Supporting Information

O-Benzoyl Pyridine Aldoxime and Amidoxime Derivatives: Novel Efficient DNA Photo-Cleavage Agents

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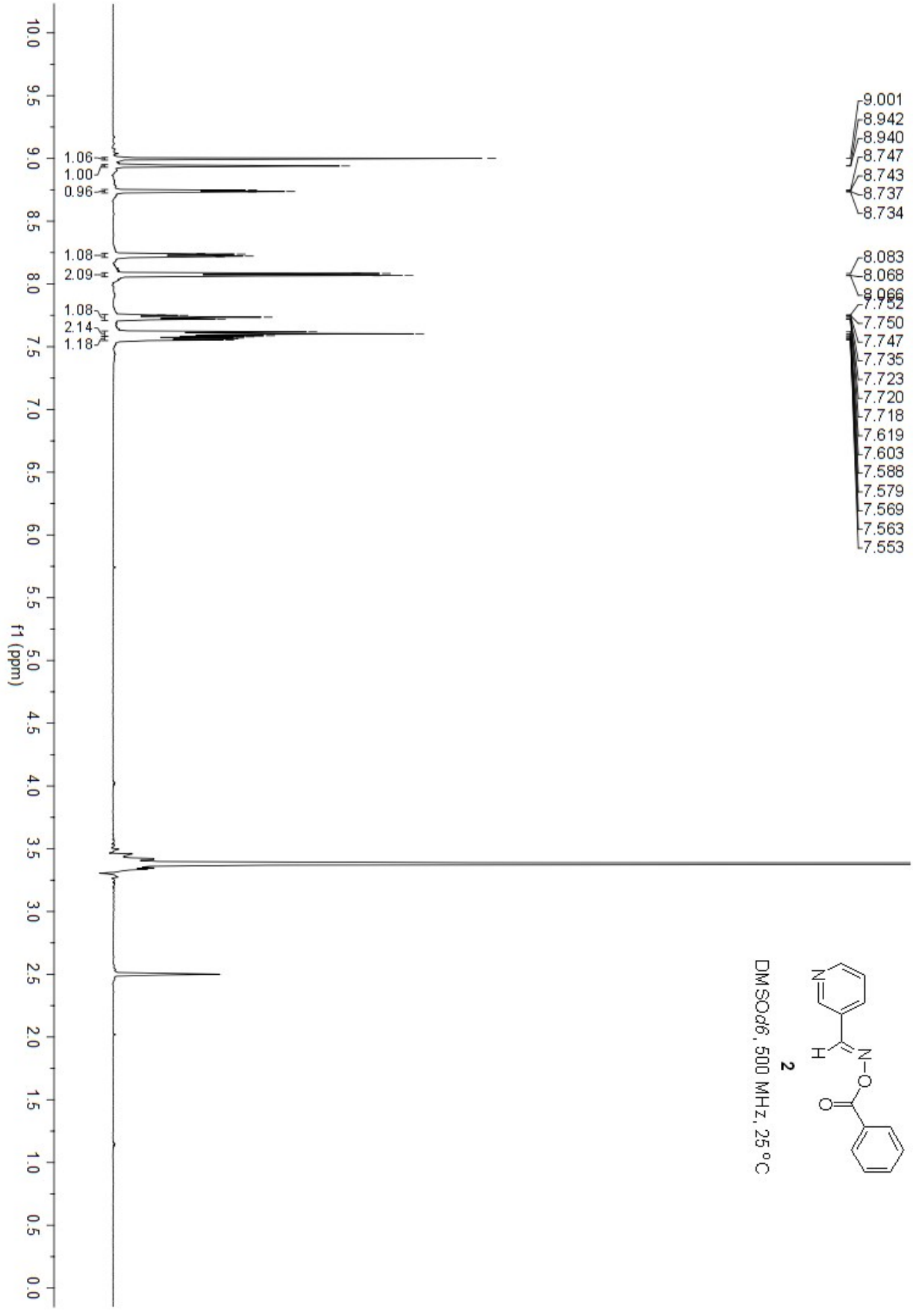
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7.750
7.747
7.735
7.723
7.720
7.718
7.619
7.603
7.588
7.579
7.569
7.563
7.553
1.06
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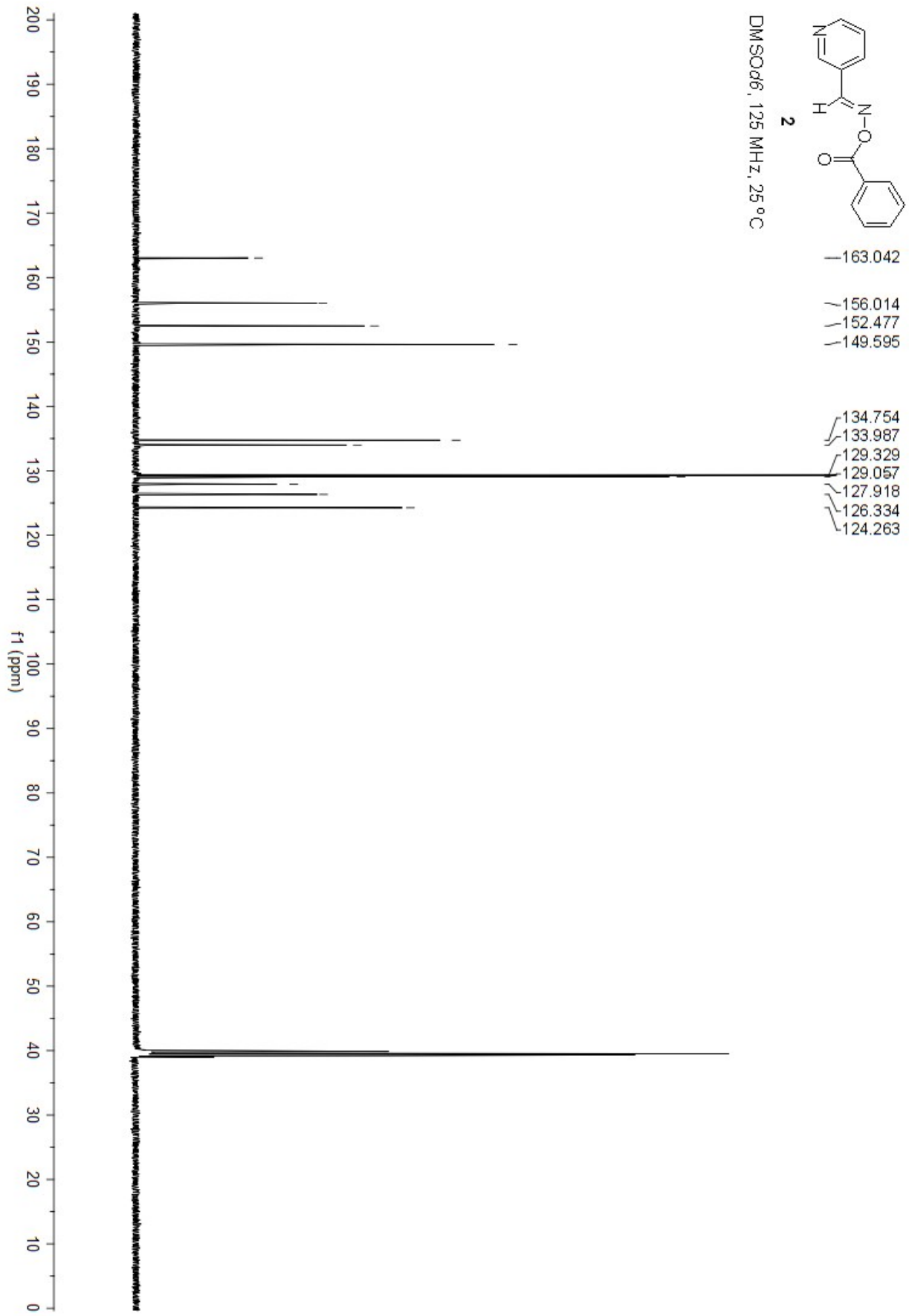
1.08
2.09
1.08
2.14
1.18
f1 (ppm)
2
DMSO-d6, 500 MHz, 25 °C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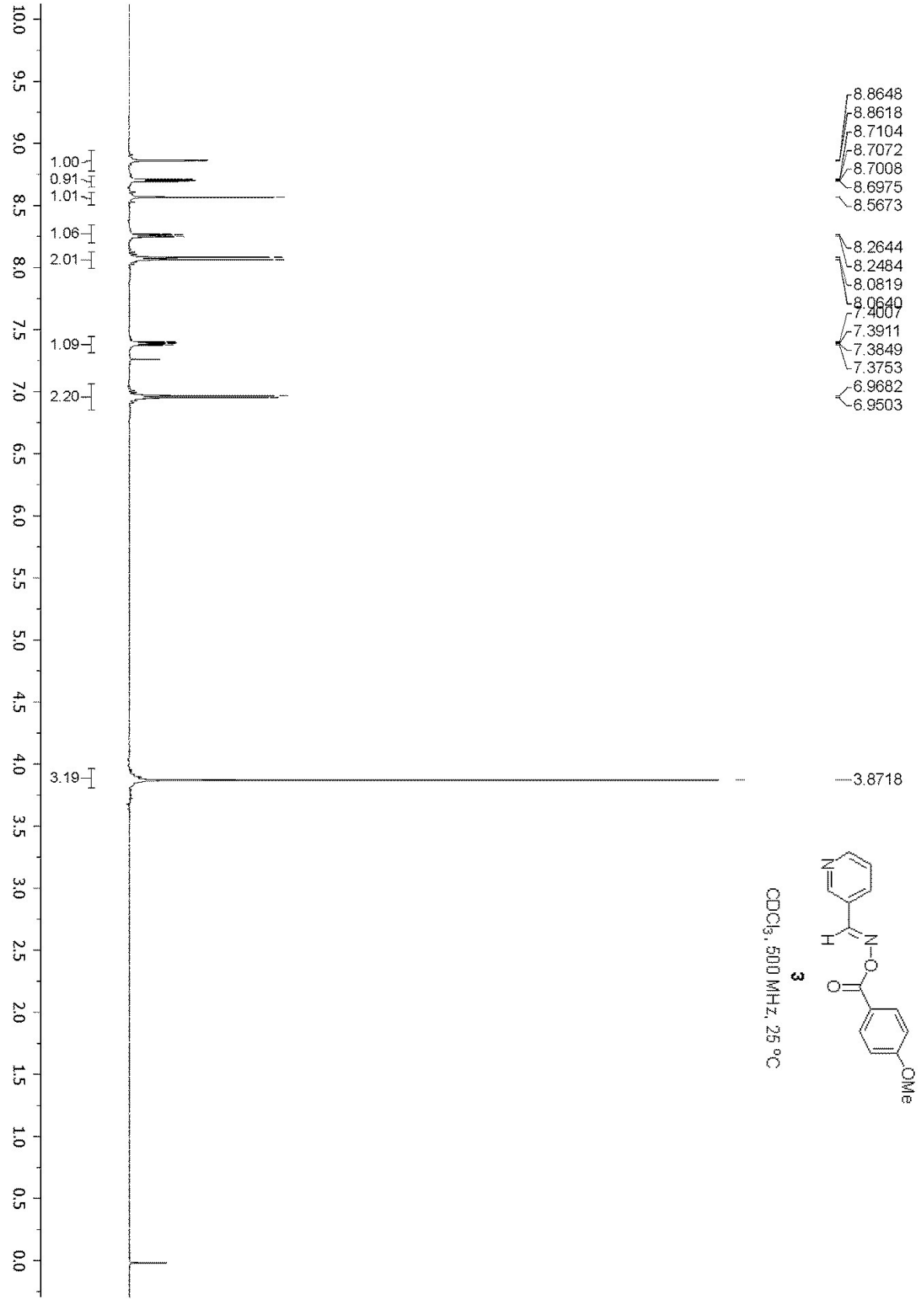
126.334
124.263
f1 (ppm)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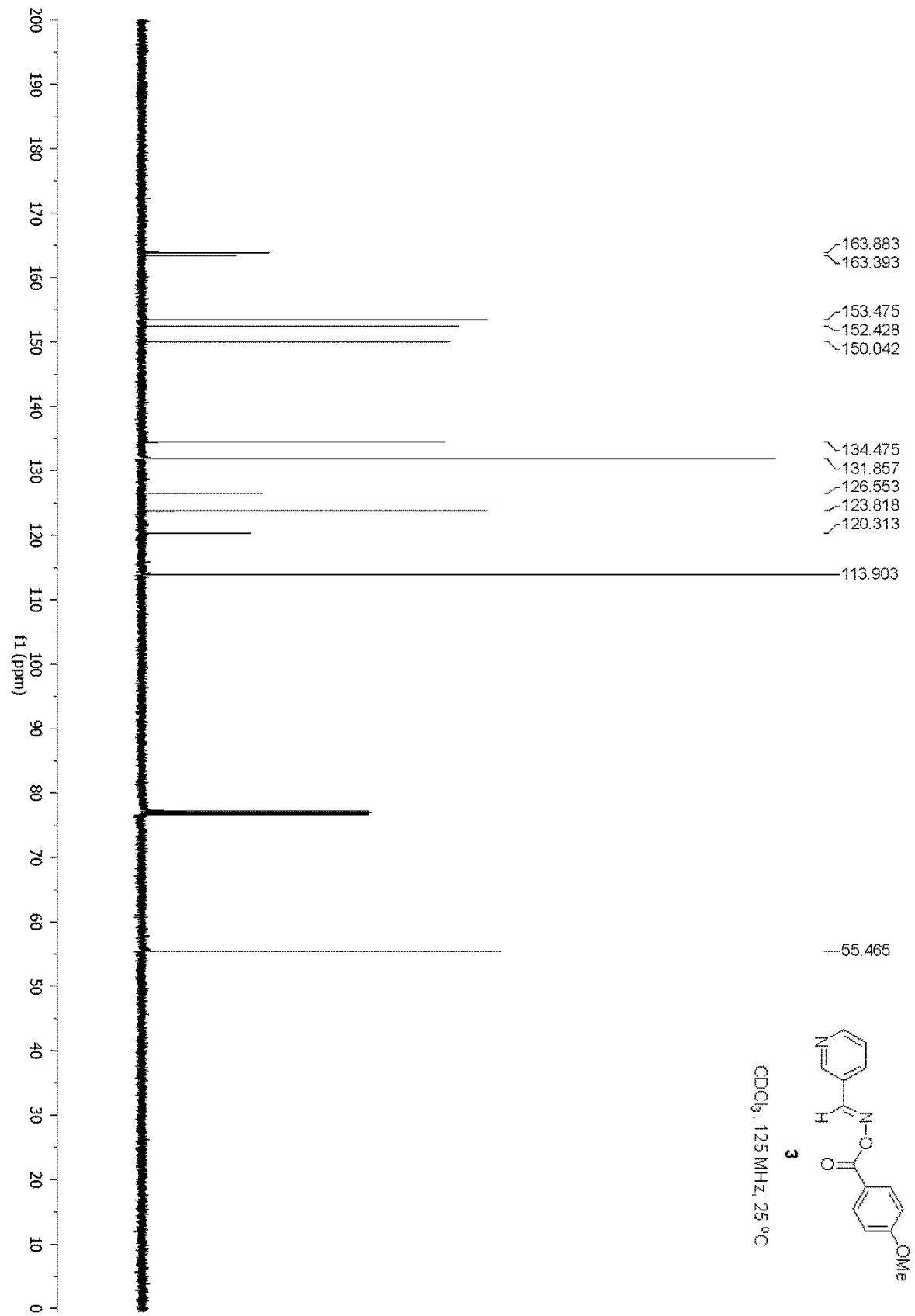
8.0640
7.4007
7.3911
7.3849
7.3753
6.9682
6.9503
3.8718
1.00
0.91
1.01
1.06
2.01
1.09
2.20
3.19
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
3
CDCl3, 500 MHz, 25 °C
N
H
N
O
O
OMe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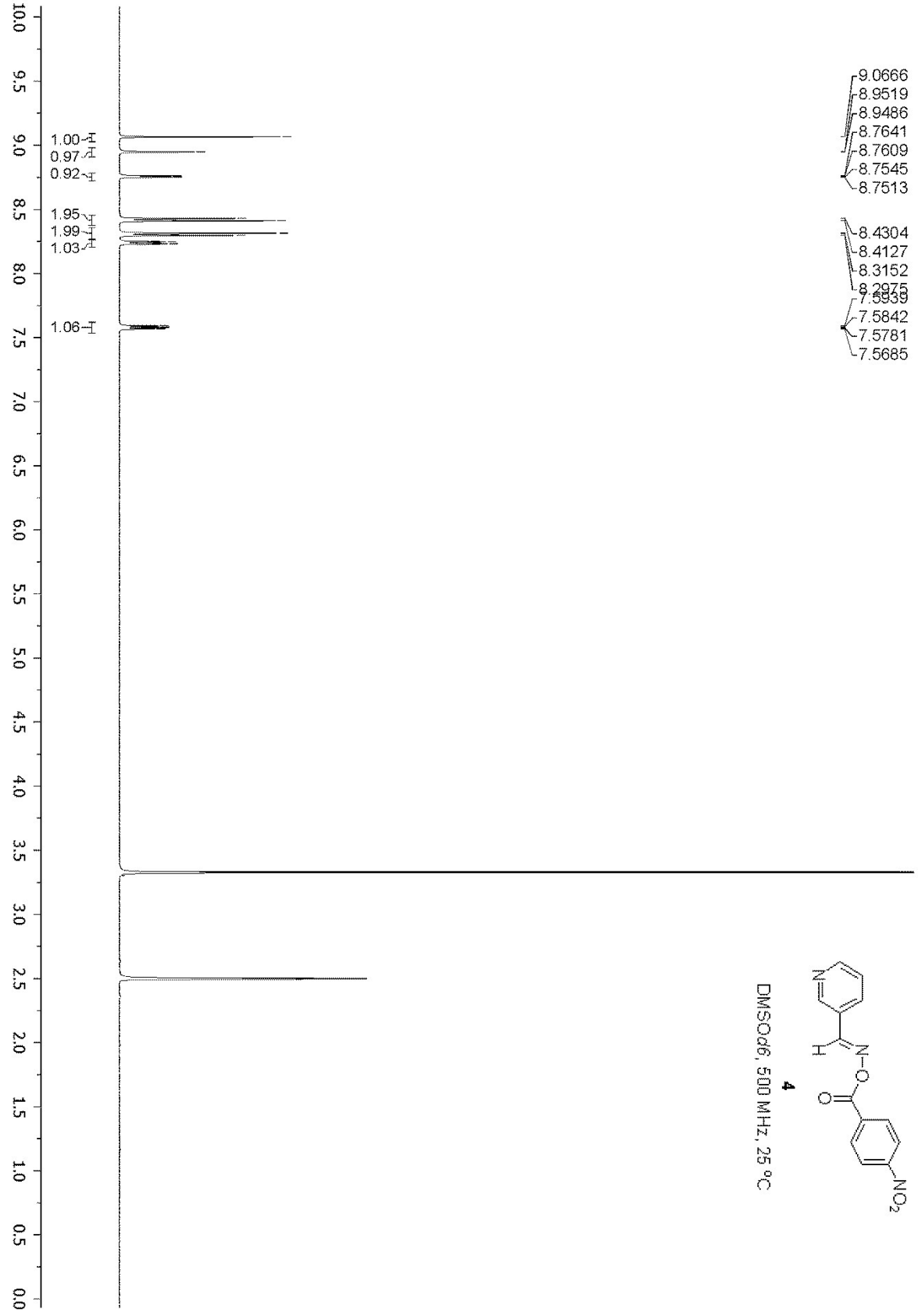
152.428
150.042
134.475
131.857
126.553
123.818
120.313
113.903
55.465
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
3
CDCl3, 125 MHz, 25 °C
N
H
N
O
O
OMe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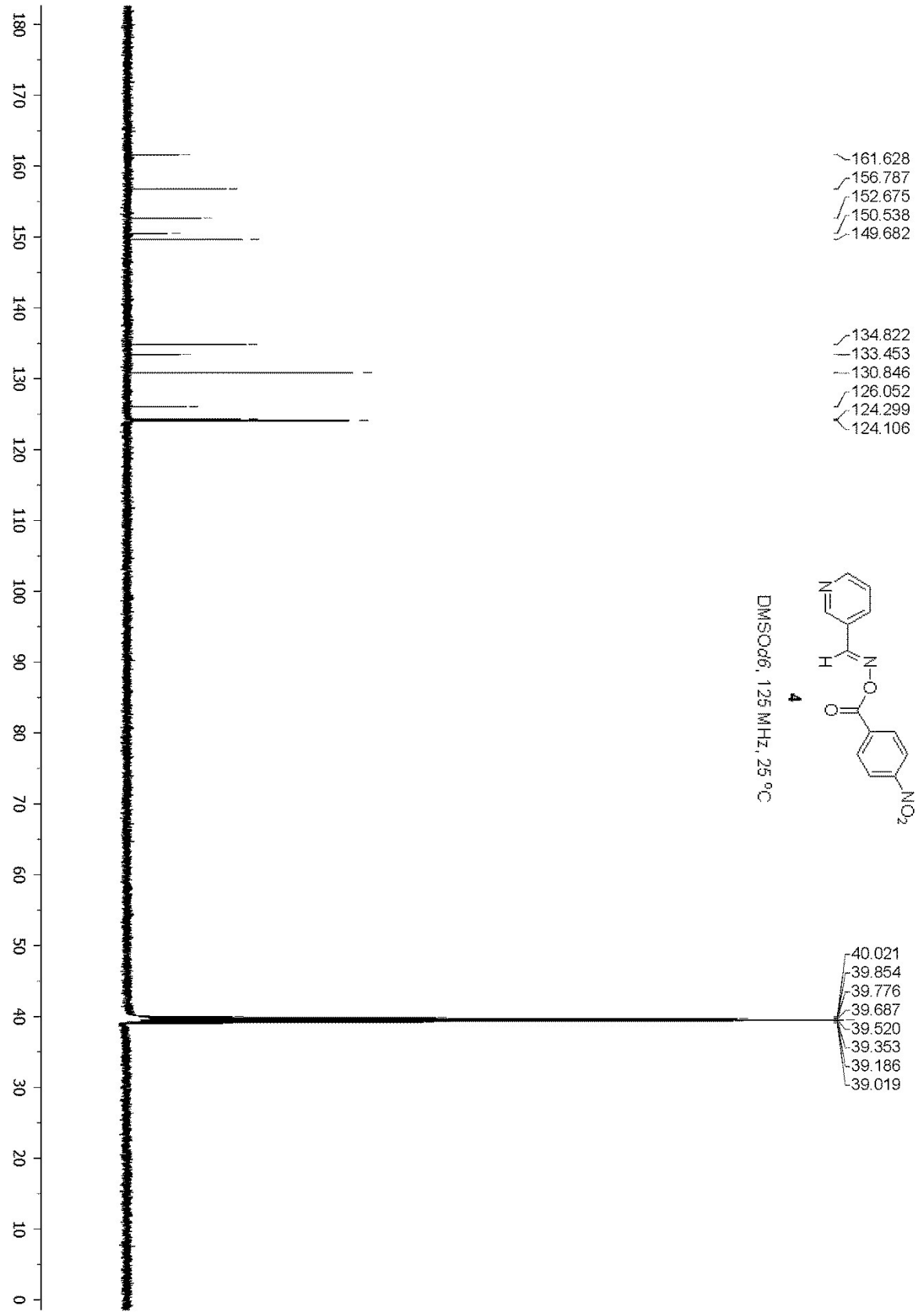
7.5939
7.5842
7.5781
7.5685
1.00
0.97
0.92
1.95
1.99
1.03
1.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
4
DMSO-d6, 500 MHz, 25 °C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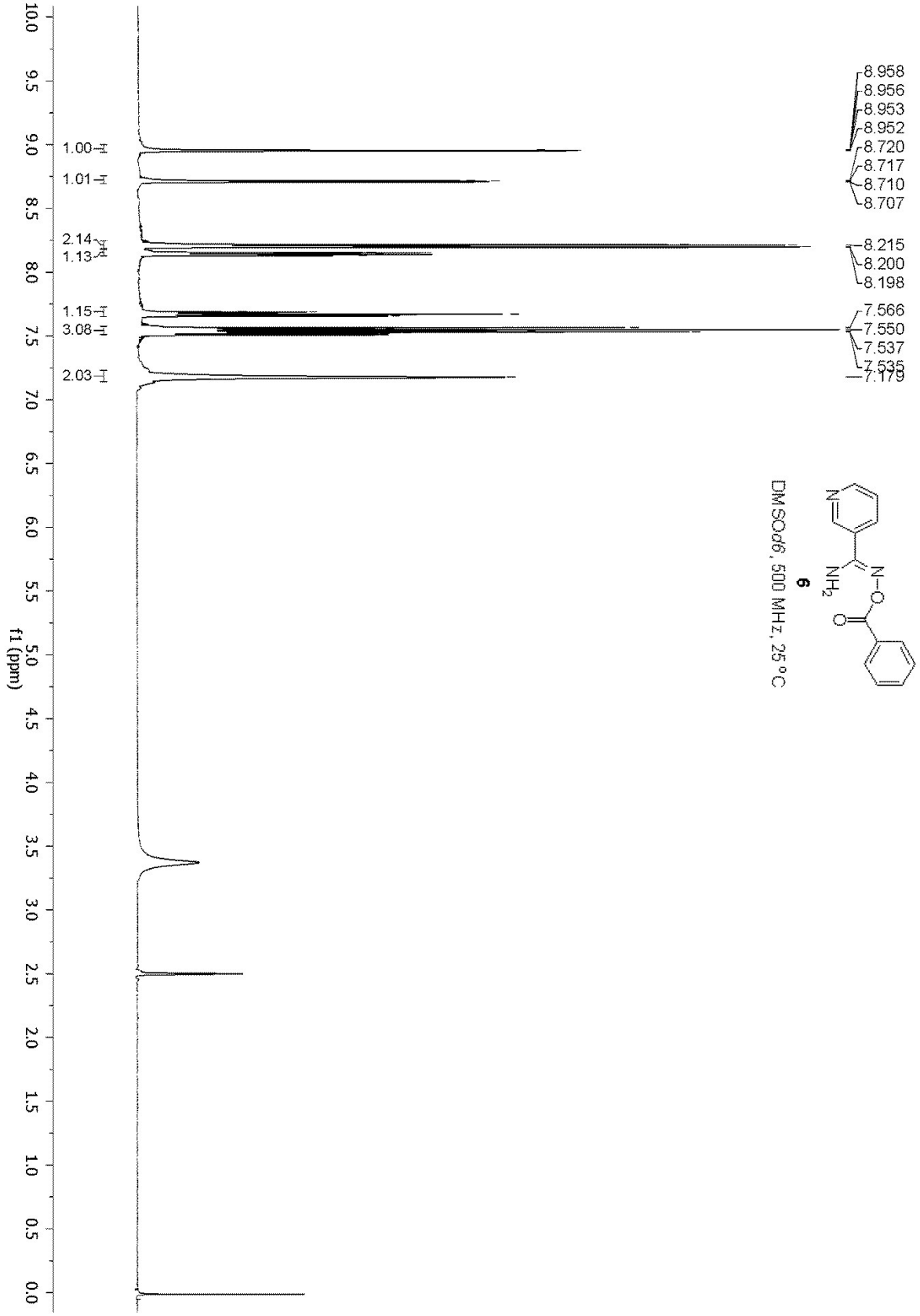
124.299
124.106
40.021
39.854
39.776
39.687
39.520
39.353
39.186
39.019
DMSO-d6, 125 MHz, 25 °C
4
N
H
N
O
O
NO2
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0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8.720
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8.707
8.215
8.200
8.198
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7.550
7.537
7.535
7.179
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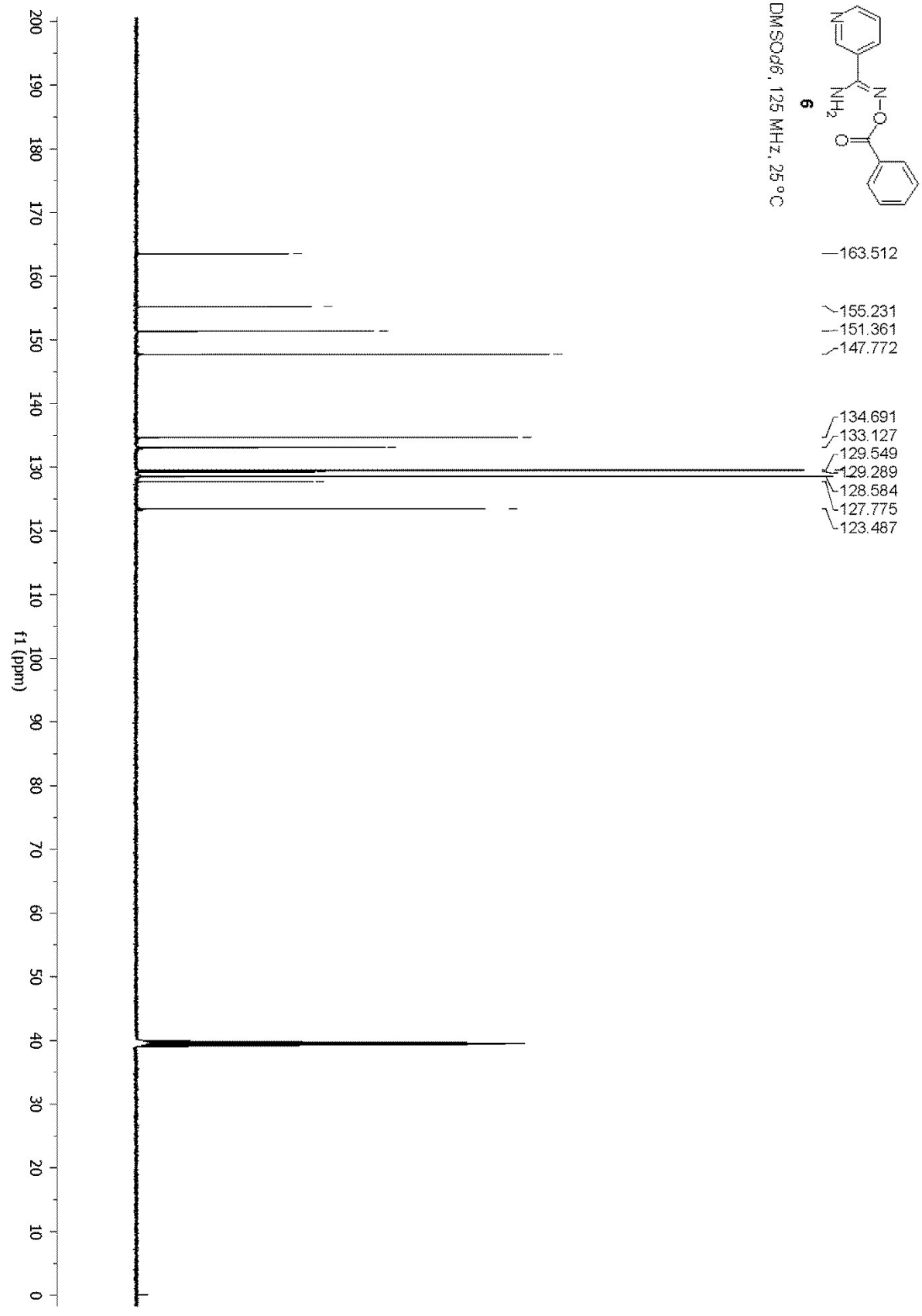
2.14
1.13
1.15
3.08
2.03
f1 (ppm)
6
DMSO-d6, 500 MHz, 25 °C


DMSO-d6, 125 MHz, 25 °C
6
163.512
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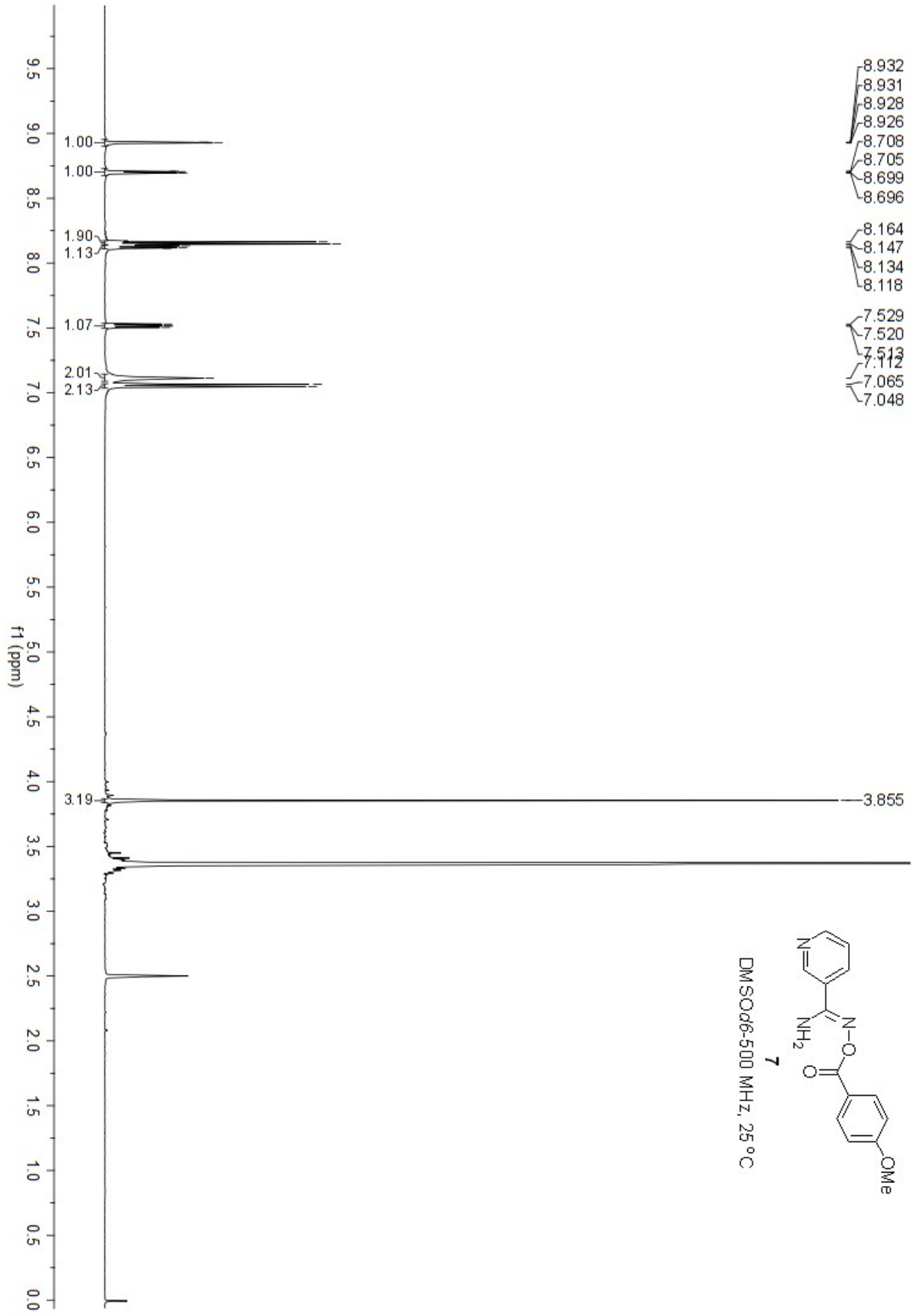
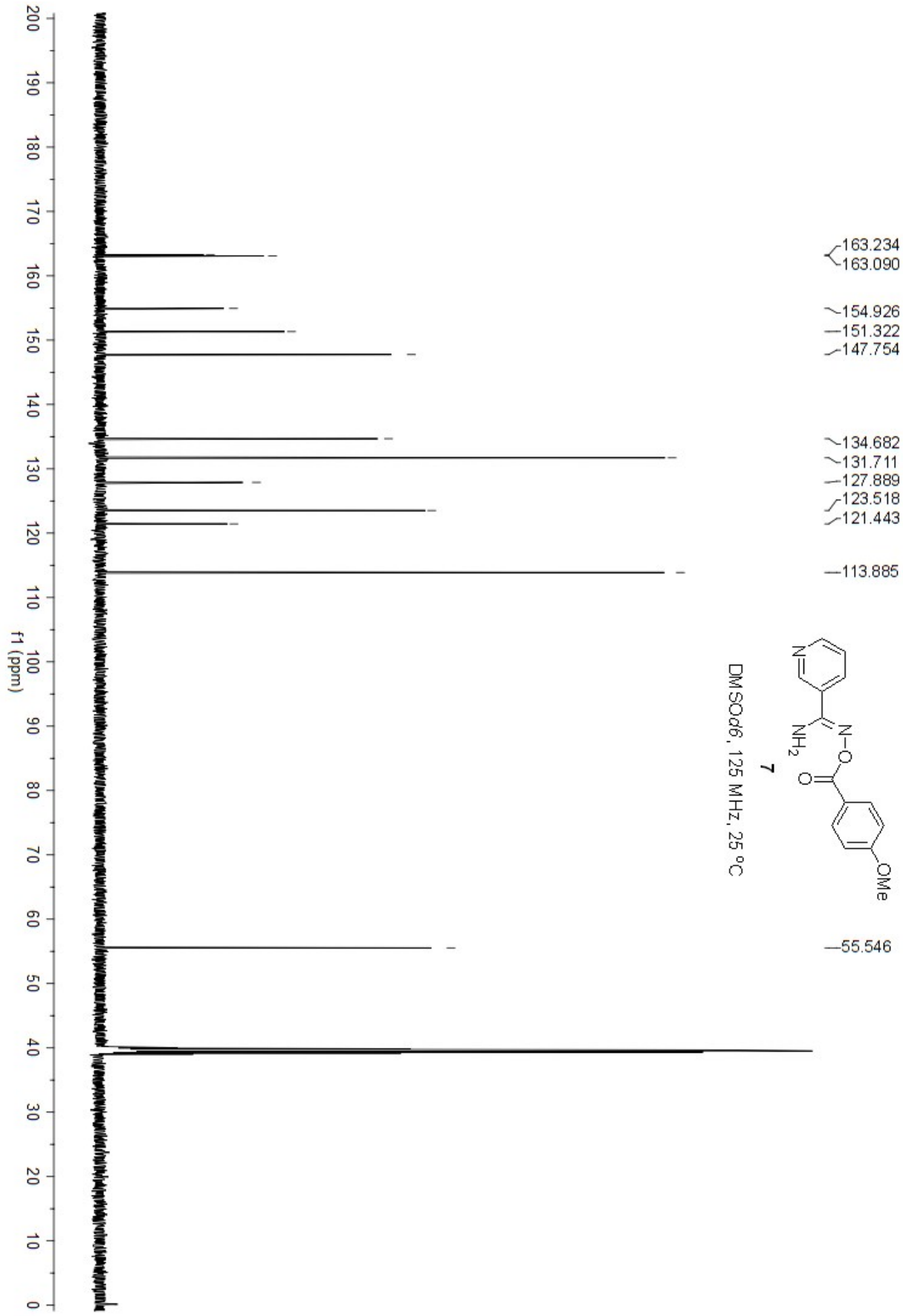
147.772
134.691
133.127
129.549
129.289
128.584
127.775
123.487
f1 (ppm)


8.932
8.931
8.928
8.926
8.708
8.705
8.699
8.696
8.164
8.147
8.134
8.118
7.529
7.520
7.513
7.112
7.065
7.048
3.855
1.00
1.00
1.90
1.13
1.07
2.01
2.13
3.19
f1 (ppm)
DMSO-d6-500 MHz, 25 °C
7
N
NH2
N–O
O
OMe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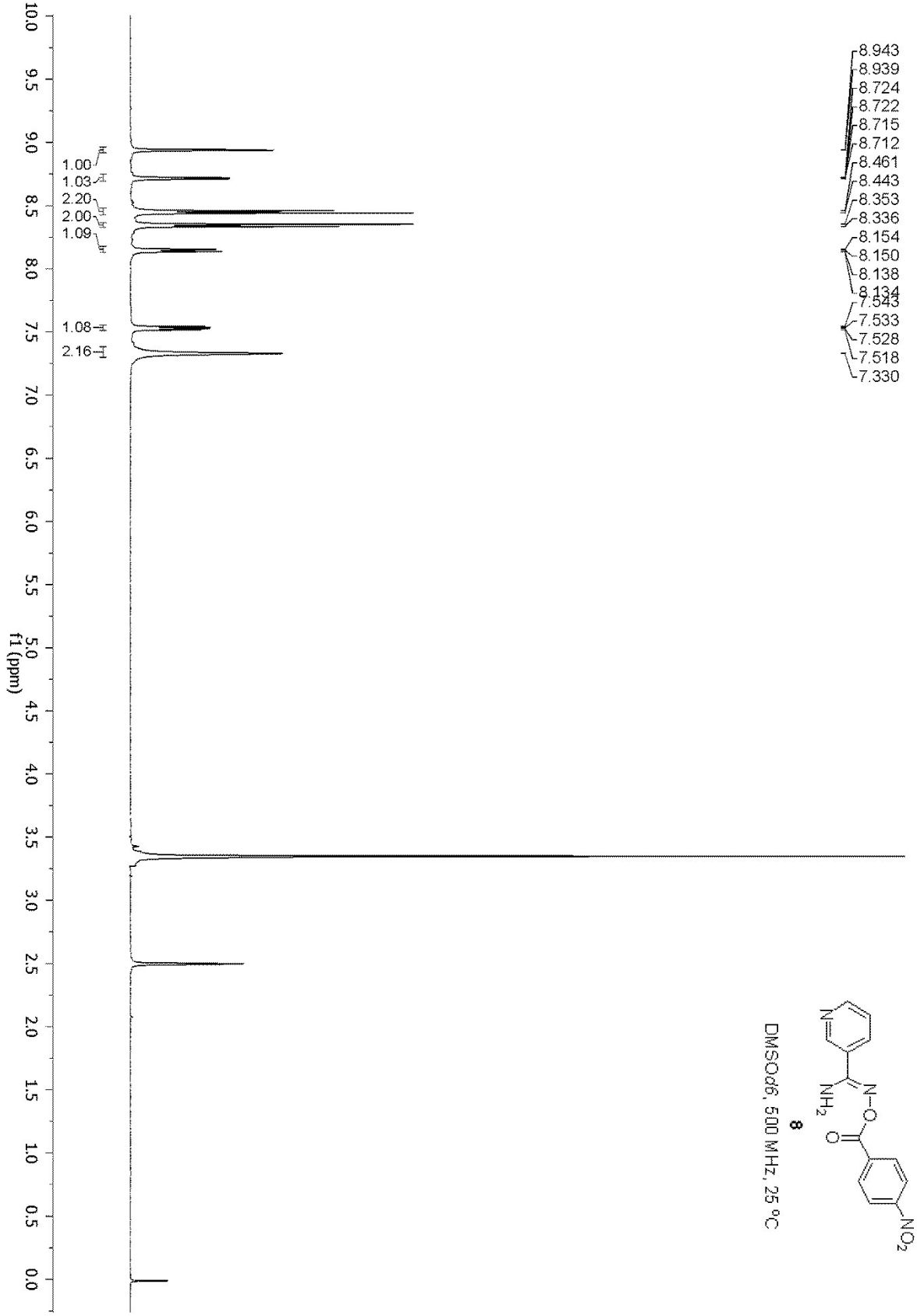
154.926
151.322
147.754
134.682
131.711
127.889
123.518
121.443
113.885
55.546
DMSO@6, 125 MHz, 25 °C
7
f1 (ppm)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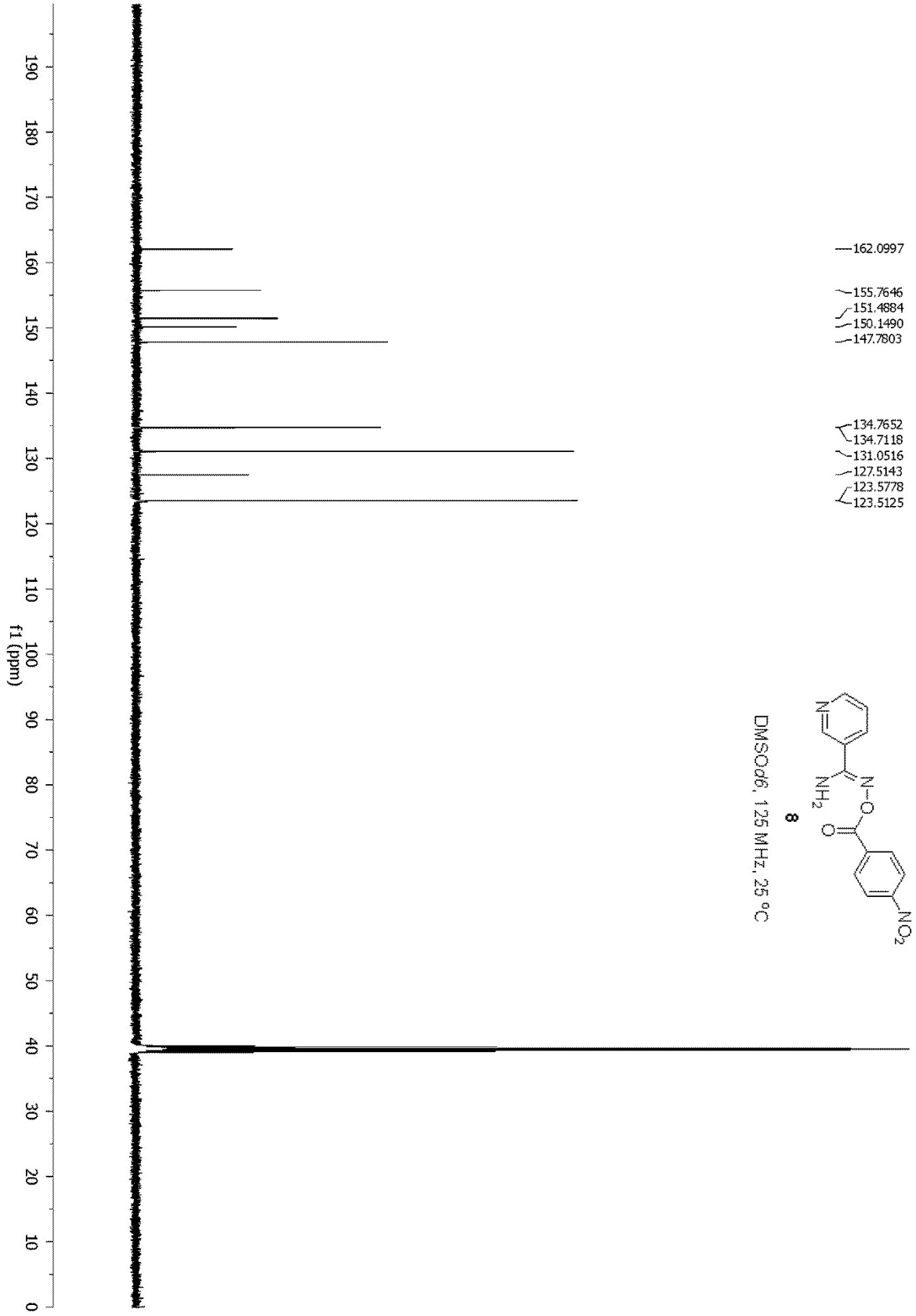
8.724
8.722
8.715
8.712
8.461
8.443
8.353
8.336
8.154
8.150
8.138
8.134
7.543
7.533
7.528
7.518
7.330
1.00
1.03
2.20
2.00
1.09
1.08
2.16
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
DMSO-d6, 600 MHz, 25 °C
8
N
NH2
N
O
O
NO2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155.7646
151.4884
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147.7803
134.7652
134.7118
131.0516
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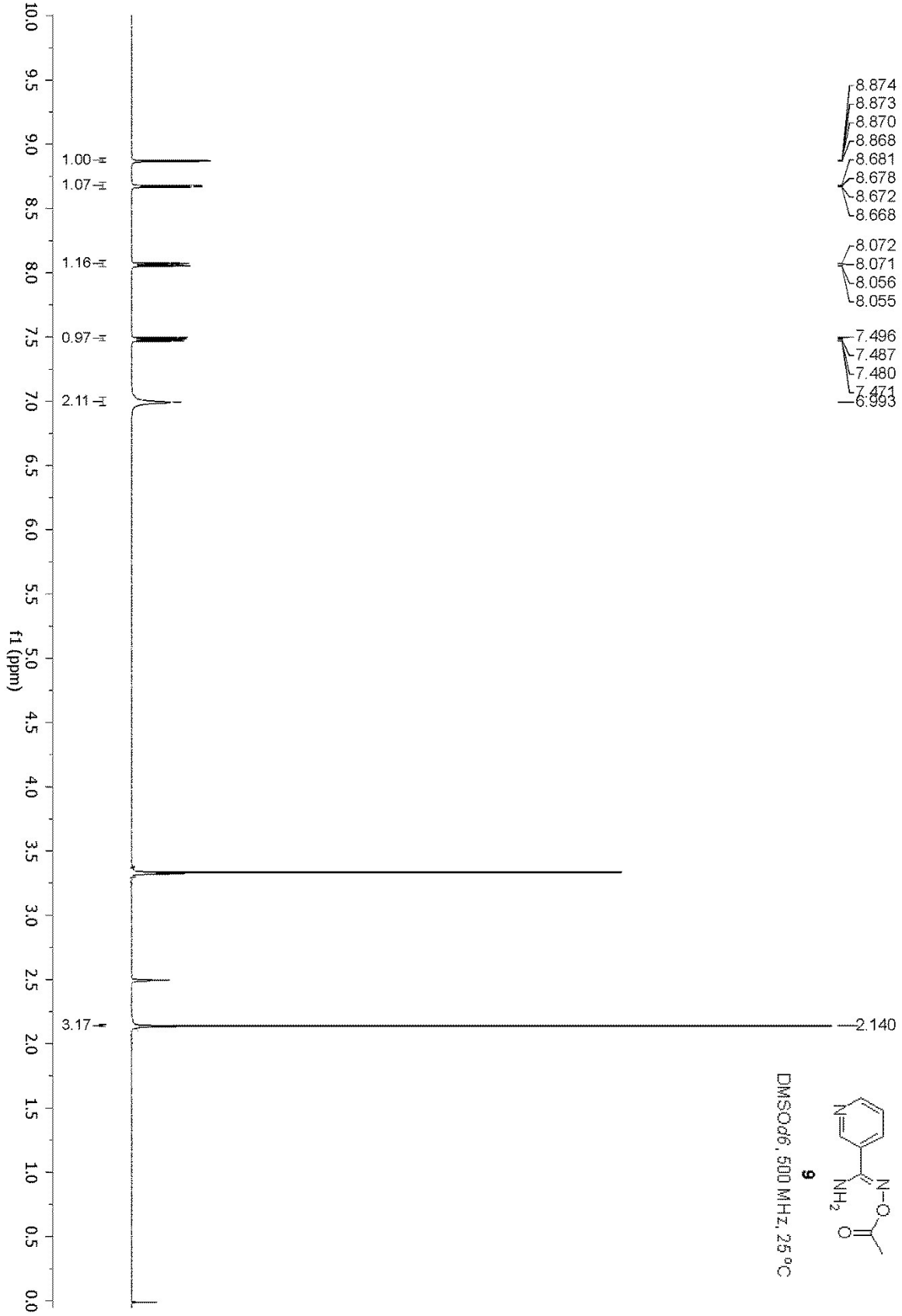
123.5778
123.5125
f1 (ppm)
DMSOd6, 125 MHz, 25 °C
8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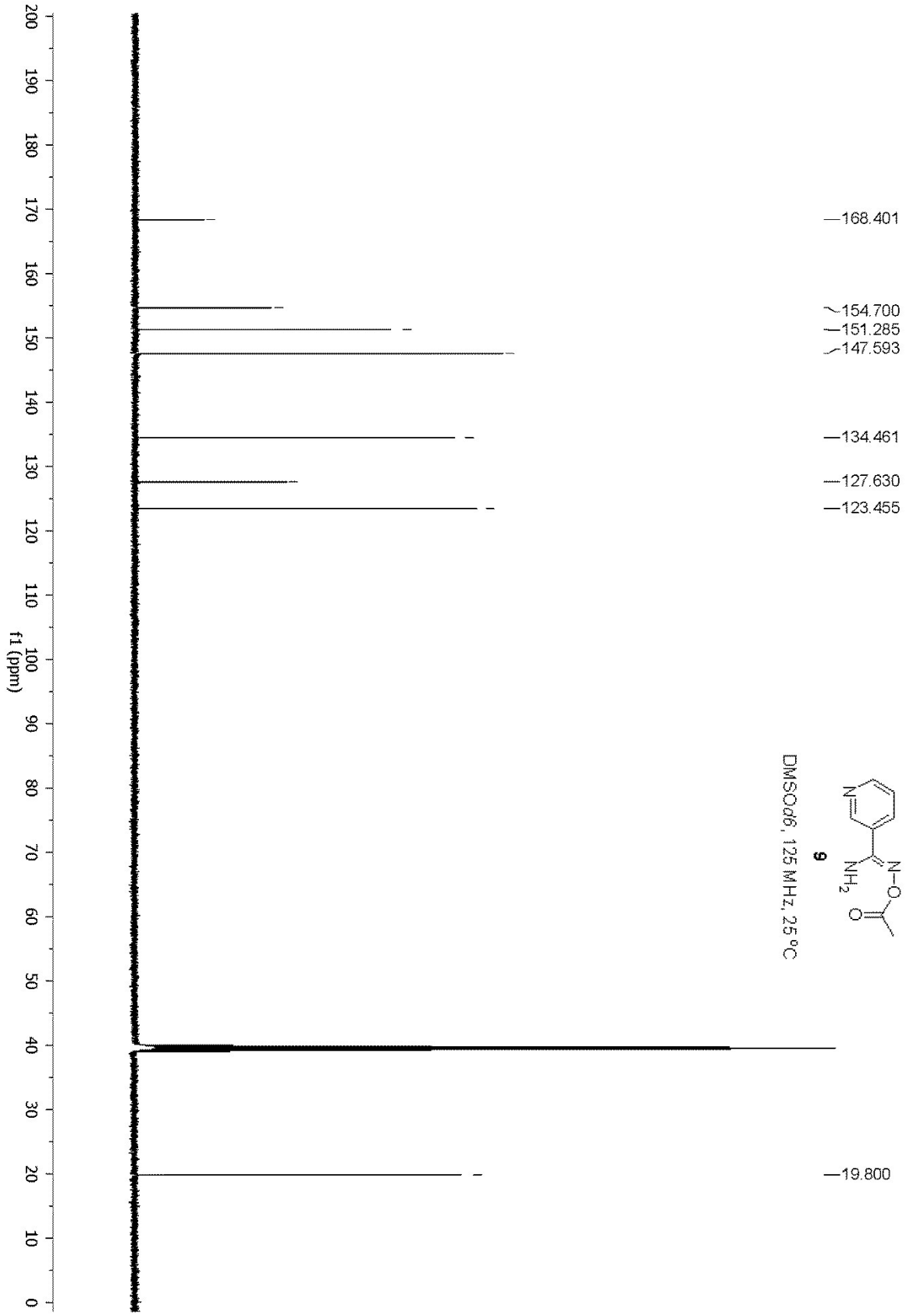
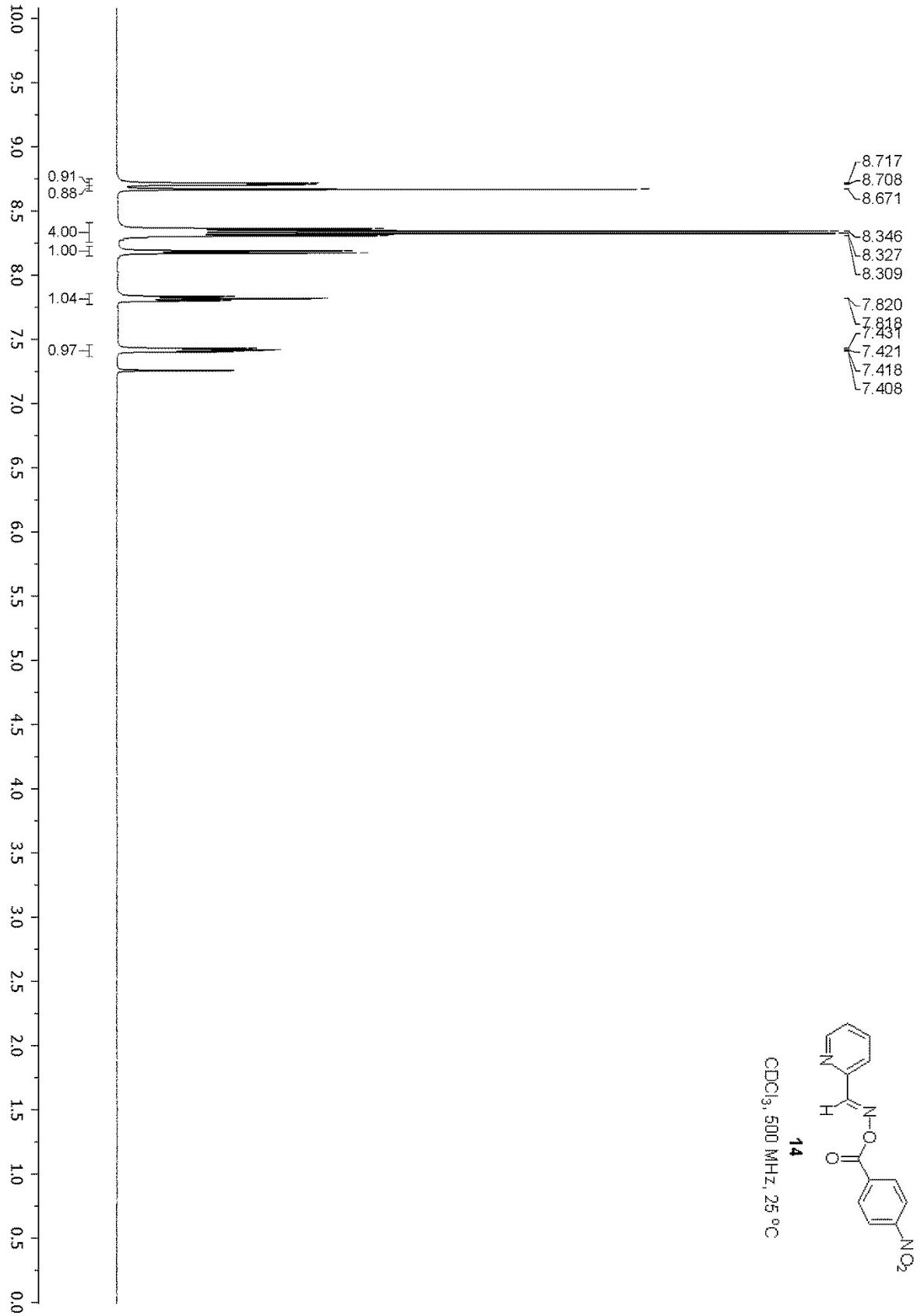
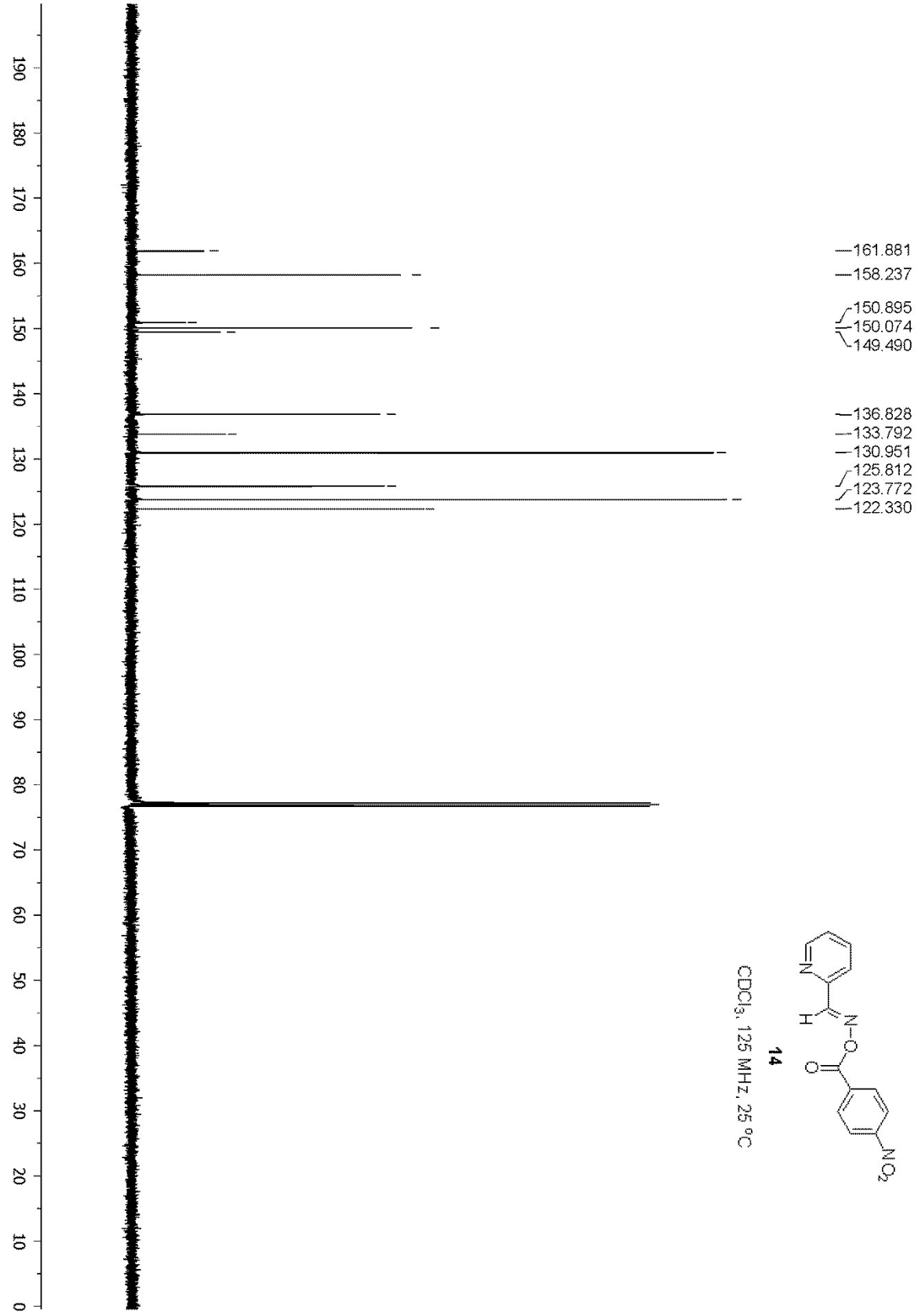
8.870
8.868
8.681
8.678
8.672
8.668
8.072
8.071
8.056
8.055
7.496
7.487
7.480
7.471
6.993
2.140
1.00
1.07
1.16
0.97
2.11
3.17
f1 (ppm)
9
DMSOd6, 500 MHz, 25 °C


168.401
154.700
151.285
147.593
134.461
127.630
123.455
19.800
f1 (ppm)
DMSOd6, 125 MHz, 25 °C
9



14

$CDCl_3$, 500 MHz, 25 °C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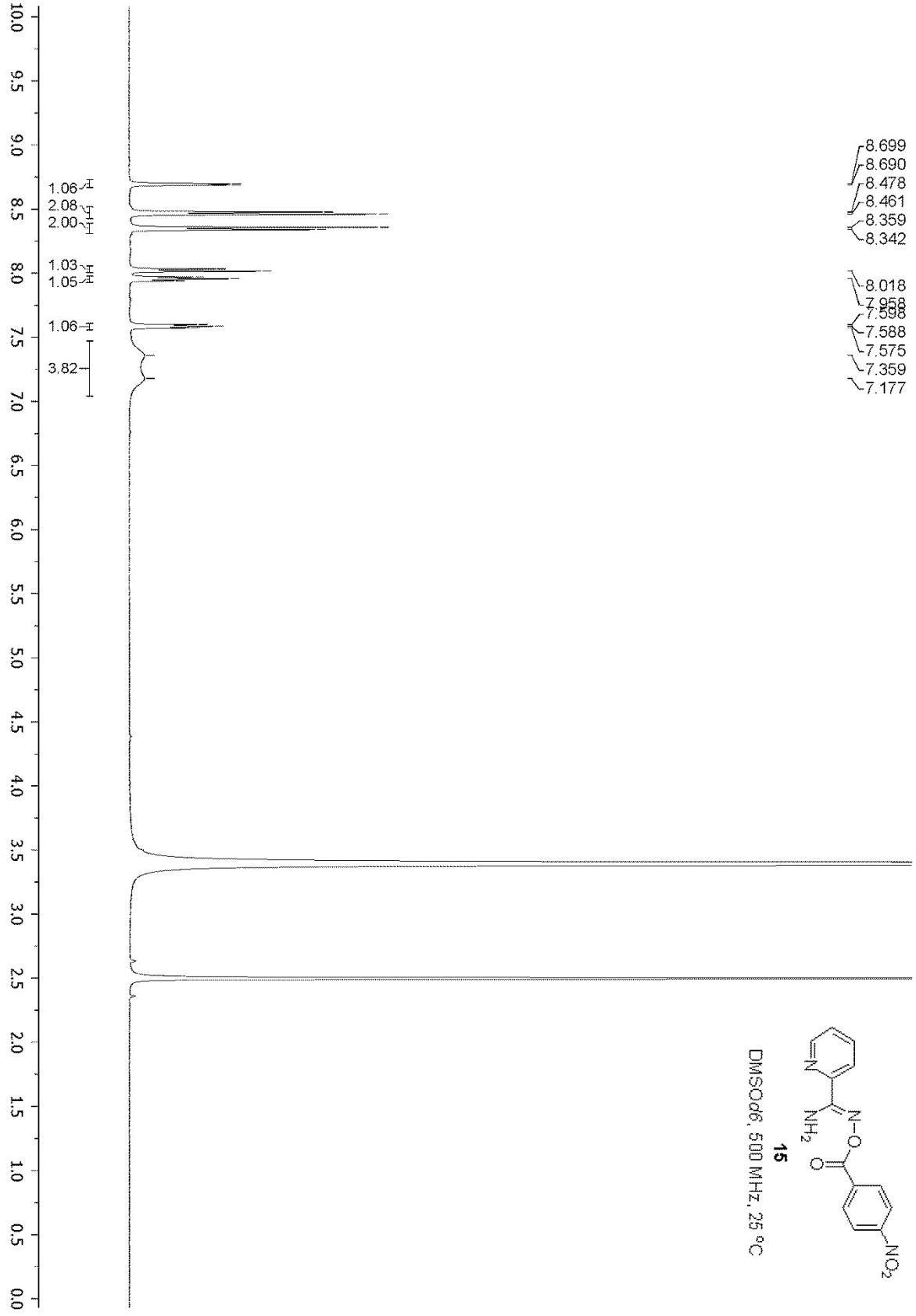
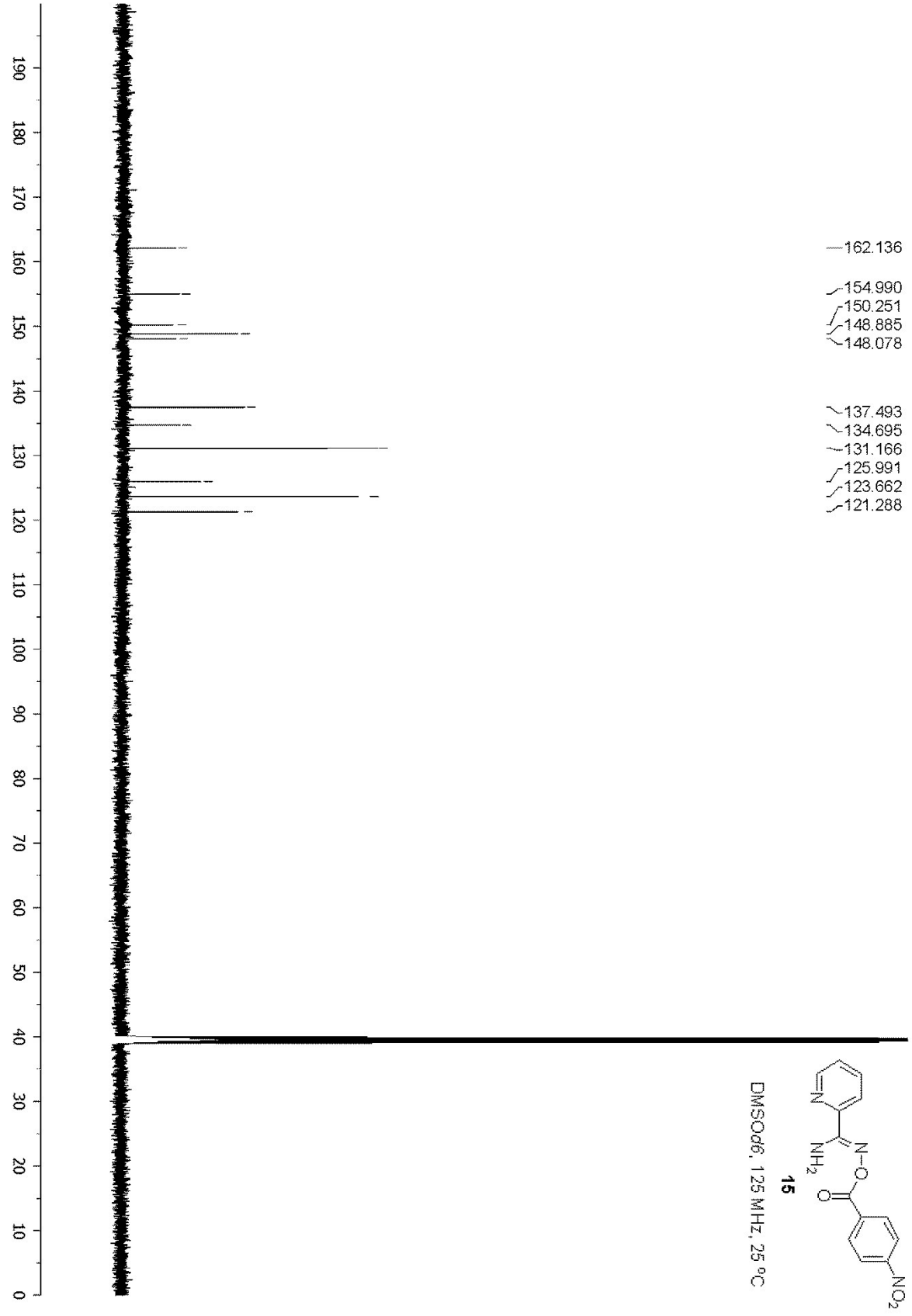
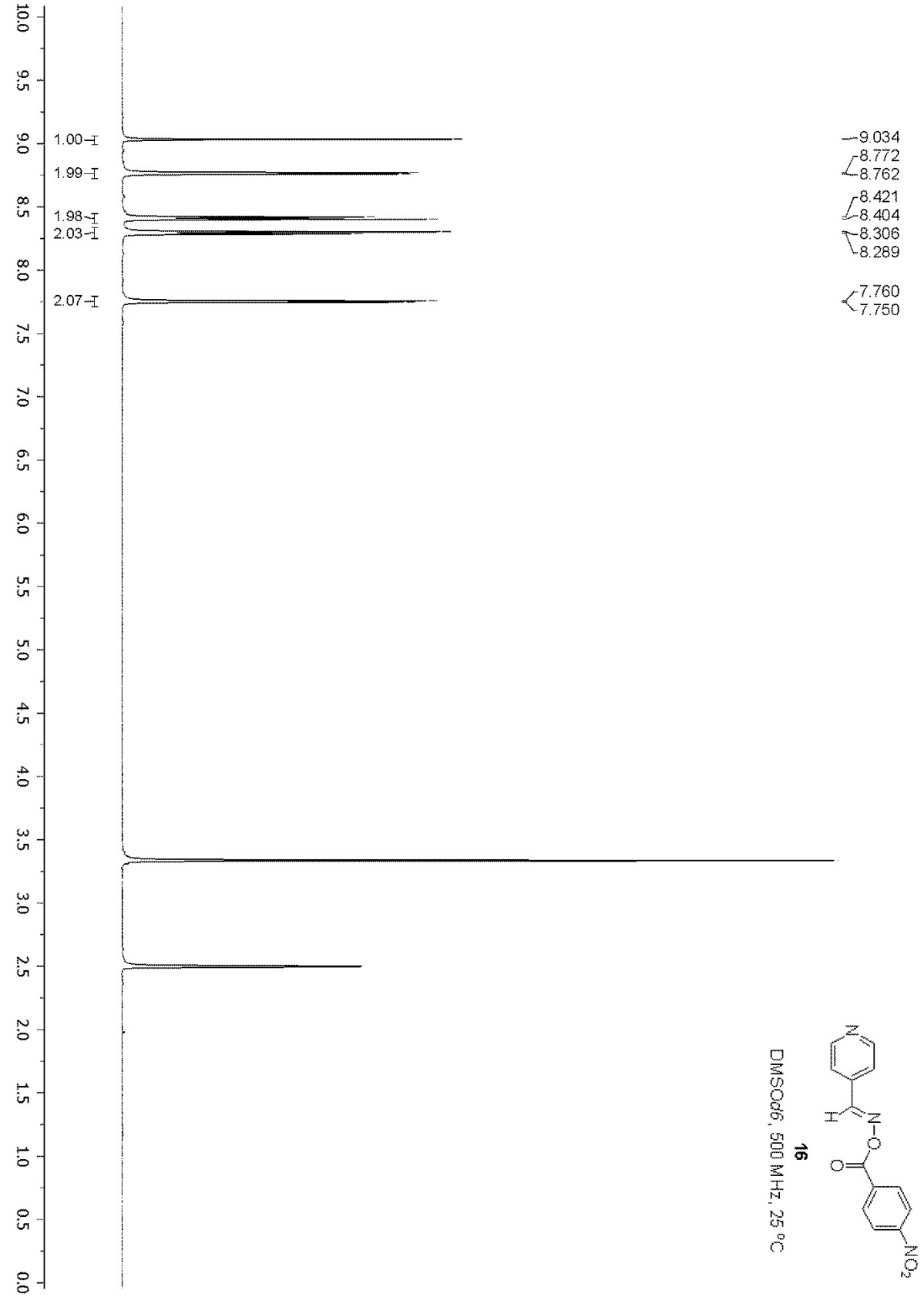
158.237
150.895
150.074
149.490
136.828
133.792
130.951
125.812
123.772
122.330
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
CDCl3, 125 MHz, 25 °C
14
N
H
N
O
O
NO2


8.699
8.690
8.478
8.461
8.359
8.342
8.018
7.958
7.598
7.588
7.575
7.359
7.177
1.06
2.08
2.00
1.03
1.05
1.06
3.82
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
15
DMSO-d6, 500 MHz, 25 °C


162.136
154.990
150.251
148.885
148.078
137.493
134.695
131.166
125.991
123.662
121.288
DMSOd6, 125 MHz, 25 °C
15
NH2
N
O
NO2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8.762
8.421
8.404
8.306
8.289
7.760
7.750
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1.99
1.98
2.03
2.07
10.0
9.5
9.0
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6.5
6.0
5.5
5.0
4.5
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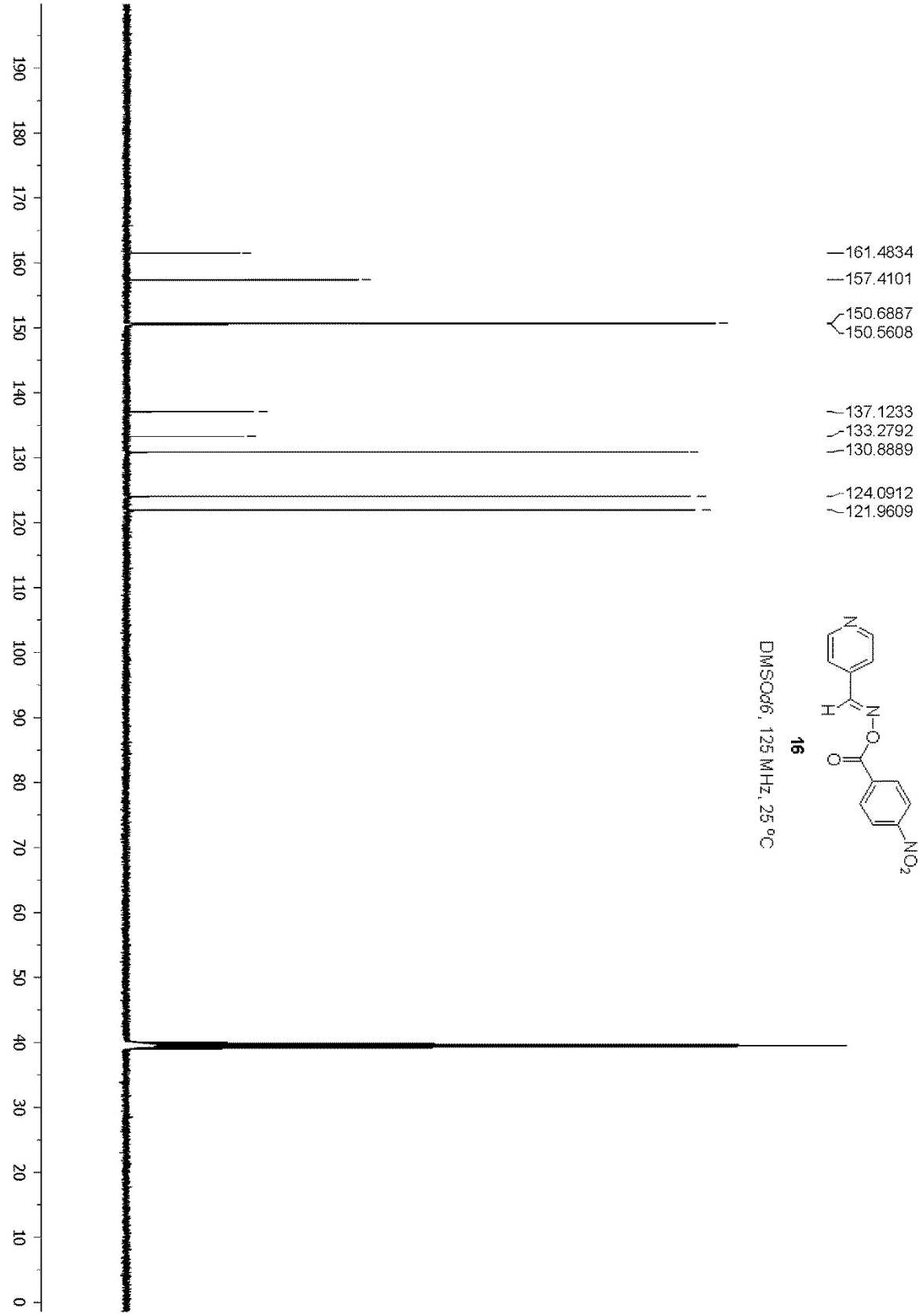
0.0
16
DMSO-d6, 500 MHz, 25 °C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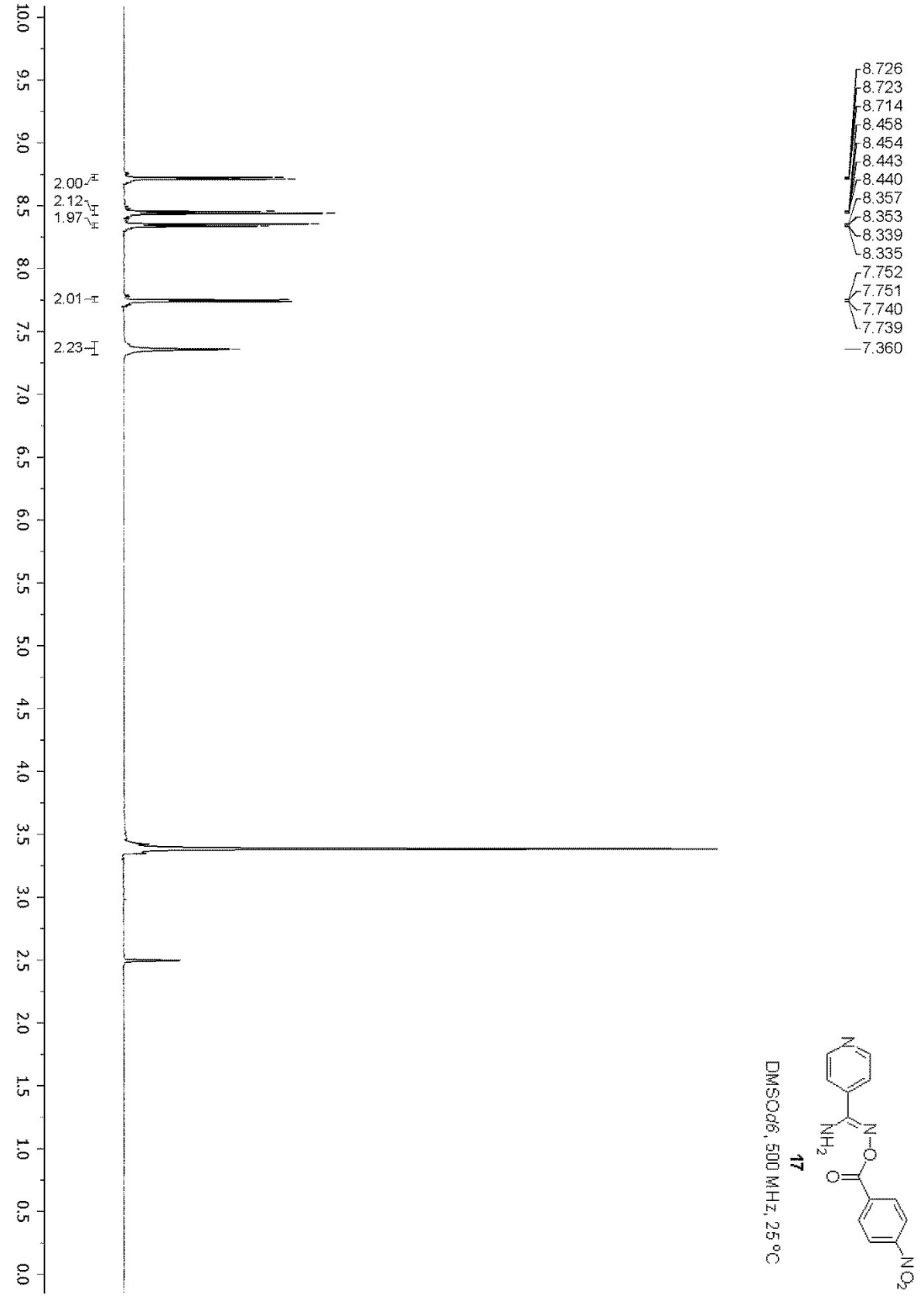
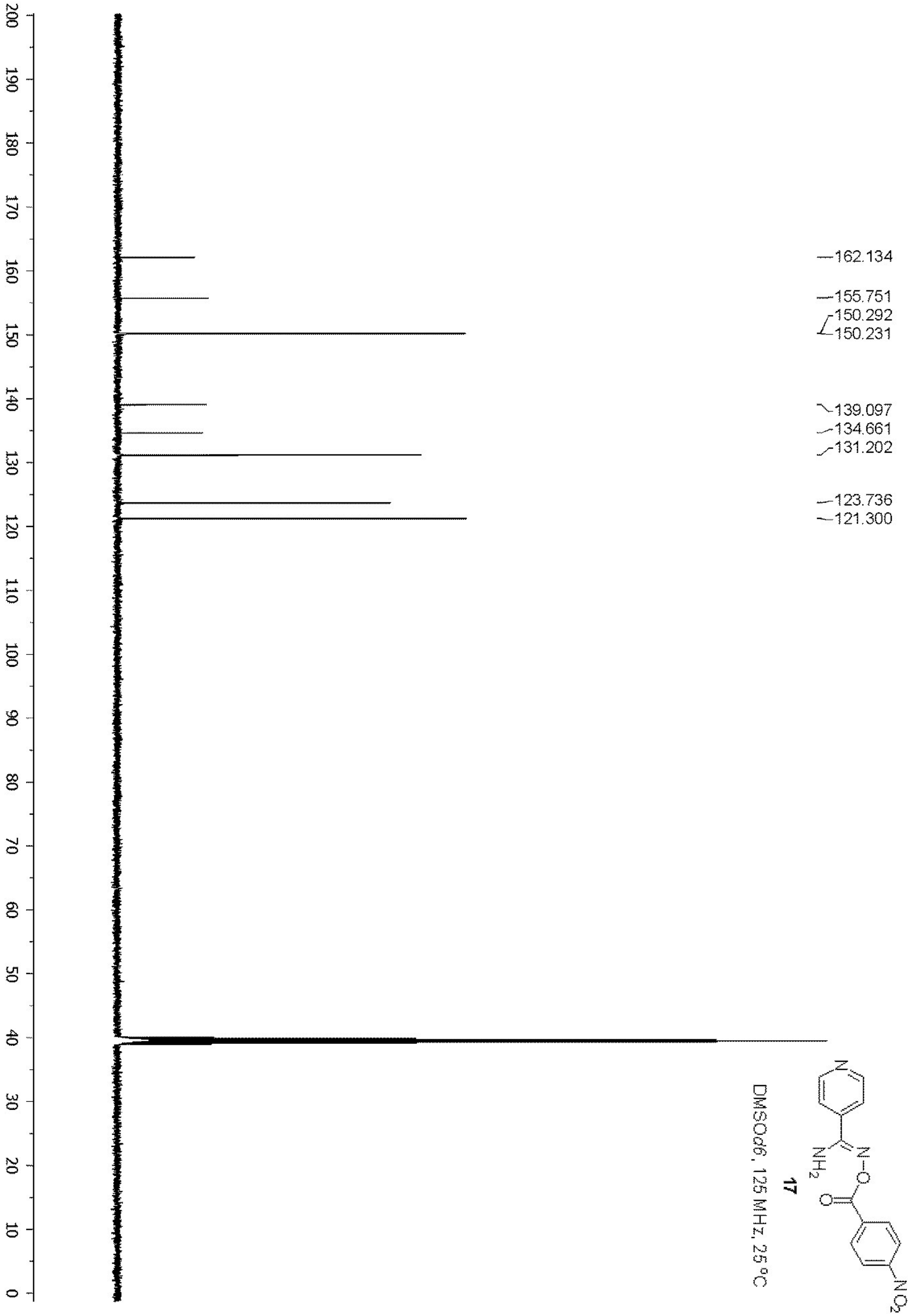
150.6887
150.5608
137.1233
133.2792
130.8889
124.0912
121.9609
16
DMSOd6, 125 MHz, 25 °C
N
H
N
O
O
NO2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



17

DMSO-*d6*, 500 MHz, 25 °C



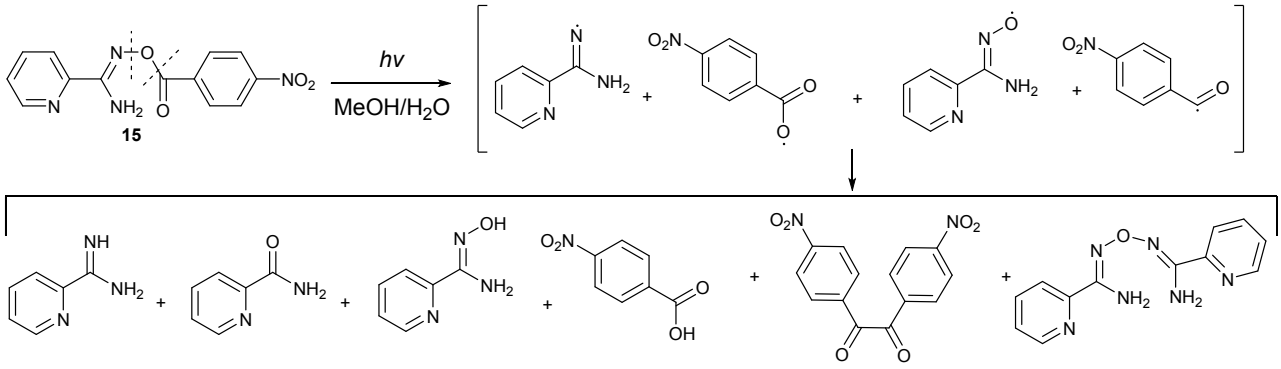
162.134
155.751
150.292
150.231
139.097
134.661
131.202
123.736
121.300
17
DMSOd6, 125 MHz, 25 °C

Photochemistry

Irradiation of derivative 15 under various conditions at 312 nm.

1. Irradiation of *N′*-((4-nitrobenzoyl)oxy)picolinimidamide (**15**) in MeOH/H_2O 9:1.

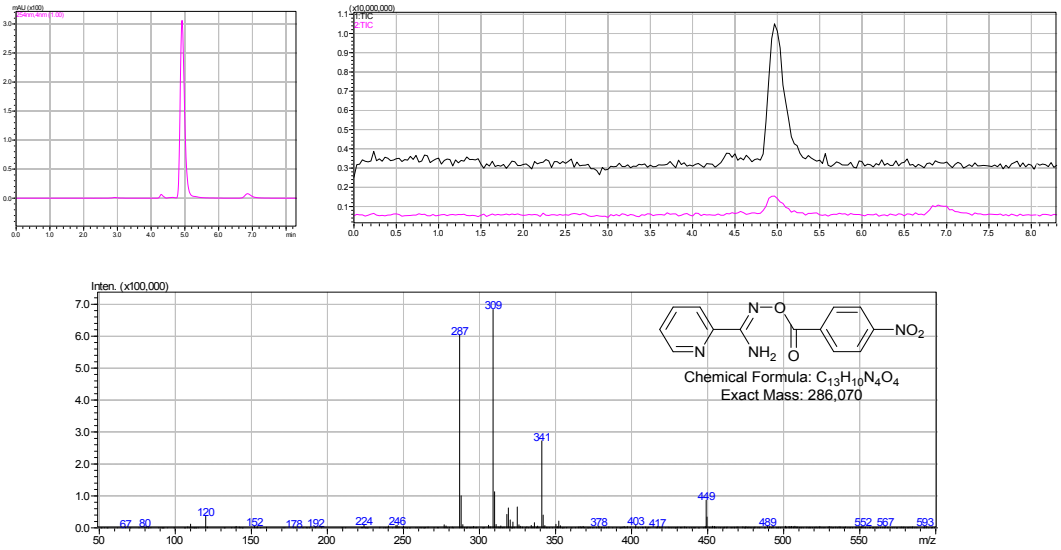
N′-((4-nitrobenzoyl)oxy)picolinimidamide **15** (13 mg) was placed into a quartz tube containing a mixture of MeOH/H_2O 9:1 (2 mL). The resulting heterogeneous mixture was degassed for 1 h and then irradiated at 312 nm for 5 h. The floating solid was removed by filtration to give 9 mg of unreacted starting material. Samples of the solid and the filtrate were analyzed with LC-MS.



Scheme 1. Proposed structures for the products obtained by the irradiation *N′*-((4-nitrobenzoyl)oxy)picolinimidamide **15** in MeOH/H_2O 9:1. The assignment is based on the fragments observed by the analysis of the LC-MS.

Solid

UV detection MS detection

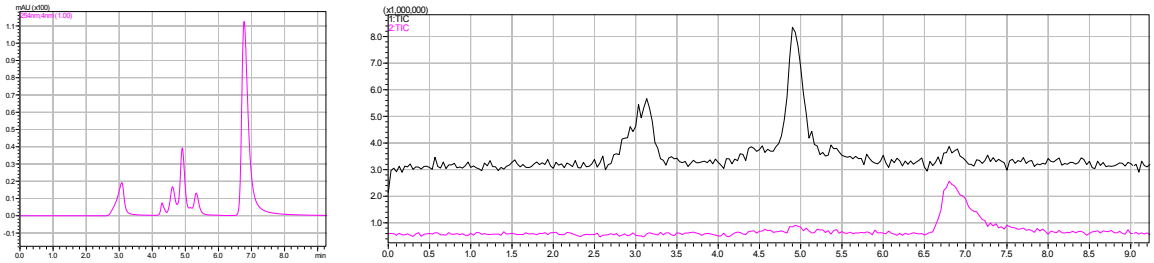


Time 4.9 min

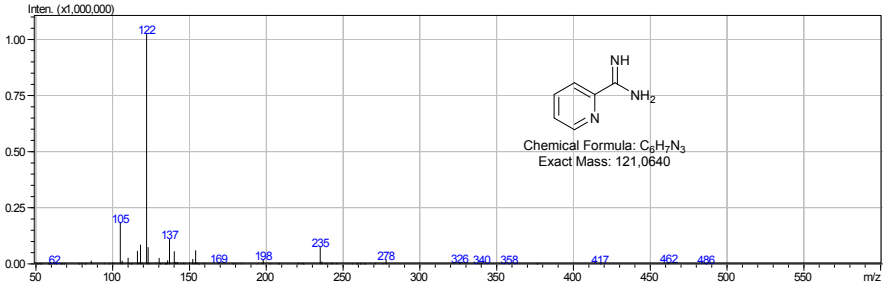
Positive: 287 [**M**+H]$^+$, 309 [**M**+Na]$^+$, 341 [**M**+Na+MeOH]$^+$.

Filtrate

UV detection MS detection

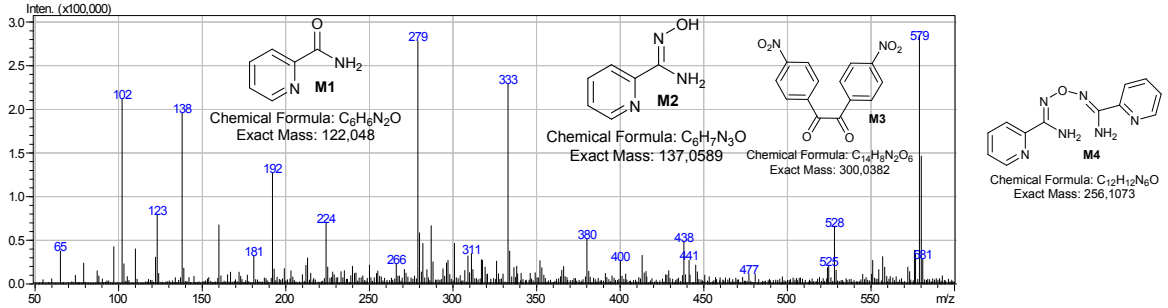


Time 3.1 min

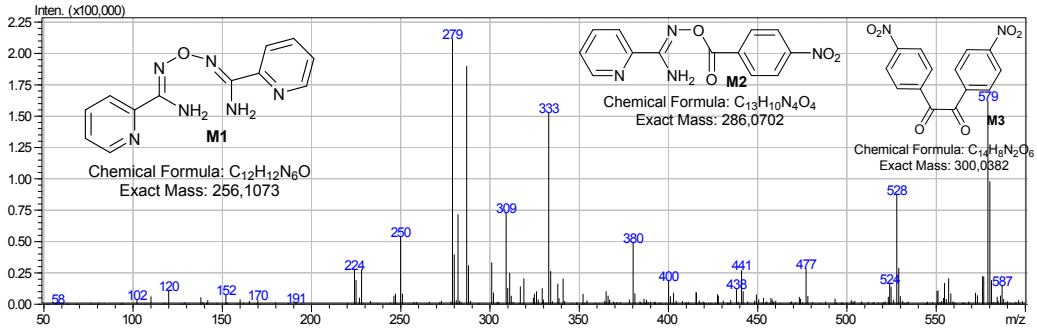


Positive: 122 [**M**+H]$^+$.

Time 4.9 min

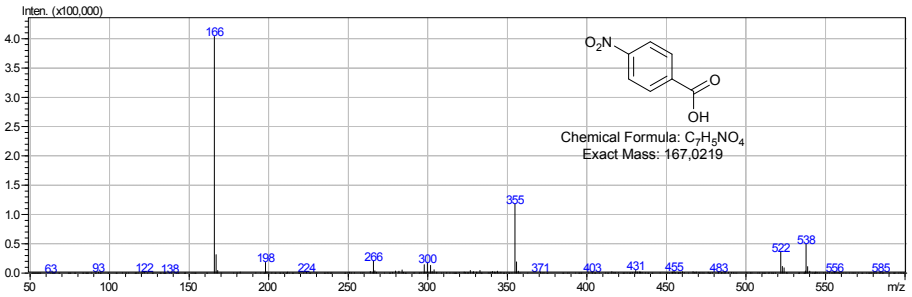


Positive: 123 [**M1**+H]$^+$, 138 [**M2**+H]$^+$, 279 [**M4**+Na]$^+$, 333 [**M3**+H+MeOH]$^+$.



Positive: 279 [**M1**+Na]$^+$, 287 [**M2**+H]$^+$, 309 [**M2**+Na]$^+$, 333 [**M3**+H+MeOH]$^+$.

Time 6.8 min

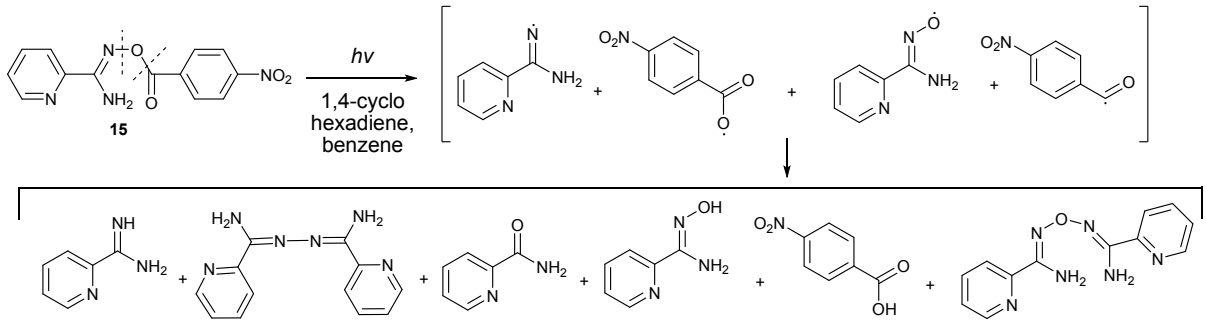


Negative: 166 [**M**-H]$^-$.

The starting material **15** is highly insoluble in the reaction solvent. From the integration of the UV detection of the filtrate it seems that the N-O cleavage dominates, as fragment with m/z 166 appears in high percentage. Amidine is consumed in side reactions.

2. Irradiation of *N′*-((4-nitrobenzoyl)oxy)picolinimidamide (**15**) in benzene.

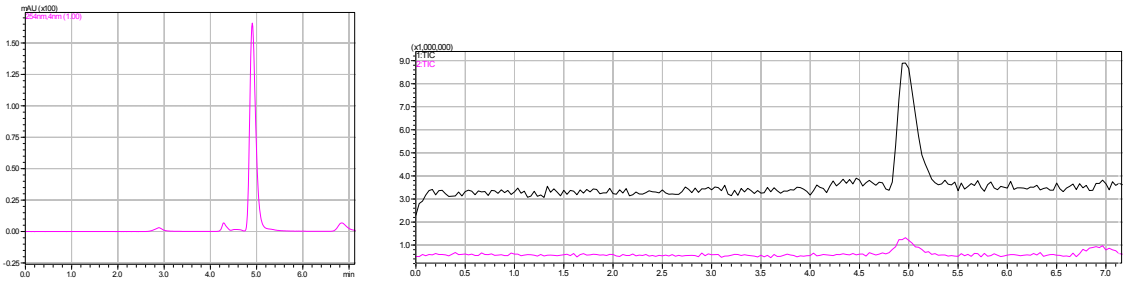
N′-((4-nitrobenzoyl)oxy)picolinimidamide **15** (13 mg) was placed into a quartz tube containing benzene (2 mL). The resulting heterogeneous mixture was degassed for 1 h, 1,4-cyclohexadiene (10 eq) was added and then irradiated at 312 nm for 5 h. The floating solid was removed by filtration to give 8 mg of unreacted starting material. Samples of the solid and the filtrate were analyzed with LC-MS.



Scheme 2. Proposed structures for the products obtained by the irradiation *N′*-((4-nitrobenzoyl)oxy)picolinimidamide **15** in benzene. The assignment is based on the fragments observed by the analysis of the LC-MS.

Solid

UV detection MS detection

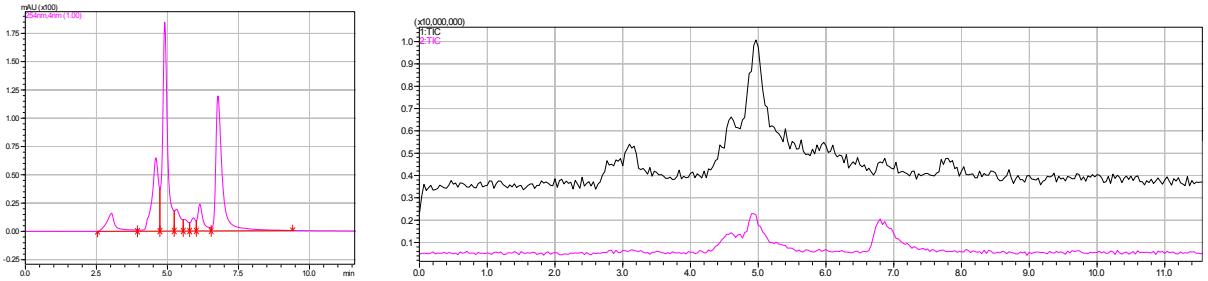


Time 4.9 min

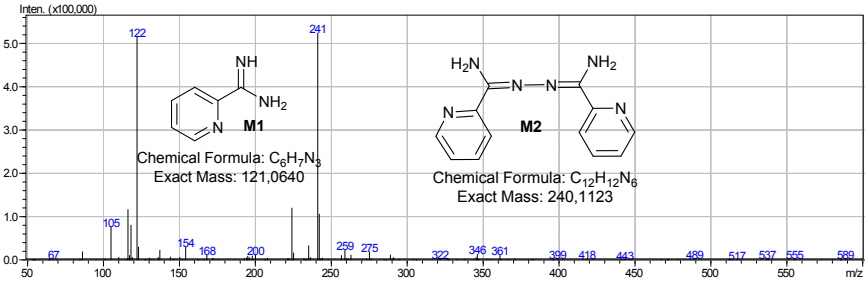
Same as before for solid.

Filtrate

UV detection MS detection

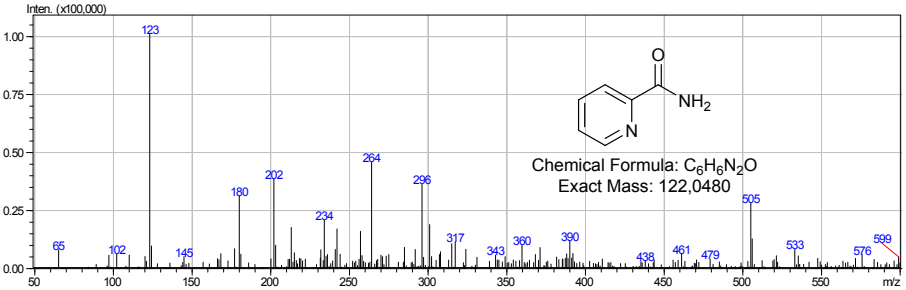


Time 3.1 min



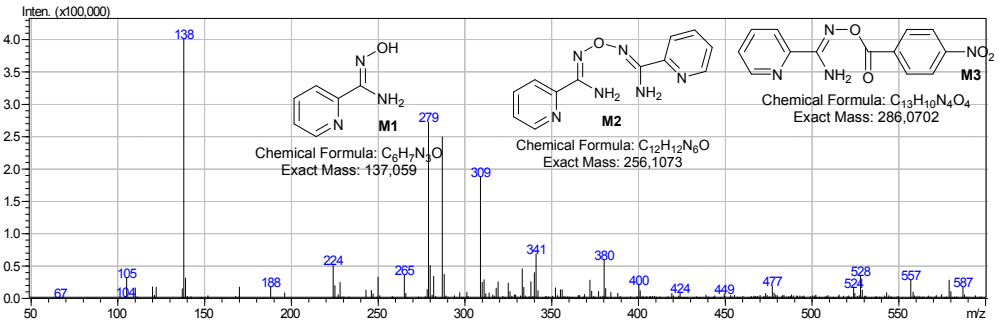
Positive: 122 [**M1**+H]$^+$, 241 [**M2**+H]$^+$.

Time 4.6 min



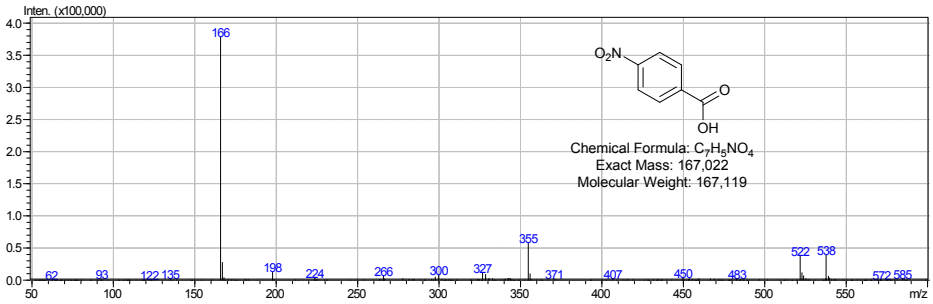
Positive: 123 [**M**+H]$^+$.

Time 4.9 min



Positive: 138 [**M1**+H]$^+$, 279 [**M2**+Na]$^+$, 309 [**M3**+Na]$^+$.

Time 6.8 min

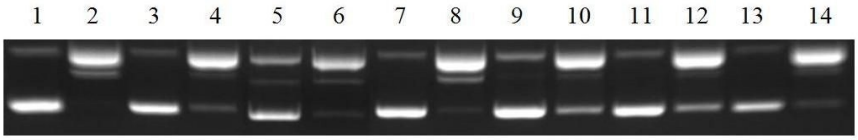


Negative: 166 [**M**-H]$^-$.

The starting material **15** is highly insoluble in the reaction solvent. From the integration of the UV detection of the filtrate it seems that the N-O cleavage dominates, as fragment with m/z 166 appears in high percentage. Amidine is consumed in side reactions.

References for irradiation of oxime acyl compounds: a) J J.-P. Vermes and R. Beugelmans, *Tetrahedron Lett.*, 1969, **10**, 2091–2092; b) J. Lalevée, X. Allonas, J. P. Fouassier, H. Tachi, A. Izumitani, M. Shirai and M. Tsunooka, *J. Photochem. Photobiol. A, Chem*., 2002, **151**, 27–37; c) R. Alonso, P. J. Campos, M. A. Rodríguez and D. Sampedro, *J. Org. Chem.*, 2008, **73**, 2234–2239.

Gel electrophoresis of plasmid with or without *N′*-((4-nitrobenzoyl)oxy) isonicotinimidamide (17) at various pHs



1 Plasmid + tris buffer pH 4
2 Plasmid + **17** (500 µM) – tris buffer pH 4 + UV
3 Plasmid + tris buffer pH 5
4 Plasmid + **17** (500 µM) – tris buffer pH 5 + UV
5 Plasmid + tris buffer pH 6
6 Plasmid + **17** (500 µM) – tris buffer pH 6 + UV
7 Plasmid + tris buffer pH 7
8 Plasmid + **17** (500 µM) – tris buffer pH 7 + UV
9 Plasmid + tris buffer pH 8
10 Plasmid + **17** (500 µM) – tris buffer pH 8 + UV
11 Plasmid + tris buffer pH 9
12 Plasmid + **17** (500 µM) – tris buffer pH 9 + UV
13 Plasmid + tris buffer pH 10
14 Plasmid + **17** (500 µM) – tris buffer pH 10 + UV

UV-Vis spectra of compounds 4, 8, 14-17 in DMSO