SUPPORTING INFORMATION

Journal of Organic Chemistry

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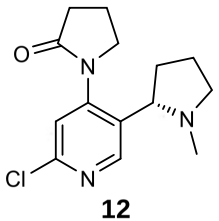
"*Synthesis of C-4 Substituted Amido Nicotine Derivatives via Copper (I)- and (II)-Catalyzed Cross-Coupling Reactions*"

I. Genenral Information----------Page 1
II. ^{1}H and ^{13}C NMR spectra for **12**-**18**, **22**----------Page 2-27

Total pages of supporting information : (27).

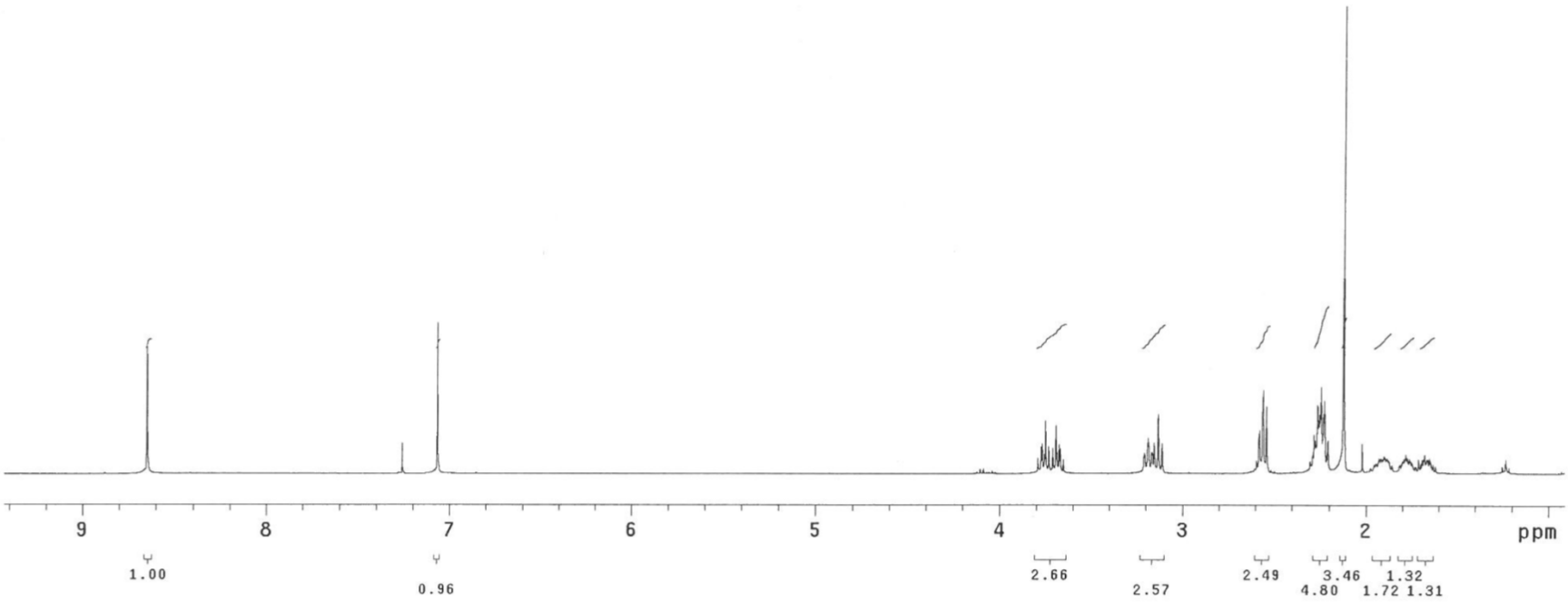
General Information

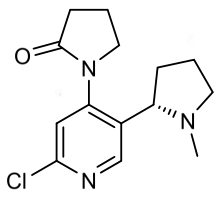
Unless otherwise noted, all reactions were performed in oven and flame-dried glassware under nitrogen atmosphere and stirred magnetically. Thin layer chromatography was performed on silica gel coated chips. Column chromatography was processed on silica gel, 60 Å, (200-400 mesh). Radial preparative layer chromatography (Radial PLC) was performed on glass plates coated with 1 or 2 mm layers of Kieselgel 60 PF254 containing gypsum. (*S*)-Nicotine was distilled under vacuum using aspiration and stored over 4 Å molecular sieves before use. Tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl before use. All the other solvents were stored over 4 Å molecular sieves. Alkyllithium reagents were titrated against diphenylacetic acid to re-determine the concentration before use respectively. Other reagents were directly used after purchase. Nuclear Magnetic Resonance spectra (NMR) were obtained from a 100 MHz, 300 MHz, 400 MHz or 700 MHz spectrometer. Chemical shifts are in δ units (ppm) with TMS (0.0 ppm) used as an internal standard. The mass analyzer type used for the HRMS measurements was TOF with electrospray as the ionization method.



12

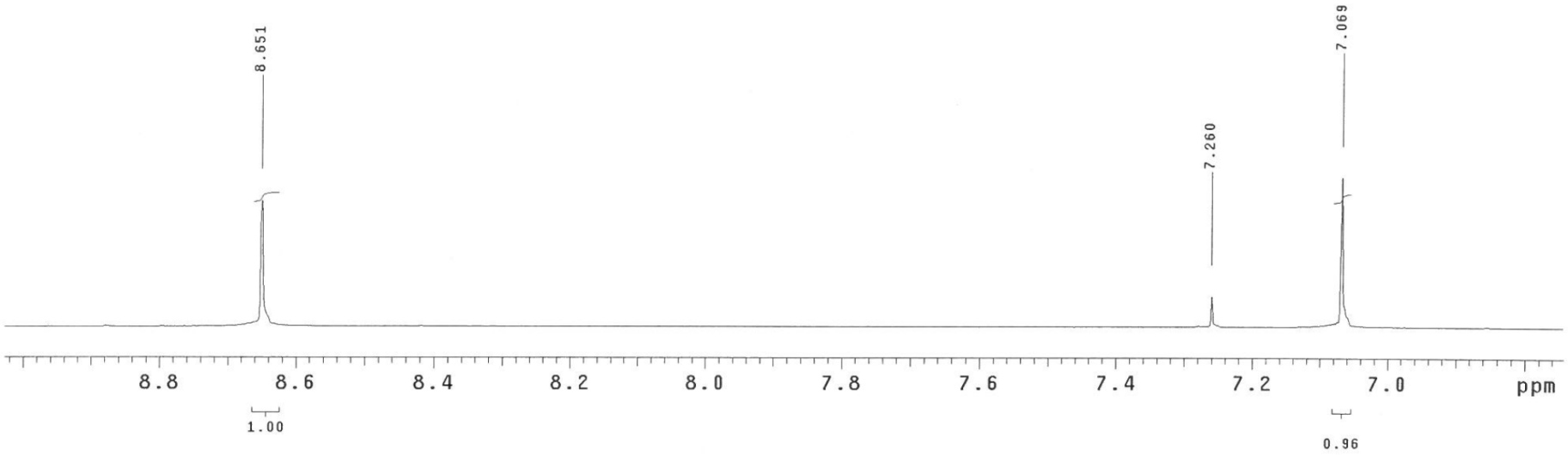
^{1}H NMR (400 MHz, $CDCl_3$)

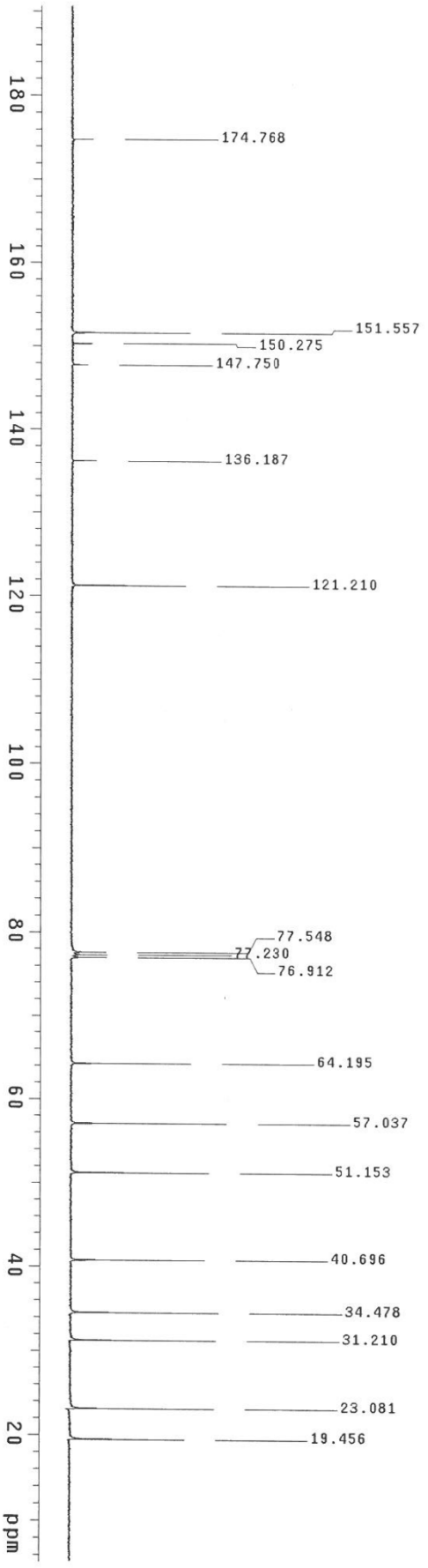




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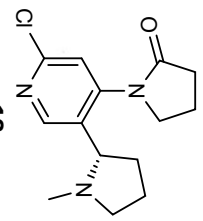
^{1}H NMR (400 MHz, $CDCl_3$)

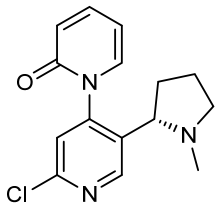




^{13}C NMR (100 MHz, $CDCl_3$)

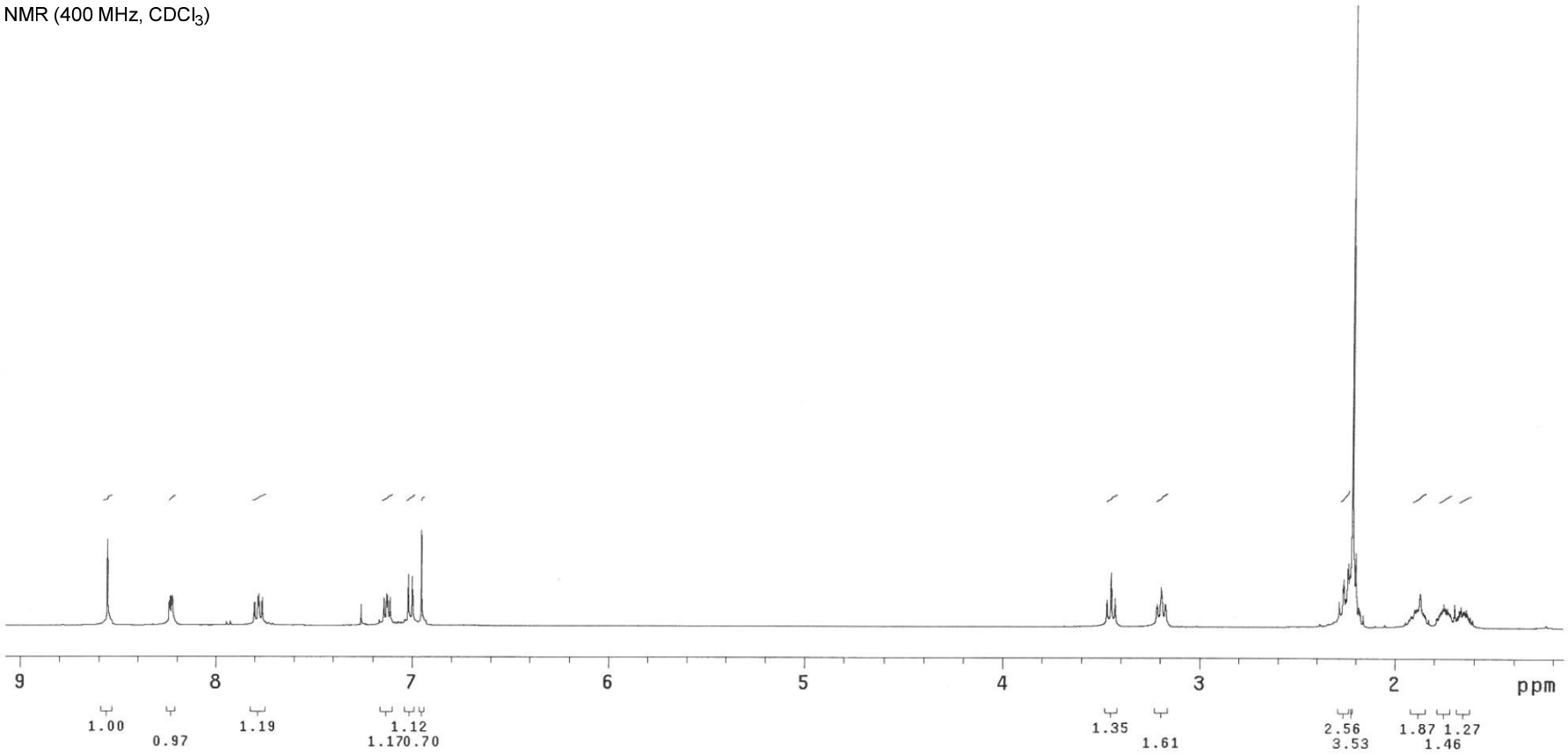
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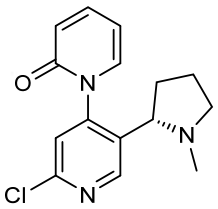




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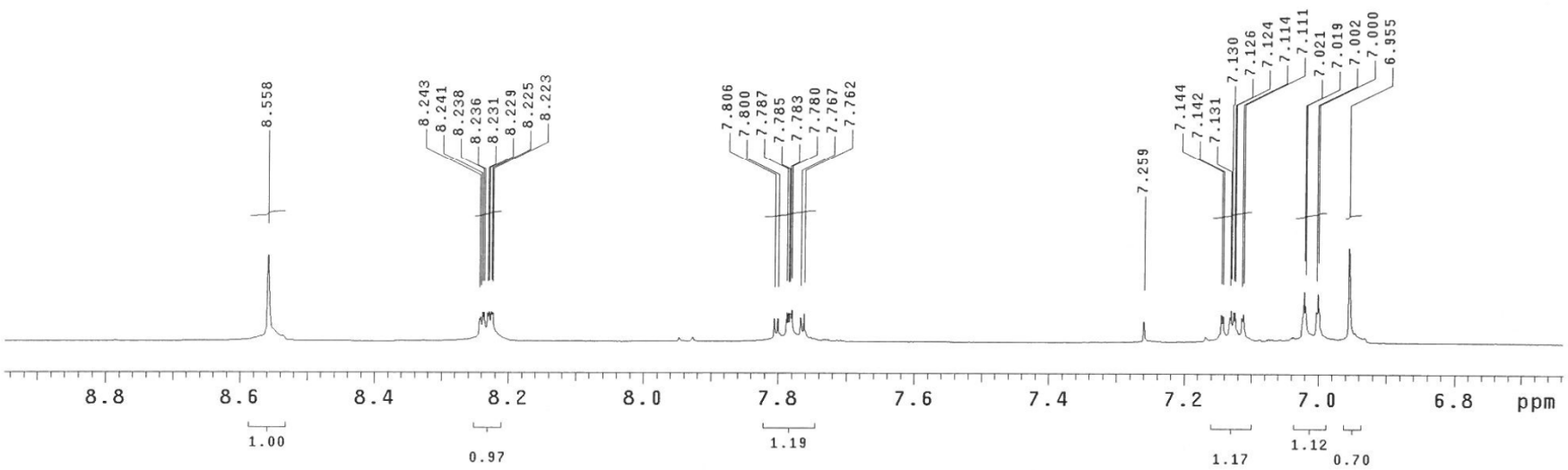
^{1}H NMR (400 MHz, $CDCl_3$)

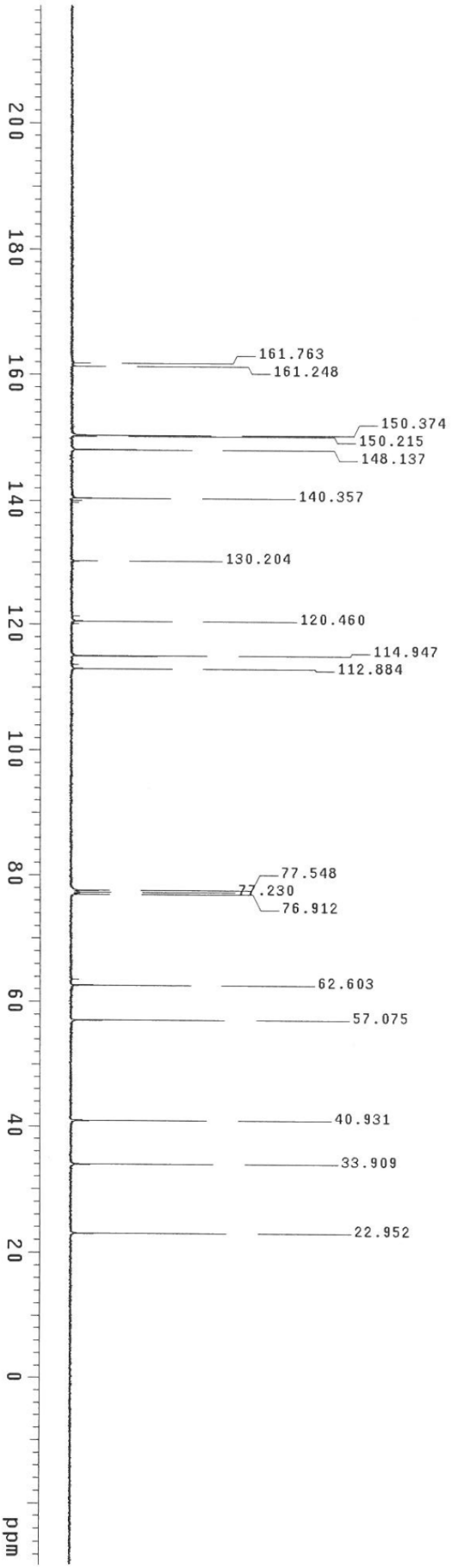




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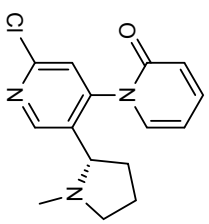
^{1}H NMR (400 MHz, $CDCl_3$)

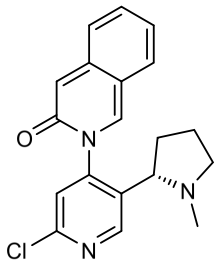




^{13}C NMR (100 MHz, $CDCl_3$)

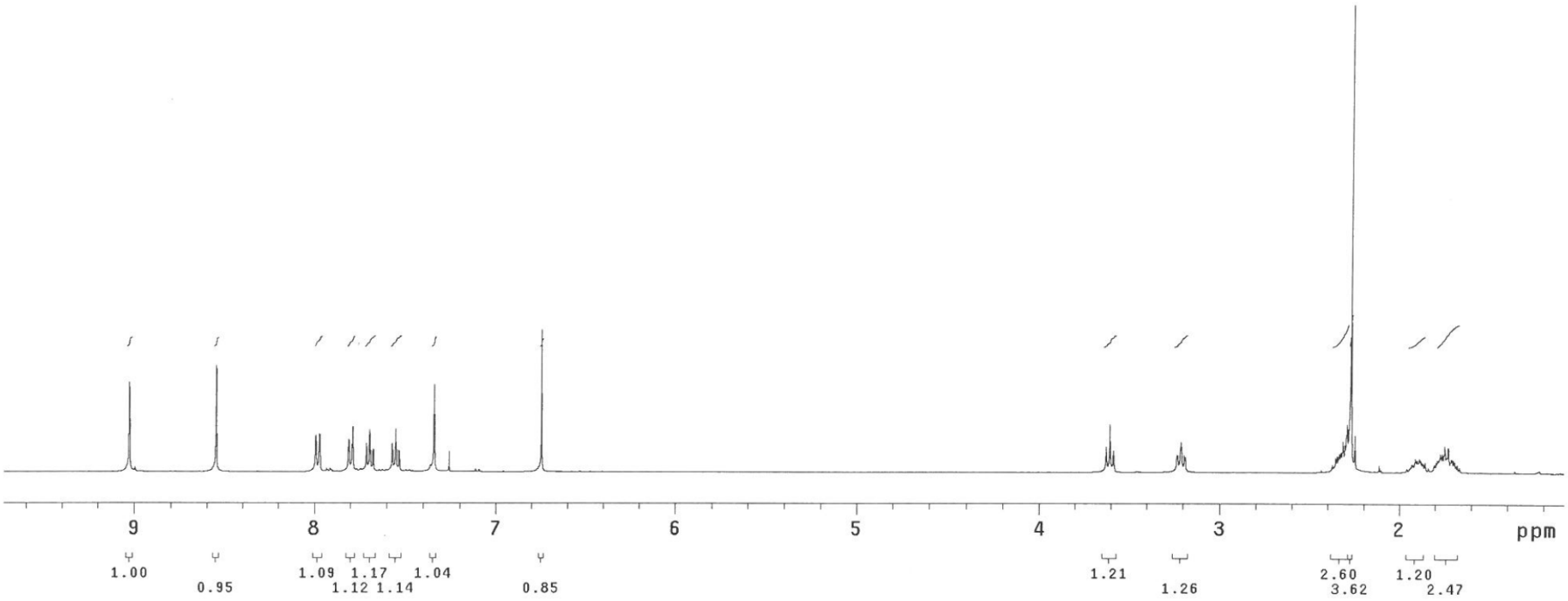
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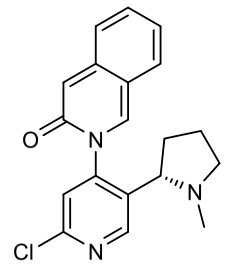




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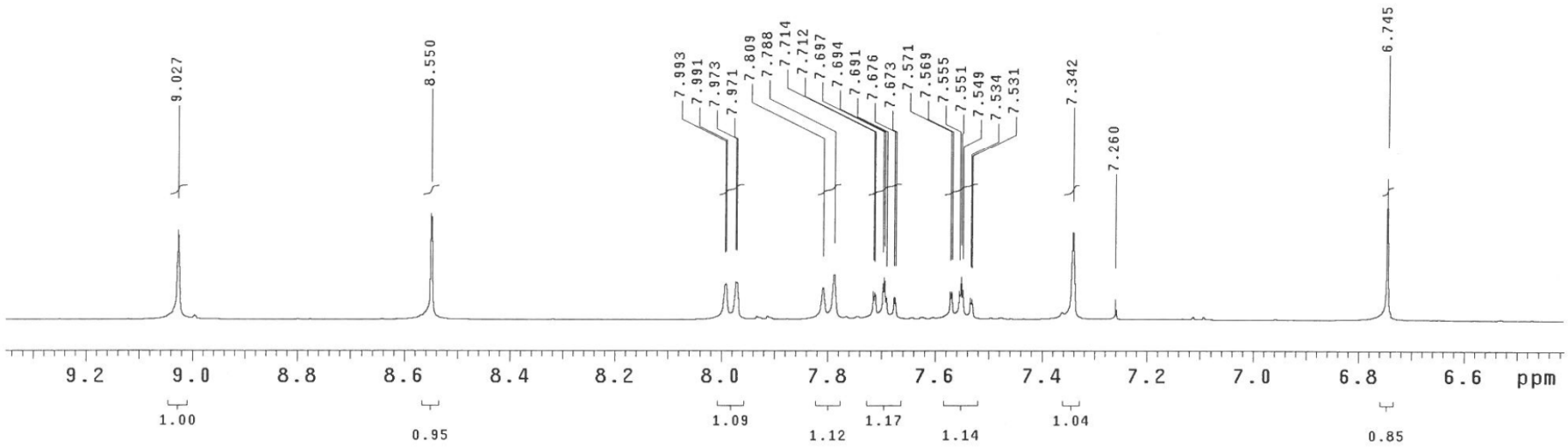
^{1}H NMR (400 MHz, $CDCl_3$)





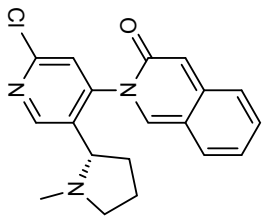
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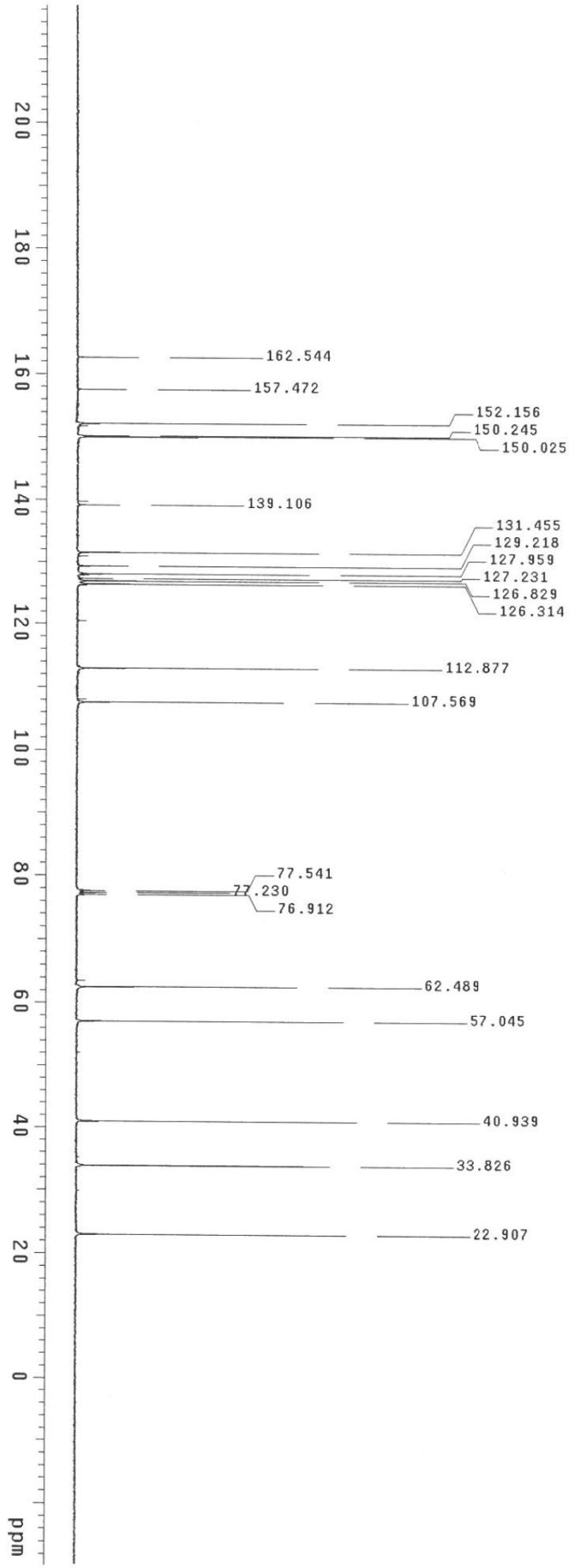
^{1}H NMR (400 MHz, $CDCl_3$)

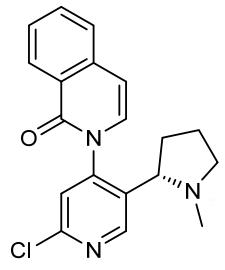


14

^{13}C NMR (100 MHz, $CDCl_3$)

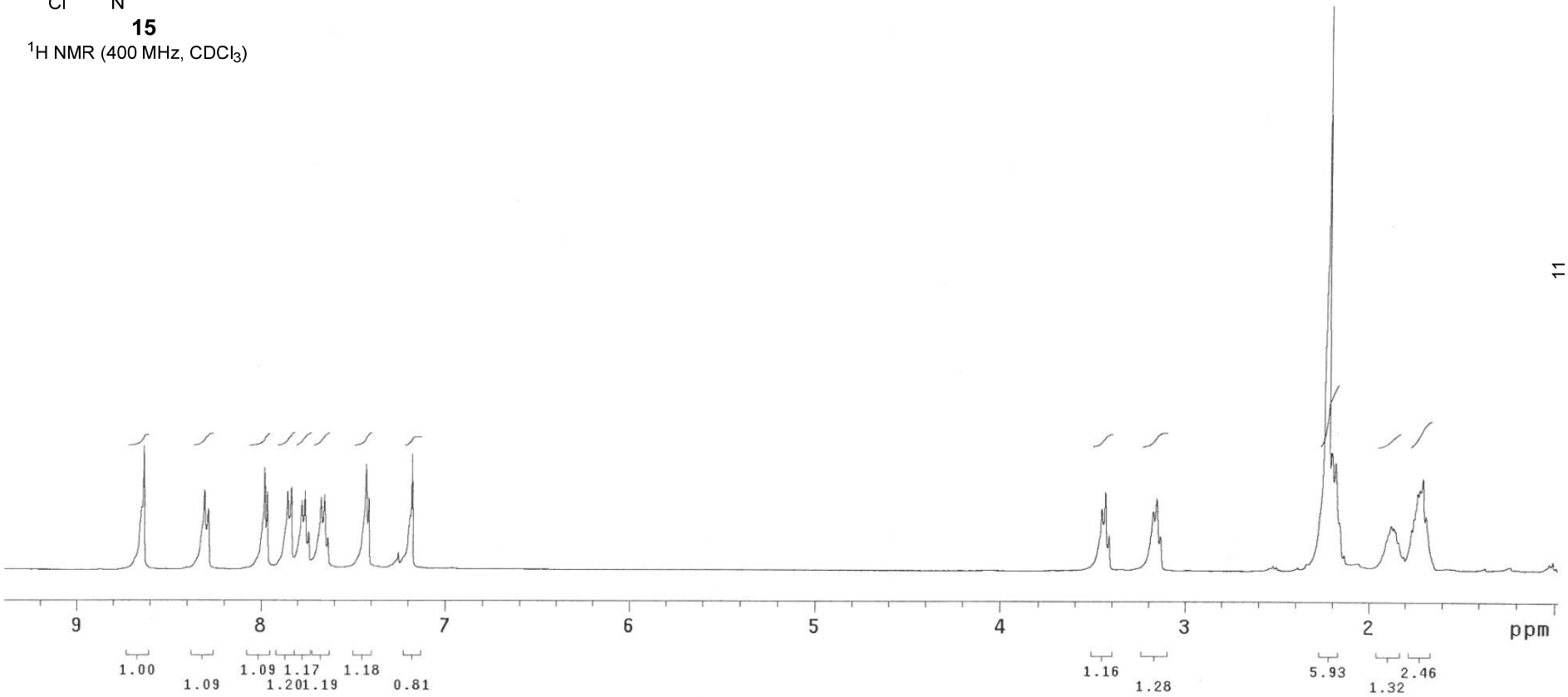


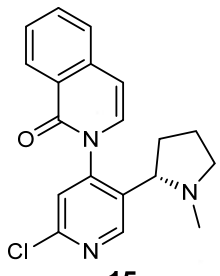




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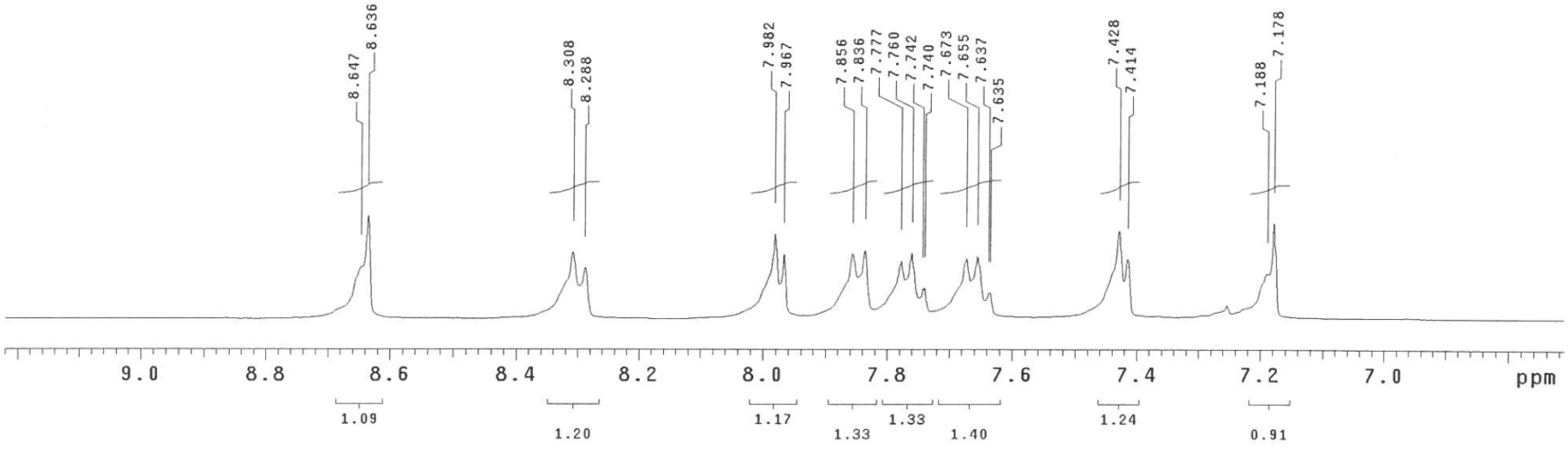
^{1}H NMR (400 MHz, $CDCl_3$)

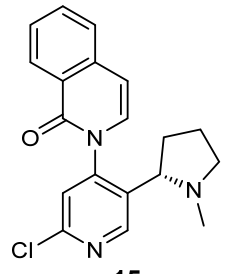




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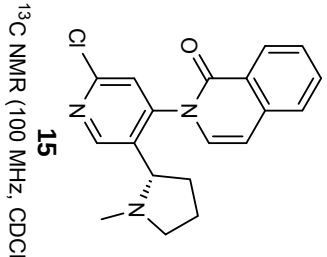
^{1}H NMR (400 MHz, $CDCl_3$)





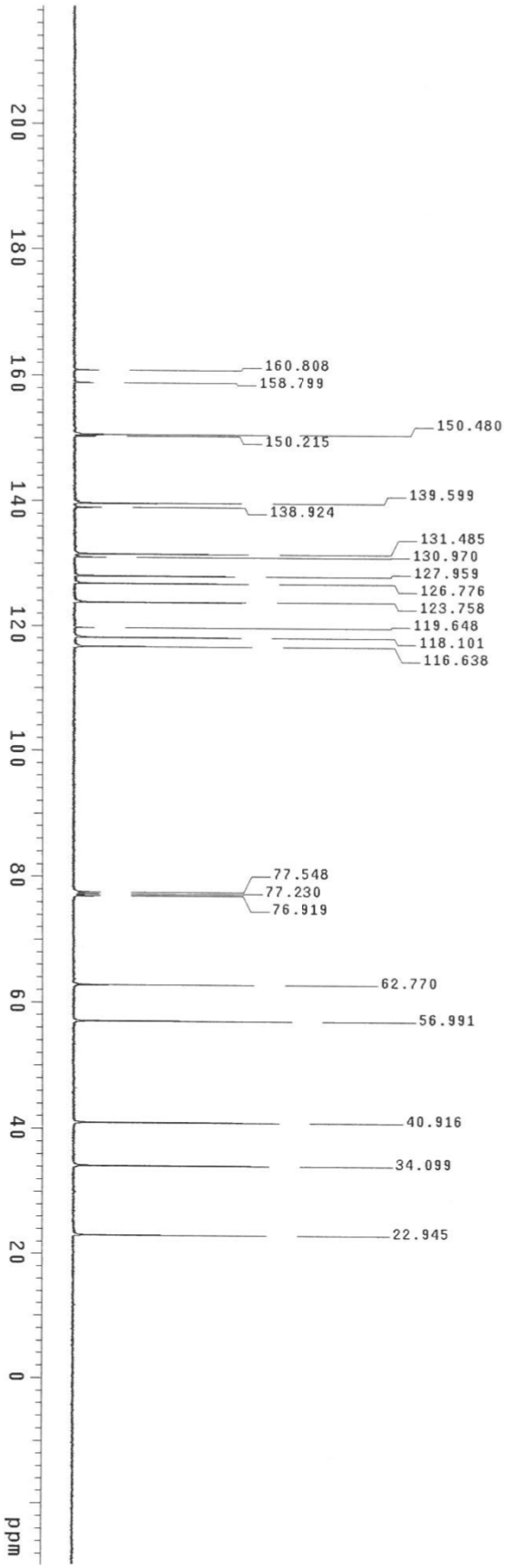
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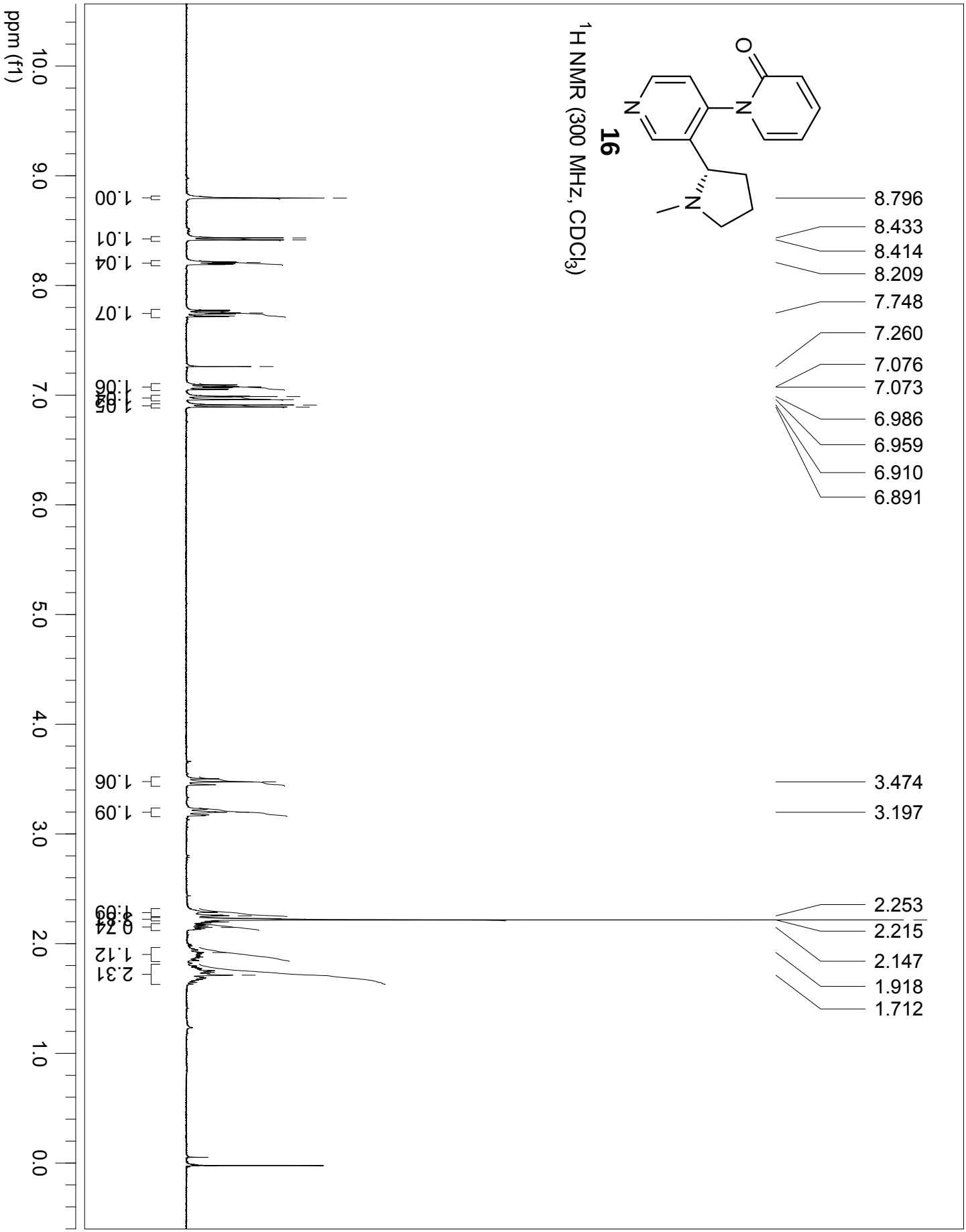
^{1}H NMR (400 MHz, $CDCl_3$)

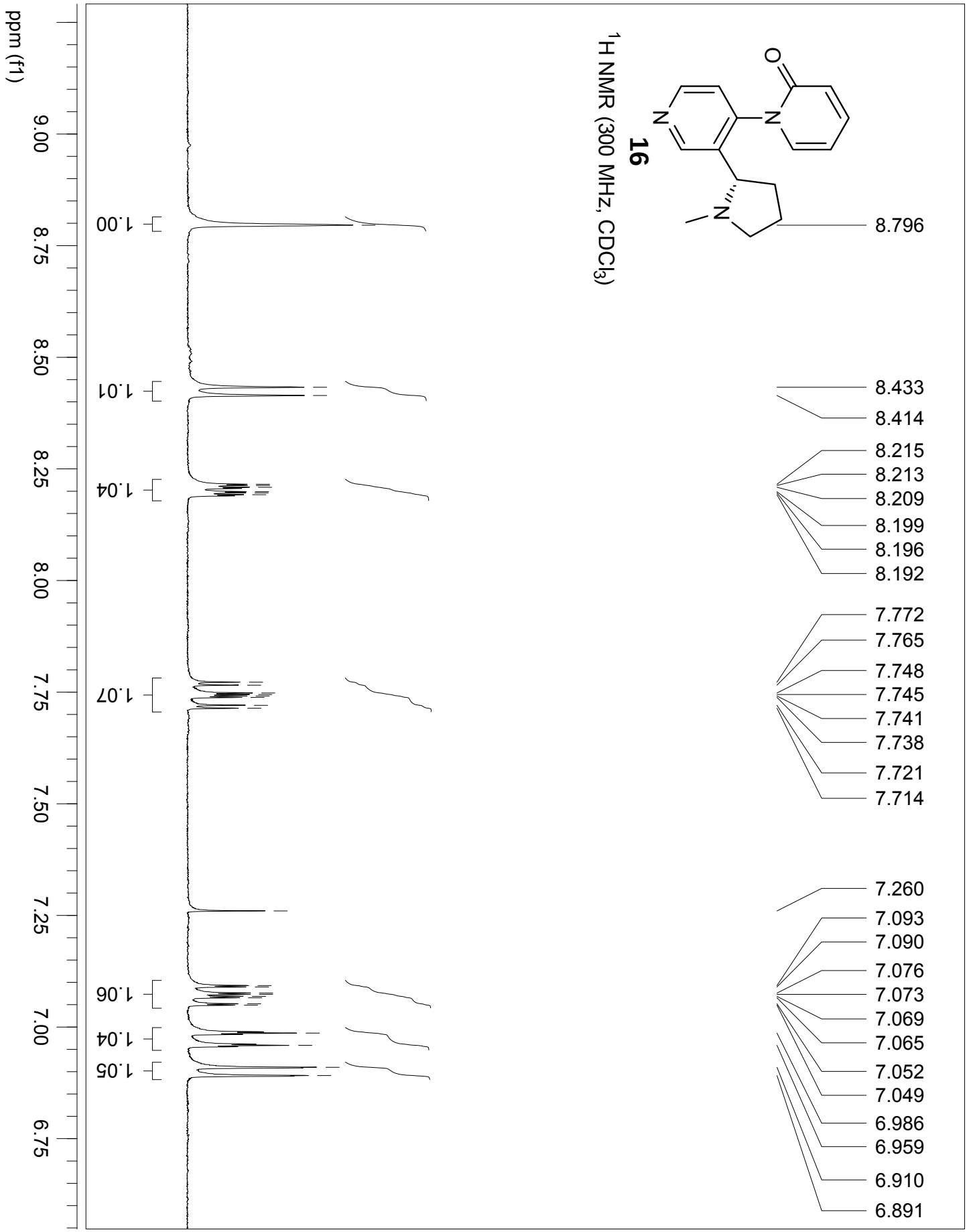


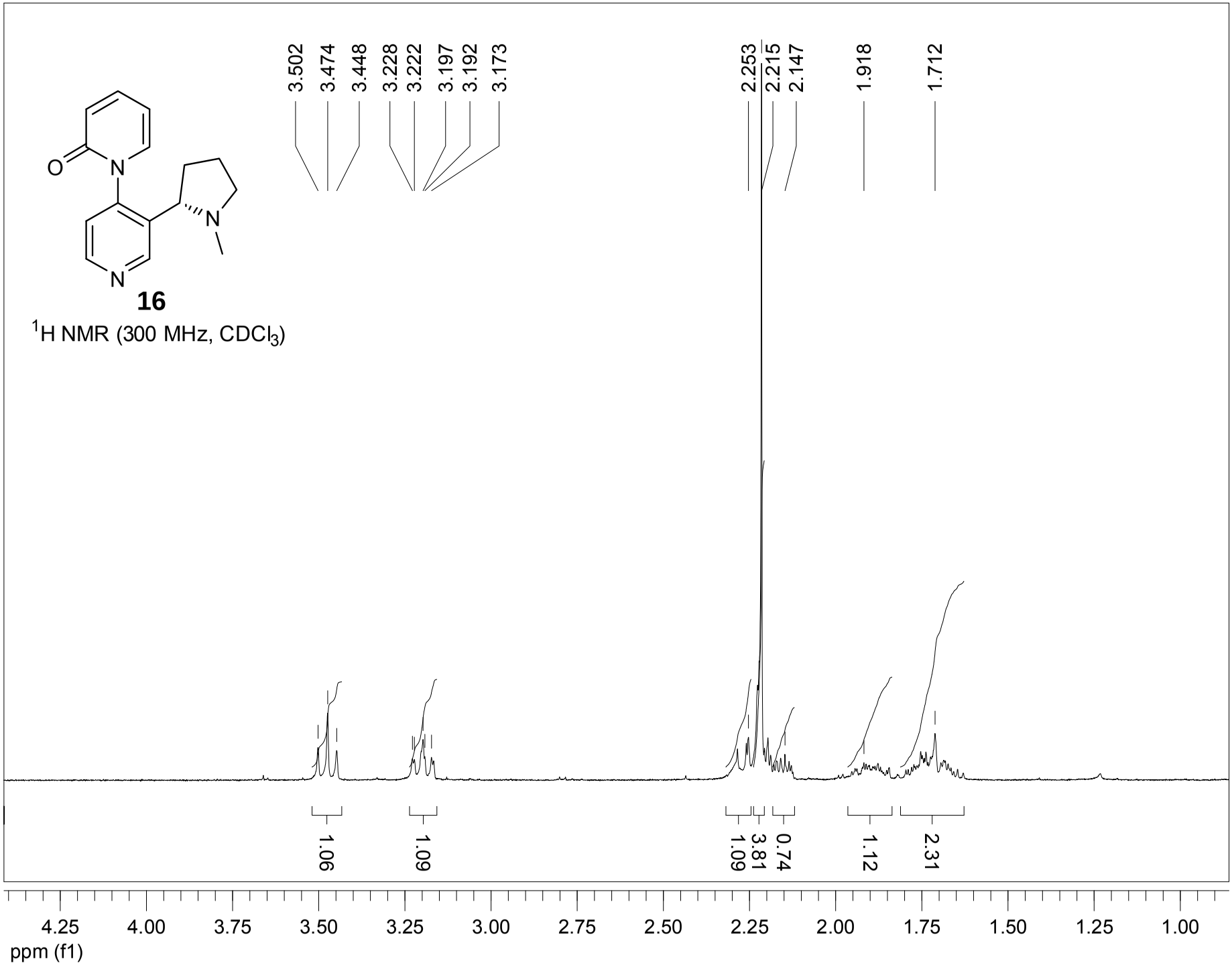
15

^{13}C NMR (100 MHz, $CDCl_3$)



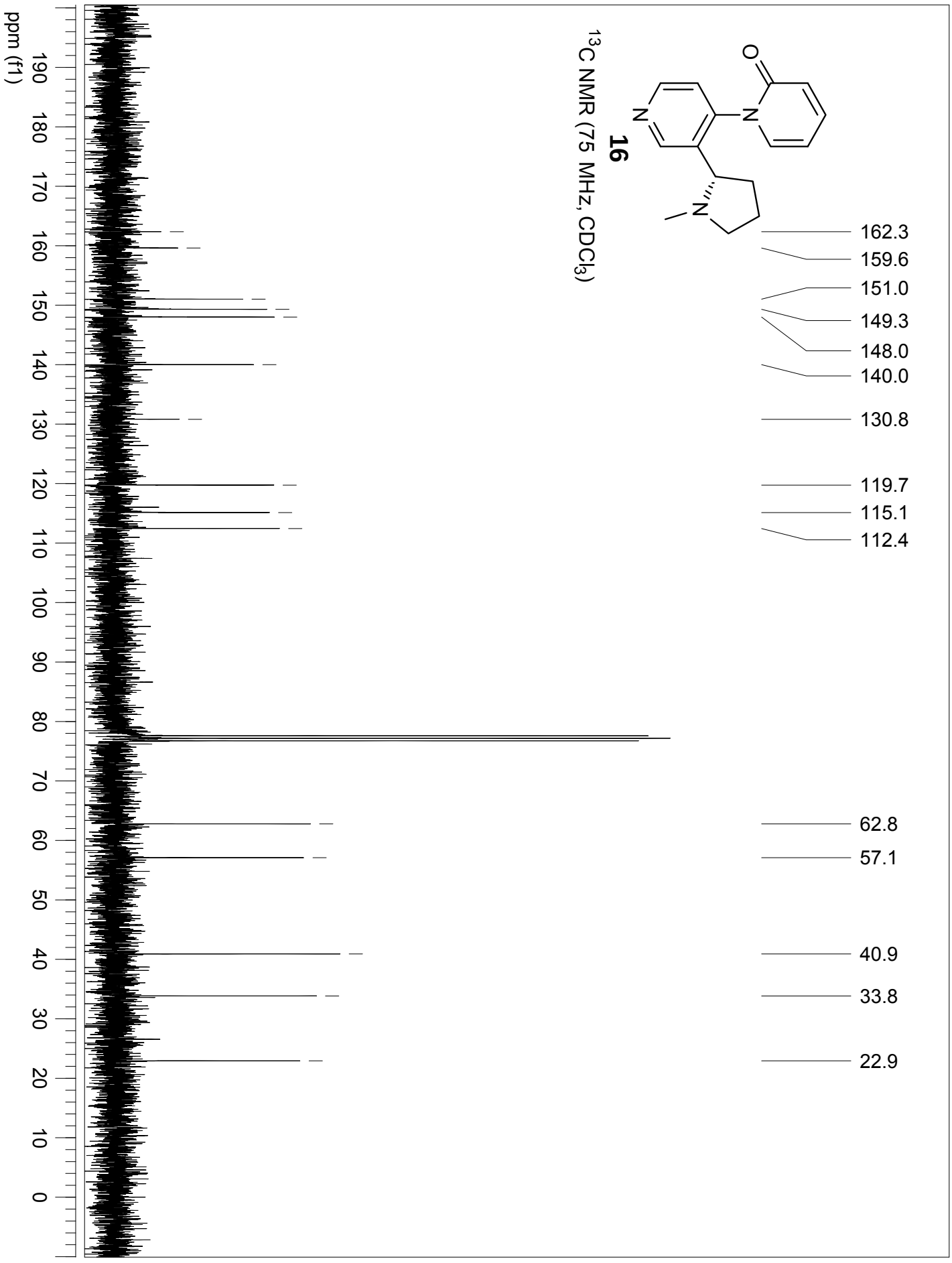

16
^{1}H NMR (300 MHz, $CDCl_3$)
ppm (f1)
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
1.00
1.01
1.04
1.07
1.06
1.05
1.06
1.09
2.31
1.12
0.24
1.09
8.796
8.433
8.414
8.209
7.748
7.260
7.076
7.073
6.986
6.959
6.910
6.891
3.474
3.197
2.253
2.215
2.147
1.918
1.712

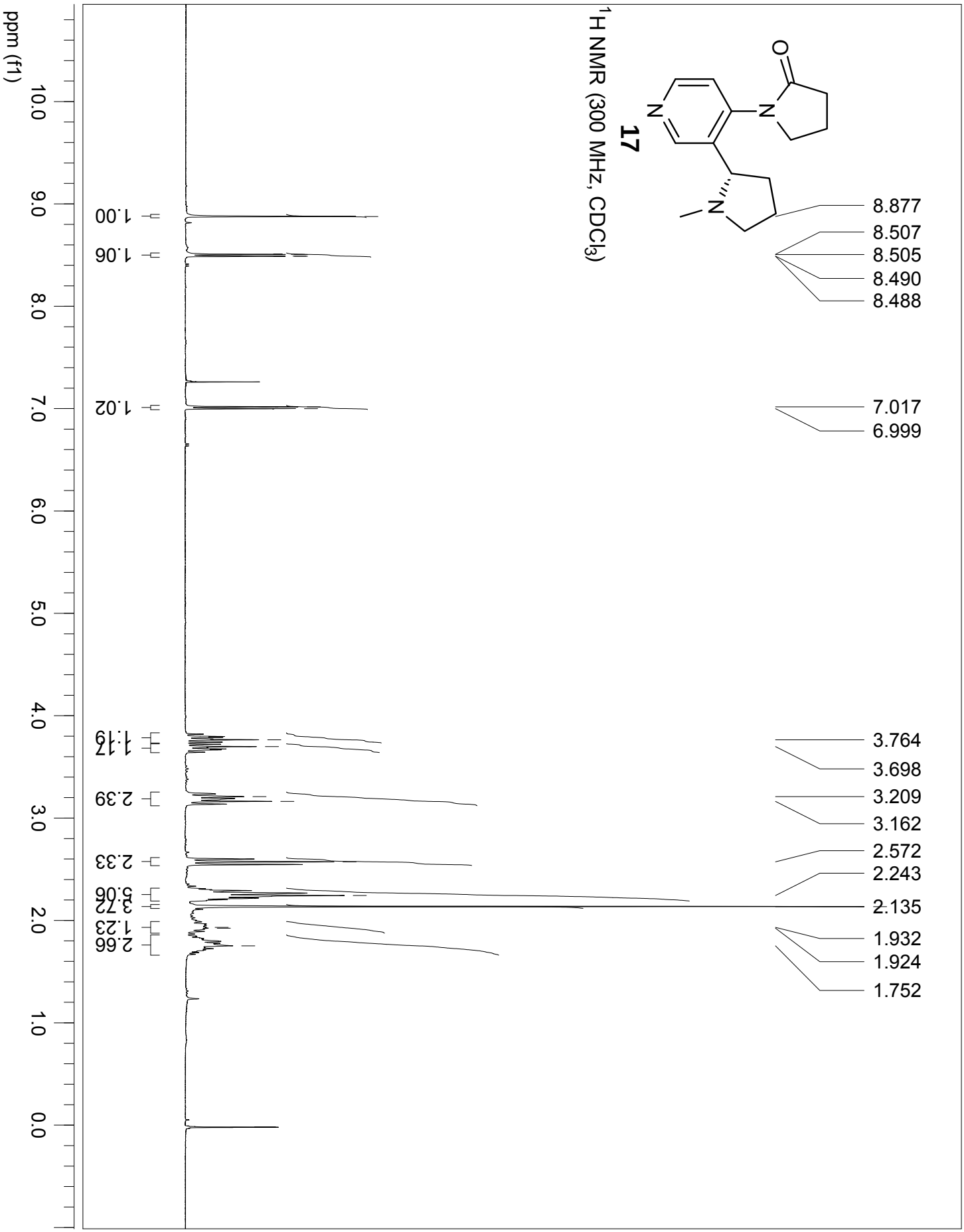

16
^{1}H NMR (300 MHz, $CDCl_3$)
ppm (f1)
9.00
8.75
8.50
8.25
8.00
7.75
7.50
7.25
7.00
6.75
1.00
1.01
1.04
1.07
1.06
1.04
1.05
8.796
8.433
8.414
8.215
8.213
8.209
8.199
8.196
8.192
7.772
7.765
7.748
7.745
7.741
7.738
7.721
7.714
7.260
7.093
7.090
7.076
7.073
7.069
7.065
7.052
7.049
6.986
6.959
6.910
6.891

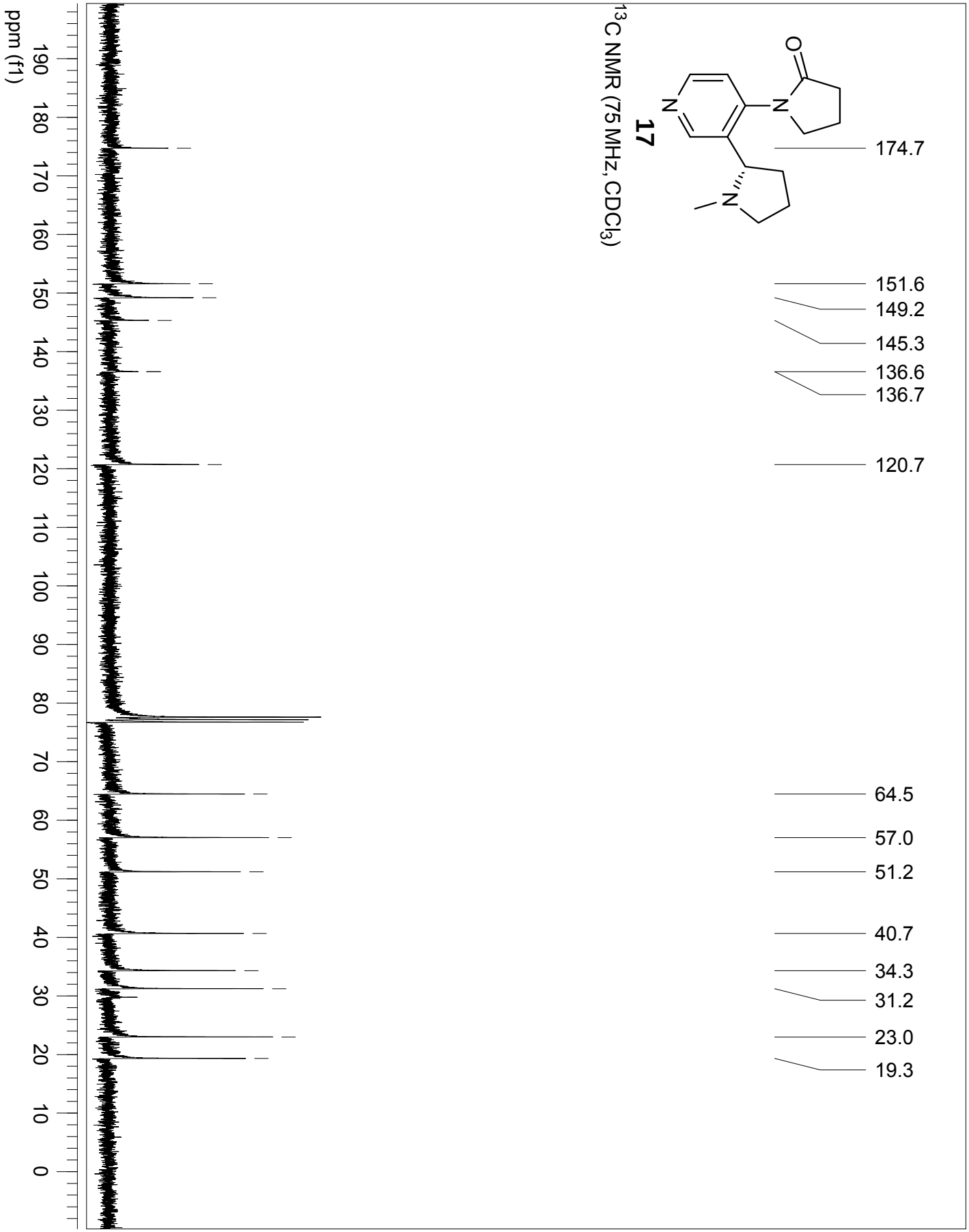


16

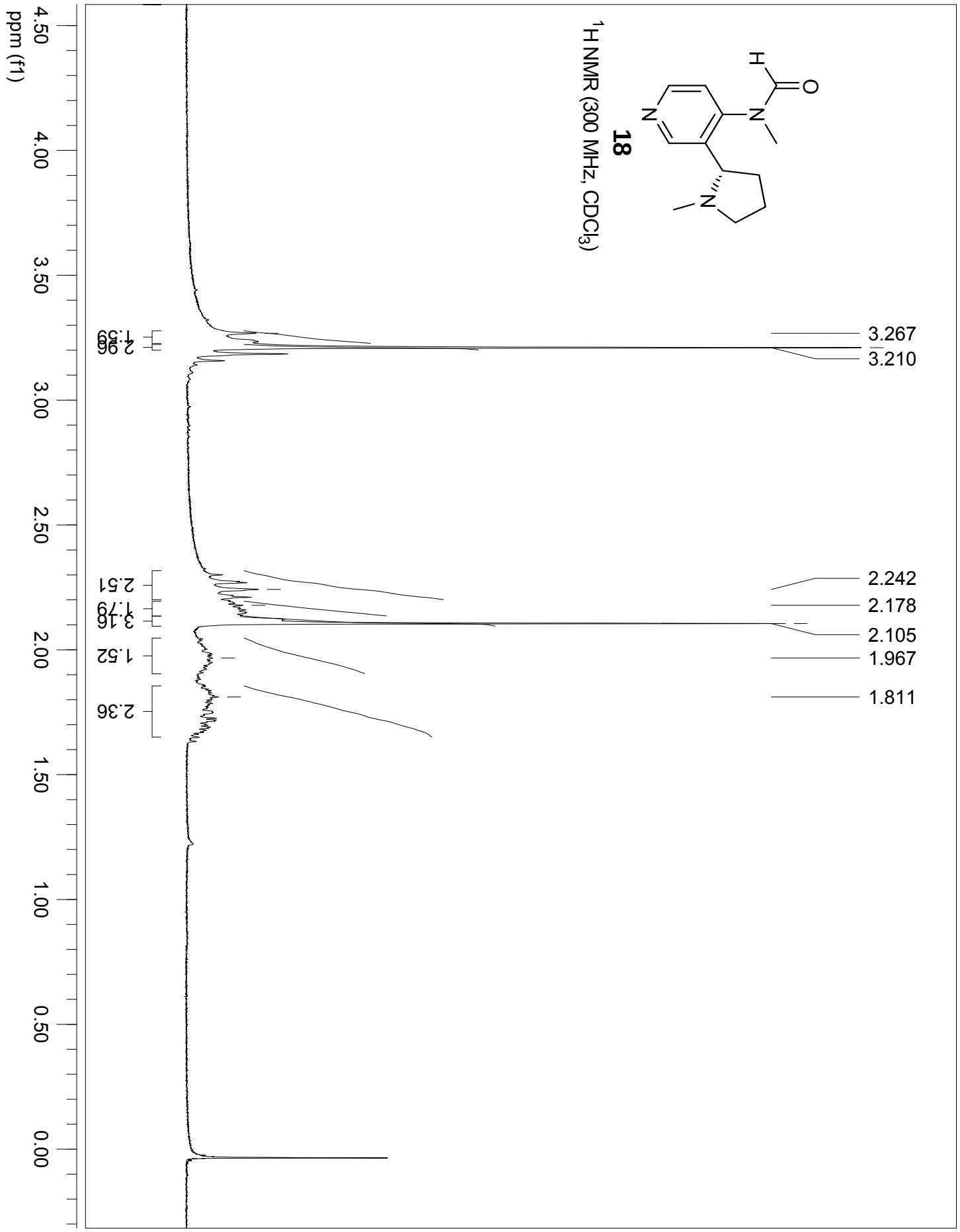
^{1}H NMR (300 MHz, $CDCl_3$)

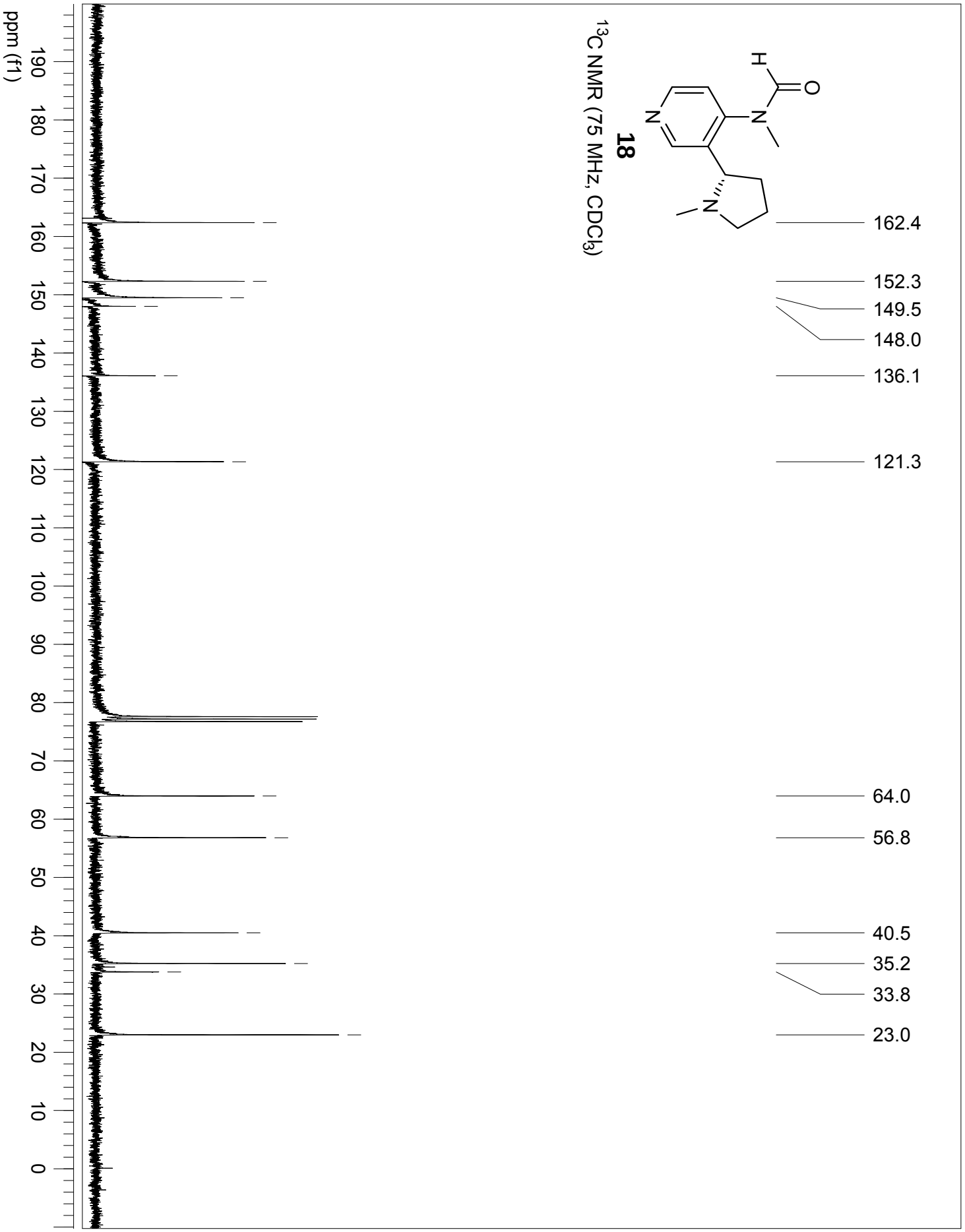

16
^{13}C NMR (75 MHz, $CDCl_3$)
ppm (f1)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
162.3
159.6
151.0
149.3
148.0
140.0
130.8
119.7
115.1
112.4
62.8
57.1
40.9
33.8
22.9

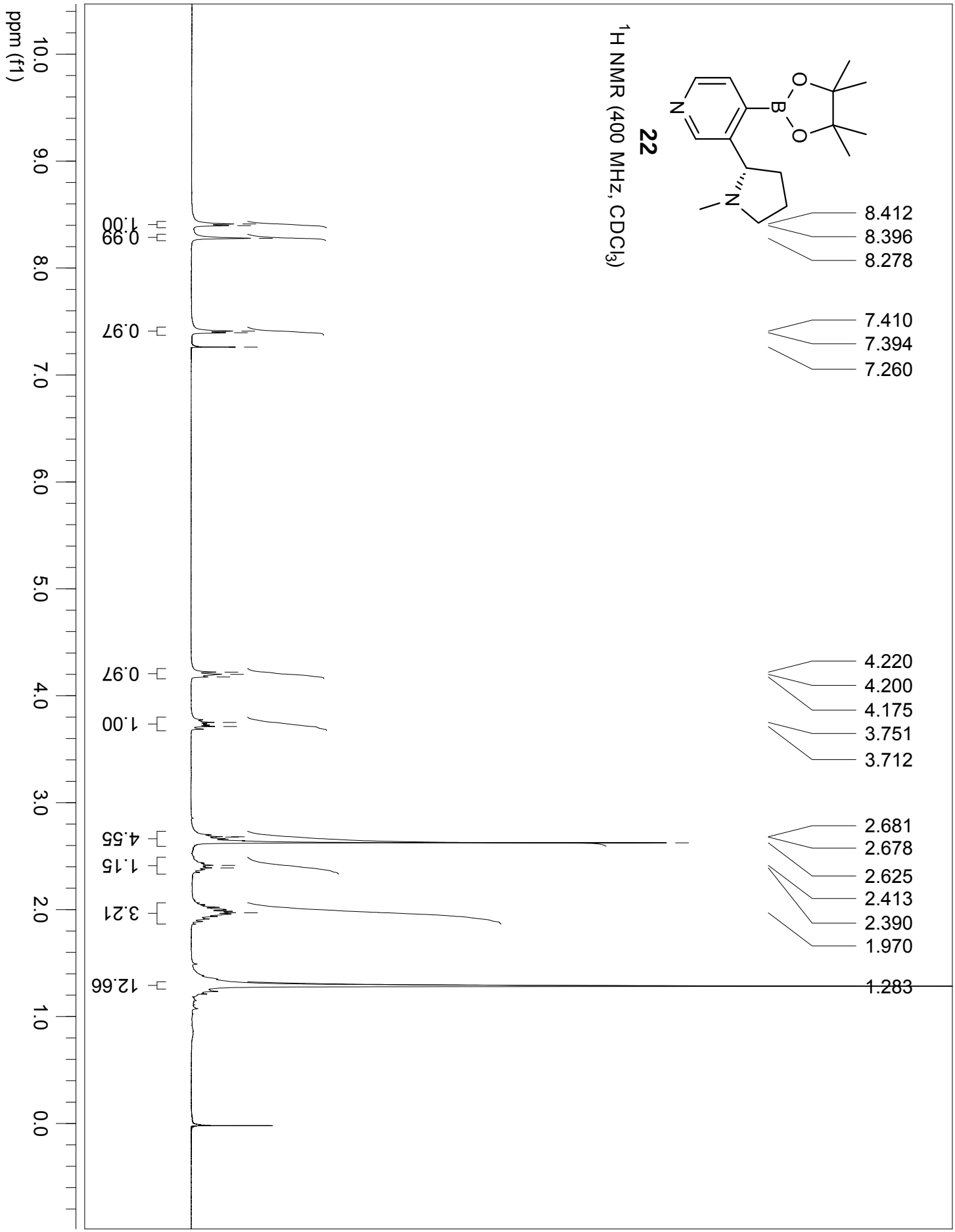

ppm (f1)
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
1.00
1.06
1.02
1.17
1.19
2.39
2.33
5.06
3.22
1.23
2.66
^{1}H NMR (300 MHz, CDCl$_3$)
17
8.877
8.507
8.505
8.490
8.488
7.017
6.999
3.764
3.698
3.209
3.162
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2.243
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1.932
1.924
1.752

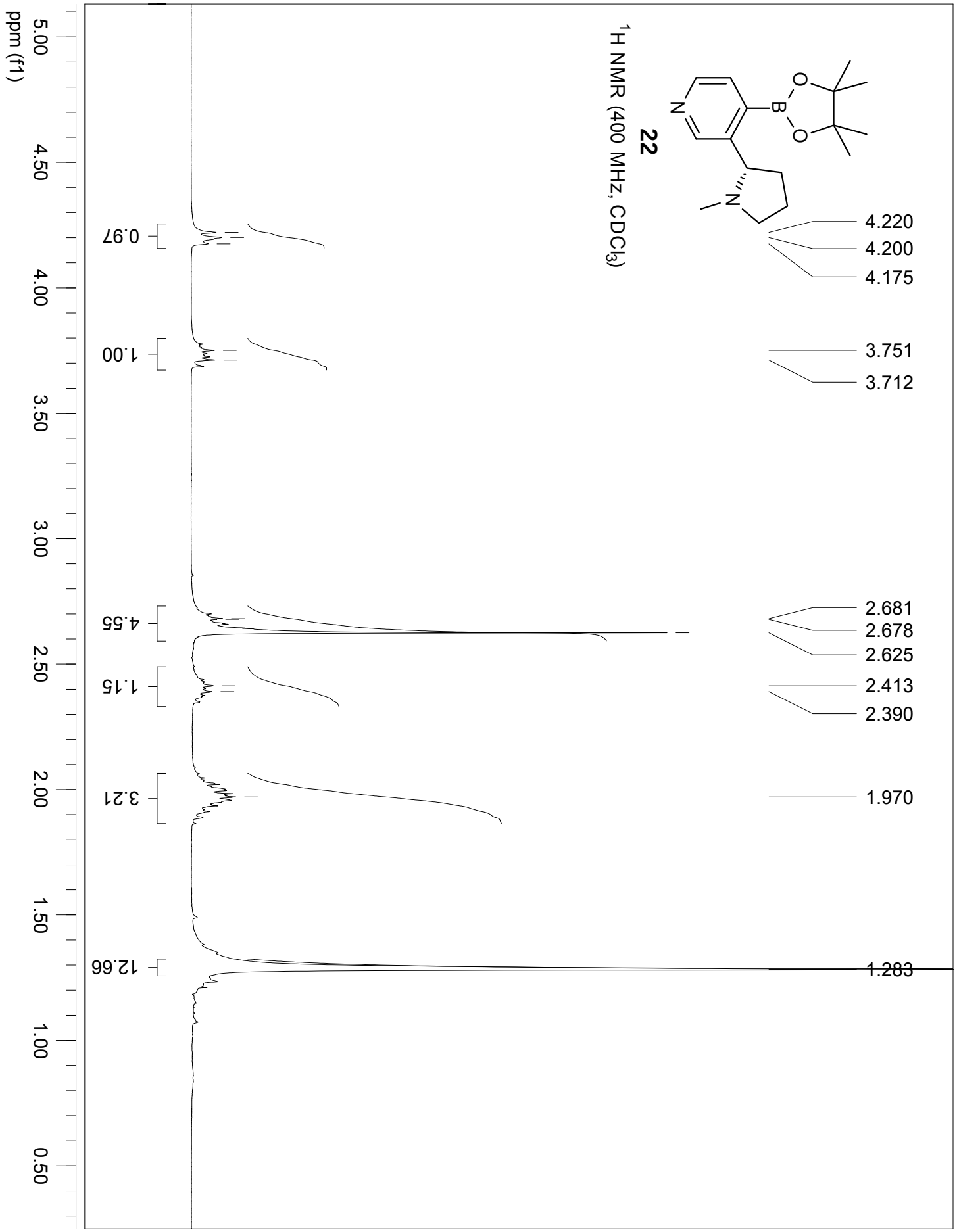

^{13}C NMR (75 MHz, $CDCl_3$)
17
O
N
N
N
174.7
151.6
149.2
145.3
136.6
136.7
120.7
64.5
57.0
51.2
40.7
34.3
31.2
23.0
19.3
ppm (f1)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

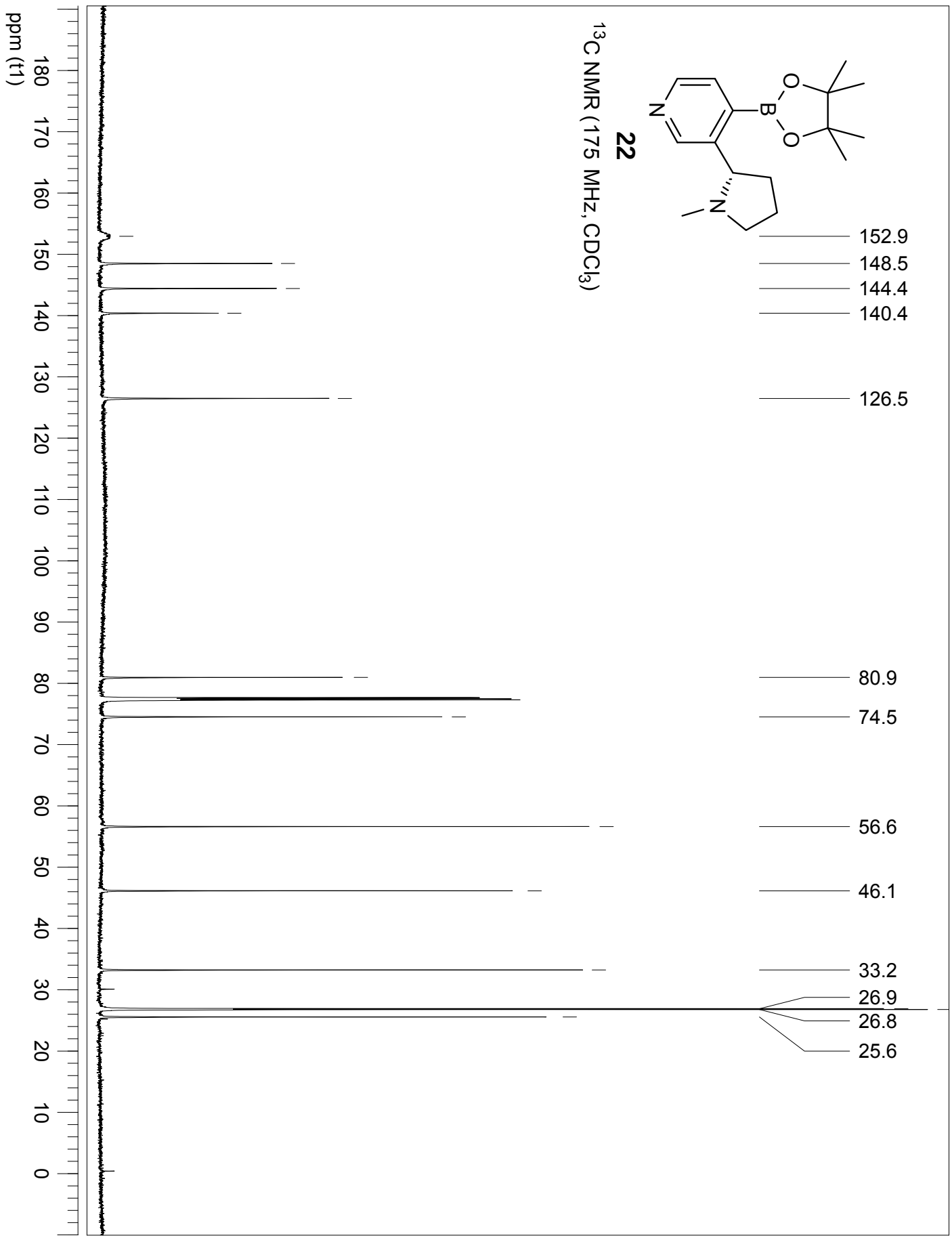
18
^{1}H NMR (300 MHz, CDCl$_3$)
ppm (f1)
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
1.00
0.98
0.84
0.92
2.86
4.99
2.51
3.79
1.52
2.36
8.908
8.536
8.519
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2.242
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2.105
1.967
1.811

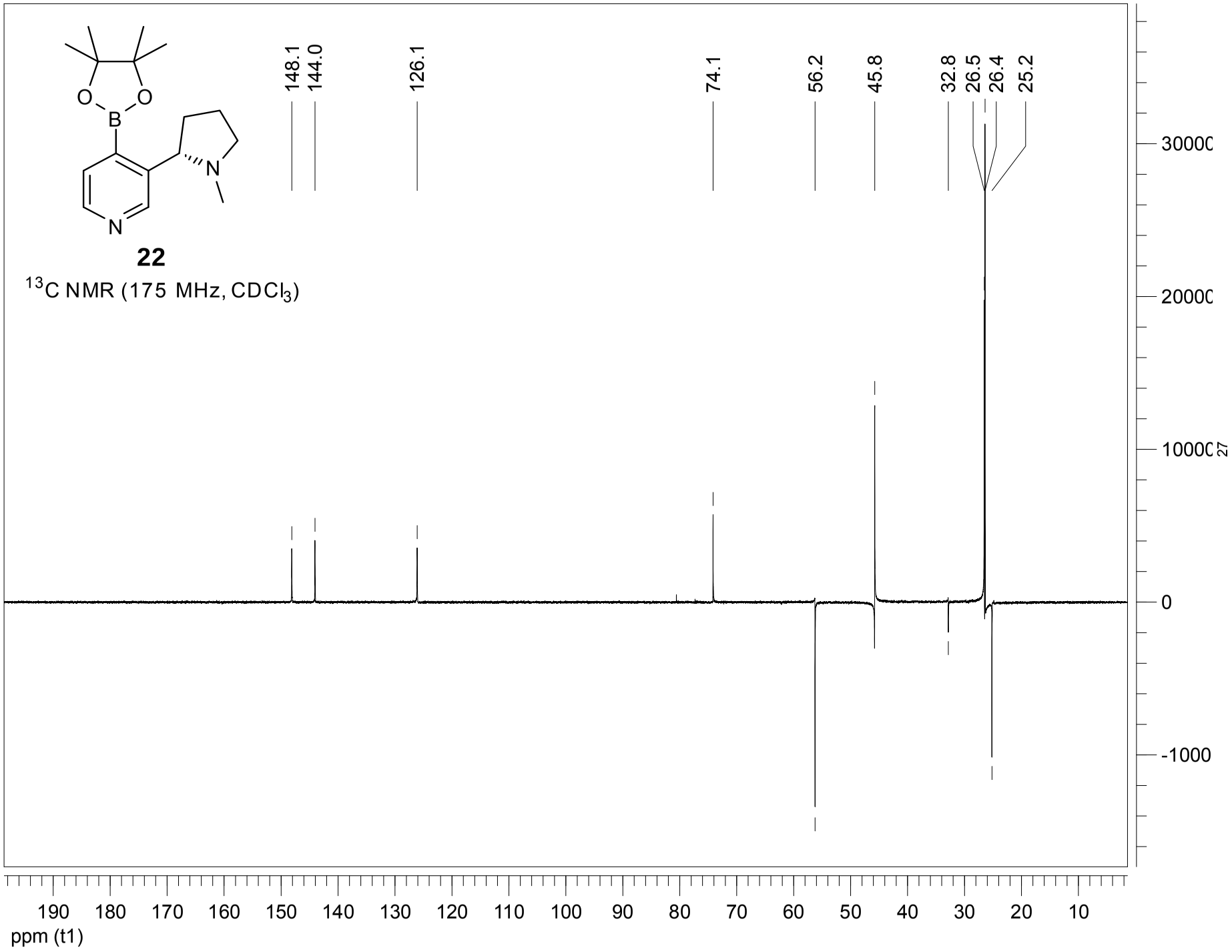

18
^{1}H NMR (300 MHz, $CDCl_3$)
ppm (f1)
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
1.59
2.96
2.51
1.79
3.16
1.52
2.36
3.267
3.210
2.242
2.178
2.105
1.967
1.811


ppm (f1)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
^{13}C NMR (75 MHz, $CDCl_3$)
18
H
O
N
N
N
162.4
152.3
149.5
148.0
136.1
121.3
64.0
56.8
40.5
35.2
33.8
23.0


22
^{1}H NMR (400 MHz, CDCl$_3$)
ppm (f1)
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
1.00
0.99
0.97
0.97
1.00
4.55
1.15
3.21
12.66
8.412
8.396
8.278
7.410
7.394
7.260
4.220
4.200
4.175
3.751
3.712
2.681
2.678
2.625
2.413
2.390
1.970
1.283


22
^{1}H NMR (400 MHz, CDCl$_3$)
ppm (f1)
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.97
1.00
4.55
1.15
3.21
12.66
4.220
4.200
4.175
3.751
3.712
2.681
2.678
2.625
2.413
2.390
1.970
1.283


22
^{13}C NMR (175 MHz, $CDCl_3$)
ppm (t1)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
152.9
148.5
144.4
140.4
126.5
80.9
74.5
56.6
46.1
33.2
26.9
26.8
25.6
N
B
O
O
N


148.1
144.0
126.1
74.1
56.2
45.8
32.8
26.5
26.4
25.2
22
^{13}C NMR (175 MHz, $CDCl_3$)
30000
20000
10000
0
-1000
27
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm (t1)