Electronic Supplementary Material (ESI) for RSC Advances.

Supporting information

One-step Synthesis of Imidazo[1,2-*a*]pyridines in Water

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Contents:

Preparation of thioformamidinium salts **2**:

Part A- Preparation of thioamide derivatives from the corresponding benzaldehydes:

In a 50 mL two-neck round-bottom flask, equipped with a reflux condenseranda thermometer, benzaldehyde derivative (50 mmol), morpholine (100 mmol, 8.6 mL), and sulfur (70 mmol, 2.24 g) were heated to 130 °C for 5h. After cooling to 65 °C, the reaction mixture was poured in warm MeOH (50 °C, 25 mL) and set aside in a refrigerator for 2h. Then, the precipitated crystals were filtered and washed with cold MeOH (0 °C, 2×10 mL) to obtain the corresponding thioamides as light yellow to yellow needles.

Part B- Preparation of the 4-((methylthio)(aryl)methylene)morpholinium iodide **2**:

In a 100 mL flask, thioamide derivative (20 mmol) was dissolved in dry THF (40 mL) and MeI (25 mmol, 3.55 g, 1.56 mL) was added dropwise during 10 min. The reaction mixture was stirred at room temperature overnight and the precipitated salt was filtered and washed with cold THF (10 mL) to gain the pure salt as light yellow powders.

Synthetic procedure for the preparation of 3-(4-nitrophenyl)-2-phenylimidazo[1,2-a]pyridine **3a** in acetonitrile:

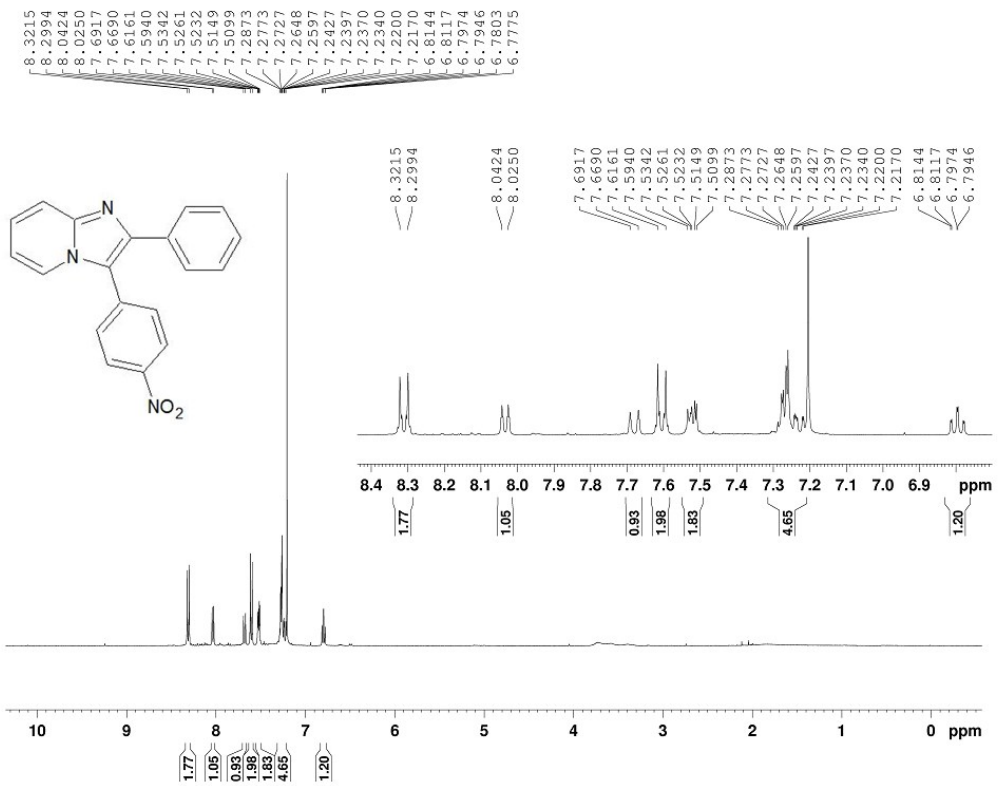
In a 25 mL round bottom flask, 2-amino-1-(4-nitrobenzyl)pyridinium bromide **1a** (1 mmol, 310 mg) and 4-(methylthio)(phenyl)methylene)morpholinium iodide **2a** (1 mmol, 349 mg) were dissolved in CH_3CN (5 mL) and DBU (2 mmol, 0.3 ml) was added dropwise during 5 min at room temperature. The reaction mixture was stirred vigorously and the reaction temperature raised to 75 °C and heated at this temperature overnight (12 h). After stripping off the half of solvent under reduced pressure, water (1 mL) was added and set it aside to crystallize. The crude crystals were recrystallized from EtOH to obtain pure compound **3a** as deep yellow crystals (243 mg, 77%).

General procedure for the preparation of imidazo[1,2-*a*]pyridines **3a-3o** in water:

In a 25 mL round bottom flask, pyridinium salt **1** (1 mmol) and 4-(methylthio)(aryl)methylene) morpholinium iodide **2** (1 mmol) were suspended in water (5 mL) and heated to 75 °C with vigorous stirring. Then Na_2CO_3 (2 mmol, 212 mg) was added to the reaction mixture at once and heating was continued at the same temperature for 4h. After that, the reaction mixture was cooled to room temperature and the precipitated crude product was filtered and washed with water (10 mL) followed by cold MeOH (5 mL). Finally, the crude crystals were recrystallized from EtOH to obtain pure compounds **3a-3o** as deep yellow to yellowish orange crystals.

Unusual reaction of 2-amino-1-(4-nitrobenzyl)pyridinium bromide **1a** with DBU in CH_3CN:

In a 25 mL round bottom flask, pyridinium salt **1** (1 mmol) and DBU (2 mmol, 304 mg) were dissolved in CH_3CN and the reaction mixture was heated under reflux condition for 20 h. After evaporation of half of solvent, the final deep yellow product was precipitated on cooling to room temperature. The crude solid was filtered and recrystallized from EtOH to obtain compound **3p** as yellowish-orange needles in moderate yield (173 mg, 48%).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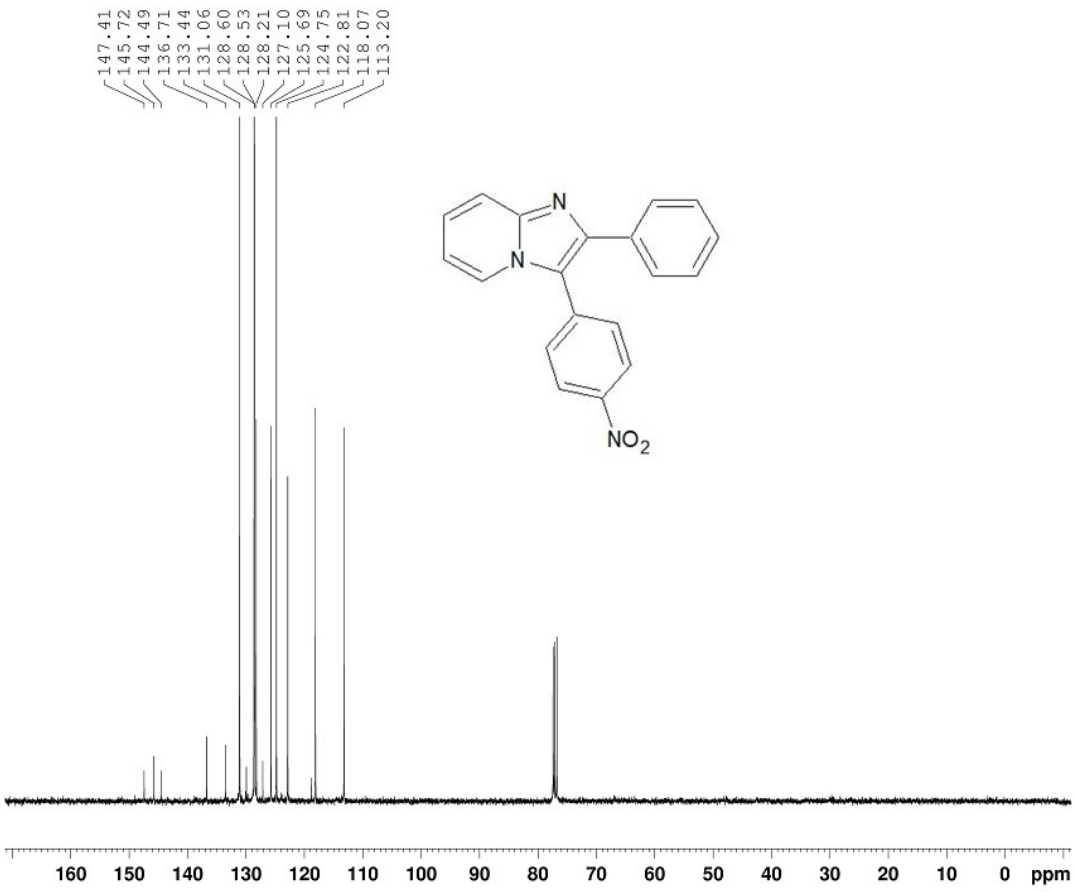
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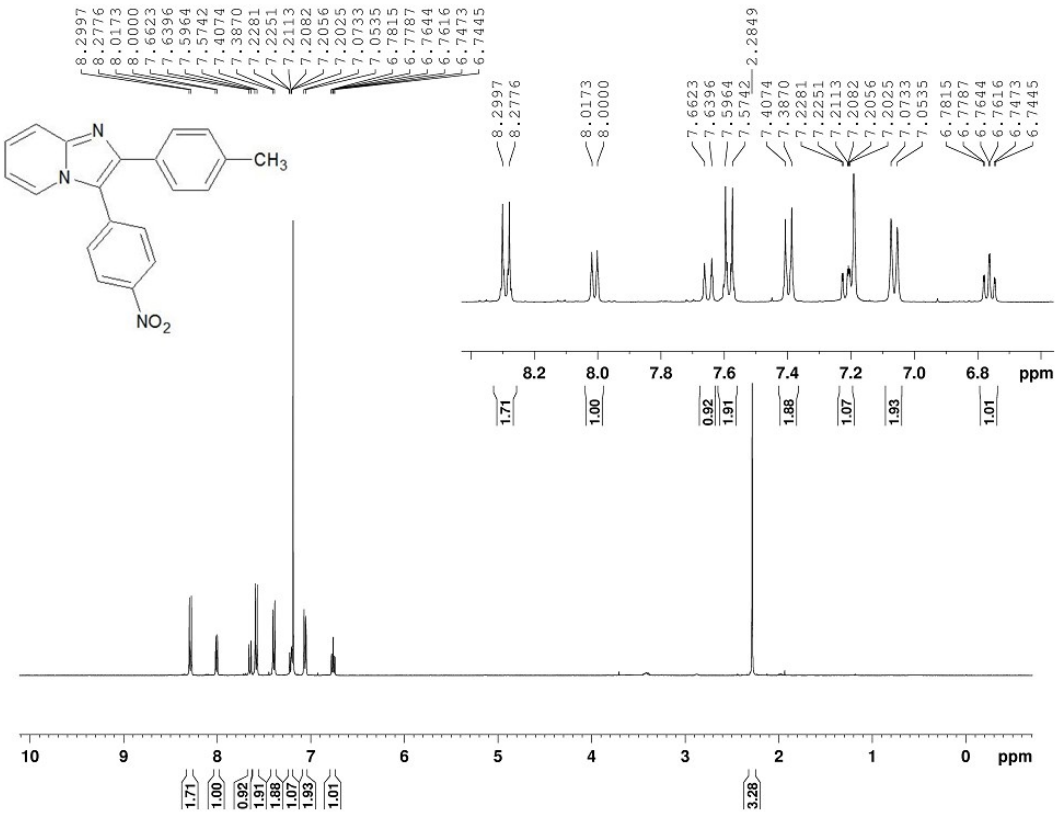
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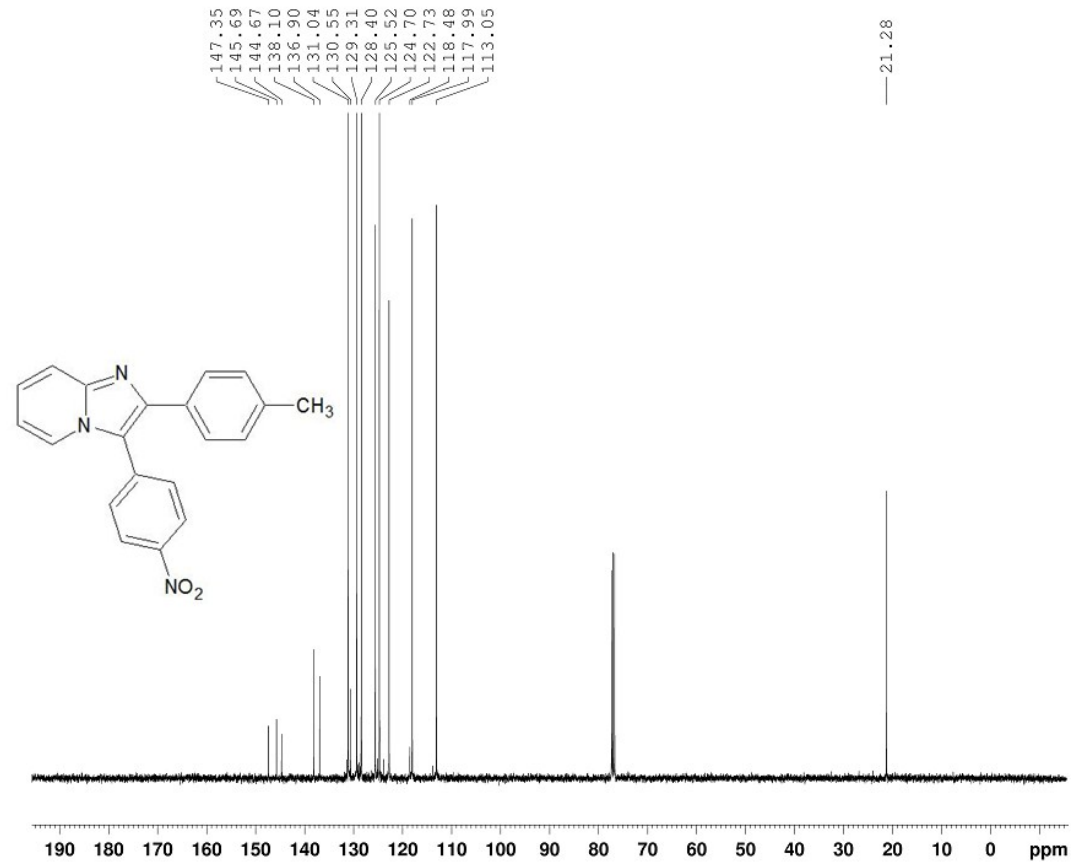
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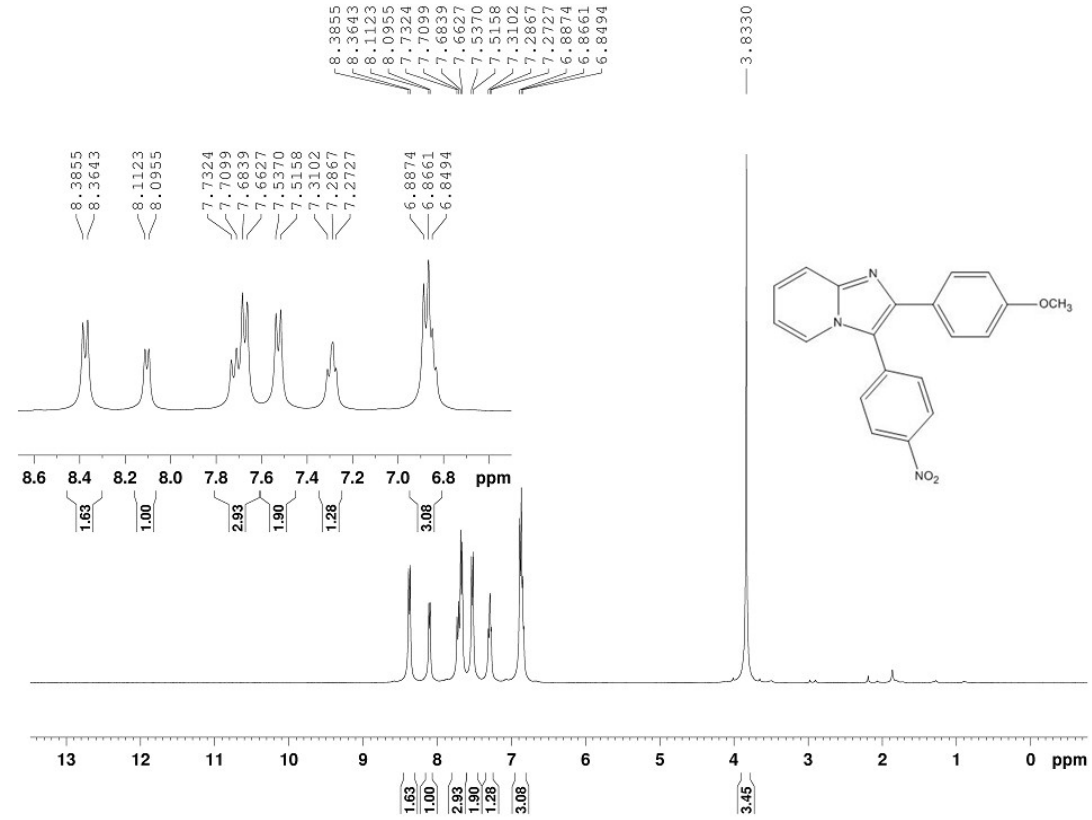
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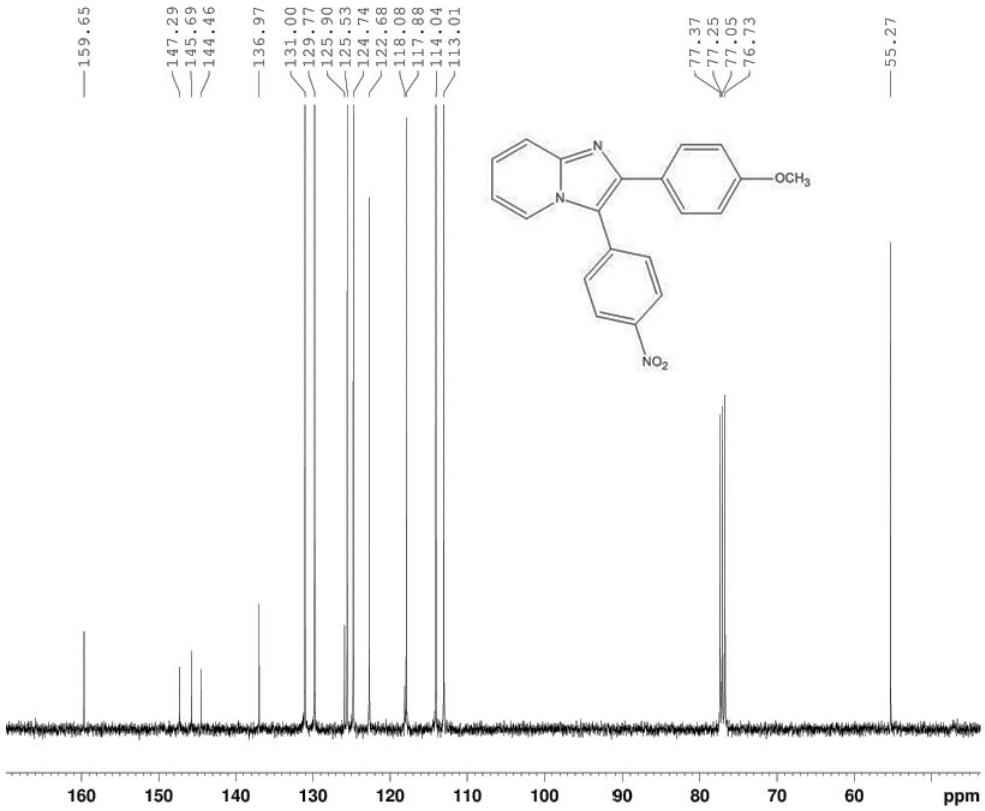
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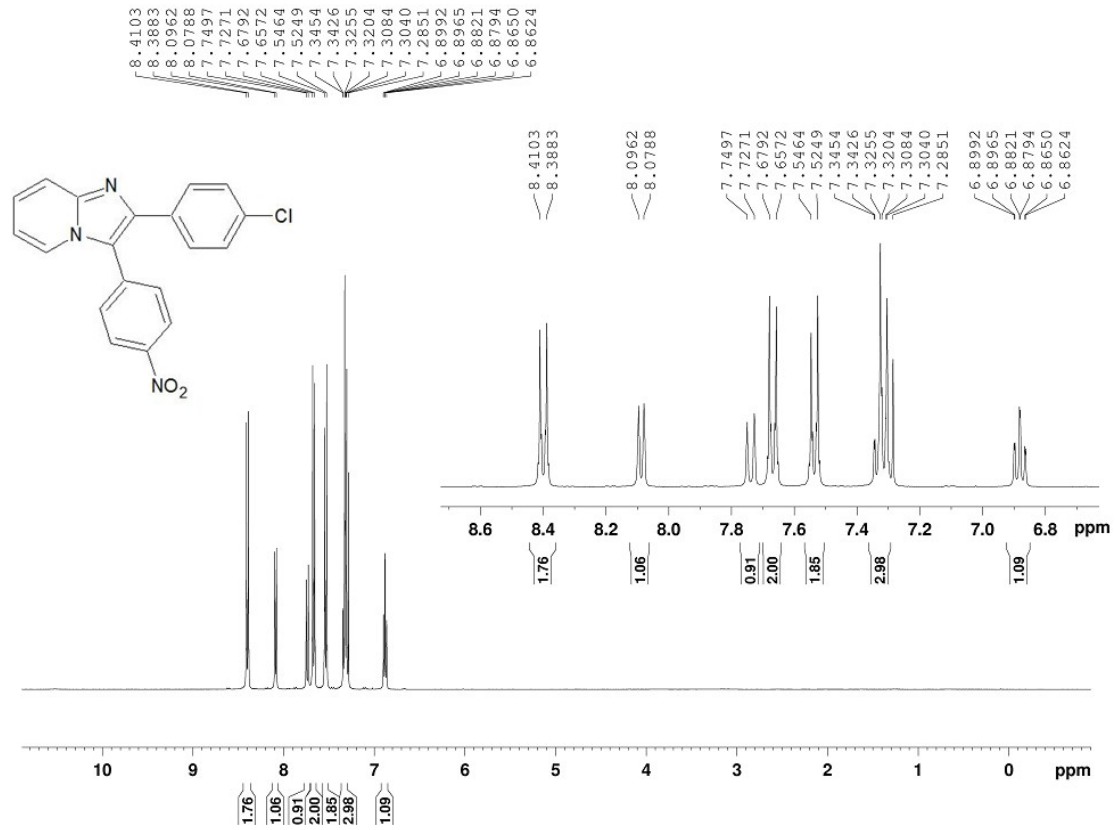
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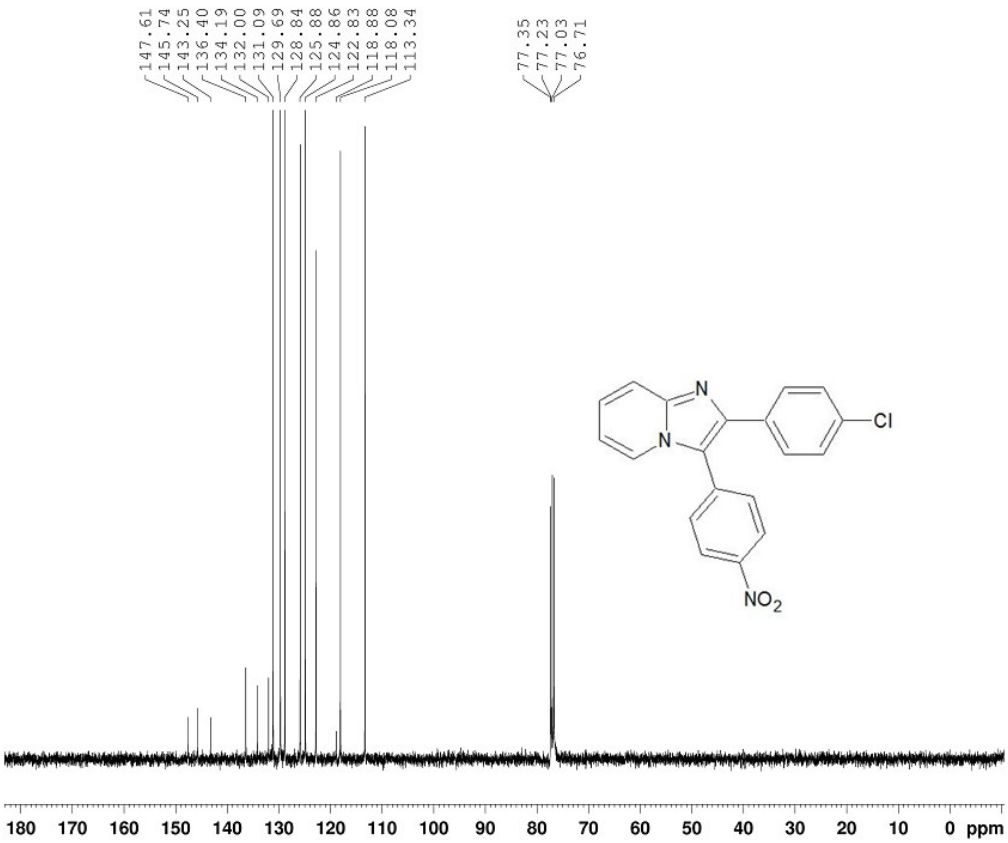
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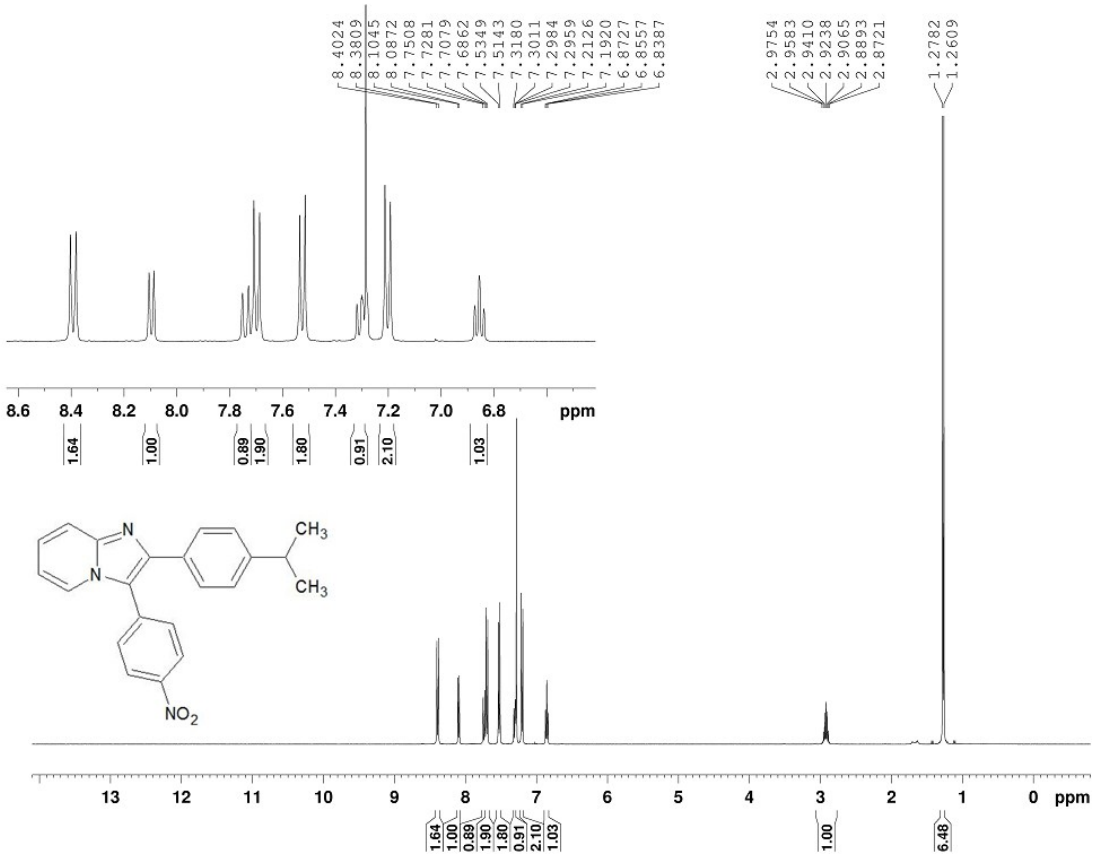
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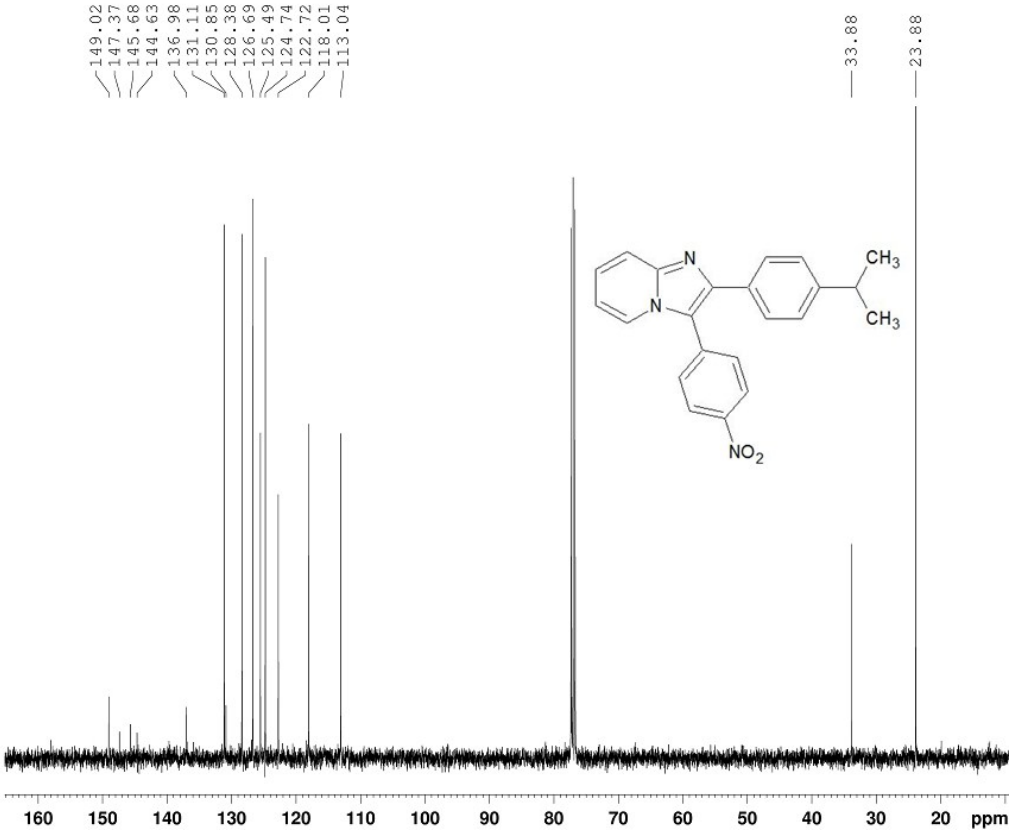
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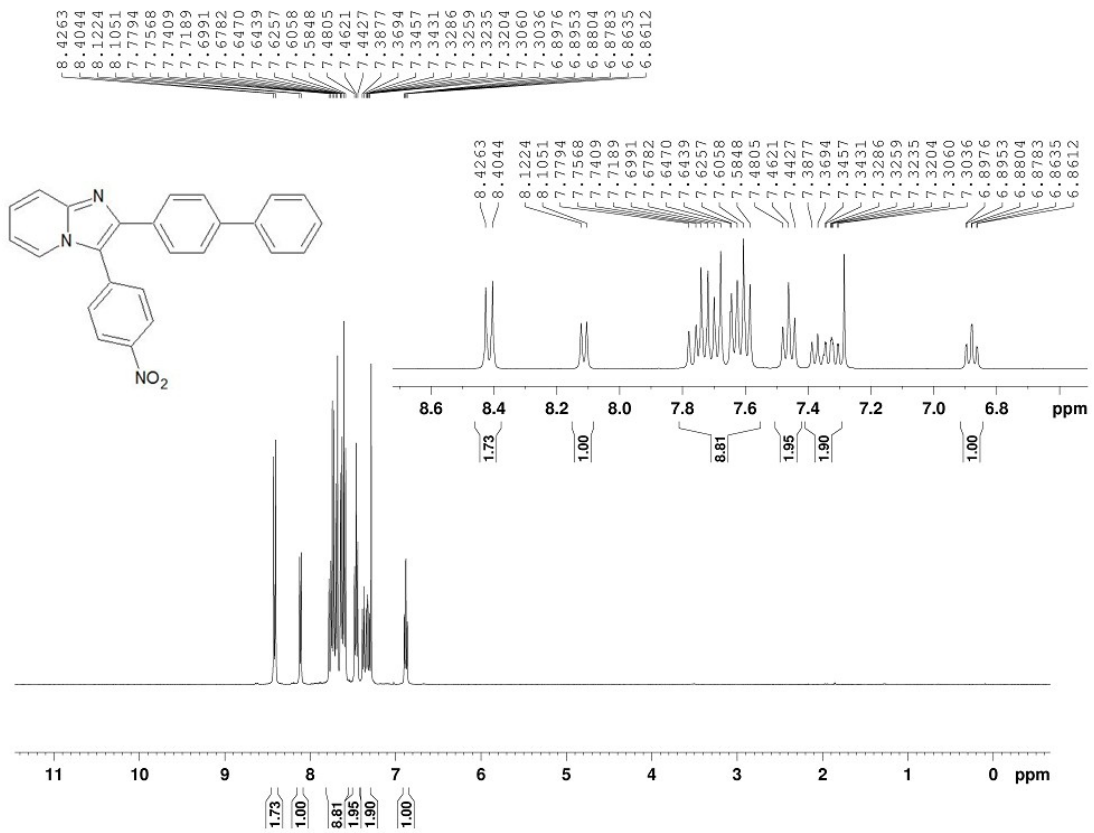
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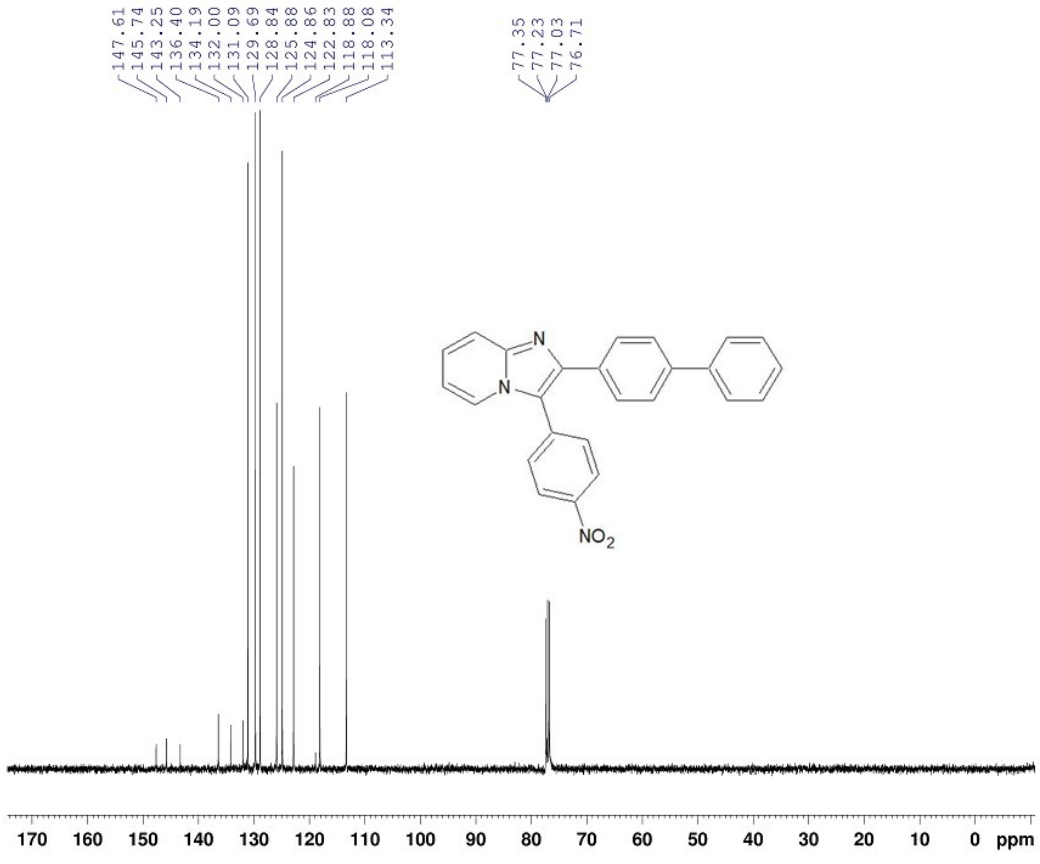
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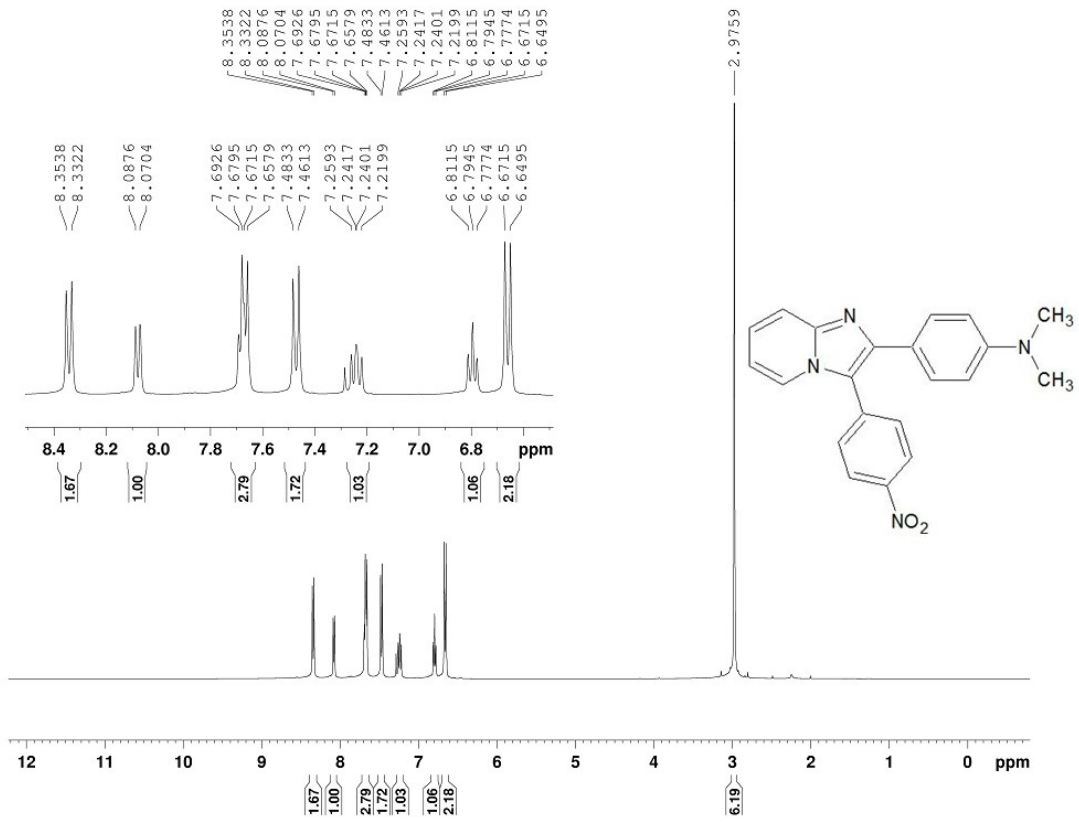
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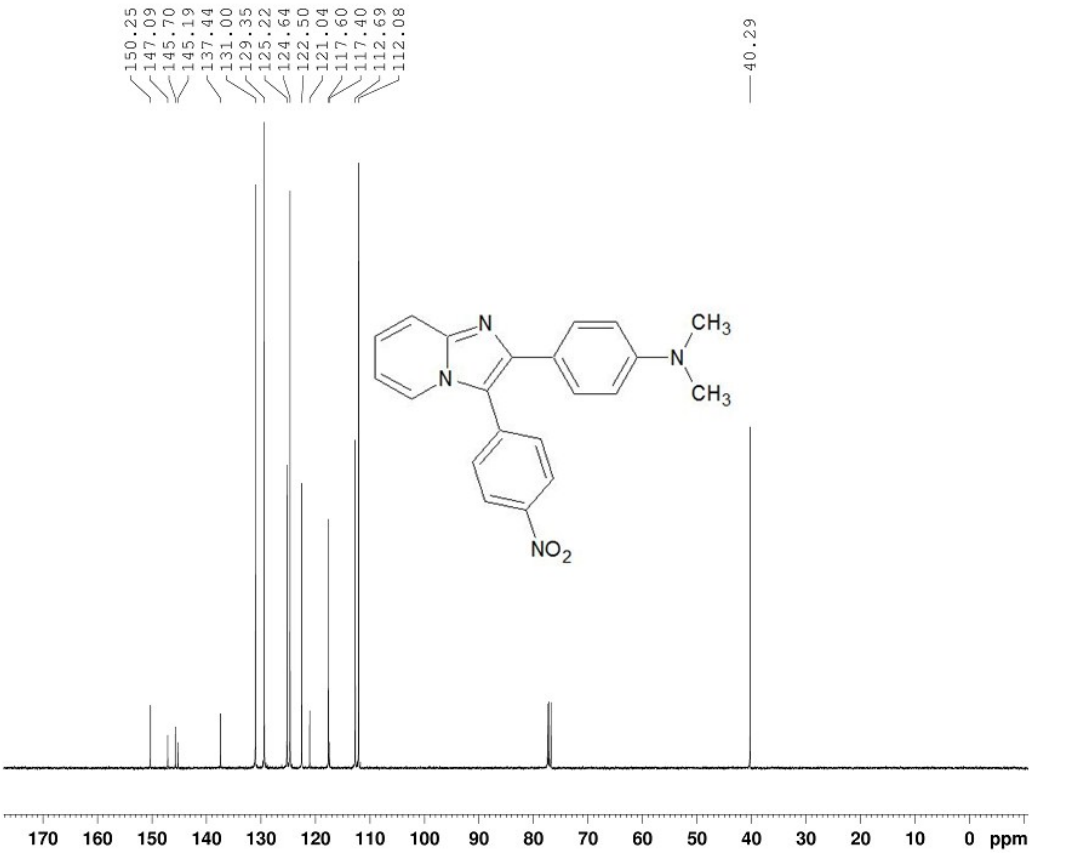
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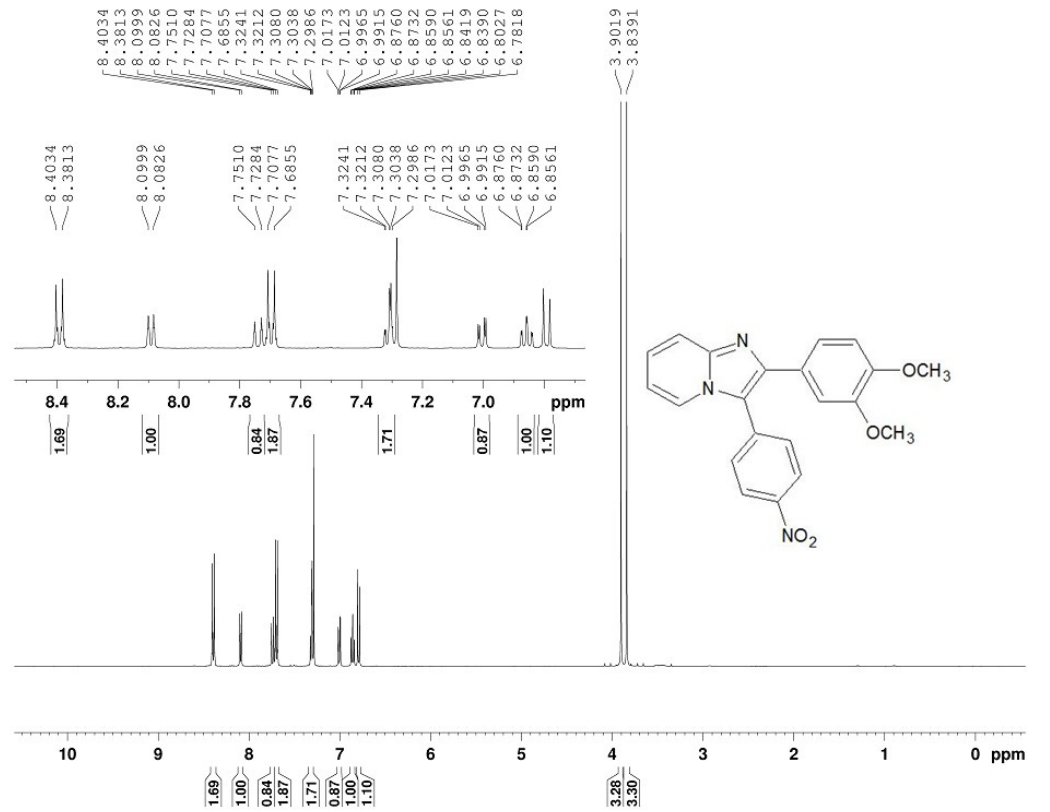
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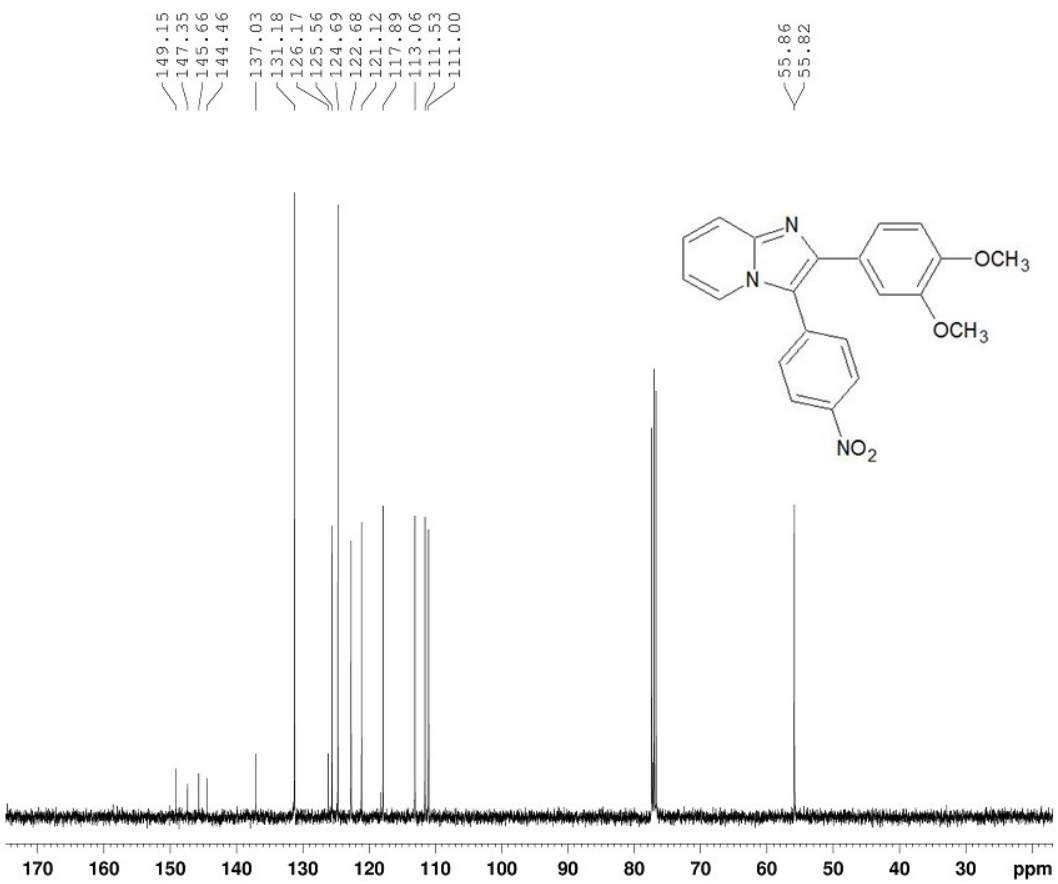
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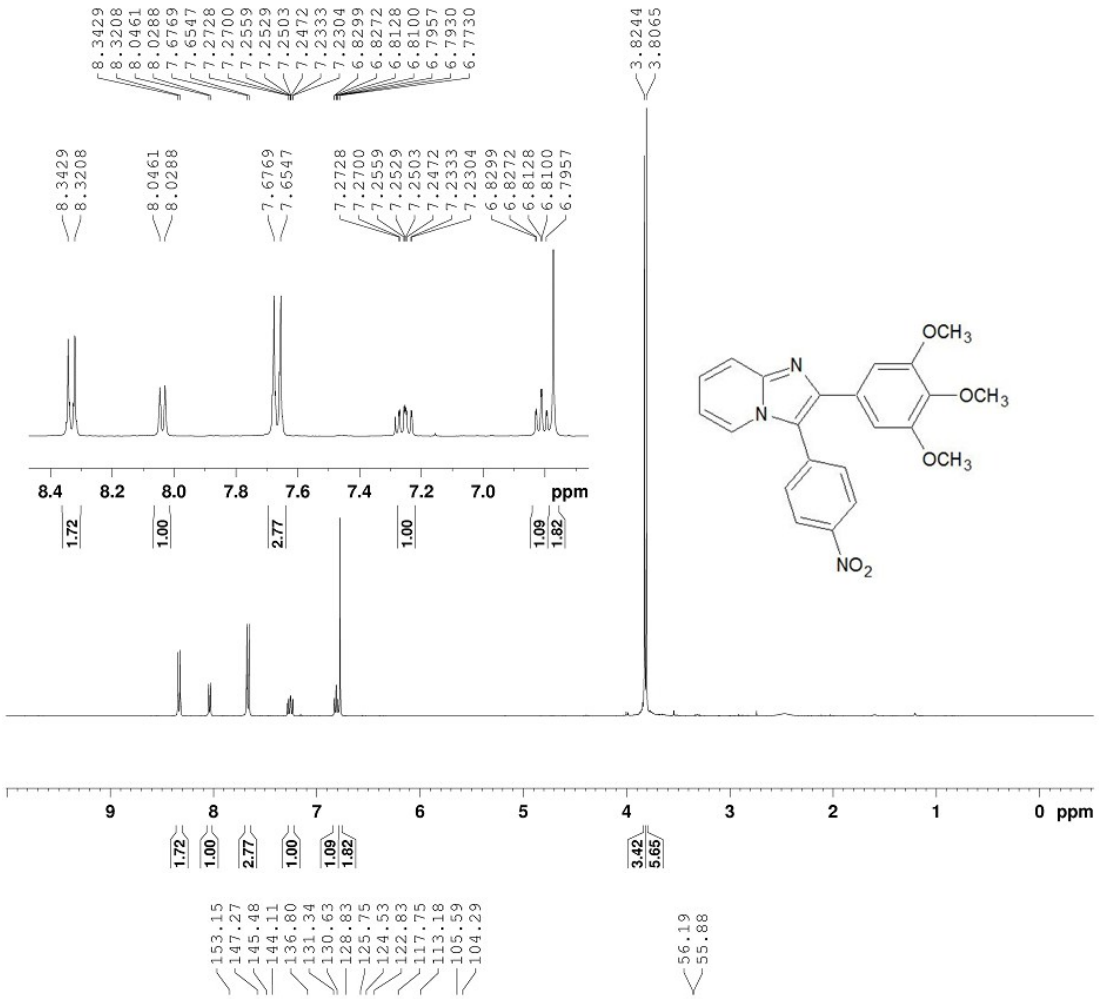
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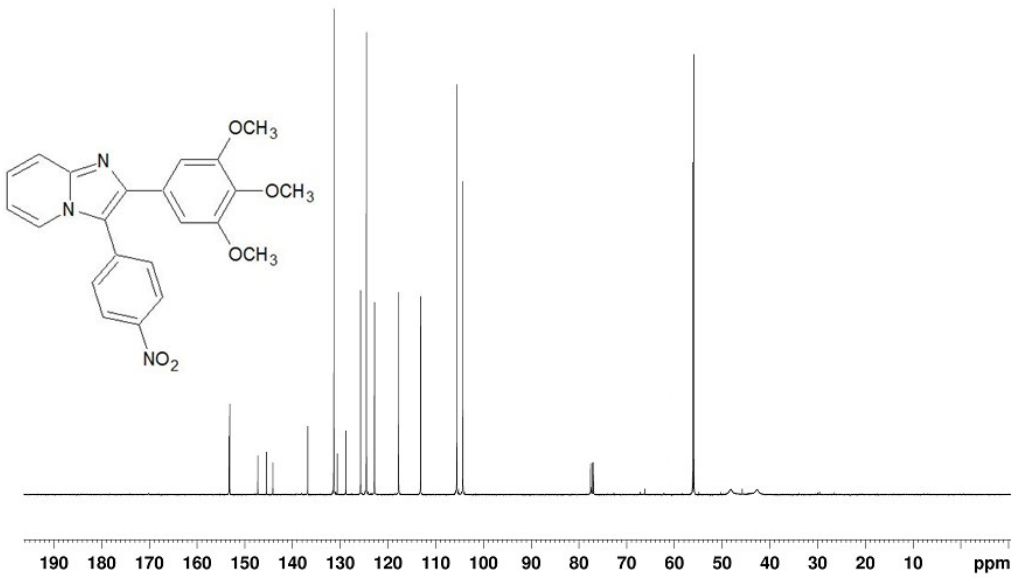
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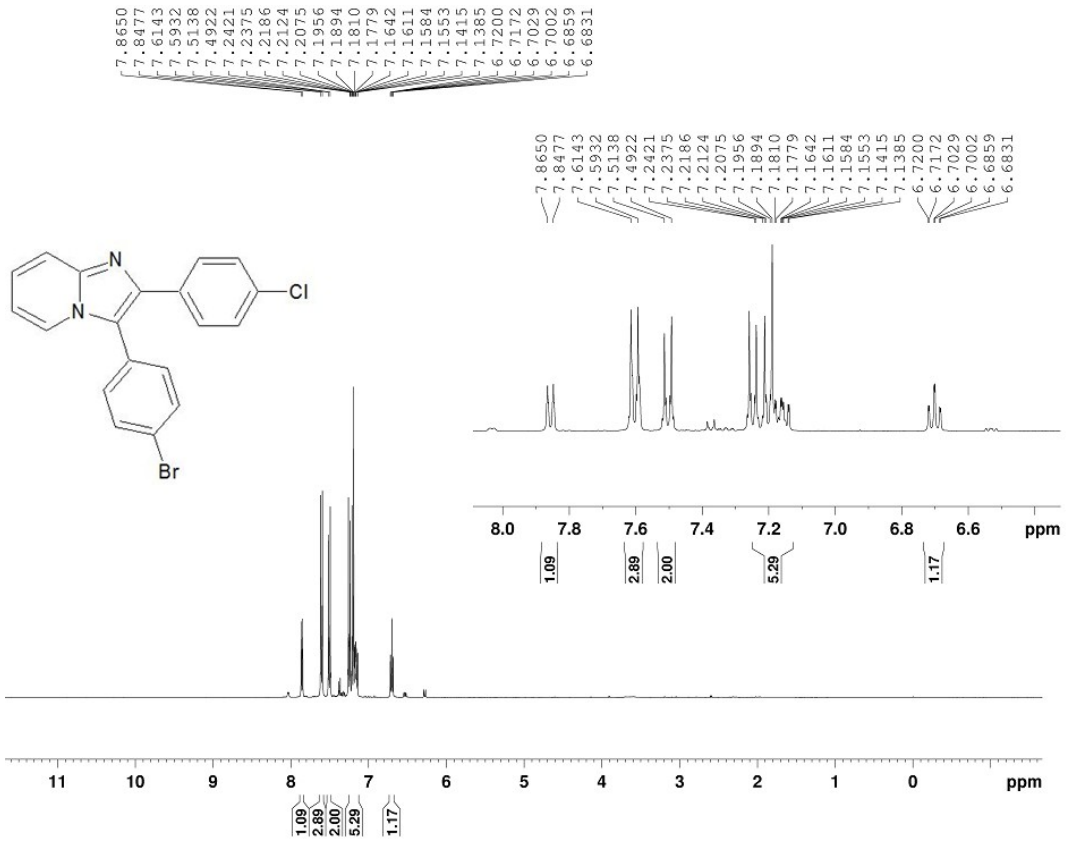
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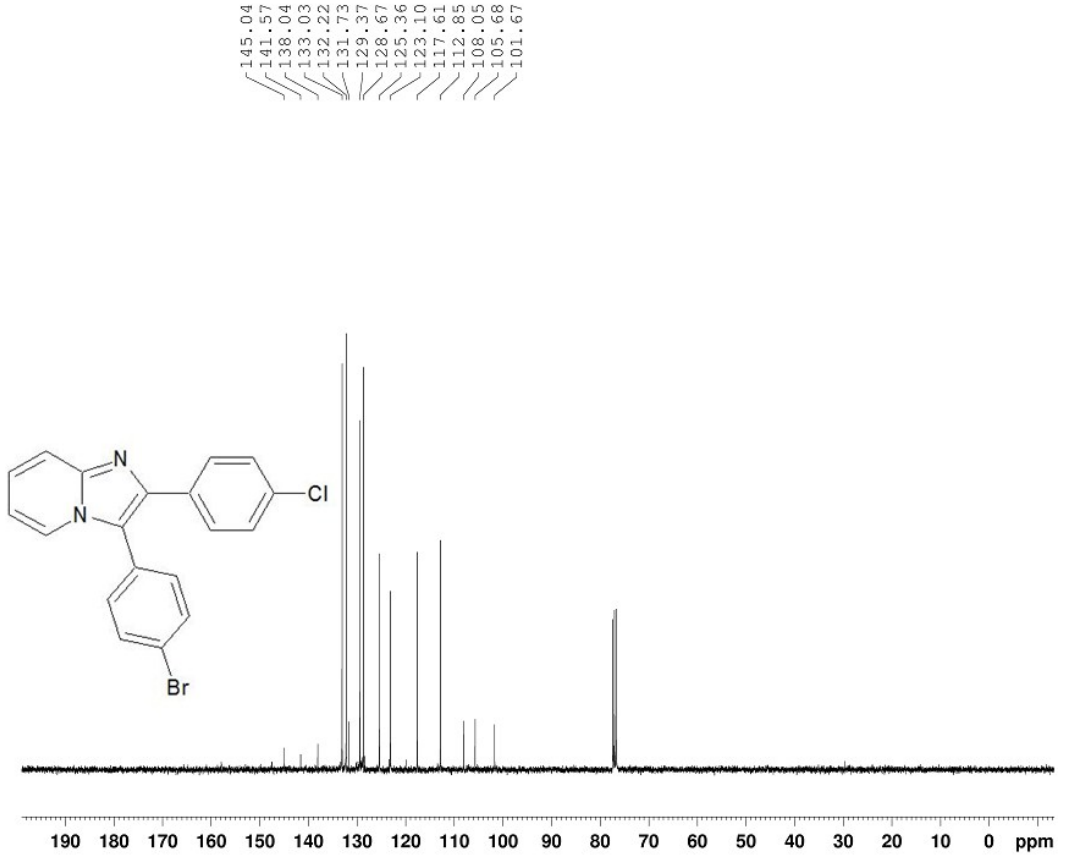
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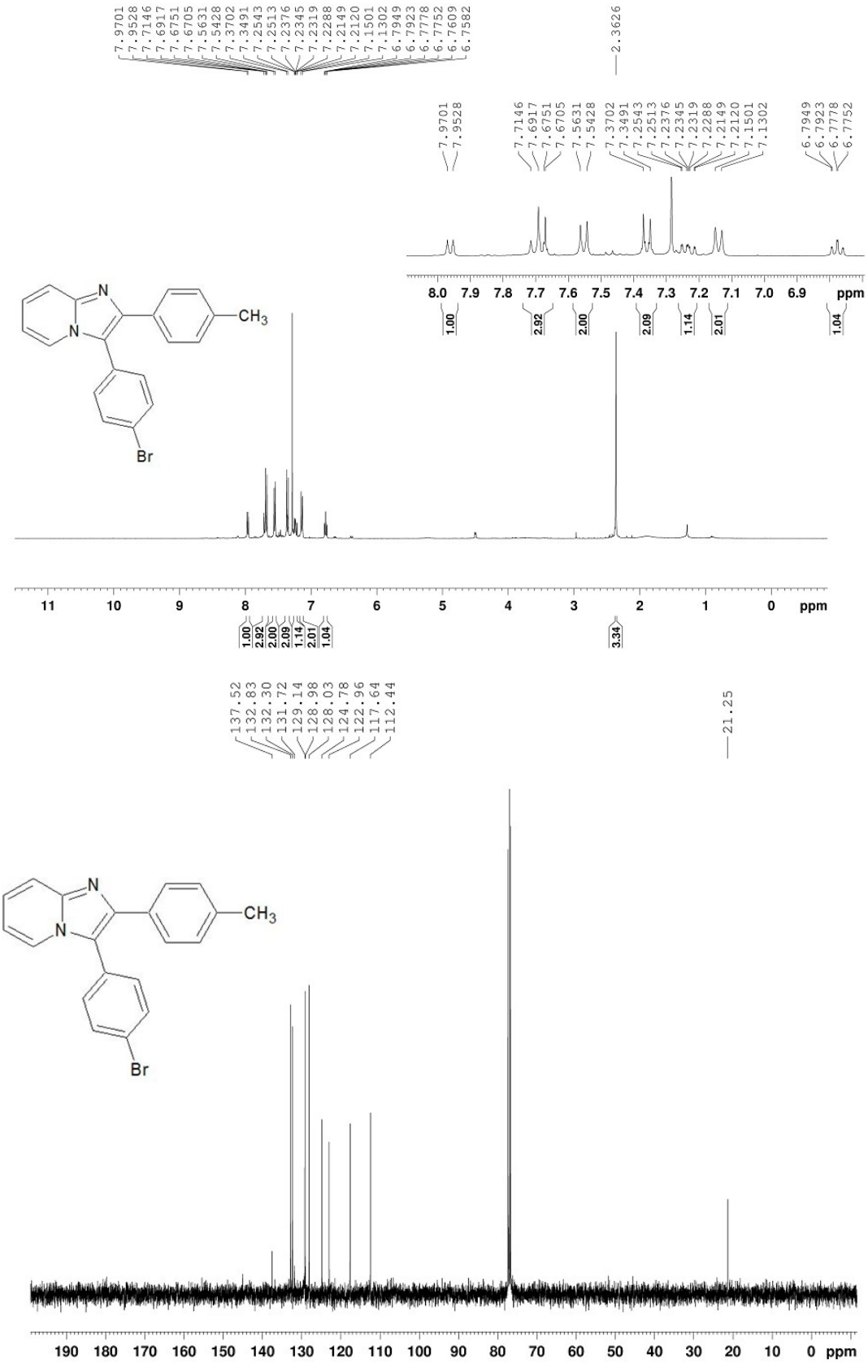
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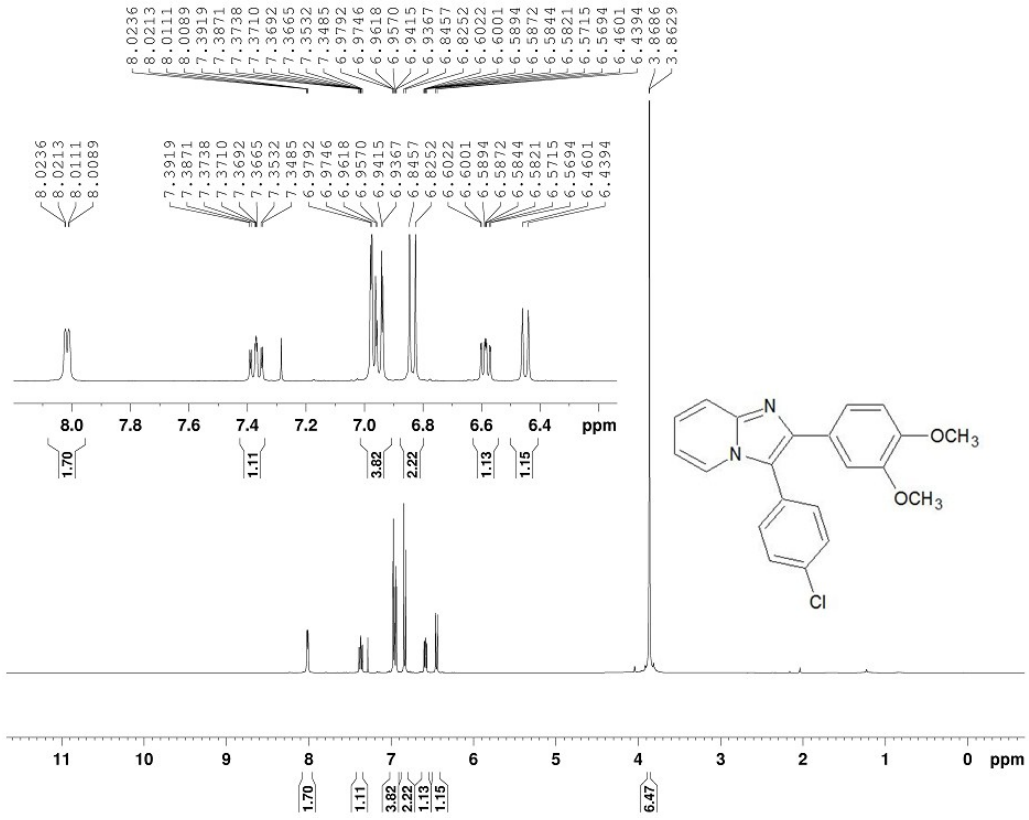
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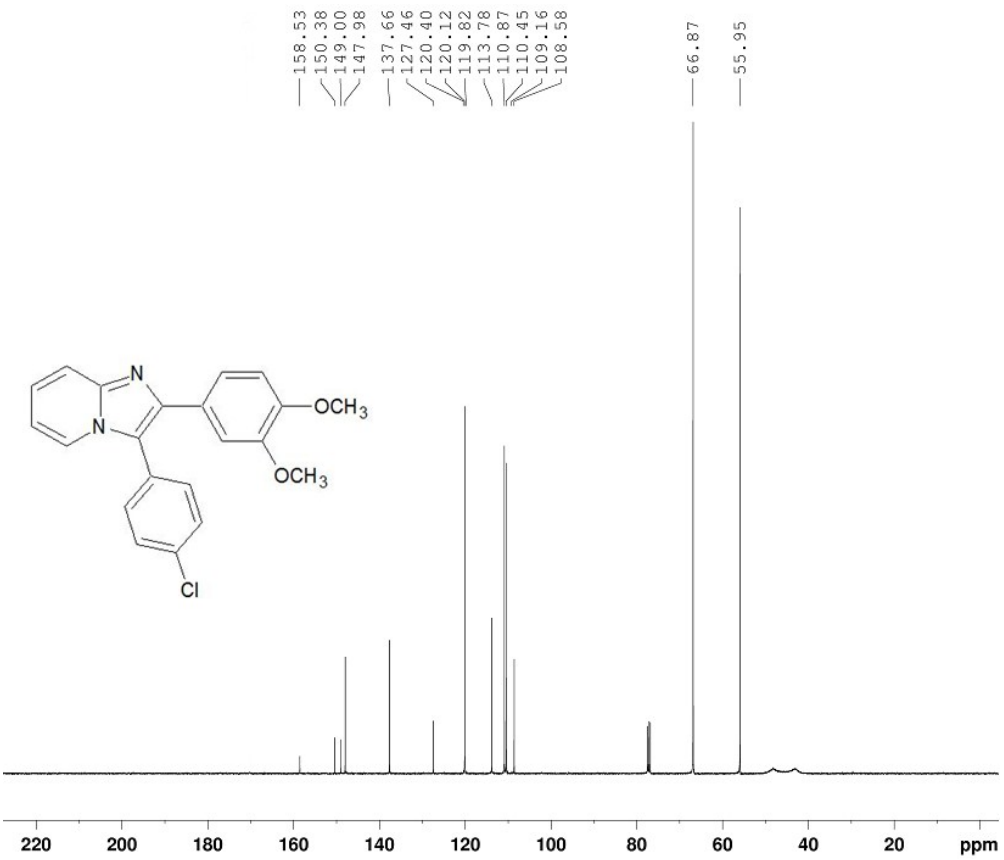
3.8629
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 ppm
1.70 1.11 3.82 2.22 1.13 1.15
11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.70 1.11 3.82 2.22 1.13 1.15 6.47
N
N
OCH3
OCH3
Cl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150.38
149.00
147.98
137.66
127.46
120.40
120.12
119.82
113.78
110.87
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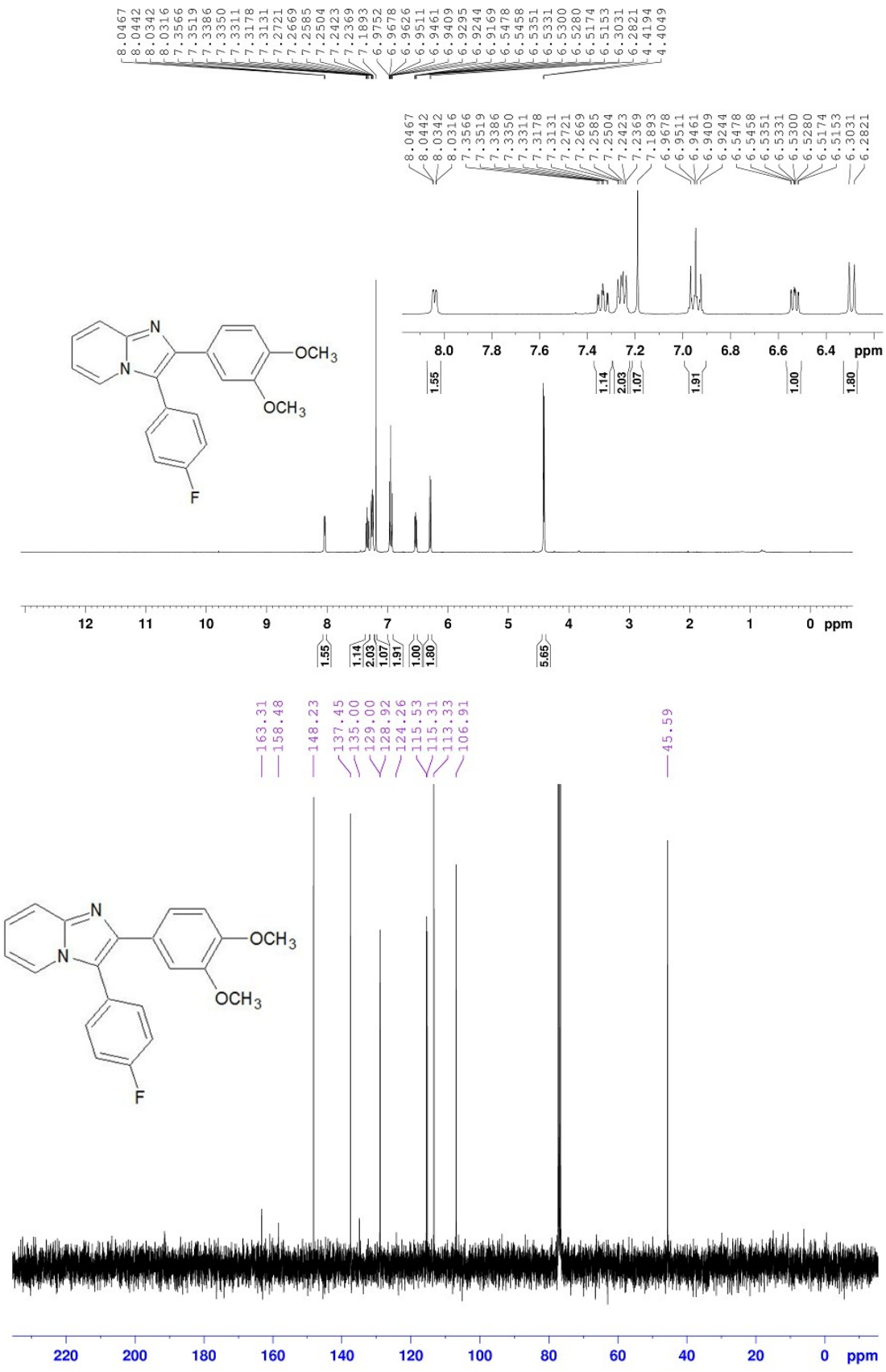
109.16
108.58
66.87
55.95
220 200 180 160 140 120 100 80 60 40 20 ppm
N
N
OCH3
OCH3
Cl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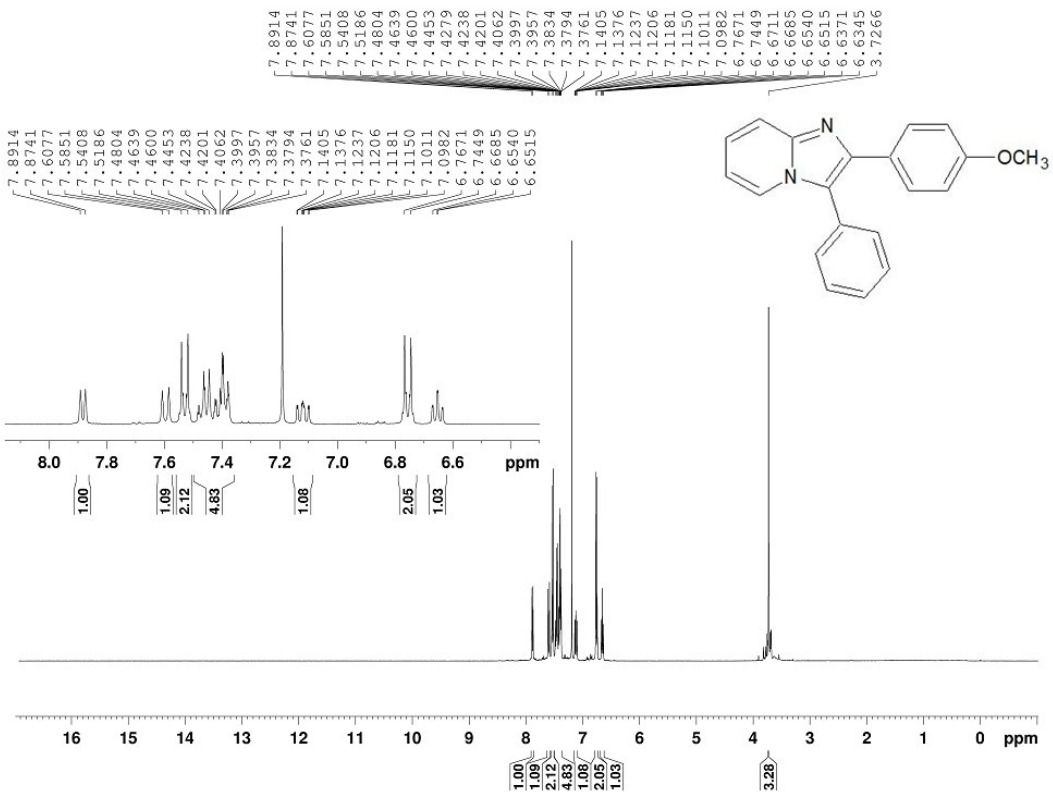
8.0442
8.0342
8.0316
7.3566
7.3519
7.3386
7.3350
7.3311
7.3178
7.3131
7.2721
7.2669
7.2585
7.2504
7.2423
7.2369
7.1893
6.9752
6.9678
6.9626
6.9511
6.9461
6.9409
6.9295
6.9244
6.9169
6.5478
6.5458
6.5351
6.5331
6.5300
6.5280
6.5174
6.5153
6.3031
6.2821
4.4194
4.4049
OCH3
OCH3
F
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 ppm
1.55 1.14 2.03 1.07 1.91 1.00 1.80
12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.55 1.14 2.03 1.07 1.91 1.00 1.80 5.65
163.31
158.48
148.23
137.45
135.00
129.00
128.92
124.26
115.53
115.31
113.33
106.91
45.59
OCH3
OCH3
F
220 200 180 160 140 120 100 80 60 40 20 0 ppm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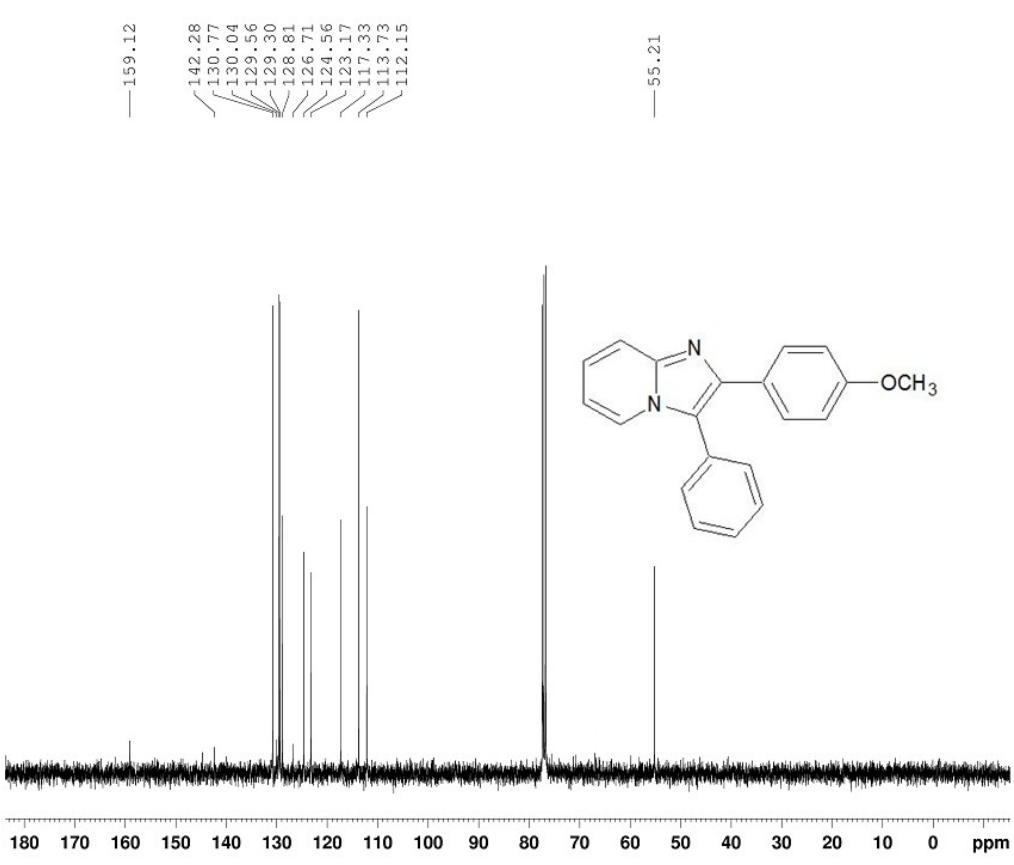
7.8741
7.6077
7.5851
7.5408
7.5186
7.4804
7.4639
7.4600
7.4453
7.4279
7.4238
7.4201
7.4062
7.3997
7.3957
7.3834
7.3794
7.3761
7.1405
7.1376
7.1237
7.1206
7.1181
7.1150
7.1011
7.0982
6.7671
6.7449
6.6711
6.6685
6.6540
6.6515
6.6371
6.6345
3.7266
OCH3
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
ppm
1.00
1.09
2.12
4.83
1.08
2.05
1.03
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
3.28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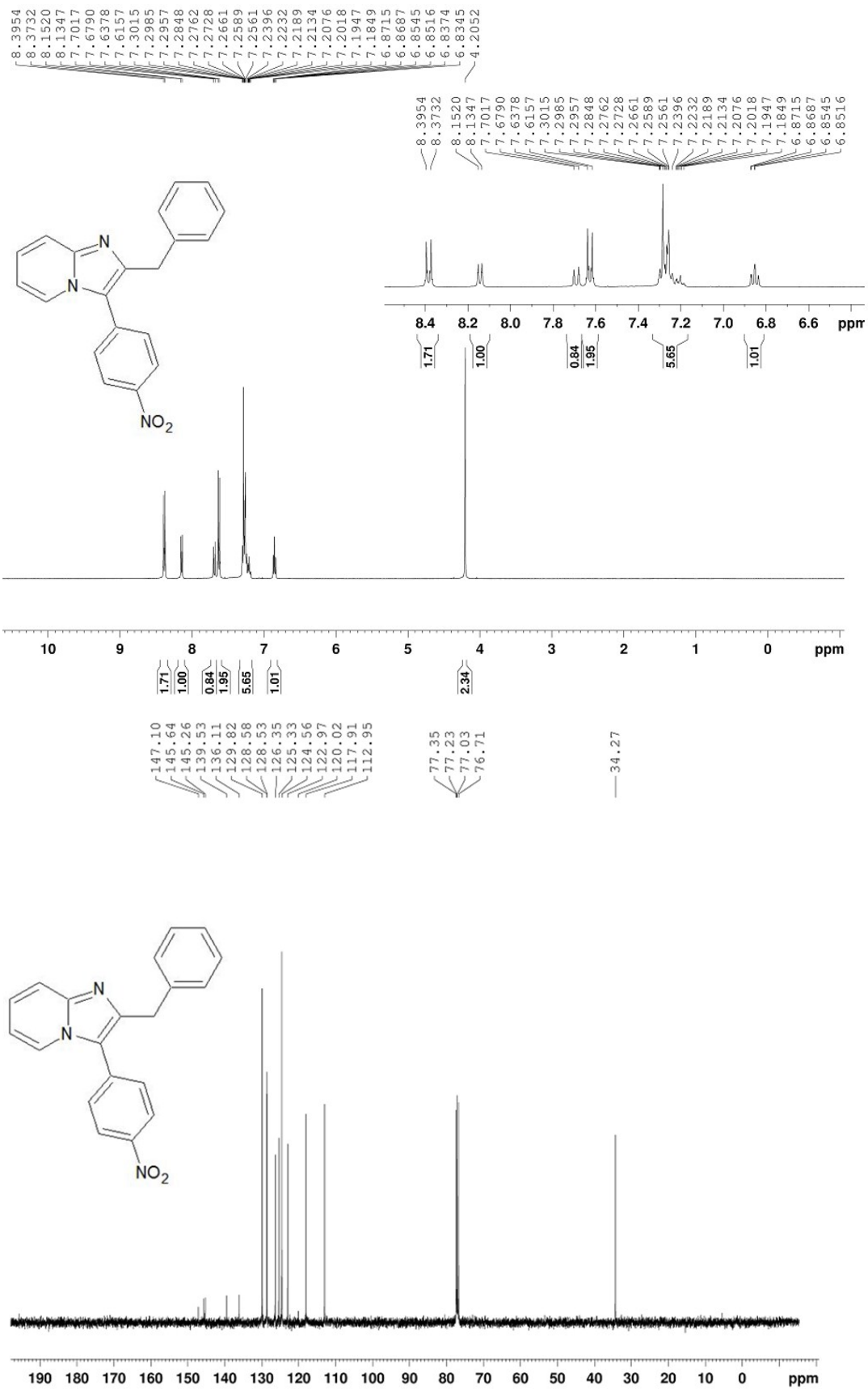
142.28
130.77
130.04
129.56
129.30
128.81
126.71
124.56
123.17
117.33
113.73
112.15
55.21
OCH3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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8.1520
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7.3015
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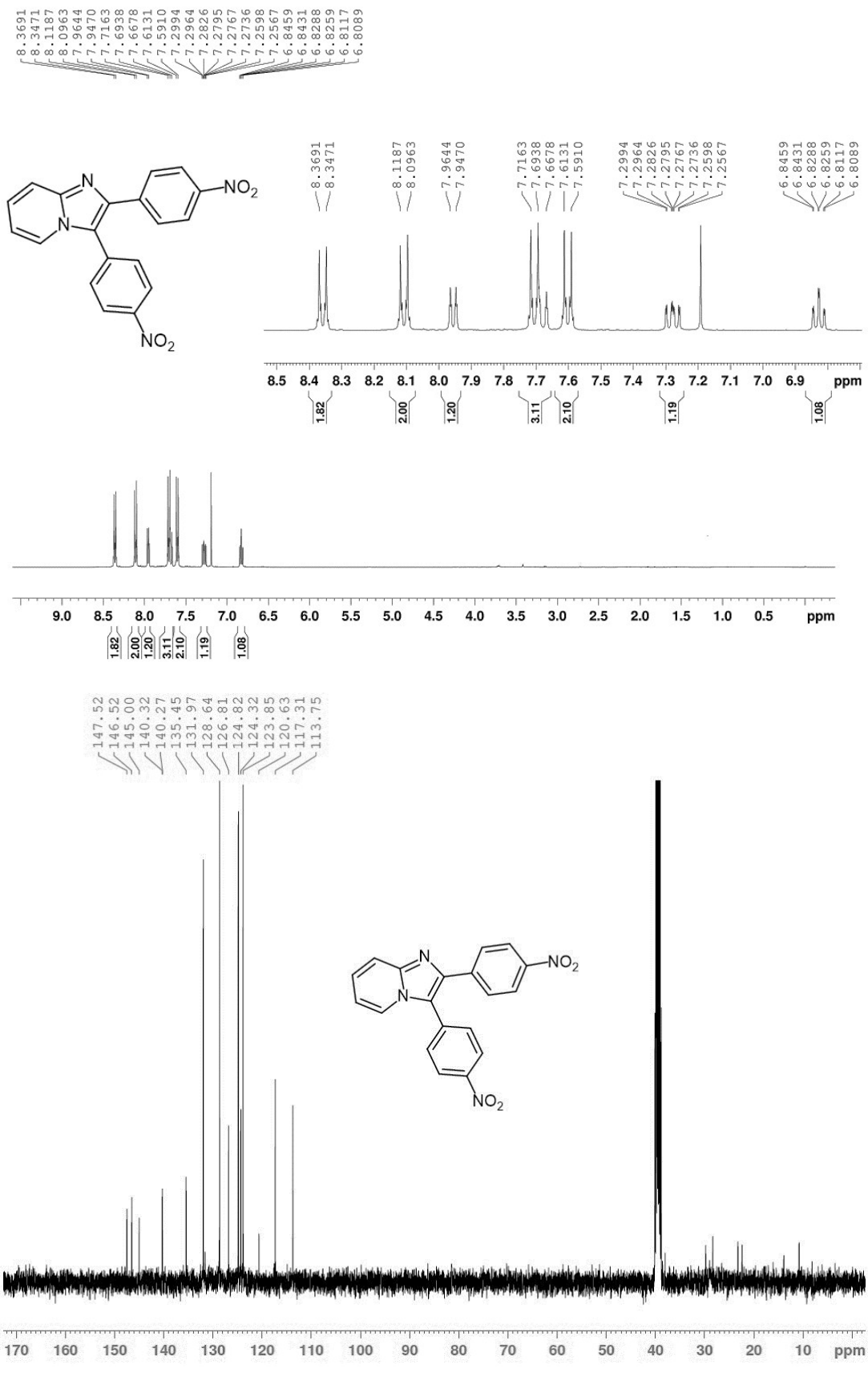
7.2957
7.2848
7.2762
7.2728
7.2661
7.2589
7.2561
7.2396
7.2232
7.2189
7.2134
7.2076
7.2018
7.1947
7.1849
6.8715
6.8687
6.8545
6.8516
6.8374
6.8345
4.2052
N
N
NO2
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
ppm
1.71
1.00
0.84
1.95
5.65
1.01
10
9
8
7
6
5
4
3
2
1
0
ppm
1.71
1.00
0.84
1.95
5.65
1.01
2.34
147.10
145.64
145.26
139.53
136.11
129.82
128.58
128.53
126.35
125.33
124.56
122.97
120.02
117.91
112.95
77.35
77.23
77.03
76.71
34.27
N
N
NO2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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8.3471
8.1187
8.0963
7.9644
7.9470
7.7163
7.6938
7.6678
7.6131
7.5910
7.2994
7.2964
7.2826
7.2795
7.2767
7.2736
7.2598
7.2567
6.8459
6.8431
6.8288
6.8259
6.8117
6.8089
NO2
NO2
ppm
1.82
2.00
1.20
3.11
2.10
1.19
1.08
147.52
146.52
145.00
140.32
140.27
135.45
131.97
128.64
126.81
124.82
124.32
123.85
120.63
117.31
113.75

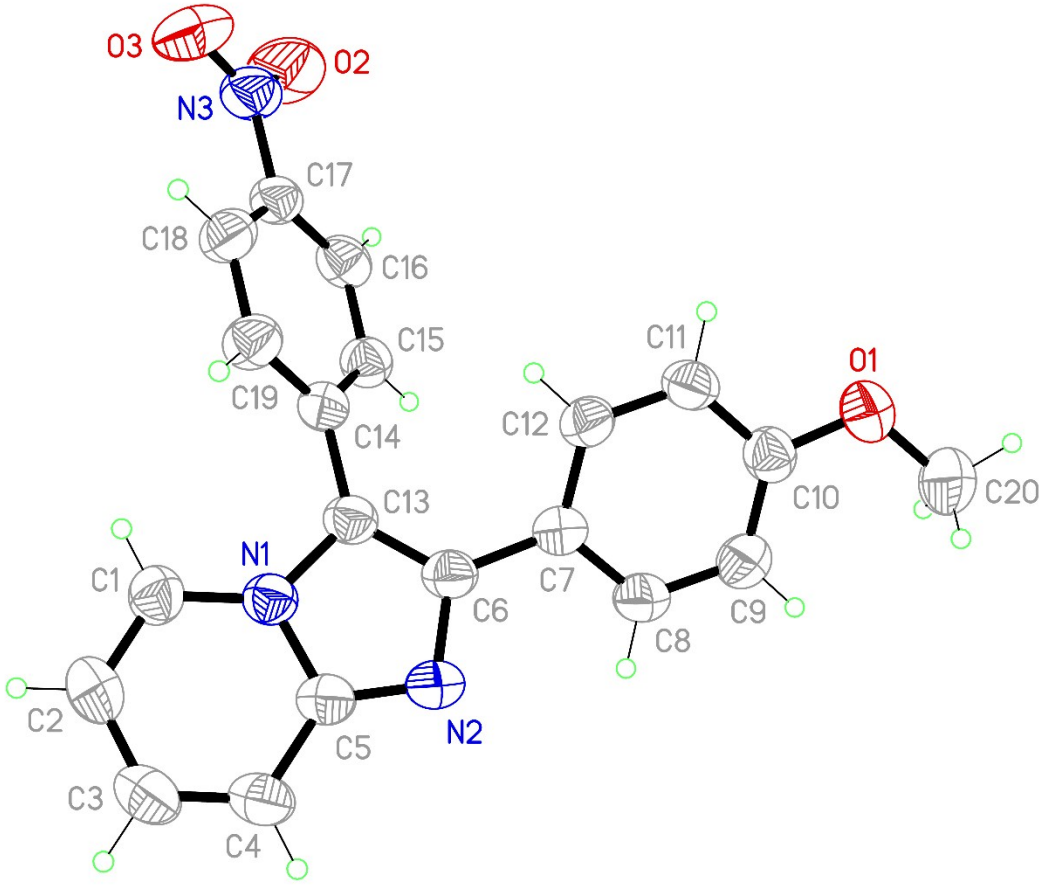

Fig. 1. ORTEP representation of **3c**. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

Table 1. Crystal data and structure refinement for compound **3c**.

Empirical formula	C20 H15 N3 O3
Formula weight	345.35
Temperature	298(2) K
Wavelength	0.71069 A
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 6.9694(14) A alpha = 84.71(3) deg.
	b = 8.0346(16) A beta = 77.42(3) deg.
	c = 15.190(3) A gamma = 87.21(3) deg.
Volume	826.3(3) A^3
Z, Calculated density	2, 1.388 Mg/m^3
Absorption coefficient	0.096 mm^-1
F(000)	360
Theta range for data collection	2.76 to 24.99 deg.
Limiting indices	-8<=h<=7, -8<=k<=9, -18<=l<=18
Reflections collected / unique	6123 / 2900 [R(int) = 0.0298]
Completeness to theta = 24.99	99.6 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2900 / 0 / 236
Goodness-of-fit on F^2	0.837
Final R indices [I>2sigma(I)]	R1 = 0.0331, wR2 = 0.0719
R indices (all data)	R1 = 0.0560, wR2 = 0.0760
Largest diff. peak and hole	0.105 and -0.157 e.A^-3

Table 2. Bond lengths [A] and angles [deg] for compound **3c**.

O(1)-C(10)	1.3654(17)
O(1)-C(20)	1.4297(19)
N(1)-C(1)	1.3735(18)
N(1)-C(13)	1.3938(18)
N(1)-C(5)	1.3958(17)
C(19)-C(18)	1.383(2)
C(19)-C(14)	1.3943(19)
C(19)-H(19)	0.9300
C(13)-C(6)	1.3886(18)
C(13)-C(14)	1.4754(19)
C(17)-C(18)	1.373(2)
C(17)-C(16)	1.380(2)
C(17)-N(3)	1.4726(19)
C(7)-C(8)	1.3896(18)
C(7)-C(12)	1.396(2)
C(7)-C(6)	1.477(2)
C(12)-C(11)	1.375(2)
C(12)-H(12)	0.9300
C(10)-C(9)	1.388(2)
C(10)-C(11)	1.3882(19)
N(2)-C(5)	1.3312(19)
N(2)-C(6)	1.3732(18)
C(5)-C(4)	1.414(2)
C(18)-H(18)	0.9300
C(11)-H(11)	0.9300

N(3)-O(2)	1.2224(18)
N(3)-O(3)	1.2234(18)
C(1)-C(2)	1.351(2)
C(1)-H(1)	0.9300
C(14)-C(15)	1.395(2)
C(15)-C(16)	1.384(2)
C(15)-H(15)	0.9300
C(16)-H(16)	0.9300
C(4)-C(3)	1.351(2)
C(4)-H(4)	0.9300
C(9)-C(8)	1.381(2)
C(9)-H(9)	0.9300
C(2)-C(3)	1.414(2)
C(2)-H(2)	0.9300
C(8)-H(8)	0.9300
C(3)-H(3)	0.9300
C(20)-H(20A)	0.9600
C(20)-H(20B)	0.9600
C(20)-H(20C)	0.9600

C(10)-O(1)-C(20)	117.47(13)
C(1)-N(1)-C(13)	131.88(12)
C(1)-N(1)-C(5)	121.50(12)
C(13)-N(1)-C(5)	106.39(11)
C(18)-C(19)-C(14)	120.89(14)
C(18)-C(19)-H(19)	119.6
C(14)-C(19)-H(19)	119.6
C(6)-C(13)-N(1)	105.42(11)

C(6)-C(13)-C(14)	132.17(13)
N(1)-C(13)-C(14)	122.40(12)
C(18)-C(17)-C(16)	122.10(13)
C(18)-C(17)-N(3)	118.42(14)
C(16)-C(17)-N(3)	119.48(14)
C(8)-C(7)-C(12)	117.09(13)
C(8)-C(7)-C(6)	120.48(12)
C(12)-C(7)-C(6)	122.37(12)
C(11)-C(12)-C(7)	121.30(13)
C(11)-C(12)-H(12)	119.3
C(7)-C(12)-H(12)	119.3
O(1)-C(10)-C(9)	124.79(13)
O(1)-C(10)-C(11)	116.81(13)
C(9)-C(10)-C(11)	118.40(13)
C(5)-N(2)-C(6)	105.78(11)
N(2)-C(5)-N(1)	111.38(12)
N(2)-C(5)-C(4)	130.43(13)
N(1)-C(5)-C(4)	118.19(13)
C(17)-C(18)-C(19)	118.92(14)
C(17)-C(18)-H(18)	120.5
C(19)-C(18)-H(18)	120.5
C(12)-C(11)-C(10)	121.01(14)
C(12)-C(11)-H(11)	119.5
C(10)-C(11)-H(11)	119.5
O(2)-N(3)-O(3)	123.56(14)
O(2)-N(3)-C(17)	118.23(15)
O(3)-N(3)-C(17)	118.20(15)
C(2)-C(1)-N(1)	119.50(14)

C(2)-C(1)-H(1)	120.3
N(1)-C(1)-H(1)	120.3
C(19)-C(14)-C(15)	118.50(13)
C(19)-C(14)-C(13)	121.47(13)
C(15)-C(14)-C(13)	120.03(12)
C(16)-C(15)-C(14)	121.12(14)
C(16)-C(15)-H(15)	119.4
C(14)-C(15)-H(15)	119.4
C(17)-C(16)-C(15)	118.47(14)
C(17)-C(16)-H(16)	120.8
C(15)-C(16)-H(16)	120.8
N(2)-C(6)-C(13)	111.03(12)
N(2)-C(6)-C(7)	119.77(12)
C(13)-C(6)-C(7)	129.17(12)
C(3)-C(4)-C(5)	119.81(15)
C(3)-C(4)-H(4)	120.1
C(5)-C(4)-H(4)	120.1
C(8)-C(9)-C(10)	120.24(13)
C(8)-C(9)-H(9)	119.9
C(10)-C(9)-H(9)	119.9
C(1)-C(2)-C(3)	120.56(15)
C(1)-C(2)-H(2)	119.7
C(3)-C(2)-H(2)	119.7
C(9)-C(8)-C(7)	121.94(14)
C(9)-C(8)-H(8)	119.0
C(7)-C(8)-H(8)	119.0
C(4)-C(3)-C(2)	120.34(15)
C(4)-C(3)-H(3)	119.8

C(2)-C(3)-H(3)	119.8
O(1)-C(20)-H(20A)	109.5
O(1)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
O(1)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5