Supporting information

Facile construction of novel imidazolidine-spirooxindoles via diastereoselective cycloaddition of *N*-acylhydrazine-derived imines with 3-isothiocyanato oxindoles

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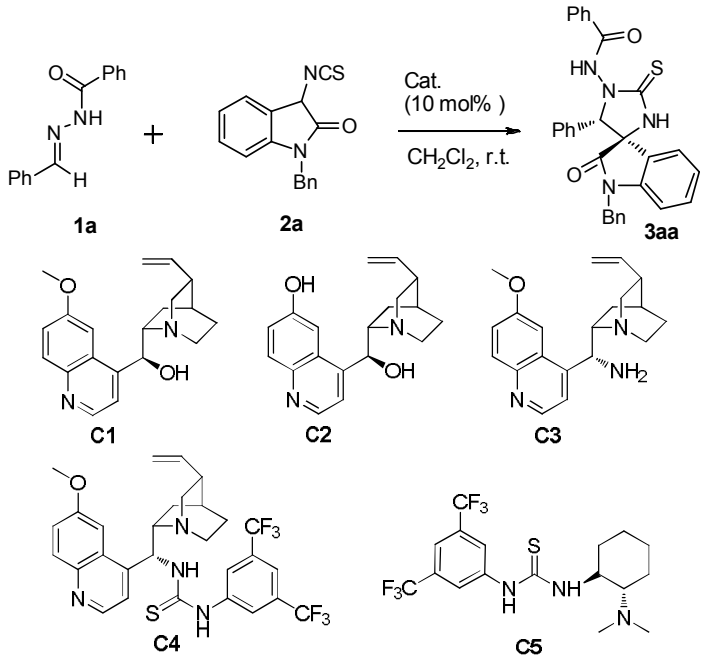
General information

Unless noted otherwise, all reagents were commercially available and used without further purification. All solvents were distilled from the appropriate drying agents immediately before use. All air and moisture sensitive reactions were carried out under an inert atmosphere of dry nitrogen. Reactions were monitored by TLC carried out on 0.25 mm SDS silica gel coated glass plates (60F254) and compounds were detected with UV light and/or with iodide. Specific optical rotations were measured with a polarimeter. NMR spectra were recorded on 400 MHz instrument and calibrated using tetramethylsilane (TMS) as internal reference. High resolution mass spectra (HRMS) were recorded under electrospray ionization (ESI) conditions. Enantiomeric excess was determined by HPLC analyses using Chiralpak AD (25 cm × 0.46 cm) column.(solvent: hexane/ethanol = 70/30).

Typical procedure for organocatalytic synthesis of imidazolidine-spirooxindole 3aa

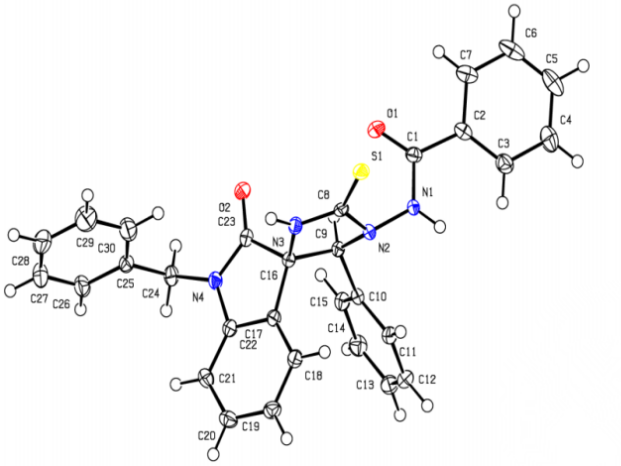


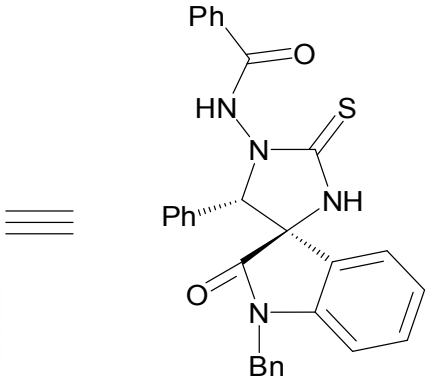
Catalyst (0.01 mmol) was added to a mixture of *N*-acylhadrazine-based imines **1a** (0.1 mmol) and 3-isothiocyanato oxindole **2a** (0.1 mmol) in anhydrous CH_2Cl_2 (1.0 mL). The reaction mixture was stirred at room temperature for 2 h. After completion of the reaction, the crude product was purified by flash column chromatography on silica gel (petroleum ether / ethyl acetate = 4:1) to afford the pure product **3aa** as white powder (64-74% yield; >99:1 dr).

Entry	Catalyst	Time (min)	Yield (%) [b]	ee (%)[c]	dr[d]
1	**C1**	120	68	0	>99:1
2	**C2**	120	64	0	>99:1
3	**C3**	120	69	0	>99:1
4	**C4**	120	74	0	>99:1
5	**C5**	120	70	0	>99:1

[a] Reactions were carried out with 0.1 mmol of **1a**, and 0.1 mmol of **2a** in the presence of 10 mol% of catalyst in 1.0 mL of CH_2Cl_2 examined at room temperature. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] Determined by ^{1}H NMR spectroscopy.

X-Ray crystal data of comopound 3aa



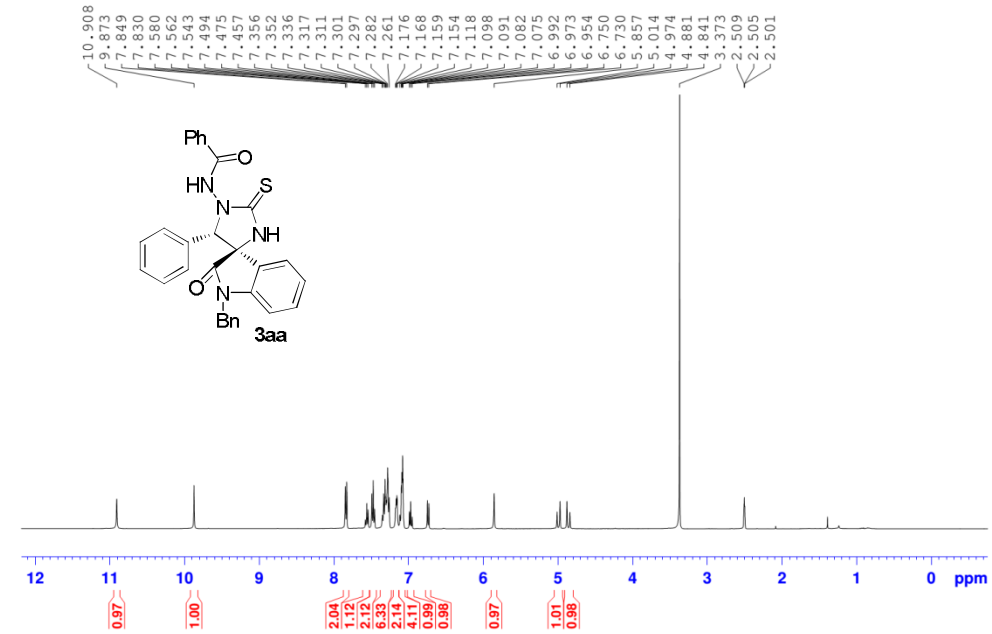


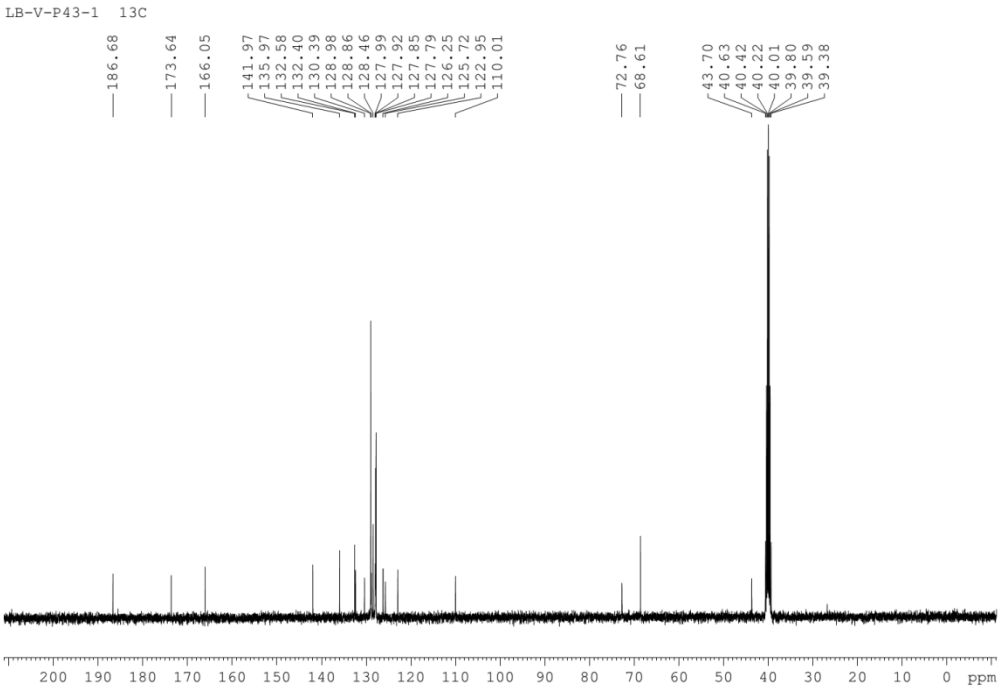
3aa

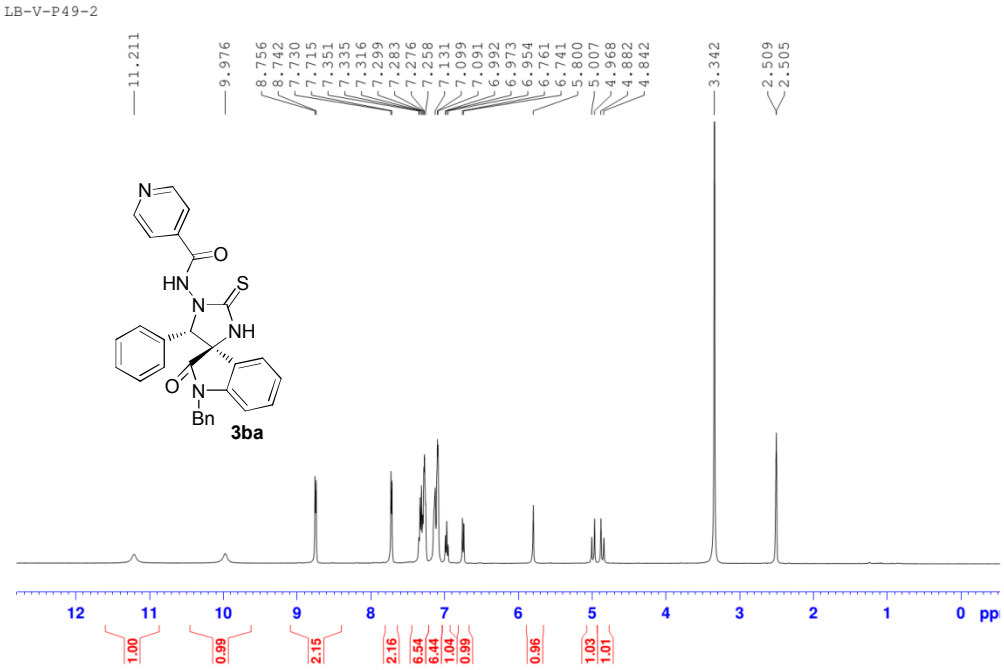
Identification code	**3aa**
Empirical formula	$C_{30}H_{24}N_4O_2S$
Formula weight	504.16
Temperature	113(2) K
Wavelength	0.71073 A
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 9.9840(13) A alpha = 117.420(7) deg. b = 12.9333(14) A beta = 99.869(13) deg. c = 13.6529(18) A gamma = 96.128(10) deg.
Volume	1506.6(3) A^3
Z, Calculated density	2, 1.307 Mg/m^3
Absorption coefficient	0.153 mm^-1
F(000)	624
Crystal size	0.20 x 0.18 x 0.12 mm
Theta range for data collection	3.03 to 27.55 deg.
Limiting indices	-12<=h<=12, -15<=k<=16, -17<=l<=17

Reflections collected / unique	15520 / 6658 [R(int) = 0.0164]
Completeness to theta = 27.55	96.00%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9819 and 0.9701
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6658 / 2 / 396
Goodness-of-fit on F^2	1.033
Final R indices [I>2sigma(I)]	R1 = 0.0326, wR2 = 0.0828
R indices (all data)	R1 = 0.0386, wR2 = 0.0864
Largest diff. peak and hole	0.325 and -0.213 e.A^-3

Copies of ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra for imidazolidine-spirooxindoles (3)



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7.258
7.131
7.099
7.091
6.992
6.973
6.954
6.761
6.741
5.800
5.007
4.968
4.882
4.842
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2.505
N
O
HN
S
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O
N
Bn
3ba
12
11
10
9
8
7
6
5
4
3
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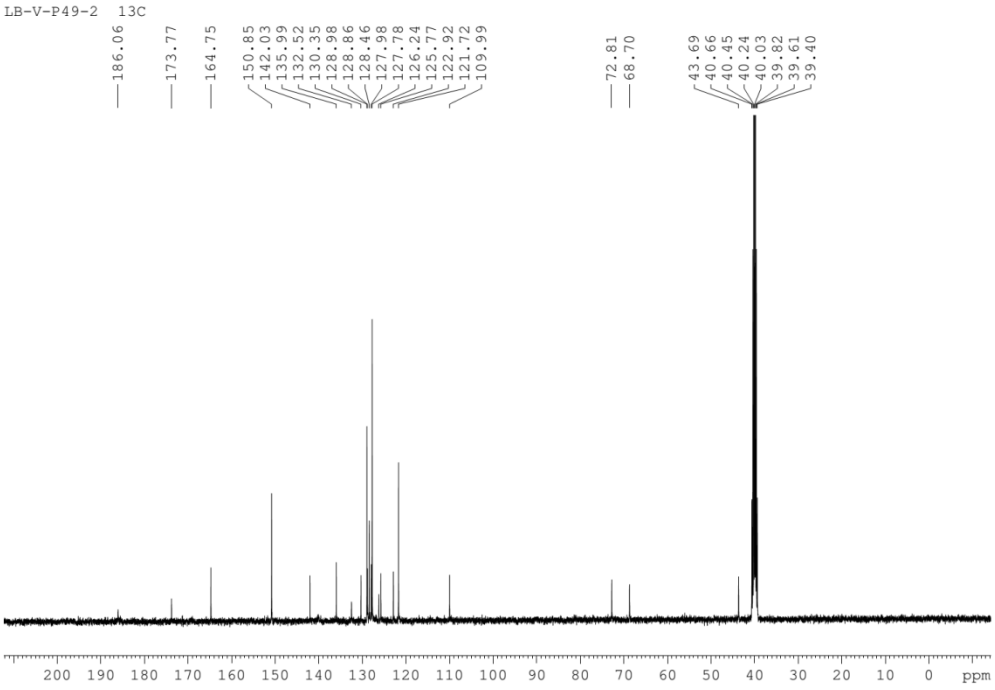
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128.46
127.98
127.78
126.24
125.77
122.92
121.72
109.99
72.81
68.70
43.69
40.66
40.45
40.24
40.03
39.82
39.61
39.40
200
190
180
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160
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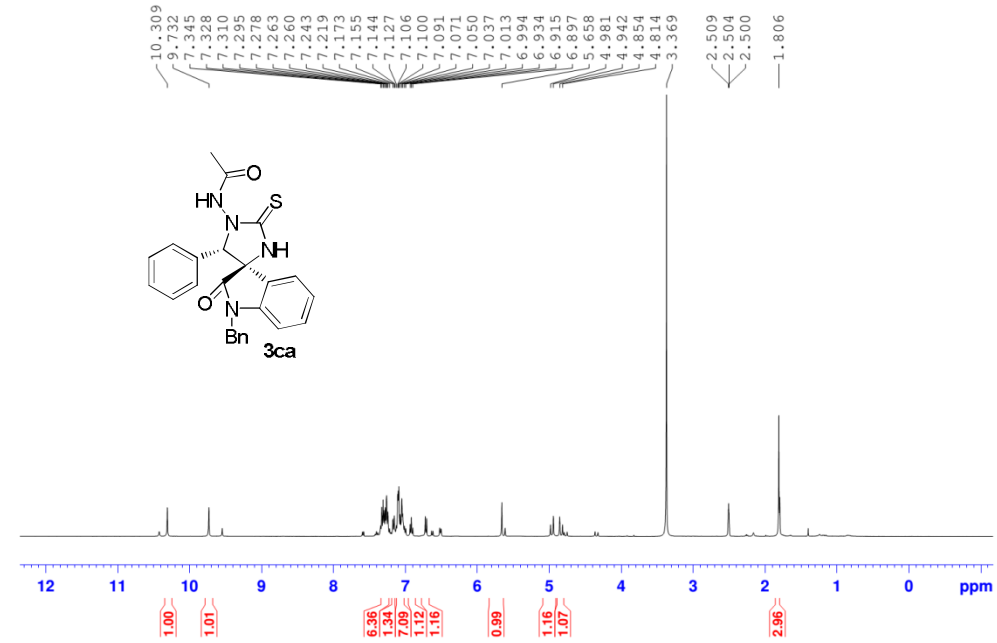
ppm

LB-V-P49-3



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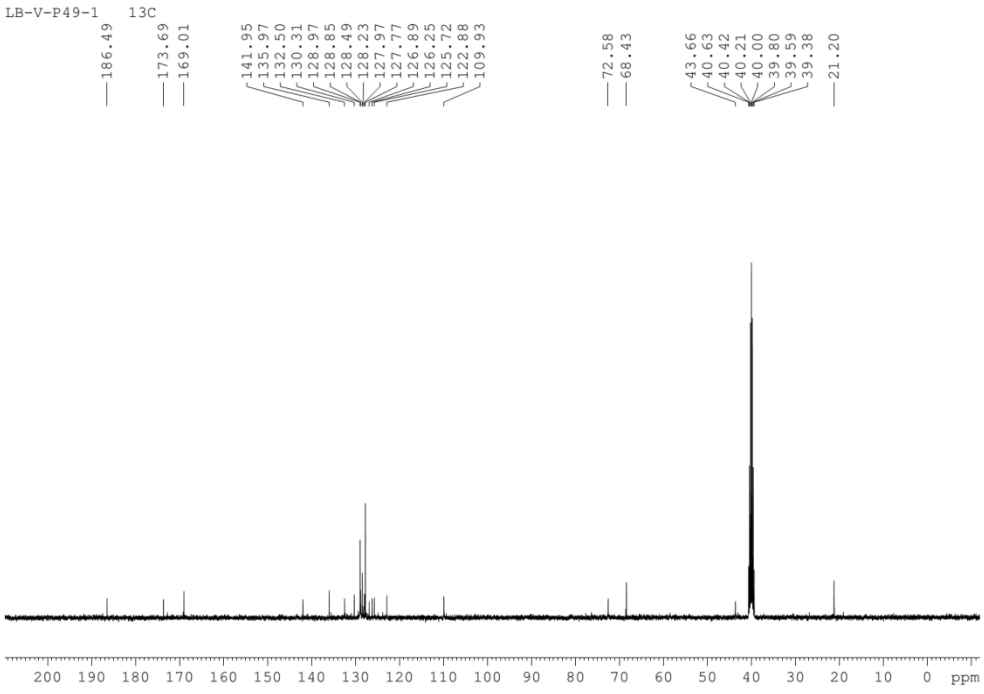

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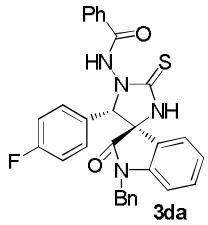
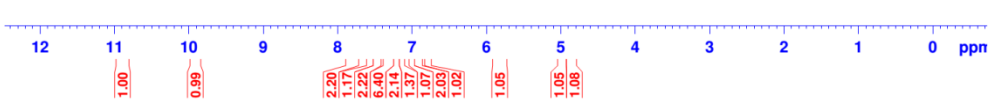


3da



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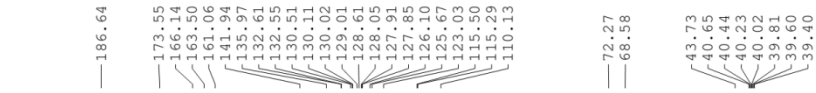
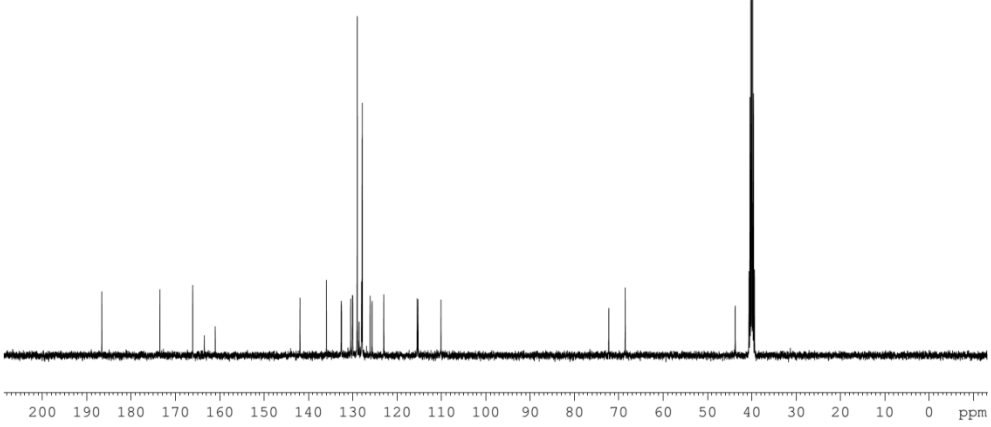
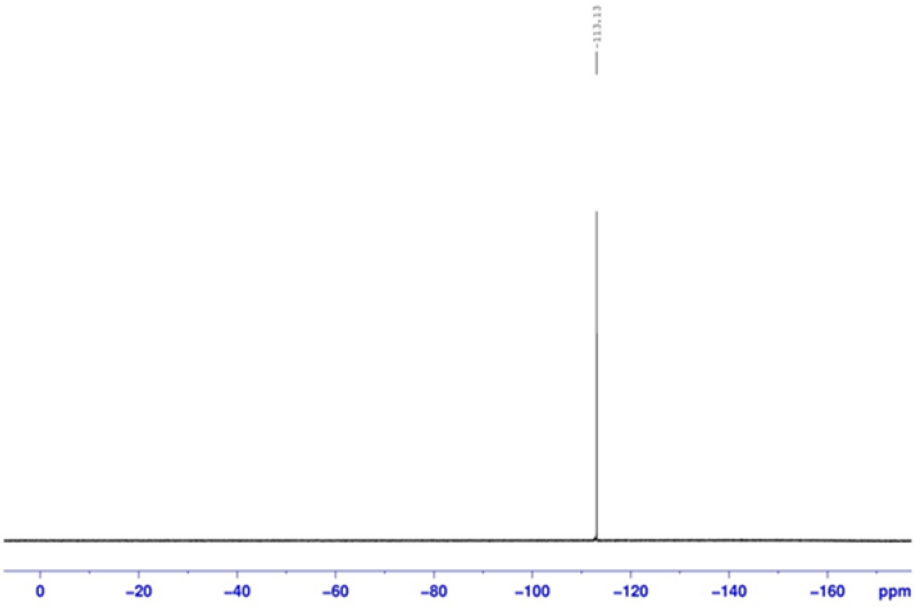
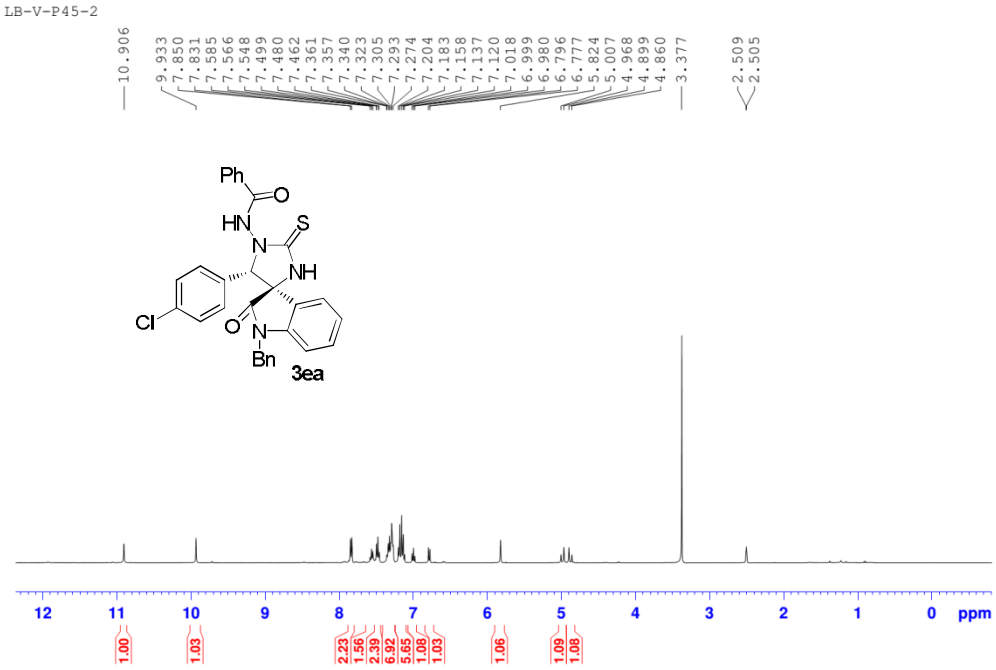




^{19}F NMR

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7.462
7.361
7.357
7.340
7.323
7.305
7.293
7.274
7.204
7.183
7.158
7.137
7.120
7.018
6.999
6.980
6.796
6.777
5.824
5.007
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4.899
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3.377
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2.505
Ph
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HN
S
N
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Cl
O
N
Bn
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11
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9
8
7
6
5
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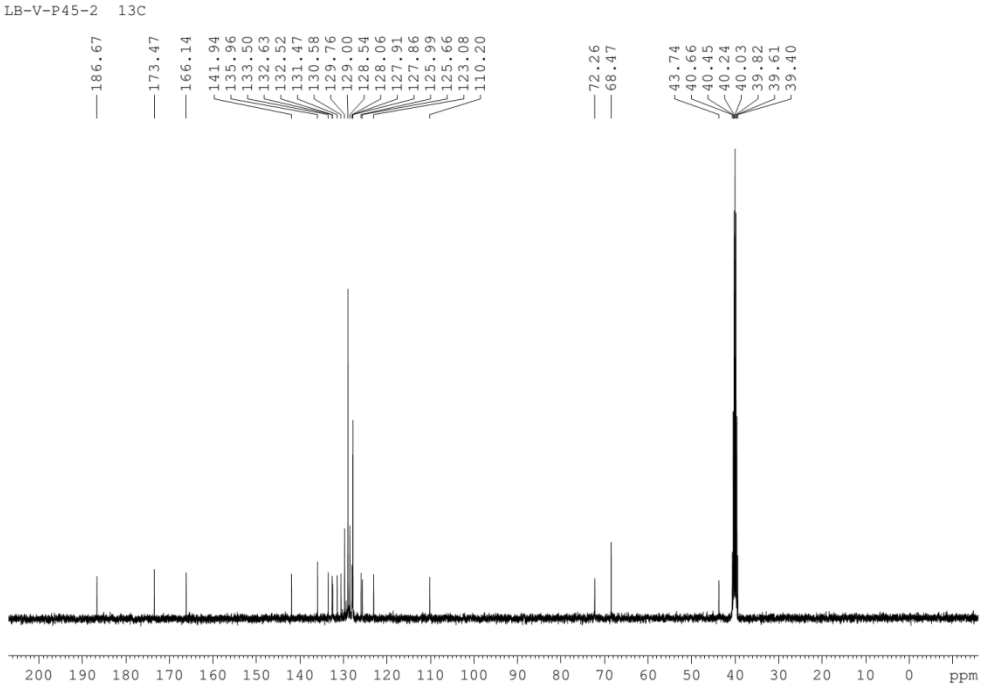
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141.94
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132.52
131.47
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129.00
128.54
128.06
127.91
127.86
125.99
125.66
123.08
110.20
72.26
68.47
43.74
40.66
40.45
40.24
40.03
39.82
39.61
39.40
200
190
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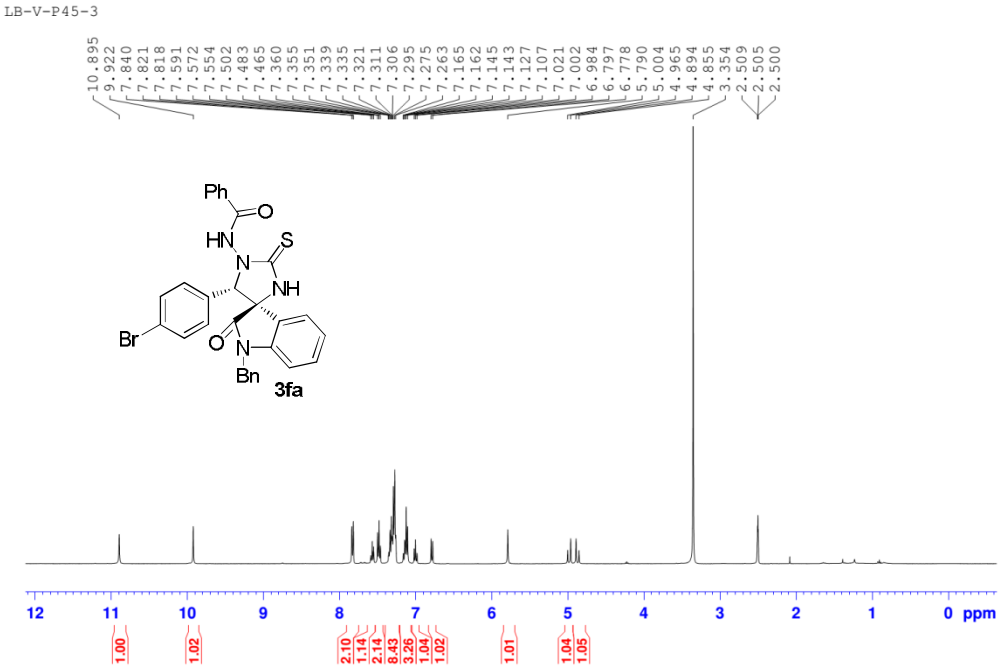
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7.465
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7.351
7.339
7.335
7.321
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7.306
7.295
7.275
7.263
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7.162
7.145
7.143
7.127
7.107
7.021
7.002
6.984
6.797
6.778
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5.004
4.965
4.894
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2.505
2.500
Ph
O
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N
S
NH
Br
O
N
Bn
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11
10
9
8
7
6
5
4
3
2
1
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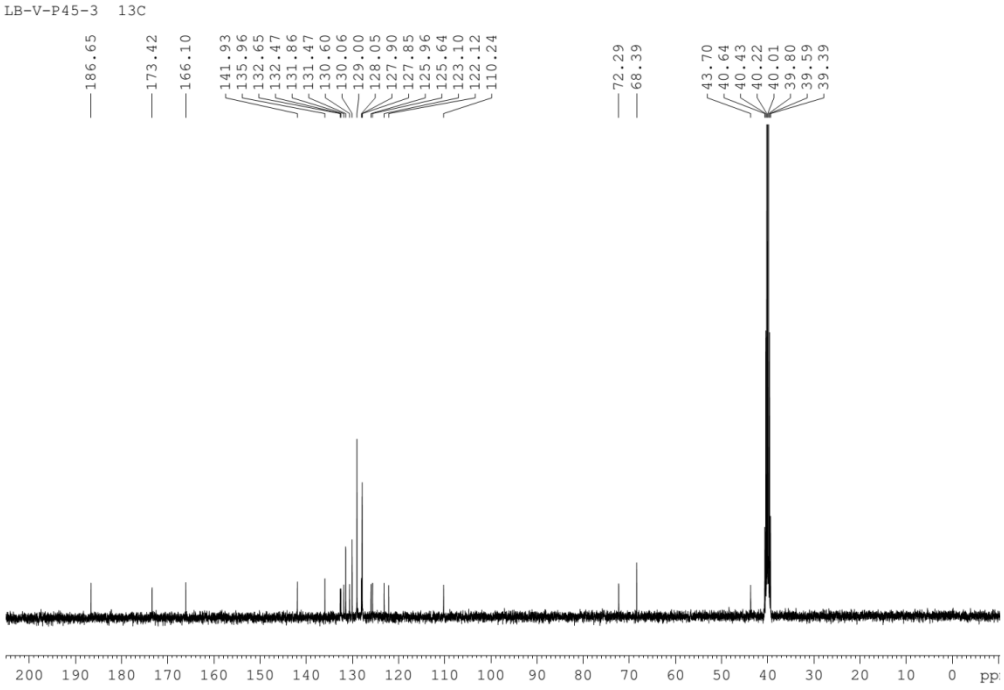
1.04
1.05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129.00
128.05
127.90
127.85
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125.64
123.10
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39.39
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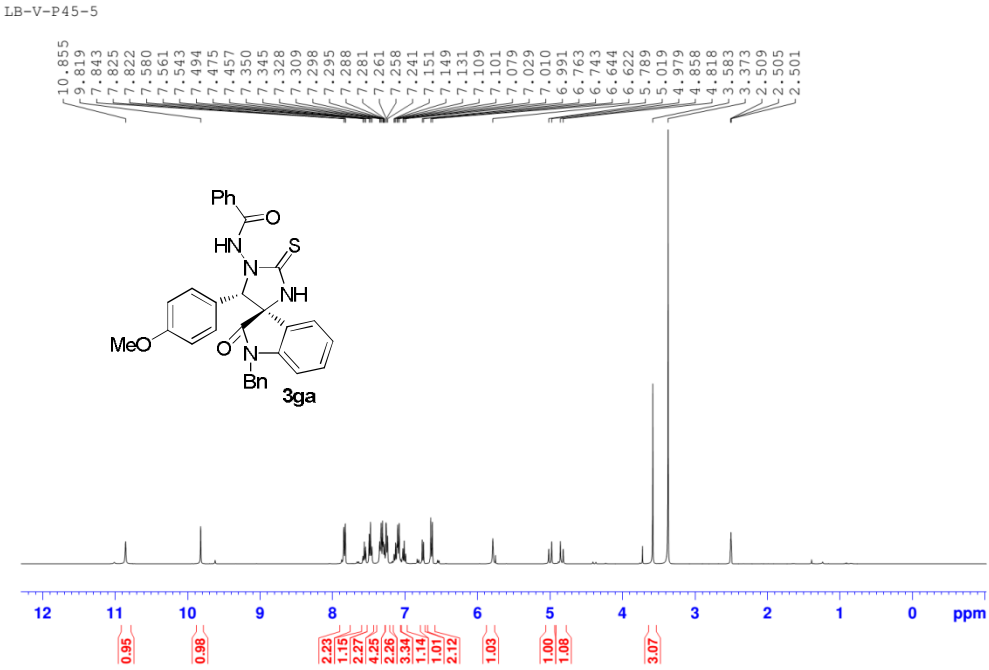
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7.350
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7.295
7.288
7.281
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7.151
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7.101
7.079
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4.818
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2.501
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Bn
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9
8
7
6
5
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3
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ppm
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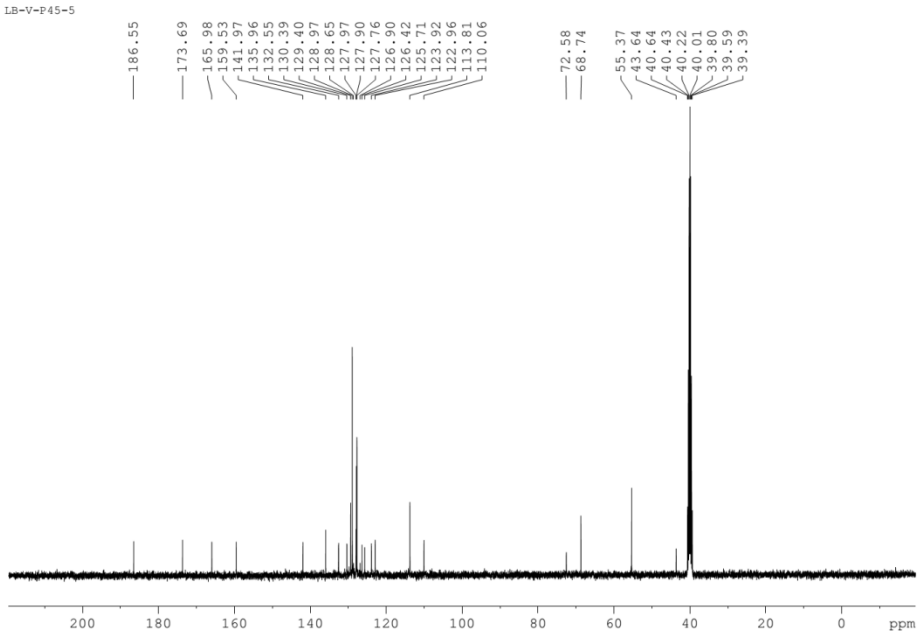
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173.69
165.98
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141.97
135.96
132.55
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128.65
127.97
127.90
127.76
126.90
126.42
125.71
123.92
122.96
113.81
110.06
72.58
68.74
55.37
43.64
40.64
40.43
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60
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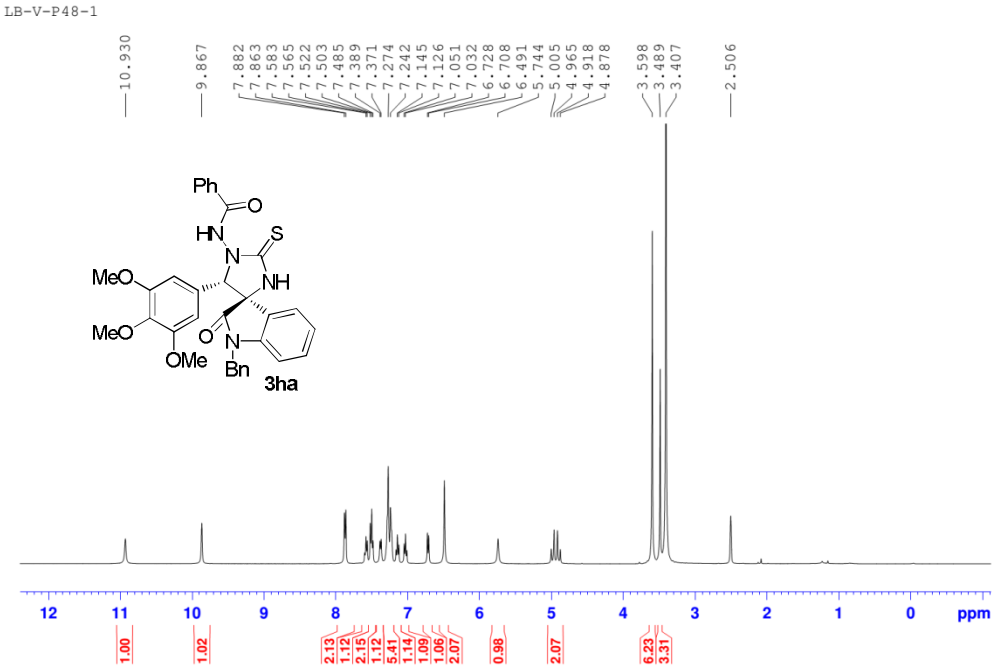
ppm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7.503
7.485
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7.371
7.274
7.242
7.145
7.126
7.051
7.032
6.728
6.708
6.491
5.744
5.005
4.965
4.918
4.878
3.598
3.489
3.407
2.506
Ph
O
HN
S
N
NH
MeO
MeO
OMe
O
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Bn
3ha
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
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1.02
2.13
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1.06
2.07
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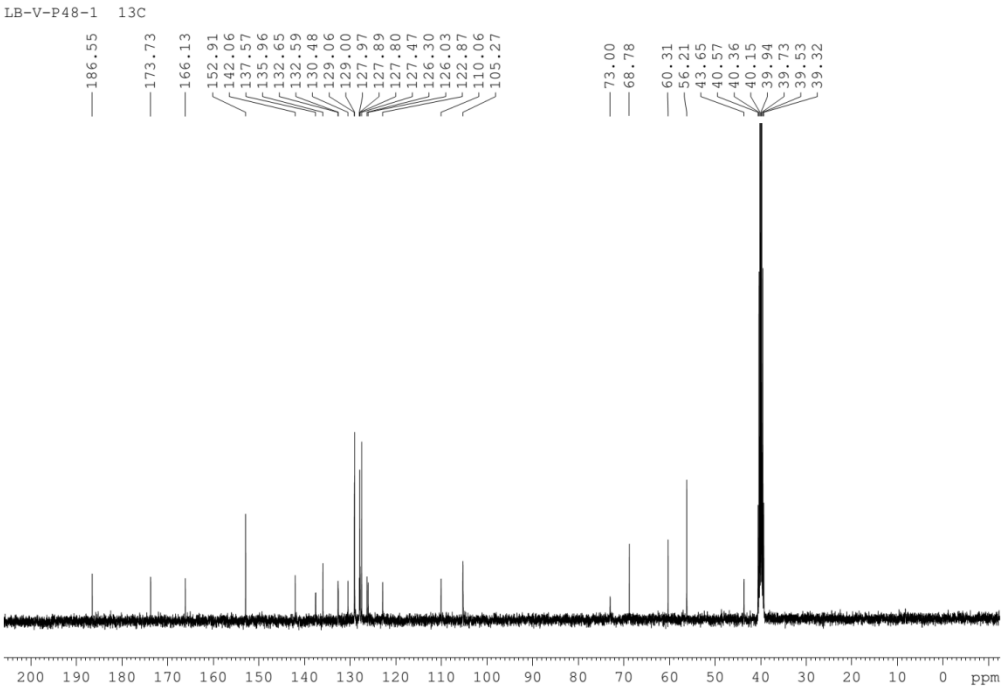
2.07
6.23
3.31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137.57
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132.65
132.59
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129.00
127.97
127.89
127.80
127.47
126.30
126.03
122.87
110.06
105.27
73.00
68.78
60.31
56.21
43.65
40.57
40.36
40.15
39.94
39.73
39.53
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200
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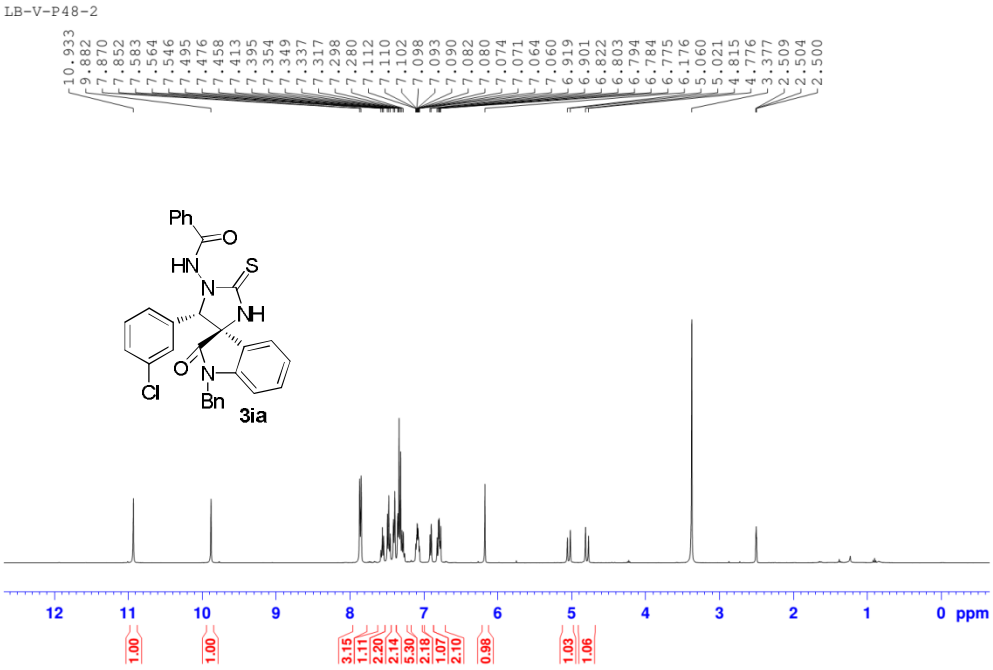
ppm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7.395
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7.349
7.337
7.317
7.298
7.280
7.112
7.110
7.102
7.098
7.093
7.090
7.082
7.080
7.074
7.071
7.064
7.060
6.919
6.901
6.822
6.803
6.794
6.784
6.775
6.176
5.060
5.021
4.815
4.776
3.377
2.509
2.504
2.500
Ph
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HN
S
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NH
O
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Cl
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12
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10
9
8
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3
2
1
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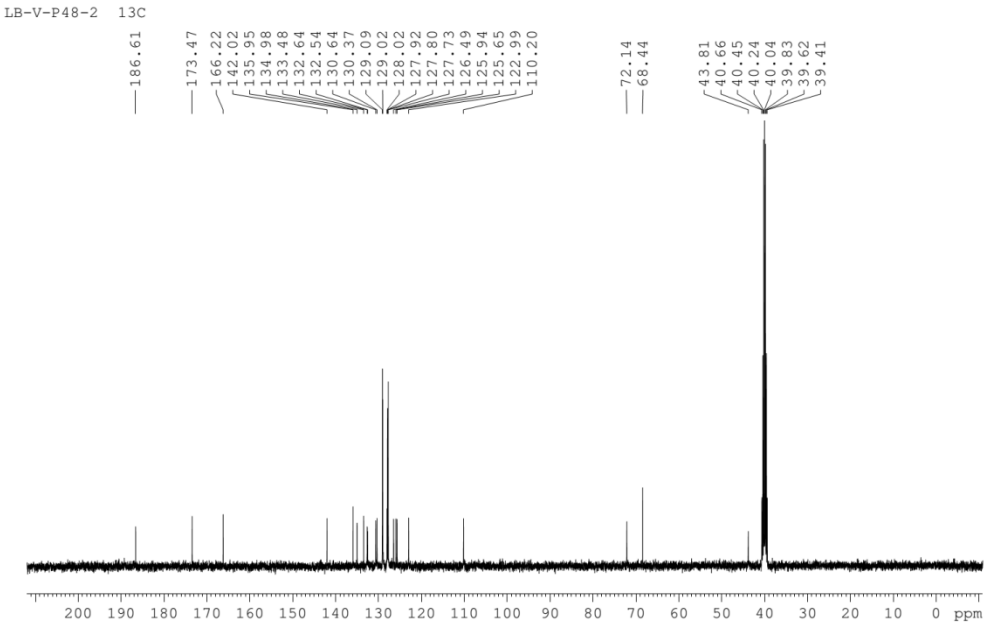
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166.22
142.02
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132.64
132.54
130.64
130.37
129.09
129.02
128.02
127.92
127.80
127.73
126.49
125.94
125.65
122.99
110.20
72.14
68.44
43.81
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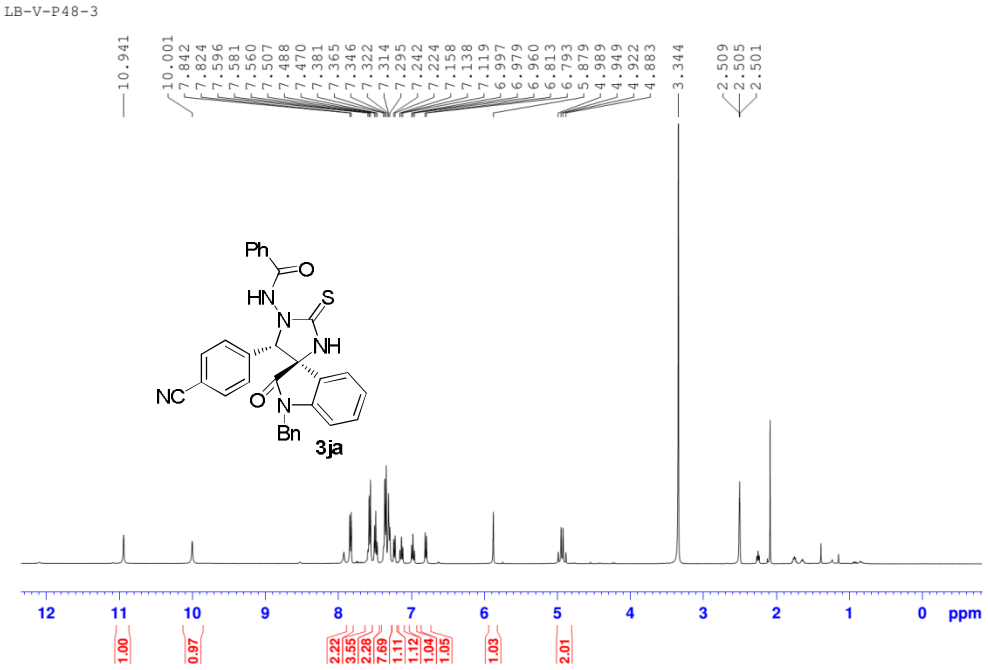
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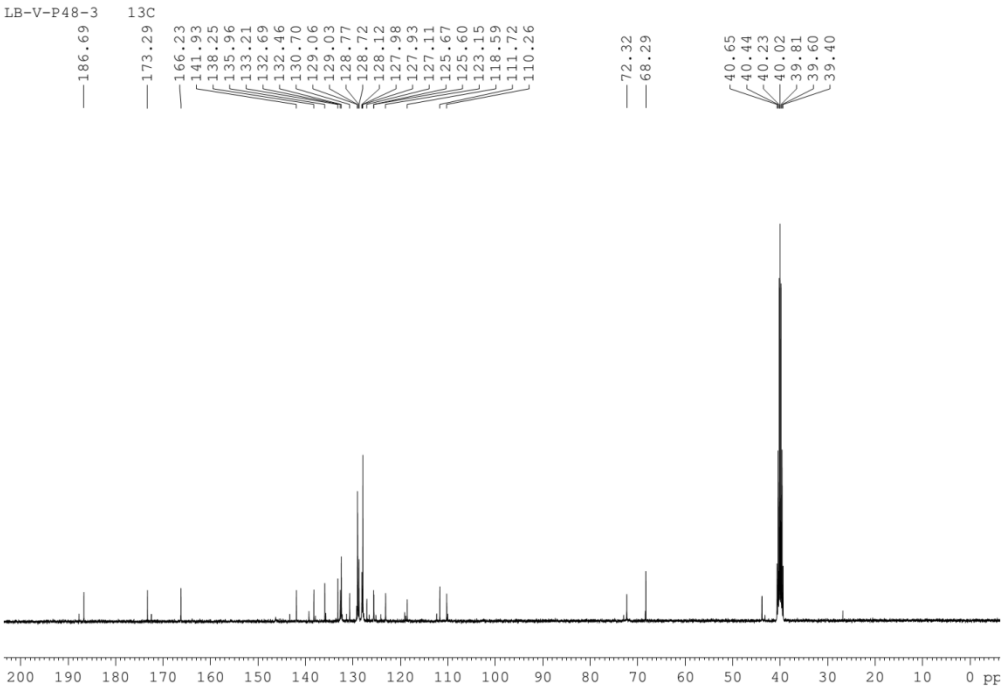
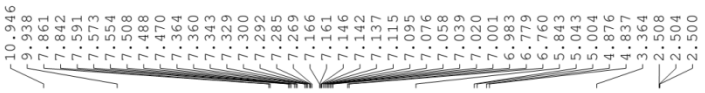
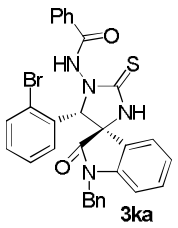
7.381
7.365
7.346
7.322
7.314
7.295
7.242
7.224
7.158
7.138
7.119
6.997
6.979
6.960
6.813
6.793
5.879
4.989
4.949
4.922
4.883
3.344
2.509
2.505
2.501
Ph
O
HN
S
N
NH
NC
O
N
Bn
3ja
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.97
2.22
3.55
2.28
7.69
1.11
1.12
1.04
1.05
1.03
2.01

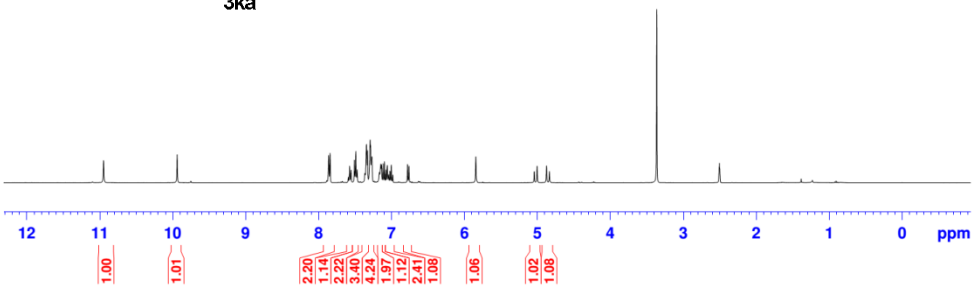

LB-V-P48-3 13C
186.69
173.29
166.23
141.93
138.25
135.96
133.21
132.69
132.46
130.70
129.06
129.03
128.77
128.72
128.12
127.98
127.93
127.11
125.67
125.60
123.15
118.59
111.72
110.26
72.32
68.29
40.65
40.44
40.23
40.02
39.81
39.60
39.40
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

LB-V-P48-4

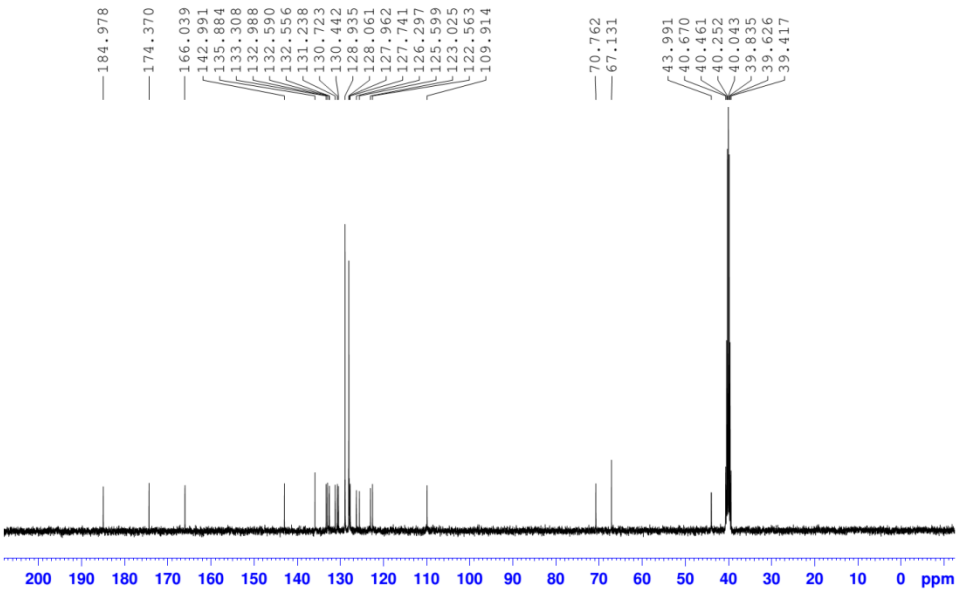


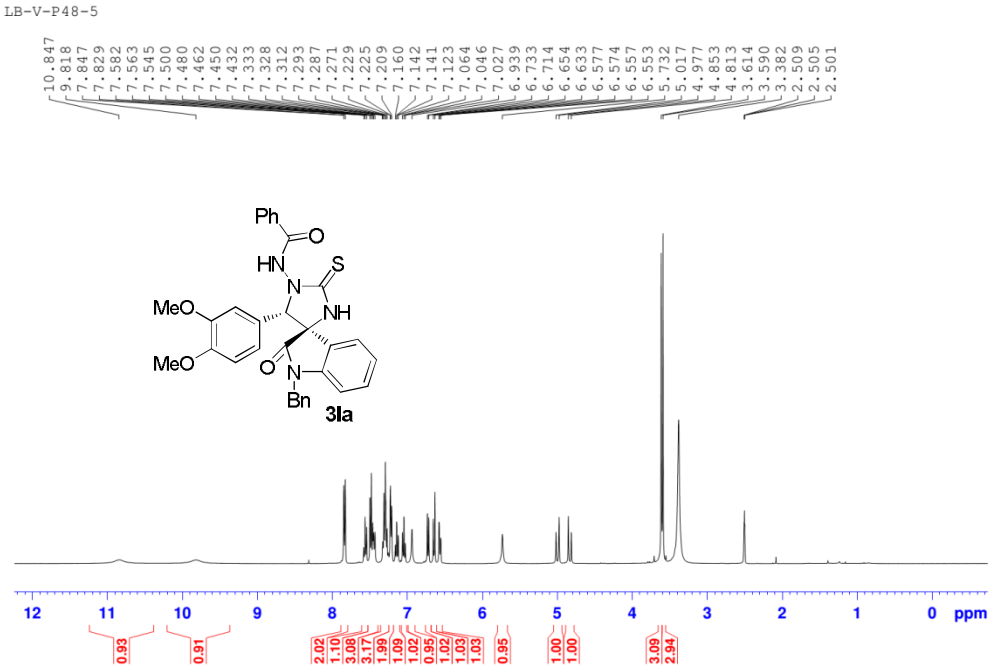


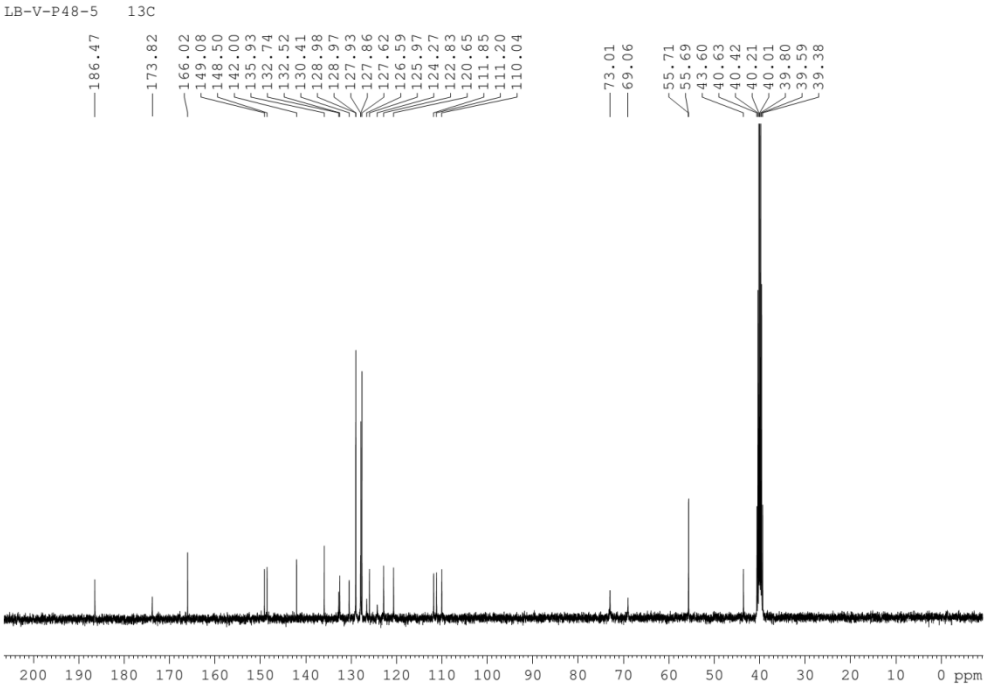
3ka

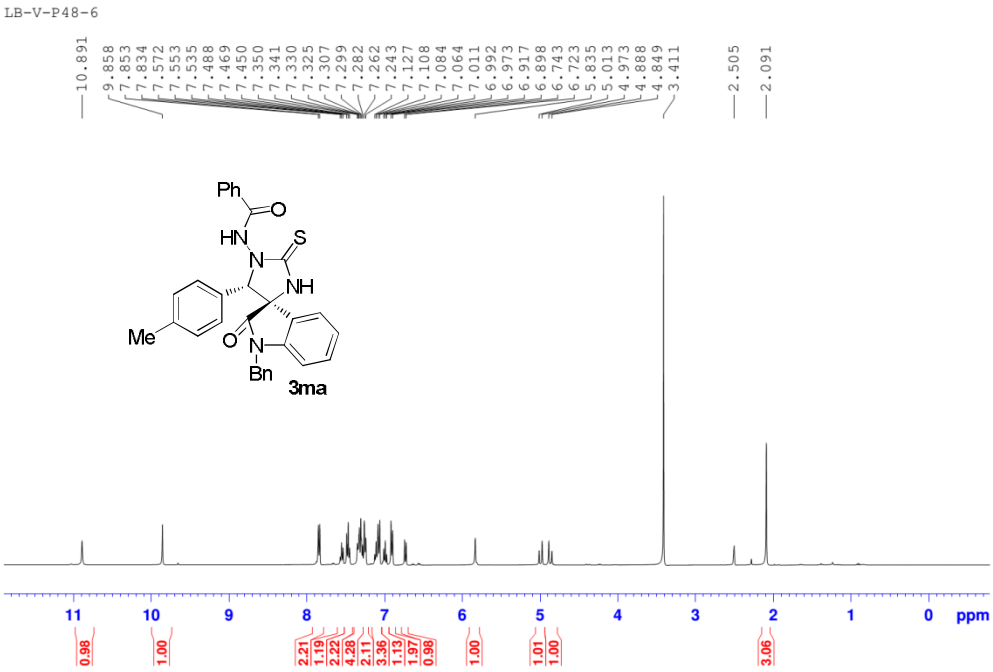


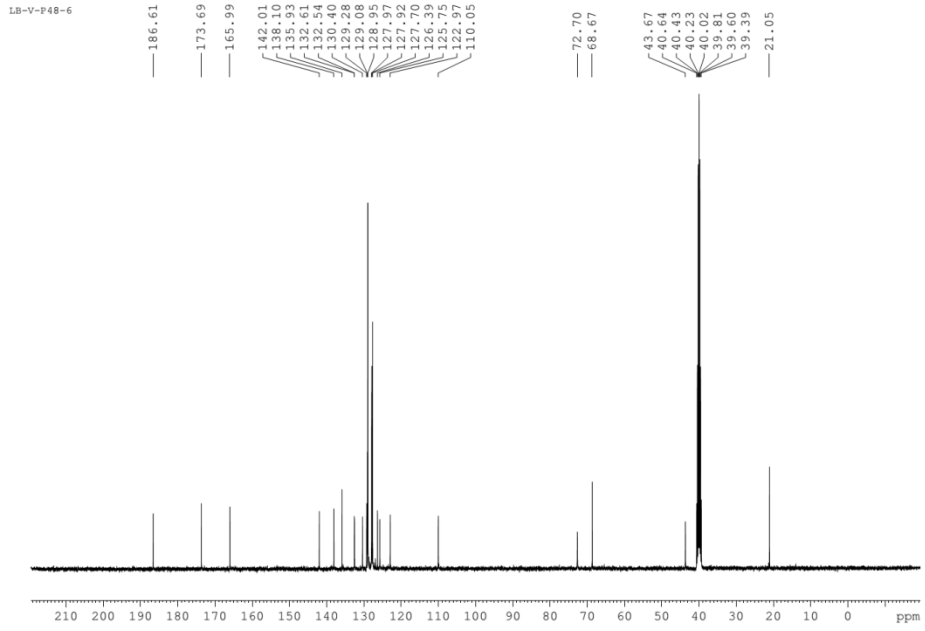
LB-V-P48-4 13C



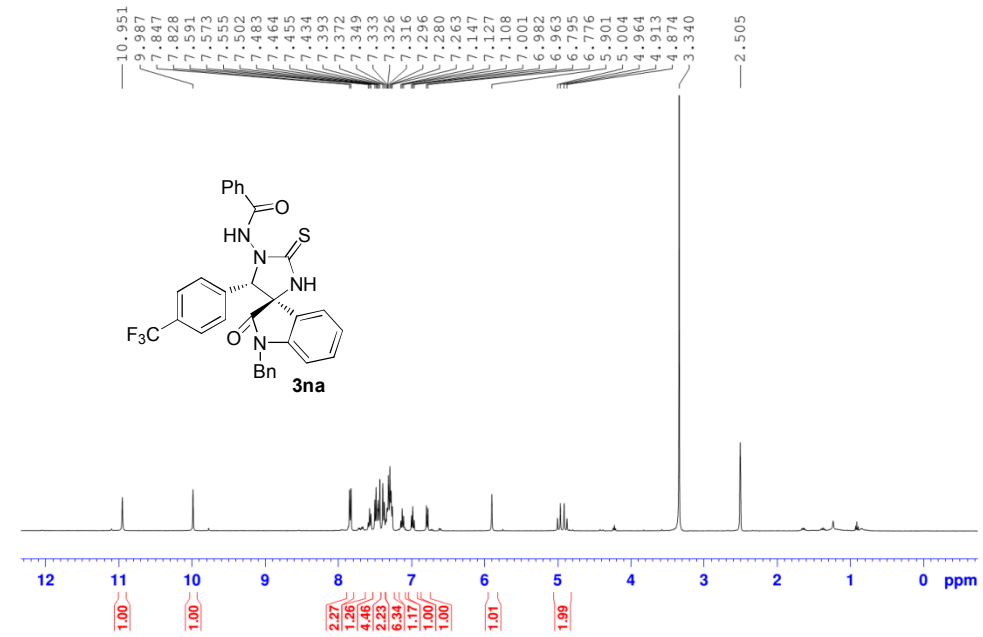

LB-V-P48-5
10.847
9.818
7.847
7.829
7.582
7.563
7.545
7.500
7.480
7.462
7.450
7.432
7.333
7.328
7.312
7.293
7.287
7.271
7.229
7.225
7.209
7.160
7.142
7.141
7.123
7.064
7.046
7.027
6.939
6.733
6.714
6.654
6.633
6.577
6.574
6.557
6.553
5.732
5.017
4.977
4.853
4.813
3.614
3.590
3.382
2.509
2.505
2.501
Ph
O
HN
S
N
NH
MeO
MeO
O
N
Bn
3la
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.93
0.91
2.02
1.10
3.08
3.17
1.99
1.09
1.02
0.95
1.02
1.03
1.03
0.95
1.00
1.00
3.09
2.94


LB-V-P48-5 13C
186.47
173.82
166.02
149.08
148.50
142.00
135.93
132.74
132.52
130.41
128.98
128.97
127.93
127.86
127.62
126.59
125.97
124.27
122.83
120.65
111.85
111.20
110.04
73.01
69.06
55.71
55.69
43.60
40.63
40.42
40.21
40.01
39.80
39.59
39.38
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

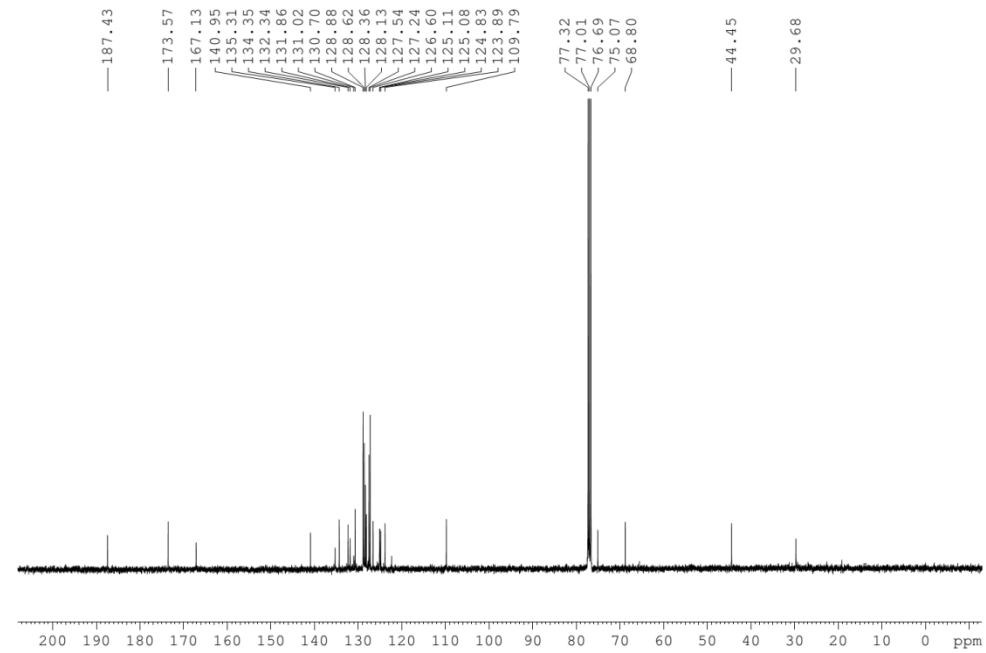

LB-V-P48-6
10.891
9.858
7.853
7.834
7.572
7.553
7.535
7.488
7.469
7.450
7.350
7.341
7.330
7.325
7.307
7.299
7.282
7.262
7.243
7.127
7.108
7.084
7.064
7.011
6.992
6.973
6.917
6.898
6.743
6.723
5.835
5.013
4.973
4.888
4.849
3.411
2.505
2.091
Ph
O
HN
S
N
NH
Me
O
N
Bn
3ma
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.98
1.00
2.21
1.19
2.22
4.28
2.11
3.36
1.13
1.97
0.98
1.00
1.01
1.00
3.06

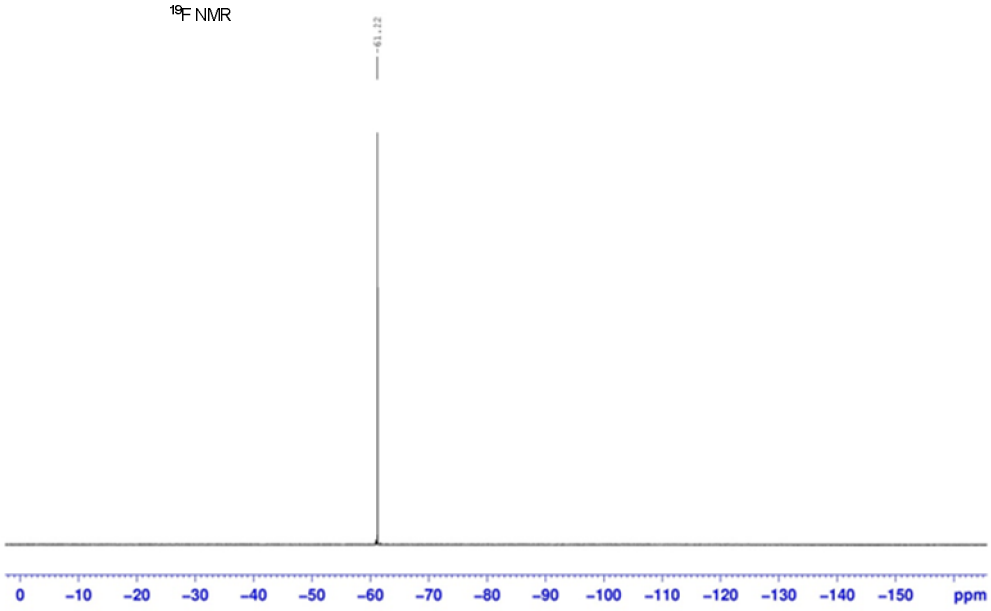

LB-V-P48-6
186.61
173.69
165.99
142.01
138.10
135.93
132.61
132.54
130.40
129.28
129.08
128.55
127.97
127.92
127.70
126.79
125.75
122.37
110.05
72.70
68.67
43.67
40.64
40.43
40.23
40.02
39.81
39.60
39.39
21.05
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

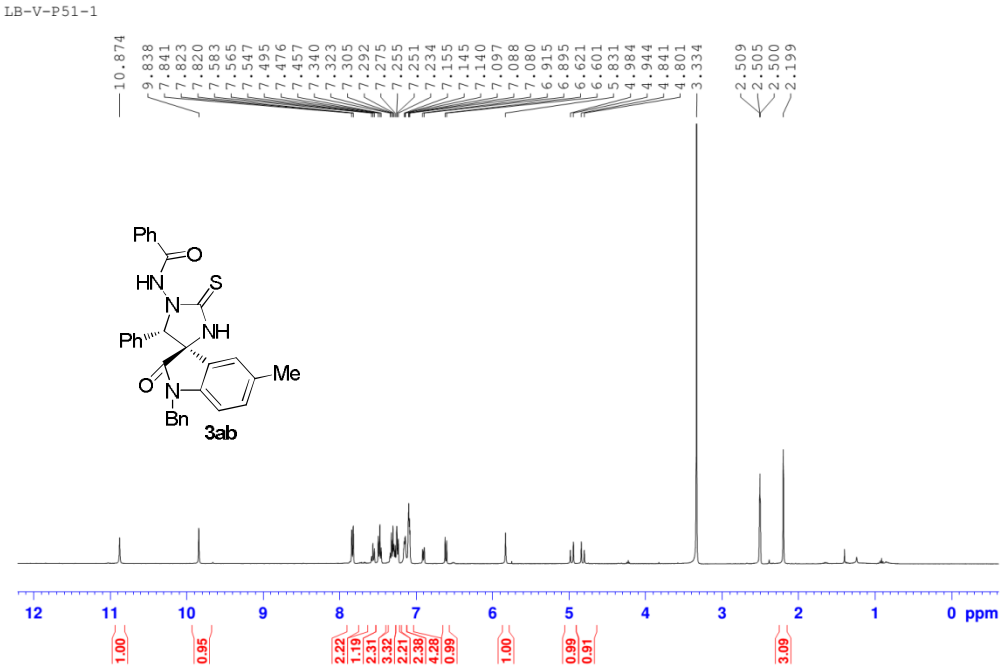
LB-V-P48-7

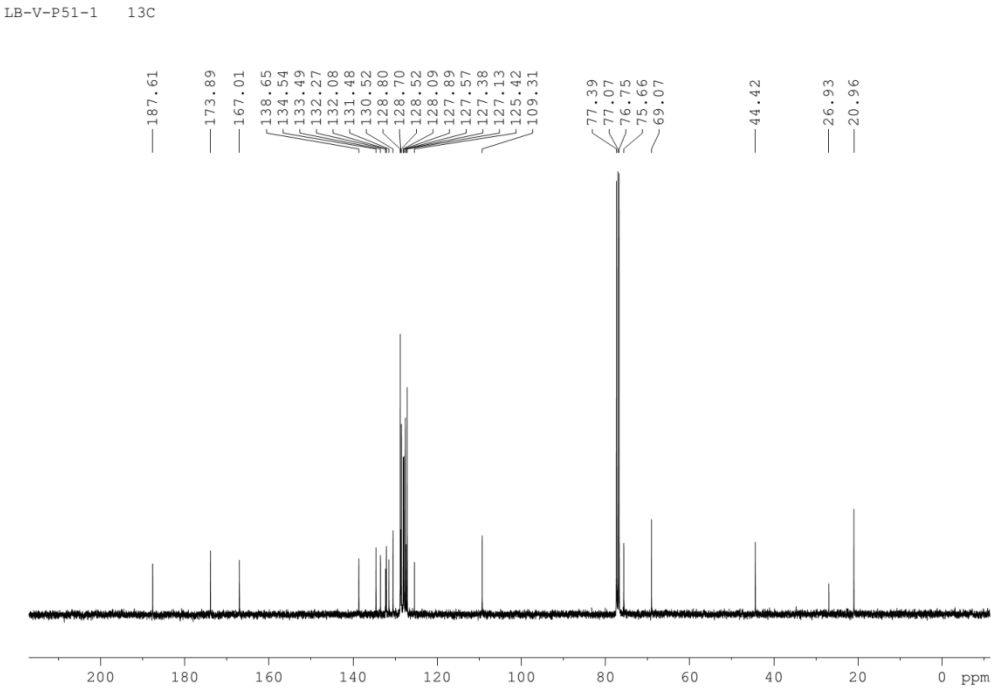


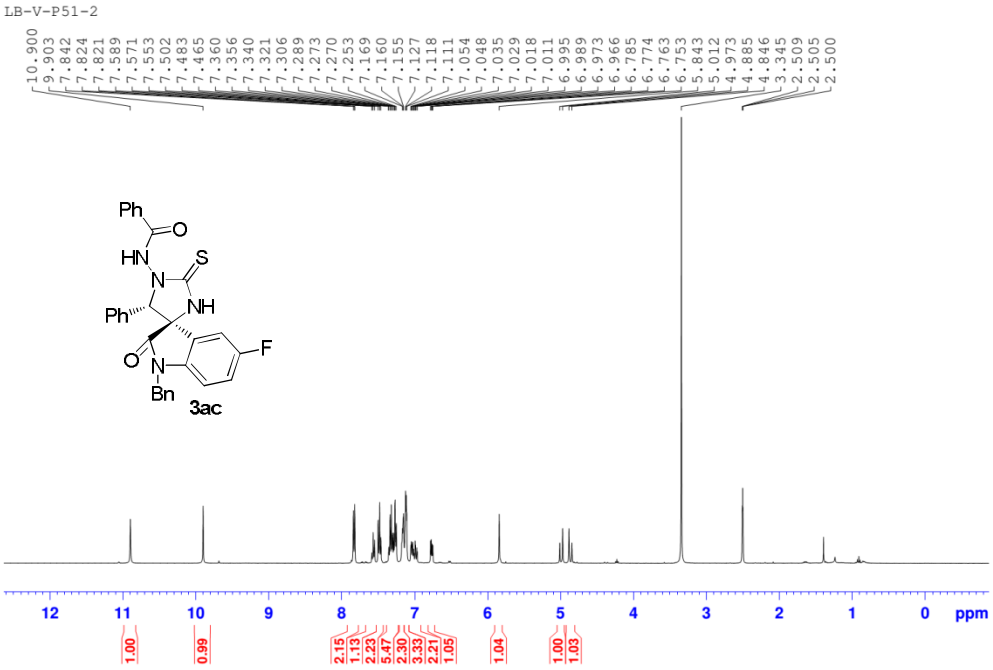
LB-V-P40-7 13c

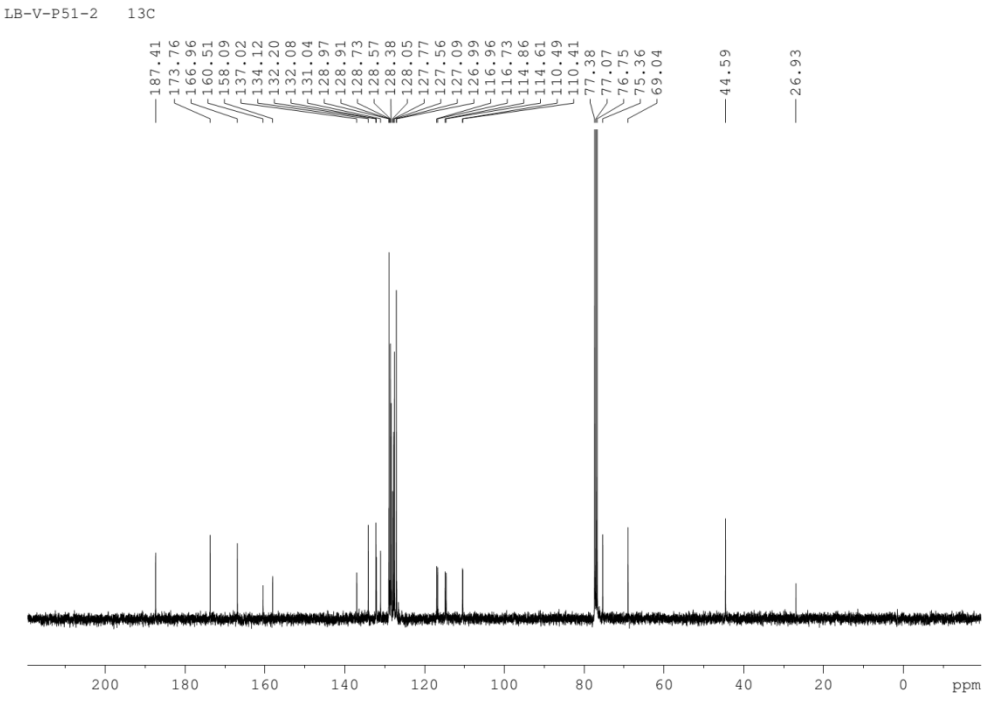



19F NMR
-61.22
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
ppm

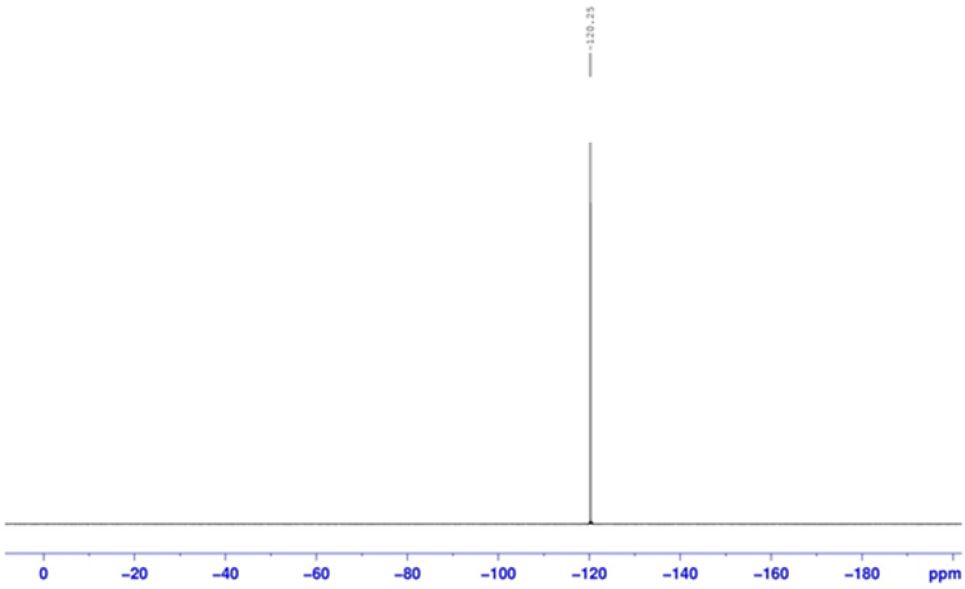

LB-V-P51-1
10.874
9.838
7.841
7.823
7.820
7.583
7.565
7.547
7.495
7.476
7.457
7.340
7.323
7.305
7.292
7.275
7.255
7.251
7.234
7.155
7.145
7.140
7.097
7.088
7.080
6.915
6.895
6.621
6.601
5.831
4.984
4.944
4.841
4.801
3.334
2.509
2.505
2.500
2.199
Ph
O
HN
S
N
NH
Ph
Me
O
N
Bn
3ab
12
11
10
9
8
7
6
5
4
3
2
1
0 ppm
1.00
0.95
2.22
1.19
2.31
3.32
2.21
2.38
4.28
0.99
1.00
0.99
0.91
3.09

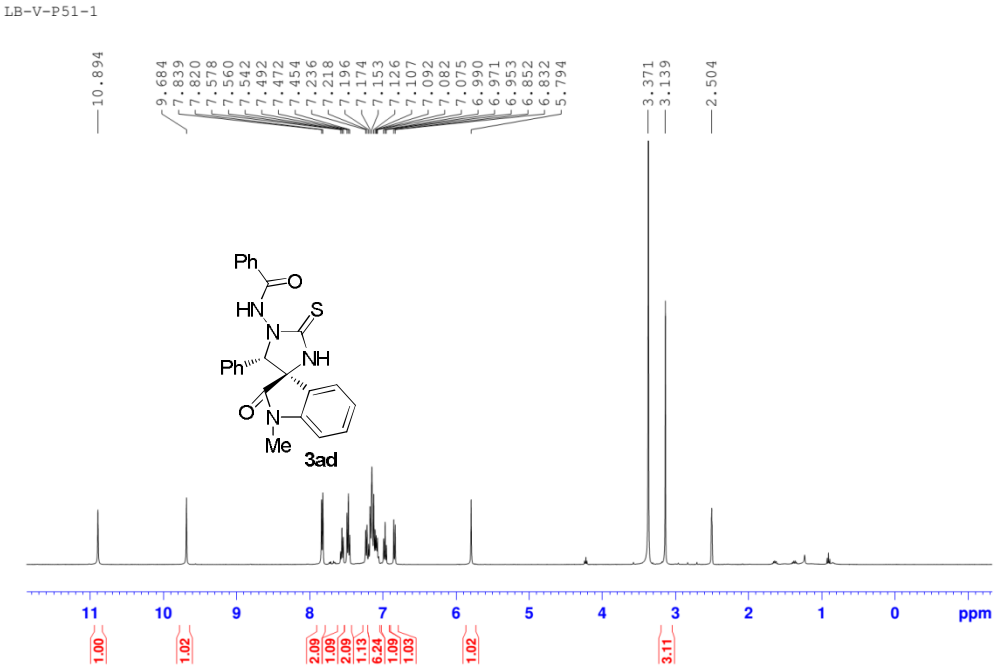

LB-V-P51-1 13C
187.61
173.89
167.01
138.65
134.54
133.49
132.27
132.08
131.48
130.52
128.80
128.70
128.52
128.09
127.89
127.57
127.38
127.13
125.42
109.31
77.39
77.07
76.75
75.66
69.07
44.42
26.93
20.96
200
180
160
140
120
100
80
60
40
20
0 ppm

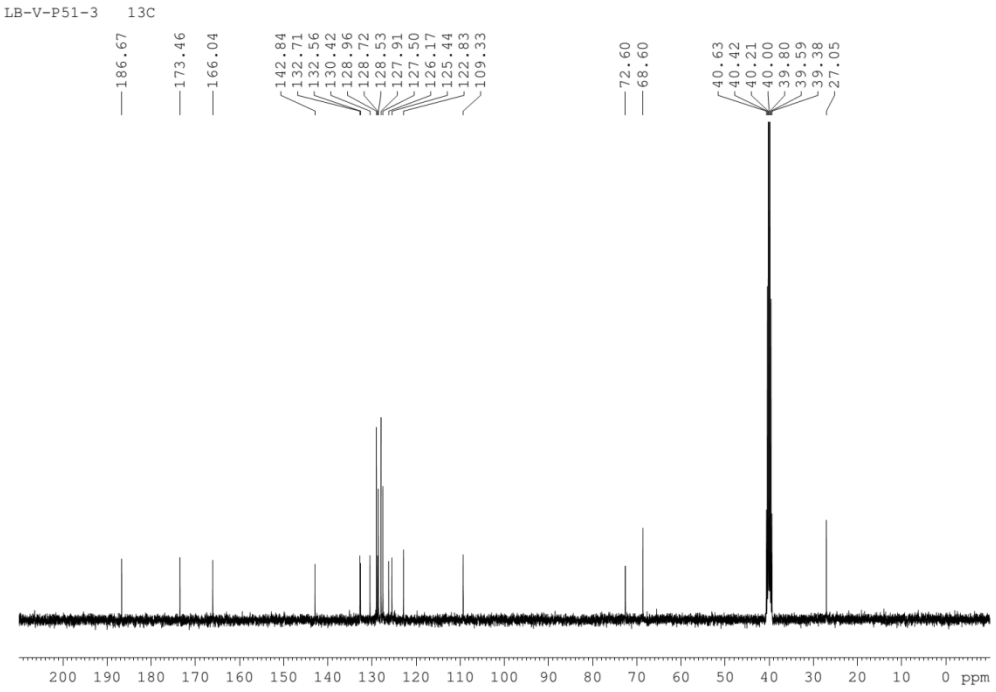

LB-V-P51-2
10.900
9.903
7.842
7.824
7.821
7.589
7.571
7.553
7.502
7.483
7.465
7.360
7.356
7.340
7.321
7.306
7.289
7.273
7.270
7.253
7.169
7.160
7.155
7.127
7.118
7.111
7.054
7.048
7.035
7.029
7.018
7.011
6.995
6.989
6.973
6.966
6.785
6.774
6.763
6.753
5.843
5.012
4.973
4.885
4.846
3.345
2.509
2.505
2.500
Ph
O
HN
S
N
NH
Ph
O
N
F
Bn
3ac
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.99
2.15
1.13
2.23
5.47
2.30
3.33
2.21
1.05
1.04
1.00
1.03


LB-V-P51-2 13C
187.41
173.76
166.96
160.51
158.09
137.02
134.12
132.20
132.08
131.04
128.97
128.91
128.73
128.57
128.38
128.05
127.77
127.56
127.09
126.99
116.96
116.73
114.86
114.61
110.49
110.41
77.38
77.07
76.75
75.36
69.04
44.59
26.93
200
180
160
140
120
100
80
60
40
20
0
ppm

^{19}F NMR




LB-V-P51-1
10.894
9.684
7.839
7.820
7.578
7.560
7.542
7.492
7.472
7.454
7.236
7.218
7.196
7.174
7.153
7.126
7.107
7.092
7.082
7.075
6.990
6.971
6.953
6.852
6.832
5.794
3.371
3.139
2.504
Ph
O
HN
N
S
NH
Ph
O
N
Me
3ad
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.02
2.09
1.09
2.09
1.13
6.24
1.09
1.03
1.02
3.11


LB-V-P51-3 13C
186.67
173.46
166.04
142.84
132.71
132.56
130.42
128.96
128.72
128.53
127.91
127.50
126.17
125.44
122.83
109.33
72.60
68.60
40.63
40.42
40.21
40.00
39.80
39.59
39.38
27.05
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm