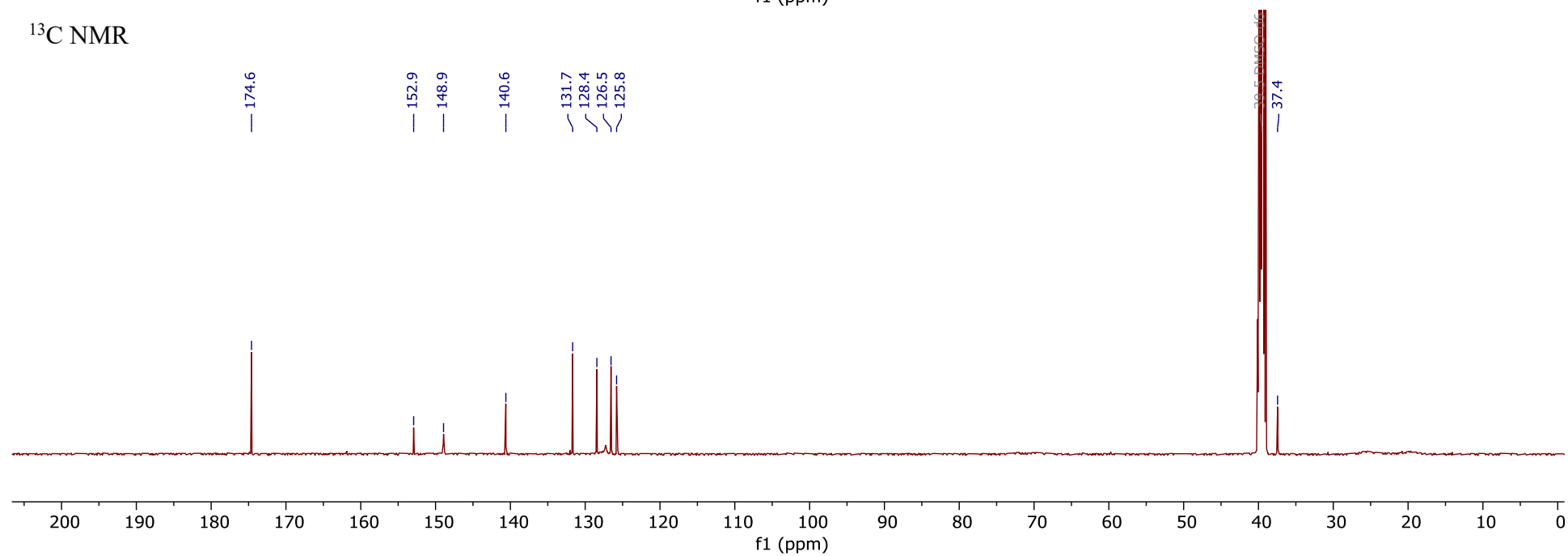
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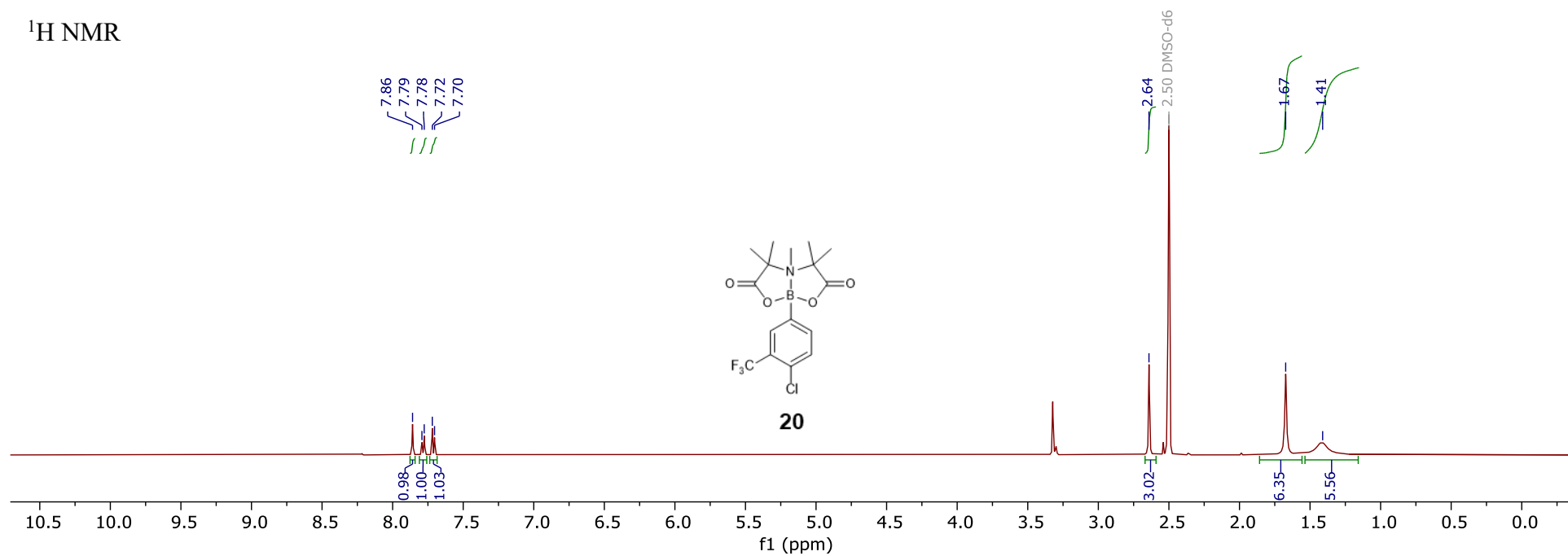
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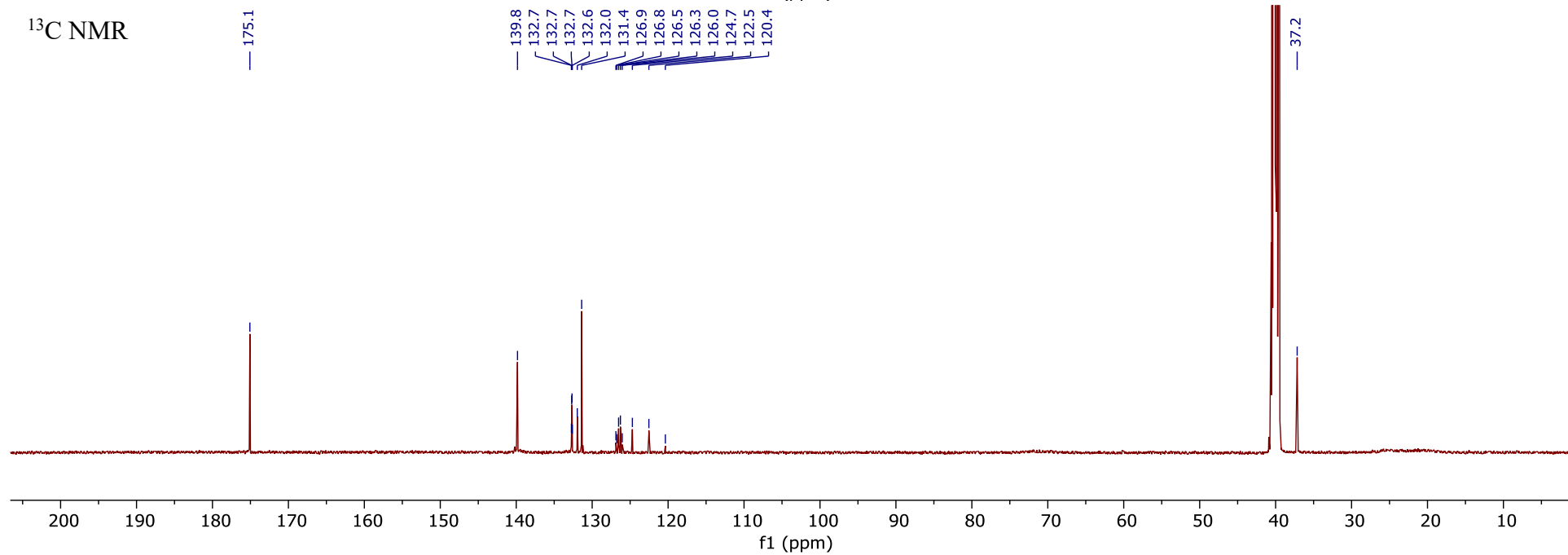
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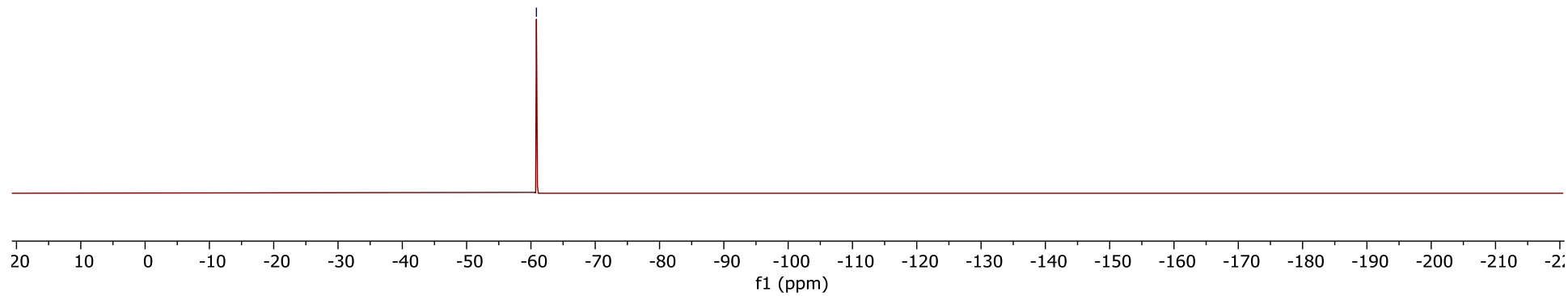


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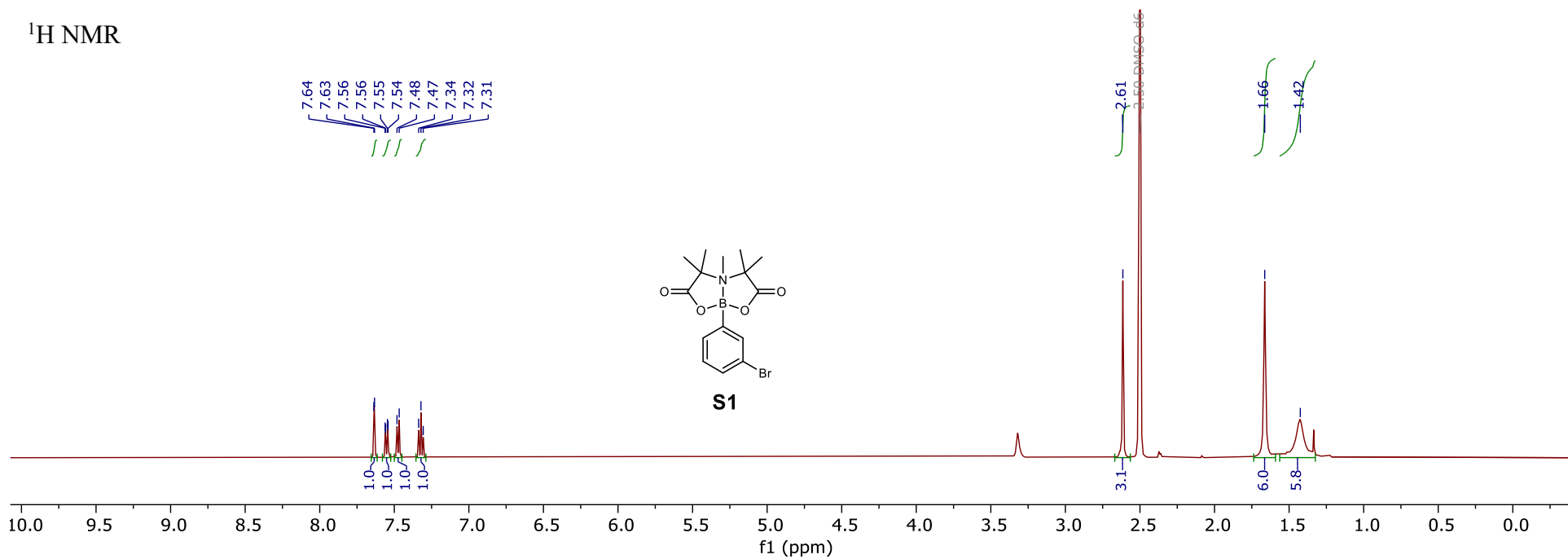


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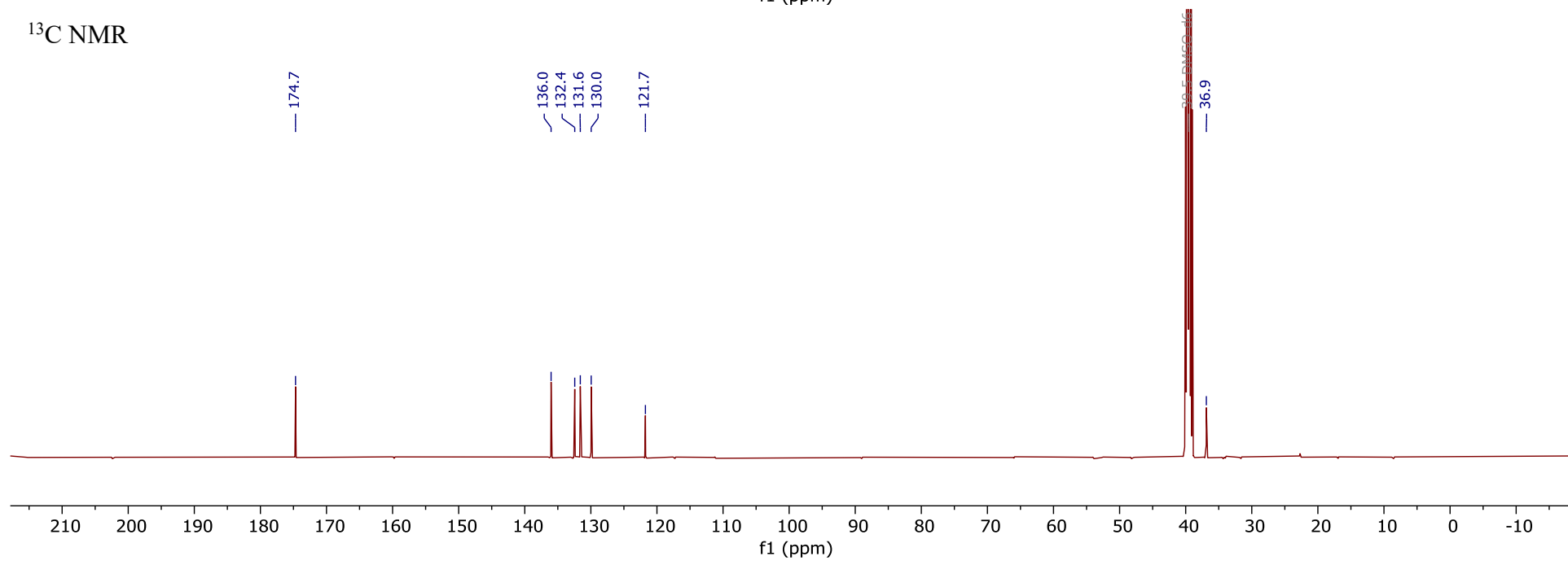
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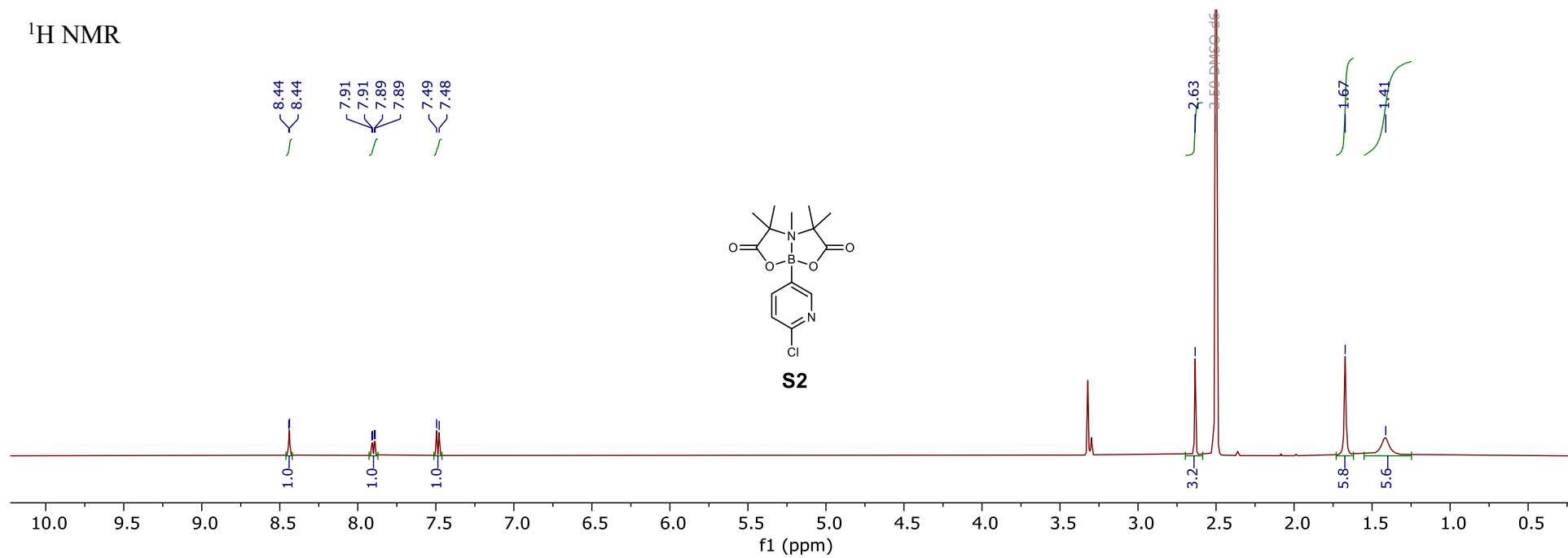
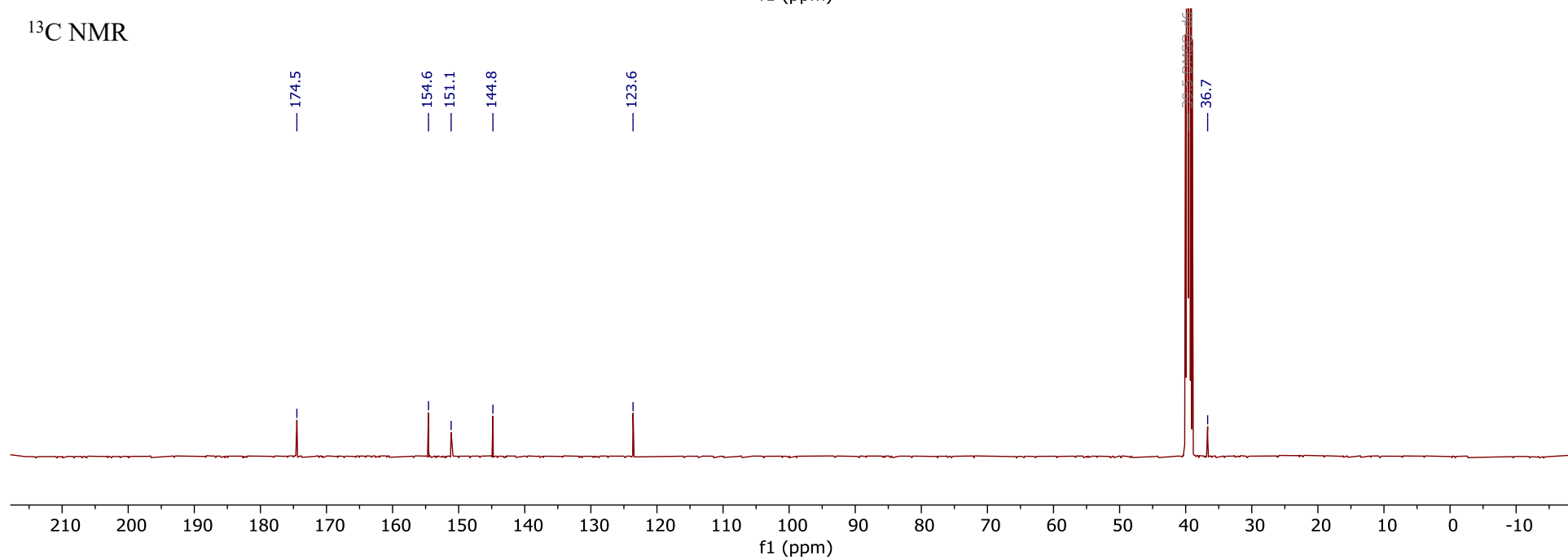


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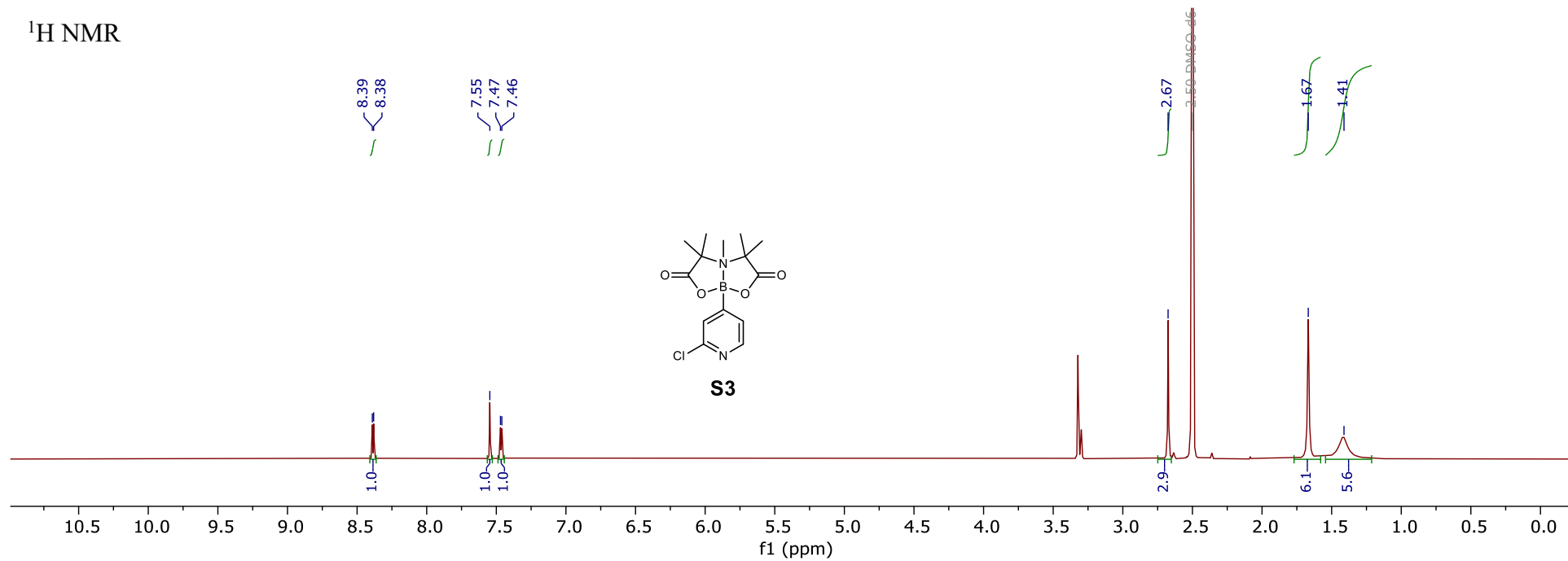


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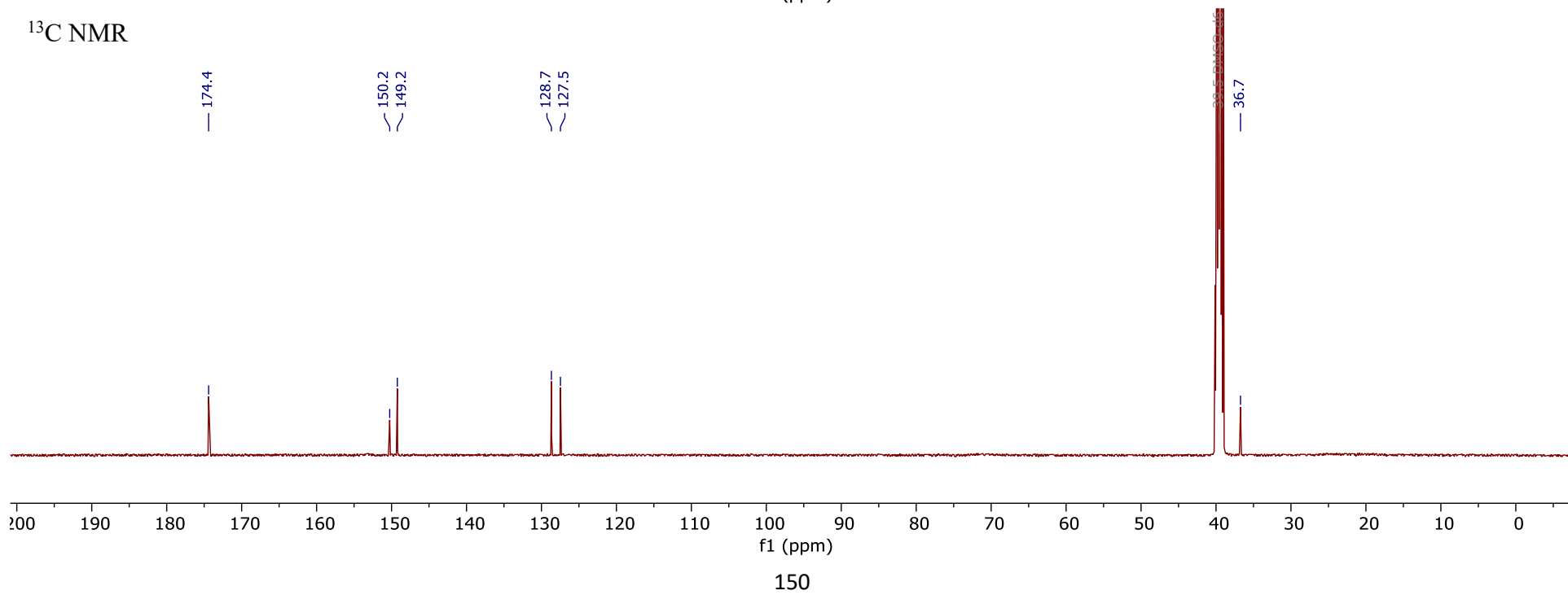


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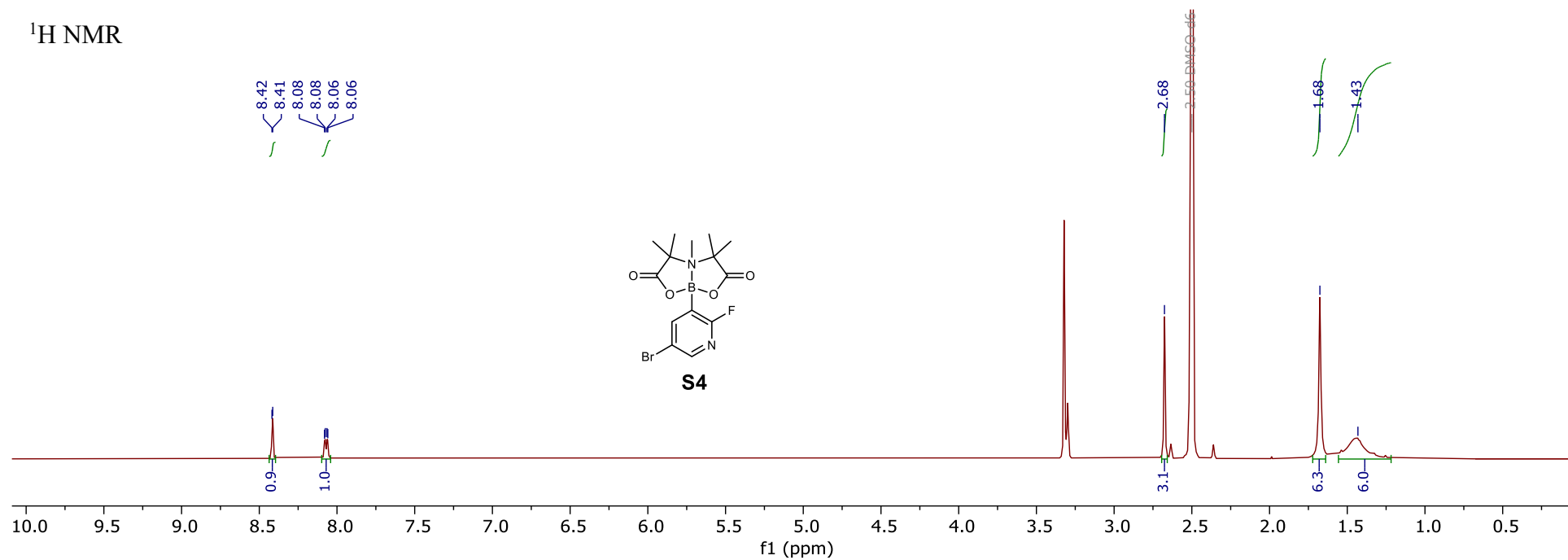
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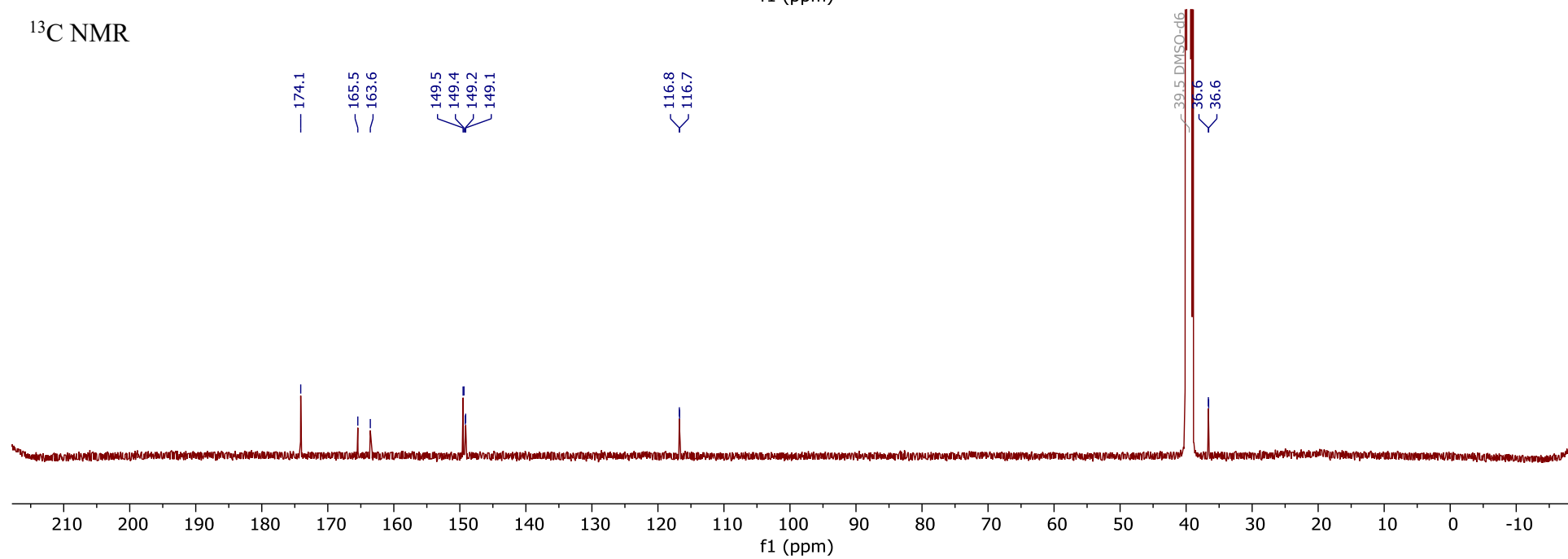
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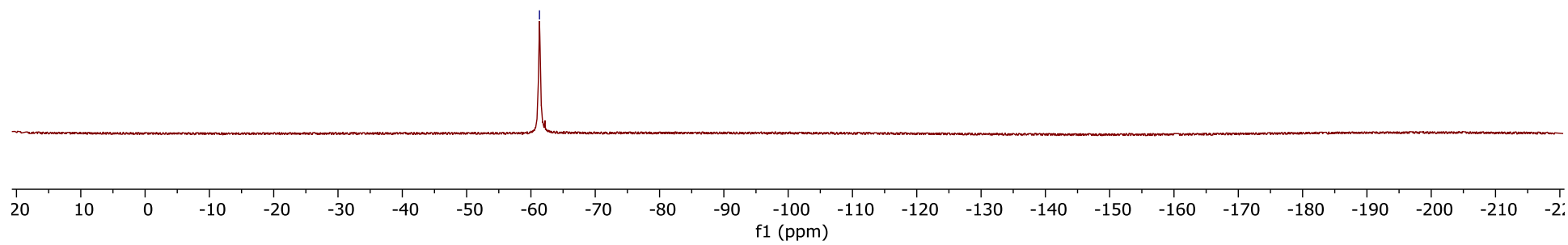


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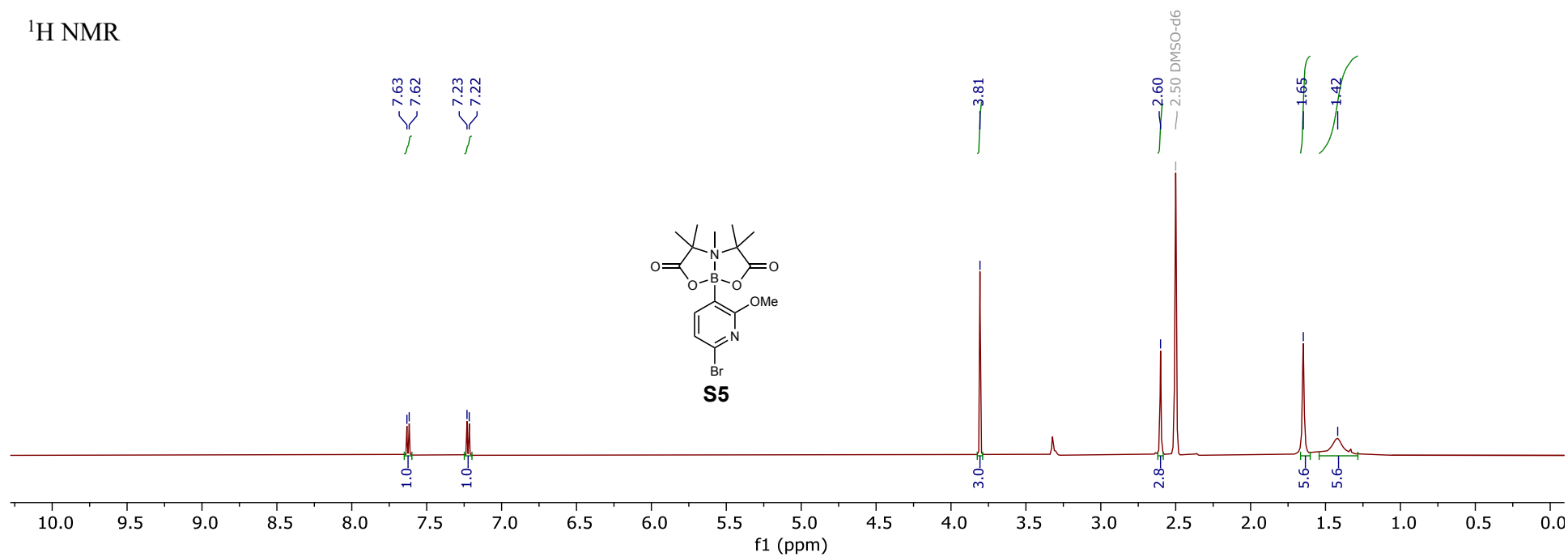


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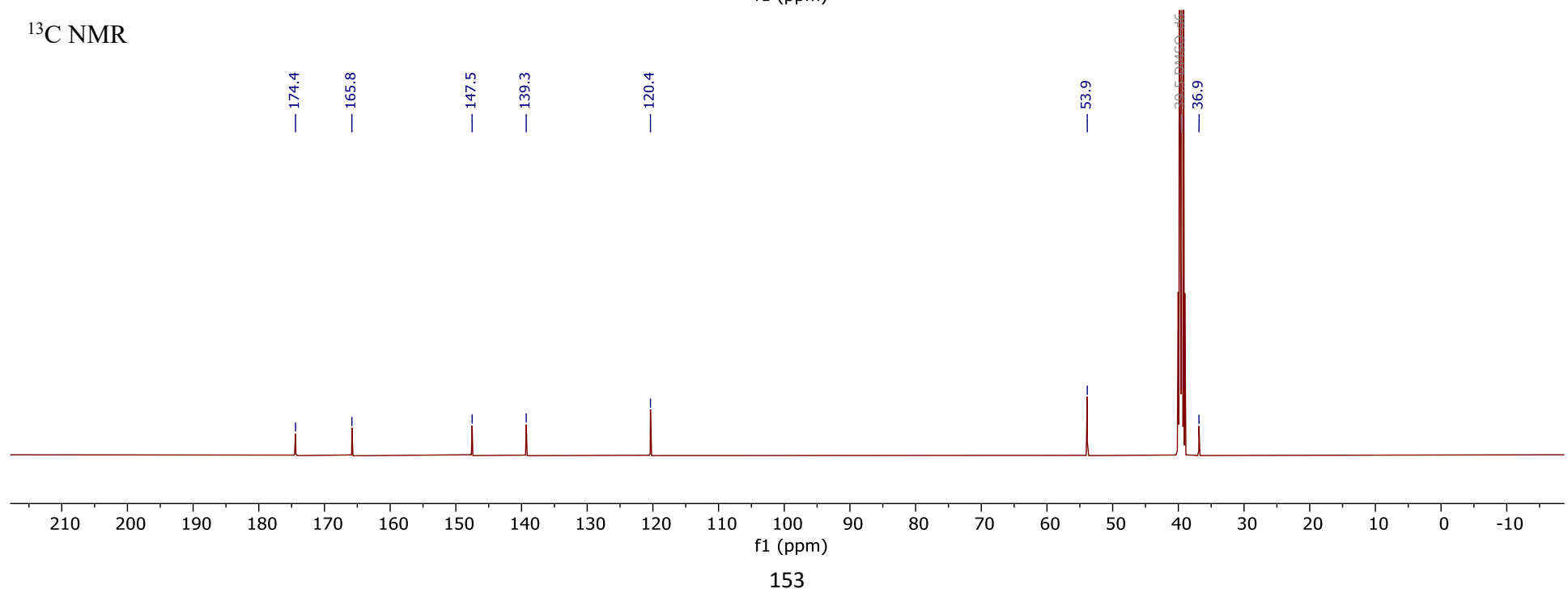
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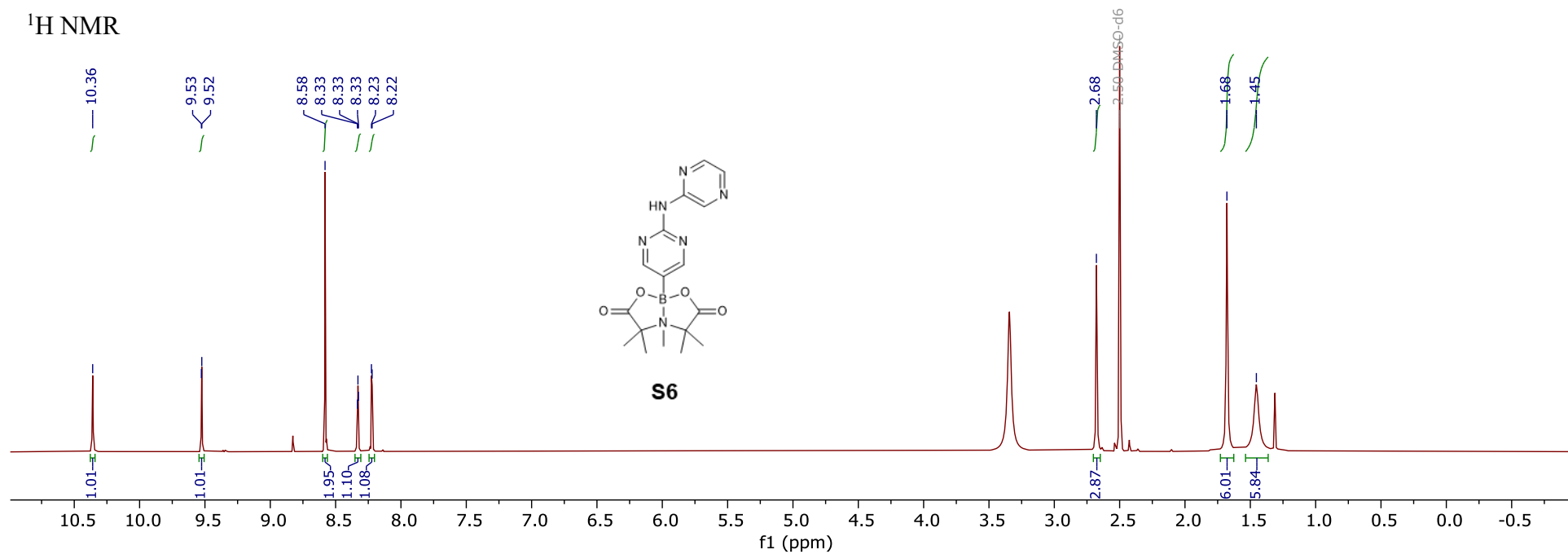
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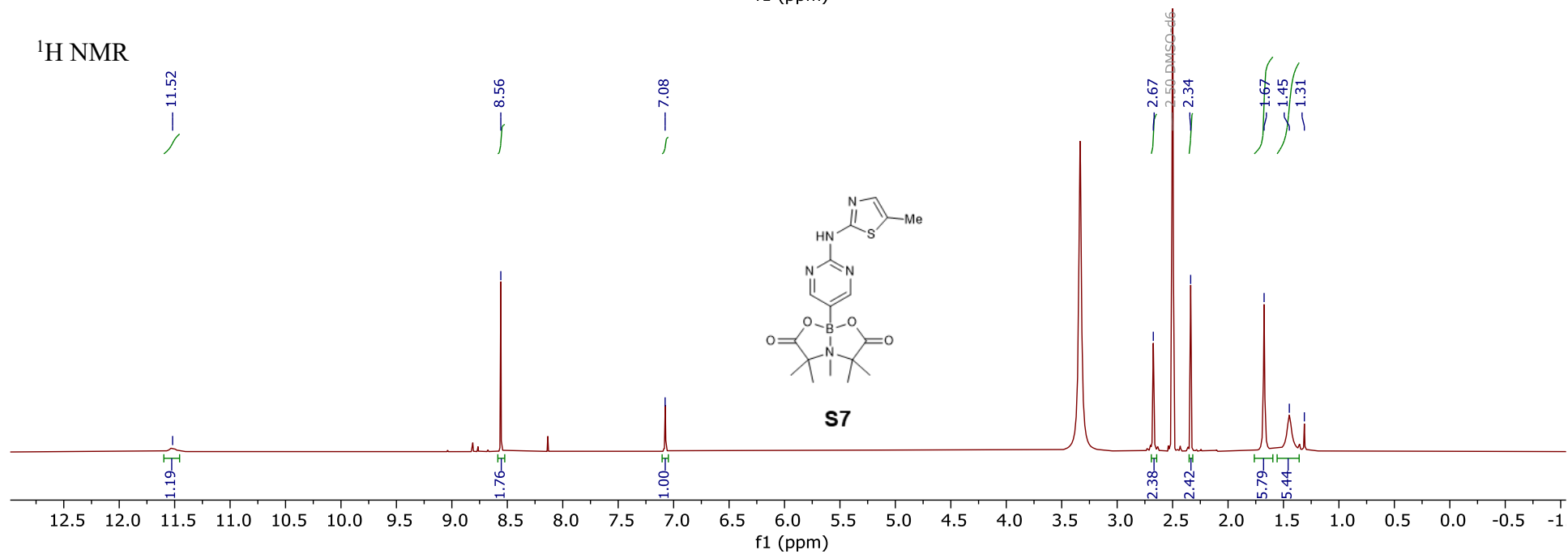
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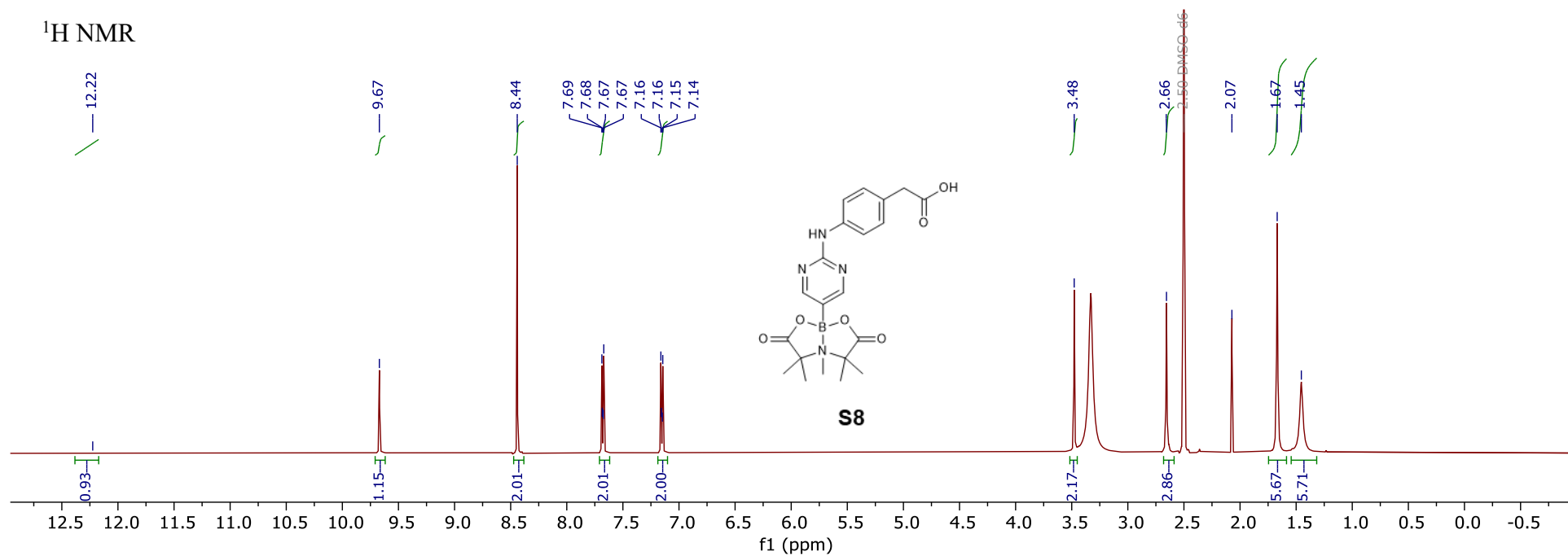
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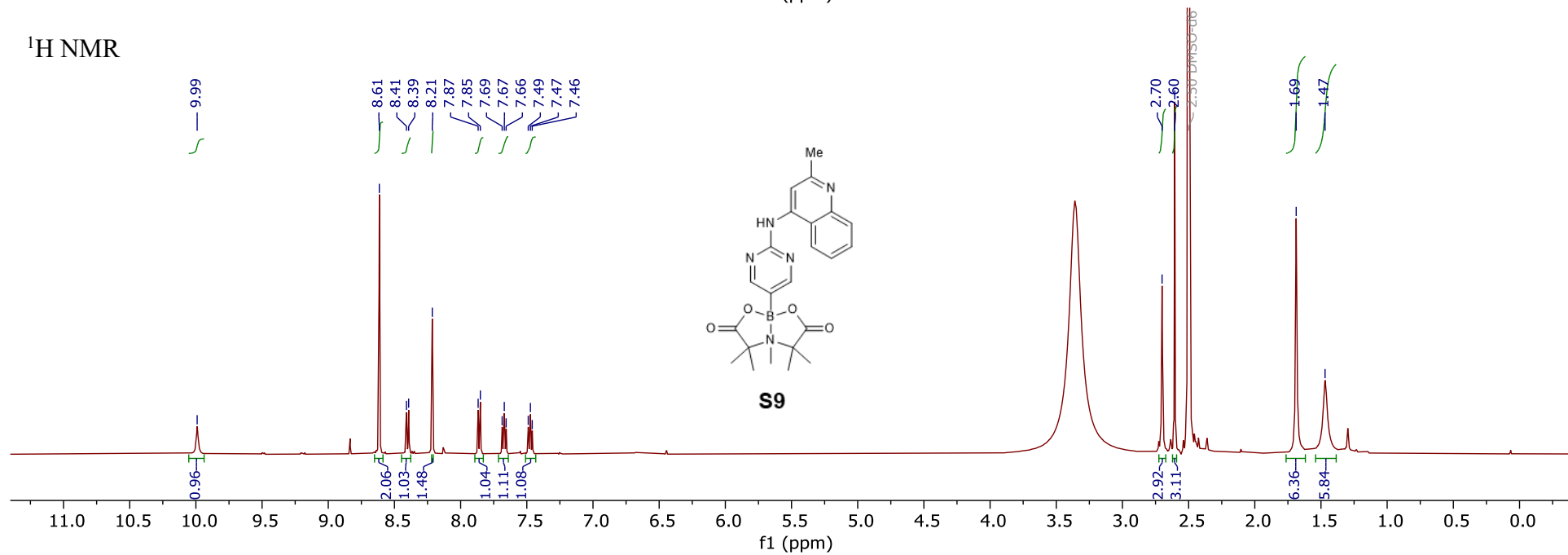
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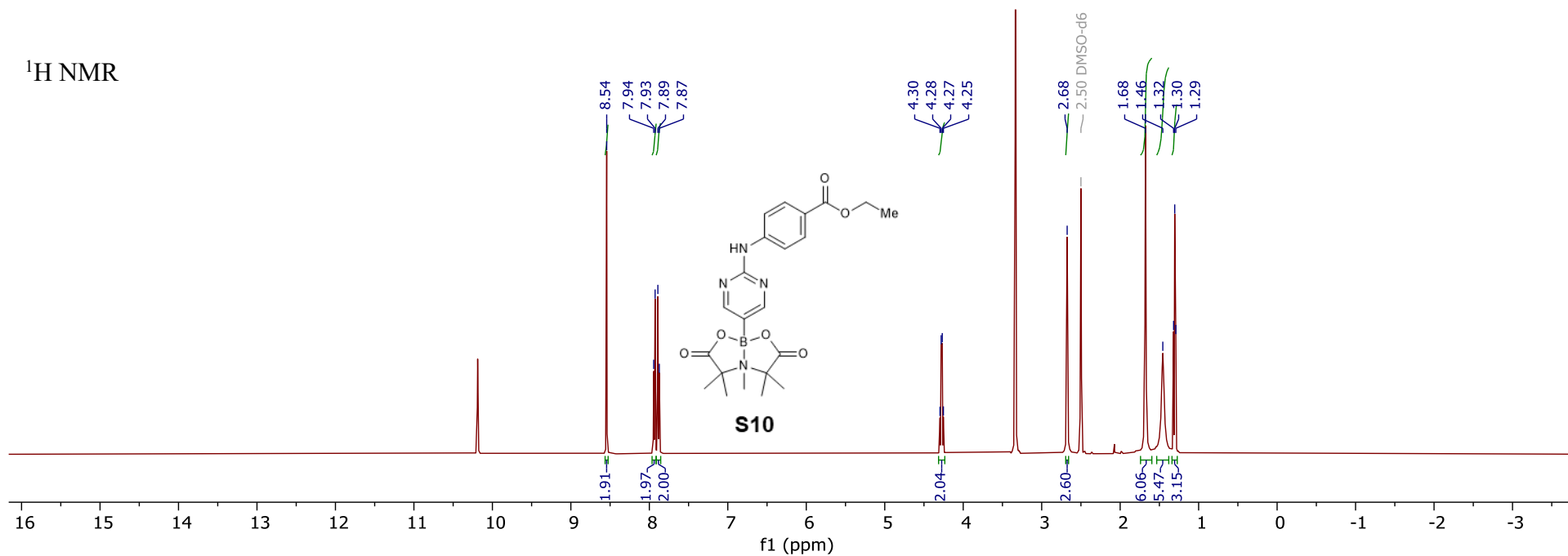
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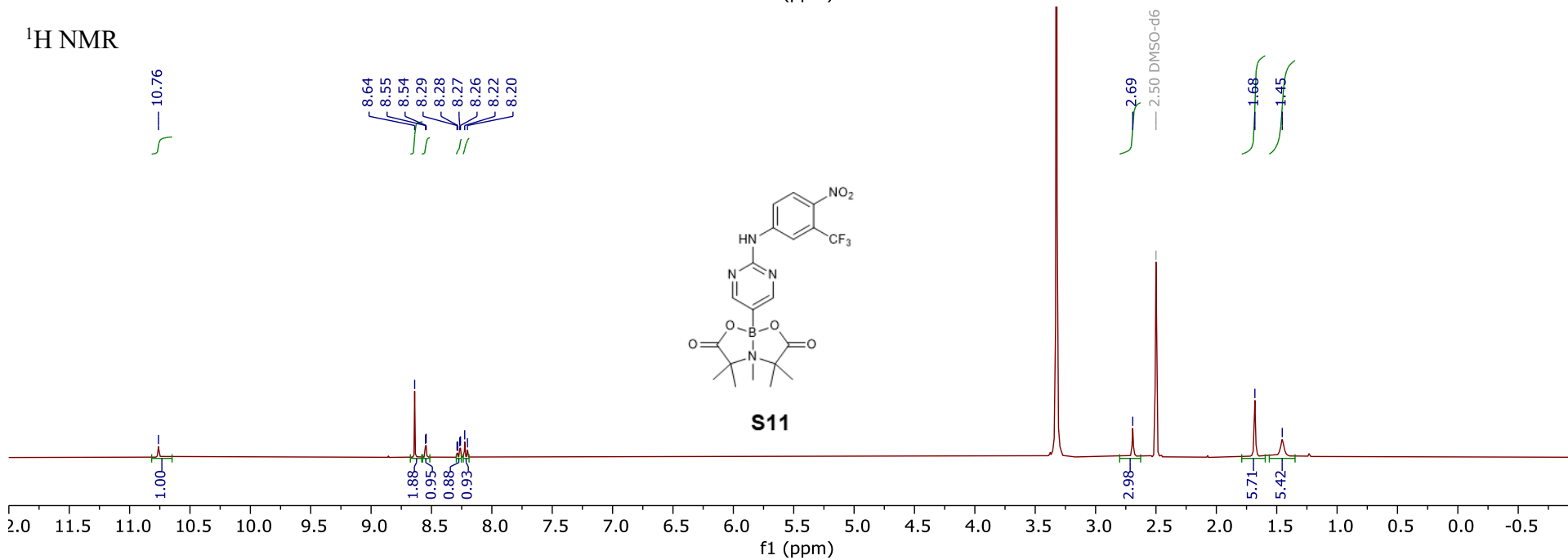
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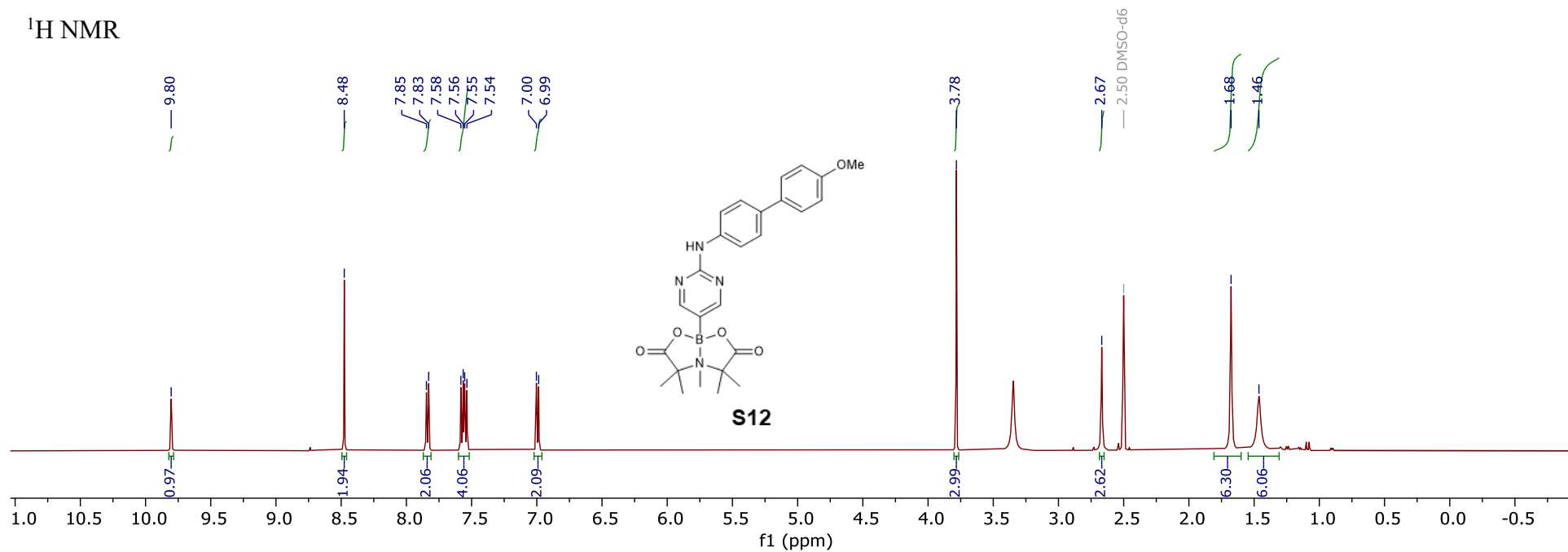
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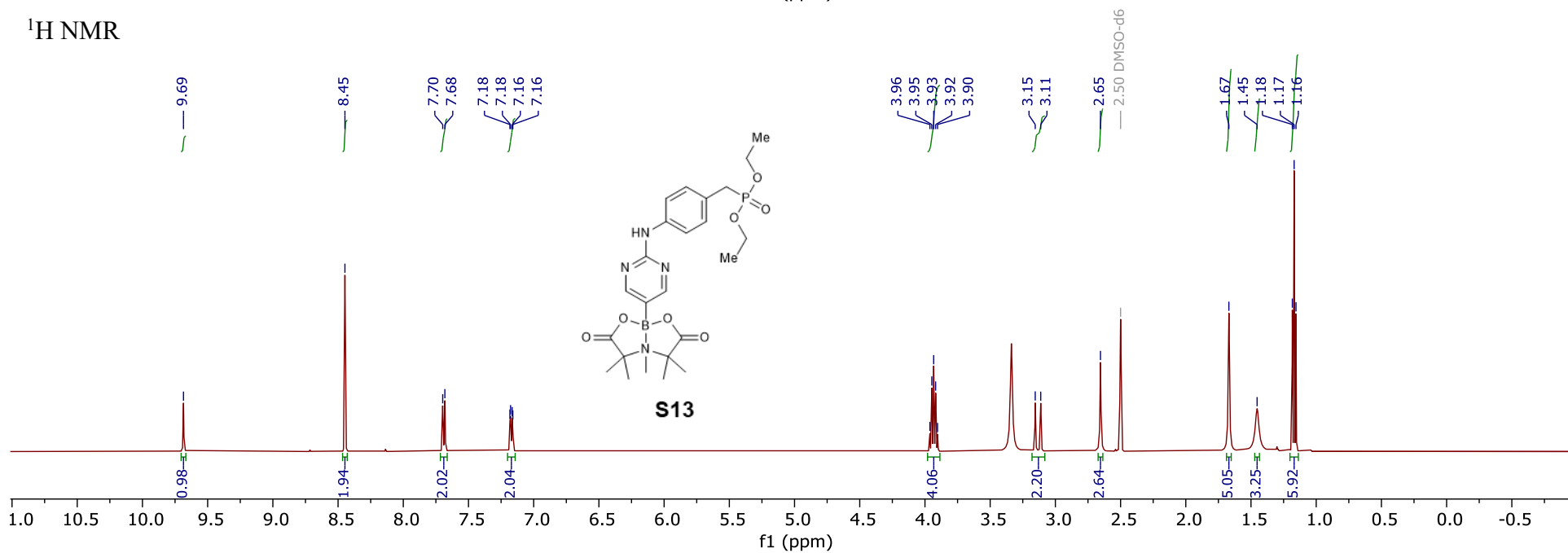
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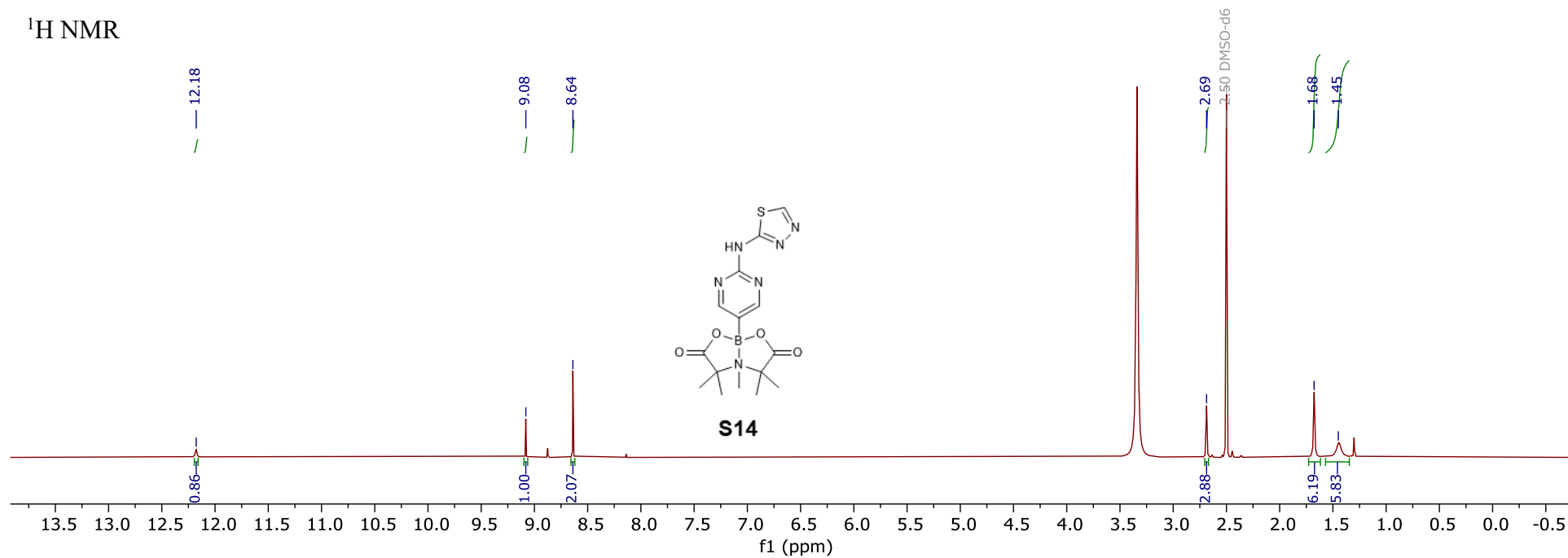
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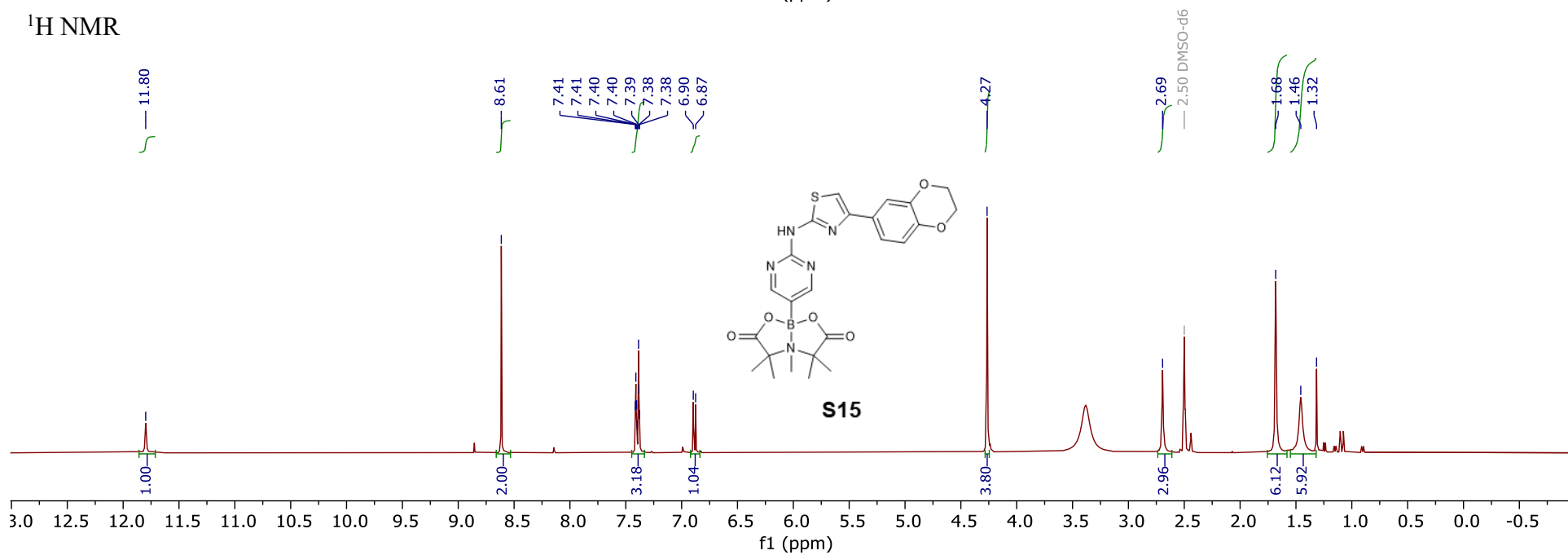
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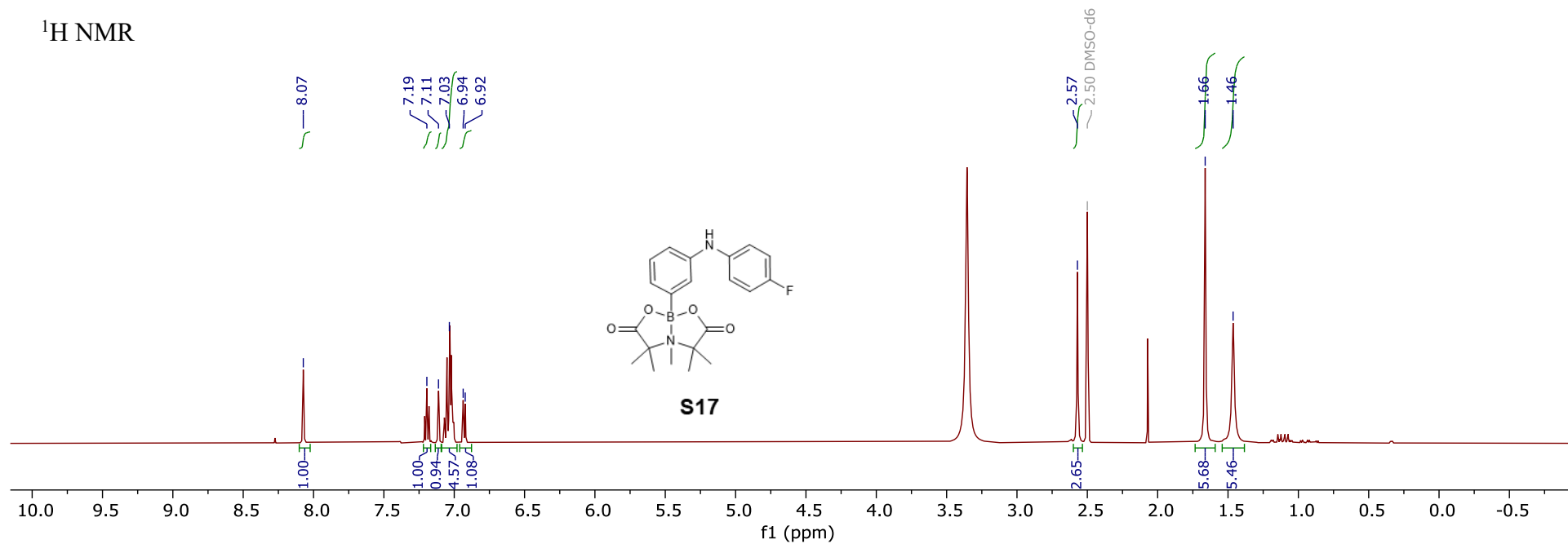
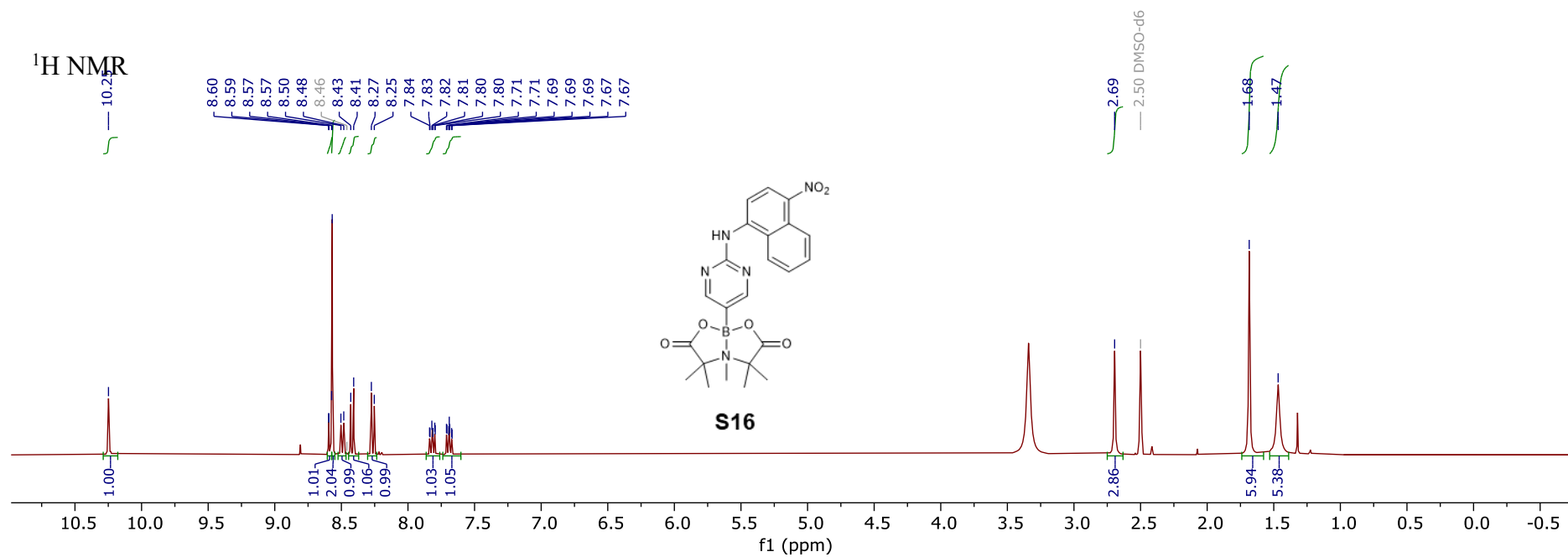


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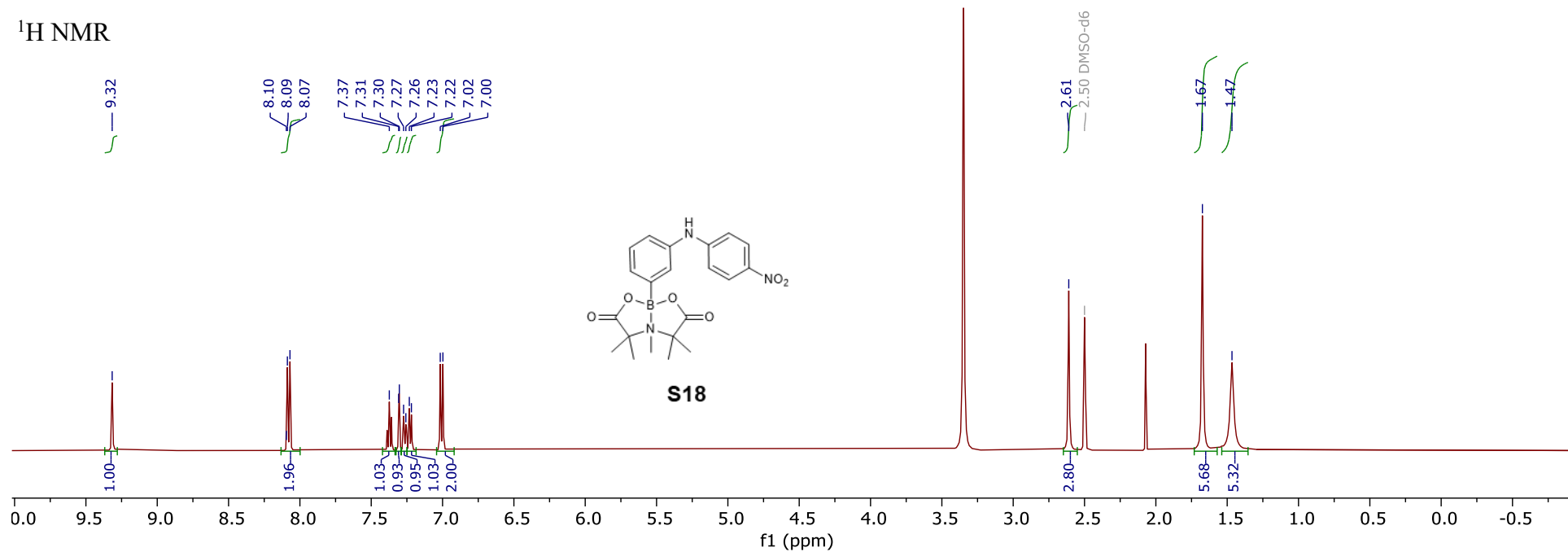


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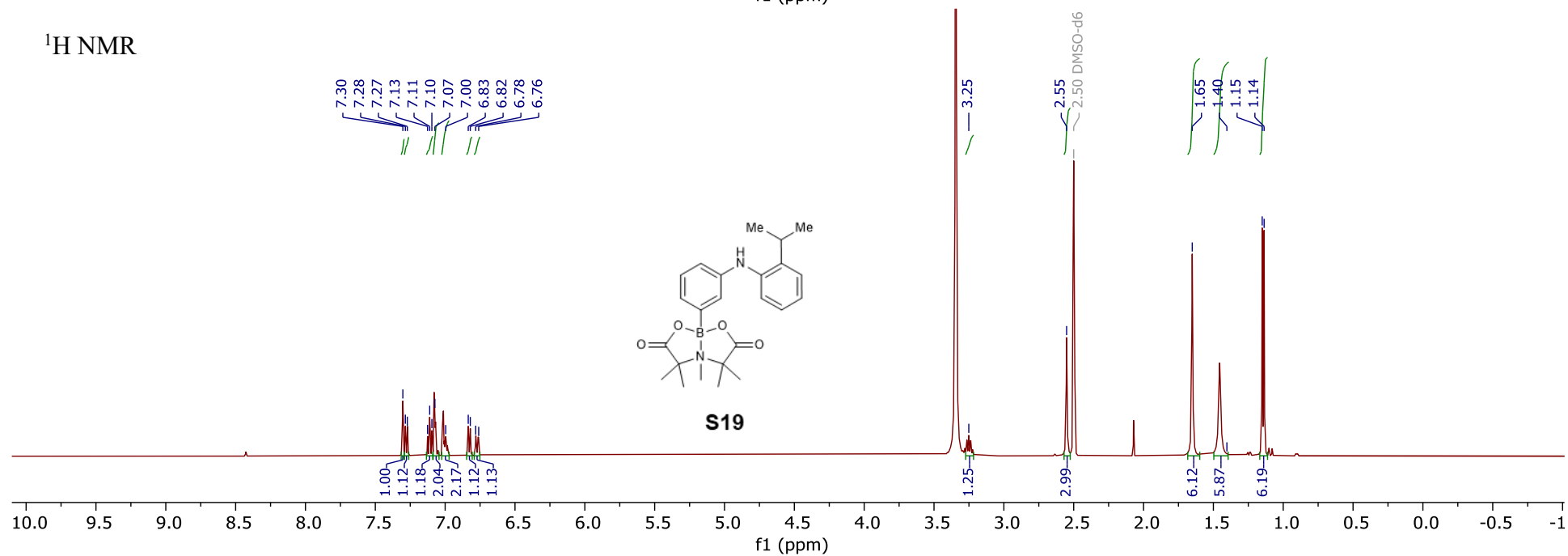




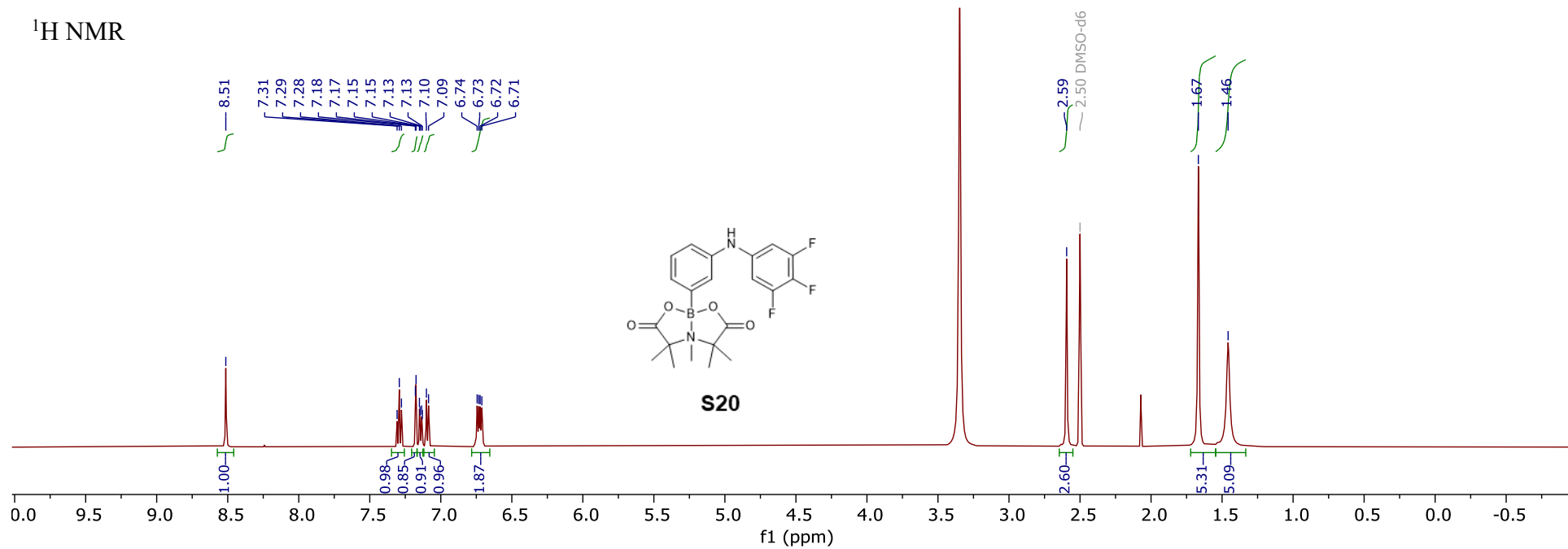
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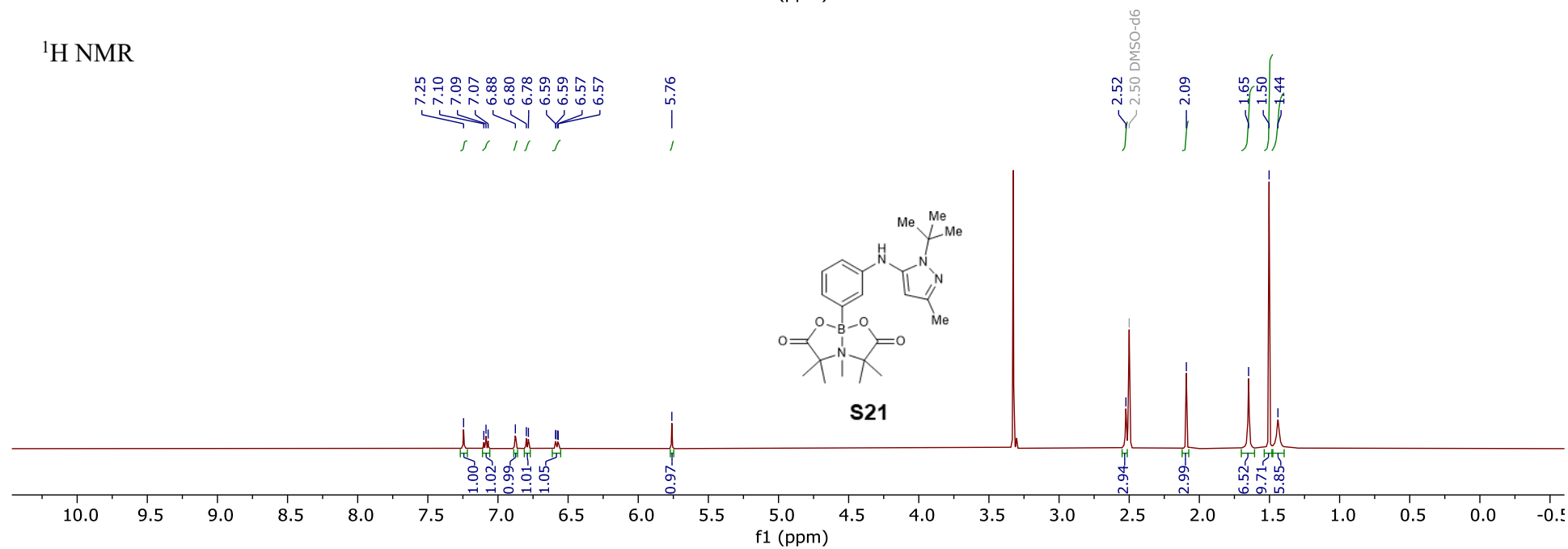
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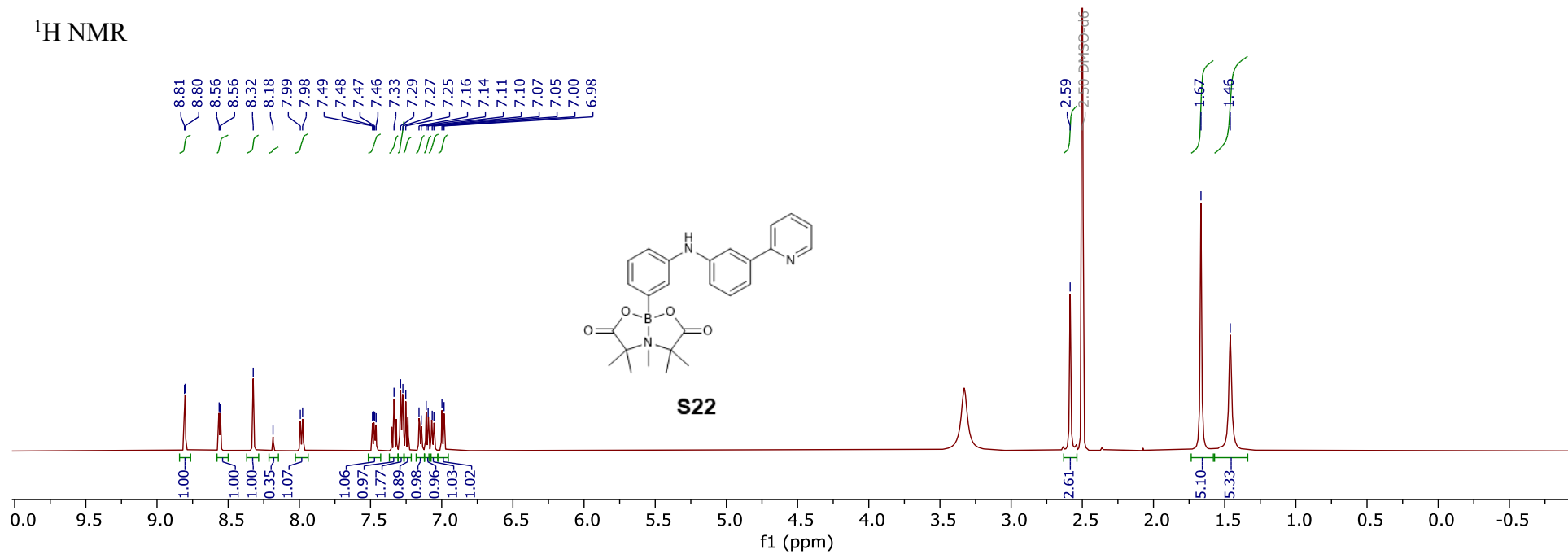
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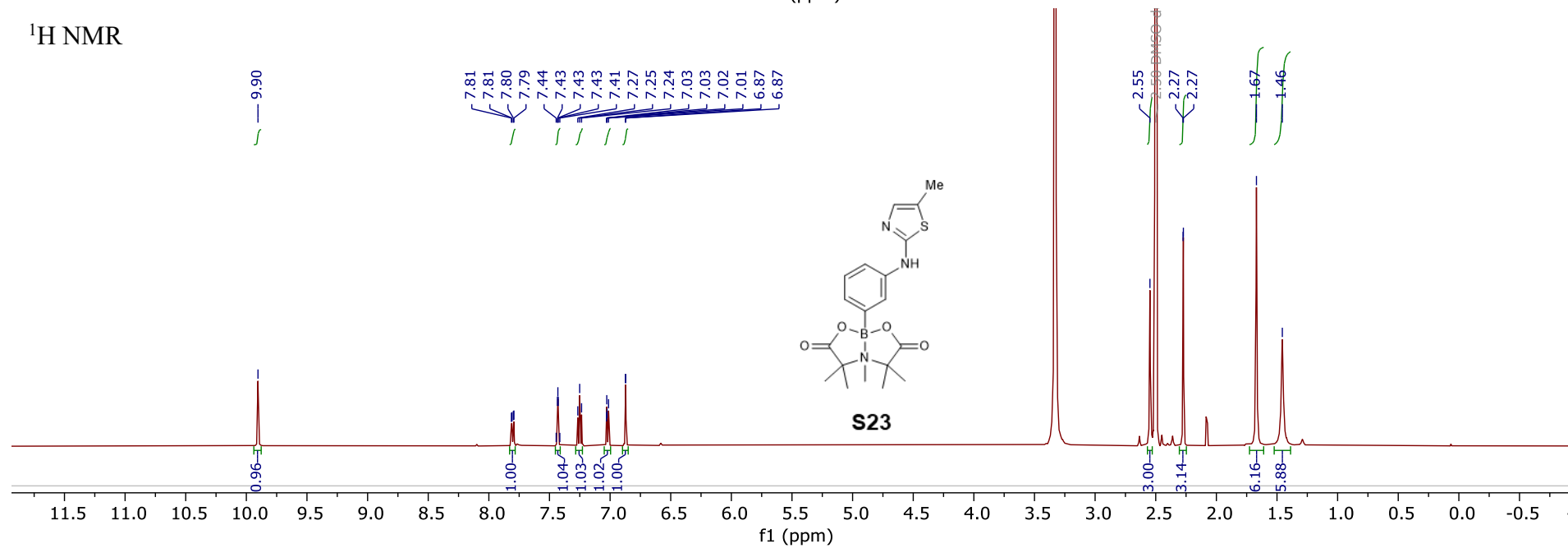
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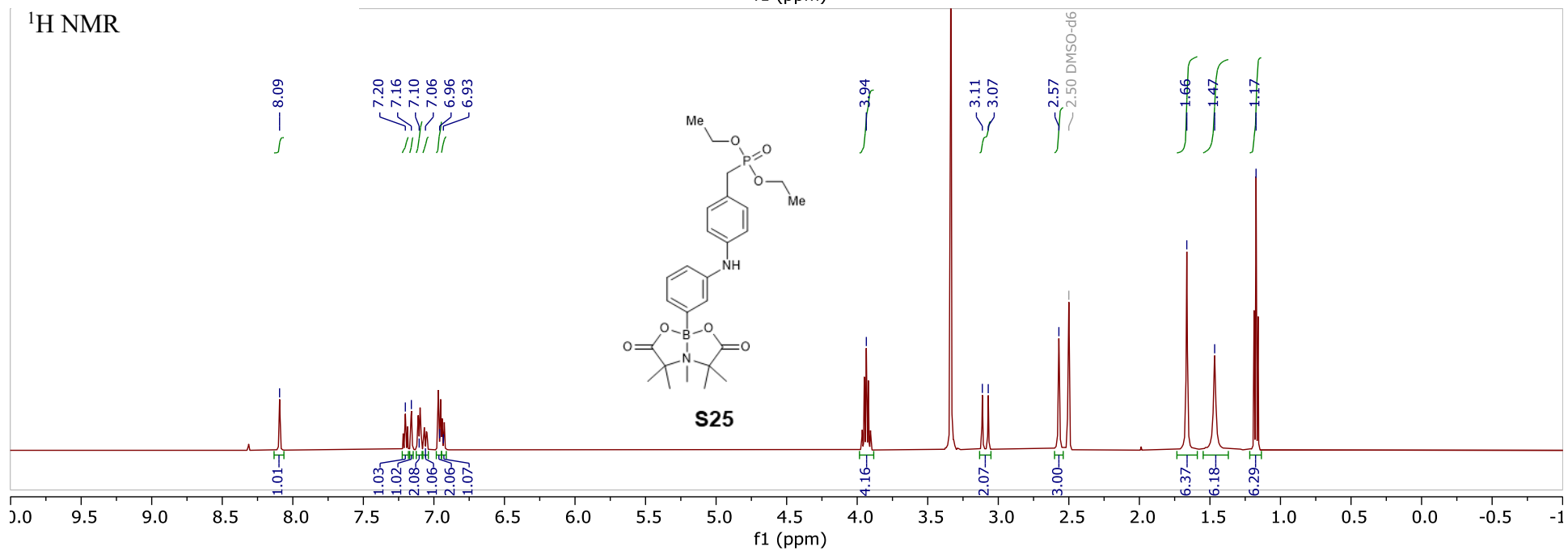
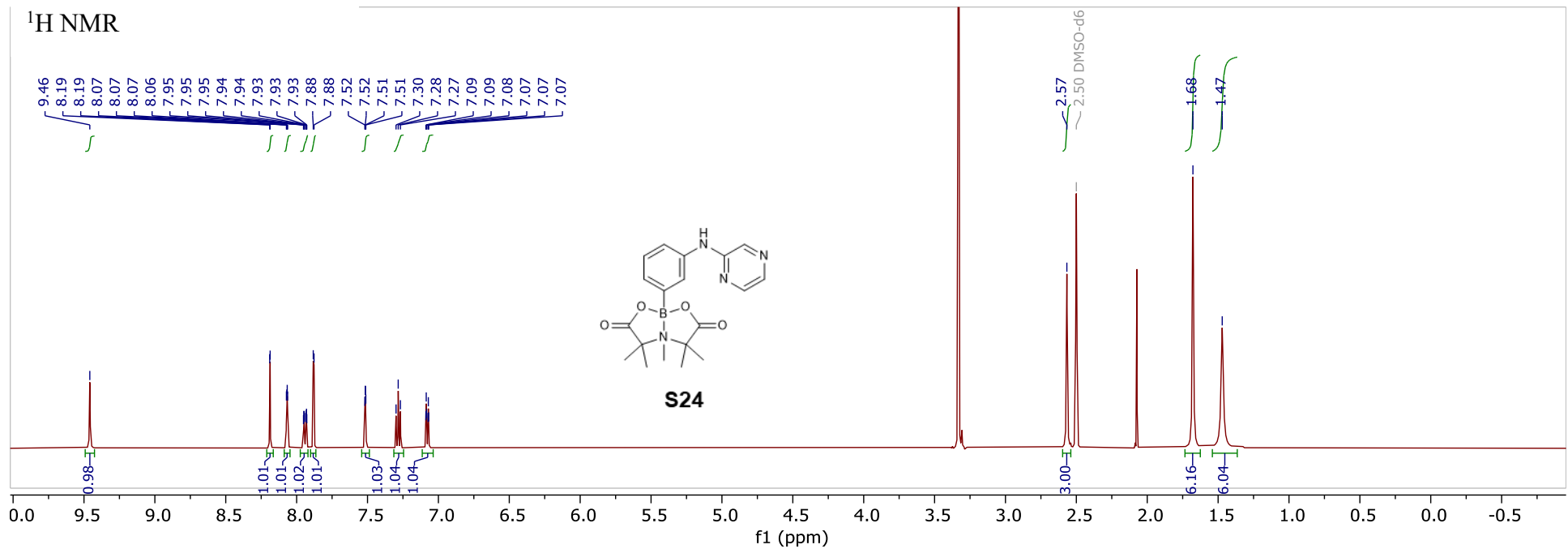


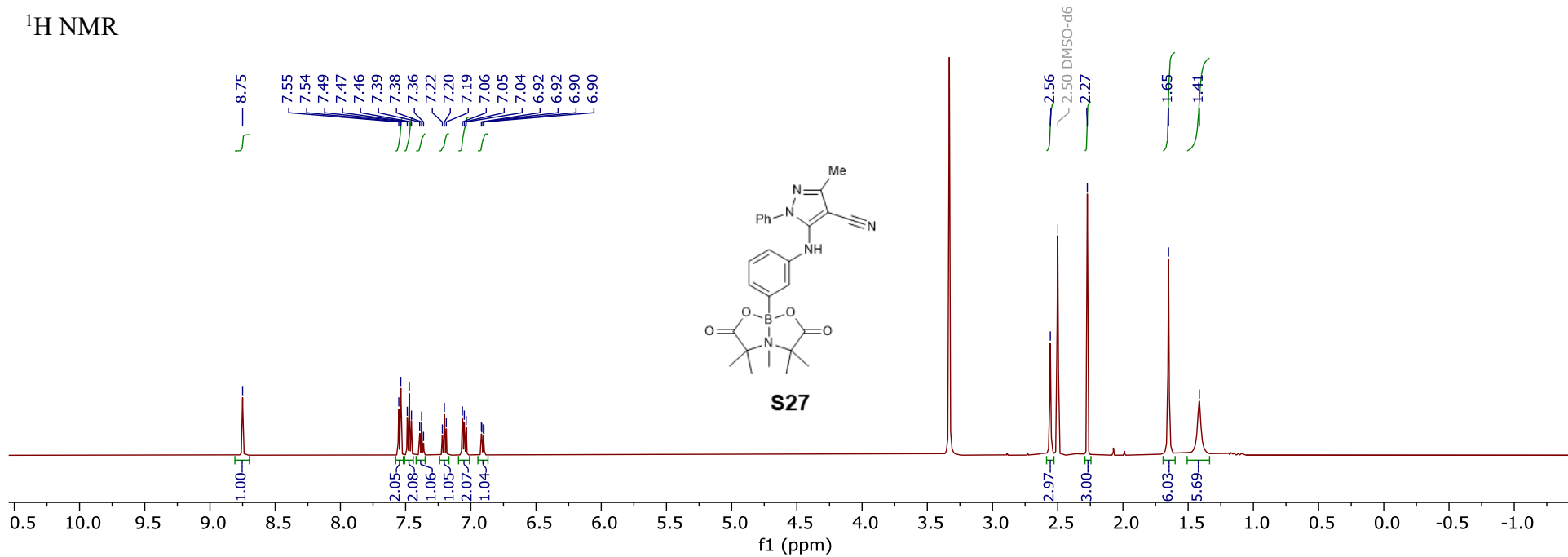
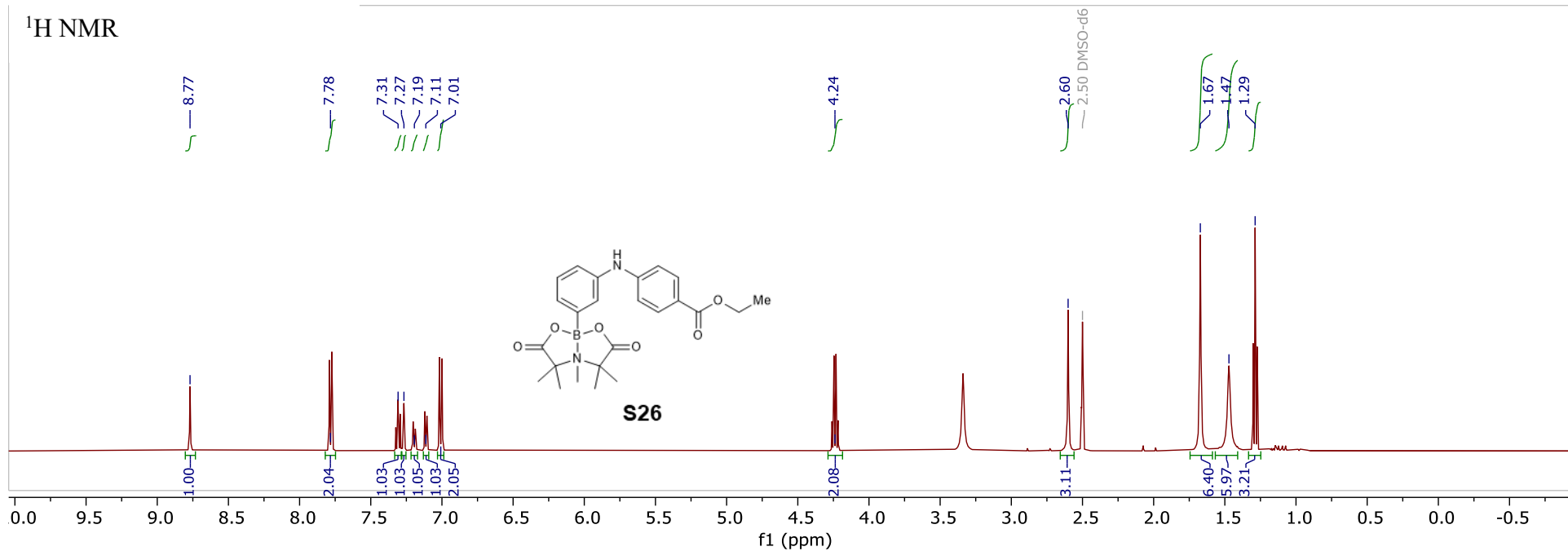
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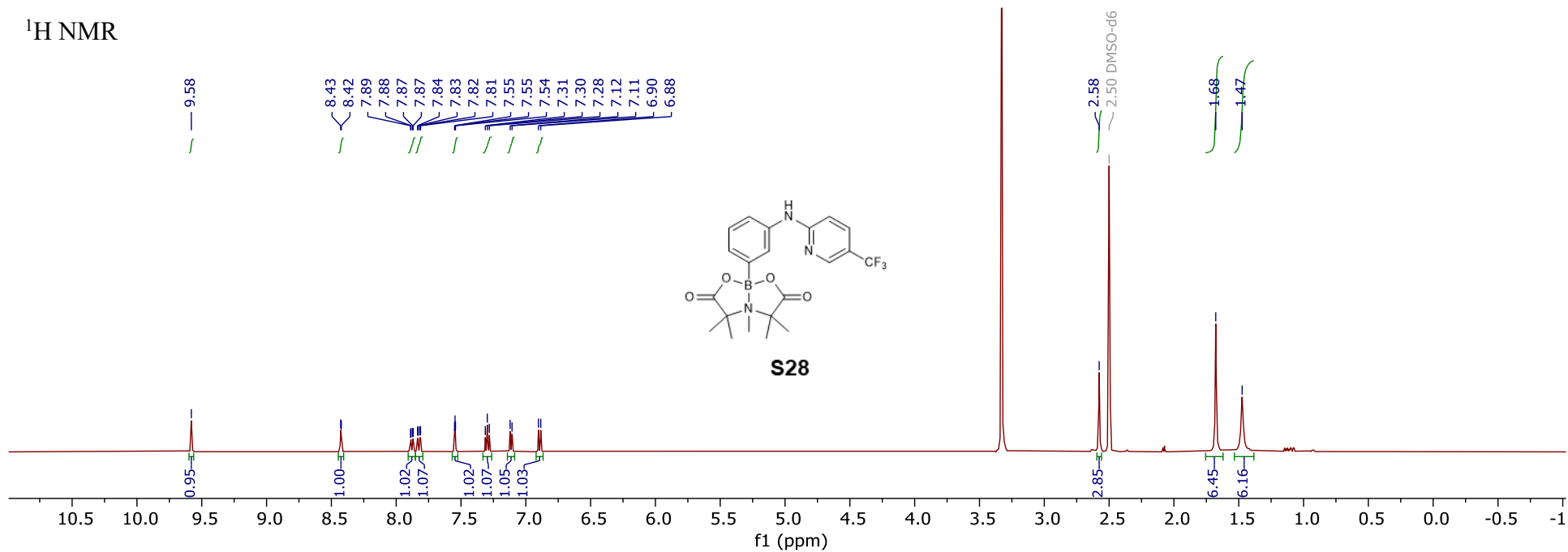
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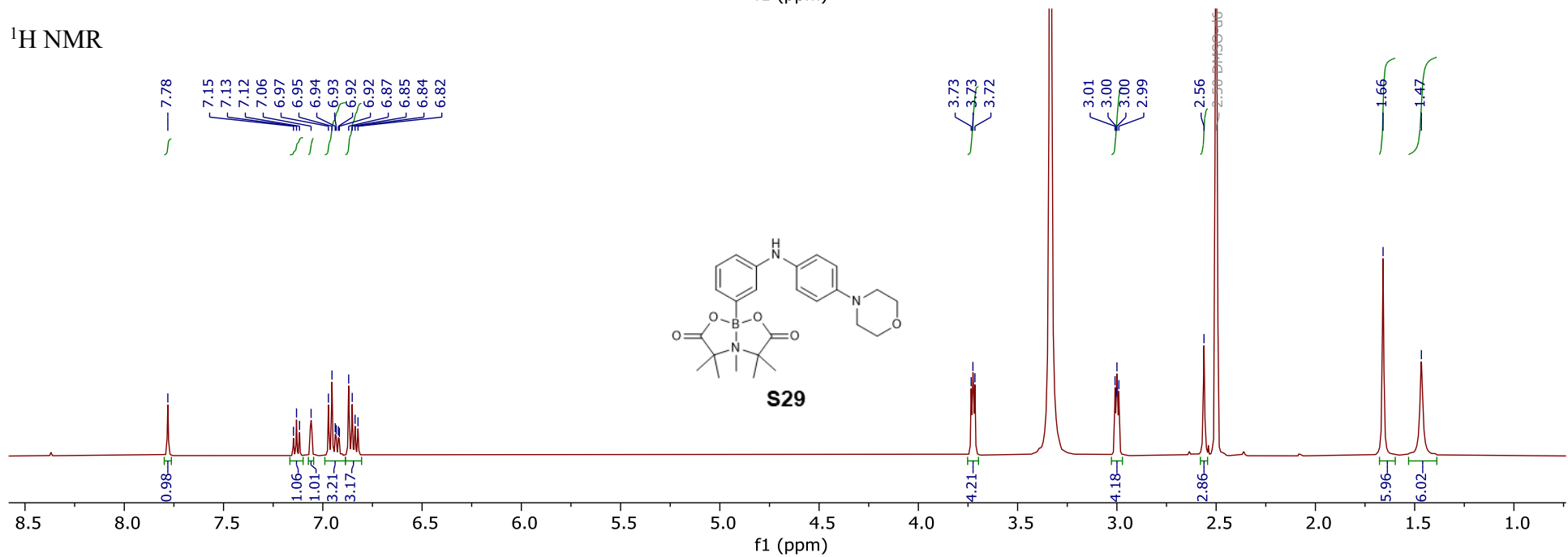


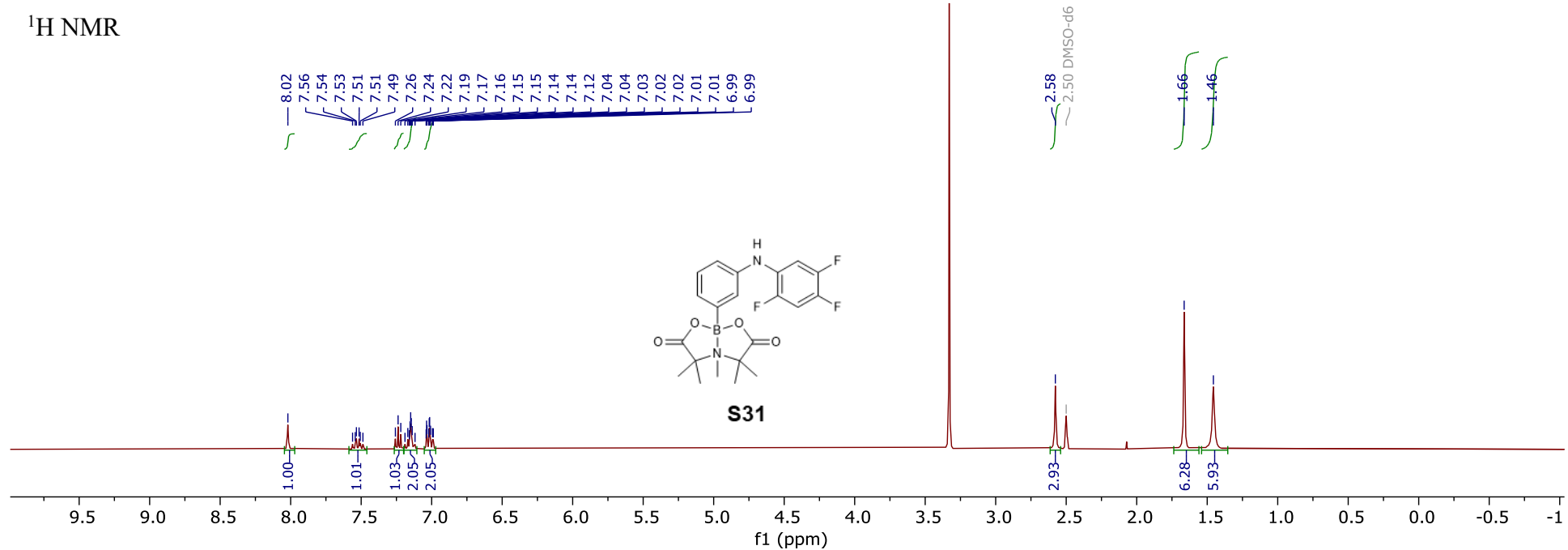
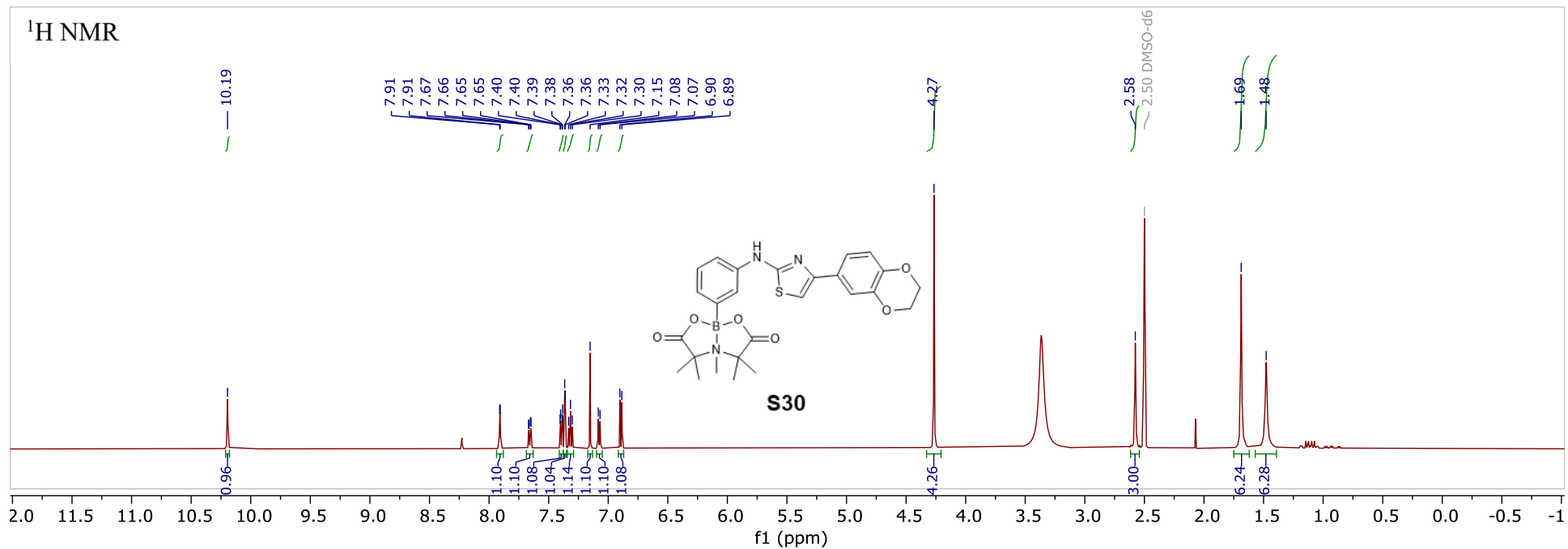


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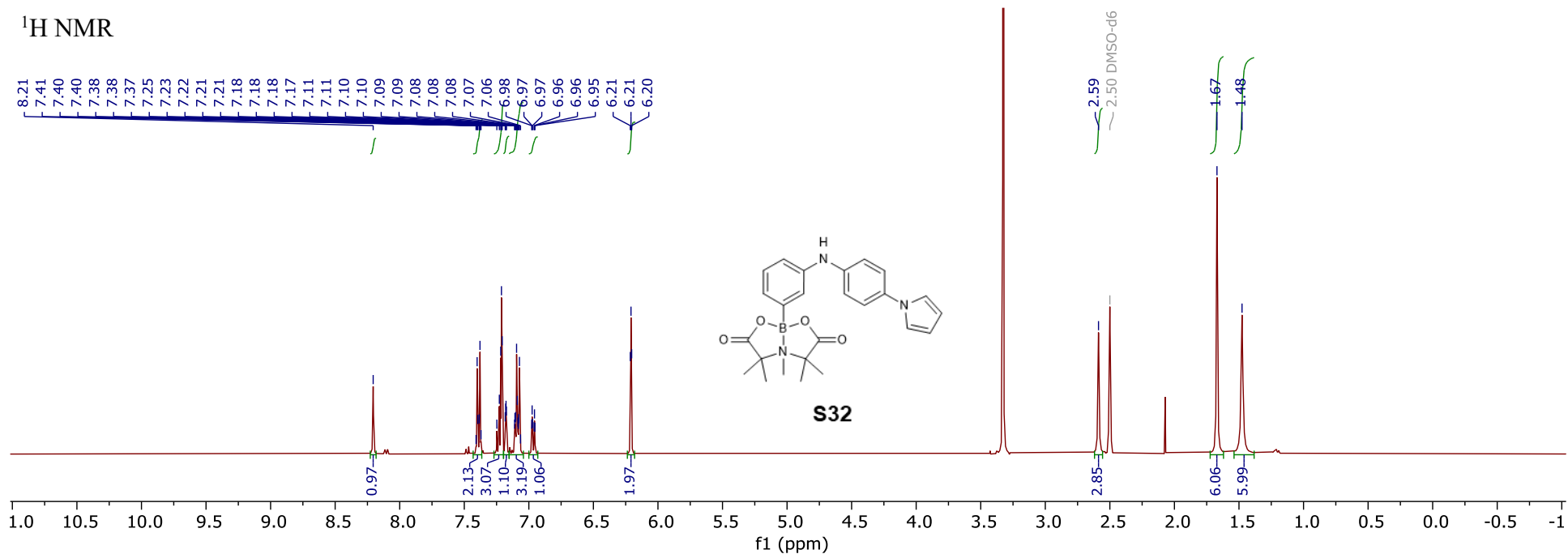


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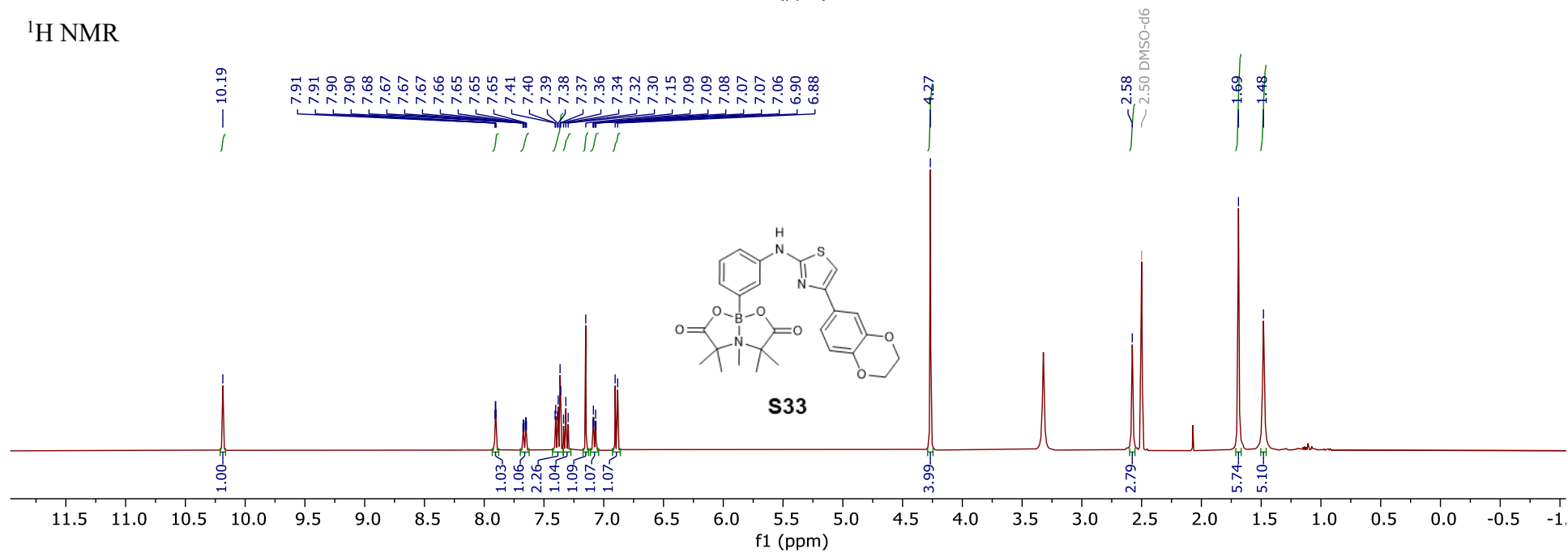




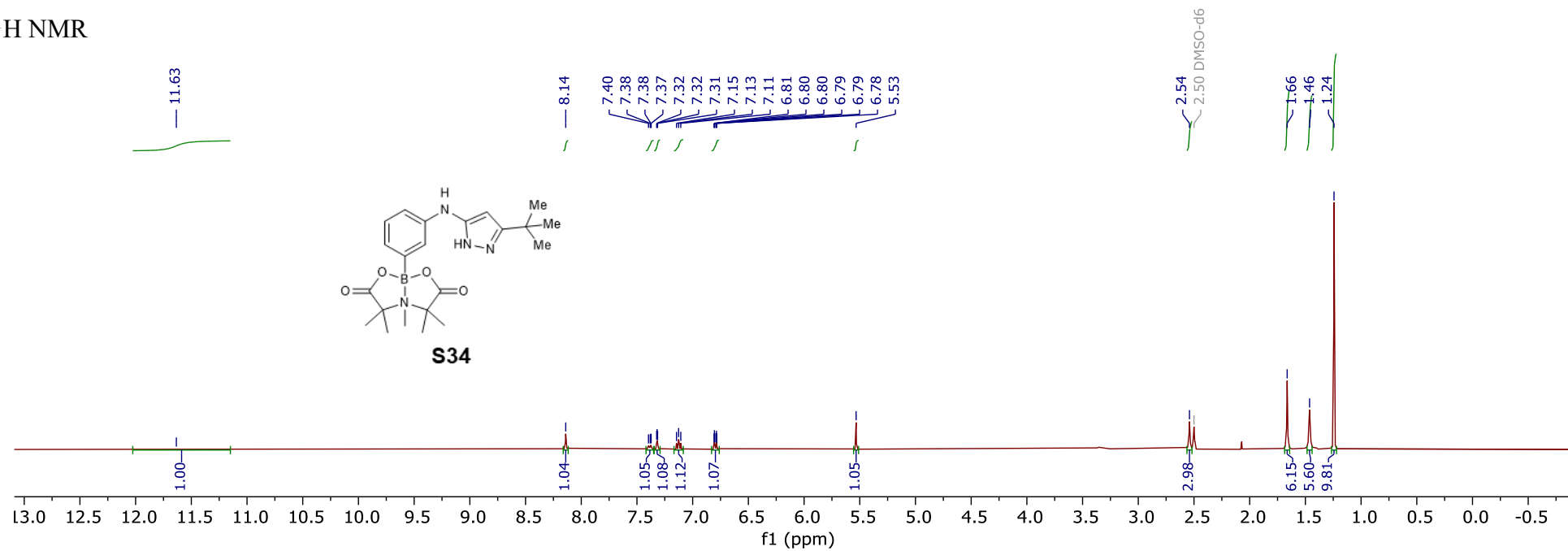
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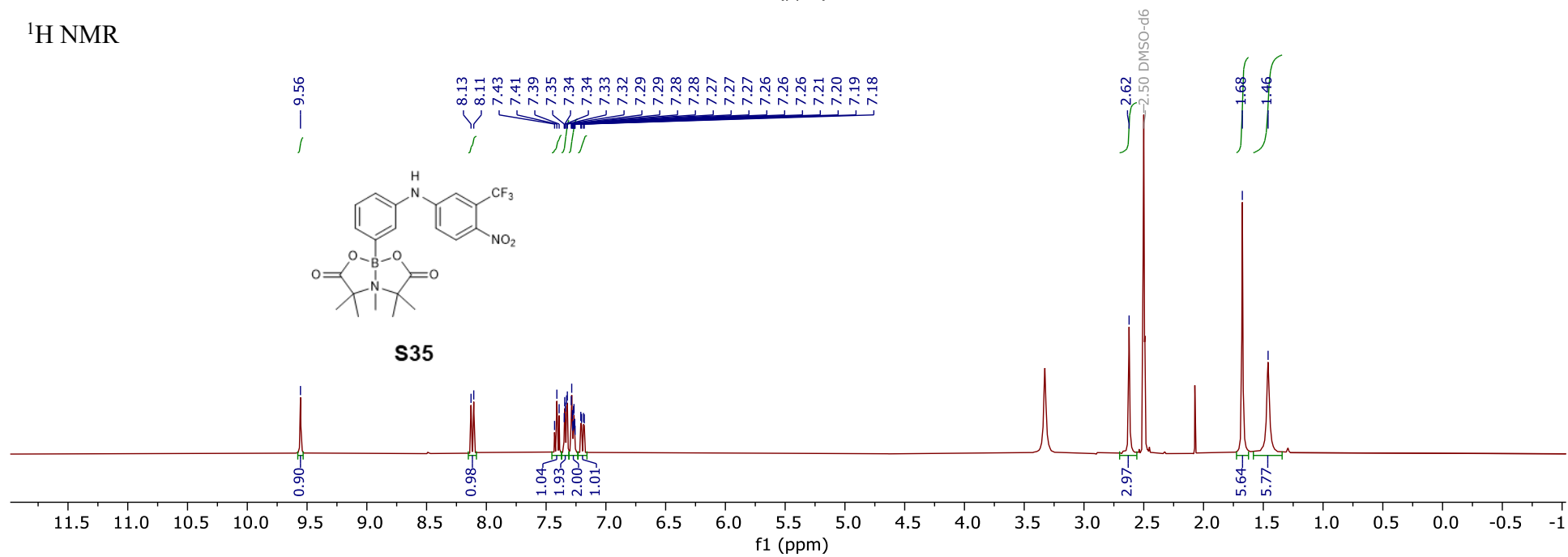
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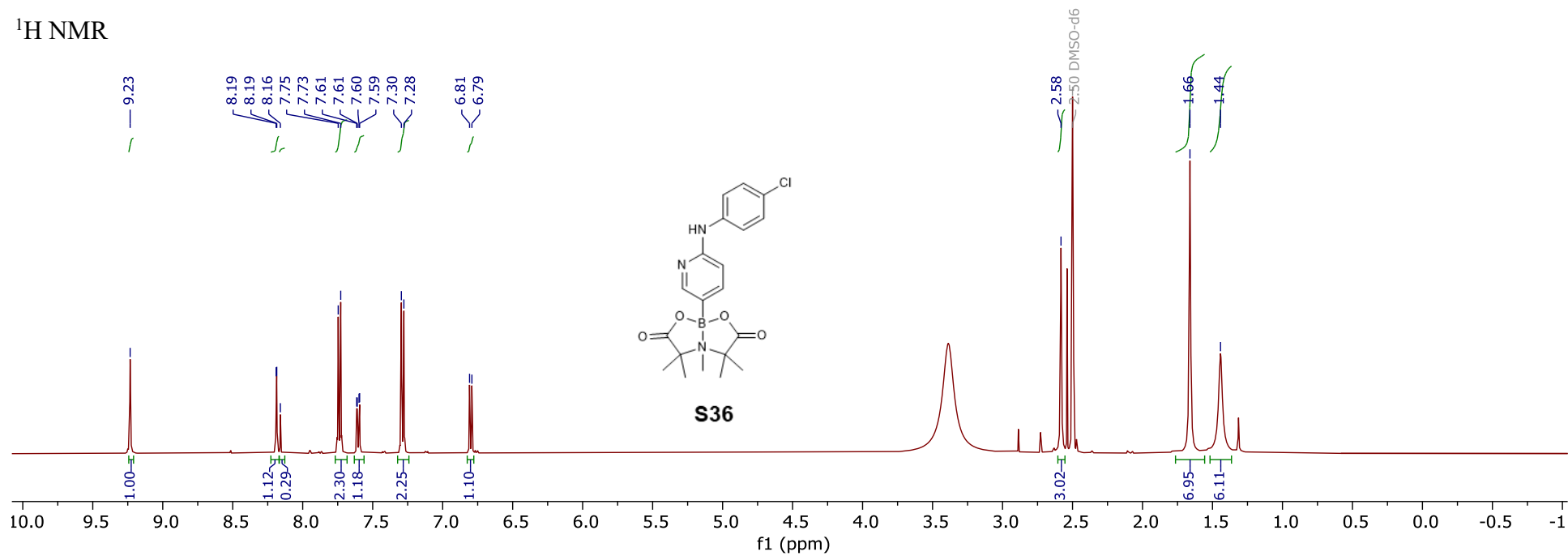
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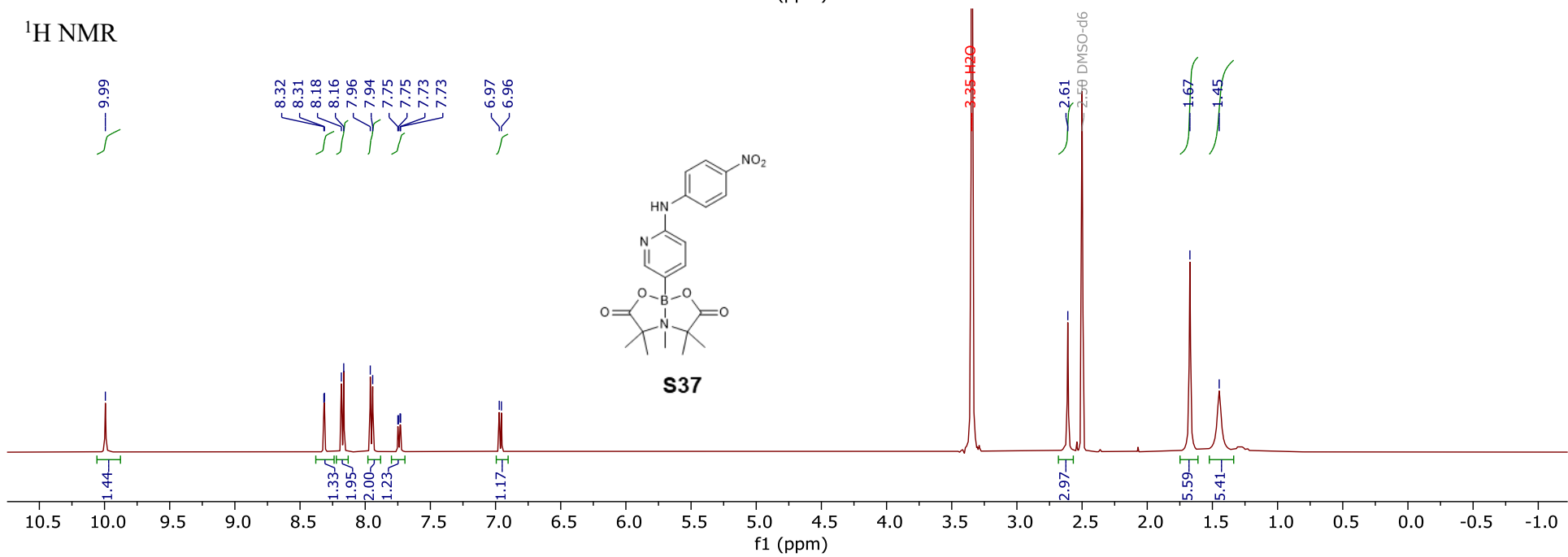
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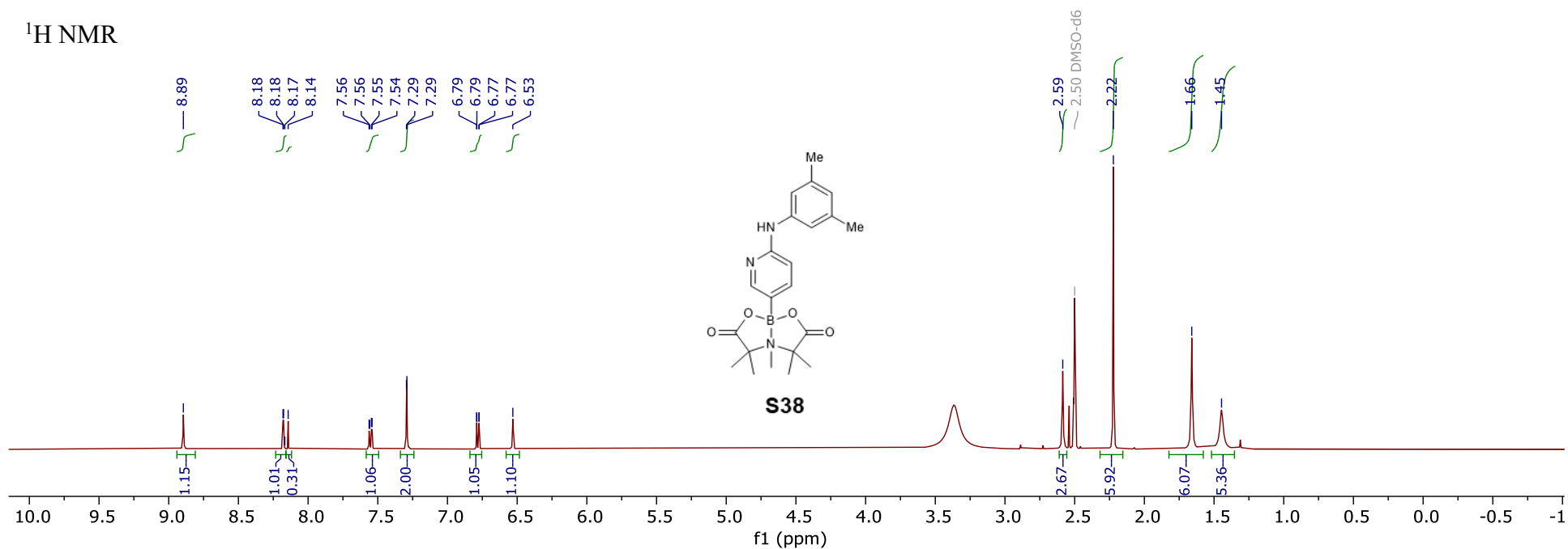
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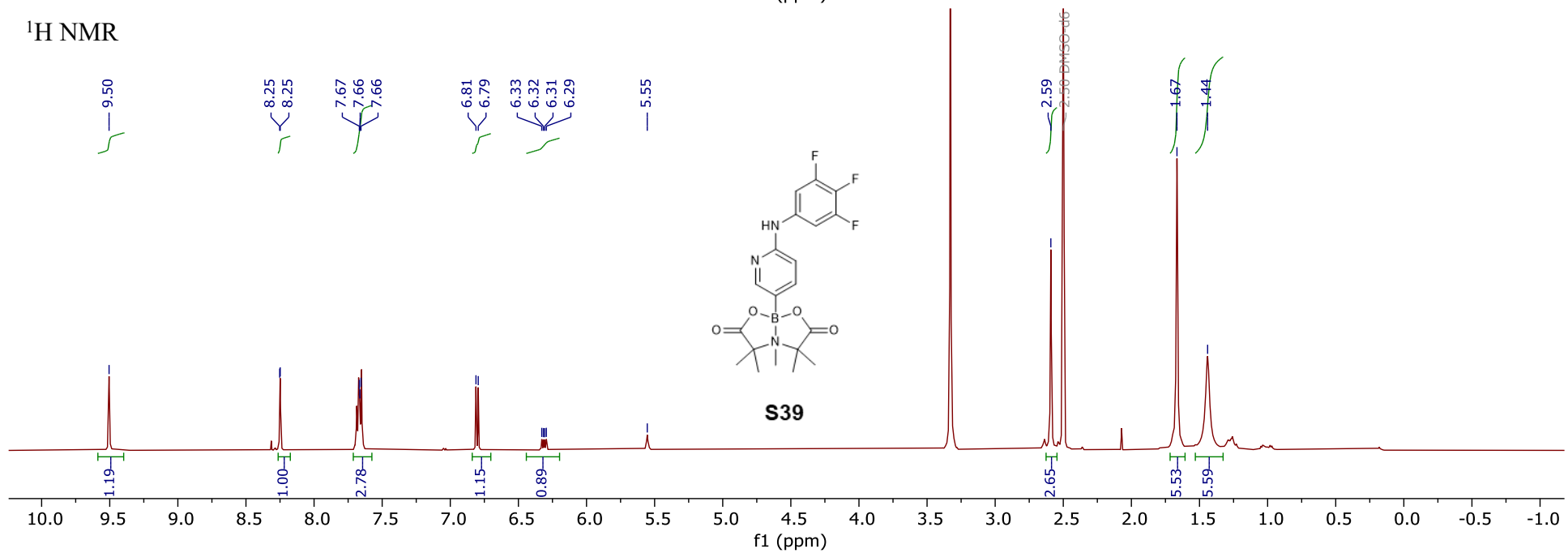
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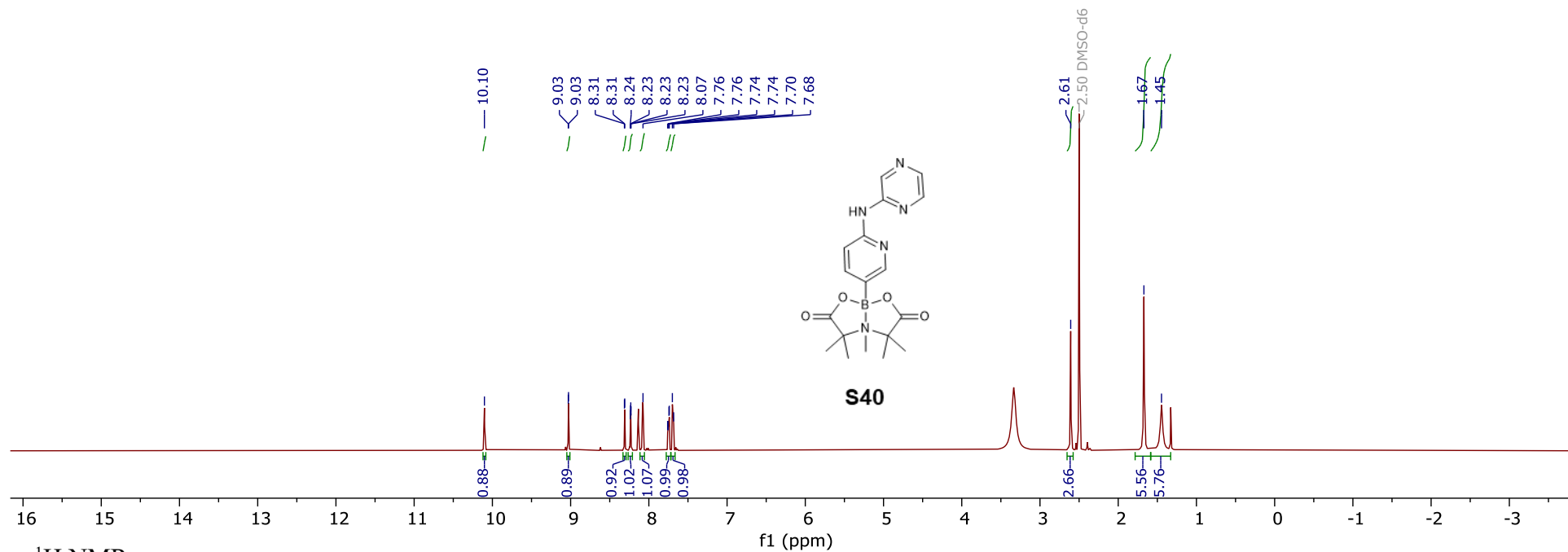
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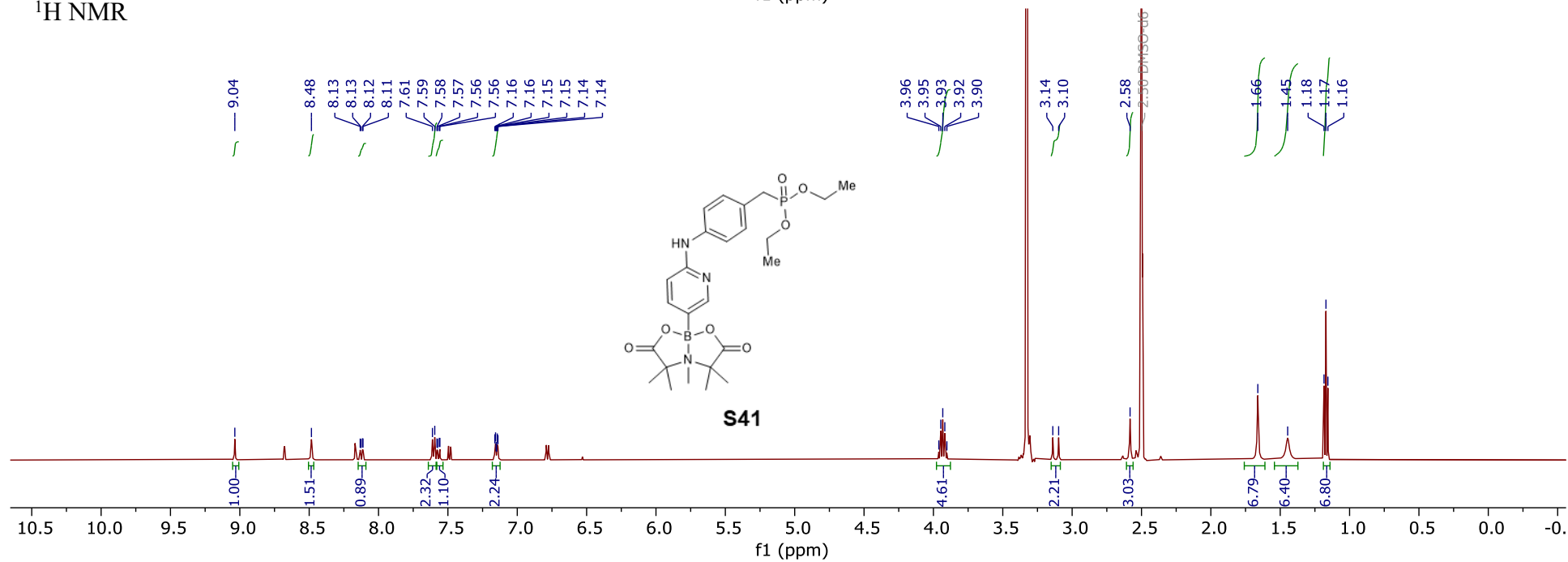
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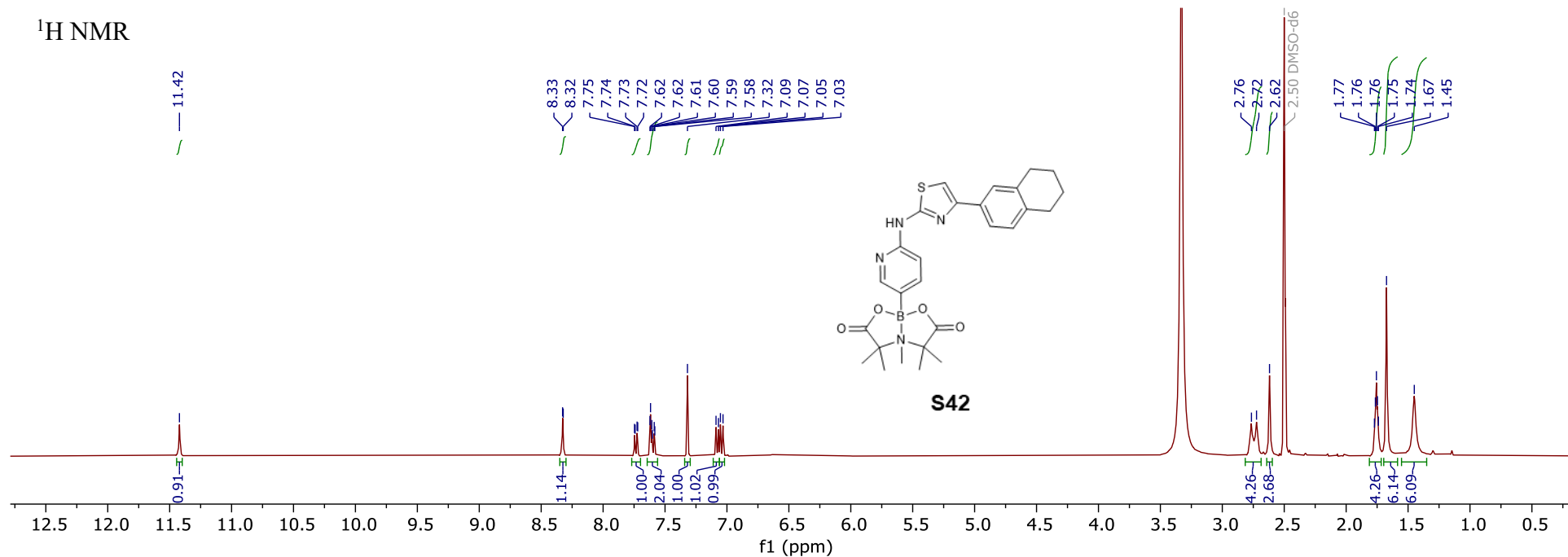


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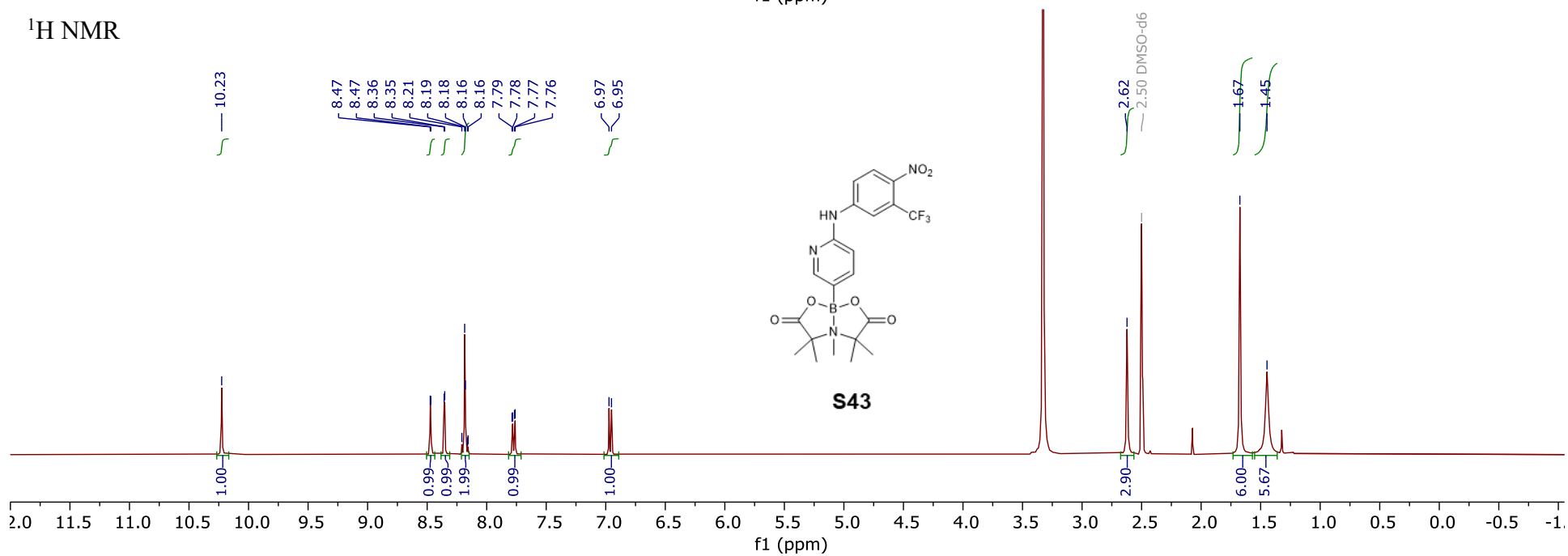


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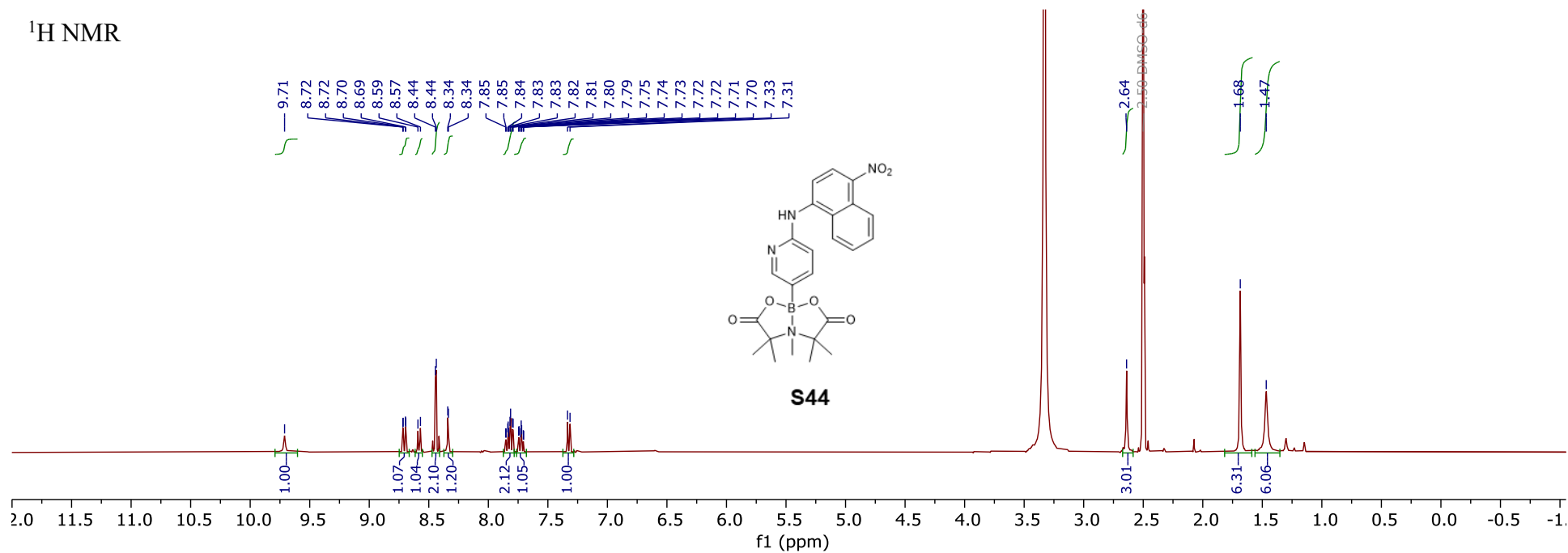
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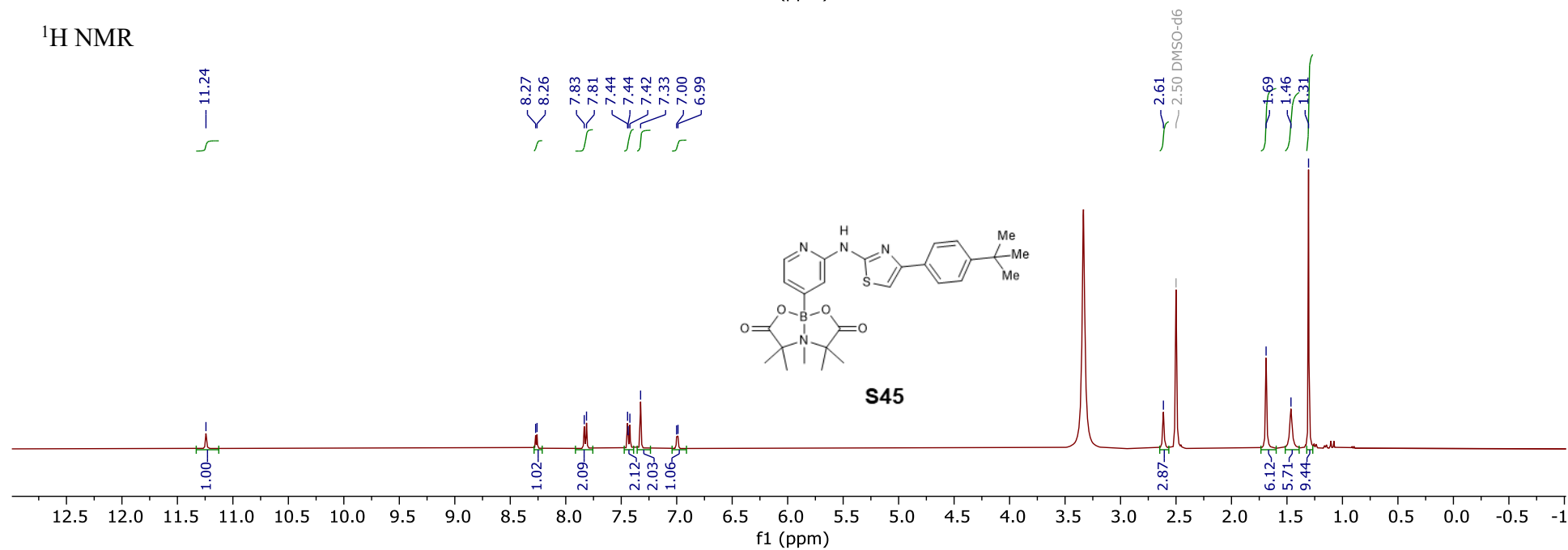
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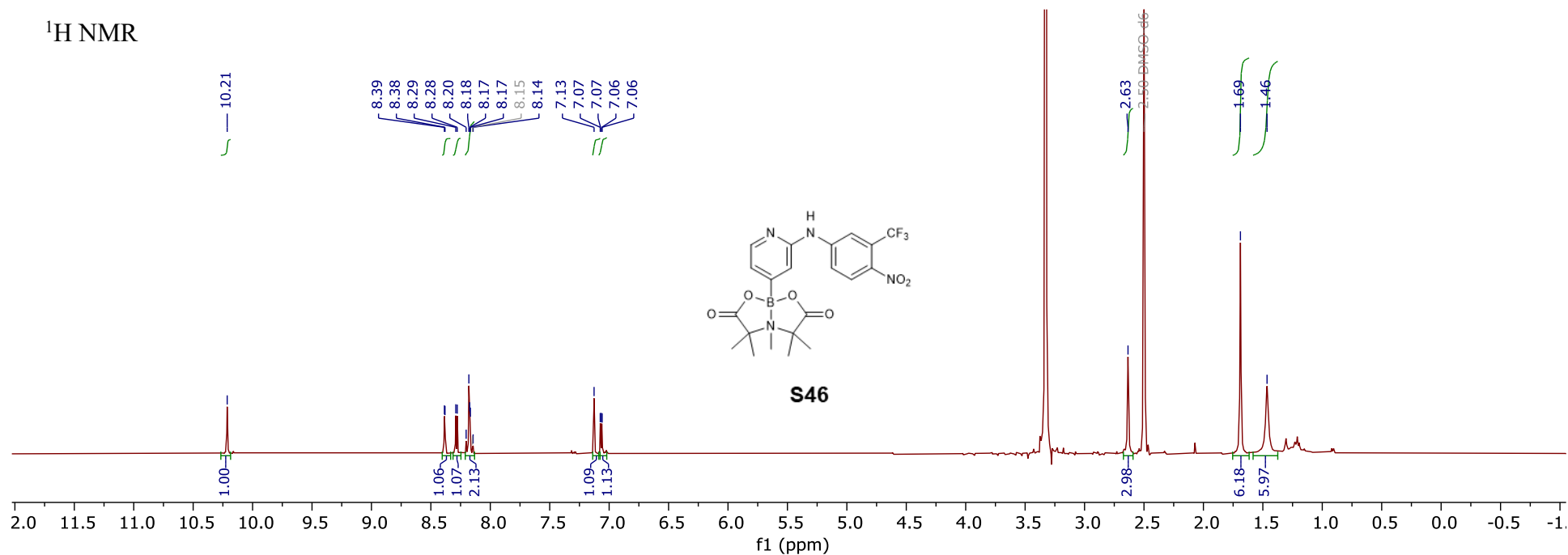
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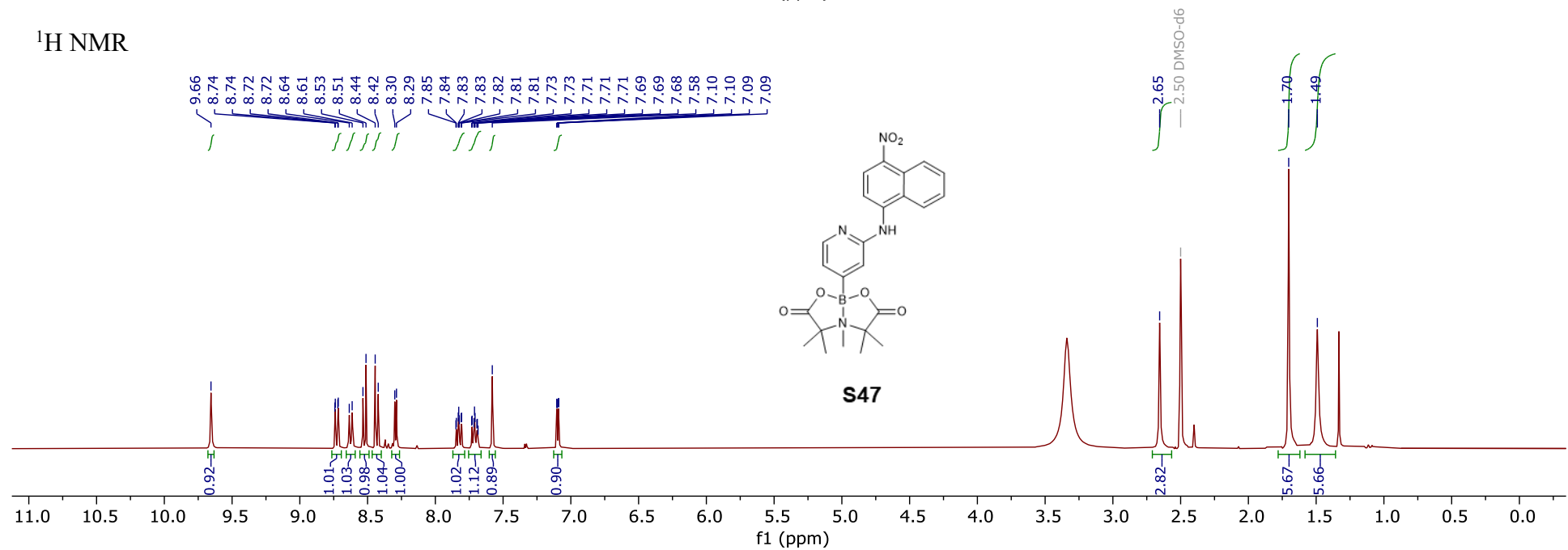
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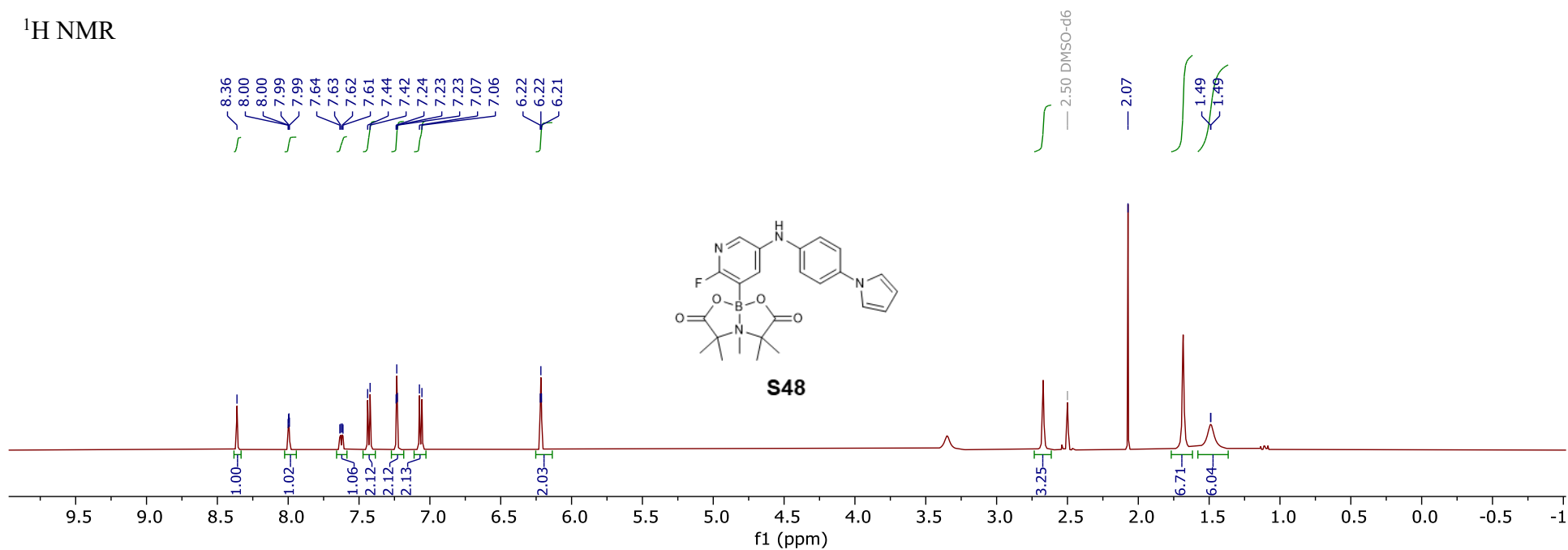
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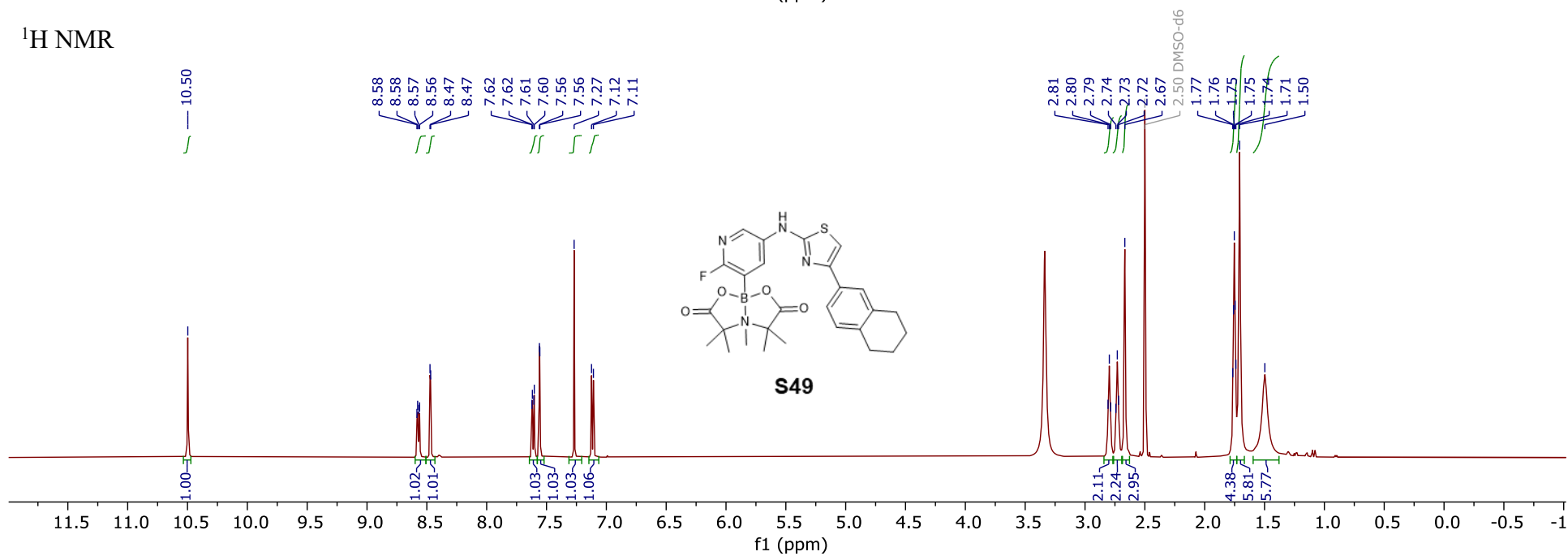
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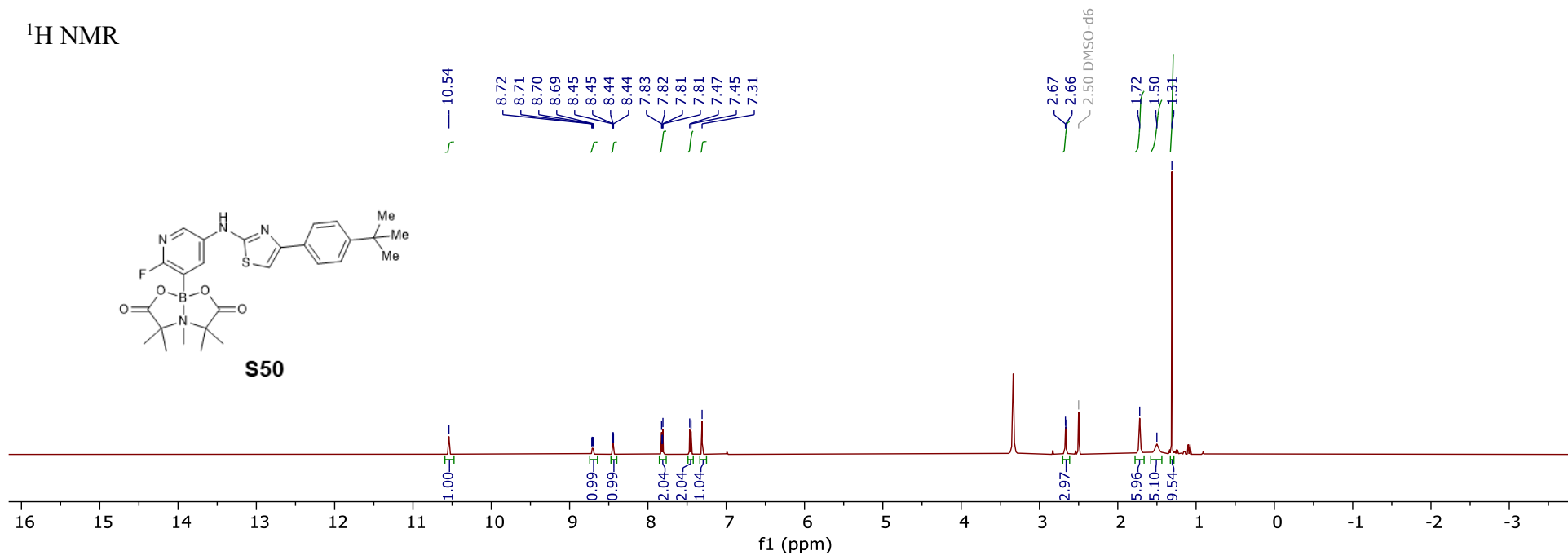
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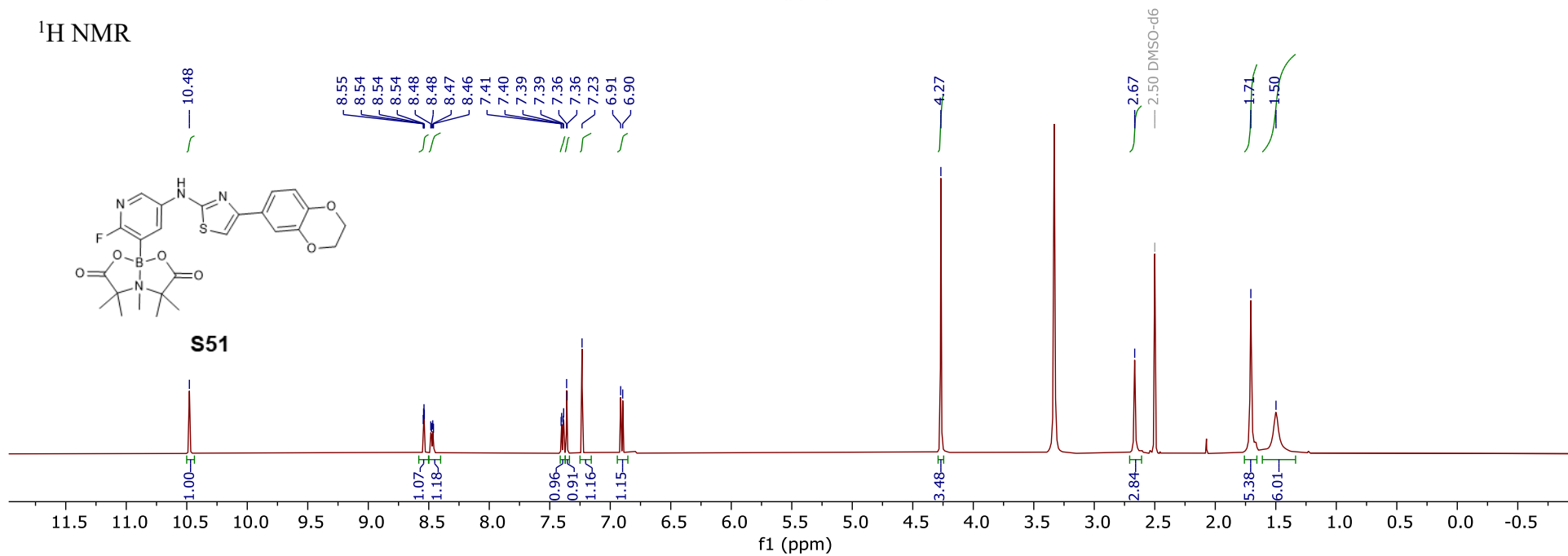
¹H NMR



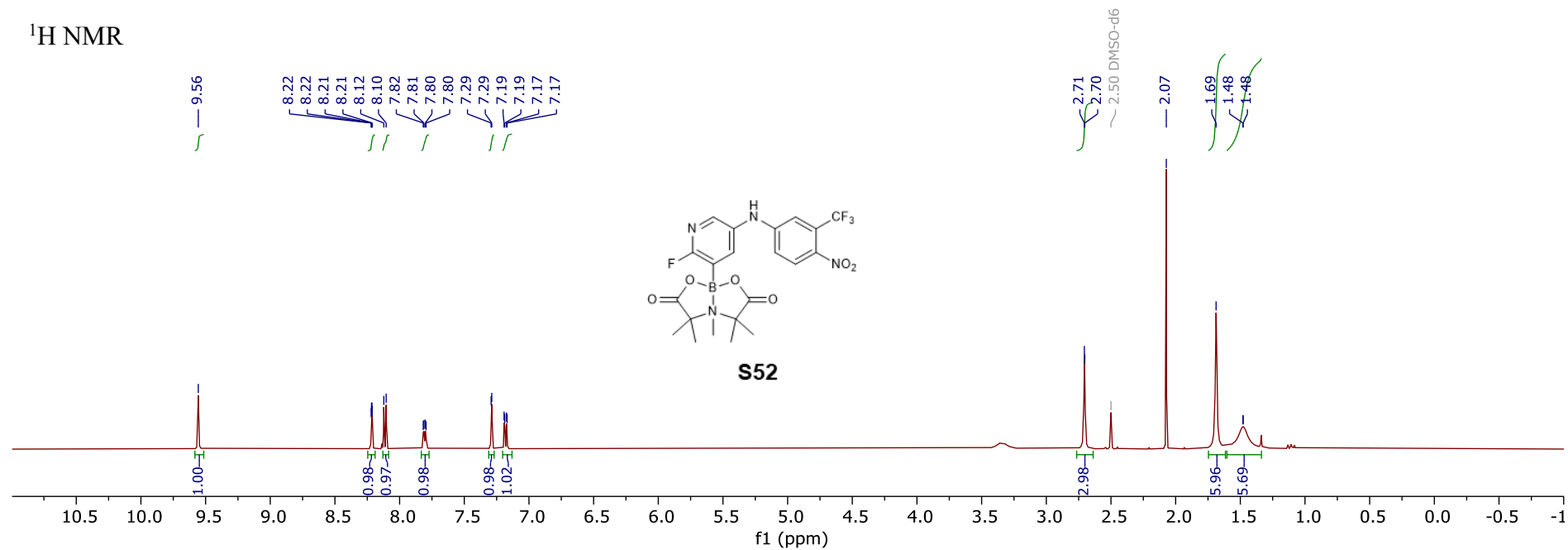
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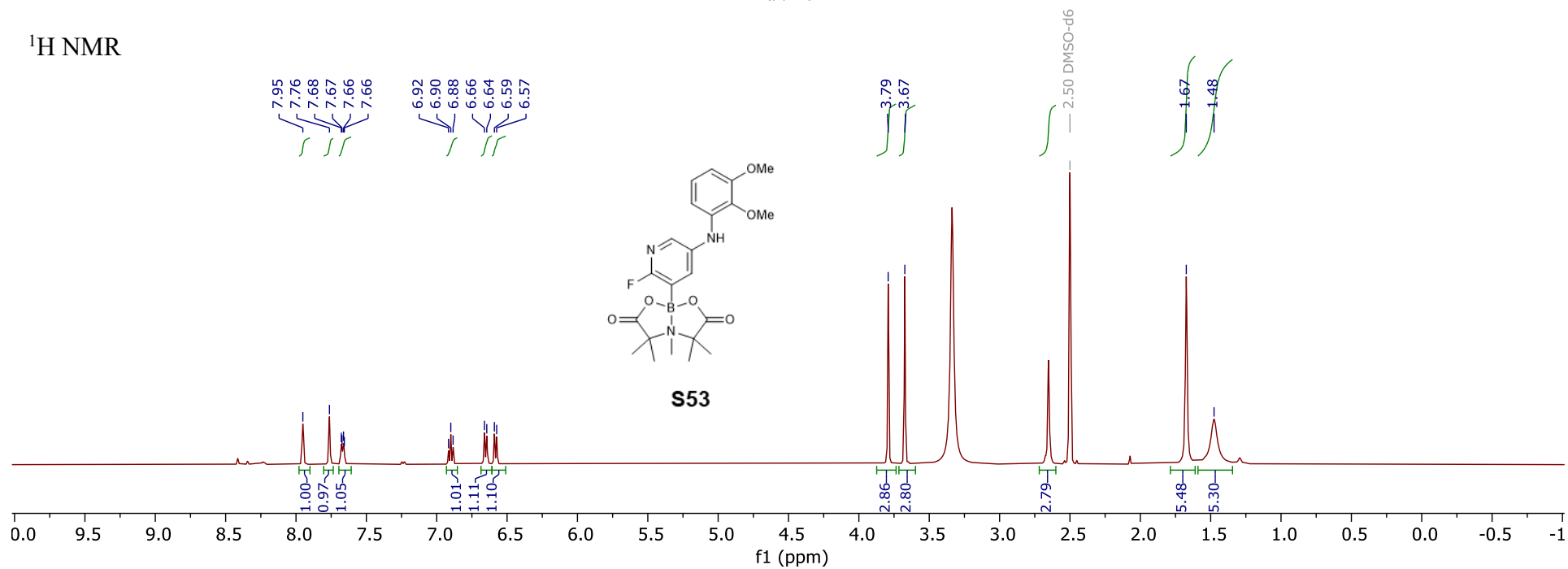
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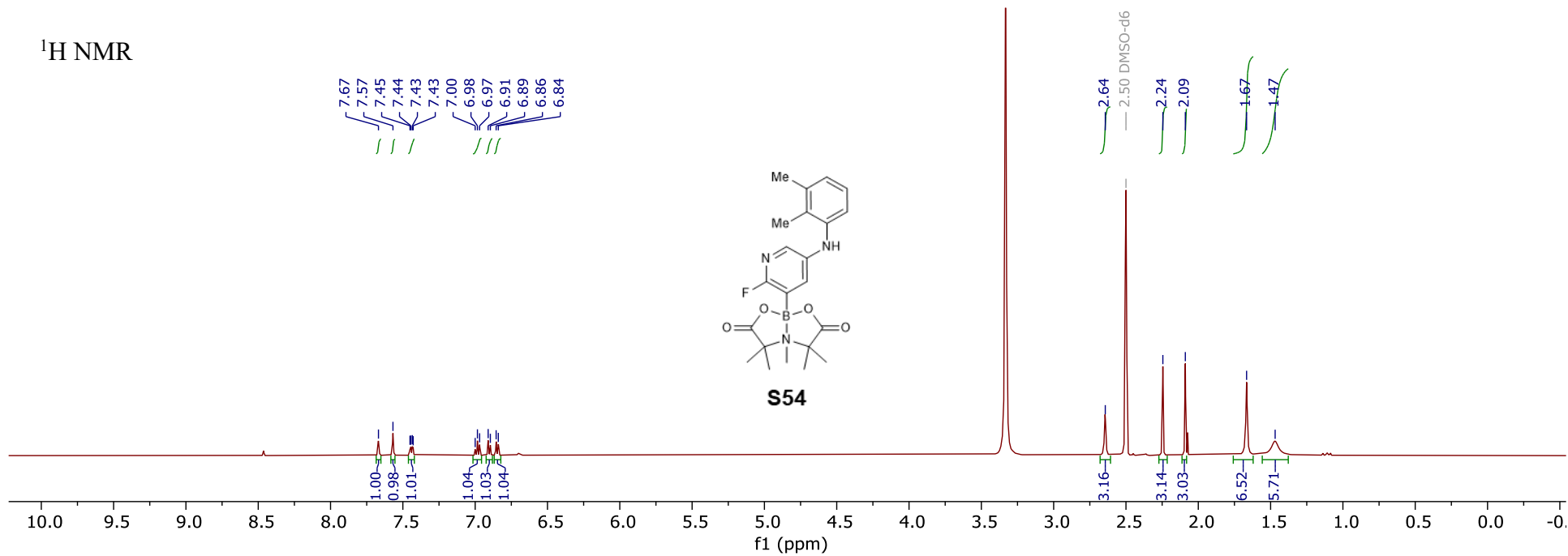
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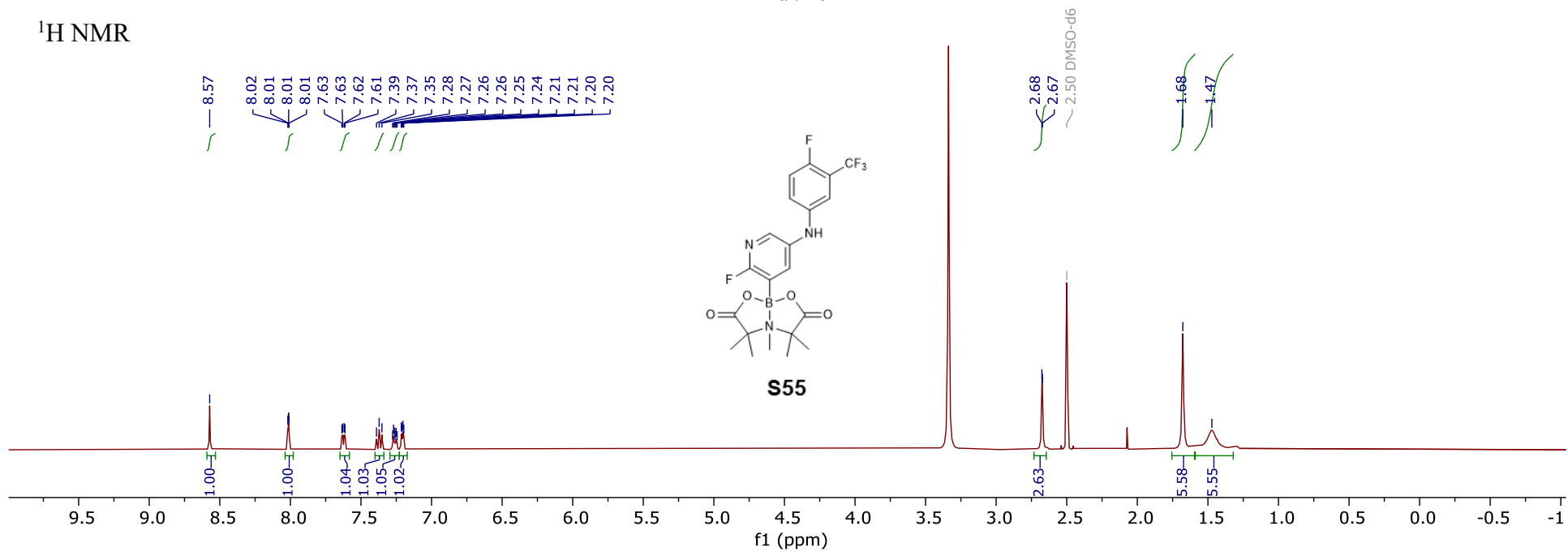
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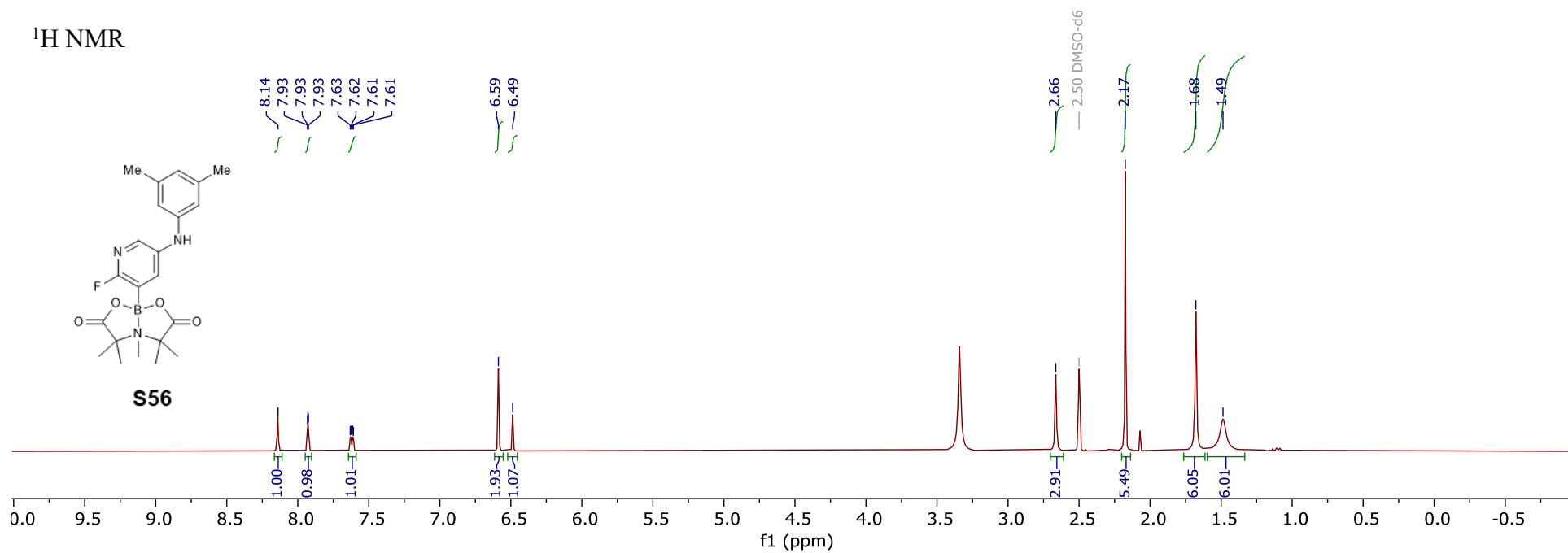
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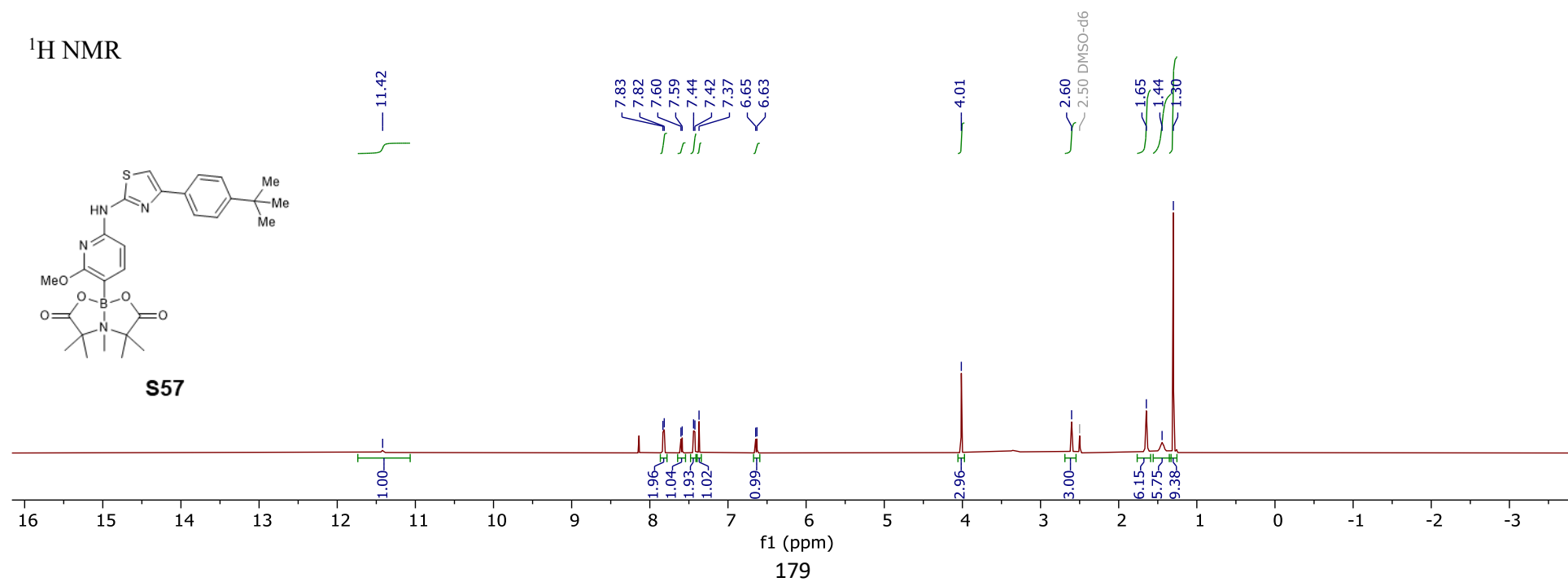
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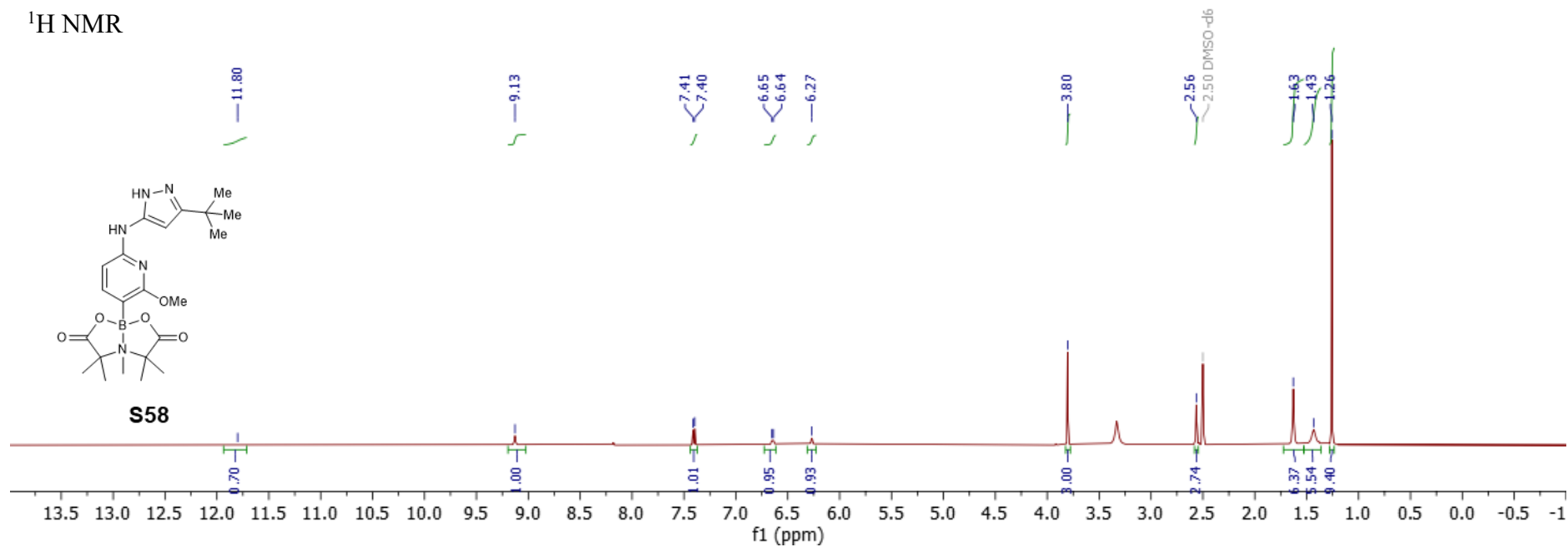
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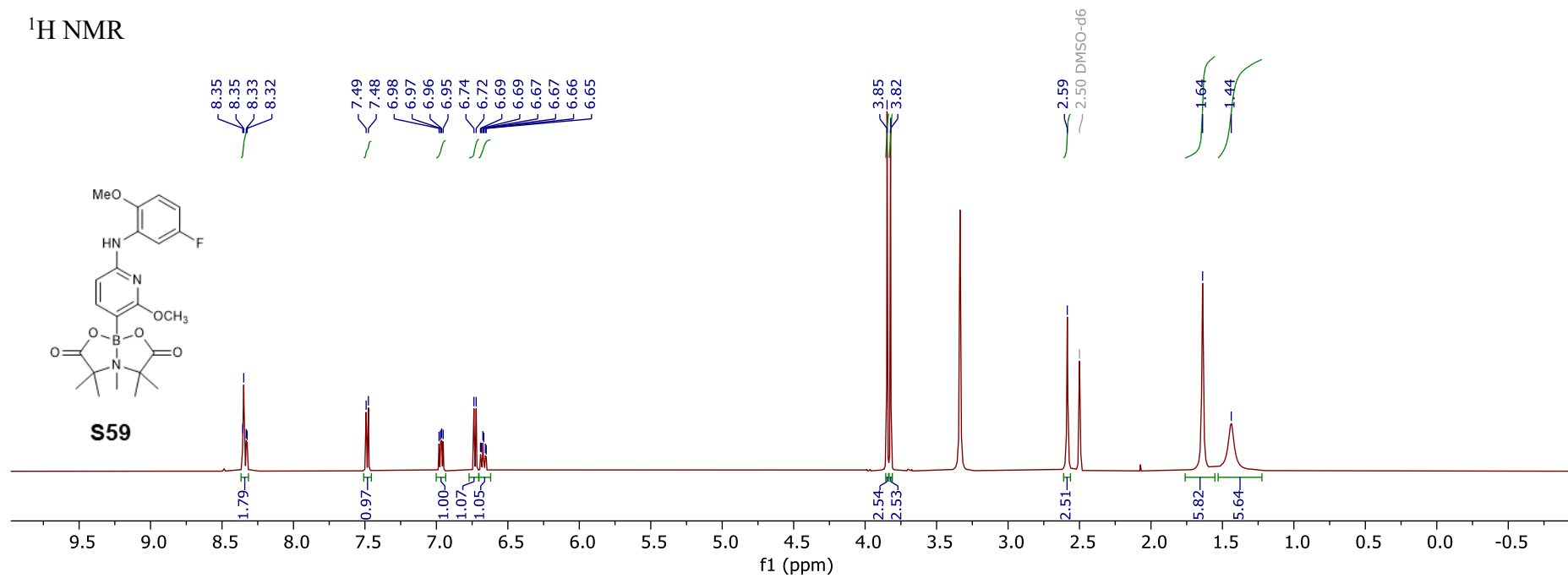
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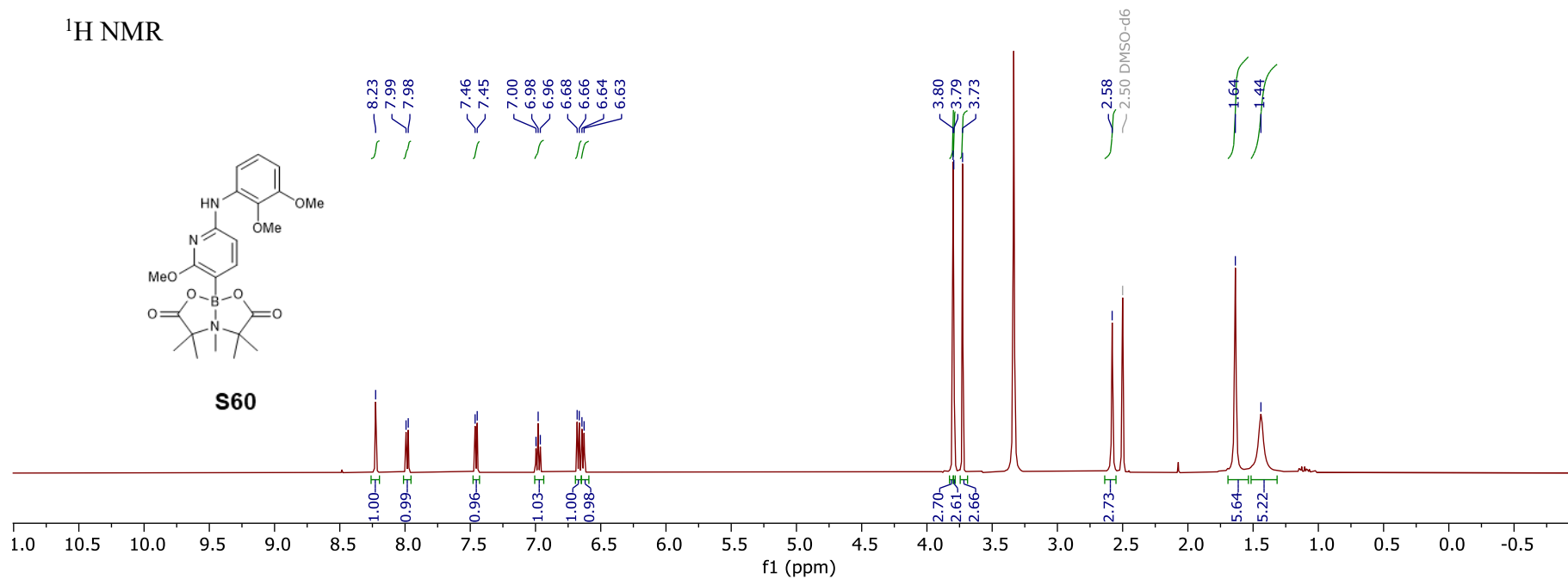
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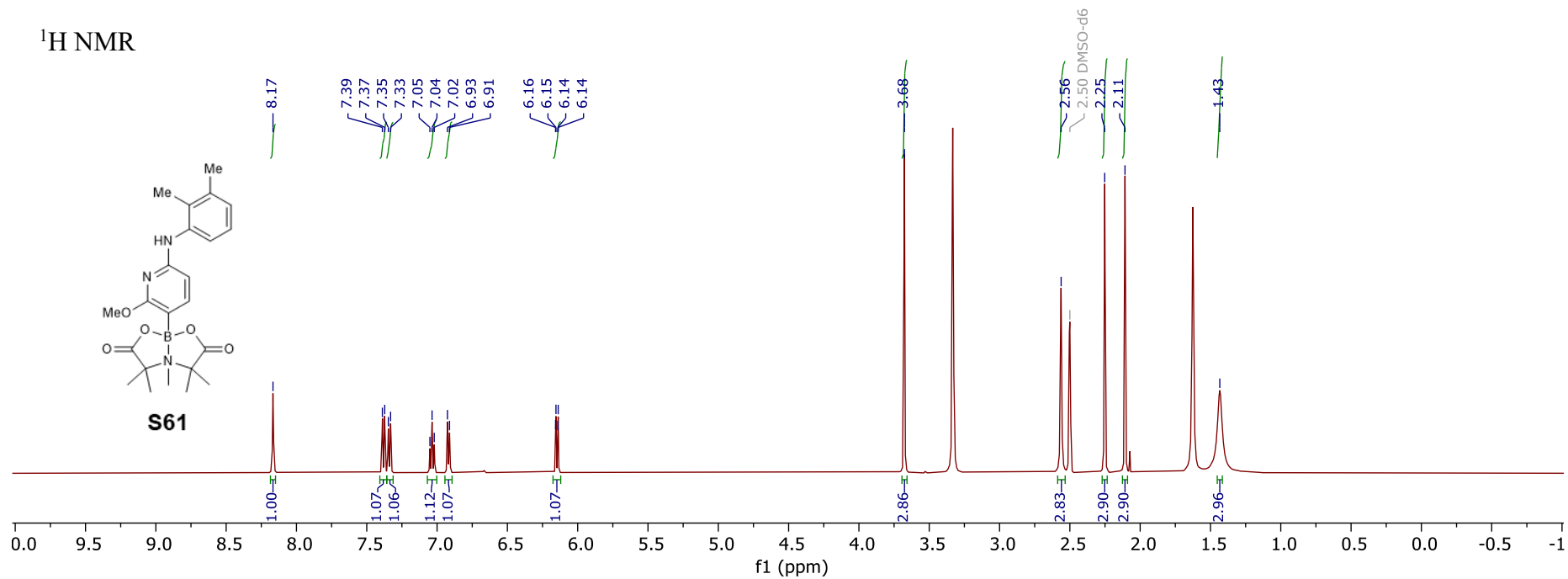
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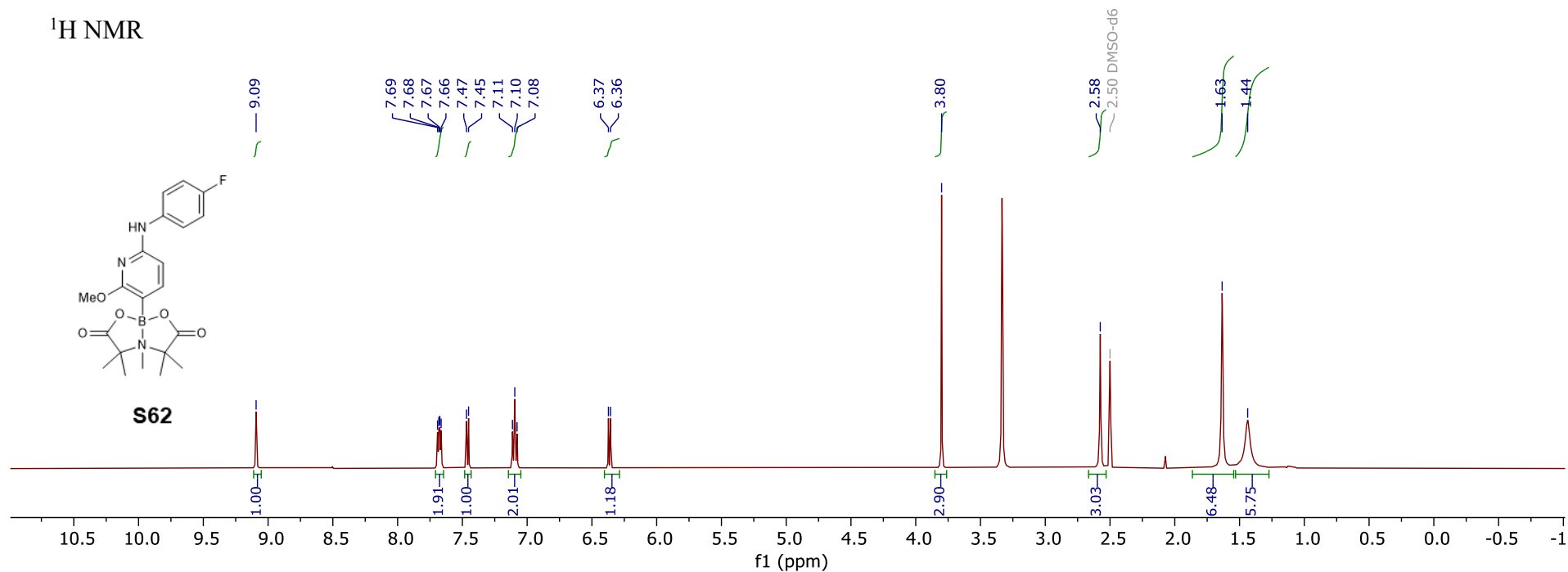
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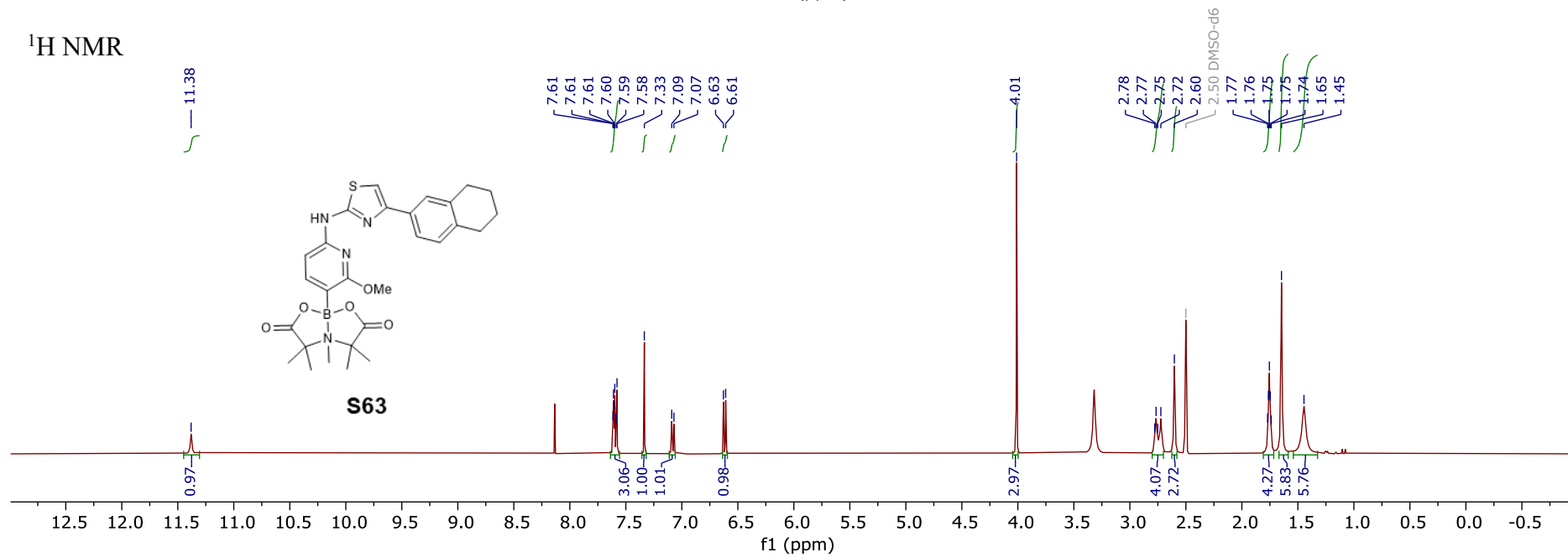
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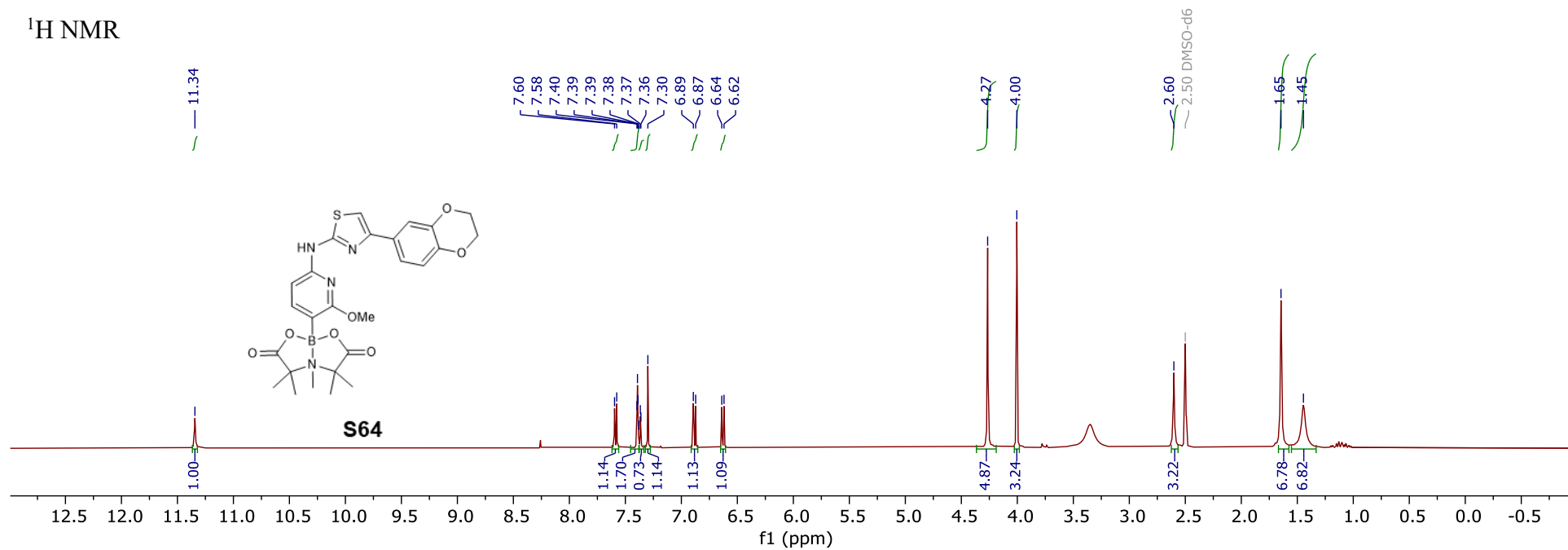
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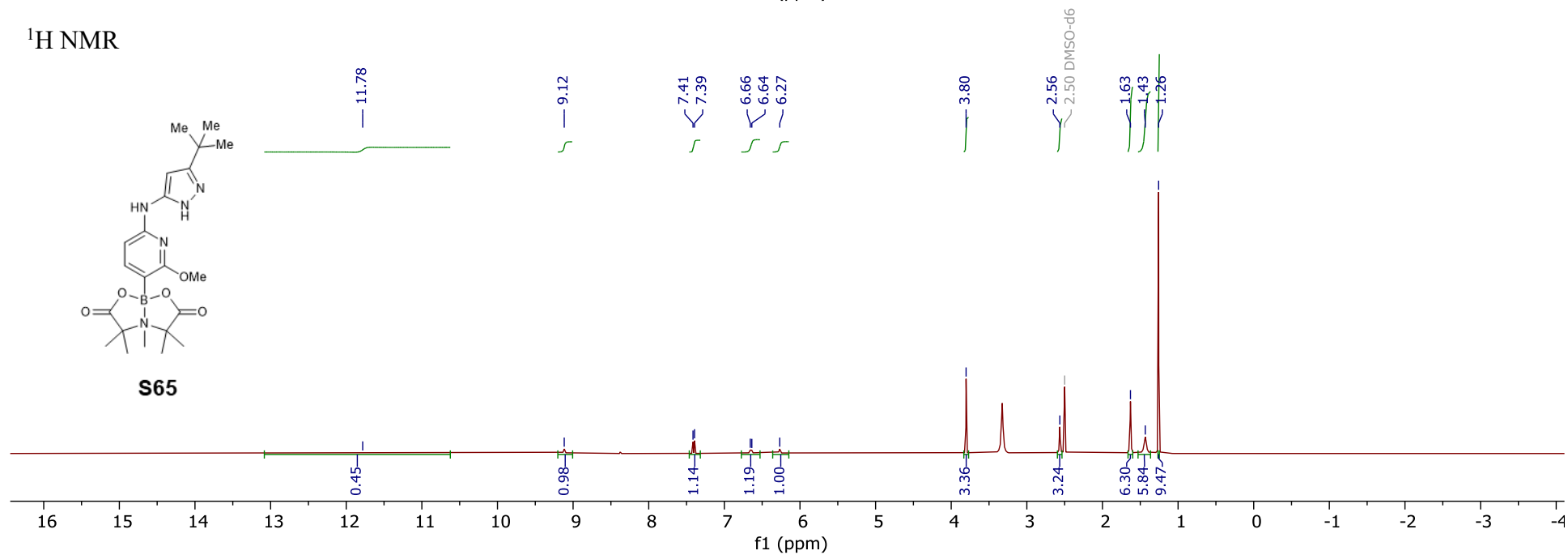
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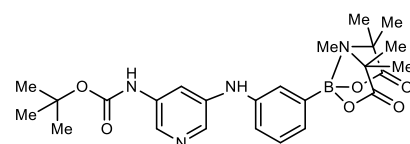
¹H NMR



¹H NMR



¹H NMR



S96

