SUPPORTING INFORMATION FOR:

A Chemoenzymatic Total Synthesis of (+)-Clividine

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Oxalate salt of C11b-epi-ent-***1***.* $C_{17}H_{20}NO_5^+ \bullet C_2HO_4^-$, M = 407.38, T = 200 K, monoclinic, space group $P2_1$, Z = 2, a = 7.8532(4), b = 7.8328(4), c = 15.1100(8) Å, β = 93.534(3)°, V = 927.69(8) Å^3, D_x = 1.458 g cm^{-3}, 1761 unique data (θ = 2.7–25°), R = 0.035 [for 1629 with $I > 2.0\sigma(I)$]; Rw = 0.086 (all data), S = 1.03.

Picrate salt of ent-***1***. $2(C_{17}H_{20}NO_5^+) \bullet 2(C_6H_2N_3O_7^-) \bullet 7.87H_2O \bullet 0.315CH_3CN$, M = 1247.6, T = 200 K, monoclinic, space group $P2_1$, Z = 2, a = 8.6590(2), b = 35.4747(9), c = 9.0925(2) Å, β = 101.1071(12)°, V = 2740.68(11) Å^3, D_x = 1.512 g cm^{-3}, 4933 unique data (θ = 2.6–25.1°), R = 0.050 [for 3901 with $I > 2.0\sigma(I)$]; Rw = 0.110 (all data), S = 1.02.

Compound ***6***. $C_{11}H_{14}BrNO_3$, M = 288.14, T = 200 K, monoclinic, space group $P2_1$, Z = 2, a = 10.0349(3), b = 5.8790(1), c = 11.4499(3) Å, β = 113.6267(15)°, V = 618.87(3) Å^3, D_x = 1.546 g cm^{-3}, 2718 unique data (θ = 2.6–27.5°), R = 0.025 [for 2619 with $I > 2.0\sigma(I)$]; Rw = 0.065 (all data), S = 1.01, Flack parameter = –0.015(7).

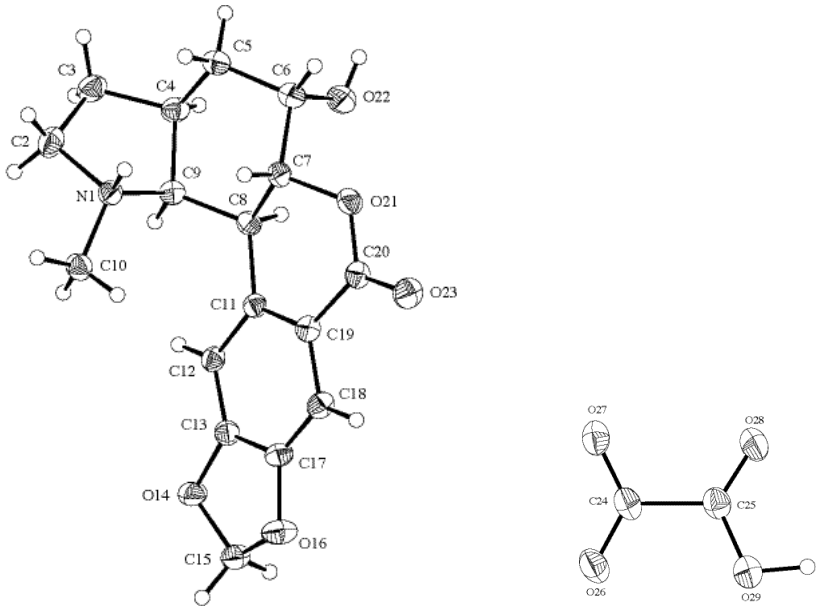
Compound ***10***. $C_{20}H_{21}NO_6$, M = 371.39, T = 200 K, orthorhombic, space group $P2_12_12_1$, Z = 4, a = 9.7236(2), b = 13.2103(2), c = 14.0965(2) Å, V = 1810.72(6) Å^3, D_x = 1.362 g cm^{-3}, 2977 unique data (θ = 2.6–30°), R = 0.034 [for 2703 with $I > 2.0\sigma(I)$]; Rw = 0.087, S = 1.00.

Compound ***15***. $C_{17}H_{19}NO_5$, M = 317.34, T = 200 K, monoclinic, space group $P2_1$, Z = 2, a = 8.6115(8), b = 7.9108(8), c = 11.2630(12) Å, β = 105.651(6)°, V = 738.83(13) Å^3, D_x = 1.426 g cm^{-3}, 1411 unique data (θ = 2.7–25.1°), R = 0.081 [for 1103 with $I > 2.0\sigma(I)$]; Rw = 0.236 (all data), S = 1.02.

Structure Determination

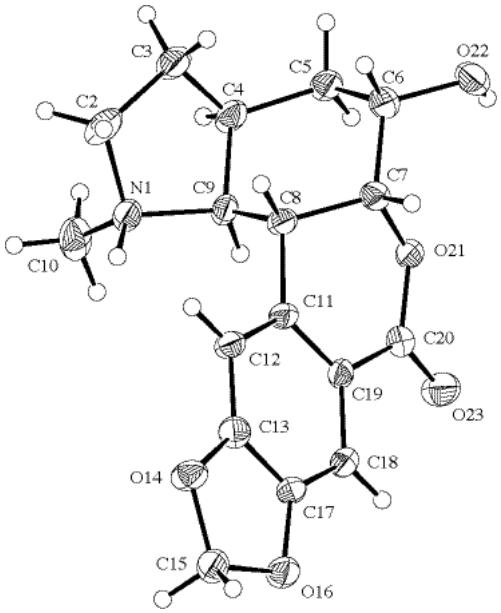
Images were measured on a Nonius Kappa CCD diffractometer (MoKα, graphite monochromator, λ = 0.71073 Å) and data extracted using the DENZO package.[1] Structure solution was by direct methods (SIR92).[2] The structures of the abovementioned compounds were refined using the CRYSTALS program package.[3] Atomic coordinates, bond lengths and angles, and displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC nos. 813598–813602 for the oxalate salt of compound C11b-*epi*-*ent*-**1**, the picrate salt of compound *ent*-**1** and compounds **6**, **10** and **15**, respectively). These data can be obtained free-of-charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

Anisotropic Displacement Ellipsoid Plots

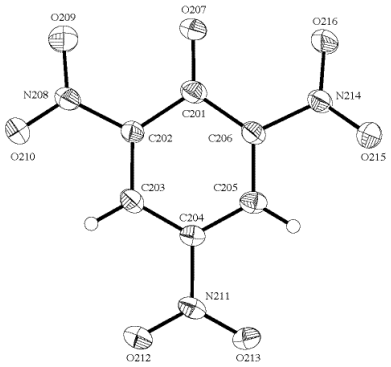


a **b**

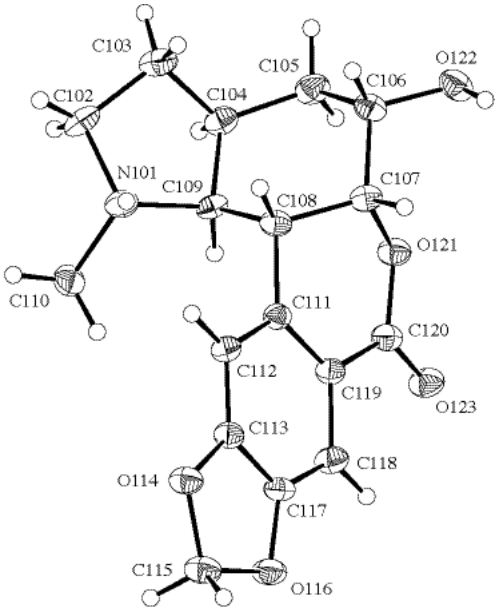
Figure S1. Structure of the oxalate salt of C11b-*epi*-*ent*-**1** (CCDC 813598, **a** = $C_{17}H_{20}NO_5^+$ cation, **b** = $C_2HO_4^-$ anion) with labelling of selected atoms. Anisotropic displacement ellipsoids display 30% probability levels. Hydrogen atoms are drawn as circles with small radii.



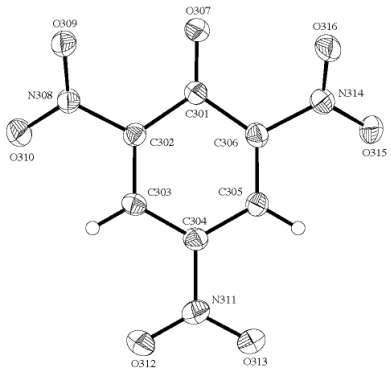
a



b



c



d

Figure S2. Structure of the picrate salt of *ent*-**1** (CCDC 813599, **a** = $C_{17}H_{20}NO_5^+$ cation one, **b** = $C_6H_2N_3O_7^-$ anion one, **c** = $C_{17}H_{20}NO_5^+$ cation two, **d** = $C_6H_2N_3O_7^-$ anion two) with labelling of selected atoms. Anisotropic displacement ellipsoids display 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

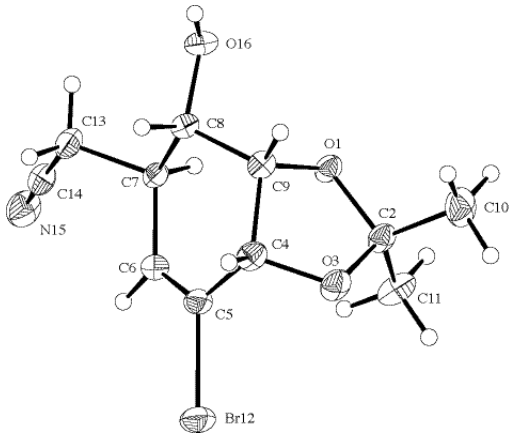
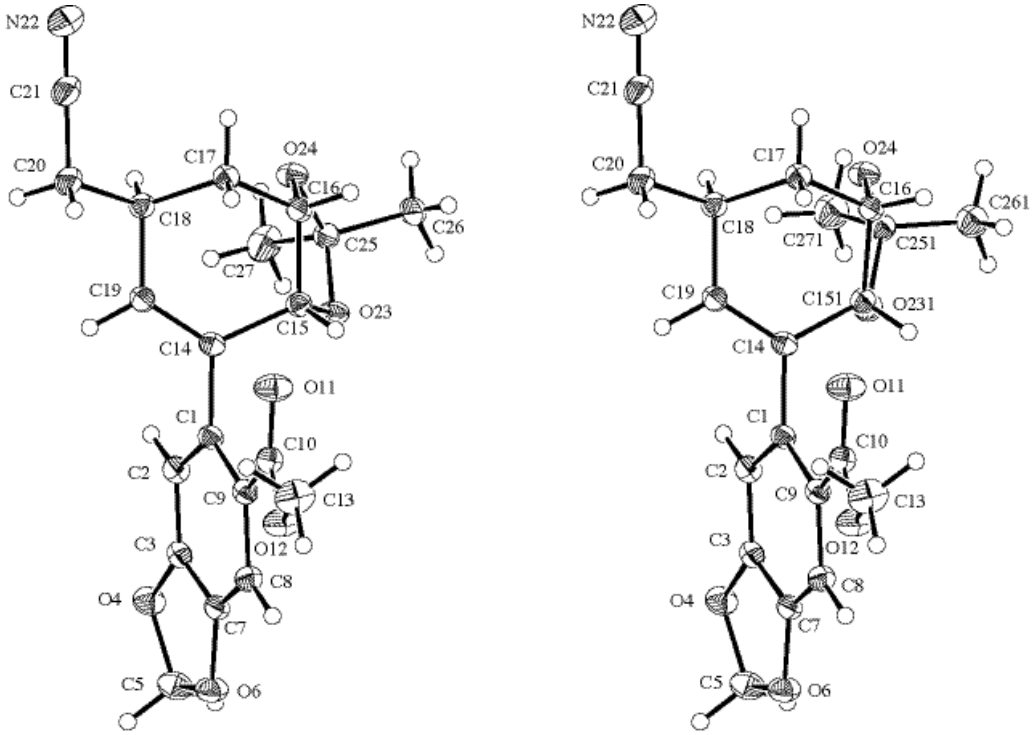


Figure S3. Structure of compound **6** (CCDC 813600, $C_{11}H_{14}BrNO_3$) with labelling of selected atoms. Anisotropic displacement ellipsoids display 30% probability levels. Hydrogen atoms are drawn as circles with small radii.



a **b**

Figure S4. Structure of compound **10** (CCDC 813601, **a** = $C_{20}H_{21}NO_6$ showing the major sites of the disordered atoms, **b** = $C_{20}H_{21}NO_6$ showing the minor sites of the disordered atoms) with labelling of selected atoms. Anisotropic displacement ellipsoids display 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

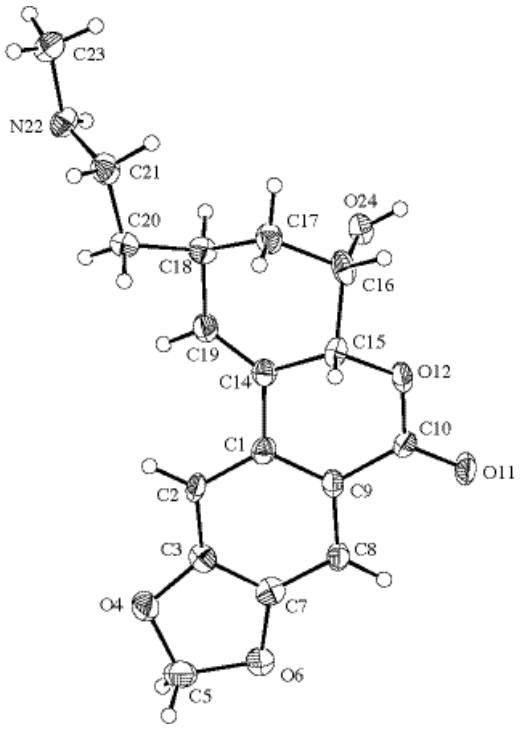


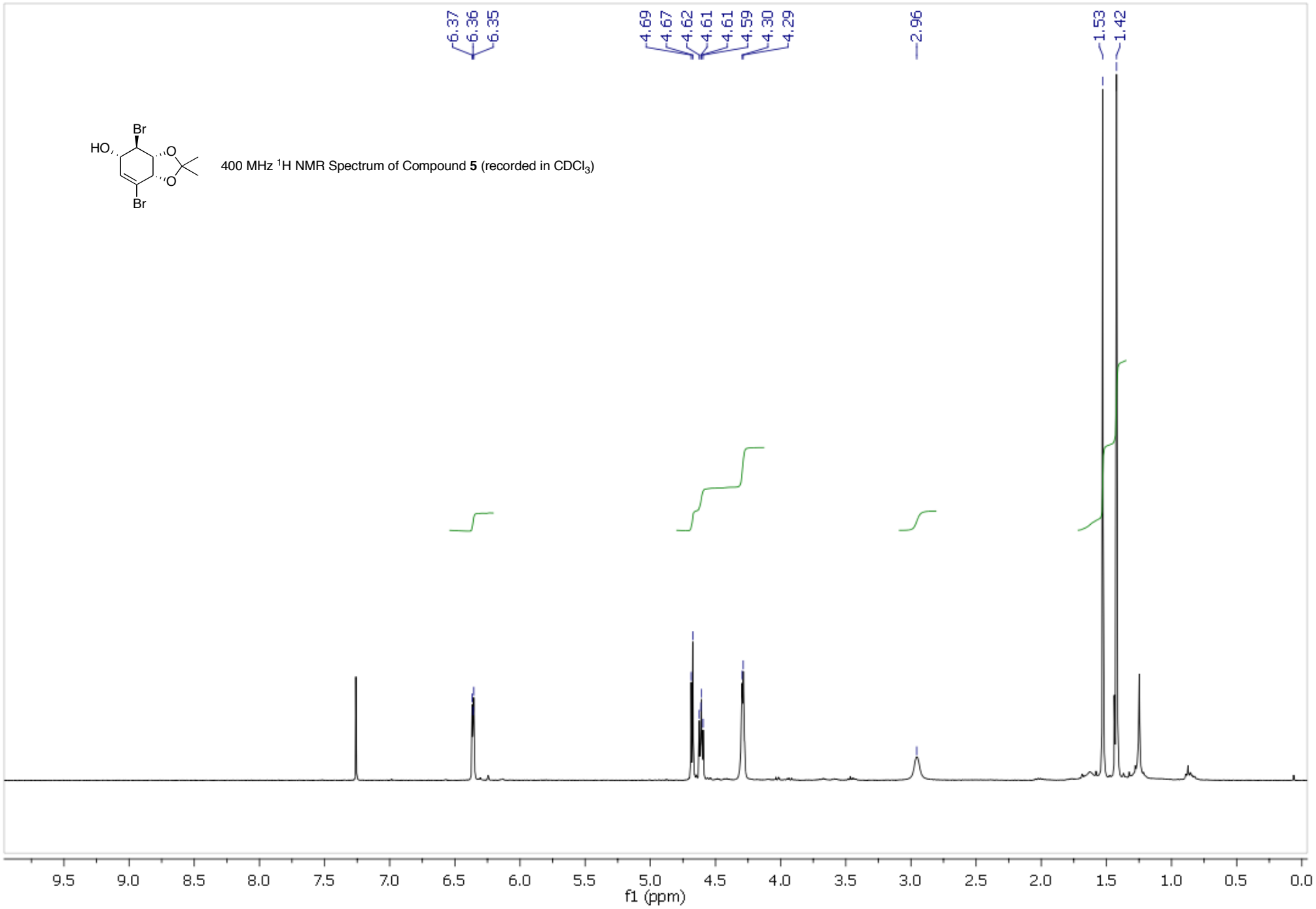
Figure S5. Structure of compound **15** (CCDC 813602, $C_{17}H_{19}NO_5$) with labelling of selected atoms. Anisotropic displacement ellipsoids display 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

References

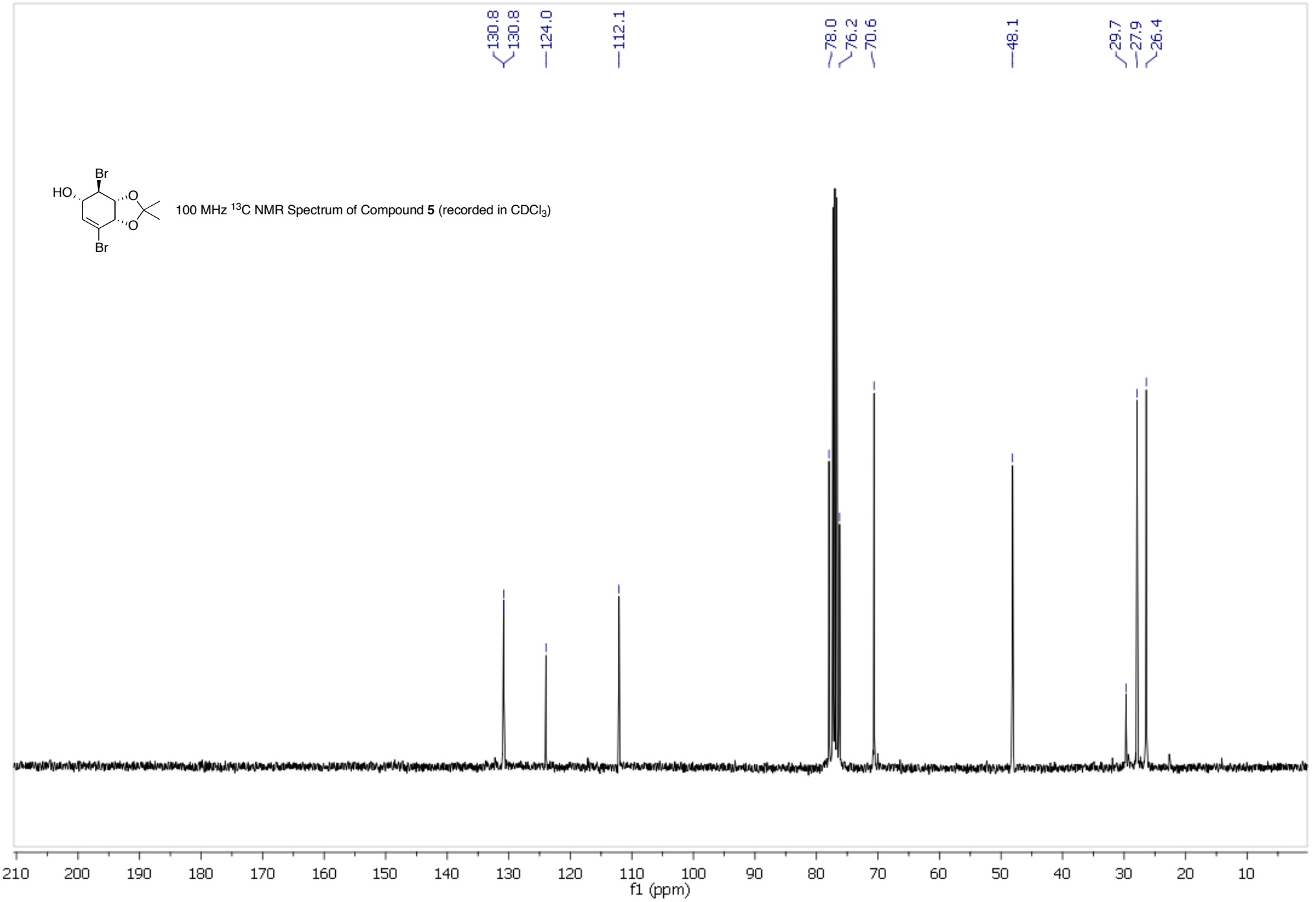
(1) DENZO–SMN. Otwinowski, Z.; Minor, W. Processing of X-ray diffraction data collected in oscillation mode. In *Methods in Enzymology, Volume 276: Macromolecular Crystallography, Part A*; Carter Jr., C. W.; Sweet, R. M., Eds.; Academic Press: New York, 1997; pp. 307–326.

(2) SIR92. Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli, M. *J. Appl. Crystallogr.*, **1994**, *27*, 435.

(3) Betteridge, P. W.; Carruthers, J. R.; Cooper, R. I.; Prout, K.; Watkin, D. J. *J. Appl. Crystallogr.*, **2003**, *36*, 1487.



400 MHz ^{1}H NMR Spectrum of Compound **5** (recorded in $CDCl_3$)



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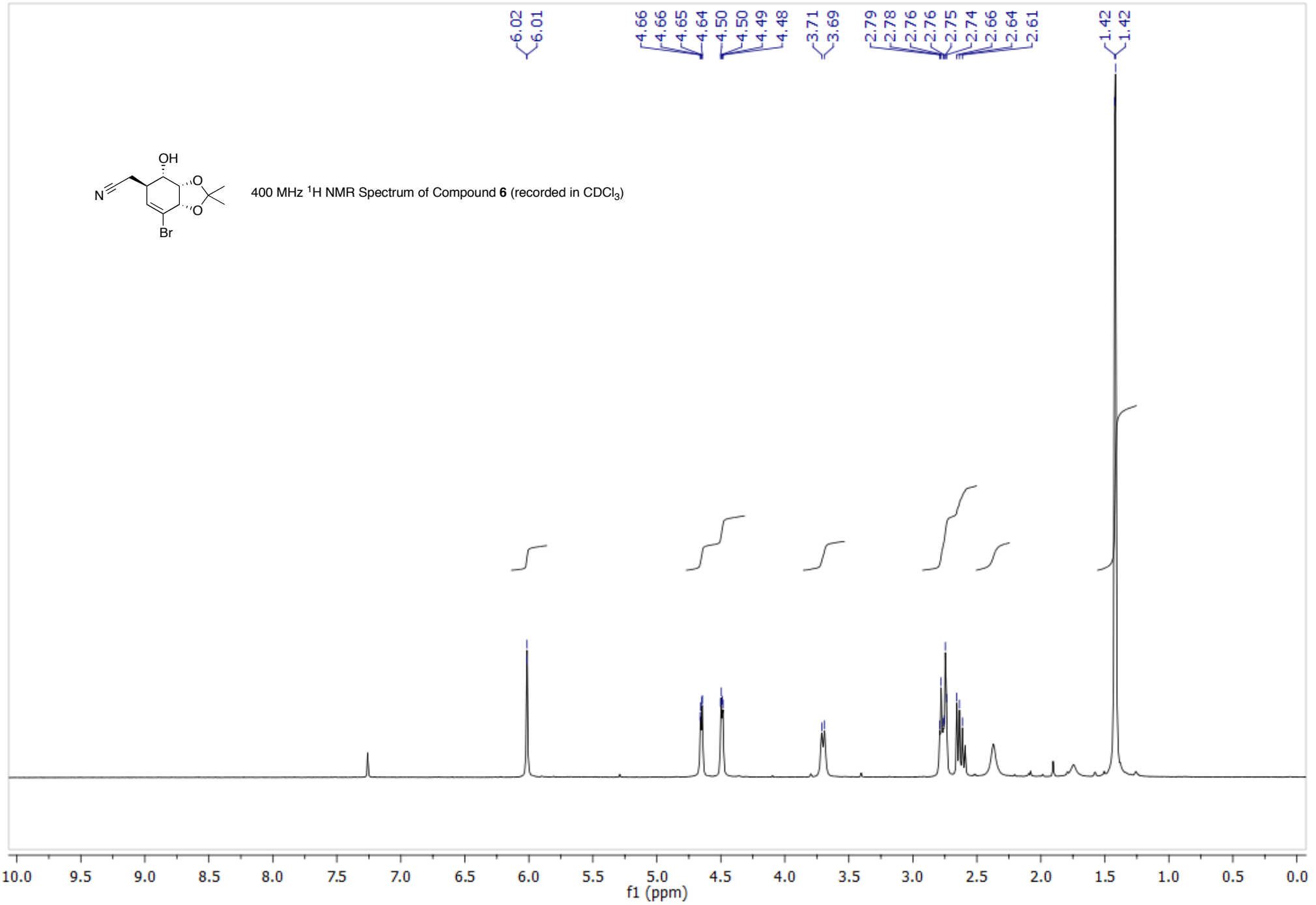

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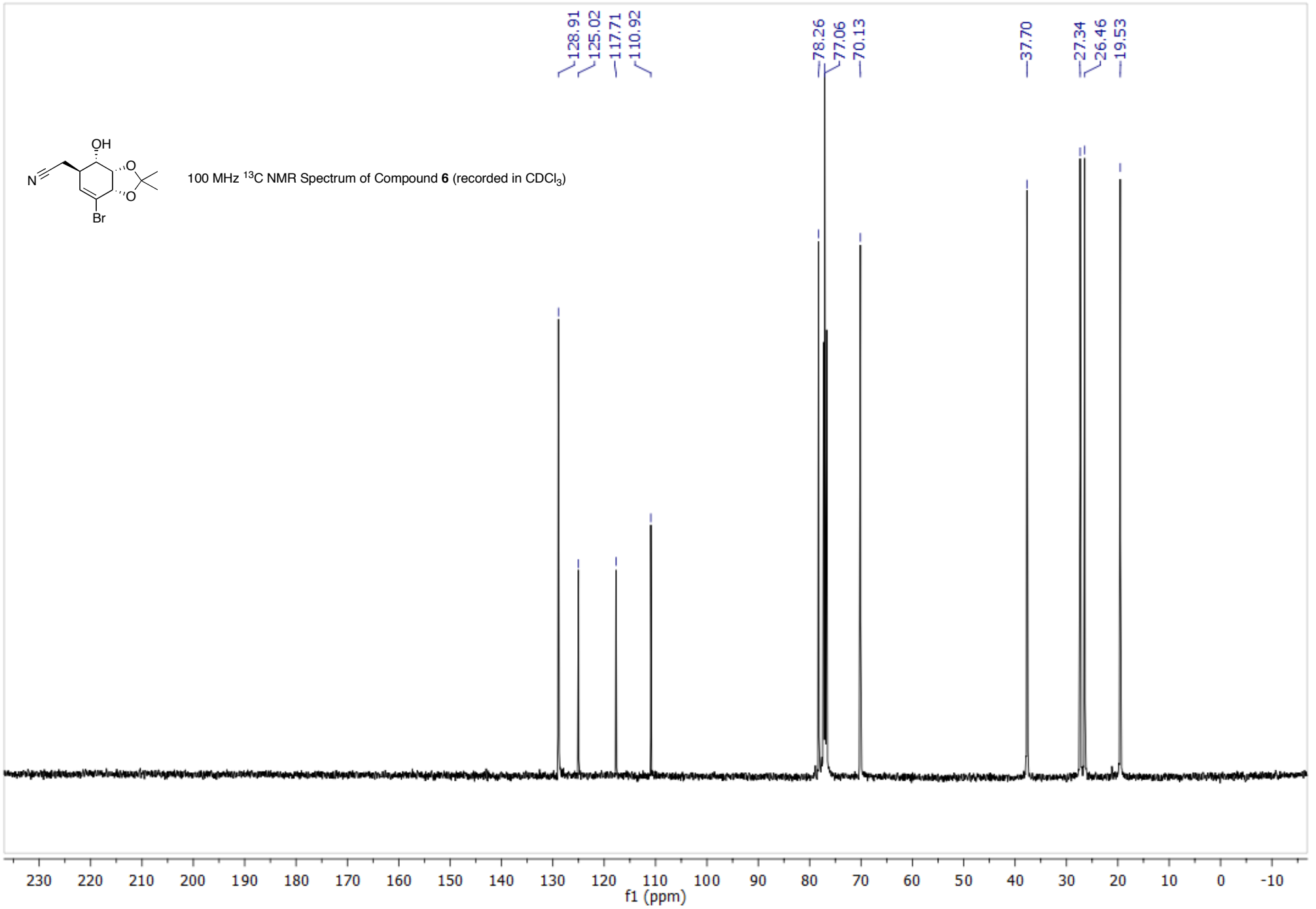

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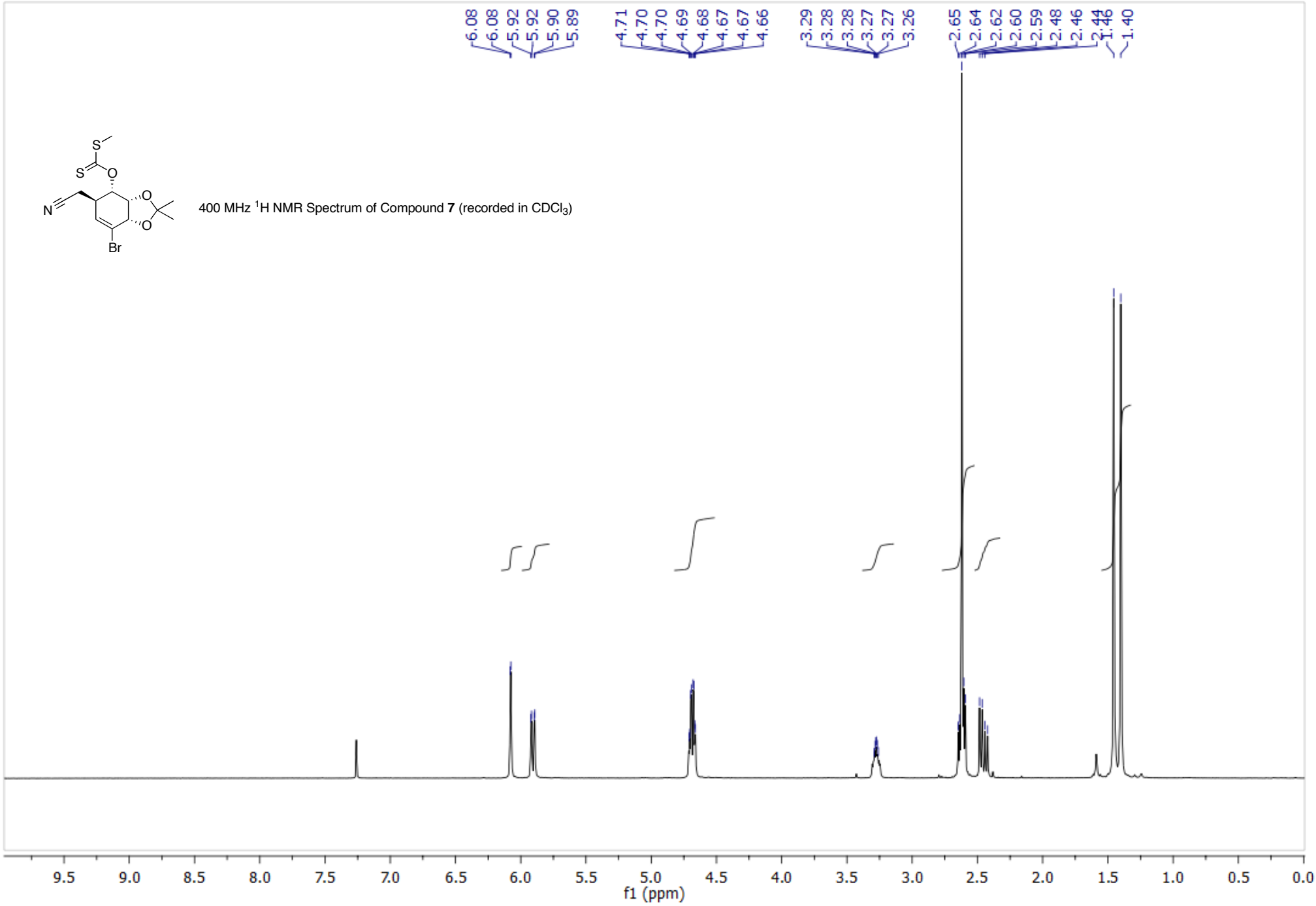

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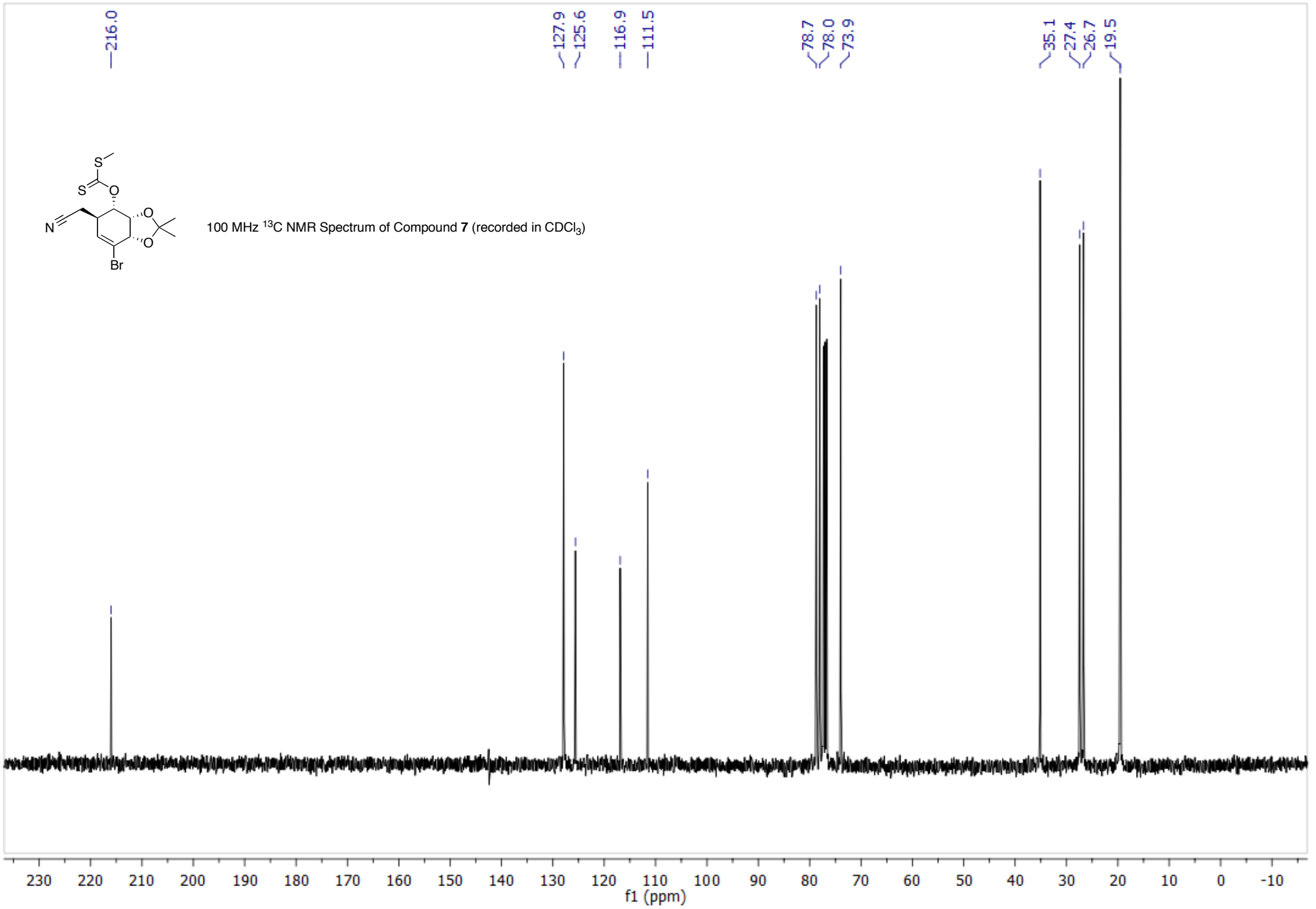
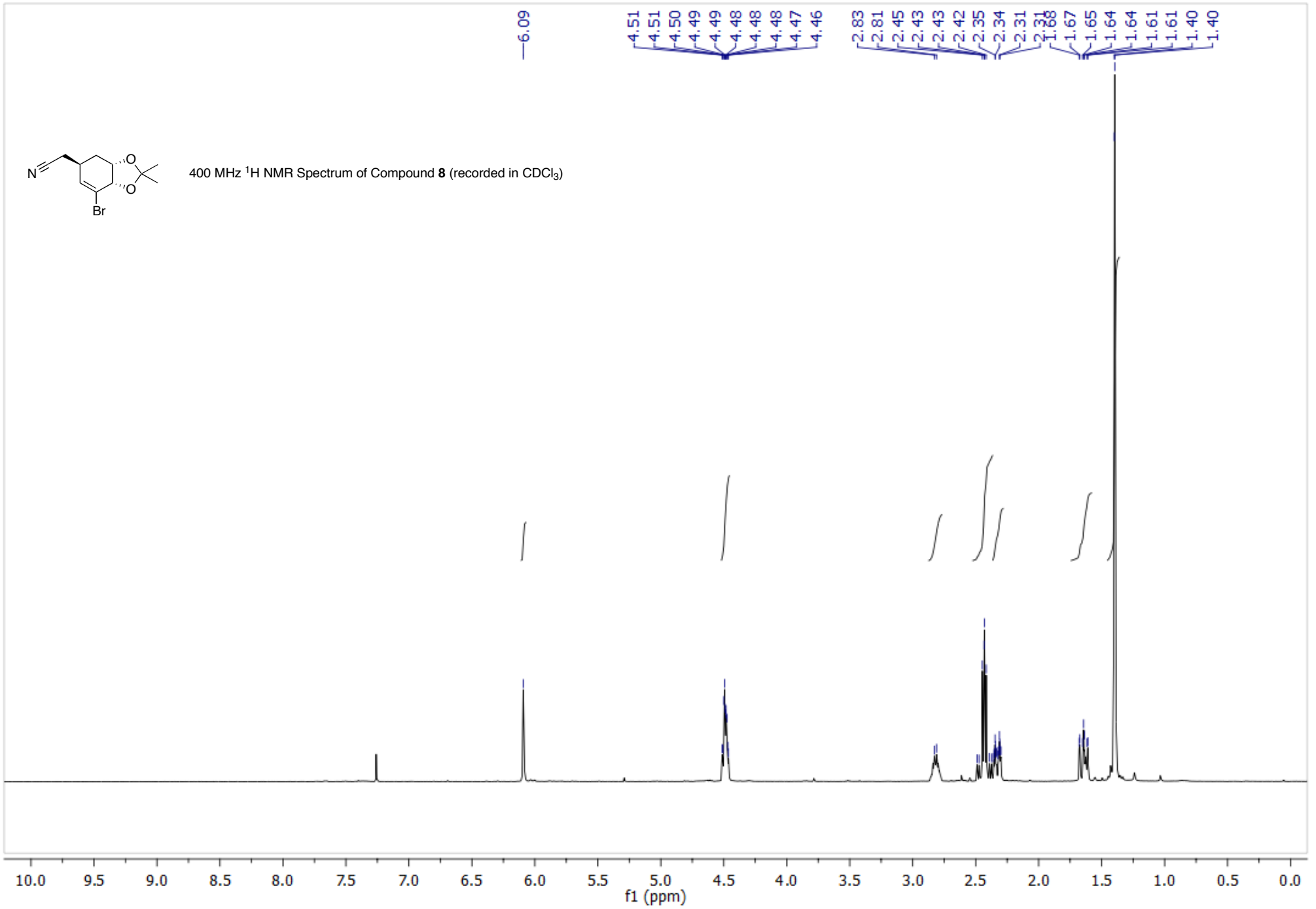
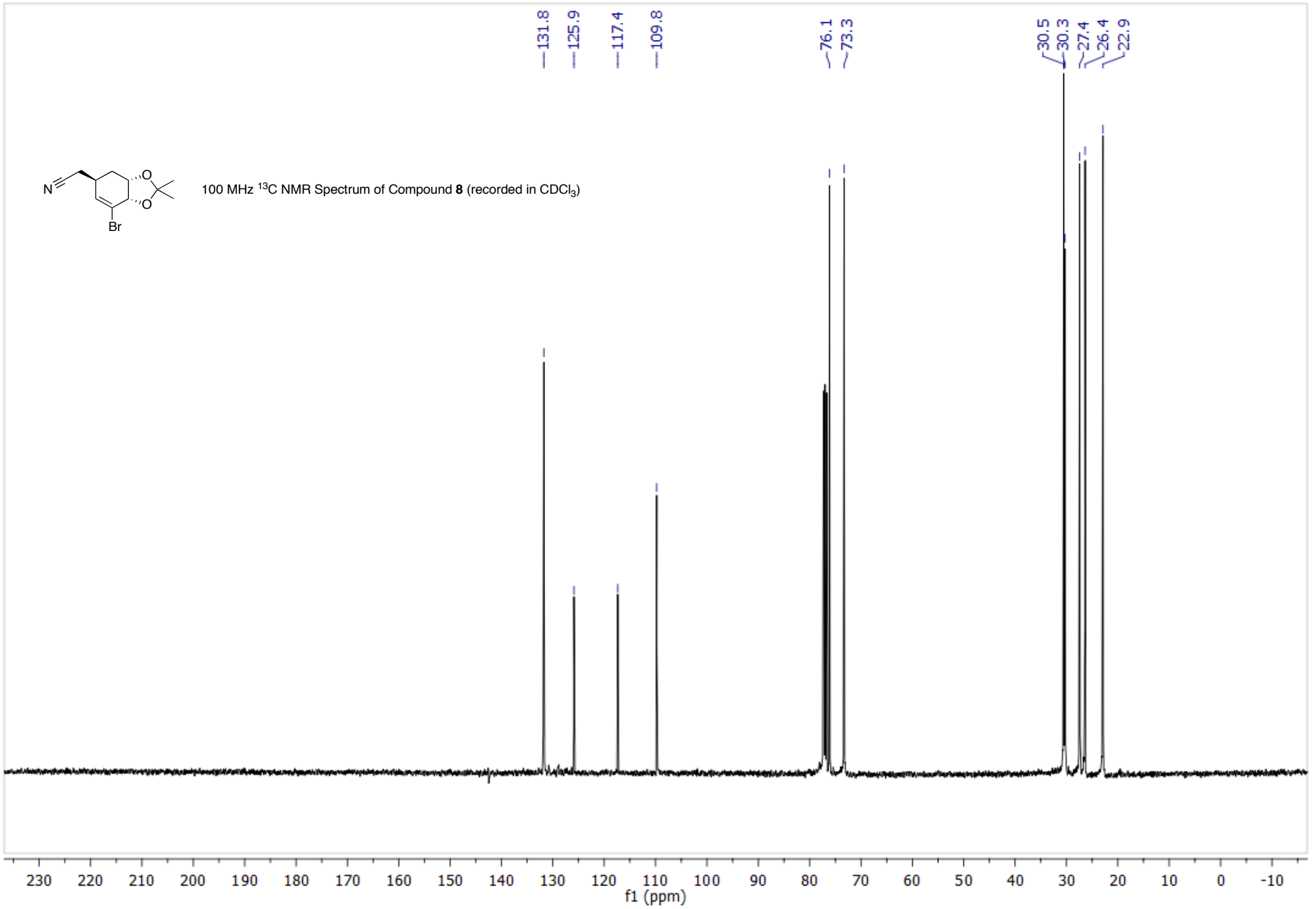
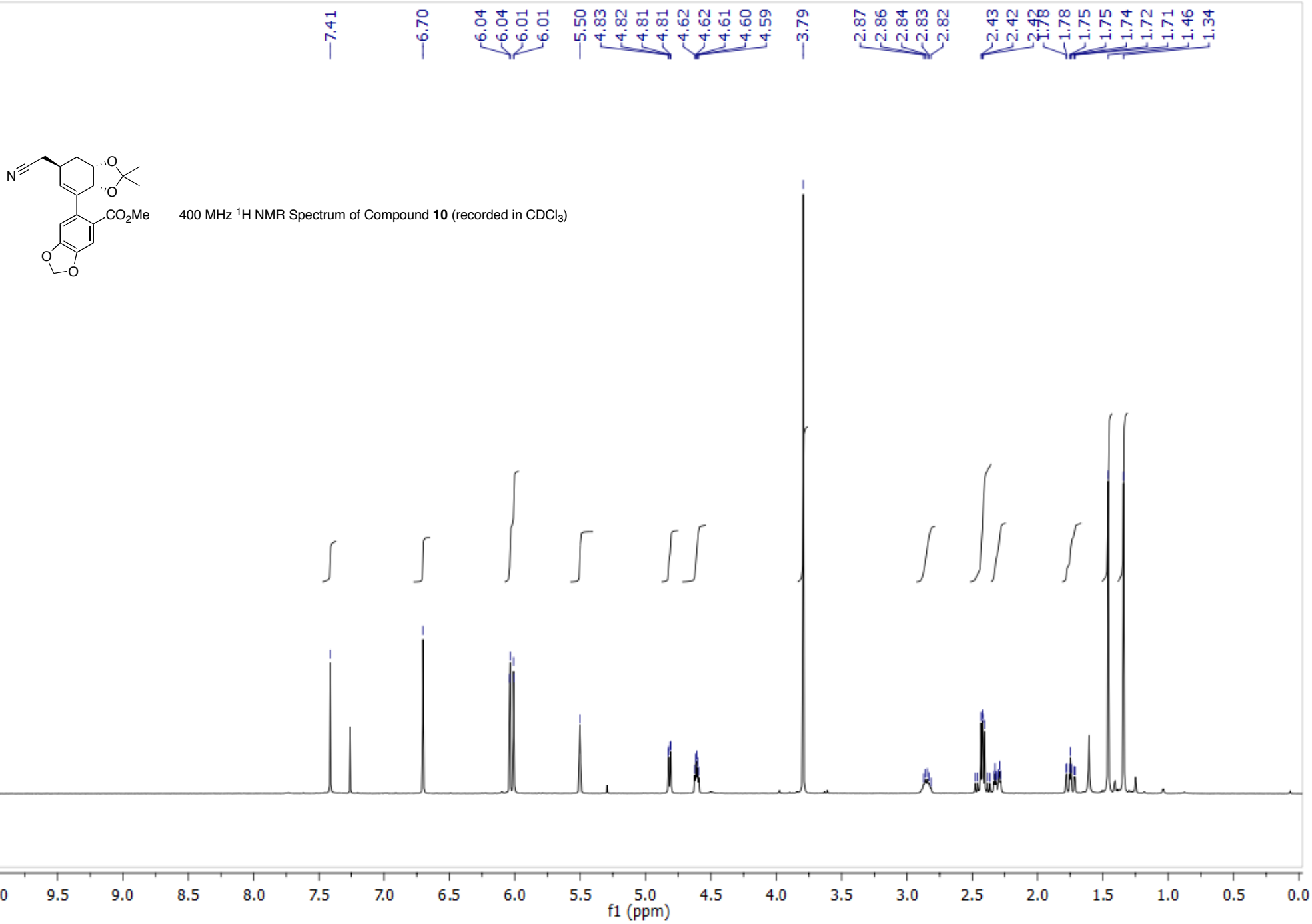


100 MHz ^{13}C NMR Spectrum of Compound **7** (recorded in $CDCl_3$)

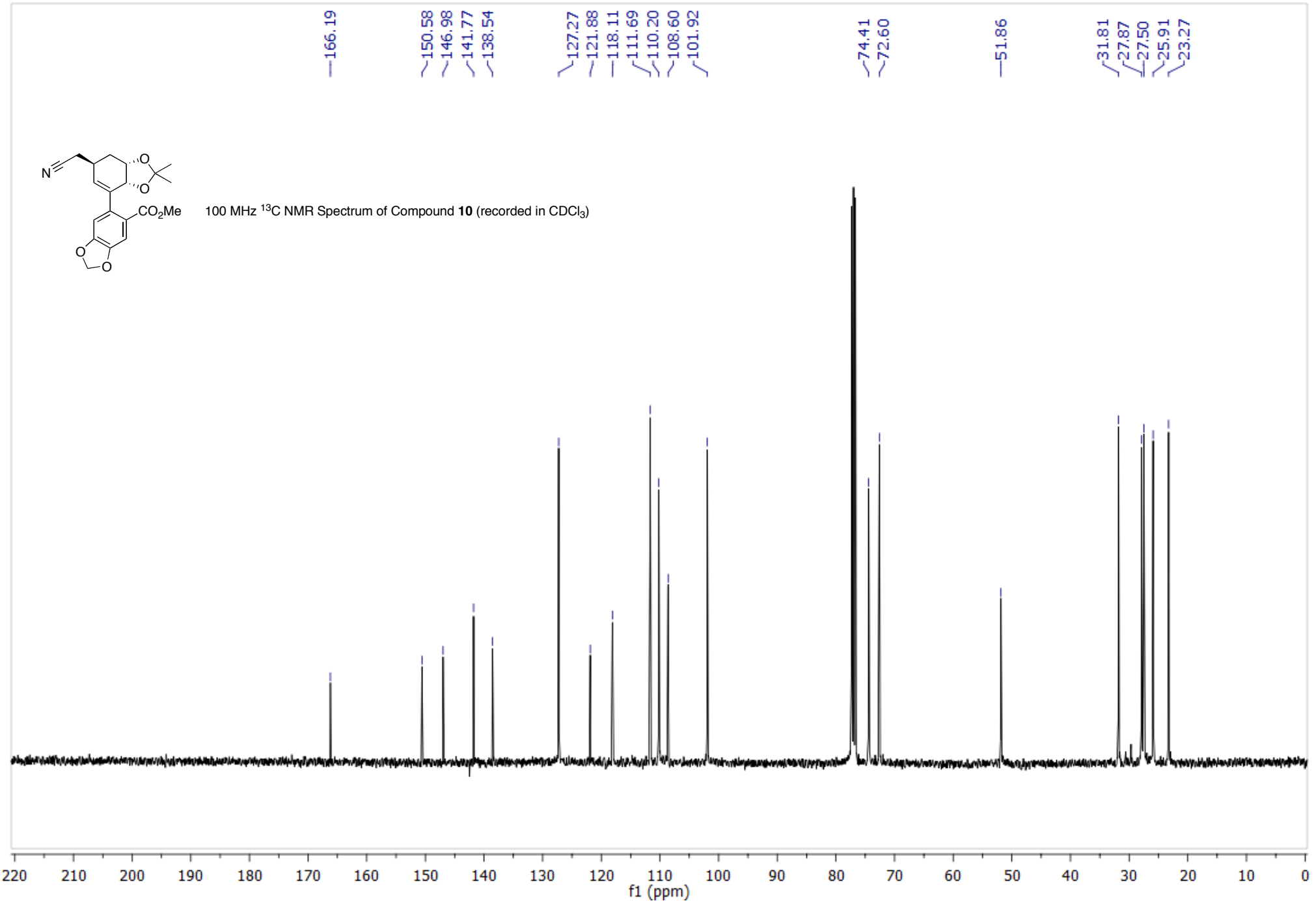

6.09
4.51
4.51
4.50
4.49
4.49
4.48
4.48
4.48
4.47
4.46
2.83
2.81
2.45
2.43
2.43
2.42
2.35
2.34
2.31
2.31
1.68
1.67
1.65
1.64
1.64
1.61
1.61
1.40
1.40
N
O
O
Br
400 MHz ^{1}H NMR Spectrum of Compound **8** (recorded in $CDCl_3$)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



100 MHz ^{13}C NMR Spectrum of Compound **8** (recorded in $CDCl_3$)



400 MHz ^{1}H NMR Spectrum of Compound **10** (recorded in $CDCl_3$)



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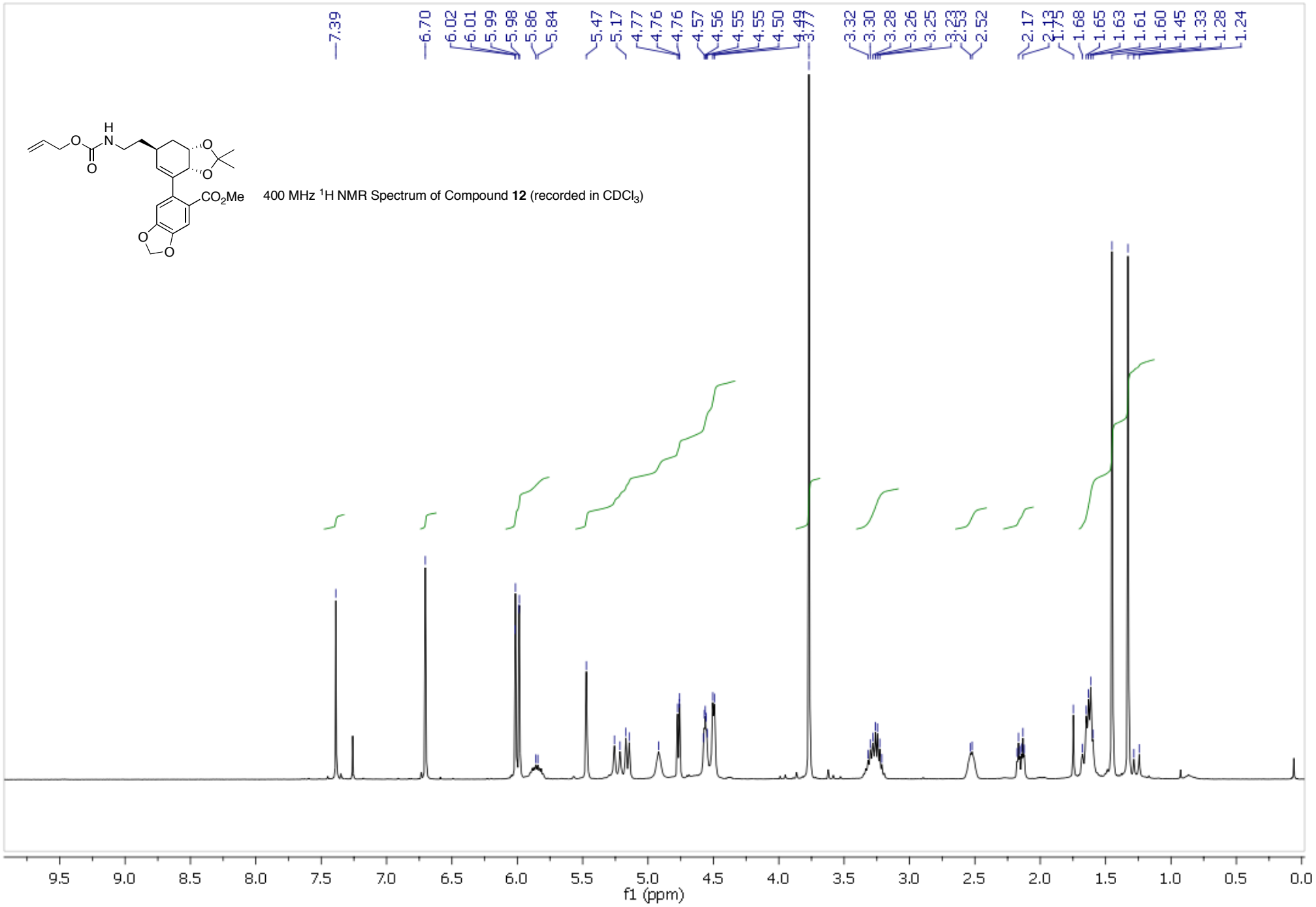
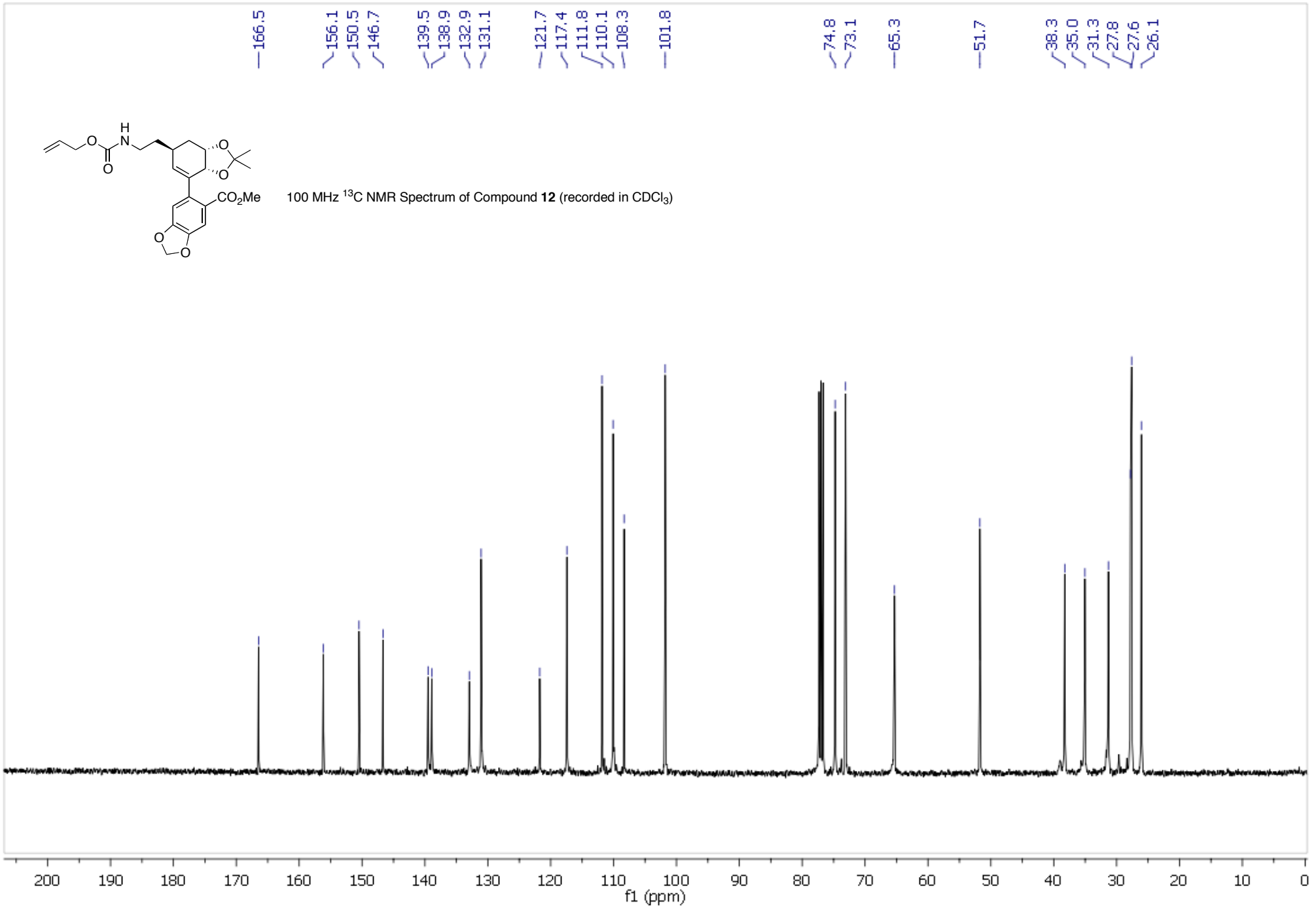
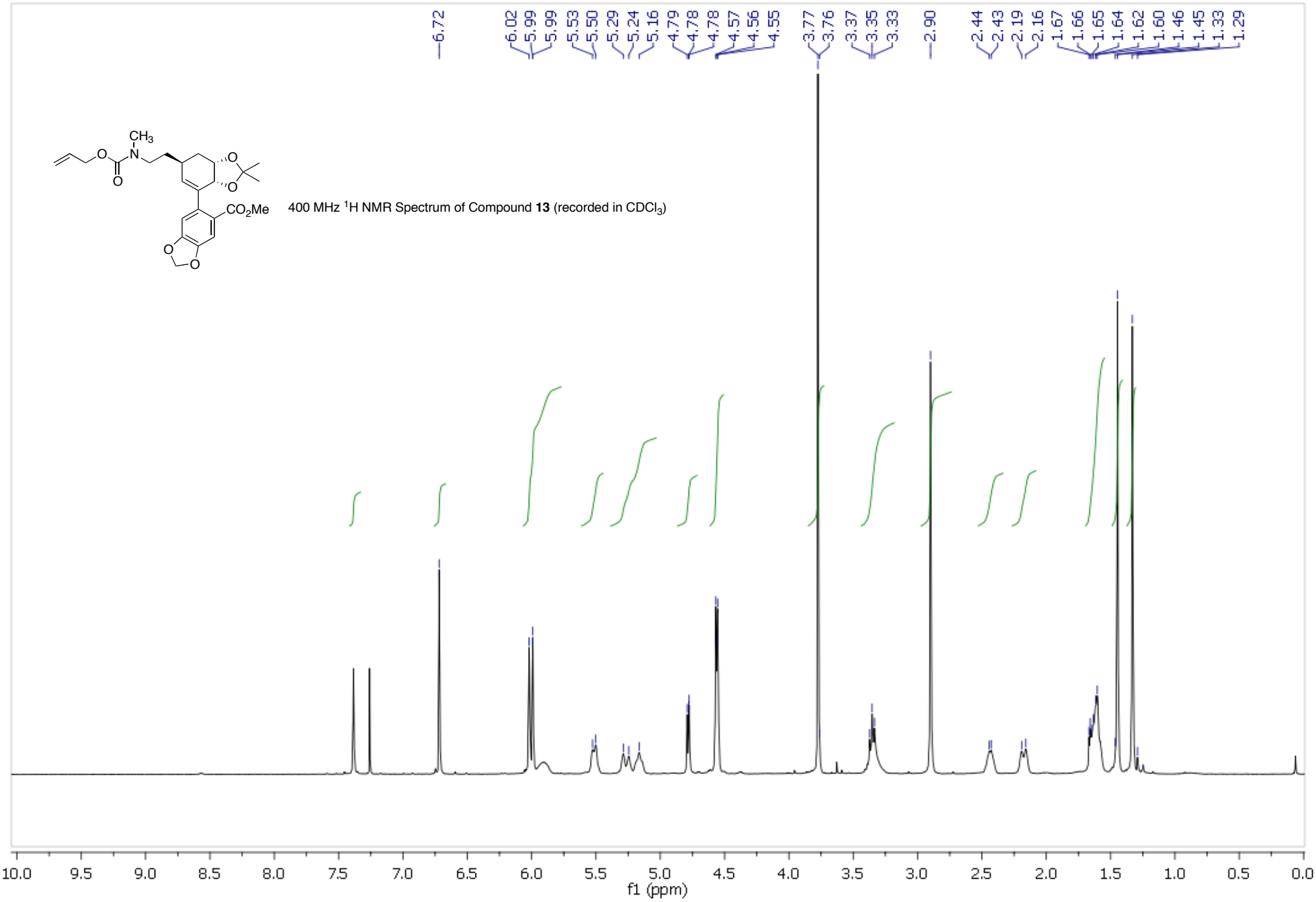


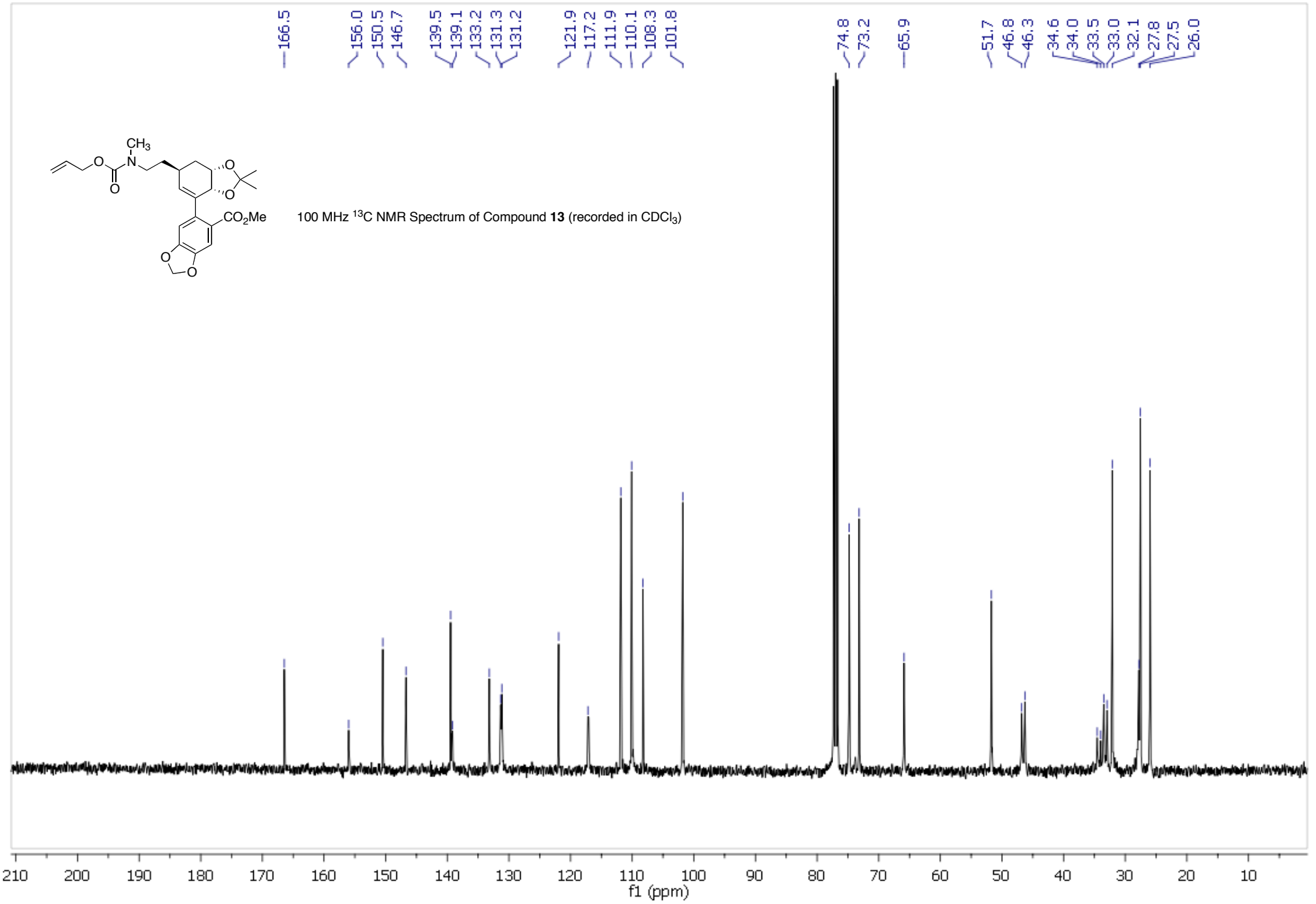
400 MHz ^{1}H NMR Spectrum of Compound **12** (recorded in $CDCl_3$)



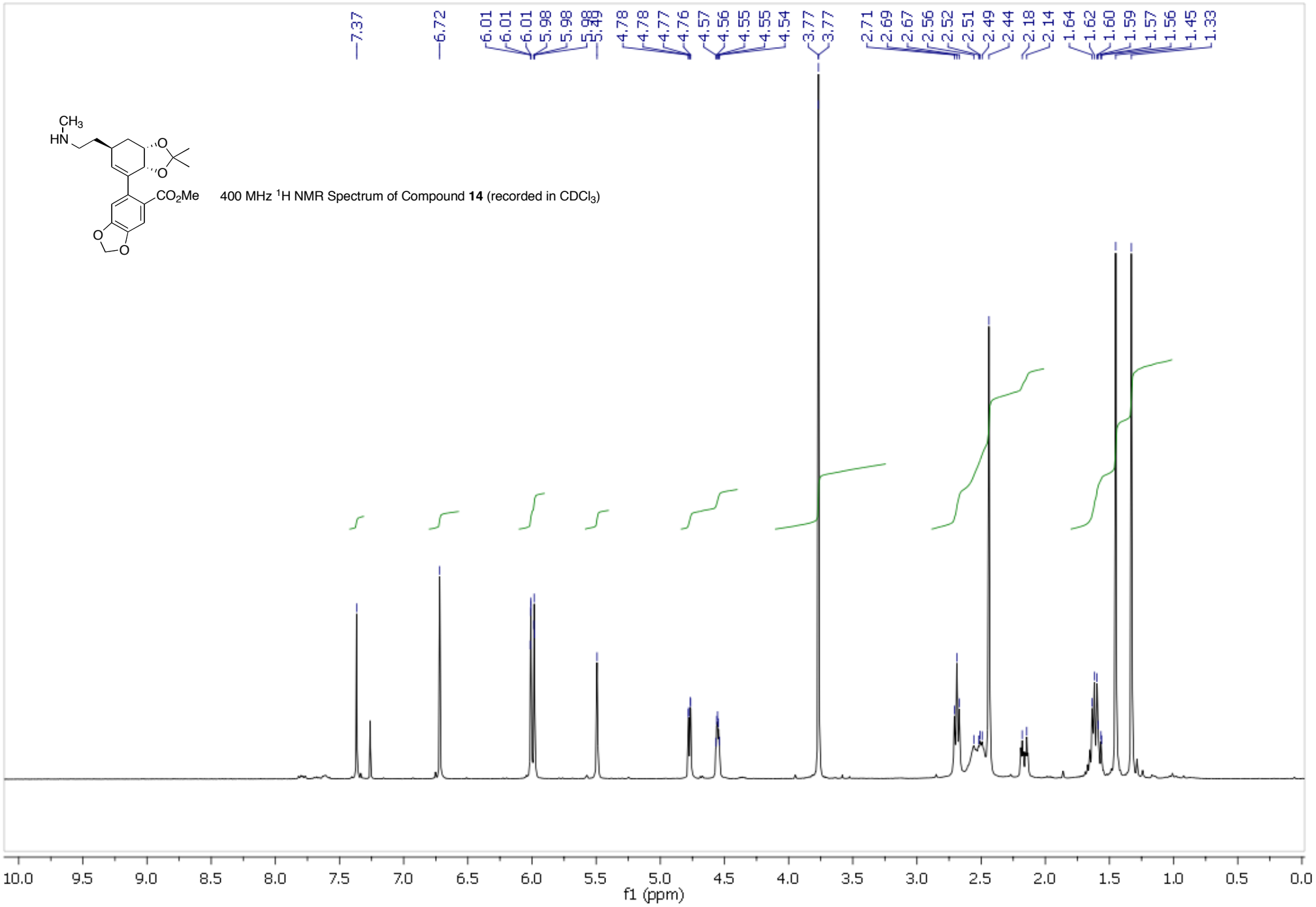
100 MHz ^{13}C NMR Spectrum of Compound **12** (recorded in $CDCl_3$)



400 MHz ^{1}H NMR Spectrum of Compound **13** (recorded in $CDCl_3$)



100 MHz ^{13}C NMR Spectrum of Compound **13** (recorded in $CDCl_3$)



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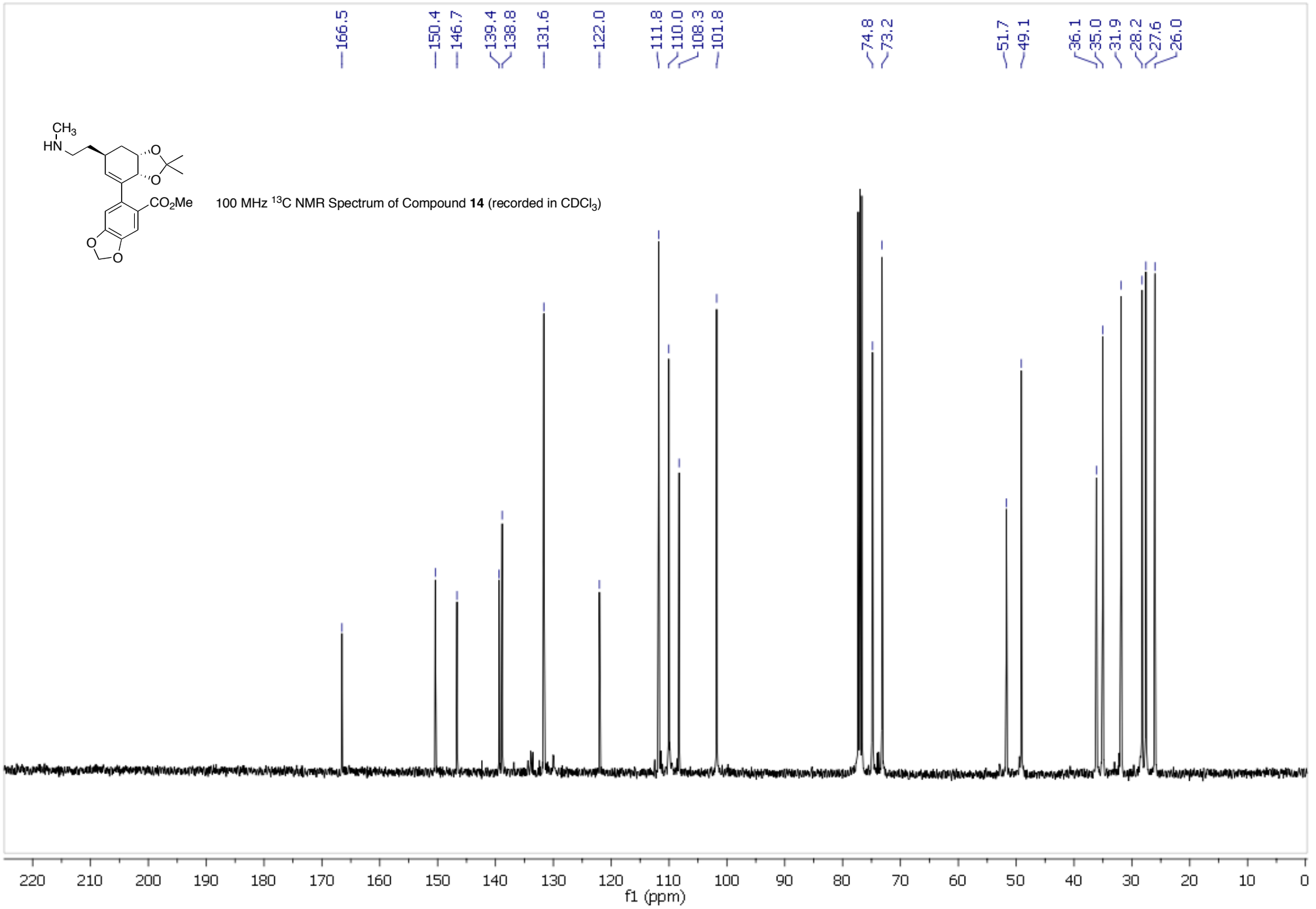
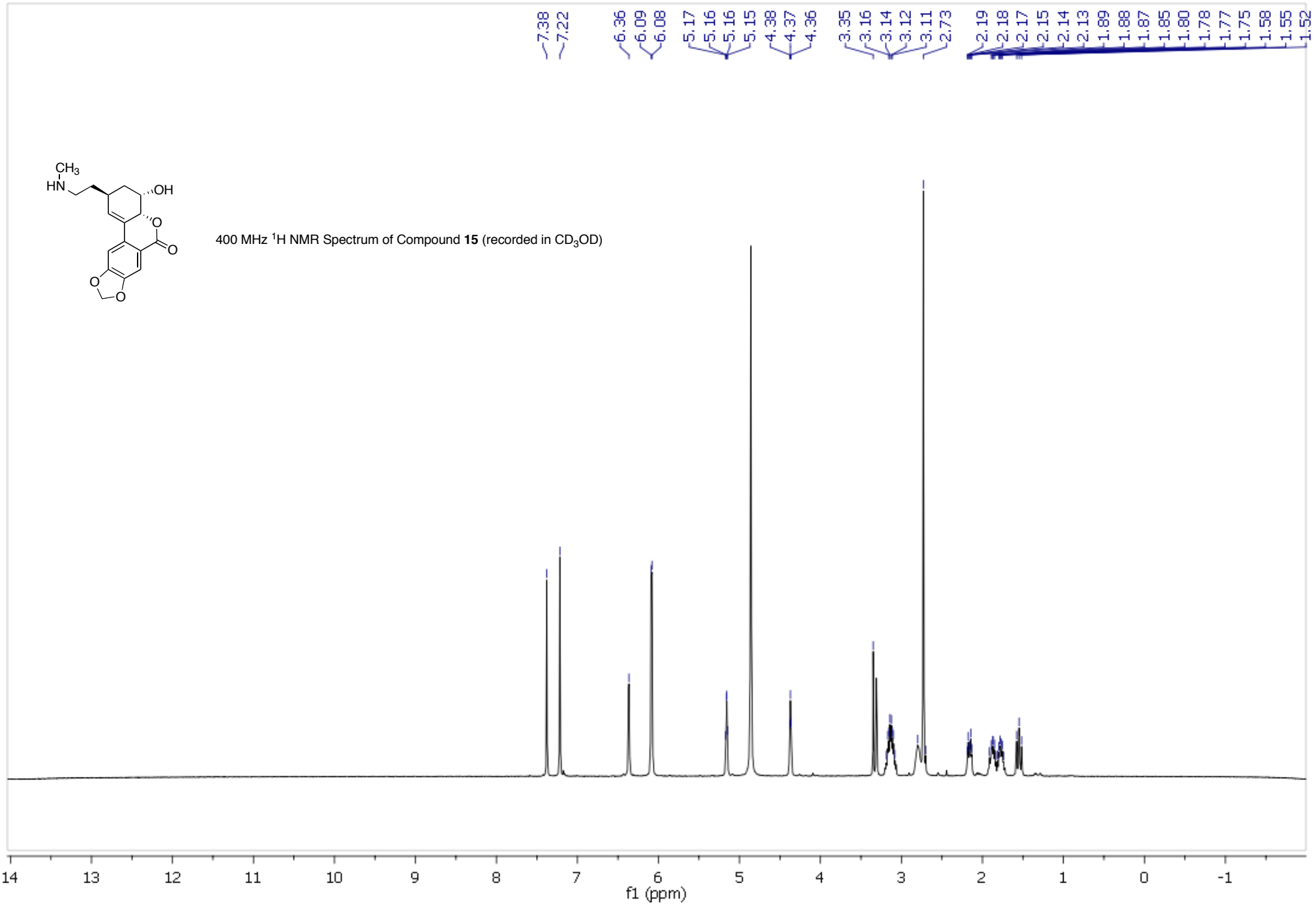
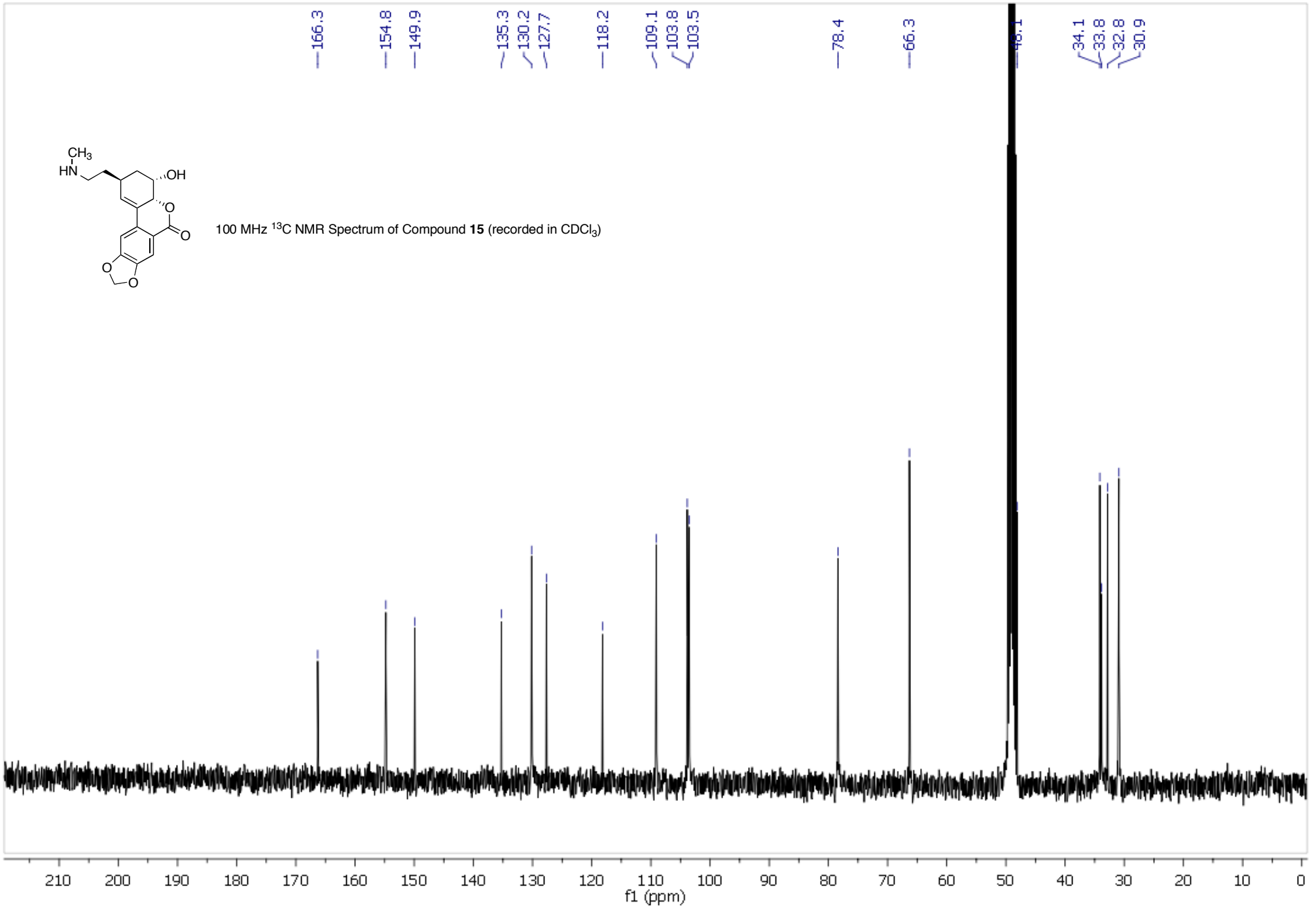


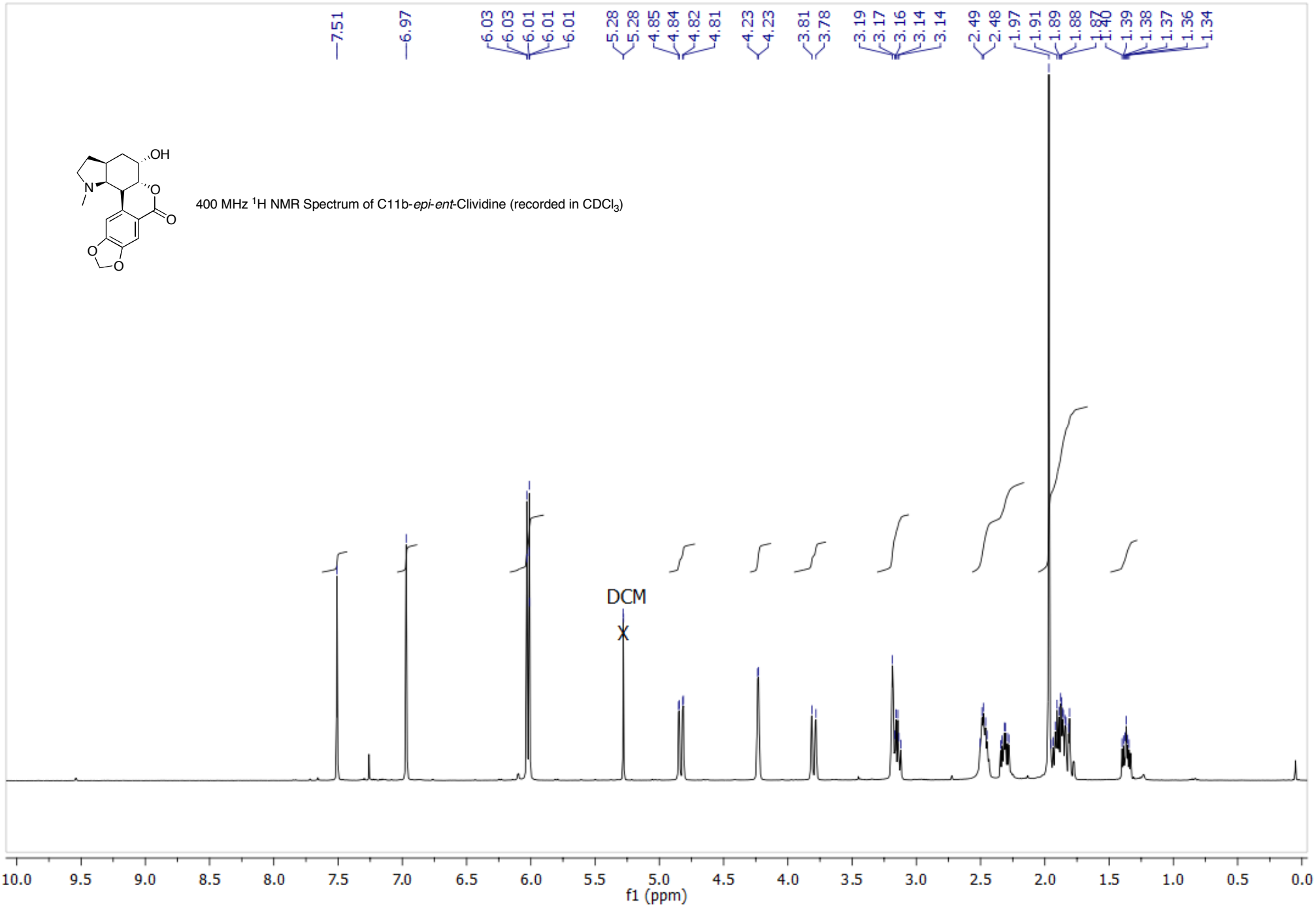
100 MHz ^{13}C NMR Spectrum of Compound **14** (recorded in $CDCl_3$)



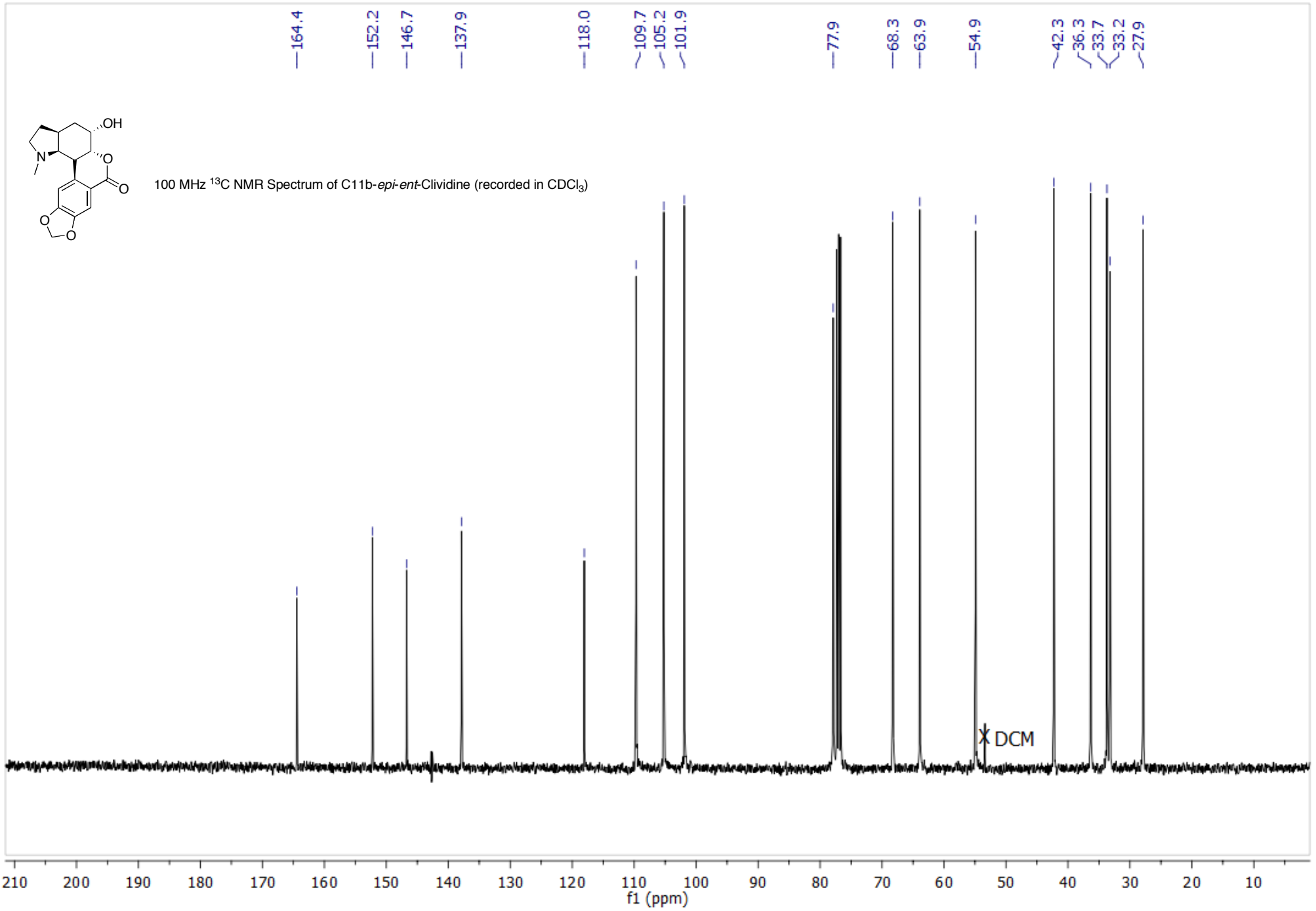
400 MHz ^{1}H NMR Spectrum of Compound **15** (recorded in CD_3OD)

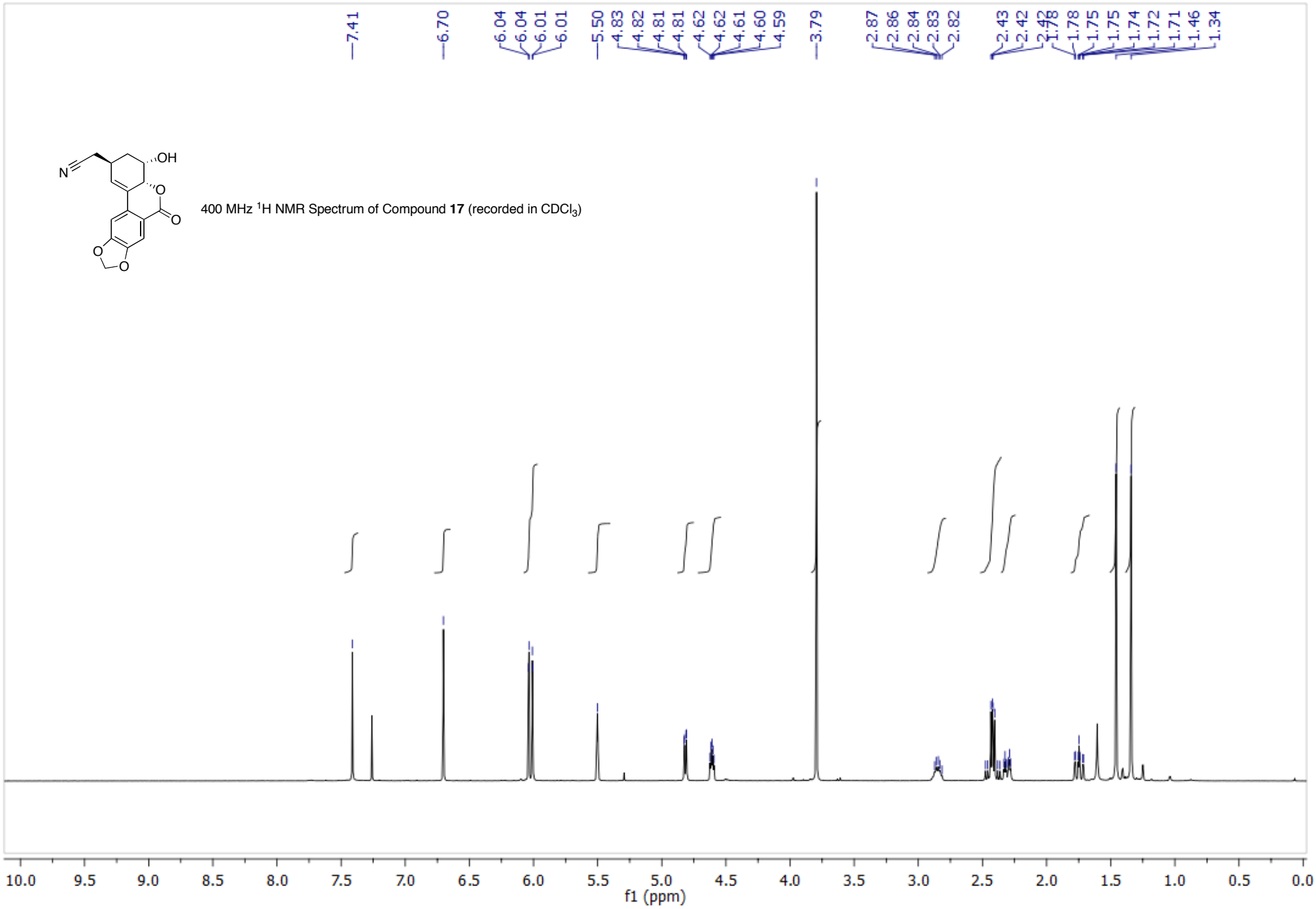


100 MHz ^{13}C NMR Spectrum of Compound **15** (recorded in $CDCl_3$)



400 MHz ^{1}H NMR Spectrum of C11b-*epi*-*ent*-Clividine (recorded in $CDCl_3$)


164.4
152.2
146.7
137.9
118.0
109.7
105.2
101.9
77.9
68.3
63.9
54.9
42.3
36.3
33.7
33.2
27.9
OH
N
O
O
O
O
100 MHz ^{13}C NMR Spectrum of C11b-*epi*-*ent*-Clividine (recorded in $CDCl_3$)
DCM
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.41
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6.04
6.04
6.01
6.01
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4.82
4.81
4.81
4.62
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4.61
4.60
4.59
3.79
2.87
2.86
2.84
2.83
2.82
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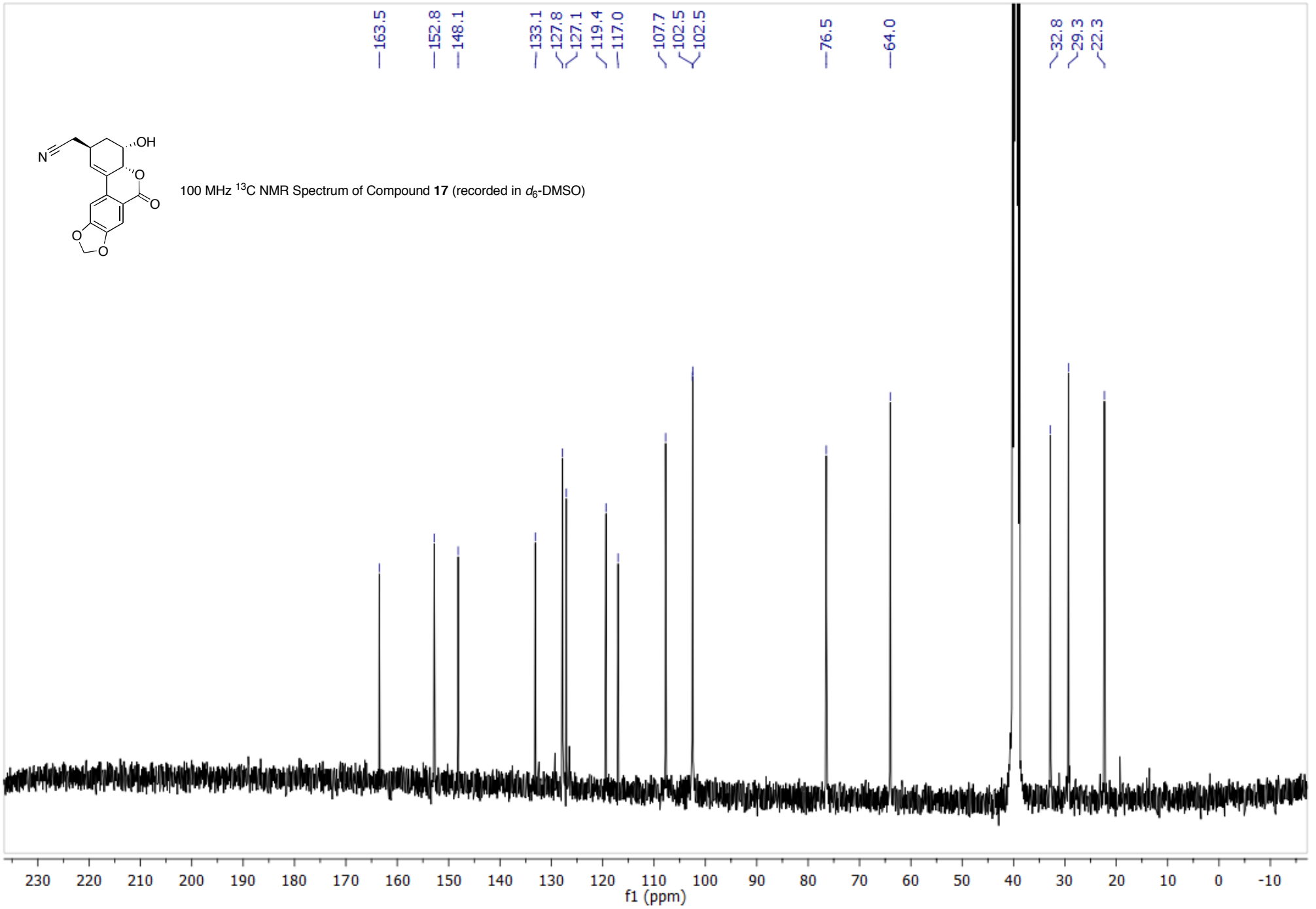
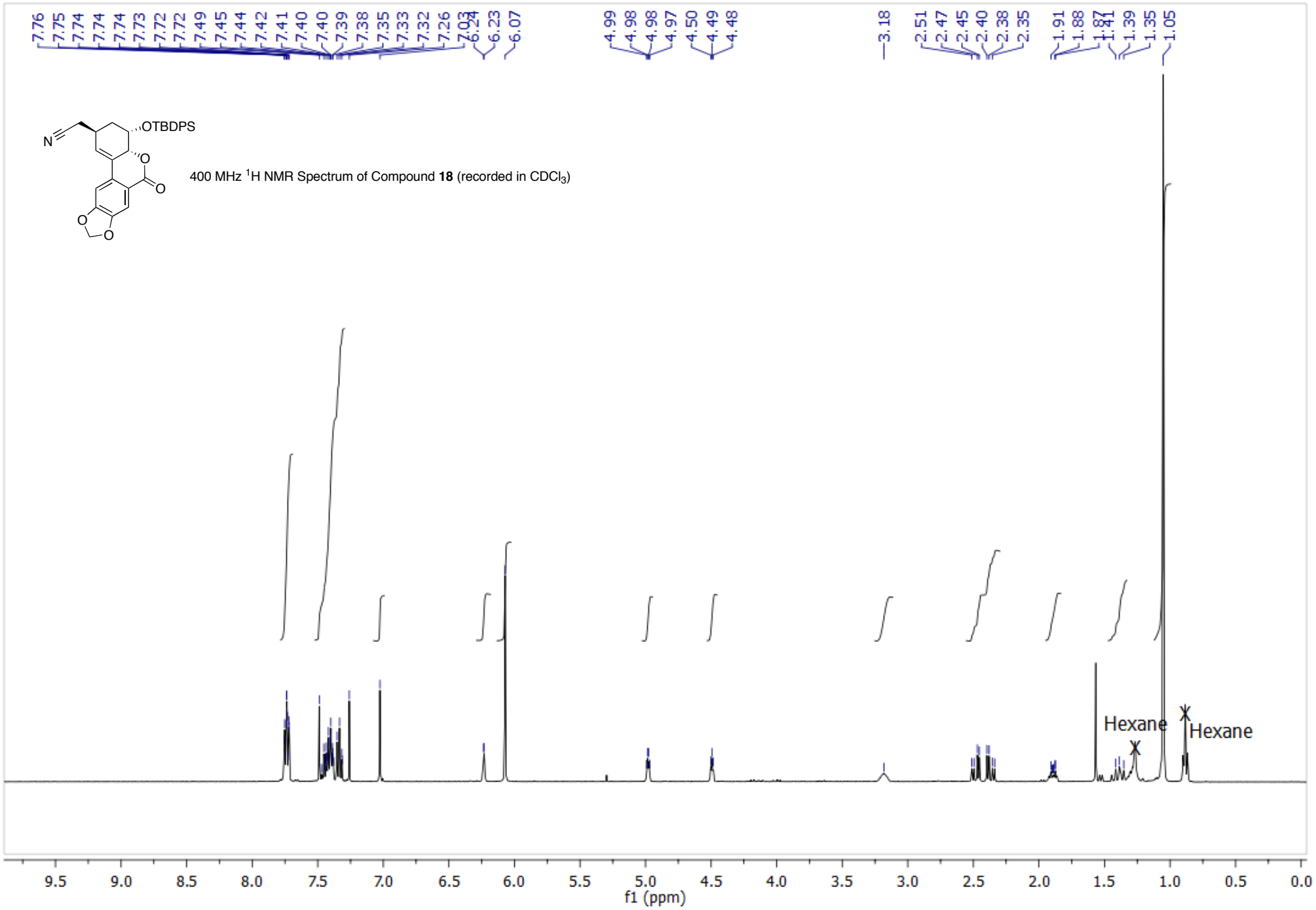
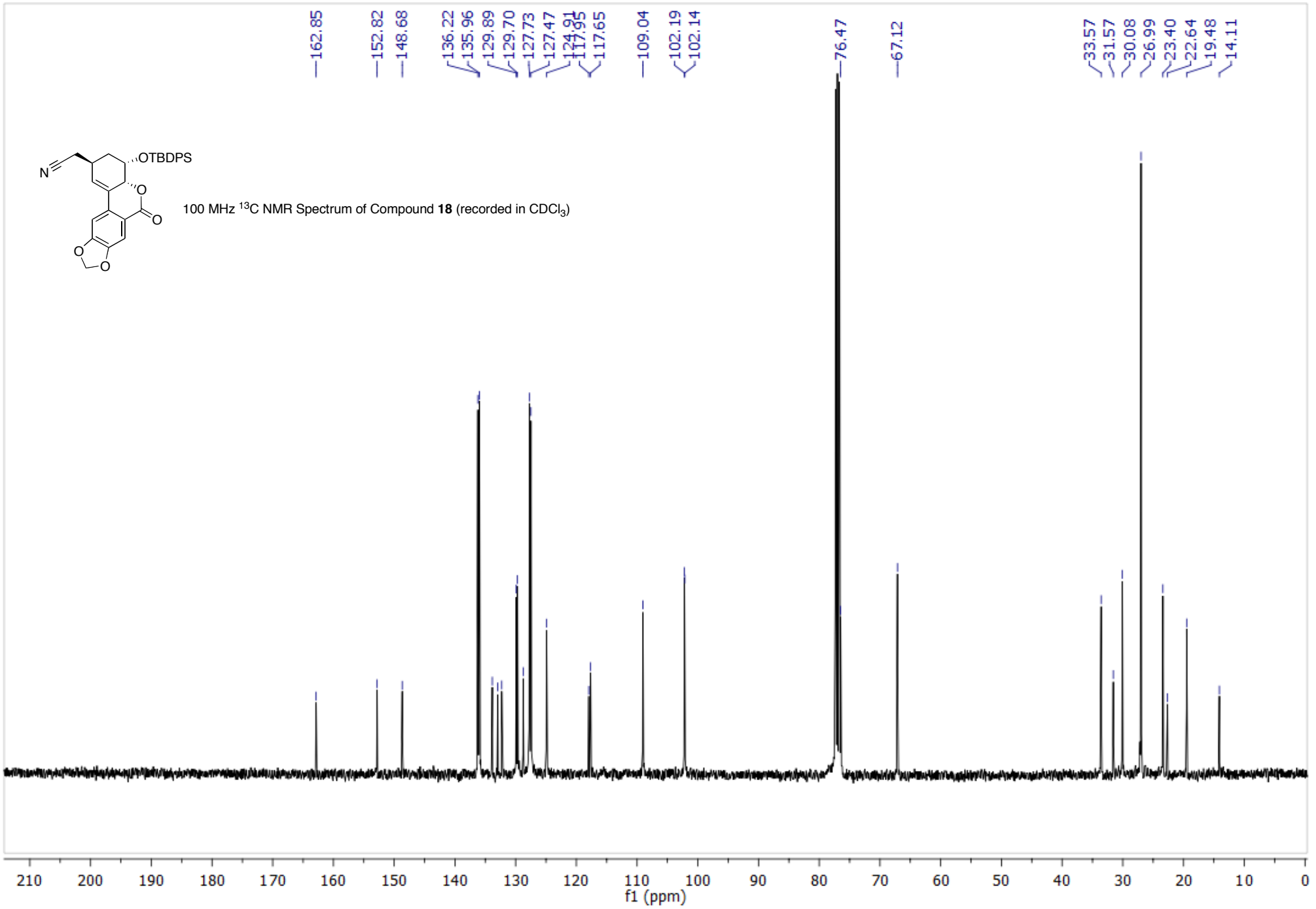
2.42
2.42
1.78
1.78
1.75
1.75
1.74
1.72
1.71
1.46
1.34
OH
N
O
O
O
O
400 MHz ^{1}H NMR Spectrum of Compound **17** (recorded in $CDCl_3$)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



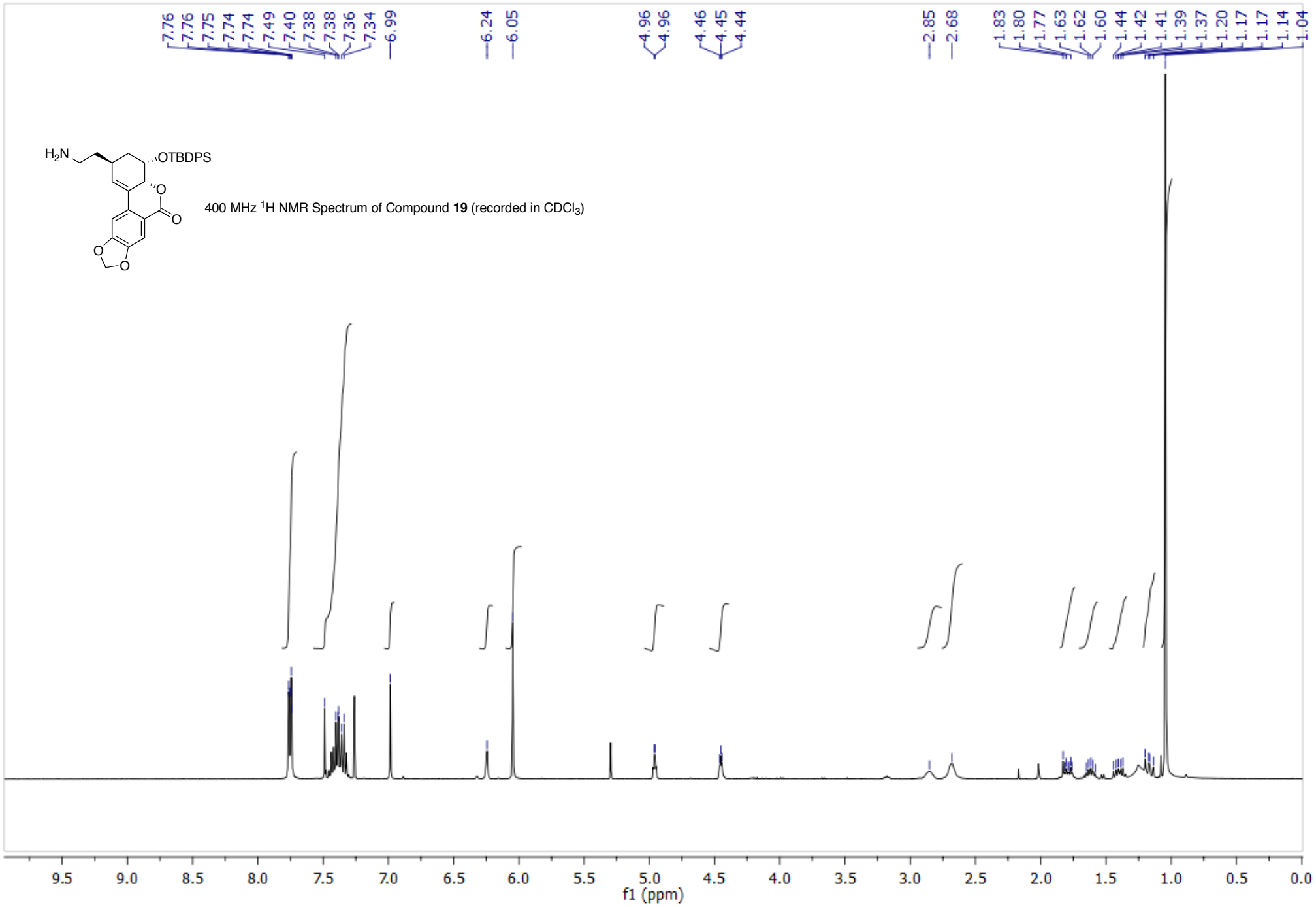
100 MHz ^{13}C NMR Spectrum of Compound **17** (recorded in d_6-DMSO)



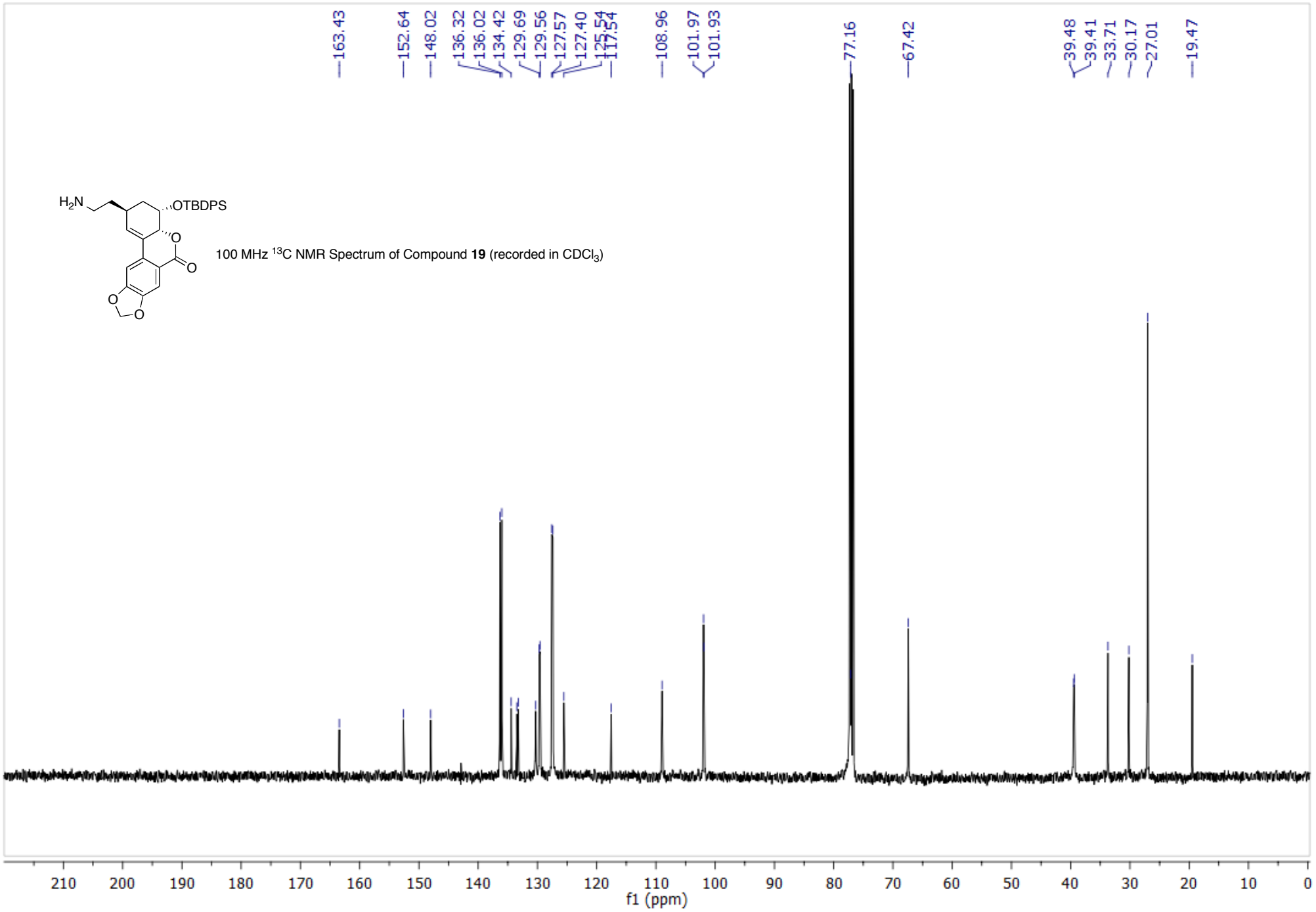
400 MHz ^{1}H NMR Spectrum of Compound **18** (recorded in $CDCl_3$)



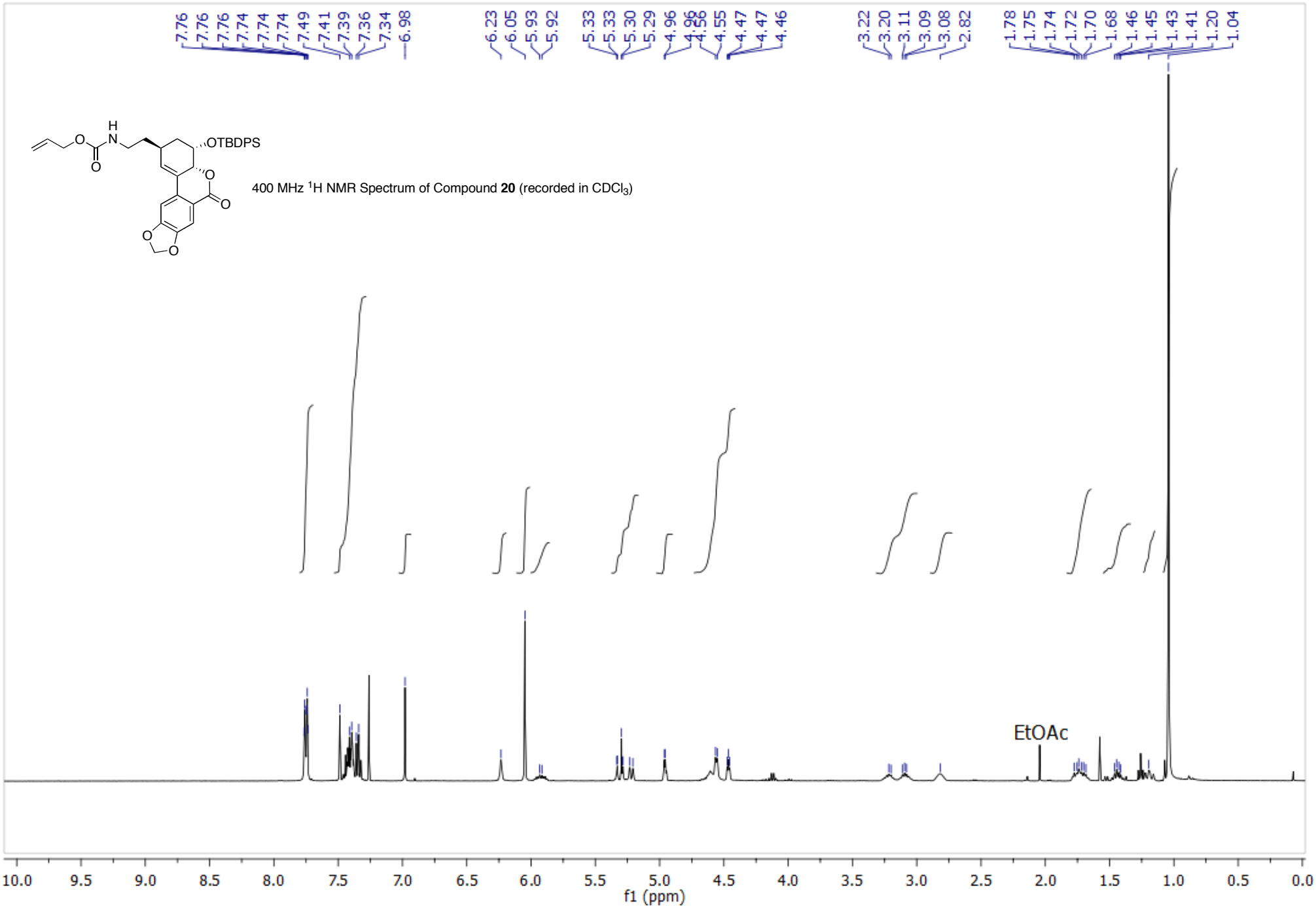
100 MHz ^{13}C NMR Spectrum of Compound **18** (recorded in $CDCl_3$)



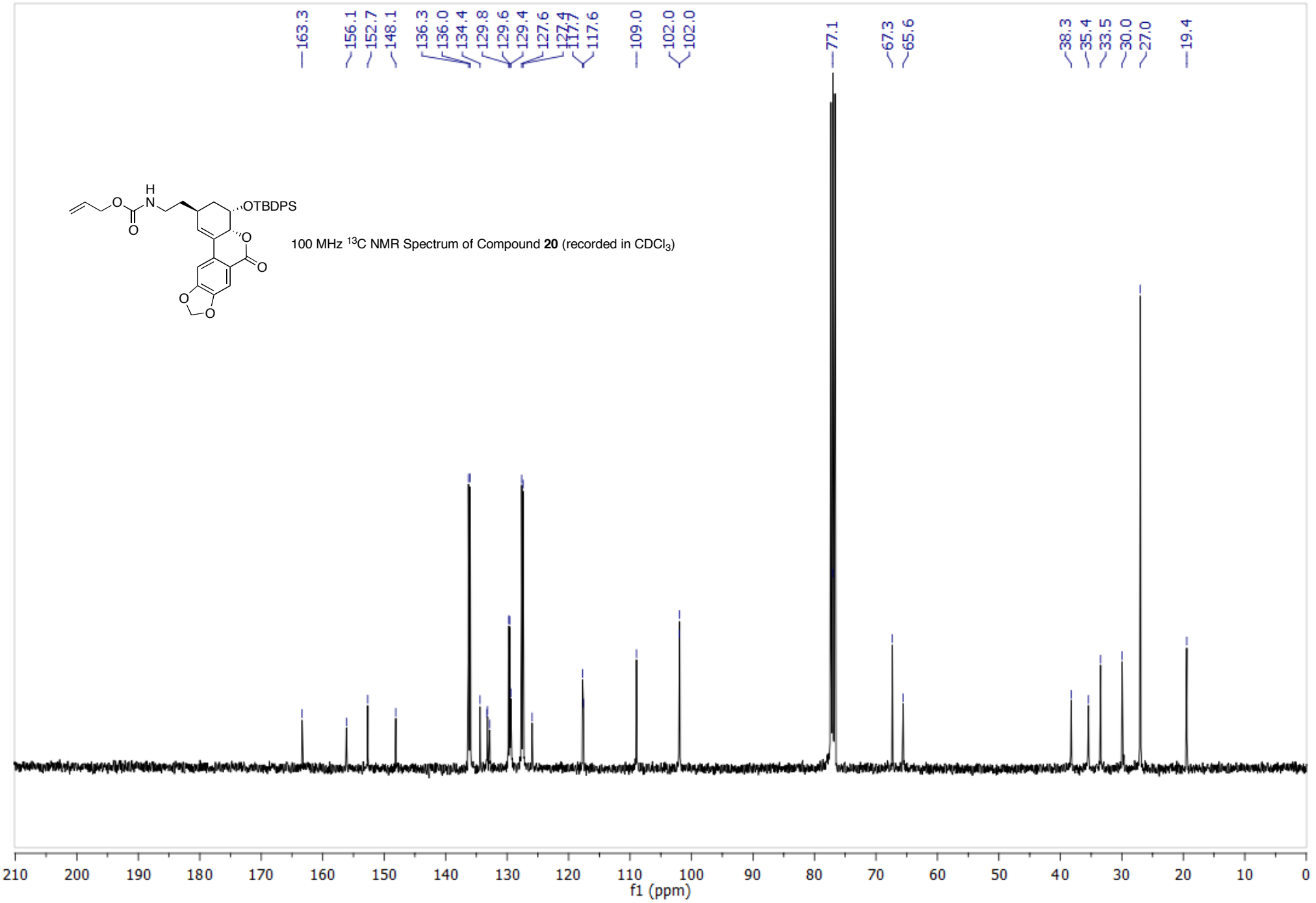
400 MHz ^{1}H NMR Spectrum of Compound **19** (recorded in $CDCl_3$)



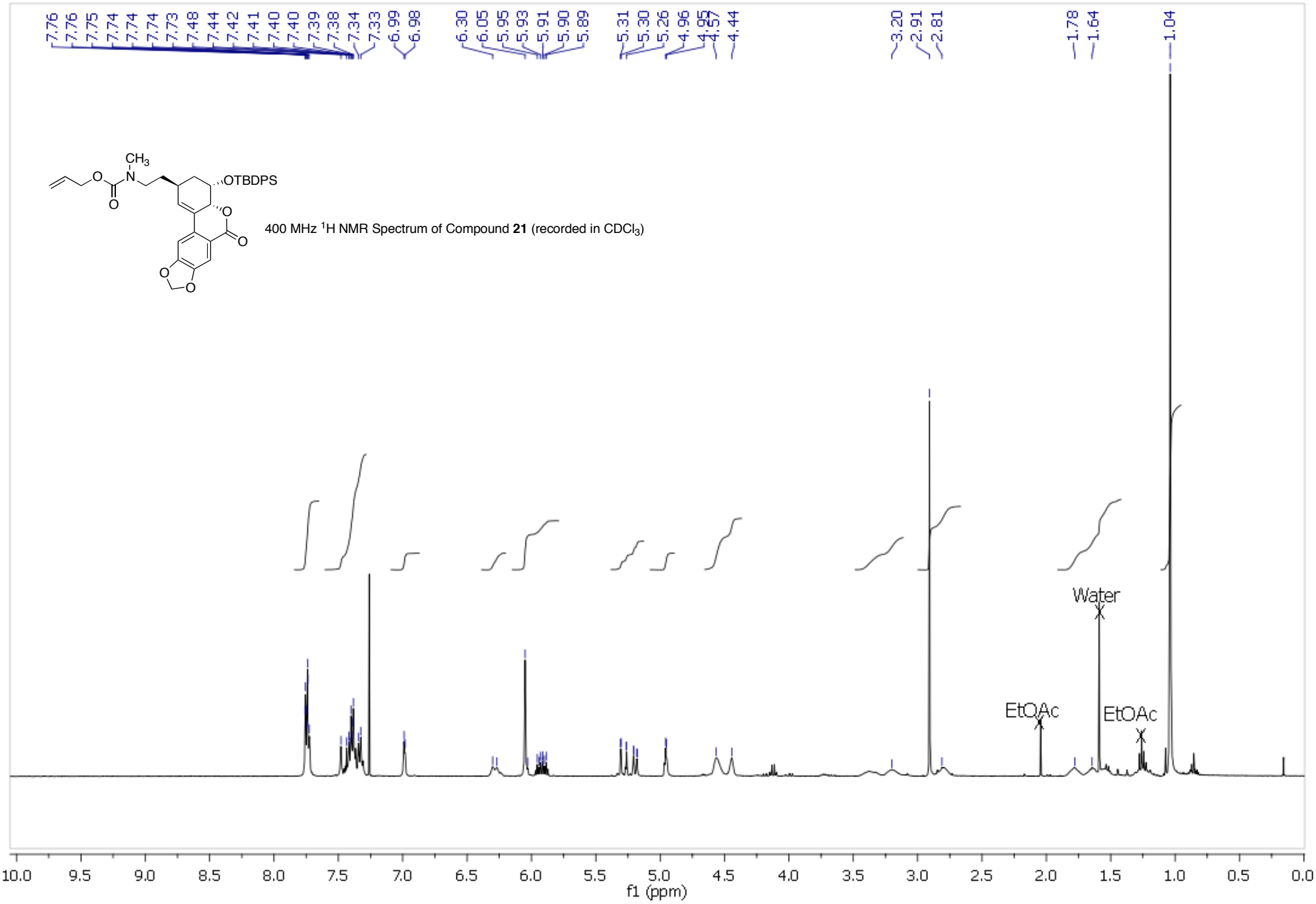
100 MHz ^{13}C NMR Spectrum of Compound **19** (recorded in $CDCl_3$)



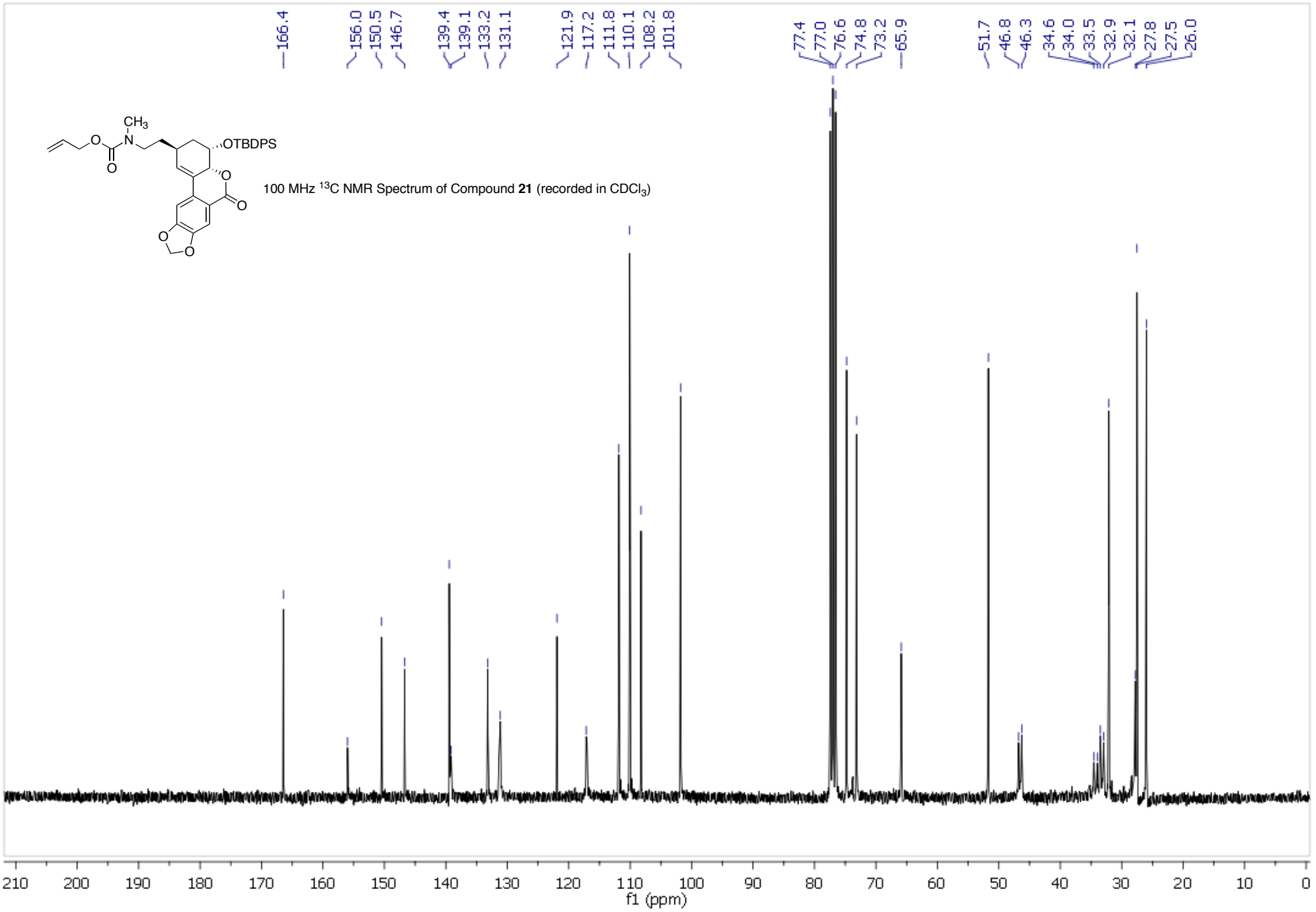
400 MHz ^{1}H NMR Spectrum of Compound **20** (recorded in $CDCl_3$)



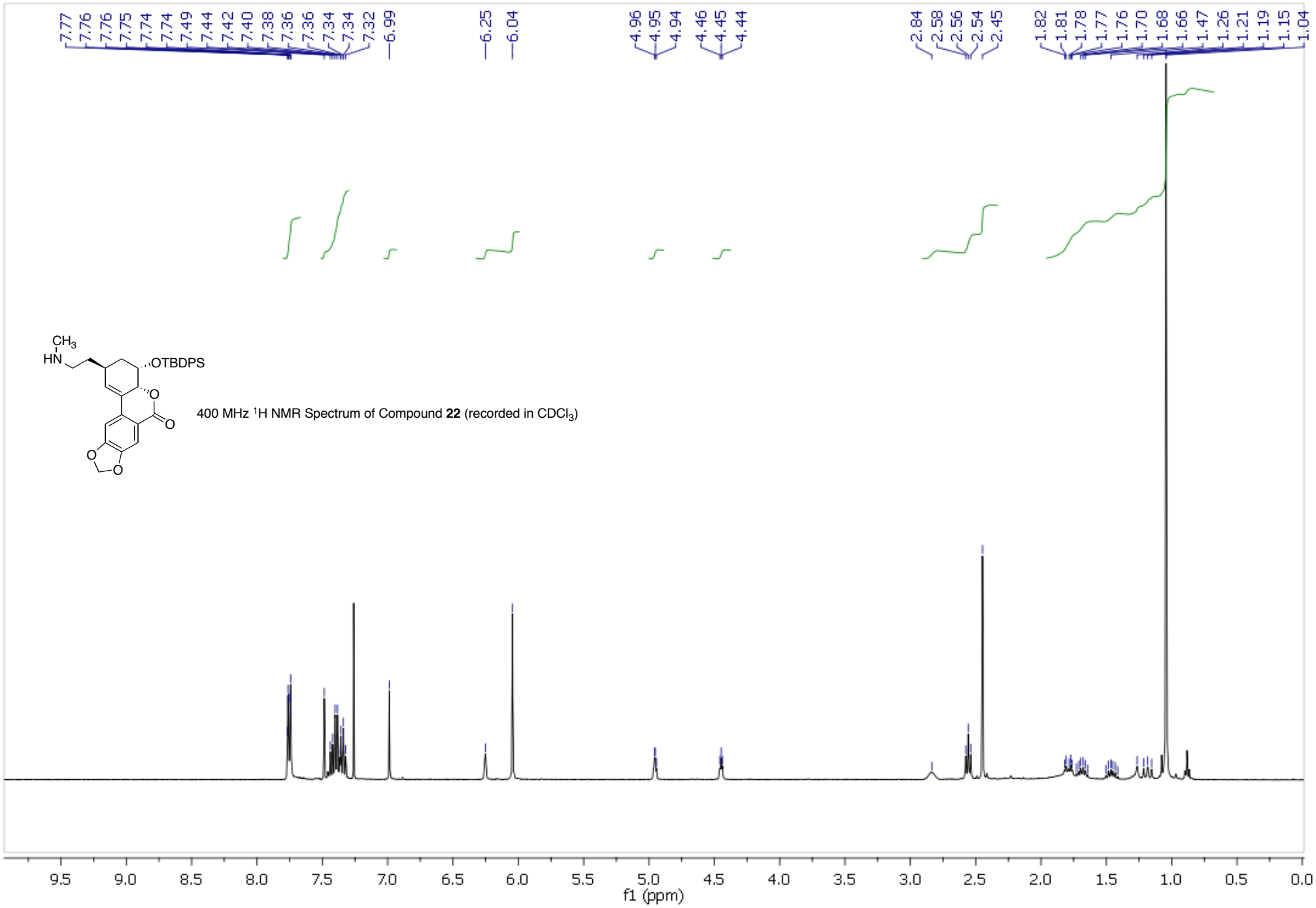
100 MHz ^{13}C NMR Spectrum of Compound **20** (recorded in $CDCl_3$)



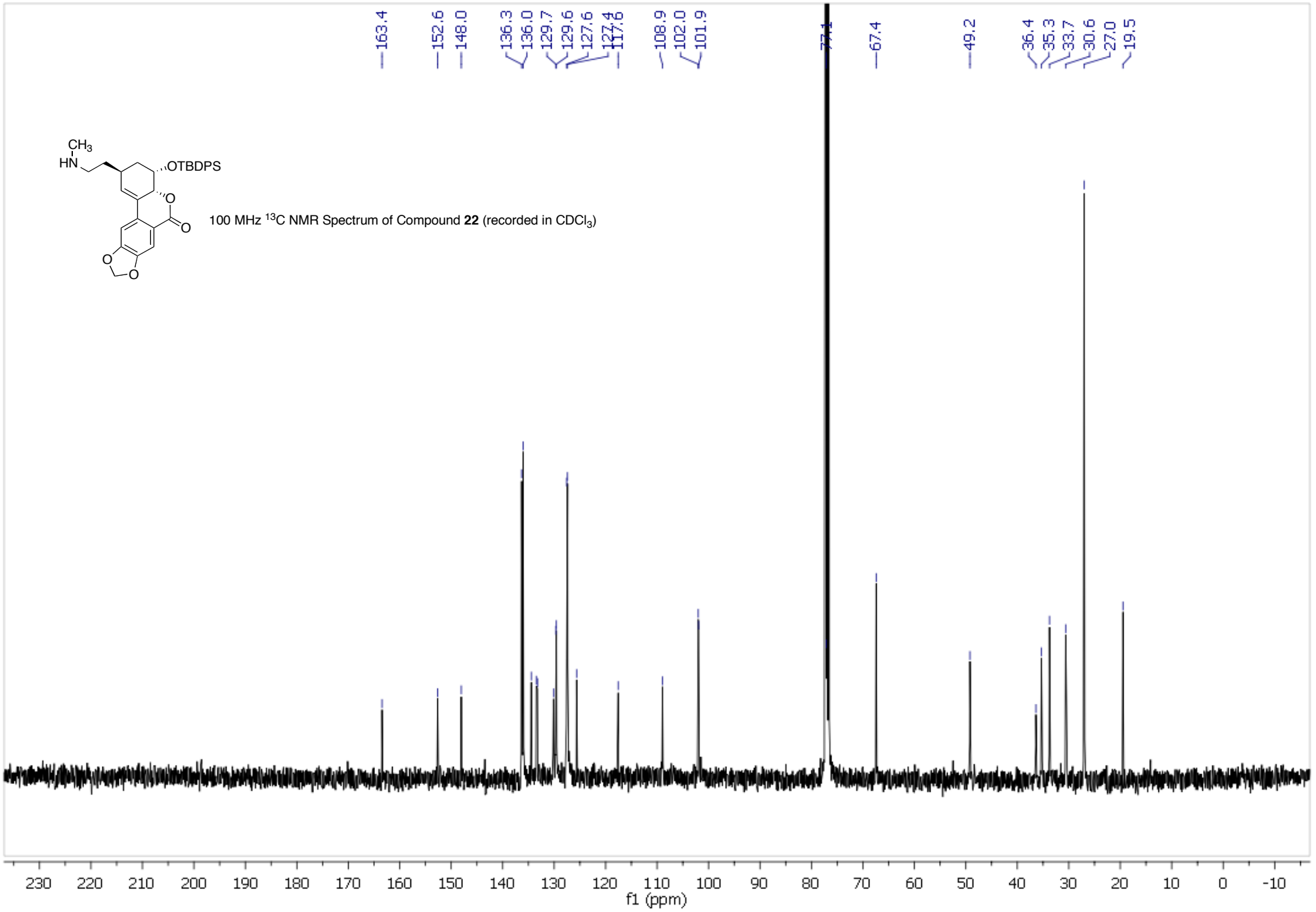
400 MHz ^{1}H NMR Spectrum of Compound **21** (recorded in $CDCl_3$)



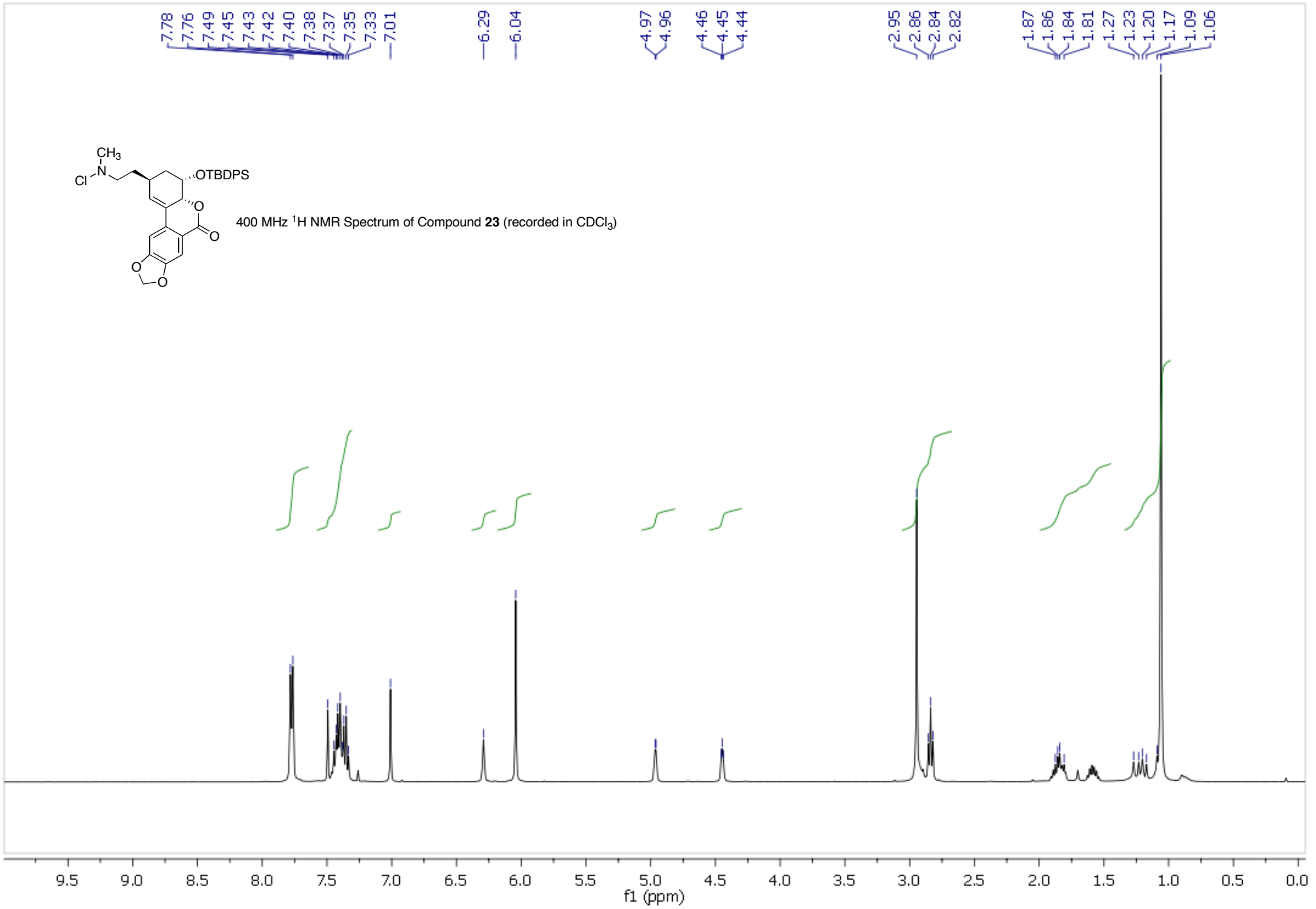
100 MHz ^{13}C NMR Spectrum of Compound **21** (recorded in $CDCl_3$)



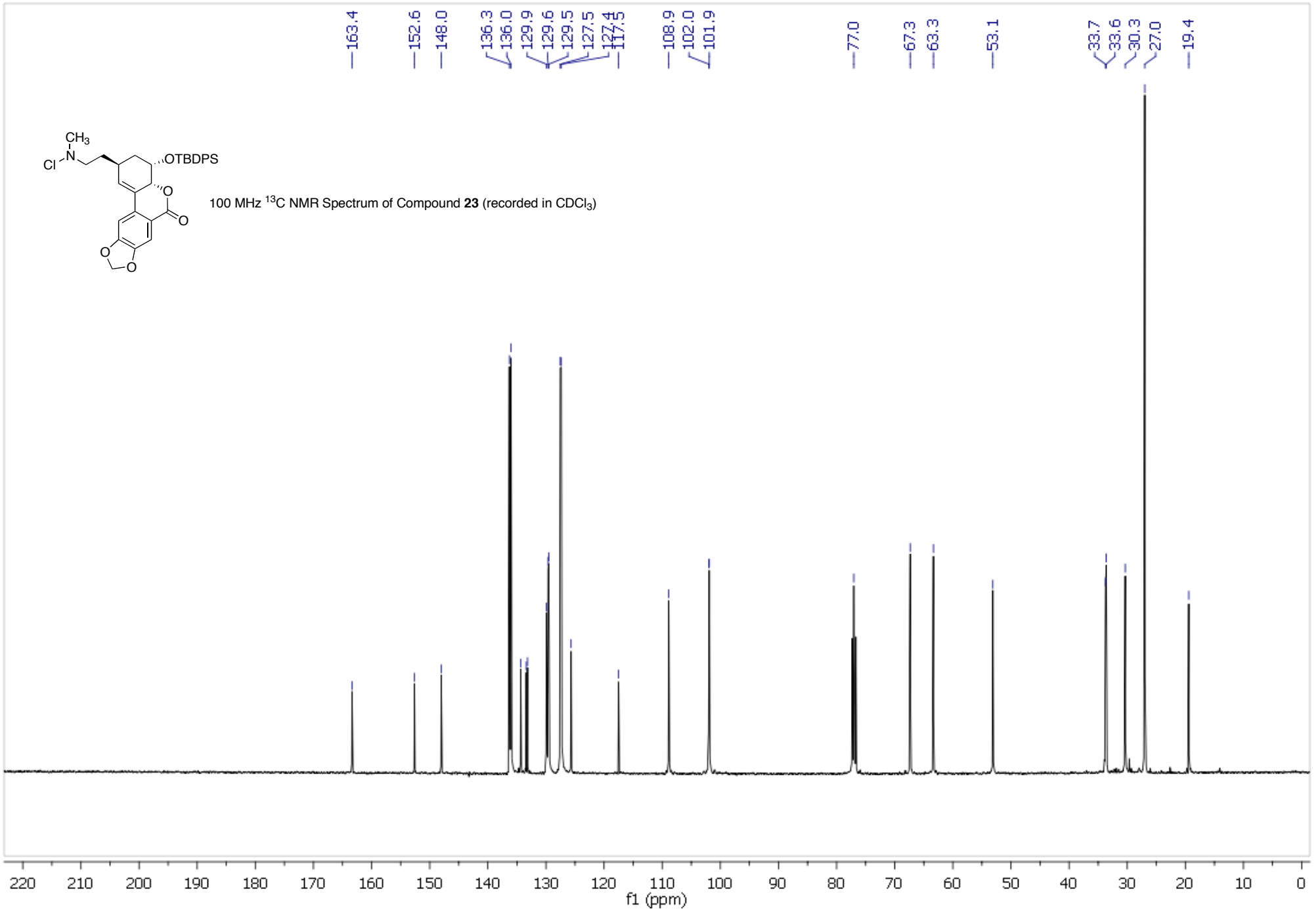
400 MHz ^{1}H NMR Spectrum of Compound **22** (recorded in $CDCl_3$)



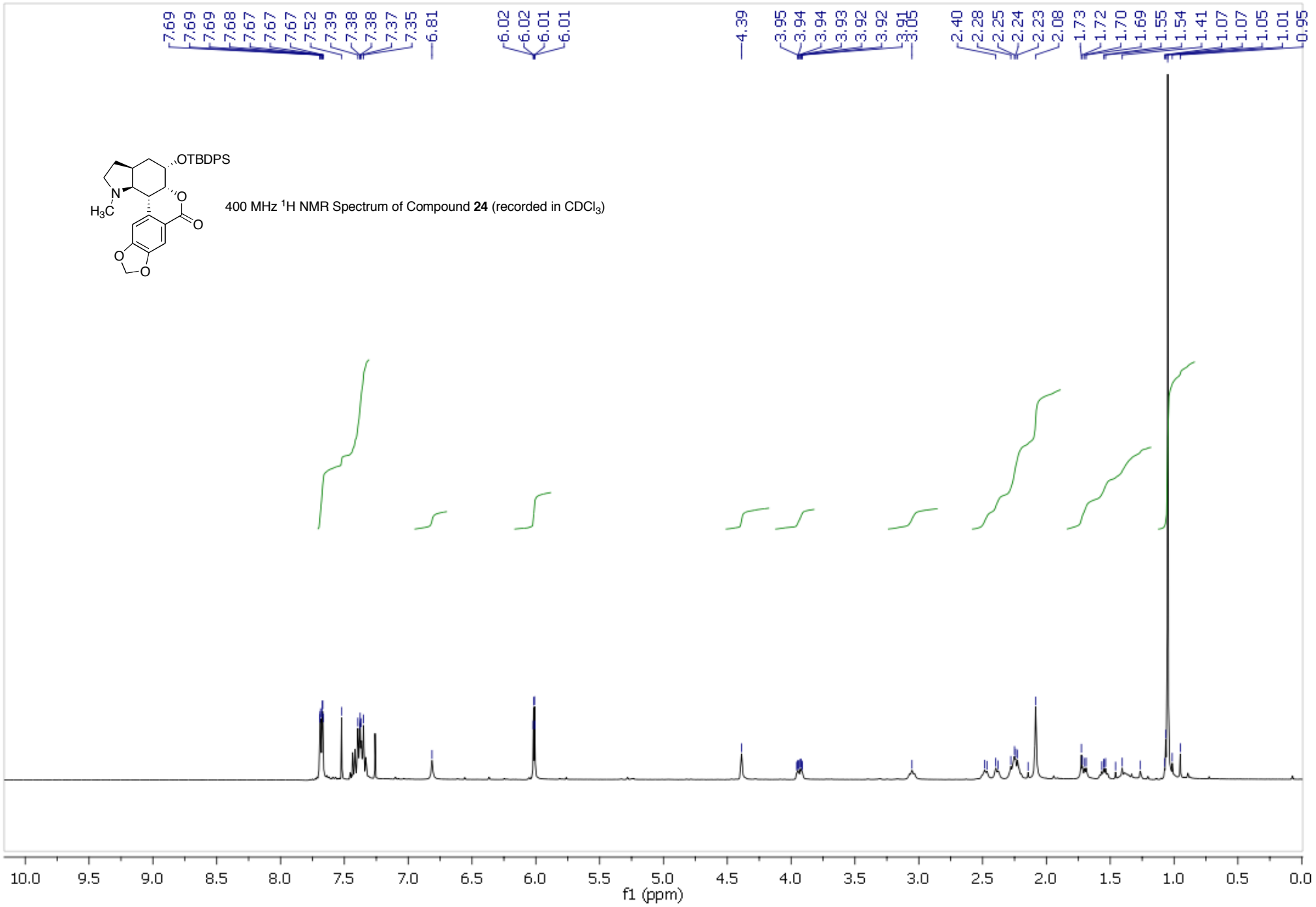
100 MHz ^{13}C NMR Spectrum of Compound **22** (recorded in $CDCl_3$)

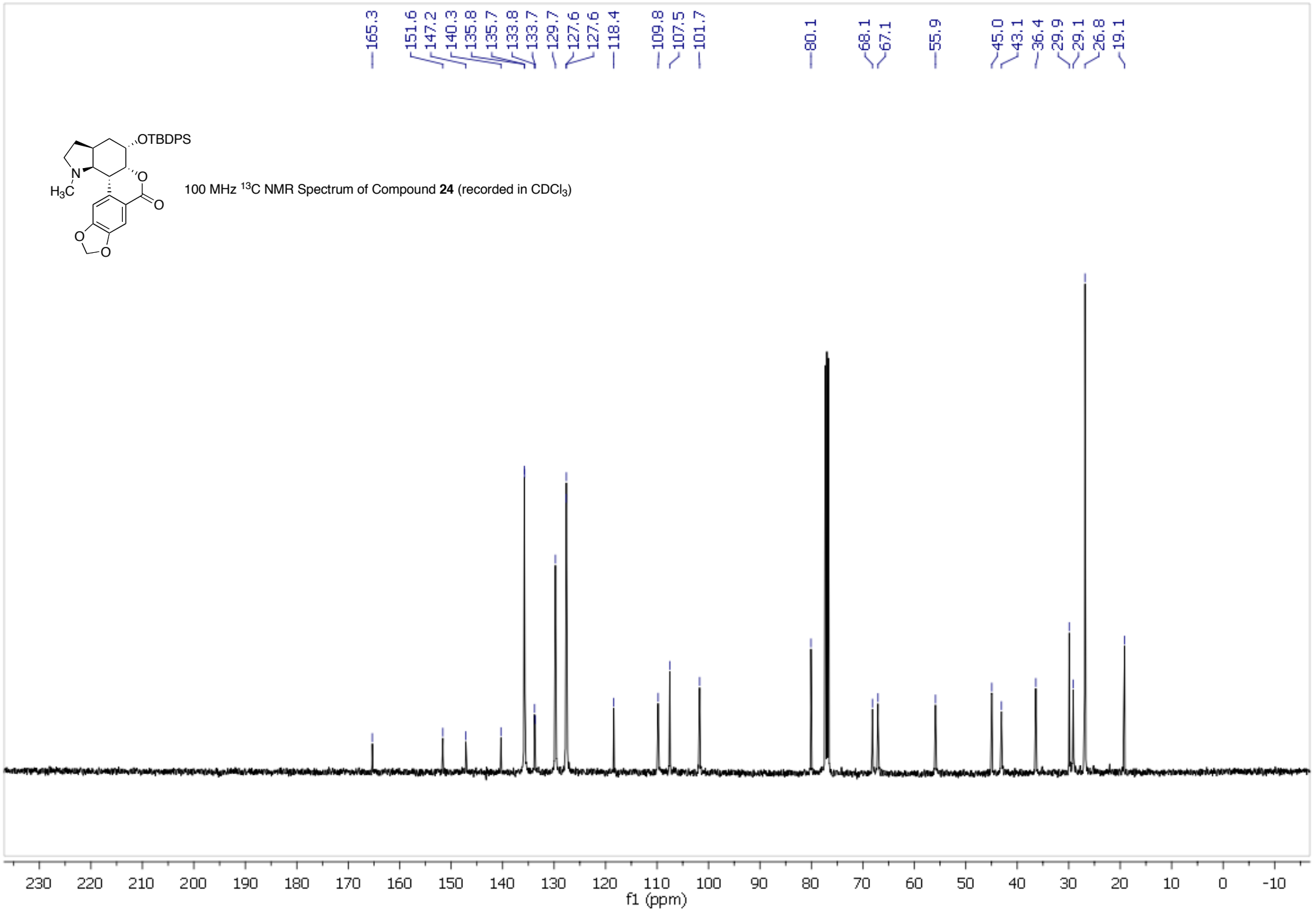


400 MHz ^{1}H NMR Spectrum of Compound **23** (recorded in $CDCl_3$)

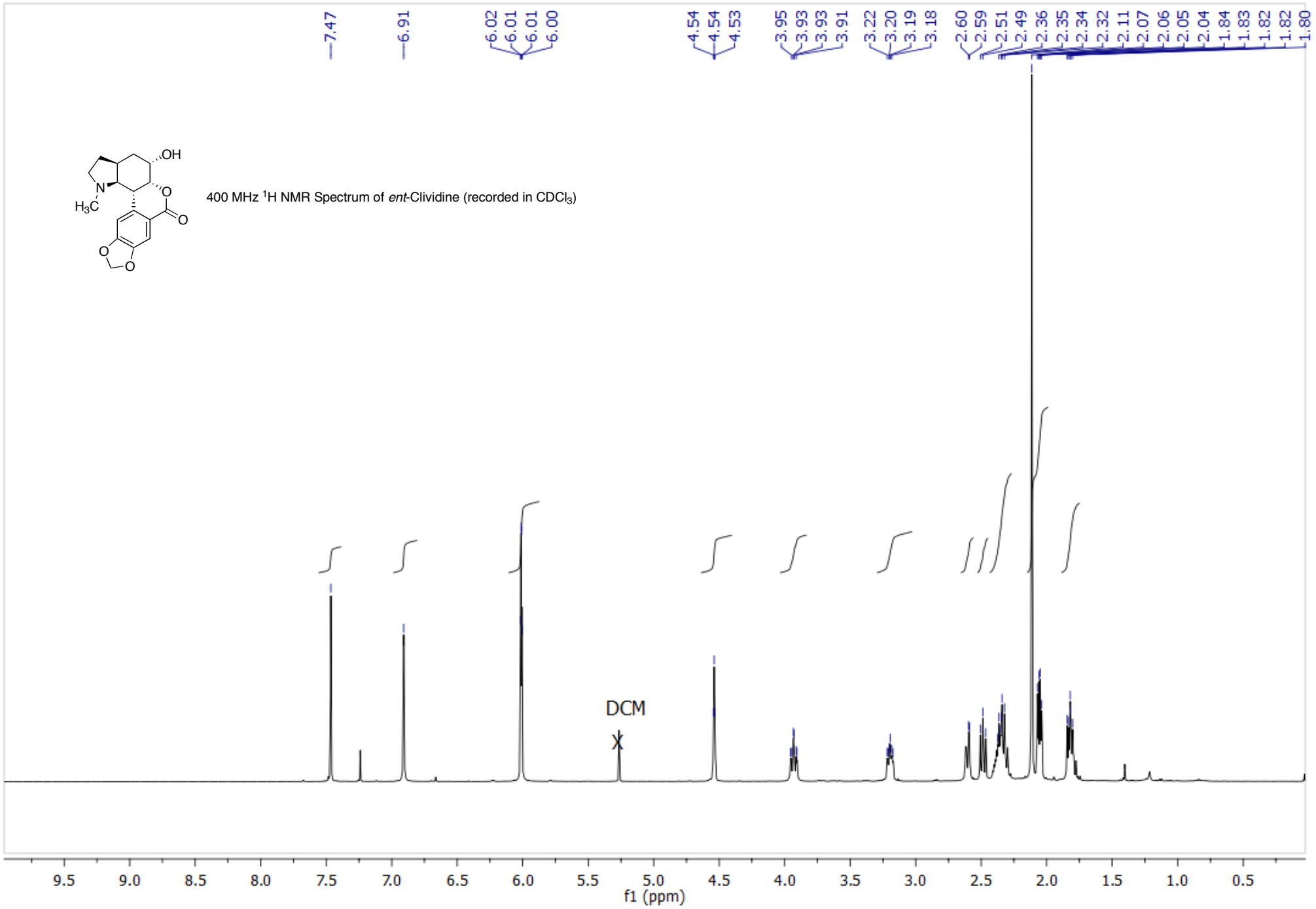


100 MHz ^{13}C NMR Spectrum of Compound **23** (recorded in $CDCl_3$)

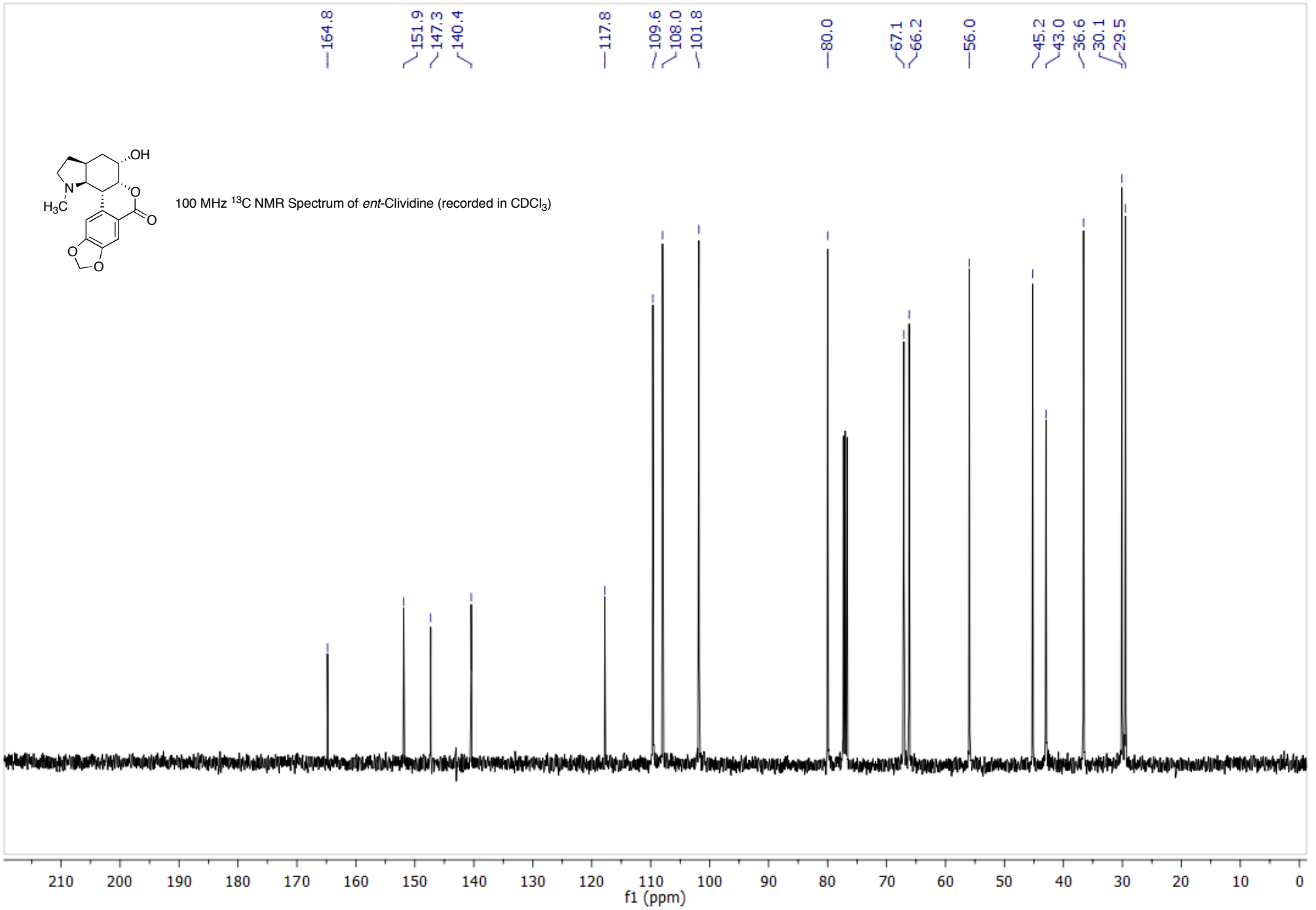

7.69 7.69 7.69 7.68 7.67 7.67 7.67 7.52 7.39 7.38 7.38 7.37 7.35 6.81
6.02 6.02 6.01 6.01
4.39
3.95 3.94 3.94 3.93 3.92 3.92 3.91 3.85
2.40 2.28 2.25 2.24 2.23 2.08
1.73 1.72 1.70 1.69 1.55 1.54 1.41 1.07 1.07 1.05 1.01 0.95
OTBDPS
N
H3C
O
O
O
O
O
400 MHz 1H NMR Spectrum of Compound 24 (recorded in CDCl3)
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
f1 (ppm)



100 MHz ^{13}C NMR Spectrum of Compound **24** (recorded in $CDCl_3$)



400 MHz ^{1}H NMR Spectrum of *ent*-Clividine (recorded in $CDCl_3$)


164.8
151.9
147.3
140.4
117.8
109.6
108.0
101.8
80.0
67.1
66.2
56.0
45.2
43.0
36.6
30.1
29.5
OH
N
H3C
O
O
O
O
100 MHz 13C NMR Spectrum of ent-Clividine (recorded in CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)