PEt_3-Mediated Deoxygenative C–N Coupling of Nitroarenes and Boronic Acids

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Contents

I. General Methods

All reagents (including commercial phosphorus reagents used in optimization studies) were purchased from commercial vendors (Sigma-Aldrich, Alfa Aesar, Acros, TCI, or Oakwood Chemical, Combi-Blocks) and used without further purification unless otherwise indicated. Nitrobenzene was distilled over CaH prior to use. Anhydrous *m*-xylene was obtained from a Sigma-Aldrich (sure-seal® bottle) and used as received. All other solvents were ACS grade or better and were used without further purification. Manipulations were conducted under an atmosphere of dry N_2 gas unless otherwise noted. The phosphine-mediated C–N coupling reactions were carried out in glass culture tubes with threaded end (20 x 125 mm; Fisher Scientific part # 14-959-35A), outfitted with a phenolic screw-thread open top cap (Kimble-Chase part #73804-15425), and PTFE-lined silicone septum (Thermo Fisher part # B7995-15). Column chromatography was carried out on silica gel (SiliFlash® Irregular Silica Gel, P60 40-63µm. ^{1}H, ^{13}C, and ^{19}F NMR were collected with a Bruker AVANCE III DRX 400 spectrometer and processed using MestReNova. ^{1}H NMR chemical shifts are given in ppm with respect to solvent residual peak ($CDCl_3$, δ 7.26 ppm) and $^{13}C\{^1H\}$ NMR shifts are given in ppm with respect to ($CDCl_3$ δ 77.16 ppm). Multiplicities are described as s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, tt = triplet of triplets, m = multiplet. Coupling constants are reported in Hertz (Hz). High-resolution ESI mass spectra were obtained from the MIT department of chemistry instrumentation facility on an Agilent 6545 Q-TOF instrument.

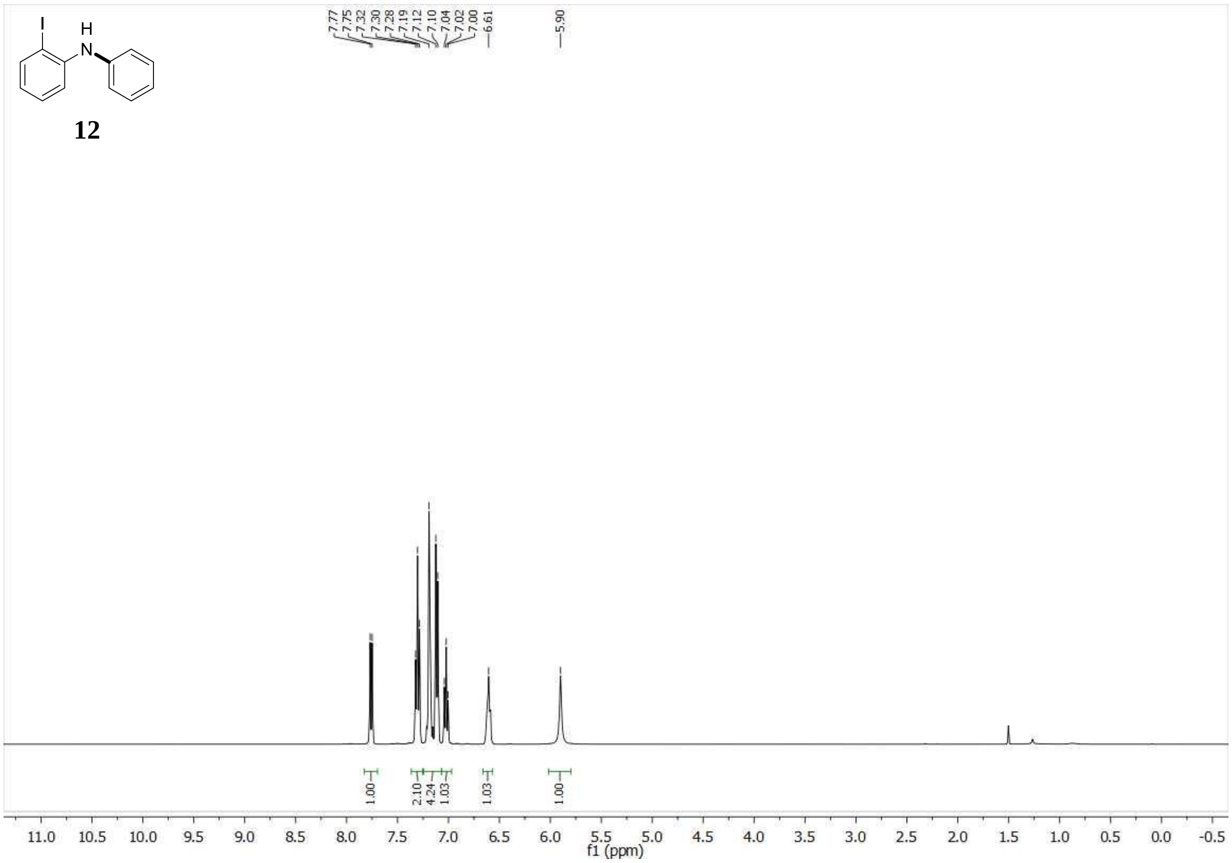
II. Reaction Optimization

Procedure:

Reaction vessels as described in the General Methods section were equipped with a PTFE stir bar and charged with phenylboronic acid (67 mg, 0.55 mmol, 1.1 equiv), nitrobenzene (51 µL, 0.50 mmol, 1 equiv), and dodecane as standard (~0.50 mmol, gravimetrically determined). The vessels were sealed, evacuated on a Schlenk line for 30 sec, and backfilled with N_2 (1x). Each vessel was then charged with 1 mL of *m*-xylene via syringe, followed by the appropriate phosphine reagent via microliter syringe. In instances where the phosphine reagent was a solid, the solid was added prior to evacuation. The reactions were then heated to 120 ˚C and stirred for 4 h. Then the reaction mixtures were cooled to room temperature and diluted with 1 mL of denatured EtOH. After stirring thoroughly, a 40 µL reaction aliquot was taken from each reaction mixture and charged into a GC vial containing 1.5 mL of denatured EtOH. The GC vial was capped and the shaken in order to mix thoroughly. Reaction yields were quantified by GC-FID by reference to calibration curves that were made using authentic analytes prior to the start of this study.

GC-FID information:

An Agilent 7890A gas chromatograph was used for the analysis, outfitted with a J&W 127-1012 column (10m X 100 µm X 0.1µm). The initial carrier gas flow rate was 0.38586 mL/min (He) and the temperature program started at 70 ˚C holding for 1 min, then ramped at 50 ºC/min until 250 ºC, and held at that temperature for 2 min. The retention times are as follows: 2.3 minutes (nitrobenzene), 2.7 minutes (dodecane), 3.9 minutes (diphenylamine).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1.00
2.10
4.24
1.03
1.03
1.00
11.0
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10.0
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9.0
8.5
8.0
7.5
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6.5
6.0
5.5
5.0
4.5
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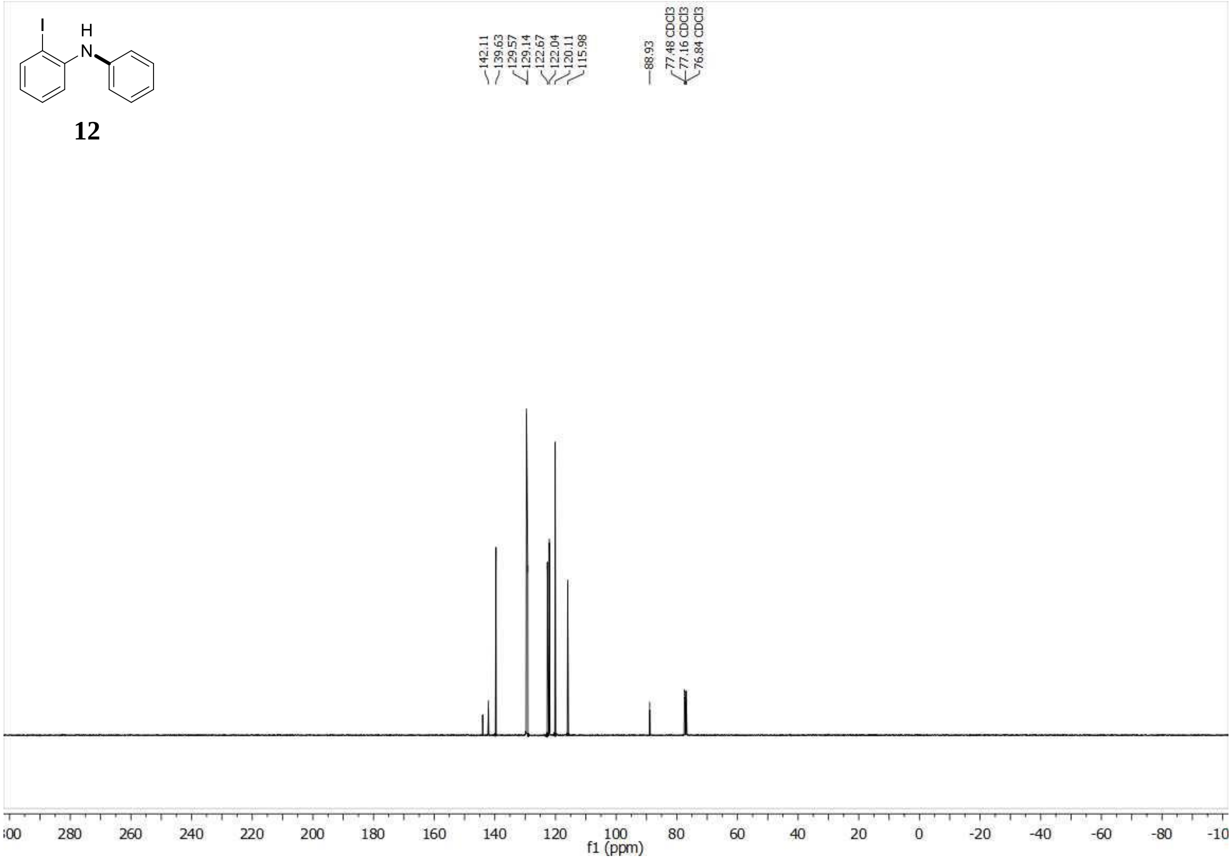
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77.16 CDCl3
76.84 CDCl3
00
280
260
240
220
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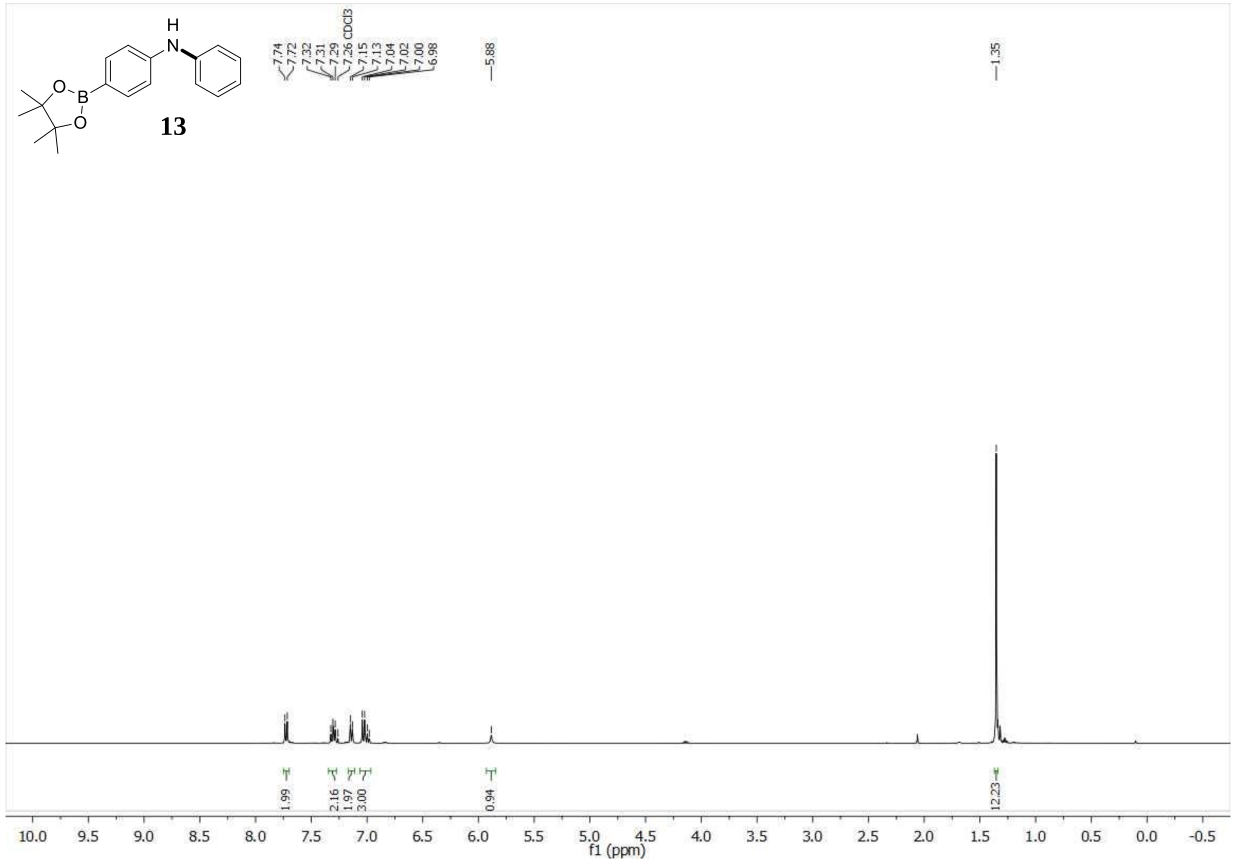
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3.00
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9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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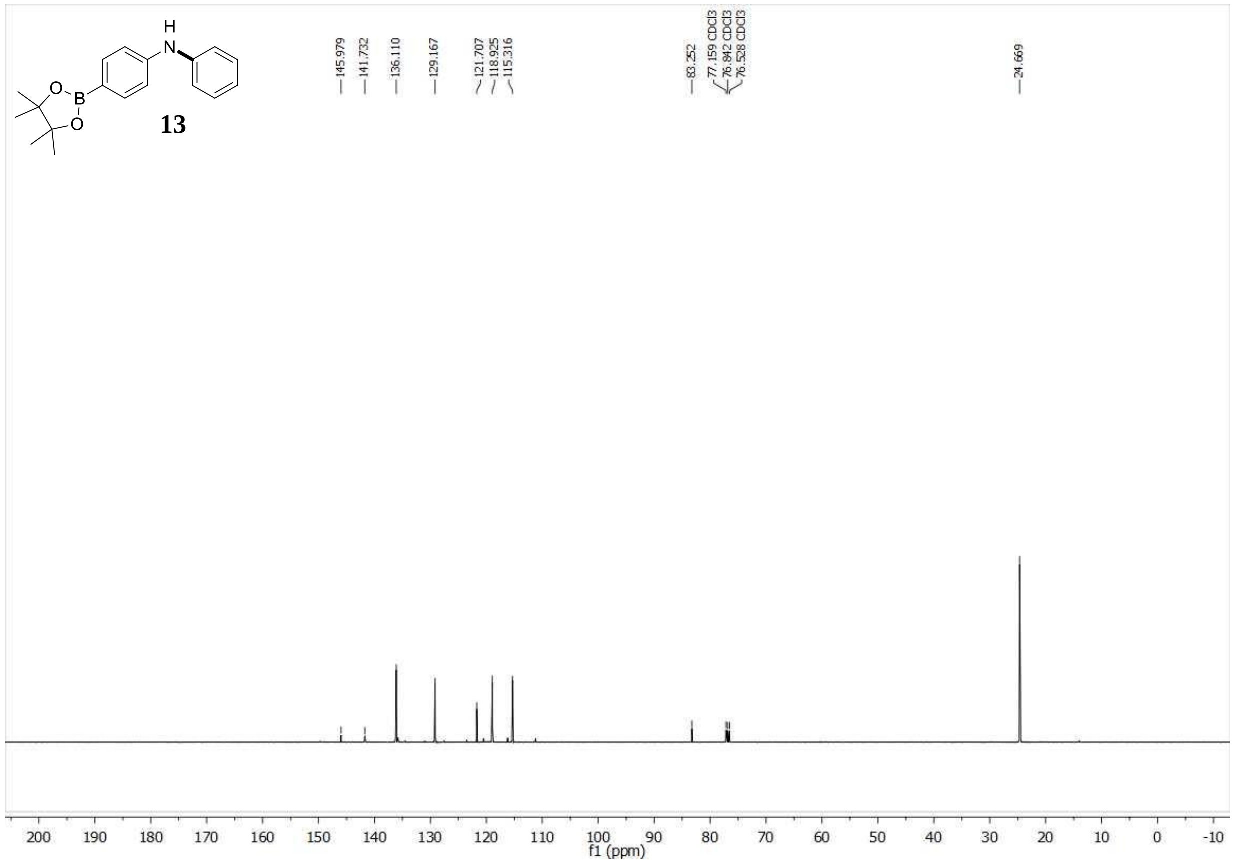
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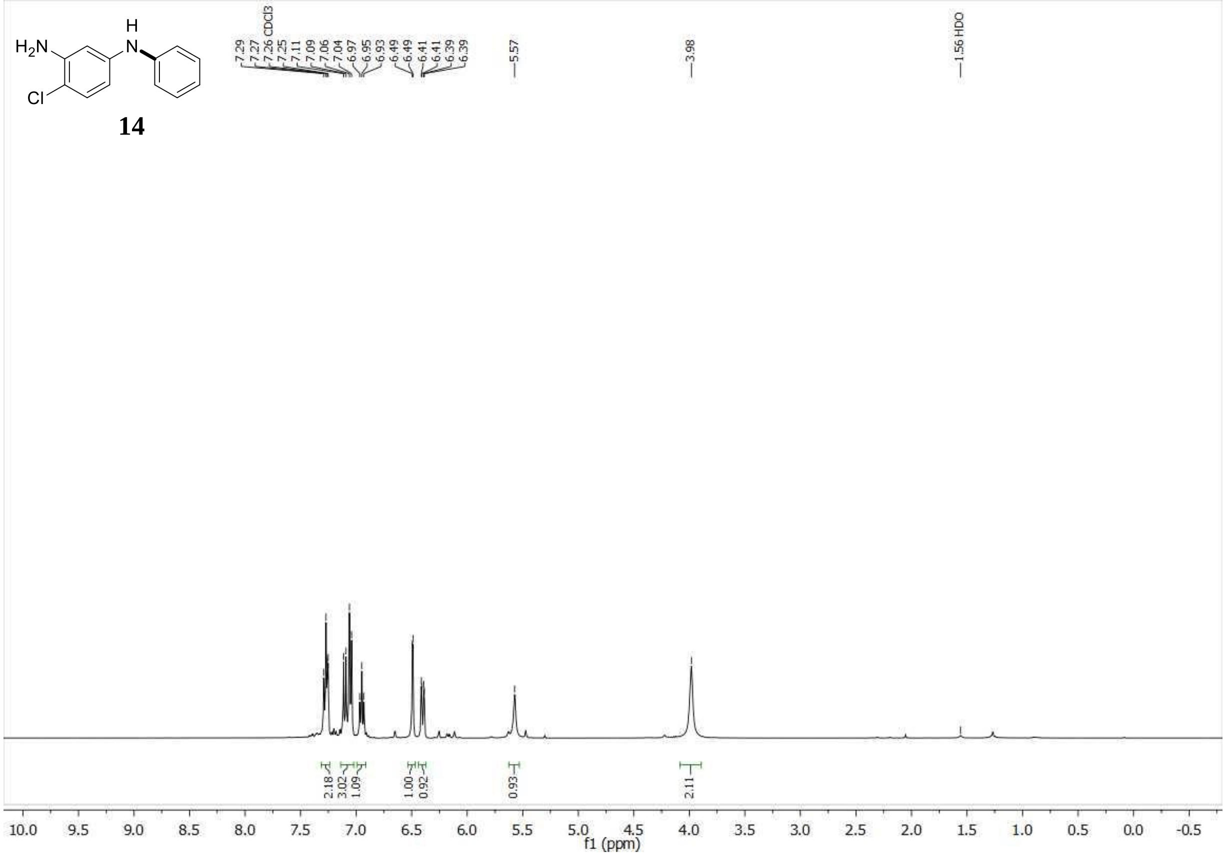
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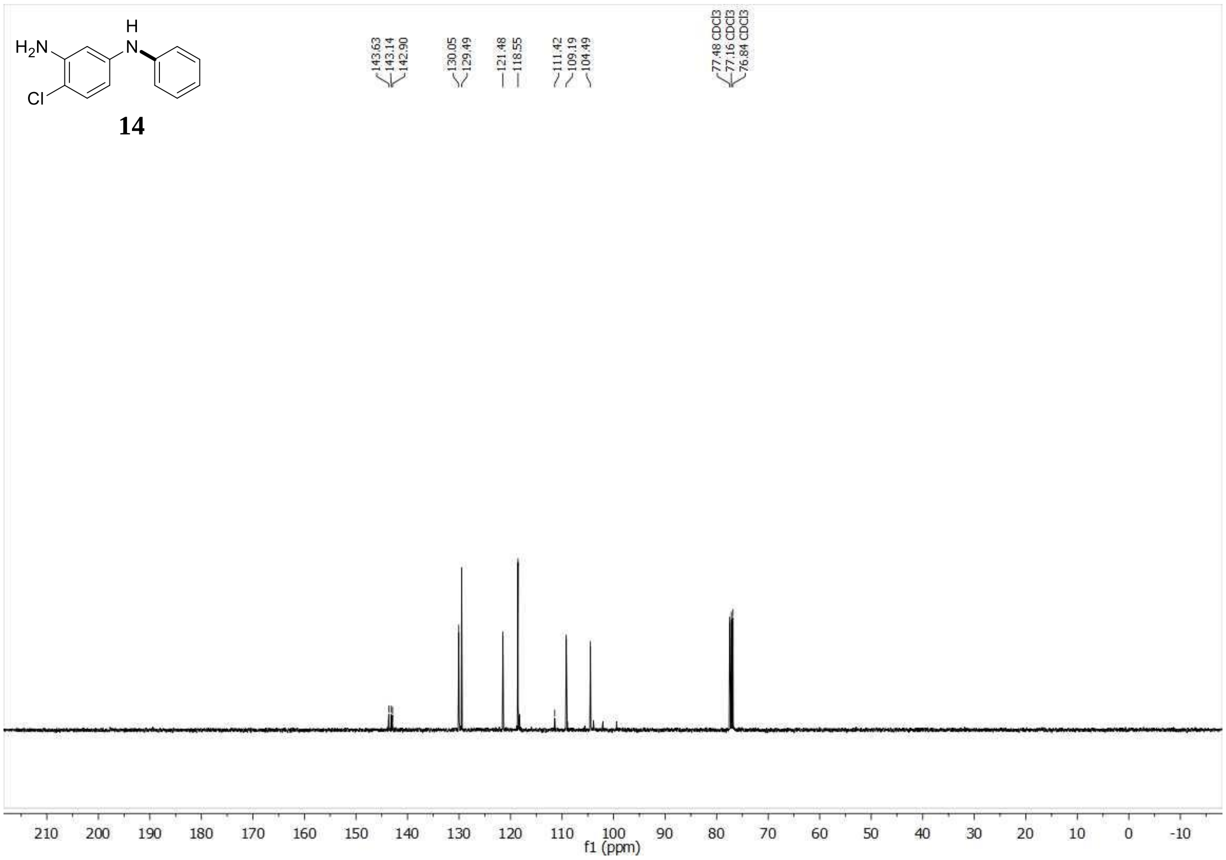
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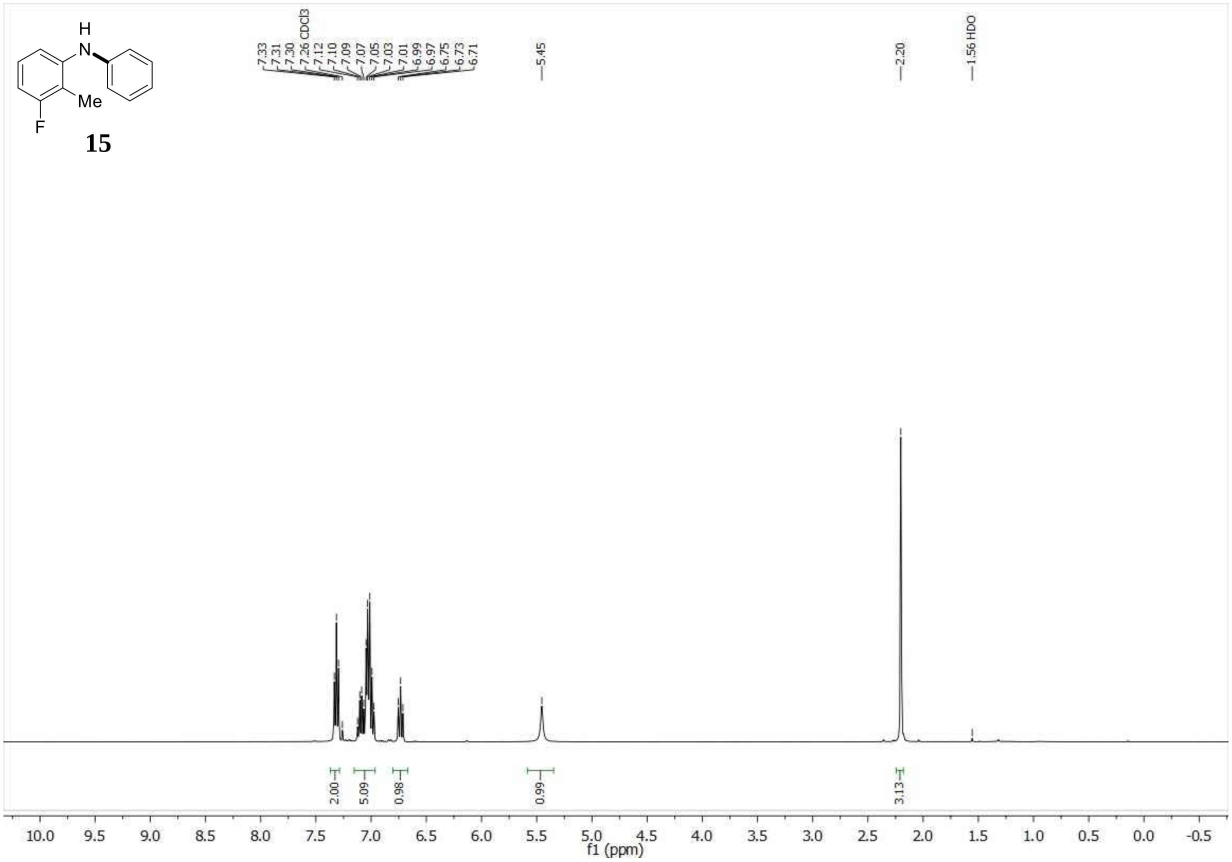
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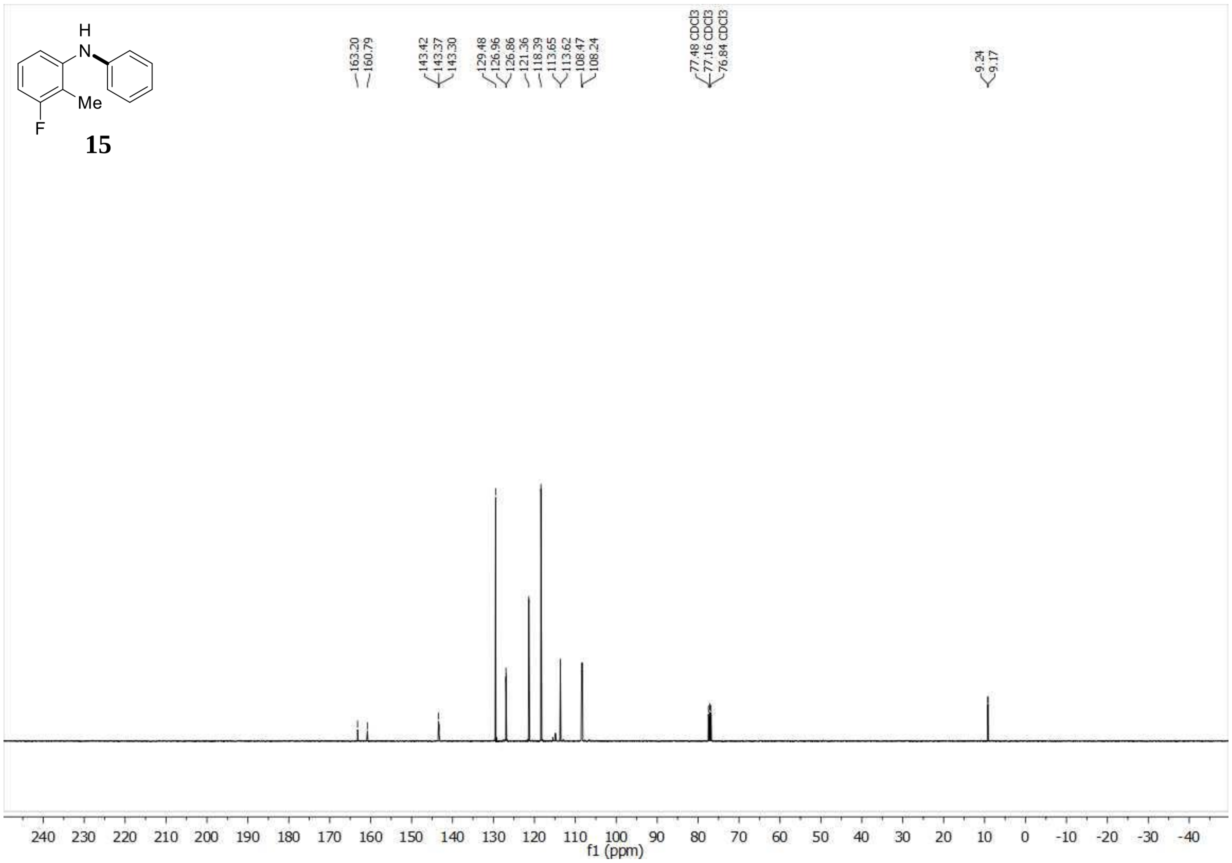
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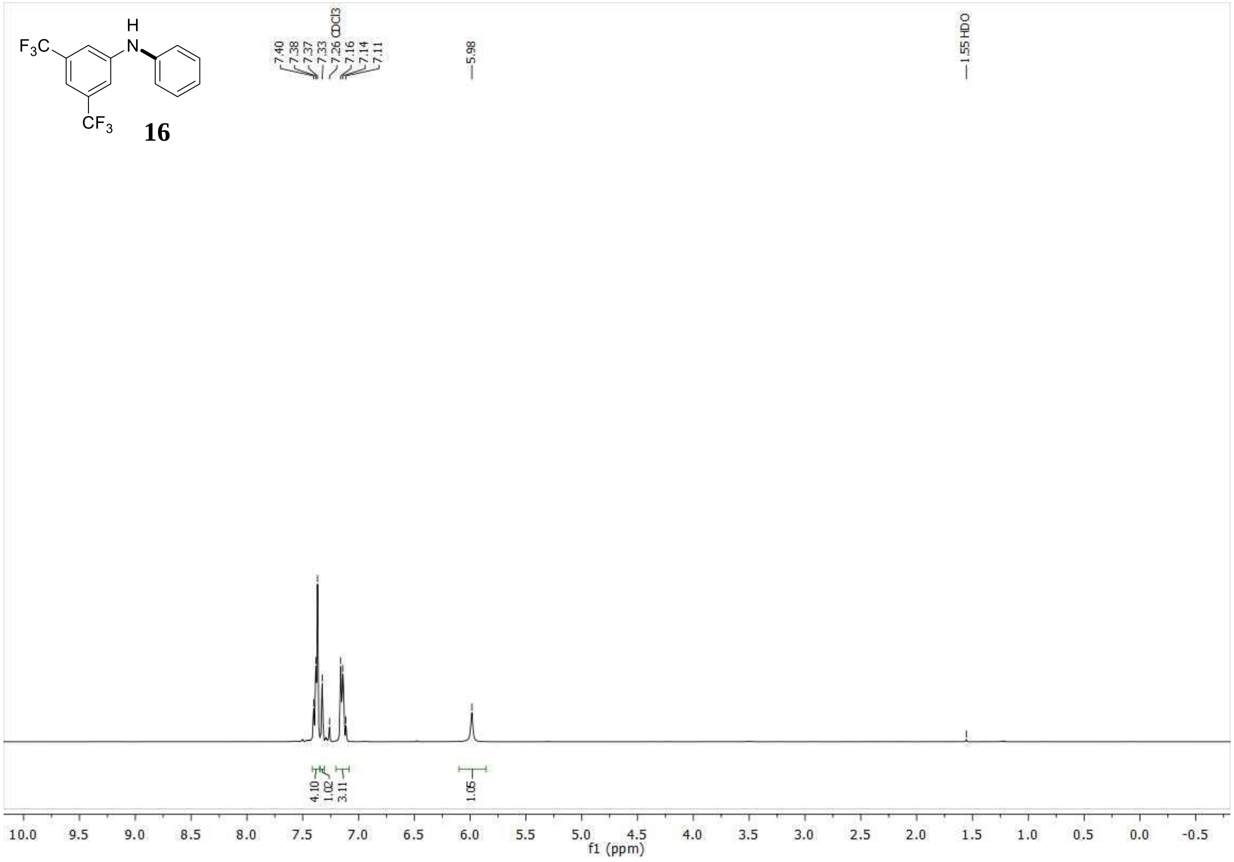
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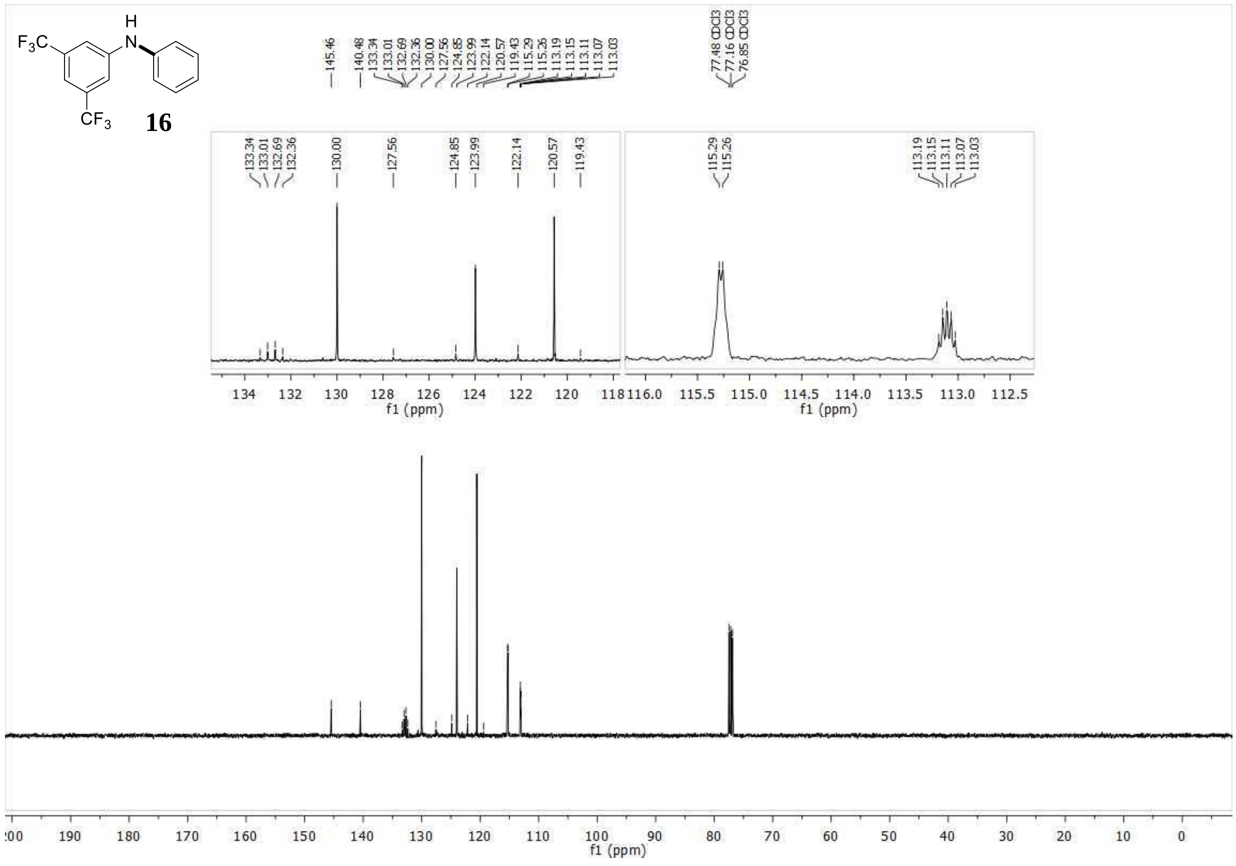
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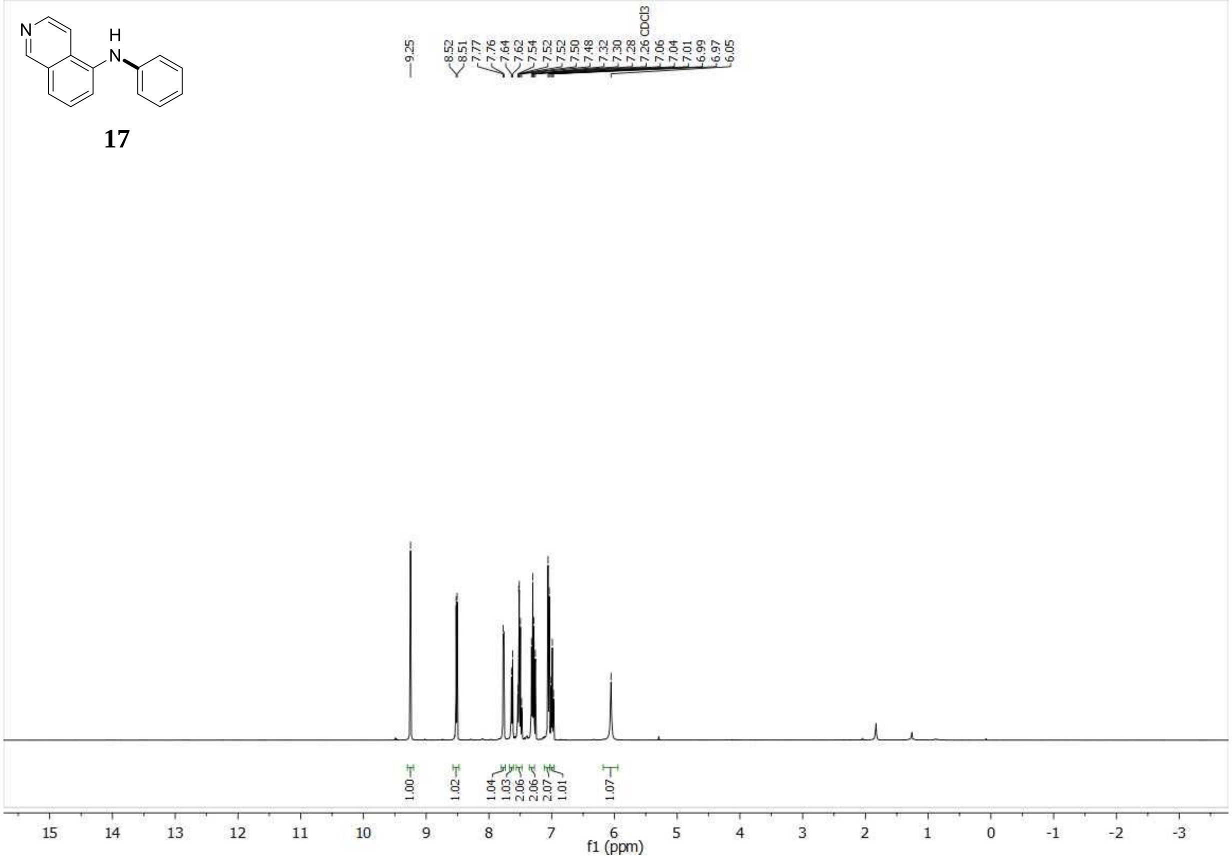
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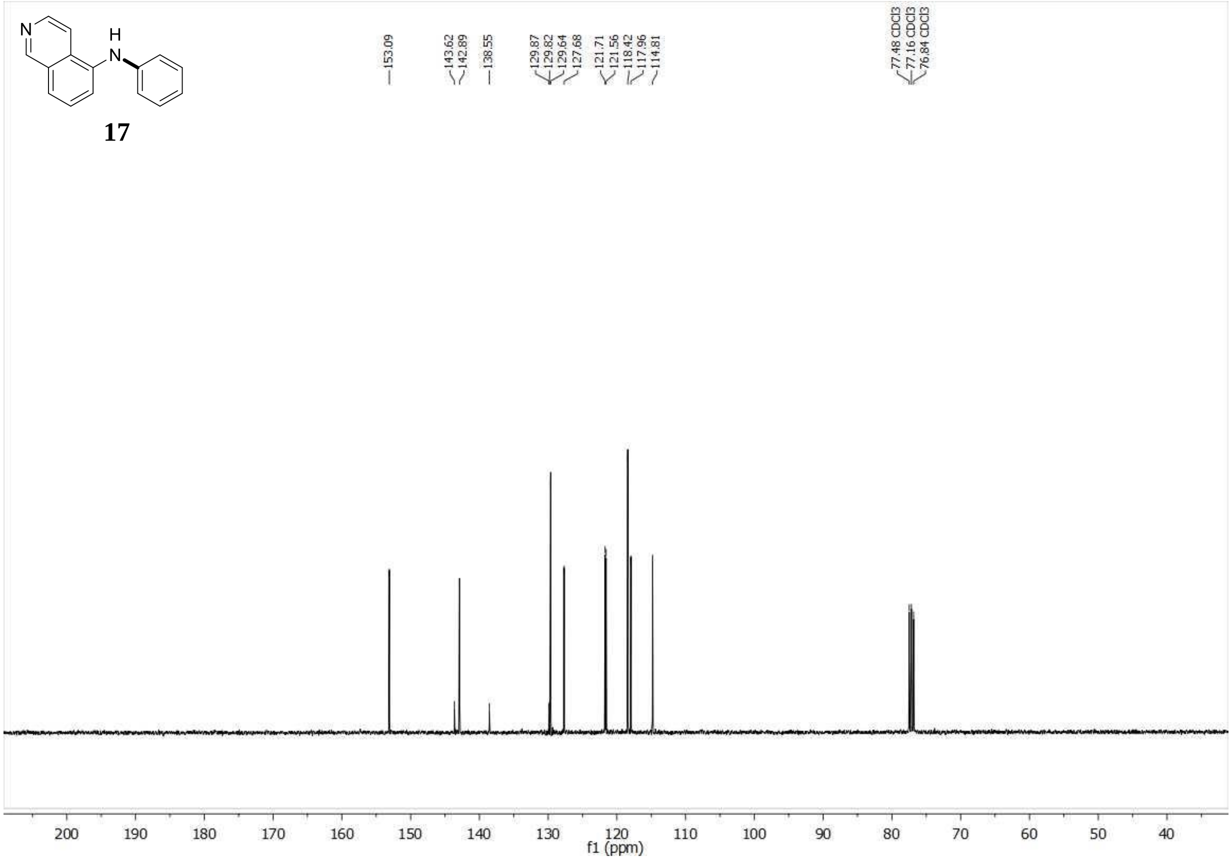
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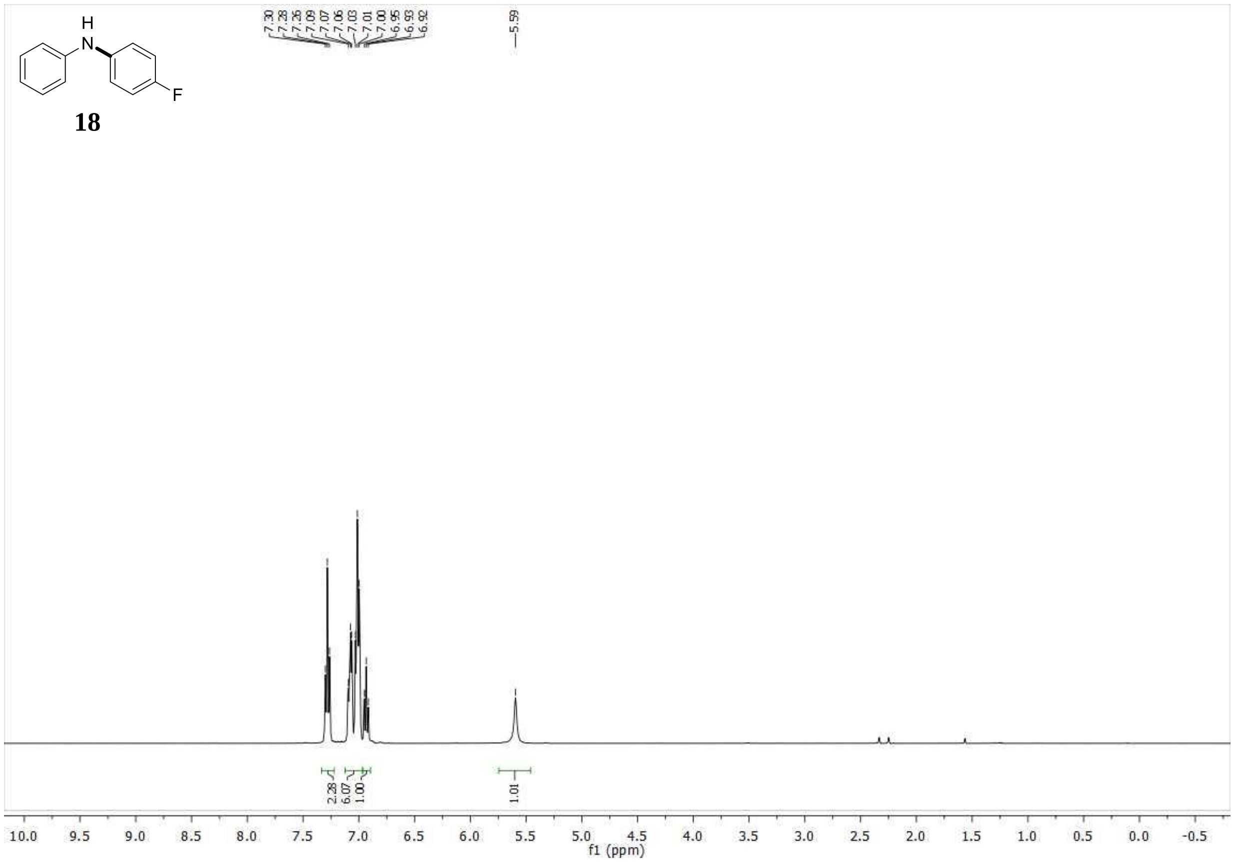
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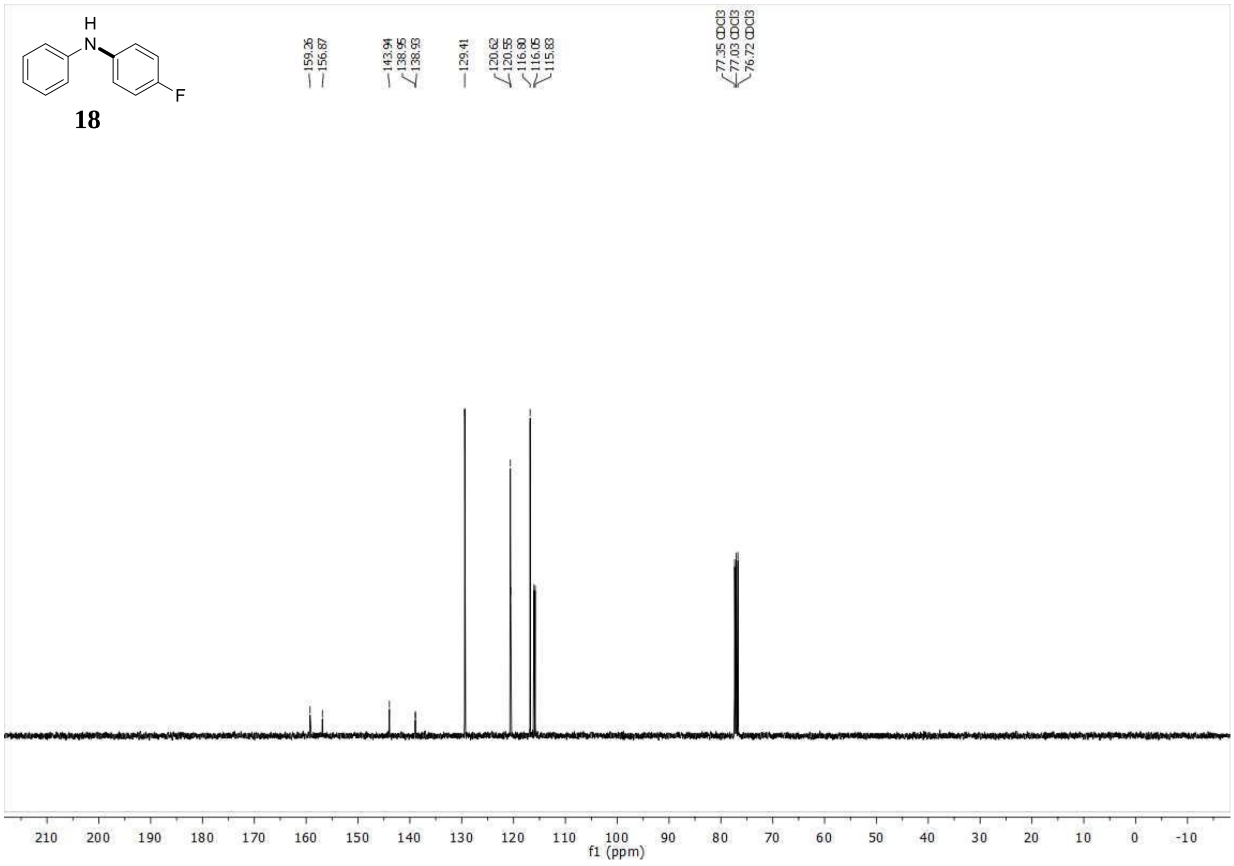
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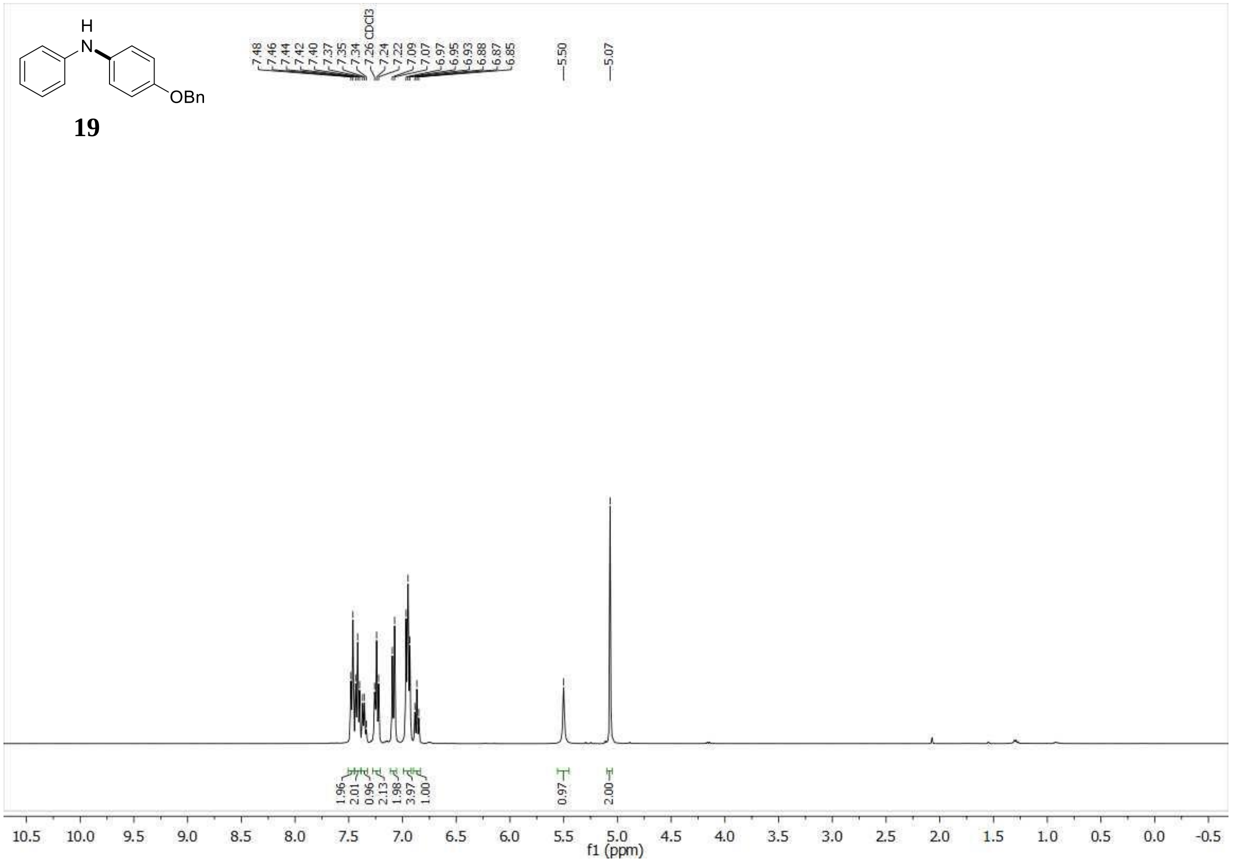
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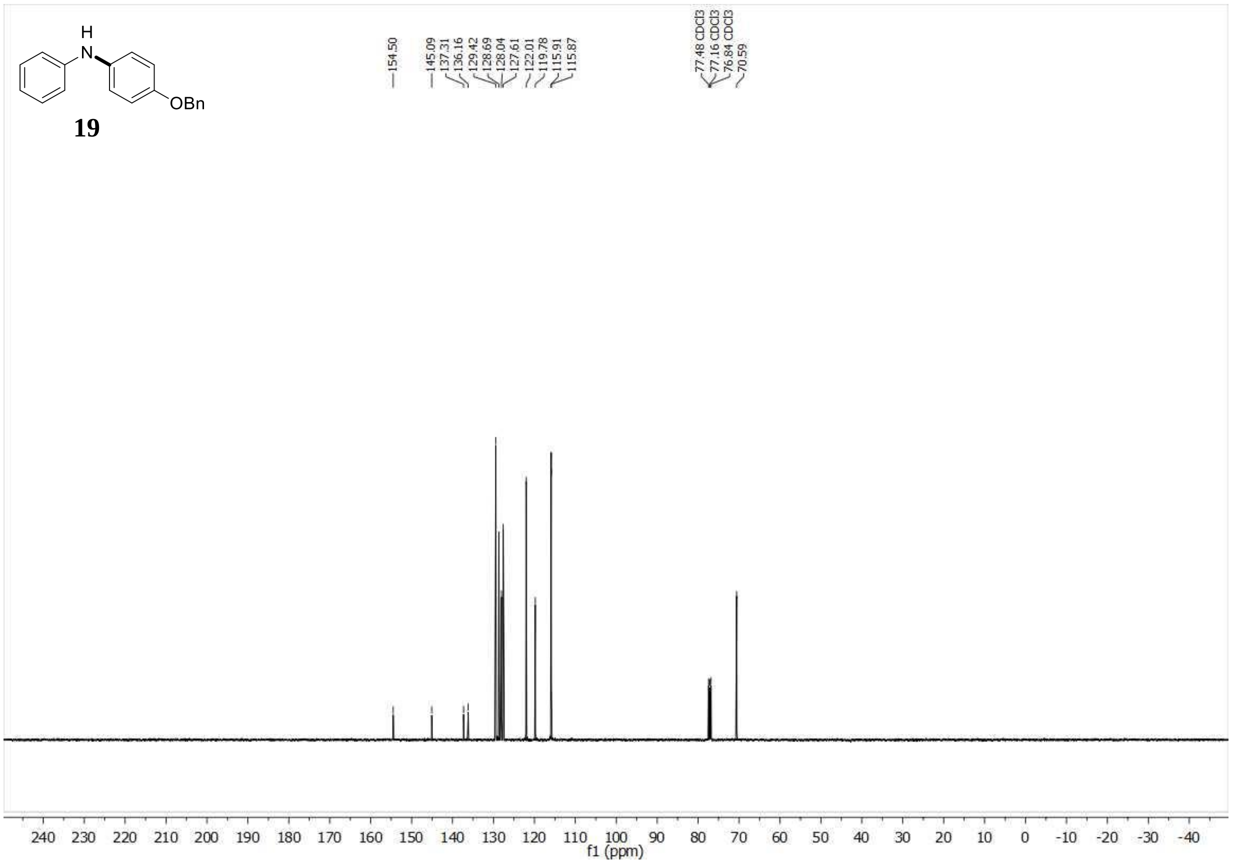
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77.16 CDCl3
76.84 CDCl3
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220
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200
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170
160
150
140
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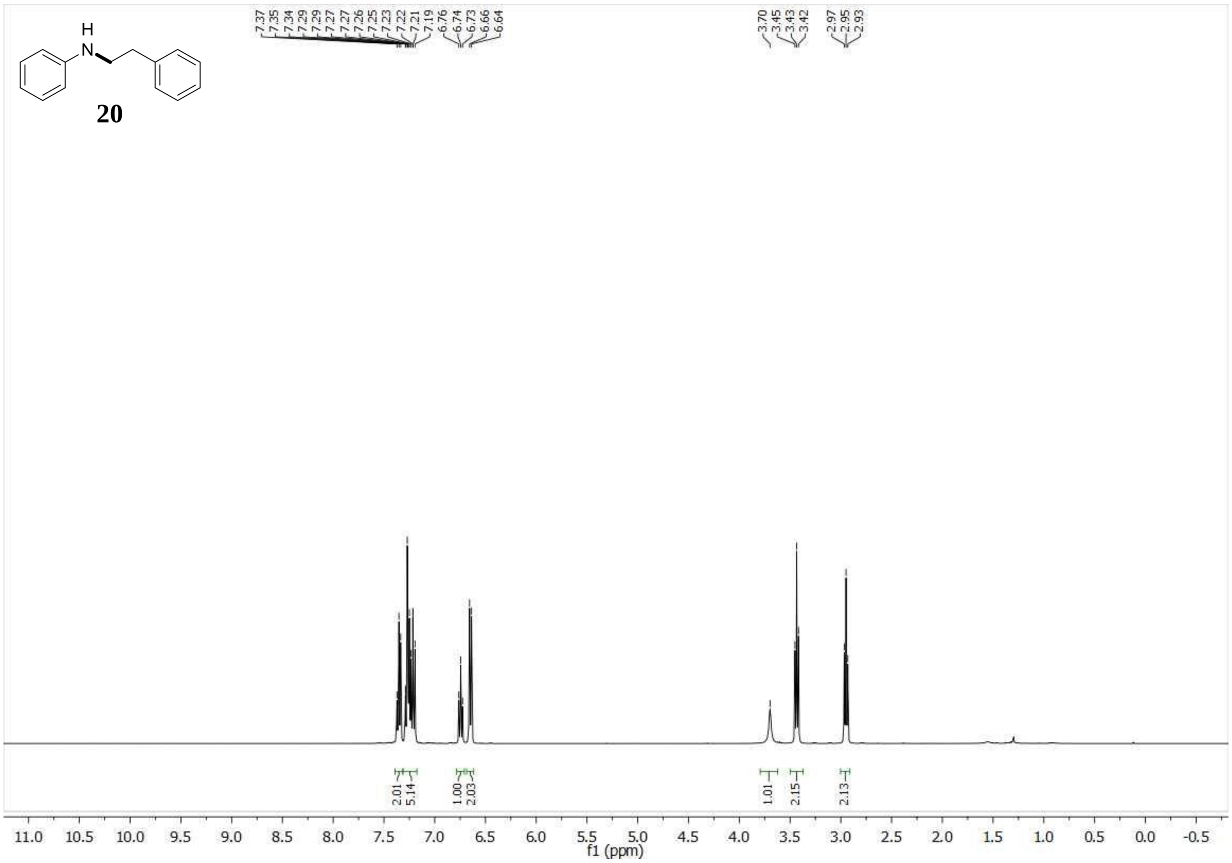
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2.95
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1.01
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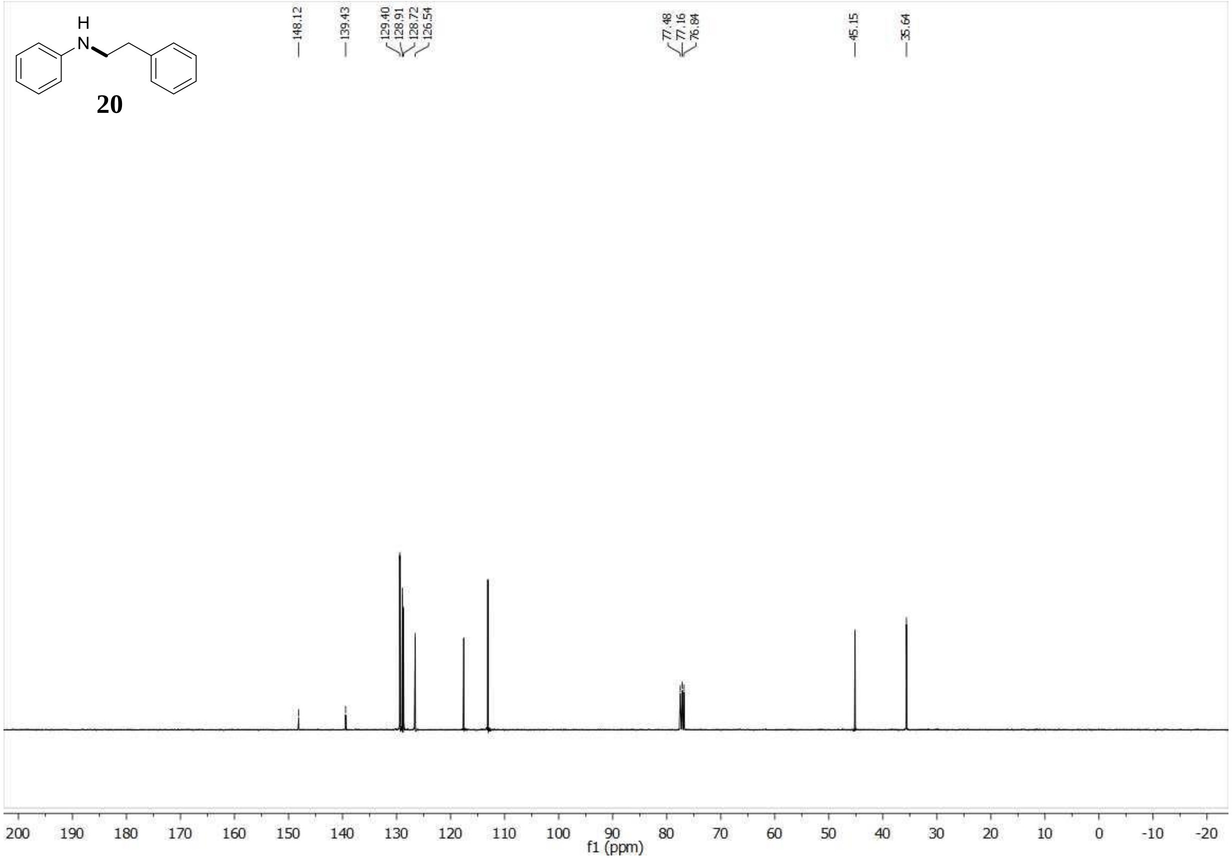
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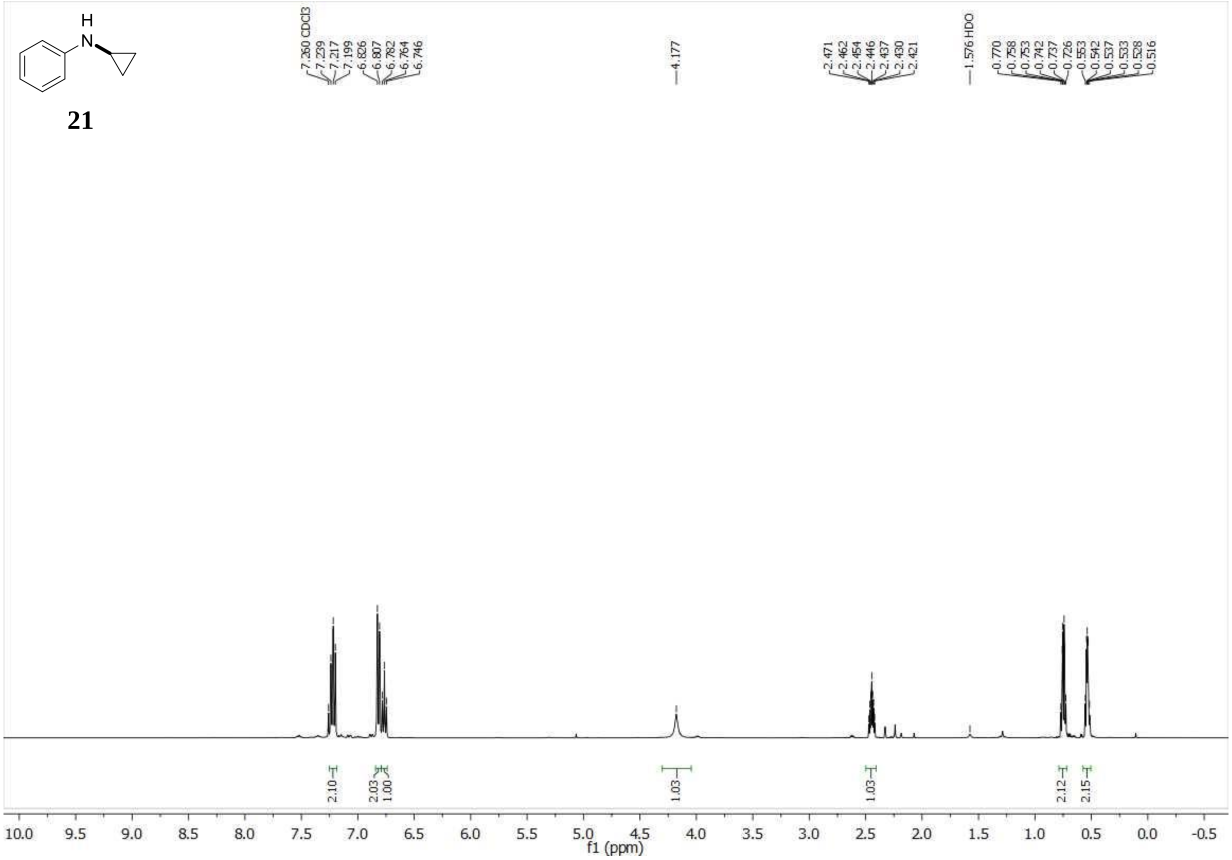
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0.533
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6.0
5.5
5.0
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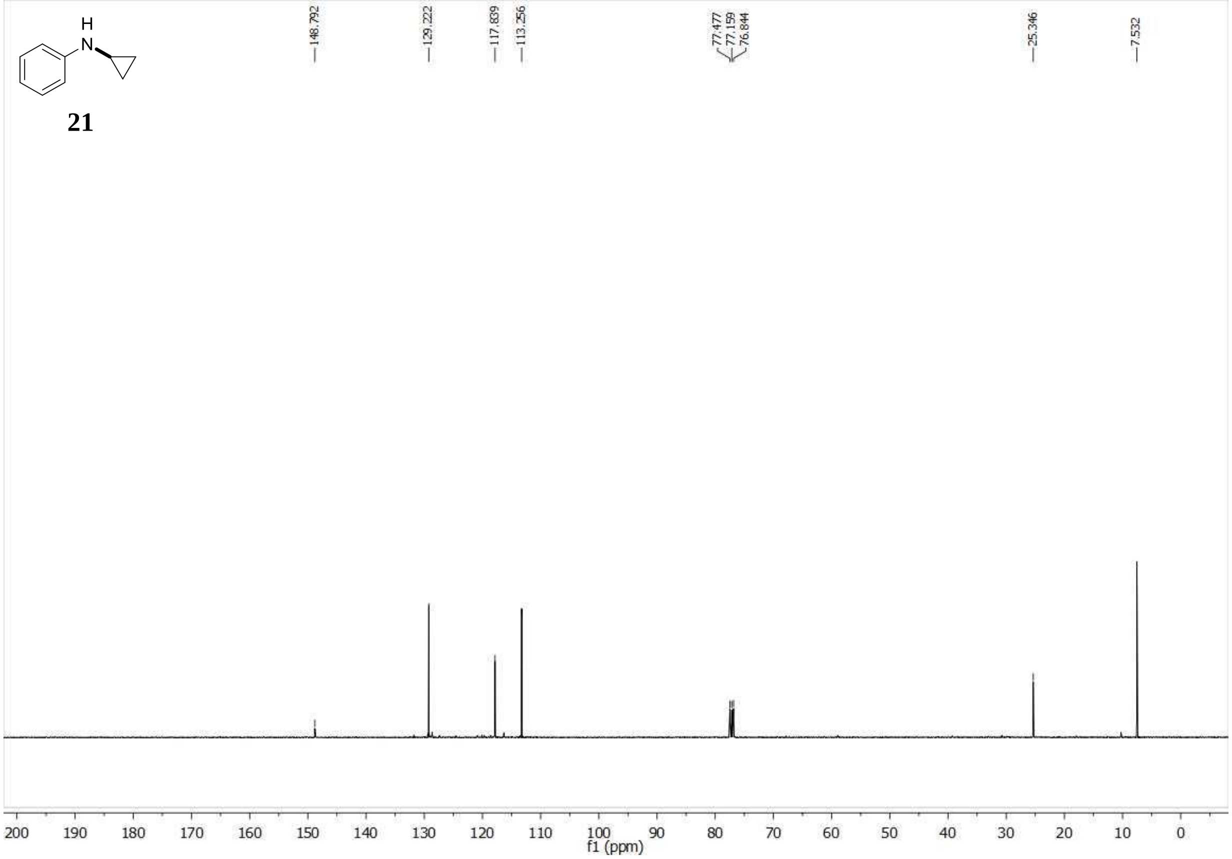
f1 (ppm)

21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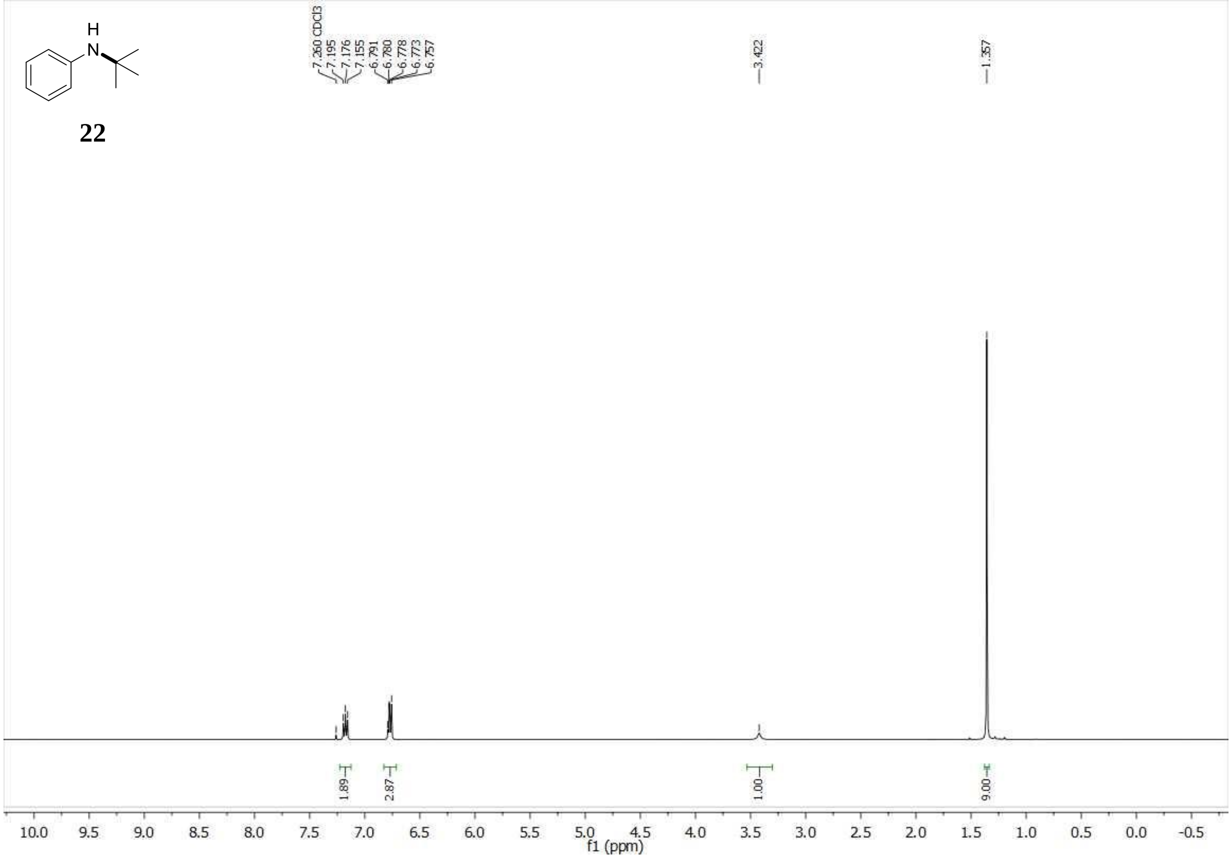
21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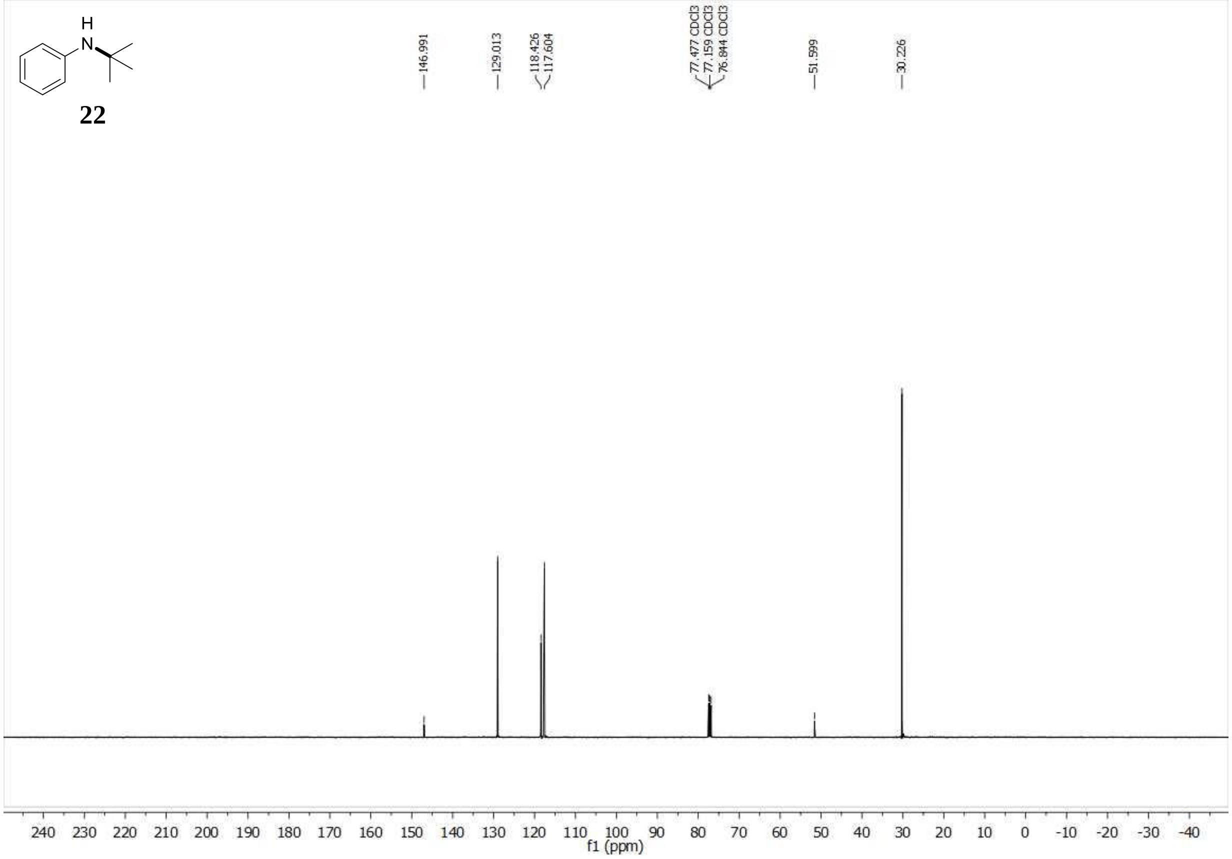
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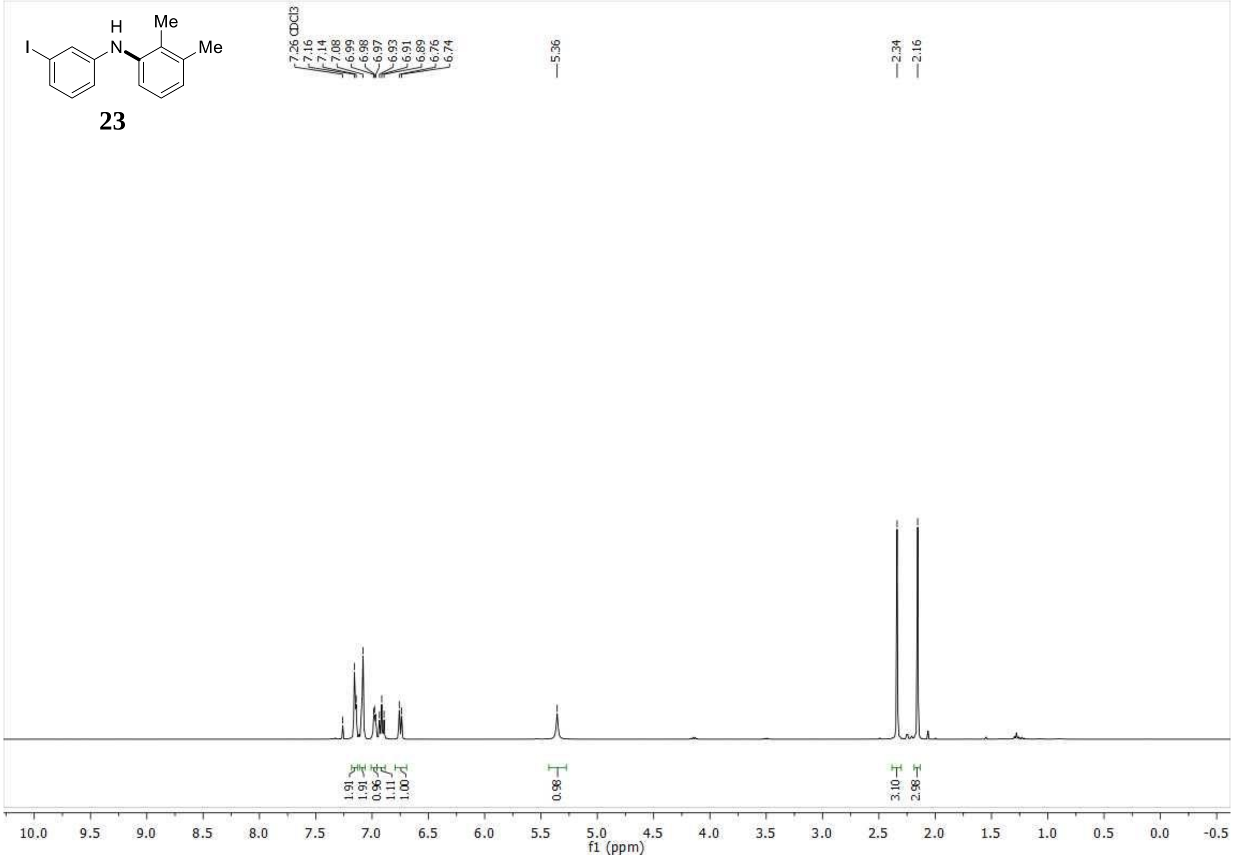
f1 (ppm)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6.74
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1.91
0.96
1.11
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0.98
3.10
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8.0
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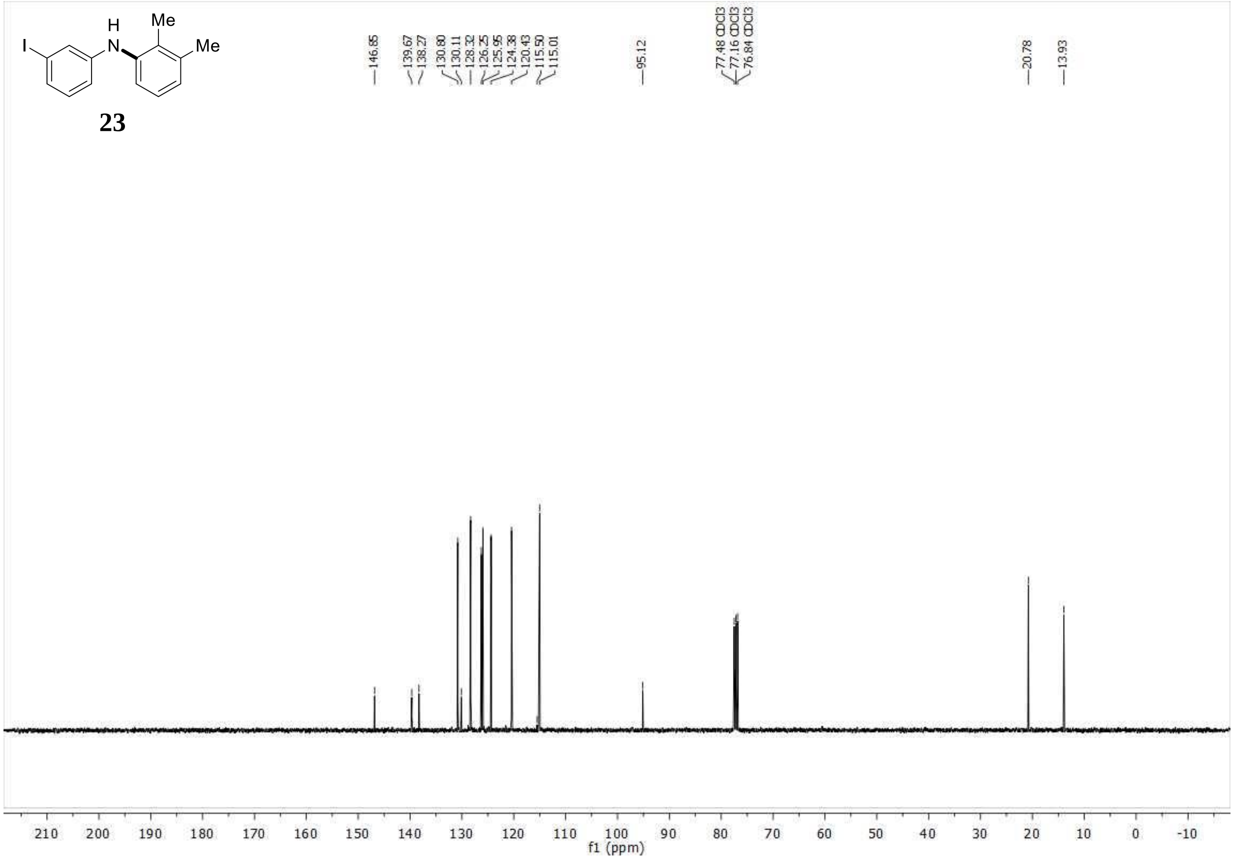
f1 (ppm)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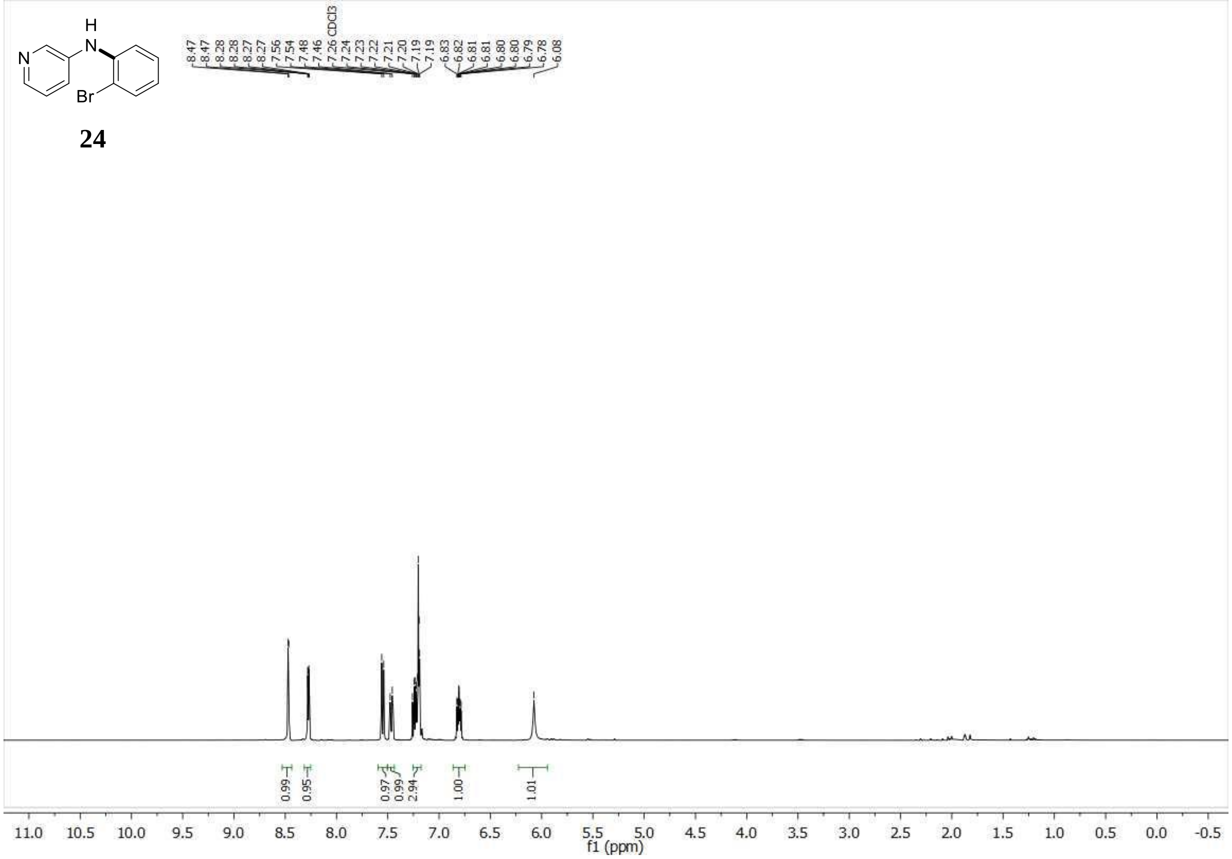
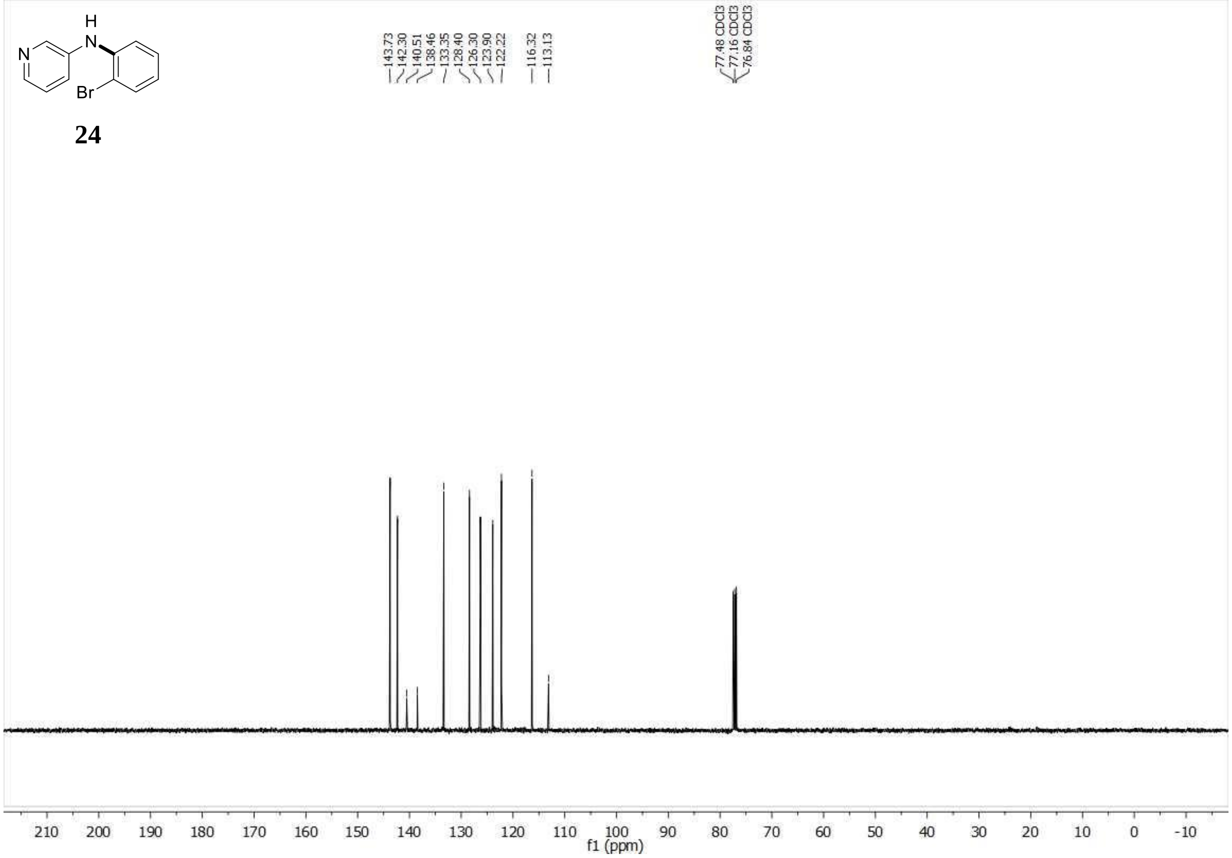
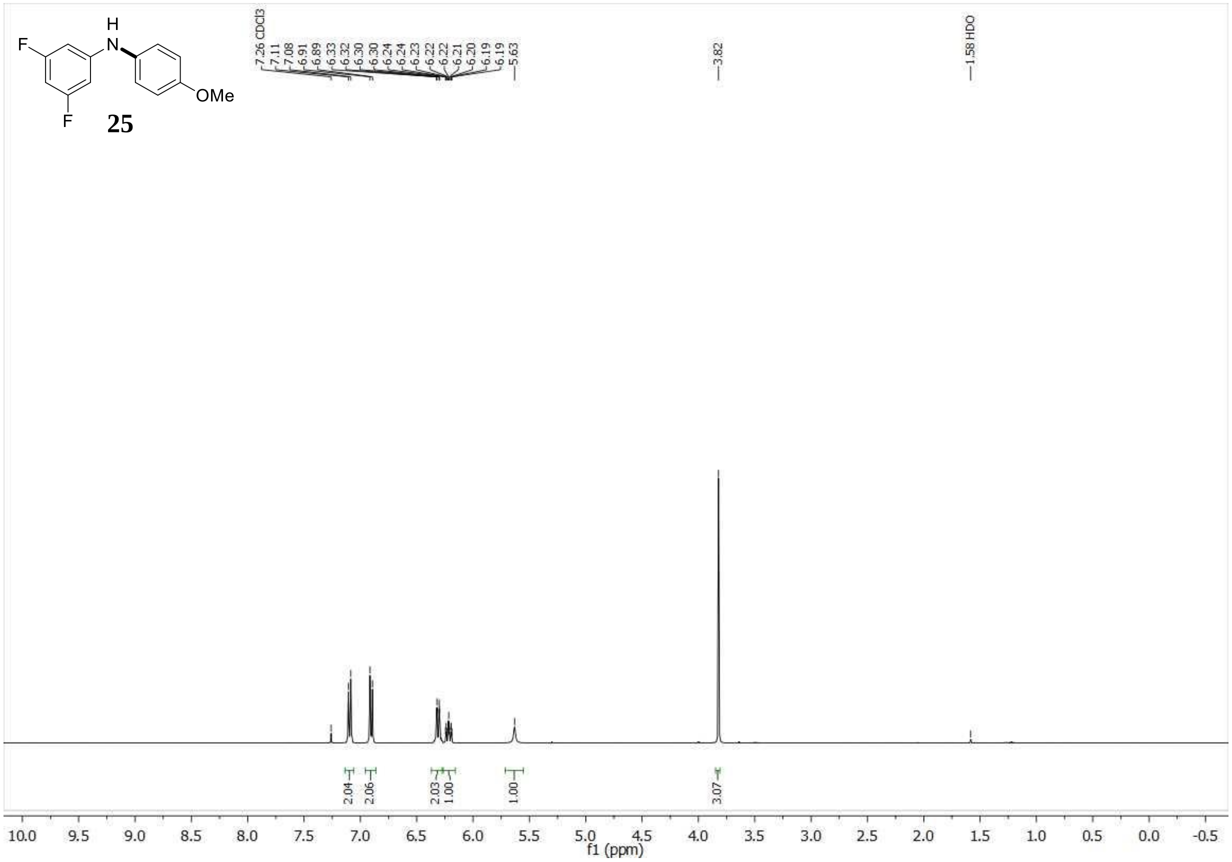
120.43
115.50
115.01
95.12
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
20.78
13.93
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


H
N
N
Br
8.47
8.47
8.28
8.28
8.27
8.27
7.56
7.54
7.48
7.46
7.26 CDCl3
7.24
7.23
7.22
7.21
7.20
7.19
7.19
6.83
6.82
6.81
6.81
6.80
6.79
6.78
6.08
0.99
0.95
0.97
0.99
2.94
1.00
1.01
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

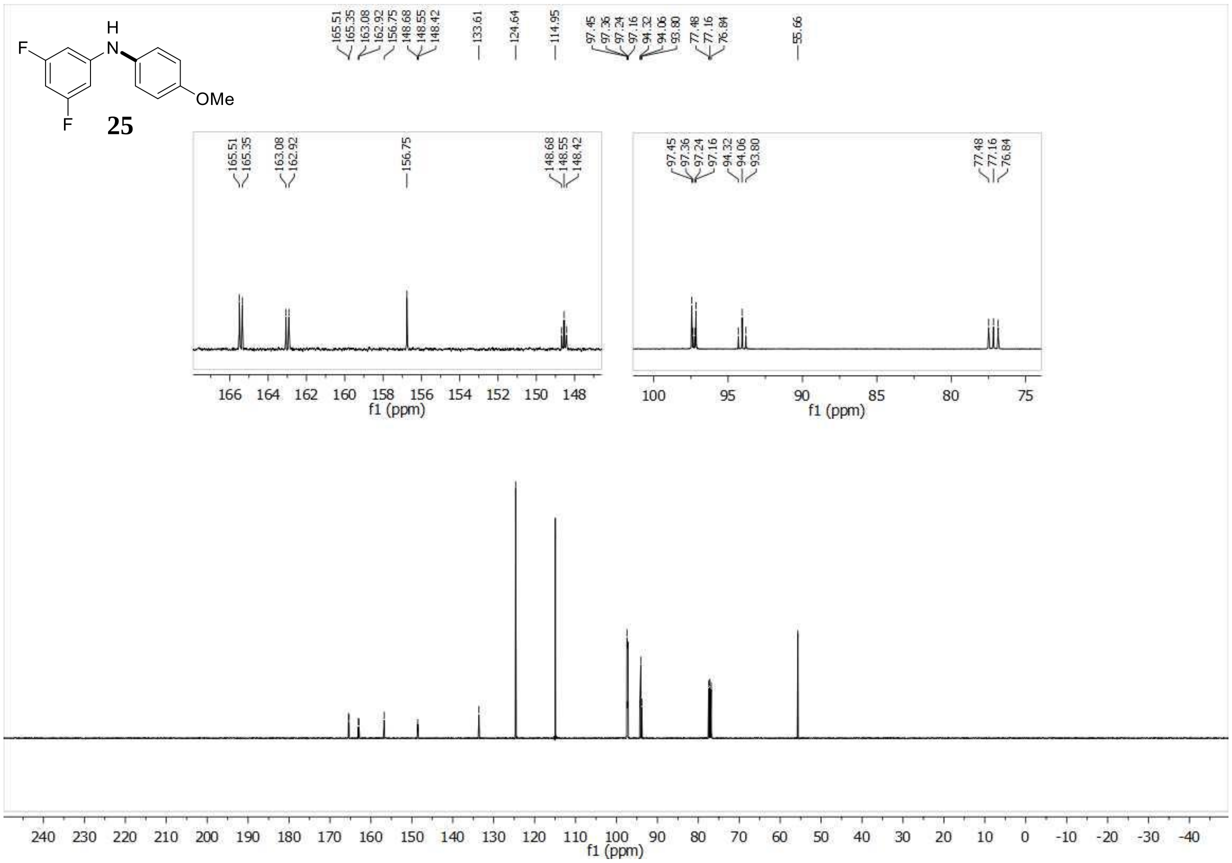
24


H
N
N
Br
143.73
142.30
140.51
138.46
133.35
128.40
126.30
123.90
122.22
116.32
113.13
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

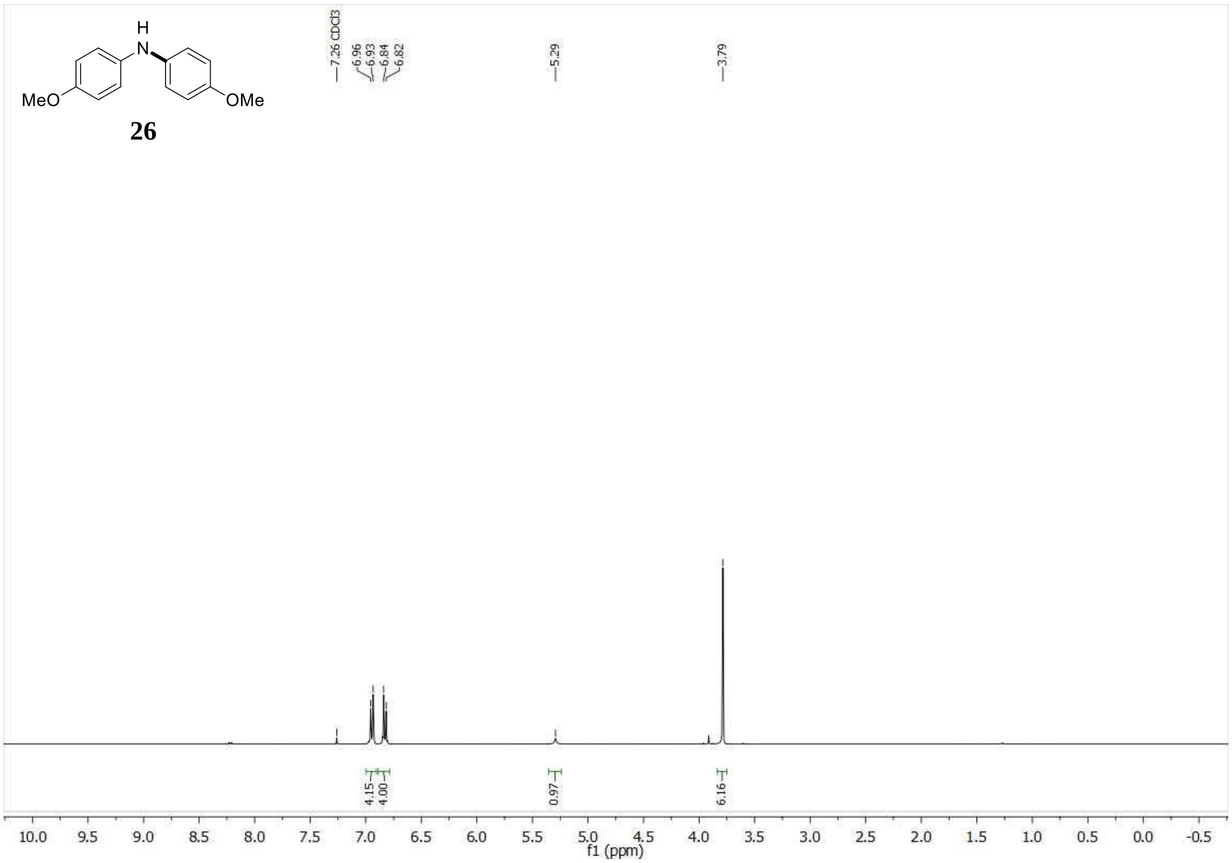
24


25

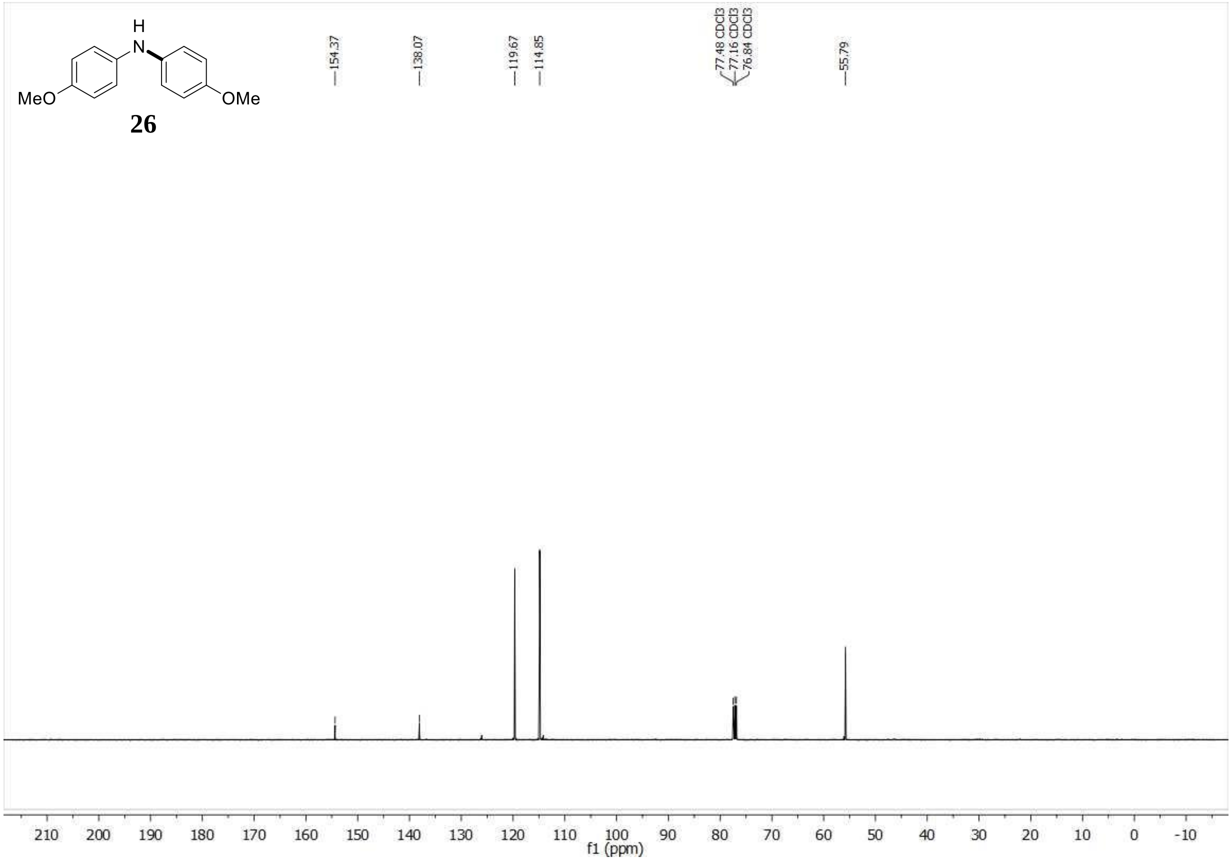
F
H
N
OMe
F
7.26 CDCl3
7.11
7.08
6.91
6.89
6.33
6.32
6.30
6.30
6.24
6.24
6.23
6.22
6.22
6.21
6.20
6.19
6.19
5.63
3.82
1.58 HDO
2.04
2.06
2.03
1.00
1.00
3.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


25

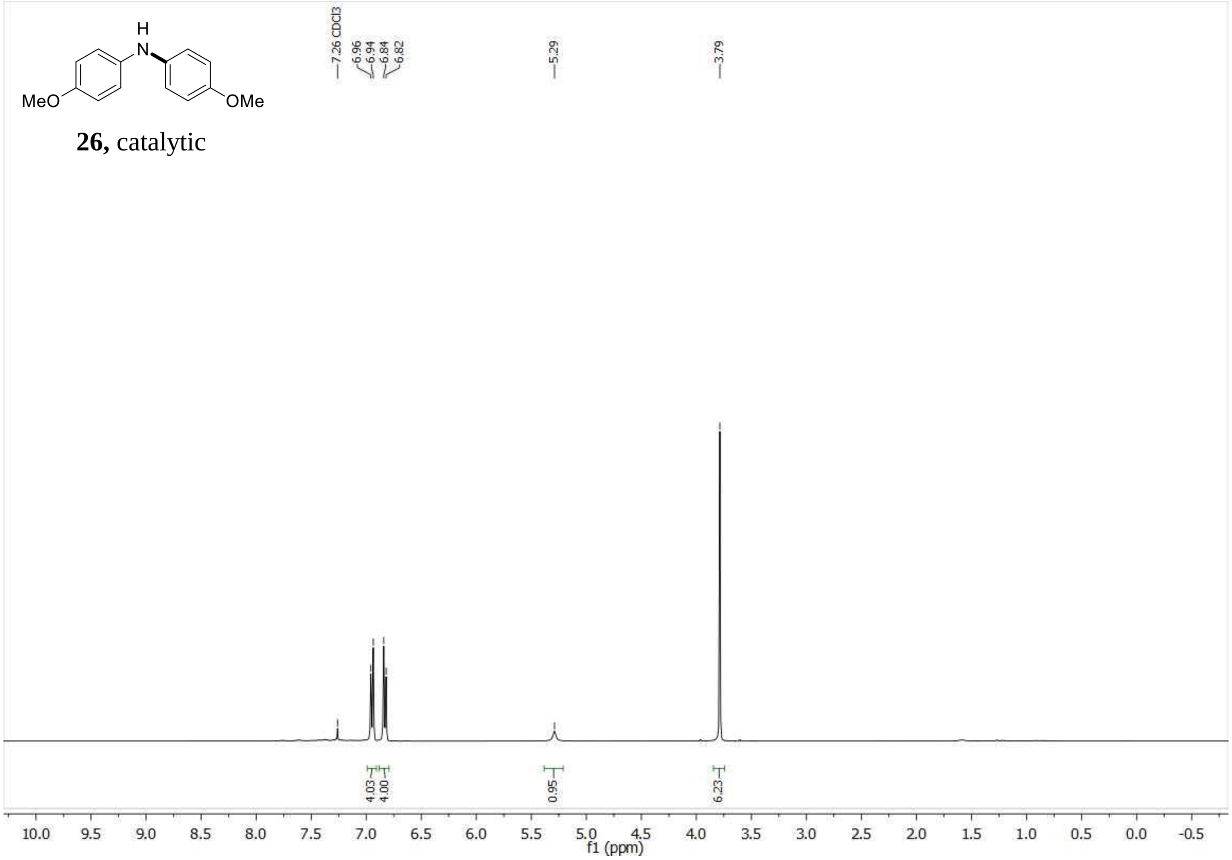
F
H
N
OMe
F
165.51
165.35
163.08
162.92
156.75
148.68
148.55
148.42
133.61
124.64
114.95
97.45
97.36
97.24
97.16
94.32
94.06
93.80
77.48
77.16
76.84
55.66
166 164 162 160 158 156 154 152 150 148
f1 (ppm)
100 95 90 85 80 75
f1 (ppm)
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)


H
N
MeO
OMe
7.26 CDCl3
6.96
6.93
6.84
6.82
5.29
3.79
4.15
4.00
0.97
6.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

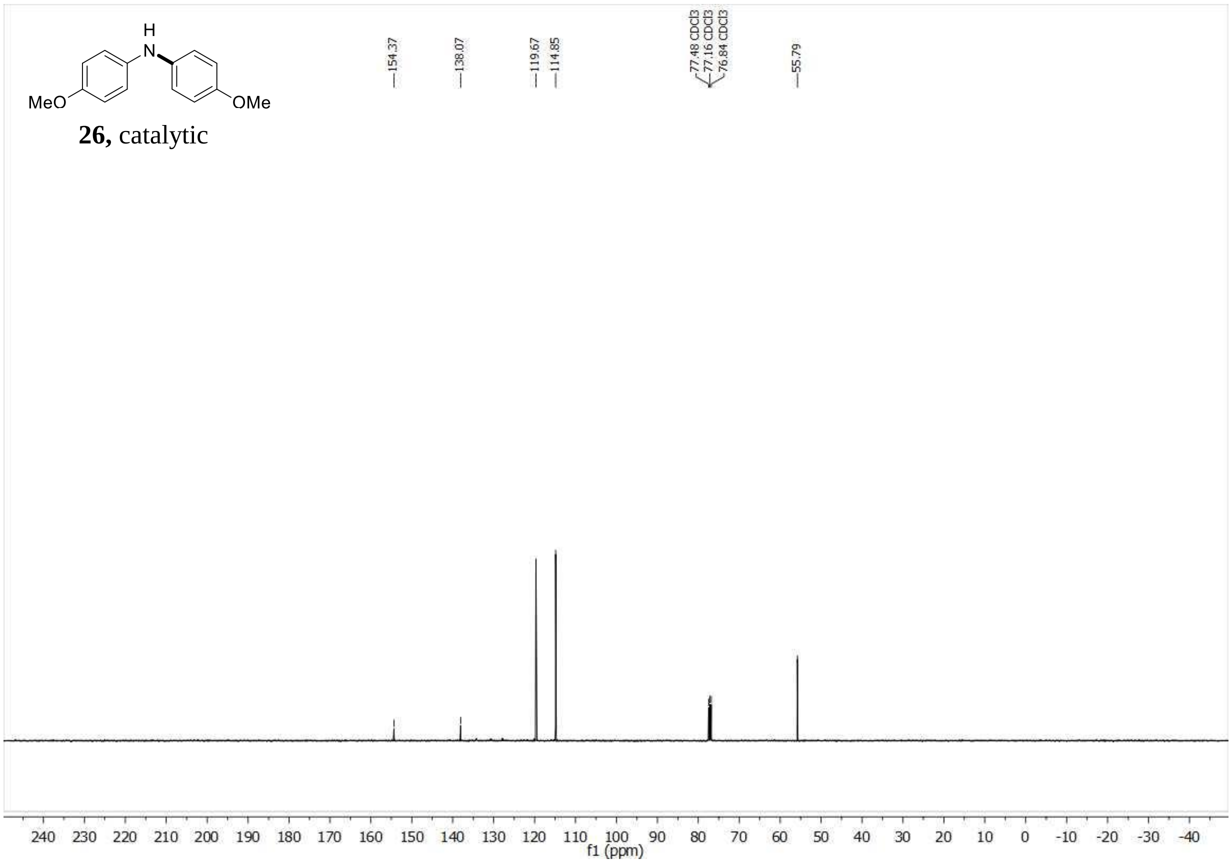
26


H
N
MeO
OMe
154.37
138.07
119.67
114.85
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.79
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

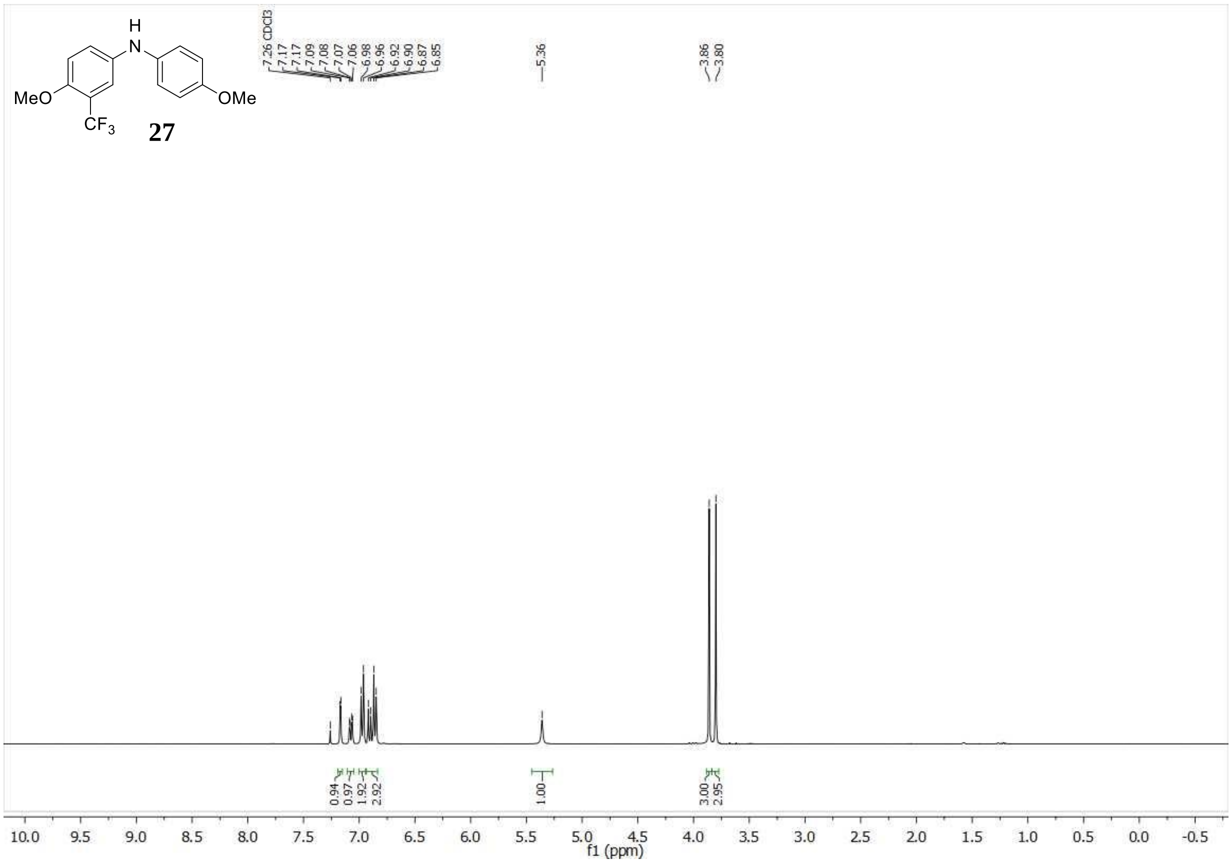
26



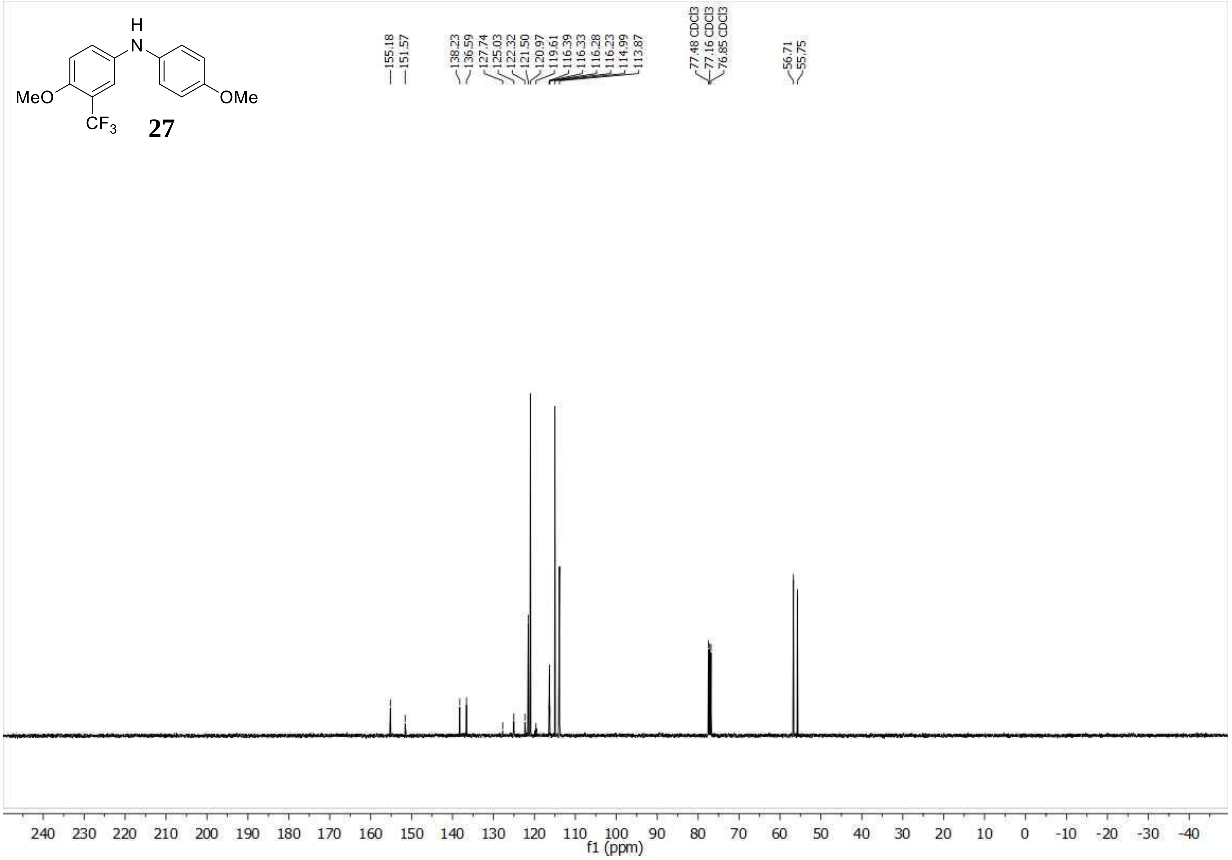
26, catalytic



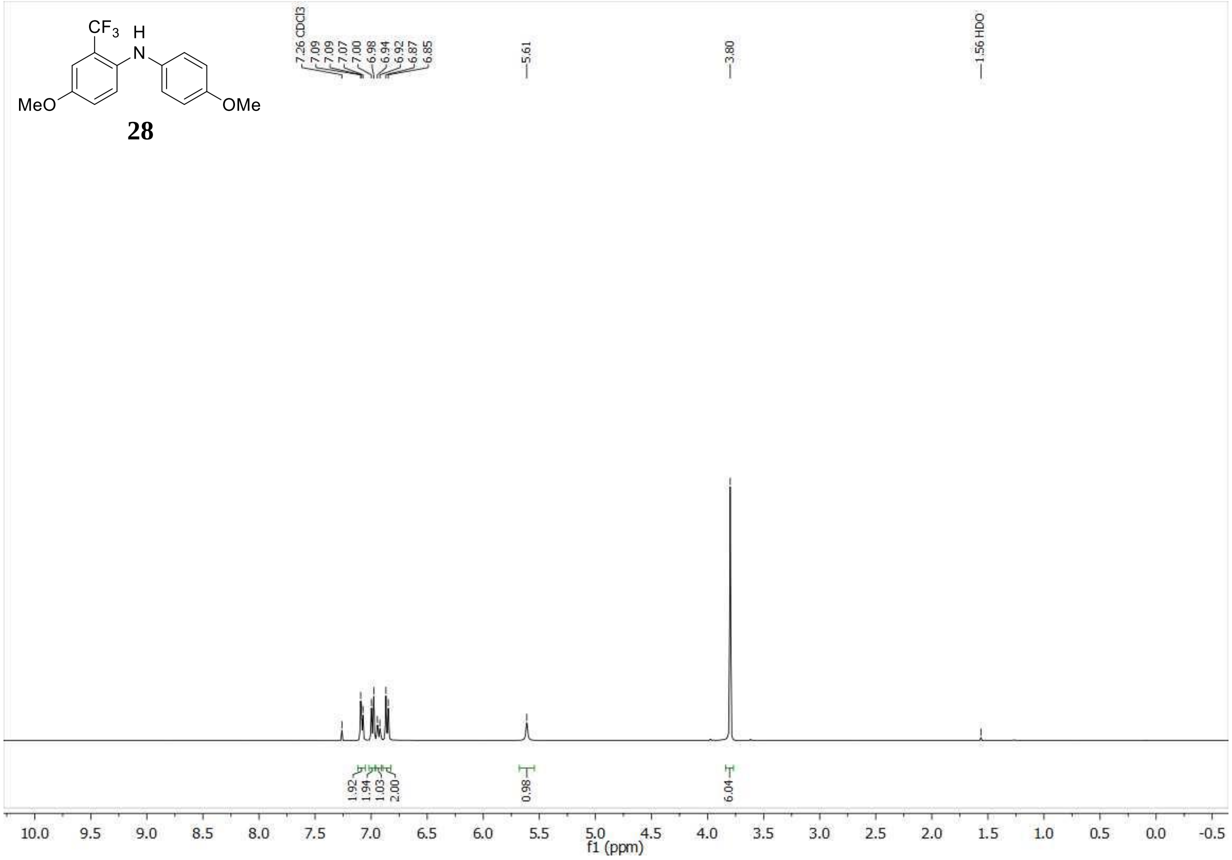
26, catalytic


H
N
MeO
OMe
CF3
7.26 CDCl3
7.17
7.17
7.09
7.08
7.07
7.06
6.98
6.96
6.92
6.90
6.87
6.85
5.36
3.86
3.80
0.94
0.97
1.92
2.92
1.00
3.00
2.95
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

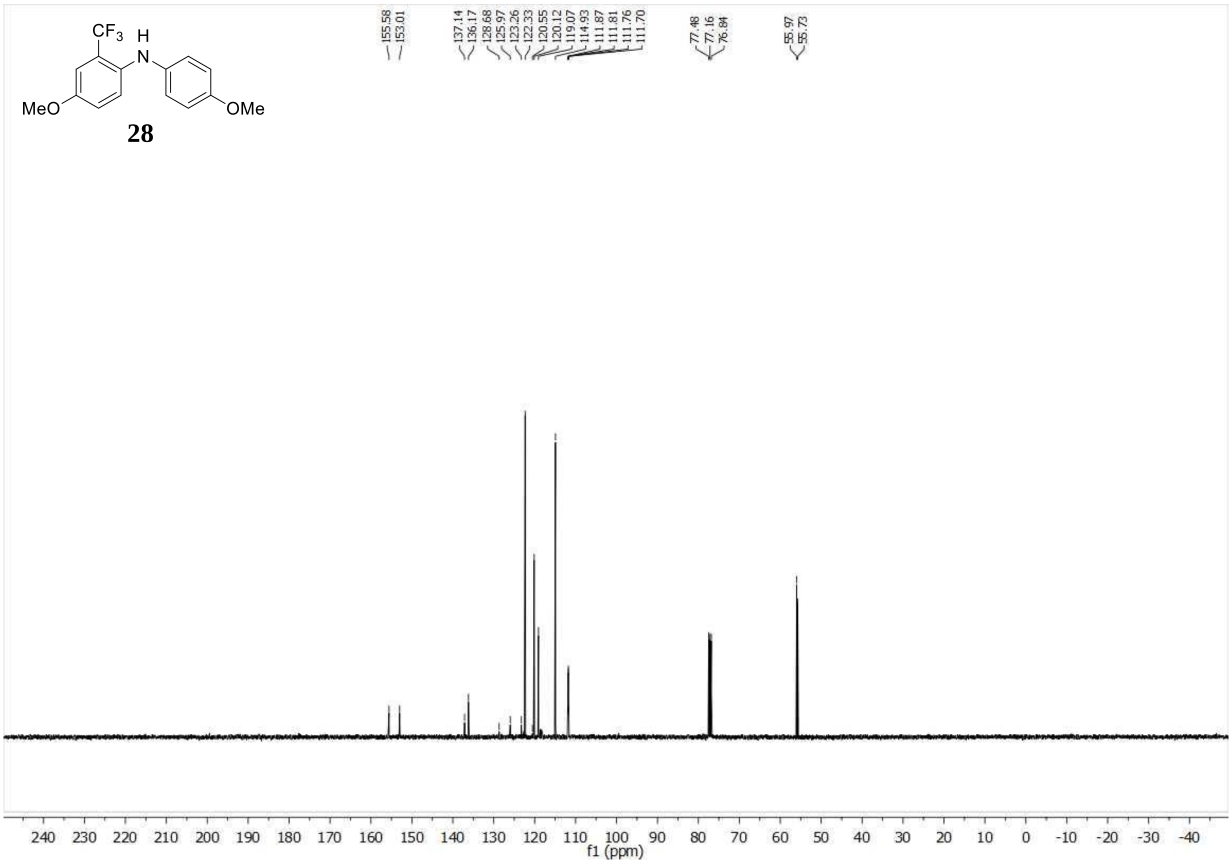
27


H
N
MeO
OMe
CF3
155.18
151.57
138.23
136.59
127.74
125.03
122.32
121.50
120.97
119.61
116.39
116.33
116.28
116.23
114.99
113.87
77.48 CDCl3
77.16 CDCl3
76.85 CDCl3
56.71
55.75
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

27



CF3
H
N
MeO
OMe
28
7.26 CDCl3
7.09
7.09
7.07
7.00
6.98
6.94
6.92
6.87
6.85
5.61
3.80
1.56 HDO
1.92
1.94
1.03
2.00
0.98
6.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



CF3
H
N
MeO
OMe
28
155.58
153.01
137.14
136.17
128.68
125.97
123.26
122.33
120.55
120.12
119.07
114.93
111.87
111.81
111.76
111.70
77.48
77.16
76.84
55.97
55.73
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
f1 (ppm)