Electronic Supplementary Information (ESI)

An efficient Sn(II)-catalyzed one-pot synthesis of 3-substituted azetidine-2,4-dione framework†

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1. General Remarks:

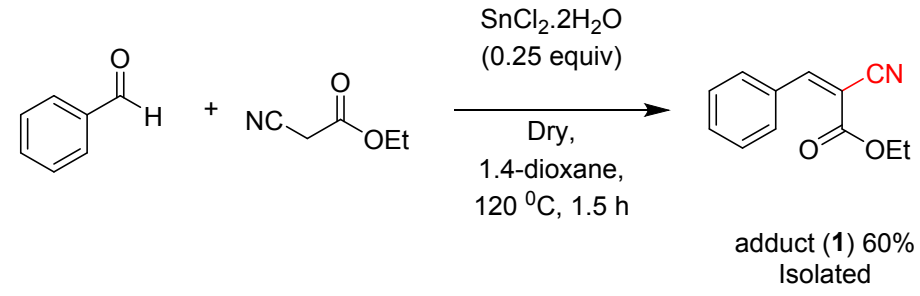
Unless otherwise specified, all reactions were carried out under an open atmosphere in solvent free condition and Reaction temperatures are reported as the temperature of the bath surrounding the reaction vessel. All reagents and solvents were obtained from commercial suppliers and Aldrich, Merck Millipore, Alfa Aesar and Avra Synthesis. Aldehydes were purified either by distillation or washing with $NaHCO_3$ after dissolving in ether, prior to use and all AR grade solvents were used without further purification.

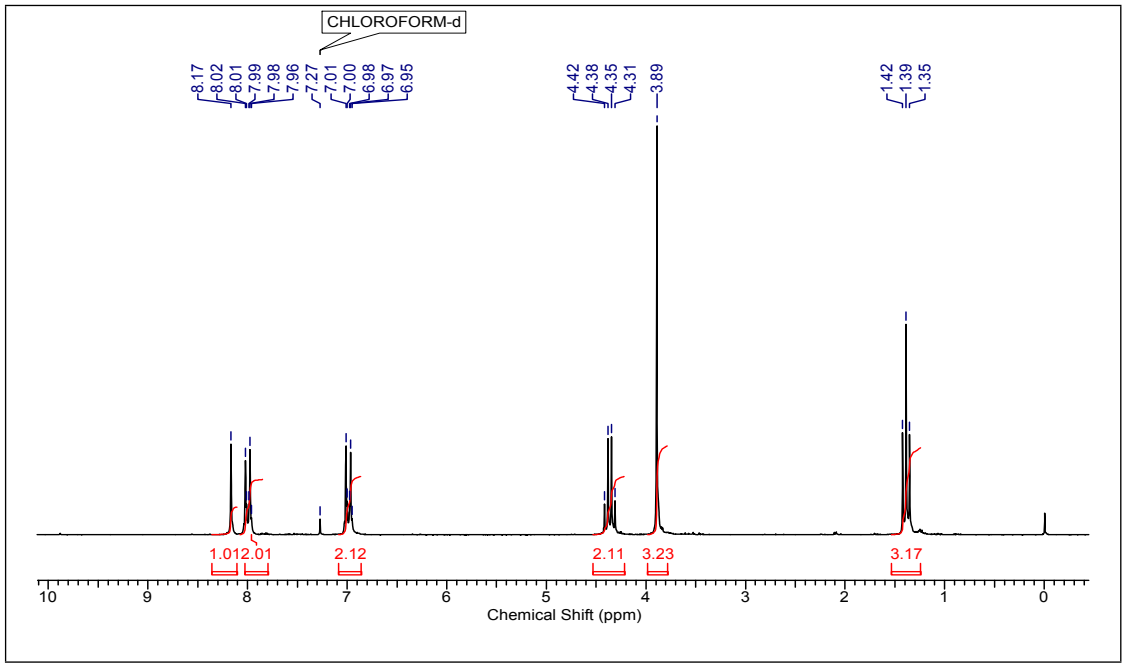
Analytical thin layer chromatography was performed on Polygram SIL G/UV254 plates. Visualization was accomplished with short UV light or KMnO4 staining solutions followed by heating. Flash chromatography was performed on Merck silica gel (100-200 mesh) by standard techniques eluting with solvents as indicated.

All compounds were fully characterized. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV 200, 400, 500 MHz INOVA instruments in solvents as indicated. Chemical shifts (δ) are given in ppm relative to TMS. Abbreviations for signal couplings are: s, singlet; d, doublet; t, triplet; m, multiplet; brs, brosilet. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δH = 7.26 ppm, δC =77.16 ppm and DMSO-D_6: δH = 2.5 ppm, δC =39.5 ppm). HRMS data were recorded on a Thermo Scientific Q-Exactive, Accela 1250 pump.

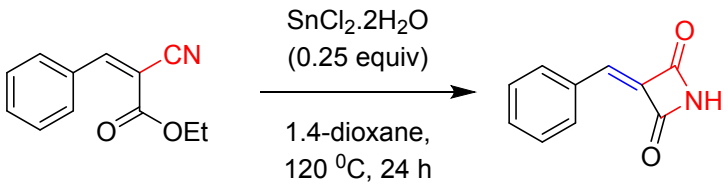
2. Control Experiments

2.1 General Procedure for the Synthesis of Azetidine 3a from Adduct



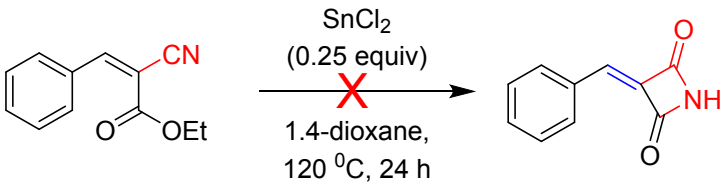


Adduct (**I**) was isolated after 1.5 h. in 60% yield. ^{1}H NMR (200 MHz, $CDCl_3$) d ppm 8.17 (s, 1 H) 7.85 - 8.08 (m, 2 H) 6.86 - 7.08 (m, 2 H) 4.36 (q, *J*=7.2 Hz, 2 H) 3.89 (s, 3 H) 1.39 (t, *J*=7.1 Hz, 3 H)



adduct **(I)** **3a,** 93%

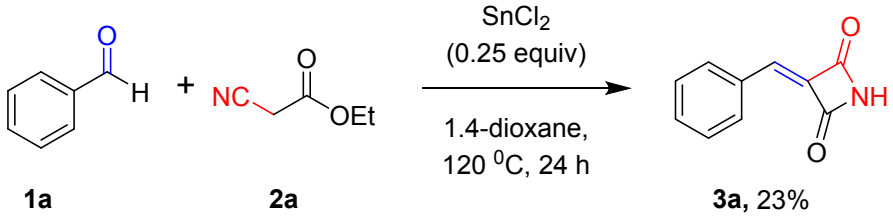
In a 10 mL round bottom flask equipped with a magnetic stir bar was added the adduct **(I)** (1 mmol), $SnCl_2.2H_2O$ (25 mol %) and 1,4-dioxane (4 mL) were taken. Then the resultant reaction mixture was kept in stirring at 120 ^{0}C for 24. Upon completion of the reaction, reaction mixture was dried under vacuum. Then the crude reaction mixture was diluted with ethyl acetate (10 mL) and filtered through a pad of silica gel and eluted with EtOAc (20 mL). The solvent was evaporated and the crude residue was preadsorbed on silica gel and purified by column chromatography to afford the corresponding azetidines **3a** in 93% yields.



adduct **(I)** **3a,** trace

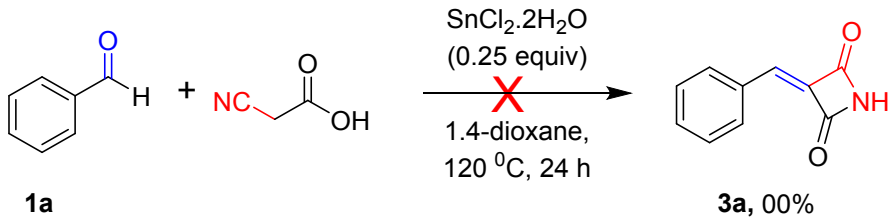
The above same reaction condition was applied while using $SnCl_2$ as catalyst then the reaction was failed to generate the corresponding azetidine derivative **3a** in high yield.

2.2 General Procedure for the Synthesis of Azetidine 3a from Adduct



1a **2a** **3a,** 23%

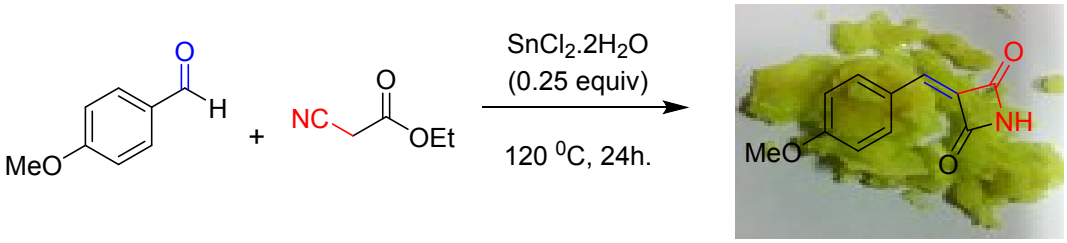
In a 10 mL round bottom flask equipped with a magnetic stir bar was added the benzaldehyde **1a** (1 mmol), ethyl cyanoacetate **2a** (1.5 mmol), $SnCl_2$ (25 mol %) and 1,4-dioxane (4 mL) were taken. Then the resultant reaction mixture was kept in stirring at 120 ^{0}C for 24. Upon completion of the reaction, reaction mixture was dried under vacuum. Then the crude reaction mixture was diluted with ethyl acetate (10 mL) and filtered through a pad of silica gel and eluted with EtOAc (20 mL). The solvent was evaporated and the crude residue was preadsorbed on silica gel and purified by column chromatography to afford the corresponding azetidines **3a** in 23% yields.



1a **3a,** 00%

In a 10 mL round bottom flask equipped with a magnetic stir bar was added the benzaldehyde **1a** (1 mmol), 2-cyanoacetic acid (1.5 mmol), $SnCl_2.2H_2O$ (25 mol %) and 1,4-dioxane (4 mL) were taken. Then the resultant reaction mixture was kept in stirring at 120 ^{0}C for 24. The progress of the reaction was monitored by TLC, but reaction was failed to generate the desired compound **3a**.

3. General Procedure for the Gram Scale Synthesis of Azetidine 3g



8 g,
58.3 mmol

9.89 g,
87.5 mmol

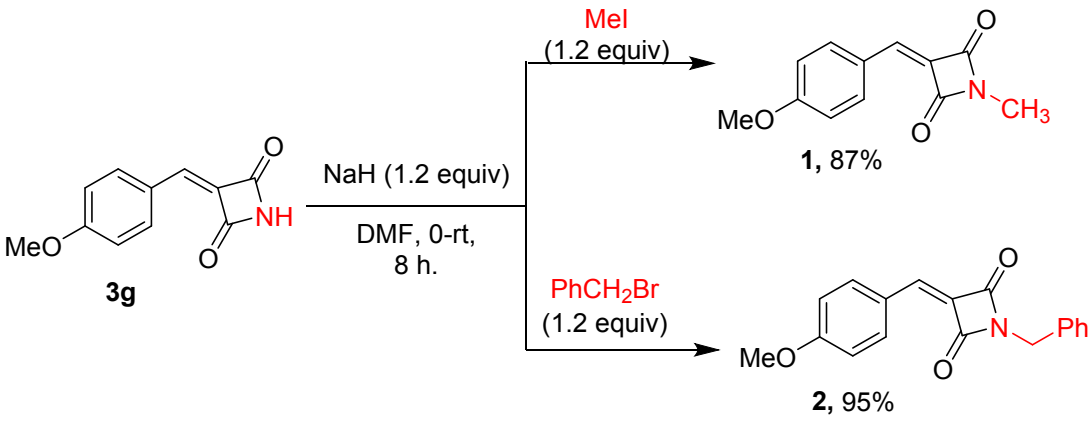
10.533 g,
51.8 mmol (89 %)

In a 100 mL bottom flask charged with the magnetic stirrer and 4-anisaldehyude (**8 g**, 58.3 mmol), Ethyl cyanoacetate (**9.89 g**, 87.5 mmol), catalyst $SnCl_2.2H_2O$ (**3.30 g**, 0.0147 mmol) and 1,4-dioxane (80 mL) were taken. The round bottom flask was equipped with condenser and the resultant reaction mixture was refluxed at 120 ^{0}C for 24 h. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the reaction mixture was dried under vacuum. Then the crude reaction mixture was diluted with ethyl acetate (50 mL) and filtered through a pad of silica gel and eluted with EtOAc (100 mL). The solvent was evaporated and the crude residue was preadsorbed on silica gel and purified by column chromatography with eluted solvent (pet.ether + ethylaceate 6:4) to afford the corresponding azetidine derivate **3g** in (10.53 g, 89%) yields.

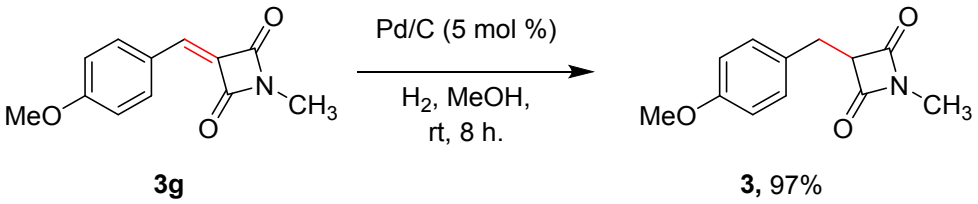
4. Transformation of 3-benzylideneazetidine-2,4-dione

4.1 General Procedure for the Synthesis of *N*-protected Azetidine Derivative 1 and 2

N-alkylated azetidine derivatives were prepared from commercially available methyl iodide, benzyl bromide with **3g** in the presence of NaH in DMF at room temperature for 8 h. MeI or $PhCH_2Br$ (1.2 equiv) was added to a stirred solution of 3-benzylideneazetidine-2,4-dione **3g** (1 equiv) and NaH (1.2 equiv) in DMF and stirred for 8 h at room temperature. The reaction mixture was quenched with water and extracted with dichloromethane (3 x 20 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuum*. The crude residue was then purified by column chromatography on silica gel with ethyl acetate-pet.ether (10/90 to 20/80) to provide compounds **1** and **2**.

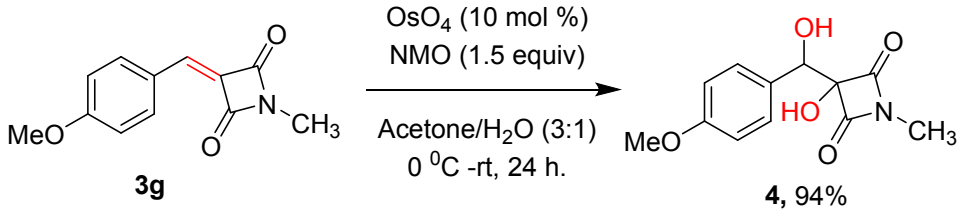


4.2 General Procedure for the Hydrogenation



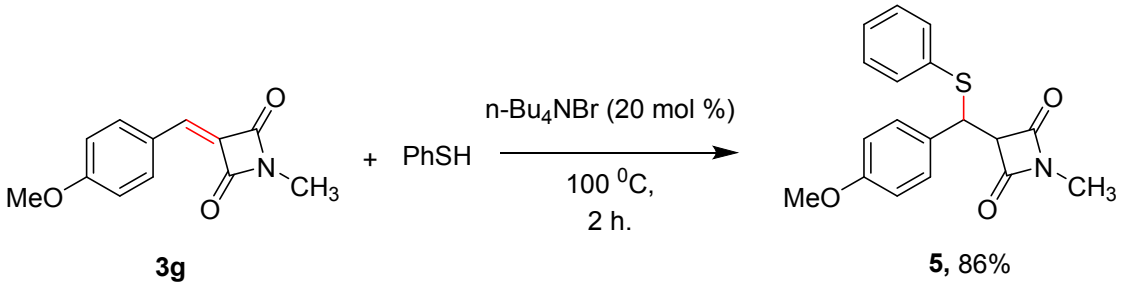
A oven dried 10 ml round bottom flask charged with a magnetic stir bar and vacuum/H_2 cycles flushed twice, then the added 3-(4-methoxybenzylidene)-1-methylazetidine-2,4-dione **1** (0.108 g, 1 mmol), 10% Pd/C (10% of the weight of comp.) in an absolute solvent (4 mL) was hydrogenated at ambient pressure (balloon) and temperature (*ca.* 25 °C) for 24 h. The reaction mixture was filtered through a pad of silica gel and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash silica gel column chromatography (pet.ether/ethyl acetate, 9:1) to give compound **3** as a pale yellow solid (97%).

4.3 General Procedure for the Dihydroxylation



To a stirred solution of compound 3-(4-methoxybenzylidene)-1-methylazetidine-2,4-dione (0.217 g, 1 mmol) in acetone/ H_2O (3:1, 4 mL) was added NMO monohydrate (0.202 g, 1.5 mmol) followed by OsO4 (0.025 g, 0.10 mmol) at 0 ^{0}C and stirred at room temperature for 24 h. After the addition of Na_2SO_3 (0.158 g, 1.1 mmol), acetone was removed under reduced pressure and the reaction mixture was diluted with water and extracted with dichloromethane (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, purified by column chromatography (pet. ether/ethyl acetate, 7:3) to give compound **4** as a yellow solid (94%).

4.4 General Procedure for the Thiophenol Addition

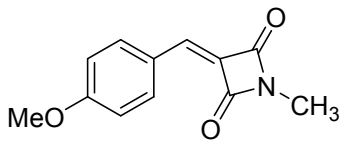


3g **5,** 86%

A mixture of azetidine (1 mmol) and thiophenol (1.2 mmol) was added to molten tetrabutylammonium bromide (20 mol %) and the whole mixture was stirred at 100 ^{o}C (oil bath) for 2. TLC was monitored and after completion of reaction. The reaction mixture was then allowed to cool to room temperature and extracted with ethyl acetate (20 mL). The ethyl acetate extract was washed with water and dried over Na_2SO_4. Evaporation of solvent followed by column chromatography of the crude product over silica gel (Pet. Ether/ethyl acetate 80:20) furnished the pure (**5)** 3-((4-methoxyphenyl)(phenylthio)methyl)-1-methylazetidine-2,4-dioneas a off white solid (86%).

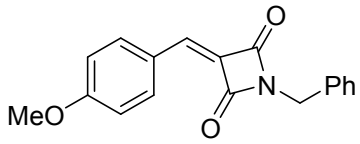
5. Spectral Data of Azetidine

3-(4-methoxybenzylidene)-1-methylazetidine-2,4-dione (1)



R*f*: 0.25 (Pet. ether /EtOAc = 90/10); Yield: 93 mg, 87%; Yellow solid; mp: 134-136 °C; **^{1}H NMR (200 MHz, CDCl$_3$)** δ ppm 8.19 (s, 1 H) 7.96 - 8.06 (m, 2 H) 6.96 - 7.05 (m, 2 H) 3.92 (s, 3 H) 3.90 (s, 3 H); **^{13}C NMR (50 MHz, CDCl$_3$)** δ ppm 163.8, 163.6, 154.6, 133.7, 124.3, 116.2, 114.8, 98.8, 55.6, 53.1; **HRMS** (ESI) calculated $[M+H]^+$ for $C_{12}H_{12}NO_3$: 218.0815, found: 218.0812.

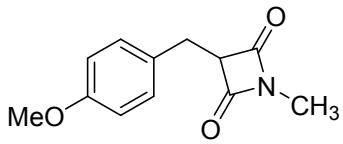
1-benzyl-3-(4-methoxybenzylidene)azetidine-2,4-dione (2)



R*f*: 0.30 (Pet. ether /EtOAc = 85/15); Yield: 137 mg, 95%; Off white solid; mp: 171-173 °C; **^{1}H NMR (200 MHz, CDCl$_3$)** δ ppm 8.20 (s, 1 H) 7.96 - 8.06 (m, 2 H) 7.35 - 7.49 (m, 5 H) 6.97 - 7.04 (m, 2 H) 5.35 (s, 2 H) 3.90 (s, 3 H); **^{13}C NMR (50 MHz, CDCl$_3$)** δ ppm 163.9, 163.0, 154.8, 135.1, 133.7, 128.6, 128.5, 128.2, 124.3, 116.0, 114.8, 113.6, 110.3, 105.9, 99.0, 67.8, 55.6; **HRMS** (ESI) calculated $[M+Na]^+$ for $C_{18}H_{15}NO_3Na$: 316.0947, found: 316.0950.

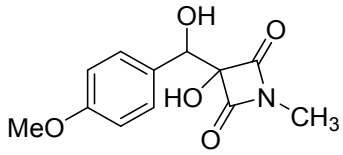
3-(4-methoxybenzyl)-1-methylazetidine-2,4-dione(3)

R*f*: 0.27 (Pet. ether /EtOAc = 95/05); Yield: 97 mg, 97%; white solid; mp: 133-134 °C; **^{1}H NMR (200 MHz, CDCl$_3$)** δ ppm 7.50 - 7.56 (d, 2 H) 7.12 - 7.24 (m, 2 H) 4.46 - 4.61 (m, 1 H)



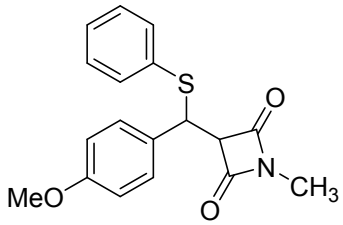
4.18 (s, 3 H) 4.10 (s, 3H) 3.41 - 3.59 (m, 2 H); **^{13}C NMR (50 MHz, $CDCl_3$)** δ ppm164.3, 159.2, 132.5, 130.1, 129.2, 126.9, 114.3, 114.0, 113.8, 55.5, 55.3, 34.9; **HRMS** (ESI) calculated $[M+H]^+$ for $C_{12}H_{14}NO_3$: 220.0966, found: 220.0974.

3-hydroxy-3-(hydroxy(4-methoxyphenyl)methyl)-1-methylazetidine-2,4-dione (4)



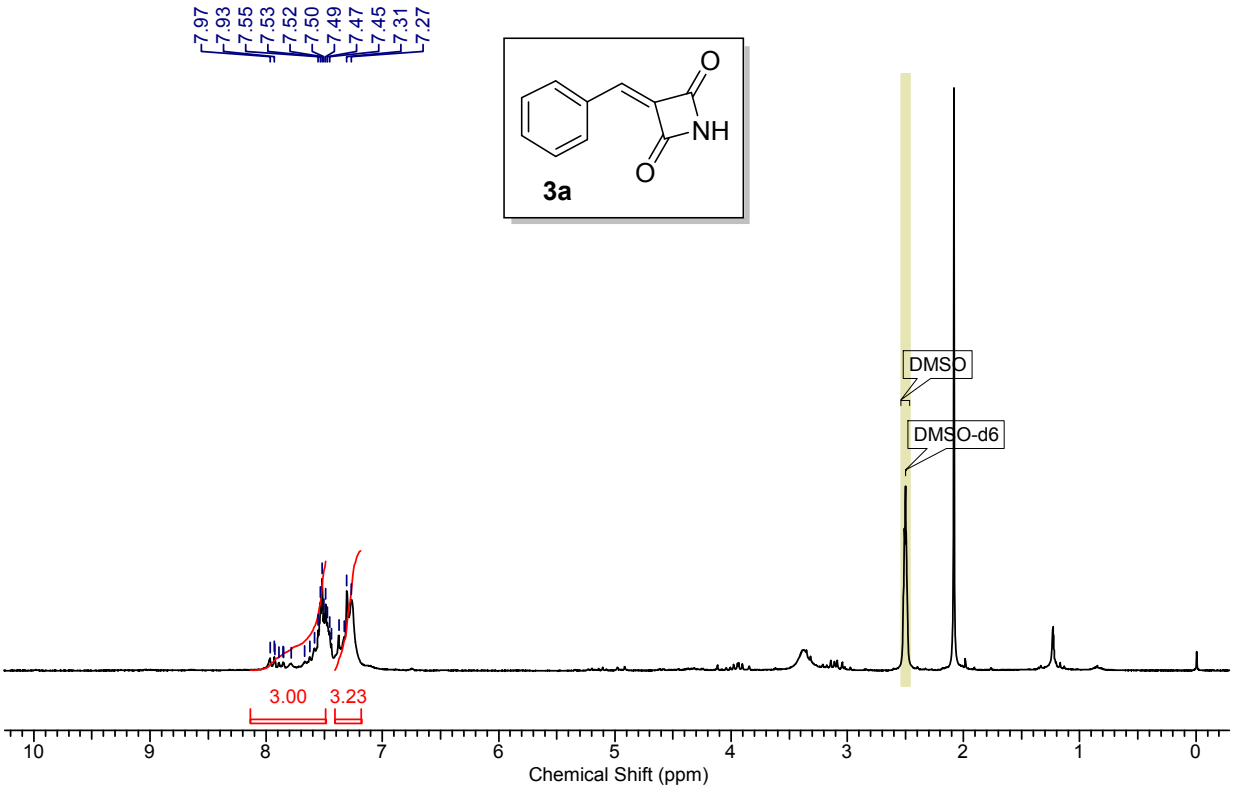
R*f*: 0.37 (Pet. ether /EtOAc = 80/20); Yield: 108 mg, 94%; white solid; mp: 159-160 °C; **^{1}H NMR (200 MHz, $CDCl_3$)** δ ppm 7.46 - 7.55 (m, 2 H) 7.38 - 7.44 (m, 1 H) 6.88 - 6.96 (m, 3 H) 4.88 (s, 1 H) 4.25 (s, 3 H) 3.84 (s, 3H); **^{13}C NMR (50 MHz, $CDCl_3$)** δ ppm 170.9, 162.0, 150.1, 131.0, 129.1, 128.2, 126.4, 126.3, 118.7, 118.0, 114.5, 114.0, 93.4, 69.0, 59.6, 55.5; **HRMS** (ESI) calculated $[M+H]^+$ for $C_{12}H_{14}NO_5$: 252.0874, found: 252.0872.

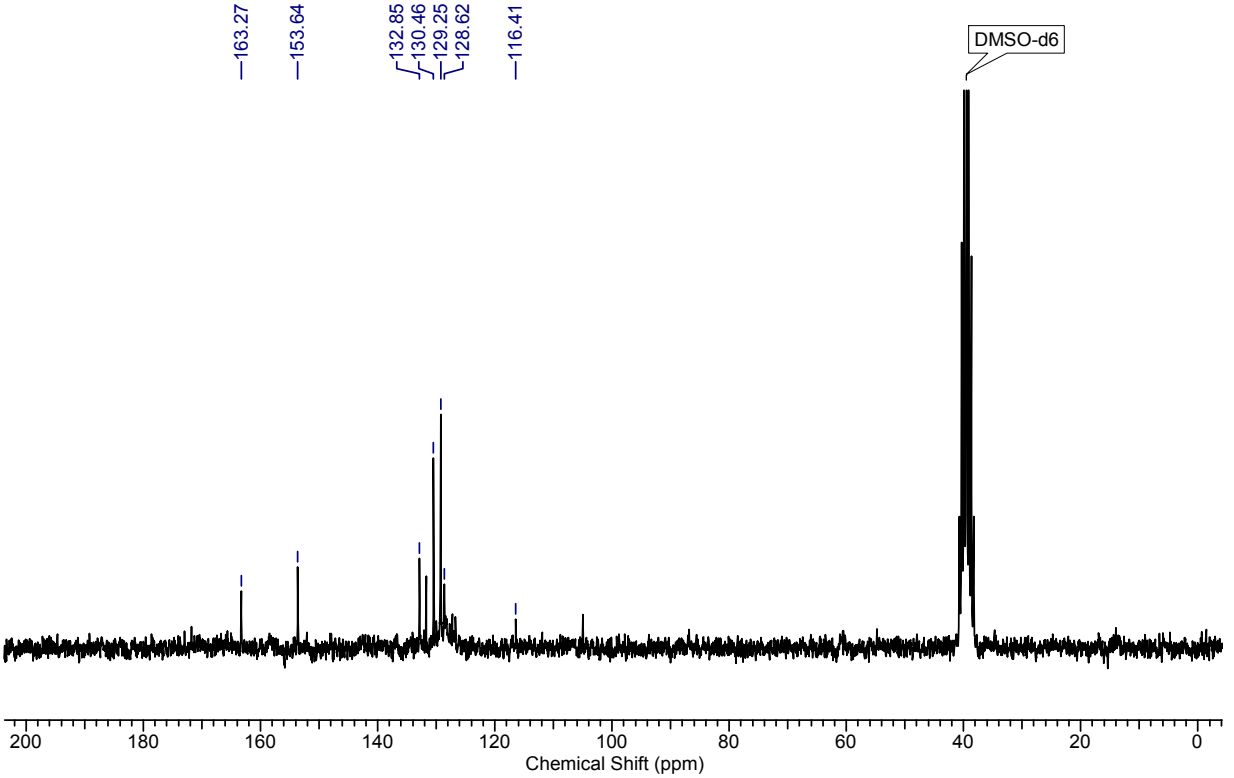
3-((4-methoxyphenyl)(phenylthio)methyl)-1-methylazetidine-2,4-dione (5)

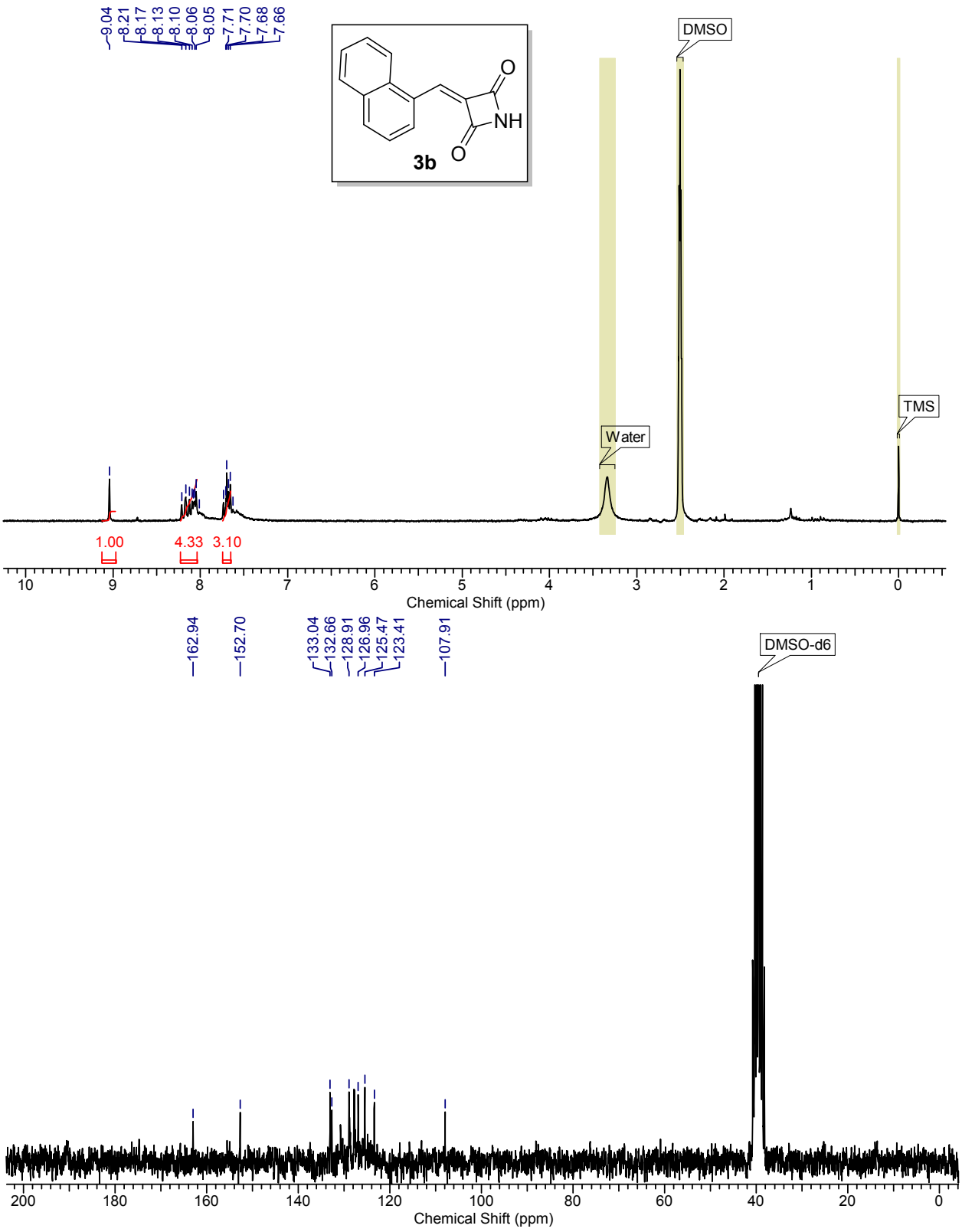


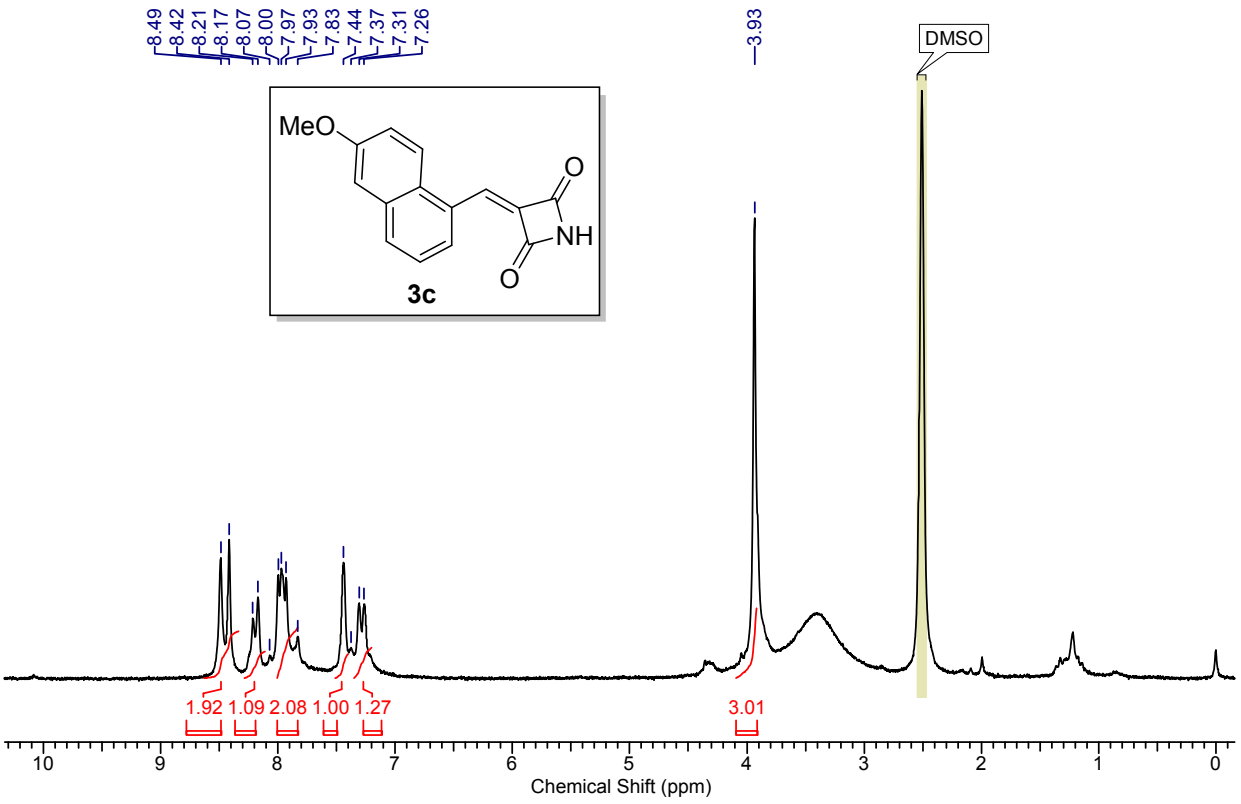
R*f*: 0.30 (Pet. ether /EtOAc = 80/20); Yield: 86%; white solid; mp: 140-141 °C; **^{1}H NMR (200 MHz, $CDCl_3$)** δ ppm 7.81 (d, *J*=9.0 Hz, 1 H) 7.37 - 7.43 (m, 4 H) 6.89 - 7.02 (m, 4 H) 5.73 (d, *J*=16.5 Hz, 1 H) 5.30 (d, *J*=12.1 Hz, 1 H) 3.75 - 3.97 (m, 6 H); **^{13}C NMR (50 MHz, $CDCl_3$)** δ ppm 159.6, 157.6, 144.5, 139.1, 133.7, 130.1, 129.3, 128.6, 118.1, 114.3, 65.0, 55.3, 48.7, 25.3; **HRMS** (ESI) calculated $[M+H]^+$ for $C_{18}H_{18}NO_3S$: 328.1002, found: 328.1010.

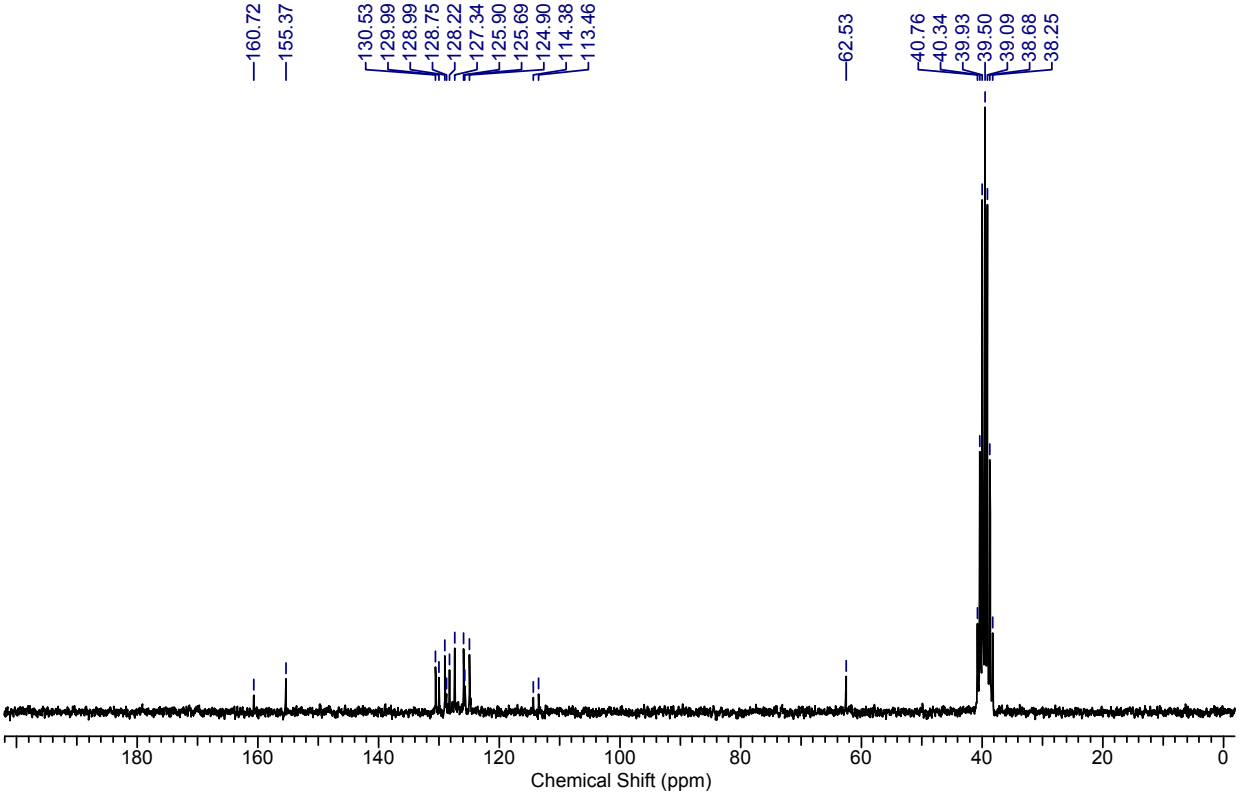
6) ^{1}H NMR and ^{13}C NMR Spectra of Azetidine:

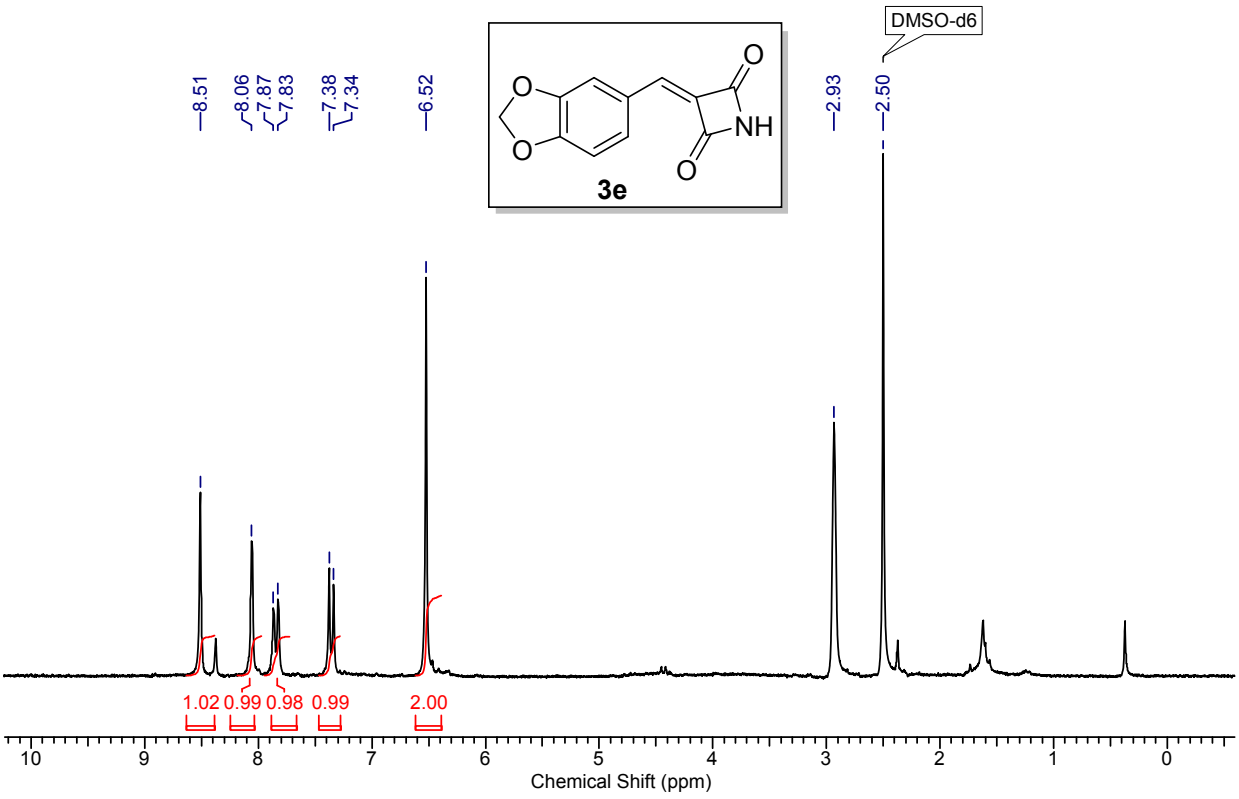


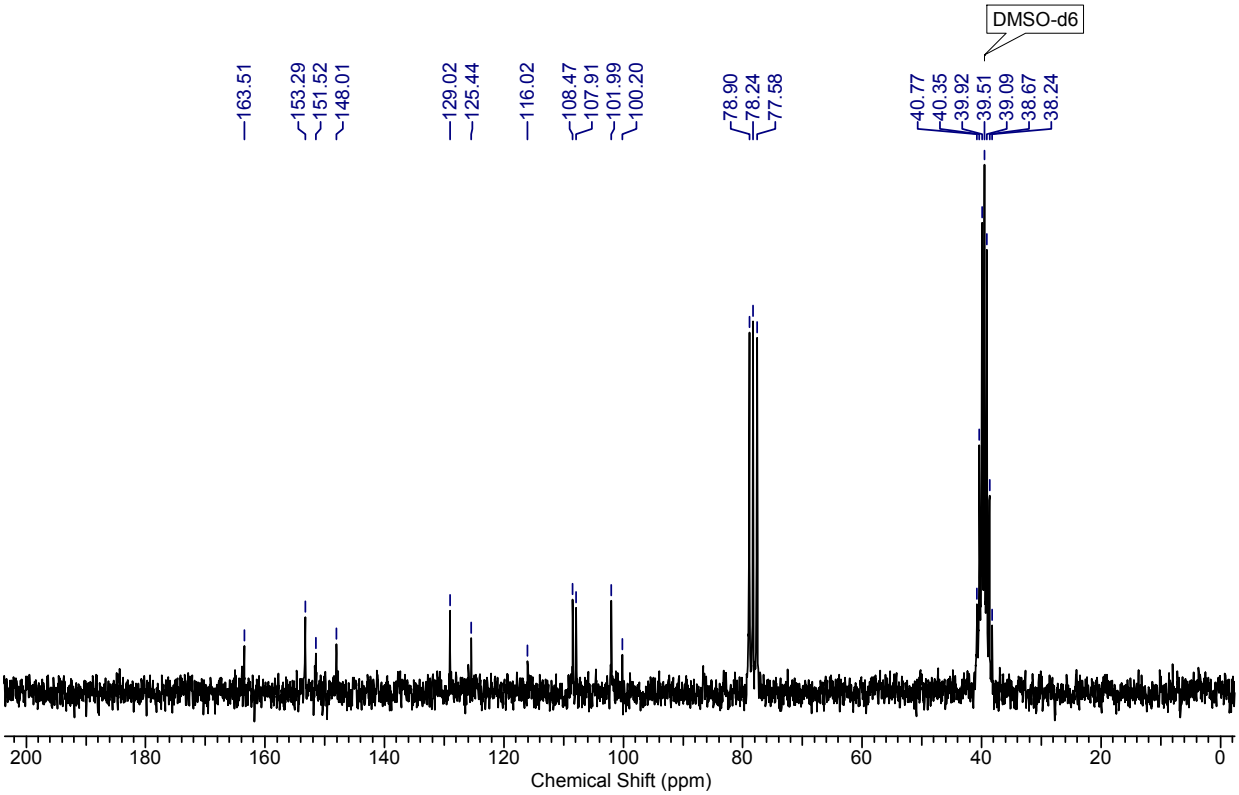


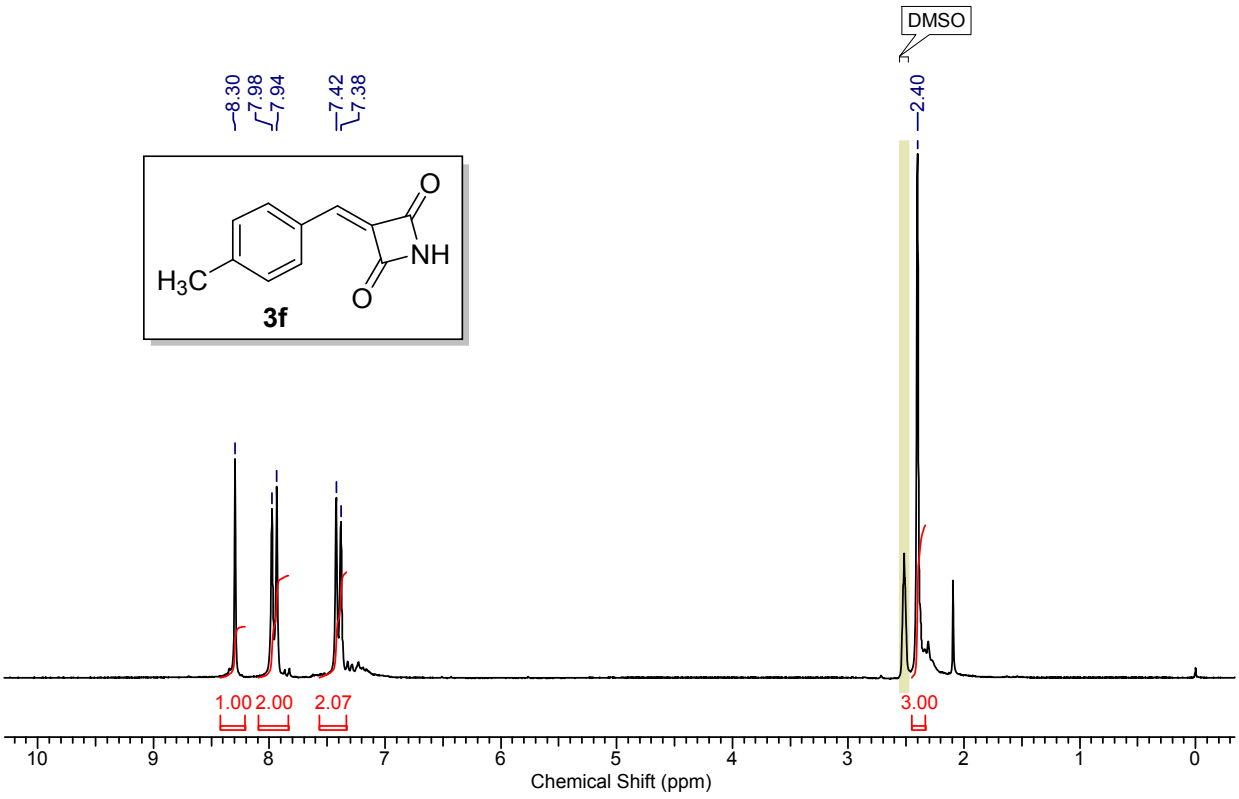

9.04
8.21
8.17
8.13
8.10
8.06
8.05
7.71
7.70
7.68
7.66
O
NH
O
3b
DMSO
Water
TMS
1.00
4.33
3.10
Chemical Shift (ppm)
162.94
152.70
133.04
132.66
128.91
126.96
125.47
123.41
107.91
DMSO-d6
Chemical Shift (ppm)

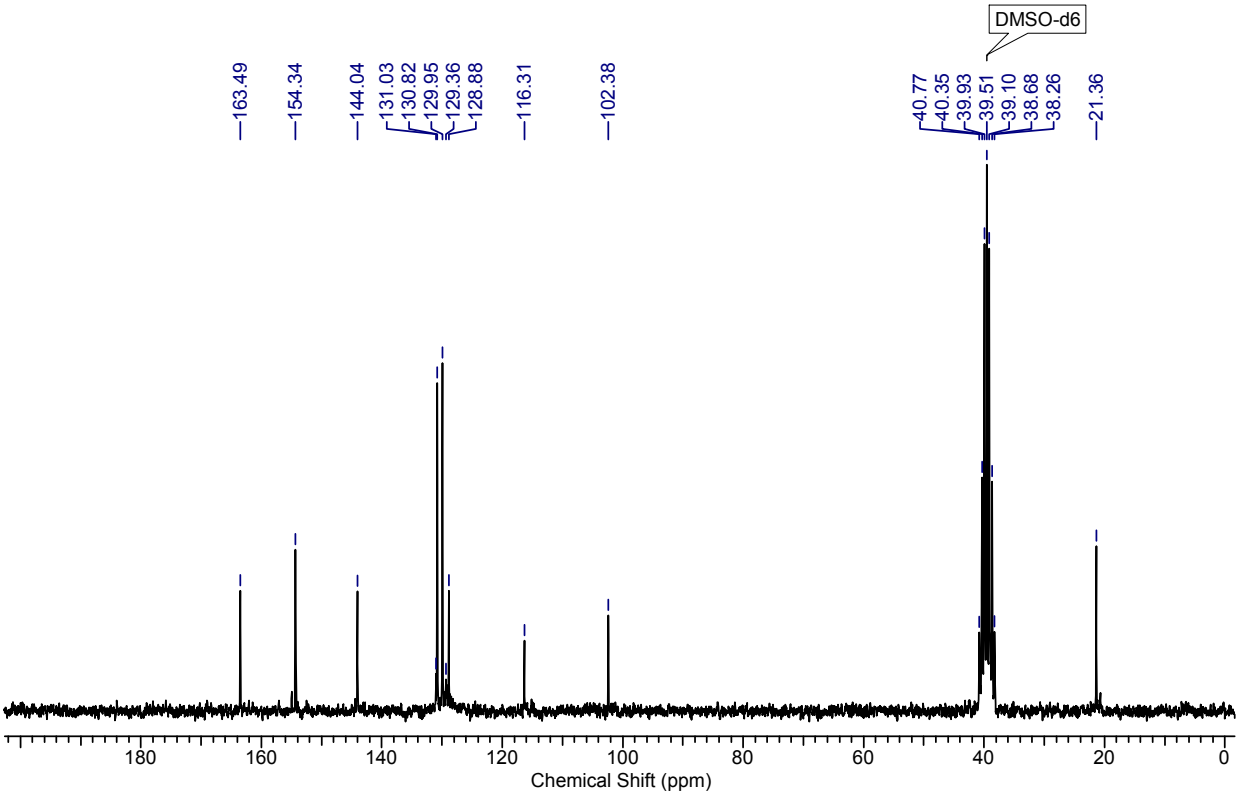

8.49
8.42
8.21
8.17
8.07
8.00
7.97
7.93
7.83
7.44
7.37
7.31
7.26
3.93
DMSO
MeO
O
NH
O
3c
1.92 1.09 2.08 1.00 1.27
3.01
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

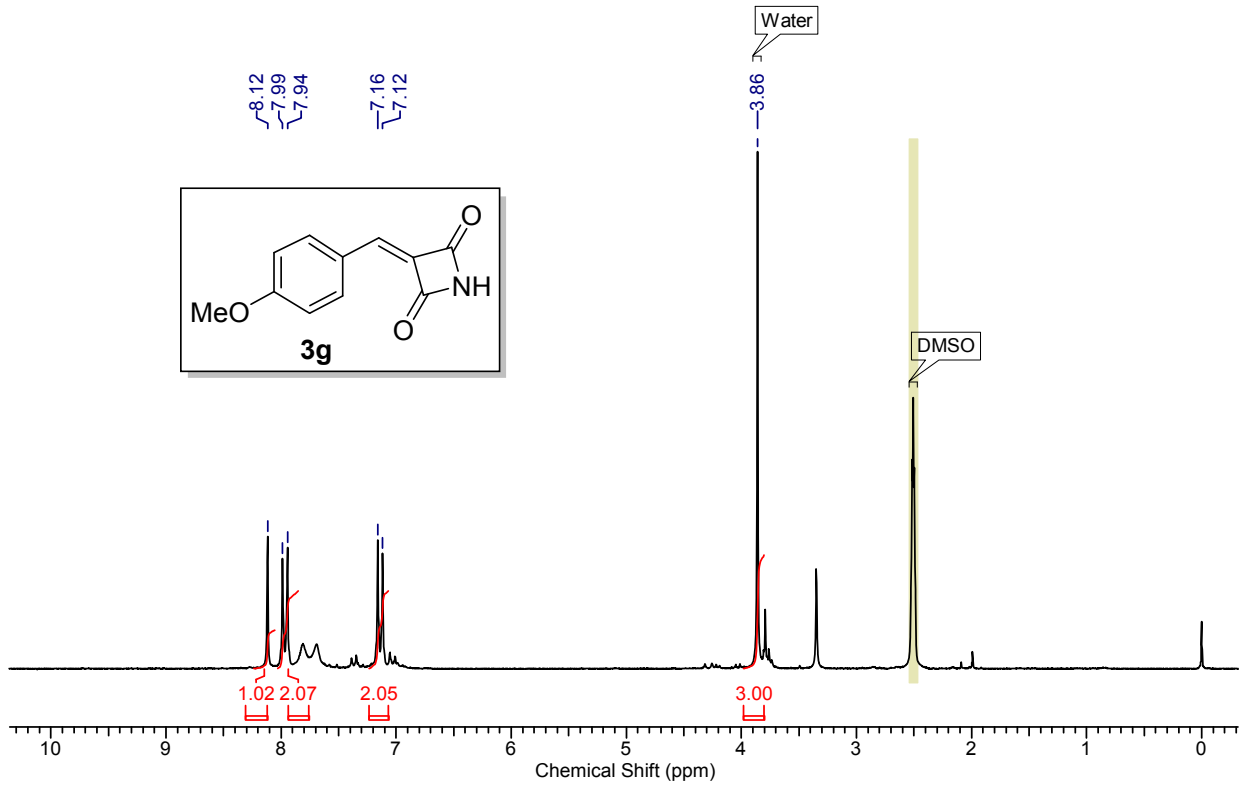

160.72
155.37
130.53
129.99
128.99
128.75
128.22
127.34
125.90
125.69
124.90
114.38
113.46
62.53
40.76
40.34
39.93
39.50
39.09
38.68
38.25
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

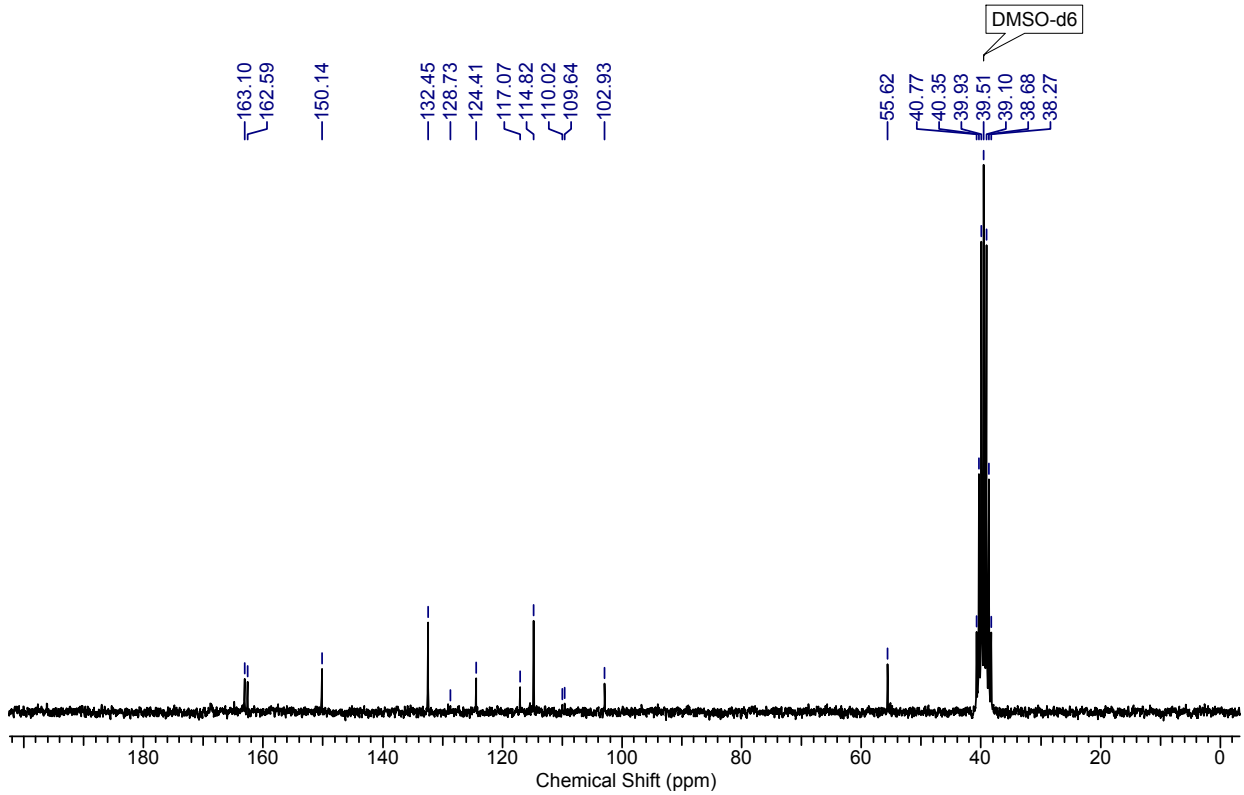

DMSO-d6
8.51
8.06
7.87
7.83
7.38
7.34
6.52
2.93
2.50
O
O
O
NH
O
3e
1.02 0.99 0.98 0.99 2.00
10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

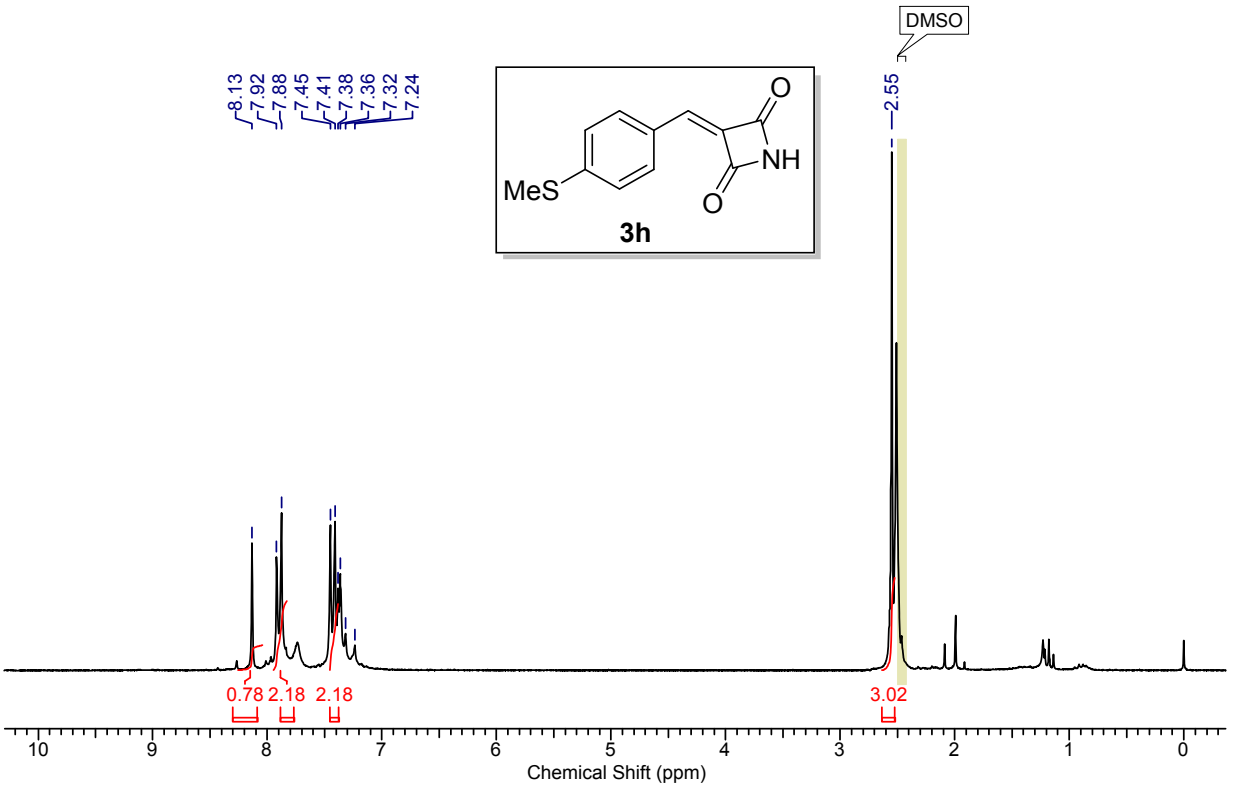

DMSO-d6
163.51
153.29
151.52
148.01
129.02
125.44
116.02
108.47
107.91
101.99
100.20
78.90
78.24
77.58
40.77
40.35
39.92
39.51
39.09
38.67
38.24
200 180 160 140 120 100 80 60 40 20 0
Chemical Shift (ppm)

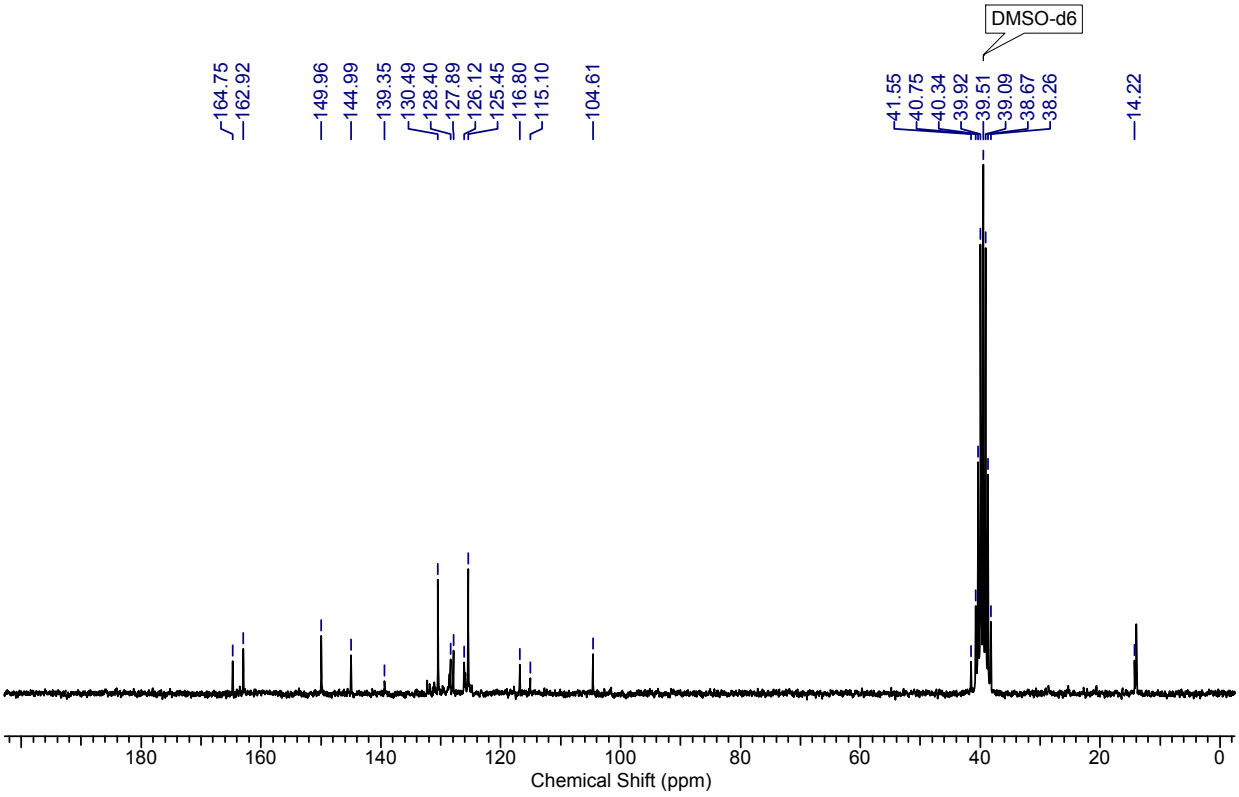

DMSO
8.30
7.98
7.94
7.42
7.38
2.40
O
NH
O
H_3C
3f
1.00
2.00
2.07
3.00
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

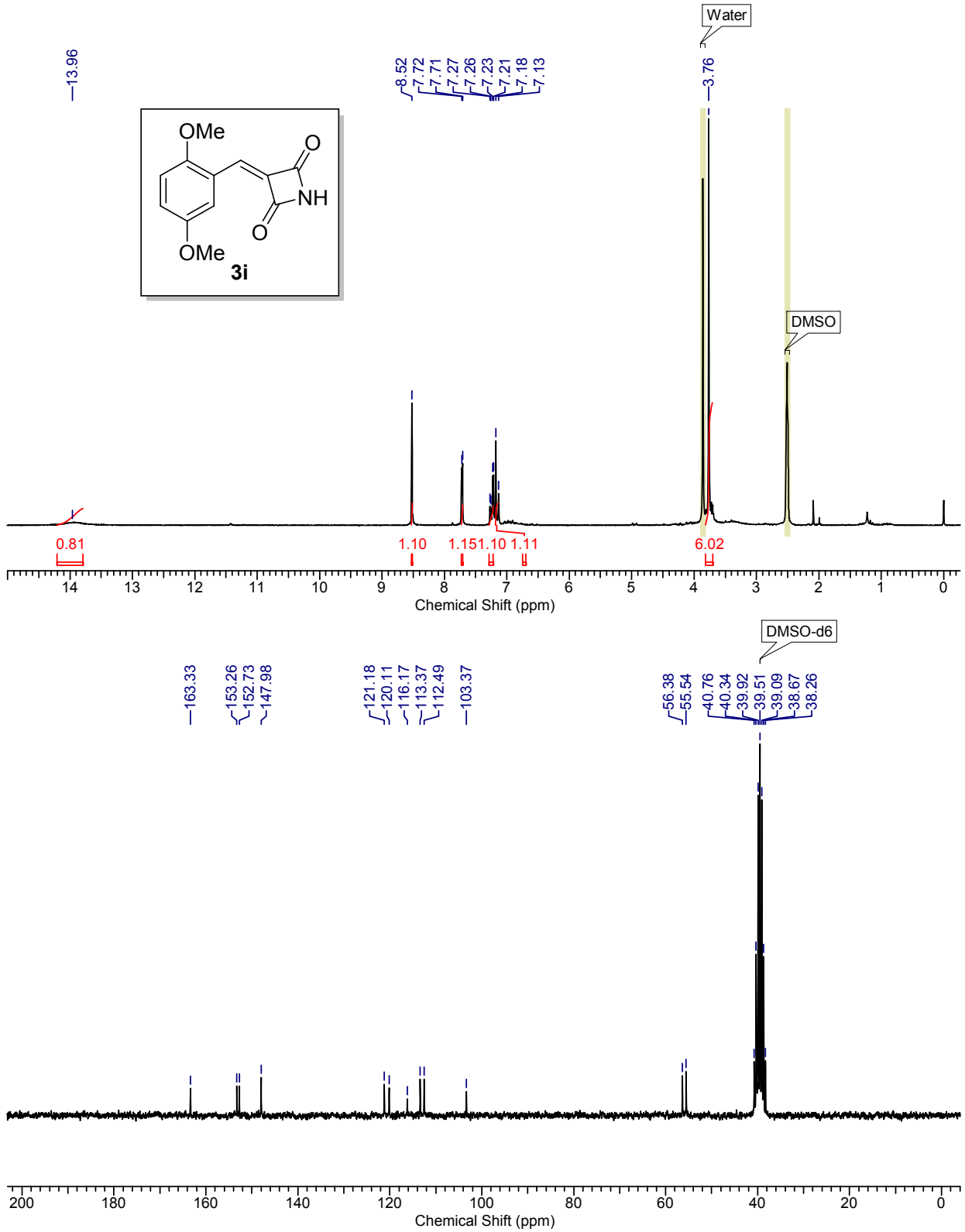

DMSO-d6
163.49
154.34
144.04
131.03
130.82
129.95
129.36
128.88
116.31
102.38
40.77
40.35
39.93
39.51
39.10
38.68
38.26
21.36
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

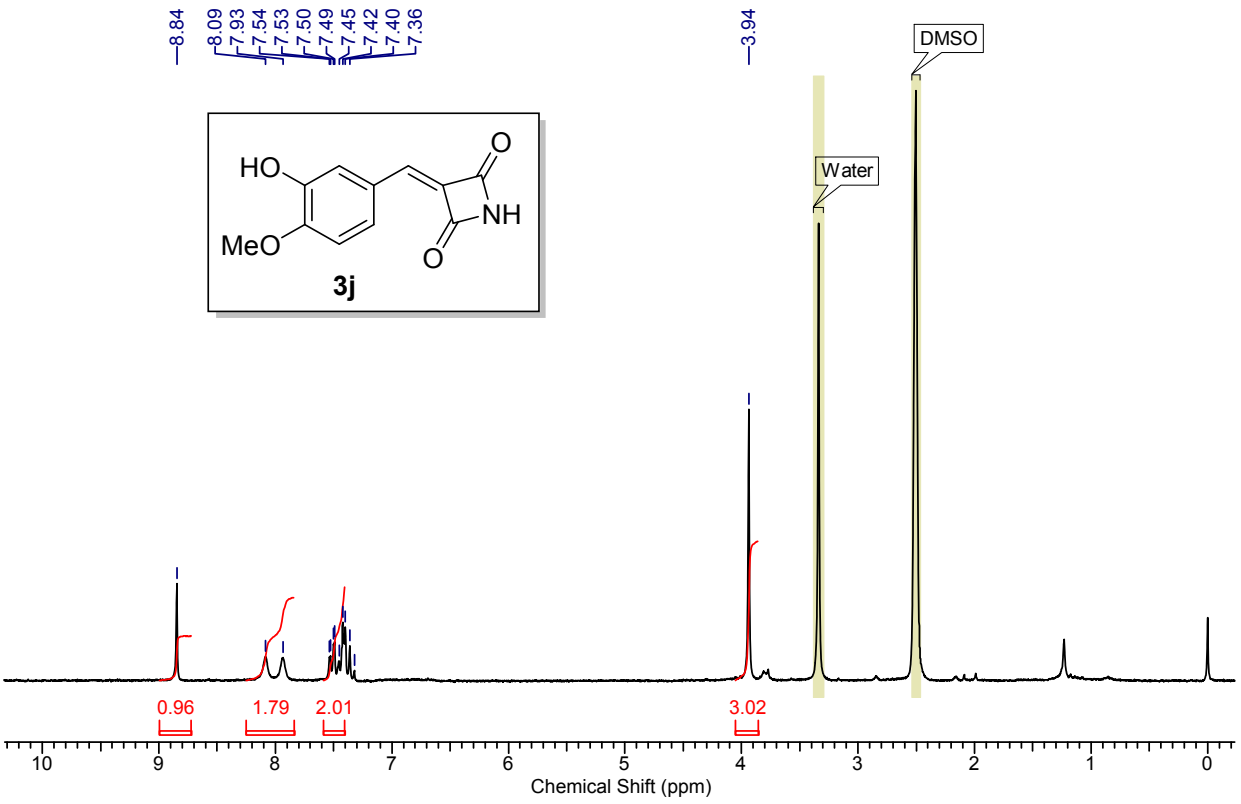

Water
8.12
7.99
7.94
7.16
7.12
3.86
DMSO
MeO
NH
O
O
3g
1.02
2.07
2.05
3.00
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

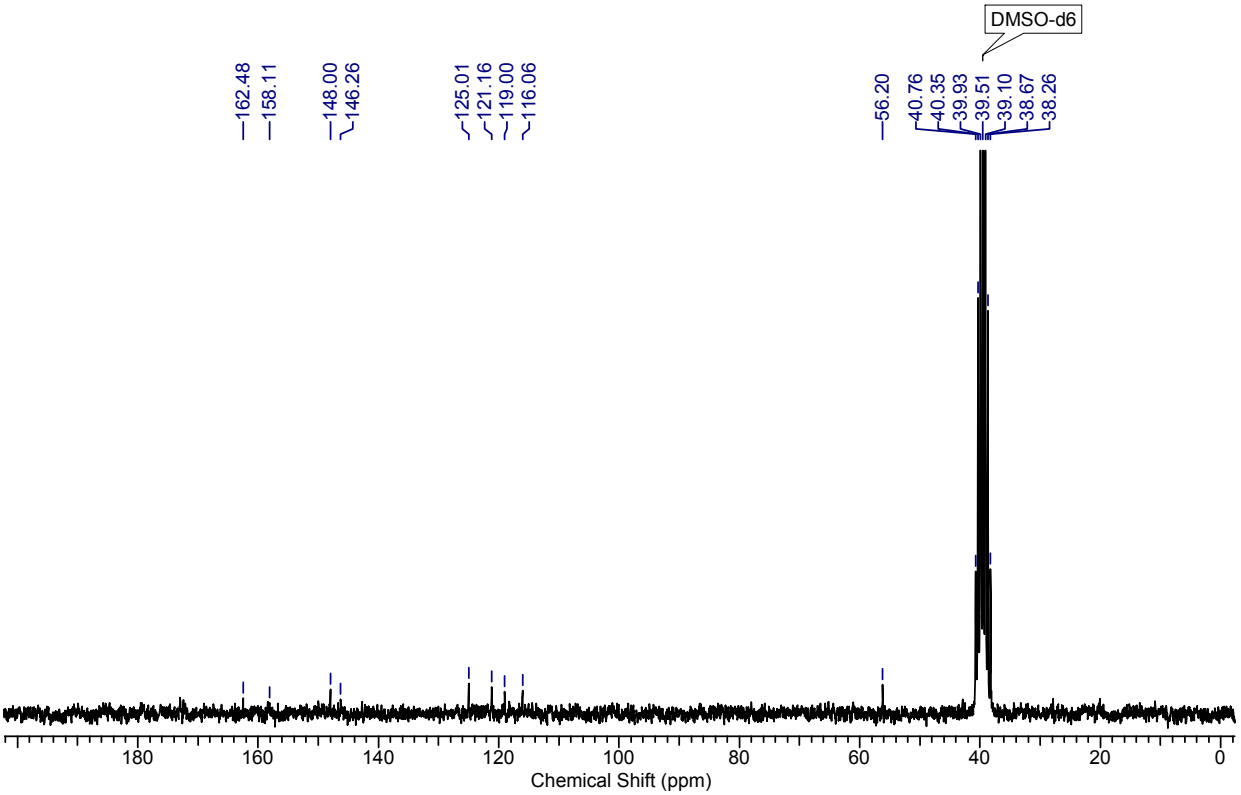

DMSO-d6
163.10
162.59
150.14
132.45
128.73
124.41
117.07
114.82
110.02
109.64
102.93
55.62
40.77
40.35
39.93
39.51
39.10
38.68
38.27
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

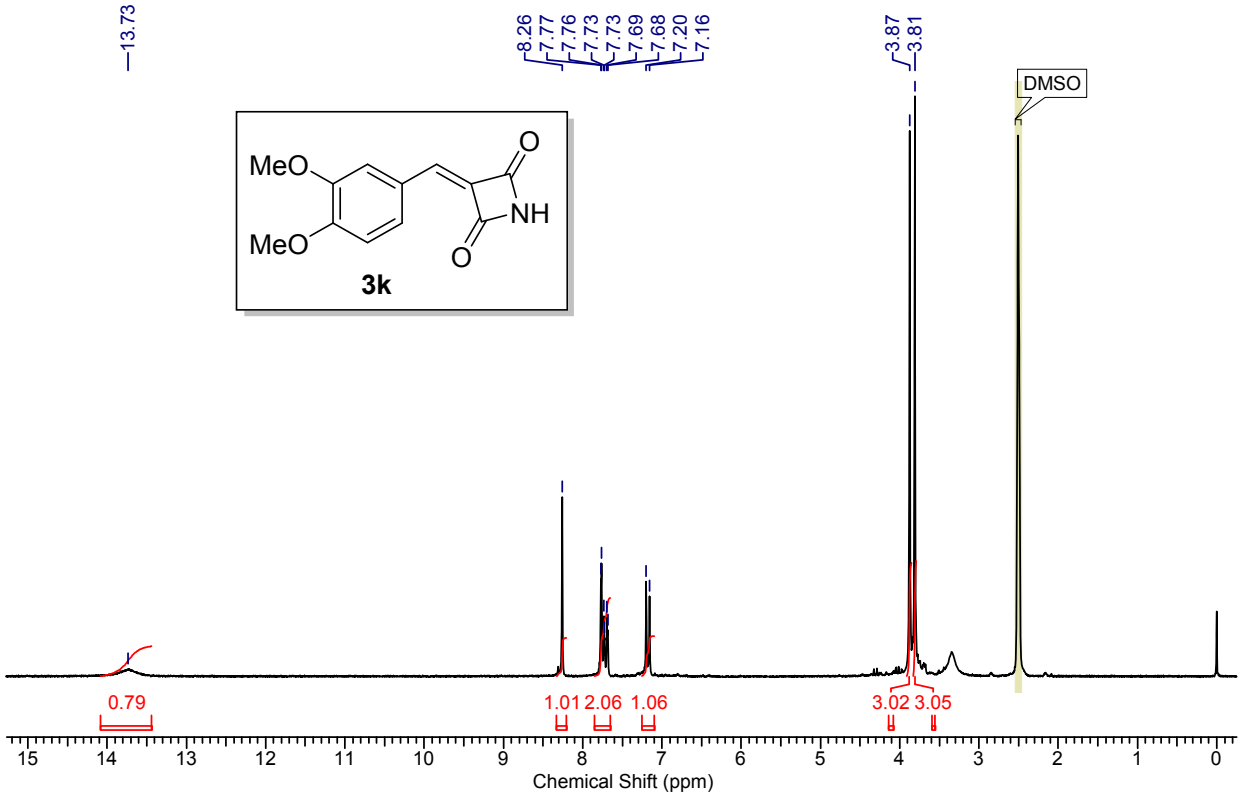

DMSO
8.13
7.92
7.88
7.45
7.41
7.38
7.36
7.32
7.24
2.55
O
NH
O
MeS
3h
0.78
2.18
2.18
3.02
Chemical Shift (ppm)

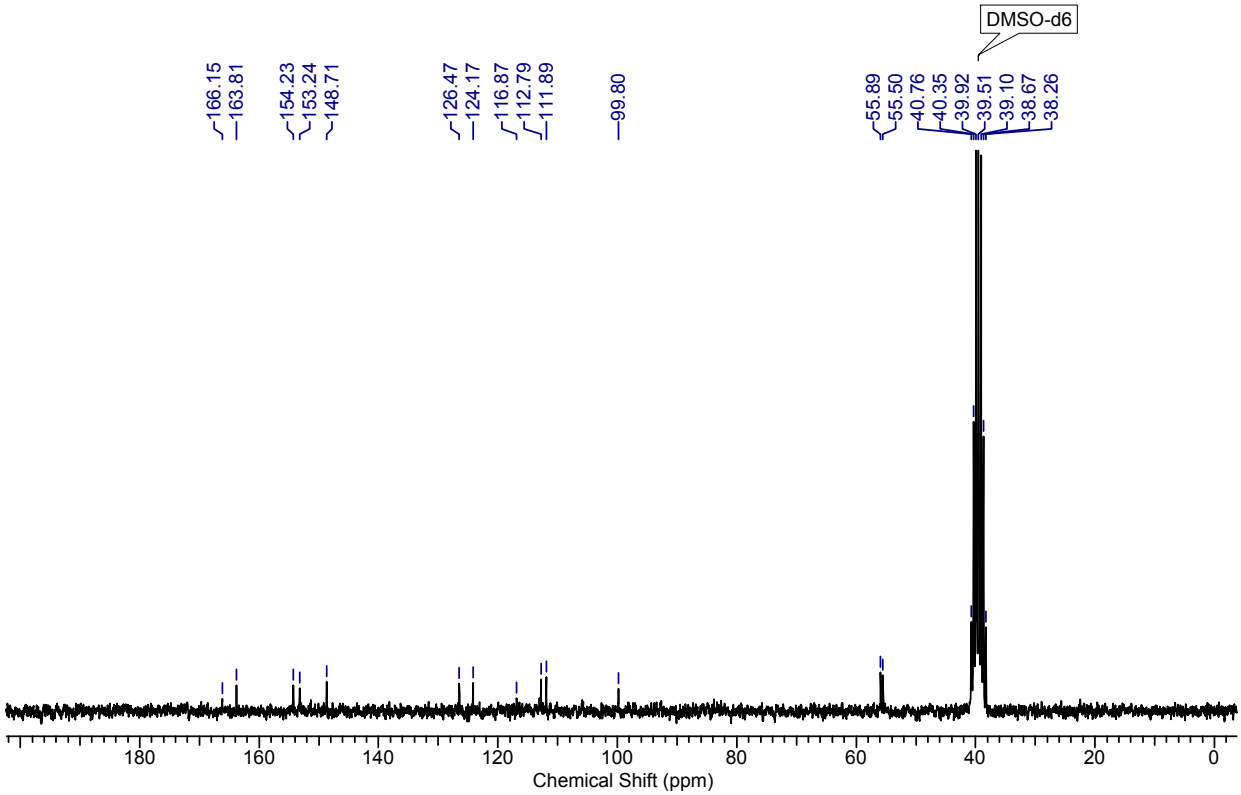

DMSO-d6
164.75
162.92
149.96
144.99
139.35
130.49
128.40
127.89
126.12
125.45
116.80
115.10
104.61
41.55
40.75
40.34
39.92
39.51
39.09
38.67
38.26
14.22
Chemical Shift (ppm)

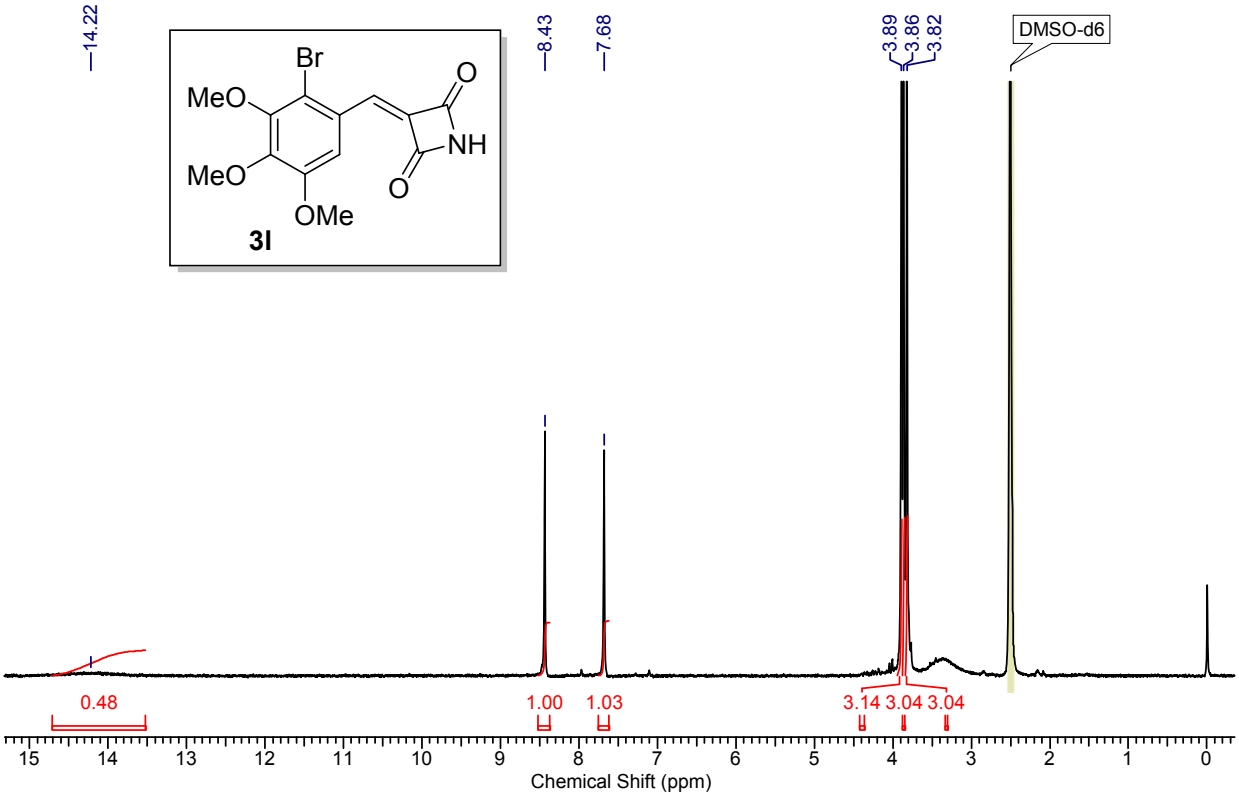

13.96
8.52
7.72
7.71
7.27
7.26
7.23
7.21
7.18
7.13
3.76
Water
DMSO
OMe
OMe
O
NH
O
3i
0.81
1.10
1.15
1.10
1.11
6.02
Chemical Shift (ppm)
DMSO-d6
163.33
153.26
152.73
147.98
121.18
120.11
116.17
113.37
112.49
103.37
56.38
55.54
40.76
40.34
39.92
39.51
39.09
38.67
38.26
Chemical Shift (ppm)

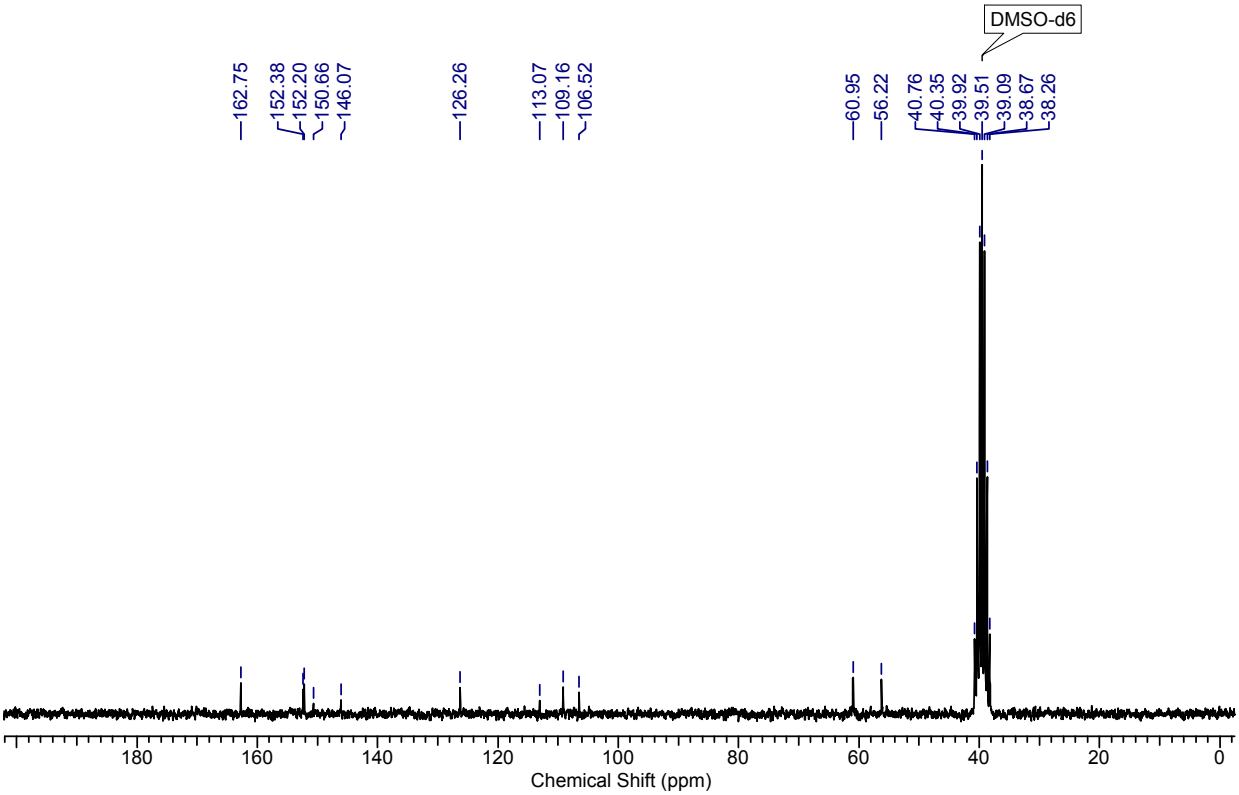

8.84
8.09
7.93
7.54
7.53
7.50
7.49
7.45
7.42
7.40
7.36
3.94
DMSO
Water
HO
MeO
O
NH
O
3j
0.96
1.79
2.01
3.02
Chemical Shift (ppm)

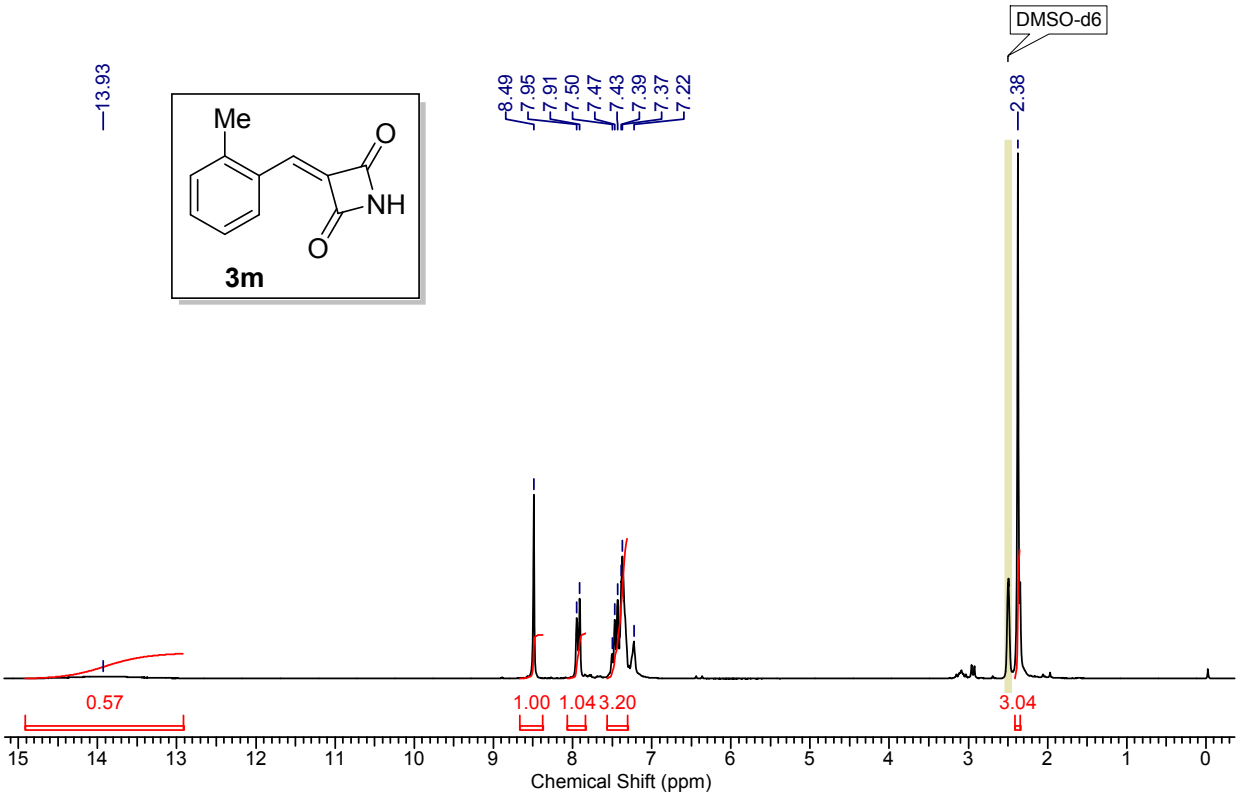

DMSO-d6
162.48
158.11
148.00
146.26
125.01
121.16
119.00
116.06
56.20
40.76
40.35
39.93
39.51
39.10
38.67
38.26
Chemical Shift (ppm)

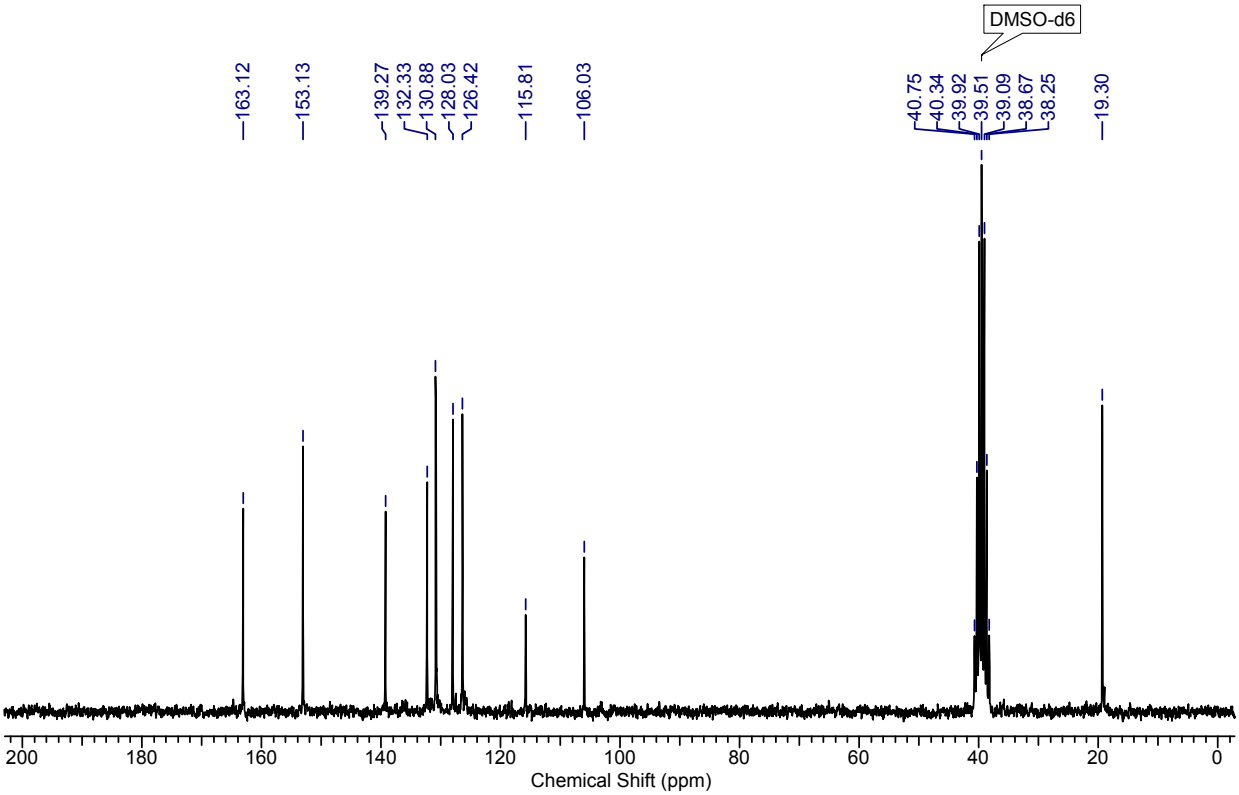

13.73
8.26
7.77
7.76
7.73
7.73
7.69
7.68
7.20
7.16
3.87
3.81
DMSO
MeO
MeO
O
NH
O
3k
0.79
1.01
2.06
1.06
3.02
3.05
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

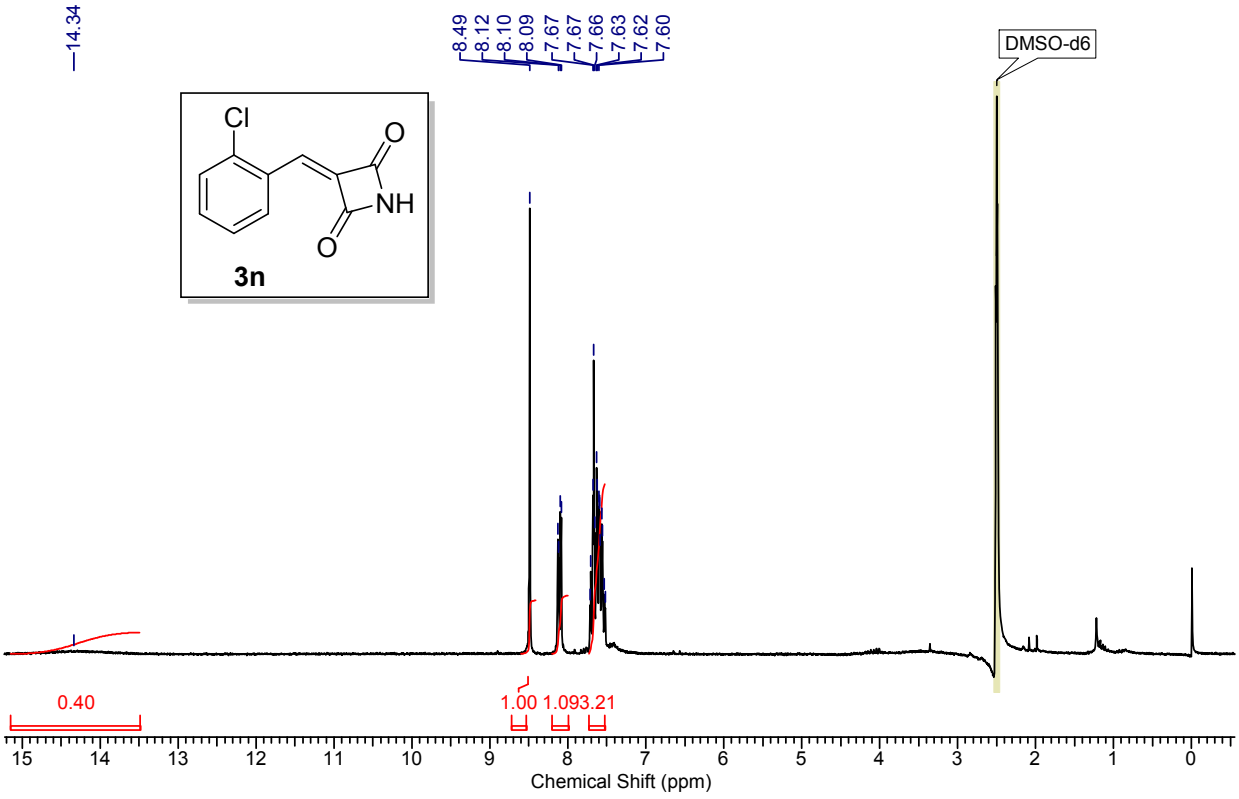

DMSO-d6
166.15
163.81
154.23
153.24
148.71
126.47
124.17
116.87
112.79
111.89
99.80
55.89
55.50
40.76
40.35
39.92
39.51
39.10
38.67
38.26
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

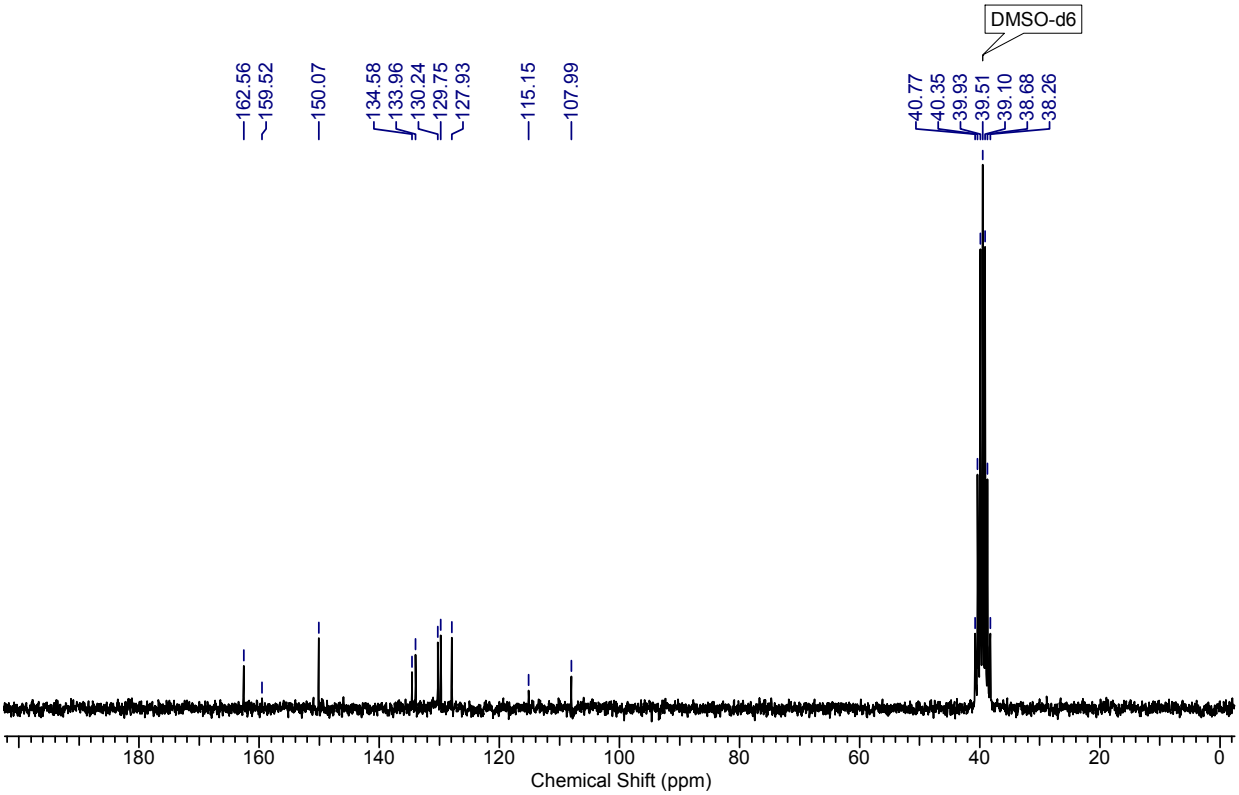

14.22
8.43
7.68
3.89
3.86
3.82
DMSO-d6
Br
MeO
MeO
OMe
O
NH
O
3l
0.48
1.00
1.03
3.14
3.04
3.04
Chemical Shift (ppm)

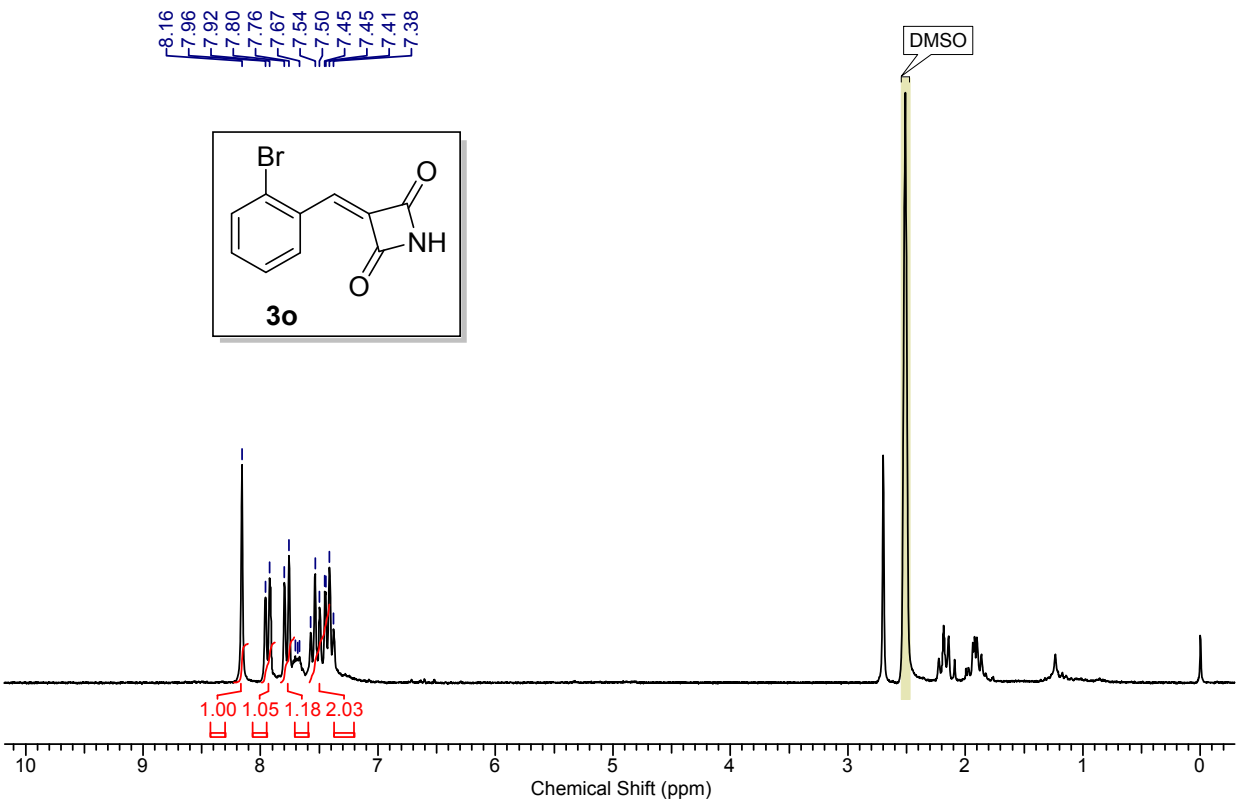

DMSO-d6
162.75
152.38
152.20
150.66
146.07
126.26
113.07
109.16
106.52
60.95
56.22
40.76
40.35
39.92
39.51
39.09
38.67
38.26
Chemical Shift (ppm)

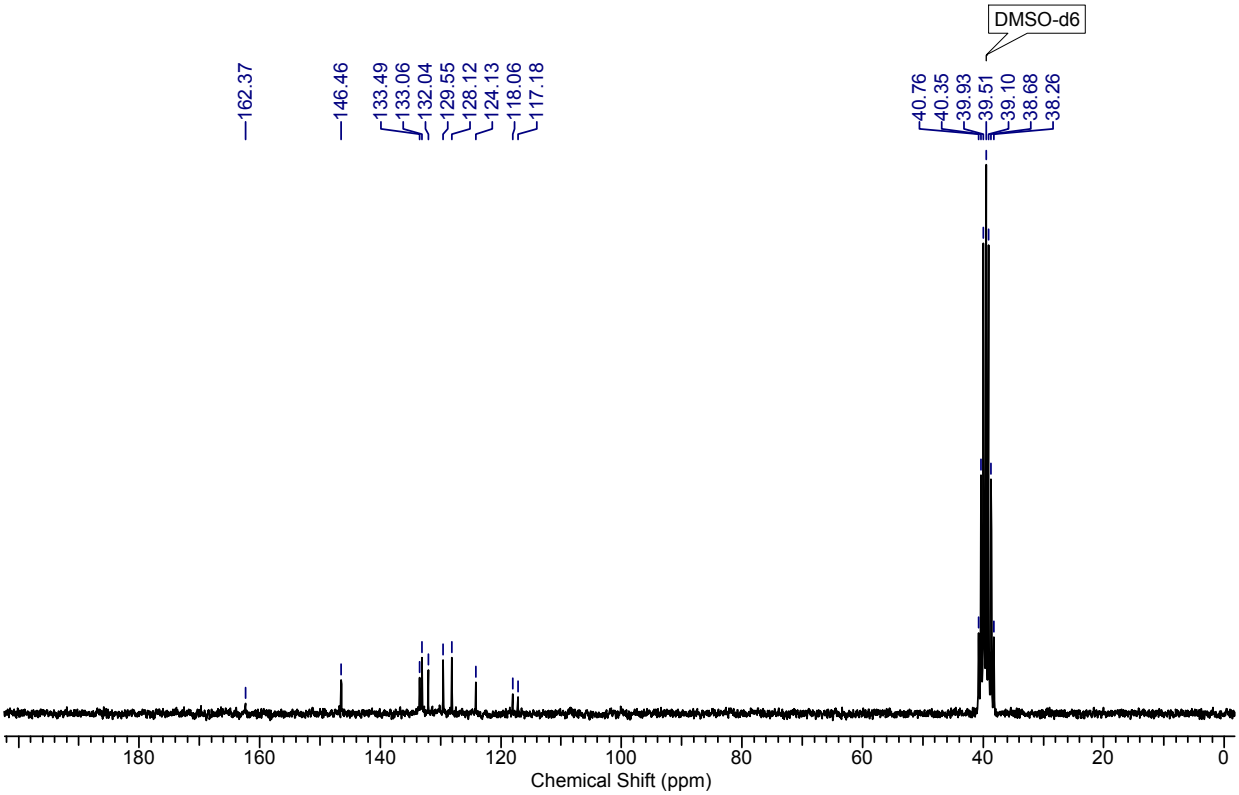

DMSO-d6
13.93
8.49
7.95
7.91
7.50
7.47
7.43
7.39
7.37
7.22
2.38
Me
O
NH
O
3m
0.57
1.00
1.04
3.20
3.04
Chemical Shift (ppm)

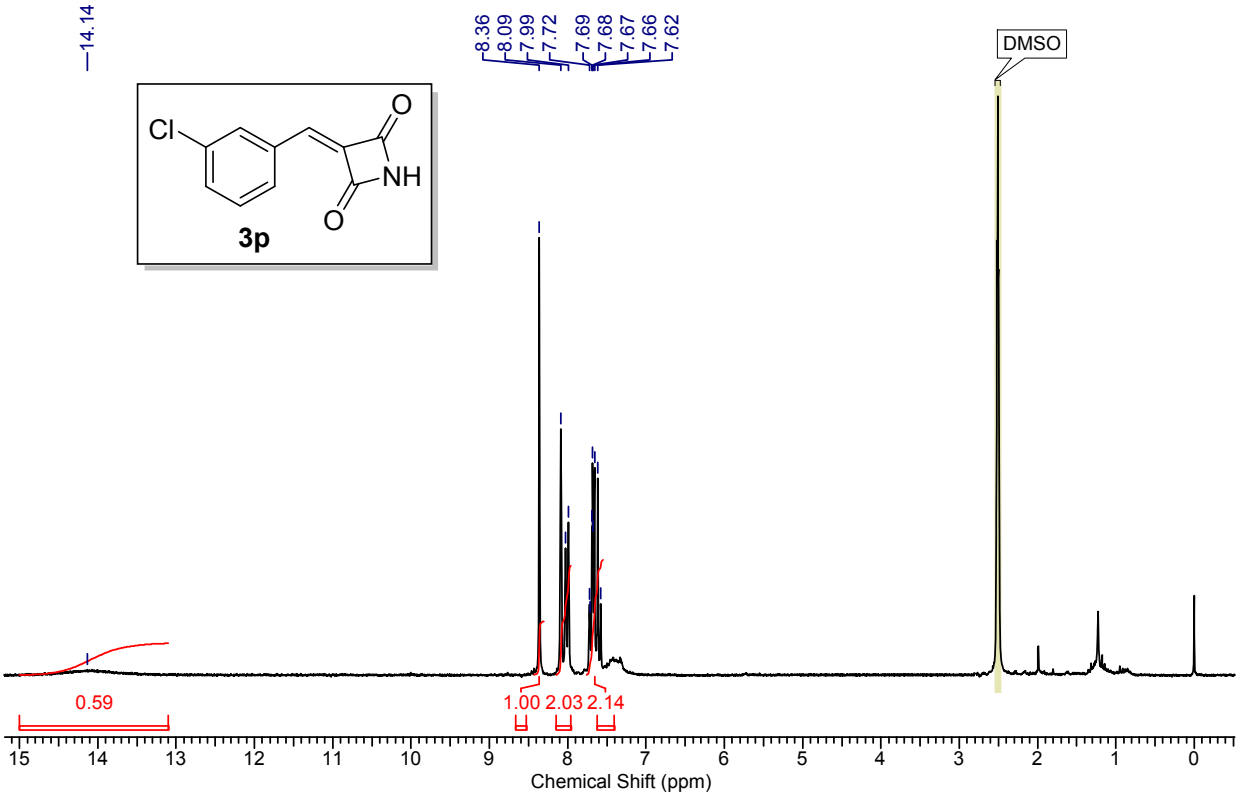

DMSO-d6
163.12
153.13
139.27
132.33
130.88
128.03
126.42
115.81
106.03
40.75
40.34
39.92
39.51
39.09
38.67
38.25
19.30
Chemical Shift (ppm)

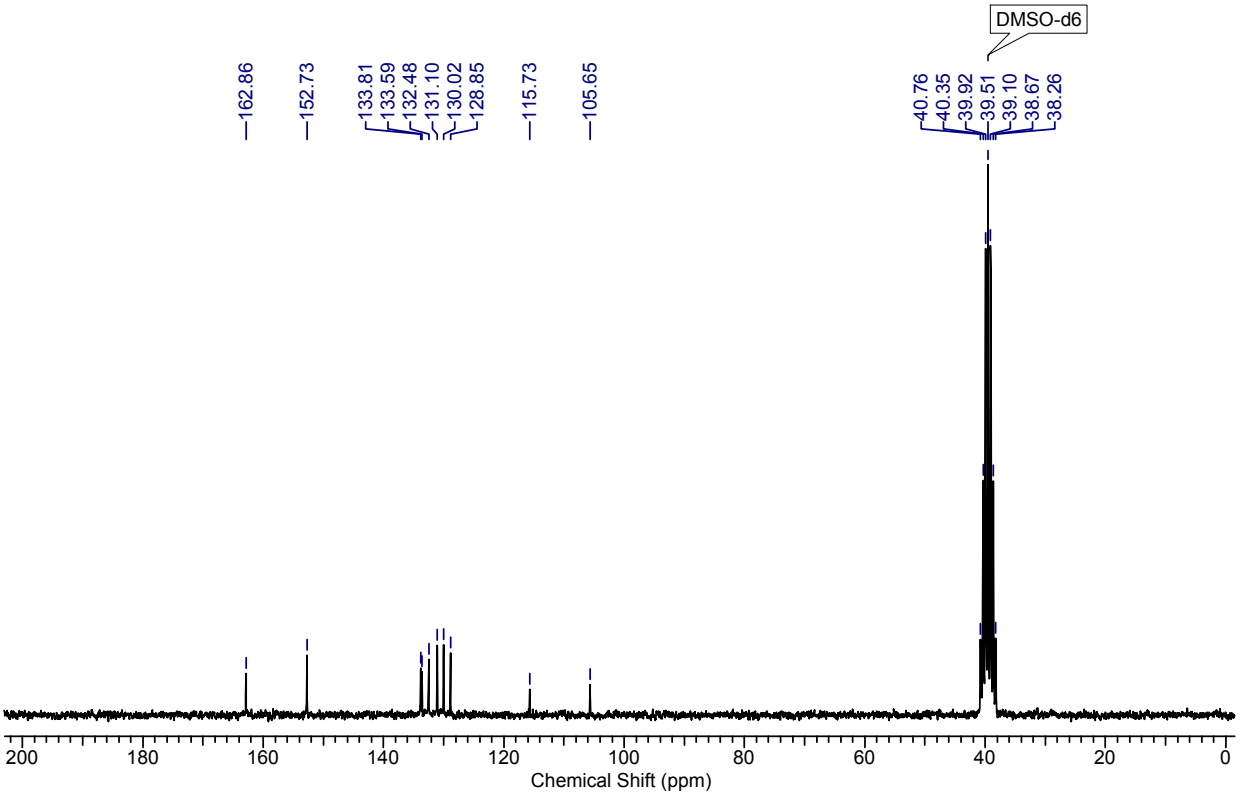

14.34
8.49
8.12
8.10
8.09
7.67
7.67
7.66
7.63
7.62
7.60
DMSO-d6
Cl
O
NH
O
3n
0.40
1.00
1.09
3.21
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

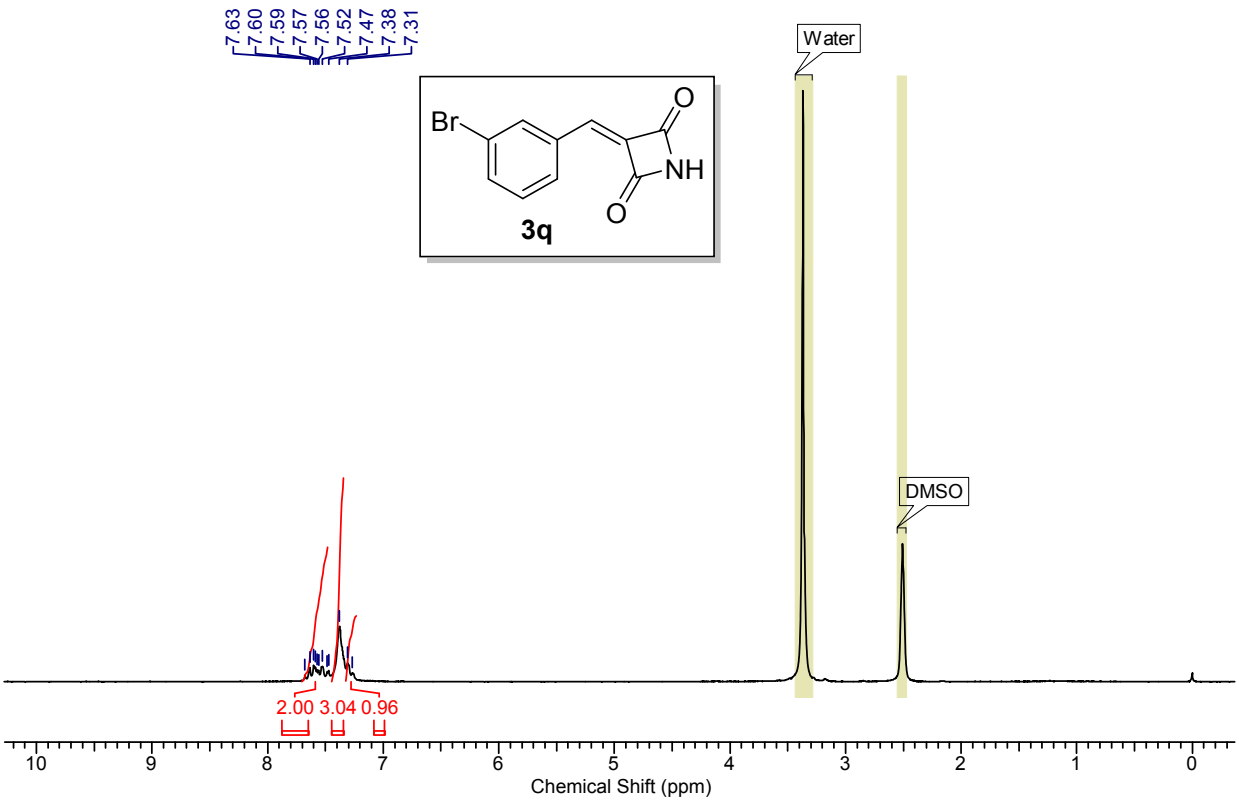

DMSO-d6
162.56
159.52
150.07
134.58
133.96
130.24
129.75
127.93
115.15
107.99
40.77
40.35
39.93
39.51
39.10
38.68
38.26
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

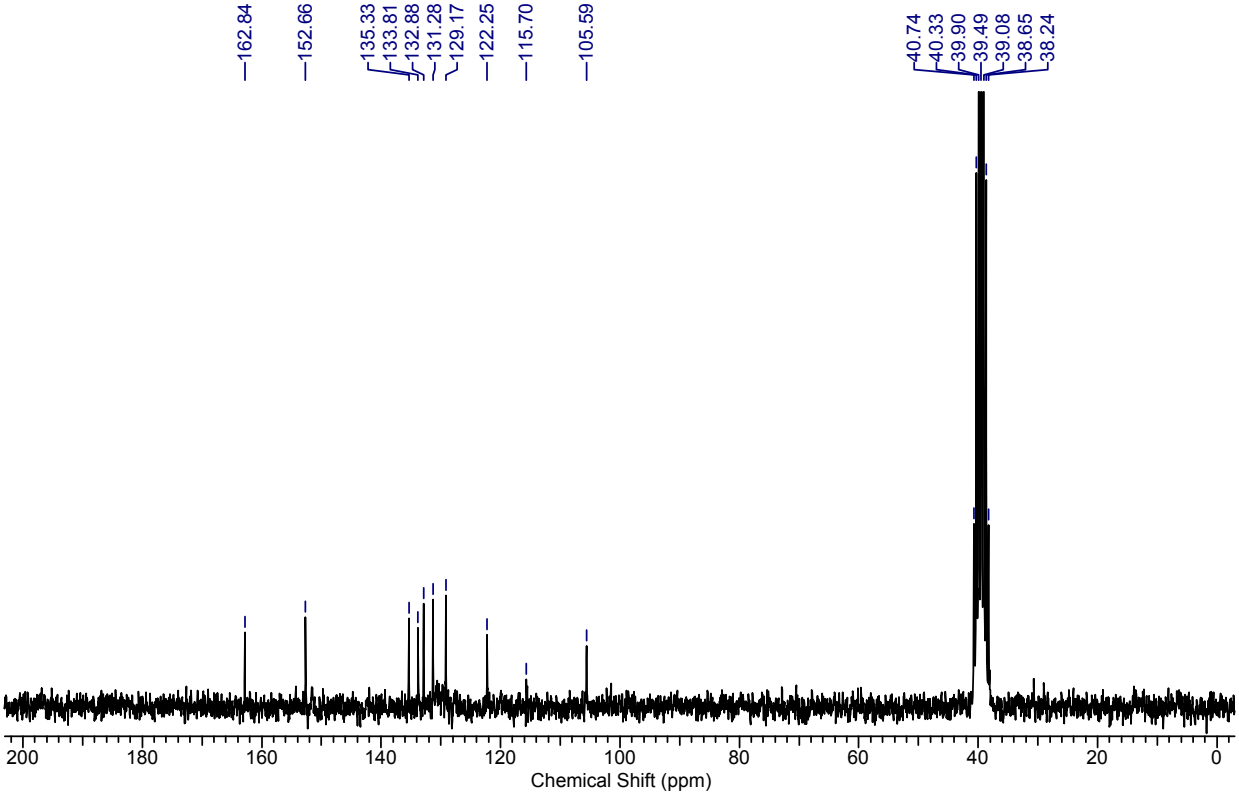

8.16
7.96
7.92
7.80
7.76
7.67
7.54
7.50
7.45
7.45
7.41
7.38
Br
O
NH
O
3o
DMSO
1.00 1.05 1.18 2.03
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

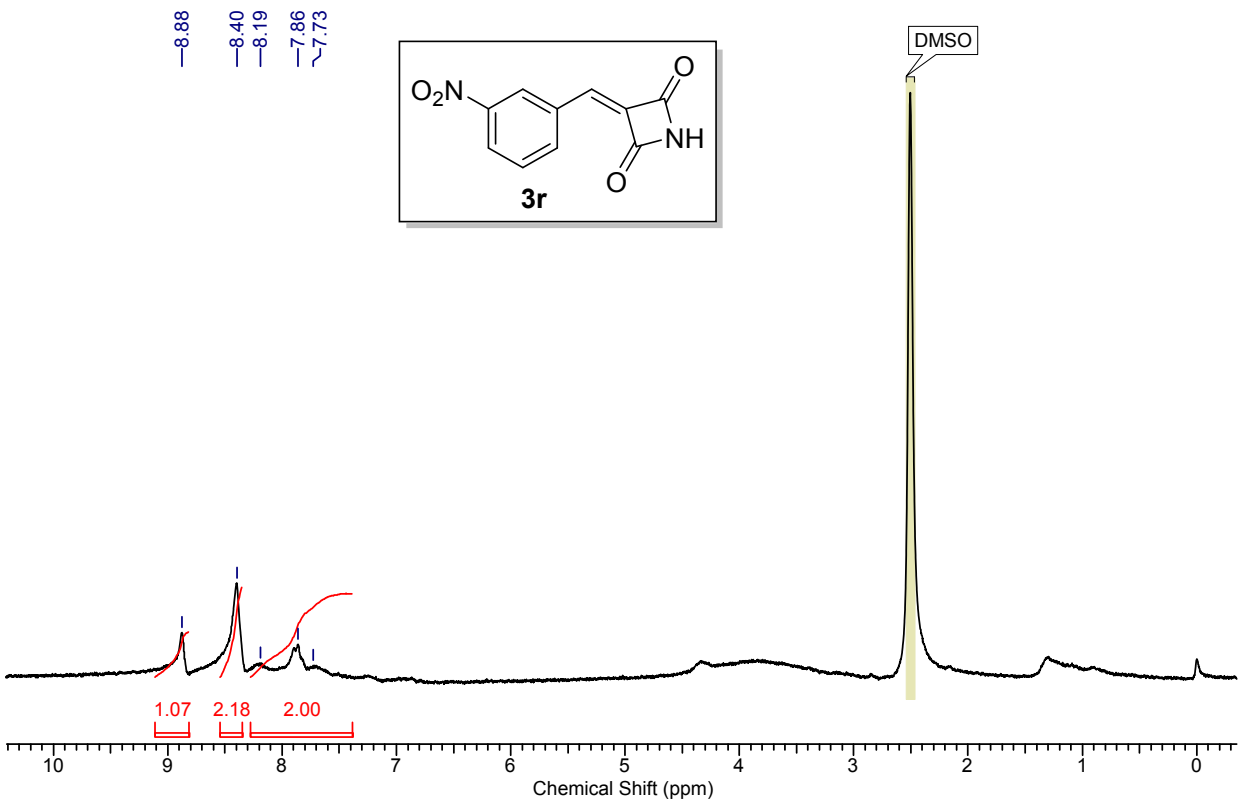

DMSO-d6
162.37
146.46
133.49
133.06
132.04
129.55
128.12
124.13
118.06
117.18
40.76
40.35
39.93
39.51
39.10
38.68
38.26
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

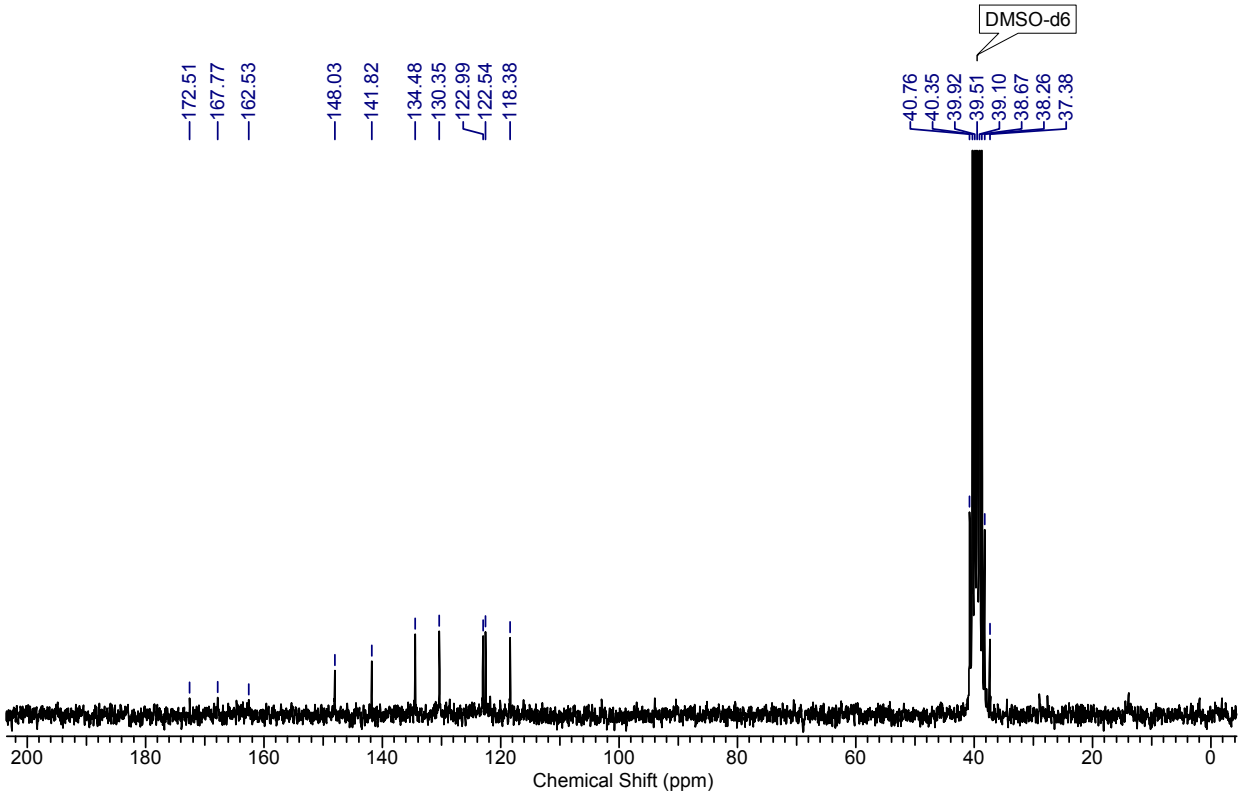

14.14
8.36
8.09
7.99
7.72
7.69
7.68
7.67
7.66
7.62
DMSO
Cl
O
NH
O
3p
0.59
1.00
2.03
2.14
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

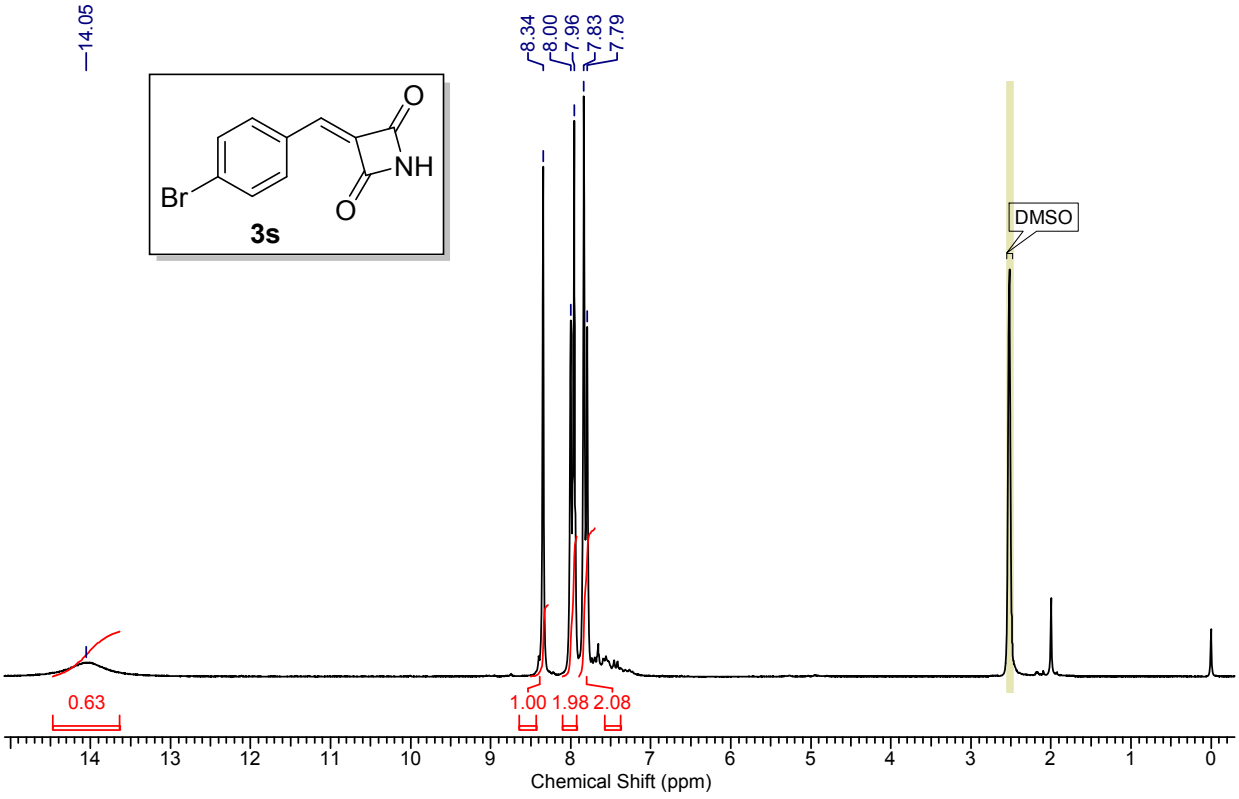

DMSO-d6
162.86
152.73
133.81
133.59
132.48
131.10
130.02
128.85
115.73
105.65
40.76
40.35
39.92
39.51
39.10
38.67
38.26
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

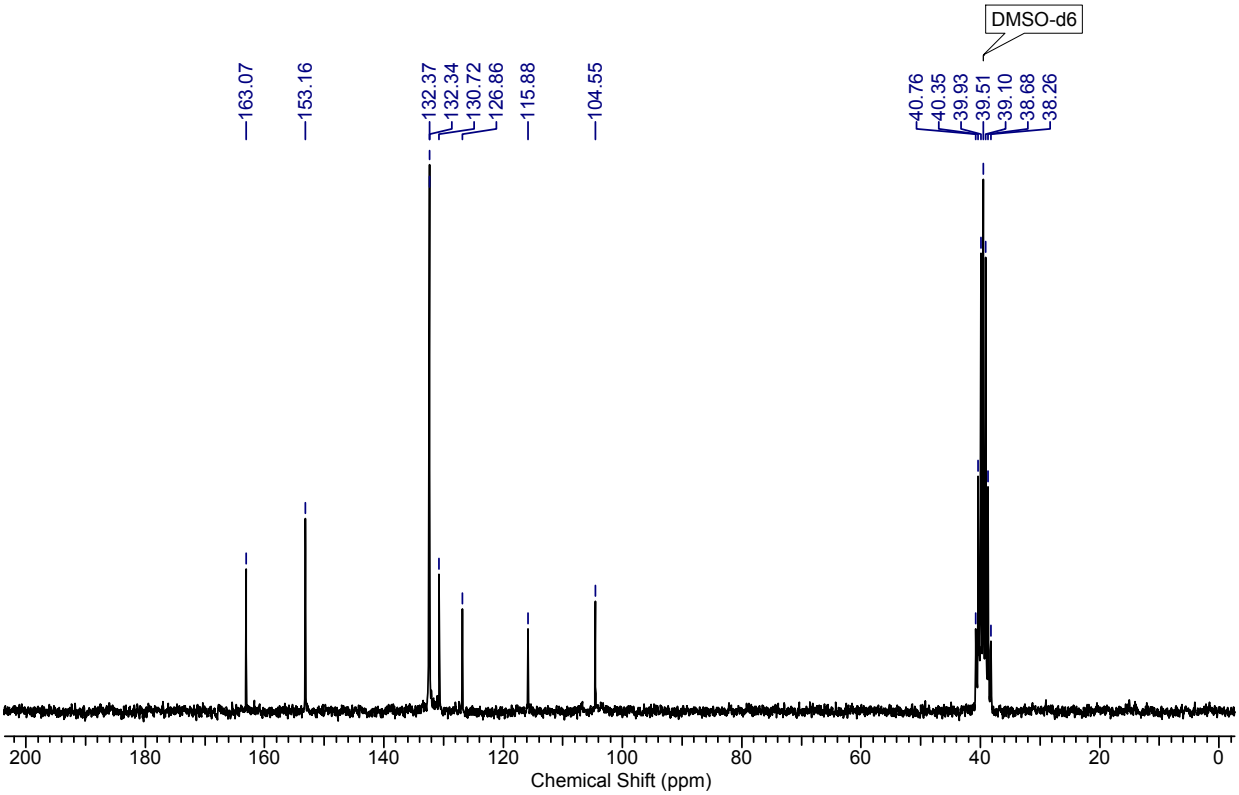

7.63
7.60
7.59
7.57
7.56
7.52
7.47
7.38
7.31
Water
DMSO
Br
O
NH
O
3q
2.00 3.04 0.96
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

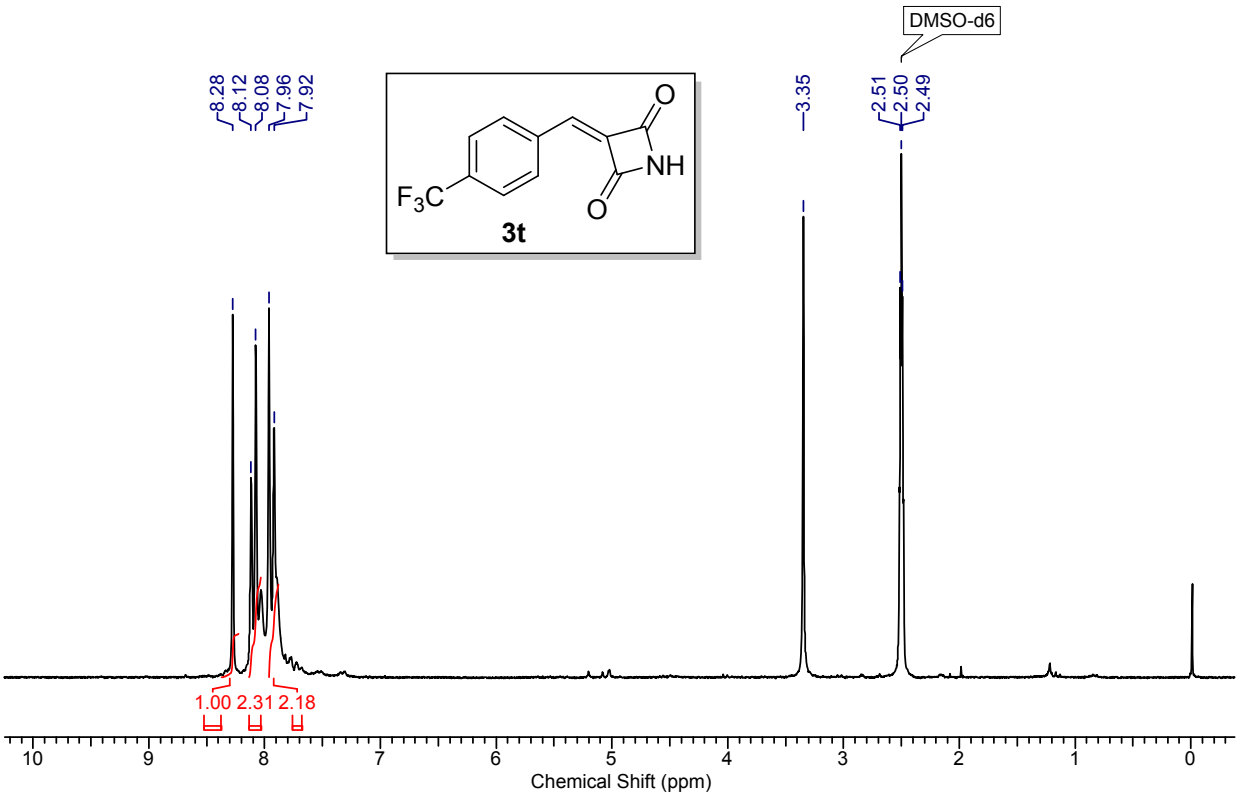

162.84
152.66
135.33
133.81
132.88
131.28
129.17
122.25
115.70
105.59
40.74
40.33
39.90
39.49
39.08
38.65
38.24
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

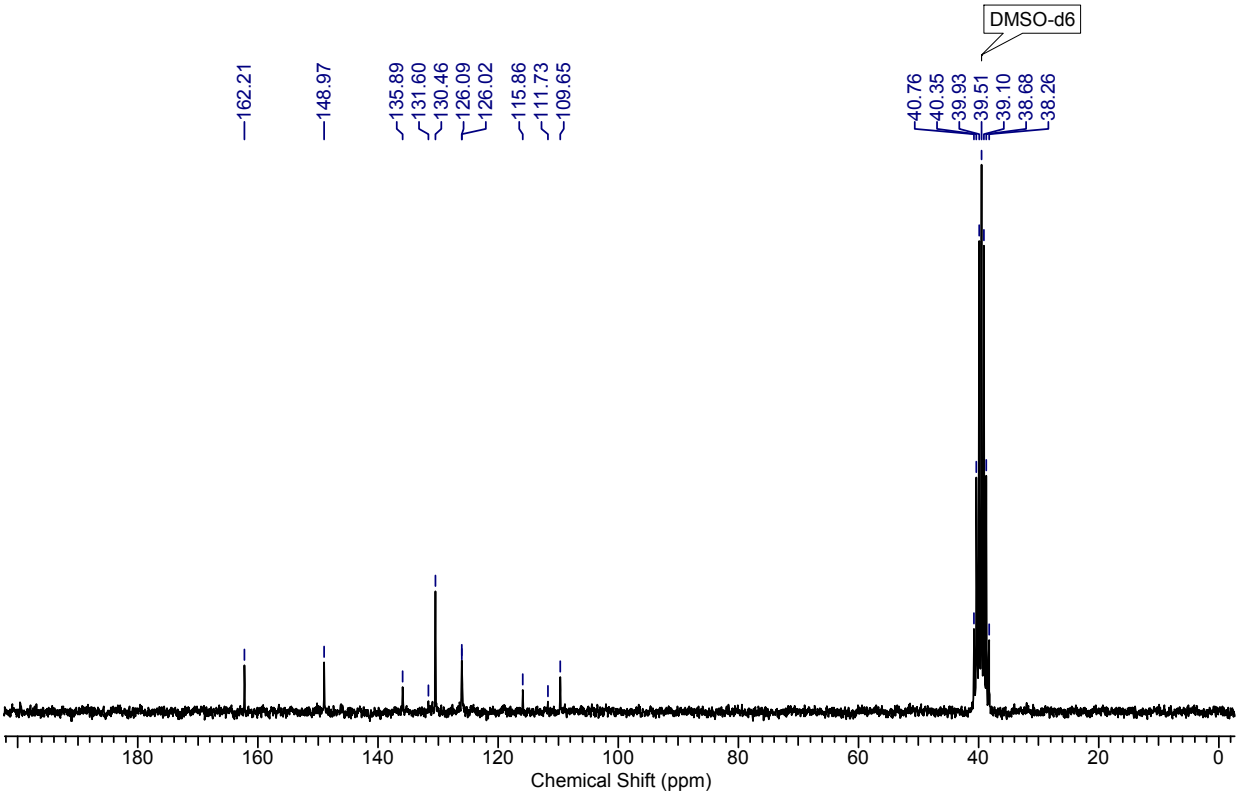

8.88
8.40
8.19
7.86
7.73
O2N
O
NH
O
3r
DMSO
1.07
2.18
2.00
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

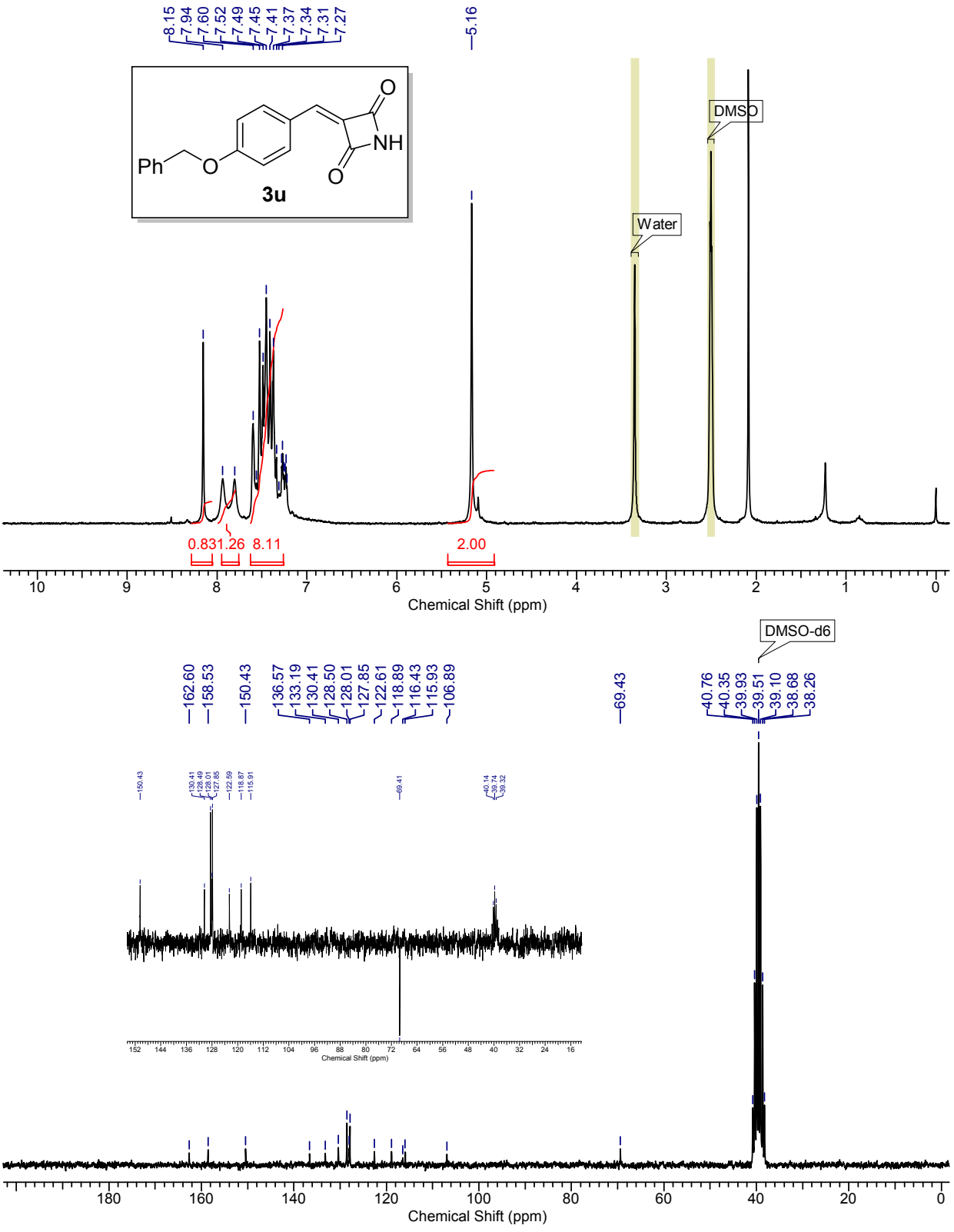

DMSO-d6
172.51
167.77
162.53
148.03
141.82
134.48
130.35
122.99
122.54
118.38
40.76
40.35
39.92
39.51
39.10
38.67
38.26
37.38
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

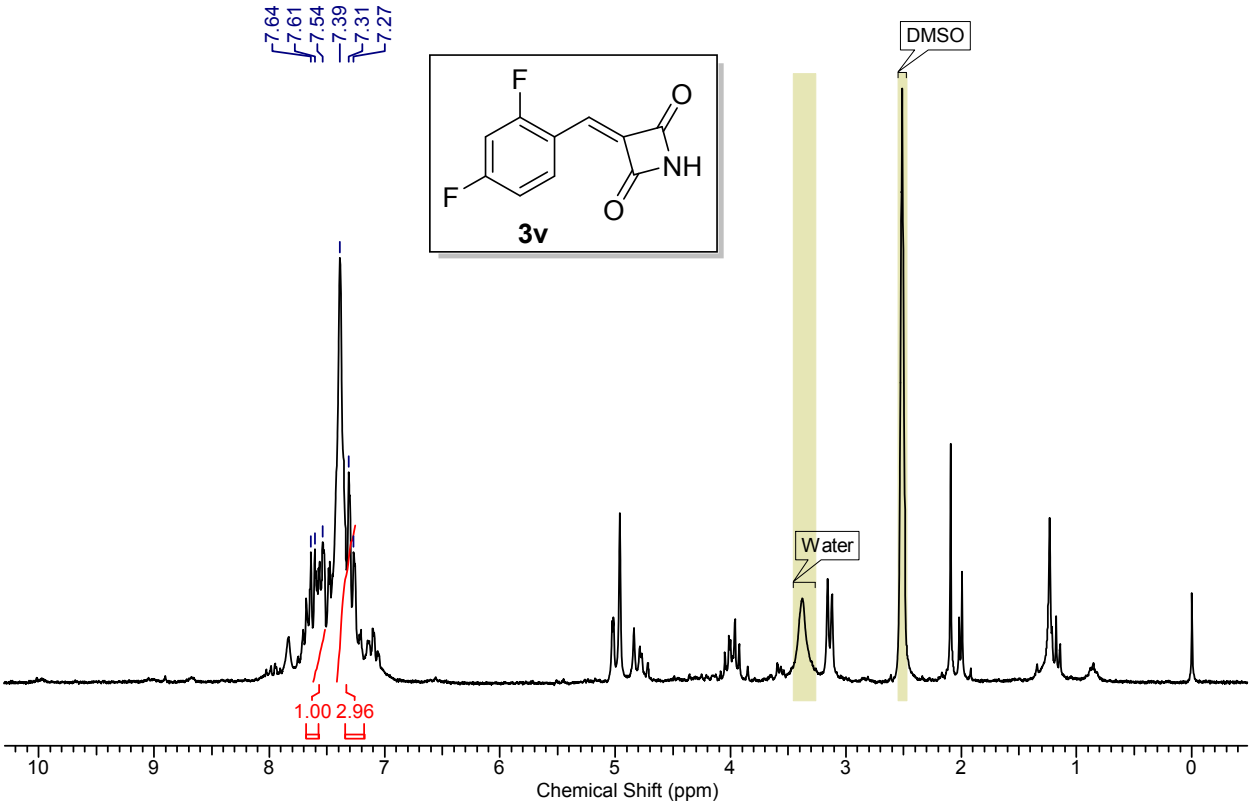

14.05
8.34
8.00
7.96
7.83
7.79
O
NH
O
Br
3s
DMSO
0.63
1.00
1.98
2.08
Chemical Shift (ppm)

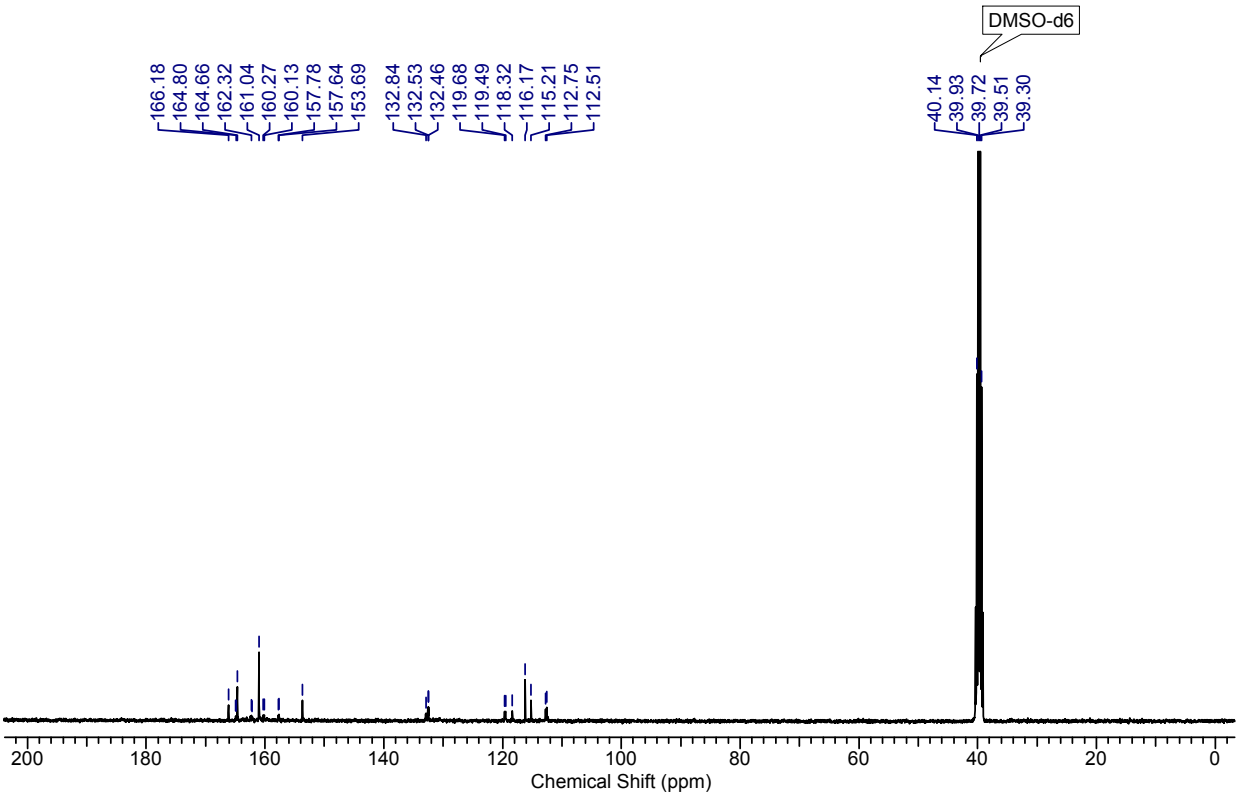

DMSO-d6
163.07
153.16
132.37
132.34
130.72
126.86
115.88
104.55
40.76
40.35
39.93
39.51
39.10
38.68
38.26
Chemical Shift (ppm)

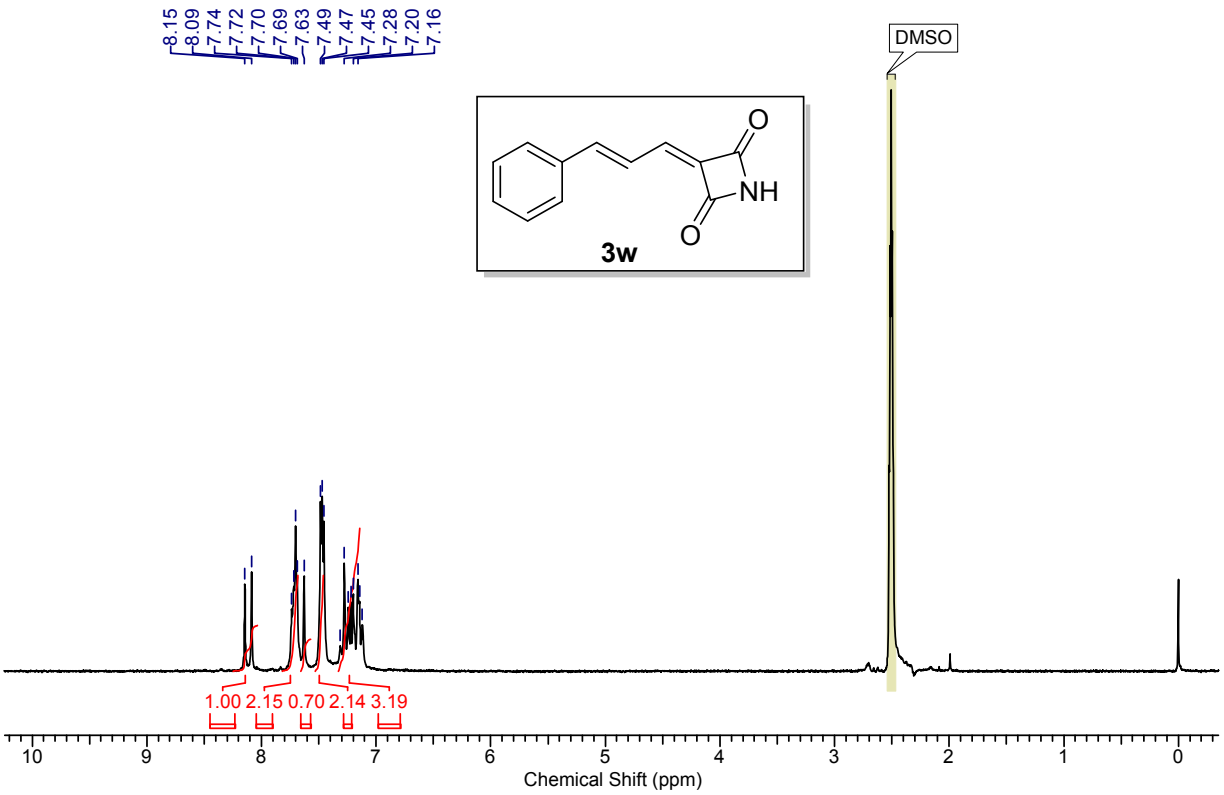

DMSO-d6
8.28
8.12
8.08
7.96
7.92
3.35
2.51
2.50
2.49
O
NH
O
F3C
3t
1.00 2.31 2.18
10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

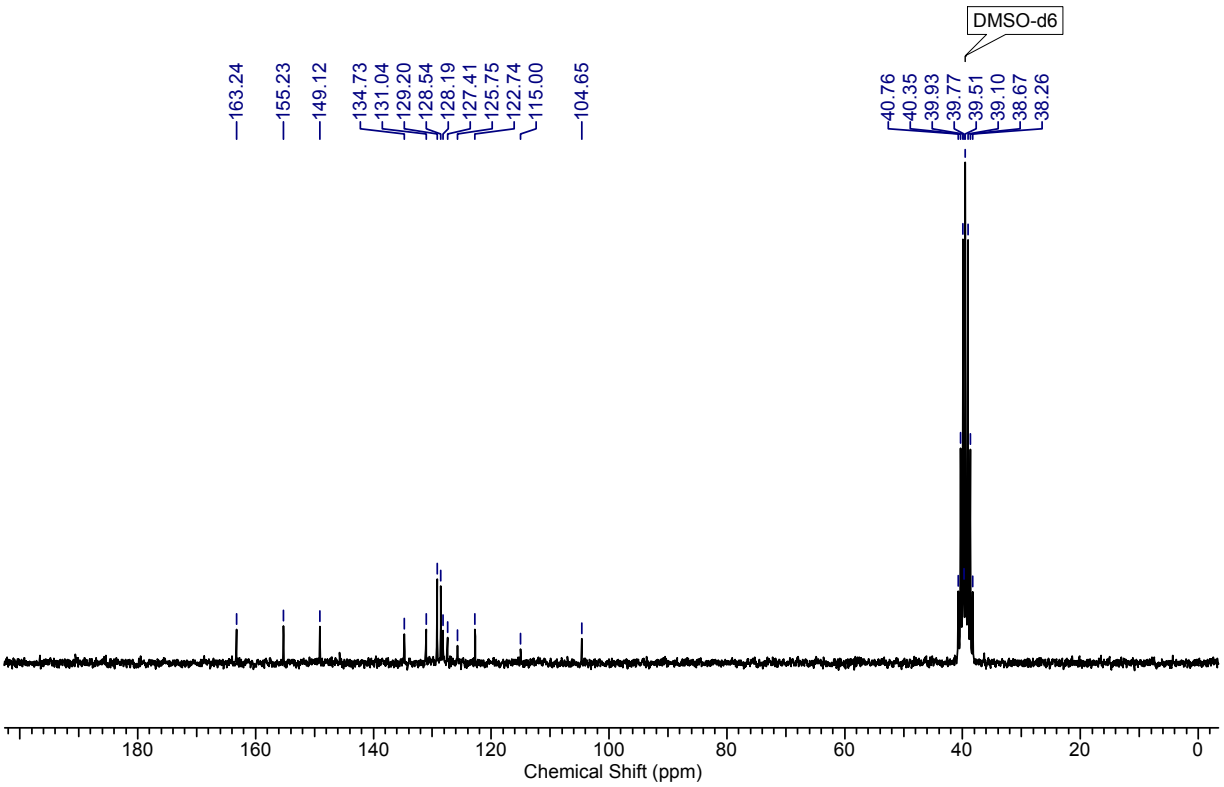

DMSO-d6
162.21
148.97
135.89
131.60
130.46
126.09
126.02
115.86
111.73
109.65
40.76
40.35
39.93
39.51
39.10
38.68
38.26
180 160 140 120 100 80 60 40 20 0
Chemical Shift (ppm)

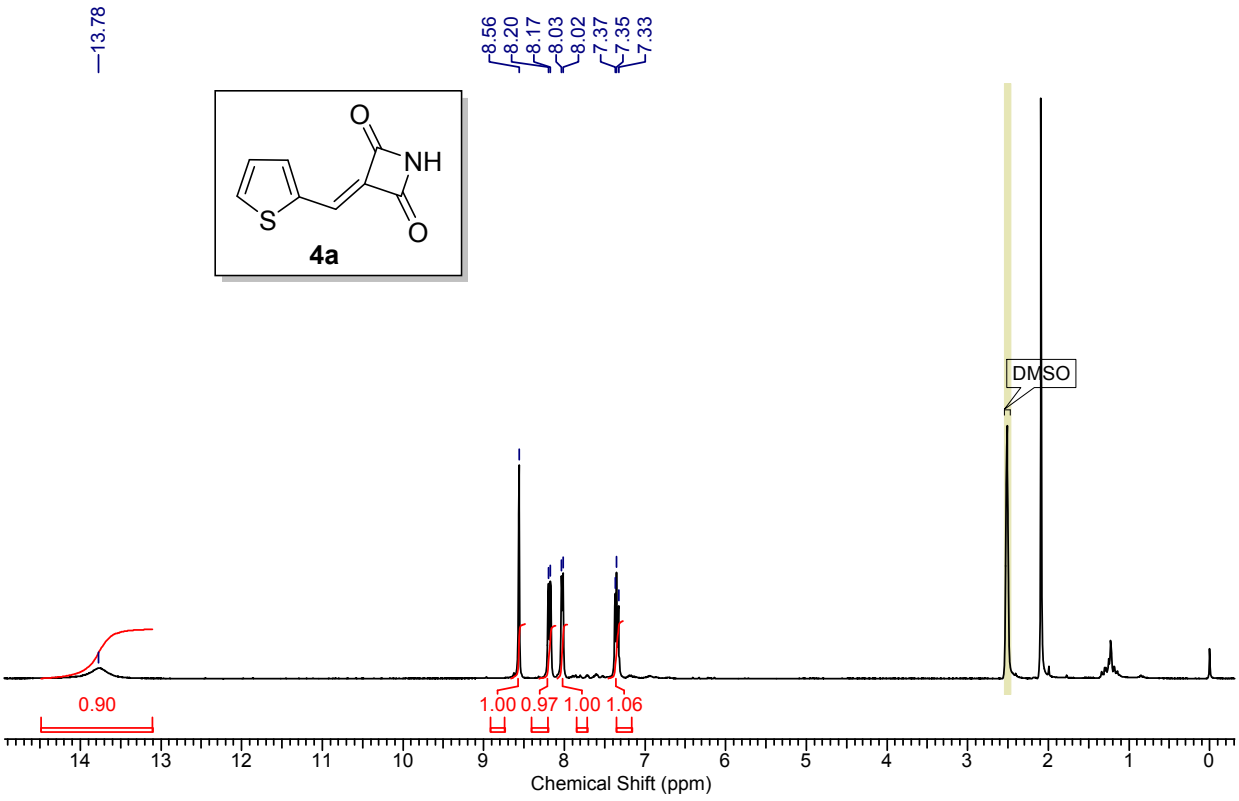

8.15
7.94
7.60
7.52
7.49
7.45
7.41
7.37
7.34
7.31
7.27
5.16
O
NH
O
Ph
O
3u
DMSO
Water
0.83
1.26
8.11
2.00
Chemical Shift (ppm)
DMSO-d6
162.60
158.53
150.43
136.57
133.19
130.41
128.50
128.01
127.85
122.61
118.89
116.43
115.93
106.89
69.43
40.76
40.35
39.93
39.51
39.10
38.68
38.26
Chemical Shift (ppm)

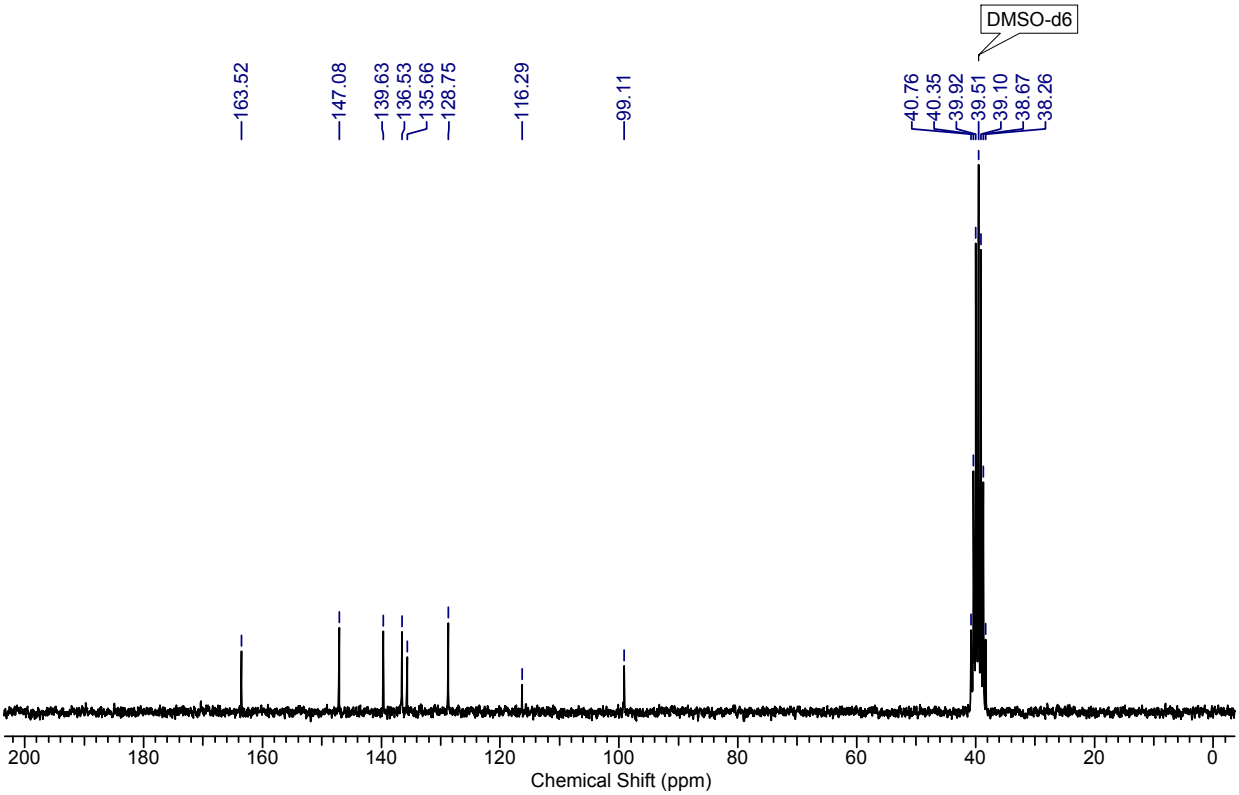

7.64
7.61
7.54
7.39
7.31
7.27
F
F
O
NH
O
3v
DMSO
Water
1.00
2.96
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

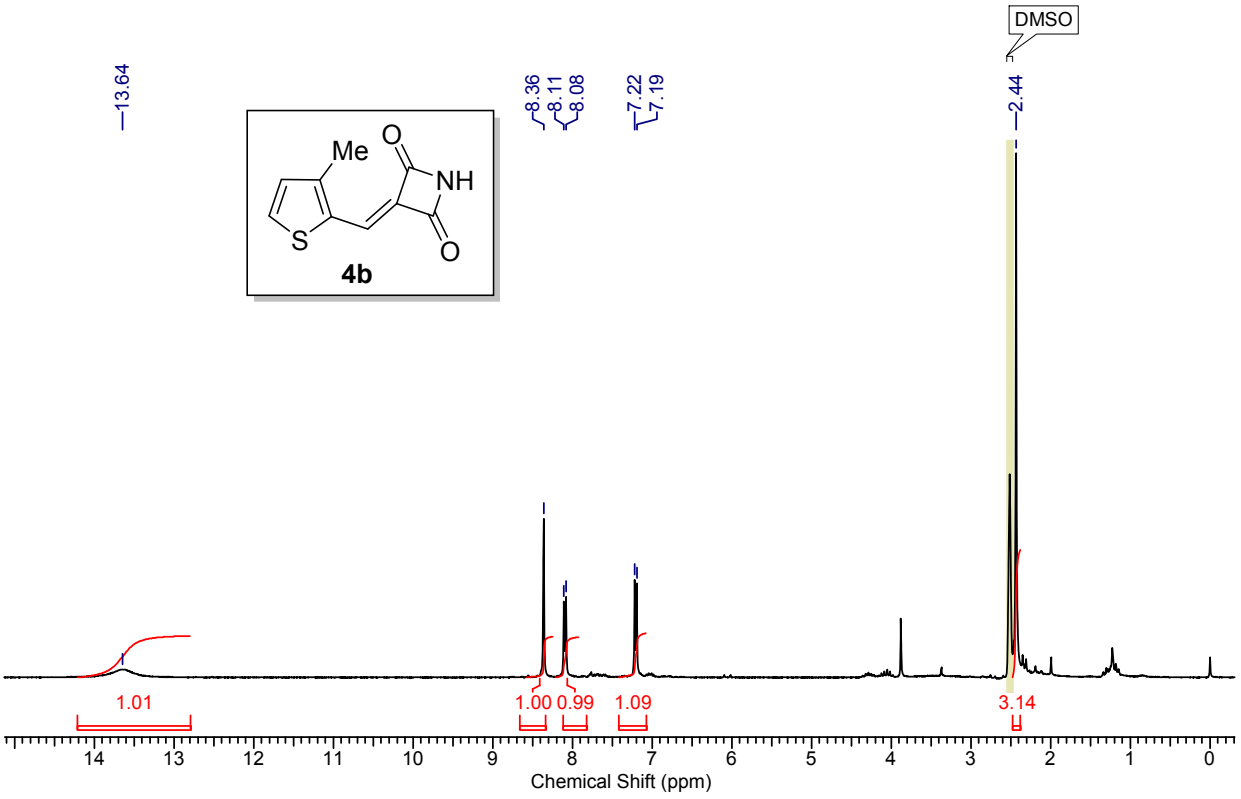

166.18
164.80
164.66
162.32
161.04
160.27
160.13
157.78
157.64
153.69
132.84
132.53
132.46
119.68
119.49
118.32
116.17
115.21
112.75
112.51
DMSO-d6
40.14
39.93
39.72
39.51
39.30
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

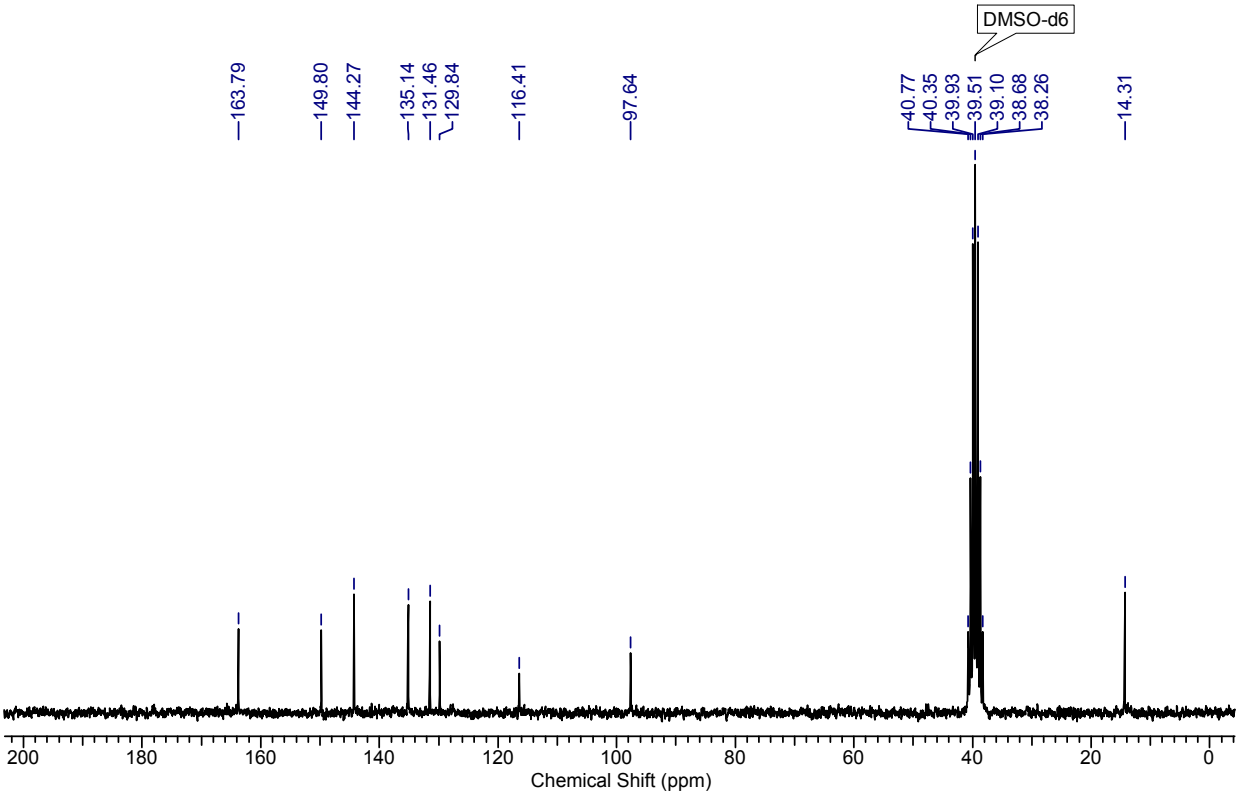

8.15
8.09
7.74
7.72
7.70
7.69
7.63
7.49
7.47
7.45
7.28
7.20
7.16
DMSO
O
NH
O
3w
1.00 2.15 0.70 2.14 3.19
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

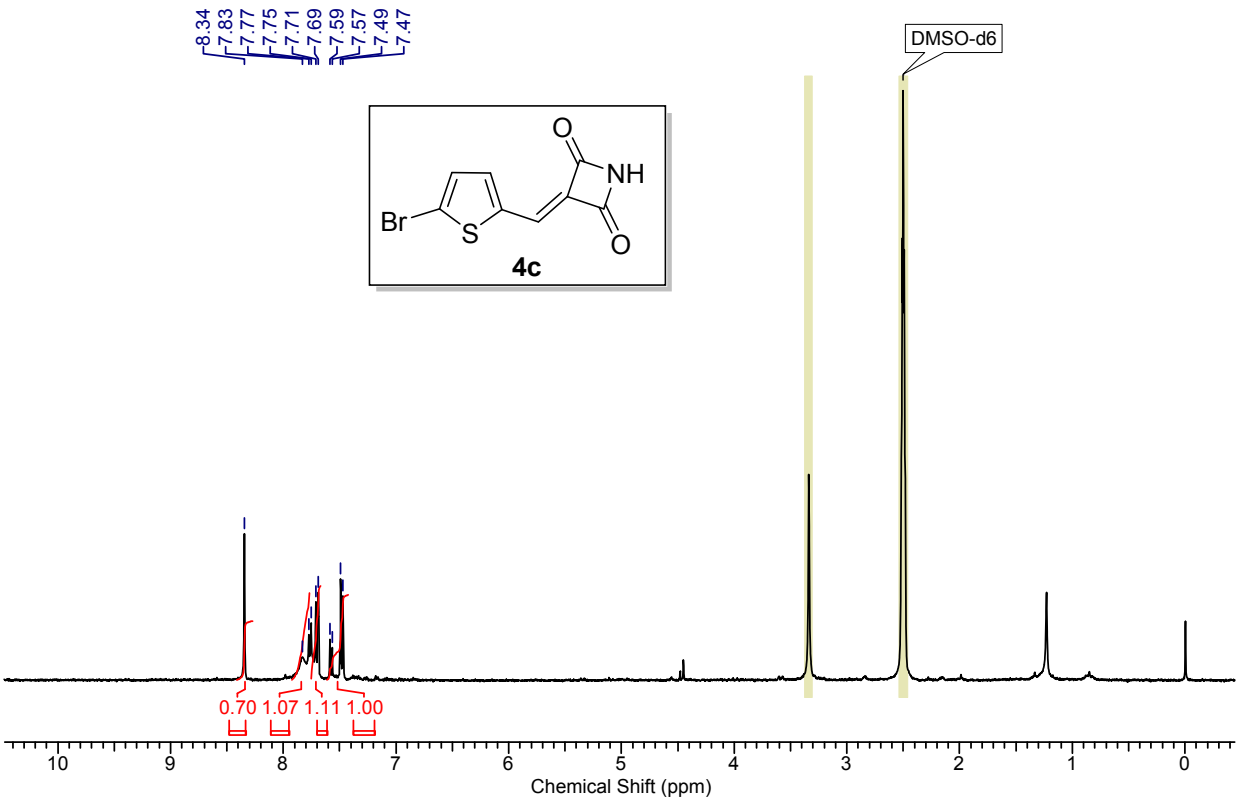

DMSO-d6
163.24
155.23
149.12
134.73
131.04
129.20
128.54
128.19
127.41
125.75
122.74
115.00
104.65
40.76
40.35
39.93
39.77
39.51
39.10
38.67
38.26
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

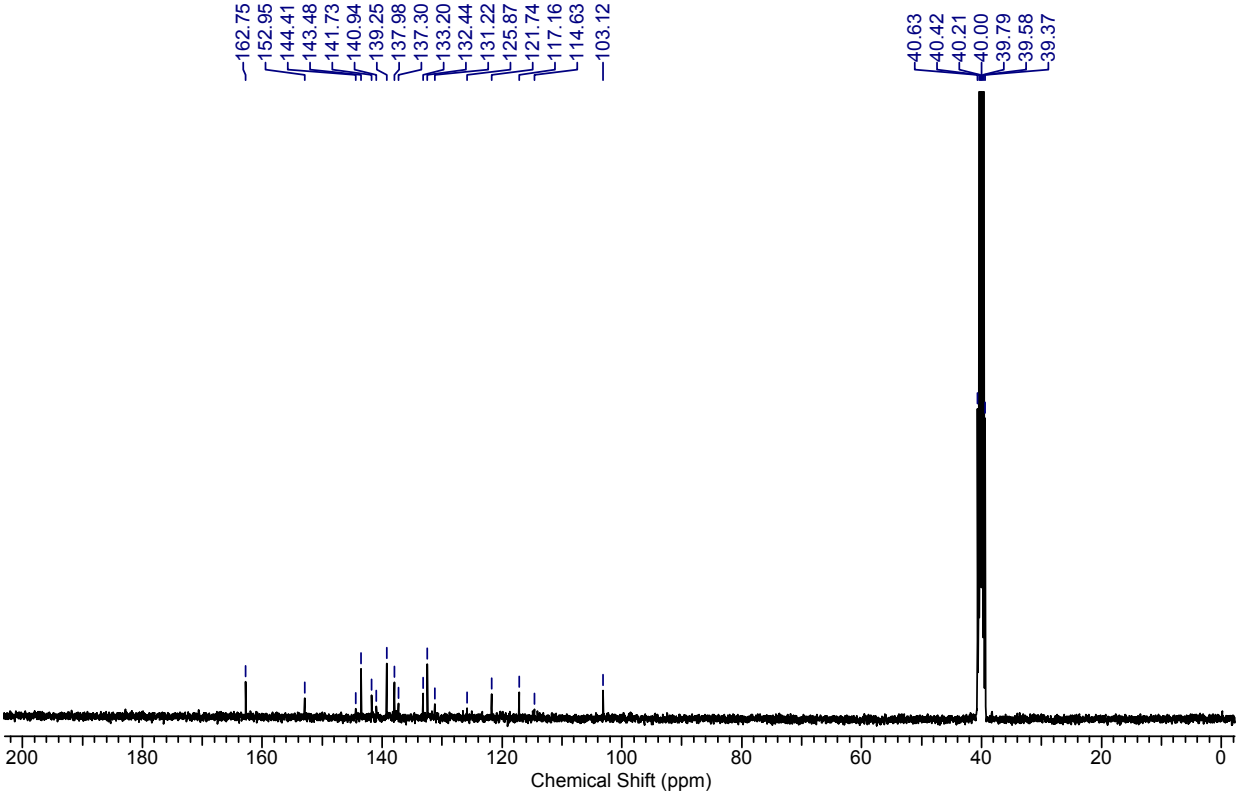

13.78
8.56
8.20
8.17
8.03
8.02
7.37
7.35
7.33
O
NH
O
S
4a
DMSO
0.90
1.00
0.97
1.00
1.06
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

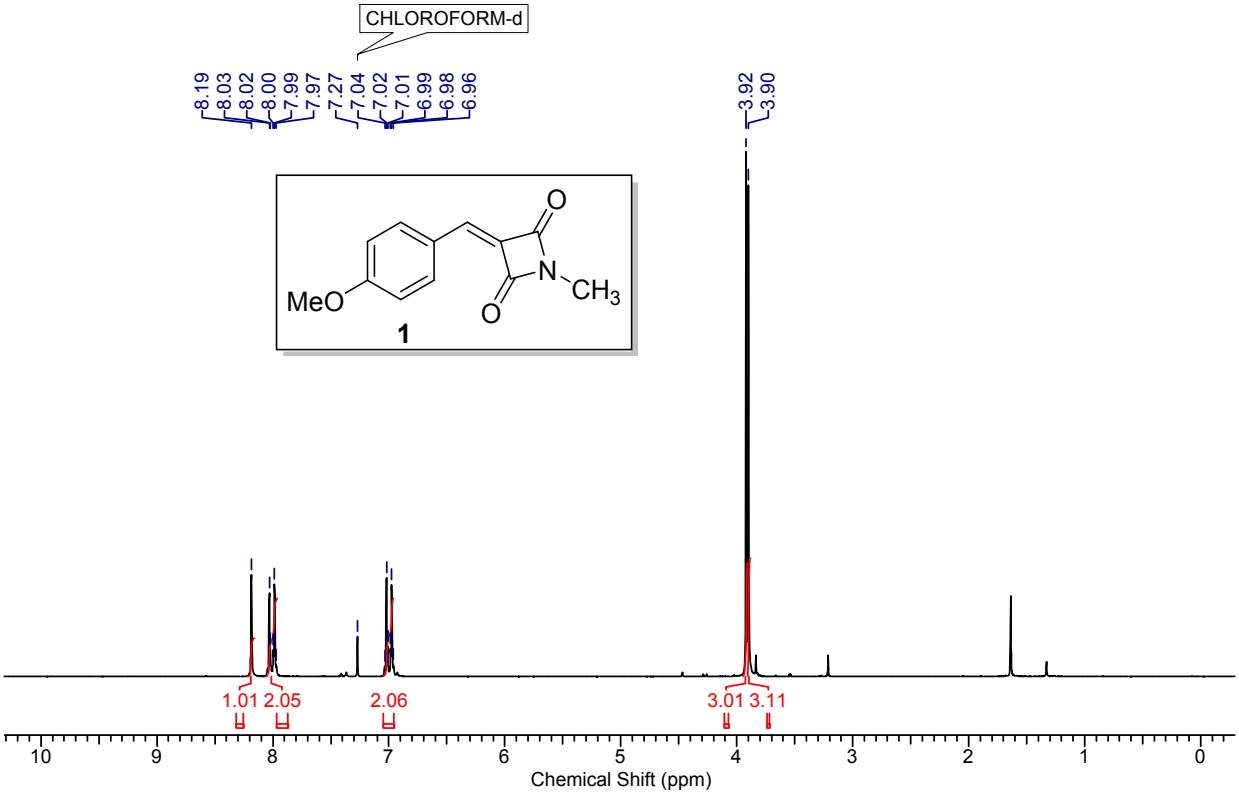

DMSO-d6
163.52
147.08
139.63
136.53
135.66
128.75
116.29
99.11
40.76
40.35
39.92
39.51
39.10
38.67
38.26
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

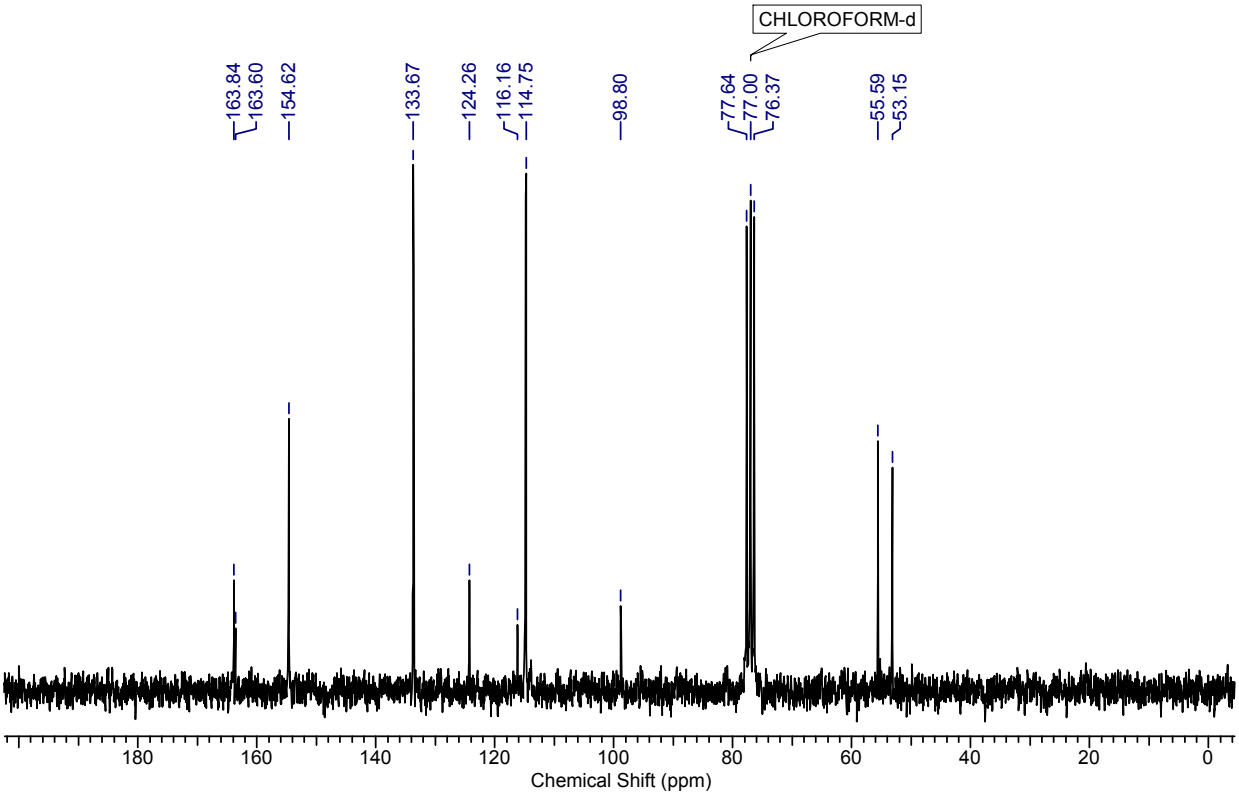

DMSO
13.64
8.36
8.11
8.08
7.22
7.19
2.44
Me
O
NH
S
O
4b
1.01
1.00
0.99
1.09
3.14
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

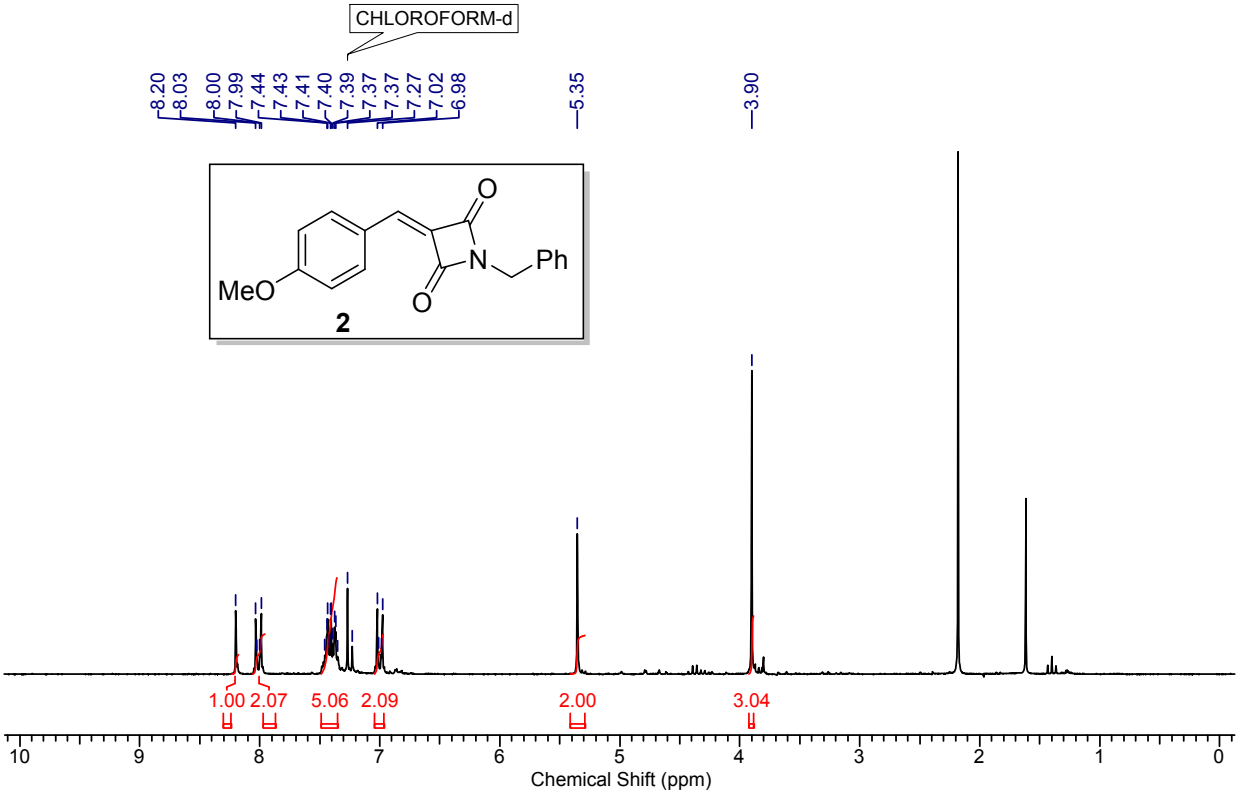

DMSO-d6
163.79
149.80
144.27
135.14
131.46
129.84
116.41
97.64
40.77
40.35
39.93
39.51
39.10
38.68
38.26
14.31
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

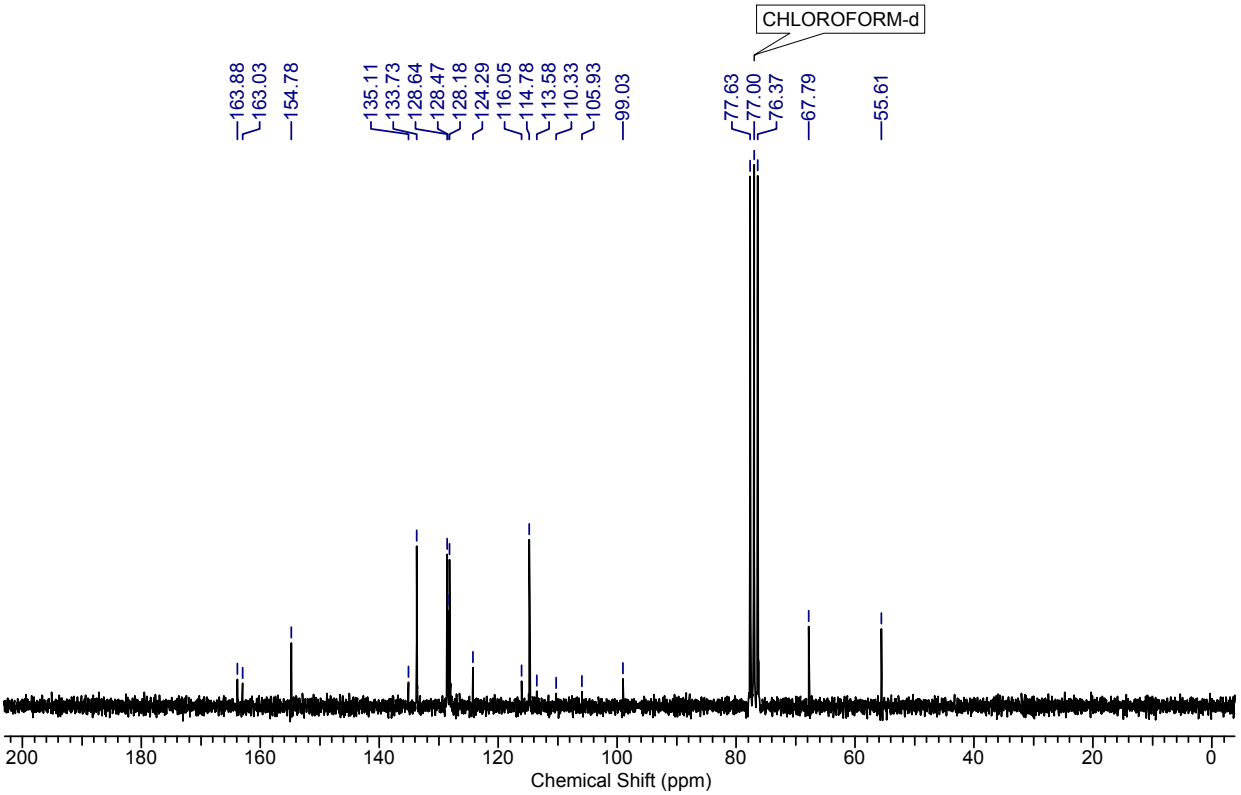

8.34
7.83
7.77
7.75
7.71
7.69
7.59
7.57
7.49
7.47
DMSO-d6
O
NH
Br
S
O
4c
0.70 1.07 1.11 1.00
10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

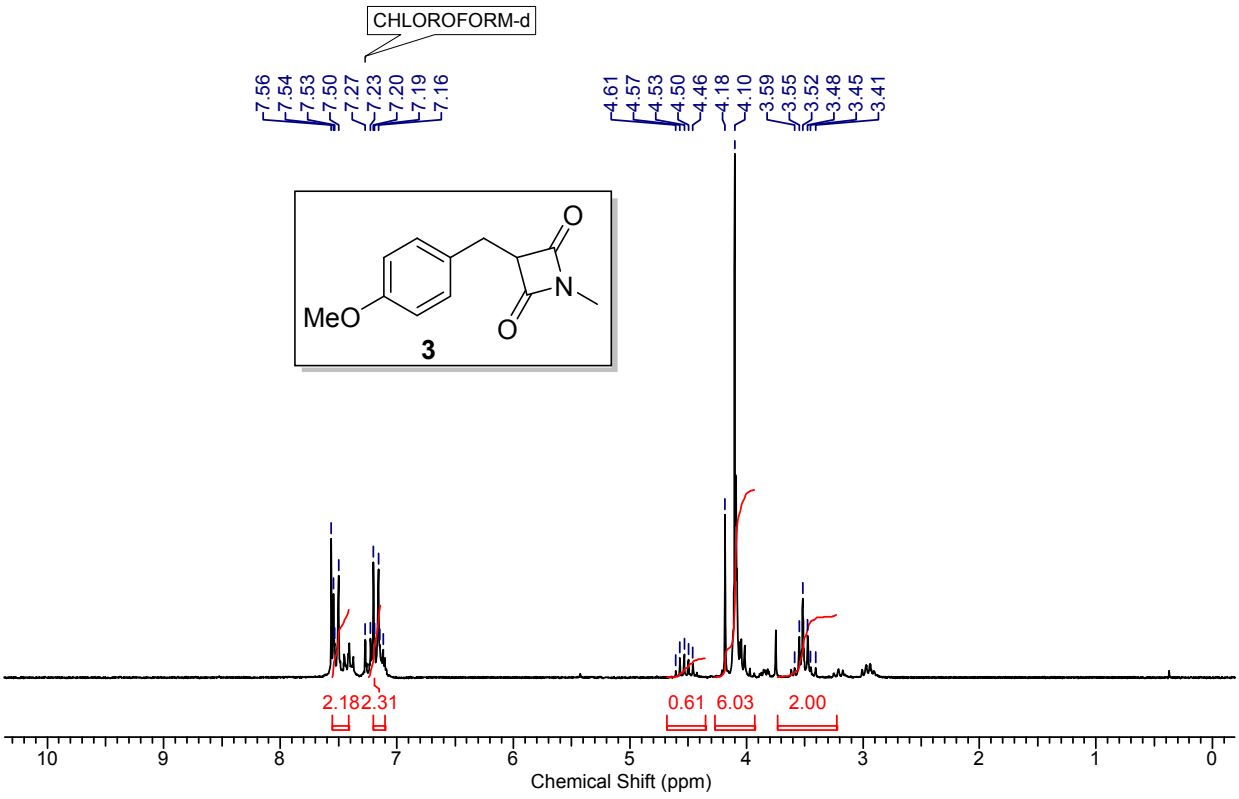

162.75
152.95
144.41
143.48
141.73
140.94
139.25
137.98
137.30
133.20
132.44
131.22
125.87
121.74
117.16
114.63
103.12
40.63
40.42
40.21
40.00
39.79
39.58
39.37
200 180 160 140 120 100 80 60 40 20 0
Chemical Shift (ppm)

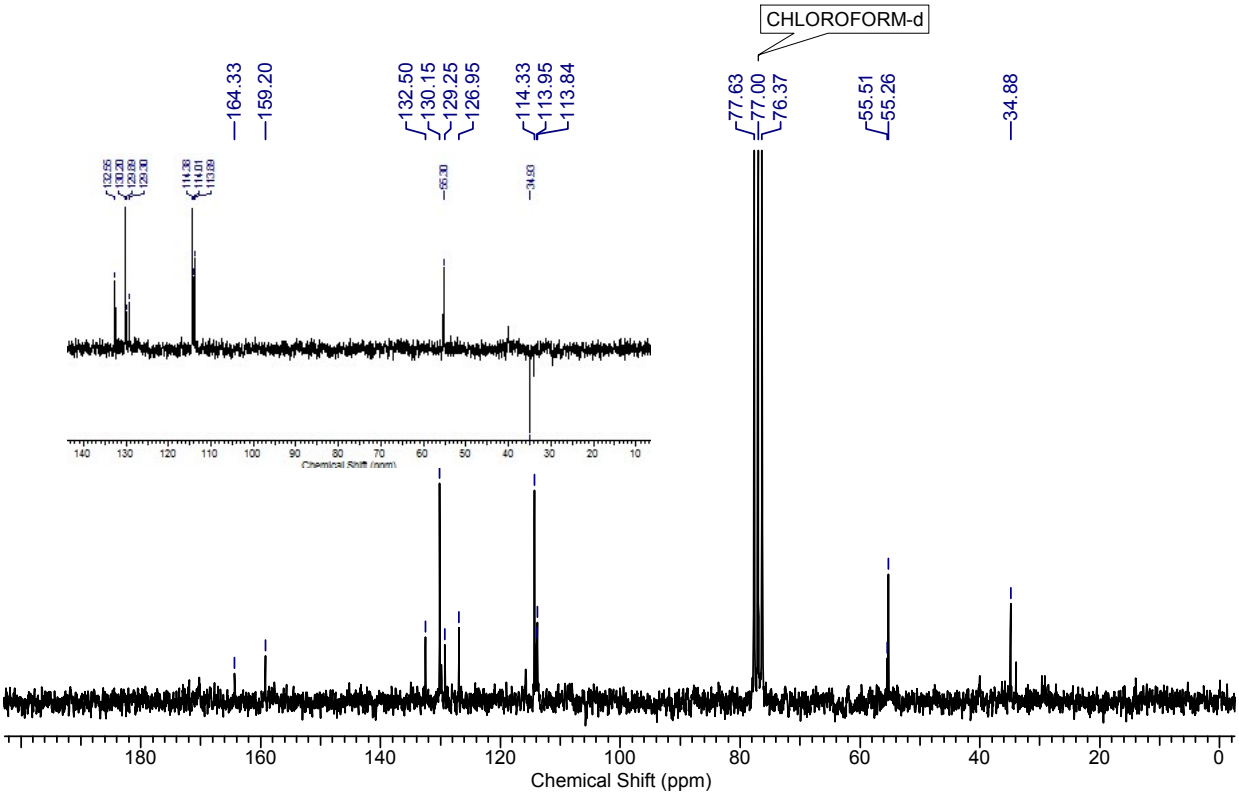

CHLOROFORM-d
8.19
8.03
8.02
8.00
7.99
7.97
7.27
7.04
7.02
7.01
6.99
6.98
6.96
3.92
3.90
MeO
N
CH3
O
O
1
1.01
2.05
2.06
3.01
3.11
Chemical Shift (ppm)

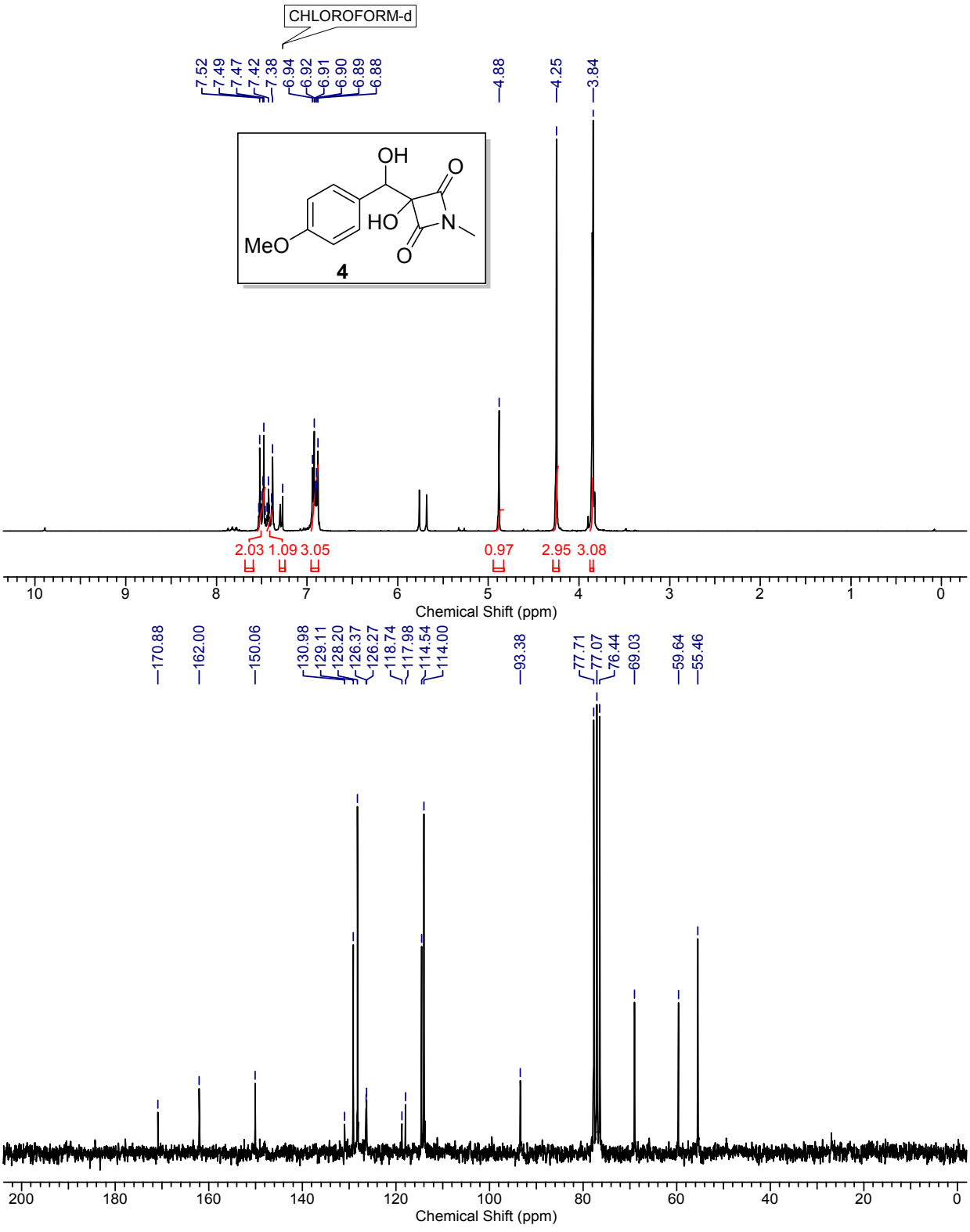

CHLOROFORM-d
163.84
163.60
154.62
133.67
124.26
116.16
114.75
98.80
77.64
77.00
76.37
55.59
53.15
Chemical Shift (ppm)

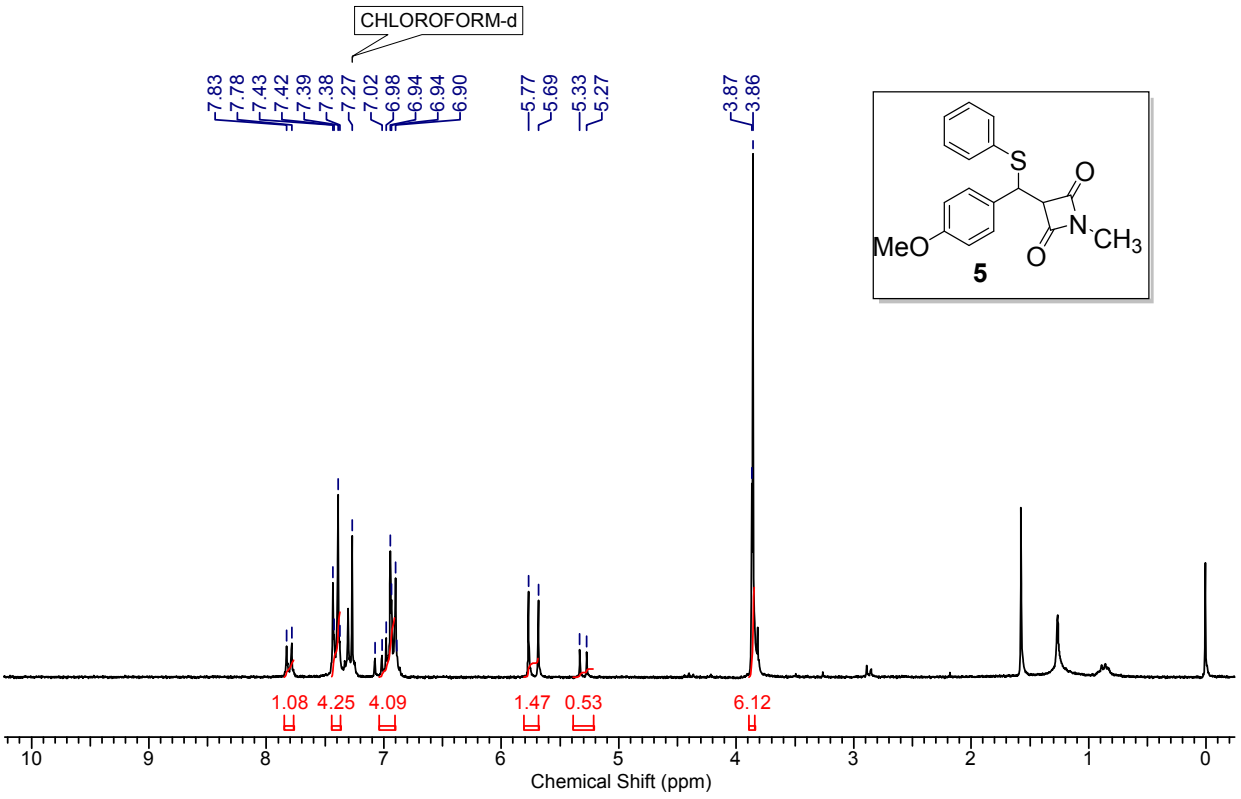

CHLOROFORM-d
8.20
8.03
8.00
7.99
7.44
7.43
7.41
7.40
7.39
7.37
7.37
7.27
7.02
6.98
5.35
3.90
O
N
Ph
MeO
O
2
1.00
2.07
5.06
2.09
2.00
3.04
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

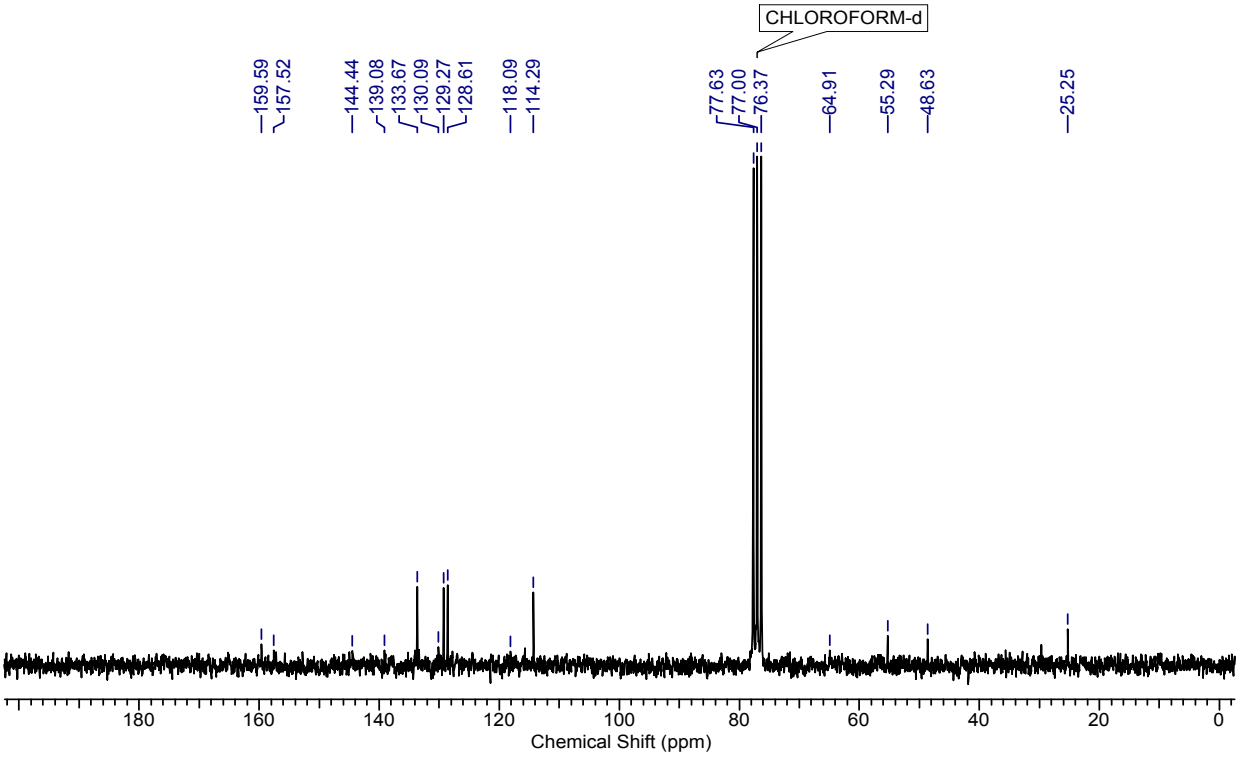

CHLOROFORM-d
163.88
163.03
154.78
135.11
133.73
128.64
128.47
128.18
124.29
116.05
114.78
113.58
110.33
105.93
99.03
77.63
77.00
76.37
67.79
55.61
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


CHLOROFORM-d
7.56
7.54
7.53
7.50
7.27
7.23
7.20
7.19
7.16
4.61
4.57
4.53
4.50
4.46
4.18
4.10
3.59
3.55
3.52
3.48
3.45
3.41
MeO
O
N
O
3
2.18
2.31
0.61
6.03
2.00
Chemical Shift (ppm)


CHLOROFORM-d
164.33
159.20
132.50
130.15
129.25
126.95
114.33
113.95
113.84
77.63
77.00
76.37
55.51
55.26
34.88
Chemical Shift (ppm)


CHLOROFORM-d
7.52
7.49
7.47
7.42
7.38
6.94
6.92
6.91
6.90
6.89
6.88
4.88
4.25
3.84
OH
O
HO
N
MeO
O
4
2.03
1.09
3.05
0.97
2.95
3.08
Chemical Shift (ppm)
170.88
162.00
150.06
130.98
129.11
128.20
126.37
126.27
118.74
117.98
114.54
114.00
93.38
77.71
77.07
76.44
69.03
59.64
55.46
Chemical Shift (ppm)


CHLOROFORM-d
7.83
7.78
7.43
7.42
7.39
7.38
7.27
7.02
6.98
6.94
6.94
6.90
5.77
5.69
5.33
5.27
3.87
3.86
S
O
N
CH3
O
MeO
5
1.08
4.25
4.09
1.47
0.53
6.12
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


CHLOROFORM-d
159.59
157.52
144.44
139.08
133.67
130.09
129.27
128.61
118.09
114.29
77.63
77.00
76.37
64.91
55.29
48.63
25.25
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)