Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Electronic Supporting Information

Synthesis and biological evaluation of isatin oxime ether-tethered aryl 1*H*-1,2,3 triazoles as inhibitors of *Mycobacterium tuberculosis*

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c. *Medicinal Chemistry & Antimycobacterial Research laboratory, Pharmacy group, Birla Institute of Technology and Science-Pilani, Hyderabad campus, Telangana state-500078, India.*
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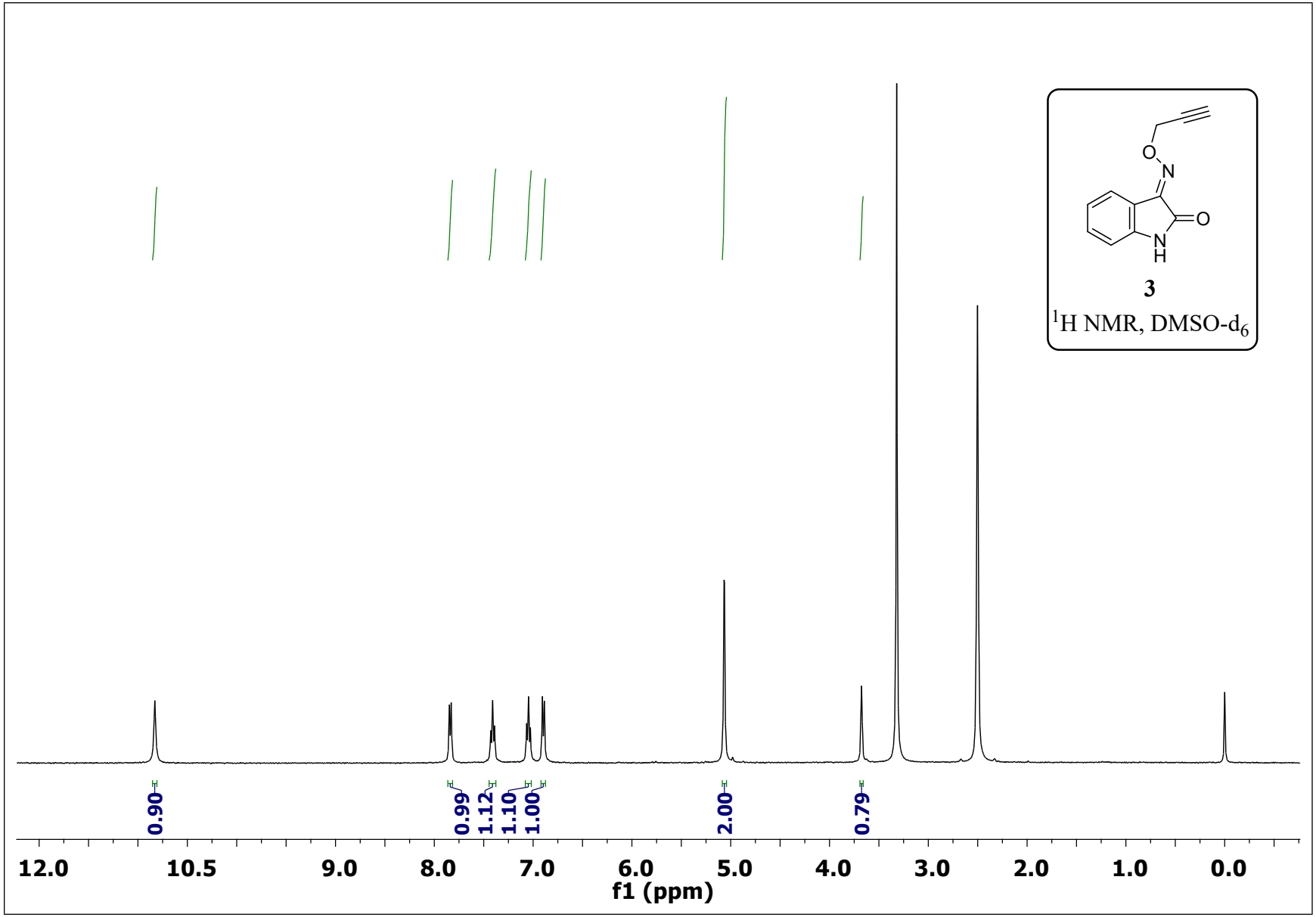
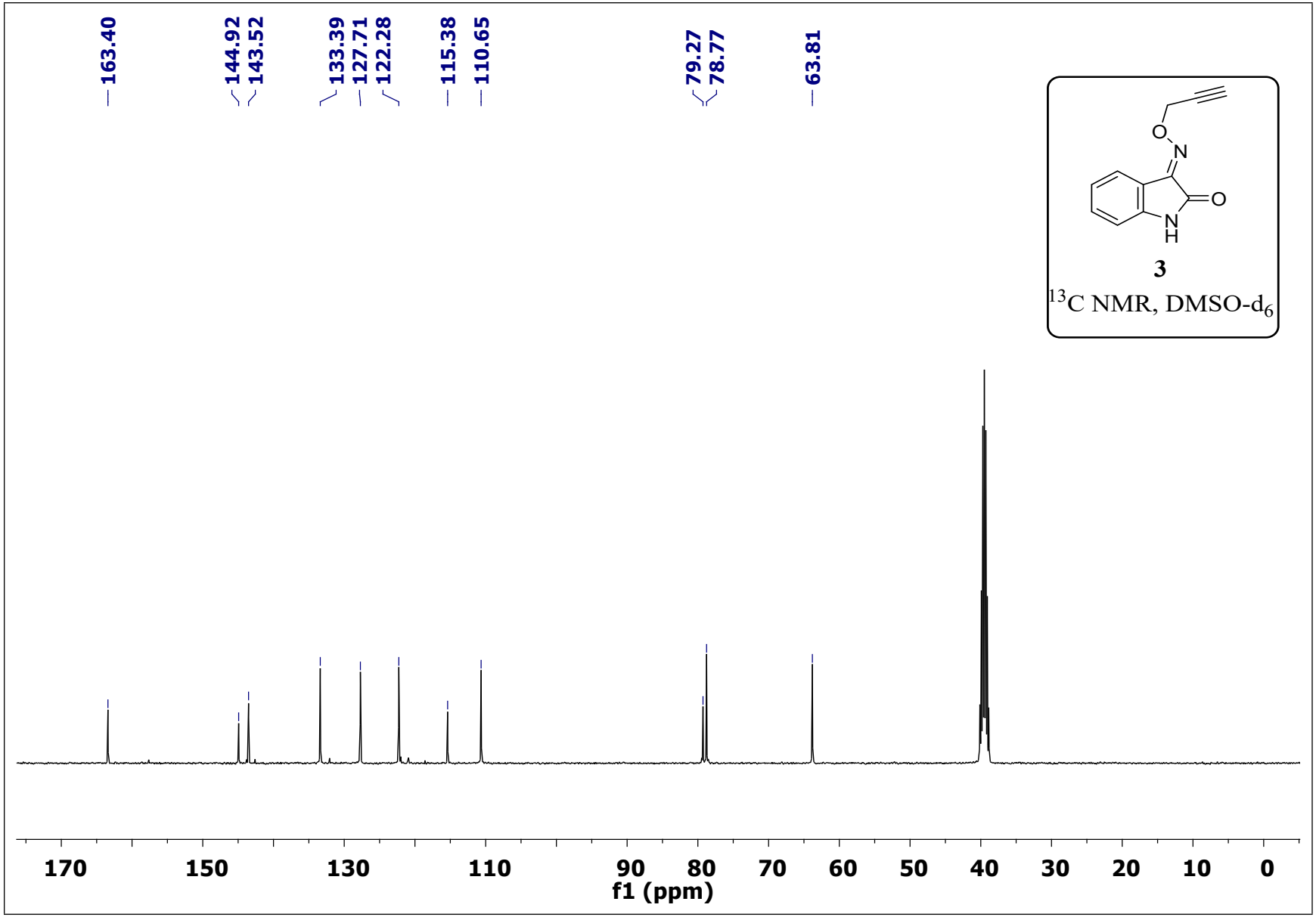
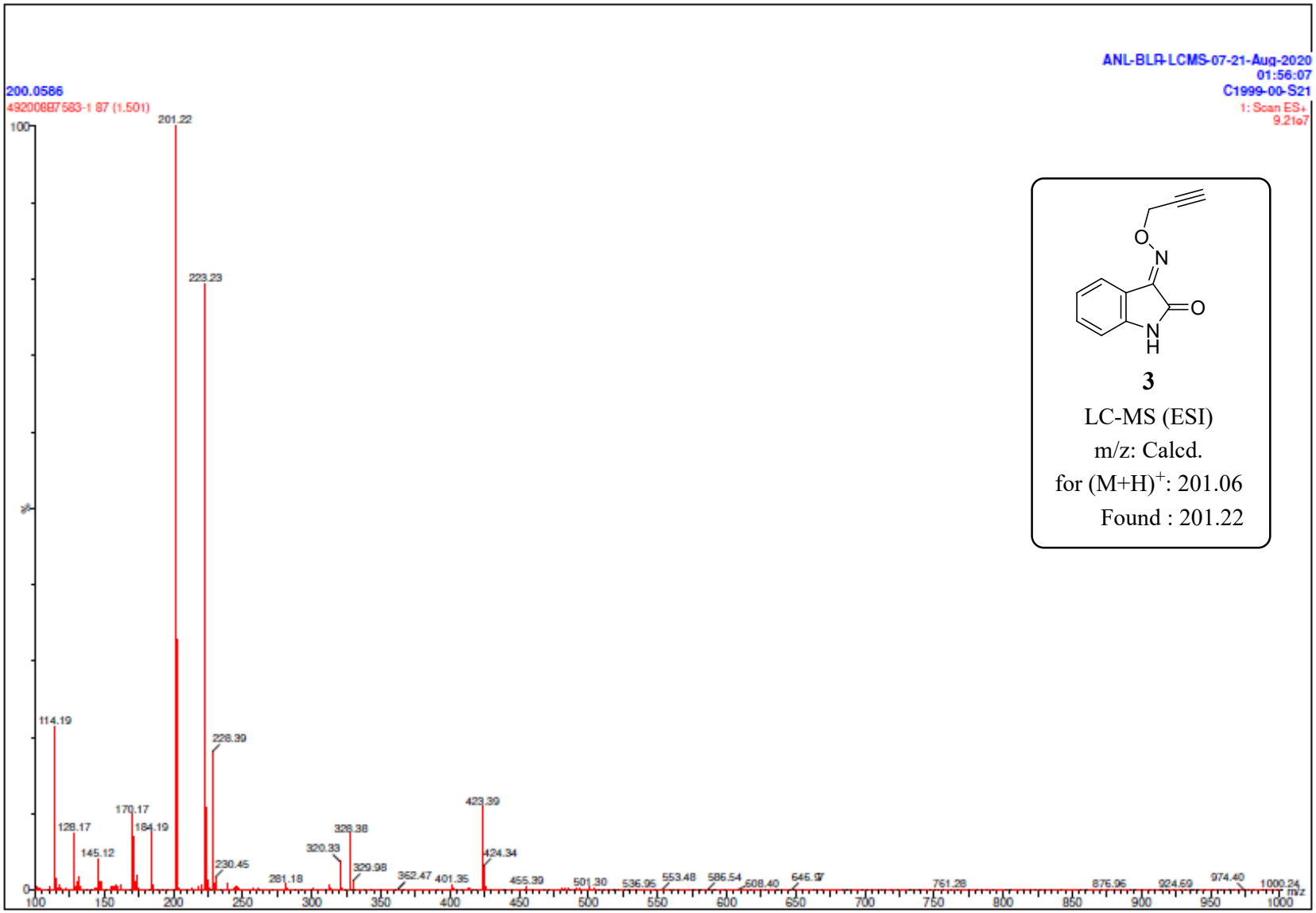

3
^{1}H NMR, DMSO-d$_6$
0.90
0.99
1.12
1.10
1.00
2.00
0.79
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


163.40
144.92
143.52
133.39
127.71
122.28
115.38
110.65
79.27
78.77
63.81
O
N
O
N
H
3
13C NMR, DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



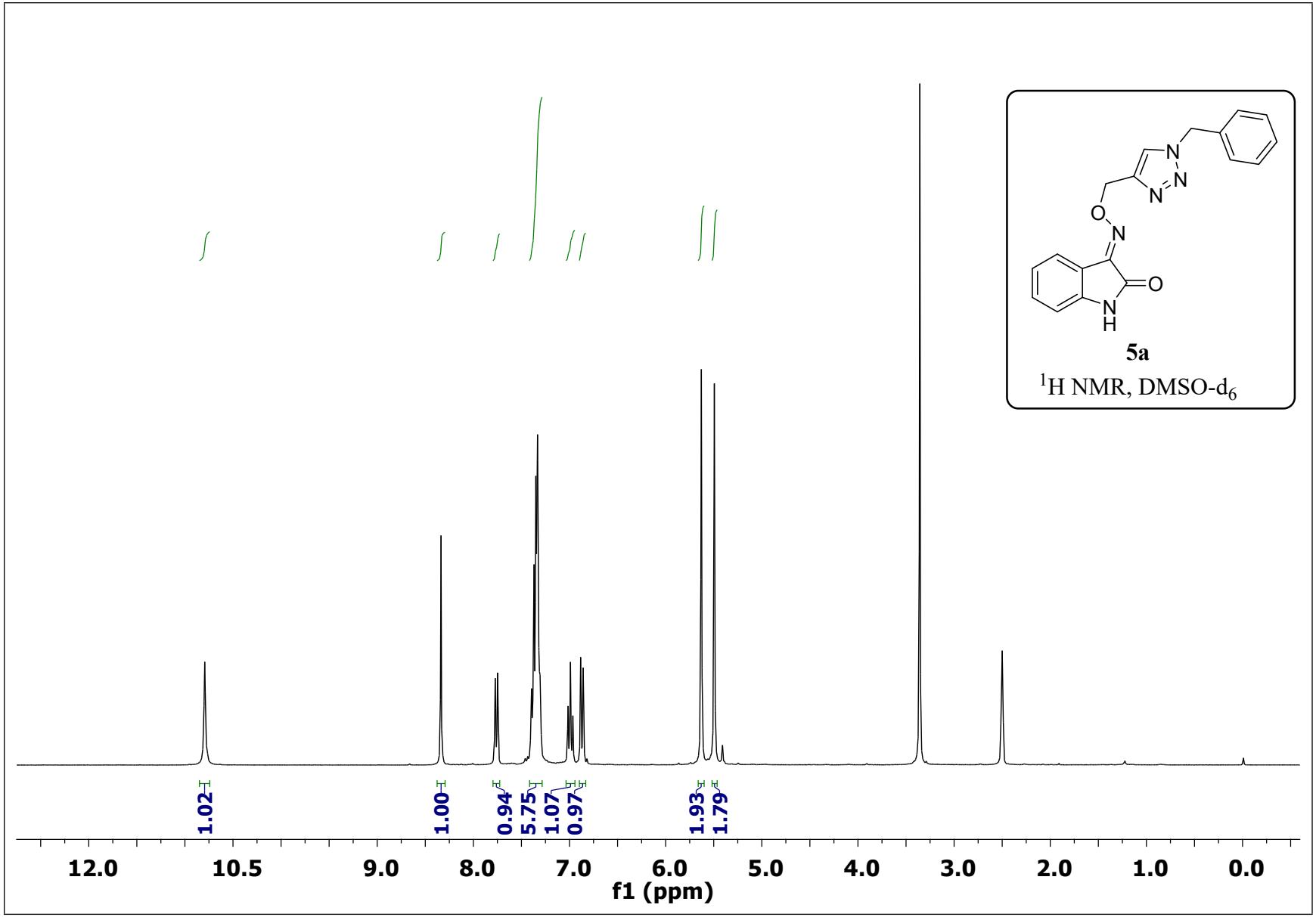
3

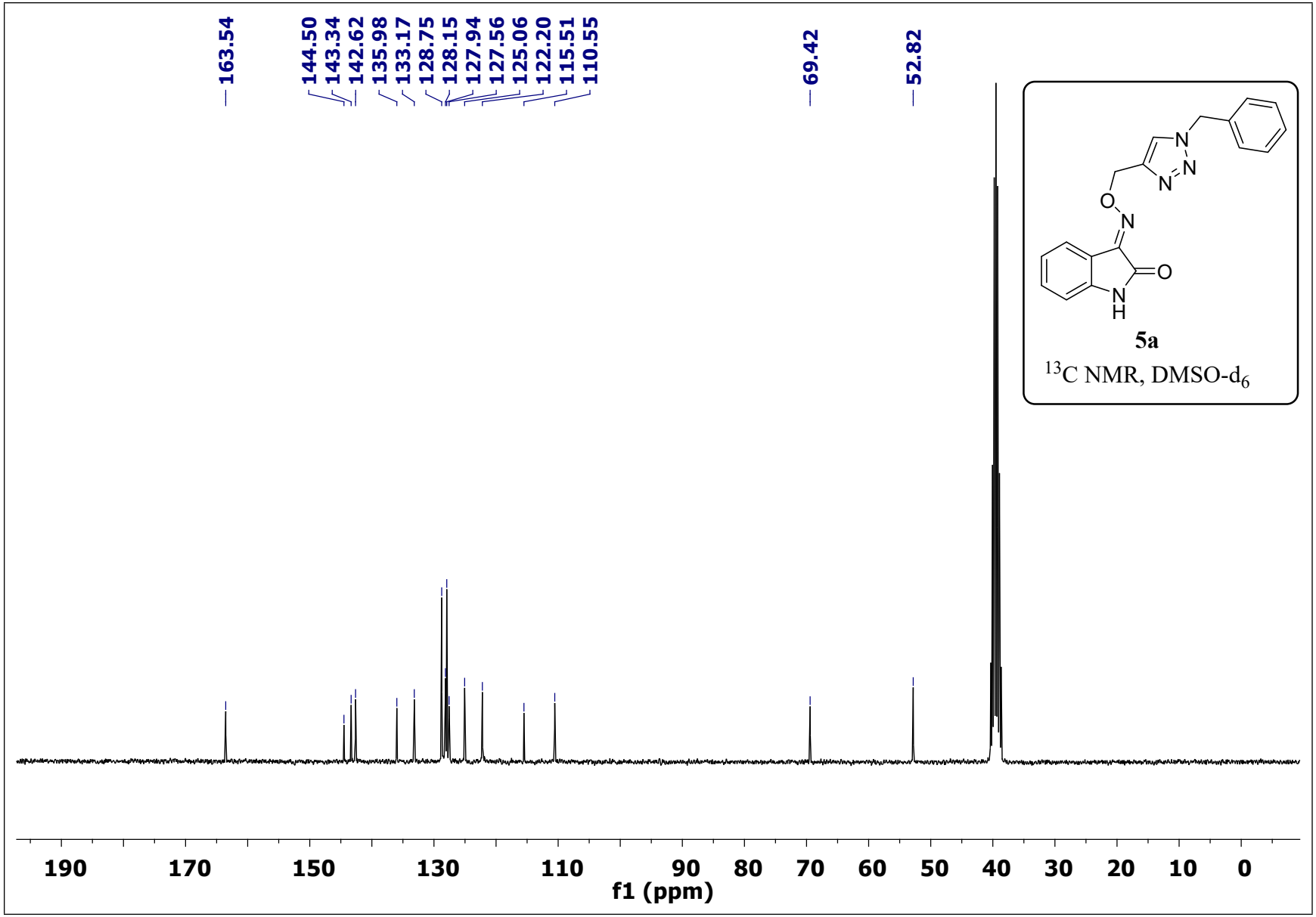
LC-MS (ESI)

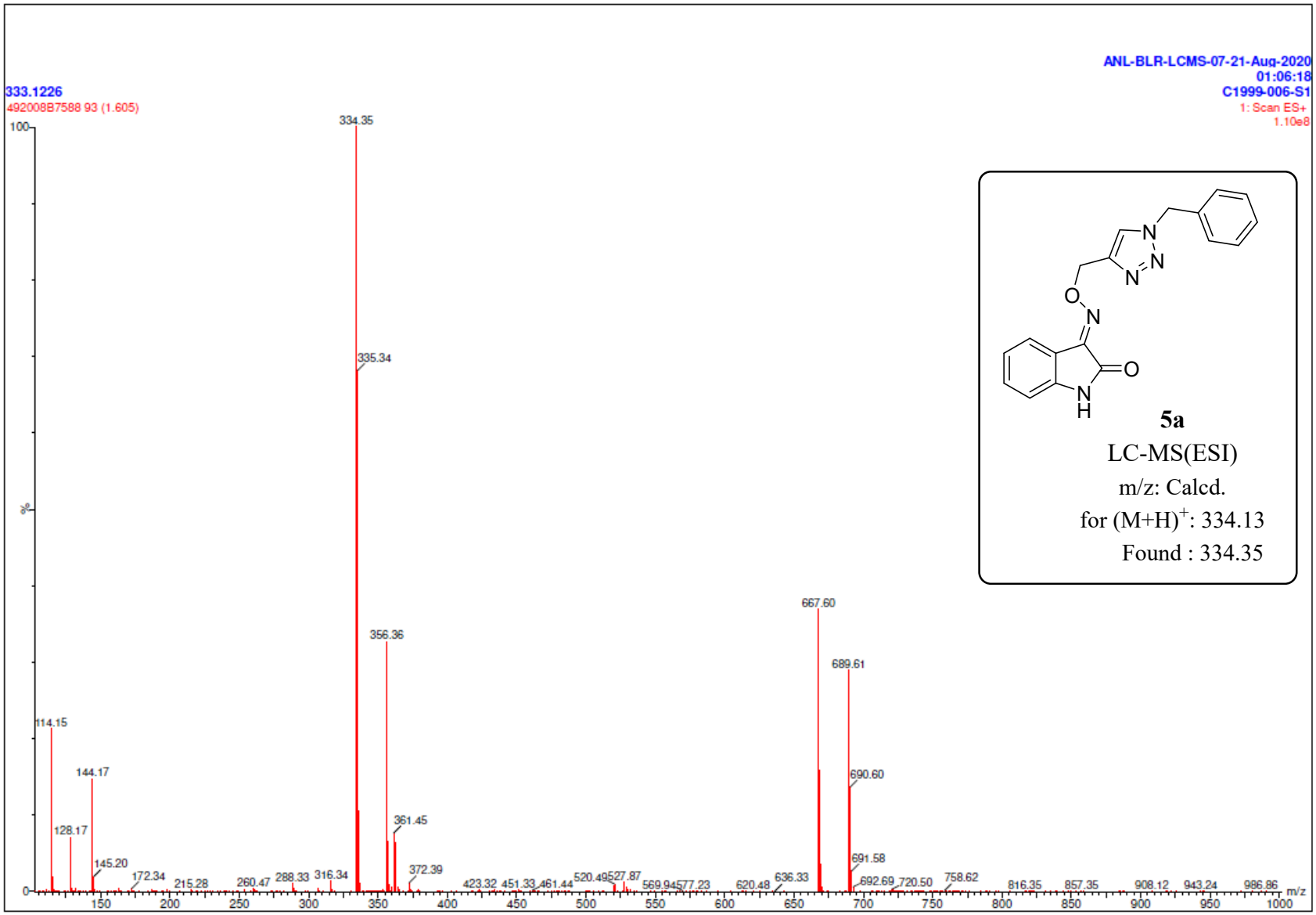
m/z: Calcd.

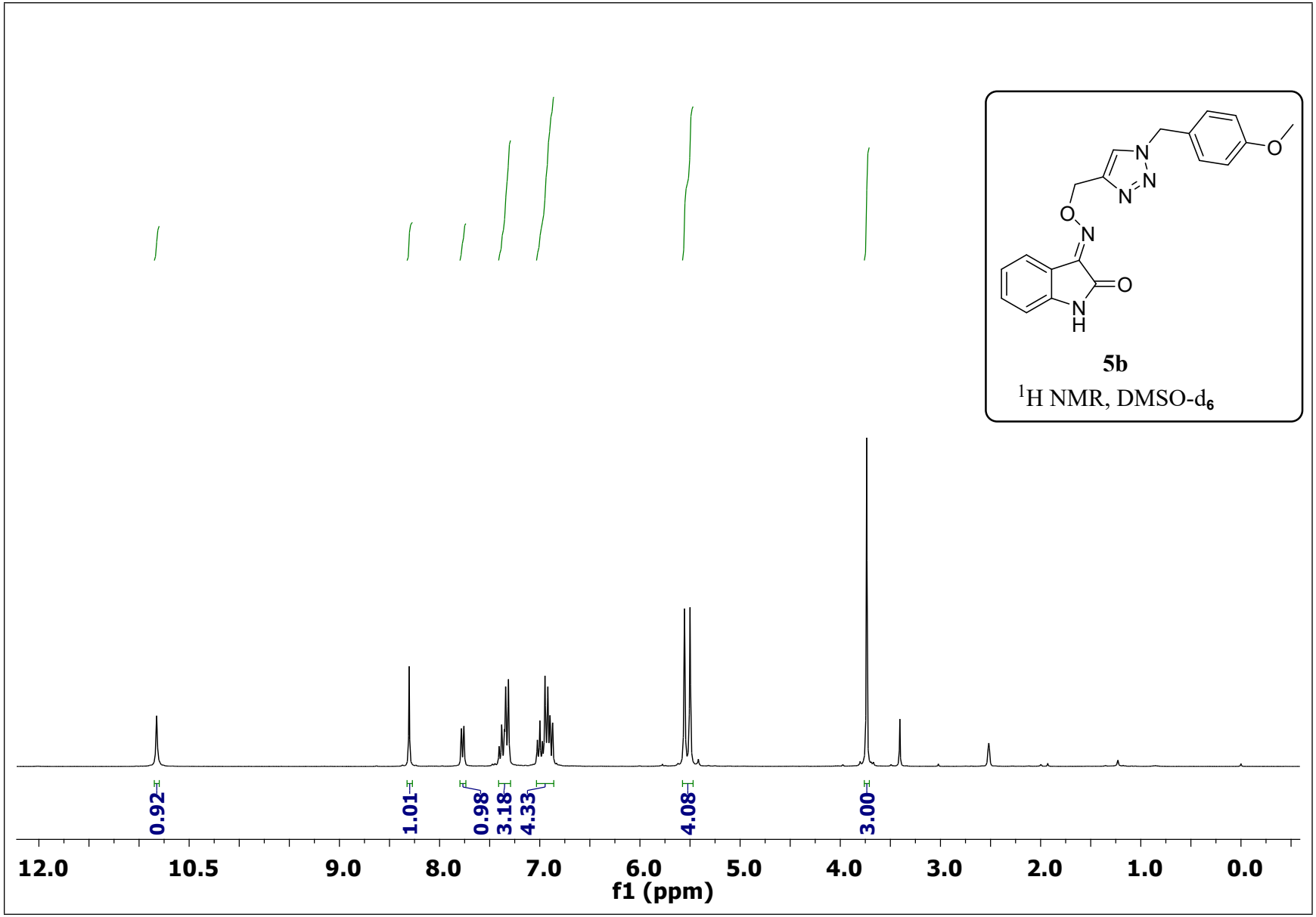
for $(M+H)^+$: 201.06

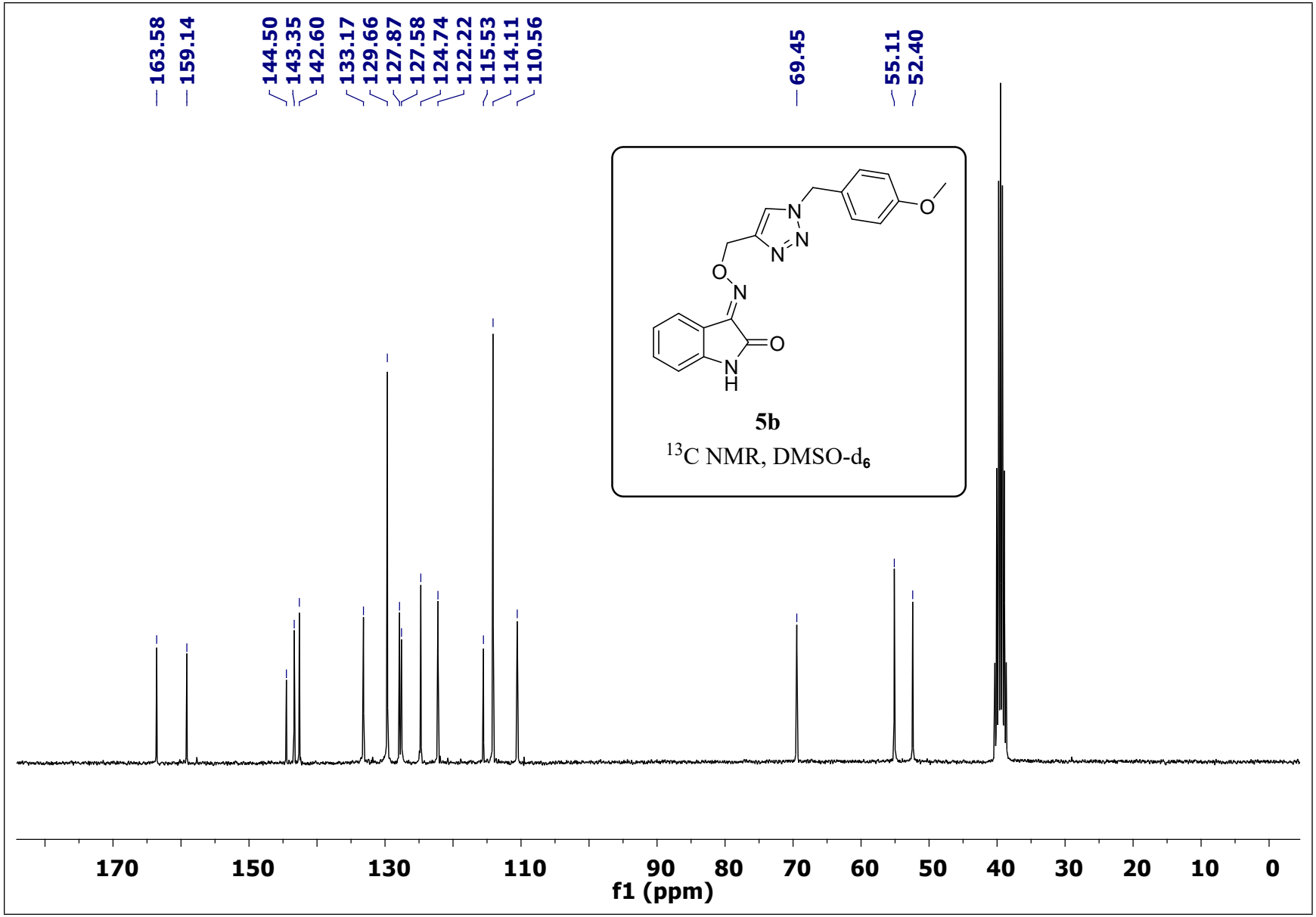
Found : 201.22

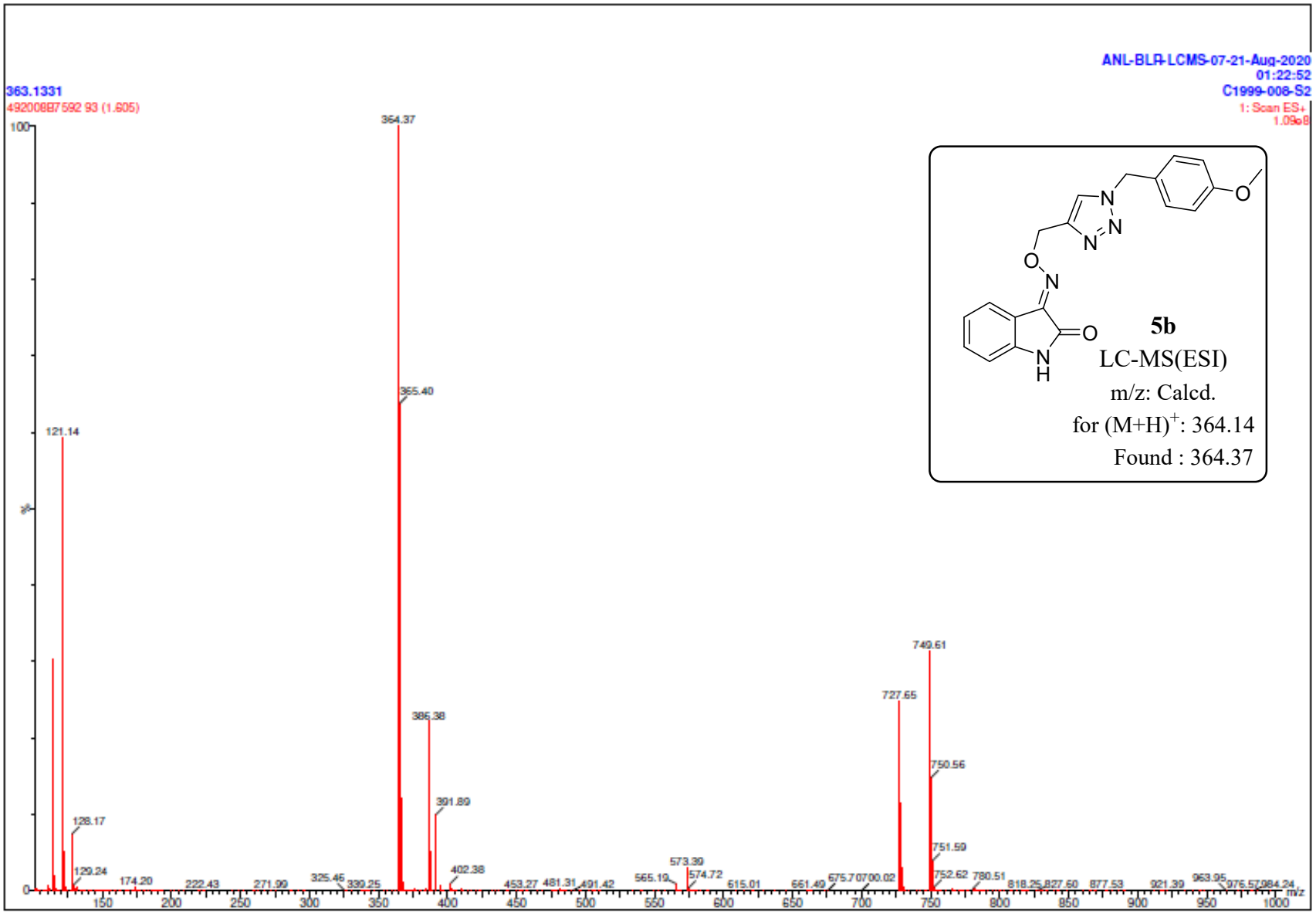

5a
^{1}H NMR, DMSO-d$_6$
1.02
1.00
0.94
5.75
1.07
0.97
1.93
1.79
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

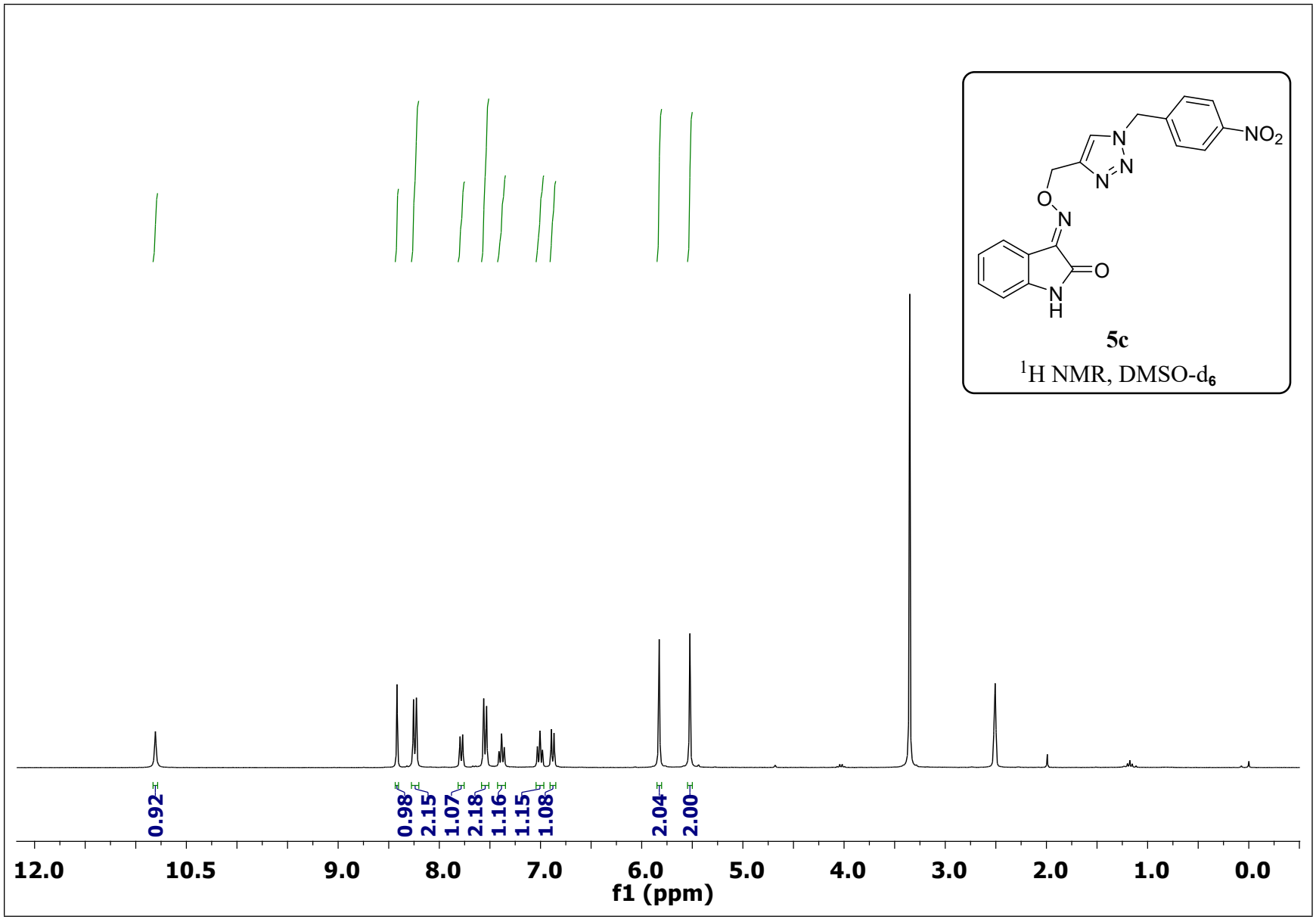

163.54
144.50
143.34
142.62
135.98
133.17
128.75
128.15
127.94
127.56
125.06
122.20
115.51
110.55
69.42
52.82
5a
13C NMR, DMSO-d6
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

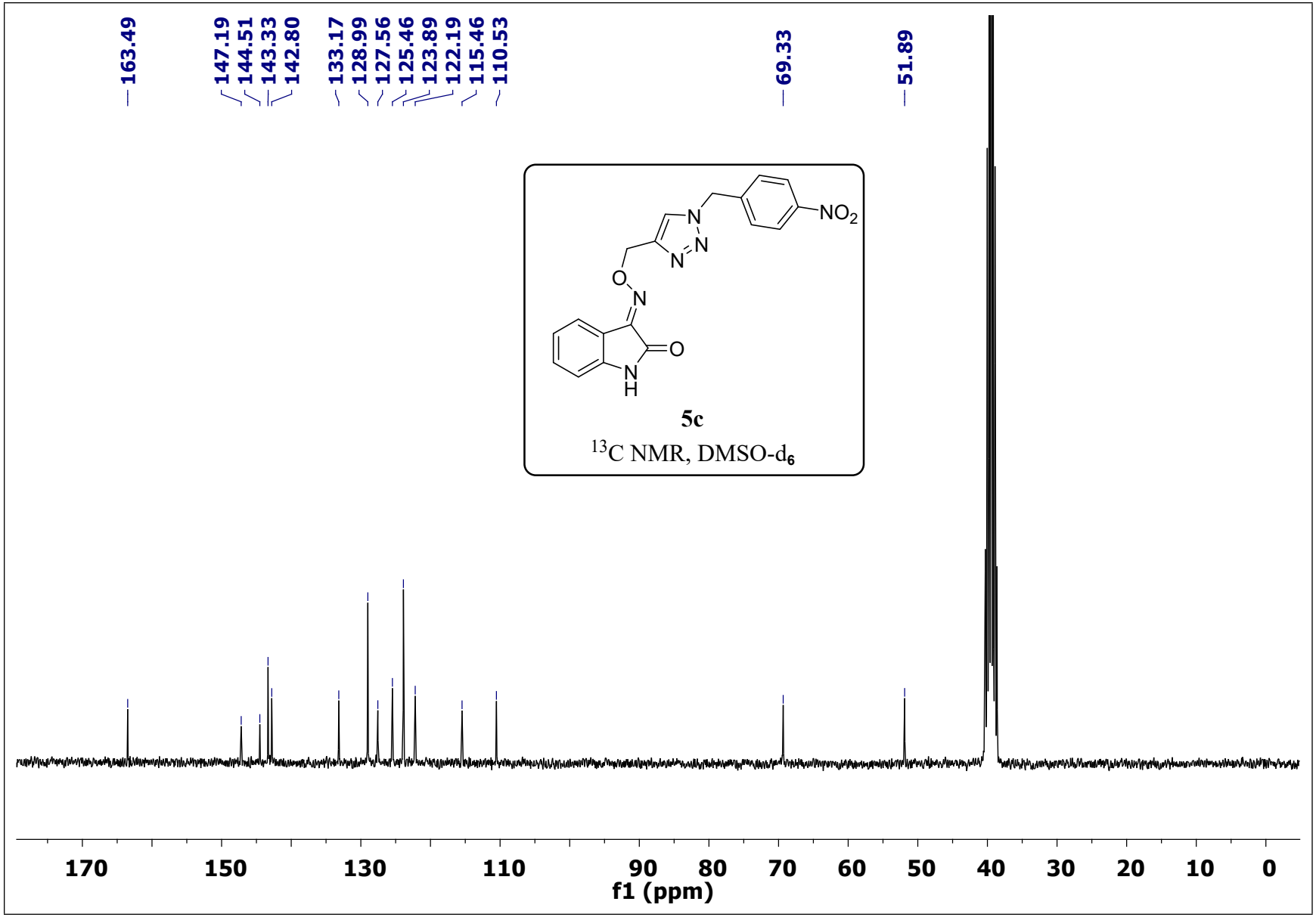

ANL-BLR-LCMS-07-21-Aug-2020
01:06:18
C1999-006-S1
1: Scan ES+
1.10e8
333.1226
492008B7588 93 (1.605)
100
%
0
334.35
335.34
356.36
667.60
689.61
690.60
691.58
114.15
144.17
128.17
145.20
172.34
215.28
260.47
288.33
316.34
361.45
372.39
423.32
451.33
461.44
520.49
527.87
569.94
577.23
620.48
636.33
692.69
720.50
758.62
816.35
857.35
908.12
943.24
986.86
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900
950
1000
m/z
5a
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 334.13
Found : 334.35

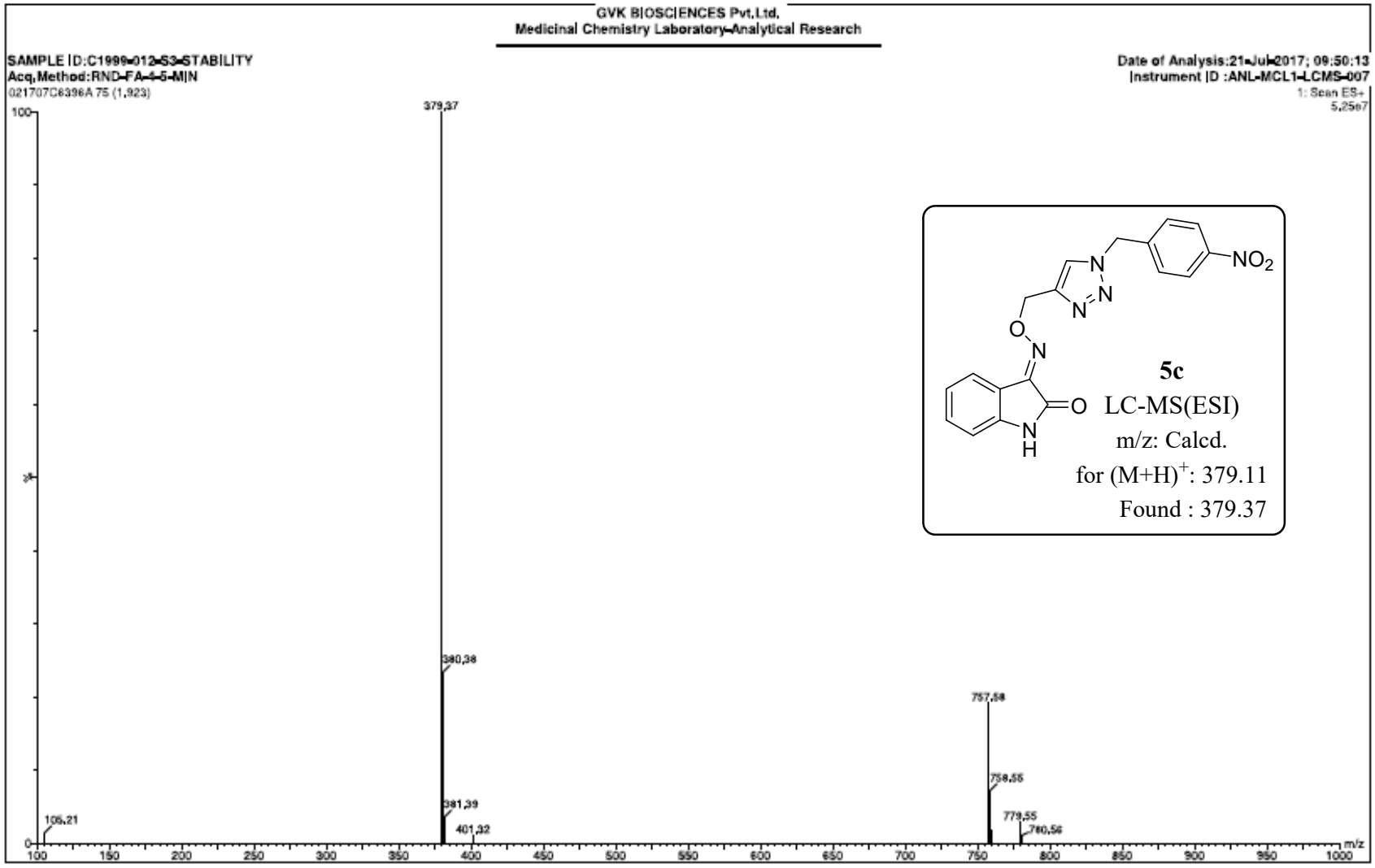

5b
1H NMR, DMSO-d6
0.92
1.01
0.98
3.18
4.33
4.08
3.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

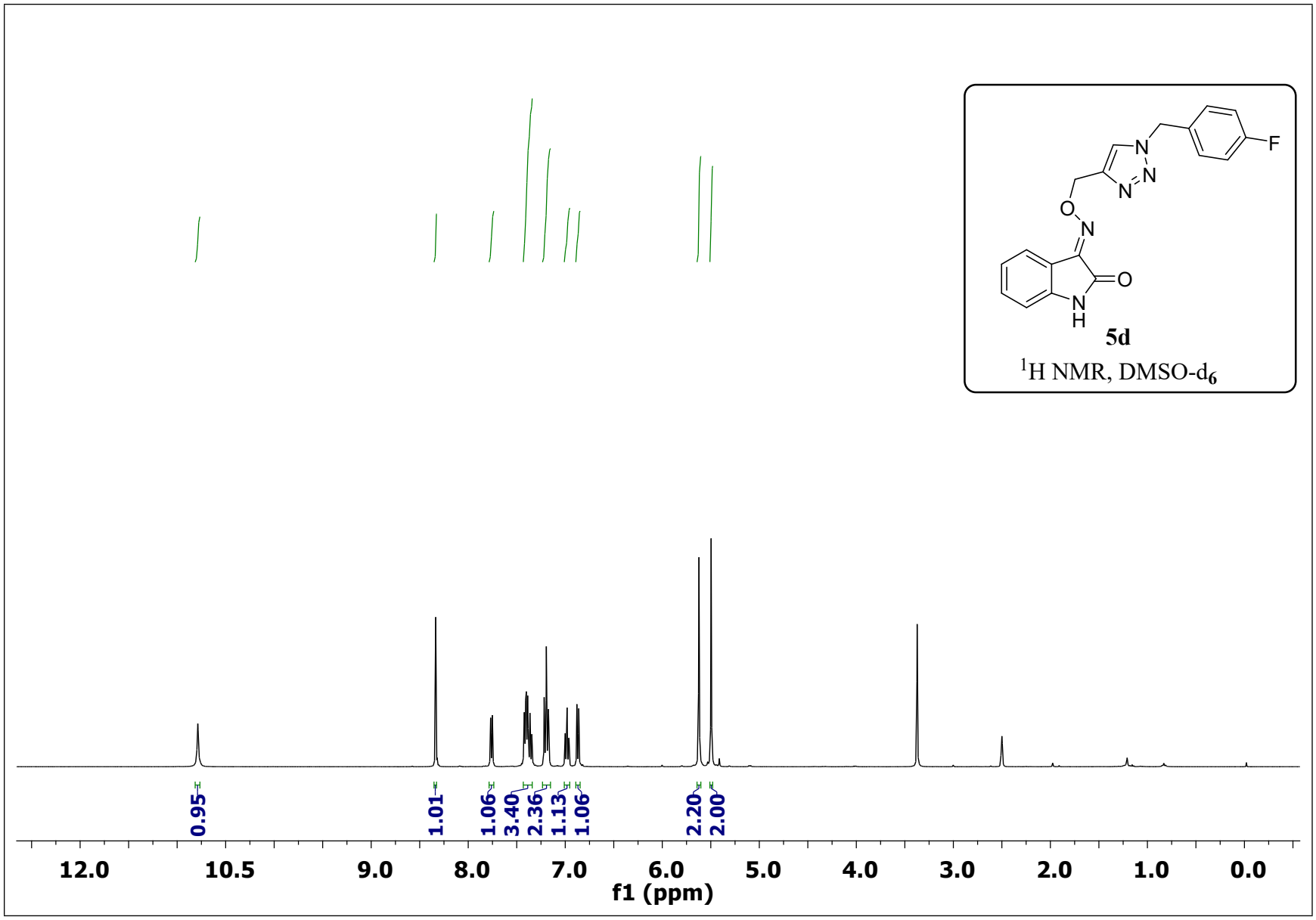

163.58
159.14
144.50
143.35
142.60
133.17
129.66
127.87
127.58
124.74
122.22
115.53
114.11
110.56
69.45
55.11
52.40
O
N
N
N
O
N
O
N
H
5b
13C NMR, DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

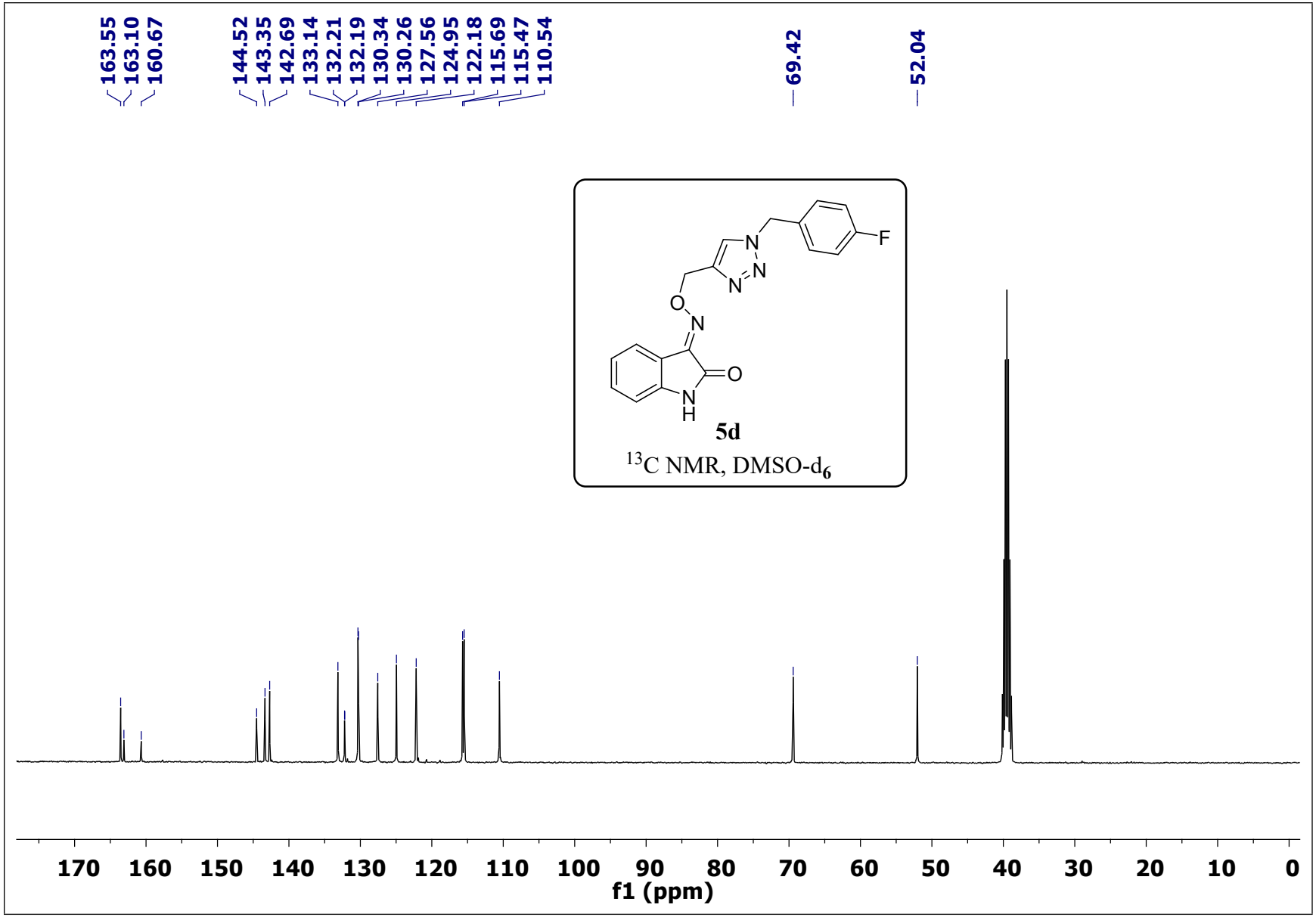

ANL-BLR-LCMS-07-21-Aug-2020
01:22:52
C1999-008-S2
1: Scan ES+
1.09e8
363.1331
4920088 7592 93 (1.605)
364.37
365.40
121.14
386.38
301.89
128.17
129.24
749.61
727.65
750.56
751.59
752.62
573.39
574.72
402.38
5b
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 364.14
Found : 364.37

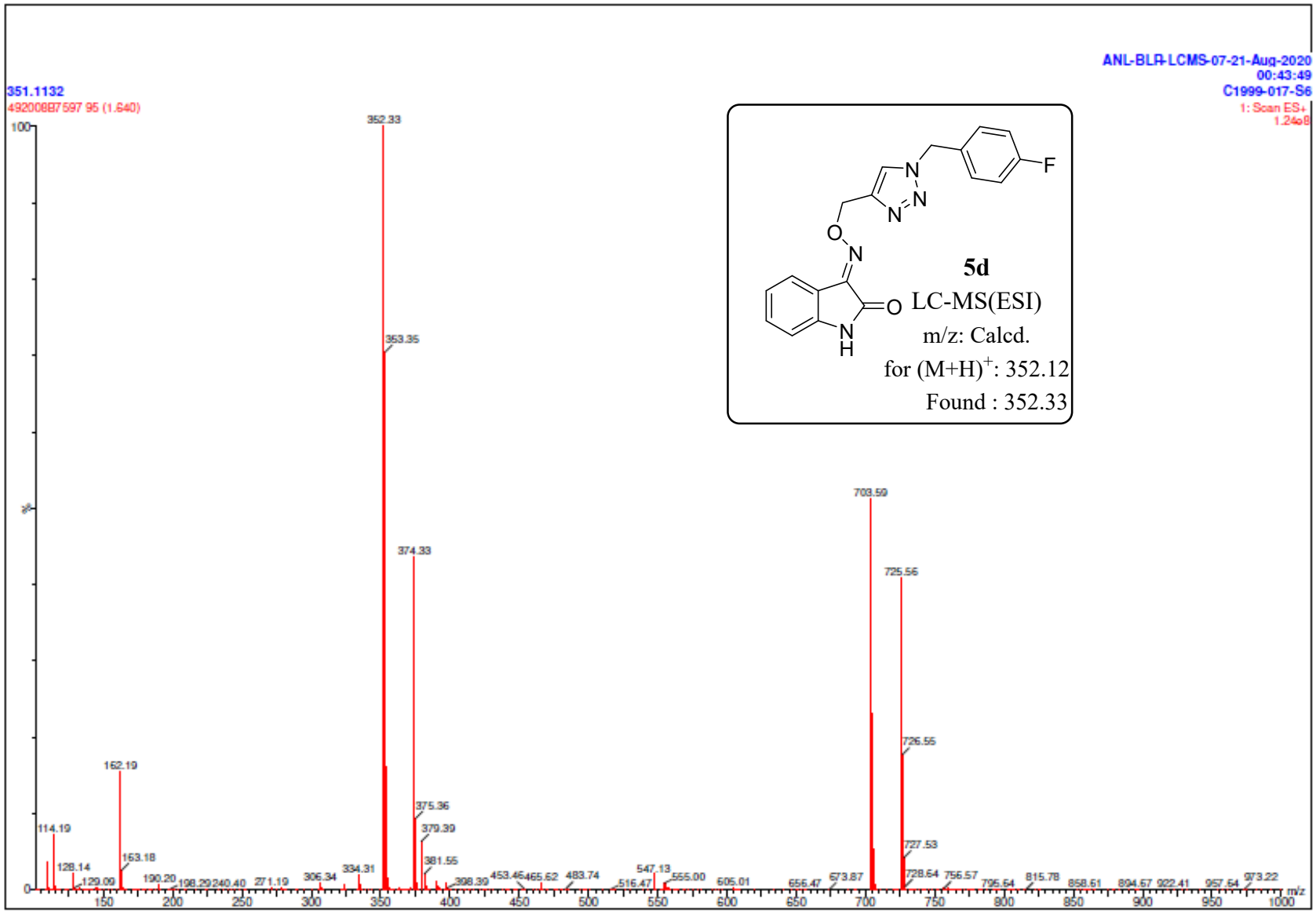

NO2
N
N
N
O
N
O
N
H
5c
1H NMR, DMSO-d6
0.92
0.98
2.15
1.07
2.18
1.16
1.15
1.08
2.04
2.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

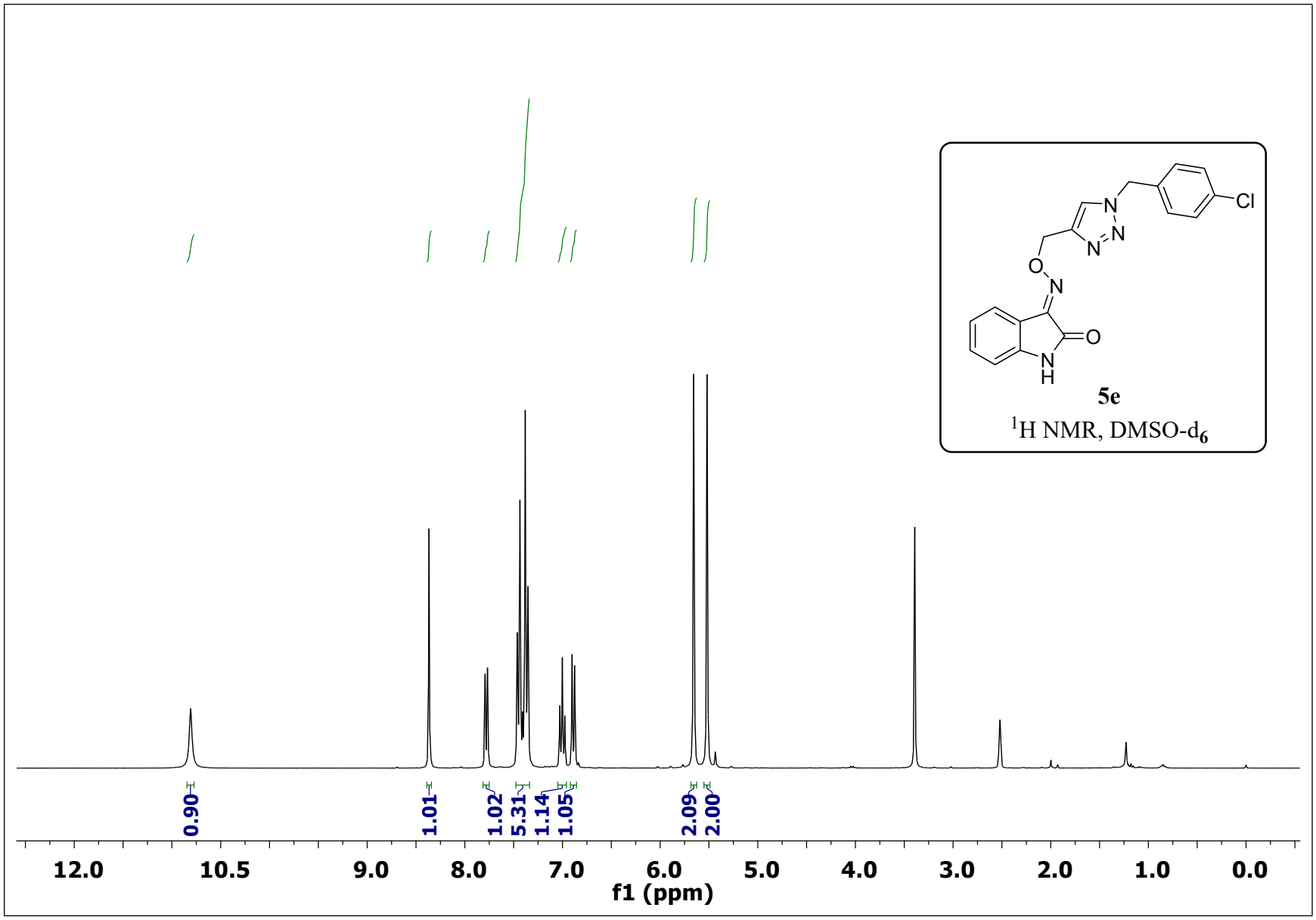

163.49
147.19
144.51
143.33
142.80
133.17
128.99
127.56
125.46
123.89
122.19
115.46
110.53
69.33
51.89
NO2
N
N
N
O
N
O
N
H
5c
13C NMR, DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

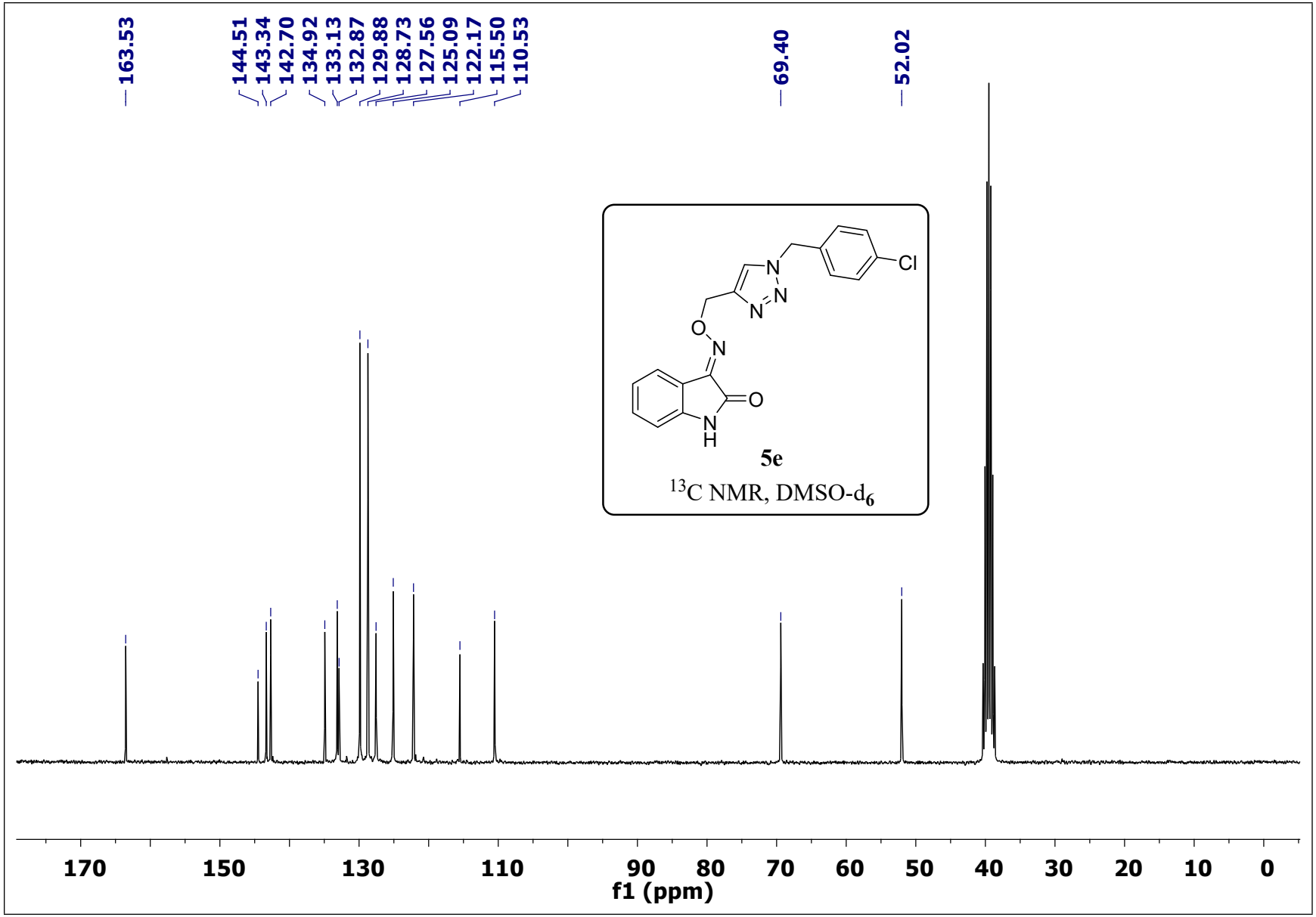

GVK BIOSCIENCES Pvt.Ltd.
Medicinal Chemistry Laboratory-Analytical Research
SAMPLE ID:C1999-012-S3-STABILITY
Acq.Method:RND-FA-4-5-MIN
021707C6396A 75 (1.923)
Date of Analysis:21-Jul-2017; 09:50:13
Instrument ID :ANL-MCL1-LCMS-007
1: Scan ES+
5.25e7
379.37
380.38
381.39
401.32
757.58
758.55
779.55
780.56
105.21
NO2
5c
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 379.11
Found : 379.37
m/z

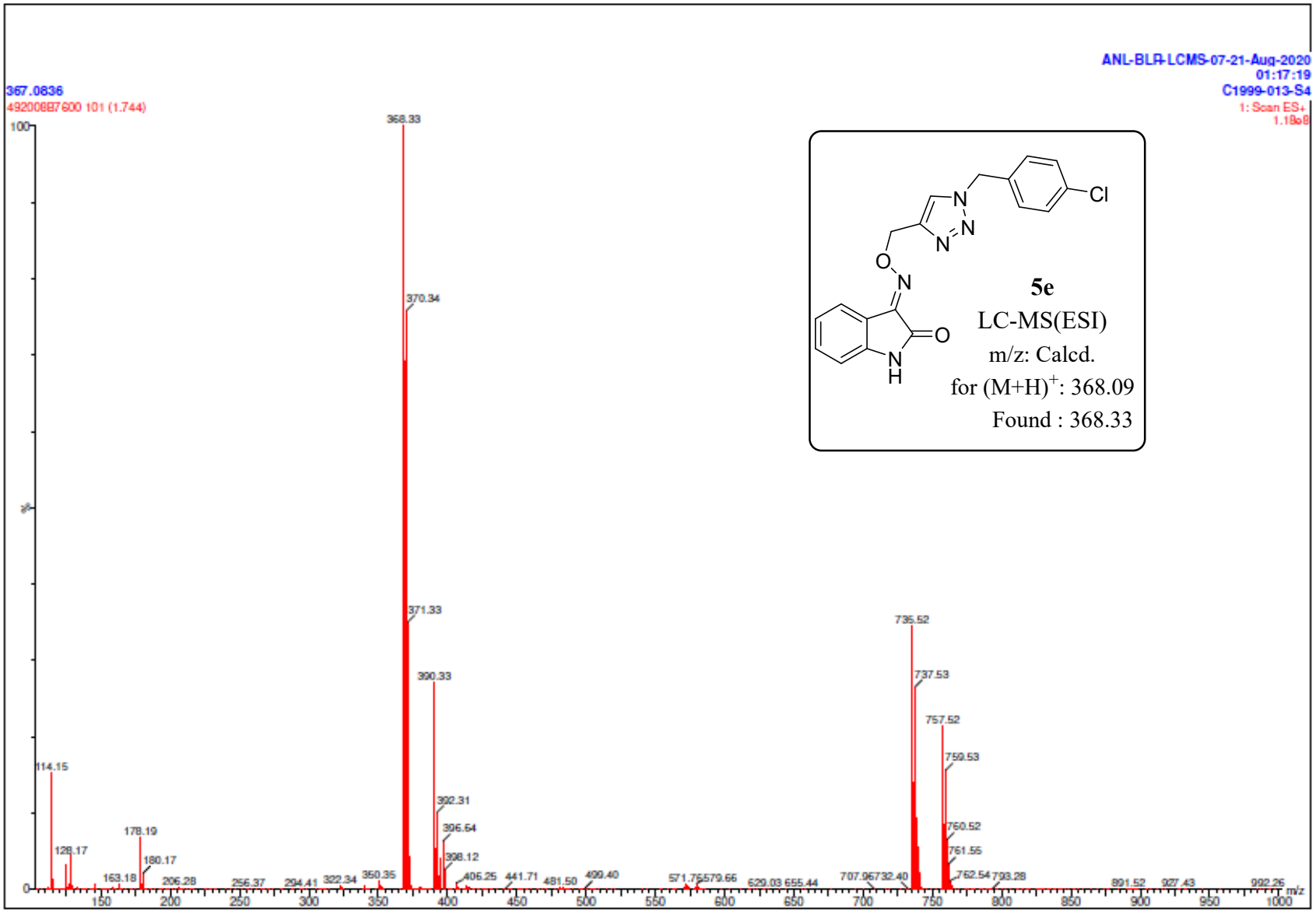

F
N
N
N
O
N
O
N
H
5d
^{1}H NMR, DMSO-d$_6$
0.95
1.01
1.06
3.40
2.36
1.13
1.06
2.20
2.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

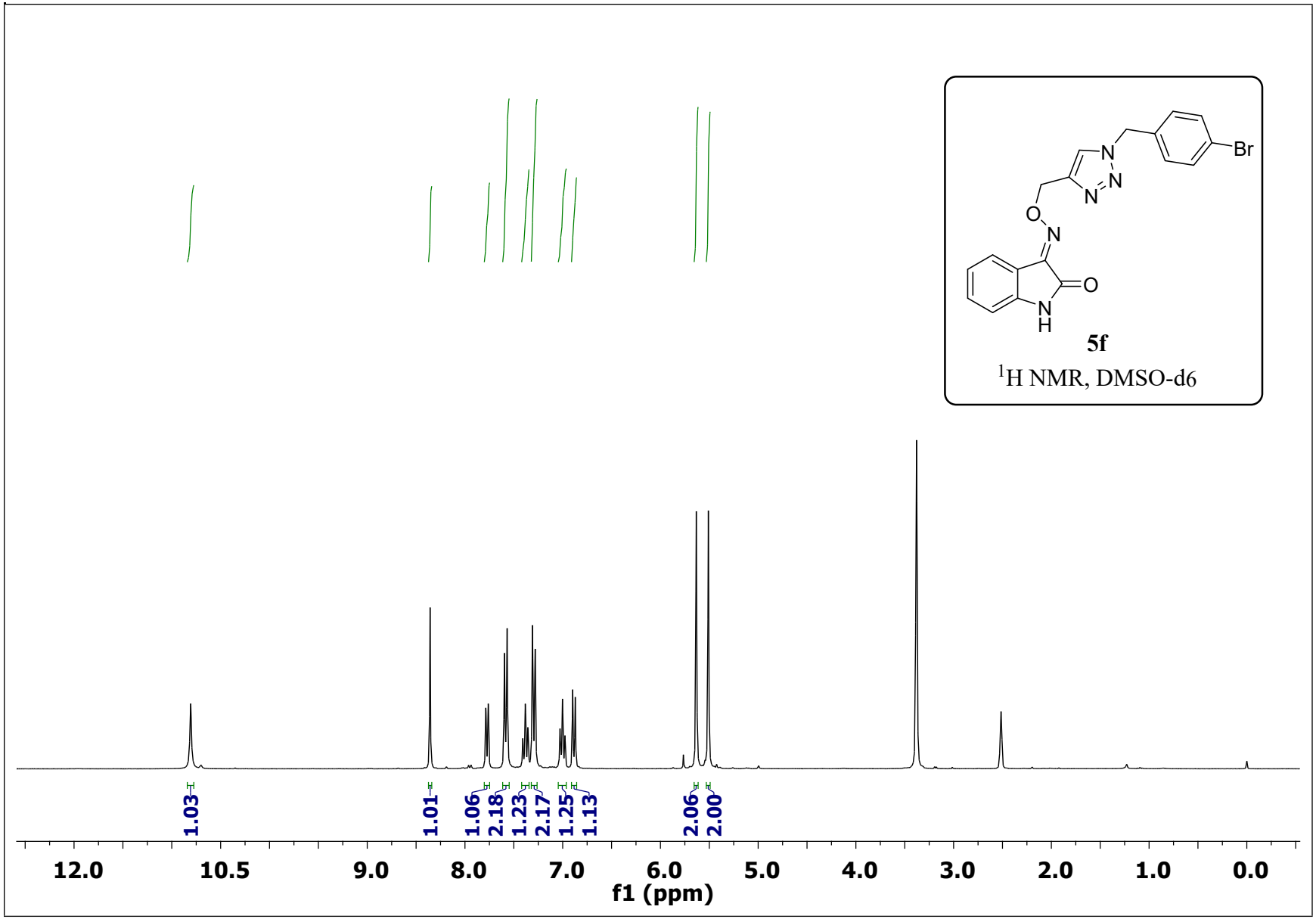

163.55
163.10
160.67
144.52
143.35
142.69
133.14
132.21
132.19
130.34
130.26
127.56
124.95
122.18
115.69
115.47
110.54
69.42
52.04
F
N
N
N
O
N
O
N
H
5d
13C NMR, DMSO-d6
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

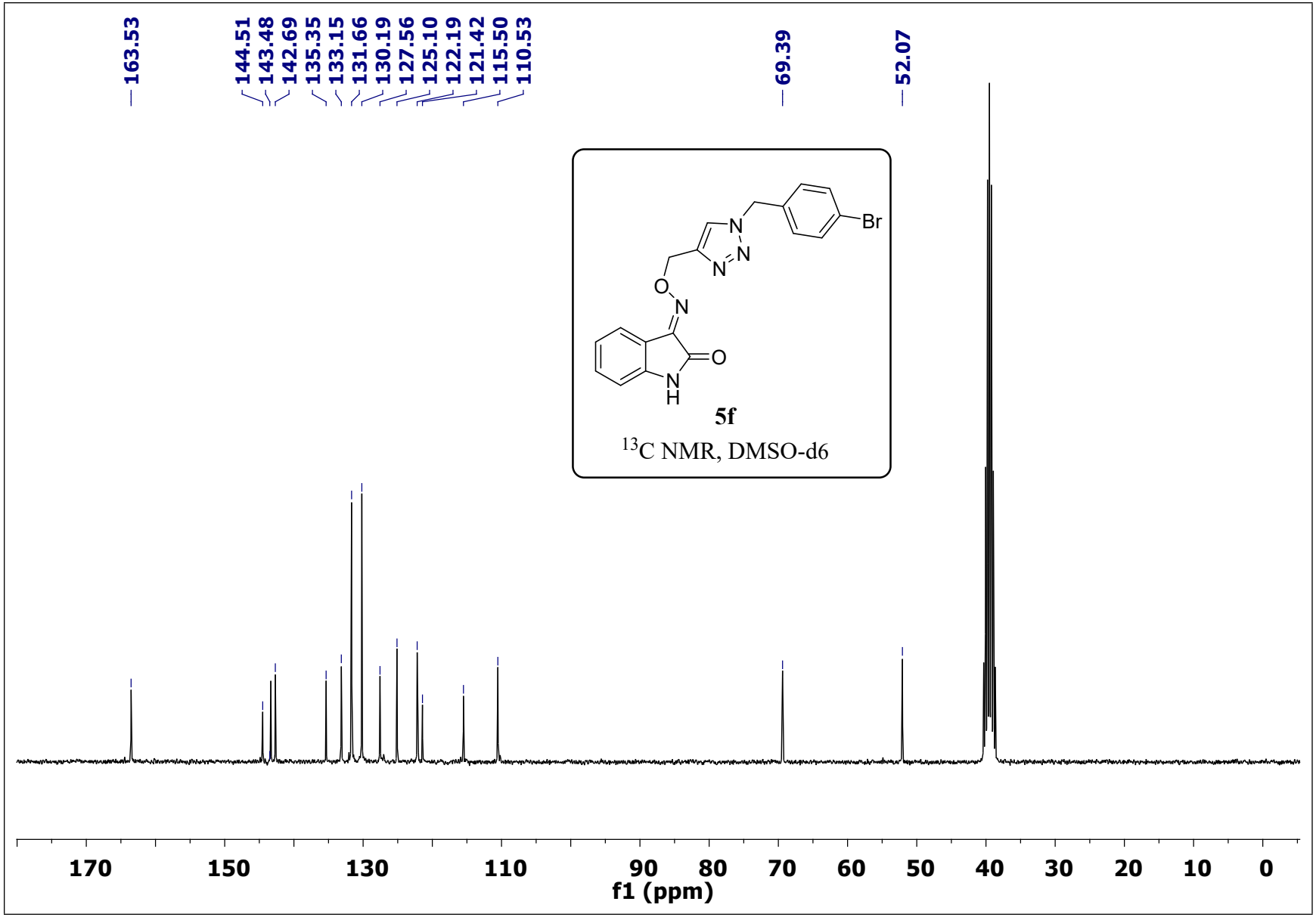

ANL-BLR-LCMS-07-21-Aug-2020
00:43:49
C1999-017-S6
1: Scan ES+
1.24e8
351.1132
492008B7597 95 (1.640)
5d
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 352.12
Found : 352.33
352.33
353.35
374.33
703.59
725.56
726.55
727.53
162.19
114.19
375.36
379.39
381.55
153.18
128.14
129.09
190.20
198.29
240.40
271.19
306.34
334.31
398.39
453.46
465.62
483.74
516.47
547.13
555.00
505.01
656.47
673.87
728.64
756.57
795.64
815.78
858.61
894.67
922.41
957.64
973.22
m/z

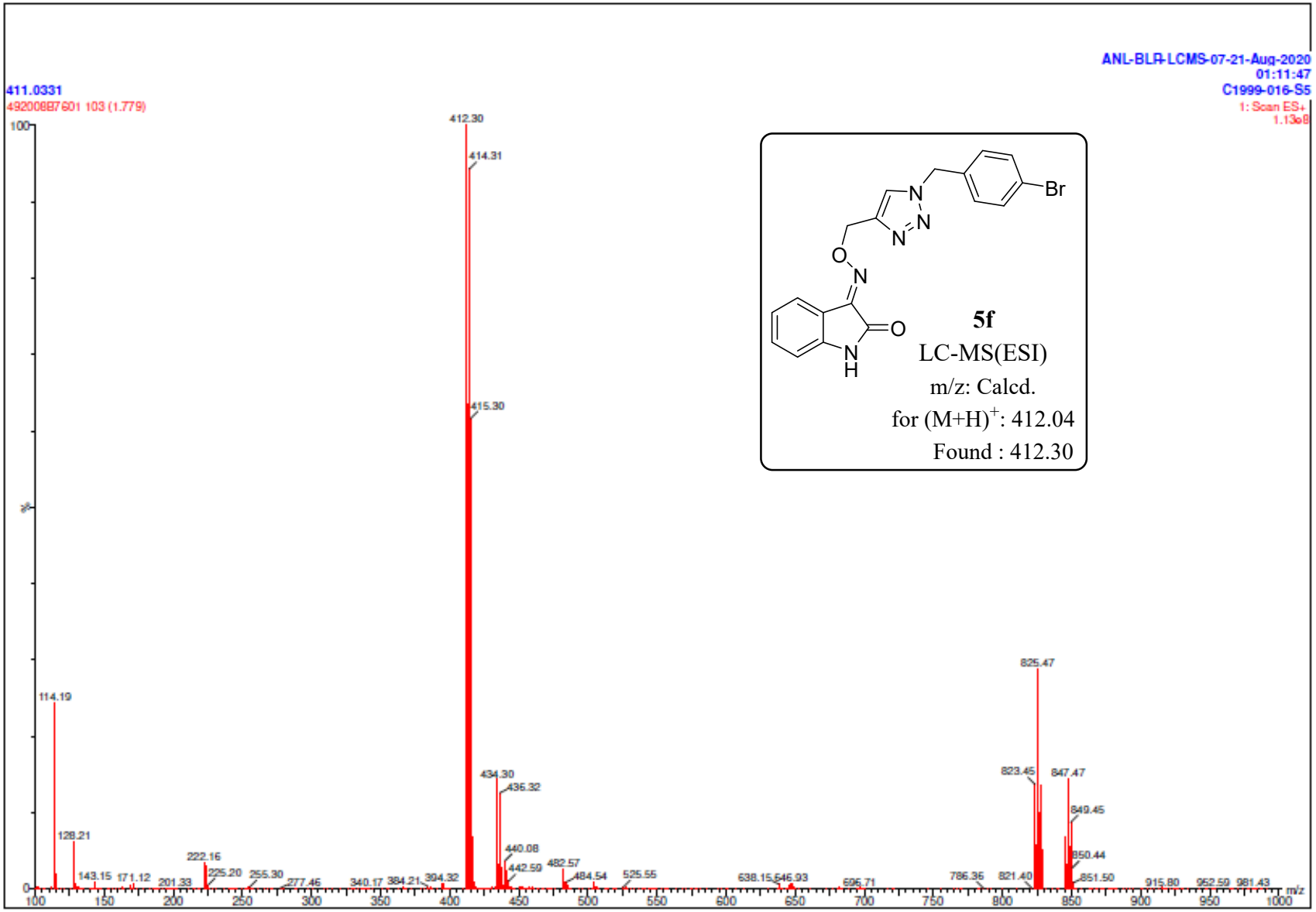

Cl
N
N
N
O
N
O
N
H
5e
^{1}H NMR, DMSO-d$_6$
0.90
1.01
1.02
5.31
1.14
1.05
2.09
2.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

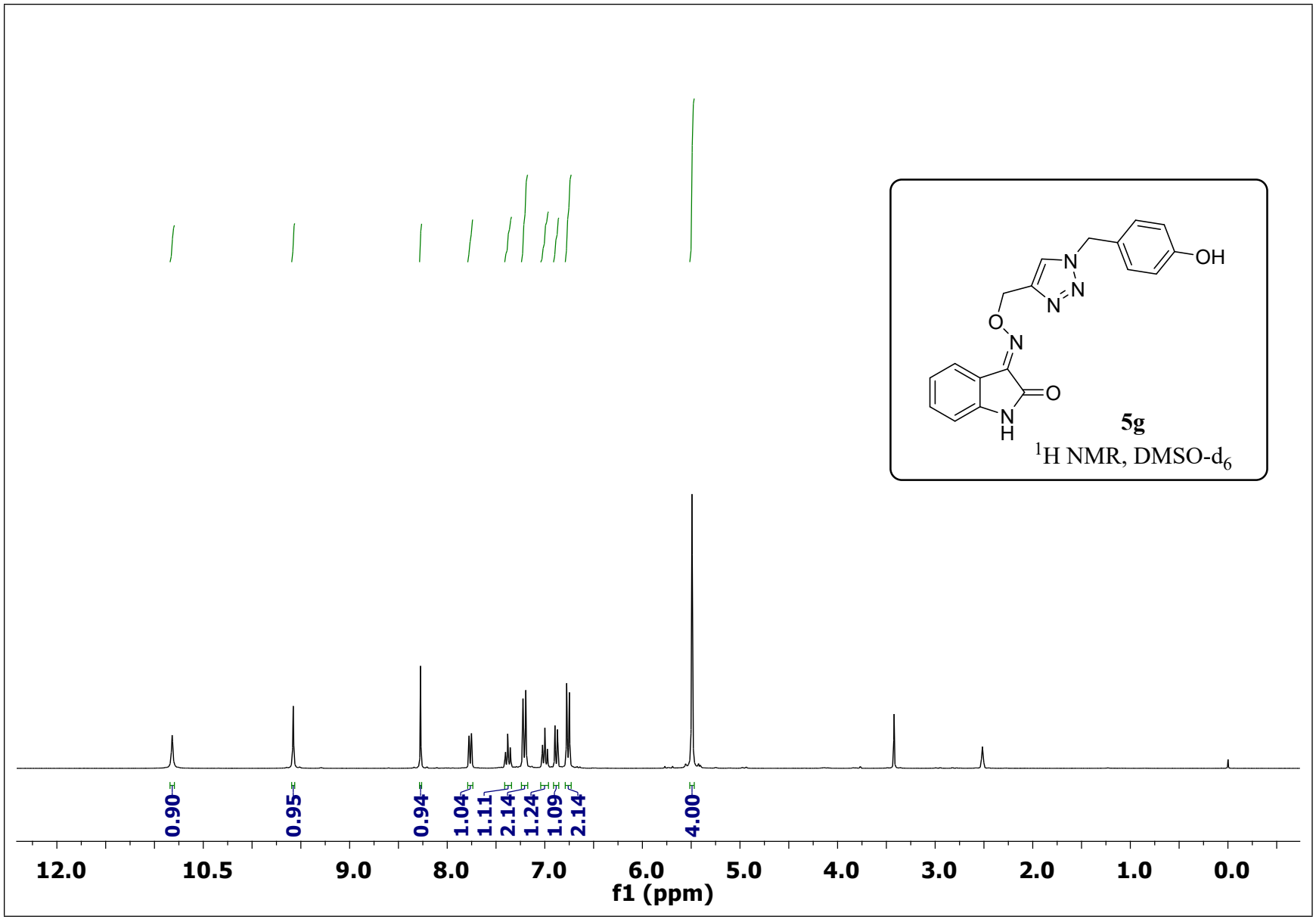

163.53
144.51
143.34
142.70
134.92
133.13
132.87
129.88
128.73
127.56
125.09
122.17
115.50
110.53
69.40
52.02
Cl
N
N
N
O
N
O
N
H
5e
13C NMR, DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

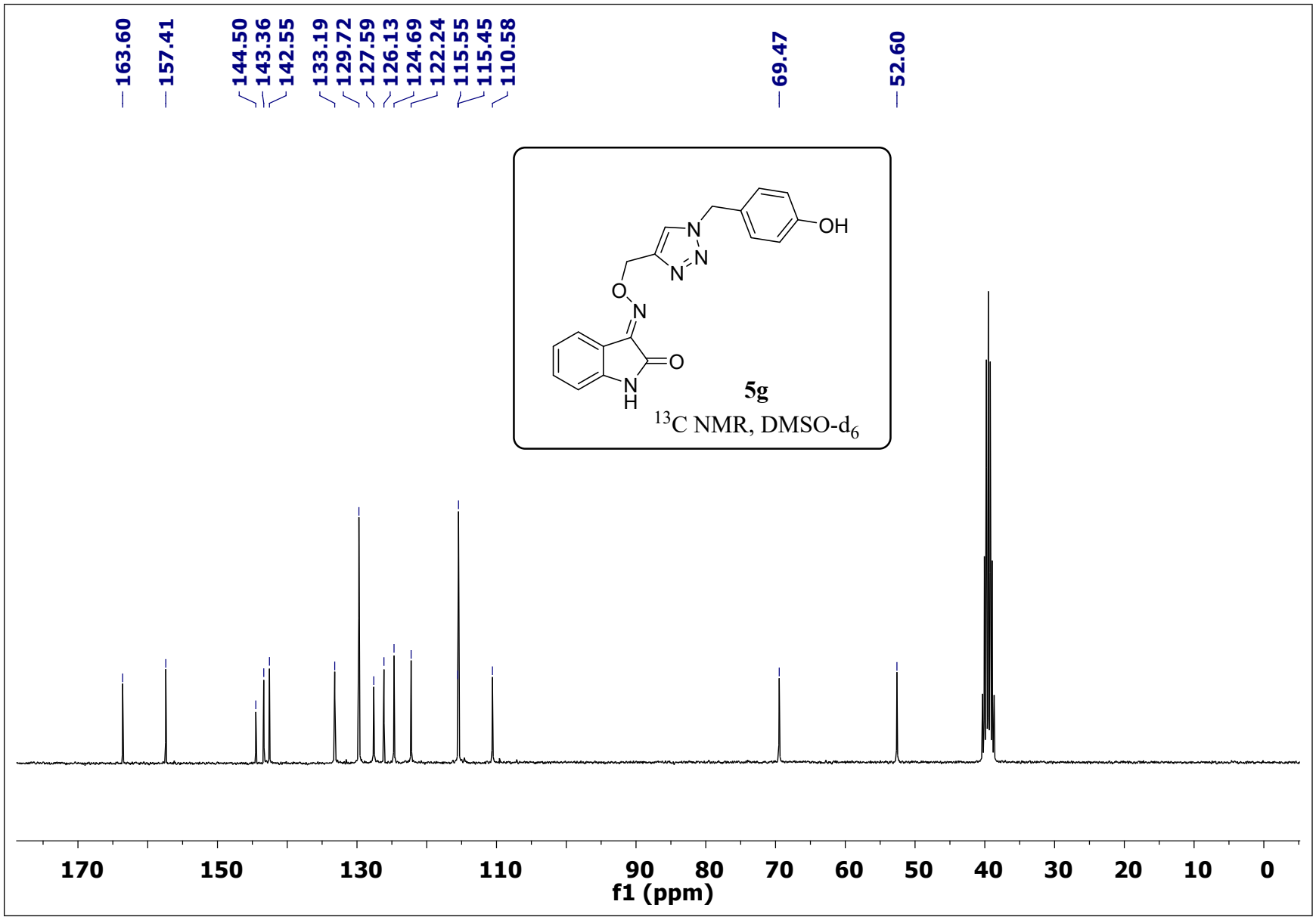

ANL-BLR-LCMS-07-21-Aug-2020
01:17:19
C1999-013-S4
1: Scan ES+
1.18e8
367.0836
492008877600 101 (1.744)
100
%
0
368.33
370.34
371.33
390.33
392.31
396.64
398.12
114.15
128.17
178.19
180.17
153.18
206.28
256.37
294.41
322.34
350.35
406.25
441.71
481.50
499.40
571.75579.66
629.03 655.44
707.95732.40
735.52
737.53
757.52
759.53
760.52
761.55
762.54
793.28
891.52
927.43
992.26
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900
950
1000
m/z
Cl
N
N
N
O
N
O
N
H
5e
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 368.09
Found : 368.33

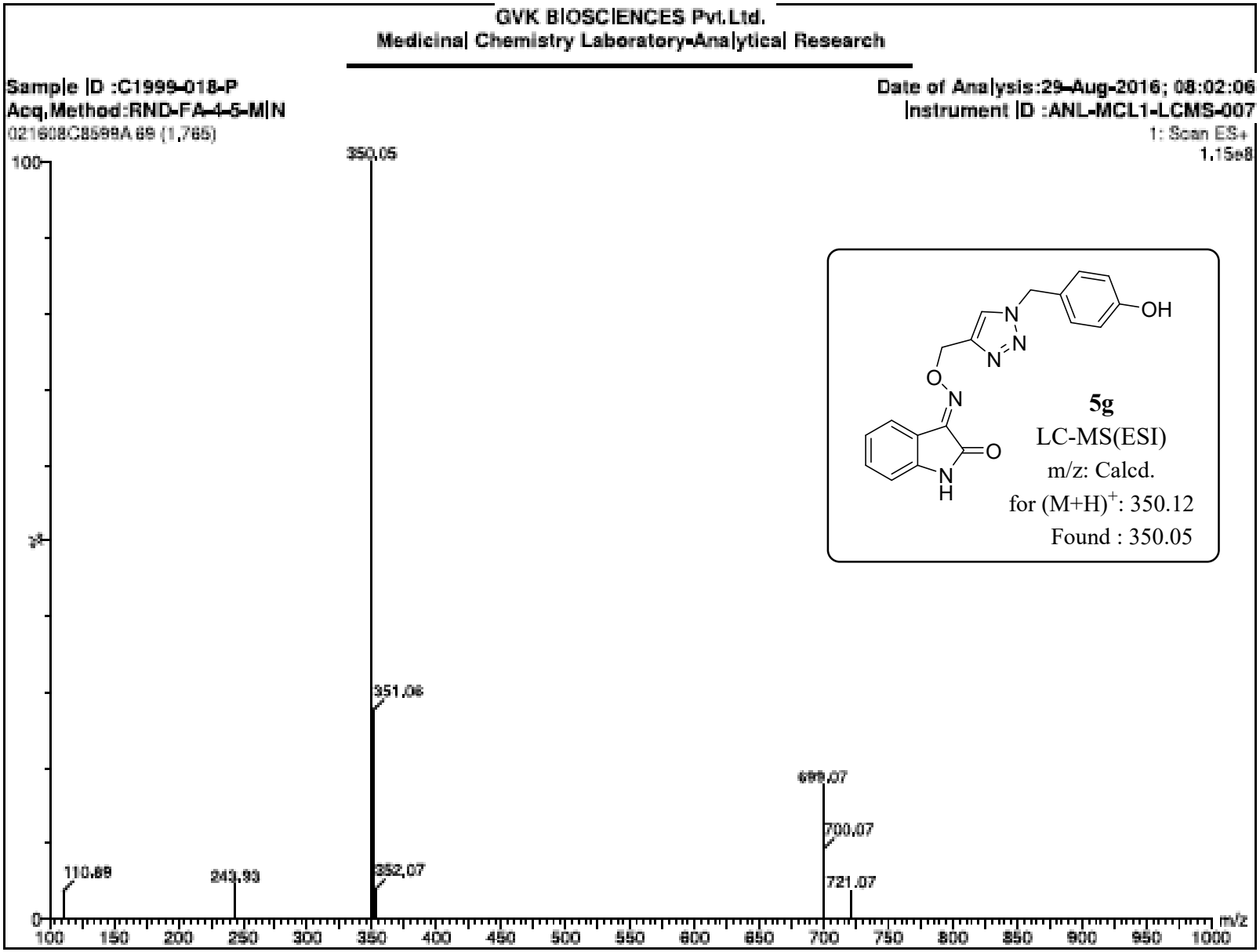

Br
N
N
N
O
N
O
N
H
5f
1H NMR, DMSO-d6
1.03
1.01
1.06
2.18
1.23
2.17
1.25
1.13
2.06
2.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

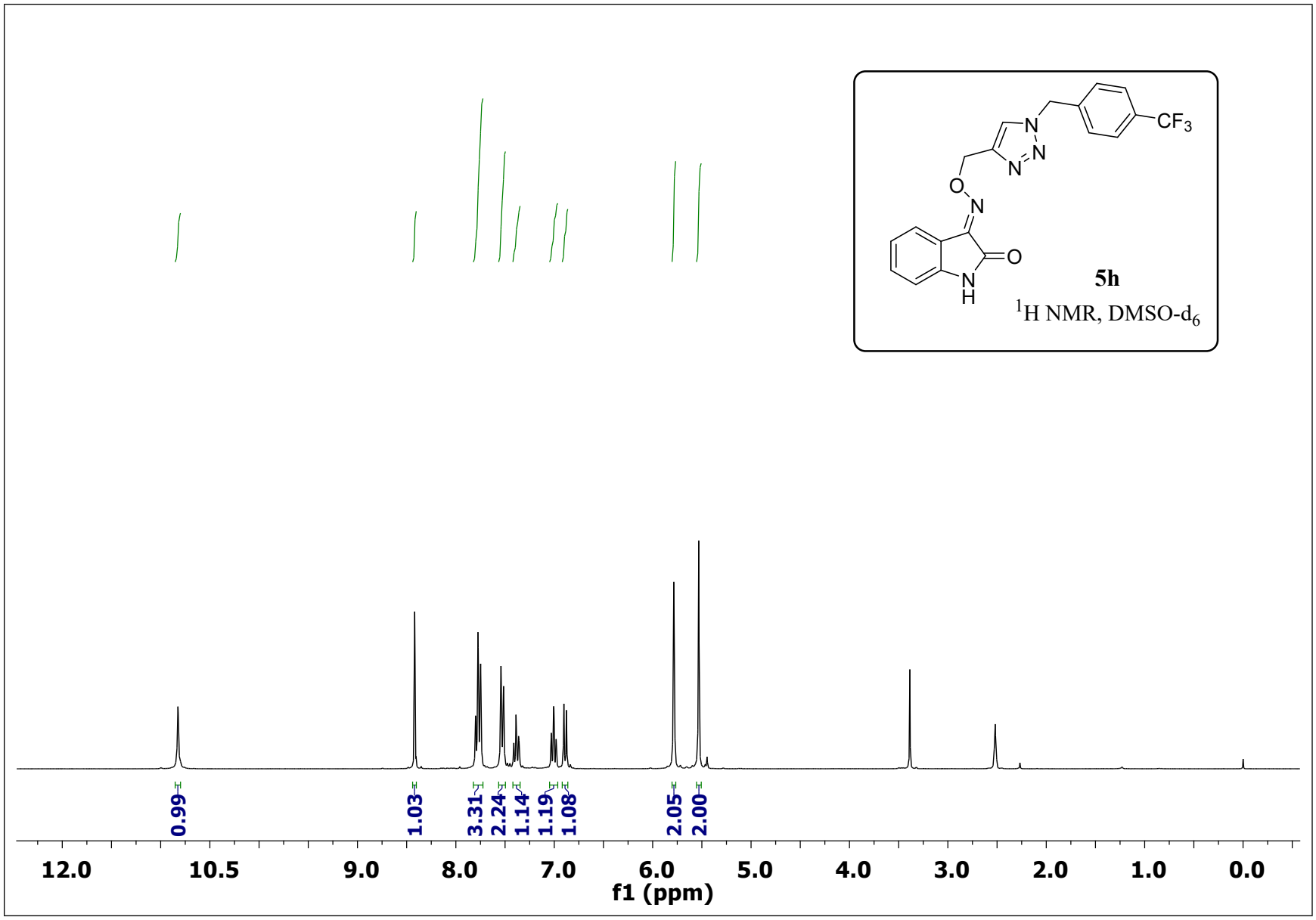

163.53
144.51
143.48
142.69
135.35
133.15
131.66
130.19
127.56
125.10
122.19
121.42
115.50
110.53
69.39
52.07
Br
N
N
N
O
N
O
N
H
5f
13C NMR, DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

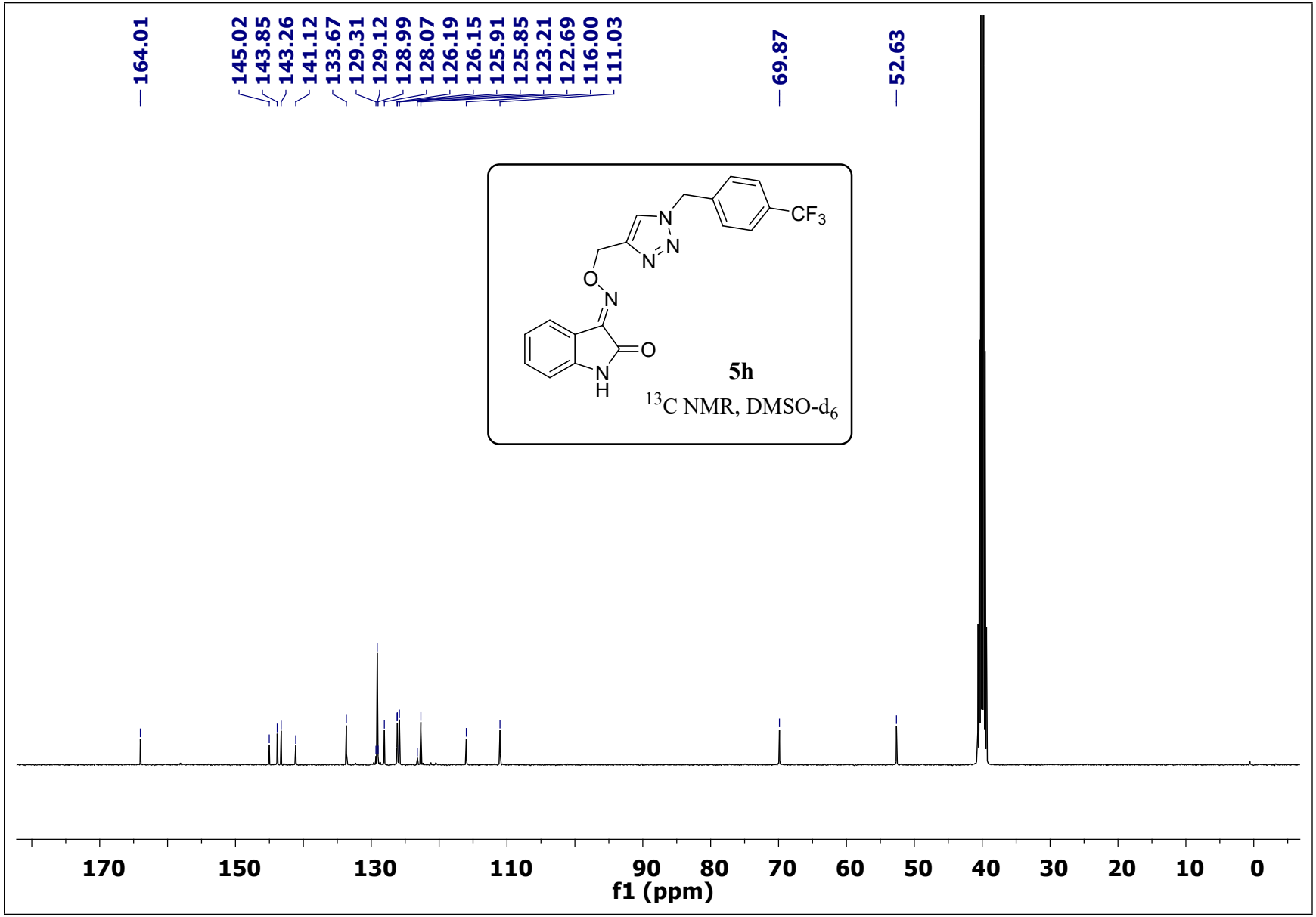

ANL-BLR-LCMS-07-21-Aug-2020
01:11:47
C1999-016-S5
1: Scan ES+
411.0331
412.30
414.31
415.30
114.19
128.21
222.16
434.30
436.32
440.08
442.59
482.57
825.47
823.45
847.47
849.45
850.44
851.50
5f
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 412.04
Found : 412.30

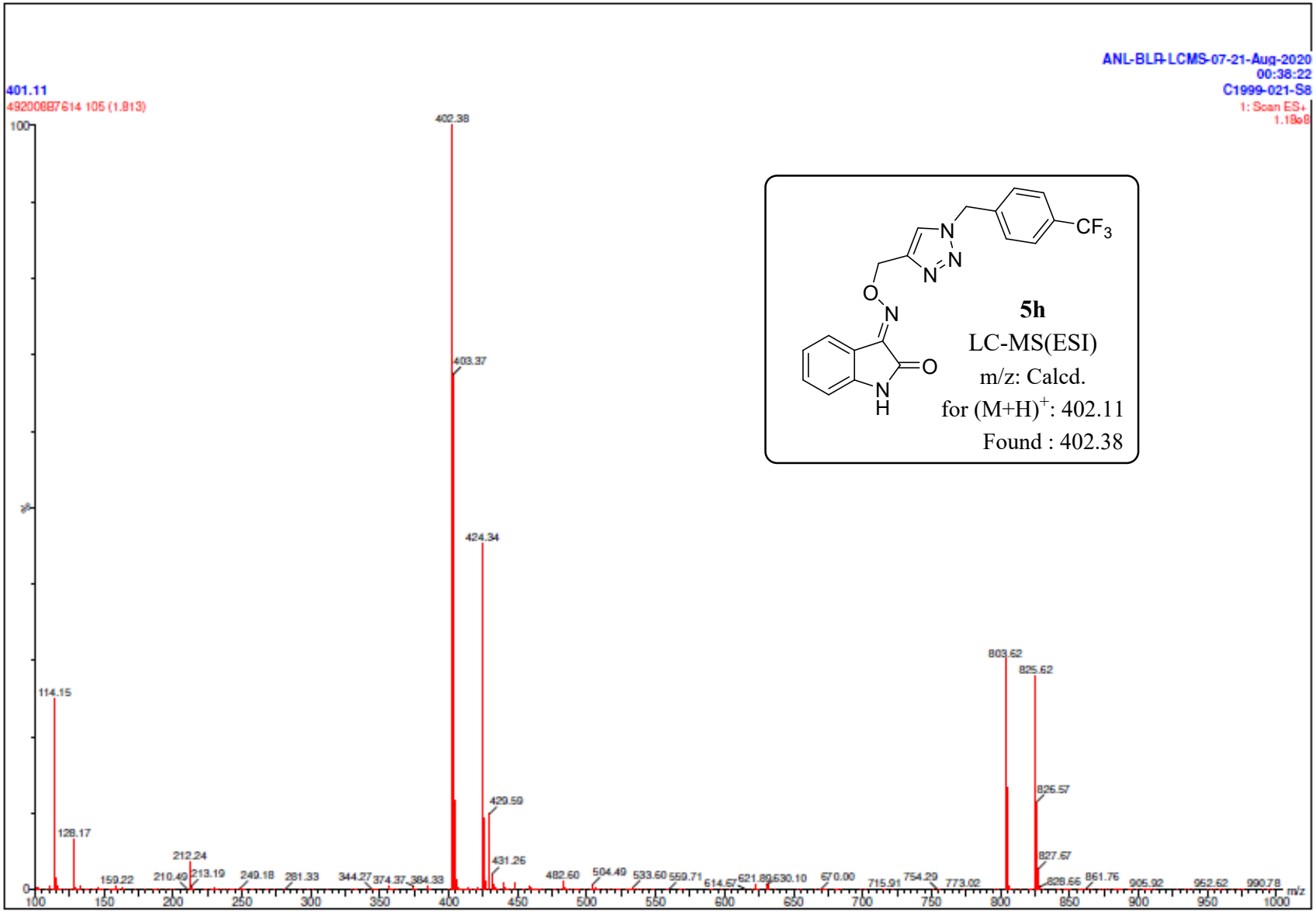

OH
N
N
N
O
N
O
N
H
5g
^{1}H NMR, DMSO-d$_6$
0.90
0.95
0.94
1.04
1.11
2.14
1.24
1.09
2.14
4.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

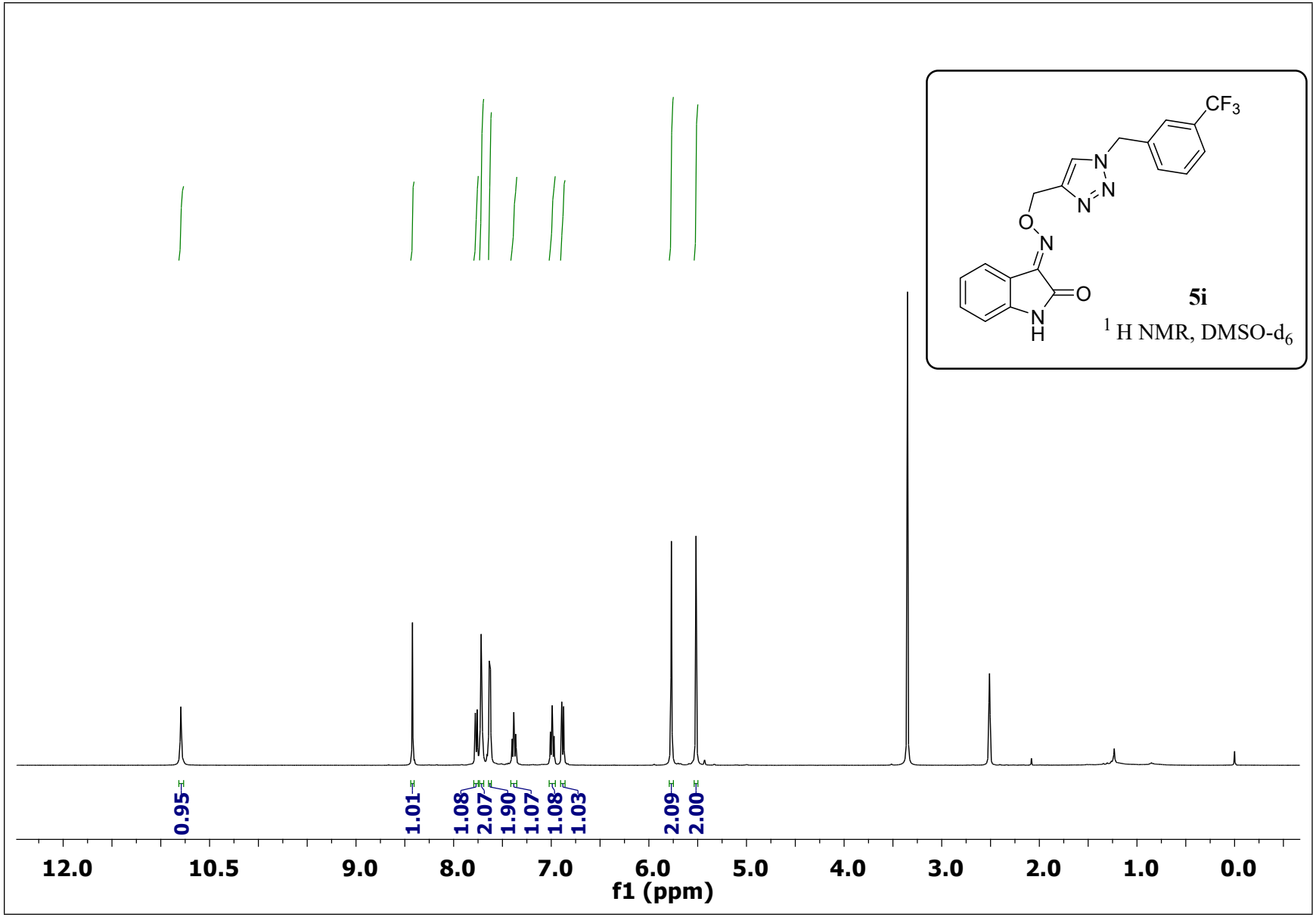

163.60
157.41
144.50
143.36
142.55
133.19
129.72
127.59
126.13
124.69
122.24
115.55
115.45
110.58
69.47
52.60
OH
N
N
N
O
N
O
N
H
5g
13C NMR, DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

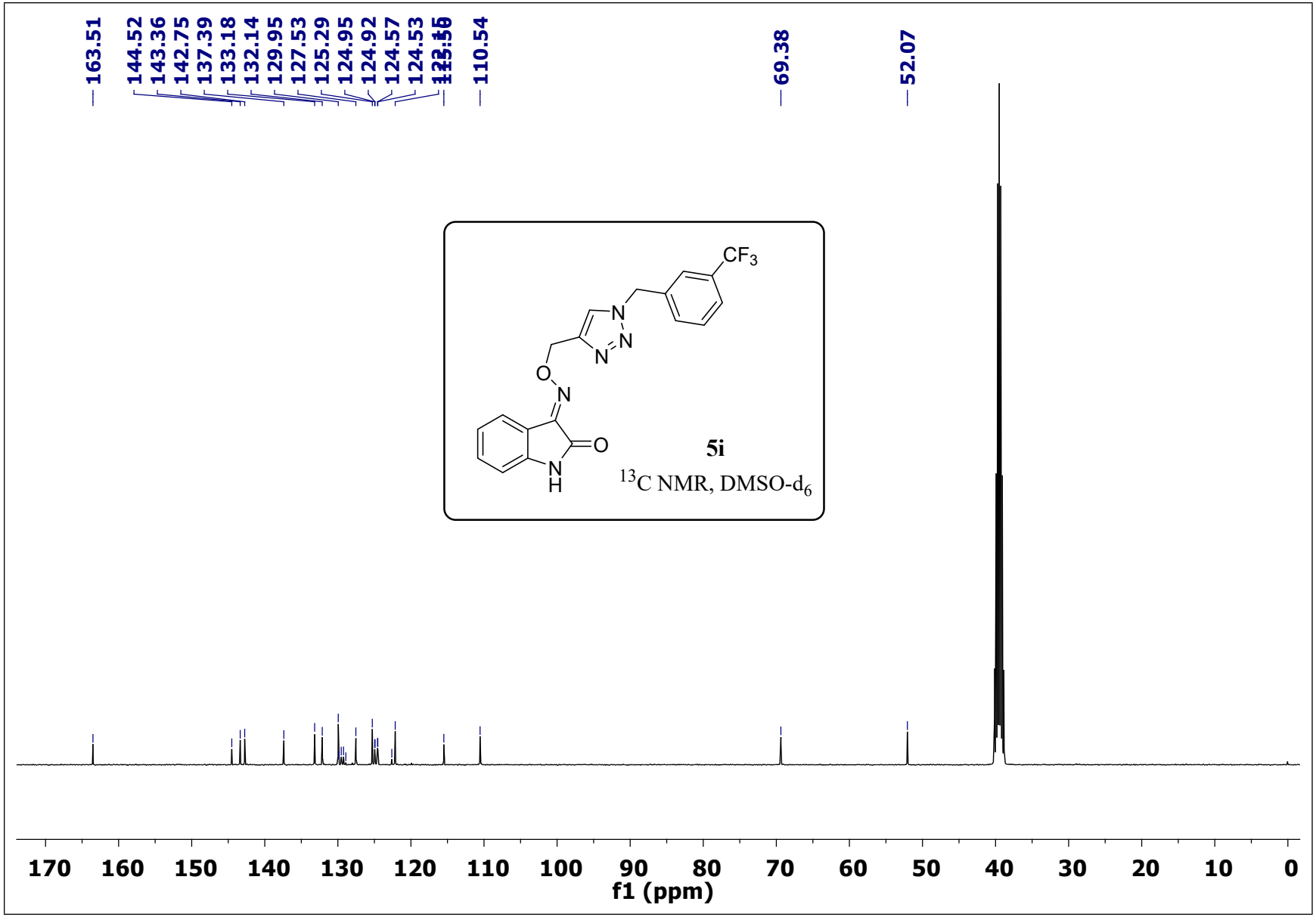

GVK BIOSCIENCES Pvt.Ltd.
Medicinal Chemistry Laboratory-Analytical Research
Sample ID :C1999-018-P
Acq.Method:RND-FA-4-5-M.M
021608C8599A 69 (1,765)
Date of Analysis:29-Aug-2016; 08:02:06
Instrument ID :ANL-MCL1-LCMS-007
1: Scan ES+
1.15e8
100
%
0
350.05
351.06
352.07
699.07
700.07
721.07
110.89
243.93
m/z
100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000
OH
N
N
N
O
N
O
N
H
5g
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 350.12
Found : 350.05

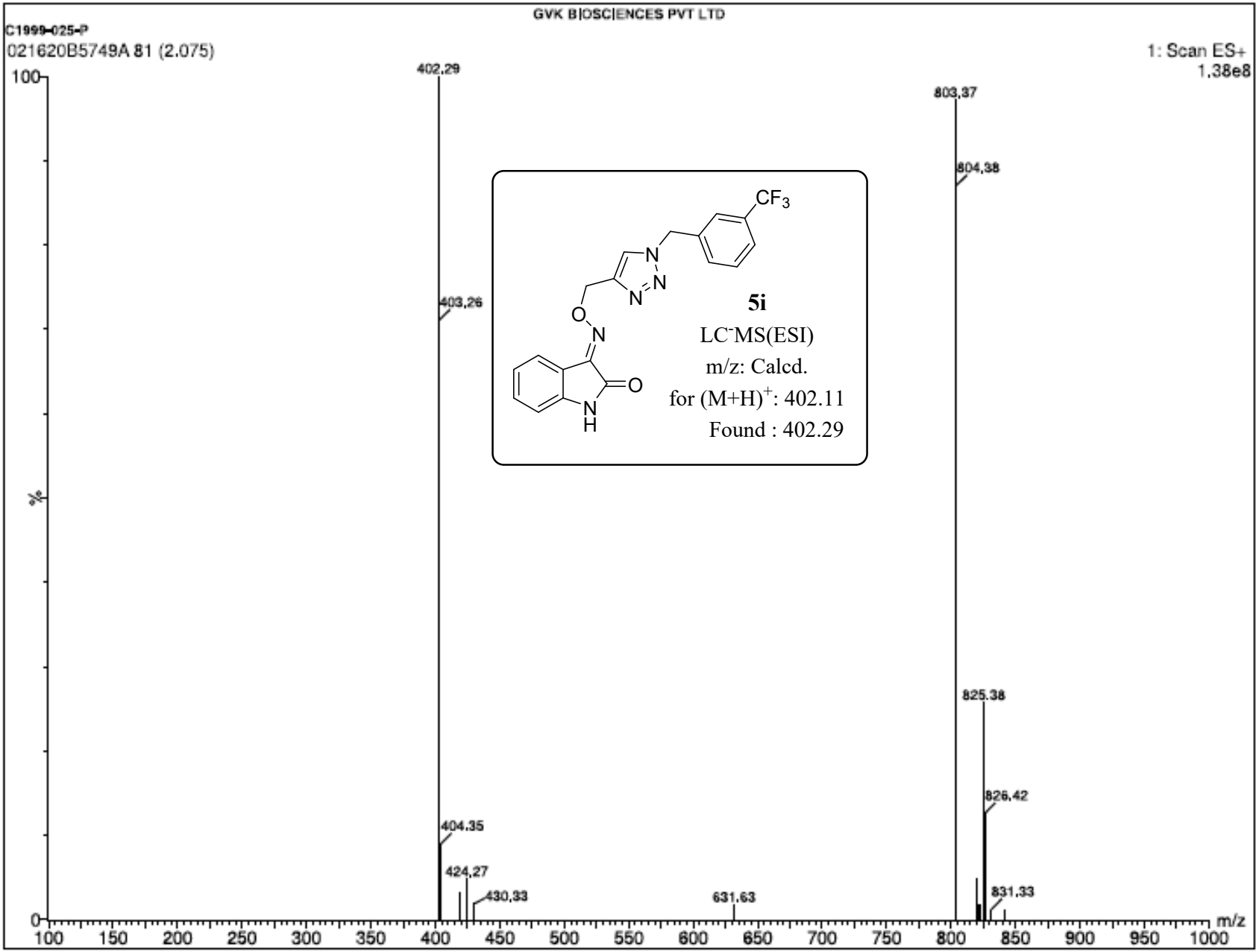

CF3
N
N
N
O
N
O
N
H
5h
1H NMR, DMSO-d6
0.99
1.03
3.31
2.24
1.14
1.19
1.08
2.05
2.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

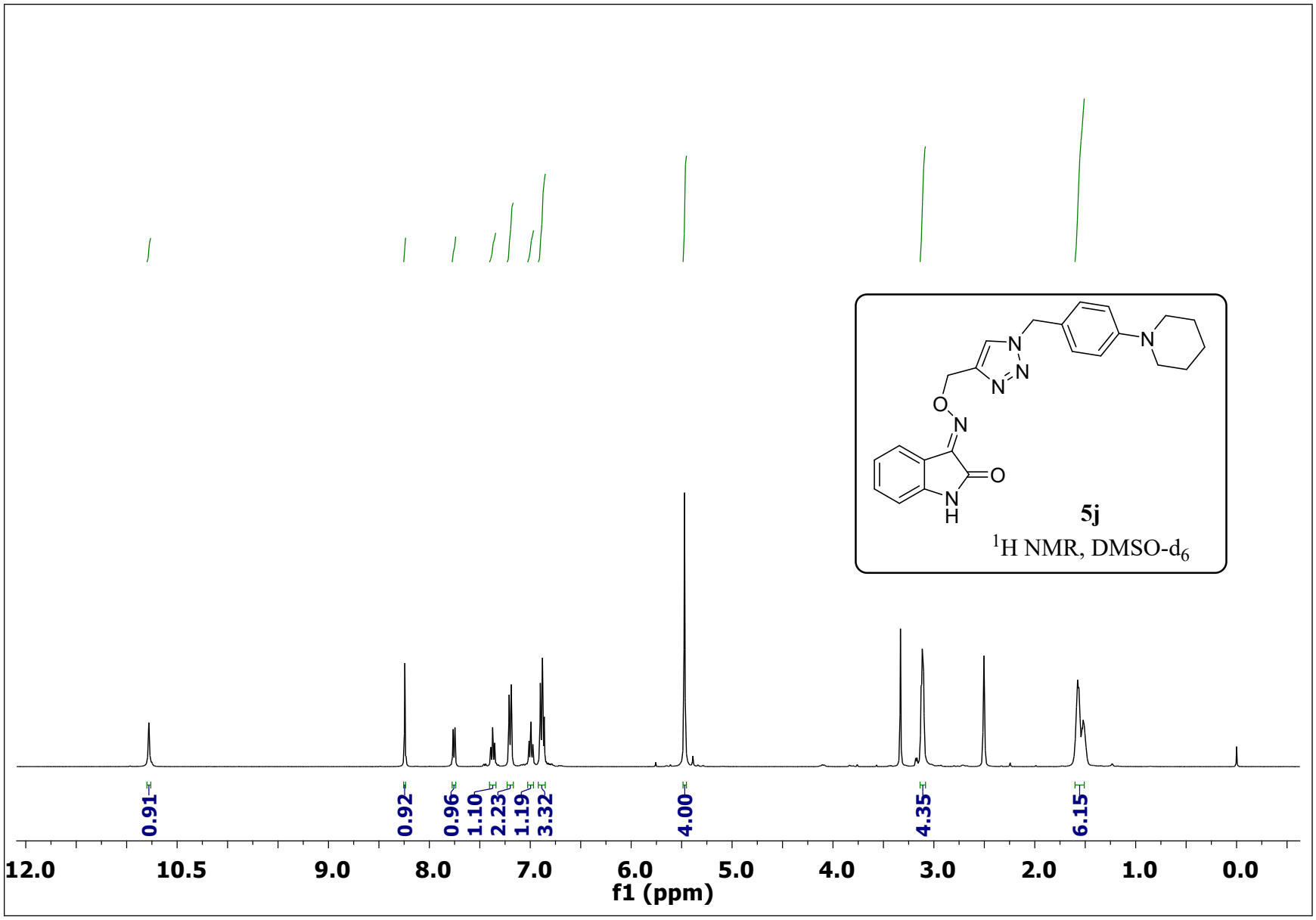

164.01
145.02
143.85
143.26
141.12
133.67
129.31
129.12
128.99
128.07
126.19
126.15
125.91
125.85
123.21
122.69
116.00
111.03
69.87
52.63
CF3
N
N
N
O
N
O
N
H
5h
13C NMR, DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

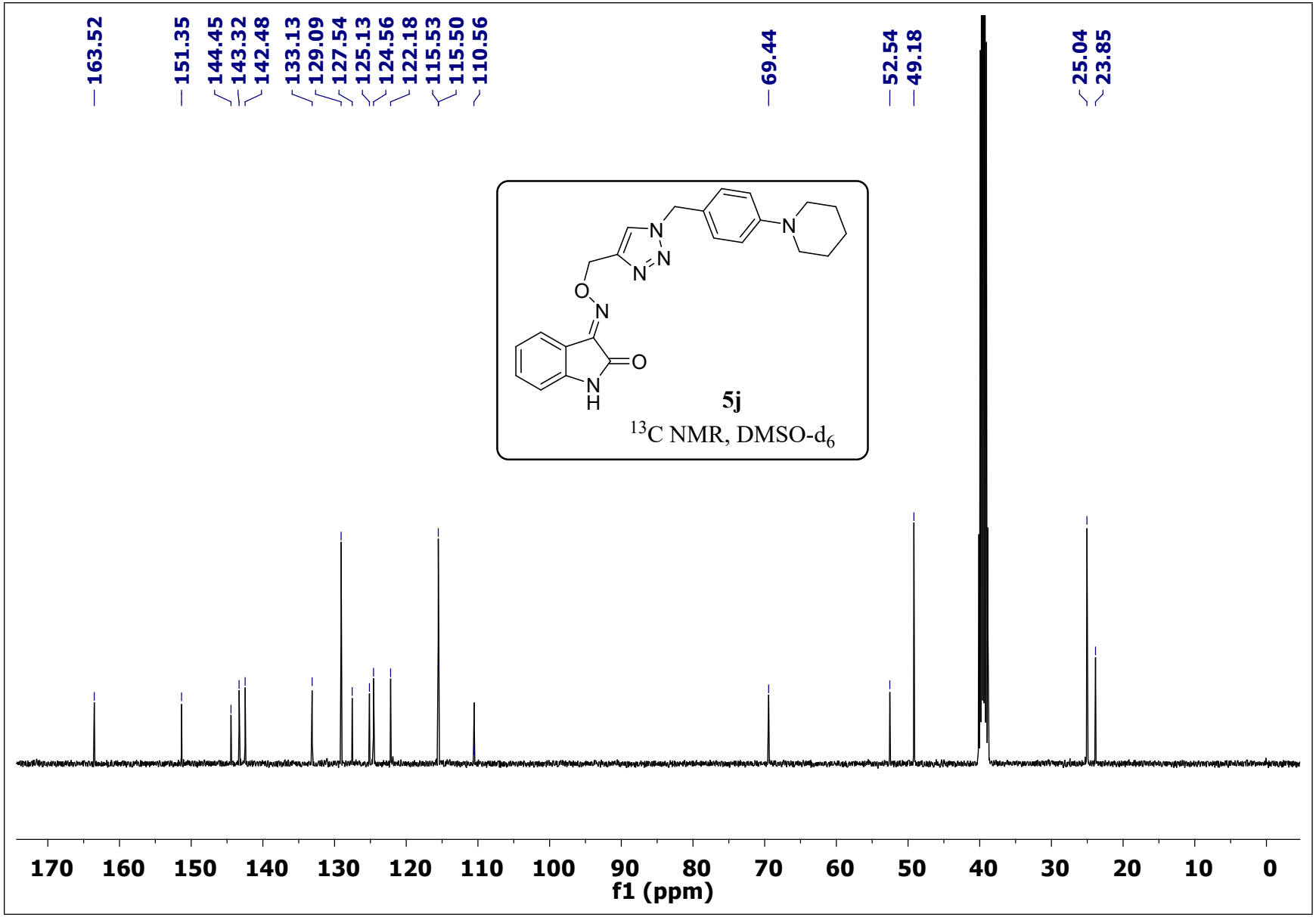

ANL-BLR-LCMS-07-21-Aug-2020
00:38:22
C1999-021-S8
1: Scan ES+
401.11
492008B7614 105 (1.813)
5h
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 402.11
Found : 402.38

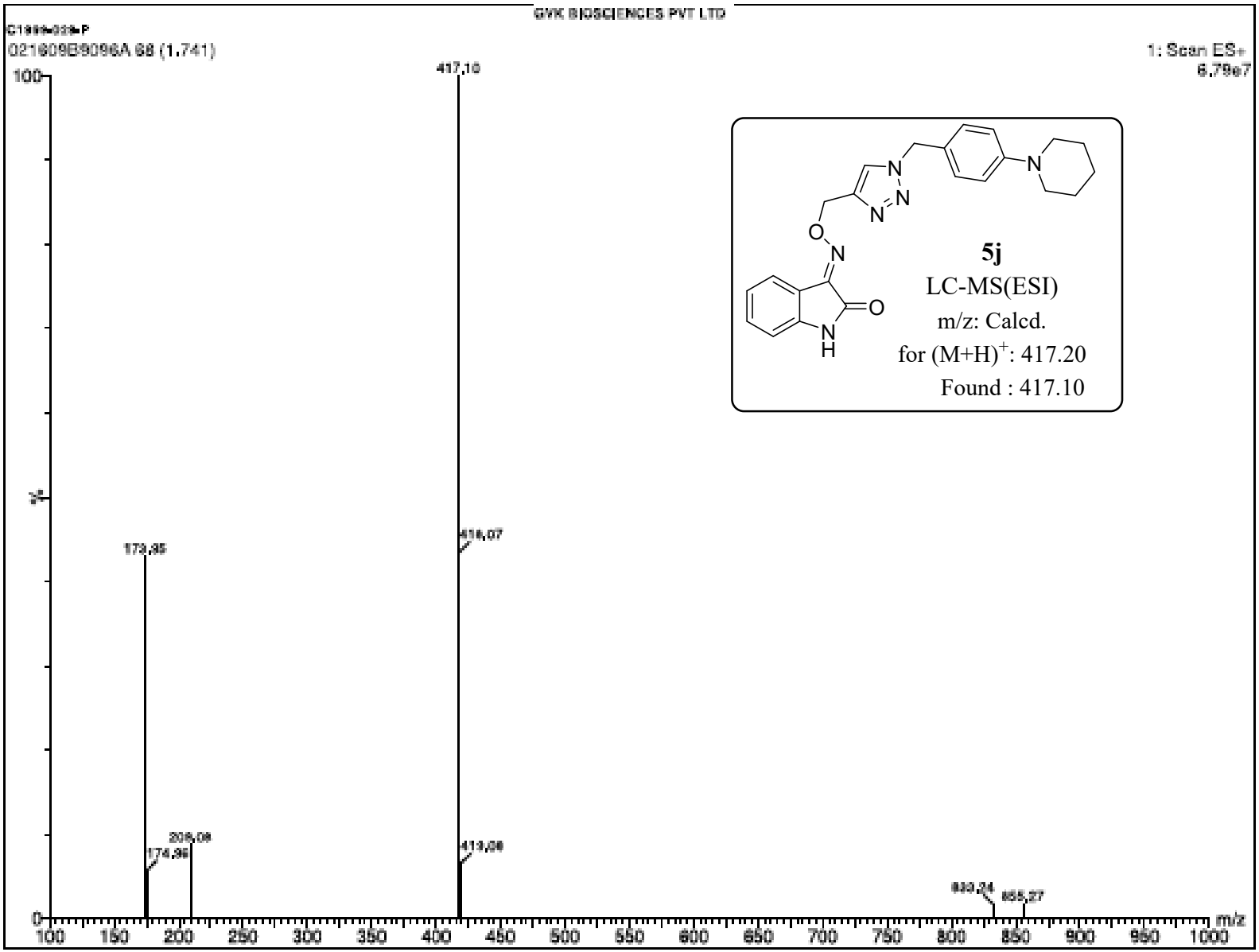

CF3
N
N
N
O
N
O
N
H
5i
1 H NMR, DMSO-d6
0.95
1.01
1.08
2.07
1.90
1.07
1.08
1.03
2.09
2.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

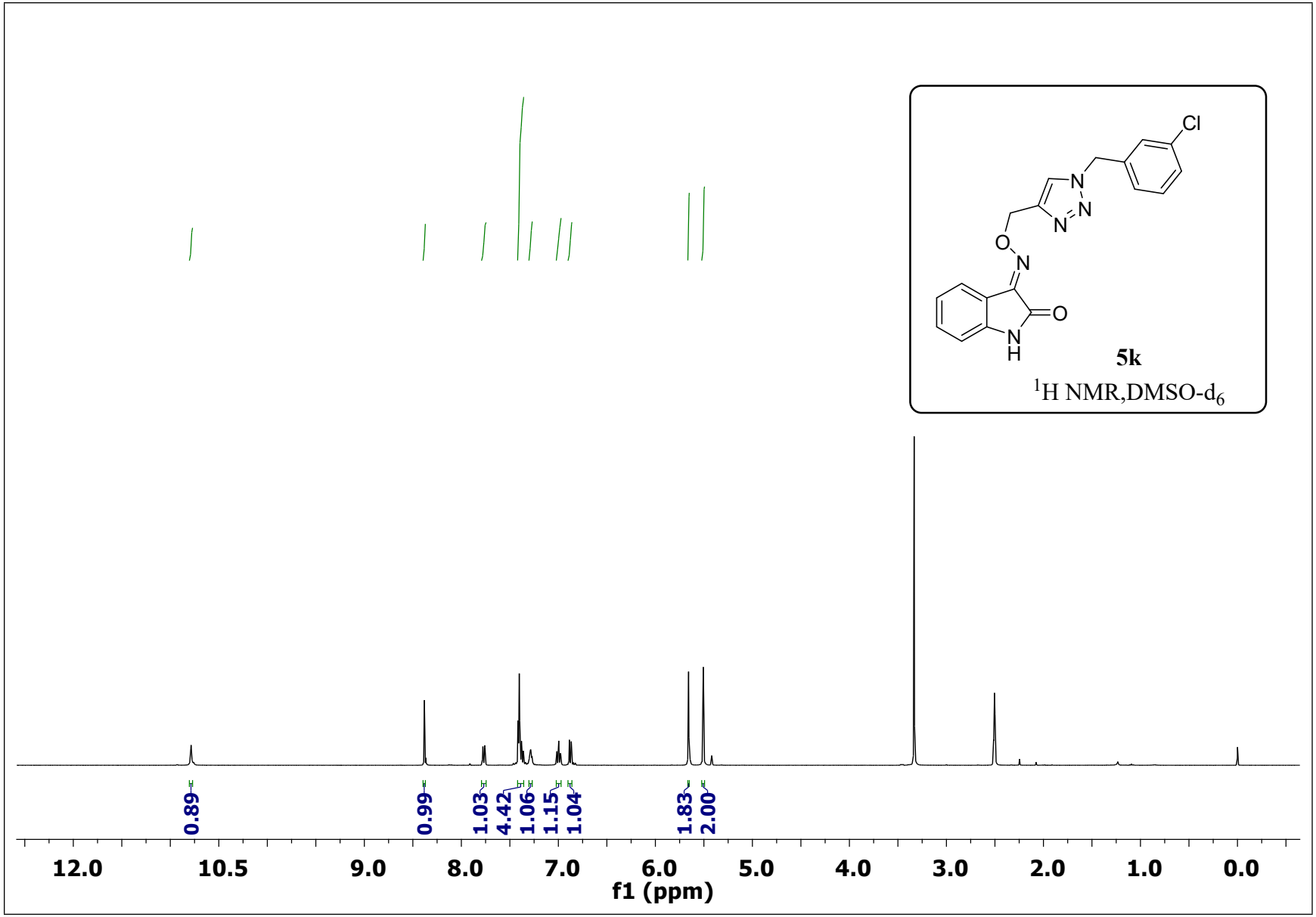

163.51
144.52
143.36
142.75
137.39
133.18
132.14
129.95
127.53
125.29
124.95
124.92
124.57
124.53
110.54
69.38
52.07
CF3
N
N
N
O
N
O
N
H
5i
13C NMR, DMSO-d6
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

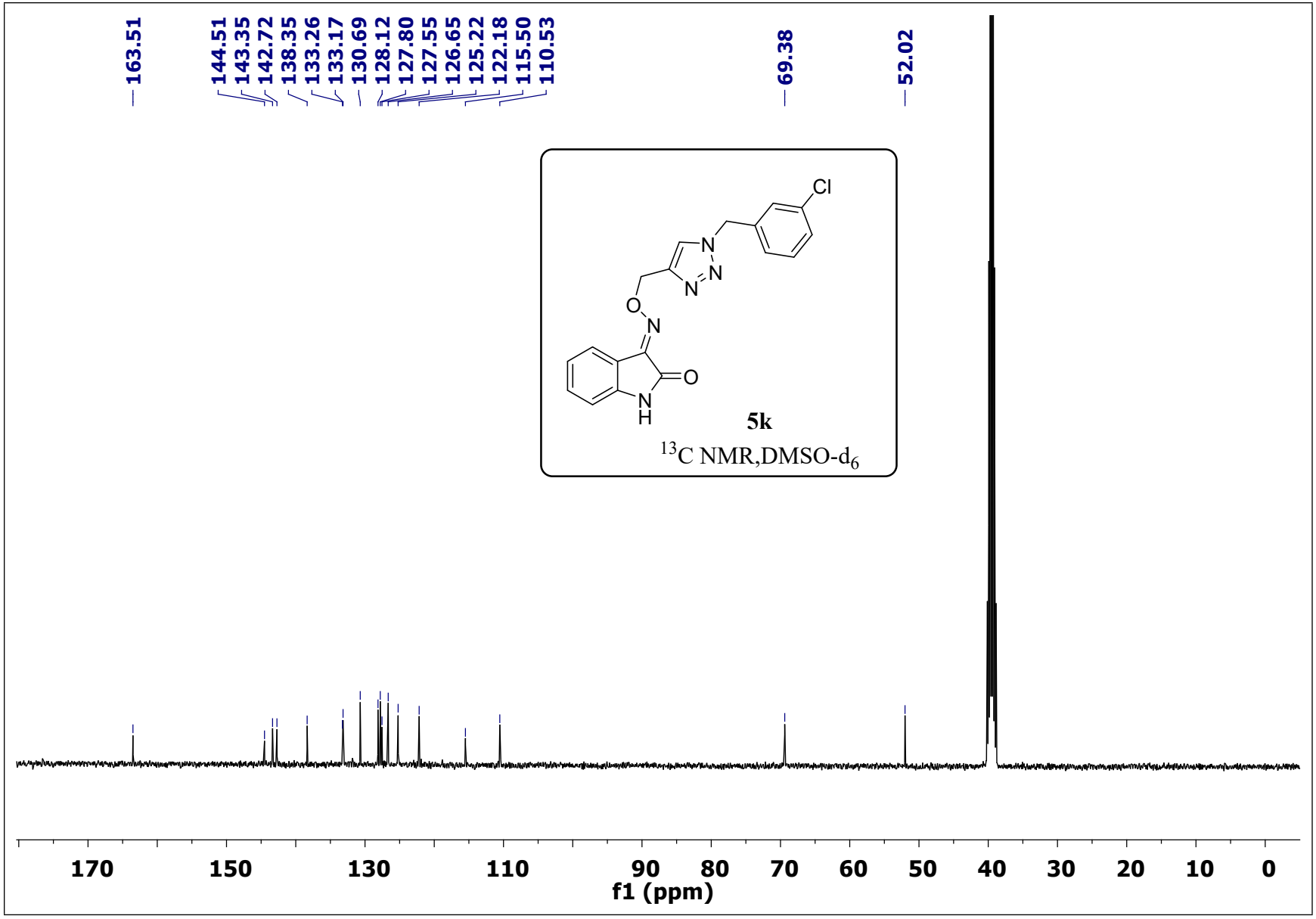

GVK BIOSCIENCES PVT LTD
C1999-025-P
021620B5749A 81 (2.075)
1: Scan ES+
1.38e8
100
%
0
402.29
403.26
404.35
424.27
430.33
631.63
803.37
804.38
825.38
826.42
831.33
m/z
100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000
CF3
N
N
N
O
N
O
N
H
5i
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 402.11
Found : 402.29

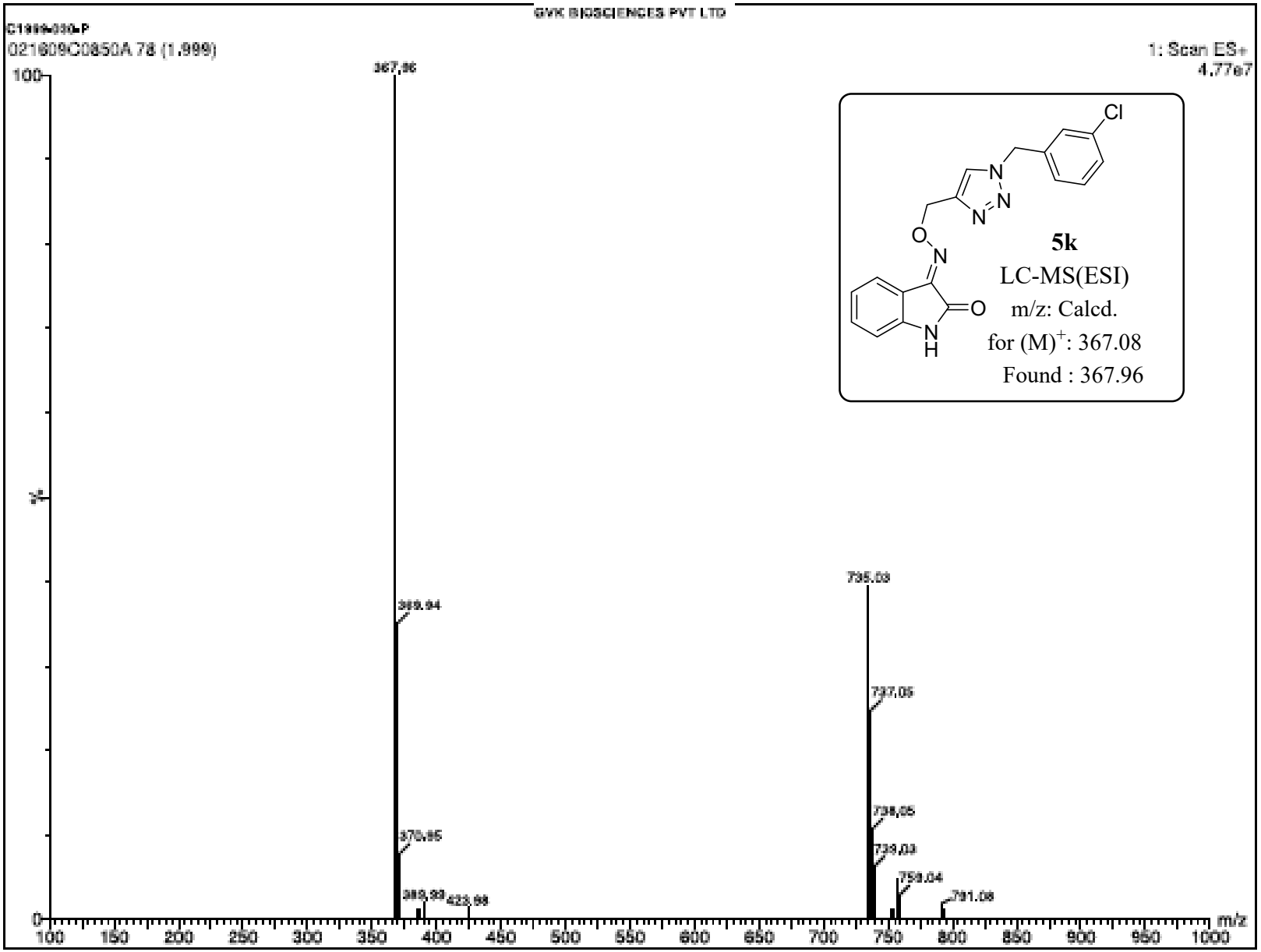

5j
^{1}H NMR, DMSO-d$_6$
0.91
0.92
0.96
1.10
2.23
1.19
3.32
4.00
4.35
6.15
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

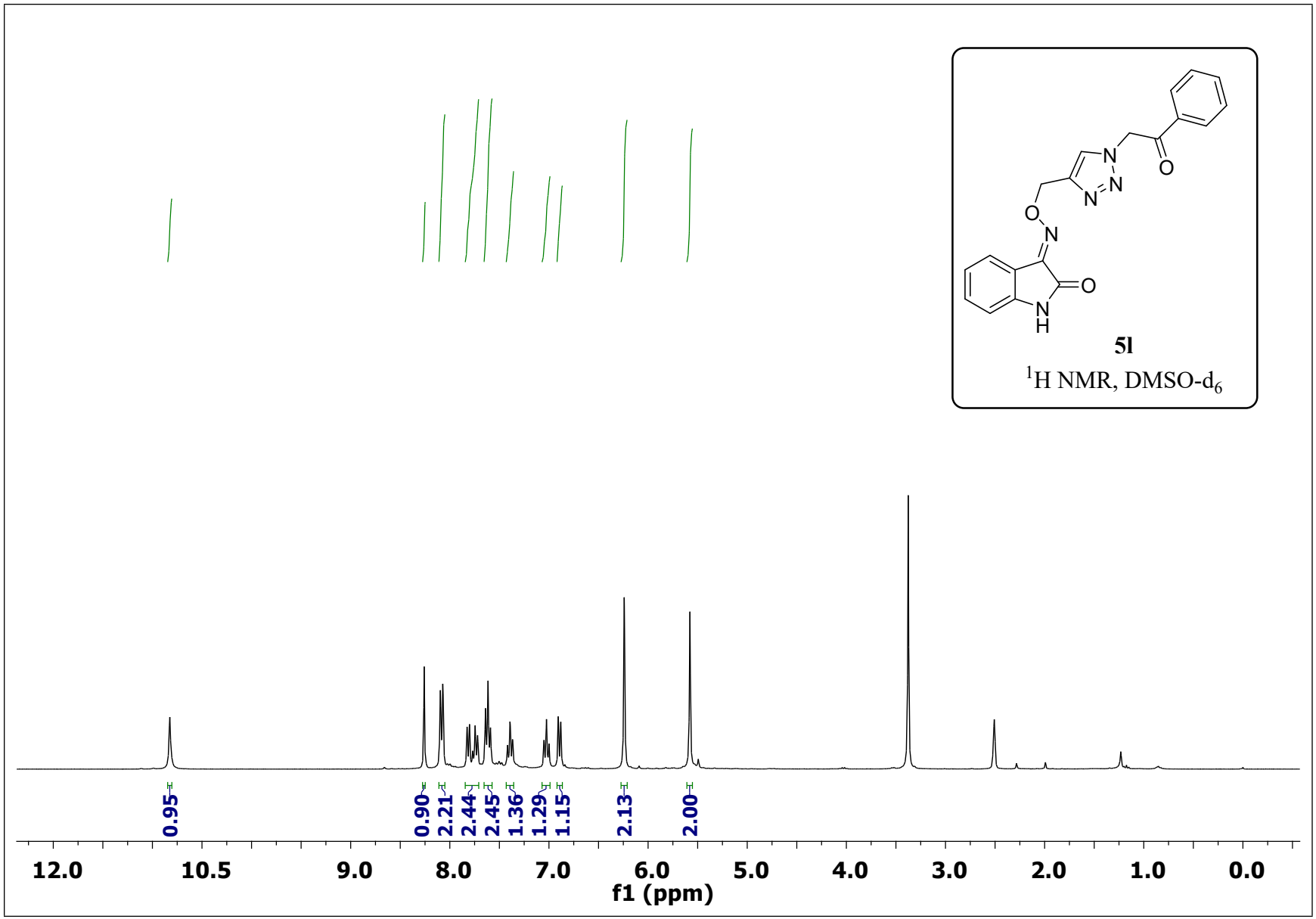

163.52
151.35
144.45
143.32
142.48
133.13
129.09
127.54
125.13
124.56
122.18
115.53
115.50
110.56
69.44
52.54
49.18
25.04
23.85
5j
13C NMR, DMSO-d6
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

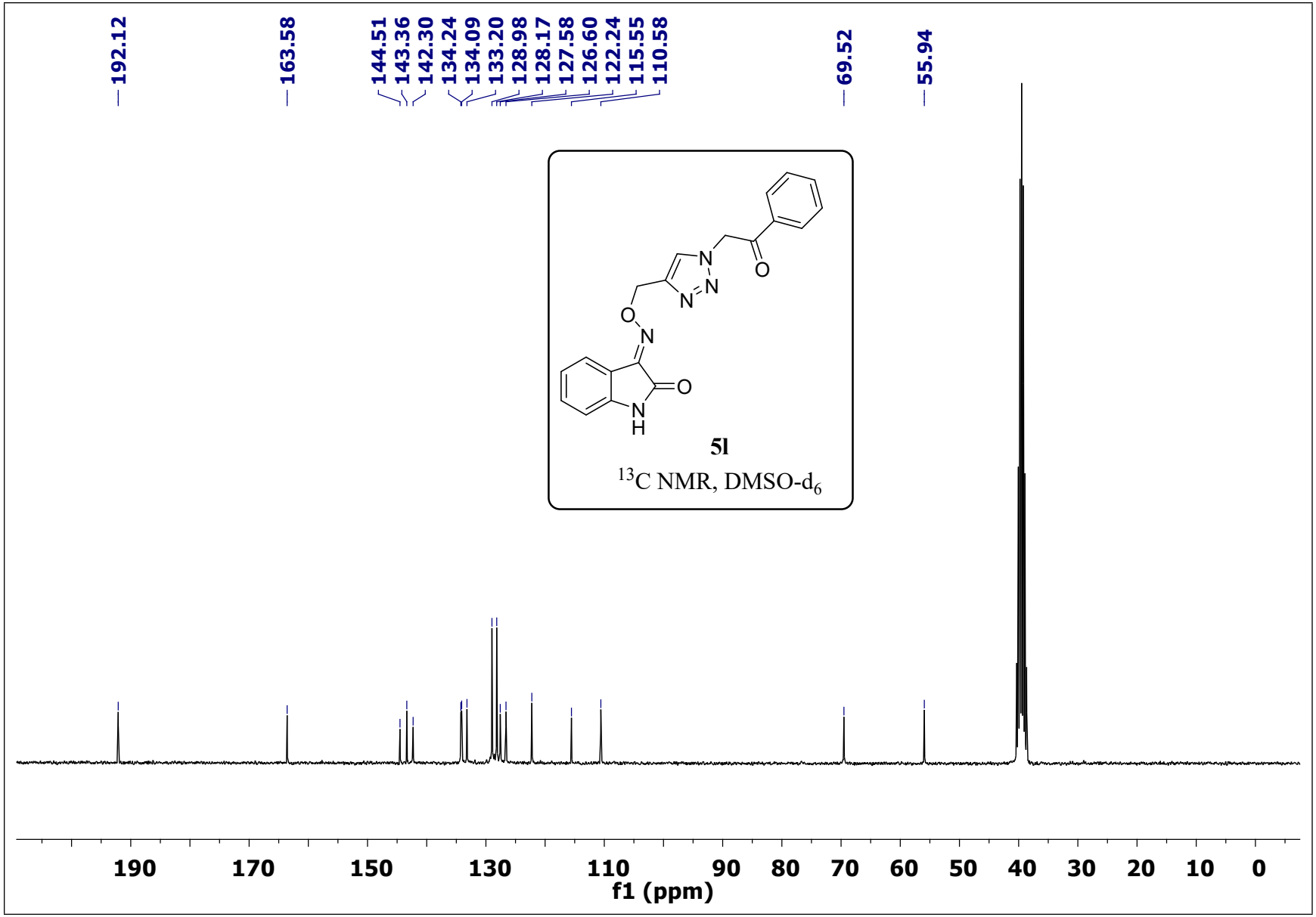

GVK BIOSCIENCES PVT LTD
021609B9096A 88 (1.741)
1: Scan ES+
6.79e7
100
%
0
417.10
416.07
413.04
173.95
174.96
208.08
833.24
855.27
m/z
100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000
5j
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 417.20
Found : 417.10

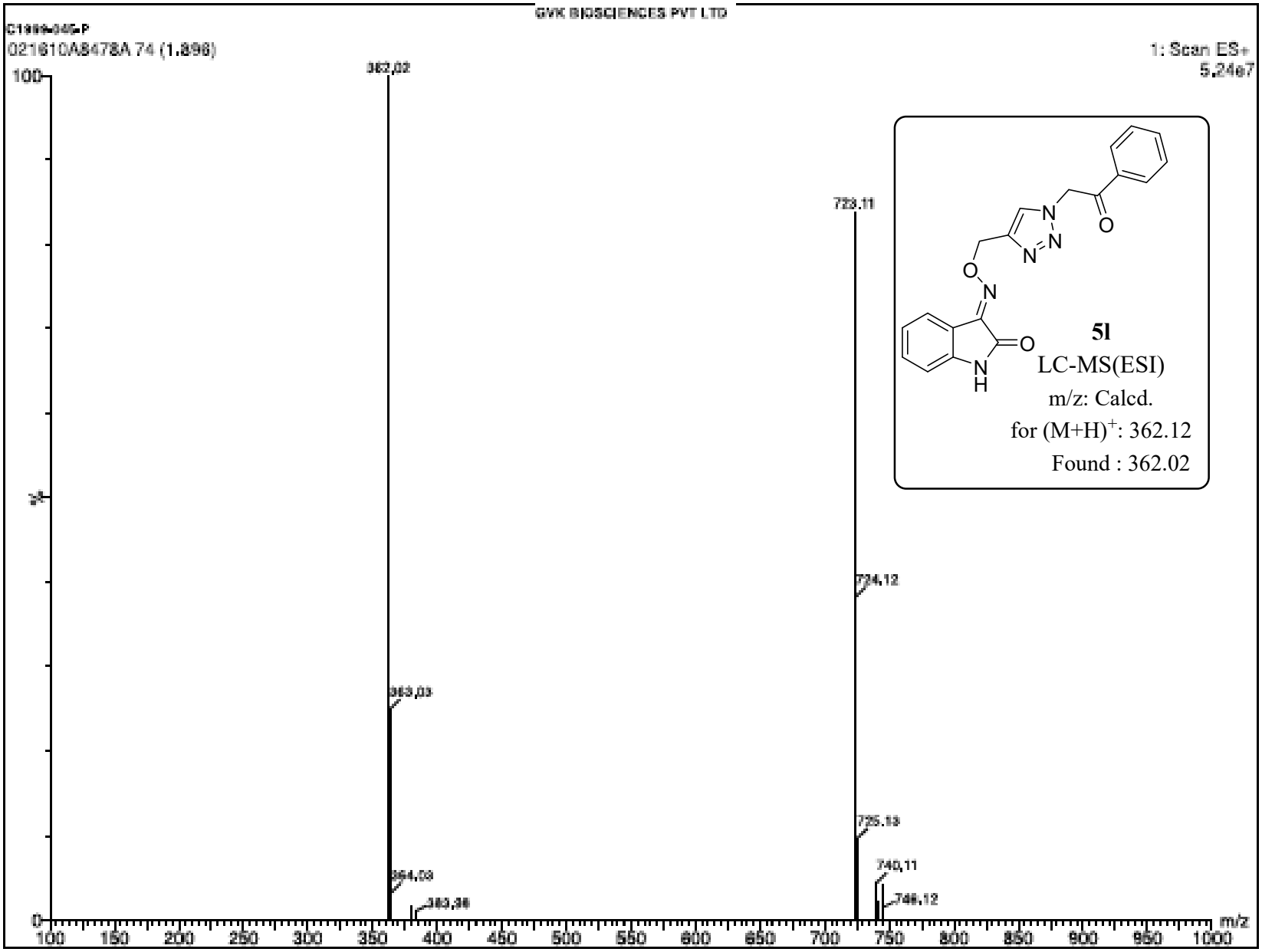

Cl
N
N
N
O
N
O
N
H
5k
^{1}H NMR,DMSO-d$_6$
0.89
0.99
1.03
4.42
1.06
1.15
1.04
1.83
2.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

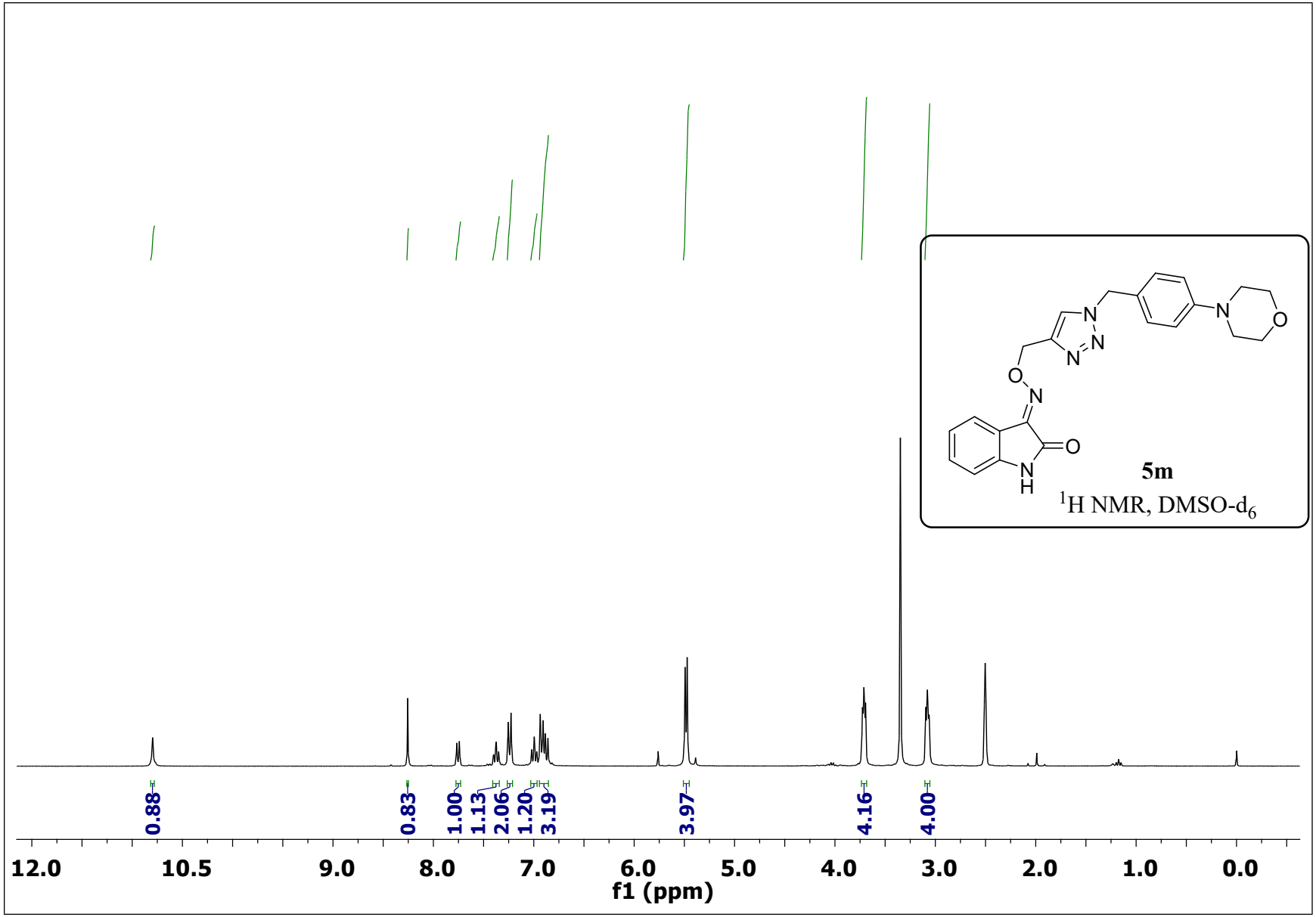

163.51
144.51
143.35
142.72
138.35
133.26
133.17
130.69
128.12
127.80
127.55
126.65
125.22
122.18
115.50
110.53
69.38
52.02
Cl
N
N
N
O
N
O
N
H
5k
13C NMR,DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

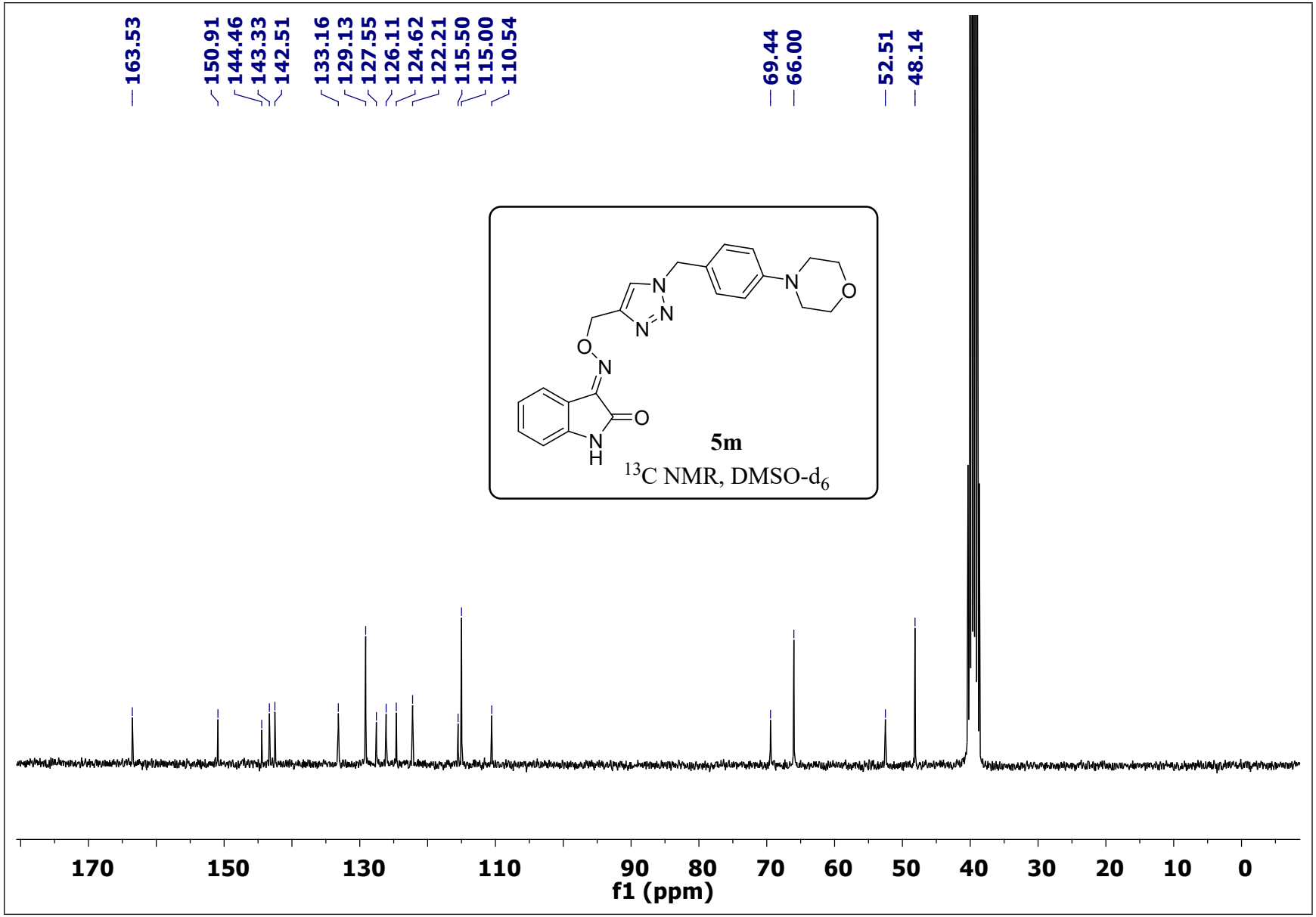

GVK BIOSCIENCES PVT LTD
021909C0850A 78 (1.999)
1: Scan ES+
4.77e7
367.86
389.94
735.03
737.05
738.05
739.03
759.04
791.08
5k
LC-MS(ESI)
m/z: Calcd.
for (M)+: 367.08
Found : 367.96
m/z

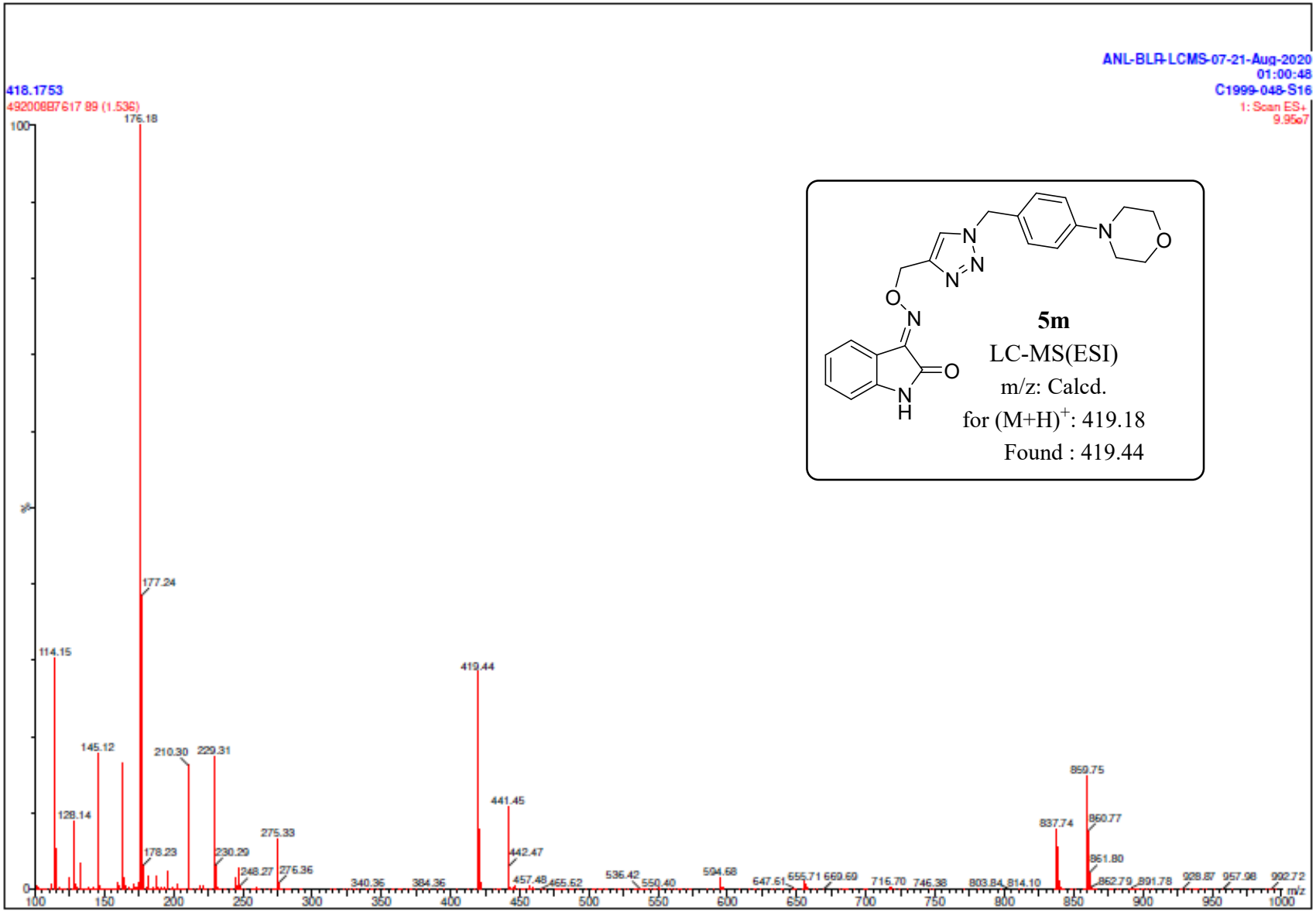

5l
^{1}H NMR, DMSO-d$_6$
0.95
0.90
2.21
2.44
2.45
1.36
1.29
1.15
2.13
2.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

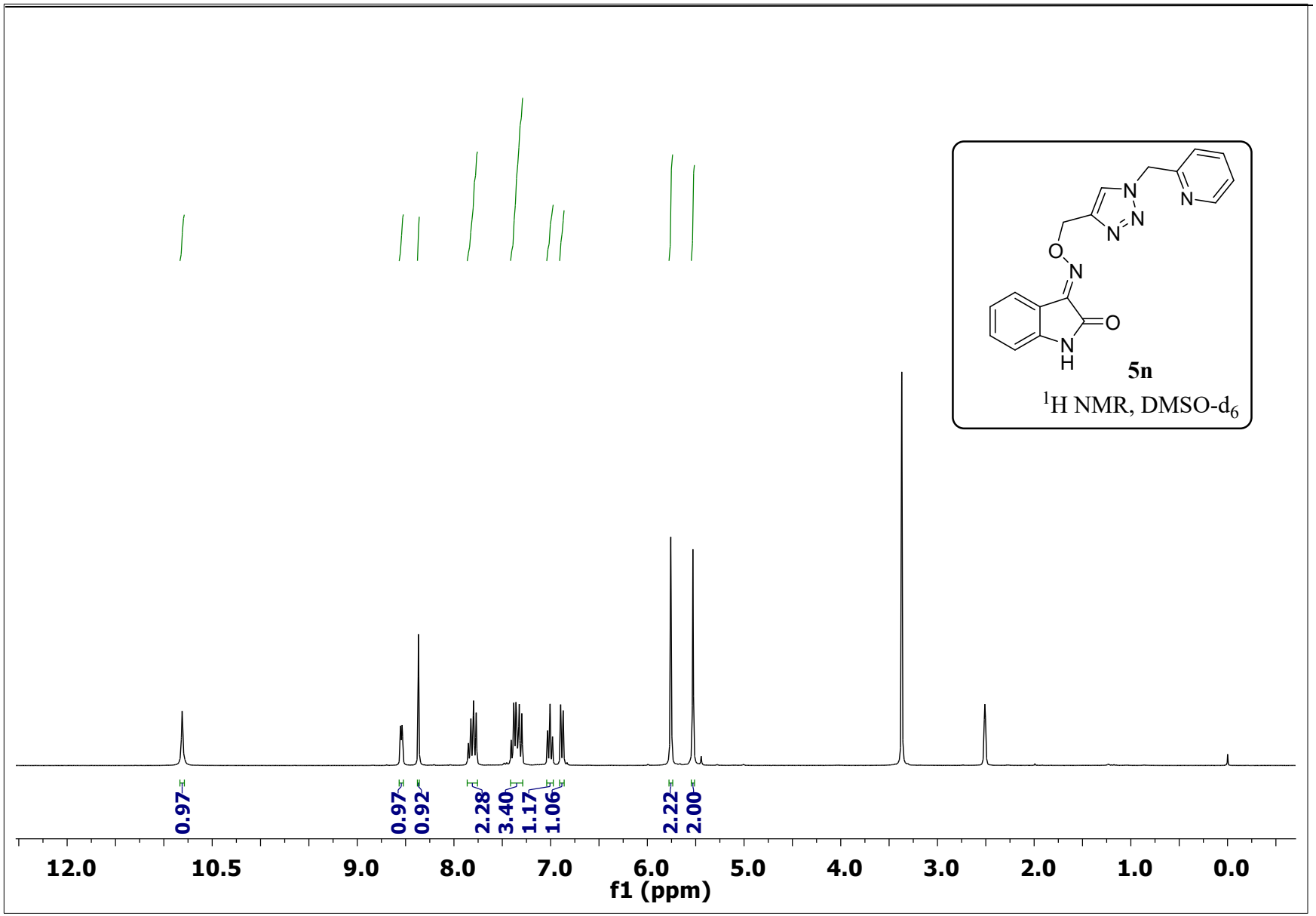

192.12
163.58
144.51
143.36
142.30
134.24
134.09
133.20
128.98
128.17
127.58
126.60
122.24
115.55
110.58
69.52
55.94
5l
13C NMR, DMSO-d6
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

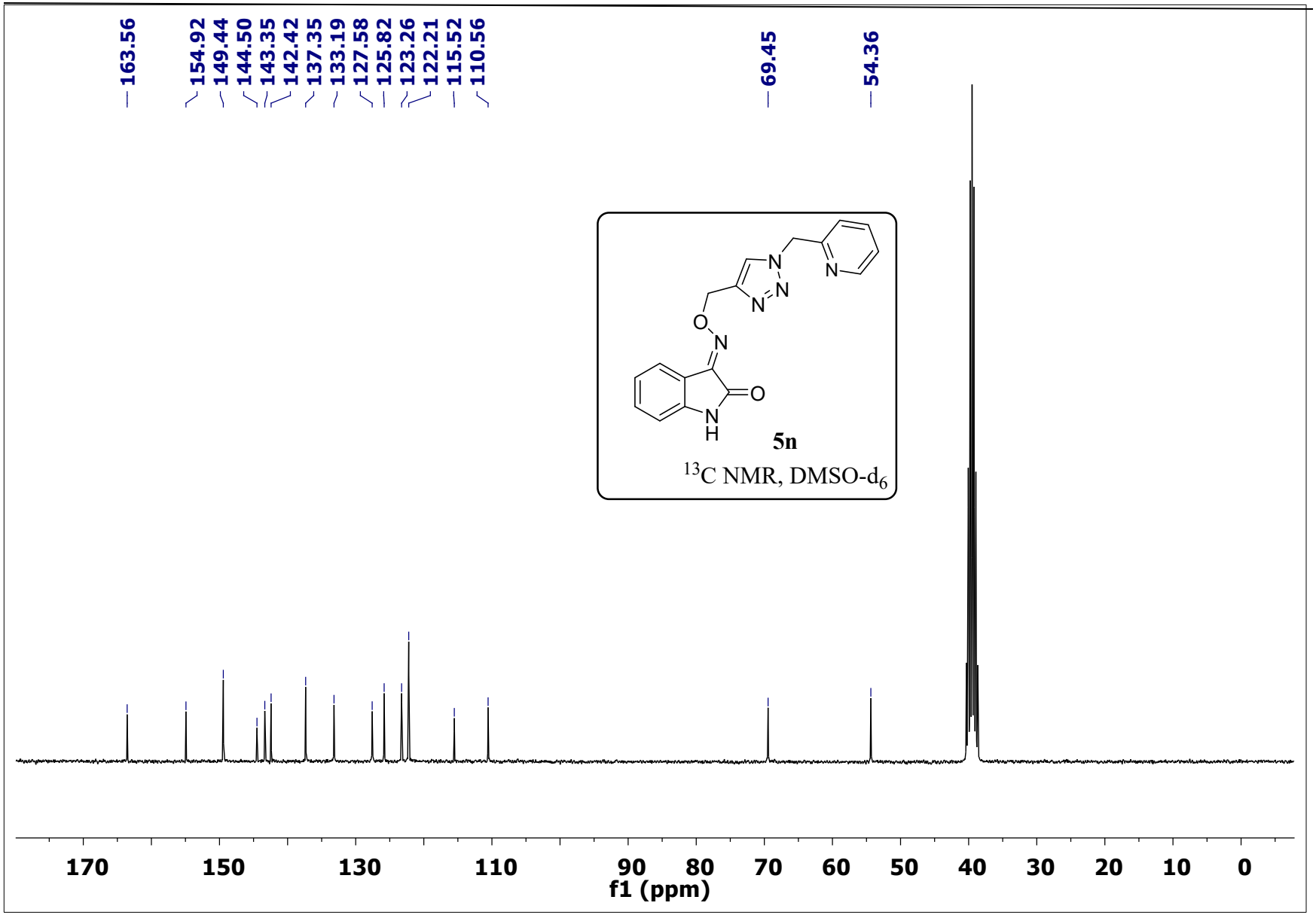

GVK BIOSCIENCES PVT LTD
021610A8478A 74 (1.896)
1: Scan ES+
5.24e7
362.02
723.11
724.12
363.03
725.13
740.11
746.12
364.08
383.38
100
%
0
m/z
100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000
5l
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 362.12
Found : 362.02

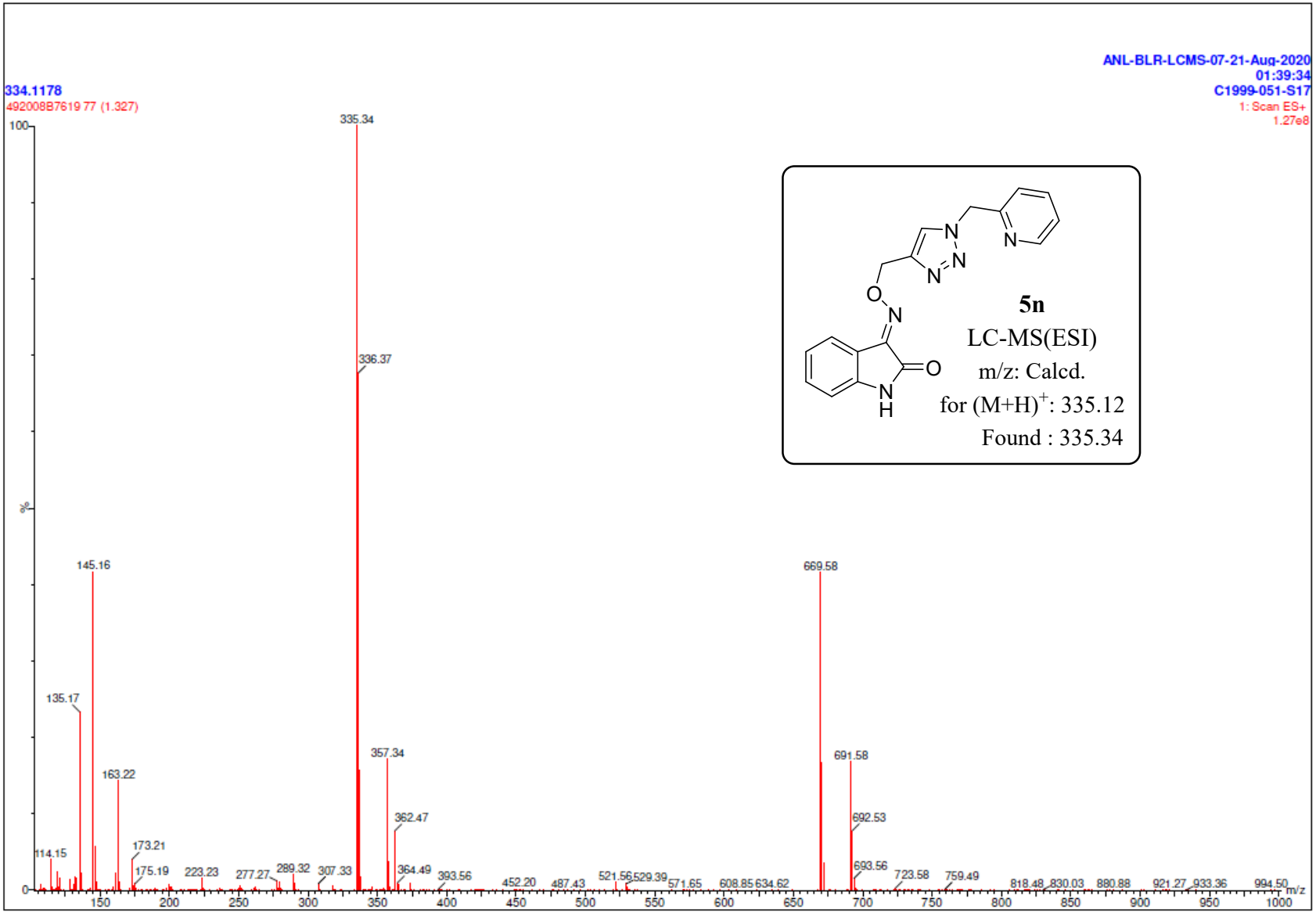

0.88
0.83
1.00
1.13
2.06
1.20
3.19
3.97
4.16
4.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)
5m
^{1}H NMR, DMSO-d$_6$

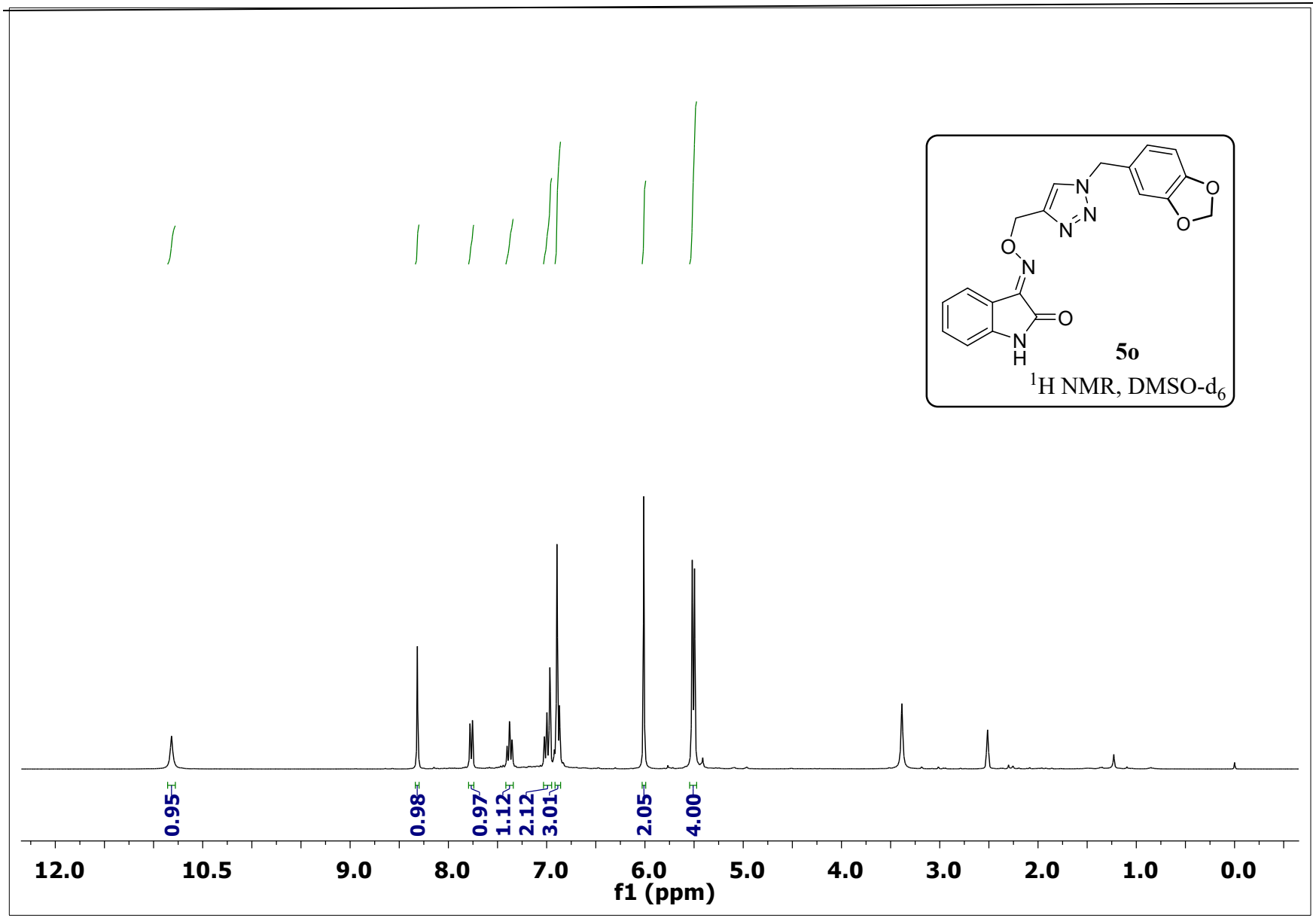

163.53
150.91
144.46
143.33
142.51
133.16
129.13
127.55
126.11
124.62
122.21
115.50
115.00
110.54
69.44
66.00
52.51
48.14
5m
13C NMR, DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

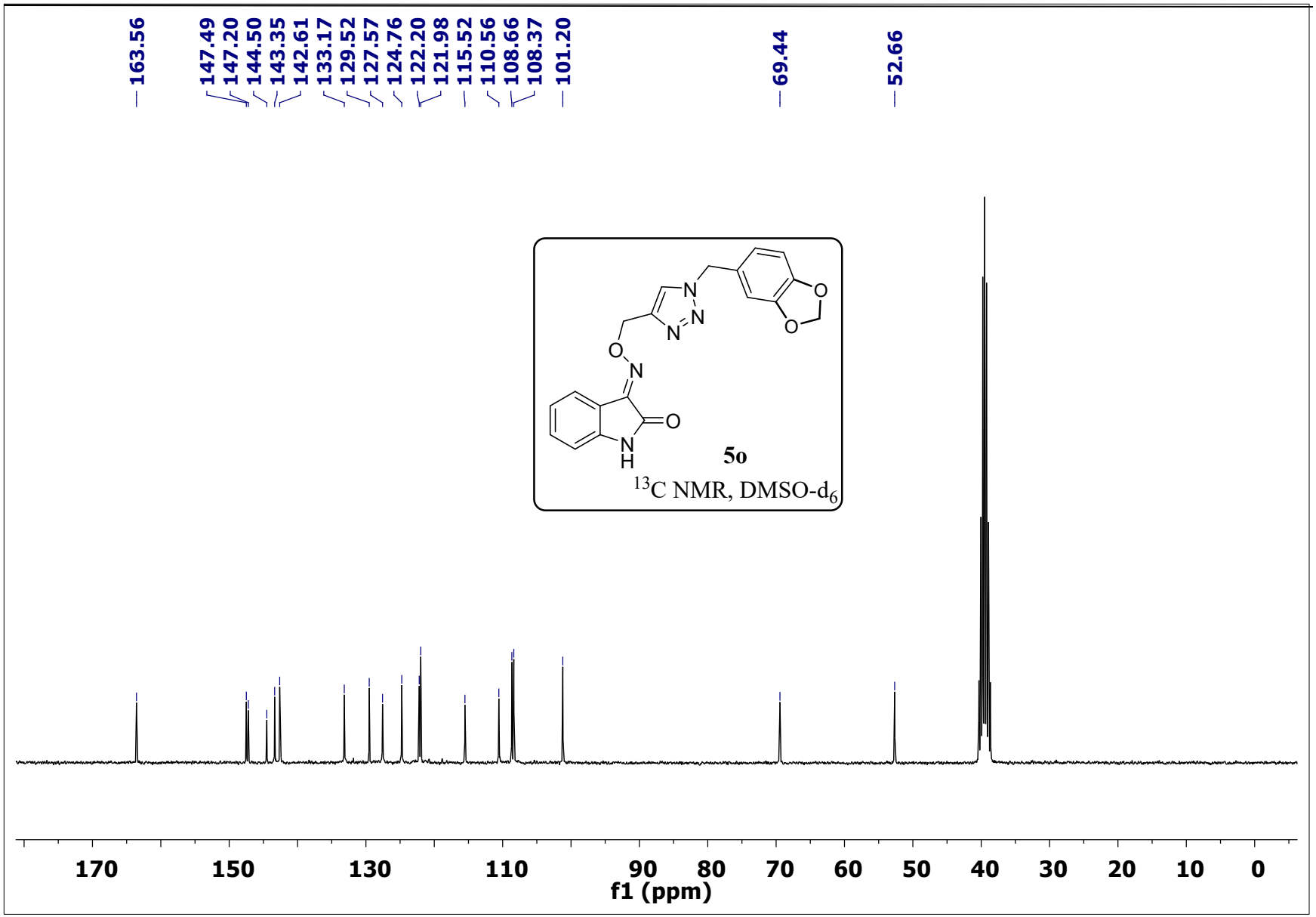

ANL-BLR-LCMS-07-21-Aug-2020
01:00:48
C1999-048-S16
1: Scan ES+
9.95e7
418.1753
4920088 7617 89 (1.536)
5m
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 419.18
Found : 419.44
176.18
177.24
114.15
419.44
145.12
210.30
229.31
441.45
128.14
275.33
178.23
230.29
442.47
248.27
276.36
340.36
384.36
457.48
455.62
536.42
550.40
594.58
647.61
655.71
669.69
716.70
746.38
803.84
814.10
837.74
859.75
860.77
861.80
862.79
891.78
928.87
957.98
992.72
m/z

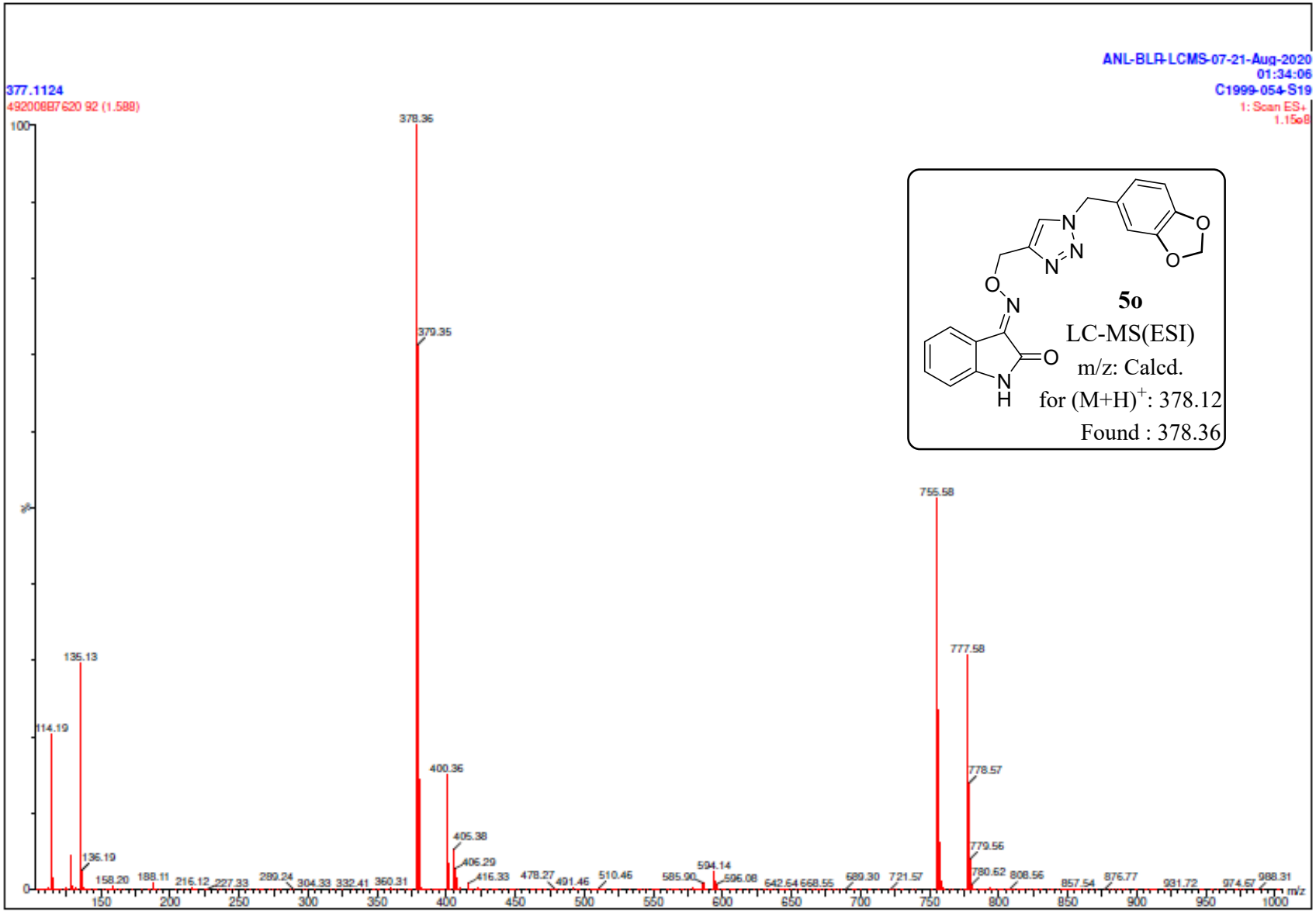

5n
^{1}H NMR, DMSO-d$_6$
0.97
0.97
0.92
2.28
3.40
1.17
1.06
2.22
2.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

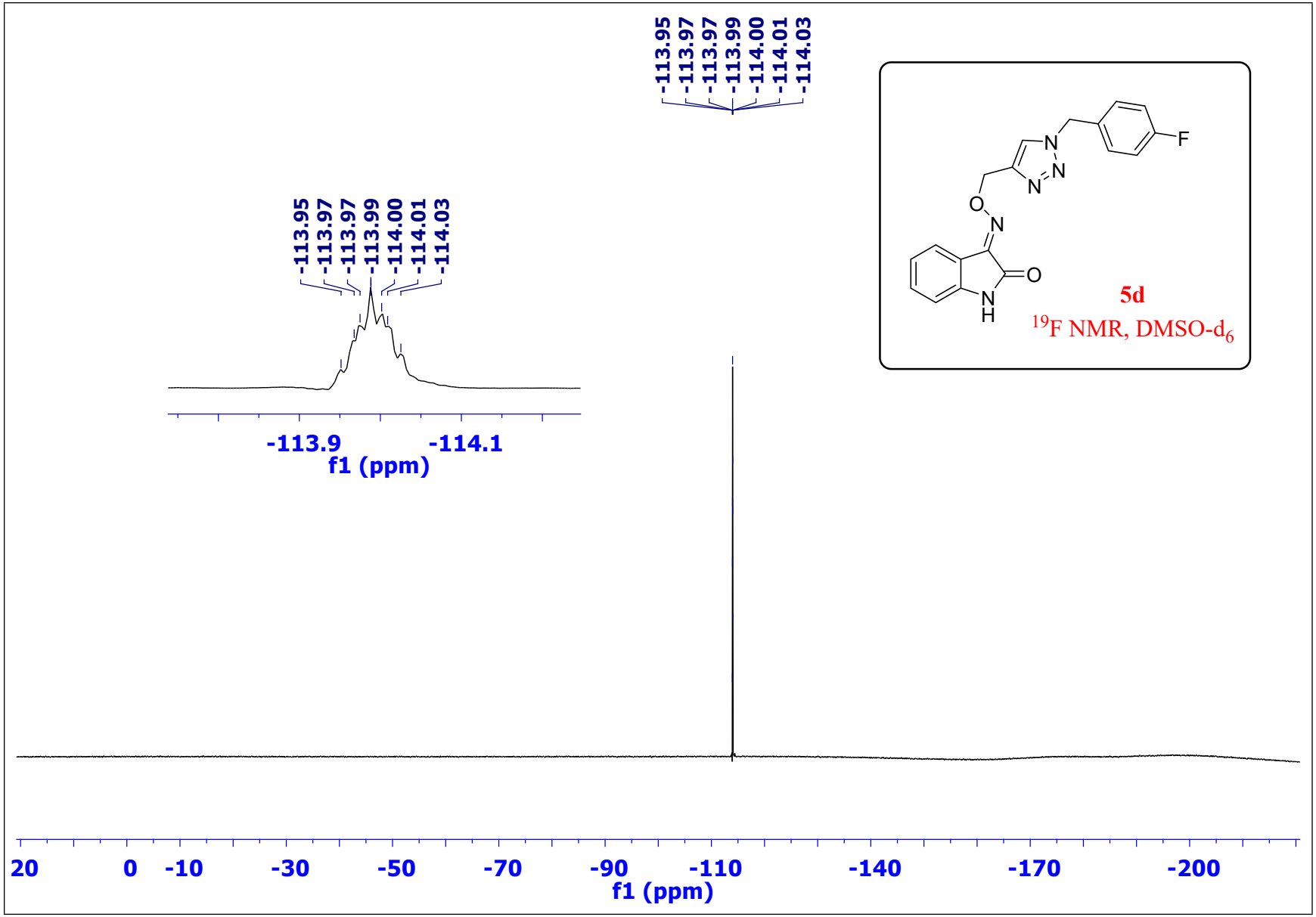

163.56
154.92
149.44
144.50
143.35
142.42
137.35
133.19
127.58
125.82
123.26
122.21
115.52
110.56
69.45
54.36
5n
13C NMR, DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

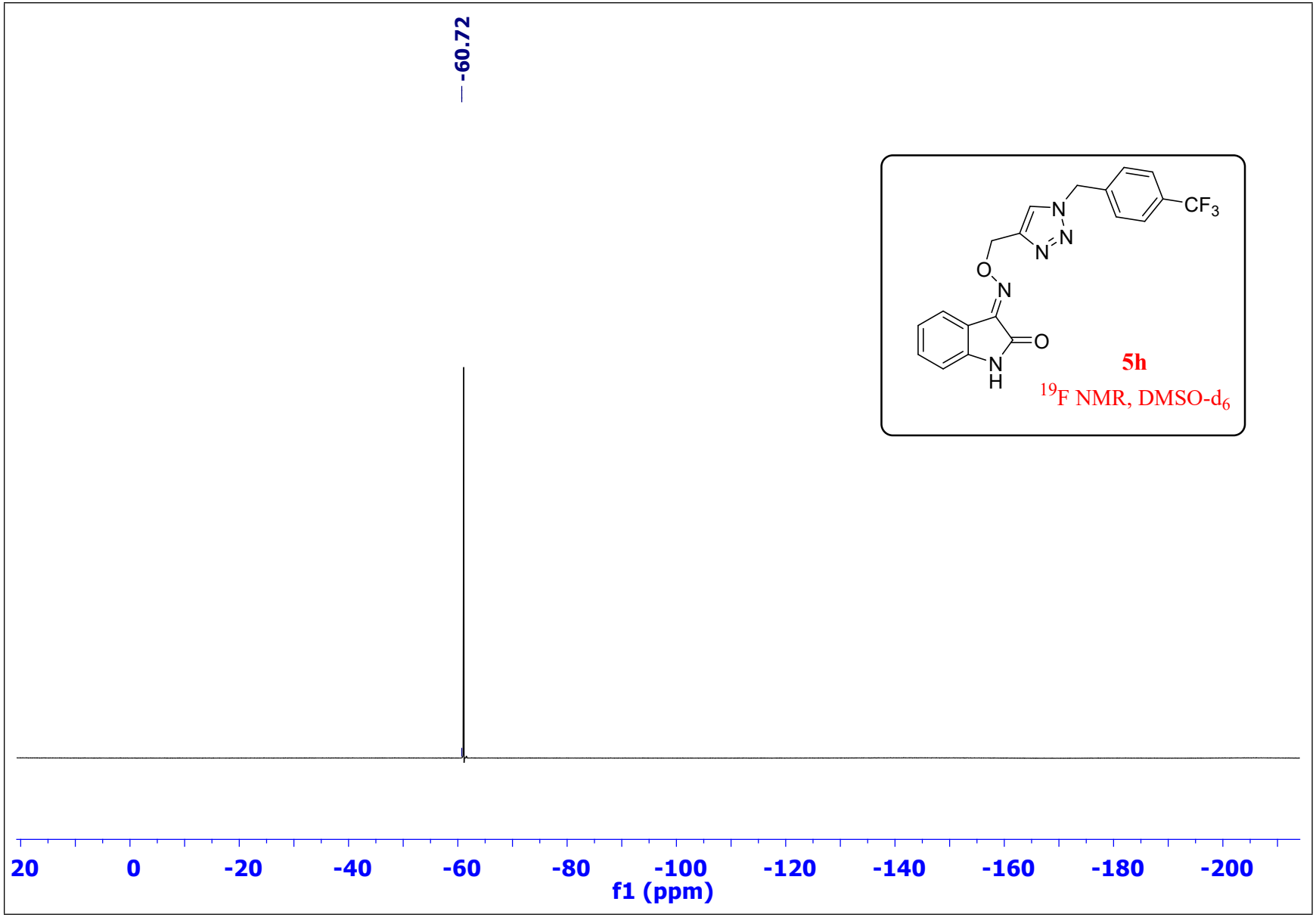

ANL-BLR-LCMS-07-21-Aug-2020
01:39:34
C1999-051-S17
1: Scan ES+
1.27e8
334.1178
492008B7619 77 (1.327)
100
%
0
335.34
336.37
145.16
135.17
163.22
357.34
362.47
173.21
114.15
175.19
223.23
277.27
289.32
307.33
364.49
393.56
452.20
487.43
521.56
529.39
571.65
608.85
634.62
669.58
691.58
692.53
693.56
723.58
759.49
818.48
830.03
880.88
921.27
933.36
994.50
m/z
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900
950
1000
5n
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 335.12
Found : 335.34

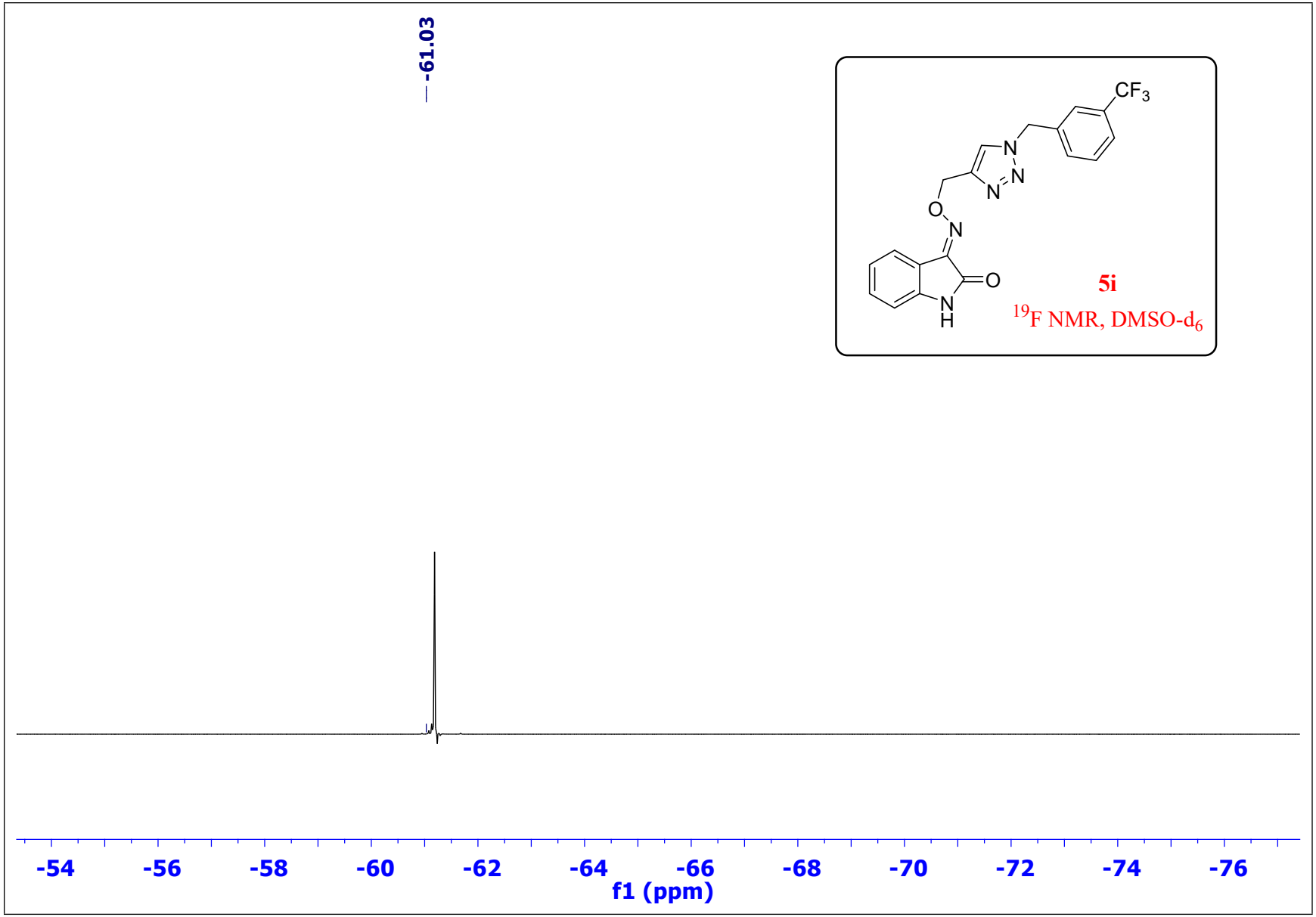

5o
^{1}H NMR, DMSO-d$_6$
0.95
0.98
0.97
1.12
2.12
3.01
2.05
4.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


163.56
147.49
147.20
144.50
143.35
142.61
133.17
129.52
127.57
124.76
122.20
121.98
115.52
110.56
108.66
108.37
101.20
69.44
52.66
5o
13C NMR, DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


ANL-BLR-LCMS-07-21-Aug-2020
01:34:06
C1999-054-S19
1: Scan ES+
1.15e8
377.1124
4920088 7620 92 (1.588)
100
%
0
378.36
379.35
135.13
114.19
136.19
400.36
405.38
406.29
755.58
777.58
778.57
779.56
780.62
5o
LC-MS(ESI)
m/z: Calcd.
for (M+H)+: 378.12
Found : 378.36
m/z


-113.95
-113.97
-113.97
-113.99
-114.00
-114.01
-114.03
-113.9
-114.1
f1 (ppm)
F
N
N
N
O
N
O
N
H
5d
19F NMR, DMSO-d6
20
0
-10
-30
-50
-70
-90
-110
-140
-170
-200
f1 (ppm)


-60.72
CF3
N
N
N
O
N
O
N
H
5h
19F NMR, DMSO-d6
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)


-61.03
CF3
N
N
N
O
N
O
N
H
5i
19F NMR, DMSO-d6
-54
-56
-58
-60
-62
-64
-66
-68
-70
-72
-74
-76
f1 (ppm)

3. 2d NMR studies of compound 3

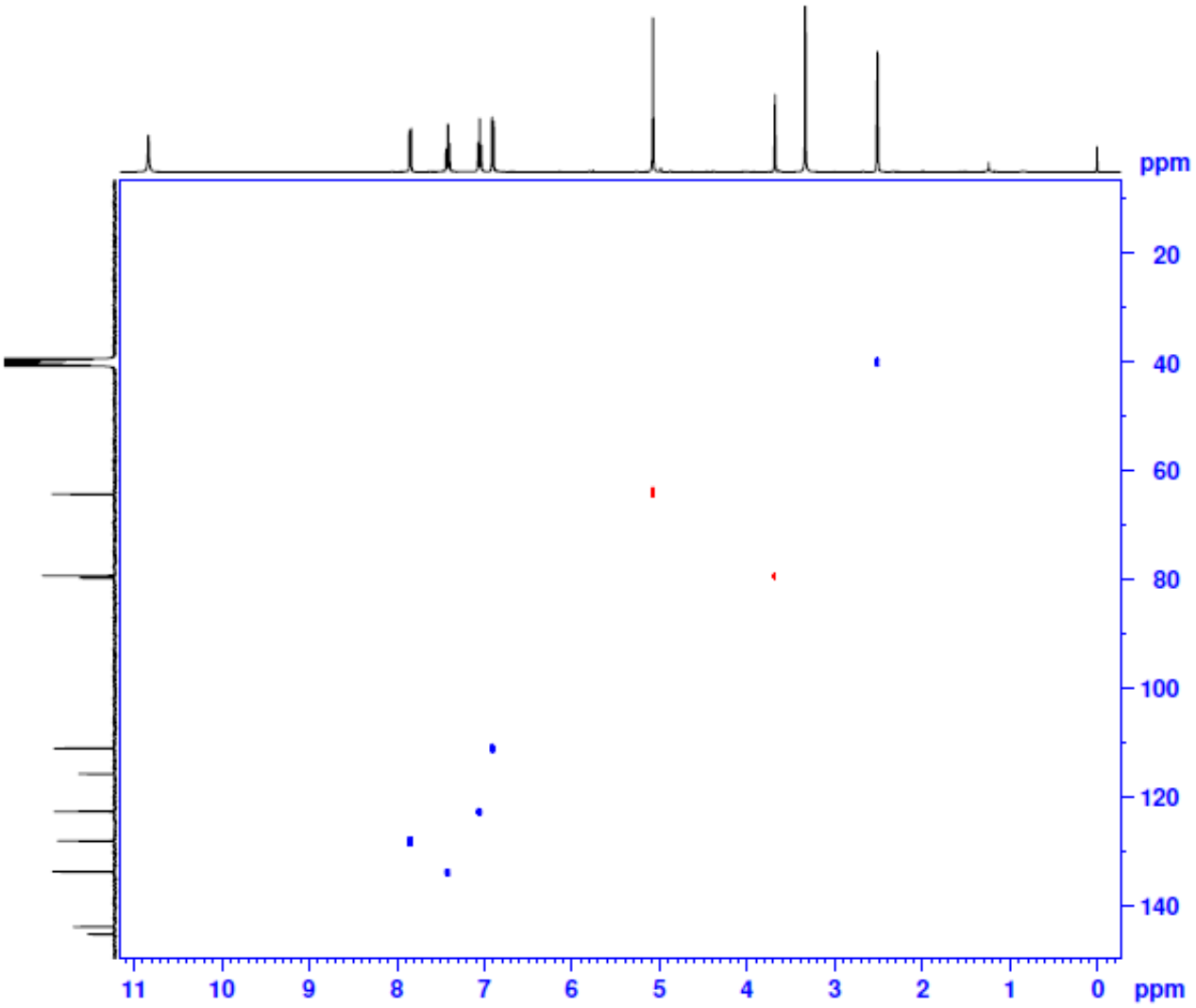


Fig S1. ^{1}H-^{13}C HSQC spectrum of compound **3** in DMSO-d_6 at 400 MHz.

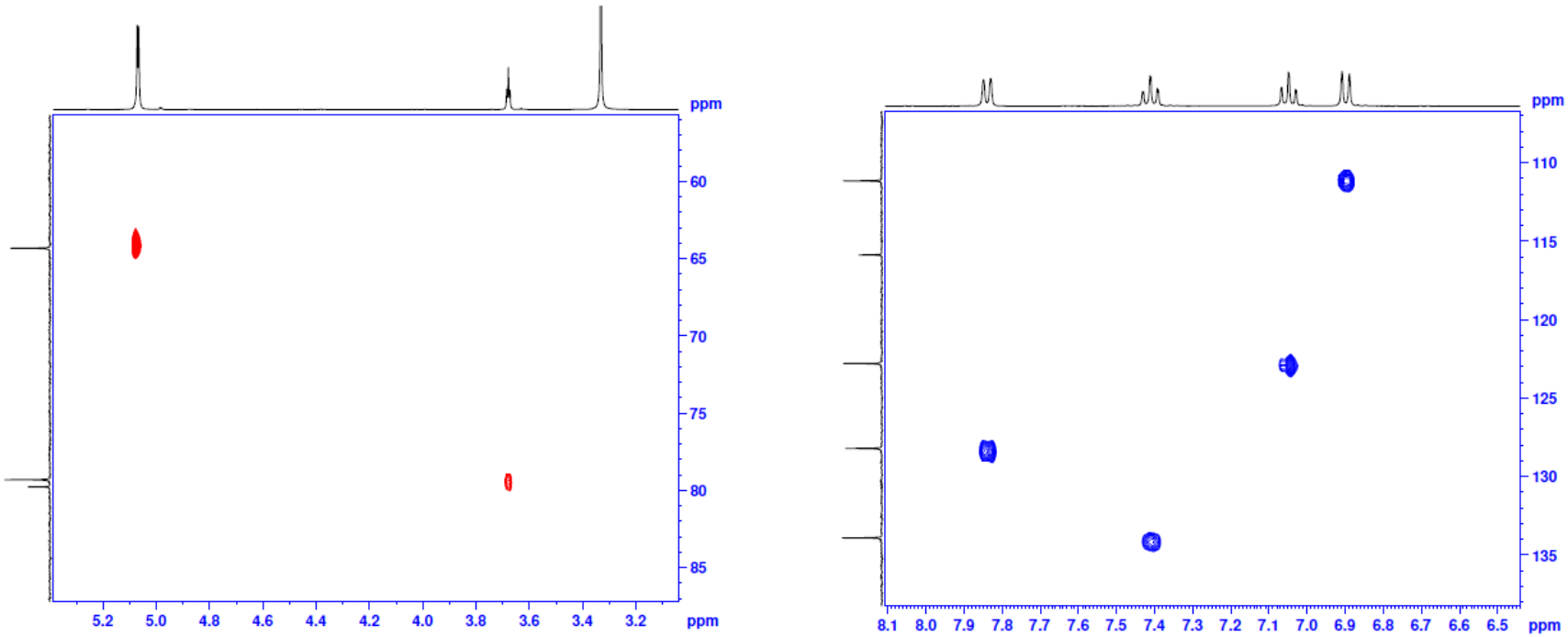


Fig S2.Expanded area of ^{1}H-^{13}C HSQC spectrum of compound **3** (**Blue** indicates **CH** and **Red** indicates **CH_2** and **ethynyl CH**).

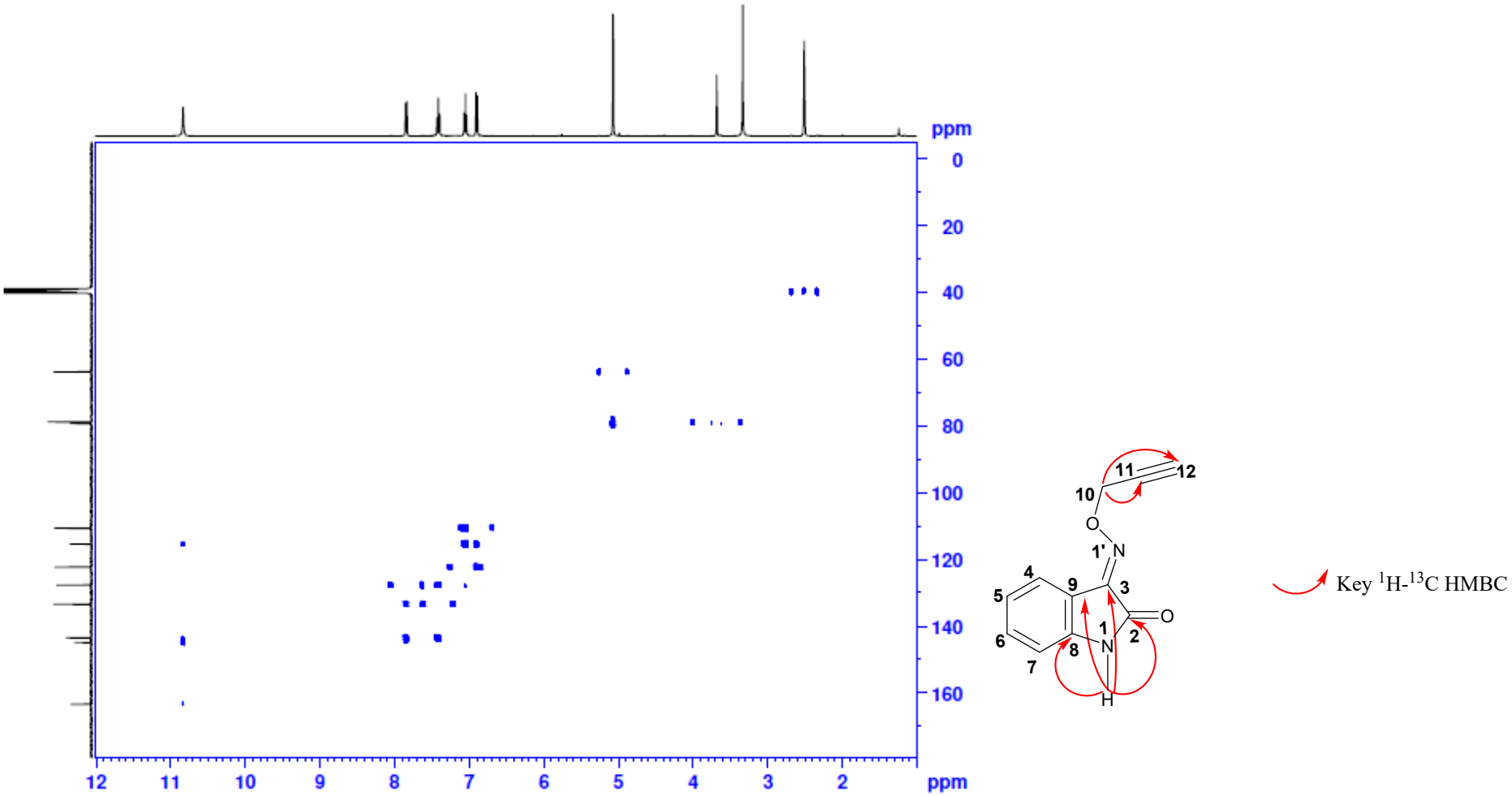


Fig S3.^{1}H-^{13}C HMBC spectrum of compound **3** in DMSO-d_6 at 400 MHz.

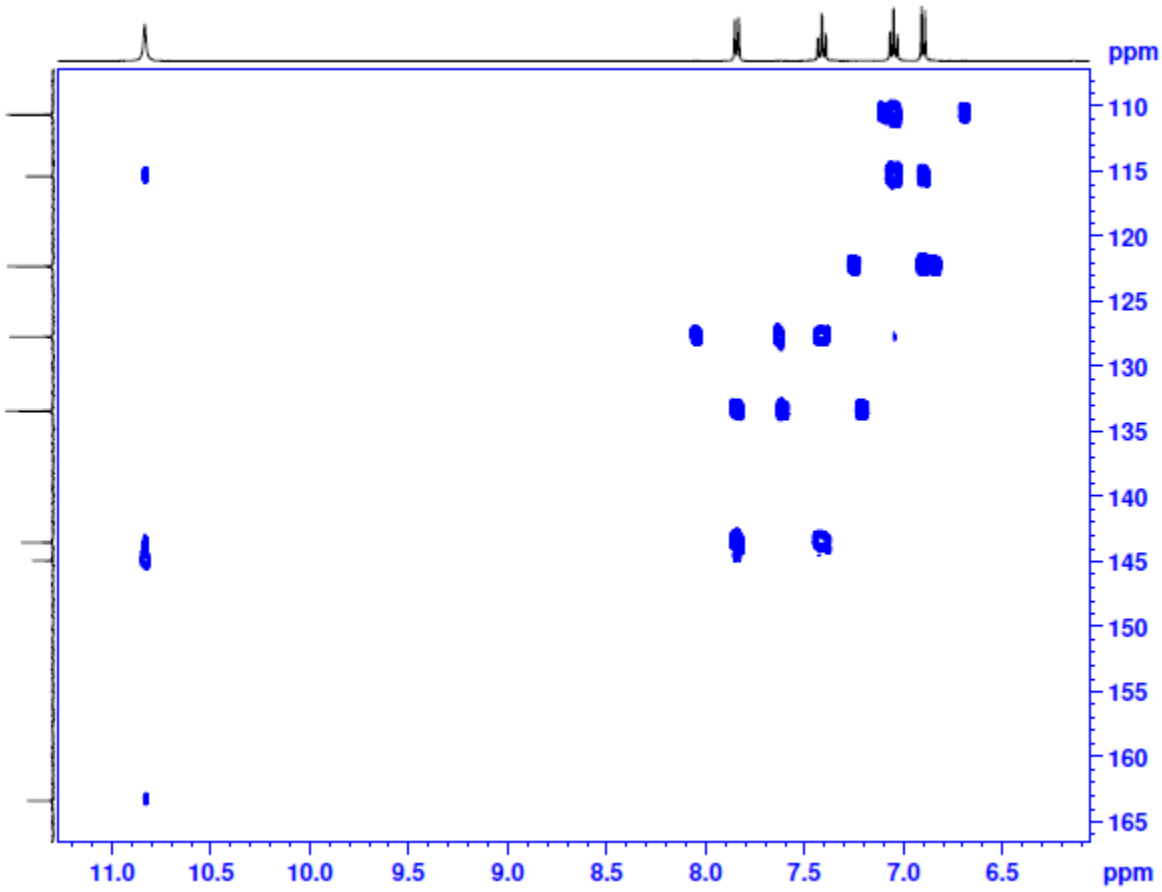


Fig S4. Expanded area of ^{1}H-^{13}C HMBC spectrum of compound **3** in DMSO-d_6 at 400 MHz.

Table S1. Assignments of NMR shift values for compound **3.**

S.NO	Assignment	Type of Atom	^{1}H Chemical Shift (ppm)	^{13}C Chemical shift (ppm)
1	1	NH	10.83	-
2	2	CO	-	163.4
3	3	C	-	144.9
4	4	**CH**	7.83	127.7
5	5	**CH**	7.05	122.2
6	6	**CH**	7.41	133.3
7	7	**CH**	6.89	110.6
8	8	C	-	143.5
9	9	C	-	115.3
10	10	CH_2	5.06	63.8
11	11	C	-	79.2
12	12	CH	3.67	78.7

Key Points:

- The direct attachment of proton with carbon was assigned by ^{1}H-^{13}C HSQC experiment.
- In ^{1}H-^{13}C HMBC experiment **H-10** protons showing correlation to C-11 and C-12 carbons.
- In ^{1}H-^{13}C HMBC experiment **H-1** proton showing correlation to C-2, C-3, C-8 and C-9 carbons.

4. 2d NMR studies of compound 5a

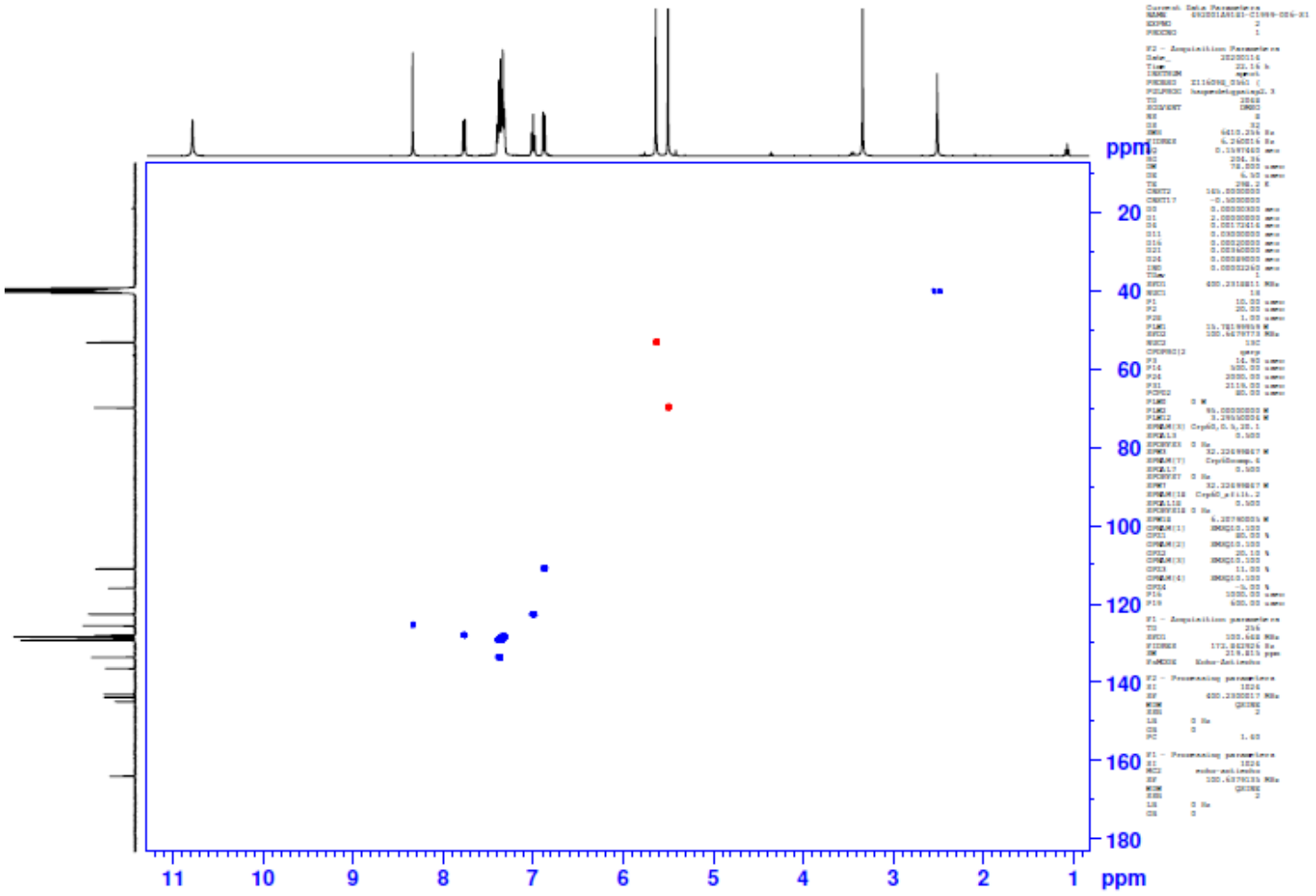


Fig S5. ^{1}H-^{13}C HSQC spectrum of compound **5a** in DMSO-d_6 at 400 MHz

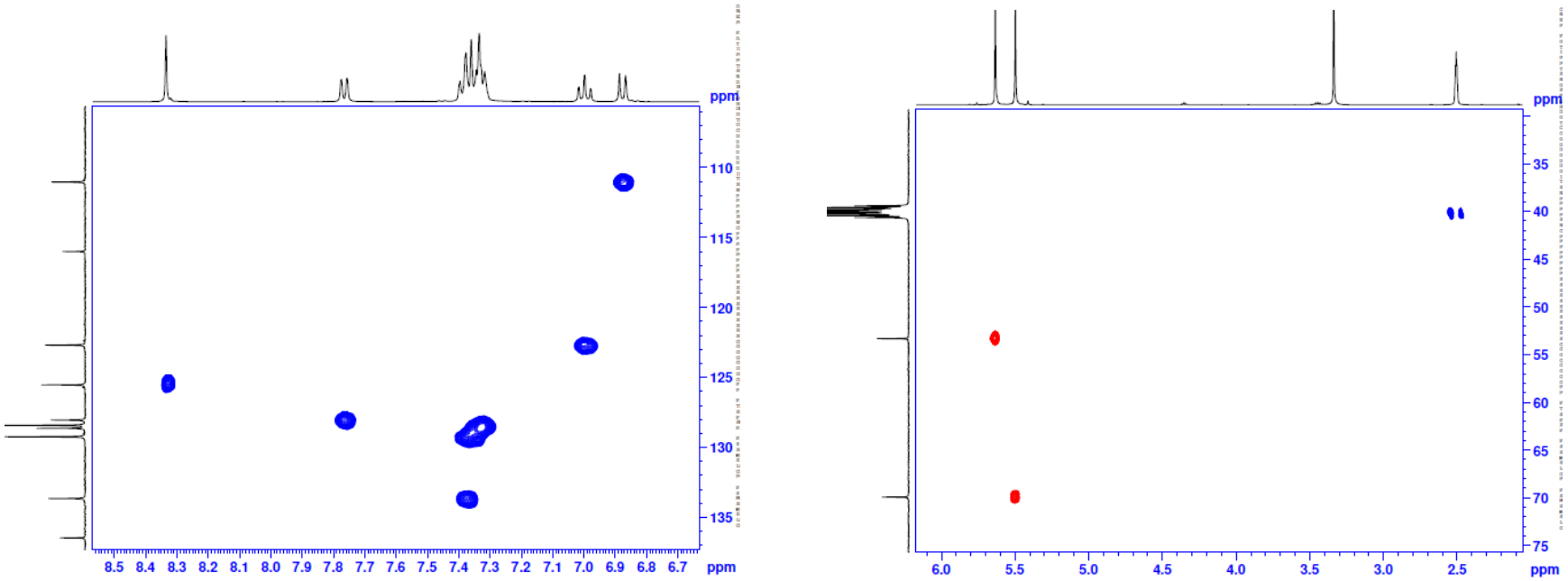


Fig.S6. Expanded area of ^{1}H-^{13}C HSQC spectrum of compound **5a** (**Blue** indicates **CH** and **Red** indicates **CH_2**).

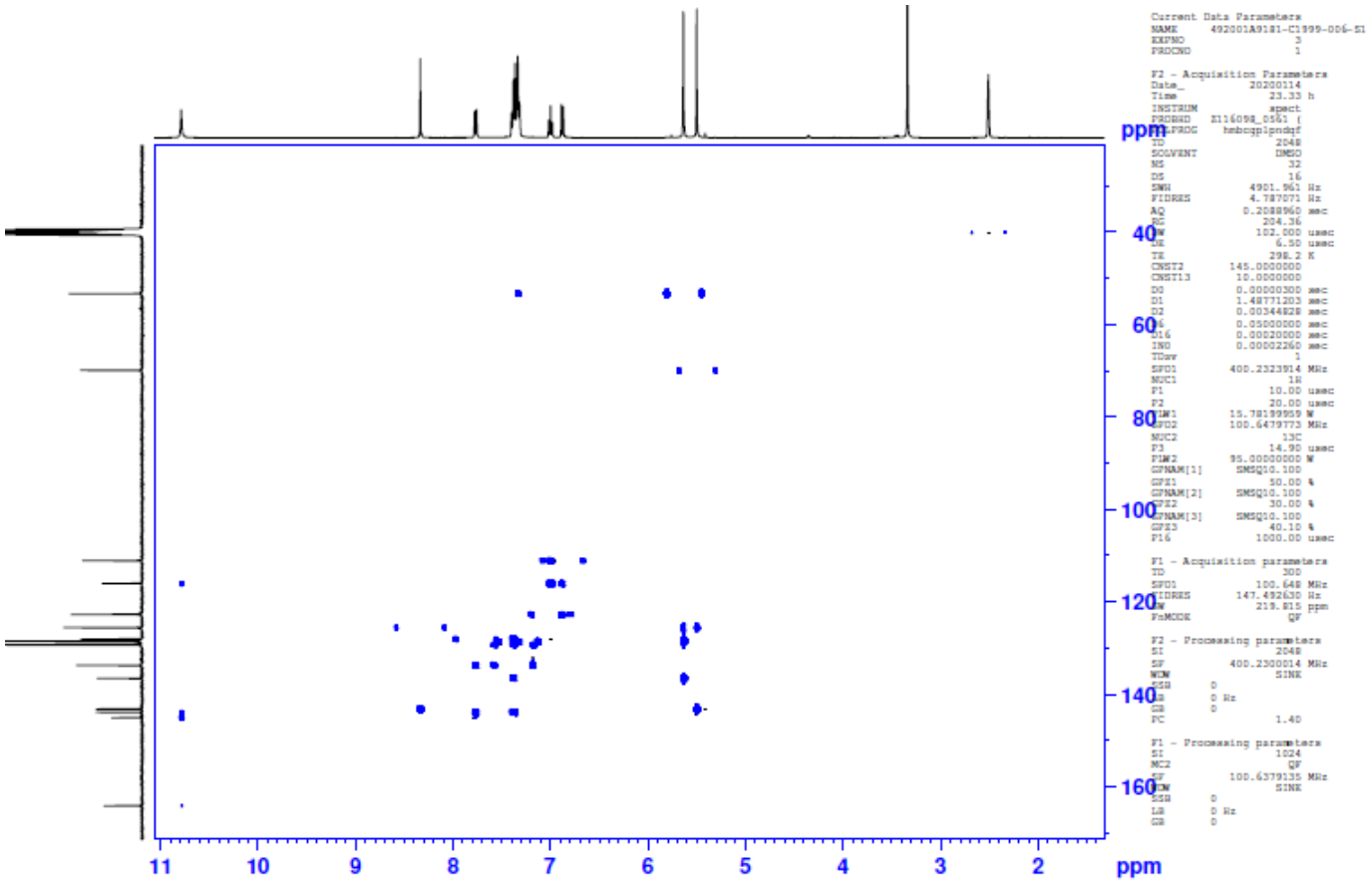


Fig S7.^{1}H-^{13}C HMBC spectrum of compound **5a** in DMSO-d_6 at 400 MHz.

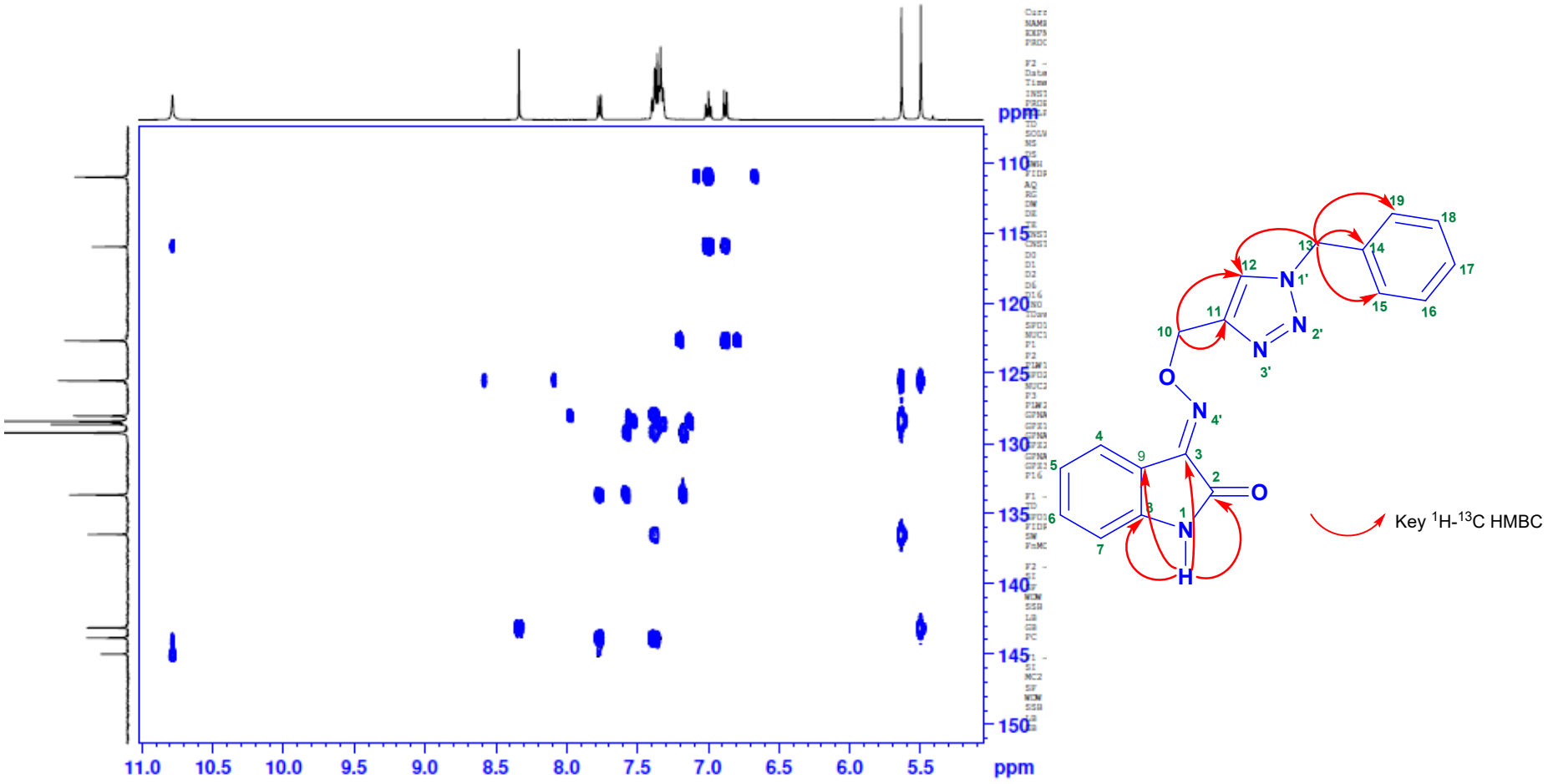


Fig S8. Expanded area of ^{1}H-^{13}C HMBC spectrum of compound **5a** in DMSO-d_6 at 400 MHz.

Table S2. Assignments of NMR shift values for compound **5a.**

S.NO	Assignment	Type of Atom	^{1}H Chemical Shift (ppm)	^{13}C Chemical shift (ppm)
1	1	NH	10.78	-
2	2	CO	-	163.5
3	3	C	-	144.4
4	4	CH	7.75	127.5
5	5	CH	6.97	122.1
6	6	CH	7.39	133.2
7	7	CH	6.86	110.5
8	8	C	-	143.3
9	9	C	-	115.5
10	10	CH_2	5.49	69.4
11	11	C	-	142.6
12	12	CH	8.33	125.0
13	13	CH_2	5.63	52.8
14	14	C	-	135.9
15	15,19	CH	7.32	127.9
16	16,18	CH	7.37	128.7

17	17	CH	7.36	128.1
18	1′	N	-	-
19	2′	N	-	-
20	3′	N	-	-
21	4′	N	-	-

Key Points:

- The direct attachment of proton with carbon was assigned by ^{1}H-^{13}C HSQC experiment.
- In ^{1}H-^{13}C HSQC experiment **H-10** protons attached carbon showing at 69.4 ppm.
- In ^{1}H-^{13}C HMBC experiment **H-10** protons showing connectivity to C-11 and C-12 carbons.
- In ^{1}H-^{13}C HMBC experiment **H-1** proton showing connectivity to C-2, C-3, C-8 and C-9 carbons.
- In ^{1}H-^{13}C HMBC experiment **H-13** protons showing correlations to C-12, C-14, C-15and C-19 carbons.

5 **SwissADME evaluation of compounds 5d, 5e, 5h and 5i along with standard drugs isoniazid and rifampicin.**

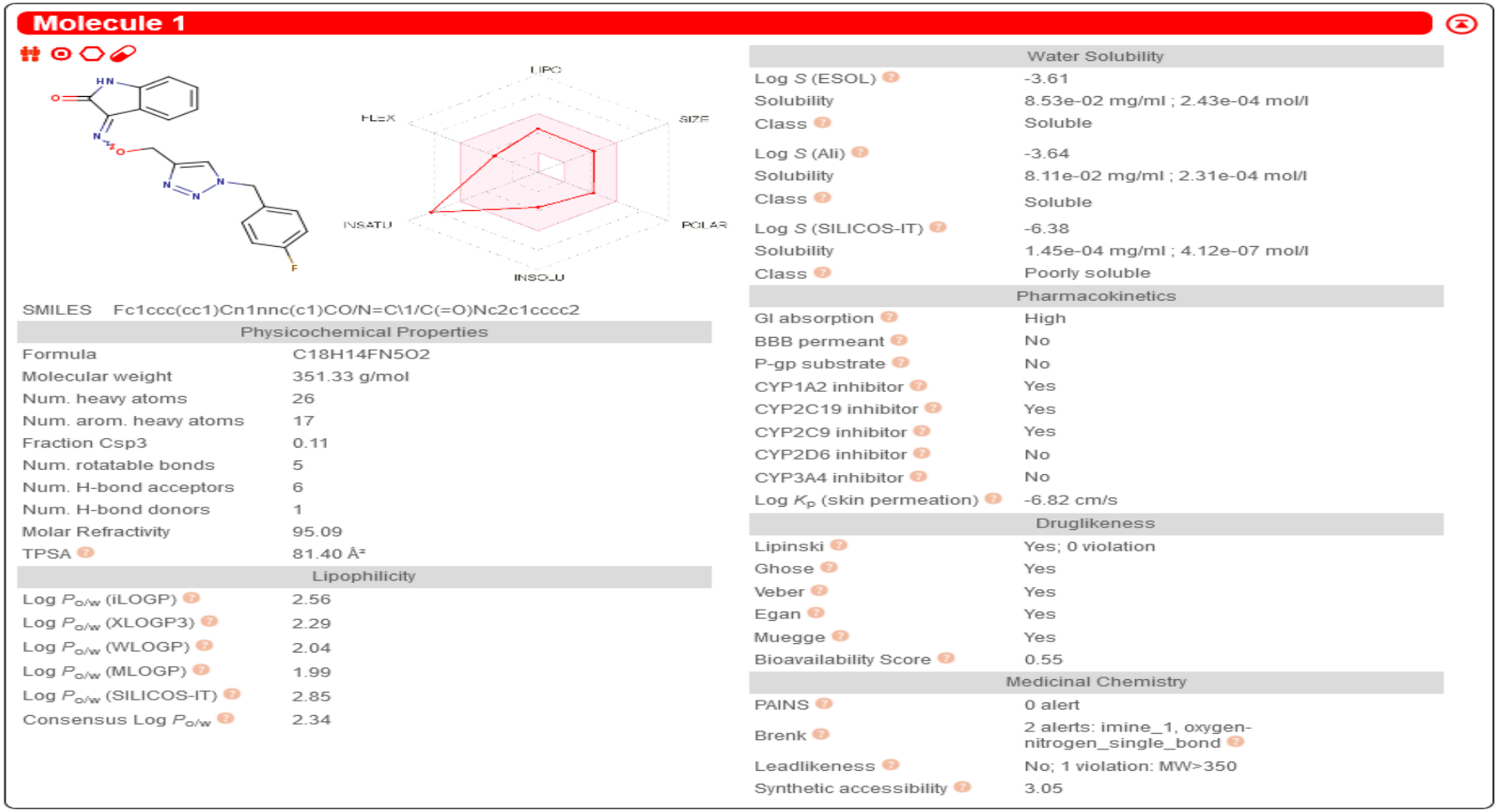
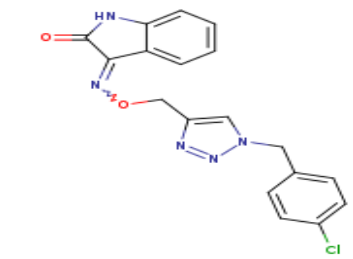
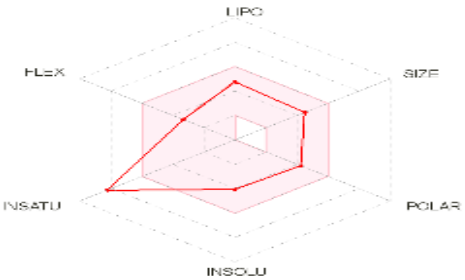


Fig S9. SwissADME prediction of compound **5d**.

Molecule 2





SMILES Clc1ccc(cc1)Cn1nnc(c1)CO/N=C\1/C(=O)Nc2c1cccc2

Physicochemical Properties	
Formula	C18H14ClN5O2
Molecular weight	367.79 g/mol
Num. heavy atoms	26
Num. arom. heavy atoms	17
Fraction Csp3	0.11
Num. rotatable bonds	5
Num. H-bond acceptors	5
Num. H-bond donors	1
Molar Refractivity	100.14
TPSA	81.40 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	2.74
Log $P_{o/w}$ (XLOGP3)	2.82
Log $P_{o/w}$ (WLOGP)	2.13
Log $P_{o/w}$ (MLOGP)	2.10
Log $P_{o/w}$ (SILICOS-IT)	3.07
Consensus Log $P_{o/w}$	2.57

Water Solubility	
Log *S* (ESOL)	-4.05
Solubility	3.27e-02 mg/ml ; 8.90e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-4.19
Solubility	2.39e-02 mg/ml ; 6.50e-05 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-6.71
Solubility	7.17e-05 mg/ml ; 1.95e-07 mol/l
Class	Poorly soluble
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	Yes
Log K_p (skin permeation)	-6.54 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, oxygen-nitrogen_single_bond
Leadlikeness	No; 1 violation: MW>350
Synthetic accessibility	3.04

Fig S10. SwissADME prediction of compound **5e**.

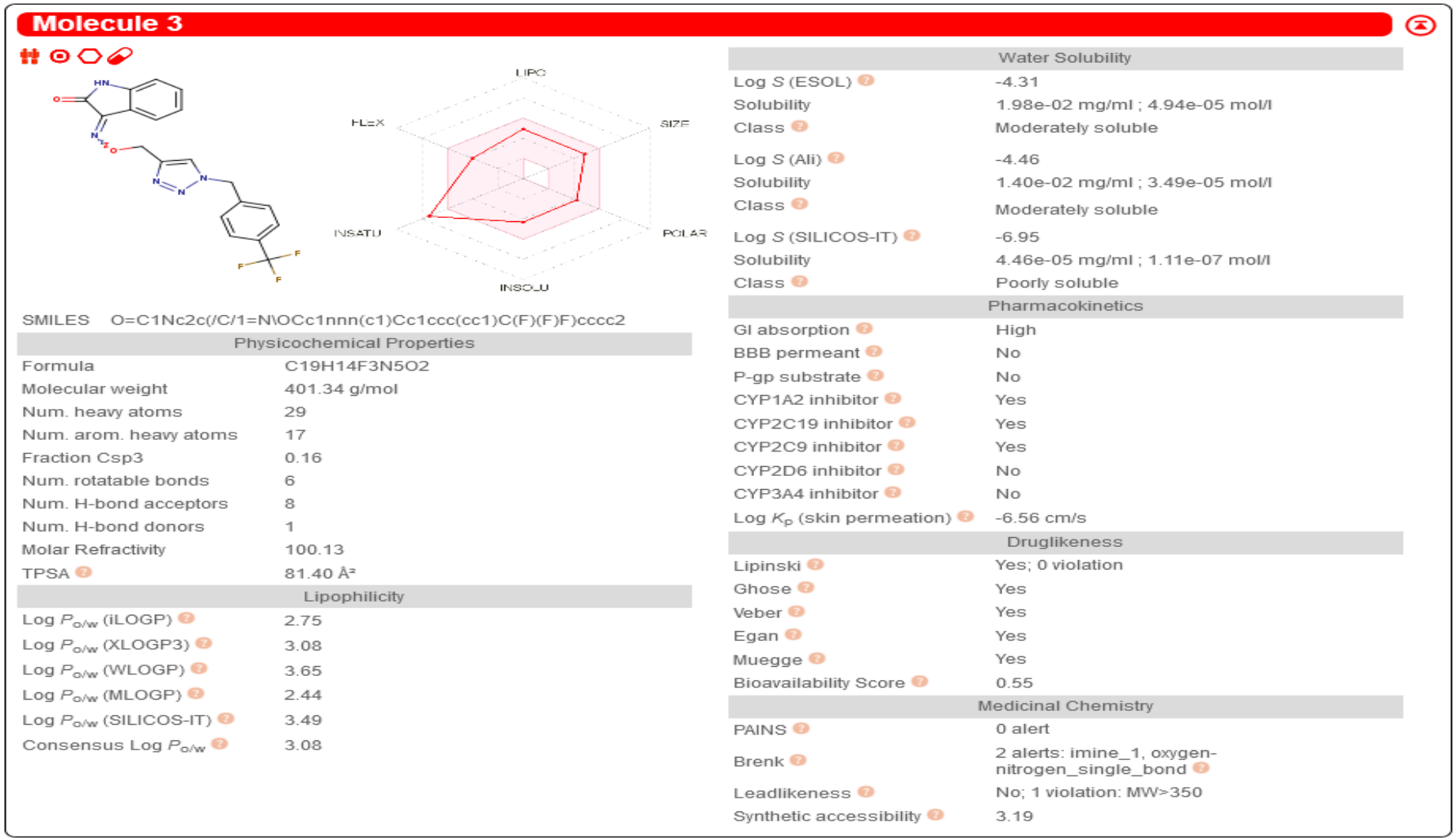
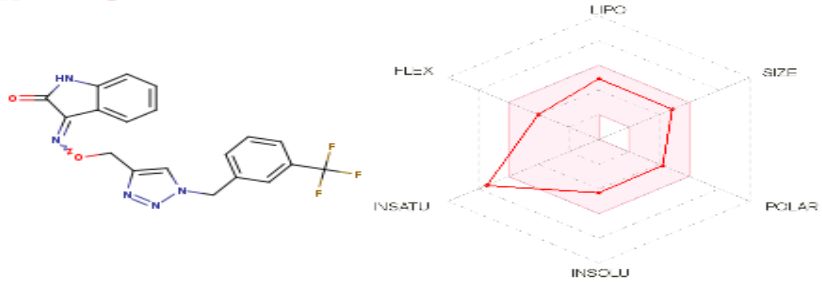


Fig S11. SwissADME prediction of compound **5h**.

Molecule 4



SMILES O=C1Nc2c(/C/1=N\OCc1nnn(c1)Cc1cccc(c1)C(F)(F)F)cccc2

Physicochemical Properties	
Formula	C19H14F3N5O2
Molecular weight	401.34 g/mol
Num. heavy atoms	29
Num. arom. heavy atoms	17
Fraction Csp3	0.16
Num. rotatable bonds	6
Num. H-bond acceptors	8
Num. H-bond donors	1
Molar Refractivity	100.13
TPSA	81.40 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	2.69
Log $P_{o/w}$ (XLOGP3)	3.08
Log $P_{o/w}$ (WLOGP)	3.65
Log $P_{o/w}$ (MLOGP)	2.44
Log $P_{o/w}$ (SILICOS-IT)	3.49
Consensus Log $P_{o/w}$	3.07

Water Solubility	
Log *S* (ESOL)	-4.31
Solubility	1.98e-02 mg/ml ; 4.94e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-4.46
Solubility	1.40e-02 mg/ml ; 3.49e-05 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-6.95
Solubility	4.46e-05 mg/ml ; 1.11e-07 mol/l
Class	Poorly soluble

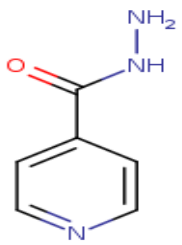
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.56 cm/s

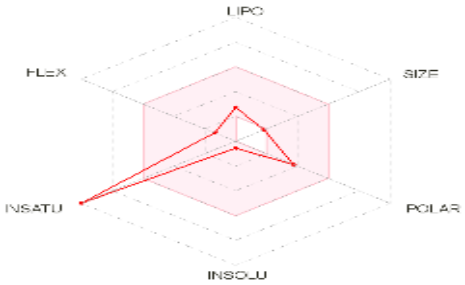
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, oxygen-nitrogen_single_bond
Leadlikeness	No; 1 violation: MW>350
Synthetic accessibility	3.21

Fig S12. SwissADME prediction of compound **5i**.

Molecule 5





SMILES NNC(=O)c1ccncc1

Physicochemical Properties	
Formula	C6H7N3O
Molecular weight	137.14 g/mol
Num. heavy atoms	10
Num. arom. heavy atoms	6
Fraction Csp3	0.00
Num. rotatable bonds	2
Num. H-bond acceptors	3
Num. H-bond donors	2
Molar Refractivity	35.13
TPSA	68.01 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	0.03
Log $P_{o/w}$ (XLOGP3)	-0.70
Log $P_{o/w}$ (WLOGP)	-0.31
Log $P_{o/w}$ (MLOGP)	-0.47
Log $P_{o/w}$ (SILICOS-IT)	-0.27
Consensus Log $P_{o/w}$	-0.35

Water Solubility	
Log *S* (ESOL)	-0.56
Solubility	3.77e+01 mg/ml ; 2.75e-01 mol/l
Class	Very soluble
Log *S* (Ali)	-0.25
Solubility	7.66e+01 mg/ml ; 5.58e-01 mol/l
Class	Very soluble
Log *S* (SILICOS-IT)	-1.64
Solubility	3.17e+00 mg/ml ; 2.31e-02 mol/l
Class	Soluble

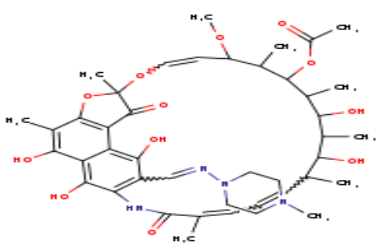
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-7.63 cm/s

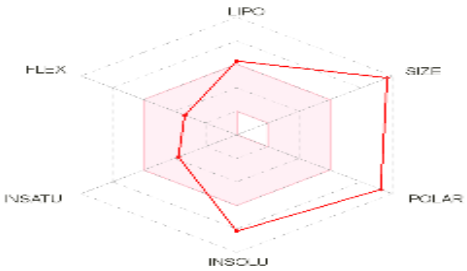
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	No; 3 violations: MW<160, MR<40, #atoms<20
Veber	Yes
Egan	Yes
Muegge	No; 1 violation: MW<200
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: acyl_hydrazine, hydrazine
Leadlikeness	No; 1 violation: MW<250
Synthetic accessibility	1.24

Fig S13. SwissADME prediction of **isoniazid**.

Molecule 6





SMILES COC1C=COC2(C)Oc3c(C2=O)c2c(O)c(C=NN4CCN(CC4)C)c(c(c2c(c3C)O)O)NC(=O)C(=CC=CC(C(C(C(C(C(C1C)OC(=O)C)C)O)C)O)C)C

Physicochemical Properties	
Formula	C43H58N4O12
Molecular weight	822.94 g/mol
Num. heavy atoms	59
Num. arom. heavy atoms	10
Fraction Csp3	0.53
Num. rotatable bonds	5
Num. H-bond acceptors	14
Num. H-bond donors	6
Molar Refractivity	234.22
TPSA	220.15 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	5.25
Log $P_{o/w}$ (XLOGP3)	5.46
Log $P_{o/w}$ (WLOGP)	3.00
Log $P_{o/w}$ (MLOGP)	0.14
Log $P_{o/w}$ (SILICOS-IT)	2.07
Consensus Log $P_{o/w}$	3.19

Water Solubility	
Log *S* (ESOL)	-8.18
Solubility	5.47e-06 mg/ml ; 6.65e-09 mol/l
Class	Poorly soluble
Log *S* (Ali)	-9.84
Solubility	1.19e-07 mg/ml ; 1.44e-10 mol/l
Class	Poorly soluble
Log *S* (SILICOS-IT)	-4.74
Solubility	1.50e-02 mg/ml ; 1.83e-05 mol/l
Class	Moderately soluble

Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-7.44 cm/s

Druglikeness	
Lipinski	No; 3 violations: MW>500, NorO>10, NHorOH>5
Ghose	No; 3 violations: MW>480, MR>130, #atoms>70
Veber	No; 1 violation: TPSA>140
Egan	No; 1 violation: TPSA>131.6
Muegge	No; 5 violations: MW>600, XLOGP3>5, TPSA>150, H-acc>10, H-don>5
Bioavailability Score	0.17

Medicinal Chemistry	
PAINS	3 alerts: hzone_phenol_A, hzone_pipzn, keto_naphthol_A
Brenk	3 alerts: catechol, hydroquinone, imine_1
Leadlikeness	No; 2 violations: MW>350, XLOGP3>3.5
Synthetic accessibility	9.23

Fig S14. SwissADME prediction of **rifampicin**.

The bioavailability radar for compounds 5d, 5e, 5h and 5i along with standard drugs isoniazid and rifampicin

The pink area represents the optimal range for each property (lipophilicity: XLOGP3 between −0.7 and +5.0, size: MW between 150 and 500 g/mol, polarity: TPSA between 20 and 130 Å, solubility: log S not higher than 6, saturation: fraction of carbons in the sp^3 hybridization not less than 0.25, and flexibility: no more than 9 rotatable bonds).

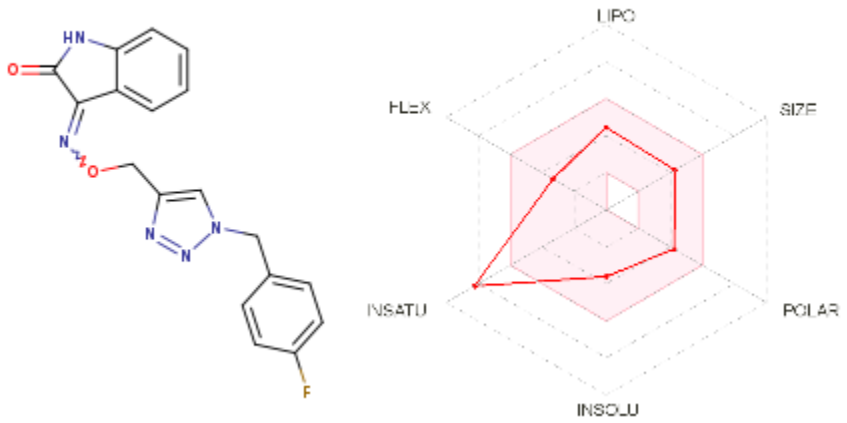


Fig S15. The bioavailability radar for compound **5d**.

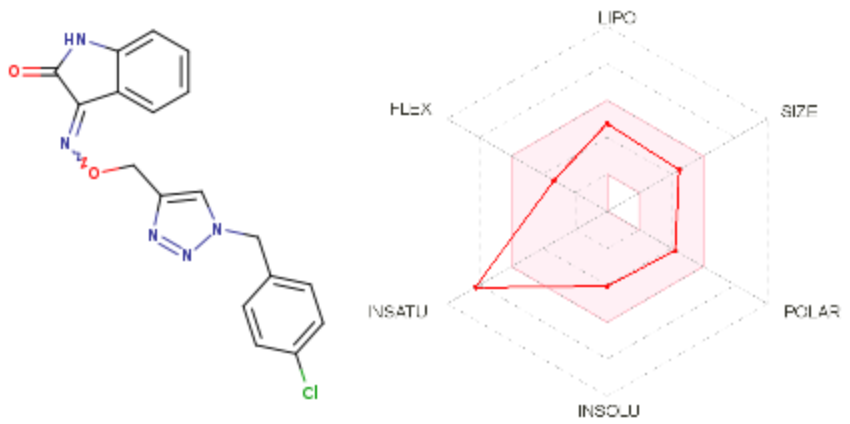


Fig S16. The bioavailability radar for compound **5e**.

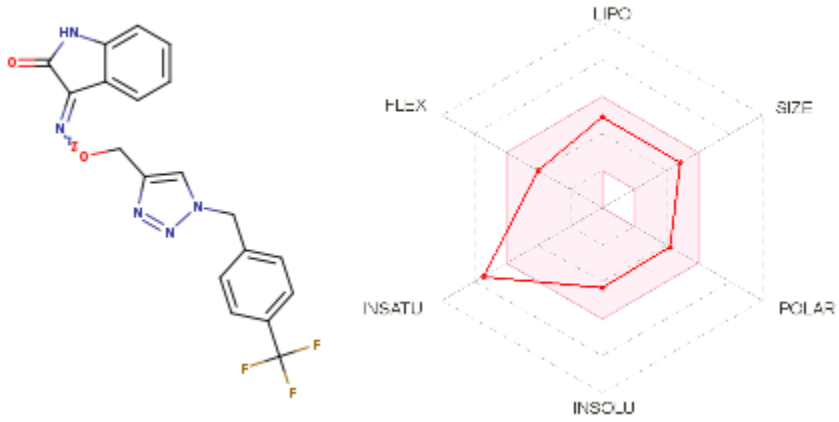


Fig S17. The bioavailability radar for compound **5h**.

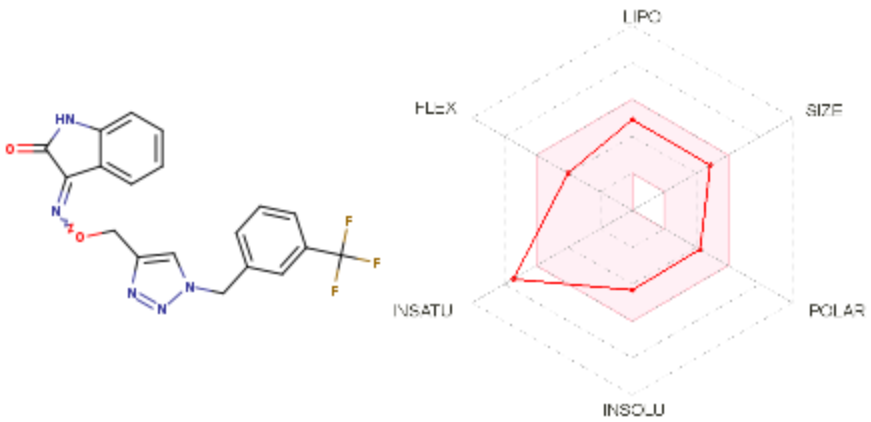


Fig S18. The bioavailability radar for compound **5i**.

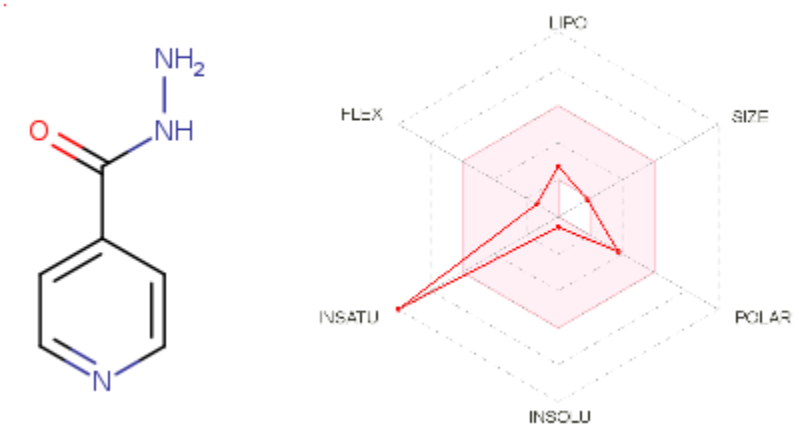


Fig S19. The bioavailability radar for isoniazid.

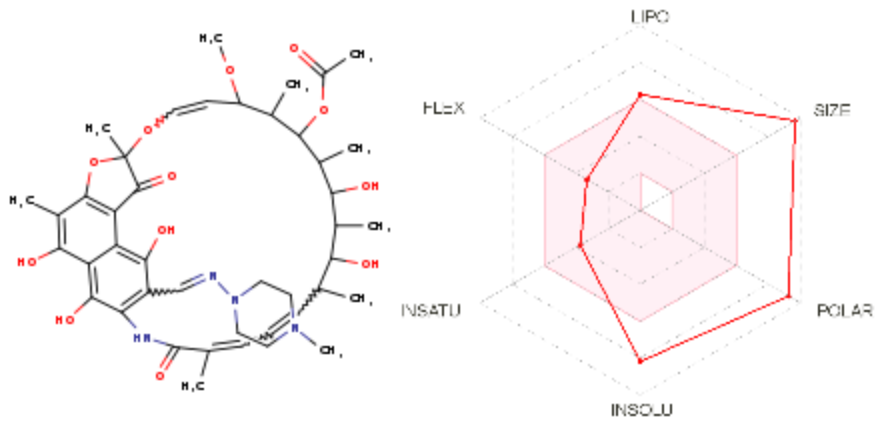


Fig S20. The bioavailability radar for **rifampicin.**

BOILED-Egg representation for compounds 5d, 5e, 5h and 5i along with standard drugs isoniazid and rifampicin

The BOILED-Egg representation allows for intuitive evaluation of passive gastrointestinal absorption (HIA) and brain penetration (BBB) in function of the position of the molecules in the WLOGP-versus-TPSA referential. The **white region** is for high probability of passive absorption by the gastrointestinal tract, and the **yellow region (yolk)** is for high probability of brain penetration.

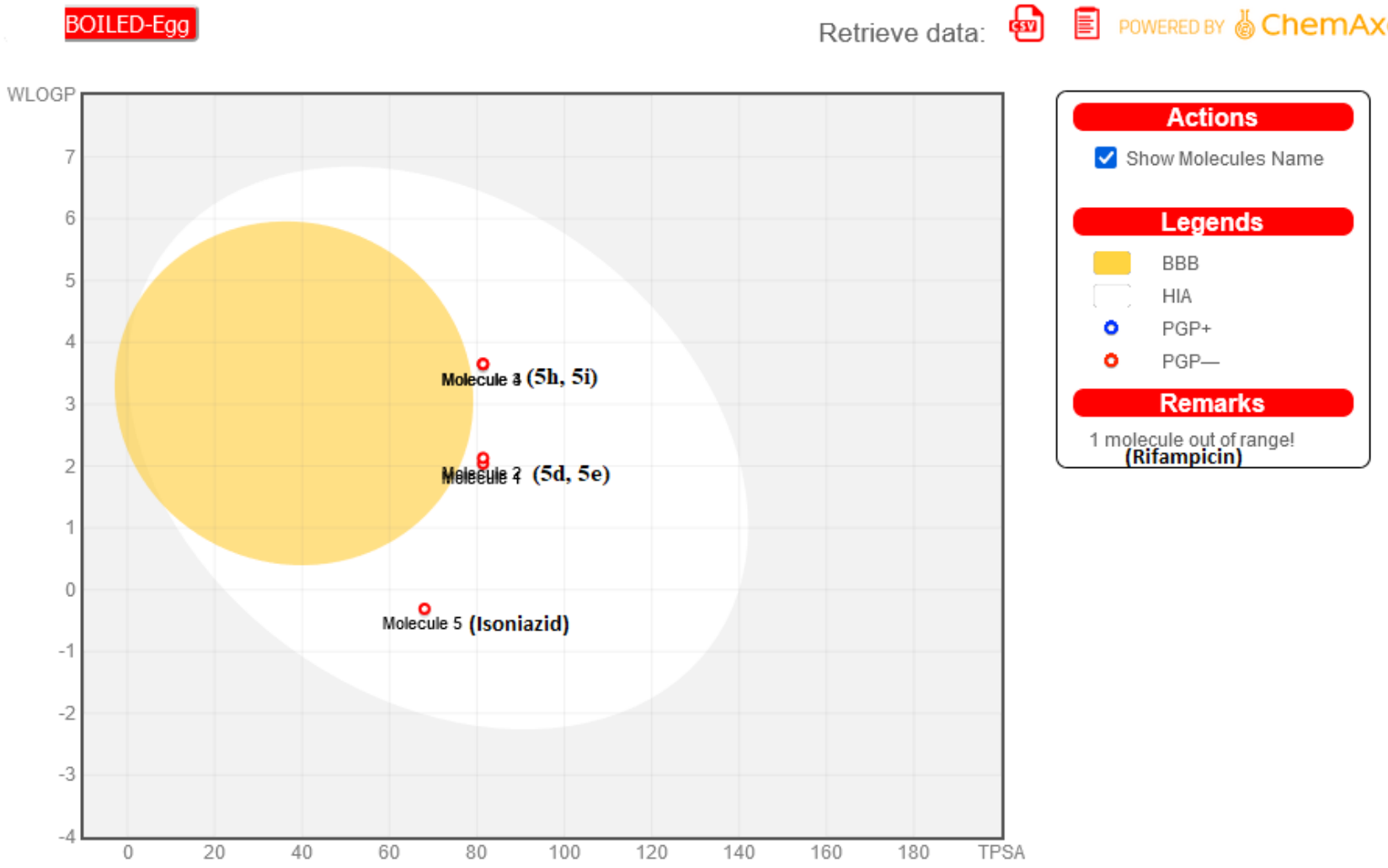


Fig S21. BOILED-Egg representation for compounds **5d**, **5e**, **5h** and **5i** along with standard drugs isoniazid and rifampicin.