Supporting Information for:

Reagent Design and Ligand Evolution for the Development of a Mild Copper-Catalyzed Hydroxylation Reaction

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General experimental details

All hydroxylation reactions were assembled in screw-cap vials in a nitrogen-filled glovebox, unless otherwise noted. Reactions to prepare **L4** were performed under N_2 using standard air-free techniques. Reagents and common substrates were purchased from commercial suppliers and used as received. Complex substrates were received from the Merck comound collection. Anhydrous DMSO was purchased from Sigma Aldrich and stored in a nitrogen-filled glovebox. NMR chemical shifts are reported in ppm and referenced to residual solvent peaks. Coupling constants are reported in hertz.

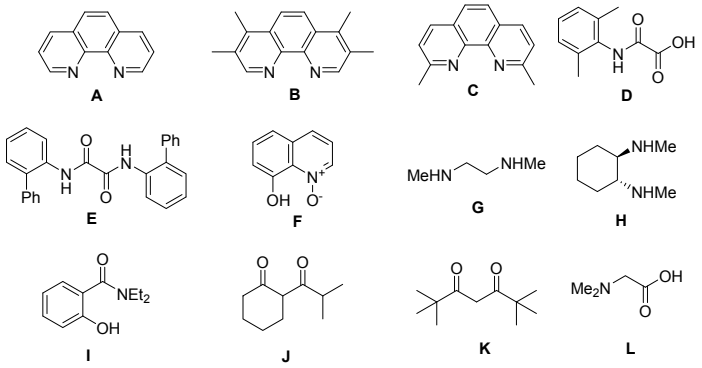
General procedure for the conversion of aryl halides to phenols

To a screw-cap vial was added aryl halide (1.0 equiv), benzaldehyde oxime (2.0 equiv), cesium carbonate (2.5 equiv), CuI (0.05 equiv), and ligand **L4** (0.05 equiv). Anhydrous DMSO was added such that the aryl halide concentration was 0.2 M. The vessel was sealed and heated at 80 ^{o}C with rapid stirring for 18 h.

For cases where assay yields were determined, the entire reaction mixture was diluted in a volumetric flask with 3:1 MeCN : 0.1% aqueous H_3PO_4 and the resulting solution was analyzed on an HPLC instrument calibrated to the product standard. The concentration of the phenol product was determined and used to calculate the yield of the product.

For cases where the product was isolated, the reaction mixture was quenched with 0.1 M HCl and extracted twice with DCM. The combined organic solutions were dried over $MgSO_4$, and purified by silica gel chromatography using a TeleDyne Isco CombiFlash purification system.

Ligands screened in initial high-throughput experiments (Scheme 1)



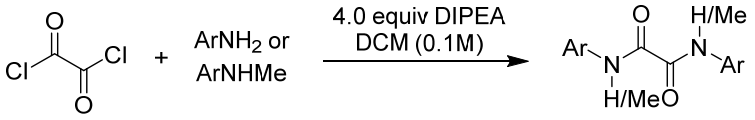
96-well reaction screening paramters: CuI (5 mol %), ligand (5 mol %), benzaldoxime (1.2 equiv), base (2.0 equiv), solvent (1.0 M), 80 °C, 18 h

Bases: K_3PO_4, K_2CO_3, Cs_2CO_3, DBU

Solvents: DMSO, DMF

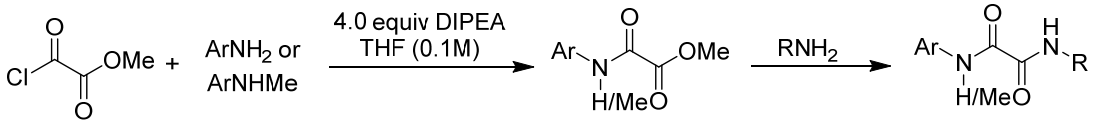
Procedure and Results: A 96-well plate with 250 µL vials was charged with stock solutions containing aryl halide (1.0 equiv, 1.0 M concentration), benzaldoxime (1.2 equiv), base (2.0 equiv), CuI (0.05 equiv), and ligand (0.05 equiv) in a glove box. The reaction plate was sealed and heated at 80 ^{o}C with rapid stirring for 18 h. The yield of **2** was determind by diluting each reaction vial with 0.2 mL of a 3:1 MeCN : 0.1% aqueous H_3PO_4 mixture and the resulting solution was analyzed on an HPLC instrument calibrated to the product standard. The best results obtained in the screen were 15% and 11% resulting from ligand **E** in DMSO with Cs_2CO_3 and K_2CO_3 respectively. All other conditions gave compound **2** in yields ranging from 0-8%.

Synthesis of modular ligand library



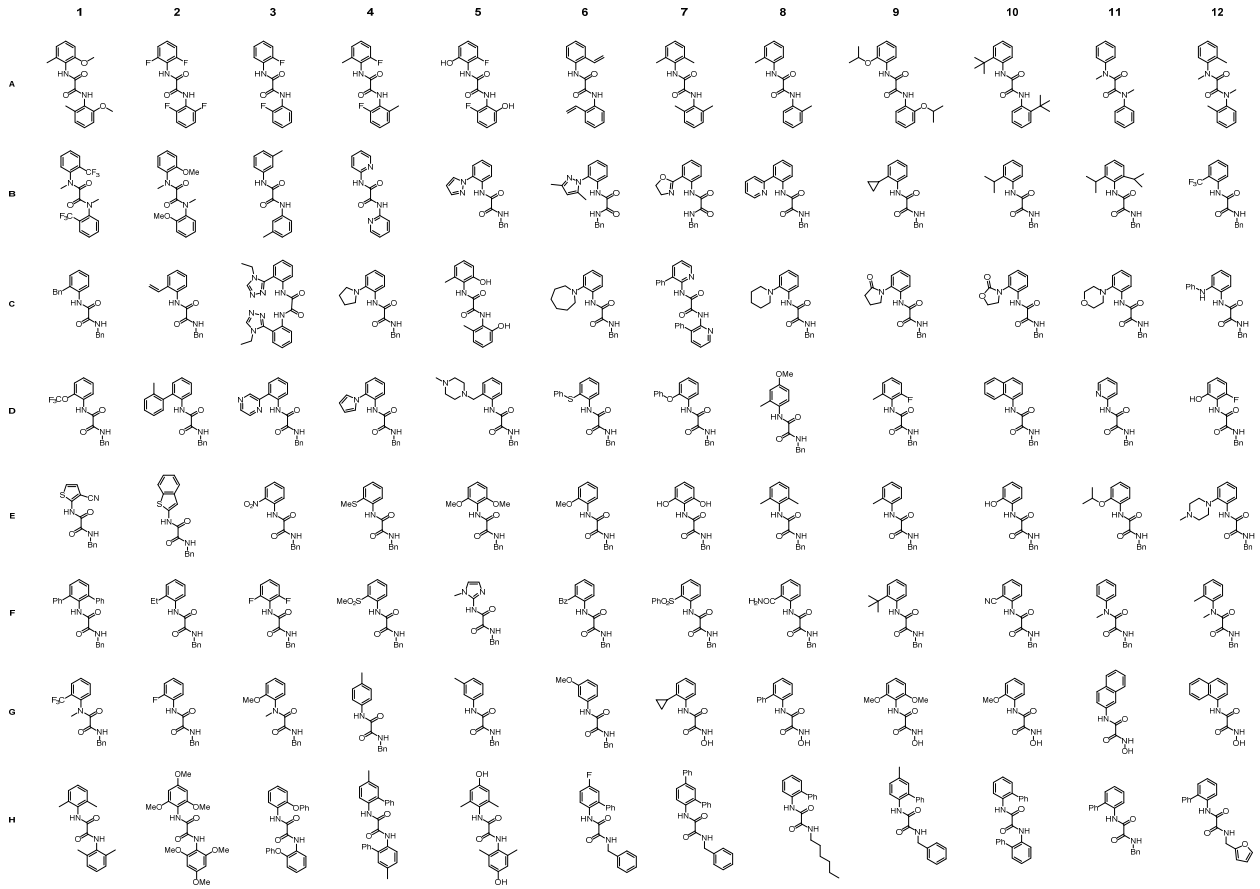
Symmetrical Ligands

General Procedure for Symmetrical Ligands: The aniline reagent (2.3 equiv, 0.30 mmol) in DCM (1 mL) at room temperature was treated with oxalyl dichloride (1.0 equiv, 0.065 mL, 0.13 mmol) and Hunig's Base (4.0 equiv, 0.091 mL, 0.52 mmol). The reaction mixture was stirred at room temperature for 17 h, filtered, and concentrated. The residues were dissolved in DMSO, filtered, and purified via Mass Spectrometry-directed purification (Reverse phase C-18, Water/Acetonitrile with 0.1% TFA). The resulting enriched fractions were concentrated in pre-tared vials to afford the symmetrical ligands.



Unsymmetrical Ligands

General Procedure for Unsymmetrical Ligands: The aniline reagent (1.07 equiv, 0.15 mmol) in THF (1 mL) at room temperature was treated with methyl 2-chloro-2-oxoacetate (1.0 equiv, 0.017 g, 0.14 mmol) and Hunig's Base (4.0 equiv, 0.098 ml, 0.56 mmol). The reaction was stirred for 18 h. To the crude reaction mixture was added alkylamine (1.6 equiv, 0.024 g, 0.224 mmol), and the reaction was stirred at 70 °C for 18 h. The reaction mixture was then cooled to room temperature, filtered, and concentrated. The residues were then dissolved in DMSO, filtered, and purified via Mass Spectrometry-directed purification (Reverse phase C-18, Water/Acetonitrile with 0.1% TFA). The resulting enriched fractions were concentrated in pre-tared vials to afford the unsymmetrical ligands.

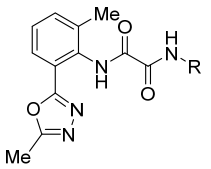

1
2
3
4
5
6
7
8
9
10
11
12
A
B
C
D
E
F
G
H

Yields for the Reactions of 1 to 2 with the 96 Oxamide Library (Scheme 2)

	Benzaldehyde	p-CF3	p-OMe	Mesityl			Benzaldehyde	p-CF3	p-OMe	Mesityl
A:1	11	15	14	0		E:1	0	0	0	0
A:2	3	7	5	0		E:2	12	4	3	0
A:3	10	0	0	0		E:3	22	13	12	0
A:4	6	0	2	0		E:4	37	29	44	10
A:5	0	0	0	0		E:5	36	24	32	5
A:6	20	16	18	0		E:6	20	15	18	4
A:7	8	6	6	0		E:7	0	0	0	0
A:8	24	6	5	0		E:8	44	9	47	4
A:9	8	4	2	5		E:9	29	9	24	5
A:10	12	0	0	0		E:10	0	0	0	0
A:11	0	0	0	0		E:11	34	15	18	5
A:12	0	0	0	0		E:12	40	18	39	13
B:1	0	0	0	0		F:1	12	8	16	0
B:2	0	0	0	0		F:2	41	29	33	6
B:3	13	6	8	0		F:3	42	24	28	5
B:4	0	0	0	0		F:4	36	15	15	6
B:5	40	11	16	6		F:5	10	0	0	0
B:6	38	18	9	1		F:6	24	16	18	6
B:7	61	17	21	16		F:7	19	13	3	0
B:8	46	19	21	19		F:8	5	5	8	0
B:9	33	4	2	6		F:9	24	8	6	0
B:10	32	6	3	0		F:10	35	20	17	5
B:11	36	7	4	6		F:11	0	0	0	0
B:12	41	21	19	5		F:12	0	0	0	0
C:1	42	27	24	5		G:1	0	0	0	0
C:2	41	33	28	4		G:2	45	29	28	5
C:3	8	3	2	0		G:3	3	0	0	0
C:4	20	12	12	5		G:4	25	14	15	0
C:5	0	0	0	0		G:5	15	13	13	0
C:6	18	15	13	0		G:6	15	6	5	4
C:7	3	0	0	0		G:7	0	0	0	0
C:8	18	3	3	0		G:8	0	4	0	0
C:9	35	13	11	4		G:9	6	4	3	0
C:10	0	5	3	0		G:10	8	0	0	0
C:11	21	14	15	0		G:11	0	0	0	0
C:12	10	0	6	0		G:12	11	11	10	7
D:1	33	22	23	4		H:1	15	10	14	5
D:2	25	14	14	0		H:2	22	14	17	0
D:3	41	19	23	0		H:3	20	13	11	0
D:4	39	3	23	4		H:4	17	14	9	4
D:5	15	4	13	0		H:5	39	19	34	9
D:6	26	30	23	11		H:6	29	21	21	5
D:7	36	8	16	0		H:7	31	10	28	0
D:8	34	17	18	0		H:8	16	9	9	0
D:9	20	25	24	6		H:9	22	11	14	6
D:10	35	5	33	8		H:10	14	14	13	0
D:11	5	0	2	0		H:11	18	18	17	5
D:12	0	0	0	0		H:12	15	11	6	0

Reaction conditions: 5.0 μmol of **1**, 2.0 equiv oxime, 2.5 equiv of Cs_2CO_3, 5 mol % CuI and ligand, DMSO (25 μL, 0.2 M), 80 °C, 18 h. Yields were determined by HPLC against an authentic product standard.

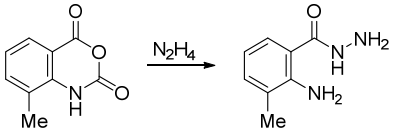
Yields for the conversion of 1 to 2 with ligands related to L4 (Scheme 3)



R=
1-napthylmethyl: 75%
3,5-dimethoxybenzyl: 78%
3,4,5-trimethoxybenzyl:71%
1-phenylethyl: 65%
cyclohexyl: 55%
cyclohexylmethyl: 74%
4-dimethylaminobenzyl: 74%
1-pyrrolidinyl: 58%
2-pyridylmethyl: 55%
Tertiary amide derived from piperidine: 7%

Synthesis of Ligand L4

Step 1:

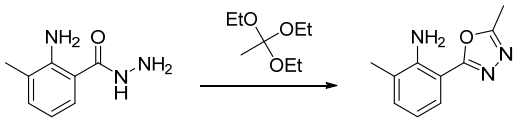


3-methyl isatoic anhdyride (6.50 g, 36.7 mmol, 1.00 equiv, CAS #66176-17-8) was suspended in 100 mL of EtOH. Hydrazine (35% solution in water, 5.00 equiv) was added at once and the resulting reaction mixture was aged at room temperature for 1 h. The reaction mixture was concentrated to ~20 mL on a rotovap, during which time a white solid formed. The solid was collected via filtration and washed 3 x 20 mL MTBE to afford a white solid (4.75 g, 78% yield).

^{1}H NMR (500 MHz, Methanol-d4) δ 7.28 (dd, J = 8.0, 1.4 Hz, 1H), 7.19 – 7.06 (m, 1H), 6.59 (t, J = 7.6 Hz, 1H), 4.86 (s, 5 N-H bonds, overlapping with H_2O peak), 2.17 (s, 3H).

^{13}C NMR (126 MHz, Methanol-d4) δ 170.47, 146.50, 132.67, 125.28, 123.63, 115.79, 114.71, 16.25.

Step 2:

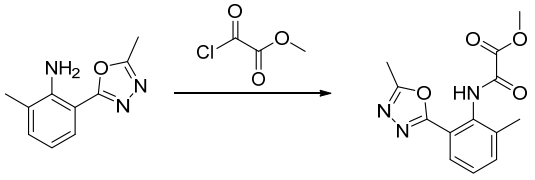


The product from step 1 (4.70 g, 28.5 mmol) was mixed with anhydrous digylme (60 mL) and triethyl orthoacetate (31.3 mmol, 1.1 equiv) at 140°C for 12 h. The reaction mixture was cooled to room temperature and poored into 500 mL of water with rapid stirring, and the resulting slurry was aged at room temperature for 20 minutes. The solid was collected and washed 3 x 40 mL water, then dried under vacuum with a nitrogen sweep to afford a white solid (2.88 g, 54% yield).

^{1}H NMR (500 MHz, Methanol-d4) δ 7.62 (dd, J = 7.9, 1.4 Hz, 1H), 7.19 (d, J = 7.1 Hz, 1H), 6.68 (t, J = 7.6 Hz, 1H), 4.85 (s, 2 N-H bonds, overlapping with H_2O peak), 2.62 (s, 3H), 2.24 (s, 3H).

^{13}C NMR (126 MHz, Methanol-d4) δ 165.35, 162.52, 145.66, 132.86, 125.23, 123.13, 115.84, 104.74, 16.34, 9.11.

Step 3:

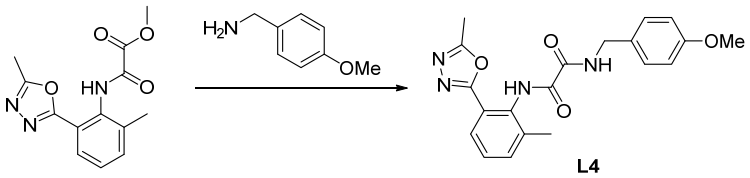


The product from step 2 (2.80 g, 14.8 mmol) was dissolved in 74 mL of anhydrous THF (0.2 M) and treated with triethylamine (1.2 equiv). The resulting solution was cooled to -40°C. Methyl chlorooxoacetate (1.1 equiv) was added dropwise over approximately 1 minute. The resulting mixture was aged at -40°C for 10 minutes, and then warmed to room temperature and aged for an additional 10 minutes. MeOH (0.5 equiv) was added to quench any remaining chlorooxoacetate. The mixture was filtered to remove Et_3N-HCl, and the solid was rinsed with MTBE. The filtrate was concentrated to afford a yellow oil, which was purified on silica gel with a gradient of 0-5% MeOH in DCM. Concentration of the fractions afforded a colorless oil, which was mixed with heptane and reconcentrated to afford a white solid (3.7 g, 91% yield).

^{1}H NMR (500 MHz, Methanol-d4) δ 7.88 (dd, J = 7.8, 1.5 Hz, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.51 – 7.41 (m, 1H), 4.85 (N-H bond), 3.98 (s, 3H), 2.60 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (126 MHz, Methanol-d4) δ 164.31, 163.44, 160.31, 156.58, 137.39, 133.79, 132.49, 127.83, 126.57, 120.82, 52.62, 17.07, 9.19.

Step 4:



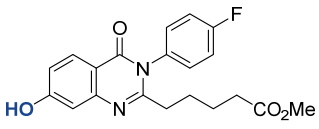
The product from step 3 (2.75 g, 10.0 mmol) was treated with THF (20 mL, 0.5 M) and 4-methoxybenzylamine (12.0 mmol, 1.20 equiv) at 65°C for 30 minutes. The reaction mixture was cooled to room temperature and concentrated to an oil. The oil was mixed well with 50 mL of MTBE to afford a slurry. The solid was collected and washed 2 x 15 mL MTBE to afford a white solid (3.65 g, 96% yield).

^{1}H NMR (500 MHz, DMSO-d6) δ 10.53 (s, 1H), 9.36 (t, J = 6.4 Hz, 1H), 7.79 (dd, J = 8.0, 1.5 Hz, 1H), 7.60 – 7.48 (m, 1H), 7.42 (t, J = 7.7 Hz, 1H), 7.33 – 7.18 (m, 2H), 6.94 – 6.83 (m, 2H), 4.31 (d, J = 6.5 Hz, 2H), 3.74 (s, 3H), 2.44 (s, 3H), 2.25 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d6) δ 163.83, 163.40, 159.93, 159.83, 158.82, 137.38, 133.99, 131.20, 129.38, 127.87, 127.14, 121.66, 114.18, 55.55, 42.45, 18.56, 10.83.

HRMS calculated (M+1): 381.1563
HRMS observed (M+1): 381.1554

Synthesis of 4s



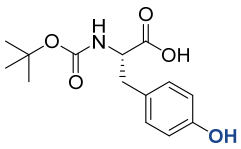
The compound was prepared using the standard procedure on 1.0 mmol scale. The product was purified on silica gel with a gradient of 0-10% methanol in dichloromethane, and obtained as a white solid (296 mg, 80% yield).

^{1}H NMR (500 MHz, Methanol-d4) δ 8.04 (d, J = 8.7 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.38 – 7.29 (m, 2H), 7.06 – 6.96 (m, 2H), 3.64 (s, 3H), 2.52 – 2.40 (m, 2H), 2.26 (t, J = 7.2 Hz, 2H), 1.75 – 1.64 (m, 2H), 1.56 (p, J = 7.3 Hz, 2H).

^{13}C NMR (126 MHz, Methanol-d4) δ 174.07, 163.86, 163.79, 162.51, 161.89, 157.53, 149.49, 133.24 (d, J = 3.4 Hz), 130.59 (d, J = 8.9 Hz), 128.24, 127.66 (d, J = 110.4 Hz), 112.49, 109.79, 50.59, 34.90, 32.77, 26.01, 23.95.

HRMS calculated (M+1): 371.1407
HRMS observed (M+1): 371.1401

Synthesis of 4t



The compound was prepared using the standard procedure on 1.0 mmol scale. The product was purified on silica gel with a gradient of 0-10% methanol in dichloromethane, and obtained as a white solid (176 mg, 63% yield).

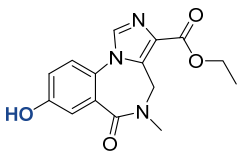
Note: The NMR spectra are complicated due to the presence of N-Boc rotamers

^{1}H NMR (500 MHz, Methanol-d_4) δ 7.05 (d, J = 8.4 Hz, 2H), 6.72 (dd, J = 9.0, 2.7 Hz, 2H), 4.30 m, 1H), 3.06 (m, 1H), 2.84 (m, 1H), 1.41 (9H).

^{13}C NMR (126 MHz, Methanol-d_4) δ 174.14, 156.38, 155.85, 129.89, 127.81, 114.74, 79.10, 55.11, 36.54, 27.28.

HRMS calculated (M+1): 282.1341
HRMS observed (M+1): 282.1333

Synthesis of 4u



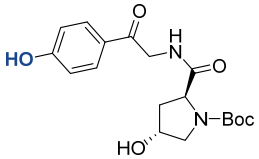
The compound was prepared using the standard procedure on 1.0 mmol scale. The product was purified on silica gel with a gradient of 0-10% methanol in dichloromethane, and obtained as a white solid (239 mg, 79% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.20 (br, 1H), 8.25 (s, 1H), 7.55 (d, J = 8.7 Hz, 1H), 7.26 (d, J = 2.8 Hz, 1H), 7.09 (dd, J = 8.7, 2.8 Hz, 1H), 4.94 (br, 1H), 4.38 (br, 3H), 3.08 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 166.03, 162.87, 157.42, 136.53, 135.69, 130.27, 127.68, 124.77, 124.31, 120.04, 117.56, 60.45, 42.56, 35.47, 14.69.

HRMS calculated (M+1): 302.1141
HRMS observed (M+1): 302.1149

Synthesis of 4v



The compound was prepared using the standard procedure on 1.0 mmol scale. The product was purified on silica gel with 10% methanol in dichloromethane, and obtained as a white solid (262 mg, 72% yield).

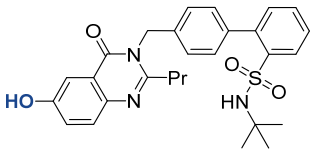
Note: The NMR spectra are complicated due to the presence of N-Boc rotamers

^{1}H NMR (500 MHz, Acetonitrile-d3) δ 7.90 (br, 3H), 7.13 (d, J = 65.2 Hz, 1H), 6.99 – 6.86 (m, 2H), 4.60 (dd, J = 9.6, 4.9 Hz, 2H), 4.45 – 4.27 (m, 2H), 3.56 – 3.39 (m, 2H), 3.17 (br, 1H), 2.28 – 2.02 (m, 2H), 1.44 (9H).

^{13}C NMR (126 MHz, Acetonitrile-d3) δ 192.77, 173.09, 172.63, 161.93, 155.12, 154.27, 130.41, 127.32, 115.34, 79.50, 69.34, 68.79, 59.63, 59.08, 54.97, 54.66, 45.47, 45.35, 39.55, 38.24, 27.62, 27.47.

HRMS calculated (M+1): 365.1713
HRMS observed (M+1): 365.1704

Synthesis of 4w

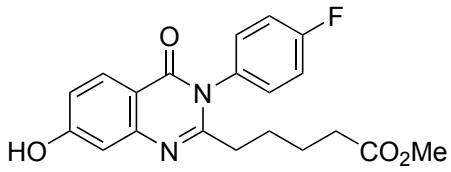


The compound was prepared using the standard procedure on 1.0 mmol scale. The product was purified on silica gel with 10% methanol in dichloromethane, and obtained as a tan solid (423 mg, 84% yield).

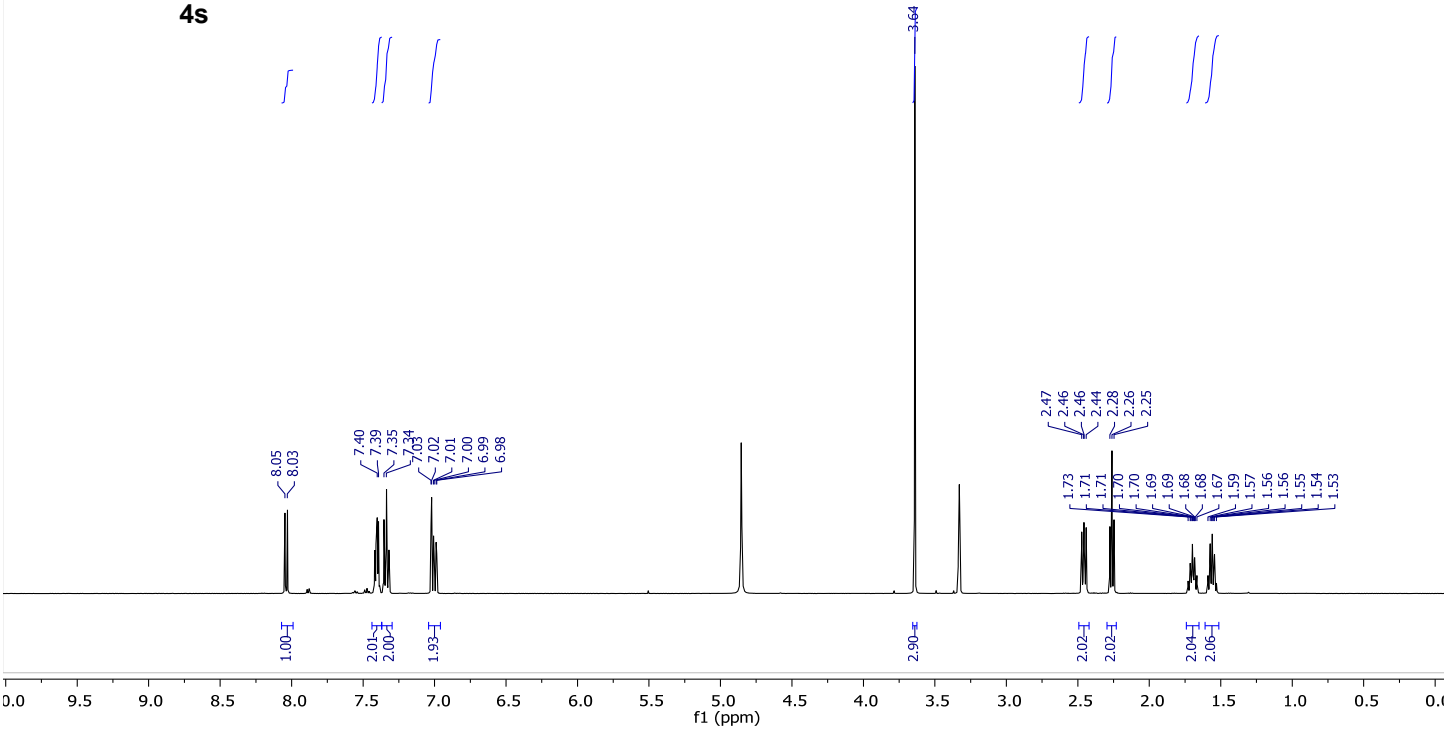
^{1}H NMR (500 MHz, DMSO-d6) δ 10.06 (s, 1H), 8.04 (dd, J = 7.9, 1.4 Hz, 1H), 7.61 (td, J = 7.5, 1.4 Hz, 1H), 7.57 – 7.51 (m, 2H), 7.48 (d, J = 2.8 Hz, 1H), 7.39 (d, J = 8.0 Hz, 2H), 7.31 – 7.26 (m, 2H), 7.19 (d, J = 8.0 Hz, 2H), 6.52 (s, 1H), 5.43 (s, 2H), 2.76 – 2.67 (m, 2H), 1.73 (h, J = 7.4 Hz, 2H), 0.94 (m, 12H).

^{13}C NMR (126 MHz, DMSO-d6) δ 161.90, 156.39, 154.28, 142.53, 140.81, 140.06, 139.20, 136.45, 133.03, 132.19, 130.09, 129.01, 128.52, 128.17, 125.98, 124.46, 121.25, 109.60, 53.82, 45.80, 36.02, 29.75 (d, J = 3.3 Hz), 19.96, 14.04.

HRMS calculated (M+1): 506.2114
HRMS observed (M+1): 506.2120


O
F
N
HO
N
CO2Me

4s


8.05
8.03
7.40
7.39
7.35
7.34
7.03
7.02
7.01
7.00
6.99
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2.47
2.46
2.46
2.44
2.28
2.26
2.25
1.73
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1.70
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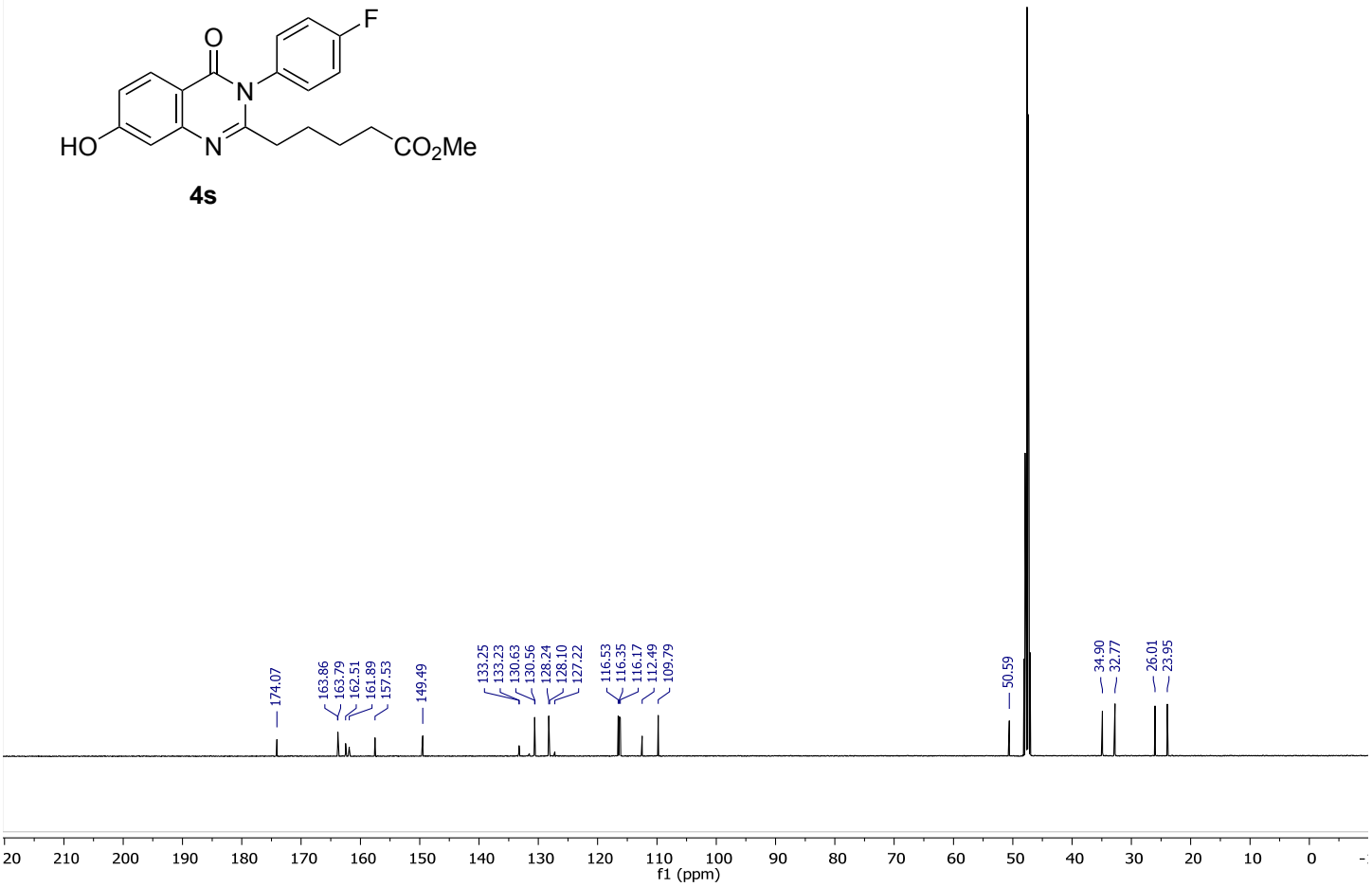
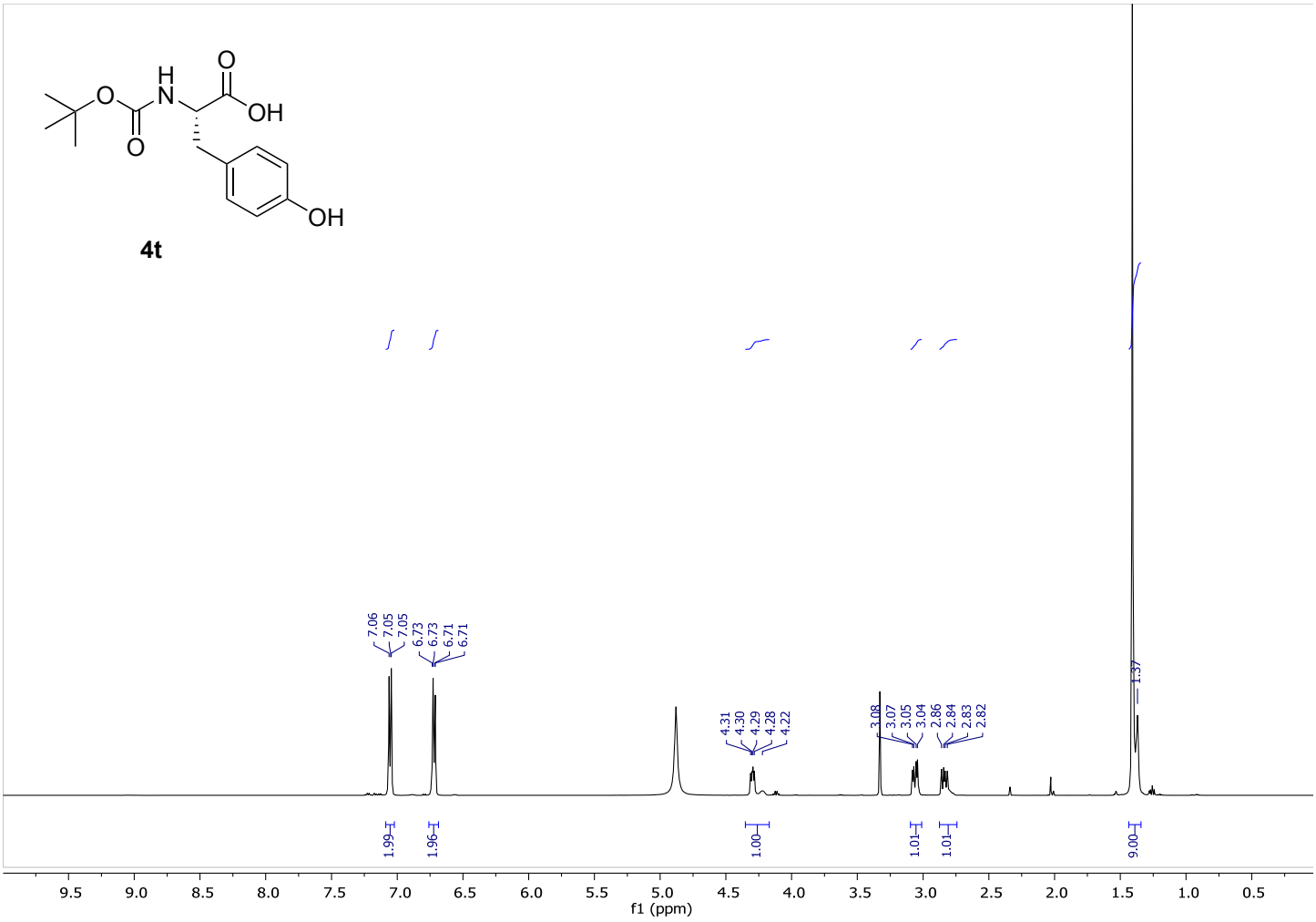
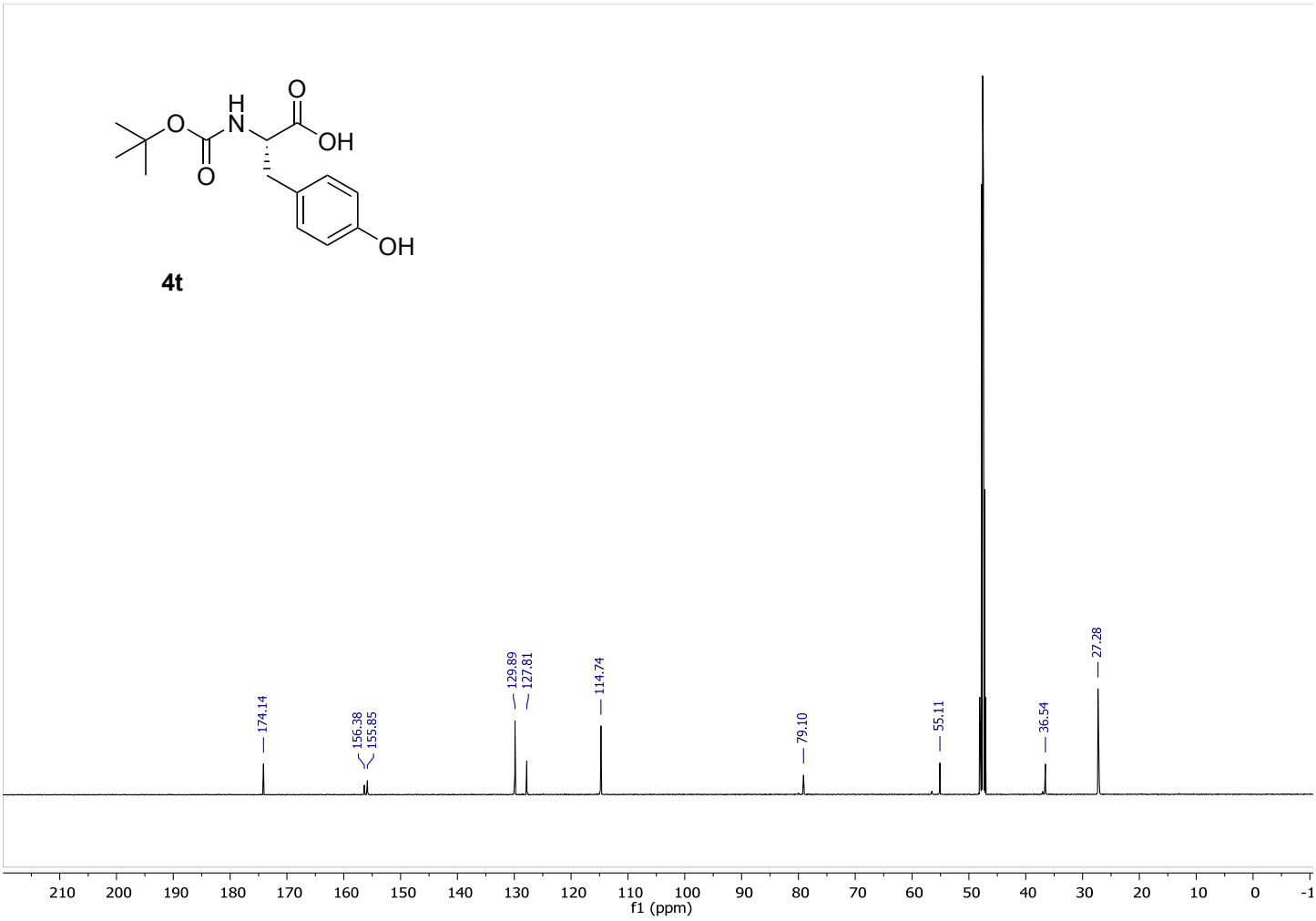
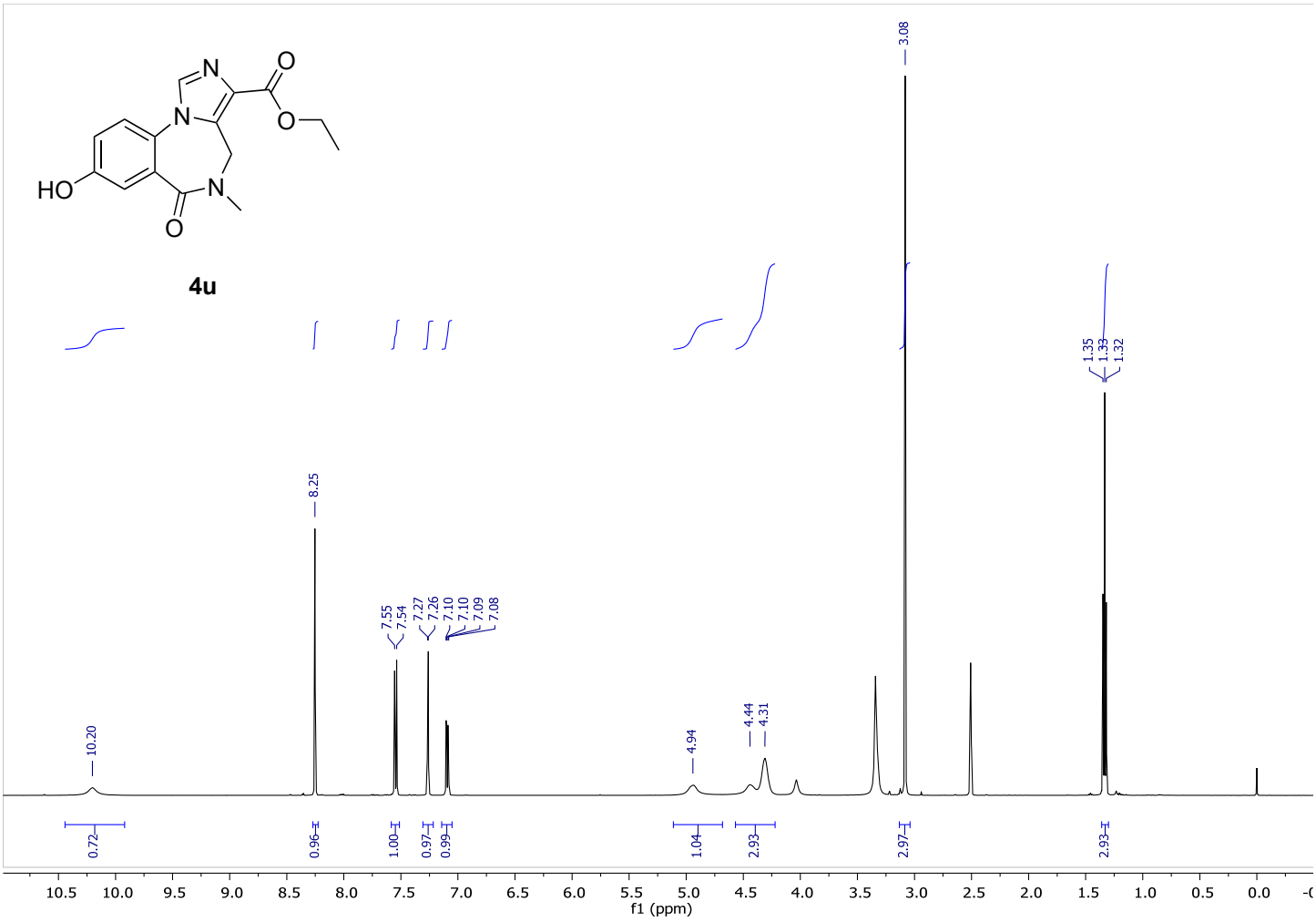
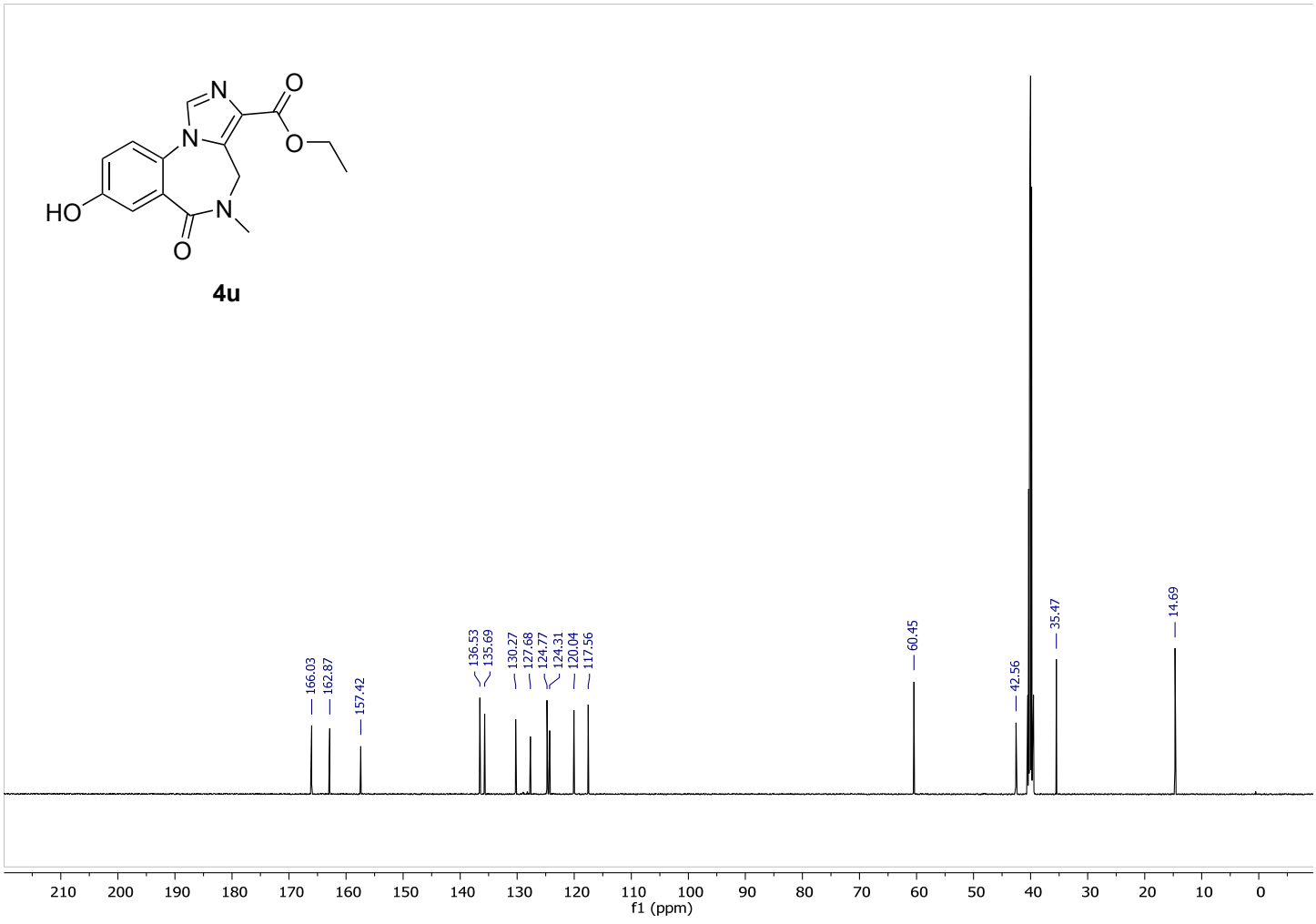
1.56
1.55
1.54
1.53
1.00
2.01
2.00
1.93
2.90
2.02
2.02
2.04
2.06
f1 (ppm)


O
F
N
HO
N
CO2Me
4s
174.07
163.86
163.79
162.51
161.89
157.53
149.49
133.25
133.23
130.63
130.56
128.24
128.10
127.22
116.53
116.35
116.17
112.49
109.79
50.59
34.90
32.77
26.01
23.95
f1 (ppm)

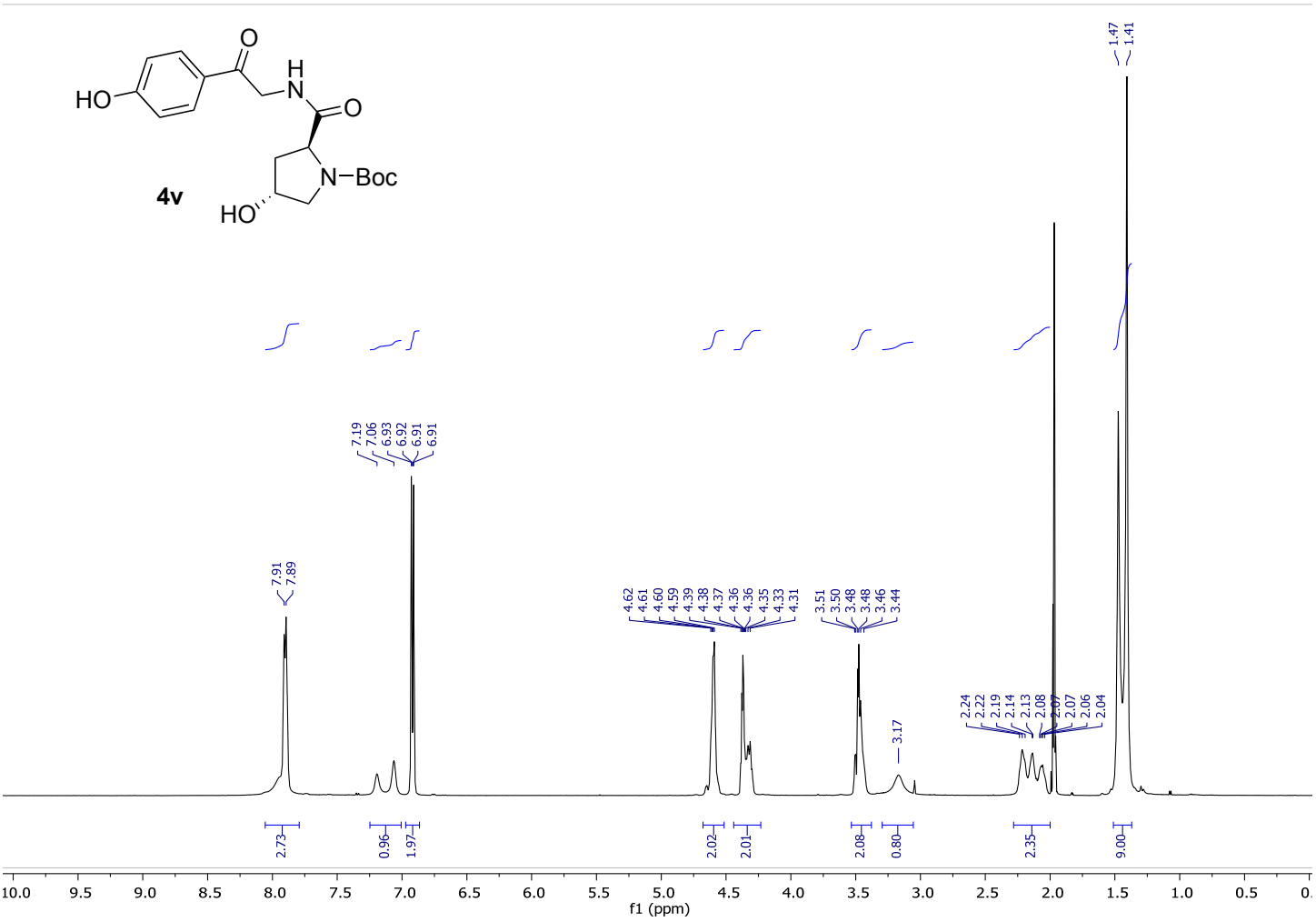

4t
7.06
7.05
7.05
6.73
6.73
6.71
6.71
4.31
4.30
4.29
4.28
4.22
3.08
3.07
3.05
3.04
2.86
2.84
2.83
2.82
1.37
1.99
1.96
1.00
1.01
1.01
9.00
f1 (ppm)


O
H
N
O
OH
O
OH
4t
174.14
156.38
155.85
129.89
127.81
114.74
79.10
55.11
36.54
27.28
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

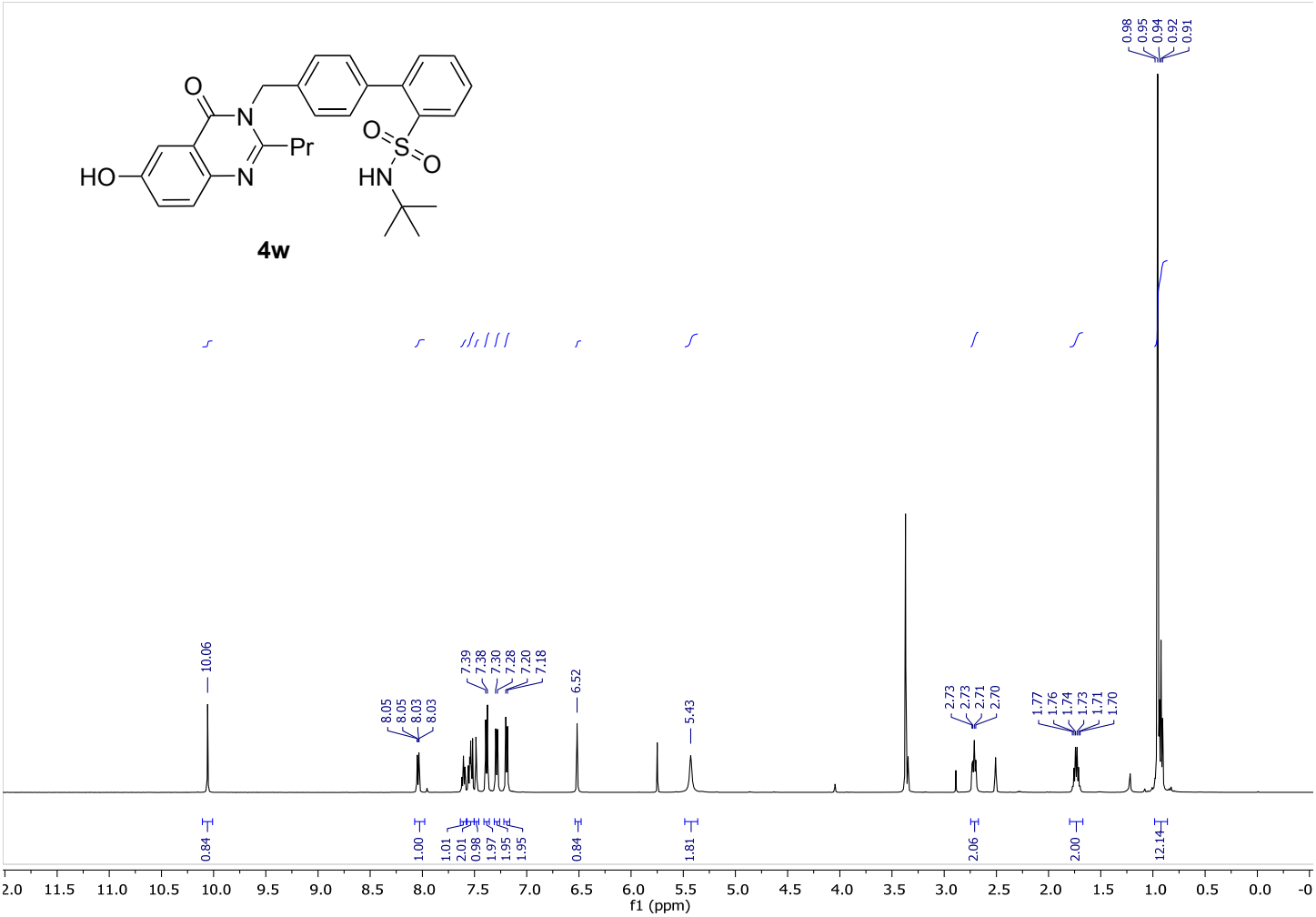

HO
N
N
O
O
N
O
4u
3.08
8.25
7.55
7.54
7.27
7.26
7.10
7.10
7.09
7.08
10.20
4.94
4.44
4.31
1.35
1.33
1.32
0.72
0.96
1.00
0.97
0.99
1.04
2.93
2.97
2.93
f1 (ppm)

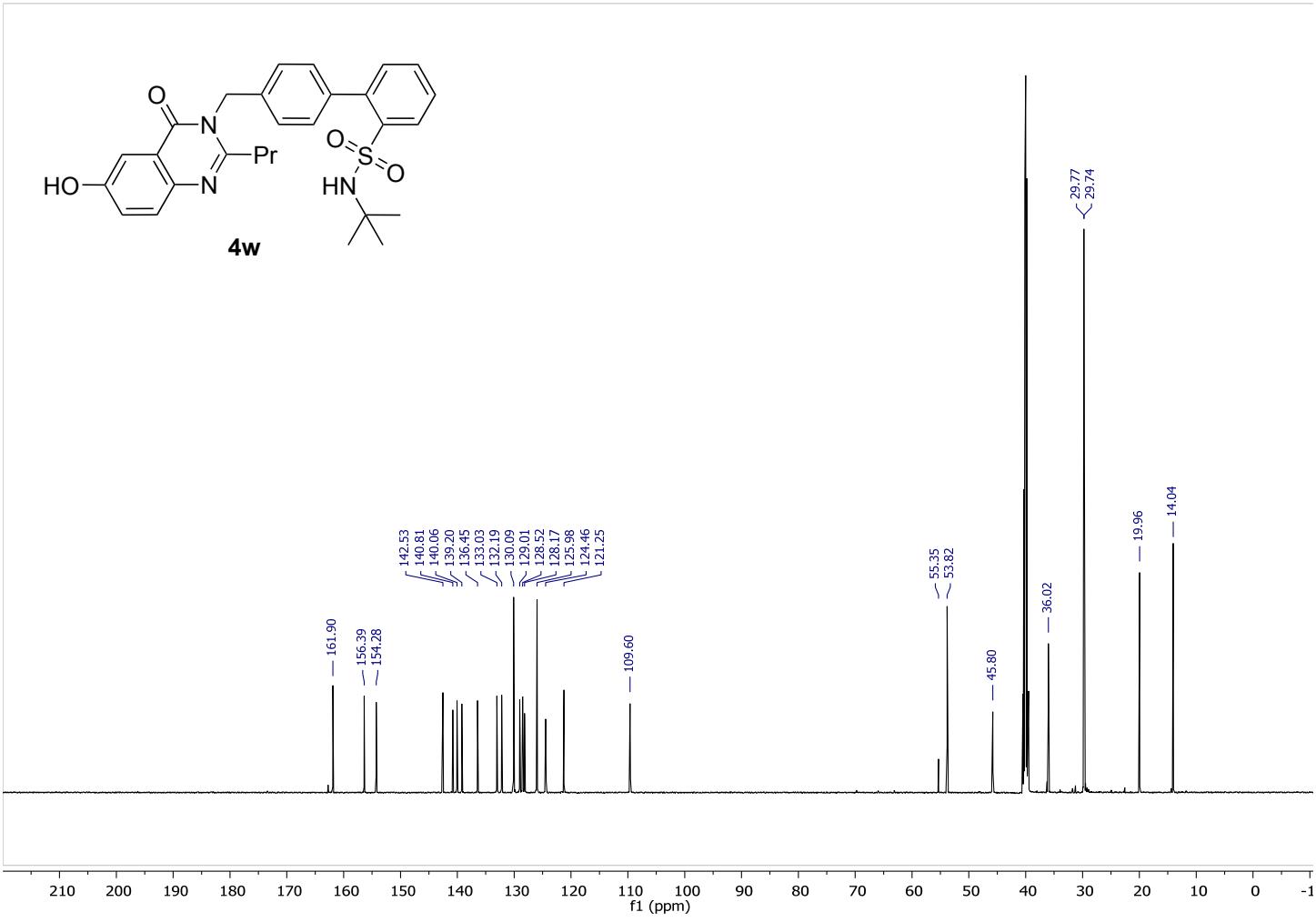

HO
N
N
O
O
O
N
O
166.03
162.87
157.42
136.53
135.69
130.27
127.68
124.77
124.31
120.04
117.56
60.45
42.56
35.47
14.69
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

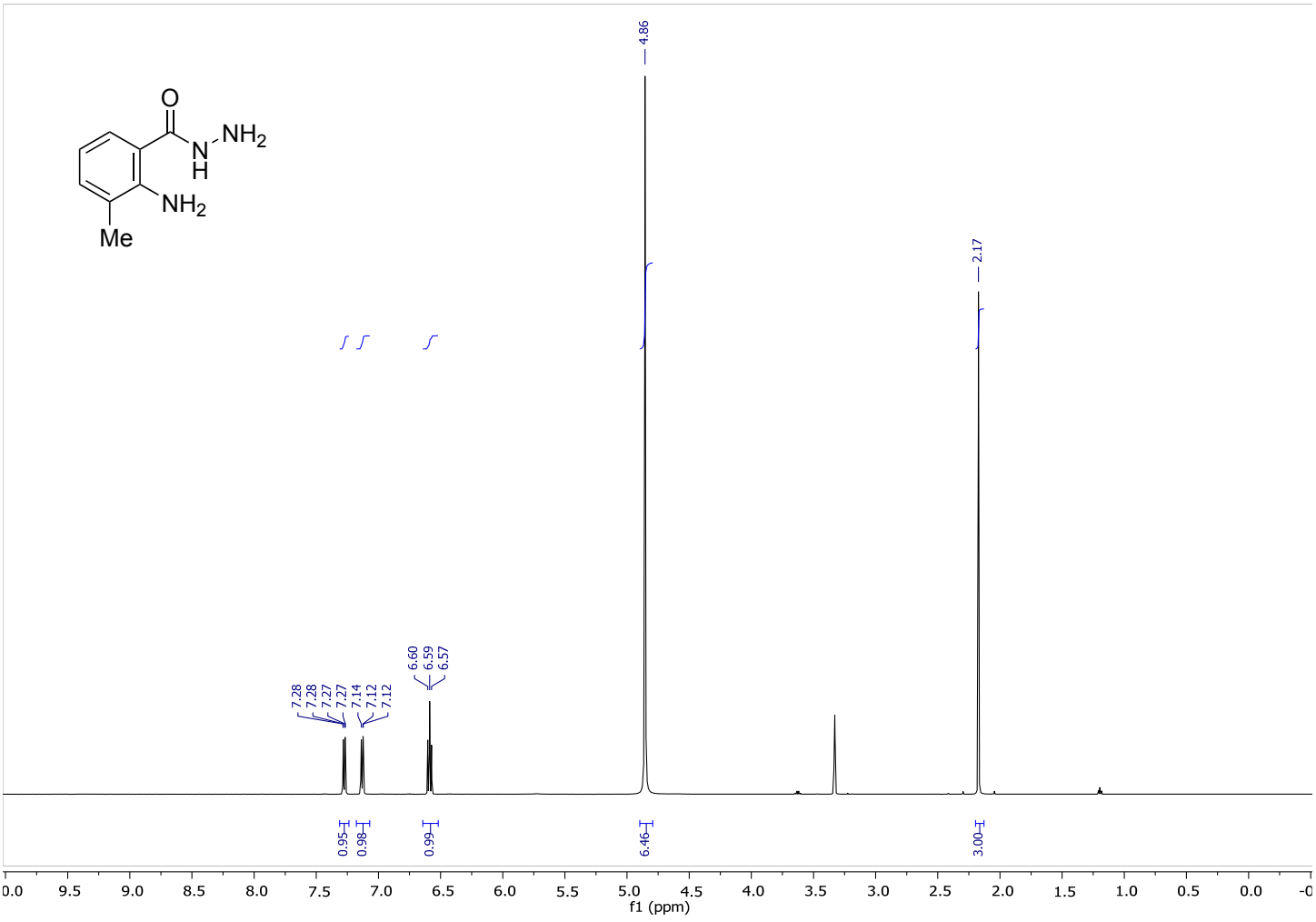
4u

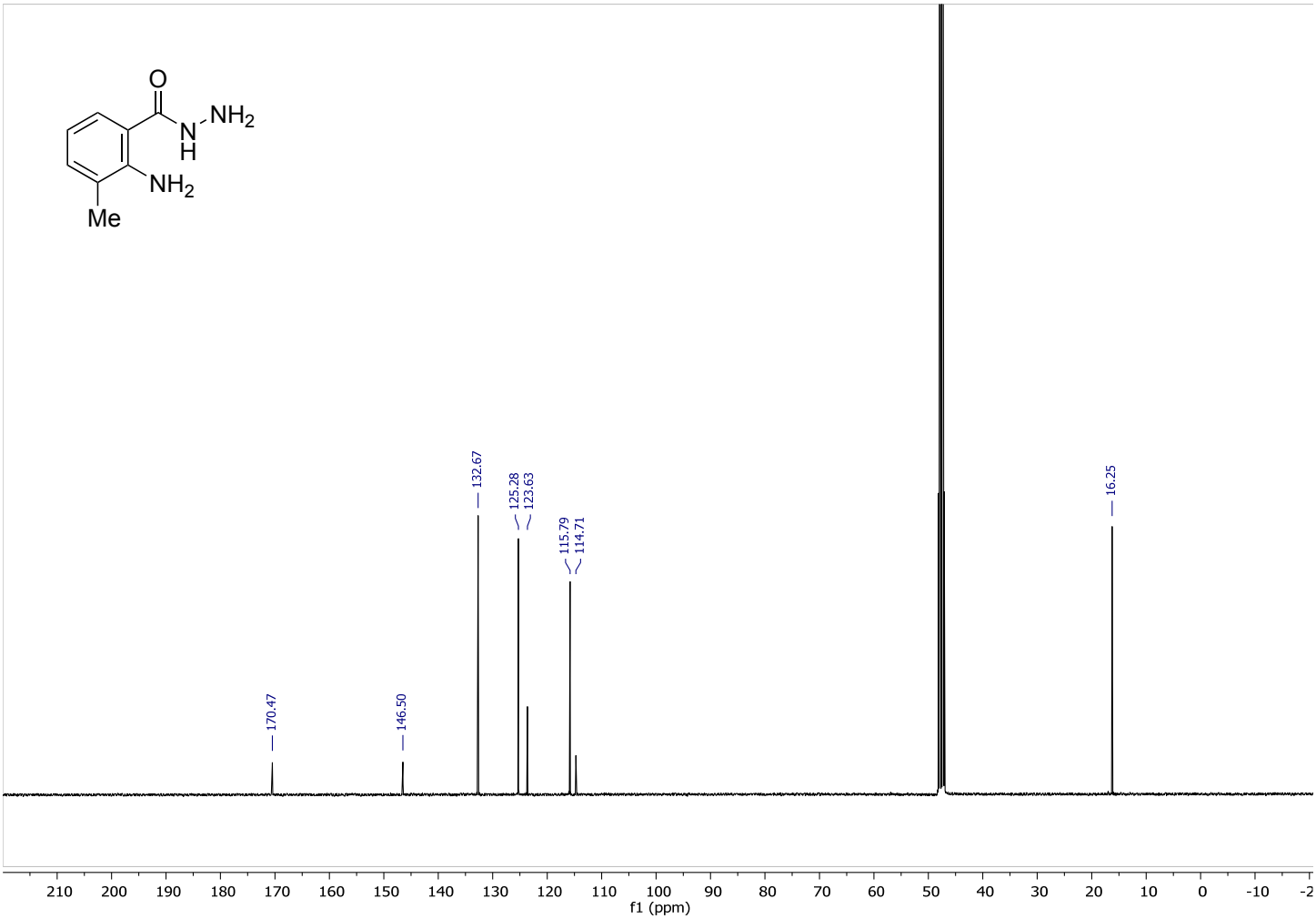

HO
O
H
N
O
N−Boc
HO
4v
1.47
1.41
7.19
7.06
6.93
6.92
6.91
6.91
7.91
7.89
4.62
4.61
4.60
4.59
4.39
4.38
4.37
4.36
4.36
4.35
4.33
4.31
3.51
3.50
3.48
3.48
3.46
3.44
3.17
2.24
2.22
2.19
2.14
2.13
2.08
2.07
2.07
2.06
2.04
2.73
0.96
1.97
2.02
2.01
2.08
0.80
2.35
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

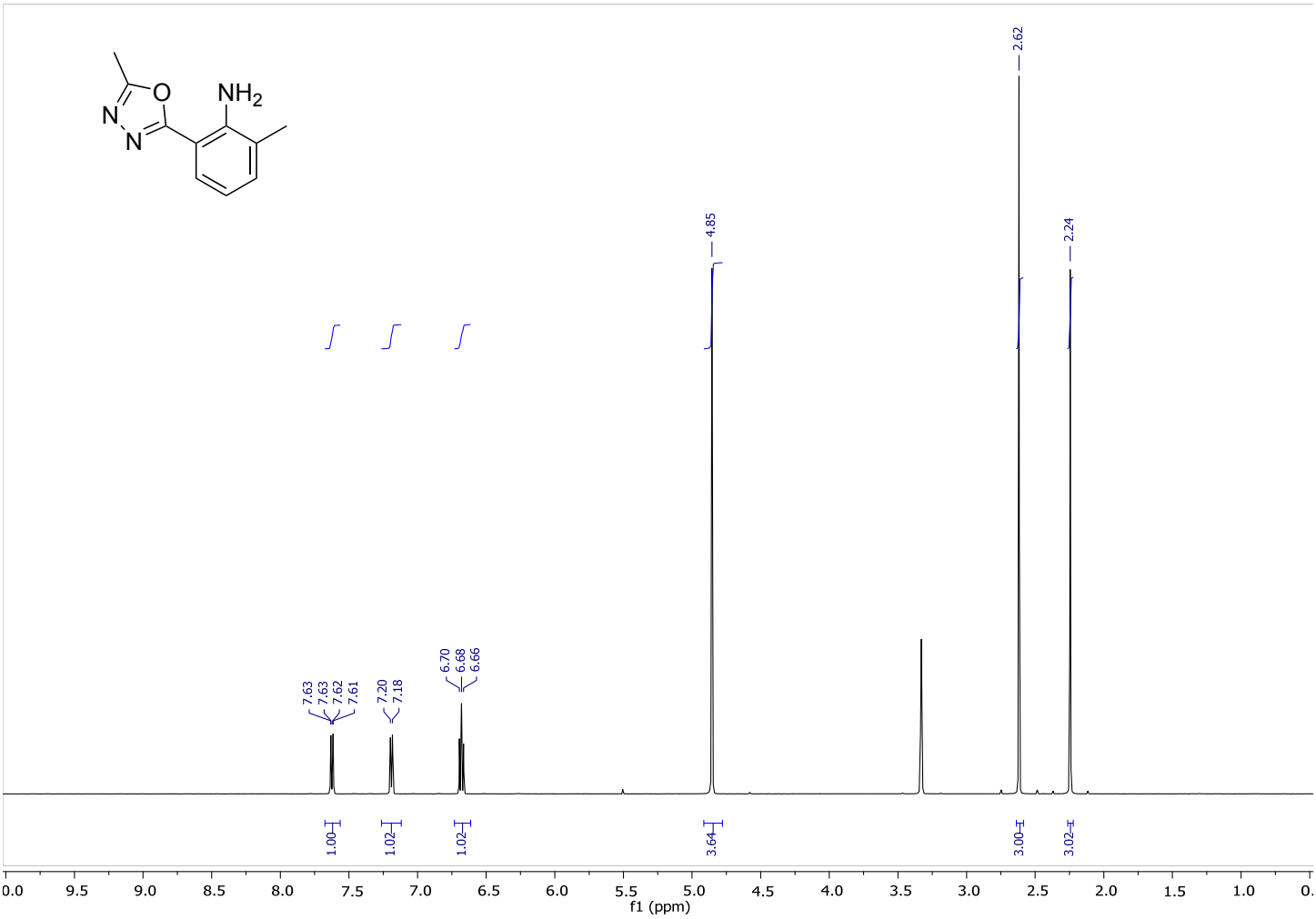

HO
O
H
N
O
N−Boc
HO
4v
192.77
173.09
172.63
161.93
155.12
154.27
130.41
127.32
115.34
79.50
69.34
68.79
59.63
59.08
54.97
54.66
45.47
45.35
39.55
38.24
27.62
27.47
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

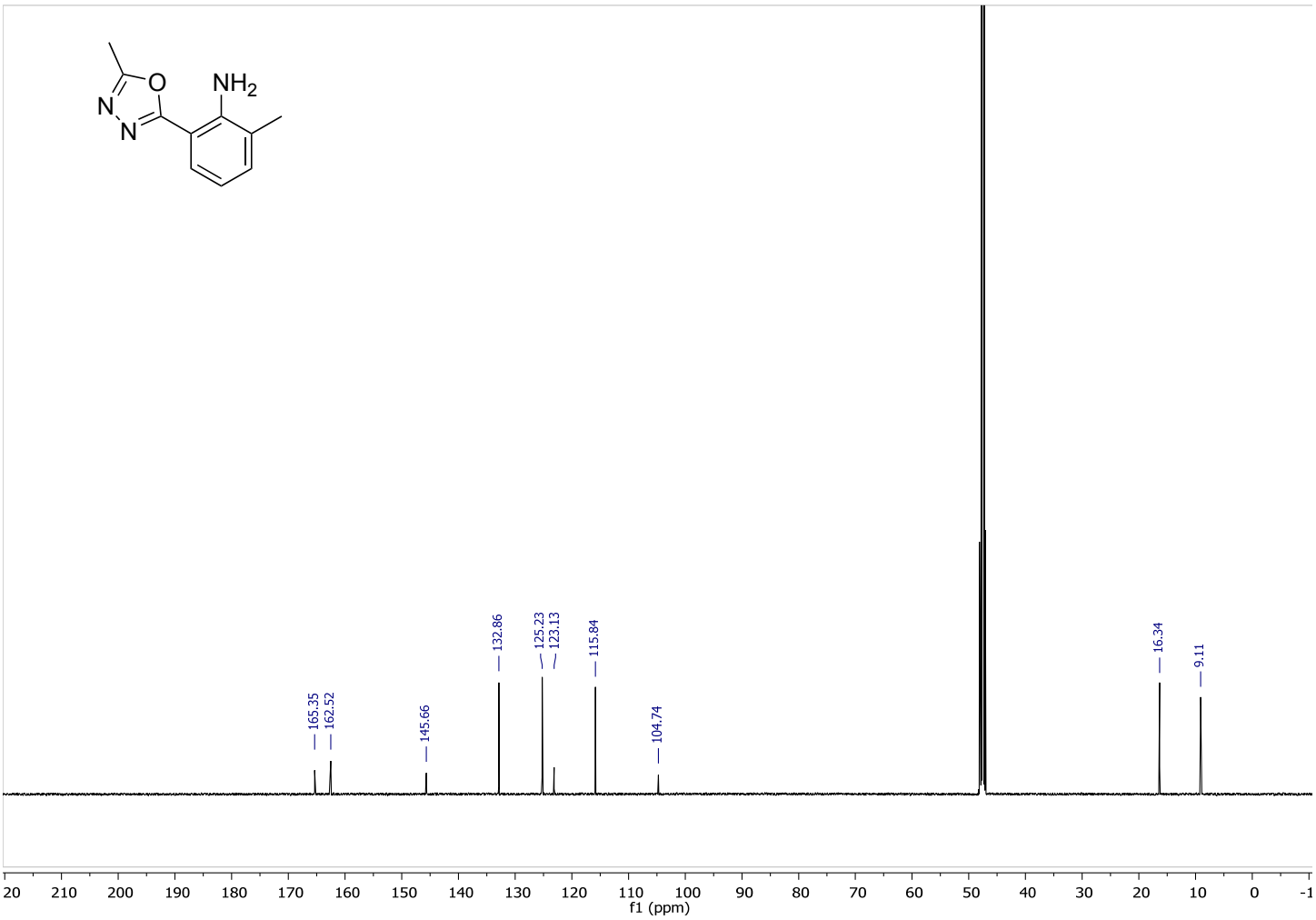

O
N
Pr
HO
N
O
S
O
HN
4w
0.98
0.95
0.94
0.92
0.91
10.06
8.05
8.05
8.03
8.03
7.39
7.38
7.30
7.28
7.20
7.18
6.52
5.43
2.73
2.73
2.71
2.70
1.77
1.76
1.74
1.73
1.71
1.70
0.84
1.00
1.01
2.01
0.98
1.97
1.95
1.95
0.84
1.81
2.06
2.00
12.14
f1 (ppm)

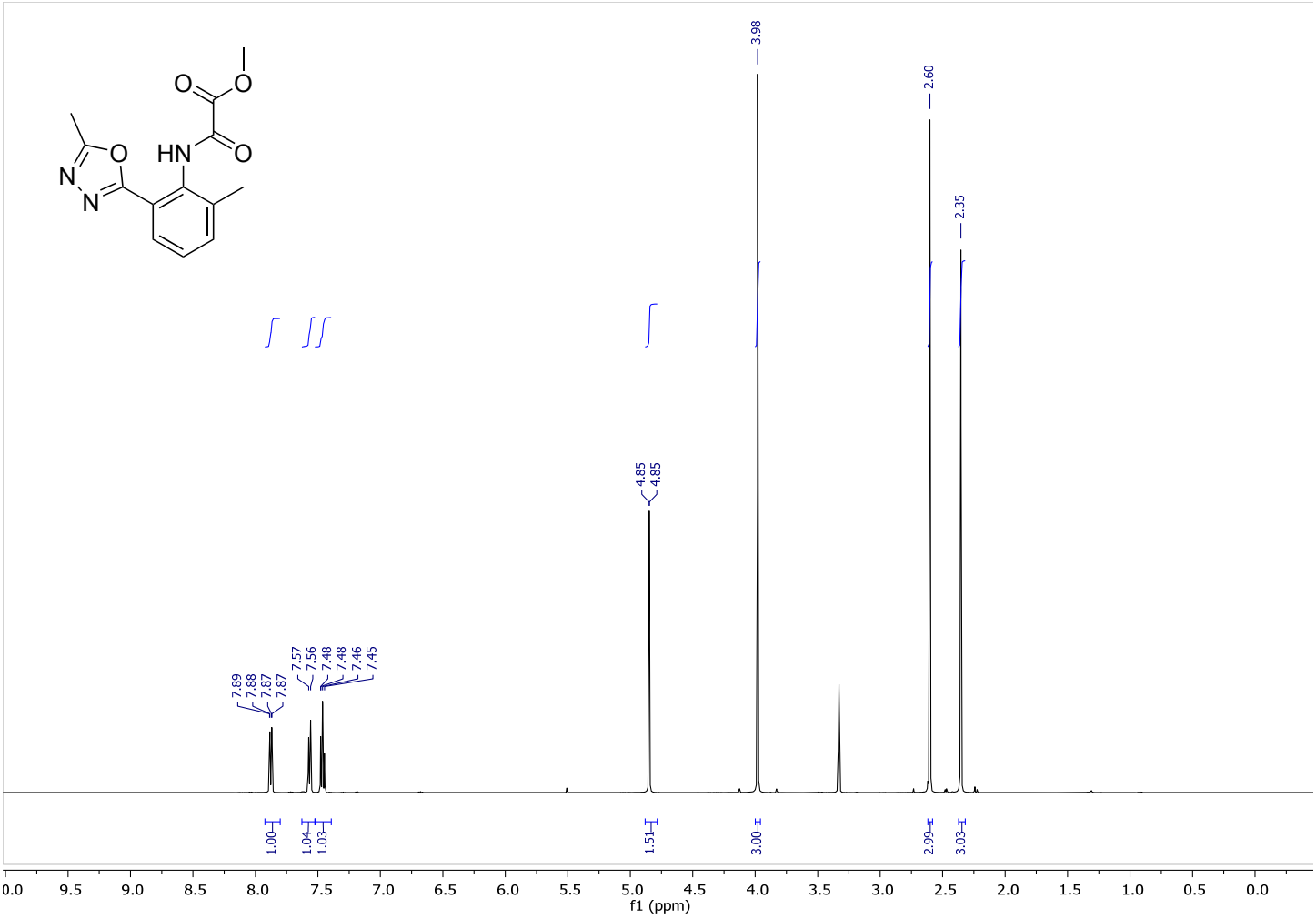

O
N
Pr
HO
N
O
S
O
HN
4w
161.90
156.39
154.28
142.53
140.81
140.06
139.20
136.45
133.03
132.19
130.09
129.01
128.52
128.17
125.98
124.46
121.25
109.60
55.35
53.82
45.80
36.02
29.77
29.74
19.96
14.04
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

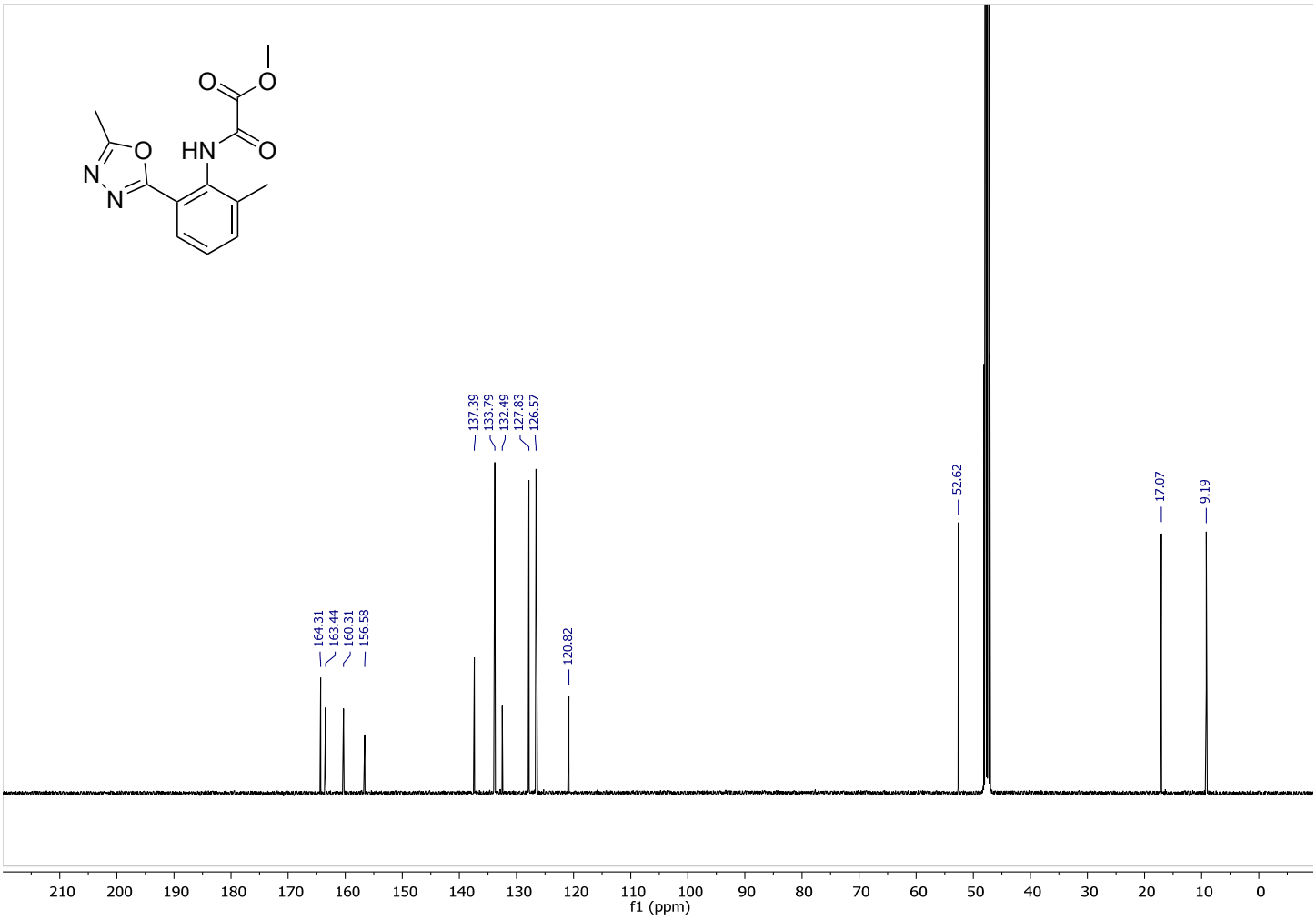

O
NH2
N
H
NH2
Me
4.86
2.17
7.28
7.28
7.27
7.27
7.14
7.12
7.12
6.60
6.59
6.57
0.95
0.98
0.99
6.46
3.00
f1 (ppm)

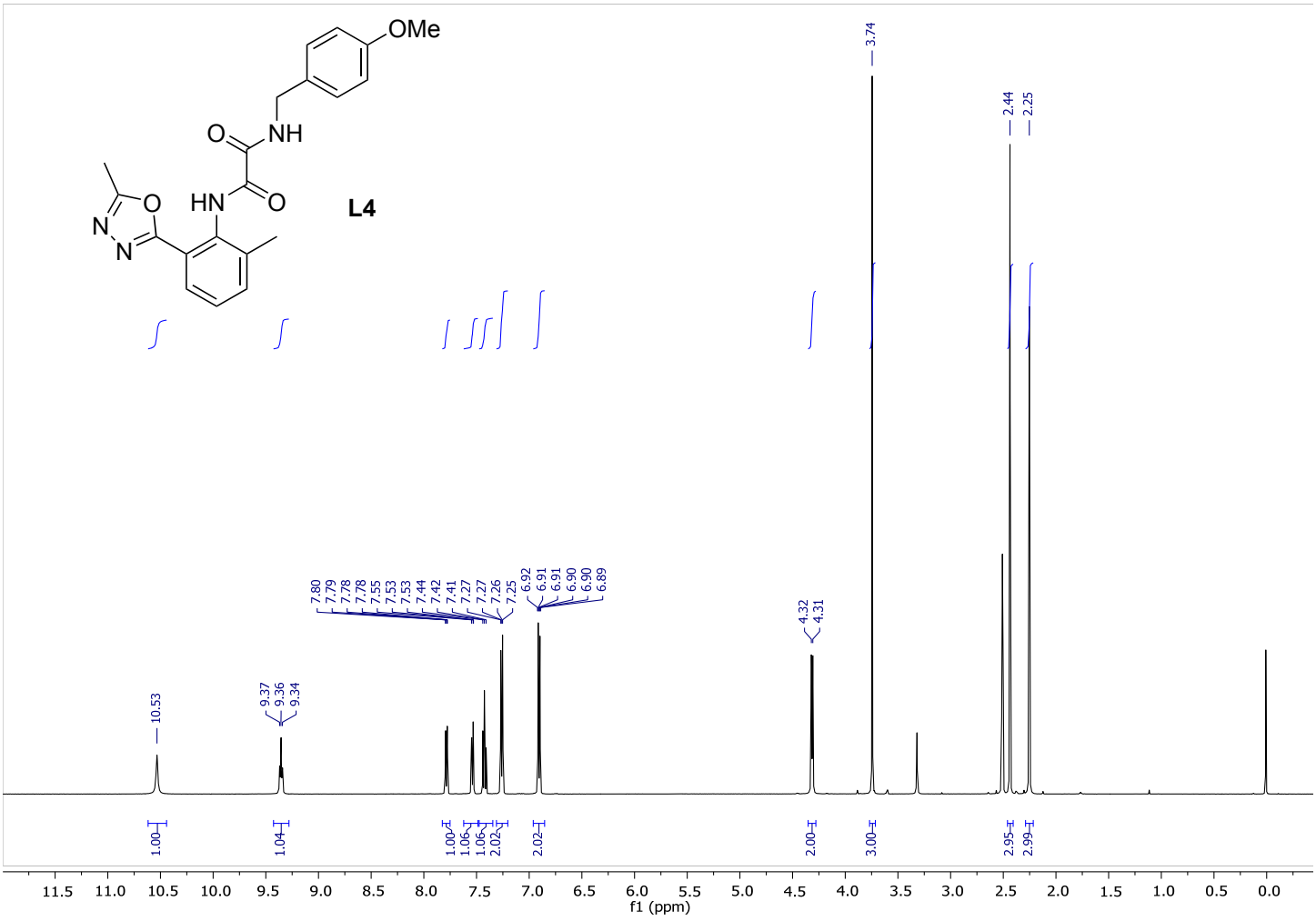

O
NH2
N
H
NH2
Me
170.47
146.50
132.67
125.28
123.63
115.79
114.71
16.25
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -2
f1 (ppm)

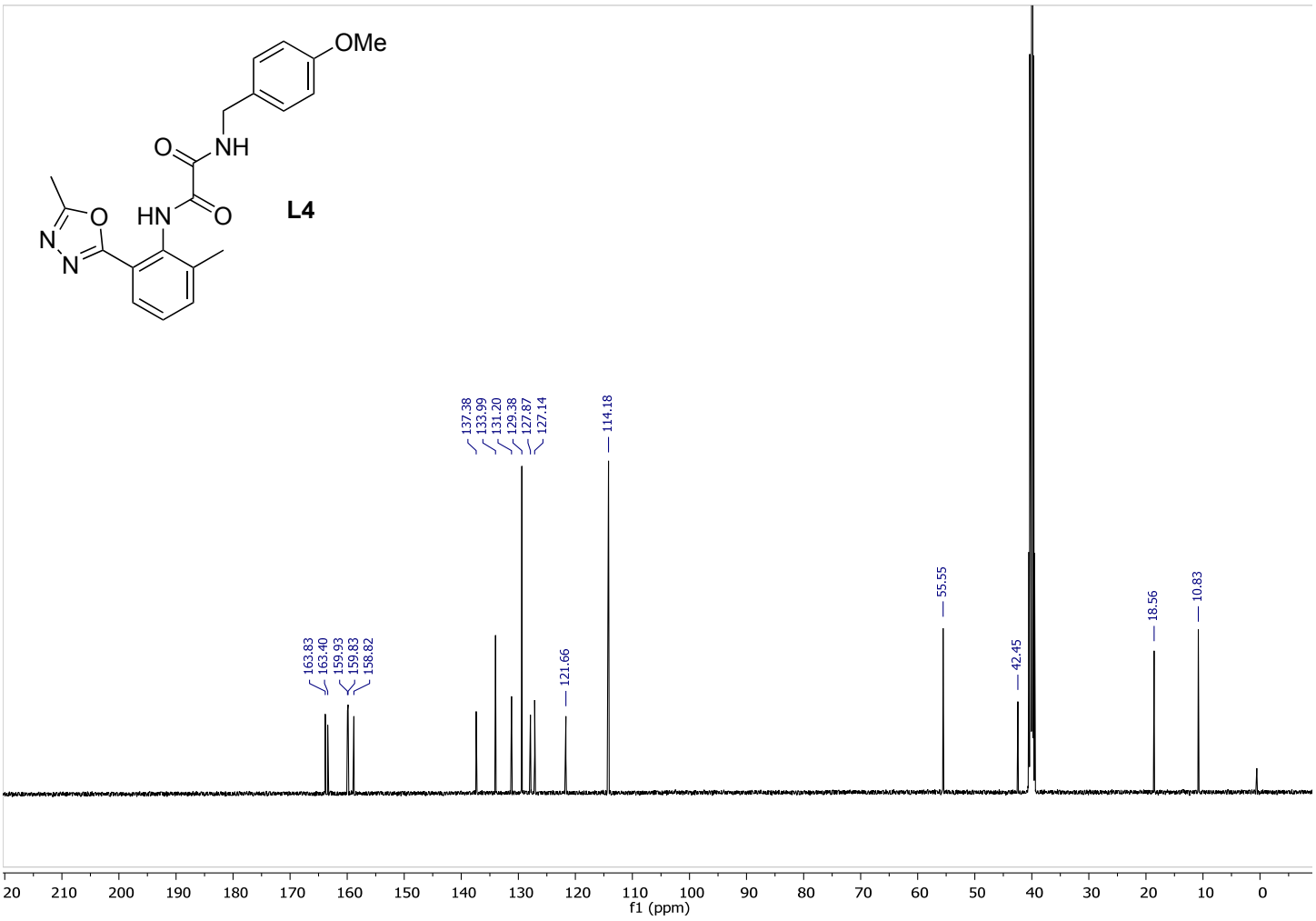

NH2
O
N
N
2.62
4.85
2.24
7.63
7.63
7.62
7.61
7.20
7.18
6.70
6.68
6.66
1.00
1.02
1.02
3.64
3.00
3.02
f1 (ppm)


NH2
O
N
N
165.35
162.52
145.66
132.86
125.23
123.13
115.84
104.74
16.34
9.11
f1 (ppm)


O
O
HN
O
N
N
O
3.98
2.60
2.35
4.85
4.85
7.89
7.88
7.87
7.87
7.57
7.56
7.48
7.48
7.46
7.45
1.00
1.04
1.03
1.51
3.00
2.99
3.03
f1 (ppm)


O
O
HN
O
O
N
N
164.31
163.44
160.31
156.58
137.39
133.79
132.49
127.83
126.57
120.82
52.62
17.07
9.19
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


OMe
O
NH
HN
O
O
N
N
O
L4
3.74
2.44
2.25
7.80
7.79
7.78
7.78
7.55
7.53
7.53
7.44
7.42
7.41
7.27
7.27
7.26
7.25
6.92
6.91
6.91
6.90
6.90
6.89
4.32
4.31
10.53
9.37
9.36
9.34
1.00
1.04
1.00
1.06
1.06
2.02
2.02
2.00
3.00
2.95
2.99
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


OMe
O
NH
HN
O
O
N
N
L4
163.83
163.40
159.93
159.83
158.82
137.38
133.99
131.20
129.38
127.87
127.14
121.66
114.18
55.55
42.45
18.56
10.83
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)