Synthesis of Indazolones via Friedel-Crafts Cyclization of Blocked (Masked) *N*-Isocyanates

Eslam B. Elkaeed,[ab] Jing An,[a] André M. Beauchemin[a]*

a) Centre for Catalysis Research and Innovation, Department of Chemistry and Biomolecular Sciences, University of Ottawa, 10 Marie-Curie, Ottawa, ON, K1N 6N5, Canada.

b) Department of Organic Chemistry, Faculty of Pharmacy, Al-Azhar University, Cairo 11884, Egypt.

*andre.beauchemin@uottawa.ca

Supporting information

Table of Contents page

Difficult Substrates - Further Calibration on the Scope of this Reactivity

Additional data on attempted cyclizations of other substrates is provided below. Unfortunately, the cyclization of some electron-rich and electron-poor substrates was not observed under the standard conditions, or at a higher temperature. In addition, cyclization of the *N*-*t*-butyl substrate could not be achieved. This result suggests that the cyclization is sensitive to destabilizing interactions (Ar ⇔ Me group on *t*-Bu), as hinted by the low yield obtained for the cyclization to form product **2f**. The result with the *m*-methyl substrate was unexpected.

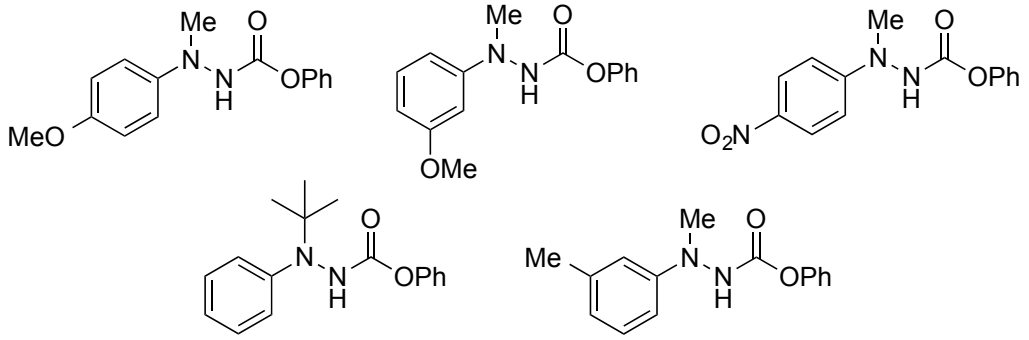
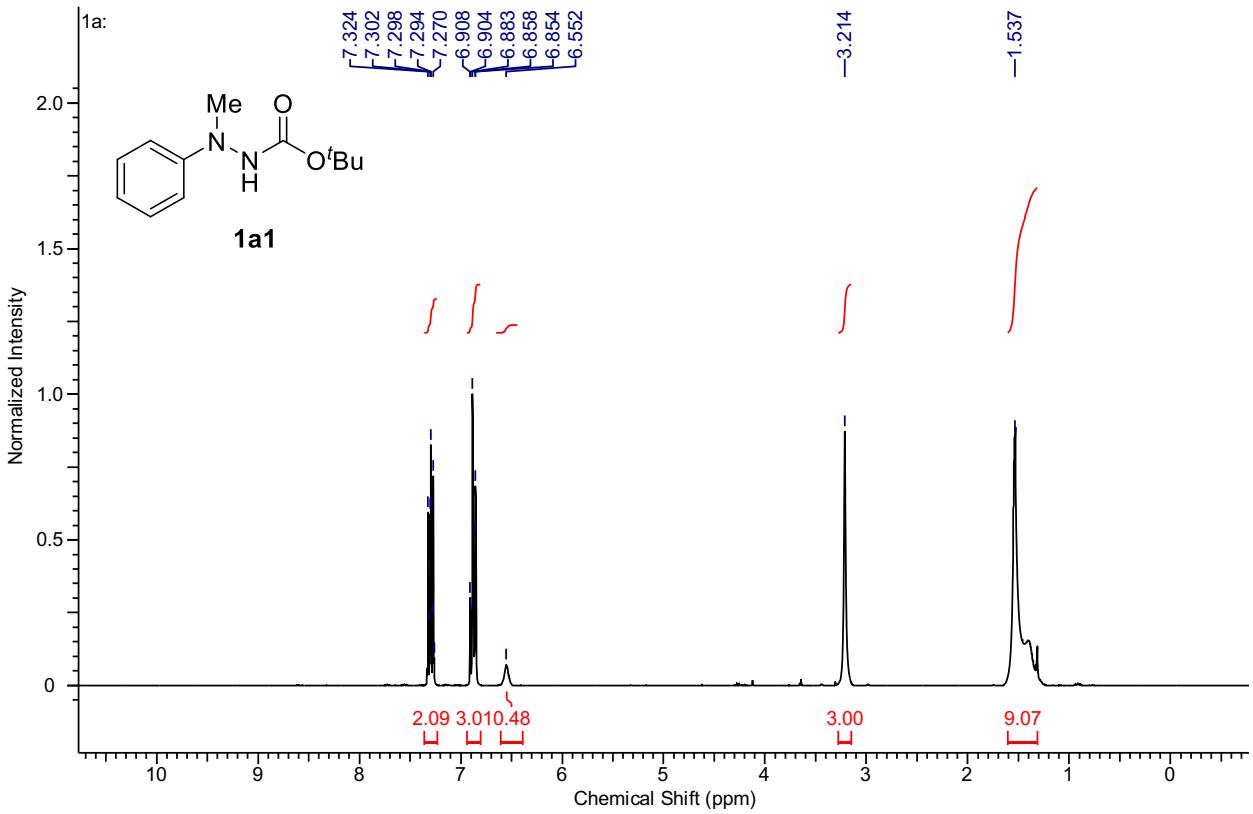
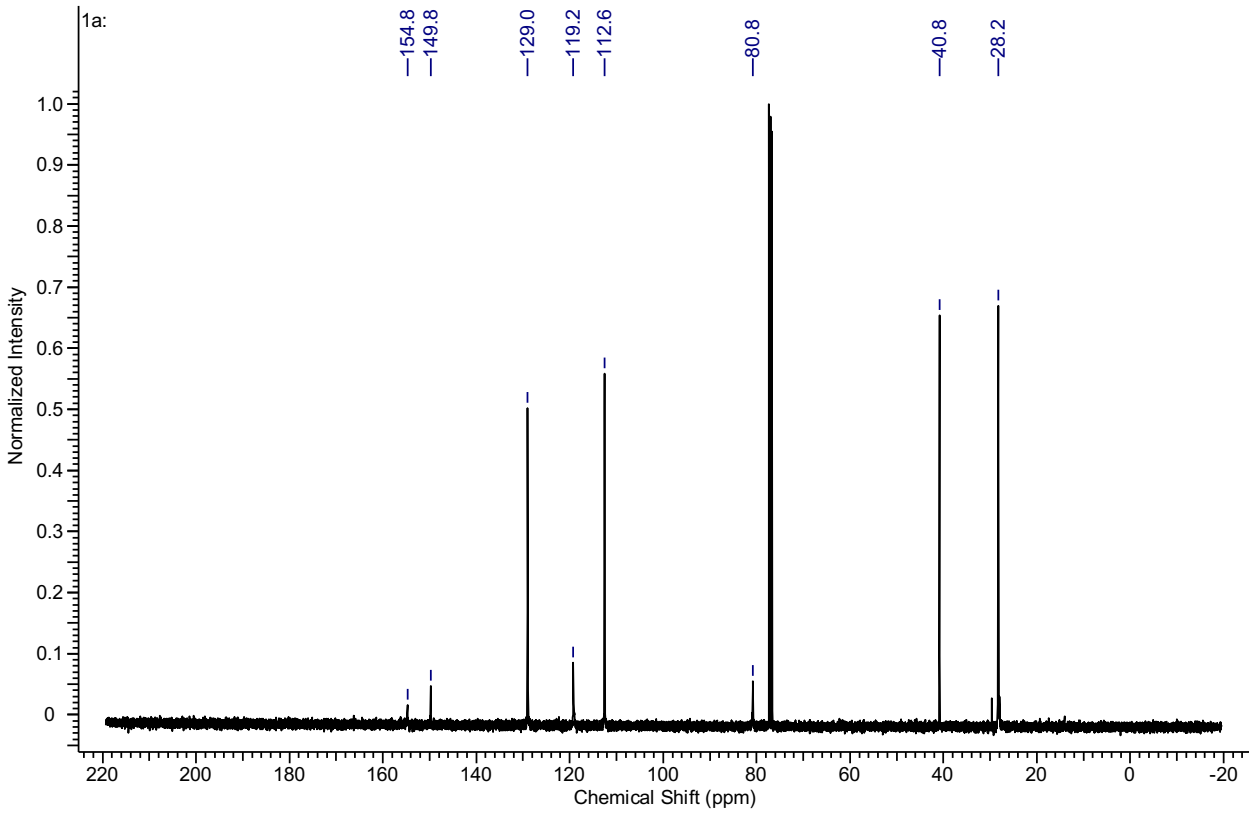
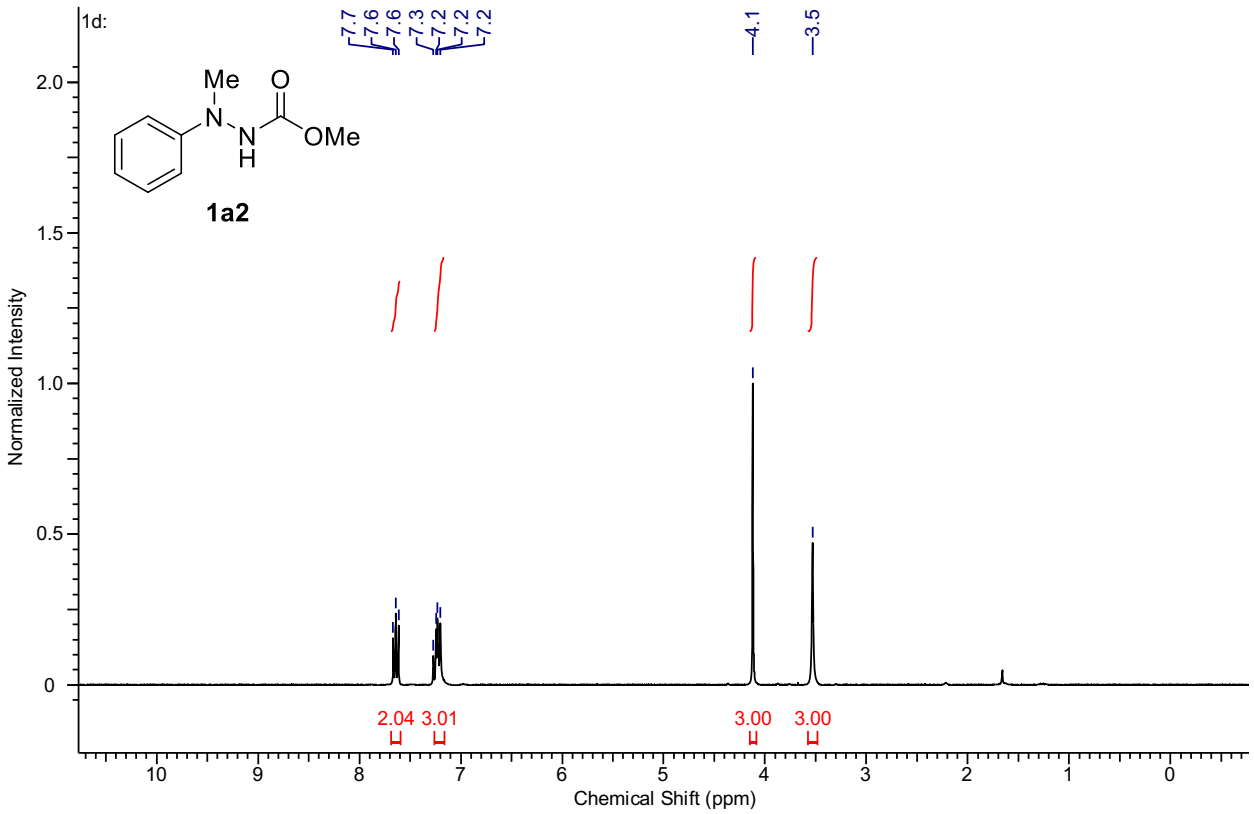
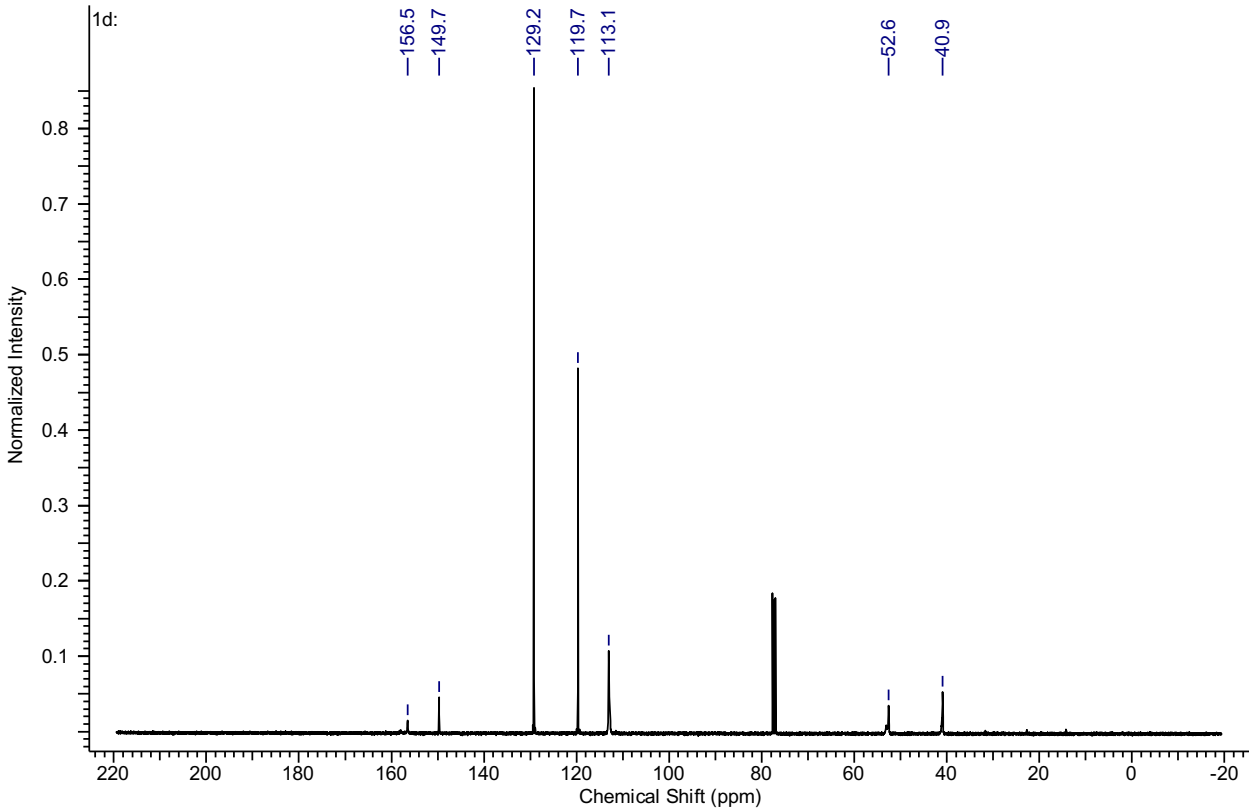


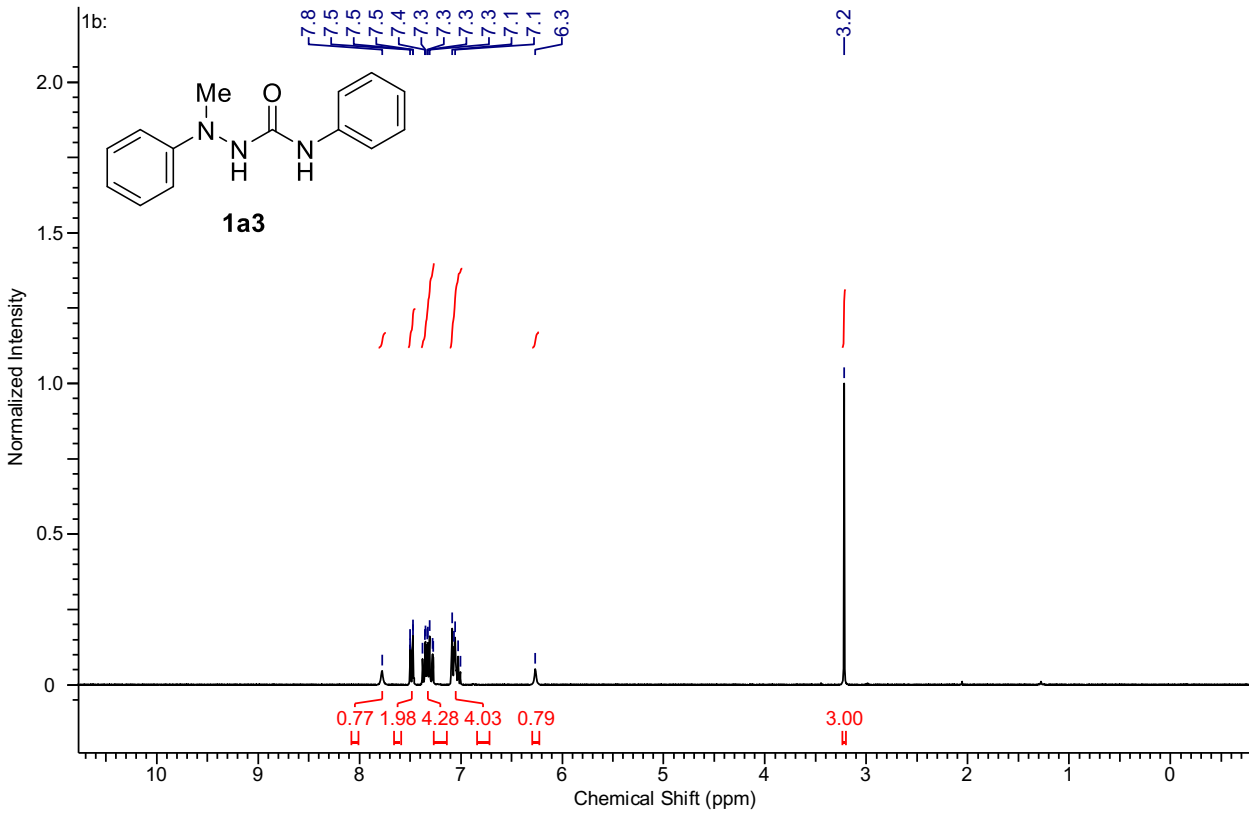
Figure S1. Substrates that failed to cyclize under the standard reaction conditions

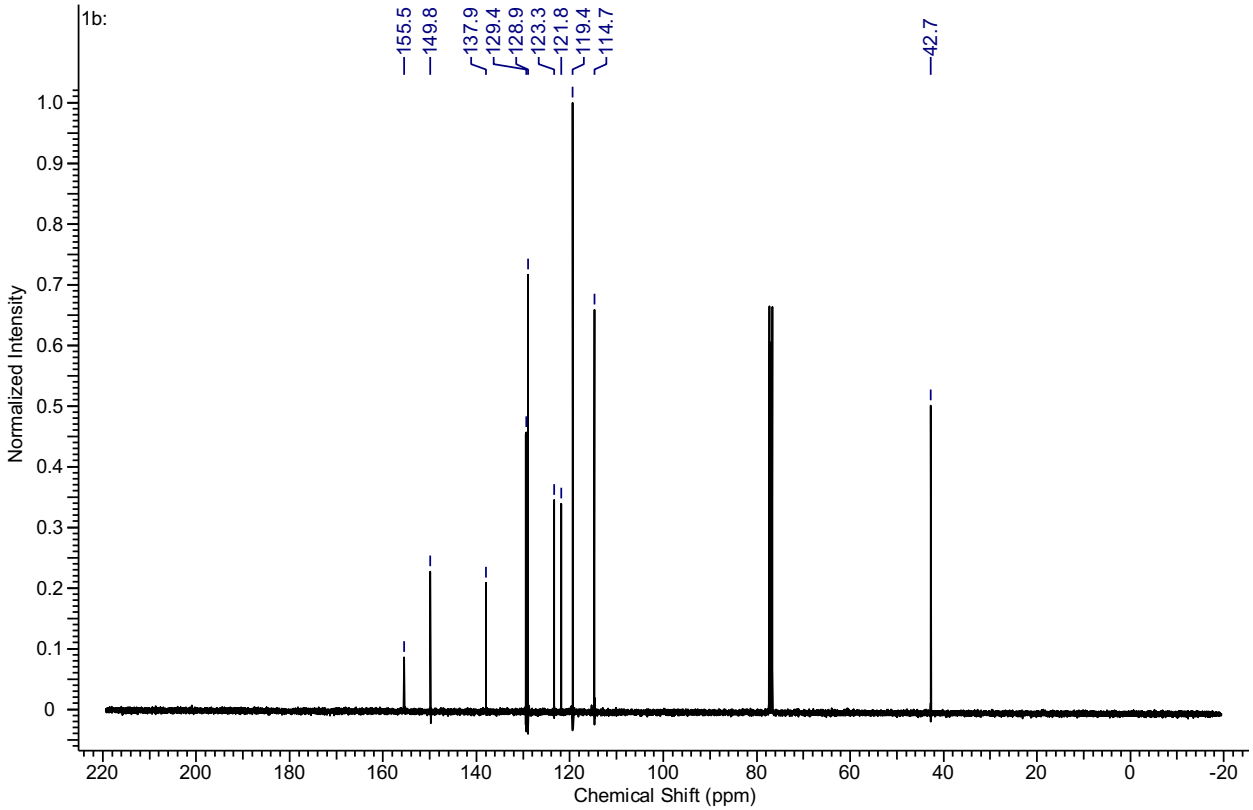

1a:
7.324
7.302
7.298
7.294
7.270
6.908
6.904
6.883
6.858
6.854
6.552
3.214
1.537
Me
O
N
N
H
O^{t}Bu
1a1
Normalized Intensity
2.09
3.01
0.48
3.00
9.07
Chemical Shift (ppm)

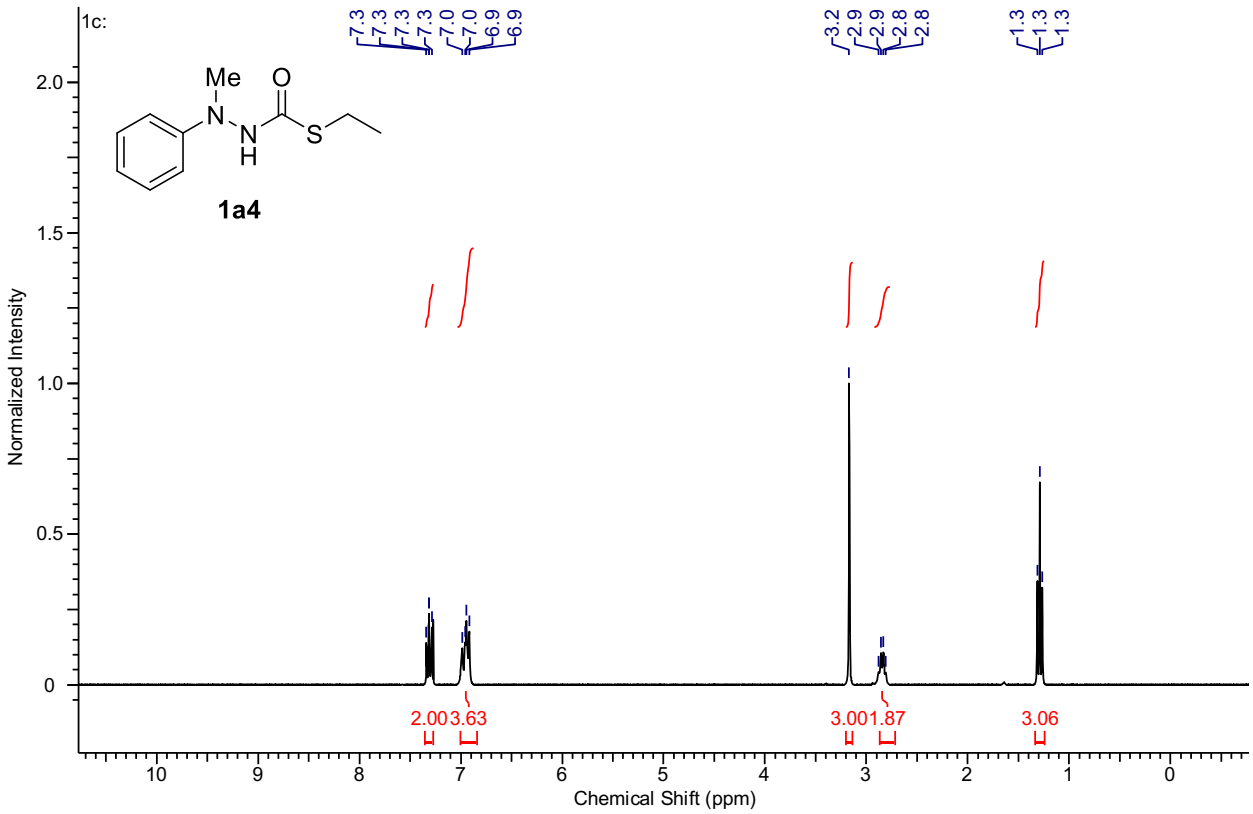

1a:
154.8
149.8
129.0
119.2
112.6
80.8
40.8
28.2
Normalized Intensity
Chemical Shift (ppm)

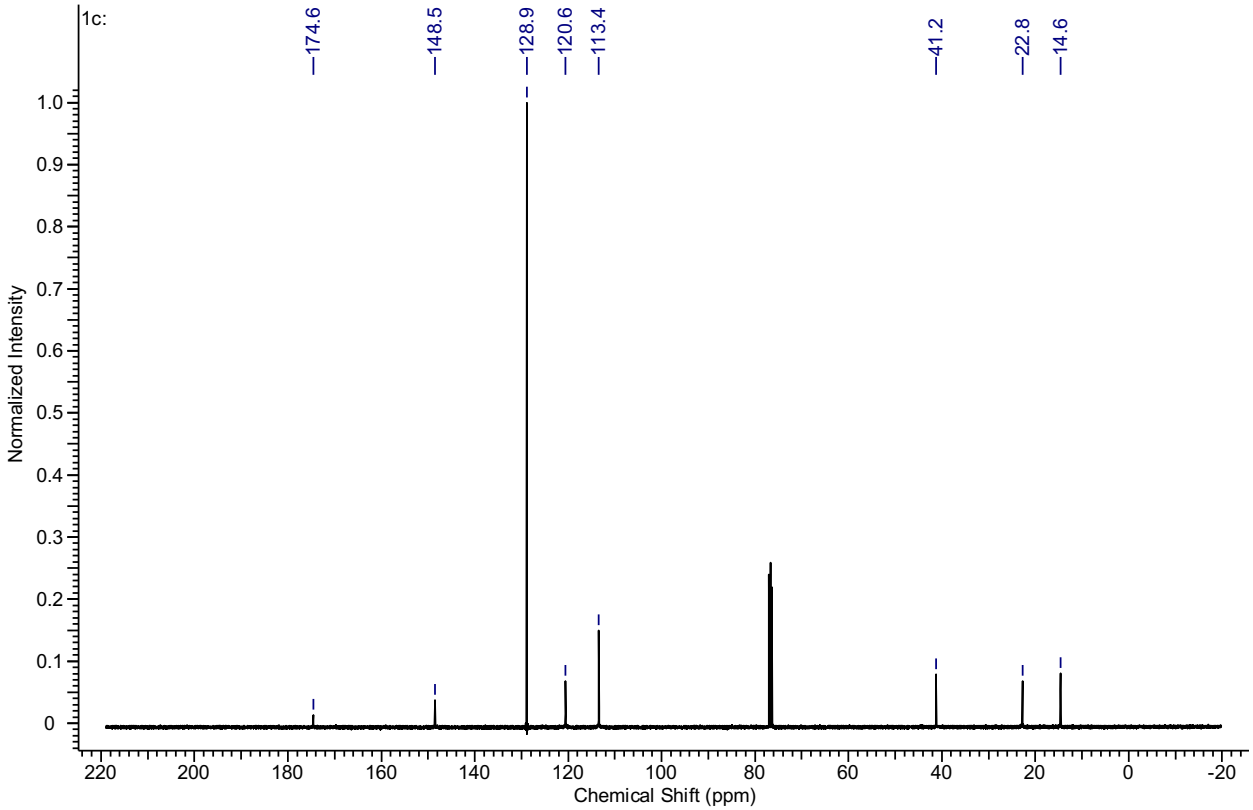

1d:
7.7
7.6
7.6
7.3
7.2
7.2
7.2
4.1
3.5
Me
O
N
N
H
OMe
1a2
2.04
3.01
3.00
3.00
Normalized Intensity
Chemical Shift (ppm)

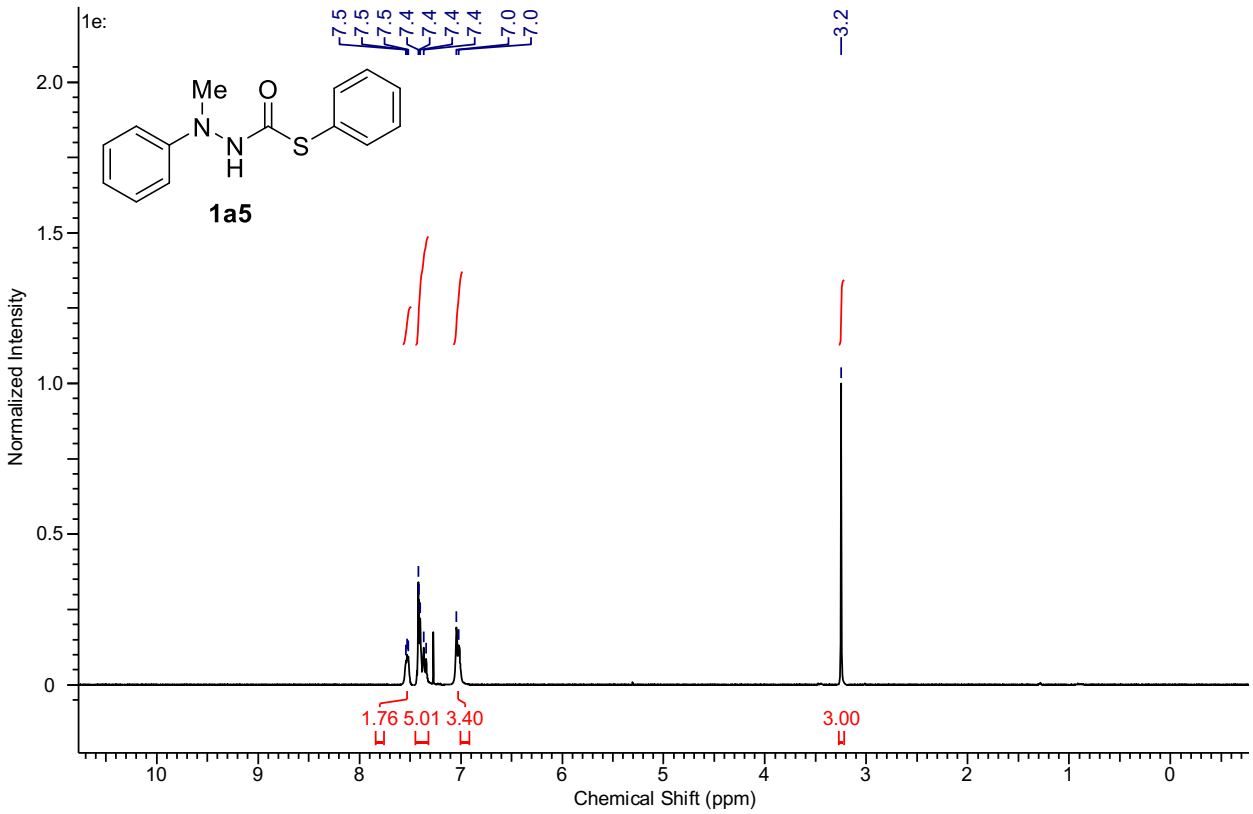

1d:
156.5
149.7
129.2
119.7
113.1
52.6
40.9
Normalized Intensity
Chemical Shift (ppm)

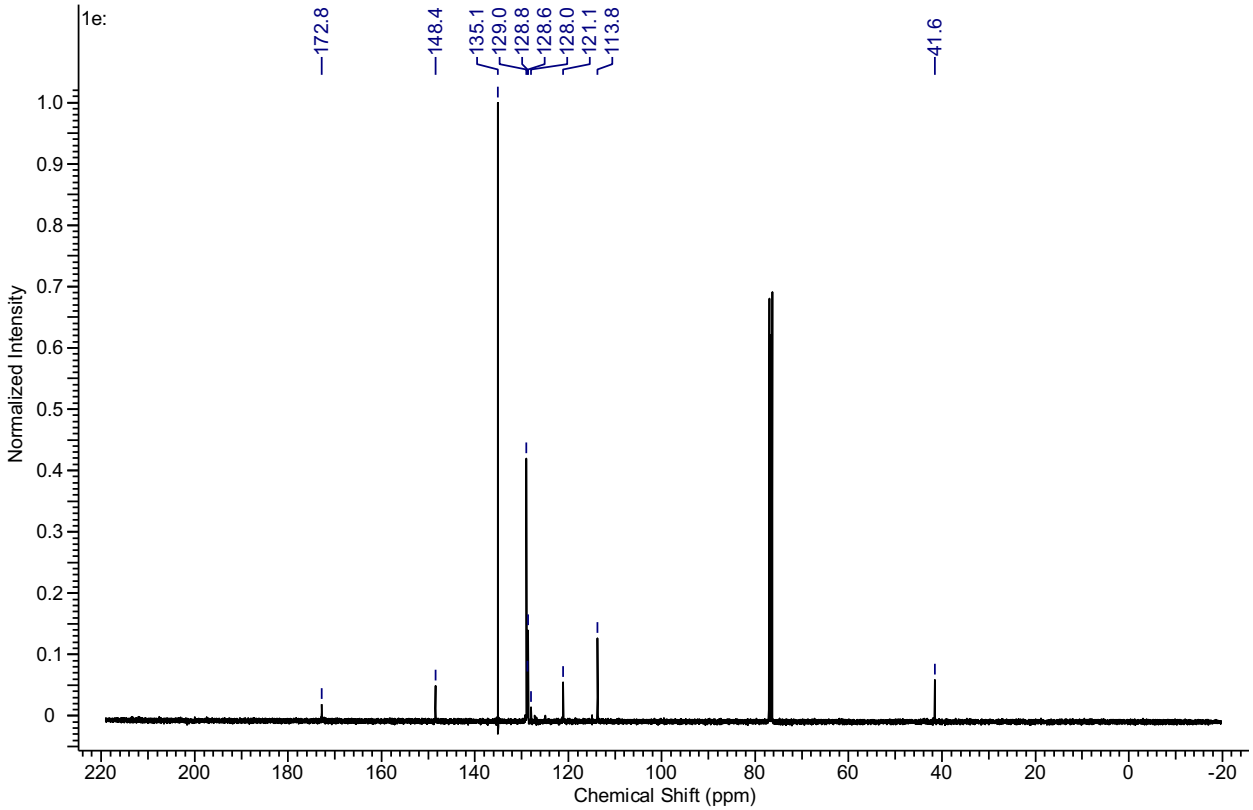

1b:
7.8
7.5
7.5
7.5
7.4
7.3
7.3
7.3
7.3
7.1
7.1
6.3
3.2
Me
O
N
N
H
N
H
1a3
Normalized Intensity
0.77 1.98 4.28 4.03 0.79
3.00
Chemical Shift (ppm)

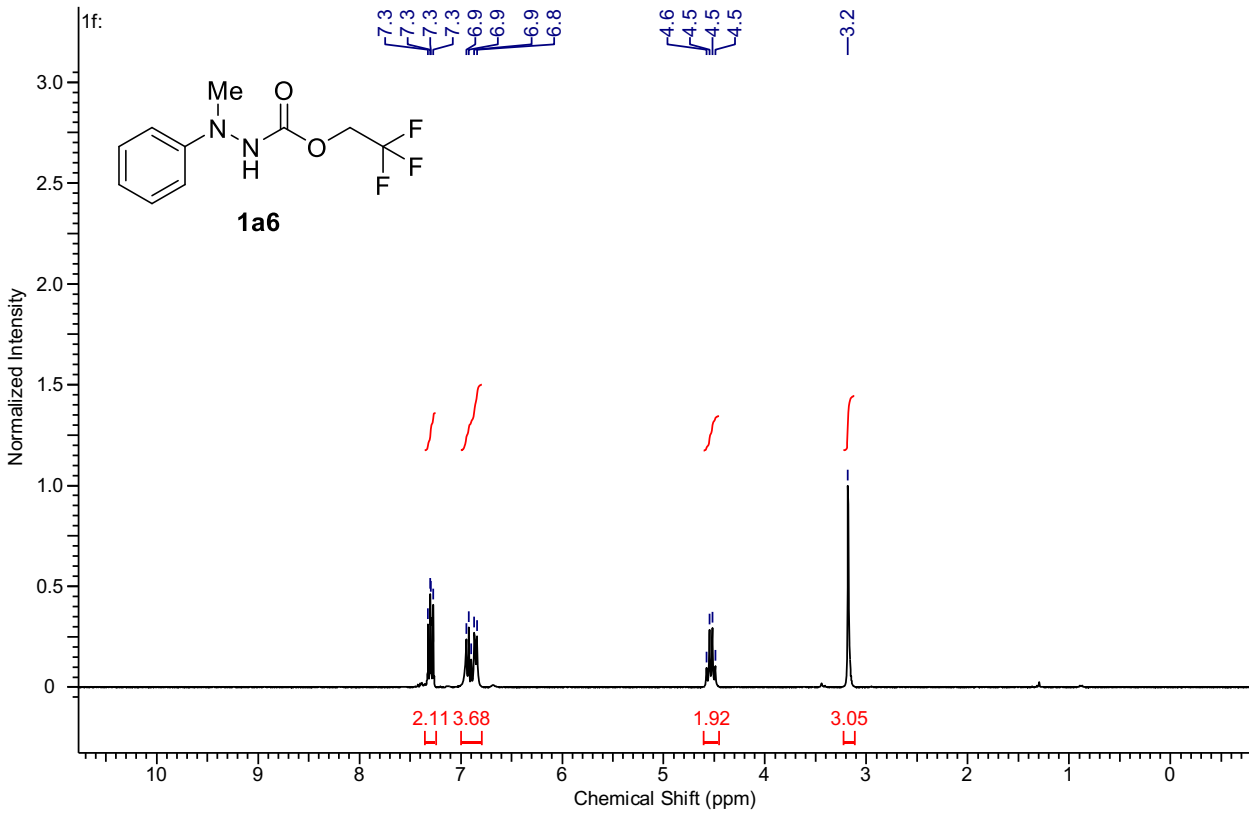

1b:
155.5
149.8
137.9
129.4
128.9
123.3
121.8
119.4
114.7
42.7
Normalized Intensity
Chemical Shift (ppm)

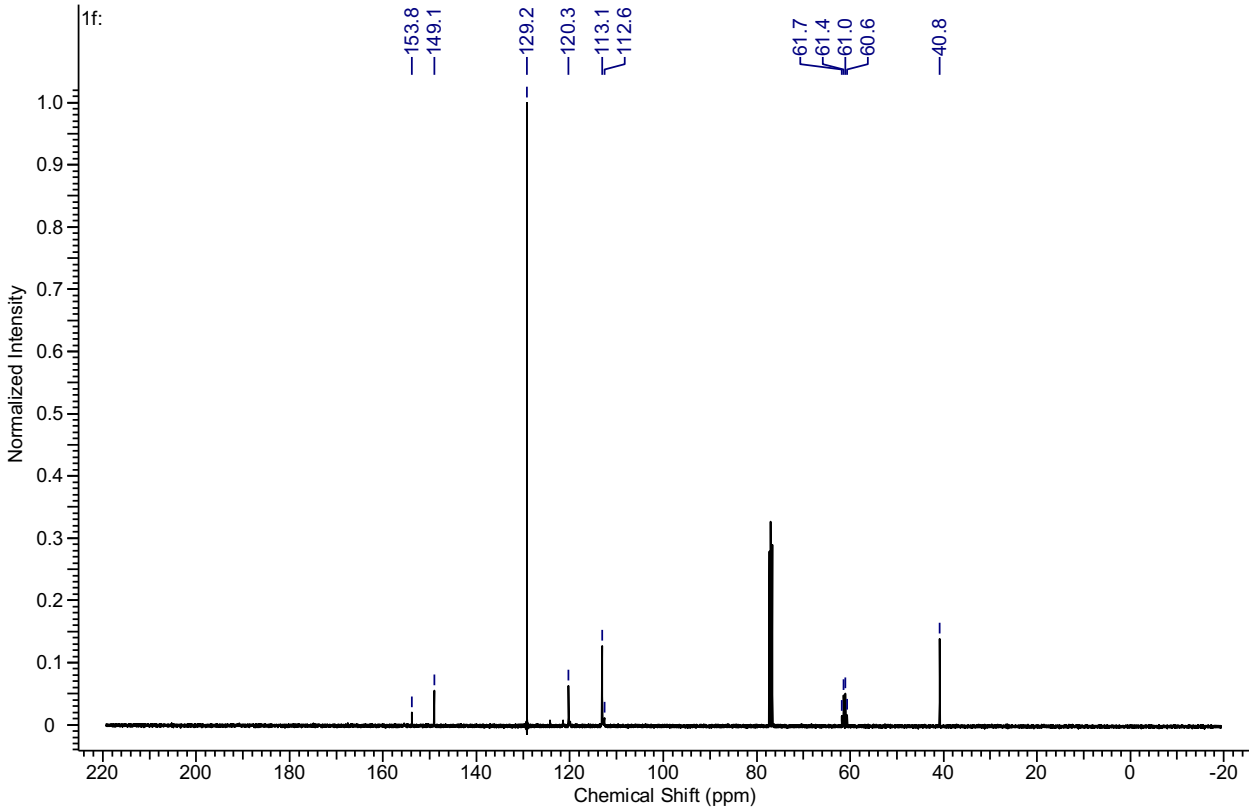

1c:
7.3
7.3
7.3
7.3
7.0
7.0
6.9
6.9
3.2
2.9
2.9
2.8
2.8
1.3
1.3
1.3
Me
O
N
N
H
S
1a4
Normalized Intensity
2.00
3.63
3.00
1.87
3.06
Chemical Shift (ppm)

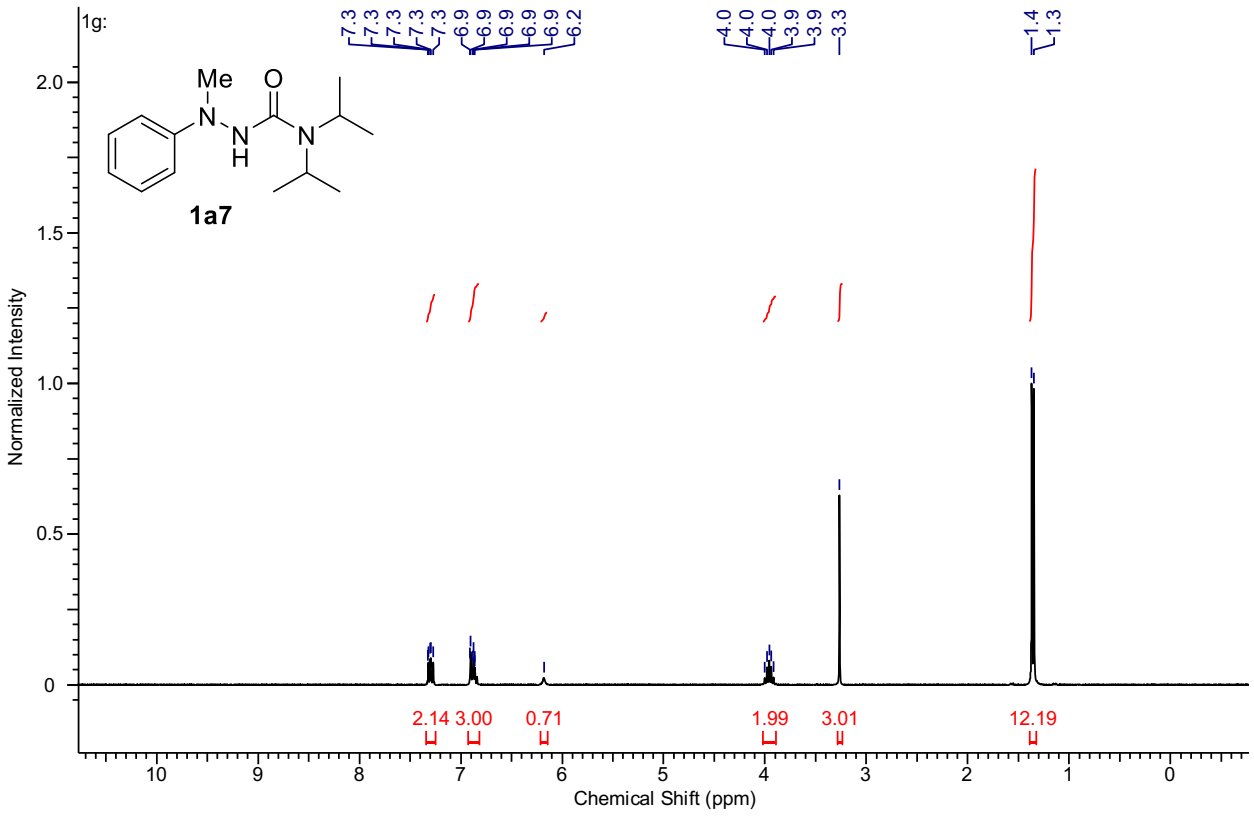

1c:
174.6
148.5
128.9
120.6
113.4
41.2
22.8
14.6
Normalized Intensity
Chemical Shift (ppm)

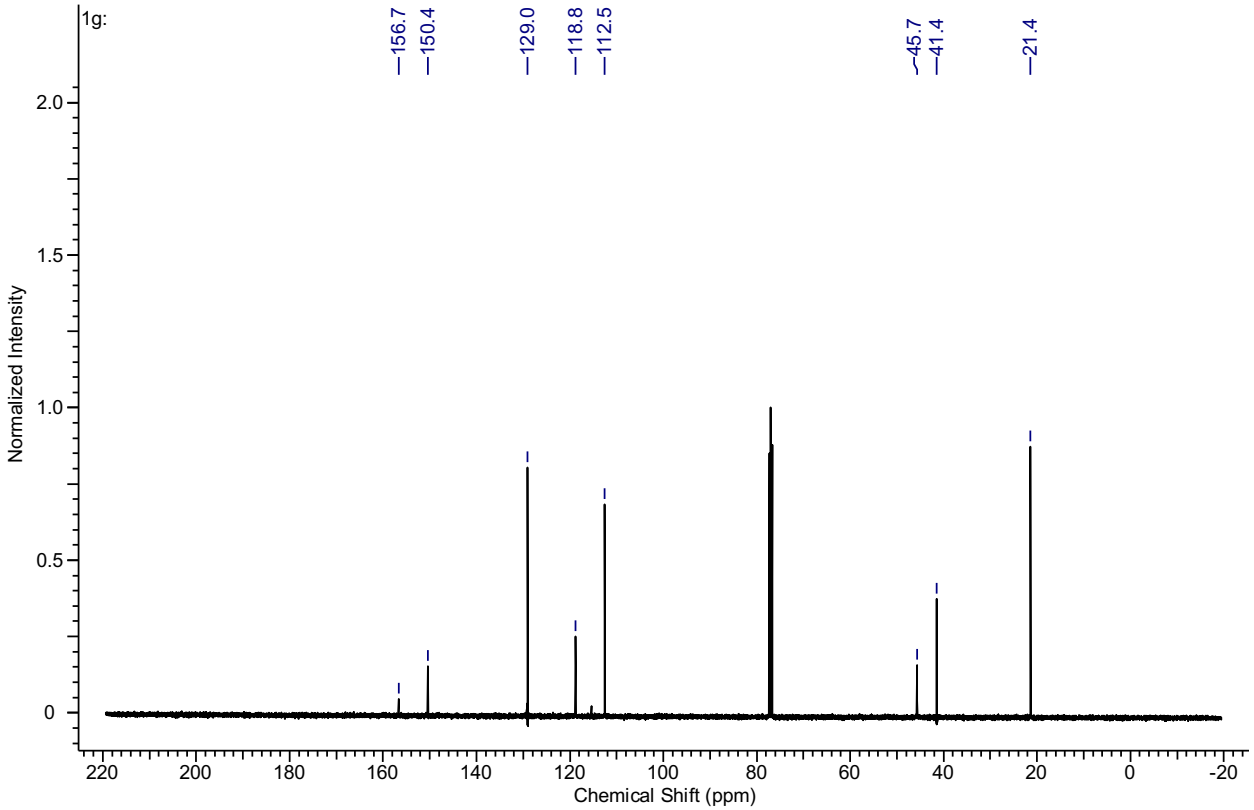

1e:
7.5
7.5
7.5
7.4
7.4
7.4
7.4
7.0
7.0
3.2
Me
O
N
N
H
S
1a5
Normalized Intensity
1.76
5.01
3.40
3.00
Chemical Shift (ppm)

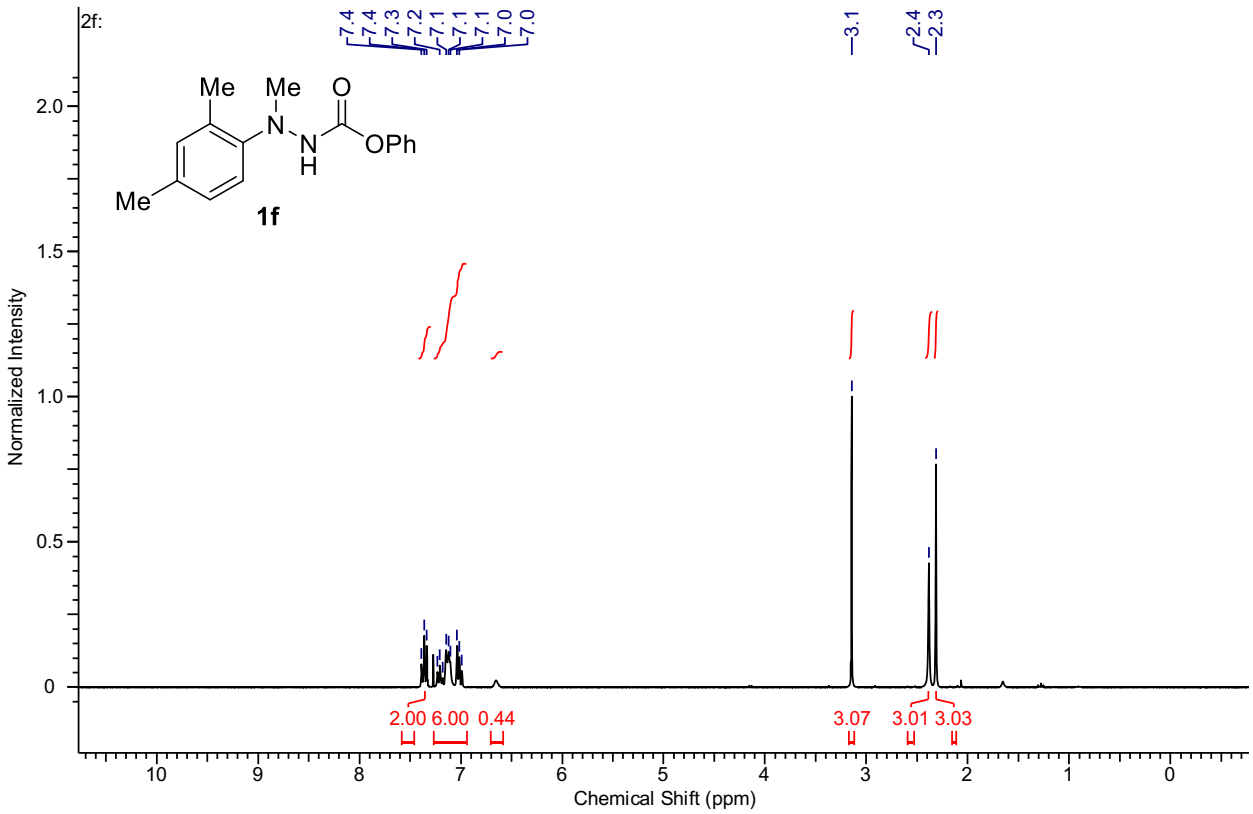

1e:
172.8
148.4
135.1
129.0
128.8
128.6
128.0
121.1
113.8
41.6
Normalized Intensity
Chemical Shift (ppm)

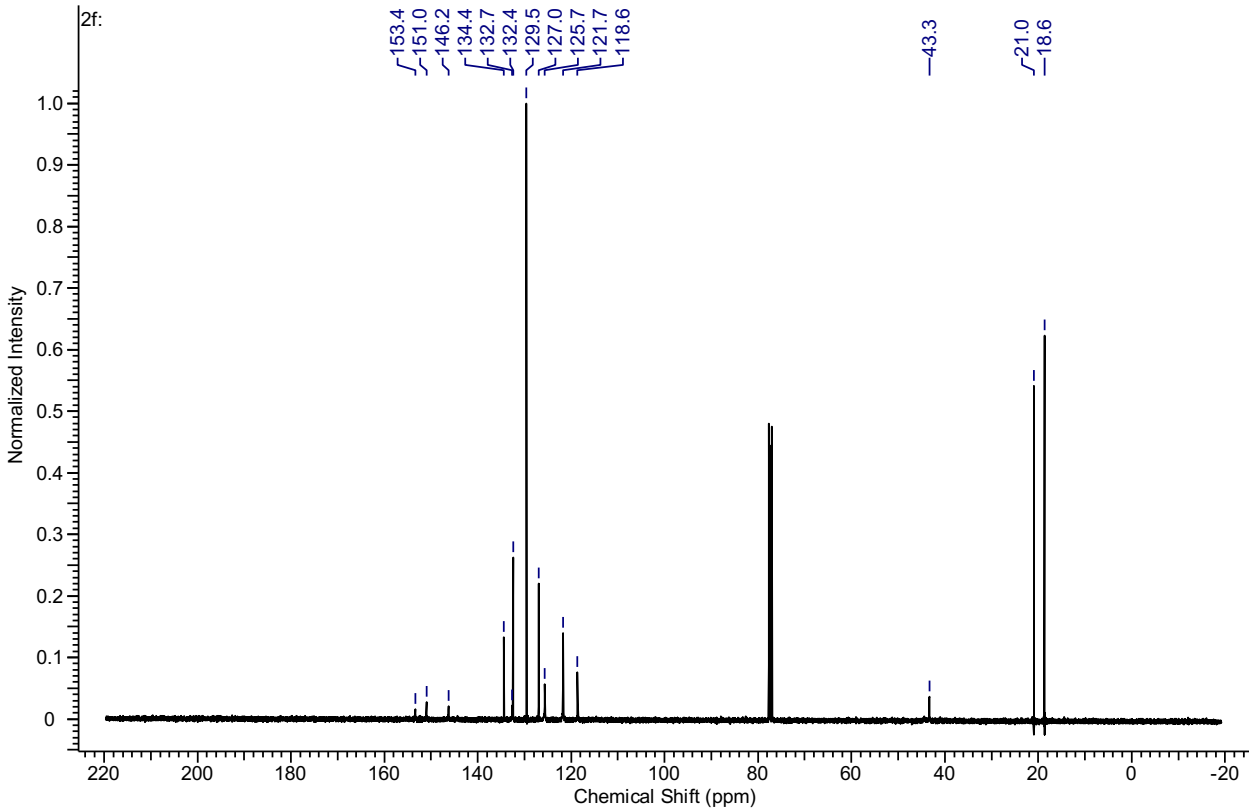

1f:
7.3
7.3
7.3
7.3
6.9
6.9
6.9
6.8
4.6
4.5
4.5
4.5
3.2
Me
O
N
N
H
O
F
F
F
1a6
Normalized Intensity
2.11
3.68
1.92
3.05
Chemical Shift (ppm)

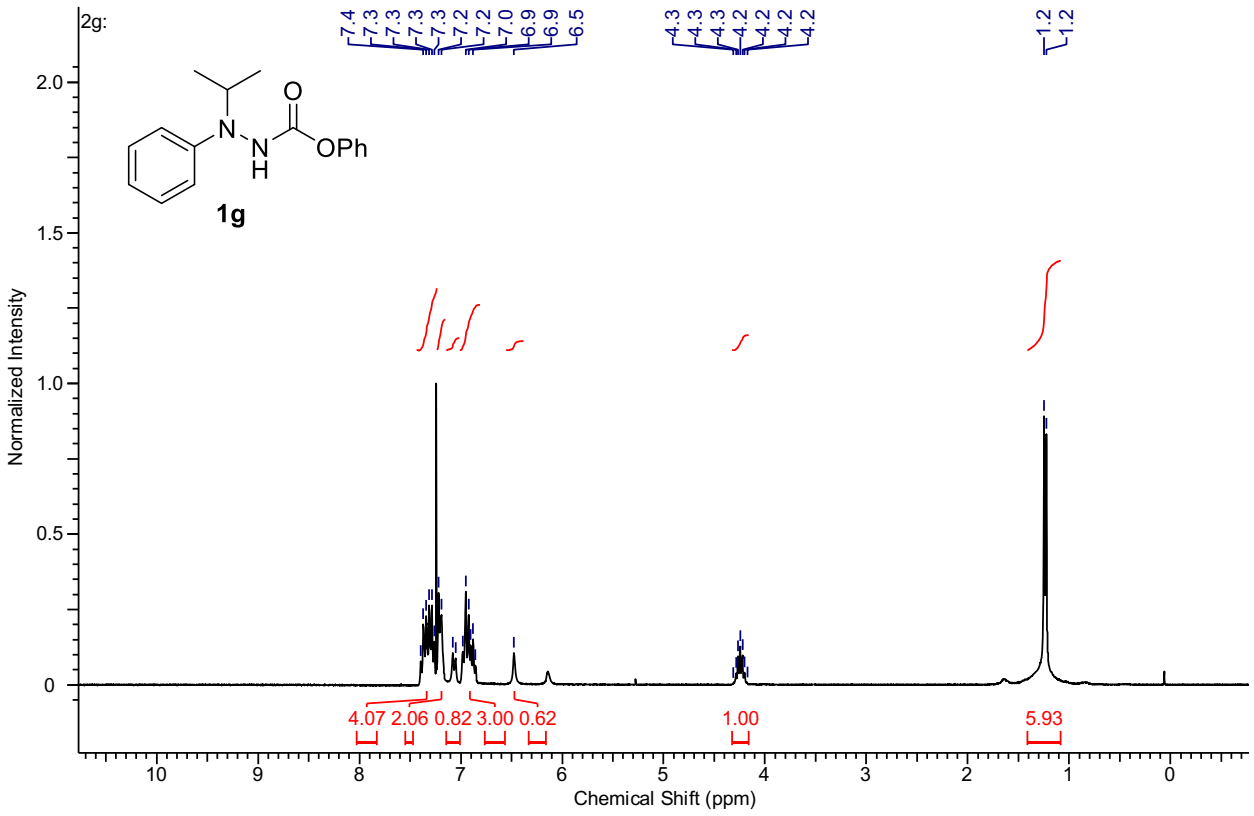

1f:
153.8
149.1
129.2
120.3
113.1
112.6
61.7
61.4
61.0
60.6
40.8
Normalized Intensity
Chemical Shift (ppm)

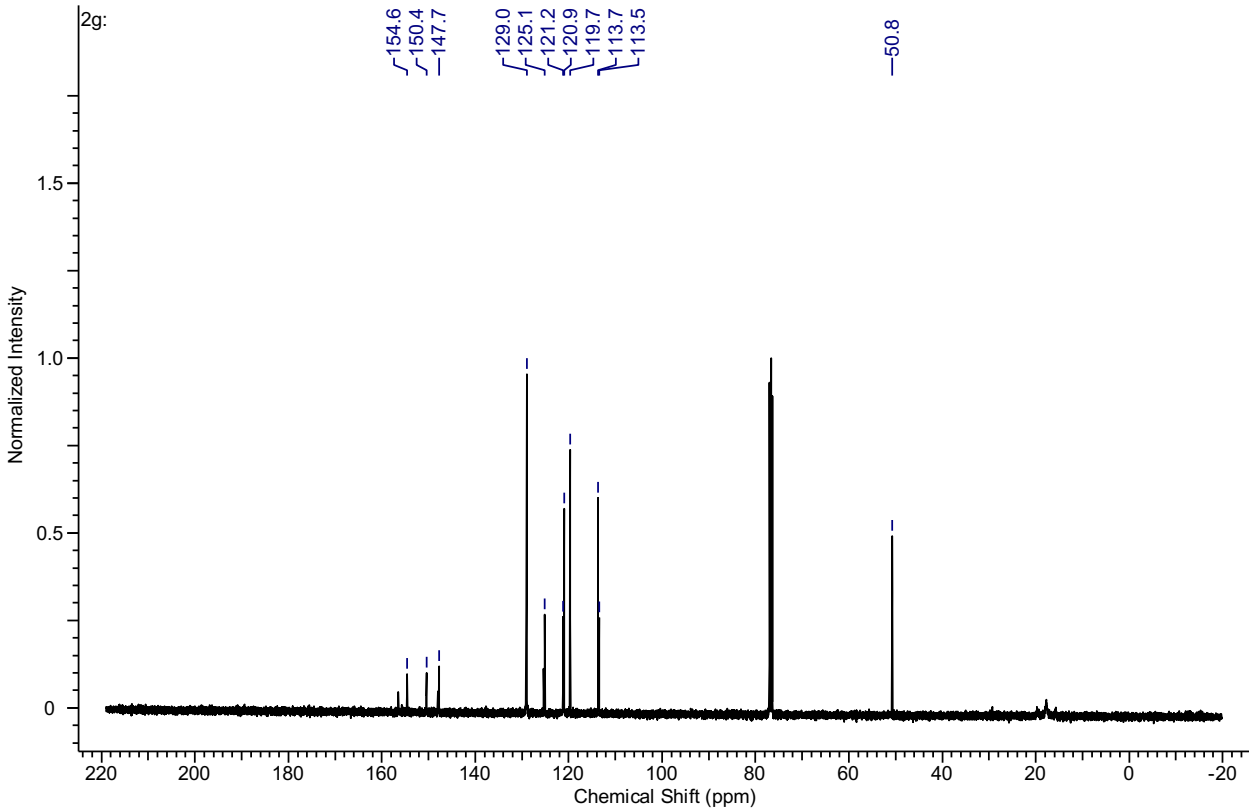

1g:
7.3
7.3
7.3
7.3
7.3
6.9
6.9
6.9
6.9
6.9
6.2
4.0
4.0
4.0
3.9
3.9
3.3
1.4
1.3
Me
O
N
N
H
N
1a7
Normalized Intensity
2.14
3.00
0.71
1.99
3.01
12.19
Chemical Shift (ppm)

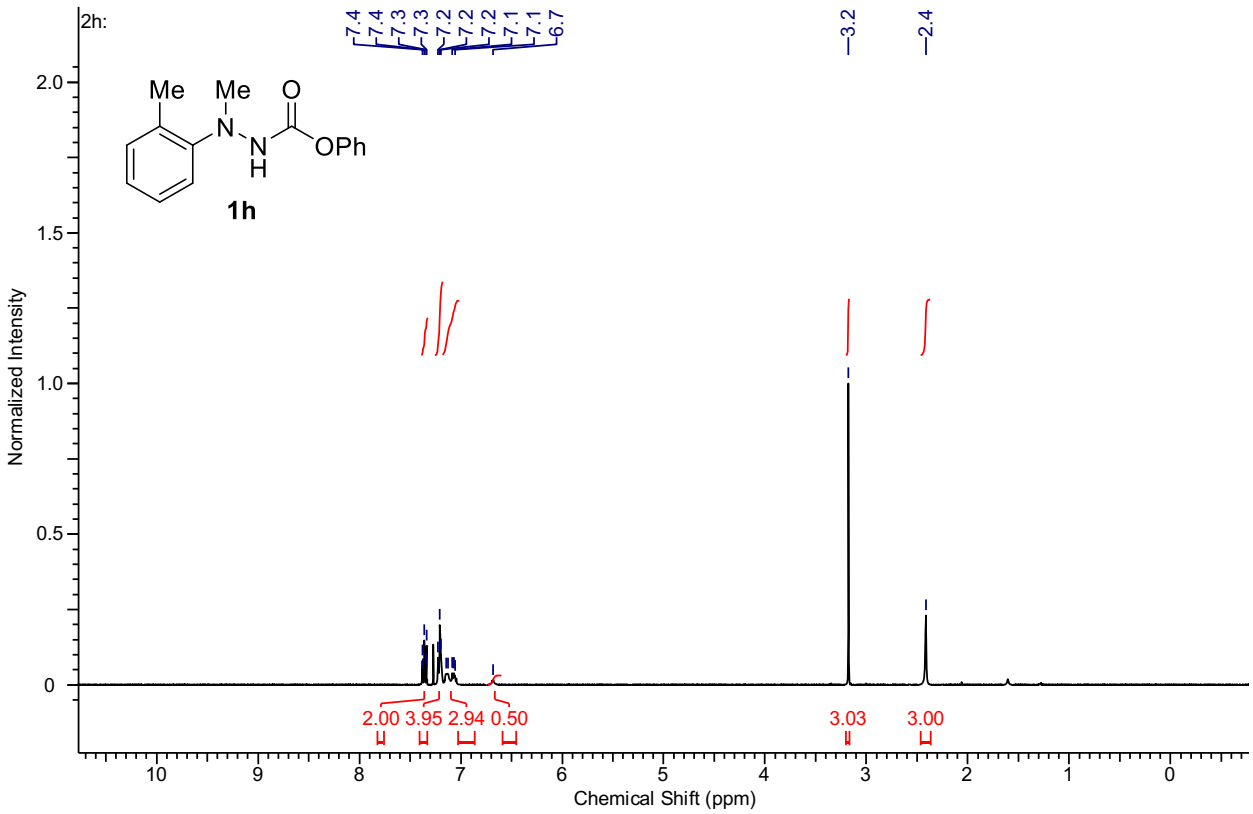

1g:
156.7
150.4
129.0
118.8
112.5
45.7
41.4
21.4
Normalized Intensity
Chemical Shift (ppm)

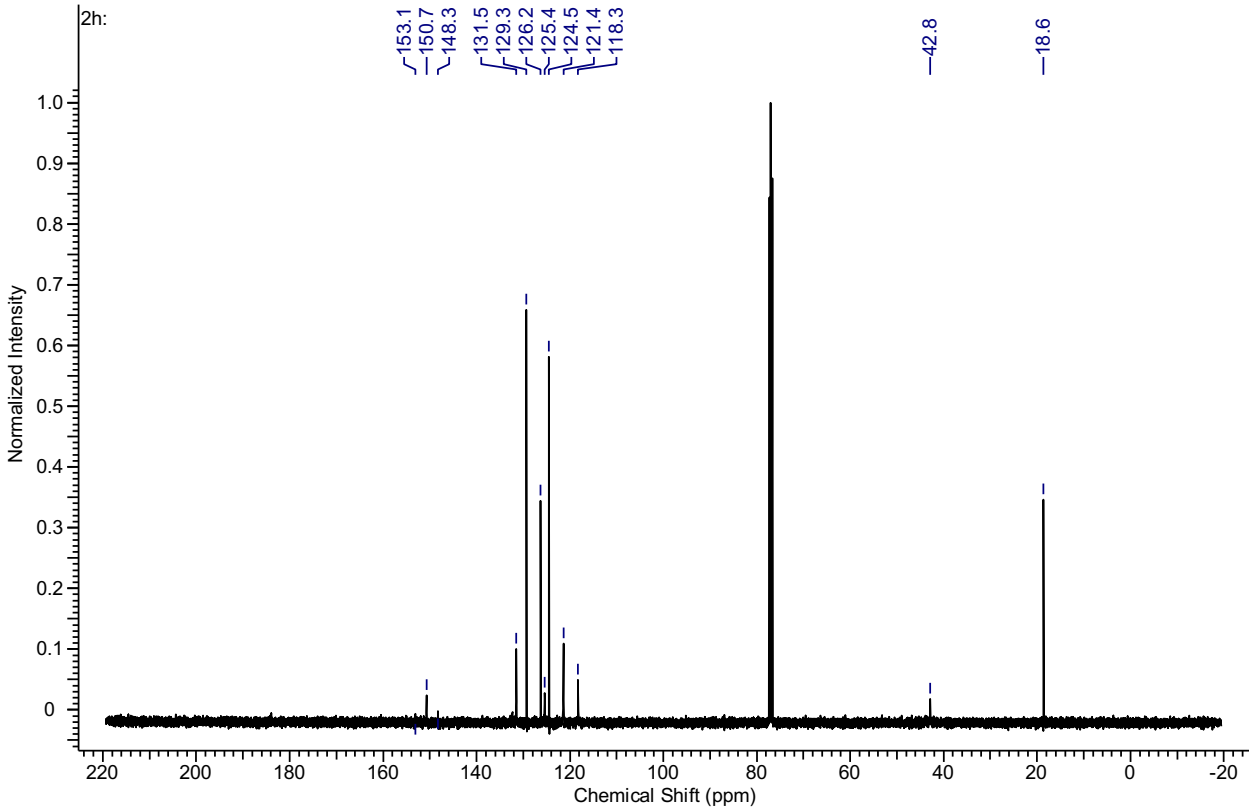

2f:
7.4
7.4
7.3
7.2
7.1
7.1
7.1
7.0
7.0
3.1
2.4
2.3
Me
Me
O
N
N
H
OPh
Me
1f
Normalized Intensity
2.00
6.00
0.44
3.07
3.01
3.03
Chemical Shift (ppm)

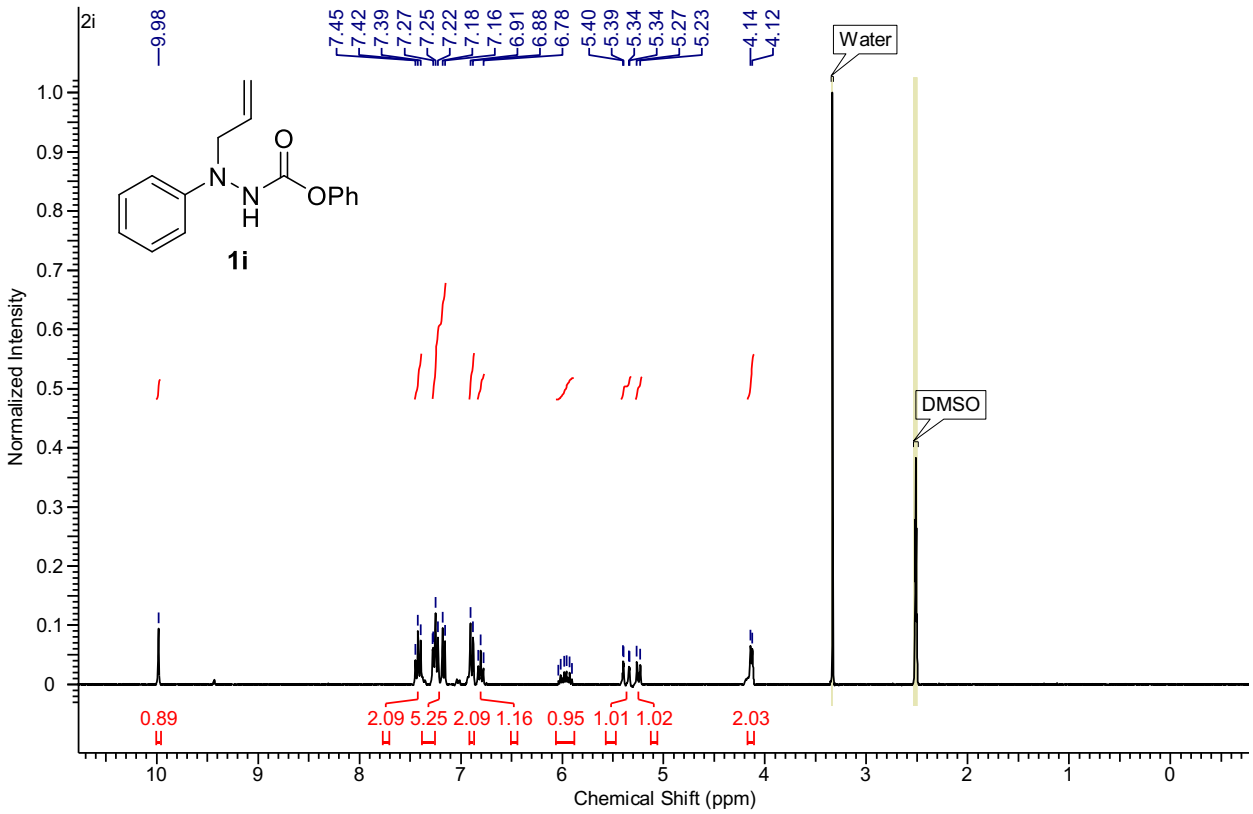

2f:
153.4
151.0
146.2
134.4
132.7
132.4
129.5
127.0
125.7
121.7
118.6
43.3
21.0
18.6
Normalized Intensity
Chemical Shift (ppm)

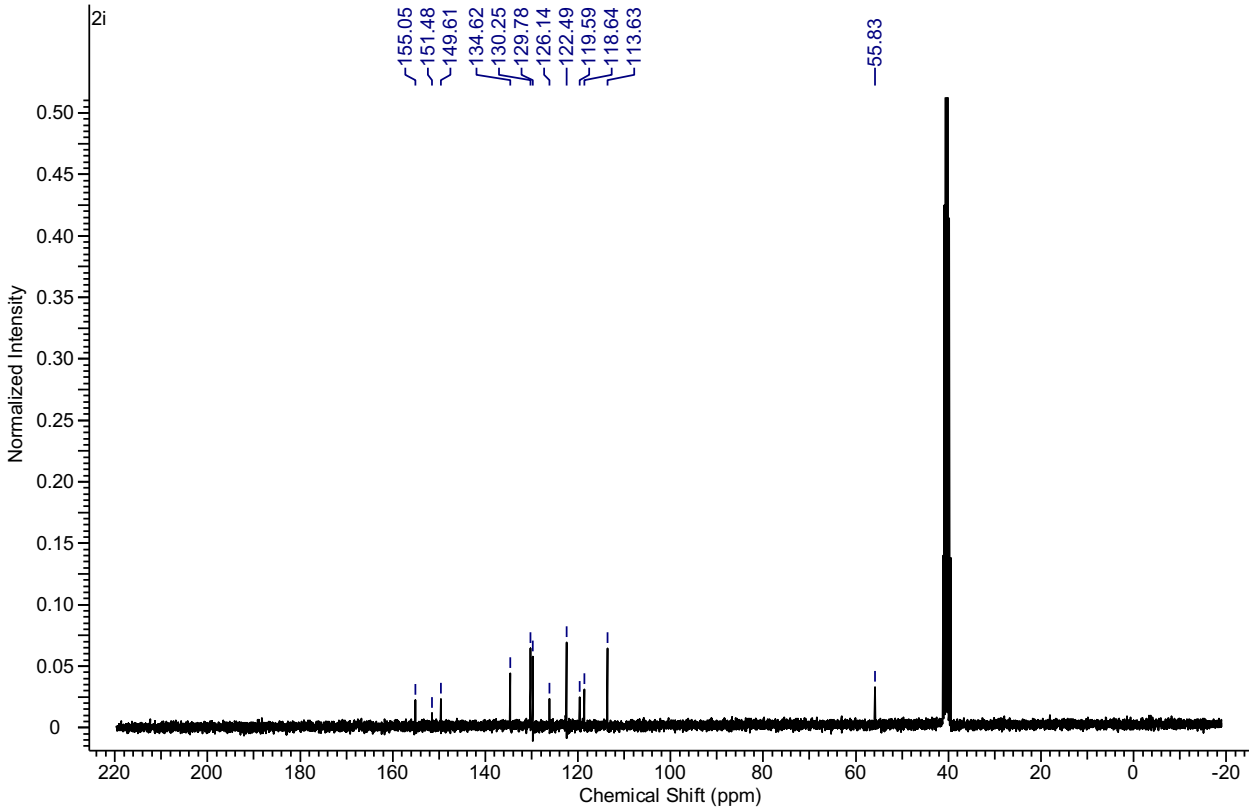

2g:
7.4
7.3
7.3
7.3
7.3
7.2
7.2
7.0
6.9
6.9
6.5
4.3
4.3
4.3
4.2
4.2
4.2
4.2
1.2
1.2
O
N
N
H
OPh
1g
Normalized Intensity
4.07 2.06 0.82 3.00 0.62
1.00
5.93
Chemical Shift (ppm)

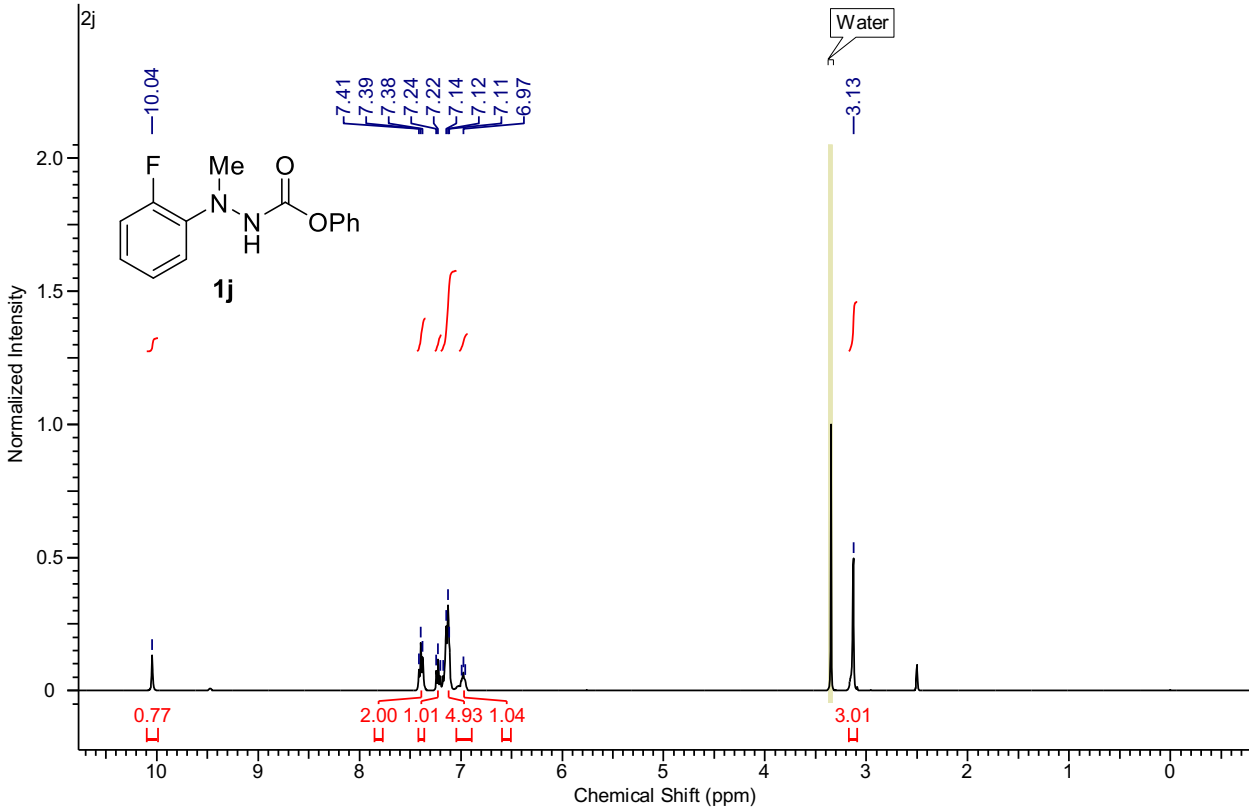

2g:
154.6
150.4
147.7
129.0
125.1
121.2
120.9
119.7
113.7
113.5
50.8
Normalized Intensity
Chemical Shift (ppm)

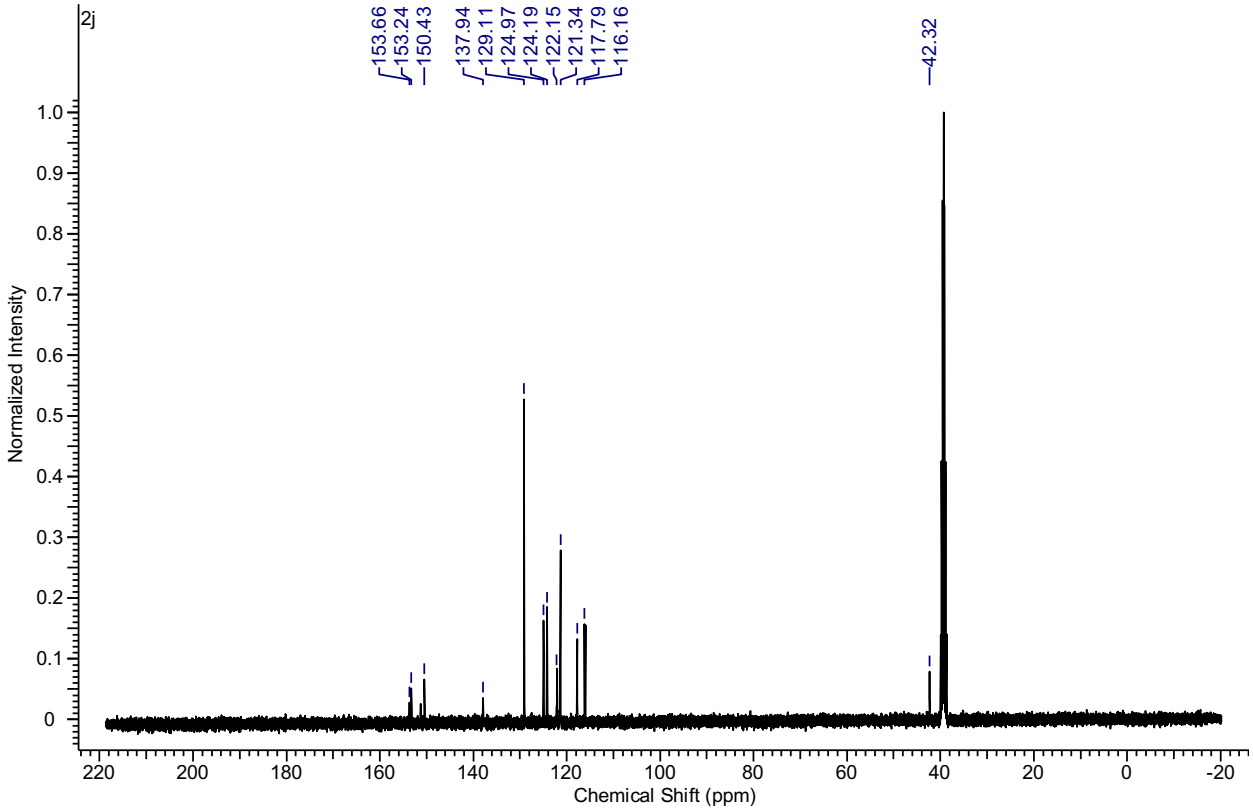

2h:
7.4
7.4
7.3
7.3
7.2
7.2
7.2
7.1
7.1
6.7
3.2
2.4
Me
Me
O
N
N
H
OPh
1h
Normalized Intensity
2.00 3.95 2.94 0.50
3.03
3.00
Chemical Shift (ppm)

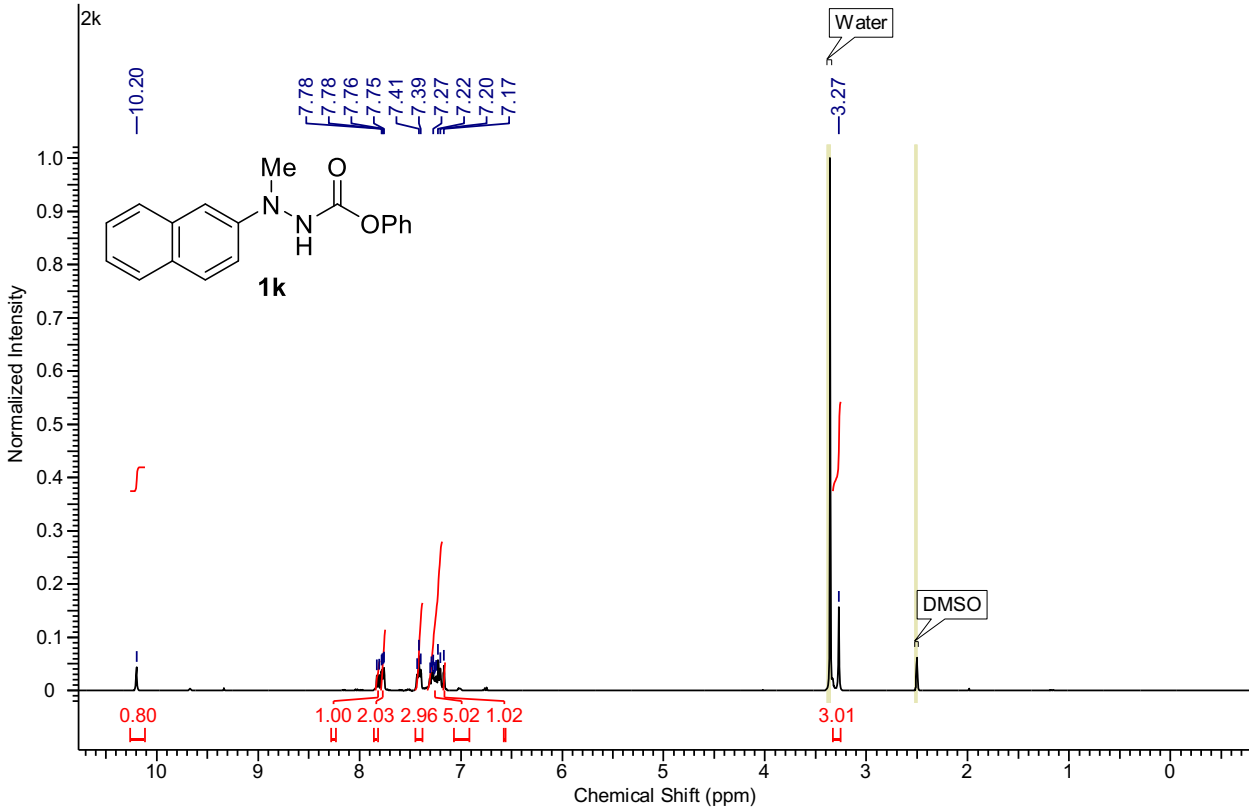

2h:
153.1
150.7
148.3
131.5
129.3
126.2
125.4
124.5
121.4
118.3
42.8
18.6
Normalized Intensity
Chemical Shift (ppm)

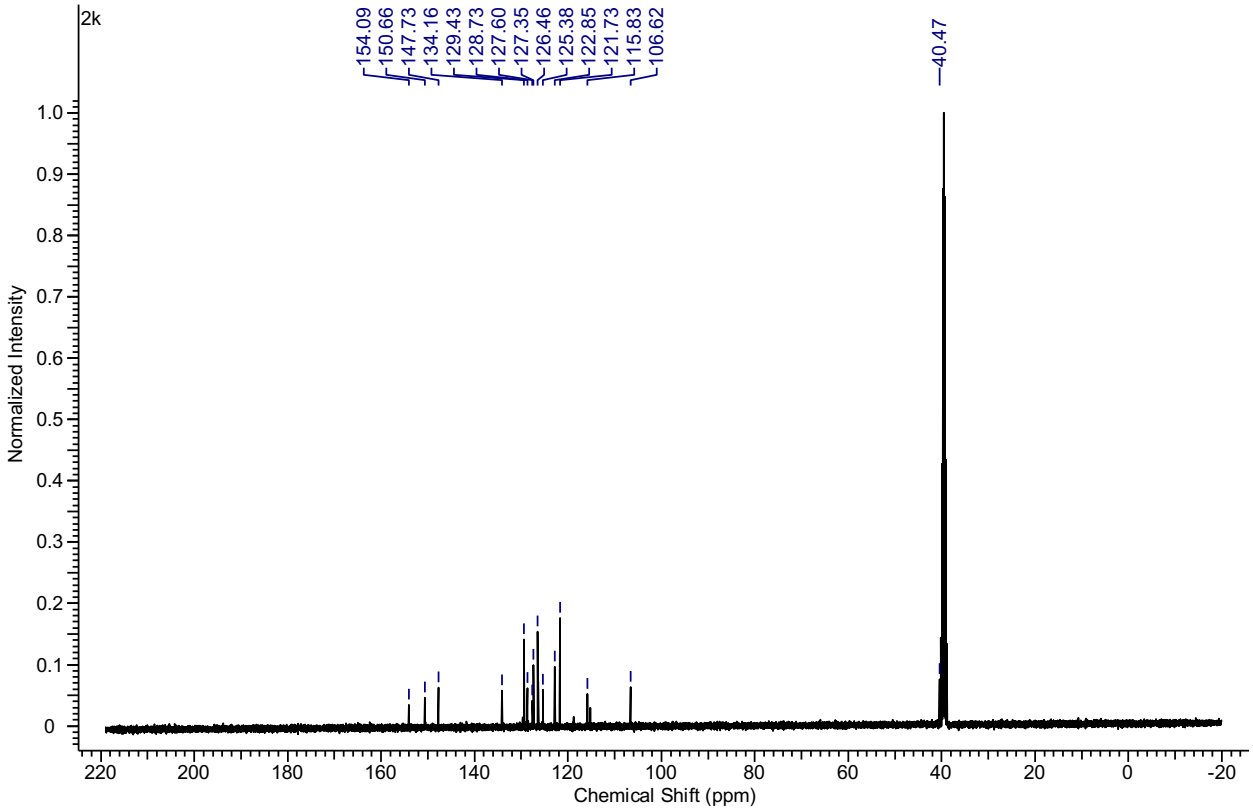

2i
9.98
7.45
7.42
7.39
7.27
7.25
7.22
7.18
7.16
6.91
6.88
6.78
5.40
5.39
5.34
5.34
5.27
5.23
4.14
4.12
Water
DMSO
O
N
N
H
OPh
1i
Normalized Intensity
0.89
2.09
5.25
2.09
1.16
0.95
1.01
1.02
2.03
Chemical Shift (ppm)

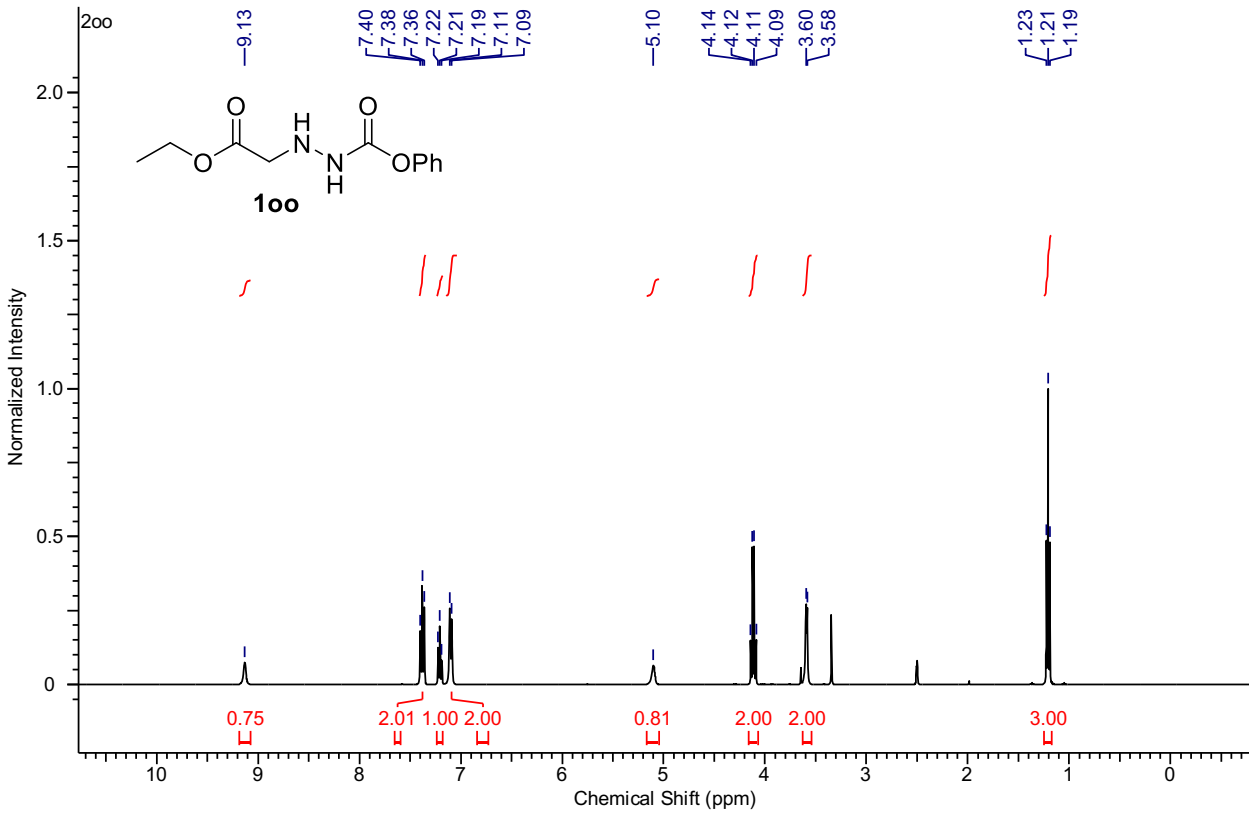

2i
155.05
151.48
149.61
134.62
130.25
129.78
126.14
122.49
119.59
118.64
113.63
55.83
Normalized Intensity
Chemical Shift (ppm)

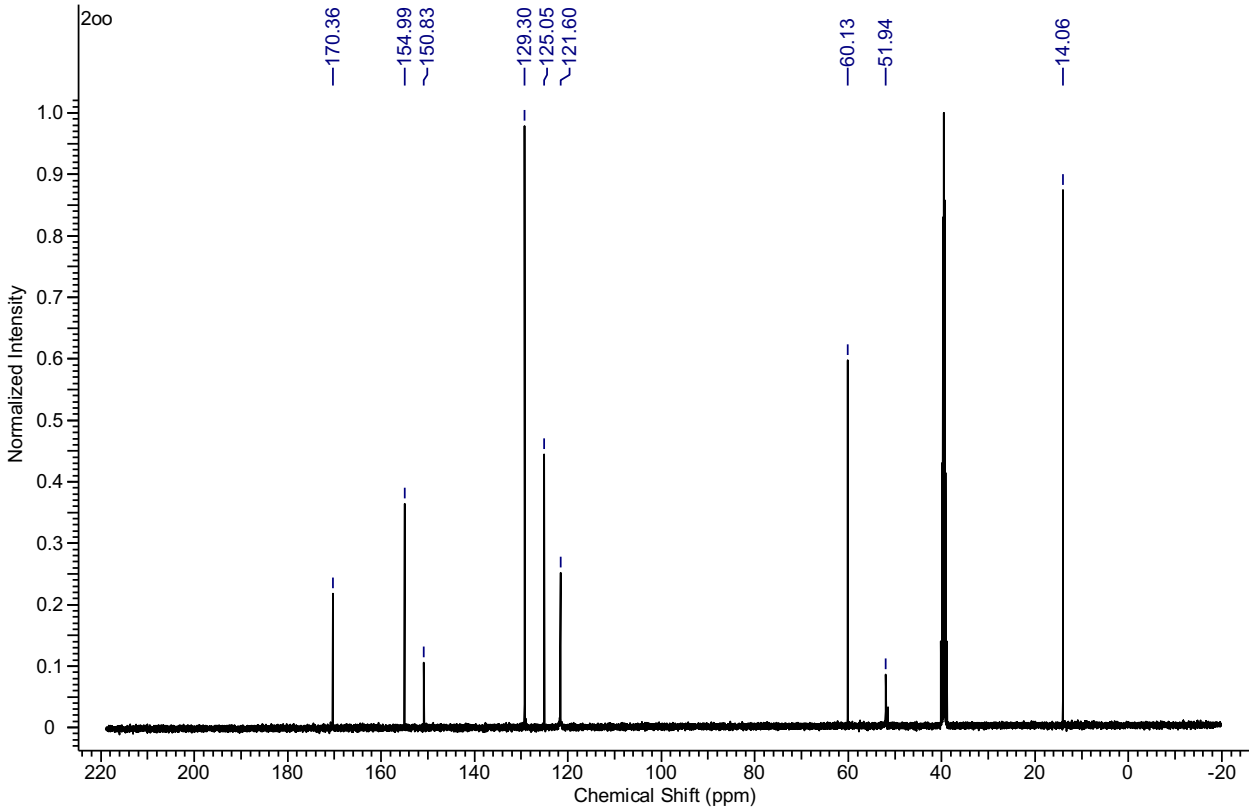

2j
Water
10.04
7.41
7.39
7.38
7.24
7.22
7.14
7.12
7.11
6.97
3.13
F
Me
O
N
N
H
OPh
1j
Normalized Intensity
0.77
2.00
1.01
4.93
1.04
3.01
Chemical Shift (ppm)

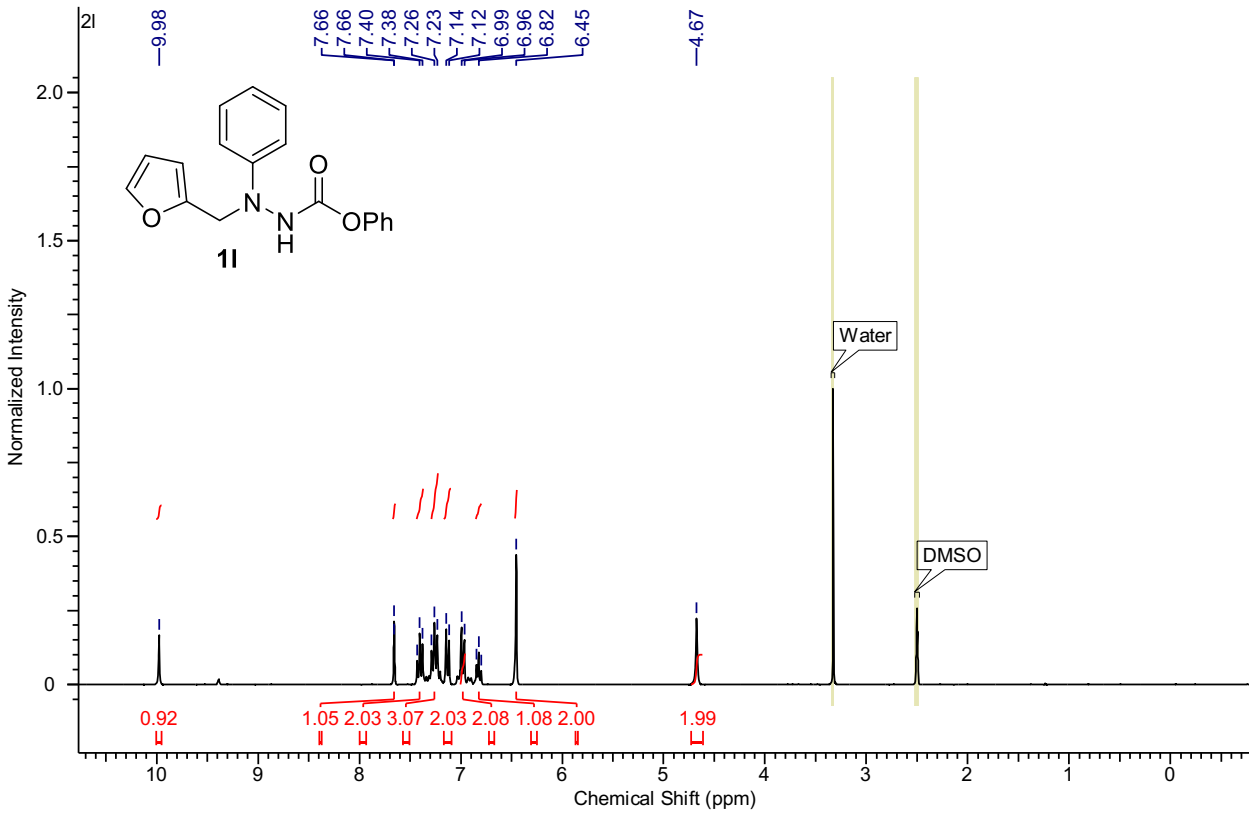

2j
153.66
153.24
150.43
137.94
129.11
124.97
124.19
122.15
121.34
117.79
116.16
42.32
Normalized Intensity
Chemical Shift (ppm)

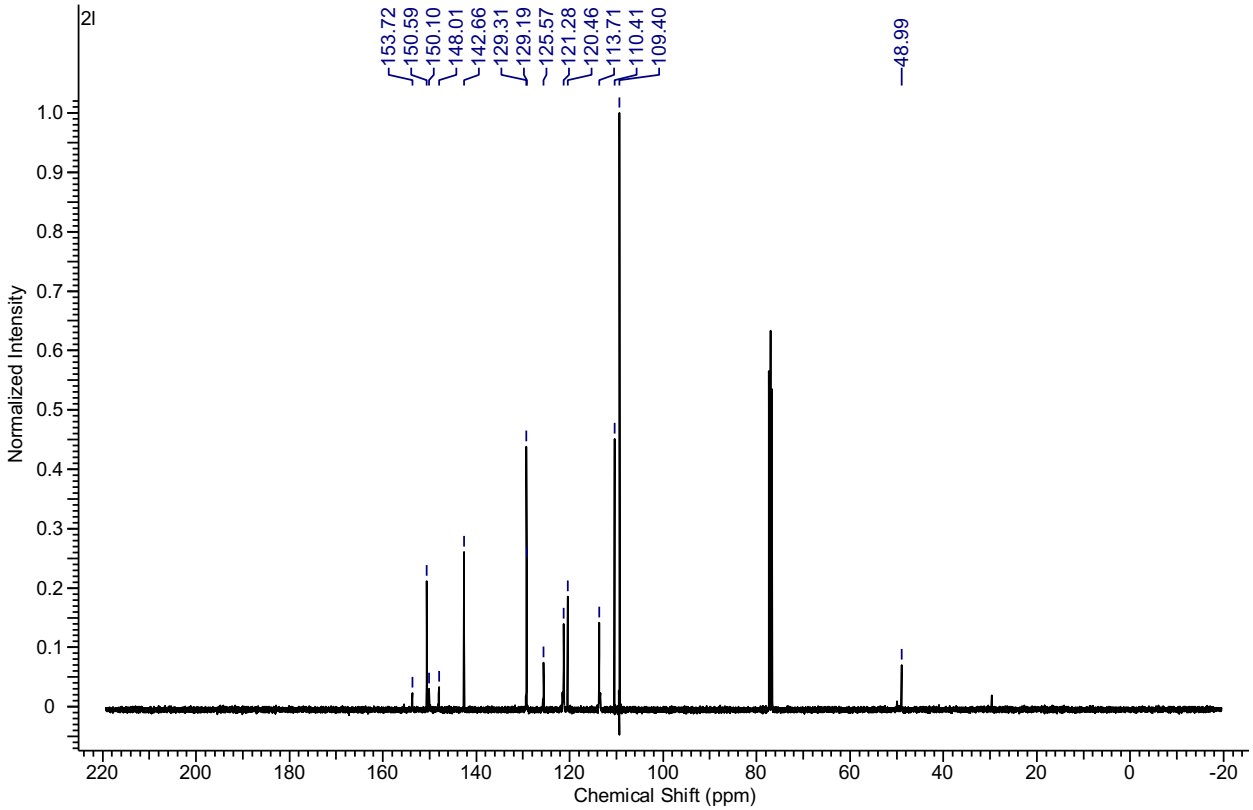

2k
Water
10.20
7.78
7.78
7.76
7.75
7.41
7.39
7.27
7.22
7.20
7.17
3.27
Me
O
N
N
H
OPh
1k
DMSO
Normalized Intensity
0.80
1.00
2.03
2.96
5.02
1.02
3.01
Chemical Shift (ppm)

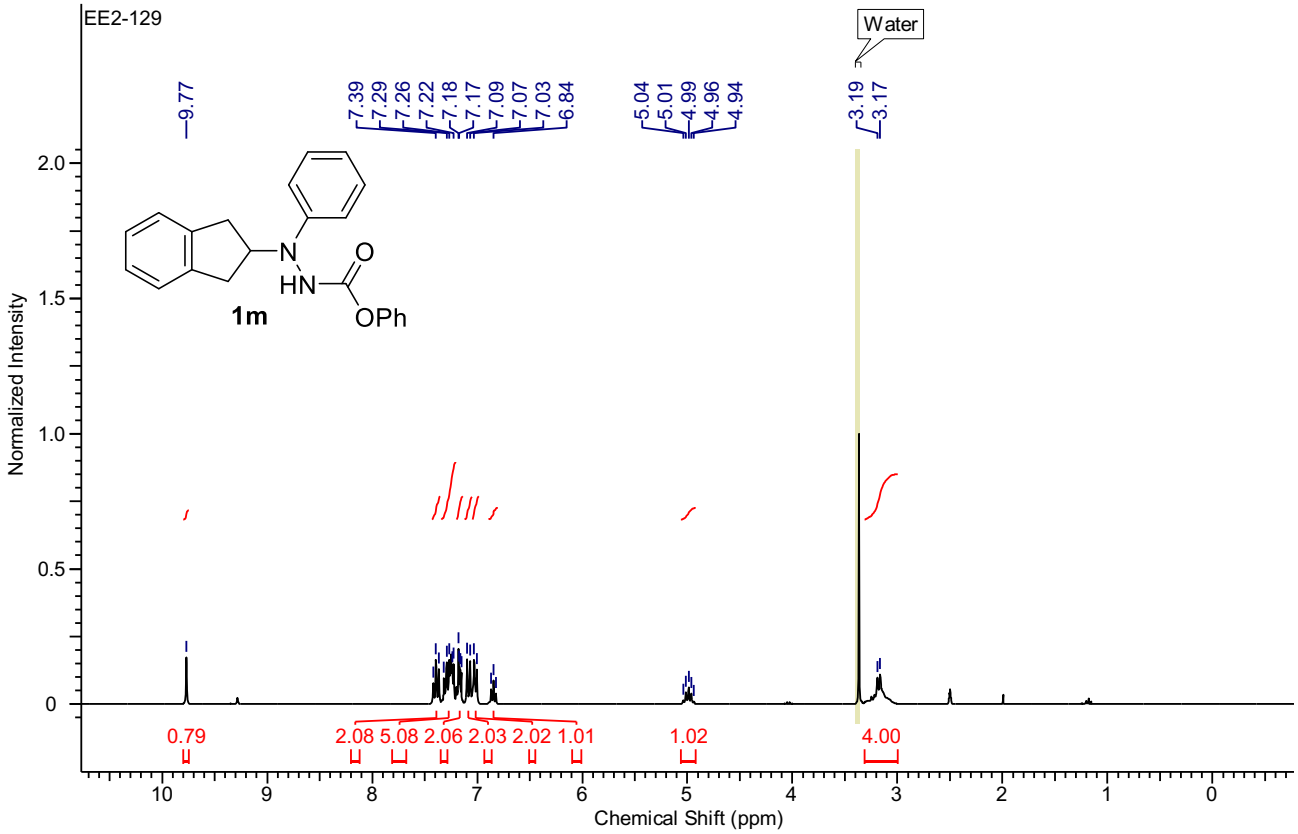

2k
154.09
150.66
147.73
134.16
129.43
128.73
127.60
127.35
126.46
125.38
122.85
121.73
115.83
106.62
40.47
Normalized Intensity
Chemical Shift (ppm)

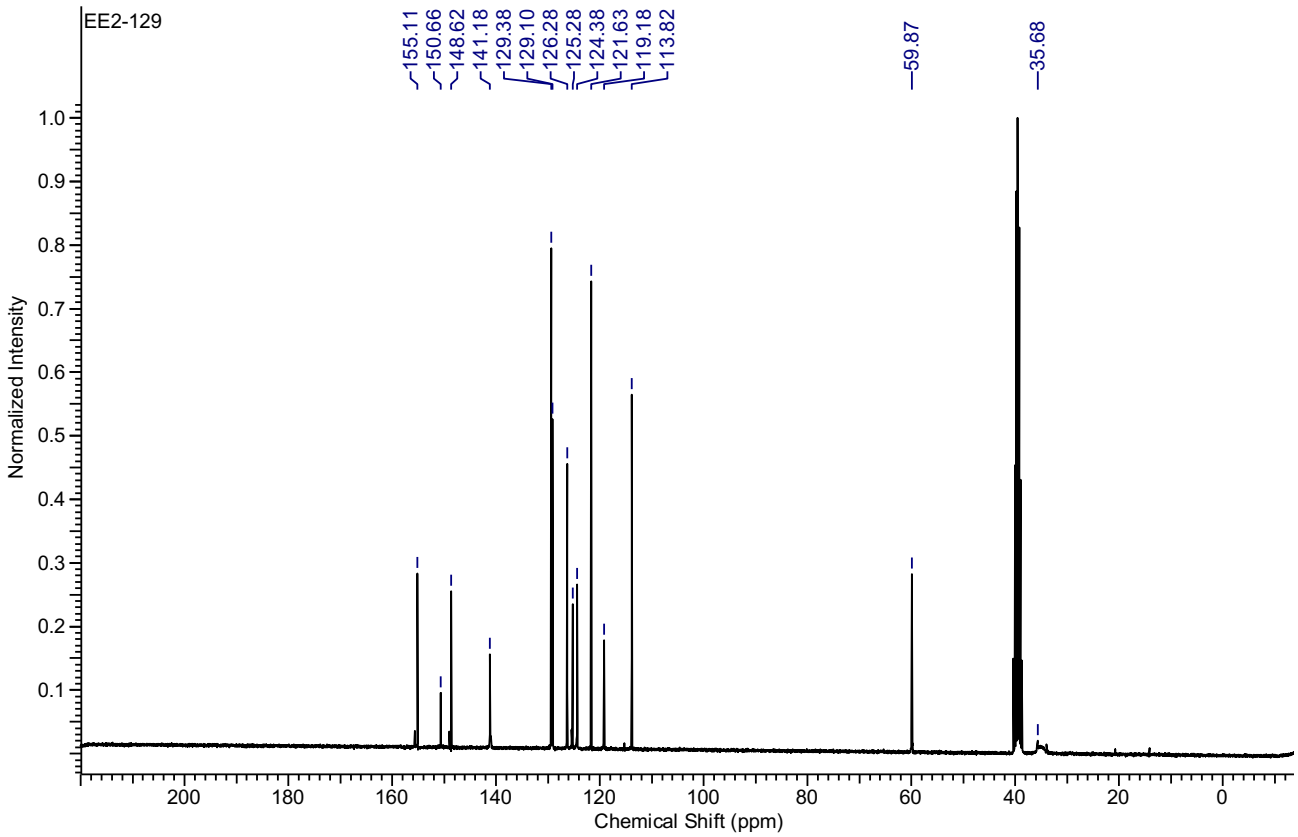

2oo
9.13
7.40
7.38
7.36
7.22
7.21
7.19
7.11
7.09
5.10
4.14
4.12
4.11
4.09
3.60
3.58
1.23
1.21
1.19
O
H
N
N
H
O
O
OPh
1oo
Normalized Intensity
0.75
2.01
1.00
2.00
0.81
2.00
2.00
3.00
Chemical Shift (ppm)

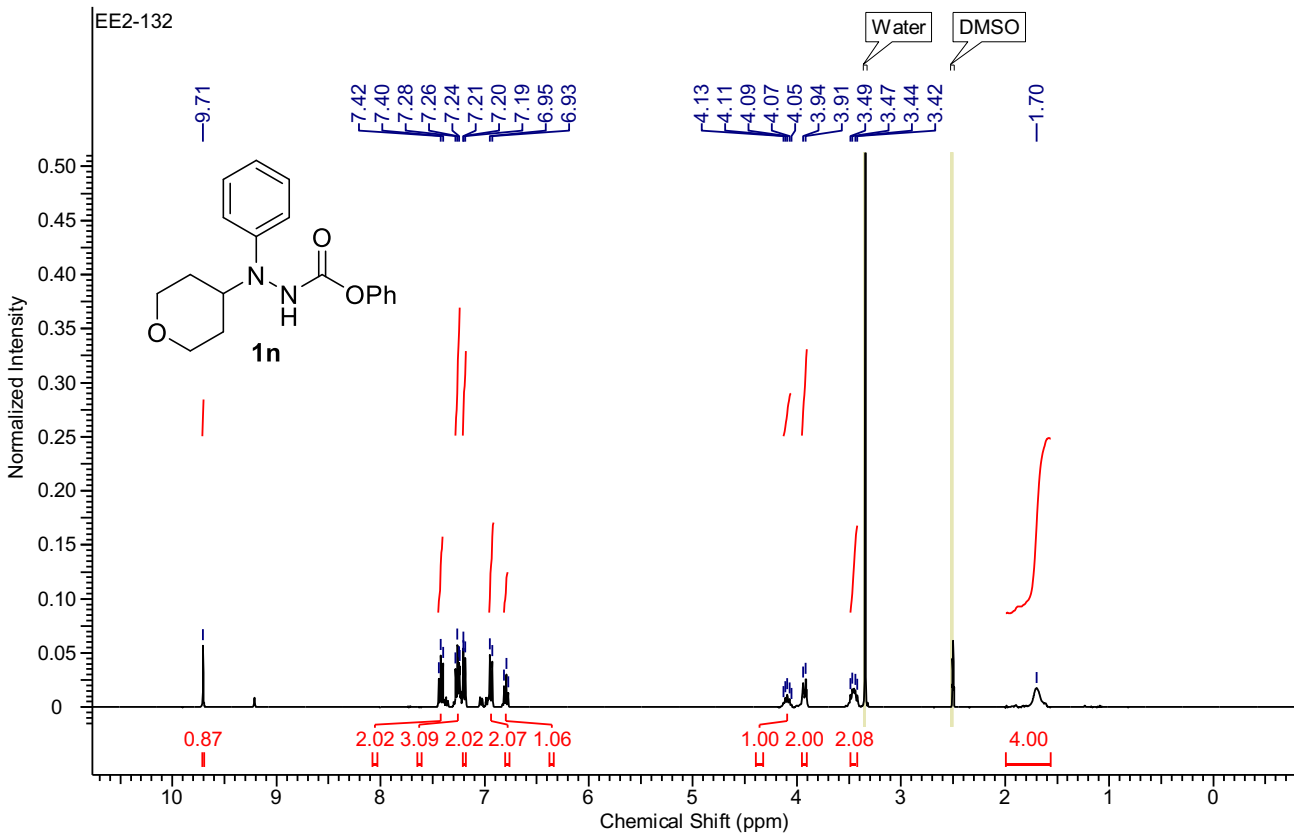

2oo
170.36
154.99
150.83
129.30
125.05
121.60
60.13
51.94
14.06
Normalized Intensity
Chemical Shift (ppm)

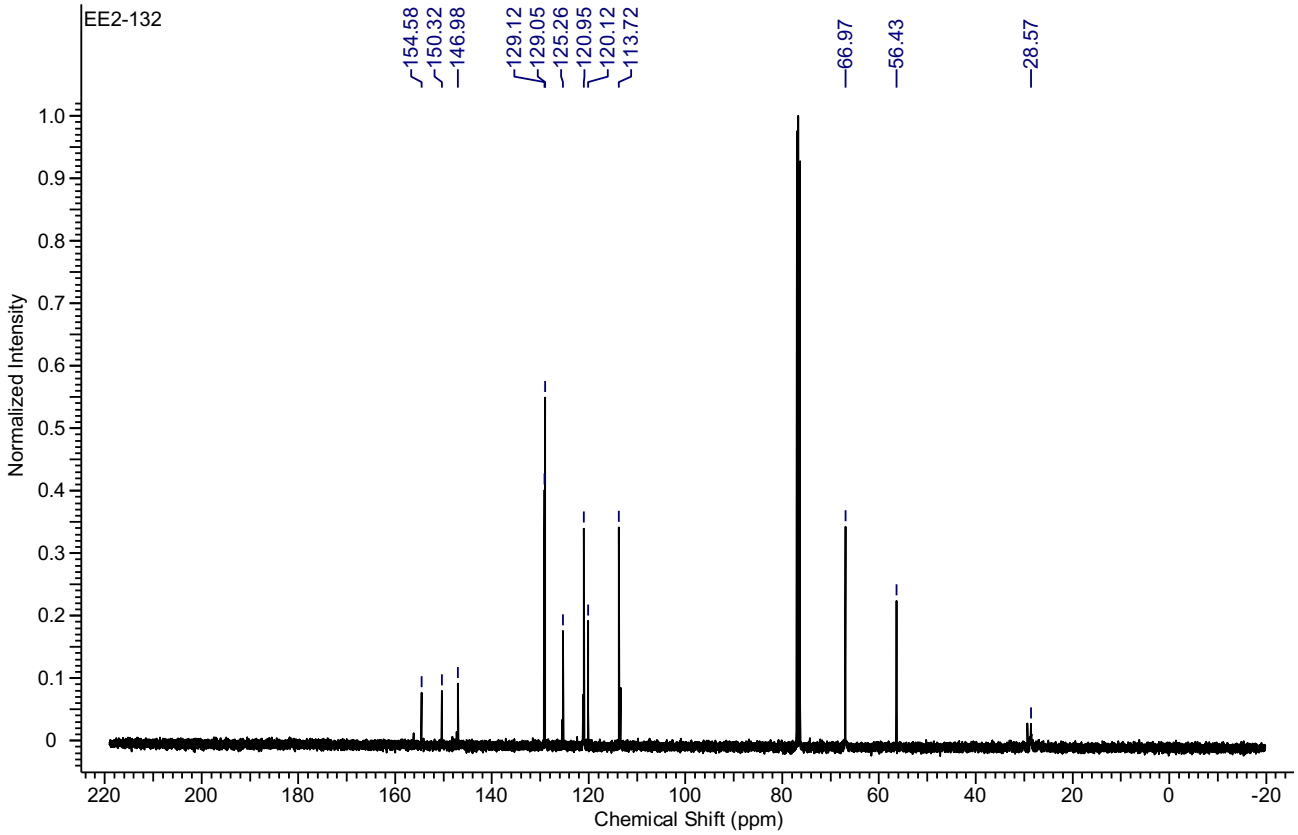

2l
9.98
7.66
7.66
7.40
7.38
7.26
7.23
7.14
7.12
6.99
6.96
6.82
6.45
4.67
O
N
N
H
O
OPh
1l
Water
DMSO
Normalized Intensity
0.92
1.05 2.03 3.07 2.03 2.08 1.08 2.00
1.99
Chemical Shift (ppm)

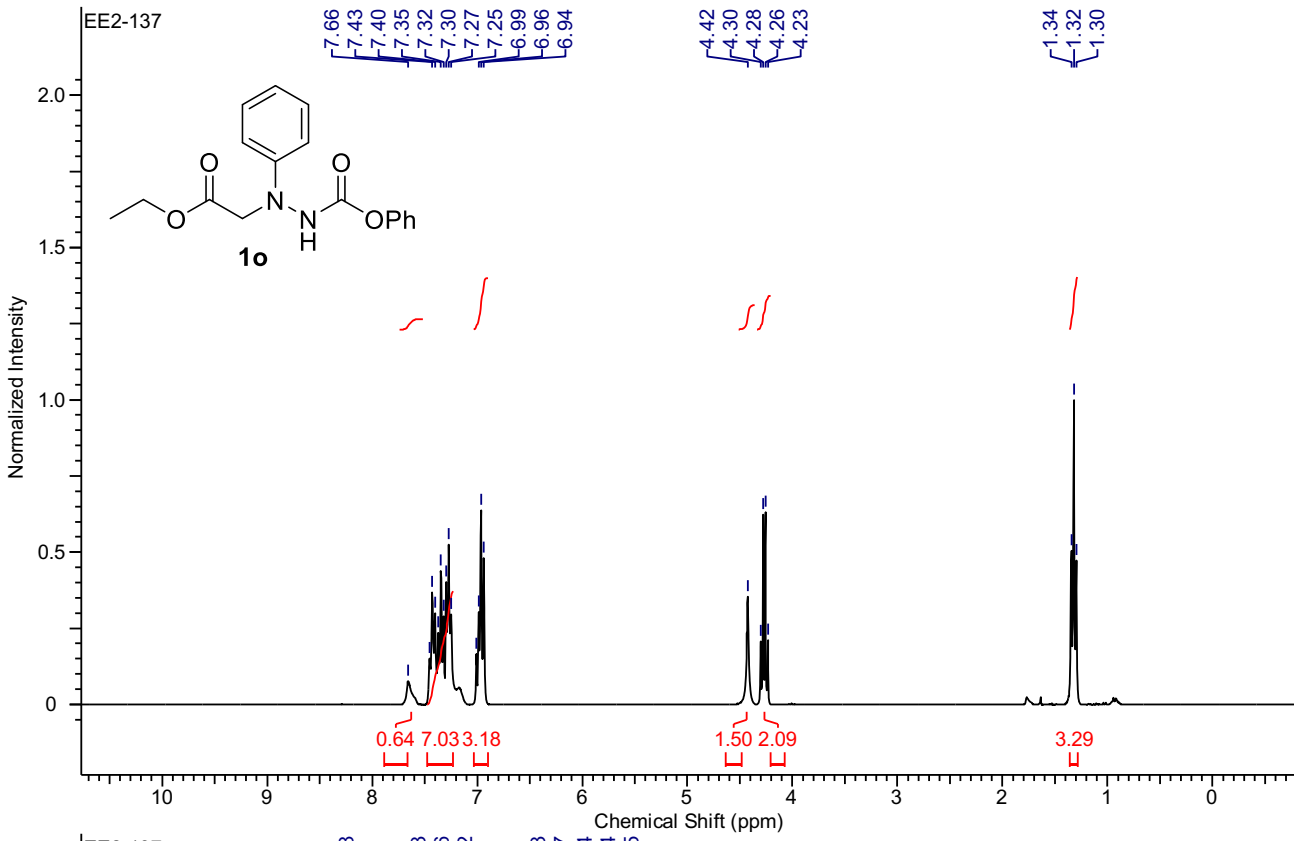

2l
153.72
150.59
150.10
148.01
142.66
129.31
129.19
125.57
121.28
120.46
113.71
110.41
109.40
48.99
Normalized Intensity
Chemical Shift (ppm)

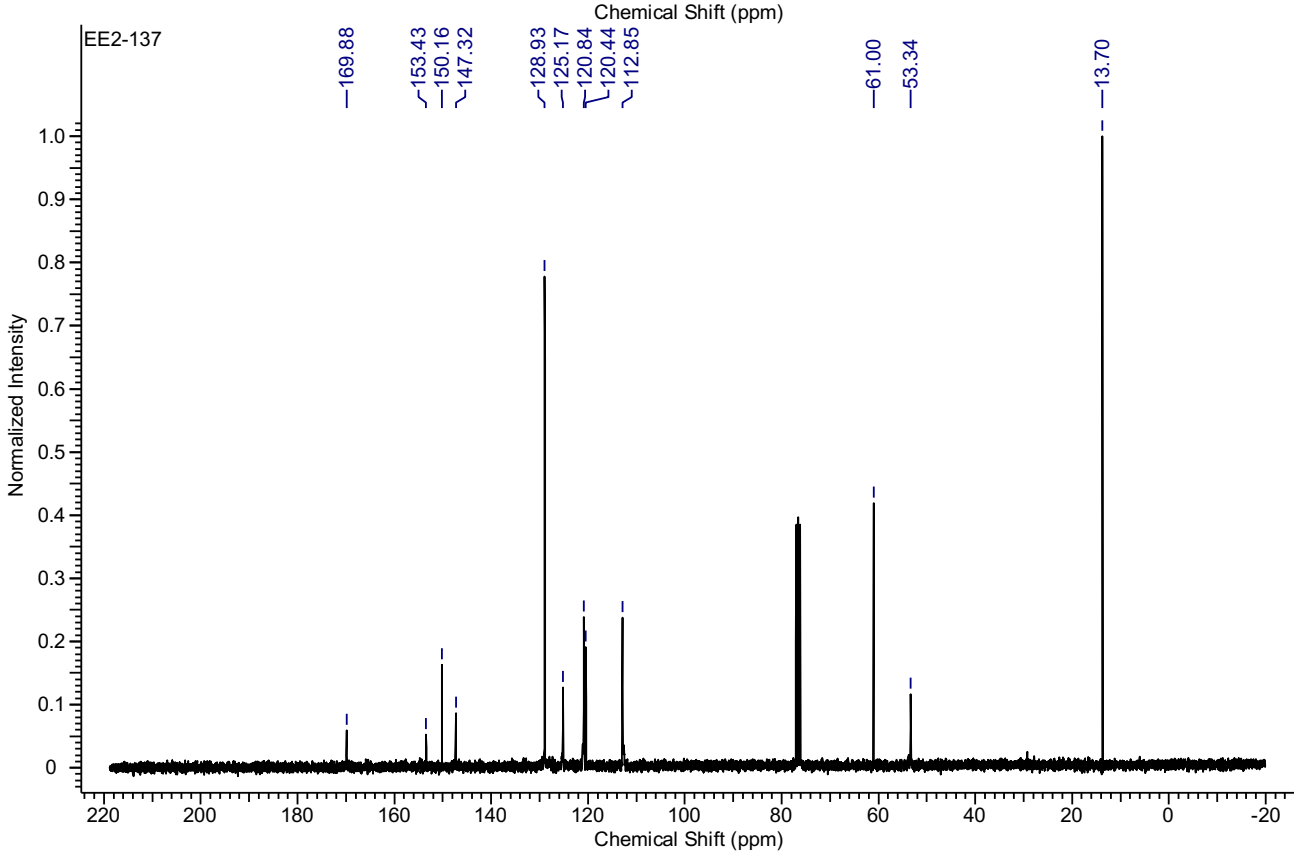

EE2-129
Water
9.77
7.39
7.29
7.26
7.22
7.18
7.17
7.09
7.07
7.03
6.84
5.04
5.01
4.99
4.96
4.94
3.19
3.17
1m
Normalized Intensity
Chemical Shift (ppm)
0.79
2.08
5.08
2.06
2.03
2.02
1.01
1.02
4.00

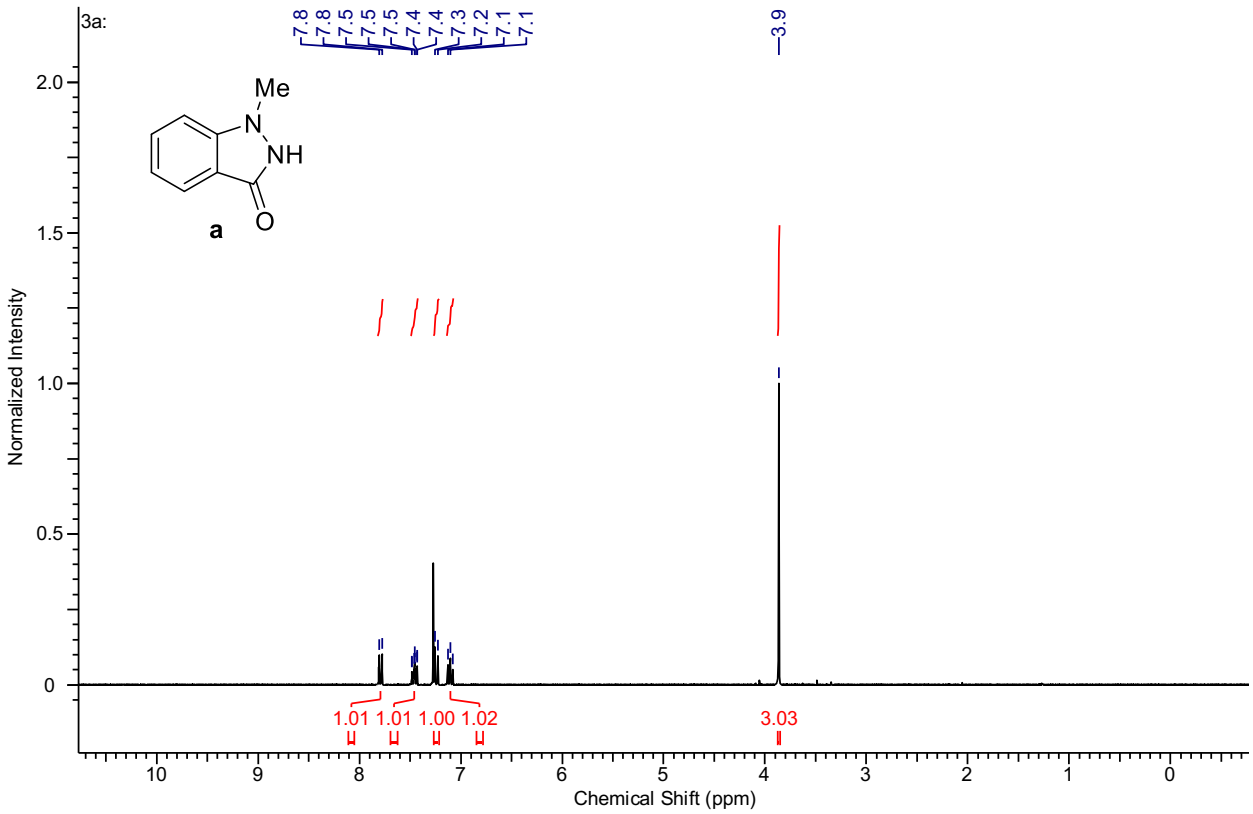

EE2-129
155.11
150.66
148.62
141.18
129.38
129.10
126.28
125.28
124.38
121.63
119.18
113.82
59.87
35.68
Normalized Intensity
Chemical Shift (ppm)

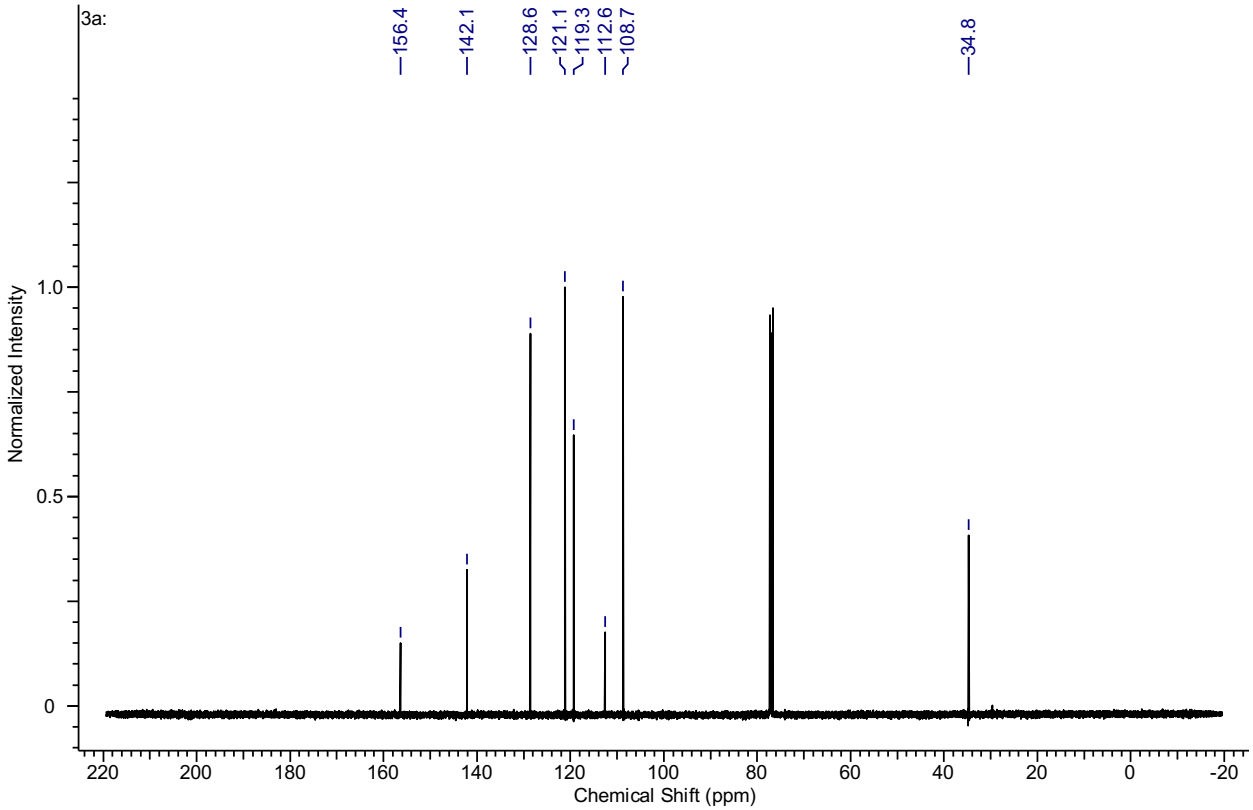

EE2-132
Water
DMSO
9.71
7.42
7.40
7.28
7.26
7.24
7.21
7.20
7.19
6.95
6.93
4.13
4.11
4.09
4.07
4.05
3.94
3.91
3.49
3.47
3.44
3.42
1.70
1n
Normalized Intensity
0.87
2.02
3.09
2.02
2.07
1.06
1.00
2.00
2.08
4.00
Chemical Shift (ppm)

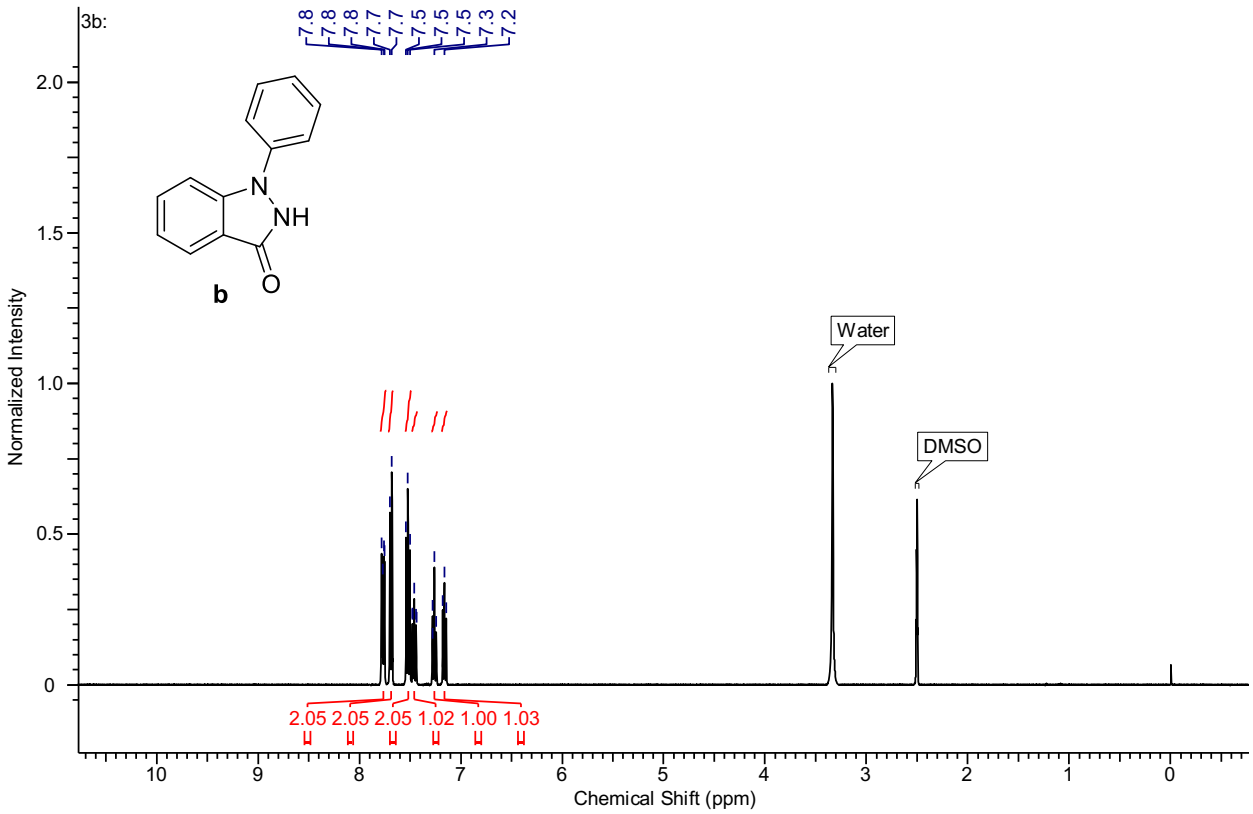

EE2-132
154.58
150.32
146.98
129.12
129.05
125.26
120.95
120.12
113.72
66.97
56.43
28.57
Normalized Intensity
Chemical Shift (ppm)

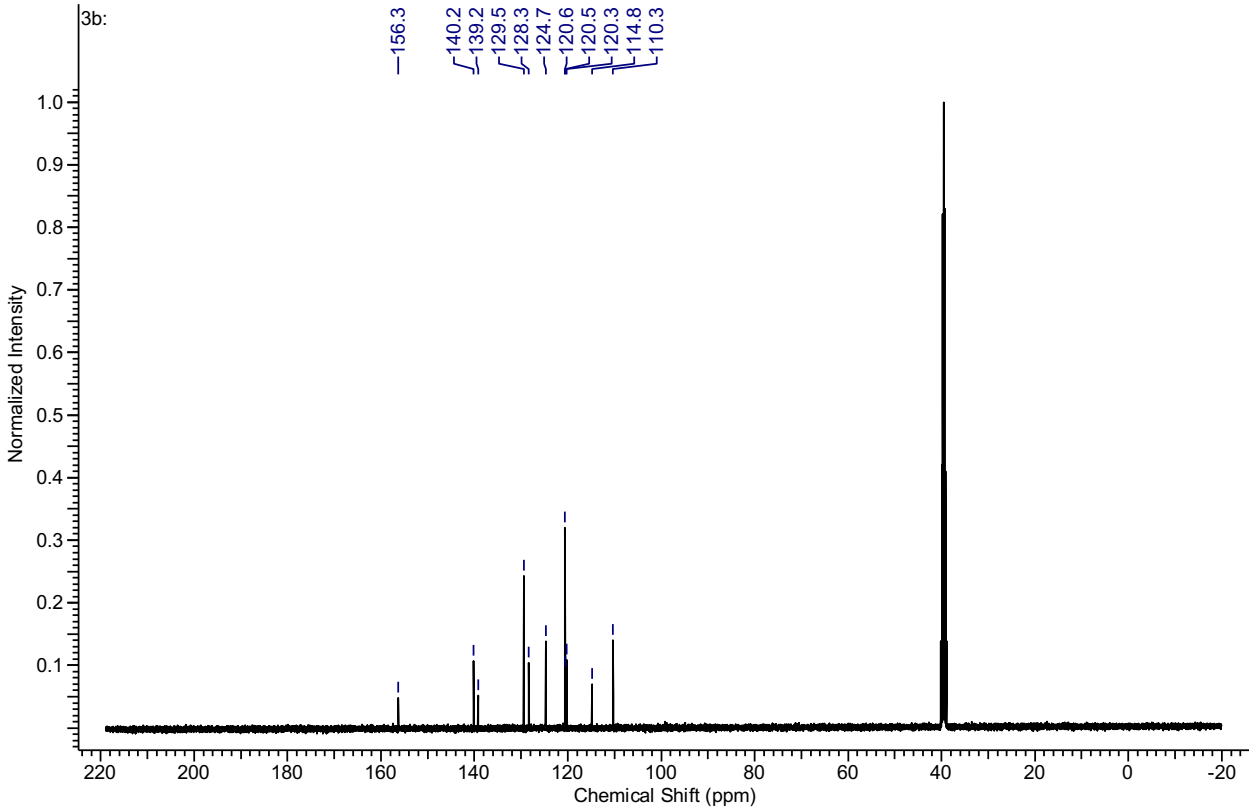

EE2-137
7.66
7.43
7.40
7.35
7.32
7.30
7.27
7.25
6.99
6.96
6.94
4.42
4.30
4.28
4.26
4.23
1.34
1.32
1.30
O
O
N
N
H
O
OPh
1o
Normalized Intensity
0.64
7.03
3.18
1.50
2.09
3.29
Chemical Shift (ppm)

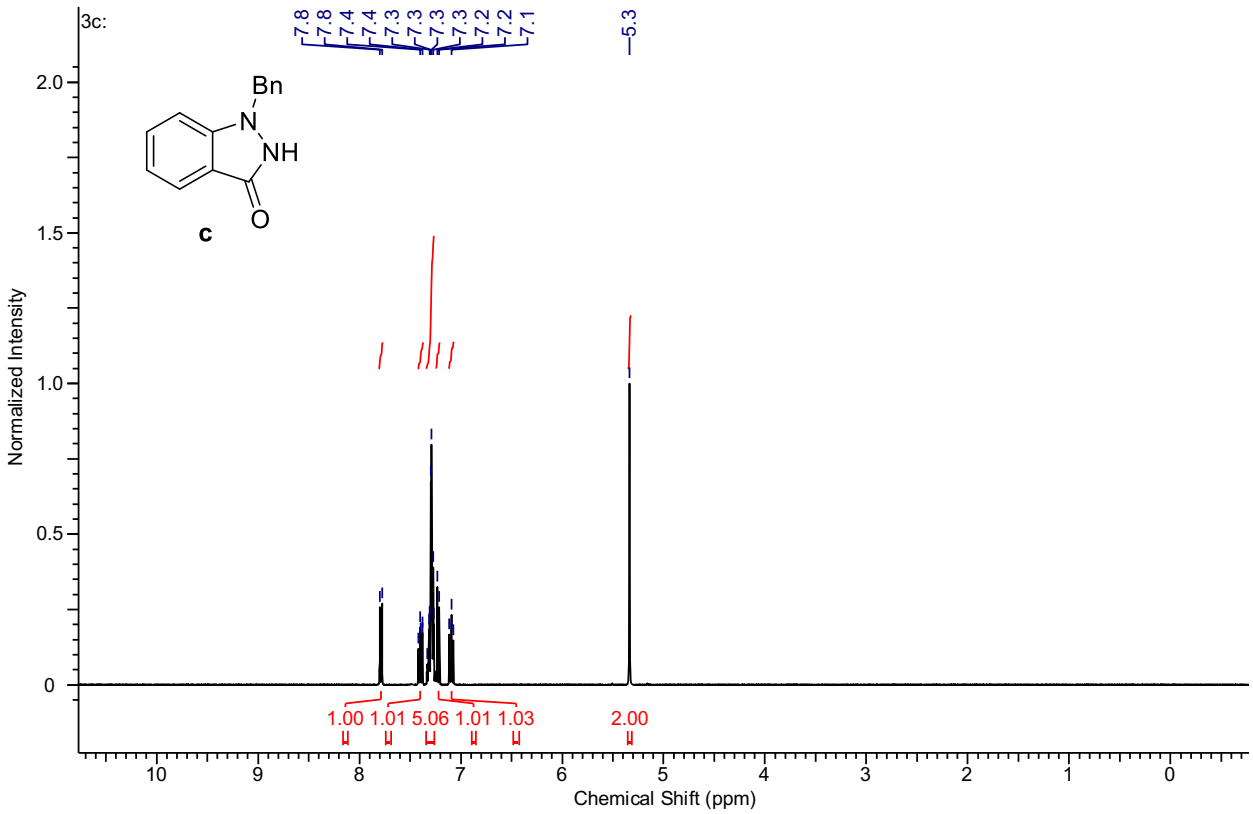

EE2-137
169.88
153.43
150.16
147.32
128.93
125.17
120.84
120.44
112.85
61.00
53.34
13.70
Normalized Intensity
Chemical Shift (ppm)

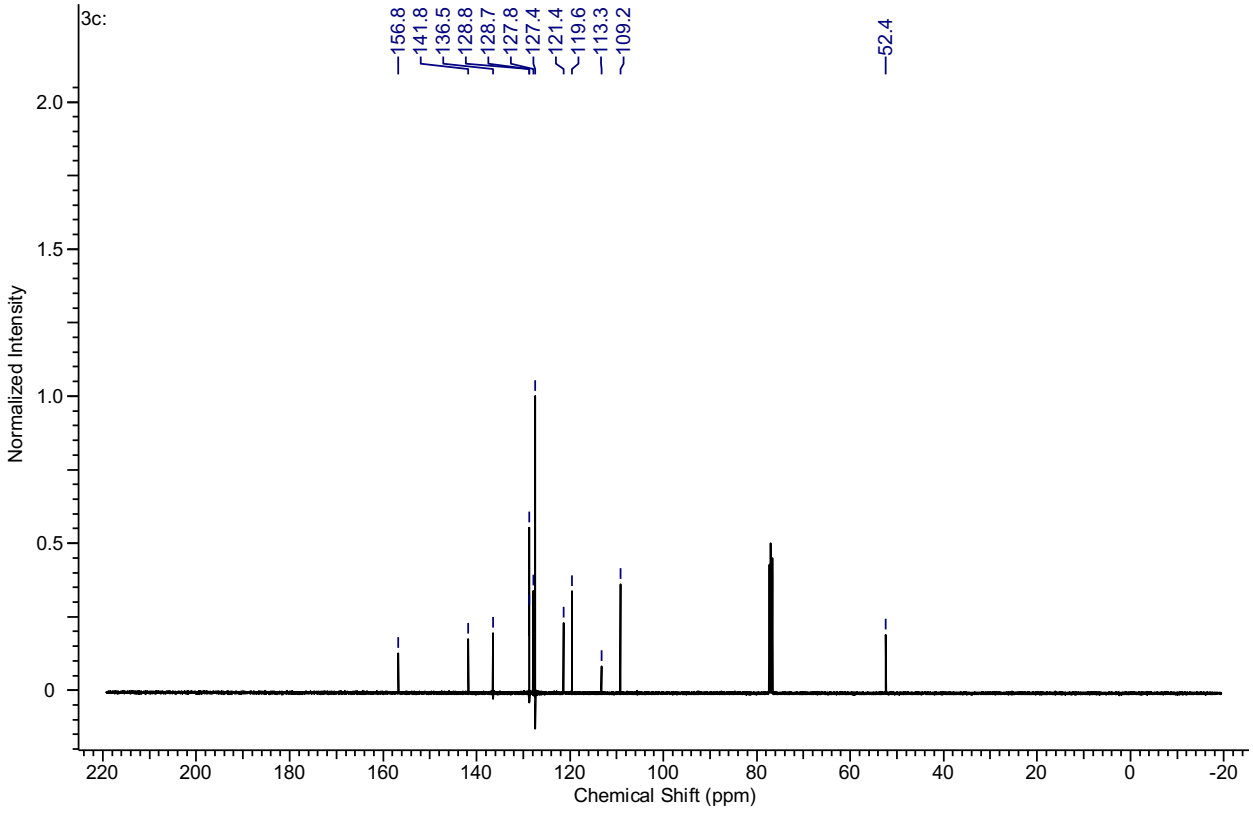

3a:
7.8
7.8
7.5
7.5
7.5
7.4
7.4
7.3
7.2
7.1
7.1
3.9
Me
N
NH
O
a
Normalized Intensity
2.0
1.5
1.0
0.5
0
1.01 1.01 1.00 1.02
3.03
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

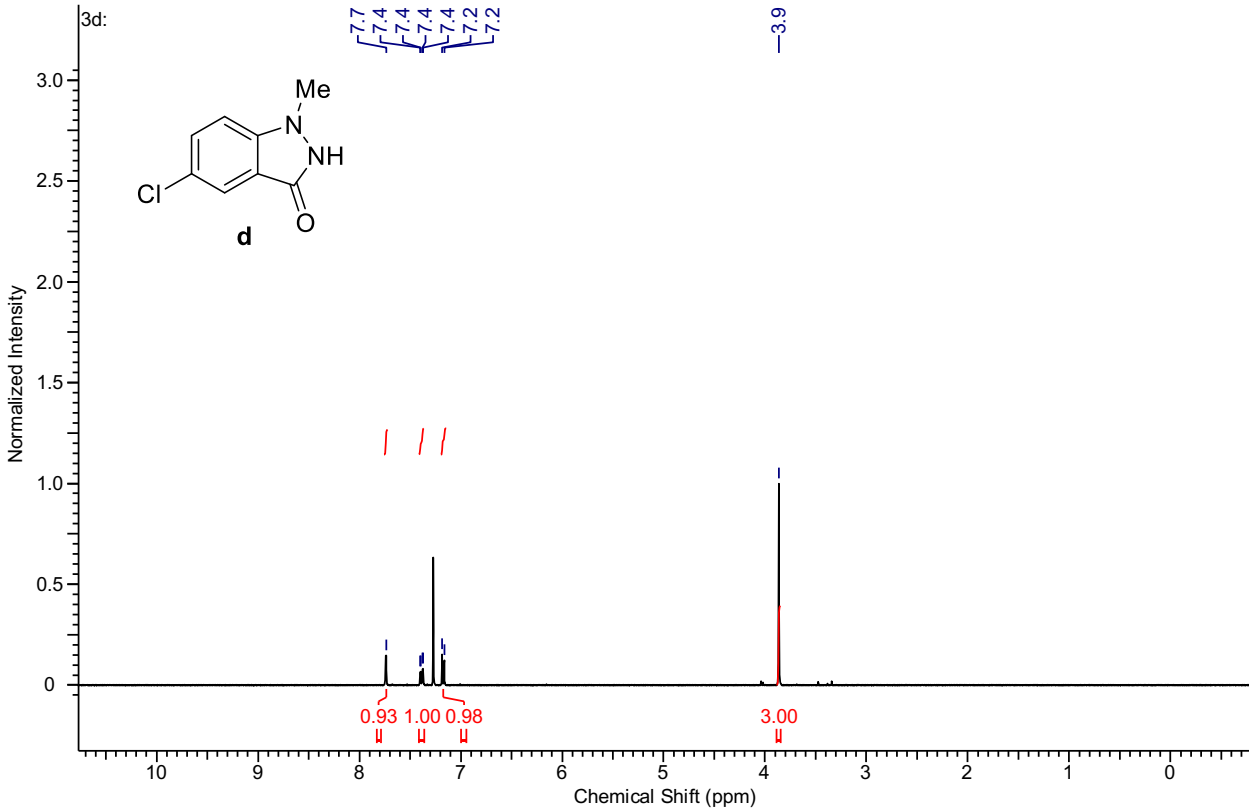

3a:
156.4
142.1
128.6
121.1
119.3
112.6
108.7
34.8
Normalized Intensity
1.0
0.5
0
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

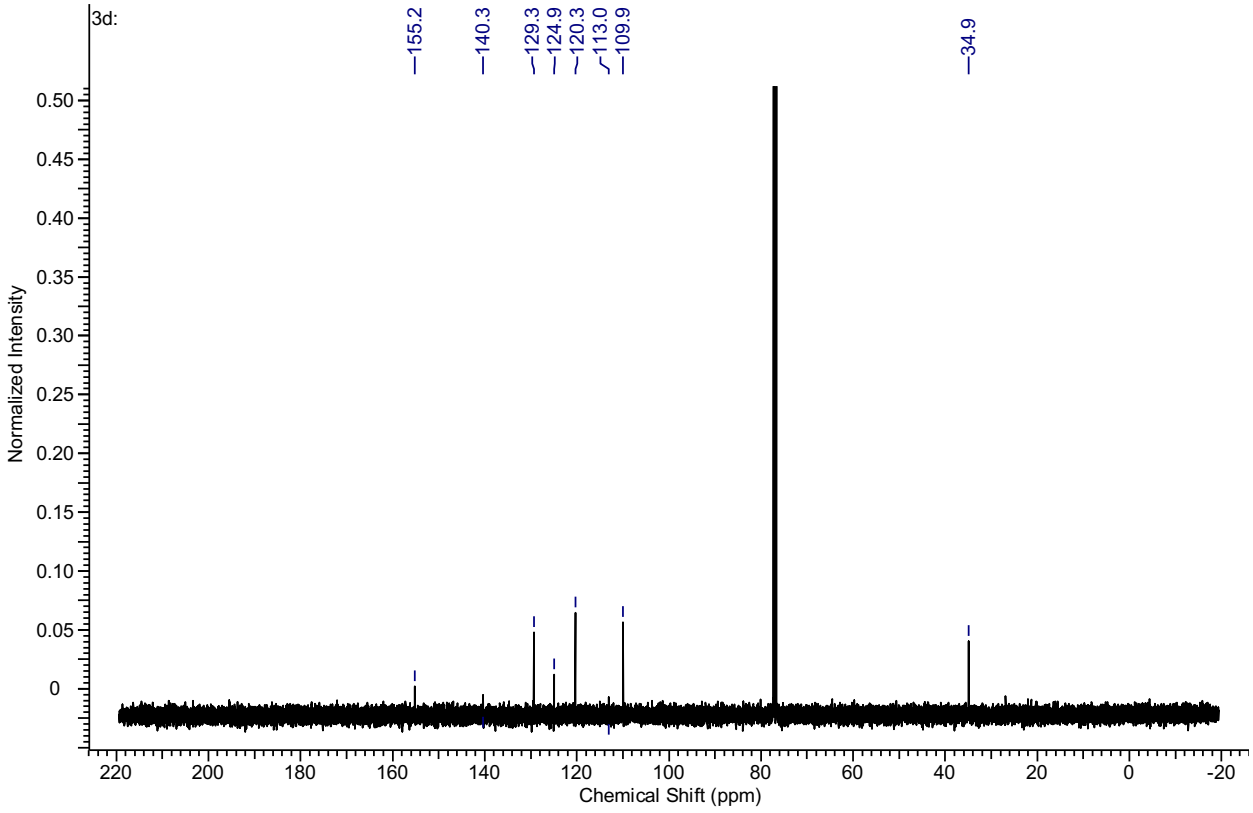

3b:
7.8
7.8
7.8
7.7
7.7
7.5
7.5
7.5
7.3
7.2
N
NH
O
b
Water
DMSO
Normalized Intensity
2.05 2.05 2.05 1.02 1.00 1.03
Chemical Shift (ppm)

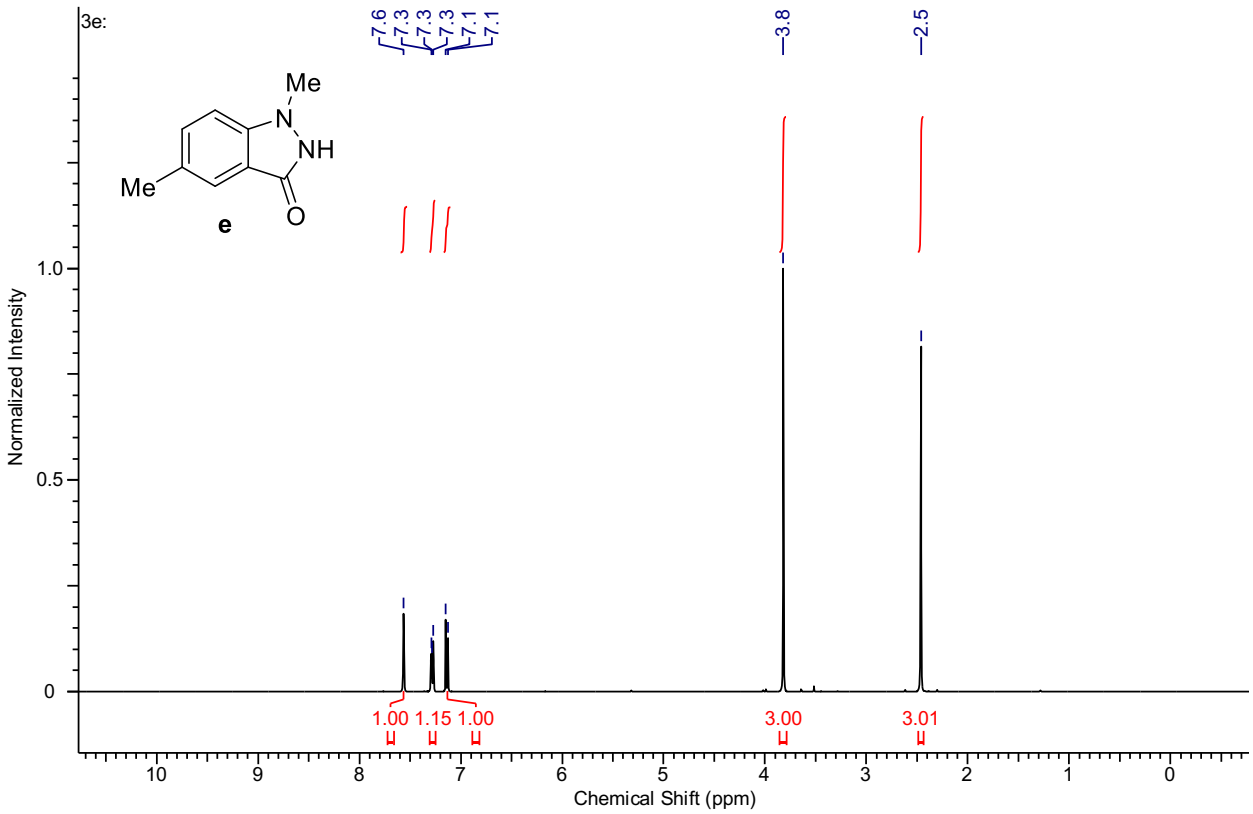

3b:
156.3
140.2
139.2
129.5
128.3
124.7
120.6
120.5
120.3
114.8
110.3
Normalized Intensity
Chemical Shift (ppm)

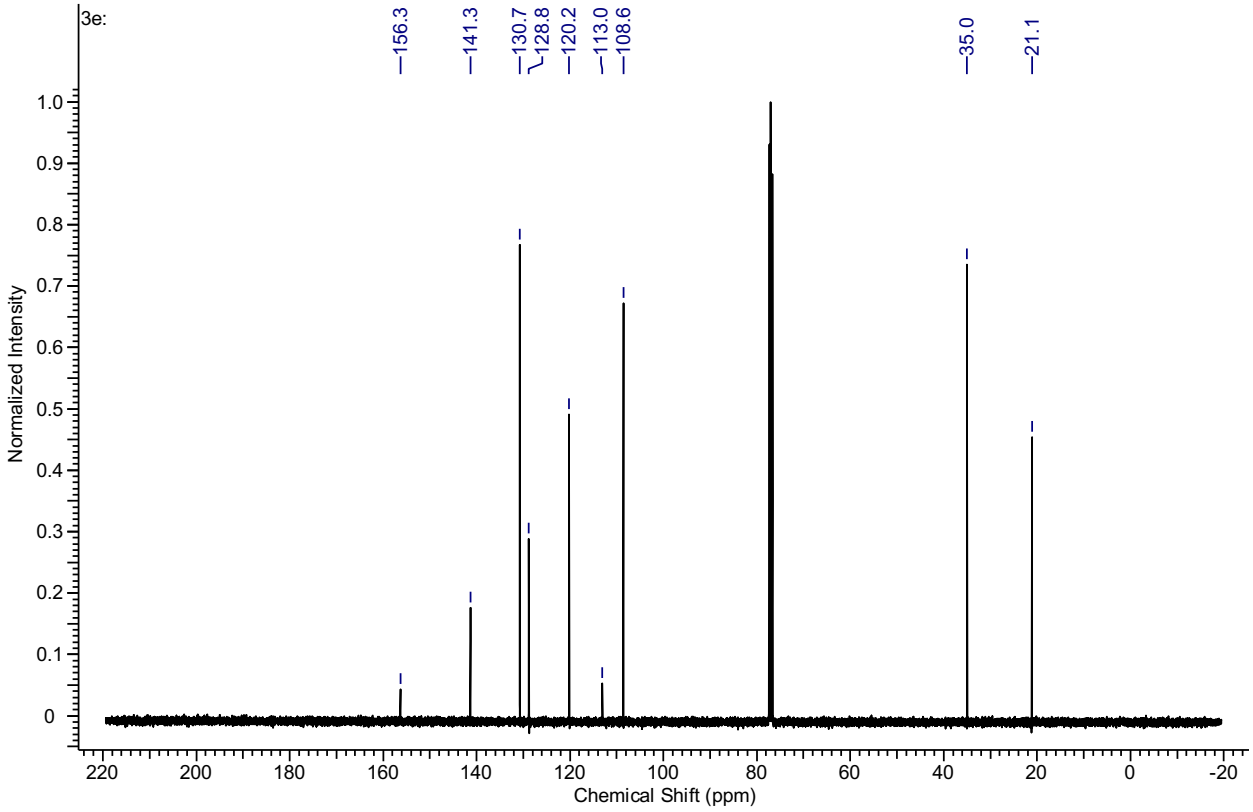

3c:
7.8
7.8
7.4
7.4
7.3
7.3
7.3
7.3
7.2
7.2
7.1
5.3
Bn
N
NH
O
c
Normalized Intensity
2.0
1.5
1.0
0.5
0
1.00 1.01 5.06 1.01 1.03
2.00
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

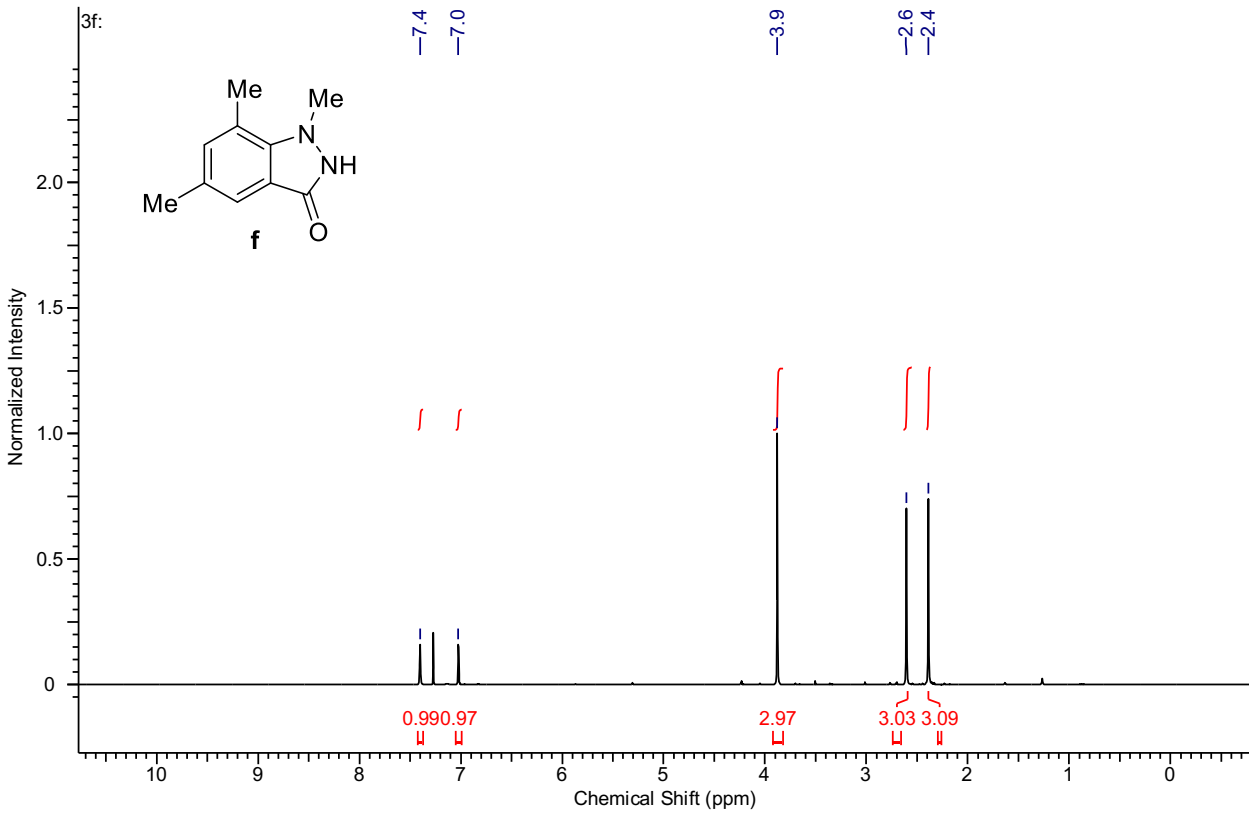

3c:
156.8
141.8
136.5
128.8
128.7
127.8
127.4
121.4
119.6
113.3
109.2
52.4
Normalized Intensity
2.0
1.5
1.0
0.5
0
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

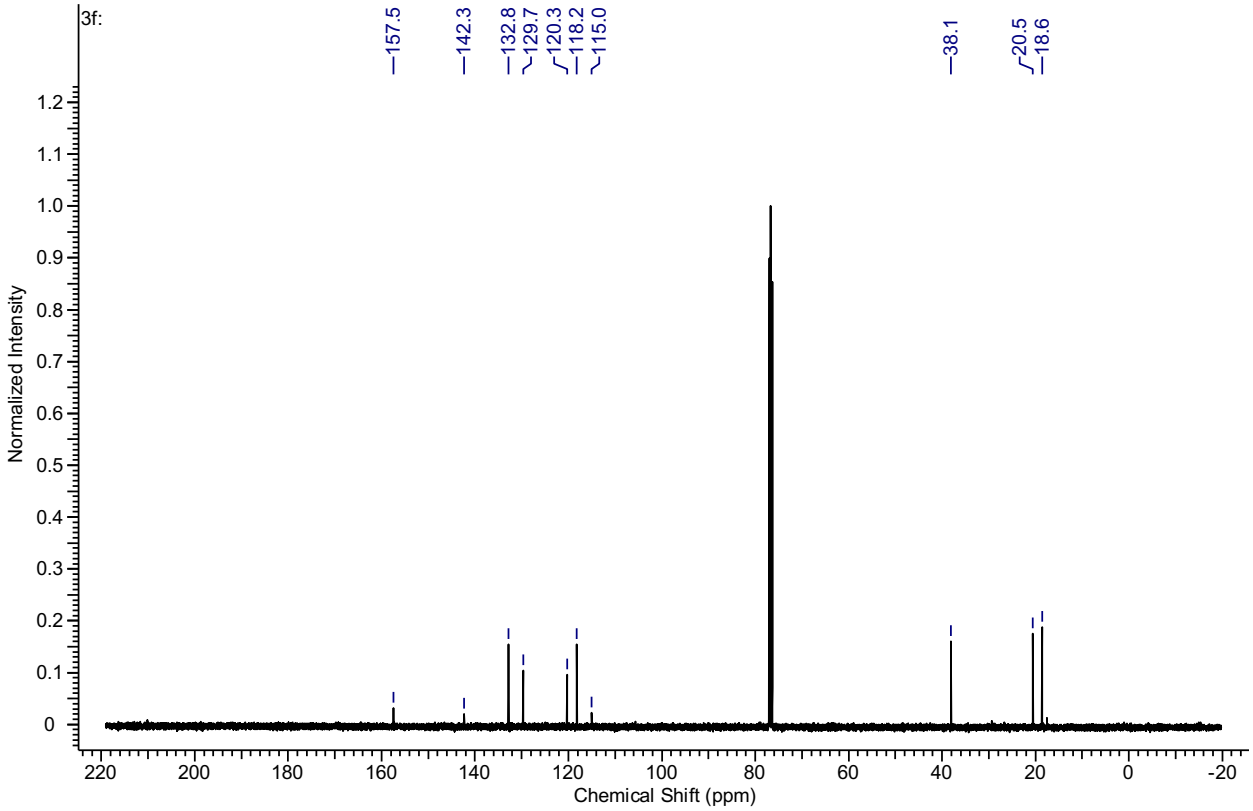

3d:
7.7
7.4
7.4
7.4
7.4
7.2
7.2
3.9
Me
N
NH
Cl
O
d
Normalized Intensity
0.93 1.00 0.98
3.00
Chemical Shift (ppm)

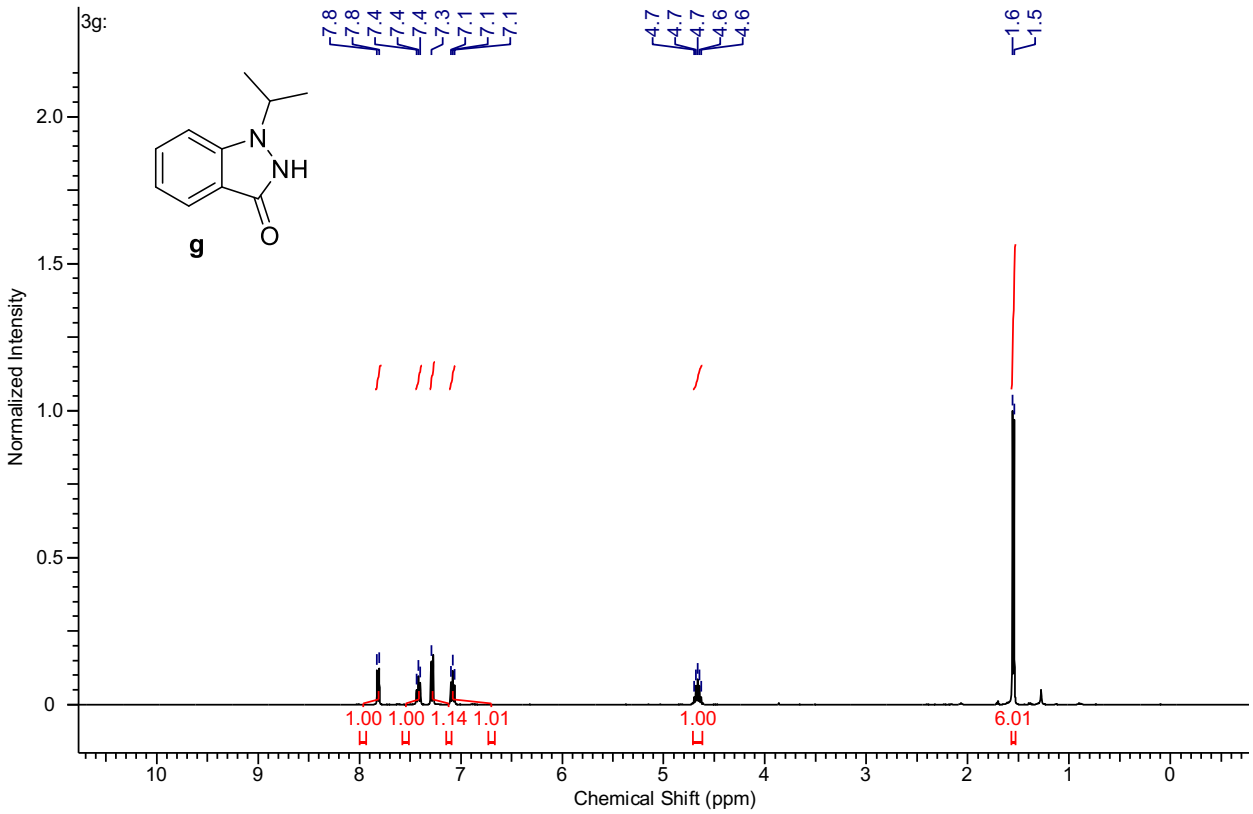

3d:
155.2
140.3
129.3
124.9
120.3
113.0
109.9
34.9
Normalized Intensity
Chemical Shift (ppm)

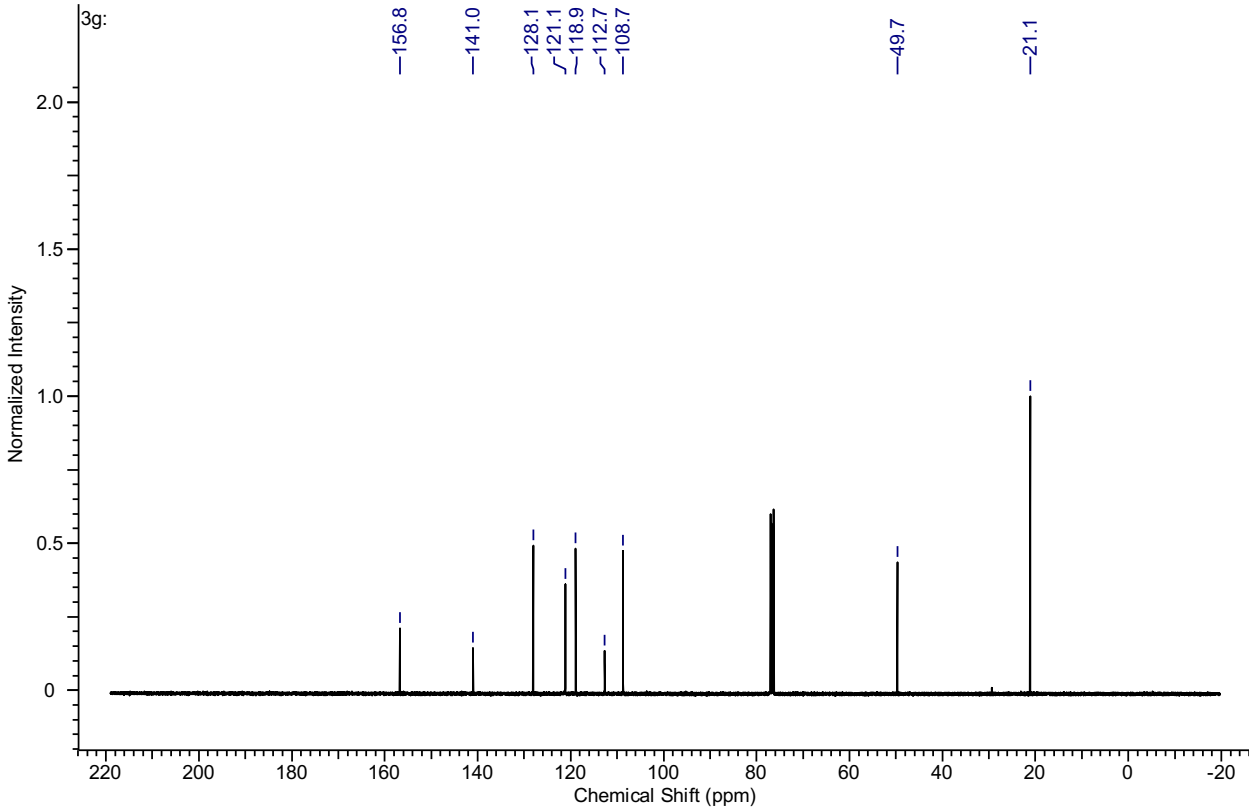

3e:
Me
N
NH
Me
O
e
7.6
7.3
7.3
7.3
7.1
7.1
3.8
2.5
1.00
1.15
1.00
3.00
3.01
Normalized Intensity
Chemical Shift (ppm)

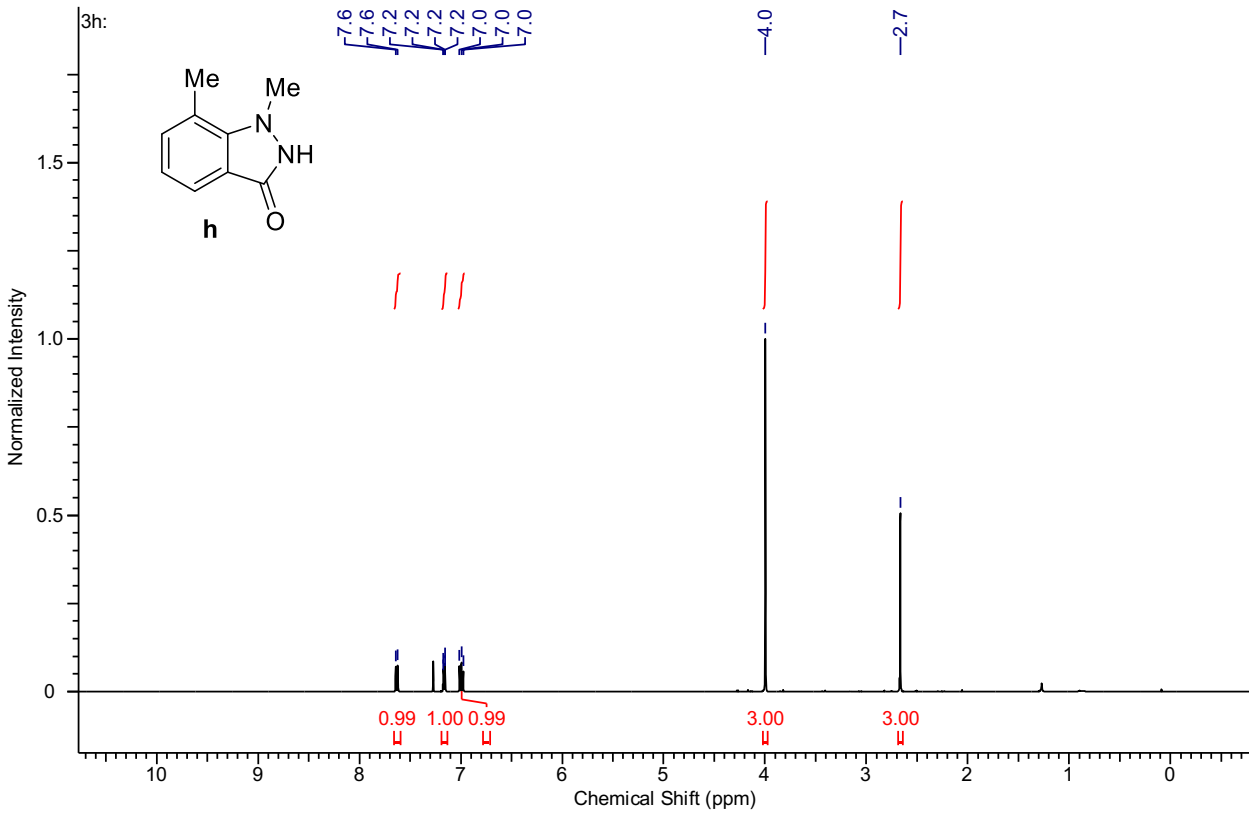

3e:
156.3
141.3
130.7
128.8
120.2
113.0
108.6
35.0
21.1
Normalized Intensity
Chemical Shift (ppm)

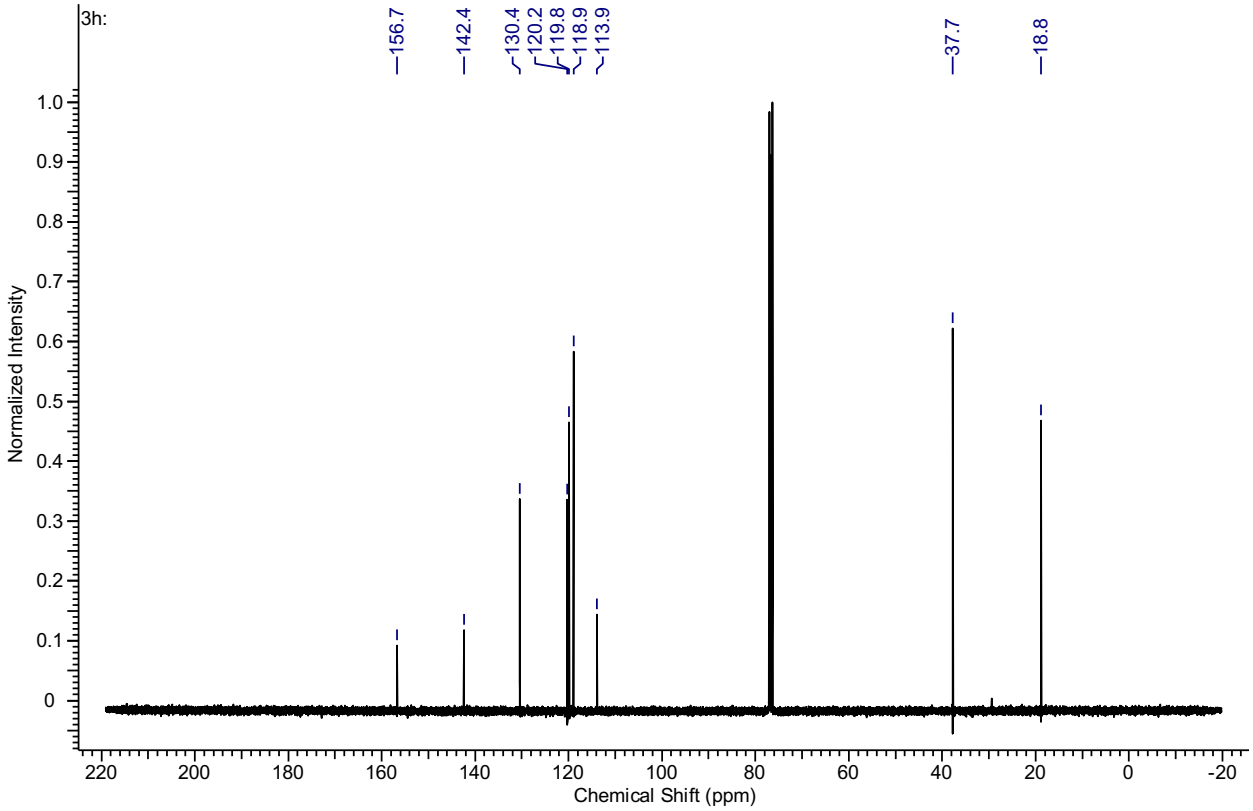

3f:
7.4
7.0
3.9
2.6
2.4
Me
Me
N
NH
Me
O
f
Normalized Intensity
0.99
0.97
2.97
3.03
3.09
Chemical Shift (ppm)

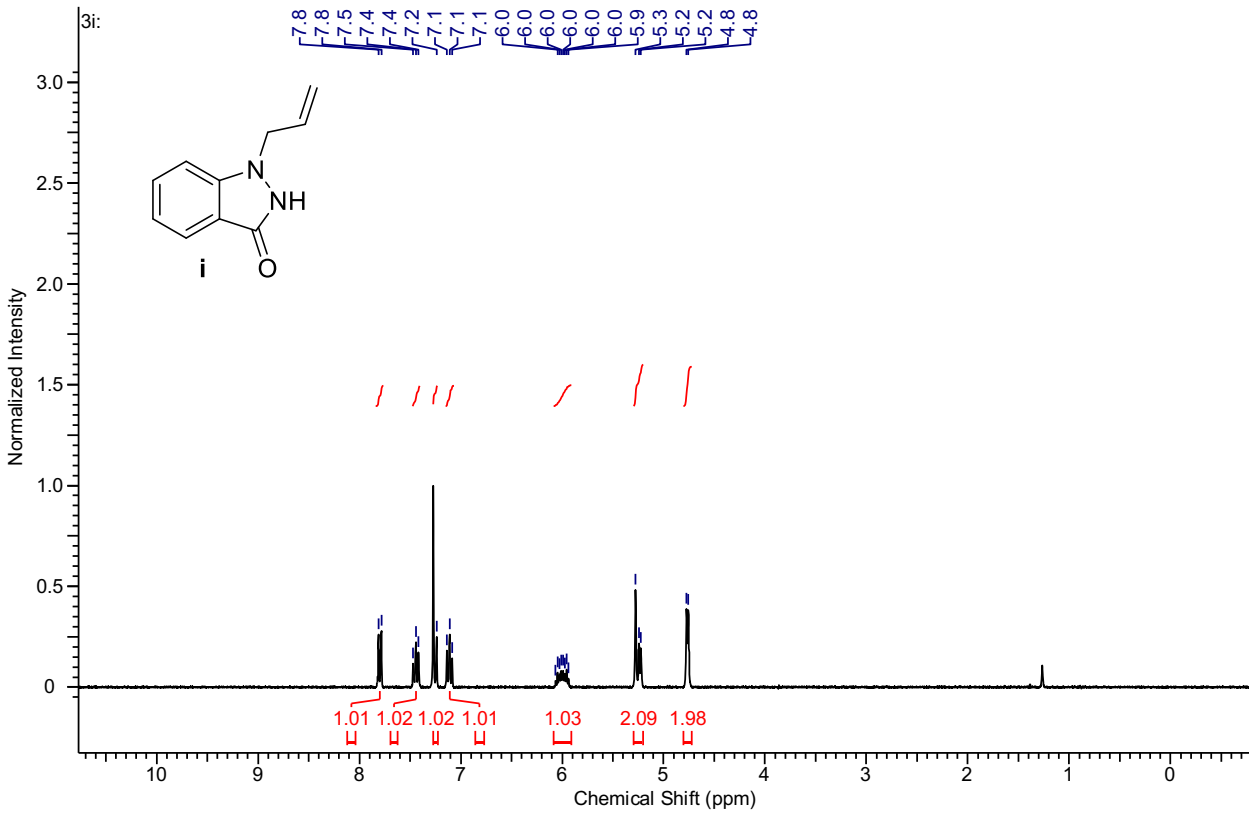

3f:
157.5
142.3
132.8
129.7
120.3
118.2
115.0
38.1
20.5
18.6
Normalized Intensity
Chemical Shift (ppm)

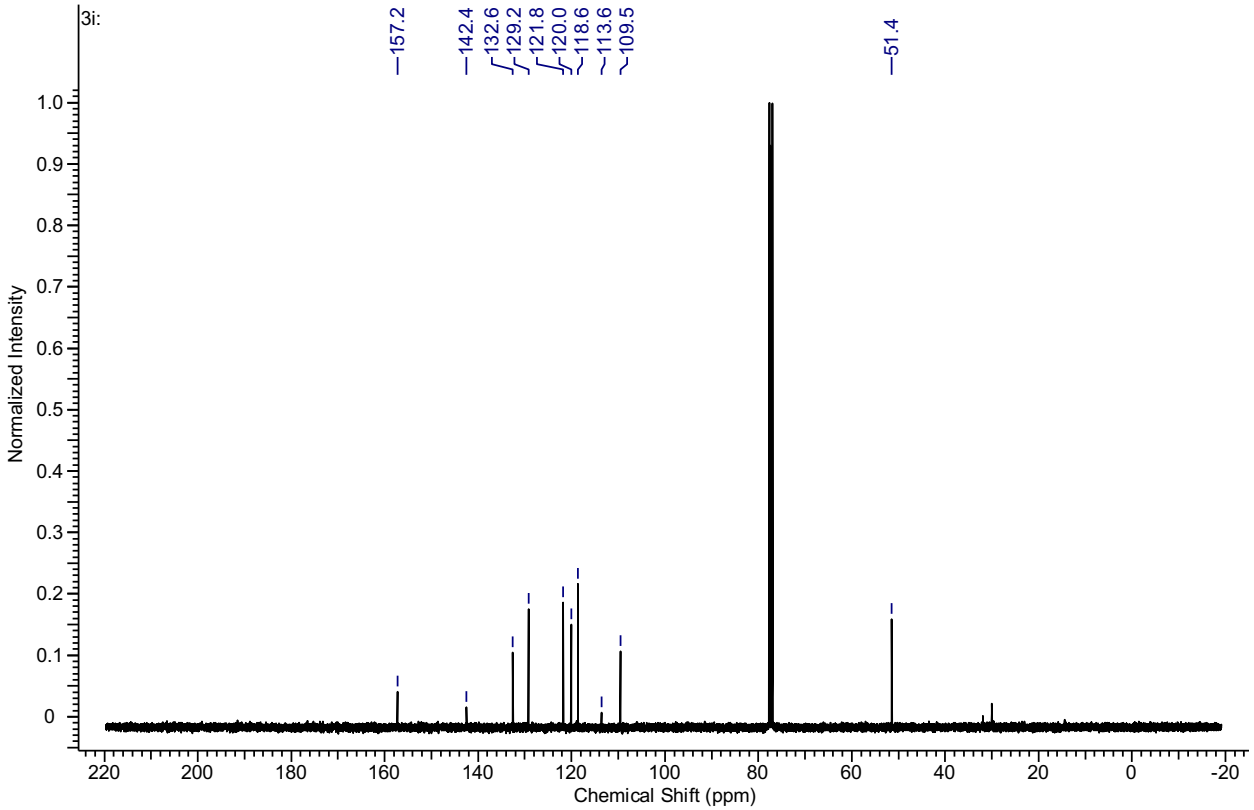

3g:
7.8
7.8
7.4
7.4
7.4
7.3
7.1
7.1
7.1
4.7
4.7
4.7
4.6
4.6
1.6
1.5
N
NH
O
g
Normalized Intensity
2.0
1.5
1.0
0.5
0
1.00 1.00 1.14 1.01
1.00
6.01
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

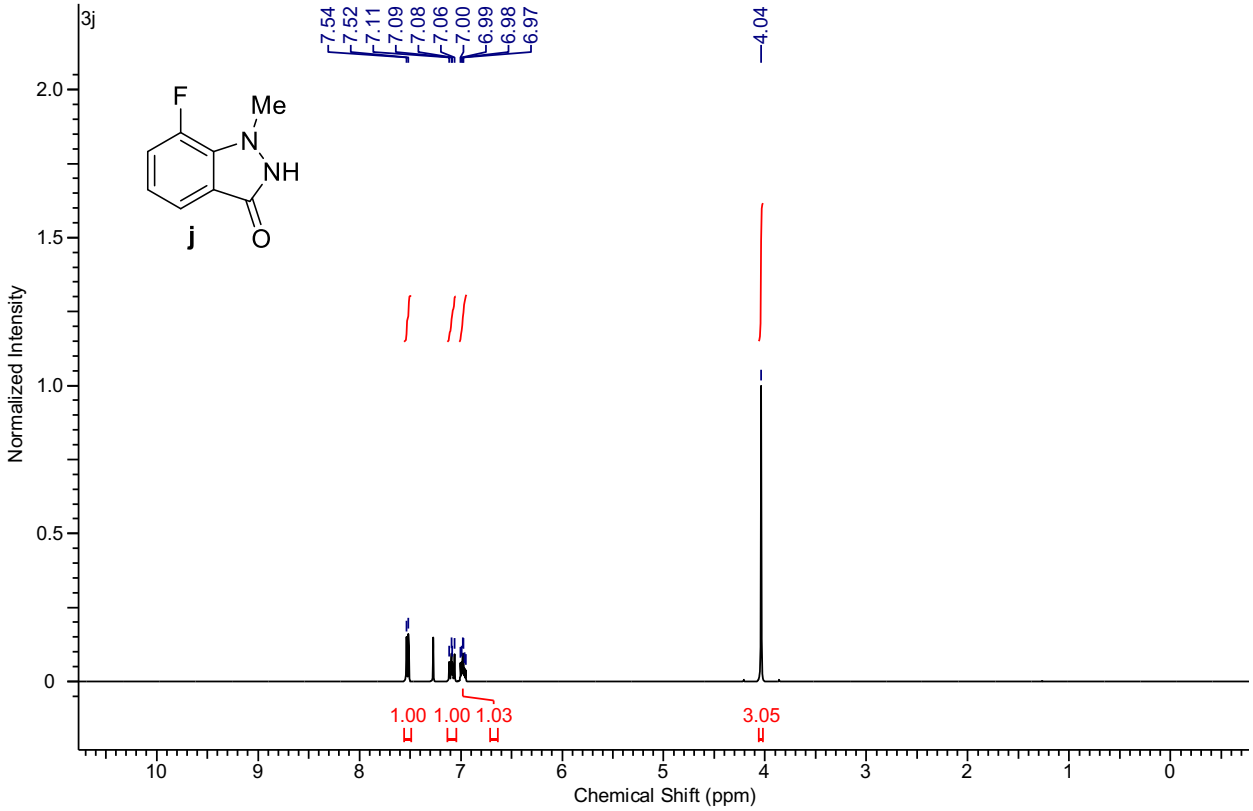

3g:
156.8
141.0
128.1
121.1
118.9
112.7
108.7
49.7
21.1
Normalized Intensity
2.0
1.5
1.0
0.5
0
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

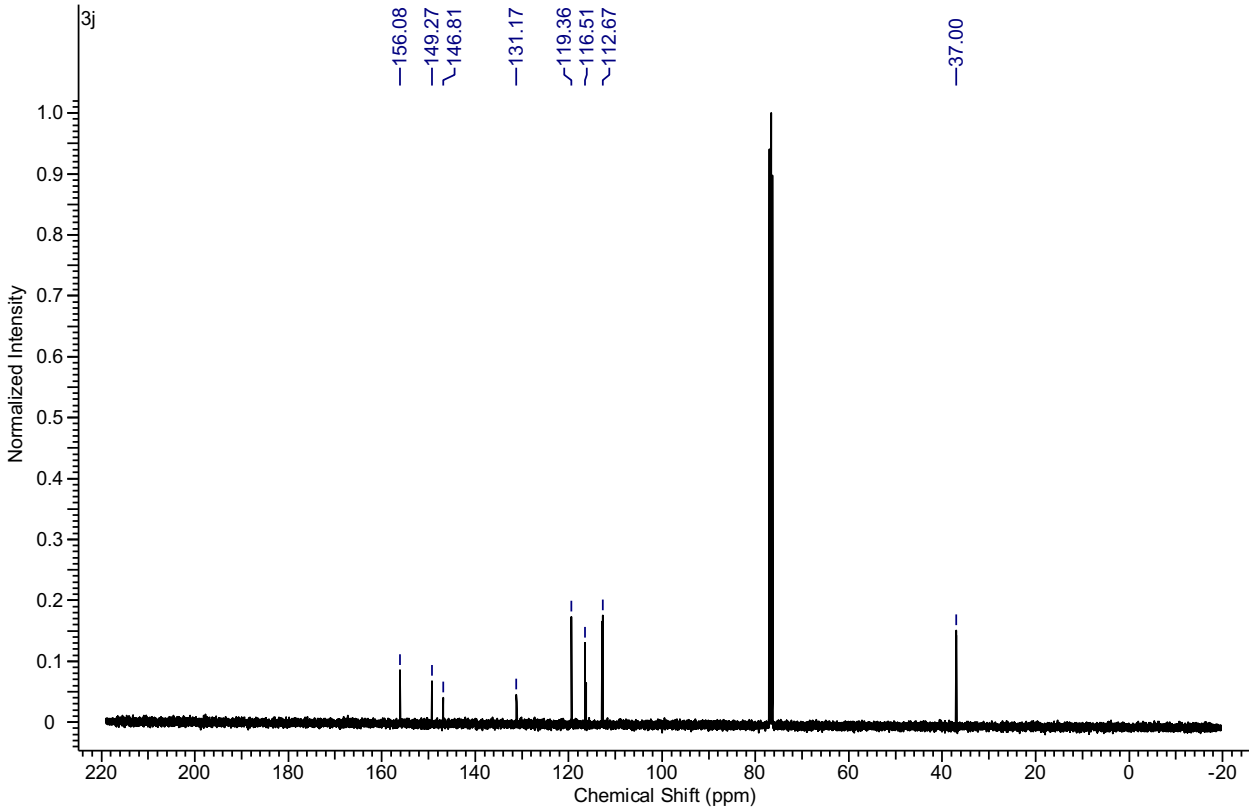

3h:
7.6
7.6
7.2
7.2
7.2
7.2
7.0
7.0
7.0
4.0
2.7
Me
Me
N
NH
O
h
Normalized Intensity
0.99
1.00
0.99
3.00
3.00
Chemical Shift (ppm)

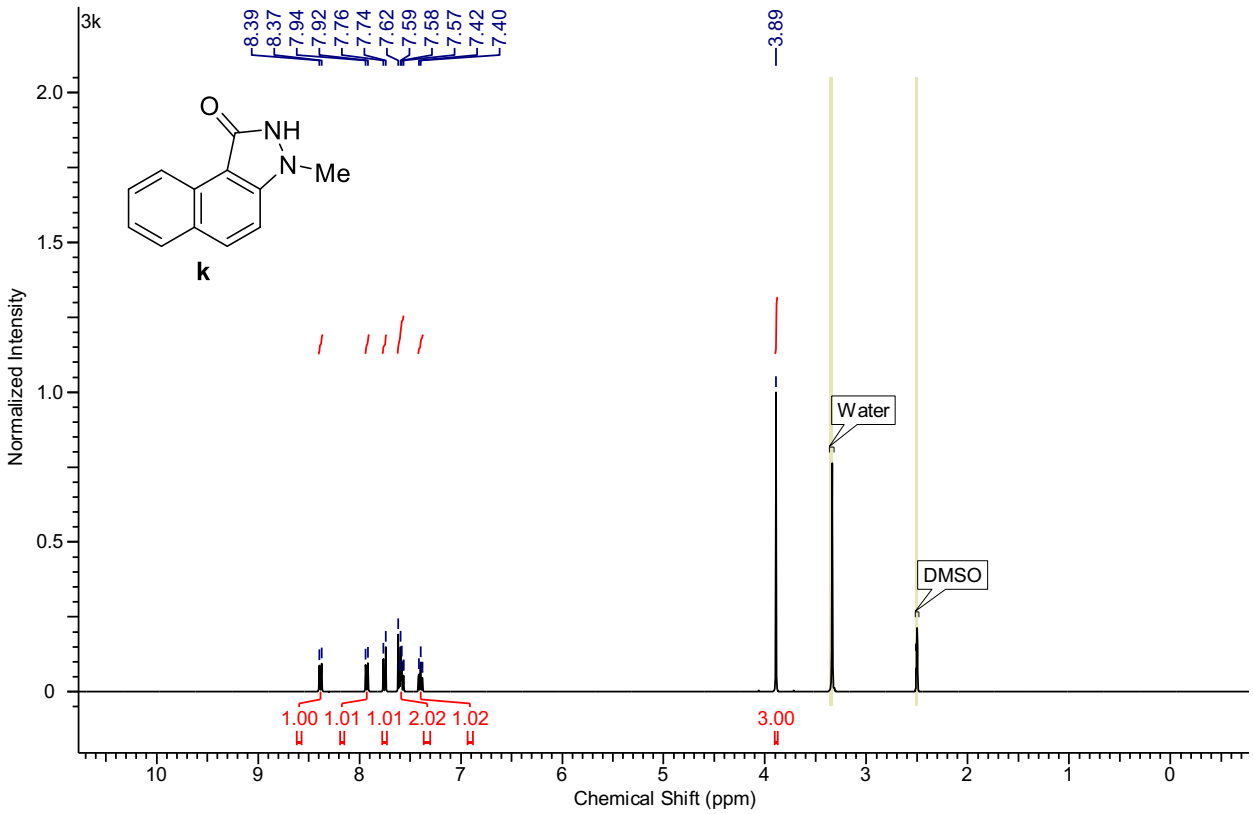

3h:
156.7
142.4
130.4
120.2
119.8
118.9
113.9
37.7
18.8
Normalized Intensity
Chemical Shift (ppm)

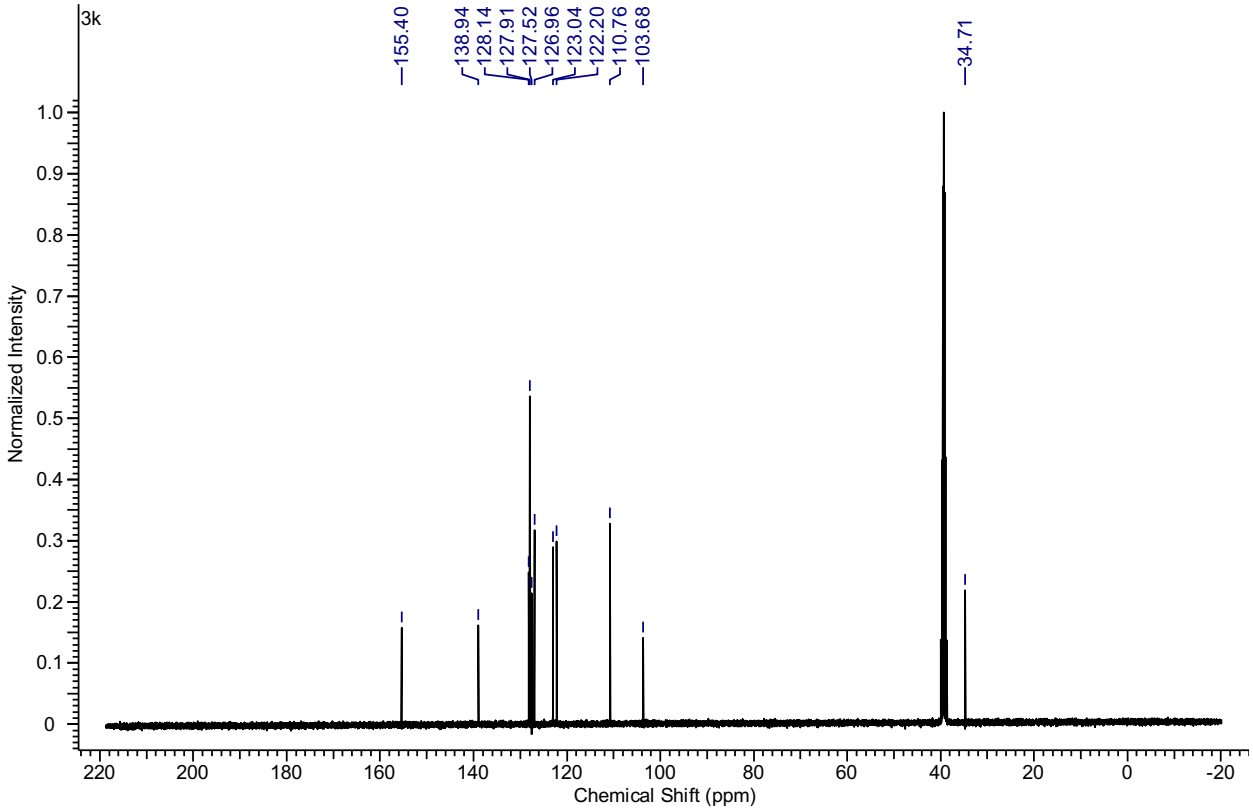

3i:
7.8
7.8
7.5
7.4
7.4
7.4
7.2
7.1
7.1
7.1
6.0
6.0
6.0
6.0
6.0
5.9
5.3
5.2
5.2
4.8
4.8
N
NH
O
i
Normalized Intensity
1.01
1.02
1.02
1.01
1.03
2.09
1.98
Chemical Shift (ppm)

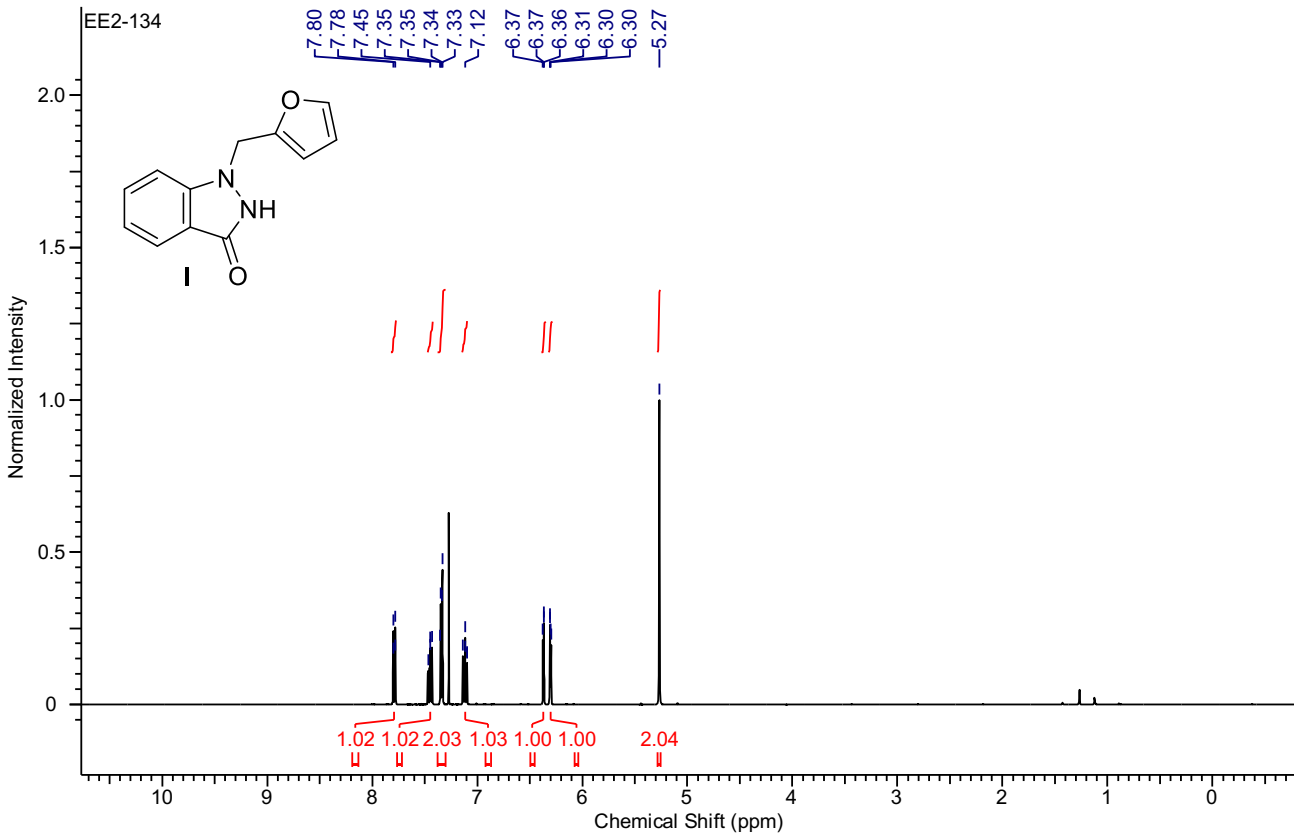

3i:
157.2
142.4
132.6
129.2
121.8
120.0
118.6
113.6
109.5
51.4
Normalized Intensity
Chemical Shift (ppm)

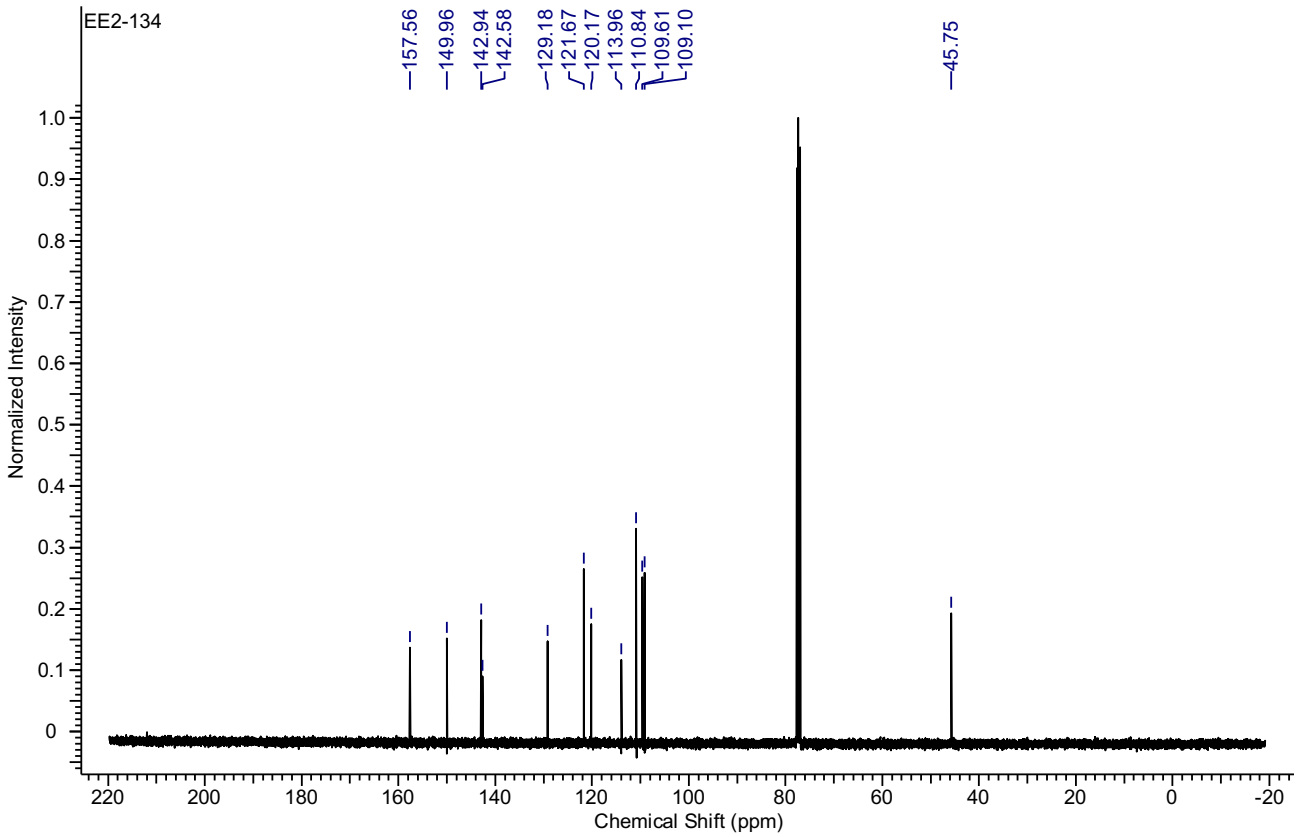

3j
7.54
7.52
7.11
7.09
7.08
7.06
7.00
6.99
6.98
6.97
4.04
F
Me
N
NH
O
j
Normalized Intensity
1.00
1.00
1.03
3.05
Chemical Shift (ppm)

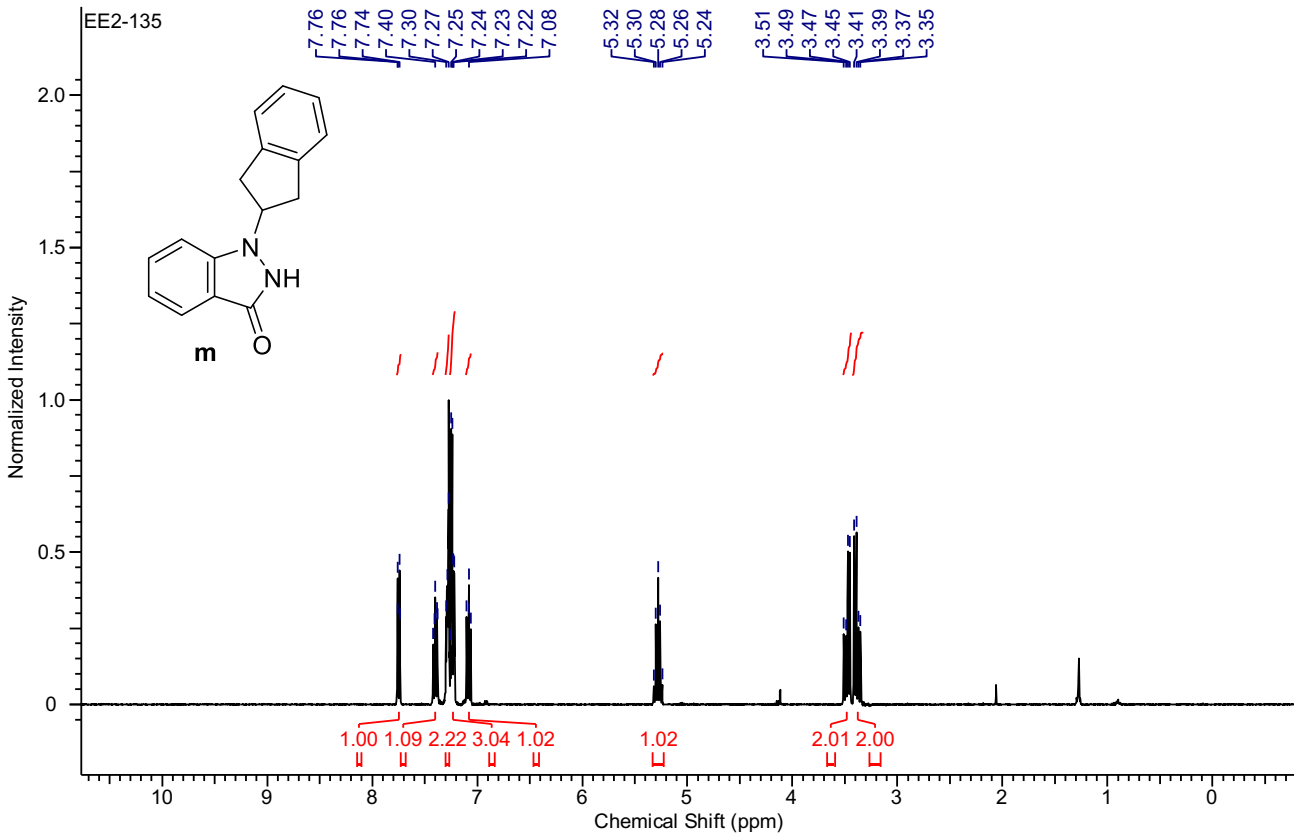

3j
156.08
149.27
146.81
131.17
119.36
116.51
112.67
37.00
Normalized Intensity
Chemical Shift (ppm)

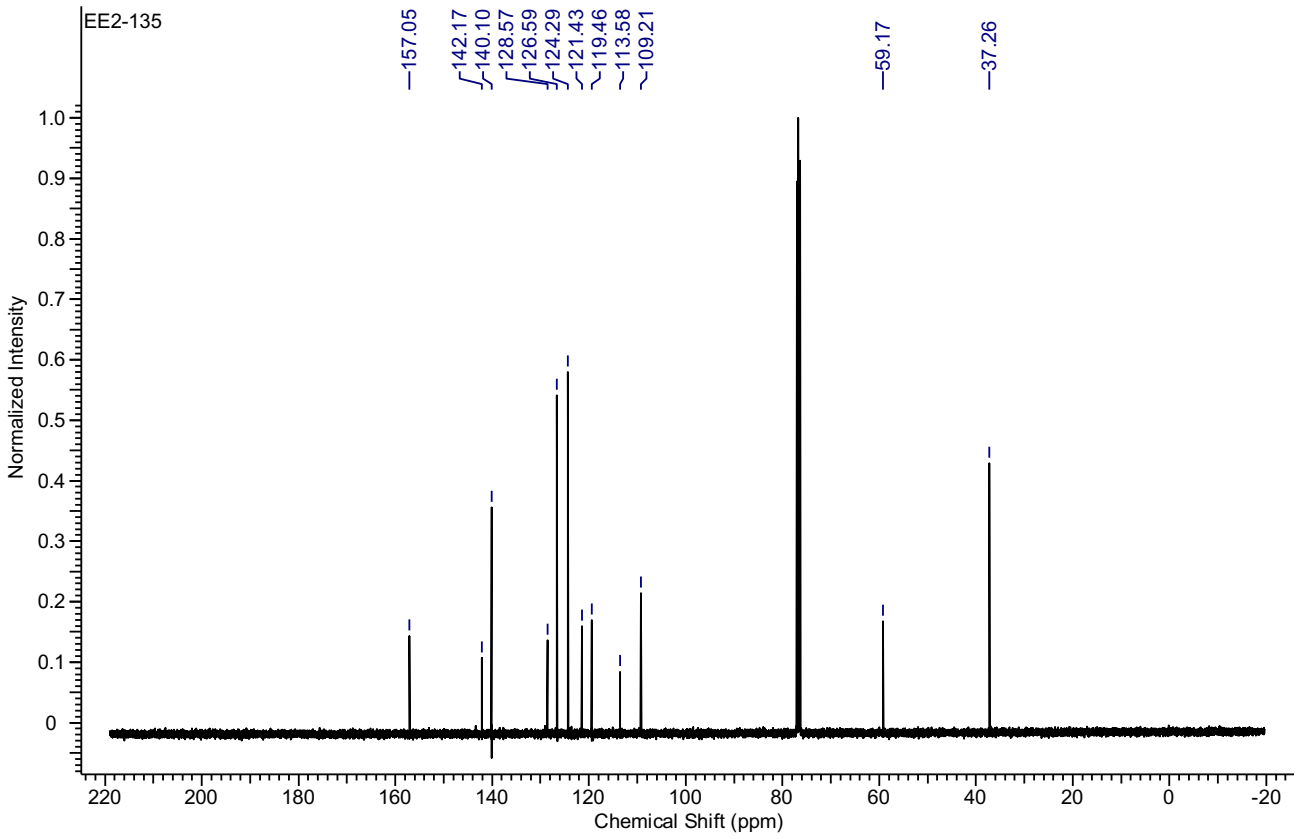

3k
8.39
8.37
7.94
7.92
7.76
7.74
7.62
7.59
7.58
7.57
7.42
7.40
3.89
O
NH
N
Me
k
Water
DMSO
1.00 1.01 1.01 2.02 1.02
3.00
Normalized Intensity
Chemical Shift (ppm)

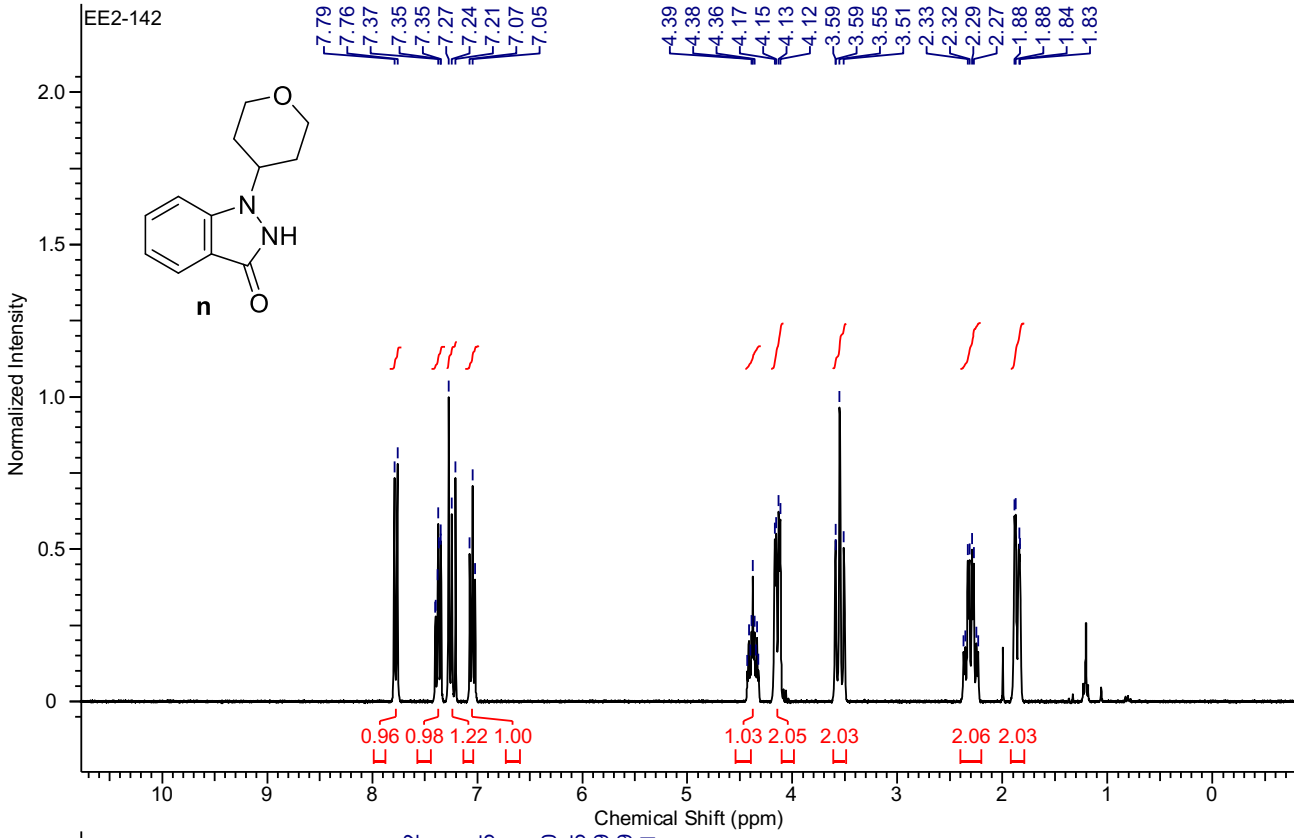

3k
155.40
138.94
128.14
127.91
127.52
126.96
123.04
122.20
110.76
103.68
34.71
Normalized Intensity
Chemical Shift (ppm)

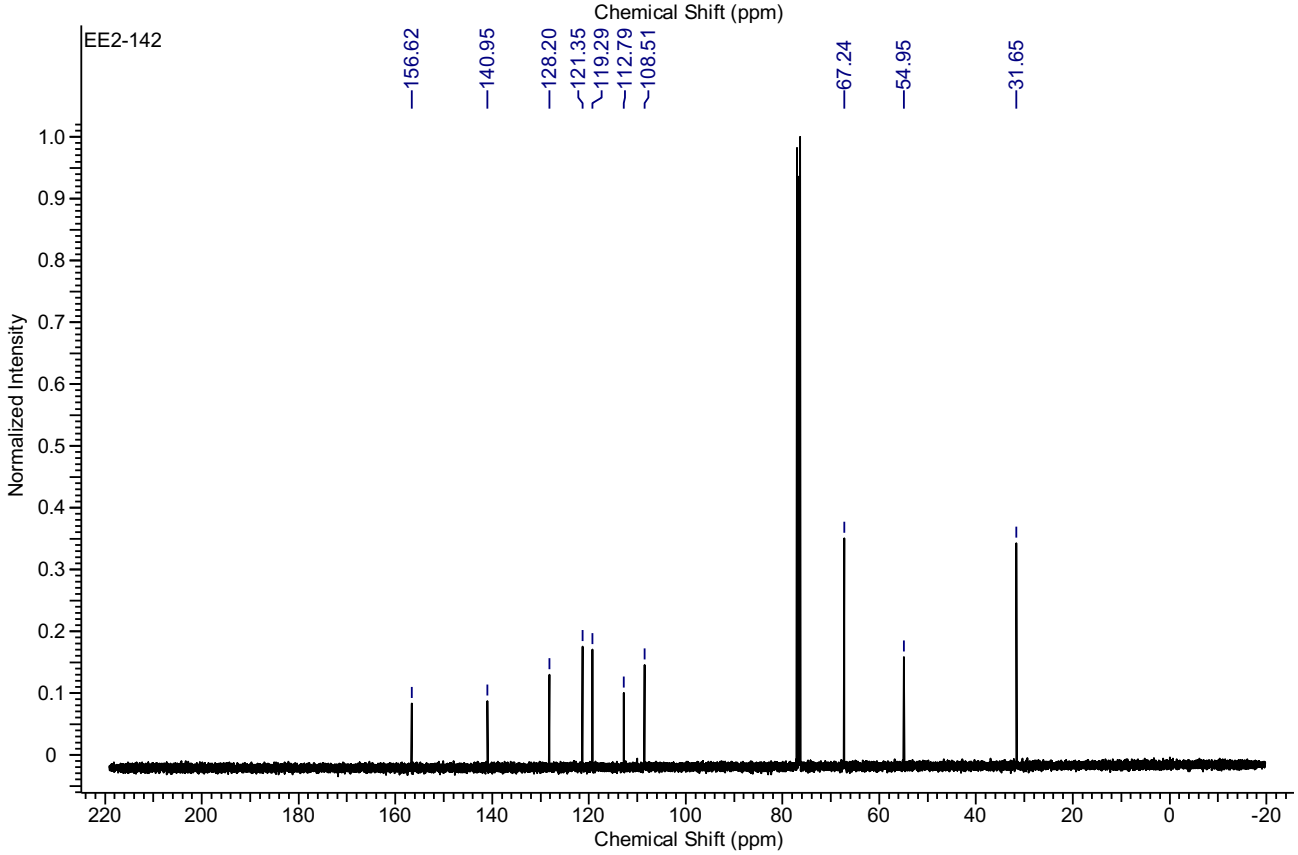

EE2-134
7.80
7.78
7.45
7.35
7.35
7.34
7.33
7.12
6.37
6.37
6.36
6.31
6.30
6.30
5.27
O
N
NH
O
I
Normalized Intensity
1.02 1.02 2.03 1.03 1.00 1.00 2.04
Chemical Shift (ppm)

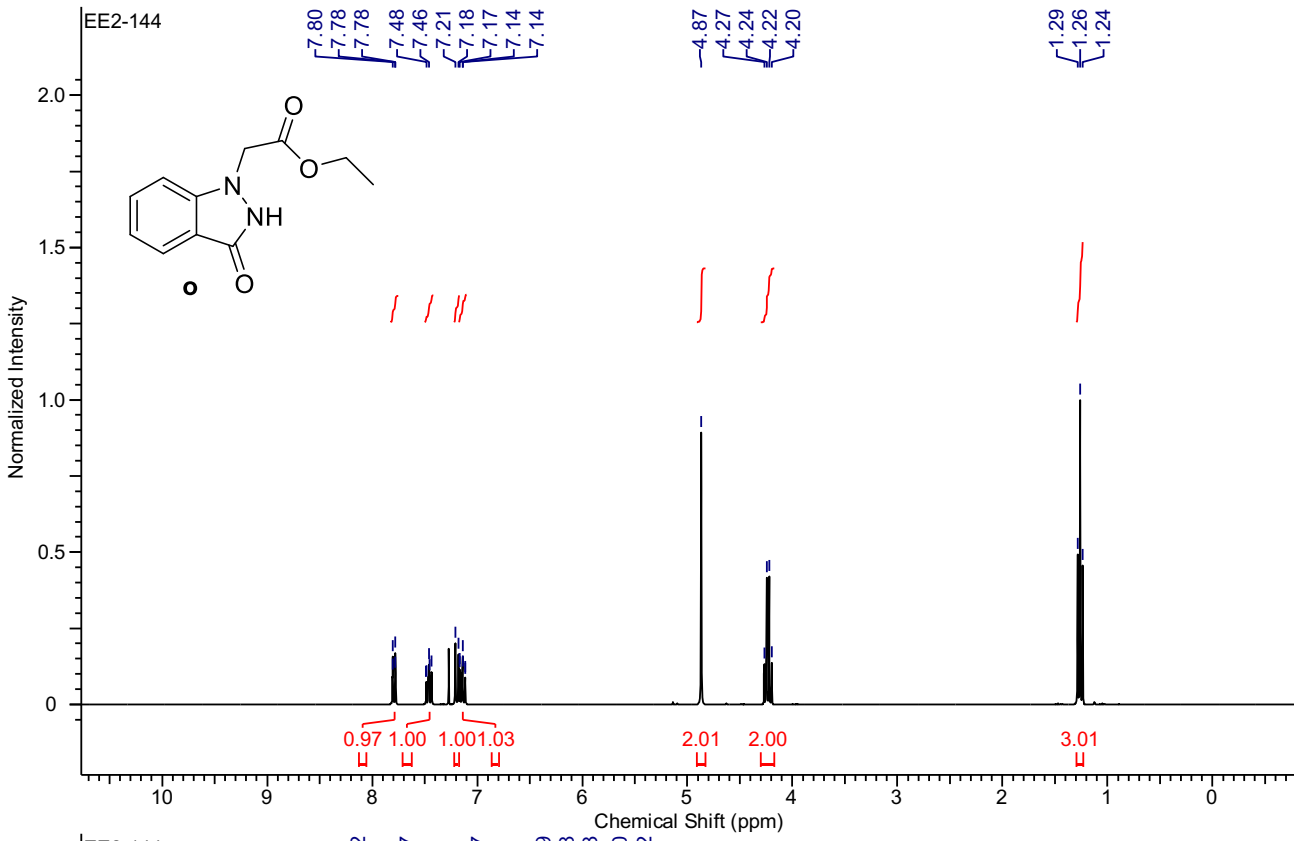

EE2-134
157.56
149.96
142.94
142.58
129.18
121.67
120.17
113.96
110.84
109.61
109.10
45.75
Normalized Intensity
Chemical Shift (ppm)

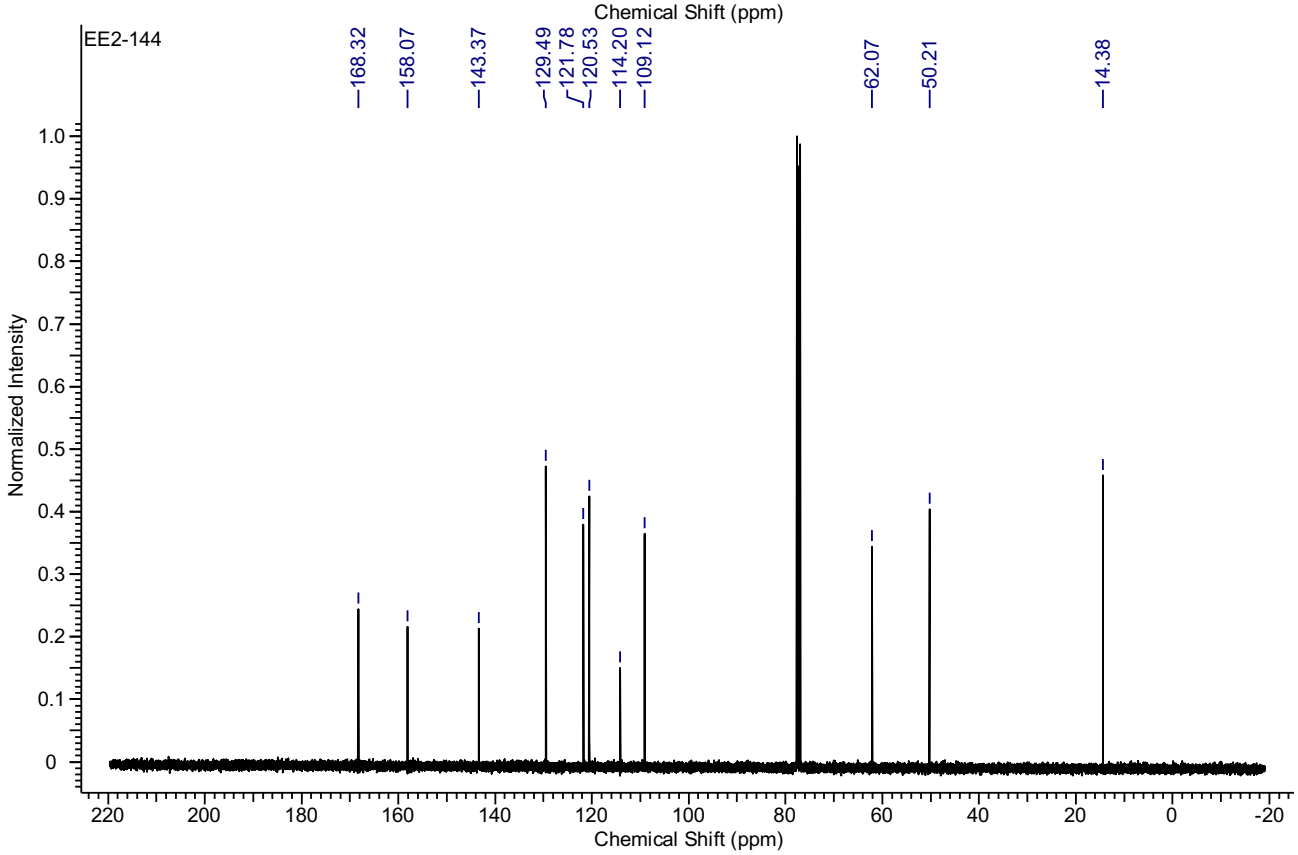

EE2-135
7.76
7.76
7.74
7.40
7.30
7.27
7.25
7.24
7.23
7.22
7.08
5.32
5.30
5.28
5.26
5.24
3.51
3.49
3.47
3.45
3.41
3.39
3.37
3.35
N
NH
O
m
Normalized Intensity
Chemical Shift (ppm)
1.00 1.09 2.22 3.04 1.02
1.02
2.01 2.00


EE2-135
157.05
142.17
140.10
128.57
126.59
124.29
121.43
119.46
113.58
109.21
59.17
37.26
Normalized Intensity
Chemical Shift (ppm)


EE2-142
7.79
7.76
7.37
7.35
7.35
7.27
7.24
7.21
7.07
7.05
4.39
4.38
4.36
4.17
4.15
4.13
4.12
3.59
3.59
3.55
3.51
2.33
2.32
2.29
2.27
1.88
1.88
1.84
1.83
O
N
NH
O
n
Normalized Intensity
0.96 0.98 1.22 1.00
1.03 2.05 2.03
2.06 2.03
Chemical Shift (ppm)


EE2-142
156.62
140.95
128.20
121.35
119.29
112.79
108.51
67.24
54.95
31.65
Normalized Intensity
Chemical Shift (ppm)


EE2-144
7.80
7.78
7.78
7.48
7.46
7.21
7.18
7.17
7.14
7.14
4.87
4.27
4.24
4.22
4.20
1.29
1.26
1.24
O
O
N
NH
O
Normalized Intensity
0.97
1.00
1.00
1.03
2.01
2.00
3.01
Chemical Shift (ppm)


EE2-144
168.32
158.07
143.37
129.49
121.78
120.53
114.20
109.12
62.07
50.21
14.38
Normalized Intensity
Chemical Shift (ppm)