SUPPLEMENTARY INFORMATION

Configuration-guided reactions: the case of highly decorated spiro[cyclopropane-1,2'(3'*H*)-pyrrolo[1,2-*b*]isoxazole derivatives en route to polyhydroxyindolizidines

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X-Ray Data Collection:

Crystals, mounted on a glass fiber, were analyzed using a Goniometer Oxford Diffraction KM4 Xcalibur2 with a graphite-monochromated Cu/Kα radiation (40mA/-40KV). For all of them measures were carried out at 100°K, except for compound **12** which temperature was held at 150°K.

Structures refinement:

The integrated intensities, measured using the ω scan mode, were corrected for Lorentz and polarization effects.*

The substantial redundancy in data allows empirical absorption corrections to be applied using multiple measurements of symmetry-equivalent reflections.

Structures were solved by direct methods of SIR2004** and refined using the full-matrix least squares on F^2 provided by SHELXL-2014/6 (Sheldrick, 2014)***.

The non-hydrogen atoms were refined anisotropically.

In all cases hydrogen atoms were assigned in calculated positions and all of them were refined as isotropic.

Copies of the data can be obtained, free of charge, from CCDC, 12 Union Road, Cambridge, CB2 1EZ UK (e-mail: deposit@ccdc.cam.ac.uk; internet://www.ccdc.cam.ac.uk) with the deposition numbers reported below for each compound.

- * Walker, N.; Stuart, D.; *Acta Cystallogr*. *Sect.A*, **1983**, 39, 158-166
- ** Burla M.C., Camalli M., Carrozzini B., Cascarano G.L., Giacovazzo C., Polidori G., Spagna R., Caliandro, R., De Caro L. *SIR2004: An Improved Tool for Crystal Structure Determination and Refinement*,
  Journal of Applied Crystallography 38(2): 381-388
- *** Sheldrick, G, M. *Crystal Structure Refinement with SHELXL*; Acta Cryst. (2015).
  C71, 3-8

The following programs have been used for solution, refinement, graphic and deposition of data:

WinGX: Farrugia, L. J. (2012). J. Appl. Cryst. 45, 849-854.

ORTEP-3: Farrugia, L. J. (2012). J. Appl. Cryst. 45, 849-854.

enCIFer: Allen, F. H., Johnson, O., Shields, G. P., Smith, B. R. & Towler, M. (2004).
J. Appl. Cryst. 37, 335-338.

Cristallographic data 10 (exp_1273):

$C_{17}H_{31}NO_4$, M=313.43, Orthorhombic, space group P 21 21 2, a=17.643(1), b=16.144(1), c=6.601(1)Å, V=1880.2(3)Å^3, Z=4 D_c=1.107 Mg/m^3, μ=0.625 mm^{-1}, F(000)=688.

5913 reflections were collected with a 5.013°<θ<70.844° range with a completeness to theta 99,1%; 3079 were independent, the parameters were 199 and the final R index was 0.0456 for reflections having I>2σI.

Deposition number at the Cambridge Crystallographic Data Center: **CCDC 1496575**.

An intermolecular hydrogen bond is present between O2-H2-N1(1):

Distance X-H	Distance X-Y	Distance H-Y	Angle X-H-Y
0.820 Å	2.742 Å	1.939 Å	166.38°

The relative symmetry operation is (1)= x,+y,+z+1

Cristallographic data 11 (exp_1272):

$C_{17}H_{31}NO_4$, M=313.43, Orthorhombic, space group P 21 21 21, a=6.030(1), b=16.334(1), c=18.224(1)Å, V=1795.0(3)Å^3, Z=4 D_c=1.160 Mg/m^3, μ=0.665 mm^{-1}, F(000)=688.

5696 reflections were collected with a 4.853°<θ<70.654° range with a completeness to theta 99,0%; 2886 were independent, the parameters were 200 and the final R index was 0.0333 for reflections having I>2σI.

Deposition number at the Cambridge Crystallographic Data Center: **CCDC 1496576**.

Also in this case an intermolecular hydrogen bond is present between O2-H2-N1(1):

Distance X-H	Distance X-Y	Distance H-Y	Angle X-H-Y
0.820 Å	2.842 Å	2.079 Å	154.63°

The relative symmetry operation is (1)= x-1,+y,+z

Cristallographic data 12 (exp_1121):

4x($C_{13}H_{21}NO_3$), M=957.23, Monoclinic, space group P 21, a=10.178(1), b=21.780(1), c=11.615(1)Å, ß=90.547(1)°, V=2574.7(4) Å^3, Z=2 D_c=1.235 Mg/m^3, μ=0.705 mm^{-1}, F(000)=1040.

14484 reflections were collected with a 4.314°<θ<70.399° range with a completeness to theta 93,4%; 7357 were independent, the parameters were 613 and the final R index was 0.0450 for reflections having I>2σI.

Deposition number at the Cambridge Crystallographic Data Center: **CCDC 1496577**.

No significant interactions were detected.

Cristallographic data 25 (exp_24):

$C_{13}H_{21}NO_3$, M=239.31, Orthorhombic, space group P 21 21 21, a=6.078(1), b=10.204(1), c=19.957(1)Å, V=123770(1)Å^3, Z=4 D_c=1.284 Mg/m^3, μ=0.733 mm^{-1}, F(000)=520.

3937 reflections were collected with a 4.867°<θ<70.378° range with a completeness to theta 98,3%; 1946 were independent, the parameters were 154 and the final R index was 0.0404 for reflections having I>2σI.

Deposition number at the Cambridge Crystallographic Data Center: **CCDC 1496578**.

No significant interactions were detected.

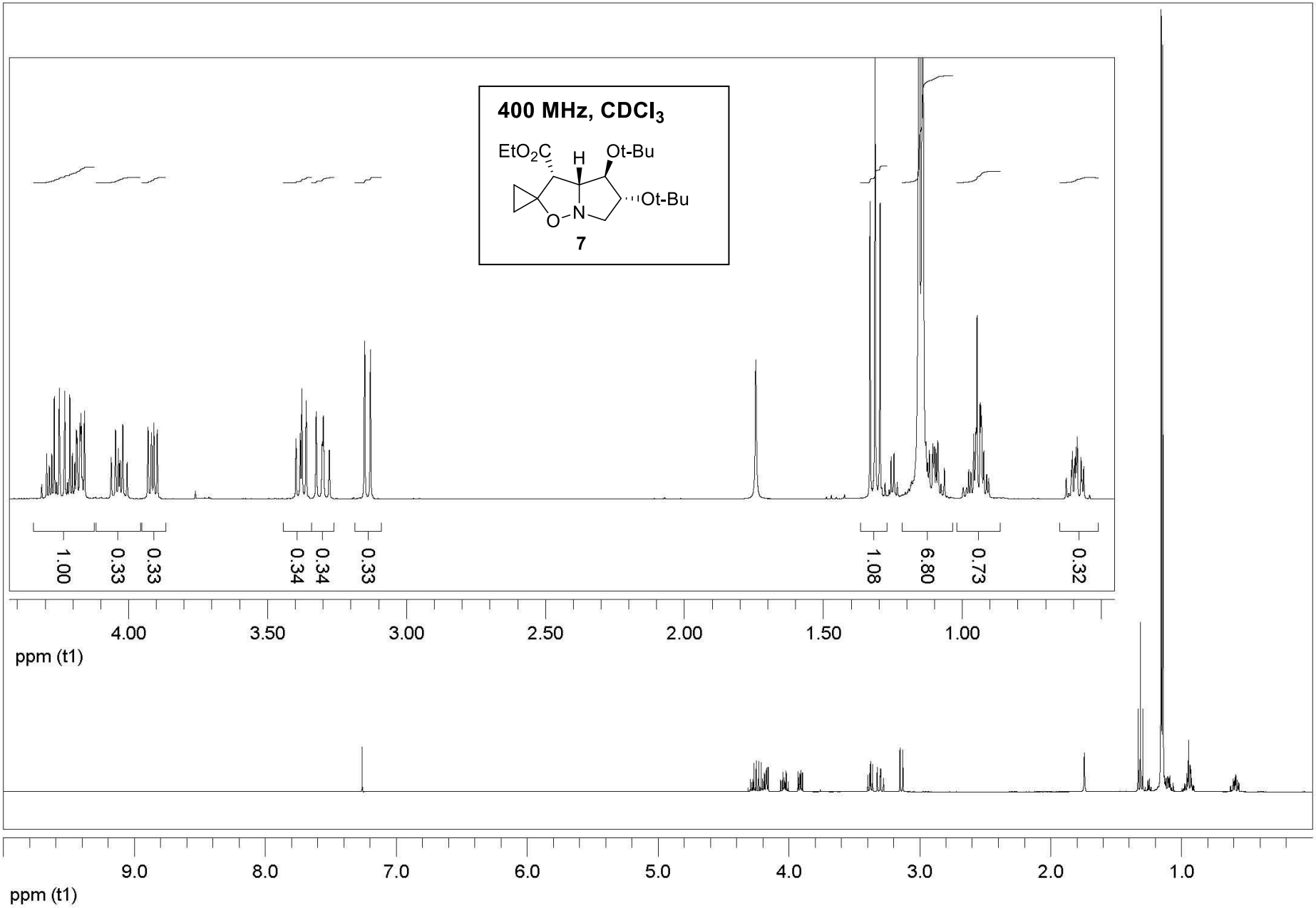
Cristallographic data 26 (exp_94):

2x($C_{26}H_{42}N_2O_6$), M=957.23, Monoclinic, space group P 21, a=7.252(1), b=25.570(1), c=14.465(1)Å, ß=100.170(2)°, V=2640.2(4) Å^3, Z=2 D_c=1.204 Mg/m^3, μ=0.687 mm^{-1}, F(000)=1040.

11770 reflections were collected with a 4.648°<θ<72.537° range with a completeness to theta 99,4%; 7615 were independent, the parameters were 613 and the final R index was 0.0492 for reflections having I>2σI.

Deposition number at the Cambridge Crystallographic Data Center: **CCDC 1496579**.

No significant interactions were detected.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Ot-Bu
O
N
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0.33
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6.80
0.73
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3.00
2.50
2.00
1.50
1.00
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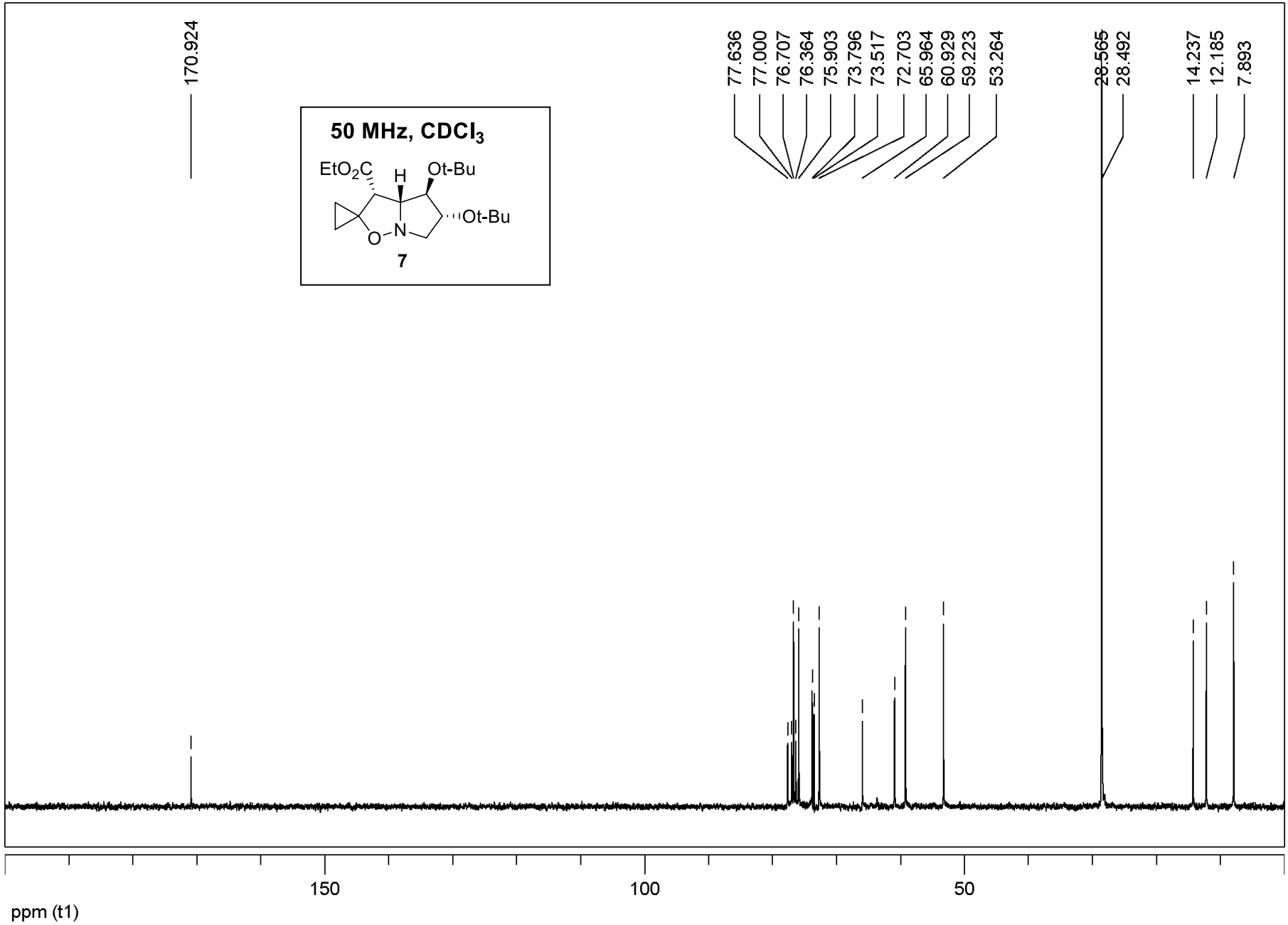
1.0
ppm (t1)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28.565
28.492
14.237
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Ot-Bu
O
N
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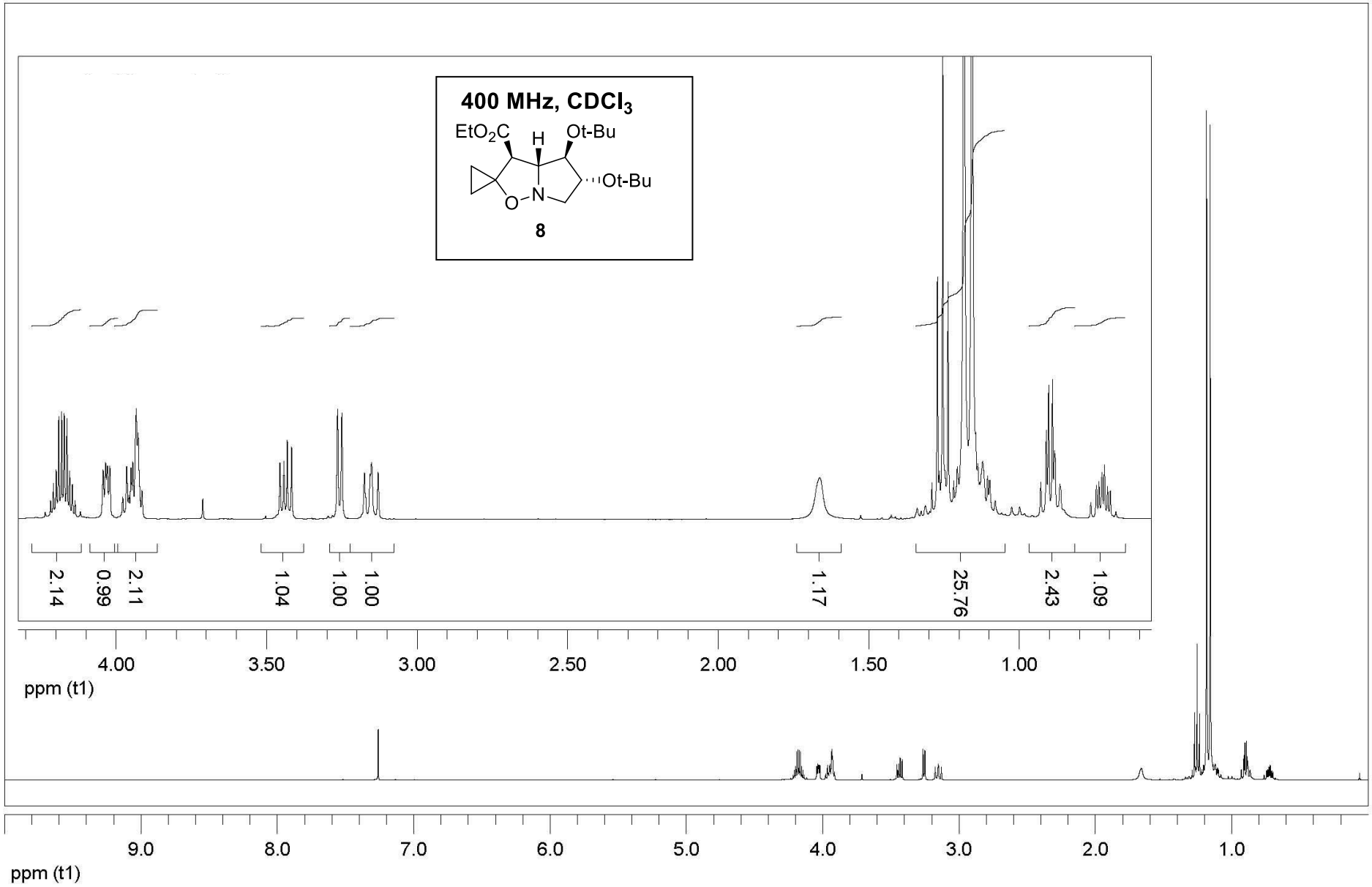
150
100
50
ppm (t1)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Ot-Bu
Ot-Bu
O
N
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2.11
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1.00
1.17
25.76
2.43
1.09
4.00
3.50
3.00
2.50
2.00
1.50
1.00
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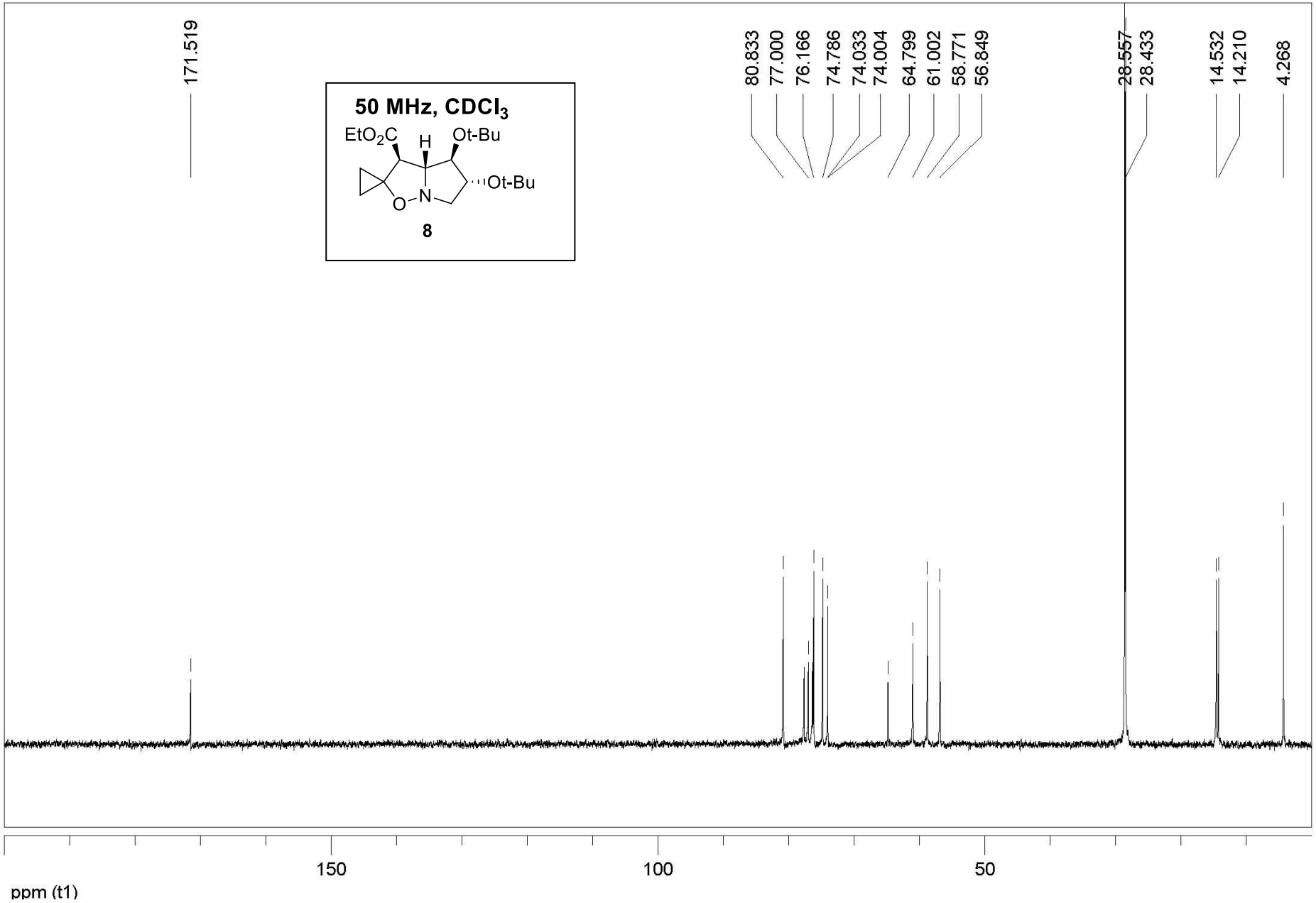
ppm (t1)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28.433
14.532
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Ot-Bu
O
N
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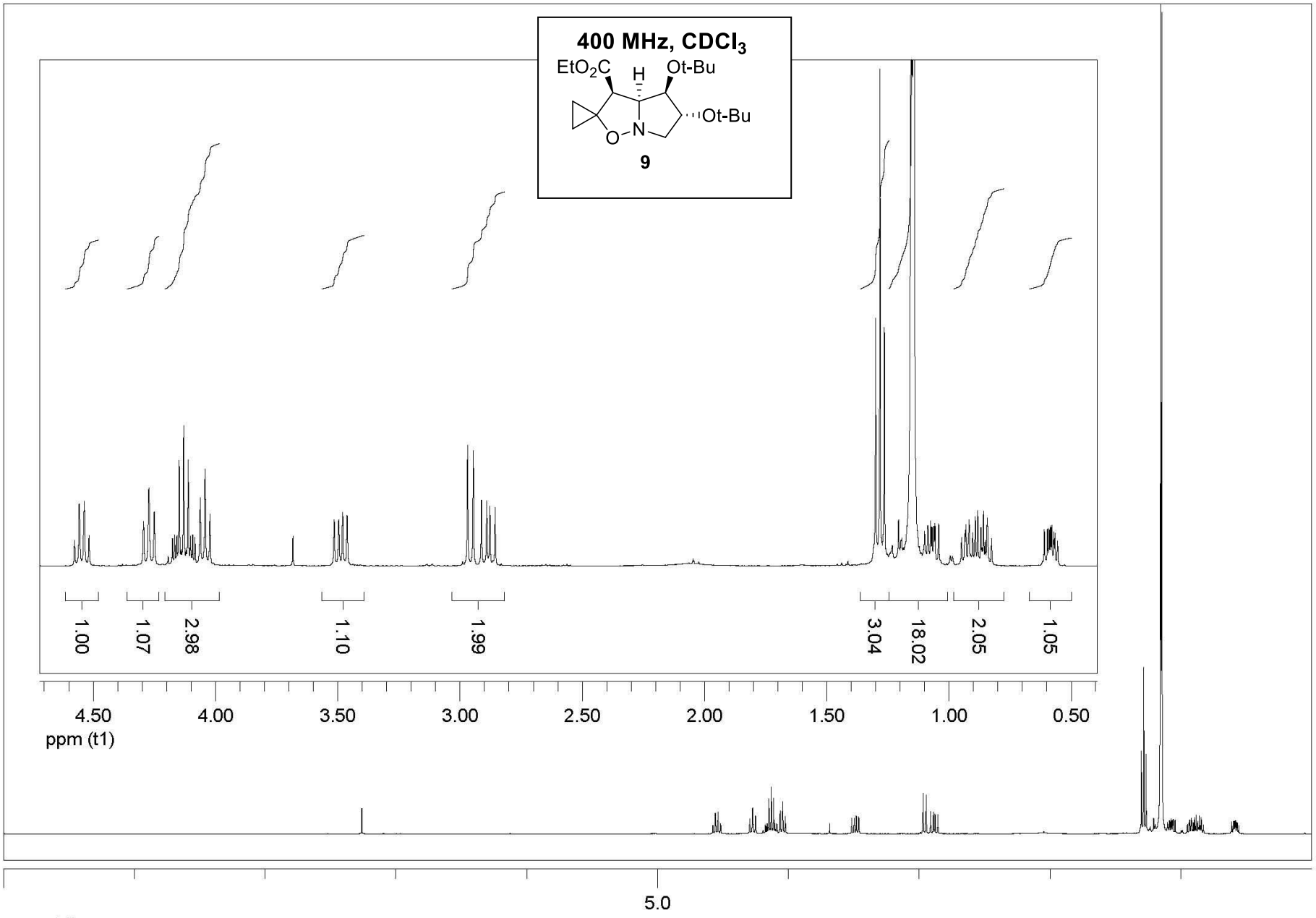
100
50
ppm (t1)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O
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3.04
18.02
2.05
1.05
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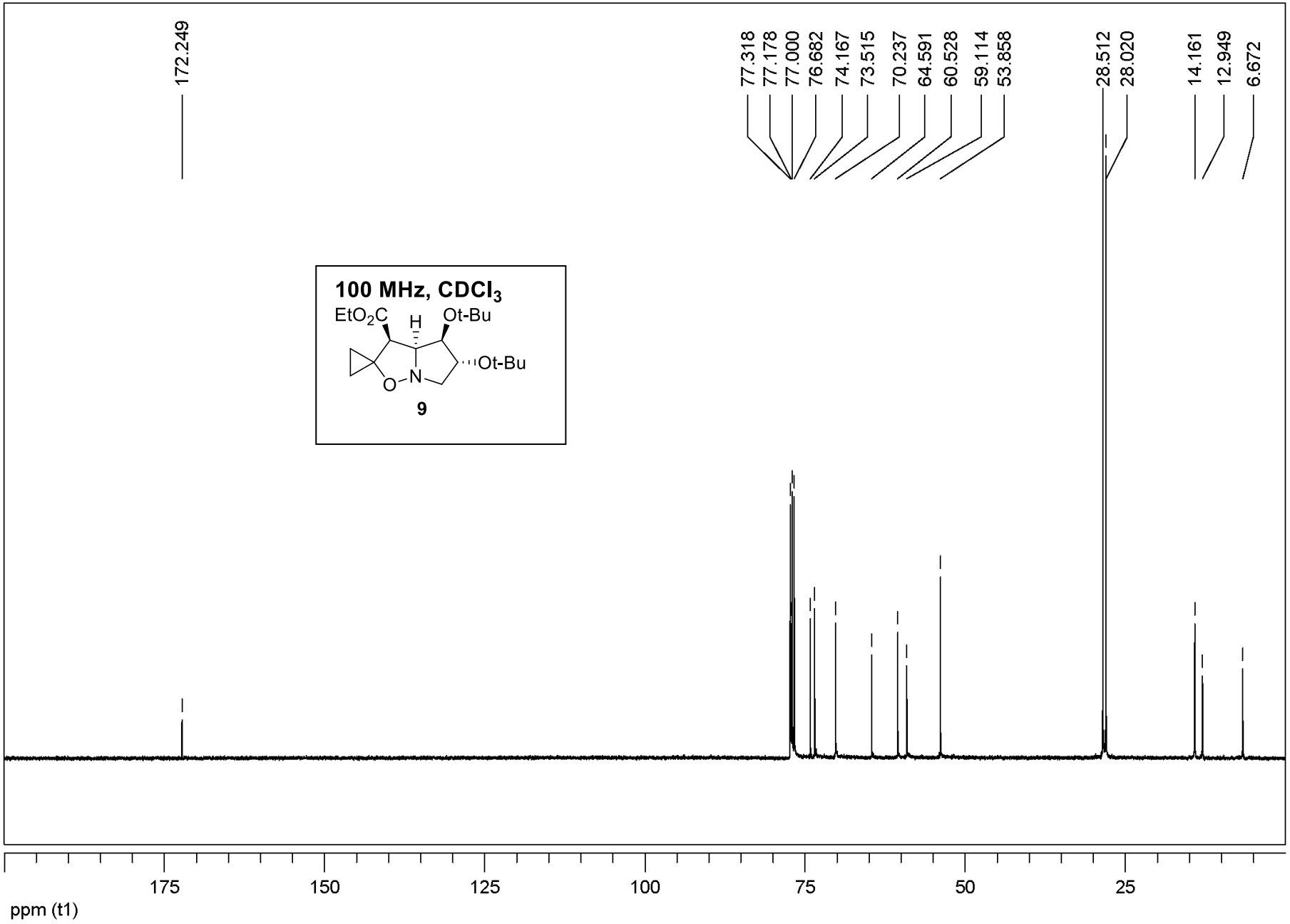
ppm (t1)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28.020
14.161
12.949
6.672
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O
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50
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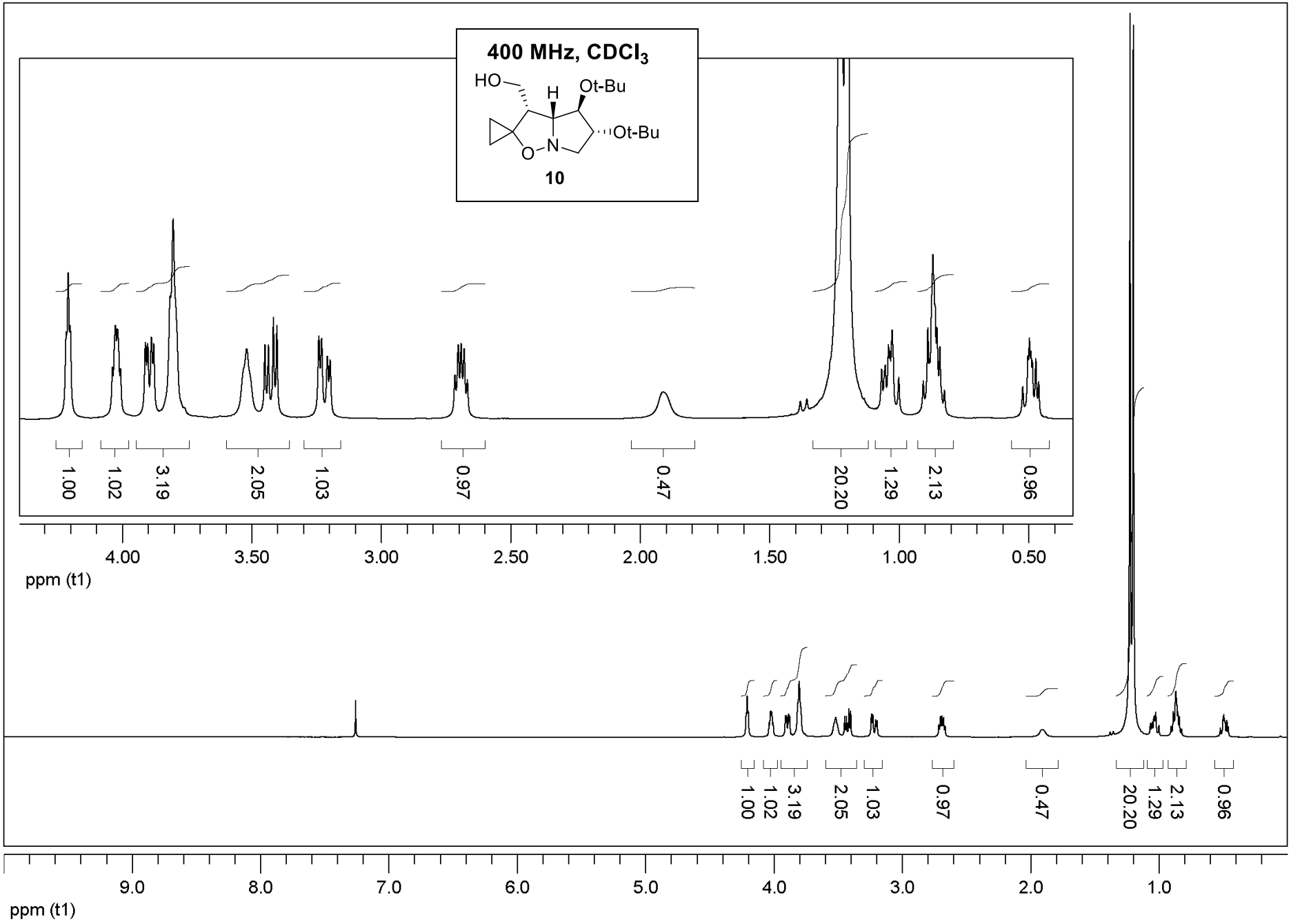
ppm (t1)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Ot-Bu
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0.47
20.20
1.29
2.13
0.96
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3.50
3.00
2.50
2.00
1.50
1.00
0.50
ppm (t1)
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1.02
3.19
2.05
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0.47
20.20
1.29
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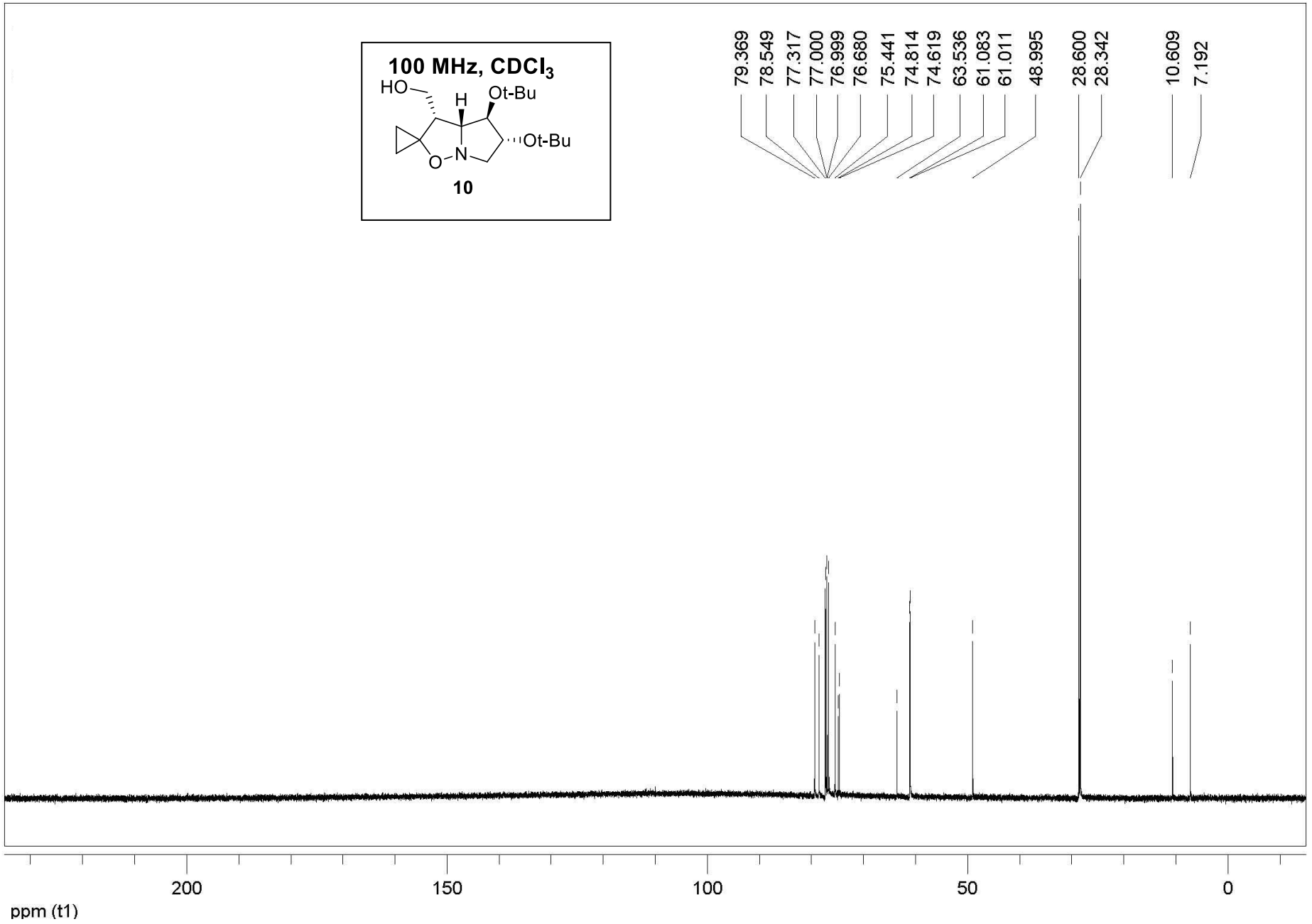
ppm (t1)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74.619
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50
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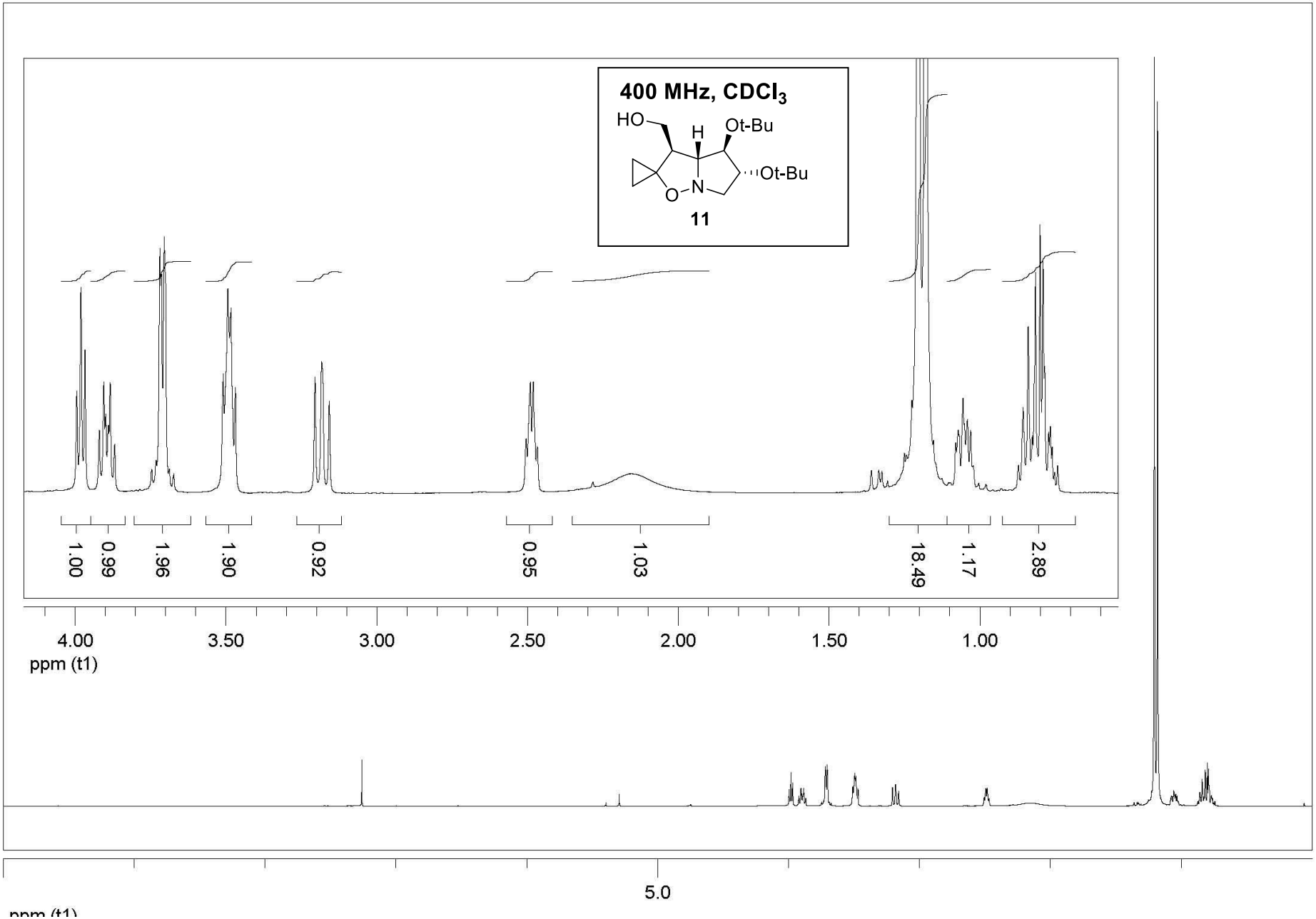
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0.95
1.03
18.49
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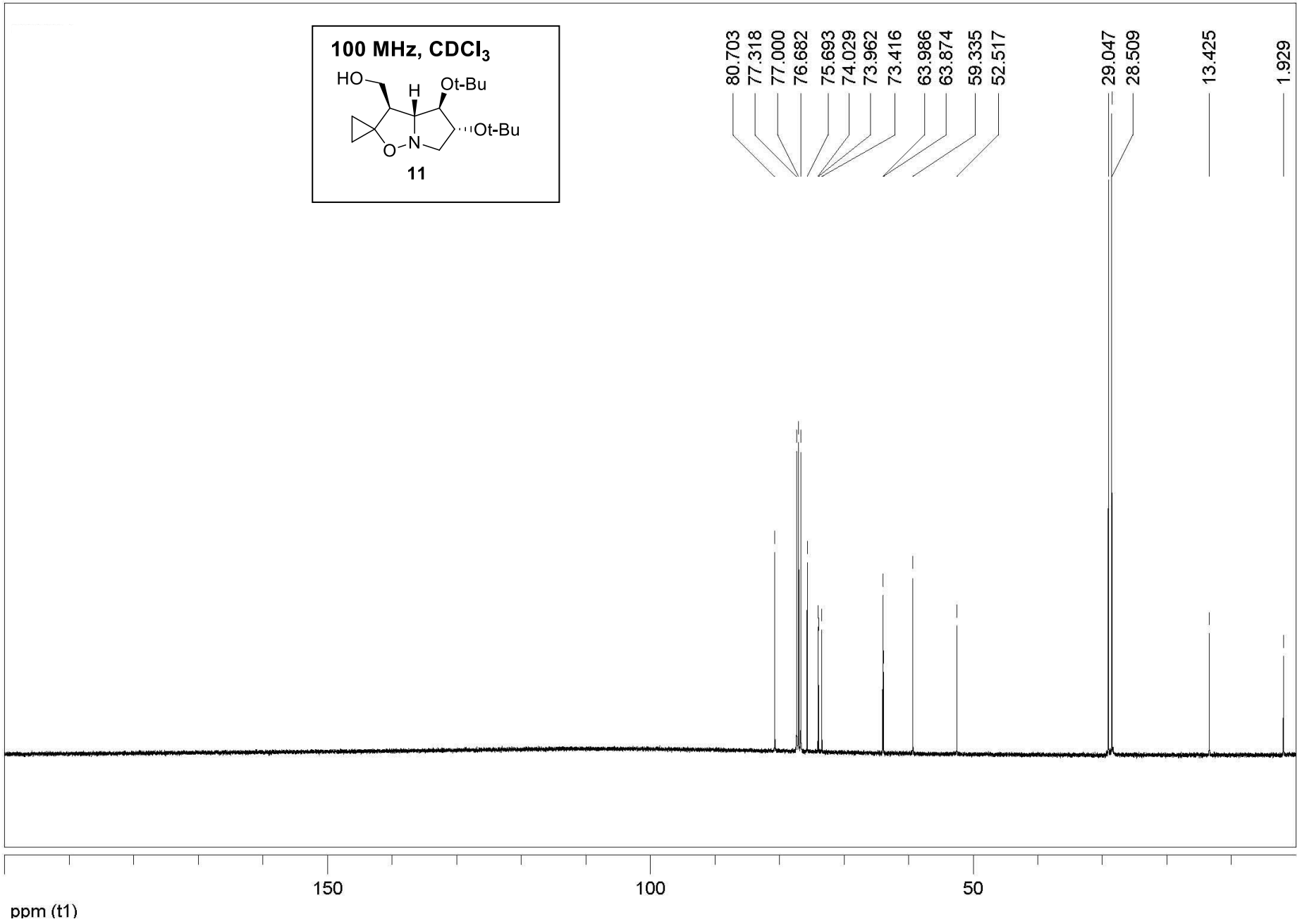
1.50
1.00
ppm (t1)
5.0
ppm (t1)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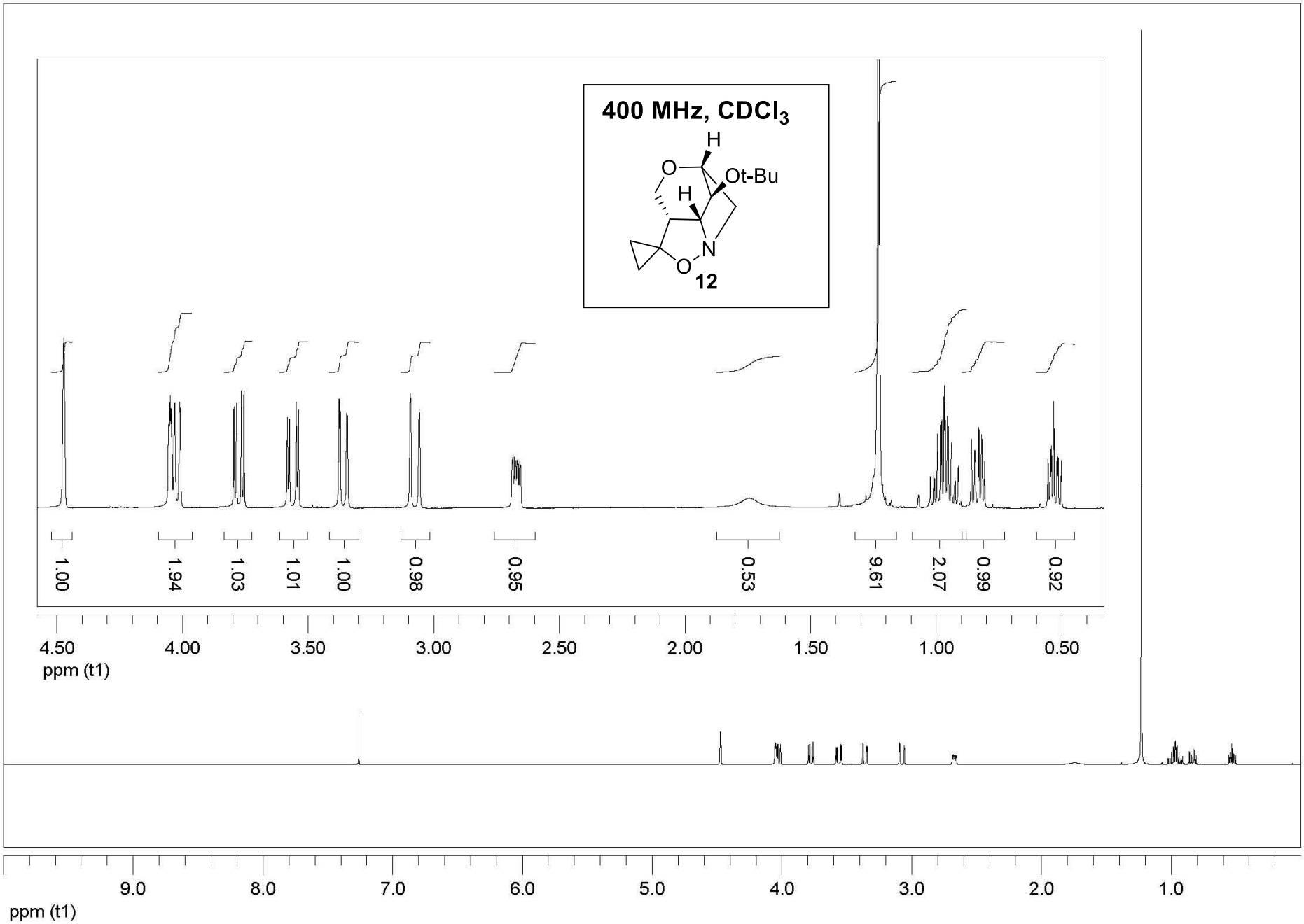
ppm (t1)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4.00
3.50
3.00
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2.00
1.50
1.00
0.50
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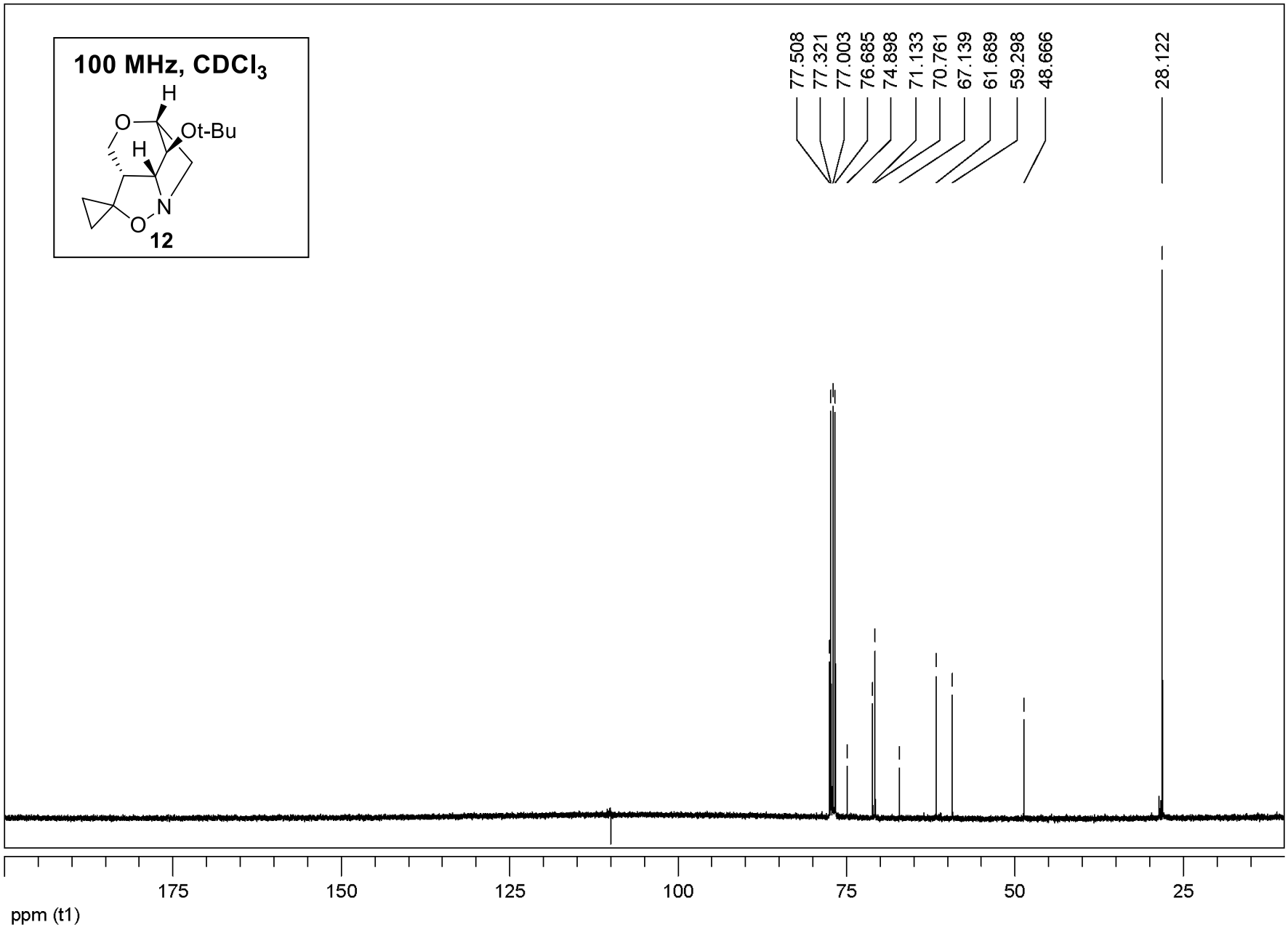
1.0
ppm (t1)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75
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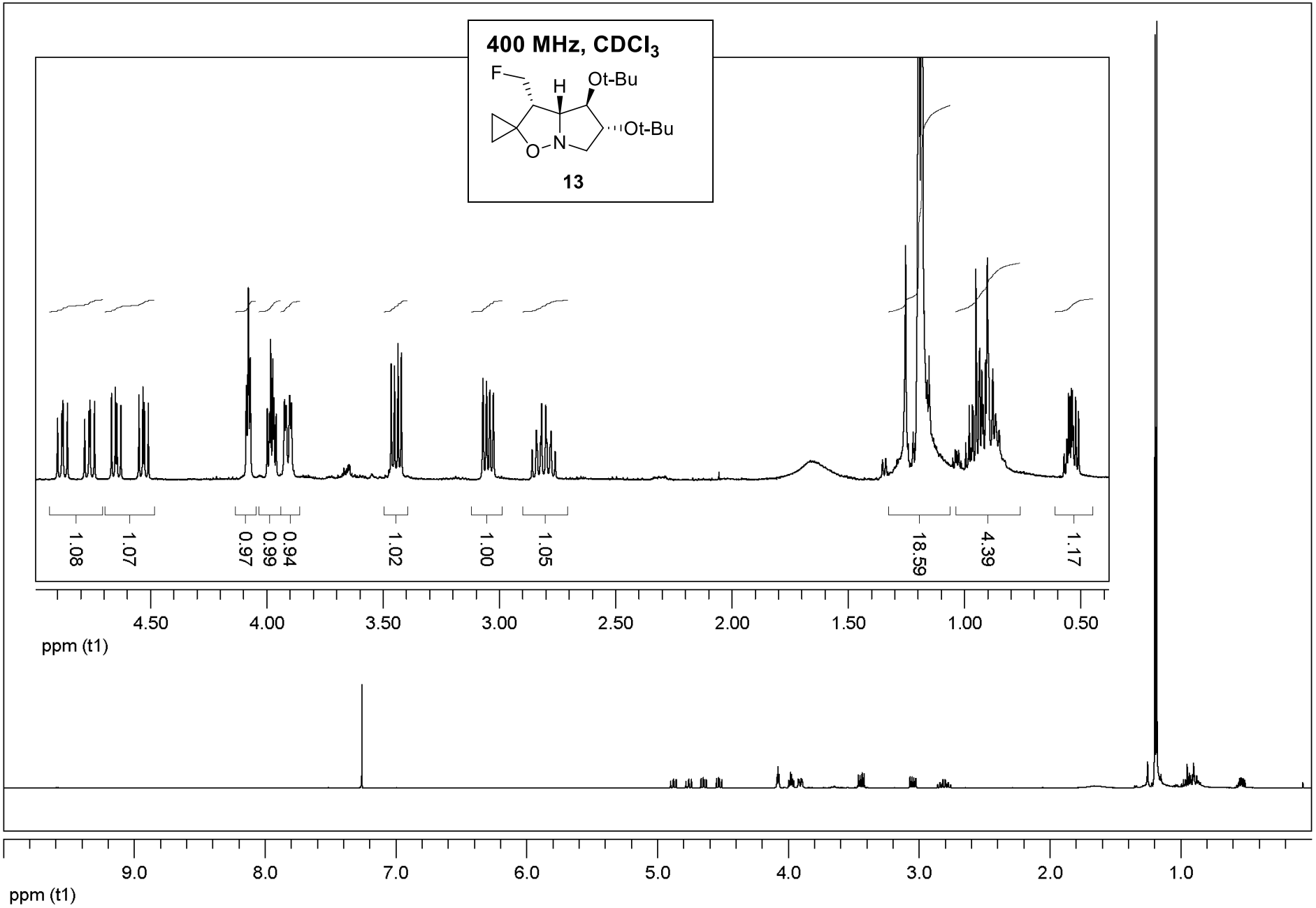
25
ppm (t1)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1.05
18.59
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3.00
2.50
2.00
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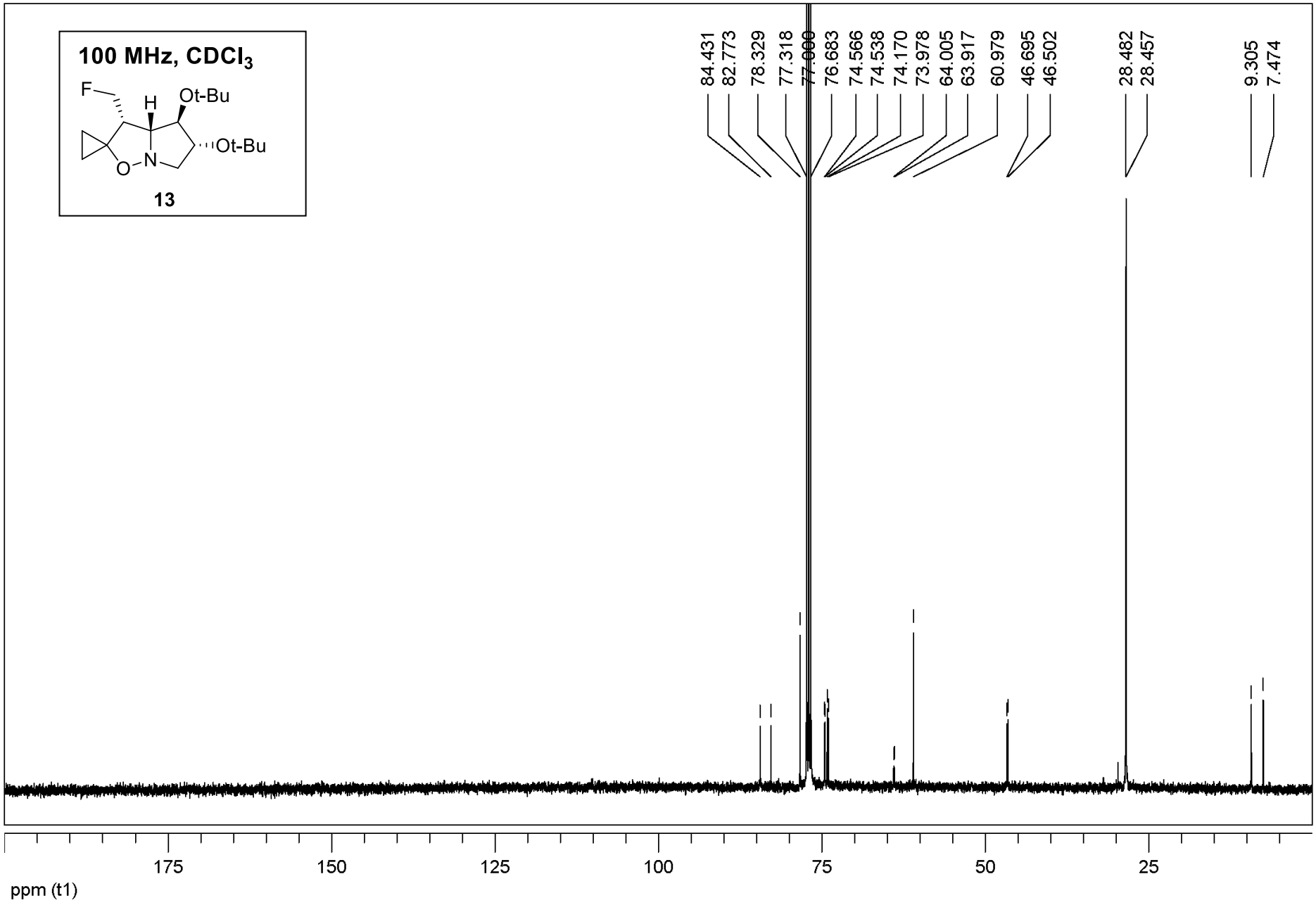
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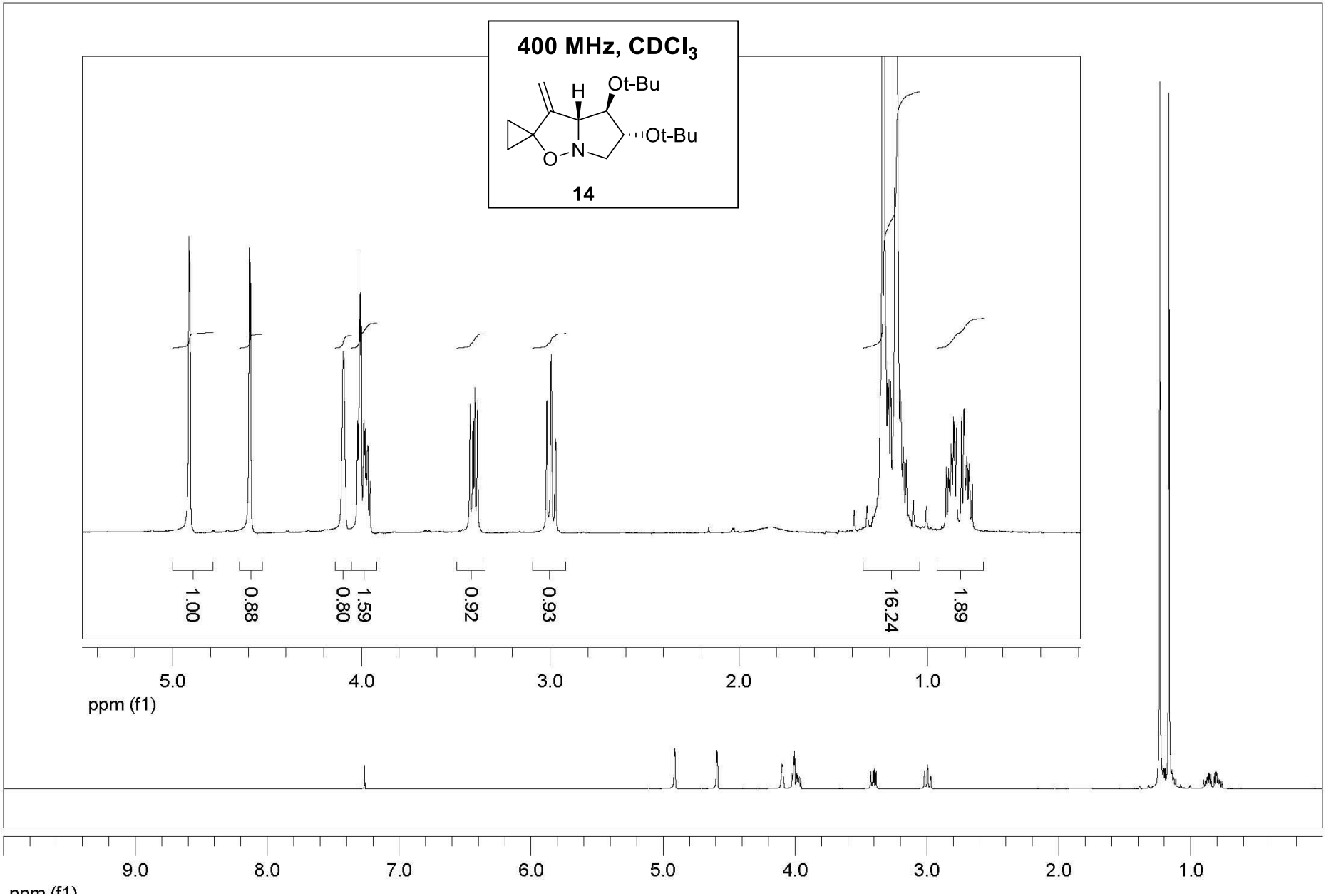
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4.0
3.0
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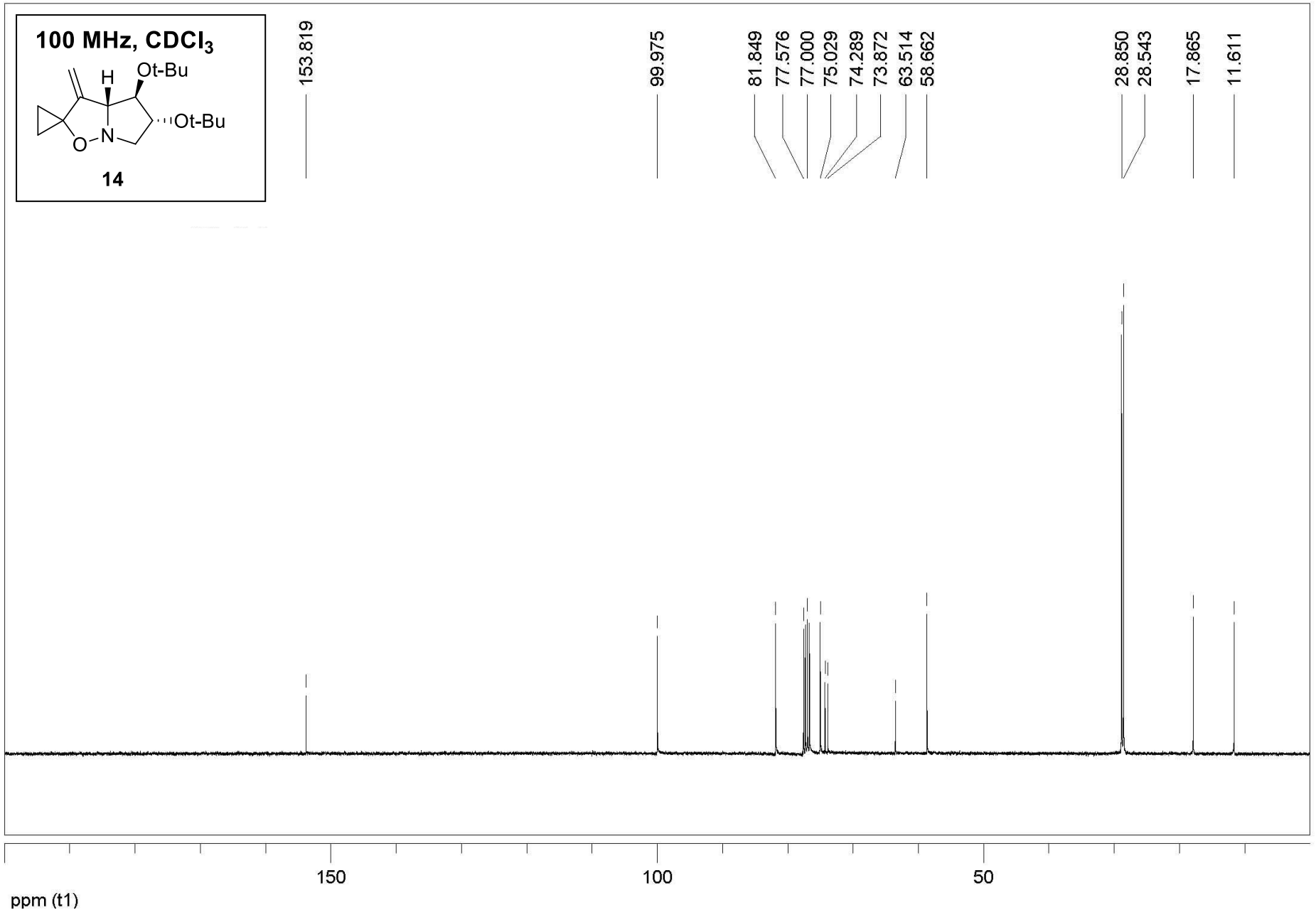
2.0
1.0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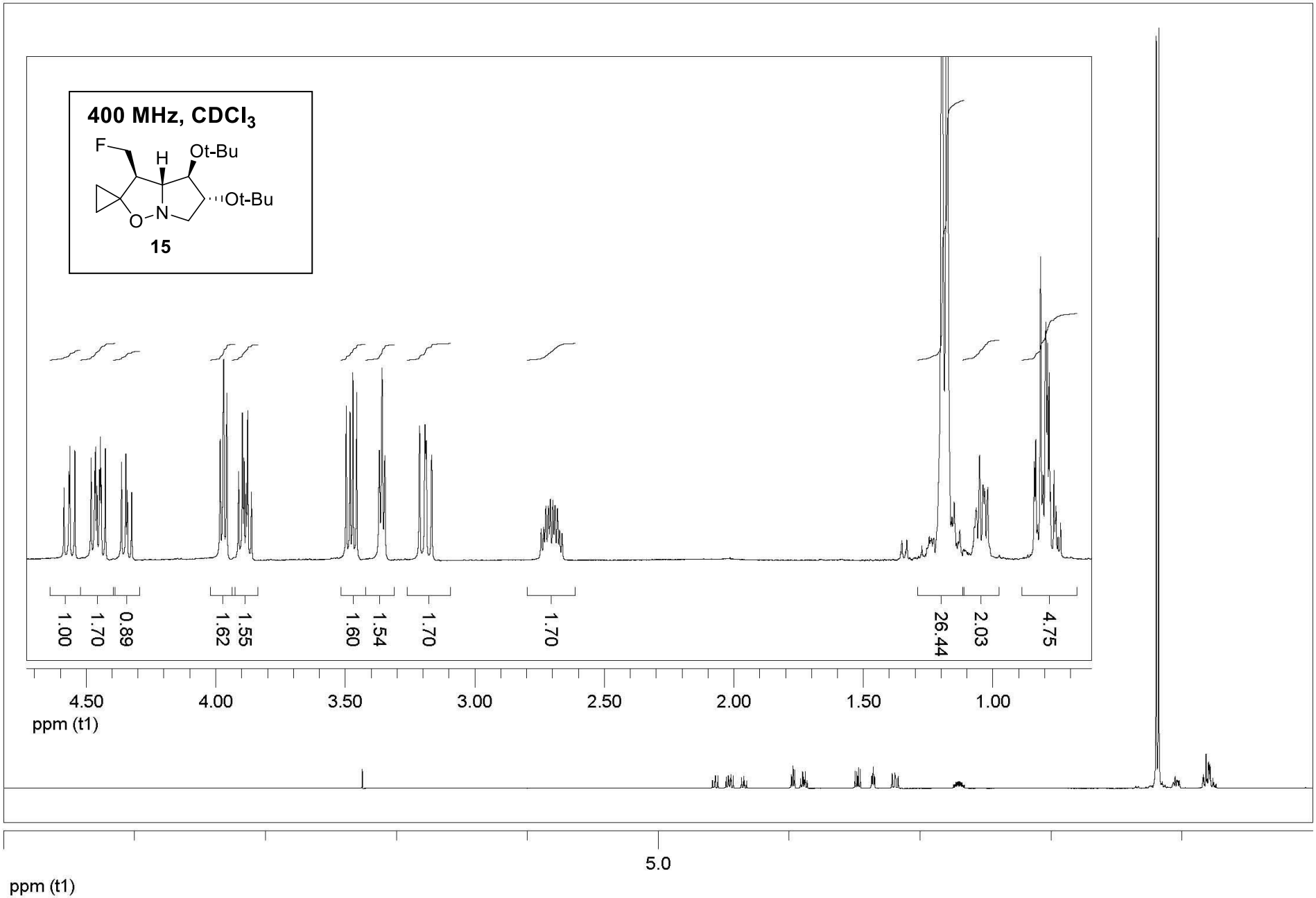
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1.70
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4.75
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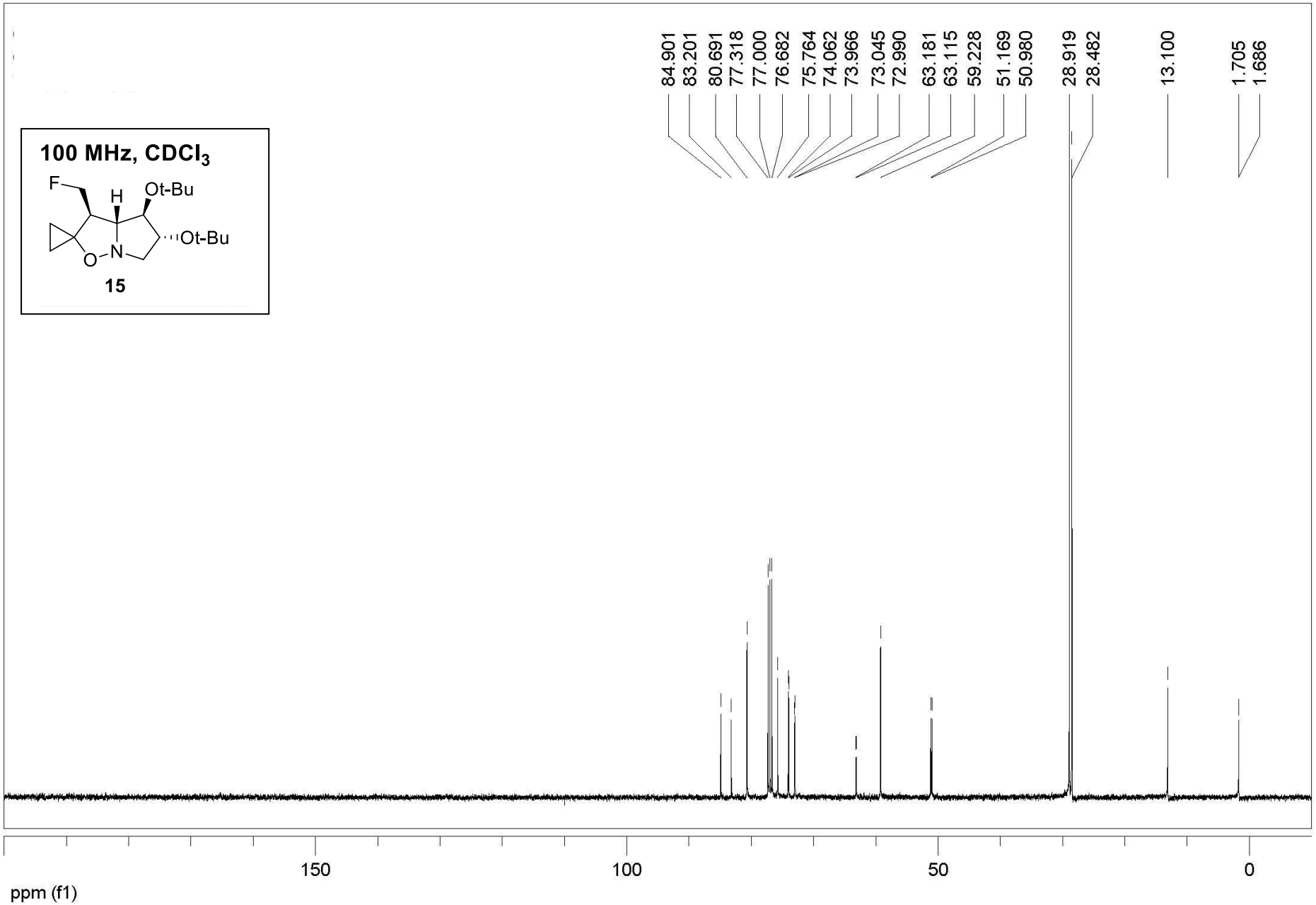
ppm (t1)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74.062
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63.181
63.115
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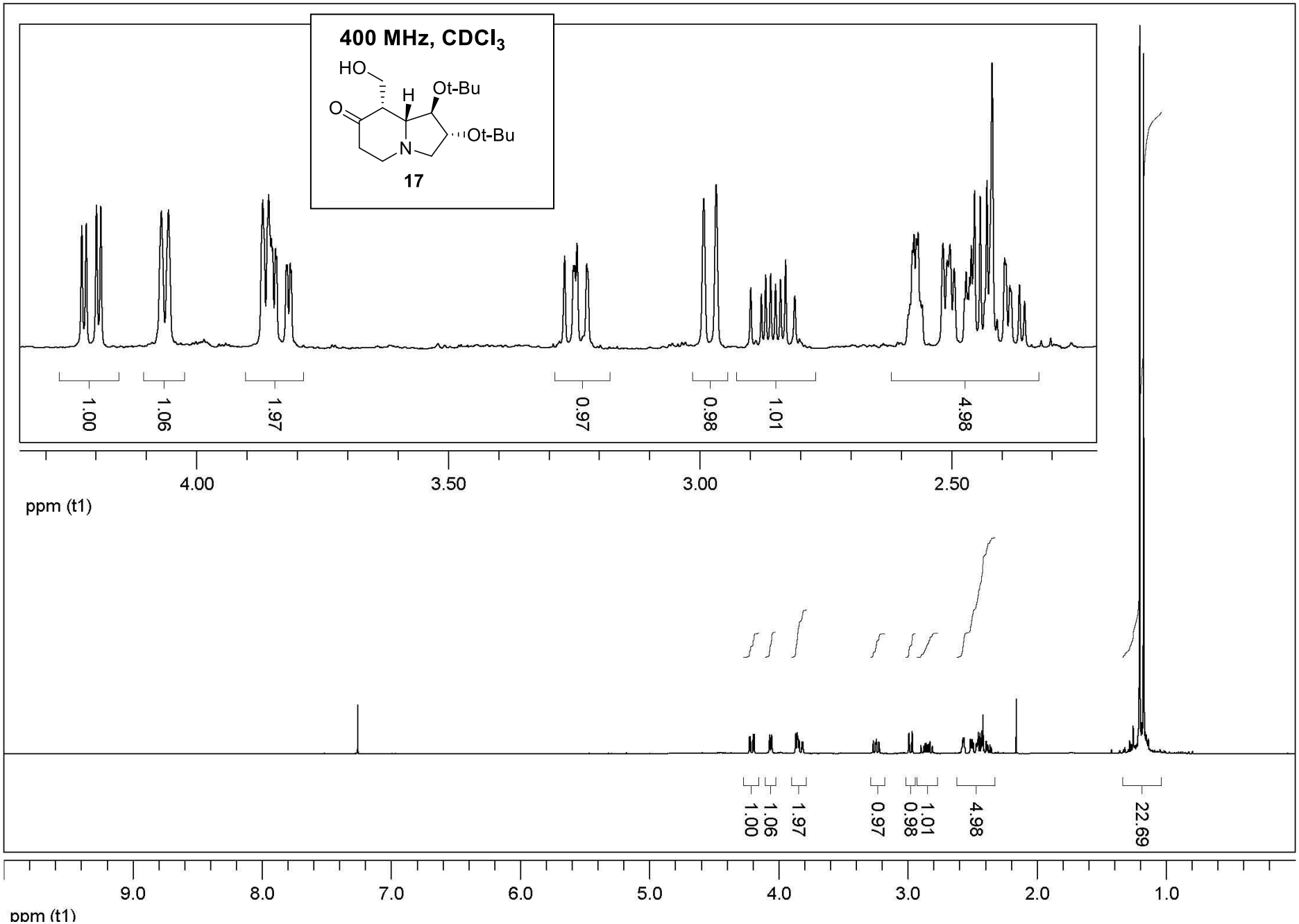
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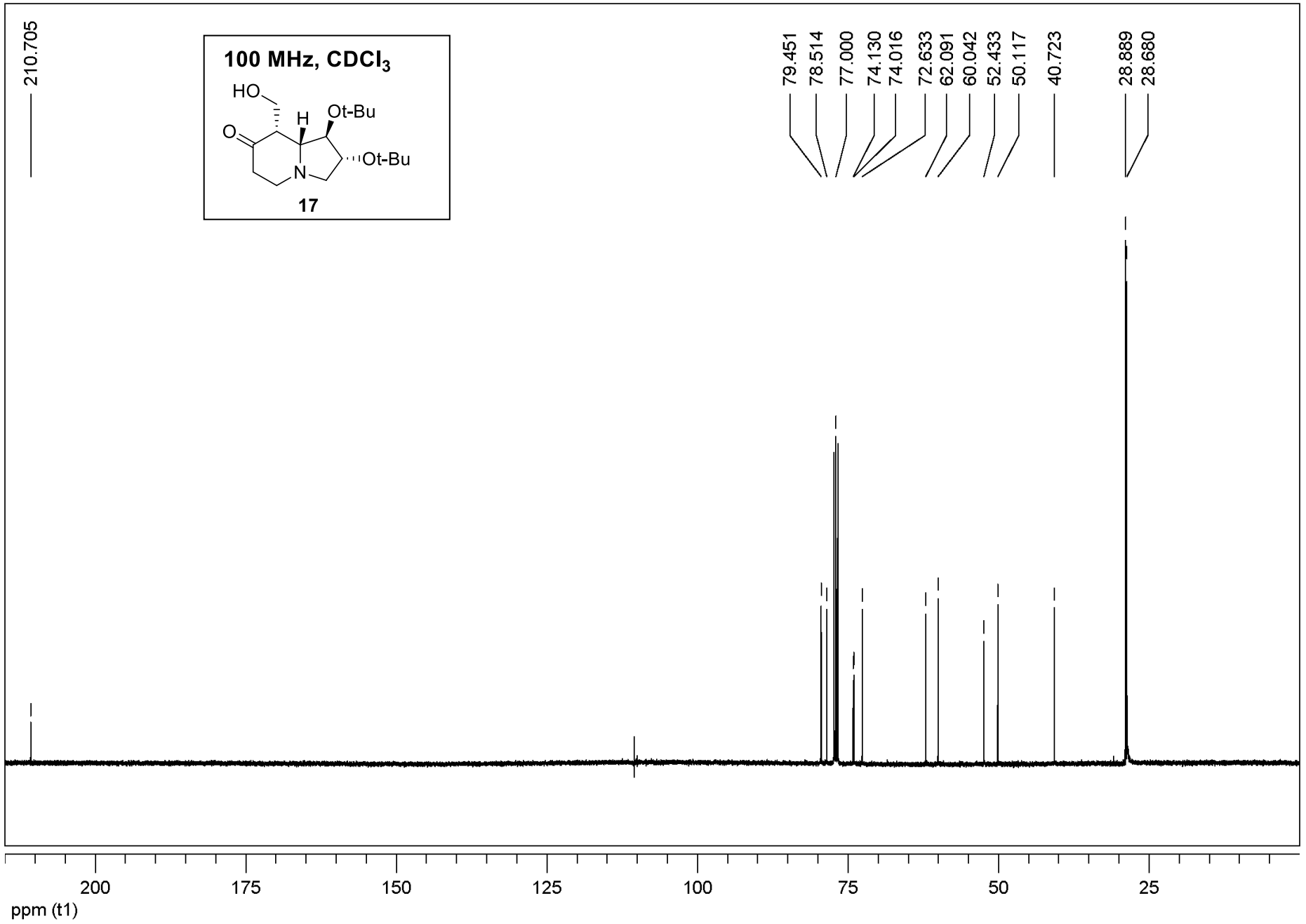
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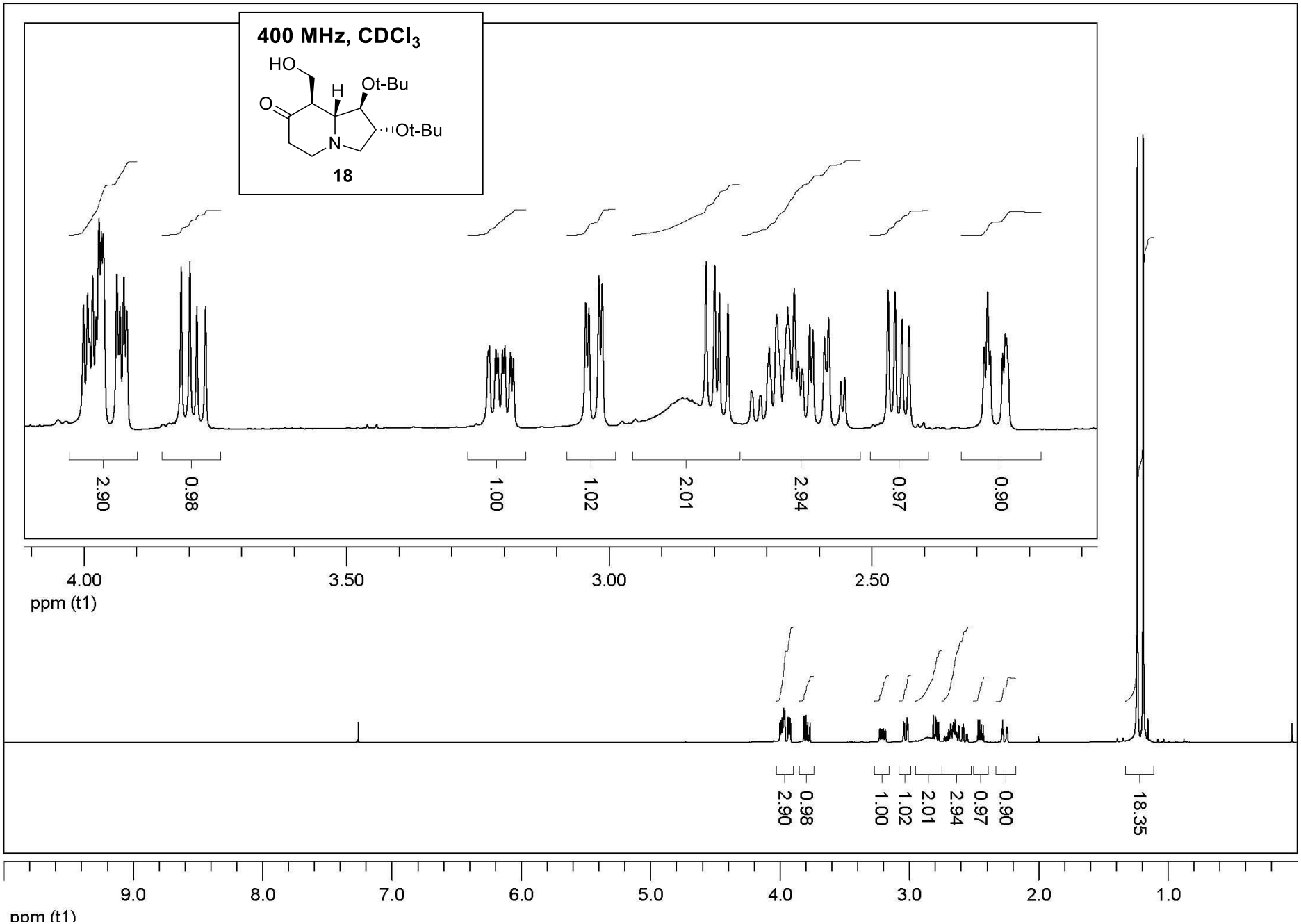
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Ot-Bu
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N
Ot-Bu
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1.02
2.01
2.94
0.97
0.90
4.00
3.50
3.00
2.50
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0.98
1.00
1.02
2.01
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0.97
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1.0
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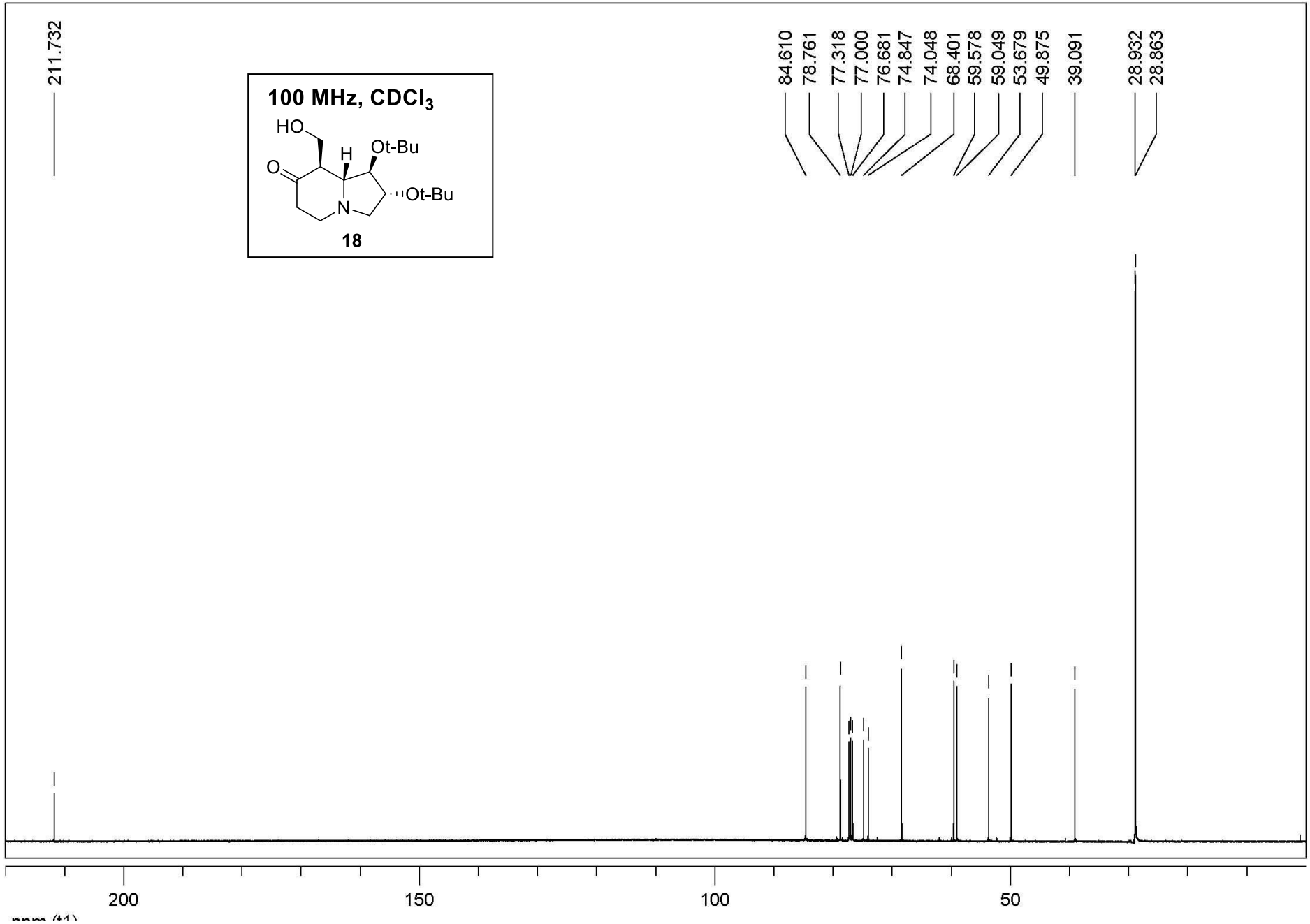
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74.048
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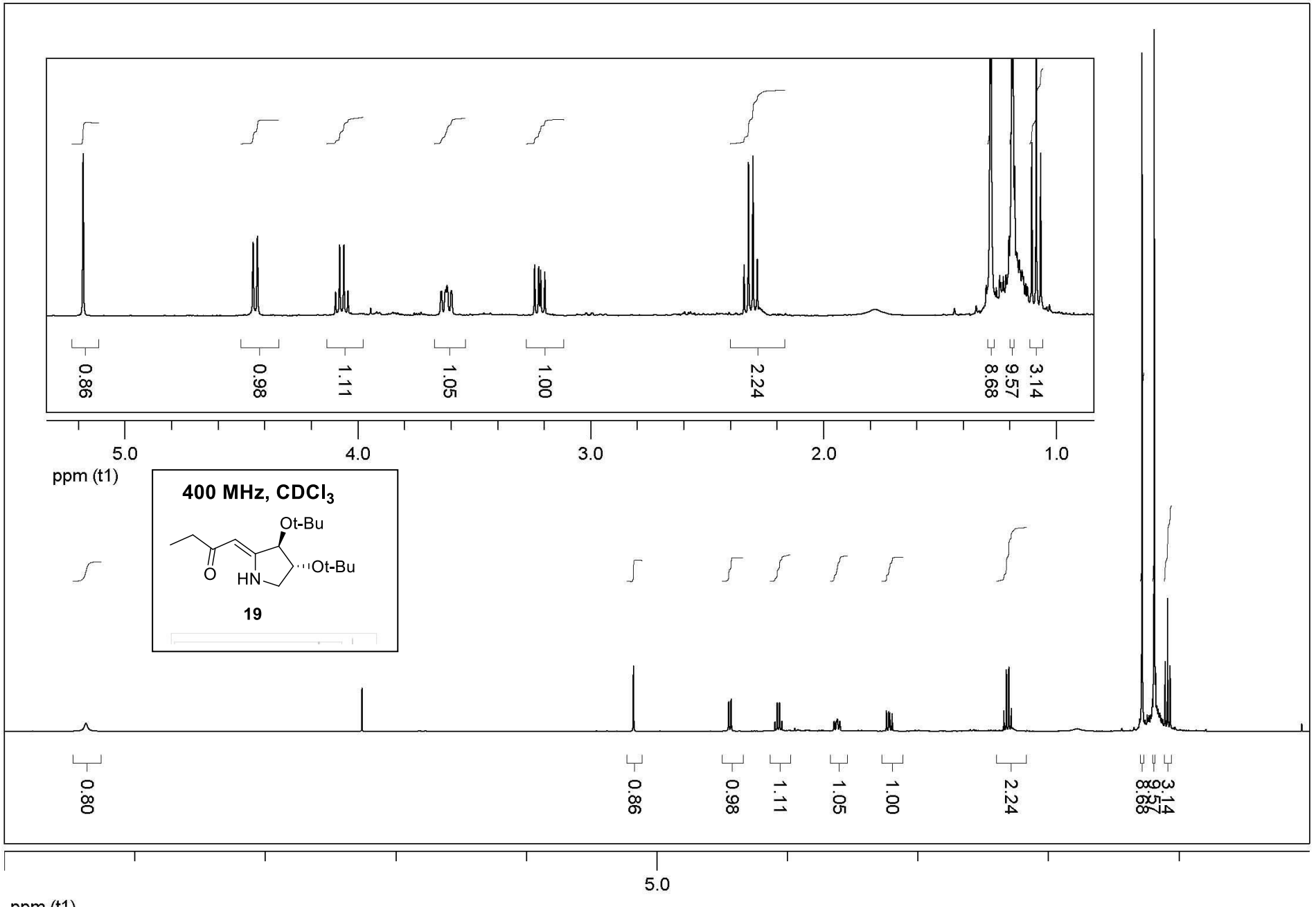
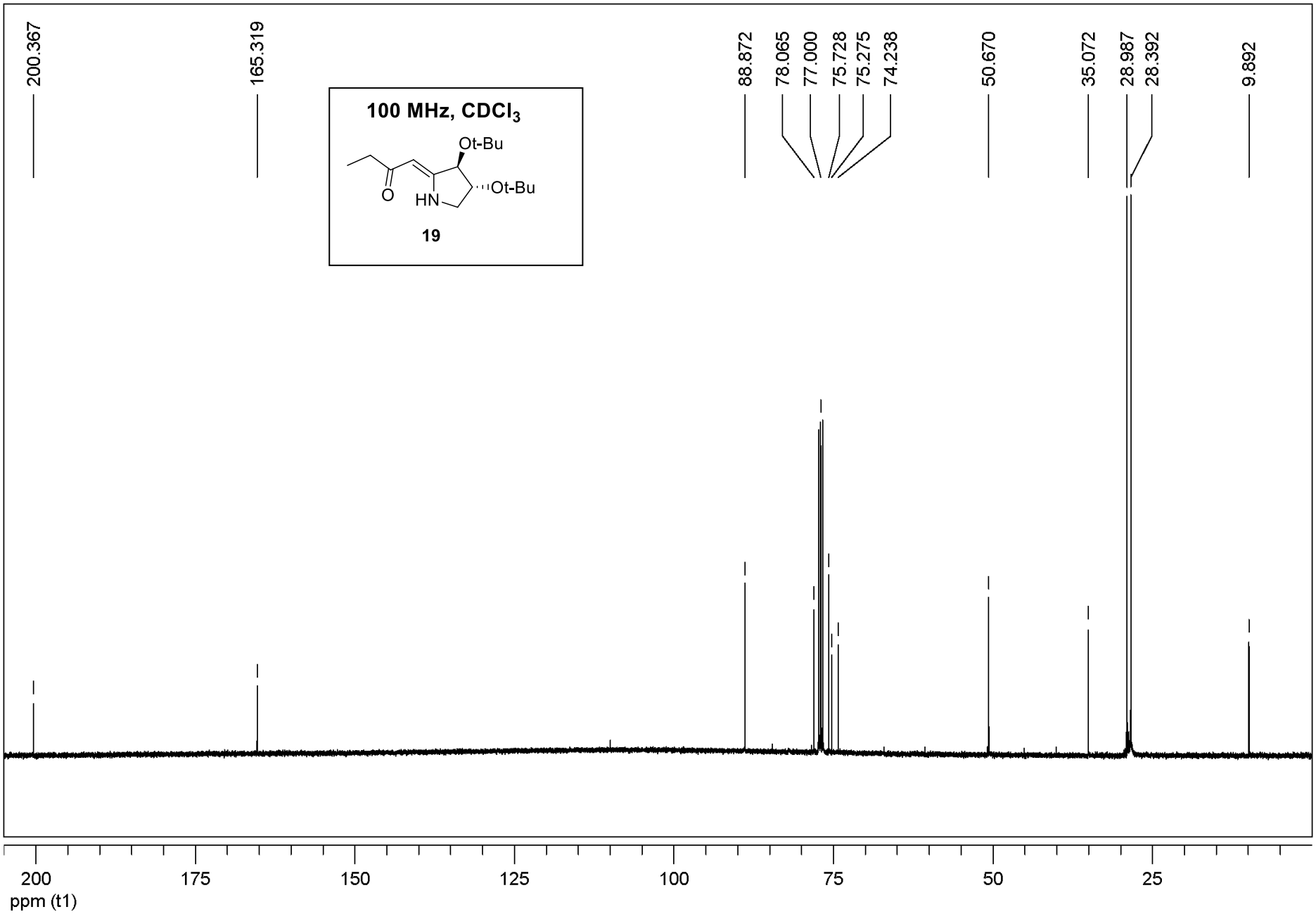
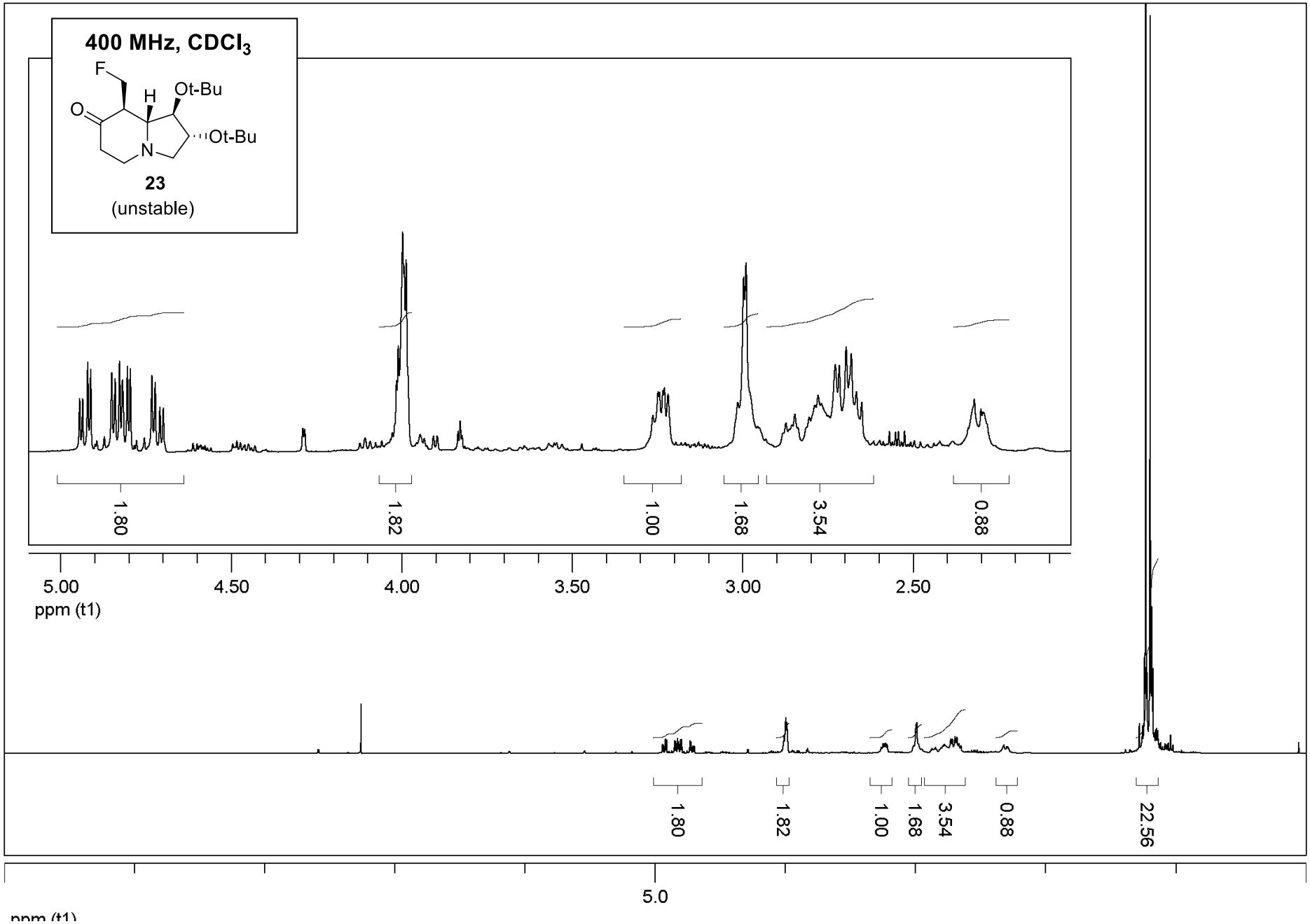
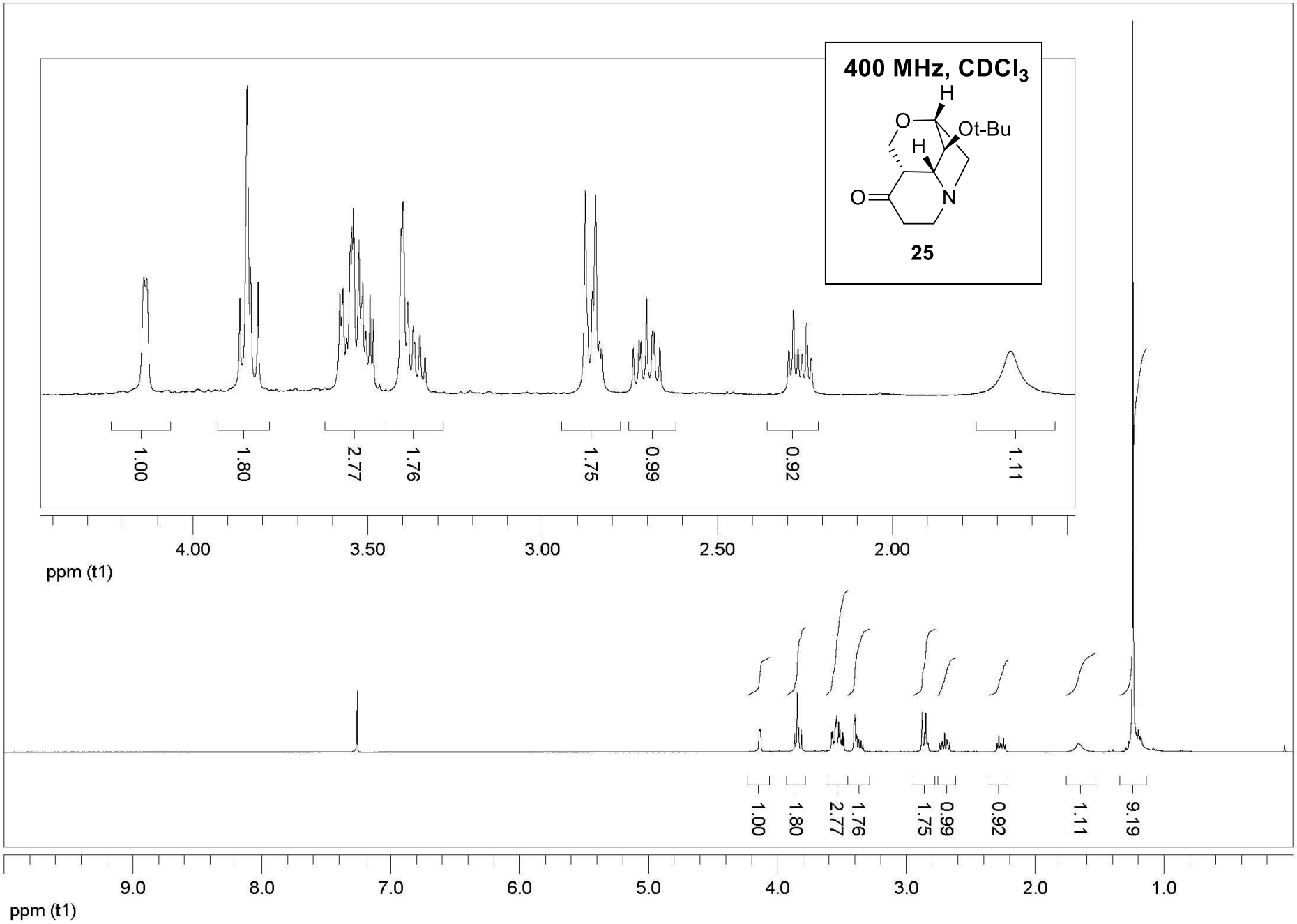
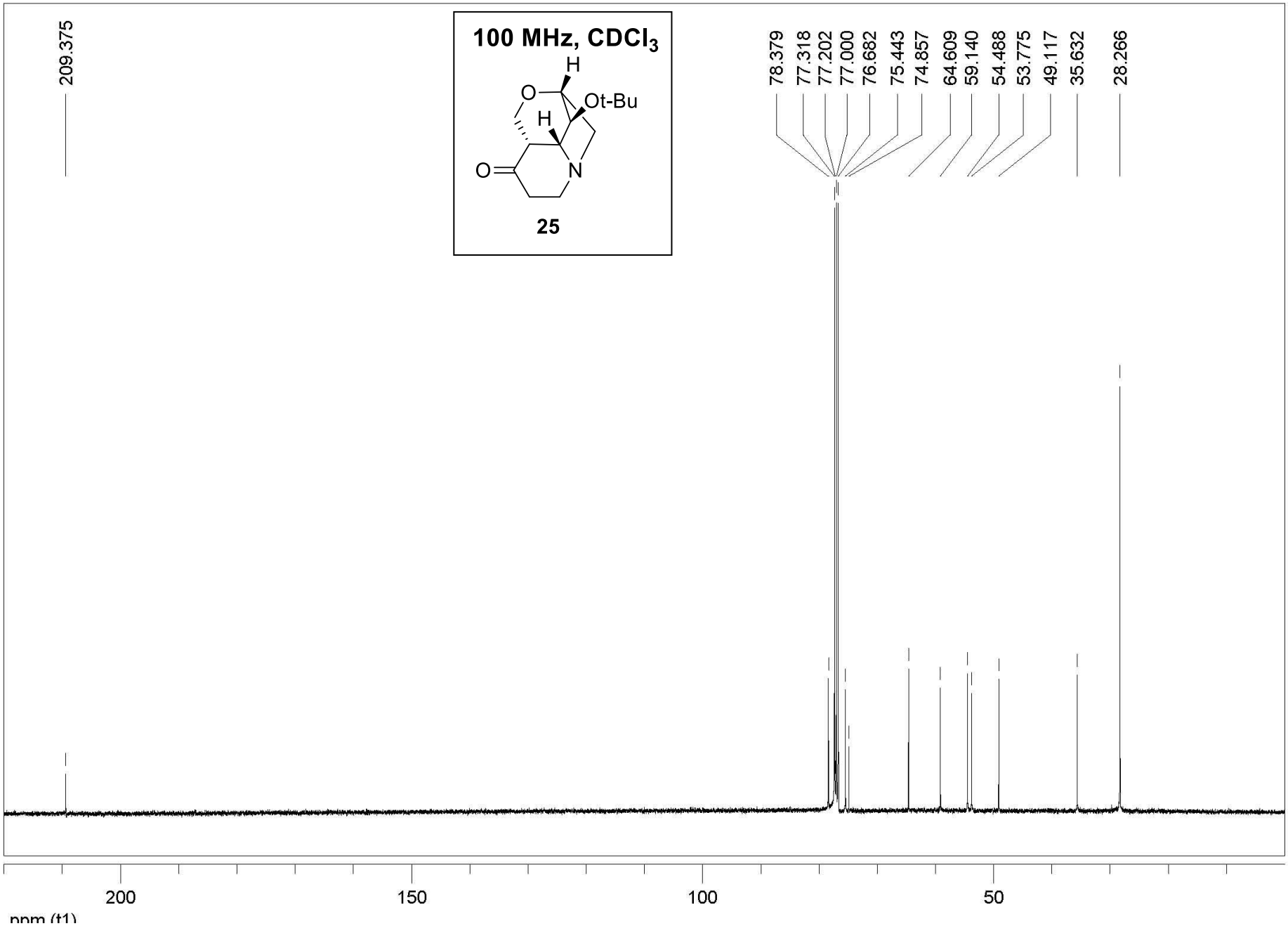
49.875
39.091
28.932
28.863
100 MHz, CDCl3
HO
H
Ot-Bu
O
Ot-Bu
N
18
200
150
100
50
ppm (t1)

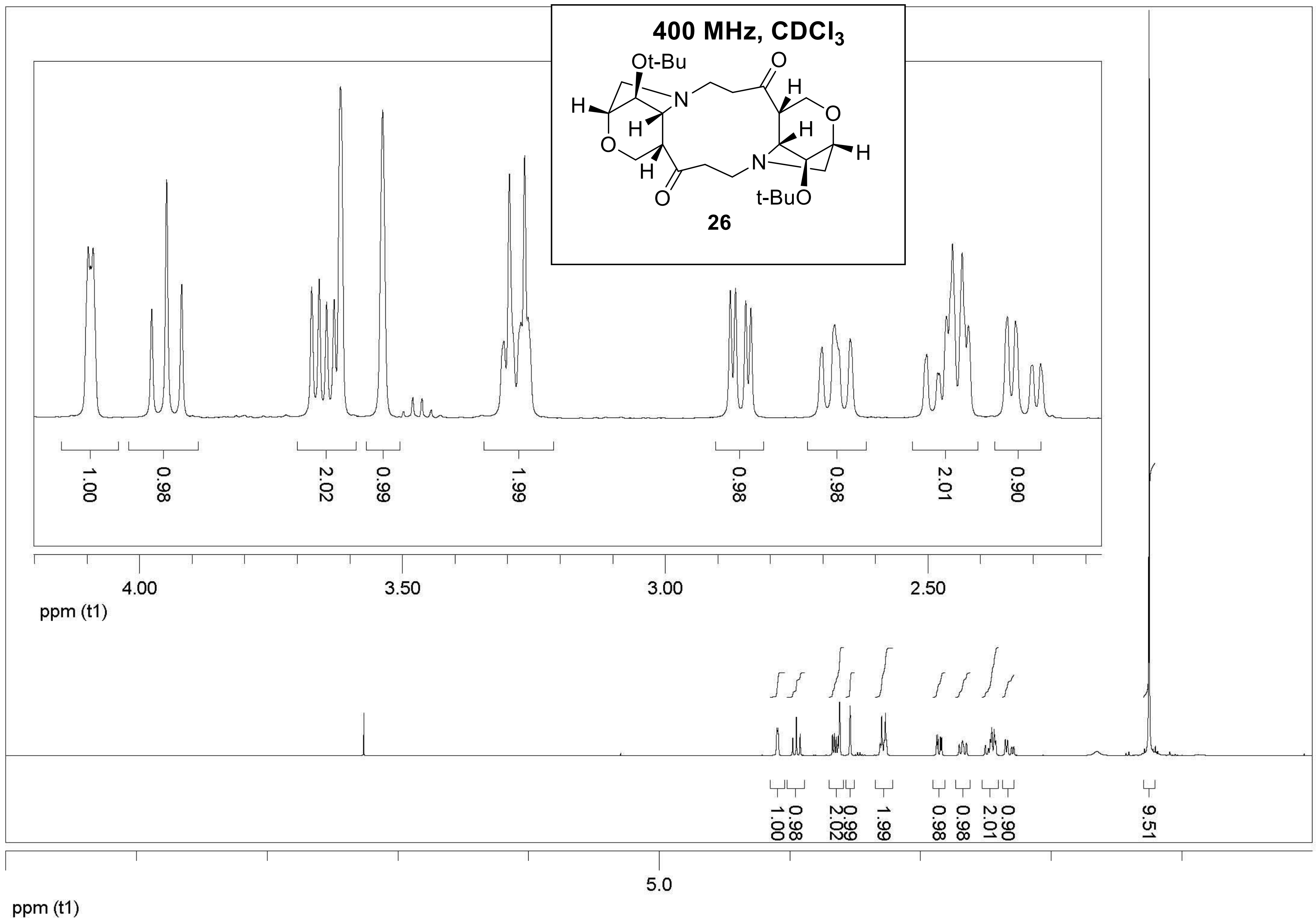

0.86
0.98
1.11
1.05
1.00
2.24
8.68
9.57
3.14
5.0
4.0
3.0
2.0
1.0
ppm (t1)
400 MHz, CDCl3
Ot-Bu
Ot-Bu
O
HN
19
0.80
0.86
0.98
1.11
1.05
1.00
2.24
8.68
9.57
3.14
5.0
ppm (t1)

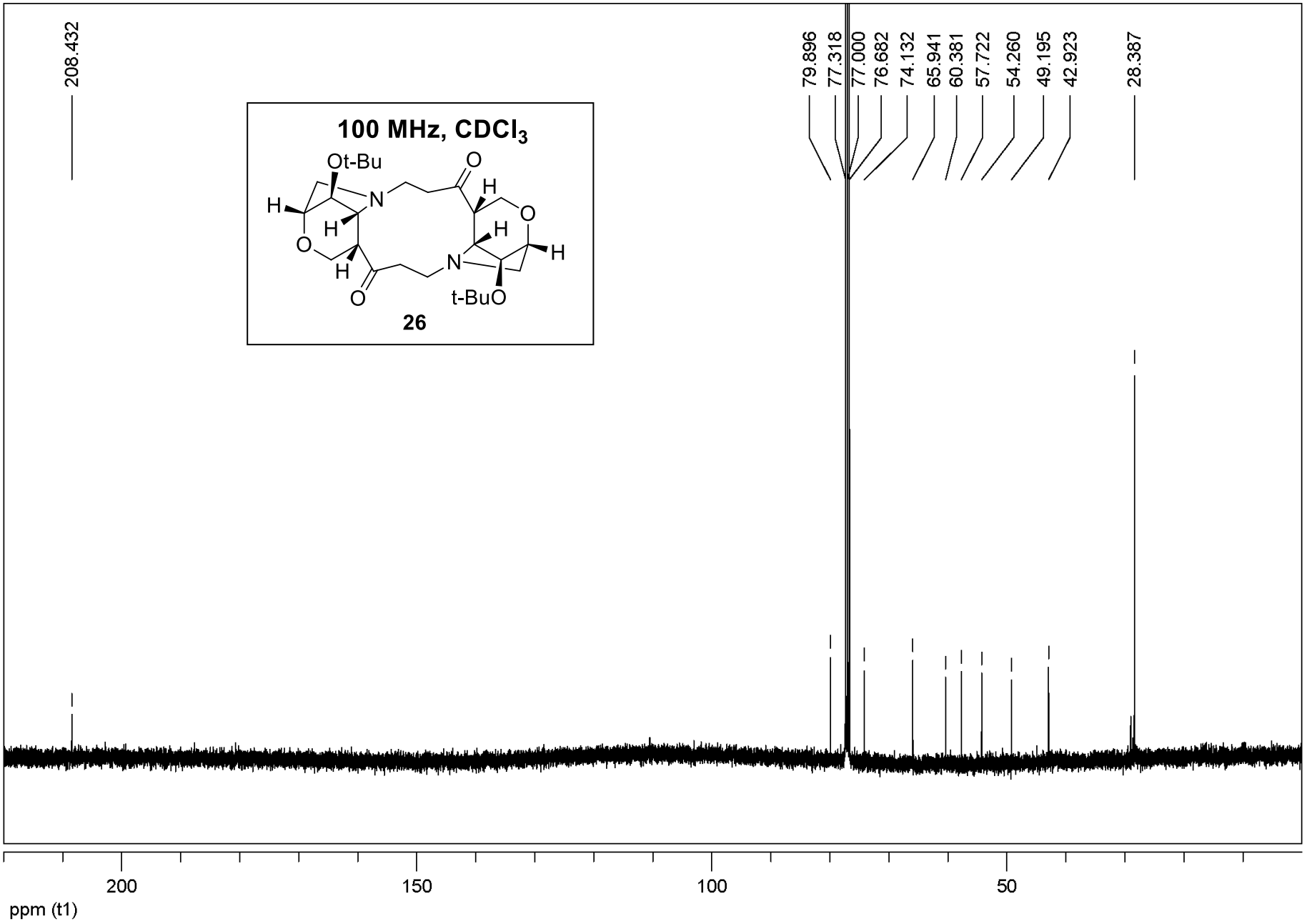

200.367
165.319
88.872
78.065
77.000
75.728
75.275
74.238
50.670
35.072
28.987
28.392
9.892
100 MHz, CDCl3
Ot-Bu
Ot-Bu
O
HN
19
200
175
150
125
100
75
50
25
ppm (t1)

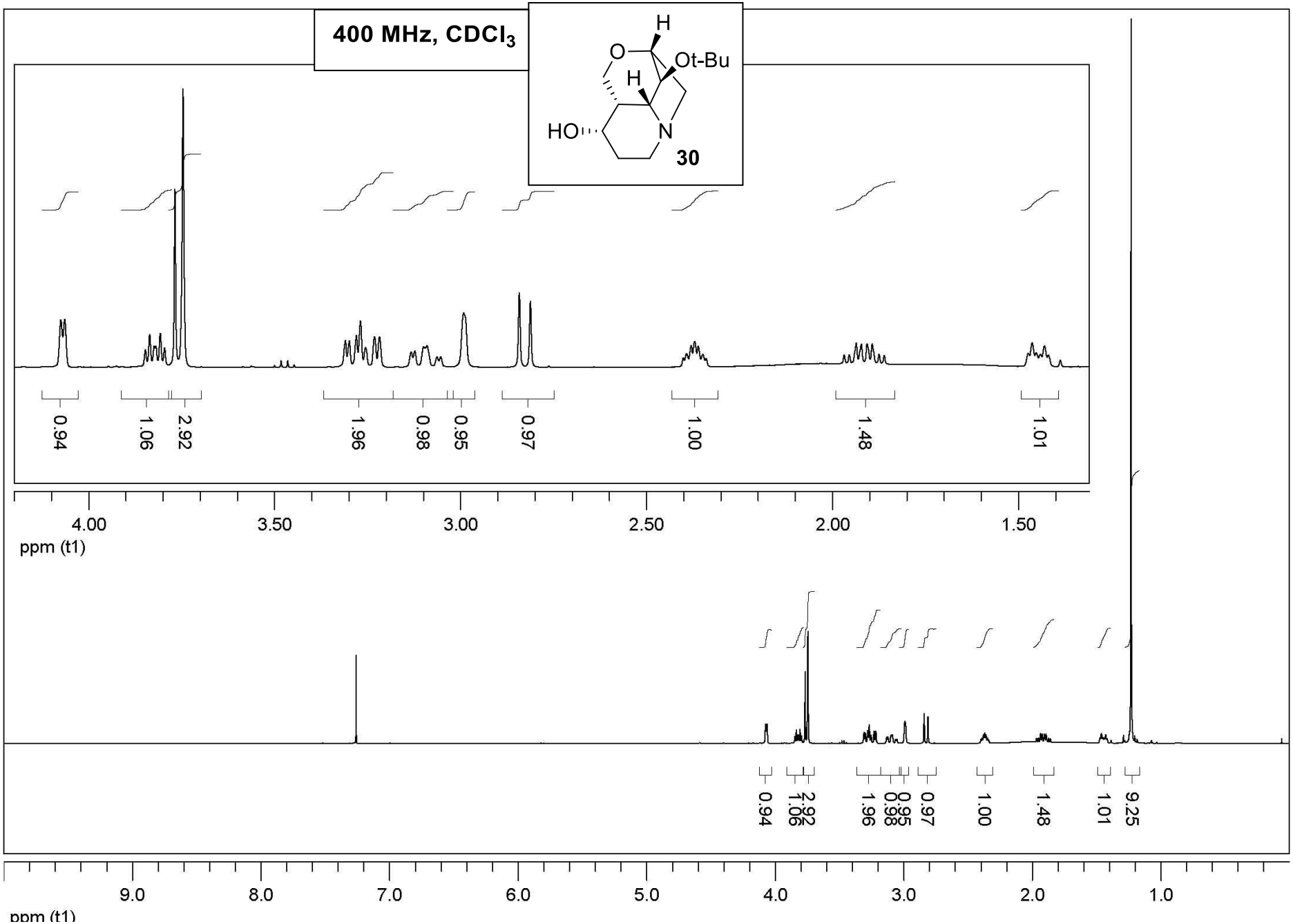

400 MHz, CDCl3
F
H
Ot-Bu
O
Ot-Bu
N
23
(unstable)
1.80
1.82
1.00
1.68
3.54
0.88
5.00
4.50
4.00
3.50
3.00
2.50
ppm (t1)
1.80
1.82
1.00
1.68
3.54
0.88
22.56
5.0
ppm (t1)

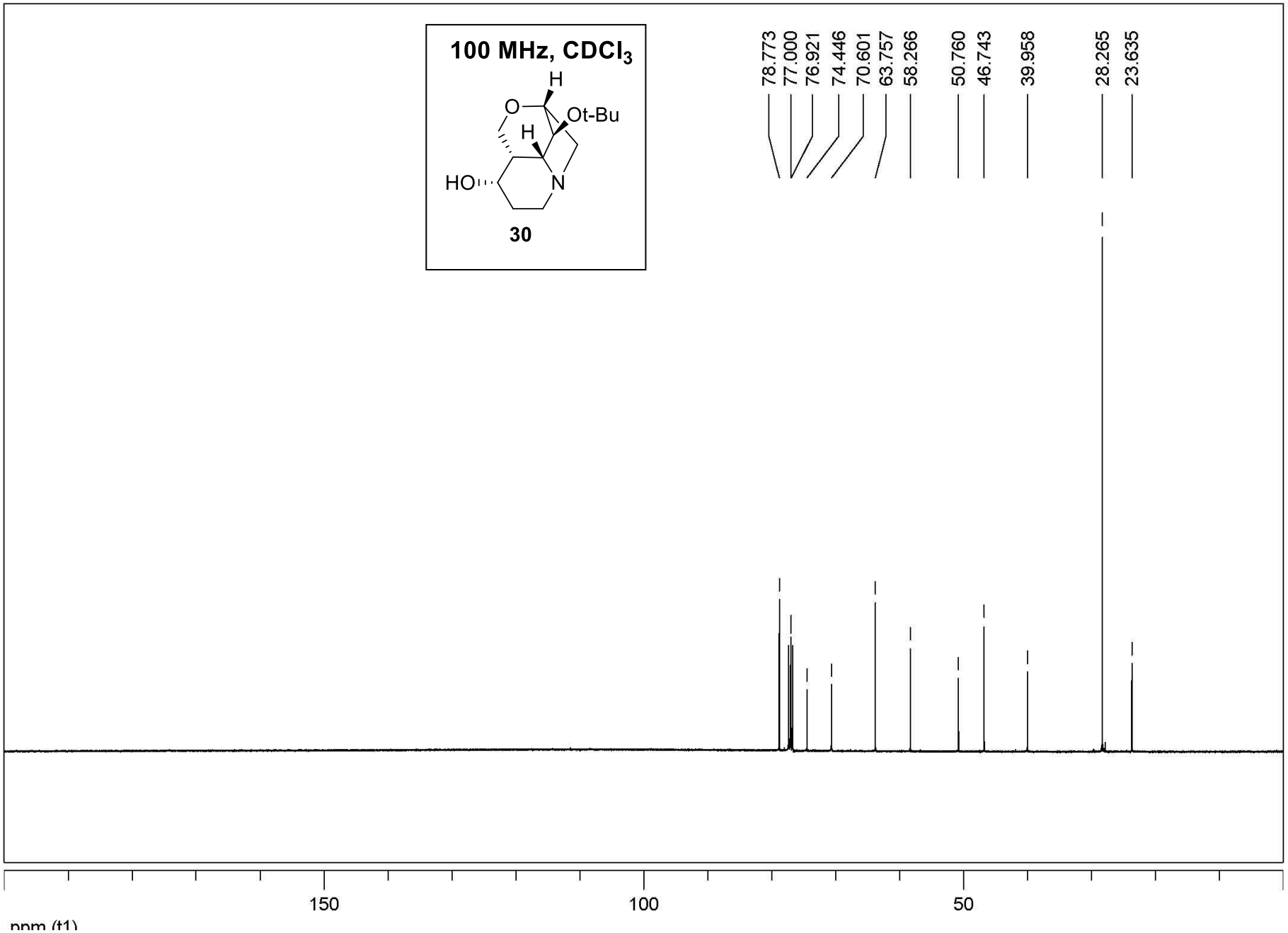

400 MHz, CDCl3
H
O
Ot-Bu
H
O
N
25
1.00
1.80
2.77
1.76
1.75
0.99
0.92
1.11
4.00
3.50
3.00
2.50
2.00
ppm (t1)
1.00
1.80
2.77
1.76
1.75
0.99
0.92
1.11
9.19
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

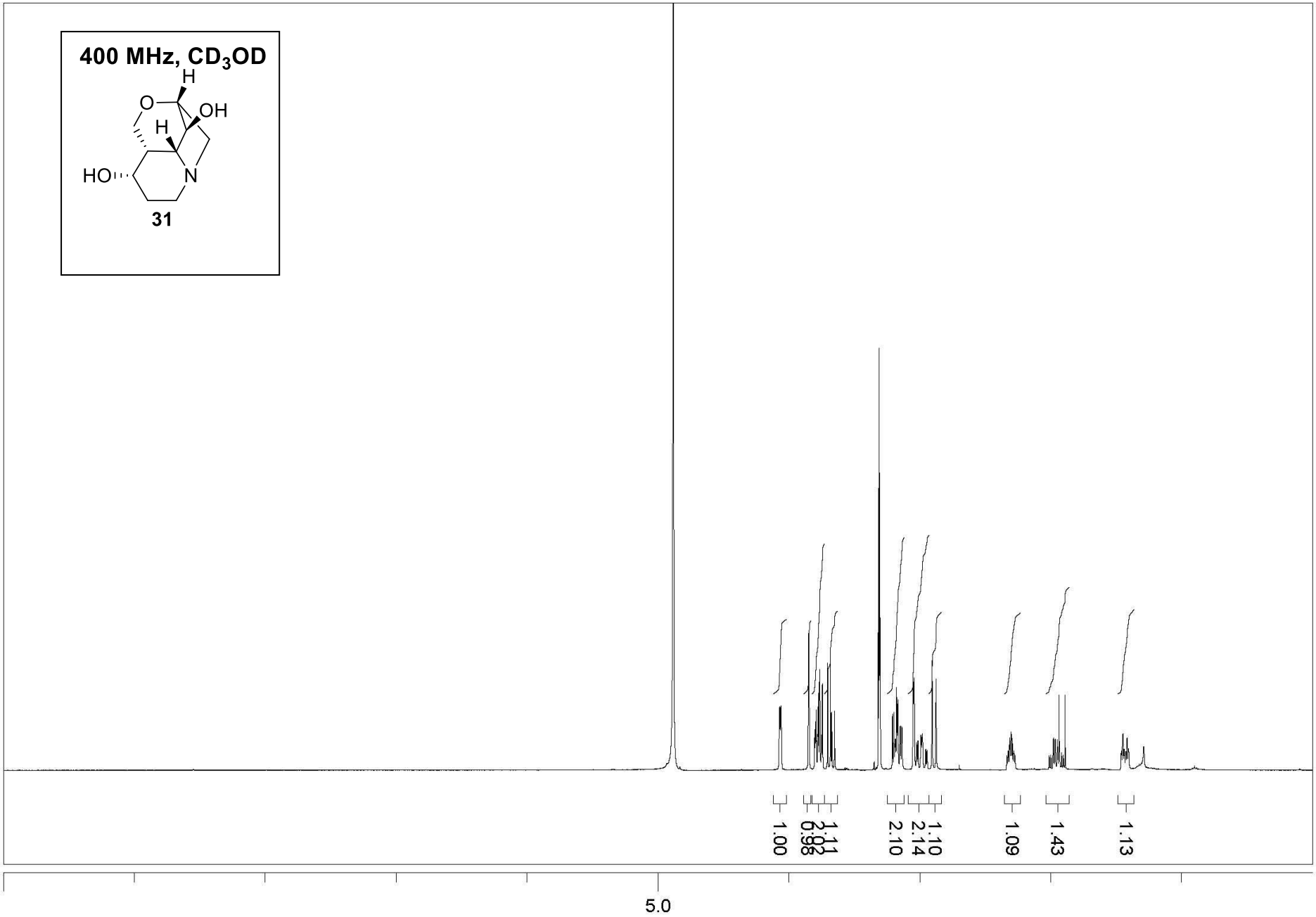

100 MHz, CDCl3
25
209.375
78.379
77.318
77.202
77.000
76.682
75.443
74.857
64.609
59.140
54.488
53.775
49.117
35.632
28.266
200
150
100
50
ppm (t1)

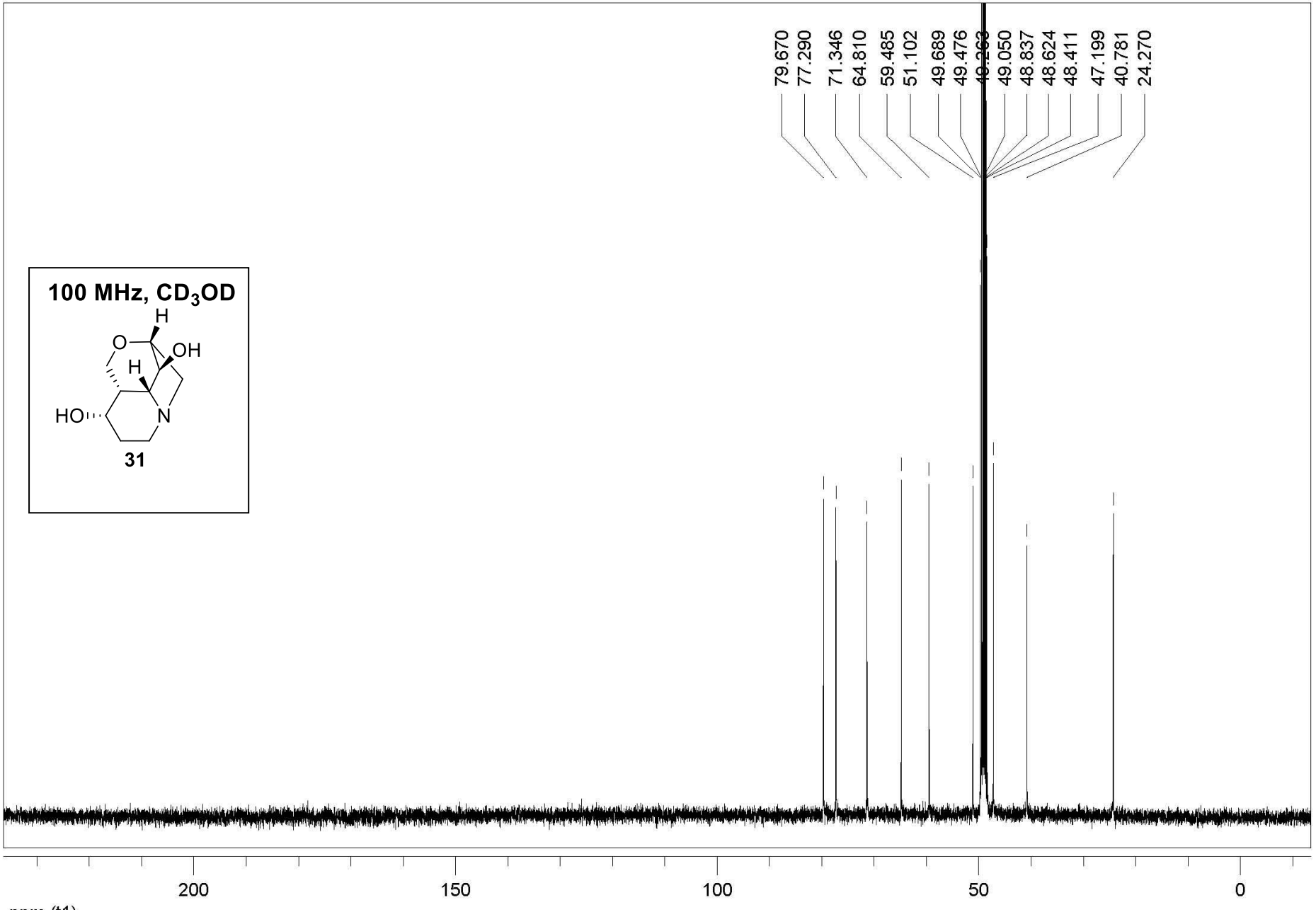

400 MHz, CDCl3
Ot-Bu
t-BuO
26
1.00
0.98
2.02
0.99
1.99
0.98
0.98
2.01
0.90
9.51
4.00
3.50
3.00
2.50
5.0
ppm (t1)

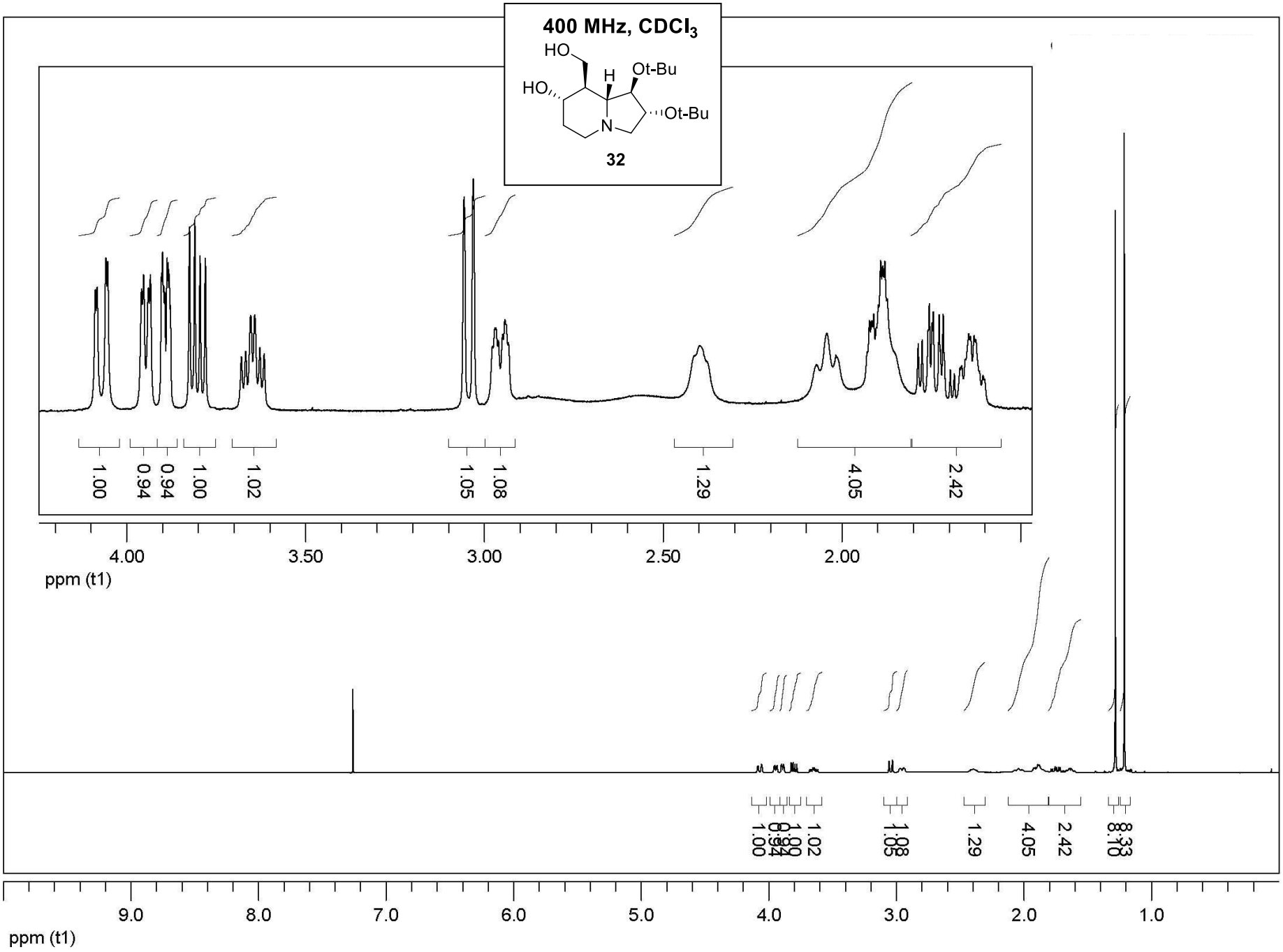

208.432
79.896
77.318
77.000
76.682
74.132
65.941
60.381
57.722
54.260
49.195
42.923
28.387
100 MHz, CDCl3
Ot-Bu
O
H
N
H
H
O
O
H
H
N
H
O
t-BuO
26
200
150
100
50
ppm (t1)

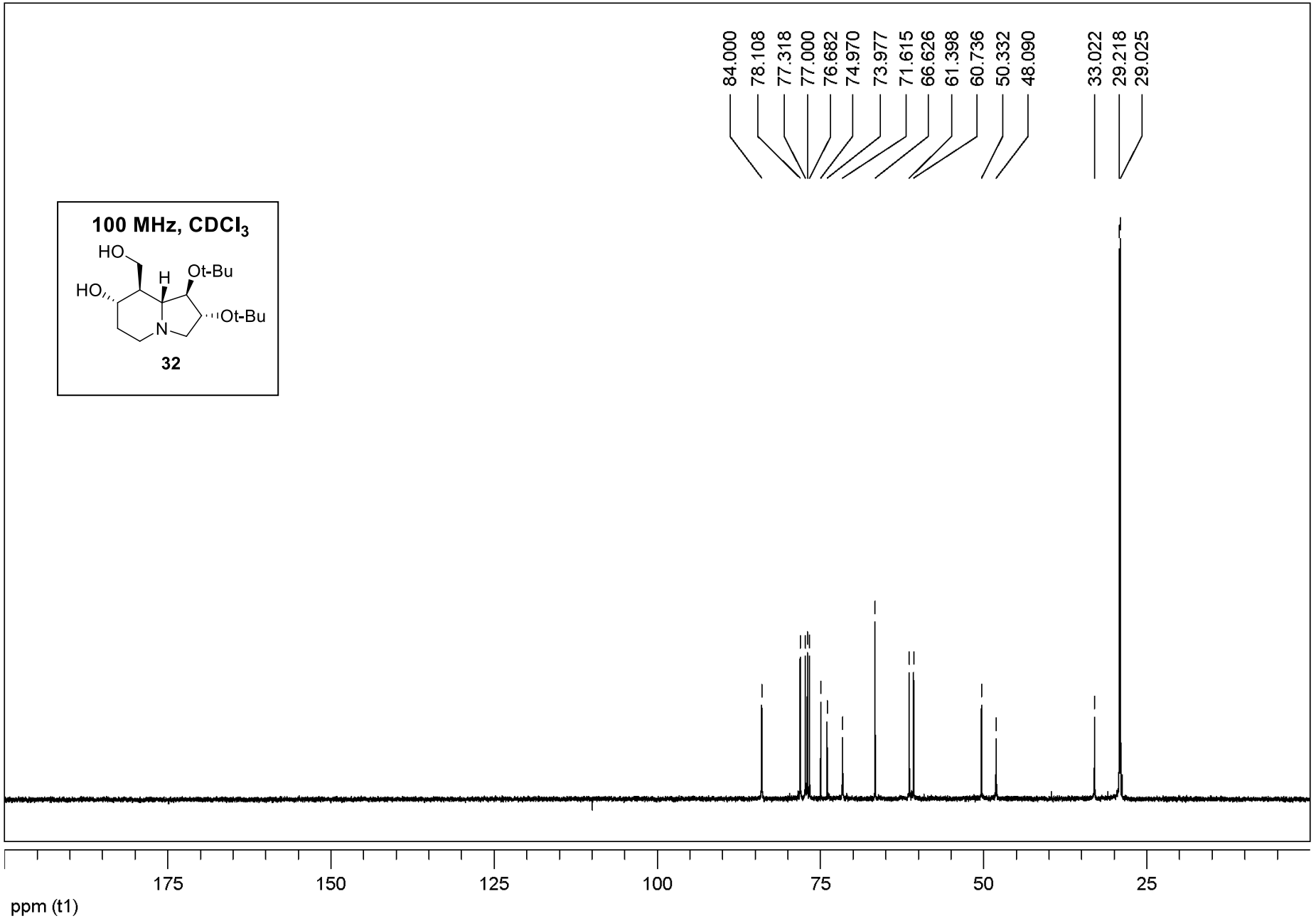

400 MHz, CDCl3
H
O
Ot-Bu
H
HO
N
30
0.94
1.06
2.92
1.96
0.98
0.95
0.97
1.00
1.48
1.01
4.00
3.50
3.00
2.50
2.00
1.50
ppm (t1)
0.94
1.06
2.92
1.96
0.98
0.95
0.97
1.00
1.48
1.01
9.25
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

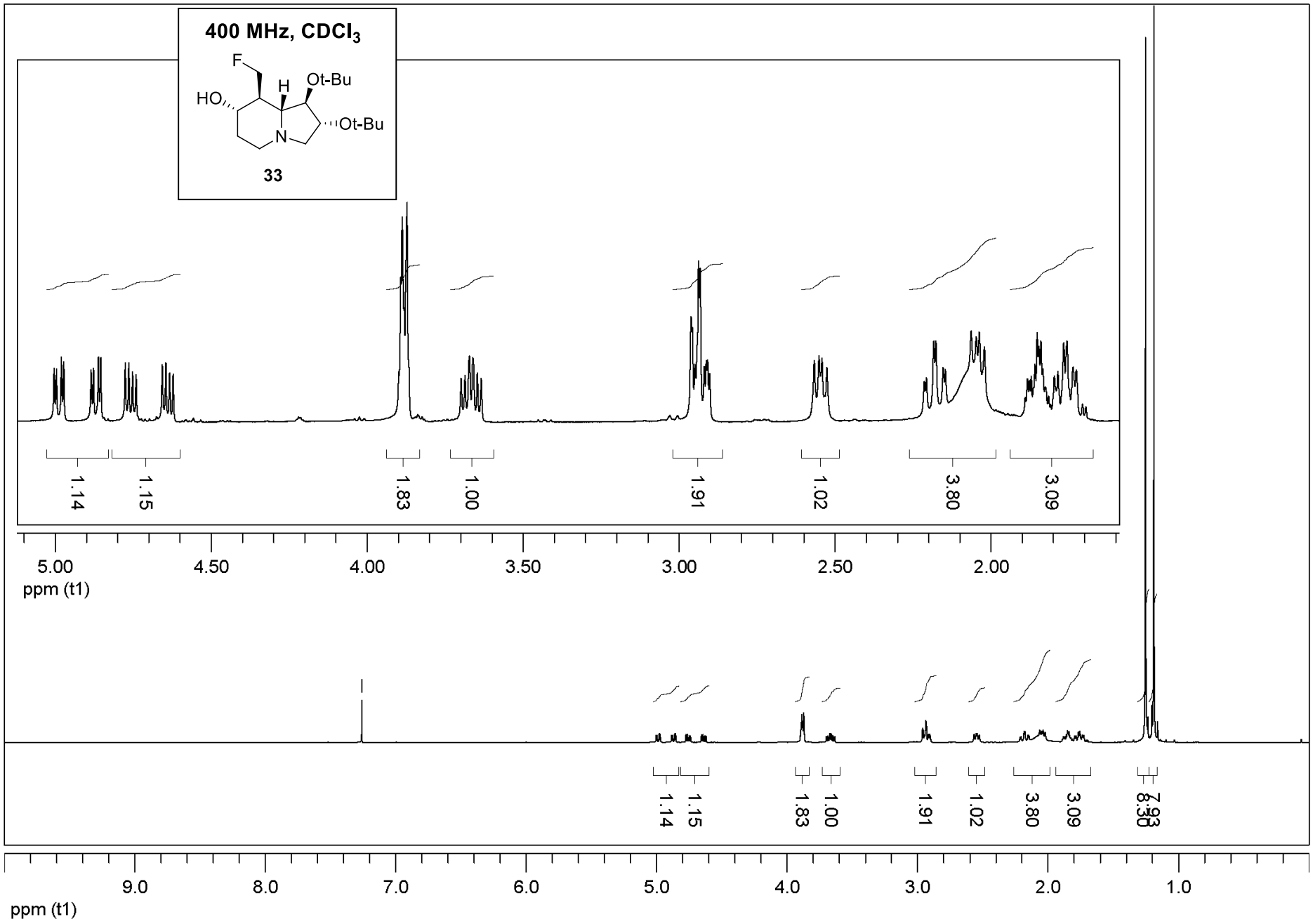

100 MHz, CDCl3
H
O
Ot-Bu
H
HO
N
30
78.773
77.000
76.921
74.446
70.601
63.757
58.266
50.760
46.743
39.958
28.265
23.635
150
100
50
ppm (t1)

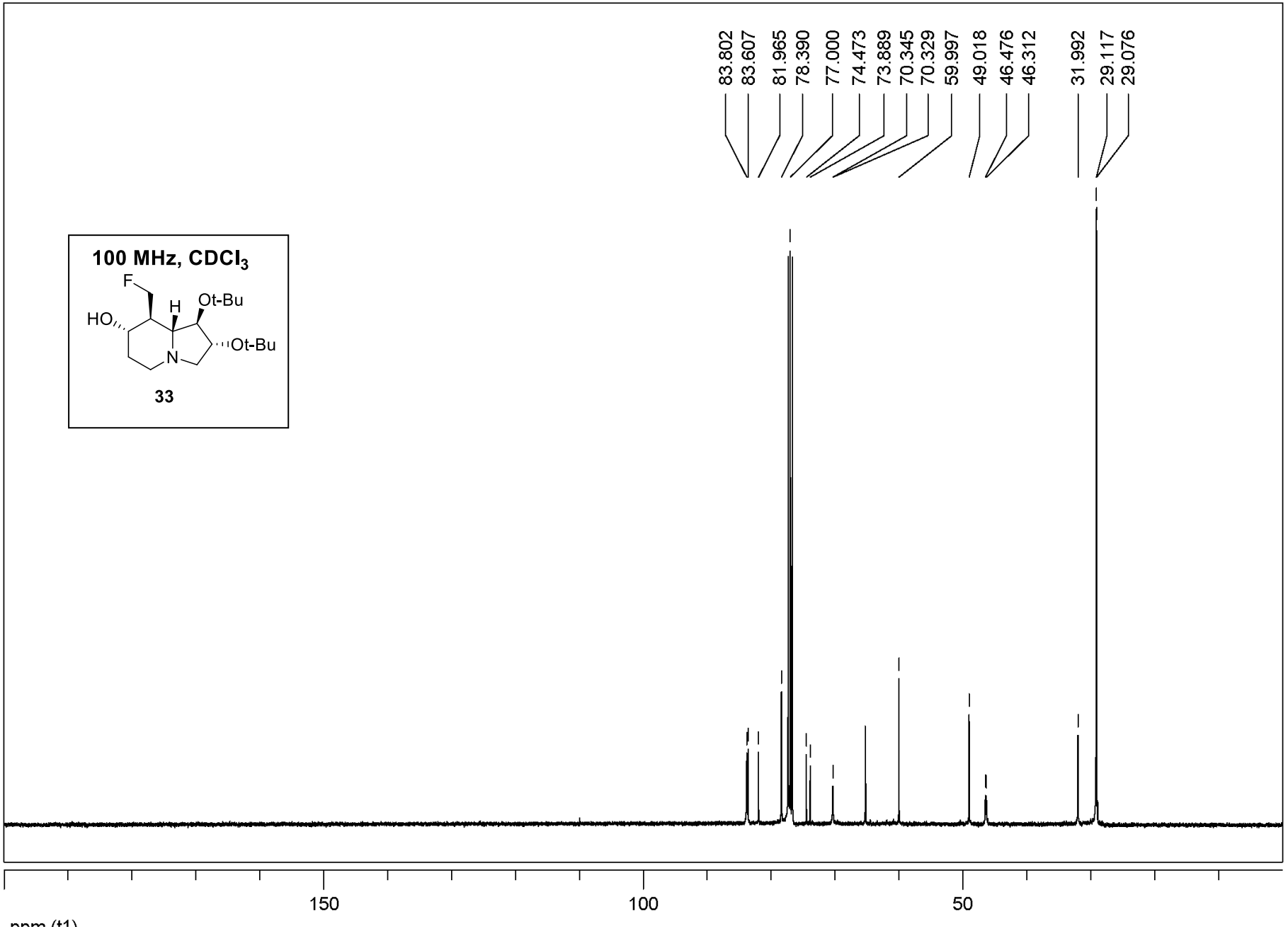

400 MHz, CD3OD
H
O
OH
H
HO
N
31
1.00
0.98
1.02
1.11
2.10
2.14
1.10
1.09
1.43
1.13
5.0
ppm (t1)

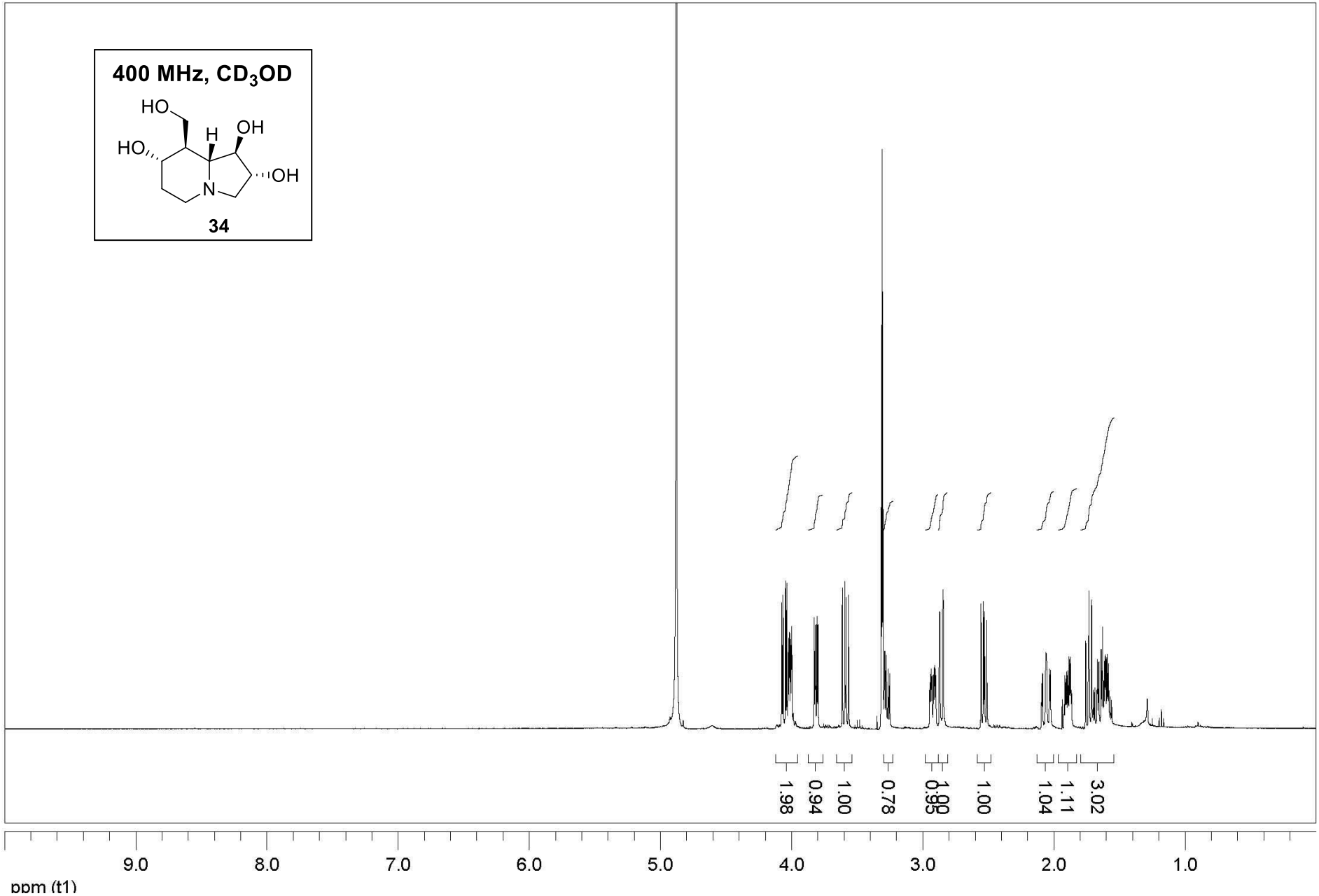

79.670
77.290
71.346
64.810
59.485
51.102
49.689
49.476
49.263
49.050
48.837
48.624
48.411
47.199
40.781
24.270
100 MHz, CD3OD
H
O
OH
H
HO
N
31
200
150
100
50
0

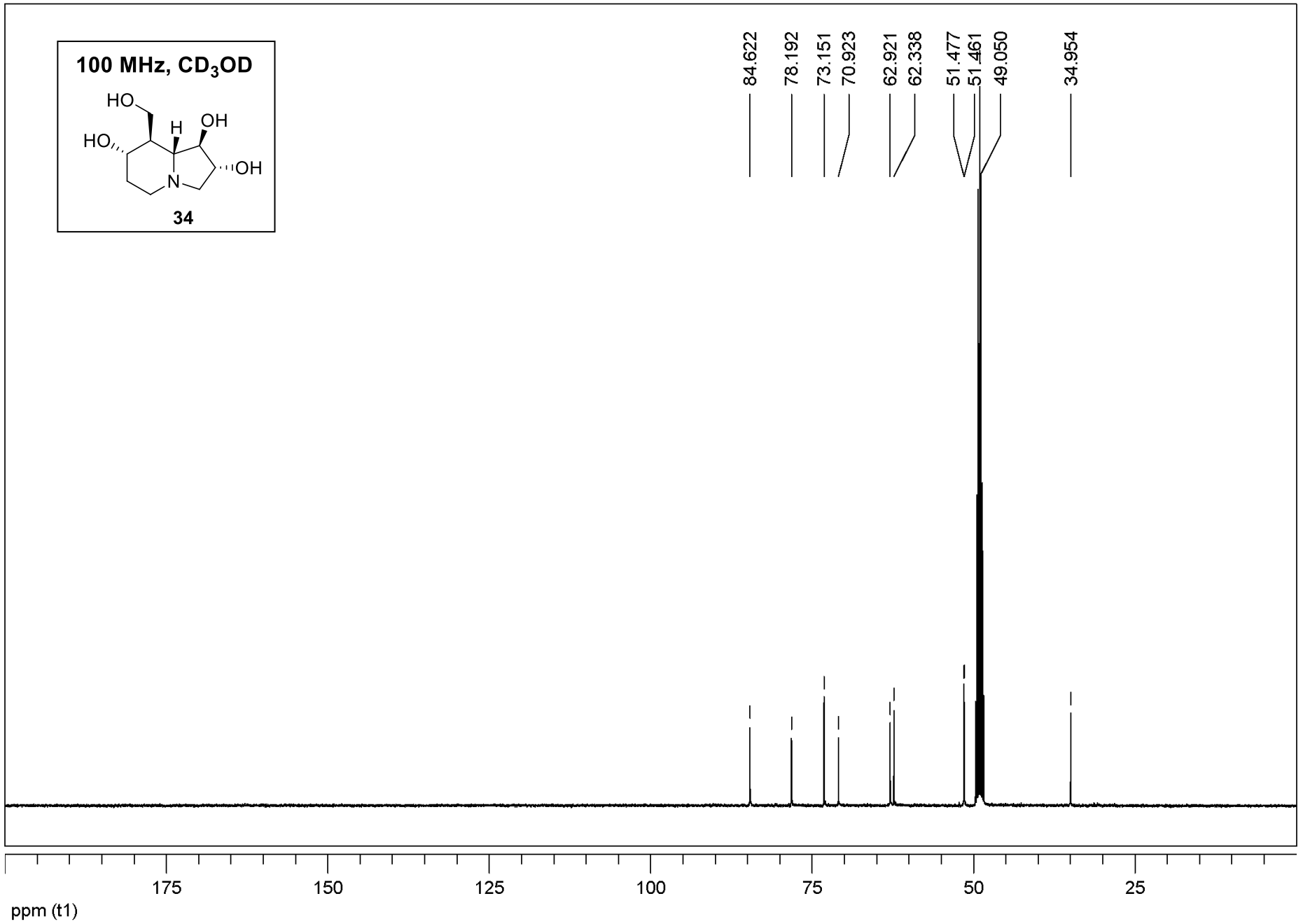

400 MHz, CDCl3
HO
H
Ot-Bu
HO
Ot-Bu
N
32
1.00
0.94
0.94
1.00
1.02
1.05
1.08
1.29
4.05
2.42
4.00
3.50
3.00
2.50
2.00
ppm (t1)
1.00
0.94
0.94
1.00
1.02
1.05
1.08
1.29
4.05
2.42
8.10
8.33
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

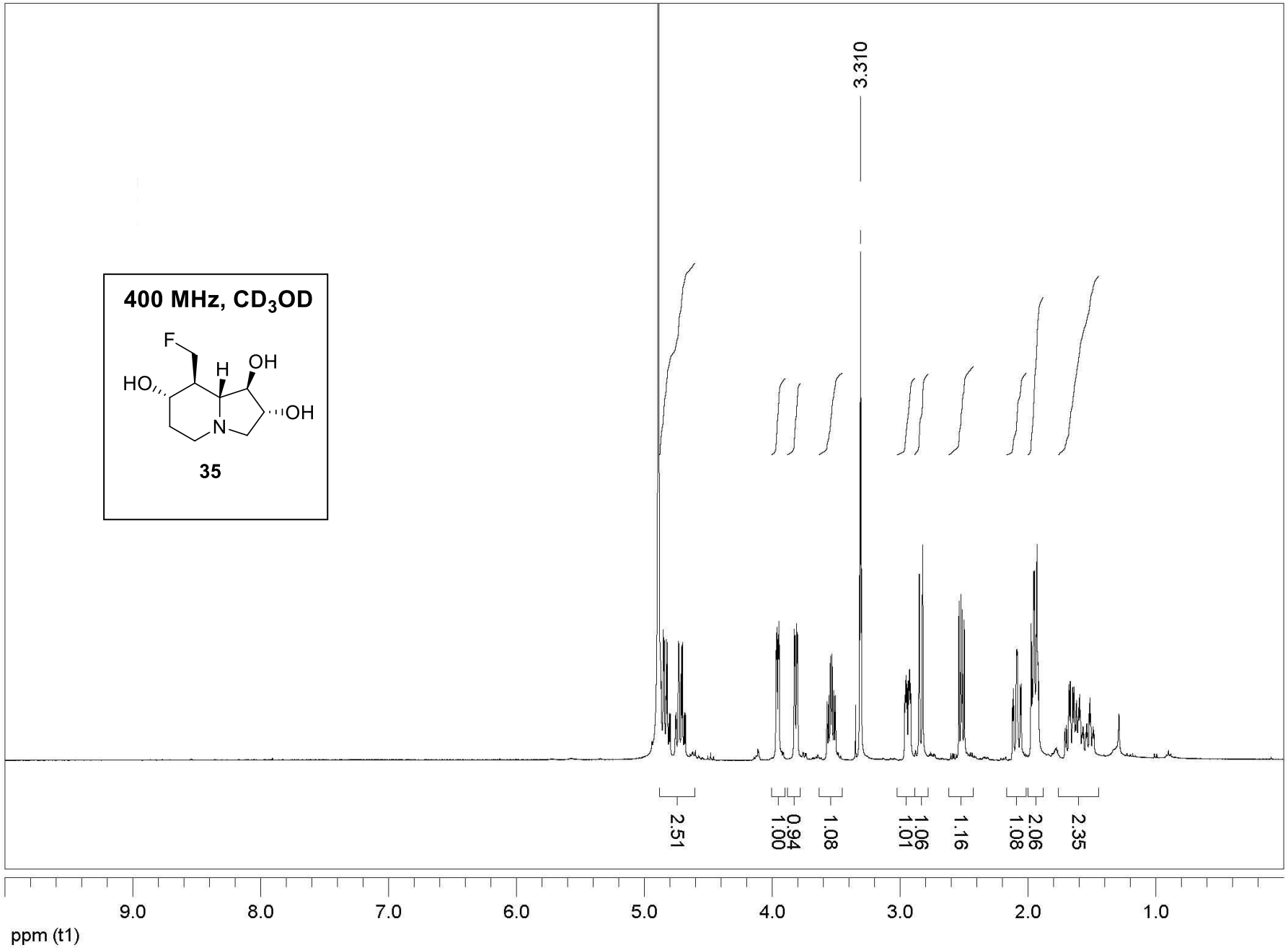

84.000
78.108
77.318
77.000
76.682
74.970
73.977
71.615
66.626
61.398
60.736
50.332
48.090
33.022
29.218
29.025
100 MHz, CDCl3
HO
H
Ot-Bu
HO
Ot-Bu
N
32
175
150
125
100
75
50
25
ppm (t1)

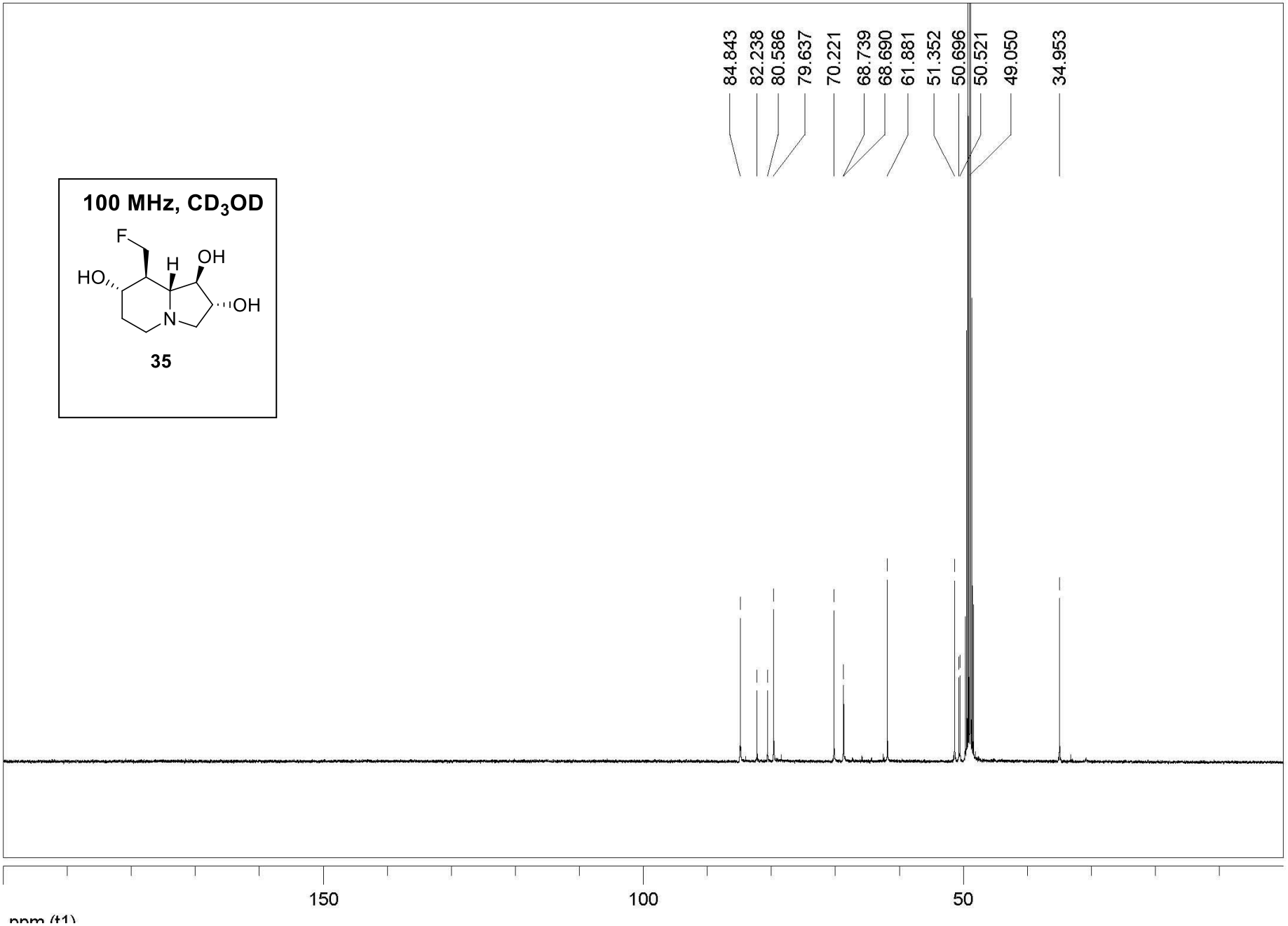

400 MHz, CDCl3
F
H
Ot-Bu
HO
Ot-Bu
N
33
1.14
1.15
1.83
1.00
1.91
1.02
3.80
3.09
5.00
4.50
4.00
3.50
3.00
2.50
2.00
ppm (t1)
1.14
1.15
1.83
1.00
1.91
1.02
3.80
3.09
7.93
8.30
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


83.802
83.607
81.965
78.390
77.000
74.473
73.889
70.345
70.329
59.997
49.018
46.476
46.312
31.992
29.117
29.076
100 MHz, CDCl3
F
H
Ot-Bu
HO
Ot-Bu
N
33
150
100
50
ppm (t1)


400 MHz, CD3OD
HO
H
OH
HO
OH
N
34
1.98
0.94
1.00
0.78
0.95
1.00
1.04
1.11
3.02
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


100 MHz, CD3OD
HO
H
OH
HO
OH
N
34
84.622
78.192
73.151
70.923
62.921
62.338
51.477
51.461
49.050
34.954
175
150
125
100
75
50
25
ppm (t1)


400 MHz, CD3OD
F
H
OH
HO
OH
N
35
3.310
2.51
1.00
0.94
1.08
1.01
1.06
1.16
1.08
2.06
2.35
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


84.843
82.238
80.586
79.637
70.221
68.739
68.690
61.881
51.352
50.696
50.521
49.050
34.953
100 MHz, CD3OD
F
H
OH
HO
OH
N
35
150
100
50
ppm (t1)