

Bilateral metalloheterocyclic systems based on palladacycle and piperidine-2,4-dione pharmacophores

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General. The manipulations with sensitive to air components compounds were carried out under inert atmosphere of dry Ar. NMR spectra were recorded on Bruker Avance-400 and Inova 400 instruments. Chemical shifts are reported in ppm relative to the solvent signals. Column chromatography was carried out using silica gel 60–230 mesh (Merck) as well as using automated flash chromatograph Biotage Isolera with cartridges Agilent SF15-12g for gradient elution. Thin layer chromatography was run on AlugramSilG/UV₂₅₄ (Macherey-Nagel). Corrected melting points were measured on Buchi B-540 capillary melting point apparatus. 6-Phenylpiperidine-2,4-dione **5a**, [1,2]palladium(II) acetate[3] were synthesized according to the described procedures.

X-Ray crystallographic data for compounds 11b, 11d and 11g

The structures of the complexes **11b**, **11g** and **11d** (Figure 1) were confirmed by X-ray diffraction data collected from their solvates with chloroform (1:3), ethyl acetate (1:1) and chloroform-d₁ (1:1); the latter was treated as a diffuse contribution to the overall scattering without specific atom positions. They all crystallize in the racemic space groups P-1 or C2/c with the palladium(II) ion in a distorted square-planar environment of the *N*-heterocyclic ligand, triphenylphosphine oxide and chloride anion (Table 1). The two aromatic fragments of the ligand coordinated by the metal ion are planar while the second *N*-heterocyclic fragment adopts a half-chair conformation with the atom C(7) deviating from the mean plane of the others by 0.567(5) Å in **11b** (0.463(5) Å for the minor component of the disordered C-phenyl moiety), 0.599(4) and 0.563(7) Å (0.551(12) Å for the minor component of the disordered *N*-heterocyclic ligand) in **11g** and **11d**, respectively. The angle between the latter plane and that of the phenyl substituent at the atom C(7) is 81.39(15)° in **11b** (88.13(16)° for the minor component of the disordered C-phenyl moiety), 87.57(11) and 45.96(14)° (76.5(3)° for the minor component of the disordered *N*-heterocyclic ligand) in **11g** and **11d**, respectively.

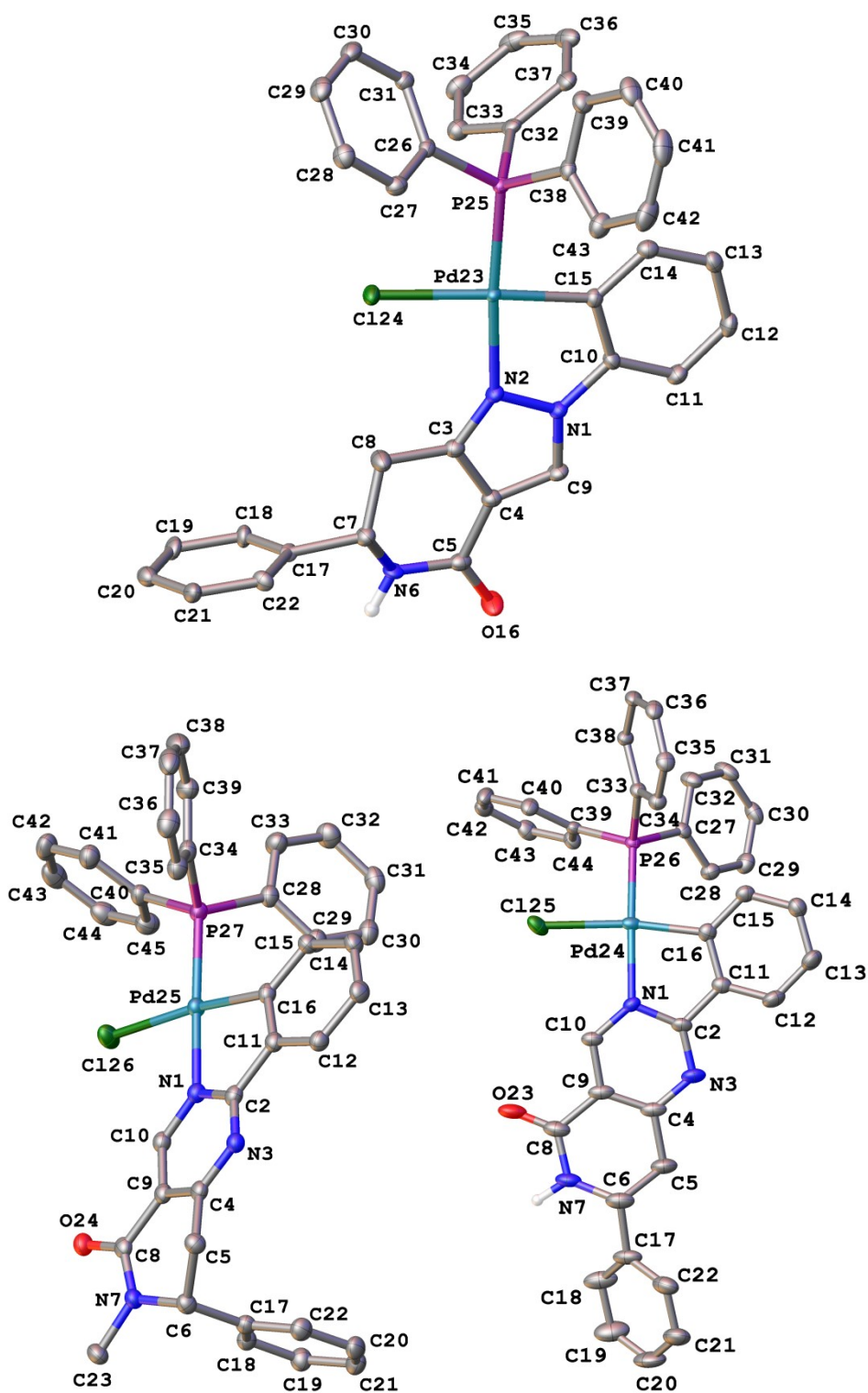


Fig. 1. General view of the complexes **11b** (top), **11d** (bottom right) and **11g** (bottom left) in representation of atoms *via* thermal ellipsoids at 30% probability level. Hydrogen atoms except those of NH groups in **11b** and **11d** are omitted, as are the solvent molecules of chloroform in **11b**, ethyl acetate in **11g** and the minor components of the disordered *N*-heterocyclic ligand in **11b** and **11d**.

Table 1. Main geometric parameters of **11b**, **11d** and **11g**.

Parameter	11b	11d	11g
Pd-Cl, Å	2.3675(6)	2.3897(8)	2.3772(14)
Pd-P, Å	2.2450(5)	2.2439(7)	2.2611(9)
Pd-N, Å	2.0834(17)	2.082(11)	2.095(2)
Pd-C, Å	2.024(2)	1.976(5)	2.029(3)
NPdP, °	174.79(5)	165.4(3)	175.55(6)
CPdCl, °	171.33(6)	166.9(2)	170.93(7)

In **11b** and **11d**, the NH group of the non-coordinating N-heterocyclic fragment form the N-H...O bonds that assemble the molecules of the complexes into centrosymmetric dimers; the appropriate N...O distance and NHO angle are 2.914(2) Å and 163.13(13)°, 2.588(6) Å and 155.8(4)° (3.562(14) Å and 148.3(8)° for the minor component of the disordered *N*-heterocyclic ligand), respectively.

X-ray crystallography. X-ray diffraction data for **11g** were collected at the K4.4 station of the Kurchatov Center for Synchrotron Radiation and Nanotechnology in Moscow (Russia) at a wavelength of 0.745 Å; those for **11b** and **11d** were collected with a Bruker Quest D8 CMOS diffractometer, using graphite monochromated Mo-K α radiation ($\lambda = 0.71073$ Å, ω -scans). Structures were solved using Intrinsic Phasing with the ShelXT[4] structure solution program in Olex2[5] and then refined with the XL[6] refinement package using Least-Squares minimization against F^2 in the anisotropic approximation for non-hydrogen atoms. Hydrogen atoms of NH groups were found in difference Fourier synthesis while positions of other hydrogen atoms were calculated, and they were refined in the isotropic approximation within the riding model. The C-phenyl moiety of the *N*-heterocyclic ligand in **11b** is disordered over two positions with the occupancies of 0.514(3):0.486(3) while the *N*-heterocyclic ligand in **11d** is disordered over two positions with the occupancies of 0.637(2):0.363(2). Disordered solvate molecules of chloroform-d₁ in **11d** were treated as a diffuse contribution to the overall scattering without specific atom positions by SQUEEZE/PLATON [7]. Crystal data and structure refinement parameters are given in Table 2. CCDC 2217768, 2217769 and 2217770 contain the supplementary crystallographic data for **11b**, **11g** and **11d**, respectively.

Table 2. Crystal data and structure refinement parameters for **11b**, **11d** and **11g**.

	11b	11g	11d
Empirical formula	C ₃₉ H ₃₂ Cl ₁₀ N ₃ OPPd	C ₄₂ H ₃₉ ClN ₃ O ₃ PPd	C ₃₇ H ₂₉ ClN ₃ OPPd
Formula weight	1050.54	806.58	704.45
T, K	100	100	100
Crystal system	Triclinic	Triclinic	Monoclinic
Space group	P-1	P-1	C2/c
Z	2	2	8
a, Å	9.24000(10)	10.923(2)	35.7466(13)
b, Å	15.0951(2)	11.870(2)	9.2750(3)
c, Å	16.2876(2)	15.665(3)	26.6696(10)
α, °	68.4410(10)	96.22(3)	90
β, °	87.7750(10)	101.71(3)	127.8700(10)
γ, °	85.8250(10)	113.13(3)	90
V, Å ³	2107.06(5)	1788.6(8)	6980.2(4)
D _{calc} (g cm ⁻³)	1.656	1.498	1.341
Linear absorption, μ (cm ⁻¹)	11.49	7.7	6.86
F(000)	1052	828	2864
2θ _{max} , °	50	53	50
Reflections measured	24426	22484	76544
Independent reflections	9199	7957	7614
Observed reflections [<i>I</i> > 2σ(<i>I</i>)]	8010	6670	7174
Parameters	504	464	419
R1	0.0296	0.0337	0.0364
wR2	0.0643	0.0849	0.0889
GOF	1.016	1.037	1.193
Δρ _{max} / Δρ _{min} (e Å ⁻³)	0.696/-0.661	0.675/-1.121	0.651/-0.562

¹ Kuznetsov, N. Yu.; Maleev, V. I.; Khrustalev, *et al.* *Eur. J. Org. Chem.* **2012**, 334-344.

² Kuznetsov, N. Yu.; Tikhov, R. M.; Strelkova, T. V.; Bubnov, Yu. N. *Org. Lett.* **2018**, *20*, 3549-3552.

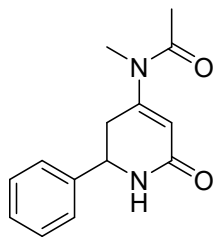
³ Stolyarov, I.P., Demina, L.I.; Cherkashina, N.V. *Russ. J. Inorg. Chem.* **2011**, *56*, 1532-1537.

⁴ Sheldrick, G.M. *Acta Cryst.* **2015**, *A71*, 3-8.

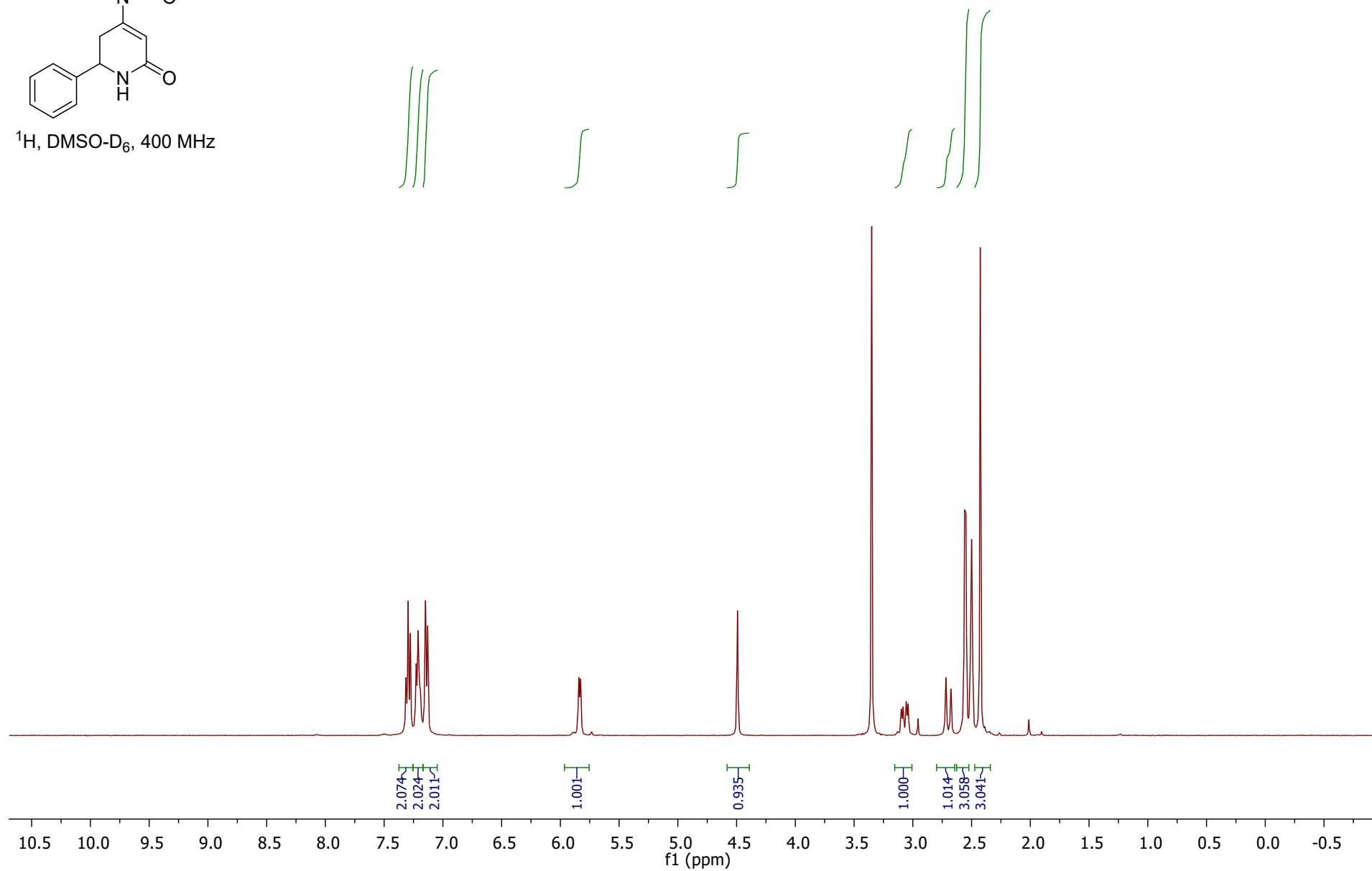
⁵ Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J.A.K.; Puschmann, H. *J. Appl. Cryst.* **2009**, *42*, 339-341.

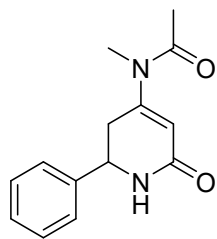
⁶ Sheldrick, G.M. *Acta Cryst.* **2008**, *A64*, 112-122.

⁷ Spek, A.L. *Acta Cryst. D* **2009**, *65*, 148-155.



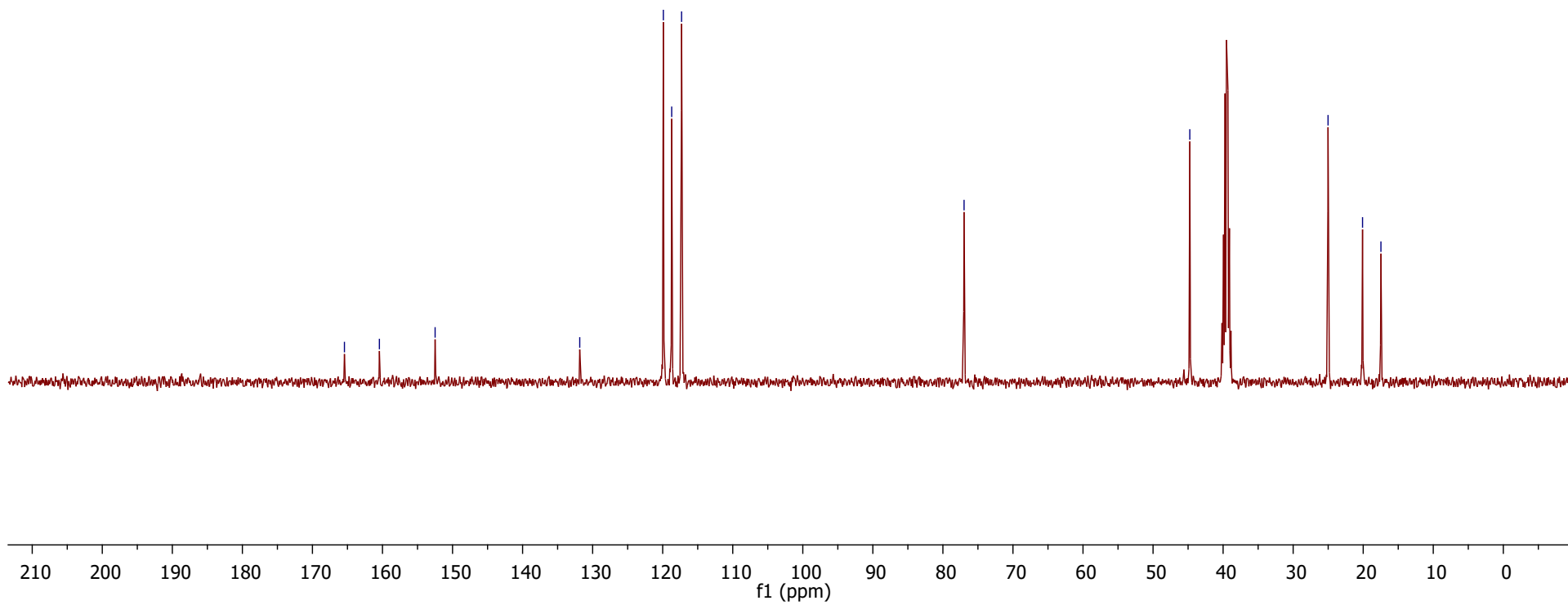
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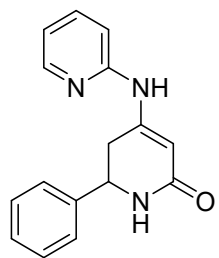




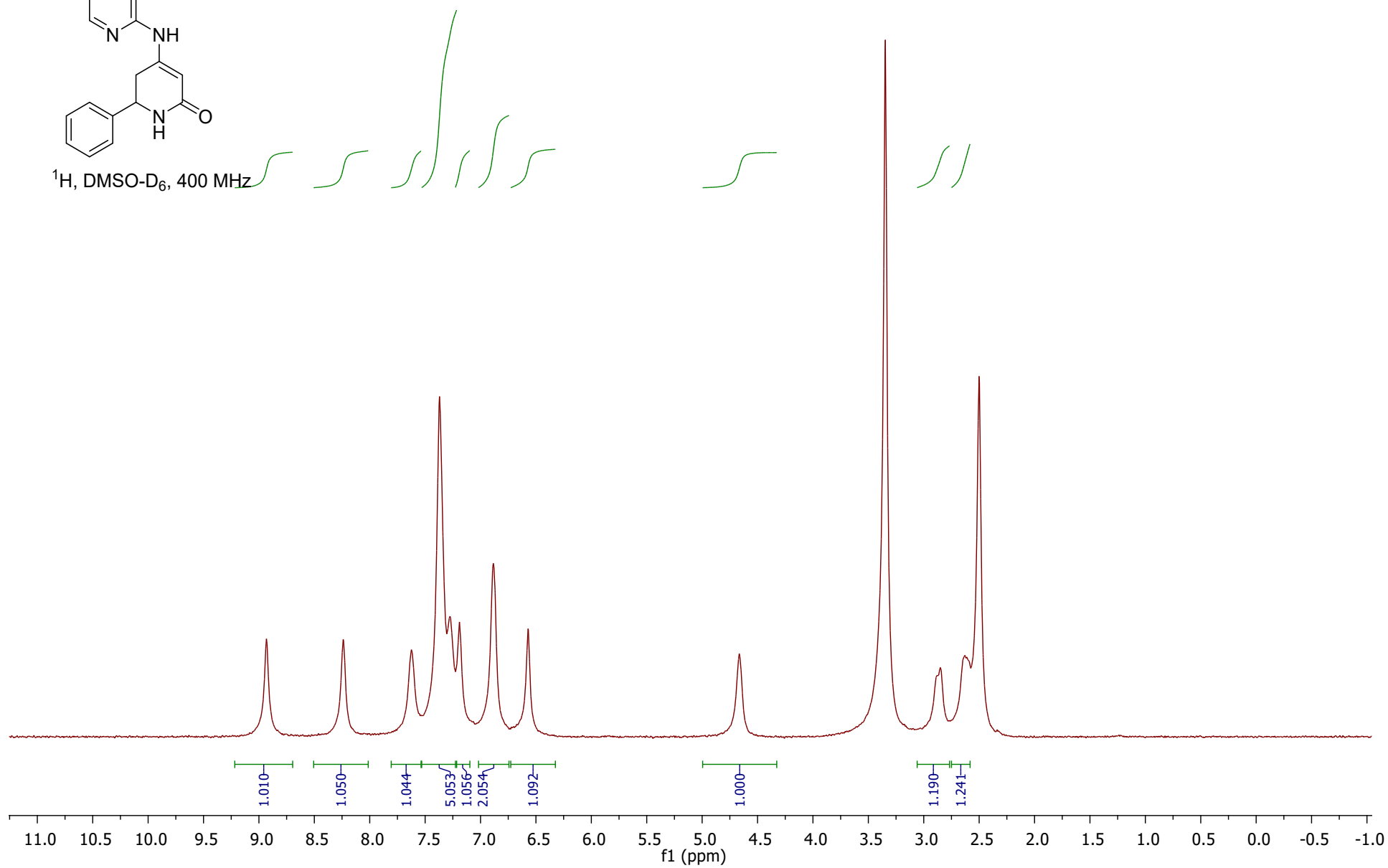
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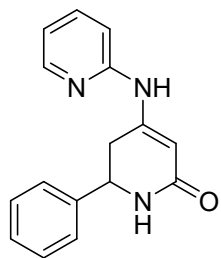
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- 160.4415
- 152.4877
- 131.8419
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- 25.0198
- 20.0949
- 17.4703



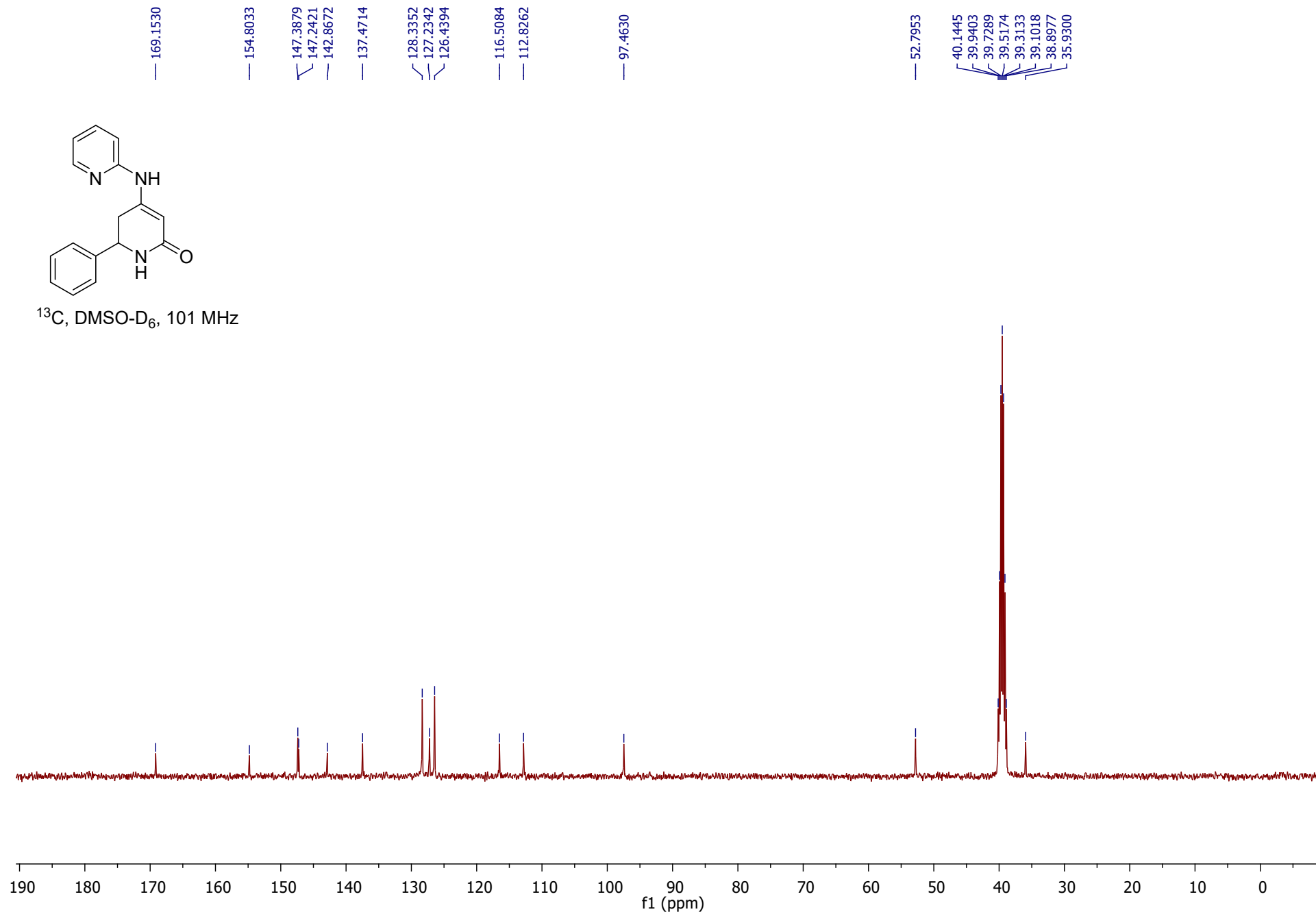


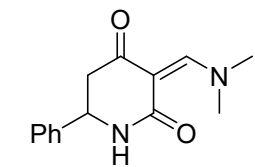
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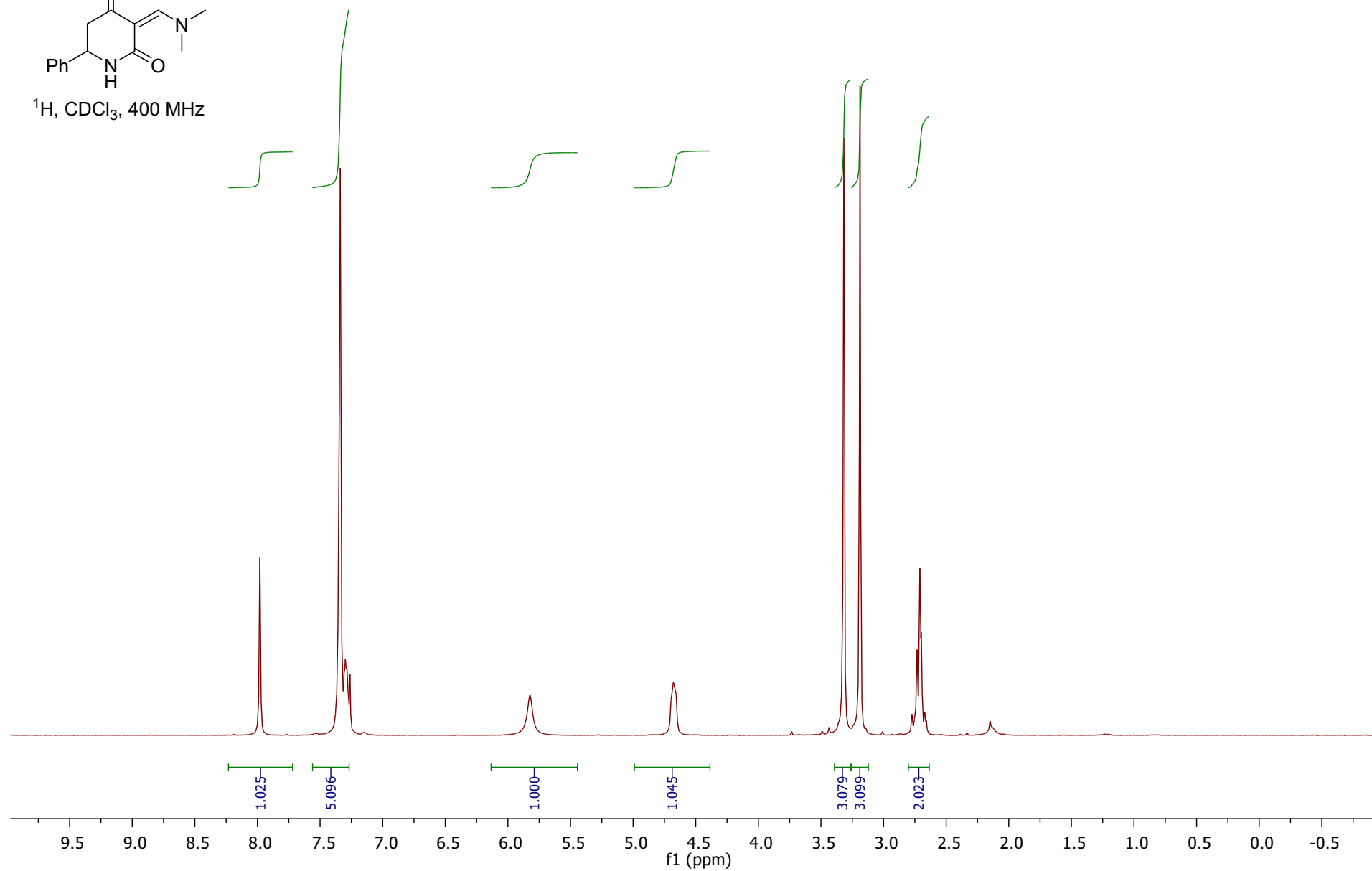


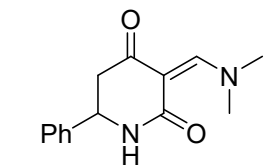
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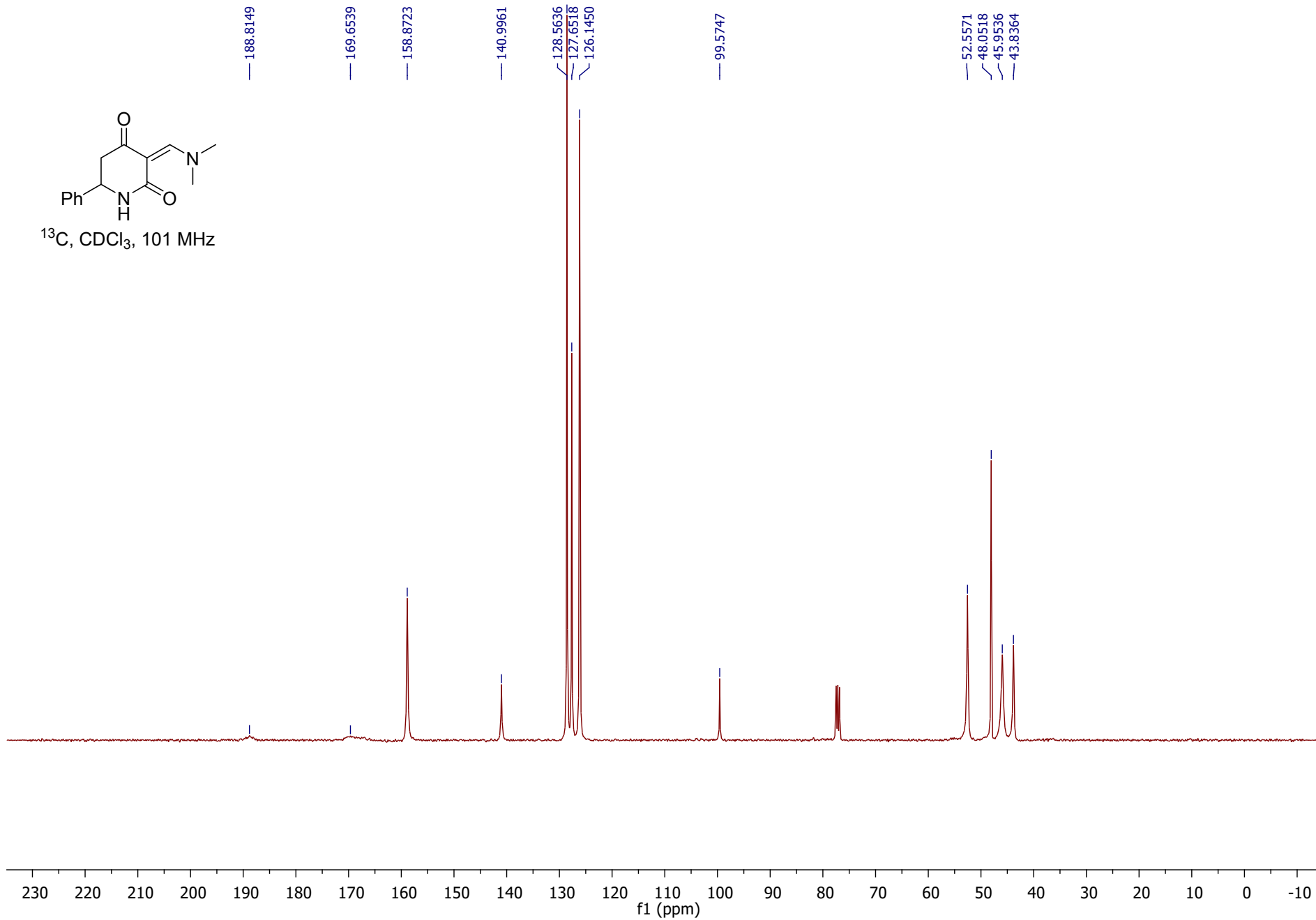


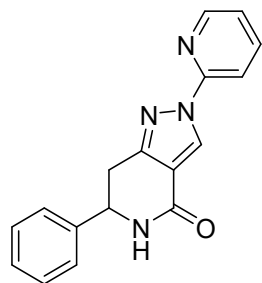
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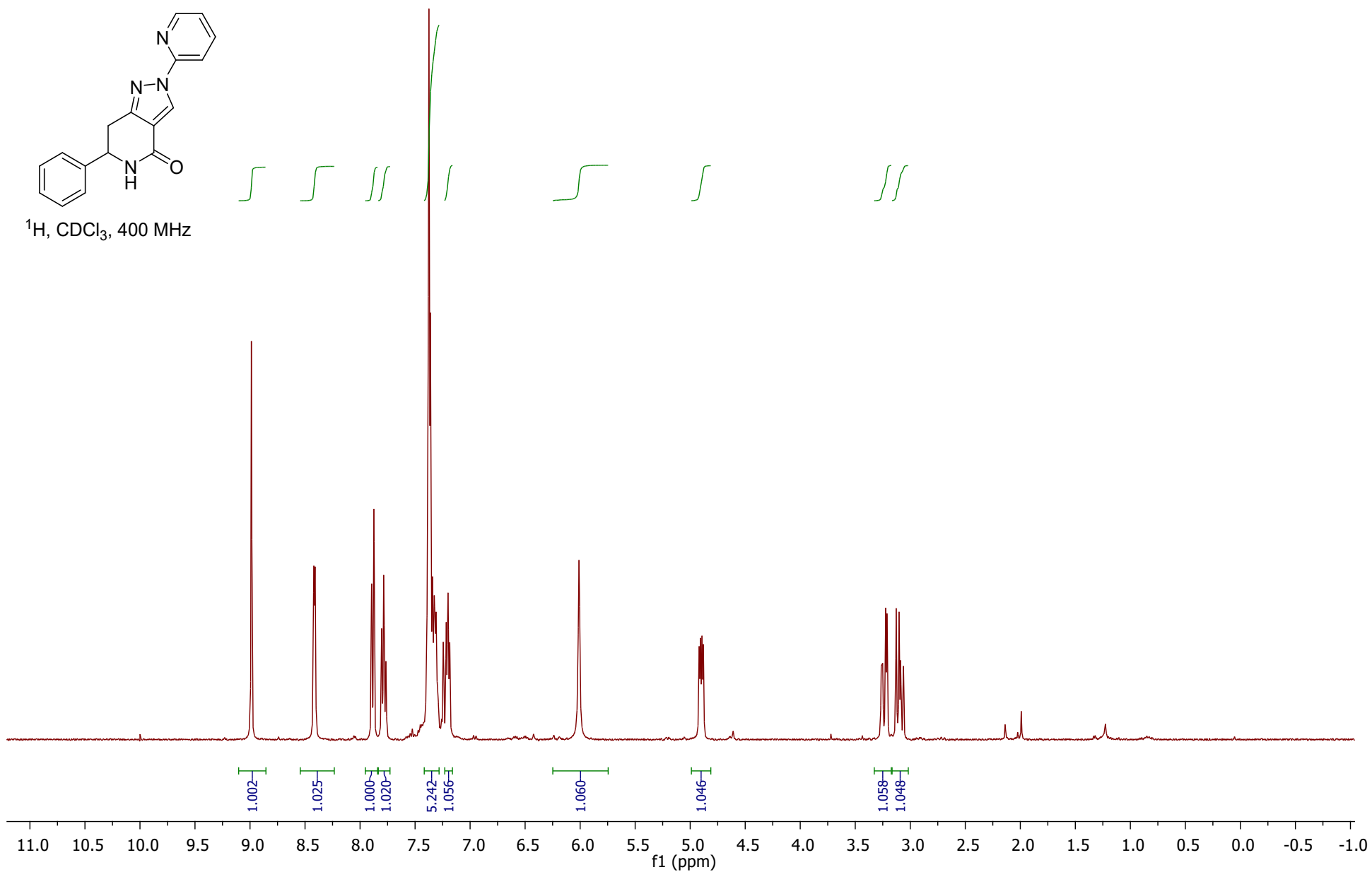


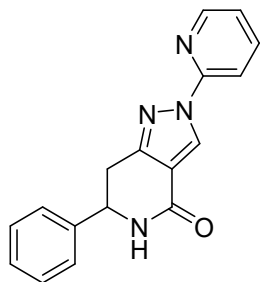
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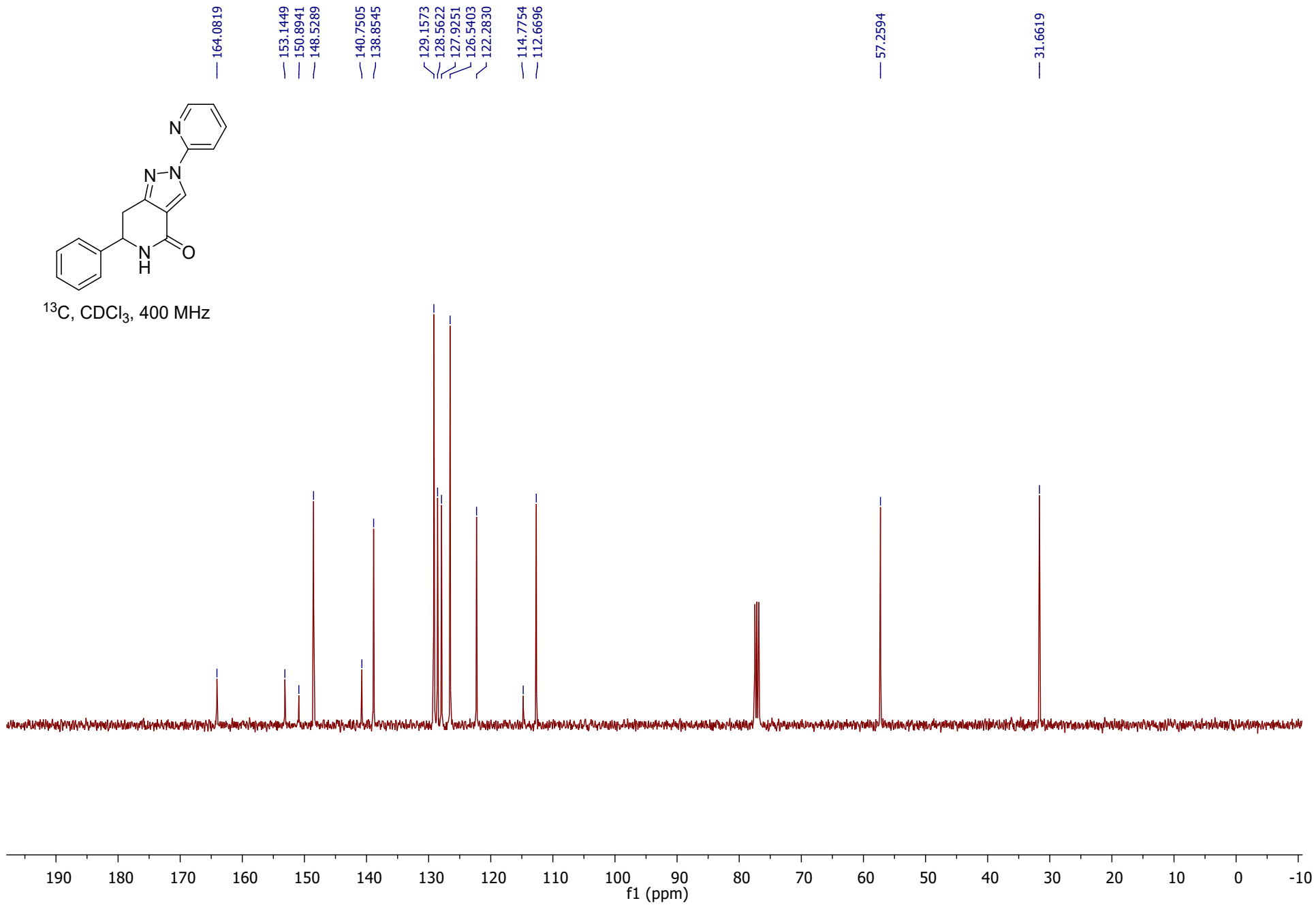


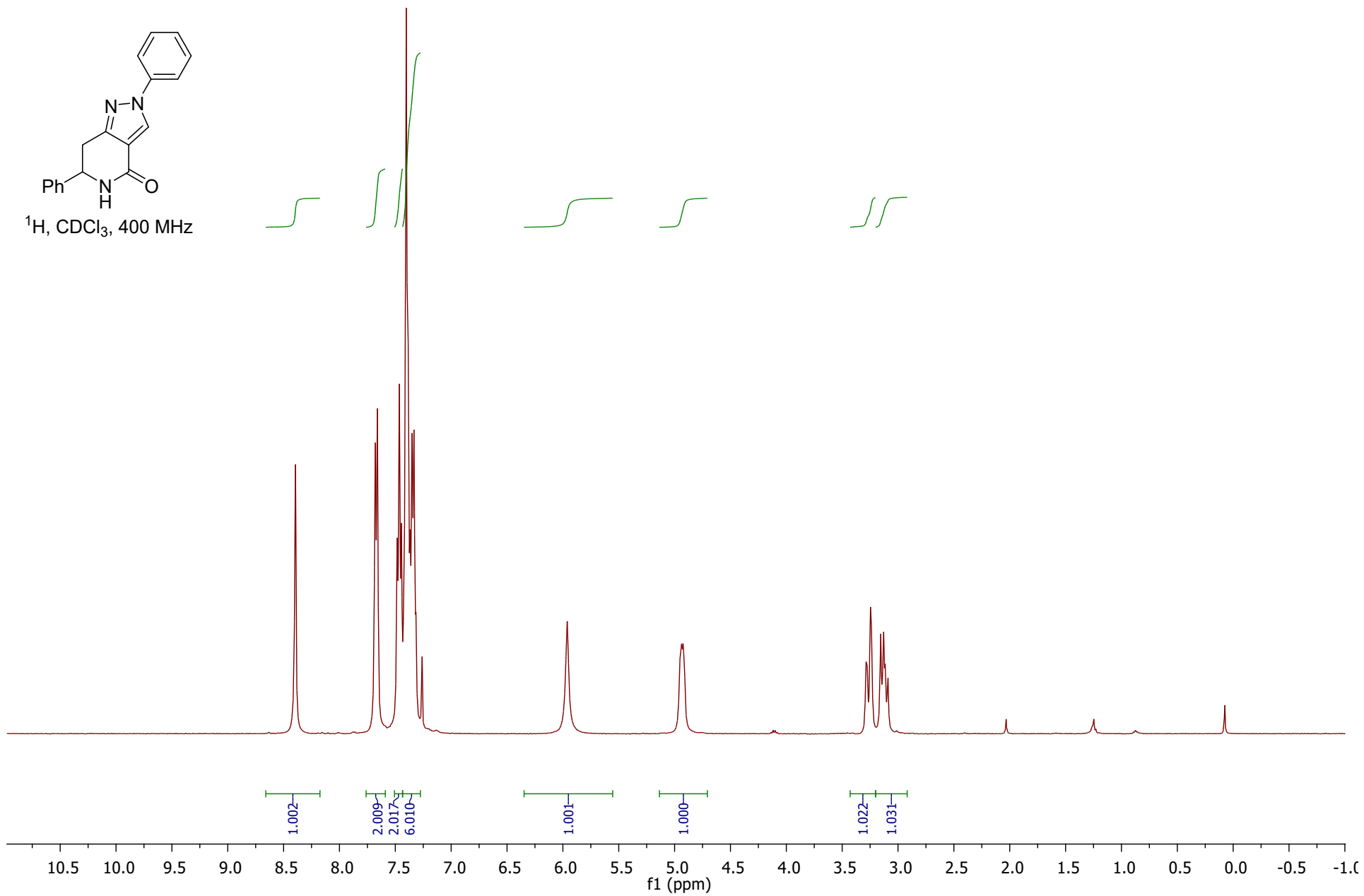
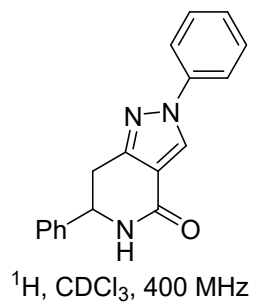
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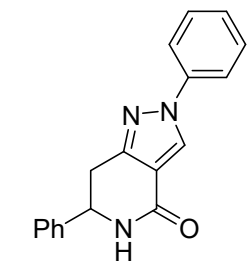




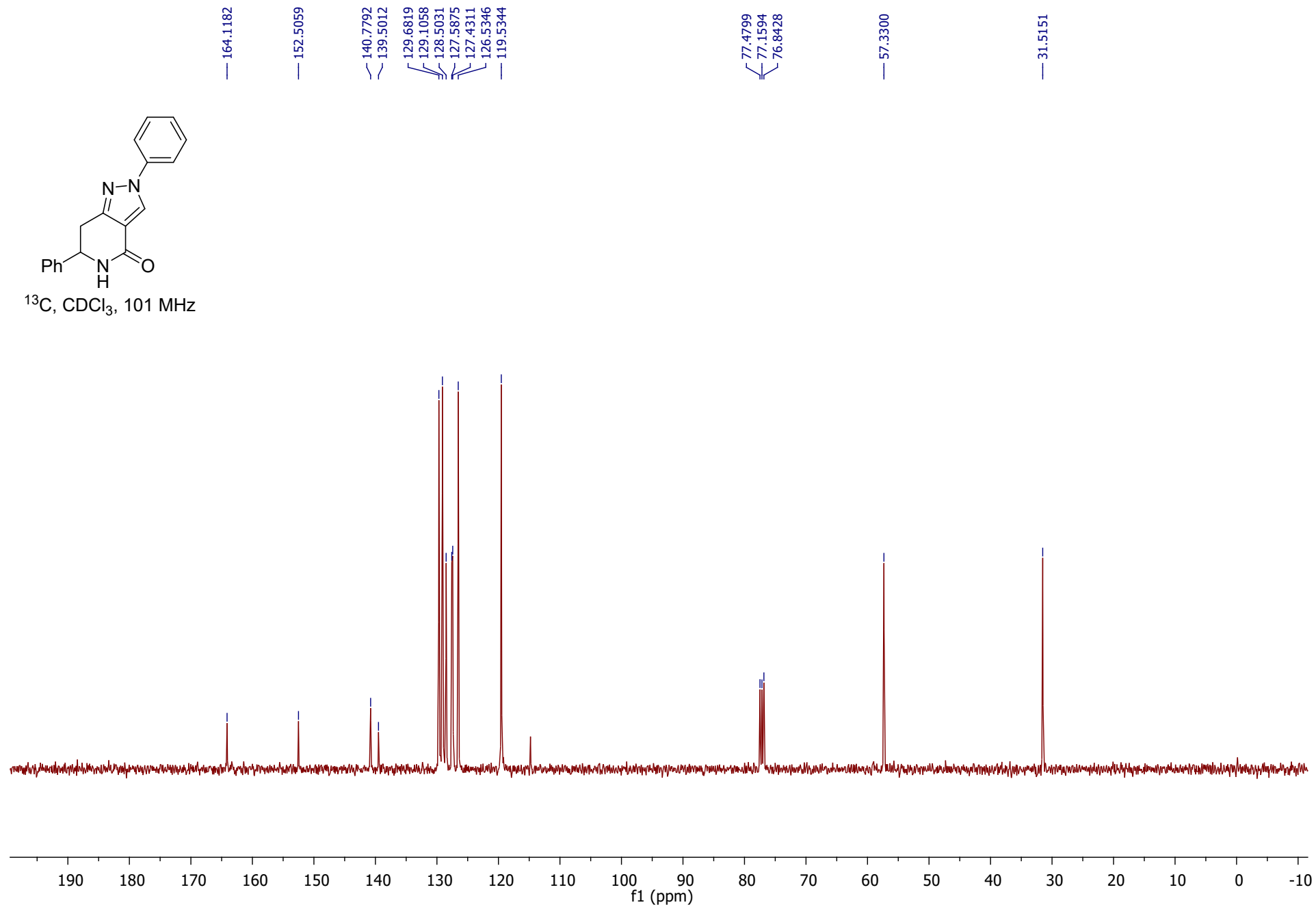
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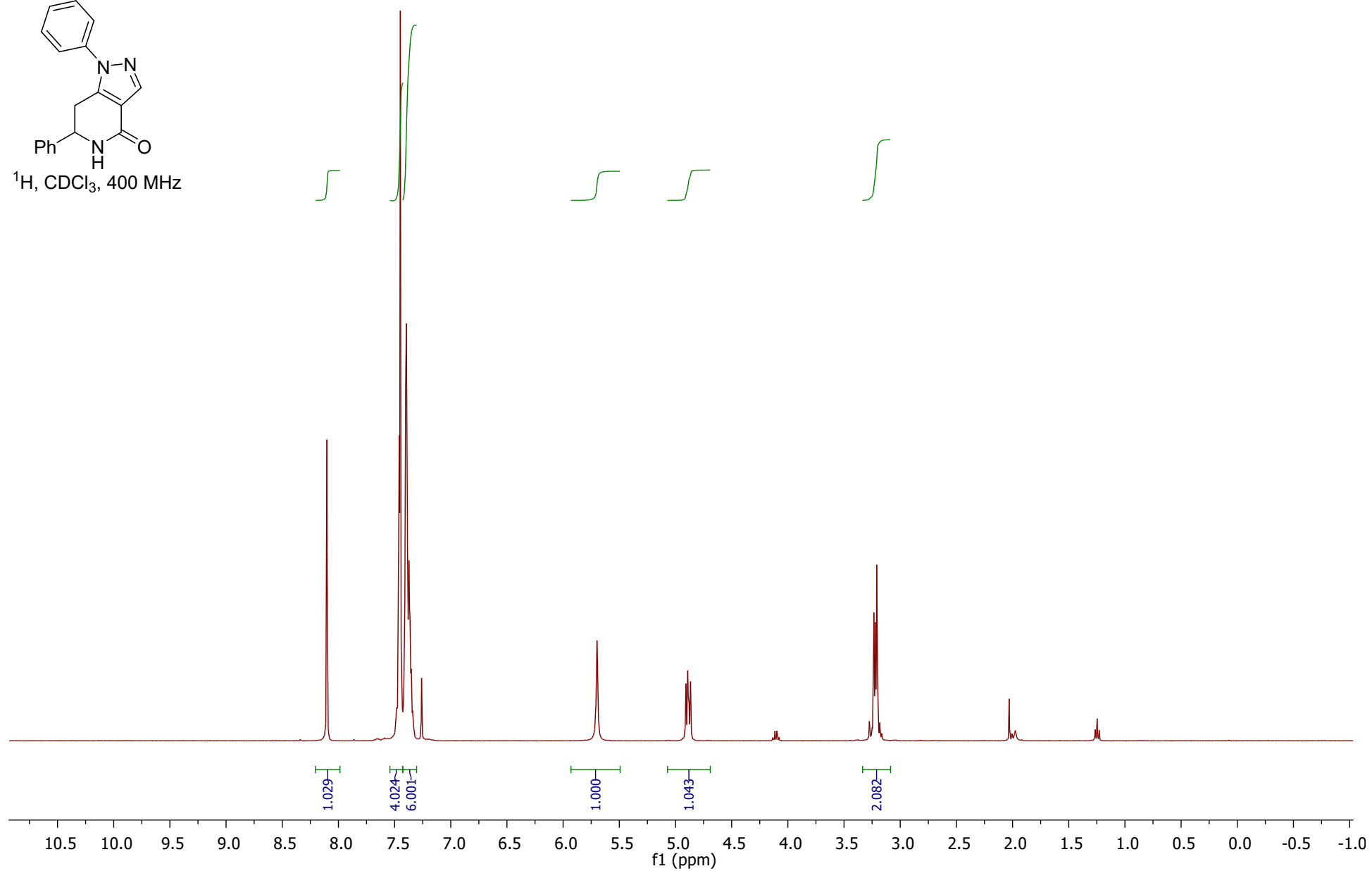
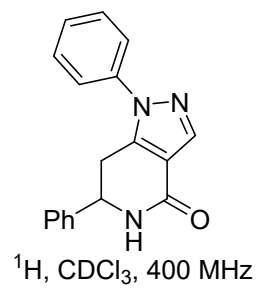


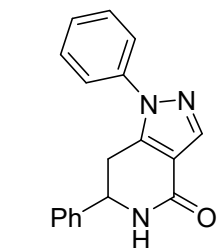




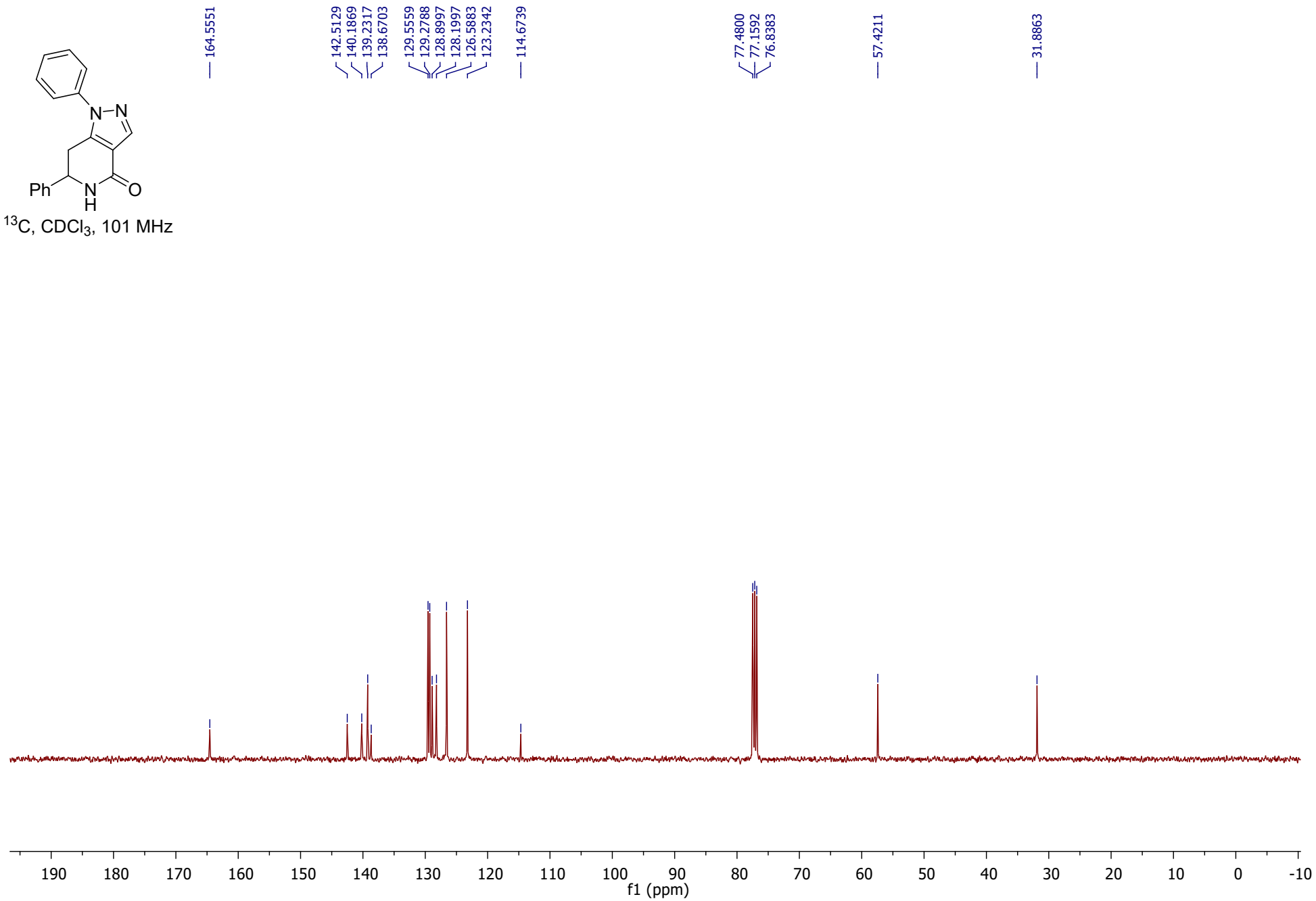
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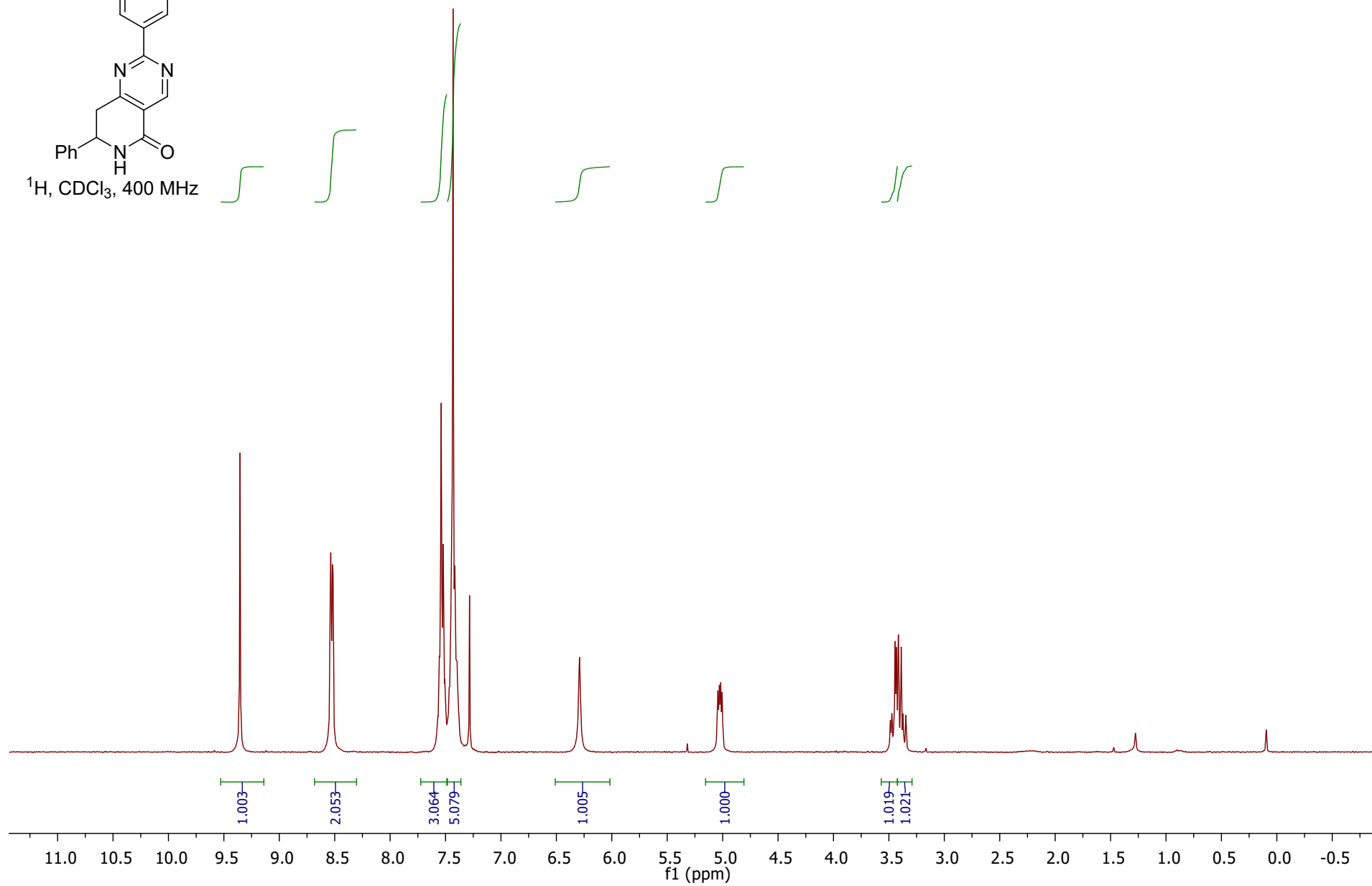
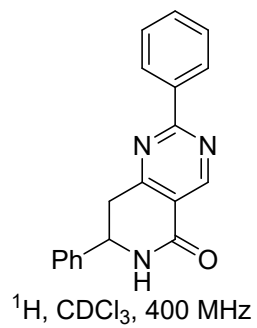


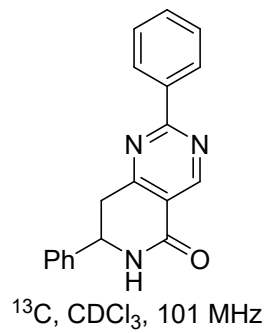




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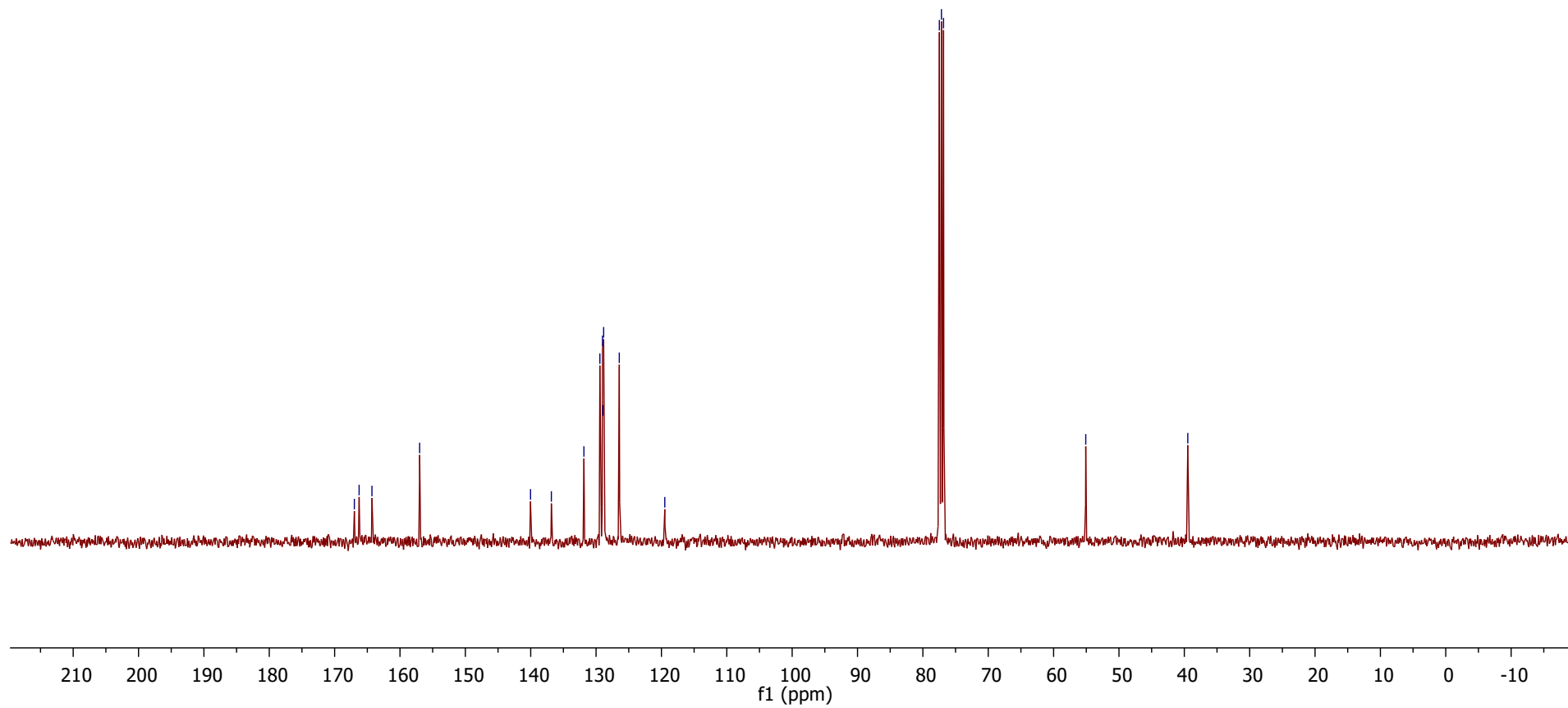
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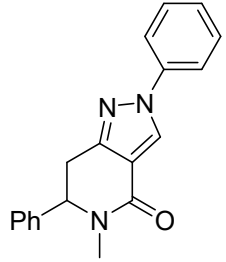
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128.8409
126.4493
— 119.4859

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77.1587
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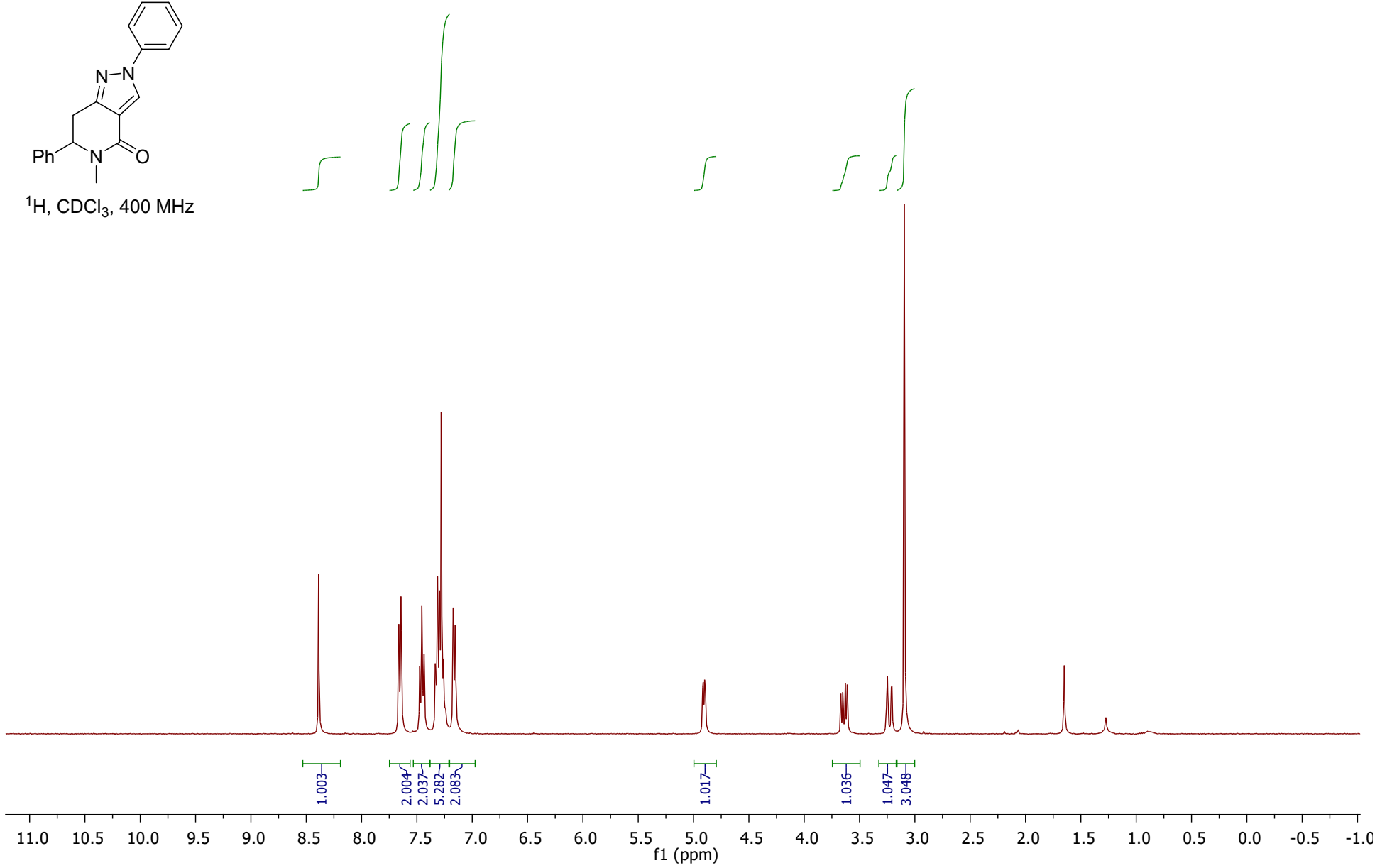
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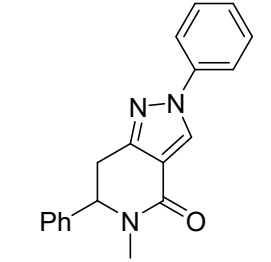
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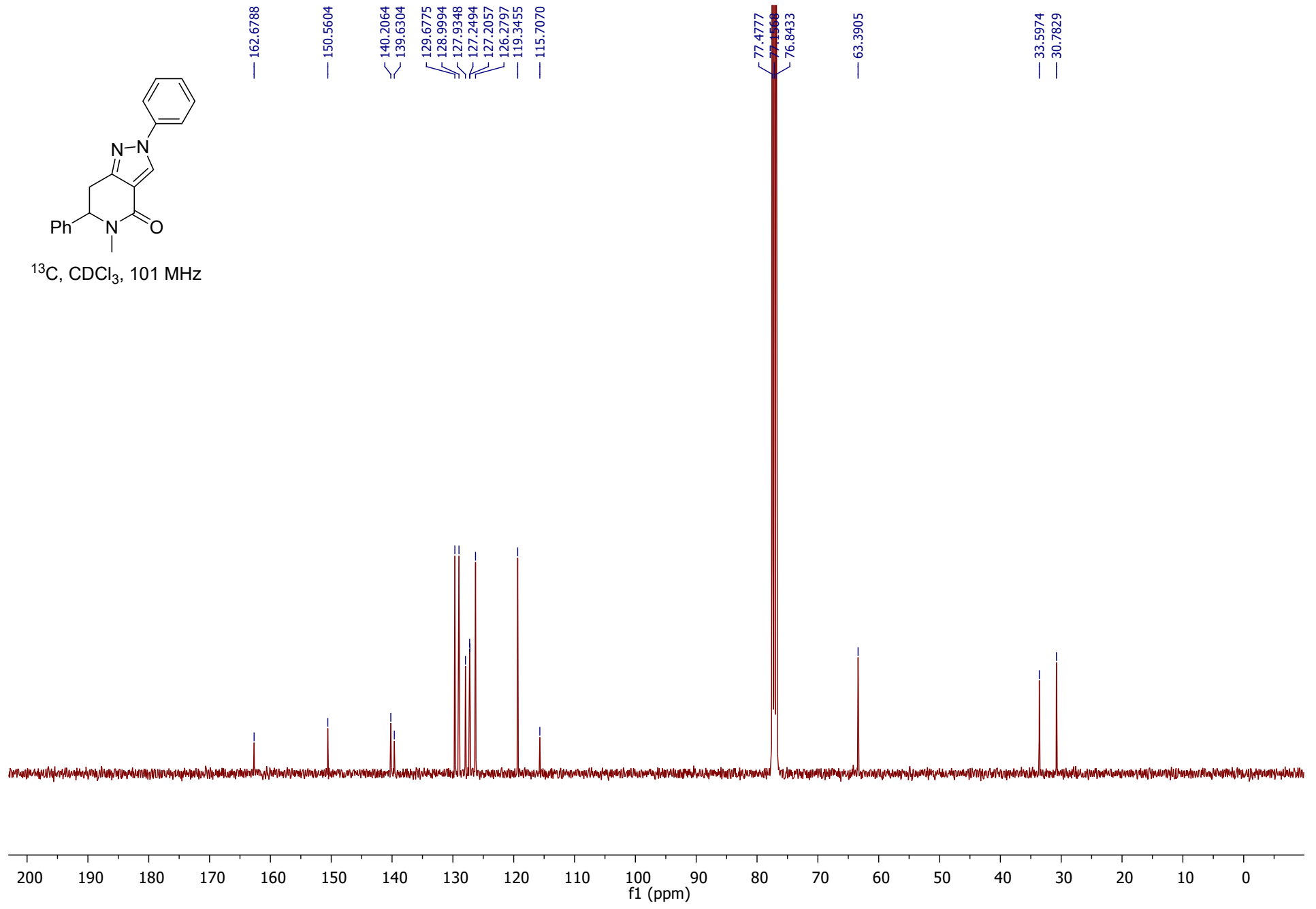


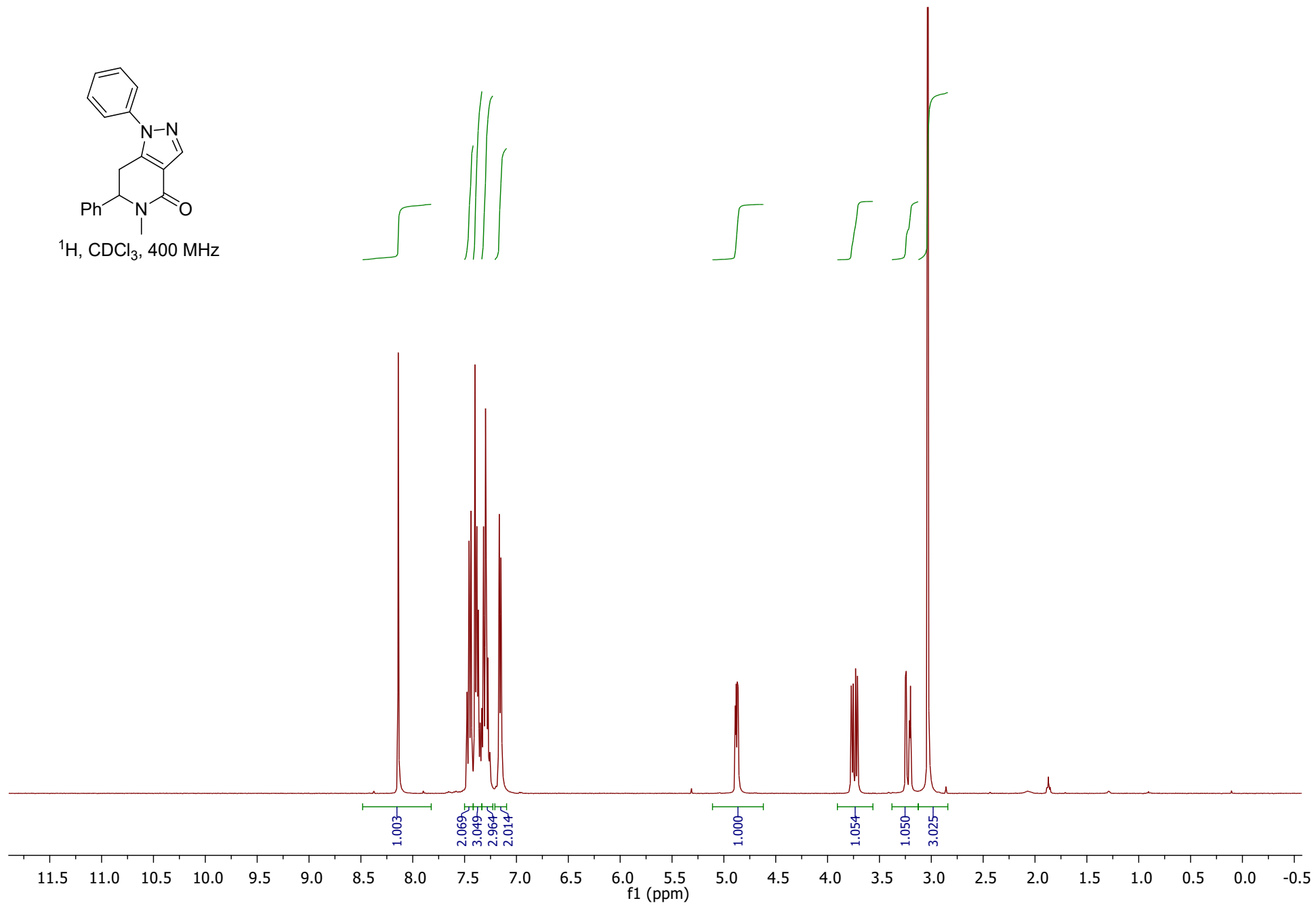
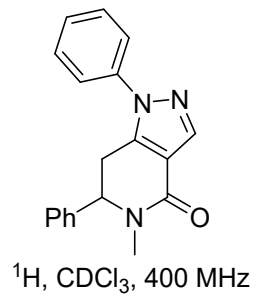
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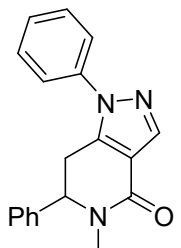




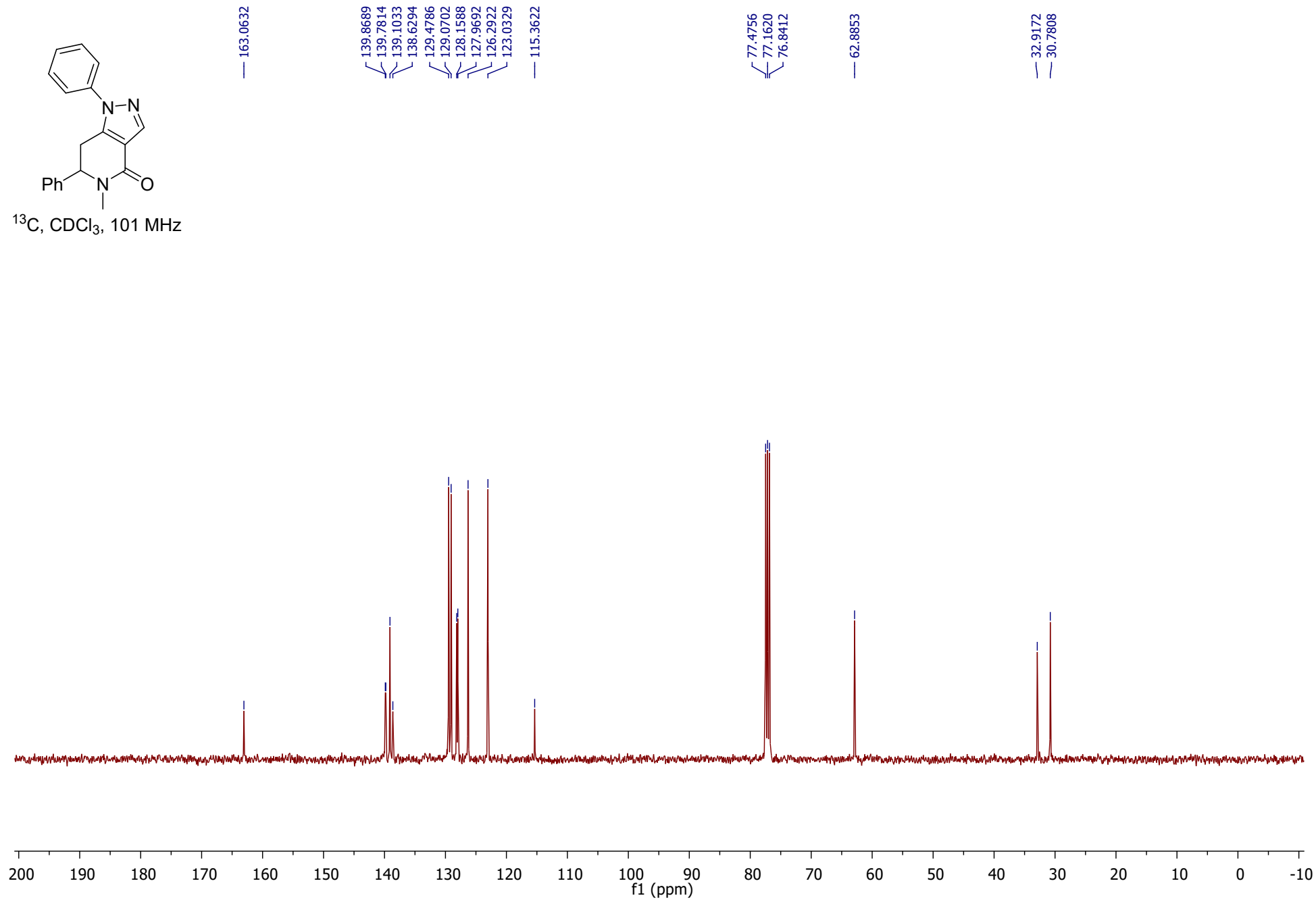
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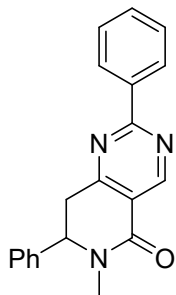




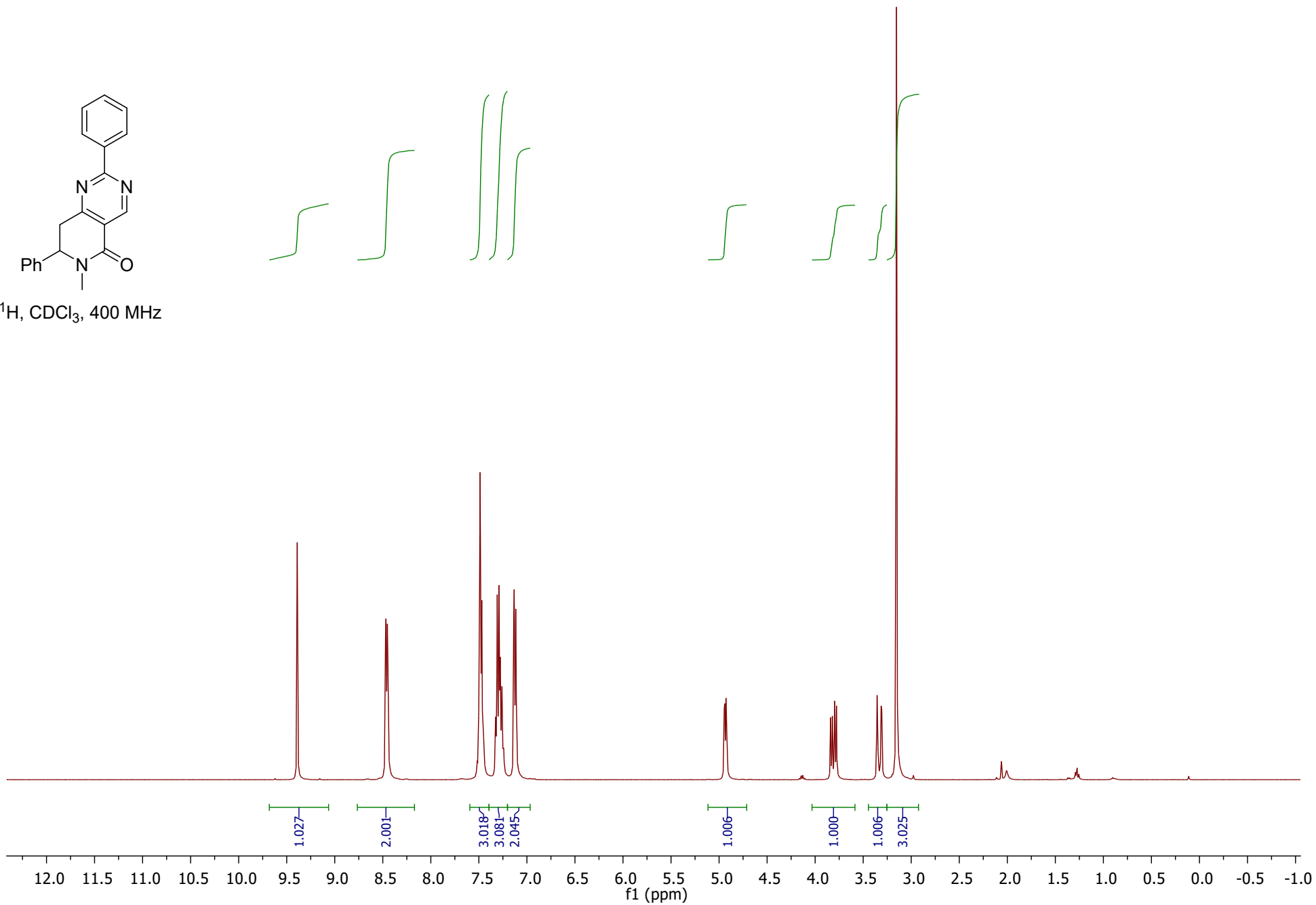


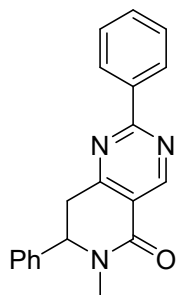
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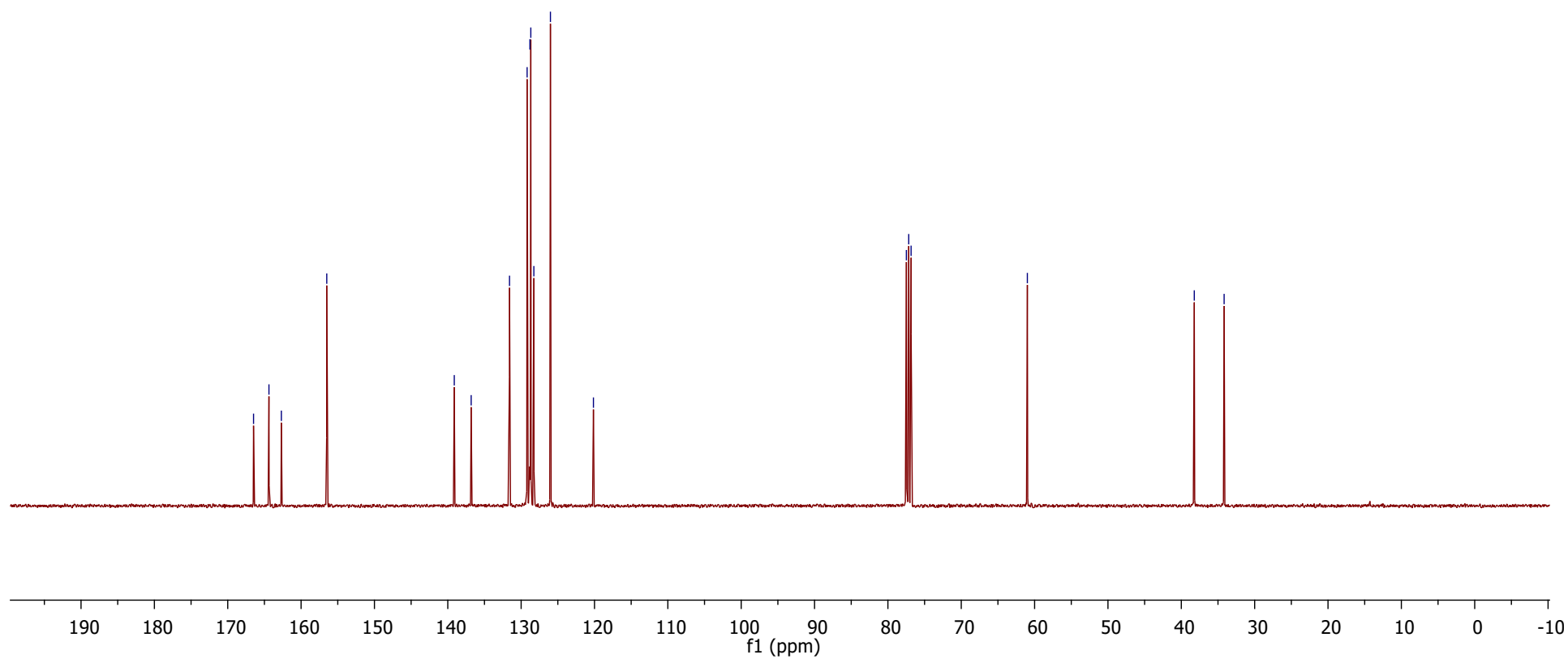
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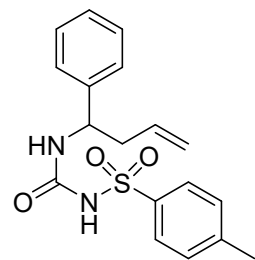
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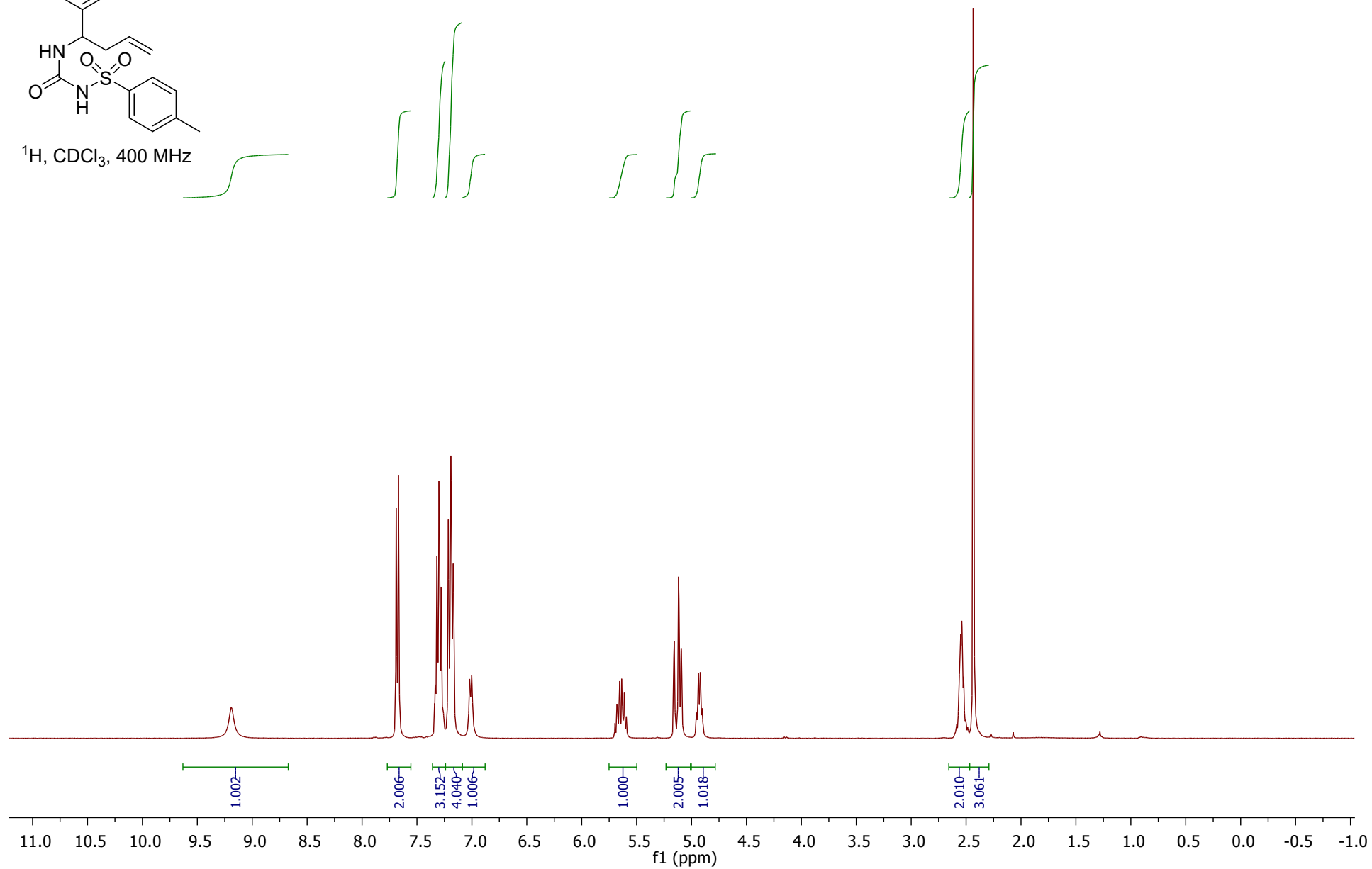
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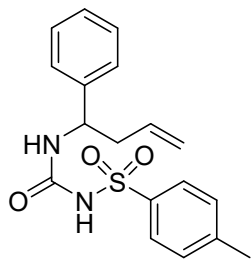
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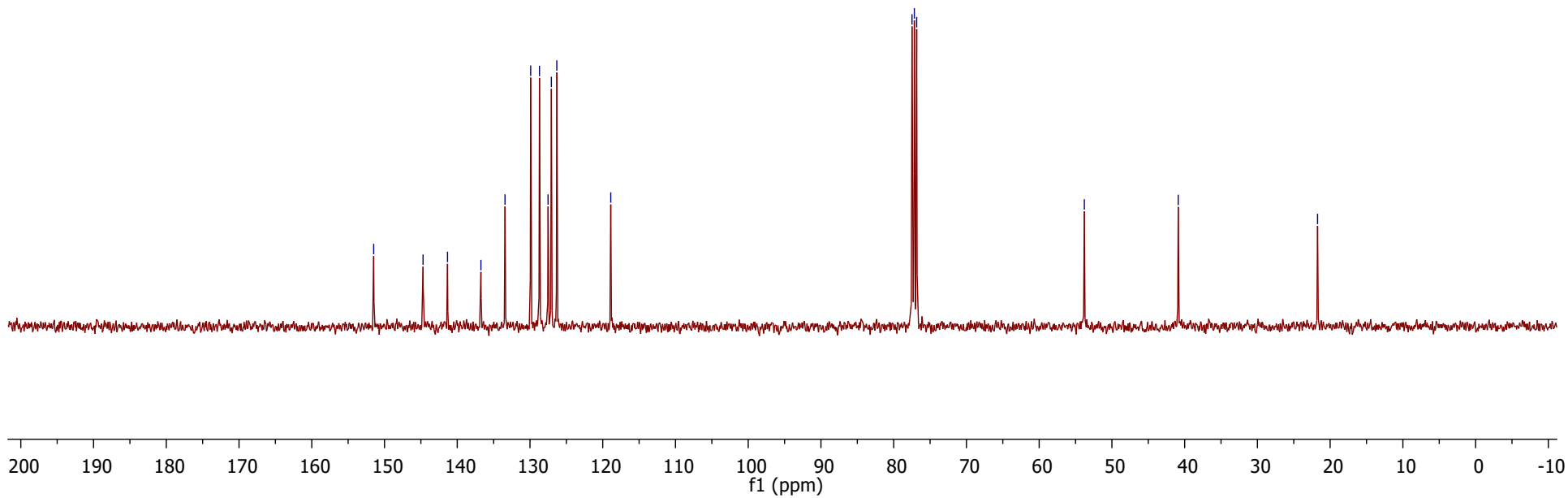
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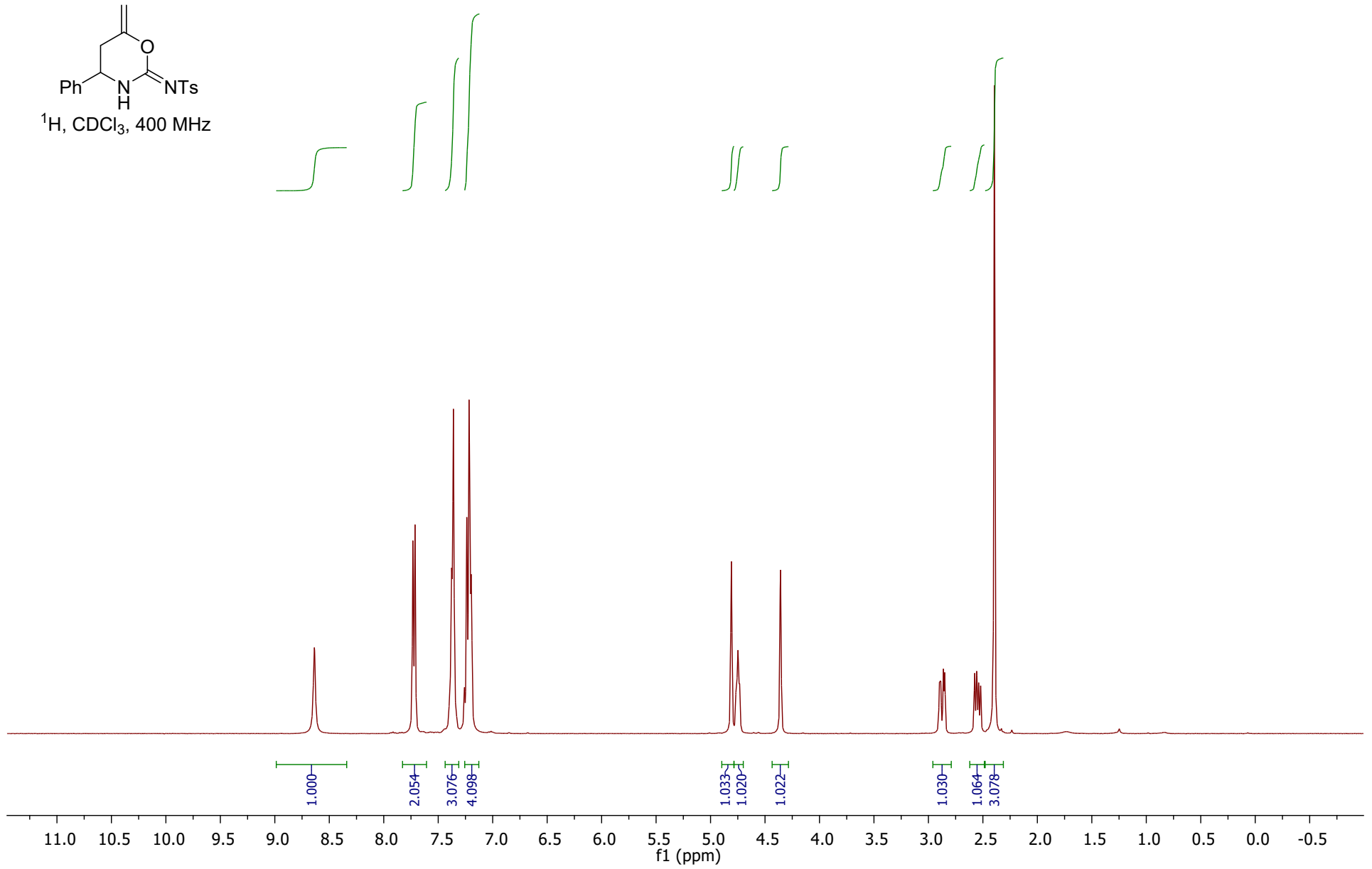
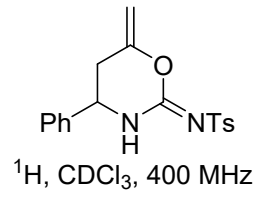
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{ 77.1596
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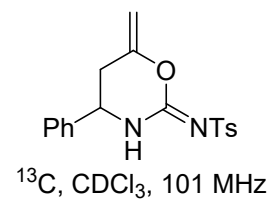
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— 40.8844

— 21.7296







— 154.5295
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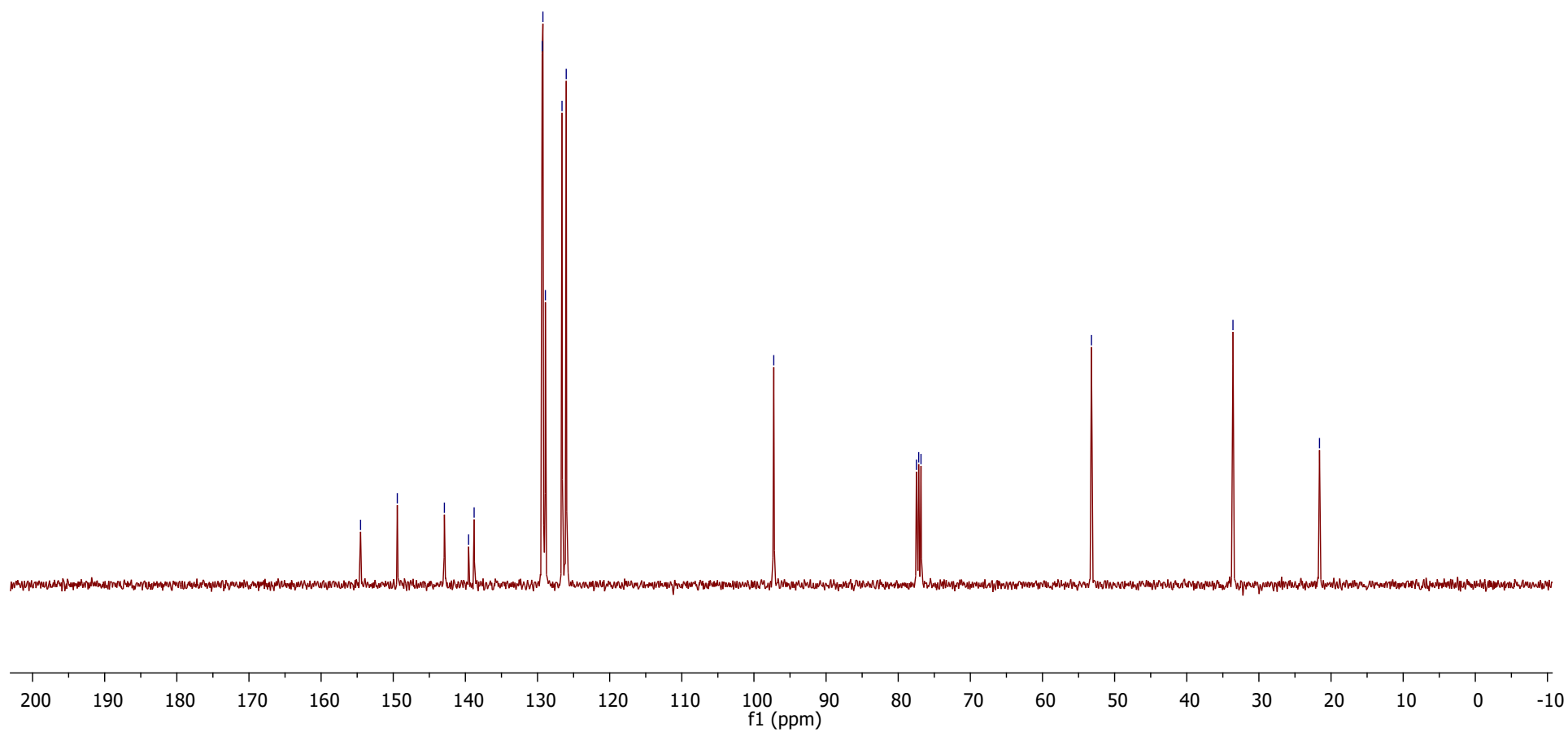
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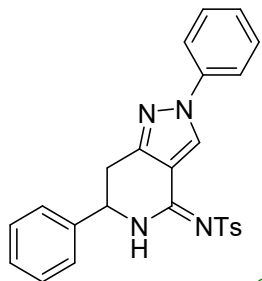
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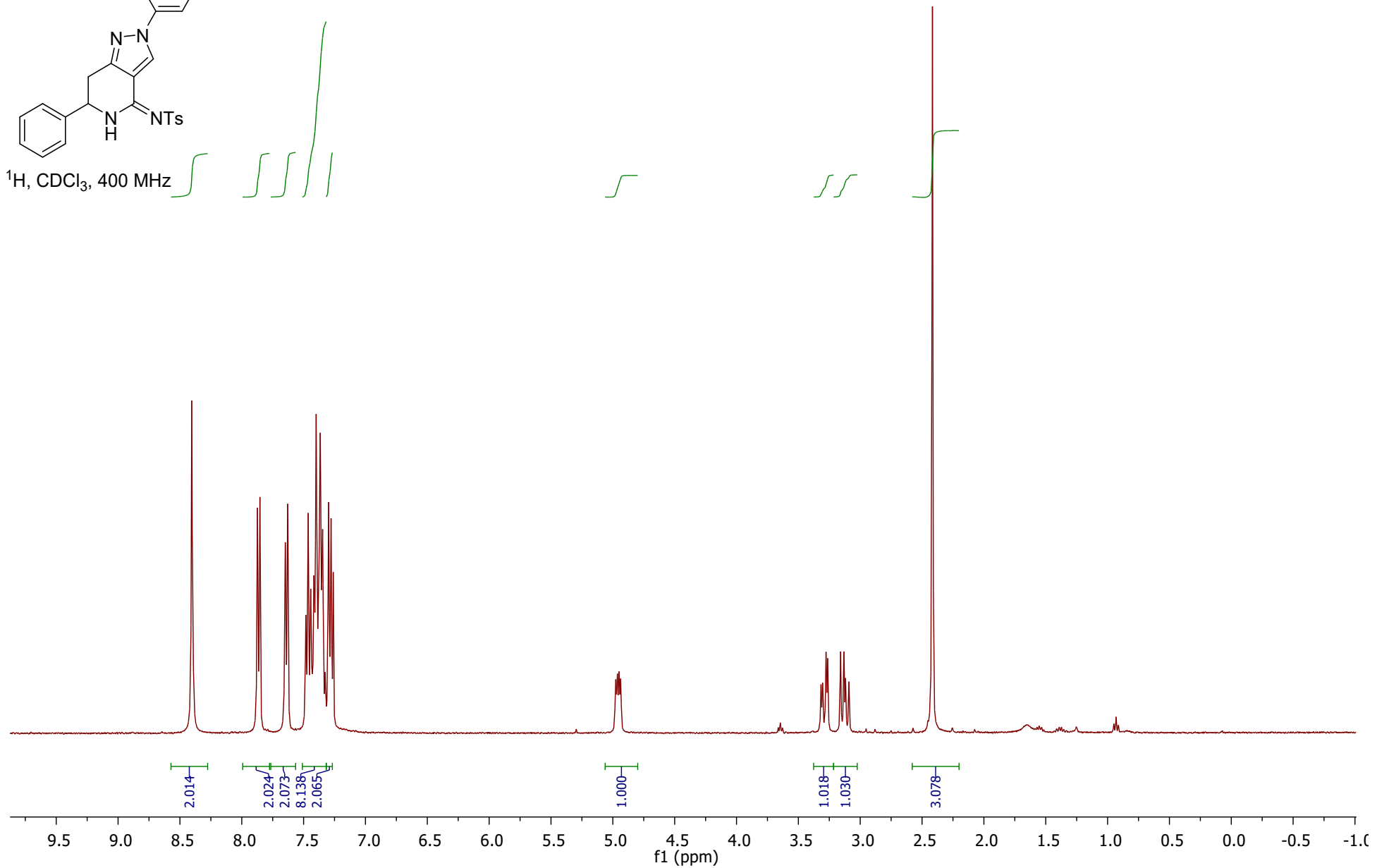
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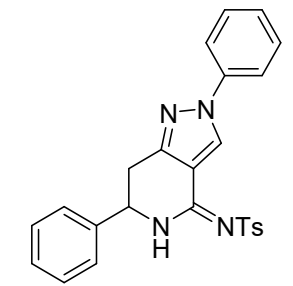
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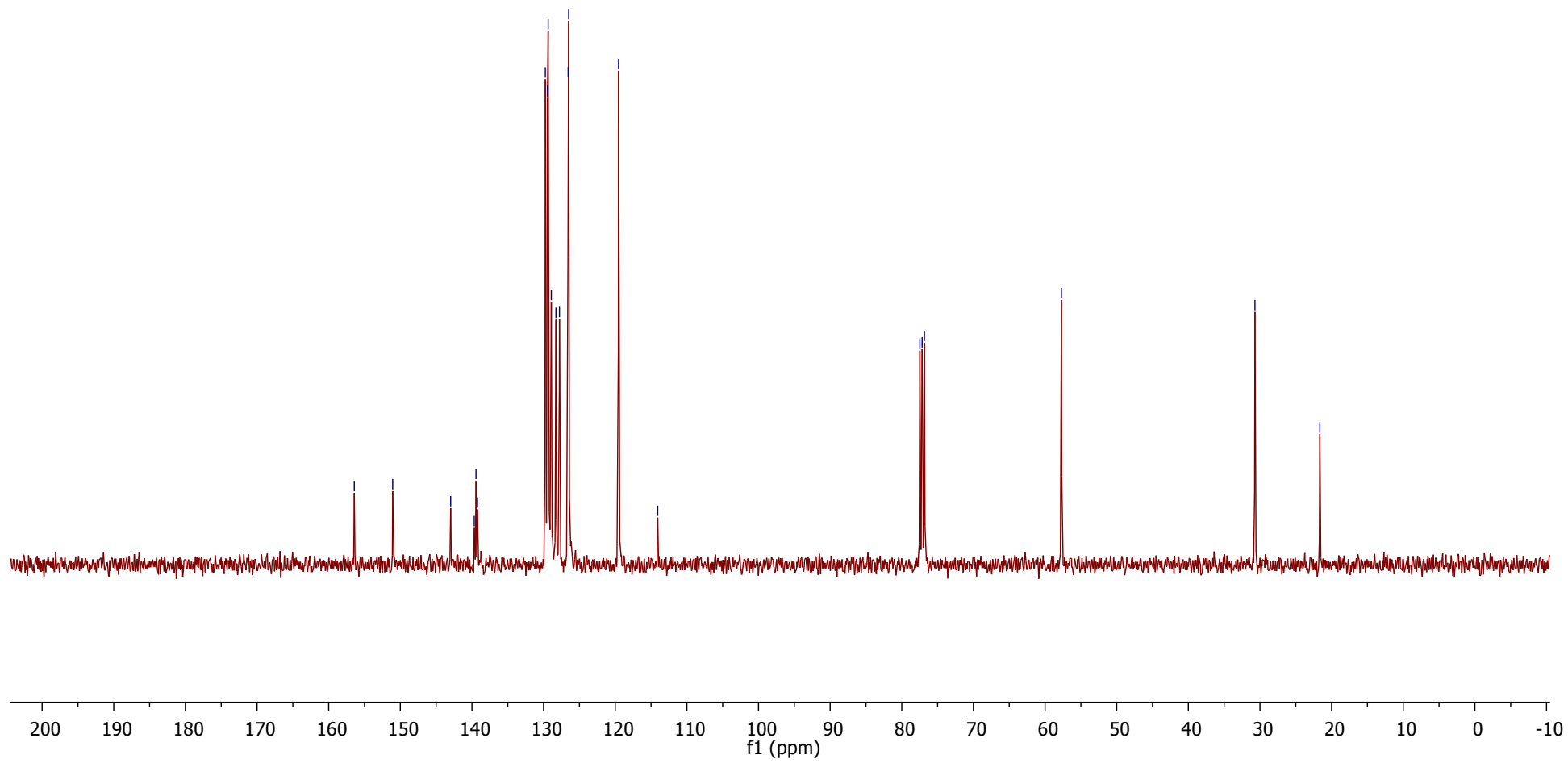
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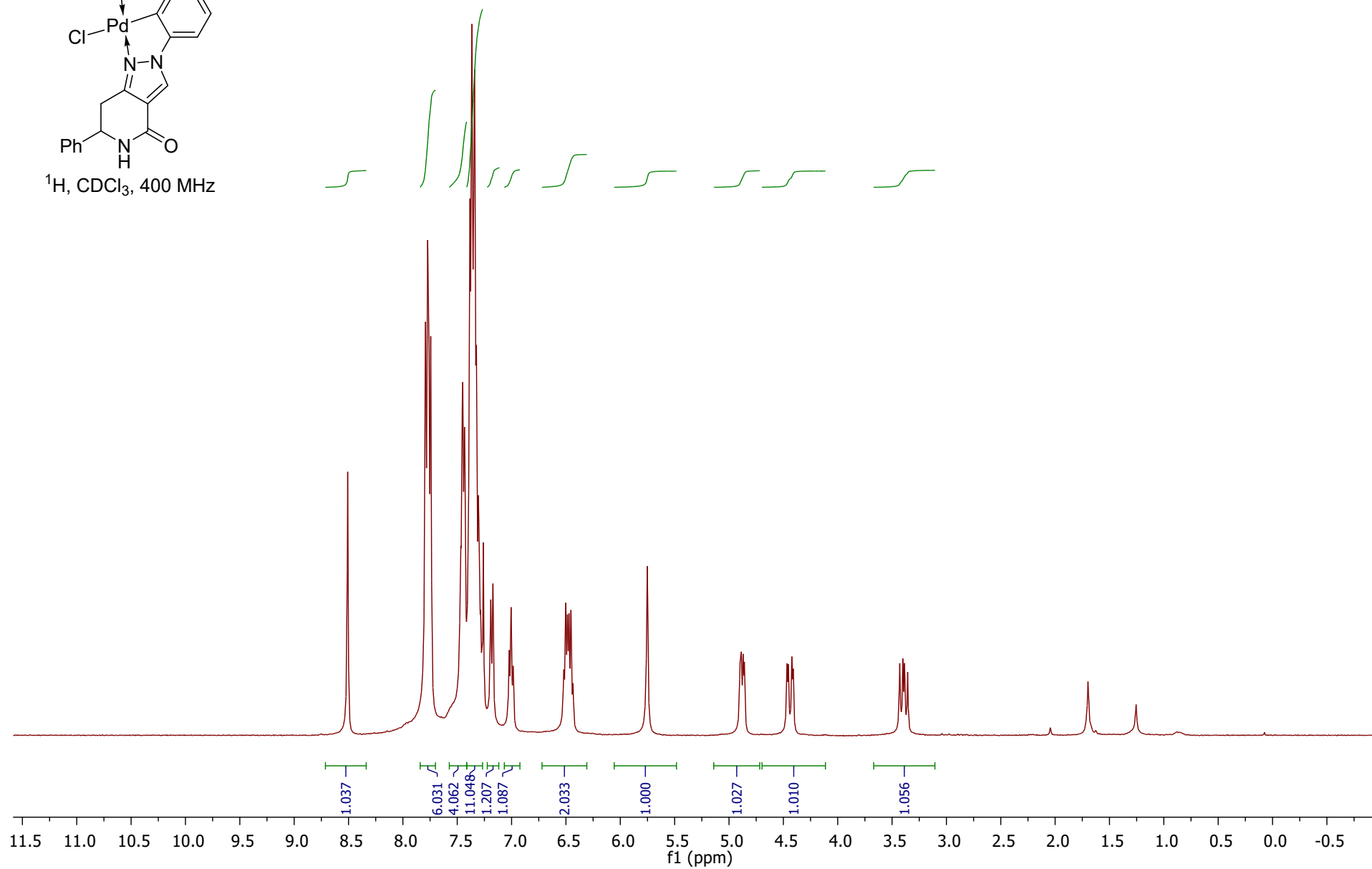
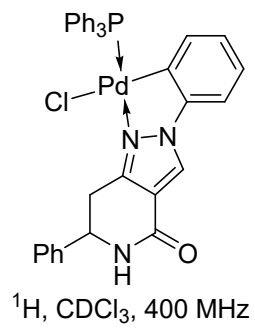


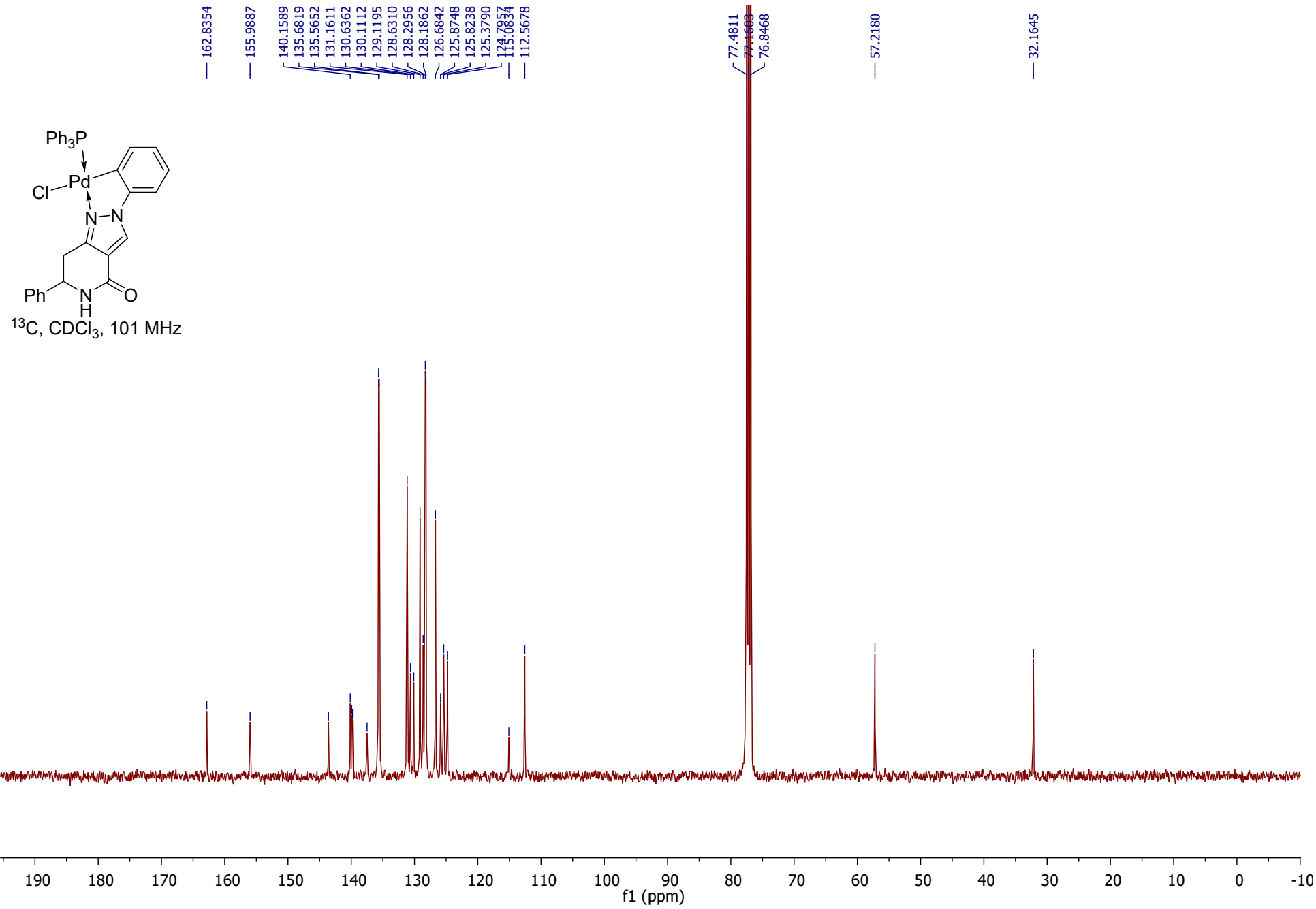


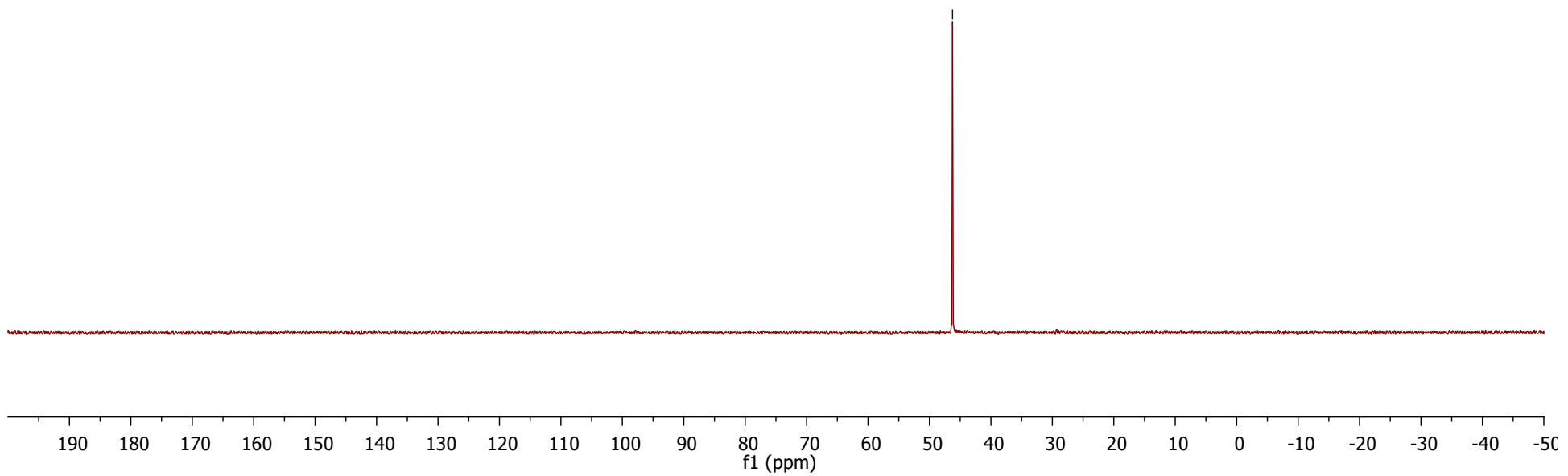
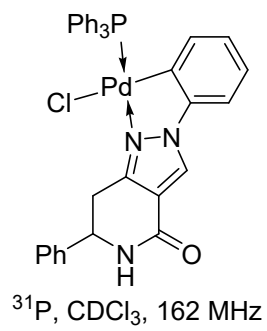
^{13}C , CDCl_3 , 101 MHz

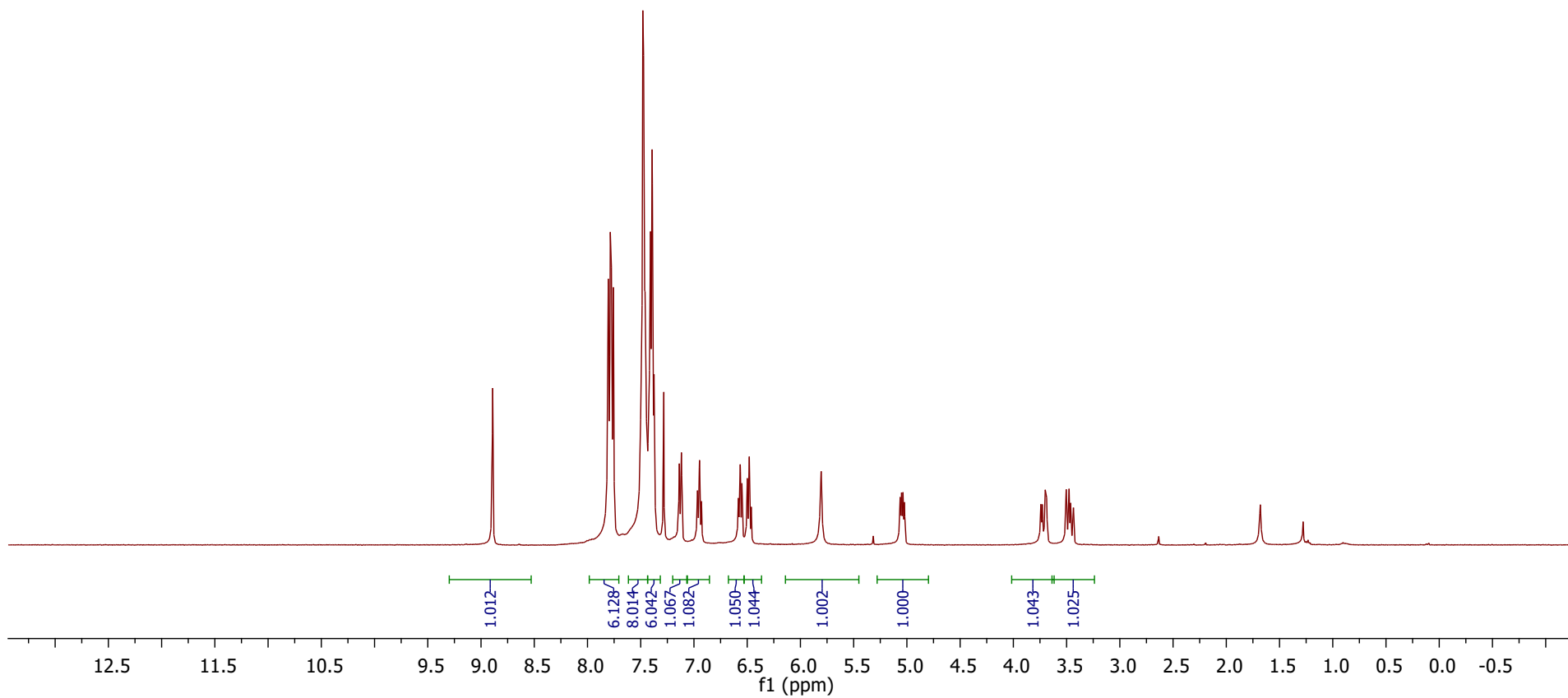
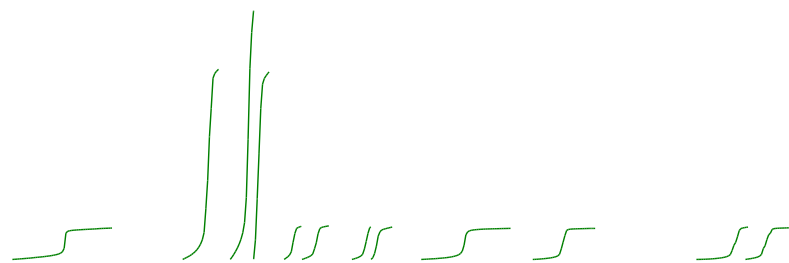
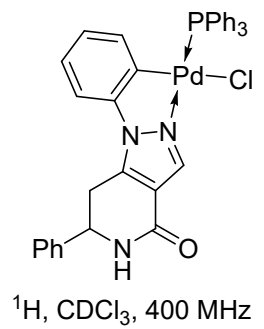
- 156.4240
- 151.0604
- 142.9692
- 139.6808
- 139.4367
- 139.2307
- 129.7585
- 129.4609
- 129.3617
- 126.5731
- 119.5995
- 114.0681
- 77.4802
- 77.1597
- 76.8431
- 57.7156
- 30.6990
- 21.6388

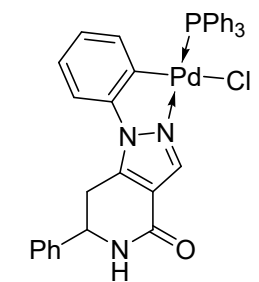




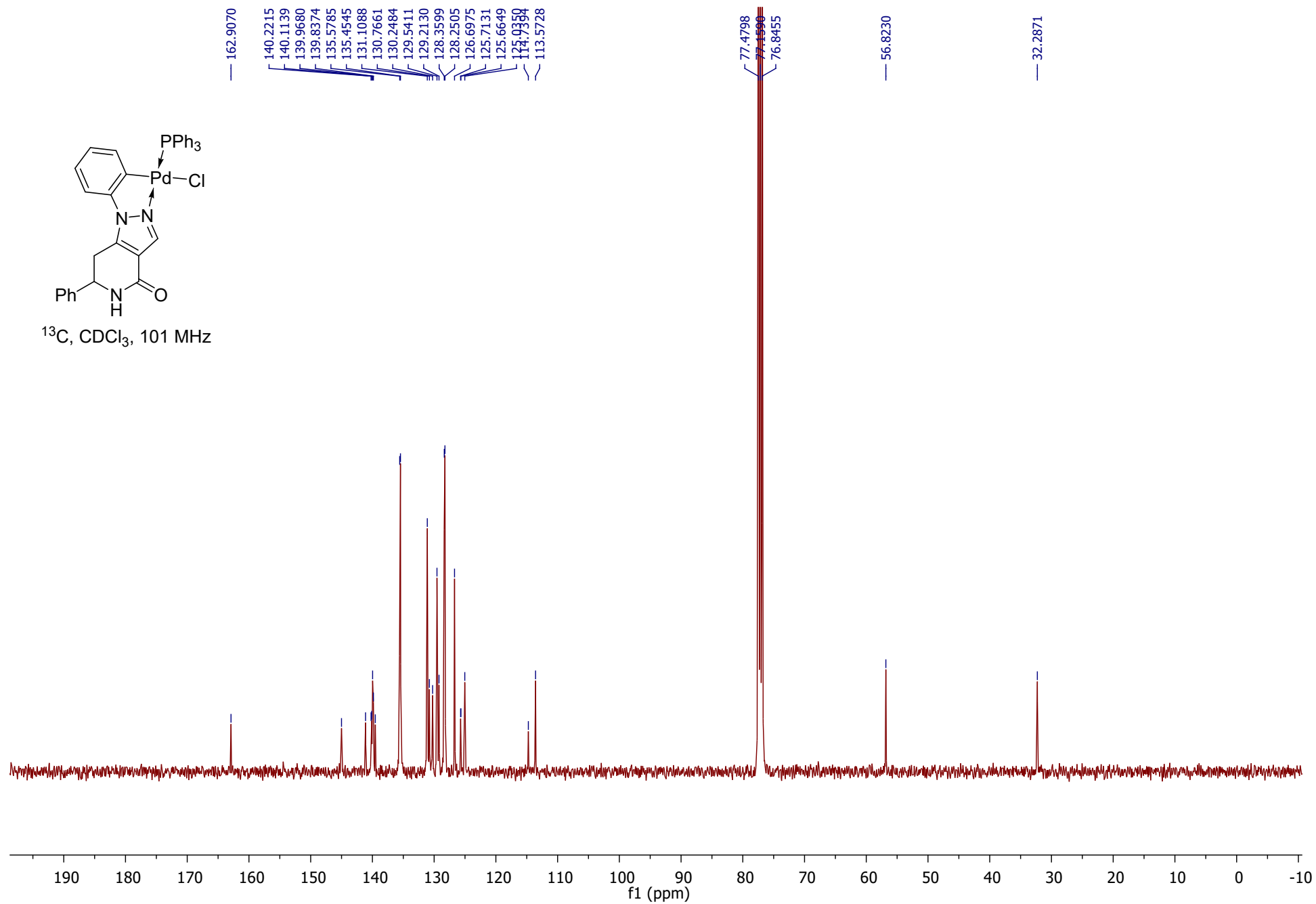


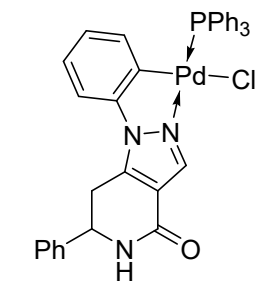






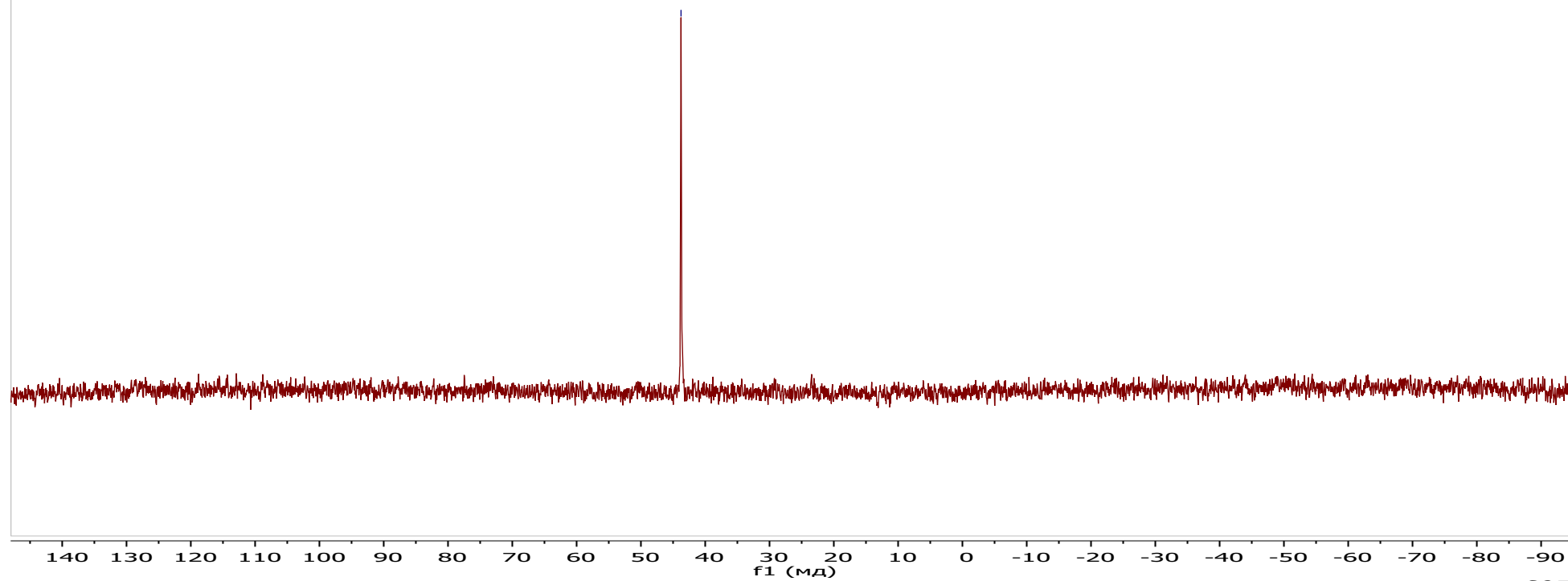
¹³C, CDCl₃, 101 MHz

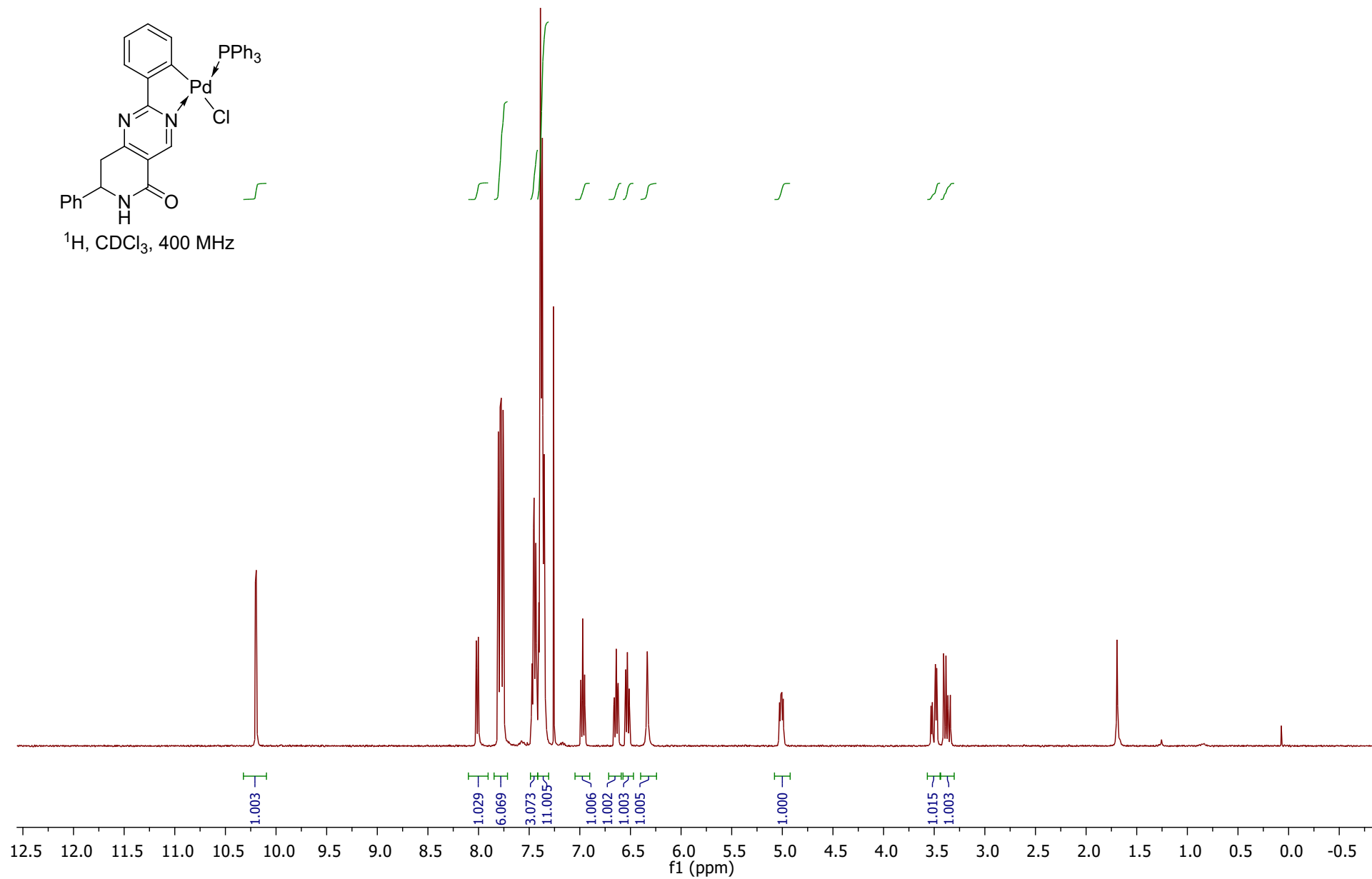
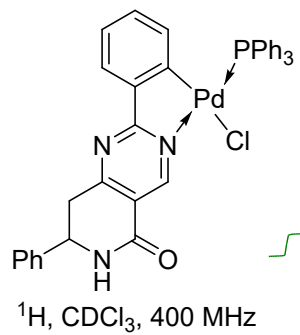


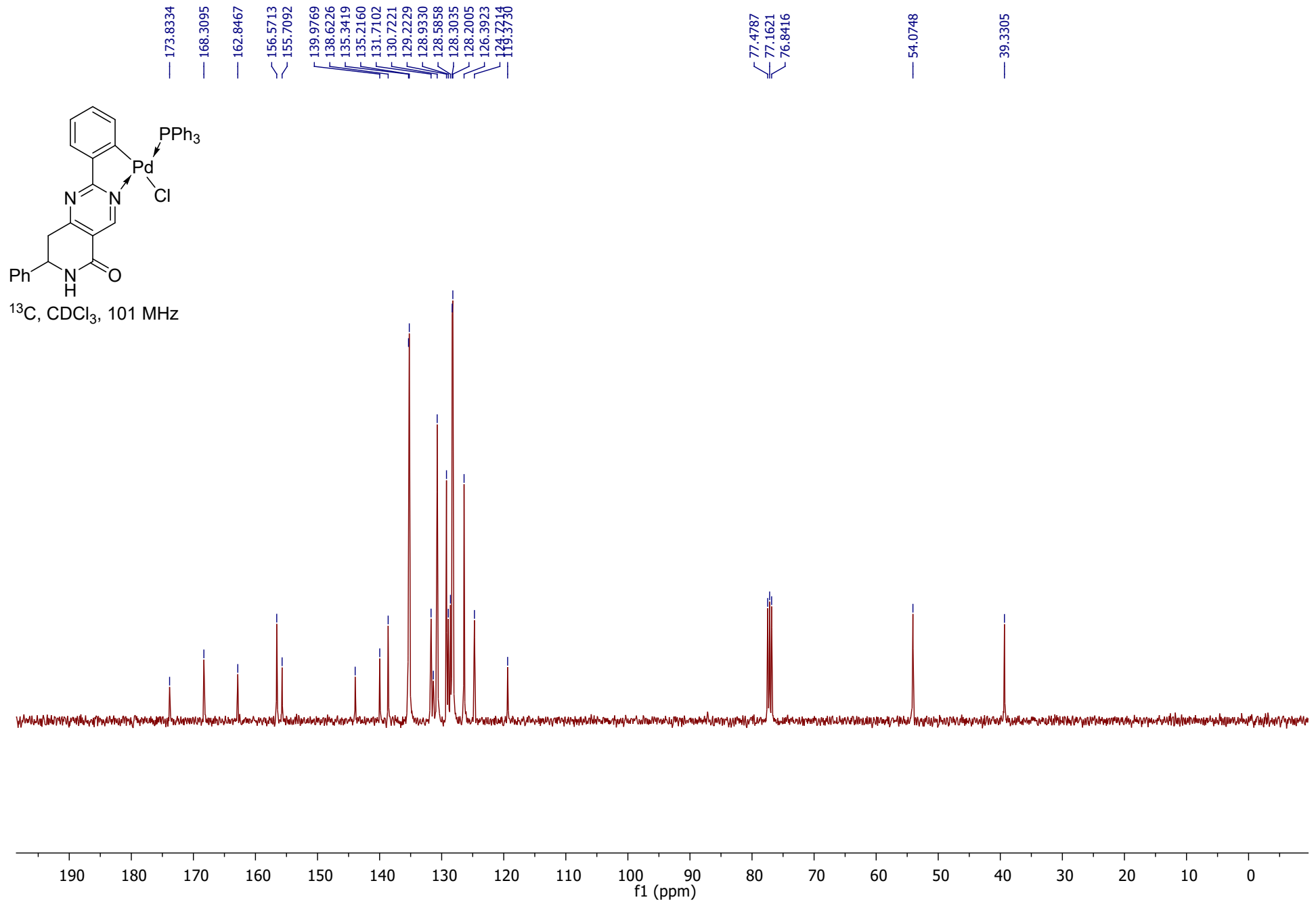


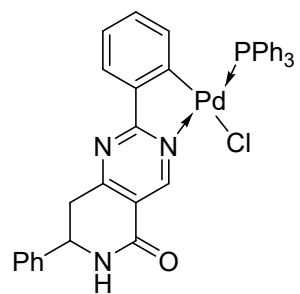
^{31}P , CDCl_3 , 121 MHz

-43.7621



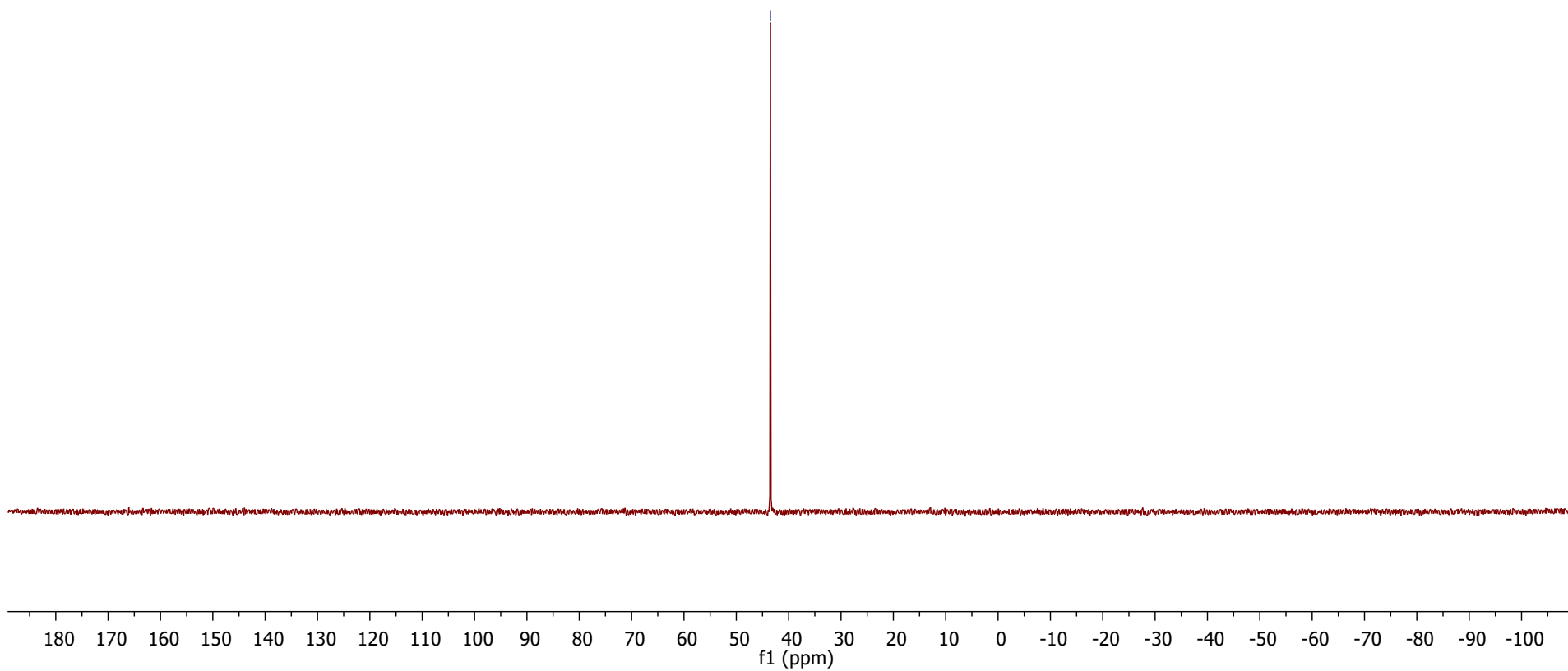


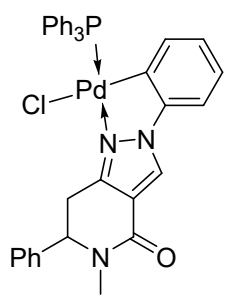




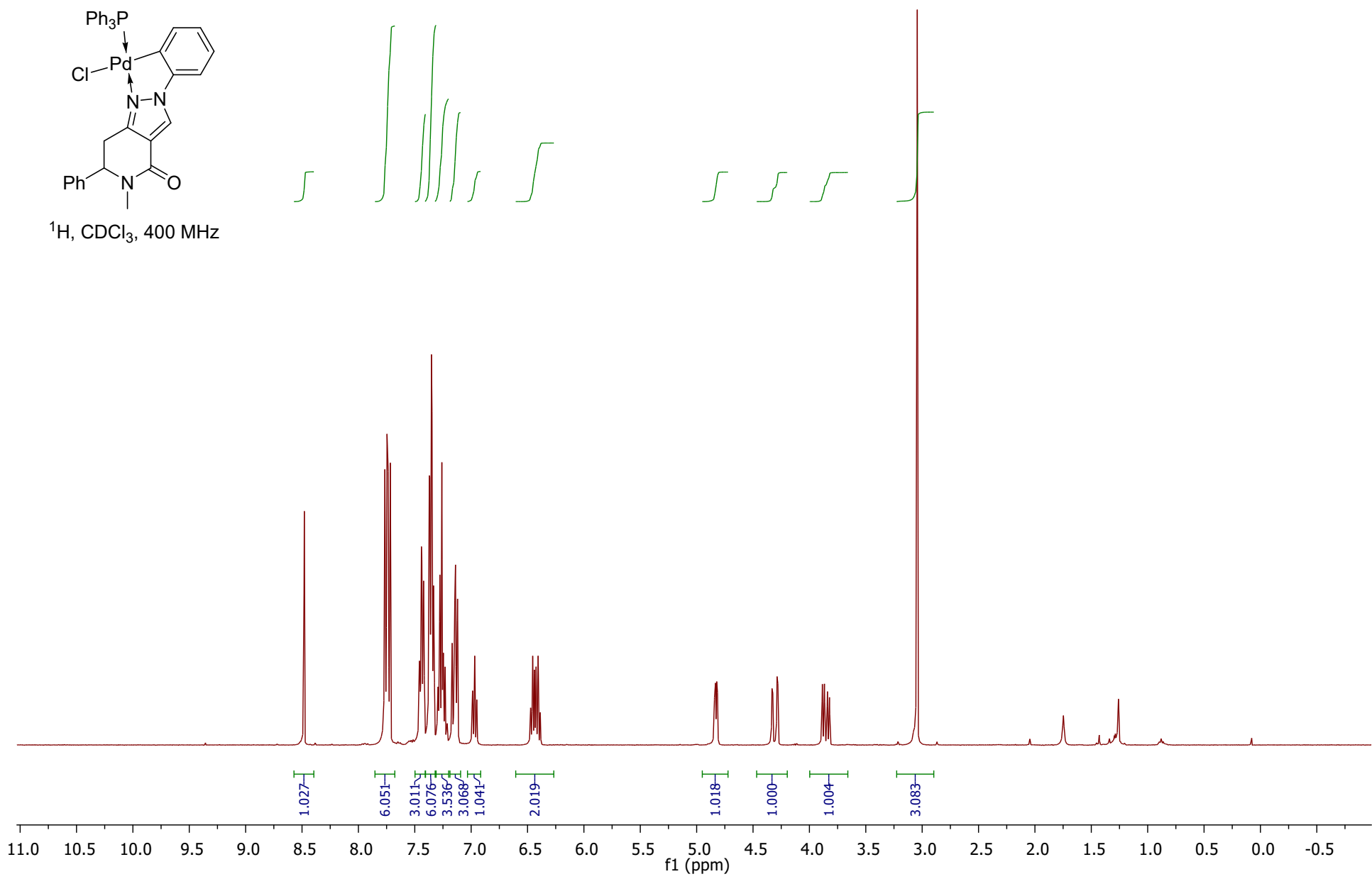
^{31}P , CDCl_3 , 162 MHz

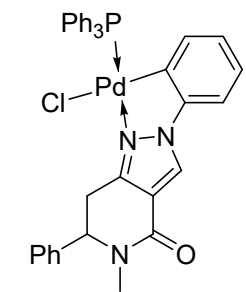
— 43.5073



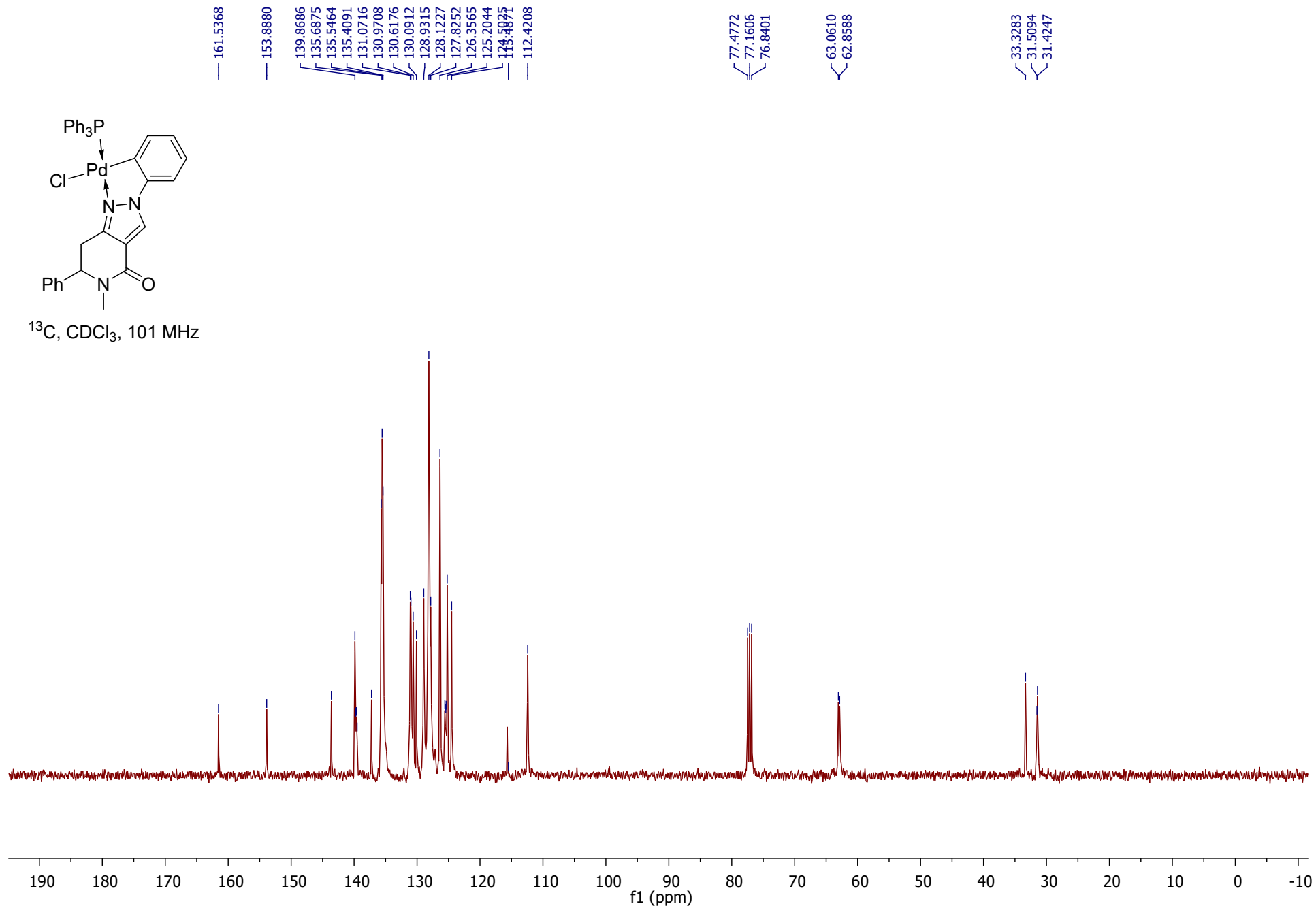


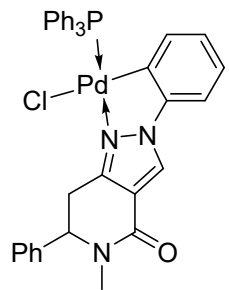
¹H, CDCl₃, 400 MHz





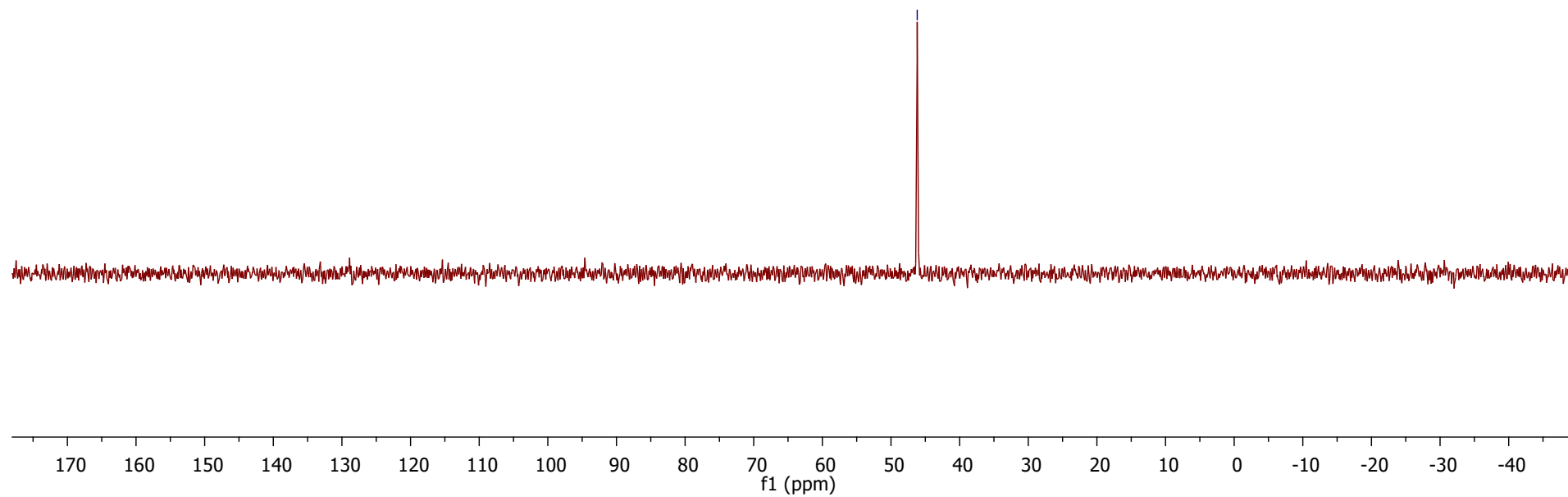
^{13}C , CDCl_3 , 101 MHz

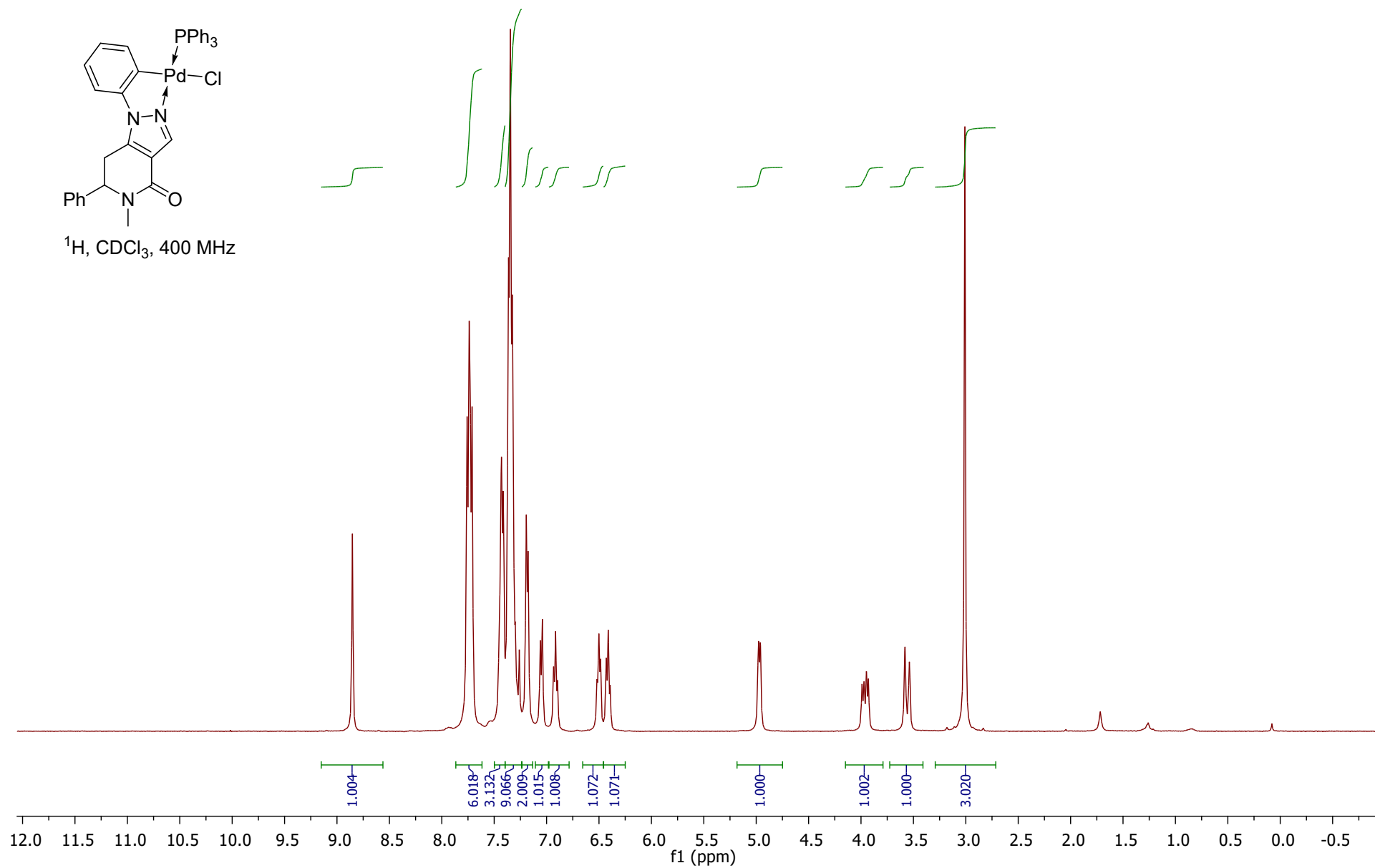
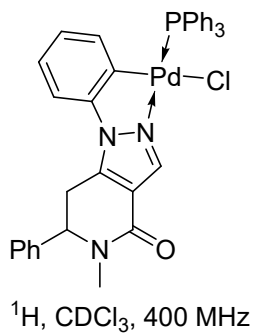


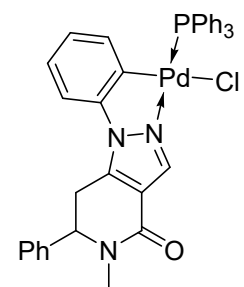


^{31}P , CDCl_3 , 162 MHz

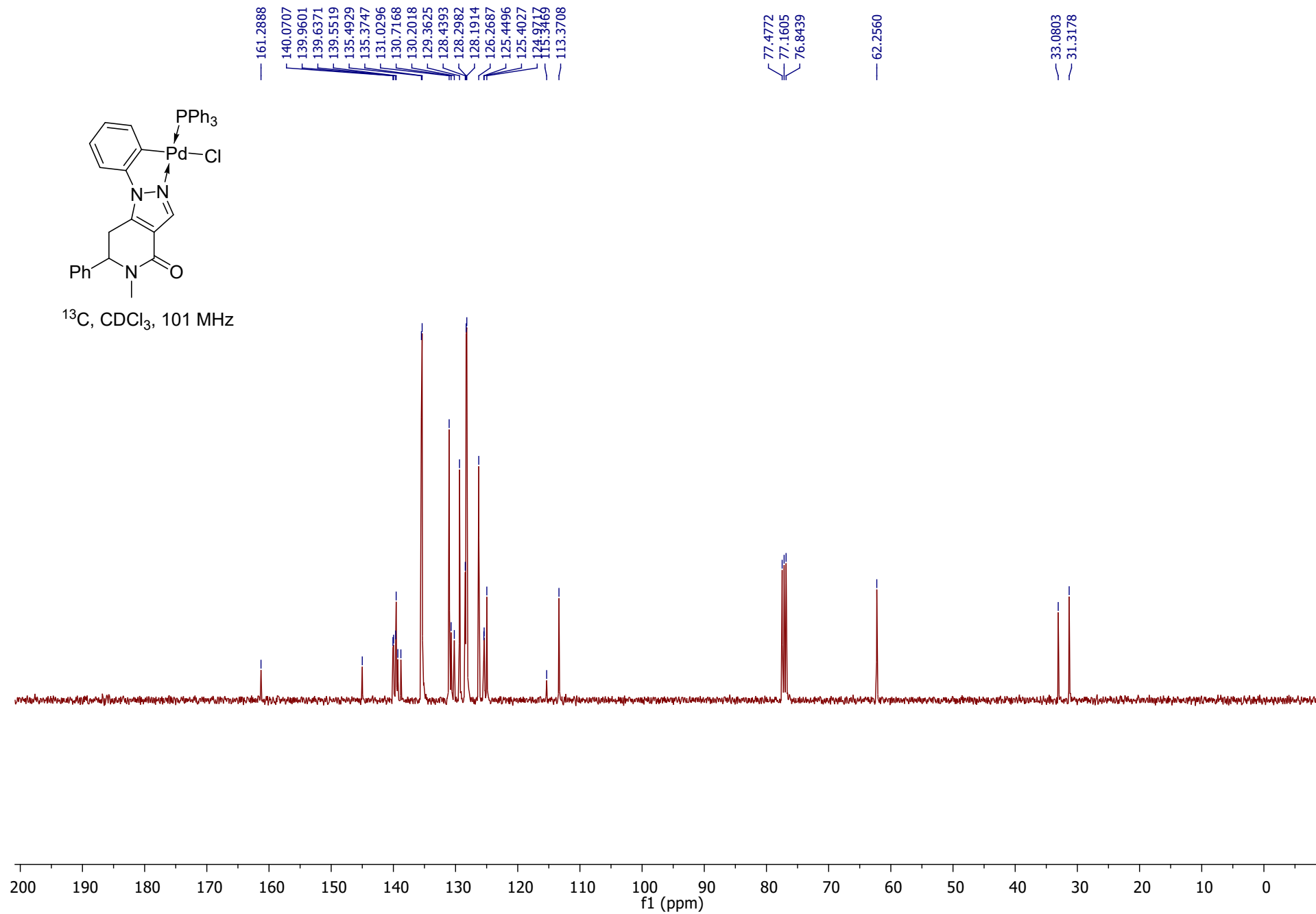
— 46.1801

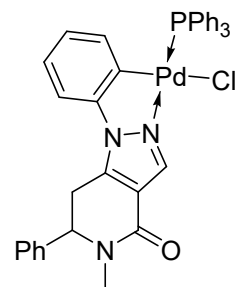




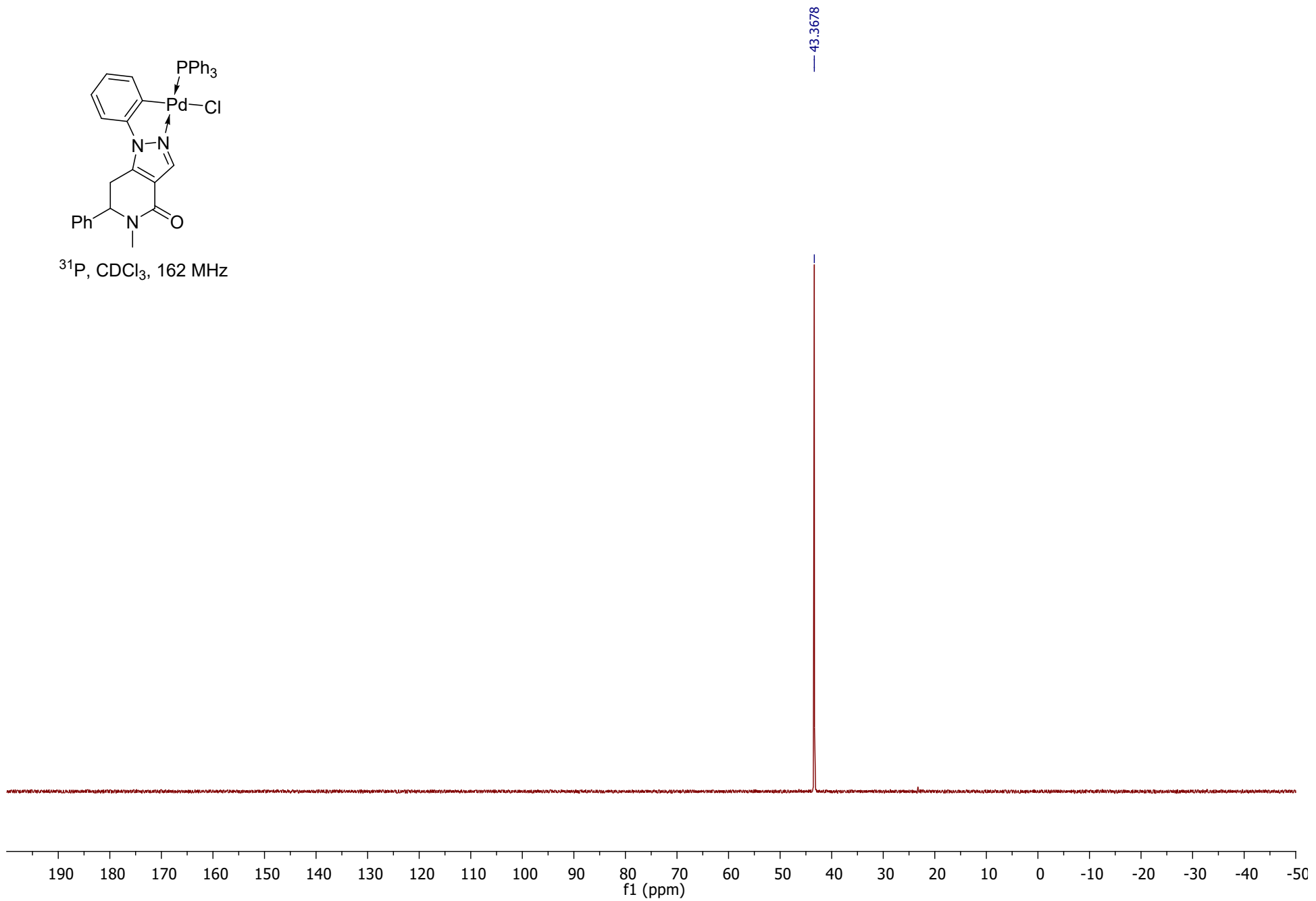


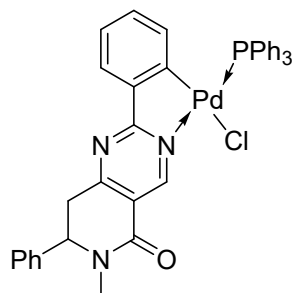
^{13}C , CDCl_3 , 101 MHz



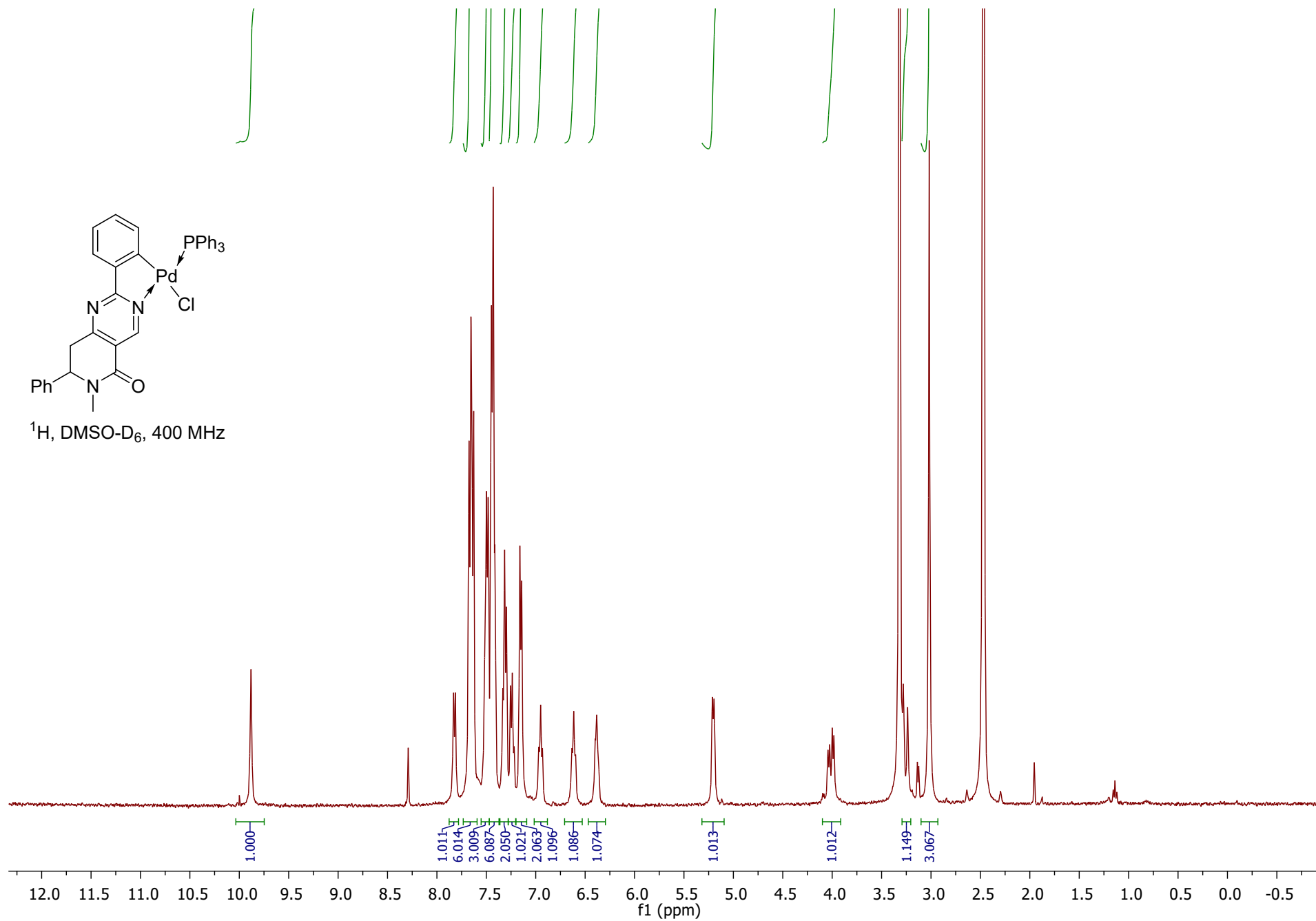


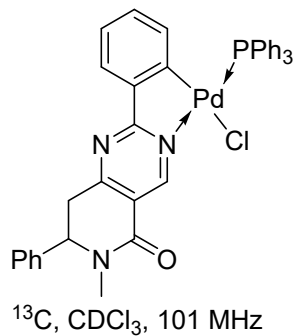
³¹P, CDCl₃, 162 MHz





¹H, DMSO-D₆, 400 MHz





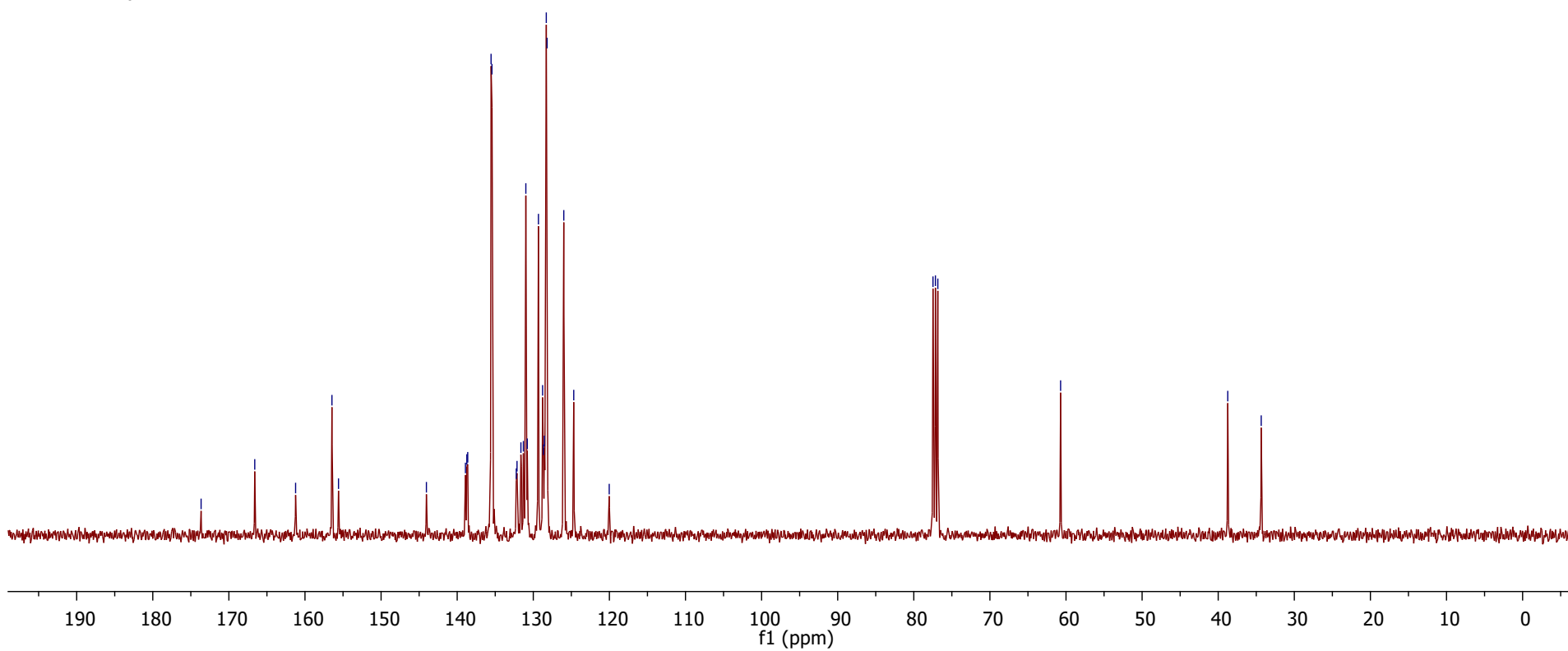
— 173.6503
 — 166.6005
 — 161.2331
 — 156.4569
 — 155.5948

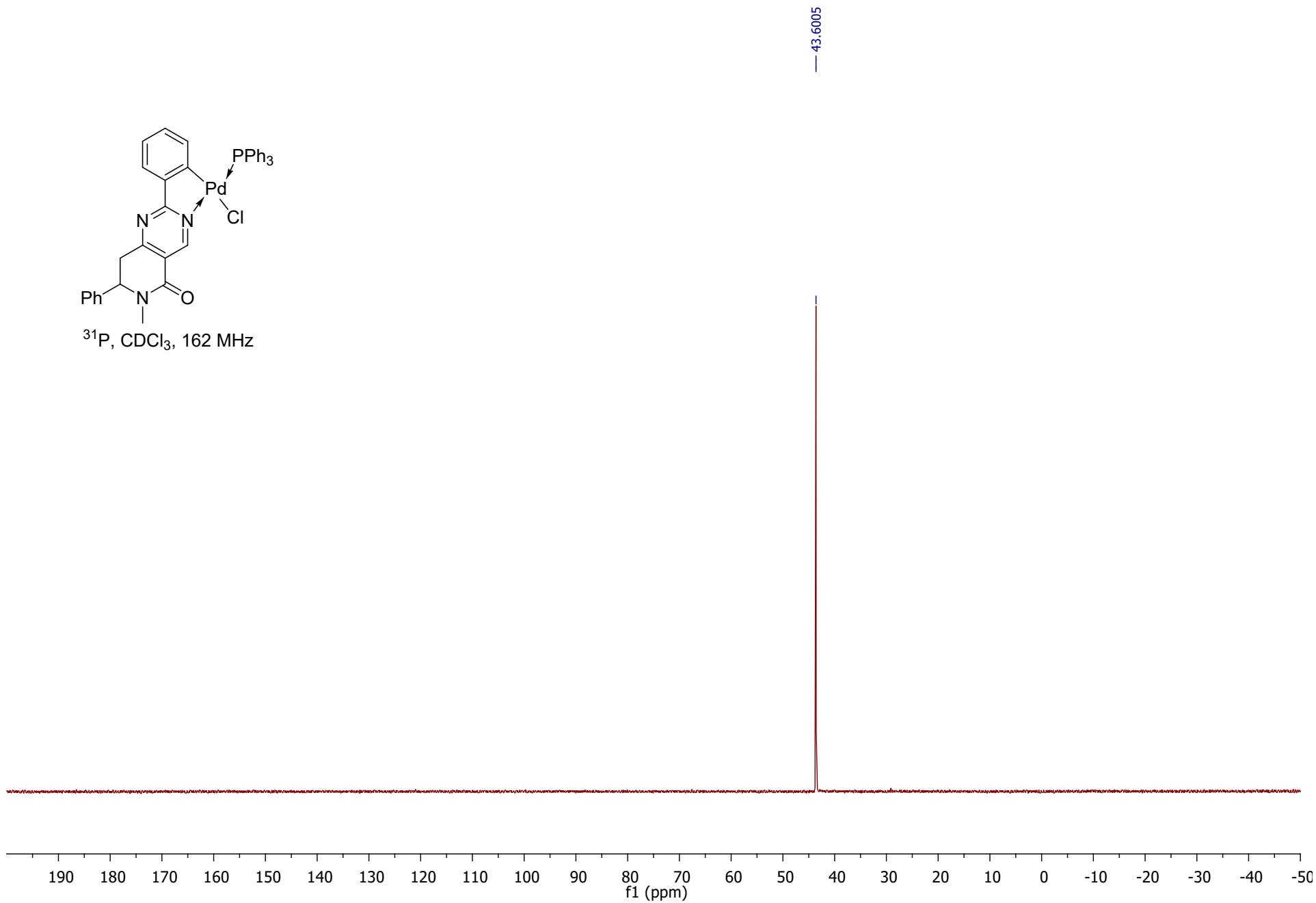
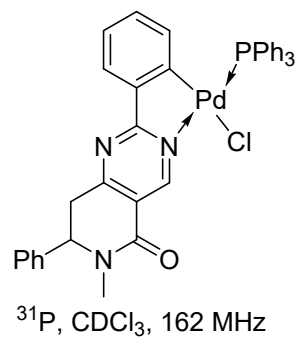
— 144.0435
 — 138.9126
 — 138.7333
 — 138.6150
 — 135.5479
 — 135.4296
 — 132.2366
 — 132.1375
 — 131.6263
 — 131.3020
 — 130.9778
 — 130.7908
 — 129.3221
 — 128.7766
 — 128.6660
 — 128.5439
 — 128.2921
 — 128.1815
 — 125.9918
 — 124.6833
 — 120.0216

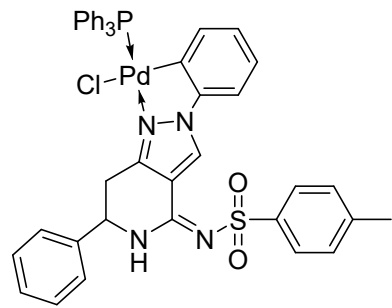
— 77.4787
 — 77.1583
 — 76.8416

— 60.7088

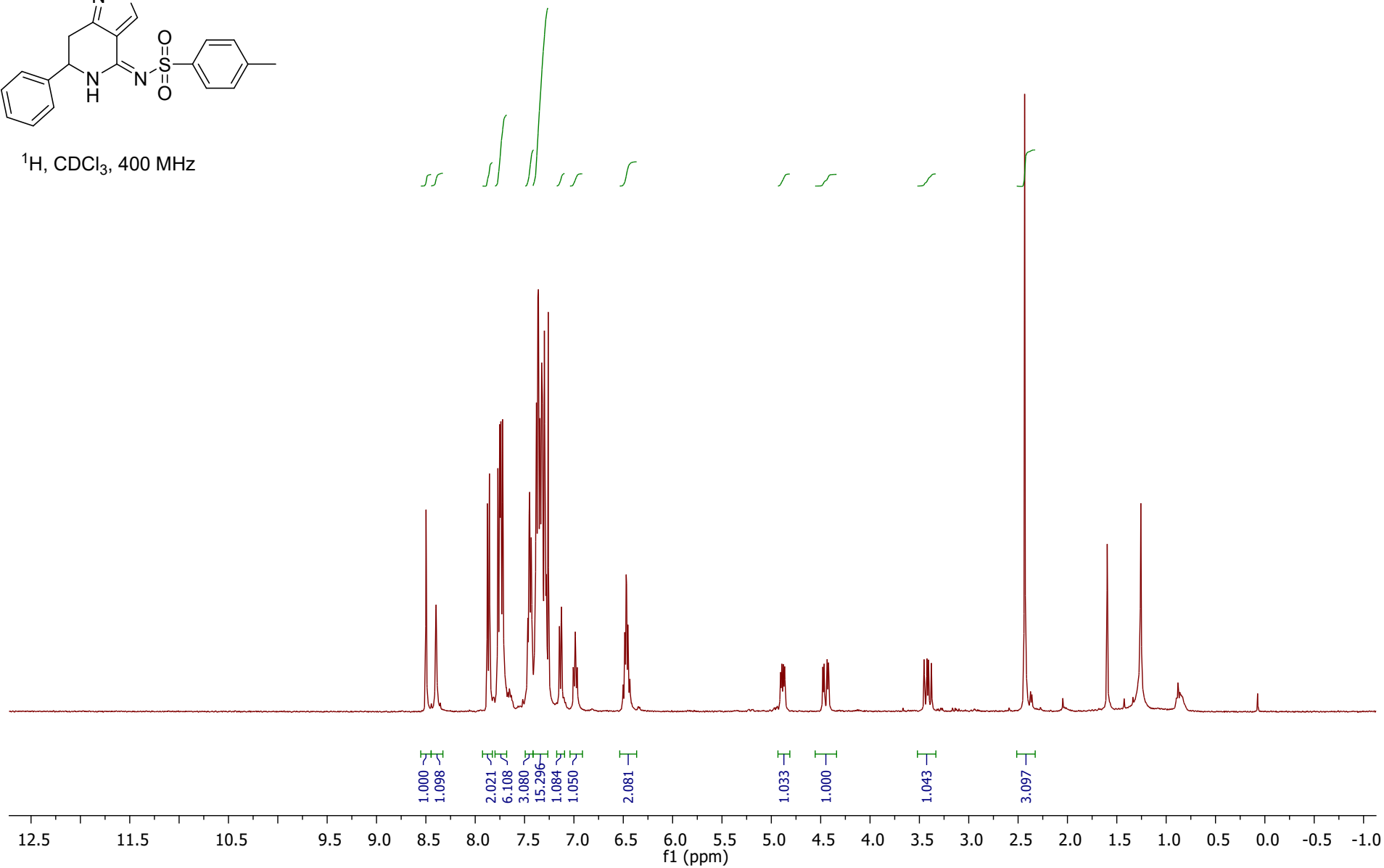
— 38.7430
 — 34.3484

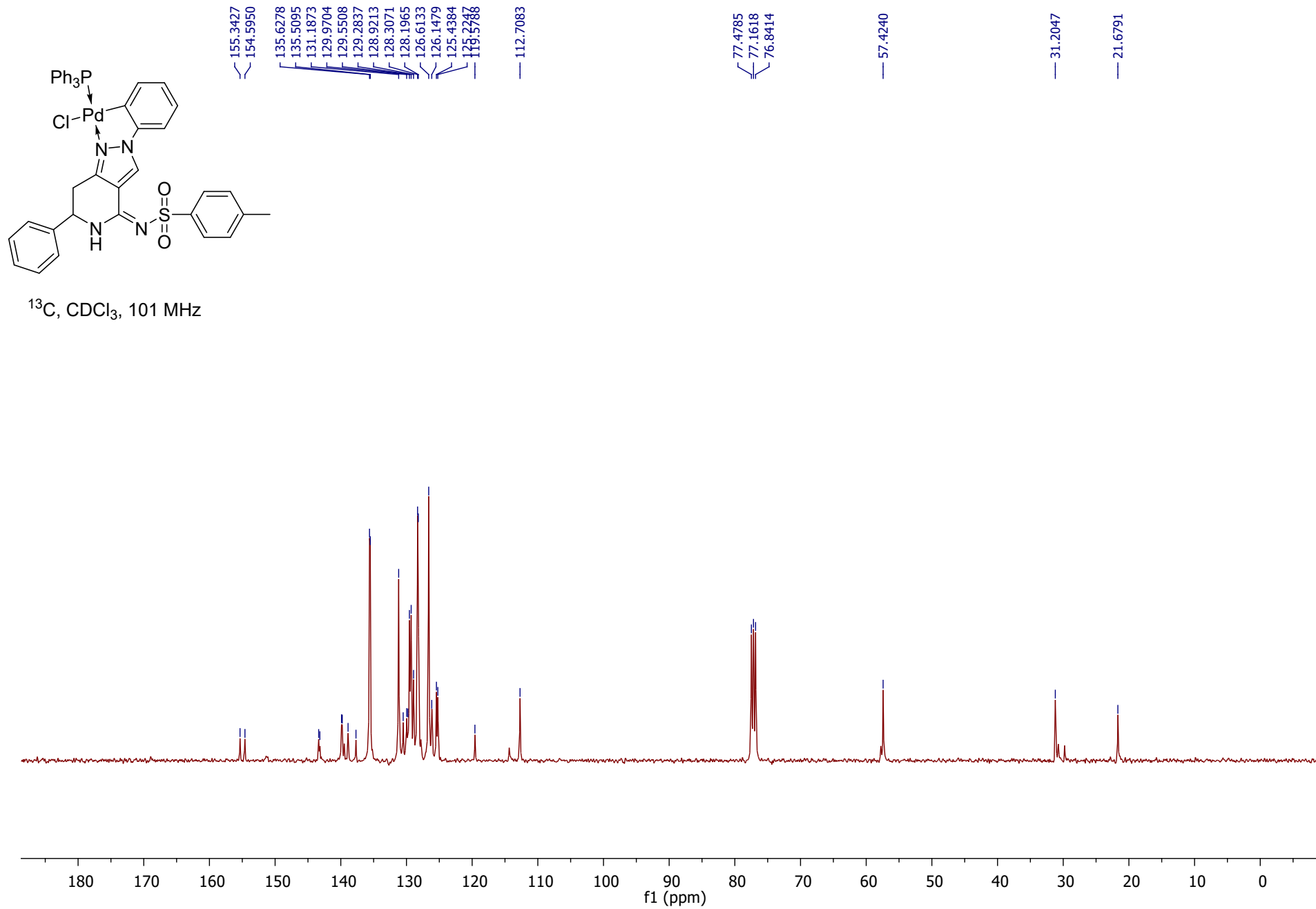


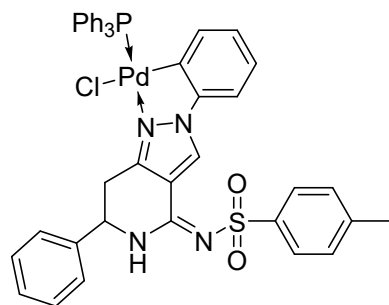




¹H, CDCl₃, 400 MHz

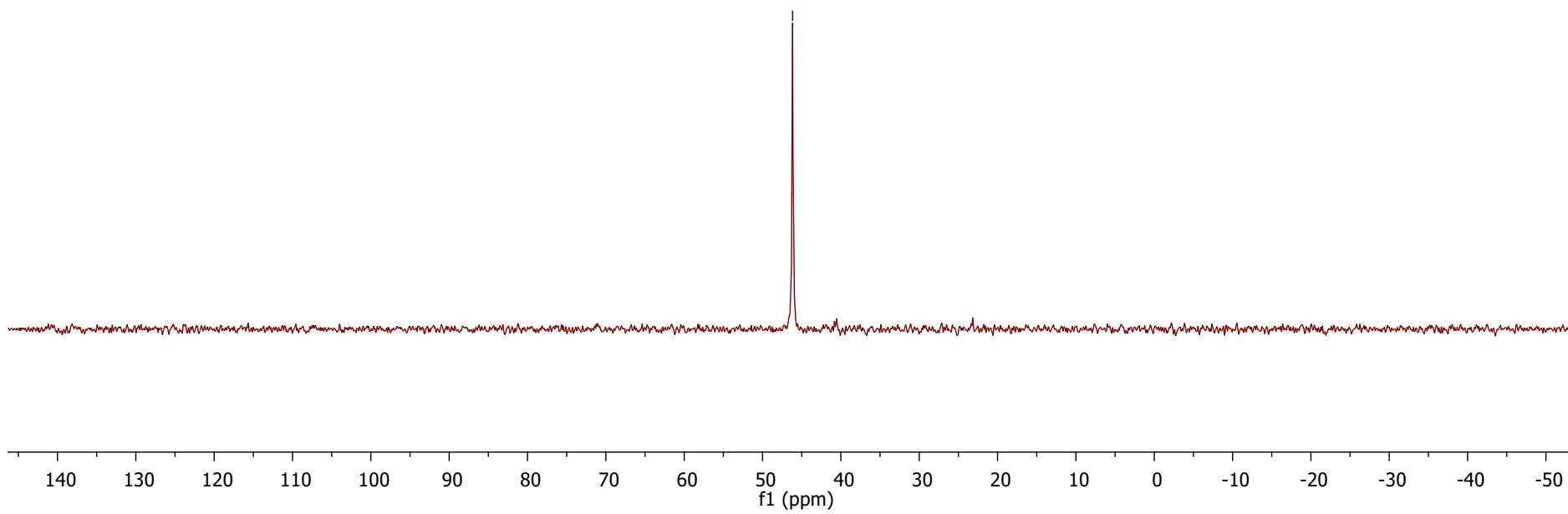


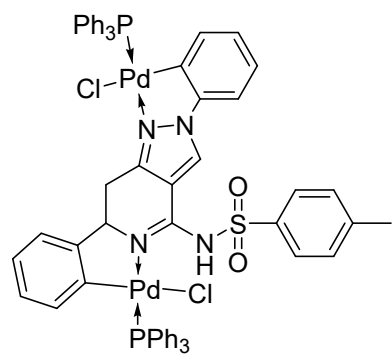




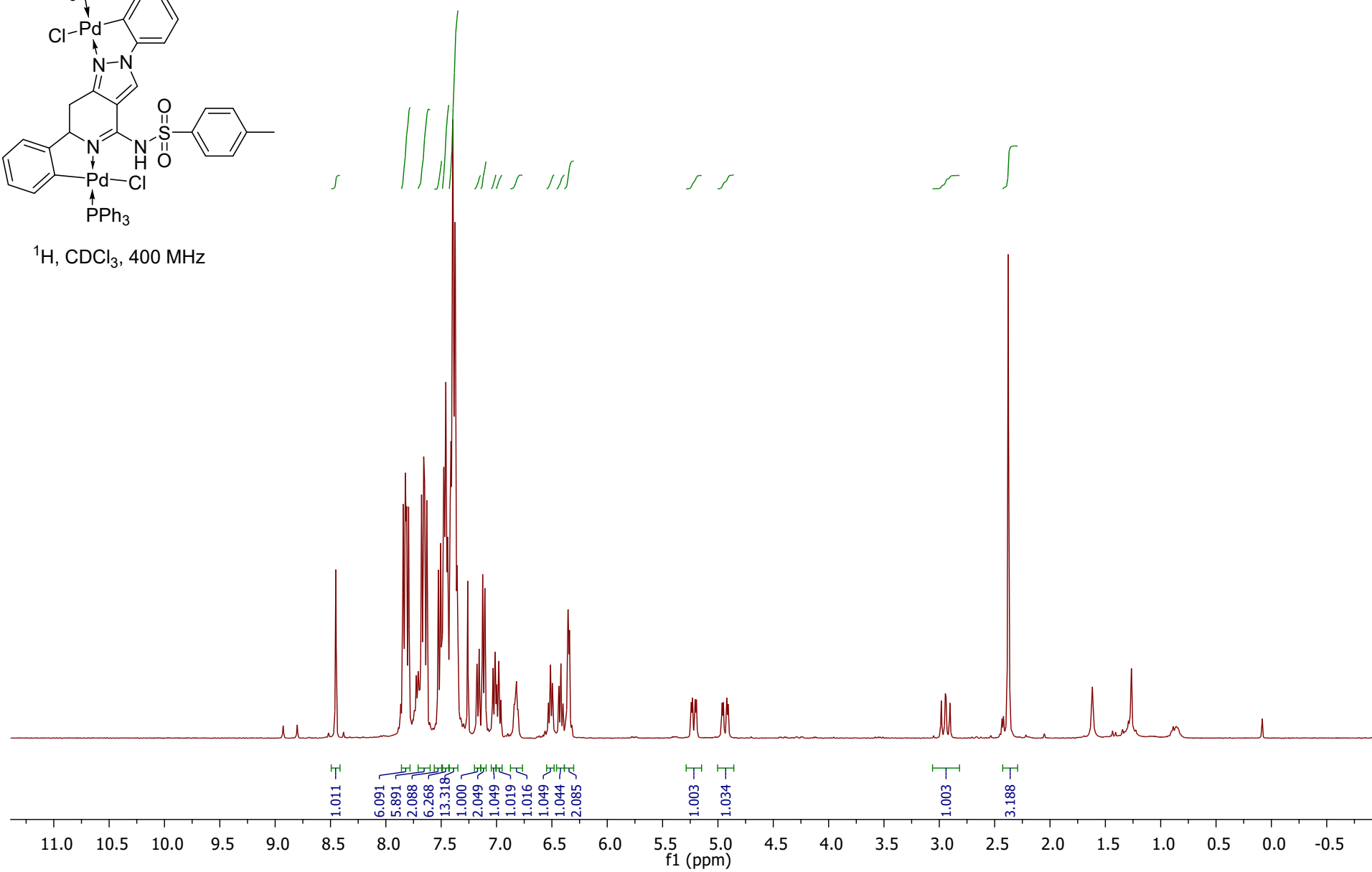
³¹P, CDCl₃, 162 MHz

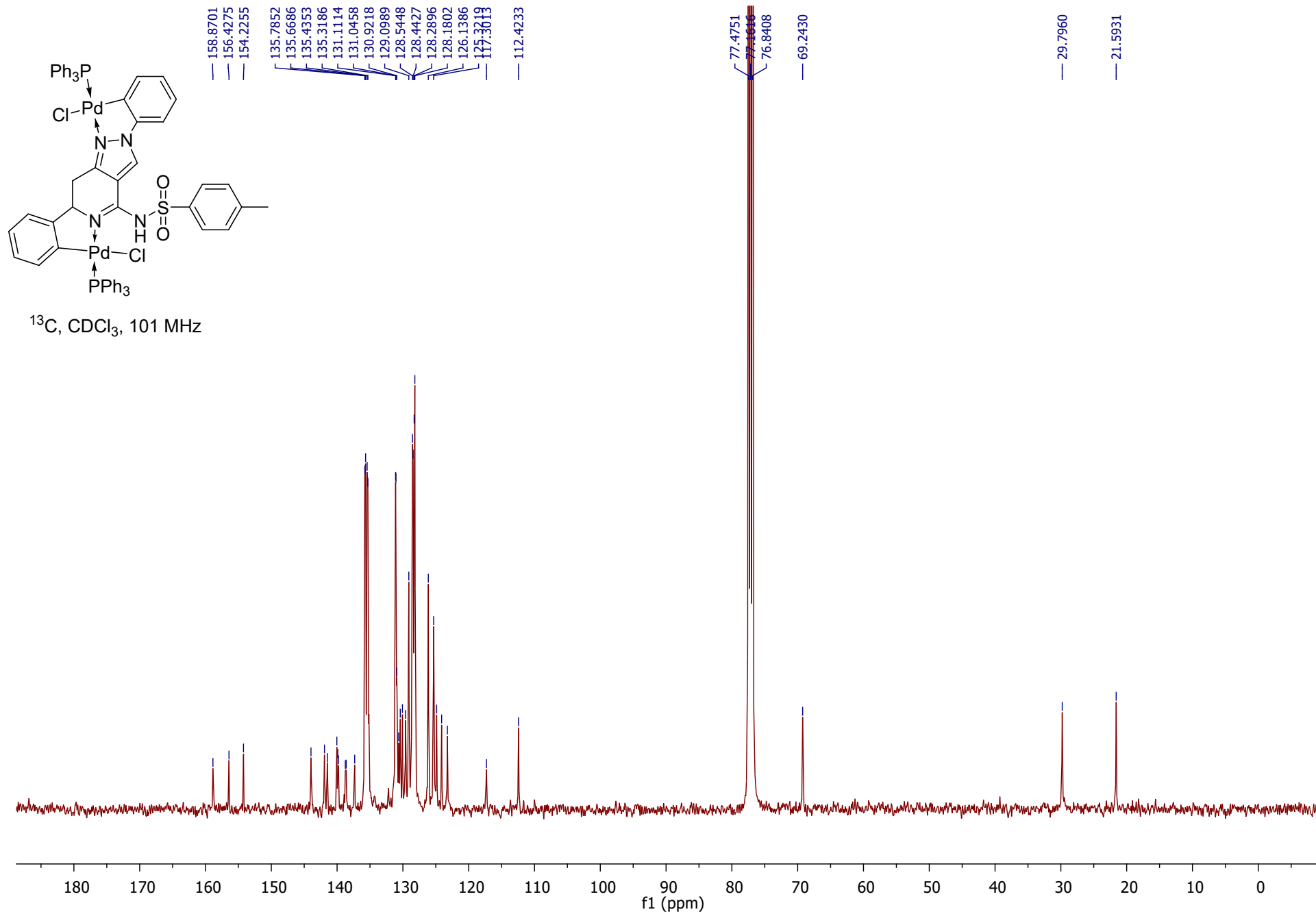
— 46.1676

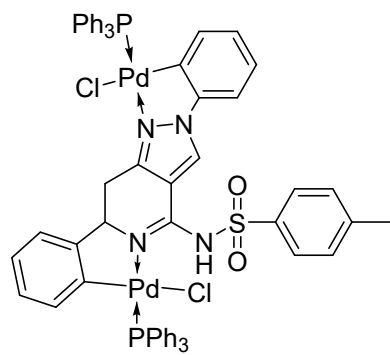




^1H , CDCl_3 , 400 MHz

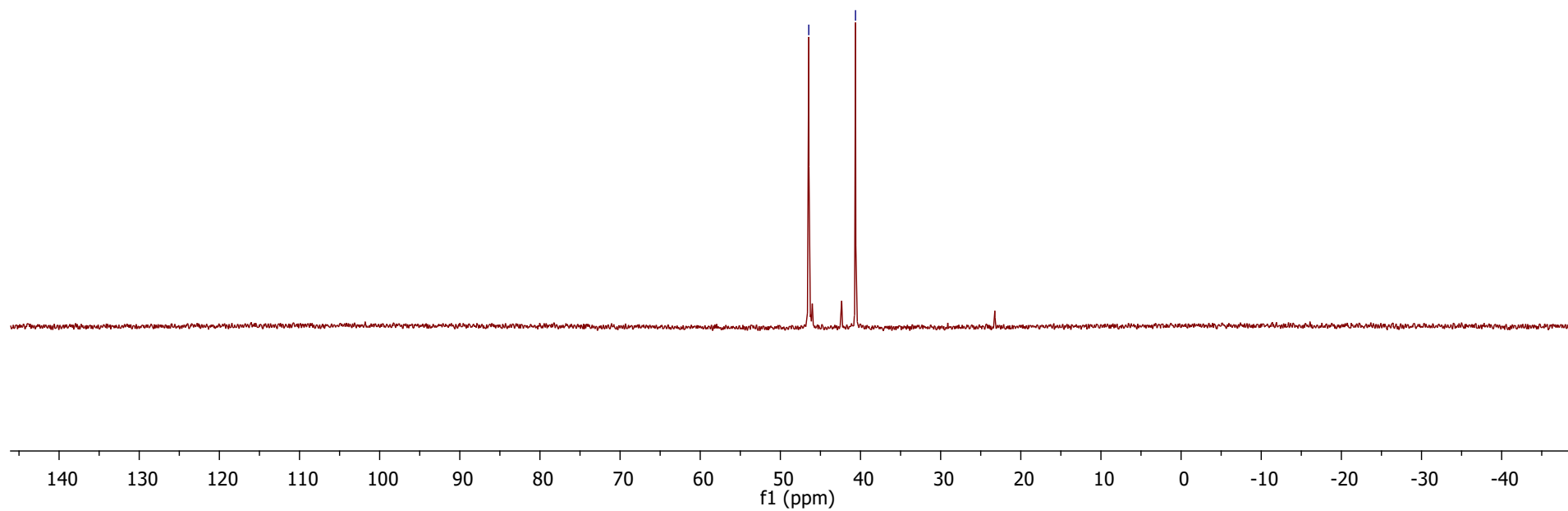




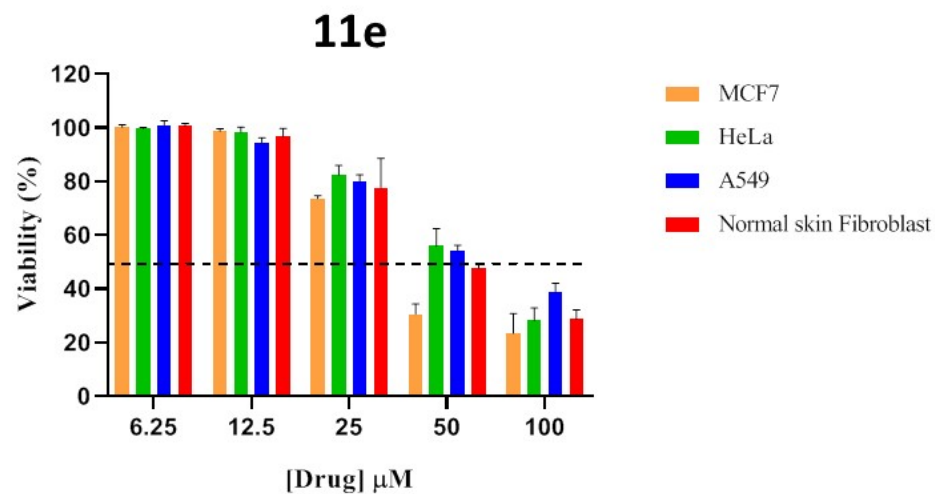
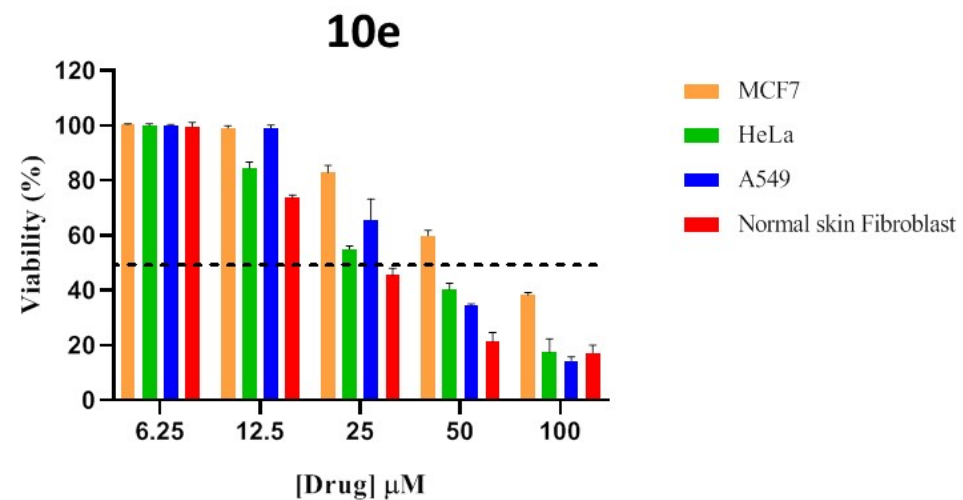
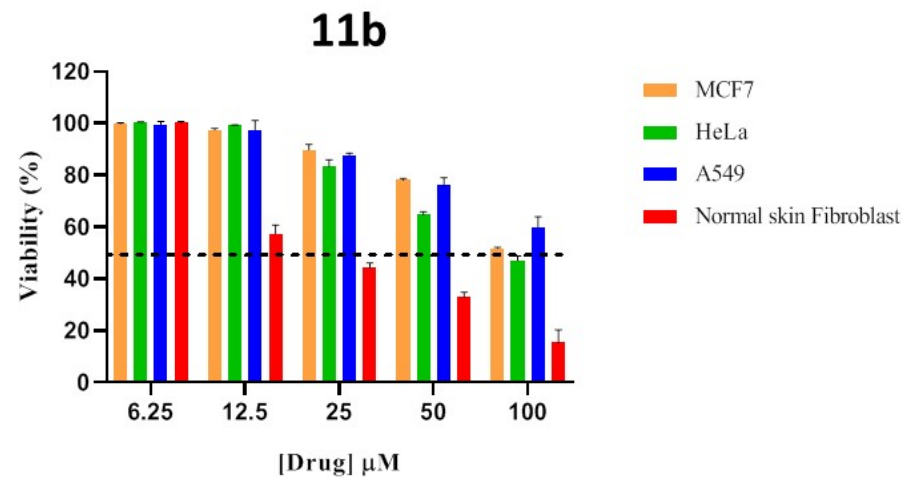
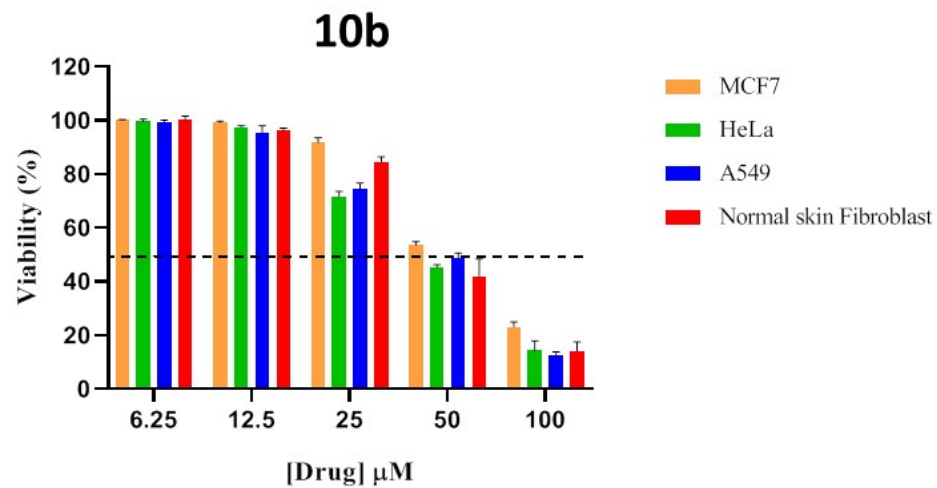


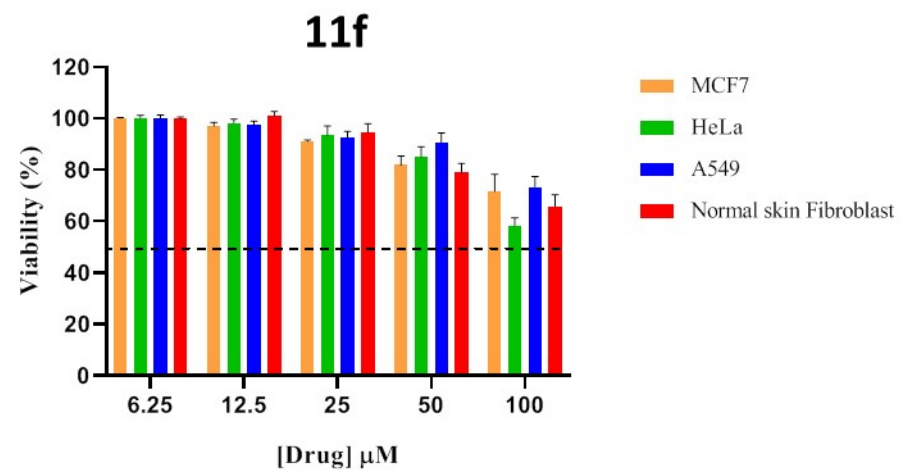
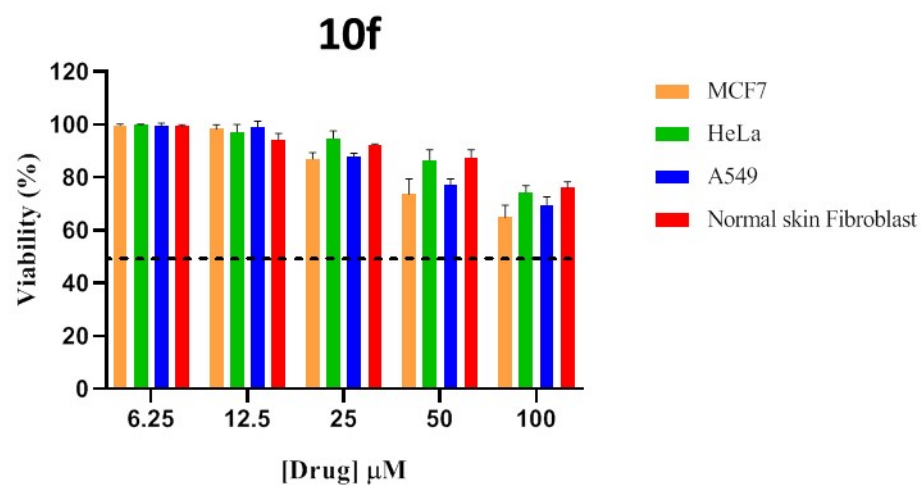
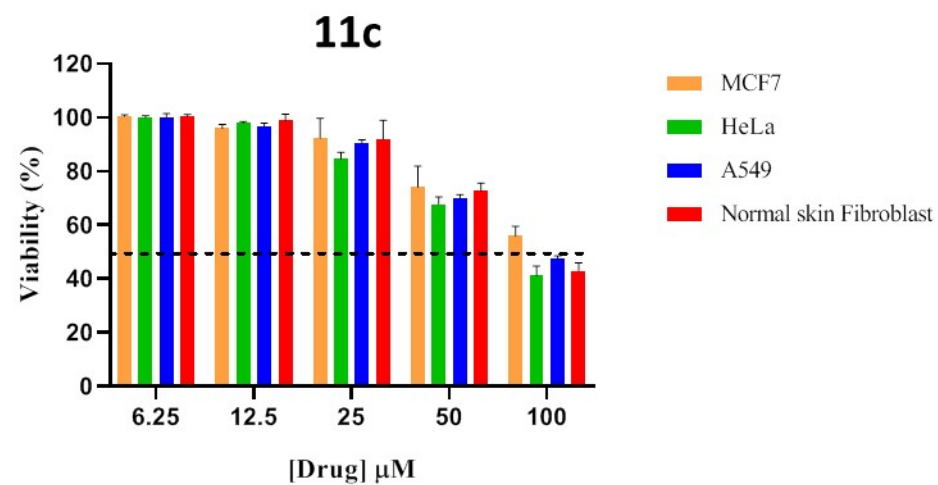
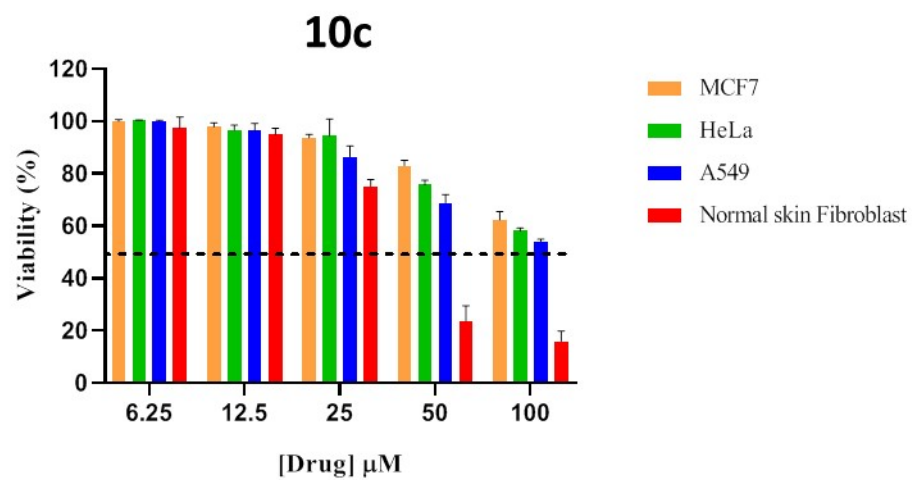
^{31}P , CDCl_3 , 162 MHz

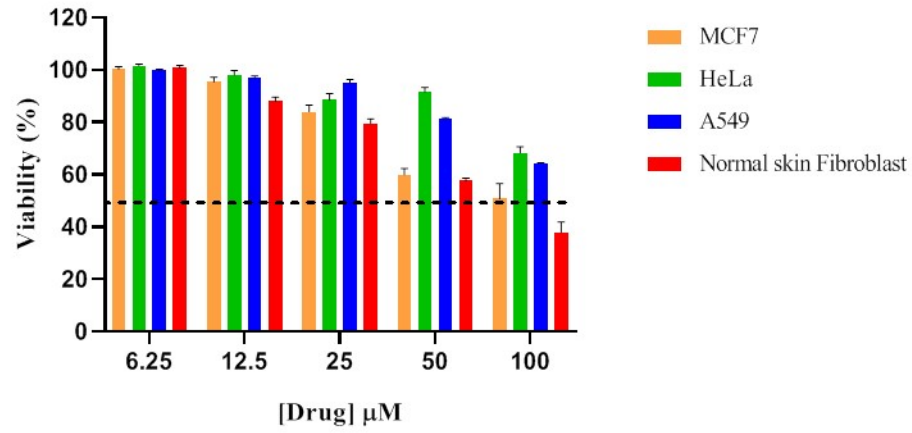
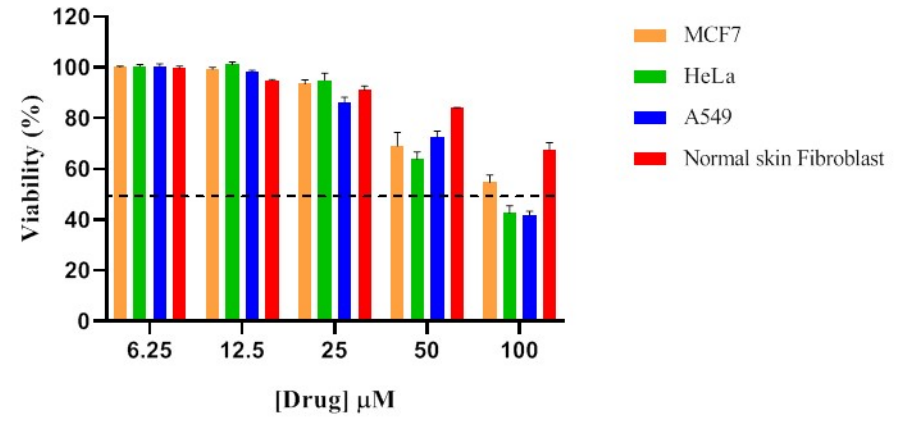
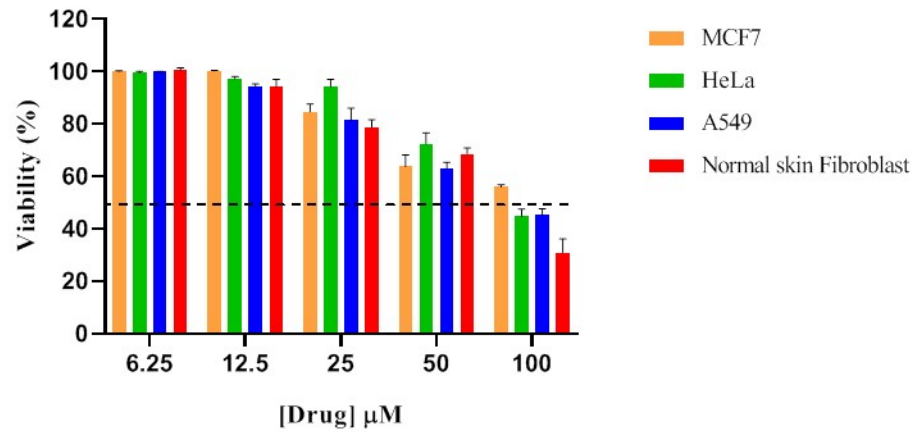
— 46.4578
— 40.6250



Biological activity data





10d**11d****10g****11g**