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

Supporting Information

Ligand-free, palladacycle-facilitated Suzuki coupling yields potent and selective COX-2 inhibitors

Mohamed S. A. Elsayed, Siran Chang, and Mark Cushman*

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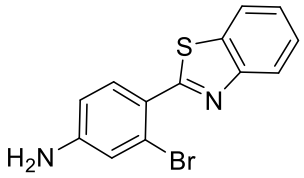
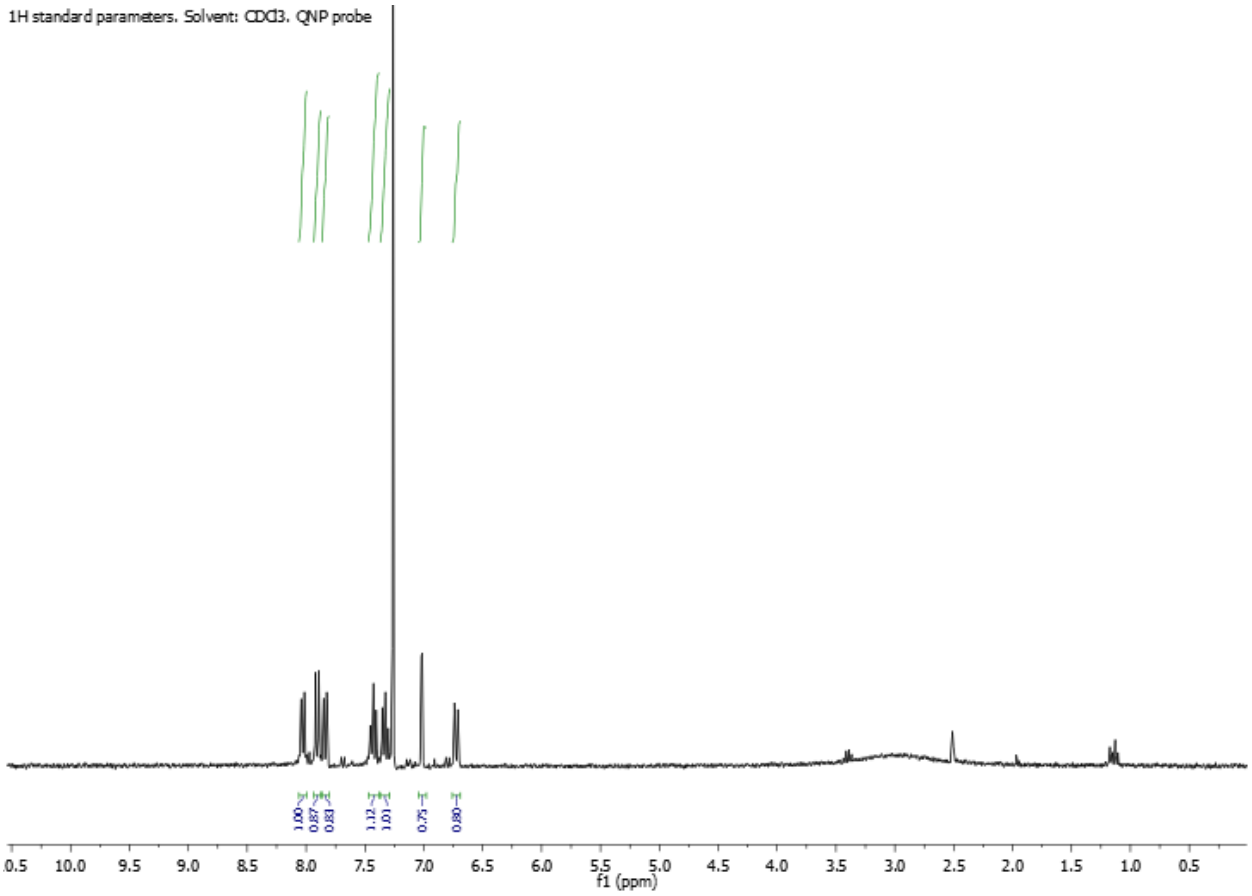

S
N
H2N
Br

6a


1H standard parameters. Solvent: CDCl3. QNP probe
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10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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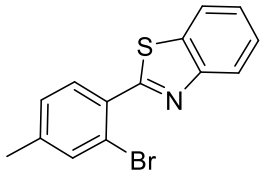
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)



6b

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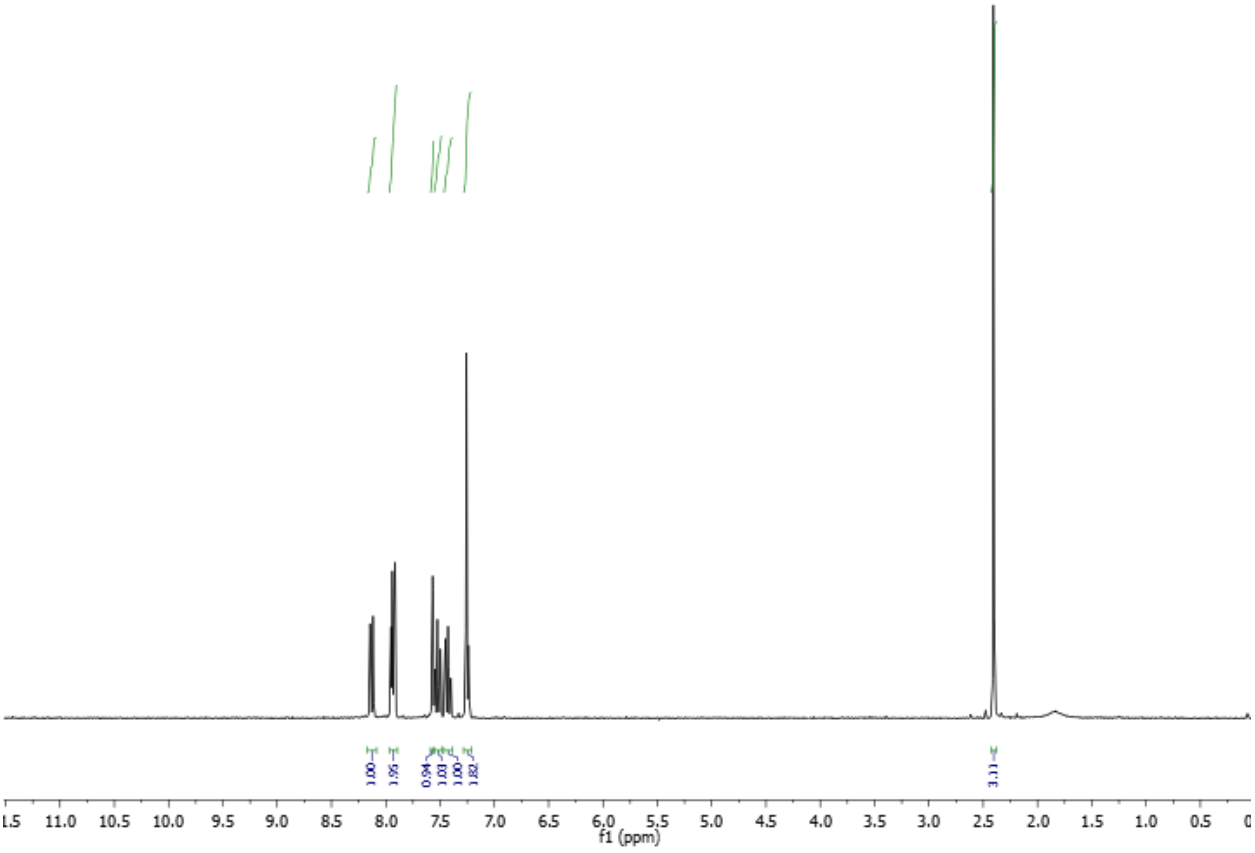
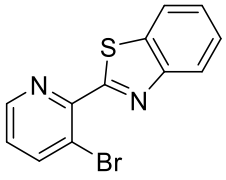
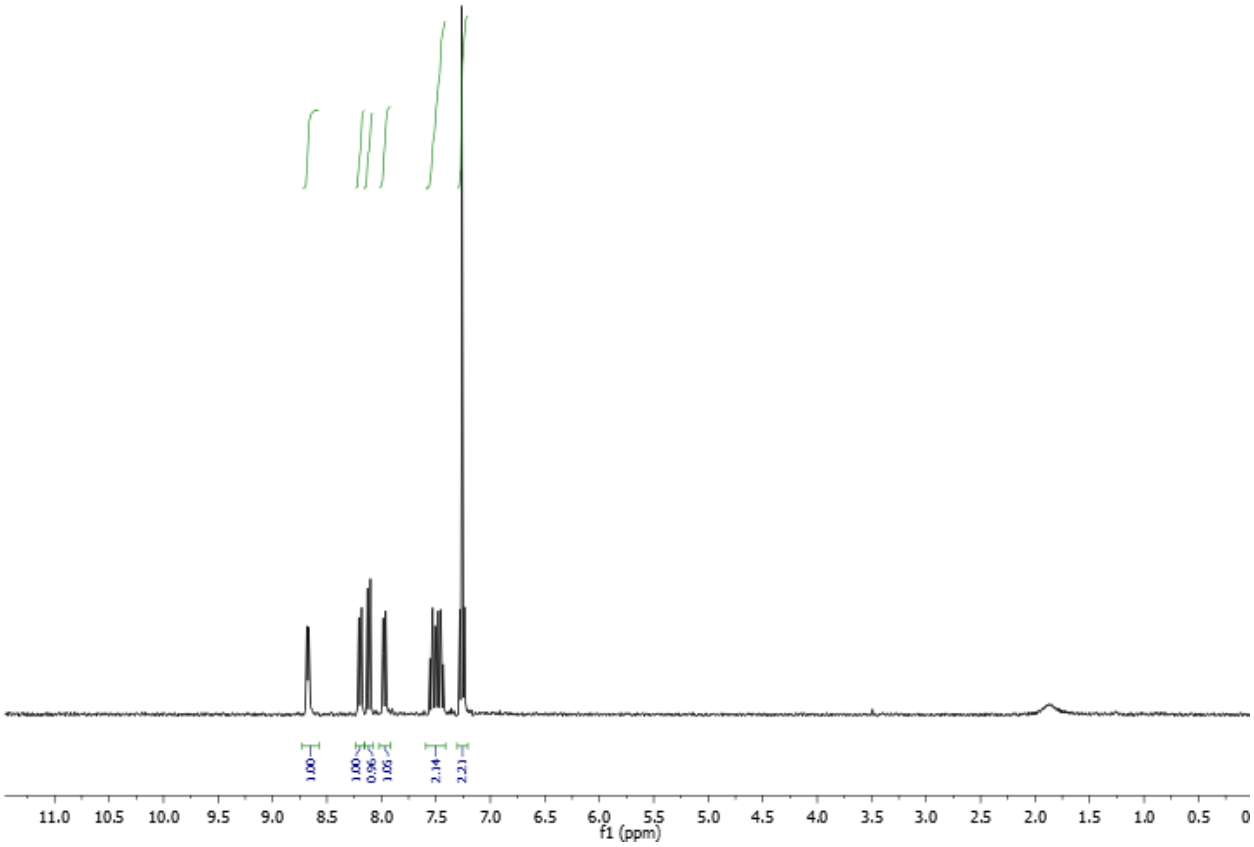
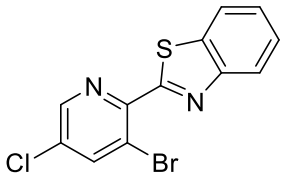




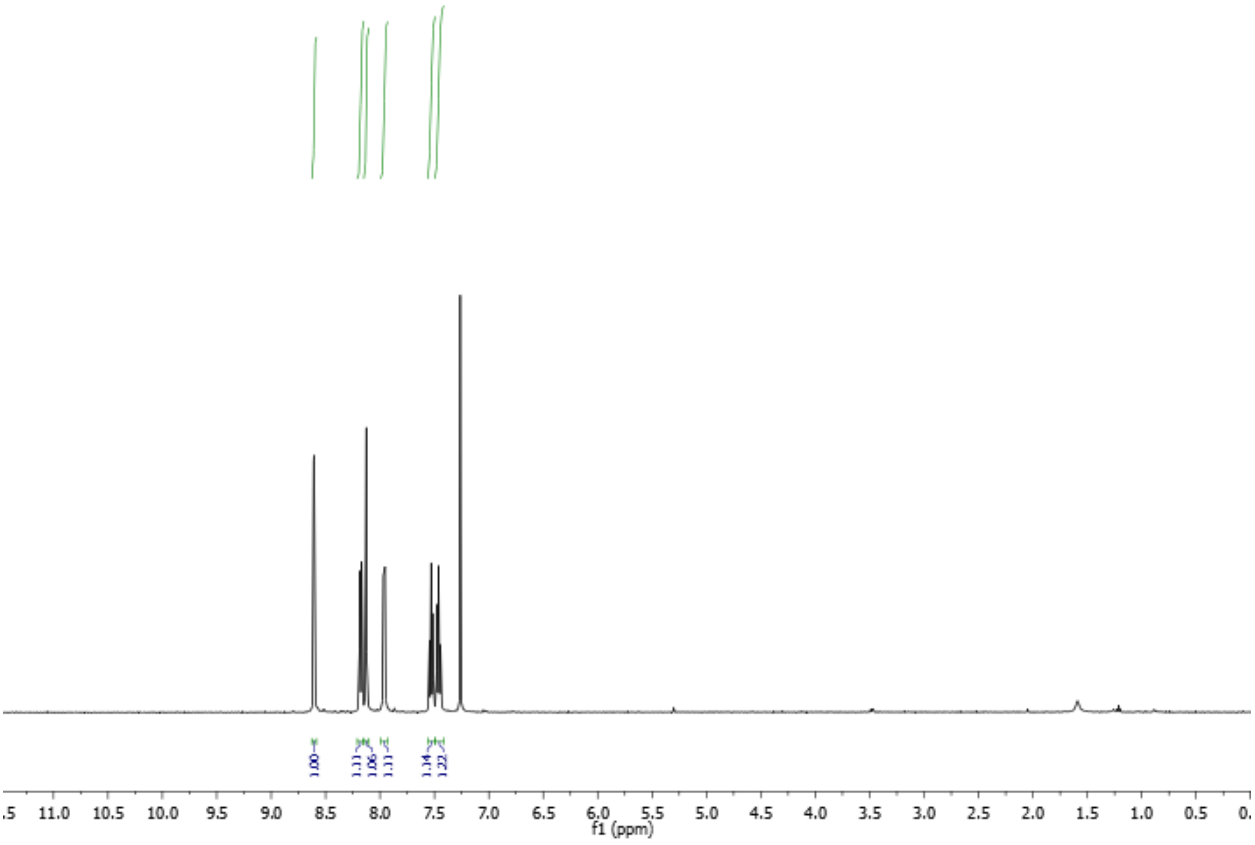
6c

1H standard parameters. Solvent: CDCl3. QNP probe




S
N
N
Cl
Br

6d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6.5
6.0
5.5
5.0
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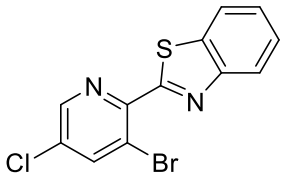
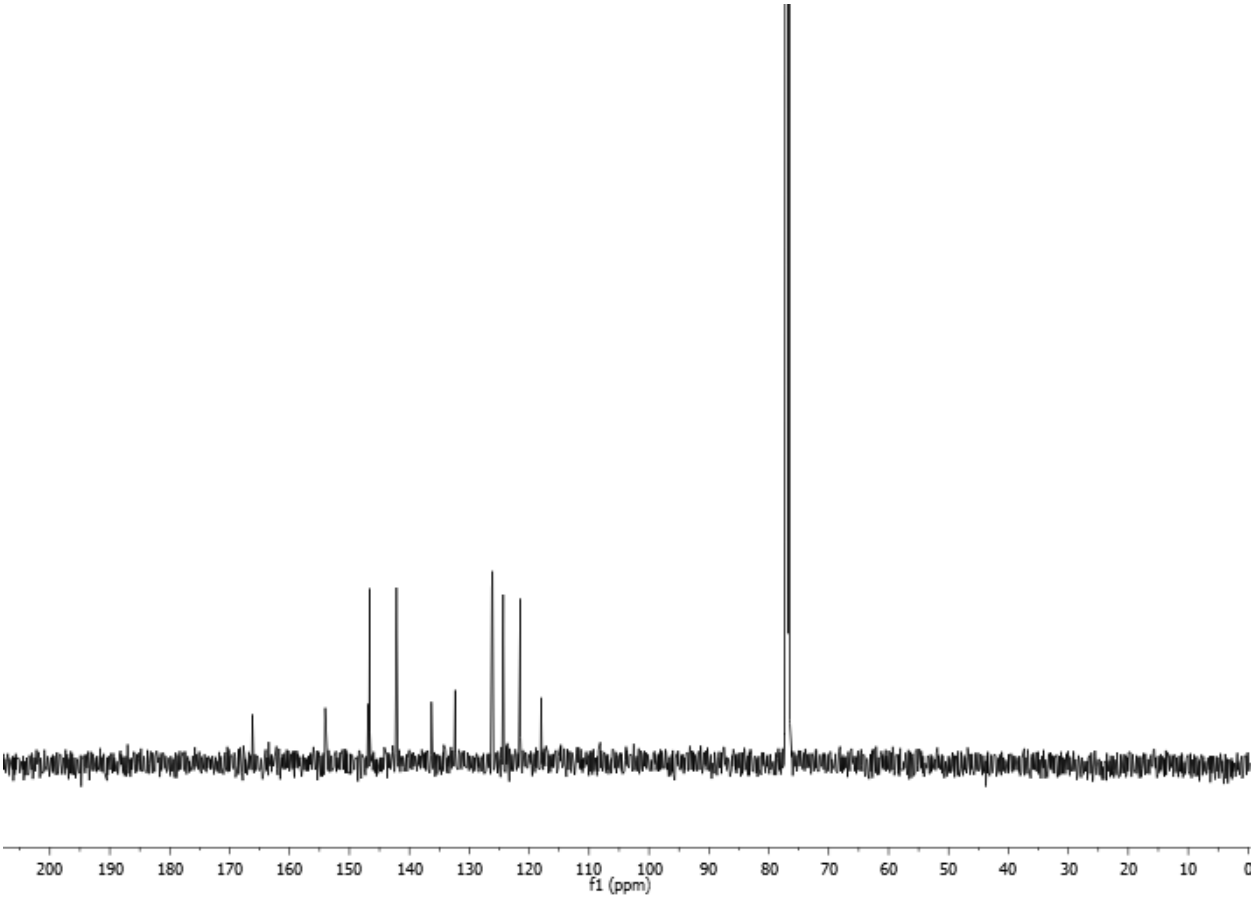
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


S
N
N
Cl
Br

6d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100
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80
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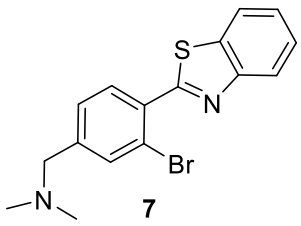
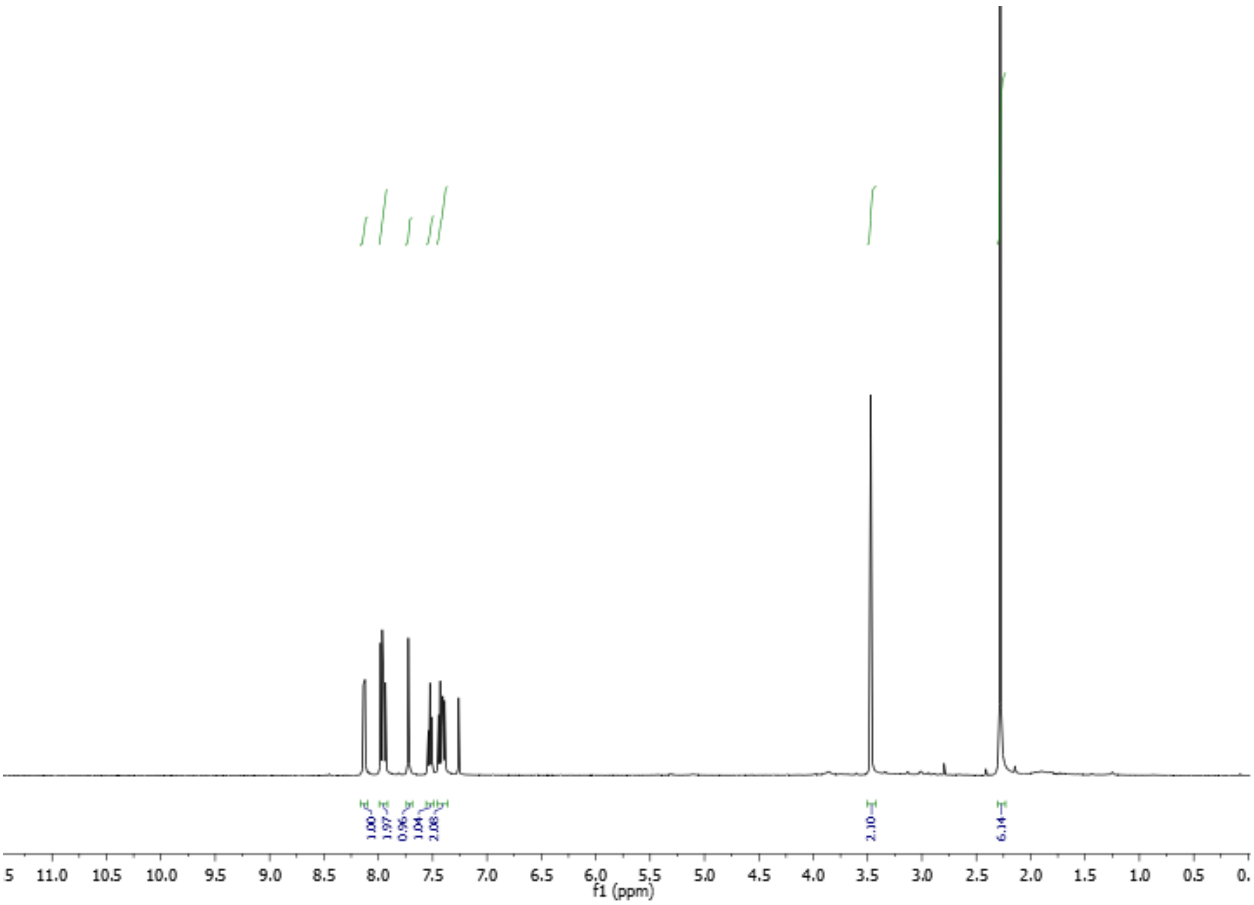
60
50
40
30
20
10
f1 (ppm)


S
N
Br
N

7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1.97
0.96
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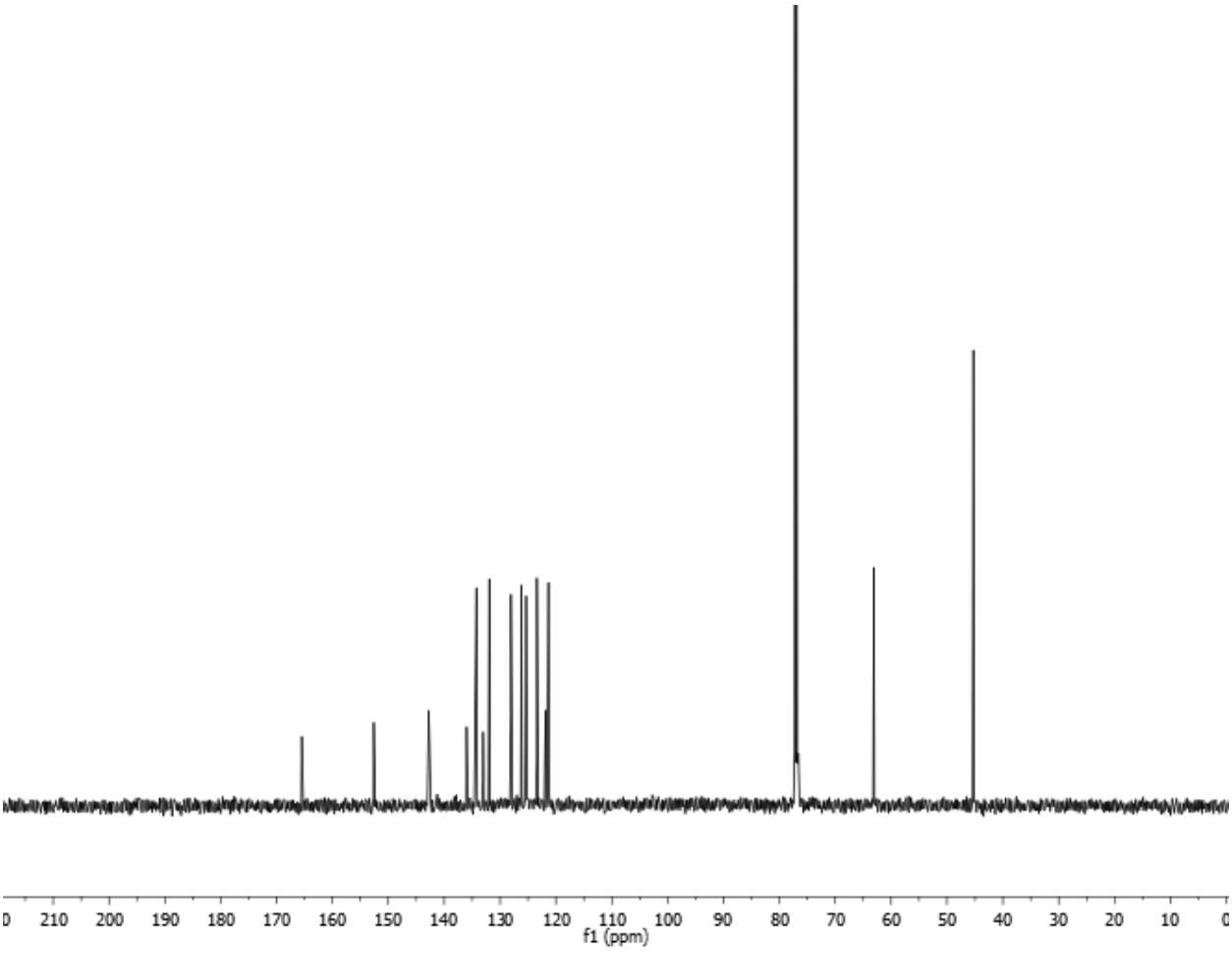
2.08
2.10
6.14
5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)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200
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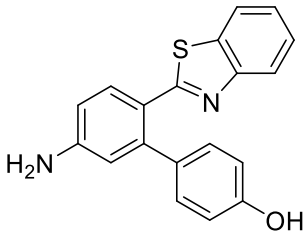
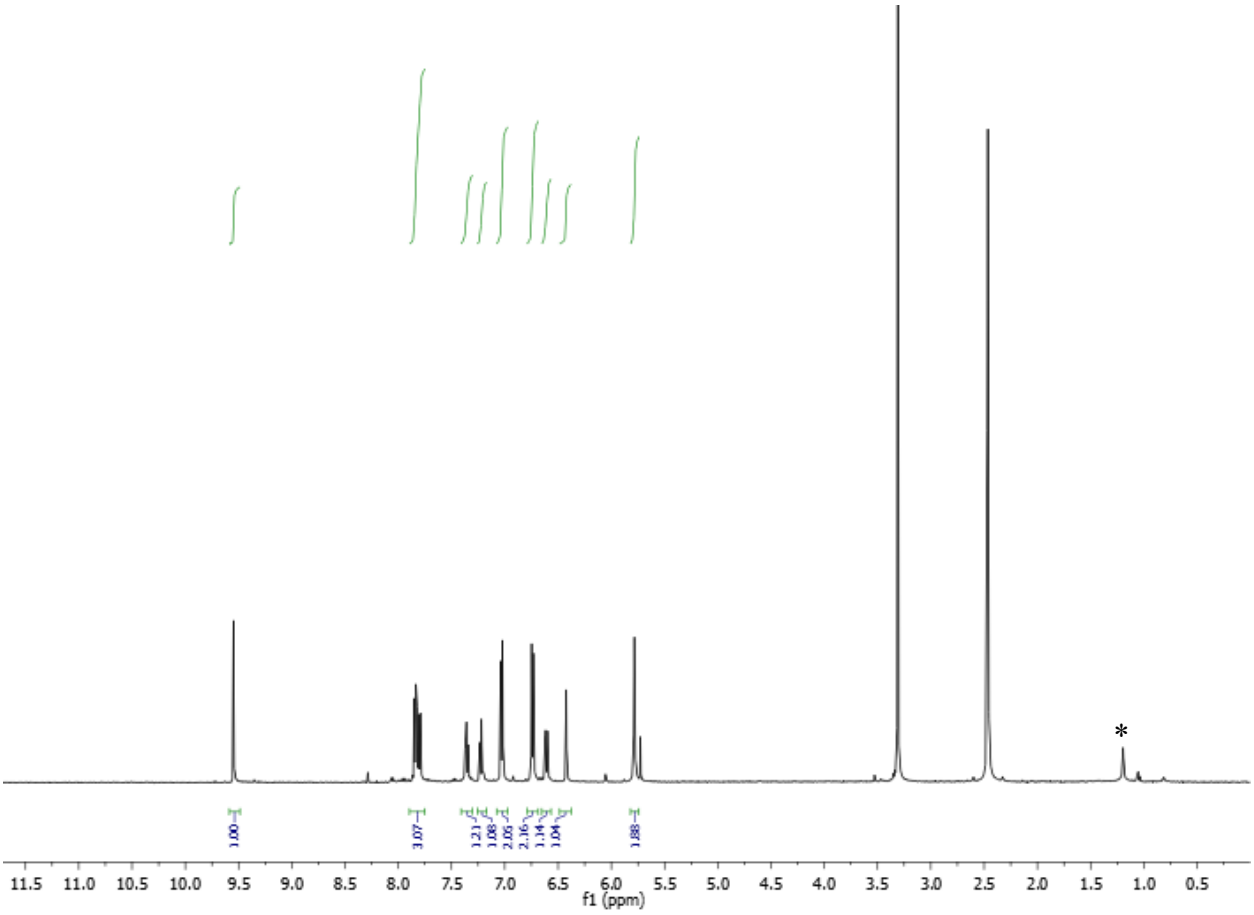
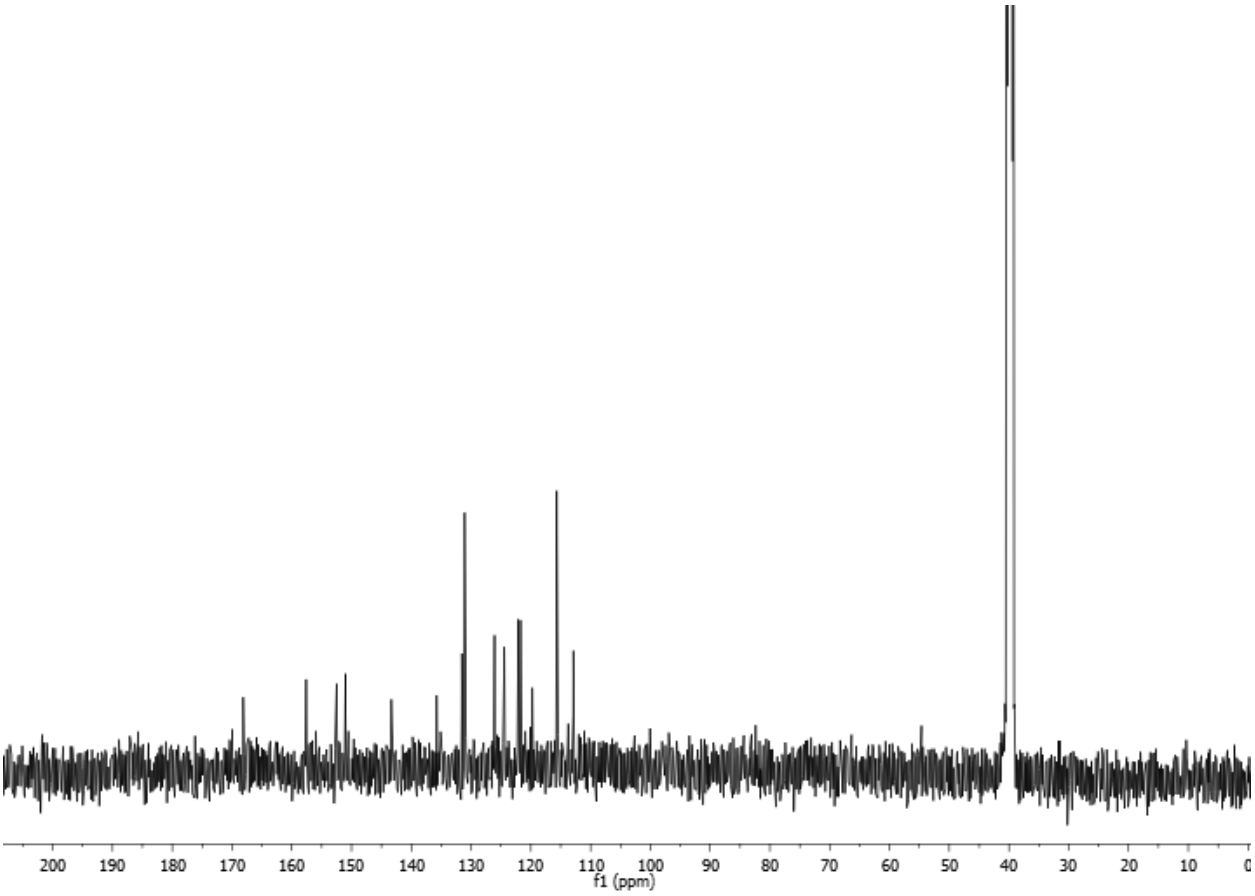
60
50
40
30
20
10
f1 (ppm)


S
N
H2N
OH

8a


*
1.00
3.07
1.21
1.08
2.05
2.16
1.14
1.04
1.88
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
f1 (ppm)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190
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80
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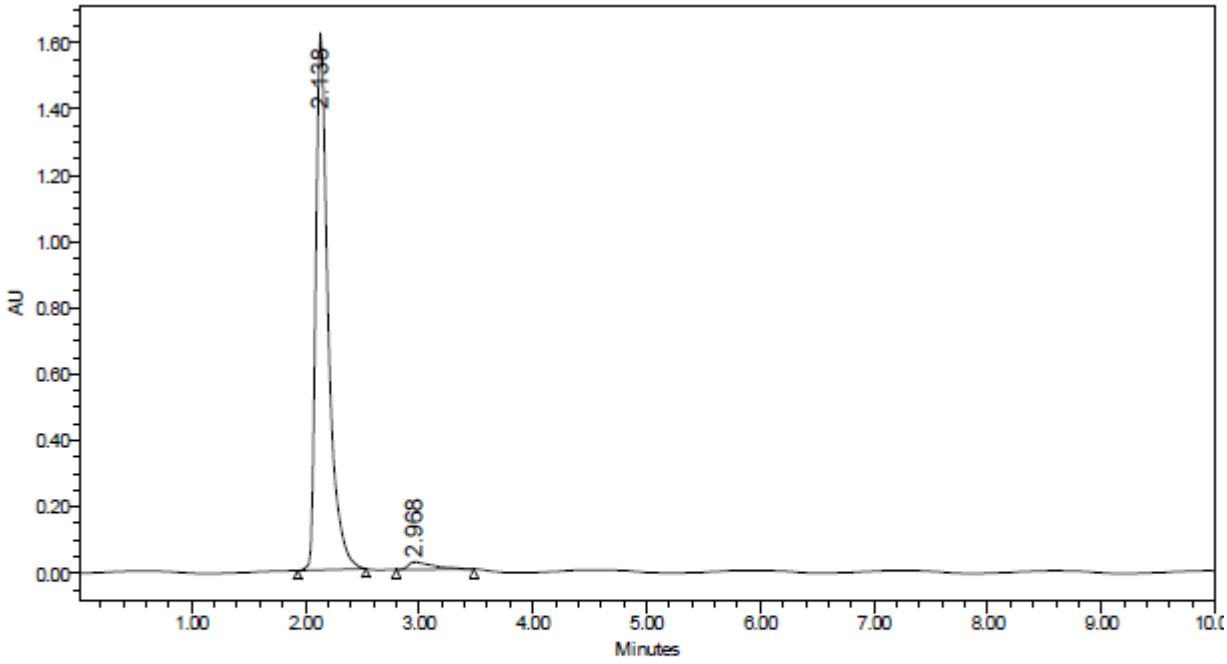
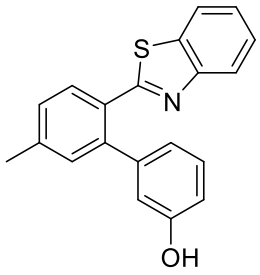
50
40
30
20
10
0
f1 (ppm)

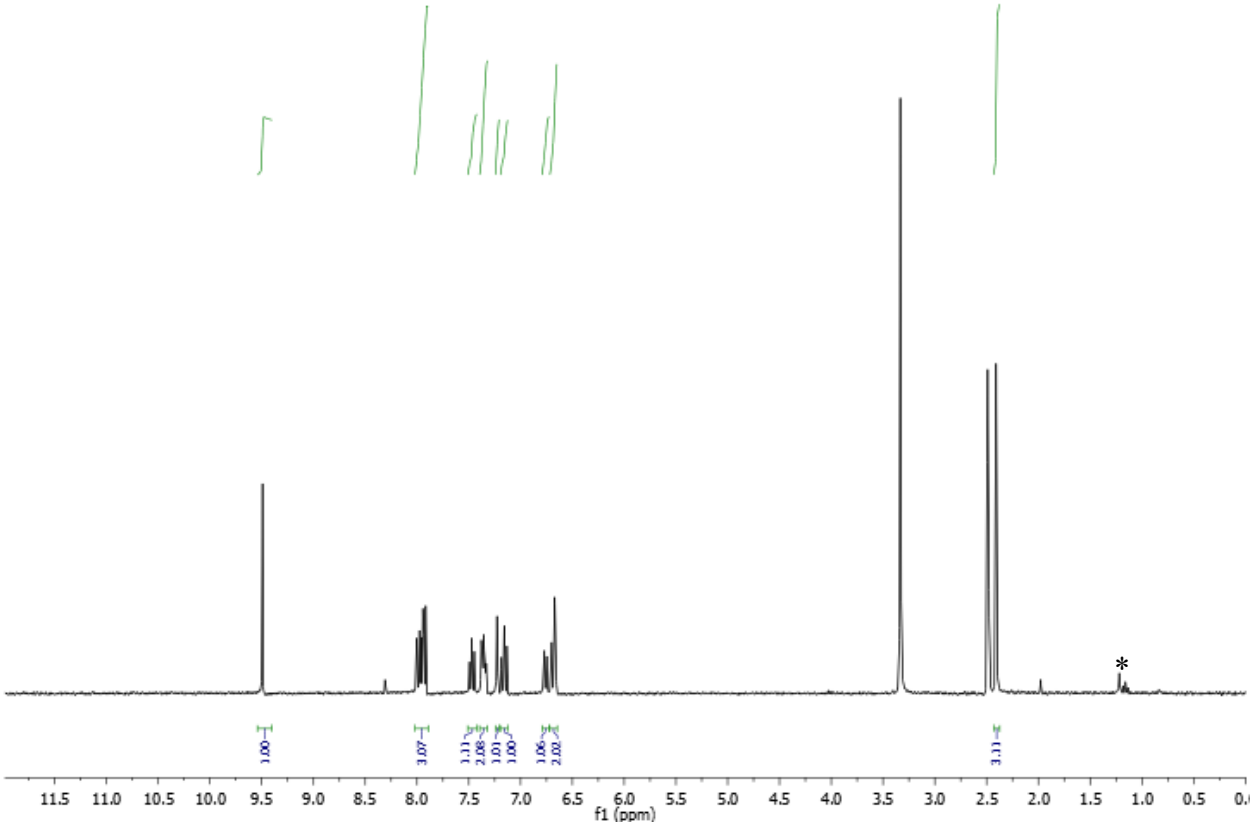


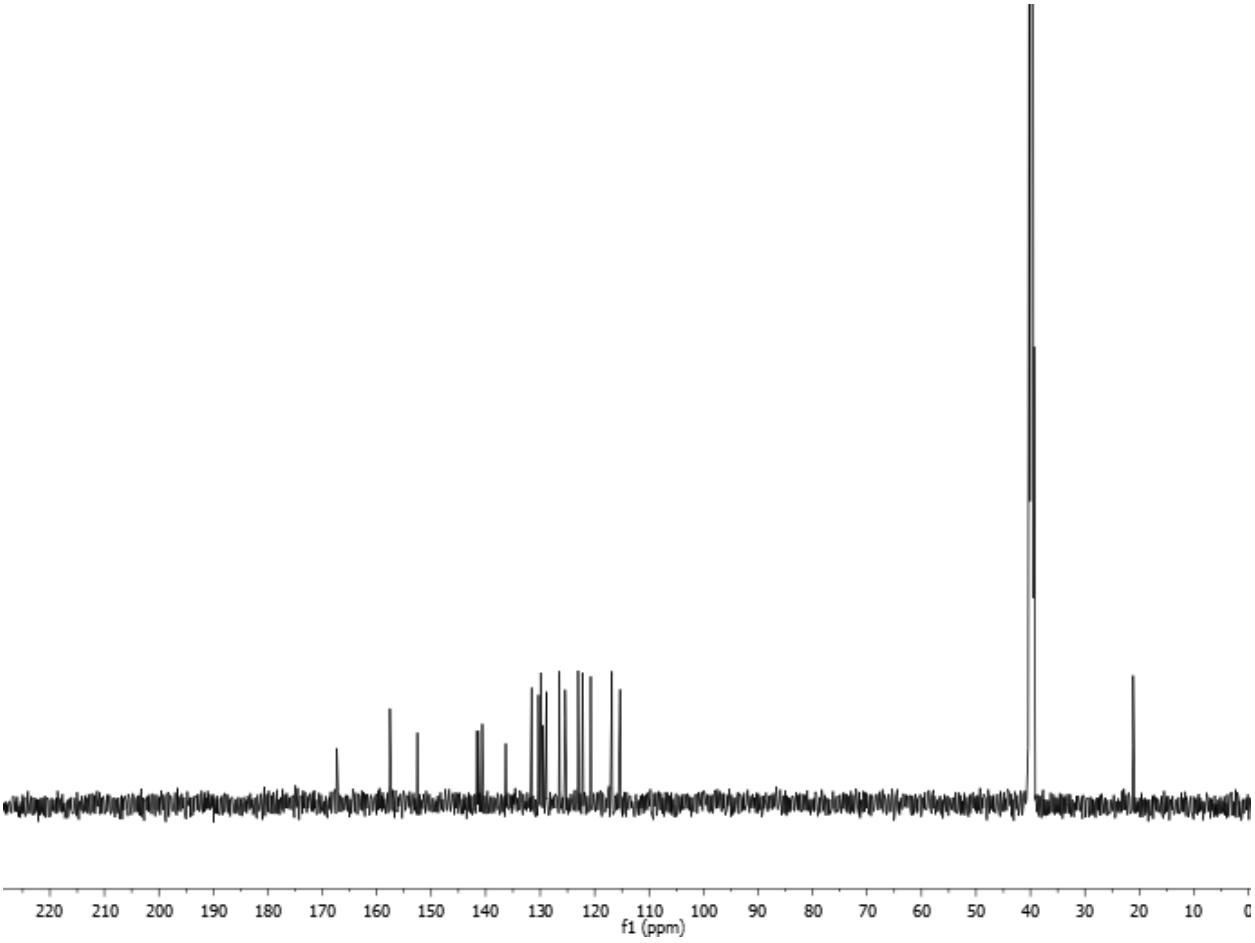
	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	2.138	Unknown	12276479	97.31	1617922	98.59	bb	36	1.933	2.533
2	2.968	Unknown	338754	2.69	23108	1.41	bb	41	2.800	3.483



8b

1H standard parameters. Solvent: DMSO. QNP probe

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200
190
180
170
160
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130
120
110
100
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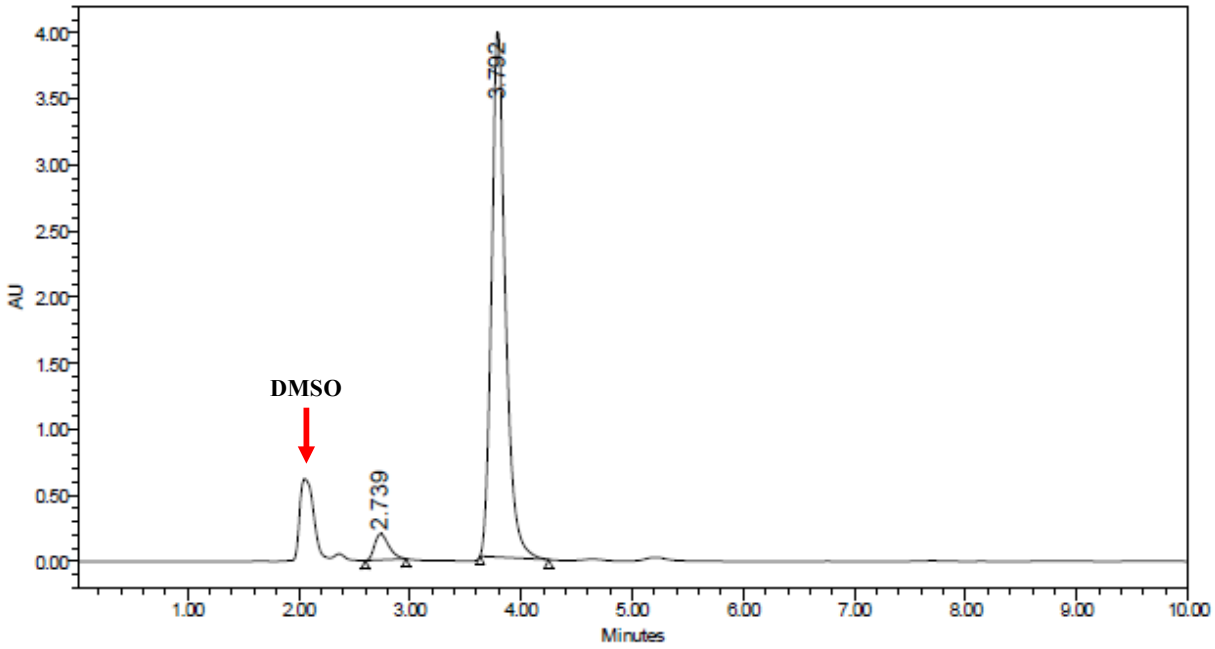
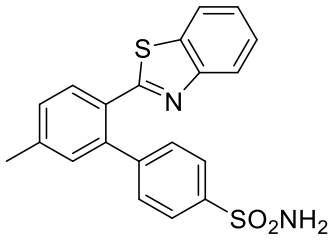
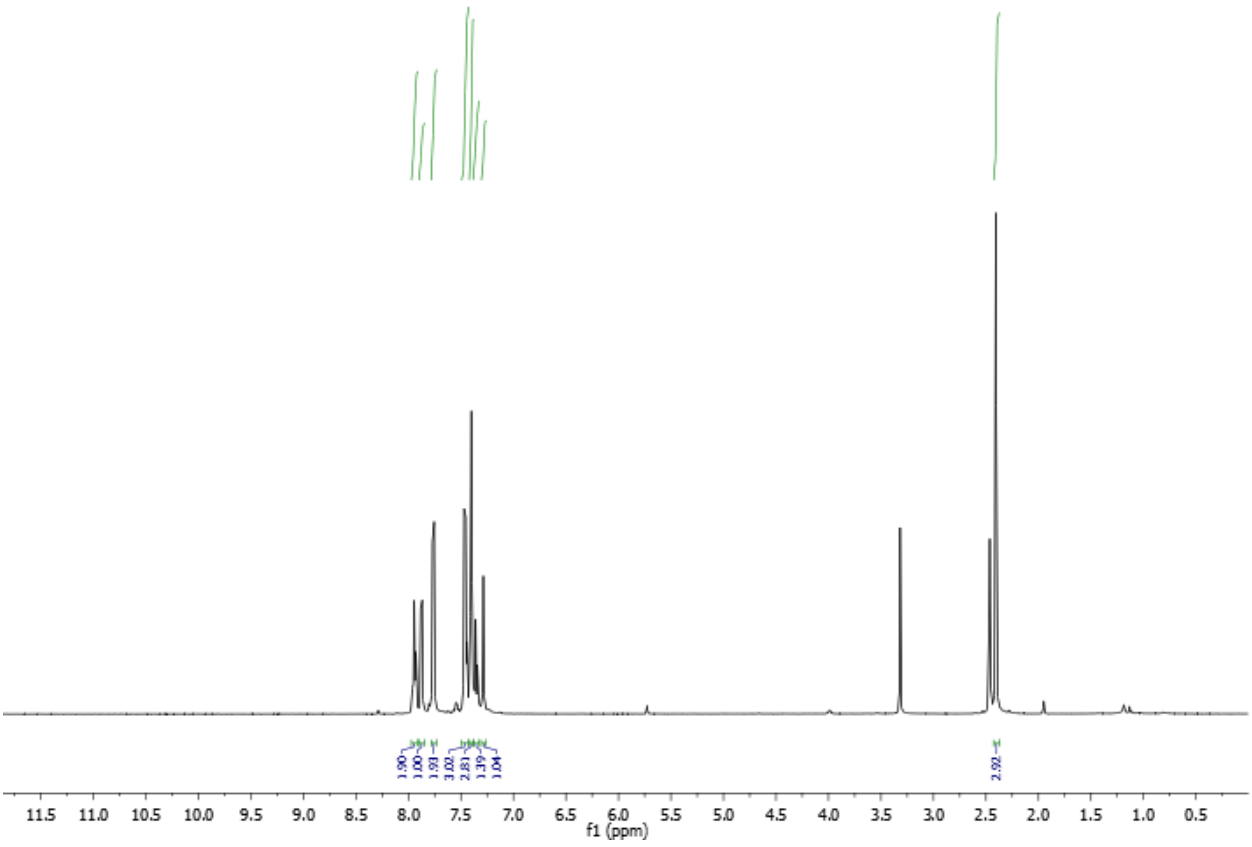
70
60
50
40
30
20
10
0
f1 (ppm)



	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	2.739	Unknown	1740262	4.75	197046	4.65	bb	22	2.600	2.967
2	3.792	Unknown	34908649	95.25	4036614	95.35	bb	37	3.633	4.250


S
N
SO2NH2

8c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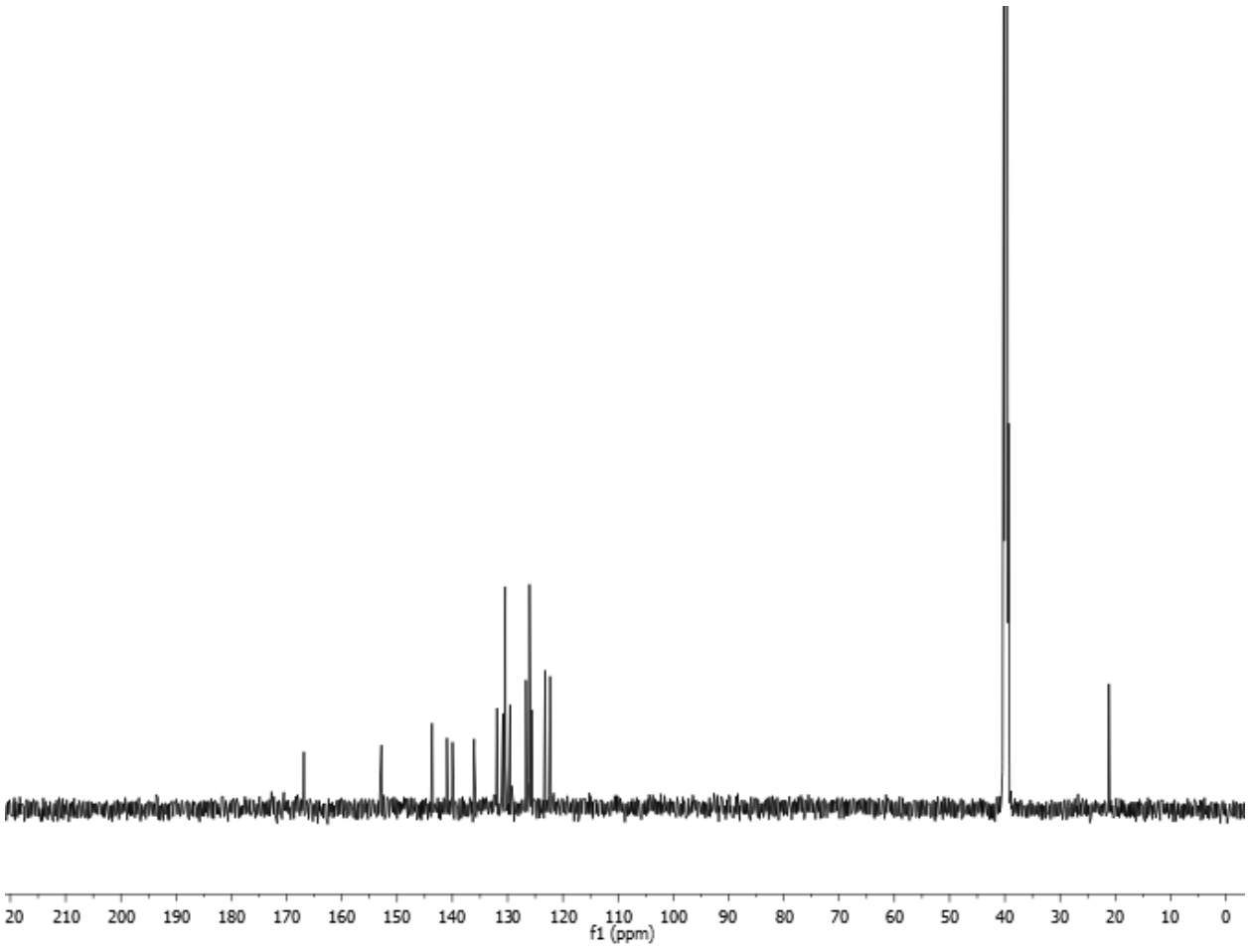
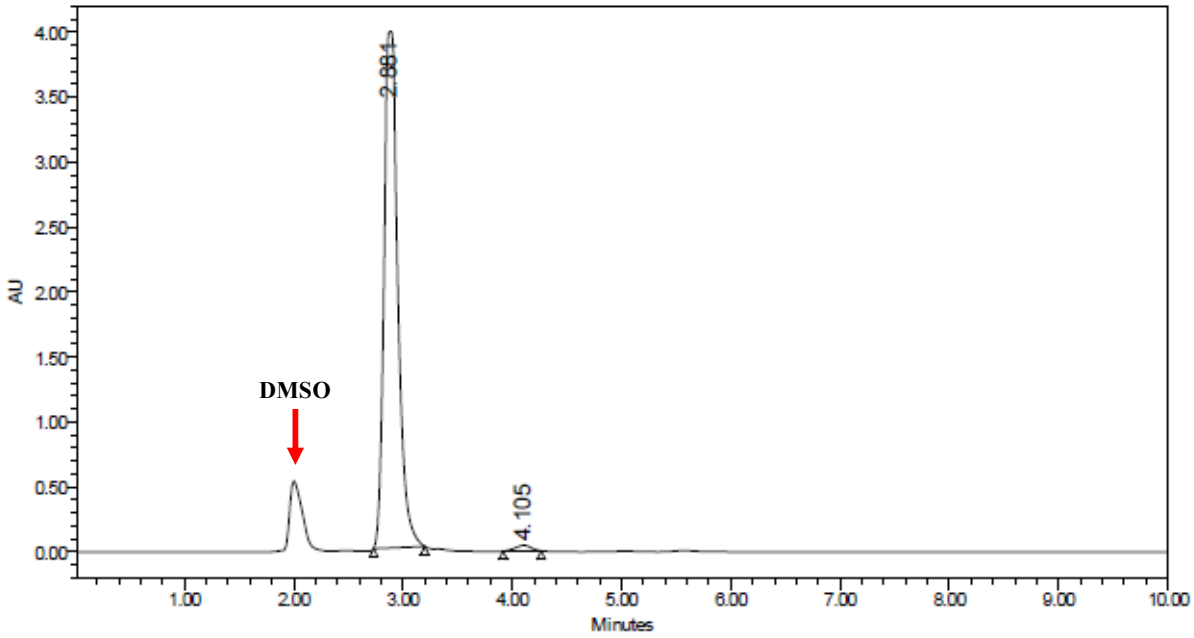
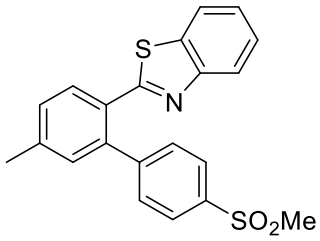
1.93
3.02
2.81
1.39
1.04
2.92
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

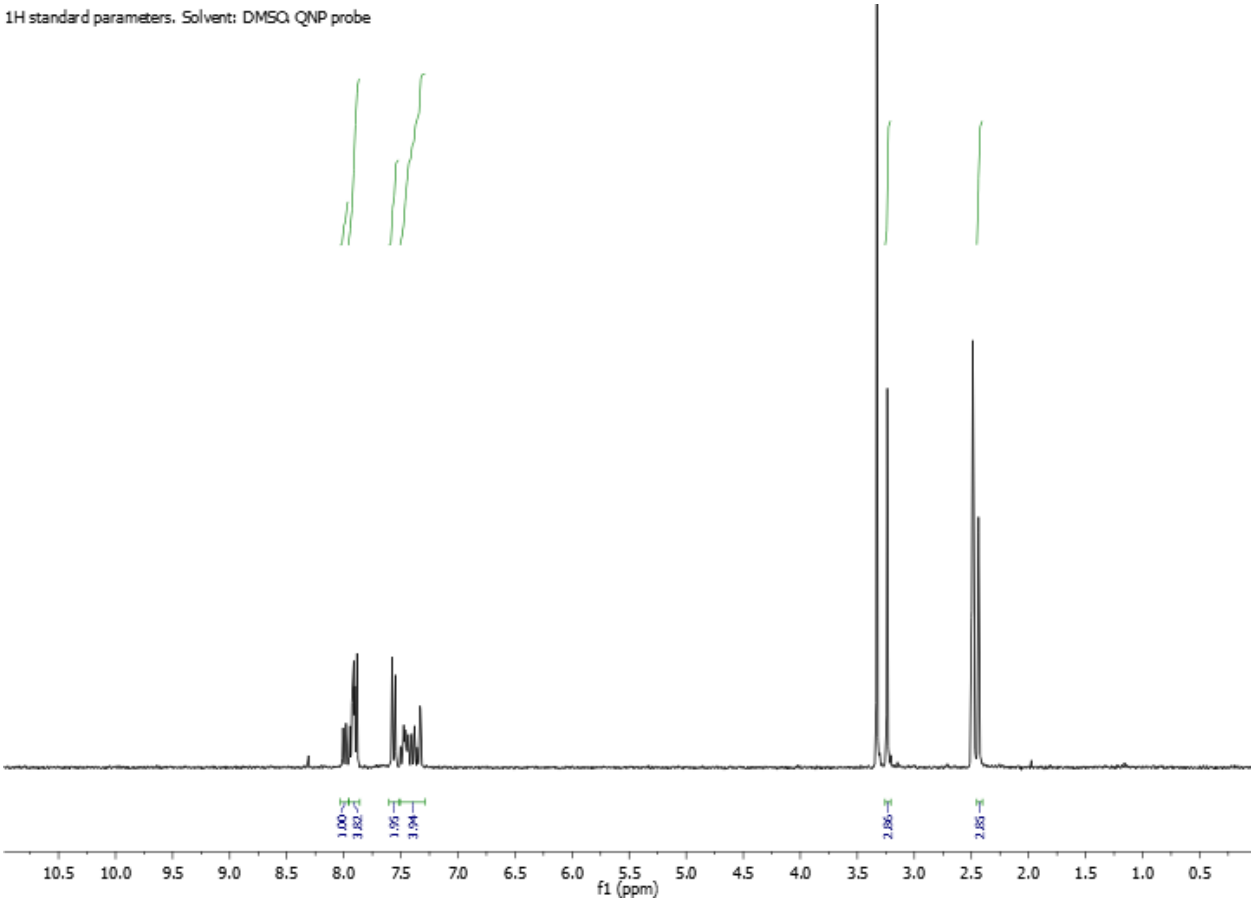

20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	2.881	Unknown	35014447	98.75	4140333	98.94	bb	28	2.733	3.200
2	4.105	Unknown	442791	1.25	44251	1.06	bb	21	3.917	4.267


S
N
SO2Me

8d


1H standard parameters. Solvent: DMSO. QNP probe
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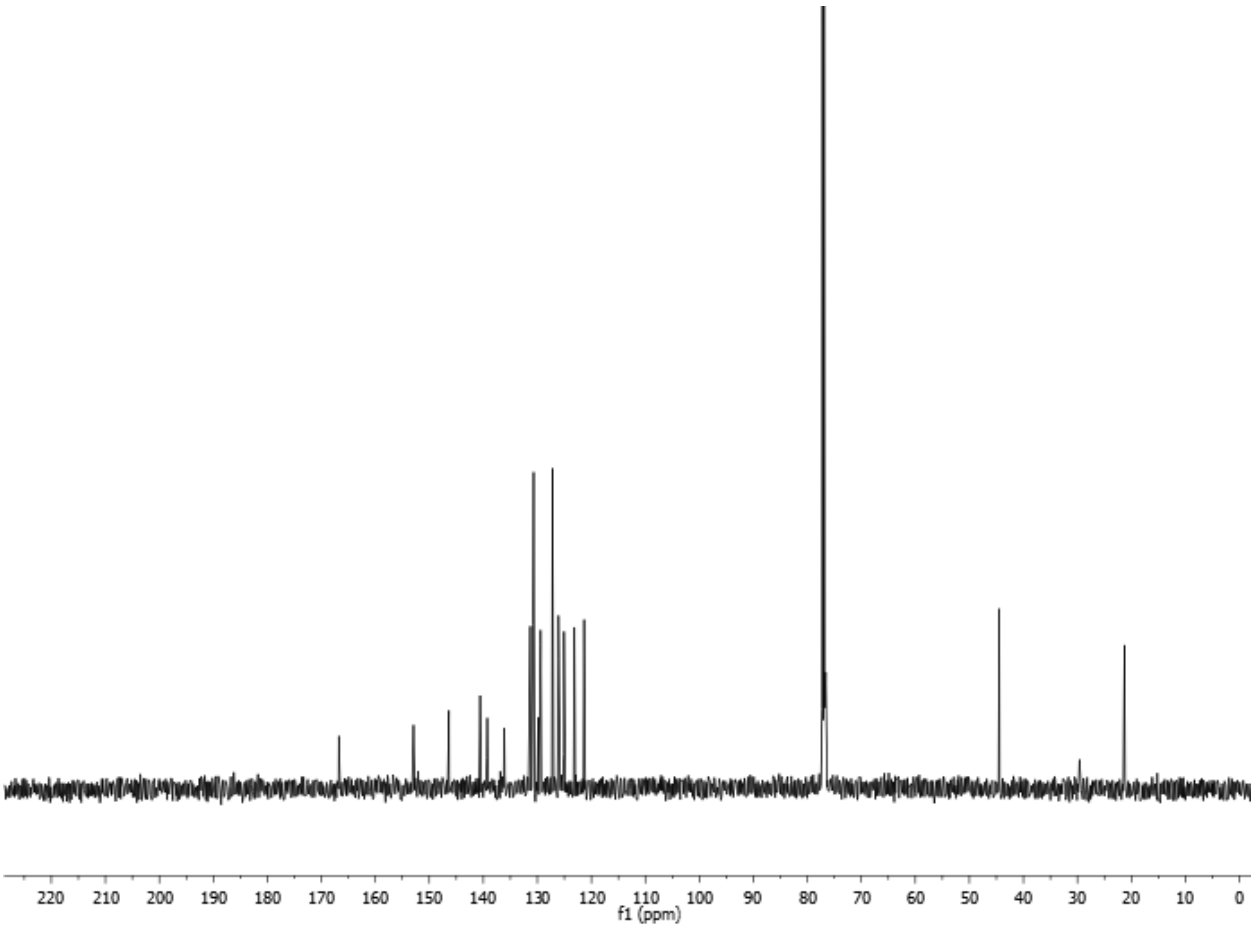
1.95
3.94
2.86
2.85
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


220
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180
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120
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100
90
80
70
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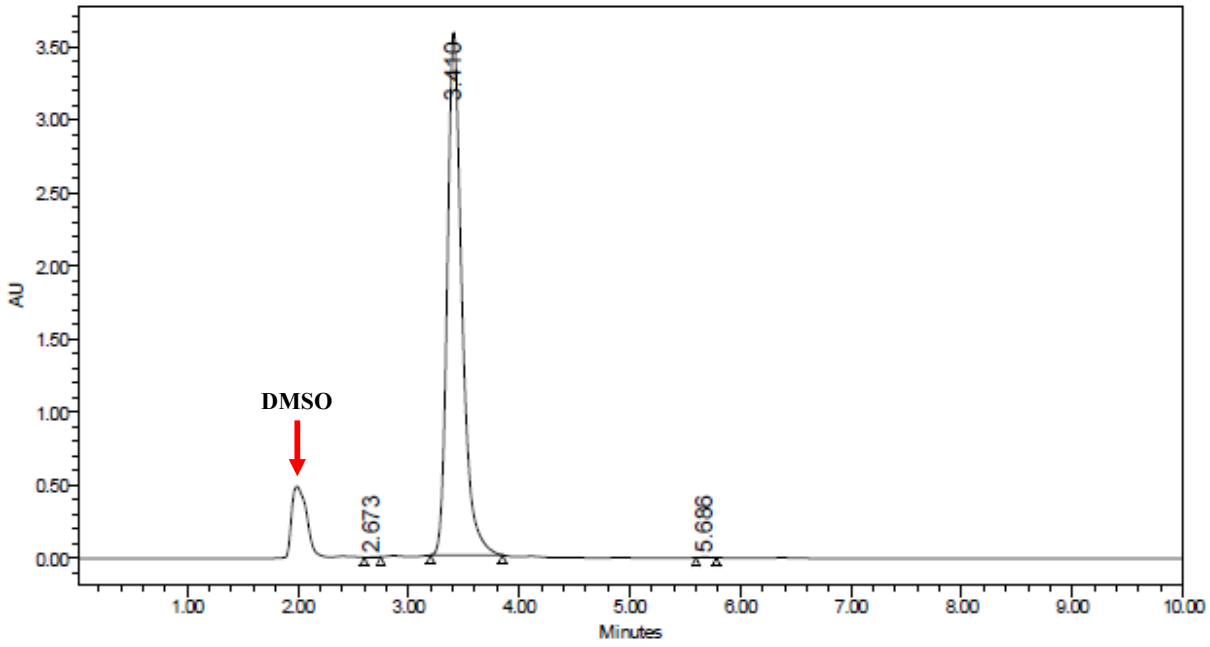
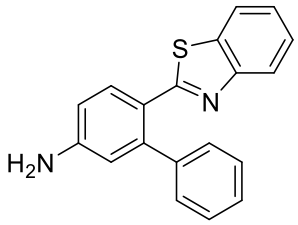
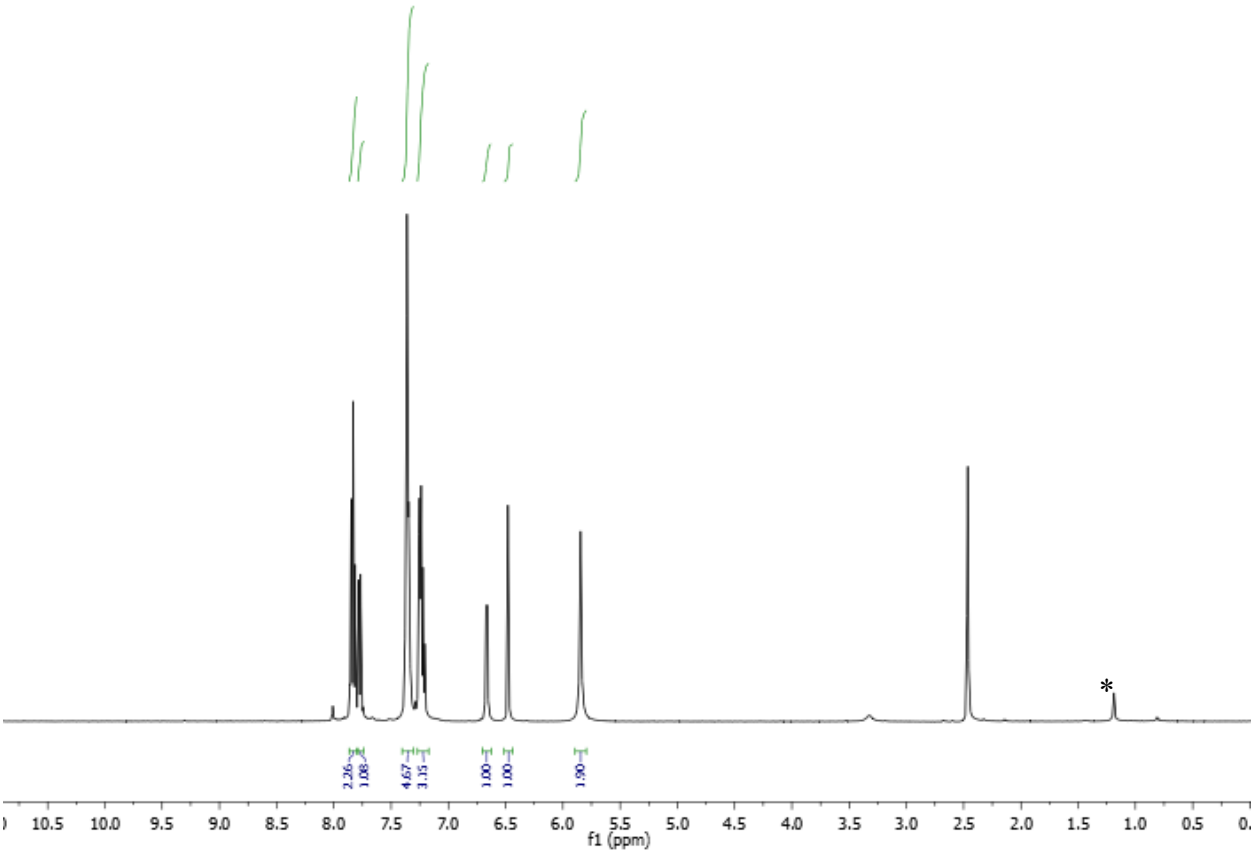
50
40
30
20
10
0
f1 (ppm)

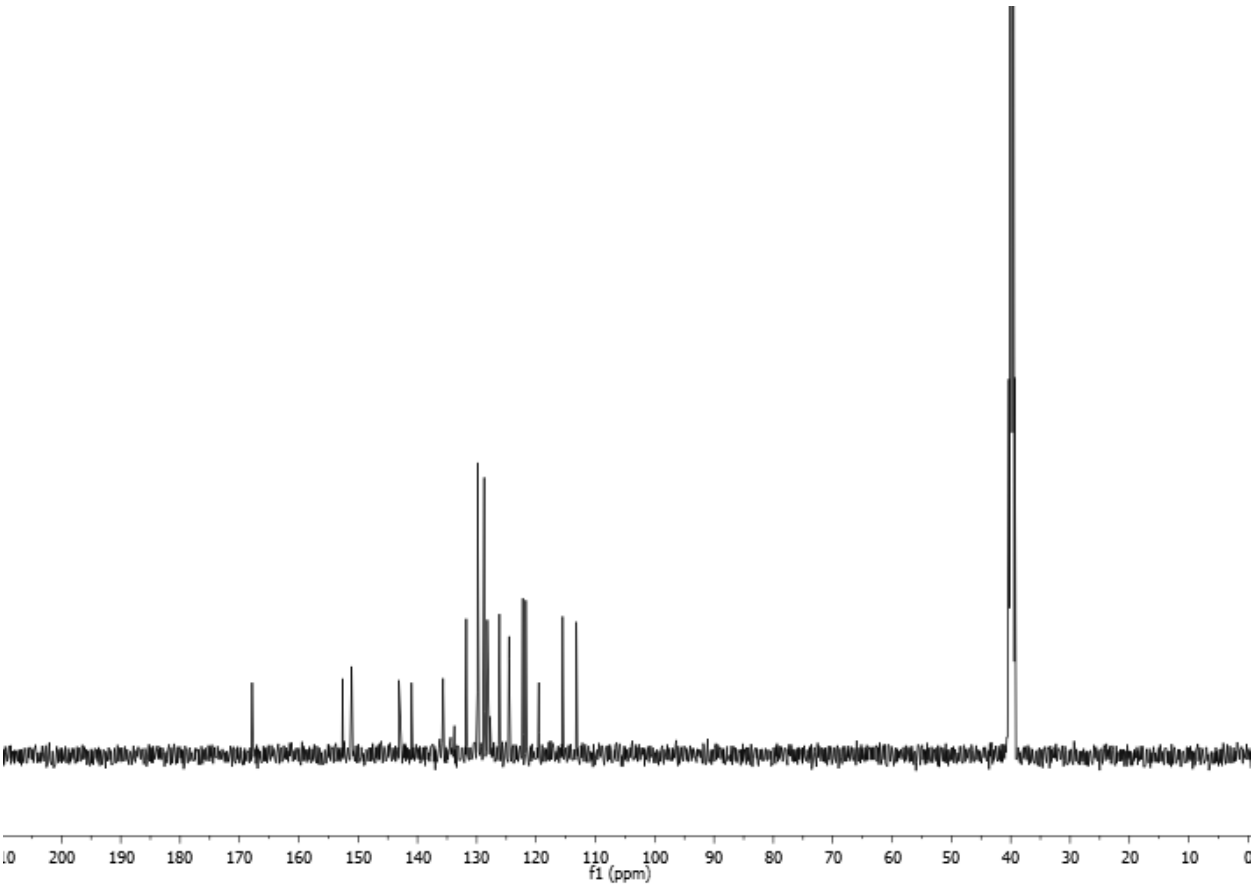


	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	2.673	Unknown	16530	0.05	-2738	0.08	bb	9	2.600	2.750
2	3.410	Unknown	32960475	99.89	3586090	99.84	bb	39	3.200	3.850
3	5.686	Unknown	19683	0.06	2866	0.08	bb	11	5.600	5.783


S
N
H2N

8e


2.26
1.08
4.67
3.15
1.00
1.00
1.90
*
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
f1 (ppm)


200
190
180
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140
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120
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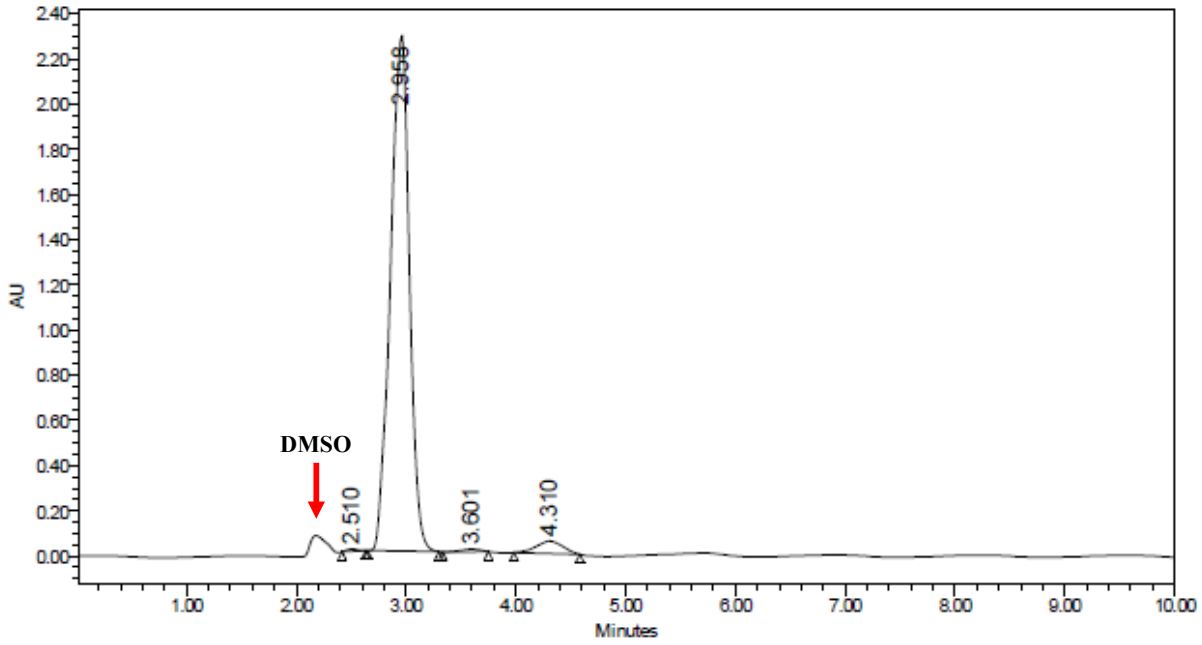
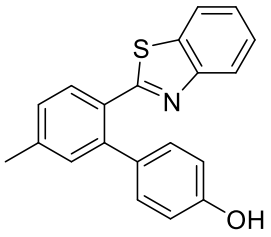
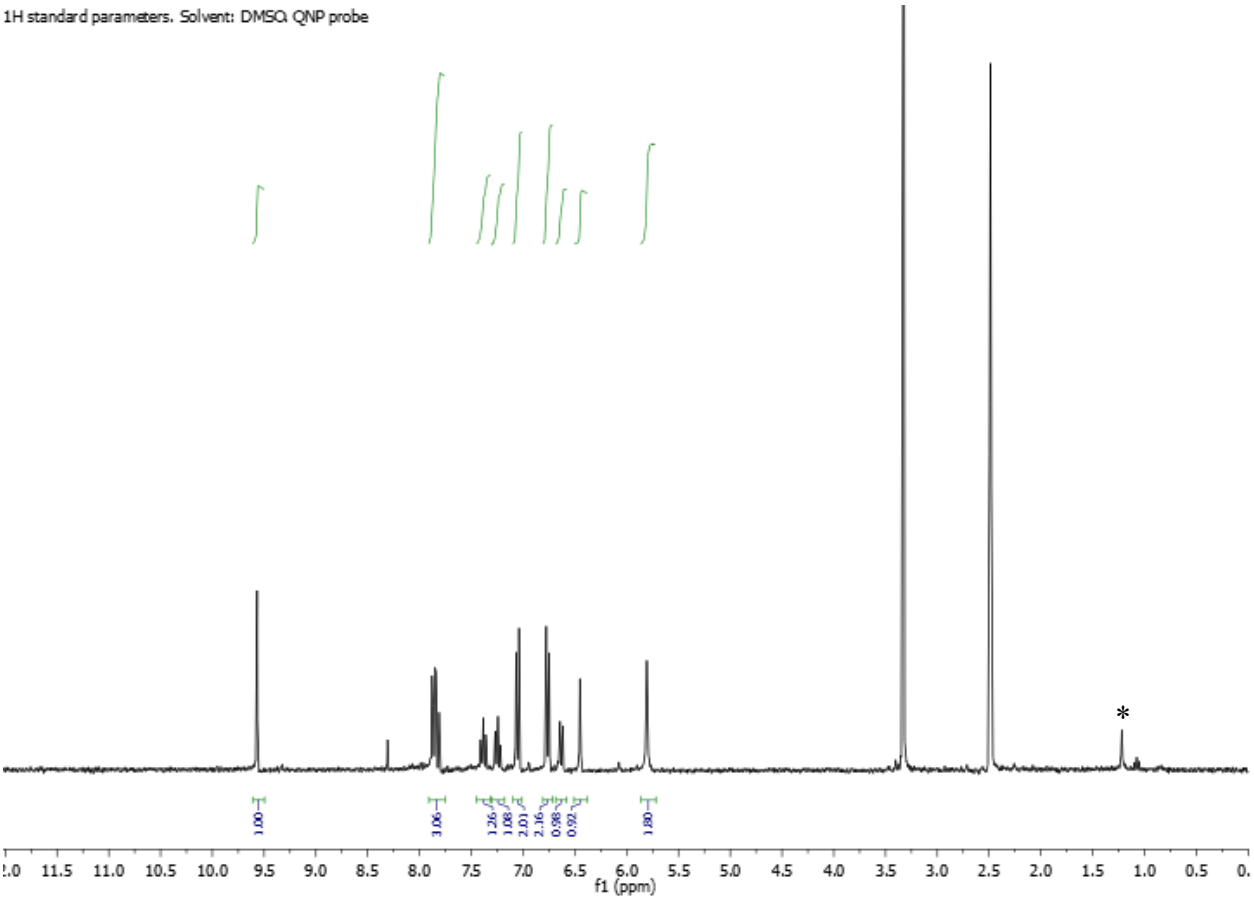
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

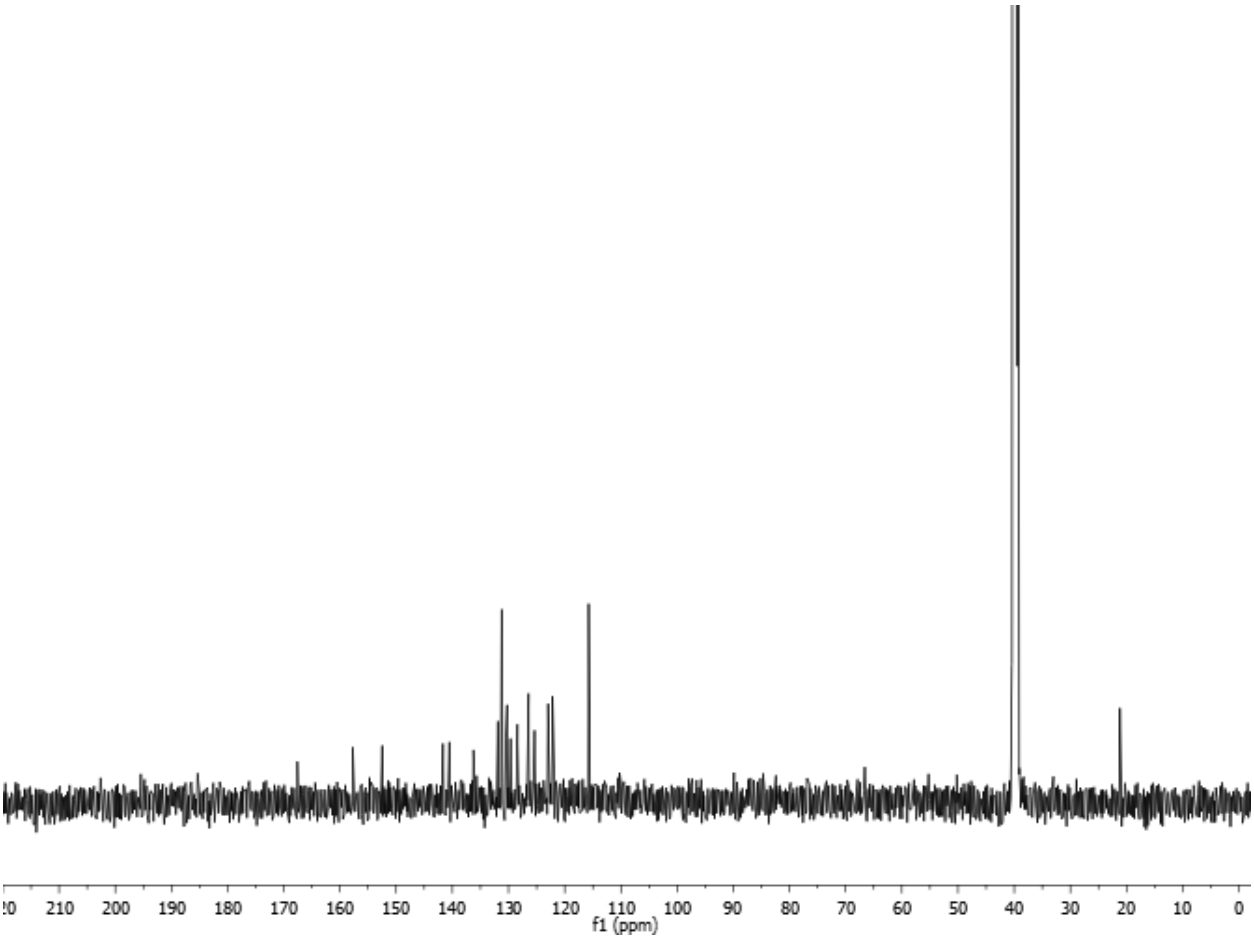


	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	2.510	Unknown	70383	0.25	10486	0.44	bb	13	2.417	2.633
2	2.958	Unknown	27293082	95.96	2293281	96.71	bb	39	2.650	3.300
3	3.601	Unknown	136245	0.48	11376	0.48	bb	25	3.333	3.750
4	4.310	Unknown	942521	3.31	56156	2.37	bb	36	3.983	4.583


S
N
OH

8f


1H standard parameters. Solvent: DMSO. QNP probe
*
1.00
3.06
1.26
1.08
2.01
2.16
0.98
0.92
1.80
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
f1 (ppm)


210
200
190
180
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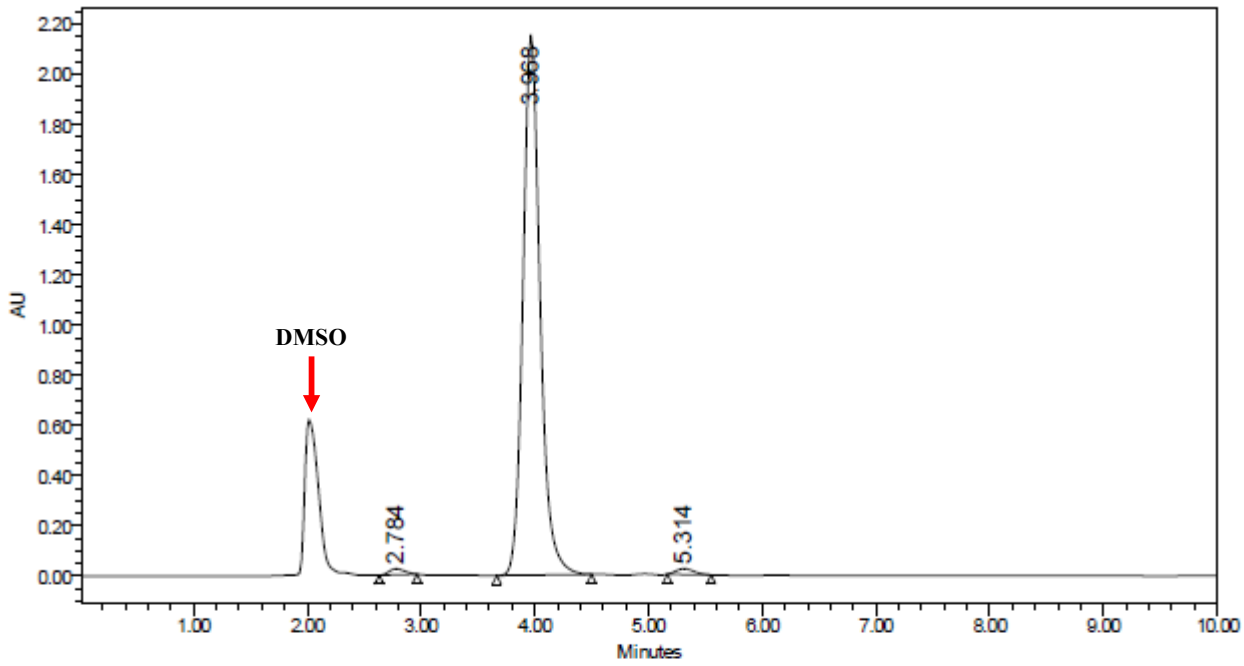
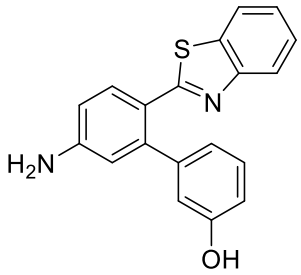
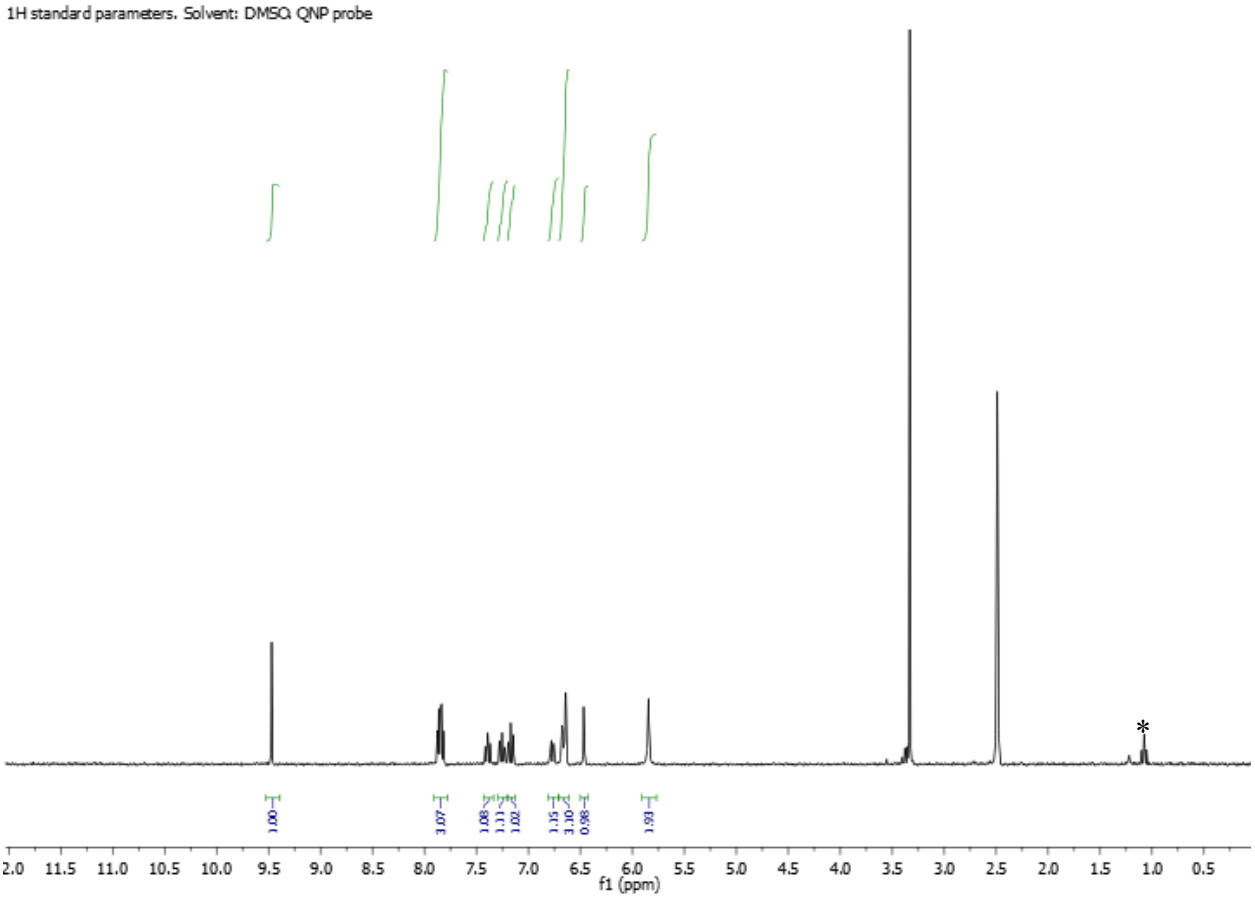
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

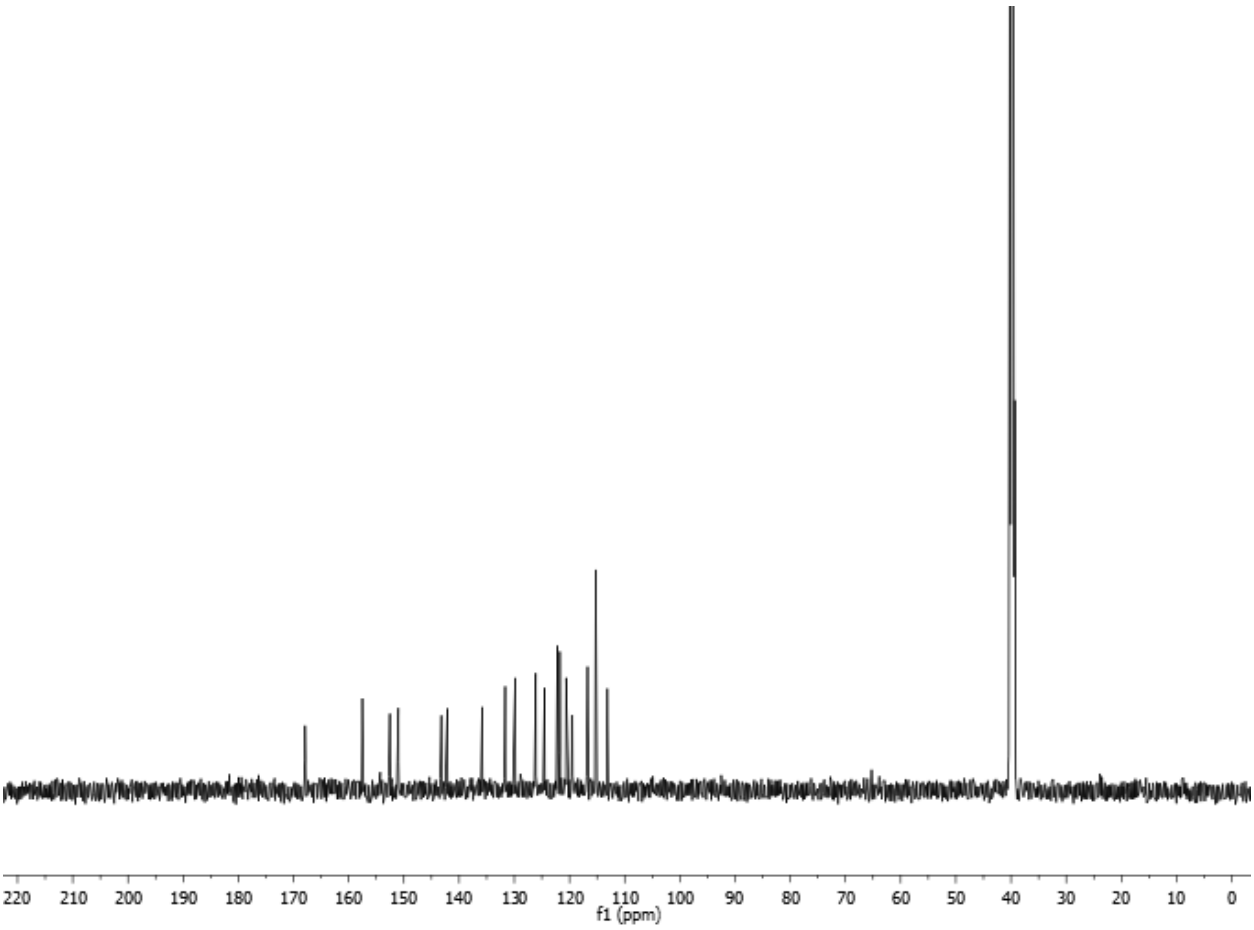


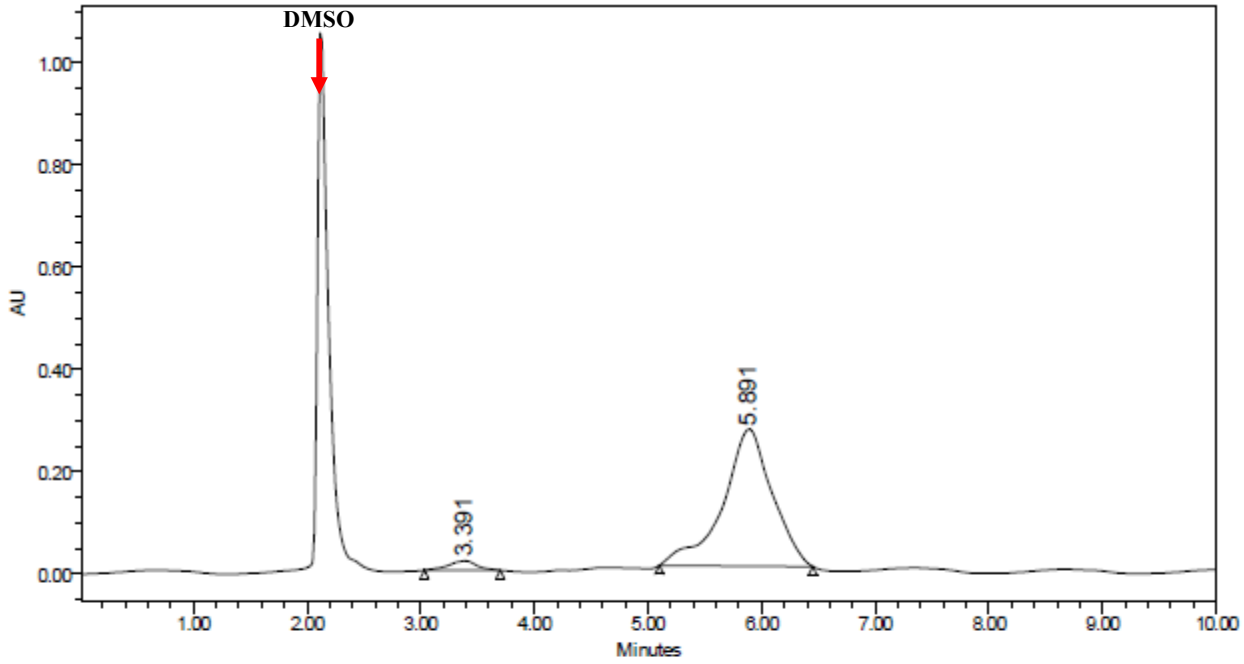
	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	2.784	Unknown	221692	0.96	23619	1.07	bb	20	2.633	2.967
2	3.968	Unknown	22596379	97.94	2153329	97.87	bb	50	3.667	4.500
3	5.314	Unknown	254553	1.10	23348	1.06	bb	23	5.167	5.550


S
N
H2N
OH

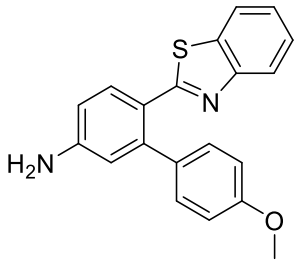
8g


1H standard parameters. Solvent: DMSO. QNP probe
1.00
3.07
1.08
1.11
1.02
1.15
3.10
0.98
1.93
*
f1 (ppm)

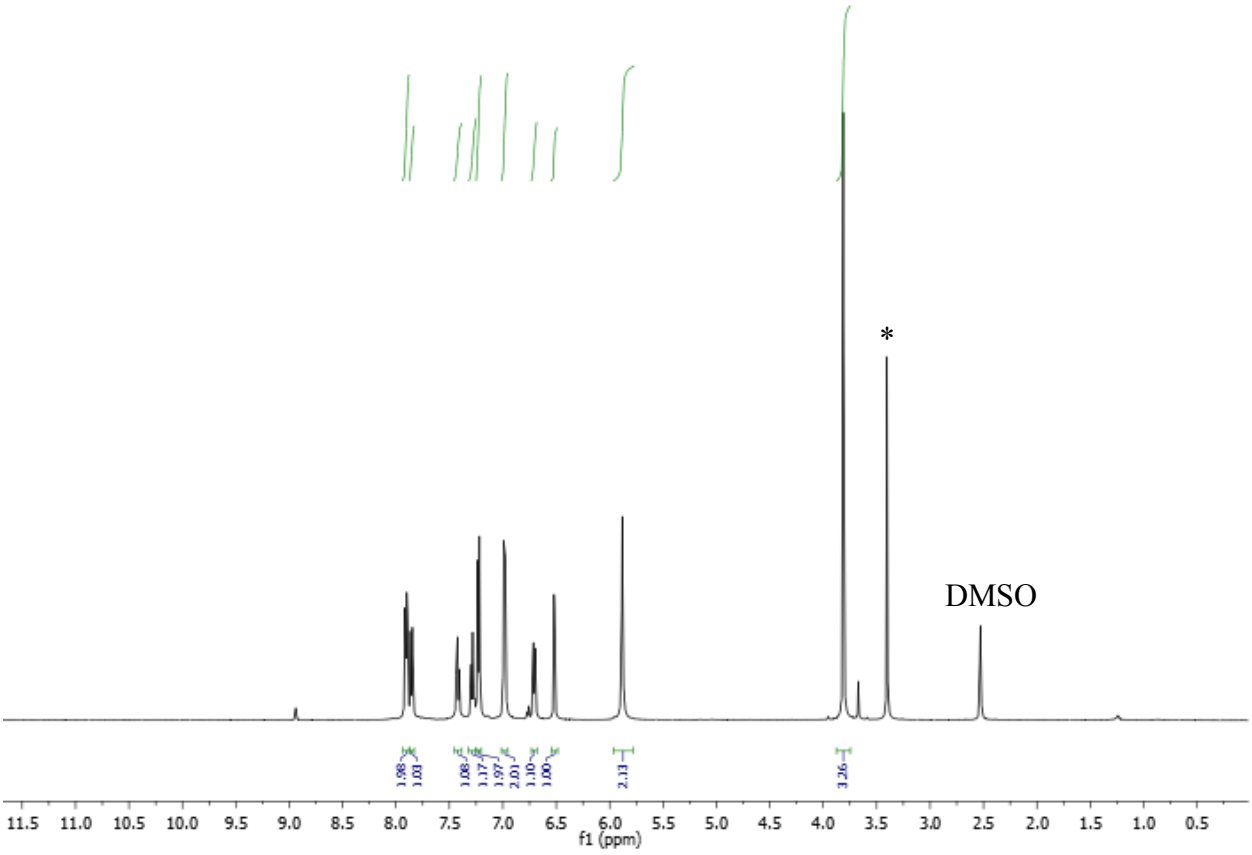

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

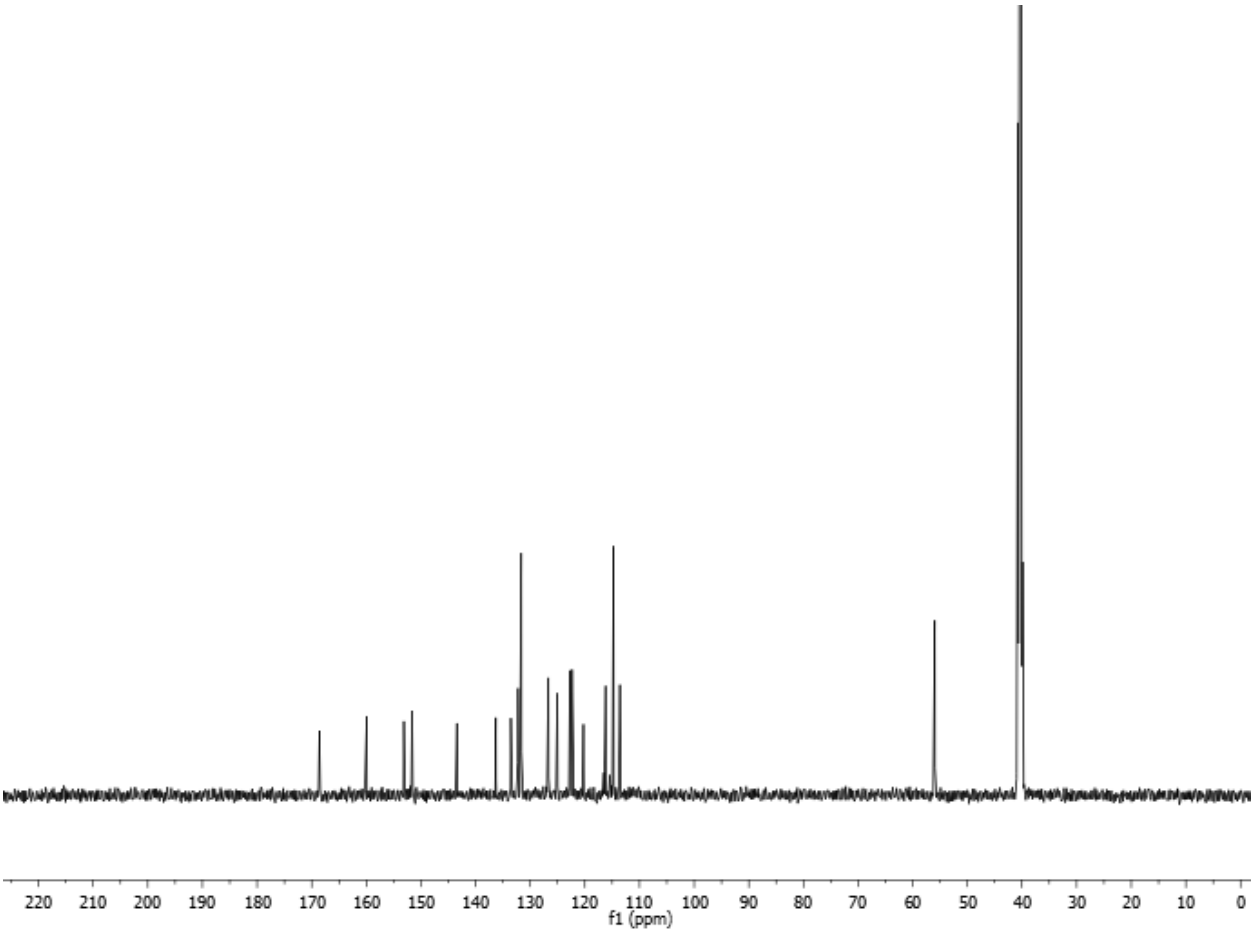


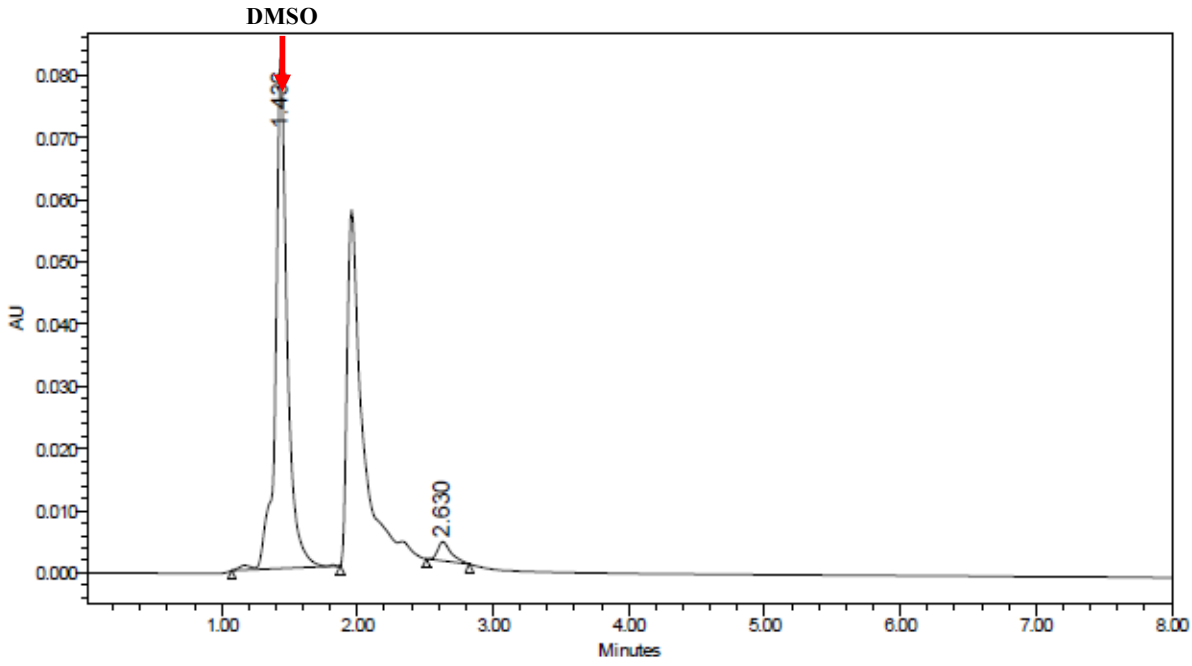
	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	3.391	Unknown	315999	3.76	18386	6.42	bb	40	3.033	3.700
2	5.891	Unknown	8088409	96.24	267982	93.58	bb	81	5.100	6.450


S
N
H2N
O

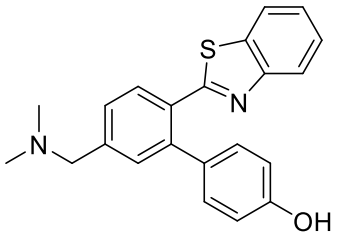
8h


*
DMSO
1.98
1.03
1.08
1.17
1.97
2.01
1.10
1.00
2.13
3.26
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
f1 (ppm)


220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

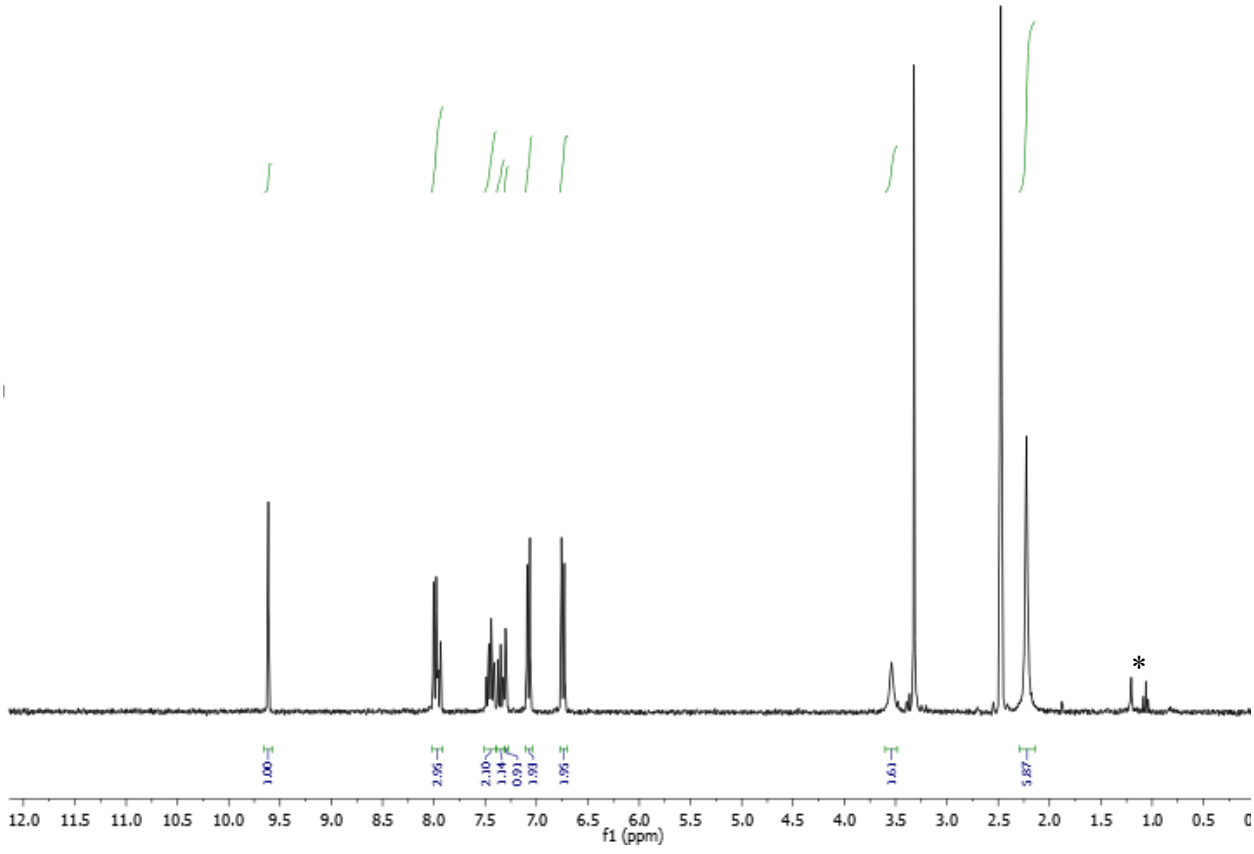


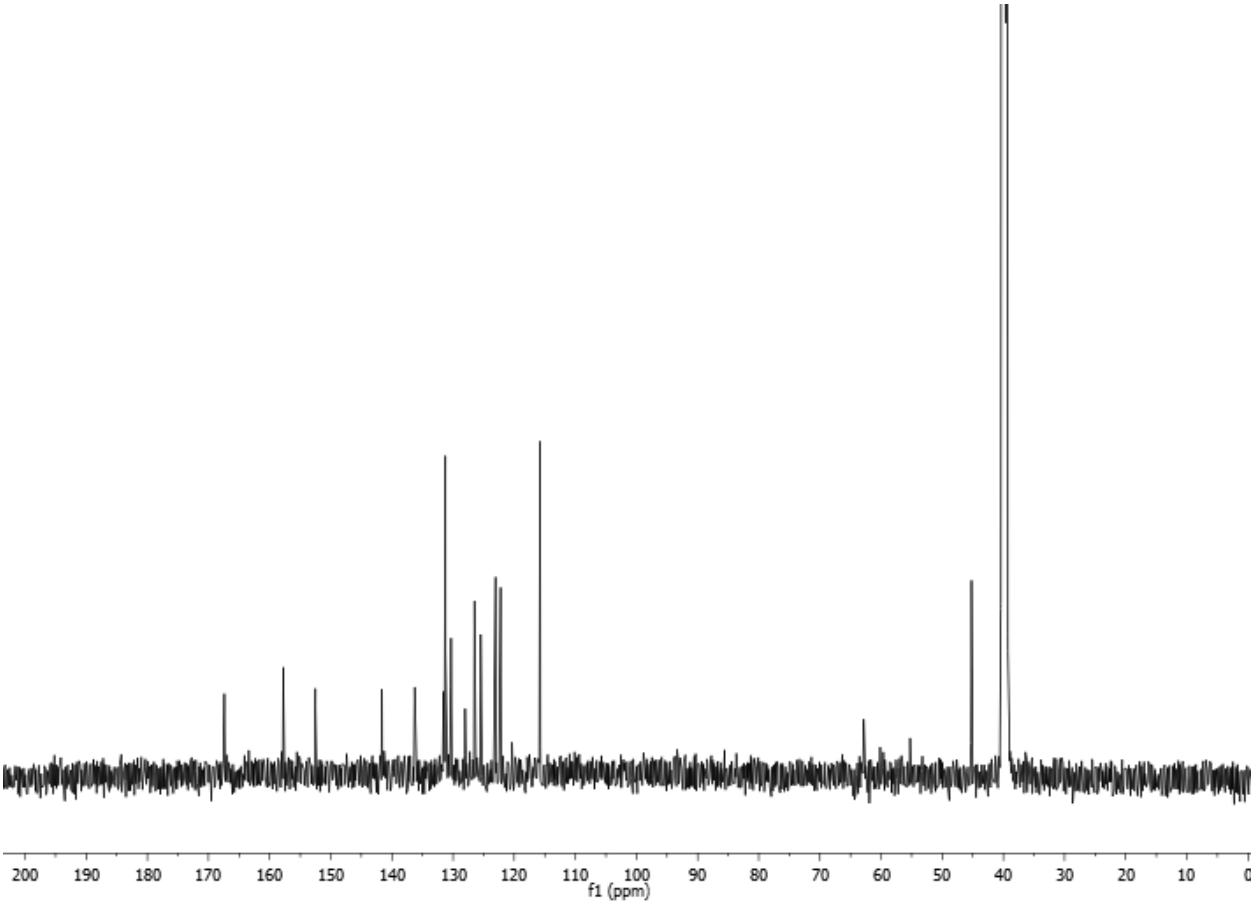
	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	1.436	Unknown	492890	95.88	82041	96.39	bb	96	1.075	1.875
2	2.630	Unknown	21178	4.12	3077	3.61	bb	38	2.508	2.825

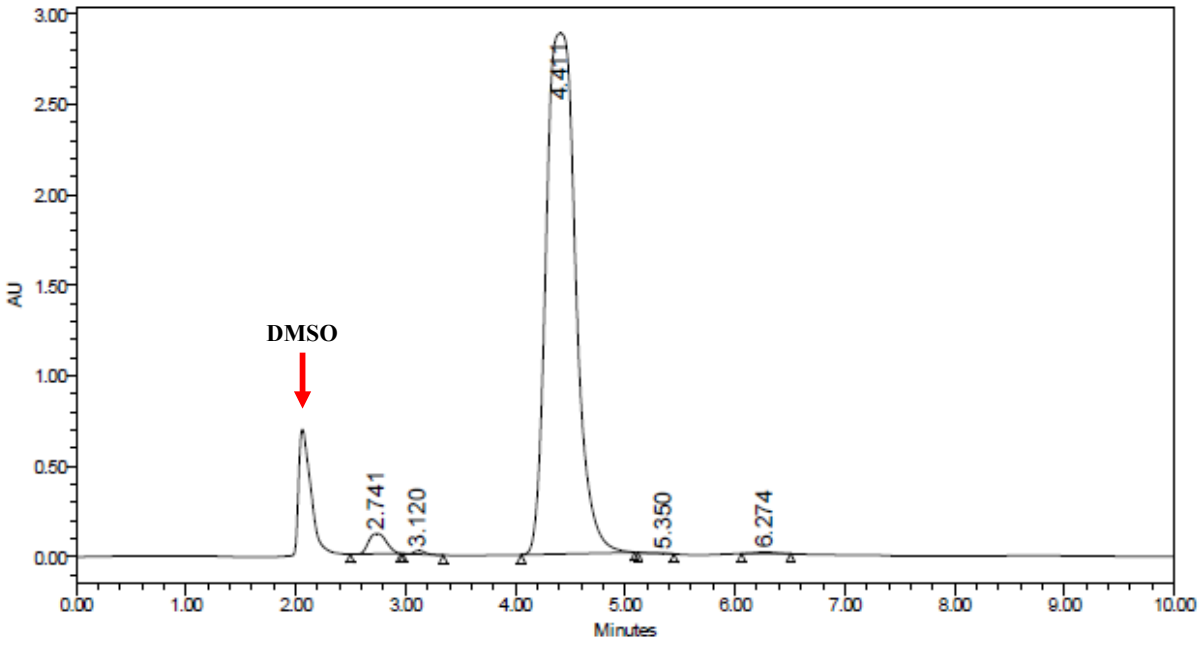


8i

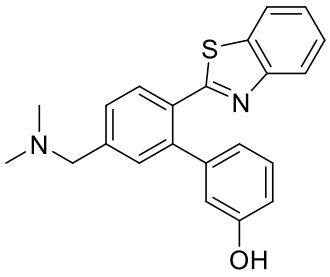
1H standard parameters. Solvent: DMSO QNP probe



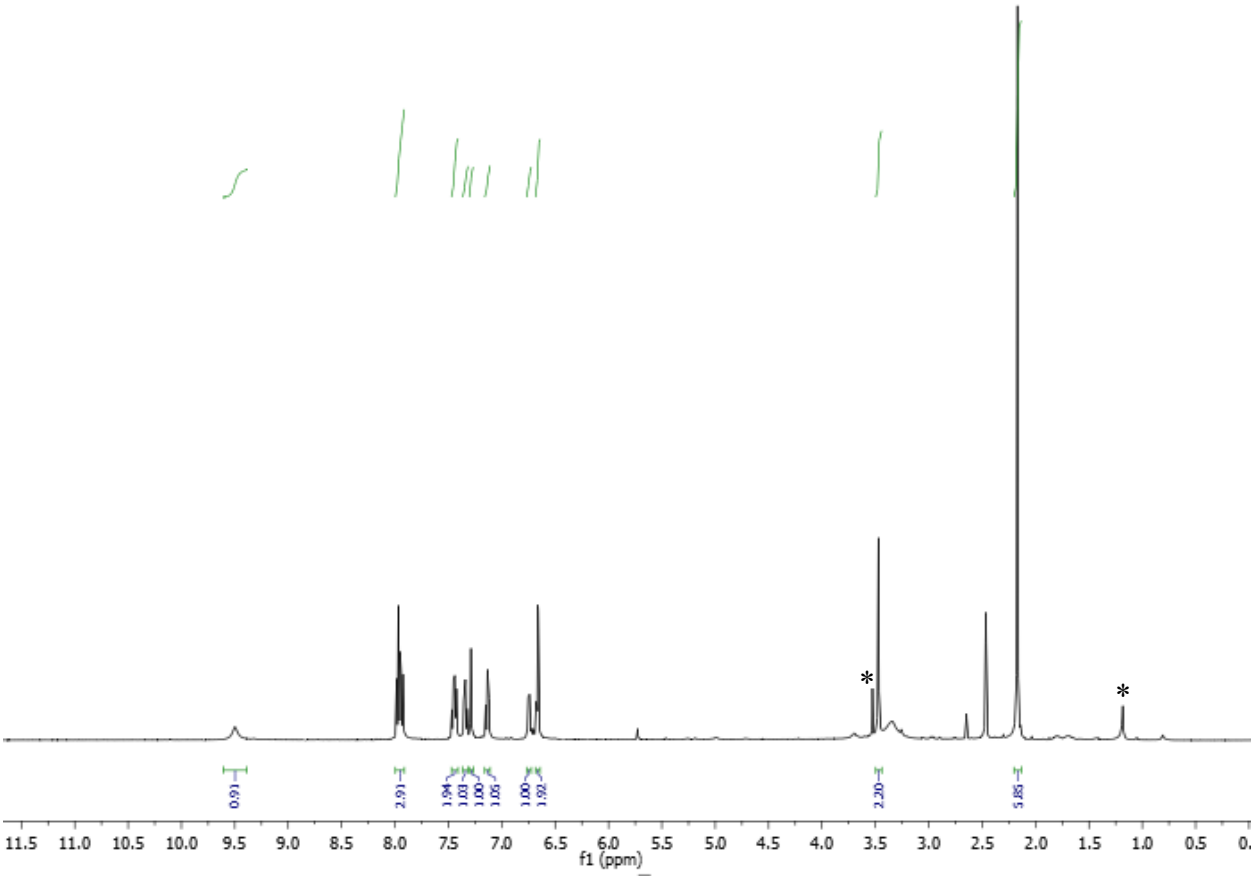

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

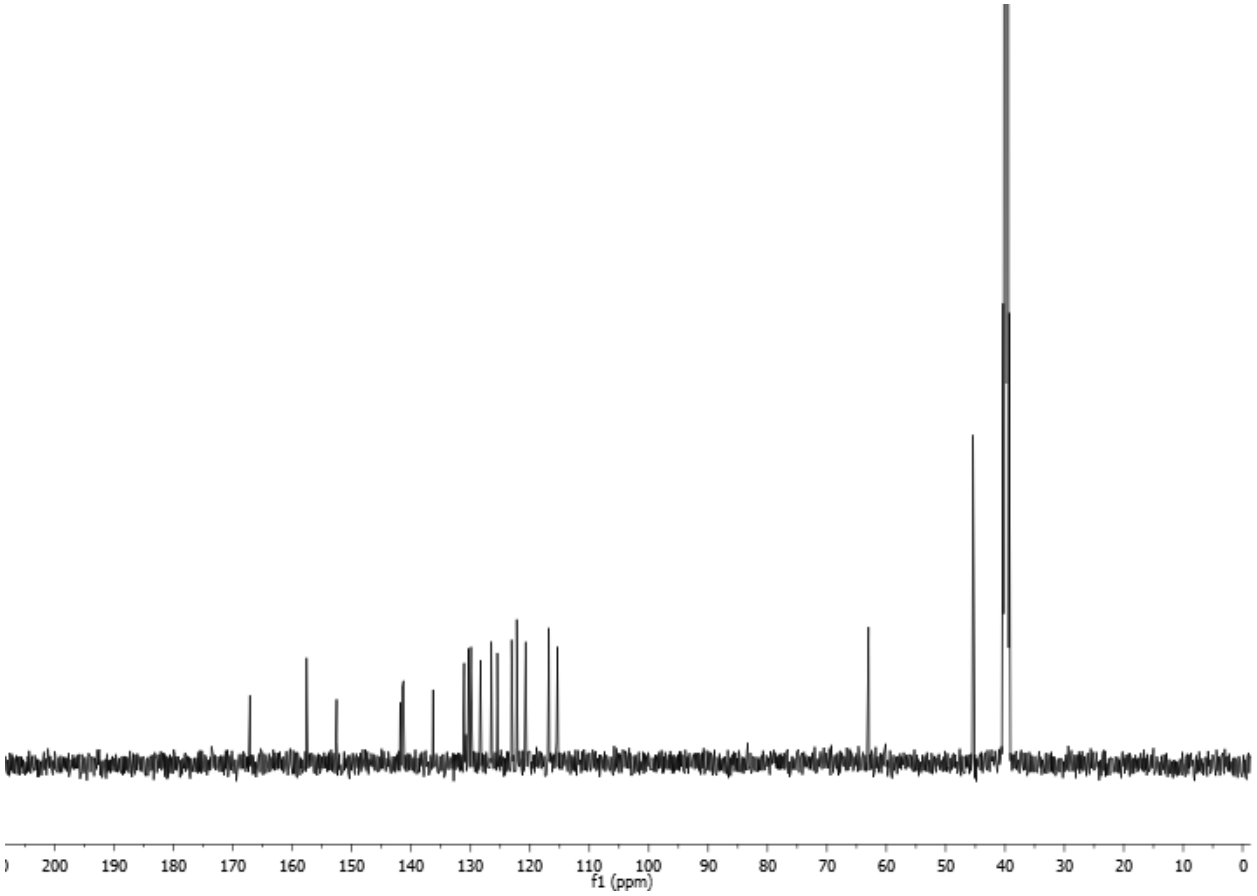


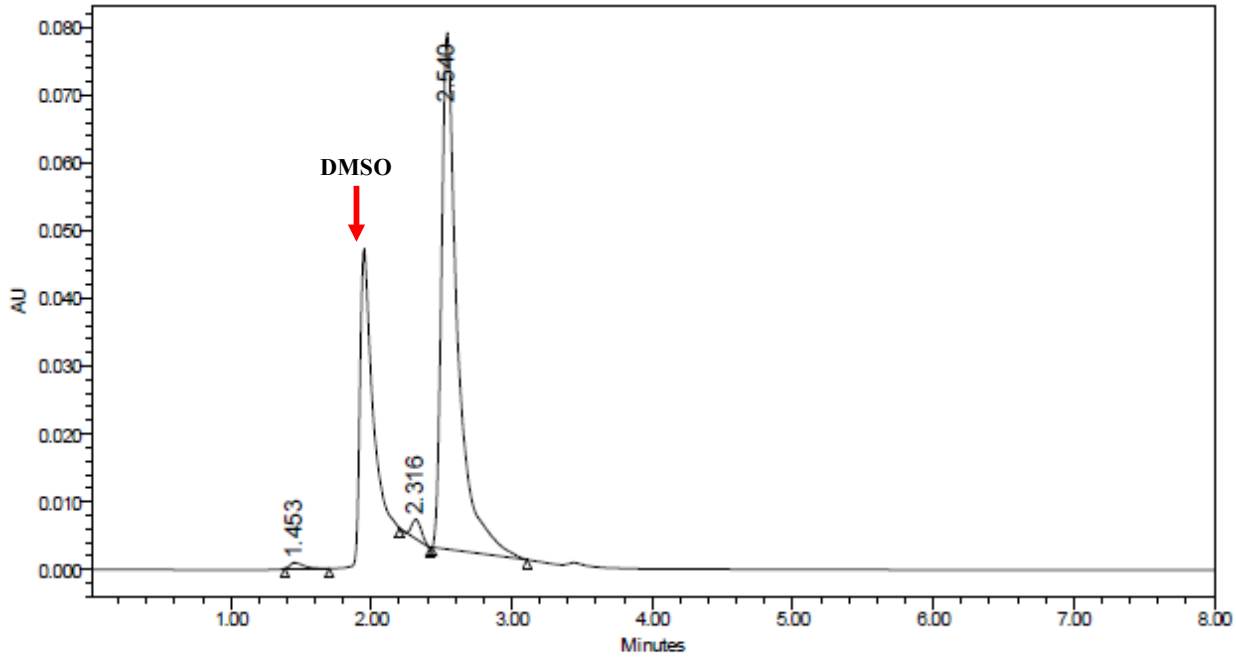
	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Peak Codes	Points Across Peak	Start Time (min)
1	2.741	Unknown	1252979	2.26	111029	3.68	bb		138	2.497
2	3.120	Unknown	135605	0.24	20938	0.69	bb		110	2.977
3	4.411	Unknown	53866803	97.26	2879078	95.32	bb		310	4.053
4	5.350	Unknown	17346	0.03	1676	0.06	bb	I08	98	5.117


S
N
N
OH

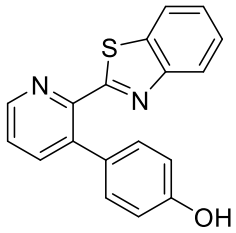
8j


*
*
0.91
2.91
1.94
1.03
1.00
1.05
1.00
1.92
2.20
5.85
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.
f1 (ppm)

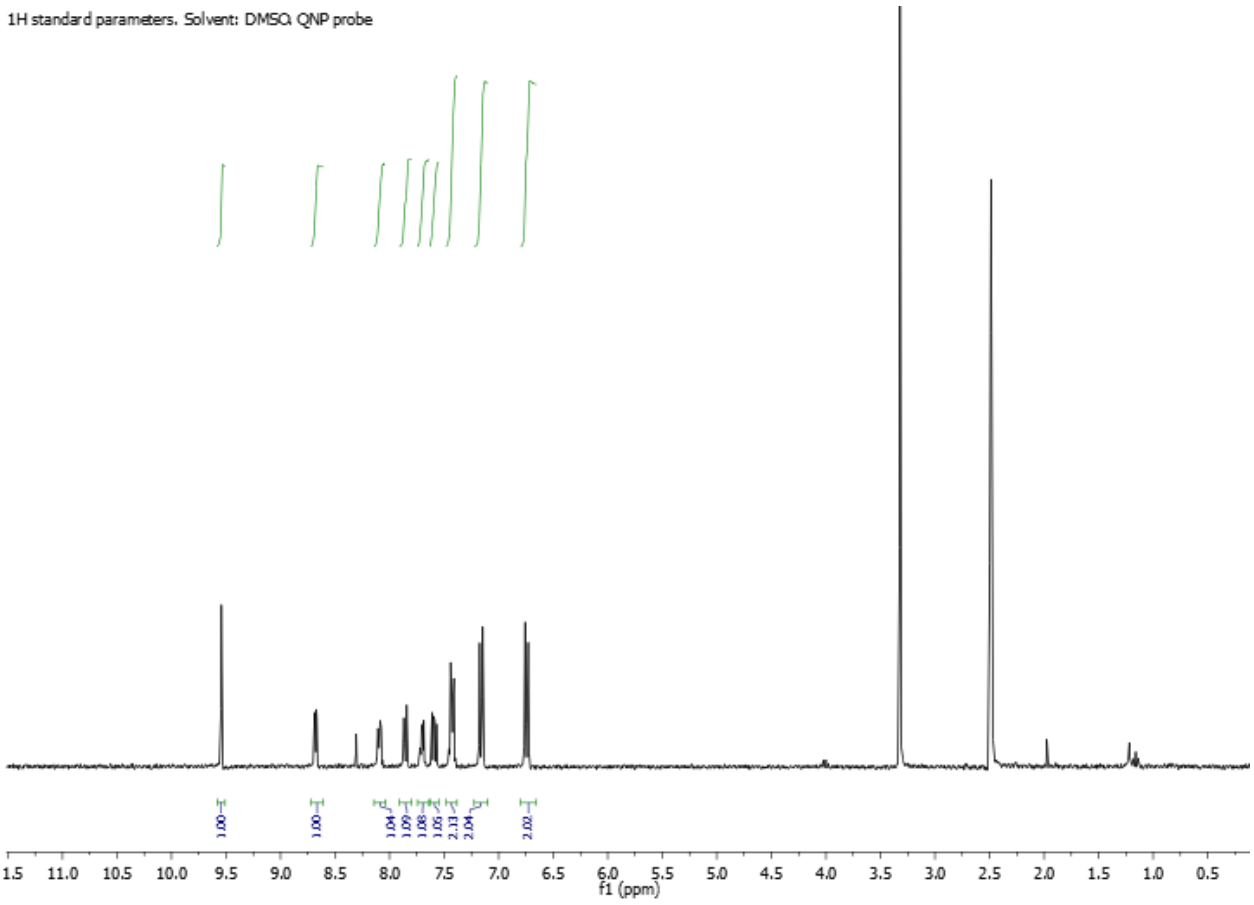

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

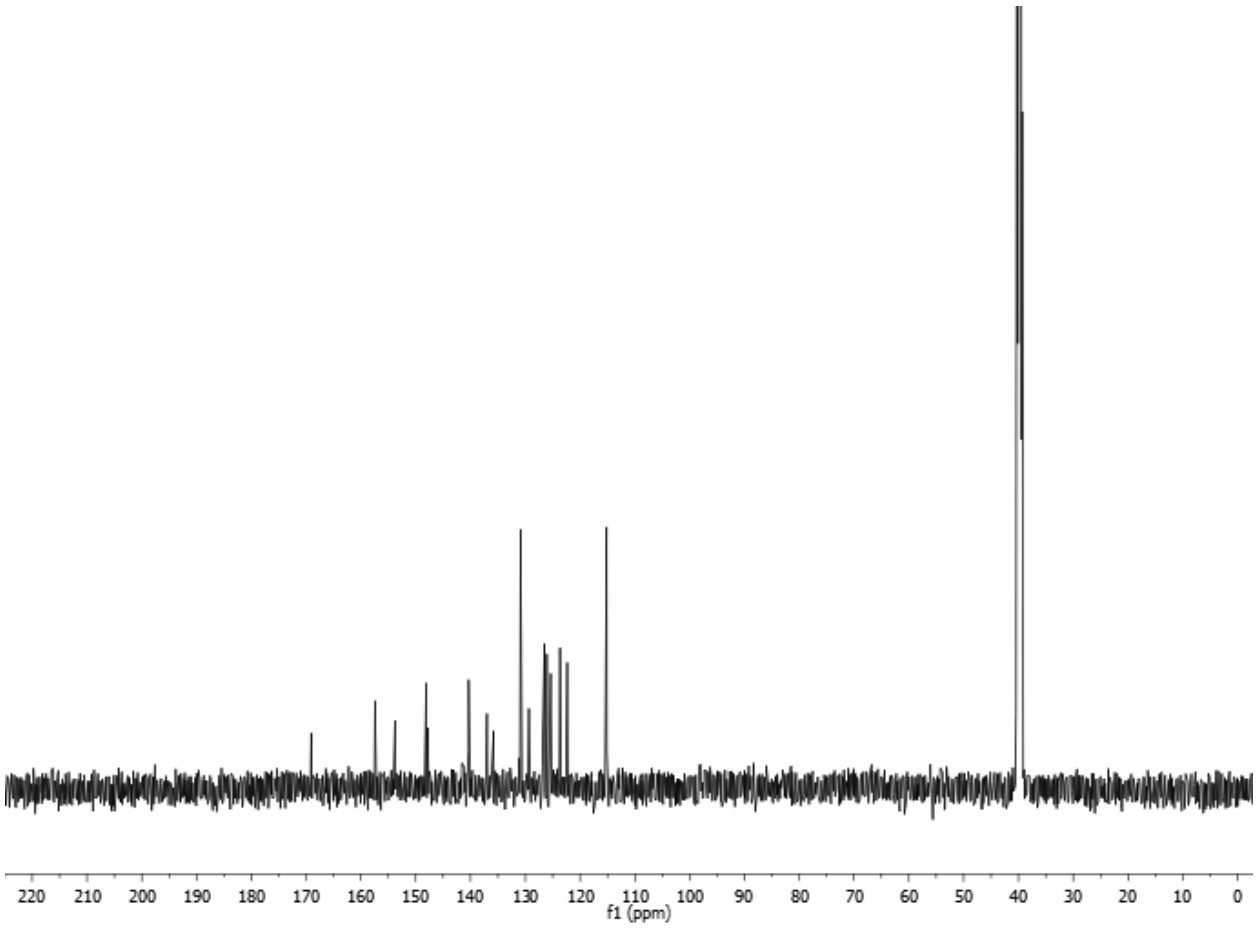


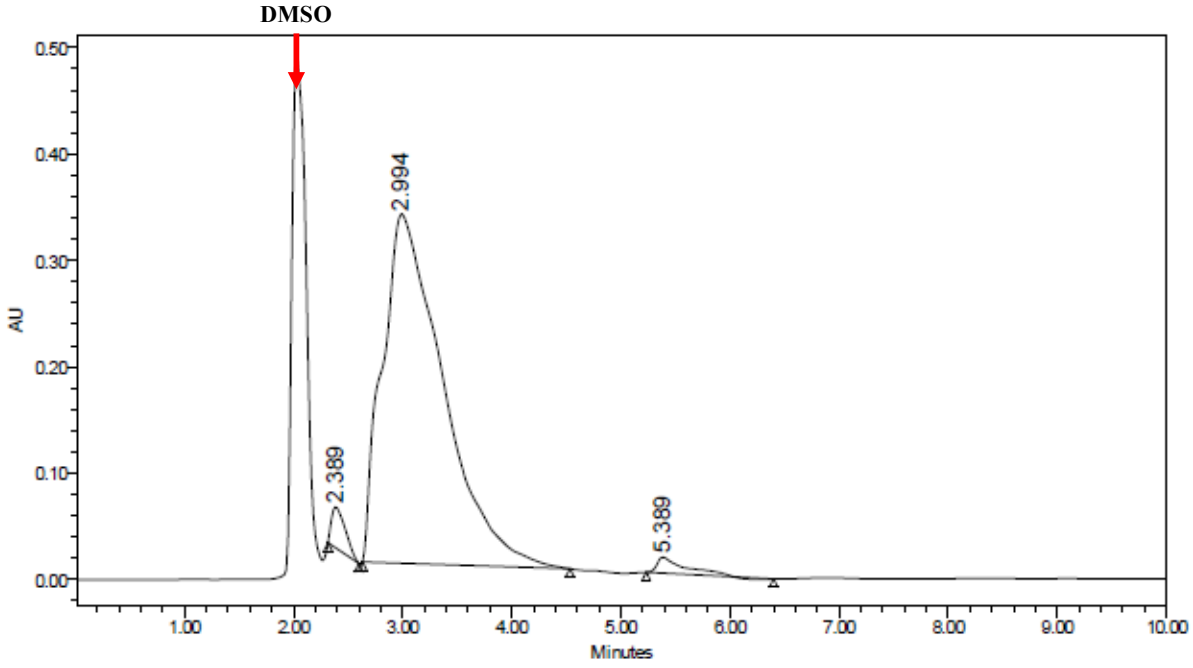
	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	1.453	Unknown	5664	0.90	856	1.07	bb	38	1.383	1.700
2	2.316	Unknown	14076	2.25	2877	3.59	bb	26	2.200	2.417
3	2.540	Unknown	606111	96.85	76299	95.34	bb	81	2.433	3.108


S
N
N
OH

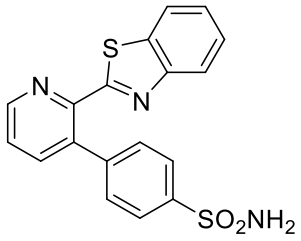
8k


1H standard parameters. Solvent: DMSO. QNP probe
1.00
1.00
1.04
1.09
1.08
1.05
2.13
2.04
2.02
1.5 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
f1 (ppm)

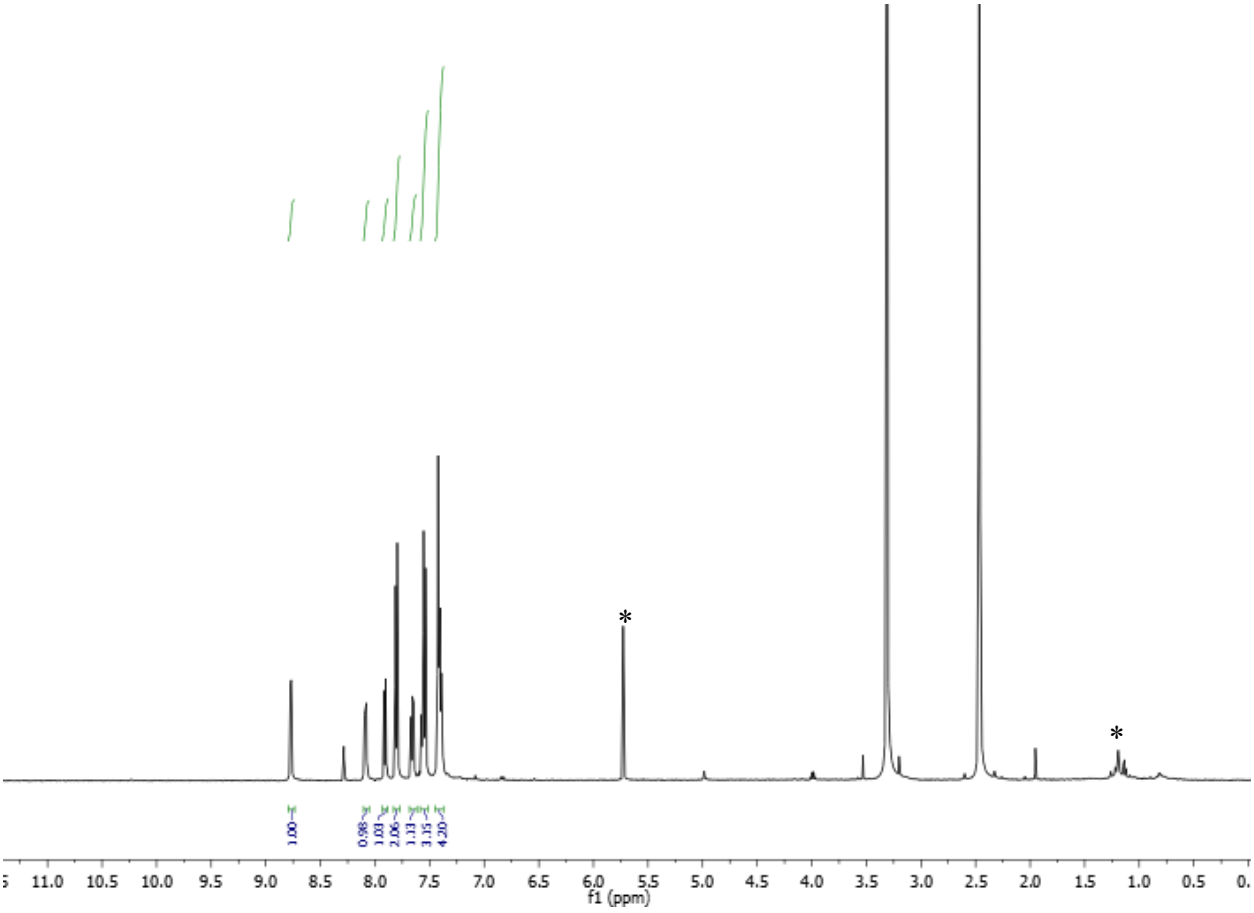

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

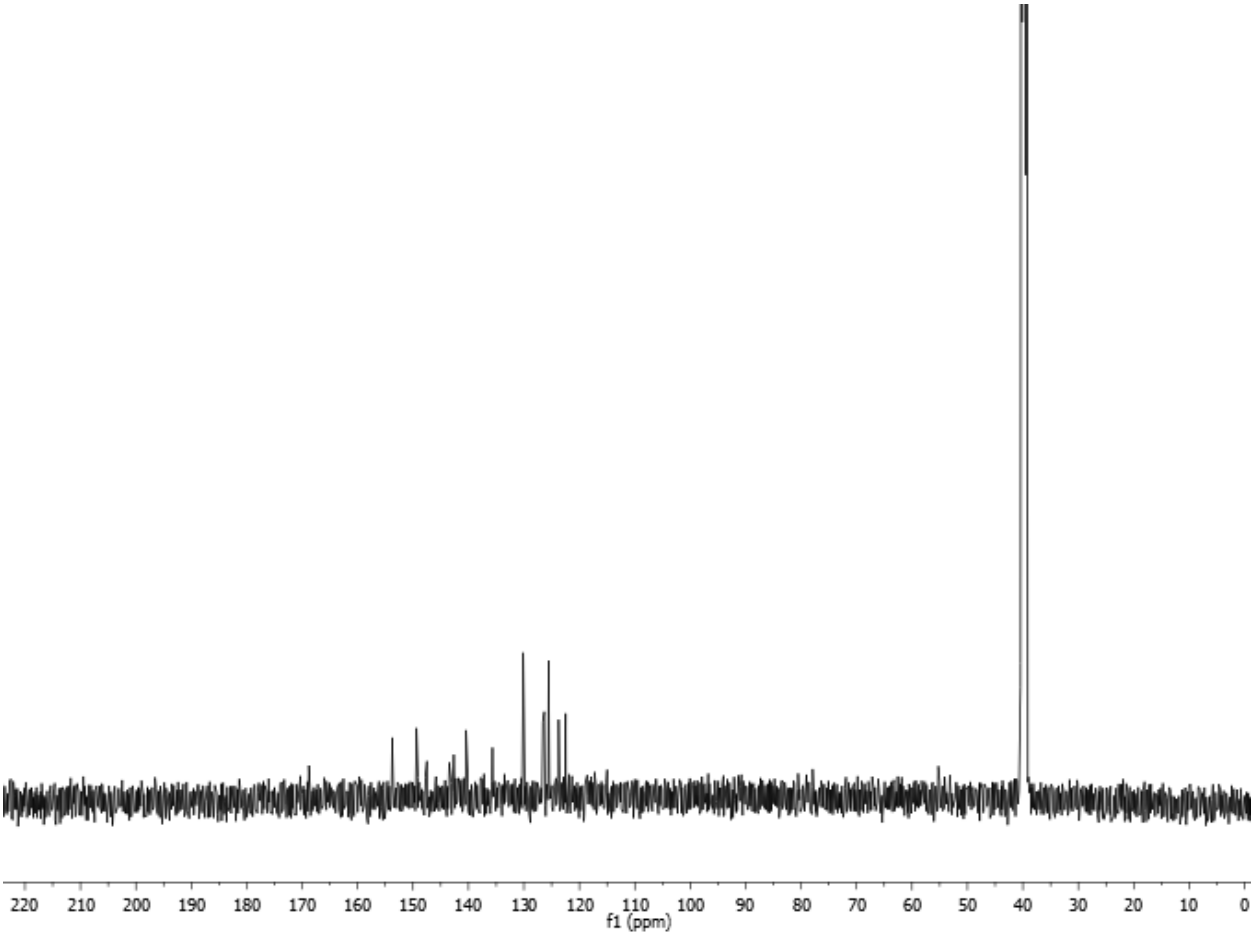


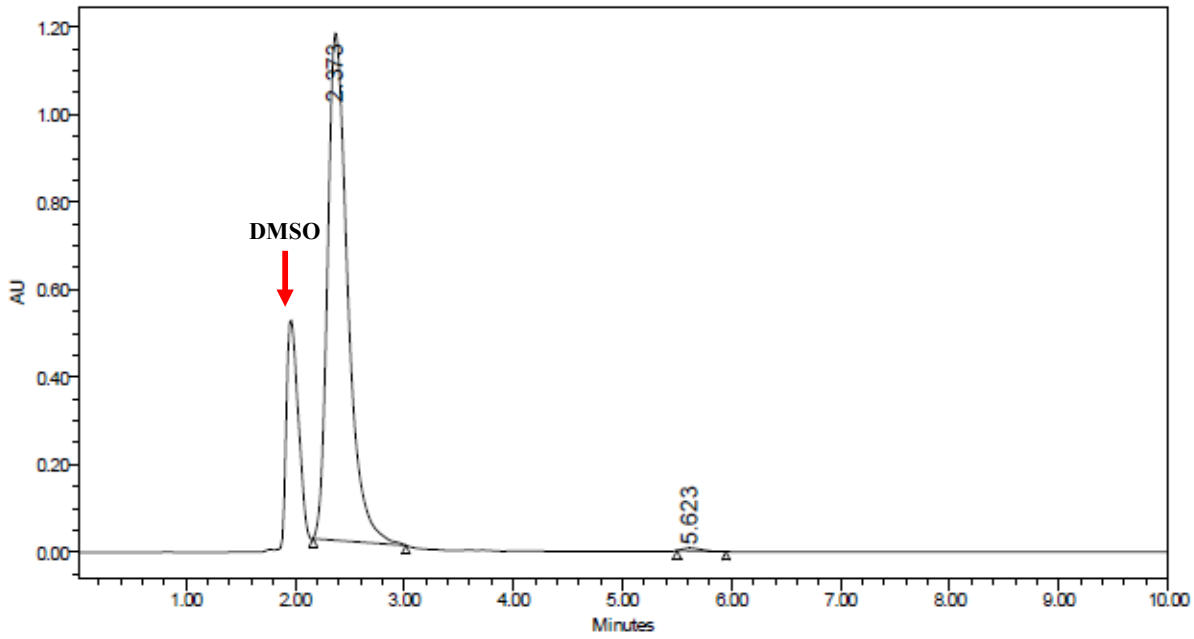
	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	2.389	Unknown	344469	2.59	38135	10.00	bb	17	2.317	2.600
2	2.994	Unknown	12658816	95.15	327934	86.03	bb	114	2.633	4.533
3	5.389	Unknown	300929	2.26	15113	3.96	bb	70	5.233	6.400


S
N
N
SO2NH2

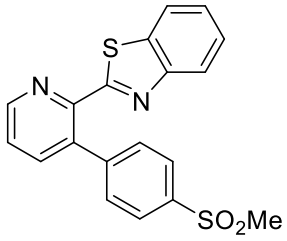
8l


*
*
1.00
0.98
1.03
2.06
1.13
3.15
4.20
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
f1 (ppm)

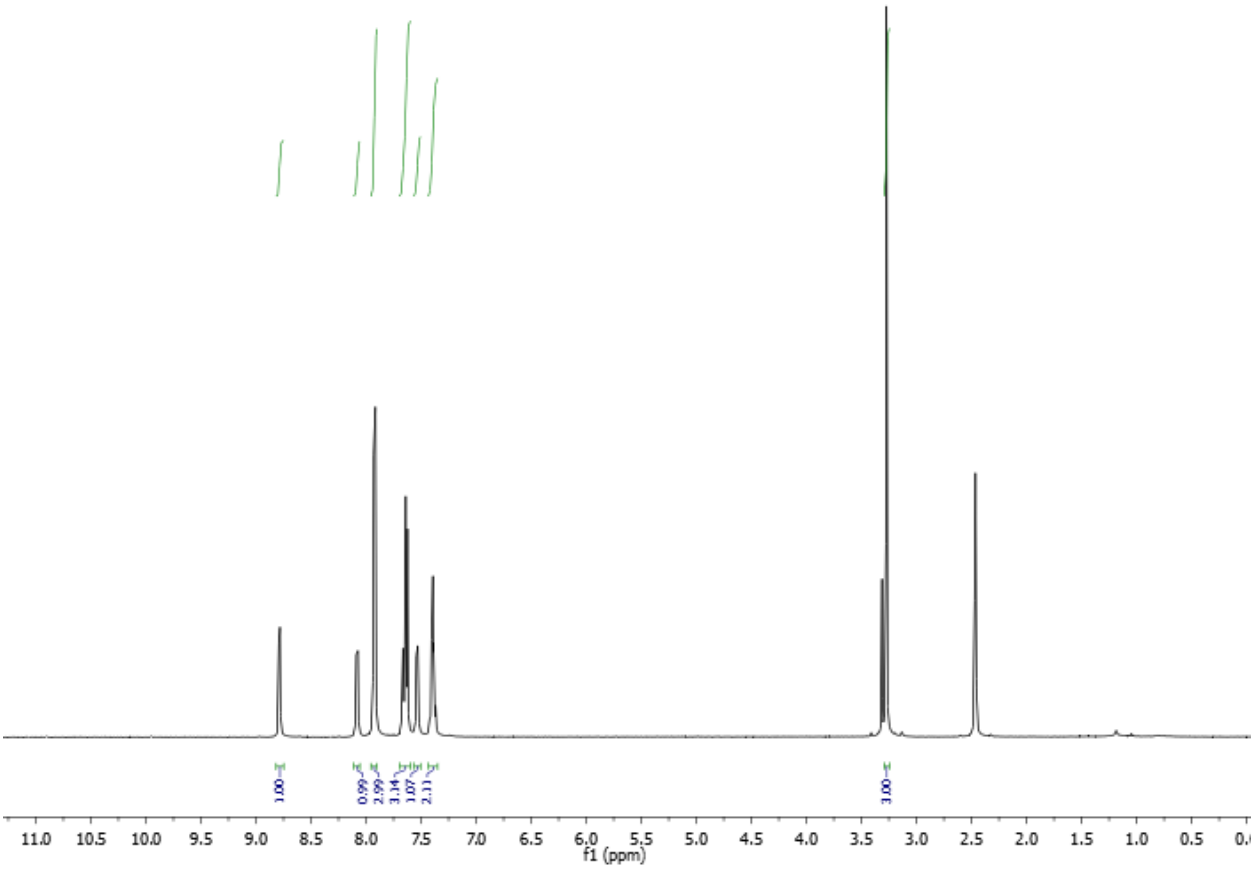

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

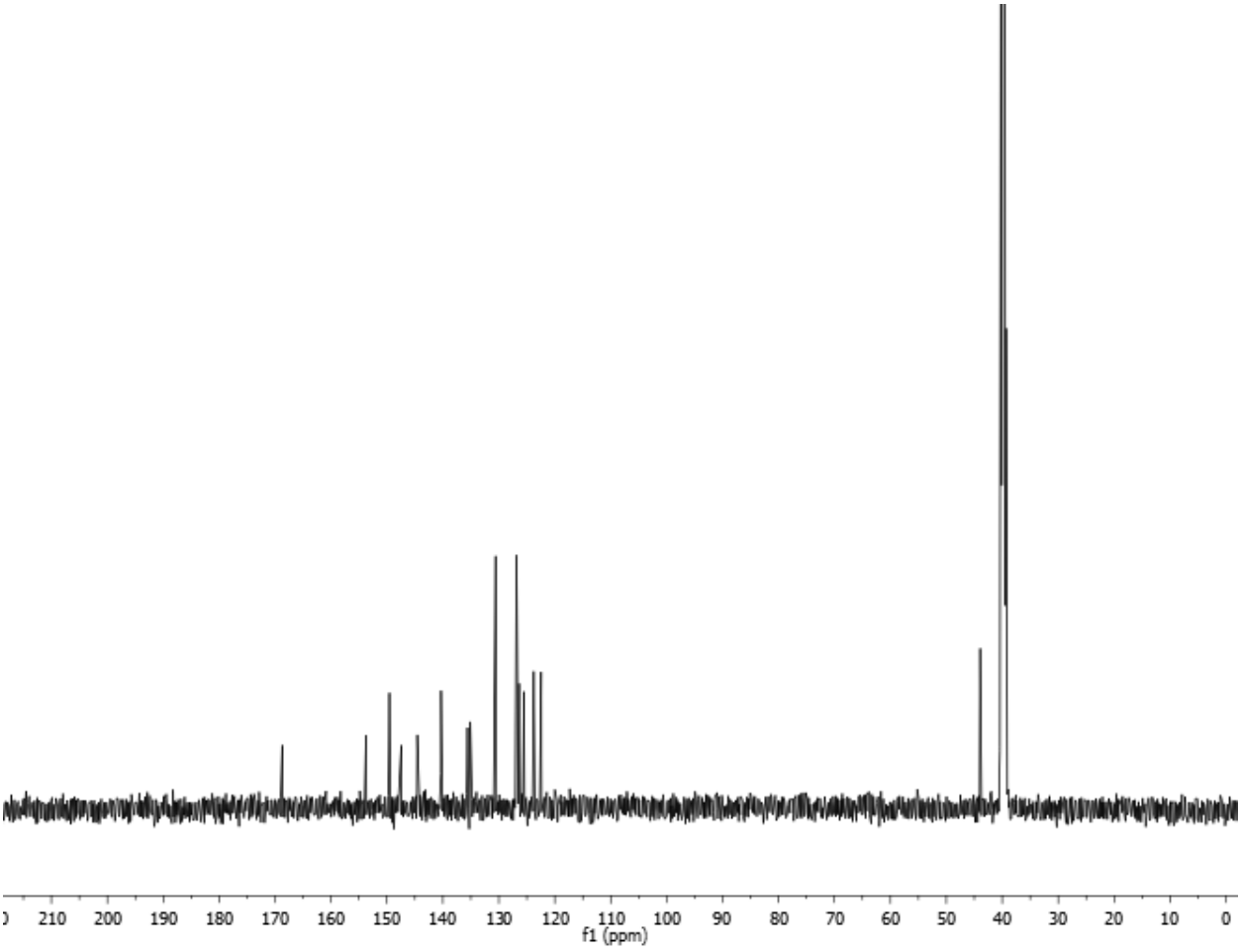


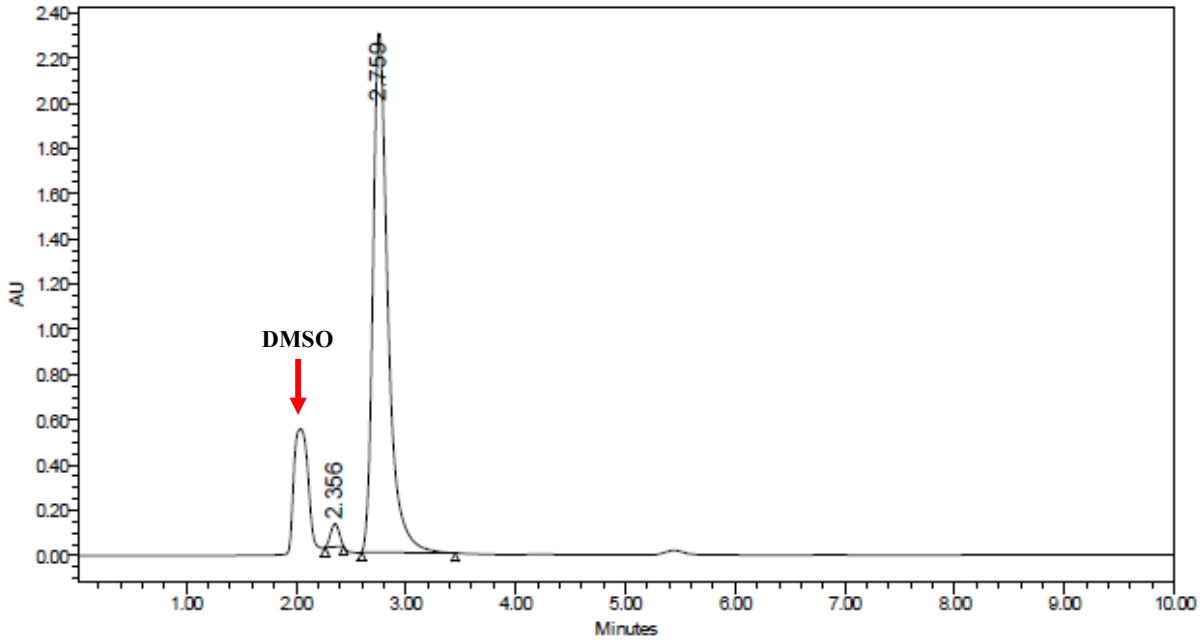
	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	2.373	Unknown	14860825	99.53	1163714	99.45	bb	51	2.167	3.017
2	5.623	Unknown	69810	0.47	6419	0.55	bb	27	5.500	5.950


S
N
N
SO2Me

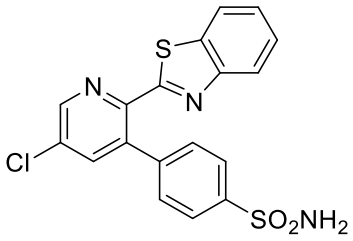
8m


1.00
0.99
2.99
3.14
1.07
2.11
3.00
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
f1 (ppm)

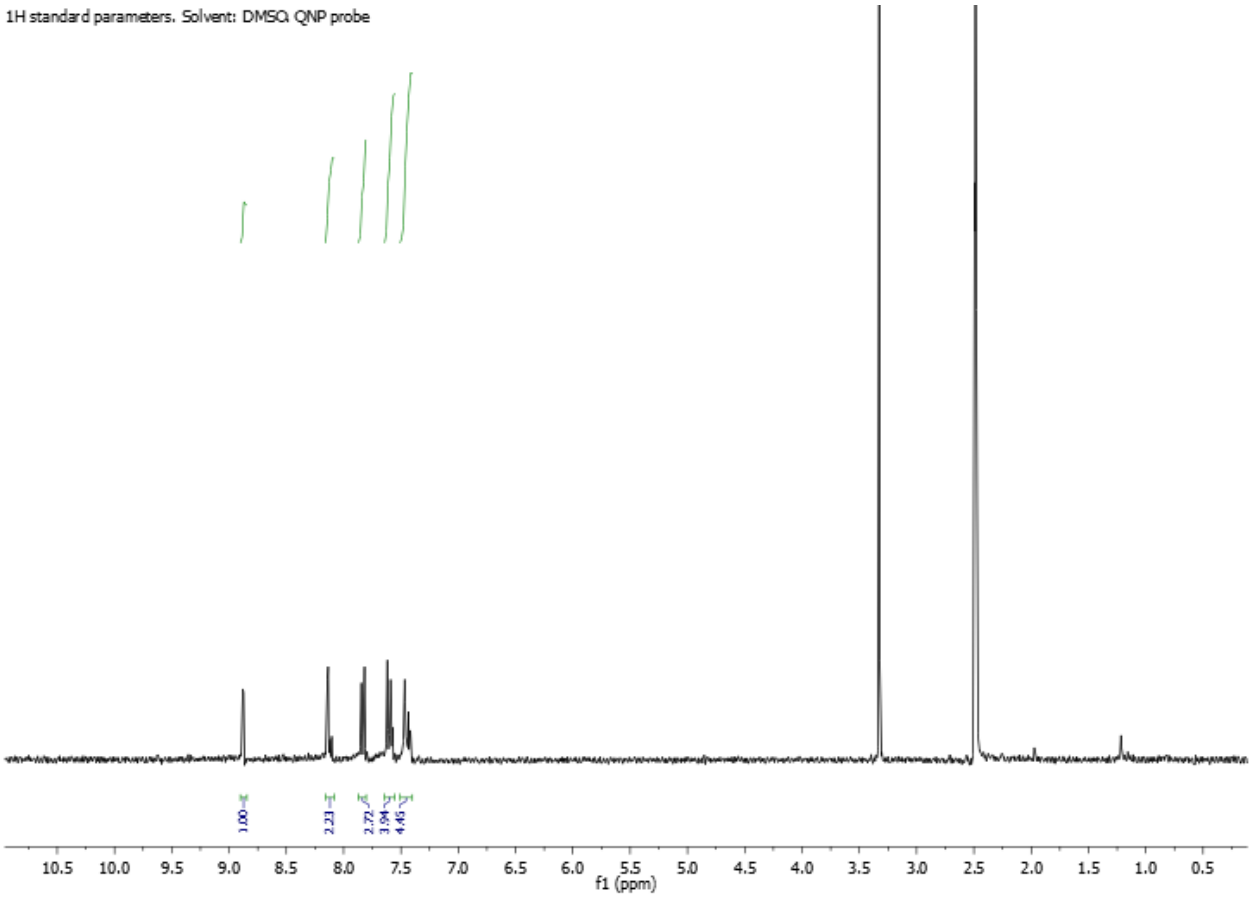

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

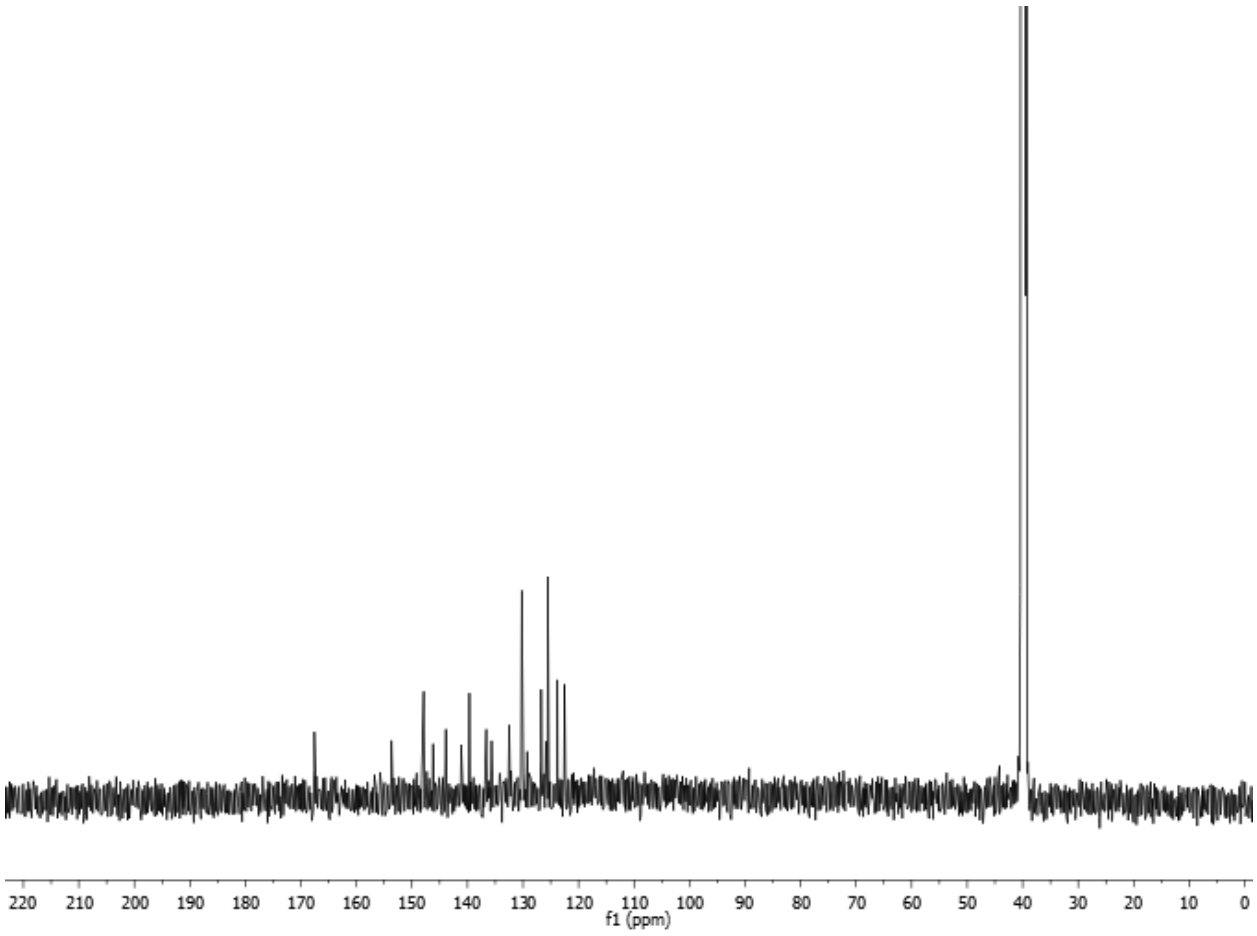


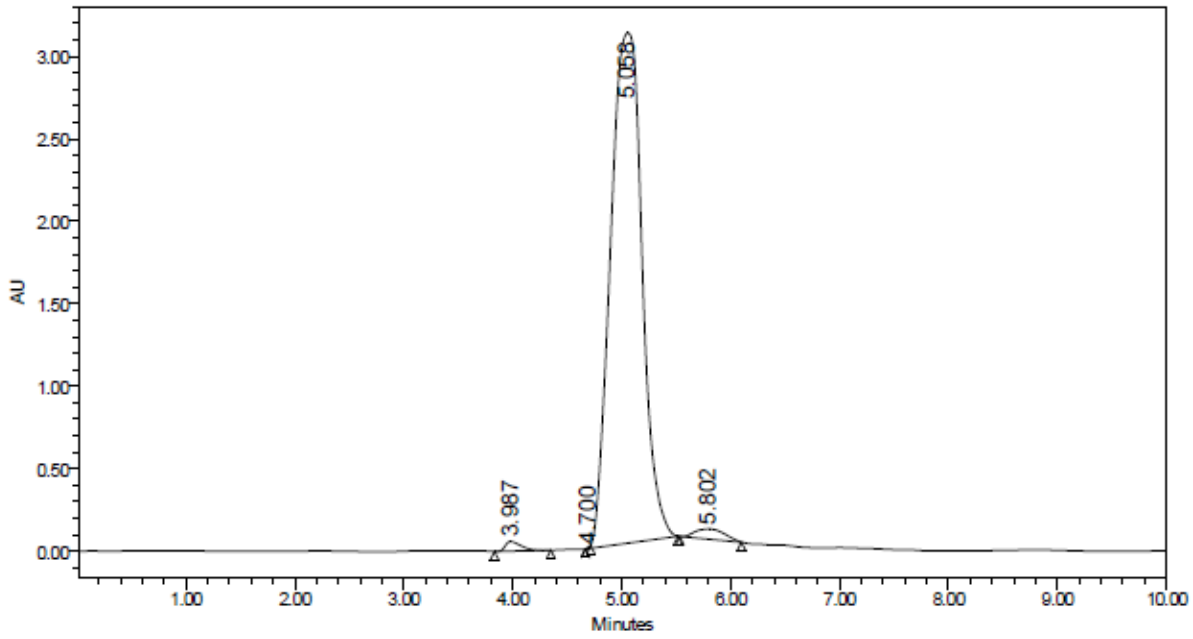
	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	2.356	Unknown	542749	2.44	101933	4.21	bb	10	2.267	2.433
2	2.759	Unknown	21674967	97.56	2318468	95.79	bb	51	2.600	3.450


S
N
N
Cl
SO2NH2

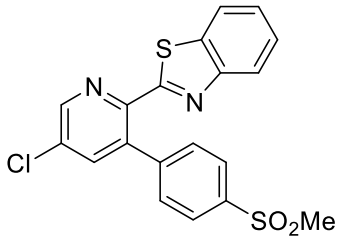
8n


1H standard parameters. Solvent: DMSO. QNP probe
1.00
2.23
2.72
3.94
4.45
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
f1 (ppm)

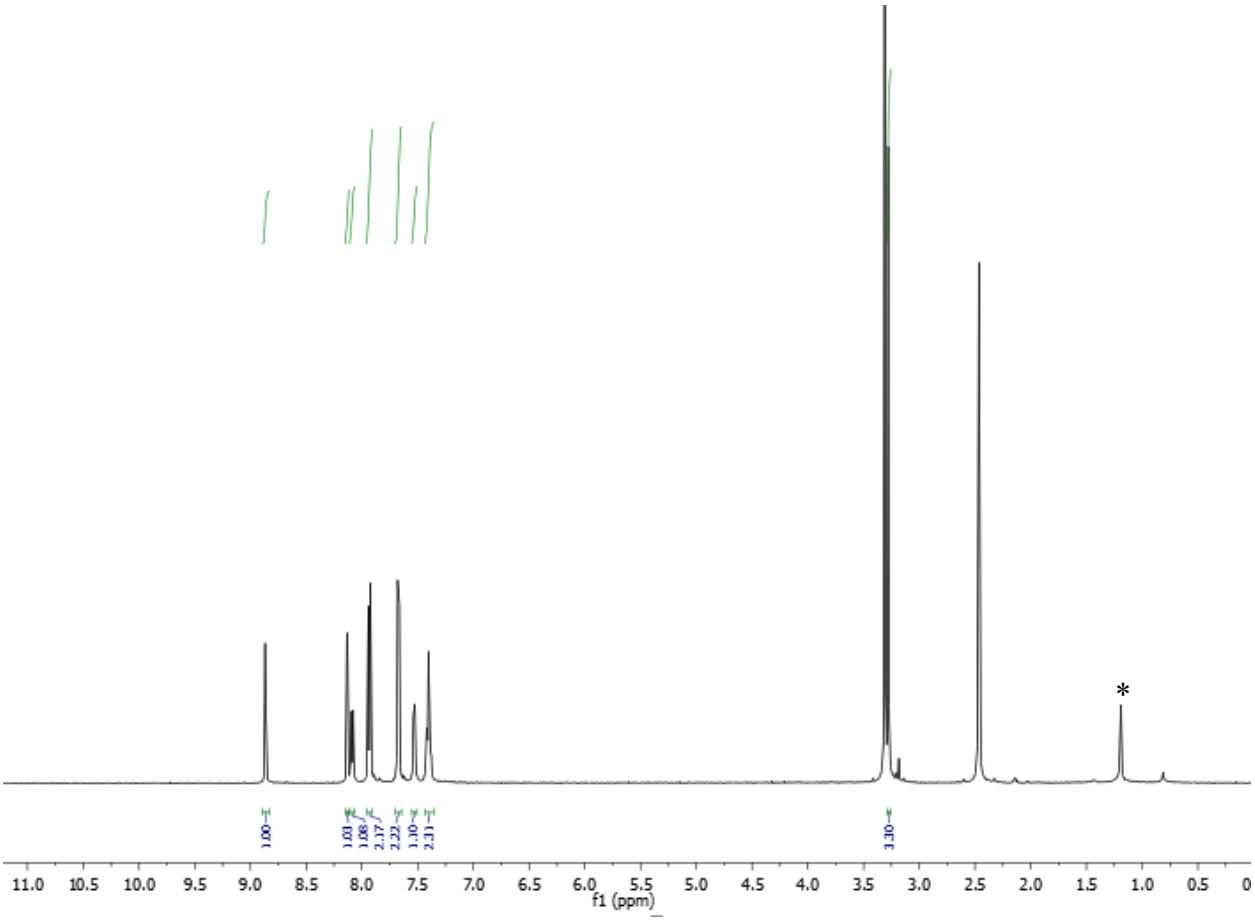

220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

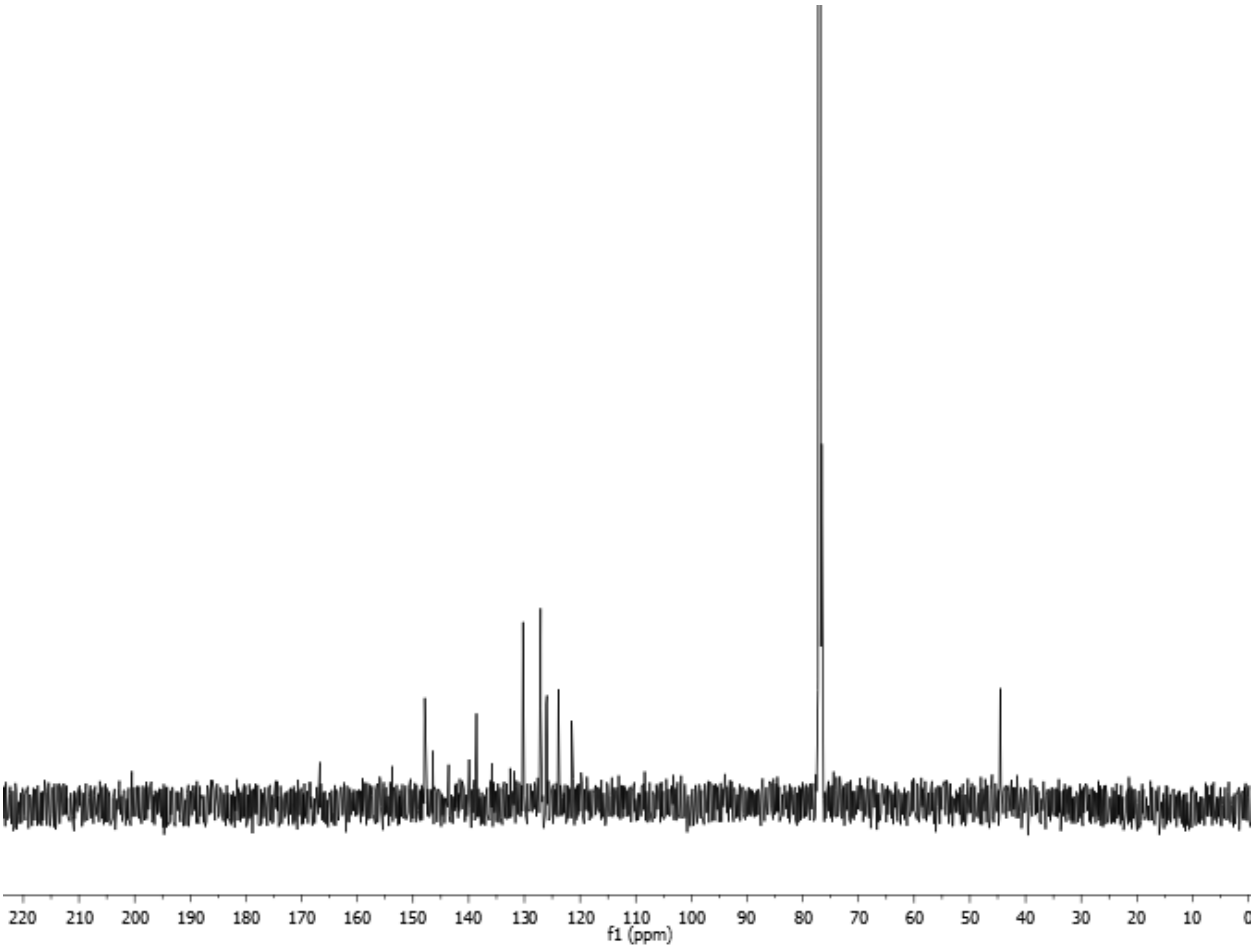


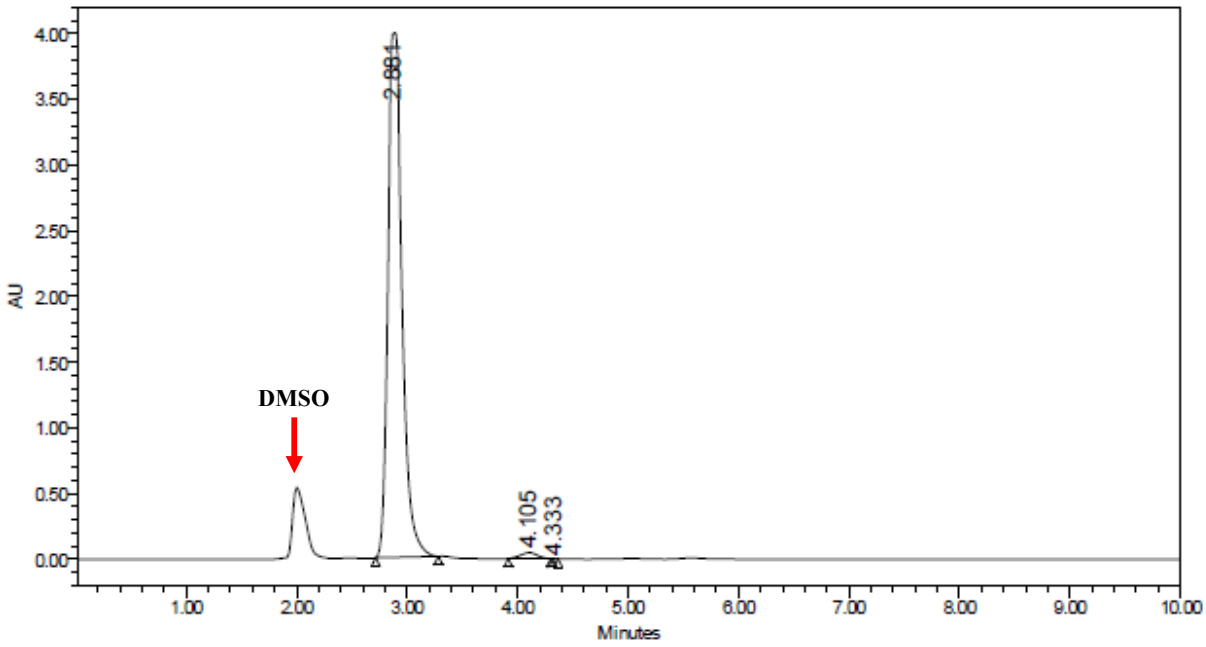
	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Peak Codes	Points Across Peak	Start Time (min)
1	3.987	Unknown	578599	0.90	59812	1.85	bb		31	3.833
2	4.700	Unknown	11809	0.02	-6777	0.21	tt	I05	3	4.667
3	5.058	Unknown	62305388	97.26	3097181	96.01	bb		51	4.667
4	5.802	Unknown	1165698	1.82	62256	1.93	bb		34	5.533


S
N
N
Cl
SO2Me

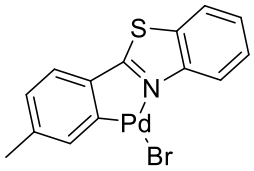
8o


*
1.00
1.03
1.08
2.17
2.22
1.10
2.31
3.30
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
f1 (ppm)

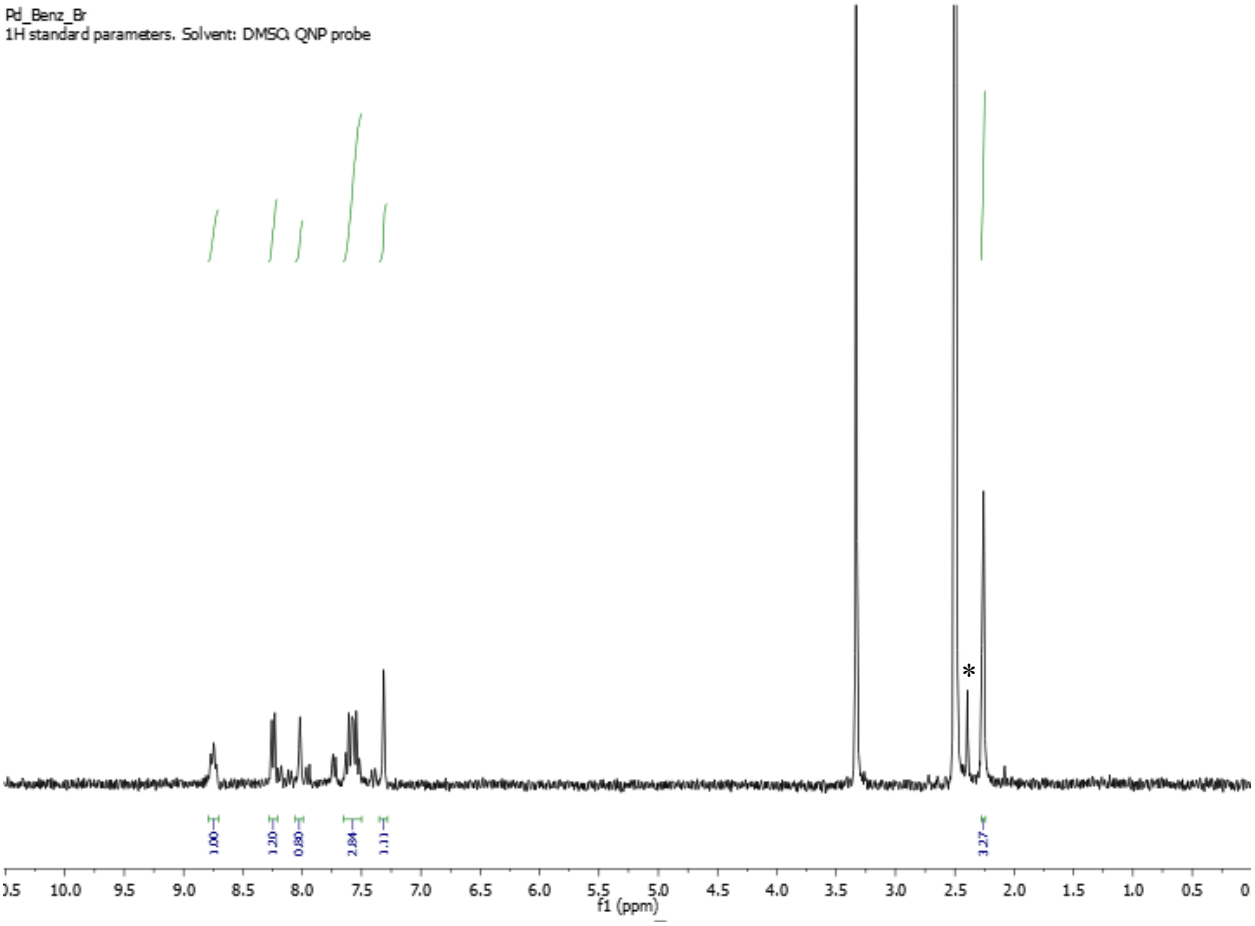

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

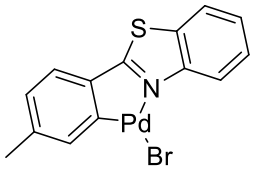


	RT (min)	Peak Type	Area (µV*sec)	% Area	Height (µV)	% Height	Integration Type	Peak Codes	Points Across Peak	Start Time (min)
1	2.881	Unknown	35543871	98.68	4156739	98.91	bb		34	2.717
2	4.105	Unknown	473534	1.31	45703	1.09	bb		23	3.917
3	4.333	Unknown	259	0.00	-137	0.00	bb	I05	3	4.317

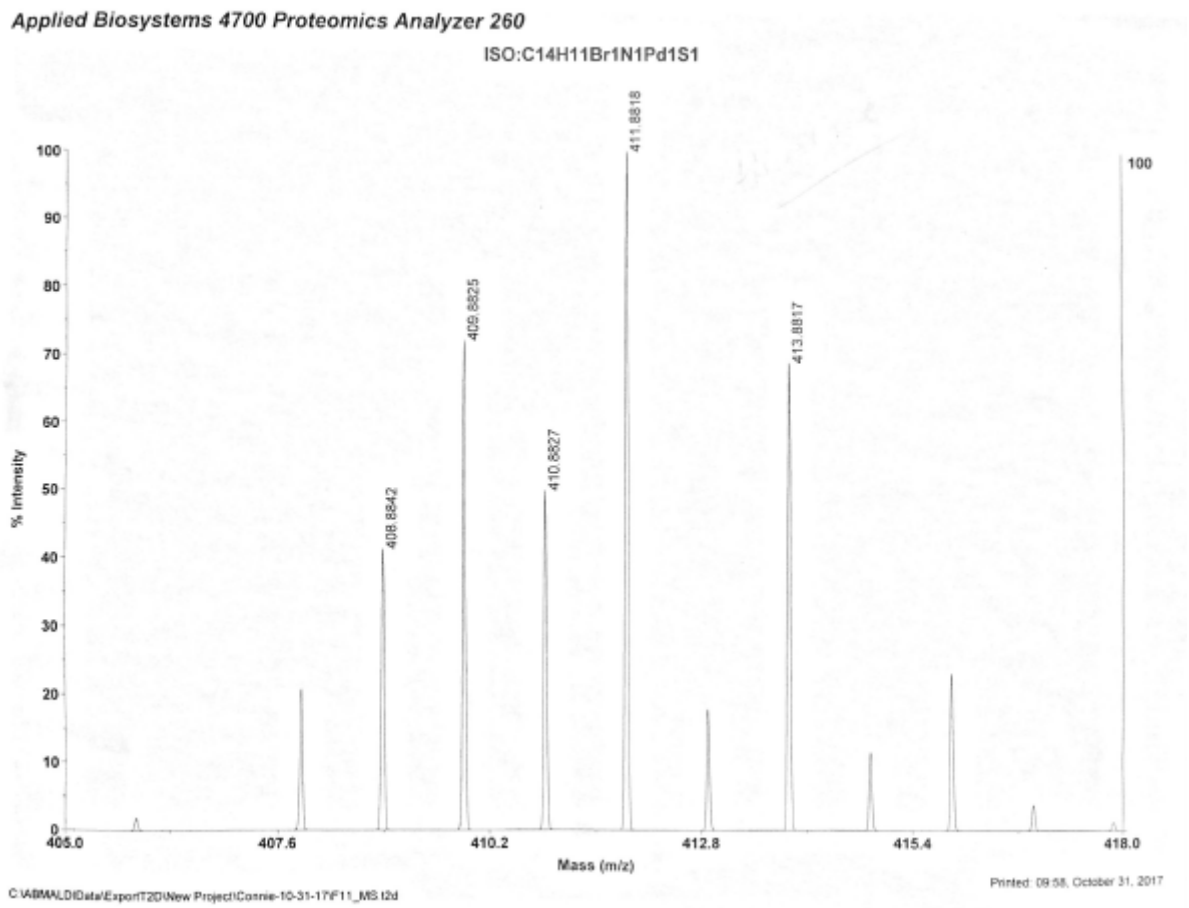

S
N
Pd
Br

9


Pd_Benz_Br
1H standard parameters. Solvent: DMSO; QNP probe
*
1.00
1.20
0.80
2.84
1.11
3.27
f1 (ppm)


S
N
Pd
Br

9


Applied Biosystems 4700 Proteomics Analyzer 260
ISO:C14H11Br1N1Pd1S1
411.8818
100
409.8825
413.8817
408.8842
410.8827
% Intensity
Mass (m/z)
405.0
407.6
410.2
412.8
415.4
418.0
C:\ABMALDIData\Export\T2D\New Project\Connie-10-31-17\F11_MS.t2d
Printed: 09:58, October 31, 2017