Supporting Information

Diastereoselective [3+2]-Cycloaddition of Oxindoles with α,β-Disubstituted Nitroethylenes: Regioreversed Spiropyrrolidines Posed Potent MRSA Activity

Madhuri P. Rao[a], Shubha S. Gunaga[b], Johannes Zuegg[c], Rambabu Pamarthi[a] and Madhu Ganesh[*a]

[a]*Department of Chemistry, B.M.S. College of Engineering, Bull Temple Rd, Bengaluru 560019, India*

[b]*Solid State & Structural Chemistry Unit, Indian Institute of Science, CV Raman Rd, Bengaluru 560012, India*

[c]*CO-ADD, Institute of Molecular Bioscience, University of Queensland, Carmody Rd 306, Brisbane 4072, Australia*

E-mail: *madhug.chem@bmsce.ac.in*

Contents

I. X-ray crystal structure and data of 13a, 13l & 14a

Instrumental details about crystal **13a**

Good quality single crystals were collected under an optical microscope equipped with polarizer. A high resolution data set of crystal $C_{18}H_{16}BrN_3O_3$ was collected on Bruker APEX-II CCD diffractometer using MoKα radiation (λ=0.71073 Å) at 298K. The single crystal was affixed to a Hampton Research cryoloop using Paratone-N oil. Data collection and reduction was performed using Bruker APEX2 and Bruker SAINT, respectively. The structure was solved by patterson methods using SHELXS-97 (Sheldrick, 2008) and were refined by SHELXL-97 (Sheldrick, 2008). The computing molecular graphics were prepared with ORTEP diagram using Mercury software (Mercury CSD 3.10.3 (Build 205818).

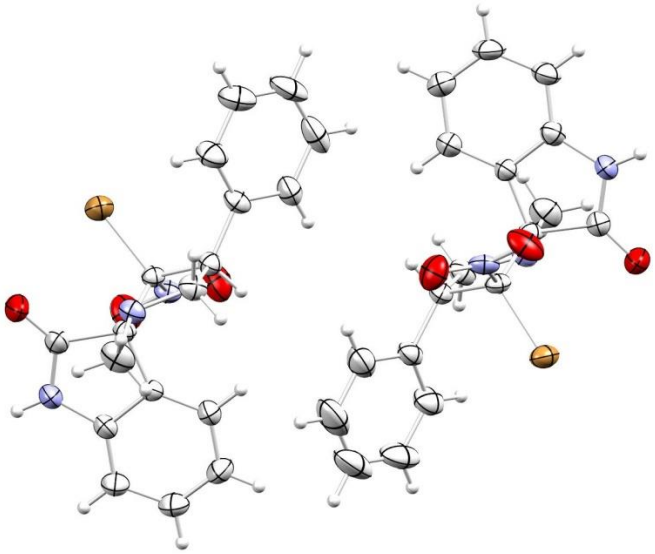


Figure S1: ORTEP representation of compound **13a**

Instrumental details about crystal **13l**

Good quality single crystals were collected under an optical microscope equipped with polarizer. A high resolution data set of crystal $C_{19}H_{18}FN_3O_3$ was collected on an Oxford Xcaliber Mova diffractometer equipped with an EOS CCD detector using MoKα radiaton (λ=0.71073 Å) and a Mova microsource. The single crystal to was affixed to a Hampton Research cryoloop using Paratone-N oil and was cooled with a liquid nitrogen stream using an Oxford Cryosystem nitrogen gas-stream cooling device. Data collection and reduction was performed using CrysAlisPro (version 1.171.38.43). The structure was solved by direct methods using SHELXS-2013/1 (Sheldrick, 2008) and structures were refined by SHELXL-2016/6 (Sheldrick, 2016). The computing molecular graphics were with ORTEP diagram using Mercury software (Mercury CSD 3.10.3 (Build 205818).

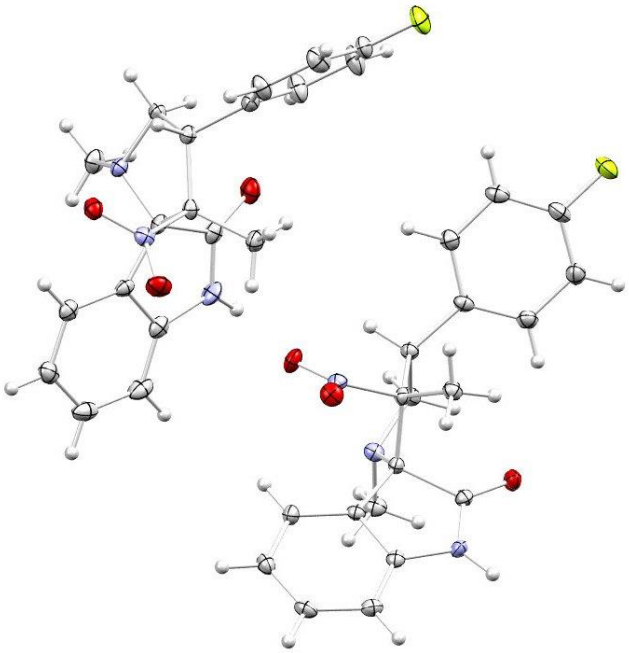


Figure S2: ORTEP representation of compound **13l**

Instrumental details about crystal **14a**

Good quality single crystals were collected under an optical microscope equipped with polarizer. A high resolution data set of crystal $C_{46}H_{45}Br_2N_6O_6$ was collected on an Oxford Xcaliber Mova diffractometer equipped with an EOS CCD detector using MoKα radiaton (λ=0.71073 Å) and a Mova microsource. The single crystal to was affixed to a Hampton Research cryoloop using Paratone-N oil and was cooled with a liquid nitrogen stream using an Oxford Cryosystem nitrogen gas-stream cooling device. Data collection and reduction was performed using CrysAlisPro (version 1.171.38.43) and WINGX(version 2018.3).All non-hydrogen atoms were refined anisotropically. Hydrogen atoms on heteroatoms were located from difference electron density maps. All C-H atoms were fixed geometrically. The structure was solved by direct methods using SHELXS-2013/1 (Sheldrick, 2008) and structures were refined by SHELXL-2016/6 (Sheldrick, 2016). The computing molecular graphics were with Ortep diagram using Mercury software (Mercury CSD 3.10.3 (Build 205818).

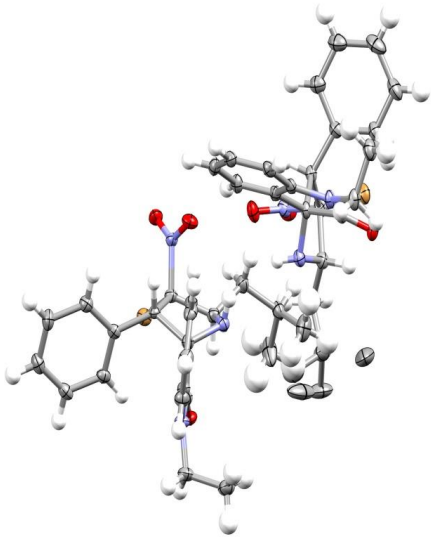
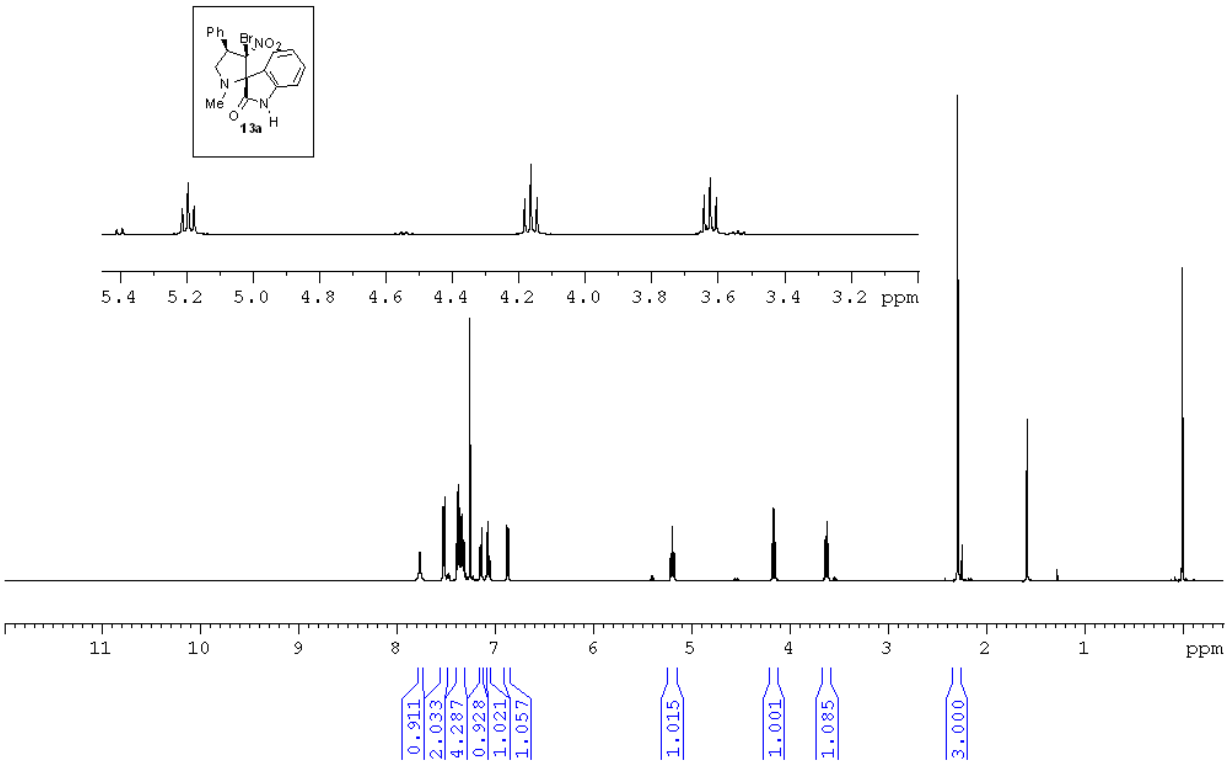
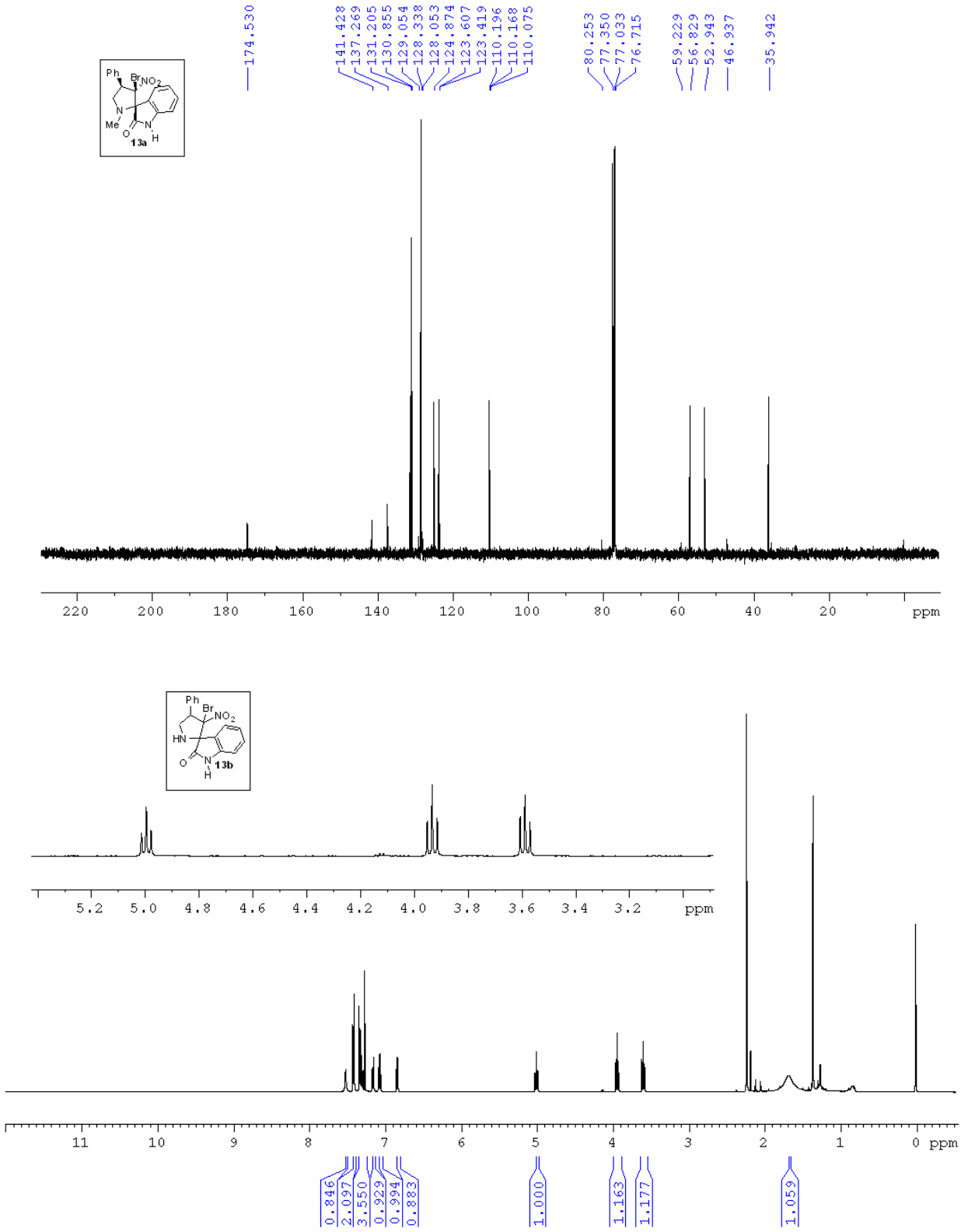


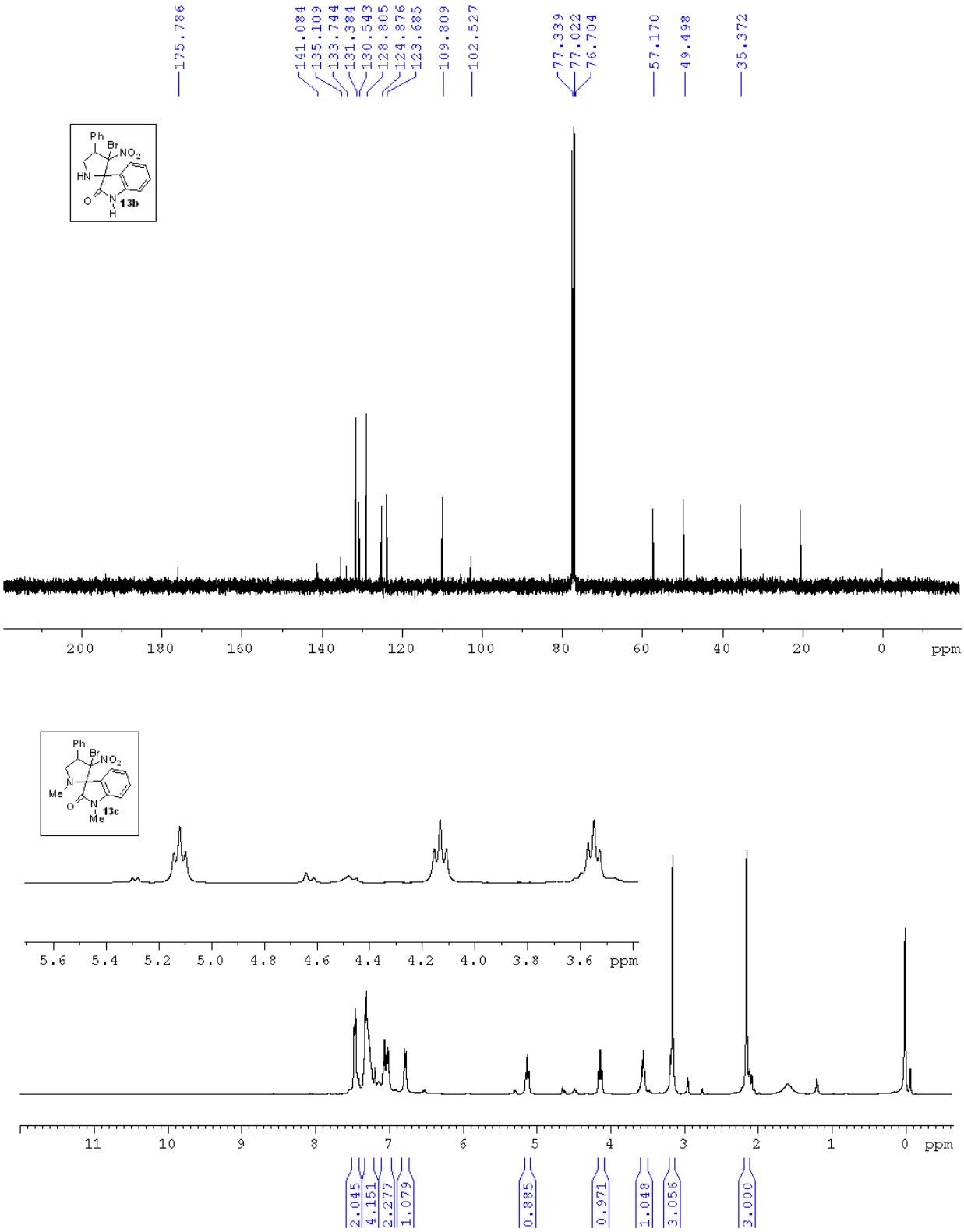
Figure S3: ORTEP representation of compound **14a**

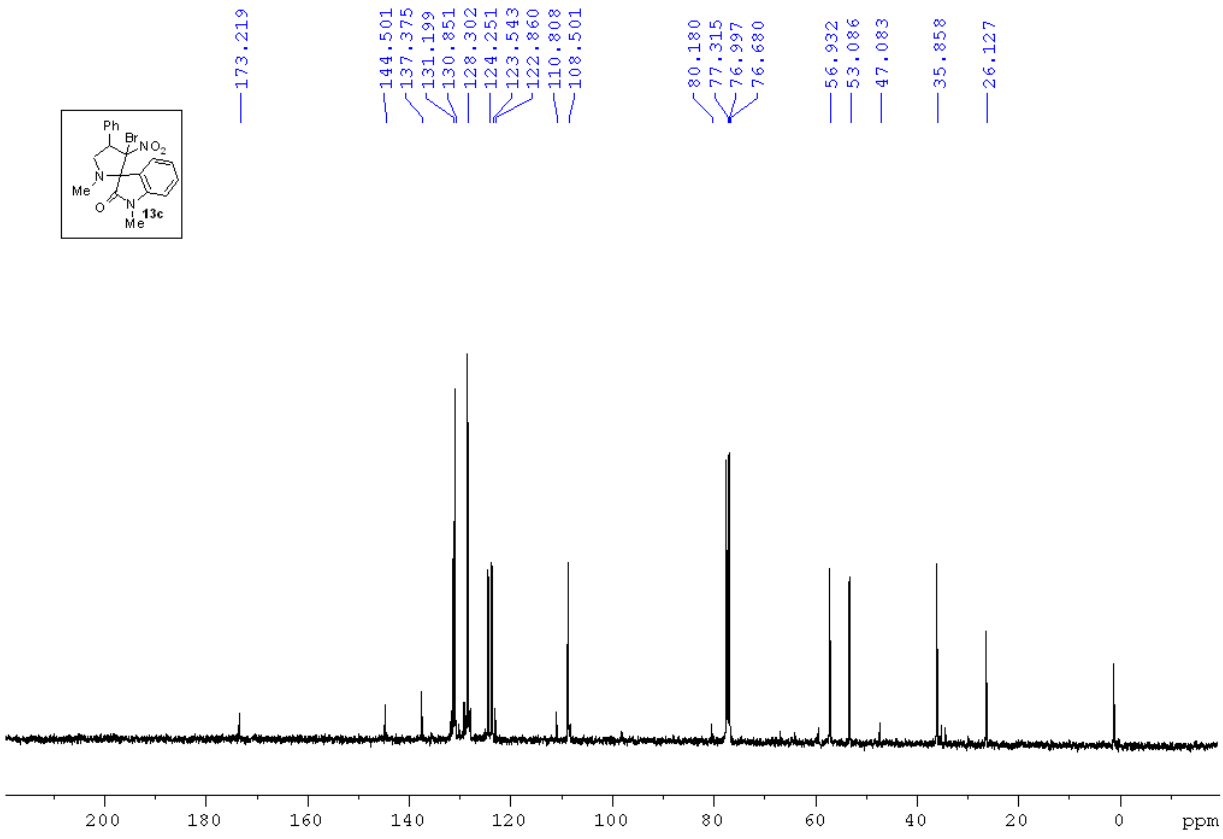
Identification code	**13a**	**13l**	**14a**
Empirical formula	$C_{18}H_{16}Br\ N_3O_3$	$C_{19}H_{18}FN_3O_3$	$C_{23}H_{26}Br_2N_3O_3$
Formula weight	804.50	355.36	937.70
Temperature/K	296(2) K	99.97(10)	99.97(10)
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	P12(1)/n1	P 21/n	C 2/c
a/Å	15.516(5) Å	19.0038(6) Å	24.8162(5) Å
b/Å	9.876(4) Å	7.3040(2) Å	11.0757(2) Å
c/Å	23.035(7) Å	25.2096(7) Å	34.2851(7) Å
α/°	90°	90°	90°
β/°	104.61(2)°	108.964(3)°	100.280(2)°
γ/°	90°	90°	90°
Volume/$Å^3$	3415.8(19) $Å^3$	3309.26(18) $Å^3$	9272.2(3) $Å^3$
Z	4	8	8
$\rho_{calc}g/cm^3$	1.564 x 10^{-9}	1.427 x 10^{-9}	1.343 x 10^{-9}
μ/mm^{-1}	2.429 mm^{-1}	0.106 mm-1	1.801 mm^{-1}
F(000)	1632	1488	3848
Crystal size/mm^3	0.262 x 0.243 x 0.236	0.263 x 0.251 x 0.238	0.275 x 0.269 x 0.257
Radiation	MoKα (□□ 0.71073 Å)	MoKα (□□ 0.71073 Å)	MoKα (□□ 0.71073 Å)
2θ range for data collection/°	1.82 to 27.75°	3.418 to 27.482°	3.337 to 27.483°
Index ranges	-20<=h<=20, -12<=k<=12, -29<=l<=29	-24<=h<=24, -9<=k<=9, -32<=l<=32	-32<=h<=32, -14<=k<=14, -44<=l<=44
Reflections collected	54024	46806	67257
Independent reflections	7878 [R_{int} = 0.0960]	7580 [R(int)= 0.0679]	10619 [R(int)= 0.0476]
Data/restraints/parameters	7878 / 0 / 453	7580 / 0 / 480	10619 / 0 / 568
Goodness-of-fit on F^2	0.897	1.036	1.077
Final R indexes [I>=2σ(I)]	R_1 = 0.0499, wR2 = 0.1295	R_1 = 0.0464, wR2 = 0.0959	R_1 = 0.0512, wR2 = 0.1577
Final R indexes [all data]	R_1 = 0.0991, wR2 = 0.1566	R_1 = 0.0639, wR2 = 0.1069	R_1 = 0.0604, wR2 = 0.1653
Largest diff. peak/hole/$eÅ^3$	0.524 and -0.669 e.$Å^{-3}$	0.301 and -0.239 e.$Å^{-3}$	3.621 and -0.407 e.$Å^{-3}$
CCDC	1887027	1886930	1895444

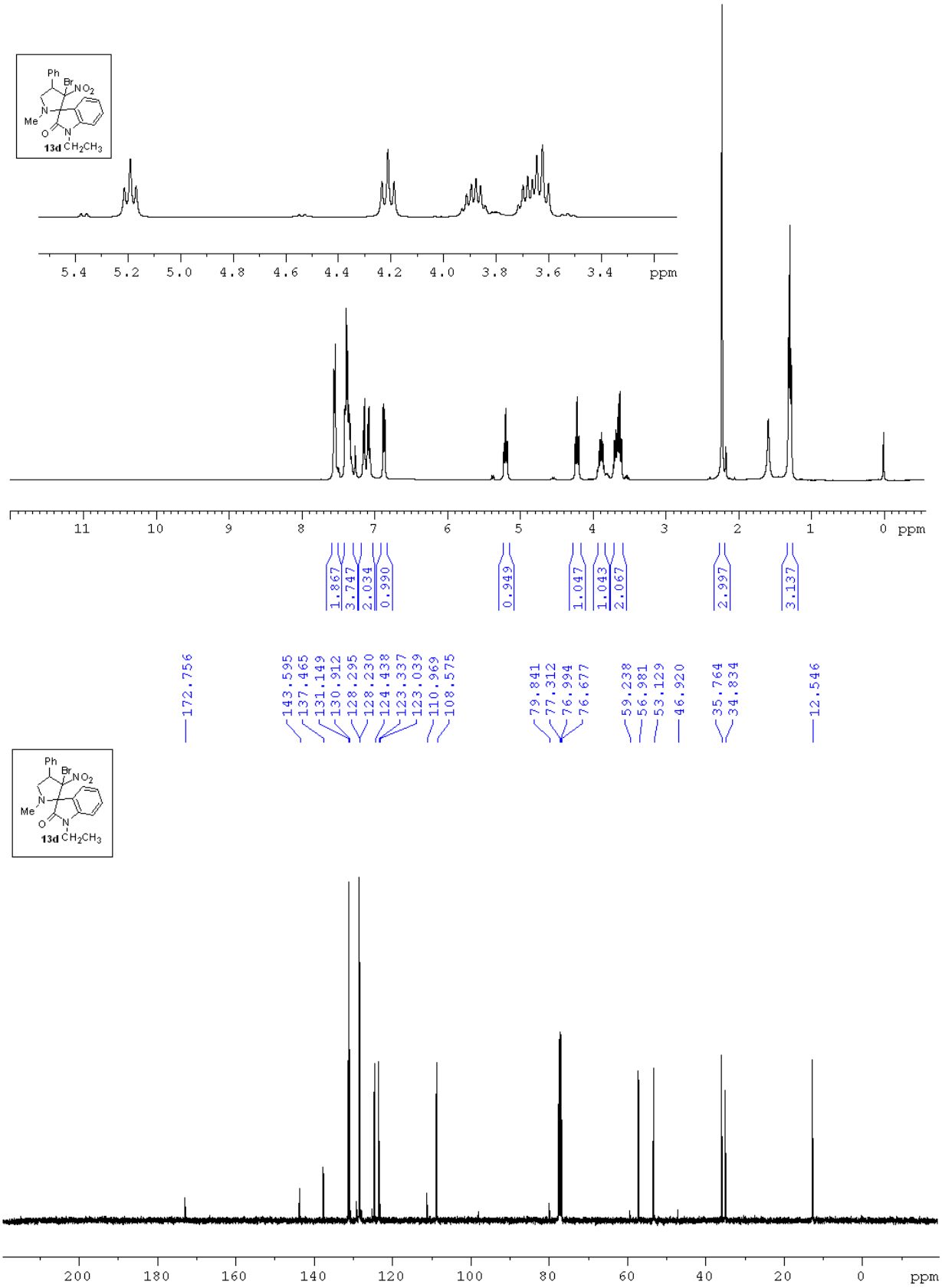
II. Copies of NMR Spectra of 13a-13k

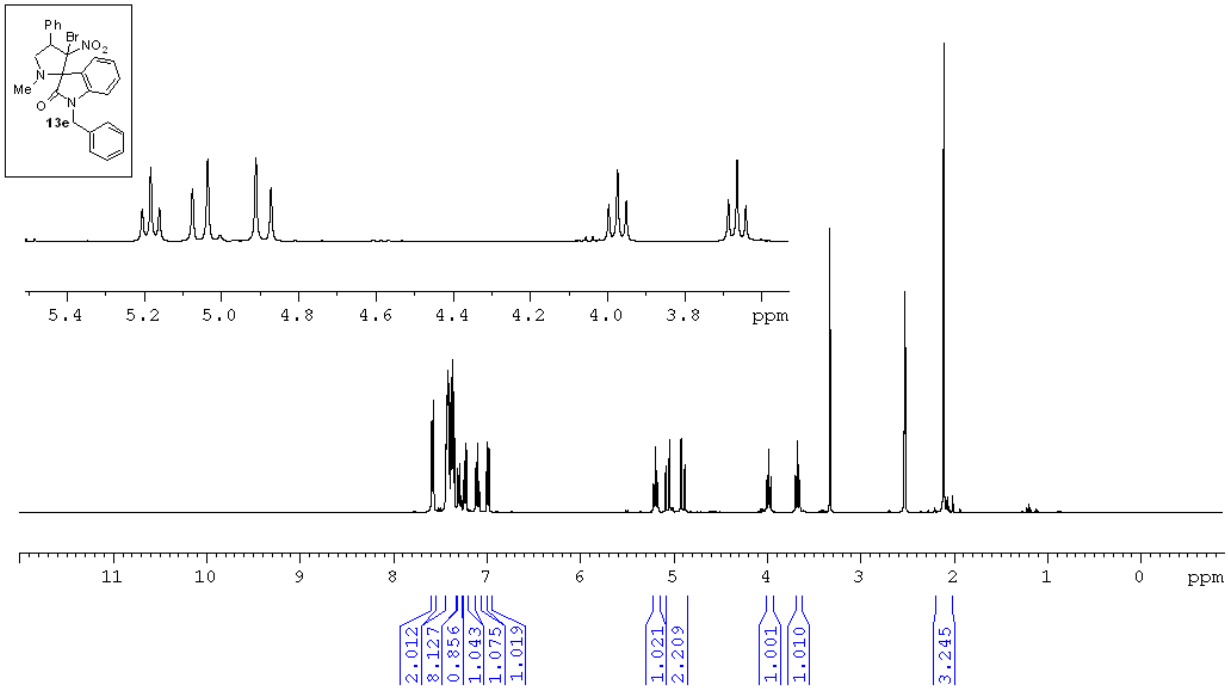


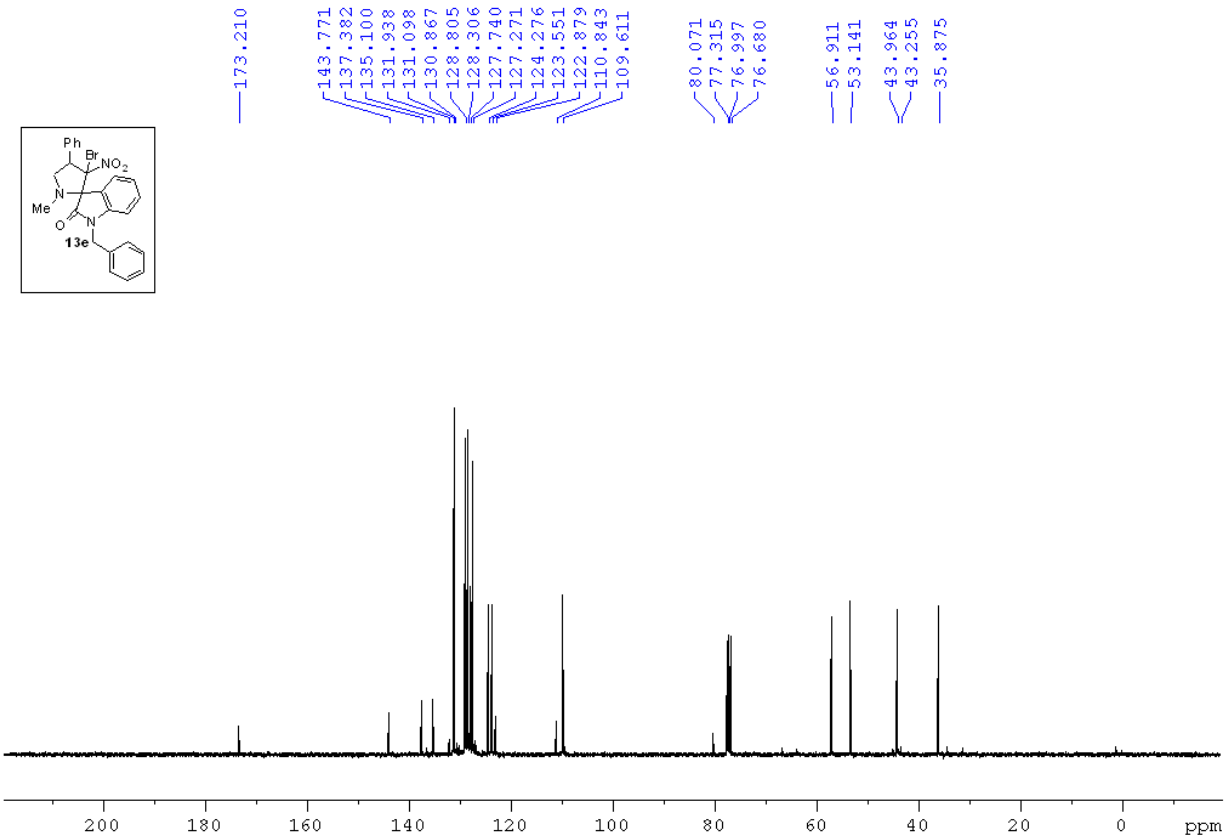

174.530
141.428
137.269
131.205
130.855
129.054
128.338
128.053
124.874
123.607
123.419
110.196
110.168
110.075
80.253
77.350
77.033
76.715
59.229
56.829
52.943
46.937
35.942
13a
13b
ppm
0.846
2.097
3.550
0.929
0.994
0.883
1.000
1.163
1.177
1.059

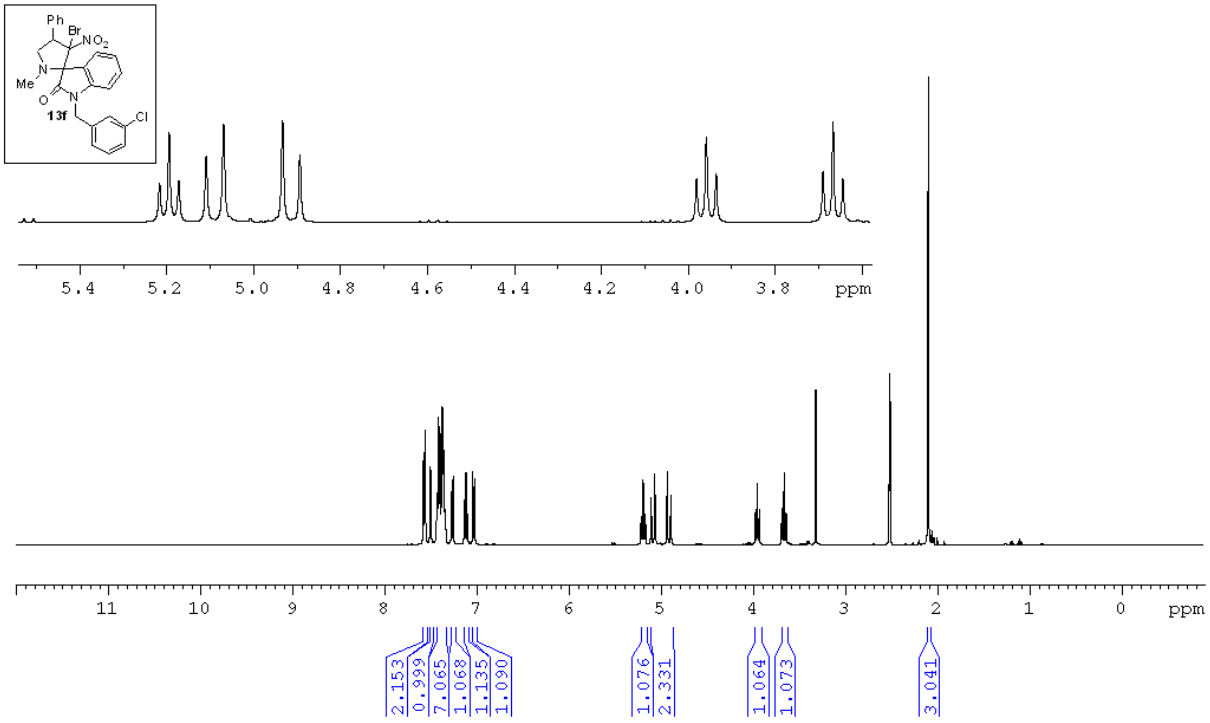

175.786
141.084
135.109
133.744
131.384
130.543
128.805
124.876
123.685
109.809
102.527
77.339
77.022
76.704
57.170
49.498
35.372
Ph
Br
NO2
HN
O
N
H
13b
200
180
160
140
120
100
80
60
40
20
0
ppm
Ph
Br
NO2
N
Me
O
N
Me
13c
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
ppm
11
10
9
8
7
6
5
4
3
2
1
0
ppm
2.045
4.151
2.277
1.079
0.885
0.971
1.048
3.056
3.000

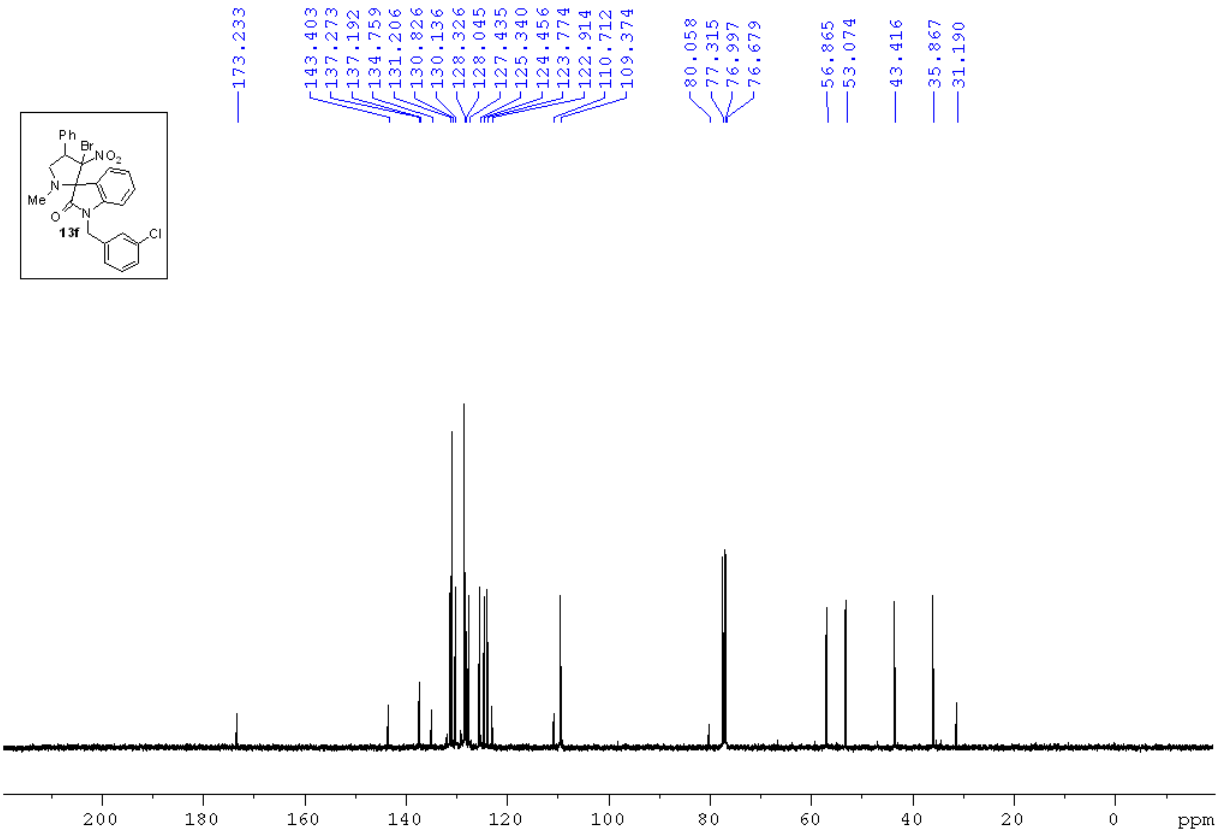

173.219
144.501
137.375
131.199
130.851
128.302
124.251
123.543
122.860
110.808
108.501
80.180
77.315
76.997
76.680
56.932
53.086
47.083
35.858
26.127
Ph
Br
NO2
N
Me
O
N
Me
13c
200
180
160
140
120
100
80
60
40
20
0
ppm

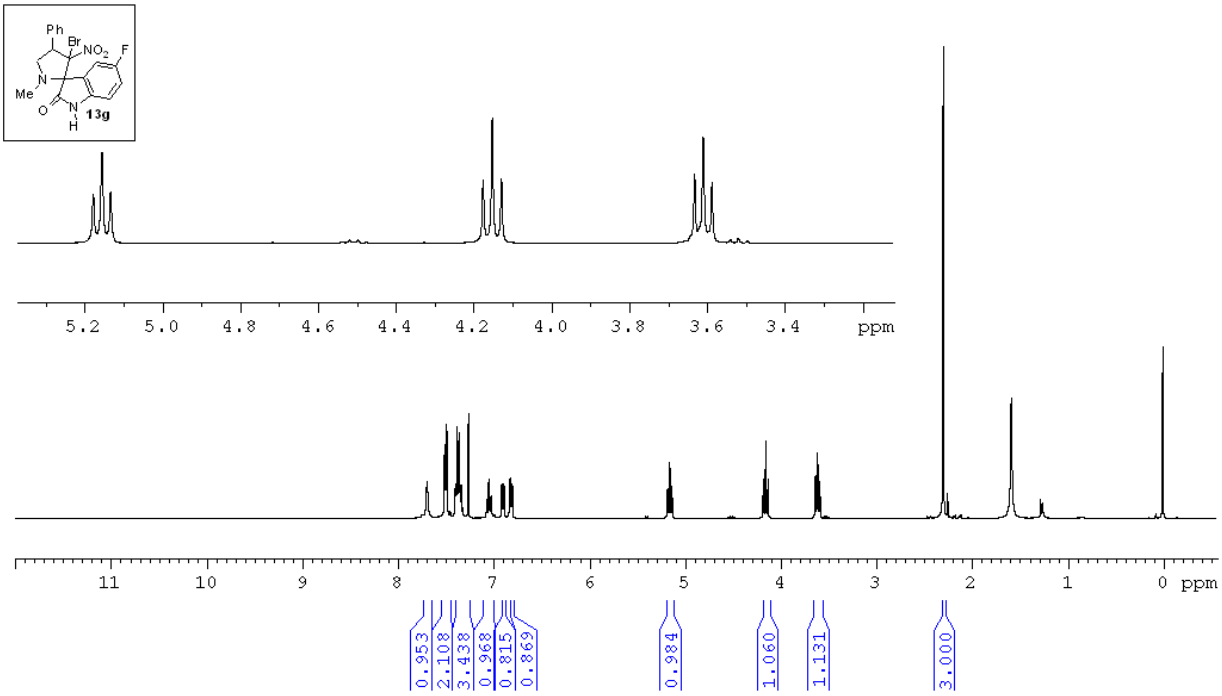

Ph
Br
NO2
Me
N
O
N
CH2CH3
13d
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
ppm
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.867
3.747
2.034
0.990
0.949
1.047
1.043
2.067
2.997
3.137
172.756
143.595
137.465
131.149
130.912
128.295
128.230
124.438
123.337
123.039
110.969
108.575
79.841
77.312
76.994
76.677
59.238
56.981
53.129
46.920
35.764
34.834
12.546
200
180
160
140
120
100
80
60
40
20
0
ppm

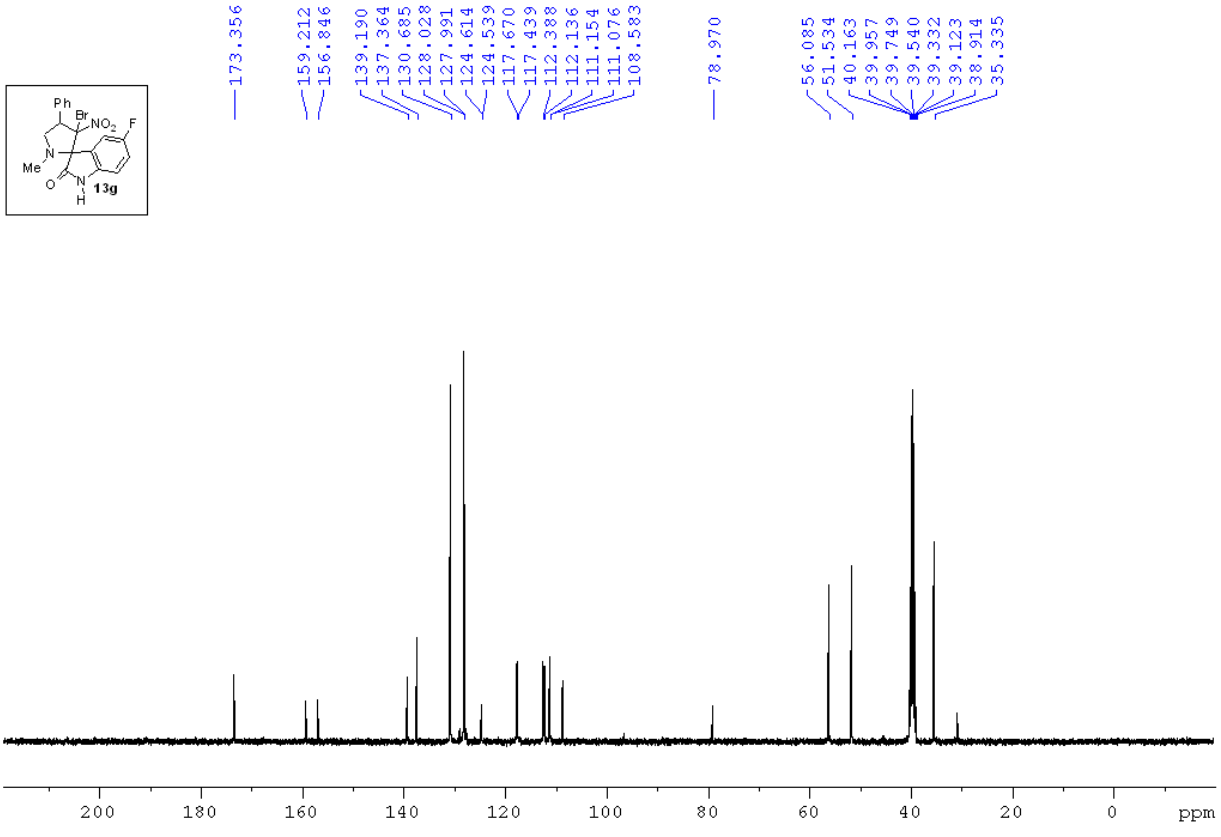

Ph
Br
NO2
Me
N
O
N
13e
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
ppm
11
10
9
8
7
6
5
4
3
2
1
0
ppm
2.012
8.127
0.856
1.043
1.075
1.019
1.021
2.209
1.001
1.010
3.245

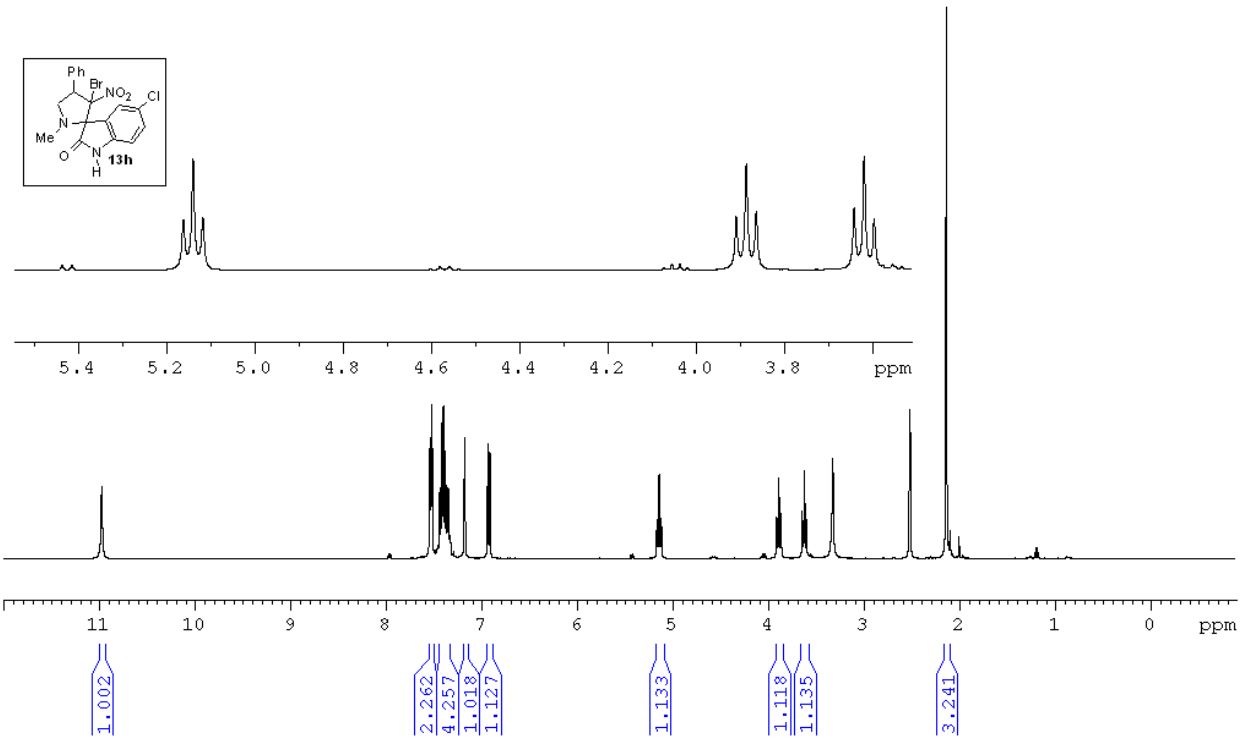

173.210
143.771
137.382
135.100
131.938
131.098
130.867
128.805
128.306
127.740
127.271
124.276
123.551
122.879
110.843
109.611
80.071
77.315
76.997
76.680
56.911
53.141
43.964
43.255
35.875
Ph
Br
NO2
Me
N
O
N
13e
200
180
160
140
120
100
80
60
40
20
0
ppm

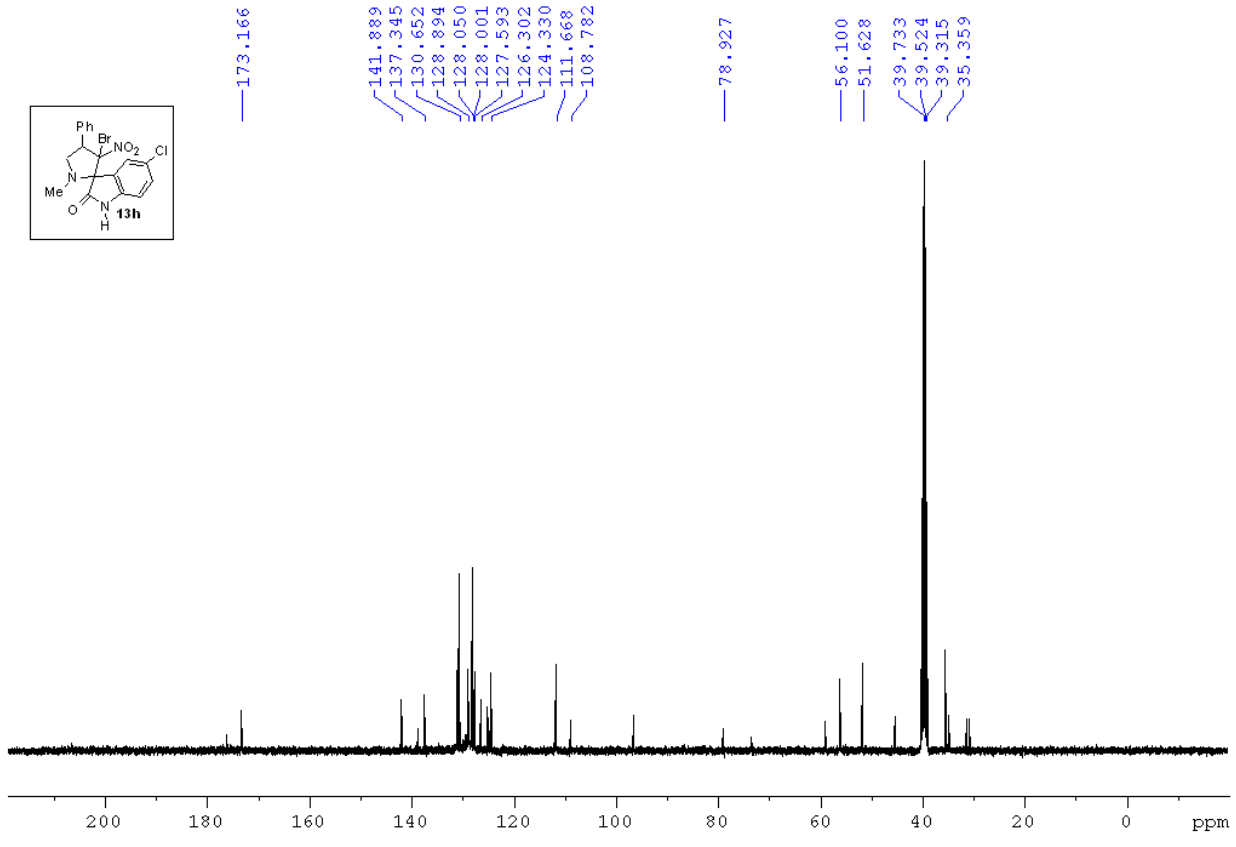

Ph
Br
NO2
Me
N
O
N
13f
Cl
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
ppm
11
10
9
8
7
6
5
4
3
2
1
0
ppm
2.153
0.999
7.065
1.068
1.135
1.090
1.076
2.331
1.064
1.073
3.041

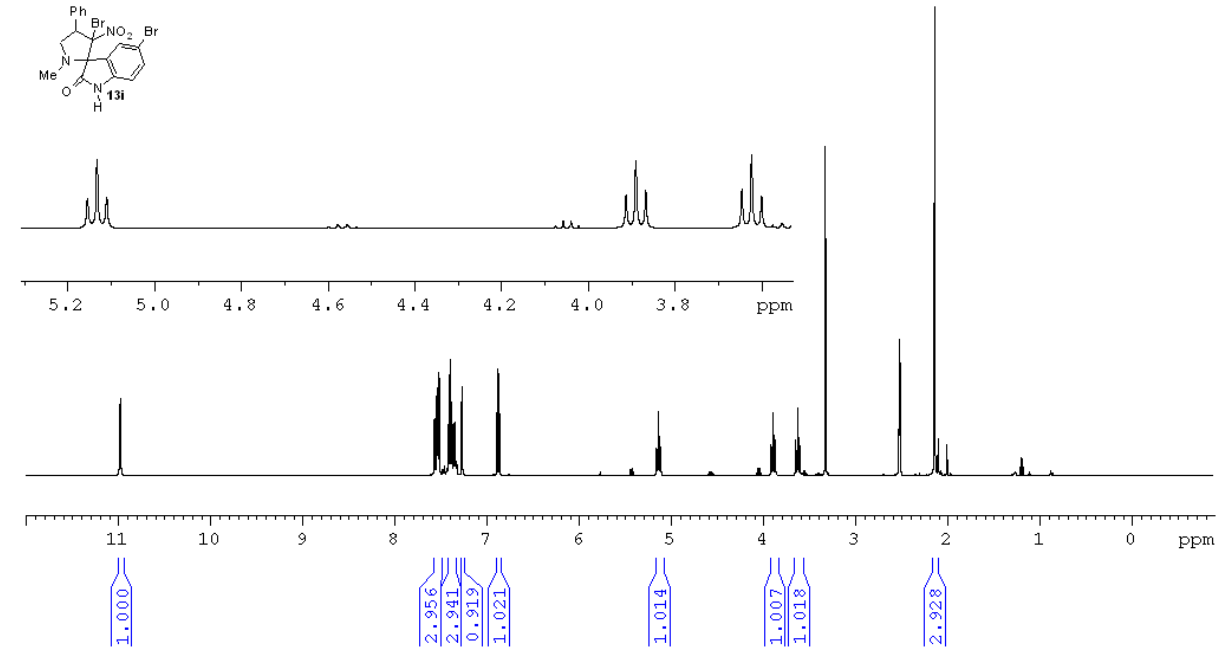

173.233
143.403
137.273
137.192
134.759
131.206
130.826
130.136
128.326
128.045
127.435
125.340
124.456
123.774
122.914
110.712
109.374
80.058
77.315
76.997
76.679
56.865
53.074
43.416
35.867
31.190
Ph
Br
NO2
Me
N
O
N
13f
Cl
200
180
160
140
120
100
80
60
40
20
0
ppm

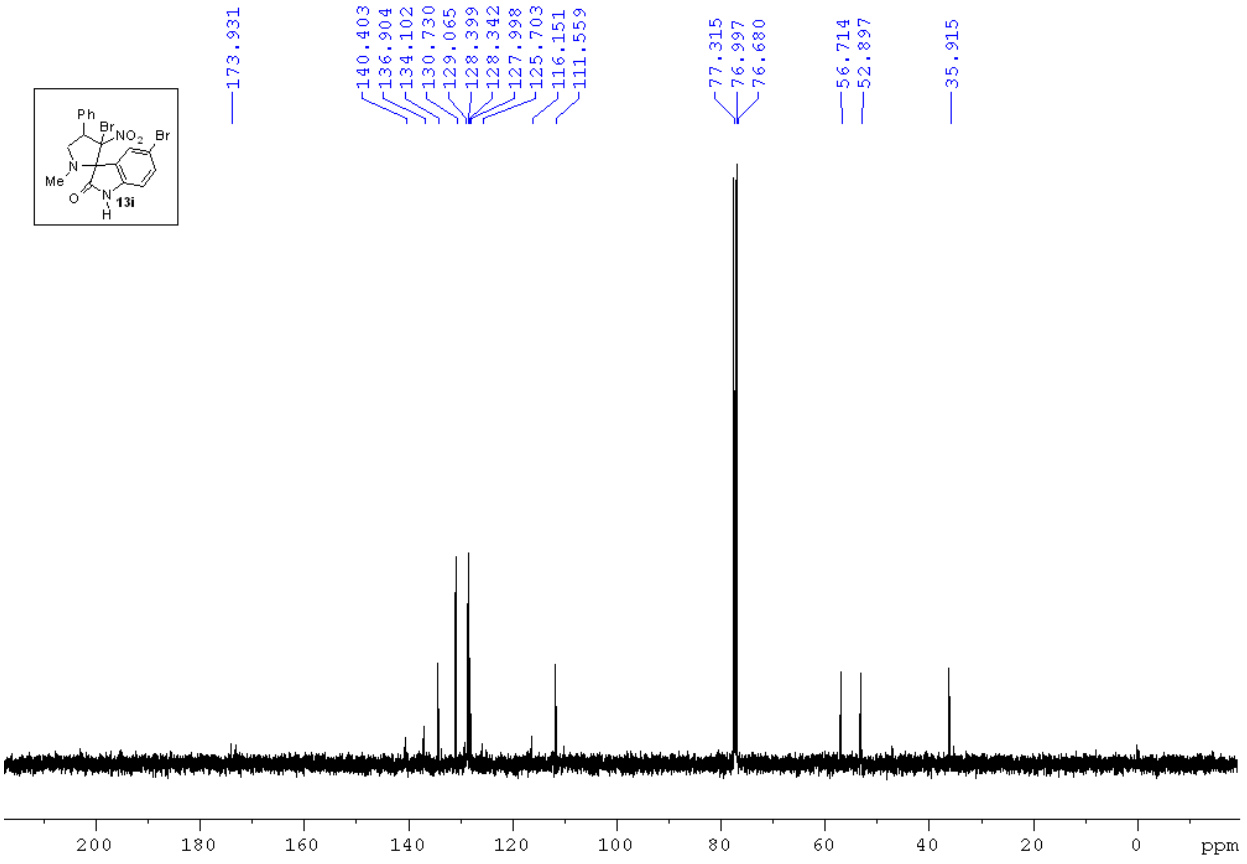

Ph
Br
NO2
F
Me
N
O
N
H
13g
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
ppm
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.953
2.108
3.438
0.968
0.815
0.869
0.984
1.060
1.131
3.000

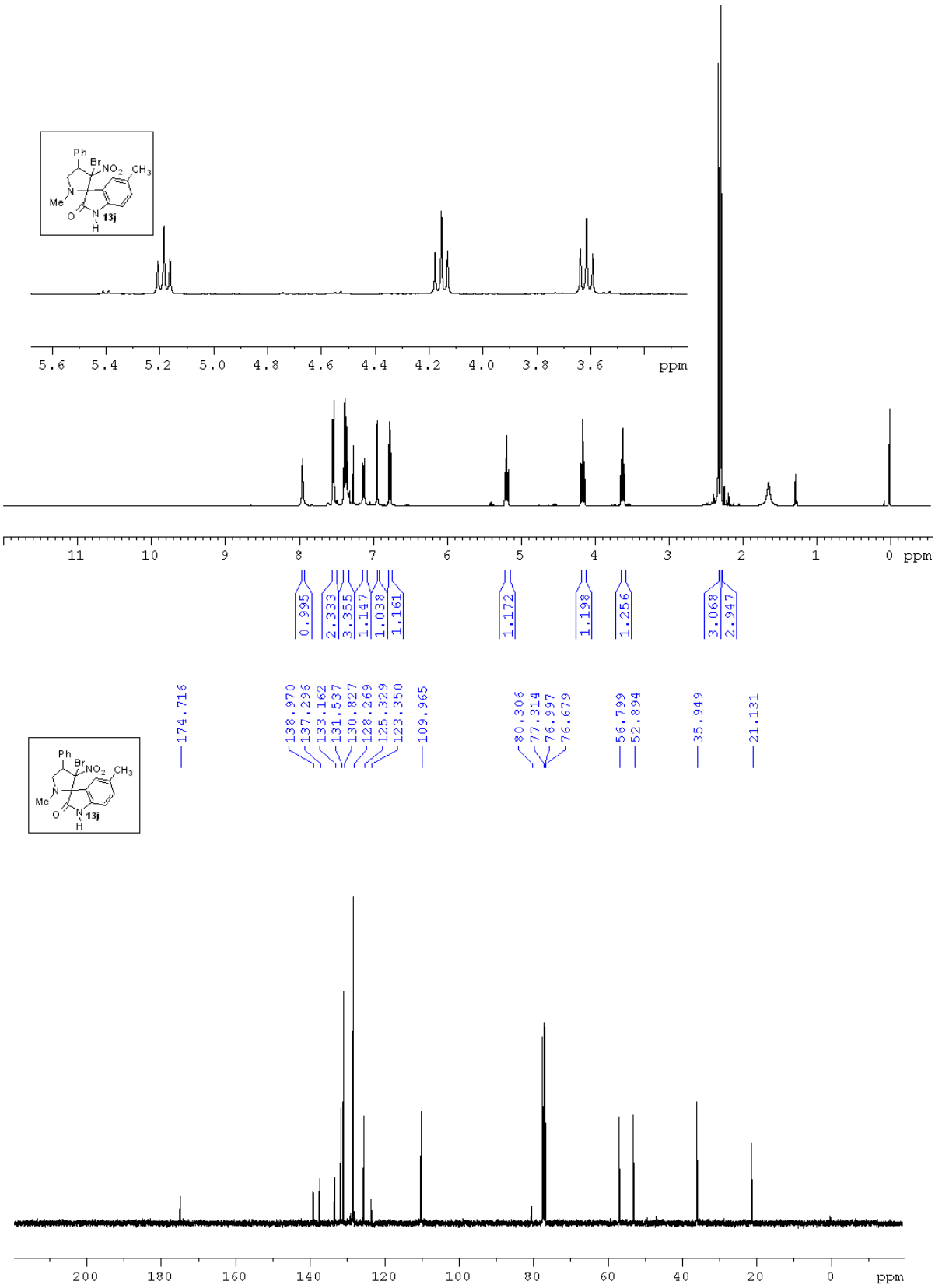

173.356
159.212
156.846
139.190
137.364
130.685
128.028
127.991
124.614
124.539
117.670
117.439
112.388
112.136
111.154
111.076
108.583
78.970
56.085
51.534
40.163
39.957
39.749
39.540
39.332
39.123
38.914
35.335
Ph
Br
NO2
F
Me
N
O
N
H
13g
200
180
160
140
120
100
80
60
40
20
0
ppm

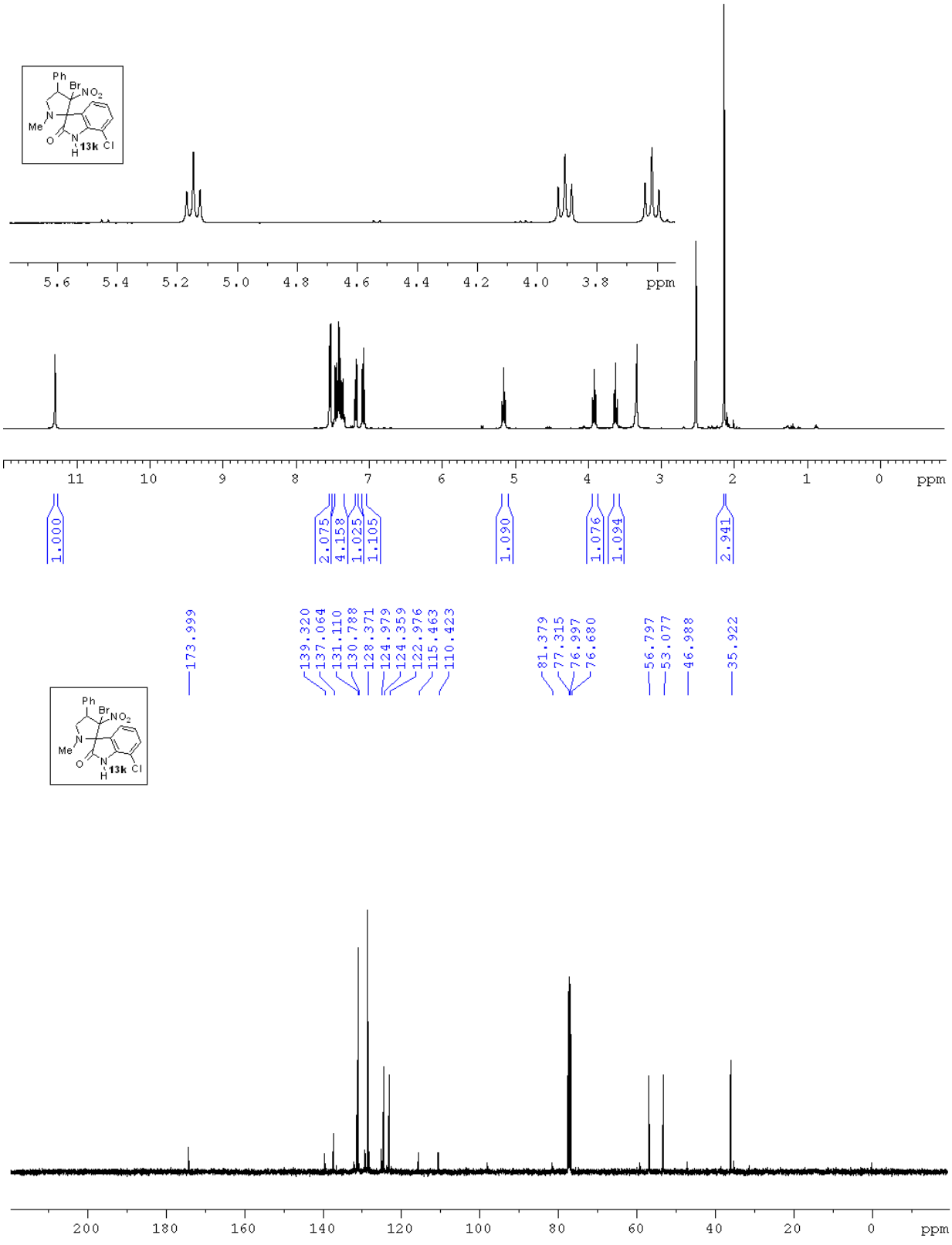

Ph
Br
NO2
Cl
Me
N
O
N
H
13h
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
ppm
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.002
2.262
4.257
1.018
1.127
1.133
1.118
1.135
3.241


173.166
141.889
137.345
130.652
128.894
128.050
128.001
127.593
126.302
124.330
111.668
108.782
78.927
56.100
51.628
39.733
39.524
39.315
35.359
Ph
Br
NO2
Cl
Me
N
O
N
H
13h
200
180
160
140
120
100
80
60
40
20
0
ppm

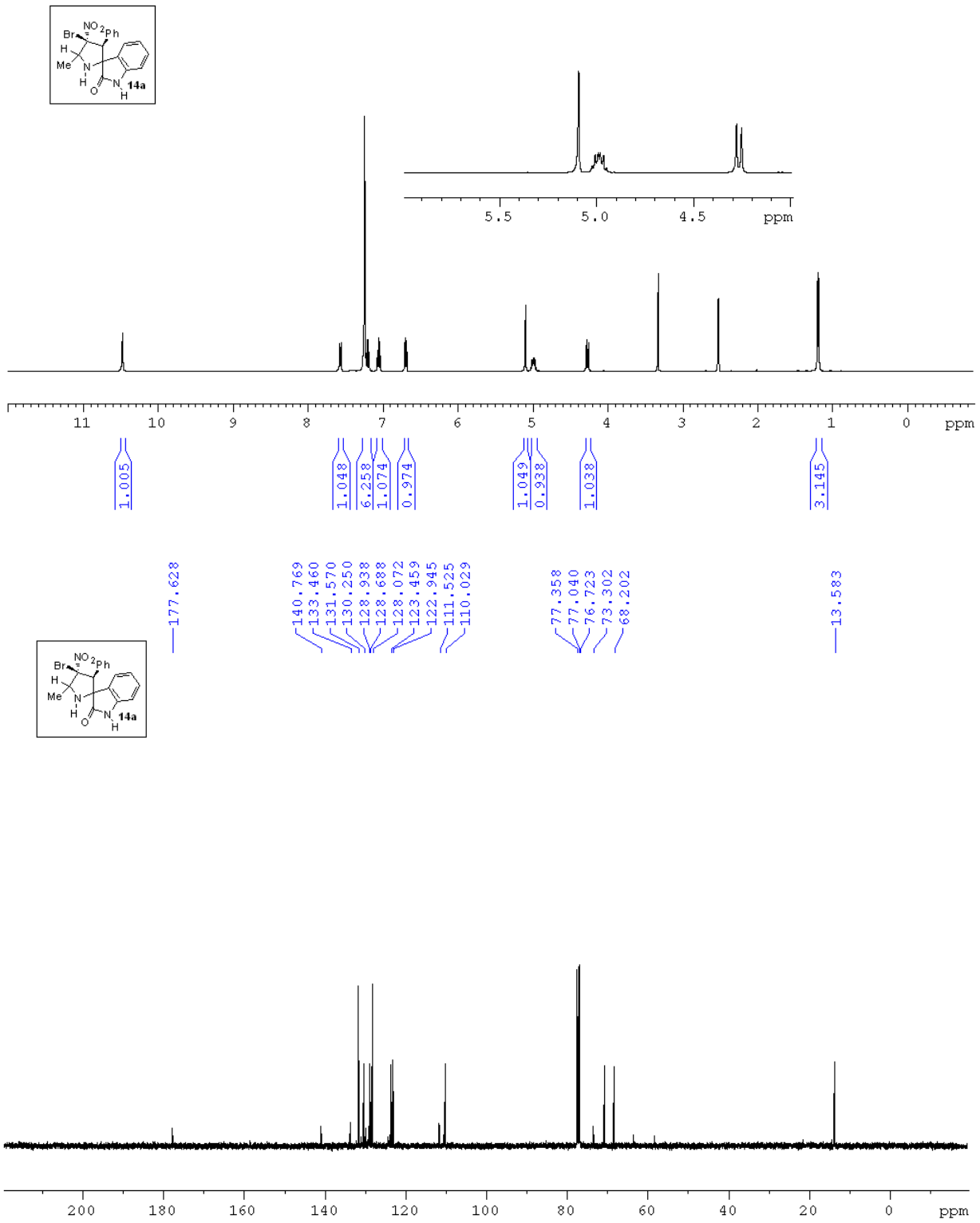

Ph
Br
NO2
Br
Me
N
O
N
H
13i
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
ppm
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
2.956
2.941
0.919
1.021
1.014
1.007
1.018
2.928


173.931
140.403
136.904
134.102
130.730
129.065
128.399
128.342
127.998
125.703
116.151
111.559
77.315
76.997
76.680
56.714
52.897
35.915
Ph
Br
NO2
Br
Me
N
O
N
H
13i
200
180
160
140
120
100
80
60
40
20
0
ppm

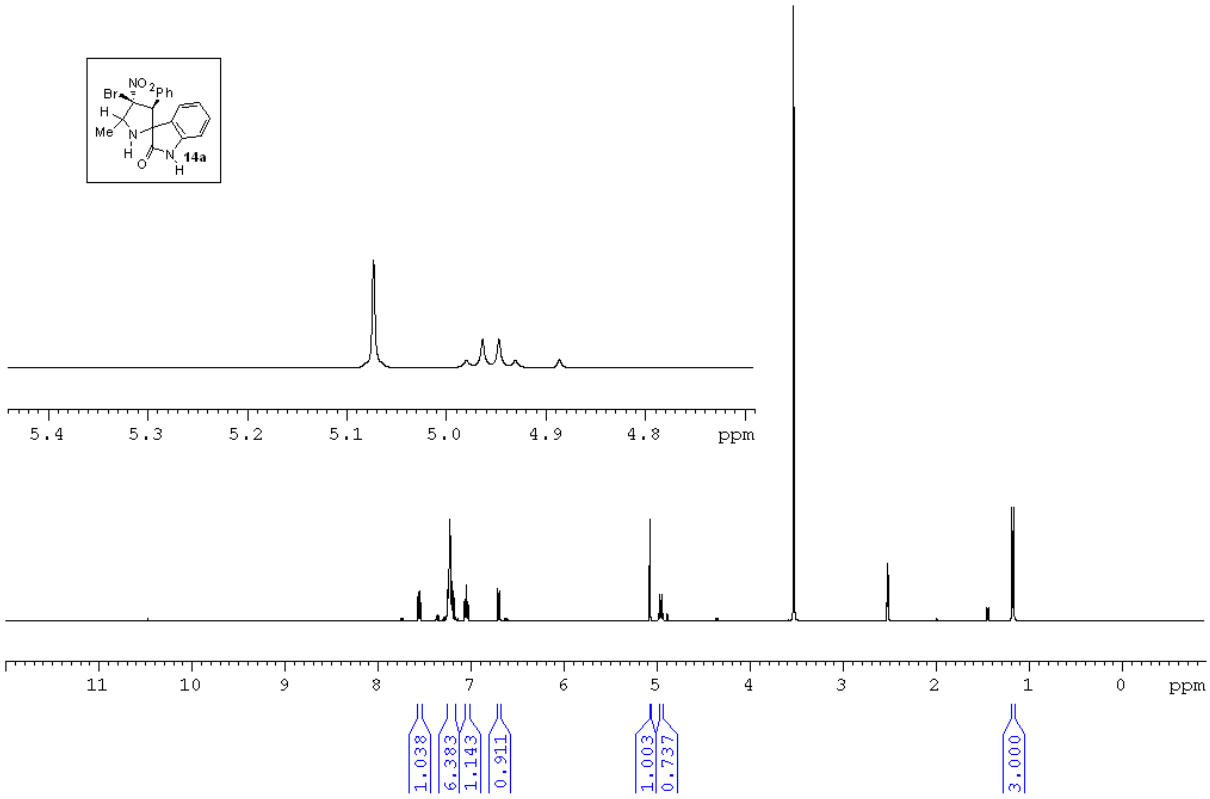

Ph
Br
NO2
CH3
Me
N
O
N
H
13j
5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 ppm
11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.995
2.333
3.355
1.147
1.038
1.161
1.172
1.198
1.256
3.068
2.947
174.716
138.970
137.296
133.162
131.537
130.827
128.269
125.329
123.350
109.965
80.306
77.314
76.997
76.679
56.799
52.894
35.949
21.131
200 180 160 140 120 100 80 60 40 20 0 ppm

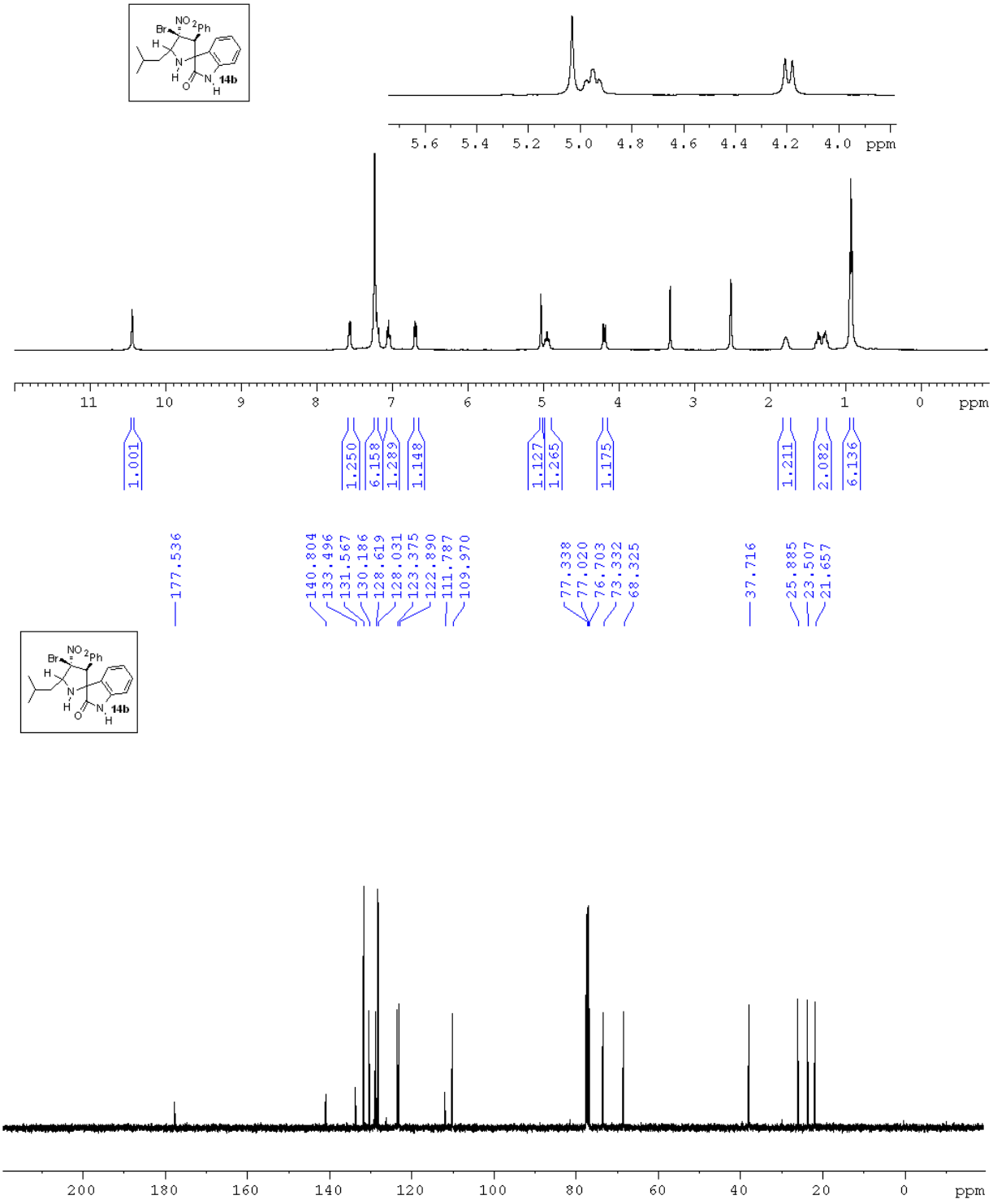

Ph
Br
NO2
Me
N
O
N
H
13k
Cl
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
ppm
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
2.075
4.158
1.025
1.105
1.090
1.076
1.094
2.941
173.999
139.320
137.064
131.110
130.788
128.371
124.979
124.359
122.976
115.463
110.423
81.379
77.315
76.997
76.680
56.797
53.077
46.988
35.922
200
180
160
140
120
100
80
60
40
20
0
ppm

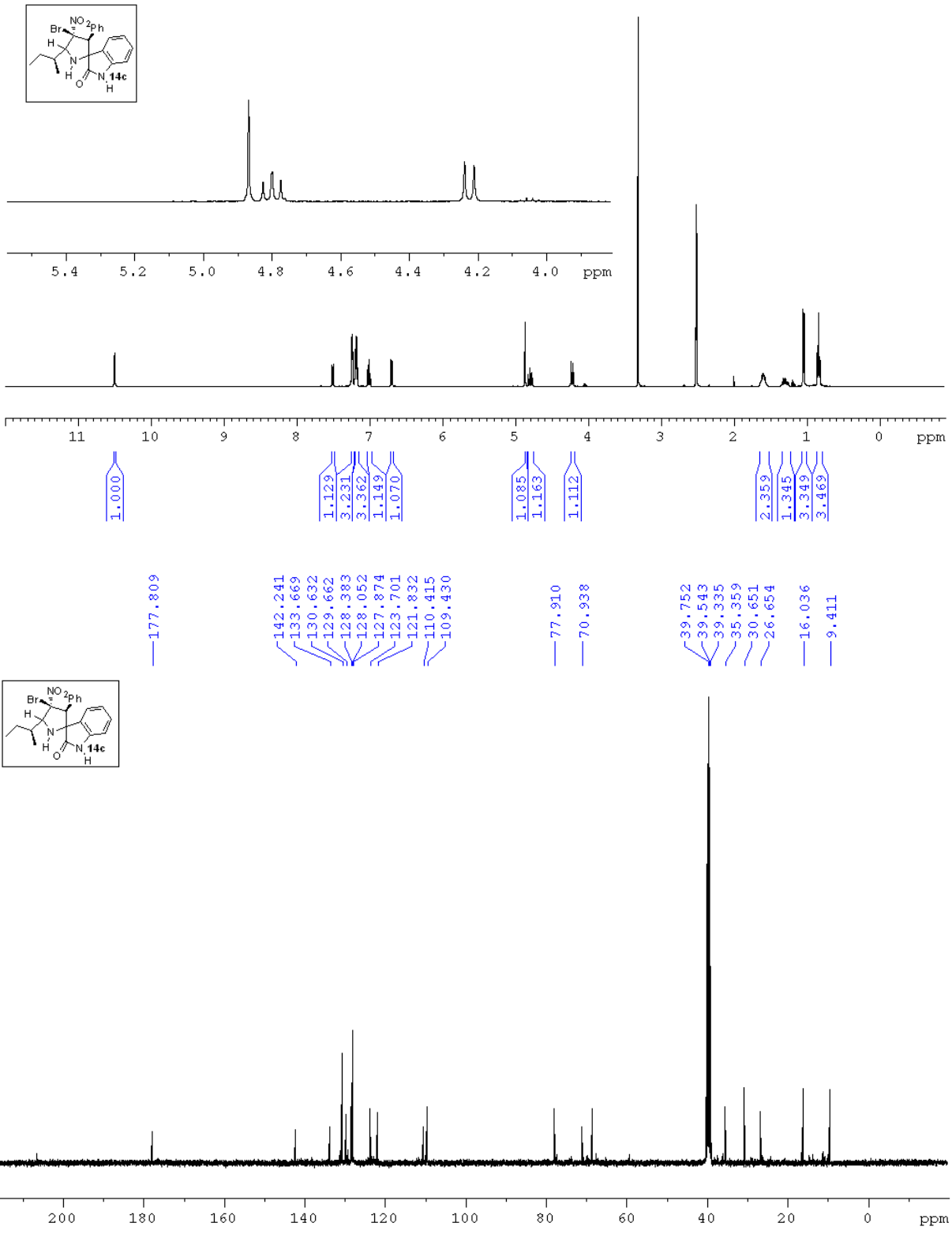
III. Copies of NMR Spectra of 14a-14h

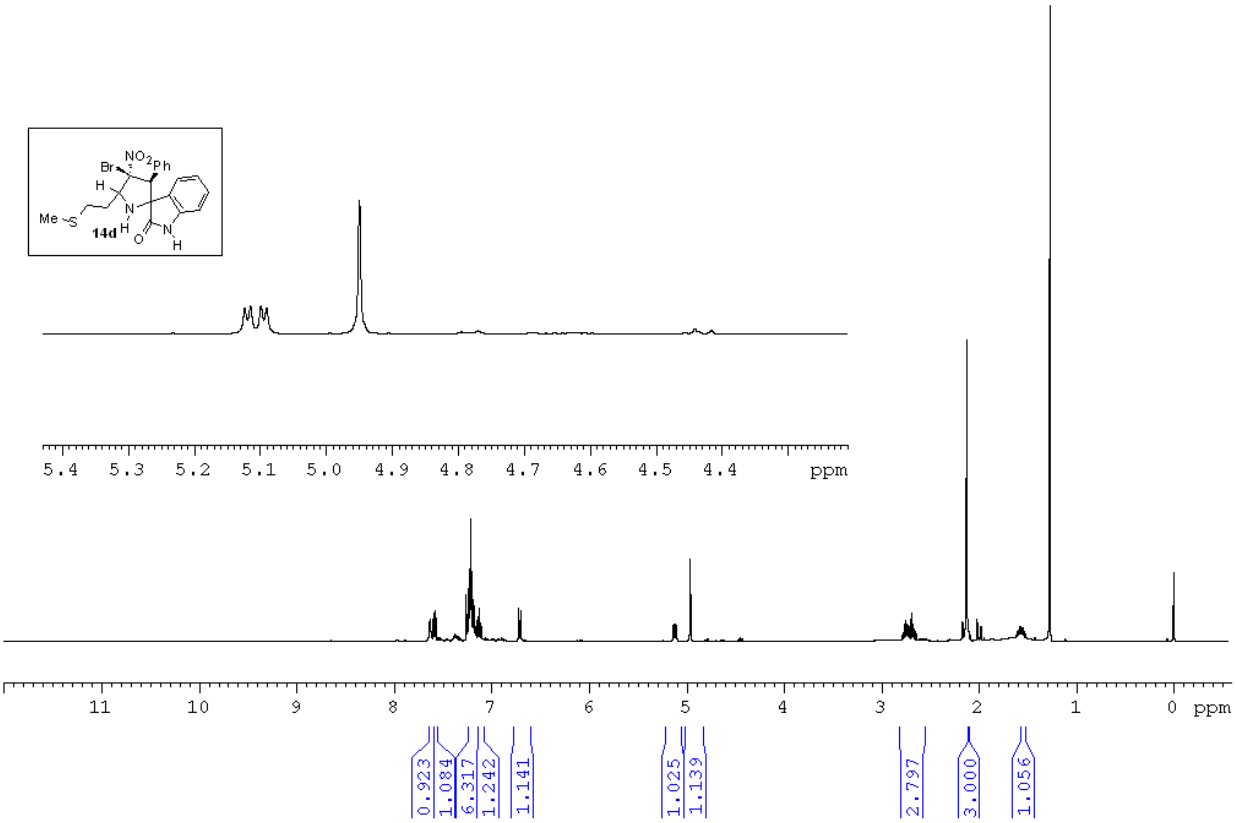


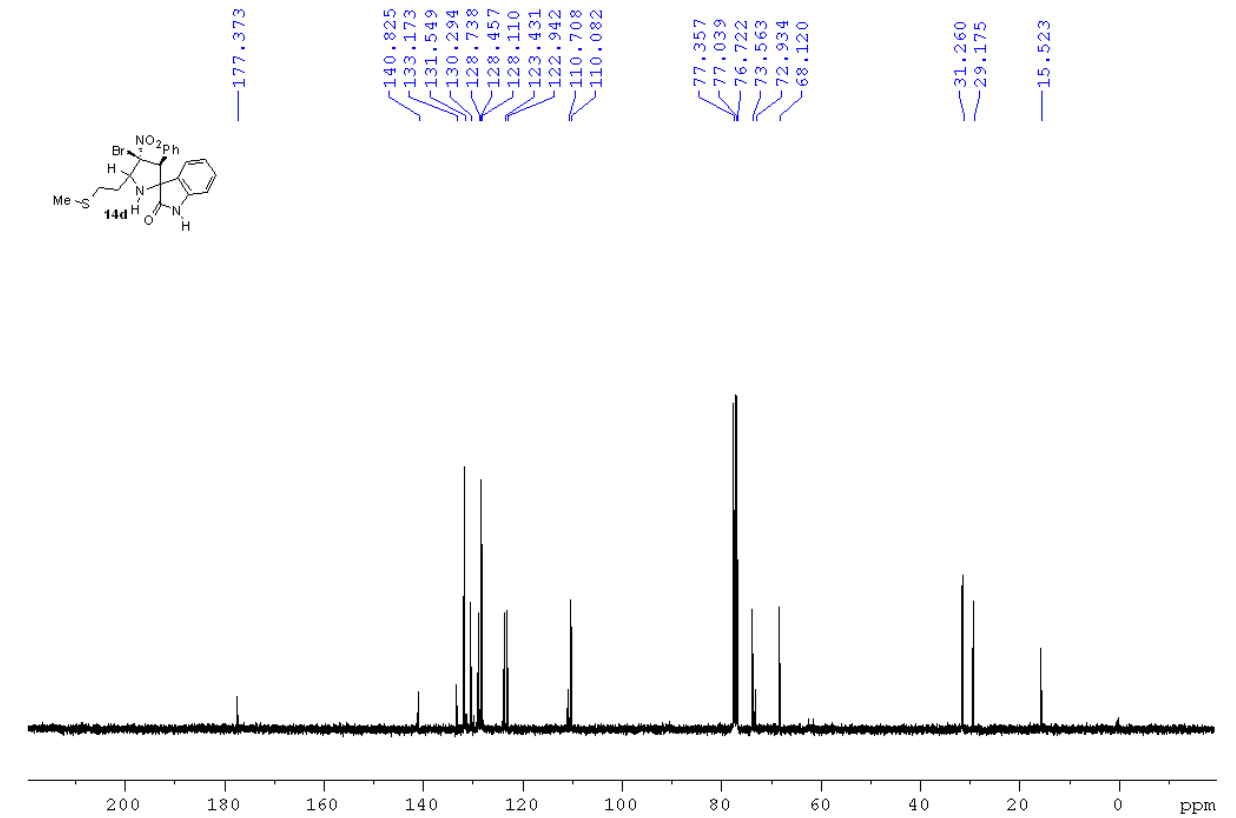
D_2O exchange experiment for the compound **14a**

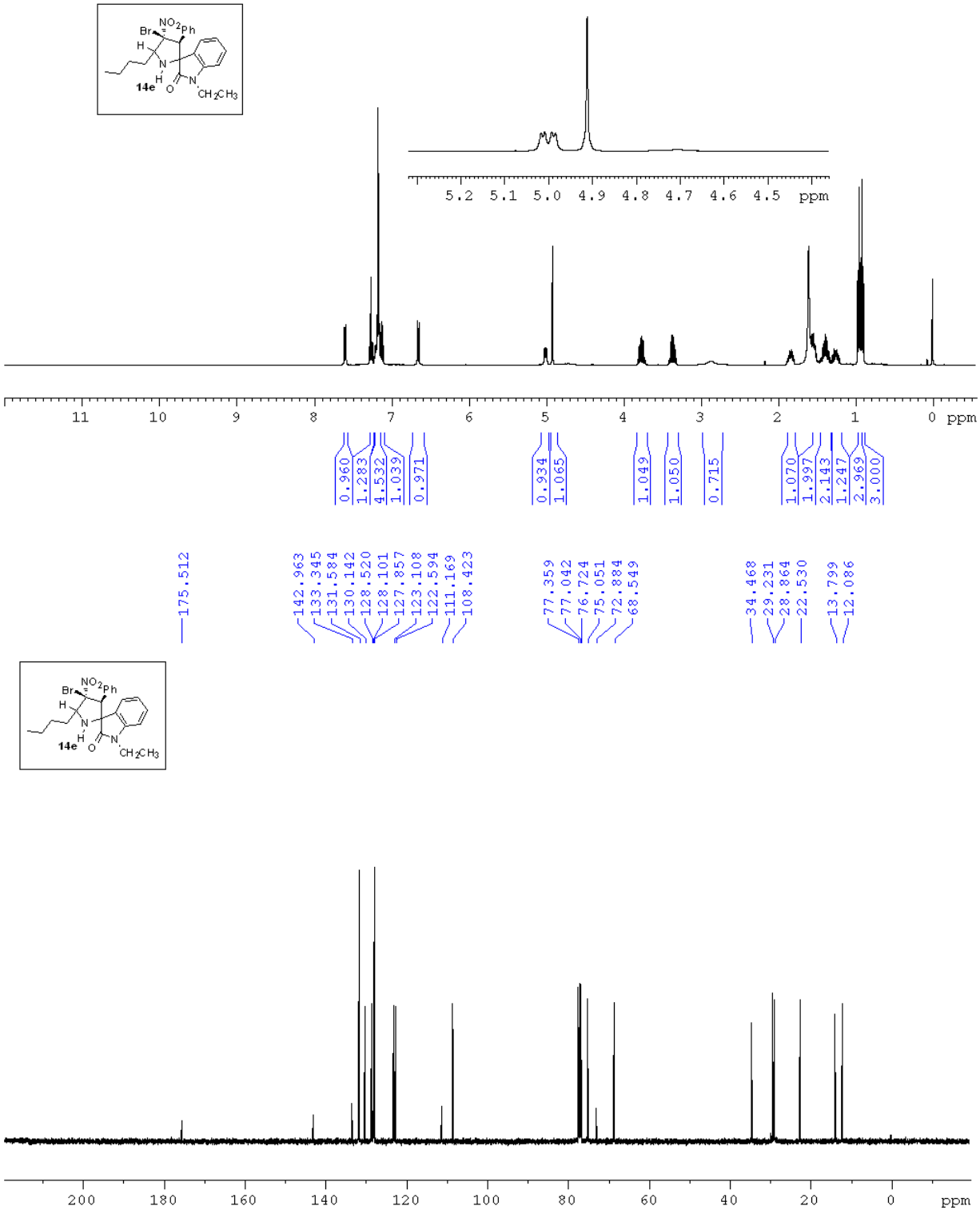


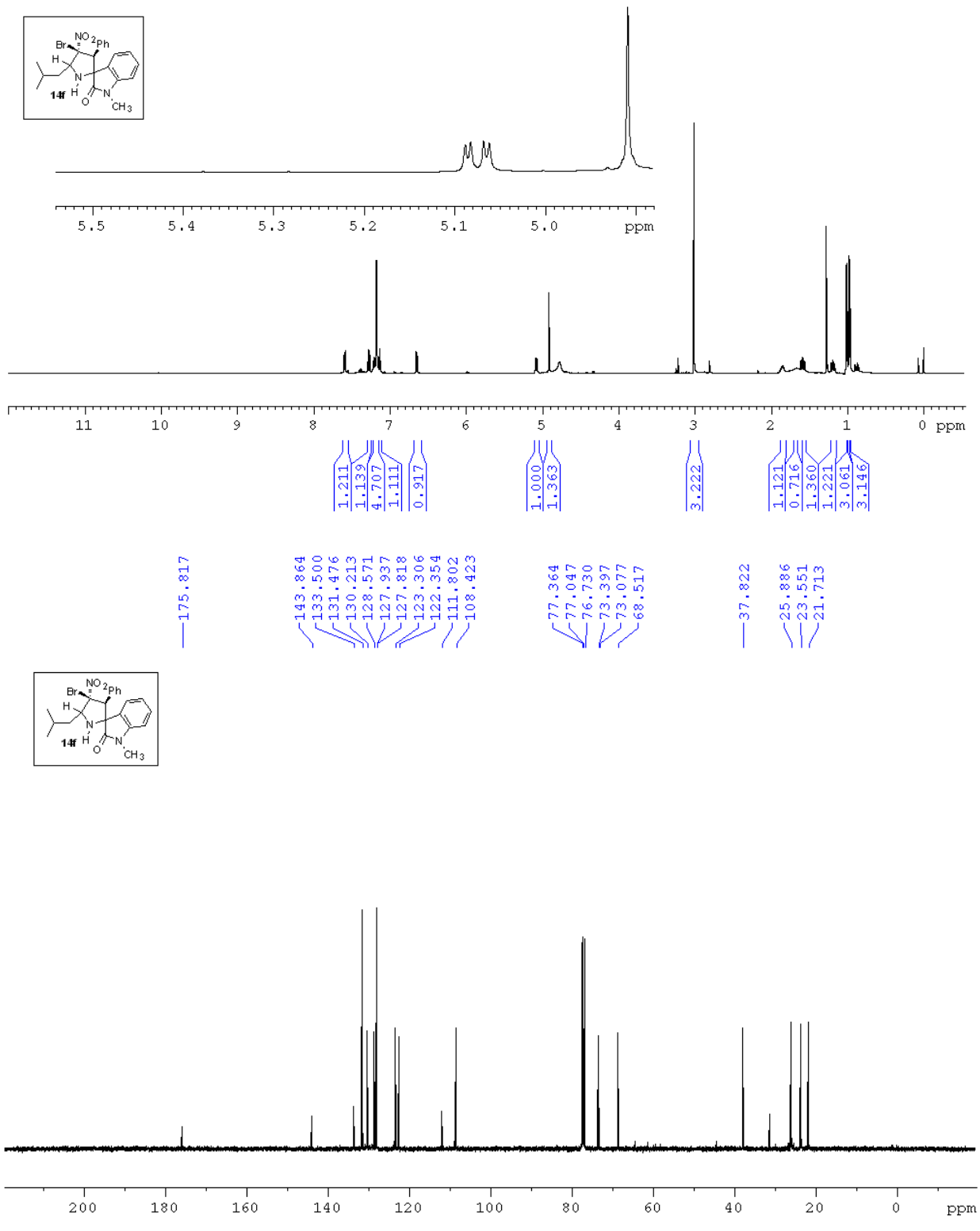

NO2Ph
Br
H
N
H
O
N
H
14b
5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 ppm
11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.001
1.250
6.158
1.289
1.148
1.127
1.265
1.175
1.211
2.082
6.136
177.536
140.804
133.496
131.567
130.186
128.619
128.031
123.375
122.890
111.787
109.970
77.338
77.020
76.703
73.332
68.325
37.716
25.885
23.507
21.657
200 180 160 140 120 100 80 60 40 20 0 ppm

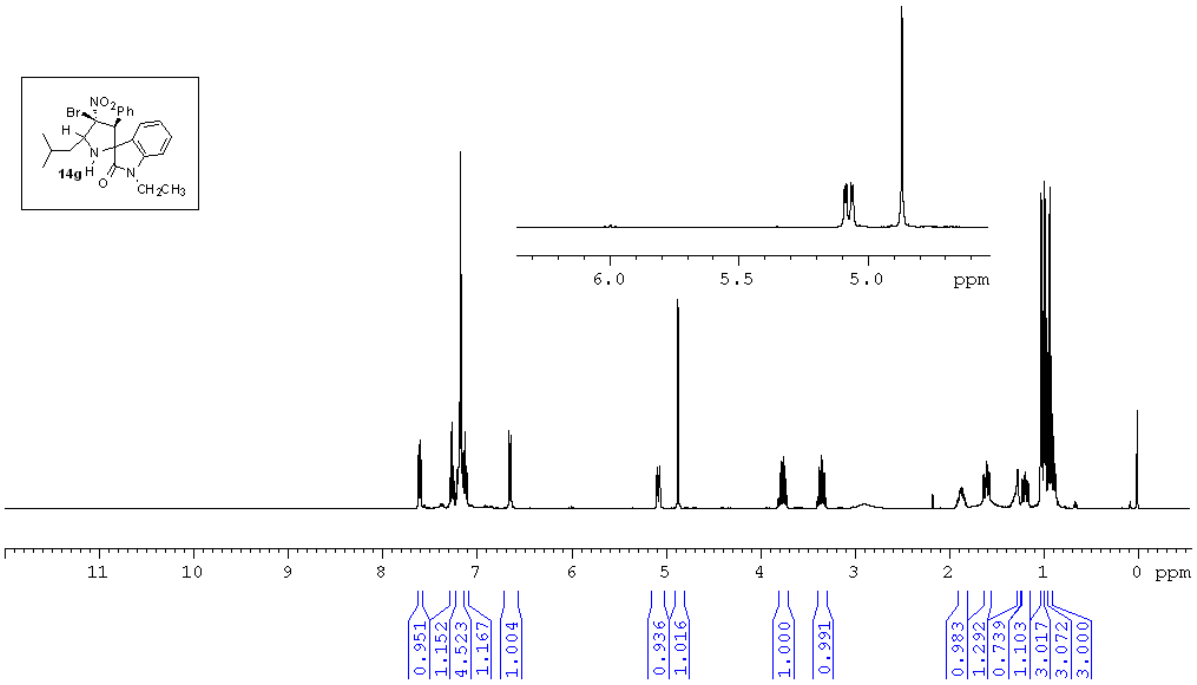

14c
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
ppm
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
1.129
3.231
3.362
1.149
1.070
1.085
1.163
1.112
2.359
1.345
3.349
3.469
177.809
142.241
133.669
130.632
129.662
128.383
128.052
127.874
123.701
121.832
110.415
109.430
77.910
70.938
39.752
39.543
39.335
35.359
30.651
26.654
16.036
9.411
14c
200
180
160
140
120
100
80
60
40
20
0
ppm

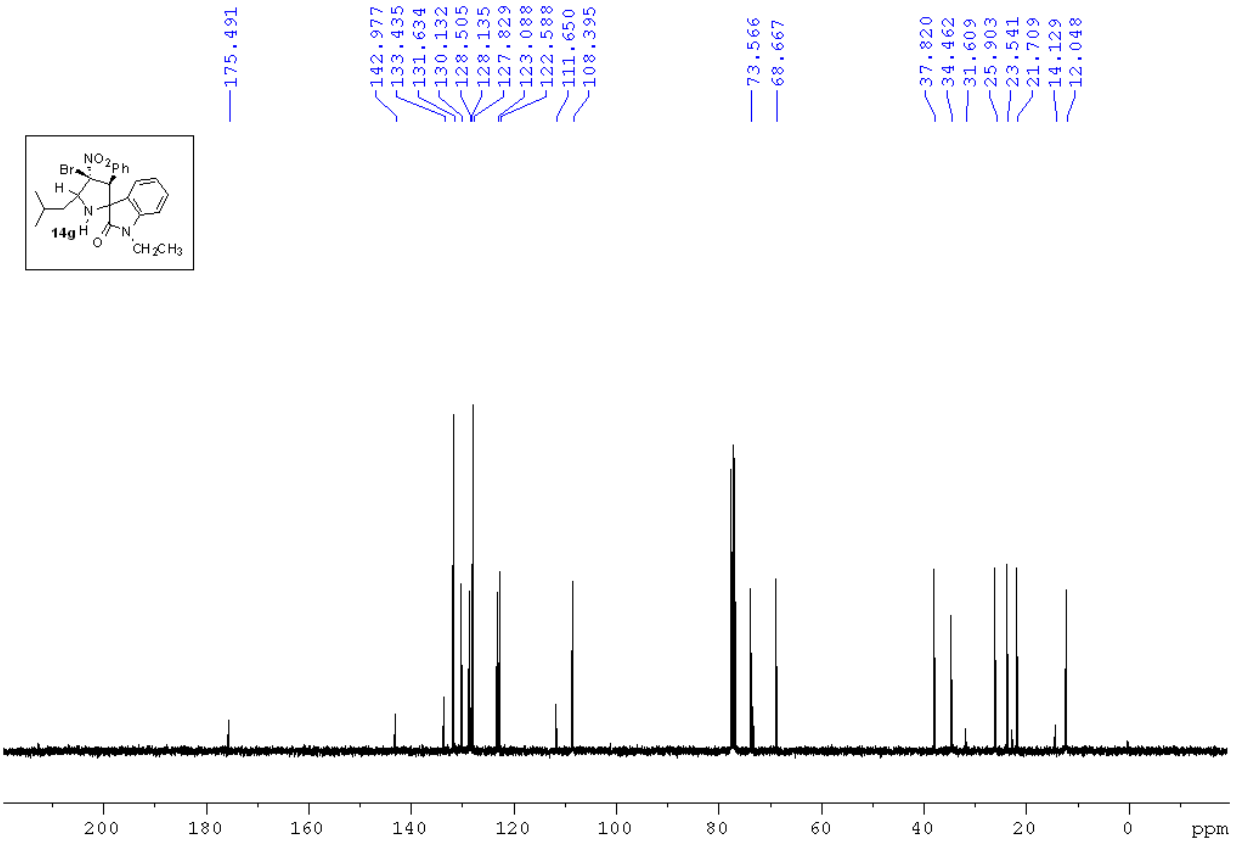

Br
NO2Ph
H
N
H
Me
S
14d
O
N
H
5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 ppm
11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.923
1.084
6.317
1.242
1.141
1.025
1.139
2.797
3.000
1.056

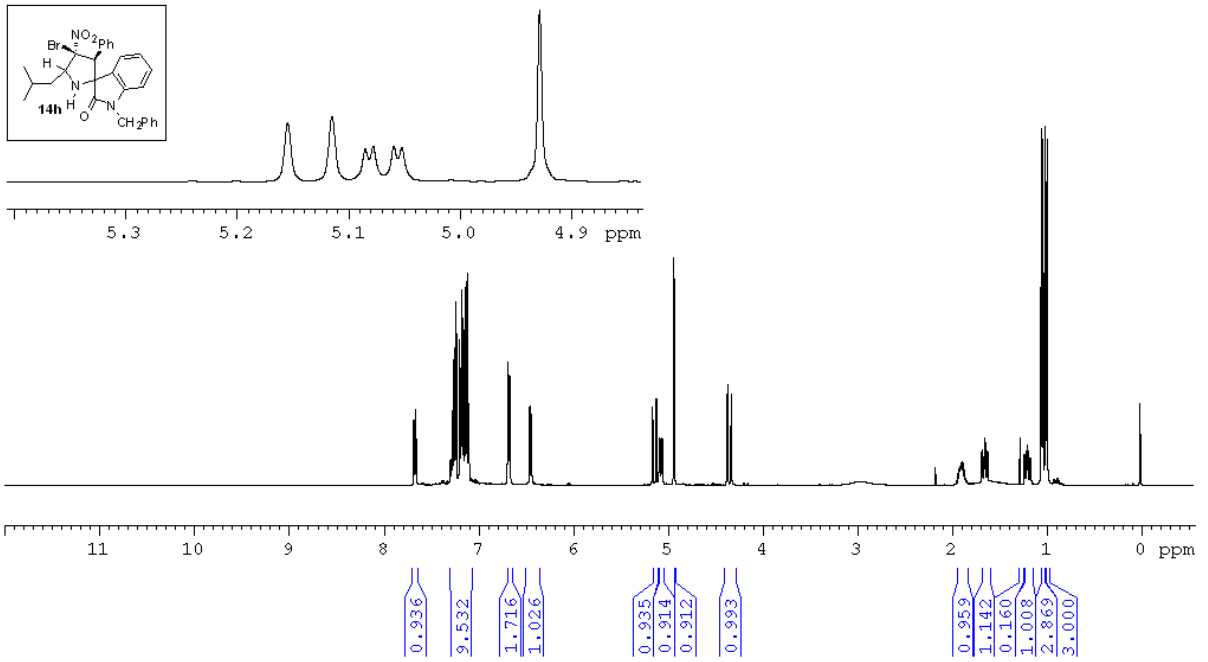

177.373
140.825
133.173
131.549
130.294
128.738
128.457
128.110
123.431
122.942
110.708
110.082
77.357
77.039
76.722
73.563
72.934
68.120
31.260
29.175
15.523
Br
NO2Ph
H
N
H
Me
S
14d
O
N
H
200 180 160 140 120 100 80 60 40 20 0 ppm

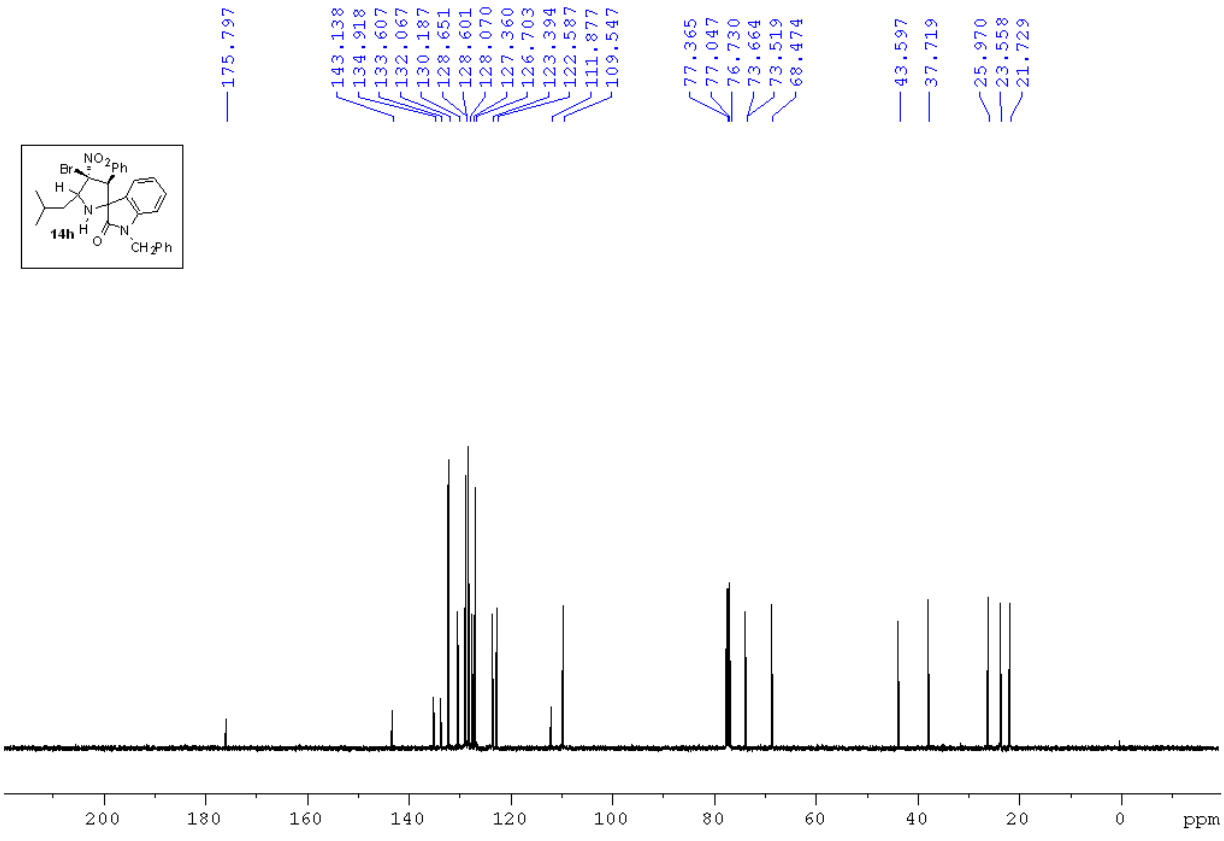

14e
5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 ppm
11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.960 1.283 4.532 1.039 0.971 0.934 1.065 1.049 1.050 0.715 1.070 1.997 2.143 1.247 2.969 3.000
175.512 142.963 133.345 131.584 130.142 128.520 128.101 127.857 123.108 122.594 111.169 108.423 77.359 77.042 76.724 75.051 72.884 68.549 34.468 29.231 28.864 22.530 13.799 12.086
14e
200 180 160 140 120 100 80 60 40 20 0 ppm


14f
5.5
5.4
5.3
5.2
5.1
5.0
ppm
11
10
9
8
7
6
5
4
3
2
1
0 ppm
1.211
1.139
4.707
1.111
0.917
1.000
1.363
3.222
1.121
0.716
1.360
1.221
3.061
3.146
175.817
143.864
133.500
131.476
130.213
128.571
127.937
127.818
123.306
122.354
111.802
108.423
77.364
77.047
76.730
73.397
73.077
68.517
37.822
25.886
23.551
21.713
200
180
160
140
120
100
80
60
40
20
0
ppm

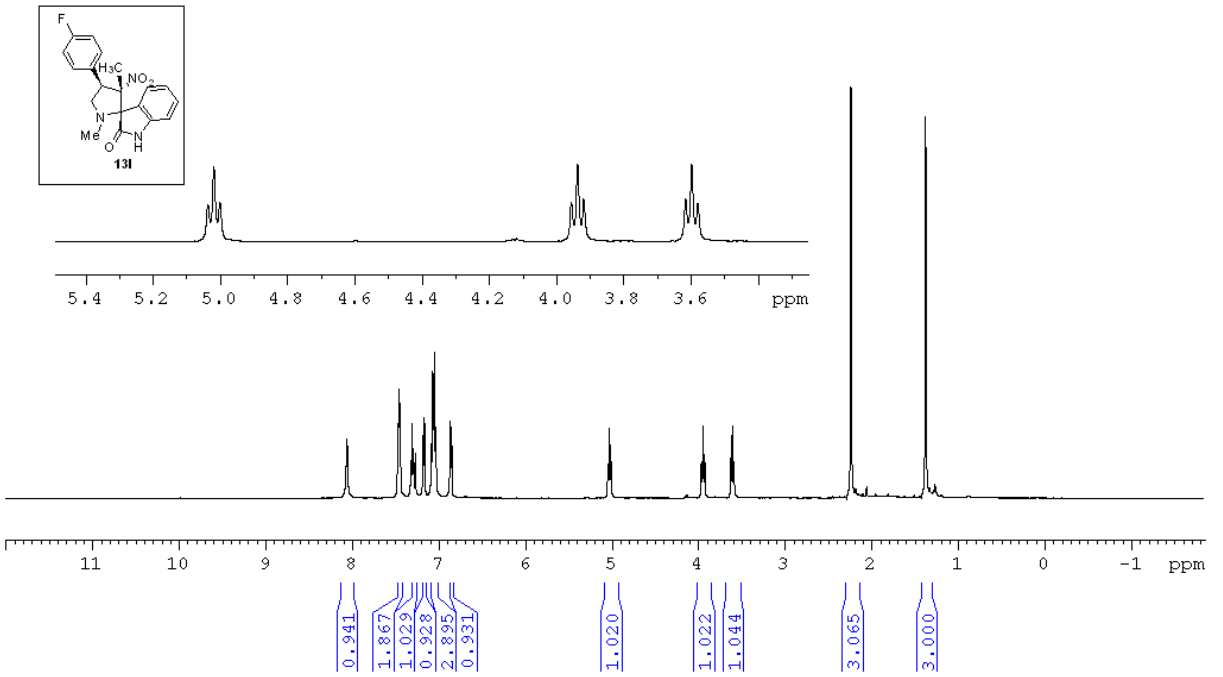

14g
6.0
5.5
5.0
ppm
11
10
9
8
7
6
5
4
3
2
1
0 ppm
0.951
1.152
4.523
1.167
1.004
0.936
1.016
1.000
0.991
0.983
1.292
0.739
1.103
3.017
3.072
3.000

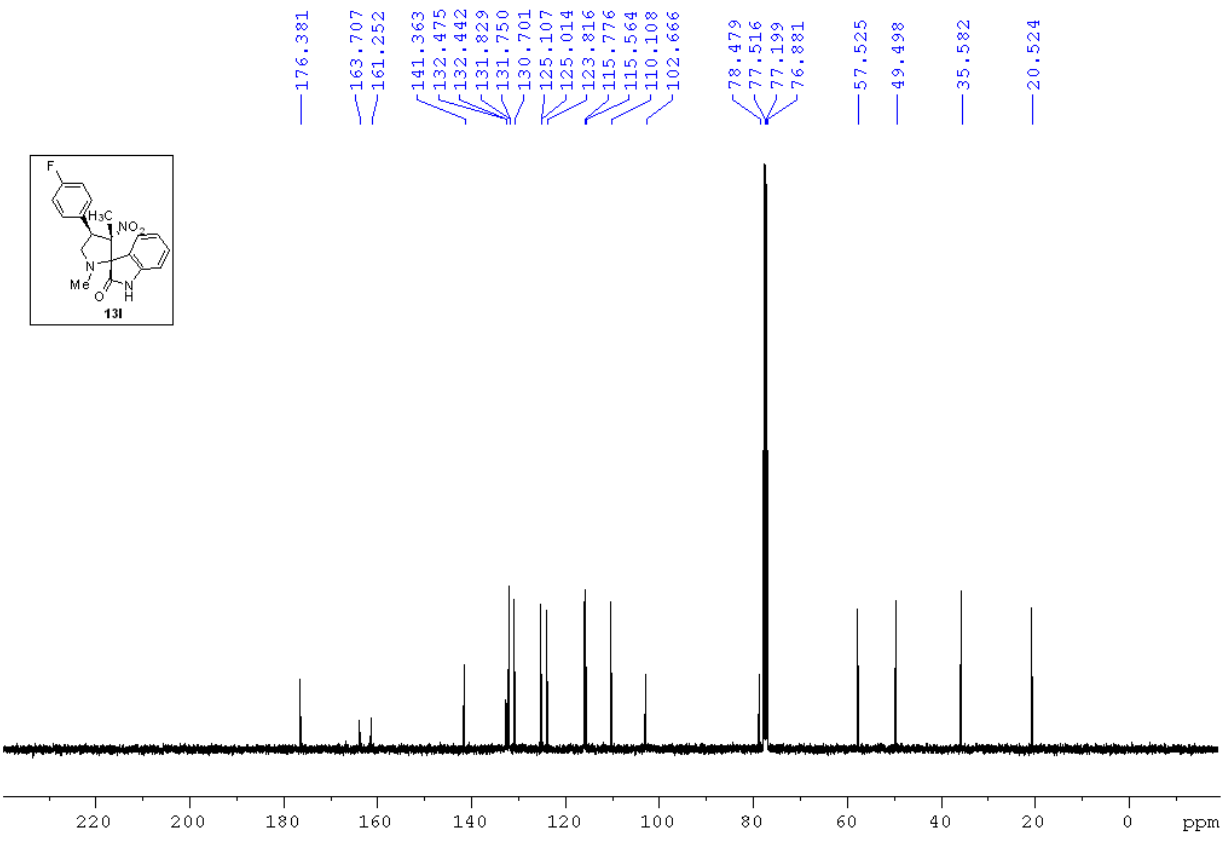

175.491
142.977
133.435
131.634
130.132
128.505
128.135
127.829
123.088
122.588
111.650
108.395
73.566
68.667
37.820
34.462
31.609
25.903
23.541
21.709
14.129
12.048
14g
200
180
160
140
120
100
80
60
40
20
0
ppm

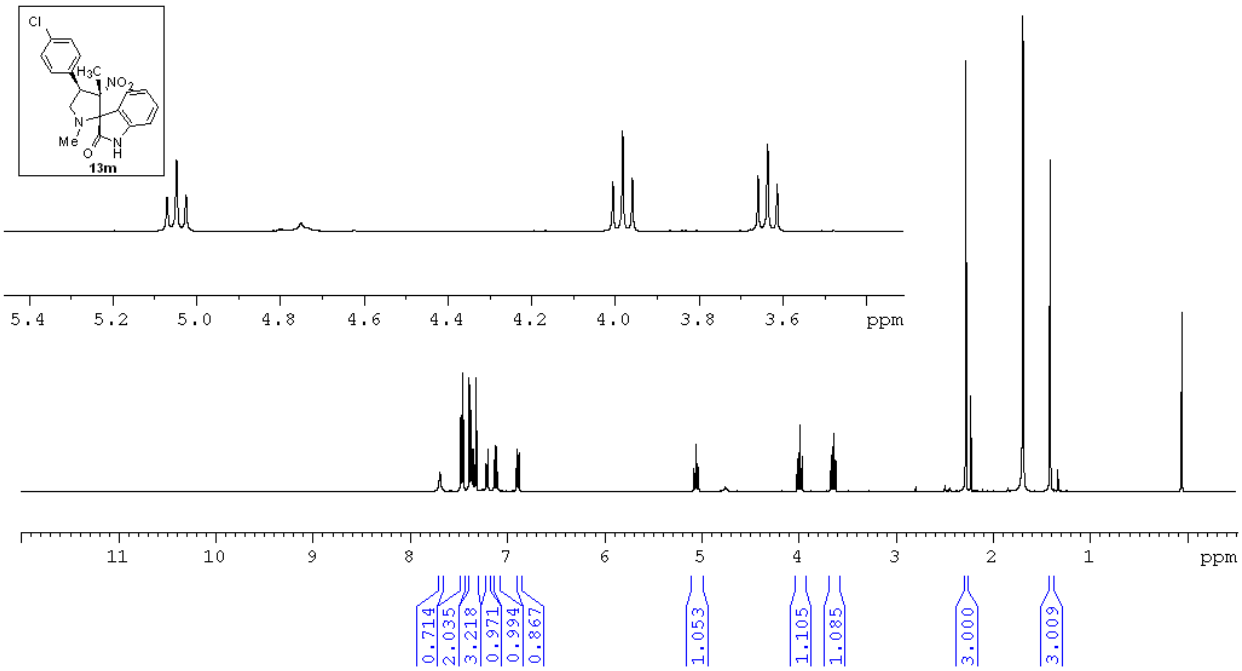

14h
5.3
5.2
5.1
5.0
4.9 ppm
11
10
9
8
7
6
5
4
3
2
1
0 ppm
0.936
9.532
1.716
1.026
0.935
0.914
0.912
0.993
0.959
1.142
0.160
1.008
2.869
3.000

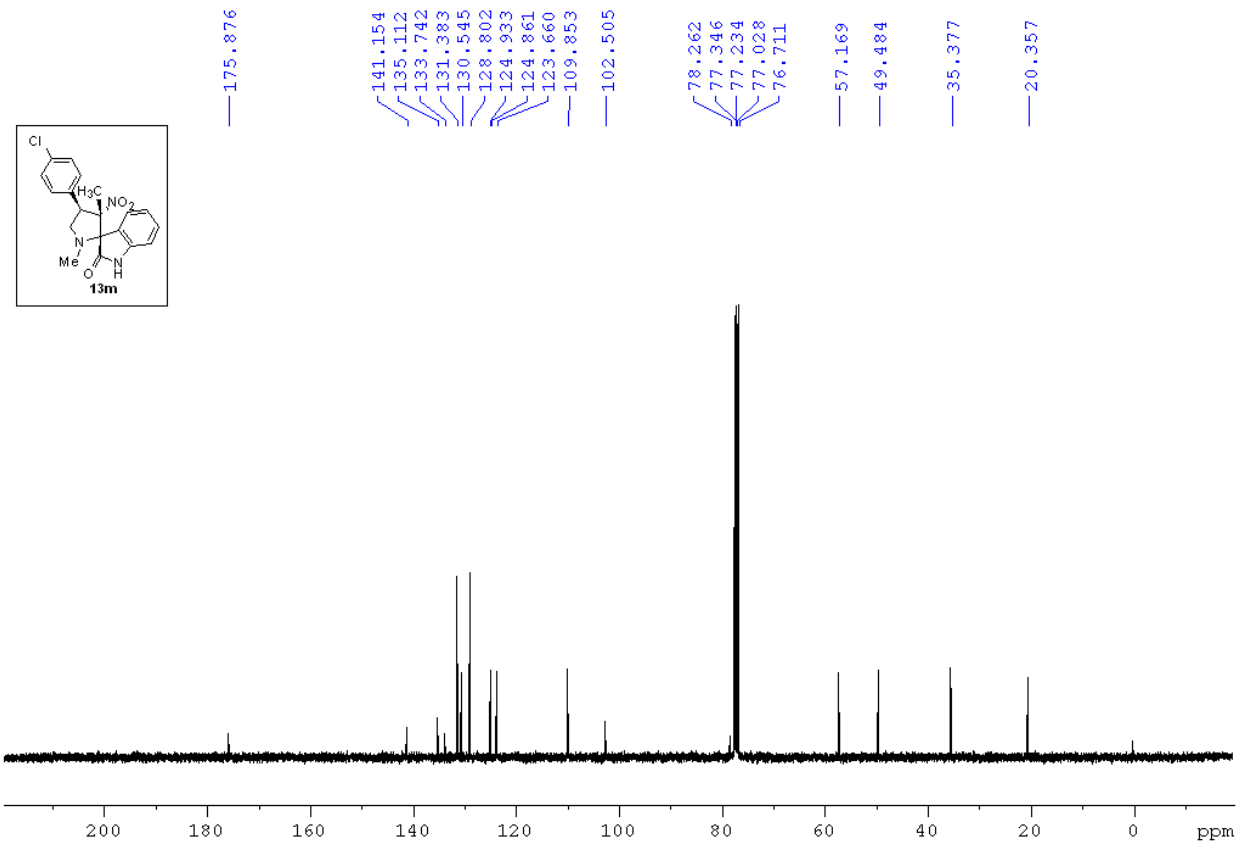

175.797
143.138
134.918
133.607
132.067
130.187
128.651
128.601
128.070
127.360
126.703
123.394
122.587
111.877
109.547
77.365
77.047
76.730
73.664
73.519
68.474
43.597
37.719
25.970
23.558
21.729
14h
200
180
160
140
120
100
80
60
40
20
0
ppm

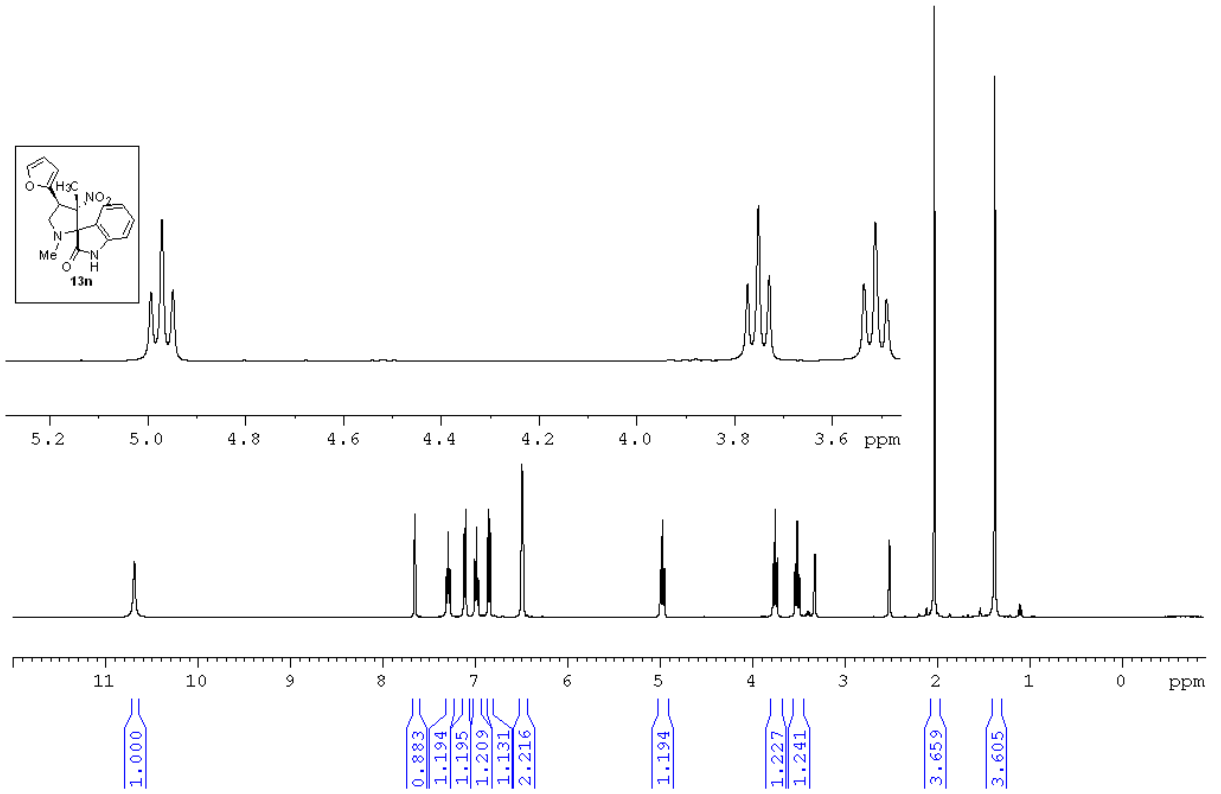
IV. Copies of NMR Spectra of 13l-13s

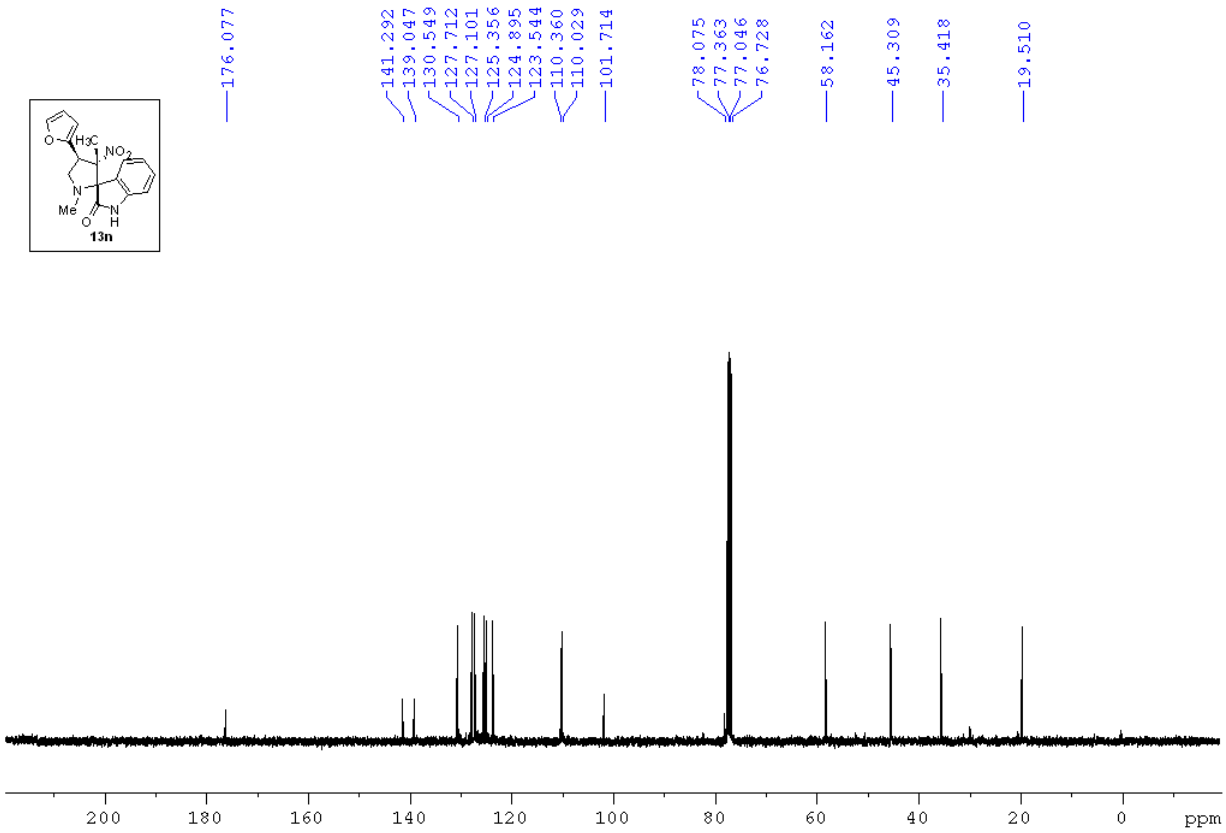


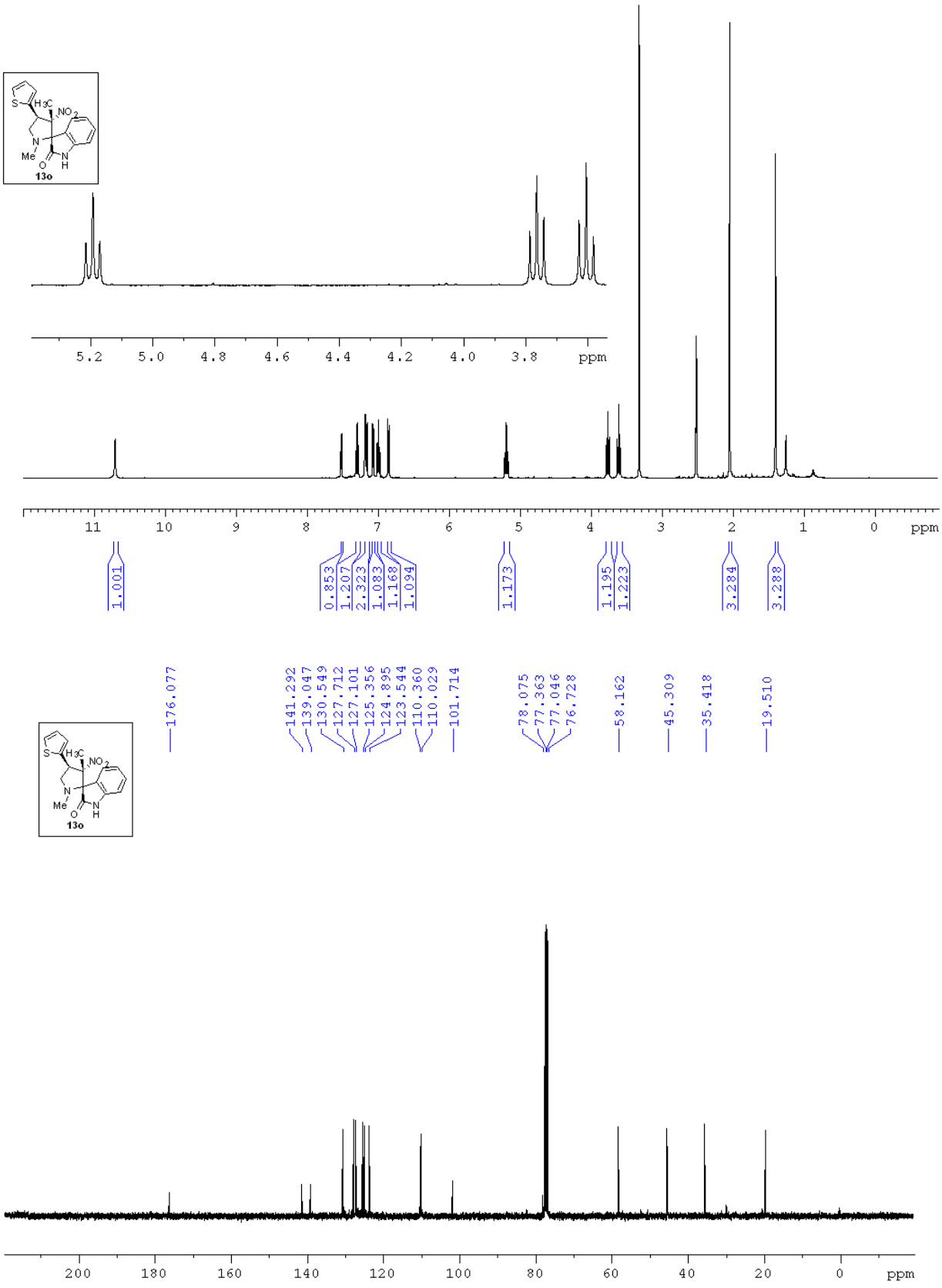


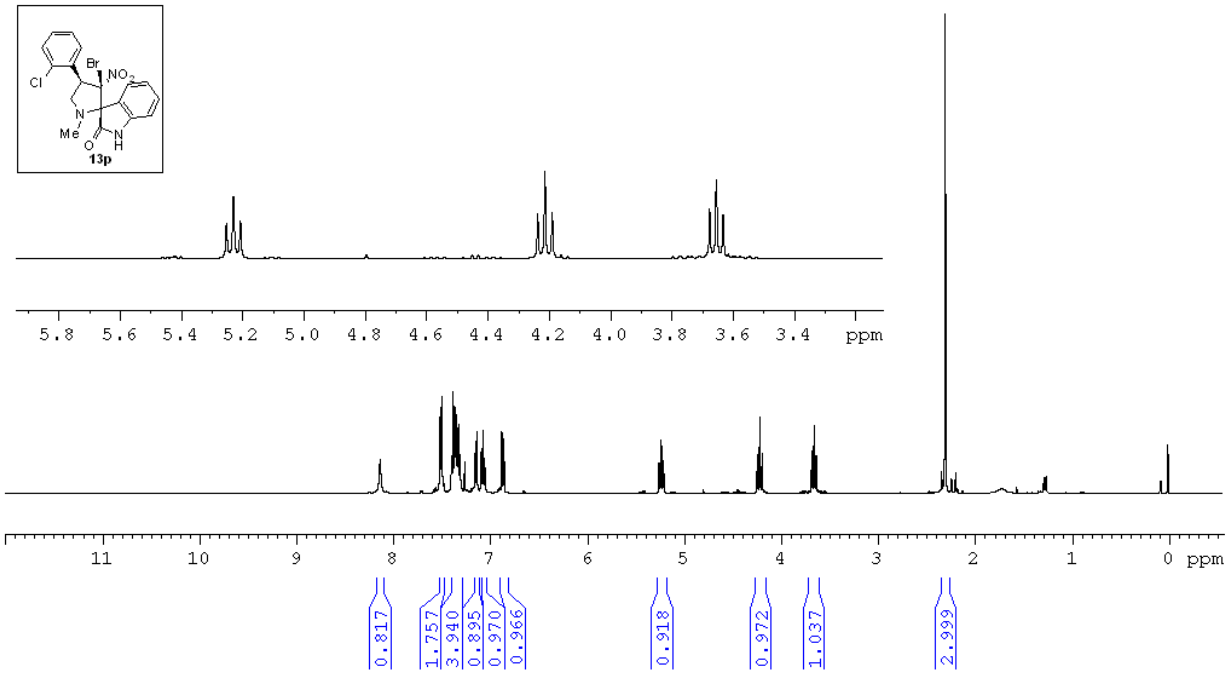

Cl
H3C
NO2
N
Me
O
N
H
13m
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
ppm
11
10
9
8
7
6
5
4
3
2
1
ppm
0.714
2.035
3.218
0.971
0.994
0.867
1.053
1.105
1.085
3.000
3.009

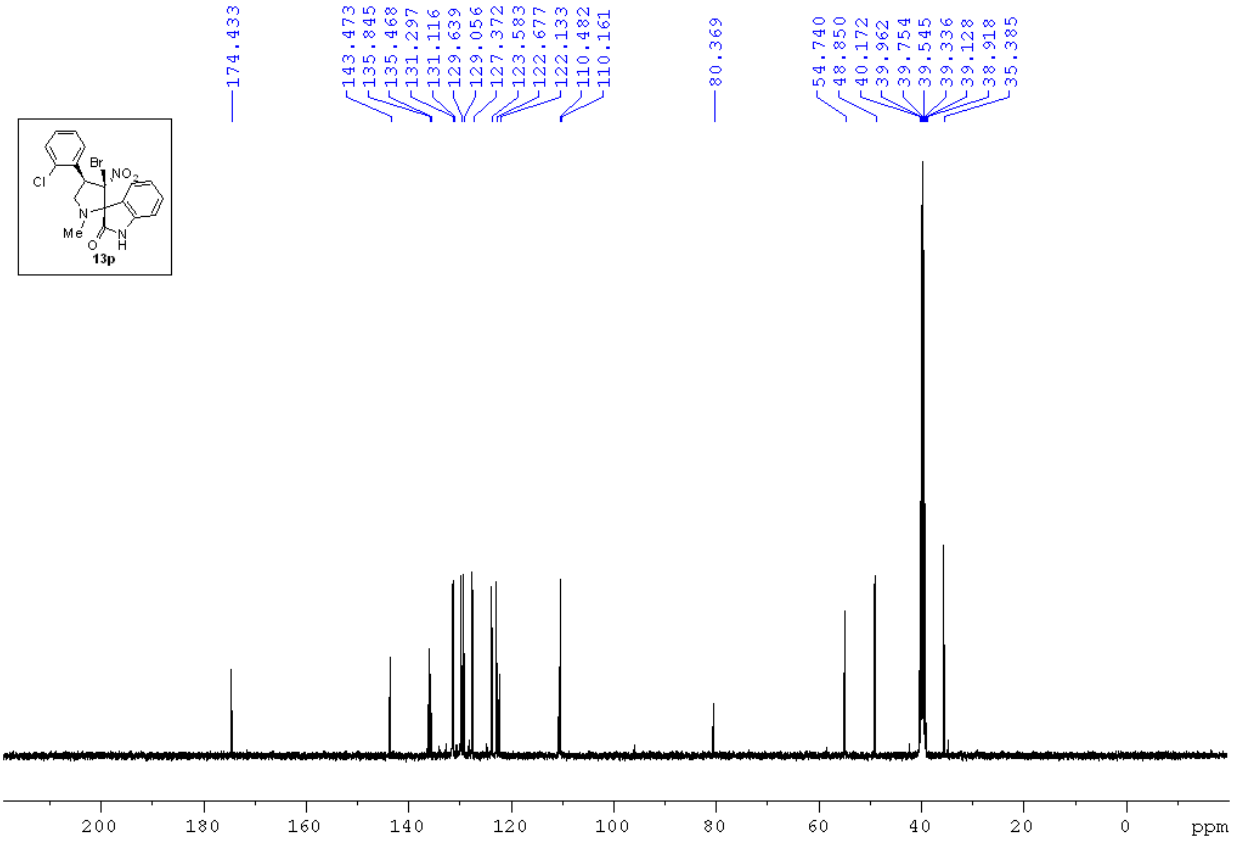

175.876
141.154
135.112
133.742
131.383
130.545
128.802
124.933
124.861
123.660
109.853
102.505
78.262
77.346
77.234
77.028
76.711
57.169
49.484
35.377
20.357
Cl
H3C
NO2
N
Me
O
N
H
13m
200
180
160
140
120
100
80
60
40
20
0
ppm

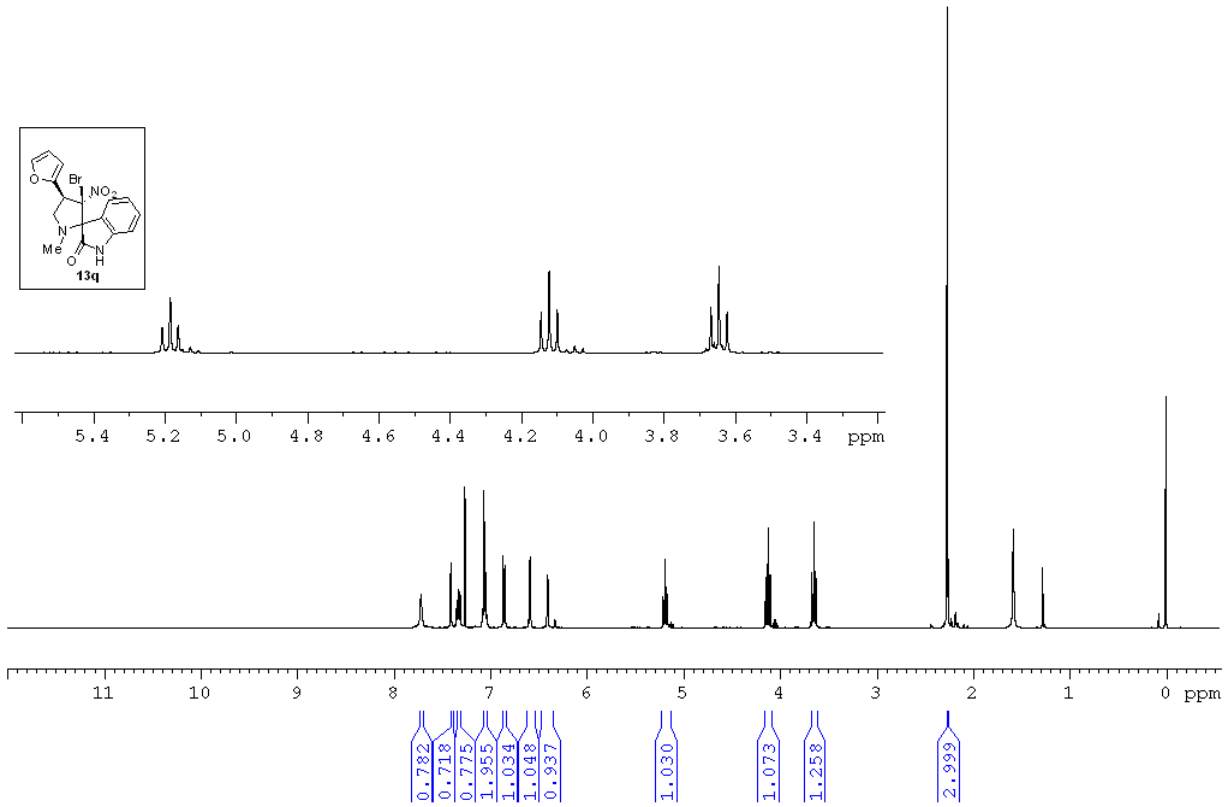

13n
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
ppm
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
0.883
1.194
1.195
1.209
1.131
2.216
1.194
1.227
1.241
3.659
3.605

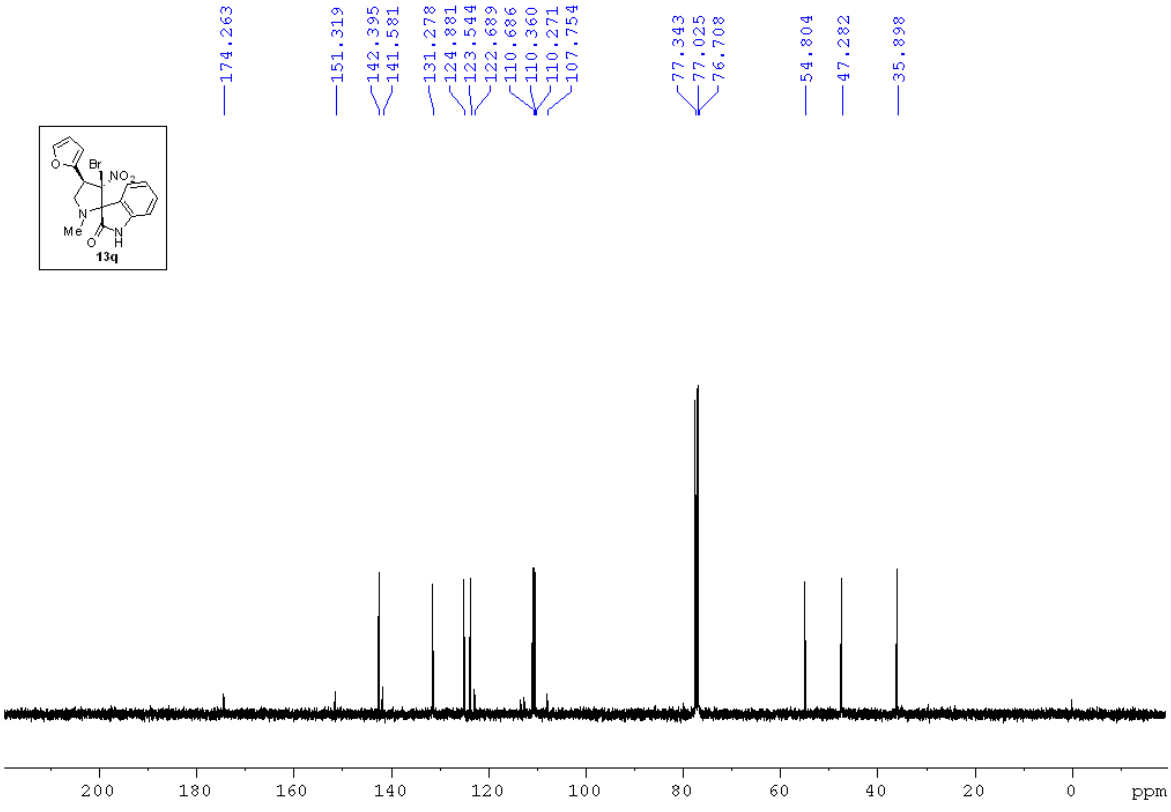

176.077
141.292
139.047
130.549
127.712
127.101
125.356
124.895
123.544
110.360
110.029
101.714
78.075
77.363
77.046
76.728
58.162
45.309
35.418
19.510
13n
200
180
160
140
120
100
80
60
40
20
0
ppm

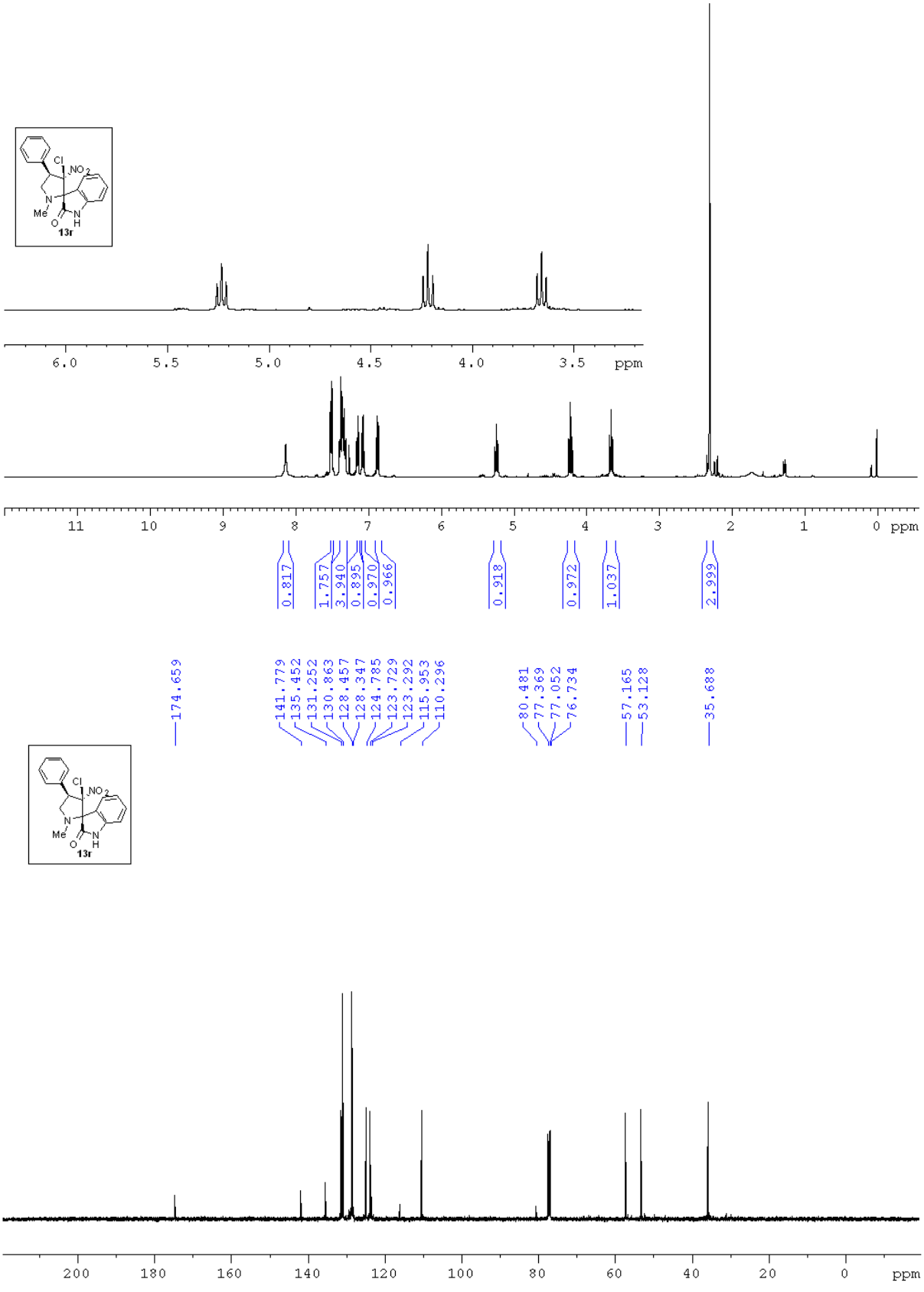

13o
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
ppm
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.001
0.853
1.207
2.323
1.083
1.168
1.094
1.173
1.195
1.223
3.284
3.288
176.077
141.292
139.047
130.549
127.712
127.101
125.356
124.895
123.544
110.360
110.029
101.714
78.075
77.363
77.046
76.728
58.162
45.309
35.418
19.510
13o
200
180
160
140
120
100
80
60
40
20
0
ppm

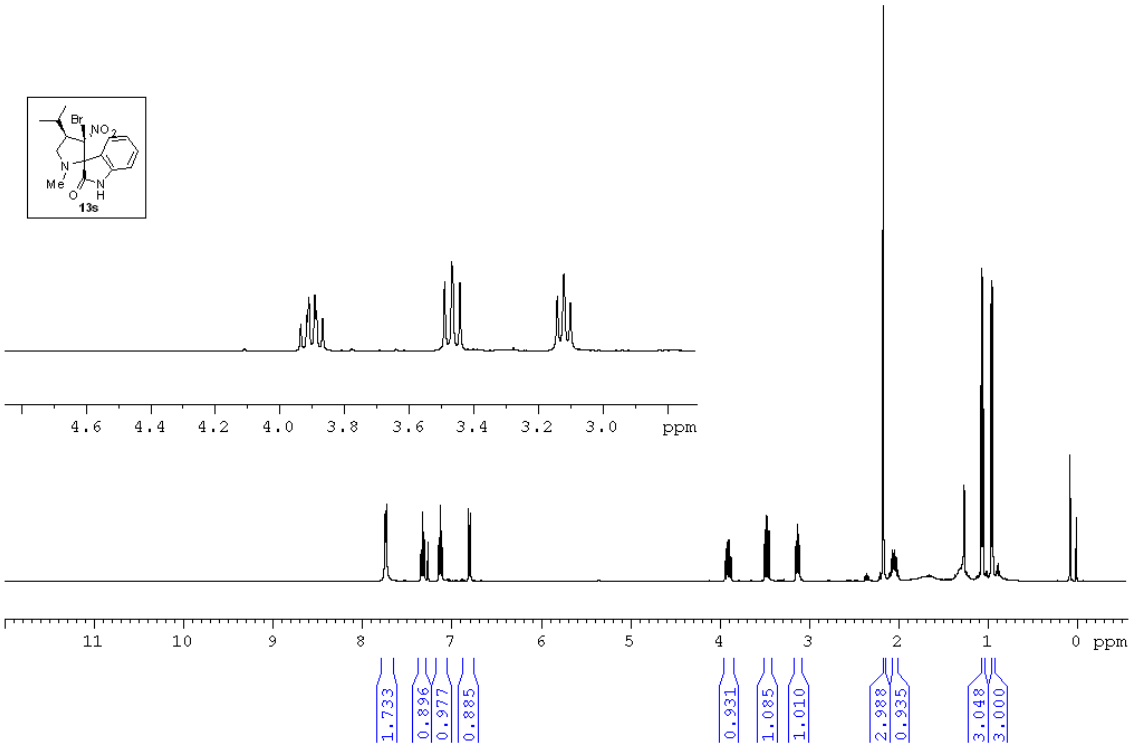

Cl
Br
NO2
N
Me
O
N
H
13p
5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 ppm
11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.817
1.757
3.940
0.895
0.970
0.966
0.918
0.972
1.037
2.999

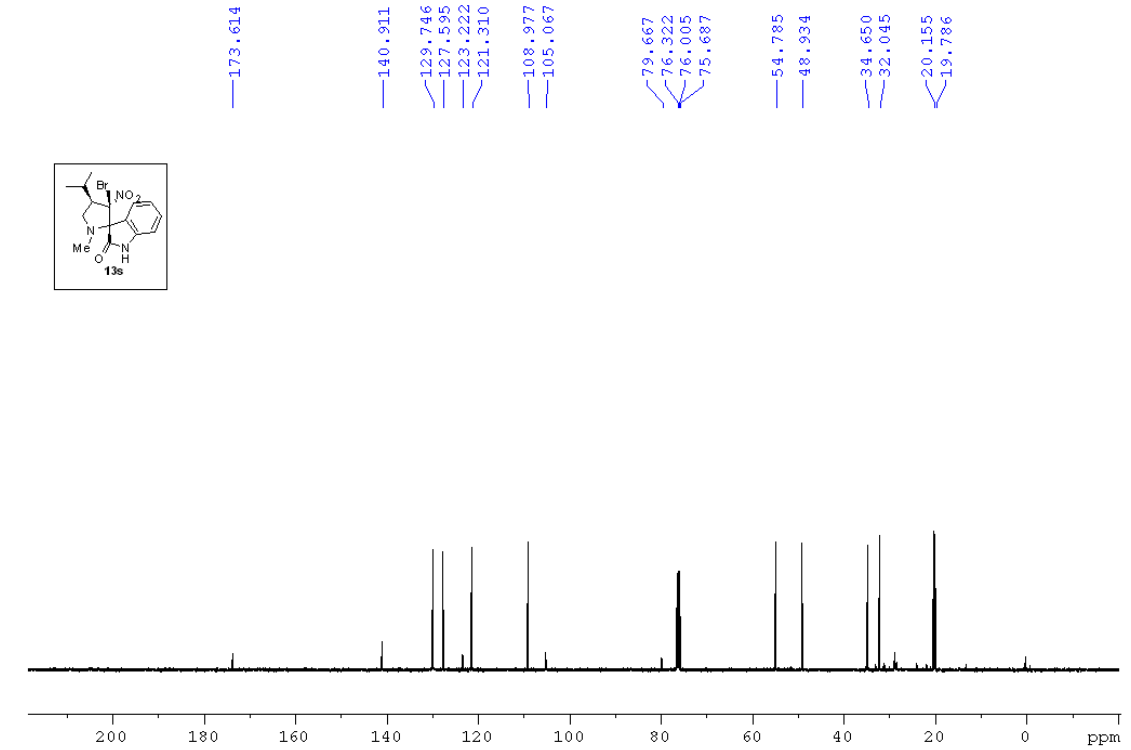

174.433
143.473
135.845
135.468
131.297
131.116
129.639
129.056
127.372
123.583
122.677
122.133
110.482
110.161
80.369
54.740
48.850
40.172
39.962
39.754
39.545
39.336
39.128
38.918
35.385
Cl
Br
NO2
N
Me
O
N
H
13p
200 180 160 140 120 100 80 60 40 20 0 ppm


13q
5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 ppm
11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.782
0.718
0.775
1.955
1.034
1.048
0.937
1.030
1.073
1.258
2.999

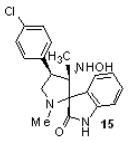

174.263
151.319
142.395
141.581
131.278
124.881
123.544
122.689
110.686
110.360
110.271
107.754
77.343
77.025
76.708
54.804
47.282
35.898
13q
200 180 160 140 120 100 80 60 40 20 0 ppm

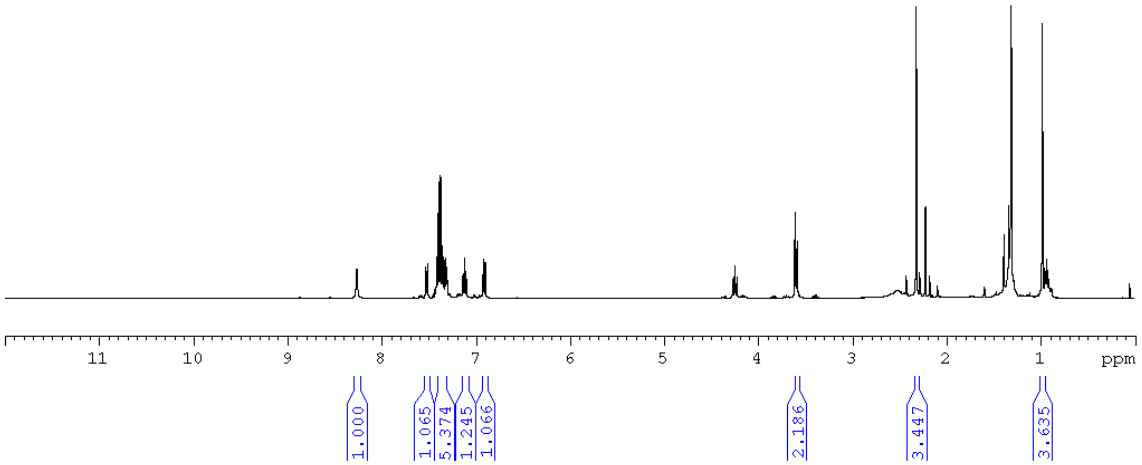

Cl
NO2
N
Me
O
N
H
13r
6.0
5.5
5.0
4.5
4.0
3.5
ppm
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.817
1.757
3.940
0.895
0.970
0.966
0.918
0.972
1.037
2.999
174.659
141.779
135.452
131.252
130.863
128.457
128.347
124.785
123.729
123.292
115.953
110.296
80.481
77.369
77.052
76.734
57.165
53.128
35.688
200
180
160
140
120
100
80
60
40
20
0
ppm

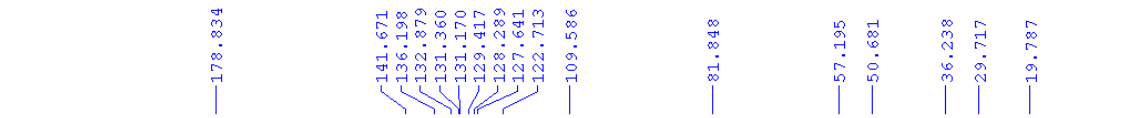

13s
4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 ppm
11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.733 0.896 0.977 0.885 0.931 1.085 1.010 2.988 0.935 3.048 3.000

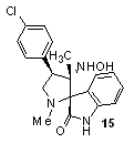

173.614
140.911
129.746
127.595
123.222
121.310
108.977
105.067
79.667
76.322
76.005
75.687
54.785
48.934
34.650
32.045
20.155
13.786
13s
200 180 160 140 120 100 80 60 40 20 0 ppm

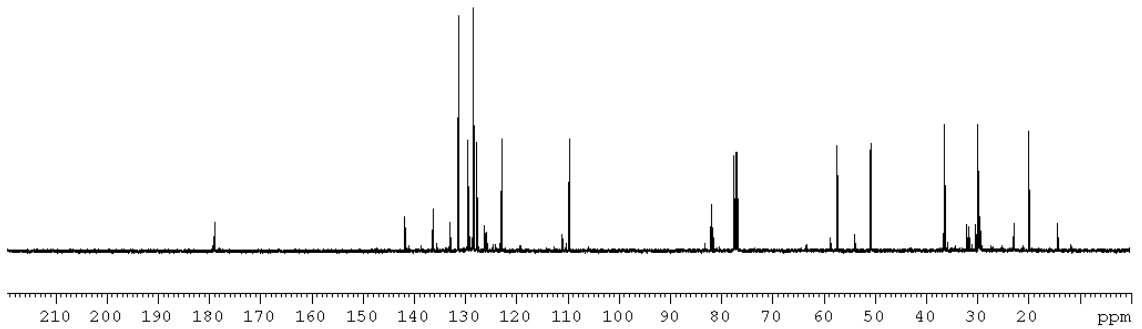
V. Copies of NMR Spectra of **15** & **16**

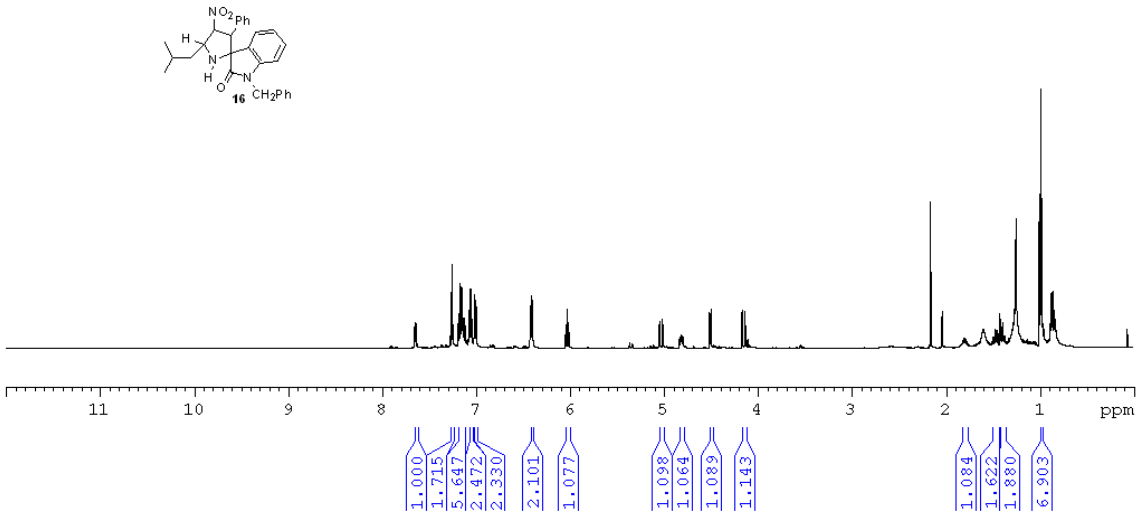


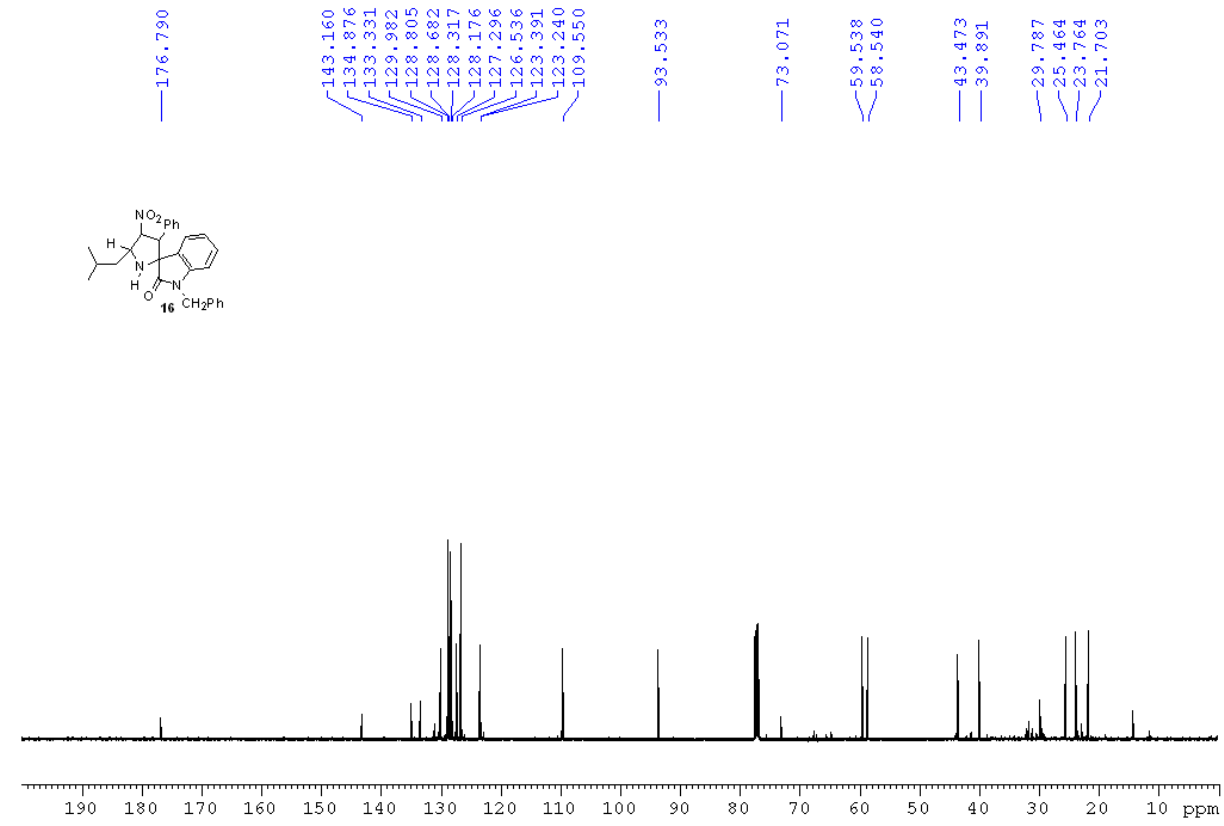






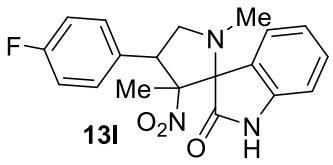



NO2
Ph
H
N
H
O
16
N
CH2Ph
11
10
9
8
7
6
5
4
3
2
1
ppm
1.000
1.715
5.647
2.472
2.330
2.101
1.077
1.098
1.064
1.089
1.143
1.084
1.622
1.880
6.903

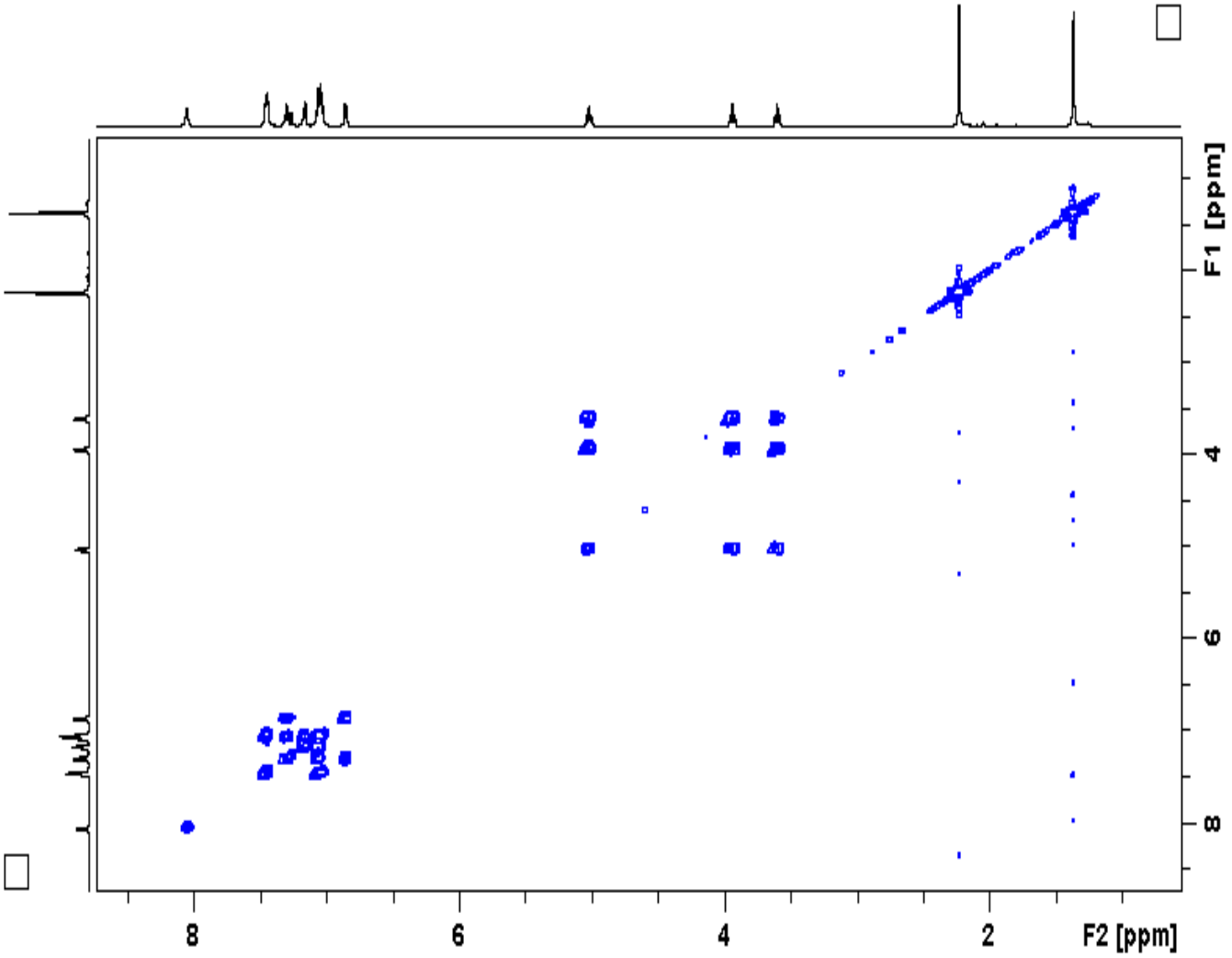

176.790
143.160
134.876
133.331
129.982
128.805
128.682
128.317
128.176
127.296
126.536
123.391
123.240
109.550
93.533
73.071
59.538
58.540
43.473
39.891
29.787
25.464
23.764
21.703
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

VI. Copies of 2D-NMR spectra of 13l

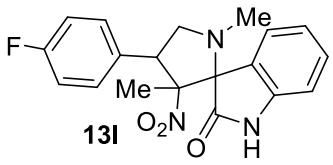
a) COSY for the compound 13l



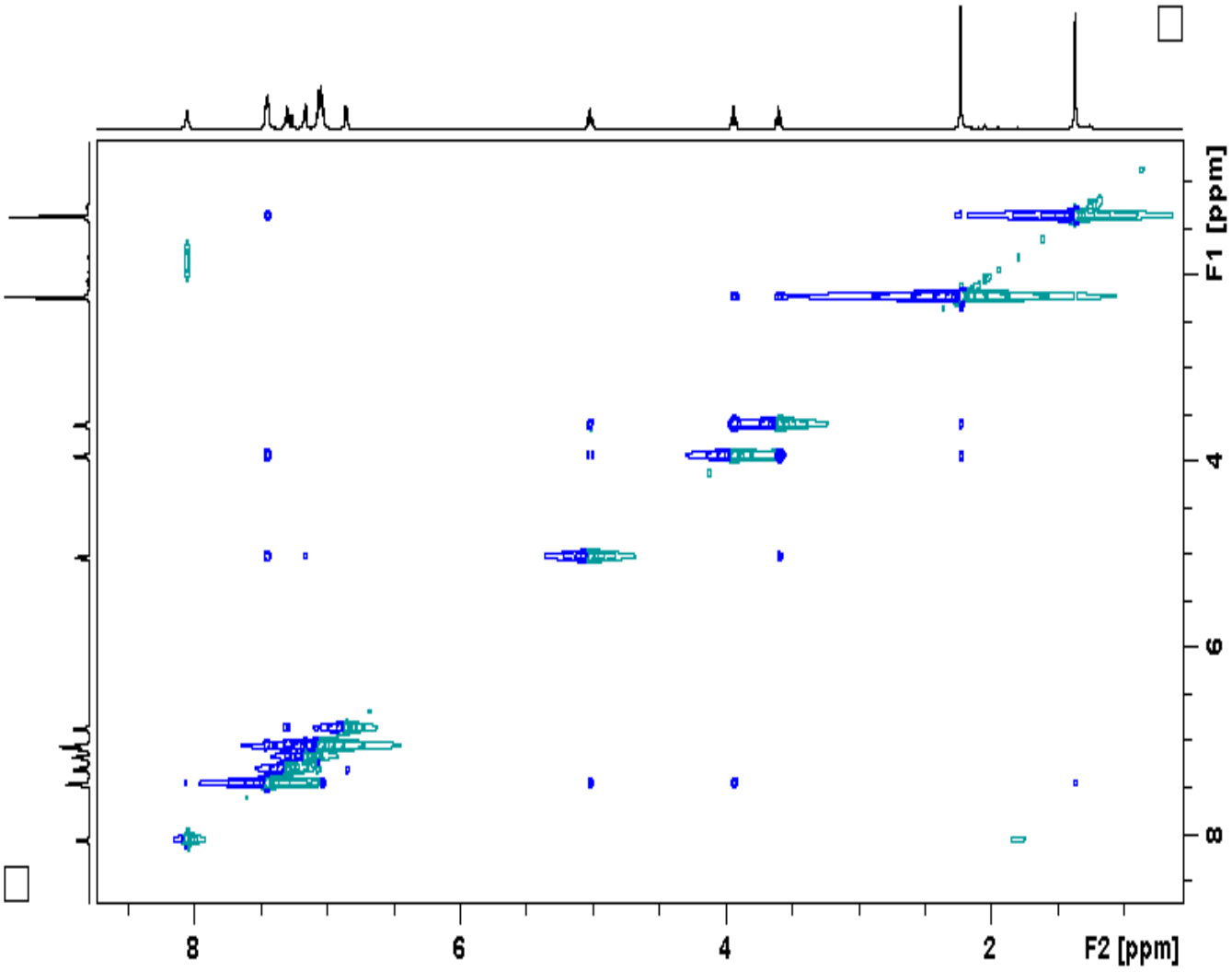
13l



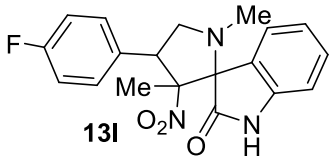
b) NOESY for the compound 13l



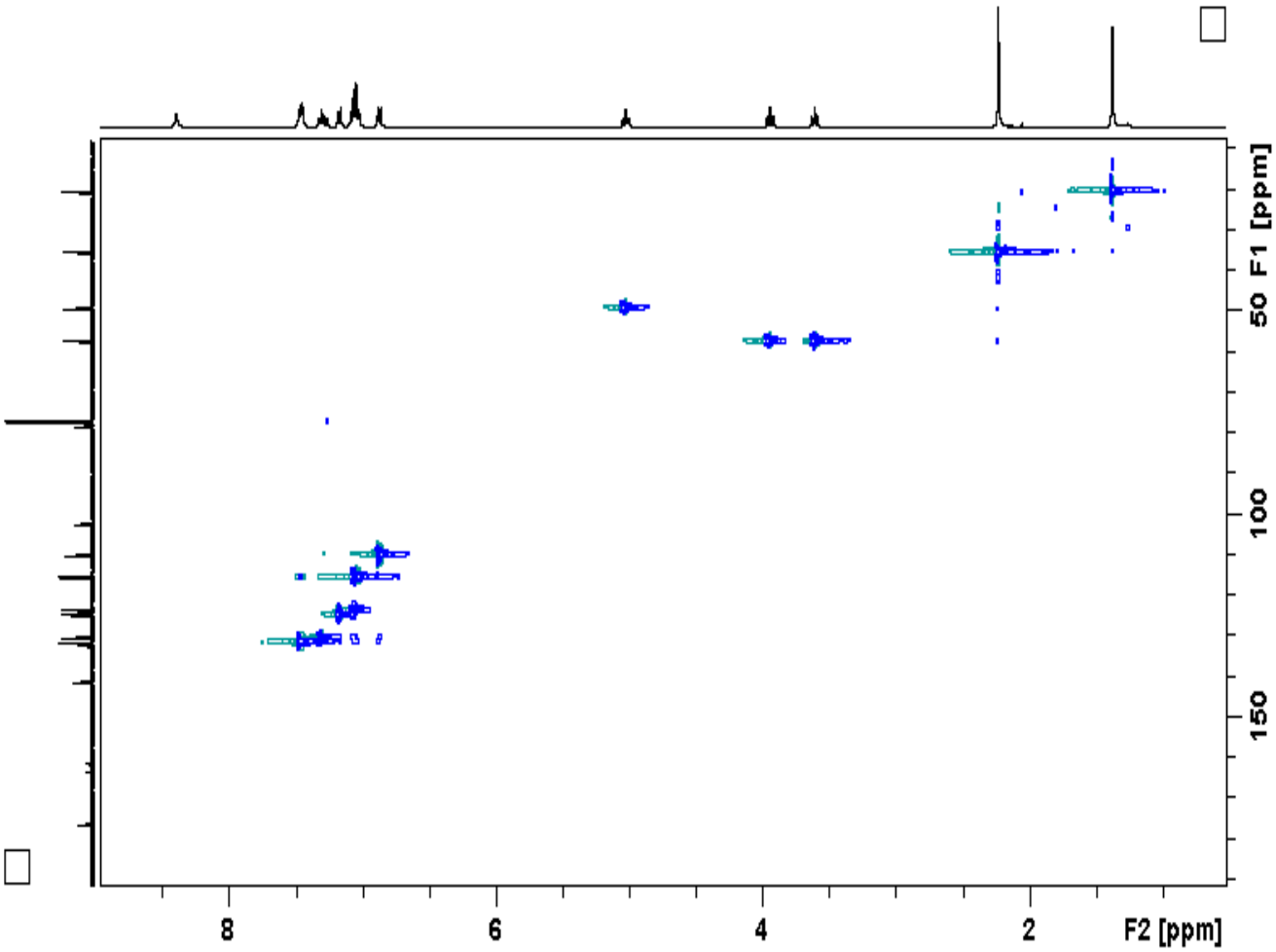
13l



c) HSQC for the compound 13l



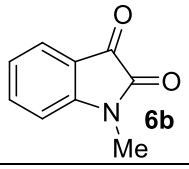
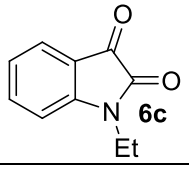
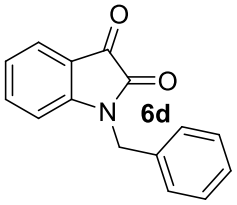
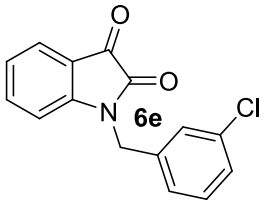
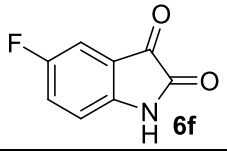
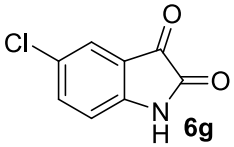
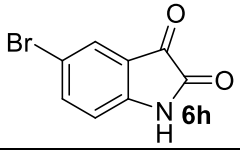
13l

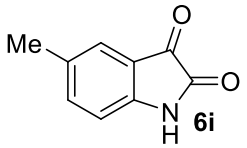
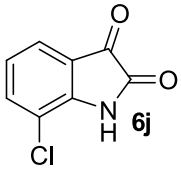
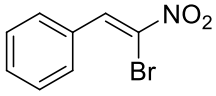
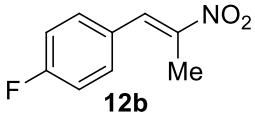
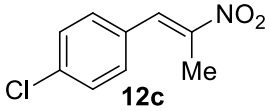
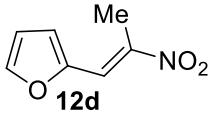
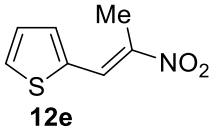
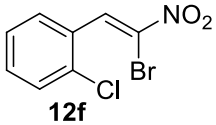
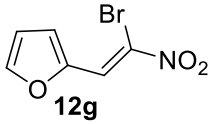
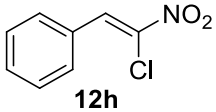
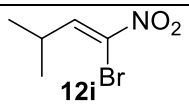


VII. Copies of HPLC chromatograms for starting materials

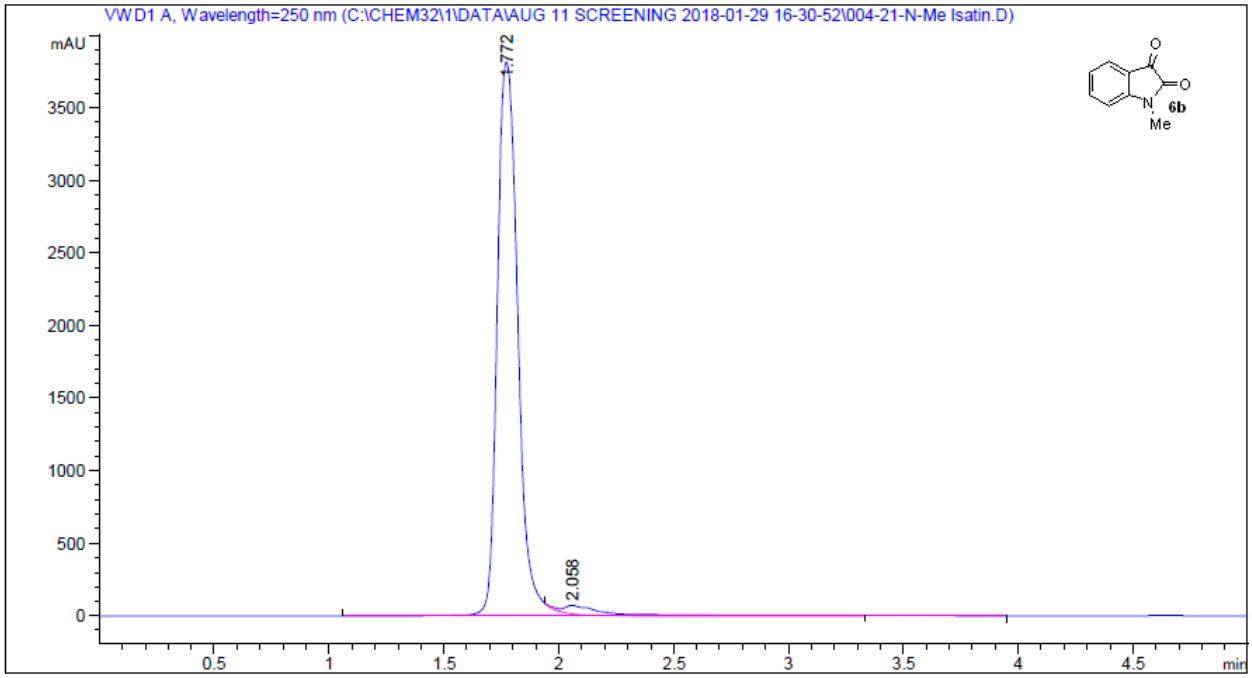
Synthesis of Starting materials

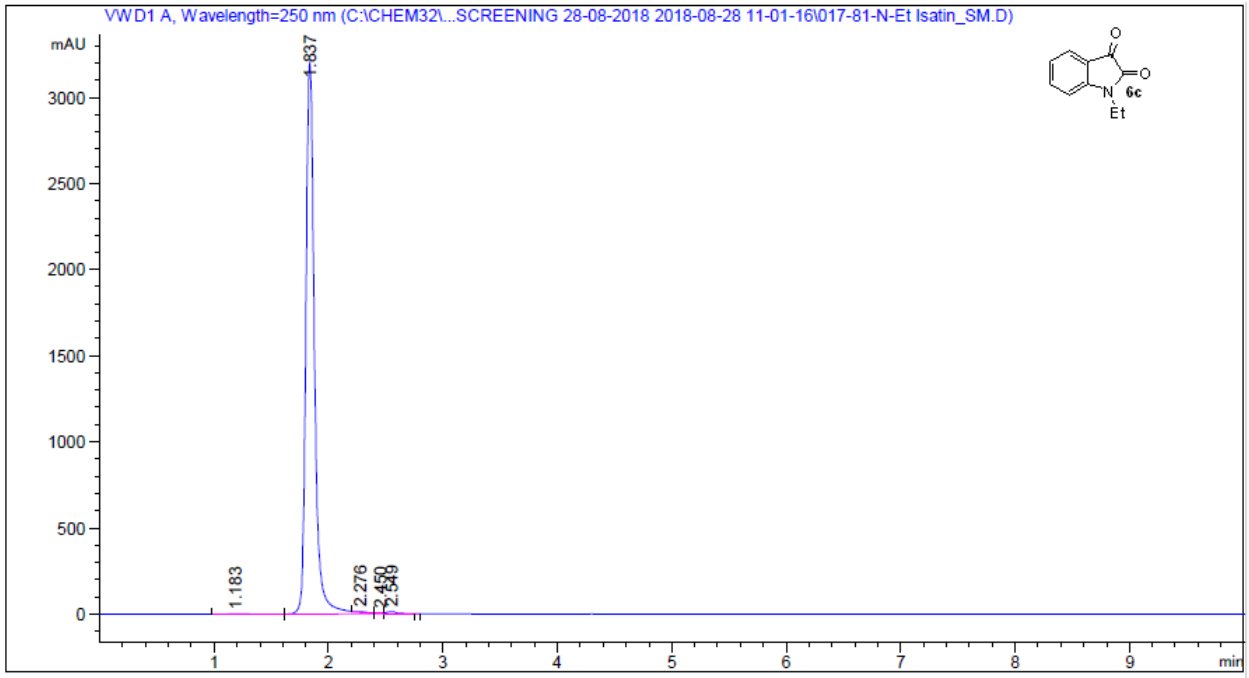
All the starting materials (**6b**-**6j** & **12a**-**12i**) were synthesized according to the procedure in the literature. [1-5] The purity of the compounds were confirmed by reverse-phase HPLC screening Agilent 1220 Infinity II LC instrument.

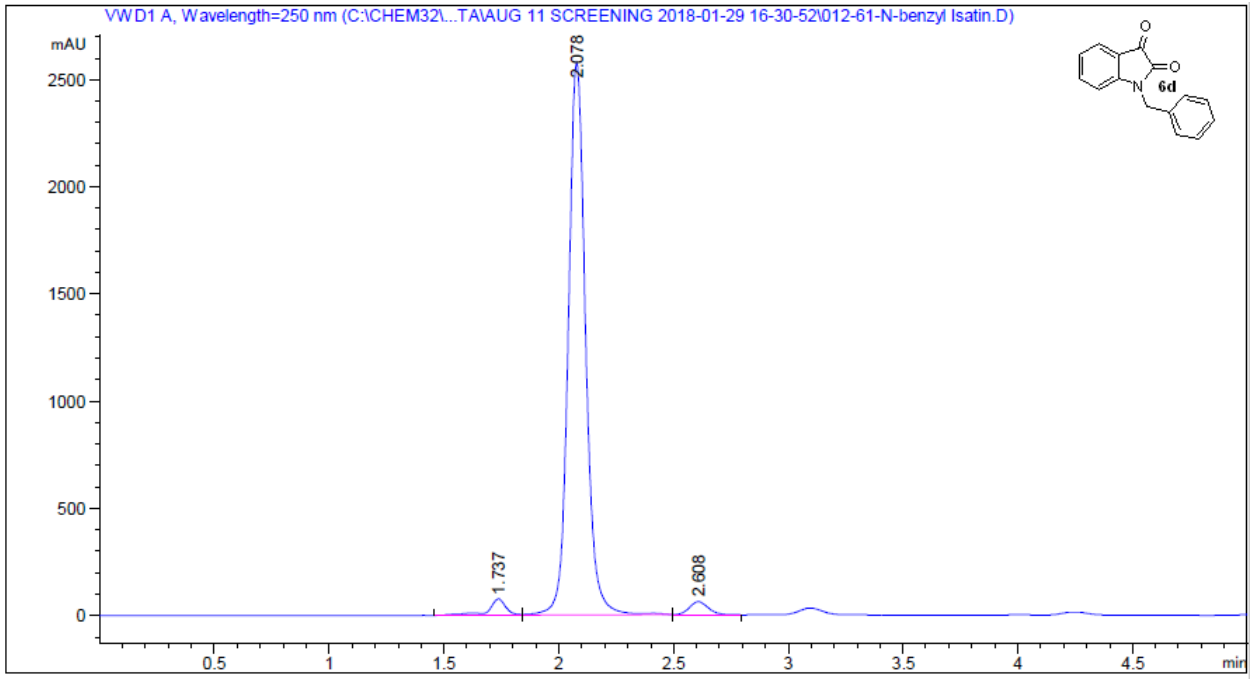
Sl.No.	Sample code & Structure	IUPAC Name	% Purity by HPLC	Reference
1	 **6b**	1-methylindoline-2,3-dione	96.88	1
2	 **6c**	1-ethylindoline-2,3-dione	99.21	1
3	 **6d**	1-benzylindoline-2,3-dione	94.83	1
4	 **6e**	1-(3-chlorobenzyl)indoline-2,3-dione	98.08	1
5	 **6f**	5-fluoroindoline-2,3-dione	99.83	2
6	 **6g**	5-chloroindoline-2,3-dione	95.50	2
7	 **6h**	5-bromoindoline-2,3-dione	96.76	2

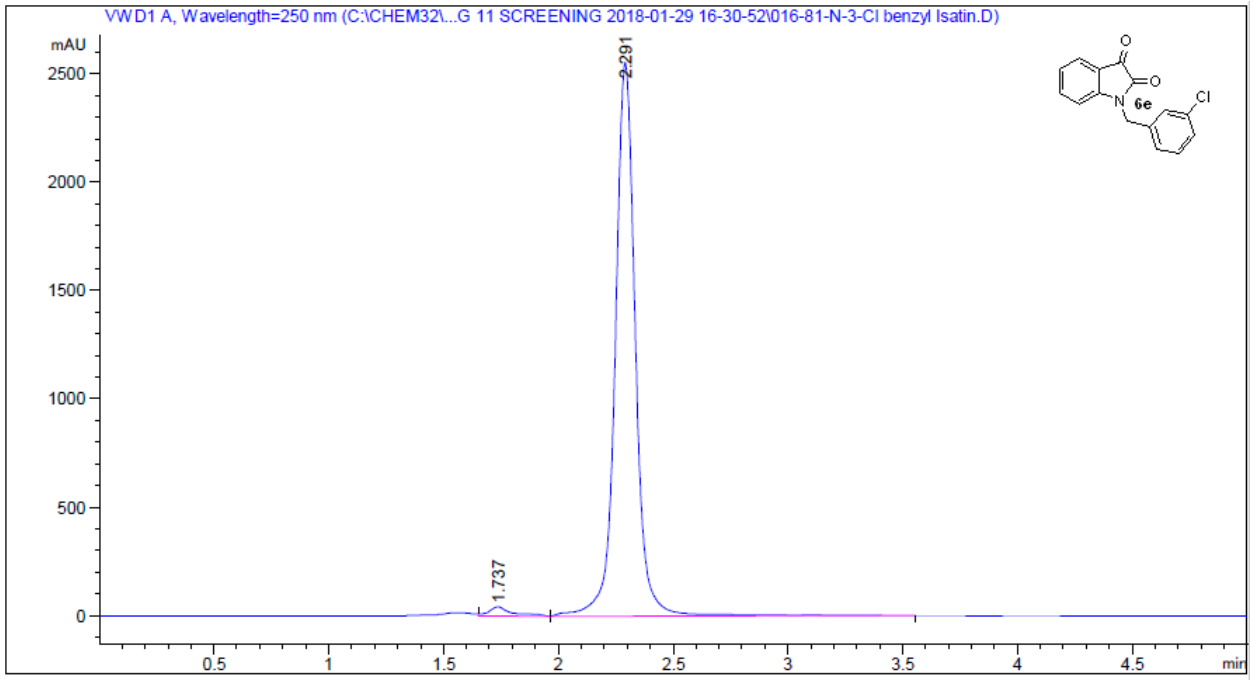
8	 **6i**	5-methylindoline-2,3-dione	96.68	2
9	 **6j**	7-chloroindoline-2,3-dione	91.59	2
10	 **12a**	(Z)-(2-bromo-2-nitrovinyl)benzene	96.59	5
11	 **12b**	(E)-1-fluoro-4-(2-nitroprop-1-enyl)benzene	99.81	3
12	 **12c**	(E)-1-chloro-4-(2-nitroprop-1-enyl)benzene	97.65	3
13	 **12d**	(E)-2-(2-nitroprop-1-enyl)furan	99.86	3
14	 **12e**	(E)-2-(2-nitroprop-1-enyl)thiophene	91.72	3
15	 **12f**	(Z)-1-(2-bromo-2-nitrovinyl)-2-chlorobenzene	92.56	5
16	 **12g**	(Z)-2-(2-bromo-2-nitrovinyl)furan	91.30	5
17	 **12h**	(Z)-(2-chloro-2-nitrovinyl)benzene	92.56	4
18	 **12i**	(Z)-1-bromo-3-methyl-1-nitrobut-1-ene	91.85	5

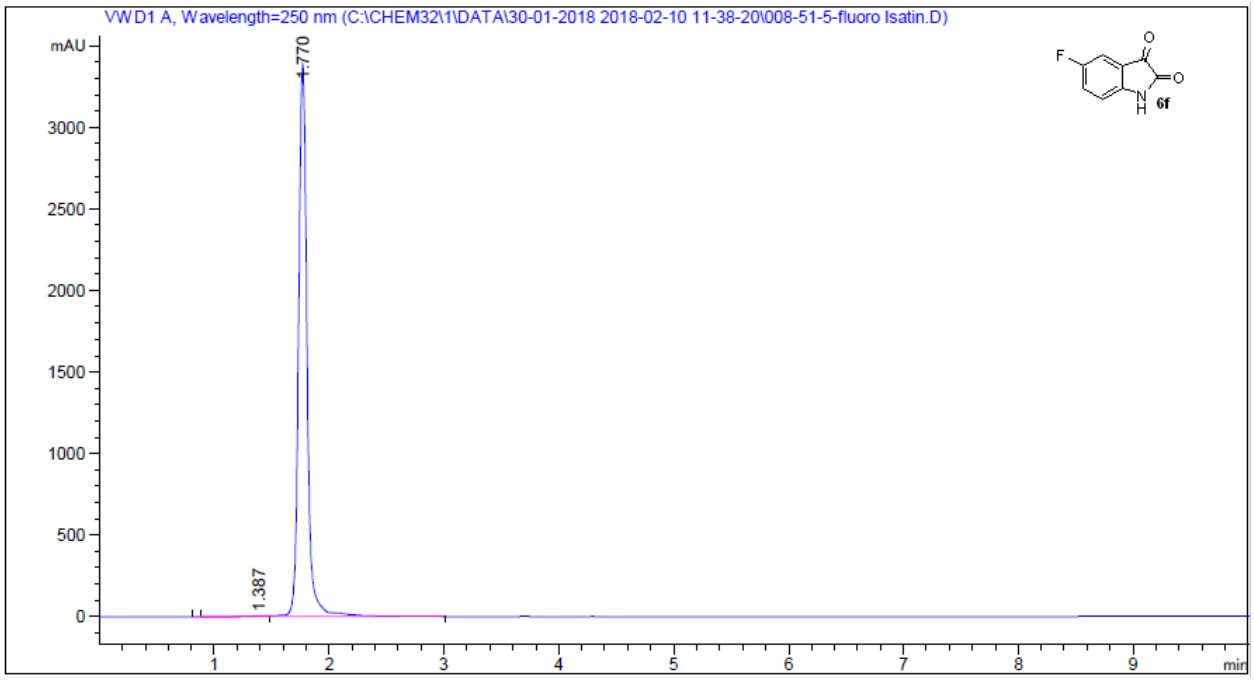
RP-HPLC analysis were carried out on Agilent HPLC (autosampler) on C-18 column using MeOH- H_2O binary solvent (90:10)

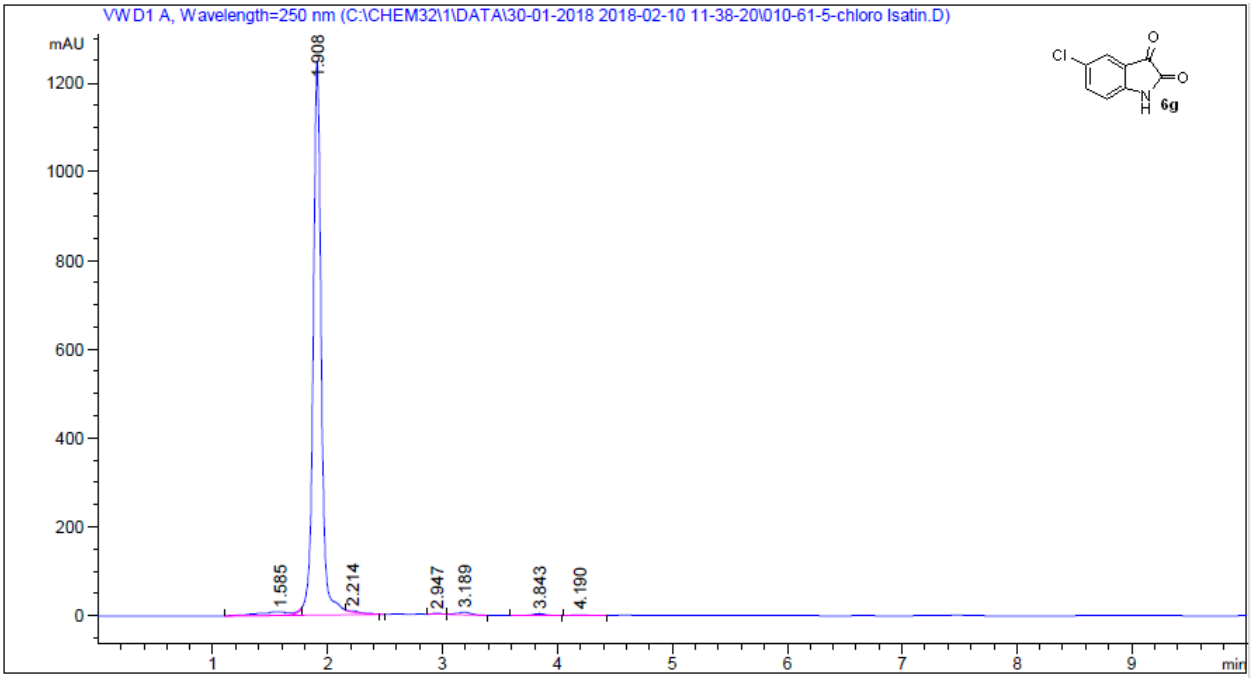

VWD1 A, Wavelength=250 nm (C:\CHEM32\1\DATA\AUG 11 SCREENING 2018-01-29 16-30-52\004-21-N-Me Isatin.D)
mAU
3500
3000
2500
2000
1500
1000
500
0
1.772
2.058
0.5
1
1.5
2
2.5
3
3.5
4
4.5
min
6b
Me

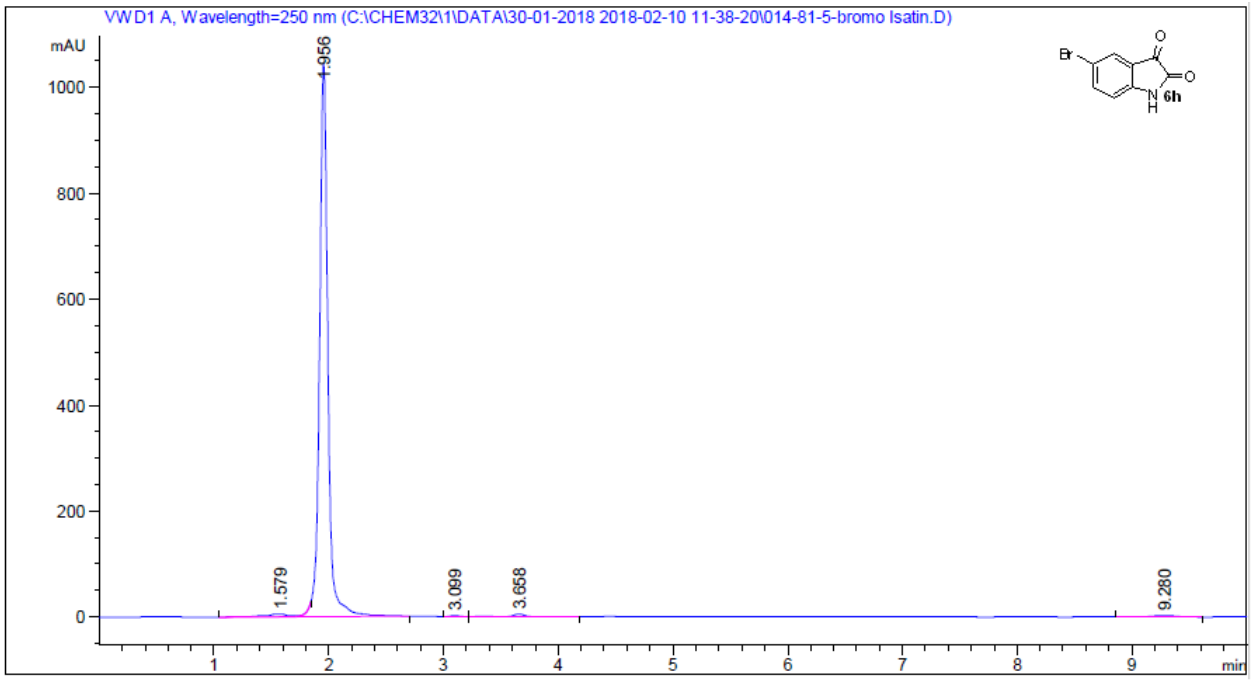

VWD1 A, Wavelength=250 nm (C:\CHEM32\...SCREENING 28-08-2018 2018-08-28 11-01-16\017-81-N-Et Isatin_SM.D)
mAU
3000
2500
2000
1500
1000
500
0
1.837
1.183
2.276
2.450
2.549
1
2
3
4
5
6
7
8
9
min
6c
Et

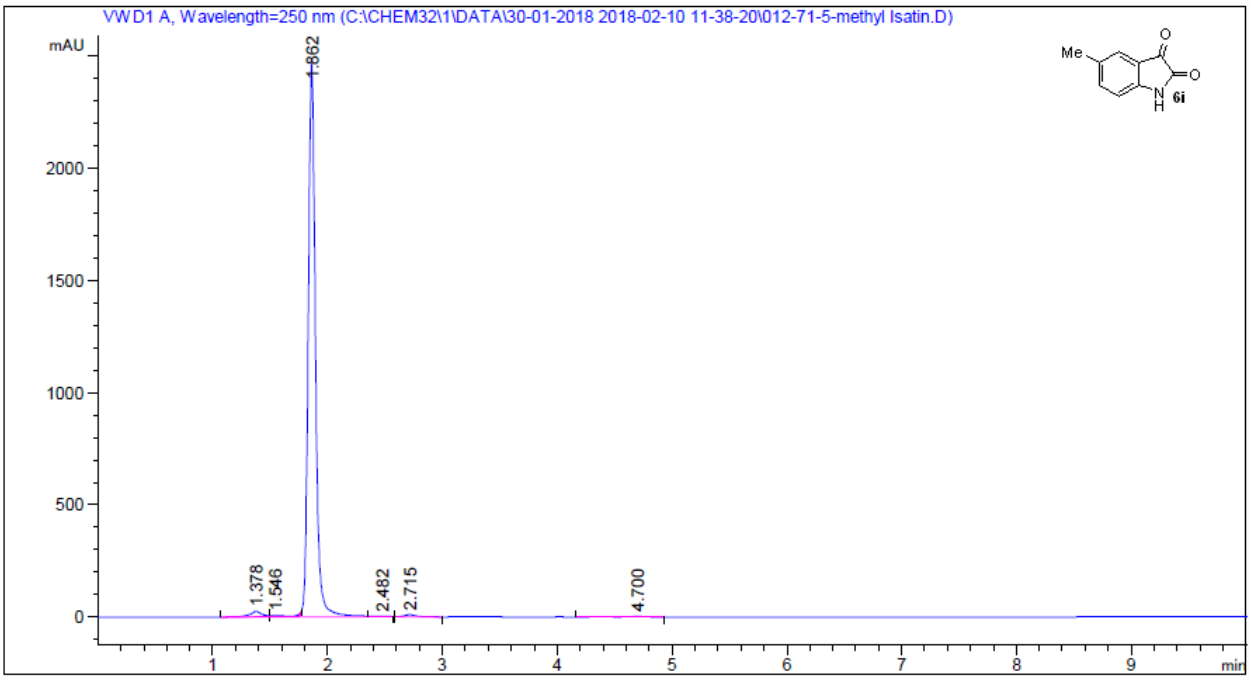

VWD1 A, Wavelength=250 nm (C:\CHEM32\...TA\AUG 11 SCREENING 2018-01-29 16-30-52\012-61-N-benzyl Isatin.D)
mAU
2500
2000
1500
1000
500
0
2.078
1.737
2.608
0.5
1
1.5
2
2.5
3
3.5
4
4.5
min
6d

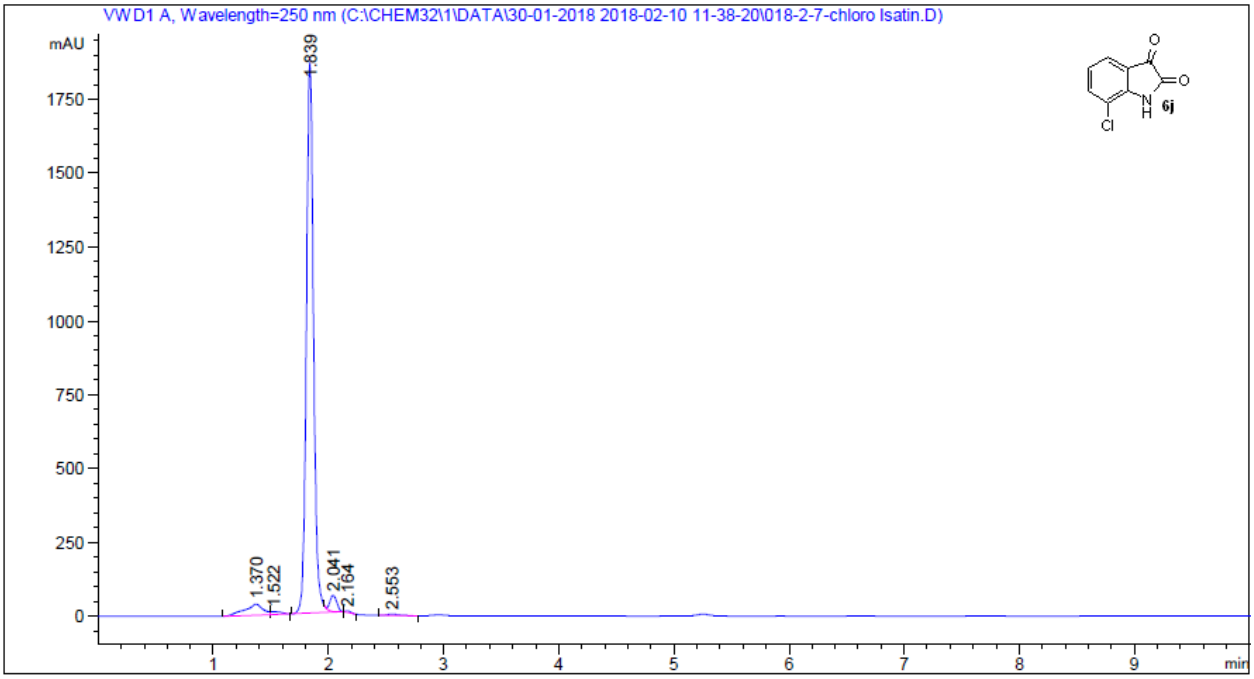

VWD1 A, Wavelength=250 nm (C:\CHEM32\...G 11 SCREENING 2018-01-29 16-30-52\016-81-N-3-Cl benzyl Isatin.D)
mAU
2500
2000
1500
1000
500
0
2.291
1.737
0.5
1
1.5
2
2.5
3
3.5
4
4.5
min
6e
Cl

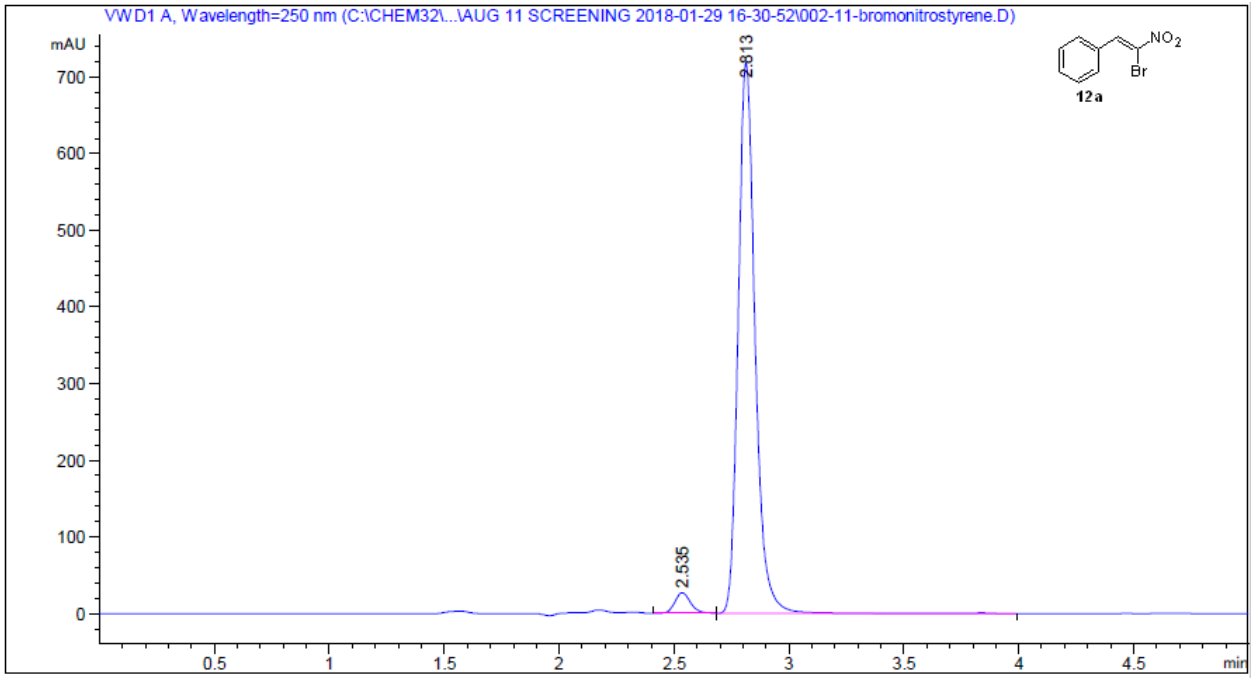

VWD1 A, Wavelength=250 nm (C:\CHEM32\1\DATA\30-01-2018 2018-02-10 11-38-20\008-51-5-fluoro Isatin.D)
mAU
3000
2500
2000
1500
1000
500
0
1.387
1.770
1
2
3
4
5
6
7
8
9
min
F
O
O
N
H
6f

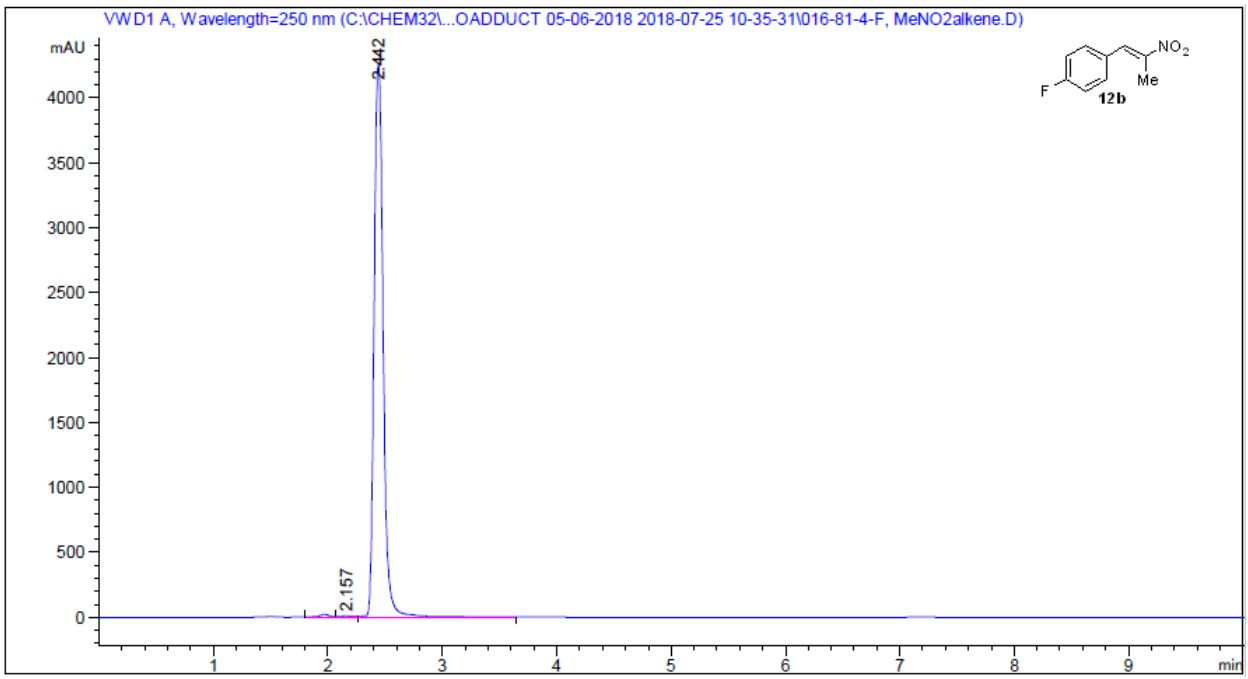

VWD1 A, Wavelength=250 nm (C:\CHEM32\1\DATA\30-01-2018 2018-02-10 11-38-20\010-61-5-chloro Isatin.D)
mAU
1200
1000
800
600
400
200
0
1.585
1.908
2.214
2.947
3.189
3.843
4.190
1
2
3
4
5
6
7
8
9
min
Cl
O
O
N
H
6g

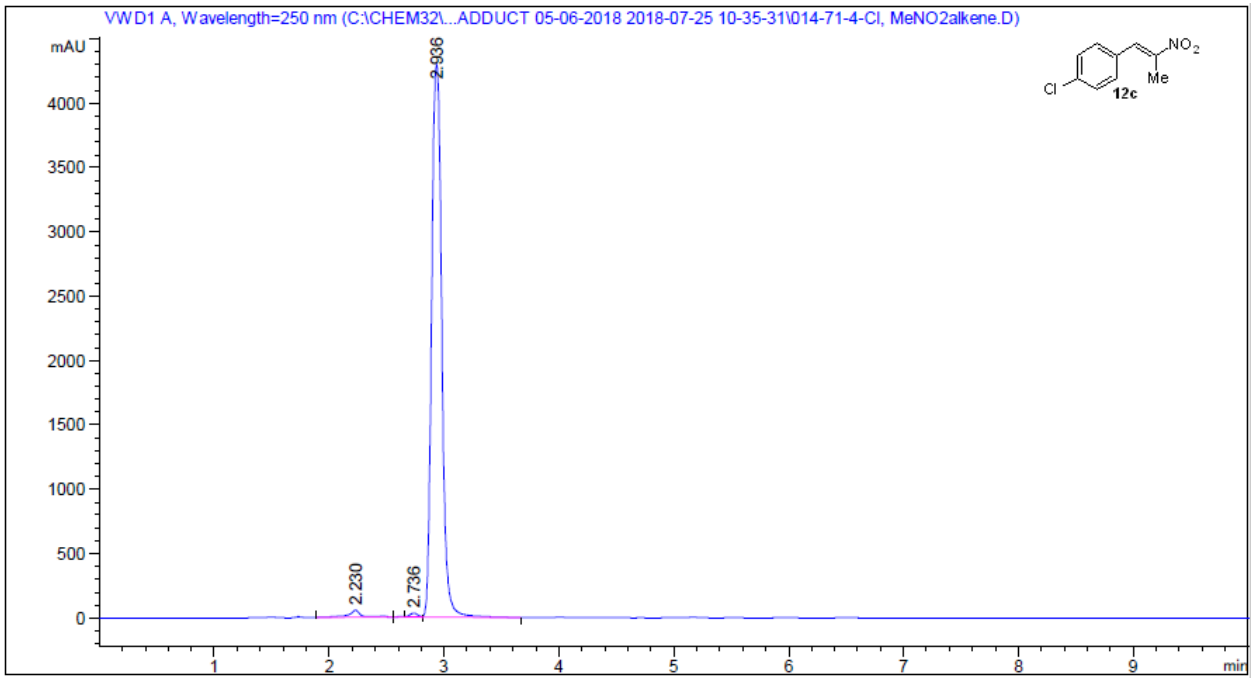

VWD1 A, Wavelength=250 nm (C:\CHEM32\1\DATA\30-01-2018 2018-02-10 11-38-20\014-81-5-bromo Isatin.D)
mAU
1000
800
600
400
200
0
1.579
1.956
3.099
3.658
9.280
1
2
3
4
5
6
7
8
9
min
Br
O
O
N
H
6h

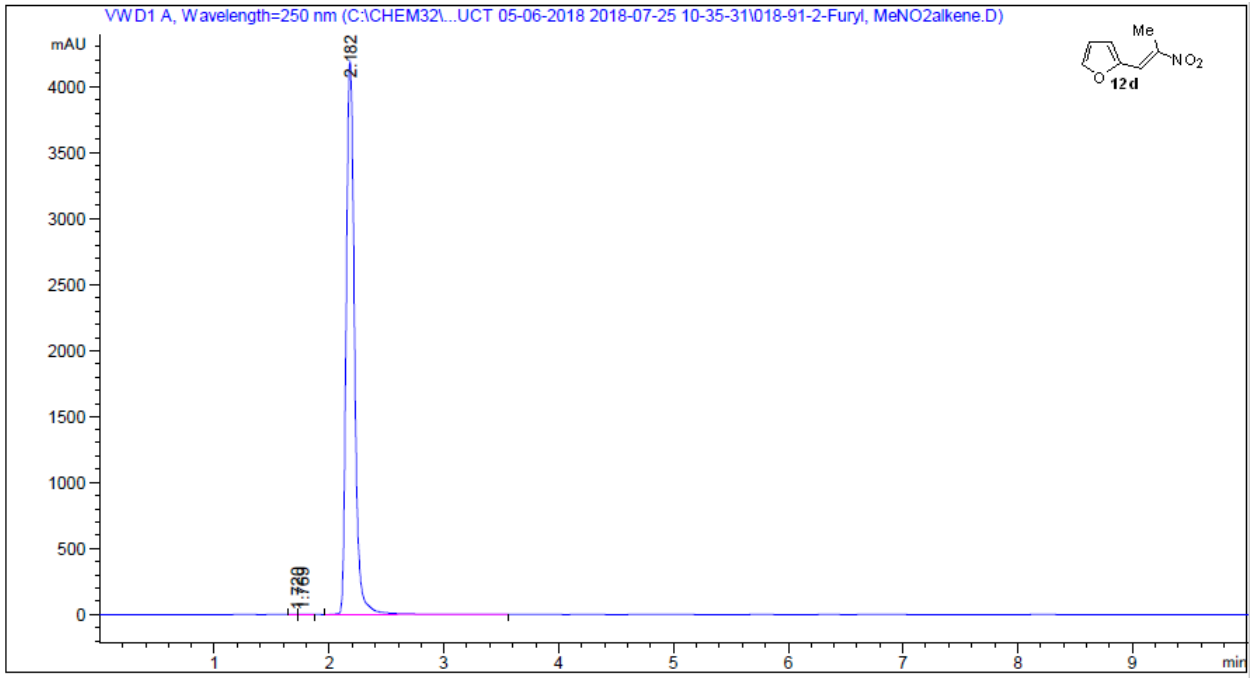

VWD1 A, Wavelength=250 nm (C:\CHEM32\1\DATA\30-01-2018 2018-02-10 11-38-20\012-71-5-methyl Isatin.D)
mAU
2000
1500
1000
500
0
1.378
1.546
1.862
2.482
2.715
4.700
1
2
3
4
5
6
7
8
9
min
Me
O
O
N
H
6i

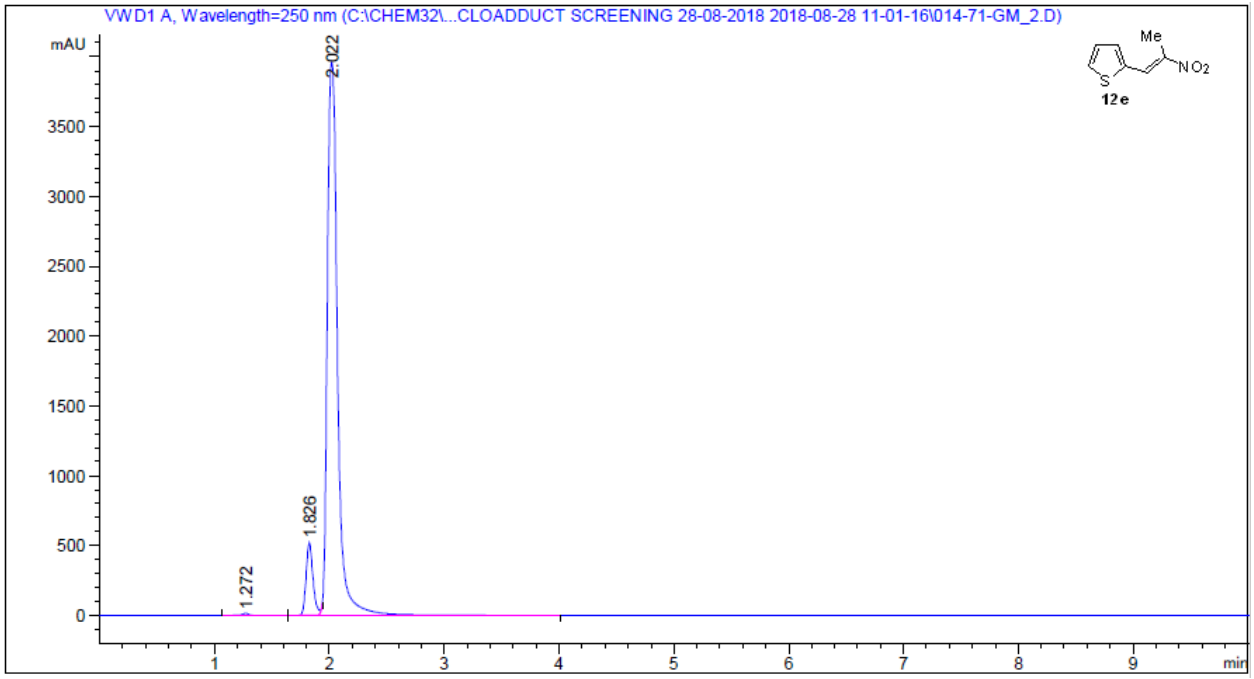

VWD1 A, Wavelength=250 nm (C:\CHEM32\1\DATA\30-01-2018 2018-02-10 11-38-20\018-2-7-chloro Isatin.D)
mAU
1.839
1.370
1.522
2.041
2.164
2.553
min
6j

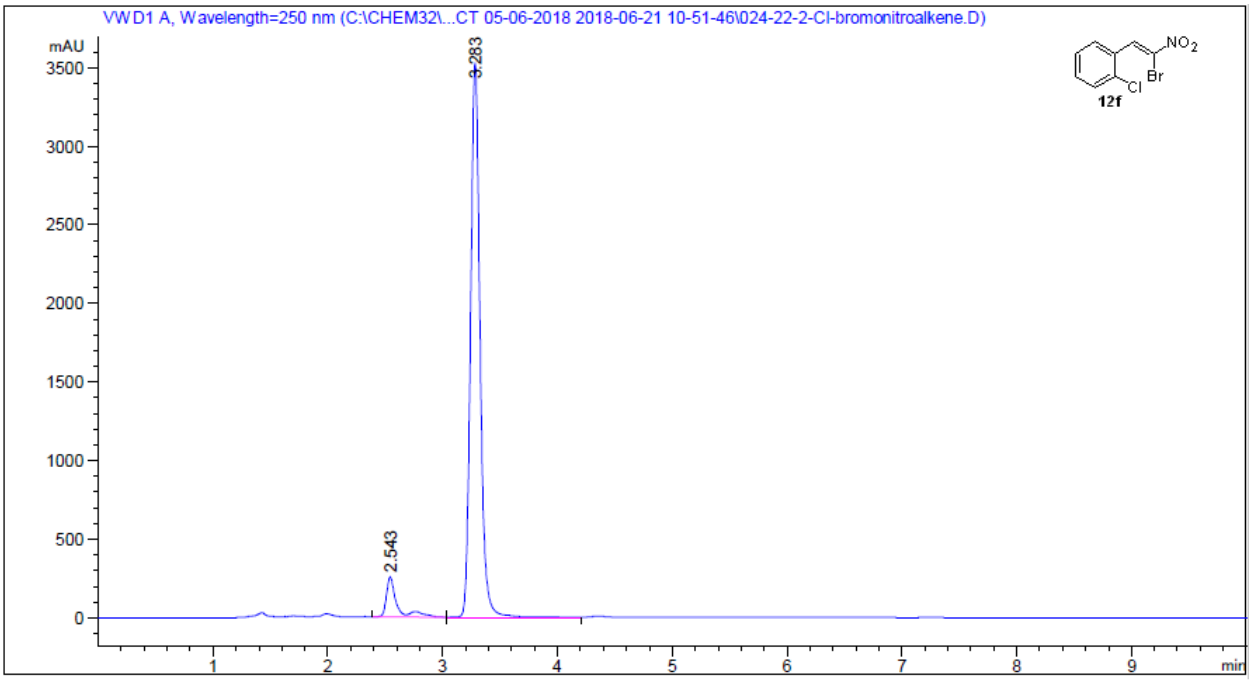

VWD1 A, Wavelength=250 nm (C:\CHEM32\...\AUG 11 SCREENING 2018-01-29 16-30-52\002-11-bromonitrostyrene.D)
mAU
2.813
2.535
min
12a

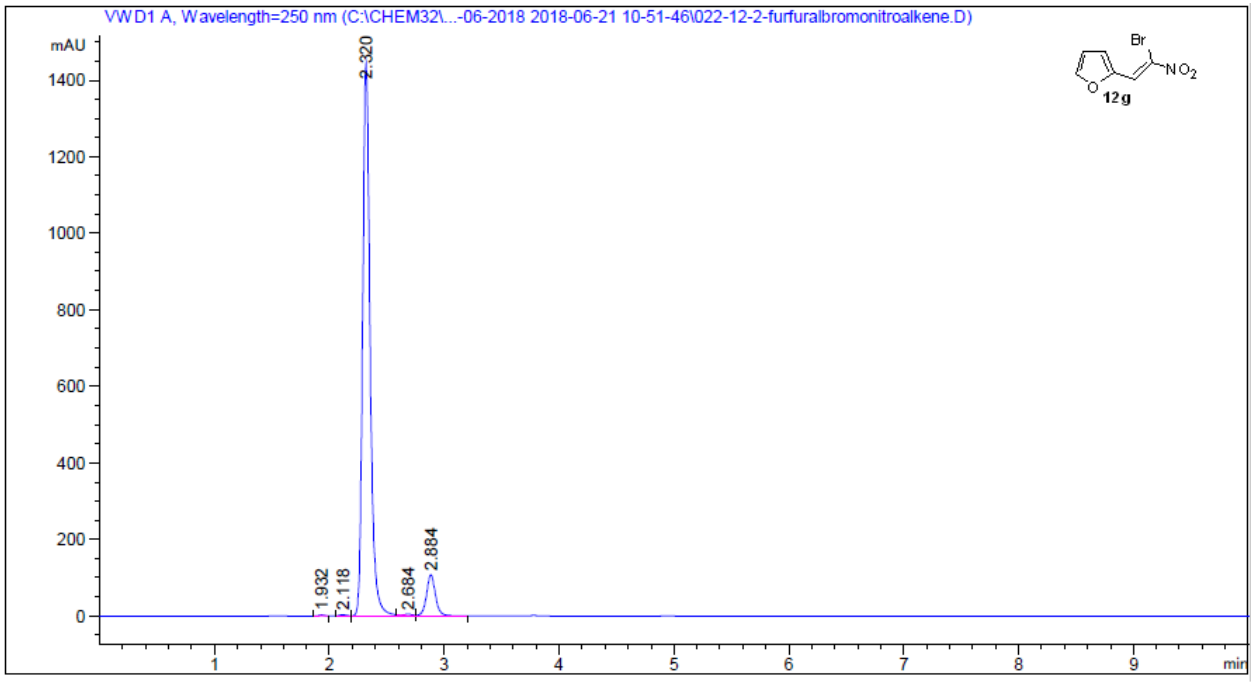

VWD1 A, Wavelength=250 nm (C:\CHEM32\...OADDUCT 05-06-2018 2018-07-25 10-35-31\016-81-4-F, MeNO2alkene.D)
mAU
2.442
2.157
NO2
Me
F
12b
min

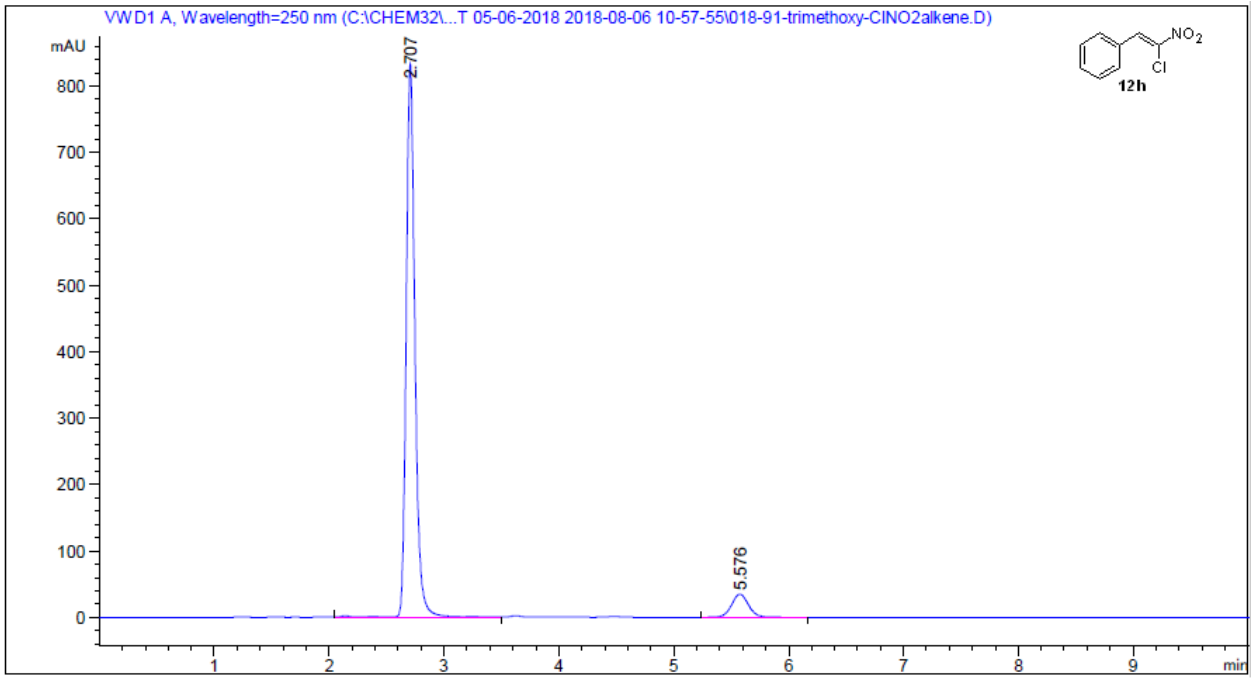

VWD1 A, Wavelength=250 nm (C:\CHEM32\...ADDUCT 05-06-2018 2018-07-25 10-35-31\014-71-4-Cl, MeNO2alkene.D)
mAU
2.936
2.230
2.736
NO2
Me
Cl
12c
min

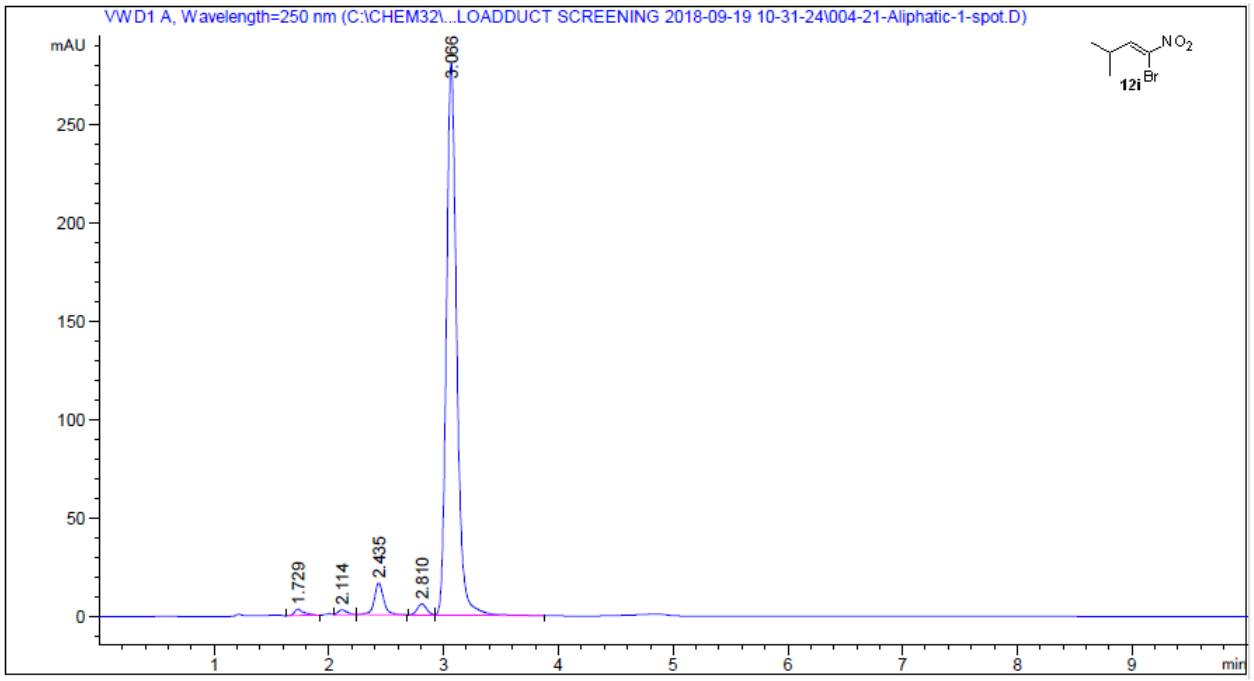

VWD1 A, Wavelength=250 nm (C:\CHEM32\...UCT 05-06-2018 2018-07-25 10-35-31\018-91-2-Furyl, MeNO2alkene.D)
mAU
4000
3500
3000
2500
2000
1500
1000
500
0
2.182
1.769
1.739
1
2
3
4
5
6
7
8
9
min
Me
NO2
O
12d


VWD1 A, Wavelength=250 nm (C:\CHEM32\...CLOADDUCT SCREENING 28-08-2018 2018-08-28 11-01-16\014-71-GM_2.D)
mAU
3500
3000
2500
2000
1500
1000
500
0
2.022
1.826
1.272
1
2
3
4
5
6
7
8
9
min
Me
NO2
S
12e


VWD1 A, Wavelength=250 nm (C:\CHEM32\...CT 05-06-2018 2018-06-21 10-51-46\024-22-2-Cl-bromonitroalkene.D)
mAU
3500
3000
2500
2000
1500
1000
500
0
2.543
3.283
1
2
3
4
5
6
7
8
9
min
NO2
Br
Cl
12f

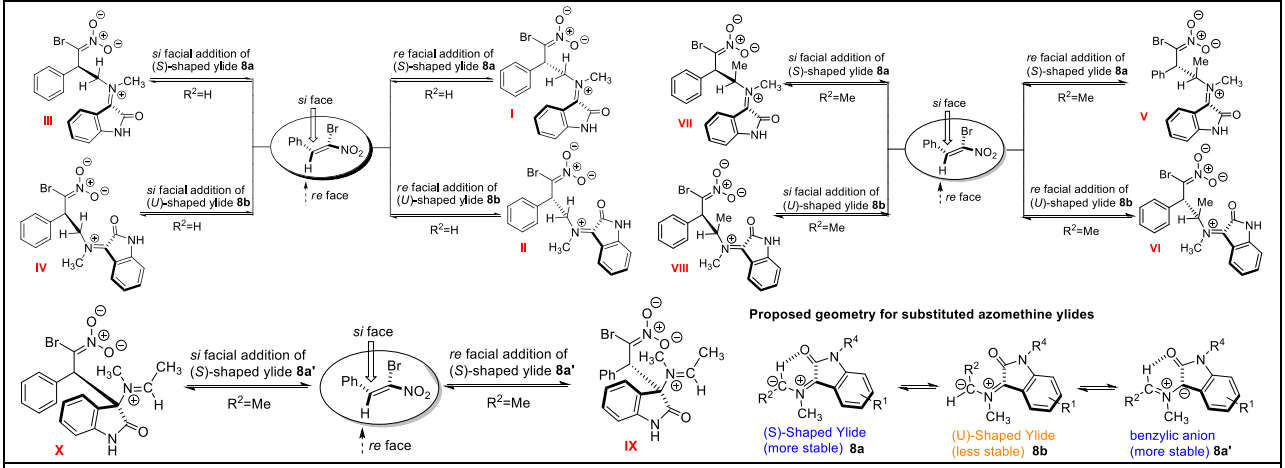

VWD1 A, Wavelength=250 nm (C:\CHEM32\...-06-2018 2018-06-21 10-51-46\022-12-2-furfuralbromonitroalkene.D)
mAU
1400
1200
1000
800
600
400
200
0
1.932
2.118
2.320
2.684
2.884
1
2
3
4
5
6
7
8
9
min
Br
NO2
O
12g


VWD1 A, Wavelength=250 nm (C:\CHEM32\...T 05-06-2018 2018-08-06 10-57-55\018-91-trimethoxy-ClNO2alkene.D)
mAU
2.707
5.576
min
12h

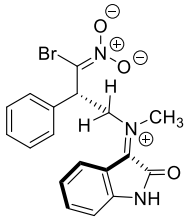
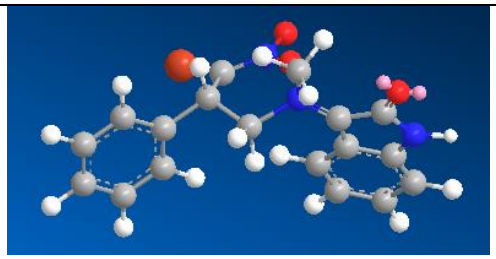
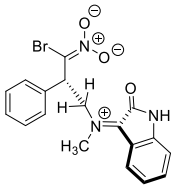
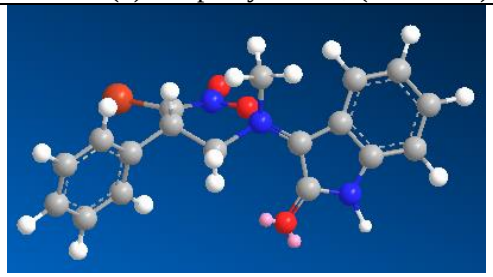

VWD1 A, Wavelength=250 nm (C:\CHEM32\...LOADDUCT SCREENING 2018-09-19 10-31-24\004-21-Aliphatic-1-spot.D)
mAU
1.729
2.114
2.435
2.810
3.066
min
12i

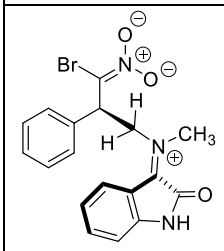
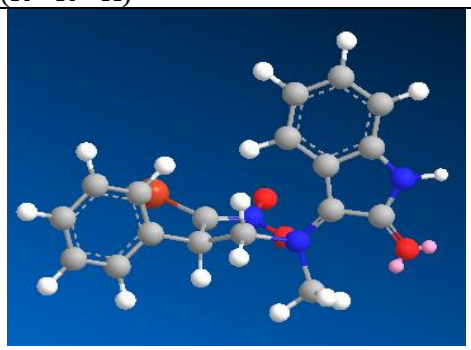
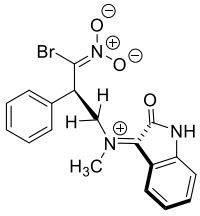
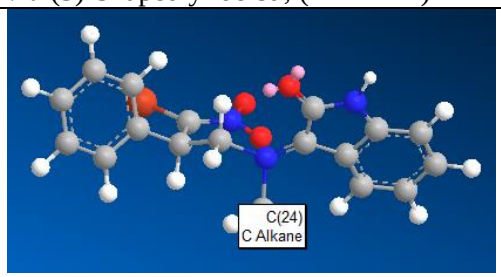
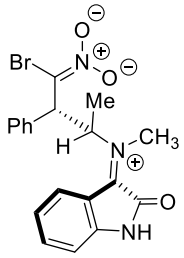
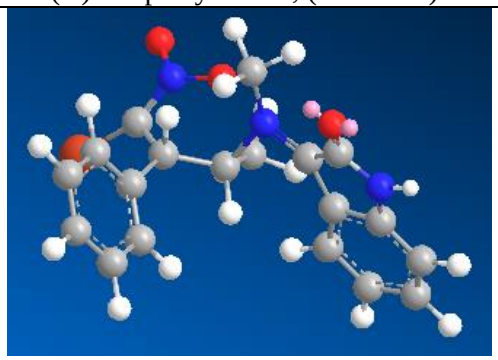
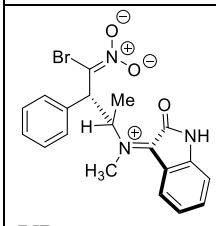
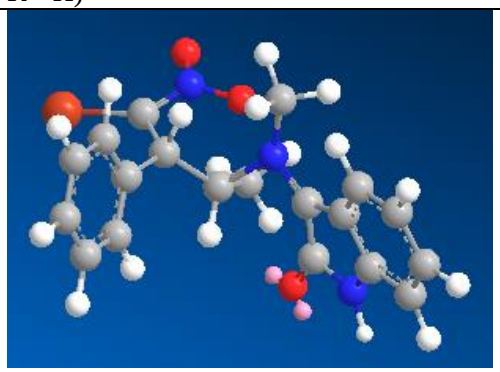
VIII. Chem3D GS Single point MM2 Calculations on the Intemediate Structures

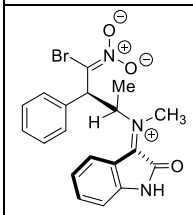
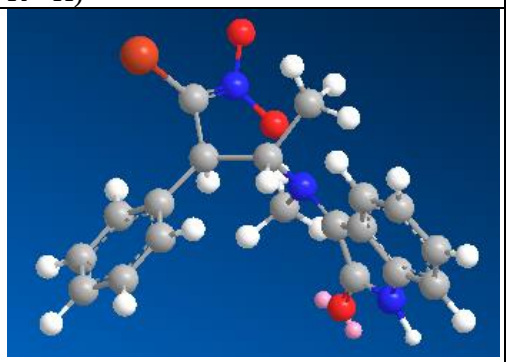
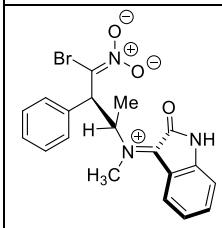
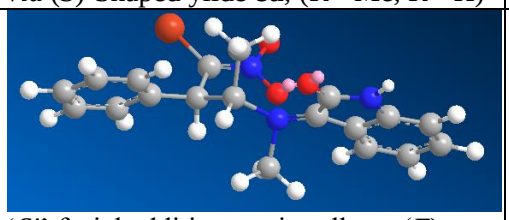
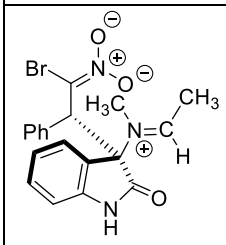
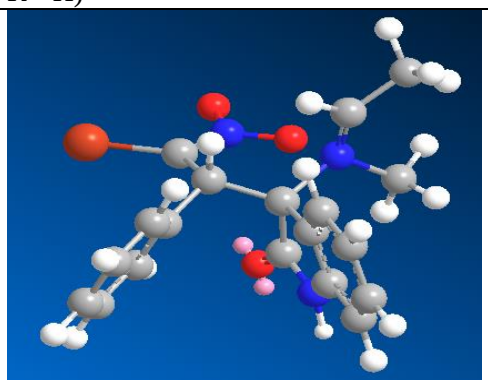
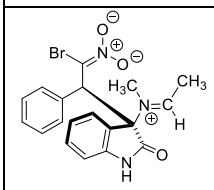
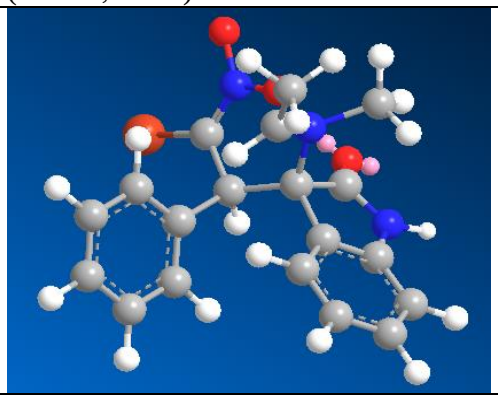
Chem3D GS Single point MM2 Calculations on the Intemediate Structures
(stepwise mechanism, presumably of highest occupied molecular orbital of the iminium)



Although the total energy of these conformations do not actually reflects the reaction pathway nor the energy of the transition states, it provides an input on ground state energies of these intermediates. As far as the intermediates **I-IV** are concerned, it is apparent that the nitronate resulted from '*re*' facial or '*si*' facial additions of (*S*)-shaped ylide **8a** has relatively lower energies compared to (*U*)-shaped ylide **8b**. More importantly, the corresponding energies of intermediates **V-VIII** of either (*S*)-shaped ylide **8a** or (*U*)-shaped ylide **8b** resulted from addition of azo-methine ylide of *α*-methyl glycine has resulted in higher energy structures. This leads to speculation that azo-methine ylide of *α*-methyl glycine adds *via* carbanion **8a'** to '*re*' facial 1-bromo-nitrostyrene to result in opposite regioisomer. Grossly these energy values agree with the stereochemical outcome with regard to regioselectivity of the reaction (R^2=H, Me).

Intermediate Structure	Chem3D GS Single point MM2 minimized structures	Torsion	Non-1,4 VDW	1,4 VDW	Total Energy
		(KCal/mol)			
 I	 '*Re*' facial addition to nitroalkene (*E*)-**12a** *via* (*S*)-Shaped ylide **8a**; (R^2=R^4=H)	-6.0915	100.8209	17.4190	-337.0586
 **II**	 '*Re*' facial addition to nitroalkene (*E*)-	-6.2391	102.9775	17.0651	-335.3876

	12a *via* (*U*)-Shaped ylide **8b**; (R^2=R^4=H)				
 **III**	 '*Si*' facial addition to nitroalkene (*E*)-**12a** *via* (*S*)-Shaped ylide **8a**; (R^2=R^4=H)	-6.0869	100.8038	17.4193	-337.0585
 **IV**	 '*Si*' facial addition to nitroalkene (*E*)-**12a** *via* (*U*)-Shaped ylide **8b**; (R^2=R^4=H)	-6.1971	102.9784	17.0564	-335.3889
 **V**	 '*Re*' facial addition to nitroalkene (*E*)-**12a** *via* (*S*)-Shaped ylide **8a**; (R^2=Me, R^4=H)	4.2126	73.2864	28.2502	-209.6299
 **VI**	 *'Re*' facial addition to nitroalkene (*E*)-	1.1283	72.6976	26.9846	-202.7997

	12a *via* (*U*)-Shaped ylide **8b**; (R^2=Me, R^4=H)				
 **VII**	 '*Si*' facial addition to nitroalkene (*E*)-**12a** *via* (*S*)-Shaped ylide **8a**; (R^2=Me, R^4=H)	2.5241	73.1824	25.9114	-205.2397
 **VIII**	 '*Si*' facial addition to nitroalkene (*E*)-**12a** *via* (*U*)-Shaped ylide **8b**; (R^2=Me, R^4=H)	2.0156	104.5159	18.5822	-321.8889
 **IX**	 *'Re'* facial addition to nitroalkene (*E*)-**12a** *via* (*S*)-Shaped benzylic anion **8a'**; (R^2=Me, R^4=H)	-5.5806	100.8601	17.0326	-328.6635
 **X**		-5.1472	101.3293	17.4431	-325.7844

	'Si' facial addition to nitroalkene (*E*)-**12a** *via* (*S*)-Shaped benzylic anion **8a'**; (R^2=Me, R^4=H)				